Employing Arynes in Multicomponent Reactions and Rearrangements Triggered by Nitrogen Nucleophiles

Thesis Submitted to AcSIR

For the Award of the Degree of

DOCTOR OF PHILOSOPHY

In

CHEMICAL SCIENCES

By

Tony Roy
(Registration Number: 10CC15J26013)

Under the guidance of
Dr. A. T. Biju

Organic Chemistry Division
CSIR-National Chemical Laboratory
Pune-411 008, India.

May 2018

Dedicated to

My Family, Friends and Teachers

सीएसआयआर-राष्ट्रीय रासायनिक प्रयोगशाला
(वैज्ञानिक तथा औद्योगिक अनुसंधान परिषद)
डॉ. होमी भाभा मार्ग, पुणे - 411 008 भारत
CSIR-NATIONAL CHEMICAL LABORATORY
(Council of Scientific & Industrial Research)
Dr. Homi Bhabha Road, Pune - 411 008 India

Dr. A. T. Biju
Senior Scientist
at.biju@ncl.res.in
Organic Chemistry Division

Thesis Certificate

This is to certify that the work incorporated in this Ph.D. thesis entitled **"Employing Arynes in Multicomponent Reactions and Rearrangements Triggered by Nitrogen Nucleophiles"** submitted by **Mr. Tony Roy** to Academy of Scientific and Innovative Research (AcSIR) in fulfilment of the requirements for the award of the Degree of Doctor of Philosophy, embodies original research work under my supervision. I further certify that this work has not been submitted to any other University or Institution in part or full for the award of any degree or diploma. Research material obtained from other sources has been duly acknowledged in the thesis. Any text, illustration, table etc., used in the thesis from other sources, have been duly cited and acknowledged.

Tony Roy
(Research Student)

Dr. A. T. Biju
(Research Supervisor)

Declaration by the Candidate

I hereby declare that the original research work embodied in this thesis entitled, **"Employing Arynes in Multicomponent Reactions and Rearrangements Triggered by Nitrogen Nucleophiles"** submitted to Academy of Scientific and Innovative Research for the award of degree of Doctor of Philosophy (Ph.D.) is the outcome of experimental investigations carried out by me under the supervision of **Dr. A. T. Biju**, Senior Scientist, Organic Chemistry Division, CSIR-National Chemical Laboratory, Pune. I affirm that the work incorporated is original and has not been submitted to any other academy, university or institute for the award of any degree or diploma.

May 2018
CSIR-National Chemical Laboratory
Pune-411 008

Tony Roy
(Research Student)

Acknowledgment

It is my pleasure to be indebted to various people, who directly or indirectly contributed in the development of this work and who influenced my thinking, behavior, and acts during the course of study.

First and foremost, I wish to express my heartfelt gratitude to my research supervisor **Dr. A. T. Biju** for believing in my abilities and providing me an incredible opportunity to pursue my career as a Ph. D. student. I thank him for his excellent guidance, constant encouragement, sincere advice, understanding and unstinted support throughout of my doctoral research. I would like to thank him for encouraging my research and for allowing me to grow in research. His advice on both research as well as on my career have been priceless.

I wish to express my sincere thanks to my Doctoral Advisory Committee members Dr. Ulhas K. Kharul, Dr. D. S. Reddy and Dr. Pradip Maity for their continued support, guidance and suggestions. I am grateful to Prof. Ashwini Kumar Nangia, Director, NCL, Dr. Sourav Pal (Former Director, NCL), Dr. Subhash P. Chavan, Head, Division of Organic Chemistry, and Dr. Pradeep Kumar, (Former HoD, Organic Chemistry Division) for giving me this opportunity and providing all necessary infrastructure and facilities.

My sincere thanks to Dr. T. G. Ajithkumar, Dr. S. B. Sukumaran, Dr. C. V. Ramana, Dr. Muthukrishnan, Dr. Nitin Patil, Dr. G. J. Sanjayan, Dr. Shashidhar, Dr. N. P. Argade, Dr. S. K. Asha, and all other scientists of NCL for their motivation, constant encouragement and support.

I was very fortunate to work with a fantastic group of colleagues in Dr. Biju's research group. My sincere thanks to Sachin Bhojgude, Anup Bhunia, Santhivardhana Reddy Yetra, Trinadh Kaicharla, Atanu Patra**,** Manikandan Thangaraj**,** Santigopal Mondal, Subrata Mukherjee**,** Dnyaneshwar R. Baviskar**,** Tamal Kanti Das, Rahul Gaykar, Arghya Ghosh, Subrata Bhattacharjee, Kuruva Balanna, and Anu Jacob for devoting their precious time and for providing many valuable suggestions which indeed helped me during this research work. It has been a great learning experience for me through our group seminars. A special thank goes to Sachin Bhojgude, Trinadh Kaicharla, T.

Manikandan**,** Dnyaneshwar R. Baviskar, Anjali and Rupa Kamath for their help in completing various projects.

I wish to express my deep sense of gratitude to my teachers at St. Antony's Public School, Kanjirapally, St. Dominics College, Kanjirapally and School of Chemical Sciences, M. G. University for their sincere efforts and patience in guiding me during my graduation and post-graduation studies.

No words can suffice to acknowledge my prized seniors and friends in and out of NCL who have helped me at various stages of my work in NCL. I wish to thank Dr. Rajesh, Dr. Sunil, Dr. Jijil, Dr. Kiran, Dr. Leena, Dr. Prajitha, Dr. Sarath, Dr. Vijayadas, Dr. Bihag, Dr. Sreekuttan, Dr. Remya, Dr. Nisha, Dr. Anumon, Dr. Alson, Dr. Lenin, Mohan, Anish Lazar, Shoy, Aswathy, Jaise, Subin, Unnikuttan, Gifty, Sanoop, Ranjeesh, Shibin, Pranav, Rajith, Vipin, Zinoy, ArunTorris, Vidyanand, Rashid, Shabeeb, Fayis, Munavar, Kayum, Manjunadh, Sethulekshmi, Sumi, Anjima, Neethu, Elizabeth, Litty, Kavya, Betsy, Anupriya, Emmanuel, Prasenjit, Vijay, Fayaz, Sharvani, for helping me in various aspects of life as well as work.

I would like to extend my thanks to Dr. Rajamohanan, for their timely help with NMR spectra recording, Dr. Rajesh Gonnade, Mr. Shridhar, Ms. Ekta, Mr. Bikash for the X-ray analysis, Mrs. Shantakumari for Mass/HRMS facility and Dr. Borikar for recording GCMS. Help from IR facility is also acknowledged.

Without the funding I received, this Ph.D. would not have been possible and I would like to express my sincere appreciation to DST for awarding Inspire-JRF and SRF.

Finally, I dedicate this thesis to the people who mean the most to me, my dearest **Papa**, loving **Mummy**, beloved **Georgekutty**, caring **Chechy**, my sweet little angel **Serah** and all my well-wishers whose continuous encouragement and support have been a source of inspiration in completion of this tough task.

Above all, I owe it all to Almighty God for granting me the wisdom, health and strength to undertake this research task and enabling me to its completion.

Tony Roy

List of Abbreviations

Ac	Acetyl
Ar	Aryl
1-Ad	1-Adamantyl
bs	Broad singlet
BSA	Bis(trimethylsilyl)acetamide
Bn	Benzyl
t-Bu	tertiaryButyl
n-BuLi	*n*-Butyllithium
Cy	Cyclohexyl
Cat.	Catalytic
DCE	1,2-Dichloroethane
DCM	Dichloromethane
Dipp	2,6-Diisopropylphenyl
DME	1,2-Dimethoxyethane
DMF	*N*,*N*-Dimethylformamide
DMSO	Dimethyl sulfoxide
E^+	Electrophile
Et	Ethyl
g	gram(s)
h	hour(s)
HMDS	Bis(trimethylsilyl)amine
HMPT	Hexamethylphosphoramide
HRMS	High-resolution mass spectrometry
Hz	Hertz
IR	Infra red
J	Coupling constant in NMR
LDA	Lithium diisopropyl amide
M	Multiplet
Me	Methyl

MCC	Multicomponent coupling
min	Minute(s)
mL	Millilitres
mmol	Millimole
MW	Microwave
NMR	Nuclear magnetic resonance
Nu^-	Nucleophile
ORTEP	Oak Ridge Thermal Ellipsoid Plot
Ph	Phenyl
i-Pr	Isopropyl
q	Quartet
rt	Room temperature
s	Singlet
t	Triplet
TBAF	Tetrabutylammonium fluoride
TBAT	Tetrabutylammoniumdifluorotriphenylsilicate
TEMPO	2,2,6,6-Tetramethylpiperidin-1-yl)oxyl
Tf	Trifluromethanesulfonyl
TFA	Trifluoroacetic acid
Tf_2O	Trifluoromethanesulfonic anhydride
THF	Tetrahydofuran
TLC	Thin layer chromatography
TMS	Trimethylsilyl
p-Tol	para-Tolyl

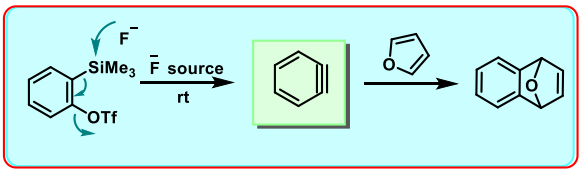
Synopsis

Synopsis of the Thesis to be submitted to the Academy of Scientific and Innovative Research for Award of the Degree of Doctor of Philosophy in Chemistry	
Name of the Candidate	Mr. Tony Roy
Degree Enrolment No. & Date	Ph. D. in Chemical Sciences (10CC15J26013); January 2015
Title of the Thesis	Employing Arynes in Multicomponent Reactions and Rearrangements Triggered by Nitrogen Nucleophiles
Research Supervisor	Dr. A. T. Biju (CSIR-NCL, Pune)

The thesis is divided into five chapters. A brief introduction to aryne chemistry has been provided in the first chapter. Synthesis of *N*-aryl β-amino alcohols by trifluoroacetic acid-promoted multicomponent coupling of aziridines, arynes and water is described in the second chapter. The third chapter deals with employing carboxylic acids in aryne multicomponent coupling using aziridines/azetidines as the nucleophilic trigger. Synthesis of functionalized amino epoxides by a three-component coupling involving aziridines, arynes and aldehydes forms the focal theme of the fourth chapter. In the fifth and final chapter, synthesis of functionalized homoallylic amines *via* an aryne [2,3] Stevens rearrangement tertiary allylic amines is discussed. The details are presented below.

Chapter 1: A Brief Introduction to Aryne Chemistry

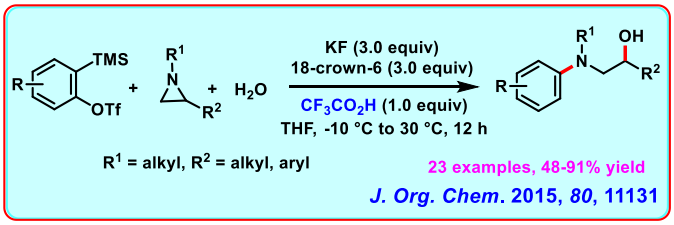
Arynes are highly reactive intermediates discovered more than a century ago, having several applications in organic synthesis for the construction of various 1,2-disubstituted arenes.[1] Presence of the carbon-carbon triple bond in a six-membered ring creates a ring strain, which make them highly electrophilic in nature, kinetically unstable and highly reactive. Consequently, arynes have been extensively used for the 1,2-difunctionalisation of aromatic ring along with the construction of benzo-fused carbocycles and heterocycles. Aryne chemistry had a rebirth when a mild condition for their generation by the fluoride-induced 1,2-elimination of 2-(trimethylsilyl)aryltriflates has been uncovered by Kobayashi and co-workers (Scheme 1).[2] This strategy is mild compared to the conventional harsh conditions. A brief introduction on the transition-metal-free applications of arynes in carbon-carbon and carbon-heteroatom bond-forming reactions is presented in the introduction chapter.



Scheme 1: Fluoride-Induced Generation of Aryne and Subsequent Cycloaddition

Chapter 2: **Synthesis of *N*-Aryl β-Amino Alcohols by Trifluoroacetic Acid-Promoted Multicomponent Coupling of Aziridines, Arynes and Water**

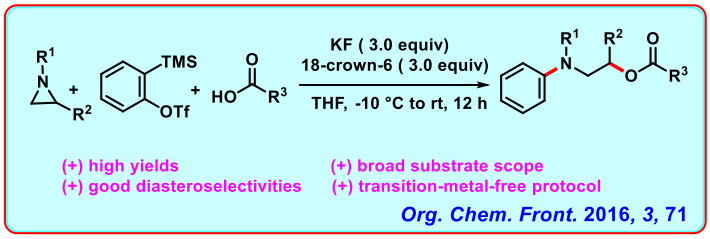
β-Amino alcohols are an important class of compounds having widespread applications in pharmaceutical industry. A transition-metal-free protocol for the synthesis of medicinally important *N*-aryl β-amino alcohol derivatives using a three-component coupling involving *N*-substituted aziridines, arynes and water promoted by trifluoroacetic acid (TFA) has been discussed in detail in this chapter (Scheme 2). The reaction furnished medicinally important *N*-aryl β-amino alcohol derivatives in moderate to good yields. The role of trifluoroacetic acid in promoting the reaction has been investigated with several mechanistic experiments. Additionally, the use of azetidines in this reaction afforded *N*-aryl γ-amino alcohol derivatives.[3]



Scheme 2: TFA Mediated Synthesis of *N*-Aryl β-Amino Alcohols

Chapter 3: **Employing Carboxylic Acids in Aryne Multicomponent Coupling Triggered by Aziridines/Azetidines**

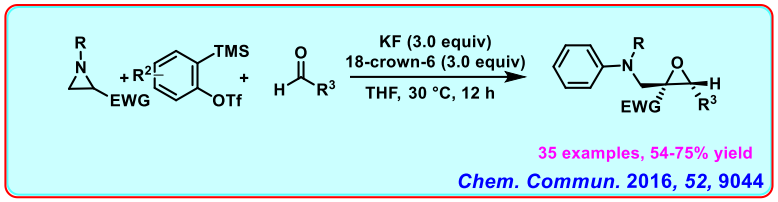
This chapter focuses on a transition-metal-free aryne multicomponent coupling (MCC) involving carboxylic acids initiated by aziridines/azetidines. The use of aziridines as nucleophile afforded *N*-aryl β-amino alcohol derivatives and the application of azetidines as nucleophilic trigger furnished *N*-aryl γ-amino alcohol derivatives in moderate to good yields. These reactions proceed under mild conditions and result in the formation of a new carbon-nitrogen bond and a new carbon-oxygen bond (Scheme 3). The utility of carboxylic acids in aryne MCCs have been demonstrated, and the synthetic potential of phenols as acid surrogates in the present aryne MCCs has been realized.Interestingly, the reaction of enantiomerically pure aziridine under the optimized conditions afforded the chiral amino alcohol derivative with retention of enantiopurity.[4]



Scheme 3: MCC Involving Aziridines, Arynes and Carboxylic acids

Chapter 4: **Synthesis of Functionalized Amino Epoxides by a Three-Component Coupling Involving Aziridines, Arynes and Aldehydes**

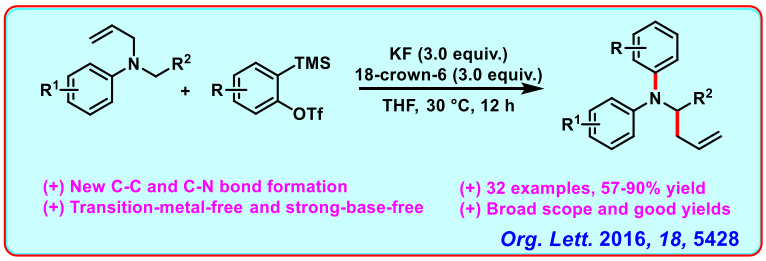
Functionalized epoxides are versatile intermediates for the synthesis of various biologically important molecules and this moiety is found in many natural products.The details on a mild and transition-metal-free procedure for the three-component coupling of aziridines, arynes and aldehydes form the subject matter of the 4thchapter of the thesis. The reaction afforded *N*-aryl α-amino epoxides in moderate to good yields and diastereoselectivity (Scheme 4). All the three-components can easily be varied under the present reaction conditions. Given the significance of α-amino epoxides as a precursor for the synthesis of amino sugars and polyoxygenated α-amino acids, the one-pot transition-metal-free method presented herein is likely to find application for the synthesis of these molecules.[5]



Scheme 4: Three-Component Coupling Involving Aziridines, Arynes and Aldehydes

Chapter 5: **The Aryne [2,3] Stevens Rearrangement**

The Stevens rearrangement involves the conversion of ammonium/sulfonium salts into complex nitrogen/sulfur containing products, usually takes place in the presence of a strong base. A mild and transition-metal-free procedure for the [2,3] Stevens rearrangement induced by arynes for the synthesis of functionalized homoallylic amines has been uncovered (Scheme 5). The reaction proceeds *via* the generation of the nitrogen ylide intermediate from arynes and tertiary allyl amines. A variety of tertiary allyl amines were well tolerated under the present reaction conditions. Formation of a new carbon-carbon and carbon-nitrogen bond under mild and strong-base-free reaction conditions, broad substrate scope and high yields of products are the notable features of the present reaction. The reaction of arynes with chiral allyl amines afforded chiral homoallylic amines with retention of enantiopurity and inversion in configuration.[6]



Scheme 5: Aryne [2,3] Stevens Rearrangement

References

1. For selected reviews, (a) Wenk, H. H.; Winkler, M.; Sander, W. *Angew. Chem. Int. Ed.***2003**, *42*, 502. (b) Bhunia, A.; Yetra, S. R.; Biju, A. T. *Chem. Soc. Rev.* **2012**, *41*,

3140. (c) Tadross, P. M.; Stoltz, B. M. *Chem. Rev.* **2012**,*112*, 3550.(d) Bhojgude**,** S. S.; Bhunia**,** A.; Biju A. T**.** *Acc. Chem. Res.* **2016***, 49,* 1658**.**

2. Himeshima, Y.; Sonoda, T.; Kobayashi, H. *Chem. Lett*. **1983**,1211.
3. Roy, T.; Baviskar, D. R.; Biju, A. T. *J. Org. Chem*. **2015**, *80*, 11131.
4. Roy, T.; Bhojgude, S. S.; Kaicharla, T.; Thangaraj, M.; Garai, B.; Biju, A. T. *Org. Chem. Front.***2016**, *3*, 71.
5. Roy, T.; Thangaraj, M.; Gonnade, R. G.; Biju, A. T. *Chem. Commun.* **2016**, *52*, 9044.
6. Roy, T.; Thangaraj, M.; Kaicharla, T.; Kamath, R. V.; Gonnade, R. G.; Biju, A. T. *Org. Lett.* **2016***, 18,* 5428

A TABLE OF CONTENTS

Chapter 1: A Brief Introduction to Aryne Chemistry

Chapter 2: Synthesis of *N*-Aryl β-Amino Alcohols by Trifluoroacetic Acid-Promoted Multicomponent Coupling (MCC) of Aziridines, Arynes and Water

Chapter 3: Employing Carboxylic Acids in Aryne Multicomponent Coupling Triggered by Aziridines/Azetidines

Contents Page

Chapter 4: Synthesis of Functionalized Amino Epoxides by a Three-Component Coupling Involving Aziridines, Arynes and Aldehydes

Contents Page

Chapter 5: The Aryne [2,3] Stevens Rearrangement

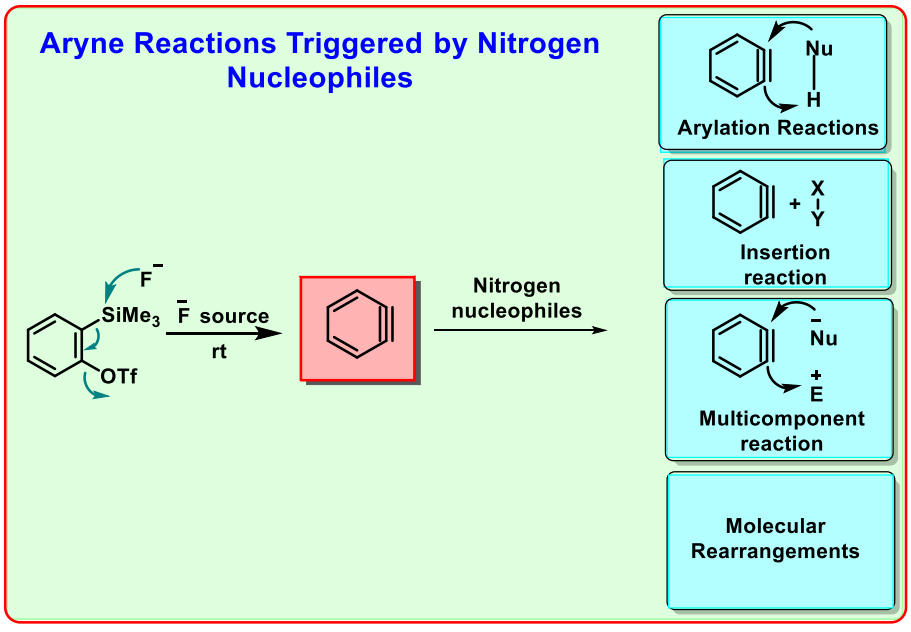
Contents Page

List of Publications

Chapter 1

A Brief Introduction to Aryne Chemistry

Arynes are highly reactive intermediates discovered more than a century ago, having several applications in organic synthesis for the construction of various 1,2-disubstituted arenes. Presence of the carbon-carbon triple bond in a six-membered ring creates a ring strain, which make them highly electrophilic in nature, kinetically unstable and highly reactive. Consequently, arynes have been extensively used for the 1,2-difunctionalization of aromatic rings for the construction of benzo-fused carbocycles and heterocycles. In this chapter, aryne reactions triggered by nitrogen nucleophiles have been discussed in detail.



1.1. Introduction

Arynes are highly reactive intermediates discovered more than a century ago and these transient intermediates have encountered an unprecedented resurgence in the past decades. The chemists have exploited this reactive intermediate for the synthesis of an array of 1,2-disubstituted benzene derivatives and also benzo-fused carbocycles and heterocycles, which are otherwise difficult to achieve by conventional methods.[1] Our focus has been on the utilization of arynes in transition metal-free multicomponent and rearrangement reactions. To put things in perspective, a brief overview of the aryne chemistry from its discovery, methods of generation, and particularly recent advances in the reaction of arynes triggered by nitrogen nucleophiles are provided in the following sections.

Benzyne or aryne or 1,2-dehydroarene is an uncharged reactive intermediate formally contained a highly strained C-C triple bond generated by removal of two vicinal-substituents from an aromatic system.[2] The *p*-orbitals overlap is reduced and they are no longer parallel to each other as in normal alkynes due to the geometric constraints on the C-C triple bond in a six-membered ring. (Figure 1.1). This reduced *p*-orbital overlap results in significant lowering of the LUMO energy of arynes. This strain created by the distorted triple bond and the increased energy gap between HOMO and LUMO in this kinetically unstable intermediate makes them highly reactive towards various charged and uncharged electrophiles. Hence, a wide variety of anionic as well as uncharged nucleophiles can add to this intermediate.[3]

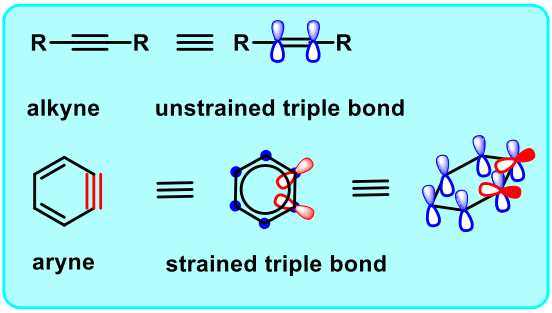
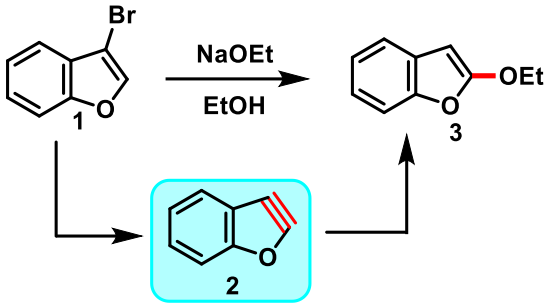


Figure 1.1: Geometry of aryne

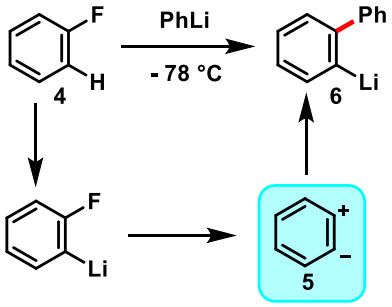
The first hint about the existence of aryne intermediate was provided in 1902 by Stoermer and Kahlert.[4] The formation of 2-ethoxybenzofuran **3** upon treatment of 3-bromobenzofuran **1** with sodium ethoxide in ethanol was studied and they postulated that

the reactive intermediate involved could be an aryne (Scheme 1.1). But they could not provide any direct experimental evidence about the intermediate **2**.



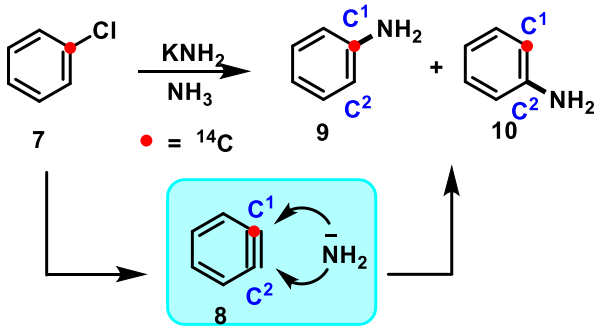
Scheme 1.1. Stoermer and Kahlert experiment

In 1942, Wittig synthesized biphenyl **6** from fluorobenzene **4** and phenyllithium and proposed that the reaction proceeds *via* a zwitterionic intermediate **5** (Scheme 1.2).[5]



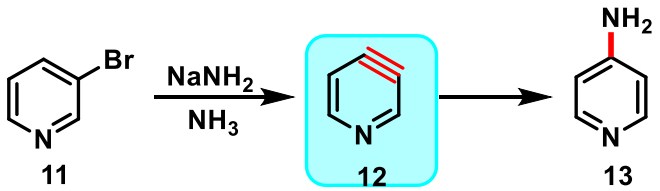
Scheme 1.2. Wittig's experiment

In 1953, Roberts and co-workers performed a seminal ^{14}C labelling experiment, which proved the existence of the reactive intermediate "benzyne".[6] The treatment of isotopically labelled chlorobenzene-1-^{14}C **7** with potassium amide delivered a mixture of labelled isomers, of aniline-1 **9** and aniline-2 **10**. The observed mixture of products proves that the $\mathbf{C^1}$ and $\mathbf{C^2}$ are equivalent in the intermediate **8** (Scheme 1.3).



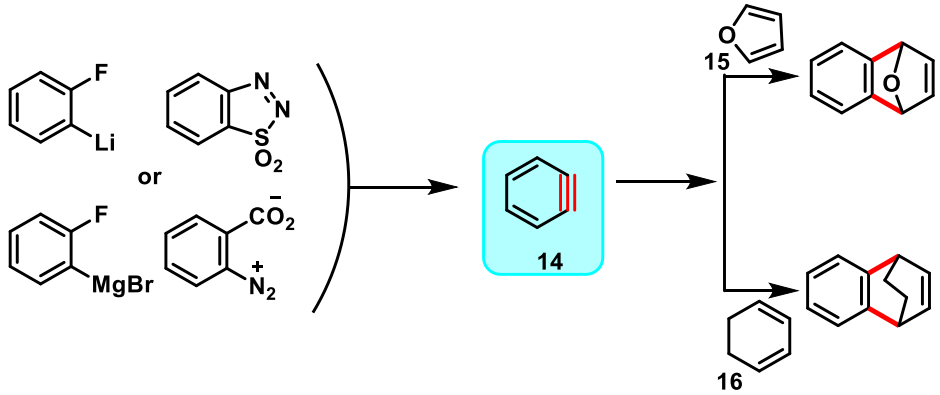
Scheme 1.3. Roberts's experiment

First heteroaryne was uncovered by Levine and co-workers when they generated pyridyne from pyridine[7] using the reaction of 3-bromopyridine **11** with sodamide. The pyridyne **12** formed upon treatment with excess sodamide delivered 4-amino pyridine **13** (Scheme 1.4).



Scheme 1.4. Heteroaryne generation

Later, Wittig and Pohmer successfully trapped the aryne intermediate **14** with furan **15** *via* a [4+2] cycloaddition reaction. The reaction furnished epoxynaphthalene derivative (Scheme 1.5).[8] Independently, Huisgen and Knorr have utilized aryne as an electrophilic dienophile when they demonstrated the reaction of aryne generated from different precursors with furan **15** or cyclohexadiene **16**.[9]



Scheme 1. 5. Wittig and Huisgen's Aryne Trapping Experiment

1.1.1. Different Class of Arynes

Arynes have found growing applications in various carbon-carbon and carbon-heteroatom bond-forming reactions. In the last few decades, several new arynes have been reported. Few popular aryne intermediates, which are generally used for synthetic transformations are shown in Figure 1.2.[10]

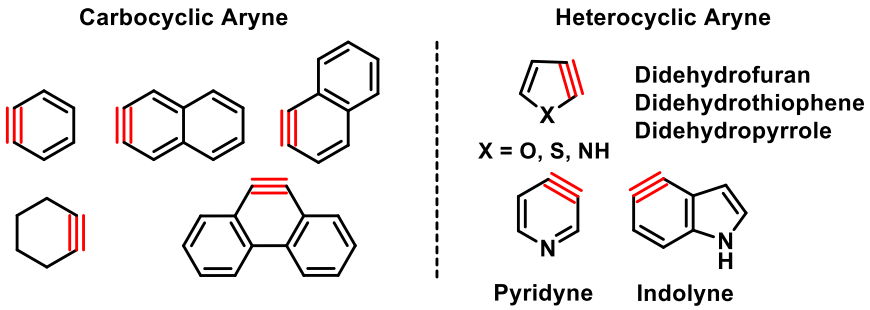


Figure 1.2. Different classs of aryne

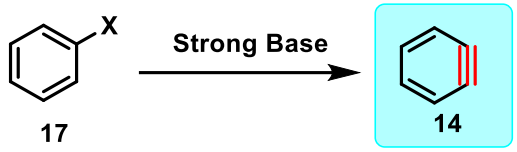
1.2. Methods of Aryne Generation

Due to the high reactivity, arynes cannot be isolated. Instead they are generated *in situ* in solution. In last decades, different research groups realized various protocols for aryne generation.

1.2.1. Traditional methods of aryne generation

(*a*) Deprotonation of aryl halides

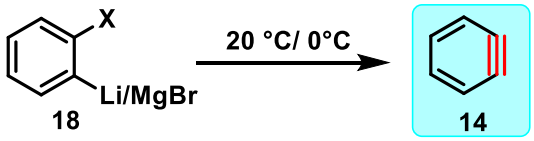
Deprotonation of aryl halides **17** using strong bases such as sodamide or *n*-BuLi generated aryne *via* the dehalogenation of the anionic intermediate.[11] However, strong basic reaction conditions are not compatible for the base-sensitive functional groups and hence have limited applications (Scheme 1.6).



Scheme 1.6. Aryne from halobenzene

(*b*) Metal-halogen exchange/elimination

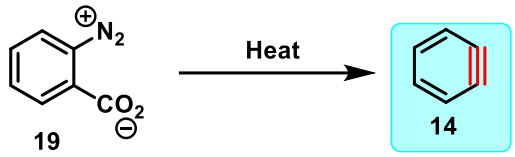
Another approach involves the metal-halogen exchange/elimination of 1,2-disubtituted haloarenes **18** or haloaryl triflates with the action of metals (Mg or Li) or organometallic reagents derived from Li, and Mg.[12] Organometallic reagents itself can act as nucleophiles making this route less practical (Scheme 1.7).



Scheme 1.7. Metal-halogen exchange/elimination

(*c*) From anthranilic acids

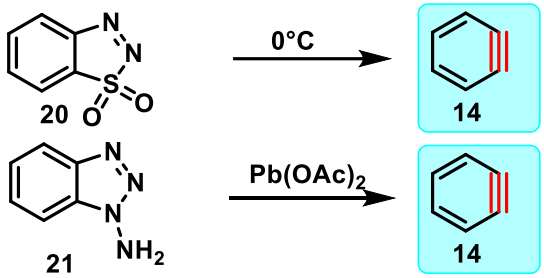
Arynes can also be generated from anthranilic acids **19**, converting them into the zwitterionic benzenediazonium 2-carboxylates in the reaction course. Benzenediazonium 2-carboxylate upon heating decomposes to form aryne with the liberation of nitrogen and carbon dioxide.[13] The main problem associated with this method is the explosive nature of diazonium compounds (Scheme 1.8).



Scheme 1.8. Arynes from anthranilic acids

(*d*) Fragmentation of aminotriazole

Fragmentation of benzo[d][1,2,3]thiadiazole 1,1-dioxide **20** and aminotriazole **21** produces aryne with evolution of nitrogen gas, but has explosive nature and requires lead tetraacetate oxidant, resulting in less functional group tolerance (Scheme 1.9). [14]



Scheme 1.9. Arynes from benzothiadiazoledioxide and aminotriazole

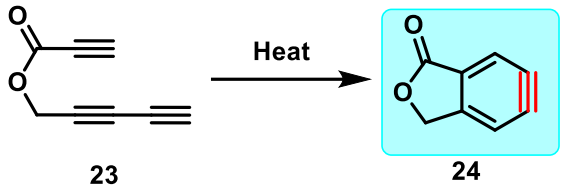
(*e*) From phenyl(2-(trimethylsilyl)phenyl)iodonium triflate

Fluoride-induced elimination of the aryne precursor phenyl(2-(trimethylsilyl)phenyl)iodonium triflate **22** is an additional process for the generation of aryne, but preparation of starting material involves complex process[15] which makes its synthesis unfeasible (Scheme 1.10).

Scheme 1.10. Arynes from phenyl(2-(trimethylsilyl)phenyl)iodonium triflate

(*f*) Using hexadehydro Diels-Alder (HDDA) reaction

Recently, Hoye and co-workers developed a new method of aryne generation by the intramolecular hexadehydro Diels-Alder reaction (HDDA) of triynes **23**. This method allows reagent-free and metal-free generation of arynes **24**, but requires elevated temperature for the formation of arynes (Scheme 1.11). [16]

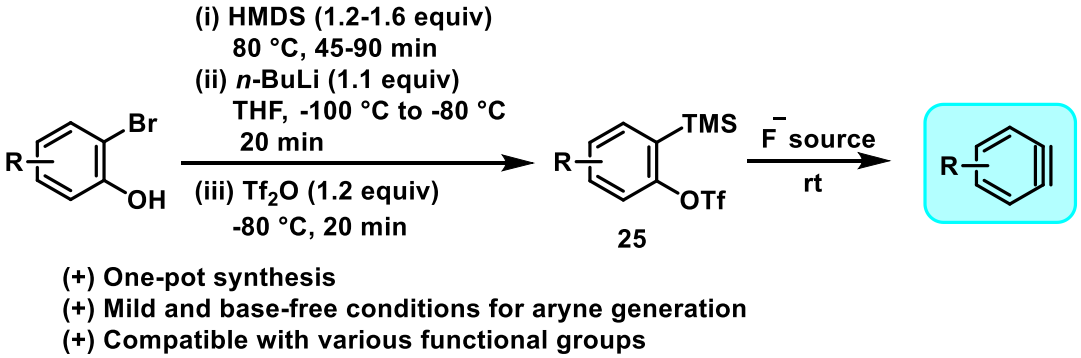


Scheme 1.11. Arynes using HDDA strategy

All these methods requires stoutly basic or harsh reaction conditions. The use of metals, strongly basic conditions and high temperature are not compatible with large number of functional groups, which considerably restricted the scope of aryne reactions in organic synthesis.

1.2.2. Kobayashi's fluoride induced aryne generation

In 1983, Kobayashi and co-workers, through a pioneering work uncovered a facile method for the generation of arynes under base-free and mild reaction conditions by the fluoride-induced 1,2-elimination of 2-(trimethylsilyl)aryl triflates **25** as aryne precursor. This seminal discovery led to a rapid development in the field of aryne chemistry (Scheme 1.12).[17] The precursor could easily be synthesized from 2-bromophenol in two steps.



Scheme 1.12. Kobayashi's method of aryne generation

Kobayashi's method is compatible with a range of functional groups and reagents. KF (with 18-crown-6 as additive) in THF, CsF in CH_3CN, TBAT in THF and tetrabutyl

ammonium fluoride (TBAF) in THF are generally used as fluoride sources for the generation aryne from **25**. Cautious selection of fluoride source and solvent combination was found to be beneficial to control the rate of aryne generation as well as the regioselectivity in the product formation. In past three decades, Kobayashi's method is highly prefered by synthetic chemists over traditional methods for aryne generation. Mild and efficient Kobayashi's procedure of aryne generation has urged chemists to revisit traditional aryne reactions to enhance the scope and yield.

1.3. Possible Reactivity Modes of Arynes

Arynes are one of the most important class of reactive intermediates primarily due to their electron-deficient nature and have been widely used as electrophiles in various reactions. In recent years, these fascinating intermediates gathered much attention of organic chemists by virtue of their different modes of action in various bond forming processes. Transition-metal-free reactions of arynes can be rationalized into five main groups such as

(a) Pericyclic reactions[18]

(b) Multicomponent couplings (MCCs)[19]

(c) Arylation Reactions

(d) Insertion reactions[20]

(e) Rearrangement reactions[21]

Owing to their distinct electrophilic nature, arynes form excellent dienophile and dipolarophile in Diels-Alder reactions and dipolar cycloaddition reactions respectively.

Arynes have the inherent ability to react with wide range of nucleophiles, even with neutral nucleophiles. Recently, arynes have been efficiently utilized for the synthesis of valuable molecules *via* transition-metal-free multicomponent couplings (MCCs). The concept of this multicomponent reaction involves the addition of nucleophiles to arynes to form the aryl anion intermediate, which is successfully trapped by various electrophiles leading to the synthesis of a variety of 1,2-disustituted benzene derivatives in a single step transformation. A reactant with acidic protons can quench the reactive aryl anion intermediate leading to arylation reactions.

Arynes are extensilvely utilized for the insertion reactions as well. A variety of functionalized 1,2-disubstituted arenes are synthesized as a result of the element-element σ-bond and π-bond insertion.

Recently a new class of reactions of arynes has attracted the attention of synthetic chemists called the rearrangement reactions. Rearrangement reaction of aryne involves the sigmatrotropic rearrangements or migration reactions involving arynes.

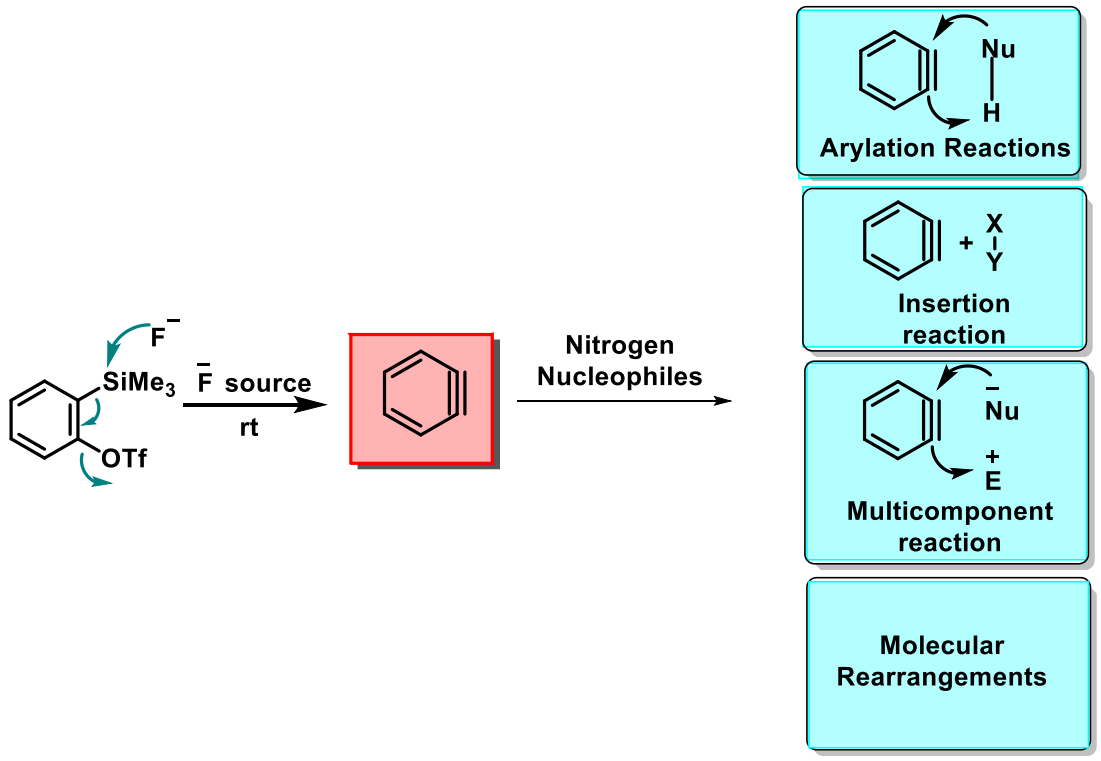
The focus of this chapter is on the reactions of arynes triggered by nitrogen nucleophiles. Majority of aryne reactions involves the nitrogen containing nucleophilic initiators. The reactions of arynes initiated by nitrogen nucleophiles can be primarily classified into four categories (Scheme 1.13).

(a) Insertion reactions

(b) Arylation Reactions

(c) Multicomponent couplings (MCCs)

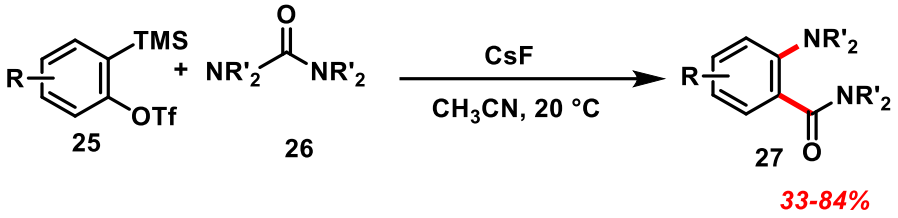
(d) Rearrangement reactions



Scheme 1.13. Reactions of aryne with nitrogen nucleophiles

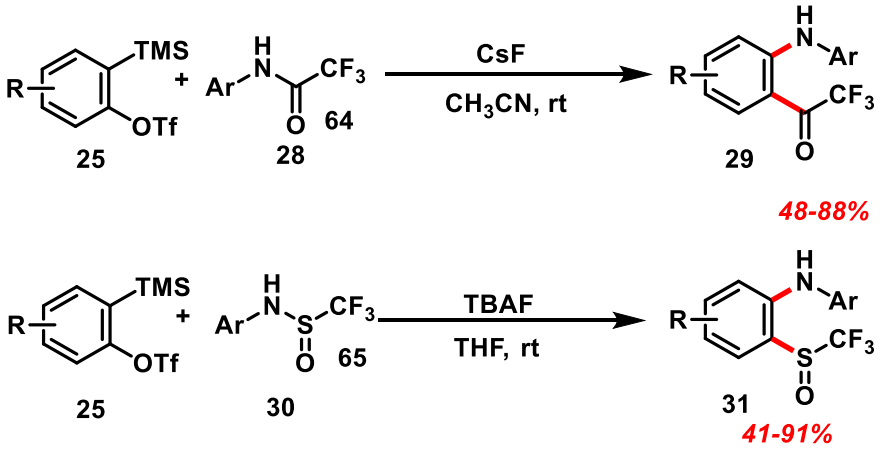
1.3.1. Insertion Reactions Involving Nitrogen Nucleophiles

To utilize the ability of arynes to insert into various element-element σ-bonds and π-bonds, they have been extensively employed in the synthesis of functionalized 1,2-disubstituted arenes. Shirakawa, Hiyama and co-workers synthesized 2-aminobenzamides **27** by the insertion of arynes into the N-CO bond of ureas **26** under mild reaction conditions, which are difficult to access by conventional methods (Scheme 1.14).[22]



Scheme 1.14. Insertion of arynes into the N-CO bond in urea

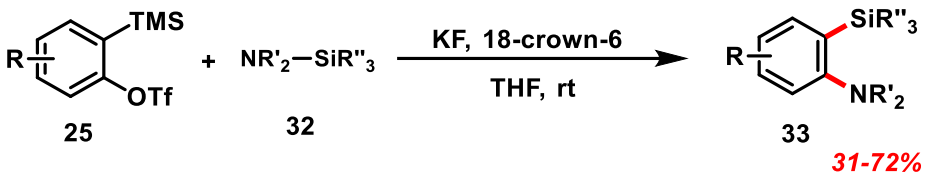
Moreover, Liu and Larock demonstrated an efficient insertion of arynes to the C-N bond of amides **25** and S-N bond of sulfinamides **30** leading to a transition-metal-free synthesis of 1,2-disubstituted arenes **29** and **31** respectively under mild reaction conditions with broad substrate scope (Scheme 1.15).[23]



Scheme 1.15. Insertion of arynes into the C-N bond of amides and S-N bond of sulfinamides

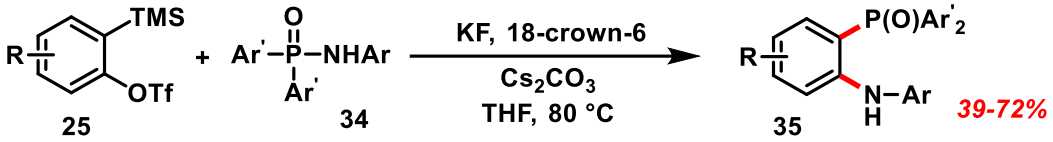
Yoshida, Kunai and co-workers demonstrated the insertion of arynes into the nitrogen-silicon σ-bond of aminosilanes **32** resulting in variety of functionalized 2-

silylaniline derivatives (Scheme 1.16).[24] Notably, this aminosilylation reaction worked under mild reaction conditions (Scheme 1.16).



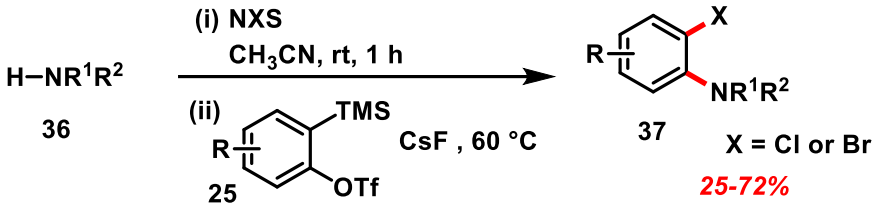
Scheme 1.16. Insertion of arynes into N-Si bond

In 2013, Zhang and co-workers reported the insertion reaction of arynes to P-N bond of arylphosphoryl amides **34** leading to the formation of *ortho*-amine substituted arylphosphine oxides **35** (eq 22).[25] It has to be noted that this method provides straightforward access to the number of useful bidentate aminophosphine ligands (Scheme 1.17).



Scheme 1.17. Insertion of arynes into N-P bond

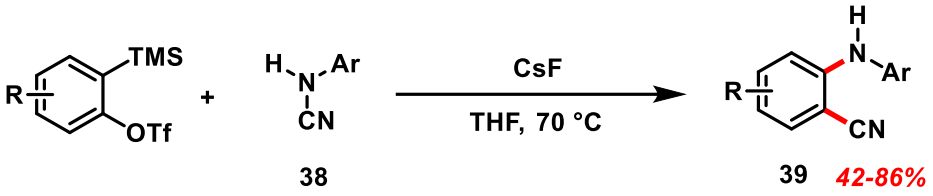
Subsequently, Wang and co-workers disclosed a transition-metal-free one-pot procedure for the synthesis of *ortho*-haloaminoarenes **37** by the insertion of arynes into a nitrogen-halogen bond (N-X) formed *in situ* by the treatment of secondary amines **36** with *N*-halosuccinimide (N-X) (Scheme 1.18).[26] The *ortho*-haloaminoarene products has been functionalized easily using Pd-catalyzed coupling reactions demonstrating the synthetic utility of present method.



Scheme 1.18. Insertion of arynes into N-X bond

Recently, Zeng and co-workers developed an efficient protocol for the synthesis of 1,2-bifunctional aminobenzonitriles **39** by the insertion of arynes to N-CN bond of aryl cyanamides **38** (Scheme 1.19).[27] Broad substrate scope, transition-metal-free conditions and

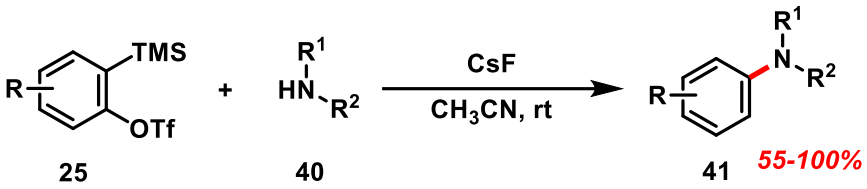
good yields of products and post-synthetic functionalization of aminocyanation products makes this methodology valuable in synthesis.



Scheme 1.19. Insertion of arynes into N-CN bond

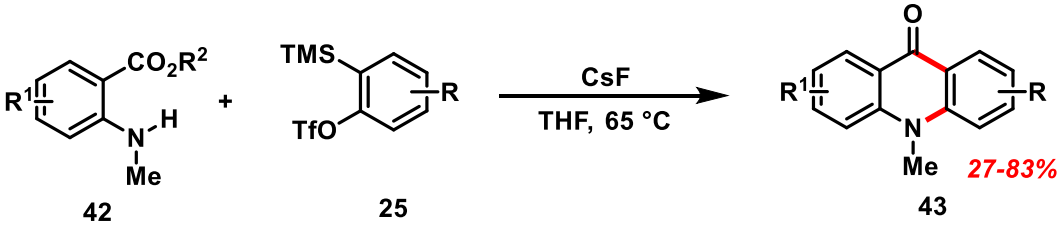
1.3.2. *N*-Arylation Reactions

In 2003, Larock and co-workers developed an efficient transition-metal-free method for the *N*-arylation of primary and secondary amines and sulfonamides by the insertion of arynes into the N-H bonds. Interestingly, selective monoarylation and diarylation of primary amines has easily been achieved by the simple control of the ratio of the reactants.[28]



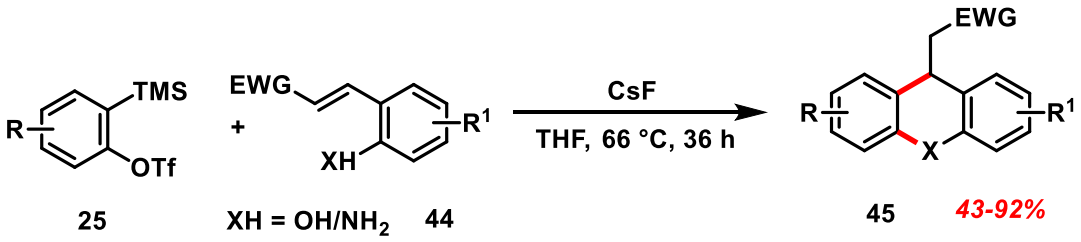
Scheme 1.20. *N*-Arylation of Amines and Sulfonamides

An efficient, mild and transition-metal-free method for the synthesis of xanthones has been uncovered by Liu and Larock (Scheme 1.21).[29] The mechanism involves a tandem insertion-cyclization sequence of arynes with 2-substituted benzoates **43** in excellent yields.[30] The reaction proceeds *via* the intermolecular nucleophilic addition of aniline nitrogen to the arynes to form the aryl anion intermediate followed by an intramolecular electrophilic cyclization.



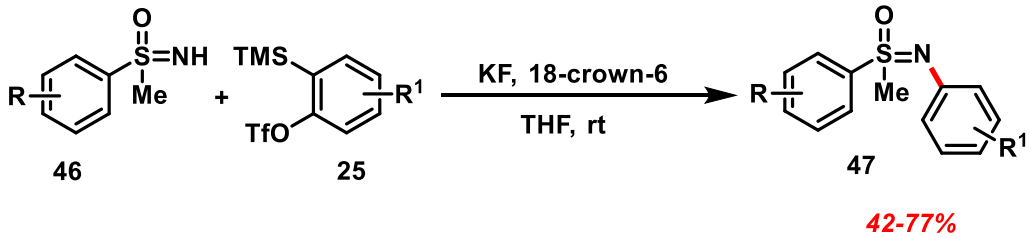
Scheme 1.21. Tandem Insertion-Cyclization of Arynes

Moreover, Huang and Zhang uncovered a cascade process for the synthesis of 9-functionalized xanthenes/acridines **45**.[31] The reaction involves the nucleophilic addition of -OH/NH_2 groups of phenols/anilines **44** having a Michael acceptor at the 2-position to arynes followed by intramolecular cyclic Michael addition of *in situ* formed aryl anion intermediate to give final products **45** (Scheme 1.22).



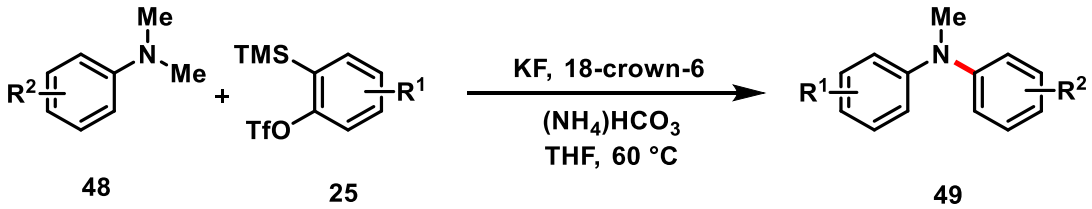
Scheme 1.22. Cascade Insertion-Cyclization Involving Arynes

A transition-metal-free process with mild reaction conditions, shorter reaction time, and broad substrate scope for the *N*-arylation of sulfoximines **46** *via* the insertion of arynes to the N-H bond leading to the synthesis of *N*-aryl sulfoximine derivatives **47** has been reported by Singh and co-workers (Scheme 1.23).[32]



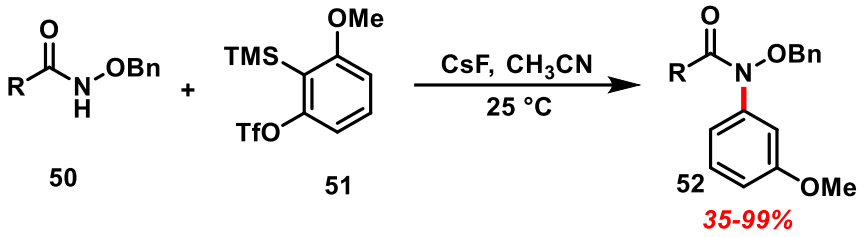
Scheme 1.23. *N*-Arylation of Sulfoximines

In 2013, Biju group developed a highly monoselective and transition-metal-free *N*-arylation of aromatic tertiary amines **48** using arynes leading to the formation of functionalized diaryl amine derivatives **49** in good yields (Scheme 1.24). High yields, broad substrate scope are the noteworthy features of this reaction.[33]



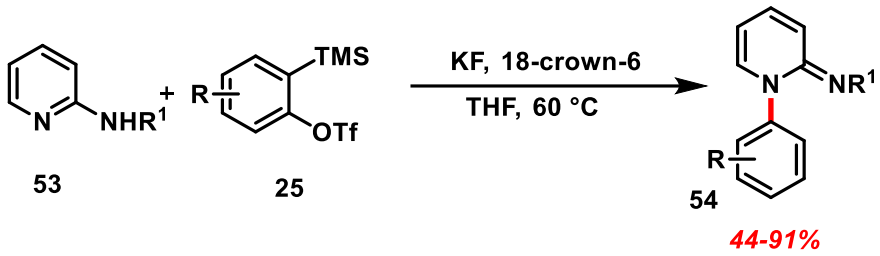
Scheme 1.24. *N*-Arylation of aromatic tertiary amines

An efficient and transition-metal-free *N*-arylation of amides *via* the insertion of arynes generated from silyl triflate **51** into the N−H bonds in the *N*-alkoxy amides **50** was demonstrated recently by Jin group. This protocol is applicable for the construction of structurally diverse *N*-aryl hydroxamates and hydroxamic acids derived from *N*-protecting amino acids and peptides (Scheme 1.25).[34]



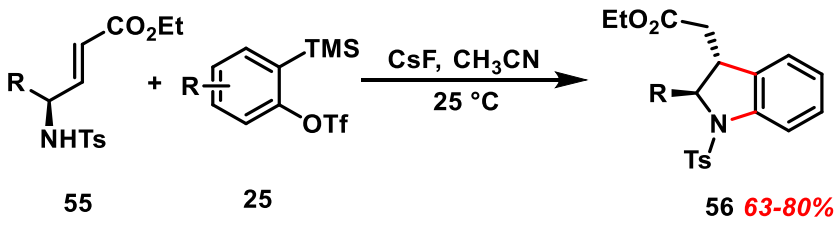
Scheme 1.25. *N*-Arylation of *N*-alkoxy amides

In 2017, Zhai and co-workers uncovered a chemoselective *N*-arylation reaction of 2-aminopyridine **53** derivatives with arynes. The dearomatized pyridine products **54** could be further applied to the facile construction of benzoisoquinuclidines and isoquinuclidines (Scheme 1.26).[35]



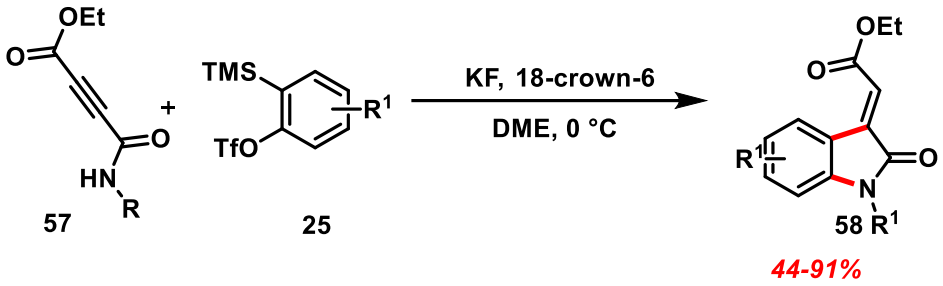
Scheme 1.26. *N*-Arylation of of 2-aminopyridines

A one step formal [3+2]-annulation protocol for the synthesis of 2,3-disubstituted indolines **56** has been demonstrated by Sudalai and co-workers (Scheme 1.27). The *in situ* generated aryne reacts with γ-amino-α,β-unsaturated esters to deliver indolines **56** with high regio- and diastereoselectivities.[36]



Scheme 1.27. *N*-Arylation/Michael cascade

An aryne route towards the preparation of various (*E*)-oxindolylidene acetates **58** using arynes and carbamoylpropiolates **57** has been developed by Mhaske group (Scheme 1.28). The utility of this milder and transition-metal-free protocol is further extended to the one pot synthesis of complex spirooxindolopyrrolidones as well.[37]

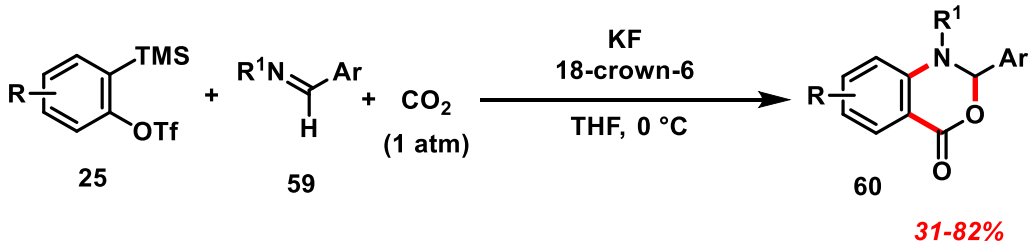


Scheme 1.28. *N*-Arylation for the (*E*)-oxindolylidene acetate synthesis

1.3.3. Multicomponent Couplings (MCCs) Involving Nitrogen Nucleophiles

In recent years, aryne-based reactions have achieved astonishing success, mainly in transition-metal-free multicomponent couplings (MCCs). The success in using aryne in multicomponent reactions can be attributed to the mild reaction conditions involved in Kobayashi's method for aryne generation, which allows the reactive intermediate to serve as connector between the nucleophilic and electrophilic couling partners. A large number of aryne multicomponent reactions are triggered by nitrogen nucleophiles. Following are some of the selected aryne multicomponent reactions triggered by nitrogen nucleophiles.

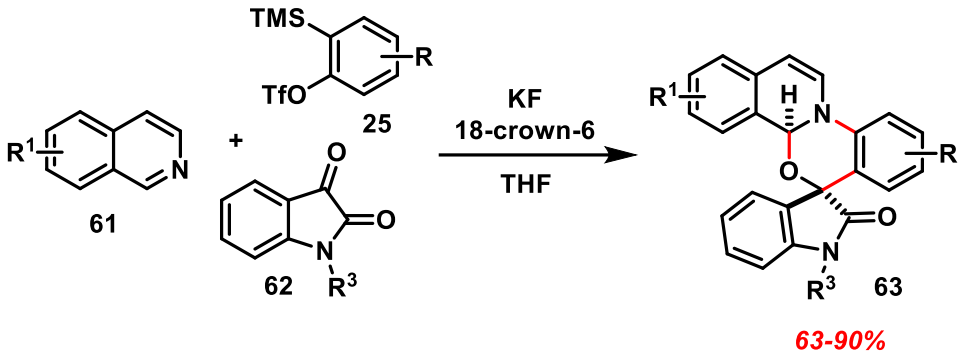
In 2006, Yoshida group has demonstrated the imine triggered multicomponent reaction utilizing carbon dioxide as the third component. The zwitterion arising from nucleophilic addition of imines **59** to arynes is captured using CO_2, leading to the synthesis of benzoxazinone derivatives **60** (Scheme 1.29).[38]



Scheme 1.29. MCCs involving arynes, imines and CO_2

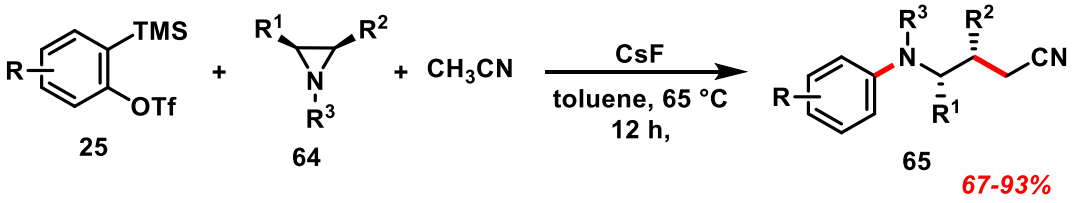
In 2013, Biju and co-workers demonstrated the transition-metal-free multicomponent coupling (MCC) involving arynes, *N*-heterocycles, and isatins.[39]

Employing isoquinoline **61** as the nucleophilic initiator with *N*-substituted isatin **62** as third component, the reaction afforded a mixture of spirooxazino isoquinoline derivatives **63** in good yield and diastereoselectivity (Scheme 1.30).



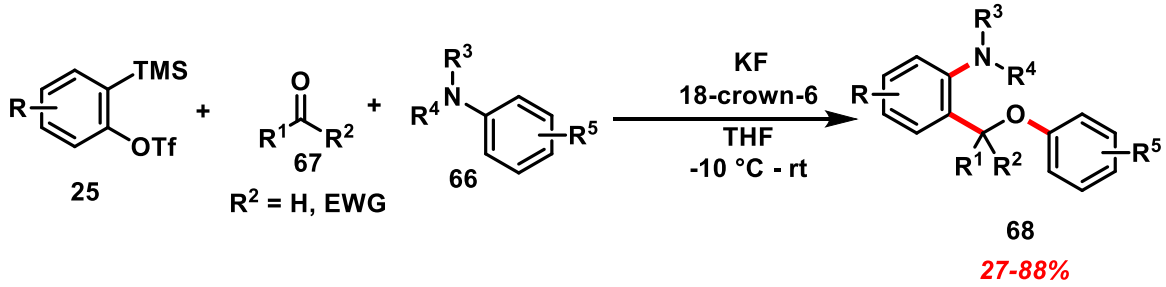
Scheme 1.30. MCCs involving arynes, quinolines/isoquinolines and carbonyls

In 2013, a stereospecific aryne MCCs triggered by aziridines **64** with CH_3CN as the third-component was uncovered by Larionov and co-workers. This protocol furnished biologically relevant *N*-aryl γ-aminobutyronitriles **65** in good yields (Scheme 1.31).[40]



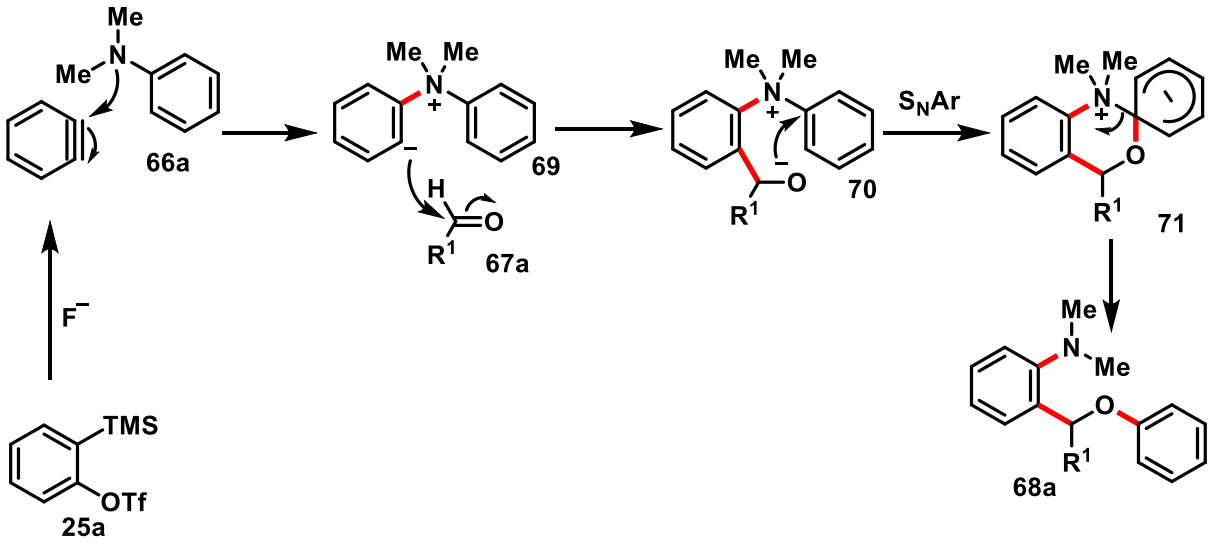
Scheme 1.31. Arynes MCCs involving CH_3CN

In 2015, a facile route towards the synthesis of *ortho*-functionalized tertiary amines **68** from arynes **1**, aromatic tertiary amines **66**, and carbonyls **67** has been demonstrated by Biju and co-workers. The reaction involves an aryl–aryl tertiary amino group migration similar to that of the Smiles rearrangement (Scheme 1.32).[41] Activated carbonyls like various isatins, phenyl ethyl glyoxylate etc. also worked well under the reaction conditions.



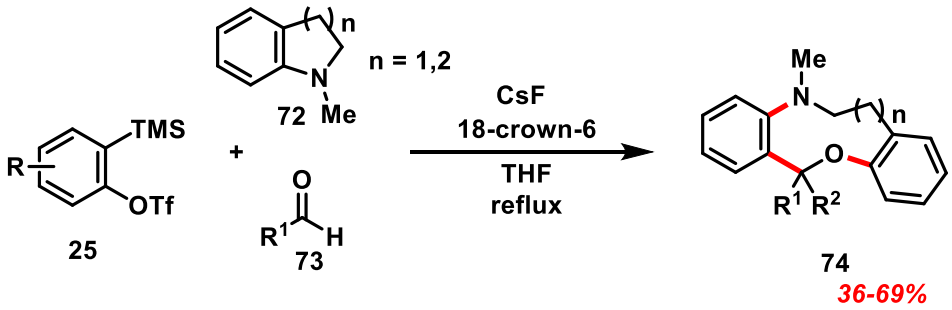
Scheme 1.32. MCCs involving arynes, carbonyls and tertiary amines

The mechanism involves the nucleophilic attack of tertiary amine **66a** on aryne generating the dipolar intermediate **69**. This intermediate upon addition to carbonyls leads to the key tetrahedral intermediate **70**. An intramolecular nucleophilic aromatic substitution reaction (S_NAr) results in the formation of the *ortho*-functionalized tertiary amine product **68a** *via* the σ-complex **71** (Scheme 1.33).



Scheme 1.33. Proposed mechanism for aryne Smiles rearrangement

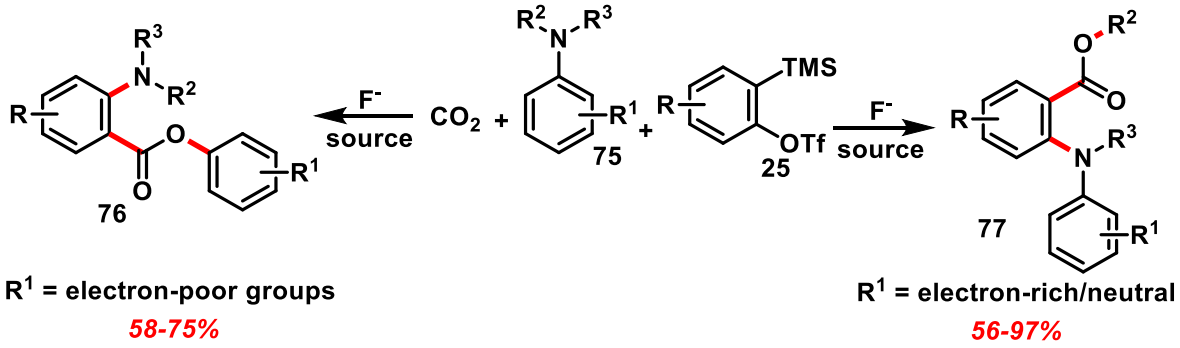
Subsequently, Okuma and co-workers developed the three-component reaction of aromatic cyclic tertiary amines **72** with arynes and aldehydes. This protocol is a facile method for the synthesis of 9- and 10-membered cyclic dibenzo[1,5]oxazonines and dibenzo[1,5]oxazecines **74** (Scheme 1.34).[42]



Scheme 1.34. MCC involving aryne, aldehydes and cyclic tertiary amines

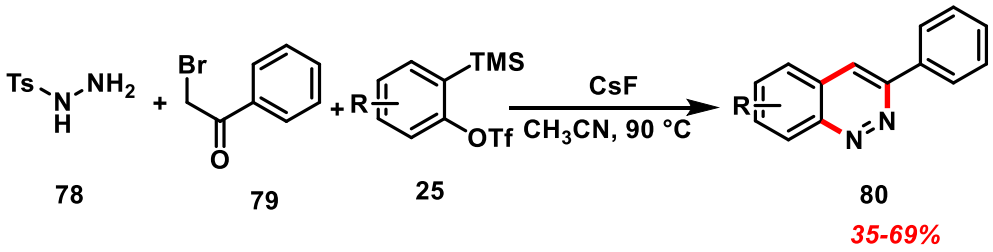
Recently, Biju and co-workers disclosed a the teriary amine triggered multicomponent reaction involving arynes, aromatic tertiary amines **75** and CO_2. When the

amine coupling partner possesses an electron-releasing/neutral groups, the reaction delivered 2-arylamino benzoates **77** *via* a nitrogen to oxygen alkyl group migration. However, employing electron-deficient amines in the reaction delivered 2-aminoaryl benzoates **76** in which reaction proceeds *via* an aryl migration similar to that of the Smiles rearrangement (Scheme 1.35).[43]



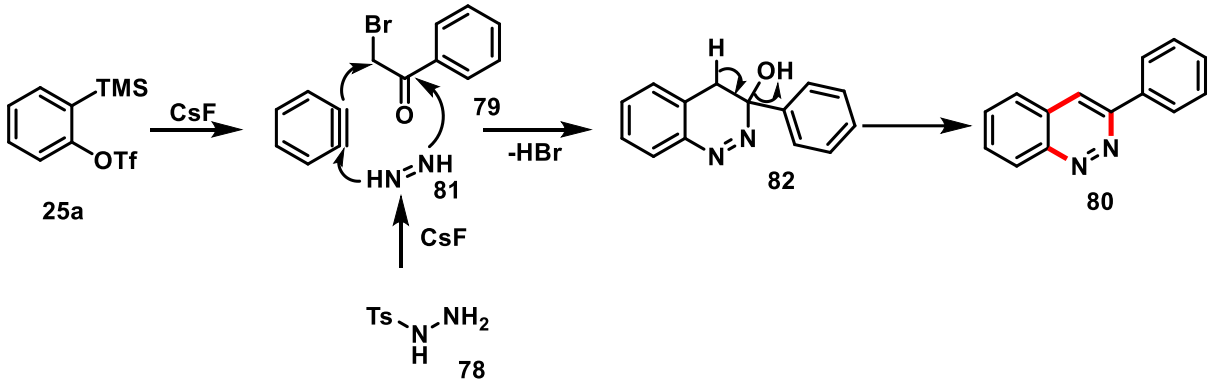
Scheme 1.35. MCC involving aryne, CO_2 and tertiary amines

Recent studies from Wu group has shown a novel transition-metal-free multicomponent coupling cyclization reaction for the efficient and convenient synthesis of cinnoline derivatives **80** with an *in situ* generated diazene as the nucleophilic partner. This aryne multicomponent reaction allows the formation of new C-C and C-N bonds in a single step (Scheme 1.36).[44]



Scheme 1.36. Synthesis of cinnolines using aryne MCC

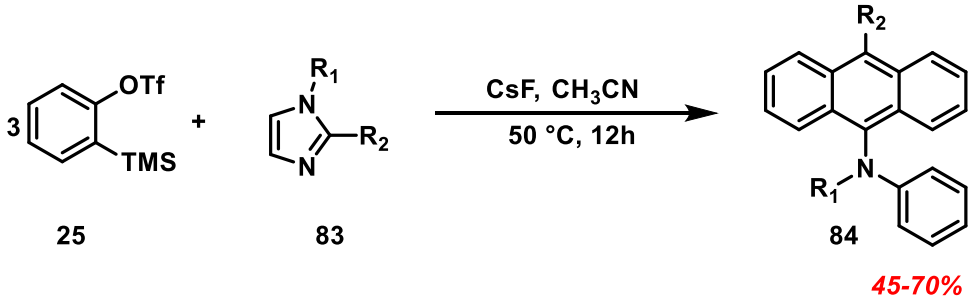
The tosylhydrazine **78** decomposes into the 4-methylbenzenesulfinate anion and intermediate diazene **81** adds nucleophilically to the aryne generated. A coupling annulation α-bromoacetophenone **79** reaction to afford intermediate **82**. Finally, intermediate **82** is converted to the desired product **80** through an aromatization reaction with elimination of H_2O (Scheme 1.37).



Scheme 1.37. Proposed mechanism for the cinnoline synthesis

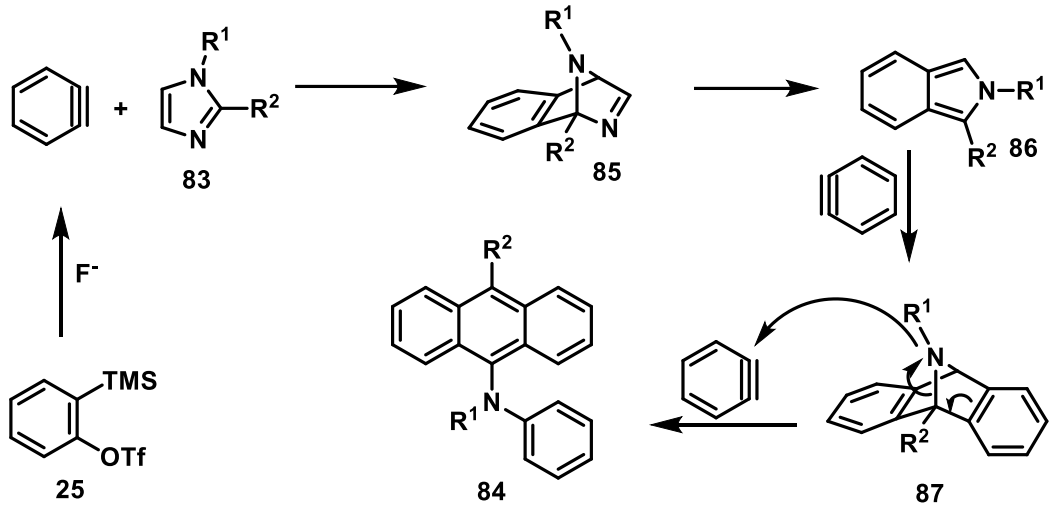
1.3.4. Rearrangement Reactions

Xie and Zhang demonstrated a tandem reaction of arynes for the synthesis of arylamines containing anthracene moiety **84** with *N*-substituted imidazoles **83**, where three molecules of aryne were incorporated in the final product (Scheme 1.38).[45]



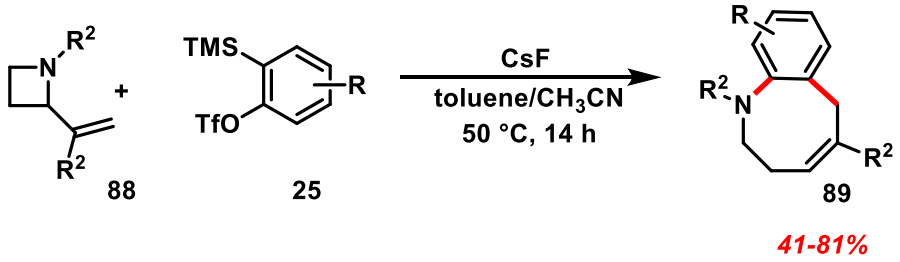
Scheme 1.38. Reaction of *N*-substituted imidazole with aryne

The mechanism involves an initial Diels-Alder reaction of substituted imidazole **83** with the *in situ* generated aryne leading to the nitrogen-bridged isoquinoline intermediate **85**. Elimination of a molecule of HCN *via* the retro Diels-Alder reaction results in the formation of **86**. A second Diels-Alder followed by nucleophilic *N* arylation leads to arylamines containing anthracenes (Scheme 1.39).



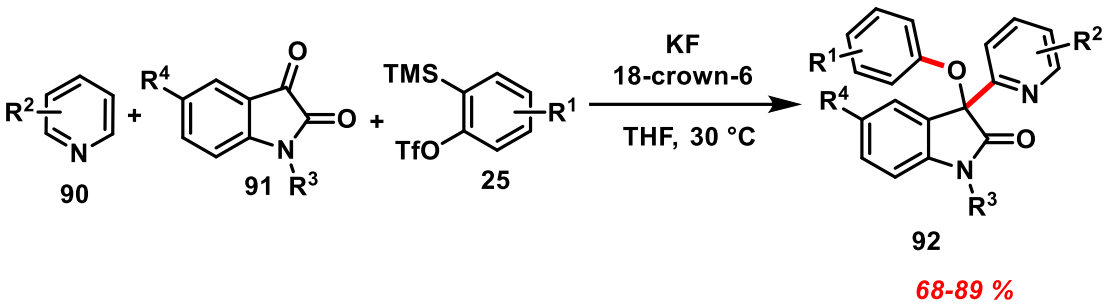
Scheme 1.39. Mechanism for the reaction of *N*-substituted imidazole with aryne

Inspired by the Greaney report on aryne aza-Claisen rearrangement (For details, see Chapter 5), Saito and co-workers have disclosed the reaction of 2-vinylazetidines **88** with arynes resulting in the smooth synthesis of 1-benzazocine derivatives **89** *via* Claisen rearrangement (Scheme 9).[46] The reaction proceeds *via* the nuclophilic addition of azetidine **88** to aryne generated from **1** followed by protonation of the aryl anion and a subsequent aza-Claisen rearrangement (Scheme 1.40).



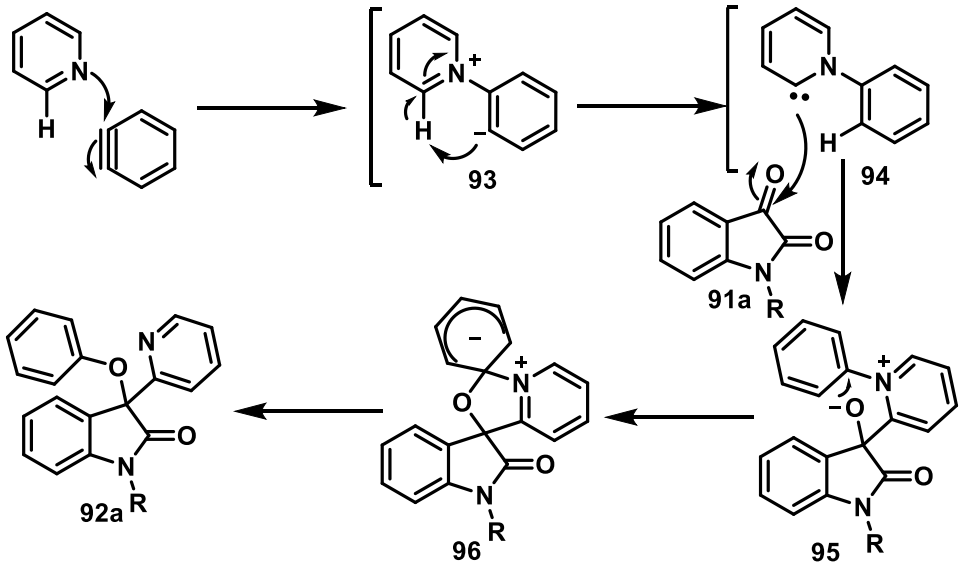
Scheme 1.40. Aryne aza-Claisen rearrangement

Biju group, in 2013, observed that when pyridine **90** was engaged as the nucleophilic coupling partner in aryne MCCs with isatins **91** as the third component, no expected pyridooxazino derivatives were observed, but instead indolin-2-one derivatives **92** was obtained in good yields (Scheme 1.41).[39] The reaction proceeds *via* a conceptually new highly nucleophilic pyridylidene intermediate.



Scheme 1.41. MCC involving aryne, pyridine and isatin

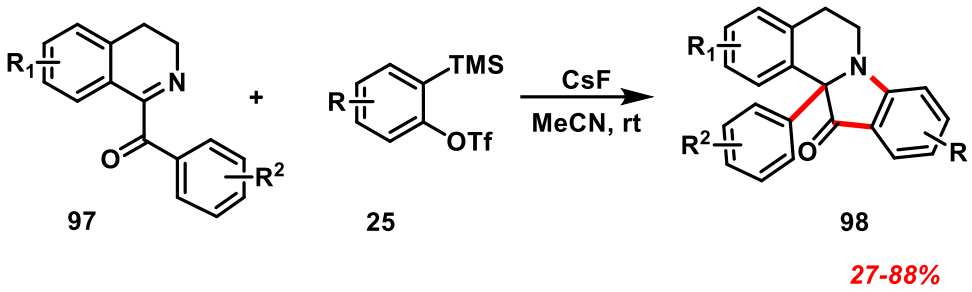
The reaction was initiated with the nucleophilic attack of pyridine on aryne leading to the 1,4-dipolar intermediate **93**. This intermediate undergoes an intramolecular proton transfer to generate a highly unstable and nucleophilic pyridylidene intermediate **94**. This highly nucleophilic pyridylidene intermediate **94** adds to the electrophilic carbonyl group of isatin derivatives **91a** forming the intermediate **95**, which undergoes an intramolecular nucleophilic aromatic substitution (S_NAr) reaction to furnish indolin-2-one **92a** *via* the intermediate **96** (Scheme 1.42).



Scheme 1.42. Mechanism of MCC involving aryne, pyridine and isatin

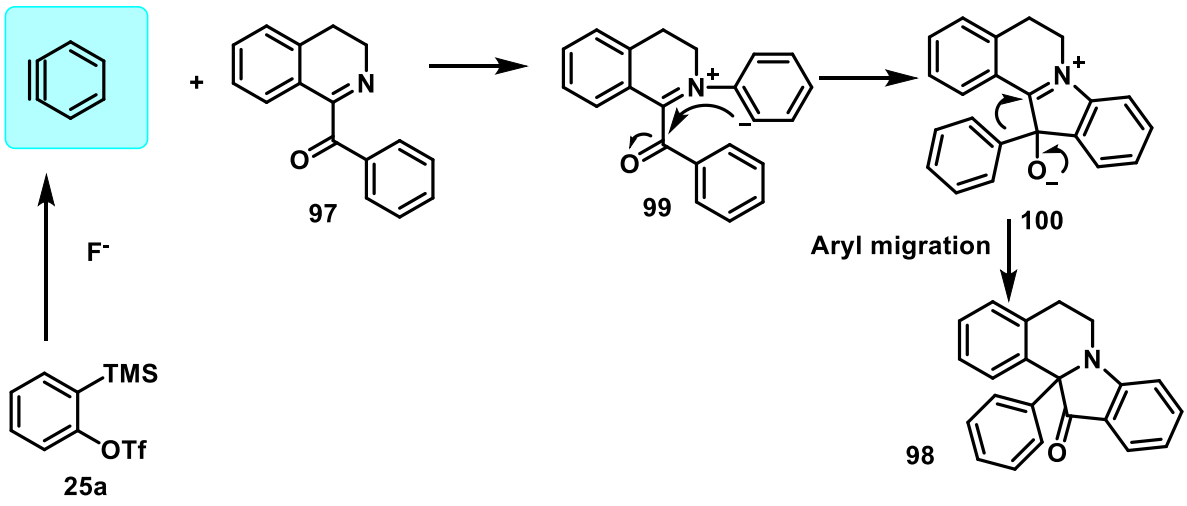
In 2016, Voskressensky and co-workers demonstrated the synthesis of indoxylisoquinolines **98** by the reaction of 1-aryloxy substituted 3,4-dihydroisoquinolines **97** and arynes. This reaction involves an aryl-anion migration

(Scheme 18).[47] This new rearrangement reaction involving arynes provides direct route to the synthesis of biologically important indoxylisoquinoline cores (Scheme 1.43).



Scheme 1.43. Synthesis of indoxylisoquinolines

Mechanistically, the reaction proceeds *via* the initial nucleophilic attack of dihydroisoquinoline **97** onto aryne, leading to the generation of the zwitterion **99**. Intramolecular attack of aryl anion to the carbonyl centre forms the intermediate **100**. A migration of aryl substituent to the iminium carbon occurs forming the indoloisoquinolinones **98**. This migration has close connection with benzylic rearrangement and quasi-Favorskii rearrangements of α-haloarylketones (Scheme 1.44).



Scheme 1.44. Plausible reaction mechanism

1.4. Focal Theme of the Thesis

This chapter has described the brief history, generation and reactions of arynes. The success of this reactive intermediate in organic synthesis can be attributed to their inherent electrophilic nature and the mild reaction conditions involved in Kobayashi's method for aryne generation by fluoride-induced 1,2-elimanation of 2-(trimethylsilyl)aryl triflates. The central theme of this thesis is the transition-metal-free applications of arynes in multicomponent and rearrangement reactions triggered by nitrogen nucleophiles using Kobayashi's method of aryne generation. A brief introduction on the transition-metal-free applications of arynes in carbon-carbon and carbon-heteroatom bond-forming reactions with special emphasis to nitrogen nucleophiles has been discussed so far.

A transition-metal-free protocol for the synthesis of medicinally important *N*-aryl β-amino alcohol derivatives using a three-component coupling involving *N*-substituted aziridines, arynes and water promoted by trifluoroacetic acid (TFA) has been discussed in detail in the 2nd chapter of the thesis. β-Amino alcohols are an important class of compounds having widespread applications in pharmaceutical industry. Moreover, the use of aziridines as nucleophile with carboxylic acids as the third component afforded *N*-aryl β-amino alcohol derivatives and the details form the subject matter of the 3rd chapter of the thesis.

Functionalized epoxides are versatile intermediates for the synthesis of various biologically important molecules and this moiety is found in many natural products. A mild and transition-metal-free coupling of aziridines, arynes and aldehydes afforded *N*-aryl α-amino epoxides in moderate to good yields and diastereoselectivity. Investigations of these reactions are documented in the 4th chapter of the thesis.

The Stevens rearrangement involves the conversion of ammonium/sulfonium salts into complex nitrogen/sulfur containing products, which usually takes place in the presence of a strong base. A mild and transition-metal-free procedure for the [2,3] Stevens rearrangement induced by arynes for the synthesis of functionalized homoallylic amines is presented in the last chapter of the thesis.

1.5. References

1. For recent reviews; (a) Idiris, F. I. M.; Jones, C. R. *Org. Biomol. Chem*. **2017**, *15*, 9044. (b) García-López, J.-A.; Greaney, M. F. *Chem. Soc. Rev.***2016**, *45*, 6766. (c) Bhojgude, S. S.; Bhunia, A.; Biju, A. T. *Acc. Chem. Res*. **2016**, *49*, 1658. (d) Goetz, A. E.; Shah, T. K.; Garg, N. K. *Chem. Commun*. **2015**, *51*, 34. f) (e) Dubrovskiy, A. V.; Markina, N. A.; Larock, R. C. *Org. Biomol. Chem.* **2013**, *11*, 191. (f) Wu, C.; Shi, F. *Asian J. Org. Chem.* **2013**, *2*, 116. (g) Pérez, D.; Peña, D.; Guitián, E. *Eur. J. Org. Chem.* **2013**, 5981. (h) Tadross, P. M.; Stoltz, B. M. *Chem. Rev.* **2012**, *112*, 3550. (i) Gampe, C. M.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2012**, *51*, 3766. (j) Bhunia, A.; Yetra, S. R.; Biju, A. T. *Chem. Soc. Rev.* **2012**, *41*, 3140. (k) Okuma, K. *Heterocycles* **2012**, *85*, 515. (l) Yoshida, H.; Ohshita, J.; Kunai, A. *Bull. Chem. Soc. Jpn.* **2010**, *83*, 199
2. Gilchrist T.C.; Rees C.W.; (1969) *Carbenes, Nitrenes and Arynes* Nelson. London.
3. Heaney, H. *Chem. Rev*. **1962**, 62, 81.
4. Stoermer, R.; Kahlert, B. *Ber. Dtsch. Chem. Ges.* **1902,** *35*, 1633.
5. Wittig, G. *Naturwissenschaften* **1942**, *30*, 696.
6. Roberts, J. D.; Simmons, H. E. Jr.; Carlsmith, L. A.; Vaughan, C. W. *J. Am. Chem. Soc*. **1953**, *75*, 3290.
7. Levine, R.; Leake, W. W. *Science* **1955**, *121*, 780.
8. Wittig, G.; Pohmer, L. *Angew. Chem.* **1955**, *67*, 348.
9. Huisgen, R.; Knorr, R. *Tetrahedron Lett*. **1963**, 1017
10. Kessar, S. V. In *Comprehensive Organic Synthesis;* Pergamon Press: New York, **1991**; Vol. 4, pp 483.
11. Kitamura, T. *Aust. J. Chem*. **2010**, *63*, 987.
12. Matsumoto, T.; Hosoya, T.; Katsuki, M.; Suzuki, K. *Tetrahedron Lett.* **1991**, *32*, 6735.
13. (a) Stiles, M.; Miller, R. G. *J. Am. Chem. Soc.* **1960**, *82*, 3802. (b) Friedman, L.; Logullo, F. M. *J. Am. Chem. Soc*. **1963**, *85*, 1549.
14. Campbell, C. D.; Rees, C. W. *J. Chem. Soc., C* **1969**, 742.
15. Kitamura, T.; Yamane, M. *J. Chem. Soc., Chem. Commun.* **1995**, 983.

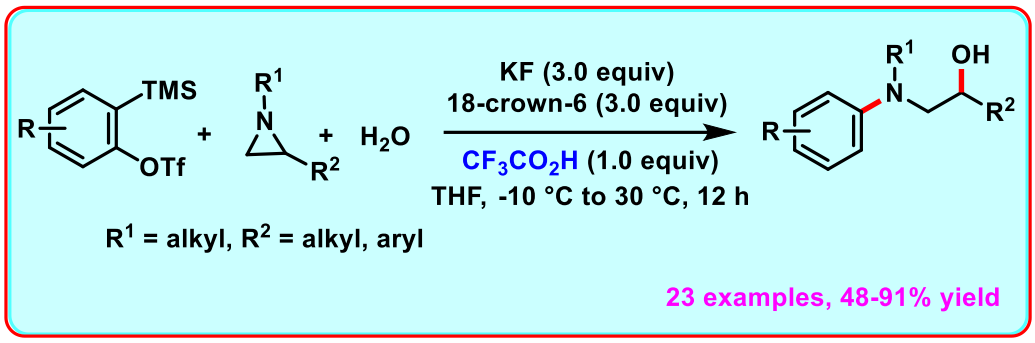
16. (a) Hoye, T. R.; Baire, B.; Niu, D.; Willoughby, P. H.; Woods, B. P. *Nature* **2012**, *490*, 208. (b) Holden (née Hall), C.; Greaney, M. F. *Angew. Chem. Int. Ed.* 2014, *53*, 5746.
17. (a) Himeshima, Y.; Sonoda, T.; Kobayashi, H. *Chem. Lett.* **1983**, 1211. For a modified procedure, see: (b) Peña, D.; Cobas, A.; Pérez, D.; Guitián, E. *Synthesis* **2002**, 1454.
18. Pellissier, H.; Santelli, M. *Tetrahedron* **2003**, *59*, 701.
19. For highlights on aryne MCCs, see: (a) Bhunia, A.; Biju, A. T. *Synlett* **2014**, 608. (b) Bhojgude, S. S.; Biju, A. T. *Angew. Chem., Int. Ed.* **2012**, *51*, 1520.
20. (a) Peña, D.; Pérez, D.; Guitián, E. *Angew. Chem., Int. Ed.* **2006**, *45*, 3579. For Account, see: (b) Yoshida, H.; Takaki, K. *Synlett*, **2012**, *23*, 1725.
21. Roy, T.; Biju, A. T. *Chem. Commun.***, 2018**, *54*, 2580.
22. Yoshida, H.; Shirakawa, E.; Honda Y.; Hiyama, T. *Angew. Chem., Int. Ed*. **2002**, *41*, 3247.
23. Liu, Z.; Larock, R. C. *J. Am. Chem. Soc.* **2005**, *127*, 13112.
24. Yoshida, H.; Minabe, T.; Ohshita, J.; Kunai, A. *Chem. Commun.* **2005**, 3454.
25. Shen, C.; Yang, G.; Zhang. W. *Org. Lett.* **2013**, *15*, 5722.
26. Hendrick, C, E.; McDonald, S, L.; Wang, Q. *Org. Lett.* **2013**, *15*, 3444.
27. Rao, B.; Zeng. X. *Org. Lett.* **2014**, *16*, 314.
28. Liu, Z.; Larock, R. C. *Org. Lett.* **2003**, *5*, 4673.
29. (a) Liu, Z.; Larock, R. C. *Org. Lett.* **2004**, *6***,** 99. (b) Liu, Z.; Larock, R. C. *J. Org. Chem.* **2006**, *71*, 3198.
30. (a) Zhao, J.; Larock, R. C. *Org. Lett.* **2005**, *7***,** 4273. (b) Zhao, J.; Larock, R. C. *J. Org. Chem.* **2007**, *72*, 583.
31. Huang, X.; Zhang, T. *J. Org. Chem.* **2010**, *75***,** 506.
32. Aithagani, S. K.; Dara, S.; Munagala, G.; Aruri, H.; Yadav, M.; Sharma, S.; Vishwakarma, R, A.; Singh, P. P. *Org. Lett*. **2015**, *17***,** 5574.
33. Bhojgude, S.; Kaichala T.; Biju, A. T. *Org. Lett*. **2013**, *15*, 5452.
34. Zhang, L; Geng, Y.; Jin, Z. *J. Org. Chem.* **2016**, *81*, 3542.
35. Cheng, B.; Wei, J.; Zu, B.; Zhao, J.; Wang, T.; Duan, X.; Wang, R.; Li, Y.; Zhai, H. *J. Org. Chem.* **2017**, *82*, 9410.

36. Aher, R. D.; Suryavanshi, G. M.; Sudalai. A. *J. Org. Chem.* **2017**, *82*, 5940.
37. Pandya, V.G.; Mhaske, S. B. *Org. Lett.* **2018**, *20*, 1483.
38. Yoshida, H.; Fukushima, H.; Ohshita, J.; Kunai, A. *J. Am. Chem. Soc.* **2006**, *128*, 11040.
39. Bhunia, A.; Roy, T.; Pachfule, P.; Rajamohanan P. R.; Biju, A. T. *Angew. Chem., Int. Ed.*, **2013**, *52*, 10040.
40. Stephens, D.; Zhang, Y.; Cormier, M.; Chavez, G.; Arman, H.; Larinov, O. V. *Chem. Commun.* **2013**, *49*, 6558.
41. Bhojgude, S. S.; Baviskar, D. B.; Gonnade R. G.; Biju, A. T. *Org. Lett.*, **2015**, *17*, 6270.
42. Okuma, K.; Kinoshita, H.; Nagahora N.; Shioji, K. *Eur. J. Org. Chem.*, **2016**, 2264.
43. Bhojgude, S. S.; Roy, T.; Gonnade R. G.; Biju, A. T. *Org. Lett*., 2016, **18**, 5424.
44. Shu, W. M.; Ma, J. R.; Zheng, K. L.; Wu, A. X. *Org. Lett.* **2016**, *18*, 196.
45. Xie, C.; Zhang, Y. *Org. Lett.* **2007**, *9*, 781.
46. Aoki, T.; Koya, S.; Yamasaki R.; Saito, S. *Org. Lett.* **2012**, *14*, 4506.
47. Varlamov, A. V.; Guranova, N.I.; Novikov, R. A.; Ilyushenkova, V. V.; Khrustalev, V. N.; Baleeva, N. S.; Borisova T. N.; Voskressensky, L. G. *RSC Adv.*, **2016**, *6*, 12642.

Chapter 2

Synthesis of *N*-Aryl β-Amino Alcohols by Trifluoroacetic Acid-Promoted Multicomponent Coupling (MCC) of Aziridines, Arynes and Water

A transition-metal-free, three-component coupling involving *N*-substituted aziridines, arynes and water promoted by trifluoroacetic acid (TFA) has been reported. The reaction furnished medicinally important *N*-aryl β-amino alcohol derivatives in moderate to good yields. In addition, the use of azetidines in this reaction afforded *N*-aryl γ-amino alcohol derivatives. The use of water as a coupling partner is accomplished in the aziridine/azetidine initiated aryne multicomponent coupling.



J. Org. Chem. **2015**, *80*, 11131

2.1. Introduction

β-Amino alcohols are an important class of compounds having numerous applications in the pharmaceutical industry.[1] They serves as versatile intermediates for many organic compounds in the synthesis of natural and synthetically originated biologically active compounds. The most common class of naturally occurring compounds containing β-amino alcohol subunit are hydroxy amino acids. β-Amino alcohol derived sphingoids or sphingoid bases are the characteristic or defining structural unit of the sphingolipids and the antifungal agent sphingofungin (Figure 2.1).[2]

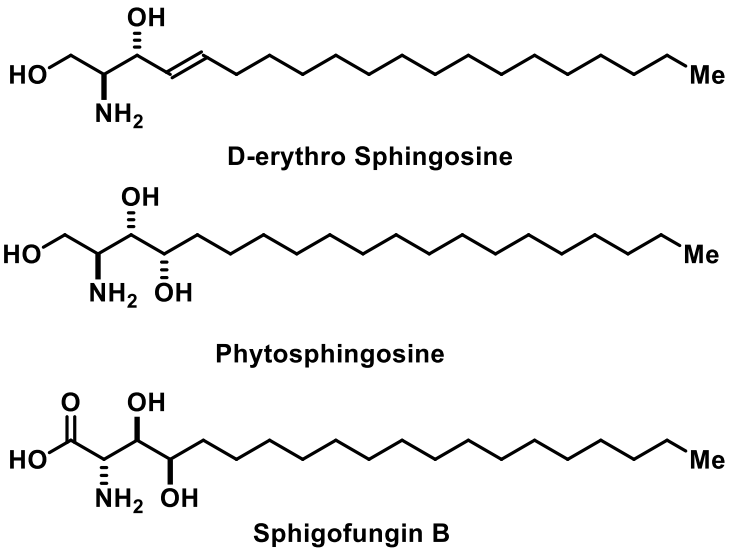


Figure 2.1. Sphingoid Bases

β-amino alcohol derivative salbutamol (**A**) is a selective β_2-receptor agonist used in the treatment of asthma (Figure 2.2).[3] Additionally, terbutaline (**B**) is used in the asthma treatment,[4] and propranolol (**C**) is used in the treatment of high blood pressure and heart diseases.[5] In addition, β-amino alcohols are used as ligands (pybox ligands **D**)[6] and also as chiral auxiliaries (Evans's auxiliary **E**) in organic synthesis.[7] They are useful for the synthesis of various N-heterocyclic carbenes (triazolium salt **F**), which are widely used for the umpolung reactivities in organocatalysis.[8] Given the importance of β-amino alcohols in drug discovery and in organic synthesis, development of practical and mild synthetic routes to this moiety is highly desirable.

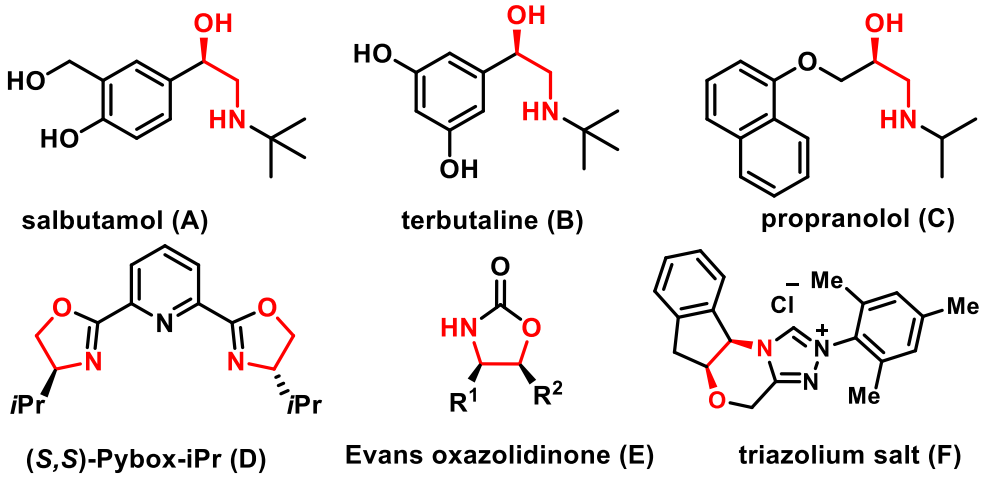
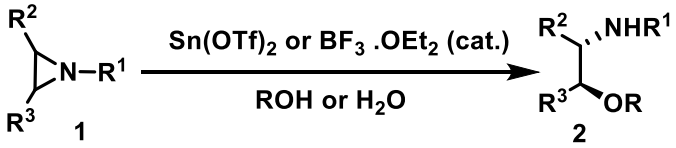


Figure 2.2. Importance of β-amino alcohol moiety

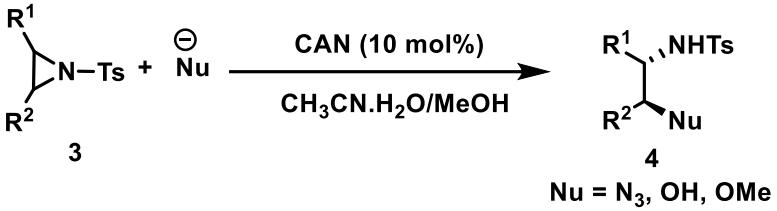
2.2. Synthesis of β-Amino Alcohols *via* Ring-Opening of Aziridines

The ring-opening of aziridines with H_2O under the protic or Lewis acid activation is one of the practical methods to access β-amino alcohols.[9] The ring-opening of both activated and non-activated aziridines with a water molecule using protic or Lewis acid catalyzed conditions is well explored for the synthesis of amino alcohols. Although the stereochemistry of the ring-opened product is *anti* in general, the regiochemistry is determined based on the reaction conditions chosen. There are other factors including steric effects and functional group effects playing key roles in governing the site of the ring-opening. The ring-opening of activated aziridines with the water as the nucleophile has been achieved using mineral acids[10] and recently using Lewis acids, such as $BF_3{\cdot}OEt_2$ and $Sn(OTf)_2$. In 2000, Singh group has demonstrated the ring-opening of a variety of *N*-activated aziridines **1** with water, primary, allylic, and propargyl alcohols at rt in high yield using a catalytic amount of $Sn(OTf)_2$ or $BF_3.OEt_2$ (Scheme 2.1).[11] The water molecule opens up the ring *anti* to the aziridine nitrogen to give *trans* aminols **2**. However, Lewis acids, such as $Cu(OTf)_2$, $CuCl_2$, $SnCl_2$, $AlCl_3$, $FeCl_3$ and $LiClO_4$ could also open up the aziridine ring but with less functional group tolerance and reduced yields.



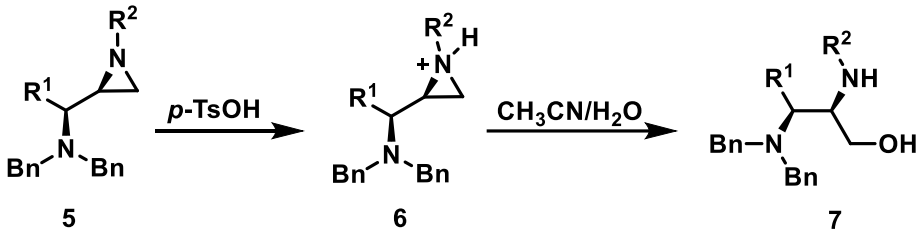
Scheme 2.1. Synthesis of β-amino alcohols using $Sn(OTf)_2$ or BF_3 .OEt_2 catalyst

In 2002, Chandrasekhar group has developed an efficient protocol for the ring-opening of *N*-tosylaziridines **3** with H_2O, MeOH and NaN_3 as nucleophiles using catalytic ceric ammonium nitrate (CAN) lading to the synthesis of vicinal amino alcohols **4**. However poor regio-chemistry was observed in water addition (Scheme 2.2).[12]



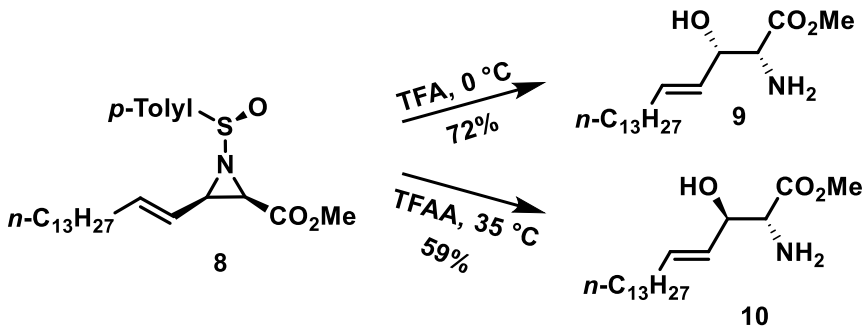
Scheme 2.2. Synthesis of β-amino alcohols using CAN catalyst

In 2003, a highly regio-selective aziridine ring-opening was demonstrated by Concellon and Riego in a stereoselective manner, obtaining the corresponding amino alcohols **7** in high yield (Scheme 2.3). Stoichiometric amount of *p*-TsOH in a mixed solvent CH_3CN/H_2O provided the addition of hydroxyl at the less hindered methylene *via* a protonated aziridinium intermediate **6**. However, a shift in the selectivity was observed when $BF_3{\cdot}OEt_2$ was used to promote the ring-opening of aziridine **5**. In this case, the reaction was carried out in CH_3CN on heating and amino alcohols were obtained in low to good yields with addition at the more hindered carbon.[13]



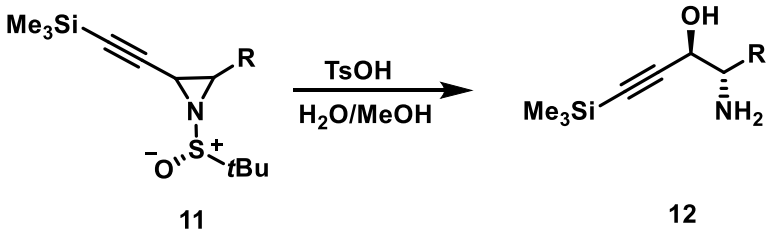
Scheme 2.3. Regioselective ring-opening of aziridines using *p*-TsOH

A switchable stereoselectivity was observed when trifluoroacetic acid (TFA) and trifluoroacetic anhydride (TFAA) was used in the ring-opening of carboxylate aziridine **8** delivering amino alcohols **9** and **10** respectively (Scheme 2.4). Opposite chirality between the ring-opened products are obtained with the tuning of the reaction conditions. Because of the competing S_N1 and S_N2 reactivities, selectivity in aziridine ring-opening largely depends on the ring substituents, the activating group on nitrogen and the reaction conditions.[14]



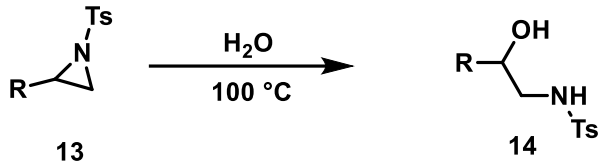
Scheme 2.4. Switchable stereoselectivity in ring-opening of aziridines

Enantiopure *trans* and *cis* 2,3-disubstituted ethynyl *N-tert*-butanesulfinylaziridines **11** were used for the regioselective ring-opening by water under acidic conditions leading to the diasteroselective synthesis of enantiopure *anti* and *syn* acetylenic α-amino alcohols **12** (Scheme 2.5). Treatment of an aqueous solution of sulfinylaziridines with TsOH delivered the amino alcohols in good yield and selectivity.[15]



Scheme 2.5. Synthesis of acetylenic α-amino alcohols

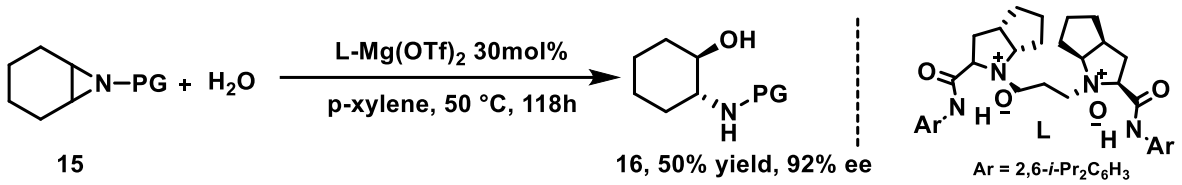
In 2007, an efficient hydrolysis of epoxides and aziridines has been developed by just heating these strained ring molecules in water (Scheme 2.6). A variety of nucleophiles including amines, sodium azide, and thiophenol could also be used in this protocol. The absence of any protic or Lewis acid catalyst make it a practical method to access amino alcohol derivatives.[16]



Scheme 2.6. Aziridine opening in hot water

In 2014, Feng group demonstrated the first direct enantioselective desymmetrization of meso-aziridines **15** with primary alcohols (Scheme 2.7). The chiral Mg(II) complex

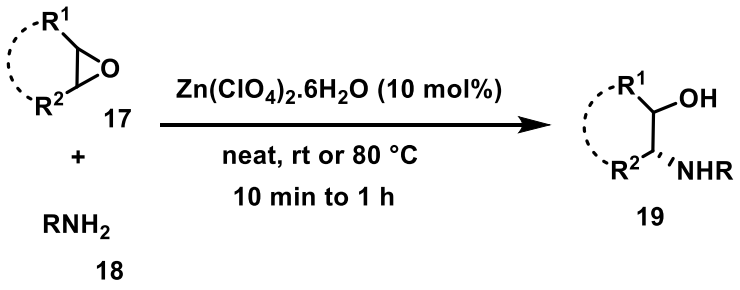
mediated the asymmetric ring-opening to generate a variety of optically active β-amino alcohols **16** in good yields (up to 96%) with excellent enantioselectivities (up to 92% ee). This catalytic system can also be applied towards the nucleophilic ring-opening of meso-aziridine with aniline and water, giving 1,2-amino alcohols and 1,2-diamines in excellent enantioselectivities, respectively.[17]



Scheme 2.7. Enantioselective desymmetrization of meso-aziridines

2.3. Synthesis of β-Amino Alcohols from Epoxides

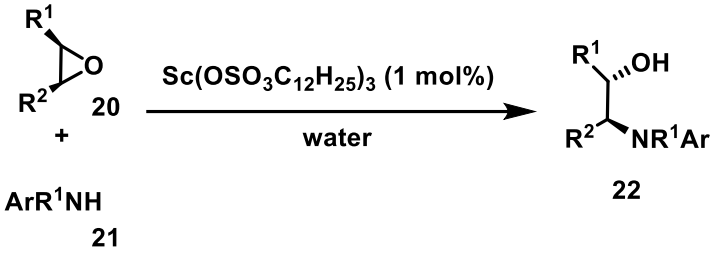
Moreover, the reaction of epoxides with anilines is a useful protocol for accessing the *N*-arylated β-amino alcohols.[18] In 2007, Chakraborti and co-workers reported the utility of the commercially available zinc(II) perchlorate hexahydrate [$Zn(ClO_4)_2 \cdot 6H_2O$] as a catalyst for opening of epoxide rings by amines affording 2-amino alcohols **19** in good yields (Scheme 2.8).[19] The reaction delivered amino alcohols with excellent chemo-, regio-, and stereoselectivities under solvent free conditions. The methodology was utilized for the synthesis of cardiovascular drugs propranolol and naftopidil as racemates and optically active enantiomers.



Scheme 2.8. Zinc-catalyzed epoxide opening

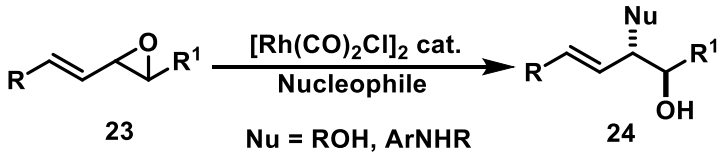
Kobayashi group has uncovered a catalytic, stereoselective addition of amines **21** to meso-epoxides **20** employing a scandium-bipyridine complex with water as the solvent (Scheme 2.9). Chiral amino alcohols **22** were prepared in good yields and

enantioselectivities in water. Low catalyst loading and the use of water as the solvent makes it a green strategy for the stereoselective synthesis of amino alcohols.[20]



Scheme 2.9. Stereoselective addition of amines to meso-epoxides

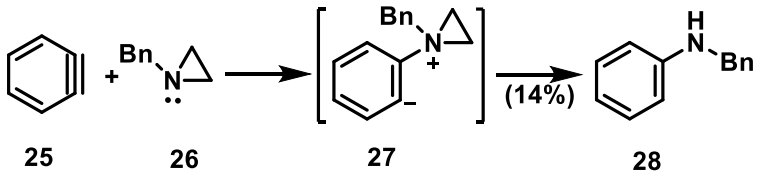
In 2000, Fagnou and Lautens developed a Rh-catalyzed aminolysis of vinyl epoxides **23** for the synthesis of *N*-aryl β-amino alcohols **24**.[21] Moreover, Job and Buchwald demonstrated the Cu-catalyzed arylation route to the synthesis of *N*-aryl β-amino alcohols (Scheme 2.10).[22]



Scheme 2.10. Synthesis of β-amino alcohols using ring-opening strategy

2.4. Statement of the Problem

Though there are several methodologies for the synthesis of valuable β-amino alcohols, the limitations associated with such as the low reactivity of anilines, use of excess reagents and high temperature, and concerns on regioselectivity urge synthetic chemists to develop new and efficient methods handling these problems. Keeping the utility of *N*-aryl β-amino alcohols in mind, a transition-metal-free synthesis of *N*-aryl β-amino alcohols using arynes[23] as the aryl source is worth to explore.



Scheme 2.11. Reaction of aziridine with aryne

Notably, the formation of a zwitterion **27** from arynes **25** and aziridines is known as early as 1972 (Scheme 2.11).[24,25] The nucleophilic addition of the aziridine **26** onto aryne

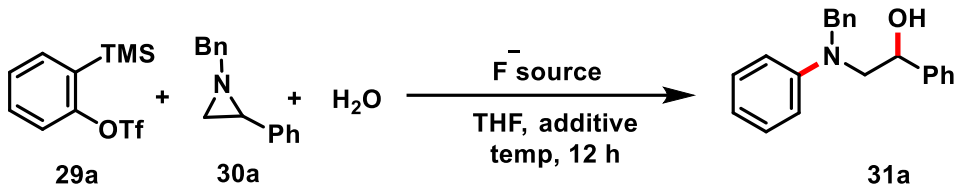
25 followed by the extrusion of a molecule of acetylene delivered arylated amine **28** in 14% yield. Moreover, the reaction of arynes with aziridines, where the solvent CH_3CN has been incorporated as the third-component has been recently disclosed by Larionov and co-workers.[26] A study on transition-metal-free, trifluoroacetic acid (TFA)-promoted three-component coupling involving arynes, aziridines and H_2O for the rapid access to *N*-aryl β-amino alcohols is presented in the following sections.[27]

2.5. Results and Discussion

2.5.1. Optimization Studies

With a view to synthesize pharmaceutically relevant β-amino alcohols, the present study was initiated by treating the aryne precursor **29a**[28] with *N*-benzyl aziridine **30a** and H_2O. When aryne was generated from **29a** using KF and 18-crown-6, the expected β-amino alcohol **31a** was formed only in 28% yield (Table 2.1, entry 1). The use of CsF as the fluoride source returned inferior results (entry 2). When CsF was substituted with tetrabutyl ammonium fluoride (TBAF), the aminoalcohol was formed in 28% yield (entry 3). However, in the case of TBAF, the reaction also furnished the α-fluoro-β-amino acid derivative recently reported by Wu and Sha in 30% yield.[29] When a reaction was carried out at -10 °C and slowly allowed to warm to room temperature over 12 hours, the expected product was formed in reduced yield (entry 4). Performing the reaction at higher temperature did not improve the yield of the product. At this stage, we considered addition of Brønsted acids as additives in this ring-opening reaction. Surprisingly, the use of 20 mol % of trifluoroacetic acid (TFA) improved the yield of **31a** to 55% (entry 6).[30] Increasing the amount of TFA to 30 mol% enhanced the yield of product **31a** (entry 7). A semi-stoichiometric amount of TFA as additive improved the yield to 64% (entry 8). Moreover, further increase in the stoichiometry of TFA has shown slight progress in the yield (entry 9). When the reaction was carried out using 1.0 equiv of TFA at -10 °C to 30 °C, the desired amino alcohol **31a** was formed in 72% yield (entry 10). Further increase in the amount of additive did not give any yield enhancement (entry 11). With the result of enhancement of yields in presence of Brønsted acid we have peformed a screening of a variety of Brønsted acids. Disappointingly, the use of other Brønsted acids such as triflic acid, *p*-toluene sulfonic acid, and methane sulfonic acid delivered only traces of the

expected product (entries 12-14). Moreover, using TFA as additive, the use of CsF and TBAF as fluoride sources were also not found to be beneficial (entries 15,16).



entry	F⁻ source	additive (mol %)	temp (°C)	yield of 31a (%)[b]
1	KF/18-crown-6	----	30	28
2[c]	CsF	----	30	13
3	TBAF	----	30	28
4	KF/18-crown-6	----	-10 to 30	10
5	KF/18-crown-6	----	60	19
6	KF/18-crown-6	TFA (20)	30	55
7	KF/18-crown-6	TFA (30)	30	60
8	KF/18-crown-6	TFA (50)	30	64
9	KF/18-crown-6	TFA (100)	30	69
10	**KF/18-crown-6**	**TFA (100)**	**-10 to 30**	**72**
11	KF/18-crown-6	TFA (200)	-10 to 30	71
12	KF/18-crown-6	TfOH(100)	-10 to 30	<5
13	KF/18-crown-6	*p*TSA·H_2O (100)	-10 to 30	<5
14	KF/18-crown-6	$MeSO_3H$ (100)	-10 to 30	<5
15[c]	CsF	TFA (100)	-10 to 30	20
16	TBAF	TFA (100)	-10 to 30	45

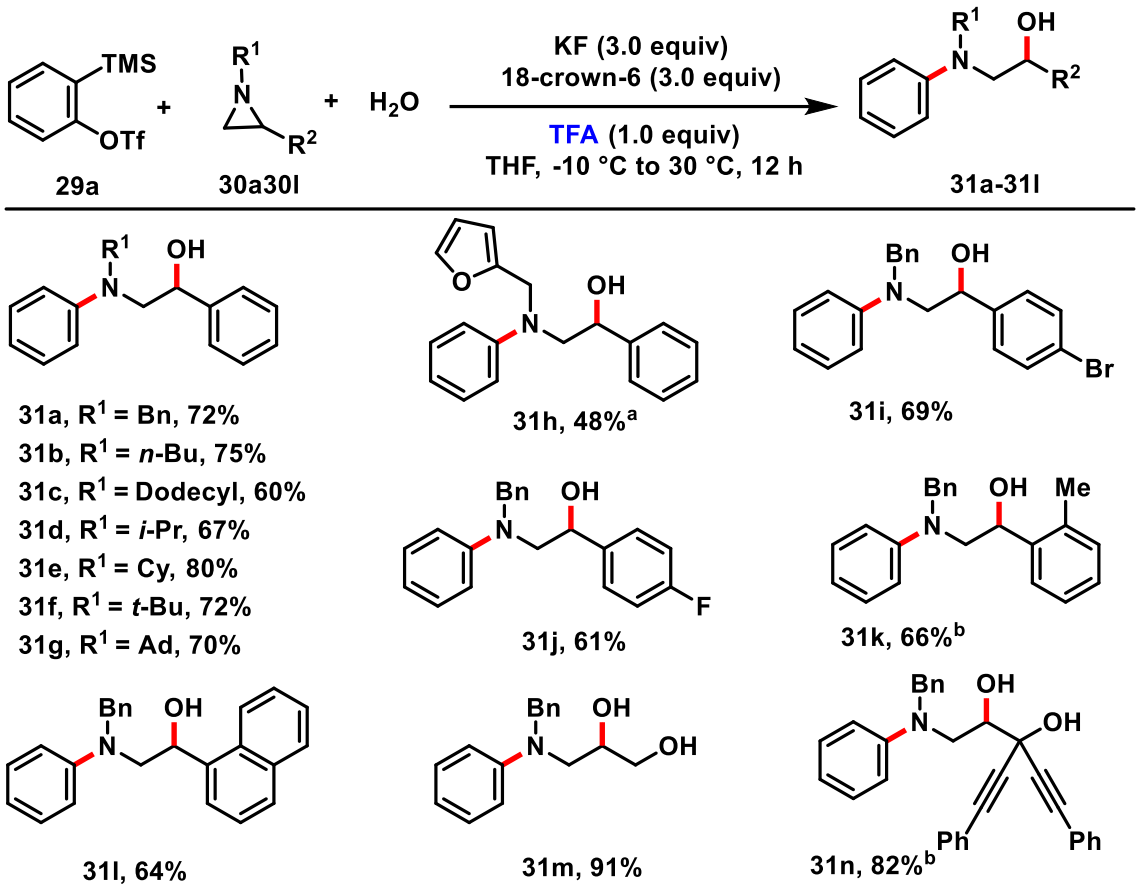
[a] Standard conditions: **29a** (0.375 mmol), **30a** (0.25 mmol), H_2O (0.5 mmol), fluoride source (3.0 equiv), THF (1.0 mL), stirred for 12 h. [b] Yield of isolated products are given. [c] The reaction performed using CH_3CN as the solvent.

Table 2.1. Optimization of the reaction conditions[a]

2.5.2. Synthesis of *N*-Aryl β-Amino Alcohols by TFA promoted MCC

After optimizing the reaction conditions for this TFA mediated multicomponent coupling (MCC), we examined the scope and limitations of this reaction. First, we evaluated the variation of aziridines (Scheme 2.12). The variation in the *N*-substituents in aziridines which includes linear, branched and even sterically demanding ones underwent

smooth coupling reaction promoted by TFA leading to the formation of the *N*-alkyl *N*-phenyl β-amino alcohol in good yields (**31a-31g**).



General conditions: **29a** (0.75 mmol), **30** (0.50 mmol), H_2O (1.0 mmol), TFA (0.50 mmol), KF (3.0 equiv), 18-crown-6 (3.0 equiv), THF (2.0 mL), -10 °C to 30 °C, 12 h. Yields of the isolated products are given. [a] Reaction was performed on 0.25 mmol scale with TBAF as fluoride source. [b] Reaction was performed on 0.25 mmol scale.

Scheme 2.12. Synthesis of *N*-aryl β-amino alcohols: Scope of aziridines.

The aziridine-derived from furfuryl amine afforded the desired product **31h** in 48% by using TBAF as the fluoride source as the cycloaddition was predominant in presence of KF as the fluoride source. The substituents at the 2-aryl moiety of aziridines did not affect the outcome of the reaction, and in all cases the expected regioselectively opened product was isolated in good yields (**31i-31l**). Furthermore, alkyl substitution at the 2-position of aziridine was well-tolerated, and the corresponding amino alcohols were isolated in excellent yields (**31m, 31n**) thus demonstrating the versatility of the present reaction. Disappointingly, *N*-phenyl aziridine, **32a,** aziridines-derived from sulfonamides **32b**, and

unprotected aziriidine **32c** were not ideal substrates for the present methodology. Disappointingly, thiirane **33** failed to deliver desired product.

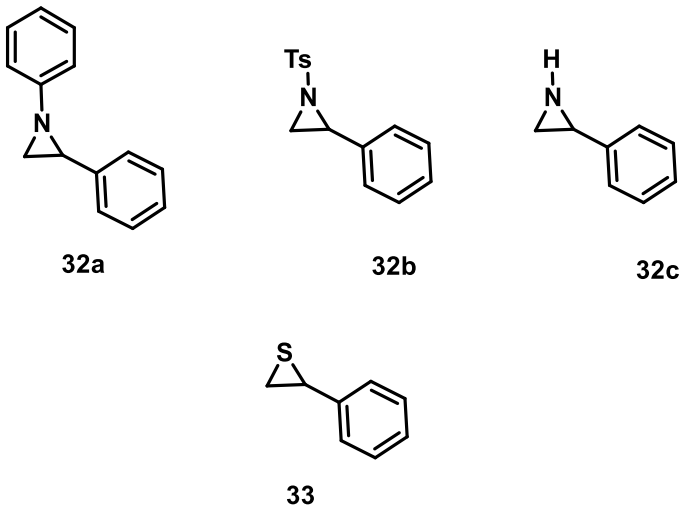
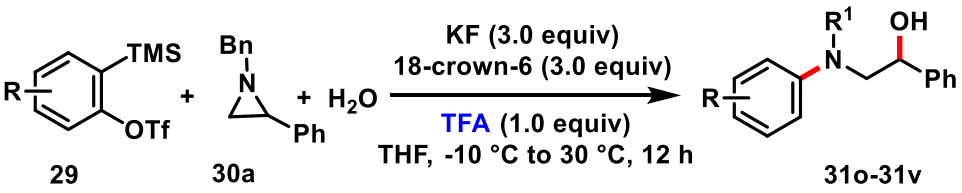
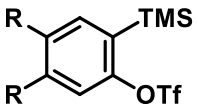
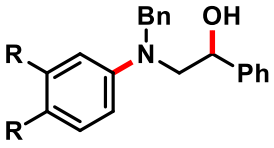
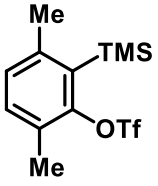
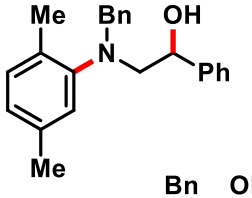
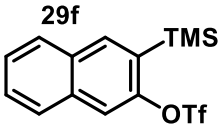
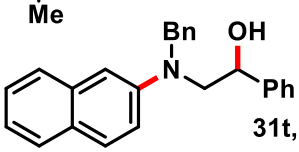
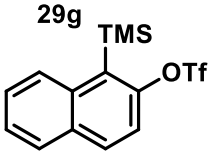
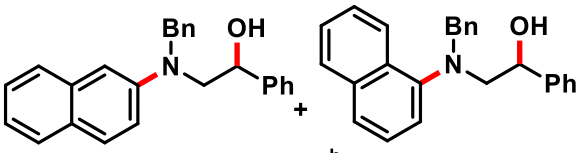
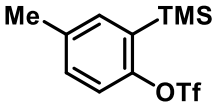
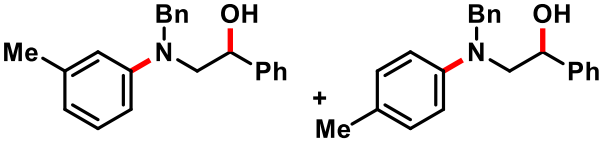
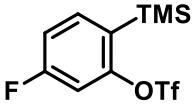
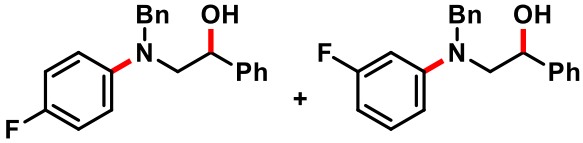


Figure 2.3. Substrates that failed to afford desired products

Inspired by these interesting results, we then examined the effect of varying the substituents on the aryne precursor (Table 2.2). To our delight, electronically dissimilar 4,5-disubstituted symmetrical arynes generated from precursors **29b**-**29e** readily afforded the *N*-aryl β-amino alcohols in good yields upon treatment with aziridine **30a** and H_2O promoted by TFA under the optimized conditions (**31o**-**31r**). In addition, 3,6-dimethyl aryne generated from **29f** and the symmetrical naphthalyne generated from **29g** resulted in the formation of the desired products in moderate yields (**31s**-**31t**). Moreover, the reaction of **30a** and H_2O with unsymmetrical aryne generated from **29h** furnished 2-naphthyl amino alcohol **31t** in 59% yield and in excellent regioselectivity of >20:1. The use of unsymmetrical 4-methyl aryne precursor **29i** in the present methodology afforded the mixture of regioisomers in 1:1 ratio and 70% yield. Similarly, the unsymmetrical 4-fluoroaryne formed from **29j** resulted in the formation of mixture of regioisomers **31v** and **31v'** in 3:1 and 65% yield, thus further expanding the scope of this aryne three-component coupling.



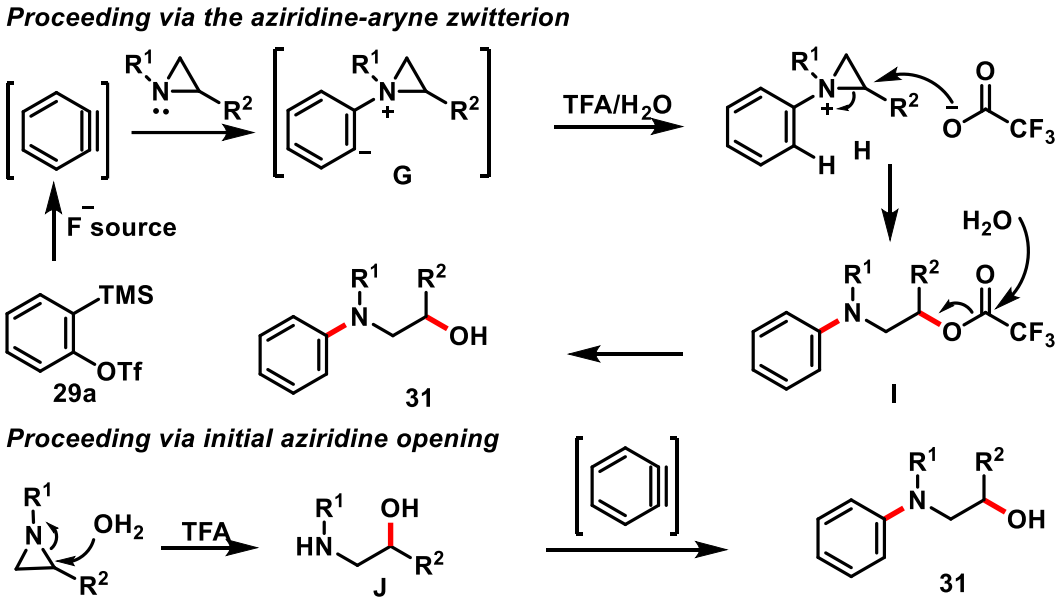
entry	aryne precursor	product(s), yield (%)
1 2 3 4	 29b-e	 31o, R = Me, (60%)[a] 31p, R = $(CH_2)_3$, (68%) 31q, R = $O(CH_2)O$, (66%) 31r, R = F, (65%)
5		 31s, (57%)
6	29f 	 31t, (57%)
7	29g  29h	 31t, (>20:1)[b], (59%) 31t'
8	 29i	 31u, (1:1)[b], (70%) 31u'
9	 29j	 31v, (3:1)[b], (65%) 31v'

General conditions: **29** (0.75 mmol), **30a** (0.50 mmol), H_2O (1.0 mmol), TFA (0.5 mmol), KF (3.0 equiv), 18-crown-6 (3.0 equiv), THF (2.0 mL), -10 °C to 30 °C, 12 h. Yields of the isolated products are given. [a] Reaction was performed on 0.25 mmol scale. [b] The regioisomer ratio was determined by ^{1}H NMR analysis of crude reaction mixture.

Table 2.2 Variation of the Aryne Moiety

2.5.3. Mechanism of Trifluoroacetic Acid-Promoted MCC

The proposed mechanism of this TFA-promoted MCC is presented in Scheme 2.13. There are two possible pathways for this reaction.

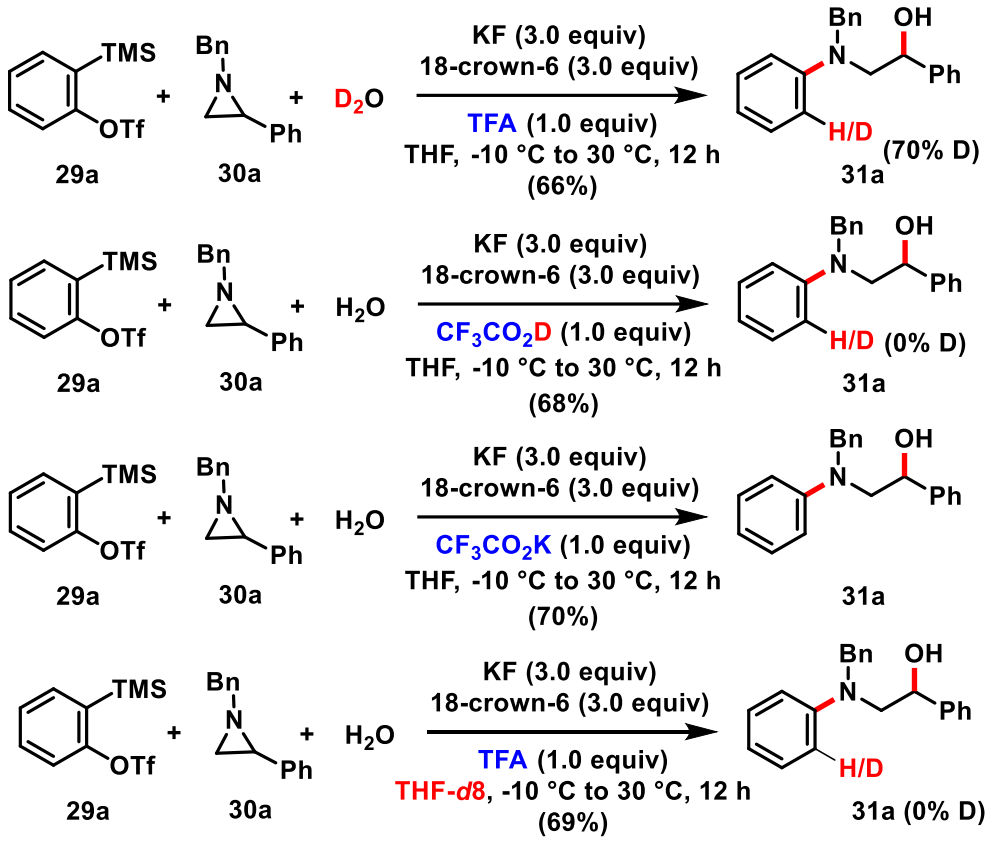


Scheme 2.13. Plausible mechanism of the reaction

The highly strained and nucleophilic aziridine can add to aryne generating the zwitterionic intermediate **G**,[31] which could possibly be protonated by TFA/H_2O to form the quaternary ammonium salt **H**. This highly strained quaternary salt is attacked by the trifluoroacetate anion (most likely proceeding via S_N2 pathway) generating the ester intermediate **I**. This ester intermediate upon hydrolysis affords the desired product **31**. The other possibility involves the aziridine opening using H_2O promoted by TFA leading to the formation of the amino alcohol **J**, which on *N*-arylation using aryne can result in the formation of **31**.[32]

Moreover, the reaction of aziridine **30a** with aryne generated from **29a** in the absence of H_2O did not afford the expected product **31a**. This also indicates the role of H_2O in the reaction. However, when the reaction mixture was exposed to air, the reaction proceeded slowly. This may be due to the moisture content in the air. When the reaction was performed under the optimized conditions in the absence of the aryne precursor **29a**, the amino alcohol **J** (Scheme 3) was not observed, and the aziridine **30a** was recovered in 80% yield. Moreover, the observation of product **31a** in 28% yield even in the absence of

TFA (Table 1, entry 1) sheds light on the initial addition of aziridines to arynes (*via* the aziridine-aryne zwitterion).



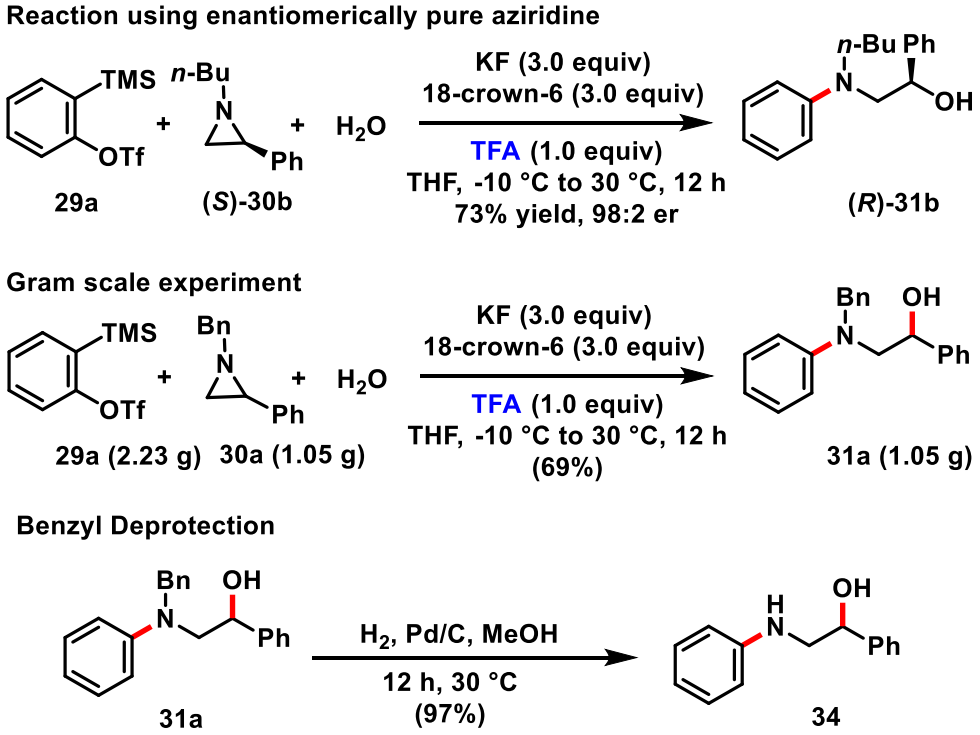
Scheme 2.14. Mechanistic experiments

Several mechanistic experiments were carried out to derive at the mechanism of this transformation. 70% D incorporation at the 2-position of the ring was observed when the reaction was performed using D_2O instead of H_2O with 66% yield of the amino alcohol product. This experiment confirms the role of H_2O in protonating the aryl anion intermediate **G** generated from aziridine and aryne (Scheme 2.14). Moreover, a reaction was carried out using TFA-*d* to get insight into the role of TFA in the protonation of aryl anion intermediate **G**, (Scheme 2.14). However, amino alcohol with 68% yield was obtained with no incorporation of D at the 2-position of the ring. This experiment rules out the possibility of protonation of the aryl anion intermediate by TFA. To find out of the role of TFA in this reaction, we have performed additional experiment using CF_3CO_2K (Scheme 2.14). Comparable yield of **31a** was obtained giving hint about the generation of CF_3CO_2K in the reaction mixture. Thus it is likely that CF_3CO_2K is formed under the reaction

conditions from TFA and KF. Performing the reaction under optimized conditions using THF-d_8 afforded **31a** in 69% yield with no deuterium incorporation ruling out the possibility of solvent protontion.

2.5.4. Stereospecific Reaction and Gram Scale Experiment

The reaction of enantiomerically pure aziridine **(*S*)-30b** with **29a** and H_2O under the optimized conditions afforded the enantiopure β-amino alcohol derivative **(*R*)-31b** in 73% yield and 98:2 er (Scheme 2.15). The formation of **(*R*)-31b** with preservation of enantiopurity and inversion of configuration rules out the possibility of S_N1 opening of the intermediate **H** (Scheme 3). When a gram scale experiment was performed to prove the practical application of the present method, 1.05 g (69%) of the desired amino alcohol product **31a** was isolated (Scheme 2.15). Debenzylation of **31a** under Pd-C conditions afforded the unprotected *N*-aryl β-amino alcohol **37** in 97% yield.

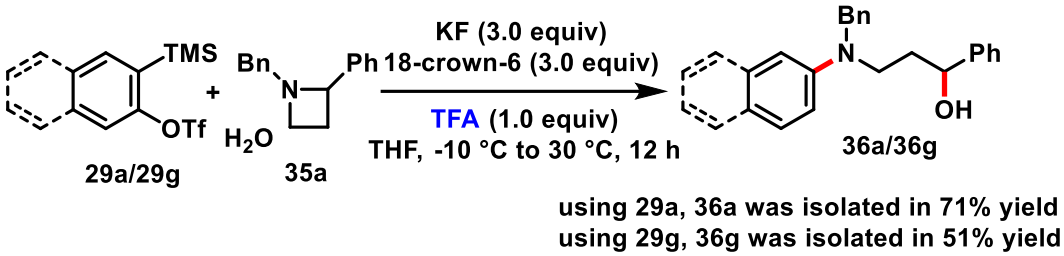


Scheme 2.15. Stereospecific reaction and gram scale experiment

2.5.5. Use of Azetidines as the Aziridine Analogues

In order to expand the utility of this protocol, azetidines were used as a substitute for aziridines with the view to synthesize γ-amino alcohols. As expected, treatment of **29a**

with 2-phenyl azetidine **35a** and H_2O in the presence of TFA and KF/18-crown-6 resulted in the formation of the *N*-phenyl γ-amino alcohol **36a** in 71% yield (Scheme 2.16). The scope of azetidine derived reaction was further expanded using symmetrical naphthalyne generated from **29g** on reaction with **35a** and H_2O afforded the desired γ-amino alcohol **36g** in 51% yield.



Scheme 2.16. Use of azetidine as the nucleophilic trigger

2.6. Conclusion

An operationally simple, transition-metal-free and mild three-component coupling involving aziridines, arynes and water promoted by TFA is discussed in detail. The reaction afforded pharmaceutically relevant *N*-aryl β-amino alcohols in moderate to good yields. Azetidines could also be used as the nucleophilic trigger in the present methodology.[36]

2.7. Experimental Details

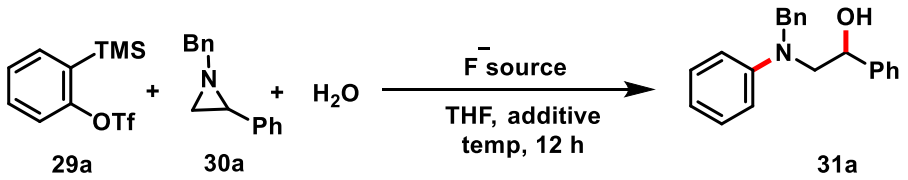
2.7.1 General Information

Unless otherwise specified, all reactions were carried out under an atmosphere of argon in flame-dried reaction vessels with Teflon screw caps. 30 °C corresponds to the room temperature of the lab when the experiments were carried out. THF was freshly purified by distillation over Na-benzophenone and was transferred under argon. 18-Crown-6 was recrystallized from dry CH_3CN and KF was dried by heating at 110 °C for 12 h and left to cool under argon and stored in argon filled glove-box. Trifluoroacetic acid and potassium trifluoroacetate were purchased from commercial sources and used as received without any further purification. All the aziridines and azetidines were prepared following the literature procedure.[33] The 2(trimethylsilyl)phenyl trifluoromethanesulfonate **29a** and the other symmetric and unsymmetric aryne precursors were synthesized following literature procedure.[34]

Analytical thin layer chromatography was performed on TLC Silica gel 60 F254. Visualization was accomplished with short wave UV light. Chromatography was performed on silica gel (230-400 mesh) by standard techniques eluting with solvents as indicated.

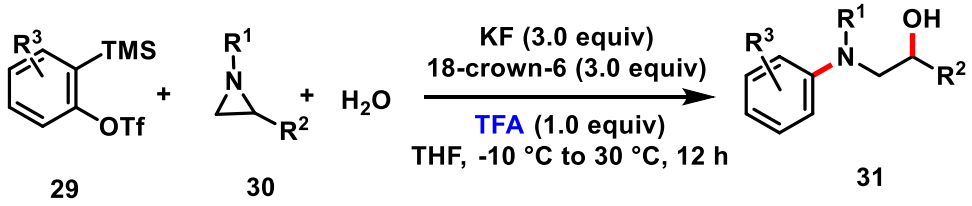
All compounds were fully characterized. ^{1}H and ^{13}C NMR spectra were recorded on Bruker AV 400, 500 in solvents as indicated. Chemical shifts (δ) are given in ppm. The residual solvent signals were used as references and the chemical shifts converted to the TMS scale ($CDCl_3$: δH = 7.26 ppm, δC = 77.16 ppm). Infrared spectra were recorded on a Bruker Alpha-E Infrared Spectrophotometer. The wave numbers (n) of recorded IR-signals are quoted in cm^{-1}. HRMS data were recorded on either Thermo Scientific Q-Exactive, Accela 1250 pump.

2.7.2. General Procedure for the Optimization of the Reaction Conditions



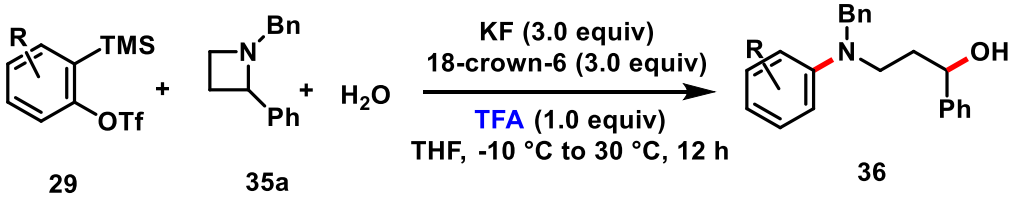
To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added the fluoride source (3.0 equiv) inside a glove-box. THF (1.0 mL) was added outside the glove-box under argon atmosphere. To this solution were added corresponding additives (1.0 equiv) and continued stirring for five minutes at 30 °C. After five minutes of stirring, 1-benzyl-2-phenylaziridine **30a** (0.105 g, 0.5 mmol, 1 equiv) was added. After attaining the indicated temperature aryne precursor **29a** (0.75 mmol, 1.5 equiv) was added. After stirring for ten minutes at this temperature, H_2O (18 μL, 2.0 equiv) was added. Then the reaction mixture was allowed to react at mentioned temperature for 12 h. After 12 h, the reaction was stopped, the solvent was evaporated and the crude residue pre-adsorbed on silica gel and purified by flash column chromatography (Pet. ether /EtOAc = 95/05) on silica gel to afford 2-(benzyl(phenyl)amino)-1-phenylethan-1-ol **31a** as yellow oil.

2.7.3. General Procedure for the TFA-Promoted Reaction of Aziridines, Arynes and H_2O



To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added the KF (87 mg, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) inside a glove-box. THF (2.0 mL) was added outside the glove-box under argon atmosphere. To this solution was added trifluoroacetic acid (0.057 g, 39 µL, 0.50 mmol) and continued stirring for five minutes at 30 °C. After five minutes of stirring, aziridine **30** (0.5 mmol) was added. Then the reaction mixture was cooled to -10 °C and aryne precursor **29** (0.75 mmol) was added. After stirring for ten minutes at -10 °C, H_2O (18 µL, 1.0 mmol) was added. Then the reaction mixture was slowly warmed to 30 °C and kept stirring for 12 h. After 12 h, the reaction was stopped, the solvent was evaporated and the crude residue pre-adsorbed on silica gel and purified by flash column chromatography (Pet. ether /EtOAc = 95/05) on silica gel to afford the corresponding 2-amino alcohols **31** in moderate to good yields.

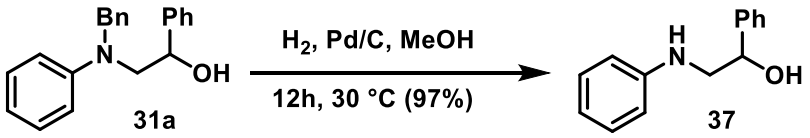
2.7.4. Procedure for the TFA-Promoted Reaction of Azetidine, Arynes and H_2O



To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added the KF (87 mg, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) inside a glove-box. THF (2.0 mL) was added outside the glove-box under argon atmosphere. To this solution was added trifluoroacetic acid (0.057 g, 39 µL, 0.50 mmol) and continued stirring for five minutes at 30 °C. After five minutes of stirring, 1-benzyl-2-phenylazetidine **35a** (0.112 g, 0.5 mmol) was added. Then the reaction mixture was cooled to -10 °C and **29** (0.75 mmol) was added. After stirring for ten minutes at -10 °C, H_2O (18 µL, 1.0 mmol) was added.

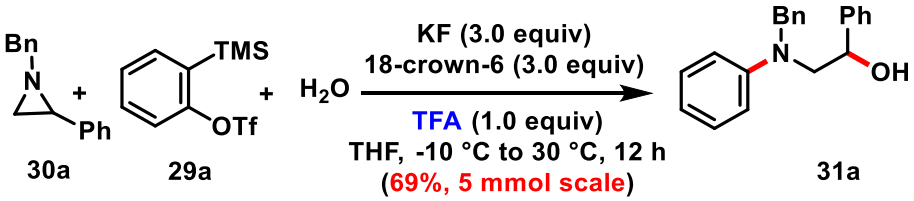
Then the reaction mixture was slowly warmed to 30 °C and kept stirring for 12 h. After 12 h, the reaction was stopped, the solvent was evaporated and the crude residue pre-adsorbed on silica gel and purified by flash column chromatography (Pet. ether /EtOAc = 93/7) on silica gel to afford the product as a yellow oil **36**.

2.7.4.1. Procedure for the Preparation of Unprotected *N*-aryl β-Amino Alcohol



An oven dried round bottomed flask was charged with 2-(benzyl(phenyl)amino)-1-phenylethan-1-ol **31a** (0.152 g, 0.50 mmol) and Pd 10% on activated carbon (20 mg, 0.03 equiv) in methanol (10 mL). The reaction mixture was continued stirring at 30 °C for 12 h under H_2 atmosphere in balloon pressure. Upon consumption of the starting material **31a,** the crude reaction mixture was passed through celite and concentrated under reduced pressure to get a sufficiently pure 1-phenyl-2-(phenylamino)ethan-1-ol **37** in 97% yield (103 mg) as yellow sticky oil.

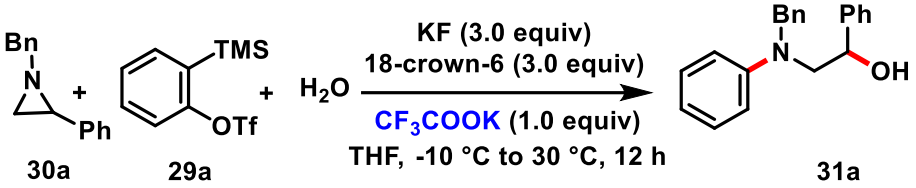
2.7.4.2. Gram Scale Synthesis of 2-(benzyl(phenyl)amino)-1-phenylethan-1-ol 31a



An oven dried round bottomed flask with a magnetic stir bar was charged with KF (0.870 g, 15.0 mmol) and 18-crown-6 (3.96 g, 15.0 mmol) inside a glove-box. THF (20 mL) was added outside the glove-box under argon atmosphere. To this solution was added trifluoroacetic acid (0.570 g, 0.390 µL, 5.0 mmol) and continued stirring for five minutes at 30 °C. After five minutes of stirring, 1-benzyl-2-phenylaziridine **30a** (1.05 g, 5.0 mmol) was added. Then the reaction mixture was cooled to -10 °C and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **29a** (2.23 g, 1.82 mL, 7.5 mmol) was added. After stirring for ten minutes at -10 °C, H_2O (180 µL, 10.0 mmol) was added. Then the reaction mixture was

slowly warmed to 30 °C and kept stirring for 12 h. After 12 h the reaction was stopped, the solvent was evaporated and the crude residue pre-adsorbed on silica gel and purified by flash column chromatography (Pet. ether /EtOAc = 95/05) on silica gel to afford the 2-(benzyl(phenyl)amino)-1-phenylethan-1-ol as yellow oil **31a** (1.05 g, 69% yield).

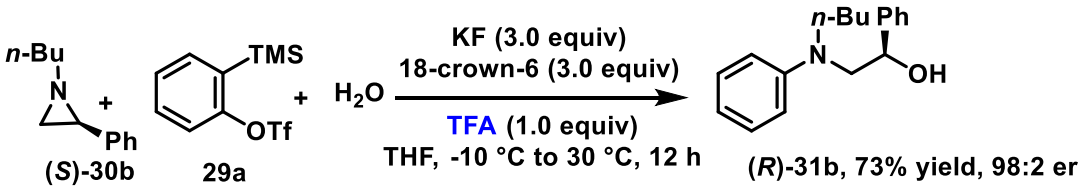
2.7.4.3. Procedure for the Potassium Trifluoroactetae Promoted Reaction of Aziridine, Aryne and H_2O



To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added the KF (87 mg, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) inside a glove-box. THF (2.0 mL) was added outside the glove-box under argon atmosphere. To this solution was added potassium trifluoroacetate (0.076 g, 0.50 mmol) and continued stirring for five minutes at 30 °C. After five minutes of stirring, 1-benzyl-2-phenylaziridine **30a** (0.105 g, 0.5 mmol) was added. Then the reaction mixture was cooled to -10 °C and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **29a** (0.223 g, 182 µL, 0.75 mmol) was added. After stirring for ten minutes at -10 °C, H_2O (18 µL, 2.0 equiv) was added. Then the reaction mixture was slowly warmed to 30 °C and kept stirring for 12 h. After 12 h, the reaction was stopped, the solvent was evaporated and the crude residue pre-adsorbed on silica gel and purified by flash column chromatography (Pet. ether /EtOAc = 95/05) on silica gel to afford the 2-(benzyl(phenyl)amino)-1-phenylethan-1-ol as yellow oil **31a** (0.106 g, 70% yield).

2.7.5. Mechanistic Experiments

2.7.5.1. Reaction using enantiopure (*S*)-1-butyl-2-phenylaziridine

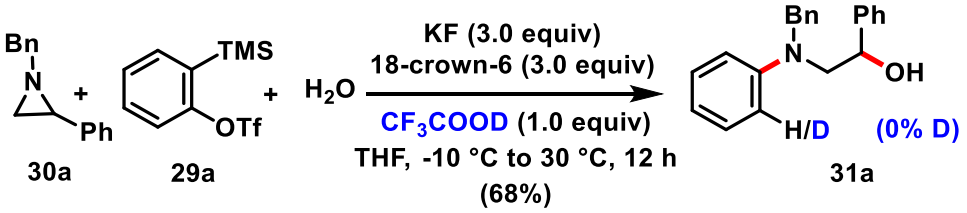


To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added the KF (87 mg, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) inside a glove-box. THF (2.0 mL) was added outside the glove-box under argon atmosphere. To this solution was added trifluoroacetic acid (0.057 g, 39 µL, 0.50 mmol) and continued stirring for five minutes at 30 °C. After five minutes of stirring, (*S*)-1-butyl-2-phenylaziridine[35] **(*S*)-30b** (0.088 g, 0.5 mmol) was added. Then the reaction mixture was cooled to -10 °C and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **29a** (0.223 g, 182 µL, 0.75 mmol) was added. After stirring for ten minutes at -10 °C, H_2O (18 µL, 2.0 eq) was added. Then the reaction mixture was slowly warmed to 30 °C and kept stirring for 12 h. After 12 h, the reaction was stopped, the solvent was evaporated and the crude residue pre-adsorbed on silica gel and purified by flash column chromatography (Pet. ether /EtOAc = 95/05) on silica gel to afford afforded (*R*)-2-(butyl(phenyl)amino)-1-phenylethan-1-ol as yellow oil ***(R)*-31b** (0.098 g, 73% yield).

*The formation of **(R)-31b** in high er rules out the possibility of S_N1 opening of intermediate* **H** (Scheme 3 of manuscript).

2.7.5.2. Deuterium Labeling Experiment

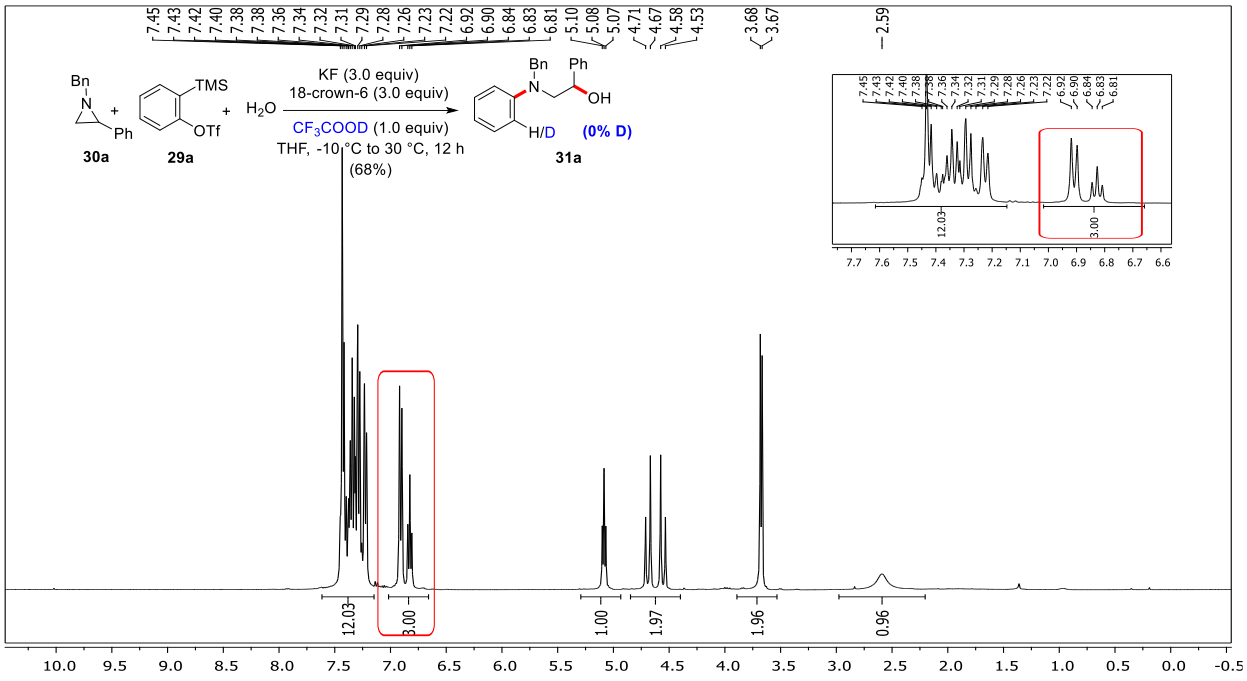
(i) Experiment using CF_3CO_2D



To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added the KF (87 mg, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) inside a glove-box. THF (2.0 mL) was added outside the glove-box under argon atmosphere. To this solution was added trifluoroacetic acid-*d* (0.058 g, 0.50 mmol) and continued stirring for five minutes at 30 °C. After five minutes of stirring, 1-benzyl-2-phenylaziridine **30a** (0.105 g, 0.5 mmol) was added. Then the reaction mixture was cooled to -10 °C and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **29a** (0.223 g, 182 µL, 0.75 mmol) was added. After stirring for ten minutes at -10 °C, H_2O (18 µL, 2.0 eq) was added. Then the reaction mixture was slowly warmed to 30 °C and kept stirring for 12 h. After 12 h, the

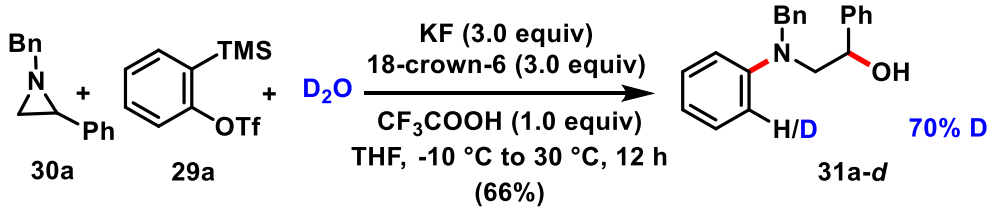
reaction was stopped, the solvent was evaporated and the crude residue pre-adsorbed on silica gel and purified by flash column chromatography (Pet. ether /EtOAc = 95/05) on silica gel to afford the 2-(benzyl(phenyl)amino)-1-phenylethan-1-ol as yellow oil **31a** (0.103 g, 68% yield) with 0% deuterium incorporation.

^{1}H NMR Spectrum, 400 MHz (Experiment using CF_3CO_2D)



The incorporation of no Deuterium in the product indicates that ***CF_3CO_2H*** *may not be involved in protonating the aryl anion intermediate H* (Scheme 3 of manuscript).

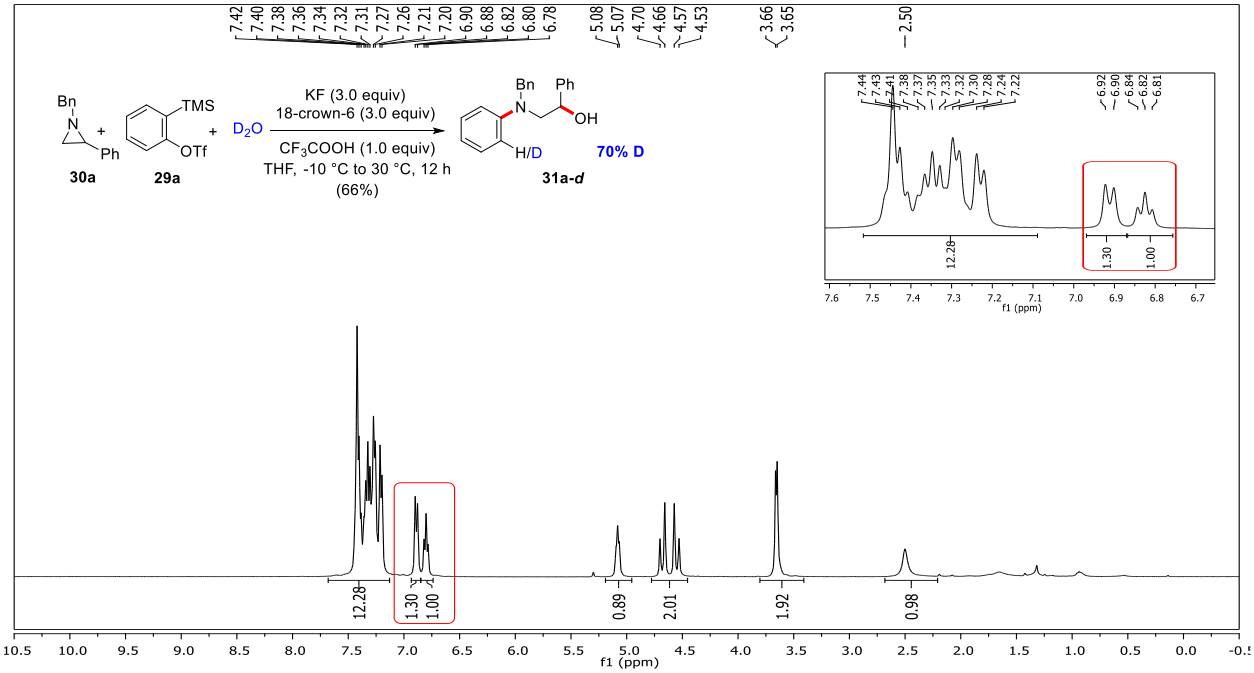
(ii) Experiment using D_2O



To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added the KF (87 mg, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) inside a glove-box. THF (2.0 mL) was added outside the glove-box under argon atmosphere. To this solution was added trifluoroacetic acid (0.057 g, 39 µL, 0.50 mmol) and continued stirring for five

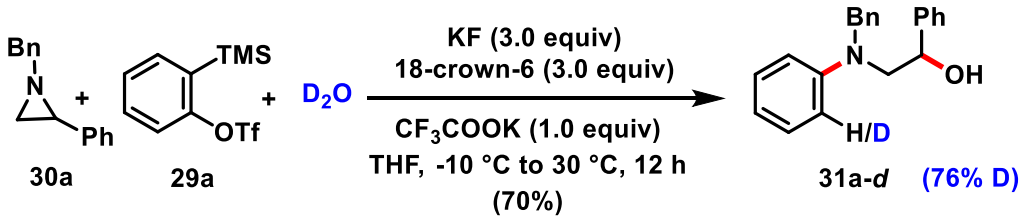
minutes at 30 °C. After five minutes of stirring, 1-benzyl-2-phenylaziridine **30a** (0.105 g, 0.5 mmol) was added. Then the reaction mixture was cooled to -10 °C and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **29a** (0.223 g, 182 µL, 0.75 mmol) was added. After stirring for ten minutes at -10 °C, D_2O (18 µL, 2.0 eq) was added. Then the reaction mixture was slowly warmed to 30 °C and kept stirring for 12 h. After 12 h the reaction was stopped, the solvent was evaporated and the crude residue pre-adsorbed on silica gel and purified by flash column chromatography (Pet. ether /EtOAc = 95/05) on silica gel to afford the 2-(benzyl(phenyl)amino)-1-phenylethan-1-ol as yellow oil **31a-*d*** (0.100 g, 66% yield) with 70% deuterium incorporation.

^{1}H NMR Spectrum, 400 MHz (Experiment using D_2O)



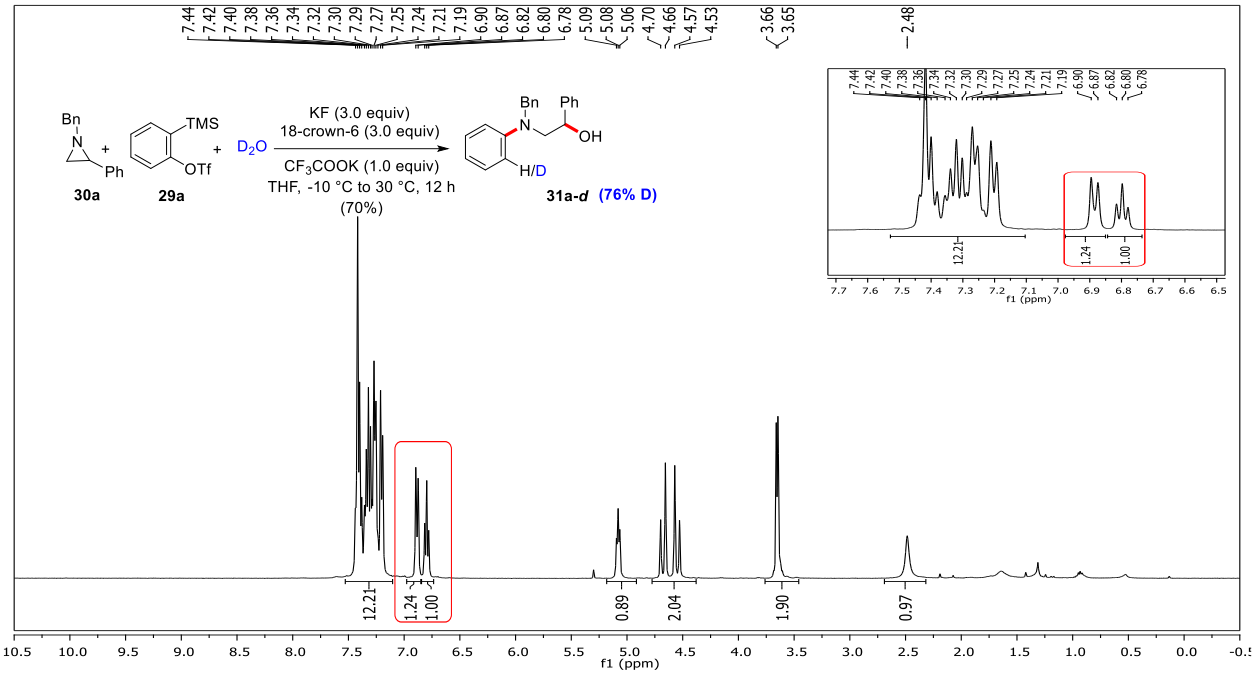
The incorporation of 70% D in the product sheds light on the role of ***H_2O*** *in protonating the aryl anion intermediate H* (Scheme 3 of manuscript).

(iii) Experiment using CF_3COOK and D_2O



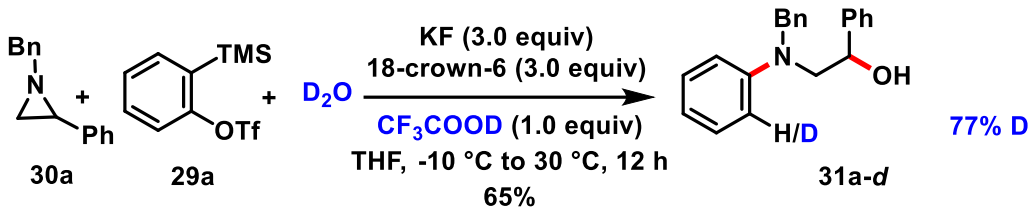
To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added the KF (87 mg, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) inside a glove-box. THF (2.0 mL) was added outside the glove-box under argon atmosphere. To this solution was added potassium trifluoroacetate (0.076 g, 0.50 mmol) and continued stirring for five minutes at 30 °C. After five minutes of stirring, 1-benzyl-2-phenylaziridine **30a** (0.105 g, 0.5 mmol) was added. Then the reaction mixture was cooled to -10 °C and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **29a** (0.223 g, 182 µL, 0.75 mmol) was added. After stirring for ten minutes at -10 °C, D_2O (18 µL, 2.0 eq) was added. Then the reaction mixture was slowly warmed to 30 °C and kept stirring for 12 h. After 12 h the reaction was stopped, the solvent was evaporated and the crude residue pre-adsorbed on silica gel and purified by flash column chromatography (Pet. ether /EtOAc = 95/05) on silica gel to afford the 2-(benzyl(phenyl)amino)-1-phenylethan-1-ol as yellow oil **31a-*d*** (0.106 g, 70% yield) with 76% deuterium incorporation.

^{1}H NMR Spectrum 400 MHz (Experiment using CF_3COOK and D_2O)



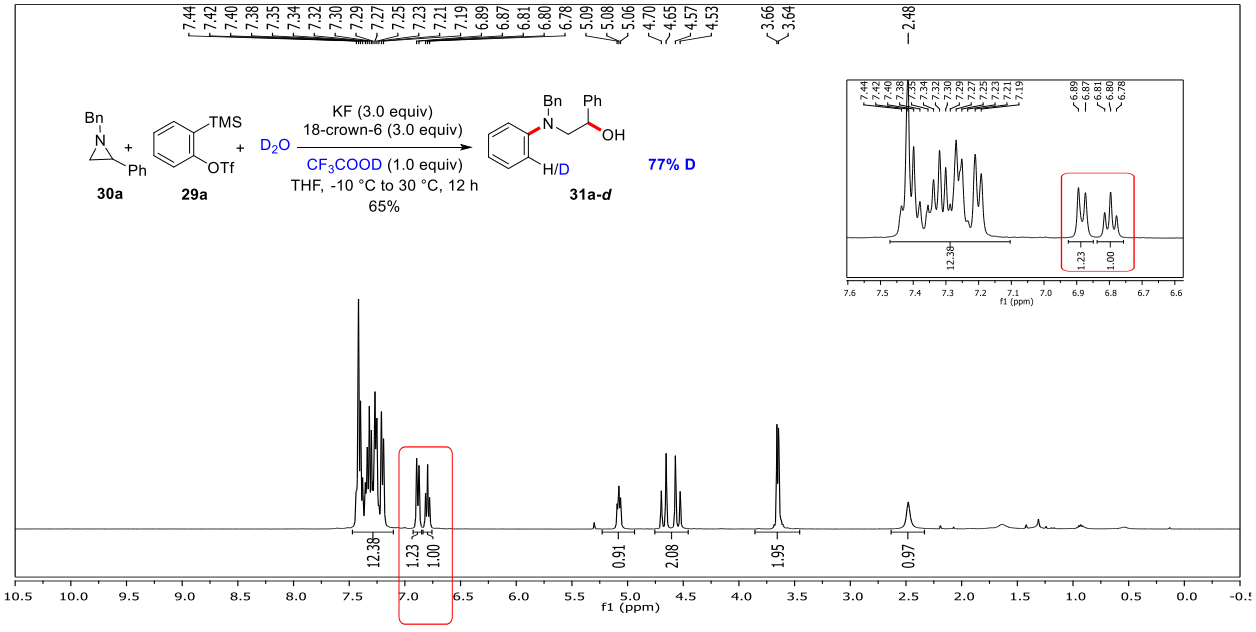
The formation of product in 70% using CF_3CO_2K indicates the generation of CF_3CO_2K under the reaction conditions from TFA and KF. Moreover 76% D incorporation sheds light on the role of water in protonating the aryl anion intermediate H.

(iv) Experiment using both CF_3CO_2D and D_2O

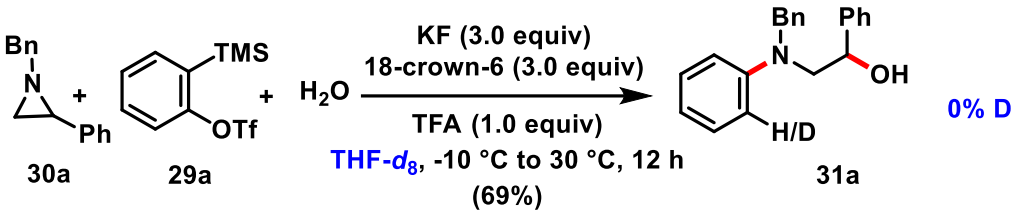


To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added the KF (87 mg, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) inside a glove -box. THF (2.0 mL) was added outside the glove-box under argon atmosphere. To this solution was added trifluoroacetic acid-*d* (0.058 g, 0.50 mmol) and continued stirring for five minutes at 30 °C. After five minutes of stirring, 1-benzyl-2-phenylaziridine **30a** (0.105 g, 0.5 mmol) was added. Then the reaction mixture was cooled to -10 °C and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **29a** (0.223 g, 182 µL, 0.75 mmol) was added. After stirring for ten minutes at -10 °C, D_2O (18 µL, 2.0 eq) was added. Then the reaction mixture was slowly warmed to 30 °C and kept stirring for 12 h. After 12 h the reaction was stopped, the solvent was evaporated and the crude residue pre-adsorbed on silica gel and purified by flash column chromatography (Pet. ether /EtOAc = 95/05) on silica gel to afford the 2-(benzyl(phenyl)amino)-1-phenylethan-1-ol as yellow oil **31a** (0.099 g, 65% yield) with 77% deuterium incorporation.

^{1}H NMR Spectrum 400 MHz (Experiment using both CF_3CO_2D and D_2O)

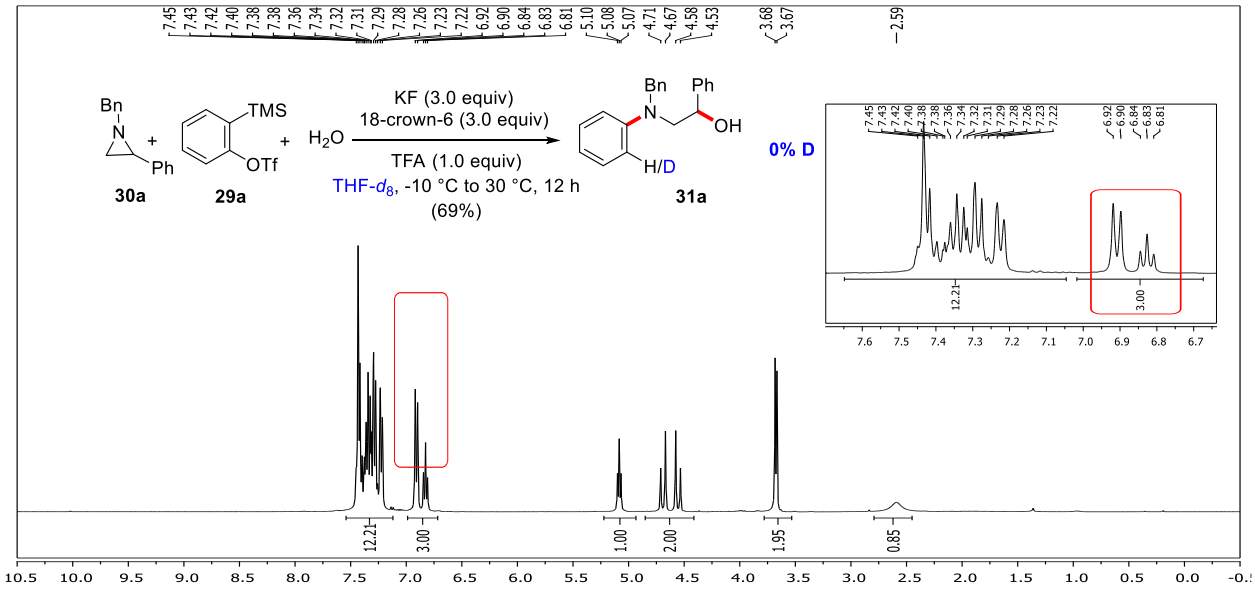


(v) Experiment using THF-d_8 as the solvent



To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added the KF (44 mg, 0.75 mmol) and 18-crown-6 (198 g, 0.75 mmol) inside a glove-box. THF-d_8 (1.0 mL) was added outside the glove-box under argon atmosphere. To this solution was added trifluoroacetic acid (0.029 g, 20 µL, 0.25 mmol) and continued stirring for five minutes at 30 °C. After five minutes of stirring, 1-benzyl-2-phenylaziridine **30a** (0.53 g, 0.25 mmol) was added. Then the reaction mixture was cooled to -10 °C and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **29a** (0.112 g, 91 µL, 0.375 mmol) was added. After stirring for ten minutes at -10 °C, H_2O (9 µL, 1.0 mmol) was added. Then the reaction mixture was slowly warmed to 30 °C and kept stirring for 12 h. After 12 h the reaction was stopped, the solvent was evaporated and the crude residue pre-adsorbed on silica gel and purified by flash column chromatography (Pet. ether /EtOAc = 95/05) on silica gel to afford the 2-(benzyl(phenyl)amino)-1-phenylethan-1-ol as yellow oil **31a-*d*** (0.52 g, 69% yield) w ith 0% deuterium incorporation.

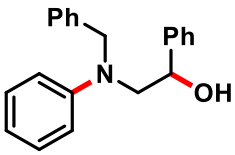
^{1}H NMR Spectrum 400 MHz (Experiment using THF-d_8 as the solvent)



This experiment indicates that solvent THF is not involved in the protonation of the aryl anion intermediate H.

2.7.6. Synthesis and Characterization of *N*-aryl β-Amino Alcohols

2-(Benzyl(phenyl)amino)-1-phenylethan-1-ol (31a)



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **30a** (0.105 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **29a** (0.223 g, 182 μL, 0.75 mmol) with trifluoroacetic acid (0.057 g, 39 μL, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol), 18-crown-6 (0.396 g, 1.5 mmol) and H_2O (18 μL, 1.0 mmol) in THF (2.0 mL) from -10 °C to 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 97/03) of the crude reaction mixture using silica gel afforded 2-(benzyl(phenyl)amino)-1-phenylethan-1-ol as yellow oil **31a** (0.109 g, 72% yield).

***R*f** (Pet. ether /EtOAc = 80/20): 0.51.

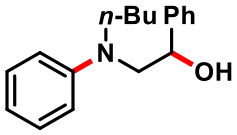
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.22 (m, 12H), 6.91 (d, *J* = 8.3 Hz, 2H), 6.83 (t, *J* = 7.2 Hz, 1H), 5.09 (t, *J* = 6.4 Hz, 1H), 4.69 (d, *J* = 17.1 Hz, 1H), 4.56 (d, *J* = 17.1 Hz, 1H), 3.68 (d, *J* = 6.4 Hz, 2H), 2.59 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 148.81, 142.16, 138.45, 129.45, 128.73, 128.68, 127.99, 126.98, 126.83, 126.03, 117.50, 113.43, 72.11, 59.81, 55.42.

HRMS (ESI) calculated $[M+H]^+$ for $C_{21}H_{22}NO$: 304.1696, found: 304.1694.

FTIR (cm^{-1}) 3339, 3055, 2912, 2352, 1687, 1600, 1501, 1460, 1355, 1267, 1110, 957, 899, 839, 705.

2-(Butyl(phenyl)amino)-1-phenylethan-1-ol (31b)



Following the general procedure, treatment of 1-butyl-2-phenylaziridine **30b** (0.088 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **29a** (0.223 g, 182 μL, 0.75 mmol) with trifluoroacetic acid (0.057 g, 39 μL, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol), 18-crown-6 (0.396 g, 1.5 mmol) and H_2O (18 μL, 1.0 mmol) in THF (2.0 mL) from -10 °C to 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 97/03) of the crude reaction mixture using silica gel afforded 2-(butyl(phenyl)amino)-1-phenylethan-1-ol as yellow oil **31b** (0.101 g, 75% yield).

***R*f** (Pet. ether /EtOAc = 90/10): 0.51.

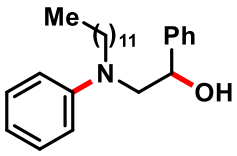
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 - 7.40 (m, 4H), 7.36 – 7.28 (m, 3H), 6.88 (d, *J* = 8.0 Hz, 2H), 6.80 (t, *J* = 7.2 Hz, 1H), 5.00 (dd, J_1 = 9.1, J_2 = 3.9 Hz, 1H), 3.54 (dd, J_1 = 14.7, J_2 = 4.0 Hz, 1H), 3.43 (dd, J_1 = 14.7, J_2 = 9.1 Hz, 1H), 3.37 – 3.31 (m, 2H), 2.59 (s, 1H), 1.62 – 1.51 (m, 2H), 1.40 – 1.31 (m, 2H), 0.95 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 148.58, 142.09, 129.46, 128.67, 127.94, 126.04, 117.41, 113.82, 71.53, 60.19, 52.34, 28.83, 20.44, 14.10.

HRMS (ESI) calculated $[M+H]^+$ for $C_{18}H_{24}NO$: 270.1852, found: 270.1863.

FTIR (cm^{-1}) 3357, 3055, 2304, 1598, 1500, 1425, 1365, 1260, 897, 741.

2-(Dodecyl(phenyl)amino)-1-phenylethan-1-ol (31c)



Following the general procedure, treatment of 1-dodecyl-2-phenylaziridine **30c** (0.144 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **29a** (0.223 g, 182 μL, 0.75 mmol) with trifluoroacetic acid (0.057 g, 39 μL, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol), 18-crown-6 (0.396 g, 1.5 mmol) and H_2O (18 μL, 1.0 mmol) in THF (2.0 mL) from -10 °C to 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 97/03) of the crude reaction mixture using silica gel afforded 2-(dodecyl(phenyl)amino)-1-phenylethan-1-ol **31c** as yellow oil (0.115 g, 60% yield).

***R*f** (Pet. ether /EtOAc = 90/10): 0.55.

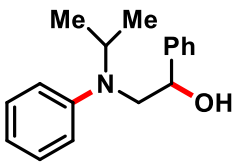
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.10 (m, 7H), 6.75 (d, *J* = 8.2 Hz, 2H), 6.67 (t, *J* = 7.2 Hz, 1H), 4.86 (dd, J_1 = 8.9 Hz, J_2 = 3.9 Hz, 1H), 3.41 (dd, J_1 = 14.7 Hz, J_2 = 4.0 Hz, 1H), 3.31 (dd, J_1 = 14.7 Hz, J_2 = 9.0 Hz, 1H), 3.24 – 3.10 (m, 2H), 2.50 (s, 1H), 1.45 (s, 2H), 1.18 (s, 18H), 0.80 (t, *J* = 6.7 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$ δ 148.55, 142.13, 129.44, 128.63, 127.89, 126.02, 117.33, 113.75, 71.52, 60.14, 52.59, 32.05, 29.76, 29.61, 29.48, 27.23, 26.66, 22.82, 14.26.

HRMS (ESI) calculated $[M+H]^+$ for $C_{26}H_{40}NO$: 396.3261, found: 396.3264.

FTIR (cm^{-1}) 3427, 3029, 2924, 2857, 1956, 1600, 1501, 1458, 1360, 1298, 1219, 1045, 762.

2-(Isopropyl(phenyl)amino)-1-phenylethan-1-ol (31d)



Following the general procedure, treatment of 1-isopropyl-2-phenylaziridine **30d** (0.081 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **29a** (0.223 g, 182 µL, 0.75 mmol) with trifluoroacetic acid (0.057 g, 39 µL, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol), 18-crown-6 (0.396 g, 1.5 mmol) and H_2O (18 µL, 1.0 mmol) in THF (2.0 mL) from -10 °C to 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 97/03) of the crude reaction mixture using silica gel afforded 2-(isopropyl(phenyl)amino)-1-phenylethan-1-ol **31d** (0.086 g, 67% yield).

***R*f** (Pet. ether /EtOAc = 90/10): 0.60.

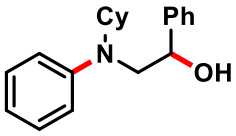
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 – 7.34 (m, 7H), 7.13 (d, *J* = 8.0 Hz, 2H), 6.98 (t, *J* = 7.2 Hz, 1H), 4.80 (dd, J_1 = 9.9 Hz, J_2 = 3.3 Hz, 1H), 3.96 (dt, J_1 = 13.2 Hz, J_2 =6.6 Hz, 1H), 3.43 (dd, J_1 = 14.2 Hz, J_2 = 3.4 Hz, 1H), 3.16 - 3.10 (m, 2H), 1.31 (d, *J* = 6.7 Hz, 3H), 1.05 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 148.88, 142.32, 129.18, 128.48, 127.69, 125.98, 120.46, 119.20, 70.29, 53.20, 53.13, 20.99, 19.07.

HRMS (ESI) calculated $[M+H]^+$ for $C_{17}H_{22}NO$: 256.1696, found: 256.1698.

FTIR (cm^{-1}) 3442, 3018, 2972, 1596, 1498, 1458, 1333, 1217, 1182, 1054, 762, 698.

2-(Cyclohexyl(phenyl)amino)-1-phenylethan-1-ol (31e)



Following the general procedure, treatment of 1-cyclohexyl-2-phenylaziridine **30e** (0.105 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **29a** (0.223 g, 182 µL, 0.75 mmol) with trifluoroacetic acid (0.057 g, 39 µL, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol), 18-crown-6 (0.396 g, 1.5 mmol) and H_2O (18 µL, 1.0 mmol) in THF (2.0 mL) from -10 °C to 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 97/03) of the crude reaction mixture using silica gel afforded 2-(cyclohexyl(phenyl)amino)-1-phenylethan-1-ol as yellow oil **31e** (0.118 g, 80% yield).

***R*f** (Pet. ether /EtOAc = 90/10): 0.60.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 - 7.32 (m, 7H), 7.12 (d, *J* = 8.0 Hz, 2H), 6.97 (t, *J* = 7.2 Hz, 1H), 4.86 - 4.69 (m, 1H), 3.60 - 3.40 (m, 2H), 3.17 (dd, J_1 = 13.9 Hz, J_1 = 10.3 Hz,

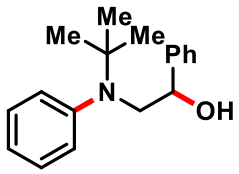
2H), 2.00 (d, *J* = 11.7 Hz, 1H), 1.91 (d, *J* = 12.4 Hz, 1H), 1.80 (d, *J* = 9.8 Hz, 2H), 1.69 (d, *J* = 11.5 Hz, 1H), 1.58 – 1.01 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 148.92, 142.30, 129.14, 128.47, 127.65, 125.97, 120.32, 119.10, 70.44, 61.97, 54.36, 31.61, 30.10, 26.23, 25.87.

HRMS (ESI) calculated $[M+H]^+$ for $C_{20}H_{26}NO$: 296.2009, found: 296.2008.

FTIR (cm^{-1}) 3440, 3018, 2933, 2858, 2404, 1951, 1596, 1497, 1453, 1395, 1338, 1273, 1046, 764.

2-(*Tert*-Butyl(phenyl)amino)-1-phenylethan-1-ol (31f)



Following the general procedure, treatment of 1-(*tert*-butyl)-2-phenylaziridine **30f** (0.088 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **29a** (0.223 g, 182 µL, 0.75 mmol) with trifluoroacetic acid (0.057 g, 39 µL, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol), 18-crown-6 (0.396 g, 1.5 mmol) and H_2O (18 µL, 1.0 mmol) in THF (2.0 mL) from -10 °C to 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 97/03) of the crude reaction mixture using silica gel afforded 2-(*tert*-butyl(phenyl)amino)-1-phenylethan-1-ol as yellow oil **31f** (0.097 g, 72 % yield).

***R*$_f$** (Pet. ether /EtOAc = 90/10): 0.45

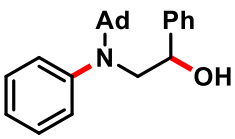
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.28 (m, 10H), 4.22 (d, *J* = 10.5 Hz,1H), 4.15 (s, 1H), 3.36 (d, *J* = 12.6 Hz, 1H), 3.09 (t, *J* = 11.7 Hz, 1H), 1.20 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 147.26, 142.38, 129.81, 128.73, 128.31, 127.42, 126.25, 126.01, 69.82, 57.62, 55.73, 28.53.

HRMS (ESI) calculated $[M+H]^+$ for $C_{18}H_{24}NO$: 270.1852, found: 270.1865.

FTIR (cm^{-1}) 3439, 3018, 2974, 2871, 1594, 1486, 1459, 1399, 1361, 1331, 1267, 1208, 1090, 1061, 927, 761, 706.

2-(Adamantan-1-yl)(phenyl)amino)-1-phenylethan-1-ol (31g)



Following the general procedure, treatment of 1-(adamantan-1-yl)-2-phenylaziridine **30g** (0.127 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **29a** (0.223 g, 182 µL, 0.75 mmol) with trifluoroacetic acid (0.057 g, 39 µL, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol), 18-crown-6 (0.396 g, 1.5 mmol) and H_2O (18 µL, 1.0 mmol) in THF (2.0 mL)

from -10 °C to 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 97/03) of the crude reaction mixture using silica gel afforded 2-(adamantan-1-yl)(phenyl)amino)-1-phenylethan-1-ol as yellow solid **31g** (0.122 g, 70% yield).

***R*f** (Pet. ether /EtOAc = 90/10): 0.54.

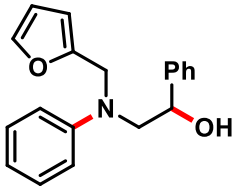
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-– 7.24 (m, 10H), 4.15 (dd, J_1 = 10.6, J_2 = 3.1 Hz, 2H), 3.28 (dd, J_1 = 12.9, J_2 = 3.1 Hz, 1H), 3.09 (dd, J_1 = 12.8, J_2 = 10.7 Hz, 1H), 2.07 (s, 3H), 1.86 (d, J = 10.9 Hz, 3H), 1.62 (d, J = 12.1 Hz, 3H), 1.54 (d, J = 11.8 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 146.55, 142.54, 130.34, 128.68, 128.34, 127.43, 126.25, 126.04, 69.76, 56.02, 55.69, 41.48, 36.56, 29.87.

HRMS (ESI) calculated $[M+H]^+$ for $C_{24}H_{30}NO$: 348.2322, found: 348.2328.

FTIR (cm^{-1}) 3432, 3017, 2920, 2855, 1593, 1490, 1319, 1214, 1117, 1901, 765, 705.

2-((Furan-2-ylmethyl)(phenyl)amino)-1-phenylethan-1-ol (31h)



Following the general procedure, treatment of 1-(furan-2-ylmethyl)-2-phenylaziridine **30h** (0.050 g, 0.25 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **29a** (0.112 g, 91 μL, 0.375 mmol) with trifluoroacetic acid (0.028 g, 18 μL, 0.25 mmol) in the presence of TBAF.3H_2O (3.0 equiv) and H_2O (9 μL, 0.5 mmol) in THF (1.0 mL) from -10 °C to 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 97/03) of the crude reaction mixture using silica gel afforded 2-((furan-2-ylmethyl)(phenyl)amino)-1-phenylethan-1-ol as yellow oil **31h** (0.035 g, 48% yield).

***R*f** (Pet. ether /EtOAc = 90/10): 0.44.

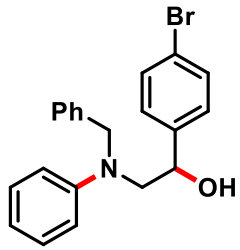
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.21 (m, 6H), 7.21 – 7.16 (m, 2H), 6.87 (d, J = 8.1 Hz, 2H), 6.73 (t, J = 7.3 Hz, 1H), 6.21 (dd, J_1 = 3.0 Hz, J_2 = 1.9 Hz, 1H), 6.07 (d, J = 2.8 Hz, 1H), 4.90 (dd, J_1 = 9.1 Hz, J_1 = 3.7 Hz, 1H), 4.41 (q, J = 16.7 Hz, 2H), 3.54 – 3.39 (m, 2H), 2.68 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 152.16, 148.77, 142.12, 141.89, 129.38, 128.69, 127.97, 126.04, 118.37, 114.27, 110.45, 107.80, 71.90, 60.25, 49.38.

HRMS (ESI) calculated $[M+H]^+$ for $C_{19}H_{20}NO_2$: 294.1489, found: 294.1490.

FTIR (cm^{-1}) 3386, 3020, 2926, 2400, 1599, 1505, 1216, 1044, 929, 877, 772.

2-(Benzyl(phenyl)amino)-1-(4-bromophenyl)ethan-1-ol (31i)



Following the general procedure, treatment of 1-benzyl-2-(4-bromophenyl)aziridines **30i** (0.144 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **29a** (0.223 g, 182 µL, 0.75 mmol) with trifluoroacetic acid (0.057 g, 39 µL, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol), 18-crown-6 (0.396 g, 1.5 mmol) and H_2O (18 µL, 1.0 mmol) in THF (2.0 mL) from -10 °C to 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 97/03) of the crude reaction mixture using silica gel afforded 2-(benzyl(phenyl)amino)-1-(4-bromophenyl)ethan-1-ol as yellow solid **31i** (0.132 g, 69% yield).

***R*f** (Pet. ether /EtOAc = 90/10): 0.59.

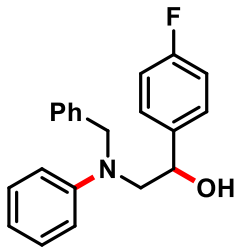
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.2 Hz, 2H), 7.32 – 7.18 (m, 9H), 6.89 – 6.80 (m, 3H), 5.00 (t, *J* = 6.5 Hz , 1H), 4.65 (d, *J* = 17.0 Hz, 1H), 4.53 (d, *J* = 17.0 Hz, 1H), 3.60 – 3.58 (m, 2H), 2.58 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 148.68, 141.05, 138.20, 131.73, 129.49, 128.76, 127.73, 127.07, 126.84, 121.73, 117.80, 113.58, 71.37, 59.68, 55.56.

HRMS (ESI) calculated $[M+H]^+$ for $C_{21}H_{21}NOBr$: 382.0801, found: 382.0804.

FTIR (cm^{-1}) 3440, 3018, 2926, 2404, 1599, 1500, 1453, 1216, 1037, 950, 764.

2-(Benzyl(phenyl)amino)-1-(4-fluorophenyl)ethan-1-ol (31j)



Following the general procedure, treatment of 1-benzyl-2-(4-fluorophenyl)aziridine **30j** (0.114 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **29a** (0.223 g, 182 µL, 0.75 mmol) with trifluoroacetic acid (0.057 g, 39 µL, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol), 18-crown-6 (0.396 g, 1.5 mmol) and H_2O (18 µL, 1.0 mmol) in THF (2.0 mL) from -10 °C to 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 97/03) of the crude reaction mixture using silica gel afforded 2-(benzyl(phenyl)amino)-1-(4-fluorophenyl)ethan-1-ol as yellow oil **31j** (0.098 g, 61% yield).

***R*f** (Pet. ether /EtOAc = 90/10): 0.45.

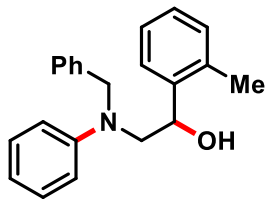
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.15 (m, 9H), 7.07 (t, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 8.5 Hz, 2H), 6.81 (t, *J* = 7.3 Hz, 1H), 5.04 (t, *J* = 6.5 Hz, 1H), 4.65 (d, *J* = 17.0 Hz, 1H), 4.53 (d, *J* = 17.1 Hz, 1H), 3.61 (d, *J* = 6.5 Hz, 2H), 2.55 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 163.71, 161.27, 148.76, 138.30, 137.85, 137.82, 129.48, 128.77, 127.73, 127.65, 127.06, 126.84, 117.71, 115.63, 115.42, 113.53, 71.40, 59.83, 55.50.

HRMS (ESI) calculated $[M+H]^+$ for $C_{21}H_{21}FNO$: 322.1602, found: 322.1617.

FTIR (cm^{-1}) 3431, 3018, 2920, 2404, 1600, 1504, 1356, 1222, 1067, 953, 838, 762, 698.

2-(Benzyl(phenyl)amino)-1-(o-tolyl)ethan-1-ol (31k)



Following the general procedure, treatment of 1-benzyl-2-(o-tolyl)aziridine **30k** (0.066 g, 0.25 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **29a** (0.112 g, 91 µL, 0.375 mmol) with trifluoroacetic acid (0.029 g, 20 µL, 0.25 mmol) in the presence of KF (0.044 g, 0.75 mmol), 18-crown-6 (0.198 g, 0.75 mmol) and H_2O (9 µL, 0.5 mmol) in THF (1.0 mL) from -10 °C to 30 °C rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 97/03) of the crude reaction mixture using silica gel afforded 2-(benzyl(phenyl)amino)-1-(o-tolyl)ethan-1-ol as yellow oil **31k** (0.052 g, 66% yield).

***R*$_f$** (Pet. ether /EtOAc = 90/10): 0.48.

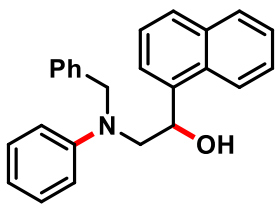
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.5 Hz, 1H), 7.37 – 7.19 (m, 10H), 6.95 (d, *J* = 8.0 Hz, 2H), 6.83 (t, *J* = 7.3 Hz, 1H), 5.34 (dd, J_1 = 7.7, J_2 = 5.1 Hz, 1H), 4.70 (d, *J* = 17.0 Hz, 1H), 4.60 (d, *J* = 17.0 Hz, 1H), 3.67-3.65 (m, 2H), 2.47 (s, 1H), 2.36 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 149.04, 140.22, 138.40, 134.74, 130.51, 129.44, 128.74, 127.70, 127.03, 126.89, 126.60, 125.87, 117.66, 113.57, 77.48, 77.16, 76.84, 68.60, 58.52, 55.29, 19.38. **HRMS (ESI)** calculated $[M+H]^+$ for $C_{22}H_{23}NO$: 318.1852, found: 318.1867.

FTIR (cm^{-1}) 3552, 3018, 2935, 2406, 1599, 1500, 1453, 1357, 1297, 1217, 1118, 1037, 763.

2-(Benzyl(phenyl)amino)-1-(naphthalen-1-yl)ethan-1-ol (31l)

Following the general procedure, treatment of 1-benzyl-2-(naphthalen-1-yl)aziridine **30l** (0.130 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **29a** (0.223 g,



182 μL, 0.75 mmol) with trifluoroacetic acid (0.057 g, 39 μL, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol), 18-crown-6 (0.396 g, 1.5 mmol) and H_2O (18 μL, 1.0 mmol) in THF (2.0 mL) from -10 °C to 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 97/03) of the crude reaction mixture using silica gel afforded 2-(benzyl(phenyl)amino)-1-(naphthalen-1-yl)ethan-1-ol as yellow oil **31l** (0.112 g, 64% yield).

***R*f** (Pet. ether /EtOAc = 90/10): 0.50.

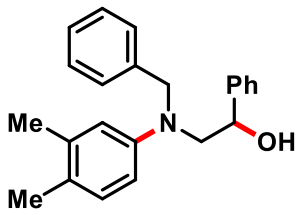
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.7 Hz, 1H), 7.93 – 7.90 (m, 1H), 7.84 (d, *J* = 8.2 Hz, 1H), 7.77 (d, *J* = 7.1 Hz, 1H), 7.54 – 7.48 (m, 3H), 7.35 – 7.20 (m, 7H), 6.97 (d, *J* = 8.1 Hz, 2H), 6.84 (t, *J* = 7.2 Hz, 1H), 5.79 (dd, *J* = 8.1, 4.4 Hz, 1H), 4.67 (d, *J* = 16.9 Hz, 1H), 4.59 (d, *J* = 16.9 Hz, 1H), 3.88 - 3.78 (m, 2H), 2.65 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 149.08, 138.46, 137.95, 130.62, 129.48, 129.07, 128.75, 128.39, 127.06, 127.01, 126.24, 125.70, 123.78, 123.07, 117.79, 113.85, 69.43, 58.87, 55.50.

HRMS (ESI) calculated $[M+H]^+$ for $C_{25}H_{24}NO$: 354.1852, found: 354.1870.

FTIR (cm^{-1}) 3554, 3062, 2924, 1598, 1504, 1452, 1390, 1217, 1167, 1092, 1029, 956, 758.

2-(Benzyl(3,4-dimethylphenyl)amino)-1-phenylethan-1-ol (31m)



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **30a** (0.053 g, 0.25 mmol) and 4,5-dimethyl-2-(trimethylsilyl)phenyl trifluoromethanesulfonate **29b** (0.122 g, 0.375 mmol) with trifluoroacetic acid (0.029 g, 20 μL, 0.25 mmol) in the presence of KF (0.044 g, 0.75 mmol), 18-crown-6 (0.198 g, 0.75 mmol) and H_2O (9 μL, 0.5 mmol) in THF (1.0 mL) from -10 °C to 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 97/03) of the crude reaction mixture using silica gel afforded 2-(benzyl(3,4-dimethylphenyl)amino)-1-phenylethan-1-ol as yellow oil **31m** (0.050 g, 60% yield).

***R*f** (Pet. ether /EtOAc = 90/10): 0.45.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.38 (m, 10H), 7.04 (d, *J* = 8.3 Hz, 1H), 6.76 (s, 1H), 6.68 (dd, J_1 = 8.2 Hz, J_2 = 2.3 Hz, 1H), 5.04 (dd, J_1 = 8.5 Hz, J_2 = 4.3 Hz, 1H), 4.57

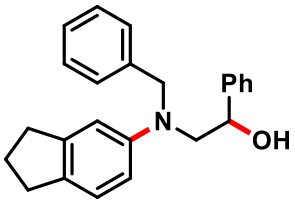
(dd, J_1 = 45.7 Hz, J_2 = 16.8 Hz, 2H), 3.59 (qd, J_1 = 14.8 Hz, J_2 = 6.5 Hz, 2H), 2.61 (s, 1H), 2.27 (s, 3H), 2.23 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 147.20, 142.15, 138.70, 137.42, 130.46, 128.64, 128.58, 127.84, 127.02, 126.90, 125.98, 115.70, 111.65, 71.82, 59.99, 55.83, 20.49, 18.70.

HRMS (ESI) calculated $[M+H]^+$ for $C_{23}H_{26}NO$: 332.2009, found: 332.2006.

FTIR (cm^{-1}) 3445, 3018, 2927, 2405, 1955, 1878, 1611, 1569, 1507, 1452, 1217, 1026, 767.

2-(Benzyl(2,3-dihydro-1*H*-inden-5-yl)amino)-1-phenylethan-1-ol (31n)



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **30a** (0.105 g, 0.5 mmol) and 6-(trimethylsilyl)-2,3-dihydro-1*H*-inden-5-yl trifluoromethanesulfonate **29c** (0.254 g, 0.75 mmol) with trifluoroacetic acid (0.057 g, 39 μL, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol), 18-crown-6 (0.396 g, 1.5 mmol) and H_2O (18 μL, 1.0 mmol) in THF (2.0 mL) from -10 °C to 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 97/03) of the crude reaction mixture using silica gel afforded 2-(benzyl(2,3-dihydro-1*H*-inden-5-yl)amino)-1-phenylethan-1-ol **31n** (0.091 g, 68% yield).

***R*$_f$** (Pet. ether /EtOAc = 90/10): 0.50.

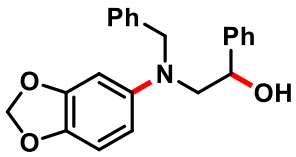
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.43 - 7.38 (m, 4H), 7.33 (t, J = 7.51 Hz, 3H), 7.28 – 7.22 (m, 3H), 7.13 (d, J = 8.2 Hz, 1H), 6.85 (s, 1H), 6.73 (dd, J_1 = 8.2 Hz, J_2 = 1.8 Hz, 1H), 5.04 (dd, J_1 = 8.5 Hz, J_2 = 4.3 Hz, 1H), 4.64 (d, J = 16.8 Hz, 1H), 4.52 (d, J = 16.8 Hz, 1H), 3.59 (qd, J_1 = 14.7 Hz, J_2 = 6.5 Hz, 2H), 2.89 (dd, J_1 = 16.7 Hz, J_2 = 7.7 Hz, 4H), 2.63 (s, 1H), 2.10 (p, J = 7.4 Hz, 2H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 147.95, 145.69, 142.16, 138.69, 133.81, 128.68, 128.61, 127.88, 127.07, 126.94, 126.04, 124.91, 112.53, 110.50, 71.82, 60.31, 56.17, 33.48, 32.01, 25.81.

HRMS (ESI) calculated $[M+H]^+$ for $C_{24}H_{26}NO$: 344.2009, found: 344.2010.

FTIR (cm^{-1}) 3425, 3063, 3012, 2950, 2868, 2845, 1615, 1573, 1498, 1452, 1385, 1356, 1322, 1217, 1169, 1060, 799, 773.

2-(Benzo[*d*][1,3]dioxol-5-yl(benzyl)amino)-1-phenylethan-1-ol (31o)



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **30a** (0.105 g, 0.5 mmol) and 6-(trimethylsilyl)benzo[d][1,3]dioxol-5-yl trifluoromethanesulfonate **29d** (0.257 g, 0.75 mmol) with trifluoroacetic acid (0.057 g, 39 µL, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol), 18-crown-6 (0.396 g, 1.5 mmol) and H_2O (18 µL, 1.0 mmol) in THF (2.0 mL) from -10 °C to 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 97/03) of the crude reaction mixture using silica gel afforded 2-(benzo[*d*][1,3]dioxol-5-yl(benzyl)amino)-1-phenylethan-1-ol as yellow oil **31o** (0.114 g, 66% yield).

***R*f** (Pet. ether /EtOAc = 90/10): 0.46.

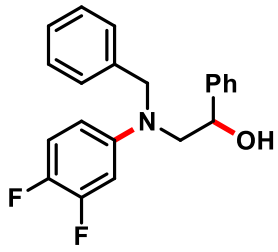
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 4.3 Hz, 4H), 7.36 – 7.24 (m, 4H), 7.21 (d, *J* = 7.1 Hz, 2H), 6.73 (d, *J* = 8.5 Hz, 1H), 6.57 (d, *J* = 2.4 Hz, 1H), 6.35 (dd, *J* = 8.5, 2.5 Hz, 1H), 5.89 (d, *J* = 0.9 Hz, 2H), 4.96 (dd, *J* = 8.8, 4.2 Hz, 1H), 4.53 (d, *J* = 16.4 Hz, 1H), 4.43 (d, *J* = 16.4 Hz, 1H), 3.54 - 3.42 (m,, 2H), 2.81 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 148.52, 144.88, 142.02, 140.47, 138.25, 128.64, 128.59, 127.88, 127.31, 127.08, 126.00, 108.54, 107.68, 100.86, 98.36, 77.48, 77.16, 76.84, 71.60, 60.93, 57.13.

HRMS (ESI) calculated $[M+H]^+$ for $C_{22}H_{22}NO_3$: 348.1594, found: 348.1604.

FTIR (cm^{-1}) 3442, 3019, 2886, 2404, 1621, 1496, 1355, 1209, 1041, 945, 762.

2-(Benzyl(3,4-difluorophenyl)amino)-1-phenylethan-1-ol (31p)



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **30a** (0.105 g, 0.5 mmol) and 4,5-difluoro-2-(trimethylsilyl)phenyl trifluoromethanesulfonate **29e** (0.261 g, 0.75 mmol) with trifluoroacetic acid (0.057 g, 39 µL, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol), 18-crown-6 (0.396 g, 1.5 mmol) and H_2O (18 µL, 1.0 mmol) in THF (2.0 mL) from -10 °C to 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 97/03) of the crude reaction mixture using silica gel afforded 2-(benzyl(3,4-difluorophenyl)amino)-1-phenylethan-1-ol as yellow oil **31p** (0.110 g, 65% yield).

***R*f** (Pet. ether /EtOAc = 90/10): 0.48.

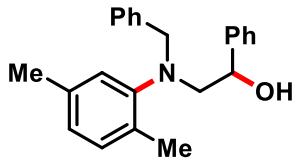
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.31 (m, 7H), 7.26 (t, *J* = 7.3 Hz, 1H), 7.16 (d, *J* = 7.3 Hz, 2H), 6.99 (dd, J_1 = 19.1 Hz, J_2 = 9.3 Hz, 1H), 6.62 (ddd, J_1 = 13.8 Hz, J_2 = 6.6 Hz, J_3 = 3.1 Hz, 1H), 6.49 – 6.47 (m, 1H), 5.01 (dd, J_1 = 8.3 Hz, J_1 = 4.5 Hz, 1H), 4.58 (d, *J* = 17.1 Hz, 1H), 4.47 (d, *J* = 17.1 Hz, 1H), 3.60 (qd, J_1 = 15.1, J_2 = Hz, 2H), 2.40 (s, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 150.84 (dd, J_1 = 244.6, J_2 = 13.4 Hz), 145.99 (d, *J* = 8.2 Hz), 143.00 (dd, J_1 = 236.9, J_2 = 12.7 Hz), 141.94, 137.72, 128.85, 128.80, 128.22, 127.23, 126.72, 125.99, 117.47 (d, *J* = 17.3 Hz), 108.53, 102.44 (d, *J* = 21.7 Hz), 72.23, 60.08, 55.69.

HRMS (ESI) calculated $[M+H]^+$ for $C_{21}H_{20}F_2NO$: 340.1507, found: 340.1508.

FTIR (cm^{-1}) 3429, 3069, 3019, 2968, 2866, 2404, 1599, 1517, 1218, 1123, 1023, 768.

2-(Benzyl(2,5-dimethylphenyl)amino)-1-phenylethan-1-ol (31q)



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **30a** (0.105 g, 0.5 mmol) and 3,6-dimethyl-2-(trimethylsilyl)phenyl trifluoromethanesulfonate **29f** (0.249 g, 0.75 mmol) with trifluoroacetic acid (0.057 g, 39 μL, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol), 18-crown-6 (0.396 g, 1.5 mmol) and H_2O (18 μL, 1.0 mmol) in THF (2.0 mL) from -10 °C to 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 97/03) of the crude reaction mixture using silica gel afforded 2-(benzyl(2,5-dimethylphenyl)amino)-1-phenylethan-1-ol as yellow oil **31q** (0.094 g, 57% yield).

***R*$_f$** (Pet. ether /EtOAc = 90/10): 0.53

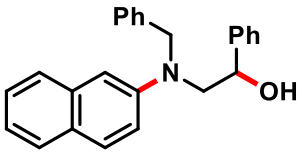
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.29 (m, 8H), 7.21 – 7.19 (m, 2H), 7.13 (d, *J* = 7.9 Hz, 1H), 6.91 (d, *J* = 6.9 Hz, 2H), 4.63 (dd, J_1 = 10.3, J_2 = 3.2 Hz, 1H), 4.14 (d, *J* = 13.8 Hz, 1H), 4.07 (d, *J* = 13.8 Hz, 1H), 3.41 (s, 1H), 3.29 (dd, J_1 = 13.0, J_2 = 3.2 Hz, 1H), 2.94 (dd, J_1 = 13.0, J_2 = 10.3 Hz, 1H), 2.36 (s, 3H), 2.30 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 149.04, 142.08, 137.55, 136.30, 131.32, 129.41, 128.42, 128.40, 127.63, 127.54, 126.06, 125.72, 124.06, 70.37, 60.83, 60.18, 21.24, 18.17.

HRMS (ESI) calculated $[M+H]^+$ for $C_{23}H_{26}NO$: 332.2009, found: 332.2022.

FTIR (cm^{-1}) 3441, 3019, 2927, 2405, 1604, 1501, 1452, 1324, 1217, 1121, 1057, 767.

2-(Benzyl(naphthalen-2-yl)amino)-1-phenylethan-1-ol (31r)



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **30a** (0.105 g, 0.5 mmol) and 3-(trimethylsilyl)naphthalen-2-yl trifluoromethanesulfonate **29g** (0.261 g, 0.75 mmol) with trifluoroacetic acid (0.057 g, 39 μL, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol), 18-crown-6 (0.396 g, 1.5 mmol) and H_2O (18 μL, 1.0 mmol) in THF (2.0 mL) from -10 °C to 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 97/03) of the crude reaction mixture using silica gel afforded 2-(benzyl(naphthalen-2-yl)amino)-1-phenylethan-1-ol as yellow oil **31r** (0.101 g, 57% yield).

***R*f** (Pet. ether /EtOAc = 90/10): 0.57.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.9 Hz, 2H), 7.70 (d, *J* = 8.2 Hz, 1H), 7.49 – 7.26 (m, 13H), 7.15 (s, 1H), 5.17 (dd, J_1 = 7.6, J_2 = 5.2 Hz, 1H), 4.79 (d, *J* = 17.0 Hz, 1H), 4.66 (d, *J* = 17.0 Hz, 1H), 3.96 – 3.60 (m, 2H), 2.66 (s, 1H).

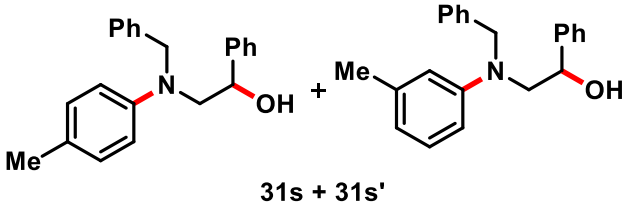
^{13}C NMR (100 MHz, $CDCl_3$) δ 146.63, 142.17, 138.31, 134.99, 129.21, 128.73, 128.04, 127.53, 127.37 – 126.74, 126.43, 126.05, 122.52, 116.68, 107.53, 72.06, 59.67, 55.45.

HRMS (ESI) calculated $[M+H]^+$ for $C_{25}H_{24}NO$: 354.1852, found: 354.1855.

FTIR (cm^{-1}) 3417, 3020, 2926, 2403, 1629, 1597, 1507, 1448, 1393, 1217, 1045, 958, 767, 670.

The reaction of aryne precursor 1-(trimethylsilyl)naphthalen-2-yl trifluoromethanesulfonate **29h** (0.261 g, 0.75 mmol) with 1-benzyl-2-phenylaziridine **30a** (0.105 g, 0.5 mmol) under the reaction conditions has resulted in the formation of mixture of regioisomers **31r** and **31r'** in the ratio >20:1 in 59% yield.

2-Amino alcohols 31s and 31s' (1:1)



31s + 31s'

Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **30a** (0.105 g, 0.5 mmol) and 4-methyl-2-(trimethylsilyl)phenyl trifluoromethanesulfonate **29i** (0.234 g, 0.75 mmol) with trifluoroacetic acid (0.057 g, 39 μL, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol), 18-crown-6 (0.396 g, 1.5 mmol) and H_2O (18 μL, 1.0 mmol) in THF

(2.0 mL) from -10 °C to 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 97/03) of the crude reaction mixture using silica gel afforded inseparable mixture of 2-amino alcohols **31s** and **31s'** in (1:1) ratio as yellow oil (0.111 g, 70% yield).

***R*f** (Pet. ether /EtOAc = 90/10): 0.54.

^{1}H NMR of 31s (400 MHz, $CDCl_3$) δ 7.46 - 7.21 (m, 10H), 7.12 (d, *J* = 8.25 Hz, 2H), 6.85 (d, *J* = 8.67 Hz, 2H), 5.11- 5.07 (m, 1H), 4.71 - 4.73 (m, 2H), 3.67 - 3.57 (m, 2H), 2.66 (s, 1H), 2.38 (s, 3H).

^{13}C NMR of 31s (100 MHz, $CDCl_3$) δ 146.69, 142.13, 138.55, 129.29, 128.64, 128.61, 127.89, 126.93, 126.85, 114.15, 110.68, 71.89, 59.66, 55.35, 20.37.

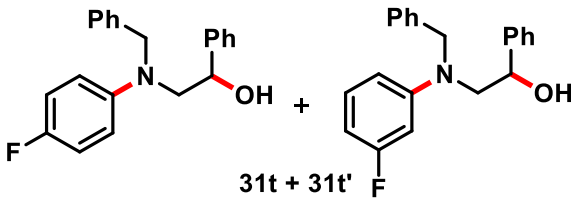
^{1}H NMR of 31s' (400 MHz, $CDCl_3$) δ 7.46 - 7.21 (m, 10H), 7.18 (d, *J* = 7.8 Hz, 1H), 6.75 - 6.72 (m, 2H), 6.67 (d, *J* = 7.6 Hz, 1H), 5.07 - 5.04(m, 1H), 4.57 - 4.51 (m, 2H), 3.67 - 3.57 (m, 2H), 2.58 (s, 1H), 2.34 (s, 3H).

^{13}C NMR of 31s' (100 MHz, $CDCl_3$) δ 148.91, 142.18, 139.11, 129.95, 128.68, 128.66, 127.93, 126.97, 126.01, 118.49, 114.07, 72.00, 60.09, 55.83, 22.08.

HRMS (ESI) calculated $[M+H]^+$ for $C_{22}H_{24}NO$: 318.1852, found: 318.1852.

FTIR (cm^{-1}) 3442, 3018, 2405, 1955, 1877, 1812, 1605, 1508, 1451, 1218, 1045, 955, 766, 704.

2-Amino alcohols 31t and 31t' (3:1)



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **30a** (0.105 g, 0.5 mmol) and 5-fluoro-2-(trimethylsilyl)phenyl trifluoromethanesulfonate **29j** (0.237 g, 0.75 mmol) with trifluoroacetic acid (0.057 g, 39 μL, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol), 18-crown-6 (0.396 g, 1.5 mmol) and H_2O (18 μL, 1.0 mmol) in THF (2.0 mL) from -10 °C to 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 97/03) of the crude reaction mixture using silica gel afforded inseparable mixture of 2-amino alcohols **31t** and **31t'** in (3:1) ratio as yellow oil (0.104 g, 65% yield).

***R*f** (Pet. ether /EtOAc = 90/10): 0.47.

^{1}H NMR of Major isomer 31t (400 MHz, $CDCl_3$) δ 7.42 – 7.14 (m, 10H), 6.96 (t, *J* = 8.7 Hz, 2H), 6.83 – 6.80 (m, 2H), 4.99 (dd, *J* = 7.8, 5.0 Hz, 1H), 4.68 - 4.47 (m, 2H), 3.61 - 3.52 (m, 2H), 2.57 (s, 1H).

^{13}C NMR of Major isomer 31t (100 MHz, $CDCl_3$) δ 157.38, 150.54 (d, *J* = 10.4 Hz), 142.00, 138.16, 130.45 (d, *J* = 10.4 Hz), 128.83, 127.15, 127.09, 126.02, 115.91, 115.69, 103.64 (d, *J* = 22.1 Hz, 100.07 (d, *J* = 25.3 Hz), 71.97, 60.57, 56.40.

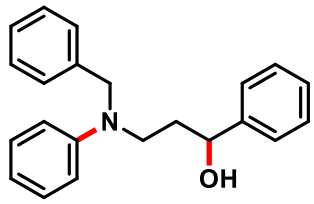
^{1}H NMR of Minor isomer 31t' (400 MHz, $CDCl_3$) δ 7.42 – 7.14 (m, 11H), .60 (dd, J_1 = 8.3 Hz, J_2 = 1.9 Hz, 1H), 6.54 (d, *J* = 12.8 Hz, 1H), 6.46 (t, *J* = 8.1 Hz, 1H), 5.08 (dd, *J* = 7.9, 4.7 Hz, 1H),), 4.68 - 4.47 (m, 2H), 3.71 - 3.64 (m, 2H), 2.34 (s, 1H)

Representative ^{13}C NMR peaks of Minor isomer 31t' (100 MHz, $CDCl_3$) δ 155.03, 137.93, 128.19, 128.06, 126.61, 115.54(d, *J* = 7.2 Hz), 108.55, 72.27, 59.63, 55.23.

HRMS (ESI) calculated $[M+H]^+$ for $C_{21}H_{21}FNO$: 322.1602, found: 322.1604.

FTIR (cm^{-1}) 3245, 3018, 2926, 2404, 1892, 1600, 1504, 1450, 1356, 1299, 1222, 1067, 828, 737.

3-(Benzyl(phenyl)amino)-1-phenylpropan-1-ol (36a)



Following the general procedure, treatment of 1-benzyl-2-phenylazetidine **35a** (0.112 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **29a** (0.223 g, 182 μL, 0.75 mmol) with trifluoroacetic acid (0.057 g, 39 μL, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol), 18-crown-6 (0.396 g, 1.5 mmol) and H_2O (18 μL, 1.0 mmol) in THF (2.0 mL) from -10 °C to 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 93/07) of the crude reaction mixture using silica gel afforded 3-(benzyl(phenyl)amino)-1-phenylpropan-1-ol as yellow oil **36a** (0.113 g, 71% yield).

***R*$_f$** (Pet. ether /EtOAc = 80/20): 0.40.

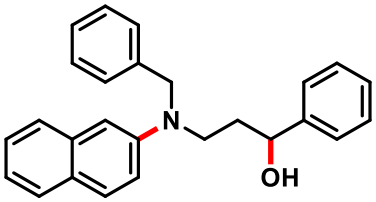
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.20 (m, 12H), 6.77 - 6.72 (m, 7.7 Hz, 3H), 4.77 (t, *J* = 6.4 Hz, 1H), 4.57 (s, 2H), 3.65 – 3.51 (m, 2H), 2.28 (s, 1H), 2.10 (dd, *J* = 13.8, 7.2 Hz, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 148.66, 144.53, 138.95, 129.34, 128.67, 127.80, 126.93, 126.87, 125.83, 116.83, 113.09, 72.86, 55.09, 48.22, 36.27.

HRMS (ESI) calculated $[M+H]^+$ for $C_{22}H_{24}NO$: 318.1852, found: 318.1847.

FTIR (cm^{-1}) 3425, 3060, 2926, 2253, 1640, 1601, 1501, 1453, 1363, 1035, 908, 737.

3-(Benzyl(naphthalen-2-yl)amino)-1-phenylpropan-1-ol (36g)



Following the general procedure, treatment of 1-benzyl-2-phenylazetidine **35a** (0.028 g, 0.125 mmol) and 3-(trimethylsilyl)naphthalen-2-yl trifluoromethanesulfonate **29g** (0.065 g, 0.1875 mmol) with trifluoroacetic acid (0.014 g, 10 μL, 0.50 mmol) in the presence of KF (0.022 g, 0.375 mmol), 18-crown-6 (0.99 g, 0.375 mmol) and H_2O (5 μL, 0.25 mmol) in THF (0.5 mL) from -10 °C to 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 93/07) of the crude reaction mixture using silica gel afforded 3-(benzyl(naphthalen-2-yl)amino)-1-phenylpropan-1-ol as yellow oil **36g** (0.023 g, 51% yield).

***R*$_f$** (Pet. ether /EtOAc = 80/20): 0.45.

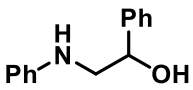
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77– 7.66 (m, 4H), 7.56 (d, *J* = 8.2 Hz, 1H), 7.43 (t, *J* = 7.2 Hz, 1H), 7.39 – 7.18 (m, 9H), 7.14 – 7.11 (m, 1H), 6.91 (s, 1H), 4.79 (t, *J* = 6.3 Hz, 1H), 4.66 (s, 2H), 3.71 – 3.57 (m, 2H), 2.33 – 2.11 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) 146.51, 144.48, 138.81, 135.07, 129.08, 128.72, 127.87, 127.66, 127.05, 126.98, 126.42, 126.31, 125.89, 124.14, 122.89, 122.18, 116.59, 106.97, 72.87, 55.16, 48.16, 36.27.

HRMS (ESI) calculated $[M+H]^+$ for $C_{26}H_{26}NO$: 368.2009, found: 368.2005.

FTIR (cm^{-1}) 3422, 3055, 2929, 2254, 1641, 1610, 1481, 1453, 1373, 1035, 910, 730.

1-Phenyl-2-(phenylamino)ethan-1-ol (37)



An oven dried round bottomed flask was charged with 2-(benzyl(phenyl)amino)-1-phenylethan-1-ol **31a** (0.152g, 0.50 mmol) and Pd 10% on activated carbon (20 mg, 0.03 equiv) in methanol (10 mL). The reaction mixture was continued stirring at 30 °C for 12h under H_2 atmosphere in balloon pressure. Upon consumption of the starting material **31a,** the crude reaction mixture was passed through celite and concentrated under reduced pressure to get a sufficiently pure 1-phenyl-2-(phenylamino)ethan-1-ol **37** in 97% yield (103 mg) as yellow sticky oil.

***R*$_f$** (Pet. ether /EtOAc = 70/30): 0.51.

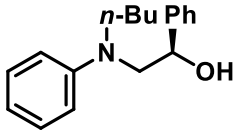
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.33 (m, 5H, H_{ar}), 7.26 (t, *J* = 7.5 Hz, 2H, H_{ar}), 6.83 (t, *J* = 7.2 Hz, 1H, H_{ar}), 6.70 (d, *J* = 8.0 Hz, 2H, H_{ar}), 4.89 (dd, J_1 = 8.6, J_2 = 3.8 Hz, 1H), 3.42 (dd, J_1 = 13.1, J_2 = 3.8 Hz, 1H), 3.29 (dd, J_1 = 13.1, J_2 = 8.7 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 147.88, 142.12, 129.37, 128.63, 127.98, 125.95, 118.14, 113.55, 72.38, 51.74.

HRMS (ESI) calculated $[M+H]^+$ for $C_{14}H_{16}NO$: 214.1226, found: 214.1226.

FTIR (cm^{-1}) 3413, 3019, 2405, 1602, 1504, 1446, 1317, 1254, 1216, 1057, 911, 768, 703.

(*R*)-2-(Butyl(phenyl)amino)-1-phenylethan-1-ol ((*R*)-31b)



Following the general procedure, treatment of (*S*)-1-butyl-2-phenylaziridine **(*S*)-30b** (0.088 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **29a** (0.223 g, 182 μL, 0.75 mmol) with trifluoroacetic acid (0.057 g, 39 μL, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol), 18-crown-6 (0.396 g, 1.5 mmol) and H_2O (18 μL, 1.0 mmol) in THF (2.0 mL) from -10 °C to 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 97/03) of the crude reaction mixture using silica gel afforded (*R*)-2-(butyl(phenyl)amino)-1-phenylethan-1-ol as yellow oil **(*R*)-31b** (0.098 g, 73% yield).

***R*$_f$** (Pet. ether /EtOAc = 90/10): 0.51.

HPLC (Chiralpak AD, 95:05 (Hexane:IPA, 1.0 mL/min), Major: 8.7 min, Minor: 8.1 min, er = 98: 2, $[\alpha]_D^{26}$ = -11.2 (c 1.0, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 – 7.40 (m, 4H), 7.37 – 7.29 (m, 3H), 6.89 (d, *J* = 8.0 Hz, 2H), 6.81 (t, *J* = 7.2 Hz, 1H), 4.99 (dd, J_1 = 8.9 Hz, J_2 = 4.1 Hz, 1H), 3.54 (dd, J_1 = 14.7 Hz, J_2 = 4.1 Hz, 1H), 3.45 (dd, J_1 = 14.7 Hz, J_2 = 9.0 Hz, 1H), 3.37 – 3.30 (m, 2H), 2.67 (s, 1H), 1.62 - 1.55 (m, 7.7, 2.7 Hz, 2H), 1.39 - 1.33 (m, 7.5 Hz, 2H), 0.97 (t, *J* = 7.4 Hz, 3H).

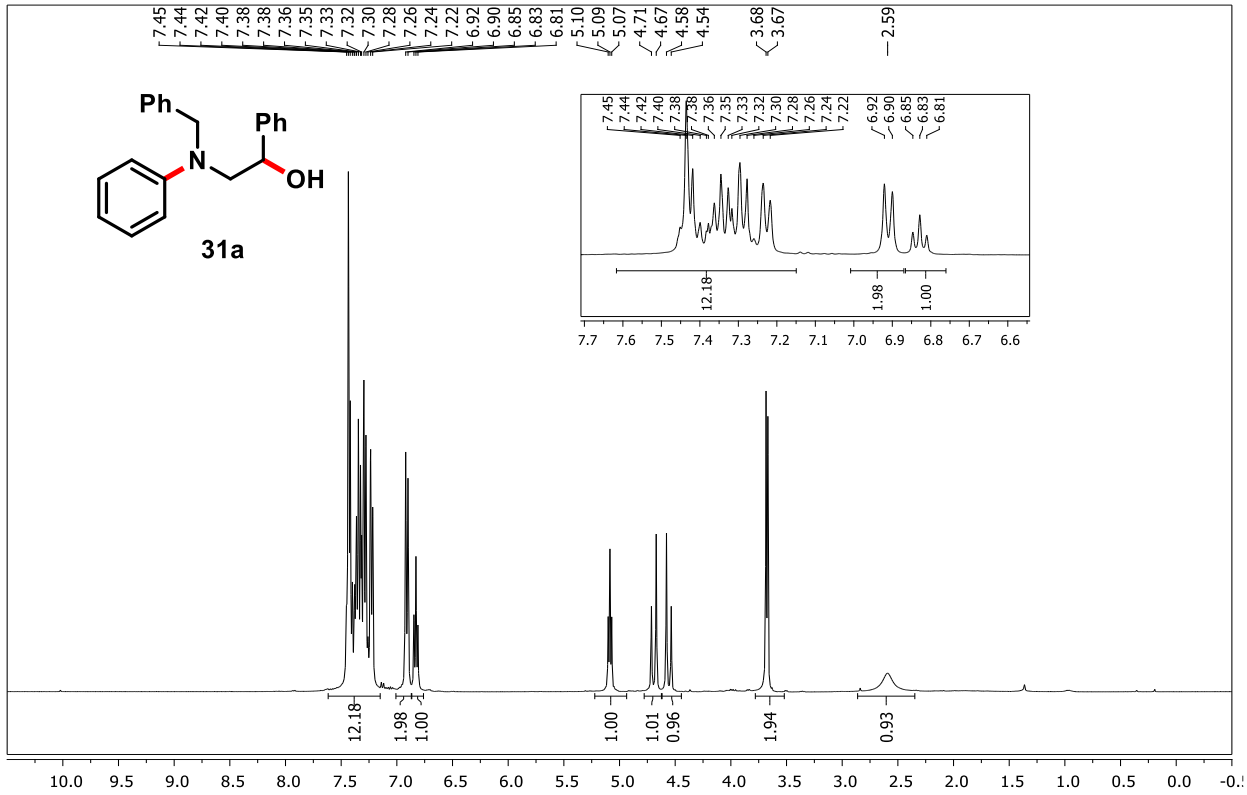
^{13}C NMR (125 MHz, $CDCl_3$) δ 148.54, 142.12, 129.43, 128.61, 127.87, 126.01, 117.34, 113.76, 71.49, 60.11, 52.28, 28.80, 20.40, 14.07.

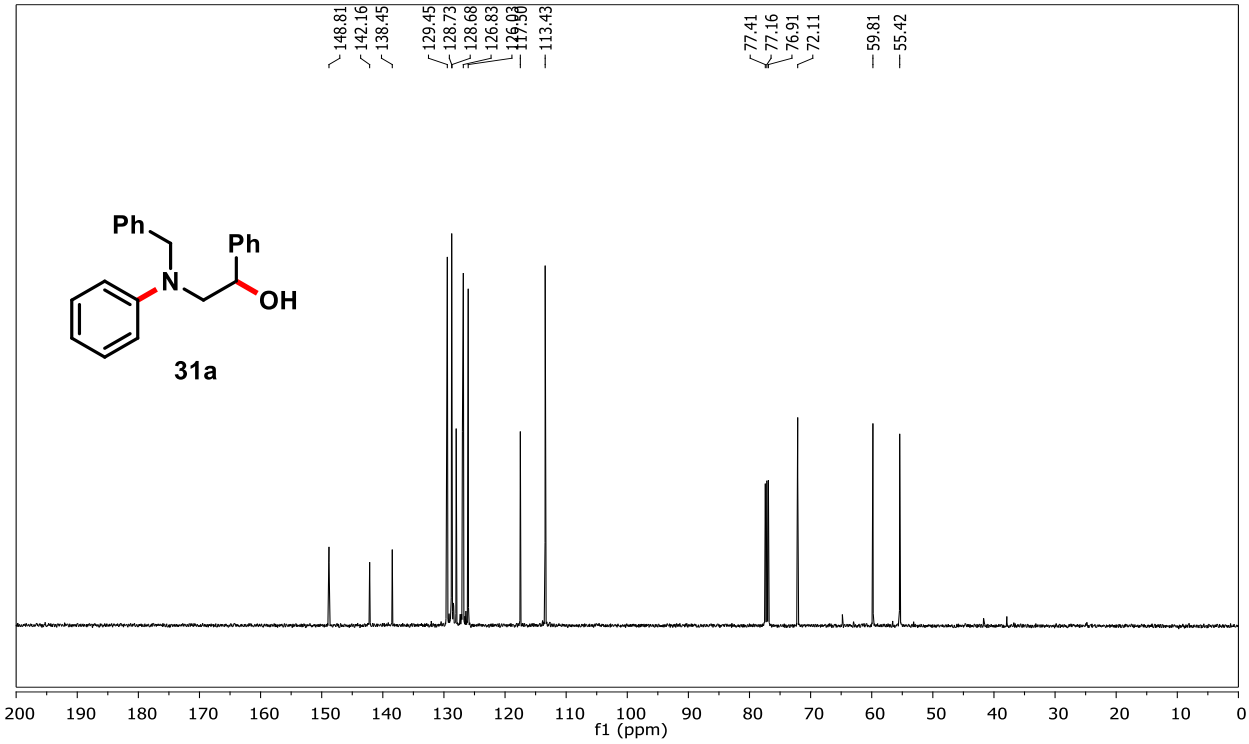
HRMS (ESI) calculated $[M+H]^+$ for $C_{18}H_{24}NO$: 270.1852, found: 270.1855.

FTIR (cm^{-1}) 3451, 3018, 2958, 2872, 2404, 1598, 1501, 1459, 1361, 1216, 1125, 1095, 929, 770.

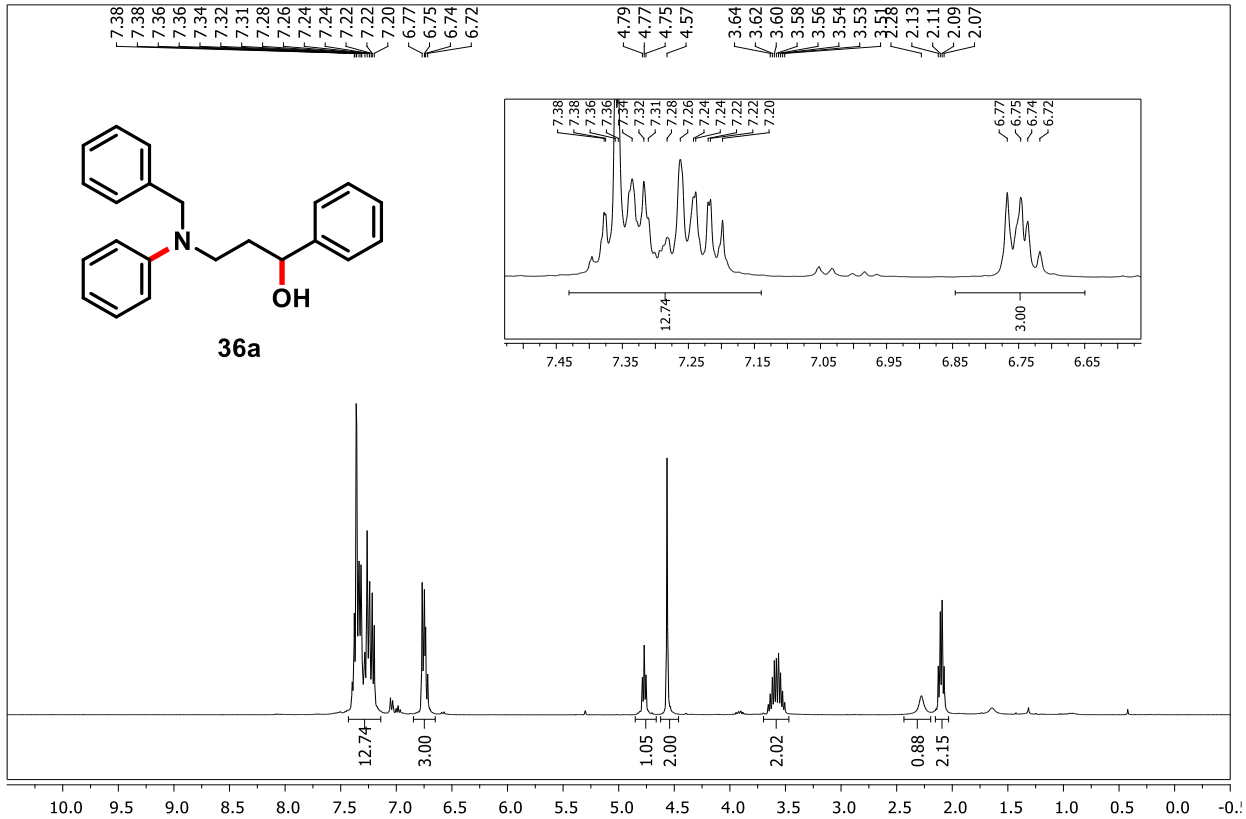
2.7.7. ^{1}H and ^{13}C NMR Spectra of Selected Compounds

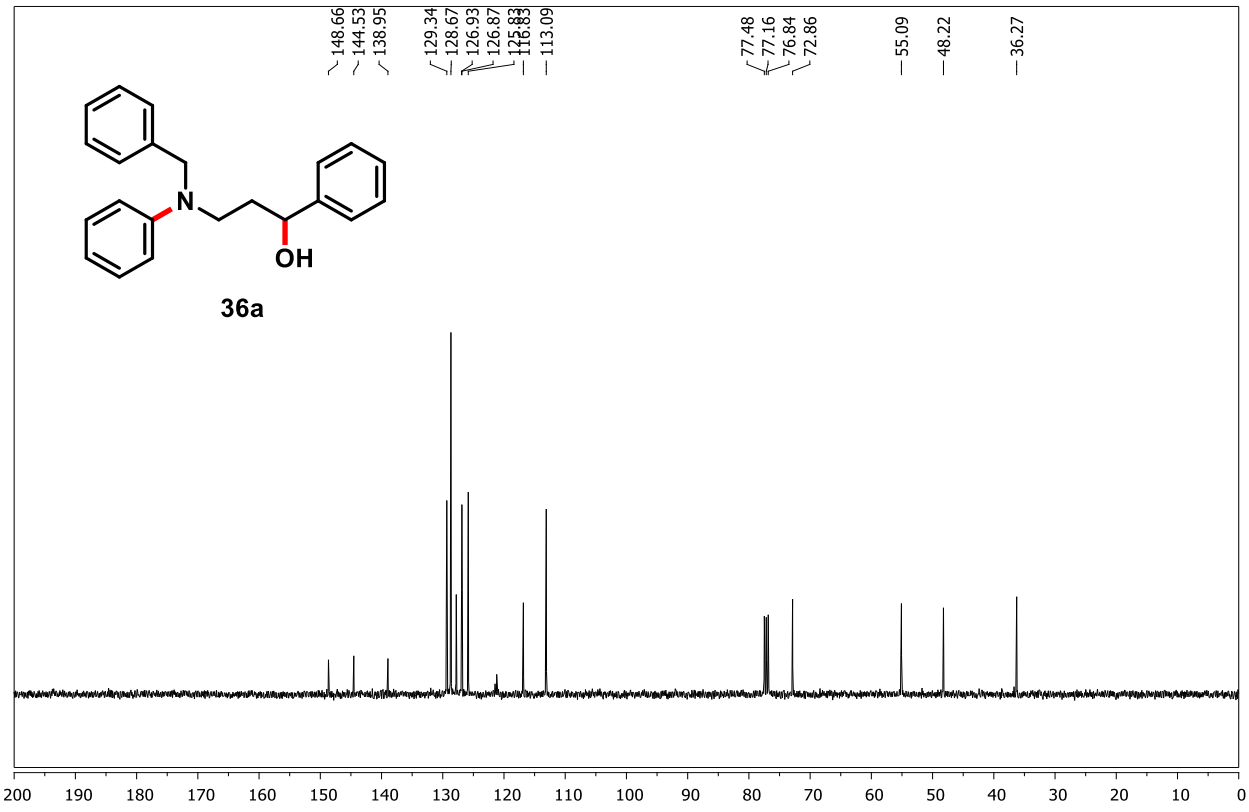
2-(Benzyl(phenyl)amino)-1-phenylethan-1-ol (31a)



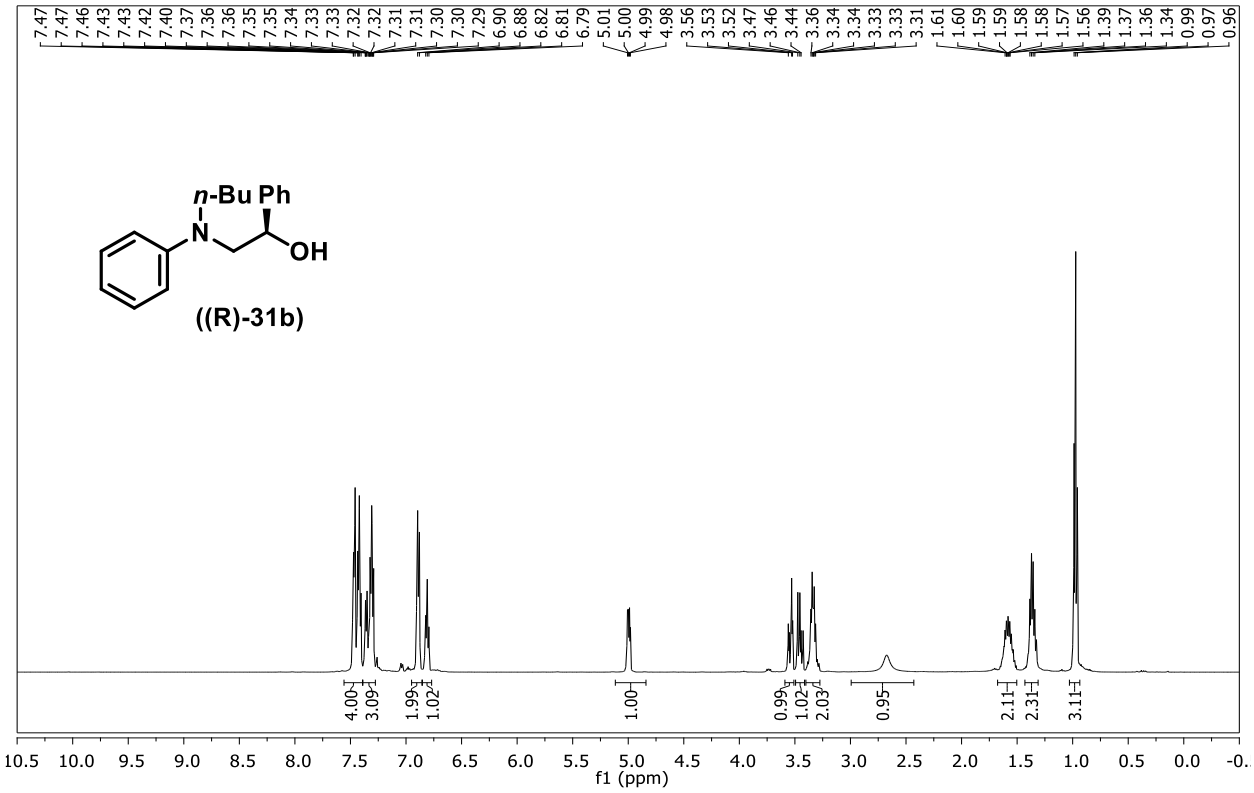


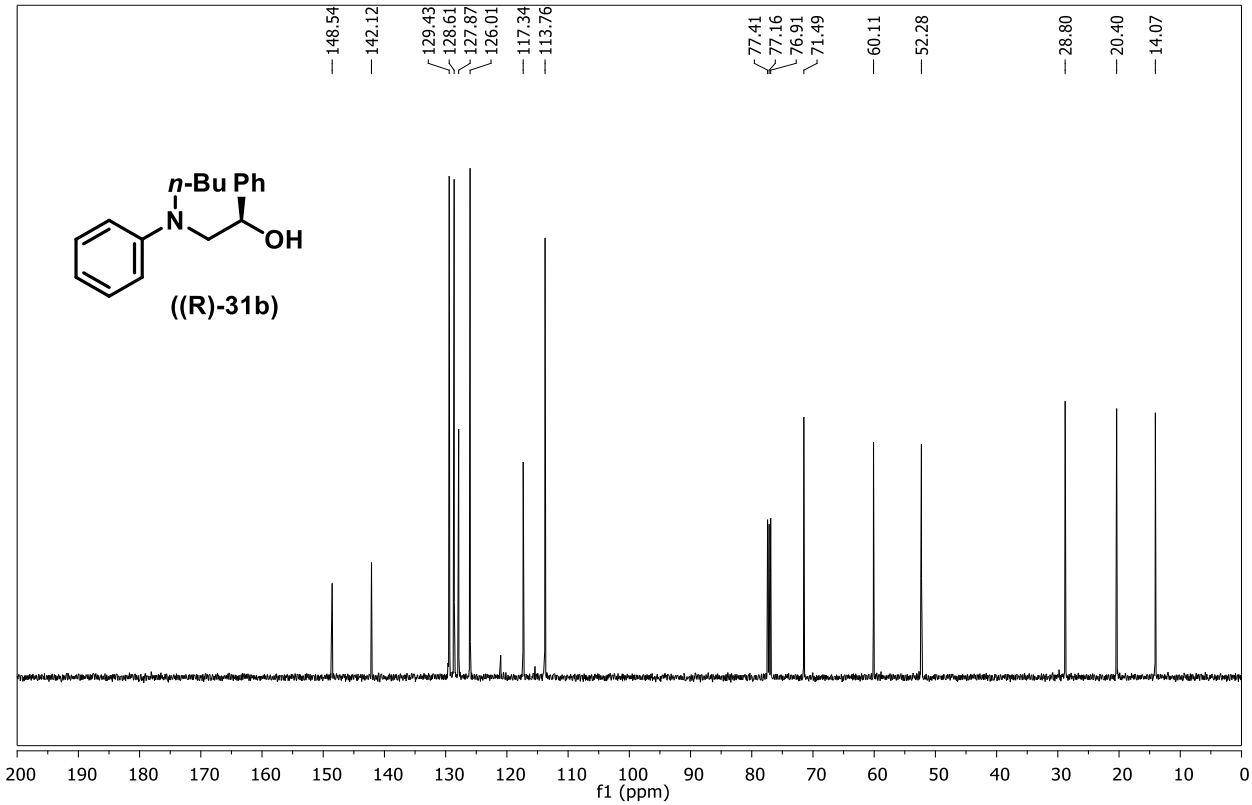
3-(Benzyl(phenyl)amino)-1-phenylpropan-1-ol (36a)





(*R*)-2-(Butyl(phenyl)amino)-1-phenylethan-1-ol ((*R*)-31b)





2.8. References

1. For selected reviews, see: (a) Anaya de Parrodi, C.; Juaristi, E. *Synlett* **2006**, 2699. (b) Bergmeier, S. C. *Tetrahedron* **2000**, *56*, 2561. (c) Ager, D. J.; Prakash, I.; Schaad, D. R. *Chem. Rev*. **1996**, *96*, 835. (d) Reetz, M. T. *Angew. Chem., Int. Ed.* **1991**, *30*, 1531.
2. Merrill, A. H. *Chem. Rev*. **2011**, *111*, 6387.
3. Desai, P. H.; Salvi, N. J.; Patravale, B. S.; Seetharaman, S.; Patil, D. J.; Ghogare, K. S. US Pat. Appl. US 8,063,251 B2.
4. (a) Effenberger, F.; Jäger, J. *J. Org. Chem.* **1997,** *62*, 3867. (b) Wetterlin, K. *J. Med. Chem*. **1972**, *15*, 1182.
5. Stahlberg, J.; Henriksson, H.; Divne, C.; Isaksson, R.; Pettersson, G.; Johansson, G.; Jones, T. A. *J. Mol. Biol.* **2001**, *305*, 79.
6. (a) Desimoni, G.; Faita, G.; Quadrelli, P. *Chem. Rev*. **2003**, *103*, 3119. (b) Nishiyama, H.; Sakaguchi, H.; Nakamura, T.; Horihata, M.; Kondo, M.; Itoh, K. *Organometallics* **1989**, *8*, 846.
7. (a) Evans, D. A.; Kim, A. S. In *Chiral Reagents for Asymmetric Synthesis*, Ed.: Paquette, L. A. Wiley, New York, 2003, p 57. (b) Ager, D. J.; Prakash, I.; Schaad, D. R. *Aldrichimica Acta* **1997**, *30*, 3.
8. (a) Struble, J. R.; Bode, J. W. *Org. Synth.* **2010**, *87*, 362. (b) Vora, H. U.; Lathrop, S. P.; Reynolds, N. T.; Kerr, M. S.; Read de Alaniz, J.; Rovis, T. *Org. Synth.* **2010**, *87*, 350.
9. For reviews, see: (a) Stanković, S.; D'hooghe, M.; Catak, S.; Eum, H.; Waroquier, M.; Speybroeck, V. V.; De Kimpe, N.; Ha, H.-J. *Chem. Soc. Rev*. **2012**, *41*, 643. (b) Hu, X. E. *Tetrahedron* **2004**, *60*, 2701.
10. Stamm, H.; Speth, D. *Arch. Pharm.* (Weinheim) **1989**, *332*, 277.
11. Prasad, B. A. B.; Sekar, G.; Singh, V. K. *Tetrahedron Lett.* **2000**, *41*, 4677.
12. Chandrasekhar, S.; Narsihmulu, C.; Sultana, S. S. *Tetrahedron Lett.* **2002**, *43*, 7361.
13. Concellon, J. M.; Riego, E. *J. Org. Chem.* **2003**, *68*, 6407.
14. Davis, F. A.; Reddy, G. V. *Tetrahedron Lett.* **1996**, *37*, 4349.
15. Palais, L.; Chemla, F.; Fereira, F. *Synlett* **2006**, *7*, 1039.
16. Wang, Z.; Cui, Y.-T.; Xu, Z.-B.; Qu, J. *J. Org. Chem.* **2008**, *73*, 2270.
17. Li, J.; Liao, Y.; Zhang, Y.; Liu, X.; Lin, L.; Feng. X. *Chem. Commun.*, **2014**, *50*, 6672.

18. For selected reports, see: (a) Liu, G.; Stahl, S. S. *J. Am. Chem. Soc.* **2006**, *128*, 7179. (b) Sello, G.; Orsini, F.; Bernasconi, S.; Gennaro, P. D. *Tetrahedron:Asymmetry* **2006**, *17*, 372. (c) (e) Azizi, N.; Saidi, M. R. *Org. Lett*. **2005**, *7*, 3649.
19. Shivani, Pujala, B.; Chakraborti, A. K. *J. Org. Chem.* **2007**, *72*, 3713.
20. Azoulay, S.; Manabe, K.; Kobayashi, S. *Org. Lett.* **2005**, *7*, 4593.
21. Fagnou, K.; Lautens, M. *Org. Lett*. **2000**, *2*, 2319.
22. (a) Job, G. E.; Buchwald, S. L. *Org. Lett*. **2002**, *4*, 3703. For selected reports on amino alcohol synthesis using hydroamination of alkenes, see: (b) Nakamura, Y.; Ohta, T.; Oe, Y. *Chem. Commun.* **2015**, *51*, 7459. (c) Barry, C. S.; Simpkins, N. S. *Tetrahedron Lett*. **2007**, *48*, 8192.
23. For recent reviews on aryne chemistry, see: (a) Shi, J.; Li, Y.; Li, Y. *Chem. Soc. Rev.* **2017**, *46*, 1707. (a) Idiris, F. I. M.; Jones, C. R. *Org. Biomol. Chem*. **2017**, *15*, 9044. (b) García-López, J.-A.; Greaney, M. F. *Chem. Soc. Rev*.**2016**, *45*, 6766. (c) Bhojgude, S. S.; Bhunia, A.; Biju, A. T. *Acc. Chem. Res*. **2016**, *49*, 1658. (d) Goetz, A. E.; Shah, T. K.; Garg, N. K. *Chem. Commun*. **2015**, *51*, 34. f) (e) Dubrovskiy, A. V.; Markina, N. A.; Larock, R. C. *Org. Biomol. Chem.* **2013**, *11*, 191. (f) Wu, C.; Shi, F. *Asian J. Org. Chem.* **2013**, *2*, 116. (g) Pérez, D.; Peña, D.; Guitián, E. *Eur. J. Org. Chem.* **2013**, 5981. (h) Tadross, P. M.; Stoltz, B. M. *Chem. Rev.* **2012**, *112*, 3550. (i) Gampe, C. M.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2012**, *51*, 3766. (j) Bhunia, A.; Yetra, S. R.; Biju, A. T. *Chem. Soc. Rev.* **2012**, *41*, 3140. (k) Okuma, K. *Heterocycles* **2012**, *85*, 515. (l) Yoshida, H.; Ohshita, J.; Kunai, A. *Bull. Chem. Soc. Jpn.* **2010**, *83*, 199
24. For a related aziridine opening using water, see: (a) Gaebert, C.; Mattay, J. *Tetrahedron* **1997**, *53*, 14297. For highlights on aryne three-component couplings, see: (b) Bhojgude, S. S.; Biju, A. T. *Angew. Chem., Int. Ed.* **2012**, *51*, 1520. (c) Bhunia, A.; Biju, A. T. *Synlett*, **2014**, *25*, 608.
25. (a) Giumanini, A. G. *J. Org. Chem.* **1972**, *37*, 513. For the reaction of arynes with 1-azirines, see: (b) Nair, V.; Kim, K. H. *J. Org. Chem.* **1975**, *40*, 3784.
26. (a) Stephens, D.; Zhang, Y.; Cormier, M.; Chavez, G.; Arman, H.; Larionov, O. V. *Chem. Commun.* **2013**, *49*, 6558. Performing the TFA promoted reaction in CH_3CN, **3a** was observed in 20% yield (Table 1, entry 13). However, the CH_3CN incorporated product reported by Larionov was not observed under these conditions. Notably, the

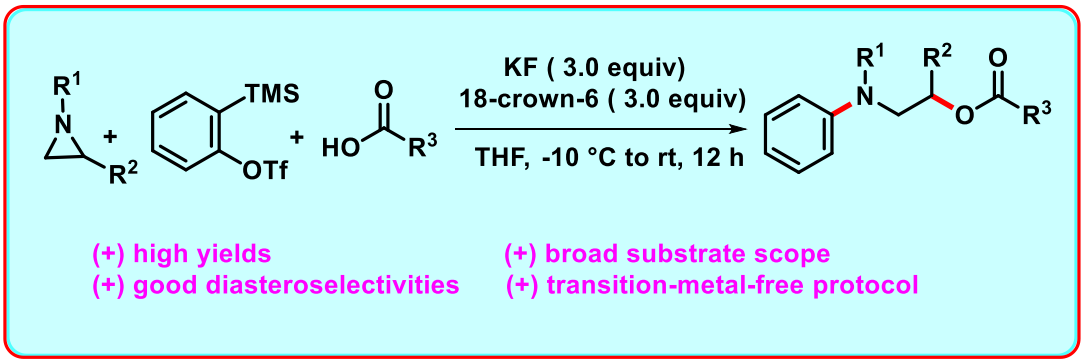
present work differs from Larionov protocol in the use of H_2O as a third-component and the crucial role of TFA in promoting this reaction.

27. For related work on use of H_2O as third component in aryne coupling, see: (b) Kaicharla, T.; Thangaraj, M.; Biju, A. T. *Org. Lett.* **2014**, *16*, 1728. (c) Rigby, J. H.; Laurent, S. *J. Org. Chem.* **1998**, *63*, 6742.
28. (a) Himeshima, Y.; Sonoda, T.; Kobayashi, H. *Chem. Lett.* **1983**, 1211.See also: (b) Peña, D.; Cobas, A.; Pérez, D.; Guitián, E. *Synthesis* **2002**, 1454.
29. (a) Tang, C.-Y.; Wang, G.; Yang, X.-Y.; Wu, X.-Y.; Sha, F. *Tetrahedron Lett*. **2014**, *55*, 6447.
30. For a review on the applications of TFA in organic synthesis, see: López, S. E.; Salazar, J. *J. Fluorine Chem.* **2013**, *156*, 73.
31. For related three-component couplings, see: (a) Bhunia, A.; Roy, T.; Pachfule, P.; Rajamohanan, P. R.; Biju, A. T. *Angew. Chem., Int. Ed.* **2013**, *52*, 10040. (b) Bhunia, A.; Porwal, D.; Gonnade, R. G.; Biju, A. T. *Org. Lett.* **2013**, *15*, 4620. (c) Nawaz, F.; Mohanan, K.; Charles, L.; Rajzmann, M.; Bonne, D.; Chuzel, O.; Rodriguez, J.; Coquerel, Y. *Chem. Eur. J.* **2013**, *19*, 17578. (d) Liu, P.; Lei, M.; Hu, L. *Tetrahedron* **2013**, *69*, 10405. (e) Jeganmohan, M.; Bhuvaneswari, S.; Cheng, C.-H. *Chem. Asian J*. **2010**, 5,153. (f) Sha, F.; Huang, X. *Angew. Chem., Int. Ed.* **2009**, *48*, 3458. (g) Okuma, K.; Hino, H.; Sou, A.; Nagahora, N.; Shioji, K. *Chem. Lett.* **2009**, *38*, 1030. (h) Jeganmohan, M.; Cheng, C.-H. *Chem. Commun*. **2006**, 2454.
32. For efficient *N*-arylation and *O*-arylation using arynes, see: Liu, Z.; Larock, R. C. *J. Org. Chem.* **2006**, *71*, 3198.
33. Dou, X. Y.; He, L. N.; Yang, Z. Z.; Wang, J. L. *Synlett* **2010**, 2159. (b) Drouillat, B.;d'Aboville, E.; Bourdreux, F.; Couty, F. *Eur. J. Org. Chem*. **2014**,1103.
34. Sato, Y.; Tamura, T.; Kinbara, A.; Morib, M. *Adv. Synth. Catal*. **2007**, *349*, 647. (b) Peña, D.; Cobas, A.; Pérez, D.; Guitián, E. *Synthesis* **2002**, 1454.
35. Du, Y.; Wu, Y.; Liu, A. H.; He, L. N. *J. Org. Chem.* **2008**, *73*, 4709.
36. Roy, T.; Baviskar, D. R.; Biju, A. T. *J. Org. Chem.* **2015**, *80*, 11131.

Chapter 3

Employing Carboxylic Acids in Aryne Multicomponent Coupling Triggered by Aziridines/Azetidines

The transition-metal-free aryne multicomponent coupling (MCC) involving carboxylic acids initiated by aziridines/azetidines has been reported. The use of aziridines as nucleophile afforded *N*-aryl β-amino alcohol derivatives and the application of azetidines as nucleophilic trigger furnished *N*-aryl γ-amino alcohol derivatives in moderate to good yields. Moreover, phenols could also be used as a substituent for carboxylic acids in this reaction.



Org. Chem. Front. **2016**, *3*, 71

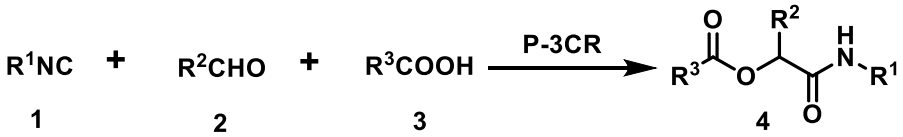
3.1. Introduction

Multicomponent couplings (MCCs) play leading role among the various synthetic methods to build molecular complexity and MCCs are routinely used in medicinal and combinatorial chemistry. MCCs can be defined as a synthetic methodology in which more than two reactants react together in a single reaction vessel to form a new product containing almost all part of the substrates, generating negligible by-products. That makes MCCs an extremely ideal and eco-friendly reaction system. Molecules which are of high level of complexity can be obtained in one pot with reduced number of steps. Therefore, MCCs have been paid much attention in various research fields, such as discovery of lead compounds in medicinal chemistry, or combinatorial chemistry. Carboxylic acids stand as important component in many multicomponent reactions due its less cost and ready availability.

3.2. Classic Multicomponent Reactions Employing Carboxylic Acids/Phenols

3.2.1. Passerini Reaction

Among MCCs, Passerini reaction holds a distinction for the efficient and green multicomponent reaction utilizing readily available substrates like aldehydes or ketones (oxo compounds), carboxylic acids and their analogues. The 1,1-amphoteric nature of the isocyanide is utilized for the efficient coupling of three functional groups. Passerini and Ugi reactions are the two most well-known isocyanide-based MCCs which utilizes the unique reactivity of isocyanides.

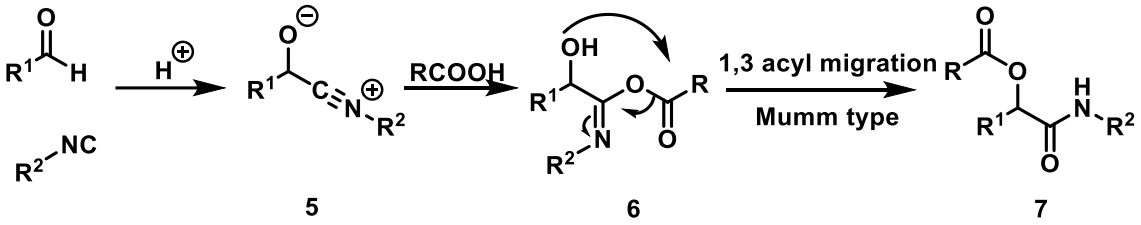


Scheme 3.1. Classical three-component Passerini reaction

The first isocyanide based MCC was revealed by Passerini in 1921,[1] where carbonyl compounds **2** such as an aldehydes or ketones, carboxylic acid **3**, and an isocyanide **1** react together to provide α-acyloxycarboxamide derivatives **4** without any side product obeying all aspects of an efficient multicomponent reaction. The α-acyloxyamide scaffold **4** synthesized using this methodology is found in a number of drug-like molecules,

and can be applied in the total syntheses of biologically active natural products (Scheme 3.1).

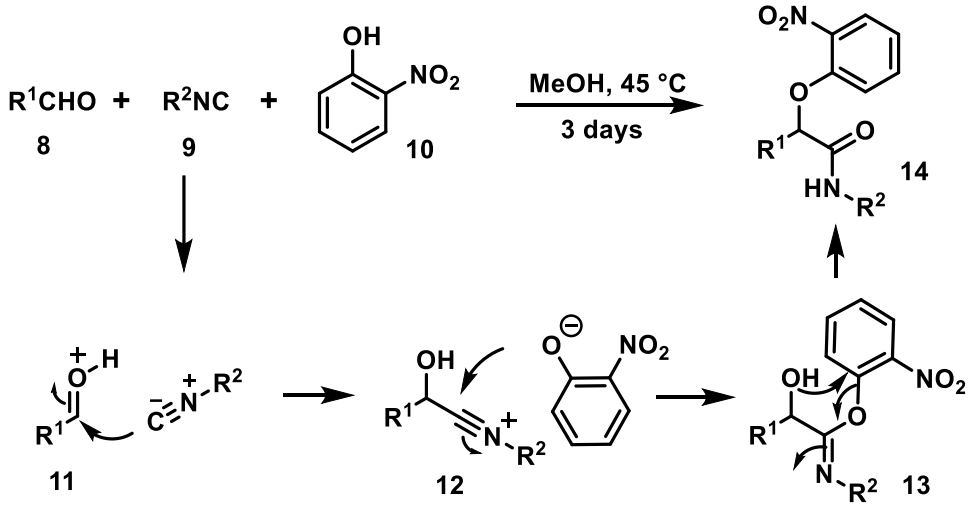
The mechanism of this three-component reaction involves the electrophilic activation of the carbonyl, followed by nucleophilic attack of the isocyanide generating the zwitterion **5** which was attacked by acetate anion leading to the intermediate **6** followed by 1,3 acyl migration to deliver α-acyloxyamide **7** (Scheme 3.2).[2] The Passerini reaction meets one of the main goals of green chemistry providing 100% atom-economy.



Scheme 3.2. Mechanism of the Passerini reaction

3.2.2. *O*-Arylative Passerini Reactions

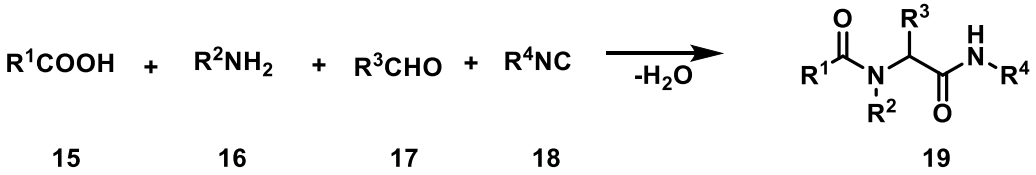
In 2006, Grimaud group reported an *O*-arylative Passerini reaction substituting the carboxylic acid with electron deficient phenols.[3] The key step of the conversion lies in an irreversible Smiles rearrangement of intermediate phenoxyimidate adducts. The phenoxide traps the resulting nitrilium intermediate **12**, generated from oxonium **11** and isocyanide **9,** forming imidate **13**. The latter undergoes a Smiles rearrangement to provide the more stable α-aryloxy amides **14** (Scheme 3.3).



Scheme 3.3. *O*-Arylative Passerini reactions

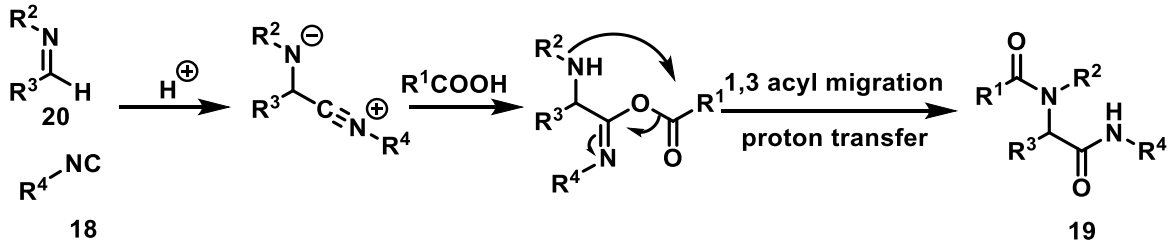
3.2.3. Ugi Reaction

Another important multicomponent reaction that utilizes carboxylic acids as one of the component is Ugi reaction. The Ugi reaction is a four-component reaction which is typically an expansion of the Passerini reaction with the addition of ammonia or a primary or secondary amine.[4] There is a possibility of competing Passerini reaction. However, high selectivity of Ugi product is observed in the case of this four-component reaction (Scheme 3.4).



Scheme 3.4. Ugi four-component reaction

The mechanism of Ugi reaction is similar to that of the Passerini Reaction. Condensation of the amine **16** and carbonyls **17** gives rise to an electrophilic iminium ion that reacts with the isocyanide and carboxylate to give the four-component Ugi product **19** *via* the acyl migration and proton transfer (Scheme 3.5).



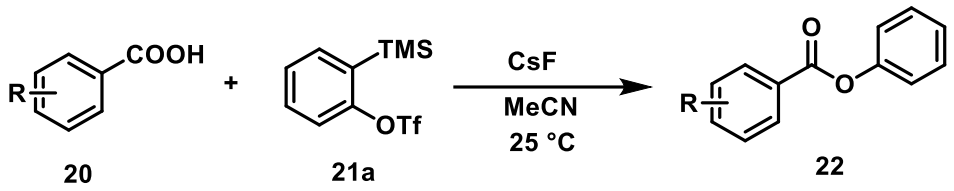
Scheme 3.5. Mechanism of the Ugi reaction

3.3. Reaction of Arynes with Carboxylic Acids

3.3.1. Arynes with Aromatic Carboxylic Acids

In 2003, Larock group has uncovered an efficient, mild, transition-metal-free method for the *O*-arylation of aromatic carboxylic acids **20** with arynes **21a**.[5] A variety carboxylic acids **20** with wide range of functional groups were well tolerated and delivered the ester products **22** in high yields. However, aliphatic carboxylic acids failed to give reasonable yields under the optimized reaction condtions. Apart from carboxylic acids

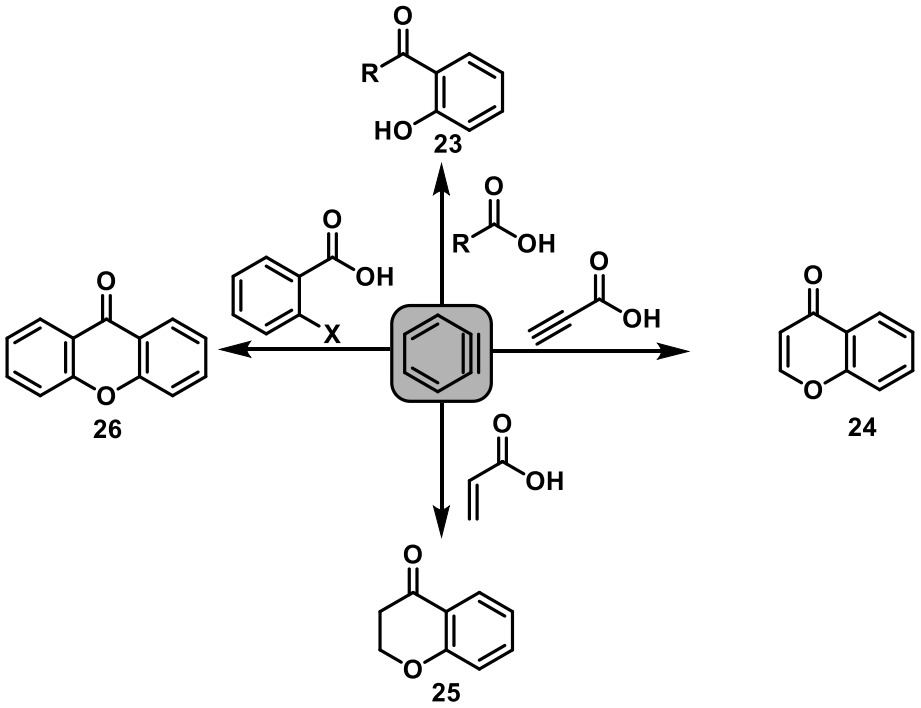
phenols could also be arylated using arynes to give diaryl ethers in good yields (Scheme 3.6).



Scheme 3.6. *O*-arylation of aromatic carboxylic acids

3.3.2. Arynes with Aliphatic Carboxylic Acids

In 2010, the same group has developed an efficient strategy to synthesize *o*-hydroxyaryl ketones **23**, 4-chromanones **24**, flavones **25**, xanthones **26**, and their analogues by aryne insertion into the C-O bond of readily available carboxylic acids (Scheme 3.7). This method could be employed for the synthesis of complex heterocycles and disubstituted arenes utilizing carboxylic acids.[6]

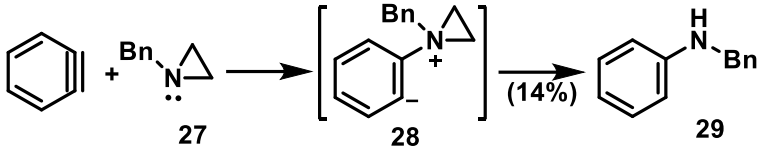


Scheme 3.7. Reaction of arynes with aliphatic carboxylic acids

3.4. Reaction of Arynes with Aziridines

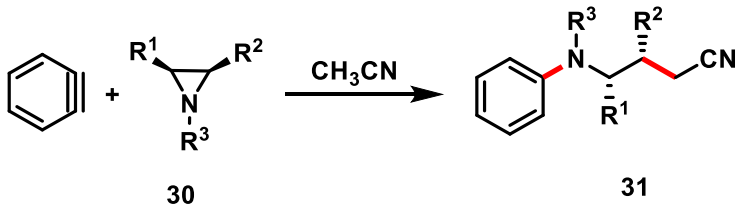
The reaction of arynes with aziridines **27** is known as early as 1971. Giumanini observed the formation of *N*-benzylaniline **29** when aziridine was treated with aryne

generated from chlorobenzene. The reaction generated the zwitterion **28** *via* the initial nucleophlic addition of aziridine to aryne. The ylide formation followed by acetylene elimination forms the benzylaniline product (Scheme 3.8).[7]



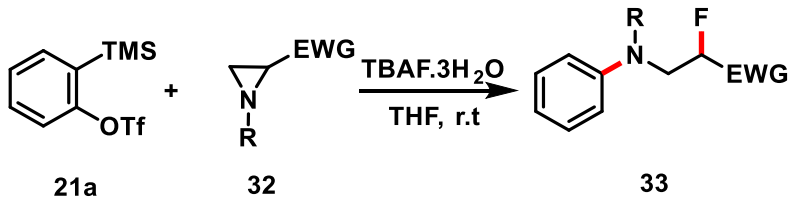
Scheme 3.8. Reaction of arynes with aziridines

In 2013, Larionov and co-workers developed three-component reaction of aziridines **30** with arynes and acetonitrile. Acetonitrile, well known for the aryl anion protonation was explored using this aziridine initiated MCC. The reaction afforded *N*-aryl γ-aminobutyronitriles **31** in moderate to good yields. The products obtained are congeners of a number of bioactive compounds, such as pregabalin and lergotrile. The reaction could tolerate azetidines as well, delivering δ-aminovaleronitriles (Scheme 3.9).[8]



Scheme 3.9. MCC involving arynes, aziridines and acetonitrile

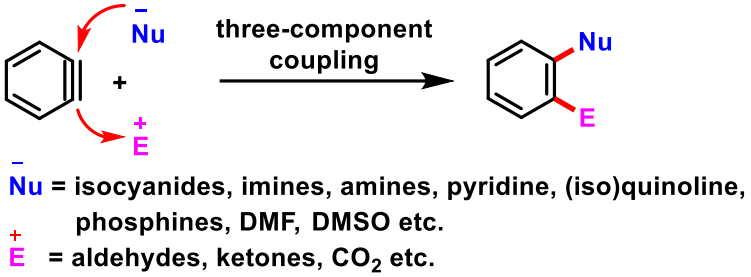
In 2014, Sha group reported the synthesis of α-fluoro-β-amino acid **33** derivatives using a multicomponent strategy. The nucleophilic addition of arynes and aziridines **32** followed by the ring opening by the fluoride anion delivered the fluorinated amino acid derivatives in good yields. This is a rare example of utilizing TBAF hydrate as a fluorinating reagent in aryne chemistry (Scheme 3.10).[9]



Scheme 3.10. TBAF as fluoride source in aryne MCC

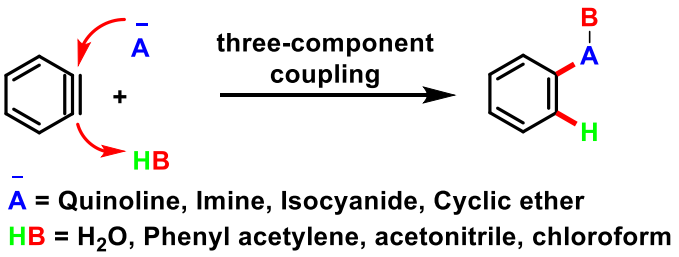
3.5. Statement of the Problem

Engaging arynes in MCCs is one of the transition-metal-free protocols for the synthesis of complex 1,2-disubstituted benzene derivatives and benzofused heterocycles. Usually in aryne MCCs the nucleophilic addition of the first component to aryne generates the zwitterionic intermediate which in turn is trapped using suitable electrophile (Scheme 3.11).[10] The nucleophiles include isocyanides,[11] imines,[12] amines,[13] N-heterocycles[14] such as pyridine, (iso)quinoline, phosphines,[15] and solvents such as THF,[11d] DMF[16] and DMSO.[17]



Scheme 3.11. General aryne MCCs

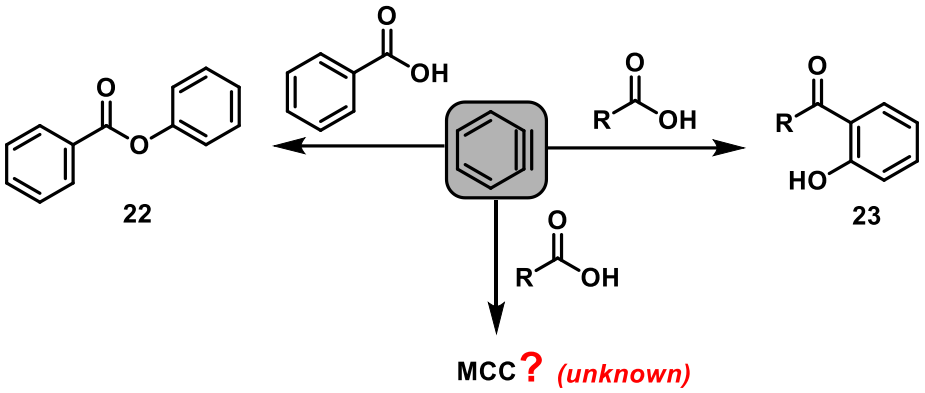
However, there are a class of aryne MCCs where the third component has an acidic proton which protonates the aryl anion. This protonation generates a pro-nucleophile which adds to complete the multicomponent process. These third components include phenyl acetylene, acetonitrile, H_2O, chloroform etc (Scheme 3.12).



Scheme 3.12. Aryne MCCs with proton rich third component

Utility of carboxylic acids in aryne multicomponent reactions is very broad. The *O*-arylation with the aromatic carboxylic acid and the C-O insertion with aliphatic carboxylic acids are eminent transformations in the history of aryne chemistry (Scheme 3.13). However, the use of carboxylic acids in aryne multicomponent coupling is not reported to the best of our knowledge. This could be due to the rapid formation of arylation product

with aromatic acids or insertion product with aliphatic acids, preventing their utility in aryne multicomponent coupling.



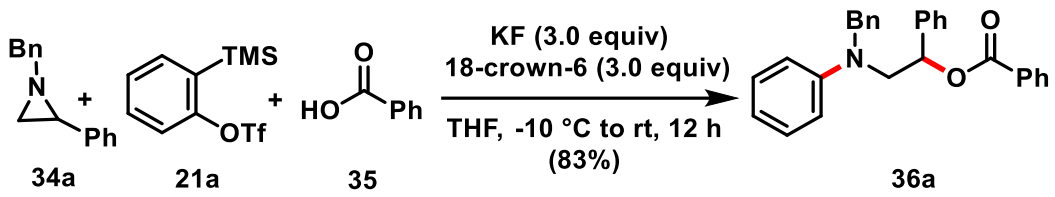
Scheme 3.13. Utility of carboxylic acids in aryne chemistry

To efficiently utilize carboxylic acids in multicomponent reactions one has to control the two-component reaction between the aryne and acid. A highly strained and electron rich nucleophile could be used as the initiator in the multicomponent reaction thus preventing the carboxylic acid addition to arynes. Aziridines are well explored in synthetic organic chemistry due to their high reactivity arising from the elevated ring strain. With a view to employ carboxylic acids in aryne MCCs we envisaged the use of aziridines as the nucleophilic trigger. Moreover, Cu-catalyzed aryne MCCs involving alkenyl aziridines and alkynes have been reported by Pineschi and co-workers.[18] A detailed study of the aryne MCCs with aziridine as the nucleophile utilizing carboxylic acids as an efficient multicomponent partner has been discussed in detail in the present chapter.

3.6. Results and Discussion

3.6.1. Optimization Studies

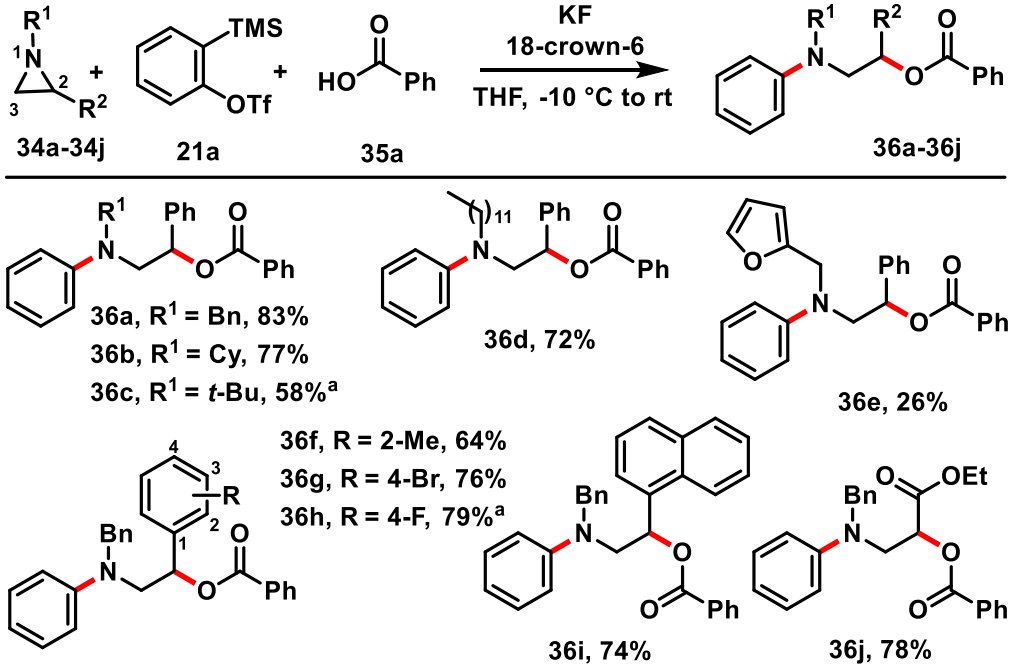
The present study was initiated by treating *N*-benzyl aziridine **34**, and benzoic acid **35**, with the aryne generated in situ from 2-(trimethylsilyl)aryl triflate **21a** using KF and 18-crown-6.[19] A facile reaction took place leading to the formation of 2-(benzyl(phenyl)amino)-1-phenylethyl benzoate **36a** in 83% yield (Scheme 3.14). It is noteworthy that under the present reaction conditions, the reaction proceeded in a three-component pathway rather than the well established insertion of aryne into the OH sigma bond of the acids or a CO insertion.



Scheme 3.14. MCC involving *N*-benzyl aziridine, aryne and benzoic acid

3.6.2. Synthesis of *N*-Aryl β-Amino Alcohol Derivatives

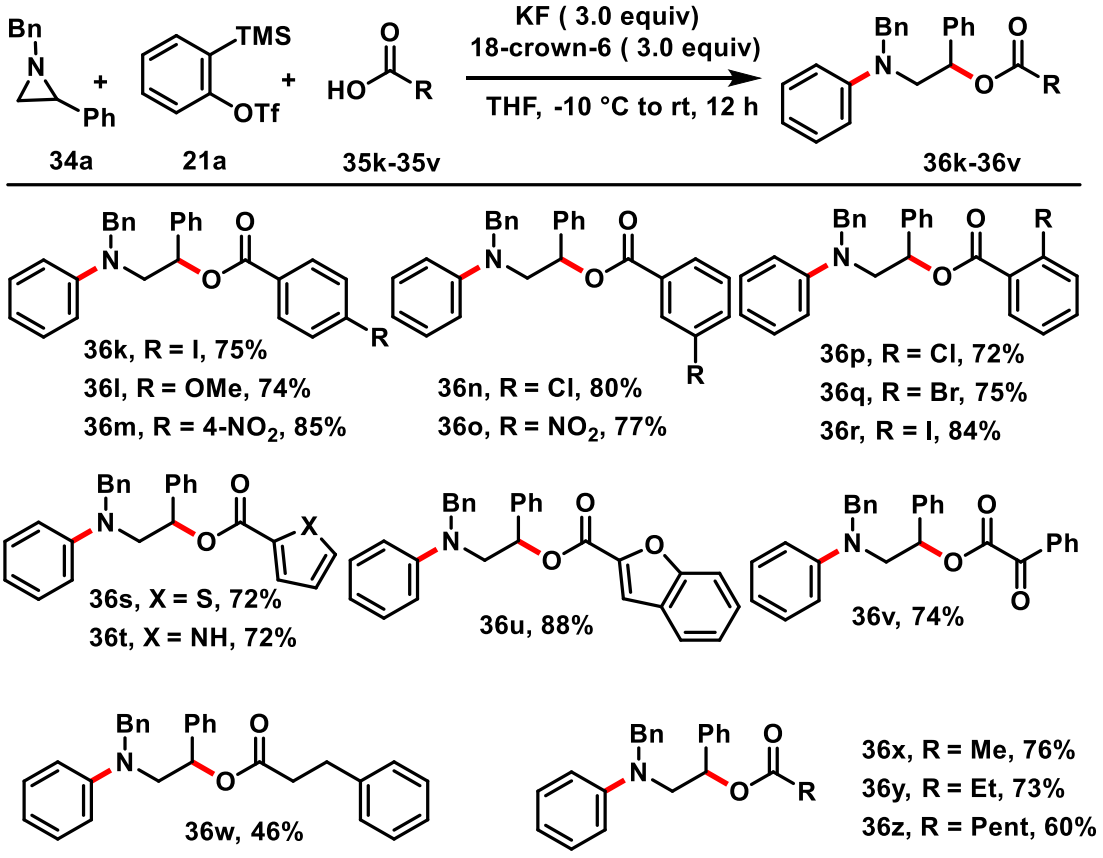
With the optimized reaction condition in hand, we then studied the scope of aziridines in this new aryne MCC. Interestingly, linear, branched and even sterically demanding substituent on aziridine nitrogen was found tolerable in the present methodology (Scheme 3.15). It has been found that good yields are maintained with a broad range of aziridines with different *N*-substituents (**36a-36d**). Interestingly, *N*-furyl substituted aziridine also gave the desired product (**36e**), though the yield is low. Moreover, aziridines with substitution at the 2-aryl ring also worked smoothly under the present condition (**36f-36i**). Additionally, the aziridines with ester substituents also gave the three-component product in very good yields (**36j**).



General conditions: **34** (0.50 mmol), **21a** (0.75 mmol), **35a** (0.75 mmol) KF (3.0 equiv), 18-crown-6 (3.0 equiv), THF (2.0 mL), -10 °C to rt, 12 h. Yields of the isolated products are given.

Scheme 3.15. Scope of aziridines

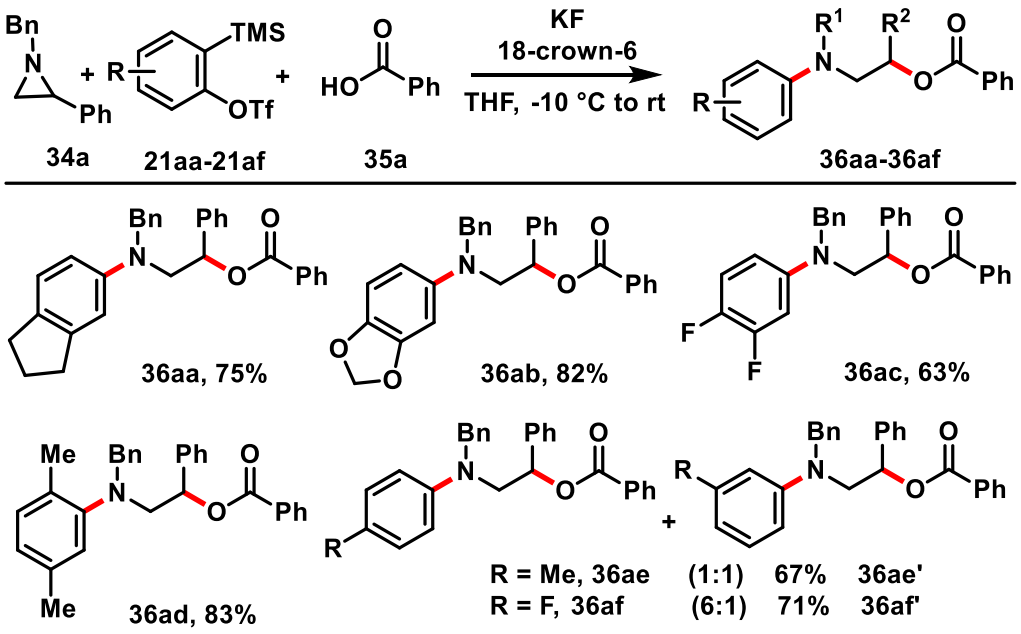
Next we started the screening of carboxylic acid component in this novel multicomponent coupling reaction (Scheme 3.16). Various carboxylic acids with both electron withdrawing and electron donating group at the 4 position of the acid worked very well under the present conditions (**36k-36i**). Different *ortho* and *meta* substituted carboxylic acids also underwent smooth conversion to the product (**36n-36r**). Gratifyingly various hererocyclic carboxylic acids furnished the desired products in moderate yields further expanding the scope of this aryne multicomponent reaction (**36s-36u**). Other carboxylic acids like phenylpropionic acid and phenylglyoxilic acid worked well to afford the products in moderate yields (**36v**, **36w**). Moreover, aliphatic acids including acetic acid and propionic acid were smoothly transformed into the desired products in high yields (**36x-36z**).



[a] General conditions: **34a** (0.50 mmol), **21a** (0.75 mmol), **35** (0.75 mmol) KF (3.0 equiv), 18-crown-6 (3.0 equiv), THF (2.0 mL), -10 °C to rt, 12 h. Yields of the isolated products are given.

Scheme 3.16. Scope of carboxylic acids

We next examined the effect of varying the substituents on the aryne precursor **21** (Scheme 3.17). Electronically dissimilar 4,5- disubstituted symmetrical aryne precursors readily furnished the MCC products derivatives in good yields (**36aa-36ac**). Also the 2,6 disubstituted aryne precursor also worked well under the preset optimised condition(**36ad**). As expected the unsymmetrical monosubstituted aryne precursors gave a mixture of regioisomers in good yields (**36ae, 36af**).



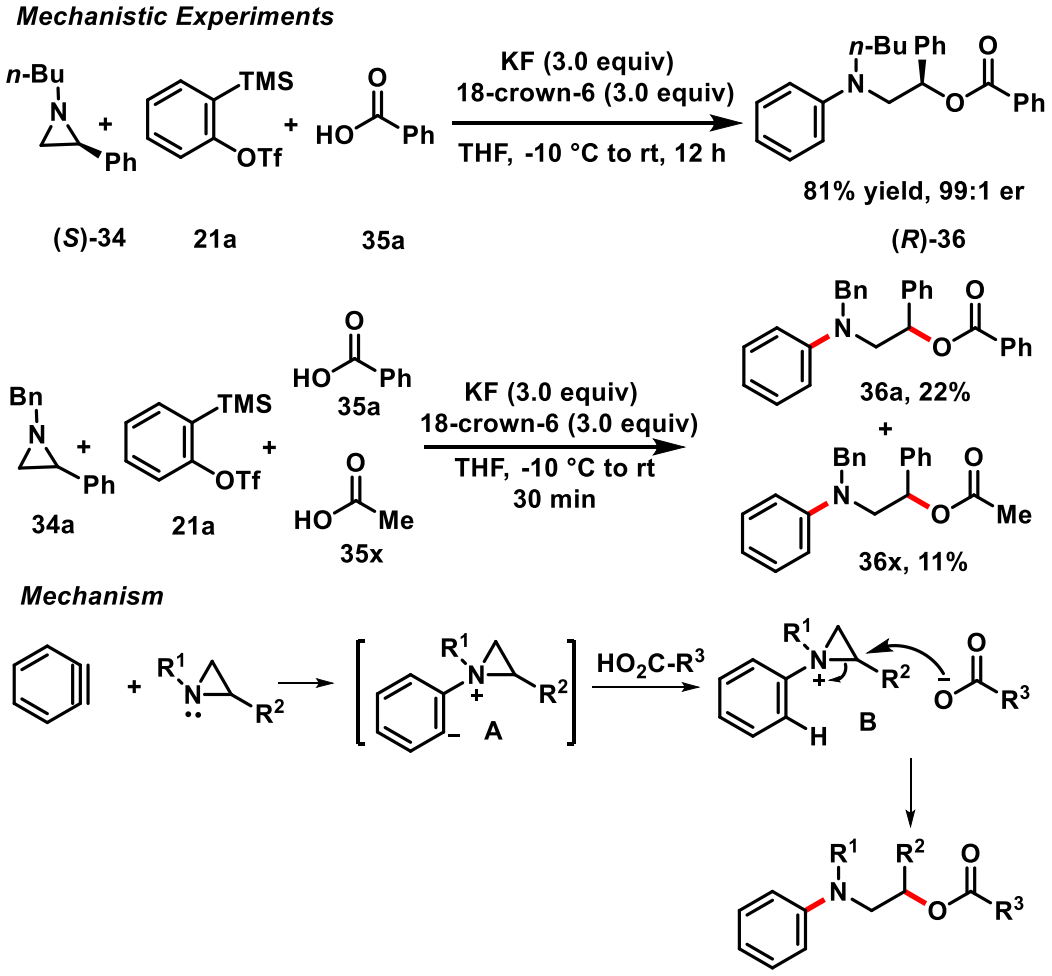
General conditions: **34a** (0.50 mmol), **21** (0.75 mmol), **35a** (0.75 mmol) KF (3.0 equiv), 18-crown-6 (3.0 equiv), THF (2.0 mL), -10 °C to rt, 12 h. Yields of the isolated products are given.

Scheme 3.17. Variation of arynes

3.6.3. Mechanistic Experiments and Mechanism

Further experiments have shed light on the mechanism of this transformation. The reaction using enantiomerically pure aziridine **(*S*)-34** with **21a** and **35a** under the optimized conditions afforded the chiral amino alcohol derivative **(*R*)-36** in 81% yield with retention of enantiopurity (Scheme 3.18). The formation of **(*R*)-36** in high er rules out the possibility of S_N1 opening of the intermediate **B**. Moreover, competition experiment carried out using **34a** and aryne generated from **21a** with aromatic acid **35a** and aliphatic acid **35x.** The results revealed that **35a** reacted almost two times faster than **35x** when the reaction was quenched after 30 minutes under the optimized conditions (Scheme 3.18). Similar result

was obtained when the reaction was quenched after 60 minutes (See experimental section). These results indicate that the aromatic acid being stronger can protonate the aryl anion intermediate **A** faster than the aliphatic acid.



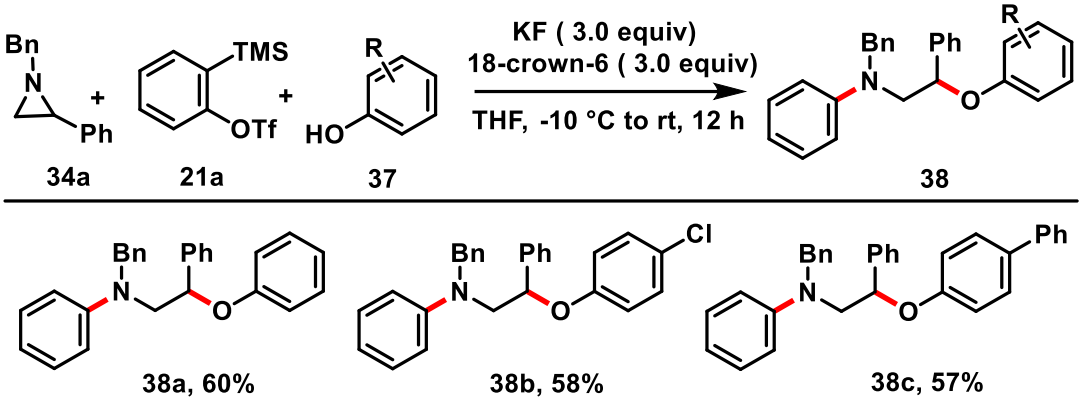
Scheme 3.18. Mechanistic experiments and mechanism

Based on the mechanistic experiments it was proposed that the reaction proceeds *via* the initial attack by aziridine onto aryne generating the 1,3 zwitterionic intermediate **A**. This intermediate gets protonated and the strained aziridinium ring **B** gets opened by carboxylate anion to deliver the final products.

3.6.4. Employing Phenols as Multicomponent Partner

The versatility of this novel aryne multicomponent reaction has been demonstrated by utilizing phenols as the acid component in the reaction. The treatment of aziridines **34a**

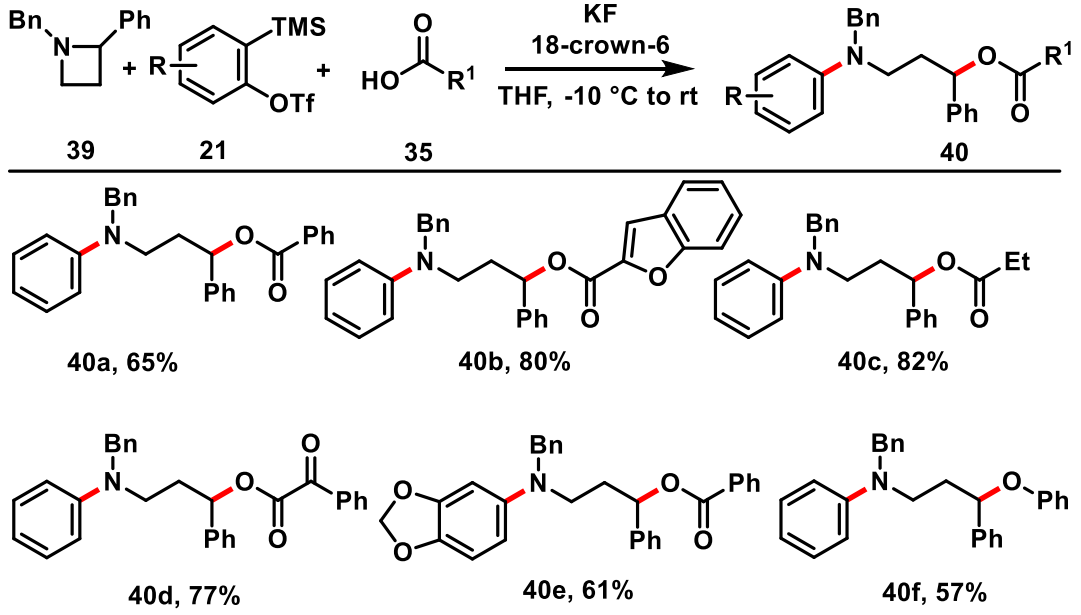
and aryne precursor **21a** with various phenols **37** resulted in the synthesis of the 2-phenoxy amine derivatives in moderate yields (**38a-38c**) (Scheme 3.19).[20]



Scheme 3.19. Phenols as multicomponent partner

3.6.5. Azetidines as Nucleophilic Trigger

It was found that the present aryne MCCs are not limited to *N*-substituted aziridines as the nucleophilic trigger, but instead *N*-substituted azetidines **39** afforded the corresponding *N*-aryl γ-amino alcohol derivatives in good yields (Scheme 3.20).



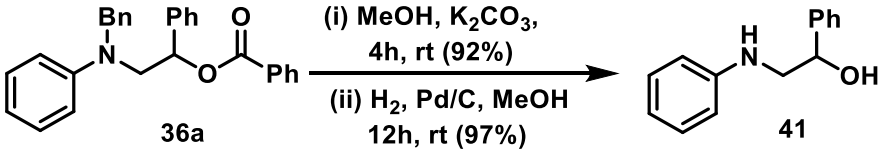
Scheme 3.20. MCCs Involving Arynes, Acids and Azetidines

The reaction worked well with aromatic, heteroaromatic and aliphatic carboxylic acids and in all cases, the desired product was formed in good yields (**40a-40c**). In addition,

α-ketoacid and 4,5-disubstituted symmetrical aryne generated from the precursor also underwent smooth aryne MCCs under the present conditions using azetidine as the nucleophilic trigger (**40d-40e**). In addition, phenol was also used as the acid surrogate in this reaction leading to the formation of the aryloxy derivative **40f** in 57% yield.

3.6.6. Synthesis of β-Amino Alcohol Derivative

The synthetic utility of the present methodology was further examined by the 2 step synthesis of β-amino alcohol **41** (Scheme 3.21). β-Amino alcohol derivatives like Isoetarine, Pindolol, Propranolol, Valinol, Sphingosine, Epinephrine, Noradrenalin are active compounds in biological systems. Since they are ubiquitous functionalities in biological systems, the present methodology give access to their synthesis under mild conditions and excellent yields.



Scheme 3.21. Synthesis of β-amino alcohol

3.7. Conclusion

In conclusion, we have developed a practical, high yielding and efficient multicomponent reaction involving aziridines, arynes and carboxylic acids. The reaction facilitated the transition metal free synthesis of β-amino alcohol derivatives in good yields. Moreover, unconventional multicomponent partners like phenols and peracids also were found tolerable with this novel multicomponent reaction. The synthetic utility of the methodology has been demonstrated by the two step synthesis of β-Amino alcohol derivative in excellent yield. Extensively broad substrate scope, high yields, and mild reaction conditions are the noteworthy features of the present reaction.[24]

3.8. Experimental Details

3.8.1. General Information

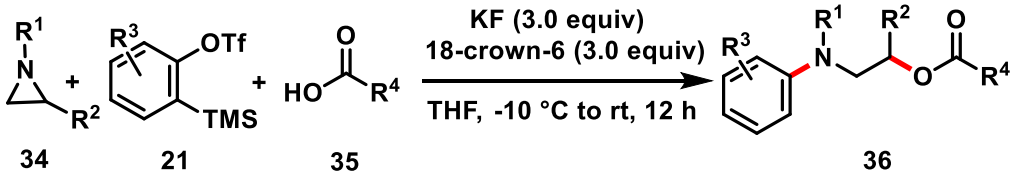
Unless otherwise specified, all reactions were carried out under an atmosphere of argon in flame-dried reaction vessels with Teflon screw caps. 30 °C corresponds to the room temperature of the lab when the experiments were carried out. THF was freshly

purified by distillation over Na-benzophenone and was transferred under argon. 18-Crown-6 was recrystallized from dry CH_3CN, and KF was dried by heating at 110 °C for 12 h and left to cool under argon and stored in an argon filled glove box. The acids and phenols were purchased from either Sigma Aldrich, Acros Organics or from other commercial sources and used as received without any further purification. All the aziridines and azetidine derivatives used in this study were prepared following the literature procedure.[21] The 2(trimethylsilyl)phenyl trifluoromethanesulfonate **21a** and the other symmetrical and unsymmetrical aryne precursors were synthesized following literature procedure.[22]

Analytical thin layer chromatography was performed on TLC Silica gel 60 F_{254}. Visualization was accomplished with short wave UV light. Chromatography was performed on silica gel (230-400 mesh) by standard techniques eluting with solvents as indicated.

All compounds were fully characterized. ^1H and ^{13}C NMR spectra were recorded on Bruker AV 400, 500 in solvents as indicated. Chemical shifts (δ) are given in ppm. The residual solvent signals were used as references and the chemical shifts converted to the TMS scale ($CDCl_3$: δH = 7.26 ppm, δC = 77.16 ppm). Infrared spectra were recorded on a Bruker Alpha-E Infrared Spectrophotometer as thin films using NaCl plates. The wave numbers (n) of recorded IR-signals are quoted in cm^{-1}. HRMS data were recorded on Thermo Scientific Q-Exactive, Accela 1250 pump. X-ray intensity data measurements were carried out on a Super Nova Dual source X-ray Diffractometer system (Agilent Technologies) with graphite monochromatized (Mo Kα= 0.71073Å) radiation. HPLC analysis was performed on Shimadzu Class-VP V6.12 SP5 with UV detector.

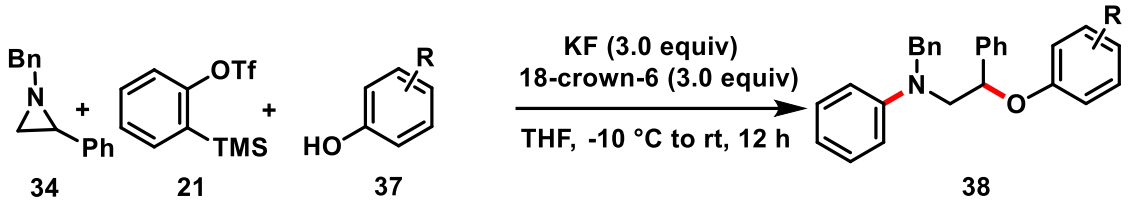
3.8.2. General Procedure for the MCC Involving Aziridines, Arynes and Carboxylic Acids



To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added the KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) inside a glove box. Carboxylic acid **35** (0.75 mmol) was added outside the glove box under argon atmosphere. The mixture was dissolved in THF (2.0 mL) under argon atmosphere and continued stirring

for five minutes at 30 °C. After five minutes of stirring, aziridine **34** (0.5 mmol) was added. Then the reaction mixture was cooled to -10 °C and kept stirring for five minutes. To the stirring solution, aryne precursor **21** (0.75 mmol) was added. Then the reaction mixture was slowly warmed to rt and kept stirring for 12 h. After 12 h the reaction was stopped, the solvent was evaporated and the crude residue pre-adsorbed on silica gel and purified by flash column chromatography (Pet. ether /EtOAc = 98/02) on silica gel to afford the corresponding *N*-aryl β-amino alcohol derivatives **36** in moderate to good yields.

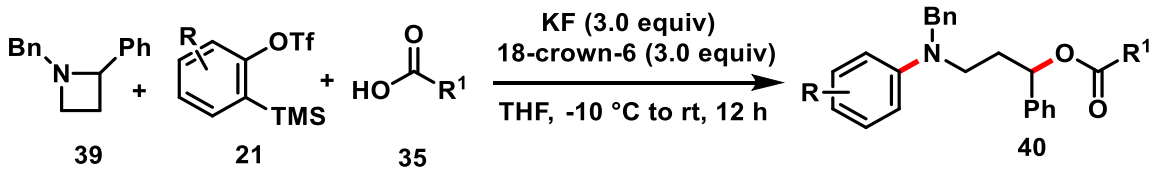
3.8.3. General Procedure for the MCC Involving Aziridines, Arynes and Phenols



34 21 37 38

To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added the KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) inside a glove box. Phenol **37** (0.75 mmol) was added outside the glove box under argon atmosphere. The mixture was dissolved in THF (2.0 mL) under argon atmosphere and continued stirring for five minutes at 30 °C. After five minutes of stirring, aziridine **34** (0.5 mmol) was added. Then the reaction mixture was cooled to -10 °C and kept stirring for five minutes. To the stirring solution aryne precursor **21**(0.75 mmol) was added. Then the reaction mixture was slowly warmed to rt and kept stirring for 12 h. After 12 h the reaction was stopped, the solvent was evaporated and the crude residue pre-adsorbed on silica gel and purified by flash column chromatography (Pet. ether /EtOAc = 98/02) on silica gel to afford the corresponding *N*-aryl β-amino alcohol derivatives **38** in moderate to good yields.

3.8.4. General Procedure for the MCC Involving Azetidines, Arynes and Carboxylic Acids



39 21 35 40

To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added the KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) inside a glove box. Carboxylic acid/Phenol **35/37** (0.75 mmol) was added outside the glove box under argon atmosphere. The mixture was dissolved in THF (2.0 mL) under argon atmosphere and continued stirring for five minutes at 30 °C. After five minutes of stirring, azetidine **39** (0.5 mmol) was added. Then the reaction mixture was cooled to -10 °C and kept stirring for five minutes. To the stirring solution, aryne precursor **21** (0.75 mmol) was added. Then the reaction mixture was slowly warmed to rt and kept stirring for 12 h. After 12 h the reaction was stopped, the solvent was evaporated and the crude residue pre-adsorbed on silica gel and purified by flash column chromatography (Pet. ether /EtOAc = 98/02) on silica gel to afford the corresponding *N*-aryl γ-amino alcohol derivatives **40** in moderate to good yields.

3.8.5. Competition Experiments

Experiment 1: Reaction quenched after 30 minutes

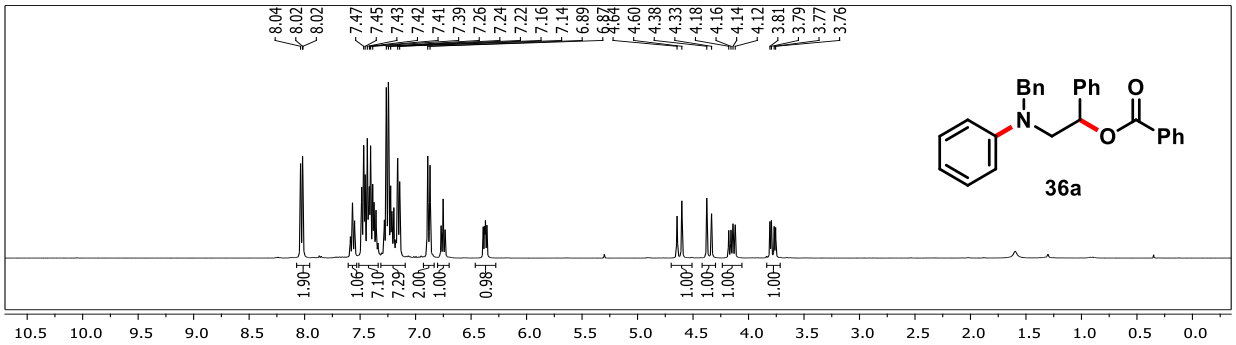
To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added the KF (0.044 g, 0.75 mmol) and 18-crown-6 (0.198 g, 0.75 mmol) inside a glove box. Benzoic acid **35a** (0.023 g, 0.188 mmol) and acetic acid **35x** (0.011 g, 11 μL, 0.188 mmol) were added outside the glove box under argon atmosphere. The mixture was dissolved in THF (1.0 mL) under argon atmosphere and continued stirring for five minutes at 30 °C. After five minutes of stirring, 1-benzyl-2-phenylaziridine **34a** (0.053 g, 0.25 mmol) was added. Then the reaction mixture was cooled to -10 °C and kept stirring for five minutes. To the stirring solution 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **21a** (0.112 g, 91 μL, 0.375 mmol) was added. Then the reaction mixture was slowly warmed to rt and kept stirring for 30 min. Then the reaction mixture was diluted with CH_2Cl_2 (2.0 mL) and filtered through a short pad of silica gel and eluted with CH_2Cl_2 (10.0 mL). The solvent was evaporated to obtain the crude products whose yield was determined by ^1H NMR analysis using CH_2Br_2 (18.0 μL, 0.25 mmol) as the internal standard.

Experiment 2: Reaction quenched after 60 minutes

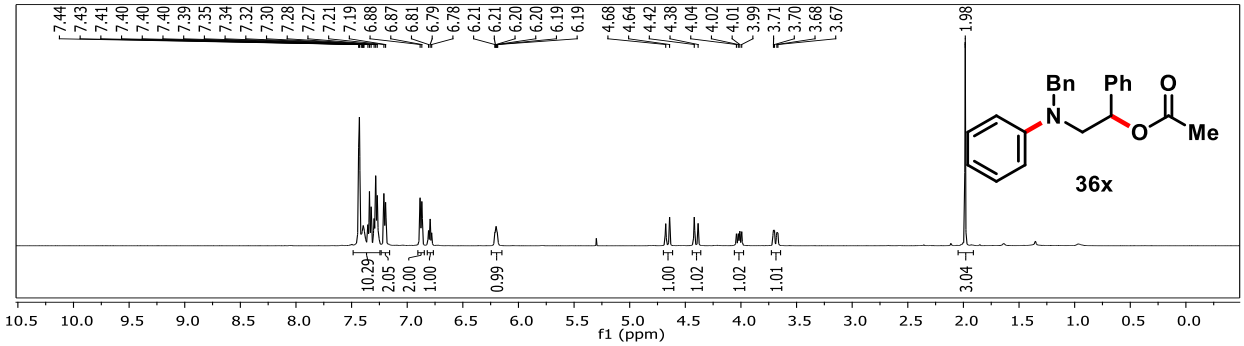
To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added the KF (44 mg, 0.75 mmol) and 18-crown-6 (198 mg, 0.75 mmol) inside a glove box. Benzoic acid **35a** (23 mg, 0.188 mmol) and acetic acid **35x** (11 mg, 11 μL, 0.188

mmol) were added outside the glove box under argon atmosphere. The mixture was dissolved in THF (1.0 mL) under argon atmosphere and continued stirring for five minutes at 30 °C. After five minutes of stirring, 1-benzyl-2-phenylaziridine **34a** (0.053 g, 0.25 mmol) was added. Then the reaction mixture was cooled to -10 °C and kept stirring for five minutes. To the stirring solution 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **21a** (0.112 g, 91 µL, 0.375 mmol) was added. Then the reaction mixture was slowly warmed to rt and kept stirring for 60 min. Then the reaction mixture was diluted with CH_2Cl_2 (2.0 mL) and filtered through a short pad of silica gel and eluted with CH_2Cl_2 (10.0 mL). The solvent was evaporated to obtain the crude products whose yield was determined by ^{1}H NMR analysis using CH_2Br_2 (18.0 µL, 0.25 mmol) as the internal standard.

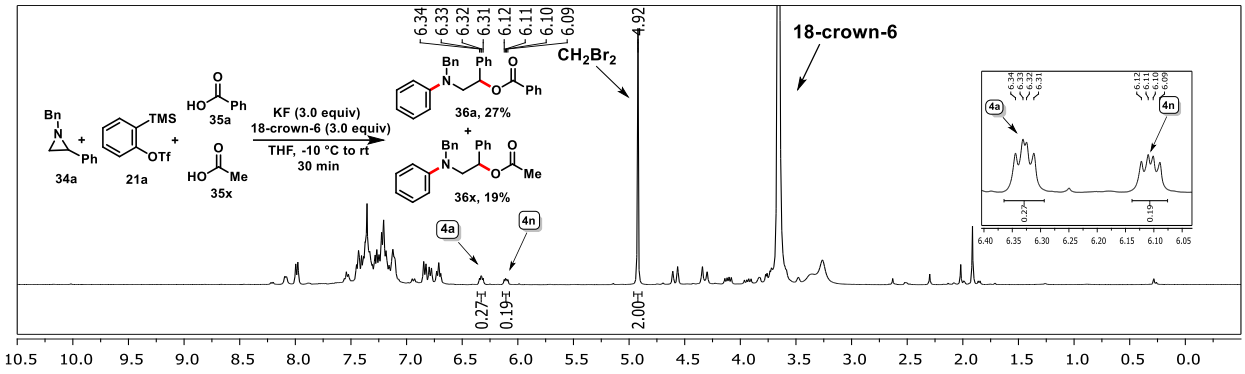
^{1}H NMR (400 MHz) Spectra of 2-(benzyl(phenyl) amino)-1-phenylethyl benzoate (36a)



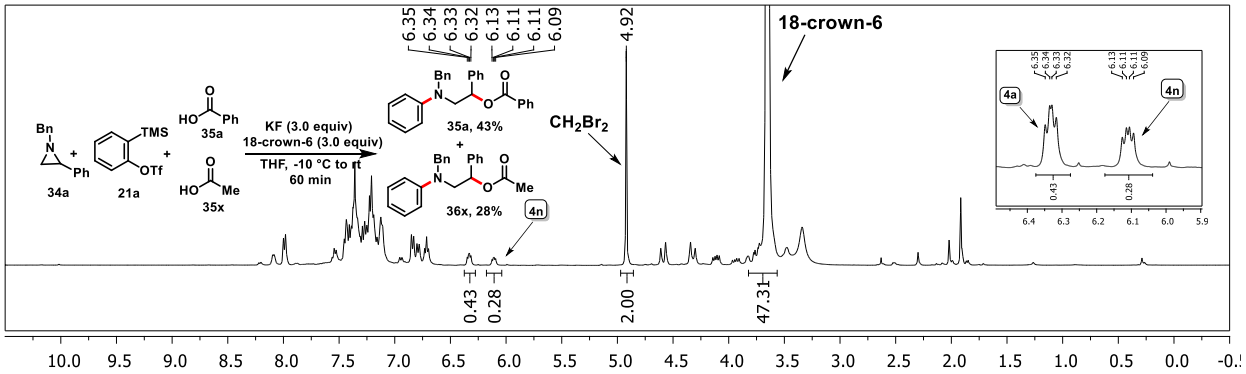
^{1}H NMR (400 MHz) Spectra of 2-(benzyl(phenyl)amino)-1-phenylethyl acetate (36x)



^{1}H-NMR (400 MHz) of Reaction Mixture after 30 minutes

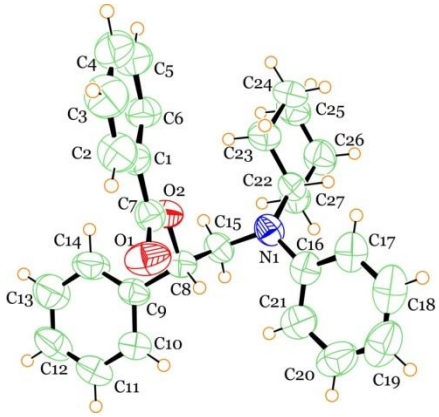


^{1}H-NMR (400 MHz) of Reaction Mixture after 60 minutes



3.8.6. X-ray data of 36b

Crystal data of **36b** $C_{27}H_{29}NO_2$, M = 399.51, colorless block, 0.45 x 0.32 x 0.26 mm^3, monoclinic, space group *P*-2_1/c, *a* = 15.5737(5) Å, *b* = 12.7774(4) Å, *c* = 11.4615 (3) Å, α = 90.00°, β = 91.399(3)°, γ = 90.00°, *V* = 2280.08 (12) $Å^3$, Z = 4, *T* = 298 K, ρ_{calc}mg/mm^3 = 1.164, m/mm^{-1} = 0.072, F(000) = 856.0, Crystal size/mm^3 = 0.4 × 0.2 × 0.2, 2Θ range for data collection = 6.38 to 58.02°, Index ranges = $-21 \leq h \leq 11$, $-4 \leq k \leq 16$, $-11 \leq l \leq 15$, Reflections collected = 10221, Independent reflections = 5313[R(int) = 0.0280], Data/restraints/parameters = 5313/0/271, Goodness-of-fit on F^2 = 1.095, Final R indexes [I>=2σ (I)] = R_1 = 0.0678, wR_2 = 0.1884, Final R indexes [all data] = R_1 = 0.1180, wR_2 = 0.2219, Largest diff. peak/hole / e $Å^{-3}$ = 0.34/-0.15

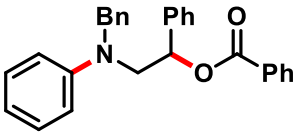


Crystal structure of **36b** (thermal ellipsoids are shown with 50% probability).

CCDC-1050176 (**36b**) contains the supplementary crystallographic data. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

3.8.7. Synthesis and Characterization of *N*-Aryl β/γ-Amino Alcohol Derivatives

2-(Benzyl(phenyl)amino)-1-phenylethyl benzoate (36a)



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **34a** (0.105 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **21a** (0.223 g, 182 μL, 0.75 mmol) with benzoic acid **35a** (0.92 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-(benzyl(phenyl) amino)-1-phenylethyl benzoate as a colourless oil **36a** (0.170 g, 83% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.53.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 7.2 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.48-7.34 (m, 7H), 7.28-7.18 (m, 5H), 7.15 (d, *J* = 7.2 Hz, 2H), 6.88 (d, *J* = 8.3 Hz, 2H), 6.75 (t, *J* = 7.2 Hz, 1H), 6.39-6.36 (m, 1H), 4.62 (d, *J* = 17.2 Hz, 1H), 4.35 (d, *J* = 17.3 Hz, 1H), 4.15 (dd, J_1 = 8.1 Hz, J_2 = 15.4 Hz, 1H), 3.78 (dd, J_1 = 5.2 Hz, J_2 = 15.3 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 148.4, 138.9, 138.4, 133.1, 130.2, 129.8, 129.4, 128.8, 128.7, 128.5, 128.5, 126.9, 126.7, 126.6, 117.1, 112.8, 74.6, 56.8, 54.7.

HRMS (ESI) calculated $[M+H]^+$ for $C_{28}H_{26}O_2N$: 408.1958, found: 408.1957.

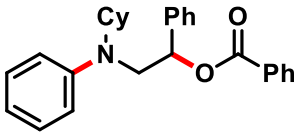
FTIR (cm^{-1}) 3022, 2929, 2358, 1718, 1598, 1503, 1451, 1359, 1311, 1268, 1217, 1108, 995, 767.

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 147.9, 139.0, 133.1, 130.2, 129.8, 129.4, 128.72 128.4, 128.3, 126.5, 116.3, 112.4, 74.5, 56.8, 51.3, 28.9, 20.3, 14.0.

HRMS (ESI) calculated $[M+Na]^+$ for $C_{25}H_{28}O_2N$: 374.2115, found: 374.2114.

FTIR (cm^{-1}) 3022, 2957, 2870, 1719, 1598, 1502, 1456, 1216, 1108, 987, 763, 705.

2-(Cyclohexyl(phenyl)amino)-1-phenylethyl benzoate (36b)



Following the general procedure, treatment of 1-cyclohexyl-2-phenylaziridine **34b** (0.101 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **21a** (0.223 g, 182 μL, 0.75 mmol) with benzoic acid **35a** (0.92 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-(cyclohexyl(phenyl)amino)-1-phenylethyl benzoate as a white solid **36b** (0.154 g, 77% yield). CCDC-1050176 (**36b**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

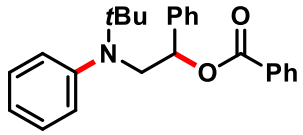
***R*$_f$** (Pet. ether /EtOAc = 95/05): 0.61.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.2 Hz, 2H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.47-7.41 (m, 4H), 7.38 (t, *J* = 7.2 Hz, 2H), 7.32 (t, *J* = 7.2 Hz, 1H), 7.29-7.25 (m, 2H), 6.98 (d, *J* = 8.2 Hz, 2H), 6.78 (t, *J* = 7.2 Hz, 1H), 6.19-6.17 (m, 1H), 3.88 (dd, J_1 = 8.2 Hz, J_2 = 15.2 Hz, 1H), 3.54 (dd, J_1 = 5.1 Hz, J_2 = 15.3 Hz, 1H), 3.50-3.47 (m, 1H), 1.88-1.77 (m, 3H), 1.66 (d, *J* = 10.6 Hz, 2H), 1.48-1.40 (m, 1H), 1.35-1.25 (m, 3H), 1.15-1.09 (m, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 165.9, 149.1, 139.5, 133.0, 130.4, 129.9, 129.2, 128.6, 128.4, 128.3, 126.6, 117.9, 115.7, 75.4, 59.8, 50.7, 31.2, 30.7, 26.4, 26.3, 26.0.

HRMS (ESI) calculated $[M+H]^+$ for $C_{27}H_{30}O_2N$: 400.2271, found: 400.2273. **FTIR (cm^{-1})** 3022, 2934, 2858, 2357, 1719, 1597, 1498, 1452, 1269, 1218, 1168, 1110, 1024, 760, 705.

2-(*tert*-Butyl(phenyl)amino)-1-phenylethyl benzoate (36c)



Following the general procedure, treatment of 1-(tert-butyl)-2-phenylaziridine **34c** (0.044 g, 0.25 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **21a** (0.112 g, 91 μL, 0.375 mmol) with benzoic acid **35a** (0.046 g, 0.375 mmol) in the presence of KF (0.044 g, 0.75 mmol) and 18-crown-6 (0.198 g, 0.75 mmol) in THF (1.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 99.5/0.5) of the crude reaction mixture using silica gel afforded 2-(*tert*-butyl(phenyl)amino)-1-phenylethyl benzoate as a colourless oil **36c** (0.054 g, 58% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.57.

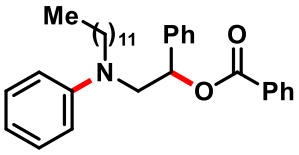
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 7.3 Hz, 2H), 7.57-7.43 (m, 3H), 7.37-7.29 (m, 7H), 7.22-7.19 (m, 3H), 5.86-5.83 (m, 1H), 3.75 (dd, J_1 = 8.8 Hz, J_2 = 5.3 Hz, 1H), 3.55 (dd, J_1 = 4.3 Hz, J_2 = 9.6 Hz, 1H), 1.11 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.77, 149.24, 139.81, 132.81, 130.68, 129.81, 128.41, 128.34, 128.29, 127.88, 126.68, 125.39, 76.47, 55.52, 55.22, 28.40.

HRMS (ESI) calculated $[M+H]^+$ for $C_{25}H_{28}O_2N$: 374.2115, found: 374.2114.

FTIR (cm^{-1}) 3022, 2972, 2930, 2866, 1715, 1594, 1489, 1457, 1362, 1273, 930, 670.

2-(Dodecyl(phenyl)amino)-1-phenylethyl benzoate (36d)



Following the general procedure, treatment of 1-dodecyl-2-phenylaziridine **34d** (0.144 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **21a** (0.223 g, 182 μL, 0.75 mmol) with benzoic acid **35a** (0.92 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-(dodecyl(phenyl)amino)-1-phenylethyl benzoate as a colourless oil **36d** (0.192 g, 72% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.56.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.4 Hz, 2H), 7.59 – 7.52 (m, 1H), 7.49 – 7.41 (m, 4H), 7.38 (t, *J* = 7.4 Hz, 2H), 7.33 (t, *J* = 7.3 Hz, 1H), 7.27 – 7.22 (m, 2H), 6.80 (d, *J* = 8.3 Hz, 2H), 6.70 (t, *J* = 7.2 Hz, 1H), 6.24 (dd, J_1 = 5.4 Hz, J_2 = 7.8 Hz, 1H), 3.97 (dd, J_1 =

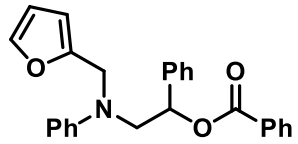
7.9 Hz, J_2 = 15.3 Hz, 1H), 3.63 (dd, J_1 = 5.3 Hz, J_2 = 15.3 Hz, 1H), 3.32 – 3.22 (m, 1H), 3.15 – 3.03 (m, 1H), 1.31-1.23 (m, 20H), 0.89 (t, J = 6.9 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 165.9, 148.0, 139.1, 133.1, 130.3, 129.8, 129.4, 128.8, 128.5, 128.4, 126.6, 116.4, 112.5, 74.6, 56.9, 51.7, 32.1, 29.8, 29.6, 29.5, 27.2, 26.8, 22.8, 14.3.

HRMS (ESI) calculated $[M+H]^+$ for $C_{33}H_{44}O_2N$: 486.3367, found: 486.3363.

FTIR (cm^{-1}) 3022, 2927, 2858, 2433, 1718, 1598, 1507, 1216, 1110, 772, 673.

2-((Furan-2-ylmethyl)(phenyl)amino)-1-phenylethyl benzoate (36e)



Following the general procedure, treatment of 1-(furan-2-ylmethyl)-2-phenylaziridine **34e** (0.105 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **21a** (0.223 g, 182 μL, 0.75 mmol) with benzoic acid **35a** (0.92 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-((furan-2-ylmethyl)(phenyl)amino)-1-phenylethyl benzoate as a colourless oil **36e** (0.051 g, 26% yield).

***R*$_f$** (Pet. ether /EtOAc = 95/05): 0.49.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (d, J = 7.4 Hz, 2H), 7.60 (t, J = 6.9 Hz, 1H), 7.55-7.36 (m, 7H), 7.34 (s, 1H), 7.29 (t, J = 7.2 Hz, 2H), 6.97 (d, J = 7.8 Hz, 2H), 6.80 (t, J = 6.9 Hz, 1H), 6.45-6.21 (m, 2H), 6.13 (s, 1H), 4.53 (d, J = 16.9 Hz, 1H), 4.31 (d, J = 16.9 Hz, 1H), 4.12 (dd, J_1 = 8.0 Hz, J_2 = 15.3 Hz, 1H), 3.76 (dd, J_1 = 4.2 Hz, J_2 = 15.4 Hz, 1H).

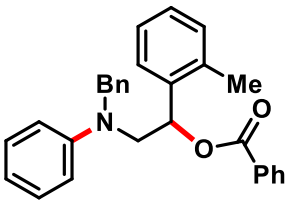
^{13}C NMR (125 MHz, $CDCl_3$) δ 165.9, 152.0, 148.1, 141.9, 138.9, 133.2, 130.2, 129.8, 129.4, 128.8, 128.5, 126.6, 117.5, 113.0, 110.3, 107.6, 74.6, 56.5, 48.1.

HRMS (ESI) calculated $[M+H]^+$ for $C_{26}H_{24}O_3N$: 398.1751, found: 398.1748.

FTIR (cm^{-1}) 3022, 2357, 1717, 1597, 1506, 1267, 1217, 1109, 1028, 766, 672.

2-(Benzyl(phenyl)amino)-1-(*o*-tolyl)ethyl benzoate (36f)

Following the general procedure, treatment of 1-benzyl-2-(o-tolyl)aziridine **34f** (0.056 g, 0.25 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **21a** (0.111 g, 91 μL, 0.38 mmol) with benzoic acid **35a** (0.046 g, 0.38 mmol) in the presence of KF (0.044 g,



0.75 mmol) and 18-crown-6 (0.198 g, 0.75 mmol) in THF (1.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-(benzyl(phenyl)amino)-1-(*o*-tolyl)ethyl benzoate as a colourless oil **36f** (0.068 g, 64% yield).

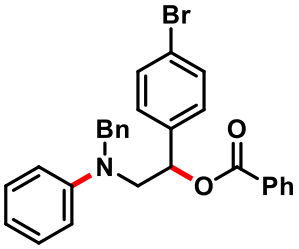
***R*f** (Pet. ether /EtOAc = 95/05): 0.39.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.1 Hz, 2H), 7.59-7.54 (m, 2H), 7.46-7.43 (m, 2H), 7.29-7.19 (m, 10H), 6.95 (d, *J* = 7.1 Hz, 2H), 6.78 (t, *J* = 6.9 Hz, 1H), 6.61-6.59 (m, 1H), 4.65 (d, *J* = 16.8 Hz, 1H), 4.40 (d, *J* = 16.8 Hz, 1H), 4.19 (dd, J_1 = 7.7 Hz, J_2 = 15.2 Hz, 1H), 3.77 (dd, J_1 = 4.7 Hz, J_2 = 15.2 Hz, 1H), 2.46 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 165.9, 148.2, 138.1, 137.3, 135.8, 133.1, 130.8, 130.2, 129.8, 129.4, 128.7, 128.5, 128.3, 127.1, 126.9, 126.6, 126.3, 117.6, 113.2, 71.3, 56.0, 54.7, 19.5. **HRMS (ESI)** calculated $[M+Na]^+$ for $C_{29}H_{27}O_2NNa$: 444.1934, found: 444.1937.

FTIR (cm^{-1}) 3057, 2357, 1718, 1598, 1503, 1354, 1271, 1106, 763.

2-(Benzyl(phenyl)amino)-1-(4-bromophenyl)ethyl benzoate (36g)



Following the general procedure, treatment of 1-benzyl-2-(4-bromophenyl)aziridine **34g** (0.144 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **21a** (0.223 g, 182 µL, 0.75 mmol) with benzoic acid **35a** (0.92 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-(benzyl(phenyl)amino)-1-(4-bromophenyl)ethyl benzoate as a colourless oil **36g** (0.185 g, 76% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.54.

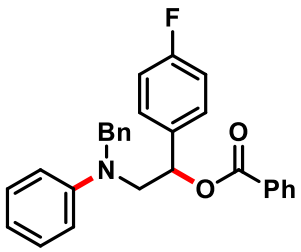
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, *J* = 7.4 Hz, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.53 (d, *J* = 8.4 Hz, 2H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.34 (d, *J* = 8.3 Hz, 2H), 7.24 (m, 5H), 7.15 (d, *J* = 7.4 Hz, 2H), 6.88 (d, *J* = 8.2 Hz, 2H), 6.78 (t, *J* = 7.2 Hz, 1H), 6.31 (dd, J_1 = 5.6 Hz, J_2 =7.7 Hz, 1H), 4.62 (d, *J* = 17.2 Hz, 1H), 4.35 (d, *J* = 17.2 Hz, 1H), 4.13 (dd, J_1 = 7.9 Hz, J_2 = 15.3 Hz, 1H), 3.74 (dd, J_1 = 5.4 Hz, J_2 =15.3 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 165.8, 148.2, 138.2, 138.0, 133.3, 132.0, 129.9, 129.8, 129.5, 128.7, 128.5, 128.3, 127.0, 126.7, 122.5, 117.4, 112.9, 73.9, 56.6, 55.0.

HRMS (ESI) calculated $[M+H]^+$ for $C_{28}H_{25}O_2NBr$: 486.1063, found: 486.1063.

FTIR (cm^{-1}) 3021, 2404, 2358, 1719, 1498, 1357, 1266, 1216, 1107, 770.

2-(Benzyl(phenyl)amino)-1-(4-fluorophenyl)ethyl benzoate (36h)



Following the general procedure, treatment of 1-benzyl-2-(4-fluorophenyl)aziridines **34h** (0.057 g, 0.25 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **21a** (0.111 g, 91 μL, 0.38 mmol) with benzoic acid **35a** (0.046 g, 0.38 mmol) in the presence of KF (0.044 g, 0.75 mmol) and 18-crown-6 (0.198 g, 0.75 mmol) in THF (1.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-(benzyl(phenyl)amino)-1-(4-fluorophenyl)ethyl benzoate as a colourless oil **36h** (0.084 g, 79% yield).

***R*$_f$** (Pet. ether /EtOAc = 95/05): 0.44.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.4 Hz, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.48-7.44 (m, 4H), 7.30-7.21 (m, 5H), 7.18 (d, *J* = 7.4 Hz, 2H), 7.11 (t, *J* = 8.6 Hz, 2H), 6.91 (d, *J* = 8.1 Hz, 2H), 6.79 (t, *J* = 7.2 Hz, 1H), 6.37 (dd, J_1 = 5.4 Hz, J_2 = 7.6 Hz, 1H), 4.64 (d, *J* = 17.2 Hz, 1H), 4.37 (d, *J* = 17.2 Hz, 1H), 4.17 (dd, J_1 = 7.8 Hz, J_2 = 15.2 Hz, 1H), 3.77 (dd, J_1 = 5.4 Hz, J_2 = 15.2 Hz, 1H).

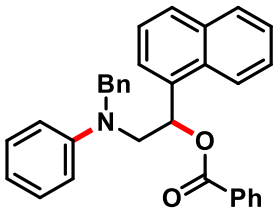
^{13}C NMR (125 MHz, $CDCl_3$) δ 165.78, 162.77 (d, *J* = 247.1 Hz), 148.10, 138.09, 134.71 (d, *J* = 2.9 Hz), 133.2, 130.0, 129.8, 129.5, 128.7, 128.5, 128.4 (d, *J* = 8.2 Hz), 127.0, 126.7, 117.5, 115.8 (d, *J* = 21.7 Hz), 113.0, 73.8, 56.7, 55.0.

HRMS (ESI) calculated $[M+H]^+$ for $C_{28}H_{25}O_2NF$: 426.1864, found: 426.1863.

FTIR (cm^{-1}) 3021, 2931, 2357, 1719, 1600, 1506, 1451, 1358, 1268, 1221, 1107, 1028, 761.

2-(Benzyl(phenyl)amino)-1-(naphthalen-1-yl)ethyl benzoate (36i)

Following the general procedure, treatment of 1-benzyl-2-(naphthalen-1-yl)aziridines **34i** (0.065 g, 0.25 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **21a** (0.111 g, 91 μL, 0.38 mmol) with benzoic acid **35a** (0.046 g, 0.38 mmol) in the presence of KF



(0.044 g, 0.75 mmol) and 18-crown-6 (0.198 g, 0.75 mmol) in THF (1.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-(benzyl(phenyl)amino)-1-(naphthalen-1-yl)ethyl benzoate as a colourless oil **36i** (0.085 g, 74% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.59.

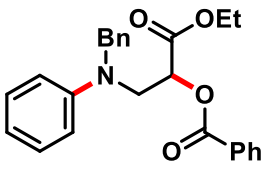
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26-8.24 (m, 1H), 8.08 (d, *J* = 7.2 Hz, 2H), 7.95-7.93 (m, 1H), 7.89 (d, *J* = 8.2 Hz, 1H), 7.75 (d, *J* = 6.9 Hz, 1H), 7.61-7.55 (m, 3H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.47 (t, *J* = 7.8 Hz, 2H), 7.32-7.27 (m, 4H), 7.25-7.15 (m, 4H), 6.99 (d, *J* = 8.0 Hz, 2H), 6.83 (t, *J* = 7.2 Hz, 1H), 4.60 (d, *J* = 16.9 Hz, 1H), 4.43-4.35 (m, 2H), 4.02 (dd, J_1 = 4.8 Hz, J_2 = 15.4 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 165.9, 148.3, 138.1, 135.0, 133.9, 133.1, 130.7, 130.1, 129.8, 129.4, 129.1, 129.0, 128.7, 128.5, 127.0, 126.9, 126.7, 126.0, 125.5, 124.6, 123.3, 117.5, 113.4, 72.2, 56.2, 54.8.

HRMS (ESI) calculated $[M+H]^+$ for $C_{32}H_{28}O_2N$: 458.2115, found: 458.2117.

FTIR (cm^{-1}) 3022, 2403, 2358, 1718, 1598, 1510, 1434, 1267, 1216, 770, 672.

3-(Benzyl(phenyl)amino)-1-ethoxy-1-oxopropan-2-yl benzoate (36j)



Following the general procedure, treatment of ethyl 1-benzylaziridine-2-carboxylate **34j** (0.103 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **21a** (0.223 g, 182 μL, 0.75 mmol) with benzoic acid **35a** (0.92 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 3-(benzyl(phenyl)amino)-1-ethoxy-1-oxopropan-2-yl benzoate as yellow oil **34j** (0.158 g, 78% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.47.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.8 Hz, 2H), 7.47 (t, *J* = 7.3 Hz, 1H), 7.31 (t, *J* = 7.7 Hz, 2H), 7.20- 7.09 (m, 7H), 6.77 (d, *J* = 8.4 Hz, 2H), 6.66 (t, *J* = 7.2 Hz, 1H), 5.49 (dd, J_1 = 3.5 Hz, J_2 = 8.3 Hz, 1H), 4.63 (q, *J* = 17.2 Hz, 2H), 4.17-4.10 (m, 2H), 4.04 (dd, J_1

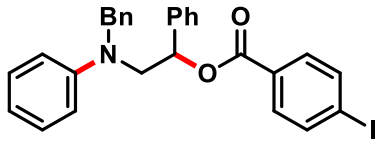
= 3.5 Hz, J_2 = 15.6 Hz, 1H), 3.95 (dd, J_1 = 8.4 Hz, J_2 = 15.7Hz, 1H), 1.19 (t, J = 7.1 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 169.0, 166.1, 147.9, 138.2, 133.4, 130.0, 129.400, 129.2, 128.7, 128.5, 127.0, 126.6, 117.6, 113.0, 72.1, 61.88, 55.1, 52.4, 14.2.

HRMS (ESI) calculated $[M+Na]^+$ for $C_{25}H_{26}O_4N$: 404.1856, found: 404.1855.

FTIR (cm^{-1}) 3202, 2357, 1729,1709, 1599, 1502, 1452, 1359, 1267, 1218, 1108, 1029, 953, 760.

2-(Benzyl(phenyl)amino)-1-phenylethyl 4-iodobenzoate (36k)



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **34a** (0.105 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **21a** (0.223 g, 182 μL, 0.75 mmol) with 4-iodobenzoic acid **35k** (0.186 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-(benzyl(phenyl) amino)-1-phenylethyl 4-iodobenzoate as a colourless oil **36k** (0.200 g, 75% yield).

R f (Pet. ether /EtOAc = 95/05): 0.54.

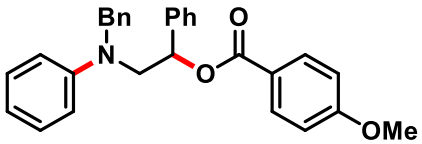
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, J = 8.3 Hz, 2H), 7.72 (d, J = 8.3 Hz, 2H), 7.50-7.48 (m, 2H), 7.45-7.38 (m, 3H), 7.31-7.26 (m, 4H), 7.24-7.18 (m, 3H), 6.92 (d, J = 8.3 Hz, 2H), 6.80 (t, J = 7.3 Hz, 1H), 6.39 (dd, J_1 = 4.9 Hz, J_2 = 8.2 Hz, 1H), 4.66 (d, J = 17.2 Hz, 1H), 4.41 (d, J = 17.2 Hz, 1H), 4.18 (dd, J_1 = 8.3 Hz, J_2 = 15.4 Hz, 1H), 3.81 (dd, J_1 = 4.9 Hz, J_2 = 15.4 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 165.4, 148.2, 138.5, 138.1, 137.7, 131.2, 129.6, 129.4, 128.9, 128.7, 128.6, 127.0, 126.7 126.5, 117.4, 113.0, 101.0, 74.8, 56.7, 54.8.

HRMS (ESI) calculated $[M+H]^+$ for $C_{28}H_{25}O_2NI$: 534.0924, found: 534.0927.

FTIR (cm^{-1})3021, 2358, 1720, 1593, 1499, 1386, 1358, 1269, 1219, 1105, 1007, 761.

2-(Benzyl(phenyl)amino)-1-phenylethyl 4-methoxybenzoate (36l)



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **34a** (0.105 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **21a**

(0.223 g, 182 μL, 0.75 mmol) with 4-methoxybenzoic acid **35l** (0.114 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-(benzyl(phenyl)amino)-1-phenylethyl 4-methoxybenzoate as a colourless oil **36l** (0.162 g, 74% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.44.

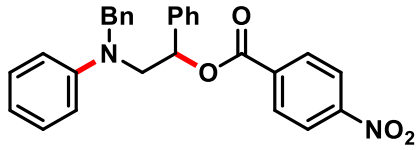
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.8 Hz, 2H), 7.44 (d, *J* = 7.1 Hz, 2H), 7.41 – 7.31 (m, 3H), 7.22 (m, 5H), 7.13 (d, *J* = 7.3 Hz, 2H), 6.88 (dd, J_1 = 22.2, J_2 = 8.5 Hz, 4H), 6.73 (t, *J* = 7.3 Hz, 1H), 6.32 (dd, J_1 = 5.3 Hz, J_2 = 7.9 Hz, 1H), 4.59 (d, *J* = 17.3 Hz, 1H), 4.31 (d, *J* = 17.3 Hz, 1H), 4.11 (dd, J_1 = 8.0 Hz, J_2 = 15.3 Hz, 1H), 3.86 (s, 3H), 3.74 (dd, J_1 = 5.3 Hz, J_2 = 15.3 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 165.6, 163.6, 148.4, 139.1, 138.4, 131.9, 129.4, 128.8, 128.7, 128.4, 126.9, 126.7, 126.6, 122.6, 117.1, 113.7, 112.8, 74.2, 56.8, 55.6, 54.7.

HRMS (ESI) calculated $[M+H]^+$ for $C_{29}H_{28}O_3N$: 438.2064, found: 438.2061.

FTIR (cm^{-1}) 3022, 2358, 1711, 1603, 1507, 1262, 1217, 1106, 1031, 766.

2-(Benzyl(phenyl)amino)-1-phenylethyl 4-nitrobenzoate (36m)



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **34a** (0.105 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **21a** (0.223 g, 182 μL, 0.75 mmol) with 4-nitrobenzoic acid **35m** (0.125 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-(benzyl(phenyl)amino)-1-phenylethyl 4-nitrobenzoate as yellow oil **36m** (0.192 g, 85% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.37.

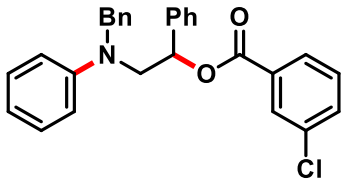
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (d, *J* = 8.8 Hz, 2H), 8.06 (d, *J* = 8.8 Hz, 2H), 7.47 – 7.37 (m, 5H), 7.26 – 7.22 (m, 4H), 7.17 (t, *J* = 7.2 Hz, 3H), 6.88 (d, *J* = 8.2 Hz, 2H), 6.76 (t, *J* = 7.3 Hz, 1H), 6.38 (dd, J_1 = 4.6, J_2 = 8.5 Hz, 1H), 4.65 (d, *J* = 17.1 Hz, 1H), 4.41 (d, *J* = 17.1 Hz, 1H), 4.17 (dd, J_1 = 8.6 Hz, J_2 = 15.5Hz, 1H), 3.80 (dd, J_1 = 4.6, J_2 = 15.5Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 164.1, 150.6, 148.4, 138.2, 138.1, 135.5, 130.8, 129.5, 129.0, 128.8, 128.7, 127.0, 126.7, 126.6, 123.5, 117.5, 113.0, 75.7, 56.7, 54.9.

HRMS (ESI) calculated $[M+H]^+$ for $C_{28}H_{25}O_4N_2$: 453.1809, found: 453.1812.

FTIR (cm^{-1}) 3023, 2358, 1726, 1599, 1520, 1451, 1351, 1271, 1217, 1108, 1025, 762.

2-(Benzyl(phenyl)amino)-1-phenylethyl 3-chlorobenzoate (36n)



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **34a** (0.105 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **21a** (0.223 g, 182 µL, 0.75 mmol) with 3-chlorobenzoic acid **35n** (0.117 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-(benzyl(phenyl)amino)-1-phenylethyl 3-chlorobenzoate as a colourless oil **36n** (0.176 g, 80% yield).

***R*$_f$** (Pet. ether /EtOAc = 95/05): 0.46.

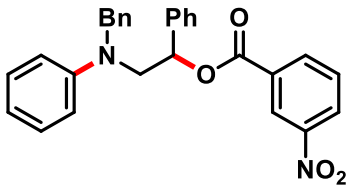
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 1.5 Hz, 1H), 7.88 (d, *J* = 7.8 Hz, 1H), 7.52-7.36 (m, 7H), 7.29-7.16 (m, 7H), 6.89 (d, *J* = 8.3 Hz, 2H), 6.77 (t, *J* = 7.3 Hz, 1H), 6.38-6.35 (m, 1H), 4.65 (d, *J* = 17.3 Hz, 1H), 4.40 (d, *J* = 17.3 Hz, 1H), 4.16 (dd, J_1 = 8.4 Hz, J_2 = 7.2 Hz, 1H), 3.80 (dd, J_1 = 4.7 Hz, J_2 = 10.7 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 148.3, 138.5, 138.3, 134.6, 133.1, 131.8, 129.8, 129.7, 129.5, 128.9, 128.7, 128.6, 127.9, 126.9, 126.6, 126.6, 117.3, 112.8, 75.1, 56.7, 54.7.

HRMS (ESI) calculated $[M+H]^+$ for $C_{28}H_{24}O_2NClNa$: 464.1388, found: 464.1389.

FTIR (cm^{-1}) 3429, 3066, 3021, 1723, 1599, 1576, 1505, 1453, 1217, 1127, 757, 698.

2-(Benzyl(phenyl)amino)-1-phenylethyl 3-nitrobenzoate (36o)



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **34a** (0.105 g, 0.5 mmol) and 2-(trimethylsilyl) phenyl trifluoromethane sulfonate **21a** (0.223 g, 182 µL, 0.75 mmol) with 3-nitrobenzoic acid **35o** (0.125 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography

(Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-(benzyl(phenyl)amino)-1-phenylethyl 3-nitrobenzoate as yellow oil **36o** (0.174 g, 77% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.40.

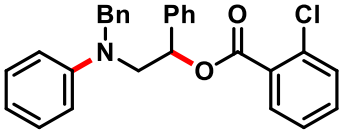
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.74 (s, 1H), 8.38 (d, *J* = 8.1 Hz, 1H), 8.23 (d, *J* = 7.7 Hz, 1H), 7.58 (t, *J* = 8.0 Hz, 1H), 7.49 (d, *J* = 7.5 Hz, 2H), 7.45-7.37 (m, 3H), 7.26-7.21 (m, 4H), 7.18- 7.12 (m, 3H), 6.88 (d, *J* = 8.2 Hz, 2H), 6.74 (t, *J* = 7.2 Hz, 1H), 6.40 (dd, J_1 = 4.2, J_2 = 8.6 Hz, 1H), 4.70 (d, *J* = 17.1 Hz, 1H), 4.47 (d, *J* = 17.1 Hz, 1H), 4.18 (dd, J_1 = 8.7 Hz, J_2 = 15.5 Hz, 1H), 3.83 (dd, J_1 = 4.2, J_2 = 15.5 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 163.8, 148.3, 138.2, 138.1, 135.4, 131.8, 129.6, 129.5, 129.0, 128.8, 128.6, 127.4, 126.9, 126.7, 126.6, 124.6, 117.4, 112.9, 75.8, 56.8, 54.9.

HRMS (ESI) calculated $[M+Na]^+$ for $C_{28}H_{24}N_2O_4Na$: 475.1628, found: 475.1629.

FTIR (cm^{-1}) 3075, 3025, 2931, 2357, 1727, 1602, 1535, 1497, 1449, 1352, 1296, 1257, 1222, 1134, 1078, 1029, 993, 960, 759.

2-(Benzyl(phenyl)amino)-1-phenylethyl 2-chlorobenzoate (36p)



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **34a** (0.105 g, 0.5 mmol) and 2-(trimethylsilyl) phenyl trifluoromethane sulfonate **21a** (0.223 g, 182 μL, 0.75 mmol) with 2-chlorobenzoic acid **35p** (0.117 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-(benzyl(phenyl)amino)-1-phenylethyl 2-chlor obenzoate as a colourless oil **36p** (0.159 g, 72% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.50.

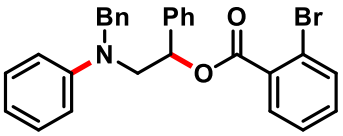
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (dd, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 1H), 7.56-7.54 (m, 2H), 7.50-7.40 (m, 5H), 7.33-7.19 (m, 8H), 6.95 (d, *J* = 8.3 Hz, 2H), 6.81 (t, *J* = 7.3 Hz, 1H), 6.46 (dd, J_1 = 5.3 Hz, J_2 = 7.6 Hz, 1H), 4.68 (d, *J* = 17.2 Hz, 1H), 4.40 (d, *J* = 17.2 Hz, 1H), 4.23 (dd, J_1 = 7.9 Hz, J_2 = 15.3 Hz, 1H), 3.82 (dd, J_1 = 5.3 Hz, J_2 = 15.3 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 164.8, 148.1, 138.4, 138.2, 133.9, 132.7, 131.7, 131.2, 129.8, 129.4, 128.0, 128.6, 128.6, 126.9, 126.8, 126.7, 126.6, 117.2, 112.9, 75.2, 56.7, 54.7.

HRMS (ESI) calculated $[M+H]^+$ for $C_{28}H_{25}O_2NCl$: 442.1568, found: 442.1572.

FTIR (cm^{-1}) 3022, 2357, 1725, 1598, 1500, 1360, 1217, 1123, 1041, 762.

2-(Benzyl(phenyl)amino)-1-phenylethyl 2-bromobenzoate (36q)



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **34a** (0.105 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **21a** (0.223 g, 182 µL, 0.75 mmol) with 2-bromobenzoic acid **35q** (0.151 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-(benzyl(phenyl)amino)-1-phenylethyl 2-bromobenzoate as a colourless oil **36q** (0.182 g, 75% yield).

***R*$_f$** (Pet. ether /EtOAc = 95/05): 0.57.

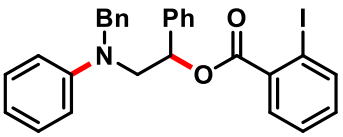
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72-7.67 (m, 2H), 8.03 (d, *J* = 7.3 Hz, 2H), 7.46-7.39 (m, 3H), 7.36-7.22 (m, 7H), 7.18 (d, *J* = 7.4 Hz, 2H), 6.91 (d, *J* = 8.2 Hz, 2H), 6.79 (t, *J* = 7.2 Hz, 1H), 6.44-6.42 (m, 1H), 4.65 (d, *J* = 17.0 Hz, 1H), 4.38 (d, *J* = 17.2 Hz, 1H), 4.22 (dd, J_1 = 8.0 Hz, J_2 = 15.3 Hz, 1H), 3.80 (dd, J_1 = 5.3 Hz, J_2 = 15.3 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 165.3, 148.3, 138.3, 138.3, 134.5, 132.7, 131.9, 131.6, 129.4, 128.8, 128.6, 128.6, 127.2, 126.9, 126.6, 121.9, 117.1, 112.8, 75.3, 56.6, 54.6.

HRMS (ESI) calculated $[M+H]^+$ for $C_{28}H_{25}O_2NBr$: 486.1063, found: 486.1068.

FTIR (cm^{-1}) 3022, 2928, 2358, 1728, 1597, 1502, 1442, 1358, 1285, 1247, 1219, 1121, 1033, 759, 697.

2-(Benzyl(phenyl)amino)-1-phenylethyl 2-iodobenzoate (36r)



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **34a** (0.105 g, 0.5 mmol) and 2-(trimethylsilyl) phenyl trifluoromethane sulfonate **21a** (0.223 g, 182 µL, 0.75 mmol) with 2-iodobenzoic acid **35r** (0.186 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-(Benzyl(phenyl)amino)-1-phenylethyl 2-iodobenzoate as a colourless oil **36r** (0.223 g, 84% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.59.

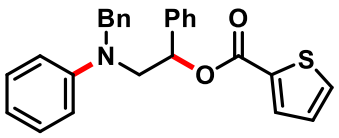
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.8 Hz, 1H), 7.74 (dd, J_1 = 1.6 Hz, J_2 = 6.2 Hz, 1H), 7.57-7.39 (m, 6H), 7.31-7.17 (m, 8H), 6.93 (d, *J* = 8.2 Hz, 2H), 6.81 (t, *J* = 6.9 Hz, 1H), 6.46-6.43 (m, 1H), 4.67 (d, *J* = 17.4 Hz, 1H), 4.40 (d, *J* = 17.3 Hz, 1H), 4.25 (dd, J_1 = 6.9 Hz, J_2 = 8.0 Hz, 1H), 3.83 (dd, J_1 = 5.0 Hz, J_2 = 10.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6 148.2, 141.4, 138.3, 138.3, 134.7, 132.7, 131.1, 129.4, 128.8, 128.6, 128.6, 127.9, 126.8, 126.6, 117.1, 112.8, 94.3, 75.3, 56.5, 54.6.

HRMS (ESI) calculated $[M+H]^+$ for $C_{28}H_{24}O_2NINa$: 556.0744, found: 556.0747.

FTIR (cm^{-1}) 3021, 1727, 1597, 1504, 1459, 1359, 1249, 1216, 1028, 761, 670, 522.

2-(Benzyl(phenyl)amino)-1-phenylethyl thiophene-2-carboxylate (36s)



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **34a** (0.105 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **21a** (0.223 g, 182 μL, 0.75 mmol) with thiophene-2-carboxylic acid **35s** (0.96 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-(Benzyl(phenyl)amino)-1-phenylethyl thiophene-2-carboxylate as a colourless oil **36s** (0.149 g, 72% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.37.

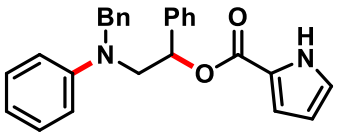
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (dd, J_1 = 1.1 Hz, J_2 = 3.7 Hz, 1H), 7.57 (dd, J_1 =1.1 Hz, J_2 = 5.0 Hz, 1H), 7.49 (d, *J* = 7.1 Hz, 2H), 7.44-7.36 (m, 3H), 7.32 – 7.21 (m, 5H), 7.19 (d, *J* = 7.3 Hz, 2H), 7.11 (dd, J_1 = 3.8 Hz, J_2 = 4.9 Hz, 1H), 6.89 (d, *J* = 8.2 Hz, 2H), 6.77 (t, *J* = 7.3 Hz, 1H), 6.35 (dd, J_1 = 4.9 Hz, J_2 = 8.3 Hz, 1H), 4.68 (d, *J* = 17.3 Hz, 1H), 4.44 (d, *J* = 17.3 Hz, 1H), 4.12 (dd, J_1 = 8.4 Hz, J_2 = 15.4 Hz, 1H), 3.79 (dd, J_1 = 4.9 Hz, J_2 = 15.4 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 161.4, 148.2, 138.6, 138.4, 133.9, 133.6, 132.7, 129.4, 128.8, 128.7, 128.5, 127.9, 126.9, 126.6, 126.5, 117.1, 112.7, 74.9, 56.7, 54.6.

HRMS (ESI) calculated $[M+H]^+$ for $C_{26}H_{23}O_2NSNa$: 436.1342, found: 414.1338.

FTIR (cm^{-1}) 3022, 2405, 2358, 1711, 1598, 1508, 1264, 1089, 1032, 766, 671.

2-(Benzyl(phenyl)amino)-1-phenylethyl 1*H*-pyrrole-2-carboxylate (36t)



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **34a** (0.105 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **21a** (0.223 g, 182 μL, 0.75 mmol) with 1*H*-pyrrole-2-carboxylic acid **35t** (0.83 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-(benzyl(phenyl)amino)-1-phenylethyl 1*H*-pyrrole-2-carboxylate as yellow oil **36t** (0.143 g, 72% yield).

***R*$_f$** (Pet. ether /EtOAc = 95/05): 0.38.

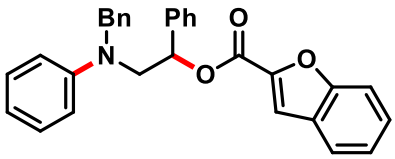
^{1}H NMR (400 MHz, CDCl$_3$) δ 9.02 (s, 1H), 7.30 (d, *J* = 7.1 Hz, 2H), 7.27-7.19 (m, 3H), 7.17- 7.07 (m, 5H), 7.03 (d, *J* = 7.3 Hz, 2H), 6.83- 6.79 (m, 1H), 6.74 (d, *J* = 8.5 Hz, 2H), 6.68-6.69 (m, 1H), 6.62 (t, *J* = 7.2 Hz, 1H), 6.14-6.10 (m, 2H), 4.48 (d, *J* = 17.2 Hz, 1H), 4.26 (d, *J* = 17.3 Hz, 1H), 3.95 (dd, J_1 = 8.4, J_2 = 15.4 Hz, 1H), 3.60 (dd, J_1 = 4.8, J_2 = 15.4 Hz, 1H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 160.5, 148.5, 139.0, 138.4, 129.4, 128.8, 128.7, 128.4, 126.9, 126.7, 126.4, 123.4, 122.6, 117.0, 115.8, 112.8, 110.5, 74.2, 56.6, 54.6.

HRMS (ESI) calculated $[M+H]^+$ for $C_{26}H_{25}O_2N_2$: 397.1911, found: 397.1908.

FTIR (cm^{-1}) 3454, 3020, 2405, 1696, 1598, 1557, 1504, 1448, 1412, 1360, 1316, 1217, 1165, 1115, 960, 766.

2-(Benzyl(phenyl)amino)-1-phenylethyl benzofuran-2-carboxylate (36u)



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **34a** (0.105 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **21a** (0.223 g, 182 μL, 0.75 mmol) with benzofuran-2-carboxylic acid **35u** (0.122 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-(benzyl(phenyl)amino)-1-phenylethyl benzofuran-2-carboxylate as a white solid **36u** (0.198 g, 88% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.53.

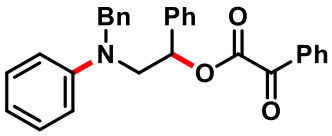
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.9 Hz, 1H), 7.60 (d, *J* = 8.4 Hz, 1H), 7.52-7.30 (m, 8H), 7.29-7.21 (m, 4H), 7.18 (d, *J* = 6.4 Hz, 3H), 6.89 (d, *J* = 7.7 Hz, 2H), 6.75 (t, *J* = 7.1 Hz, 1H), 6.45 – 6.31 (m, 1H), 4.68 (d, *J* = 17.2 Hz, 1H), 4.42 (d, *J* = 17.2 Hz, 1H), 4.15 (dd, J_1 = 8.2 Hz, J_2 = 15.3 Hz, 1H), 3.81 (dd, J_1 = 3.6 Hz, J_2 = 15.4 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 158.9, 155.9, 148.3, 145.4, 138.4, 138.3, 129.4, 128.9, 128.7, 127.8, 127.0, 126.9, 126.7, 123.9, 123.0, 117.2, 114.3, 112.9, 112.5, 75.1, 56.7, 54.7.

HRMS (ESI) calculated $[M+H]^+$ for $C_{30}H_{26}O_3N$: 448.1907, found: 448.1904.

FTIR (cm^{-1}) 3022, 2405, 2358, 1725, 1601, 1504, 1359, 1295, 1217, 1179, 766.

2-(Benzyl(phenyl)amino)-1-phenylethyl 2-oxo-2-phenylacetate (36v)



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **34a** (0.105 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **21a** (0.223 g, 182 µL, 0.75 mmol) with 2-oxo-2-phenylacetic acid **35v** (0.113 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-(benzyl(phenyl)amino)-1-phenylethyl 2-oxo-2-phenylacetate as a colourless oil **36v** (0.161 g, 74% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.47.

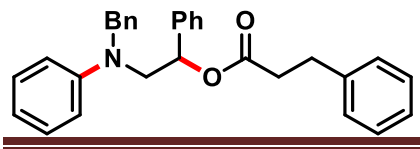
^{1}H NMR (500 MHz, $CDCl_3$ δ 7.94 (d, *J* = 8.1 Hz, 2H), 7.66 (t, *J* = 7.4 Hz, 1H), 7.52 – 7.42 (m, 7H), 7.33 – 7.23 (m, 5H), 7.19 (d, *J* = 7.5 Hz, 2H), 6.90 (d, *J* = 8.2 Hz, 2H), 6.80 (t, *J* = 7.2 Hz, 1H), 6.48 (dd, J_1 = 4.6, J_2 = 8.4 Hz, 1H), 4.68 (d, *J* = 17.3 Hz, 1H), 4.52 (d, *J* = 17.3 Hz, 1H), 4.10 (dd, J_1 = 8.6, J_2 = 15.5 Hz, 1H), 3.85 (dd, J_1 = 4.6, J_2 = 15.5 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 185.9, 163.1, 148.2, 138.4, 137.4, 134.9, 132.4, 130.1, 129.5, 129.0, 128.9, 128.7, 127.0, 126.7, 117.4, 112.8, 76.0, 56.3, 54.7.

HRMS (ESI) calculated $[M+Na]^+$ for $C_{29}H_{25}O_3NNa$: 458.1727, found: 458.1728.

FTIR (cm^{-1}) 3023, 2927, 2357, 1739, 1689, 1597, 1501, 1451, 1360, 1208, 1029, 760, 695.

2-(Benzyl(phenyl)amino)-1-phenylethyl 3-phenylpropanoate (36w)



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **34a** (0.105 g, 0.5 mmol) and 2-

(trimethylsilyl)phenyl trifluoromethane sulfonate **21a** (0.223 g, 182 µL, 0.75 mmol) with 3-phenylpropanoic acid **35w** (0.112 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-(benzyl(phenyl)amino)-1-phenylethyl 3-phenylpropanoate as a colourless oil **36w** (0.100 g, 46% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.56.

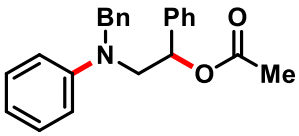
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45-7.38 (m, 5H), 7.37-7.25 (m, 8H), 7.21-7.18 (m, 4H), 6.89 (d, *J* = 8.2 Hz, 2H), 6.82 (t, *J* = 7.3 Hz, 1H), 6.24 (dd, J_1 = 4.8 Hz, J_2 = 8.6 Hz, 1H), 4.64 (d, *J* = 17.2 Hz, 1H), 4.38 (d, *J* = 17.2 Hz, 1H), 4.01 (dd, J_1 = 8.6 Hz, J_2 = 15.4 Hz, 1H), 3.67 (dd, J_1 = 4.8 Hz, J_2 = 15.4 Hz, 1H), 2.97-2.86 (m, 2H), 2.65-2.51 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 172.1, 148.2, 140.5, 138.6, 138.3, 129.4, 128.7, 128.6, 128.5, 128.4, 128.3, 126.9, 126.6, 126.5, 126.3, 117.1, 112.7, 74.0, 56.7, 54.5, 35.9, 30.8.

HRMS (ESI) calculated $[M+H]^+$ for $C_{30}H_{30}O_2N$: 436.2271, found: 436.2274.

FTIR (cm^{-1}) 3022, 2931, 2357, 1734, 1599, 1501, 1361, 1218, 1161, 761.

2-(benzyl(phenyl)amino)-1-phenylethyl acetate (36x)



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **34a** (0.105 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **21a** (0.223 g, 182 µL, 0.75 mmol) with acetic acid **35x** (0.045 g, 43 µL, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-(benzyl(phenyl)amino)-1-phenylethyl acetate as a white solid **36x** (0.132 g, 76% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.48.

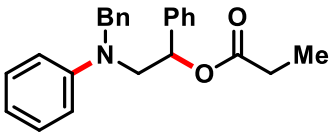
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.39 (m, 5H), 7.35-7.27 (m, 5H), 7.21-7.19 (m, 2H), 6.88 (d, *J* = 8.1 Hz, 2H), 6.79 (t, *J* = 7.3 Hz, 1H), 6.21-6.19 (m, 1H), 4.66 (d, *J* = 17.4 Hz, 1H), 4.40 (d, *J* = 17.2 Hz, 1H), 4.02 (dd, J_1 = 8.6 Hz, J_2 = 7.2 Hz, 1H), 3.69 (dd, J_1 = 4.3 Hz, J_2 = 10.8 Hz, 1H), 1.98 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 148.3, 138.7, 138.4, 129.4, 128.8, 128.7, 128.4, 126.9, 126.6, 117.0, 112.6, 73.9, 56.7, 54.6, 21.1.

HRMS (ESI) calculated $[M+H]^+$ for $C_{23}H_{23}O_2NNa$: 368.1621, found: 368.1620.

FTIR (cm^{-1}) 3023, 2931, 1738, 1598, 1502, 1365, 1232, 1033, 994, 757, 697, 609.

2-(Benzyl(phenyl)amino)-1-phenylethyl propionate (36y)



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **34a** (0.105 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **21a** (0.223 g, 182 µL, 0.75 mmol) with propionic acid **35y** (0.56 g, 56 µL, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-(benzyl(phenyl)amino)-1-phenylethyl propionate as a colourless oil **36y** (0.131 g, 73% yield).

***R*$_f$** (Pet. ether /EtOAc = 95/05): 0.55.

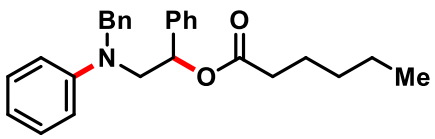
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37-7.32 (m, 5H), 7.29-7.26 (m, 2H), 7.23-7.20 (m, 3H), 7.13 (d, *J* = 7.3 Hz, 2H), 6.80 (d, *J* = 8.2 Hz, 2H), 6.73 (t, *J* = 7.3 Hz, 1H), 6.15-6.13 (m, 1H), 4.59 (d, *J* = 17.4 Hz, 1H), 4.33 (d, *J* = 17.3 Hz, 1H), 3.95 (dd, J_1 = 8.4 Hz, J_2 = 15.3 Hz, 1H), 3.61 (dd, J_1 = 4.8 Hz, J_2 = 15.3 Hz, 1H), 2.28-2.13 (m, 2H), 1.05 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 173.6, 148.3, 138.8, 138.4, 129.3, 128.7, 128.6, 128.3, 126.8, 126.6, 126.5, 117.0, 112.6, 73.7, 56.7, 54.5, 27.7, 8.9.

HRMS (ESI) calculated $[M+Na]^+$ for $C_{24}H_{25}NO_2Na$: 382.1778, found: 382.1779.

FTIR (cm^{-1}) 3022, 2934, 2358, 1731, 1599, 1452, 1359, 1291, 1217, 1084, 1028, 759, 698.

2-(Benzyl(phenyl)amino)-1-phenylethyl hexanoate (36z)



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **34a** (0.105 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **21a** (0.223 g, 182 µL, 0.75 mmol) with hexanoic acid **35z** (0.087 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-(benzyl(phenyl)amino)-1-phenylethyl hexanoate as a colourless oil **36z** (0.121 g, 60% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.47.

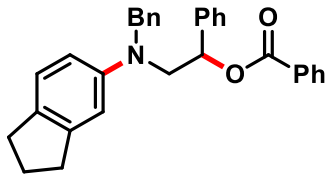
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43-7.37 (m, 5H), 7.35-7.32 (m, 2H), 7.30-7.26 (m, 3H), 7.21 (d, *J* = 7.3 Hz, 2H), 6.89 (d, *J* = 8.1 Hz, 2H), 6.80 (t, *J* = 7.3 Hz, 1H), 6.22 (dd, J_1 = 4.9 Hz, J_2 = 8.4 Hz, 1H), 4.66 (d, *J* = 17.3 Hz, 1H), 4.41 (d, *J* = 17.3 Hz, 1H), 4.03 (dd, J_1 = 8.5 Hz, J_2 = 15.4 Hz, 1H), 3.68 (dd, J_1 = 4.9 Hz, J_2 = 15.4 Hz, 1H), 2.32-2.19 (m, 2H), 1.64-1.58 (m, 2H), 1.37-1.25 (m, 4H), 0.94 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 173.0, 148.2, 138.9, 138.3, 129.3, 128.7, 128.7, 128.4, 126.9, 126.7, 126.6, 117.1, 112.8, 73.6, 56.7, 54.6, 34.4, 31.3, 24.5, 22.4, 14.0.

HRMS (ESI) calculated $[M+H]^+$ for $C_{27}H_{32}O_2N$: 402.2428, found: 402.2428.

FTIR (cm^{-1}) 3022, 2952, 2357, 1732, 1599, 1501, 1452, 1361, 1217, 762.

2-(Benzyl(2,3-dihydro-1*H*-inden-5-yl)amino)-1-phenylethyl benzoate (36aa)



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **34a** (0.105 g, 0.5 mmol) and 6-(trimethylsilyl)-2,3-dihydro-1H-inden-5-yl trifluoromethanesulfonate **21aa** (0.254 g, 0.75 mmol) with benzoic acid **35a** (0.92 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-(benzyl(2,3-dihydro-1*H*-inden-5-yl)amino)-1-phenylethyl benzoate as a colourless oil **36aa** (0.168 g, 75% yield).

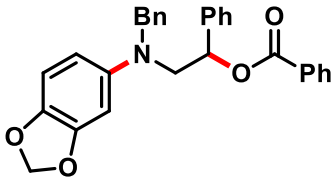
***R*f** (Pet. ether /EtOAc = 95/05): 0.57.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.2 Hz, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.51 (d, *J* = 7.4 Hz, 2H), 7.48-7.41 (m, 4H), 7.38 (t, *J* = 7.2 Hz, 1H), 7.30 (t, *J* = 7.4 Hz, 2H), 7.26-7.21 (m, 3H), 7.12 (d, *J* = 8.2 Hz, 1H), 6.85 (s, 1H), 6.72 (dd, J_1 = 1.8, J_2= 8.2 Hz, 1H), 6.42 (dd, J_1 = 8.0, J_2= 4.9 Hz, 1H), 4.64 (d, *J* = 17.1 Hz, 1H), 4.39 (d, *J* = 17.1 Hz, 1H), 4.15 (dd, J_1 = 8.2, J_2 = 15.3 Hz, 1H), 3.79 (dd, J_1 = 4.9, J_2 = 15.3 Hz, 1H), 2.90-2.85 (m, 4H), 2.09 (p, *J* = 7.4 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 165.8, 147.5, 145.5, 139.0, 138.7, 133.1, 132.9, 130.2, 129.8, 128.8, 128.6, 128.4, 126.8, 126.6, 124.9, 111.4, 109.3, 74.6, 57.1, 55.1, 33.5, 32.0, 25.8.

HRMS (ESI) calculated $[M+H]^+$ for $C_{31}H_{30}O_2N$: 448.2271, found: 448.2271.

FTIR (cm^{-1}) 3055, 2984, 2356, 1718, 1608, 1499, 1266, 1220, 1167, 1108, 1029, 908, 763.

2-(Benzo[*d*][1,3]dioxol-5-yl(benzyl)amino)-1-phenylethyl benzoate (36ab)



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **34a** (0.105 g, 0.5 mmol) and 6-(trimethylsilyl)benzo[*d*][1,3]dioxol-5-yl trifluoromethanesulfonate **21ab** (0.257 g, 0.75 mmol) with benzoic acid **35a** (0.92 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-(benzo[d][1,3]dioxol-5-yl(benzyl)amino)-1-phenylethyl benzoate as a colourless oil **36ab** (0.186 g, 82% yield).

***R*$_f$** (Pet. ether /EtOAc = 95/05): 0.32.

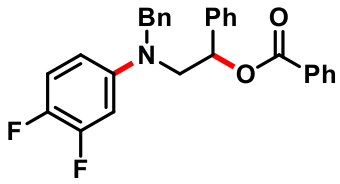
^{1}H NMR (500 MHz, CDCl$_3$) δ 8.09 (d, *J* = 7.7 Hz, 2H), 7.61 (t, *J* = 7.2 Hz, 1H), 7.54 – 7.42 (m, 6H), 7.42 – 7.29 (m, 4H), 7.22 (d, *J* = 7.3 Hz, 2H), 6.75 (d, *J* = 8.5 Hz, 1H), 6.58 (s, 1H), 6.45 – 6.33 (m, 2H), 5.89 (s, 2H), 4.58 (d, *J* = 16.8 Hz, 1H), 4.37 (d, *J* = 16.8 Hz, 1H), 4.10 (dd, J_1 = 8.2 Hz, J_2 = 15.2 Hz, 1H), 3.74 (dd, J_1 = 4.1 Hz, J_2 = 15.3 Hz, 1H).

^{13}C NMR (125 MHz, CDCl$_3$) δ 165.8, 148.6, 144.5, 139.6, 138.8, 138.4, 133.1, 130.1, 129.8, 128.8, 128.6, 128.4, 127.9, 127.0, 126.9, 126.8, 126.5, 126.3, 108.6, 105.7, 100.7, 96.8, 74.4, 57.7, 55.7.

HRMS (ESI) calculated $[M+H]^+$ for $C_{29}H_{25}O_4NNa$: 474.1676, found: 474.1673.

FTIR (cm^{-1}) 3022, 2358, 1718, 1499, 1447, 1266, 1217, 1109, 1036, 767, 673.

2-(Benzyl(3,4-difluorophenyl)amino)-1-phenylethyl benzoate (36ac)



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **34a** (0.105 g, 0.5 mmol) and 4,5-difluoro-2-(trimethylsilyl)phenyl trifluoromethanesulfonate **21ac** (0.251 g, 0.75 mmol) with benzoic acid **35a** (0.92 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-(benzyl(3,4-difluorophenyl)amino)-1-phenylethyl benzoate as a colourless oil **36ac** (0.140 g, 63% yield).

***R*$_f$** (Pet. ether /EtOAc = 95/05): 0.44.

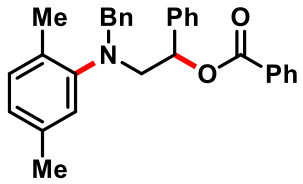
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.9 Hz, 2H), 7.58 (t, *J* = 7.1 Hz, 1H), 7.46-7.35 (m, 7H), 7.29-7.20 (m, 3H), 7.11 (d, *J* = 7.4 Hz, 2H), 6.97 (q, *J* = 9.5 Hz, 1H), 6.65-6.60 (m, 1H), 6.49 (d, *J* = 9.3 Hz, 1H), 6.33 (dd, J_1 = 5.5, J_2 = 7.5 Hz, 1H), 4.51 (d, *J* = 17.2 Hz, 1H), 4.31 (d, *J* = 17.2 Hz, 1H), 4.09 (dd, J_1 = 8.1, J_2 = 15.3 Hz, 1H), 3.70 (dd, J_1 = 5.0, J_1 = 15.4 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 150.9 (dd, J_1 = 13.0, J_2 = 243.9 Hz), 145.5 (d, *J* = 8.3 Hz), 142.9 (dd, J_1 = 13.1, J_2 = 237.6 Hz), 138.4, 137.5, 133.3, 129.9, 129.8, 128.9, 128.8, 128.7, 128.5, 127.2, 126.6, 117.5 (d, *J* = 17.4 Hz), 109.4, 108.0, 102.0 (d, *J* = 17.4 Hz), 74.2, 57.1, 55.0.

HRMS (ESI) calculated $[M+H]^+$ for $C_{28}H_{24}F_2O_2N$: 444.1770, found: 444.1766.

FTIR (cm^{-1}) 3203, 2404, 2357, 1718, 1599, 1521, 1447, 1363, 1269, 1217, 1110, 1031, 768.

2-(Benzyl(2,5-dimethylphenyl)amino)-1-phenylethyl benzoate (36ad)



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **34a** (0.105 g, 0.5 mmol) and 3,6-dimethyl-2-(trimethylsilyl)phenyl trifluoromethanesulfonate **21ad** (0.245 g, 0.75 mmol) with benzoic acid **35a** (0.092 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 99/01) of the crude reaction mixture using silica gel afforded 2-(benzyl(2,5-dimethylphenyl)amino)-1-phenylethyl benzoate as a colourless oil **36ad** (0.180 g, 83% yield).

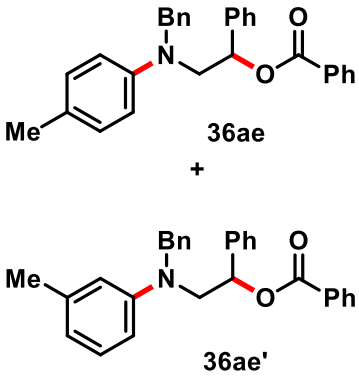
***R*$_f$** (Pet. ether /EtOAc = 95/05): 0.52.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 7.9 Hz, 2H), 7.61-7.43 (m, 3H), 7.36-7.26 (m, 10H), 7.13 (d, *J* = 7.7 Hz, 1H), 7.04 (s, 1H), 6.85 (d, *J* = 7.5 Hz, 1H), 6.20 (m, 1H), 4.22 (s, 2H), 3.64 (dd, J_1 = 5.5 Hz, J_2 = 8.7 Hz, 1H), 3.38 (dd, J_1 = 4.3 Hz, J_2 = 9.8 Hz, 1H), 2.25 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 149.9, 139.4, 138.8, 136.1, 133.0, 131.2, 129.8, 128.8, 128.7, 128.5, 128.4, 128.3, 128.04, 127.2, 126.5, 124.7, 123.3, 74.2, 59.2, 56.6, 21.1, 18.0. **HRMS (ESI)** calculated $[M+H]^+$ for $C_{30}H_{30}O_2N$: 436.2271, found: 436.2267.

FTIR (cm^{-1}) 3023, 2927, 1719, 1603, 1507, 1452, 1340, 1268, 1218, 1111, 1027, 762.

2-(Benzyl(*p*-tolyl)amino)-1-phenylethyl benzoate (36ae) and 2-(Benzyl(*m*-tolyl)amino)-1-phenylethyl benzoate (36ae')



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **34a** (0.105 g, 0.5 mmol) and 4-methyl-2-(trimethylsilyl)phenyl trifluoromethanesulfonate **21ae** (0.234 g, 0.75 mmol) with benzoic acid **35a** (0.92 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-(benzyl(*p*-tolyl)amino)-1-phenylethyl benzoate (**36ae**) and 2-(benzyl(*m*-tolyl)amino)-1-phenyl ethyl benzoate (**36ae'**) as a inseparable mixture of regioisomers in 1:1 ratio (as a colourless oil, 0.142 g, 67% yield).

***R*$_f$** (Pet. ether /EtOAc = 95/05): 0.50.

^{1}H NMR (500 MHz, CDCl$_3$) 36ae δ 8.12-8.00 (m, 2H), 7.61 (dd, J_1 = 4.2 Hz, J_2 = 10.6 Hz 1H), 7.54-7.36 (m, 7H), 7.34 – 7.27 (m, 2H), 7.25-7.15 (m, 3H), 7.09 (d, J = 8.4 Hz, 1H), 6.83 (d, J = 8.6 Hz, 1H), 6.76 (s, 1H), 6.62 (d, J = 7.3 Hz, 1H), 6.42-6.39 (m, 1H), 4.64 (t, J = 15.9 Hz, 1H), 4.38 (t, J = 16.4 Hz, 1H), 4.21-4.10 (m, 1H), 3.80 (dt, J_1 = 4.6 Hz, J_2 = 15.3 Hz, 1H), 2.35 (s, 3H).

^{13}C NMR (125 MHz, CDCl$_3$) 36ae δ 165.9, 148.5, 139.0, 138.5, 133.1, 129.8, 129.3, 128.8, 128.7, 128.4, 126.9, 126.7, 126.6, 118.1, 113.1, 74.6, 56.7, 54.6, 22.1.

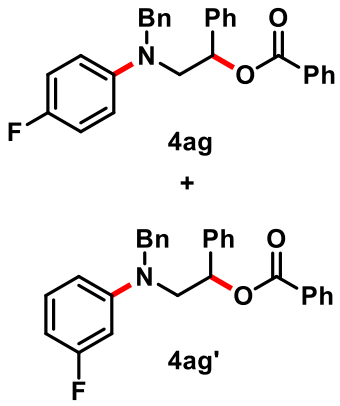
^{1}H NMR (500 MHz, CDCl$_3$) of **36ae'** δ 8.12-8.00 (m, 2H), 7.61 (dd, J_1 = 4.2 Hz, J_2 = 10.6 Hz, 1H), 7.54-7.36 (m, 7H), 7.34-7.27 (m, 2H), 7.25-7.15 (m, 4H), 7.09 (d, J = 8.4 Hz, 1H), 6.83 (d, J = 8.6 Hz, 1H), 6.72 (dd, J_1 = 2.4 Hz, J_2 = 8.2 Hz, 1H), 6.42-6.39 (m, 1H), 4.64 (t, J = 15.9 Hz, 1H), 4.38 (t, J = 16.4 Hz, 1H), 4.21 – 4.10 (m, 1H), 3.80 (dt, J_1 = 4.6 Hz, J_2 = 15.3 Hz, 1H), 2.31 (s, 3H).

^{13}C NMR (125 MHz, CDCl$_3$) of **36ae'** δ 165.9, 146.3, 138.7, 133.1, 130.2, 129.3, 128.8, 128.6, 126.8, 126.7, 126.6, 126.3 113.6, 110.1, 74.6, 57.0, 55.0, 20.3.

HRMS (ESI) calculated $[M+H]^+$ for $C_{29}H_{28}O_2N$: 422.2115, found: 422.2113.

FTIR (cm^{-1}) 3021, 2925, 2357, 1719, 1602, 1509, 1451, 1267, 1217, 1107, 760, 706.

2-(Benzyl(4-fluorophenyl)amino)-1-phenylethyl benzoate (36af) and 2-(Benzyl(3-fluoro phenyl)amino)-1-phenylethyl benzoate (36af')



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **34a** (0.105 g, 0.5 mmol) and 4-fluoro-2-(trimethylsilyl)phenyl trifluoromethanesulfonate **21af** (0.237 g, 0.75 mmol) with benzoic acid **35a** (0.092 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-(benzyl(4-fluorophenyl)amino)-1-phenylethyl benzoate **(36af)** and 2-(benzyl(3-fluorophenyl)amino)-1-phenylethyl benzoate **(36af')** as inseperable mixture of regioisomer in 6:1 ratio as yellow oil (0.152 g, 71% yield).

***R*$_f$** (Pet. ether /EtOAc = 95/05): 0.52.

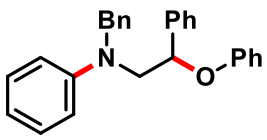
^{1}H NMR (500 MHz, $CDCl_3$) (The peaks of both the major and minor regioisomers are merged) δ 8.08-8.05 (m, 2H), 7.61-7.58 (m, 1H), 7.52-7.37 (m, 7H), 7.32-7.29 (m, 2H), 7.25-7.22 (m, 1H), 7.19-7.18 (m, 2H), 6.97-6.94 (m, 2H),6.84-6.61 (m, 2H), 6.40-6.39 (m, 1H), 4.64-4.57 (m, 1H), 4.40-4.35 (m, 1H), 4.17-4.11 (m, 1H), 3.79-3.75 (m, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) (Major Isomer **36af**) δ 165.9, 155.8 (d, *J* = 235.5 Hz), 150.1, 145.0, 138.8, 138.2, 133.2, 130.5, 129.8, 128.8, 128.7, 128.6, 128.5, 115.7 (d, *J* = 21.8 Hz), 114.2 (d, *J* = 7.34 Hz), 74.4, 57.4, 55.3.

^{13}C NMR (125 MHz, $CDCl_3$) (Minor Isomer **36af'**) δ 165.8, 155.7 (d, *J* = 238.9 Hz), 150.2, 145.0, 138.6, 137.7, 133.2, 130.4, 130.1, 128.9, 128.8, 128.5, 108.4, 103.6 (d, *J* = 21.32 Hz), 99.5 (d, *J* = 26.6 Hz), 74.3, 56.7, 54.7.

HRMS (ESI) calculated $[M+Na]^+$ for $C_{28}H_{24}O_2FNNa$: 448.1683, found: 448.1684. **FTIR (cm^{-1})** 3023, 2929, 2867, 1719, 1609, 1509, 1451, 1360, 1108, 1027, 815, 763.

***N*-Benzyl-*N*-(2-phenoxy-2-phenylethyl)aniline (38a)**



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **34a** (0.105 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **21a** (0.223 g, 182 µL, 0.75 mmol) with phenol **37a** (0.71 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5

mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded *N*-benzyl-*N*-(2-phenoxy-2-phenylethyl)aniline as a white solid **38a** (0.114 g, 60% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.55.

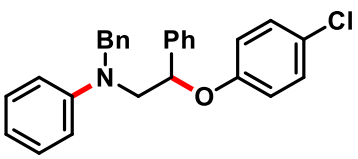
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (d, *J* = 7.4 Hz, 2H), 7.42 (t, *J* = 7.5 Hz, 2H), 7.36-7.18 (m, 10H), 6.91 (t, *J* = 7.3 Hz, 1H), 6.86-6.83 (m, 4H), 6.77 (t, *J* = 7.2 Hz, 1H), 5.56 (dd, J_1 = 3.8, J_2 = 8.1 Hz, 1H), 4.83 (d, *J* = 17.4 Hz, 1H), 4.55 (d, *J* = 17.4 Hz, 1H), 4.01 (dd, J_1 = 8.2, J_2 = 15.5 Hz, 1H), 3.85 (dd, J_1 = 3.8, J_2 = 15.5 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 158.0, 148.2, 139.9, 138.8, 129.5, 129.4, 129.0, 128.7, 128.1, 126.8, 126.6, 126.1, 121.0, 116.7, 116.0, 112.4, 78.7, 58.7, 55.1.

HRMS (ESI) calculated $[M+H]^+$ for $C_{27}H_{26}ON$: 380.2009, found: 380.2007.

FTIR (cm^{-1}) 3020, 2924, 2358, 1596, 1497, 1451, 1358, 1223, 1036, 958, 763, 697.

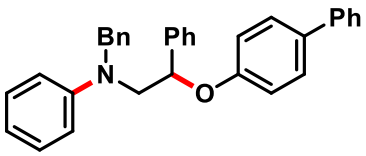
***N*-Benzyl-*N*-(2-(4-chlorophenoxy)-2-phenylethyl)aniline (38b)**



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **34a** (0.105 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **21a** (0.223 g, 182 μL, 0.75 mmol) with 4-chlorophenol **37b** (0.096 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 99/01) of the crude reaction mixture using silica gel afforded *N*-benzyl-*N*-(2-(4-chlorophenoxy)-2-phenylethyl)aniline as a white solid **38b** (0.120 g, 58% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.44; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.44-7.22 (m, 12H), 7.15-7.13 (m, 2H), 6.87-6.74 (m, 5H), 5.50-5.48 (m, 1H), 4.80 (d, *J* = 17.2 Hz, 1H), 4.56 (d, *J* = 17.2 Hz, 1H), 4.01 (dd, J_1 = 8.0 Hz, J_2 = 8.1, 1H), 3.85 (dd, J_1 = 3.7 Hz, J_2 = 11.5 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 156.6, 148.2, 139.4, 138.7, 129.5, 129.3, 129.1, 128.7, 128.3, 126.9, 126.7, 126.1, 125.9, 117.3, 116.9, 112.5, 79.3, 58.7, 55.2. **HRMS (ESI)** calculated $[M+H]^+$ for $C_{27}H_{25}ONCl$: 414.1619, found: 414.1622. **FTIR (cm^{-1})** 3021, 2963, 2925, 1597, 1496, 1448, 1359, 1219, 1036, 921, 672, 554.

_N_-(2-([1,1'-Biphenyl]-4-yloxy)-2-phenylethyl)-_N_-benzylaniline (38c)



Following the general procedure, treatment of 1-benzyl-2-phenylaziridine **34a** (0.105 g, 0.5 mmol) and 2-(trimethylsilyl) phenyl trifluoromethane sulfonate **21a** (0.223 g, 182 µL, 0.75 mmol) with [1,1'-biphenyl]-4-ol **37c** (0.127 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /DCM = 90/10) of the crude reaction mixture using silica gel afforded *N*-(2-([1,1'-biphenyl]-4-yloxy)-2-phenylethyl)-*N*-benzylaniline as a white solid **38c** (0.130 g, 57% yield).

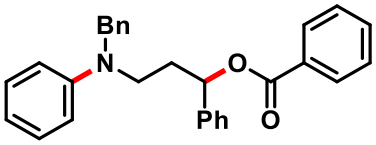
***R*f** (Pet. ether /EtOAc = 95/05): 0.55.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58-7.54 (m, 4H), 7.48-7.46 (m, 6H), 7.42-7.40 (m, 1H), 7.37-7.28 (m, 8H), 6.96-6.92 (m, 4H), 6.84 (t, *J* = 7.3 Hz, 1H), 5.66-5.65 (m, 1H), 4.88 (d, *J* = 17.2 Hz, 1H), 4.61 (d, *J* = 17.2 Hz, 1H), 4.08 (dd, J_1 = 8.1 Hz, J_2 = 15.3 Hz, 1H), 3.92 (dd, J_1 = 3.9 Hz, J_2 = 15.3 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 157.6, 140.8, 139.8, 134.1, 129.5, 129.0, 128.8, 128.7, 128.2, 128.1, 126.9, 126.8, 126.7, 126.1, 116.3, 112.6, 78.8, 58.8, 55.3.

HRMS (ESI) calculated $[M+H]^+$ for $C_{33}H_{30}ON$: 456.2322, found: 456.2324. **FTIR (cm^{-1})** 3021, 2405, 2358, 1601, 1501, 1359, 1218, 1037, 839, 769, 672.

3-(Benzyl(phenyl)amino)-1-phenylpropyl benzoate (40a)



Following the general procedure, treatment of 1-benzyl-2-phenylazetidine **39** (0.112 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **21a** (0.223 g, 182 µL, 0.75 mmol) with benzoic acid **40a** (0.092 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 3-(benzyl(phenyl)amino)-1-phenylpropyl benzoate as a white solid **8a** (0.137 g, 65% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.40.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, *J* = 7.5 Hz, 2H), 7.61 (t, *J* = 7.3 Hz, 1H), 7.51–7.45 (m, 4H), 7.40 (t, *J* = 7.4 Hz, 2H), 7.36 - 7.30 (m, 3H), 7.27 - 7.19 (m, 5H), 6.73 (t, *J* =

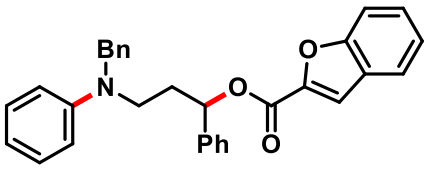
8.0 Hz, 3H), 6.09 (dd, J_1 = 7.9 Hz, J_2 = 5.3 Hz, 1H), 4.56 (q, J = 16.9 Hz, 2H), 3.71 – 3.46 (m, 2H), 2.49 - 2.42 (m, 1H), 2.38 – 2.30 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 148.3, 140.3, 138.9, 133.2, 130.3, 129.8, 129.4, 128.7, 128.7, 128.6, 128.3, 127.0, 126.8, 126.4, 116.7, 112.6, 74.9, 54.8, 47.5, 33.8.

HRMS (ESI) calculated $[M+H]^+$ for $C_{29}H_{28}NO_2$: 422.2115, found: 422.2119.

FTIR (cm^{-1}) 3022, 2974, 2403, 1716, 1599, 1505, 1443, 1363, 1269, 1217, 1111, 926, 773.

3-(Benzyl(phenyl)amino)-1-phenylpropyl benzofuran-2-carboxylate (40b)



Following the general procedure, treatment of 1-benzyl-2-phenylazetidine **7** (0.112 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **21a** (0.223 g, 182 μL, 0.75 mmol) with benzofuran-2-carboxylic acid **35u** (0.122 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 3-(benzyl(phenyl)amino)-1-phenylpropyl benzofuran-2-carboxylate as a yellow oil **40b** (0.185 g, 80% yield).

***R*$_f$** (Pet. ether /EtOAc = 95/05): 0.45.

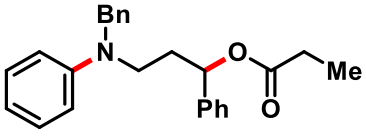
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 7.8 Hz, 1H), 7.64 (d, J = 8.4 Hz, 1H), 7.59 (s, 1H), 7.51– 7.47 (m, 3H), 7.41 (t, J = 7.3 Hz, 2H), 7.37 – 7.30 (m, 4H), 7.25 - 7.20 (m, 5H), 6.75 – 6.73 (m, 3H), 6.13 (dd, J_1 = 7.6, J_2 = 5.5 Hz, 1H), 4.57 (q, J = 17.0 Hz, 2H), 3.73 – 3.47 (m, 2H), 2.62 – 2.42 (m, 1H), 2.41 – 2.27 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0, 155.9, 148.3, 145.5, 139.6, 138.8, 130.9, 129.4, 128.8, 128.7, 128.5, 127.8, 127.0, 127.0, 126.8, 126.6, 123.9, 122.9, 116.8, 114.3, 112.7, 112.5, 75.4, 54.9, 47.4, 33.7, 19.6.

HRMS (ESI) calculated $[M+H]^+$ for $C_{31}H_{28}NO_3$: 462.2064, found: 460.2068.

FTIR (cm^{-1}) 3021, 2966, 2404, 1722, 1601, 1504, 1448, 1361, 1295, 1217, 1180, 916, 768.

3-(Benzyl(phenyl)amino)-1-phenylpropyl propionate (40c)



Following the general procedure, treatment of 1-benzyl-2-phenylazetidine **7** (0.112 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **21a** (0.223

g, 182 µL, 0.75 mmol) with propionic acid **35y** (0.056 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 3-(benzyl(phenyl)amino)-1-phenylpropyl propionate as a colorless oil, **40c** (0.153 g, 82% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.44.

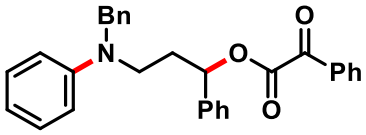
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.39 (m, 7H), 7.35 – 7.27 (m, 5H), 6.82 - 6.75 (m, *J* = 18.2, 3H), 5.93 (dd, J_1 = 7.9 Hz, J_2 = 5.5 Hz, 1H), 4.60 (q, *J* = 17.0, 2H), 3.64 – 3.47 (m, 2H), 2.50 – 2.34 (m, 3H), 2.31– 2.22 (m, 1H), 1.25 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 148.3, 140.4, 138.9, 129.3, 128.6, 128.1, 126.9, 126.7, 126.4, 116.6, 112.5, 74.0, 54.7, 47.4, 33.6, 27.9, 9.2.

HRMS (ESI) calculated $[M+H]^+$ for $C_{25}H_{28}NO_2$: 374.2115, found: 374.2118.

FTIR (cm^{-1}) 3022, 2407, 1717, 1598, 1502, 1451, 1362, 1269, 1219, 1109, 1032, 768.

3-(Benzyl(phenyl)amino)-1-phenylpropyl 2-oxo-2-phenylacetate (40d)



Following the general procedure, treatment of 1-benzyl-2-phenylazetidine **7** (0.112 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **21a** (0.223 g, 182 µL, 0.75 mmol) with 2-oxo-2-phenylacetic acid **35v** (0.113 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 3-(benzyl(phenyl)amino)-1-phenylpropyl 2-oxo-2-phenylacetate as a yellow oil **40d** (0.173 g, 77% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.41.

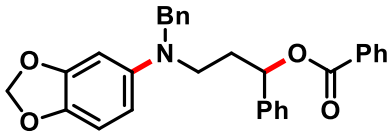
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.7 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.33 – 7.21 (m, 7H), 7.19 – 7.15 (m, 2H), 7.12 – 7.03 (m, 5H), 6.59 - 6.54 (m, 3H), 5.94 (dd, J_1 = 7.9 Hz, J_1 = 5.6 Hz, 1H), 4.40 (q, *J* = 17.1 Hz 2H), 3.48 - 3.33 (m, 2H), 2.38 – 2.23 (m, 1H), 2.22 – 2.10 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 186.2, 163.4, 148.2, 138.9, 138.7, 135.0, 132.4, 130.0, 129.4, 129.0, 128.9, 128.8, 128.7, 127.0, 126.7, 126.66, 116.9, 112.7, 76.7, 54.9, 47.4, 33.6.

HRMS (ESI) calculated $[M+H]^+$ for $C_{30}H_{28}NO_3$: 450.2064, found: 450.2067.

FTIR (cm^{-1}) 3022, 2972, 2403, 1736, 1689, 1598, 1504, 1448, 1213, 986, 919, 769.

3-(Benzo[*d*][1,3]dioxol-5-yl(benzyl)amino)-1-phenylpropyl benzoate (40e)



Following the general procedure, treatment of 1-benzyl-2-phenylazetidine **7** (0.112 g, 0.5 mmol) and 6-(trimethylsilyl)benzo[*d*][1,3]dioxol-5-yl trifluoromethanesulfonate **21ab** (0.257 g, 0.75 mmol) with benzoic acid **35a** (0.092 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 3-(benzo[*d*][1,3]dioxol-5-yl(benzyl)amino)-1-phenylpropyl benzoate as a yellow oil **40e** (0.142 g, 61% yield).

***R*$_f$** (Pet. ether /EtOAc = 95/05): 0.30.

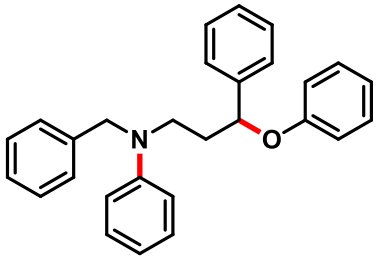
^{1}H NMR (400 MHz, CDCl$_3$) δ 8.10 (d, *J* = 7.7 Hz, 2H), 7.61 (t, *J* = 7.3 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.44 – 7.37(m, 4H), 7.35 - 7.29 (m, 3H), 7.24 (t, *J* = 6.3 Hz, 3H), 6.68 (d, *J* = 8.5 Hz, 1H), 6.40 (d, *J* = 2.0 Hz, 1H), 6.17 (dd, J_1 = 8.5 Hz, J_2 = 2.1 Hz, 1H), 6.06 (dd, J_1 = 8.1 Hz, J_2 = 5.3 Hz, 1H), 5.88 (s, 2H), 4.44 (q, *J* = 7.6 Hz., 2H), 3.53 - 3.38 (m, 2H), 2.48 – 2.34 (m, 1H), 2.34 – 2.20 (m, 1H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 165.9, 148.6, 144.7, 140.4, 139.6, 138.9, 133.2, 130.3, 129.8, 128.7, 128.6, 128.5, 128.2, 127.1, 127.0, 126.4, 108.6, 106.1, 100.7, 97.1, 74.9, 56.3, 48.4, 33.9.

HRMS (ESI) calculated $[M+H]^+$ for $C_{30}H_{28}NO_4$: 466.2013, found: 466.2009.

FTIR (cm^{-1}) 3022, 2925, 2404, 1719, 1600, 1499, 1450, 1364, 1269, 1217, 1107, 926, 769.

***N*-Benzyl-*N*-(3-phenoxy-3-phenylpropyl)aniline (40f)**



Following the general procedure, treatment of 1-benzyl-2-phenylazetidine **7** (0.112 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **21a** (0.223 g, 182 µL, 0.75 mmol) with phenol **37a** (0.71 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 99.5/0.5) of the crude reaction mixture using

silica gel afforded *N*-benzyl-*N*-(3-phenoxy-3-phenylpropyl)aniline as colourless oil **40f** (0.112 g, 57% yield).

***R*f** (Pet. ether /EtOAc = 98/02): 50.

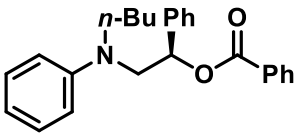
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 - 7.31 (m, 6H), 7.30 - 7.27 (m, 2H), 7.25 - 7.18 (m, 6H), 6.92 (t, *J* = 7.3 Hz, 1H), 6.87 (d, *J* = 8.1 Hz, 2H), 6.75 - 6.70 (m, 3H), 5.22 (dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz, 1H), 4.58 (q, *J* = 16.8 Hz, 2H), 3.73 - 3.68 (m, 2H), 2.34 - 2.25 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 158.11, 148.50, 141.75, 139.05, 129.47, 129.36, 128.78, 128.69, 127.69, 126.90, 126.72, 125.87, 120.94, 116.43, 115.97, 112.44, 77.96, 54.79, 47.87, 36.55.

HRMS (ESI) calculated $[M+H]^+$ for $C_{28}H_{28}NO$: 394.2165, found: 394.2170.

FTIR (cm^{-1}) 3019, 2979, 2401, 1599, 1506, 1453, 1357, 1274, 1216, 1029, 766.

(*R*)-2-(Butyl(phenyl)amino)-1-phenylethyl benzoate ((*R*)-36)[23]



Following the general procedure, treatment of (*S*)-1-butyl-2-phenylaziridine **(*S*)-34** (0.088 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **21a** (0.223 g, 182 μL, 0.75 mmol) with benzoic acid **35a** (0.092 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at -10 °C to rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 99/1) of the crude reaction mixture using silica gel afforded (*R*)-2-(butyl(phenyl)amino)-1-phenylethyl benzoate as a colourless viscous solid **((*R*)-36)** (0.150 g, 81% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.61.

HPLC (kromasil 5-Amycoat, 80:20 Pet.ether / IPA, 0.7 mL/min) *Major*: 7.7 min, *Minor*: 7.0 min, er = 99:1; $[\alpha]_D^{26}$ = -1.91 (c 1.0, $CHCl_3$).

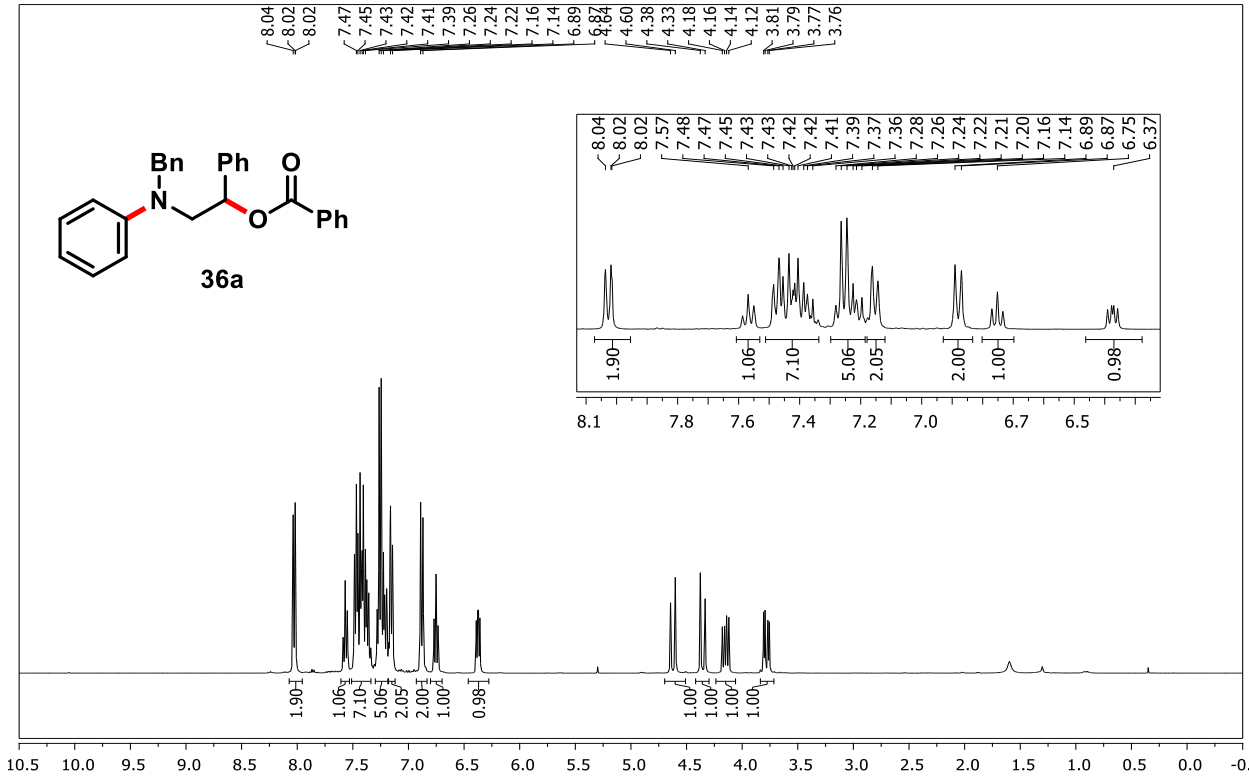
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, *J* = 7.9 Hz, 2H, H_{ar}), 7.59 (t, *J* = 7.7 Hz, 1H, H_{ar}), 7.53-7.37 (m, 7H, H_{ar}), 7.30 (t, *J* = 7.3 Hz, 2H, H_{ar}), 6.87 (d, *J* = 8.1 Hz, 2H, H_{ar}), 6.76 (t, *J* = 7.3 Hz, 1H, H_{ar}), 6.30 (t, *J* = 6.7 Hz, 1H), 4.04 (dd, J_1 = 7.9 Hz, J_2 = 15.1Hz, 1H), 3.68 (dd, J_1 = 5.2 Hz, J_2 = 15.0 Hz, 1H), 3.37-3.30 (m, 1H), 3.18-3.11 (m, 1H), 1.58-1.50 (m, 2H), 1.37-1.28 (m, 2H), 0.93 (t, *J* = 7.3 Hz, 3H)).

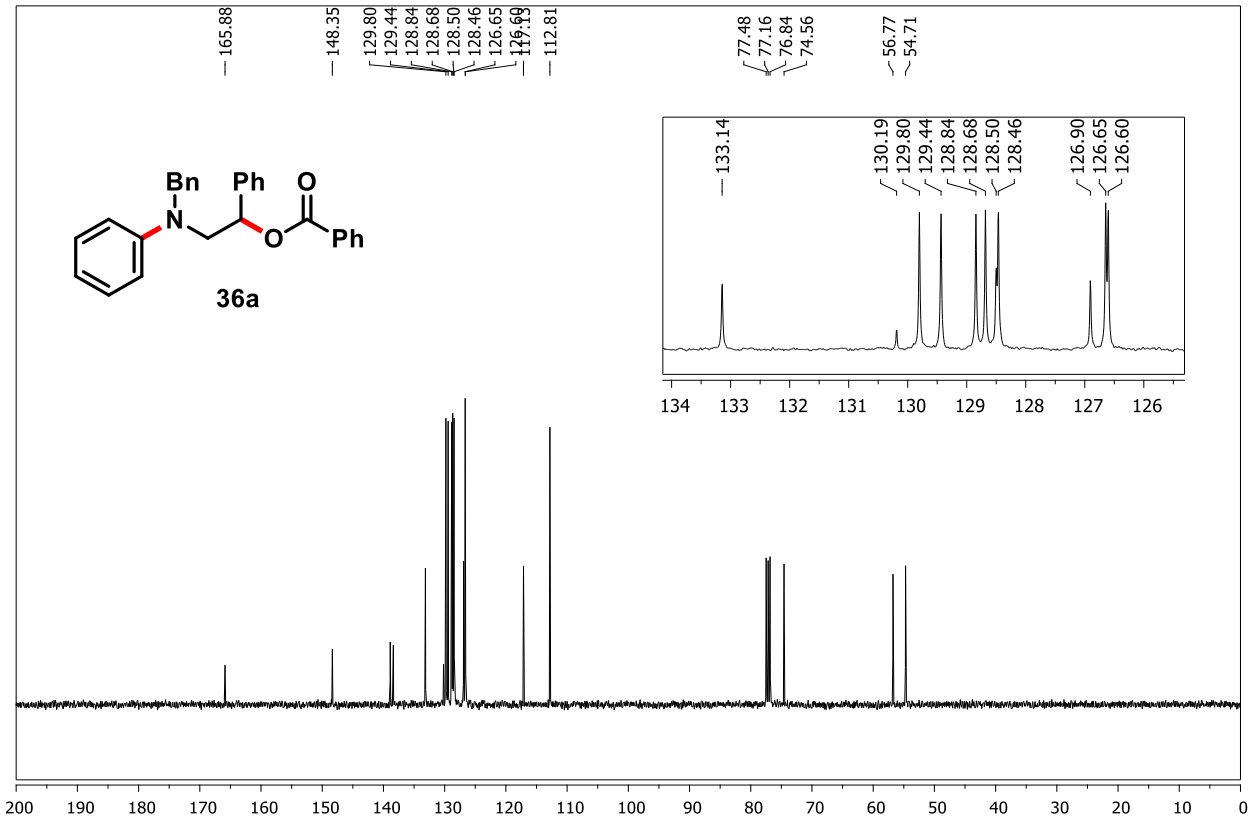
^{13}C NMR (100 MHz, $CDCl_3$) δ 165.83, 147.88, 139.01, 133.12, 130.23, 129.78, 129.40, 128.73, 128.45, 128.35, 126.56, 116.32, 112.40, 74.47, 56.84, 51.34, 28.87, 20.34, 14.01.

FTIR (cm^{-1}) 3023, 2959, 2873, 1718, 1598, 1505, 1451, 1268, 1196, 1177, 1069, 705.

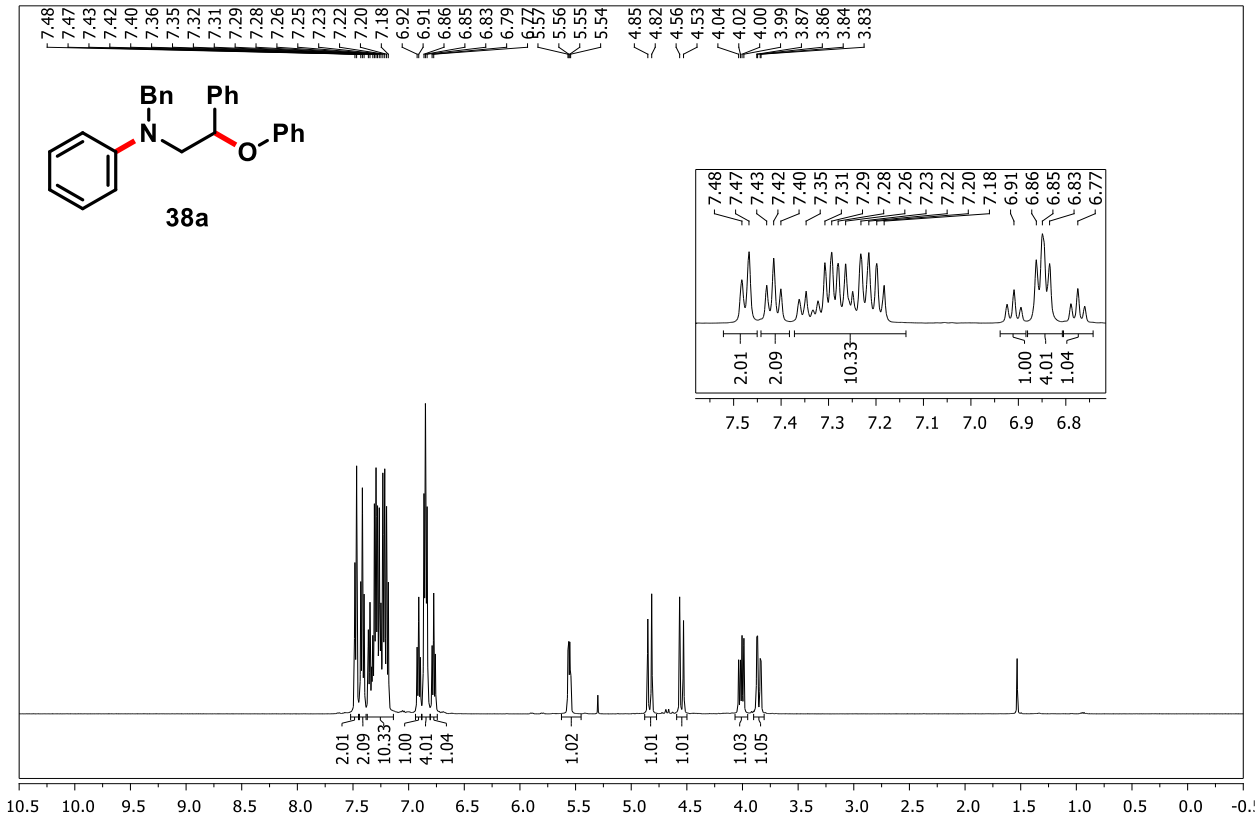
3.8.8. ^{1}H and ^{13}C NMR Spectra of Selected Compounds

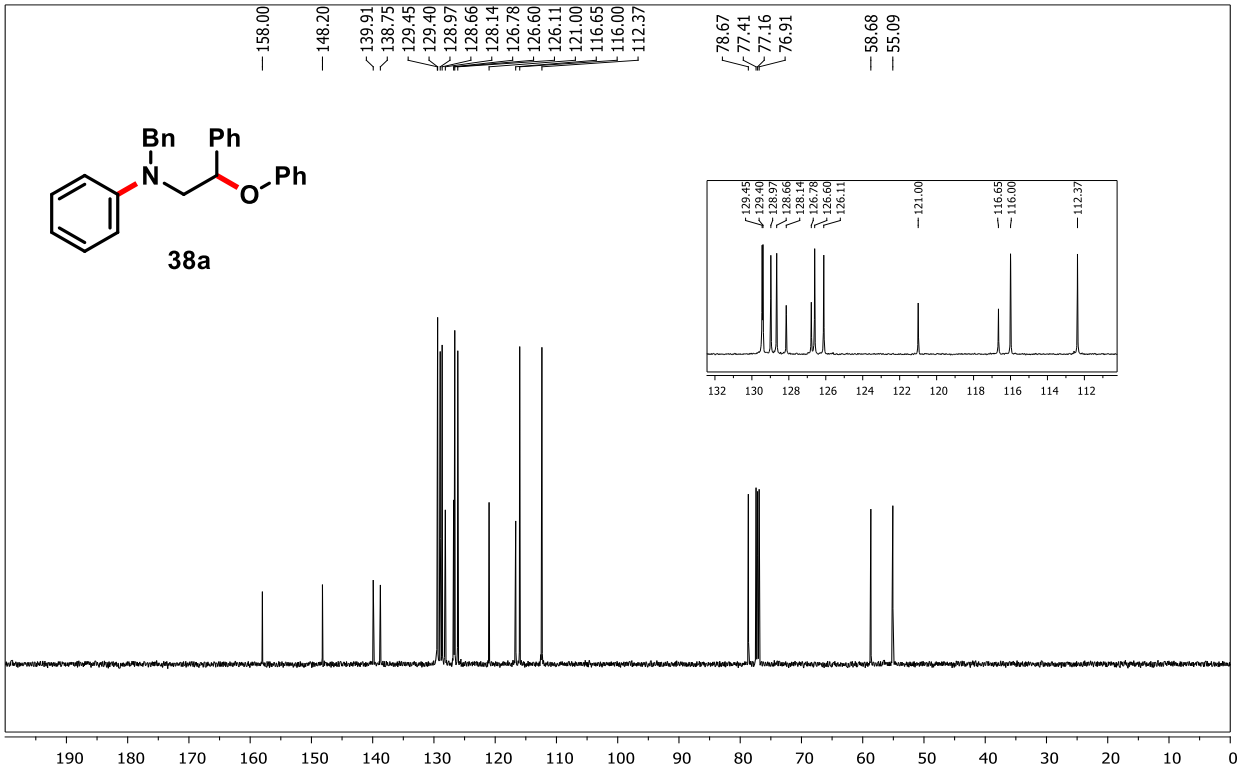
2-(Benzyl(phenyl)amino)-1-phenylethyl benzoate (36a)



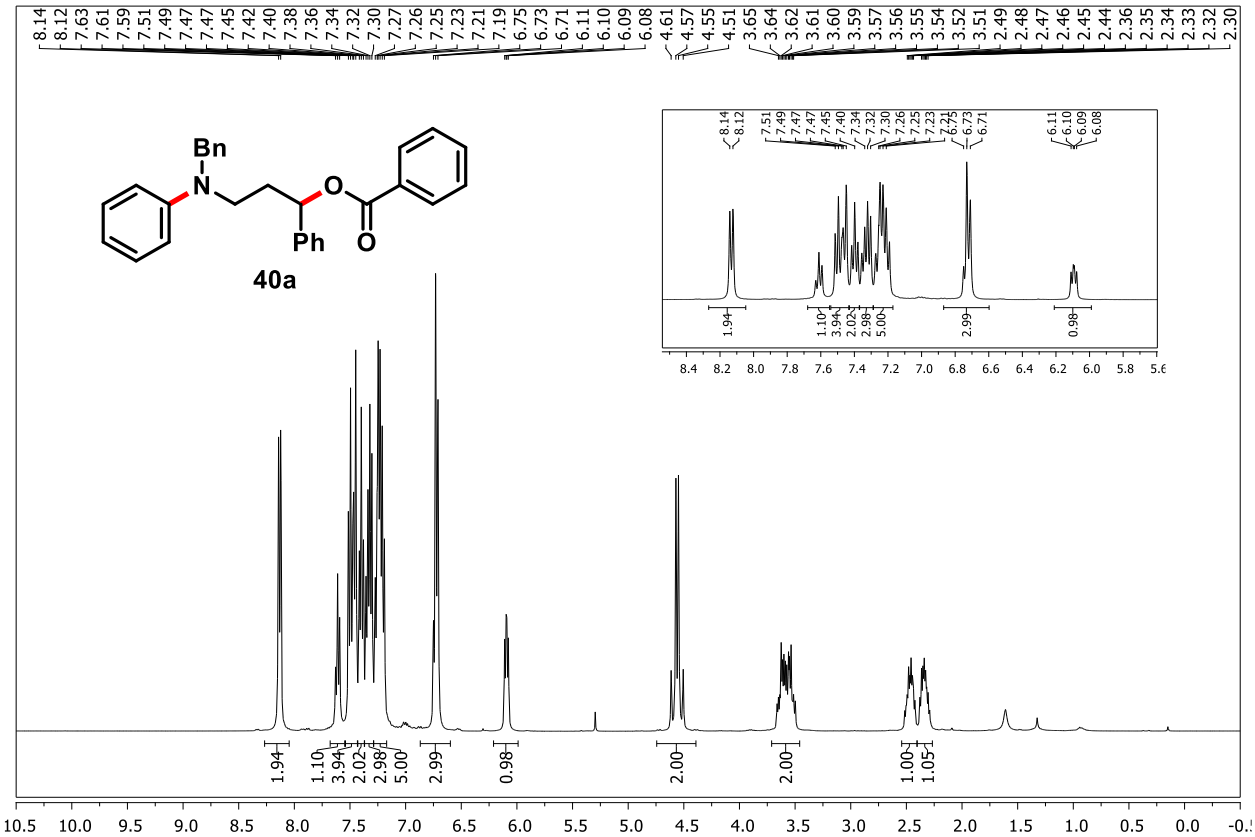


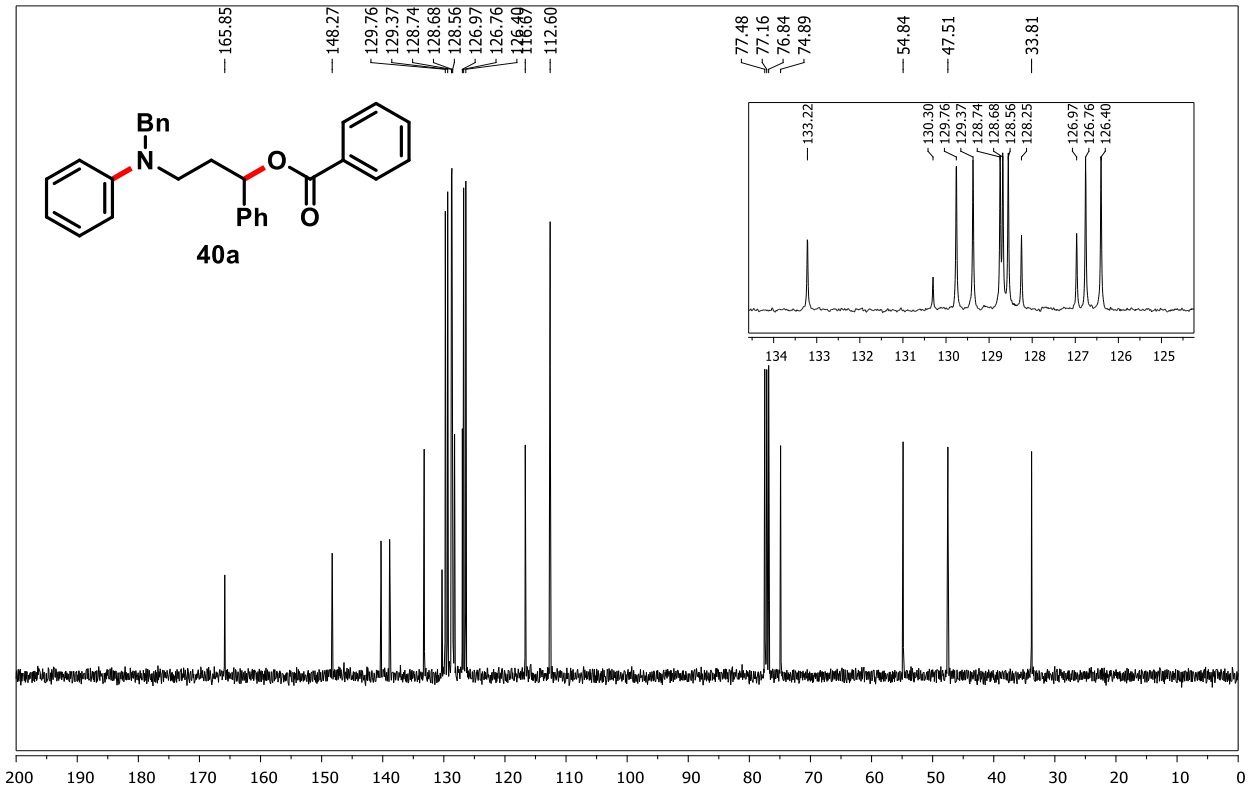
_N_-Benzyl-_N_-(2-phenoxy-2-phenylethyl)aniline (38a)





2-(Benzyl(phenyl)amino)-1-phenylpropyl benzoate (40a)


Bn
N
O
Ph
O
40a


Bn
N
O
Ph
O
40a

3.9. References

1. (a) Passerini, M.; Simone, L. *Gazz. Chim. Ital*. **1921**, *51*, 126. (b) Passerini, M.; Ragni, G. *Gazz. Chim. Ital*. **1921**, *61*, 964. (c) Riva, R.; Banfi, L.; Basso, A. In *Science of Synthesis: Multicomponent Reaction*; T. J. J. Müller, Ed.; Thieme: Stuttgart, Germany, 2012; Vol. 1.
2. Maeda, S.; Komagawa, S.; Uchiyama, M.; Morokuma, K. *Angew. Chem., Int. Ed*. **2011**, *50*, 644.
3. Yanai, H,;Oguchi, T.; Taguchi,T. *J. Org. Chem.* **2009**, *74*, 3927.
4. Soeta, T.; Kojima, Y; Ukaji, Y.; Inomata, K. *Org. Lett.* **2010**, *12*, 4341.
5. Liu, Z.; Larock, R. C. *Org. Lett.* **2004**, *6*, 99.
6. Liu, Z.; Larock, R. C. *J. Org. Chem.* **2006**, *71*, 3198.
7. (a) Giumanini, A. G. *J. Org. Chem.* **1972**, *37*, 513. For a report on the reaction of arynes with 1-azirines, see: (b) Nair, V.; Kim, K. H. *J. Org. Chem.* **1975**, *40*, 3784.
8. Stephens, D.; Zhang, Y.; Cormier, M.; Chavez, G.; Arman, H.; Larionov, O. V. *Chem. Commun.* **2013**, *49*, 6558.
9. Tang, C.-Y.; Wang, G.; Yang, X.-Y.; Wu, X.-Y.; Sha, F. *Tetrahedron Lett*. **2014**, *55*, 6447.
10. For recent reviews on aryne chemistry, see: (a) Shi, J.; Li, Y.; Li, Y. *Chem. Soc. Rev.* **2017**, *46*, 1707. (b) Idiris, F. I. M.; Jones, C. R. *Org. Biomol. Chem*. **2017**, *15*, 9044. (c) García-López, J.-A.; Greaney, M. F. *Chem. Soc. Rev.***2016**, *45*, 6766. (d) Bhojgude, S. S.; Bhunia, A.; Biju, A. T. *Acc. Chem. Res*. **2016**, *49*, 1658. (r) Goetz, A. E.; Shah, T. K.; Garg, N. K. *Chem. Commun*. **2015**, *51*, 34. (f) Dubrovskiy, A. V.; Markina, N. A.; Larock, R. C. *Org. Biomol. Chem.* **2013**, *11*, 191. (g) Wu, C.; Shi, F. *Asian J. Org. Chem.* **2013**, *2*, 116. (h) Pérez, D.; Peña, D.; Guitián, E. *Eur. J. Org. Chem.* **2013**, 5981. (i) Tadross, P. M.; Stoltz, B. M. *Chem. Rev.* **2012**, *112*, 3550. (j) Gampe, C. M.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2012**, *51*, 3766. (k) Bhunia, A.; Yetra, S. R.; Biju, A. T. *Chem. Soc. Rev.* **2012**, *41*, 3140. (l) Okuma, K. *Heterocycles* **2012**, *85*, 515. (m) Yoshida, H.; Ohshita, J.; Kunai, A. *Bull. Chem. Soc. Jpn.* **2010**, *83*, 199
11. For selected reports, see: (a) Kaicharla, T.; Thangaraj, M.; Biju, A. T. *Org. Lett.* **2014**, *16*, 1728. (b) Li, J.; Noyori, S.; Nakajima, K.; Nishihara, Y. *Organometallics*. **2014**, *33*, 3500. (c) Sha, F.; Luling Wu, L.; Huang, X. *J. Org. Chem*. **2012**, *77*, 3754. (d) Yoshida,

H.; Asatsu, Y.; Mimura, Y.; Ito, Y.; Ohshita, J.; Takaki, K. *Angew. Chem., Int. Ed.* **2011**, *50*, 9676. (e) Allan, K. M.; Gilmore, C. D.; Stoltz, B. M. *Angew. Chem., Int. Ed.* **2011**, *50*, 4488. (f) Yoshida, H.; Ito, Y.; Ohshita, J. *Chem. Commun*. **2011**, *47*, 8512. (g) Sha, F.; Huang, X. *Angew. Chem., Int. Ed.* **2009**, *48*, 3458. (h) Yoshida, H.; Fukushima, H.; Ohshita, J.; Kunai, A. *Angew. Chem., Int. Ed*. **2004**, *43*, 3935.

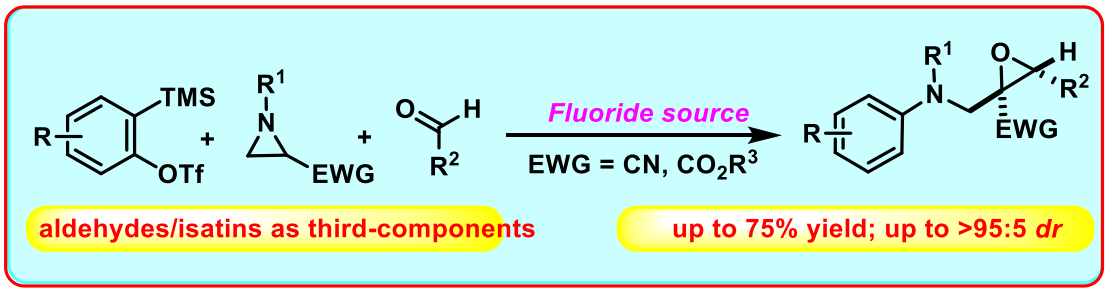
12. (a) Zhou, Y.; Chi, Y.; Zhao, F.; Zhang, W.-X.; Xi, Z. *Chem. Eur. J*. **2014**, *20*, 2463. (b) Yoshida, H.; Fukushima, H.; Ohshita, J.; Kunai, A. *J. Am. Chem. Soc.* **2006**, *128*, 11040.
13. (a) Hendrick, C. E.; McDonald, S. L.; Wang, Q. *Org. Lett.* **2013**, *15*, 3444. (b) Yoshida, H.; Morishita, T.; Ohshita, J. *Org. Lett.* **2008**, *10*, 3845. (c) Yoshida, H.; Morishita, T.; Fukushima, H.; Ohshita, J.; Kunai, A. *Org. Lett.* **2007**, *9*, 3367. (d) Morishita, T.; Fukushima, H.; Yoshida, H.; Ohshita, J.; Kunai, A. *J. Org. Chem.* **2008**, *73*, 5452.
14. (a) Bhunia, A.; Roy, T.; Pachfule, P.; Rajamohanan, P. R.; Biju, A. T. *Angew. Chem., Int. Ed.* **2013**, *52*, 10040. (b) Bhunia, A.; Porwal, D.; Gonnade, R. G.; Biju, A. T. *Org. Lett.* **2013**, *15*, 4620. For related works, see: (c) Nawaz, F.; Mohanan, K.; Charles, L.; Rajzmann, M.; Bonne, D.; Chuzel, O.; Rodriguez, J.; Coquerel, Y. *Chem. Eur. J.* **2013**, *19*, 17578. (d) Liu, P.; Lei, M.; Hu, L. *Tetrahedron* **2013**, *69*, 10405. (e) Jeganmohan, M.; Bhuvaneswari, S.; Cheng, C.-H. *Chem. Asian J.* **2010**, *5*, 153. (f) Jeganmohan, M.; Cheng, C.-H. *Chem. Commun*. **2006**, 2454.
15. (a) Bhunia, A.; Kaicharla, T.; Porwal, D.; Gonnade, R. G.; Biju, A. T. *Chem. Commun*. **2014**, *50*, 11389. (b) Bhunia, A.; Roy, T.; Gonnade, R. G.; Biju, A. T. *Org. Lett.* **2014**, *16*, 5132.
16. (a) Yoshioka, E.; Tamenga, H.; Miyabe, H. *Tetrahedron Lett.* **2014**, *55*, 1402. (b) Zhou, C.; Wang, J.; Jin, J.; Lu, P.; Wang, Y. *Eur. J. Org. Chem*. **2014**, 1832. (c) Yoshioka, E.; Tanaka, H.; Kohtani, S.; Miyabe, H. *Org. Lett.* **2013**, *15*, 3938. (d) Yoshioka, E.; Kohtani, S.; Miyabe, H. *Angew. Chem. Int. Ed*. **2011**, *50*, 6638. (e) Yoshida, H.; Ito, Y.; Ohshita, J. *Chem. Commun*. **2011**, *47*, 8512. (f) Yoshioka, E.; Kohtani, S.; Miyabe, H. *Org. Lett.* **2010**, *12*, 1956.
17. (a) Li, H.-Y.; Xing, L.-J.; Lou, M.-M.; Wang, H.; Liu, R.-H.; Wang, B. *Org. Lett.* **2015**, *17*, 1098. (b) Liu, F.-L.; Chen, J.-R.; Zou, Y.-Q.; Wei, Q.; Xiao, W.-J. *Org. Lett.* **2014**, *16*, 3768.

18. Berti, F.; Crotti, P.; Cassano, G.; Pineschi, M. *Synlett* **2012**, 2463.
19. (a) Himeshima, Y.; Sonoda, T.; Kobayashi, H. *Chem. Lett.* **1983**, 1211. For a simplified procedure, see: (b) Peña, D.; Cobas, A.; Pérez, D.; Guitián, E. *Synthesis* **2002**, 1454.
20. For an early report on use of phenol in aryne MCCs, see: Pal, R. S.; Bokadia, M. M. *Pol. J. Chem*. **1978**, *52*, 1473. See also: Nucleophilic Coupling with Arynes. Kessar, S. V. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, England, 1991; Vol. 4, p. 483.
21. (a) Dou, X. Y.; He, L. N.; Yang, Z. Z.; Wang, J. L. *Synlett* **2010**, 2159. (b) Drouillat, B.; d'Aboville, E.; Bourdreux, F.; Couty, F. *Eur. J. Org. Chem.* **2014**, 1103.
22. Sato, Y.; Tamura, T.; Kinbara, A.; Morib, M. *Adv. Synth. Catal.* **2007**, *349*, 647. (b) Peña, D.; Cobas, A.; Pérez, D.; Guitián, E. *Synthesis* **2002**, 1454.
23. For the synthesis of (*S*)-1-butyl-2-phenylaziridine, see: Du, Y.; Wu, Y.; Liu, A. H.; He, L. N. *J. Org. Chem.* **2008**, *73*, 4709.
24. Roy, T.; Bhojgude, S. S.; Kaicharla, T.; Thangaraj, M.; Garai, B.; Biju, A. T. *Org. Chem. Front.* **2016**, *3*, 71.

Chapter 4

Synthesis of Functionalized Amino Epoxides by a Three-Component Coupling Involving Aziridines, Arynes and Aldehydes

A transition-metal-free three-component coupling involving *N*-substituted aziridines, arynes and aldehydes resulting in the formation of trisubstituted *N*-aryl α-amino epoxides has been demonstrated. The reaction likely proceeds *via* the highly strained cyclic nitrogen ylide intermediates generated from aziridines and arynes. The methodology developed could also be utilized for the diastereselective synthesis of spiroepoxy oxindoles with isatin as the third component.



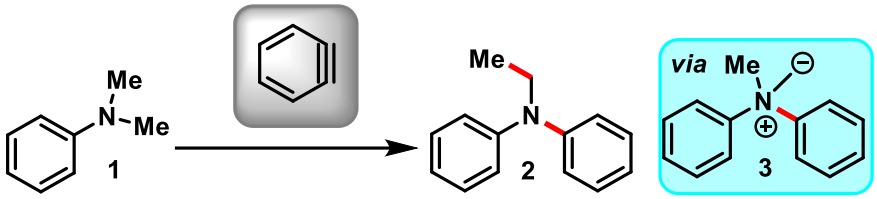
Chem. Commun. **2016**, *52*, 9094

4.1. Introduction

The fascinating chemistry of arynes, developed significantly in the last two decades has been utilized by sythetic chemists for the construction of various synthetically valuable molecules.[1] The utility of arynes has recently been explored with the intermediate's ability for proton abstraction and subsequent ylide generation. The possibility of the aryne induced ylide intermediates have been explored by various groups for the synthesis of complex molecules.

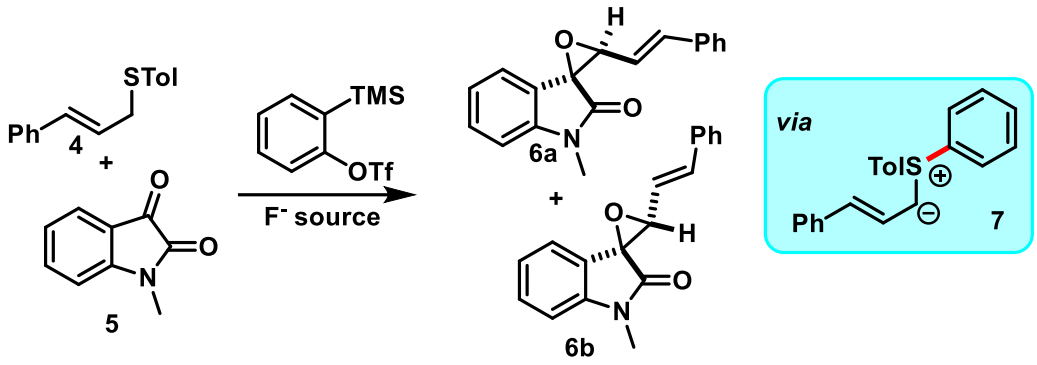
4.1.1 Reactions Involving Aryne Induced Ylides

In 1966, Lepley found that when aryne intermediate was generated using *n*-butyllithium and halobenzene and was allowed to react with dialkylanilines, alkyl transfer product was formed *via* aryne induced ylide formation.[2] For instance, the reaction of dimethylaniline **1** with aryne delivered *N*-ethyldiphenylamine **2**. The reaction proceeds *via* the generation of ylide **3** (Scheme 4.1).



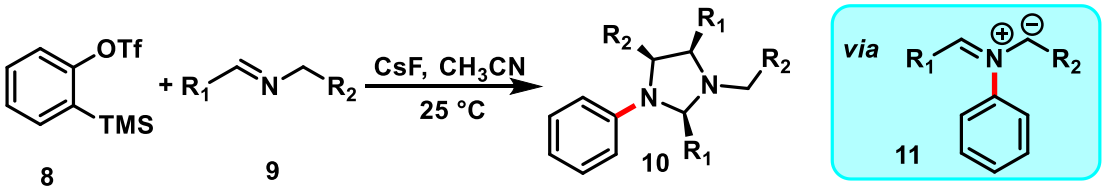
Scheme 4.1. Aryne Induced Ylide Uncovered by Lepley

In 2014 Xu and co-workers developed a synthetic route to spiroepoxyoxindoles **6** *via* aryne induced sulphur ylide generation. The sulphur ylide generated via the nucleophilic addition of sulphide **4** was trapped with isatin **5** to deliver the highly substituted epoxide product.[3] No use of preformed sulphonium salts and strong bases makes this a practical protocol for epoxidation reactions (Scheme 4.2).



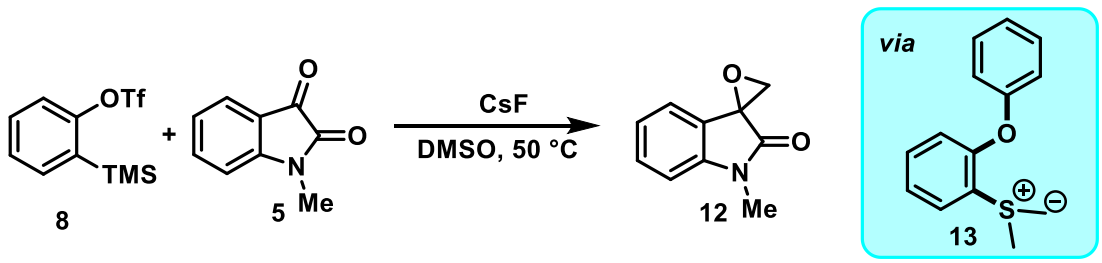
Scheme 4.2. Aryne induced ylide for epoxidation of oxindoles

In 2015, Hwu group demonstrated a new and efficient method for the direct synthesis of various imidazolidines **10** *via* the aryne induced ylides from Schiff bases **9**.[4] The mechanism involves an aryne-induced ylide formation **11**, which proceeded through a nucleophilic attack followed by a proton transfer. Subsequent [3+2] cycloaddition with another molecule of Schiff base produced imidazolidines **10** under mild conditions in good to excellent yields (Scheme 4.3).



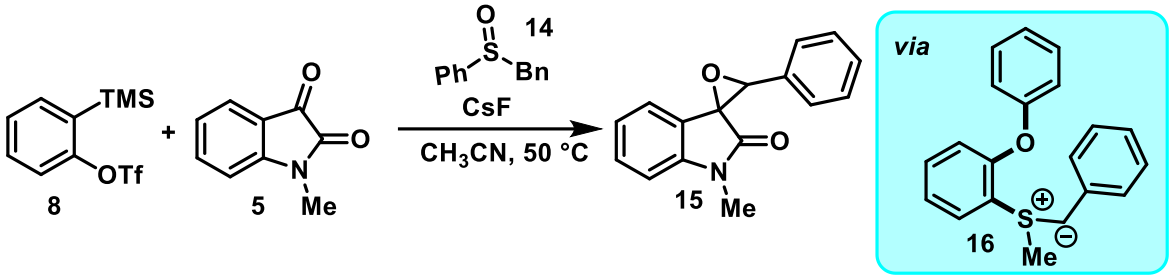
Scheme 4.3. Reaction of arynes with Schiff bases

In 2015, Wang group observed the formation of sulphur ylide in the reaction of arynes with isatin **5** in DMSO. The DMSO solvent reacted with two molecules of aryne to form sulphur ylide **13**. This aryne induced ylide is trapped with isatin to form the spiroepoxyoxindoles **12** (Scheme 4.4).[5]



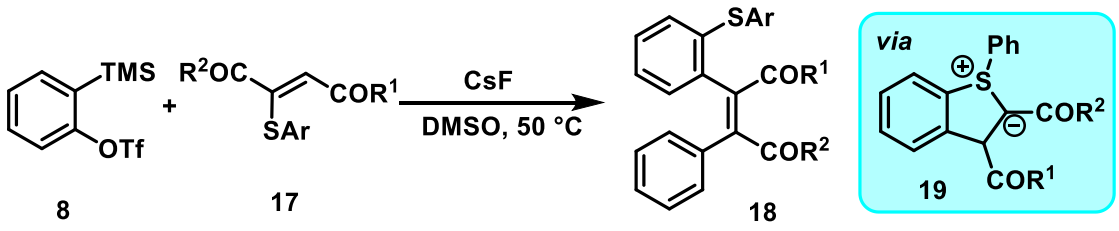
Scheme 4.4. Formation of spiroepoxyoxindole *via* ylide generation

In 2016, the same group has extended this method of sulphur ylide generation using the reaction of aryne in DMSO for the epoxidation of various carbonyl compounds.[6] The mechanism involves the in situ formation of sulphur ylide **16** from sulfoxide **14** and benzyne generated from **8** through the S–O bond insertion and deprotonation. This strong base-free approach provides a convenient way to introduce the substituted methylene groups onto the carbonyl carbon (Scheme 4.5).



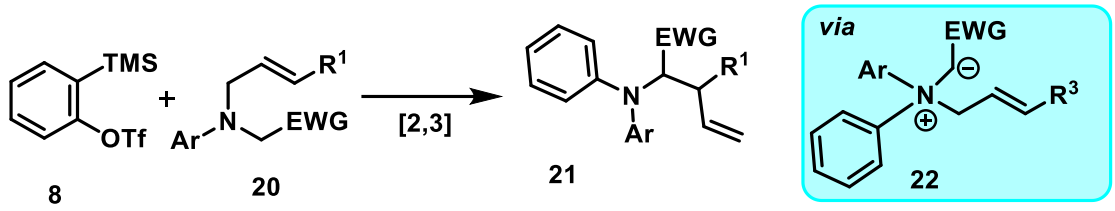
Scheme 4.5. Aryne induced epoxidation of carbonyl compounds

In 2016, Studer group uncovered the reaction of in situ generated benzannulated sulfonium ylides **19** in the reaction of arynes with vinyl sulphides **17**.[7] A [3+2] cycloaddition between arynes with vinyl sulphides generates the ylide intermediate. This reactive ylide intermediate upon trapping with electrophiles (proton transfer or a second aryne addition) and subsequent β-elimination give rise to highly substituted alkenes **18** with high stereoselectivity (Scheme 4.6).



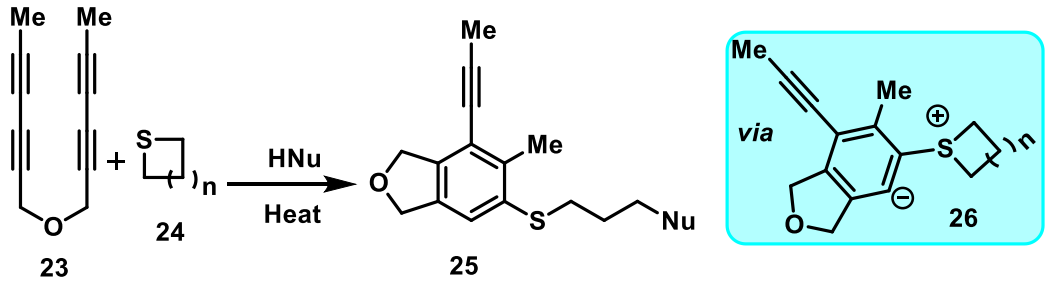
Scheme 4.6. Aryne induced ylide route to highly substituted alkenes

A transition-metal-free and mild [2,3] Stevens rearrangement of tertiary allylic amines **20** for the synthesis of functionalized homoallylic amines **21** *via* aryne induced ylide **22** has been uncovered independently by Biju, Tian and Sweaney groups recently (See chapter 5 for details) (Scheme 4.7).[8]



Scheme 4.7. Aryne induced [2,3] Stevens rearrangement

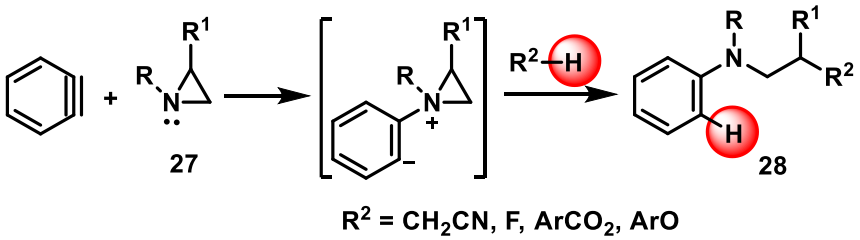
In 2016, Hoye and co-workers reported the sulphur ylide generation in the reaction of various sulphides **24** with arynes generated *via* the hexadehydro-Diels–Alder (HDDA) cycloisomerization of **23**. The initially produced 1,3-betaine undergoes intramolecular proton transfer to generate a more stable sulfur ylide **26**. Upon protonation and ring opening, this sulphur ylide gets reformed into complex molecules **25** (Scheme 4.8).[9]



Scheme 4.8. Aryne induced [2,3] Stevens rearrangement

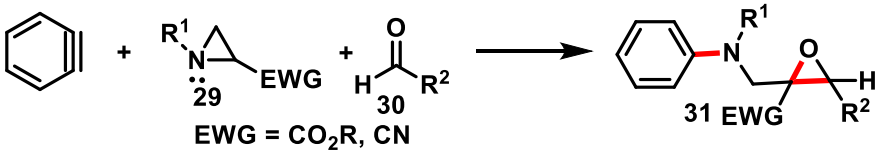
4.2. Statement of the Problem

Nitrogen nucleophiles are widely used in the reaction with arynes for the synthesis of complex aniline derivatives. Recently, our group has demonstrated the aryne three-component coupling with aziridines **27** with carboxylic acids or water as the third component for the synthesis of amino alcohol derivatives **28**.[10,11] Also, the use of acetonitrile and fluoride for the ring opening of aziridines has been uncovered by Larionov[12] and Sha group[13] respectively (Scheme 4.9).



Scheme 4.9. Three-component coupling involving arynes and aziridines

α-Amino epoxides are important class of molecules as they are key building blocks for the direct access to amino sugars and oxygenated amino acids.[14] Conventionally, α-amino epoxides are synthesized from the *N*-protected α-amino acids by converting the acid group to vinyl/aldehyde/halomethyl ketone functionality followed by the epoxidation reaction. However, this method is highly useful for the synthesis of monosubstituted α-amino epoxides, this procedure finds limited application to the synthesis of multisubstituted epoxides. The use of aryne for the generation of ylides and subsequent trapping has been one of the recently emerged strategies in aryne chemistry. In this chapter, a transition-metal-free and mild method for the straightforward and diastereoselective synthesis of *N*-aryl α–amino epoxides **31** by a three-component coupling using *N*-substituted aziridines **29**, arynes[15] and aldehydes **30** is discussed in detail (Scheme 4.10).



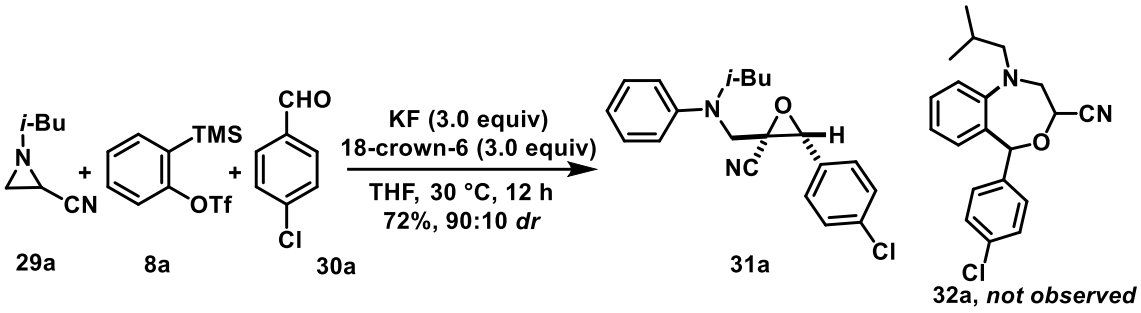
Scheme 4.10. Three-component coupling involving arynes, aziridines and aldehydes

4.3. Results and Discussion

4.3.1. Optimization Studies

The study on aryne induced ylide reaction was commenced with the treatment of *N*-isobutyl aziridines **29a** with aryne precursor **8a** and 4-chloro benzaldehyde **30a**. To our delight, the reaction furnished the amino epoxide **31a** in 72% yield (major diastereomer) with 9:1 *dr* (Scheme 4.11). The possible benzo-oxazepine derivative **32a** formed by the interception of the aziridines aryne zwitter ion with 4-chloro benzaldehyde was not observed under the present reaction conditions. Further optimization could not increase the yield of **31a**. The use of other fluoride sources such as CsF, tetrabutyl ammonium fluoride (TBAF) and tetrabutylammonium difluorotriphenylsilicate **(**TBAT) reduced the yield of **31a**, however maintained the diastereoselectivity. The presence of electron-withdrawing -CN group was mandatory for this reaction, and the attempted reactions with 2-aryl

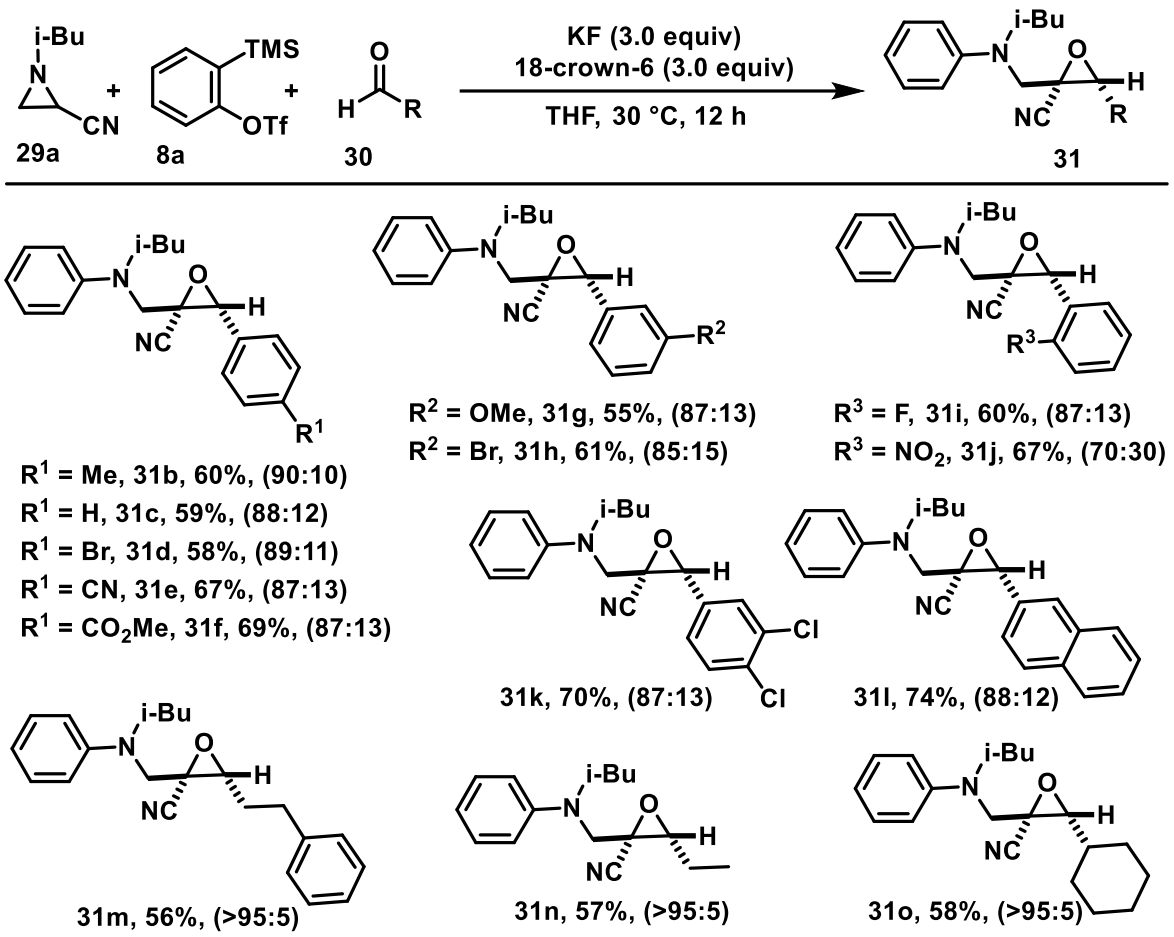
aziridines did not afford the amino epoxide product. The fluorine incorporated product in the reaction of arynes with aziridines recently reported by Wu and Sha was not observed under the optimized conditions which indicates that the reaction proceeds *via* the more favourable intramolecular proton abstraction by aryne leading to the cyclic nitrogen ylide.



Scheme 4.11. MCC involving *N*-isobutyl aziridine, aryne and aldehydes

4.3.2. Synthesis of α-Amino Epoxides

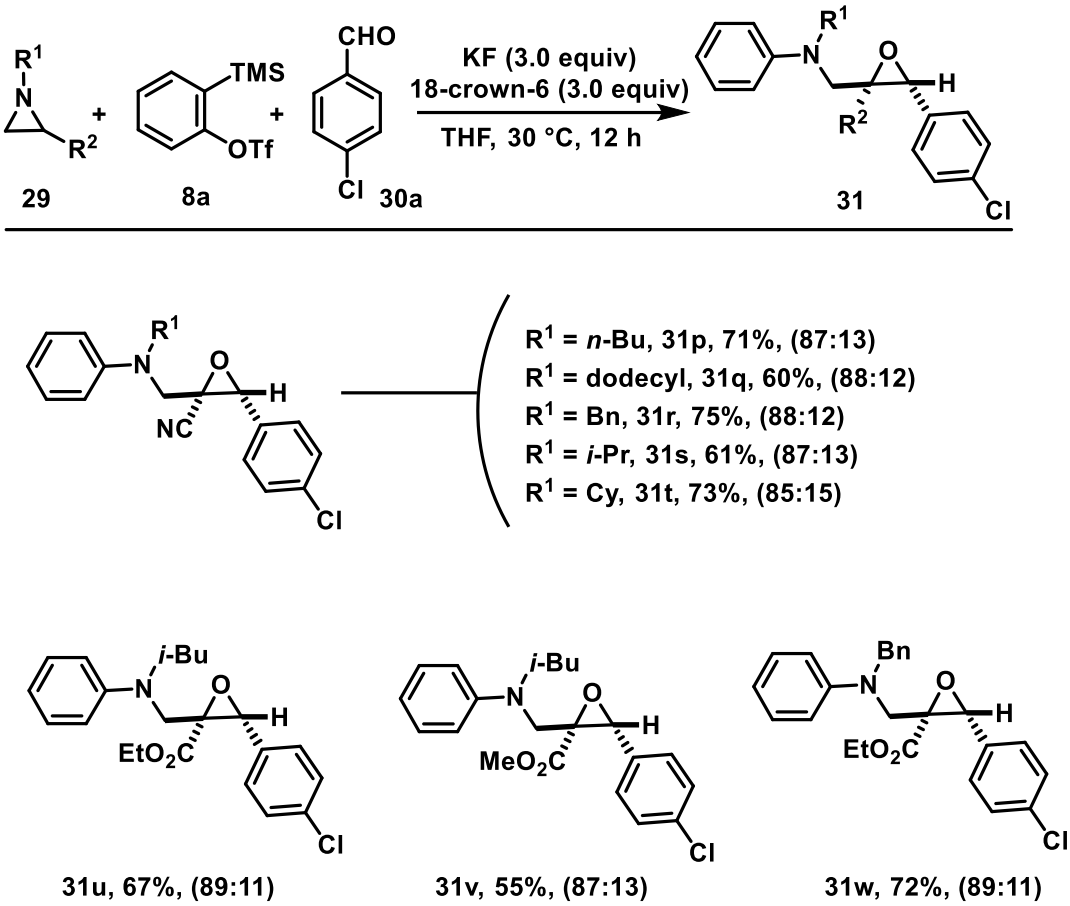
After establishing the optimized reaction conditions for the present transformation, we then investigated the scope of this reaction. A number of aldehydes were screened to check the versatility of the present methodology. First, the generality was evaluated by varying different aldehydes. To our delight, aldehydes having electronically different substituents at the para-position of the ring were well-tolerated leading to the synthesis of corresponding α-amino epoxide derivatives in good yields with moderate *dr* irrespective of the substrate electronics (**31b-31f**). Moreover, aldehydes with substituents at the *meta*- and *ortho*-positions of the ring underwent smooth conversions to amino epoxide derivatives in moderate yields and *dr* (**31g-31j**). In addition, 2-naphthaldehyde and 3,4 disubstituted aldehyde also afforded corresponding products in good yields and moderate *dr* (**31k** and **31l**). Notably, aliphatic aldehydes including cyclohexyl carboxaldehyde, hydrocinnamaldehyde and propanal funished the corresponding products in moderate yields and excellent selectivities (**31m-31o**). Disappointingly, heterocyclic aldehydes such as furfural, thiophene 2-carboxaldehyde and pyridine 2-carboxaldehyde did not afford the α-amino epoxides under the present reaction conditions possibly due to the cycloaddition side products (Scheme 4.12).



General conditions: **29a** (0.60 mmol), **8a** (0.75 mmol), **30** (0.50 mmol) KF (3.0 equiv), 18-crown-6 (3.0 equiv), THF (2.0 mL), rt, 12 h. Isolated yields of the major diastereomer are given.

Scheme 4.12. Scope of aldehydes in aryne MCC triggered by Aziridines

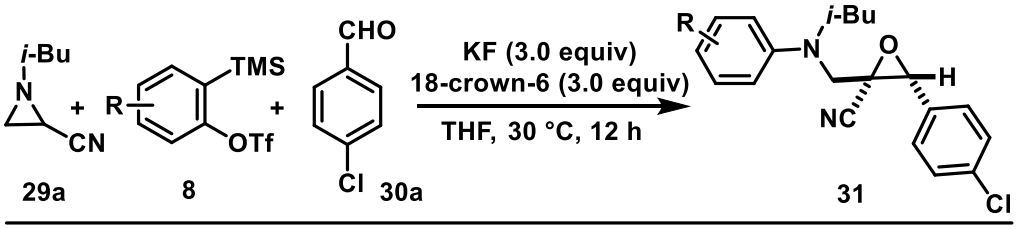
The scope of the reaction with various aziridines was also investigated (Scheme 4.13). Various *N*-alkyl substituted aziridines were well tolerated and the corresponding products were isolated in moderate to good yields (**31p**-**31t**). Notably, linear as well as branched *N*-substitution was tolerated under the present conditions. In the case of *N*-benzyl aziridine, the structure and relative stereochemistry of the major diastereomer **31r** and minor isomer **31r'** confirmed using single-crystal X-ray analysis. Apart from nitriles, esters as electron withdrawing substituents on aziridines were also well tolerated furnishing products in moderate yield and diastereoselectivity (**31u**-**31w)** (Scheme 4.13).



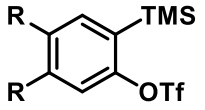
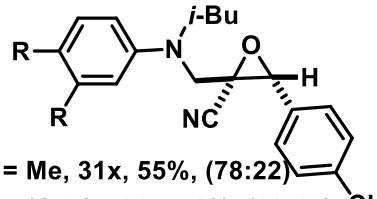
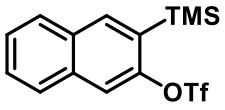
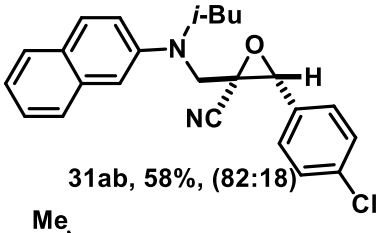
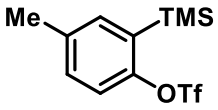
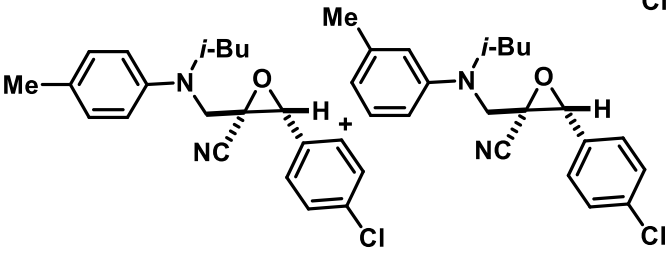
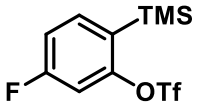
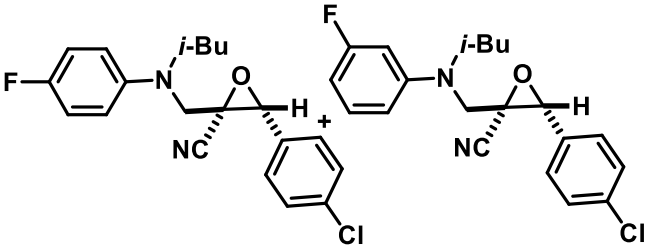
General conditions: **29** (0.60 mmol), **8a** (0.75 mmol), **30a** (0.50 mmol) KF (3.0 equiv), 18-crown-6 (3.0 equiv), THF (2.0 mL), rt, 12 h. Isolated yields of the major diastereomer are given.

Scheme 4.13. Scope of aziridines in aryne MCC triggered by aziridines

The scope of this reaction with differently substituted arynes was also carried out (Table 4.1). Electronically different symmetrical 4,5-disubstituted arynes generated from their precursors underwent efficient MCCs with aziridine **29a** and 4-chloro benzaldehyde **30a** to afford functionalized epoxides in moderate yields and diastereoselectivities (**31x-31ab**). The 4-methyl benzyne resulted in an inseparable mixture of regioisomers **31ac** and **31ac′** in a 1:1 ratio and in 64% yield with 7:1 *dr*. Moreover, an inseparable mixture of regioisomers **31ad** and **31ad′** in a 6:1 ratio and in 65% yield was obtained by using 4-fluorobenzyne as the aryne component in this reaction (Table 4.1).



29a 8 30a 31

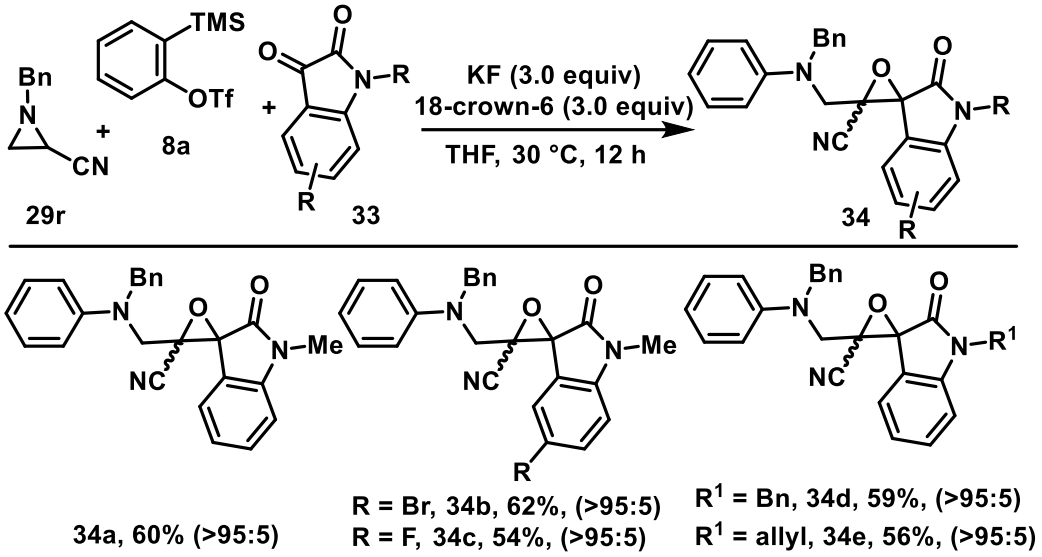
entry	aryne precursor	product, yield (%), and *dr*
		
1	8b, R = Me	R = Me, 31x, 55%, (78:22)
2	8c, R = $(CH_2)_3$	R = $(CH_2)_3$, 31y, 59%, (83:17)
3	8d, R = $O(CH_2)O$	R = $O(CH_2)O$, 31z, 55%, (72:28)[b]
4	8e, R = F	R = F, 31aa, 58%, (82:18)
5	 8f	 31ab, 58%, (82:18)
6	 8g	 31ac and 31ac', 64%, (85:15), [1:1][c]
7	 8h	 31ad and 31ad', 65%, (78:22), [2:1][c]

General conditions: **29a** (0.60 mmol), **8** (0.75 mmol), **30a** (0.50 mmol) KF (3.0 equiv), 18-crown-6 (3.0 equiv), THF (2.0 mL), rt, 12 h. Isolated yields of the major diastereomer are given.

Table 4.1. Scope of arynes in MCC triggered by aziridines

4.3.3. Synthesis of Spiroepoxy Oxindoles

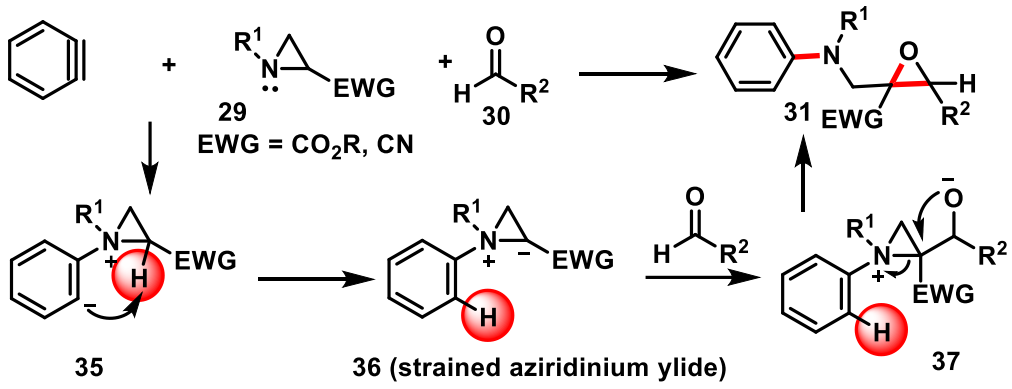
This aryne induced ylide coupling reaction triggered by aziridines is not limited to aldehydes as the third-component. *N*-substituted isatins could also be used as the ylide trapping component. Treatment of the aziridine **29r** with aryne generated from **8a** and the *N*-methyl isatin **33a** resulted in the formation of the spiroepoxy oxindole **34a** in 60% yield and in excellent diastereoselectivity of >95:5. Halogen substitution on the carbocyclic ring of isatin was well tolerated in the present protocol. Variation of *N*-substitution on isatin did not affect the outcome of the reaction. In all the cases, the spiroepoxy oxindole was formed in moderate to good yields and excellent diastereoselectivity (**34b**-**34e**) (Scheme 4.14).



Scheme 4.14. Synthesis of spiroepoxy oxindoles

4.3.4. Reaction Mechanism

The nucleophilic attack of aziridine to aryne generates the aziridine-aryne zwitterion **35,** followed by an intramolecular proton abstraction to generate a transient nitrogen ylide intermediate **36**. This strained aziridinium ylide **36** could add to aldehyde generating the alkoxide intermediate **37**, which opens the aziridinium species to furnish the trisubstituted epoxide (Scheme 4.15).[16]



Scheme 4.15. Proposed mechanism

4.4. Conclusion

In conclusion, we have developed a protocol for the synthesis of amino epoxides *via* a muticomponent pathway involving aziridines arynes and aldehydes. The reaction proceeds *via* a novel cyclic aziridinium ylide which upon interception with various carbonyls resulted in highly substituted oxiranes. A multicomponent epoxidation strategy has been applied for the first time in aryne chemistry adding to the recent success of aryne MCCs. Further investigations on this aryne induced cyclic ammonium ylides are ongoing in our laboratory.[22]

4.5. Experimental Details

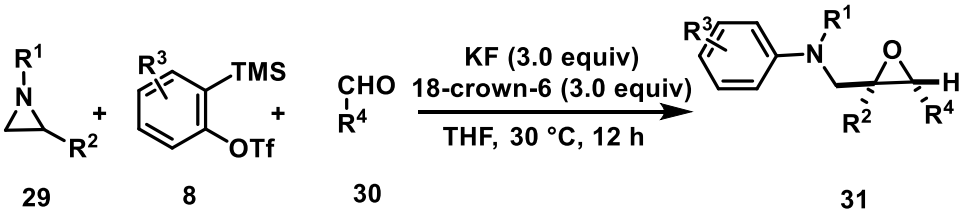
4.5.1 General Information

Unless otherwise specified, all reactions were carried out under an atmosphere of argon in flame-dried reaction vessels with Teflon screw caps. 30 °C corresponds to the room temperature of the lab when the experiments were carried out. THF was freshly purified by distillation over Na-benzophenone and was transferred under argon. [18]-Crown-6 was recrystallized from dry CH_3CN and KF was dried by heating at 110 °C for 12 h and left to cool under argon and stored in argon filled glove box. The aldehydes were purchased from either Sigma Aldrich, Acros Organics or from other commercial sources and were purified either by distillation or washing with $NaHCO_3$ solution, prior to use. All the aziridines were prepared following the literature procedure.[17] The 2(trimethylsilyl)phenyl trifluoromethanesulfonate **8a** and the other symmetric and unsymmetric aryne precursors were synthesized following literature procedure.[18]

Analytical thin layer chromatography was performed on TLC Silica gel 60 F_{254}. Visualization was accomplished with short wave UV light. Chromatography was performed on silica gel (230-400 mesh) by standard techniques eluting with solvents as indicated.

All compounds were fully characterized. ^{1}H and ^{13}C NMR spectra were recorded on Bruker AV 400, 500 in solvents as indicated. Chemical shifts (δ) are given in ppm. The residual solvent signals were used as references and the chemical shifts converted to the TMS scale ($CDCl_3$: δH = 7.26 ppm, δC = 77.16 ppm). Gas Chromatography was recorded on Agilent 7890 B GC. Infrared spectra were recorded on a Bruker Alpha-E Infrared Spectrophotometer. The wave numbers (n) of recorded IR-signals are quoted in cm^{-1}. HRMS data were recorded on either Thermo Scientific Q-Exactive, Accela 1250 pump or Waters SYNAPT G2 High Definition Mass Spectroscopy System. X-ray intensity data measurements of compound **31r** was carried out on a Bruker SMART APEX II CCD diffractometer with graphite-monochromatized (MoK_α= 0.71073Å) radiation at room temperature.

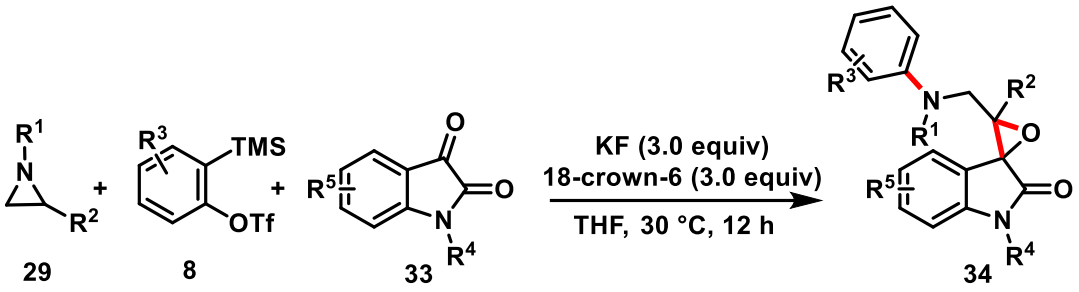
4.5.2. General Procedure for the Reaction Involving Aziridines, Arynes and Aldehydes



To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added KF (87 mg, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) inside a glove-box. Aldehyde **30** (0.50 mmol) followed by THF (2.0 mL) was added outside the glove-box under argon atmosphere (*solid* aldehydes were weighed in air and transferred to the screw-capped test tube by closing the argon flow and *liquid* aldehydes were transferred via syringe with argon flow). To this solution was added aziridine **29** (0.60 mmol) and continued stirring for five minutes at 30 °C. After five minutes of stirring, aryne precursor **8** (0.75 mmol) was added. Then the reaction mixture was kept stirring for 12 h at 30 °C. After 12 h, the reaction was stopped, the solvent was evaporated and the crude residue pre-adsorbed on silica gel and purified by flash column chromatography (Pet. ether /EtOAc =

98/02) on silica gel to afford the corresponding amino epoxides **31** in moderate to good yields. It may be mentioned that the reaction works well without glove-box techniques maintaining the isolated yield of **31**.

4.5.3. General Procedure for the Reaction Involving Aziridines, Arynes and Isatins



29 8 33 34

To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added KF (87 mg, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) inside a glove-box. Isatin **33** (0.50 mmol) followed by THF (2.0 mL) was added outside the glove-box under argon atmosphere. To this solution was added aziridine **29** (0.60 mmol) and continued stirring for five minutes at 30 °C. After five minutes of stirring, aryne precursor **8** (0.75 mmol) was added. Then the reaction mixture was kept stirring for 12 h at 30 °C. After 12 h, the reaction was stopped, the solvent was evaporated and the crude residue pre-adsorbed on silica gel and purified by flash column chromatography (Pet. ether /EtOAc = 90/10) on silica gel to afford the corresponding spiro amino epoxides **34** in moderate to good yields.

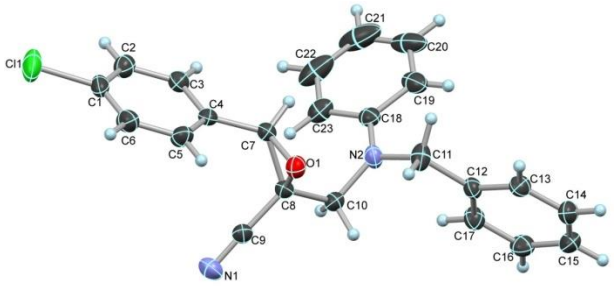
4.5.4. X-ray data of 31r and 31r'

X-ray intensity data measurements of compound **31r** and **31r'** were carried out on a Bruker SMART APEX II CCD diffractometer with graphite-monochromatized (MoK_α= 0.71073Å) radiation at room temperature. The X-ray generator was operated at 50 kV and 30 mA. A preliminary set of cell constants and an orientation matrix were calculated from three sets of 36 frames. Data were collected with ω scan width of 0.5° at different settings of φ and 2θ with a frame time of 10 secs keeping the sample-to-detector distance fixed at 5.00 cm. The X-ray data collection was monitored by APEX2

program (Bruker, 2006). All the data were corrected for Lorentzian, polarization and absorption effects using SAINT and SADABS programs (Bruker, 2006). SHELX-97 was used for structure solution and full matrix least-squares refinement on F^2. All the hydrogen atoms were placed in geometrically idealized position and constrained to ride on their parent atoms. An *ORTEP* III view of both compounds were drawn with 30% probability displacement ellipsoids and H atoms are shown as small spheres of arbitrary radii.

Crystal data for Compound 31r

Crystal data of **31r** $C_{23}H_{19}ClN_2O$, M = 374.85, colorless block, 0.40 x 0.31 x 0.17 mm^3, monoclinic, space group $P2_1/c$, a = 11.925(6) Å, b = 23.667(12) Å, c = 7.039(4) Å, β = 99.498(6)°, V = 1959.4(17) $Å^3$, Z = 4, T = 296(2) K, $2\theta_{max}$=50.00°, D_{calc} (g cm^{-3}) = 1.271, $F(000)$ = 784, μ (mm^{-1}) = 0.209, 12071 reflections collected, 3345 unique reflections (R_{int}=0.0601), 2627 observed ($I > 2\sigma(I)$) reflections, multi-scan absorption correction, T_{min} = 0.921, T_{max} = 0.965, 334 refined parameters, S = 1.416, $R1$ = 0.0559, $wR2$ = 0.1374 (all data R = 0.0722, $wR2$ = 0.1448), maximum and minimum residual electron densities; $\Delta\rho_{max}$ = 0.17, $\Delta\rho_{min}$= -0.31 ($eÅ^{-3}$).



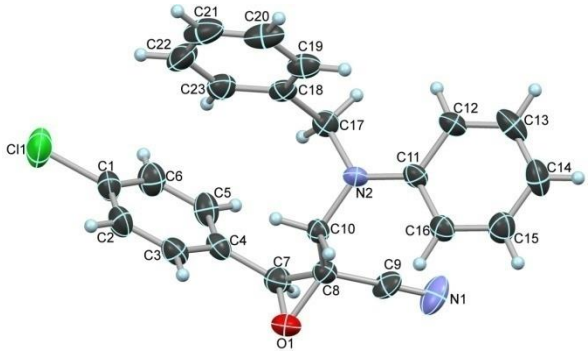
Crystal structure of **31r** (thermal ellipsoids are shown with 30% probability).

CCDC 1444745 (**31r**) contains the supplementary crystallographic data. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Crystal data for Compound 31r'

Crystal data of **31r'** $C_{23}H_{19}ClN_2O$, M = 374.85, colorless block, 0.45 x 0.32 x 0.26 mm^3, triclinic, space group P-1, a = 9.859(2) Å, b = 9.973(2) Å, c = 11.943(3) Å,

α = 103.759(14)°, β = 101.793(14)°, γ = 114.317(12)°, V = 976.9(4) Å^3, Z = 2, T = 296(2) K, $2\theta_{max}$ = 50.00°, D_{calc} (g cm^{-3}) = 1.274, $F(000)$ = 392, μ (mm^{-1}) = 0.210, 9717 reflections collected, 3288 unique reflections (R_{int}=0.0910), 1556 observed ($I > 2\sigma(I)$) reflections, multi-scan absorption correction, T_{min} = 0.911, T_{max} = 0.947, 244 refined parameters, S = 1.295, $R1$ = 0.0923, $wR2$ = 0.2626 (all data R = 0.3420, $wR2$ = 0.4100), maximum and minimum residual electron densities; $\Delta\rho_{max}$ = 0.50, $\Delta\rho_{min}$= -0.57 (eÅ^{-3}).

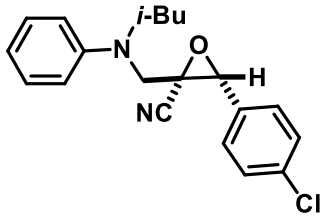


Crystal structure of **31r'** (thermal ellipsoids are shown with 30% probability).

CCDC 1444746 (**31r'**) contains the supplementary crystallographic data.These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

4.5.5. Synthesis and Characterization of *N*-Aryl Amino Epoxides

3-(4-Chlorophenyl)-2-((isobutyl(phenyl)amino)methyl)oxirane-2-carbonitrile (31a)



Following the general procedure, treatment of 1-isobutylaziridine-2-carbonitrile **29a** (0.075 g, 0.6 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **8a** (0.223 g, 182 µL, 0.75 mmol) with 4-chlorobenzaldehyde **30a** (0.070 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 3-(4-chlorophenyl)-2-((isobutyl(phenyl) amino)methyl)oxirane-2-carbonitrile as a yellow oil **31a** (0.123 g, 72% yield). [the *dr* of crude reaction mixture determined using GC analysis is 90:10]

***R*$_f$** (Pet. ether /EtOAc = 90/10): 0.53.

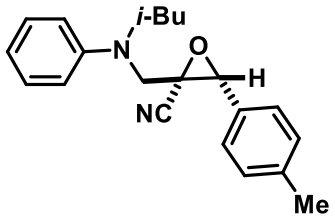
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 - 7.30 (m, 4H), 7.15 (d, *J* = 7.2 Hz, 2H) 6.85 (t, *J* = 7.2 Hz, 1H), 6.78 (d, *J* = 8.2 Hz, 2H), 4.06 (d, *J* = 16.0 Hz, 1H), 3.96 (d, *J* = 16.1 Hz, 1H), 3.91 (s, 1H), 3.34 (dd, *J* = 14.8 Hz, 6.1 Hz, 1H), 3.13 (dd, *J* = 14.8 Hz, 8.5 Hz, 1H), 2.16 - 2.06 (m, 1H), 0.96 (dd, *J* = 9.4 Hz, 6.8 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 147.51, 135.57, 130.37, 129.68, 128.97, 127.58, 118.36, 115.99, 113.47, 61.60, 60.46, 56.64, 53.75, 27.12, 20.54, 20.37.

HRMS (ESI) calculated $[M+H]^+$ for $C_{20}H_{22}ClN_2O$: 341.1415, found: 341.1413.

FTIR (cm^{-1}) 3022, 2963, 2403, 1599, 1501, 1373, 1217, 1045, 764, 672.

((Isobutyl(phenyl)amino)methyl)-3-(*p*-tolyl)oxirane-2-carbonitrile (31b)



Following the general procedure, treatment of 1-isobutylaziridine-2-carbonitrile **29a** (0.075 g, 0.60 mmol) and 2-(trimethylsilyl) phenyl trifluoromethane sulfonate **8a** (0.223 g, 182 μL, 0.75 mmol) with p-tolualdehyde **30b** (0.60 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded ((isobutyl(phenyl)amino)methyl)-3-(*p*-tolyl)oxirane-2-carbonitrile as a yellow oil **31b** (0.96 g, 60% yield). [the *dr* of crude reaction mixture determined using GC analysis is 90:10]

***R*$_f$** (Pet. ether /EtOAc = 90/10): 0.58.

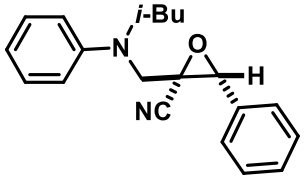
^{1}H NMR (400 MHz, $CDCl_3$ δ 7.33 (t, *J* = 7.9 Hz, 2H), 7.20 (d, *J* = 8.1 Hz, 2H), 7.15 (d, *J* = 8.1 Hz, 2H), 6.86 (t, *J* = 7.3 Hz, 1H), 6.81 (d, *J* = 9.2 Hz, 2H), 4.01 (dd, *J* = 3.7 Hz, 1.6 Hz, 2H), 4.01 (s, 1H), 3.36 (dd, *J* = 14.8 Hz, 6.3 Hz, 1H), 3.36 (dd, *J* = 14.8 Hz, 6.3 Hz, 1H), 2.37 (s, 3H), 2.26 - 2.01 (m, 1H), 1.04 - 0.95 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 147.63, 139.48, 129.58, 129.33, 128.74, 126.12, 118.15, 116.31, 113.43, 62.26, 60.32, 56.67, 53.96, 27.06, 21.39, 20.53, 20.37.

HRMS (ESI) calculated $[M+H]^+$ for $C_{21}H_{25}N_2O$: 321.1961, found: 321.1956.

FTIR (cm^{-1}) 3021, 2963, 2404, 1600, 1505, 1465, 1217, 1039, 926, 768.

2-((*Iso*-Butyl(phenyl)amino)methyl)-3-phenyloxirane-2-carbonitrile (31c)



Following the general procedure, treatment of 1-isobutylaziridine-2-carbonitrile **29a** (0.075 g, 0.6 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **8a** (0.223 g, 182 μL, 0.75 mmol) with benzaldehyde **30c** (0.053 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-((*iso*-butyl(phenyl)amino)methyl)-3-phenyloxirane-2-carbonitrile as a yellow oil **31c** (0.090 g, 59% yield). [the *dr* of crude reaction mixture determined using GC analysis is 88:12]

R_f (Pet. ether /EtOAc = 90/10): 0.53.

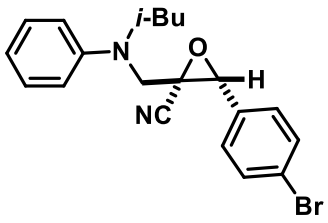
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 - 7.40 (m, 3H), 7.37-7.33 (m, 2H), 7.28 - 7.25 (m, 2H), 6.90 - 6.86 (m, 1H), 6.83 (d, *J* = 8.2 Hz, 2H), 4.12 - 3.98 (m. 3H) 3.41 (dd, *J* = 6.2 Hz, 14.9 Hz, 1H), 3.21 (dd, *J* = 8.4 Hz, 14.8 Hz, 1H), 2.18 - 2.11 (m, 1H), 1.02 (dd, *J*= 6.6 Hz, 10.1 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 147.56, 131.77, 129.63, 129.55, 128.64, 126.19, 118.17, 116.19, 113.37, 62.16, 60.35, 56.65, 53.87, 27.08, 20.55, 20.38.

HRMS (ESI) calculated $[M+H]^+$ for $C_{20}H_{23}N_2O$: 307.1805, found: 307.1801.

FTIR (cm^{-1}) 2404, 1599, 1502, 1464, 1374, 1217, 1129, 1039, 983, 920, 864, 678.

3-(4-Bromophenyl)-2-((isobutyl(phenyl)amino)methyl)oxirane-2-carbonitrile (31d)



Following the general procedure, treatment of 1-isobutylaziridine-2-carbonitrile **1a** (0.075 g, 0.60 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **2a** (0.223 g, 182 μL, 0.75 mmol) with 4-bromobenzaldehyde **3d** (0.93 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 3-(4-bromophenyl)-2-((isobutyl(phenyl)amino)methyl)oxirane-2-carbonitrile as a yellow oil **31d** (0.112 g, 58% yield). [the *dr* of crude reaction mixture determined using GC analysis is 89:11]

R_f (Pet. ether /EtOAc = 90/10): 0.55.

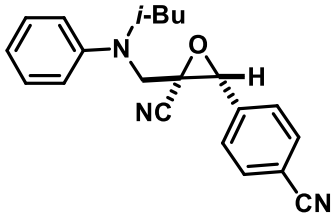
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.3 Hz, 2H), 7.34 - 7.30 (m, 4H), 6.87 (t, *J* = 7.3 Hz, 1H), 6.77 (d, *J* = 8.3 Hz, 2H), 4.10 (d, *J* = 16.3 Hz, 1H), 3.99 (d, *J* = 15.5 Hz, 1H), 3.99 (s, 1H), 3.35 (dd, *J* = 14.9 Hz, 6.2 Hz, 1H), 3.12 (dd, *J* = 14.8 Hz, 8.5 Hz, 1H), 2.13 - 2.05 (m, 1H), 0.96 (dd, *J* = 9.2 Hz, 6.6 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 147.31, 137.09, 132.44, 129.74, 126.97, 118.52, 118.30, 115.56, 113.44, 61.17, 60.49, 56.67, 53.53, 27.09, 20.49, 20.32.

HRMS (ESI) calculated $[M+H]^+$ for $C_{20}H_{22}BrN_2O$: 385.0910, found: 385.0904.

FTIR (cm^{-1}) 3022, 2965, 2235, 1645, 1599, 1504, 1218, 1122, 1036, 927, 767.

3-(4-Cyanophenyl)-2-((isobutyl(phenyl)amino)methyl)oxirane-2-carbonitrile (31e)



Following the general procedure, treatment of 1-isobutylaziridine-2-carbonitrile **29a** (0.075 g, 0.60 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **8a** (0.223 g, 182 μL, 0.75 mmol) with 4-cyanobenzaldehyde **30e** (0.66 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 3-(4-cyanophenyl)-2-((isobutyl(phenyl)amino)methyl)oxirane-2-carbonitrile as a yellow oil **31e** (0.111 g, 67% yield). [the *dr* of crude reaction mixture determined using GC analysis is 87:13]

R_f (Pet. ether /EtOAc = 90/10): 0.41.

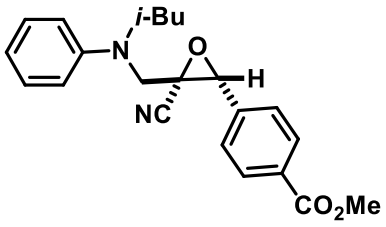
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.4 Hz, 2H), 7.32 (t, *J* = 8.4 Hz, 2H), 7.09 (d, *J* = 8.4 Hz, 2H), 6.86 (t, *J* = 7.3 Hz, 1H), 6.78 (d, *J* = 8.2 Hz, 2H), 4.01 (dd, *J* = 42.8 Hz, 16.1 Hz, 2H), 3.90 (s, 1H), 3.35 (dd, *J* = 14.8 Hz, 6.1 Hz, 1H), 3.14 (dd, *J* = 14.8 Hz, 8.5 Hz, 1H), 2.15 - 2.06 (m, 1H), 0.97 (dd, *J* = 9.4 Hz, 6.7 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 147.45, 131.88, 130.87, 129.66, 127.82, 123.76, 118.33, 115.95, 113.41, 61.62, 60.42, 56.56, 53.69, 27.08, 20.52, 20.36.

HRMS (ESI) calculated $[M+H]^+$ for $C_{21}H_{22}N_3O$: 332.1757, found: 332.1750.

FTIR (cm^{-1}) 3021, 2962, 2404, 1599, 1500, 1372, 1217, 1125, 926, 763.

Methyl 4-(3-cyano-3-((isobutyl(phenyl)amino)methyl)oxiran-2-yl)benzoate (31f)



Following the general procedure, treatment of 1-isobutylaziridine-2-carbonitrile **29a** (0.075 g, 0.60 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **8a** (0.223 g, 182 μL, 0.75 mmol) with methyl 4-formylbenzoate **3f** (0.82 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded methyl 4-(3-cyano-3-((isobutyl(phenyl)amino)methyl)oxiran-2-yl)benzoate as a yellow oil **31f** (0.126 g, 69% yield). [the *dr* of crude reaction mixture determined using GC analysis is 87:13]

***R*$_f$** (Pet. ether /EtOAc = 90/10): 0.40.

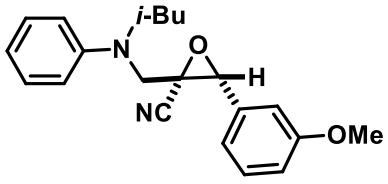
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.1 Hz, 2H), 7.33 - 7.26 (m, 7.4 Hz, 4H), 6.86 (t, *J* = 7.2 Hz, 1H), 6.78 (d, *J* = 8.2 Hz, 2H), 4.08 (d, *J* = 16.2 Hz, 1H), 3.99 d, *J* = 16.0 Hz, 1H), 3.98 (s, 1H), 3.91 (s, 3H), 3.35 (dd, *J* = 14.8 Hz, 6.1 Hz, 1H), 3.13 (dd, *J* = 14.8 Hz, 8.5 Hz, 1H), 2.18 - 2.00 (m, 1H), 0.96 (dd, *J* = 12.6 Hz, 6.6 Hz, 6H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 166.56, 147.41, 136.72, 131.23, 129.90, 129.70, 126.23, 118.35, 115.82, 113.38, 61.59, 60.42, 56.64, 53.70, 52.38, 27.09, 20.53, 20.35.

HRMS (ESI) calculated $[M+H]^+$ for $C_{22}H_{25}N_2O_3$: 365.1860, found: 365.1854.

FTIR (cm^{-1}) 3022, 2963, 2404, 1720, 1601, 1504, 1433, 1373, 1283, 1217, 1113, 1035, 769.

2-((Isobutyl(phenyl)amino)methyl)-3-(3-methoxyphenyl)oxirane-2-carbonitrile (31g)



Following the general procedure, treatment of 1-isobutylaziridine-2-carbonitrile **29a** (0.075 g, 0.60 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **8a** (0.223 g, 182 μL, 0.75 mmol) with 3-methoxybenzaldehyde **30g** (0.68 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-((isobutyl(phenyl)amino)methyl)-3-(3-methoxyphenyl)oxirane-2-

carbonitrile as a yellow oil **31g** (0.93 g, 55% yield). [the *dr* of crude reaction mixture determined using GC analysis is 87:13]

R_f (Pet. ether /EtOAc = 90/10): 0.50.

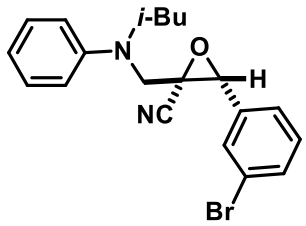
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 - 7.19 (m, 3H), 6.91 (dd, *J* = 8.2 Hz, 2.2 Hz, 1H), 6.88 - 6.72 (m, 5H), 4.01 (dd, *J* = 39.3 Hz, 16.1 Hz, 2H), 3.93 (s, 1H), 3.80 (s, 3H), 3.35 (dd, *J* = 14.8 Hz, 6.2 Hz, 1H), 3.16 (dd, *J* = 14.8 Hz, 8.4 Hz, 1H), 2.15 - 2.07 (m, 1H), 0.97 (dd, *J* = 9.5 Hz, 6.7 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 159.81, 147.59, 133.33, 129.78, 129.62, 118.57, 118.24, 116.17, 115.54, 113.49, 111.17, 62.12, 60.40, 56.56, 55.37, 53.93, 27.11, 20.54, 20.38.

HRMS (ESI) calculated $[M+H]^+$ for $C_{21}H_{25}N_2O_2$: 337.1911, found: 337.1903.

FTIR (cm^{-1}) 3021, 2962, 2404, 1600, 1500, 1466, 1218, 1044, 871, 770.

3-(3-Bromophenyl)-2-((*iso*-butyl(phenyl)amino)methyl)oxirane-2-carbonitrile (31h)



Following the general procedure, treatment of 1-isobutylaziridine-2-carbonitrile **29a** (0.075 g, 0.6 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **8a** (0.223 g, 182 μL, 0.75 mmol) with 3-bromobenzaldehyde **30h** (0.093 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 3-(3-bromophenyl)-2-((*iso*-butyl(phenyl)amino)methyl)oxirane-2-carbonitrile as a yellow oil **31h** (0.118 g, 61% yield). [the *dr* of crude reaction mixture determined using GC analysis is 85:15]

R_f (Pet. ether /EtOAc = 90/10): 0.53.

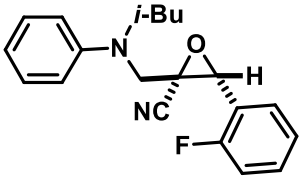
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.9 Hz, 1H), 7.37-7.33 (m, 3H), 7.29-7.25 (m, 1H), 7.19 (d, *J* = 7.6 Hz, 1H), 6.89 (t, *J* = 7.4 Hz, 1H), 6.82 (d, *J* = 8.3 Hz, 2H), 4.11 (d, *J* = 15.9 Hz, 1H), 4.01 (d, *J* = 16.6 Hz, 1H), 3.92 (s, 1H), 3.99 (dd, *J* = 6.2 Hz, 14.9 Hz, 1H), 3.18 (dd, *J* = 8.6 Hz, 14.8 Hz, 1H), 2.18 - 2.08 (m, 1H), 1.01 (dd, *J* = 6.6 Hz, 9.2 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 147.45, 134.17, 132.68, 130.25, 129.69, 129.33, 124.69, 122.74, 118.43, 113.49, 61.18, 60.43, 56.57, 53.74, 27.08, 20.53, 20.36.

HRMS (ESI) calculated $[M+H]^+$ for $C_{20}H_{22}BrN_2O$: 385.0910, found: 385.0912.

FTIR (cm^{-1}) 2404, 1599, 1502, 1433, 1372, 1217, 1129, 1039, 920, 767, 678.

3-(2-Fluorophenyl)-2-((iso-butyl(phenyl)amino)methyl)oxirane-2-carbonitrile (31i)



Following the general procedure, treatment of 1-isobutylaziridine-2-carbonitrile **29a** (0.075 g, 0.6 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **8a** (0.223 g, 182 μL, 0.75 mmol) with 2-fluorobenzaldehyde **30i** (0.062 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 3-(2-fluorophenyl)-2-((iso-butyl(phenyl)amino)methyl)oxirane-2-carbonitrile as a yellow oil **31i** (0.097 g, 60% yield). [the *dr* of crude reaction mixture determined using GC analysis is 87:13]

***R*$_f$** (Pet. ether /EtOAc = 90/10): 0.57.

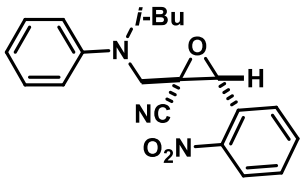
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.41 - 7.31 (m, 4H), 7.23 (t, *J* = 7.4 Hz, 1H), 7.11 (t, *J* = 8.9 Hz, 1H), 6.88-6.84 (m, 3H), 4.31 (s, 1H), 4.11 (d, *J* = 16.1 Hz, 1H), 4.05 (d, *J* = 16.1 Hz, 1H), 3.38 (dd, *J* = 6.7 Hz, 14.9 Hz, 1H), 3.27 (dd, *J* = 8.0 Hz, 14.9 Hz, 1H), 2.19 - 2.14 (m, 1H), 1.03 (dd, *J* = 6.8 Hz, 9.8 Hz, 6H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 161.42 (d, *J* = 248.8 Hz), 147.56, 131.06 (d, *J* = 8.1 Hz), 129.50, 127.01 (d, *J* = 2.7 Hz), 124.48 (d, *J* = 3.4 Hz), 119.69 (d, *J* = 13.0 Hz), 118.19, 115.89, 115.39 (d, *J* = 20.4), 113.53, 60.04, 57.24 (d, *J* = 5.6 Hz), 56.46, 53.87, 26.87, 20.51, 20.38.

HRMS (ESI) calculated $[M+H]^+$ for $C_{20}H_{22}FN_2O$: 325.1711, found: 325.1705.

FTIR (cm^{-1}) 2404, 1599, 1501, 1462, 1373, 1218, 1132, 1039, 981, 925, 869, 767, 675.

2-((*iso*-Butyl(phenyl)amino)methyl)-3-(2-nitrophenyl)oxirane-2-carbonitrile (31j)



Following the general procedure, treatment of 1-isobutylaziridine-2-carbonitrile **29a** (0.075 g, 0.6 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **8a** (0.223 g, 182 μL, 0.75 mmol) with 2-nitrobenzaldehyde **30j** (0.76 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-((*iso*-

butyl(phenyl)amino)methyl)-3-(2-nitrophenyl)oxirane-2-carbonitrile as a yellow solid **31j** (0.117 g, 67% yield). [the *dr* of crude reaction mixture determined using GC analysis is 70:30]

***R*f** (Pet. ether /EtOAc = 90/10): 0.37.

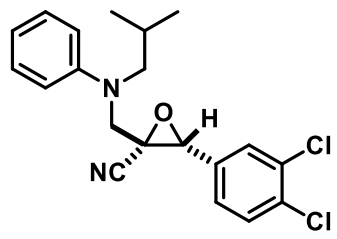
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, *J* = 8.3 Hz, 1H), 7.80 - 7.61 (m, 3H), 7.34-7.28 (m, 2H), 6.97 (d, *J* = 8.0 Hz, 2H), 6.86-6.83 (m, 1H), 4.63 (s, 1H), 4.40 (d, *J* = 16.3 Hz, 1H), 3.98 (d, *J* = 16.3 Hz, 1H), 3.47 (dd, J_1 = 7.0 Hz, J_2 = 14.9 Hz, 1H), 3.35 (dd, J_1 = 7.5, J_2 = 15.1 Hz, 1H), 2.25 - 2.20 (m, 1H), 1.04 (d, *J* = 7.0 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 147.65, 146.98, 134.90, 130.29, 129.53, 129.32, 128.53, 125.27, 118.16, 115.64, 113.94, 59.94, 59.08, 57.20, 54.20, 26.53, 20.49, 20.43.

HRMS (ESI) calculated $[M+H]^+$ for $C_{20}H_{22}N_3O_3$: 352.1656, found: 352.1651.

FTIR (cm^{-1}) 2405, 1600, 1520, 1352, 1304, 1216, 1132, 1038, 977, 923, 854, 750, 679.

3-(3,4-Dichlorophenyl)-2-((isobutyl(phenyl)amino)methyl)oxirane-2-carbonitrile (31k)



Following the general procedure, treatment of 1-isobutylaziridine-2-carbonitrile **29a** (0.075 g, 0.6 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **8a** (0.223 g, 182 μL, 0.75 mmol) with 3,4-dichlorobenzaldehyde **30k** (0.88 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 3-(3,4-dichlorophenyl)-2-((isobutyl(phenyl)amino)methyl)oxirane-2-carbonitrile as a yellow oil **31k** (0.132 g, 70% yield). [the *dr* of crude reaction mixture determined using GC analysis is 87:13]

***R*f** (Pet. ether /EtOAc = 90/10): 0.56.

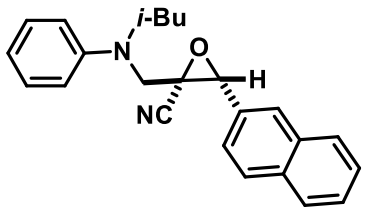
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.3 Hz, 1H), 7.32 (t, *J* = 8.0 Hz, 2H), 7.27 (t, *J* = 3.0 Hz, 1H), 7.04 (dd, *J* = 8.3 Hz, 1.8 Hz, 1H), 6.87 (t, *J* = 7.3 Hz, 1H), 6.77 (d, *J* = 8.2 Hz, 2H), 4.01 (dd, *J* = 45.5 Hz, 16.1 Hz, 2H), 3.87 (s, 1H), 3.33 (dd, *J* = 14.8 Hz, 6.1 Hz, 1H), 3.11 (dd, *J* = 14.8, 8.5 Hz, 1H), 2.21 - 2.01 (m, 1H), 0.96 (dd, *J* = 9.0 Hz, 6.7 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 147.42, 133.87, 133.15, 132.16, 130.83, 129.74, 128.30, 125.35, 118.57, 115.71, 113.57, 60.86, 60.53, 56.56, 53.66, 27.12, 20.53, 20.36.

HRMS (ESI) calculated $[M+H]^+$ for $C_{20}H_{21}Cl_2N_2O$: 375.1025, found: 375.1025.

FTIR (cm^{-1}) 3022, 2967, 2403, 1599, 1522, 1427, 1217, 1043, 977, 772.

2-((*iso*-Butyl(phenyl)amino)methyl)-3-(naphthalen-1-yl)oxirane-2-carbonitrile (31l)



Following the general procedure, treatment of 1-isobutylaziridine-2-carbonitrile **29a** (0.075 g, 0.6 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **8a** (0.223 g, 182 µL, 0.75 mmol) with 2-naphthaldehyde **30l** (0.78 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-((*iso*-butyl(phenyl)amino)methyl)-3-(naphthalen-1-yl)oxirane-2-carbonitrile as a yellow solid **31l** (0.132 g, 74% yield). [the *dr* of crude reaction mixture determined using GC analysis is 88:12]

R_f (Pet. ether /EtOAc = 90/10): 0.53.

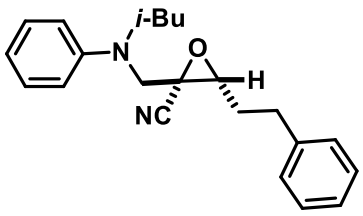
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 - 7.88 (m, 3H), 7.77 (s, 1H), 7.56-7.54 (m, 2H), 7.42-7.34 (m, 3H), 6.95-6.87 (m, 3H), 4.16-4.03 (m, 3H), 3.43 (dd, *J* = 6.2 Hz, 15.0Hz, 1H), 3.23 (dd, *J* = 8.3 Hz 14.7 Hz, 1H), 2.21 - 2.15 (m, 1H), 1.05 (dd, *J* = 6.7 Hz, 10.36 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 147.61, 133.85, 132.92, 129.66, 129.25, 128.58, 128.24, 127.94, 126.83, 126.70, 125.97, 123.10, 118.24, 116.23, 113.48, 62.34, 60.38, 56.85, 53.96, 27.08, 20.55, 20.38.

HRMS (ESI) calculated $[M+H]^+$ for $C_{24}H_{25}N_2O$: 357.1961, found357.1953.

FTIR (cm^{-1}) 2404, 1692, 1599, 1504, 1469, 1374, 1217, 1129, 1041, 977, 916, 863, 786.

2-((*iso*-Butyl(phenyl)amino)methyl)-3-phenethyloxirane-2-carbonitrile (31m)



Following the general procedure, treatment of 1-isobutylaziridine-2-carbonitrile **29a** (0.075 g, 0.6 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **8a** (0.223 g, 182 µL, 0.75 mmol) with 3-phenylpropanal **30m** (0.067 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by

flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-((*iso*-butyl(phenyl)amino)methyl)-3-phenethyloxirane-2-carbonitrile as a yellow oil **31m** (0.094g, 56% yield). [the *dr* of crude reaction mixture determined using GC analysis is >95:5]

***R*f** (Pet. ether /EtOAc = 90/10): 0.57.

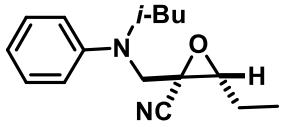
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 - 7.25 (m, 5H), 7.19 (d, *J* = 7.4 Hz, 2H), 6.83 (t, *J* = 6.9 Hz, 1H), 6.76 (d, *J* = 7.8 Hz, 2H), 3.89-3.81 (m, 2H), 3.28 (dd, *J* = 6.4Hz, 14.4 Hz, 1H), 3.13 (dd, *J* = 8.2, Hz, 14.7 Hz, 1H), 3.02 (t, *J* = 6.0 Hz, 1H), 2.78 (t, *J* = 7.8 Hz, 2H), 2.15-2.04 (m, 3H), 0.97-0.94 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 147.63, 140.03, 129.50, 128.71, 128.46, 126.51, 118.04, 116.92, 113.46, 61.13, 60.09, 53.83, 53.75, 31.79, 31.58, 26.86, 20.49, 20.38.

HRMS (ESI) calculated $[M+H]^+$ for $C_{22}H_{27}N_2O$: 335.2118, found: 335.2114.

FTIR (cm^{-1}) 2247, 1599, 1502, 1459, 1373, 1217, 1132, 1038, 984, 920, 870, 770, 677.

3-Ethyl-2-((*iso*-butyl(phenyl)amino)methyl)oxirane-2-carbonitrile (31n)



Following the general procedure, treatment of 1-isobutylaziridine-2-carbonitrile **29a** (0.075 g, 0.6 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **8a** (0.223 g, 182 μL, 0.75 mmol) with propionaldehyde **30n** (0.029 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 3-ethyl-2-((*iso*-butyl(phenyl)amino)methyl)oxirane-2-carbonitrile as a yellow oil **31n** (0.074 g, 57% yield). [the *dr* of crude reaction mixture determined using GC analysis is >95:5]

***R*f** (Pet. ether /EtOAc = 90/10): 0.60.

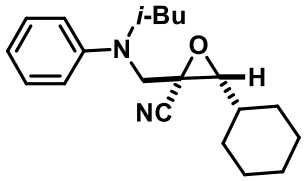
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 - 7.27 (m, 2H), 6.83-6.75 (m, 3H), 3.95 (d, *J* = 16.1 Hz, 1H), 3.88 (d, *J* = 16.0 Hz, 1H), 3.31 (dd, *J* = 6.4 Hz, 14.7 Hz, 1H), 3.16 (dd, J_1 = 8.1 Hz, 14.8 Hz, 1H), 2.95 (t, *J* = 6.7 Hz, 1H), 2.13-2.09 (m, 1H), 1.87-1.82 (m, 1H), 1.75-1.68 (m, 1H), 1.07 (t, *J* = 7.5 Hz, 3H), 0.99-0.95 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 147.62, 129.44, 117.93, 117.03, 113.36, 63.03, 60.10, 53.73, 53.42, 26.89, 23.35, 20.47, 20.35, 9.72.

HRMS (ESI) calculated $[M+H]^+$ for $C_{16}H_{23}N_2O$: 259.1805, found: 259.1803.

FTIR (cm^{-1}) 2405, 1631, 1600, 1502, 1463, 1375, 1218, 1037, 917, 767, 674.

3-Cyclohexyl-2-((*iso*-butyl(phenyl)amino)methyl)oxirane-2-carbonitrile (31o)



Following the general procedure, treatment of 1-isobutylaziridine-2-carbonitrile **29a** (0.075 g, 0.6 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **8a** (0.223 g, 182 μL, 0.75 mmol) with cyclohexanecarbaldehyde **30o** (0.056 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 3-cyclohexyl-2-((*iso*-butyl(phenyl)amino)methyl)oxirane-2-carbonitrile as a yellow oil **31o** (0.090 g, 58% yield). [the *dr* of crude reaction mixture determined using GC analysis is >95:5]

***R*$_f$** (Pet. ether /EtOAc = 90/10): 0.70.

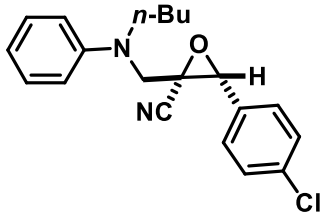
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.29 - 7.25 (m, 2H), 6.82-6.72 (m, 3H), 3.95 (d, *J* = 16.1 Hz, 1H), 3.85 (d, *J* = 16.0 Hz, 1H), 3.31 (dd, *J* = 6.4 Hz, 14.7 Hz, 1H), 3.14 (dd, *J* = 8.2 Hz, 14.8 Hz, 1H), 2.71 (d, *J* = 9.2 Hz, 1H), 2.15-2.05 (m, 1H), 1.92-1.90 (m, 1H), 1.73-1.67 (m, 5H), 1.46-1.11 (m, 5H), 0.97-0.94 (m, 6H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 205.13, 147.51, 129.41, 117.84, 117.16, 113.28, 66.13, 60.06, 53.66, 52.97, 38.91, 29.81, 28.26, 26.91, 25.94, 25.14, 25.01, 20.47, 20.34.

HRMS (ESI) calculated $[M+H]^+$ for $C_{20}H_{29}N_2O$: 313.2274, found: 313.2271.

FTIR (cm^{-1}) 2405, 1599, 1504, 1455, 1357, 1218, 1127, 1037, 982, 921, 767, 674.

2-((Butyl(phenyl)amino)methyl)-3-(4-chlorophenyl)oxirane-2-carbonitrile (31p)



Following the general procedure, treatment of 1-butylaziridine-2-carbonitrile **29p** (0.075 g, 0.60 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **8a** (0.223 g, 182 μL, 0.75 mmol) with 4-chlorobenzaldehyde **30a** (0.070 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-((butyl(phenyl)amino)methyl)-3-(4-chlorophenyl)oxirane-2-carbonitrile as a

yellow oil **31p** (0.121 g, 71% yield). [the *dr* of crude reaction mixture determined using GC analysis is 87:13]

R_f (Pet. ether /EtOAc = 90/10): 0.57.

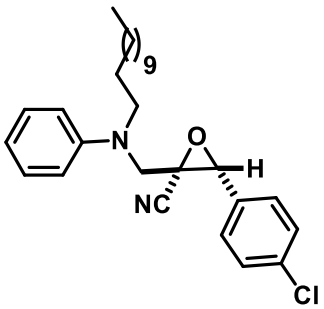
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 - 7.29 (m, 4H), 7.20 (d, *J* = 8.5 Hz, 2H), 6.84 (t, *J* = 7.3 Hz, 1H), 6.74 (d, *J* = 8.1 Hz, 2H), 4.03 - 3.87 (m, 3H), 3.39 (dd, *J* = 9.0 Hz, 6.7 Hz, 2H), 1.66 – 1.57 (m, 2H), 1.45 - 1.33 (m, 2H), 0.98 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 147.34, 135.61, 130.40, 129.74, 129.01, 127.64, 118.16, 115.98, 112.82, 61.26, 56.76, 53.06, 52.28, 28.95, 20.29, 14.07.

HRMS (ESI) calculated $[M+H]^+$ for $C_{20}H_{22}ClN_2O$: 341.1415, found: 341.1410.

FTIR (cm^{-1}) 3021, 2962, 2452, 1598, 1501, 1371, 1217, 1095, 1032, 768.

3-(4-Chlorophenyl)-2-((dodecyl(phenyl)amino)methyl)oxirane-2-carbonitrile (31q)



Following the general procedure, treatment of 1-dodecylaziridine-2-carbonitrile **29q** (0.142 g, 0.6 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **8a** (0.223 g, 182 μL, 0.75 mmol) with 4-chlorobenzaldehyde **30a** (0.070 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 3-(4-chlorophenyl)-2-((dodecyl(phenyl)amino)methyl)oxirane-2-carbonitrile as a yellow oil **31q** (0.136 g, 60% yield). [the *dr* of crude reaction mixture determined using GC analysis is 88:12]

R_f (Pet. ether /EtOAc = 90/10): 0.60.

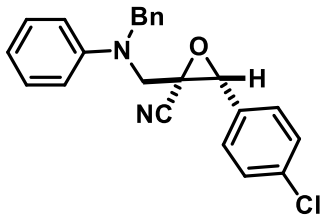
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.4 Hz, 2H), 7.31 (t, *J* = 7.9 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 6.84 (t, *J* = 7.3 Hz, 1H), 6.73 (d, *J* = 8.3 Hz, 2H), 4.00 - 3.91 (m, 3H), 3.38 (dd, *J* = 9.0 Hz, 6.6 Hz, 2H), 1.64 - 1.60 (m, 2H), 1.33 - 1.27 (m, 18H), 0.89 (t, *J* = 6.7 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 147.33, 135.62, 130.40, 129.75, 129.01, 127.65, 118.12, 115.99, 112.76, 61.25, 56.75, 53.03, 52.55, 32.05, 29.77, 29.72, 29.59, 29.48, 27.10, 26.82, 22.83, 14.27.

HRMS (ESI) calculated $[M+H]^+$ for $C_{28}H_{38}ClN_2O$: 453.2667, found: 453.2665.

FTIR (cm^{-1}) 3021, 2962, 2404, 1737, 1599, 1500, 1430, 1372, 1219, 1094, 1045, 977, 769.

2-((Benzyl(phenyl)amino)methyl)-3-(4-chlorophenyl)oxirane-2-carbonitrile (31r)



Following the general procedure, treatment of 1-benzylaziridine-2-carbonitrile **29r** (0.095 g, 0.60 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **8a** (0.223 g, 182 μL, 0.75 mmol) with 4-chlorobenzaldehyde **30a** (0.070 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 2-((benzyl(phenyl)amino)methyl)-3-(4-chlorophenyl)oxirane-2-carbonitrile as a yellow oil **31r** (0.141 g, 75% yield). [the *dr* of crude reaction mixture determined using GC analysis is 88:12]

***R*f** (Pet. ether /EtOAc = 95/05): 0.58.

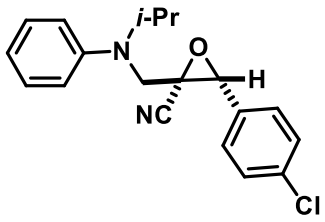
^{1}H NMR (400 MHz, $CDCl_3$ δ 7.39 - 7.21 (m, 11H), 6.90 - 6.83 (m, 3H), 4.71 (dd, *J* = 38.8 Hz, 17.2 Hz, 2H), 4.12 - 3.99 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 147.92, 137.35, 135.66, 130.22, 129.72, 129.01, 128.95, 127.66, 127.42, 126.75, 118.87, 115.86, 113.30, 61.40, 56.81, 55.38, 52.69.

HRMS (ESI) calculated $[M+H]^+$ for $C_{23}H_{20}ClN_2O$: 375.1259, found: 375.1254.

FTIR (cm^{-1}) 3022, 2924, 2403, 1599, 1501, 1440, 1361, 1217, 1092, 1027, 962, 768.

3-(4-Chlorophenyl)-2-((isopropyl(phenyl)amino)methyl)oxirane-2-carbonitrile (31s)



Following the general procedure, treatment of 1-isopropylaziridine-2-carbonitrile **29s** (0.066 g, 0.60 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **8a** (0.223 g, 182 μL, 0.75 mmol) with 4-chlorobenzaldehyde **30a** (0.070 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 3-(4-chlorophenyl)-2-((isopropyl(phenyl)amino)methyl)oxirane-2-carbonitrile as a yellow oil **31s** (0.100 g, 61% yield). [the *dr* of crude reaction mixture determined using GC analysis is 87:13]

***R*f** (Pet. ether /EtOAc = 90/10): 0.58.

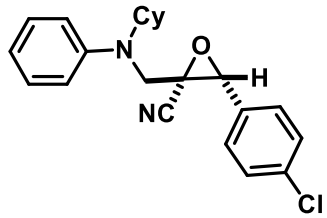
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (t, *J* = 7.8 Hz, 4H), 7.13 (d, *J* = 8.4 Hz, 2H), 6.92 (t, *J* = 7.3 Hz, 1H), 6.87 (d, *J* = 8.1 Hz, 2H), 4.08 - 4.02 (m, 1H), 3.92 (s, 1H), 3.86 (d, *J* = 16.0 Hz, 1H), 3.72 (d, *J* = 16.0 Hz, 1H), 1.24 (d, *J* = 6.6 Hz, 3H), 1.19 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 148.11, 135.48, 130.55, 129.67, 128.94, 127.59, 119.61, 116.20, 115.73, 61.65, 57.01, 49.78, 46.94, 21.02, 19.61.

HRMS (ESI) calculated $[M+H]^+$ for $C_{19}H_{20}ClN_2O$: 327.1259, found: 327.1257.

FTIR (cm^{-1}) 3021, 2964, 2405, 1737, 1600, 1500, 1374, 1220, 1121, 1022, 929, 768.

3-(4-Chlorophenyl)-2-((cyclohexyl(phenyl)amino)methyl)oxirane-2-carbonitrile (31t)



Following the general procedure, treatment of 1-cyclohexyl aziridine-2-carbonitrile **29t** (0.090 g, 0.60 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **8a** (0.223 g, 182 μL, 0.75 mmol) with 4-chlorobenzaldehyde **30a** (0.070 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 3-(4-chlorophenyl)-2-((cyclohexyl(phenyl)amino)methyl)oxirane-2-carbonitrile as a yellow oil **31t** (0.134 g, 73% yield). [the *dr* of crude reaction mixture determined using GC analysis is 85:15]

R_f (Pet. ether /EtOAc = 90/10): 0.53.

^{1}H NMR (400 MHz, $CDCl_3$ δ 7.35 - 7.26 (m, 4H), 7.12 (d, *J* = 8.5 Hz, 2H), 6.91 (t, *J* = 7.3 Hz, 1H), 6.85 (d, *J* = 8.2 Hz, 2H), 3.94 -3.90 (m, 2H), 3.76 (d, *J* = 16.1 Hz, 1H), 3.58 - 3.52 (m, 1H), 1.89 (m, 4H), 1.71 (d, *J* = 12.8 Hz, 1H), 1.44 - 1.28 (m, 4H), 1.23 - 1.09 (m, 1H).

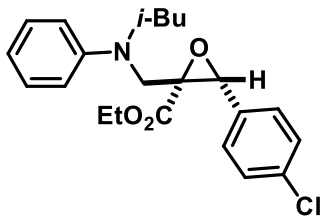
^{13}C NMR (100 MHz, $CDCl_3$) δ 148.05, 135.47, 130.57, 129.66, 128.94, 127.58, 119.48, 116.23, 115.59, 61.63, 58.49, 57.12, 47.74, 31.67, 30.39, 26.20, 26.09, 25.87.

HRMS (ESI) calculated $[M+H]^+$ for $C_{22}H_{24}ClN_2O$: 367.1572, found: 367.1570.

FTIR (cm^{-1}) 3021, 2935, 2859, 2404, 1597, 1499, 1351, 1218, 1092, 935, 767.

Ethyl 3-(4-chlorophenyl)-2-((*iso*butyl(phenyl)amino)methyl)oxirane-2-carboxylate (31u)

Following the general procedure, treatment of ethyl 1-isobutylaziridine-2-carboxylate **29u** (0.103 g, 0.6 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **8a** (0.223 g,



182 μL, 0.75 mmol) with 4-chlorobenzaldehyde **30a** (0.070 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded ethyl 3-(4-chlorophenyl)-2-((isobutyl(phenyl)amino)methyl)oxirane-2-carboxylate as a yellow oil **31u** (0.130 g, 67% yield). [the *dr* of crude reaction mixture determined using GC analysis is 89:11]

***R*f** (Pet. ether /EtOAc = 90/10): 0.56.

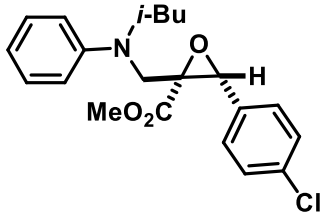
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 - 7.24 (m, 4H), 7.14 (d, *J* = 8.4 Hz, 2H), 6.86 (d, *J* = 8.3 Hz, 2H), 6.77 (t, *J* = 7.2 Hz, 1H), 4.18 (d, *J* = 16.1 Hz, 1H), 4.04 - 3.94 (m, 3H), 3.86 (s, 1H), 3.39 (dd, *J* = 14.9 Hz, 5.7 Hz, 1H), 3.11 (dd, *J* = 14.9 Hz, 8.9 Hz, 1H), 2.26 - 2.03 (m, 1H), 1.00 (t, *J* = 7.1 Hz, 3H), 0.94 (t, *J* = 7.2 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 167.55, 148.24, 134.21, 132.05, 129.46, 128.31, 127.68, 117.09, 112.68, 65.82, 61.64, 60.39, 59.83, 52.34, 27.02, 20.59, 20.37, 13.99.

HRMS (ESI) calculated $[M+H]^+$ for $C_{22}H_{27}ClNO_3$: 388.1674, found: 388.1673.

FTIR (cm^{-1}) 3021, 2964, 2404, 1737, 1599, 1501, 1376, 1305, 1219, 1120, 1022, 930, 767.

3-(4-Chlorophenyl)-2-((isobutyl(phenyl)amino)methyl)oxirane-2-carbonitrile (31v)



Following the general procedure, treatment of methyl 1-isobutylaziridine-2-carboxylate **29v** (0.094 g, 0.6 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **8a** (0.223 g, 182 μL, 0.75 mmol) with 4-chlorobenzaldehyde **30a** (0.070 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 3-(4-chlorophenyl)-2-((isobutyl(phenyl)amino)methyl)oxirane-2-carbonitrile as a yellow oil **31v** (0.103 g, 55% yield). [the *dr* of crude reaction mixture determined using GC analysis is 87:13]

***R*f** (Pet. ether /EtOAc = 90/10): 0.58.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (t, *J* = 8.4, 7.5 Hz, 2H), 7.25 (d, *J* = 8.5 Hz, 2H), 7.12 (d, *J* = 8.4 Hz, 2H), 6.85 (d, *J* = 8.3 Hz, 2H), 6.78 (t, *J* = 7.2 Hz, 1H), 4.18 (d, *J* = 16.2 Hz,

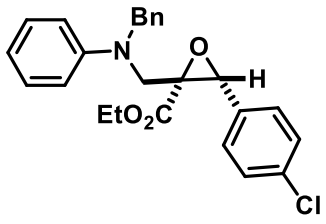
1H), 3.98 (d, *J* = 16.2 Hz, 1H), 3.86 (s, 1H), 3.52 (s, 3H), 3.38 (dd, *J* = 14.8 Hz, 5.7 Hz, 1H), 3.10 (dd, *J* = 14.9 Hz, 9.0 Hz, 1H), 2.16 - 2.10 (m, 1H), 0.94 (dd, *J* = 8.9 Hz, 6.7 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 167.98, 148.17, 134.27, 131.93, 129.48, 128.41, 127.57, 117.14, 112.67, 66.03, 60.46, 59.84, 52.38, 52.35, 27.00, 20.58, 20.37.

HRMS (ESI) calculated $[M+H]^+$ for $C_{21}H_{25}ClNO_3$: 374.1517, found: 374.1514.

FTIR (cm^{-1}) 3021, 2964, 2404, 1602, 1507, 1429, 1374, 1217, 1046, 926, 768.

Ethyl -2-((benzyl(phenyl)amino)methyl)-3-(4-chlorophenyl)oxirane-2-carboxylate (31w)



Following the general procedure, treatment of ethyl 1-benzylaziridine-2-carboxylate **29w** (0.123 g, 0.6 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **8a** (0.223 g, 182 μL, 0.75 mmol) with 4-chlorobenzaldehyde **30a** (0.070 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded Ethyl -2-((benzyl(phenyl)amino)methyl)-3-(4-chlorophenyl)oxirane-2-carboxylate as a white solid **31w** (0.152 g, 72% yield). [the *dr* of crude reaction mixture determined using GC analysis is 89:11]

***R*$_f$** (Pet. ether /EtOAc = 90/10): 0.49.

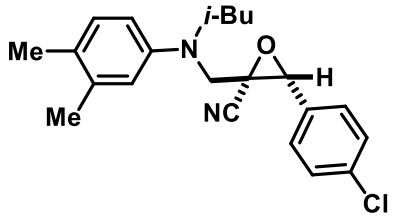
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 - 7.23 (m, 11H), 6.91 (d, *J* = 8.5 Hz, 2H), 6.83 (t, *J* = 7.1 Hz, 1H), 4.75 (q, *J* = 17.4 Hz, 2H), 4.17 (dd, *J* = 44.4, 16.2 Hz, 2H), 4.07 (s, 1H), 4.05 – 3.93 (m, 2H), 1.04 (t, *J* = 9.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 167.36, 148.57, 138.00, 134.32, 131.92, 129.51, 128.77, 128.39, 127.75, 127.05, 126.63, 117.73, 112.68, 66.10, 61.71, 60.25, 54.86, 51.68, 14.00.

HRMS (ESI) calculated $[M+H]^+$ for $C_{25}H_{25}ClNO_3$: 422.1517, found: 422.1516.

FTIR (cm^{-1}) 3020, 2968, 2401, 1745, 1601, 1506, 1495, 1389, 1217, 1123, 1016, 773.

3-(4-Chlorophenyl)-2-(((3,4-dimethylphenyl)(isobutyl)amino)methyl)oxirane-2-carbonitrile (31x)



Following the general procedure, treatment of 1-isobutyl aziridine-2-carbonitrile **29a** (0.075 g, 0.6 mmol) and 4,5-dimethyl-2-(trimethylsilyl)phenyl trifluoromethanesulfonate **8b** (0.245 g, 0.75 mmol) with 4-chlorobenzaldehyde **30a** (0.070 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 3-(4-chlorophenyl)-2-(((3,4-dimethylphenyl)(isobutyl)amino)methyl)oxirane-2-carbonitrile as a yellow oil **31x** (0.101 g, 55% yield). [the *dr* of crude reaction mixture determined using GC analysis is 78:22]

***R*f** (Pet. ether /EtOAc = 90/10): 0.57.

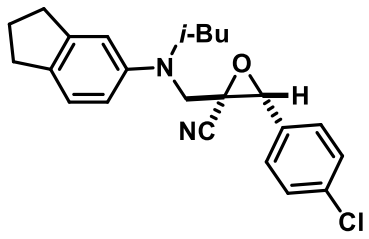
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8.2 Hz, 2H), 7.20 (d, *J* = 8.0 Hz, 2H), 7.11 (d, *J* = 8.2 Hz, 1H), 6.63-6.57 (m, 2H), 4.05-3.89 (m, 3H), 3.32 (dd, $_1$ = 6.2 Hz, 14.5 Hz, 1H), 3.16 (dd, *J* = 8.3 Hz, 14.2 Hz, 1H), 2.30 (s, 3H), 2.26 (s, 3H), 2.15 – 2.08 (m, 1H) 1.0-0.96 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 145.91, 137.69, 135.48, 130.67, 129.57, 128.93, 127.56, 116.11, 115.74, 111.61, 61.62, 60.73, 56.81, 54.33, 27.14, 20.53, 20.41, 18.76.

HRMS (ESI) calculated $[M+H]^+$ for $C_{22}H_{26}ClN_2O$: 369.1728, found: 369.1726.

FTIR (cm^{-1}) 2404, 1611, 1506, 1459, 1378, 1217, 1103, 1046, 927, 770, 671.

3-(4-Chlorophenyl)-2-(((2,3-dihydro-1*H*-inden-5-yl)(isobutyl)amino)methyl)oxirane-2-carbonitrile (31y)



Following the general procedure, treatment of 1-isobutylaziridine-2-carbonitrile **29a** (0.075 g, 0.6 mmol) and 3-(trimethylsilyl)naphthalen-2-yl trifluoromethanesulfonate **8c** (0.261 g, 182 μL, 0.75 mmol) with 4-chlorobenzaldehyde **30a** (0.070 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 3-(4-chlorophenyl)-2-(((2,3-dihydro-1*H*-inden-5-yl)(isobutyl)amino)methyl)oxirane-2-carbonitrile as a yellow oil **31y** (0.112 g, 59% yield). [the *dr* of crude reaction mixture determined using GC analysis is 87:13]

***R*$_f$** (Pet. ether /EtOAc = 90/10): 0.56.

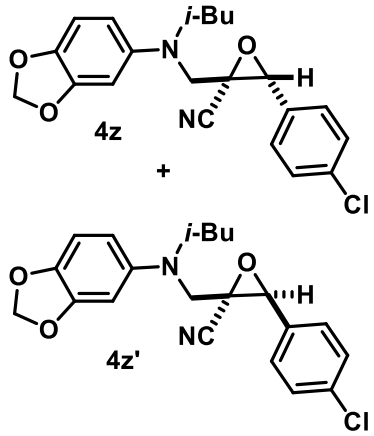
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.5 Hz, 2H), 7.19 (dd, *J* = 8.6 Hz, 2.4 Hz, 3H), 6.73 (s, 1H), 6.63 (dd, *J* = 8.2, 2.3 Hz, 1H), 4.04 (d, *J* = 15.9 Hz, 1H), 3.95 (s, 1H), 3.91 (d, *J* = 15.9 Hz, 1H), 3.30 (dd, *J* = 14.5 Hz, 6.3 Hz, 1H), 3.14 (dd, *J* = 14.6 Hz, 8.3 Hz, 1H), 2.92 (dd, *J* = 16.6, 7.7 Hz, 4H), 2.16 - 2.10 (m, 3H), 0.99 (dd, *J* = 9.5 Hz, 6.7 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 146.64, 145.91, 135.48, 134.61, 130.54, 128.92, 127.56, 125.11, 116.14, 112.63, 110.74, 61.69, 61.09, 56.81, 54.79, 33.51, 32.04, 27.08, 25.84, 20.56, 20.43.

HRMS (ESI) calculated $[M+H]^+$ for $C_{23}H_{26}ClN_2O$: 381.1728, found: 381.1727.

FTIR (cm^{-1}) 3020, 2960, 2403, 1609, 1499, 1429, 1217, 1094, 1032, 926, 766.

2-((Benzo[d][1,3]dioxol-5-yl(isobutyl)amino)methyl)-3-(4-chlorophenyl)oxirane-2-carbonitrile (31z)



Following the general procedure, treatment of 1-isobutylaziridine-2-carbonitrile **29a** (0.075 g, 0.6 mmol) and 6-(trimethylsilyl)benzo[d][1,3]dioxol-5-yl trifluoromethane sulfonate **8d** (0.257 g, 0.75 mmol) with 4-chlorobenzaldehyde **30a** (0.70 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded inseparable diastereomeric mixture of 2-((benzo[d][1,3]dioxol-5-yl(*iso*-butyl) amino)methyl)-3-(4-chlorophenyl)oxirane-2-carbonitrile as a yellow oil **31z** (0.105 g, 55% yield). [the *dr* of crude reaction mixture determined using GC analysis is 72:28]

***R*$_f$** (Pet. ether /EtOAc = 90/10): 0.40

Data for Major isomer **(4z)**: **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.39 (d, *J* = 8.4 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 6.80 (d, *J* = 8.5 Hz, 1H), 6.53 (d, *J* = 2.4 Hz, 1H), 6.31 (m, 1H), 5.96 (s, 2H), 3.92-3.73 (m, 3H), 3.19 (dd, *J* = 6.0 Hz, 13.9 Hz, 1H), 3.07 (dd, *J* = 8.2 Hz, 14.2 Hz, 1H), 2.02 – 1.95 (m, 1H), 0.98 (dd, *J* = 6.2 Hz, 11.1 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 148.79, 143.84, 141.29, 135.52, 130.36, 128.94, 128.02, 127.58, 108.67, 108.51, 101.13, 98.91, 61.94, 61.76, 56.75, 56.66, 27.02, 20.51, 20.41.

Representative peak for minor isomer (**4z'**): **^{1}H NMR (400 MHz, $CDCl_3$)** δ 6.66 (d, *J* = 7.9 Hz), 4.43 (s), 3.40 (d, *J* = 15.5 Hz), 2.94 (dd, *J* = 7.4 Hz, 13.7 Hz), 2.87 (dd, *J* = 7.3 Hz, 13.4 Hz), 1.79 (m), 0.90-0.87 (m).

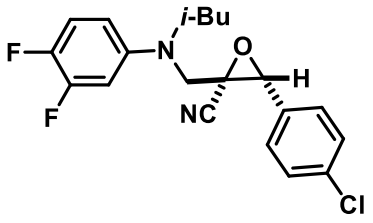
^{13}C NMR (100 MHz, $CDCl_3$) δ 116.05, 111.71, 108.24, 62.34, 62.27, 53.81, 52.71, 26.74.

HRMS (ESI) calculated $[M]^+$ for $C_{21}H_{21}ClN_2O_3$: 384.1241, found: 384.1237.

GCMS calculated $[M]^+$ for $C_{21}H_{21}ClN_2O_3$: 384.1, found: 384.2 (GCMS data recorded using Agilent 7890 B GC and 5977 A MSD mass analyzer).

FTIR (cm^{-1}) 2404, 1616, 1496, 1379, 1216, 1099, 1042, 976, 925, 768, 670.

3-(4-Chlorophenyl)-2-(((3,4-difluorophenyl)(isobutyl)amino)methyl)oxirane-2-carbonitrile (31aa)



Following the general procedure, treatment of 1-isobutylaziridine-2-carbonitrile **29a** (0.075 g, 0.6 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **8e** (0.251 g, 0.75 mmol) with 4-chlorobenzaldehyde **30a** (0.070 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 3-(4-chlorophenyl)-2-(((3,4-difluorophenyl)(isobutyl)amino)methyl)oxirane-2-carbonitrile as a yellow oil **31aa** (0.109 g, 58% yield). [the *dr* of crude reaction mixture determined using GC analysis is 82:18]

***R*$_f$** (Pet. ether /EtOAc = 90/10): 0.52.

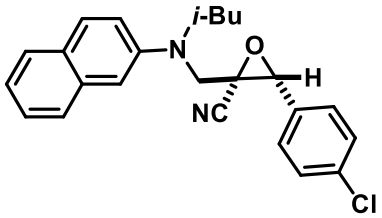
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8.4 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 2H), 7.10 (q, *J* = 9.3 Hz, 1H), 6.61 (ddd, *J* = 13.4, 6.5, 3.0 Hz, 1H), 6.47 - 6.45 (m, 1H), 4.04 - 3.84 (m, 3H), 3.28 (dd, *J* = 14.8 Hz, 6.4 Hz, 1H), 3.13 (dd, *J* = 14.8 Hz, 8.2 Hz, 1H), 2.11 - 2.07 (m, 1H), 0.97 (dd, *J* = 9.0, 6.7 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ δ 144.82 (d, *J* = 11.1 Hz),135.87, 129.98, 129.15, 127.59, 117.88 (d, *J* = 71.3 Hz), 115.67, 109.00, 103.00, (d, *J* = 21.2 Hz), 61.51, 60.79, 56.54, 54.53, 26.95, 20.47, 20.35.

HRMS (ESI) calculated $[M+H]^+$ for $C_{20}H_{20}ClF_2N_2O$: 377.1227, found: 377.1223.

FTIR (cm^{-1}) 3022, 2963, 2403, 1599, 1502, 1472, 1420, 1370, 1216, 1132, 1038, 976, 927, 763.

3-(4-Chlorophenyl)-2-((isobutyl(naphthalen-2-yl)amino)methyl)oxirane-2-carbonitrile (31ab)



Following the general procedure, treatment of 1-isobutylaziridine-2-carbonitrile **29a** (0.075 g, 0.6 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **8f** (0.261 g, 0.75 mmol) with 4-chlorobenzaldehyde **30a** (0.070 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded 3-(4-Chlorophenyl)-2-((isobutyl(naphthalen-2-yl)amino)methyl)oxirane-2-carbonitrile as a yellow oil **31ab** (0.113 g, 58% yield). [the *dr* of crude reaction mixture determined using GC analysis is 82:18]

***R*$_f$** (Pet. ether /EtOAc = 90/10): 0.52.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 15.0 Hz, 8.6 Hz, 2H), 7.68 (d, *J* = 8.2 Hz, 1H), 7.42 (t, *J* = 7.3 Hz, 1H), 7.30 (d, *J* = 6.7 Hz, 3H), 7.15 (dd, *J* = 9.1 Hz, 2.5 Hz, 1H), 7.09 (d, *J* = 8.4 Hz, 2H), 6.97 (d, *J* = 2.2 Hz, 1H), 4.18 (d, *J* = 16.1 Hz, 1H), 4.05 (d, *J* = 16.1 Hz, 1H), 3.95 (s, 1H), 3.47 (dd, *J* = 14.8 Hz, 6.3 Hz, 1H), 3.23 (dd, *J* = 14.8 Hz, 8.4 Hz, 1H), 2.25 - 2.10 (m, 1H), 0.99 (t, *J* = 6.9 Hz, 6H).

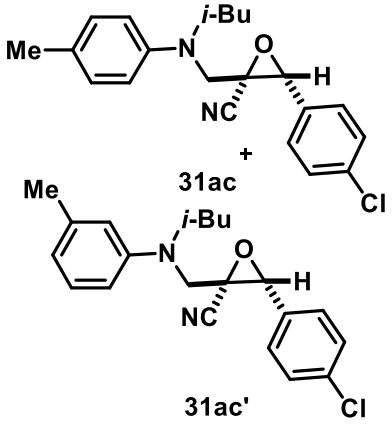
^{13}C NMR (100 MHz, $CDCl_3$) δ 145.29, 135.59, 134.90, 130.28, 129.59, 128.99, 127.65, 127.53, 126.91, 126.43, 123.17, 116.13, 116.01, 107.97, 61.65, 60.56, 56.61, 53.85, 27.31, 20.55, 20.41.

HRMS (ESI) calculated $[M+H]^+$ for $C_{24}H_{24}ClN_2O$: 391.1572, found: 391.1570.

FTIR (cm^{-1}) 3022, 2962, 2404, 1731, 1602, 1496, 1355, 1265, 1217, 1164, 1122, 1040, 984, 770.

3-(4-Chlorophenyl)-2-((isobutyl(p-tolyl)amino)methyl)oxirane-2-carbonitrile (31ac) and 3-(4-chlorophenyl)-2-((isobutyl(m-tolyl)amino)methyl)oxirane-2-carbonitrile (31ac')

Following the general procedure, treatment of 1-isobutylaziridine-2-carbonitrile **29a** (0.075 g, 0.6 mmol) and 4-fluoro-2-(trimethylsilyl)phenyl trifluoromethanesulfonate **8g** (0.237 g, 0.75 mmol) with 4-chlorobenzaldehyde **30a** (0.070 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h



followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded inseparable mixture of 3-(4-chlorophenyl)-2-((isobutyl(p-tolyl)amino)methyl)oxirane-2-carbonitrile (**31ac**) and 3-(4-chlorophenyl)-2-((isobutyl(m-tolyl)amino)methyl)oxirane-2-carbonitrile (**31ac'**) as a yellow oil (0.114 g, 64% yield). [the *dr* of crude reaction mixture determined using GC analysis is 85:15]

***R*f** (Pet. ether /EtOAc = 90/10): 0.56.

^{1}H NMR of 4ac (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.5 Hz, 2H), 7.23 - 7.12 (m, 4H) 6.70 (t, *J* = 8.1 Hz, 2H), 4.06 (d, *J* = 16.7 Hz, 1H), 3.94 (d, *J* = 17.2 Hz, 1H), 3.92 (s, 1H), 3.35 - 3.25 (m, 1H), 3.15 - 3.08 (m, 1H), 2.36 (s, 3H) 2.14 - 2.04 (m, 1H), 0.98 - 0.94 (m, 6H).

^{13}C NMR of 4ac (100 MHz, $CDCl_3$) δ 147.58, 139.39, 135.52, 130.44, 130.16, 129.50, 128.95, 127.88, 127.53, 119.28, 116.02, 114.09, 110.69, 61.63, 60.46, 56.67, 54.28, 53.75, 27.14, 22.10, 20.53, 20.38.

^{1}H NMR of 4ac' (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.5 Hz, 2H), 7.23 - 7.12 (m, 3H) 6.70 (t, *J* = 8.1 Hz, 1H), 6.59 - 6.58 (m, 2H), 4.01 (d, *J* = 16.8 Hz, 1H), 3.92 (s, 1H), 3.90 (d, *J* = 17.1 Hz, 1H), 3.35 - 3.25 (m, 1H), 3.15 - 3.08 (m, 1H), 2.32 (s, 3H) 2.14 - 2.04 (m, 1H), 0.98 - 0.94 (m, 6H).

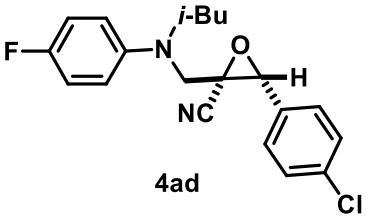
^{13}C NMR of 4ac' (100 MHz, $CDCl_3$) δ 145.46, 139.39, 135.52, 130.44, 130.16, 129.50, 128.95, 127.88, 127.53, 119.28, 116.07, 114.24, 110.69, 61.57, 60.73, 56.75, 54.28, 53.75, 27.09, 22.10, 20.53, 20.38.

HRMS (ESI) calculated $[M+H]^+$ for $C_{21}H_{24}ClN_2O$: 355.1572, found: 355.1568.

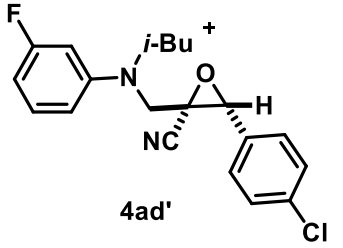
FTIR (cm^{-1}) 3021, 2962, 2404, 1601, 1506, 1374, 1217, 1095, 1046, 927, 767.

3-(4-Chlorophenyl)-2-(((4-fluorophenyl)(isobutyl)amino)methyl)oxirane-2-carbonitrile (31ad) and -3-(4-Chlorophenyl)-2-(((3-fluorophenyl)(isobutyl)amino)methyl)oxirane-2-carbonitrile (31ad')

Following the general procedure, treatment of 1-isobutylaziridine-2-carbonitrile **29a** (0.075 g, 0.6 mmol) and 4-methyl-2-(trimethylsilyl)phenyl trifluoromethanesulfonate **8h** (0.234 g, 0.75 mmol) with 4-chlorobenzaldehyde **30a** (0.070 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h



4ad



4ad'

followed by flash column chromatography (Pet. ether /EtOAc = 98/02) of the crude reaction mixture using silica gel afforded inseparable 2:1 regioisomeric mixture of 3-(4-chlorophenyl)-2-(((4-fluorophenyl)(isobutyl)amino)methyl)oxirane-2-carbonitrile (**31ad**) and -3-(4-chlorophenyl)-2-(((3-fluorophenyl)(isobutyl)amino)methyl)oxirane-2-carbonitrile (**31ad'**) as a yellow oil (0.116 g, 65% yield). [the *dr* of crude reaction mixture determined using GC analysis is 78:22]

***R*$_f$** (Pet. ether /EtOAc = 90/10): 0.51.

^{1}H NMR of 4ad (400 MHz, $CDCl_3$) δ 7.43 - 7.29 (m, 2H), 7.29 - 7.10 (m, 2H), 7.10 - 6.91 (m, 2H), 6.87 - 6.62 (m, 1H), 6.52 - 6.44 (m, 1H), 3.93 (d, *J* = 15.9 Hz, 1H), 3.89 (s, 1H) 3.85 (d, *J* = 15.9 Hz, 1H), 3.23 (dd, *J* = 14.5 Hz, 6.4 Hz, 1H), 3.09 (dd, *J* = 14.5 Hz, 8.2 Hz, 1H), 2.04 - 1.97 (m, 1H), 0.97 - 0.92 (m, 6H).

^{13}C NMR of 4ad (100 MHz, $CDCl_3$) δ 157.66 (d, *J* = 239.6 Hz), 149.24 (d, *J* = 10.6 Hz), 144.36, 135.69, 130.22, 129.04, 127.58, 116.26, 116.03, 108.58, 104.70 (d, *J* = 21.4 Hz), 100.32 (d, *J* = 26.4 Hz), 61.62, 61.27, 56.71, 55.17, 27.02, 20.52, 20.40.

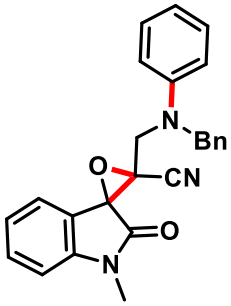
^{1}H NMR of 4ad' (400 MHz, $CDCl_3$) δ 7.43 - 7.29 (m, 2H), 7.29 - 7.10 (m, 2H), 7.10 - 6.91 (m, 1H), 6.87 - 6.62 (m, 2H), 6.64 - 6.28 (m, 1H), 4.00 (q, *J* = 16.7 Hz, 1H), 3.91 (s, 1H), 3.33 (dd, *J* = 15.0, 6.3 Hz, 1H), 3.13 (dd, *J* = 15.2, 8.5 Hz, 1H), 2.16 - 2.06 (m, 1H), 0.97 - 0.92 (m, 6H). **^{13}C NMR of 4ad' (100 MHz, $CDCl_3$)** δ 164.29 (d, *J* = 243.5 Hz), 149.18, 144.36, 135.69, 130.79 (d, *J* = 10.1 Hz), 130.11, 129.04, 127.58, 116.26, 116.03, 115.95, 104.70 (d, *J* = 21.4 Hz), 100.32 (d, *J* = 26.4 Hz),, 61.57, 61.27, 60.35, 56.44, 53.53, 27.02, 20.47, 20.32.

HRMS (ESI) calculated $[M+H]^+$ for $C_{20}H_{21}FClN_2O$: 359.1321, found: 359.1318.

FTIR (cm^{-1}) 3021, 2925, 1725, 1601, 1503, 1452, 1371, 1279, 1107, 977, 765.

4.5.5. Synthesis and Characterization of *N*-Aryl Spiro Amino Epoxides

3'-((Benzyl(phenyl)amino)methyl)-1-methyl-2-oxospiro[indoline-3,2'-oxirane]-3'-carbonitrile (34a)



Following the general procedure, treatment of 1-benzylaziridine-2-carbonitrile **29r** (0.095 g, 0.6 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **8a** (0.223 g, 182 µL, 0.75 mmol) with 1-methylindoline-2,3-dione **33a** (0.081 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 90/10) of the crude reaction mixture using silica gel afforded 3'-((benzyl(phenyl)amino)methyl)-1-methyl-2-oxospiro[indoline-3,2'-oxirane]-3'-carbonitrile **34a** (0.119 g, 60% yield). [the *dr* of crude reaction mixture determined using GC analysis is >95:5]

***R*f** (Pet. ether /EtOAc = 70/30): 0.40.

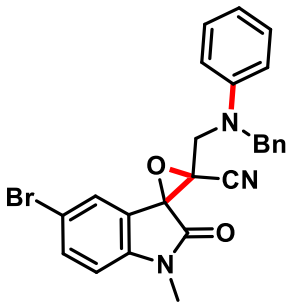
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 - 7.44 (m, 2H), 7.28 – 7.14 (m, 8H), 7.00 (d, *J* = 8.2 Hz, 2H), 6.89 - 6.82 (m, 2H), 4.80 - 4.70 (m, 2H), 4.65 (d, *J* = 16.3 Hz, 1H), 4.21 (d, *J* = 16.3 Hz, 1H), 3.19 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 168.33, 148.29, 144.96, 137.83, 131.83, 129.44, 128.66, 127.14, 126.87, 124.55, 123.53, 118.91, 118.72, 115.76, 114.40, 109.15, 63.37, 59.62, 55.92, 49.91, 26.94.

HRMS (ESI) calculated $[M+H]^+$ for $C_{25}H_{22}N_3O_2$: 396.1707, found: 396.1703.

FTIR (cm^{-1}) 3018, 2921, 2404, 1952, 1815, 1599, 1501, 1450, 1356, 1216, 1036, 763.

3'-((benzyl(phenyl)amino)methyl)-5-bromo-1-methyl-2-oxospiro[indoline-3,2'-oxirane]-3'-carbonitrile (34b)



Following the general procedure, treatment of 1-benzylaziridine-2-carbonitrile **29r** (0.095 g, 0.6 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **8a** (0.223 g, 182 µL, 0.75 mmol) with 5-bromo-1-methylindoline-2,3-dione **33b** (0.120 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether

/EtOAc = 90/10) of the crude reaction mixture using silica gel afforded 3'-((benzyl(phenyl)amino)methyl)-5-bromo-1-methyl-2-oxospiro[indoline-3,2'-oxirane]-3'-carbonitrile **34b** (0.147 g, 62% yield). [the *dr* of crude reaction mixture determined using GC analysis is >95:5]

***R*f** (Pet. ether /EtOAc = 70/30): 0.42.

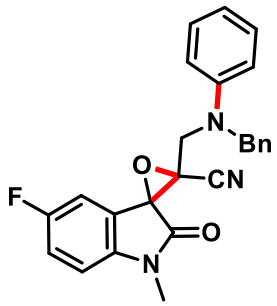
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 6.1 Hz, 2H), 7.38 – 7.09 (m, 7H), 7.00 (d, *J* = 8.3 Hz, 2H), 6.86 (t, *J* = 7.2 Hz, 1H), 6.76 (d, *J* = 8.8 Hz, 1H), 4.73 (q, *J* = 17.0 Hz, 2H), 4.63 (d, *J* = 16.3 Hz, 1H), 4.21 (d, *J* = 16.2 Hz, 1H), 3.17 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 167.78, 148.28, 143.94, 137.82, 134.71, 129.48, 128.68, 127.61, 127.19, 126.91, 120.70, 119.17, 116.23, 115.45, 114.58, 110.56, 62.77, 59.69, 56.09, 49.79, 27.07.

HRMS (ESI) calculated $[M+H]^+$ for $C_{25}H_{21}BrN_3O_2$: 474.0812, found: 474.0811.

FTIR (cm^{-1}) 3018, 2958, 2404, 1598, 1501, 1459, 1361, 1288, 1216, 929, 770.

3'-((Benzyl(phenyl)amino)methyl)-5-fluoro-1-methyl-2-oxospiro[indoline-3,2'-oxirane]-3'-carbonitrile (34c)



Following the general procedure, treatment of 1-benzylaziridine-2-carbonitrile **29r** (0.095 g, 0.6 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **8a** (0.223 g, 182 µL, 0.75 mmol) with 5-fluoro-1-methylindoline-2,3-dione **33c** (0.090 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 90/10) of the crude reaction mixture using silica gel afforded 3'-((benzyl(phenyl)amino)methyl)-5-fluoro-1-methyl-2-oxospiro[indoline-3,2'-oxirane]-3'-carbonitrile **34c** (0.112 g, 54% yield). [the *dr* of crude reaction mixture determined using GC analysis is >95:5]

***R*f** (Pet. ether /EtOAc = 70/30): 0.39.

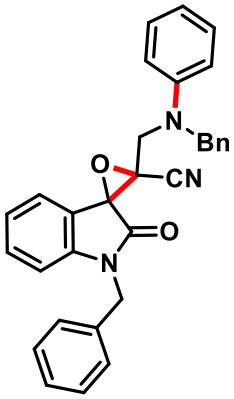
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 - 7.23 (m, 7H), 7.20 – 7.15 (m, 2H), 7.02 (d, *J* = 8.2 Hz, 2H), 6.88 (t, *J* = 7.2 Hz, 1H), 6.82 (dd, *J* = 8.6 Hz, 3.9 Hz, 1H), 4.80 (d, *J* = 17.0 Hz, 1H), 4.71 (d, *J* = 17.5 Hz, 1H), 4.66 (d, *J* = 16.4 Hz, 1H), 4.24 (d, *J* = 16.2 Hz, 1H), 3.19 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 167.98, 160.47, 158.05, 148.22, 140.86, 137.77, 129.44, 128.62, 127.14, 126.84, 120.26 (d, *J* = 8.3 Hz), 119.03, 118.24 (d, *J* = 23.6 Hz), 115.51, 114.41, 112.80 (d, *J* = 26.5 Hz), 109.88 (d, *J* = 7.7 Hz), 59.63, 55.96, 49.72, 27.05.

HRMS (ESI) calculated $[M+H]^+$ for $C_{25}H_{21}FN_3O_2$: 414.1612, found: 414.1609.

FTIR (cm^{-1}) 3021, 2966, 2929, 2873, 2596, 1498, 1454, 1374, 1276, 1219, 1030, 991, 764.

1-Benzyl-3'-((benzyl(phenyl)amino)methyl)-2-oxospiro[indoline-3,2'-oxirane]-3'-carbonitrile (34d)



Following the general procedure, treatment of 1-benzylaziridine-2-carbonitrile **29r** (0.095 g, 0.6 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **8a** (0.223 g, 182 μL, 0.75 mmol) with 1-benzylindoline-2,3-dione **33d** (0.119 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 90/10) of the crude reaction mixture using silica gel afforded 1-benzyl-3'-((benzyl(phenyl)amino)methyl)-2-oxospiro[indoline-3,2'-oxirane]-3'-carbonitrile **34d** (0.139 g, 59% yield). [the *dr* of crude reaction mixture determined using GC analysis is >95:5]

***R*$_f$** (Pet. ether /EtOAc = 70/30): 0.38.

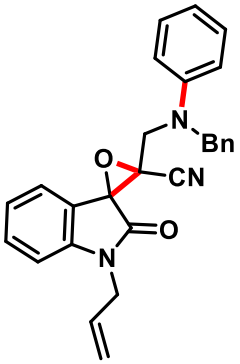
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 7.5 Hz, 1H), 7.37 - 7.28 (m, 6H), 7.28 - 7.18 (m, 7H), 7.13 (t, *J* = 7.6 Hz, 1H), 6.98 (d, *J* = 8.3 Hz, 2H), 6.83 (dd, *J* = 7.5 Hz, 4.0 Hz, 2H), 4.90 (dd, *J* = 34.8 Hz, 15.6 Hz, 2H), 4.79 (s, 2H), 4.67 (d, *J* = 16.4 Hz, 1H), 4.28 (d, *J* = 16.4 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 168.60, 148.12, 144.21, 137.69, 134.78, 131.83, 129.48, 129.16, 128.76, 128.25, 127.56, 127.19, 126.88, 124.71, 123.63, 118.80, 118.72, 115.67, 114.24, 110.21, 63.42, 59.88, 55.75, 50.02, 44.72.

HRMS (ESI) calculated $[M+H]^+$ for $C_{31}H_{26}N_3O_2$: 472.2020, found: 472.2018.

FTIR (cm^{-1}) 3019, 2928, 2404, 1956, 1604, 1501, 1452, 1324, 1217, 1121, 914, 763.

1-Allyl-3'-((benzyl(phenyl)amino)methyl)-2-oxospiro[indoline-3,2'-oxirane]-3'-carbonitrile (34e)



Following the general procedure, treatment of 1-benzylaziridine-2-carbonitrile **29r** (0.095 g, 0.6 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **8a** (0.223 g, 182 μL, 0.75 mmol) with 1-allylindoline-2,3-dione **33e** (0.081 g, 0.50 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 90/10) of the crude reaction mixture using silica gel afforded 1-allyl-3'-((benzyl(phenyl)amino)methyl)-2-oxospiro[indoline-3,2'-oxirane]-3'-carbonitrile **34e** (0.119 g, 56% yield). [the *dr* of crude reaction mixture determined using GC analysis is >95:5]

***R*$_f$** (Pet. ether /EtOAc = 70/30): 0.43.

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.54 (d, *J* = 8.0 Hz, 1H), 7.46 (t, *J* = 7.8, 1H), 7.31 - 7.26 (m, 6H), 7.24 - 7.17 (m, 2H), 7.01 (d, *J* = 8.1 Hz, 2H), 6.94 (d, *J* = 7.9 Hz, 1H), 6.86 (t, *J* = 7.3 Hz, 1H), 5.90 - 5.80 (m, 1H), 5.34 (d, *J* = 4.2 Hz, 1H), 5.31 (d, *J* = 1.4 Hz, 1H), 4.81 (s, 2H), 4.68 (d, *J* = 16.3 Hz, 1H), 4.36 (d, *J* = 5.5 Hz, 2H), 4.27 (d, *J* = 16.3 Hz, 1H).

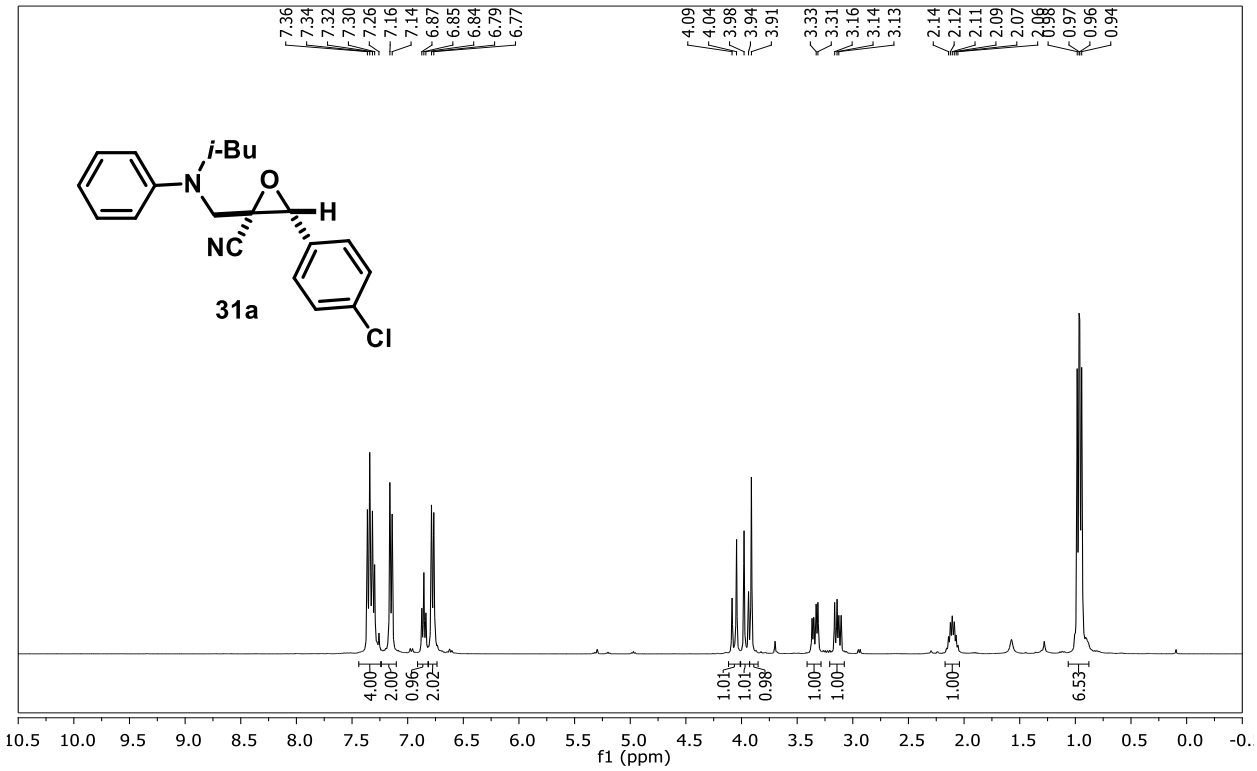
^{13}C NMR (100 MHz, CDCl$_3$) δ 168.13, 148.09, 144.20, 137.67, 131.79, 130.50, 129.42, 128.71, 127.14, 126.81, 124.62, 123.51, 118.75, 118.64, 115.66, 114.18, 110.06, 63.32, 59.74, 55.71, 49.90, 43.21.

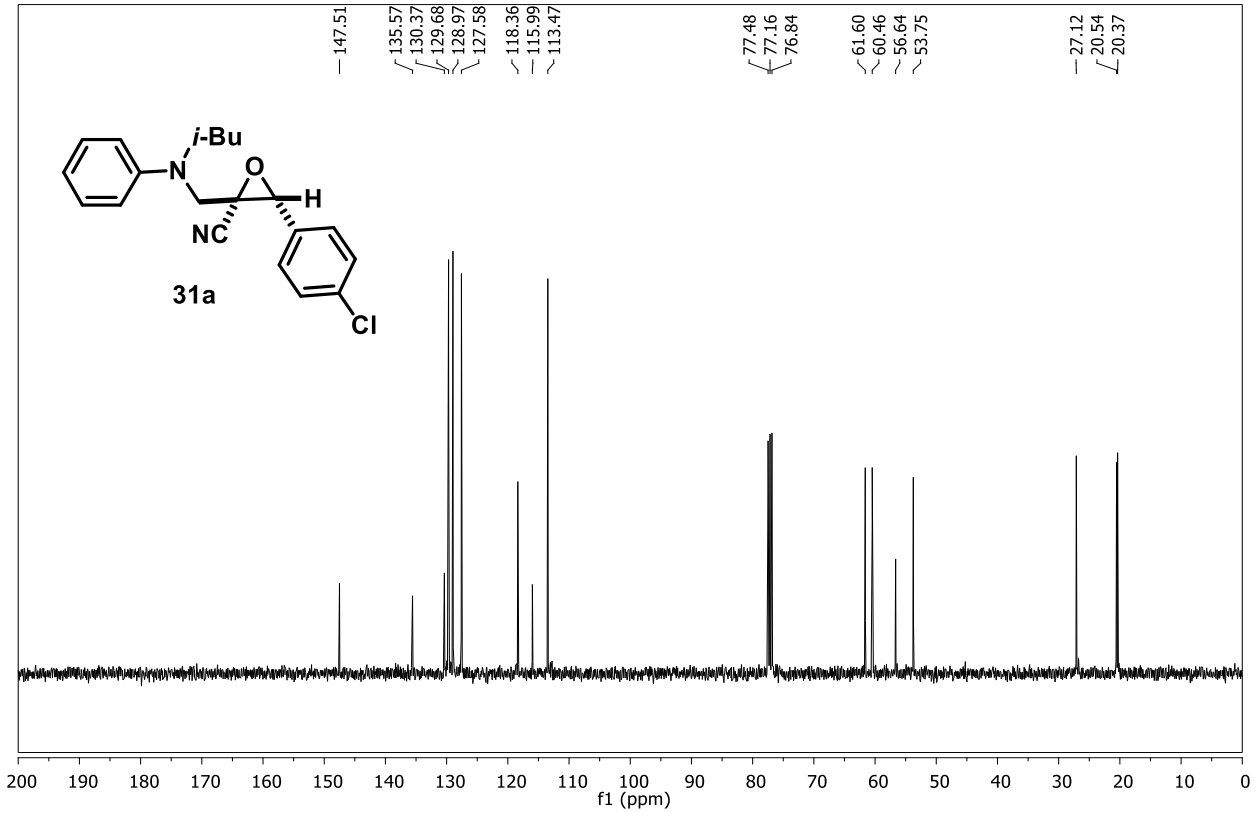
HRMS (ESI) calculated $[M+H]^+$ for $C_{27}H_{24}N_3O_2$: 422.1863, found: 422.1859.

FTIR (cm^{-1}) 3019, 2970, 2404, 1596, 1499, 1450, 1376, 1218, 1033, 937, 769.

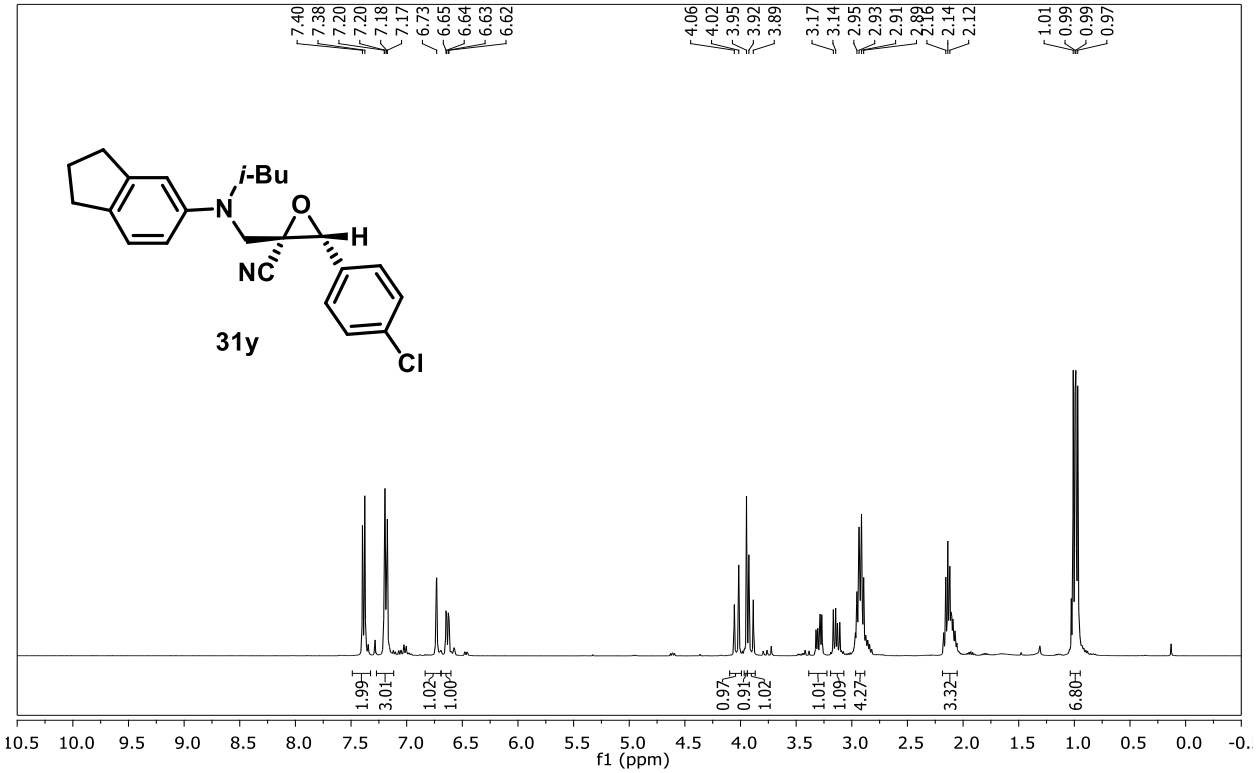
4.5.6. ^{1}H and ^{13}C NMR Spectra of Selected Compounds

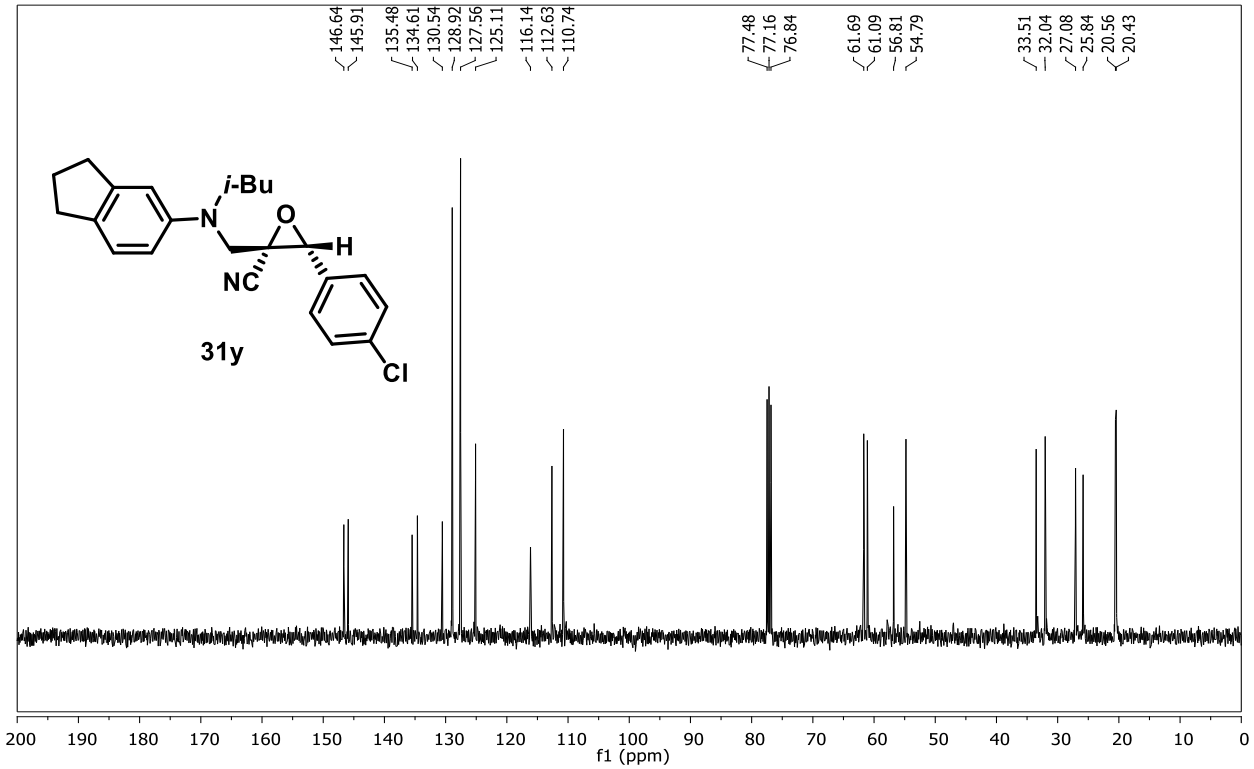
3-(4-Chlorophenyl)-2-((isobutyl(phenyl)amino)methyl)oxirane-2-carbonitrile (31a)



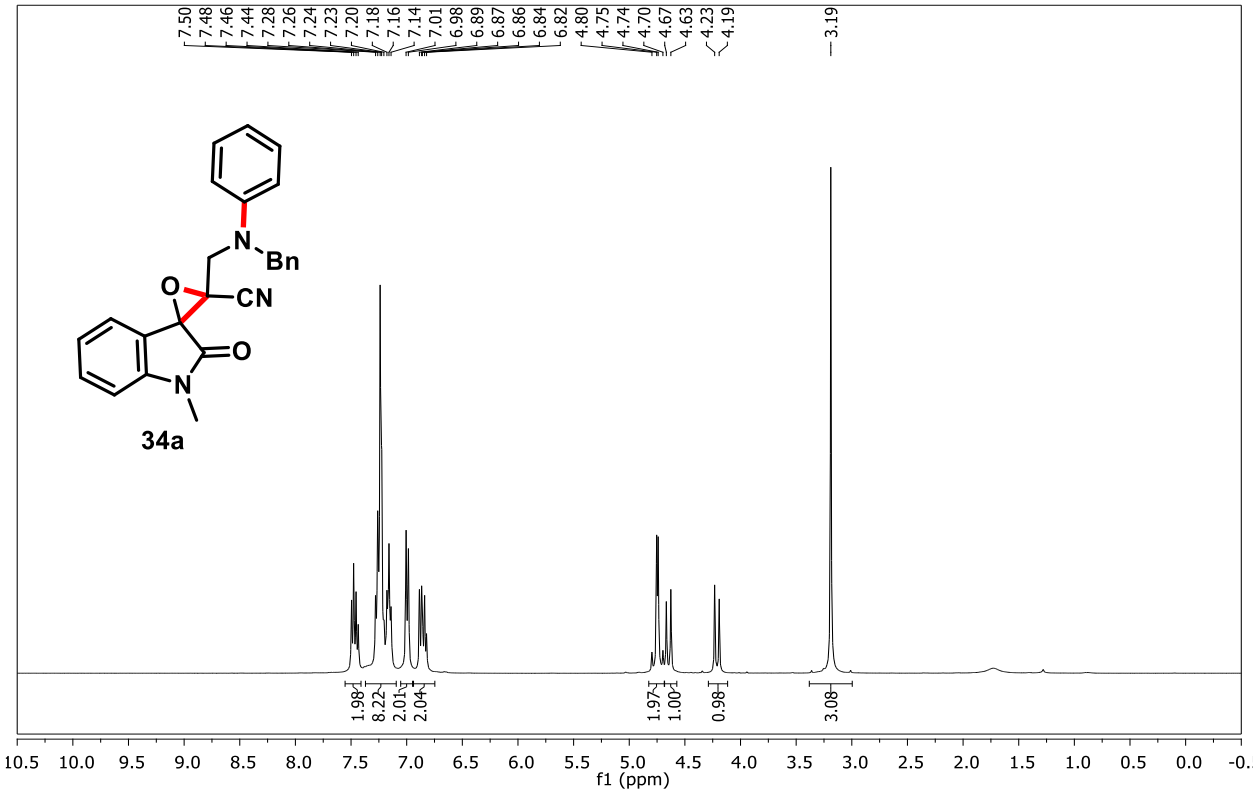


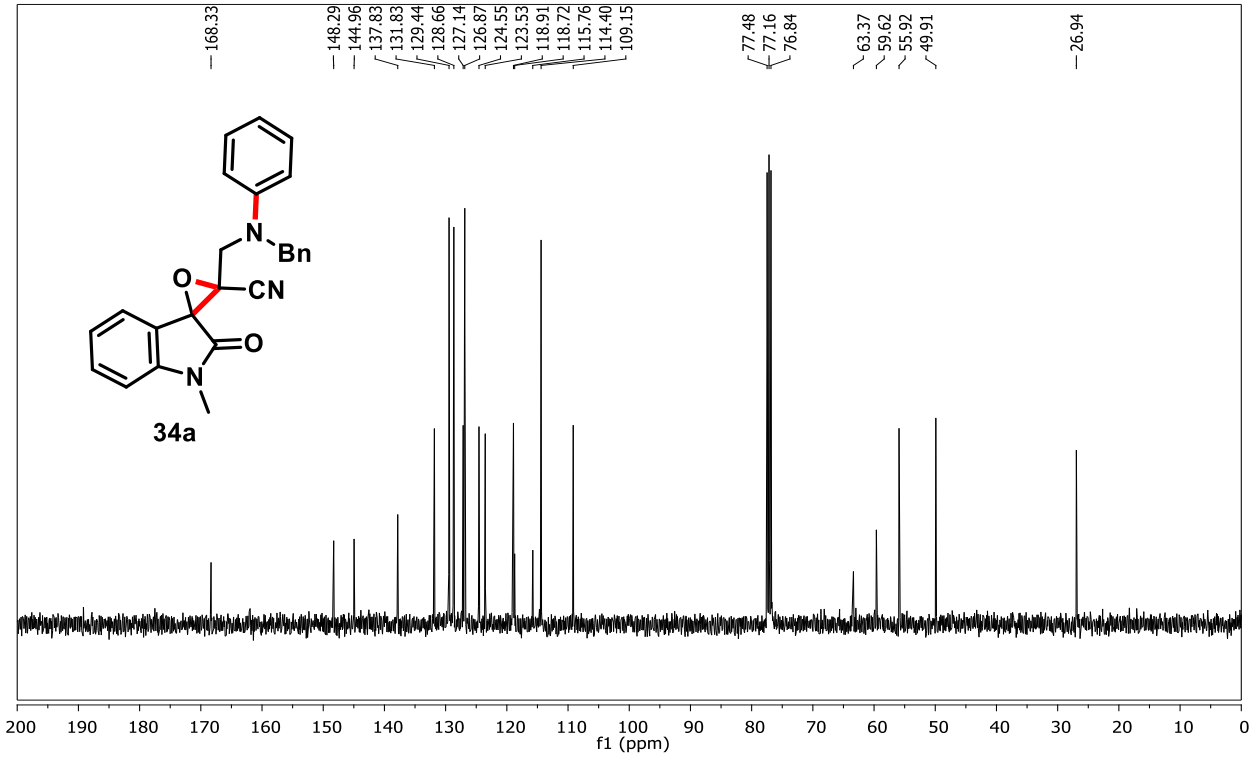
3-(4-Chlorophenyl)-2-(((2,3-dihydro-1*H*-inden-5-yl)(isobutyl)amino)methyl)oxirane-2-carbonitrile (31y)





3'-((Benzyl(phenyl)amino)methyl)-1-methyl-2-oxospiro[indoline-3,2'-oxirane]-3'-carbonitrile (34a)





4.6. References

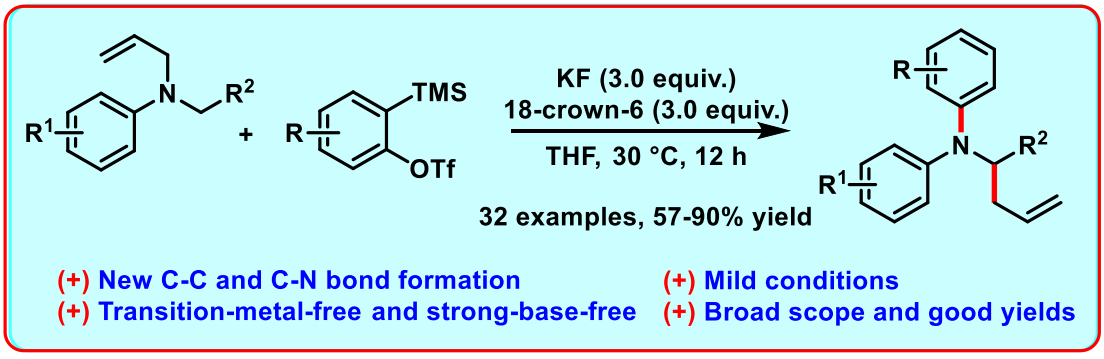
1. For recent reviews on arynes, see: (a) Shi, J.; Li, Y.; Li, Y. *Chem. Soc. Rev.* **2017**, *46*, 1707. (b) Idiris, F. I. M.; Jones, C. R. *Org. Biomol. Chem*. **2017**, *15*, 9044. (c) García-López, J.-A.; Greaney, M. F. *Chem. Soc. Rev.***2016**, *45*, 6766. (d) Bhojgude, S. S.; Bhunia, A.; Biju, A. T. *Acc. Chem. Res*. **2016**, *49*, 1658. (r) Goetz, A. E.; Shah, T. K.; Garg, N. K. *Chem. Commun*. **2015**, *51*, 34. (f) Dubrovskiy, A. V.; Markina, N. A.; Larock, R. C. *Org. Biomol. Chem.* **2013**, *11*, 191. (g) Wu, C.; Shi, F. *Asian J. Org. Chem.* **2013**, *2*, 116. (h) Pérez, D.; Peña, D.; Guitián, E. *Eur. J. Org. Chem.* **2013**, 5981. (i) Tadross, P. M.; Stoltz, B. M. *Chem. Rev.* **2012**, *112*, 3550. (j) Gampe, C. M.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2012**, *51*, 3766. (k) Bhunia, A.; Yetra, S. R.; Biju, A. T. *Chem. Soc. Rev.* **2012**, *41*, 3140. (l) Okuma, K. *Heterocycles* **2012**, *85*, 515. (m) Yoshida, H.; Ohshita, J.; Kunai, A. *Bull. Chem. Soc. Jpn.* **2010**, *83*, 199
2. Lepley, A. R.; Giumanini, A. G.; Giumanini A. B.; A.Khan, W. *J. Org. Chem.*, **1966**, *31*, 2051
3. Xu, H.-D.; Cai, M.-Q.; He, W.-J.; Hu W.-H.; Shen, M.-H. *RSC Adv.*, **2014**, *4*, 7623.
4. Swain, S. P.; Shih, Y.-C.; Tsay, S.-C.; Jacob, J.; Lin, C.-C.; Hwang, K. C.; Horng J.-C.; Hwu, J. R. *Angew. Chem., Int. Ed.*, **2015**, *54*, 9926.
5. Li, H.-Y.; Xing, L-J.; Lou, M-M.; Wang H.; Liu, R-H.; Wang, B. *Org. Lett.*, **2015**, *17*, 1098.
6. M.-M. Lou, H. Wang, L. Song, H.-Y. Liu, Z.-Q. Li, X.-S. Guo, F.-G Zhang and B. Wang, *J. Org. Chem.*, 2016, **81**, 5915.
7. Li, Y.; Muck-Lichtenfeld C.; Studer, A. *Angew. Chem., Int. Ed.*, **2016**, *55*, 14435.
8. (a) Roy, T.; Thangaraj, M.; Kaicharla, T.; Kamath, R. V.; Gonnade R. G.; Biju, A. T. *Org. Lett.*, **2016**, *18*, 5428. (b) Zhang, J.; Chen, Z.-X.; Du, T.; Li, B.; Gu Y.; Tian, S.-K. *Org. Lett.*, **2016**, *18*, 4872 (c) Moss, S. G.; Pocock, I. A.; Sweeney, J. B.; *Chem. - Eur. J.*, **2017**, *23*, 101.
9. Chen, J.; Palani, V.; Hoye, T. R. *J. Am. Chem. Soc.*, **2016**, *138*, 4318.
10. Roy, T.; Bhojgude, S. S.; Kaicharla, T.; Thangaraj, M.; Garai B.; Biju, A. T. *Org. Chem. Front*., **2015**, *3*, 71.
11. Roy, T.; Baviskar, D. R.; Biju, A. T. *J. Org. Chem.*, **2015**, *80*, 11131

12. Stephens, D.; Zhang, Y.; Cormier, M.; Chavez, G.; Arman H.; Larionov, O. V.; *Chem. Commun.*, **2013**, *49*, 6558.
13. Tang, C.-Y.; Wang, G.; Yang, X.-Y.; Wu X.-Y.; Sha F. *Tetrahedron Lett.*, **2014**, *55*, 6447.
14. For selected reports, see: (a) Siciliano, C.; Barattucci, A.; Bonaccorsi, P.; Gioia, M. L. D.; Leggio, A.; Minuti, L.; Romio E.; Temperini, A. *J. Org. Chem.*, **2014**, *79*, 5320; (b) Concellón, J. M.; Solar, V.; García-Granda S.; Díaz, M. R. *J. Org. Chem.*, **2007**, *72*, 7567; (c) Concellón, J. M.; Suárez J. R.; Solar, V. *Org. Lett.*, **2006**, *8*, 349; (d) Concellón, J. M.; Suárez J. R. Solar, V. *J. Org. Chem.*, **2005**, *70*, 7447.
15. (a) Himeshima, Y.; Sonoda T.; Kobayashi, H. *Chem. Lett.*, **1983**, 1211; (b) Peña, D.; Cobas, A.; Pérez D.; Guitián, E. *Synthesis*, **2002**, 1454.
16. For a related epoxidation using strained azetidinium ylides, see: (a) Alex, A.; Larmanjat, B.; Marrot, J.; Couty F.; David, O. *Chem. Commun.*, **2007**, 2500; see also: (b) Couty, F.; David, O.; Larmanjat B.; Marrot, J. *J. Org. Chem.*, **2007**, *72*, 1058.
17. Gunderman, K.-D.; Holtman, G.; Rose H. -J.; Schulze, H. *Chem. Ber.*, **1960**, *93*, 1632.
18. (a) Sato, Y.; Tamura, T.; Kinbara, A.; Morib, M. *Adv. Synth. Catal.* **2007**, *349*, 647; (b) Peña, D.; Cobas, A.; Pérez, D.; Guitián, E. *Synthesis* **2002**, 1454.
19. Bruker (**2006**). *APEX2*, *SAINT* and *SADABS*. Bruker AXS Inc., Madison, Wisconsin, USA.
20. Sheldrick, G. M. *Acta Crystallogr*. **2008**, *A64*, 112.
21. Farrugia, L. J. *J. Appl. Cryst.* **1997**, *30*, 565.
22. Roy, T.; Thangaraj, M.; Gonnade, R. G.; Biju, A. T. *Chem. Commun.* **2016**, *52*, 9044.

Chapter 5

The Aryne [2,3] Stevens Rearrangement

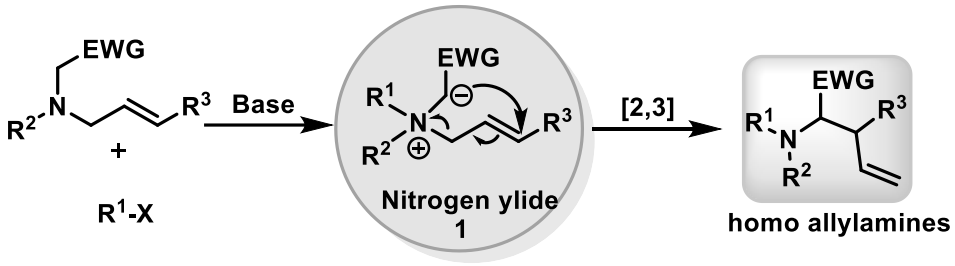
An aryne induced transition-metal-free and mild [2,3] Stevens rearrangement of tertiary allylic amines for the synthesis of functionalized homoallylic amines in moderate to good yield and broad substrate scope is presented in this chapter. The key nitrogen ylide intermediate was generated by the *N*-arylation of allyl amines using arynes. Moreover, the reaction of chiral allyl amines with arynes resulted in the enantiospecific synthesis of homoallylic amines. In addition, preliminary studies on [1,2] Stevens rearrangement is also presented.



Org. Lett. **2016**, *18*, 5428

5.1. Introduction

The Stevens rearrangement involves the rearrangement of ammonium/sulfonium salts into complex nitrogen/sulfur containing products *via* either [1,2] or [2,3] sigmatropic rearrangement. Normally, the reaction usually takes place in the presence of a strong base.[1,2] The key intermediate is a nitrogen ylide **1** which is formed by the deprotonation of the ammonium/sulphonium salts (Scheme 5.1). [3] There are improved synthetic procedures to generate the ylides selectively and have been extensively utilized in past two decades for the synthesis of several important molecules.

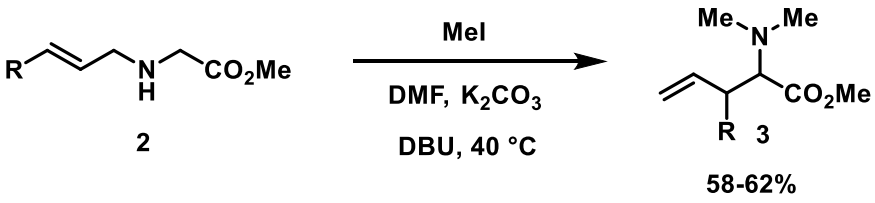


Scheme 5.1. [2,3] Stevens rearrangement

5.2. Stevens Rearrangement

5.2.1 By Deprotonation of Ammonium Salts

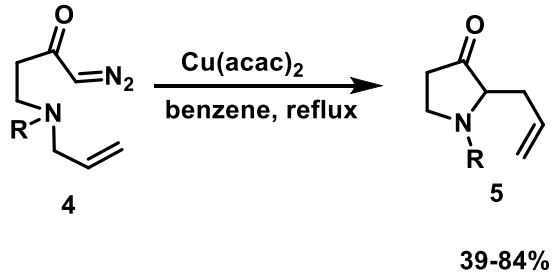
There are several reports on Stevens rearrangements of ammonium salts using base. One-pot protocols are also developed for the preparation of products of [2,3]-rearrangement without isolating the quaternary ammonium salt precursors. The direct reactions of secondary allylic amines **2** with methyl iodide (primary amines and allyl iodide/bromide) in basic media delivered the rearranged products **3** in good yields (Scheme 5.2).[4]



Scheme 5.2. [2,3] Stevens rearrangement with in situ formed ammonium salt

5.2.2. Intramolecular Additions of Allylic Amines to Carbenes and Carbenoids

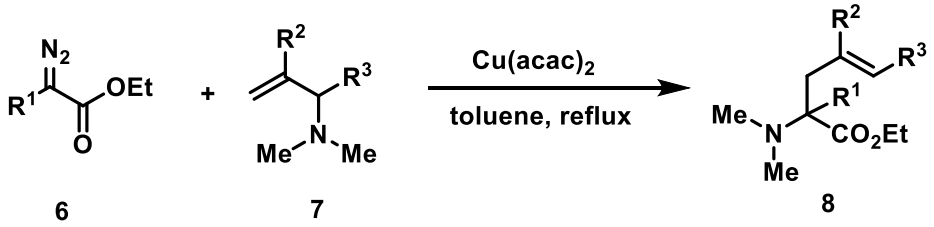
Transition metal-catalyzed methods can also be employed for the generation of nitrogen ylides. The metal-catalyzed cross-coupling of tertiary allyl amines with diazoesters is a convenient method for the direct access to nitrogen ylides. As early as 1994, tandem intramolecular formations of allylic ammonium ylides from the allylic amine **4** followed by [2,3]-Stevens rearrangement to form **5** were studied by Clark and co-workers (Scheme 5.3).[5]



Scheme 5.3. Intramolecular metal catalyzed [2,3] Stevens rearrangement

5.2.3. Intermolecular Additions of Allylic Amines to Carbenes and Carbenoids

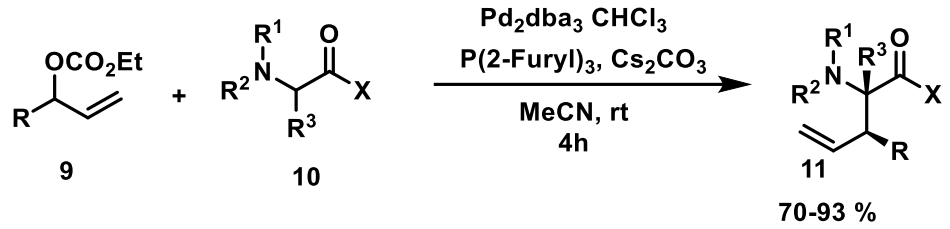
The [2,3]-Stevens rearrangement has also been explored in its intermolecular variant. The diazo derivatives **6** and allylic amines **7** reacted, usually in presence of $Cu(acac)_2$ to form the rearranged products **8** (Scheme 5.4).[6]



Scheme 5.4. Intermolecular additions of allylic amines to carbenoids

In 2011, the Tambar group demonstrated the Pd-catalyzed allylic amination strategy using tertiary amino esters **10** and allyl carbonates **9**. The in situ generated the nitrogen ylide underwent diasteroselective Stevens rearrangement to afford

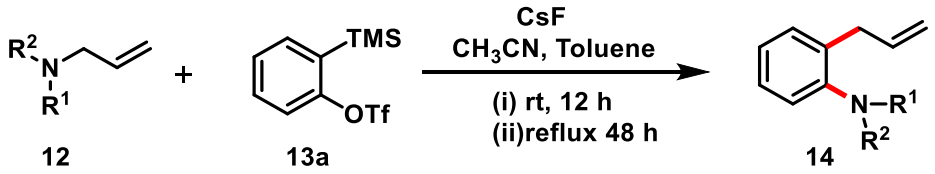
corresponding homoallylic amines **11**. This is a mild method for the tandem ylide generation/[2,3] rearrangement (Scheme 5.5).[7]



Scheme 5.5. Palladium catalyzed diasteroselective Stevens rearrangement

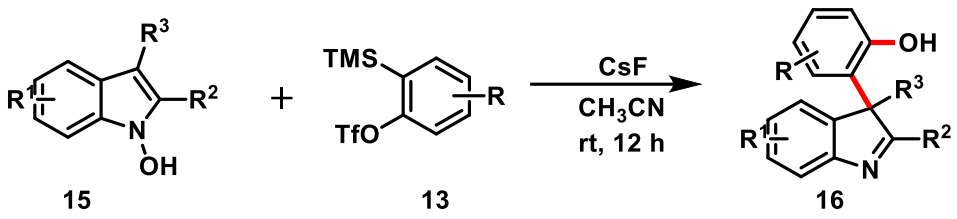
5.3. Selected Sigmatropic Rearrangements Involving Aryne Intermediates

The aza-Claisen rearrangement of allylenamines is a well known [3,3]-rearrangement for the synthesis of functionalized amines. To overcome the drawbacks of traditional methods of aza-Claisen rearrangement, Greaney and co-workers came up with a simpler protocol for the same employing arynes. The addition of aryne **13a** to a tertiary allylamine **12** afforded the rearranged product **14** *via* an aza-Claisen rearrangement and the methodology developed is a milder strategy to synthesize functionalized anilines (Scheme 5.6).[8]



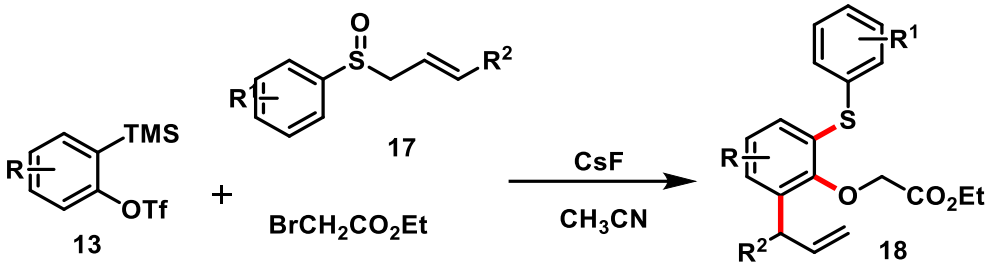
Scheme 5.6. Aryne aza-Claisen rearrangement

Wang and co-workers reported the synthesis of C3-aryl indoles **16** *via* a [3,3]-rearrangement in the reaction of *N*-hydroxyindoles **15** with arynes. (Scheme 5.7).[9] The initially formed *O*-arylated *N*-hydroxyindole undergoes a [3,3] sigmatropic rearrangement to afford the 3-aryl indoles **16**.



Scheme 5.7. Aryne route towards the synthesis of C3-aryl indoles

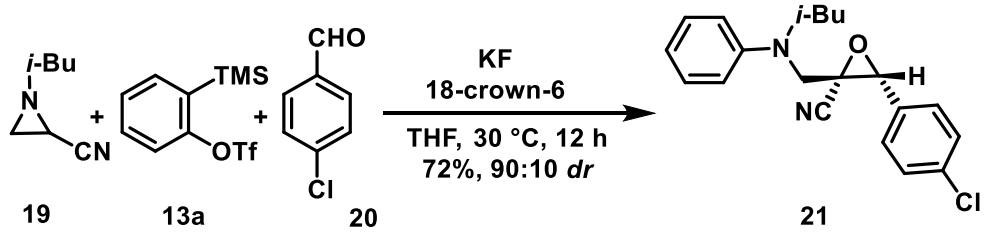
Recently Li and co-workers reported an aryne 1,2,3-trisubstitution with aryl allyl sulfoxides with the formation of three new bonds including C-S, C-O, and C-C bonds in a single transformation on consecutive positions of a benzene ring. For the first time, aryne 1,2,3-trifunctionalization is achieved using a smartly designed aryl allyl sulfoxides **17** (Scheme 5.8).[10] The reaction proceeds *via* a sigmatropic rearrangement and delivers the trifunctionalized product **18**.



Scheme 5.8. Aryne 1,2,3-trifunctionalization

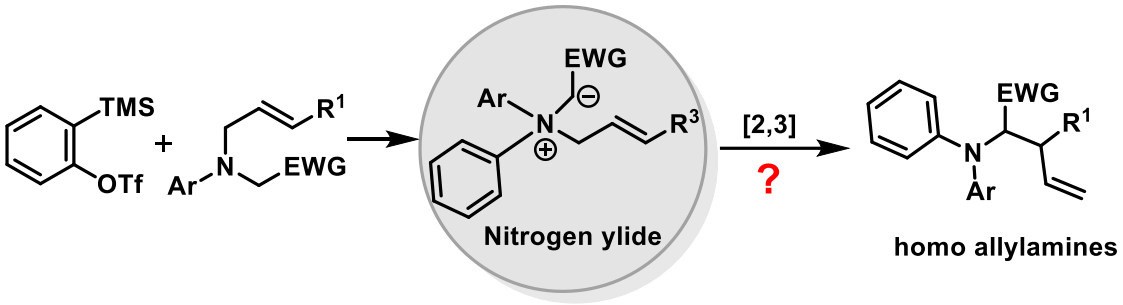
5.4. Statement of the Problem

Arynes are well known for triggering the in situ generation of ylides.[11] Recently, our group has demonstrated the utility of aryne induced ylide for the synthesis of functionalized amino epoxides (For details, see chapter 4). The cyclic ammonium ylide formed by the nucleophilic addition of aziridine **19** to aryne **13a** followed a proton transfer is intercepted with aldehyde **20** for the synthesis of biologically important amino epoxides **21** (Scheme 5.9).[12]



Scheme 5.9. Functionalized amino epoxides using aryne induced ylides

Traditionally, the nitrogen ylides for Stevens rearrangement are generated from the corresponding ammonium salts (prepared from tertiary amines and alkyl halides) by treatment with a base. However, the harsh reaction conditions needed for the synthesis of many ammonium salt precursors and use of strong base limit the broad application of this method. Thus, studies towards the mild, metal free and general methods for the [1,2], and [2,3] rearrangements are highly desirable (Scheme 5.10).



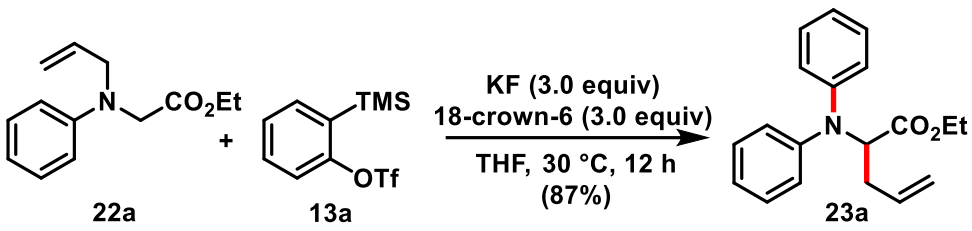
Scheme 5.10. Aryne induced ammonium ylide

An aryne induced transition-metal-free and mild [2,3] Stevens rearrangement of tertiary allylic amines for the synthesis of functionalized homoallylic amines is discussed in the following sections.

5.5. Results and Discussion

5.5.1. Optimization Studies

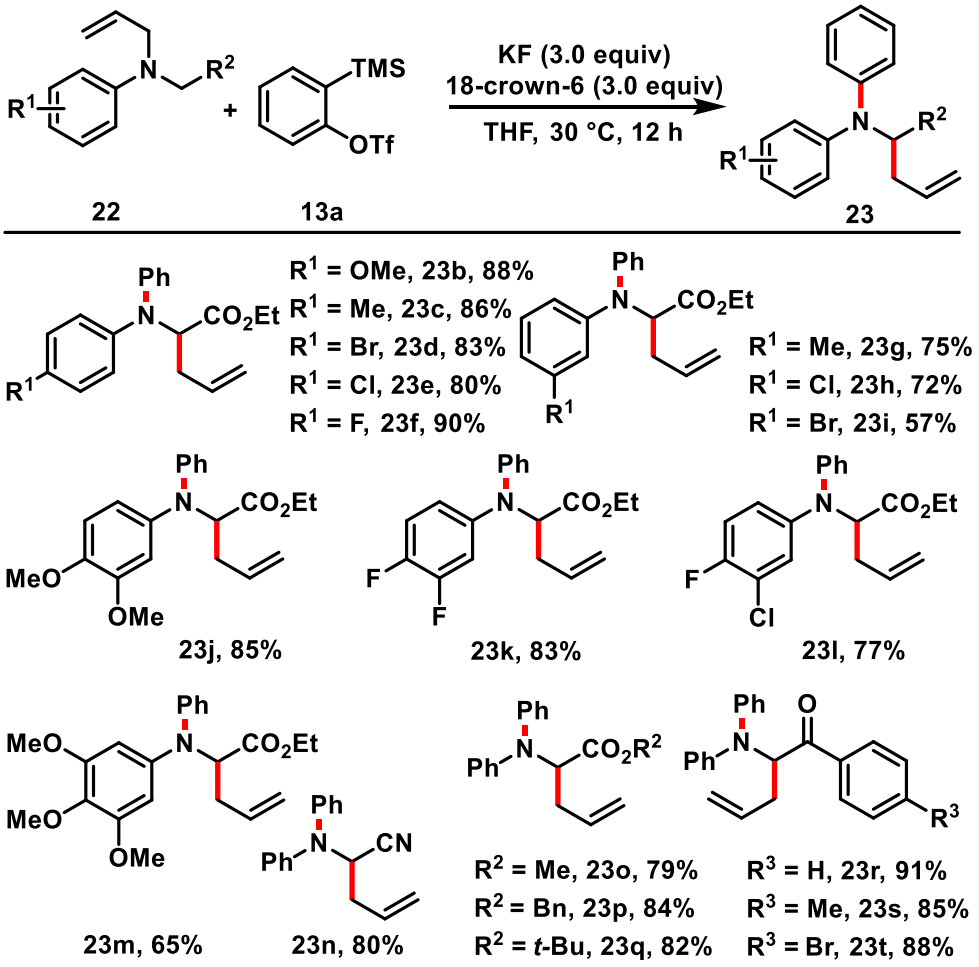
With the experience of generating the nitrogen ylides from arynes and electron-deficient aziridines, the present study was commenced with the treatment of ethyl *N*-allyl-*N*-phenylglycinate **22a** with the aryne generated from the 2-(trimethylsilyl)aryl triflate precursor **13a**[13] using KF in presence of 18-crown-6 as additive in THF at 30 °C. Under these reaction conditions, the homoallylic amine 2**3a** derived from the [2,3] Stevens rearrangement was formed in 87% yield (Scheme 5.11). Notably, the aza-Claisen product reported by Greaney and co-workers was not observed under the reaction conditions. The use of CsF (in CH_3CN as solvent) and tetrabutyl ammonium fluoride (TBAF) as the fluoride source afforded 2**3a** in 68% and 32% yield respectively.



Scheme 5.11. Aryne induced [2,3] Stevens rearrangement

5.5.2. Synthesis of Homoallylic Amines

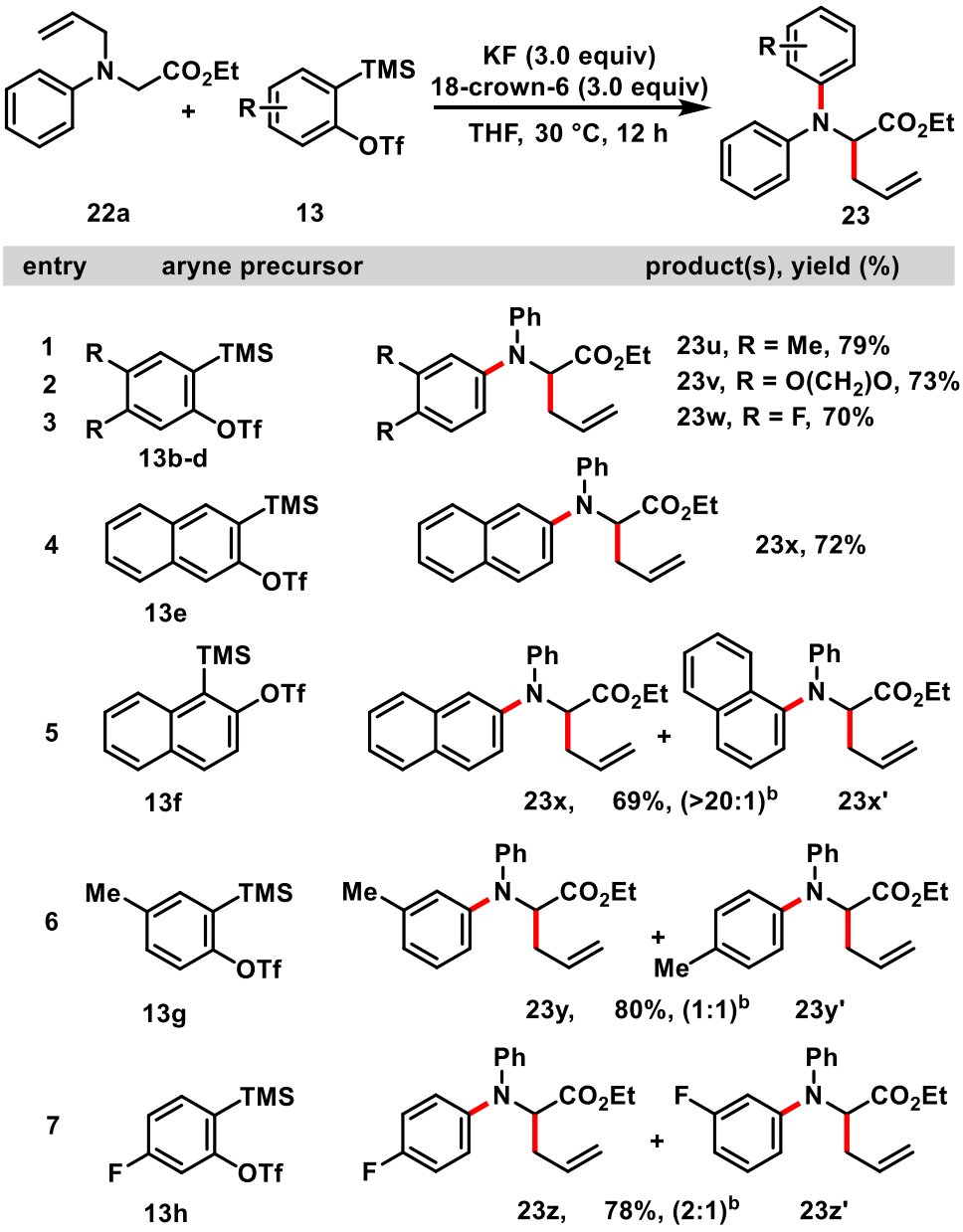
With the optimized reaction conditions in hand, we evaluated the scope of the allylic amines in this reaction (Scheme 5.12).[14,15] Various electronically different *para*-substituted allylic anilines underwent smooth rearrangement to the correcsponding *N, N*-diaryl homoallylic amines in good yields (**23b-23f**). Moreover, *meta*-substituted anilines were well tolerated furnishing the desired homo allylic amines in high yields (**23g-23i**). However, *ortho*-substituted anilines afforded only traces of the expected product, probably due to the steric hindrance during the formation of the aryne induced ylide. Additionally, various disubstituted allylic anilines worked well in this rearrangement reaction delivering the products in good yields (**23j-23l**). Trisubstituted aniline derived allylic amine also afforded the desired product **23m** in 65% yield. The reactivity was unaltered when the electron-withdrawing ester group was replaced by a nitrile group affording the α-amino cyano compound **23n** in 80% yield. Various alkoxy carbonyl groups including methyl, benzyl and *tert*-butyl as the electron-withdrawing group delivered good yields (**23o-23q**). The use of differently substituted benzoyl groups as the electron-withdrawing group was well tolerable under the present conditions and the rearranged products are formed in good yields (**23r-23t)**.



General conditions: **22** (0.50 mmol), **13a** (0.75 mmol), KF (3.0 equiv), 18-crown-6 (3.0 equiv), THF (2.0 mL), 30 °C and 12 h. Yields of the isolated products are given.

Scheme 5.12. Scope of amines in the aryne induced [2,3] Stevens rearrangement

We next examined the scope of differently substituted arynes (Table 5.1). Electronically dissimilar 4,5-disubstituted symmetrical arynes readily furnished the respective homoallylic amines in good yields (**23u-23w**). The reaction of the tertiary allylic amine **22a** with symmetrical and unsymmetrical naphthalyne generated from the precursors **13e** and **13f**, resulted in the formation of 2-naphthyl substituted homoallyl amine **23x** in good yield. In the case of unsymmetrical naphthalyne, **23x** was exclusively formed with high regioselectivity. As expected, the unsymmetrical 4-methyl aryne generated from **13g** afforded the mixture of regioisomers **23y** and **23y'** in 80% yield and 1:1 ratio. Furthermore, the reaction of **22a** with unsymmetrical 4-fluoroaryne generated from **13h** resulted in the mixture of regioisomers **23z** and **23z'** in 78% yield and 2:1 ratio.



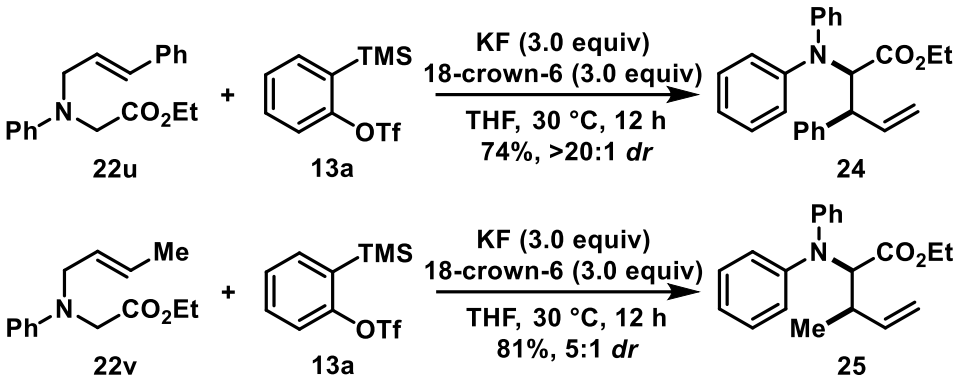
General conditions: **22a** (0.50 mmol), **13** (0.75 mmol), KF (3.0 equiv), 18-crown-6 (3.0 equiv), THF (2.0 mL), 30 °C and 12 h. Yields of the isolated products are given. [b] The regioisomer ratio was determined by ^{1}H NMR analysis of crude reaction mixture.

Table 5.1. Scope of arynes in the aryne induced [2,3] Stevens rearrangement

5.5.3. Diastereoselective Synthesis of Homoallylic Amines

The outcome of this rearrangement with allyl amines[16] having substituent at the allylic position has been examined. To our delight, the reaction of arynes with the tertiary

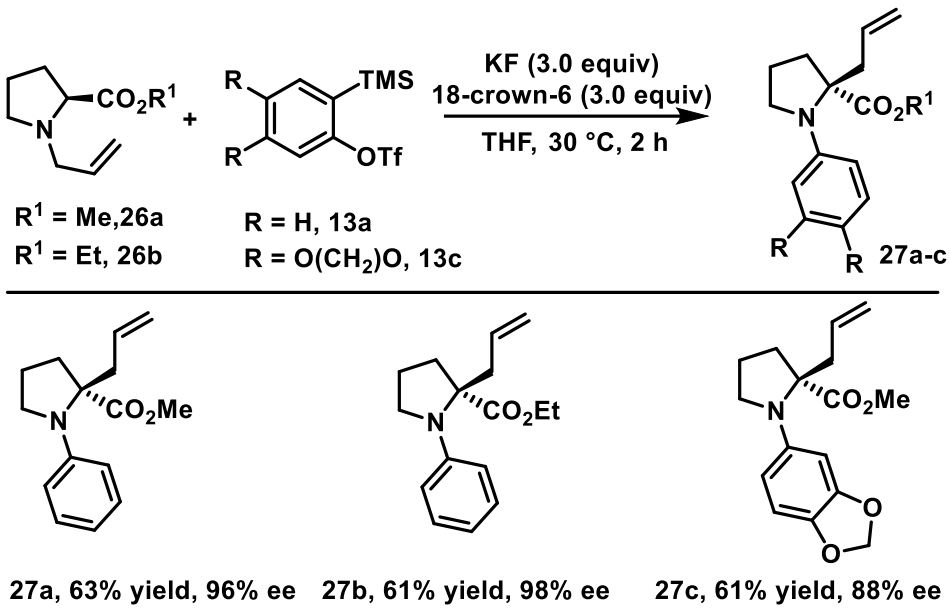
cinnamyl amine **22u** afforded functionalized homoallylic amine **24** in 74% yield and in excellent selectivity (>20:1, determined by ^{1}H NMR) (Scheme 5.13). Additionally, the reaction of aryne with the crotyl substituted substrate **22v** afforded the desired product **25** in 81% yield and 5:1 *dr* (Scheme 5.13).



Scheme 5.13. Aryne induced diastereoselective [2,3] Stevens rearrangement

5.5.4. Stereospecific [2,3] Stevens Rearrangement

This aryne induced [2,3] rearrangement could also be applied to enantiomerically pure proline-derived allyl amines. Treatment of the chiral proline-derived allylic amine **26a** (>99% ee) with aryne generated from **13a** resulted in the formation of the *N*-aryl α-allyl proline derivative **27a** bearing a quaternary stereocentre in 63% yield with retention of enantiopurity and inversion of configuration (Scheme 5.14).[16,17] It is happening *via* the transfer of chirality from carbon to nitrogen and then back to carbon. Additionally, the ethyl ester **26b** afforded the stereoselective product **27b** in 61% yield and 98% ee. Moreover, 4,5-disubstituted aryne generated from the triflate precursor **13c** also afforded the corresponding rearranged proline derivative **27c** in 61% yield and 88% ee.

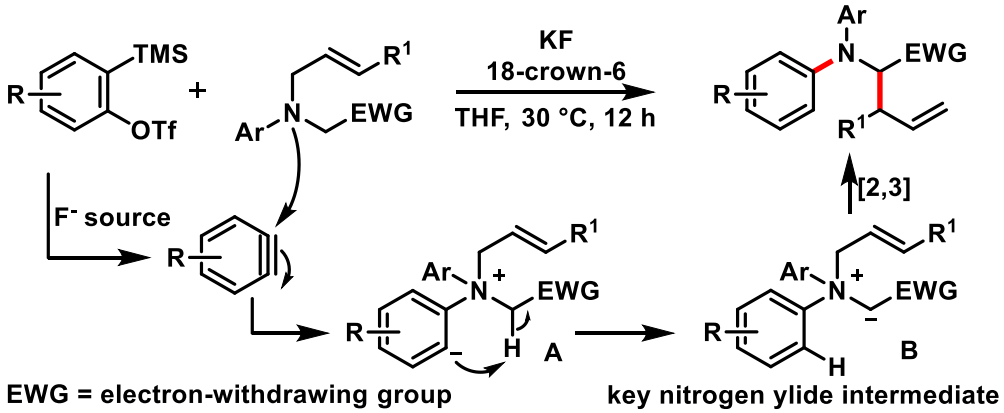


General conditions: **26** (0.50 mmol), **13** (0.75 mmol), KF (3.0 equiv), 18-crown-6 (3.0 equiv), THF (2.0 mL), 30 °C and 2 h. Yields of the isolated products are given and the ee was determined by HPLC analysis on a chiral column.

Scheme 5.14. Aryne induced enantiospecific [2,3] Stevens rearrangement

5.5.5. Mechanism of [2,3] Stevens Rearrangement

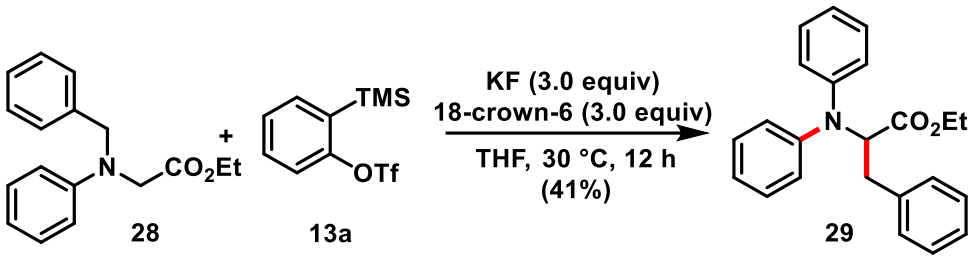
The mechanism involves the addition of tertiary amine to aryne generated from the 2-(trimethylsilyl) aryl triflate generating the 1,3-zwitterionic intermediate **A**. This intermediate undergoes an intramolecular proton transfer to form the key nitrogen ylide intermediate **B**. The ylide **B** upon a [2,3] Stevens rearrangement forms the homoallylic amine (Scheme 5.15).



Scheme 5.15. Mechanism for the aryne [2,3] Stevens rearrangement

5.5.6. [1,2] Stevens Rearrangement

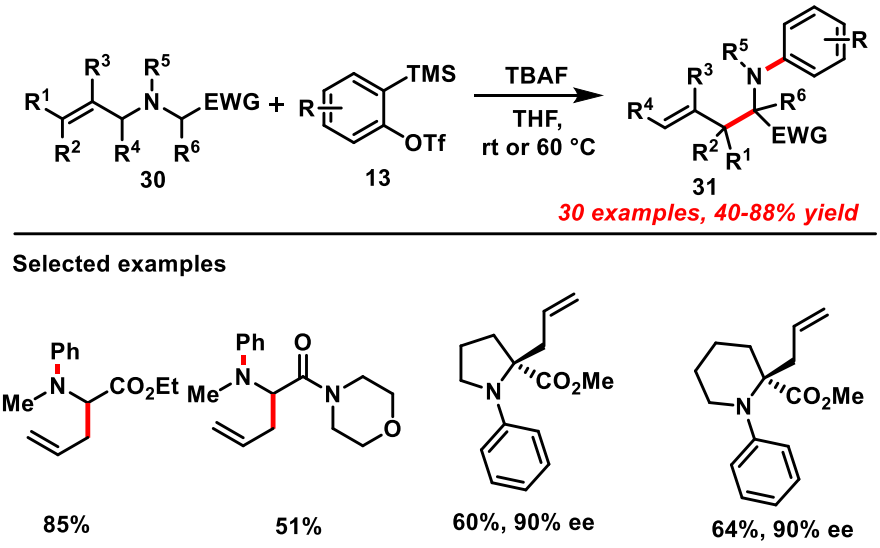
Preliminary study on [1,2] Stevens rearrangement has shown that *N*-benzyl aniline derivative **28** with aryne generated from **13a** using KF in presence of 18-crown-6 as additive in THF at 30 °C delivered the functionalized tertiary amine **29** in 41% yield (Scheme 5.16). Futher optimization did not improve the yield of **29**. The reaction involves the initial generation of nitrogen ylide from aryne and **28**, followed by a [1,2] Stevensrearrangement.



Scheme 5.16. Aryne induced [1,2] Stevens rearrangement

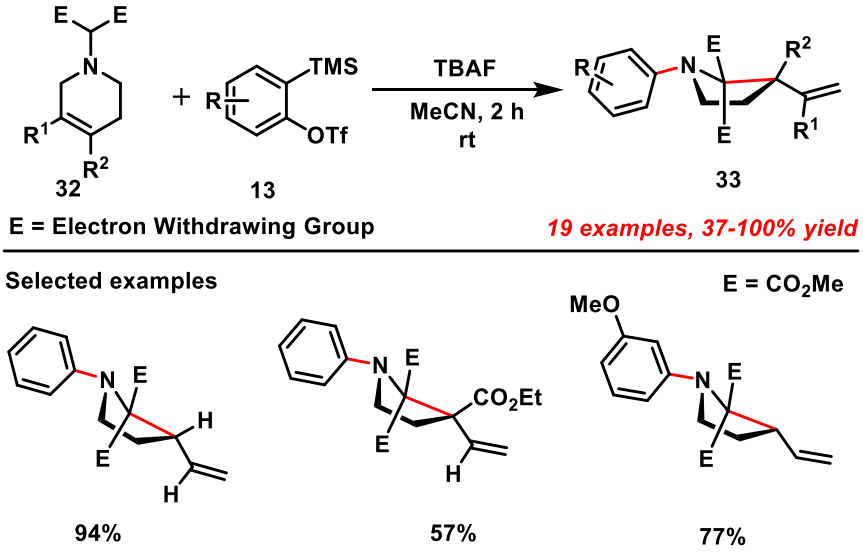
5.6. Simultaneous Developments on Aryne Stevens Rearrangement

A conceptually similar [2,3]-sigmatropic rearrangement of quaternary allylic ammonium ylides was reported independently by Tian and co-workers demonstrating the synthesis of functionalized homoallylic amines **31** in good yields (Scheme 5.17).[18]



Scheme 5.17. Aryne mediated [2,3] Stevens rearrangement

Also, a [2,3]-sigmatropic rearrangement of *N*-(2-malonyl) tetrahydropyridines **32** for the synthesis *of N*-aryl proline derivative **33** *via* an aryne induced sigmatropic rearrangement analogues was demonstrated by Sweeney and co-workers (Scheme 5.18).[19]



Scheme 5.18. Synthesis of *N*-aryl-pyrrolidines using aryne [2,3] Stevens rearrangement

5.7. Conclusion

In conclusion, a mild and transition-metal-free [2,3] Stevens rearrangement induced by arynes for the synthesis of functionalized homoallylic amines have been developed. The reaction proceeds *via* the generation of the nitrogen ylide intermediate from arynes and tertiary allyl amines followed by a sigmatropic rearrangement. A variety of tertiary allyl amines were well tolerated forming of a new carbon-carbon and carbon-nitrogen bond under mild and strong-base-free reaction conditions. The reaction of arynes with proline derived chiral allyl amines afforded the coresponding homoallylic amines with retention of enantiopurity and inversion in configuration.[20]

5.8. Experimental Details

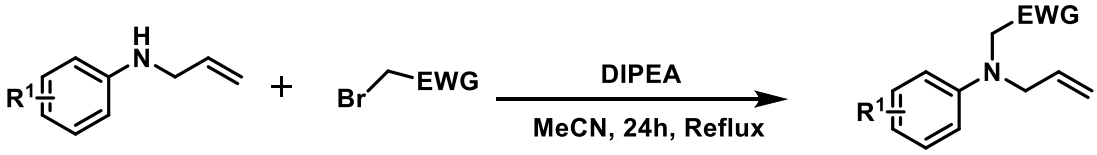
5.8.1. General Information

Unless otherwise specified, all reactions were carried out under an atmosphere of argon in flame-dried reaction vessels with Teflon screw caps. 30 °C corresponds to the room temperature of the lab when the experiments were carried out. THF was freshly purified by distillation over Na-benzophenone and was transferred under argon. 18-Crown-6 was recrystallized from dry CH_3CN and KF was dried by heating at 110 °C for 12 h and left to cool under argon and stored in argon filled glove-box. The 2(trimethylsilyl)phenyl trifluoromethanesulfonate **13a** and the other symmetric and unsymmetric aryne precursors were synthesized following literature procedure.[21]

Analytical thin layer chromatography was performed on TLC Silica gel 60 F_{254}. Visualization was accomplished with short wave UV light. Chromatography was performed on silica gel (230-400 mesh) by standard techniques eluting with solvents as indicated.

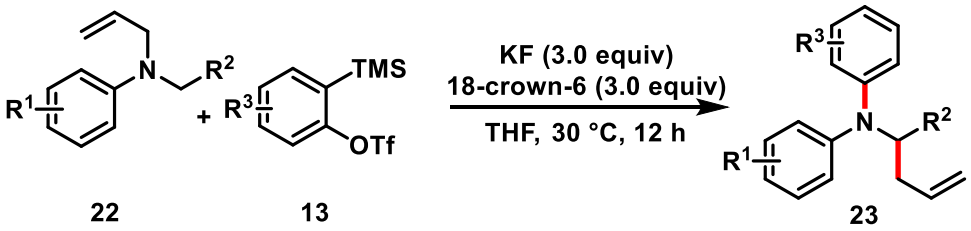
All compounds were fully characterized. ^1H and ^{13}C NMR spectra were recorded on Bruker AV 400, 500 in solvents as indicated. Chemical shifts (δ) are given in ppm. The residual solvent signals were used as references and the chemical shifts converted to the TMS scale ($CDCl_3$: δH = 7.26 ppm, δC = 77.16 ppm). Infrared spectra were recorded on a Bruker Alpha-E Infrared Spectrophotometer. The wave numbers (n) of recorded IR-signals are quoted in cm^{-1}. HRMS data were recorded on either Thermo Scientific Q-Exactive, Accela 1250 pump. HPLC analysis was performed on Agilent Technologies 1260 Infinity with UV detector. Optical rotation was measured with a JASCO P 2000 digital polarimeter at rt using 50 mm cell of 1 mL capacity.

5.8.2. General Procedure for the preparation of *N*-Allyl Aniline Substrates



Following the literature procedure, the allyl aniline is treated with the corresponding bromo compounds to afford the allyl amine starting materials for the aryne [2,3] Stevens rearrangement.[22]

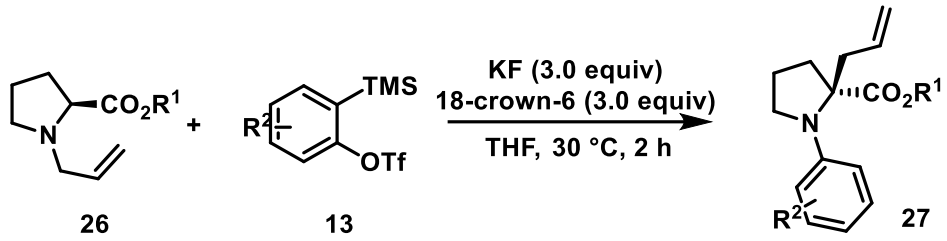
5.8.3. General Procedure for the Aryne [2,3] Stevens Rearrangement



22 13 23

To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added the KF (87 mg, 1.5 mmol) and 18-crown-6 (0.396 mg, 1.5 mmol) in a glove box. The mixture was dissolved in THF (2.0 mL) under argon atmosphere. Allyl amine **22** (0.50 mmol) was added outside the glove box under argon atmosphere. To the stirring solution, aryne precursor **13** (0.75 mmol) was added. Then the reaction mixture was allowed to react at 30 °C for 12 h. After 12 h, the reaction was stopped, the solvent was evaporated and the crude residue pre-adsorbed on silica gel and purified by flash column chromatography (Pet. ether /EtOAc = 99/01) on silica gel to afford the corresponding homoallylic amines **23** in moderate to good yields.

5.8.4. General Procedure for the Enantiospecific [2,3] Stevens Rearrangement



26 13 27

To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added the KF (87 mg, 1.5 mmol) and 18-crown-6 (0.396 mg, 1.5 mmol) in a glove box. The mixture was dissolved in THF (2.0 mL) under argon atmosphere. The *N*-allyl proline derivative **26** (0.50 mmol) was added outside the glove box under argon atmosphere. To the stirring solution aryne precursor **13** (0.75 mmol) was added. Then the reaction mixture was allowed to react at 30 °C for 2 h. After 2 h the reaction was stopped, the solvent was evaporated and the crude residue pre-adsorbed on silica gel and purified by flash column

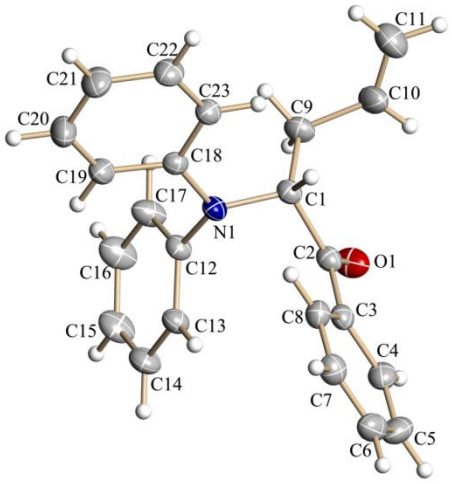
chromatography (Pet. ether /EtOAc = 99/01) on silica gel to afford the corresponding *N*-aryl proline derivatives **27** in moderate to good yields.

5.8.5. X-ray Data of 23r

X-ray intensity data measurements of compound **23r** was carried out on a Bruker D8 VENTURE Kappa Duo PHOTON II CPAD diffractometer equipped with Incoatech multilayer mirrors optics. The intensity measurements were carried out with micro-focus sealed tube diffraction source (MoK_α= 0.71073Å) at 150(2) K temperature using OXFORD LN2 cryosystem. The X-ray generator was operated at 50 kV and 1.4 mA. A preliminary set of cell constants and an orientation matrix were calculated from three sets of 36 frames. Data were collected with ω scan width of 0.5° at different settings of φ and 2θ with a frame time of 15 secs keeping the sample-to-detector distance fixed at 4.00 cm. The X-ray data collection was monitored by APEX3 program (Bruker, 2016).[21] All the data were corrected for Lorentzian, polarization and absorption effects using SAINT and SADABS programs (Bruker, 2016). SHELX-97 was used for structure solution and full matrix least-squares refinement on F^2. All the hydrogen atoms were placed in a geometrically idealized position and constrained to ride on their parent atoms.. The molecules of compound **23r** crystallized in tricinic *P*-1 space group containing two symmetry independednt moleucles in the asymmetriuc unit. The allyl moiety of one of the molecules showed statistical disorder over two position with occupancy 40% and 60%. An *ORTEP* III[3] view of unprimed moleucle was drawn with 50% probability displacement ellipsoids and H atoms are shown as small spheres of arbitrary radii.[23]

Crystal data of **23r**: ($C_{23}H_{21}NO$), M = 327.41, colorless block crystals, 0.27 x 0.24 x 0.22 mm^3, triclinic, space group *P*-1, a = 10.2062(6) Å, b = 13.2507(8) Å, c = 13.9258(8) Å, α = 91.429(2)°, β = 104.805(2)°, γ = 98.033(2)°, V = 1799.30(18) $Å^3$, Z = 4, T = 150(2) K, $2\theta_{max}$=61.096°, D_{calc} (g cm^{-3}) = 1.209, $F(000)$ = 696, μ (mm^{-1}) = 0.073, 126850 reflections collected, 10988 unique reflections (R_{int}=0.0659), 8900 observed ($I > 2\sigma(I)$) reflections, multi-scan absorption correction, T_{min} = 0.980, T_{max} = 0.984, 469 refined parameters, S = 1.041, $R1$ = 0.0536, $wR2$ = 0.1215 (all data R =

0.0684, *wR*2 = 0.1288), maximum and minimum residual electron densities; $\Delta\rho_{max}$ = 0.32, $\Delta\rho_{min}$= -0.20 (eÅ^{-3}).

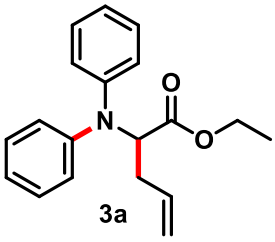


Ortep Diagram of **23r** (thermal ellipsoids are shown with 50% probability).

CCDC 1504535 (**23r**) contains the supplementary crystallographic data. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

5.8.6. Synthesis and Characterization of Homoallylic Amines

Ethyl-2-(diphenylamino)pent-4-enoate (23a)



Following the general procedure, treatment of ethyl *N*-allyl-*N*-phenylglycinate **22a** (0.110 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **13a** (0.223 g, 182 µL, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 99/01) of the crude reaction mixture using silica gel afforded ethyl-2-(diphenylamino)pent-4-enoate **23a** as yellow oil (0.128 g, 87% yield).

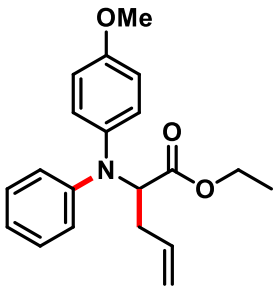
***R*$_f$** (Pet. ether /EtOAc = 95/05): 0.53.

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.31 (t, *J* = 7.8 Hz, 4H), 7.06 - 7.03 (m, 6H), 5.91 - 5.81 (m, 1H), 5.12 - 5.07 (m, 2H), 4.69 (t, *J* = 7.5 Hz, 1H), 4.29 - 4.17 (m, 2H), 2.69 (t, *J* = 7.0 Hz, 2H), 1.27 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.77, 146.67, 134.56, 129.19, 122.68, 122.30, 117.71, 62.72, 61.12, 34.48, 14.27.

HRMS (ESI) calculated $[M+H]^+$ for $C_{19}H_{22}O_2N$: 296.1645, found: 296.1637. **FTIR (cm^{-1})** 3022, 2951, 1722, 1598, 1517, 1445, 1363, 1289, 1261, 1218, 1082, 951, 909, 757.

Ethyl-2-((4-methoxyphenyl)(phenyl)amino)pent-4-enoate (23b)



Following the general procedure, treatment of ethyl N-allyl-N-(4-methoxyphenyl)glycinate **22b** (0.125 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **13a** (0.223 g, 182 μL, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 99/01) of the crude reaction mixture using silica gel afforded ethyl-2-((4-methoxyphenyl)(phenyl)amino)pent-4-enoate **23b** as yellow oil (0.144 g, 88% yield).

***R*$_f$** (Pet. ether /EtOAc = 95/05): 0.48.

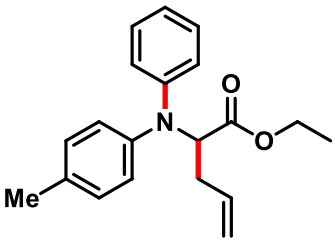
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 - 7.09 (m, 4H), 6.93 (d, *J* = 8.8 Hz, 2H), 6.79 (t, *J* = 7.2 Hz, 1H), 6.68 (d, *J* = 8.2 Hz, 2H), 5.87 - 5.77 (m, 1H), 5.09 (s, 1H), 5.06 (d, *J* = 5.9 Hz, 1H), 4.62 (t, *J* = 7.5 Hz, 1H), 4.24 - 4.18 (m, 2H), 3.85 (s, 3H), 2.59 (t, *J* = 7.1 Hz, 2H), 1.27 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.96, 157.65, 148.77, 137.35, 134.60, 130.46, 129.00, 118.65, 117.69, 115.92, 114.67, 62.33, 61.11, 55.54, 34.85, 14.35.

HRMS (ESI) calculated $[M+H]^+$ for $C_{20}H_{24}O_3N$: 326.1751, found: 326.1747.

FTIR (cm^{-1}) 3018, 2983, 2909, 2402, 1732, 1597, 1509, 1245, 1183, 1035, 993, 923, 772, 668, 501.

Ethyl -2-(phenyl(*p*-tolyl)amino)pent-4-enoate (23c)



Following the general procedure, treatment of ethyl *N*-allyl-N-(*p*-tolyl)glycinate **22c** (0.117 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **13a** (0.223 g, 182 μL, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at 30 °C

for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 99/01) of the crude reaction mixture using silica gel afforded ethyl -2-(phenyl(*p*-tolyl)amino)pent-4-enoate **23c** as yellow oil (0.133 g, 86% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.52;

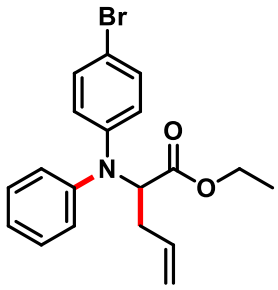
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (t, *J* = 7.9 Hz, 2H), 7.17 (d, *J* = 8.2 Hz, 2H), 7.06 (d, *J* = 8.3 Hz, 2H), 6.94 - 6.87 (m, 3H), 5.91 -5.80 (m, 1H), 5.12 - 5.08 (m, 2H), 4.65 (t, *J* = 7.5 Hz, 1H), 4.26 - 4.19 (m, 2H), 2.66 (t, *J* = 7.1 Hz, 2H), 2.38 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.89, 147.74, 143.22, 134.66, 133.59, 129.97, 129.06, 125.74, 120.46, 119.49, 117.67, 62.64, 61.10, 34.59, 20.94, 14.31.

HRMS (ESI) calculated $[M+H]^+$ for $C_{20}H_{24}O_2N$: 310.1802, found: 310.1800.

FTIR (cm^{-1}) 3026, 2936, 1718, 1588, 1523, 1453, 1369, 1311, 1227, 1108, 998.

Ethyl-2-((4-bromophenyl)(phenyl)amino)pent-4-enoate (23d)



Following the general procedure, treatment of ethyl *N*-allyl-*N*-(4-bromophenyl)glycinate **22d** (0.149 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **13a** (0.223 g, 182 μL, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 99/01) of the crude reaction mixture using silica gel afforded ethyl-2-((4-bromophenyl)(phenyl)amino)pent-4-enoate **23d** as yellow oil (0.156 g, 83% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.57

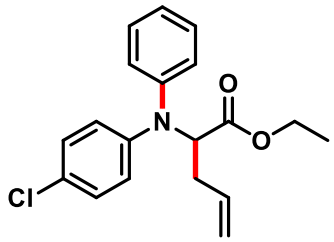
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 - 7.27 (m, 4H), 7.13 - 7.06 (m, 3H), 6.80 (d, *J* = 8.8 Hz, 2H), 5.99 - 5.66 (m, 1H), 5.10 - 5.04 (m, 2H), 4.61 (t, *J* = 7.5 Hz, 1H), 4.30 - 4.14 (m, 2H), 2.74 - 2.44 (m, 2H), 1.26 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.56, 146.27, 145.90, 134.32, 132.06, 129.58, 129.47, 124.48, 123.73, 122.63, 118.01, 114.59, 113.98, 62.80, 61.34, 34.37, 14.34.

HRMS (ESI) calculated $[M+H]^+$ for $C_{19}H_{21}O_2NBr$: 374.0750, found: 374.0749.

FTIR (cm^{-1}) 3066, 3017, 2938, 1732, 1585, 1444, 1377, 1217, 1097, 924, 771, 668.

Ethyl-2-((4-chlorophenyl)(phenyl)amino)pent-4-enoate (23e)



Following the general procedure, treatment of ethyl *N*-allyl-N-(4-chlorophenyl)glycinate **22e** (0.127 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **13a** (0.223 g, 182 µL, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 99/01) of the crude reaction mixture using silica gel afforded ethyl-2-((4-chlorophenyl)(phenyl)amino)pent-4-enoate **23e** as yellow oil (0.132 g, 80% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.45.

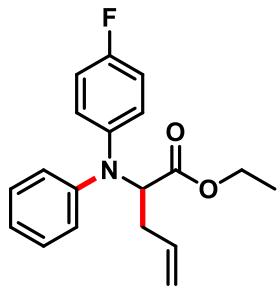
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (t, *J* = 7.8 Hz, 2H), 7.23 (d, *J* = 8.6 Hz, 2H), 7.10 - 7.03 (m, 3H), 6.90 (d, *J* = 8.5 Hz, 2H), 5.86 - 5.76 (m, 1H), 5.11 - 5.04 (m, 2H), 4.62 (t, *J* = 7.8 Hz, 1H), 4.25 - 4.18 (m, 2H), 2.69 - 2.60 (m, 2H), 1.26 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.61, 146.18, 145.58, 134.33, 129.41, 129.17, 126.92, 123.71, 123.26, 122.99, 117.98, 62.81, 61.32, 34.40, 14.32.

HRMS (ESI) calculated $[M+H]^+$ for $C_{19}H_{21}O_2NCl$: 330.1255, found: 330.1258.

FTIR (cm^{-1}) 3022, 2358, 1718, 1712, 1590, 1509, 1460, 1359, 1316, 1278, 1227, 998.

Ethyl-2-((4-fluorophenyl)(phenyl)amino)pent-4-enoate (23f)



Following the general procedure, treatment of ethyl *N*-allyl-*N*-(4-fluorophenyl)glycinate **22f** (0.119 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **13a** (0.223 g, 182 µL, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 99/01) of the crude reaction mixture using silica gel afforded ethyl-2-((4-fluorophenyl)(phenyl)amino)pent-4-enoate **23f** as yellow oil (0.141 g, 90% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.50.

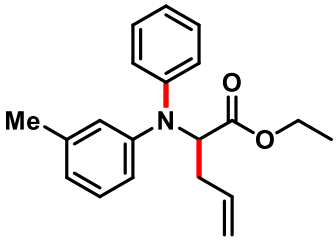
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (t, *J* = 7.8 Hz, 2H), 7.16-7.12 (m, 2H), 7.02 (t, *J* = 8.6 Hz, 2H), 6.89 (t, *J* = 7.3 Hz, 1H), 6.78 (d, *J* = 8.1 Hz, 2H), 5.84-5.74 (m, 1H), 5.19 – 4.91 (m, 2H), 4.60 (t, *J* = 7.5 Hz, 1H), 4.33 – 4.08 (m, 2H), 2.74 – 2.47 (m, 2H), 1.24 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.80, 159.92 (d, *J* = 244.5), 147.77, 134.41, 129.19, 128.26 (d, *J* = 8.44), 120.47, 118.76, 117.89, 116.19, 115.97, 62.62, 61.24, 34.64, 14.34.

HRMS (ESI) calculated $[M+H]^+$ for $C_{19}H_{21}O_2NF$: 314.1551, found: 314.1546.

FTIR (cm^{-1}) 3018, 2983, 2936, 1733, 1504, 1443, 1218, 1094, 994, 839, 772.

Ethyl -2-(phenyl(*m*-tolyl)amino)pent-4-enoate (23g)



Following the general procedure, treatment of ethyl *N*-allyl-*N*-(m-tolyl)glycinate **22g** (0.117 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **13a** (0.223 g, 182 µL, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 99/01) of the crude reaction mixture using silica gel afforded ethyl -2-(phenyl(*m*-tolyl)amino)pent-4-enoate **23g** as yellow oil (0.116 g, 75% yield).

***R*$_f$** (Pet. ether /EtOAc = 95/05): 0.51.

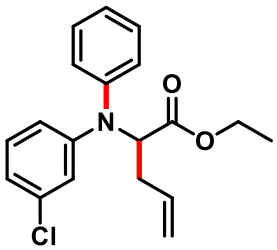
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (t, *J* = 7.8 Hz, 2H), 7.18 (t, *J* = 7.6 Hz, 1H), 7.03 - 6.97 (m, 3H), 6.88 - 6.82 (m, 3H), 5.87 - 5.78 (m, 1H), 5.10 - 5.05 (m, 2H), 4.64 (t, *J* = 7.5 Hz, 1H), 4.24 - 4.17 (m, 2H), 2.65 (t, *J* = 6.8 Hz, 2H), 2.31 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.90, 146.83, 146.59, 139.05, 134.70, 129.18, 129.06, 123.83, 123.47, 122.31, 122.01, 120.23, 117.72, 62.76, 61.15, 34.60, 21.71, 14.34.

HRMS (ESI) calculated $[M+H]^+$ for $C_{20}H_{24}O_2N$: 310.1802, found: 310.1799.

FTIR (cm^{-1}) 3027, 2939, 1716, 1592, 1523, 1441, 1357, 1315, 1278, 1118, 995.

Ethyl 2-((3-chlorophenyl)(phenyl)amino)pent-4-enoate (23h)



Following the general procedure, treatment of ethyl *N*-allyl-*N*-(3-chlorophenyl)glycinate **22h** (0.126 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **13a** (0.223 g, 182 µL, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at 30 °C for 12

h followed by flash column chromatography (Pet. ether /EtOAc = 99/01) of the crude reaction mixture using silica gel afforded ethyl 2-((3-chlorophenyl)(phenyl)amino)pent-4-enoate **23h** as yellow oil (0.119 g, 72% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.54.

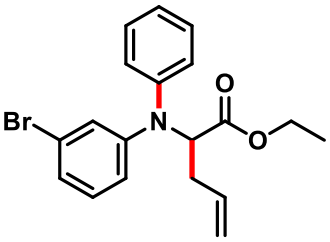
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (t, *J* = 7.7 Hz, 2H), 7.19 - 7.10 (m, 3H), 6.87 - 6.81 (m, 2H), 6.71 - 6.69 (m, 1H), 5.83 - 5.77 (m, 1H), 5.14 - 5.04 (m, 2H), 4.61 (t, *J* = 7.5 Hz, 1H), 4.28 - 4.15 (m, 2H), 2.69 - 2.57 (m, 2H), 1.29 – 1.24 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.41, 148.91, 144.96, 134.81, 134.25, 129.99, 129.56, 126.36, 124.86, 120.39, 119.08, 118.01, 117.13, 62.73, 61.34, 34.44, 14.30.

HRMS (ESI) calculated $[M+H]^+$ for $C_{19}H_{21}O_2NCl$: 330.1255, found: 330.1255.

FTIR (cm^{-1}) 3016, 2925, 2401, 1691, 1640, 1587, 1396, 1217, 1032, 1009, 918, 841, 771.

Ethyl-2-((3-bromophenyl)(phenyl)amino)pent-4-enoate (23i)



Following the general procedure, treatment of ethyl *N*-allyl-*N*-(3-bromophenyl)glycinate **22i** (0.149 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **13a** (0.223 g, 182 μL, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 99/01) of the crude reaction mixture using silica gel afforded ethyl-2-((3-bromophenyl)(phenyl)amino)pent-4-enoate **23i** as yellow oil (0.107 g, 57% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.45.

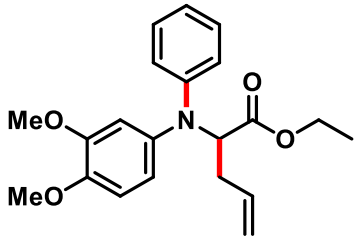
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (t, *J* = 7.7 Hz, 2H), 7.21 - 7.17 (m, 3H), 7.11 - 7.01 (m, 3H), 6.77 (d, *J* = 7.3 Hz, 1H), 5.87 - 5.77 (m, 1H), 5.12 - 5.06 (m, 2H), 4.63 (t, *J* = 7.5 Hz, 1H), 4.26 - 4.22 (m, 2H), 2.68 - 2.62 (m, 2H), 1.29 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.39, 149.01, 144.95, 134.22, 130.28, 129.55, 126.20, 124.80, 123.39, 123.00, 122.08, 118.03, 117.76, 62.72, 61.35, 34.42, 14.32.

HRMS (ESI) calculated $[M+H]^+$ for $C_{19}H_{21}O_2NBr$: 374.0750, found: 374.0751.

FTIR (cm^{-1}) 3023, 2936, 1728, 1588, 1523, 1451, 1369, 1321, 1258, 1108, 996.

Ethyl-2-((3,4-dimethoxyphenyl)(phenyl)amino)pent-4-enoate (23j)



Following the general procedure, treatment of ethyl *N*-allyl-N-(3,4-dimethoxyphenyl)glycinate **22j** (0.140 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **13a** (0.223 g, 182 µL, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 99/01) of the crude reaction mixture using silica gel afforded ethyl-2-((3,4-dimethoxyphenyl)(phenyl)amino)pent-4-enoate **23j** as yellow oil (0.142 g, 85% yield).

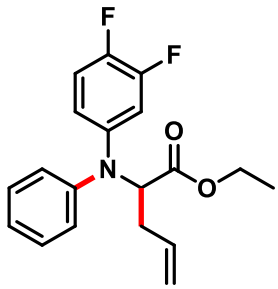
***R*f** (Pet. ether /EtOAc = 95/05): 0.21.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (t, *J* = 7.6 Hz, 2H), 6.92 - 6.86 (m, 3H), 6.82 (t, *J* = 7.1 Hz, 1H), 6.72 (d, *J* = 8.1 Hz, 2H), 5.88 - 5.81 (m, 1H), 5.11 - 5.07 (m, 2H), 4.65 (t, *J* = 7.4 Hz, 1H), 4.25 - 4.21 (m, 2H), 3.93 (s, 3H), 3.85 (s, 3H), 2.63 (t, *J* = 6.9 Hz, 2H), 1.29 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 172.89, 149.42, 148.42, 147.12, 137.47, 134.59, 128.93, 121.04, 118.71, 117.57, 115.91, 112.69, 111.38, 62.21, 61.00, 55.99, 55.86, 34.73, 14.29.

HRMS (ESI) calculated $[M+H]^+$ for $C_{21}H_{26}O_4N$: 356.1856, found: 356.1852.

FTIR (cm^{-1}) 3025, 2928, 1716, 1598, 1515, 1453, 1361, 1321, 1272, 1108, 998.

Ethyl-2-((3,4-difluorophenyl)(phenyl)amino)pent-4-enoate (23k)



Following the general procedure, treatment of ethyl ethyl *N*-allyl-*N*-(3,4-difluorophenyl)glycinate **22k** (0.128 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **13a** (0.223 g, 182 µL, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 99/01) of the crude reaction mixture using silica gel afforded ethyl-2-((3,4-difluorophenyl)(phenyl)amino)pent-4-enoate **23k** as yellow oil (0.138 g, 83% yield).

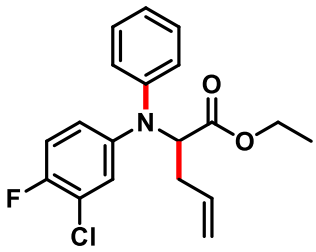
***R*f** (Pet. ether /EtOAc = 95/05): 0.47.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.28 (m, 2H), 7.11 – 6.93 (m, 4H), 6.86-6.81 (m, 1H), 6.71 – 6.69 (m, 1H), 5.87-5.76 (m, 1H), 5.09 (t, *J* = 14.2 Hz, 2H), 4.62-4.49 (m, 1H), 4.25-4.22 (m, 2H), 2.67-2.61 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.38, 151.70 (dd, J_1= 13.4, J_2= 246.89), 147.24 (dd, J_1= 13.5, J_2= 242.84), 145.90, 143.59, 134.08, 129.38, 123.21, 117.96, 117.18 (d, *J* = 17.97), 111.31 (d, *J* = 19.66), 62.72, 61.27, 34.37, 14.20.

HRMS (ESI) calculated $[M+H]^+$ for $C_{19}H_{20}O_2NF_2$: 332.1457, found: 332.1452.

FTIR (cm^{-1}) 3060, 2935, 2360, 1746, 1642, 1611, 1513, 1454, 1097, 958, 921, 816.



Ethyl 2-((3-chloro-4-fluorophenyl)(phenyl)amino)pent-4-enoate (23l)

Following the general procedure, treatment of ethyl *N*-allyl-*N*-(3-chloro-4-fluorophenyl)glycinate **22l** (0.135 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **13a** (0.223 g, 182 µL, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 99/01) of the crude reaction mixture using silica gel afforded ethyl (*R*)-2-((3-chloro-4-fluorophenyl)(phenyl)amino)pent-4-enoate **23l** as yellow oil (0.133 g, 77% yield).

***R*$_f$** (Pet. ether /EtOAc = 95/05): 0.46.

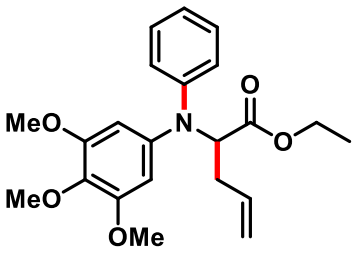
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (t, *J* = 7.7 Hz, 2H), 7.11 - 6.88 (m, 6H), 5.84 - 5.77 (m, 1H), 5.12 - 5.04 (m, 2H), 4.60 (t, *J* = 7.5 Hz, 1H), 4.27 - 4.16 (m, 2H), 2.69-2.56 (m, 2H), 1.30 - 1.25 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.43, 154.157 (d, J = 248.1 Hz), 146.27, 143.41, 143.38, 134.14, 129.54, 129.43, 125.21, 122.93 (d, *J* = 6.6 Hz), 122.74, 122.26, 121.25, 121.07, 120.77, 118.07, 116.86, 116.64, 114.57, 62.77, 61.35, 34.46, 14.30.

HRMS (ESI) calculated $[M+H]^+$ for $C_{19}H_{20}O_2NClF$: 348.1161, found: 348.1159.

FTIR (cm^{-1}) 3018, 2929, 2401, 1733, 1641, 1596, 1498, 1371, 1217, 1129, 993, 824, 772.

Ethyl 2-(phenyl(3,4,5-trimethoxyphenyl)amino)pent-4-enoate (23m)



Following the general procedure, treatment of ethyl *N*-allyl-*N*-(3,4,5-trimethoxyphenyl)glycinate **22m** (0.154 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **13a** (0.223 g, 182 µL, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0

mL) at 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 99/01) of the crude reaction mixture using silica gel afforded Ethyl 2-(phenyl(3,4,5-trimethoxyphenyl)amino)pent-4-enoate **23m** as yellow oil (0.125 g, 65% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.41.

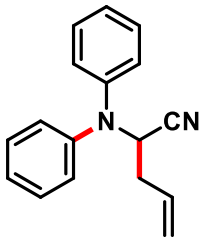
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (t, *J* = 7.8 Hz, 2H), 6.94 - 6.86 (m, 3H), 6.45 (s, 2H), 5.90 - 5.80 (m, 1H), 5.12 - 5.08 (m, 2H), 4.64 (t, *J* = 7.5 Hz, 1H), 4.29 - 4.17 (m, 2H), 3.89 (s, 3H), 3.80 (s, 6H), 2.67 - 2.64 (m, 2H), 1.29 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.82, 153.50, 147.14, 141.43, 134.89, 134.57, 129.00, 120.51, 119.10, 117.61, 103.30, 62.47, 61.04, 60.94, 55.96, 34.59, 14.26.

HRMS (ESI) calculated $[M+Na]^+$ for $C_{21}H_{27}O_5NNa$: 408.1781, found: 408.1777.

FTIR (cm^{-1}) 3014, 2938, 2836, 2250, 1640, 1590, 1495, 1462, 1369, 1229, 1007, 856, 747.

2-(Diphenylamino)pent-4-enenitrile (23n)



Following the general procedure, treatment of 2-(allyl(phenyl)amino) acetonitrile **22n** (0.086 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **13a** (0.223 g, 182 μL, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 99/01) of the crude reaction mixture using silica gel afforded 2-(diphenylamino)pent-4-enenitrile **23n** as yellow oil (0.099 g, 80% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.52.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (t, *J* = 7.8 Hz, 4H), 7.18 (t, *J* = 7.3 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 4H), 5.94 - 5.84 (m, 1H), 5.27 (dd, *J* = 13.5, 7.5 Hz, 2H), 4.86 (t, *J* = 5.4 Hz, 1H), 2.72 - 2.49 (m, 2H).

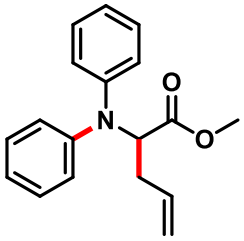
^{13}C NMR (100 MHz, $CDCl_3$) δ 145.73, 131.73, 129.67, 124.07, 123.20, 120.02, 118.60, 51.28, 36.59.

HRMS (ESI) calculated $[M+H]^+$ for $C_{17}H_{17}N_2$: 249.1386, found: 249.1382 .

FTIR (cm^{-1}) 3019, 2948, 1719, 11604, 1446, 1342, 1291, 1086, 963, 760.

Methyl-2-(diphenylamino)pent-4-enoate (23o)

Following the general procedure, treatment of methyl *N*-allyl-*N*-phenylglycinate **22o** (0.103 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **13a** (0.223 g, 182 μL,



0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 99/01) of the crude reaction mixture using silica gel afforded methyl-2-(diphenylamino)pent-4-enoate **23o** as yellow oil (0.111 g, 79% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.56.

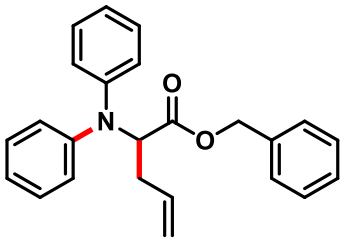
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (t, *J* = 7.8 Hz, 4H), 7.08-7.04 (m, *J* = 9.4 Hz, 6H), 5.92-5.82 (m, 1H), 5.22 – 5.00 (m, 2H), 4.73 (t, *J* = 7.5 Hz, 1H), 3.77 (s, 3H), 2.71 (t, *J* = 7.1 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 173.28, 146.54, 134.44, 129.24, 122.58, 122.36, 117.77, 62.51, 52.06, 34.39.

HRMS (ESI) calculated $[M+H]^+$ for $C_{18}H_{20}O_2N$: 282.1489, found: 282.1487.

FTIR (cm^{-1}) 3019, 2951, 1722, 1598, 1577, 1499, 1409, 1344, 1297, 1249, 1216, 1099, 995, 759.

Benzyl 2-(diphenylamino)pent-4-enoate (23p)



Following the general procedure, treatment of ethyl benzyl *N*-allyl-*N*-phenylglycinate **22p** (0.141 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **13a** (0.223 g, 182 µL, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 99/01) of the crude reaction mixture using silica gel afforded benzyl 2-(diphenylamino)pent-4-enoate **23p** as yellow oil (0.124 g, 84% yield).

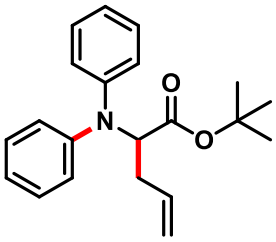
***R*f** (Pet. ether /EtOAc = 95/05): 0.55.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 - 7.24 (m, 9H), 7.12 - 6.95 (m, 6H), 5.98 - 5.76 (m, 1H), 5.24 (q, *J* = 12.3 Hz, 2H), 5.17 - 5.05 (m, 2H), 4.80 (t, *J* = 7.5 Hz, 1H), 2.73 (d, *J* = 2.9 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$** δ 172.66, 146.56, 135.60, 134.41, 129.23, 128.56, 128.37, 128.31, 122.72, 122.38, 117.85, 66.90, 62.65, 34.48.

HRMS (ESI) calculated $[M+H]^+$ for $C_{24}H_{24}O_2N$: 358.1802, found: 358.1800.

FTIR (cm^{-1}) 3018, 2982, 1732, 1641, 1565, 1440, 1371, 1216, 1028, 989, 854, 772.

***Tert*-butyl 2-(diphenylamino)pent-4-enoate (23q)**



Following the general procedure, treatment of *tert*-butyl *N*-allyl-*N*-phenylglycinate **22q** (0.124 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **13a** (0.223 g, 182 µL, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 99/01) of the crude reaction mixture using silica gel afforded *tert*-butyl 2-(diphenylamino)pent-4-enoate **23q** as yellow oil (0.133 g, 82% yield).

***R*$_f$** (Pet. ether /EtOAc = 95/05): 0.53.

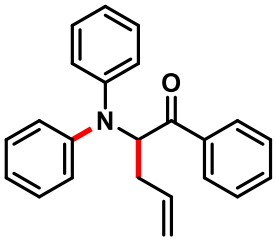
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.29 (t, *J* = 7.7 Hz, 4H), 7.04 - 7.01 (m, 6H), 5.90 - 5.80 (m, 1H), 5.10 - 5.05 (m, 2H), 4.56 (t, *J* = 7.5 Hz, 1H), 2.65 (t, *J* = 7.1 Hz, 2H), 1.45 (s, 9H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 172.00, 146.92, 134.90, 129.13, 122.73, 122.15, 117.53, 81.78, 63.63, 34.65, 28.11.

HRMS (ESI) calculated $[M+H]^+$ for $C_{21}H_{26}O_2N$: 324.1958, found: 324.1953.

FTIR (cm^{-1}) 3014, 2981, 1598, 1734, 1640, 1590, 1495, 1462, 1431, 1415, 1369, 1291, 921.

2-(Diphenylamino)-1-phenylpent-4-en-1-one (23r)



Following the general procedure, treatment of 2-(allyl(phenyl)amino)-1-phenylethan-1-one **22r** (0.126 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **13a** (0.223 g, 182 µL, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 99/01) of the crude reaction mixture using silica gel afforded 2-(diphenylamino)-1-phenylpent-4-en-1-one **23r** as yellow solid (0.149 g, 91% yield).

***R*$_f$** (Pet. ether /EtOAc = 95/05): 0.50.

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.00 (d, *J* = 7.7 Hz, 2H), 7.63 (t, *J* = 7.3 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.33 (t, *J* = 7.7 Hz, 4H), 7.10 (t, *J* = 7.3 Hz, 2H), 6.96 (d, *J* = 8.0 Hz, 4H),

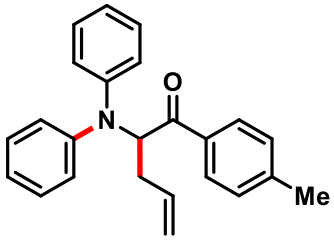
6.04 - 5.94 (m, 1H), 5.61 (t, *J* = 6.2 Hz, 1H), 5.28 (d, *J* = 17.1 Hz, 1H), 5.19 (d, *J* = 10.1 Hz, 1H), 3.06 - 2.99 (m, 1H), 2.75 - 2.69 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 197.76, 146.12, 136.59, 135.20, 133.27, 129.46, 128.77, 128.60, 122.68, 117.68, 63.29, 32.71.

HRMS (ESI) calculated $[M+H]^+$ for $C_{23}H_{22}ON$: 328.1696, found: 328.1694.

FTIR (cm^{-1}) 3019, 2947, 1721, 1593, 1495, 1449, 1356, 1274, 1132, 1036, 909, 760.

2-(Diphenylamino)-1-(*p*-tolyl)pent-4-en-1-one (23s)



Following the general procedure, treatment of 2-(allyl(phenyl)amino)-1-(p-tolyl)ethan-1-one **22s** (0.132 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **13a** (0.223 g, 182 μL, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 99/01) of the crude reaction mixture using silica gel afforded 2-(diphenylamino)-1-(*p*-tolyl)pent-4-en-1-one **23s** as yellow oil (0.145 g, 85% yield).

***R*$_f$** (Pet. ether /EtOAc = 95/05): 0.35.

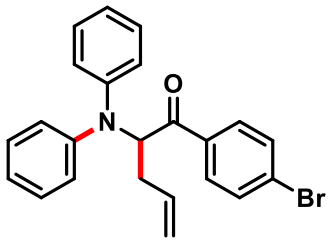
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.1 Hz, 2H), 7.32 – 7.25 (m, 6H), 7.06 (t, *J* = 7.3 Hz, 2H), 6.95 (d, *J* = 7.9 Hz, 4H), 6.02 - 5.92 (m, 1H), 5.58 (t, *J* = 7.1 Hz, 1H), 5.23 (dd, *J* = 37.7, 13.7 Hz, 2H), 3.03 - 2.95 (m, 1H), 2.72 - 2.65 (m, 1H), 2.44 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 197.23, 146.13, 144.05, 135.26, 134.01, 129.43, 129.41, 128.70, 122.66, 122.59, 117.53, 63.06, 32.74, 21.75.

HRMS (ESI) calculated $[M+H]^+$ for $C_{24}H_{24}ON$: 342.1852, found: 342.1851.

FTIR (cm^{-1}) 3024, 2921, 2348, 1716, 1578, 1513, 1451, 1356, 1313, 1278, 1108, 995.

***N*-(1-(4-bromophenyl)but-3-en-1-yl)-*N*-phenylaniline (23t)**



Following the general procedure, treatment of 2-(allyl(phenyl)amino)-1-(4-bromophenyl)ethan-1-one **22t** (0.165 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **13a** (0.223 g, 182 μL, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether

/EtOAc = 99/01) of the crude reaction mixture using silica gel afforded *N*-(1-(4-bromophenyl)but-3-en-1-yl)-*N*-phenylaniline **23t** as yellow solid (0.166 g, 88% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.51.

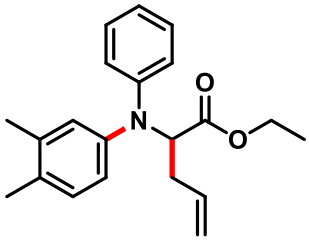
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.5 Hz, 2H), 7.57 (d, *J* = 8.4 Hz, 2H), 7.29 (t, *J* =7.3 Hz, 4H), 7.07 (t, *J* = 7.4 Hz, 2H), 6.91 (d, *J* = 7.9 Hz, 4H), 6.00 - 5.90 (m, 1H), 5.50 (dd, *J* = 7.8, 5.8 Hz, 1H), 5.25 (d, *J* = 17.1 Hz, 1H), 5.16 (d, *J* = 10.2 Hz, 1H), 3.02 – 2.95 (m, 1H), 2.79 – 2.57 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 196.71, 145.96, 135.24, 134.96, 132.02, 130.11, 129.80, 129.52, 128.37, 122.83, 122.58, 117.85, 63.35, 32.60.

HRMS (ESI) calculated $[M+H]^+$ for $C_{23}H_{21}ONBr$: 406.0801, found: 406.0803.

FTIR (cm^{-1}) 3020, 2902, 1712, 1604, 1492, 1421, 1278, 1100, 1035, 1009, 931, 865, 759.

Ethyl 2-((3,4-dimethylphenyl)(phenyl)amino)pent-4-enoate (23u)



Following the general procedure, treatment of ethyl *N*-allyl-*N*-phenylglycinate **22a** (0.110 g, 0.5 mmol) and 4,5-dimethyl-2-(trimethylsilyl)phenyl trifluoromethanesulfonate **13b** (0.245 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 99/01) of the crude reaction mixture using silica gel afforded ethyl 2-((3,4-dimethylphenyl)(phenyl)amino)pent-4-enoate **23u** as yellow oil (0.128 g, 79% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.56.

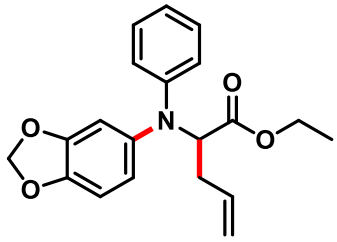
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (t, *J* = 7.8 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 1H), 6.98 (s, 1H), 6.95 – 6.83 (m, 4H), 6.05 – 5.68 (m, 1H), 5.12 (d, *J* = 12.4 Hz, 2H), 4.66 (t, *J* = 7.5 Hz, 1H), 4.32 – 4.16 (m, 2H), 2.67 (t, *J* = 7.1 Hz, 2H), 2.30 (s, 3H), 2.27 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.92, 147.76, 143.44, 137.53, 134.74, 132.44, 130.43, 129.01, 127.22, 123.37, 120.22, 119.24, 117.61, 62.62, 61.06, 34.63, 20.08, 19.26, 14.32.

HRMS (ESI) calculated $[M+H]^+$ for $C_{21}H_{26}O_2N$: 324.1958, found: 324.1953.

FTIR (cm^{-1}) 3020, 2404, 1795, 1726, 1596, 1495, 1444, 1334, 1282, 1216, 1036, 930, 760.

Ethyl-2-(benzo[*d*][1,3]dioxol-5-yl(phenyl)amino)pent-4-enoate (23v)



Following the general procedure, treatment of ethyl *N*-allyl-*N*-phenylglycinate **22a** (0.110 g, 0.5 mmol) and 6-(trimethylsilyl)benzo[*d*][1,3]dioxol-5-yl trifluoromethanesulfonate **13c** (0.257 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 99/01) of the crude reaction mixture using silica gel afforded ethyl-2-(benzo[d][1,3]dioxol-5-yl(phenyl)amino)pent-4-enoate **23v** as pale yellow oil (0.124 g, 73% yield).

***R*f** (Pet. ether/EtOAc = 95/05): 0.45.

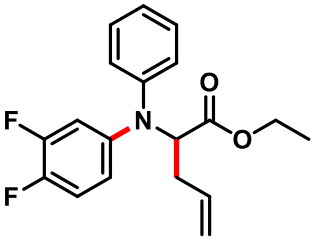
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (t, *J* = 7.9 Hz, 2H), 6.82 – 6.78 (m, 3H), 6.74 – 6.69 (m, 3H), 5.98 (s, 2H), 5.88 - 5.62 (m, 1H), 5.08 (s, 1H), 5.05 (d, *J* = 5.8 Hz, 1H), 4.57 (t, *J* = 7.5 Hz, 1H), 4.21 - 4.17 (m, 2H), 2.60 (t, *J* = 7.1 Hz, 2H), 1.25 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.85, 148.36, 145.46, 138.94, 134.57, 129.03, 121.88, 119.17, 117.76, 116.63, 109.99, 108.47, 101.46, 62.54, 61.17, 34.73, 14.35.

HRMS (ESI) calculated $[M+H]^+$ for $C_{20}H_{22}O_4N$: 340.1543, found: 340.1530.

FTIR (cm^{-1}) 3018, 2983, 2776, 2402, 1733, 1597, 1459, 1217, 1040, 994, 926, 668.

Ethyl 2-((3,4-difluorophenyl)(phenyl)amino)pent-4-enoate (23w)



Following the general procedure, treatment of ethyl *N*-allyl-*N*-phenylglycinate **22a** (0.110 g, 0.5 mmol) and 4,5-difluoro-2-(trimethylsilyl)phenyl trifluoromethanesulfonate **13d** (0.251 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 99/01) of the crude reaction mixture using silica gel afforded ethyl 2-((3,4-difluorophenyl)(phenyl)amino)pent-4-enoate **23w** as yellow oil (0.116 g, 70% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.46.

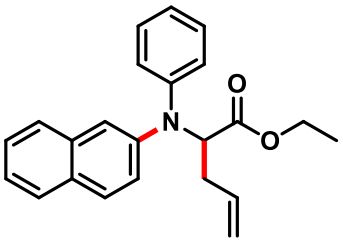
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 - 7.22 (m, 2H), 7.- 6.94 (m, 4H), 6.83-6.77 m 1H), 6.72 – 6.63 (m, 1H), 5.83-5.73 (m, 1H), 5.05 (dd, *J* = 23.3, 5.8 Hz, 2H), 4.59 - 4.55 (m, 1H), 4.27 - 4.13 (m, 2H), 2.68 - 2.50 (m, 2H), 1.25 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.49, 150.57 (dd, *J* = 144.5, 13.8 Hz), 146.14 (dd, *J* = 245.6, 12.7 Hz), 146.00, 143.63 (dd, *J* = 7.8, 2.5 Hz), 134.18, 129.48, 123.29, 118.07, 117.83 (dd, *J* = 5.2, 2.8 Hz), 117.27 (d, *J* = 17.4 Hz), 111.44 (d, 19.4 Hz), 62.82, 61.38, 34.47, 14.31.

HRMS (ESI) calculated $[M+H]^+$ for $C_{19}H_{20}O_2NF_2$: 332.1457, found: 332.1448.

FTIR (cm^{-1}) 3018, 2898, 1718, 1604, 1490, 1440, 1382, 1328, 1251, 1129, 1083, 940, 872.

Ethyl 2-(naphthalen-2-yl(phenyl)amino)pent-4-enoate (23x)



Following the general procedure, treatment of ethyl *N*-allyl-*N*-phenylglycinate **22a** (0.110 g, 0.5 mmol) and 3-(trimethylsilyl)naphthalen-2-yl trifluoromethanesulfonate **13e** (0.261 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 99/01) of the crude reaction mixture using silica gel afforded ethyl 2-(naphthalen-2-yl(phenyl)amino)pent-4-enoate **23x** as yellow oil (0.124 g, 72% yield). When 1-(trimethylsilyl)naphthalen-2-yl trifluoromethanesulfonate aryne precursor was used **23x** was isolated in 69 % yield.

***R*$_f$** (Pet. ether /EtOAc = 95/05): 0.57.

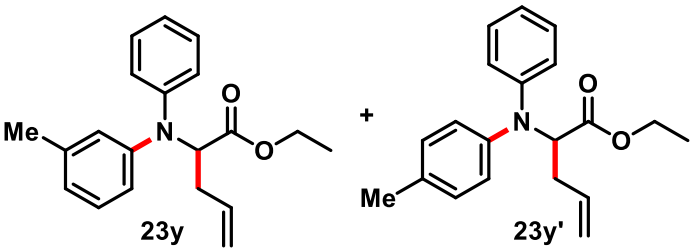
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.0 Hz, 1H), 7.71 (d, *J* = 8.6 Hz, 2H), 7.56 – 7.21 (m, 5H), 7.15 (dd, *J* = 8.8, 1.5 Hz, 1H), 7.07 (t, *J* = 7.4 Hz, 3H), 5.91-5.82 (m, 1H), 5.11-5.06 (m, 2H), 4.77 (t, *J* = 7.5 Hz, 1H), 4.38 – 4.08 (m, 2H), 2.74 (t, *J* = 7.1 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.85, 146.75, 144.39, 134.59, 134.48, 129.74, 129.30, 128.83, 127.61, 127.18, 126.31, 124.32, 123.65, 123.32, 122.78, 117.88, 117.85, 63.23, 61.26, 34.39, 14.33.

HRMS (ESI) calculated $[M+H]^+$ for $C_{23}H_{24}O_2N$: 346.1802, found: 346.1795.

FTIR (cm^{-1}) 3020, 2948, 2814, 1724, 1594, 1506, 1447, 1357, 1282, 1222, 1128, 1038, 956.

Ethyl-2-(phenyl(m-tolyl)amino)pent-4-enoate (23y) and Ethyl-2-(phenyl(p-tolyl)amino)pent-4-enoate (23y')



Following the general procedure, treatment of ethyl *N*-allyl-*N*-phenylglycinate **22a** (0.110 g, 0.5 mmol) and 4-methyl-2-(trimethylsilyl) phenyl trifluoromethanesulfonate **13g** (0.234 g, 182 µL, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 99/01) of the crude reaction mixture using silica gel afforded inseparable regioisomeric mixture of ethyl-2-(phenyl(m-tolyl)amino)pent-4-enoate **23y** and ethyl-2-(phenyl(p-tolyl)amino)pent-4-enoate **23y'** in 1:1 as yellow oil (0.124 g, 80% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.57.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.17 (m, 4H), 7.09 - 7.07 (m, 1H), 7.03-7.01 (d, *J* = 8.2 Hz, 1H), 6.93-6.85 (m, 3H), 5.90-5.83 (m, 1H), 5.13-5.09 (m, 2H), 4.70-4.66 (m, 1H), 4.25-4.22 (m, 2H), 2.69-2.67 (m, 2H), 2.39 (s, 3H), 1.31 (t, *J* = 6.7 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.83, 147.68, 146.51, 138.94, 133.53, 129.10, 125.68, 123.39. 121.94, 120.15, 117.63, 62.66, 61.05, 20.88

Representative peak for other isomer:

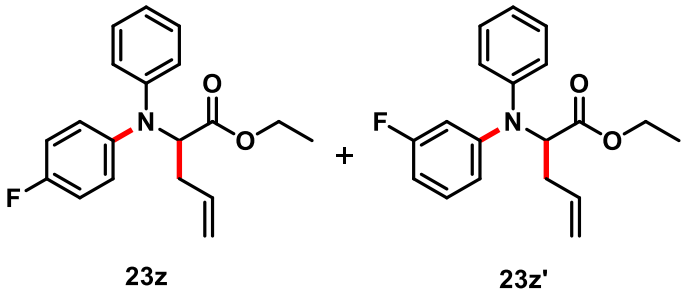
^{1}H NMR (400 MHz, $CDCl_3$) 2.34 (s).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.80, 146.75, 143.16, 134.61, 129.92, 129.0, 123.73, 122.23, 120.40, 119.42, 62.58, 21.62, 14.25.

HRMS (ESI) calculated $[M+H]^+$ for $C_{20}H_{24}O_2N$: 310.1802, found: 310.1797.

FTIR (cm^{-1}) 2982, 2929, 1733, 1641, 1498, 1217, 1129, 1030, 993, 772, 703.

Ethyl-2-((4-fluorophenyl)(phenyl)amino)pent-4-enoate (3z) and Ethyl-2-((23 fluorophenyl) (phenyl)amino)pent-4-enoate (23z′)



Following the general procedure, treatment of ethyl *N*-allyl-*N*-phenylglycinate **22a** (0.110 g, 0.5 mmol) and 4-fluoro-2-(trimethylsilyl)phenyl

trifluoromethane sulfonate **13h** (0.237 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 99/01) of the crude reaction mixture using silica gel afforded inseparable 2:1 regioisomeric mixture of ethyl-2-((4-fluorophenyl)(phenyl)amino)pent-4-enoate **23z** and ethyl-2-((3 fluorophenyl)(phenyl)amino)pent-4-enoate **23z′** as yellow oil (0.123 g, 78% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.52.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 – 7.08 (m, 4H), 7.02 (t, *J* = 8.0, 2H), 6.88 (t, *J* = 7.3 Hz, 1H), 6.77 (d, *J* = 8.1 Hz, 2H), 5.95 – 5.62 (m, 1H), 5.08-5.05 (m, 2H), 4.60 (t, *J* = 7.5 Hz, 1H), 4.29 – 4.06 (m, 2H), 2.79 – 2.39 (m, 2H), 1.24 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.81, 159.92 (d, *J* = 242.7 Hz), 147.78, 134.41, 129.19, 128.28 (d, *J* = 242.7 Hz), 127.06, 118.74, 117.90, 116.20, 62.61, 61.24, 34.64, 14.34.

Representative peak for other isomer:

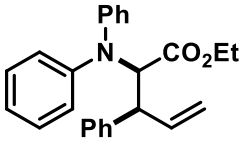
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 – 7.08 (m, 4H), 7.02 (t, *J* = 8.0, 2H), 6.88 (t, *J* = 7.3 Hz, 1H), 6.77 (d, *J* = 8.1 Hz, 2H), 5.95 – 5.62 (m, 1H), 5.08-5.05 (m, 2H), 4.60 (t, *J* = 7.5 Hz, 1H), 4.29 – 4.06 (m, 2H), 2.79 – 2.39 (m, 2H), 1.24 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.81, 159.92 (d, *J* = 242.7 Hz), 141.56, 129.58, 125.21, 120.46, 118.00, 116.20, 115.98, 62.77, 61.35, 34.51, 14.34.

HRMS (ESI) calculated $[M+H]^+$ for $C_{19}H_{21}O_2NF$: 314.1551, found: 314.1549.

FTIR (cm^{-1}) 3019, 2983, 2402, 1733, 1594, 1504, 1370, 1217, 1030, 923, 771, 669.

Ethyl 2-(diphenylamino)-3-phenylpent-4-enoate (24)



Following the general procedure, treatment of ethyl *N*-cinnamyl-*N*-phenylglycinate **22u** (0.198 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **13a** (0.223 g, 182 μL, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 99/01) of the crude reaction mixture using silica gel afforded ethyl 2-(diphenylamino)-3-phenylpent-4-enoate **24** as yellow oil (0.137 g, 74% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.51.

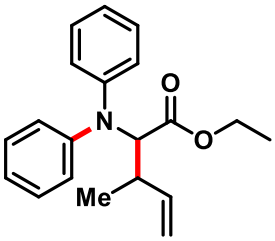
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 - 7.27 (m, 9H), 7.21 (d, *J* = 7.6 Hz, 4H), 7.10 (t, *J* = 7.2 Hz, 2H), 6.21 - 6.12 (m, 1H), 5.14 (t, *J* = 11.9 Hz, 2H), 5.01 (d, *J* = 17.3 Hz, 1H), 4.14 (dd, J_1 = 7.2 Hz, J_2 = 10.7 Hz, 1H), 4.00 - 3.72 (m, 2H), 0.95 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.97, 147.12, 140.60, 138.57, 129.18, 128.93, 128.53, 127.04, 123.19, 122.57, 116.96, 66.81, 60.67, 50.09, 13.82.

HRMS (ESI) calculated $[M+H]^+$ for $C_{25}H_{26}O_2N$: 372.1958, found: 372.1959.

FTIR (cm^{-1}) 3020, 2953, 1722, 1590, 1485, 1443, 1348, 1292, 1253, 1216, 1080, 893, 760.

Ethyl-2-(diphenylamino)-3-methylpent-4-enoate (25)



Following the general procedure, treatment of ethyl (E)-*N*-(but-2-en-1-yl)-*N*-phenylglycinate **22v** (0.117 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **13a** (0.223 g, 182 μL, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at 30 °C for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 99/01) of the crude reaction mixture using silica gel afforded Ethyl-2-(diphenylamino)-3-methylpent-4-enoate **25** as yellow oil (0.125 g, 81% yield).

***R*$_f$** (Pet. ether /EtOAc = 95/05): 0.60.

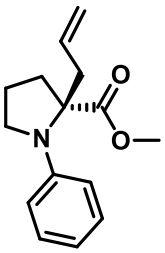
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31-7.26 (m, 4H), 7.12-7.07 (m, 3H), 7.02 (t, *J* = 7.4 Hz, 2H), 5.90 – 5.84 (m, 1H), 5.03-4.95 (m, 2H), 4.46 (d, *J* = 10.2 Hz, 1H), 4.23-4.15 (m, 2H), 3.05-3.00 (m, 1H), 1.21(t, *J* = 7.1 Hz, 3H), 1.12 (d, *J* = 6.7 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.96, 147.41, 140.76, 129.23, 129.09, 123.04, 122.32, 115.13, 68.13, 60.92, 37.80, 18.30, 14.29.

HRMS (ESI) calculated $[M+H]^+$ for $C_{20}H_{24}O_2N$: 310.1802, found: 310.1797.

FTIR (cm^{-1}) 3064, 3018, 2981, 2876, 1732, 1590, 1419, 1352, 1098, 993, 701, 668.

Methyl (*S*)-2-allyl-1-phenylpyrrolidine-2-carboxylate (27a)



Following the general procedure, treatment of methyl allyl-*L*-prolinate **26a** (0.085g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **13a** (0.223 g, 182 μL, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 2 h followed by flash column chromatography (Pet. ether /EtOAc = 99/01) of

the crude reaction mixture using silica gel afforded methyl (*S*)-2-allyl-1-phenylpyrrolidine-2-carboxylate **27a** as yellow oil (0.077 g, 63% yield).

***R*f** (Pet. ether /EtOAc = 95/05): 0.52.

HPLC (Chiralcel OD-H, 98 : 2 (hexane:IPA), 0.8 mL/min) Major: 6.9 min, Minor: 6.1 min. 96% ee. $[\alpha]_D^{25}$ = +41.22 (c 0.1, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (t, *J* = 7.8 Hz, 2H), 6.70 (t, *J* = 7.2 Hz, 1H), 6.55 (d, *J* = 8.2 Hz, 2H), 5.63 - 5.52 (m 1H), 5.06 (d, *J* = 4.8 Hz, 1H), 5.03 (s, 1H), 3.69 (s, 3H), 3.51 (dd, *J* = 9.5, 4.1 Hz, 2H), 3.11 (dd, *J* = 14.5, 5.6 Hz, 1H), 2.71 (dd, *J* = 14.5, 8.7 Hz, 1H), 2.35 - 1.88 (m, 4H).

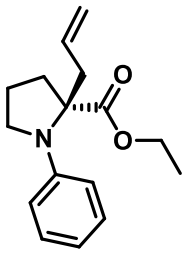
^{13}C NMR (100 MHz, $CDCl_3$) δ 177.13, 145.72, 133.49, 129.11, 118.91, 116.64, 113.22, 67.83, 52.44, 50.95, 37.87, 37.71, 23.00.

HRMS (ESI) calculated $[M+H]^+$ for $C_{15}H_{20}O_2N$: 246.1489, found: 246.1485.

FTIR (cm^{-1}) 3016, 2925, 1691, 1640, 1587, 1494, 1396, 1217, 1179, 1032, 918, 771.

Ethyl (*S*)-2-allyl-1-phenylpyrrolidine-2-carboxylate (27b)

Following the general procedure, treatment of ethyl allyl-*L*-prolinate **26b** (0.92 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **13a** (0.223 g, 182 μL, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 2 h followed by flash column chromatography (Pet. ether /EtOAc = 99/01) of the crude reaction mixture using silica gel afforded ethyl (*S*)-2-allyl-1-phenylpyrrolidine-2-carboxylate **27a** as yellow oil (0.079 g, 61% yield).



***R*f** (Pet. ether /EtOAc = 95/05): 0.50,

HPLC (Chiralpak IB, 99 : 1 (hexane:IPA), 0.7 mL/min) Major: 6.5min, Minor: 5.9 min. 98% ee; $[\alpha]_D^{25}$ = +57.16 (c 0.1, $CHCl_3$).

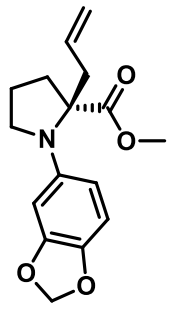
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (t, *J* = 7.8 Hz, 2H), 6.70 (t, *J* = 7.2 Hz, 1H), 6.58 (d, *J* = 8.2 Hz, 2H), 5.66 - 5.56 (m 1H), 5.07 (d, *J* = 4.8 Hz, 1H), 5.04 (s, 1H), 4.24 - 4.10 (m, 2H), 3.55 – 3.47 (m, 2H), 3.13 (dd, *J* = 9.5, 4.1 Hz, 1H), 2.72 (dd, *J* = 14.5, 5.6 Hz, 1H), 2.32 – 1.94 (m, 4H), 1.17 (t, *J* = 8.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 176.44, 145.85, 133.64, 128.98, 118.74, 116.57, 113.29, 67.93, 61.13, 51.00, 37.91, 37.83, 23.01, 14.19.

HRMS (ESI) calculated $[M+H]^+$ for $C_{16}H_{22}O_2N$: 260.1645, found: 260.1643.

FTIR (cm^{-1}) 3017, 2982, 1731, 1589, 1445, 1417, 1374, 1352, 1292, 1120, 1029, 922, 773.

Methyl (*S*)-2-allyl-1-(benzo[*d*][1,3]dioxol-5-yl)pyrrolidine-2-carboxylate (27c)



Following the general procedure, treatment of ethyl allyl-*L*-prolinate **26a** (0.085g, 0.5 mmol) and 6-(trimethylsilyl)benzo[*d*][1,3]dioxol-5-yl trifluoromethanesulfonate **13c** (0.257 g, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 2 h followed by flash column chromatography (Pet. ether /EtOAc = 99/01) of the crude reaction mixture using silica gel afforded methyl (*S*)-2-allyl-1-(benzo[*d*][1,3]dioxol-4-yl)pyrrolidine-2-carboxylate **27c** as yellow oil (0.088 g, 61% yield).

***R*$_f$** (Pet. ether /EtOAc = 95/05): 0.44.

HPLC (Chiralcel OD-H, 98 : 2 (HEXANE:IPA), 0.8 mL/min) Major: 18.1 min, Minor: 10.8 min. 88% ee; $[\alpha]_D^{25}$ = +51.74 (c 0.1, $CHCl_3$).

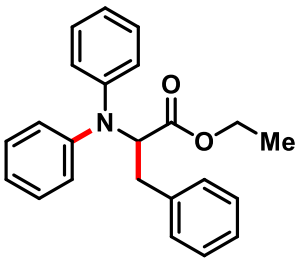
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.66 (d, *J* = 8.5 Hz, 1H), 6.20 (d, *J* = 2.0 Hz, 1H), 5.95 (dd, *J* = 8.5, 2.1 Hz, 1H), 5.84 (d, *J* = 5.6 Hz, 2H), 5.60 – 5.50 (m, 1H), 5.03 (d, *J* = 12.8 Hz, 2H), 3.69 (s, 3H), 3.43 (dd, *J* = 9.4, 4.6 Hz, 2H), 3.03 (dd, *J* = 14.6, 5.6 Hz, 1H), 2.65 (dd, *J* = 14.6, 8.7 Hz, 1H), 2.29 - 1.93 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 177.00, 148.28, 141.61, 139.02, 133.43, 118.93, 108.56, 105.30, 100.60, 96.33, 68.08, 52.42, 51.66, 37.80, 37.76, 22.98.

HRMS (ESI) calculated $[M+H]^+$ for $C_{16}H_{20}O_4N$: 290.1387, found: 290.1385.

FTIR (cm^{-1}) 3018, 2930, 2400, 1731, 1629, 1594, 1496, 1442, 1290, 1120, 994, 767.

Ethyl diphenyl-phenylalaninate (29)



Following the general procedure, treatment of ethyl *N*-benzyl-*N*-phenylglycinate **28** (0.135 g, 0.5 mmol) and 2-(trimethylsilyl)phenyl trifluoromethane sulfonate **13a** (0.223 g, 182 μL, 0.75 mmol) in the presence of KF (0.087 g, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) in THF (2.0 mL) at rt for 12 h followed by flash column chromatography (Pet. ether /EtOAc = 99/01) of the crude reaction mixture using silica gel afforded ethyl diphenyl-phenylalaninate **29** as yellow oil (0.070 g, 41% yield).

***R*$_f$** (Pet. ether /EtOAc = 95/05): 0.60.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 - 7.36 (m, 7H), 7.27 (d, *J* = 6.8 Hz, 2H), 7.15 (t, *J* = 7.3 Hz, 2H), 6.99 (d, *J* = 8.0 Hz, 4H), 4.93 (d, *J* = 8.2 Hz , 1H), 4.48 - 4.16 (m, 2H), 3.46 - 3.44 (m, 2H), 1.35 (t, *J* = 7.1 Hz, 3H).

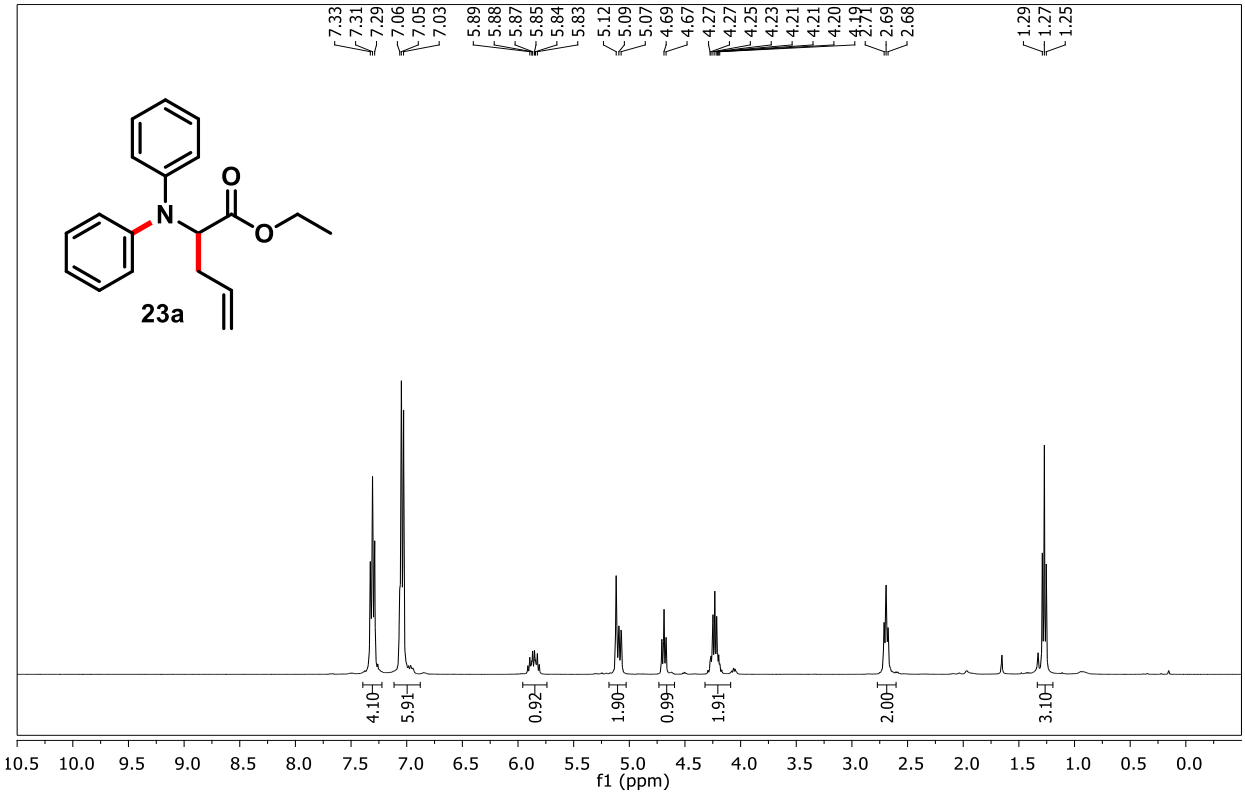
^{13}C NMR (100 MHz, $CDCl_3$) δ 172.89, 146.96, 138.40, 129.36, 129.17, 128.66, 128.49, 128.36, 126.67, 122.56, 122.18, 65.52, 61.25, 35.59, 14.18.

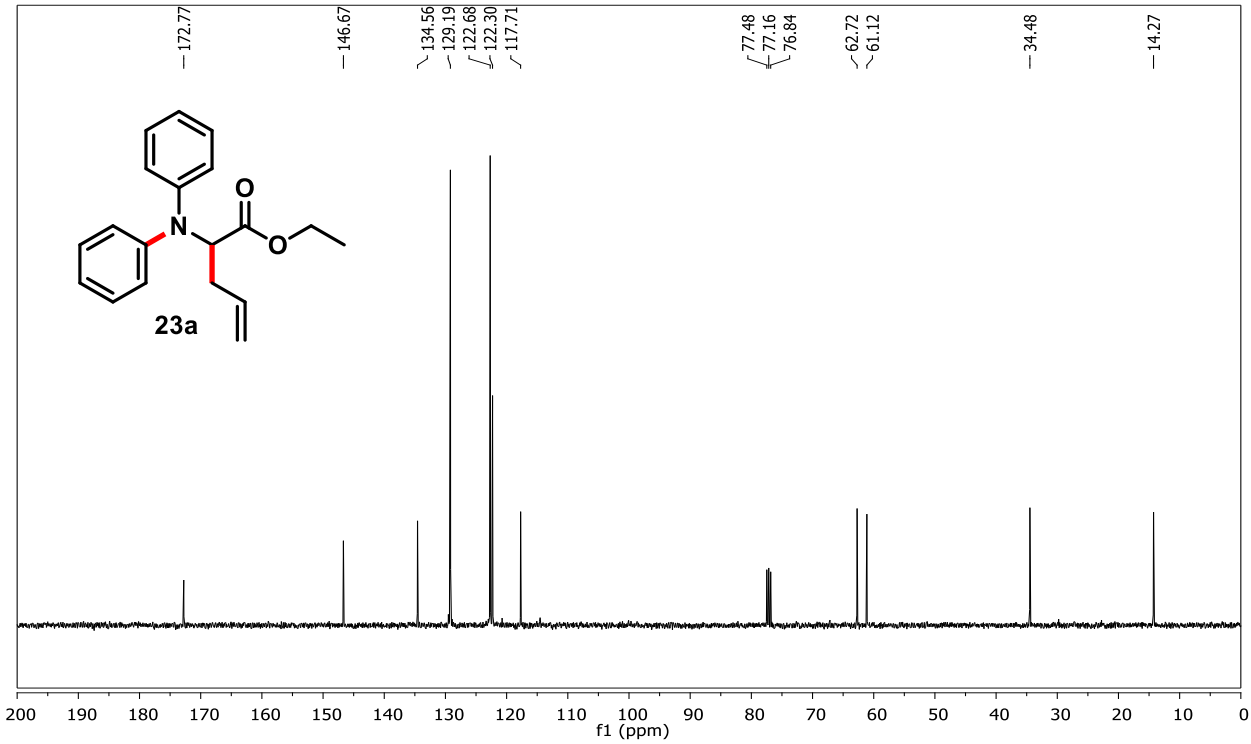
HRMS (ESI) calculated $[M+H]^+$ for $C_{23}H_{24}O_2N$: 346.1802, found: 346.1797.

FTIR (cm^{-1}) 3022, 2951, 2256, 1722, 1598, 1517, 1445, 1362, 1288, 1082, 952, 909, 760.

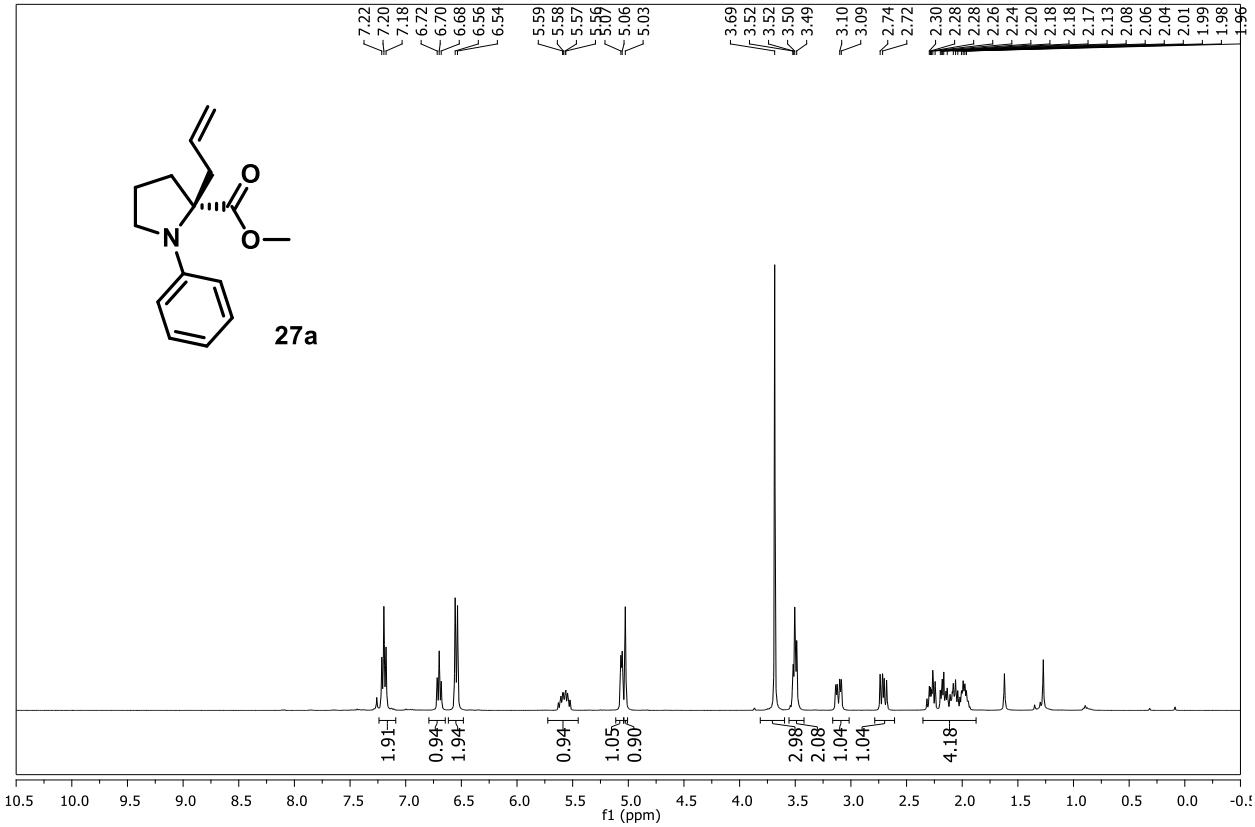
5.8.7. ^{1}H and ^{13}C NMR Spectra of Selected Compounds

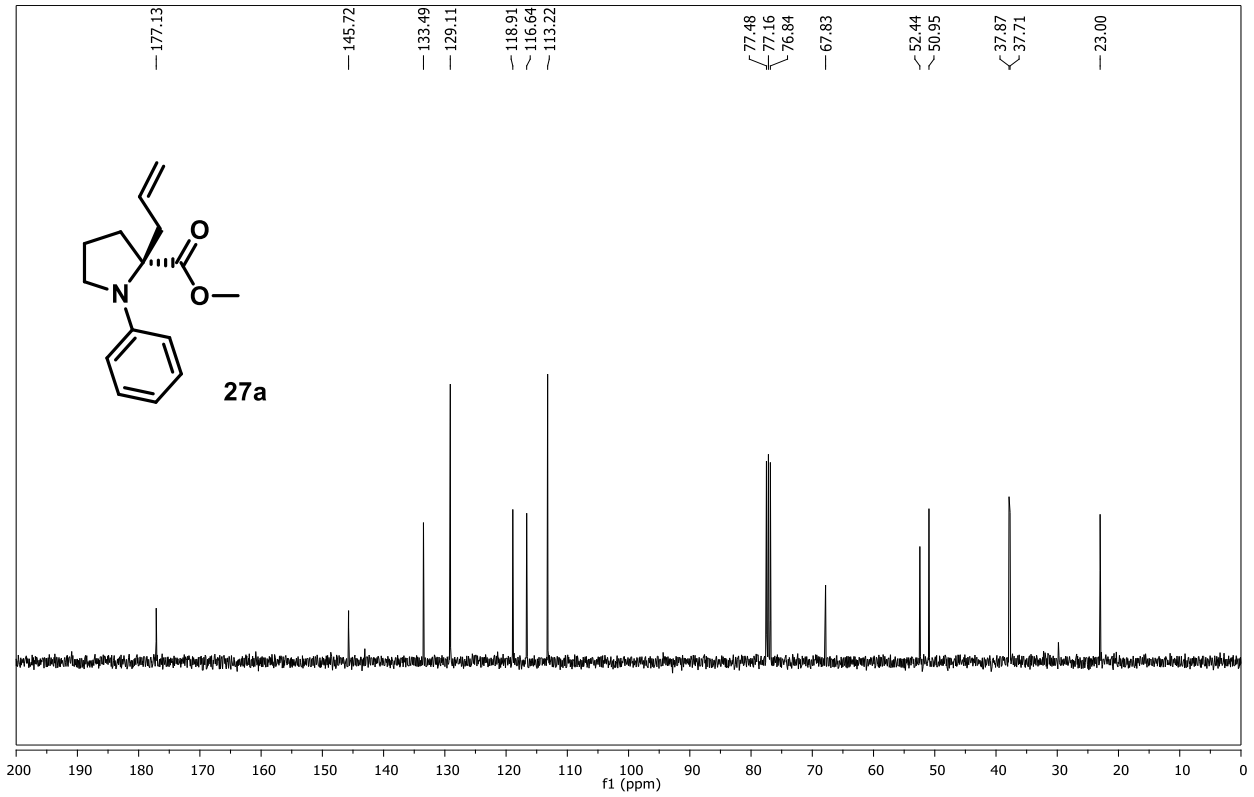
Ethyl-2-(diphenylamino)pent-4-enoate (23a)



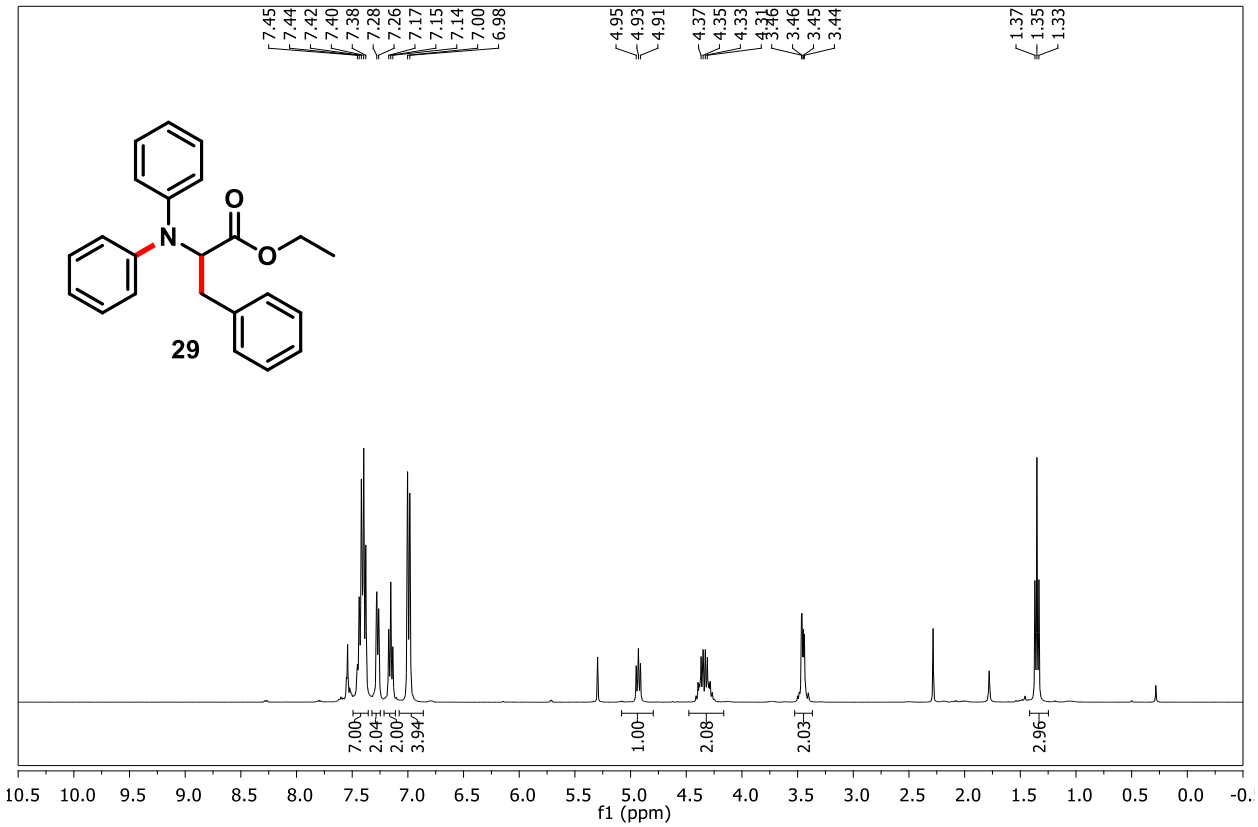


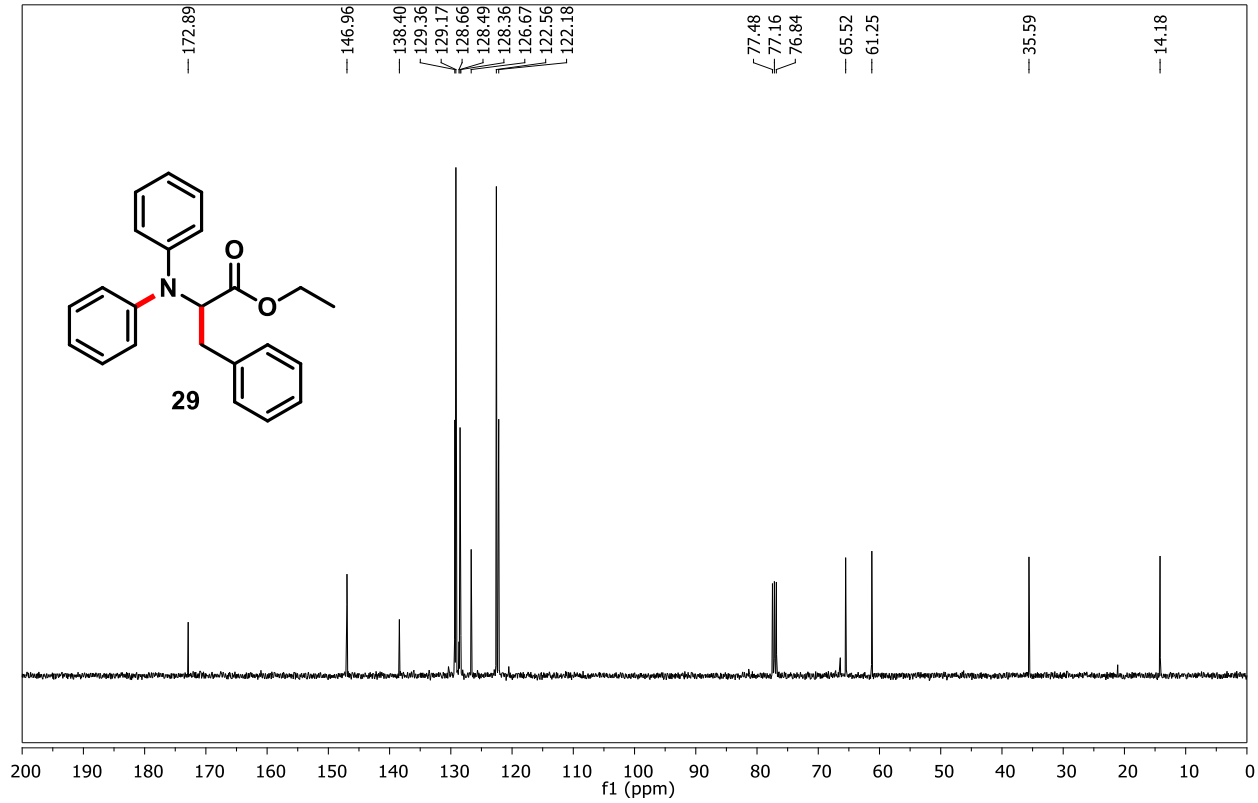
Methyl (*S*)-2-allyl-1-phenylpyrrolidine-2-carboxylate (27a)





Ethyl diphenyl-phenylalaninate (29)





5.9. References

1. Stevens, T. S.; Creighton, E. M.; Gordon, A. B.; MacNicol, M. *J. Chem. Soc.* **1928**, 3193.
2. For reviews, see: (a) West, T. H.; Spoehrle, S. S. M.; Kasten, K.; Taylor, J. E.; Smith, A. D. *ACS Catal*. **2015**, *5*, 7446. (b) Bach, R.; Harthong, S.; Lacour, J. In *Comprehensive Organic Synthesis II (Second Edition)*; Knochel, P., Ed.; Elsevier, Amsterdam, 2014; Vol. 3, pp 992-1037. (c) Lahm, G.; Pacheco, J. C. O. Opatz, T. *Synthesis* **2014**, *46*, 2413. (d) Sweeney, J. B. *Chem. Soc. Rev.* **2009**, *38*, 1027. (e) Somfai, P.; Panknin, O. *Synlett* **2007**, 1190. (f) Vanecko, J. A.; Wan, H.; West, F. G. *Tetrahedron* **2006**, *62*, 1043. (g) Li, A.-H.; Dai, L.-X.; Aggarwal, V. K. *Chem. Rev*. **1997,** *97*, 2341.
3. (a) Xu, B.; Tambar, U. K. *J. Am. Chem. Soc.* **2016**, *138*, 12073**.** (b) Biswas, B.; Collins, S. C.; Singleton, D. A. *J. Am. Chem. Soc.* **2014**, *136*, 3740.
4. Coldham, I.; Middleton, M. L.; Taylor, P. L. *J. Chem. Soc. Perkin Trans.* 1 **1997**, 2951.
5. (a) Clark, J. S.; Hodgson, P. B. *J. Chem. Soc. Chem. Commun*. **1994**, 2701. (b) Clark, J. S.; Hodgson, P. B.; Goldsmith, M. D.; Street, L. J. *J. Chem. Soc. Perkin Trans.* 1 **2001**, 3312.
6. Honda, K.; Shibuya, H.; Yasui, H.; Hoshino, Y.; Inoue, S. *Bull. Chem. Soc. Jpn*. **2008**, *81*, 142.
7. (a) Soheili, A.; Tambar, U. K. *J. Am. Chem. Soc.* **2011**, *133*, 12956. See also: (b) Nash, A.; Soheili, A.; Tambar, U. K. *Org. Lett*. **2013**, *15*, 4770. (c) Soheili, A.; Tambar, U. K. *Org. Lett*. **2013**, *15*, 5138.
8. Cant, A. A.; Bertrand, G. H. V.; Henderson, J. L.; Roberts, L.; Greaney, M. F. *Angew. Chem., Int. Ed*. **2009**, *48*, 5199.
9. Chen, Z.; Wang, Q. *Org. Lett.*, **2015**, *17*, 6130.
10. Li, Y.; Qiu, D.; Gu, R.; Wang, J.; Shi J.; Li Y., *J. Am. Chem. Soc*. **2016**, *138*, 10814.
11. For recent reviews on arynes, see(a) Shi, J.; Li, Y.; Li, Y. *Chem. Soc. Rev.* **2017**, *46*, 1707. (b) Idiris, F. I. M.; Jones, C. R. *Org. Biomol. Chem*. **2017**, *15*, 9044. (c)

García-López, J.-A.; Greaney, M. F. *Chem. Soc. Rev.***2016**, *45*, 6766. (d) Bhojgude, S. S.; Bhunia, A.; Biju, A. T. *Acc. Chem. Res*. **2016**, *49*, 1658. (r) Goetz, A. E.; Shah, T. K.; Garg, N. K. *Chem. Commun*. **2015**, *51*, 34. (f) Dubrovskiy, A. V.; Markina, N. A.; Larock, R. C. *Org. Biomol. Chem.* **2013**, *11*, 191. (g) Wu, C.; Shi, F. *Asian J. Org. Chem.* **2013**, *2*, 116. (h) Pérez, D.; Peña, D.; Guitián, E. *Eur. J. Org. Chem.* **2013**, 5981. (i) Tadross, P. M.; Stoltz, B. M. *Chem. Rev.* **2012**, *112*, 3550. (j) Gampe, C. M.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2012**, *51*, 3766. (k) Bhunia, A.; Yetra, S. R.; Biju, A. T. *Chem. Soc. Rev.* **2012**, *41*, 3140. (l) Okuma, K. *Heterocycles* **2012**, *85*, 515. (m) Yoshida, H.; Ohshita, J.; Kunai, A. *Bull. Chem. Soc. Jpn.* **2010**, *83*, 199

12. (a) Roy, T.; Thangaraj, M.; Gonnade, R. G.; Biju, A. T. *Chem. Commun.* **2016**, *52*, 9044.
13. (a) Himeshima, Y.; Sonoda, T.; Kobayashi, H. *Chem. Lett.* **1983**, 1211.See also: (b) Peña, D.; Cobas, A.; Pérez, D.; Guitián, E. *Synthesis* **2002**, 1454.
14. For reports on generation on nitrogen ylides using arynes, see: (a) Roy, T.; Thangaraj, M.; Gonnade, R. G.; Biju, A. T. *Chem. Commun.* **2016**, *52*, 9044. (b) Swain, S. P.; Shih, Y.-C.; Tsay, S.-C.; Jacob, J.; Lin, C.-C.; Hwang, K. C.; Horng, J.-C.; Hwu, J. R. *Angew. Chem., Int. Ed.*, **2015**, *54*, 9926.
15. For related aryne reactions triggered by tertiary amines proceeding *via* Smiles rearrangement, see: (a) Holden, C. M.; Sohel, S. M. A.; Greaney, M. F. *Angew. Chem., Int. Ed.* **2016**, *55*, 2450. (b) Bhojgude, S. S.; Baviskar, D. R.; Gonnade, R. G.; Biju, A. T. *Org. Lett.* **2015**, *17*, 6270. For related reports from our group, see: (c) Roy, T.; Bhojgude, S. S.; Kaicharla, T.; Thangaraj, M.; Garai, B.; Biju, A. T. *Org. Chem. Front.* **2016**, *3*, 71. (c) Roy, T.; Baviskar, D. R.; Biju, A. T. *J. Org. Chem*. **2015**, *80*, 11131. (d) Bhojgude, S. S.; Kaicharla, T.; Biju, A. T. *Org. Lett.* **2013**, *15*, 5452.
16. For reports on retention of enantiopurity and inversion of configuration in related [2,3] rearrangement involving proline derivatives, see: (a) Arboré, A. P. A.; Cane-Honeysett, D. J.; Coldham, I.; Middleton, M. L. *Synlett* **2000**, 236. (b) Glaeske, K.W.; West, F.G. *Org. Lett.* **1999**, *1*, 31. (c) Gawley, R.E.; Zhang, Q.; Campagna, S. *J. Am. Chem. Soc.* **1995**, *117*, 11817.

17. Seebach, D.; Boes, M.; Naef, R.; Schweizer, W. B. *J. Am. Chem. Soc.* **1983**, *105*, 5390.
18. Zhang, J.; Chen, Z.-X.; Du, T.; Li, B.; Gu, Y.; Tian, S.-K. *Org. Lett.* **2016**, *18*, 4872.
19. Moss, S. G.; Pocock, I. A.; Sweeney, J. B. *Chem. - Eur. J.* **2017**, *23*, 101.
20. Roy, T.; Thangaraj, M.; Kaicharla, T.; Kamath, R. V.; Gonnade, R. G.; Biju, A. T. *Org. Lett.* **2016**,*18*, 5428.
21. (a) Sato, Y.; Tamura, T.; Kinbara, A.; Morib, M. *Adv. Synth. Catal.* **2007**, *349*, 647. (b) Peña, D.; Cobas, A.; Pérez, D.; Guitián, E. *Synthesis* **2002**, 1454.
22. Everett, R. K.; John P. Wolfe, J, P. *J. Org. Chem.*, **2015**, *80*, 9041.
23. (a) Bruker (2016). *APEX3*, *SAINT* and *SADABS*. Bruker AXS Inc., Madison, Wisconsin, USA. (b) Sheldrick, G. M. *Acta Crystallogr*. **2008**, *A64*, 112. (c) Farrugia, L. J. *J. Appl. Cryst.* **1997**, *30*, 565.

List of Publications

1. **Roy, T.**; Biju, A. T., Recent Advances in Molecular Rearrangements Involving Aryne Intermediates. *Chem. Commun***. 2018,** *54***,** 2580.
2. Jacob, A.; **Roy, T.**; Kaicharla, T.; Biju, A. T., Metal-Free, Brønsted Acid-Catalyzed Formal [3+2] Annulation of Quinone Monoacetals with 2-Naphthols, *J. Org. Chem.* **2017**, *82*, 11269
3. Thangaraj, M.; Gaykar, R.N.; **Roy, T**; Biju, A.T., Synthesis of Functionalized *β*-Keto Arylthioethers by the Aryne Induced [2,3] Stevens Rearrangement of Allylthioethers. *J. Org. Chem.*, **2017**, *82*, 4470.
4. **Roy T**.; Thangaraj M.; Kaicharla T.; Kamath R. V.; Gonnade R. G.; Biju A. T., The Aryne [2,3] Stevens Rearrangement, *Org. Lett*., **2016**, *18*, 5428.
5. Bhojgude S. S.; **Roy T**.; Gonnade R. G.; Biju A. T., Substrate-Controlled Selectivity Switch in the Three-Component Coupling Involving Arynes, Aromatic Tertiary Amines, and CO_2, *Org. Lett.*, **2016**, *18*, 5424 .
6. Kaicharla, T.; **Roy T.**; Thangaraj, M.; Gonnade R. G.; Biju, A. T., Lewis Acid-Catalyzed Selective Reactions of Donor-Acceptor Cyclopropanes with 2-Naphthols. *Angew. Chem. Int. Ed.*, **2016**, *55*, 10061.
7. **Roy T.**; Thangaraj M.; Gonnade R. G.; Biju A. T., Synthesis of functionalized amino epoxides by a three-component coupling involving aziridines, arynes and aldehydes, *Chem. Commun*., **2016**, *2*, 9044.
8. **Roy T.**; Bhojgude S. S.; Kaicharla T.; Thangaraj M.; Garai B.; Biju A. T., Employing carboxylic acids in aryne multicomponent coupling triggered by aziridines/azetidines, *Org. Chem. Front.*, **2016**, *3*, 71.
9. **Roy T.**; Baviskar D. R.; Biju A. T., Synthesis of *N*-Aryl beta-Amino Alcohols by Trifluoroacetic Acid-Promoted Multicomponent Coupling of Aziridines, Arynes and Water, *J. Org. Chem.*, **2015,** *80*, 11131.
10. Bhunia A.; **Roy T.**; Gonnade R. G.; Biju A. T., Rapid Access to Benzoxaphospholes and Their Spiro Analogues by a Three-Component Coupling Involving Arynes, Phosphines, and Activated Ketones, *Org. Lett.*, **2014**, *16*, 5132.
11. Yetra S. R.; **Roy T.**; Bhunia A.; Porwal D.; Biju A. T., Synthesis of Functionalized Coumarins and Quinolinones by NHC-Catalyzed Annulation of Modified Enals with Heterocyclic C-H Acids, *J. Org. Chem.*, **2014**, *79*, 4245.
12. Bhunia A.; **Roy T.**; Pachfule P.; Rajamohanan P. R.; Biju A. T., Transition-Metal-Free Multicomponent Reactions Involving Arynes, N-Heterocycles and Isatins, *Angew. Chem., Int. Ed*., **2013**, *52*, 10040.
13. Kaicharla T.; Yetra S. R.; **Roy T.**; Biju A. T., Engaging isatins in solvent-free, sterically congested Passerini reaction, *Green Chem*., **2013**, *15*, 1608.