APPLICATION OF ZEOLITE CATALYSTS IN ESTERIFICATION, RITTER REACTION AND ALKYLATION OF AROMATIC SUBSTRATES

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PUNE - 411 008

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TO MY PARENTS

CERTIFICATE

This is to certify that the work incorporated in the thesis entitled *"Application Of Zeolite Catalysts In Esterification, Ritter Reaction And Alkylation Of Aromatic Substrates"* submitted by *Mr. V.K.GUMASTE* was carried out by him under my supervision at National Chemical Laboratory. Such material as has been obtained from other sources has been duly acknowledged in the thesis.

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(V. K. Gumaste).

one can certainly plan research,

but not the results !

Dieter Seebach

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Abbreviations

Et	:	Ethyl
Me	:	Methyl
Ph		Phenyl
i-Propyl	:	*iso*-Propyl
t-Butyl	:	Tertiary Butyl
o	:	ortho
m	:	meta
p	:	para
EDC	:	Ethylene dichloride
PTSA	:	*p*-Toluenesulfonic acid
g	:	Gram/s
h	:	Hour/s
min.		Minutes
IR	:	Infrared
NMR	:	Nuclear Magnetic Resonance
MS	:	Mass spectrum
M^+	:	Molecular ion
i.d.	:	Internal diameter
WHSV		Weight Hour Space Velocity

Synopsis of the Thesis

CHAPTER-1

Importance of zeolite in synthetic organic chemistry : A Review

Zeolite catalyzed reactions in organic chemistry have been attracted considerable attention in recent years. Zeolites are aluminosilicates with highly ordered crystalline structure. The use of zeolite as a catalyst for industrial purpose began in 1960s and slowly gained importance in synthetic organic chemistry. The combination of acidity and shape selectivity is an important property of zeolite catalysts. In recent years the utilization of this potential catalysts in the field of intermediates and fine chemicals has increased enormously. The application of zeolite catalysts for substitution reaction of aromatic as well as aliphatic moieties, addition and elimination reaction, oxidation, reduction, isomerization etc. have been reported.

In this chapter a brief discussion of some these important reactions, catalyzed by zeolite is reviewed.

CHAPTER-2

Esterification of carboxylic acids

This chapter deals with synthesis of a wide variety of esters of carboxylic acid using zeolite catalyst in a batch process or using continuous fixed bed reactor.

A mixture of acid and excess of alcohol was heated in the presence of zeolite catalyst in a Parr reactor to give esters in 37-95 % yield. To optimize the conversion and reaction efficiency, various parameters in this reaction have been systematically studied. These includes variation in reaction temperature, duration of the reaction, molar ratios of the reactants and use of various zeolite catalysts. This reaction has also been studied using a fixed bed reactor so as to make it more efficient and industrially adaptable method. The estrification of phenylacetic acid with ethanol was chosen as a model reaction. Various parameters such as temperature, WHSV (weight hour space velocity), life of the catalyst were systematically studied with this reaction.

R^1COOH + R^2OH --------> R^1COOR^2

1 2 3a-v

Ester	R^1	R^2	Ester	R^1	R^2
3a	Ph	Et	**3l**	MeCH=CH	Et
3b	$PhCH_2$	Et	**3m**	Me_2C=CH	Et
3c	$PhCH_2$	Me	**3n**	$Me(CH_2)5CH_2$	Et
3d	$PhCH_2$	n-Pr	**3o**	*o*-Tolyl	Et
3e	$PhCH_2$	*i*-Pr	**3p**	*m*-Tolyl	Et
3f	$PhCH_2$	n-Bu	**3q**	*p*-Tolyl	Et
3g	$PhCH_2$	*t*-Bu	**3r**	$PhCH_2$	*o*-Cresyl
3h	$PHCH_2$	n-Amyl	**3s**	$PhCH_2$	*m*-Cresyl
3i	$PhCH_2$	*i*-Amyl	**3t**	$PhCH_2$	*p*-Cresyl
3j	$PhCH_2$	n-Octyl	**3u**	$PhCH_2$	Phenyl
3k	PhCH=CH	Et	**3v**	$PhCH_2$	2-MeoPh

CHAPTER-3

Synthesis of N-monosubstituted amides by the reaction of olefins and alcohols with nitriles

Amides are usually prepared by the reaction of amines with carboxylic acids, esters or acid chlorides. The addition of alcohols to nitriles in the presence of strong acid is known to give amides in good yields. This reaction is known as Ritter reaction. Our aim was to replace conventional acids with zeolite for the synthesis of N-monosubstituted amides. Thus, a wide variety of amides are prepared by reacting olefins or alcohols with nitriles in the presence of zeolite catalyst. This method involves heating a mixture of alcohol/olefin and excess of nitrile in a Parr reactor at 100°C under autogenous pressure in the presence of zeolite catalyst. In this reaction good yields of amides were obtained with tertiary alcohol (**6c,h**) and poor yields with secondary alcohols (**6g**). The primary alcohols, such as methanol, ethanol failed to react with nitrile to give corresponding amides (**6a, b**). However, benzyl alcohol gave good yield of N-benzylacetamide (**6d**), as the formation of more stable benzyl carbocation is possible in this case which undergoes nucleophillic attack of acetonitrile.

R^1OH + R^2CN --------> R^1NHCOR^2

4 5 6a-k

Amide	R^1	R^2
6a	Me	Me
6b	Et	Me
6c	*t*-Bu	Me
6d	Benzyl	Me
6e	Me	$CH=CH_2$
6f	Et	$CH=CH_2$
6g	*i*-Pr	$CH=CH_2$
6h	*t*-Bu	$CH=CH_2$
6i	Benzyl	$CH=CH_2$
6j	*t*-Bu	CH_2Cl
6k	*t*-Bu	CH_2CH_2Cl
6l	*t*-Bu	Ph

The reaction of cyclohexene with various nitriles under similar condition offered amides 9a-e.

CYCLOHEXENE + RCN --------> N-Cyclohexyl-NHCOR

7 8 9a-e

Amide	R
9a	Me
9b	CH_2Cl
9c	CH_2CH_2Cl
9d	$CH=CH_2$
9e	CH=CHCl

CHAPTER-4

Section-A

An improved process for the preparation of linear alkylbenzene

Linear alkylbenzenes (LAB) are the precursor for surfactants, linear alkylbenzene sulfonates. Linear alkylbenzenes are usually prepared by alkylation of benzene with long chain olefins having 10-13 carbon atoms in the presence of hydrofluoric acid. Since HF is highly corrosive, it is difficult to handle. Moreover, disposal of fluorinated hydrocarbon by-products creates environmental problems. Our aim was to replace HF catalyst by solid acid such as zeolites. In this method a mixture of alcohol/olefin and benzene when heated at 140°C in a Parr reactor under autogenous pressure in the presence of zeolite catalyst to give alkylbenzene in very high conversion.

The alkylation of benzene has also been studied by using 1-decanol in the presence of zeolite catalyst. In this case there is possibility of formation of carbocation at five different places on a long alkyl chain to which benzene ring can be attached. All these five positional isomers were independently synthesized by earlier known method. The presence of these positional isomers in the alkylated product was determined by comparing GC-MS data with the individual isomers. Other long chain olefins on alkylation of benzene under similar condition offered corresponding alkylbenzenes with very high conversion (> 90%). A comparative study of alkylation of benzene with alcohol and olefin has been also carried out. An industrially feasible method was developed for the alkylation of benzene using readily available mixture of olefin (C_{10}-C_{13} carbon chain) and paraffin(8:92) on a fixed bed reactor. Various parameters like temperature, WHSV molar ratios of the reactants were studied to achieve maximum conversion of olefin to linear alkylbenzene.

Section-B

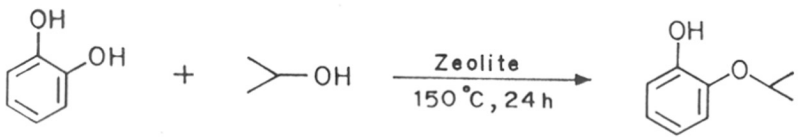
Synthesis of 2-*iso*-propoxyphenol by mono O-alkylation of catechol with *iso*-propanol

Propoxur, an important carbamate insecticide is effective against ants, bugs and cockroaches. 2-*iso*-Propoxyphenol (**11**) is a key intermediate for the synthesis of propoxur. It has been prepared by reacting catechol with alkyl halide in the presence of bases like sodium hydroxide, sodium carbonate in an autoclave at 120-160°C using phase transfer catalyst.

The above process involves the use of highly expensive and corrosive alkyl halide as starting material with strong alkali. Moreover, this method gives substantial amount of 1,2 diisopropoxybenzene as a by-product. To overcome these problems, we have carried out above transformation in the presence of zeolite catalyst using iso-propanol instead of alkyl halide. Thus, a

mixture of catechol and iso-propanol when heated in a Parr reactor at 150°C, a 20 % conversion of catechol to 2-*iso*-propoxyphenol in 100% selectivity for mono O-alkylated product was observed **(Scheme-1).**

Scheme 1



10 11

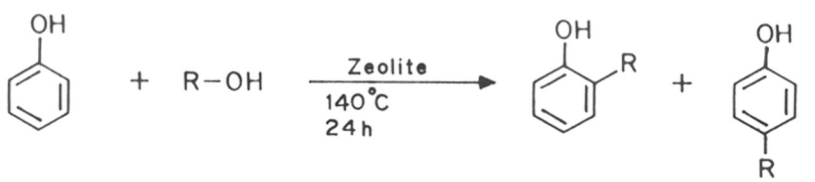
C-Alkylated and bis O-alkylated product did not formed in detectable (GC) amount at this temperature. In the presence of excess of alcohol O-alkylation is preferred over C-alkylation. The reaction was also carried on a fixed bed reactor by passing a mixture of catechol and *iso*-propanol over a catalyst bed at various temperature, molar ratios of the reactants and WHSV. It was observed that when the temperature was increased above 160°C the selectivity for mono O-alkylated product dropped gradually with increasing formation of mixture a of C-alkylated by-products.

Section-C

C-Alkylation of phenol with alcohols

Alkylation of phenol with alcohols, such as prenyl, crotyl, cinnamyl and benzyl alcohol was carried out in the presence of zeolite catalyst. The C-alkylated ortho and para product formed on alkylation of phenol with alcohol, were isolated and characterized by IR, NMR, Mass spectral analysis. It was observed that when stoechiometric ratios of reactants were used C-alkylated product **(13, 14)** is preferred over O-alkylated product**(Scheme-2).**

Scheme 2



12 13 14

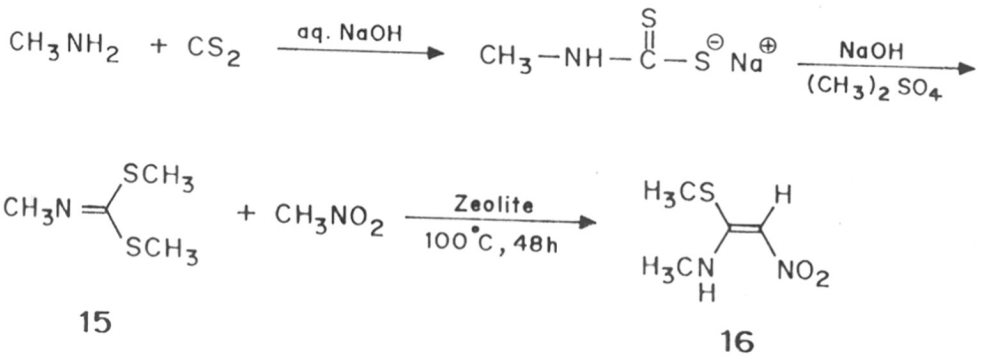
R = a) Prenyl b) Crotyl c) Cinnamyl d) Benzyl

Appendix

Synthesis of 1-methylamino-1-methylthio-2-nitroethene and hazard analysis of the reaction

1-Methylamino-1-methylthio-2-nitroethene (**16**) is a crucial intermediate for the anti-Ulcer drug Ranitidine. A novel method has been developed in our group for the synthesis of this nitroethene(**16**), which involves condensation of dimethylN-methylcarbonimidodithioate (**15**) with nitromethane in the presence of zeolite catalyst(**Scheme-3**)

Scheme 3



15 16

Although this reaction was systematically studied, there were many questions relating to the safety of the reaction: a) wether nitromethane is safe in the presence of the zeolite. b) wether the product is safe under the reaction condition. To get information on above points, this reaction has been studied using reaction calorimetry/ accelerated reaction calorimetry. Based on the above findings the process was modified for commercial operation.

Note: The compound numbers incorporated in the synopsis are different from those in the thesis.

CHAPTER 1

Importance of zeolite in synthetic organic chemistry : A Review

SUMMARY

Zeolite catalyzed reactions in organic chemistry have been attracted considerable attention in recent years. Major application of zeolite are in the reactions catalyzed by proton acids and Lewis acids, where the change from homogeneous to heterogeneous procedure brings advantage in respect of easy separation, regeneration and reuse. The use of zeolite as a catalyst for industrial purpose began in 1960s and slowly gained importance in synthetic organic chemistry. In recent years the utilization of this potential catalysts in the field of intermediates and fine chemicals has increased enormously. Since zeolites are thermally stable they can be used at higher temperatures. The application of zeolite catalyst for substitution reaction of aromatic as well as aliphatic moieties, addition and elimination reaction, reduction, isomerization etc. have been reported.

In this chapter a brief discussion of some of these important reactions, catalyzed by zeolite is reviewed.

INTRODUCTION

Zeolite catalyzed reactions in organic chemistry have been attracting considerable attention in recent years[1]. The unique features of zeolite catalysts are acidity, shape-selectivity and thermal stability. Zeolites are crystalline, hydrated, aluminosilicates having highly ordered rigid three dimensional infinite frame work; built up by the sharing of SiO_4 and AlO_4^- tetrahedra, linked through oxygen bridges. They are represented by the general empirical unit cell formulae[1,2]

$$Mx/n[(AlO_2)x(SiO_2)y].zH_2O$$

Where M is a cation with valency n. The net negative charge of the frame work generated by the presence of aluminium is compensated by cation M, which is often selected from group I, II or rare-earth metals or organic species. These cations are mobile and can be exchanged with other metal ions.

Nomenclature

The International Zeolite Association Structure Commission (IZASC) and **IUPAC** have assigned structural codes for natural and synthetic zeolites[3]. The names consisting of three capital letters have been used to identify the structures, which are generally derived from the names of the zeolite. These codes do not depend on composition as well as on distribution of various possible atoms such as Si, Al, P, Ga, Ti, etc. Some examples are given in Table 1.1.

Table 1.1. IUPAC Nomenclature of zeolites.

Name	Code
Mordenite	MOR
Faujasite	FAU
Sodalite	SOD
Laumontite	LAU
Heulandite	HEW
Erionite	ERI

Some of the synthetic zeolites are named after their inventors or institutions where they were originally synthesized.

ZSM for Zeolite Socony Mobile.

VPI for Virginia Polytechnic Institute.

Classification of zeolites

Zeolites have been classified on the basis of their morphological characteristic, crystal structure, chemical composition, effective pore diameter and natural occurrence. They have also been classified on the basis of silica/alumina ratio[4] into three types, *viz.*, low, intermediate and high silica/alumina zeolites. Typical examples of the low silica/alumina ratio are zeolite A and X types, which possess Si/Al ratio between 1 - 1.5. The intermediate (Si/Al = 2 - 5) are of Y and L type zeolites, while high (Si/Al = 10 to several thousand) are belong to ZSM-5, ZSM-11.

Barrer[4] and Sand[5] have classified zeolites into three groups, as small, intermediate, and large pore zeolites based on the effective diameter of pores. In the case of small-pore zeolites, the diameter of the cavity is 4.1 Å, formed by eight SiO_4 tetrahedra. All medium pore zeolites, are called pentasil zeolites, having ten atom ring system with tubular diameter of 5.5 Å. The third category is, the large pore zeolite having cavities of 12 atom rings with a diameter of 7.4 Å (Table 1.2). These are constructed by network of SiO_4 and AlO_4^- tetrahedra with a oxygen bridges separating the two metal atoms.

Table 1.2. Classification of zeolite based on pore diameter.

Small pore	Medium pore	Large pore
Erionite	ZSM-5	Faujasite
Carbazite	ZSM-12	X-/Y-zeolite
	TS-1	Mordenite
	Silicalite	

Structure and properties

Zeolites are microporous crystalline solids. Most of them are aluminosilicates, possessing characteristic pore and cage structures. Each Si or Al atom is surrounded by oxygen in the crystal lattice. The central atoms of the zeolite lattice can be replaced in an isomorphous manner by a large number of other tri and tetravalent atoms. For instance B, Cr, Sb, As, Ge, Ti, and Zr can be incorporated inplace of Al and Si. The isomorphous substitution results in altered lattice constants, which changes catalytic properties (acidity and activity) of the zeolite. The extent of incorporation of isomorphous replacement can be determined by MAS-NMR[6,7] spectroscopy and by appropriate test reactions[8].

In general, the neutral sodium form is obtained during the synthesis of zeolites. However, by means of ion exchange with ammonium salts and subsequent calcination of ammonium form one can obtain the proton form *i.e.,* acidic form of zeolite. The ion exchange of sodium form also allows the introduction of many other types of cations, *eg.,* alkali metal ions, transition metal ions. The Lewis acidic sites can also be introduced into zeolites by ion exchange with rare-earth metal ions.

Acidity

The acid strength and number of acidic sites can be adjusted in a controlled manner during synthesis and/or by subsequent ion exchange.

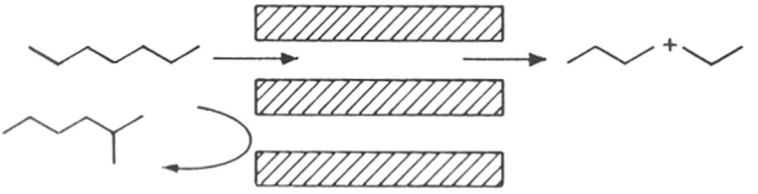
Shape-selectvity

This implies that only certain reactant molecules whose dimensions fall within specific limits of zeolite cavities can pass through the pores and reach at the site of the reaction, is termed as reactant selectivity. In the hydrocarbon cracking of n-heptane, which is linear and can easily enter into the cavities to give n-butane and n-propane whereas, in the case of *iso*-heptane the entry is restricted due to reactant selectivity. Conversely, in product selectivity only those products are obtained in the reaction, whose dimensions let them diffuse out of the pores of zeolite, the rest are trapped inside. An example of product selectivity can be illustrated by alkylation of toluene with methanol in which an equilibrium is reached between *o, m* and *p*-xylene and *p*-xylene being linear easily diffuse out of the pores. Finally, restrictions imposed by the cavity dimensions on the size of the transition state of the reaction lead to transition state selectivity[9] *m*-xylene, when reacted over mordenite, can form 1,2,4-isomer, but not 1,3,5-iosomer, since the transition state for later, with its alkyl group protruding downward, is too wide to be accommodated inside the pores (Scheme 1.1). Obviously, shape-selectivity can operate only if the reaction occur within the zeolite pores. There are some reactions which may take place on the outer surface of the zeolites without any selectivity. Shape-selectivity in zeolite catalyzed reaction has been discussed extensively[10,11] in literature.

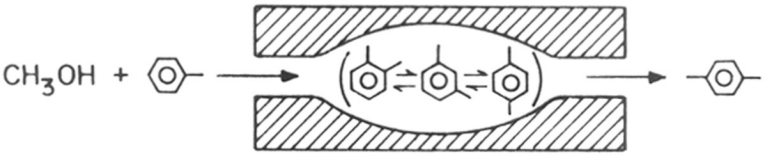
Apart from the zeolites composed of aluminosilicate, there are other families of microporous materials. One such consists of aluminium phosphates which are known as $AlPO_4$ polymorphs (ALPO). These materials also exists in a wide range of open tetrahedral network. Structural modifications have also been carried out on these materials. One such modification is referred to as SAPO in which some

Scheme - 1·1

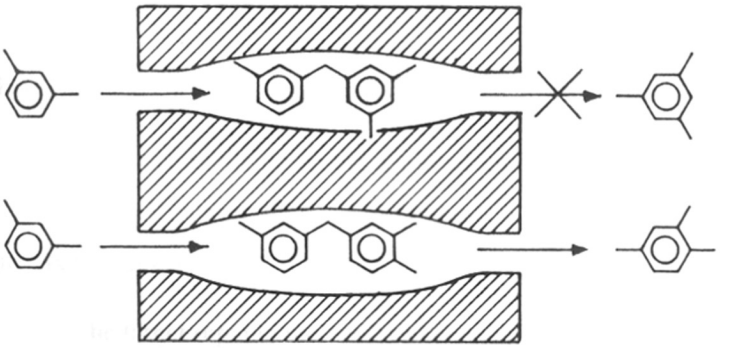
Reactant Selectivity



Product Selectivity



Restricted transition state selectivity



of the silicon atoms were replaced by phosphorus atoms. Recently, a very large pore zeolite (VPI-6)[12] containing 18 member ring has been synthesized. The synthesis and characterization of newer zeolite and other microporous materials have been reviewed recently[13].

All these variations in structure mentioned above make zeolite suitable for wide applications in petrochemicals[14,15] as well as in synthesis of organic intermediates and fine chemicals[16].

Application of zeolite in organic synthesis

Application of zeolites in organic synthesis includes non-catalytic and catalytic uses.

The non-catalytic uses of zeolites

i) Drying and purification of solvent.

ii) Separation of product.

iii) As a reactant disperser and slow release carrier.

The ability of zeolite to adsorb and retain small molecules such as water, lower alcohols, forms the basis for their non-catalytic use in synthesis of fine chemicals[17,18].

Catalytic uses of zeolites

Zeolites offer several advantages when used as catalyst. These are:

i) Thermostability.

ii) Possibility of recycle of the catalyst.

iii) Pollution and corrosion could be avoided to a greater extent.

Several reviews are available on the applications of zeolites for the synthesis of intermediate and fine chemicals[19-21]. However, their use in synthesis of organic intermediates and fine chemicals is in premature state of development. The main reasons for this are:

i) Many of the target organic molecules to be synthesized are too bulky, *i.e.,* they are bigger in size than the cavity of the zeolite.

ii) The synthetic organic chemists are not acquainted with zeolites and their potential, other than their use in industrial processes.

Some of the important organic reactions catalyzed by zeolite are discussed below:

Substitution reaction

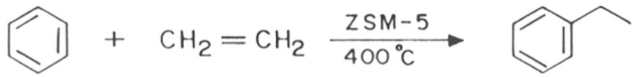
Alkylations

Fridel-Craft alkylation reactions of arenes with alcohols or olefins using Lewis acid catalyst such as $AlCl_3$[22] have been carried out on industrial scale. The use of such catalysts give rise to several problems, such as corrosivity, toxicity and effluent pollution.

Akylation on arenes

The Mobil-Badger process is an outstanding and technically proven example of alkylation of aromatic compounds using zeolite catalyst. Ethylbenzene (**3**) has been produced from ethylene (**2**) and benzene (**1**) over phosphorous doped ZSM-5 zeolite. Ethylene is completely converted to ethylbenzene with 99% selectivity[23] at about 400°C (Scheme 1.2). Similarly, alkylation of benzene with either propene or isoproponol over zeolites to give industrially important cumene has also been reported[24].

Scheme 1.2



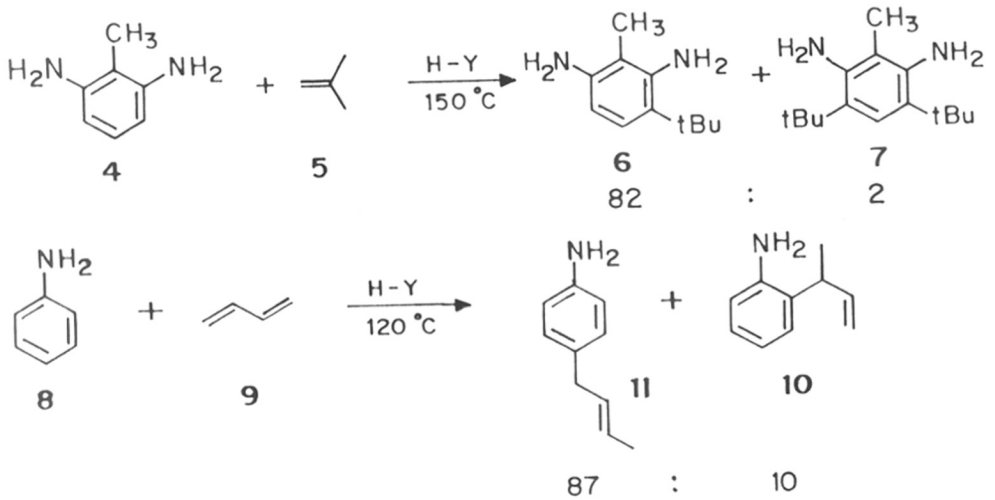
1 **2** **3**

The used catalyst can be regenerated and reused without loss of reactivity and selectivity.

Alkylation of substituted arenes

The alkylation of arylamine is highly selective. The *t*-butylation of 2,6-diaminotoluene (**4**) over H-Y zeolite shows shape selectivity as this process gives selectively mono *t*-butyl compound[25,26] **6**. Another interesting reaction of aniline (**8**) with butadiene (**9**) has been reported using H-Y zeolite at 120°C, in which preferentially para product formation was observed. The butenyl group could be attached at 2 and 4 positions in two different ways to give 2-isobutenylaniline (**10**) and 4-(but-2'-en-1'-yl)aniline (**11**) (Scheme 1.3).

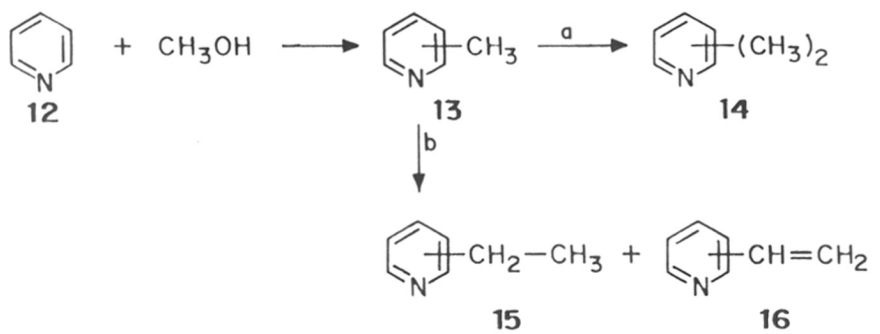
Scheme 1.3



Alkylation of heteroarenes

The alkylation of pyridine (**12**) with methanol over faujasite[27] type zeolite has been reported. Primarily, the substitution takes place at aromatic nucleus, followed by secondary reaction, in which the picoline (**13**) formed can either undergo further ring alkylation or side chain alkylation to give compound **15** or **16** respectively. Various possibilities with different zeolite are shown in (Scheme 1.4). Solinas *et al*[28] have also reported alkylation of thiophene using zeolite catalyst.

Scheme 1.4



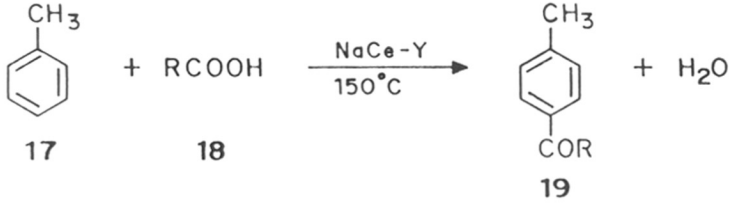
Similarly regioselective N-alkylation of imidazoles with alcohols over Y-type zeolite[29] has been reported. Vapour phase alkylation of 4(5)-methylimidazoles with methanol over Y-type zeolite selectively gave 1,5-dimethylimidazole in high yield. However, alkylation of imidazole over β-zeolite gave selectively 1,4-dimethylimidazole as a major product.

Acylations

Acylations of arenes

Friedel-Crafts acylation of aromatic compound is generally carried out by using acid chlorides or anhydrides as acylating agent in presence of stoichiometric amounts of metal chlorides such as $AlCl_3$, $FeCl_3$ as Lewis acid catalyst[30]. In this process substantial amount of catalyst is required and the work-up of the reaction involves handling of corrosive medium. To over come this problem Chiche *et al*[31] reported, for first time, the use of zeolite catalyst for acylation using carboxylic acid as acylating agent. The acylation of toluene (**17**) with aliphatic acid **18** (C_2-C_{22}) using zeolite Na(Ce 70%)Y as a catalyst have been reported to give corresponding acylated product **19** in good yield (Scheme 1.5). The shape selectivity is clearly indicated by the formation of more than 95% of para isomer **19**. Although, other catalysts including $AlCl_3$ are also known to give predominantly para isomer, the zeolite catalysts are superior in the selectivity aspect. The mechanism of this reaction has been studied by Gautheir[32] and Chichem[33]. Recently, acylation of aldehydes to diacetates using β-zeolite[34] has been reported.

Scheme 1.5

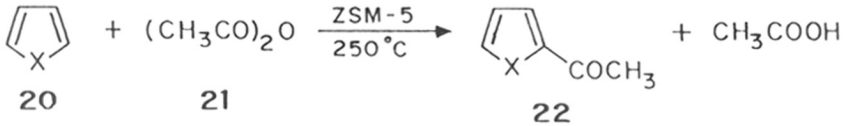


17 **18** **19**

Acylation of heteroarenes

The reaction of thiophene (**20**) with acetic anhydride (**21**) at 250°C in the presence of boron ZSM-5[35] reported to give 2-acylthiophene (**22**) with 25% conversion and 99% selectivity. Similarly pyrrole and furan gave corresponding 2-acyl products (Scheme 1.6). Holderich[36], for the first time reported the synthesis of 2-methyl-4-acetylimidazole using zeolite catalyst.

Scheme 1.6



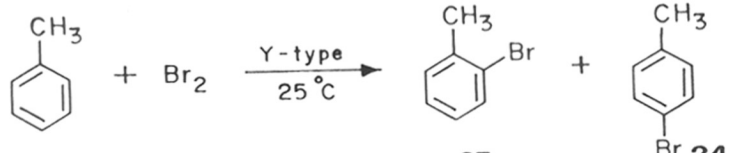
20 21 22

X = S, O, NH

Halogenation

The halogenation reaction in the presence of zeolite has been carried out in gas phase or in liquid phase. Bekkum *et al*[38] and Vega *et al*[39,40] studied halogenation using zeolite catalyst on different halobenzene (Scheme 1.7). Bromination of toluene (**17**) in presence of Y-type zeolite known to give high selectivity for para isomer[40] **24**.

Scheme 1.7

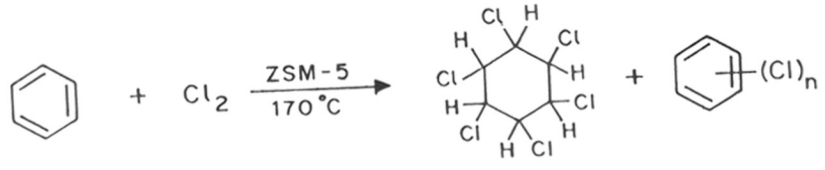


17 23 24

2 : 98

ZSM-5 type zeolite would seems to be well suited for para selective halogenation in view of geometry of the pore system. However, when chlorination of benzene (**1**) was carried out using ZSM-5 at 170°C, surprisingly, selective addition reaction was observed along with substitution, leading to a mixture of hexachlorocyclohexanes[41] (**25**) and polynuclear chlorinated product **26** (Scheme 1.8). The selective bromination of a linear alkene in presence of a branched or cyclic alkene using presence of ZSM-5 zeolite has been also reported[42].

Scheme 1.8



1 25 26

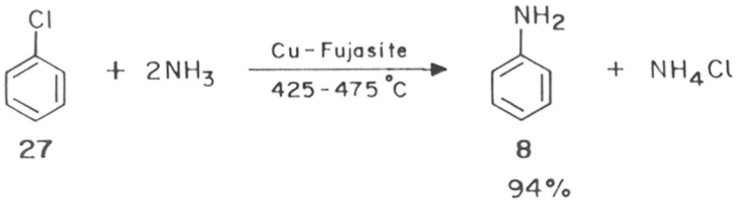
Nitration

Arenes and substituted arenes are nitrated with N_2O_4 and NO_2 in gas phase using H-ZSM-5 or H-mordenite. When benzene was nitrated with N_2O_4 in presence of H-ZSM-5 at 200°C, nitrobenzene was obtained with 98% selectivity and 64% conversion[43]. Similarly, nitration of toluene with N_2O_4 in presence of H-mordenite at 150°C gave mono nitrotoluene with 80% selectivity and 30% conversion.

Aminations

Zeolites have also been successfully used for amination reaction. Warawdekar[44] has reported synthesis of aniline (**8**) from Chlorobenzene (**27**) and ammonia using Cu-exchanged zeolite (Scheme 1.9). It has been shown that H-Y and Cu-Y exhibited maximum acidity and activity for phenol amination. Similarly, amination of phenol and anisole over cation exchanged Y-type[45] zeolite gave aniline in 94% yield.

Scheme 1.9



Reaction of alcohols with ammonia

Reaction of methanol and ammonia over Na-mordenite at 250°C for 1 h has been reported to produce methylamine along with dimethylamine and trimethylamine[46]. Recently, the use of Na-mordenite[47] catalyst treated with $SiCl_4$ reported to lower the formation of trimethylamine to 0.5%. On the other hand, the large pore H-Y zeolite, under similar conditions gave 96% trimethylamine. The exclusive formation of dimethylamine have been reported by Mochida *et al*[48].

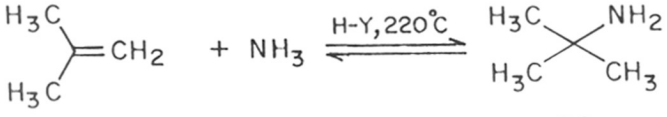
Addition reaction

Addition of ammonia to olefin

Alkylamines can be prepared from olefins and ammonia at 320°C and above using zeolite catalyst. Reaction of ethylene with ammonia over H-erionite or H-mordenite at 320°C gave only 2% of addition product, while at a higher temperature (380°C) the conversion was increased to 12%[49]. In a reaction of isobutene (**5**) with ammonia over H-Y zeolite at 220°C, a conversion of 9% with 99%

selectivity[50] for **28** was observed (Scheme 1.10). Although the conversion was low, the simplicity, selectivity and pollution factors provided advantages over the conventional HCN addition based route for the *t*-butylamine.

Scheme 1.10

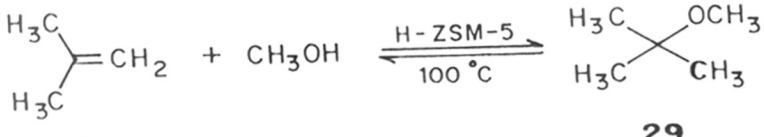


5 **28**

Addition of alcohols to olefins

Methyl *t*-butyl ether (MTBE, **29**) has been prepared from isobutene (**5**) and methanol in the presence of H-ZSM-5 zeolite at 100°C with 35% conversion and 95% selectivity (Scheme 1.11). The weakly acidic boron zeolite affords MTBE (**29**) in 86% yield[51]. However, the addition reaction of hydroxy compounds to olefins over zeolite do not offer distinct advantage over conventional Bronsted acid catalyzed reaction.

Scheme 1.11

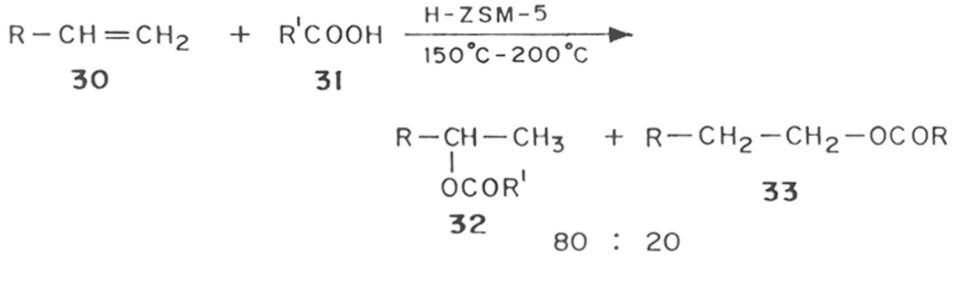


5 **29**
35%

Addition of carboxylic acid

The addition of acids (mostly acetic acid) to olefins have been achieved upto 30% conversion in presence of zeolite catalyst like H-ZSM-5, H-ZSM-12 at 150-200°C[52]. Terminal olefins **30** afford 2-acyloxy compound **32** with a selectivity of 80% (Scheme 1.12).

Scheme 1.12

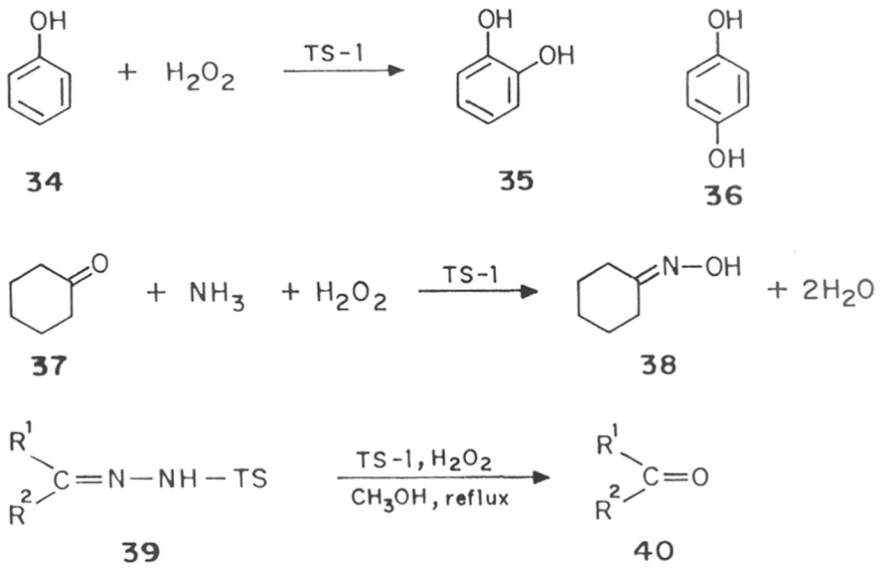


Oxidation reactions

One of the most important advances in zeolite catalysis is the introduction of titanium silicate (TS-1) for oxidation of organic substrate by means of hydrogen peroxide. A detailed reviews on the preparation, characterization[53] and utilization[54] of TS-1 catalyst have been appeared recently. The titanium on TS-1 provides a high performance, highly flexible, and highly stable catalytic sites. The selectivity and catalytic activity of TS-1 have provided the basis for the development of new technologies for some industrially important chemicals. One example in which TS-1 has already found industrial application is oxidation of phenol to hydroquinone and catechol[55-57] (Scheme 1.13). The current method of homogeneous liquid phase oxidation of phenol using perchloric acid to hydroquinone leads to substantial quantities of side products. In contrast to the above, the process using TS-1 zeolite for the oxidation of phenol (**34**) using H_2O_2 lead to 25% conversion with very high selectivity as polyhydroxylated benzene and tars is inhabited by transition state shape selectivity.

Another important application of titanium zeolite is a liquid phase conversion of cyclohexanone (**37**) to its oxime **38** in the presence of ammonia and hydrogen peroxide[58] (Scheme 1.13). The TS-1 catalyst has been found to be effective in the oxidative cleavage of tosylhydrazones[59] **39** to corresponding carbonyl compounds **40** (Scheme 1.13).

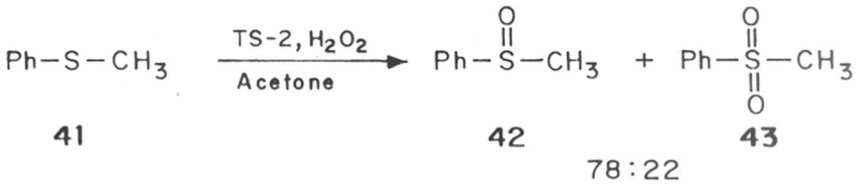
Scheme 1.13



Oxidation of sulfur

Hydroxyperoxides[60-62] and peracids[63] are well known to oxidize organic sulfides to sulfoxides and sulfones. TS-2 catalyst[64] efficiently catalyzes the oxidation of various thioethers **41** to corresponding sulfoxides **42** and sulfones **43** using dilute H_2O_2 as oxidizing agent (Scheme 1.14). Studies have been carried out to determine the mechanism[65] of the oxidation reaction.

Scheme 1.14



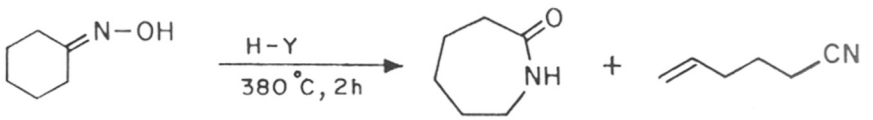
Rearrangements

The application of zeolite catalysts for some important rearrangement reactions is discussed below:

Beckmann rearrangement

The preparation of caprolactum, an important starting material for Nylon-6 involves the Beckmann rearrangement of cyclohexanone oxime. The conventional method requires concentrated sulfuric acid to carry out this transformation. The problems associated with this reaction are the formation of huge amount of ammonium sulfate as a by-product and handling of large amount of fuming sulfuric acid. Venuto and Landis[66] reported the use of zeolite to achieve this rearrangement. Zeolite X, Y and H-mordenite are effective for this reaction. Cyclohexanone oxime (**38**) in benzene (**1**) was converted over H-Y zeolite at 380°C to caprolactum (**44**) in 85% yield and 76% selectivity in only 2 h (Scheme 1.15). The main by-product in this reaction is 5-cyanopent-1-ene (**35**). As the reaction progresses the selectivity and conversion drops due to deactivation of catalyst. The detailed mechanistic studies have been carried out on this reaction[67]. In zeolite catalyzed rearrangement too, it has been proved that the group which is trans to OH group is the one which migrates.

Scheme 1.15

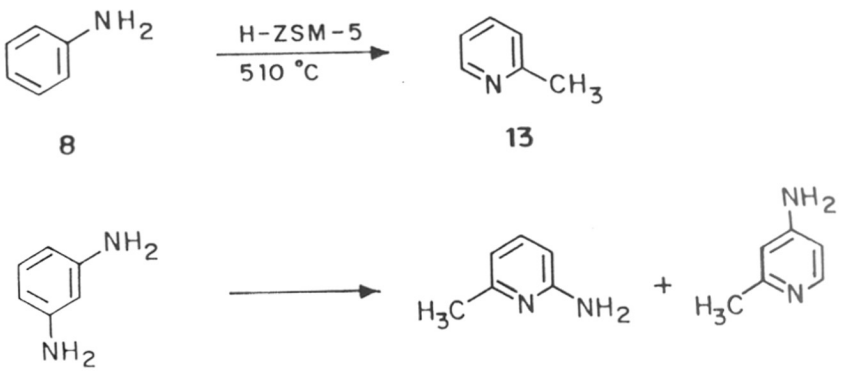


38 44 45

Benzamine rearrangement

The conversion of aniline to pyridine derivatives with the help of zeolite catalyst is very interesting, and has industrial potential as well. Aniline (**8**) has been reported to give good yield of α-picoline (**13**) when reacted with ammonia over H-ZSM-5 at 510°C with 52% selectivity[68,69]. Similarly 1,3-diaminobenzene (**46**) rearranges to a mixture of 4- and 6-aminopicolines (**48** & **47**) (Scheme 1.16).

Scheme 1.16



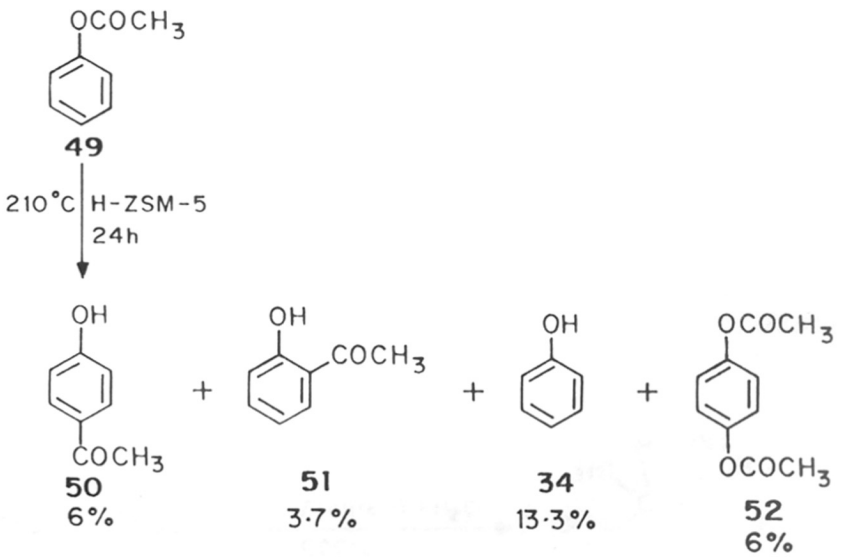
8 13

46 47 48

Fries rearrangement

The Fries rearrangement of phenylacetate (**49**) to *o*-hydroxyacetophenone (**51**) and *p*-hydroxyacetophenone (**50**) is usually performed by using $AlCl_3$ as a catalyst[70]. The use of zeolite catalyst for Fries rearrangement has also been reported[71,72]. However, the *o*/*p* selectivity obtained is very poor (Scheme 1.17). Recently, a highly selective Fries migration over H-ZSM-5 zeolite modified with Gallium[73] has been reported. 2-hydroxyacetophenone (**51**) was obtained in 46% when phenylacetate (**49**) was fed over Gallium modified H-ZSM-5 catalyst using a fixed bed reactor at 250°C. The unusual finding of *ortho* selectivity over modified catalyst has been attributed to easy migration of acetyl cation to *o*-position compare to *p*-position.

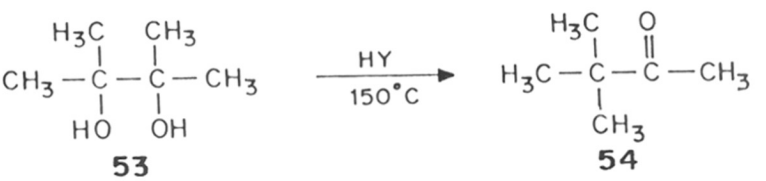
Scheme 1.17



Pinacol rearrangement

The classical method for this rearrangement involves acid treatment of glycols with proper substitution, leading to carbonyl compounds. This rearrangement has been carried out using zeolite catalyst. The rearrangement of 2,3-dimethyl-2,3-dihydroxybutane (**53**) in presence of H-Y zeolite at 105°C gave 83% of the rearranged product, 3,3-dimethyl-2-butanone[74, 75] (**54**) (Scheme 1.18).

Scheme 1.18



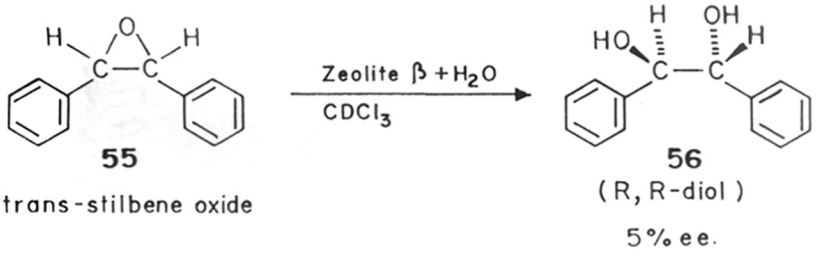
Asymmetric synthesis

To achieve an efficient catalytic asymmetric synthesis is a goal of almost all organic chemist and lot of efforts are being made in this direction. The incorporation of metal ions attached to chiral ligands inside the zeolite cage offers an attractive alternative way of achieving this objective.

Chiral rhodium complex supported on zeolite have been used as catalyst for asymmetric hydrogenation of N-acyl dehydrophenylalanine derivatives. This method provides hydrogenated products with very high enatioselectivities (95% ee)[76,77]. However, there are no reports on the large scale commercial use of such hybrid catalysts.

Davis[78] has shown, for the first time that zeolite, especially β-zeolite with an isomorph A in slight excess can be used for asymmetric synthesis of (R,R)-diol **56** with 5% ee starting from **55**. Although, the selectivity is very low, it has opened up a new area of designing chiral zeolite catalyst for asymmetric synthesis (Scheme 1.19).

Scheme 1.19



55
trans-stilbene oxide

56
(R, R-diol)
5% ee.

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CHAPTER 2

Esterification of carboxylic acids

SUMMARY

A simple and practical method for the esterification of carboxylic acids with alcohols using zeolite catalysts in good to excellent yield has been described in this chapter. To optimize the conversion and reaction efficiency, various parameters in this reaction have been systematically studied. These includes variation in reaction temperature, duration of reaction, and use of various zeolite catalysts. This reaction has also been studied using a fixed bed reactor so as to make it more efficient and industrially adaptable method. It was observed that Y-type zeolite like RE-NaY and RE-HY were found to be best catalysts for esterification reaction.

INTRODUCTION

The esters of carboxylic acids find many applications in day to day life as well as in industry. The lower esters are used in lacquers, paints, and varnishes where as higher esters are used as plasticizers. The esters in the form of natural fats, oils and waxes have been used as lubricants since ancient times. The soap industry is a very large consumer of esters. Polyol or polyethylene oxide esters of long chain fatty acids are non ionic surfactants, and used in food, pharmaceuticals, cosmetic and textile industries. The esters are also used as flavoring agents in cosmetic and food stuff. The acetates of most of the alcohols are commercially available and have diverse uses. Ethyl, *iso-propyl, butyl, iso*-butyl, amyl and *iso*-amylacetates are used in cellulose nitrate. Butyl and hexyl acetates are excellent solvents for polyurethane coating systems[1].

The most common laboratory method for the preparation of esters involves the condensation of carboxylic acid with an alcohol in presence of acid catalysts, such as HCl, H_2SO_4 or *p*-toulenesulfonic acid, methanesulfonic acid[2]. Phosphoric acid is also known to catalyze esterification, however the reaction rates are very slow. Other most frequently used methods for the preparation of esters involves the reaction of alcohol with acid chloride or acid anhydride. Diazomethane[3] is commonly used for small scale preparation of methyl esters. However, diazomethane is unsuitable for large scale preparations, as it is known to be an explosive and poisonous gas.

Esterification of carboxylic acid is a common reaction and has been studied extensively[4]. Several Lewis acids such as boron trifluoride etherate[5,6], aluminium chloride and titanium tetrachloride are known to catalyze esterification reaction of carboxylic acids with alcohols. The condensing agents such as dicyclohexylcarbodiimide (DCC)[7], cyanuric chloride (CC)[8], 2-halo-1-methylpyridinium iodide[9], triphenyl phosphine[10], 2-fluoro-1,3,5-trinitrobenzene (FTNB) have been used to bring out esterification under mild conditions[11]. The use of alkyl halides in place of alcohols for the esterification of carboxylic acids in presence of non nucleophillic bases (DBU, Et_3N)[12] has also been reported.

The carboxylate salts in the presence of crown ethers[13,14] undergo efficient esterification in polar and non-polar solvents to give esters in quantitative yields. Recently, Khurana[15] has reported the esterification of carboxylic acid with different alcohols in the presence of catalytic amount of sulfuric acid using ultrasonic waves.

The transesterification reaction has been extensively used, wherein esters are treated with alcohols, acids or other esters, in the presence of an acid or base catalyst. The transesterification reaction has also been carried out for variety of esters under mild and/or neutral conditions using several other catalysts such as iodotrimethylsilane[16], phosphoric acid salts[17], cyanide ions[18], distannoxane[19], titanium(IV) alkoxide[20] and alkali metal alkoxide[21].

PRENSENT WORK

Although many useful and reliable methods for esterification of carboxylic acids have been reported in the literature, a need still exist for a versatile, simple and environment friendly process, whereby esters may be prepared under very mild conditions.

The esterification reaction of carboxylic acid with alcohols is well known to be catalyzed by protic acids such as sulfuric acid. The use of such strong acids creates serious problem of corrosion of reaction vessels. Moreover, the acid has to be washed off prior to the isolation of the esters. The isolation process can be simplified by using heterogeneous catalysis. There are many such solid acid catalyst reported in the literature. Hino[22] et al have reported a solid super acid catalyst, which was obtained by exposing $Zr(OH)_4$ to 1N sulfuric acid and then calcining it in air at 500-600°C. This catalyst was found to be highly active for esterification reaction.

In another method, the use of heteropoly acids[23] as a catalyst for esterification reaction have been reported. Noibic acid[24] [$Nb_2O_5.nH_2O$] and Nafion[25] (fluorinated sulfonic acid) have also been successfully used as catalyst for the preparation of esters.

There are few reports in the literature wherein zeolite catalyst have been used for esterification reaction. Zeolites are salts of solid silicoaluminic acids having definite crystalline structure with regular pores in their crystal lattice[26]. The zeolite catalysts are known for their active acid sites (Bronsted and Lewis acid). Although zeolites have received much attention as the catalyst in area of petrochemicals, the area of fine chemicals[27], has not been explored extensively. Santaceriva[28] have studied kinetics of acetic acid esterification with ethanol in the presence of Y type zeolite catalysts. Mordenite[29] directly exchanged with hydrochloric acid has shown strong catalytic action in promoting esterification reaction. Recently Corma Avelino[30] has reported the use of H-Y Zeolite for the esterification of phenol with carboxylic acid.

The use of zeolite catalysts for esterification has been reported for some specific carboxylic acids and most of the reports are from patented literature[31-37]. Therefore, we felt a need for a systematic study of esterification reaction using zeolite catalysts. Our main objective was to develop an industrially viable process for esterification reaction using heterogeneous catalysts. Therefore, we decided to screen various commercially available zeolites for optimization of the reaction conditions for esterification of phenylacetic acid with ethanol and select a best catalyst for the preparation of wide variety of esters.

RESULTS AND DISCUSSION

The esterification of phenylacetic acid with ethanol was chosen as a model reaction. Several zeolite catalysts were screened for the preparation of ethyl phenylacetate.

A mixture of phenylacetic acid (5 g), ethanol (50 ml), and zeolite catalyst (5 g) was heated in a Parr reactor at 150°C under autogeneous pressure for 8 h. The reaction mixture was cooled and filtered to remove catalyst. The ethanol was removed from filtrate by distillation and the residue obtained was taken up in an organic solvent. It was further treated with a 5% solution of sodium bicarbonate to recover starting phenylacetic acid. The organic layer on concentration gave pure ethyl phenylacetate. The results of ethyl phenylacetate formation using various catalysts are summarized in Table 2.1.

Table 2.1. Preparation of ethyl phenylacetate using various catalysts.

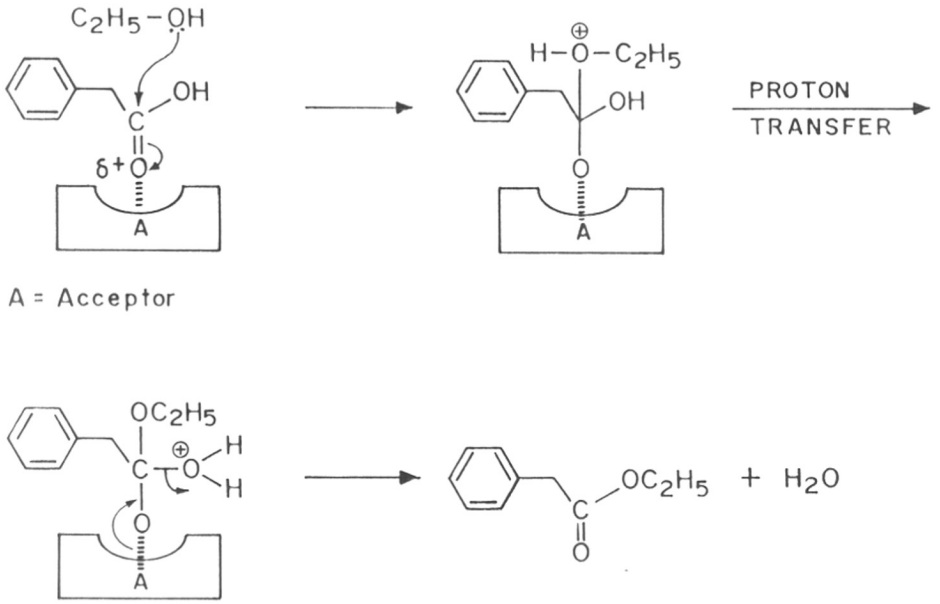
Entry No.	Catalyst used[a]	Yield[b] (%)
1	H-ZSM-5	60
2	H-Mordenite	74
3	RE-NaY	90
4	H-Y	80
5	RE-HY	92
6	US-Y	79
7	TS-1	77

[a] Reaction is carried out in a Paar reactor at 150°C for 8 h.

[b] Isolated yield of ethyl phenylacetate.

The above results reveal that all catalysts gave good conversion (60-90%) of phenyl acetic acid. However, very high yields of ethyl phenylacetate was obtained when the rare-earth exchanged H-Y and Na-Y catalysts (entries 3 & 5) were used. The rare-earth exchange is known to increase stability as well as activity (Lewis acidity) of zeolites. This Lewis acidity of zeolites helps in activation of carboxylic acids towards nucleophillic attack of alcohols. The probable mechanism is shown in Scheme 2.1. RE-NaY and RE-HY found to be the best catalysts for esterification reaction. Hence, RE-HY is selected for further studies.

Scheme 2.1



Effect of temperature on esterification reaction

The reaction of phenylacetic acid with ethanol in presence of RE-HY catalyst was studied at various temperatures. Thus, a mixture of phenylacetic acid (5 g), ethanol (50 mL) and RE-HY (5 g) was heated in a Parr reactor at temperatures ranging from 80-160°C for 8 h. The usual work up and removal of unreacted phenylacetic acid, gave ethyl phenylacetate. The results are tabulated in Table 2.2.

Table 2.2. Effect of temperature on esterification of phenylacetic acid with ethanol in presence of RE-HY catalyst.

Entry No.	Reaction Temperature(°C)	Yield[a](%)
1	78[b]	49
2	90	69
3	100	71
4	110	79
5	120	84
6	130	85
7	140	87
8	150	91
9	160	92

[a] Isolated yields of ethyl phenylacetate. [b] Reaction carried out at reflux temperature of ethanol for 8 h.

It is evident from the Table 2.2 that there is a gradual increase in the yield of ethyl phenylacetate with increase in the reaction temperature. At 150°C the yield of ester was 91%, however, there was no significant increase in the yield after further increase in the reaction temperature. A very low yield (see entry 1) of ester was observed when the reaction was carried out at reflux temperature of ethanol.

The optimum reaction temperature of 150°C was chosen to study the esterification of various carboxylic acids with different alcohols in a batch process using RE-HY catalyst in a Paar reactor. A mixture of carboxylic acid (**1**, 5 g), alcohol (**2**, 50 mL) and RE-HY (5 g) was heated in a Parr rector at 150 °C for 8 h. The usual work up gave corresponding esters **3**. The results are summarized in Table 2.3.

$$\underset{\mathbf{1}}{R^1COOH} + \underset{\mathbf{2}}{R^2OH} \text{ -------> } \underset{\mathbf{3}}{R_1COOR_2} + \mathbf{H_20}$$

Table 2.3. Esterification of carboxylic acids with various alcohols using RE-HY catalyst.

Entry No.	Ester	R^1	R^2	Yield(%)
1	**3a**	Ph	Et	37
2	**3b**	$PhCH_2$	Et	95
3	**3c**	$PhCH_2$	Me	88
4	**3d**	$PhCH_2$	n-Pr	89
5	**3e**	$PhCH_2$	*i*-Pr	47
6	**3f**	$PhCH_2$	n-Bu	88
7	**3g**	$PhCH_2$	*t*-Bu	12
8	**3h**	$PhCH_2$	n-Amyl	95
9	**3i**	$PhCH_2$	*i*-Amyl	95
10	**3j**	$PhCH_2$	n-Octyl	86
11	**3k**	PhCH=CH	Et	87
12	**3l**	MeCH=CH	Et	54
13	**3m**	Me_2C=CH	Et	70
14	**3n**	$Me(CH_2)_5CH_2$	Et	78

The esterification of phenylacetic acid with primary alcohols such as n-propanol, n-butanol, n-amyl alcohol, *i*-amyl alcohol, n-octanol gave excellent yields (entries 2,3,4,6,8,10). However, the yields dropped dramatically when secondary and tertiary alcohols (entries 5,7) such as *i*-propanol, *t*-butanol were used for esterification. The lower yields of ester with secondary and tertiary alcohol may be due to the steric factors. The α, β-unsaturated carboxylic acids such as crotonic acid, 3,3-dimethyl acrylic acid, cinnamic acid can also be esterified in reasonable yield under these conditions.

There are several limitations for the batch process. A large amount of catalyst is required in batch process. Water, a by product, formed in this reaction deactivates the catalyst, resulting in the lowering of the yield. To overcome these limitations and to make esterification reaction more efficient and industrially feasible, we decided to carry out this reaction on a fixed bed reactor. In this method a alcoholic solution of acid was passed through a preheated fixed bed of zeolite catalyst with the help of a syringe pump. A mini reactor was designed for this purpose (see Figure 1). The reactor consists of a glass tube filled with catalyst, the remaining part was filled with porcelain or glass beads. It was then placed in an electrical heating device. The lower end of the tube is attached to a water condenser and upper end is attached to an adaptor having a gas and sample inlets. A solution of acid and alcohol was passed over preheated catalyst bed with the specified rate using a syringe pump. The solution of the product in alcohol was collected at the bottom. The excess alcohol was removed by distillation to get the ester.

VARIATION OF PARAMETERS

A systematic study has been carried out by varying temperature, WHSV (weight hour space velocity, for details see experimental section) and the concentration of acid in alcohol. The effects of these parameters on the formation of ethyl phenylacetate (**3b**) using RE-NaY catalyst has been studied.

(i) Effect of temperature

The esterification was carried out at different temperatures using constant molar ratio of reactants (2.0 g phenylacetic acid/20 mL of ethanol) at WHSV 1.125 on RE-NaY catalyst (2.0 g). The results are tabulated in Table 2.4.

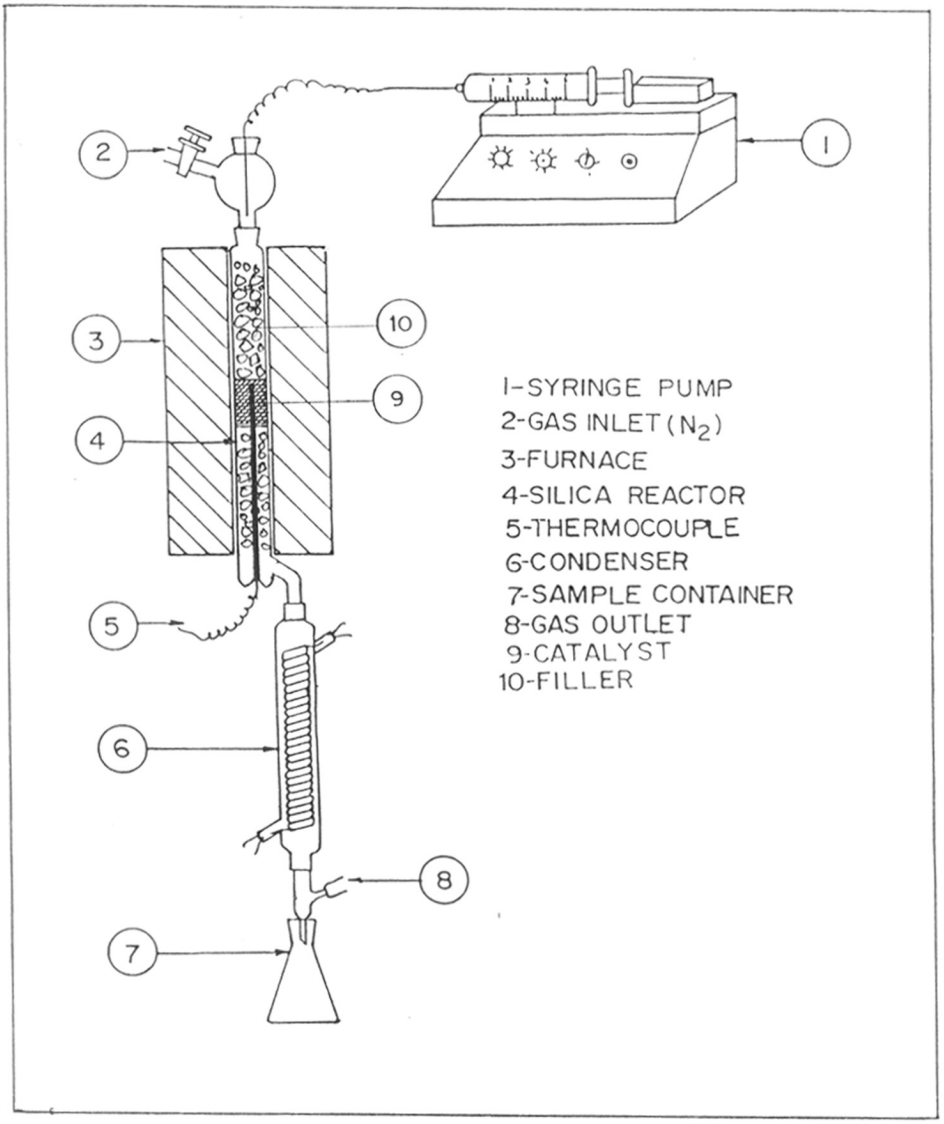


Fig. 1 : Reactor Set-up for Reactions carried out at atmospheric pressure.

Table 2.4. Effect of temperature on the conversion of phenylacetic acid to ester **3b.**

Entry No.	Temperature (°C)	% Conversion of phenylacetic acid
1	120	43
2	140	52
3	160	59
4	180	62
5	200	95

A graph of % Conversion v/s Temperature shows a steady increase in % conversion of acid to ester when temperature is raised from 120° to 200°C (Fig 2). A maximum conversion (95%) of acid to ester was observed at 200°C. Thus, the optimum temperature of 200°C is selected for the further studies.

(ii) Effect of WHSV

The esterification reaction of phenylacetic acid with ethanol was carried out by passing ethanolic solution of phenylacetic acid (2.0 g/20 mL of ethanol) over a preheated bed of RE-NaY catalyst (2.0 g) at various flow rates such as 9 mL, 22.5 mL, 30 mL and 40 mL per hour keeping the temperature constant at 200 °C. The results are summarized in Table 2.5.

Table 2.5. Effect of WHSV on the conversion of phenylacetic acid to ester **3b.**

Entry No.	WHSV	Conversion (%)
1	0.5	97
2	1.125	95
3	1.50	70
4	2.50	58

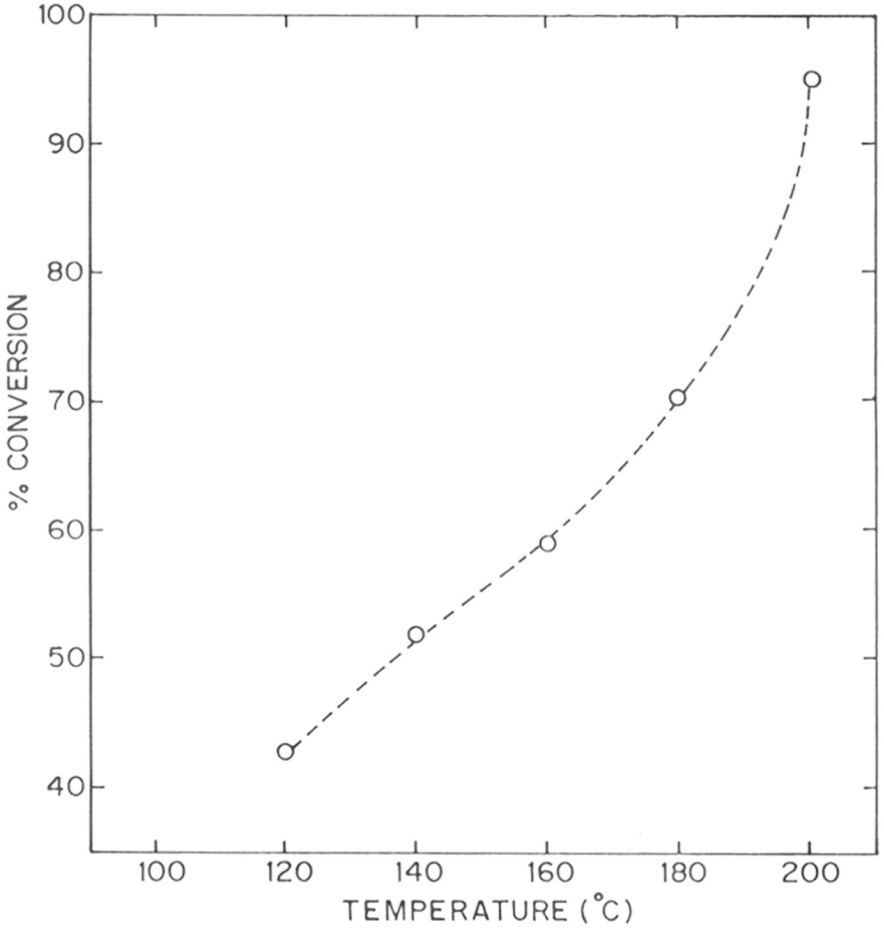


FIG.2: EFFECT OF TEMPERATURE ON THE CONVERSION OF PHENYLACETIC ACID TO ESTER **3b**

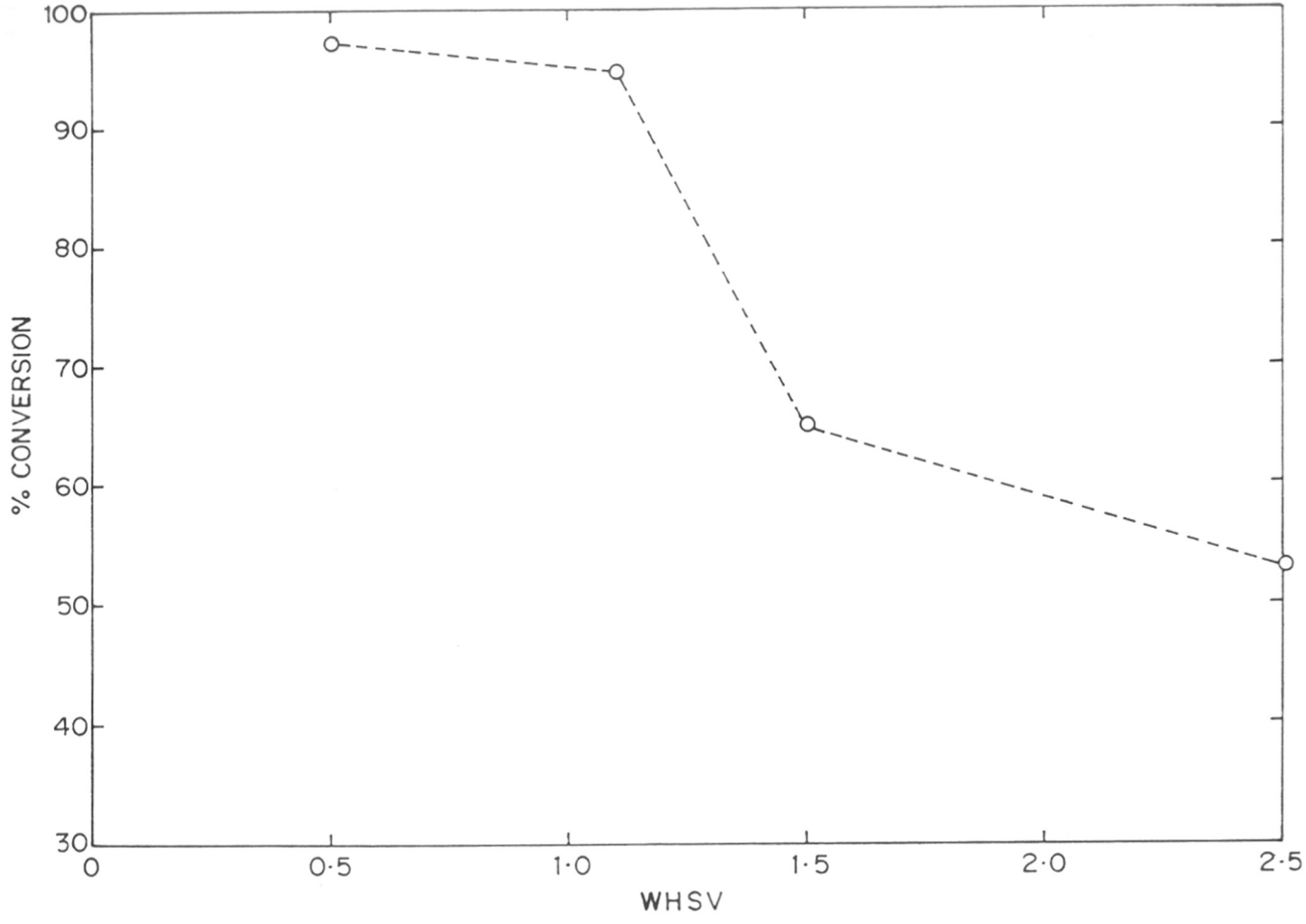


FIG. 3: EFFECT OF WHSV ON THE CONVERSION OF PHENYLACETIC ACID TO ESTER **3b**

It is clear from the above Table 2.4 and Fig 3 that conversion was maximum at WHSV 0.5 and 1.125. However, the conversion dropped considerably by further increase in WHSV due to the less contact time of the reactant with catalyst. A WHSV of 0.5 was selected for esterification as high conversion (97%) was obtained at this WHSV.

(iii) Life of the catalyst

After arriving at optimum temperature, WHSV, molar ratios of the reactants for maximum conversion of phenylacetic acid to ethyl phenylacetate (**3b**), a study on the life of the catalyst was undertaken. This was done by studying the efficiency of the catalyst, over a period of time for the optimum conversion of the phenylacetic acid to ethyl phenylacetate (**3b**). For this purpose a stock solution of phenylacetic acid (120 g) in ethanol (1200 mL) was prepared and this solution was passed over a bed RE-NaY catalyst (2.0 g) at 200°C with a rate of 10 mL/h (WHSV= 0.5). The catalyst was found to be effective even after running the reaction for 120 h without losing its activity. These results indicated that the use of continuous fixed bed reactor for esterification of phenylacetic acid with ethyl alcohol can be adopted as an industrial process for ethyl phenylacetate (**3b**).

The esterification of *o*, *m* and *p-toluic acid with ethyl alcohol was also* carried out using above mentioned fixed bed reactor with RE-NaY catalyst at 200°C. The results are summarized in Table 2.6.

Table 2.6. Esterification of *o*, *m* and *p*-toluic acid with ethanol.

Entry No.	Ester	R^1	R^2	Conversion (%)
1	**3o**	*o*-Tolyl	Et	82
2	**3p**	*m*-Tolyl	Et	70
3	**3q**	*p*-Tolyl	Et	90

Relatively low conversion in case of m-toluic acid (entry No. 2) may be due to the meta substituent, which restricts the free entry of the molecules into the zeolite cavities. However, very high conversion was observed in case of *p*-toluic acid.

Esterification of phenylacetic acid with various substituted phenols

The esterification of phenylacetic acid with *p*-cresol in presence of H-Y zeolite has been reported[30] to give *p*-cresyl phenylacetate in very low yield (13%). This prompted us to take a fresh look at the esterification of phenylacetic acid with phenols. Since, we have observed that the rare-earth exchanged Na-Y and H-Y catalysts gave very good yields in the esterification of phenylacetic acid with aliphatic alcohols, we were interested to see whether these rare-earth exchanged catalyst will improve the yield of *p*-cresyl phenylacetate.

A mixture of phenylacetic acid (4 g), *p*-cresol (5 g), RE-HY (4 g) and toluene (100 mL) was when heated at reflux temperature for 16 h with azeotropic removal of water, *p*-cresyl phenylacetate was obtained in only 8% yield. However, very high yield of *p*-cresyl phenylacetate (**3r**) was observed when toluene solvent was replaced by xylene and reaction was carried out at reflux temperature of xylene with azeotropic removal of water. Several zeolite catalysts were screened under these reaction conditions. The results are tabulated in Table 2.7.

Table 2.7. Esterification of phenylacetic acid with *p*-cresol using various catalysts.

Ester	R^1	R^2	Catalyst	Time(h)	Yield(%)
3r	$PhCH_2$	*p*-Cresyl	RE-NaY	16	85
			RE-HY	16	87
			H-Y	16	12
			H-ZSM-5	16	6

Among the catalyst screened, RE-NaY and RE-HY were found to give high yields of *p*-cresyl phenylacetate. Various esters were prepared by reacting phenylacetic acid with different phenols using RE-NaY as catalyst at xylene reflux temperature. The results are given in Table 2.8.

Table 2.8. Esterification of phenylacetic acid with substituted phenols using RE-NaY catalyst.

$$\underset{1}{R^1COOH} + \underset{2}{R^2OH} \text{ -------> } \underset{3}{R^1COOR^2} + H_2O$$

Ester	R^1	R^2	Catalyst	Time(h)	Yield(%)
3s	$PhCH_2$	*o*-Cresyl	RE-NaY	16	75
3t		*m*-Cresyl	RE-NaY	16	66
3u		Ph	RE-NaY	16	50
3v		2-MeoPh	RE-NaY	16	51

CONCLUSION

In conclusion, zeolite catalysts provide a practical, clean and efficient method for esterification of wide variety of carboxylic acids with alcohols, some of which are industrially important. This method has distinct advantages over other methods since it avoids use of strong acids such as concentrated sulfuric acid, hydrochloric acid, hazardous reagents such as diazomethane, dimethyl sulfate, expensive reagent like DCC. The work-up procedure is reduced to mere filtration and the zeolite can be recovered and reused after regeneration by calcination. This method is adaptable for commercial process and offers an environmentally safer alternative method to the existing processes.

EXPERIMENTAL

General

All the chemicals used in the study were commercial grade materials and were used after distillation. All the reactions were monitored by employing standard TLC technique using appropriate solvent system and plates were exposed to UV light or iodine vapor for developing the spots. All the solvent extracts were washed with brine then dried over anhydrous sodium sulfate. Yields reported are isolated yields.

Melting points

All melting points were recorded on Campbell Electronics (India) instrument using open capillary and are uncorrected.

Boiling points

Distillations were carried out under vacuum using oil bath for all liquid samples and boiling points refer to vapor temperatures and are uncorrected.

Nuclear magnetic resonance (NMR) spectra

^{1}H NMR spectra were recorded on varian T-60, FT 80A and BRUKER AC 200. All the samples were dissolved in chloroform-d solvent and chemical shifts are reported on δ scale using tetramethylsilane (TMS) as an internal standard. The abbreviations s, bs, d, t, q, and m, refer to singlet, broad singlet, doublet, triplet, quartet, and multiplet respectively. Coupling constant (*J*), wherever mentioned have been given in Hz.

Infrared spectra

Infrared spectra were recorded on Perkin-Elmer 599B spectrophotometer. Solid samples were recorded as Nujol mulls or in chloroform and liquids were recorded as such (neat) and absorptions were measured in cm^{-1}.

Mass spectra

Mass spectra were recorded on Finnigan MAT-1020 instrument using direct inlet system at 70 eV.

GC Analysis

GC analysis was carried out on Hewlett Packard 5890 series II instrument equipped with 3396A computing integrate. H_2 was used as carrier gas with a flow of 20 mL/min.

GC-MS Analysis

GC-MS analysis was carried out on Perkin Elmer 8000 Series GC equipped with Perkin Elmer Q-Mass 910.

Chromatography

Thin layer chromatography (TLC) was performed on 6x2 cm glass plates coated with commercial grade G-254 silica gel and visualization of the spots on TLC was achieved by exposure to iodine vapor or under UV light. Column chromatography was performed on commercial grade silica gel (100-200 mesh) supplied by M/s SD's Fine chemicals. The column was usually eluted with n-hexene or petroleum ether or with mixture of other polar solvents like ethyl acetate, acetone or methanol with pet. ether depending on the requirement.

Parr reactor

The Parr pressure reactor used in the study was Model No. 4561 with 4842 controller (Made in USA).

Fixed bed reactor

All fixed bed reactions were carried out at atmospheric pressure using a glass (15 mm i.d.) reactor and was fixed bed down flow type. The reactor was kept at constant zone of temperature in a furnace made by M/S Geomechnique, France.

WHSV (Weight Hour Space Velocity)

WHSV = 1, was achieved by passing 1 g of reactant over 1 g of zeolite bed in 1 h. The contact time of the reactants with zeolite bed could be reduced or increased by changing WHSV.

Preparation of RE-NaY catalyst[38]

A suspension of 10 g of Na-Y zeolite (Na-Y obtained from PQ Corporation U.S.A. With SiO_2/Al_2O_3 = 4.6, pore size 0.74 nm) in 100 mL of 5% aqueous solution of didymium chloride (mixture of rare earth chloride supplied by Indian Rare Earth Ltd. as didymium chloride, with the composition of trace amount of Cerium; Praseodymium 10-20%; Neodymium 35-40%; Samarium 4-6%; and 40-50% of Lathanum, Yattrium and heavier metals such as Europium, Gadolinium, Terbium, Dysprosium and Holmium) was heated on a water bath at 100°C with mechanical stirring for 4 h. The catalyst was filtered and washed with distilled water (2x25 mL). The same exchange procedure was repeated

to get the desired amount of rare earth exchange (about 70%; based on estimation of the amount of sodium ions present in the total filtrate by using atomic absorption spectrophotometer) for sodium ions present in zeolite catalyst. The exchanged zeolite RE (70%) Na-Y was thoroughly washed with distilled water, dried at 100°C for 3 h and activated at 400°C for 4 h prior to use. The crystallinity of exchanged zeolite was checked by X-ray powder pattern (XRD).

Preparation of RE-HY catalyst

RE-HY catalyst was prepared by rare earth exchange of NH_4-Y zeolite (obtained from PQ corpn. U.S.A. with SiO_2/Al_2O_3 = 4.6, pore size 0.74 nm) under similar conditions as described above, followed by calcination at 450°C for 4 h.

Preparation of H-Y catalyst

NH_4-Y obtained from PQ corpn. U. S. A. (with Si/Al = 4.6) was heated in furnace at 450°C for 4 h to get H form of NH_4-Y catalyst (H-Y catalyst).

Other zeolite catalyst like H-ZSM-5 (Si/Al = 40), H-Mordenite (Si/Al = 15), TS-1 (Si/Ti = 80) and US-Y (Ultra Stable-Y, Si/Al = 2.8) were obtained from Catalysis Division of National Chemical Laboratory, Pune.

Preparation of extrudates

The zeolite powder was mixed with binder (Catapal-B) in the ratio of (80:20) on dry basis. The mixture was initially homogenized in dry and was then mulled under 3% glacial acetic acid. The glacial acetic acid was removed by evaporation till it formed a thick lump, which was extruded through an extruder of size 1/16".

Preparation of pellets

In some cases self supported pellets were prepared using hydraulic press at a pressure of 6 tons. The self supported pellets were sized to 10-20 mesh.

Ethyl phenlyacetate (3b)

A mixture of phenylacetic acid (5 g, 0.036 mol), ethanol (50 mL) was taken in a Parr reactor and freshly activated zeolite RE-HY (5 g) was added slowly. It was then heated at 150°C under autogeneous pressure for 8 h. The reactor was cooled to room temperature and catalyst was filtered, washed with ethanol (2X25 mL). The ethanol from the filtrate was removed by distillation. The

residue was diluted with dichloromethane (50 mL) and washed with 5% sodium carbonate solution (2X25 mL) to remove unreacted acid, then with water (2X25 mL) and finally with brine (20 mL) and dried over anhydrous sodium sulfate. The removal of solvent offered pure ethyl phenylacetate (**3b**) (5.51 g, 91%), bp 142-145°C/40 mm (lit[39] bp 120-125°/17 mm).

IR (Neat) : 1720, 1600, 1500, 1450, 1020 cm^{-1}.

^{1}H NMR : 1.24 (t, J = 7 Hz); 3.56 (s, 2H); 4.12 (q, J = 7 Hz); 7.28 (s, 5H).

Following compounds were synthesized using similar procedure as described for **3b**.

Ethyl benzoate (3a)

Yield : 37%

Bp : 87-88°C/10 mm (lit[39] bp 87°C/10 mm).

IR (Neat) : 1720, 1600, 1455, 1370, 1030, 710 cm^{-1}.

^{1}H NMR : 1.45 (t, J = 7.5 Hz, 3H); 4.40 (q, J = 7.5 Hz 2H); 7.35-7.70 (m, 3H); 8.00-8.20 (m, 2H).

Methyl phenylacetate (3c)

Yield : 88%

Bp : 100-102°C/10 mm (lit[39] bp 131-132°C/50 mm).

IR (Neat) : 1735, 1600, 1500, 1020 cm^{-1}.

^{1}H NMR : 3.45 (s, 3H); 3.6 (s, 3H); 7.2 (s, 5H).

***n*-Propyl phenylacetate (3d)**

Yield : 89%

Bp : 110-112°C/20 mm (lit[40] bp 235°C).

IR (Neat) : 1735, 1610, 1500, 1400, 1260 cm^{-1}.

^{1}H NMR : 0.86 (t, J = 7 Hz, 3H); 1.16-2.0 (m, 2H); 3.46 (s, 2H); 3.93 (t, J = 7 Hz, 2H) 7.1 (s, 5H).

***i*-Propyl phenylacetate (3e)**

Yield : 47%

Bp : 68-70°C/2 mm (lit[40] bp 224°C).

IR (Neat) : 1730, 1605, 1500, 1455, 1375, 965 cm^{-1}.

^{1}H NMR : 1.30 (d, J = 6 Hz, 6H); 3.55 (s, 2H); 4.90 (m, 1H) 7.35 (s, 5H).

n-Butyl phenylacetate (3f)

Yield : 88%

Bp : 90-92°C/22 mm (lit[40] bp 249-250°C).

IR (Neat) : 1735, 1600, 1500, 1400 cm^{-1}.

^{1}**H NMR** : 0.86 (t, J = 6 Hz, 3H); 1.08-1.66 (m, 4H); 3.55(s, 2H); 4.02 (t, J = 6 Hz, 2H); 7.2 (s, 5H).

t-Butyl phenylacetate (3g)

Yield : 12%

Bp : 70-72°C/1.8 mm (lit[40] bp 230-235°C).

IR (Neat) : 1735, 1600, 1500, 1460, 1370 cm^{-1}.

^{1}**H NMR** : 1.46 (s, 9H); 3.53 (s, 2H); 7.28 (s, 5H); 7.28 (s, 5H).

n-Amyl phenylacetate (3h)

Yield : 95%

Bp : 110-112°C/5 mm (lit[41] bp 268°C).

IR (Neat) : 1740, 1600, 1500, 1455 cm^{-1}.

^{1}**H NMR** : 0.88 (t, J = 3.2 Hz, 3H); 1.04-1.74 (m, 6H); 3.58(s, 2H); 4.04 (t, J = 3.2 Hz, 2H); 7.24 (s, 5H).

i-Amyl phenylacetate (3i)

Yield : 95%

Bp : 125-126°C/10 mm (lit[42] bp 126-126°C/10 mm).

IR (Neat) : 1735, 1600, 1500, 1460 cm^{-1}.

^{1}**H NMR** : 0.91 (d, J = 5 Hz, 6H); 1.15-1.66 (m, 3H); 3.60 (s, 2H); 4.11 (t, J = 5 Hz, 2H); 7.26 (s, 5H).

n-Octyl phenylacetate (3j)

Yield : 86%

Bp : 165-166°C/3 mm.

IR (Neat) : 1740, 1610, 1500, 1475 cm^{-1}.

^{1}**H NMR** : 0.70-1.53 (m, 15H); 3.46 (s, 2H); 3.96 (t, J = 7 Hz, 2H); 7.16 (s, 5H).

Ethyl cinnamate (3k)

Yield : 87%

Bp : 135-136°C/10 mm (lit[39] bp 144°C/15 mm).

IR (Neat) : 1695, 1625, 1560, 1480 cm^{-1}.

^{1}H NMR : 1.50 (t, J = 6.5 Hz, 3H); 4.30 (q, J = 6.5 Hz, 2H); 6.70(d, J = 16 Hz, 1H); 7.55 (m, 5H); 7.70 (d, J = 16 Hz).

Ethyl crotonate (3l)

Yield : 54%

Bp : 60-62°C/50 mm (lit[39] 58-59°C/48 mm).

IR (Neat) : 1710, 1650, 1430, 1090, 1030, 960 cm^{-1}.

^{1}H NMR : 1.50 (t, J = 8 Hz, 3H); 1.82 (dd, J = 1.5 & 6 Hz, 3H); 4.20 (q, J = 8 Hz, 2H); 5.72 (m, 1H); 6.90 (m, 1H).

Ethyl 3,3-dimethyl acrylate (3m)

Yield : 70%

Bp : 70-72°C/50 mm (lit[43] bp 76-76.5°C/57.8 mm).

IR (Neat) : 1720, 1650, 1410, 1140, 1220 cm^{-1}.

^{1}H NMR : 1.28 (t, J = 7 Hz, 3H); 1.86 (s, 3H); 2.10 (s, 3H); 4.06 (q, J = 7 Hz, 2H); 5.53 (m, 1H).

Ethyl caprylate (3n)

Yield : 78%

Bp : 120-122°C/100 mm (lit[39] bp 104°C/80 mm).

IR (Neat) : 1735, 1660, 1370, 1100, 1030 cm^{-1}.

^{1}H NMR : 0.76-1.83 (m, 16H); 2.13 (t, J = 7 Hz, 2H); 4.05 (q, J = 7 Hz, 2H).

Ethyl *o*-toluate (3o)

A solution of *o*-toluic acid (2 g, 0.014 mol), in ethanol (20 mL) was passed over RE-NaY catalyst (extrudates) (2 g) placed in a fixed bed reactor [glass tube (i.d. 15 mm), the remaining part of tube was filled with porcelain beads] (Fig 1) with a rate of 22.5 mL/h (WHSV = 1.125) at 200°C. The ethanol was removed by distillation. The residue was diluted with dichloromethane (20 mL) and washed with

5% sodium carbonate solution (2X10 mL) to remove unreacted acid, then with water (2X10 mL) and finally with brine (10 mL) and dried over anhydrous sodium sulfate. The removal of solvent offered pure ethyl *o*-toluate (**3o**) (1.98 g, 82.55%), bp 100-101°C/10 mm (lit[39] bp 102.5°C/12 mm).

IR (Neat) : 1730, 1610, 1500, 1265, 1090, 750 cm^{-1}.

^{1}H NMR : 1.16 (t, J = 8 Hz, 3H); 2.56 (s, 3H); 4.36 (q, J = 8 Hz, 2H) 7.0-7.6 (m, 3H); 7.8-8.08 (m, 1H).

Following compounds were synthesized using similar procedure as described for **3o**.

Ethyl *m*-toluate (3p)

Yield : 70%

Bp : 104-105°C/10 mm (lit[39] bp 103-105°C/10 mm).

IR (Neat) : 1740, 1600, 1290, 1210, 765 cm^{-1}.

^{1}H NMR : 1.40 (t, J = 8 Hz, 3H); 2.36 (s, 3H); 4.40 (q, J = 8 Hz, 2H); 7.08-7.56 (m, 2H); 7.76-8.12 (m,2H).

Ethyl *p*-toluate (3q)

Yield : 90%

Bp : 108-110°C/10 mm (lit[39] bp 110°C/12 mm).

IR (Neat) : 1710, 1610, 1020, 840, 755 cm^{-1}.

^{1}H NMR : 1.32 (t, J = 8 Hz, 3H); 2.36 (s, 3H); 4.36 (q, J = 8 Hz, 2H); 7.0-7.5 (d, J = 8 Hz, 2H); 7.72-8.20 (d, J = 8 Hz, 2H).

***p*-Cresyl phenylacetate (3r)**

A mixture of phenylacetic acid (4.35 g, 0.031 mol), *p*-cresol (5.4 g, 0.05 mol), xylene (100 mL) was taken in a 250 mL round bottom flask to which freshly activated RE-NaY catalyst (4.5 g) was added. The mixture was heated in an oil bath at refluxing temperature of xylene (137-142°C) for 16 h. The water released during the course of the reaction was removed by azeotropic distillation with the help of Dean stark apparatus. The reaction mixture was cooled, the catalyst was filtered and washed with xylene (2 X 20 mL). The xylene from filtrate was removed by distillation under reduced pressure. The residue was diluted with ethyl acetate (50 mL), and washed with 5% sodium bicarbonate solution (2 X 25 mL) to remove unreacted acid, then with 5% sodium hydroxide solution to remove unreacted *p*-cresol. The ethyl acetate extract was finally washed with water (2 X 25 mL), brine (20 mL) and

dried over anhydrous sodium sulfate. The removal of solvent offered a white solid, which was recrystalized from *iso*-propanol to give 6.89 g (87.38%) of *p*-cresyl phenylacetate (**3r**), mp 74-75°C (lit[44] mp 76°C).

IR (Nujol) : 1750, 1600, 1500 cm^{-1}.

^{1}H NMR 2.0 (s, 3H); 3.80 (s, 3H); 6.80-7.48 (m, 9H).

Following compounds were synthesized using similar procedure as described for **3r**.

o-Cresyl phenylacetatae (3s)

Yield : 75%

Mp : 40°C (petroleum ether) (lit[45] mp 42°C).

IR (Nujol) : 1765, 1600, 1500, 1240, 850 cm^{-1}.

^{1}H NMR : 2.20(s, 3H); 3.76 (s, 2H); 6.56-7.46 (m, 9H).

m-Cresyl phenylacetate (3t)

Yield : 66%

Mp : 50-51°C (lit[45] mp 50°C).

IR (Nujol) : 1760, 1600, 1505, 1400, 930, 855 cm^{-1}.

^{1}H NMR : 2.20 (s, 3H); 3.76 (s, 2H); 6.84 (d, J = 8 Hz, 2H); 7.10 (d, J = 8 Hz, 2H); 7.35 (s, 5H).

Phenyl phenylacetate (3u)

Yield : 50%

Mp : 40-41°C (*iso*-propanol); (lit[44] mp 40.5°C).

IR (Nujol) : 1765, 1610, 1505 cm^{-1}.

^{1}H NMR : 3.80 (s, 2H); 7.0-7.78 (m, 10H).

2-methoxy phenyacetate (3v)

Yield : 51%

Bp : 153-155°C/1.5 mm (lit[46] bp 205-208°C/20 mm).

IR (Neat) : 1770, 1620, 1510, 950, 830 cm^{-1}.

^{1}H NMR : 3.70 (s, 3H); 3.84 (s, 2H); 6.36-7.48 (m, 9H).

Ethyl phenylacetate (3b) (using fixed bed reactor)

A solution of phenyl acetic acid (120 g, 0.88 mol) in ethanol (1200 mL) was passed over RE-NaY (extrudates) (2.0 g) filled in a glass tubular reactor (i.d. 15 mm) placed in a external heating device (Fig 1) with a rate of 10 mL/h (WHSV = 0.5) at 200°C. The ethanol was removed by distillation. The residue was diluted with dichloromethane (100 mL) and washed with 10% sodium carbonate solution (2X75 mL) to remove unreacted acid, then with water (100 mL) and finally with brine (50 mL) and dried over anhydrous sodium sulfate. The removal of solvent offered pure ethyl phenyl acetate (**3b**) (137.55 g, 95%).

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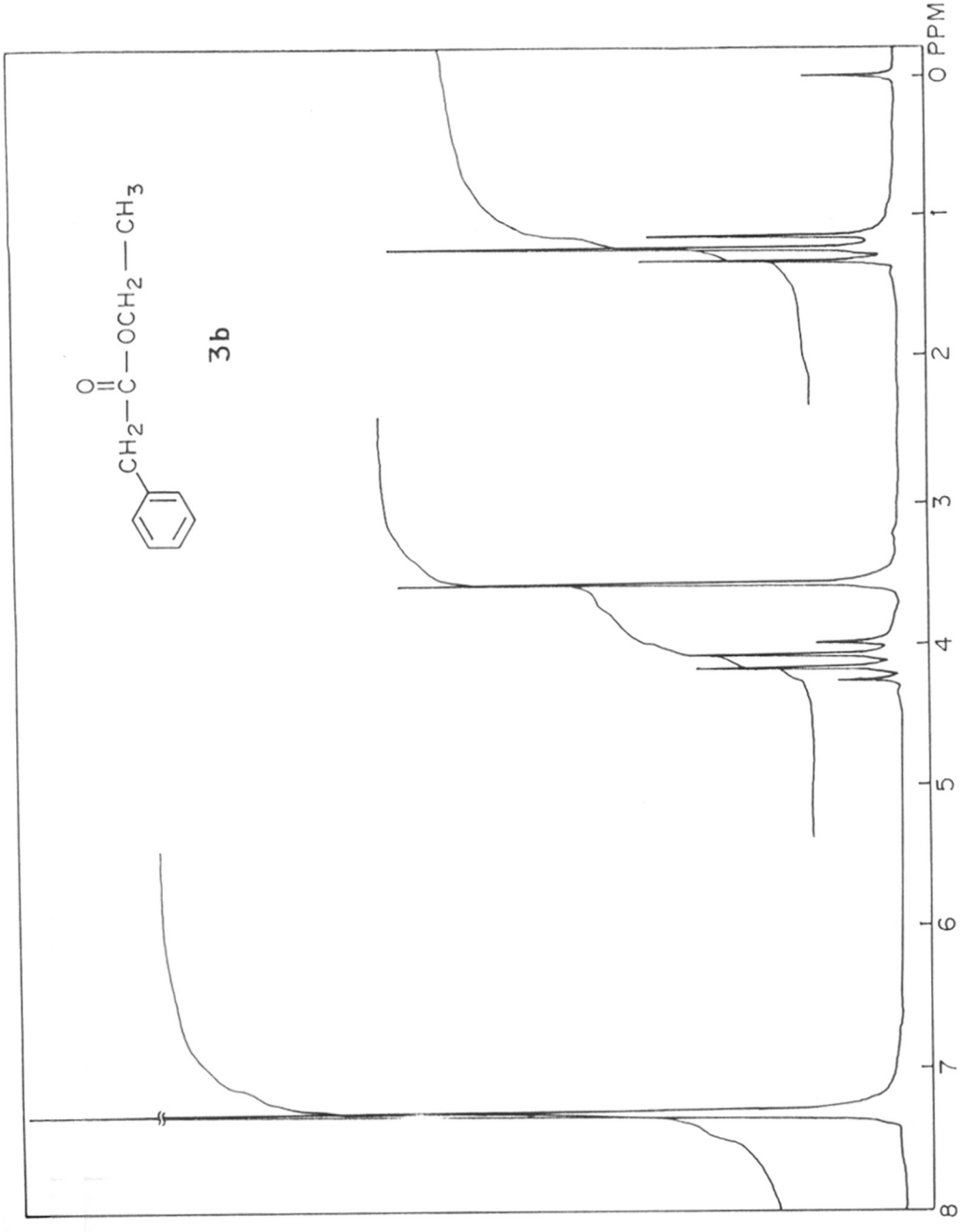
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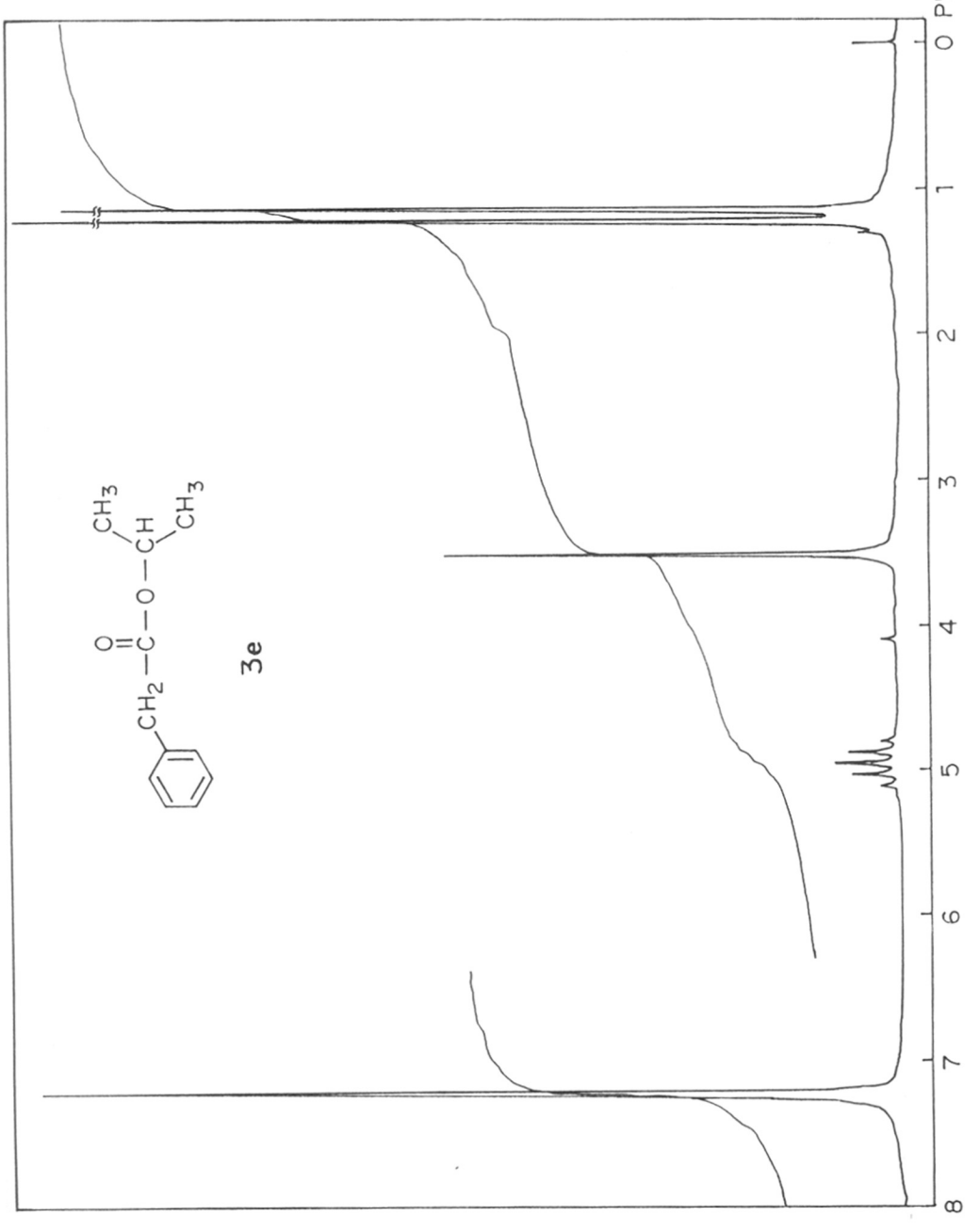
7
6
5
4
3
2
1
0 PPM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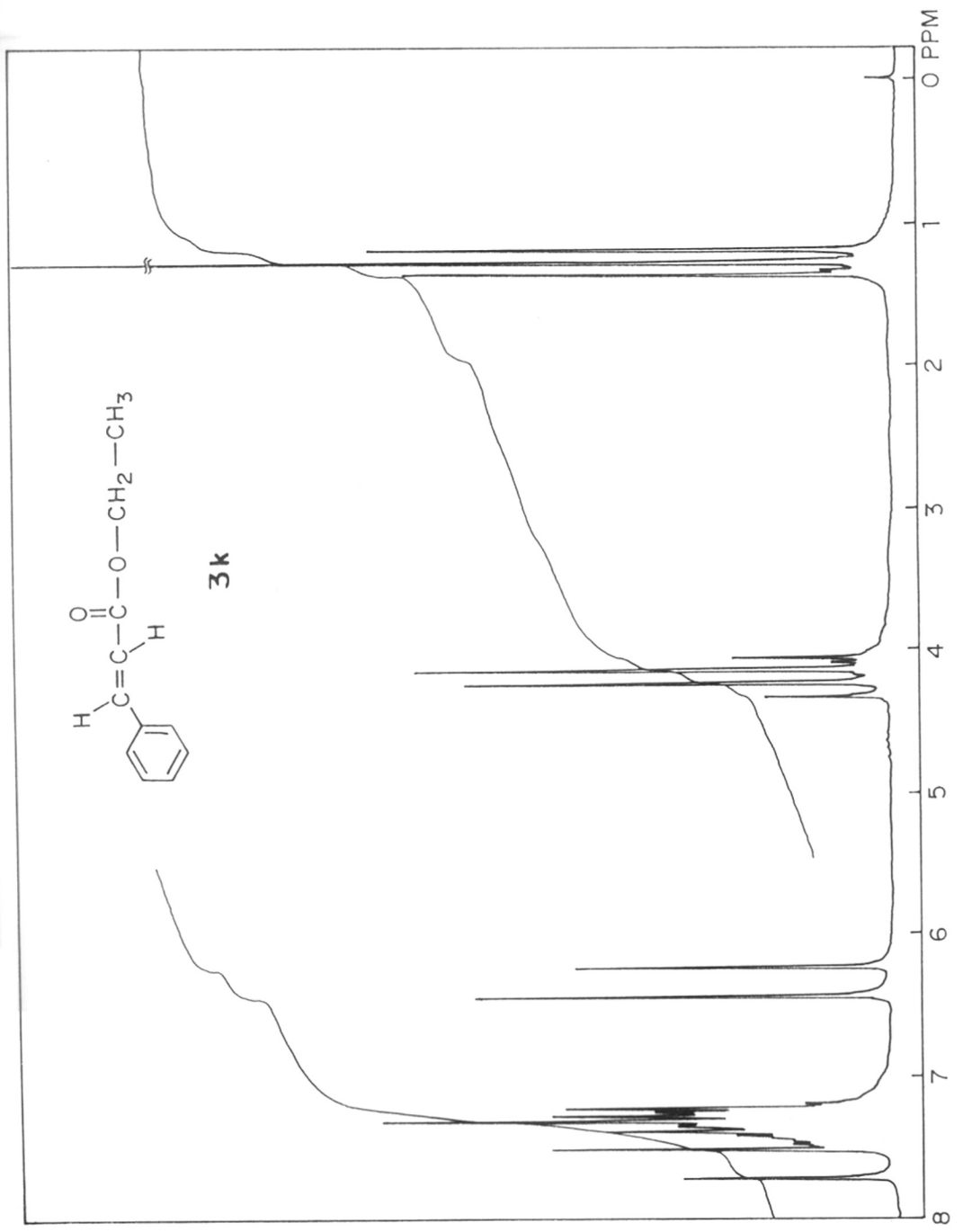
CH
O
CH2—C—O—
3e
8
7
6
5
4
3
2
1
0 PPM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C
O
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H
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7
6
5
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3
2
1
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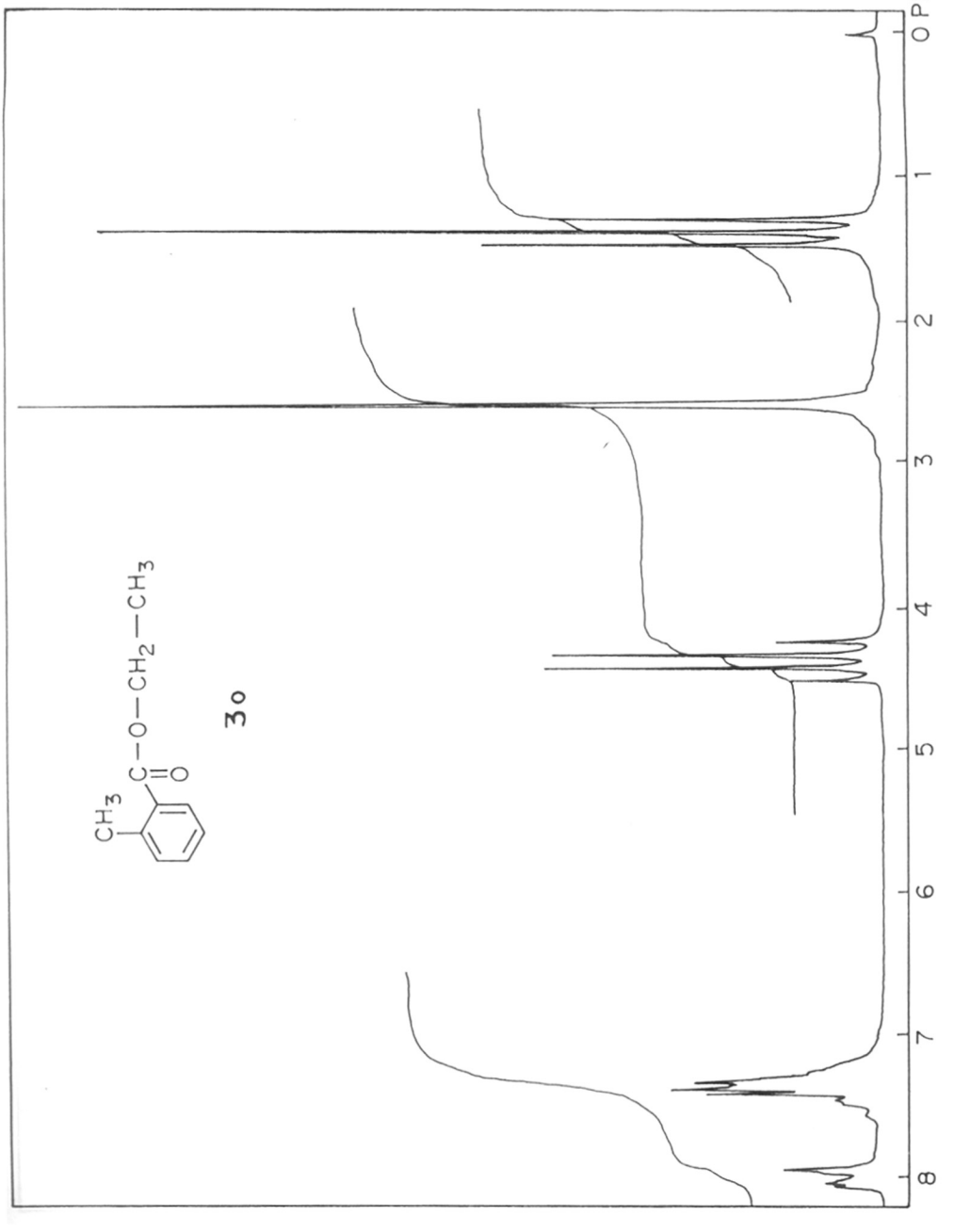
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O
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3
2
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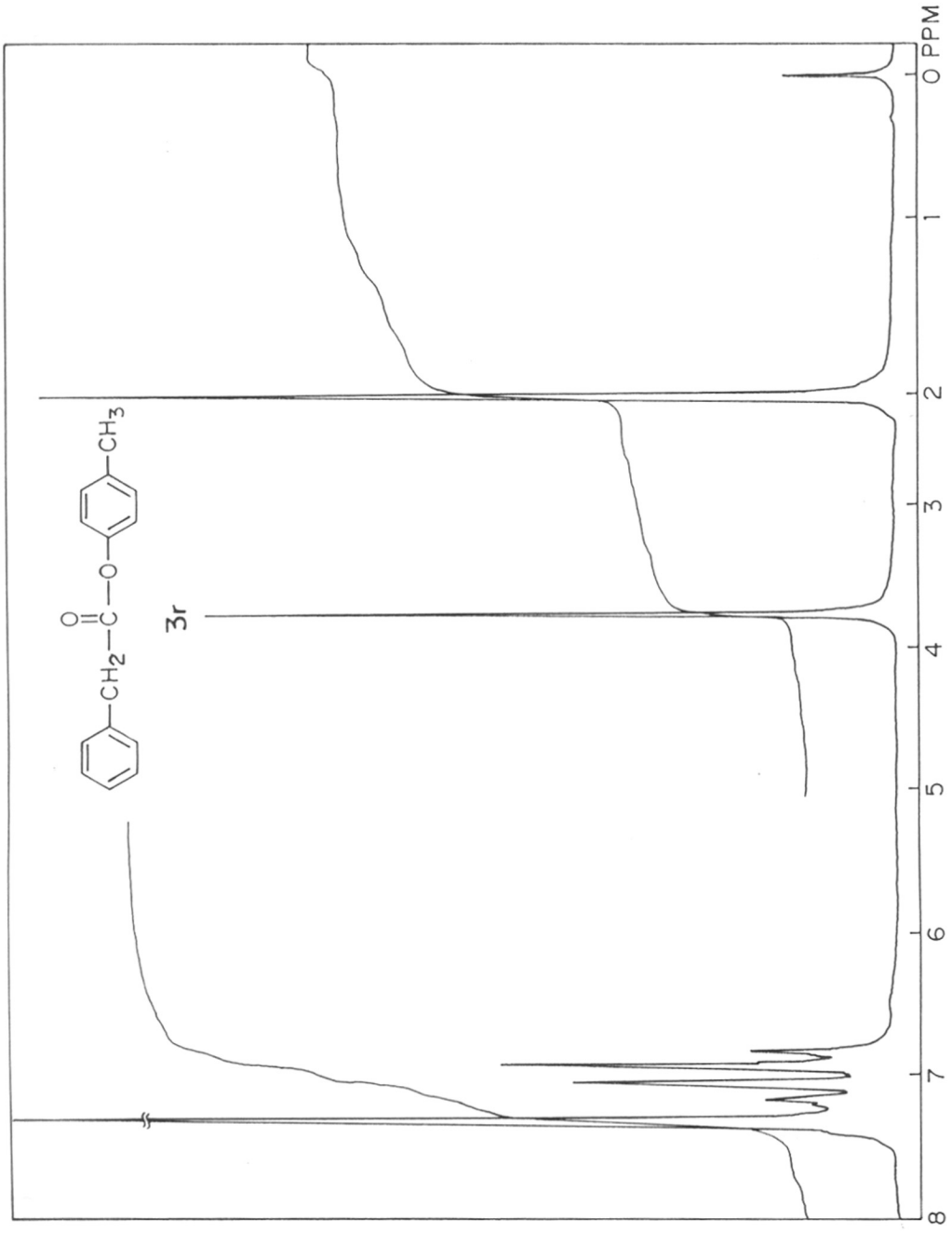
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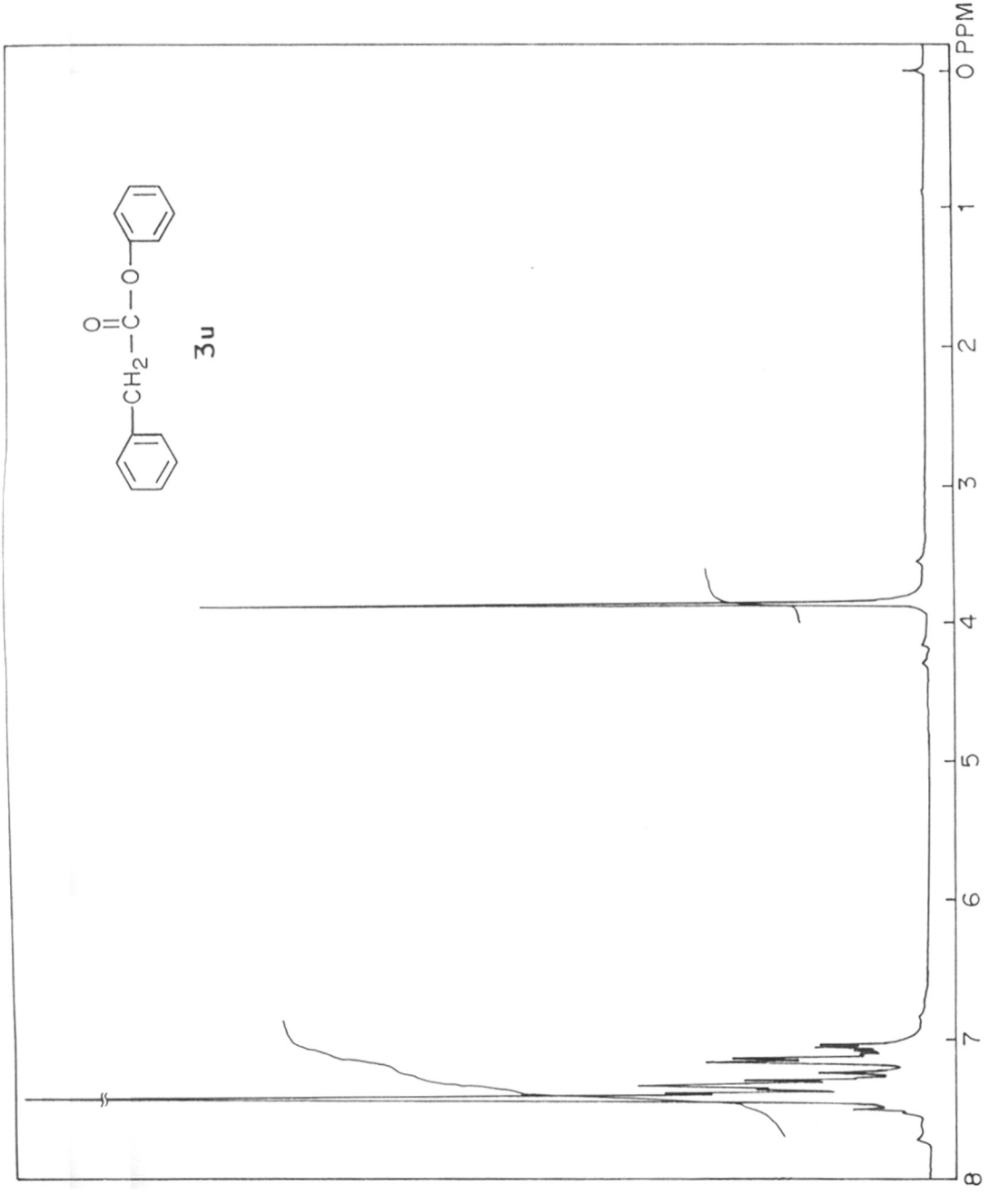
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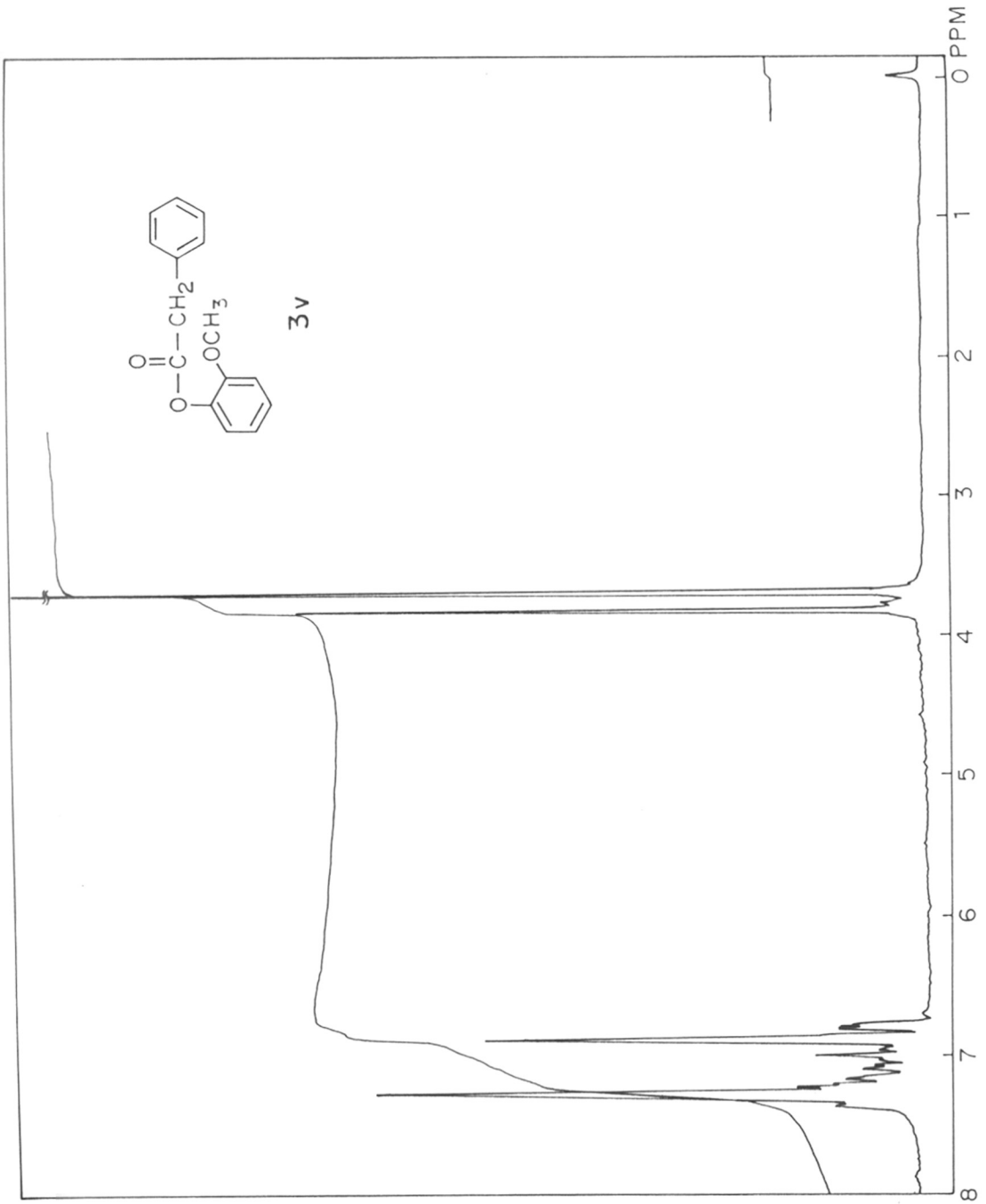
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O—C—CH2
OCH3
3v
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1
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CHAPTER 3

Synthesis of N-monosubstituted amides by the reaction of olefins and alcohols with nitriles

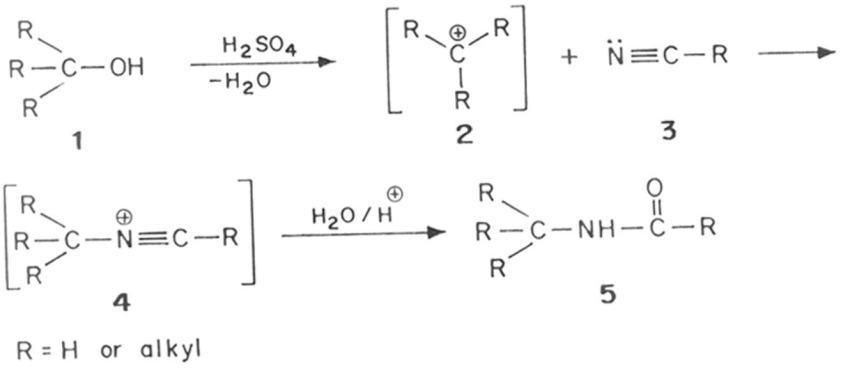
SUMMARY

This chapter describes preparation of wide variety of N-monosubstituted amides. The amides were prepared by reacting olefins or alcohols with nitriles in the presence of zeolite catalyst. Various zeolite catalysts were screened for this purpose and it was observed that, rare earth exchanged RE-HY zeolite gave best results. In this reaction good yields of amides were obtained when nitrile was reacted with tertiary alcohols. Primary alcohols failed to react with nitriles to give corresponding amides. However, benzyl alcohol gave good yield of N-benzylamides.

INTRODUCTION

The Ritter reaction[1] involves conversion of nitriles to N-substituted amides by reacting nitrile with alkenes in the presence of concentrated sulfuric acid. This reaction was discovered way back in 1948 by John J. Ritter. Since then this reaction has been extended to a wide variety of compounds capable of forming carbocation. In this reaction the carbocation is generated from alkene or alcohol (1) by strong acid such as sulfuric acid. The carbocation **2** thus formed is reacted with nitrile **3** to give nitrilium ion **4** which subsequently reacts with water to give N-alkyl amide (**5**) (Scheme 3.1).

Scheme 3.1

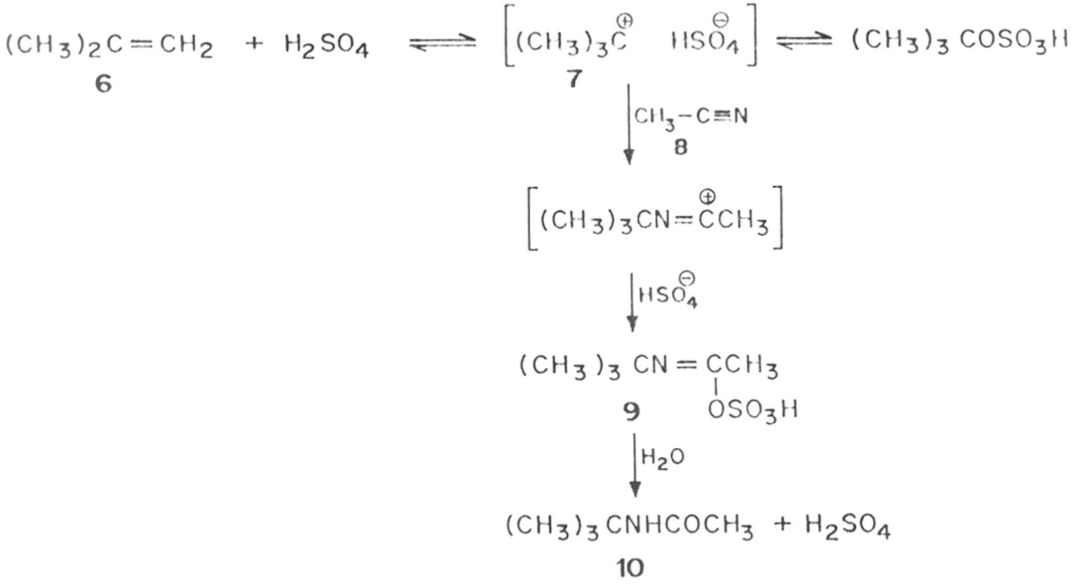


The secondary, tertiary and benzylic alcohols react readily, however, primary alcohols do not undergo this reaction[2]. The alcohols, which give fairly stable carbocation, react with nitrile. The carbocation can be generated from an alcohol or an olefin by protonation or from other sources. In general the carbocation can be generated by acids such as sulfuric acid[1], substituted sulfonic acids[3], phosphoric acid[4], polyphosphoric acid[5] or Lewis acids such as boron trifluoride[6]. This reaction has widely been used for the synthesis of large number of heterocyclic compounds. The amines can be generated by the hydrolysis of amides. Therefore, Ritter reaction is the only convenient method for the preparation of tertiary alkyl amines.

Mechanism

Ritter had suggested the formation of carbocation (Scheme 3.2). Isobutene (**6**) on protonation with sulfuric acid[7] undergo tertiary carbocation formation. The carbocation **7** thus formed reacts with acetonitrile (**8**) to give alkyl iminosulfate intermediate **9**. This alkyl iminosulfate is susceptible to water and get hydrolysed to N-alkyl amide **10**.

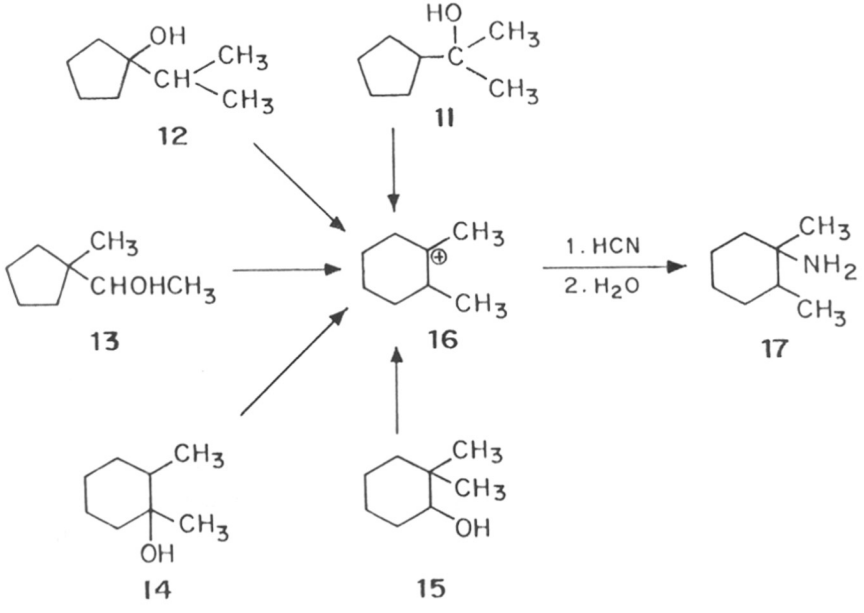
Scheme 3.2



The formation of N-alkylamide by direct alkylation of amide is ruled out as acetamide under similar reaction condition failed to give alkylated product.

Ritter's proposal, the reaction proceeds *via* carbocation intermediate, has been proved by the studies of Jacquior and Chrystol[8]. All the cycloalkynols (**11-15**) as shown in the Scheme 3.3 are

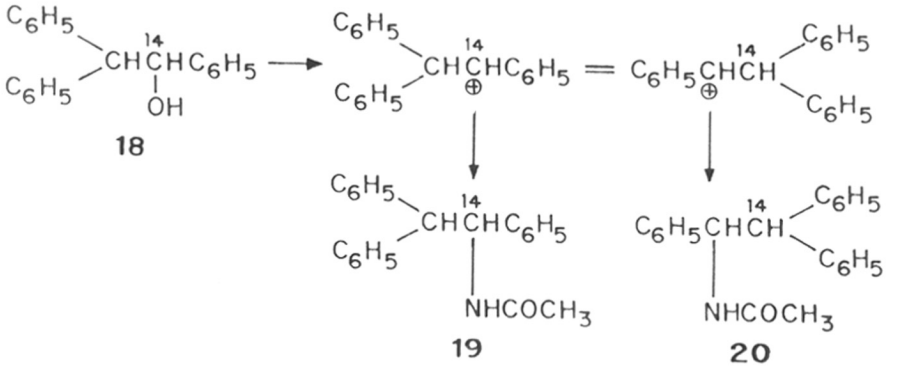
Scheme 3.3



known to rearrange to a common stable carbocation **16** under acidic condition. The alkynols, when treated with hydrogen cyanide, gave 1,2-dimethylcyclohexylamine (**17**) after hydrolysis (Scheme 3.3).

The carbocation mechanism is further supported by Roe and Swern, who employed methane sulfonic acid in place of sulfuric acid[9]. Similar investigation show that C^{14} labelled 1,2,2-tripheylethanol (**18**) when treated with acetonitrile (**8**) in the presence of sulfuric acid led to a mixture of substituted amides **19, 20** resulting from carbocation equilibrium[10,11] (Scheme 3.4).

Scheme 3.4



Other mechanisms suggested for this reaction are cyclic alkylimino sulfate intermediate[12] and ion pair mechanism[13]. Even after years of investigation, the accepted mechanism is the one, which is originally proposed by Ritter[1].

Scope and Limitations

The reaction initially has been studied on simple alkenes and alcohols which can generate carbocation easily, later on it has been extended to a large number of alkenes, alkadienes, alicyclic and spiro alcohols, alkyl chlorides, glycols, aldehydes, chlorohydrins, N-methylolamides, ethers, carboxylic acids, esters, ketones and ketoximes, which can generate carbocation[14]. Various nitriles have also been used for this reaction[14]. These includes hydrocyanic acid, aliphatic nitriles, cyanohydrins, cyano acids and their esters, cyanamide, dicyanamide and cyano complexes of inorganic acids. Ritter reaction has been employed for the synthesis of several heterocyclic compounds.

The Ritter reaction has been extensively reviewed[14]. It is difficult and impossible to include all these reactions in this chapter. Therefore we have described those reactions wherein some interesting modifications have been reported to generate carbocation, which is essential for Ritter reaction.

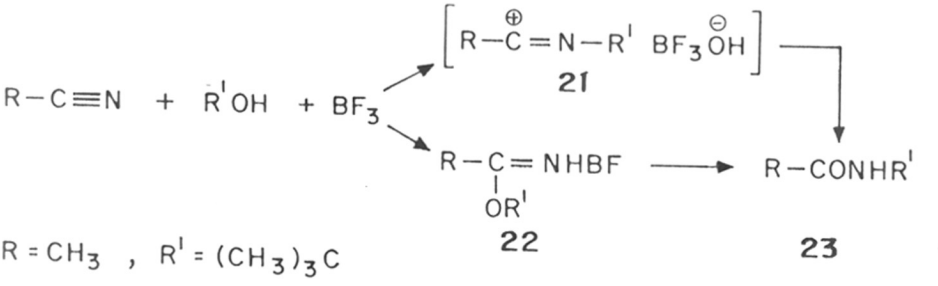
Modifications in Ritter reaction

Several modifications have been reported in the literature for Ritter reaction. The original reaction condition involves the reaction of alcohol or alkene with nitrile in the presence of concentrated sulfuric acid, either at room temperature or at lower temperature. In one of the modification the sulfuric acid is replaced by the Lewis acid such as boron trifluoride, aluminium chloride or zinc chloride[6]. It

has been shown that the reaction proceeds well with tertiary and secondary alcohols, while the primary alcohols do not react. The boron trifluoride is proved to be an excellent catalyst as compared to aluminium chloride and zinc chloride.

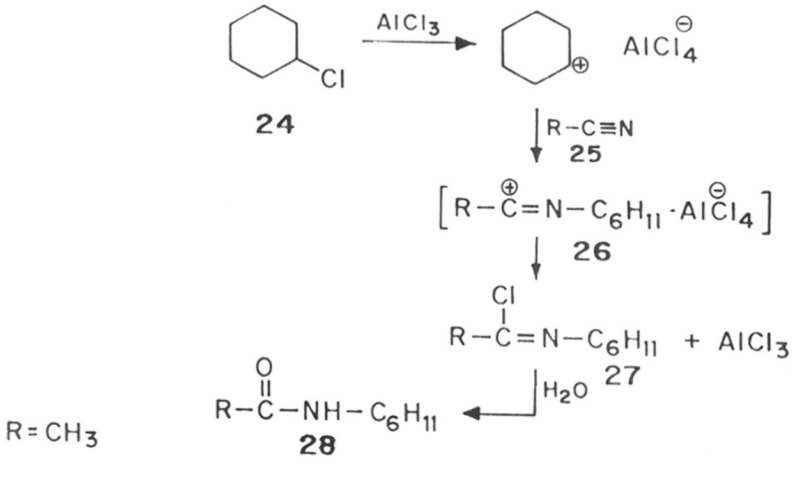
Two mechanisms for this reaction are postulated, one proceeding *via* an initial attack of nitrile nitrogen on the carbocation, to give nitrilium ion **21** and the other *via* an imidate **22** intermediate rearranging into N-alkyl amide **23** (Scheme 3.5).

Scheme 3.5



In the other report[15], the carbocation is generated from cyclopentyl or cyclohexyl chloride (**24**) by Lewis acid such as aluminium chloride. The imino chloride intermediate **27** is formed when the nitrile **25** is reacted with carbocation. This imino chloride **27** is hydrolyzed with water to get N-cyclohexylamide (**28**) (Scheme 3.6).

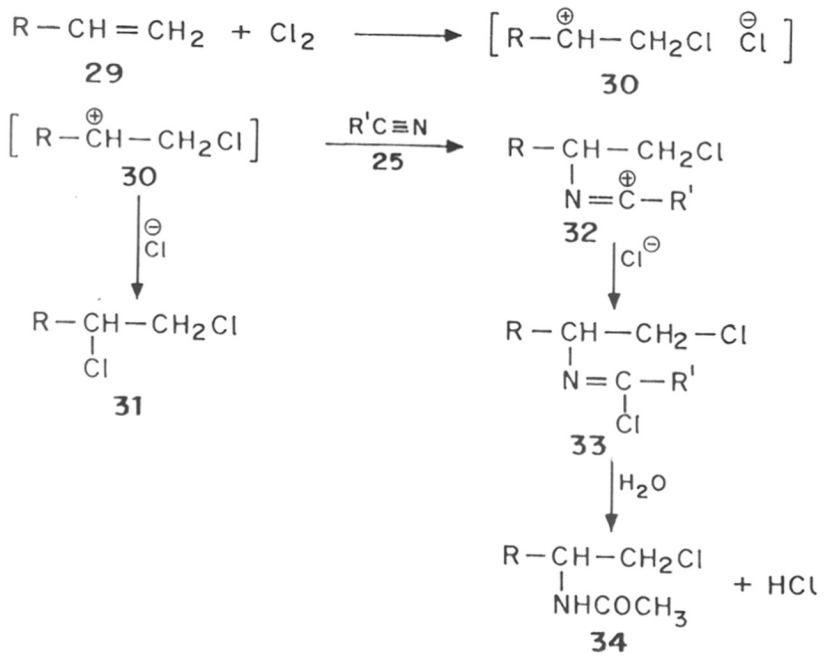
Scheme 3.6



A new three component reaction has been discovered for the synthesis of N-(2-chloroalkyl)amides[16]. This reaction involves chlorination of alkene in nitrile as a solvent. A carbocation **30** generated during chlorination of alkene **29** is either attacked by chloride ion to get

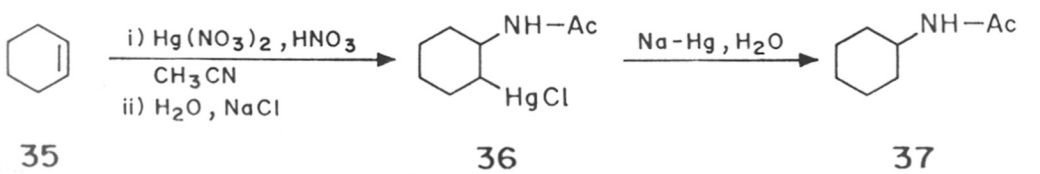
dichloroalkane **31** or by nitrile **25** to get nitrilium ion **32**. This nitrilium ion further reacts with chloride ion to get imino chloride **33**, which on hydrolysis with water gives N-(2-chloroalkyl)amide (**34**) (Scheme 3.7).

Scheme 3.7



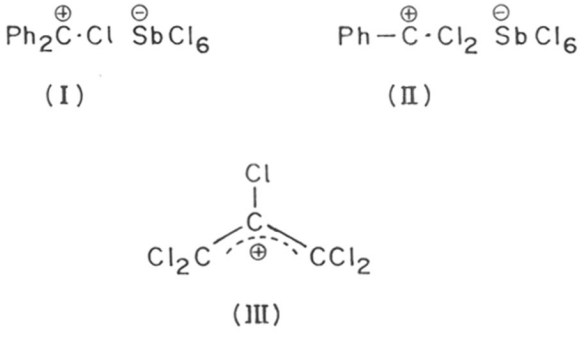
It has been shown that the carbocation can be generated by addition of Hg(II) salt on alkene[17]. This carbocation reacts with nitrile to generate nitrilium ion, which eventually hydrolyzed to amide **37**. The demercuration is achieved by reduction with sodium amalgam followed by hydrolysis with water (Scheme 3.8). H.C. Brown and J. T. Kurek[18] have also utilized Hg(II) salt for the preparation of N-alkylamides using sodium borohydride for demercuration.

Scheme 3.8



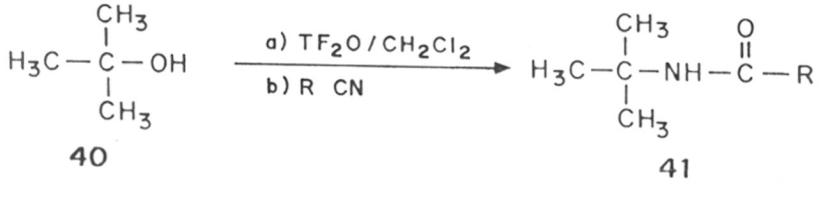
Barton *et al*[19] have used chlorodiphenylmethylium (I), dichloro(phenyl)methylium (II) and pentachloroallylium (III) ions, for generation of nitrilium ion **38** from alcohol and nitrile, which on quenching with water gives N-alkylamides **39** (Scheme 3.9).

Scheme 3.9



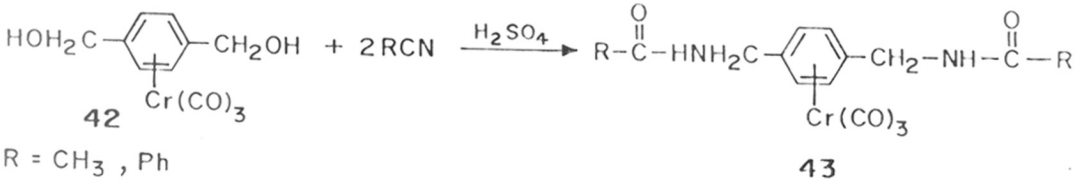
Triflic anhydride[20] has been used as an activator of alcohol **40** for the generation of carbocation, which on subsequent reaction with nitrile gives the Ritter product **41** (Scheme 3.10).

Scheme 3.10



The stability of carbocation is essential for Ritter reaction. The reaction can be considerably improved by using carbocation intermediates stabilized by transition metal complexes *eg.* Arene-$Cr(Co)_3$ Complex[21] **42**. The arene chromium complex remarkably stabilizes α carbocation. The Ritter reaction proceed with very good yields with such transition metal complexed carbocations (Scheme 3.11).

Scheme 3.11



42

R = CH_3 , Ph

43

Cation exchanged resins[22] have been successfully used to generate carbocations from alcohol or alkenes, which further reacted with nitrile to get N-monosubstituted amides. This method is particularly useful for the preparation of acid sensitive amides, like N-alkyl acrylamide.

PRESENT WORK

It is clear from the introduction that most of the modifications suggested for the Ritter reaction are either improvement on the reagent for generation carbocation or activation of alkene or alcohol for facile generation of carbocation. We believe, from our experience and knowledge on zeolites, that the zeolite would generate carbocation from alkene or alcohol at moderate reaction conditions. Most of the zeolite catalyzed reactions are either Bronsted or Lewis acid catalyzed, which is an intrinsic property of zeolite. Zeolites are also known for their shape selective catalysis. In this chapter we have exploited Bronsted acid and Lewis acid properties of zeolite for the preparation of series of N-alkylamide.

Amides are important class organic compounds. They are useful as herbicides, fungicides and insecticides. N-Monosubstituted acrylamide are effective rodent repellent when mixed with 2% food material[23]. N-*t*-Butyl acrylamide is used for the preparation of hair fixing agents and hard lotions[24]. The monomer of N-*t*-butyl acrylamide is used for food packing, adhesives as well as in drugs and cosmetics[25]. N-Cyclohexyl acetamide is used in the prevention of polyamide gelation during spinning[26]. Acrylamide derivatives are used to enhance grip of the tire[27]. The main objective of this study is to provide a method for preparation of N-monosubstituted amides using zeolite catalyst.

RESULTS AND DISCUSSION

The Ritter reaction proceeds *via* generation of carbocation, followed by nitrilium ion, which on subsequent hydrolysis with water gives N-alkylamides. Strong acids such as sulfuric acid, Lewis acid such as aluminium chloride or boron trifluoride are used for the generation of carbocation. Although zeolites act as Bronsted acid as well as Lewis acid, they have not been utilized for Ritter reaction. Apart from their acidic property, zeolites are also known for their shape selectivity, thermal stability and reusability. All these properties make zeolite a industrially important and environmentally safe catalyst. In the recent years researchers have recognized their potential as a catalyst and they have been used in fine chemical industry as well as in basic organic chemistry[28].

This chapter will deal with the utilization of zeolite catalyst for the preparation of various amides.

N-Alkyl acetamides

A mixture of *t*-BuOH and excess of acetonitrile was when heated in a Parr reactor at 100°C for 24 h in the presence of H-ZSM-5 catalyst, offered a white solid in 6% yield. This was identified as N-*t*-butyl acetamide based on following evidence. The solid had mp 98-99°C (lit[6] mp 97-98°C). The ^{1}H NMR spectrum showed a singlet at δ 1.37 for 9 protons of *t*-butyl group. A singlet at δ 1.93 for three protons (CH_3C0) and broad singlet at δ 5.5 (OH), which confirmed the product as N-*t*-butyl acetamide (**46c**). The IR spectrum showed a typical amide band at 1640 cm^{-1} and a molecular ion peak in the Mass spectrum appeared at *m/z* 115 (M^+), which further confirmed the structure of the product.

The success achieved with the help of H-ZSM-5 catalyst, although in low yield prompted us to try other zeolites in order to find out the best catalyst for this reaction. Following sections are devoted for the efforts made in this direction:

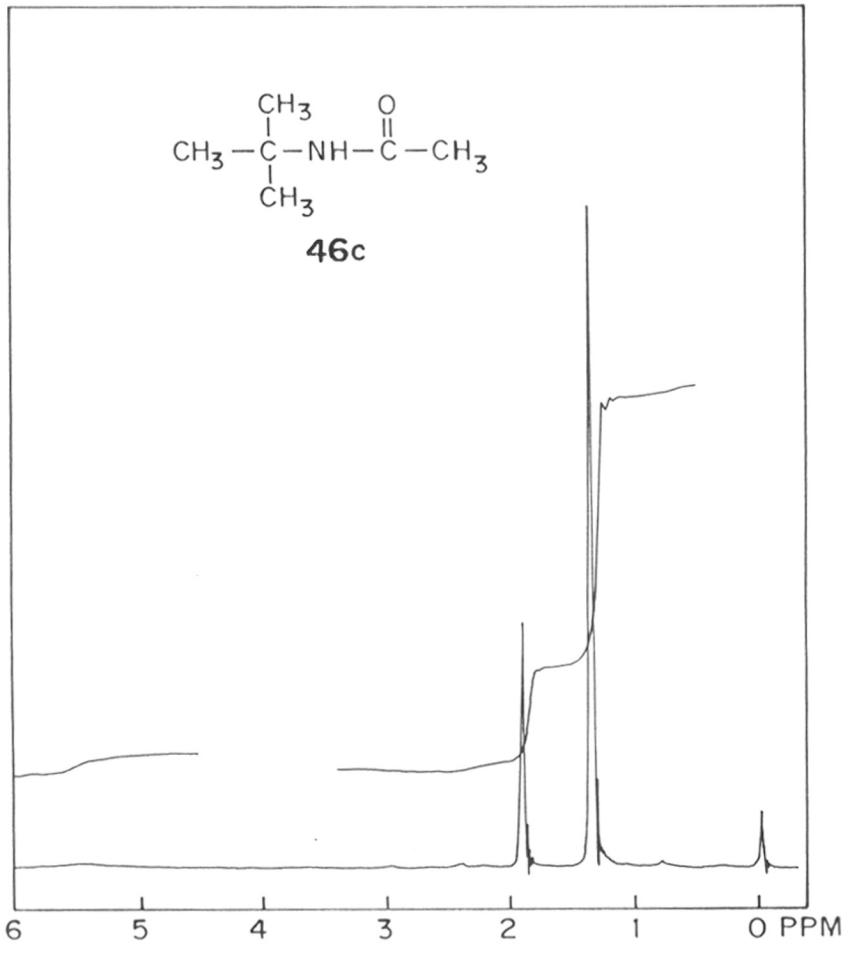
Use of Na-Y and RE-NaY catalyst

A mixture of *t*-BuOH and acetonitrile when heated in a Parr reactor at 100°C for 24 h in presence of Na-Y catalyst, failed to give even a trace of *t*-butyl acetamide. This is obvious because, Lewis or Bronsted acidic sites are required for the generation carbocation. Since Na-Y does not fulfil this condition, the desired product was not formed in presence of this catalyst. To improve the acidity of Na-Y zeolite, the sodium ions were exchanged with rare earth metal ions. The rare-earth exchanged RE-NaY was prepared as described in the experimental section of chapter 2.

A mixture of *t*-BuOH (5 g), acetonitrile (50 mL) and RE-NaY (5 g) catalyst was heated at 100°C for 24 h in a Parr reactor under autogenous pressure. The catalyst was removed by filtration and excess of acetonitrile was distilled off to get N-*t*-butyl acetamide (**46c**) in 22% yield as a pure white crystalline material. No further purification was required. The addition of water was not necessary for the hydrolysis of nitrilium ion to amide, as the water present in the zeolite is sufficient to bring out the transformation under the reaction conditions.

RE-HY catalyst

This reaction, when carried out under similar reaction condition using RE-HY catalyst, N-*t*-butyl acetamide (**46c**) was obtained in 43% yield. The reason for better yield may be attributed to the better acidity of RE-HY catalyst. However, this reaction when carried out with excess of *t*-BuOH, only 10% amide was obtained. The reason for lower yield may be due to the deactivation of the catalyst by water, which is formed by dehydration of *t*-BuOH under these reaction conditions.



NMR OF N-t-BUTYL ACETAMIDE (**46c**)

The use of other catalysts *eg.*, H-mordenite, H-Y, and Ts-1 gave lower yield of the amides (Table 3.1).

Table 3.1. Preparation of N-*t*-butyl acetamide from *t*-BuOH and acetonitrile using various zeolites at 100°C in a Parr reactor.

Entry	Catalyst Used	Yield[a] of **46c** (%)
1.	H-ZSM-5	6
2.	RE-NaY	22
3.	RE-HY	43
4.	H-Mordenite	5
5.	H-Y	5
6.	Ts-1	13

[a]Isolated yield of N-*t*-butyl acetamide (**46c**).

The Table 3.1 reveals that RE-HY (entry No 3) is the best catalyst amongst the catalyst screened. Therefore, RE-HY was selected for optimization of the reaction temperature. All the reaction were carried out by heating a mixture of acetonitrile (50 mL), *t*-BuOH (5 g) and catalyst RE-HY (5 g) at different reaction temperatures for 24 h. The results are summarized in Table 3.2.

Table 3.2. The effect of reaction temperature on the formation of N-*t*-butyl acetamide (**46c**).

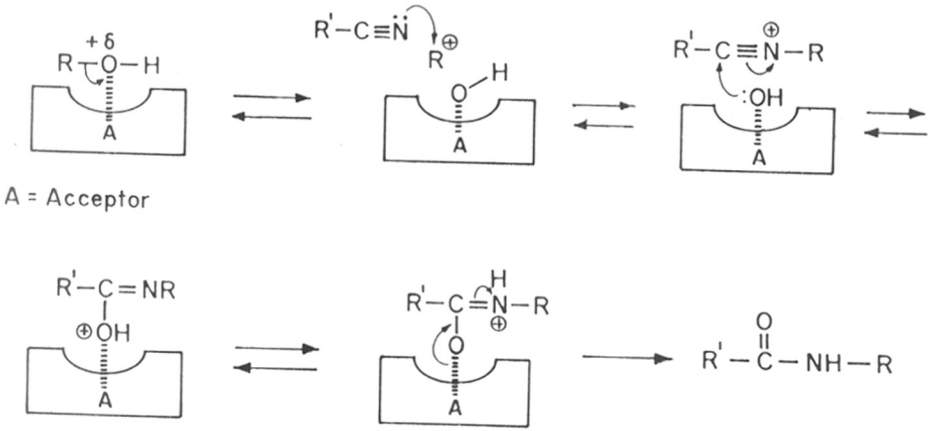
Entry	Temperature	Yield of **46c** (%)
1	50	10
2	80[a]	28
3	100	43
4	120	30
5	140	25
6	160	18

[a] Reaction is carried out in an oil bath at reflux temperature of acetonitrile.

It is evident from the Table 3.2 that the yields progressively increased from 50 to 100°C and decreased when the temperature was further increased. The optimum reaction temperature was found to be 100°C (see entry 3), which gave higher yield of amide.

Mechanism: The probable mechanism of the formation of amide is shown in Scheme 3.12.

Scheme 3.12



Variation in quantity of the catalyst

The reactions of acetonitrile with *t*-BuOH were carried out in a Parr reactor by using varying amount of RE-HY catalyst. However, the reaction time and ratio of acetonitrile and *t*-BuOH were kept constant. It was observed that when amount of catalyst was reduced to half (2.5 parts by mass to that of *t*-BuOH), the yield of amide was dropped considerably and catalytic amount of catalyst (RE-HY) did not give any amide formation.

Based on the above studies, the reaction temperature of 100°C and RE-HY as a catalyst were selected for Ritter reaction. Other N-alkyl acetamides were prepared using these optimized reaction conditions. Thus, a mixture of acetonitrile and alcohols was heated at 100°C in presence of RE-HY catalyst for 24 h in a Parr reactor under autogenous pressure to get amides (**46a-e**). The results are summarized in Table 3.3.

Table 3.3. Preparation of various amides using RE-HY catalyst.

R^1OH + R^2CN ---------> R^1NHCOR^2

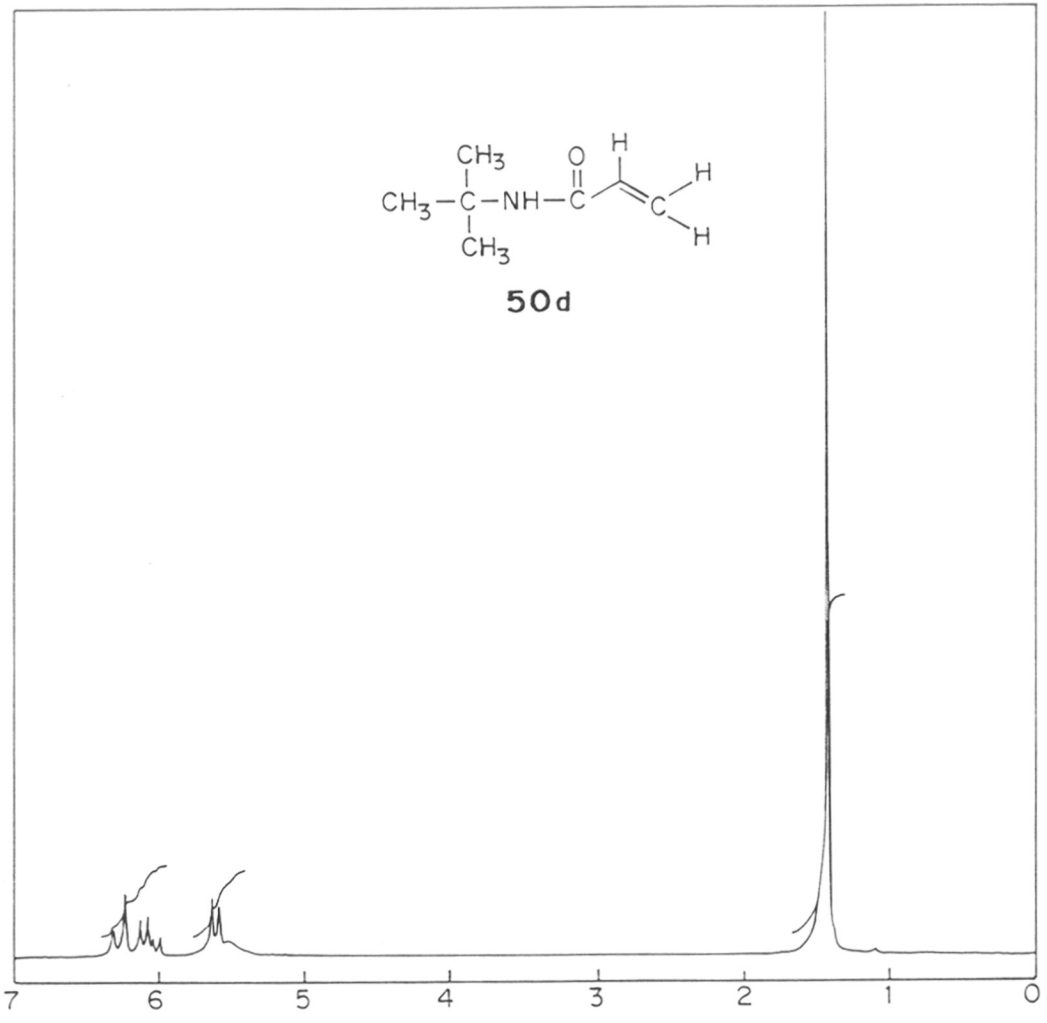
44 45 46a-e

Product	R^1	R^2	Yield(%)
46a	Me	Me	NO reaction
46b	Et	Me	NO reaction
46c	*t*-bu	Me	43
46d	Benzyl	Me	63
46e	Cyclohexyl	Me	20

In case of methanol and ethanol no amide formation was observed, this may be due to the difficulty in formation of primary carbocation under the reaction conditions. The maximum yield (63%) of N-benzyl acetamide (**46d**) was obtained when benzyl alcohol was used as one of the reactant. Since, it gives stable benzylic carbocation. Apart from N-benzyl acetamide a small amount of N,N-dibenzyl acetamide (**47**) (6%) was also obtained by further alkylation of preformed N-benzyl acetamide.

N-Alkyl acrylamides

N-Alkyl acrylamides are important monomers for polyacrylamides. Acrylonitrile as well as acrylamide polymerizes immediately in the presence of strong acid like sulfuric acid. The use of zeolites can avoid polymerization of acrylonitrile or acrylamide as they are weak acids compared to sulfuric acid. Thus, a mixture of *t*-BuOH (5 g) and acrylonitrile (50 mL) was heated in a Parr reactor at 100°C for 24 h in the presence of RE-HY catalyst. The removal of catalyst by filtration and usual work-up gave a solid product in 56% yield. This was identified as N-*t*-Butyl acrylamide (**50d**) based on the following data. The solid had mp 128-130°C (lit[6] mp 126-129°C). The ^1H NMR spectrum showed a singlet at δ 1.37 for 9 protons of *t*-butyl group and a broad signet at δ 5.37 for NH proton. The three olefinic protons showed following splitting pattern 5.56 δ (dd, J=3.5 and 10 Hz), 5.87 δ (dd, J=3.5 and 16 Hz), 6.18 (dd, J=10 and 16 Hz). IR spectrum showed characteristic amide band at 1640 cm^{-1}. Various other alcohols were also reacted with acrylonitrile to give corresponding amide. The results are summarized in Table 3.4.



NMR OF N-t-BUTYL ACRYLAMIDE (50d)

Table 3.4. Reaction of acrylonitrile with various alcohols.

R^1OH + R^2CN -------> R^1NHCOR^2

48 **49** **50a-e**

Product	R^1	R^2	Yield(%)
50a	Me	$CH=CH_2$	No reaction
50b	Et	$CH=CH_2$	No reaction
50c	*i*-Pr	$CH=CH_2$	8
50d	*t*-Bu	$CH=CH_2$	56
50e	Benzyl	$CH=CH_2$	61

The Table 3.4 reveals that methanol and ethanol did not react with acrylonitrile as these alcohols fail to give carbocation under the reaction conditions. However, *t*-BuOH reacted very well with acrylonitrile to give N-*t*-butyl acrylamide (**50d**) in 56% yield. Benzyl alcohol also gave good yield of N-benzyl acrylamide (**50e**, 61%).

Since *t*-BuOH readily forms carbocation, it was reacted with other nitriles using RE-HY catalyst. A mixture of nitrile (1.2 g), *t*-BuOH (3.9 g) and catalyst RE-HY (1.2 g) was heated in an oil bath at 85°C for 48 h. The catalyst was removed by filtration and the filtrate on usual work up gave N-*t*-butyl amide (**51a-c**) in 20-30% yield. The results are summarized in Table 3.5.

Table 3.5. Reaction of t-butanol with different nitriles using RE-HY catalyst.

R^1OH + R^2CN --------> R^1NHCOR^2

51 **52** **53a-c**

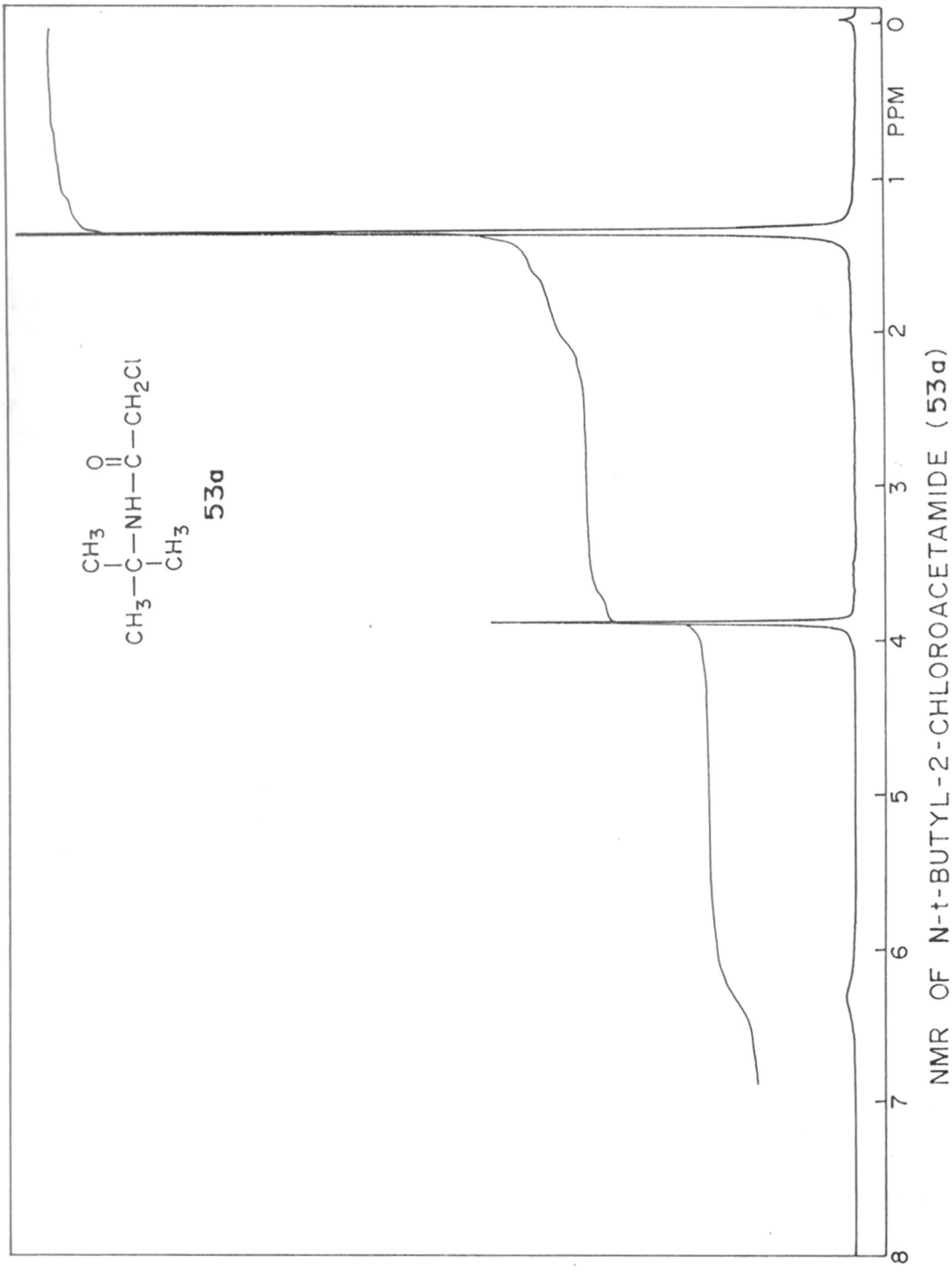
Product	R^1	R^2	Yield(%)
53a	*t*-Bu	CH_2Cl	31
53b	*t*-Bu	CH_2CH_2Cl	21
53c	*t*-Bu	Ph	12[a]

[a] The reaction was carried out in Parr reactor at 140°C using benzonitrile as a solvent.

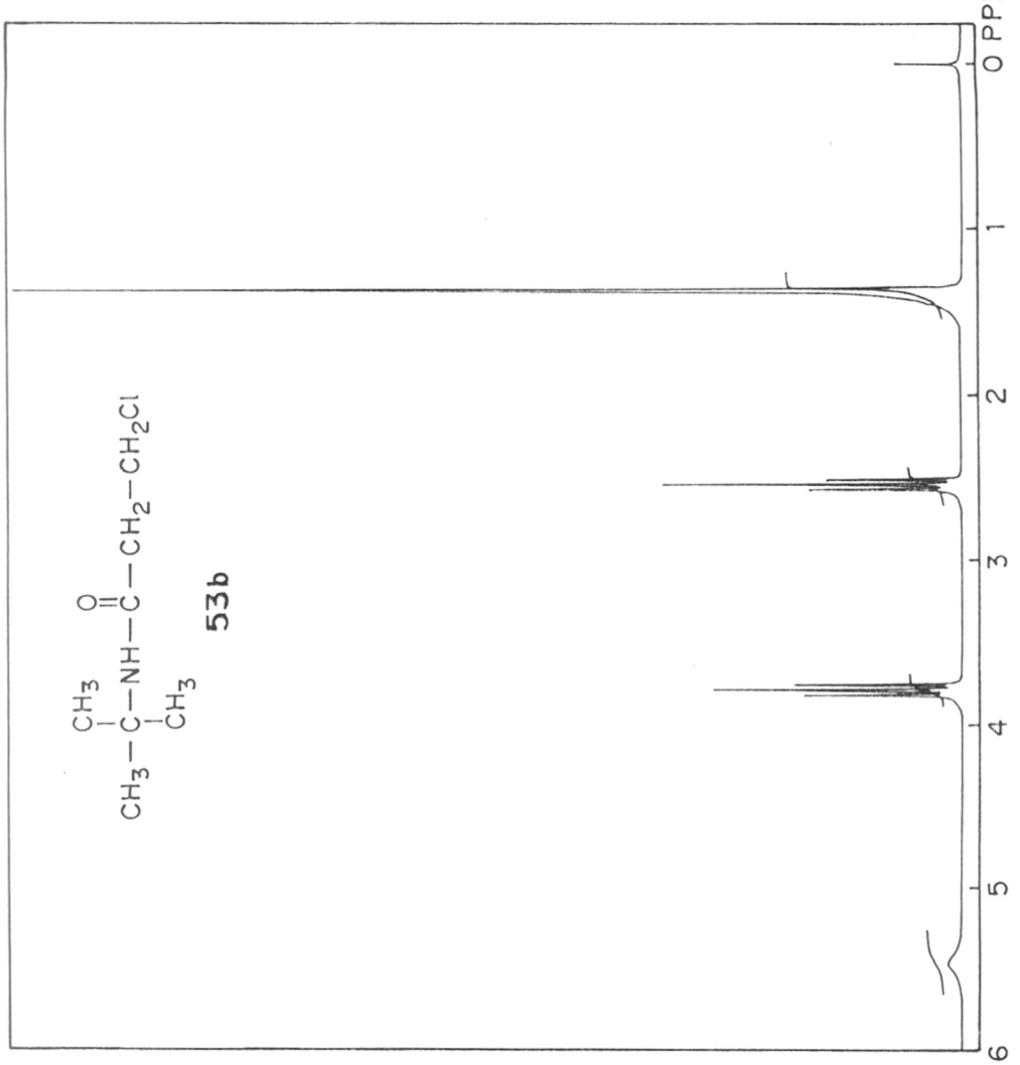
These amides were characterized by their mp, IR and ^{1}H NMR spectral analysis. N-*t*-butyl-2-chloroacetamide (**53a**) had mp 78-80°C (lit[32] mp 82-83°C). IR spectrum showed a band at 3230 cm^{-1} for amide NH and a band at 1665 cm^{-1} for amide carbonyl. ^{1}H NMR showed a singlet at δ 1.35 for 9 protons of *t*-butyl group and a singlet for 2 protons for CH_2Cl at δ3.88. A broad singlet appeared at δ 6.28 for NH proton. Similarly, N-*t*-butyl-3-chloropropanamide (**53b**), had mp 90-91°C (lit[33] mp 93-94°C). The IR spectrum showed a band at 3230 cm^{-1} for amide NH and a band at 1670 cm^{-1} for amide carbonyl. ^{1}H NMR spectrum of **51b** showed a singlet at δ 1.0 for 9 protons of *t*-butyl group. Two triplets were seen at δ 2.51 and 3.80 respectively for $COCH_2$ and CH_2Cl groups. A broad singlet appeared at δ 5.45 for NH proton. N-*t*-butyl benzamide (**53c**) had mp 132-133°C (lit[1] mp 133-134°C). The IR spectrum showed a band at 3290 cm^{-1} for amide NH and a band at 1630 cm^{-1} for amide carbonyl. A sharp band at 1520 cm^{-1} could be assigned to aromatic C=C of aromatic ring. The ^{1}H NMR spectrum showed a singlet at δ 1.5 for nine protons of *t*-butyl group. A broad singlet appeared at δ 6.0 for NH proton. The three protons on the aromatic ring appeared as multiplet at δ 7.30-7.55 and the other two protons on the aromatic ring close to carbonyl showed a multiplet at δ 7.70-7.90.

Reaction of alkene with nitrile

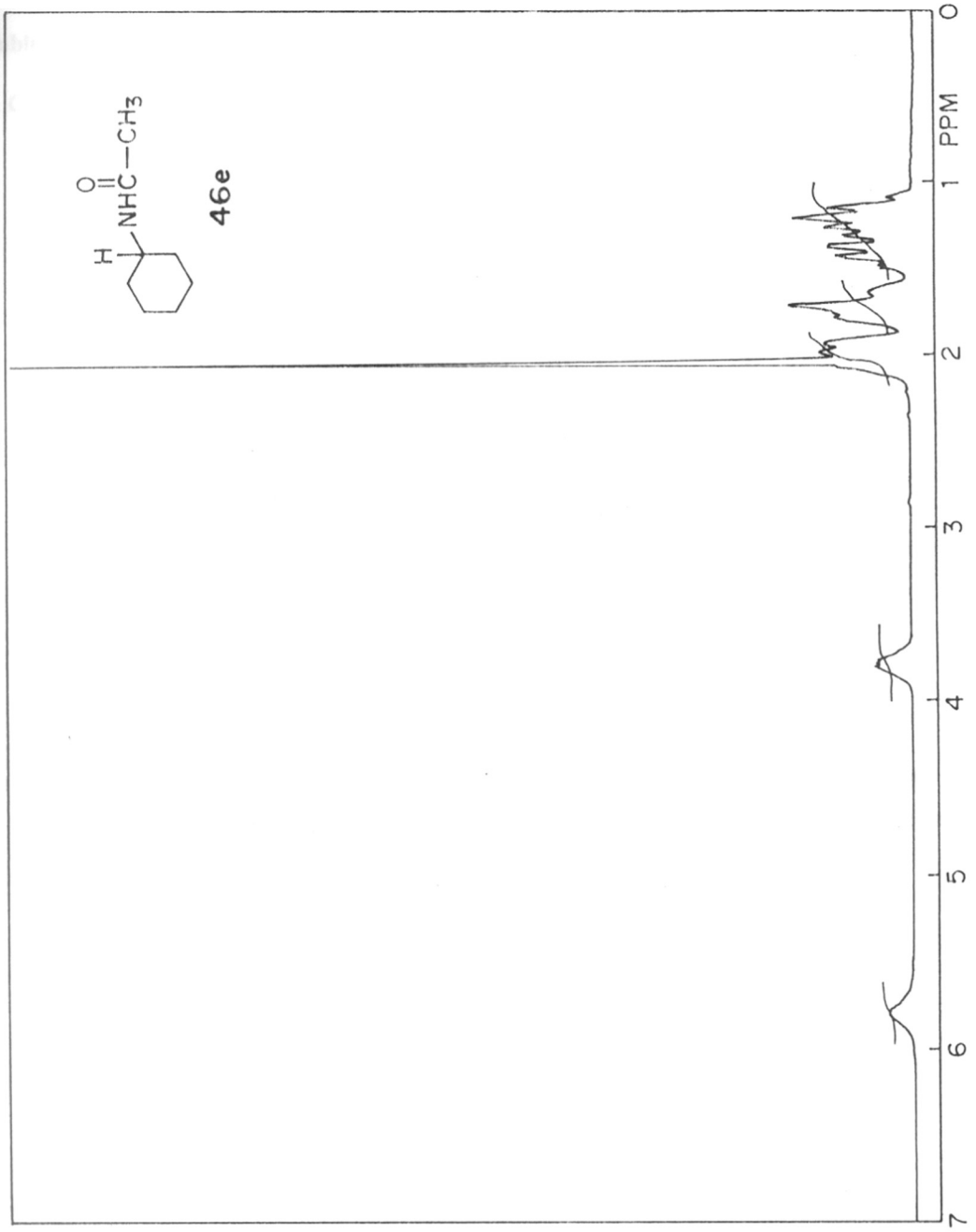
The reaction of cyclohexene with acetonitrile has been studied using zeolite catalysts to get corresponding amides. Thus, a mixture of cyclohexene (5 g), acetonitrile (50 mL) and RE-HY (5 g) was heated in a Parr reactor at 140°C for 24 h. The catalyst was removed by filtration and excess of acetonitrile was distilled off to get a solid product in 18% yield. This was identified as a N-cyclohexyl acetamide (**46e**) based on the following evidence. The solid had mp 106-108°C (lit[35] mp 105-106°C). The ^{1}H NMR spectrum of this product showed a multiplet at δ 1.0-2.0 for 10 cyclohexyl protons and a singlet at δ 2.05 for 3 protons of $COCH_3$. The protons on the carbon attached to nitrogen showed a multiplet at δ 3.55-4.00 and a broad signet was observed at δ 5.8 for NH proton. The IR spectrum showed a typical amide band at 1650 cm^{-1}. A molecular ion (M^+) peak in the mass was spectrum appeared at *m/z* 141. All these physical and spectral data confirmed the formation of N-cyclohexyl acetamide (**46e**). Similarly, other amides **56a-d** were prepared. The results are summarized in Table 3.6.



NMR OF N-t-BUTYL-2-CHLOROACETAMIDE (53a)



NMR OF N-t-BUTYL-3-CHLOROPROPANAMIDE (53b)



NMR OF N-CYCLOXEXYL ACETAMIDE (**46e**)

Table 3.6. Reaction of cyclohexene with various nitriles in the presence of RE-HY catalyst.

Cyclohexene	+	RCN	---------->	N-cyclohexyl-NHCO-R
54		55		46e & 56a-d

Entry No.	Product	R	Yield(%)
1	**46e**	$-CH_3$	18[a]
2	**56a**	$-CH_2Cl$	47[b]
3	**56b**	$-CH_2CH_2Cl$	4[c]
4	**56c**	$-CH=CH_2$	3[a]
5	**56d**	$-CCl=CH_2$	10[c]

[a] Reaction carried out in a Parr reactor at 140°C using nitrile as solvent.

[b] Reaction carried out at 80°C in an oil bath using excess cyclohexene.

[c] Reaction carried out in a Parr reactor at 140°C with cyclohexene and nitrile (1:1) using n-hexene as a solvent.

It has been found that cyclohexene efficiently reacts only with chloroacetonitrile to give N-cyclohexyl 2-chloroacetamide (**56a**) in 47% isolated yield (see entry 2). However, very poor yield of amides was obtained in case of acrylonitrile and β-chloropropionitrile. The formations these amides were confirmed by their spectral data and elemental analysis (see experimental section).

CONCLUSION

In conclusion we have developed a simple and mild method for the preparation of N-alkyl amides using solid acids. The rare earth exchanged Na-Y and H-Y catalysts were found to be suitable for this reaction. The rare earth metal present in the catalyst seems to be helping for the generation of carbocation, which further reacts with nitrile to give nitrilium ion.

The zeolite catalyzed amide formation offers fallowing advantages:

(i) The catalyst can be recovered and reused.

(ii) Use of strong acid is avoided.

(iii) No side product formation is observed.

(iv) Acid sensitive compound like acrylonitrile can be safely used without polymerization.

(v) Unreacted reactants can be recovered and reused.

EXPERIMENTAL

N-*t*-butyl acetamide (46c)

A mixture of *t*-BuOH (5 g, 0.067 mol), acetonitrile (50 mL) was taken in a Parr reactor and freshly activated zeolite RE-HY (5 g) was added slowly. It was then heated to 100°C under autogenous pressure for 24 h. The reactor was cooled to room temperature and catalyst was filtered, washed with chloroform (2x10 mL). The mixture of acetonitrile and chloroform from filtrate was removed by distillation. The residue was recrystalized from pet. ether to give N-*t*-butyl acetamide (**46c**), (2.94g, 43%), mp 98-99°C (lit[6] mp 97-98°C).

IR (Nujol) : 3300, 1655 cm^{-1}.

^{1}H NMR : 1.37 (s, 9H); 1.93 (s, 3H); 5.50 (bs, 1H).

MS (*m/z*) : 115 (M+, 100 %).

Following compounds were synthesized using similar procedure as described for **46c**.

N-benzyl acetamide (46d)

Yield : 63%

Mp : 62-63°C (Toluene-petroleum ether) (lit[29] mp 61°C).

IR (Nujol) : 3420, 1655, 1380, 1220 cm^{-1}.

^{1}H NMR : 0.94 (s, 3H); 4.32 (d, J = 6.4 Hz, 2H); 6.00 (bs, 1H); 7.22 (s, 5H).

N,N-dibenzyl acetamide (47)

Yield : 6%

: oil Purified by column chromatography (10% ethyl acetate in pet.ether).

IR (Neat) : 1640, 1500, 1420, 1370, 1240 cm^{-1}.

^{1}H NMR : 2.2 (s, 3H), 4.40 (s, 2H), 4.60 (s, 2H), 6.90-7.50 (m, 10H).

N-isopropyl acrylamide (50c)

Yield : 8%

Mp : 61-62°C (lit[30] mp 62°C).

IR (Nujol) : 3230, 1640, 1610, 1240 cm^{-1}.

^{1}H NMR : 1.20 (d, J = 9.75 Hz, 6H), 4.05-4.35 (m, 1H), 5.60 (dd, J = 2.4 Hz and 9.75 Hz, 1H), 6.10 (dd, J = 9.75 Hz and 14.6 Hz, 1H), 6.25 (dd, J = 2.4 Hz and 14.6 Hz, 1H), 7.30 (bs, 1H).

N-*t*-butyl acrylamide (50d)

Yield : 56%

Mp : 128-130°C (Benzene-pet. ether) (lit[6] mp 126-129°C).

IR (Nujol) : 3260, 1660, 1630 cm^{-1}.

^{1}H NMR : 1.37 (s, 9H); 5.37 (bs, 1H); 5.56 (dd, J = 3.5 & 10Hz, 1H); 5.87 (dd, J = 10 & 16Hz); 6.18 (dd, J = 3.5 & 16Hz).

MS (m/z) : 127 (M$^+$, 10%); 72 (100%).

N-benzyl acrylamide (50e)

Yield : 61%

Mp : 69-71°C (Toluene-pet. ether) (lit[31] mp 70-72°C).

IR (Nujol) : 3185, 1645, 1625, 1450 cm^{-1}.

^{1}H NMR : 4.50 (d, J = 4.8Hz, 2H); 5.65 (dd, J = 2.5 & 14.6Hz, 1H); 6.15 (dd, J = 9.7 & 14.6Hz, 1H); 6.35 (dd, J = 2.4 & 14.6Hz, 1H); 7.35 (m, 5H).

N-cyclohexyl acetamide (46e)

Method A: A mixture of cyclohexenol (5 g), acetonitrile (50 mL) and freshly activated zeolite RE-HY (5 g) was heated in Parr reactor at 100°C for 24 h. The usual work-up as described for **46c** gave 1.34 g (20%) of N-cyclohexyl acetamide (**46e**), mp 106-108°C (lit[35] mp 105-106°C).

IR (Nujol) : 3300, 1650 cm^{-1}.

^{1}H NMR : 1.00-2.00 (m, 10H); 2.05 (s, 3H); 3.55-4.00 (m, 1H); 5.80 (bs, 1H).

MS (m/z) : 141 (M$^+$, 100%).

Method B: A mixture of cyclohexene (5 g, 0.060 mol) and acetonitrile (50 mL) was taken in a Parr reactor and freshly activated zeolite RE-HY (5 g) was added slowly. It was then heated to 140°C under autogenous pressure for 24 h. The reactor was cooled to room temperature and catalyst was filtered,

washed with chloroform (2x10 mL). The mixture of acetonitrile and chloroform from filtrate was removed by distillation. The residue was recrystalized from benzene peroleum ether give N-cyclohexyl acetamide (**46e**) (1.45 g 18%).

N-*t*-butyl benzamide (53c)

A mixture of *t*-BuOH (5 g, 0.067 mol), benzonitrile (50 mL) was taken in a Parr reactor and freshly activated zeolite RE-HY (5 g) was added slowly. It was then heated to 140°C under autogenous pressure for 24 h. The reactor was cooled to room temperature and catalyst was filtered, washed with chloroform (2x10 mL). The mixture of benzonitrile and chloroform from filtrate was removed by distillation under reduced pressure. The residue was recrystalized from pet. ether to give N-*t*-butyl benzamide (**53c**), (1.43g, 12%), mp 133-135°C (lit[1] mp 134-134.5°C).

Yield : 12%

IR ($CHCl_3$) : 3290, 1630, 1520, 1110, 1220 cm^{-1}.

^{1}H NMR : 1.5 (s, 9H), 6.0 (bs, 1H), 7.30-7.55 (m, 3H), 7.70-7.90 (m, 3H).

N-cyclohexyl acrylamide (56c)

Yield : 3%

Mp : 110-111°C (lit[36] mp 113-114°C).

IR (Nujol) : 3245, 1640, 1605cm^{-1}.

^{1}H NMR : 0.95-2.05 (m, 10H); 3.78 (m, 1H); 5.35 (dd, J = 3.2 & 10Hz, 1H); 5.95 (dd, J = 10 & 17Hz, 1H); 6.25 (dd, J = 3.2 & 17Hz, 1H).

MS (m/z) 153 (M^+, 100%).

N-Cyclohexyl-2-chloro-2-propenamide (56d)

Yield : 10%

Mp : Low melting solid.

IR (Nujol) : 3315, 1680, 1520 cm^{-1}.

^{1}H NMR : 0.90-2.08 (m, 10H); 3.48-4.00 (m, 1H); 5.28 (bs, 1H); 5.52 (d, J = 3.2Hz, 1H) 6.25 (d, J = 3.2Hz, 1H).

N-Cyclohexyl-3-chloropropanamide (56b)

A mixture of cyclohexene (1.64 g, 0.02 mol) 3-chloropropionitrile (1.78 g, 0.02 mol) and n-hexane (50 mL) was taken in a Parr reactor and freshly activated zeolite RE-HY (1 g) was added slowly. It was then heated to 140°C under autogenous pressure for 24 h. The reactor was cooled to room temperature and catalyst was filtered, washed with chloroform (2X10 mL). The chloroform was removed by distillation. The crude solid thus obtained was recrystalized from benzene/pet. ether to get N-cyclohexyl-3-chloropropanamide (**56c**) (0.151 g 4%) mp 106-108°C (lit[36] mp 109-110°C).

IR (Nujol) : 3220, 1610 cm^{-1}.

^{1}H NMR : 0.90-2.12 (m, 10H); 2.54 (t, J = 8Hz, 2H); 3.74 (t, J = 8Hz, 2H); 5.42 (bs, 1H).

MS (*m/z*) : 189 (M^+, 18%); 108 (100%).

N-*t*-butyl-2-chloro acetamide (53a)

A mixture of *t*-BuOH (3.9 g, 0.052 mol), chloroacetonitrile (1.2 g, 0.016 mol) and freshly activated zeolite (RE-NaY, 1.2g) was heated in an oil bath with stirring at 80°C for 48 h. The catalyst was filtered off and excess of *t*-BuOH was removed by distillation. The residue was recrystalized from benzene pet. ether to give N-*t*-butyl-2-chloroacetamide (**53a**) (2.23 g 31%) mp 78-80°C (lit[32] mp 82-83°C).

IR (Nujol) : 3230, 1665 cm^{-1}.

^{1}H NMR : 1.35 (s, 9H); 3.88 (s, 2H); 6.28 (bs, 1H).

MS (*m/z*) : 149 (M^+, 33%); 134 (100%).

Following compound were synthesized using similar procedure as described for **53a**.

N-*t*-butyl-3-chloropropanamide (53b)

Yield : 21%

Mp : 90-91°C (Benzene-petroleum ether) (lit[33] mp 93-94°C).

IR (Nujol) : 3230, 1670 cm^{-1}.

^{1}H NMR : 1.40 (s, 9H); 2.51 (t, J = 2H); 3.80 (t, J = 2H); 5.45 (bs, 1H).

N-cyclohexyl-2-chloroacetamide (56a)

A mixture of cyclohexene (4.0 g, 0.048 mol), chloroacetonitrile (1.2 g, 0.016 mol) and freshly activated zeolite (RE-NaY, 1.2g) was heated in an oil bath with stirring at 80°C for 48 h. The catalyst was filtered off and excess of cyclohexene was removed by distillation. The residue was recrystalized from pet. ether : toluene (9:1), to give N-cyclohexyl-2-chloro acetamide (**56a**), (1.38 g, 47%), mp 105-106°C (lit[34] mp 106°C).

IR (Nujol) : 3240, 1635 cm^{-1}.

^{1}H NMR : 0.95-2.00 (m, 10H) 3.55-3.92 (m, 1H); 4.02 (s, 2H); 6.45 (bs, 1H).

MS (*m/z*) : 175 (M^+, 17%); 94 (100%).

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CHAPTER 4

SECTION A: An improved process for the preparation of linear alkylbenzene

SUMMARY

The use of zeolite catalysts for the alkylation of benzene with long chain alcohols/olefins is described in this section. In this method a mixture of alcohol/olefin and benzene was heated at elevated temperature under autogenous pressure in the presence of zeolite catalyst to give alkylbenzene in very high conversion. An industrially feasible method was developed for the preparation of linear alkylbenzene (LAB) used in detergents, by alkylation of benzene with a mixture of olefin (C_{10-13} carbon chain) and paraffin (8:92) on fixed bed reactor. Various parameters like, temperature, WHSV, molar ratios of the reactants were studied to achieve maximum conversion of olefin to linear alkylbenzene.

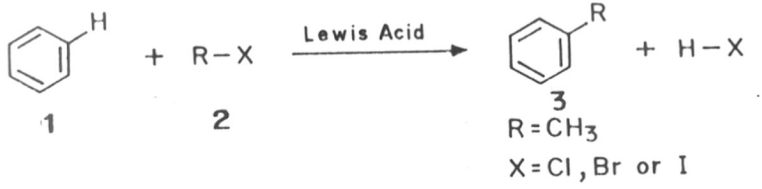
INTRODUCTION

Friedel-Crafts[1] alkylation is the most widely used reaction for nuclear alkylation of aromatic compounds. This reaction involves generation of carbocation which subsequently reacts with aromatic compounds. This is basically an electrophilic aromatic substitution reaction. The scope and limitations of this reaction is extensively studied by Olha[2,3]. The preparation of alkylbenzene using this reaction with various alkylating agent and catalyst is discussed in this chapter.

Preparation of alkylbenzene (3) from alkyl halide

Alkyl halides **2** are known to alkylate benzene (**1**) and activated benzene derivatives in the presence of strong Lewis acids such as aluminium chloride[4] or Ferric chloride. The overall reaction can be represented as shown in the Scheme 4.1.

Scheme 4.1



This is a typical electrophilic aromatic substitution reaction. The Friedel-Crafts alkylation can be carried out using primary, secondary and tertiary alkyl halides. Aluminium chloride forms a complex with alkyl halide and this complex acts as an electrophile. In case of active halides very small amount of catalyst is enough for alkylation. However, alkylation with unreactive halides such as methyl chloride, large amount of catalyst required[5].

Preparation of alkylbenzenes from alkenes

Alkenes have been used as a alkylating agent in the presence of strong acid catalyst to get alkylbenzenes. The strong acids such as H_2SO_4, HF protonate alkenes to generate carbocation, which reacts with benzene. This reaction follows Markovnikov's rule[6] for the formation of more stable carbocation, which alkylates the aromatic ring. The use of $AlCl_3$ or BF_3 as Lewis acids has also been reported for this alkylation reaction. A systematic study of alkylation of benzene with 1-dodecene in the presence of $AlCl_3$, H_2SO_4 and HF as a catalyst has been reported by Olson[7] and Alul[8].

Preparation of alkylbenzenes from alcohols

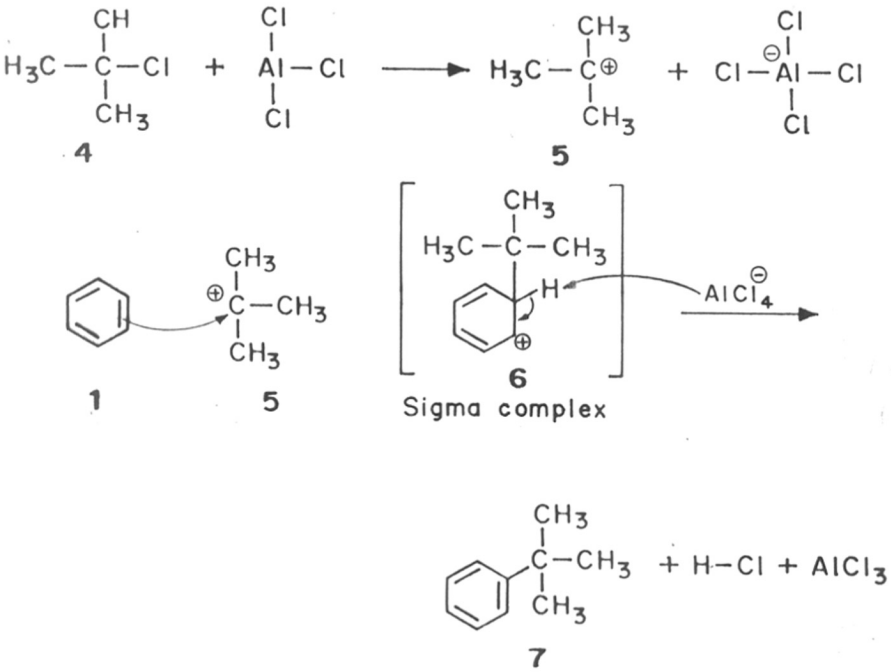
Alcohol is another alkylating agent used for Friedel-Crafts alkylation. The alkylation of benzene with amylalcohol in the presence of boron triflouride has been studied by Steitweser[9]. The excess of Lewis acid is required for this reaction as the catalyst complexes with OH group of alcohol[5]. Proton acids are also used as a catalyst for alkylation of benzene with alcohol. Protic acids such as sulfuric, sulfonic, chlorosulfonic, fluorosulfonic, phosophoric, polyphosphoric acids, hydrogen fluoride[2] possess strong catalytic activity toward Friedel-Crafts reaction. Hydrogen fluoride[10] is used as a catalyst in industry for alkylation reaction due to it's excellent catalytic activity and easy recovery.

Lewis acids like aluminium chloride and bromide are most commonly used for Friedel-Crafts reactions. Other frequently used metal halides[6] are $BeCl_2$, $ZnCl_2$, BF_3, BCl_3, $GaCl_3$, $GaBr_3$, $TiCl_4$, $TiBr_4$, $ZrCl_4$, $SnCl_2$, $SnCl_4$, $SbCl_5$, $BiCl_3$, $FeCl_3$[6], etc. A large amount of work has been carried out to establish the overall order of reactivity of these catalyst[5].

Mechanism

Friedel-Crafts alkylation proceeds *via* sigma complex, generated by the electrophilic addition of benzene to carbocationic intermediate. There is a direct evidence from IR and NMR spectra that *t*-butyl carbocation[11] (**5**) is quantitatively formed when *t*-butyl chloride (4) is reacted with $AlCl_3$ in anhydrous liquid HCl (Scheme 4.2). The *t*-butyl cation so formed, reacts with benzene (1) and give sigma complex **6**, which subsequently loses a proton to give *t*-butylbenzene (7).

Scheme 4.2



Limitations of Friedel-Crafts alkylation[6]

a) Friedel-Crafts alkylation proceeds smoothly with benzene, halobenzene and activated aromatic systems, while strongly deactivated benzene derivatives such as nitrobenzene gives poor yield of the Friedel-Crafts product.

b) Like other carbocation reaction, Friedel-Crafts alkylation is also susceptible to carbocation rearrangement. Alkylbenzene like *t*-butylbenzene, *iso*-propylbenzene, ethylbenzene can be conveniently synthesized by Friedel-Crafts alkylation as the corresponding cations are not prone to rearrangement. However, Friedel-Crafts alkylation of benzene with n-propyl halides normally gives *iso*-propylbenzene, due to more stability of secondary carbocation.

c) Di and polyalkylation are frequently observed in Friedel-Crafts alkylation, because the product of Friedel-Crafts alkylation is more reactive than starting material. The problem of polyalkylation can be avoided by using large excess of benzene. If the mole ratios of benzene:ethylbenzene is kept 50:1, the concentration of ethylbenzene will be very low in the reaction media, therefore, the electrophile will react preferentially with benzene. The product is separated from excess of benzene by distillation and unreacted benzene is recycled.

PRESENT WORK

As discussed in the introduction of this chapter, alkylbenzene preparation by alkylation of benzene with alkyl halide, alkene, or alcohol using Lewis acid such as $AlCl_3$, $FeCl_3$, BF_3 and proton acid such as H_2SO_4 or HF, suffers from various drawbacks. The $AlCl_3$ and H_2SO_4 are not only corrosive but are also not recoverable. Though HF is recoverable, it is an extremely hazardous substance to handle; in addition such homogeneous acid catalysts are a source of pollution and corrosion. It is therefore, desirable to replace these catalysts for electrophilic substitution of benzene by non-corrosive and environmentally safe heterogeneous catalysts. The manufacture of ethylbenzene from ethylene and benzene over phosphorous doped ZSM-5 zeolite[12] at 400°C is an excellent example in which conventional Lewis acid and proton acid catalyst have been successfully replaced by zeolite catalyst. This process eliminates the problem of corrosively, toxicity and effluent pollution from the earlier manufacturing process of ethylbenzene using conventional Lewis acid catalyst.

The present work describes the use of zeolite catalyst for the alkylation of benzene with long chain alcohols and alkenes. The alkylation of benzene with long chain alcohol/olefin can be extended for the manufacture of linear alkyl benzene (LAB), which is an intermediate used in the production of linear alkylbenzene sulphonate. The term linear alkylbenzene[13] has been used to describe a group of phenylalkanes having benzene ring attached at any position of a straight alkyl chain having 9-15 carbon atoms.

The linear alkylbenzene found uses in the manufacture of detergents and surfactants. The main advantages of using LAB in detergent is, they are bio-degradable and therefore environmentally safe. For the manufacture of LAB the starting materials are usually linear alpha olefins or haloalkanes[10]. The alpha olefins having 9-15 carbon atoms are prepared by catalytic dehydrogenation of n-paraffins and the olefins thus formed are used for alkylation of benzene in the presence of HF as a catalyst. n-Paraffins are chlorinated to get haloalkanes. These haloalkanes are used for alkylation of benzene with Lewis acid. A wide variety of heterogeneous catalysts have been investigated so far. The alkylation of benzene with long chain olefins have been reported over heteropoly acids[14], clays[15], pillered clays[16].

The main objective of our study is to provide an industrially viable process for alkylation of benzene using long chain olefins or alcohols at relatively lower temperature and milder reaction conditions. The long chain alcohols derived from natural sources[10], such as palm kernel oil, coconut

oil and tallow, can be alkylated with benzene to produce LAB. Thus, alkylation of benzene has been carried out using alcohols with 8-16 carbon atoms in presence of various zeolite catalyst to give alkylbenzenes. Similarly, olefins of 8-12 carbon atoms have also been used for alkylation of benzene. A comparative study of alkylation of benzene with alcohols and olefins has been carried out.

RESULTS AND DISCUSSION

Alkylation of benzene with long chain linear alcohols

A mixture of n-octanol, benzene and zeolite catalyst (H-ZSM-5) in a ratio (w/w) of 1:10:1 was refluxed for 24 h. However, these reaction condition failed to give even a trace of alkylated product and almost all unreached benzene and n-octanol was recovered from the reaction mixture. The same reaction when carried out at 140°C in a Parr reactor for 24 h also did not give any alkylated product. The reason for the failure of the reaction can be attributed to the lower strength of proton acidity of H-ZSM-5 catalyst to generate carbocation for electrophilic aromatic substitution. Therefore, we thought that it is necessary to use a catalyst with high strength of Lewis and Bronsted acidity. The rare earth exchanged Y type zeolite (RE-NaY) would be a better choice for such alkylation reaction as this catalyst is known to provide required Lewis as well as Bronsted acidity.

A mixture of n-octanol, benzene and RE-NaY catalyst (1:10:1) was heated in a Parr reactor at 140°C for 24 h. The catalyst was recovered by filtration and the excess of benzene from the filtrate was removed by distillation. A colorless oily alkylated product was obtained in 87% yield. The ^{1}H NMR spectrum of this product showed a multiplet at δ 0.5-1.7 for 15 protons and a triplet at δ 2.5 with J = 8 Hz for two benzylic protons. A singlet at δ 7.0 was observed for 5 aromatic protons. The IR spectrum did not show presence of OH group but showed absorption bands at 1600 and 1500 cm^{-1} for aromatic C=C of benzene ring. These spectral data clearly showed the presence of alkylated product. The GC analysis of this product showed 4 peaks indicating the formation of four isomeric alkylated products (Fig 1). The presence of unreacted alcohol could not be detected by GC analysis showing 100% conversion of alcohol to alkylbenzene. The R.T. (Retention Time) and area % corresponding to each peak is tabulated in Table 4.1. The four peaks may be due to 1-Phenyl, 2-Phenyl, 3-Phenyl and 4-Phenyloctanes. The formation of mixture of phenyloctane clearly indicates that the initially formed carbocation undergoes rearrangement to give different positional isomers.

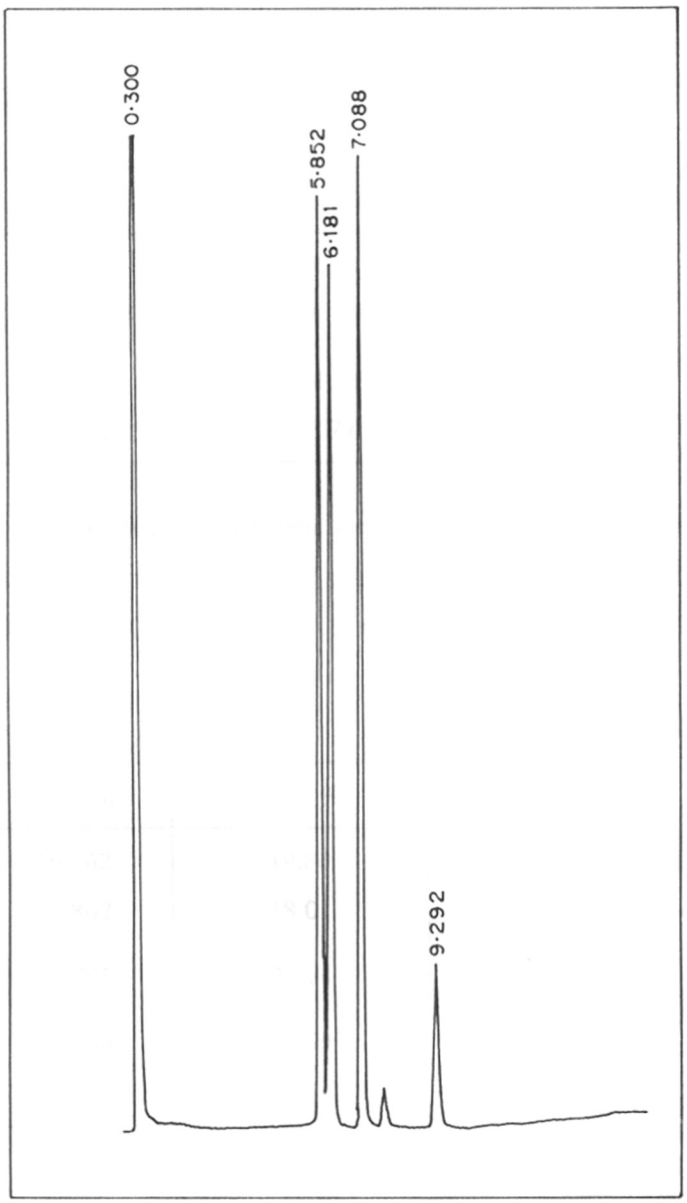


FIG. 1: GC ANALYSIS PRODUCT (BENZENE+n-OCTANOL)

Table 4.1. GC analysis of phenyloctanes.

R.T. (min)	Area (%)
5.852	29.97
6.181	29.15
7.088	34.11
9.292	6.79

1-Decanol (**8**) was reacted with benzene under similar reaction conditions using RE-NaY catalyst. The product isolated as a colorless oil obtained in 95% yield showed 5 peaks for different positional isomers (**9-13**) on GC analysis The R.T. and area % are tabulated in Table 4.2.

Table 4.2. GC analysis of phenyldecanes.

R.T. (min)	Area (%)
16.162	19.80
16.862	18.01
17.785	21.74
20.230	29.79
25.556	10.64

GC-MS Analysis

The reaction mixture was also analyzed by GC-MS which showed five peaks. The molecular ion peak (M^+) corresponding to each peak appeared at 218. However, the fragmentation pattern was found to be different for different positional isomers (Fig 2a-e).

In this case five positional isomers of the carbocation are possible due to hydride shift. All these carbocation can react with benzene to give five different isomeric products **9-13** (Scheme 4.3). To confirm the presence these positional isomers in the reaction mixture, all the five positional isomers of phenyldecane were synthesized independently as follows:

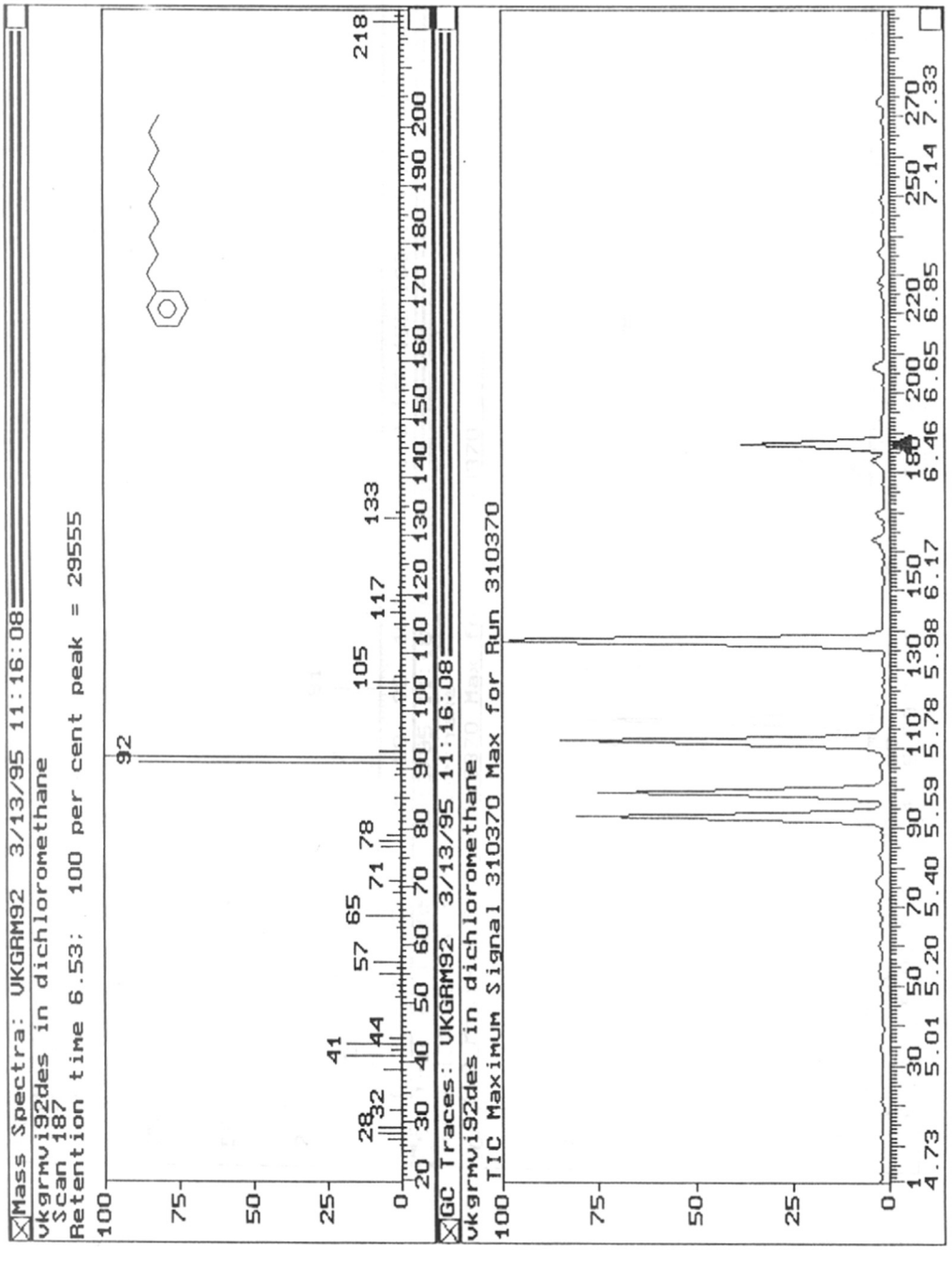


FIG.2a : GC-MS ANALYSIS OF PRODUCT (BENZENE + 1-DECANOL)

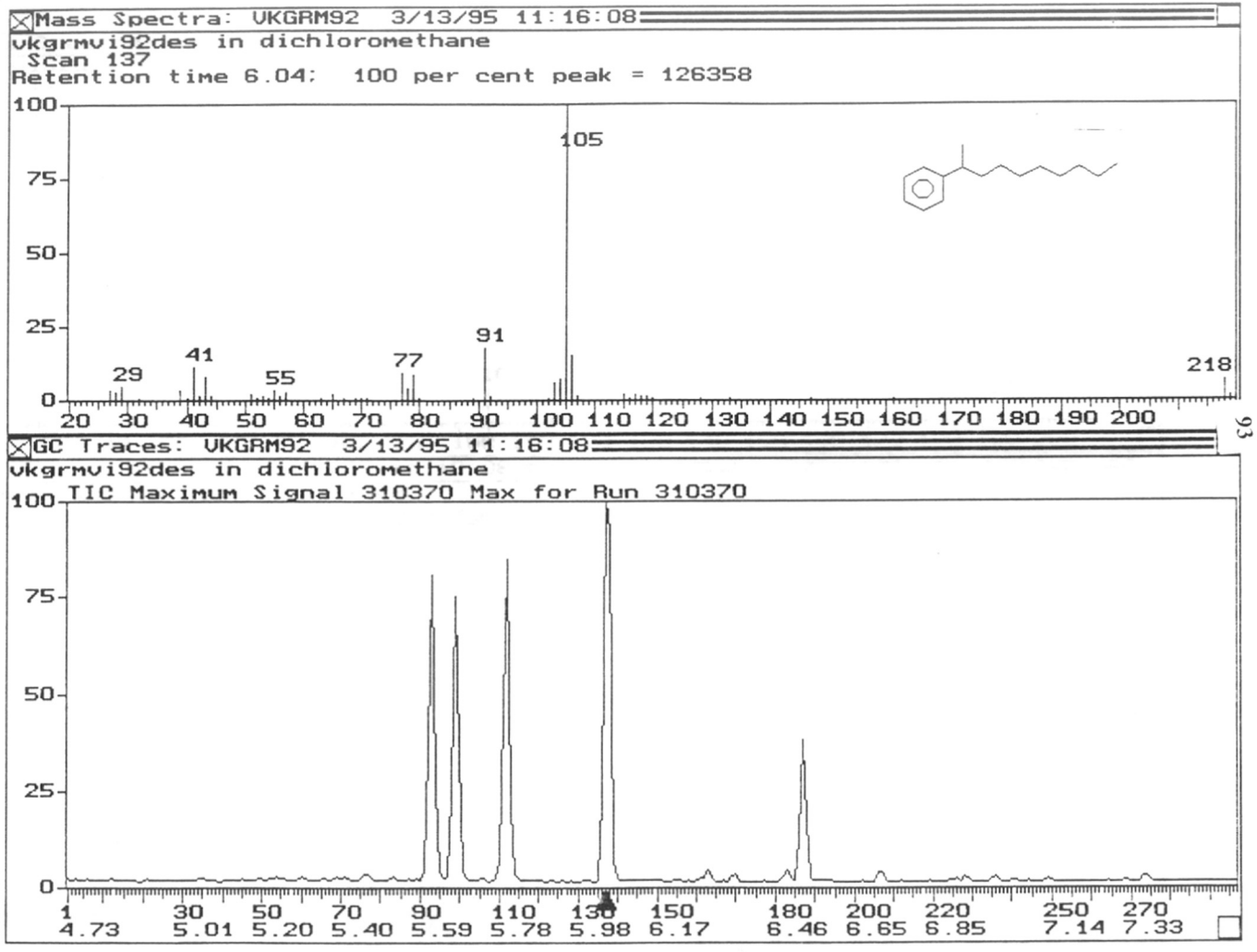


FIG. 2b: GC-MS ANALYSIS OF PRODUCT (BENZENE + 1-DECANOL)

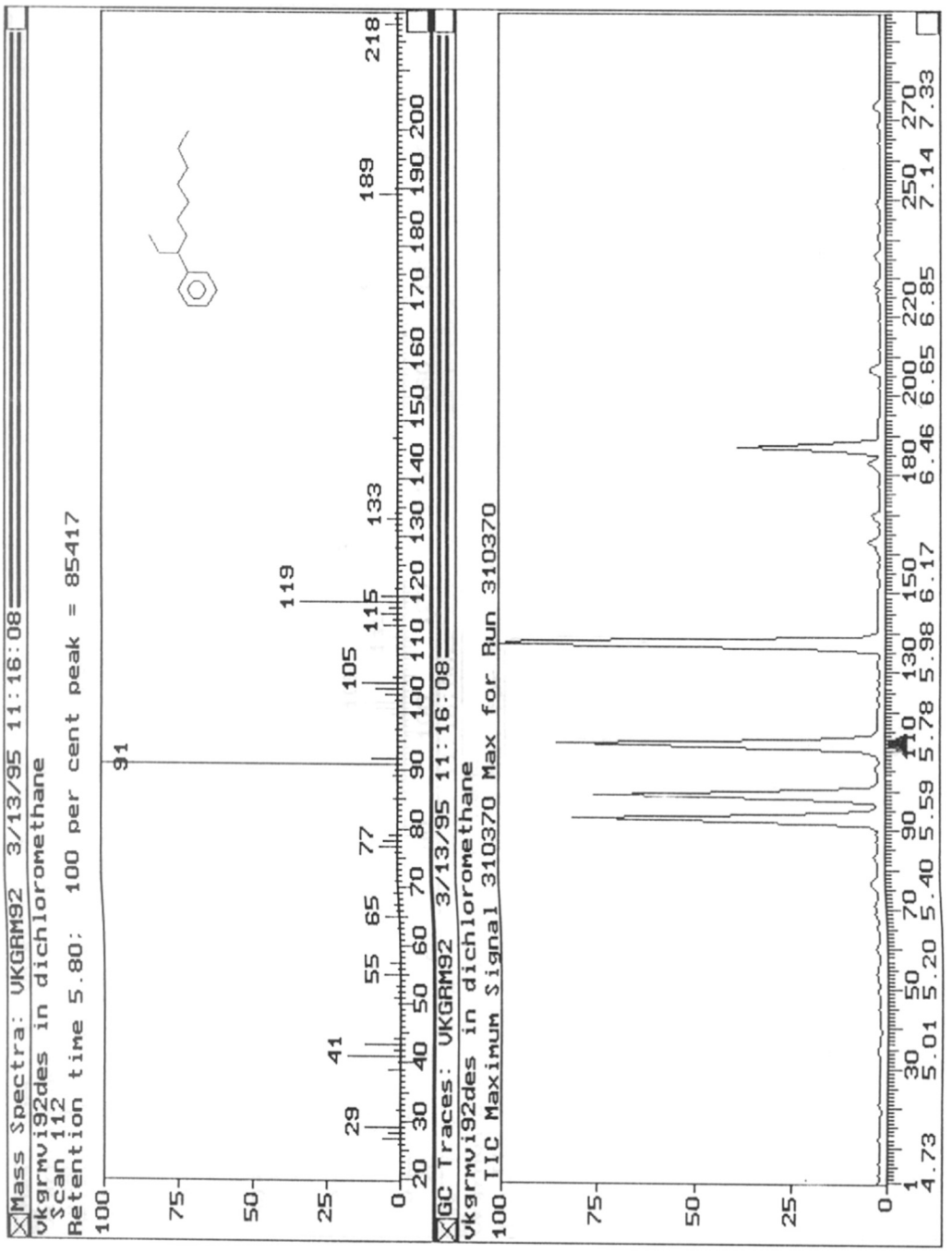


FIG. 2c: GC-MS ANALYSIS OF PRODUCT (BENZENE + 1-DECANOL)

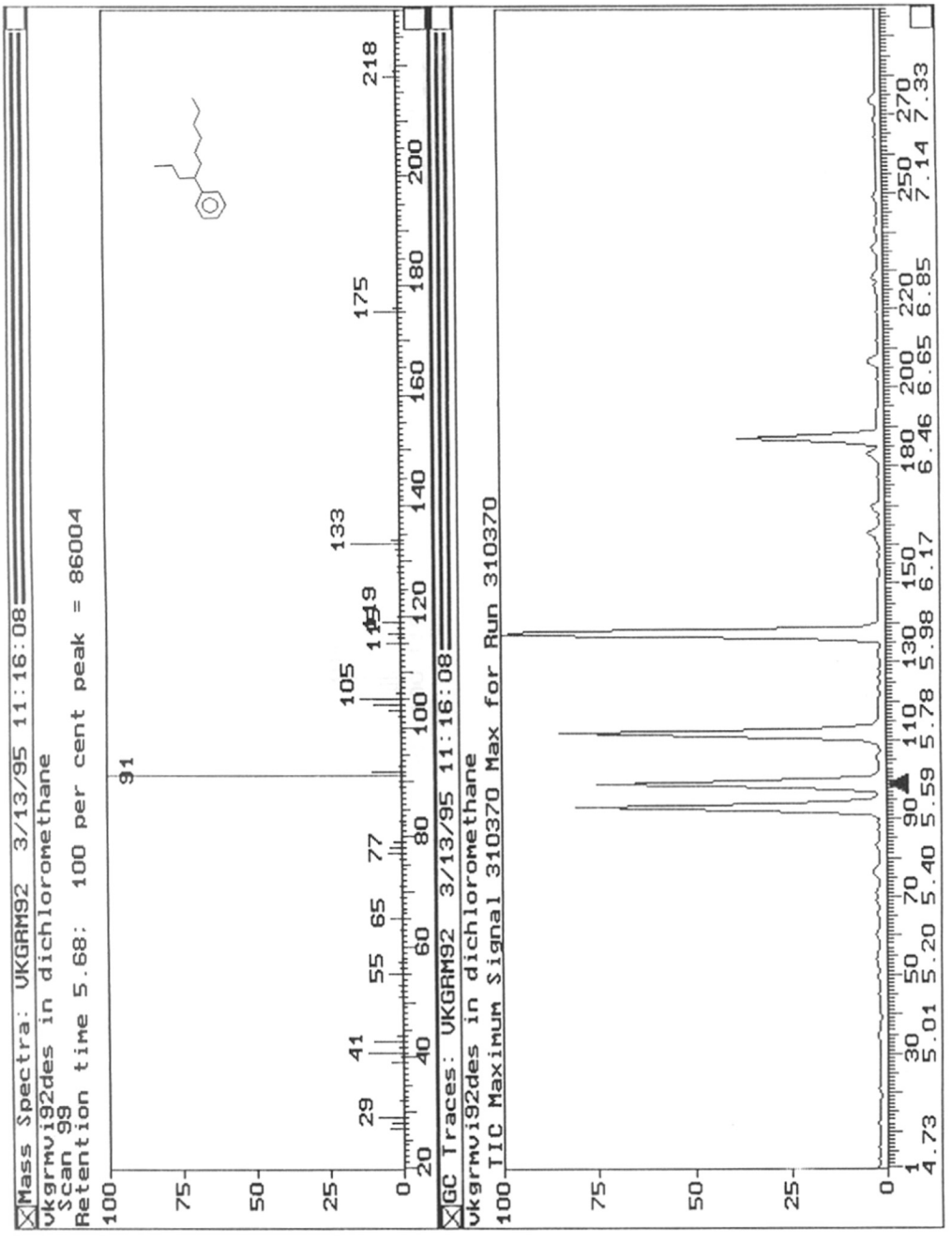


FIG.2d: GC-MS ANALYSIS OF PRODUCT (BENZENE + 1-DECANOL)

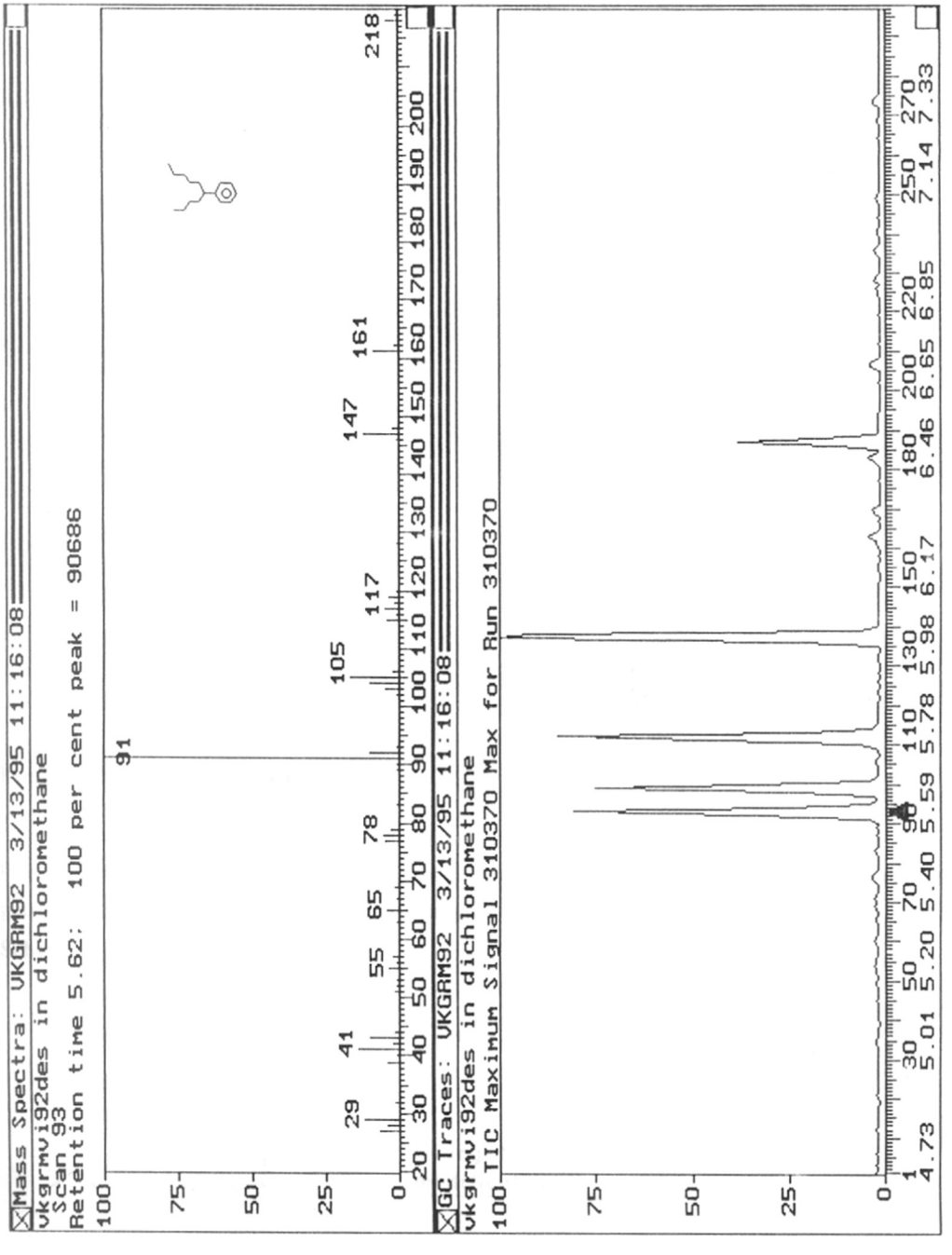
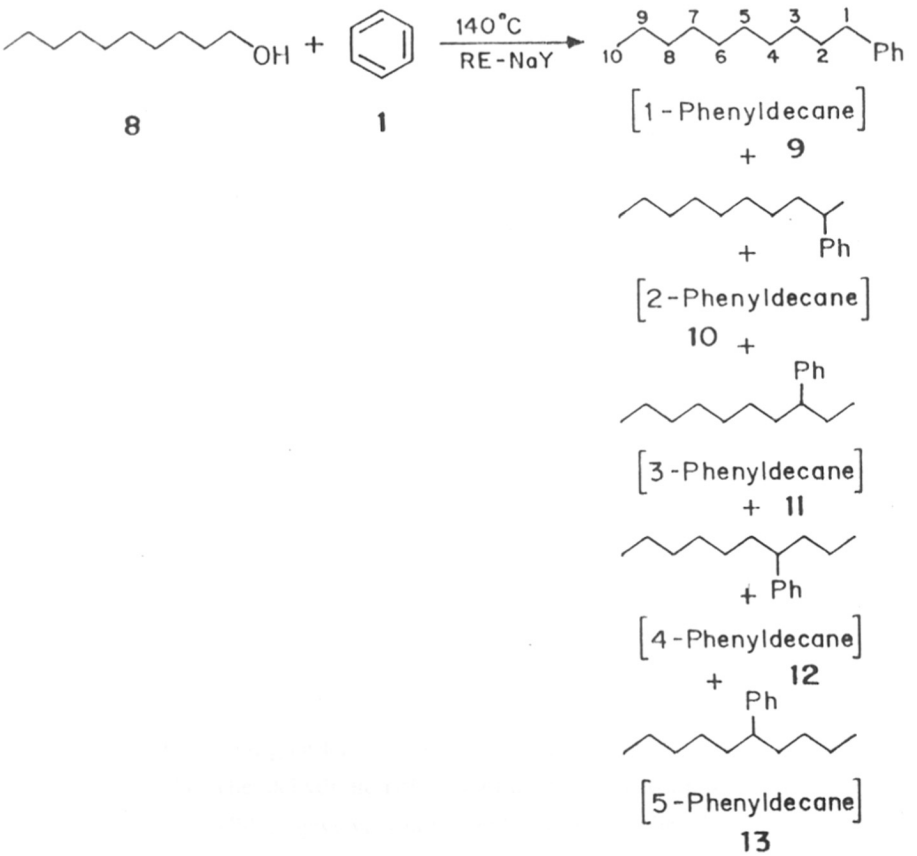


FIG.2e: GC-MS ANALYSIS OF PRODUCT (BENZENE + 1-DECANOL)

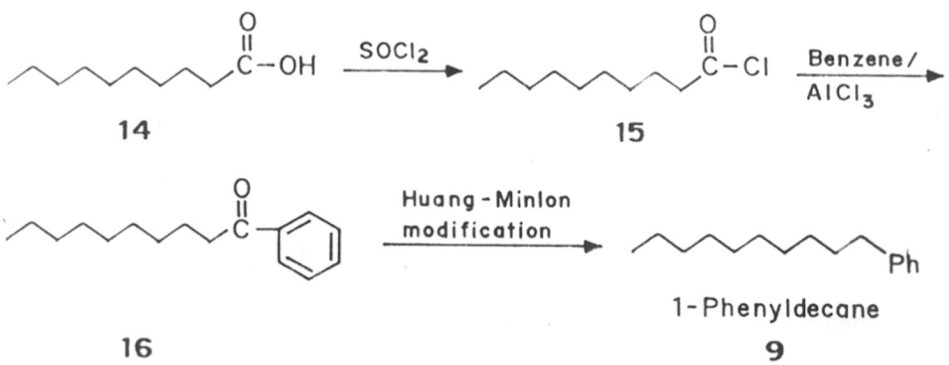
Scheme 4.3



Preparation of 1-phenyldecane (9)

Decanoic acid (**14**) on treatment with thionyl chloride gave corresponding acid chloride **15**. The Friedel-Crafts alkylation of benzene with acid chloride **15** using $AlCl_3$ as a catalyst gave ketone **16** in good yield, which on Wolff-Kishner reduction gave 1-phenyldecane (**9**) in 83% yield (Scheme 4.4).

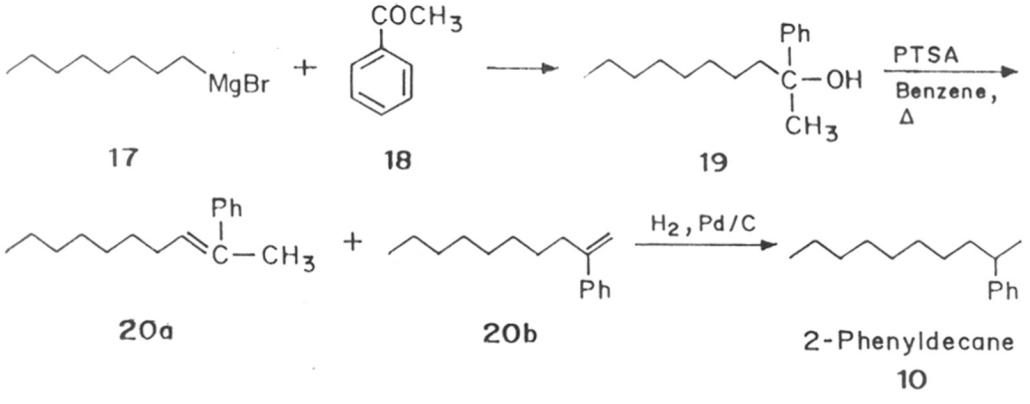
Scheme 4.4



Preparation of 2-phenyldecane (10)

The Grignard reagent prepared from octylbromide (**17**) was reacted with acetophenone (**18**) to give alcohol **19**, which on dehydration with PTSA gave a mixture of olefins **20a** and **20b** These olefins on hydrogenation gave 2-phenydecane (**10**) in very high yield (Scheme 4.5).

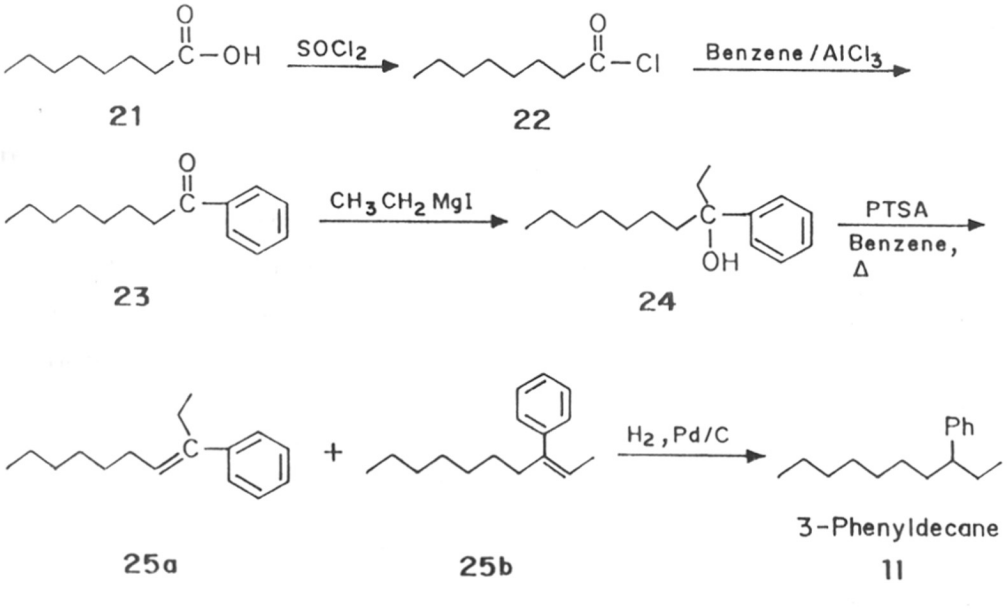
Scheme 4.5



Preparation of 3-phenyldecane (11)

Similarly, octanoic acid chloride (**22**), on Friedel-Crafts reaction with benzene in presence of $AlCl_3$ gave ketone **23**. The Grignard reagent prepared from ethyl iodide when reacted with the above ketone gave alcohol **24**. The dehydration of alcohol **24** gave a mixture of olefins **25a** and **25b**. The olefins on hydrogenation (Pd/C) gave very high yield (96%) of 3-phenyldecane (**11**) (Scheme 4.6).

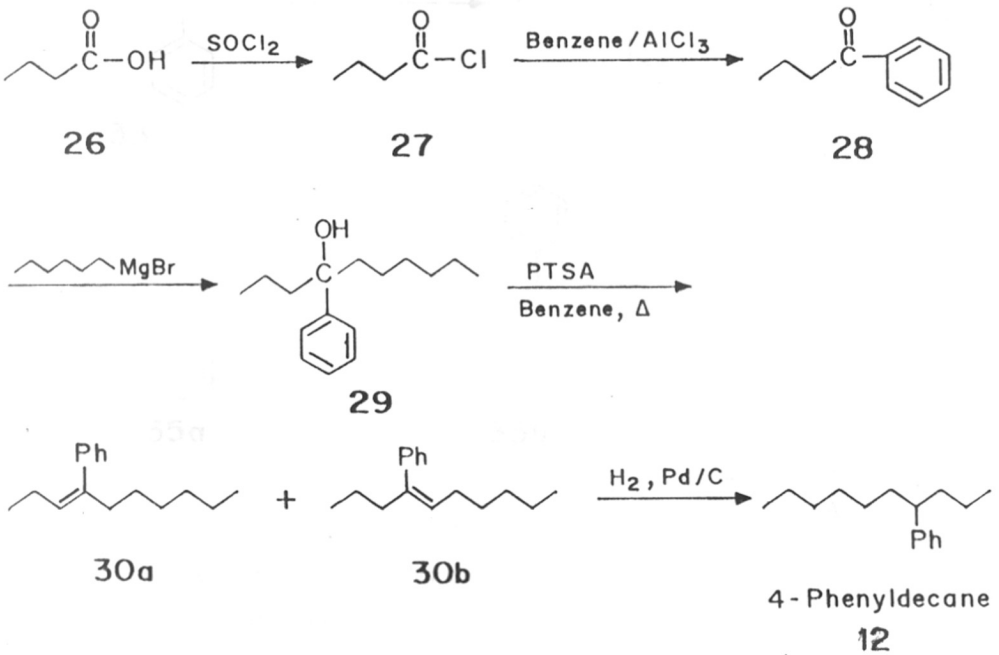
Scheme 4.6



Preparation of 4-phenyldecane (12)

Butyric acid (**26**) on treatment with thionyl chloride gave corresponding acid chloride **27**. The Friedel-Crafts alkylation of benzene with acid chloride **27** gave ketone **28**. n-Hexylmagnesium bromide when reacted with above ketone **28** gave alcohol **29**. The alcohol on dehydration gave isomeric olefins **30a** and **30b**, which on hydrogenation gave 4-phenyldecane (**12**) in 89% yield (Scheme 4.7).

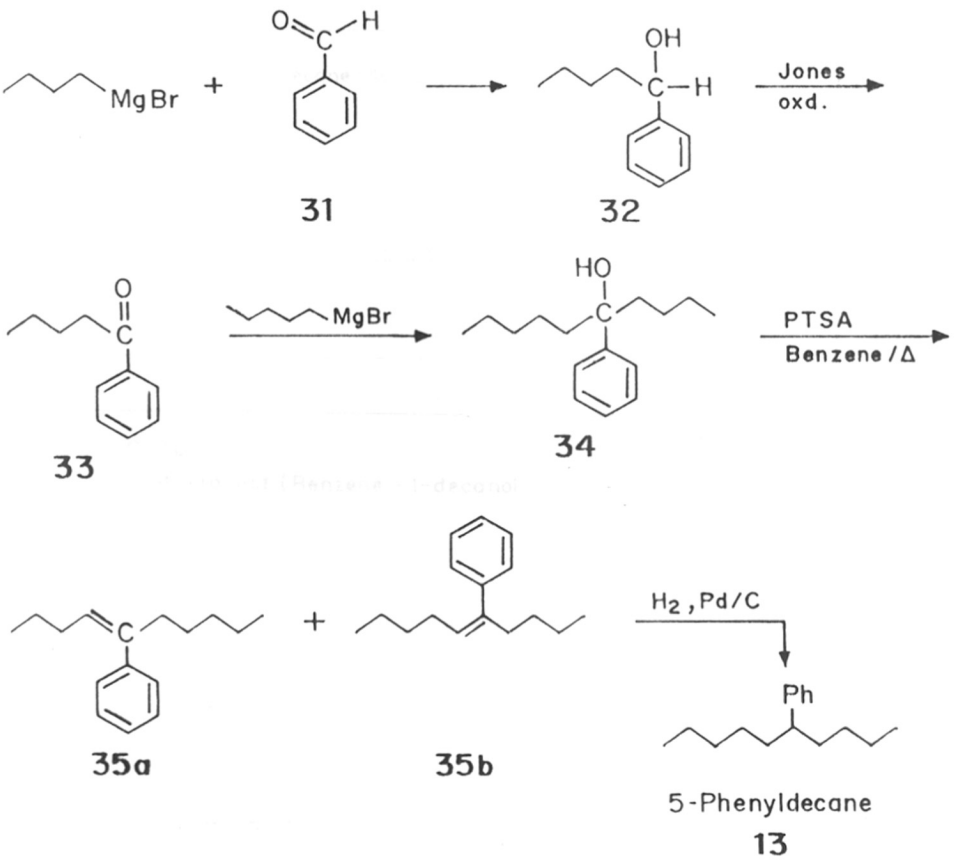
Scheme 4.7



Preparation of 5-phenyldecane (13)

The Grignard reagent prepared from n-butyl bromide when reacted with benzaldehyde (**31**) gave alcohol **32**. The alcohol **32** on Jones oxidation gave ketone **33**. The ketone when treated with Grignard reagent prepared from 1-bromopentane gave alcohol **34**, which on dehydration gave olefins **35a** and **35b**. These olefins on hydrogenation (Pd/C) gave 5-phenyldecane (**13**) in 84% yield (Scheme 4.8).

Scheme 4.8



Having prepared all these positional isomers, it was obvious to see the presence of these positional isomers in the alkylated product of benzene with 1-decanol (8). The GC analysis of alkylated product showed five peaks (Fig 3b). The GC analysis of authentic 1-phenyldecane was carried out under identical conditions and the retention time was matched with the five peaks appeared in the chromatogram of the alkylated product.

It was observed that the last peak appearing at 25.556 min in the chromatogram of the alkylated product matches very well with the retention time of authentic 1-phenyldecane (R.T. 25.551 min) (Fig 3a). This proved the presence 1-phenyldecane in the alkylated product. This was further confirmed by "Spiking" test. On externally mixing 1-phenyldecane with the alkylated product, the last peak in the chromatogram with R.T. 22.556 min was considerably enhanced (Fig 3c). Similarly the presence 2-phenyl, 3-phenyl, 4-phenyl, and 5-phenyldecane (**10-13**) was confirmed and order of elution of these positional isomers was established. The order of elution with increasing retention time is as 5-phenyl, 4-phenyl, 3-phenyl, 2-phenyl and 1-phenyldecane.

FIG. 3a:
GC of 1-phenyldecane (Authentic)

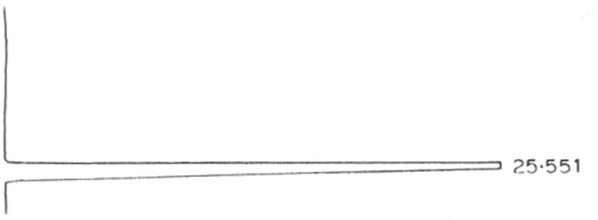


FIG. 3b:
GC of product (Benzene + 1-decanol)

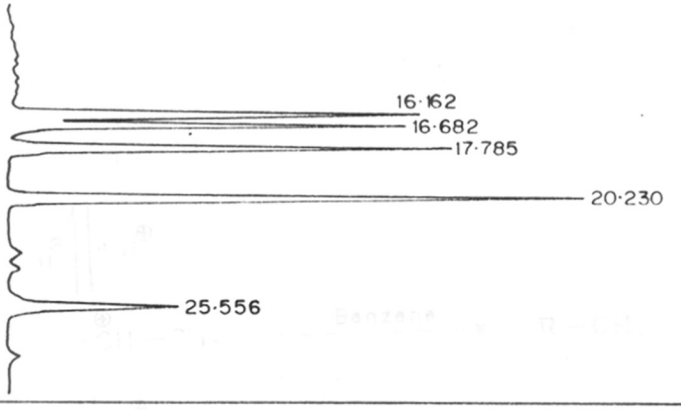
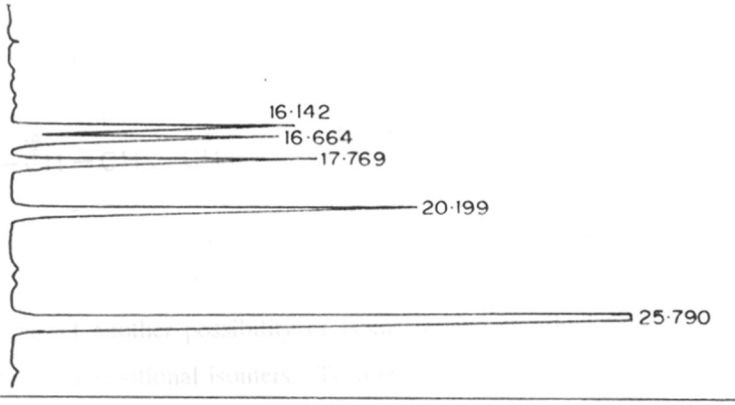
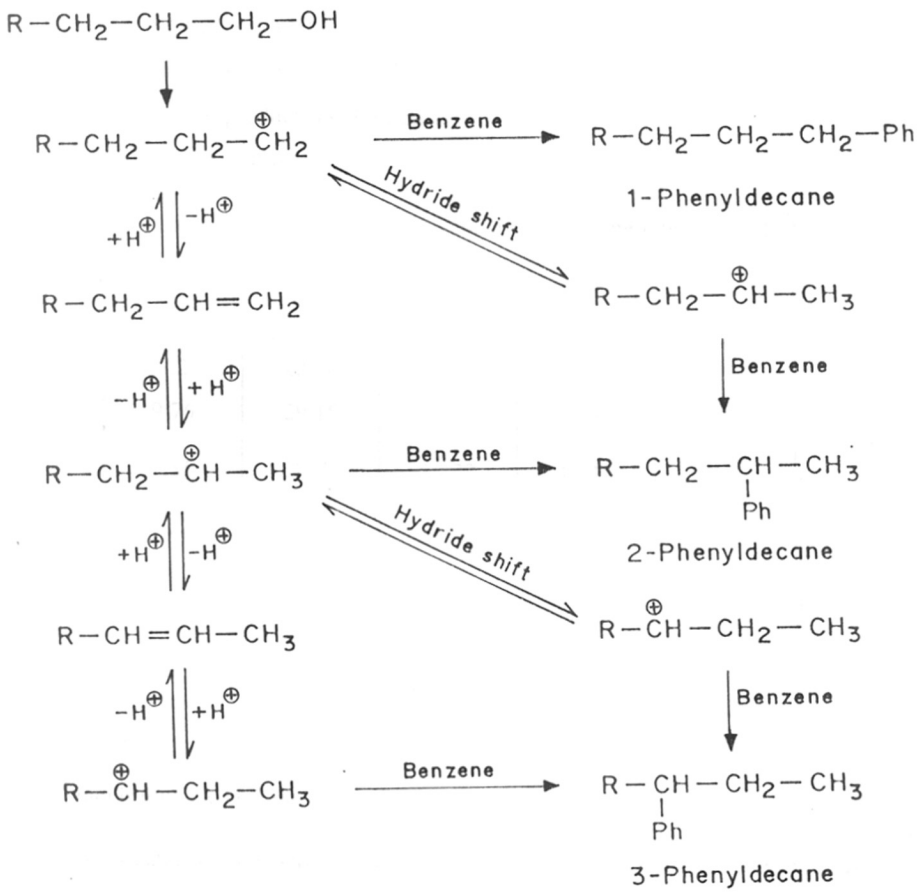


FIG. 3c:
GC of product (Benzene + 1-decanol + 1-phenyldecane)



These positional isomers may be arising from either isomerization of the primary carbocation by hydride transfer or from isomerization of terminal olefin which is the dehydration product of 1-decanol (**8**) (Scheme 4.9). 1-Phenyl decane (**9**) is formed by the reaction of primary carbocation with benzene. This primary carbocation can isomerize to most stable secondary carbocation by hydride shift or it can loose proton to give olefin. This terminal olefin can isomerize to other olefins by hydrogen transfer, which after reacting with benzene can give all five positional isomers. The cavity in the Y-zeolite (cage diameter 1.30 nm) is large enough to accommodate the transition state for the alkylation products.

Scheme 4.9



There is yet another possibility of isomerization of alkylbenzene itself under the reaction conditions to other positional isomers. To rule out this possibility, a mixture of 1-phenyldecane, benzene and RE-NaY catalyst was heated in a Parr reactor at 140°C for 6 h. The GC analysis of this

reaction mixture did not show presence of 2, 3, 4, and 5-phenyldecane. This proved that 1-phenyldecane does not isomerize under the reaction condition. 2-Phenyldecane was also heated in a Parr reactor under similar reaction conditions. The GC analysis of this reaction mixture revealed that 90% of 2-phenyldecane was found to be unchanged and only 10% of it was isomerized to other positional isomers. This means that, the isomerization of 2-phenyldecane is comparatively slower than isomerization of carbocation or alkene.

After arriving at proper reaction temperature of 140°C for alkylation reaction and confirming presence of the positional isomers, it was necessary to find out optimum time required for alkylation reaction. For this purpose a mixture of benzene (50 mL), 1-decanol (5 g), and RE-NaY catalyst (5 g) was heated in a Parr reactor at 140°C and samples were drawn at regular intervals of time and were analyzed by GC. The product distribution of positional isomers and unreacted 1-decanol at each interval is summarized in Table 4.3.

Table 4.3. Alkylation of benzene with 1-decanol at various time intervals at 140°C.

Time	1-Ph	2-Ph	3-Ph	4-Ph	5-Ph	decanol(%)
1 h	17.27	22.50	12.95	9.25	9.50	28.52
2 h	9.76	29.15	19.15	14.40	15.14	12.37
3 h	9.85	29.04	19.22	15.10	15.38	12.03
4 h	9.22	31.31	21.00	16.58	16.89	4.97
5 h	9.15	32.27	22.04	17.17	17.35	2.02

The above table reveals that the alkylation is almost complete within 5 h. The presence of 1-phenyldecane shows that initially formed primary carbocation reacts with benzene to get 1-phenyl isomer. The % of 1-phenyl isomer remains constant as it does not isomerize to other isomer. The major isomer is found to be 2-phenyldecane, which is known to give detergent of high biodegradability.

Various catalyst were screened for this alkylation reaction. A mixture of benzene (50 mL), 1-decanol (5 g), and zeolite catalysts (5 g) was heated in a Parr reactor at 140°C for 5 h. The isomer distribution in the product is tabulated in Table 4.4.

Table 4.4. Alkylation of benzene with 1-decanol using different catalyst.

Catalyst	Phenyldecanes(%)				
	1-Ph	2-Ph	3-Ph	4-Ph	5-Ph
RE-NaY	11.02	30.18	21.52	17.62	19.66
RE-HY	12.34	29.66	22.36	17.71	17.93
H-Y	8.94	29.93	23.49	18.56	19.08
H-Mordenite	0.36	1.02	0.36	Trace	Trace
H-ZSM-5	No alkylation				
TS-1	No alkylation				

It is clear from the Table 4.4 that H-ZSM-5, TS-1, H-Mordenite are not suitable catalysts for alkylation reaction. However, with Y-type zeolite (RE-NaY, RE-HY and HY) catalyst the selectivity towards LAB was very high (97-98 %). Moreover, these catalysts gave almost similar composition of positional isomers.

The position of phenyl group on the alkyl chain and the alkyl chain length is an important factor in determining surface active properties, when sulfonates are prepared from LAB. Best results are obtained with an alkyl chain in the range of 10 to 13 carbon atoms. A comparative study of alkylation of benzene with olefin and the percentage of 2-phenyl content using homogeneous catalyst like H_2S0_4, HF, $AlCl_3$, has been reported by Olson[7]. Among the several positional isomers, 2-phenylalkane has higher rate of biodegradation[7f] than the other isomers. The alkylation reaction, when carried out in the presence of zeolite catalyst, gave more percentage of 2-phenyl content in alkylated mixture as compared to H_2SO_4, $AlCl_3$ and HF. Hence, the catalyst which produces more of this isomer is preferred over other catalyst. Since the performance of RE-NaY and RE-HY was better with respect to the production of 2-phenyl isomer, RE-NaY catalyst was selected for the alkylation of benzene with other linear alcohols with 8-18 carbon chain.

A mixture of benzene (50 mL), alcohols (5 g) and RE-NaY catalyst (5 g) was heated in a Parr reactor at 140°C for 6 h. The catalyst was filtered and excess of benzene was removed by distillation and the residue was analyzed by GC to determine product distribution (positional isomers). The results are tabulated in Table 4.5.

Table 4.5. Alkylation of benzene with different alcohol.

Alcohol	Phenylalkanes(%)					
	1-Ph	2-Ph	3-Ph	4-Ph	5-Ph	6-Ph
C8	7.65	31.40	28.73	32.22	Nil	Nil
C10	11.02	30.18	21.52	17.62	19.66	Nil
C12	8.26	21.67	19.66	17.96	32.45	Trace
C16	11.61	19.32	14.89	12.09	11.14	30.95
C18	9.52	18.92	14.39	11.52	10.73	34.92

From the above table it is clear that a wide variety of alcohols can be used for alkylation of benzene using RE-NaY catalyst. The formation of 6-phenyl was also observed in case of C-16 and C-18 alcohols. However, 7-phenyl and higher isomers were not formed in detectable amounts.

After studying alkylation of benzene in the presence of zeolite catalyst using linear alcohols, we turned our attention towards alkylation of benzene using terminal olefins. The industrial process for manufacture of linear alkyl benzene uses terminal olefins with 10-13 carbon atoms in the presence of HF as a catalyst. Our aim was to replace HF by zeolite catalyst, as HF has several disadvantages such as i) it is highly corrosive ii) it is very difficult to handle iii) disposal of fluorided hydrocarbon is very difficult. Alkylation of benzene with terminal olefins was undertaken to avoid all these problems and to provide an industrially viable alternative process for the manufacture of LAB.

When a mixture of benzene (50 mL), 1-decene (5 g) and RE-NaY catalyst (5 g) was heated in a Parr reactor at 140°C for 5 h. After usual work-up, the product obtained was analyzed by GC. The GC data showed four peaks corresponding to 2-phenyl, 3-phenyl, 4-phenyl and 5-phenyldecane. The formation of 1-phenyldecane was not observed in this reaction. It is obvious, as more stable secondary carbocation formation favours over less stable primary carbocation from terminal olefin. Branched phenyldecane was not formed in detectable amount (GC).

To find out the generality of the reaction, alkylation of benzene with different olefins was carried out in a Parr reactor using RE-NaY catalyst at 140°C for 5 h under autogenous pressure. The isomer distribution in the alkylated product is tabulated in Table 4.6.

Table 4.6. Alkylation of benzene with different olefins using RE-NaY catalyst.

Olefin	Phenylalkanes(%)					
	1-Ph	2-Ph	3-Ph	4-Ph	5-Ph	6-Ph
1-Octene	-	39.28	28.36	32.36	-	--
1-Nonene	-	32.58	26.96	25.78	14.68	--
1-Decene	-	23.16	25.03	23.85	27.96	--
1-Undecene	-	19.84	19.18	18.94	22.83	19.21
1-Dodecene	-	19.64	19.29	19.08	22.70	19.29

From the above table it is clear that like alcohols, olefins can also be used for alkylation of benzene in presence of zeolite catalyst. The 2-phenyl content in the alkylted product was found to be higher than other positional isomers. However, conversion was found to be same with olefin and alcohol. The GC analysis of the product benzene and 1-octene showed 3 peaks (Fig 4). Similarly GC analysis of the product benzene and 1-decene showed 4 peaks (Fig 5).

After successful study of alkylation of benzene using terminal olefin as a alkylating agent in the batch process, we decided to simplify the process. In industry a fixed bed continuous process is always preferred over batch process. Therefore, a fixed bed, downflow tubular reactor was used for alkylation reaction.

A mixture of benzene and 1-octene is passed over a fixed bed of RE-NaY catalyst (5 g) at various conditions of temperature, pressure, WHSV and different benzene/octene ratios. The reaction conditions and conversion of 1-octene are given in the Table 4.7.

Table 4.7. Alkylation of benzene with 1-octene at 140 and 150°C.

Runs	I	II
Benzene\octene ratio (V\V)	9:1	9:1
Temperature(°C)	140	150
Pressure in Bars	Atmospheric	Atmospheric
WHSV (hr^{-1})	1	1
Conversion WT% (based on 1-octene)	100	100
WT% phenyloctane in product	84	87

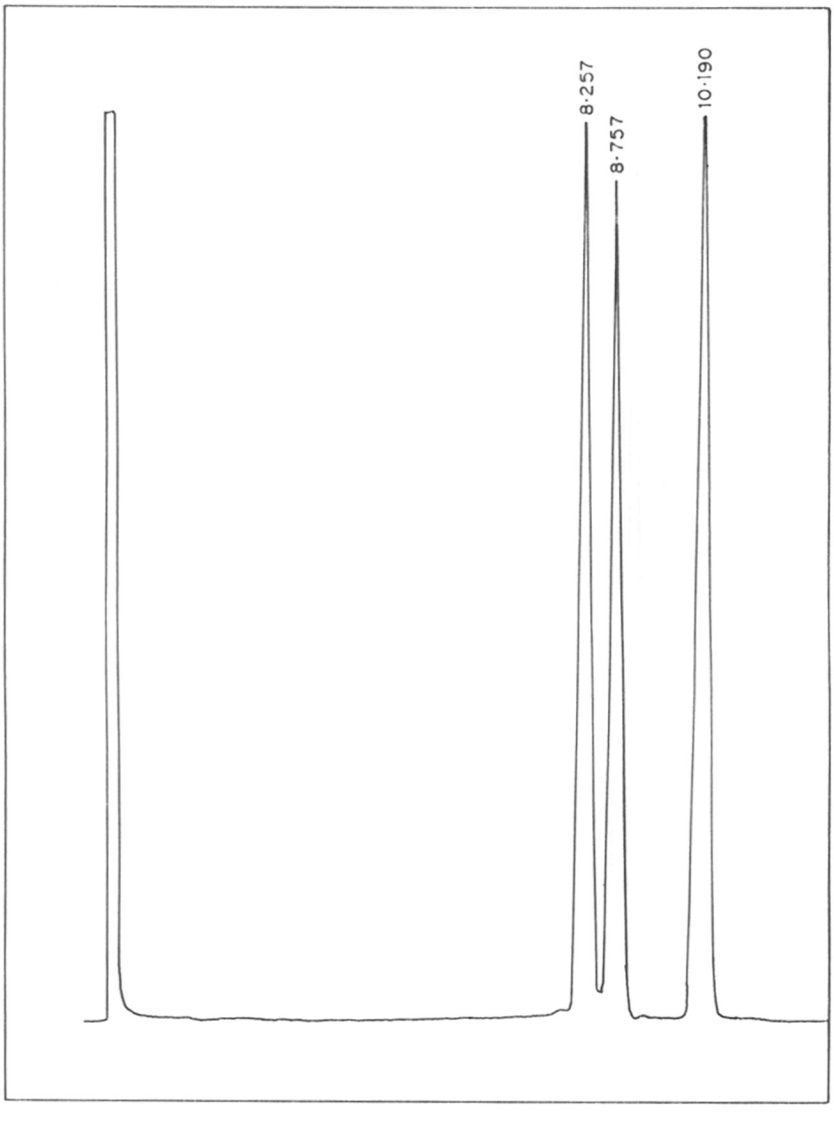


FIG. 4: GC ANALYSIS OF PRODUCT (BENZENE + 1-OCTENE)

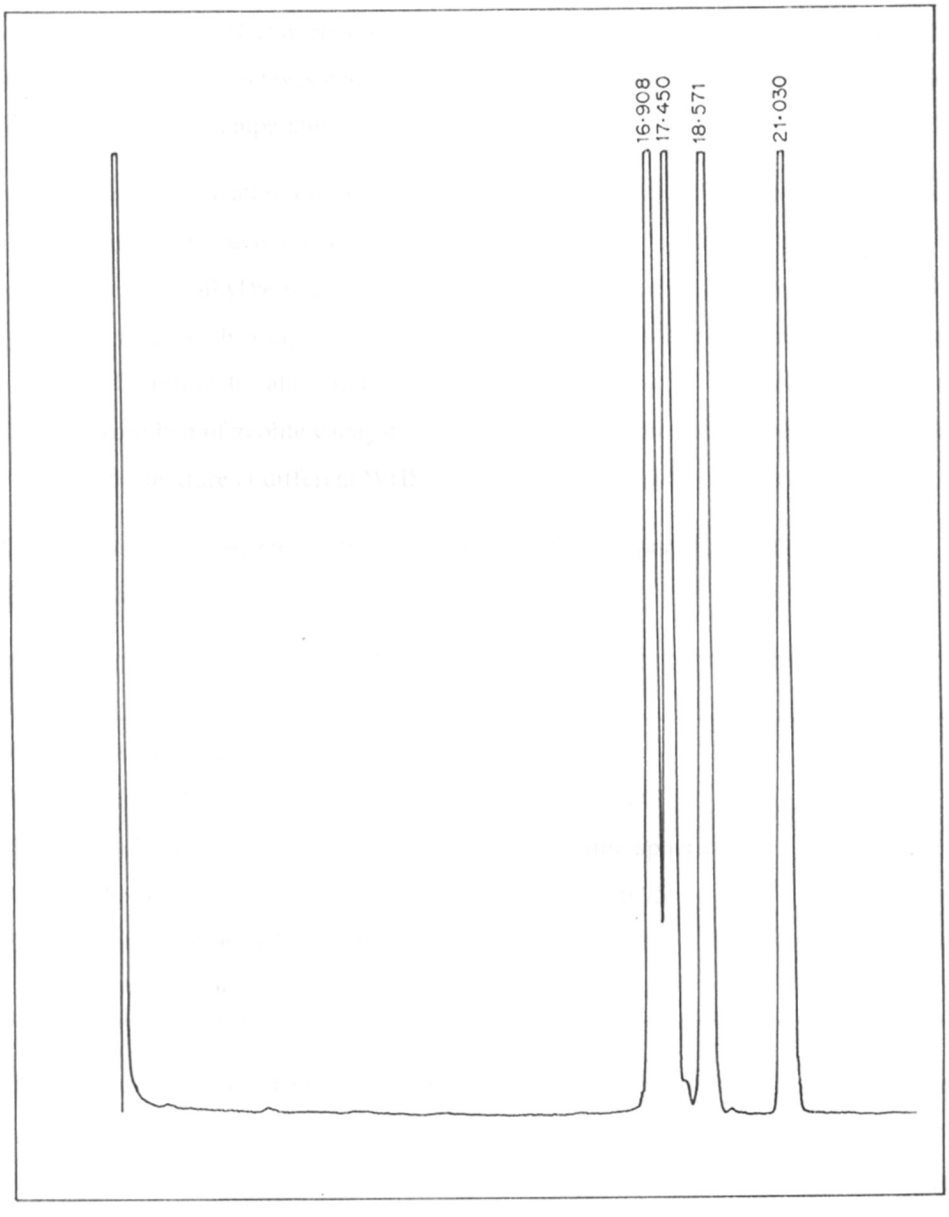


FIG.5: GC ANALYSIS OF PRODUCT (BENZENE + 1-DECENE)

When the mixture of 1-octene and benzene was passed through the preheated catalyst bed at 140°C with WHSV = 1, 100 % conversion of 1-octene to octylbenzene was observed with 84% yield. The yield of the isolated product was marginally increased when the temperature was raised by 10°C. This showed that the ideal temperature would be 140°C.

After successful utilization of fixed bed reactor for alkylation of benzene with 1-octene, an obvious extrapolation of such alkylation reaction of benzene is for the preparation of linear alkylbenzene. The linear alkyl benzenes are produced on the commercial scale by alkylation of benzene with alkylating agent, which comprises of a mixture of olefin (10-13 carbon atoms) and paraffin in the ratio of 8:92. Therefore, the alkylation of benzene was carried out with this olefin/paraffin mixture at 140°C using fixed bed of zeolite catalyst. The Table 4.8 summarizes the results of alkylation of benzene with olefin mixture at different WHSV and molar ratios of the reactants.

Table 4.8. Alkylation of benzene with a mixture of olefin and paraffin (8:92) at different WHSV using RE-NaY catalyst.

	I	II
Benzene\Alkylating agent(V\V)	1:1	2:1
Temperature (°)C	140	140
Pressure in bars	Atmospheric	Atmospheric
WHSV (hr^{-1})	0.75	1.0
Conversion, WT% based on olefin	85	100
WT% LAB in Products	80	90

The Table 4.8 reveals that benzene can be successfully alkylated with alkylating agent containing olefins (10-13 carbon atoms) using zeolite catalyst. When the ratio of benzene and alkylating agent was kept 1:1 and WHSV 0.75 the conversion was found to be 85% with isolated yield of 80%. However, when the ratio changed to 2:1 and WHSV = 1.0, the conversion was increased to 100% and isolated yield was increased to 90%. After arriving at proper conditions the study of the life of the catalyst was undertaken using RE-NaY catalyst under the following conditions: benzene:alkylating agent (2:1), WHSV = 1 and temperature 140°C. It was found that the catalyst was active for 80 h of continuous operation without loosing it's activity. The GC analysis alkylation of benzene with a mixture of olefin and paraffin (8:92) is shown in (Fig 6).

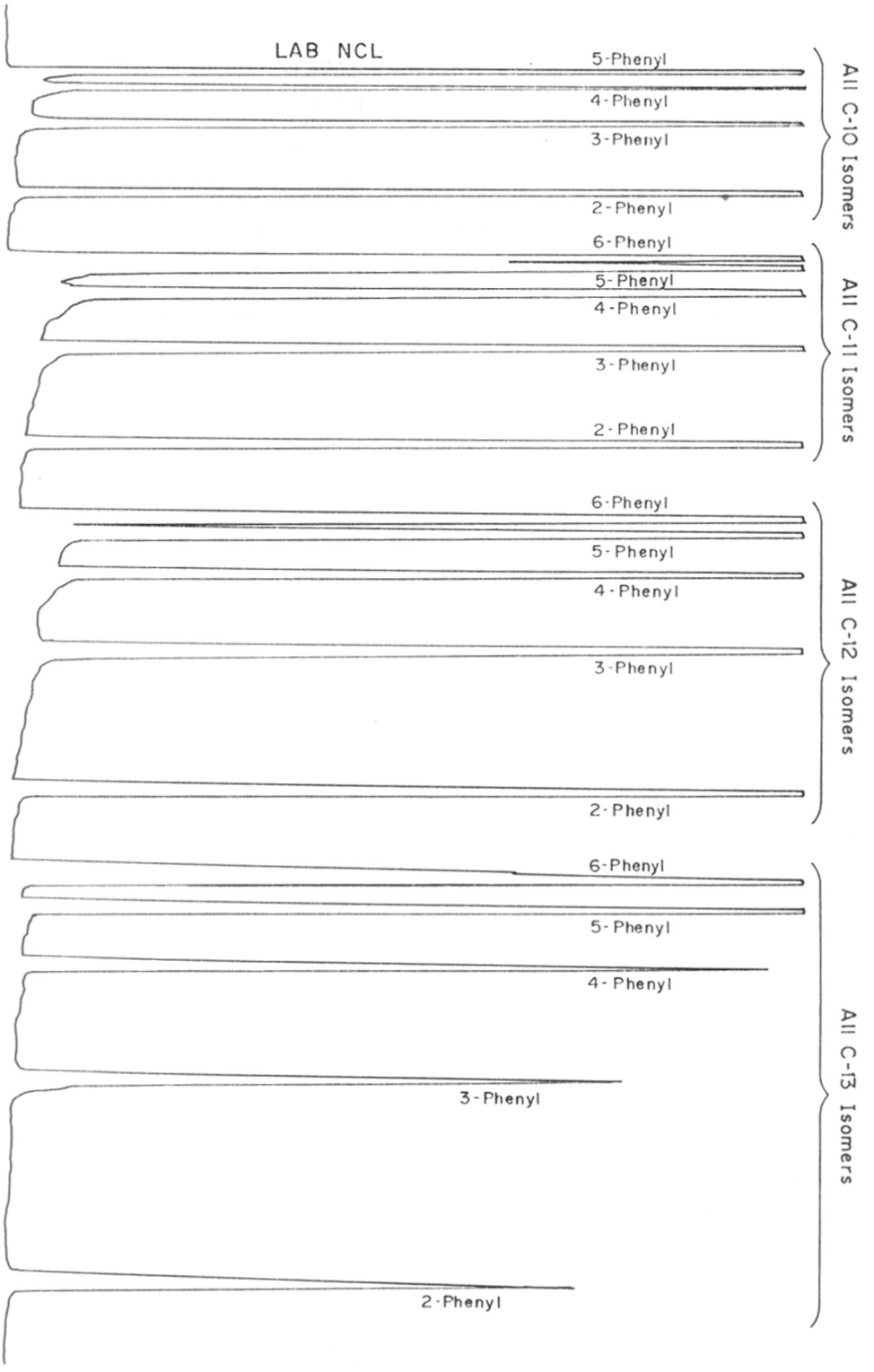


FIG. 6 : GC ANALYSIS OF THE PRODUCT (BENZENE + MIXTURE OF OLEFIN AND PARAFFIN 8:92)

The preparation of linear alkyl benzene was further developed for large scale production of LAB[17]. A thorough and systematic study of the effect of pore size and aluminium content on the alkylation of benzene by 1-dodecene in the presence of H-Y, H-ZSM-5 and H-ZSM-12 zeolite has recently been carried out by Naccache[18] and coworkers. A series of dealuminated Y-zeolites were prepared, fully characterized and then evaluated in the alkylation experiments in a batch-slurry reactor in the temperature range 100-150°C and at a pressure of 6 bars. It was observed that H-ZSM-5 and H-ZSM-12 were poor catalyst for this particular reaction which is in agreement with our results.

CONCLUSION

In conclusion, we have developed a good method for alkylation of benzene with alcohols and olefins using zeolite catalyst. All known alkylation processes available so far, suffer from various drawback such as the use of highly corrosive catalysts like aluminium chloride, hydrofluoric acid or sulfuric acid. Except HF, the other two catalyst are non recoverable. Moreover, when HF is used as a catalyst apart from the handling hazards, the disposal of other fluoride side product is also very difficult. Therefore, our method offers distinct advantages over the existing methods for the preparation LAB. It totally eliminates the highly corrosive catalyst like $AlCl_3$, HF, or $_2SO_4$. Moreover, the use of zeolite in our method for alkylation reaction can be recovered, regenerated and recycled several times, which makes the process environmentally acceptable.

EXPERIMENTAL

Alkylation of benzene with n-octanol

A mixture of n-octanol (5.01 g, 0.038 mol), benzene (50 mL) and freshly activated RE-NaY catalyst (5.10 g) was heated in a Parr reactor at 140°C under autogenous pressure for 5 h. The reactor was cooled to room temperature and the catalyst was filtered off. The excess benzene from the filtrate was removed by distillation to get a mixture of n-octylbenzenes (as a colorless oil (6.22 g, 87%).

IR (Neat) : 1600, 1500, 710 cm^{-1}

^{1}H NMR : 0.5-1.7 (m, 15H), 2.5 (t, J= 8 Hz, 2H), 7.0 (s, 5H)

GC analysis: Column, BP-1 (25 mt) with programmed oven temperature 100-200°C (2 min hold, 10°C/min); Carrier gas H_2 (12 mL/min). The GC showed the presence of four peaks of positional isomers with retention time (R.T.) and area % as follows:
5.852 (29.97), 6.181 (29.15), 7.088 (34.11) and 6.979 (9.2).

Alkylation of benzene with 1-decanol

A mixture of 1-decanol (8, 5.0 g, 0.031 mol), benzene (50 mL), freshly activated RE-NaY catalyst (5.0 g) was heated in a Parr reactor to 140 °C under autogenous pressure for 5 h. The reactor was cooled to the room temperature and the catalyst was removed by filtration. The benzene was removed from the filtrate by distillation to give a mixture of decylbenzene as a colorless oil (6.76 g, 95%).

IR (Neat) : 1610, 1500, 700 cm^{-1}.

^{1}H NMR : 0.5-1.95 (m, 19H), 2.55 (t, J= 8 Hz, 2H), 7.1 (m, 5H).

GC analysis: Column, BP-1 (25 mt) with programmed oven temperature 100-200°C (2 min hold, 10°C/min); Carrier gas H_2 (12 mL/min). The GC showed five peaks with the fallowing retention time (R.T.) and area%: 16.162 (19.80), 16.862 (18.01), 17.785 (21.74), 20.230 (29.79), 25.551 (10.64).

GC-MS Analysis: Column, BP-1 (25 mt.) with programmed oven temperature 100-180°C (2 min hold, 20°C/min); Carrier gas He (6 mL/min). The GC-MS showed five peaks due to five positional isomers. The molecular ion peak (M^+) corresponding to each positional isomer appeared at 218 with different fragmentation pattern.

Alkylation of benzene with 1-decene

To a solution of 1-decene (1.5 g, 0.010 mol) in benzene (50 mL), freshly activated RE-NaY catalyst (1.5 g) was added and it was then heated at 140°C in a Parr reactor under autogenous pressure for 5 h. The reactor was then cooled and catalyst was filtered off and washed with benzene. The excess of benzene was recovered by distillation to get a mixture of decylbenzene as a colorless oil (2.26 g, 97%).

GC analysis: Column, BP-1 (25 mt) with programmed oven temperature 100-200°C (2 min hold, 10°C/min); Carrier gas H_2 (10 mL/min). The GC showed four peaks with the following retention time and area%: 16.908 (27.96), 17.450 (23.84), 18.571 (25.03), 21.030 (23.16).

Preparation of 1-phenyldecane (9)

Preparation of decanoyl chloride (15)

A mixture of decanoic acid (**14**) (10 g, 0.058 mol) and thionyl chloride (10.37 g, 0.087 mol) was refluxed for 3 h. The excess of thionyl chloride was removed by distillation. The crude product thus obtained was distilled under reduced pressure to get decanoyl chloride (**15**) as a colorless oil (8.68 g, 78%), bp 94-96°C/5 mm; (lit[19] bp 114°C/15 mm).

*Preparation of ketone **16***

A mixture of aluminium chloride (11 g, 0.082 mol), benzene (100 mL) and acid chloride (**15**) (7.68 g, 0.04 mol) was refluxed for 3 h. The reaction mixture was cooled and poured over crushed ice and stirred for 30 min. The benzene layer was separated and the aqueous layer was extracted with benzene (2X100 mL). The combined benzene extract was washed with water (2X100 mL), aqueous sodium carbonate solution (10%, 50 mL), brine (50 mL) and dried over anhydrous sodium sulfate. The removal of solvent furnished a ketone **16** as colorless thick oil (9.10 g, 97%), bp 166-168 °C/5 mm. **IR** (neat): 1700, 1610, 1500, 1460, 1380, 765, 700 cm^{-1}. **^{1}H NMR** (80 MHz): 0.5-2.0 (m, 17H), 2.90 (t, J = 6.4 Hz, 2H), 7.10-7.45 (m, 3H), 7.50-8.0 (m, 2H).

*Reduction of ketone **16***

A mixture of ketone **16** (4.64 g, 0.02 mol), diethylene glycol (50 mL), hydrazine hydrate (80%, 4.1 g, 0.12 mol) and KOH pallets (2.66 g, 0.047 mol) was heated slowly to 80°C till all KOH pallets were dissolved completely. The heating was continued till the reaction temperature of 175°C was reached with continuous removal of low boiling liquid. The upper layer from the recovered distillate

was separated and added to the reaction mixture. The reaction mixture was further heated at 175°C for 4 h with continuous removal of lower boiling fraction. The reaction mixture was then cooled to room temperature. The upper hydrocarbon layer was separated. The aqueous layer was extracted with ether (2X50 mL). The combined extract was washed with water (2X50 mL), brine (25 mL) and dried over anhydrous sodium sulfate. The removal of solvent under reduced pressure offered pure 1-phenyldecane (**9**) as colorless oil (3.68 g, 83%). **IR (neat) :** 1600, 1490, 1450, 1380, 760, 700 cm^{-1}. ^{1}**H NMR** (200 MHz): 0.95 (t, J = 9.7 Hz, 3H), 1.20-1.50 (m, 16H), 1.60-1.80 (m, 2H), 2.63 (t, J = 9.7 Hz, 1H), 7.10-7.35 (m, 5H). **MS** (*m*/z): 218 (M^+, 19%), 91 (100%).

Preparation of 2-phenyldecane (10)

*Preparation of alcohol **19***

A Grignard reagent prepared from 1-bromooctane (**17**) (7.72 g, 0.04 mol) and magnesium (0.86 g, 0.036 mol) in dry ether (100 mL) was cooled to 0°C in an ice bath. To this cooled regent, a solution of acetophenone (**18**), (3.6 g, 0.03 mmol) in ether (25 mL) was added dropwise at 0°C. The reaction mixture was stirred at room temperature for 5 h. It was then quenched with saturated ammonium chloride solution at 10°C. The organic layer was separated and aqueous layer was extracted with ether (2X50 mL). The combined ether extract was washed with water (25 mL), brine (20 mL) and dried over sodium sulfate. The removal of solvent by distillation gave alcohol **19** (5.85 g, 83%) as an oil. **IR** (neat) : 3420, 1600, 1510, 1470, 760 cm^{-1}.

*Dehydration of alcohol **19***

A mixture of alcohol **19** (5.40 g), benzene (100 mL) and *p*-tolunesulfonic acid (0.54 g) was refluxed with azeotropic removal of water using Dean Stark azeotropic distillation assembly. The reaction mixture was cooled and benzene solution was washed with water (2X25 mL), brine (20 mL) and dried over sodium sulfate. The removal of solvent by distillation furnished a mixture of olefins **20a** and **20b** (4.10 g, 83%) as a colorless oil. **IR** (neat): 1610, 1630, 1500, 1460, 1370, 760, 700 cm^{-1}. ^{1}**H NMR** (80 MHz): 0.48-1.64 (m, 18H), 1.68-2.28 (m, 2H), 5.52-5.88 (m, 1H), 6.92-7.48 (m, 5H).

*Hydrogenation of olefin **20a,b***

A mixture of olefins **20a,b** (1.1 g, 5 mmol), ethanol (25 mL) and Pd/C (10%, 0.20 g) was placed in a Parr apparatus and H_2 gas was introduced and 45 *psi* pressure was maintained. The reaction mixture was shaken mechanically at room temperature for 4 h. The Pd/C catalyst was removed by

filtration. Ethanol solvent from filtrate was removed by distillation under reduced pressure. The residue was diluted with pet. ether (25 mL) and washed with water (10 mL), brine (10 mL) and dried over anhydrous sodium sulfate. The removal of pet. ether under reduced pressure gave 2-phenyldecane (**10**) as an oil (1.0 g, 90%). **IR** (neat): 1600, 1490, 1450, 1380, 1030, 760, 700 cm^{-1}. **^{1}H NMR** (200 MHz): 0.84-1.05 (m, 3H), 1.14-1.50 (m, 17H), 1.55-1.70 (m, 2H), 2.59-2.81 (m, 1H), 7.14-7.46 (m, 5H). **MS** (*m/z*): 218 (M^+, 10%), 91 (100%).

Preparation of 3-phenyldecane (11)

Preparation of capryloyl chloride (22)

A mixture of caprylic acid (**21**) (10.57 g, 0.073 mol), thionyl chloride (10.10 g, 0.084 mol) was refluxed for 3 h. The excess of thionyl chloride was removed by distillation and the residue was distilled under reduced pressure to give capryloyl chloride (**22**) (10.6 g, 89%) as a colorless oil, bp 83-84°C/20 mm (lit[19] bp 89°C/20 mm).

Preparation of ketone 23

The Friedel-Crafts arylation was carried out by following a similar procedure as described earlier for ketone **16** using aluminium chloride (30 g, 0.22 mol), benzene (100 mL) and acid chloride **22** (10.67 g, 0.065 mol). The ketone **23** was obtained as a colorless oil in 80% yield (10.75 g), bp 123-124°C/1 mm; (lit[20] bp 118-120°C/0.6 mm). **IR** (neat): 1690, 1600, 1580, 1450, 1220, 760, 700cm^{-1}. **^{1}H NMR** (80 MHz): 0.68-1.90 (m, 13H), 2.88 (t, J = 6.4 Hz, 2H), 7.12-7.60 (m, 3H), 7.68-8.0 (m, 2H).

Preparation of alcohol 24

A Grignard reagent prepared from ethyl iodide (9.30 g, 0.059 mol) and magnesium (1.0 g, 0.04 mol) in dry ether (100 mL) was cooled to 0°C in an ice bath. A solution of ketone **23** (4.68 g, 0.022 mol) in ether (25 mL) was then added dropwise to the cooled Grignard reagent. The reaction mixture was then allowed to warm-up to room temperature and stirred further for 6 h. Following a usual workup procedure described earlier for alcohol **19**, the alcohol **24** (5.15 g, 96%) was obtained as a colorless oil. **IR** (neat): 3430, 1600, 1500, 1460, 770, 700 cm^{-1}.

Dehydration of alcohol 24

A similar procedure as described for **19**, was followed for the dehydration of alcohol **24** (2.0 g, 0.085 mol), to get a mixture of olefins **25a** and **b** (1.85 g, 92%) as an oil. **IR** (neat): 1600, 1630, 1500,

1460, 1380, 1280, 1040, 760, 700 cm^{-1}. **^{1}H NMR** (80 MHz): 0.84-1.88 (m, 18H), 2.0-2.52 (m, 2H), 5.12-5.62 (m, 1H), 6.88-7.40 (m, 5H).

Hydrogenation of olefin 25a,b

Hydrogenation of olefin **25a,b** was carried out using a similar procedure as described earlier for **20a,b** to get 3-phenyldecane (**11**) (1.45 g, 96%). **IR** (neat): 1600, 1500, 1460, 1380, 750, 710 cm^{-1}. **^{1}H NMR** (80 MHz): 0.68-1.92 (m, 20H), 2.20-2.60 (m, 1H), 6.80-7.40 (m, 5H). **MS** (*m/z*): 218 (M^+, 6%), 91 (100%).

Preparation of 4-phenyldecane (12)

Preparation of n-butyryl chloride (27)

A mixture of n-butyric acid (**26**) (4.40 g, 0.05 mol) and thionyl chloride (7.5 g, 0.063 mol) was refluxed for 3 h. The excess of thionyl chloride was removed by distillation and the residue was distilled to get pure n-butyryl chloride (**27**) as a colorless oil (5.10 g, 95%), bp 102-103°C (lit[21] bp 100-101°C).

Preparation of butyrophenone (28)

A mixture of aluminium chloride (6.6 g, 0.049 mol) and benzene (100 mL) was taken in a three neck flask and acid chloride **27** (5.0 g, 0.055 mol) in benzene (25 mL) was added dropwise under vigorous stirring. The mixture was then refluxed for 3 h. The usual workup procedure gave 4.80 g (65%) of butyrophenone (**28**), bp 96-98°C/4 mm (lit[21] bp 227-230°C). **IR** (neat): 1680, 1610, 1450, 1220, 760, 700 cm^{-1}. **^{1}H NMR** (80 MHz): 0.72-2.12 (m, 5H), 2.92 (t, J = 6.4 Hz, 2H), 7.0-7.44 (m, 3H), 7.48-8.10 (m, 2H).

Preparation of alcohol 29

To a stirred solution of n-hexylmagnesium bromide prepared from n-hexylbromide (3.96 g, 0.024 mol) and magnesium (0.57 g, 0.024 mol) in dry ether (100 mL), a solution of ketone **28** (3.29 g, 0.021 mol) in ether (25 mL) was added at 0°C and stirred further at this temperature for 1 h. The reaction mixture was then allowed to warm up to room temperature and stirred for 6 h. By following similar work up procedure as described for alcohol **23**, 3.31 g (61%) of alcohol **19** was obtained, bp 140-143°C/4 mm. **IR** (neat): 3500, 1610, 1500, 1460, 770, 710 cm^{-1}.

Dehydration of alcohol 29

A mixture of alcohol **29** (0.82 g, 0.0035 mol), benzene (50 mL) and *p*-tolunesulfonic acid (0.10 g) was refluxed for 4 h. After usual workup olefins **30a,b** (0.75 g, 95%) was obtained as colorless oil.

IR (neat): 1600, 1620, 1500, 1470, 1380, 760, 700 cm^{-1}. **^{1}H NMR** (80 MHz): 0.52-1.72 (m, 18H), 2.0-2.60 (m, 2H), 5.20-5.80 (m, 1H), 6.85-7.40 (m, 5H).

*Hydrogenation of olefin **30a,b***

Hydrogenation of olefin **30** was carried out by following similar procedure as described earlier for **24** to get 4-phenyldecane (**12**) (0.60 g, 90%). **IR** (neat): 1600, 1500, 1460, 1380, 760, 700 cm^{-1}. **^{1}H NMR** (80 MHz): 0.65-1.85 (m, 22H), 2.20-2.72 (m, 1H), 6.85-7.45 (m, 5H). **MS** (*m/z*): 218 (M^+, 6%), 91 (100%).

Preparation of 5-phenyldecane (13)

Preparation of alcohol 32

A Grignard reagent prepared from n-butylbromide (10.27 g, 0.071 mol) and magnesium (0.44 g, 0.06 mol) in dry ether (100 mL) was cooled to 0°C in an ice bath. To this was then added dropwise a solution of benzaldehyde (**31**) (5.3 g, 0.05 mol) in ether (25 mL) and stirred at room temperature for 6 h. After usual workup 6.10 g (74%) of alcohol **32** was obtained. **IR** (neat): 3420, 1600, 1580, 1500, 1450, 1380, 1220, 710 cm^{-1}.

Oxidation of alcohol 32

To a cooled solution of alcohol **32** (5.60 g, 0.034 mol) in acetone (100 mL), Jones reagent was added dropwise till the brown color of the solution was persisted for five minutes (~15 mL). The reaction mixture was further stirred for 1/2 h and was diluted with water (150 ml) and extracted with ether (3X50 mL). The ether layer was washed with water (50 mL), brine (20 mL) and dried on anhydrous sodium sulfate. The removal of solvent offered ketone **33** (4.80 g, 86%). **IR** (neat): 1690, 1610, 1580, 1460, 1220, 760, 700 cm^{-1}. **^{1}H NMR** (80 MHz): 0.70-2.10 (m, 7H), 2.92 (t, J = 6.4 Hz, 2H), 7.0-7.45 (m, 3H), 7.48-8.10 (m, 2H).

Preparation of alcohol 34

A Grignard reagent prepared from 1-bromopentane (2.26 g, 0.014 mol) and magnesium (0.29 g, 0.012 mol) in dry ether (100 mL) was cooled to 0°C in an ice bath. To this cooled solution, a solution of ketone **38** (1.62 g, 0.01 mol) in ether (25 mL) was added dropwise and stirred at room temperature for 4 h. Usual workup furnished alcohol **34** (2.10 g, 89 %). **IR** (neat) : 3420, 1600, 1460, 1210, 920, 760, 710 cm^{-1}.

Dehydration of alcohol 34

A mixture of alcohol **39** (2.0 g, 0.0085 mol), benzene (100 mL) and PTSA (0.25 g) was refluxed for 3 h. After usual workup, a mixture of olefins **35a** and **35b** (1.66 g, 90%) was obtained as an oil. **IR** (neat): 1600, 1620, 1500, 1470, 1380, 760, 700 cm-^{1}. **^{1}H NMR** (80 MHz): 0.65-1.70 (m, 18H), 5.16-5.65 (m, 1H), 6.85-7.45 (m, 5H).

Hydrogenation of olefin 35a,b

Hydrogenation of olefin **35a,b** was carried out using similar procedure as described earlier for **20a,b** to get 5-phenyldecane (**13**) (0.76 g, 84%) as a colorless oil. **IR** (neat): 1610, 1500, 1450, 1380, 760, 710 cm^{-1}. **^{1}H NMR** (80 MHz): 0.55-1.85 (m, 18H), 2.16-2.72 (m, 1H), 6.85-7.60 (m, 5H). **MS** (*m*/*z*): 218 (M^{+}, 19%), 91 (100%).

Alkylation of benzene with 1-octene (using fixed bed reactor)

A solution of 1-octene (2.1 g, 0.017 mol) in benzene (30 mL) was passed over RE-NaY catalyst (extrudates) (2 g) with a rate of 30 mL/h (WHSV=1.05) at 140°C and benzene solution was collected at the bottom of the reactor. The excess benzene was removed under reduced pressure to get n-octyl benzene (2.74 g, 84%).

GC analysis: Column BP-1 (25 mt) with programmed oven temperature 100-200°C (2 min hold, 10°C/min); Carrier gas H_2 (10 mL/min). The GC showed the presence of three peaks of positional isomers with retention time (R.T.) and area % as follows:
8.257 (32.36), 8.757 (28.36), 10.190 (39.28).

Alkylation of benzene with a mixture of olefin and paraffin (8:92)

A mixture of olefin and paraffin (8:92, supplied by M/s Reliance Petrochemical Industries Ltd.) (25 mL) in benzene (50 mL) was passed over preheated RE-NaY catalyst (extrudates) (2 g) at a rate of 75 mL/h at 140°C. The product was collected as a solution at the bottom of the reactor. The excess benzene from the reaction mixture was removed under reduced pressure to get a of mixture of linear alkyl benzene and paraffin (22.28 g). The paraffin from the mixture was distilled under high vacuum (0.5 mm, head temperature 60°C) and the linear alkylbenzenes distilled at 120°C-145°C at 0.5 mm to give 2.31 g (100% conversion) of product.

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SECTION B: Synthesis of 2-iso-propoxyphenol by mono O-alkylation of catechol with iso-propanol

SUMMARY

Synthesis of 2-*iso*-propoxyphenol (**2**), a key intermediate for the synthesis propoxur, by mono O-alkylation of catechol (**1**) with *iso*-propanol is described in this section. The method involves heating the mixture of catachol (**1**) and excess of *iso*-propanol in the presence of zeolite catalyst to give 2-*iso*-propoxyphenol (**2**) in 20% conversion and 100% selectivity. The reaction was also carried out on a fixed bed reactor by passing a mixture of catechol (**1**) and *iso*-proponol over a catalyst bed at various temperatures, molar ratios of the reactants. It was observed that at higher temperature (>160°C) the selectivity for mono O-alkylated product dropped gradually with increasing formation of mixture of C-alkylated by-products.

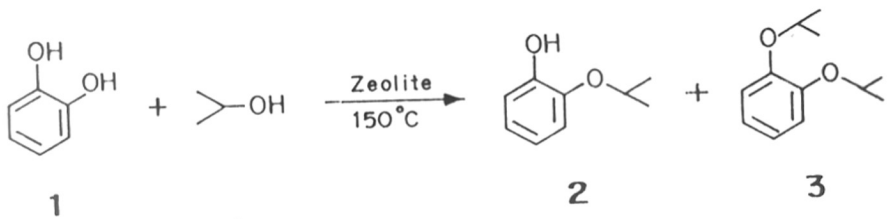
INTRODUCTION

Propoxur is an important carbamate pesticide[1]. It is non systemic insecticide effective against ants, bugs and cockroaches. 2-*iso*-Prpoxyphenol (2) is a key intermediate for the synthesis of propoxur. Various methods have been reported in the literature for the preparation of this intermediate. 2-Alkoxyphenols have been prepared by reacting catechol (1) with alkyl halides in the presence of bases (sodium hydroxide or sodium carbonate) in an autoclave at 120-160°C using terabutylammonium bromide or polyethylene glycol[2] as phase transfer catalyst. Very low yields of alkoxyphenols were obtained when acidic ion exchange resins[3] were used as a catalyst. 2-Alkoxyphenols were also prepared by dehydrogenation of 1,2-cyclohexenedione or 2-hydroxy or 2-alkoxycyclohexanones in liquid phase over noble catalyst or by vapor phase over Cu, Cr or Ni catalyst[4]. 2-*iso*-Propoxyphenol (2) can also be obtained by passing a mixture of 2-*iso*-propoxycyclohexanol or cyclohexanone and 7 fold molar excess of hydrogen over platinum or palladium[5,6] catalyst at high temperatures. When catechol (1) is alkylated with dialkyl sulfate[7] in the presence of base (potassium carbonate), 2-*iso*-propoxyphenol (2) was obtained. Preparation of 2-*iso*-propoxyphenol (2) from cyclohexanone in several steps has also been reported[8]. Recently, a simple procedure has been reported by Deodhar et al.[9] in which 2-*iso*-propoxyphenol (2) was prepared in 63% yield by refluxing catechol (1) with *iso*-propyl bromide in the presence of sodium methoxide in methanol.

PRESENT WORK

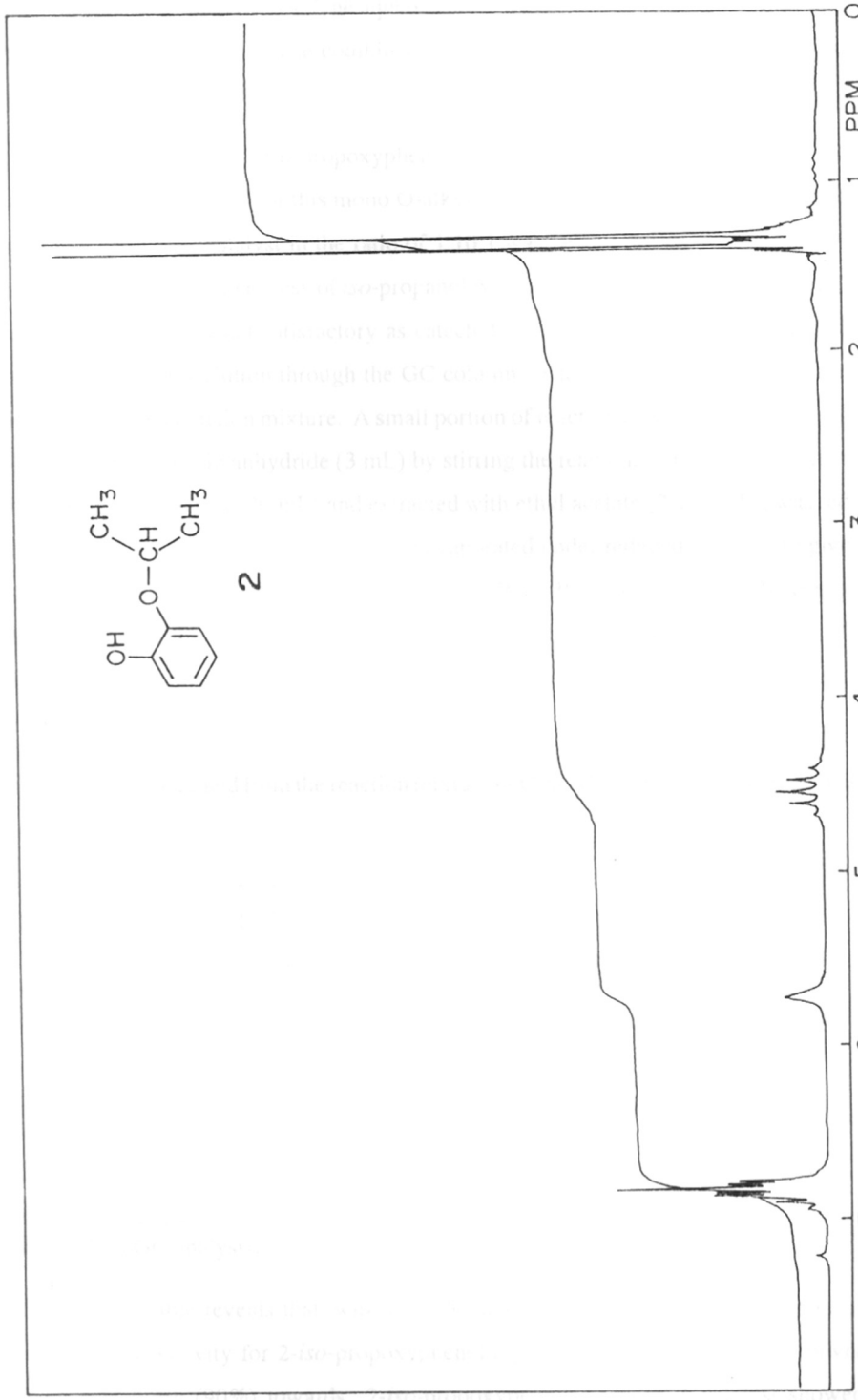
Most of the above known processes discussed in the introduction part suffers from various disadvantages such as the highly expensive and corrosive alkyl halides are used as starting material with strong alkali in the presence of phase transfer catalyst, which is difficult to recover. Moreover, some of these methods also give 1,2-diisopropoxybenzene (**3**) as a by-product. To overcome these problems, we thought that the shape selectivity of zeolite catalyst will help in selective formation of 2-*iso*-propoxyphenol (**2**). Therefore, above transformation was carried out in the presence of zeolite catalyst using *iso*-propanol instead of isopropyl halide. The main objective of the present work was to provide a method for the preparation of 2-*iso*-propoxyphenol (**2**) using zeolite catalyst (Scheme 4.10)

Scheme 4.10



RESULTS AND DISCUSSION

When a mixture of catechol (**1**), *iso*-propanol and H-ZSM-5 in a ratio of 1:10:1 was heated in a Parr reactor at 120°C for 24 h, did not give expected 2-*iso*-propoxyphenol (**2**) and all unreacted catechol (**1**) was recovered. However, when the reaction was carried out at 150°C for 24 h using same molar ratios of the reactants showed the formation of 2-*iso*-propoxyphenol (**2**) by TLC analysis (compared with authentic sample). In order to isolate the product from the reaction mixture, the catalyst was filtered, excess of *iso*-propanol was removed by distillation and the residue was treated with water (40 mL) and extracted with pet. ether (2X20 mL), which on concentration gave a colorless oil in 3% yield. This oily product was identified as 2-*iso*-propoxyphenol (**2**) based on the following evidence. The product under investigation showed IR band at 3550 cm^{-1} for hydroxyl group and bands at 1600, 1500 cm^{-1} indicated the presence of aromatic C=C. The ^1H NMR of the sample showed a doublet at δ 1.33 with J = 6 Hz coupling constant for six protons [$CH(CH_3)_2$] and a multiplet at δ 4.33-4.44 for one proton [$CH(CH_3)_2$], which is a characteristic pattern of *iso*-propyl group. The ^1H NMR spectrum also showed a broad singlet at δ 5.71 corresponding to one proton of OH group and a multiplet at δ



NMR OF 2-ISO-PROPOXYPHENOL (2)

6.66-6.93 for four aromatic protons. The aqueous layer was saturated with common salt and extracted with ethyl acetate (2X25 mL). The combined ethyl acetate on evaporation under reduced pressure gave unreacted catechol (**1**).

Since the yield of the 2-*iso*-propoxyphenol (**2**) was very low, with H-ZSM-5 catalyst, other zeolite catalyst were screened for this mono O-alkylation of catechol (**1**). A mixture of catechol (**1**), *iso*-propanol and zeolite catalyst in the ratio of 1:10:1 was heated in Parr reactor for 24 h at 150°C. The catalyst was filtered and excess of *iso*-propanol was removed by distillation. The GC analysis of this reaction mixture was not satisfactory as catechol (**1**) is highly polar and gives bad tailing and requires longer time for elution through the GC column. Therefore, it was decided to carry out GC analysis of acetylated reaction mixture. A small portion of reaction mixture (1 g) was acetylated using pyridine (2 mL) and acetic anhydride (3 mL) by stirring the reaction for 6 h at room temperature. It was then treated with water (20 mL) and extracted with ethyl acetate (2X20 mL), washed with brine and dried on sodium sulfate. The solvent was evaporated under reduced pressure to give (1.65 g) of mixture of acetates, which was analyzed by GC. The R.T. (Retention time) for 2-*iso*-propoxyphenyl acetate and catechol diacetate were found to be 5.04 and 12.68 min respectively (Fig 1). The R.T. for 1,2-diisopropoxybenzene (**3**) was 6.58 min under similar GC conditions. The results are tabulated in Table 4.9.

Table 4.9. Acetate obtained from the reaction mixture of O-alkylated product of catechol using various zeolite catalysts.

Entry	Catalyst[a]	2-*iso*-propoxy phenylacetate (%)[b]	Catechol diacetate (%)[b]	1,2-diisopropoxy benzene (%)[b]
1	RE-NaY	20	80	--
2	RE-HY	13	85	2
3	H-Y	24	66	10
4	Ts-1	3	96	1

[a]Reaction was carried out at 150°C in a Parr reactor.
[b]Yield based on GC analysis.

The above table reveals that, with RE-HY catalyst (entry 2), the conversion of catechol was 13% with 98% selectivity for 2-*iso*-propoxyphenol (**2**). H-Y catalyst gave good conversion (24%) with poor selectivity (90%) towards 2-*iso*-propoxyphenol (**2**). TS-1 catalyst showed very poor

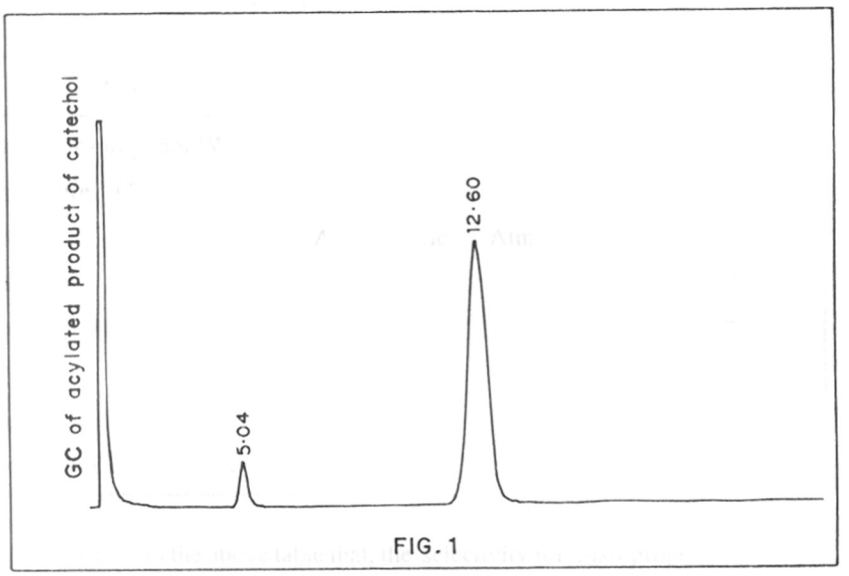


FIG. 1

conversion. RE-NaY catalyst was found to be suitable for alkylation when compared with other catalyst, which gave 100% selectivity for 2-*iso*-propoxyphenol (**2**) with 20% conversion. The O-monoalkylation of catechol (**1**) with *iso*-propanol has also been carried out using RE-NaY on a fixed bed reactor at various temperatures and molar ratios of the reactants. The results are tabulated in Table 4.10.

Table 4.10. Reaction of catechol (**1**) and *iso*-propanol on continuous fixed bed reactor.

Runs	I	II	III
Catechol:*iso*-proponol (W/V)	1:20	1:10	1:10
Temperature (°C)	150	170	200
Pressure	Atmospheric	Atmospheric	Atmospheric
WHSV	1	1	1
Conversion (%) of catechol	20	50	70
Selectivity for (2-*iso*-propoxyphenol)	100	80	60

It is clear from the above table that, the selectivity for 2-*iso*-propoxyphenol (**2**) is poor at higher temperature due the formation of complex mixture of C-alkylated product along with small amount of 1,2-diisopropoxy benzene (**3**).

CONCLUSION

In conclusion our efforts to improve the conversion of catechol (1) and selectively for 2-*iso*-propoxyphenol (2) had a little success. The conversion of more than 20% with high selectivity could not achieved even after changing various parameters and zeolite catalysts. The major hurdle was formation of a complex mixture of C-alkylated by-products at higher conversions.

EXPERIMENTAL

2-*iso*-Propoxyphenol (2)

Method A: Batch process

A mixture of catechol (**1**) (5 g, 0.045 mol) and *iso*-propanol (50 mL) was taken in a Parr reactor and RE-NaY catalyst (5 g) was added slowly. It was then heated at 150°C for 24 h. The reactor was cooled to room temperature and the catalyst was filtered. The excess of *iso*-propanol from the filtrate was removed by distillation. The residue was treated with water (40 mL) and extracted with pet. ether (2X20 mL). The pet. Ether extract on concentration gave 2-iso-propoxyphenol (**2**) as a colorless oil (1.37 g, 20%), bp 98-100°C/10 mm (lit[10] bp 100-102°C/11 mm). The aqueous layer was saturated with common salt and extracted with ethyl acetate (2X25 mL). The combined ethyl acetate extract on evaporation under reduced pressure gave 4 g (80%) of unreacted catachol (**1**).

IR (Neat) : 3560, 1610, 1510, 1280, 1130, 970, 760 cm^{-1}.

^{1}H NMR : 1.33 (d, J= 6 Hz, 6H), 4.33-4.44 (m, 1H), 5.71 (bs, 1H), 6.66-6.93 (m, 4H).

MS *(m/z)* : 152 (M^+, 10%), 41 (100%).

1,2-Diisopropoxybenzene (3)

A mixture of catechol (**1**) (5 g, 0.045 mol) and *iso*-propanol (50 mL) was taken in a Parr reactor and H-Y catalyst (5 g) was added slowly. It was then heated at 150°C for 24 h. The reactor was cooled to room temperature, the catalyst was filtered and excess of *iso*-propanol from the filtrate was removed by distillation. The residue was treated with water (40 mL) and extracted with pet. Ether (2X20 mL). The pet. Ether extract on concentration gave a mixture of two products. This mixture was separated by column chromatography to get 2-*iso*-propoxyphenol (**2**) and 1,2-diisopropoxybenzene (**3**) in pure form. The less polar product was eluted with 0.1% ethyl acetate in pet. Ether gave 1,2-diisopropoxybenzene (**3**) (0.88 g 10%), bp 140°C/4 mm (lit[11] bp 215°C/630).

IR (Neat) : 1600, 1500, 1400, 1150, 760 cm^{-1}.

^{1}H NMR : 1.36 (d, J = 6.4 Hz, 12H), 4.20-4.76 (m, 2H), 7.00 (s, 4H).

MS *(m/z)* : 194 ($M^{\pm}$, 10%), 41 (100%).

The more polar product was eluted with 2% ethyl acetate in pet. Ether to give 2-*iso*-propoxyphenol (**2**) (1.60 g 24%). The aqueous layer was saturated with common salt and extracted with ethyl acetate (2X25 mL). The combined ethyl acetate extract on evaporation under reduced pressure gave unreacted catachol (**1**) (3.30 g, 66%).

2-*iso*-Propoxyphenol (2)

Method B: Continuous procedure (using fixed bed reactor)

A mixture of catechol (2.0 g 0.018 mol) in *iso*-propanol (20 mL) was passed over preheated RE-NaY catalyst (pellets) (2.0 g) filled in tubular glass reactor (i.d. 15 mm) placed in heating device (supplied by M/S Geomechanique) with a rate of 20 mL/h at 150°C. The product was collected at the bottom of the reactor as solution in *iso*-propanol. The solvent was removed by distillation to get a residue as an oil (2.22 g). It was diluted with water (10 mL) and extracted with pet. Ether (3X25 mL). The pet. Ether layer was washed with water (10 mL), then with brine (10 mL) and dried on sodium sulfate to get 2-*iso*-propoxyphenol (**2**) (0.552 g 20%). The aqueous layer was saturated with sodium chloride and extracted with ethyl acetate (2X25 mL). The ethyl acetate layer was washed with brine (10 mL) and dried over sodium sulfate. The removal solvent under reduced pressure gave 1.58 g (79%) of unreacted catechol.

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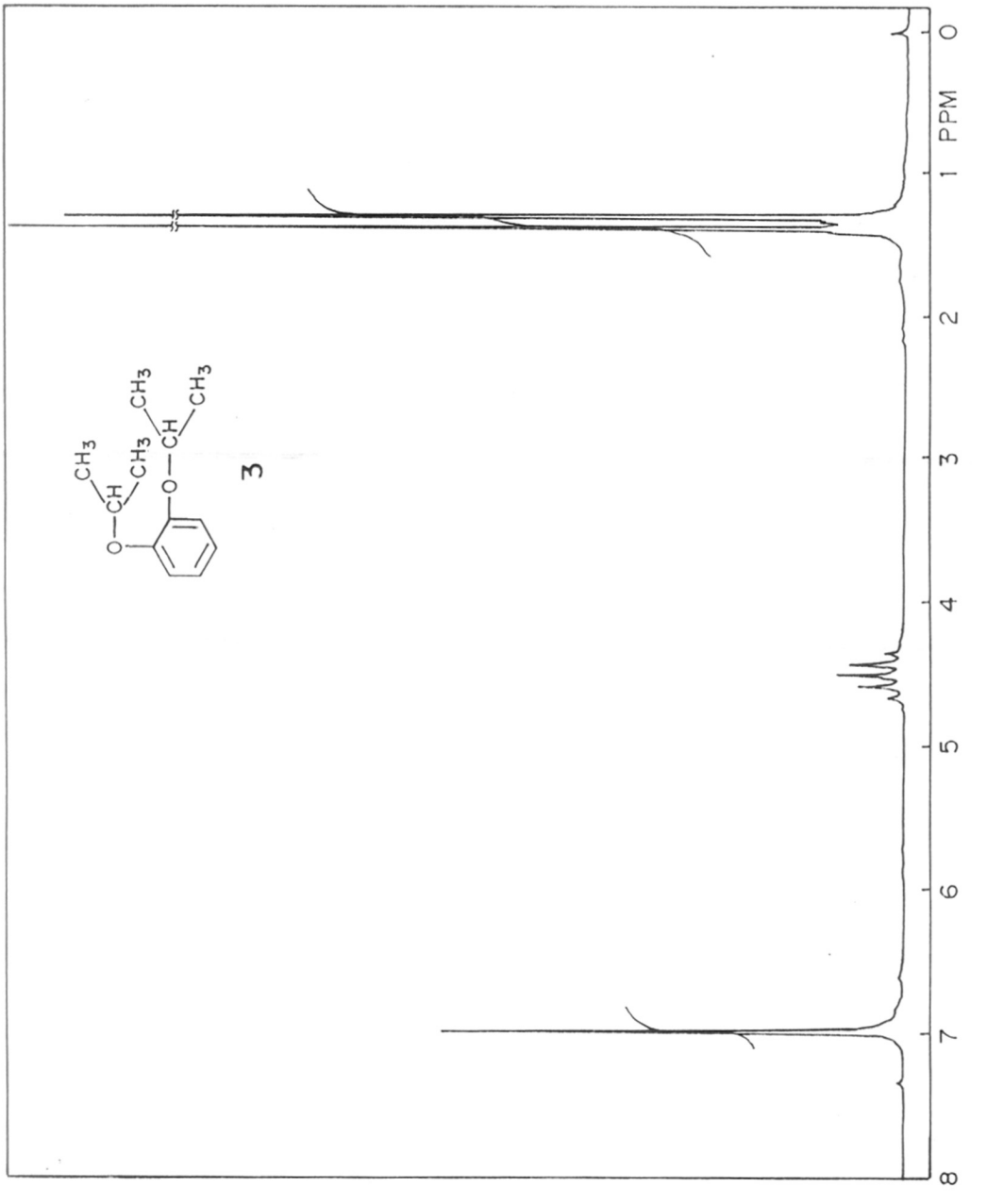
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SCETION C: C-Alkylation of phenol with alcohols

SUMMARY

The alkylation of phenol with various allylic alcohols using zeolite catalyst is described in this section. The C-alkylated *ortho* and *para* products thus obtained were isolated and characterized by usual spectroscopic technique. However, a good *o/p* selectivity could not be achieved under the reaction conditions studied. Interestingly, no appreciable O-alkylation was observed under these conditions.

INTRODUCTION

Alkylphenols have wide range of applications in industry. Some of them are useful as antioxidants and intermediates for polymers[1]. Nonylphenol is used extensively in the preparation of lubricating oil additives, resin plasticizers and surface active agents[2]. Several methods have been reported in the literature for the preparation of alkylphenols. Alkylation of phenol with primary and secondary alcohols has been carried out in the presence of $AlCl_3$,[3] BF_3[4] and other Lewis acids to give alkylphenols. Phenol when treated with *t*-butanol in the presence of $AlCl_3$ gives *t*-butylphenol in 24% yield. Proton acids like H_2S04, H_3P04[5] and polyphosphoric acid[6] have also been used for alkylation of phenols with alcohols. *p-t*-Butylphenol has been obtained in 95% yield by heating a mixture of phenol and 2-butanol at 150-160°C in the presence of ion exchanged resin KU-2[7]. Similarly, alkylation of phenol with 1,3-butadiene in the presence of 85% phosphoric acid with gaseous BF_3 is known to give *p*-crotylphenol[8]. The reaction of isoprene with phenol catalyzed by phosphoric acid[9] gave a mixture of *o*- and *p*-(3,3-dimethylallyl)phenols.

The alkylation of phenol with alcohol using zeolite catalyst has also been reported. Alkylation of phenol with ethanol has been carried out at 140°C using rare earth exchanged X type zeolite[10]. The alkylation was carried out at 316°C under 400 *psi* pressure to give mixture of *o*- and *p*- alkylated phenols. Na-Y type zeolite catalysts[11] in Al^{3+} and Fe^{3+} form have been used for alkylation of phenol with *iso*-propanol. The alkylation of phenol by ethanol, *iso*-propanol and *t*-butanol over $ZnO\text{-}Fe_2O_3$[12] catalyst has been reported. The highly selective alkylation at *ortho* position of phenol has been attributed to dissociative adsorption of phenol over the catalyst[12]. In another method phenol was alkylated with methyl, ethyl and *sec*-butyl alcohols at 285-485°C with aluminium phosphate catalyst[13] supported on alumina. In the case of reaction of phenol with methanol, the optimum methylation temperature was established as 445°C and gave *o*-cresol, *m*-cresol, *p*-cresol and dialkyl phenol, in the ratio of 25:19:8:3. When phenol was alkylated with methanol over MgO(l)[14], *o*-cresol and 2,6-xylenols were obtained. In this case selective *ortho* alkylation was observed. It has been reported that the *ortho* selectivity was governed by adsorption state of phenol. If, adsorbed phenol is in such a state that the *para* position is far from the surface, then high *ortho* selectivity is expected. Kurappannasamy et al.[15] have studied alkylation of phenol over thoria catalyst at 500°C. The main products were anisole by O-alkylation, *o*-cresol by C-alkylation and diphenyl ether by dehydration of phenol. *t*-Butylation of phenol over HY[16] zeolite at 80°C gave *ortho, para t*-butylphenols and 2,4-di-*t*-butylphenol in the ratio of 4:56:26. It has been shown that at lower temperature (30°C) O-*t*-butylation was predominant[16]. Alkylation of phenol with allyl alcohol over ultrastable Y (US-Y) type zeolite is known to give a mixture of *ortho, meta* and *para* allylated products[17].

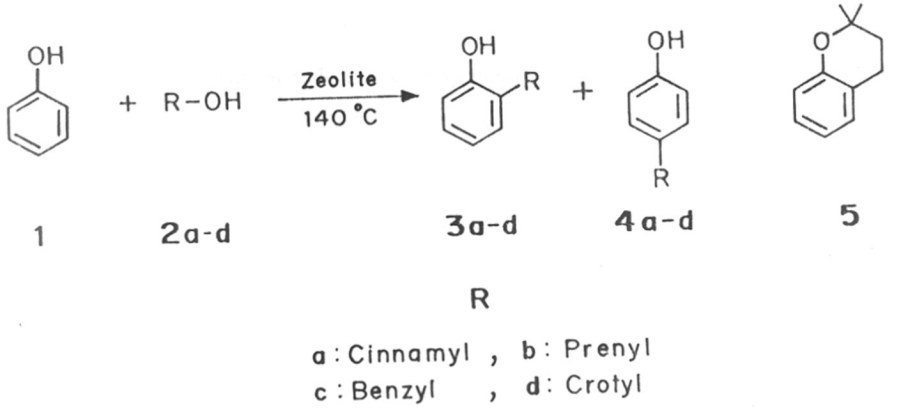
PRESENT WORK

The present work describes the regioselective alkylation of phenol with various allylic alcohols using rare earth exchanged Y type zeolite catalyst. Obtasastyrene (**4a**) a naturally occurring compound has been isolated along with neoflavanoids from *Dalbargia* and *Macherium* species[18]. Obtasastyrene (**4a**) has been synthesized by warming phenol (**1**) and cinnamyl alcohol(**2a**) in presence of 5% aqueous citric acid[19] containing ascorbic acid. In an another method it has been prepared by using formic acid[20] (100°C, 1 h) to give obtasastyrene (**4a**) as a major product. A mixture of *ortho*- and *para*-cinnamylphenols were obtained when phenol and cinnamyl bromide were reacted[21]. We therefore thought it would be worthwhile to carry out the alkylation of phenol with cinnamyl alcohol using zeolite catalyst and study the selectivity.

RESULTS AND DISCUSSION

From our earlier experience of alkylation of benzene with long chain alcohols (see Section A), we knew that the rare earth exchanged Na-Y (RE-NaY) catalyst is suitable for alkylation. Hence, this catalyst was chosen for alkylation of phenol with various allylic alcohols (Scheme 4·11).

Scheme 4.11



A mixture of phenol, (**1**) *trans*-cinnamyl alcohol (**2a**) and RE-NaY catalyst in the ratio of 1:1:1 was refluxed in n-dibutyl ether for 24 h. The catalyst was filtered and excess of n-dibutyl ether was removed by distillation under reduced pressure. The TLC of the residue showed two new spots along with starting phenol. It was treated with 5% aqueous sodium hydroxide solution and extracted with ethyl acetate. The ethyl acetate layer was washed with water and dried over anhydrous sodium sulfate.

The removal of solvent did not give any residue. This clearly indicates that there was no O-alkylated product or neutral product formation under the reaction conditions. The aqueous alkaline portion was neutralized with dilute hydrochloric acid and extracted with ethyl acetate to get mixture of phenols. The mixture was separated by column chromatography over silica gel (5% ethyl acetate in pet. ether) to give two solid products. These were identified as *ortho*- and *para*-cinnamylphenols based on fallowing evidence.

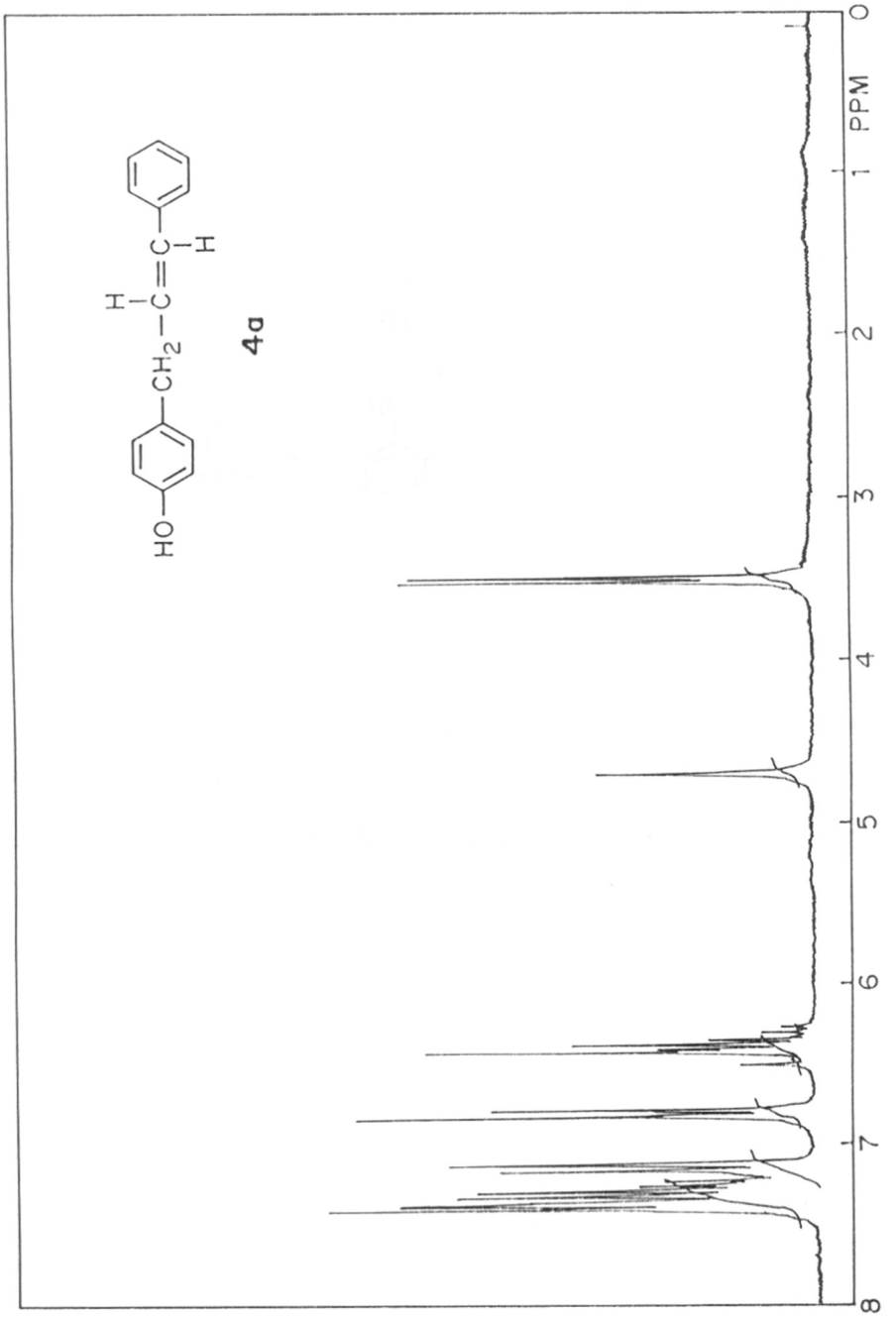
o-Cinnamylphenol (3a)

The less polar compound had mp 58-59°C (lit.mp 56-57°C for *o*-cinnamylphenol). The IR spectrum of the solid showed a band at 3420 cm^{-1} indicating presence of hydroxyl group. A band due to aromatic C=C was appeared at 1600 cm^{-1}. A sharp band at 760 cm^{-1} indicated ortho substitution. The ^1H NMR spectrum of the solid showed a doublet at δ 3.42 with J = 5 Hz for two protons of ($PhCH_2$) and a singlet at δ 4.80 for one proton of OH group. A multiplet at δ 6.30-6.40 for two protons of CH=CH group. The nine aromatic protons appeared at the usual position as multiplet between δ 6.60-7.20. The mass spectra showed a peak at 210 (M^+, 5%) and base peak 117 (100 %). All the above data confirmed the less polar compound as *o*-cinnamylphenol (3a).

p-Cinnamylphenol (4a)

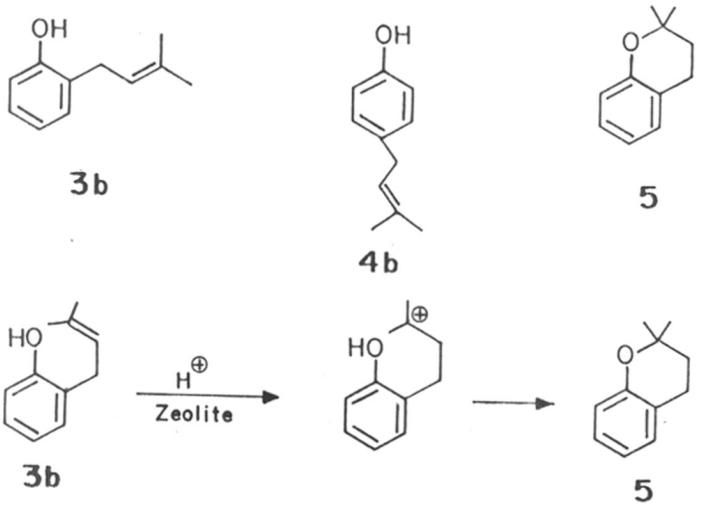
The more polar solid had mp 63-65°C (lit.mp 64-65°C for *p*-cinnamylphenol). The IR spectrum of solid displayed broad band at 3270 cm^{-1} corresponding to hydroxyl group. A band at 1590 showed the presence aromatic C=C. A band at 829 cm^{-1} could be assigned for para substitution. The ^1H NMR spectrum showed a doublet at δ 3.50 with J = 4.8 Hz for two protons of ($PhCH_2$) and a singlet at δ 4.69 for one proton of OH group, a multiplet at δ 6.24-6.52 could be assigned to two protons of CH=CH group. The two protons ortho to OH group resonated at δ 6.80 as a doublet with J = 9.7 Hz and other two protons ortho CH_2 group appeared at δ 7.14 as doublet with J = 9.7 Hz. A multiplet for five aromatic protons was seen at δ 7.25-7.55. The Mass spectrum showed a peak at 210 (M^+, 100 %).

When phenol (1) was alkylated with prenol (2b) in presence of RE-NaY catalyst under similar conditions apart from *ortho* (3b), *para* (4b) alkylated phenols, the formation of cyclic ether (5) was also observed. The cyclic ether (5) might have formed from (3b) by cyclization under the reaction conditions (Scheme 4.12). Such cyclization have been reported in the literature[22].



NMR OF P-CINNAMYLPHENOL (**4a**)

Scheme 4.12



The alkylation of phenol (**1**) with *trans*-crotyl alcohol (**2d**) gave corresponding *ortho* and *para*-crotylphenols along with a trace amount of O-alkylated product. Alkylation of phenol (**1**) with benzylalcohol (**2c**) gave *ortho* and *para*-benzylphenols. Other zeolites were also tried for the alkylation of phenol. The ratio of *o*/*p* isomers obtained in this reaction is tabulated in the Table 4.11.

Table 4.11. Alkylation of phenol (**1**) with benzylalcohol (**2c**) using various zeolite catalyst.

Entry	Catalyst	*o*-Isomer (%)[a]	*p*-Isomer (%)[a]
1.	RE-NaY	32	20
2.	RE-HY	19	15
3.	H-ZSM-5	19	9
4.	RE-X	15	11

[a] Isolated yields after column chromatography.

The above table reveals that RE-NaY (entry 1) is better catalyst for alkylation of phenols.

CONCLUSION

The C-alkylation of phenol (1) with different allylic alcohols can be achieved by using RE-NaY catalyst. However, a good *o/p* selectivity could not be achieved under the reaction conditions studied. Interestingly, there was no appreciable O-alkylation observed.

EXPERIMENTAL

Reaction of phenol (1) with *trans*-cinnamyl alcohol (2a)

To a stirred mixture of phenol (**1**) (1.88 g, 0.02 mol), *trans*-cinnamyl alcohol (**2a**) (2.68 g, 0.02 mol), n-dibutyl ether (10mL), freshly activated zeolite catalyst, RE-NaY (1.88 g) was added slowly. The reaction mixture was then refluxed for 24 h. It was then cooled to room temperature and the catalyst was filtered and washed with n-dibutyl ether. The solvent, n-dibutyl ether was removed by distillation under reduced pressure. The residue was treated with 5% aqueous solution of sodium hydroxide and extracted with ethyl acetate (2 X 25 mL) to get neutral portion. The ethyl acetate layer was washed with water (20 mL) and dried on anhydrous sodium sulfate. The removal of solvent did not give any residue. The alkali soluble aqueous portion was acidified with 2N hydrochloric acid and extracted with ethyl acetate (2X25 mL). The organic layer was washed with water (2X20 mL), brine (20 mL) and dried on sodium sulfate. The solvent was removed under reduced pressure to give 4.10 g of crude product.

GC Analysis: [Capillary Column HP-17, 25 mt., programmed temperature 140 °C to 200°C (4 °C/min. with 1 min. hold)]. GC of the crude product showed four peaks with fallowing retention time (R.T.) with area %: a) 0.535 (38.77%), b) 2.413 (4.32%), c) 16.398 (21.85%) and d) 18.420 (32.97%), which were assigned to phenol, cinnamyl alcohol, *o*-cinnamylphenol and *p*-cinnamylphenol respectively by comparing with authentic samples. The mixture was purified by column chromatography over silica gel (100 g) using ethyl acetate:pet. ether as an eluent. The less polar compound eluted with 5% ethyl acetate in pet. ether was found to be *o*-cinnamylphenol (**3a**). After progressively increasing polarity of the solvent more polar product *p*- cinnamylphenol(**4a**) and phenol (**1**) were isolated in pure form.

Recovered phenol (**1**) : 0.62 g (32%).

***o*-Cinnamylphenol** (**3a**): 0.91 g (32%, based on phenol consumed).

Mp : 58-59°C (lit[23] mp 56-57 °C).

IR (Nujol) : 3420, 1600, 1500, 1460, 760 cm^{-1}.

^{1}H NMR : 3.42 (d, J = 5 Hz, 2H), 4.80 (s, 1H), 6.30-6.40 (m, 2H), 6.60-7.20 (m, 9H).

MS (*m/z*) : 210 (M^+, 5%), 117 (100 %).

p-**Cinnamylphenol (4a)**: 1.38 g (49%, based on phenol consumed).

Mp : 63-65°C (pet. ether) (lit[23] mp 64°C).

IR (Nujol) : 3220, 1590, 1500, 1440, 829 cm^{-1}.

^{1}**H NMR** : 3.50 (d, J = 4.8 Hz, 2H), 4.69 (s, 1H), 6.24-6.52 (m, 2H), 6.80 (d, J = 9.7 Hz, 2H), 7.14 (d, J = 9.7 Hz, 2H), 7.25-7.55 (m, 5H).

MS (*m/z*) : 210 (M^+, 100 %).

Reaction of phenol (1) with prenol (2b)

A mixture of phenol (**1**) (1.88 g, 0.02 mol), prenol (**2b**) (2.76 g, 0.02 mol.), RE-NaY (1.88 g) and n-dibutyl ether (10 mL) was refluxed for 24 h. The reaction mixture was then cooled and catalyst was filtered off. The filtrate on removal of solvent, n-dibutyl ether gave 3.25 g of crude product along with unreacted starting material. The mixture was separated by column chromatography as described in the earlier experiments.

Recovered phenol (**1**) : 0.5 g (26%).

o-**(3,3-Dimethylallyl)phenol (3b)**: 0.71 g (31%, based on phenol consumed).

Bp : 152-153°C/10 mm (lit[9] bp 89-91°C/1 mm).

IR (Neat) : 3460, 1600, 1515, 1500, 1565, 765 cm^{-1}.

^{1}**H NMR** : 1.76 (s, 6H), 3.31 (d, J = 8Hz, 2H), 5.06 (s, 1H), 5.26 (t, J = 8 Hz, 1H), 6.60-7.24 (m, 4H).

MS (*m/z*) : 162 (M^+, 85 %), 107 (100 %).

p-**(3,3-Dimethylallyl)phenol** (**4b**) : 0.64 g (27%, based on phenol consumed).

Bp : 142-144°C/10 mm (lit[9] bp 104-105°C/1 mm).

IR (Neat) : 3340, 1610, 1600, 1510, 820 cm^{-1}.

^{1}**H NMR** : 1.73 (s, 6H), 3.26 (d, J = 7 Hz, 2H), 4.73 (s, 1H), 5.31 (t, J = 7 Hz, 1H), 6.77 (d, J = 8 Hz, 2H), 7.04 (d, J = 8 Hz, 2H).

MS (*m/z*) : 162 (M^+, 100 %).

2,2-Dimethylchroman (5) : 0.28 g (12%, based on phenol consumed).

: Isolated as a oil by column chromatography (2% ethyl acetate in pet. ether).

IR (Neat) : 1600, 1500, 1400, 1230 cm^{-1}.

^1H NMR : 1.32 (s, 6H), 1.76 (t, J = 6 Hz, 2H), 2.72 (t, J = 6 Hz, 2H), 6.48-7.28 (m, 4H).

MS (m/z) : 162 (M^+) 107 (100 %).

Reaction of phenol (1) with benzylalcohol (2c)

A mixture of phenol (**1**) (1.88 g, 0.02 mol), benzyl alcohol (**2c**) (2.16 g, 0.02 mol), RE-NaY (1.88 g) and n-dibutyl ether (10 mL) was refluxed for 24 h. The reaction mixture was then cooled and catalyst was filtered off. The filtrate on removal of solvent, n-dibutyl ether gave 3.50 g of crude product along with unreacted starting material. The mixture was separated by column chromatography as described in the earlier experiments.

Recovered phenol (**1**) : 0.31 g (16%).

o-**Benzylphenol (3c)** : 0.99 g (32%, based on phenol consumed).

Bp : 160-162°C/10 mm (lit[24] bp 121-123°C/1 mm).

IR (Neat) : 3500, 1600, 1500, 1460, 730 cm^{-1}.

^1H NMR : 3.96 (s, 2H), 4.74 (s, 1H), 6.50-7.40 (m, 9H).

MS (m/z) : 184 (M^+, 100 %).

p-**Benzylphenol** (4c): 0.61 g (20% based on phenol consumed).

Mp : 84-86°C (petroleum ether) (lit[25] mp 83-85°C).

IR (Nujol) : 3330, 1600, 1510, 840 cm^{-1}.

^1H NMR : 3.86 (s, 2H), 4.78 (s, 1H), 6.72 (d, J = 8 Hz, 2H), 7.04 (d, J = 8 Hz, 2H), 7.12-7.44 (m, 5H).

MS (m/z) : 184 (M^+, 100 %).

Reaction of phenol (1) with *trans*-crotylalcohol (2d)

A mixture of phenol (**1**) (1.88 g, 0.02 mol), *trans*-crotyl alcohol (**2d**) (2.88 g, 0.02 mol), RE-NaY (1.88 g), and n-dibutyl ether (10 mL) was then refluxed for 24 h. The reaction mixture was then cooled and catalyst was filtered off. The filtrate on removal of n-dibutyl ether gave 3.10 g of crude product along with unreacted starting material. The mixture was separated by column chromatography as described in the earlier experiment.

Recovered phenol (**1**) : 0.21 g (11%).

***trans*-2-Crotylphenol (3d)**: 1.27 g (49%, based on phenol consumed).

Bp : 168-170°C/10 mm (lit[26] bp 80-100°C/ 0.02mm).

IR (Neat) : 3420, 1600, 1500, 1450, 965 cm^{-1}.

^{1}H NMR : 1.48-1.84 (m, 3H), 3.28 (s, 2H), 5.00 (s, 1H), 5.40-5.72 (m, 2H), 6.32-7.24 (m, 4H).

MS (*m/z*) : 148 (M^+, 100%).

***trans*-4-Crotylphenol (4d)**: 0.97 g (37%, based on phenol consumed).

Mp : 40-41°C (lit[8] mp 39°C).

IR (Nujol) : 3320, 1600, 1510, 960 cm^{-1}.

^{1}H NMR : 1.40-1.92 (m, 3H), 3.16 (s, 2H), 5.28-5.64 (m, 2H), 6.40-7.36 (m,4H).

MS (*m/z*) : 148 (M^+, 57 %), 133 (100 %).

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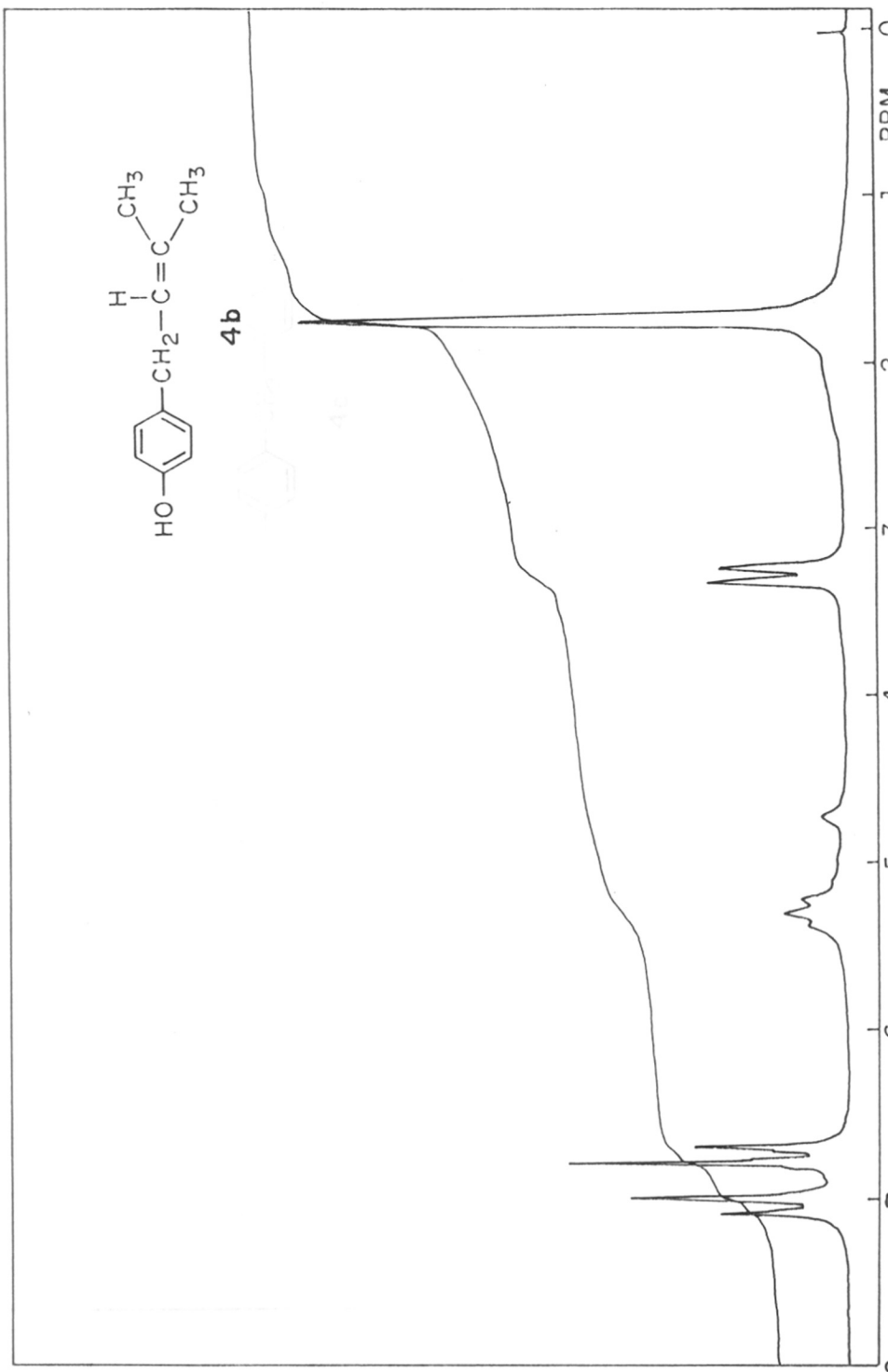
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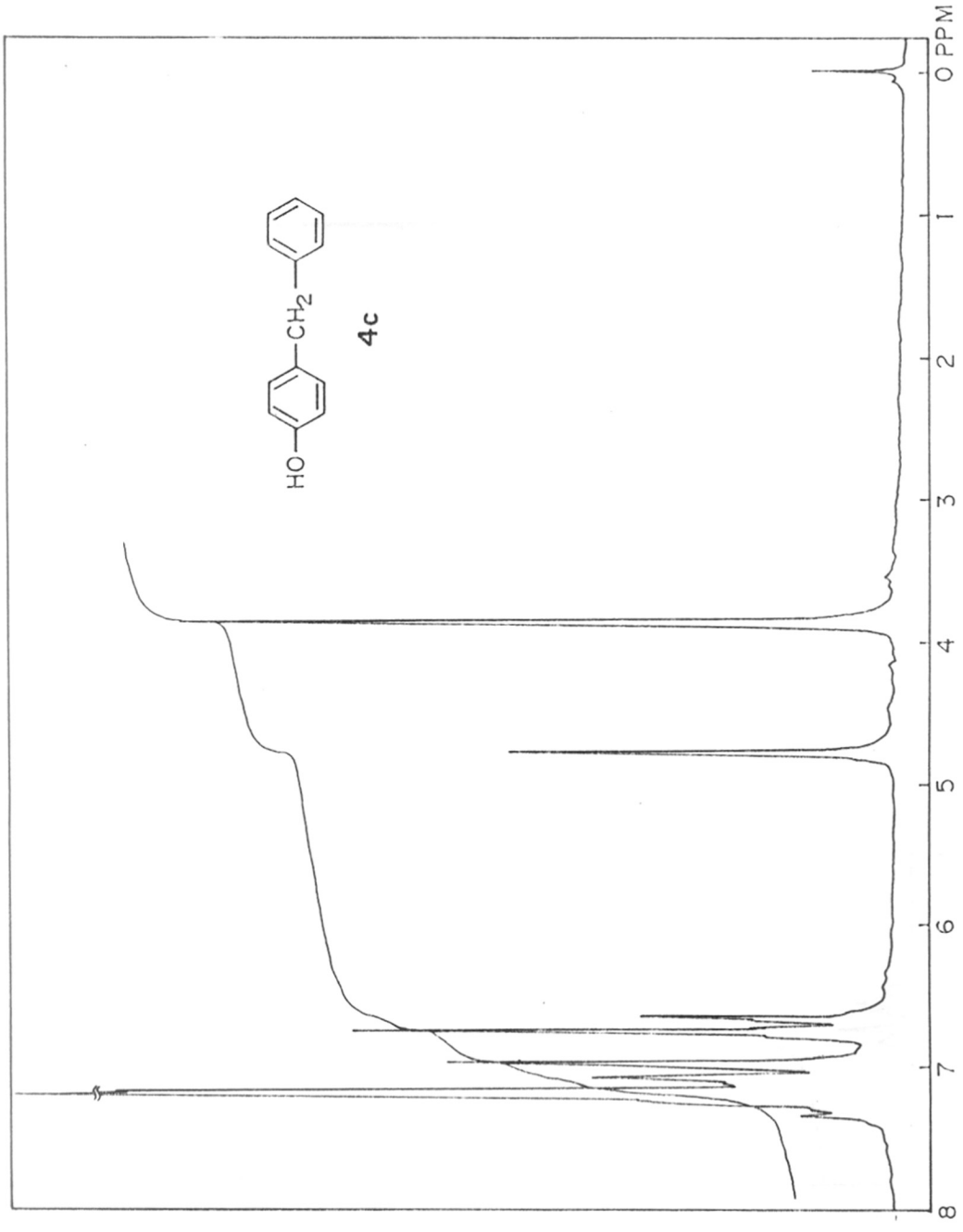
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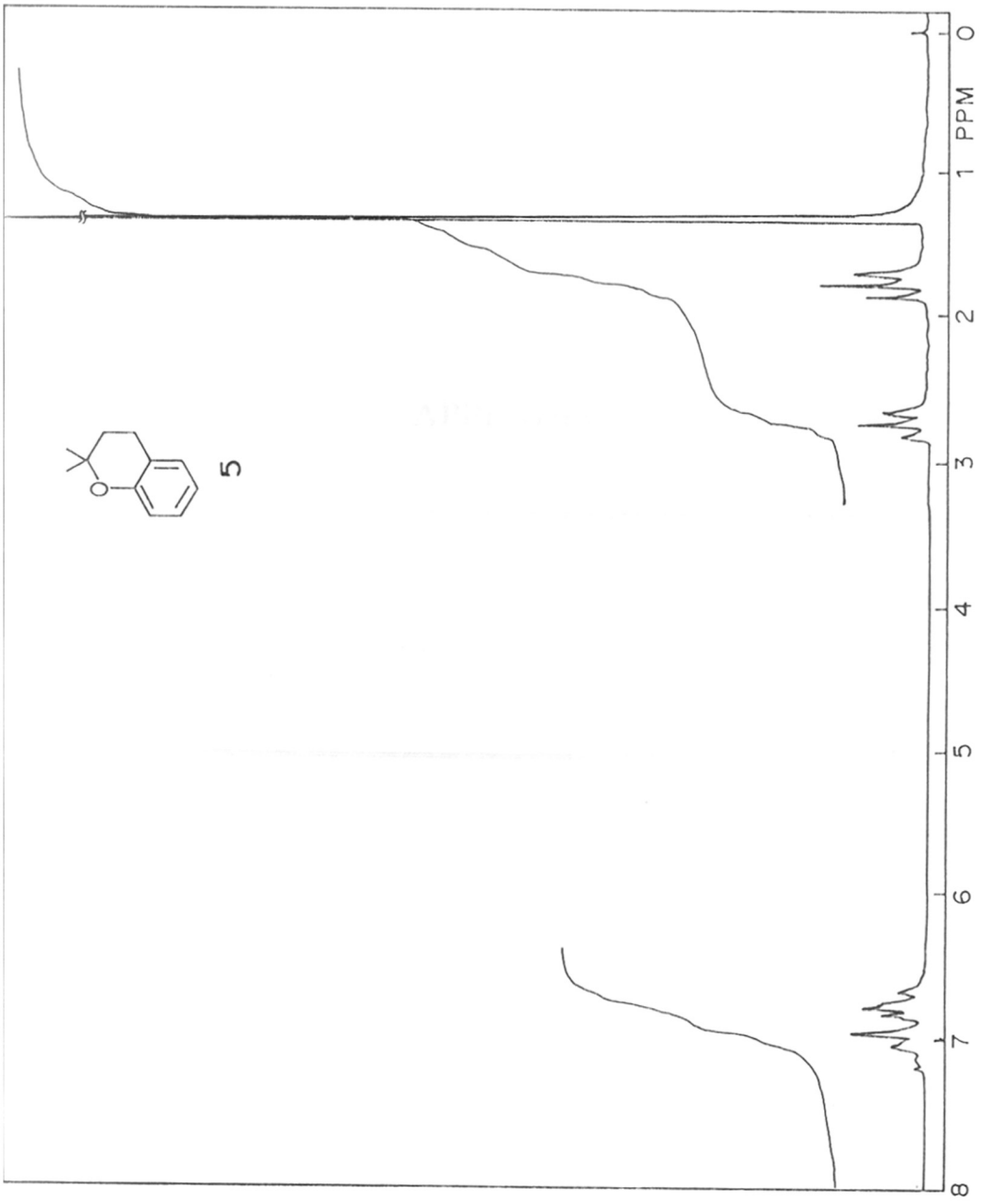
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APPENDIX

Synthesis of 1-methylamino-1-methylthio-2-nitroethene and hazard analysis of the reaction

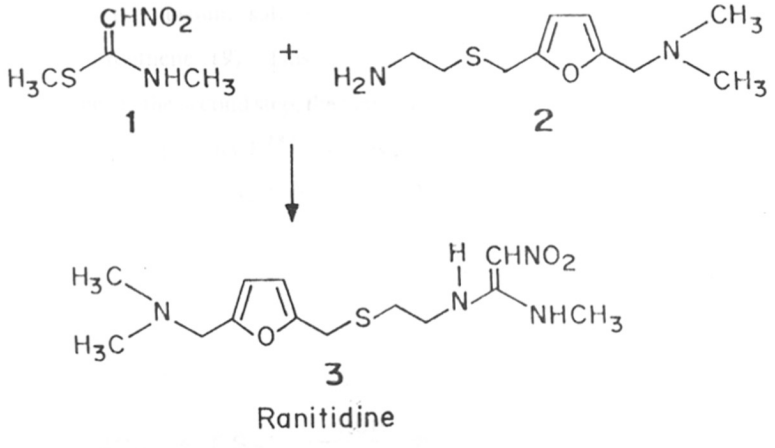
SUMMARY

1-Methylamino-1-methylthio-2-nitroethene (1) is an important intermediate for the synthesis of the anti-ulcer drug Ranitidine. A new method has been developed in our laboratory, for the synthesis 1-methylamino-1-methylthio-2-nitroethene (1) which involves condensation of nitromethane with N-methyl carbonimidodithioic acid dimethyl ester (CAD, 14) in the presence of zeolite catalyst. A systematic study of above reaction was carried out in light of explosive nature of nitro compounds. We have made use of sophisticated instruments like reaction calorimetry, accelerated reaction calorimetry, differential scanning calorimeter and thermogravimetric analyzer to generate data for intrinsic safety of this reaction, based on these findings we have modified the reaction for safe operation on commercial scale.

INTRODUCTION

1-Methylamino-1-methylthio-2-nitroethene[1,2] (MMN) (1) is an important intermediate in the synthesis of highly potent drug ranitidine.[3,4] 3 (Scheme 5.1). This drug is a powerful inhibiter of gastric acid secretion and extensively used in peptic ulcer therapy. There are very few methods reported in the literature for the synthesis of MMN (1).

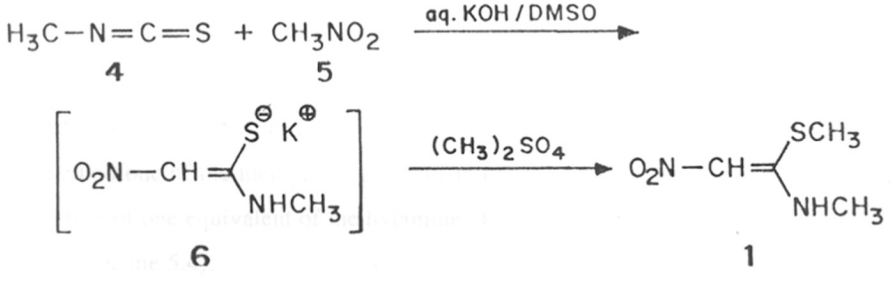
Scheme 5.1



1. Method A

In this method, nitromethane (5) was deprotonated by base[5,6] (KOH in DMSO, containing 7.5% water) and reacted with methyl isothiocyanate (4) in DMSO. The resultant potassium salt 6 was S-methylated to give 1-methylamino-1-methylthio 2-nitroehene (1) in good yield (Scheme 5.2).

Scheme 5.2



There are few drawbacks in this process.

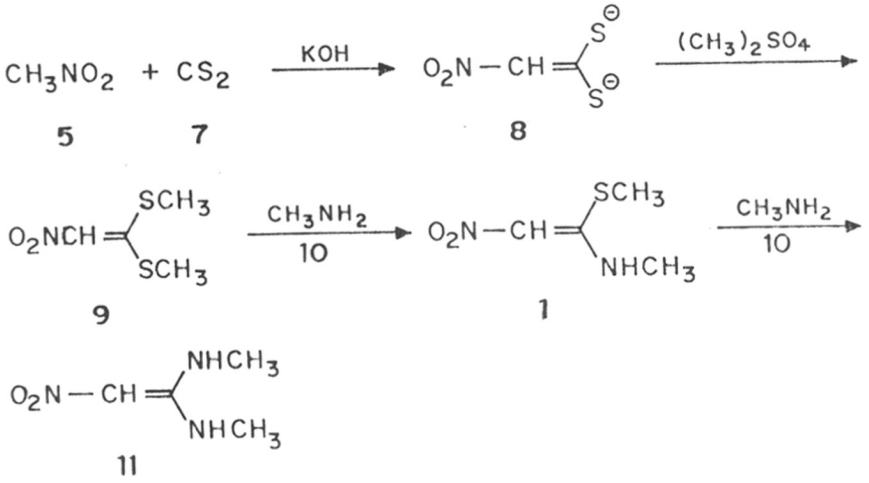
1) Nitromethane and alkali is a hazardous combination.

2) The use of DMSO as a solvent leads to serious environmental problems, moreover the recovery of DMSO from aqueous portion is difficult.

2. Method B

This method involves condensation of nitromethane (**5**) with carbon disulfide (**7**) in the presence of alkali to give the dipottasium salt **8**, which on methylation with dimethylsulfate offers 1,1-bismethylthio-2-nitroethene (**9**). This reaction is hazardous, since it involves combination of alkali and nitromethane. In the second step, the bismethylthio compound **9** is reacted with methylamine (**10**) to produce the required product **1** [7,8,9]. However, the reaction does not stop at monomethylation stage, the product **1** formed reacts further with another molecule of methylamine (**10**) to produce unwanted bismethylamino compound **11** as a by-product thereby reducing the yield of MMN (**1**) (Scheme 5.3). The process therefore has limitations.

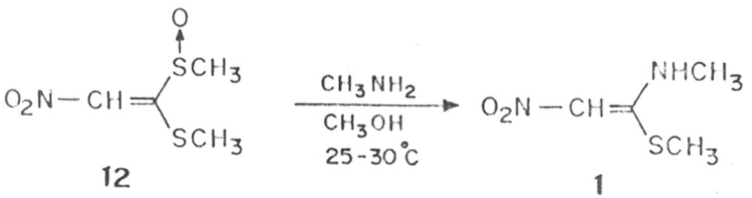
Scheme 5.3



3. Method C

The third approach for the synthesis of MMN (**1**) also starts from 1,1-bismethylthio-2-nitroethene (**9**). In this method one of the methylthio group of nitroethene was initially converted to sulfoxide **12**[10]. The reaction of one equivalent of methylamine (**10**) with this sulfoxide gives desired product **1** in high yield (Scheme 5.4).

Scheme 5.4

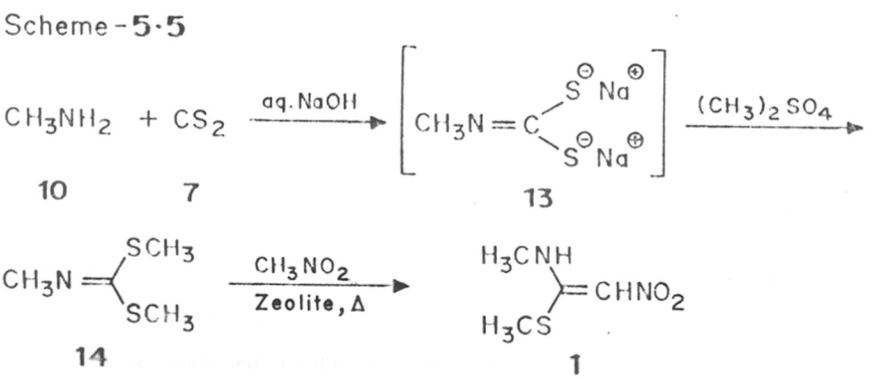


12 1

4. Method D

Recently, a novel method[11] has been developed in our laboratory for the preparation of MMN (1). This method involves condensation of methylamine (10) with carbon disulfide (7) in the presence of aqueous sodium hydroxide to give N-methyl carbonimidodithioic acid disodium salt **13**, which was then methylated with dimethyl sulfate to give corresponding dimethyl ester **14** in one pot. The condensation of this ester **14** with nitromethane (5) in the presence of zeolite catalyst gives required product **1** (Scheme 5.5). This process avoids the use of hazardous combination of alkali and nitromethane, there by making it safer than earlier processes. The catalyst used in this process is a stable alumino silicate zeolite, which can be reused several times after regeneration. The detailed computer simulation studies have been also carried out by Bhawal *et al*[12] on carbon-sulfur bond cleavage over Y-type zeolite.

Scheme 5.5



10 7 13 14 1

PRESENT WORK

Although the method developed for 1-methylamino-1-methylthio-2-nitroethene (MMN, **1**) at NCL looks superior as compared to other methods. This method involves heating a mixture of N-methyl carbonimidodithioic acid dimethyl ester (CAD) (**14**), nitromethane (**5**) and zeolite catalyst at 103-105°C (reflux temperature). In light of explosive nature of nitro compounds it was necessary to study the intrinsic safety of the reaction for commercial scale operation. Therefore, it was decided to study the thermochemical properties of the reaction. The thermal decomposition of product, reactants and catalyst were studied using DSC/TGA techniques. The thermochemical properties of reactants and product were also studied using accelerated rate calorimetry (ARC). The reaction was carried out in a reaction calorimetric (RC) apparatus under simulated process conditions.

RESULTS AND DISCUSSION

DIFFERENTIAL SCANNING AND THERMOGRAVIMETRIC STUDIES (DSC/TGA)

The DSC/TGA studies were conducted for reactants, product and used catalyst as well as regenerated catalyst to identify temperature of transitions. The results are given below in the Table 5.1.

Table 5.1. Thermogravimetric studies of reactants, product and catalyst.

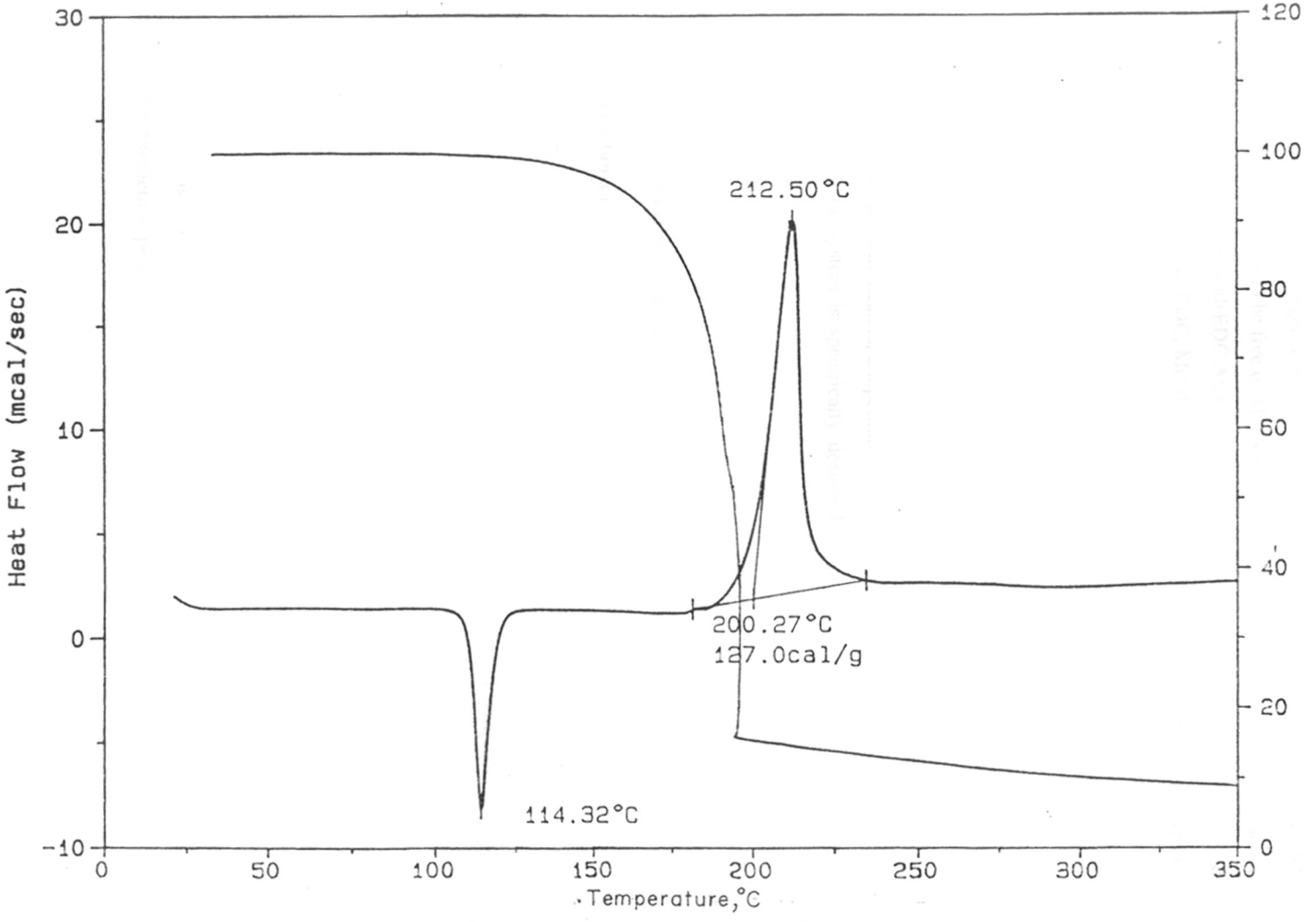
Sample	Onset of exotherm	Heat of reaction	Remarks
Nitromethane	200°C	--	
Product MMN (1)	170°C	127 cal/g	Highly exothermic
Catalyst[a]	--	--	

[a] No exotherm was observed upto 400°C

Nitromethane (**5**) showed onset of exotherm at 200°C. The product MMN (**1**), showed a sharp weight loss at around 114°C (Fig 1) and decomposed at 212°C. The fresh catalyst did not show any exotherm. It can be concluded that nitromethane (**5**) and catalyst are safe to use under the reaction conditions (100-103°C). However, the product MMN (**1**) showed a sharp weight loss at 114°C (see Fig 1), which is very close to the reaction temperature. The used catalyst retains small amount of

Sample: MM-2-NITROETHANE
Size: 4.9000 mg
Method: NCL
Comment: DSC N2 PURGE 20°C

Fig.1



MMN (1) in its cavities. Since, the regeneration of the catalyst involves heating the catalyst at 400°C, it is obvious that the catalyst should be free of MMN (1) for safe regeneration. For this purpose the catalyst was washed successively with EDC, MeOH and water. The Fig. 2 shows DSC plots for catalyst samples washed successively with EDC, MeOH and water. Mild exothermic peaks were observed for catalyst samples washed with EDC and MeOH, where as, successively water washed catalyst showed no such exotherm and it was comparable with fresh catalyst.

ACCELERATED RATE CALORIMETRY (ARC)

In this method, small quantities of liquid or solid samples are subjected to programmed temperature increase to determine the point at which the sample starts generating its own heat. This point is called onset of exotherm. The apparatus consists of a spherical bomb suspended inside a calorimeter jacket connected with heaters, temperature and pressure sensors, which are controlled by microprocessor unit. The system is specifically designed to automatically step up the sample temperature until self heat is generated.

The samples for which exothermicity was observed in DSC/TGA were further subjected to calorimetric studies employing ARC. The aim was to obtain more accurate data on the quantification of the exotherm and other related parameters *viz.,* pressure vs time, pressure vs temperature etc.

ARC test for reactants and product

i) Nitromethane (5)

Nitromethane (0.5 g) was kept in a spherical stainless steel bomb and was suspended in a calorimeter of ARC apparatus and the temperature was raised at the rate of 1°C/min. The self heat vs temperature and pressure vs temperature were recorded. The self heat rate vs temperature curve showed onset of exotherm due to decomposition of nitromethane at 250°C (Fig 3). The pressure vs temperature curve showed pressure raise upto 540 *psi* (Fig 4) at 325°C.

ii) N-methyl carbonimidodithioic acid dimethylester (CAD) (14)

CAD (14) (0.5 g) was kept in a spherical stainless steel bomb and experiment was carried out under similar conditions as described for nitromethane. The graph of temp v/s heat rate (°C/min) showed multiple exothermic peaks in ARC studies (Fig 5). The exothermic peaks were observed in

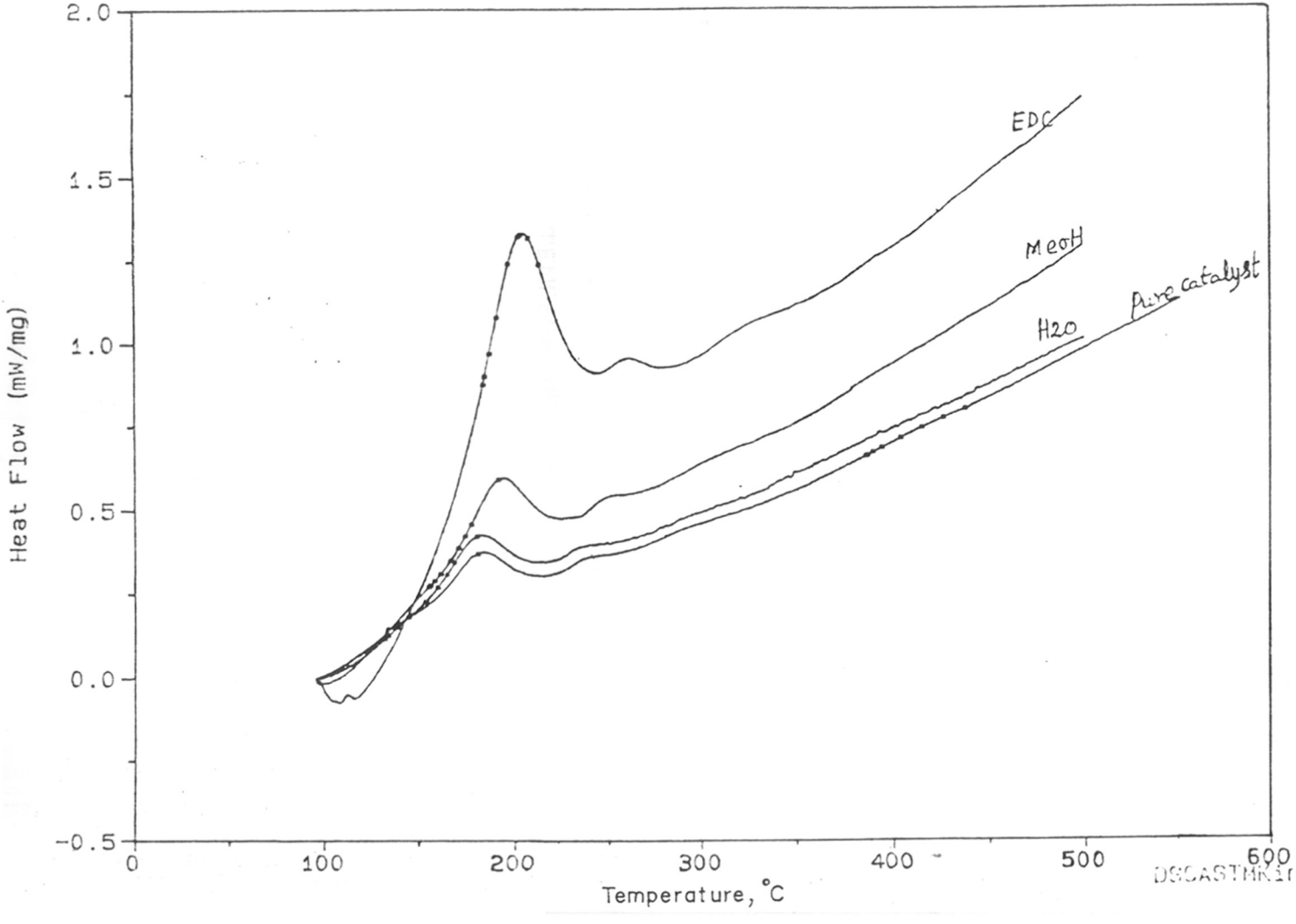
Sample : CATALYST WASHED WITH EDC

DSC

Operator: SURIANARAYANAN
Run Date: 22-Mar-92

Comment: DSC N2 PURGE 5 °C

Fig.2



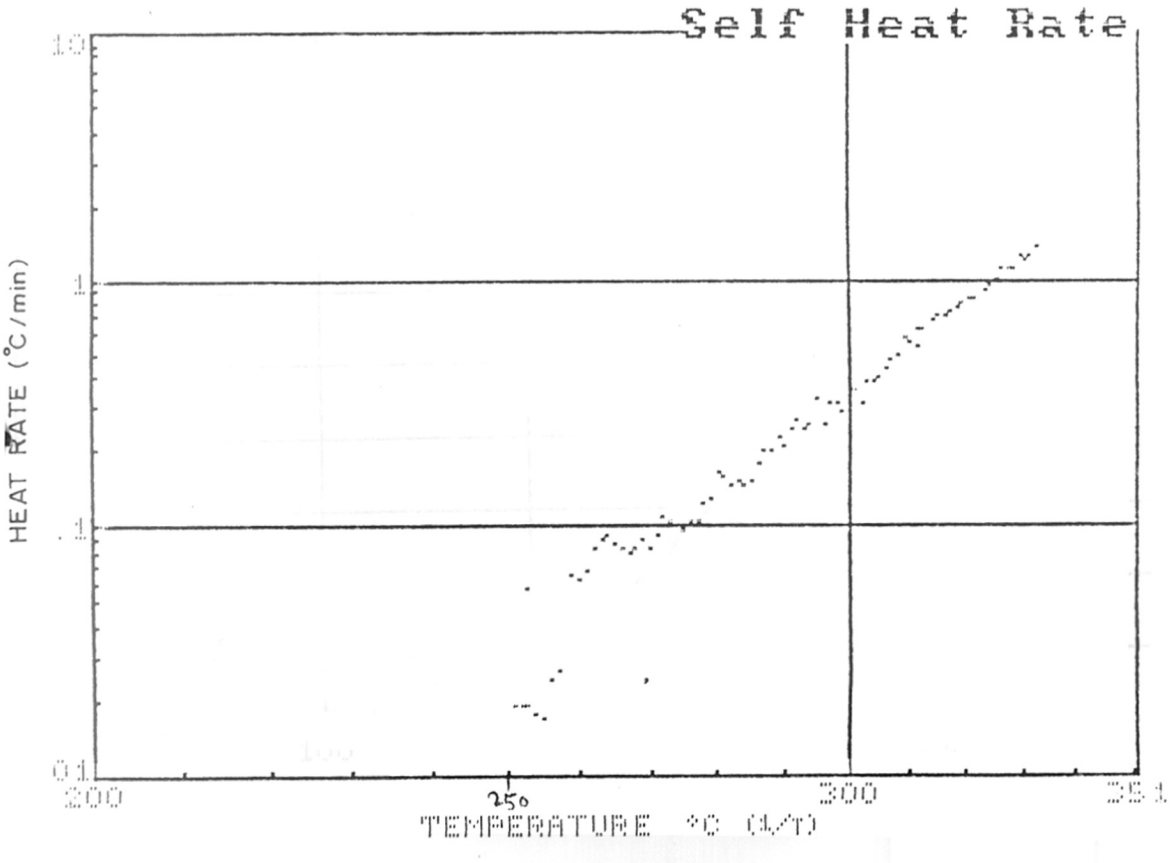


Fig. 3: Self Heat Rate (Nitromethane)

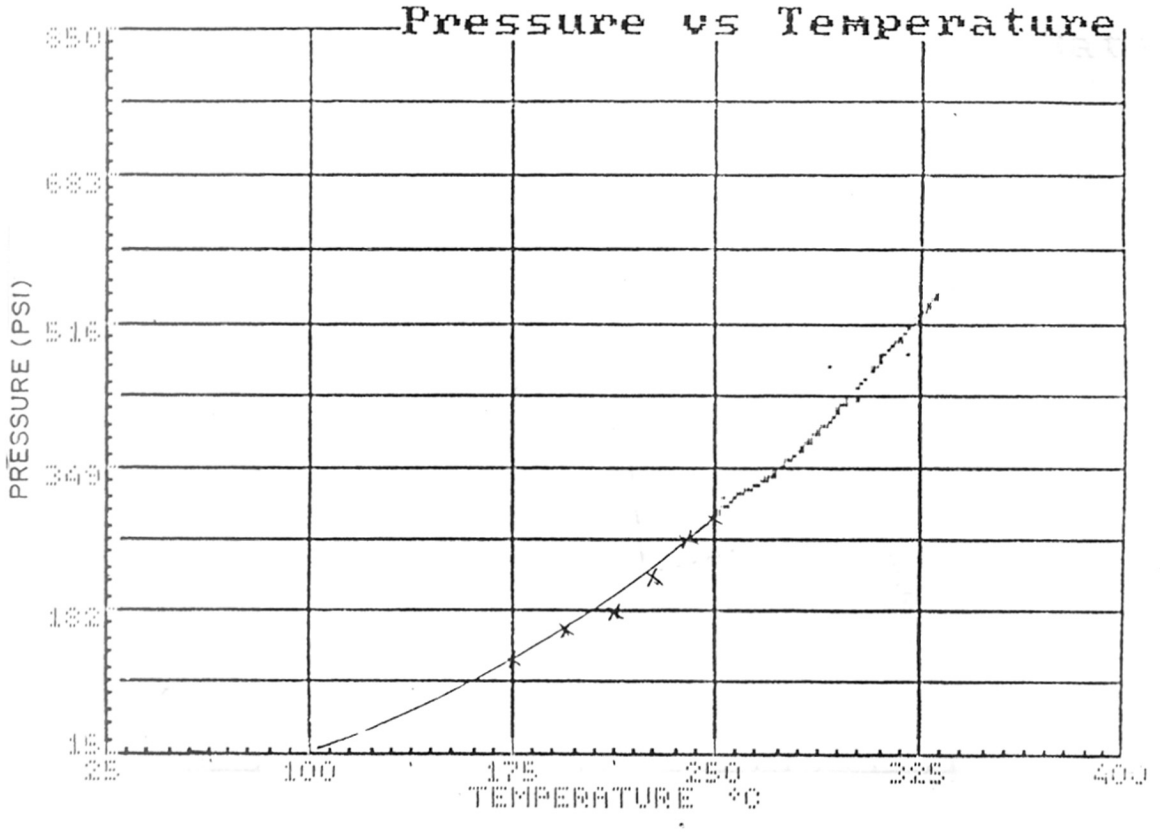


Fig. 4: Pressure vs Temperature (Nitromethane)

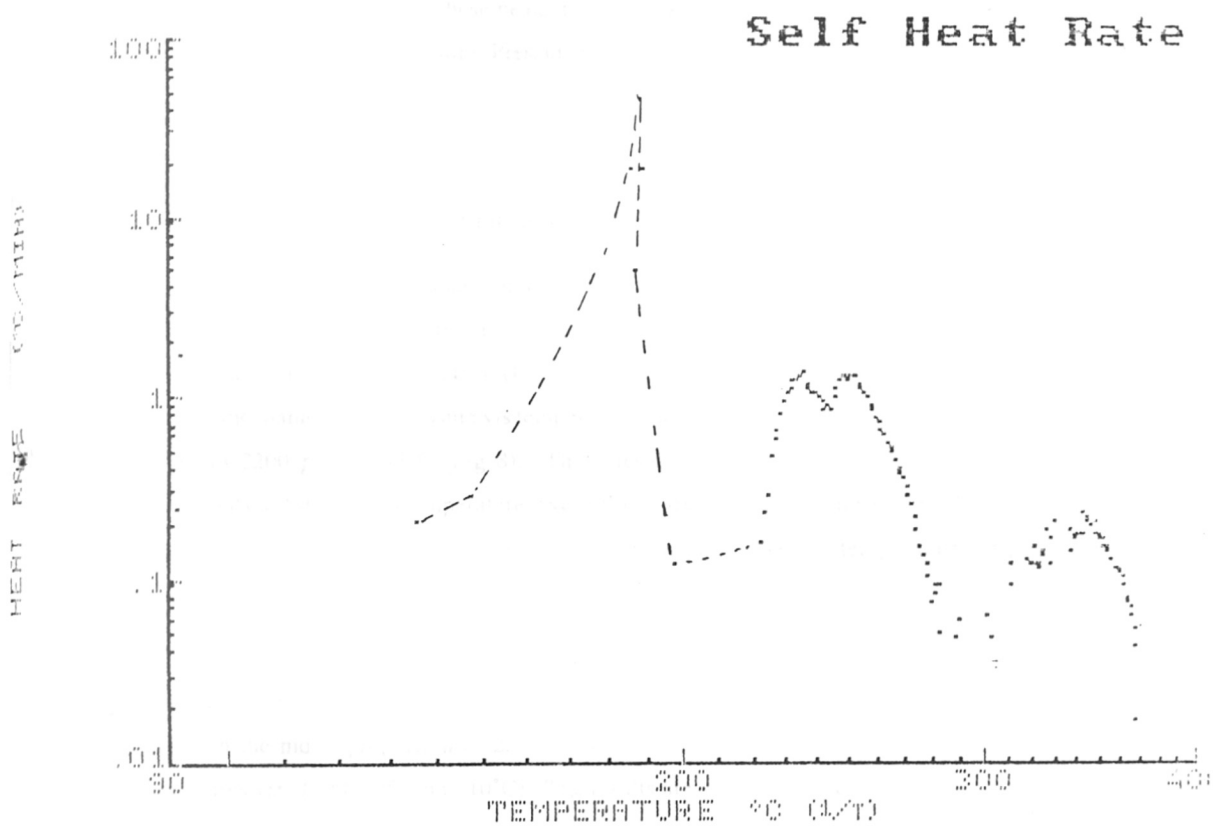


Fig. 5 : Self Heat Rate (CAD)

the range between 130-400°C. These peaks might be arising due to the decomposition of CAD (14) with increase in time and temperature. Pressure v/s temperature curve (Fig 6) showed a gradual increase in the

pressure similar to that of nitromethane (5).

iii) 1-methylamino-1-mthylthio-2-nitroethene (MMN) (1)

MMN (1) (0.5 g) when heated in a spherical bomb as described for nitromethane (5) showed decomposition with high exothermicity. Two exotherms were observed, a mild exotherm at 80°C and rapid increase in the exotherm at 110°C (Fig 7). The self heat v/s temperature looks to proceeds through a complex mechanism. The pressure v/s temperature showed a rapid increase in pressure from ambient pressure to 2200 *psi* at 145°C (Fig 8). These results indicated that the MMN (1) has onset of exothermicity at 110°C. This temperature is very close to reaction temperature (100-103°C). Therefore, the temperature of the reaction mixture should not be raised above this temperature. If possible, the reaction should be carried out much below this temperature.

Having generated data for MMN (1), CAD (14) and nitromethane (5) individually, it was decided to study the reaction under simulated process conditions. The reaction mixture of nitromethane: CAD: catalyst in the molar proportion of 2: 1: 0.5 was subjected for isothermal aging at three different temperatures *viz.*, (100, 105, and 110°C). The results are described below.

i) The reaction mixture kept at 100°C for 48 h in ARC showed no sign of exothermic behavior. After isothermal aging, it was subjected to heat-wait-search technique. The self heat rate curve shows an onset of exotherm at 140°C (Fig 9, plot 1).

ii) The reaction mixture was heated to 105°C and maintained at this temperature for 48 h. No unusual exothermic behavior was observed at any stage of reaction.

iii) The reaction mixture kept at 110°C in ARC showed an onset of exotherm (Fig 9, plot 2) within 2 h from start of the reaction and temperature started rising. The exotherm exhibited rapid self heat rate of 50°C/min around 280°C. Similarly self heat for MMN (1) and excess of nitromethane in the absence of zeolite showed an onset of exotherm after 2 h at around 110°C (Fig 9, plot 3). A pressure raise upto 1600 *psi* (Fig 10, plot 2) was observed. The pressure v/s temperature graph for MMN (1), and nitromethane (5) in the absence of zeolite at 110°C shows a pressure increase of 520 *psi* at 238°C (Fig 10, plot 3).

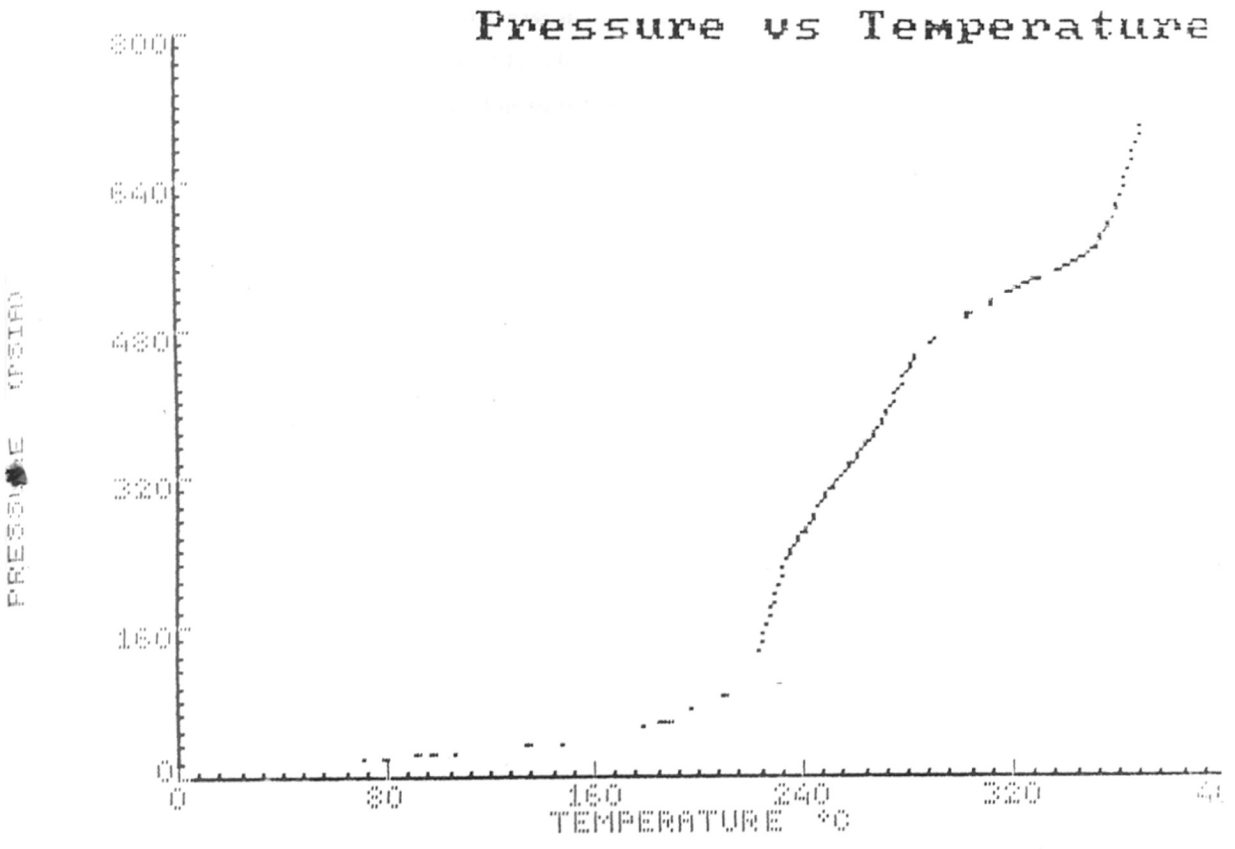


Fig. 6 : Pressure vs Temperature (CAD)

There is no appreciable increase in the pressure in case of reaction mixture kept at 100°C with isothermal aging (Fig 10 plot 1). The heat-wait-search technique indicated a slight pressure rise of about 600 psi at 232°C (Fig 10 plot 1).

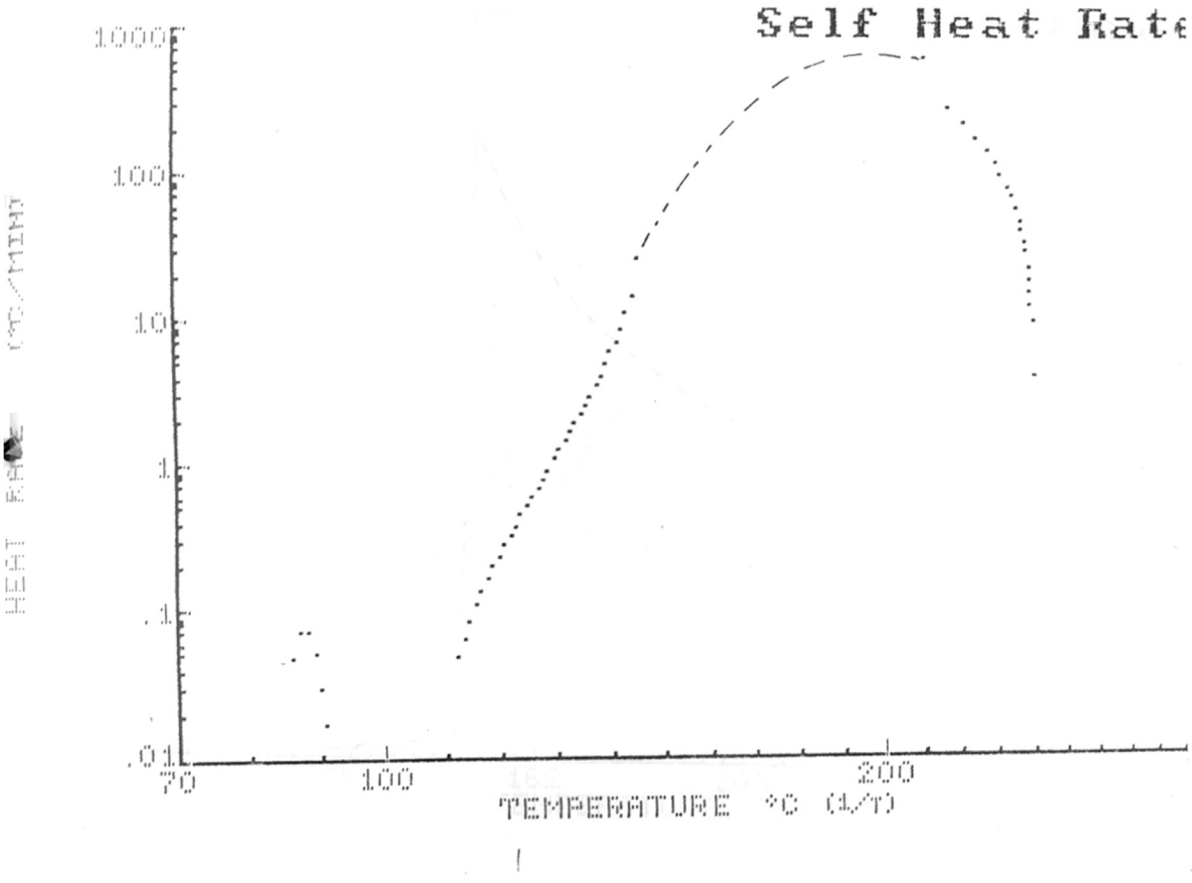


Fig. 7 : Self Heat Rate (MMN)

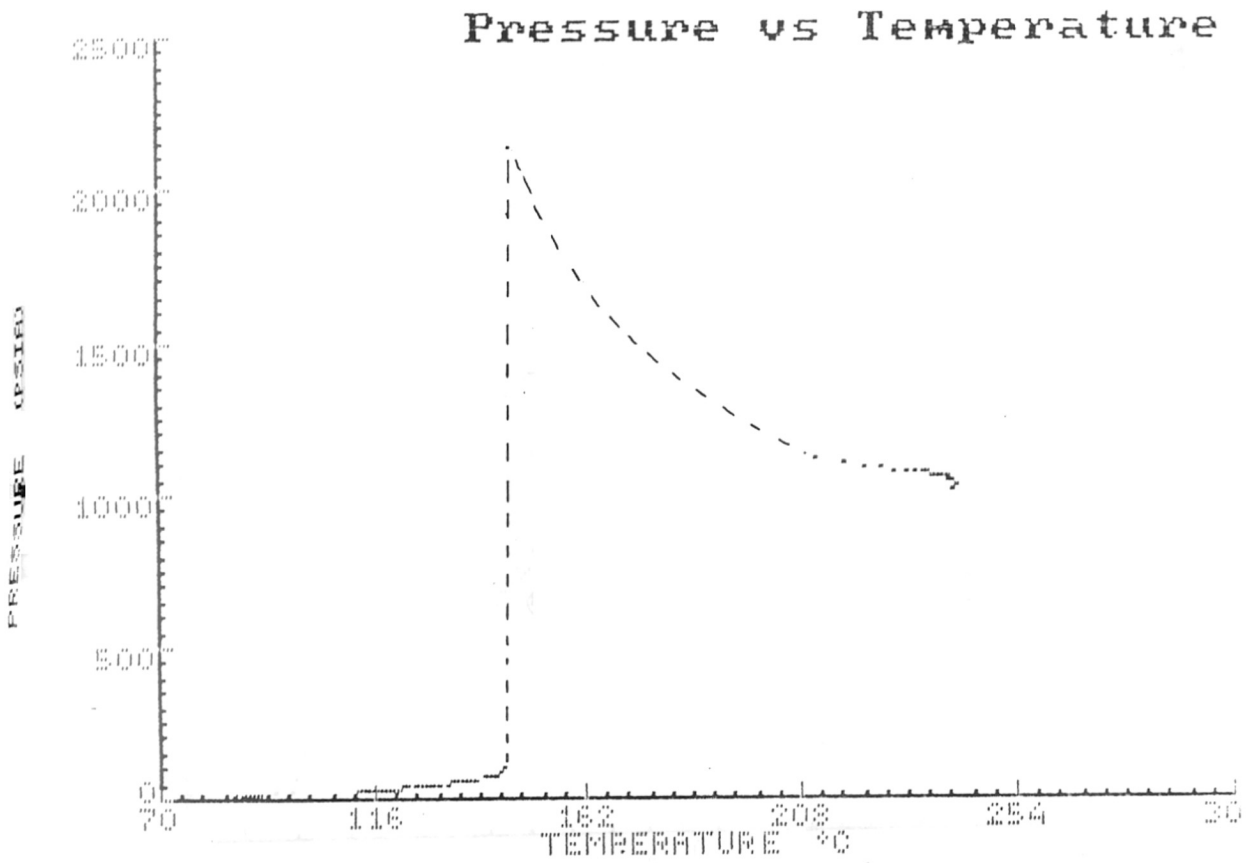


Fig. 8 : Pressure vs Temperature (MMN)

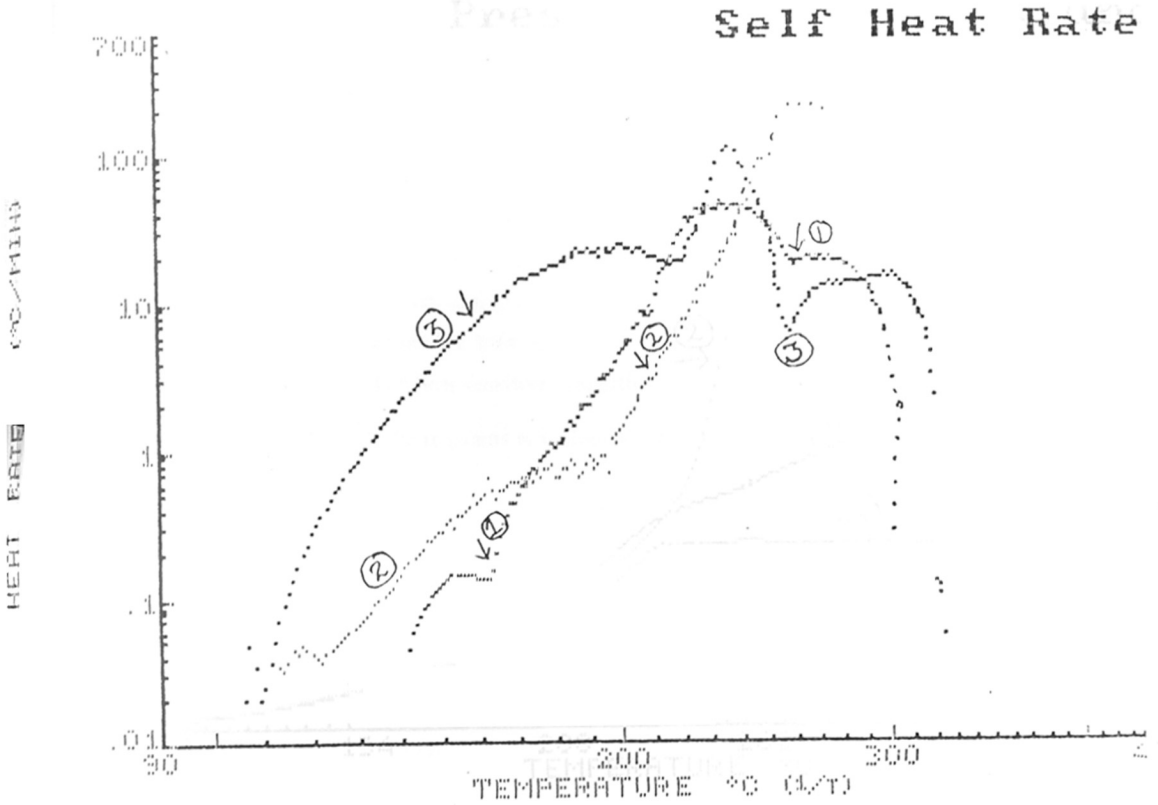


Fig.9

1. CAD + CH_3NO_2 ——Zeolite——> Heat-Wait-Search ——————>
   Iso-Aging
   o
   100 C

2. CAD + CH_3NO_2 ——Zeolite——>
   Iso-Aging
   o
   110 C

3. MMN + Excess Nitromethane

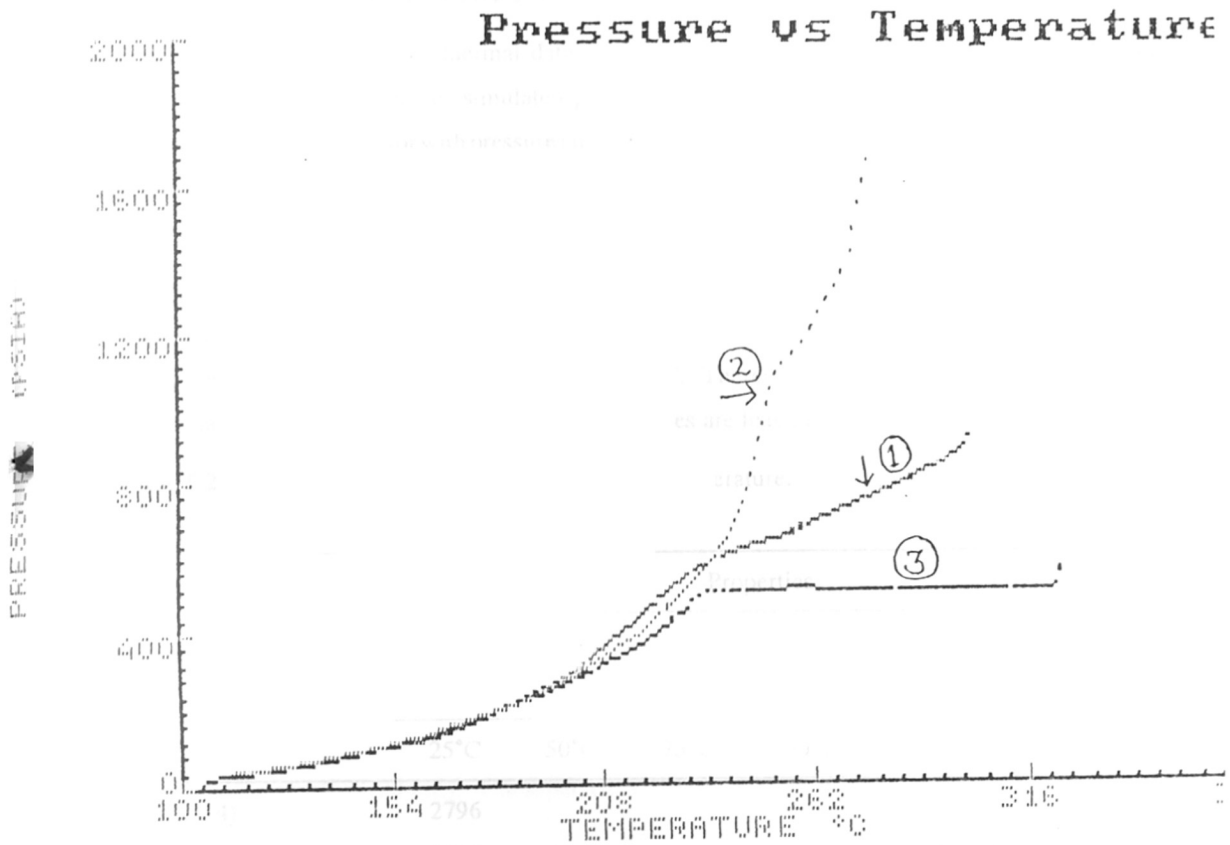


Fig. 10: Pressure vs Temperature

1. CAD + CH_3NO_2 ---Zeolite---> Heat-Wait-Search --->
   Iso-Aging
   100 °C

2. CAD + CH_3NO_2 ---Zeolite--->
   Iso-Aging
   110 °C

3. MMN + Excess Nitromethane

REACTION CALORIMETRIC STUDIES

In order to collect more thermal data at reaction conditions, the reaction was studied using reaction calorimeter (RC) under simulated process conditions. The apparatus is equipped with a medium pressure glass reactor with pressure and temperature controllers, reflux, distillation and stirring facilities.

Initially, heat capacity measurements were carried out by reaction calorimetry for CAD (14) (175 g), the zeolite catalyst was then added (75 g) and the thermal response during its addition at 25°C were measured. Finally nitromethane (300 g) was added and reaction was allowed to proceed by raising the temperature in stages 5°C/min upto 100°C. Thereafter the reaction mixture was kept at isothermal mode for 48 h. The heat sensitive properties are listed below in the Table 5.2.

Table 5.2. Heat capacity of the reactants at various temperature.

Compound	Properties				
	Heat Capacity (J/kg k)				Heat of mixing/reaction (KJ/mol)
	25°C	50°C	75°C	100°C	
CAD (14)	2796				
CAD + Zeolite	2744				-0.0020 (exothermic)
CAD + Zeolite + Nitromethane (5)	1619	1680	1752	1952	25.15 (endothermic)

From the above Table 5.2 it is clear that the reaction is endothermic in nature.

All major chemicals involved or obtained in the reaction showed exothermic behavior. This suggest that at any given time the temperature of the reaction mixture should not cross 110°C. Therefore, it was necessary to bring down the temperature of the reaction well below 110°C for safer operation. ARC studies proved that the reactants, nitromethane and CAD (14) are safe except the MMN (1), which showed the exotherm at 110°C indicating that at no point the temperature of the reaction mixture should rise above this temperature.

The reaction when carried out at 110°C in RC exhibited exothermic behavior after 2 h of operation. This possibly due to exothermic decomposition of MMN (1) formed during this period and its subsequent accumulation due to enhanced reaction rate at this temperature. This situation may lead

to thermal runway, if appropriate precautionary measures are not taken. From the operation angle, the reaction system may not tolerate positive excursions beyond 4 to 5°C over 105°C. This leaves very narrow band for temperature controls on commercial scale operation.

In conclusion the above studies have shown that the reactants and product decompositions are exothermic. Especially the MMN (**1**) quite unsafe above 110°C.

Hence, it was necessary to bring down the temperature of the reaction well below 110°C for safer operation. Therefore, the reaction was carried out at 80-85°C in nitromethane solvent for 48 h. A very poor yield of MMN (**1**) was obtained under these conditions. The nitromethane reflux condition not only provided higher temperature, but also might be helping to drive out gaseous product, methyl mercaptan formed during the reaction and thus shifting the equilibrium toward the required direction. Therefore, we thought that the reaction can be carried out at lower reflux temperature using lower boiling solvent as diluent in the reaction mixture.

Various solvents were used as a diluent to reduce the temperature of the reaction. Thus, a mixture of one equivalent of CAD (**14**), one equivalent of nitromethane, zeolite catalyst (RE-NaY) [50% of mass to that of CAD (**14**)] and n-propyl alcohol (20 mL) was refluxed for 48 h. The inside temperature was around 96-97°C. The catalyst was filtered and washed with n-propanol. The excess of n-propanol and unreacted nitromethane was removed by distillation under reduced pressure and the residue was treated with pet. ether (20 mL). The separated solid was filtered to isolated in 13% yield. The pet. Ether layer was washed with water (10 mL) and dried over anhydrous sodium sulfate. The removal of solvent gave 60% unreacted CAD (**14**). Similarly other solvents were also used as diluents in the reaction. The results are summarized in Table 5.3.

Table 5.3. Use of various solvents as diluents for MMN (**1**) preparation[a].

Entry	Solvent[a]	Reaction Temp (°C)	Yield[b] (%)
1.	Diglyme	110	13.30
2.	Toulene	112	13.70
3.	n-Propanol	97	13.65
4.	Trichloroethylene	85-87	9.90
5.	Ethylene dichloride	85	14.20

[a] In all the cases a mixture of CAD (**14**) (1 eq), nitromethane (**5**) (1 eq) and catalyst RE-NaY (50 % by mass to that of CAD) and solvent (20 mL) was refluxed for 48 h. [b] Isolated yield of pure MMN (**1**).

The poor yield of the MMN (**1**) may be due to less amount of nitromethane (**5**) used as compared to reported procedure[11] (where, five fold excess of nitromethane was used). Therefore, the effect of various amounts of nitromethane (**5**) on the yield of MMN (**1**) has been studied under above conditions using ethylene dichloride as a solvent, which is summarized in Table 5.4.

Table 5.4. Influence of nitromethane (**5**) concentration on the MMN (**1**) formation.

Entry	CAD/Nitromethane mole ratio[a]	Yield (%)
1.	1:1	13.31
2.	1:2	16.55
3.	1:3	21.00
4.	1:4	30.00
5.	1:5	34.45

[a] All reactions were carried out using EDC as diluent (30 mL) at reflux temperature for 48 h.

The above Table 5.4 showed that the yield of MMN (**1**) progressively increase with increase in the amount of nitromethane (**5**). The reaction when carried out with one equivalent of CAD (**14**) and five equivalent of nitromethane (**5**) and zeolite catalyst (RE-NaY) (50 % mass to that of CAD) with ethylene dichloride as a diluent (30 mL) gave 34% yield of the MMN (**1**) (entry 5). The reaction mixture attained a temperature of 92°C, which is well below the onset exotherm temperature (110°C) for MMN (**1**). Therefore, these reaction conditions are suitable for commercial scale operation.

CONCLUSION

In conclusion we have developed a safe method for the synthesis of 1-methylamino-1-mrthylthio-2-nitroethene (1). This procedure eliminates drawbacks involved in the earlier reported procedure. We have made use of sophisticated instruments to generate data for intrinsic safety of the reaction based on these findings, we have modified the reaction for safe operation on commercial scale.

EXPERIMENTAL

N-methyl carbonimidodithioic acid dimethyl ester (CAD, 14)[13]

To a cooled solution of carbondisulfide (**7**) (73.56 g, 1 mol) aqueous solution of methyl amine (**10**) (77.8 g, 0.97 mol) was added dropwise in 20 min. The reaction mixture was stirred for 10 min and sodium hydroxide (38.8 g, 0.97 mol) solution (60 mL) was added dropwise at 15-20°C in 15 min followed by addition of dimethyl sulfate (122 g, 0.97 mol) in about 25 min. The reaction mixture was then stirred for 1 h. The organic layer was separated and the aqueous layer was extracted with dichloromethane (2X75 mL) and the combined organic layer was washed with water (100 mL) and dried over sodium sulfate. Removal of solvent offered a pale yellow liquid (86.0 g, 74%), bp (120-122°C/70 mm (lit[13] bp 188-192°C).

IR (Neat)	:	1580 cm^{-1}
^{1}**H NMR**	:	2.30 (s, 3H), 2.55 (s, 3H), 3.15 (s, 3H)
MS (*m/z*)	:	135 (M^+, 60%), 93 (100%).

1-methylamino-1-methylthio-2-nitroethene (MMN, 1)

To a stirred mixture of CAD (**14**) (27.0 g, 0.2 mol) and EDC (30 mL), zeolite catalyst (14.0 g) was added at room temperature. To this reaction mixture nitromethane (61.0 g, 1.0 mol) in EDC (30 mL) was then added and it was refluxed for 48 h. The catalyst was filtered, washed with EDC (2X25 mL) and the solvent and excess nitromethane was removed under reduced pressure. The residue was cooled in ice bath and pet. Ether (50 mL) was added. The separated solid was filtered and dried in air to give 10.10 g (34%) of MMN (**1**). The pet. Ether filtrate was washed with water (20 mL) and dried on anhydrous sodium sulfate. The removal of solvent under reduced pressure furnished unreacted CAD (**14**) (13.95 g 51%).

The crude MMN (**1**) was recrystalized from ethanol to get pure light yellow crystals (9.65 g, 32%), mp 112-113°C (lit[11] mp 113°C).

IR (Nujol)	:	3350, 1580, 1470, 1390 cm^{-1}
^{1}**H NMR**	:	2.45 (s, 3H), 3.15 (d, *J*= Hz, 3H) 6.64 (s, 1H), 10.5 (bs, 1H).
MS (*m/z*)	:	148 (M^+, 80%), 55 (100%).

Preparation of MMN (1) using n-propyl alcohol as a diluent

To a mixture of CAD (**14**), (13.5 g, 0.1 mol), nitromethane (**5**) (6.1 g, 0.1 mol) and n-propyl alcohol (20 mL), zeolite catalyst (RE-NaY)(7.0 g) was added slowly. The reaction mixture was refluxed for 48 h. The catalyst was filtered and washed with n-propanol (20 mL). The excess of n-propanol and unreacted nitromethane was removed by distillation under reduced pressure and the residue was treated with pet. Ether (20 mL). The separated solid was filtered to get MMN (**1**) (1.98 g, 13%). The pet. Ether layer was washed with water (10 mL) and dried over anhydrous sodium sulfate. The removal of solvent furnished unreacted CAD (**14**) (8.1 g, 60%).

Similar procedure was used for the preparation of MMN (**1**) using other solvents as diluent.

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List of Publications

Patents

1. An improved Process for Manufacture of Linear Alkyl Benzenes.
   A.R.A.S. Deshmukh, **V.K. Gumaste,** and V.P. Shiralkar and B.V. Bapat.
   Ind. Patent Appl.No. 1024/DEL/90.

2. An improved Process for the Preparation of Linear Alkyl Benzenes.
   A.R.A.S. Deshmukh, **V.K. Gumaste,** and V.P. Shiralkar.
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