STUDIES IN STEREOSELECTIVE TRANSFORMATION ON ARENE-CHROMIUM TEMPLATE

A THESIS

SUBMITTED TO THE

UNIVERSITY OF POONA

FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY

(IN CHEMISTRY)

S. GANESH

NATIONAL CHEMICAL LABORATORY

PUNE-411 008

1993

CERTIFICATE

Certified that the work incorporated in the thesis entitled **"Studies in Stereoselective Transformation on Arene-Chromium Template"** submitted by **Mr. S. Ganesh** was carried out by the candidate under my supervision. Such material as has been obtained from other sources has been duly acknowledged in the thesis.

Date: 23/6/93

National Chemical Laboratory,

Pune 411 008.

(Dr. A. Sarkar)

Research Guide

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Finally I am thankful to the UGC for the financial assistance and to the Director, National Chemical Laboratory, Pune, for permitting me to submit this work in the form of a thesis.

S. Ganesh

(S. Ganesh)

DEDICATED TO MY BELOVED PARENTS

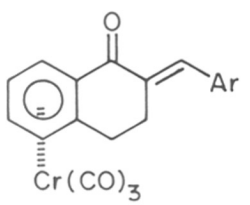
CONTENTS

Chapter - 1 : *Stereoselective Synthesis using Arene Chromium Tricarbonyl Complexes - A Review*

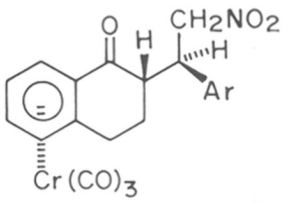
Arene chromium tricarbonyl complexes has been extensively used as a stereoface-directing group whereby considerable stereocontrol can be achieved in various organic reactions. In this review, significant results pertaining to this aspect of the arene-chromium chemistry have been discussed to serve as a background to the present work.

Chapter - 2 : *Conjugate Nucleophilic Addition to Enones Complexed with Tricarbonylchromium*

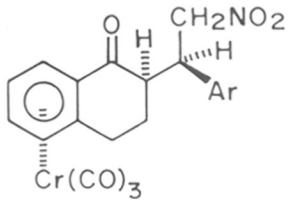
In order to investigate the steric effect of chromium tricarbonyl at a site three carbon removed from the metal-complexed arene ring, Michael reactions on suitable benzylidene substrates were carried out with different nucleophiles. Aromatic aldehydes were condensed with 1-tetralone complexed with $Cr(CO)_3$ in ethanolic potassium hydroxide to provide the substrates (**1a-d**) in excellent yield. Conjugate addition of nitromethane (solvent) was carried out with KF (stoichiometric) and 18-Crown-6 (catalytic) at room temperature. A pair of diastereomeric products (**2a-d** and **3a-d**) were obtained in good to very good yield in each case. These were separated by column chromatography and characterized.



1a-d



2a-d

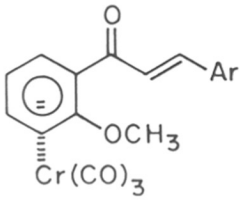


3a-d

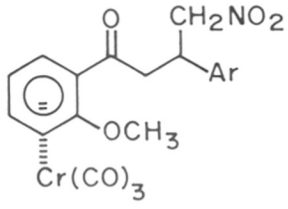
Ar

a : C_6H_5
b : $p\text{-}CH_3\text{-}C_6H_4$
c : $p\text{-}OCH_3\text{-}C_6H_4$
d : $p\text{-}NO_2\text{-}C_6H_4$

It was established that the nucleophile added to the substrate with 100% stereospecificity from the face opposite to the metal. The epimers had arisen out of a keto-enol equilibrium at the centre adjacent to the carbonyl group. The relative configuration of the major isomer was confirmed by X-ray crystal structure analysis. It was shown that preferential protonation also occurred from the face opposite to the metal, as anticipated. The NMR peak assignments were carried out with COSY and HETCOR experiments. Conjugate addition of nitromethane on the acyclic substrates **4a-c** occurred with modest selectivity. With dimethyl malonate as the nucleophile, a tricyclic product was obtained as single diastereomer. The structure of the compound was assigned as an enol lactone.



4a-c



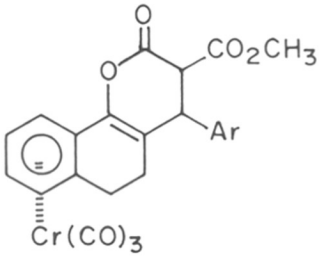
5a-c

Ar

a : C_6H_5

b : p-CH_3-C_6H_4

c : p-OCH_3-C_6H_4



6a-b

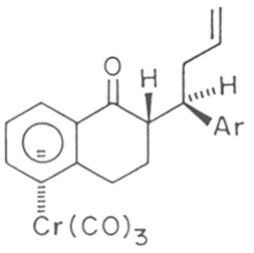
Ar

a : C_6H_5

b : p-CH_3-C_6H_4

Chapter - 3 : *Lewis Acid Mediated Conjugate Addition of Allylsilane and Allylstannane to Enones Complexed with Tricarbonylchromium*

$TiCl_4$-mediated conjugate addition of allyltrimethylsilane and allyltributylstannane to the tetralone-benzylidene complexes **1a-b** yielded the products **7a-b** as single diastereomer in very good yield. Titanium tetrachloride proved to be the most efficient Lewis acid for this reaction. The formation of a single diastereomer is probably the result of low-temperature kinetic quench of the titanium enolate. The low-temperature reaction proceeded with appreciable stereoselectivity (70 : 30) even on the acyclic substrate **4a-c** to afford the products **8a-c** in very good yield.

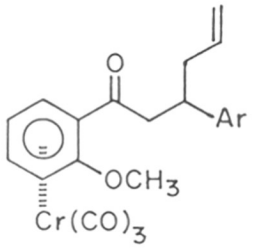


7a-b

Ar

a : C_6H_5

b : p-CH_3-C_6H_4



8a-c

Ar

a : C_6H_5

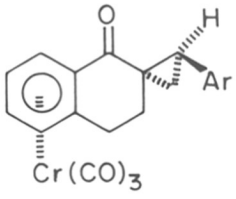
b : p-CH_3-C_6H_4

c : p-OCH_3-C_6H_4

Chapter - 4 : *Cyclopropanation of the Enones Complexed with Tricarbonylchromium*

Cyclopropanation using sulfoxonium ylides can be viewed as a nucleophilic attack followed by intramolecular electrophilic cyclization. Using trimethylsulfoxonium iodide with 50% aq sodium hydroxide

solution in dichloromethane containing 2 mol% of tetrabutylammonium bromide the cyclopropanated products **9a-c** were obtained from the substrates **1a-c**, in very high yield as single diastereomer. Uncomplexed 2-benzylidene-1-tetralone did not undergo cyclopropanation under the same condition. The X-ray crystal structure of the compound **9a** revealed that the cyclopropane was actually appended from the same face as that of the metal. Such reversal of stereoselectivity on arene-$Cr(CO)_3$ complexes is unprecedented. The steric course remained the same when the reaction was carried out in tetrahydrofuran with preformed ylide under homogeneous condition.



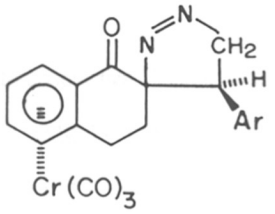
9a-c

Ar

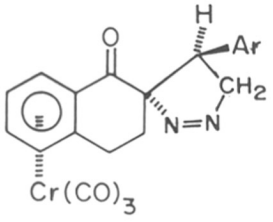
a : C_6H_5

b : $p\text{-}CH_3\text{-}C_6H_4$

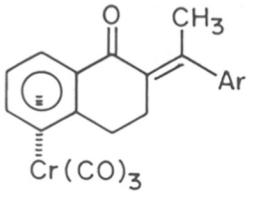
c : $p\text{-}OCH_3\text{-}C_6H_4$



10a-c



11a-c



12a-c

Ar

a : C_6H_5

b : p-CH_3 -C_6H_4

c : p-OCH_3 -C_6H_4

Chapter - 5 : *3 + 2 Cycloaddition of Diazomethane to Enones Complexed with Tricarbonylchromium*

Diazomethane reacts with enones to provide the 3 + 2 cycloaddition product. On treatment with an ethereal solution of diazomethane, the tricarbonylchromium complexes **1a-c** afforded the diastereomeric cycloaddition products **10a-c** and **11a-c**, which were separated by chromatography and characterized by spectroscopy and elemental analyses. Pyrolysis in refluxing toluene cleanly afforded the enones **12a-c** irrespective of the diastereomer used, and no cyclopropane was detected.

Note: The compound numbers incorporated in the Synopsis are different from those appearing in the Thesis.

Publications :

1. Highly Diastereoselective Michael Addition to 2-Arylidene-1-tetralones Complexed with $Cr(CO)_3$
   Sambasivam Ganesh and Amitabha Sarkar
   Tetrahedron Letters, *1991*, 32, 1085-1088.

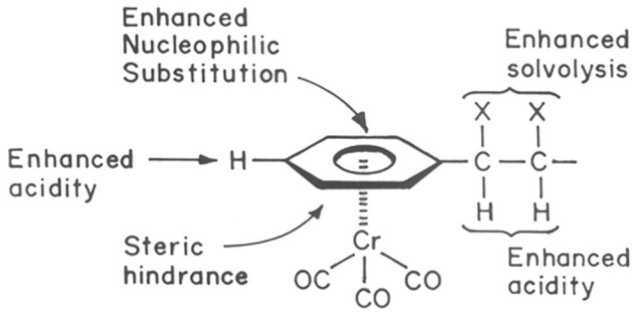
2. Complete Reversal of Stereoselectivity in Cyclopropanation of 2-Arylidene-1-Tetralone Tricarbonylchromium Complexes
   Sambasivam Ganesh, Kashinath M. Sathe, Malay Nandi, Pinak Chakrabarti and Amitabha Sarkar
   J.Chem.Soc.Chem.Commun., *1993*, 224-226.

CHAPTER - 1

Stereoselective Synthesis Using Arene Chromium Tricarbonyl Complexes : A Review

The complexation of an arene to a $Cr(CO)_3$ fragment alters its chemistry in a number of ways (Scheme 1):

Scheme 1



The aromatic ring, contrary to its usual reactivity to electrophiles, becomes susceptible to nucleophilic addition[1]. Both the rate of solvolysis[2] and acidity[3] of the protons attached to benzylic or homobenzylic site are enhanced. In addition to such modification of reactivity the stereochemical aspect recieved considerable attention over the recent years. It is possible to carry out stereospecific *anti* addition of reagents with respect to the $Cr(CO)_3$ moiety and accomplish efficient diastereoselective synthesis of a large number of complex molecular structures.

The most efficient stereocontrol has been obtained at the α carbon attached to the aromatic ring complexed with chromium tricarbonyl. Reactions at the β carbon have also been found to proceed with high diastereoselectivity. We present in the following pages a representative survey of current results concerning such diastereoselective synthesis using arene $Cr(CO)_3$ as a stereoselective template.

We recognize that an unsymmetrically substituted aromatic ring complexed with a $Cr(CO)_3$ moiety would constitute a *dl* pair[4] (Scheme 2).

Scheme 2

The chiral element is introduced by destroying the plane of symmetry of the benzene ring. Therefore, if we begin with one optical antipode of such a complex, subsequent diastereoselective transformation would result in an enantioselective synthesis leading to optically pure products.

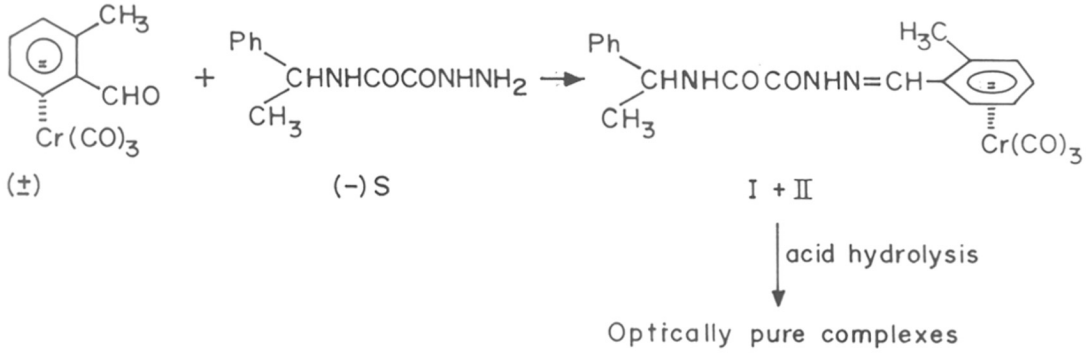
There are several methods to obtain arene $Cr(CO)_3$ complexes in optically pure form. Many of the standard resolution procedures can be readily adopted. For instance, the racemic acids can be readily resolved using optically active amines[5]. Complexed aromatic amines are too weak bases to provide diastereomeric salts with optically pure acids commonly employed in resolution. The complexes bearing aliphatic alkoxy function can be resolved *via* their hemi succinates[6].

Resolution of racemic aldehydes can be achieved by the use of S(-)-5-α-phenylethyl semioxamazide[7] (Scheme 3).

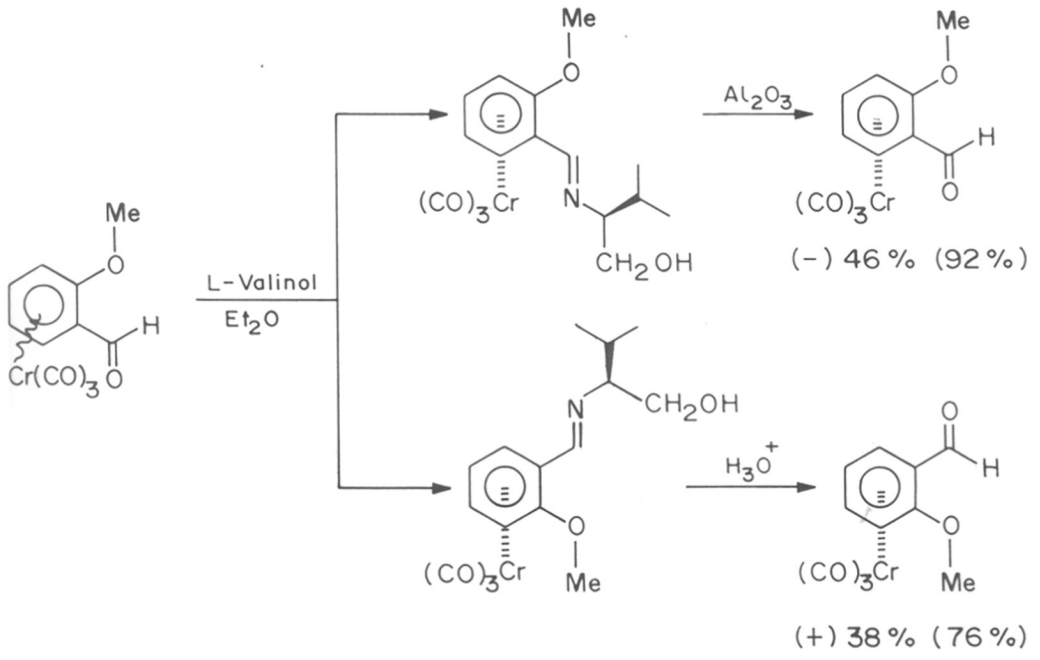
The diastereomeric derivatives were separated using column chromatography and the optically active complexed aldehydes were obtained on acid hydrolysis.

Davies et al[8] have standardised a very useful resolution method for *ortho* substituted aldehydes. Treatment of racemic complex with L-Valinol in diethyl ether containing 4A molecular sieves afforded a diastereomeric mixture of imines which could be separated by column chromatography. Subsequent hydrolysis gives optically active products(Scheme 4).

Scheme 3

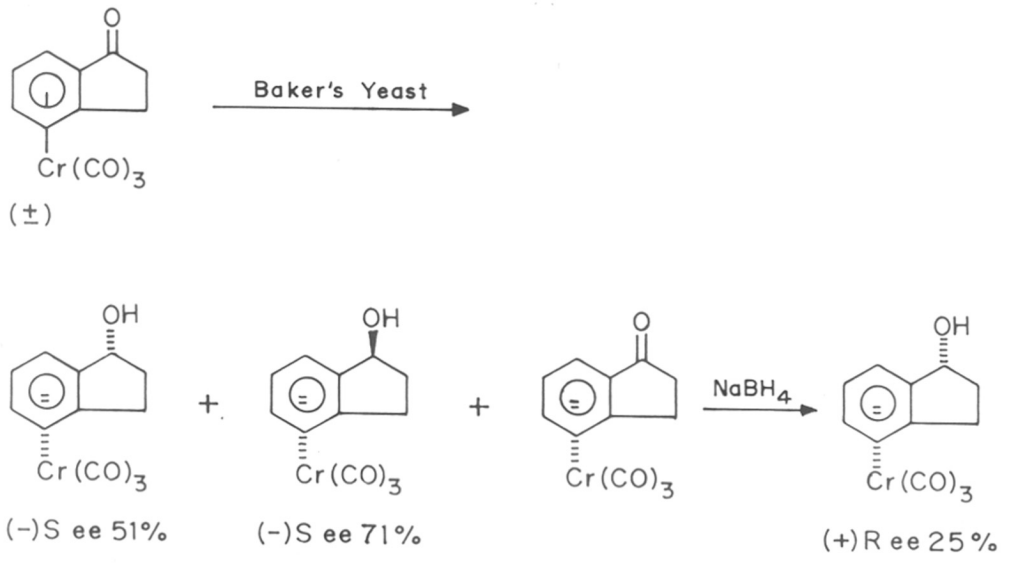


Scheme 4



Microbial and enzymatic resolutions have also been attempted on arene $Cr(CO)_3$ substrates. Characteristic of such processes, high enantiomeric excesses were obtained with a limited number of structures. For example acetophenone $Cr(CO)_3$ complex was completely reduced by baker's yeast in 24h, the chemical yield of the process was 96% with *ee* of 99%. But 1-indanone $Cr(CO)_3$ complex was reduced by baker's yeast much less efficiently[9](Scheme 5).

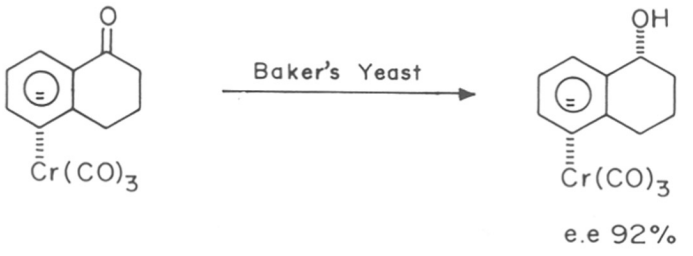
Scheme 5



On the other hand the tetralone $Cr(CO)_3$ complex was reduced with baker's yeast with 92% *ee*[10] (Scheme 6).

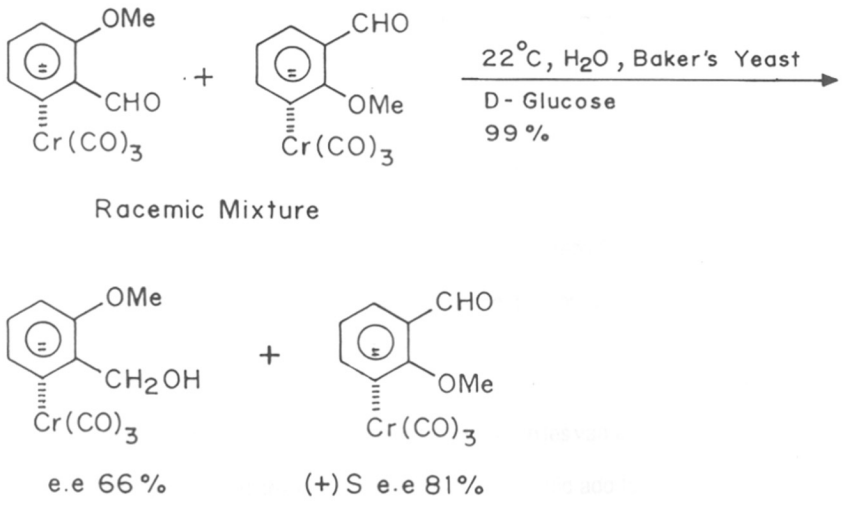
Reduction of aryl alkyl ketone complexes also proceeded with considerable success in terms of enantioselectivity depending on the substitution pattern on the aromatic ring[10].

Scheme 6



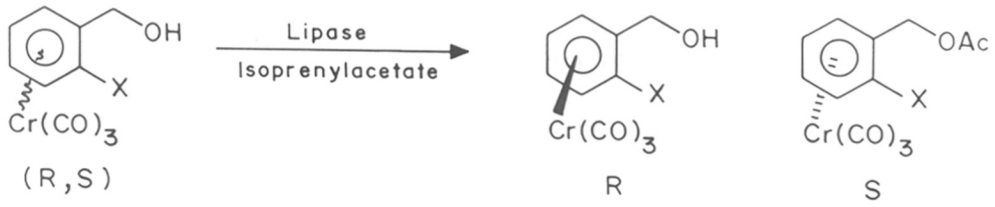
Baker's yeast reduction of racemic *ortho*-anisaldehyde $Cr(CO)_3$ complex resulted in partial formation of the corresponding alcohol. The selectivities were moderate to good[11] (Scheme 7).

Scheme 7



The enantioselective hydrolysis using lipases to obtain optically enriched products have met with considerable success with *ortho* substituted benzyl alcohol $Cr(CO)_3$ complexes[12] (Scheme 8).

Scheme 8



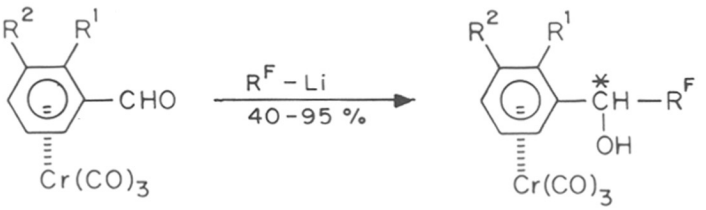
X	Lipase	(R) Yield %	ee %	(S) Yield %	ee %
Me	Amano – P	47	100	48	98
OMe	Amano – AK	46	95	47	97
$SiMe_3$	Toyobo Type A	48	85	45	84

Diastereoselective modification on aldehyde function :

A variety of nucleophiles add to substituted benzaldehydes complexed with $Cr(CO)_3$ with high diastereoselectivity. A perusal of such reactions indicate that the presence of an *ortho* substituent is a necessary condition to achieve such high stereocontrol.

When fluroalkyllithium reagents were used as nucleophiles variable diastereoselectivity were observed[13] (Scheme 9). Perfluoroalkyl iodides in the presence of zinc would add to *ortho* tolualdehyde $Cr(CO)_3$ complex in good to excellent yield. But the diastereoselectivity was less satisfactory[14] (Scheme 10).

Scheme 9



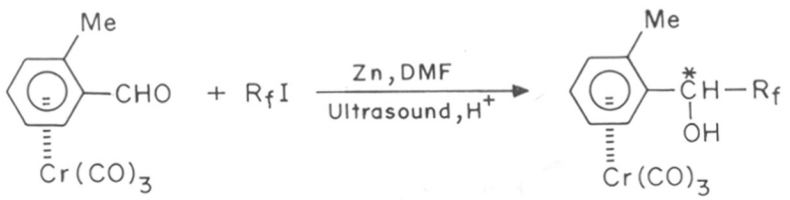
d.e 76-100 %

R^1 = Me / OMe

R^2 = H / OMe

R^F = C_2H_5 / i-C_3F_7

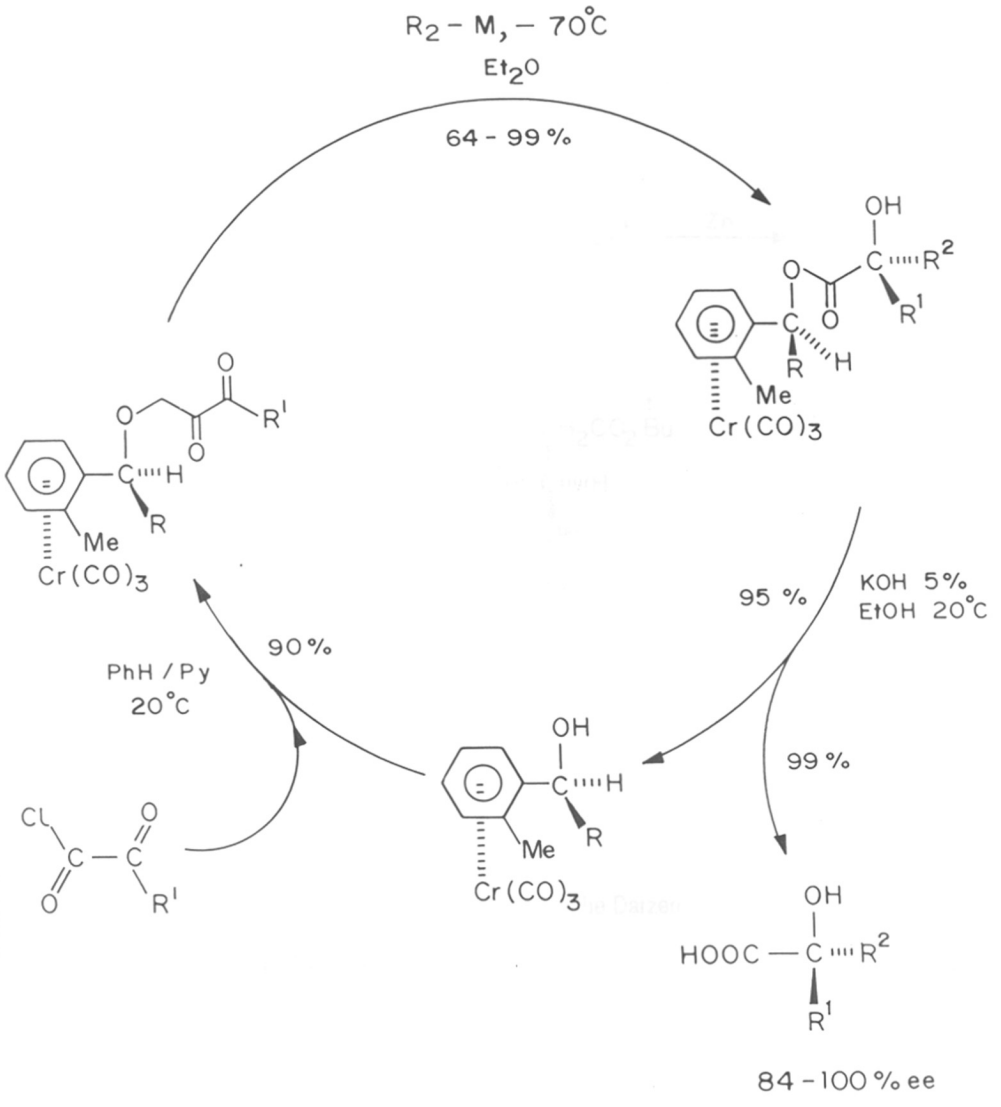
Scheme 10



	Yield (%)	Diastereomer ratio
R_f = C_2F_5	85	72/28
R_f = C_6F_{13}	80	65/35
R_f = C_3F_7	100	83/17

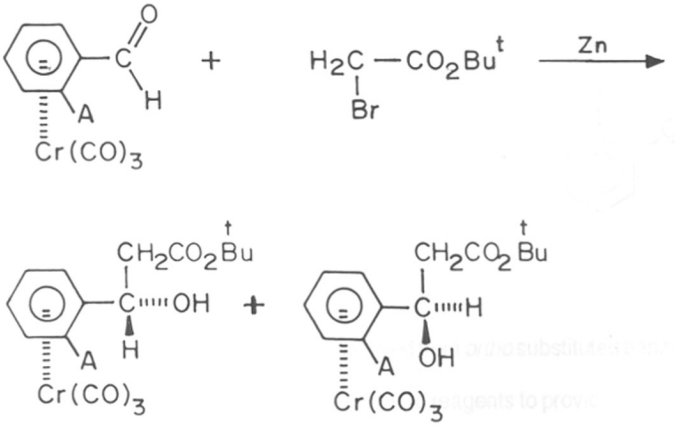
With enantiomerically pure alcohols obtained in this manner chiral induction in Prelog type synthesis was also studied. Fluroalkyllithium and various Grignard reagents were used[15] (Scheme 11).

Scheme 11



Reformatsky reaction on *ortho* anisaldehyde $Cr(CO)_3$ complex took place in high yield and excellent diastereoselectivity. For the tolualdehyde complex the diastereoselectivity was less. Though the chemical yield was comparable[16] (Scheme 12).

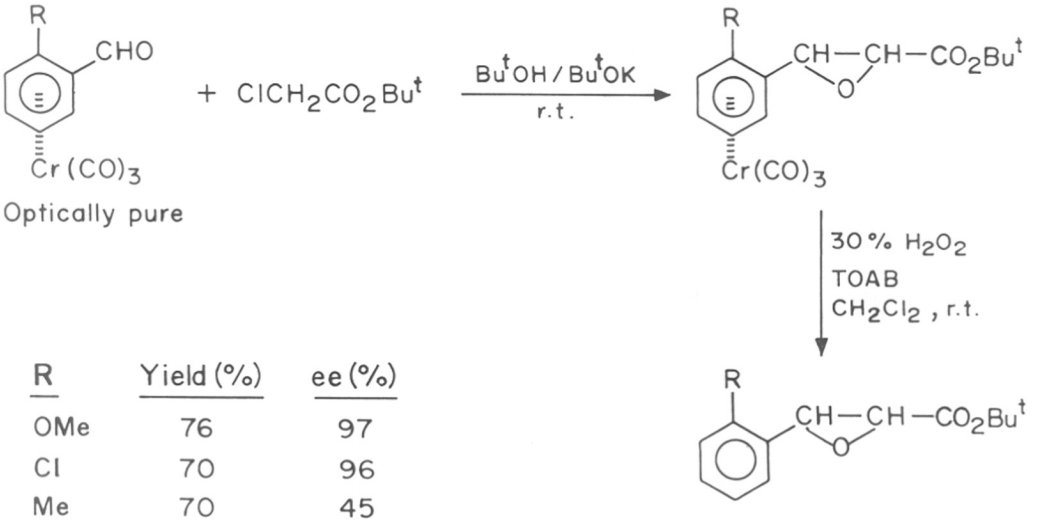
Scheme 12



A	Yield (%)	d.e.(%)
Me	80	70
OMe	70-80	100

Excellent diastereoselectivity was also obtained in the Darzen's condensation with *ortho* substituted benzaldehyde $Cr(CO)_3$ complex[17] (Scheme 13).

Scheme 13

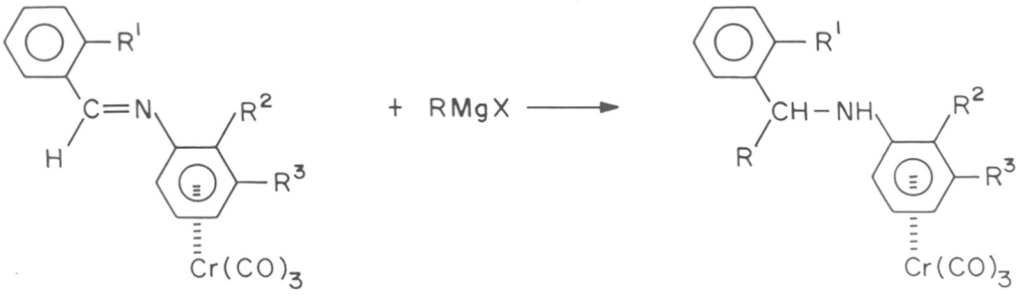


R	Yield (%)	ee (%)
OMe	76	97
Cl	70	96
Me	70	45

In an interesting variation the Schiff's base derived from *ortho* substituted benzaldehydes and substituted aryl amine complexed with $Cr(CO)_3$ reacted with Grignard reagents to provide highly stereoselective C-C bond formation. With benzylmagnesium bromide the asymmetric induction was as high as 100%[18] (Scheme 14).

Scheme 14

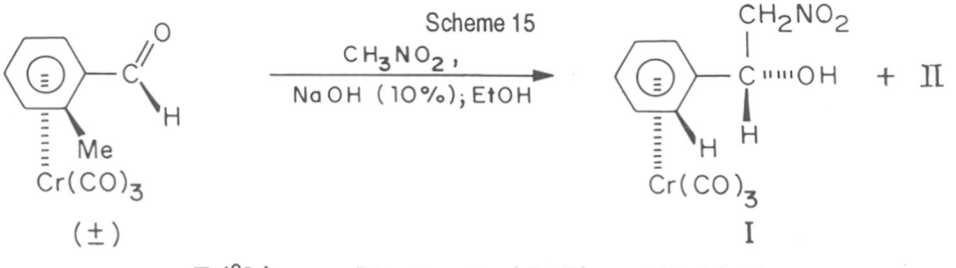
see next page



R^1	R^2	R^3	RMgX	Yield (%)	Diast Ratio
Me	Me	H	MeMgI	94	67/33
			$PhCH_2MgCl$	92	100/0
Me	H	Me	MeMgI	86	55/45
			$PhCH_2MgCl$	92	57/43

Stabilised anion like nitromethane react with *ortho* tolualdehyde $Cr(CO)_3$ complex in a manner similar to aldol reaction. The diastereoselectivity has been shown to be temperature dependant[19] (Scheme 15).

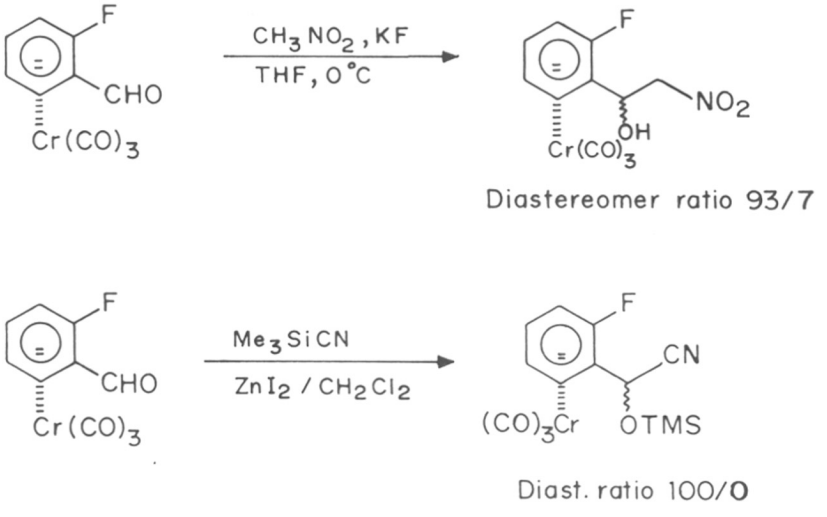
Scheme 15



T (°C)	Diast ratio (I/II)	Yield %
r.t.	64/36	~100
−20	92/8	95
−40	97/3	90

In a subsequent paper it was demonstrated that an *ortho* fluoro substituent, despite its small size, could effect a high degree of diastereoselection in similar reaction[20] (Scheme 16).

Scheme 16

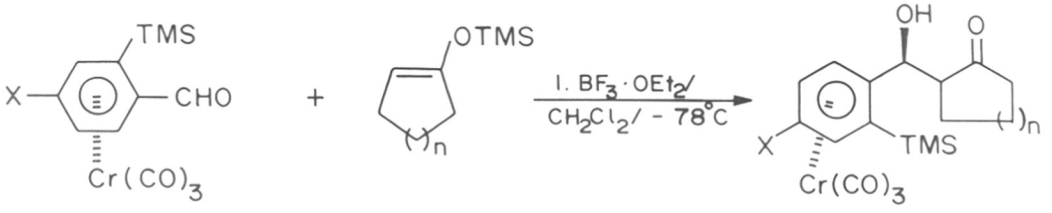


Similar nucleophilic additions have been used to prepare optically pure analogs of ephidrine[21].

Enolate addition to substituted benzaldehyde $Cr(CO)_3$ complexes were also shown to proceed with excellent stereoselectivity. Use of *ortho* trimethylsilyl group was shown to provide very high erythro selectivity[22] (Scheme 17).

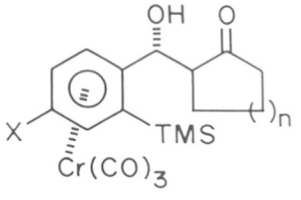
Addition of chiral allyl boronate to benzaldehyde $Cr(CO)_3$ complex resulted in a chiral benzyl alcohol after decomplexation with an *ee* of 83% while only moderate enantioselectivity (55-72% *ee*) could be obtained with uncomplexed aldehydes[23] (Scheme 18).

Scheme 17



(Erythro)

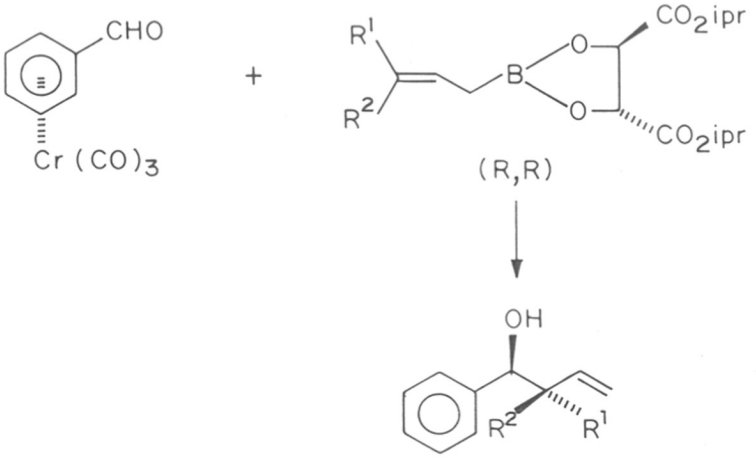
+



(Threo)

	Erythro : Threo	Yield
X = H , n = 3	> 98 : 2	75
X = OMe , n = 3	> 98 : 2	86

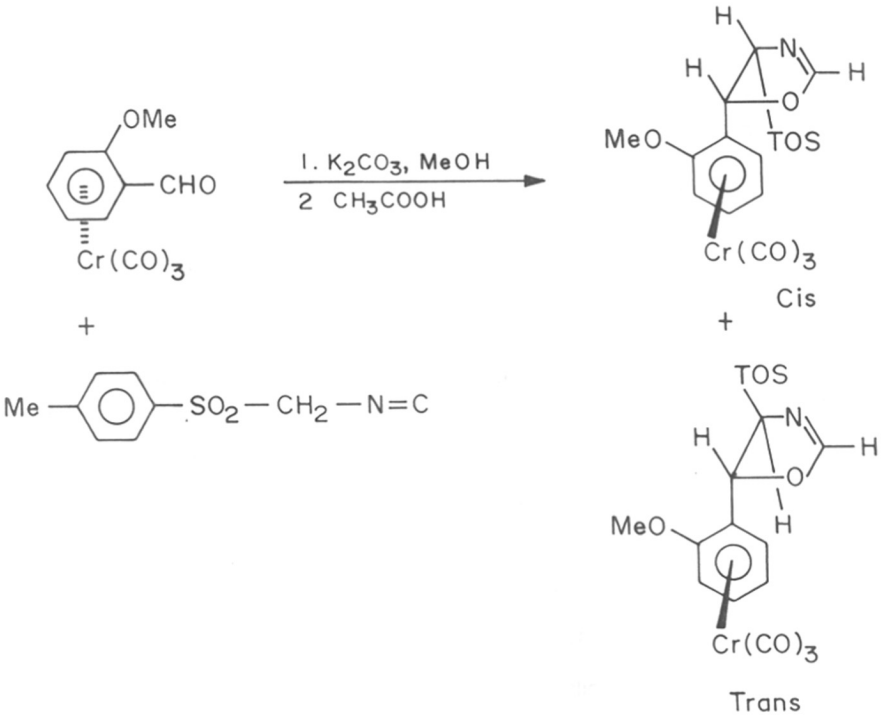
Scheme 18



R1	R2	ee (%)
H	H	83
Me	H	92

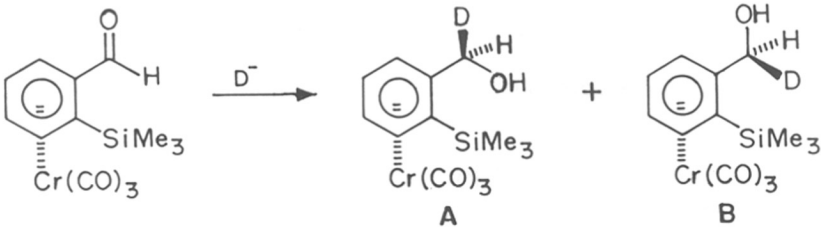
More than 98% asymmetric induction was obtained during addition of TosMic with chiral complexes. Similar selectivity was also observed with ethyl cyano acetate with chiral complexes[24] (Scheme 19).

Scheme 19



The addition of nucleophiles to tricarbonyl(η^6-*o*-trialkylsilylbenzaldehyde)chromium (0) complexes proceeds with complementary diastereoselectivities in the presence or absence of strong Lewis acids[25] (Scheme 20).

Scheme 20



Reagent	A : B	Yield %
$LiEt_3BD$	92 : 8	100
$LiEt_3BD / MgBr_2 \cdot OEt_2$	12 : 88	95

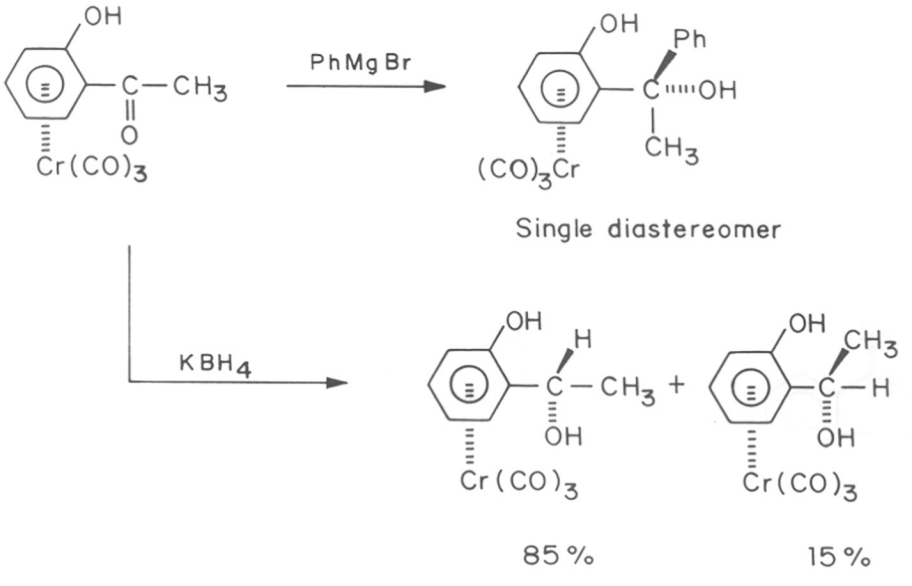
Diastereoselective addition on complexed aromatic ketones:

Addition of Grignard reagents to *ortho* substituted aromatic ketones complexed with $Cr(CO)_3$ have been reported to produce tertiary alcohols with high diastereoselectivity[26] (Scheme 21).

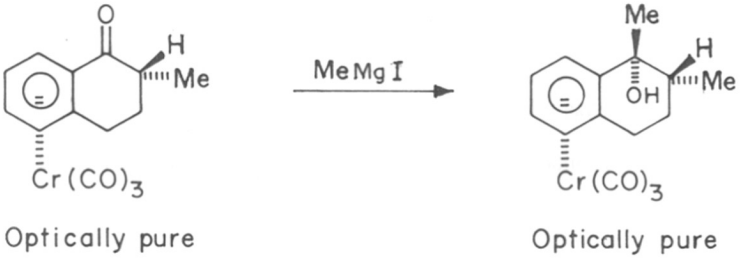
In the case of α substituted 1-tetralone $Cr(CO)_3$ complex Grignard reagents produce a single diastereomer of tertiary alcohol thereby generating two contiguous chiral centre with predictable stereochemical relationship. With optically pure substrate optically pure products can be conveniently obtained[27] (Scheme 22).

Efficient strategies to prepare optically pure indanol derivatives have been explored by Jaouen as shown below (Scheme 23)

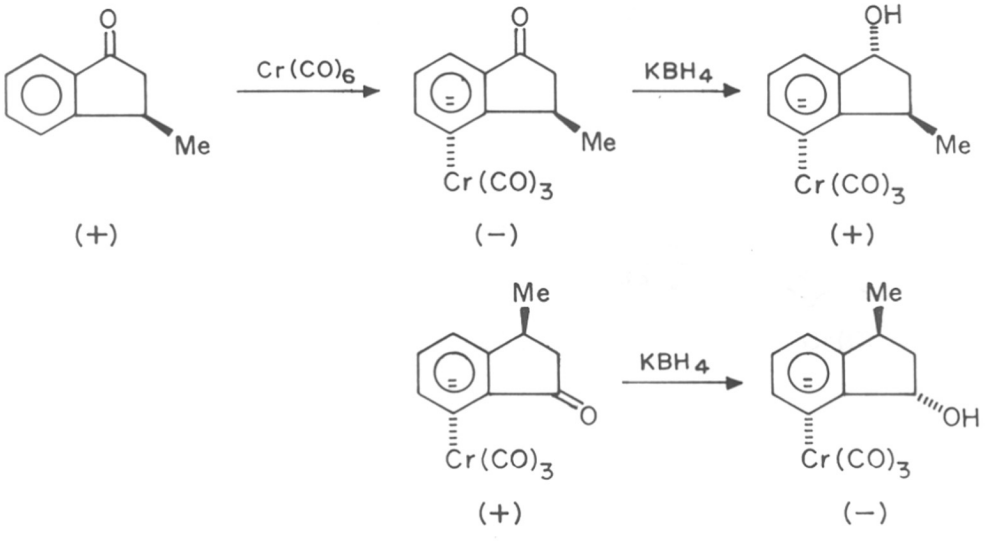
Scheme 21



Scheme 22



Scheme 23

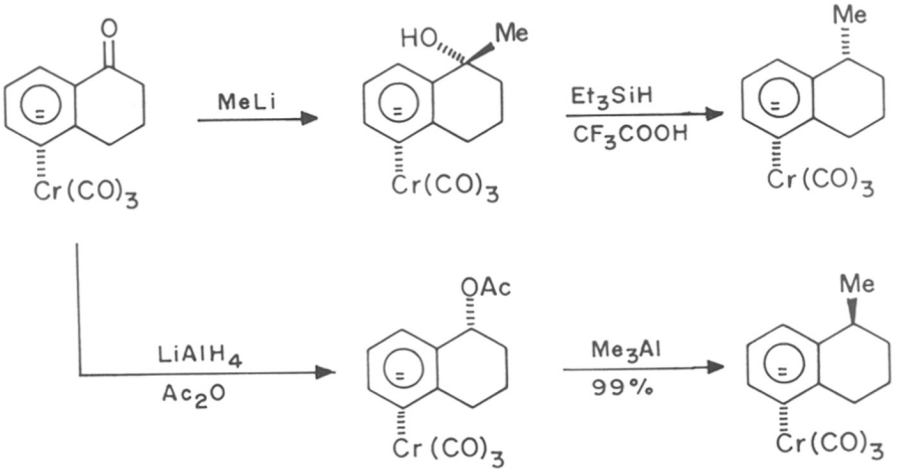


In spite of the small size of the hydride reagents high diastereoselectivity is observed in the reaction of indanone complexes. However with acyclic ketones the selectivity is reduced[28].

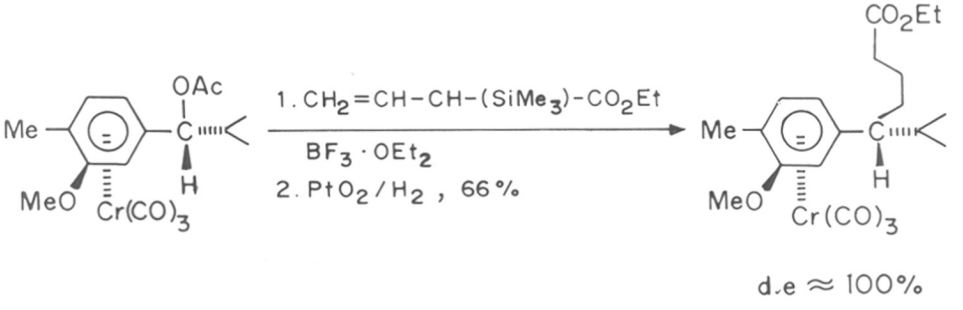
Using the favoured direction of reagent approach from the face opposite to that of the metal, αtetralone $Cr(CO)_3$ complex could be converted to α-1-methyl or β-1-methyl tetralin derivative (Scheme 24).

High selectivity is also achieved on acyclic substrates for similar transformations[29]. A useful variation of this approach resulted in stereoselective synthesis of Acorenone A and Acorenone B[30] (Scheme 25).

Scheme 24



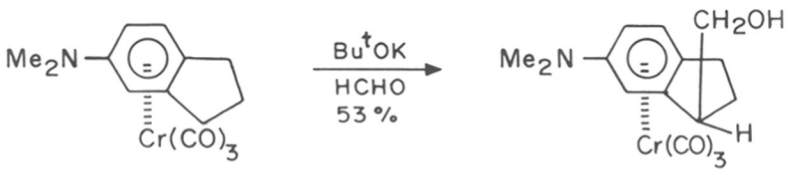
Scheme 25



Diastereoselectivity in alkylation and rearrangement:

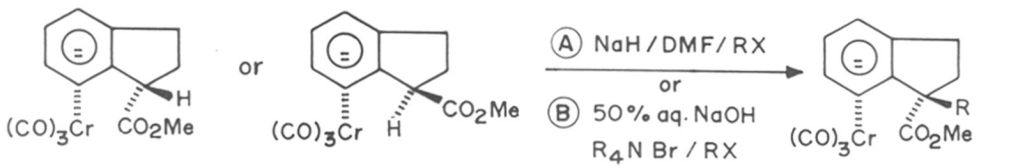
Carbanions at the benzylic position are stabilised by the $Cr(CO)_3$ group complexed to the aromatic ring. Alkylation of such anions particularly rigid indane molecule can lead to highly stereoselective C-C bond formation[31] (Scheme 26).

Scheme 26



Presence of an electron withdrawing group at the benzylic position renders such alkylation even more facile[32] (Scheme 27).

Scheme 27

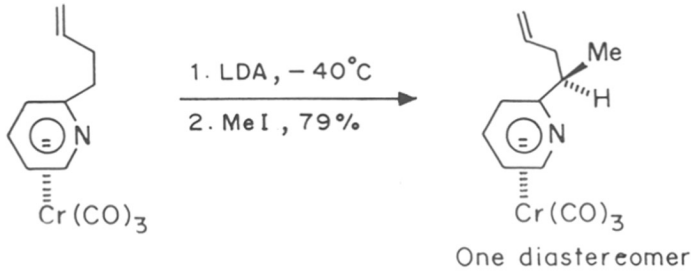


Only diastereomer

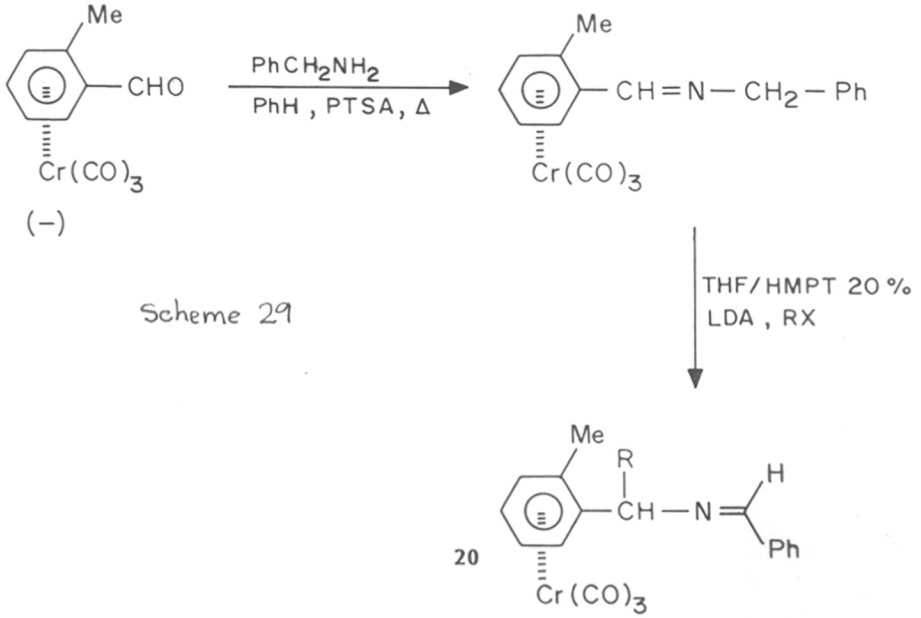
RX	Yield % (A)	(B)
MeI	100	100
	100	100
PhCH Br	100	100

(2)-3-Butenyl pyridine $Cr(CO)_3$ complex can be deprotonated at the benzylic position and alkylated at low temperature. The reaction is highly stereoselective. A planar lithiated derivative where the lithium might be complexed with nitrogen of the pyridine ring could provide the rigidity necessary to effect the observed stereoselective reaction[33] (Scheme 28).

Scheme 28



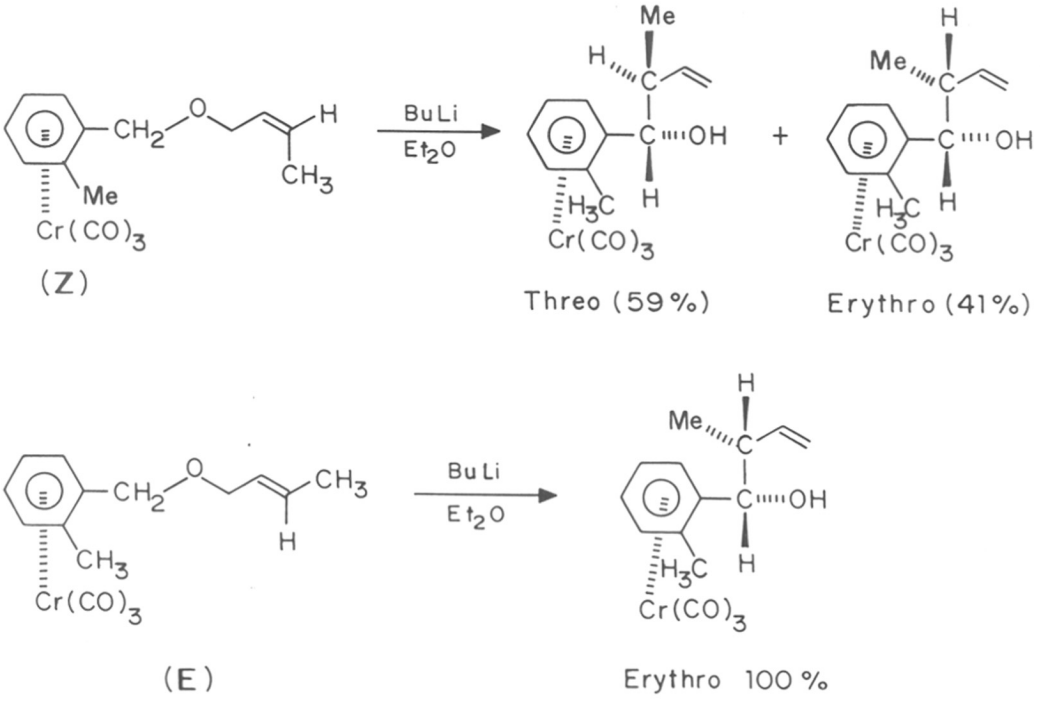
A three step reaction sequence starting from optically pure *ortho* tolualdehyde $Cr(CO)_3$ complex resulted in the transfer of a nitrogen atom from a trivial reactant(benzylamine) to yield highly enantiomerically enriched chiral benzylamine[34] (Scheme 29).



Scheme 29

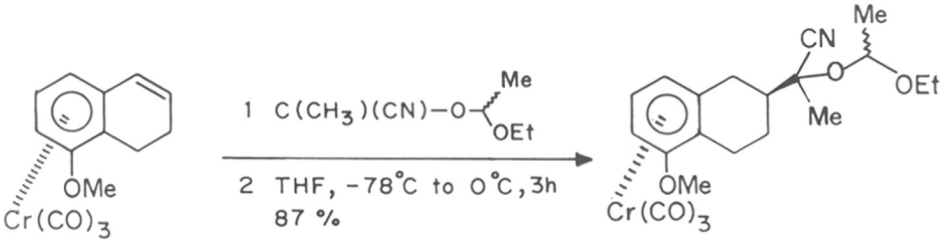
The 2,3 Wittig rearrangement of *ortho* substituted benzylallylether complexed with $Cr(CO)_3$ can occur with variable stereoselectivity depending on the configuration of the olefin. As shown below, the benzyl(*E*)crotyl ether gave the erthyro isomer while the *Z* crotyl ether gave a stereoisomeric mixture[35] (Scheme 30).

Scheme 30



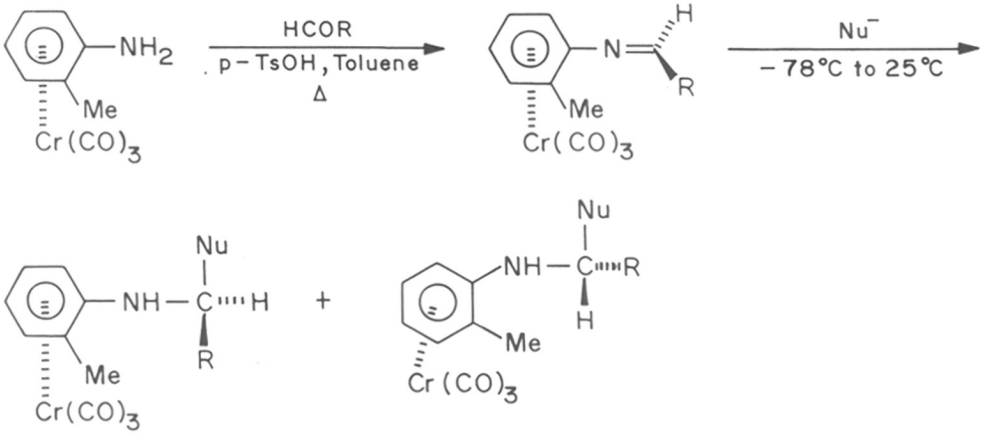
Highly diastereoselective C-C bond formation is possible at the homobenzylic position of the tetralin derivative enroute the synthesis of 11 deoxy daunomycinone[36] (Scheme 31).

Scheme 31



Similar nucleophilic addtion to imines derived from a arylamine$Cr(CO)_3$ complex can be highly diastereoselective at the β position from the aromatic ring[37] (Scheme 32).

Scheme 32

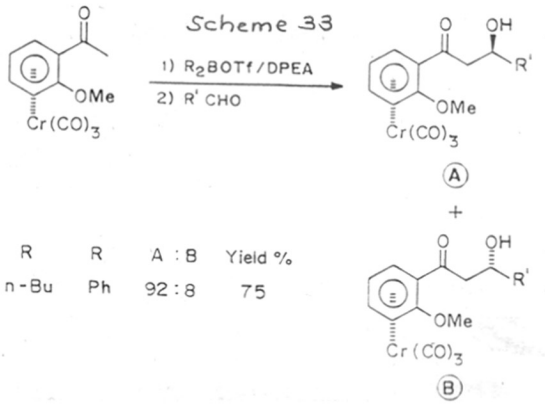


Major Minor

R	Nu	Yield (%)	Diast. Ratio
Ph	MeLi	42	90:10
Ph	$NaBD_4$	50	95:5
t Bu	$NaBD_4$	78	95:5

Diastereocontrol can be achieved even at a centre 3 atoms removed from the chromium complexed aromatic ring by a suitably designed aldol condensation[38] (Scheme 33).

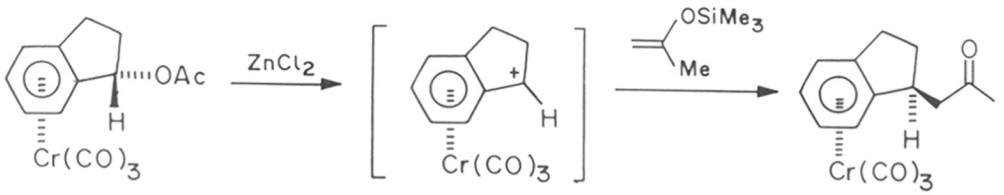
Scheme 33



R	R	A : B	Yield %
n-Bu	Ph	92 : 8	75

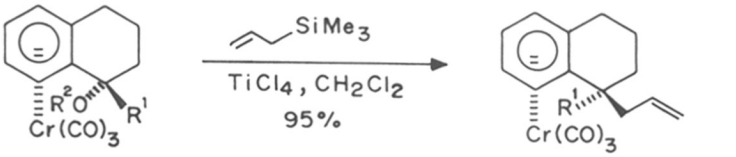
Reaction of silyl enol ethers with secondary benzyl acetate $Cr(CO)_3$ complex in the presence of Lewis acid afforded highly stereoselective α-alkylation reaction. Both cyclic and acyclic substrates have been studied[39] (Scheme 34).

Scheme 34



Such stereoselective C-C bond formation is also possible with allyl silanes[40] (Scheme 35).

Scheme 35

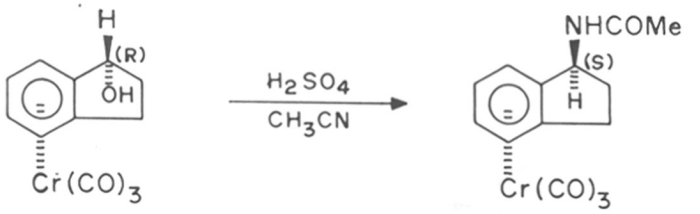


$R^1 = H$
$R^2 = Ac$

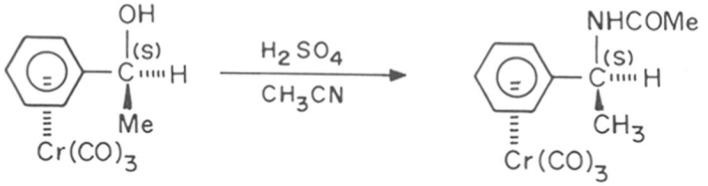
Single diastereomer

Benzylic carbocations are stabilised by metal complexation in indane or tetralin systems such carbocations can be stereoselectively trapped by nucleophilic reagents[41] (Scheme 36).

Scheme 36



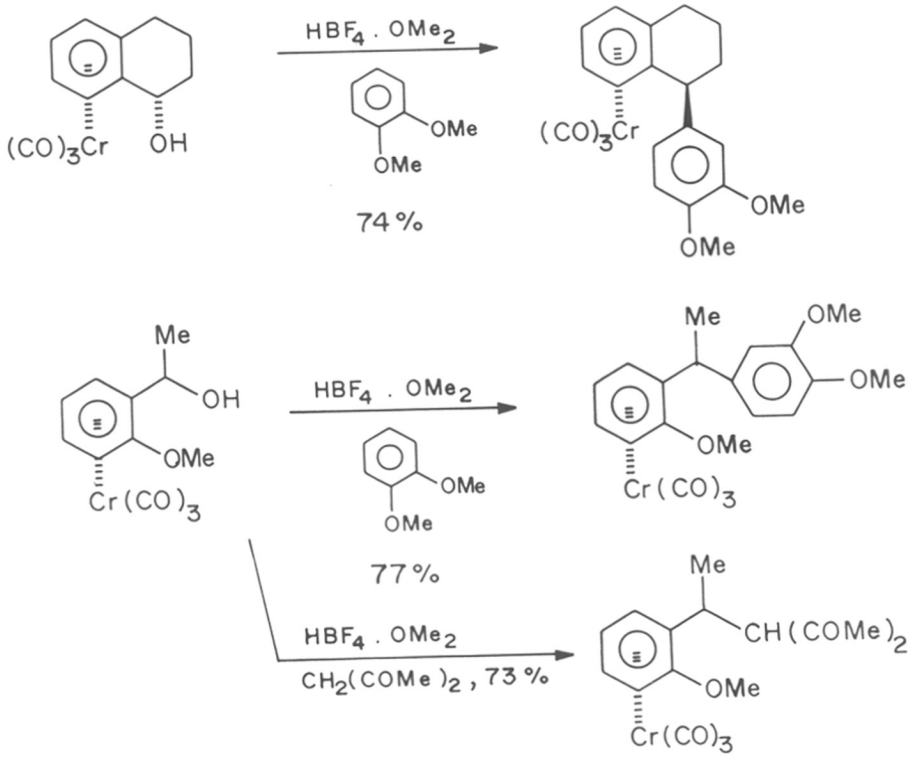
100 % inversion



100 % retention

Scheme 36

(contd.)



Summary :

Current research has clearly established the viability of using $Cr(CO)_3$ moeity as an effective stereodirecting group in a wide variety of transformations. This constitutes the background of the present work which strives to extend and explore the efficacy of stereoselection at remote sites on a arene- $CrCO)_3$ template.

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CHAPTER 2

Conjugate Nucleophilic Addition to Enones Complexed with Tricarbonylchromium

(Part of this work has been published in Tetrahedron Lett., 1991,32, 1085-1088)

INTRODUCTION

From the discussion in Chapter-1, it is clear that the chromium tricarbonyl moiety can function as an effective stereochemical template. It hinders the approach of reagents to the complexed substrate from the same face as occupied by the metal[1]. Reactions on tetralin or indane derivatives complexed with $Cr(CO)_3$ are likely to proceed with high selectivity owing to structural rigidity. In this respect, early success was reported by Jaouen and his group who studied various reactions with 1-indanone and 1-tetralone complexed to $Cr(CO)_3$ group[2a,b].

For the present study, 1-tetralone-$Cr(CO)_3$ complex was selected as the parent system in view of three distinct advantages : a) ready availability, (b) rigid structural framework, and, (c) presence of three reactive centres which can be stereoselectively functionalised.

In order to explore the efficacy of a sterically demanding $Cr(CO)_3$ group in directing the steric course of nucleophilic reactions at a remote centre, it was decided to condense the tetralone complex with aromatic aldehydes.

The resulting arylidene derivative would provide a planar π-system extending beyond the periphery of the tetralone ring. It would contain an electrophilic centre residing three carbons away from the benzene ring complexed with $Cr(CO)_3$, which is ideally suited for studying remote stereocontrol in conjugate addition of nucleophiles.

RESULTS AND DISCUSSION

Preparation of arene-chromium tricarbonyl complexes :

Thermal displacement of three CO ligands by an aromatic ring is by far the most accepted method for the preparation of arene chromium tricarbonyl complexes. Various solvents have been used, ranging from nonpolar (e.g. decalin) to polar (e.g. diglyme). The arenes themselves have also been frequently used as solvents[3].

In many cases the yields of arene-$Cr(CO)_3$ complexes are low because of their thermal instability at high temperatures. The use of donor solvents such as diglyme, α-picoline, 2,6-lutidine[4], or THF[5] leads to significantly faster reactions. Recent studies indicate that the most suitable solvent for a wide range of high yield synthesis is di-n-butyl ether containing about 10% (v/v) THF[6a,b]. This modification largely overcomes previous problems such as loss of $Cr(CO)_6$ via sublimation and removal of high boiling solvents or excess arene from products. Examination of the reaction times and yields for various substituted arenes indicate[3] that the reaction is facilitated by electron donating substituents (e.g. Me_2N, OMe) on the arene ring, and retarded by electron withdrawing groups like Cl and CO_2Me. With strongly electron withdrawing groups such as CHO, CO_2H, CN and NO_2, the reaction fails to provide significant amount of products[7].

Photochemical method of preparing arene-$Cr(CO)_3$ is not convenient for large-scale preparation. For substrates which are heat-labile, ligand exchange with $(CH_3CN)_3Cr(CO)_3$[8a], $(pyridine)_3Cr(CO)_3$[8b], or $(NH_3)_3Cr(CO)_3$[8c] have been used. In the recent years, arene-exchange with naphthalene-$Cr(CO)_3$[8d] complexes has been frequently used.

As described in a standardised procedure[6b] for the preparation of anisole-$Cr(CO)_3$ complex, 1-tetralone-$Cr(CO)_3$ was prepared for the present study from thermolysis of $Cr(CO)_6$ and 1-tetralone in the presence of a catalytic amount of THF in dibutyl ether. Despite the presence of an electron-withdrawing carbonyl function on the aromatic ring, this procedure allowed the preparation of gram quantities of the desired complex in a single step. Unreacted chromium hexacarbonyl was routinely recovered and recycled.

The solution was refluxed at 150°C (oilbath temperature) for 12 h. Occasionally, formation of a green precipitate was observed. In such cases, heating was stopped, the reaction mixture was cooled to room temperature and filtered through celite to remove the residue. Heating was continued for a total period of 12h.

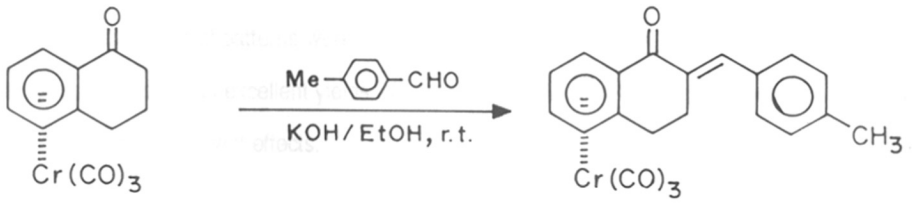
The reaction mixture was allowed to cool to room temperature, filtered through celite and the filtrate was refrigerated overnight. The red solution turned pale yellow as red crystals of the chromium complex **1** was precipitated along with unreacted $Cr(CO)_6$. They were collected by filtration. The 1-tetralone-$Cr(CO)_3$ complex was obtained in 60% yield based on recovered $Cr(CO)_6$. The spectral features were consistent with the structure of the complex and in agreement with those reported by Jaouen.

The red crystals of 1-tetralone-$Cr(CO)_3$ were stored in vials for long periods (several months). They could be used as such from time to time for preparation of suitable arylidene complexes.

Preparation of cyclic enones 2a - d and acyclic enones 3a - c :

The enones **2a - d** were prepared[9] for the first time by condensation of aromatic aldehydes with 1-tetralone-$Cr(CO)_3$ in ethanol using KOH as the base.

In a representative procedure, 1-tetralone-$Cr(CO)_3$ complex **1** and *p*-tolualdehyde in ethanol were stirred at O°C under argon. To this, ethanolic KOH was added dropwise. After the addition of base, stirring was continued at room temperature. The progress of the reaction was monitored by TLC. There was a gradual change in the colour of the reaction mixture from orange to deep red. The reaction was complete on stirring overnight. TLC (20% EtOAc - pet ether) showed that the product was more polar than the starting material. The product **2a** was isolated in excellent yield (97%). It was recrystallised from CH_2Cl_2/pet ether to obtain an analytically pure sample.



1 2a

The IR spectrum exhibited bands at 1980, 1910 for Cr-CO and 1670, 1610 corresponding to -CO-C=C(H)(Ar).

The ^{1}H NMR spectrum of this compound showed a singlet at 7.83, which was assigned to the olefinic proton. The downfield shift was due to the anisotropy of the ketone carbonyl. The *trans* stereochemistry of the olefin was thus unambiguously established.

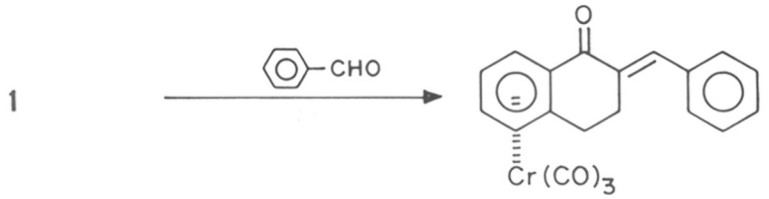
From the disappearance of this characteristic signal, subsequently, it was possible to infer complete conversion of starting material after reaction (*vide infra*).

A pair of doublets at 7.38(J=9Hz) and 7.27(J=9Hz) appeared due to the aromatic protons of the uncomplexed ring. The resonances due to the protons on the aromatic ring complexed to $Cr(CO)_3$ appeared between 6.25 and 5.15. Such upfield shift was characteristic of metal complexation and was used as a diagnostic feature for the entire series. The -CH_2- protons of the tetralone ring were diastereotopic and appeared as separate multiplets at 3.2-3.5, 2.6-3.15 and 2.56-2.58. The methyl signal appeared at 2.4.

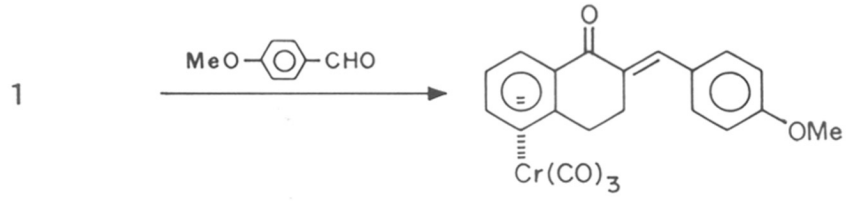
^{13}C NMR of the complex showed the expected low-field signals at 230.0 (Cr-CO) and 185.7 (-CO-). The olefinic carbon [=C(H)(Ph)] appeared at 138.0, while the [C=C(H)(Ph)] appeared at 132.0. The signals due to the carbons of the uncomplexed aromatic ring were observed between 128.4 and 134.9. The signals due to the aromatic carbons complexed to the metal appeared between 89.6 and 114.7. The methylene carbons of the tetralone ring appeared at 25.4 and 26.9. The signal at 21.2 was assigned to the methyl group.

The spectral patterns were similar in the other structurally related complexes **2b-d** prepared by analogous procedures in excellent yields. No significant shift of ^{1}H NMR signals was observed, which could be correlated by substituent effects.

Complex **2b** was prepared in the same manner in high yield (95%). The ^{13}C NMR spectrum exhibited expected signals which could be assigned unambiguously.



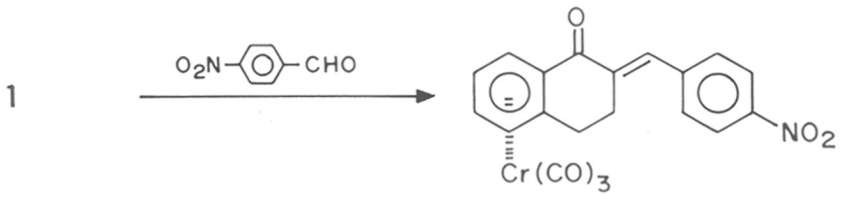
2b



2c

The IR spectrum of the complex **2c** exhibited characteristic bands at 1980, 1920, 1660 and 1620. The ^{1}H NMR spectrum exhibited a doublet at 6.95 (J=9Hz) and 7.45 (J=9Hz) corresponding to the uncomplexed aromatic ring containing a *p*-OMe substitution. The OCH_3 signal appeared as a singlet at 3.85. The ^{13}C NMR signal corresponding to this methoxy group appeared at 55.1 while the *ipso* carbon of the aromatic ring bearing the OMe substituent resonated at 160.2.

Complex **2d** showed bands at 1980, 1900, 1660 and 1600 in the IR spectrum.



2d

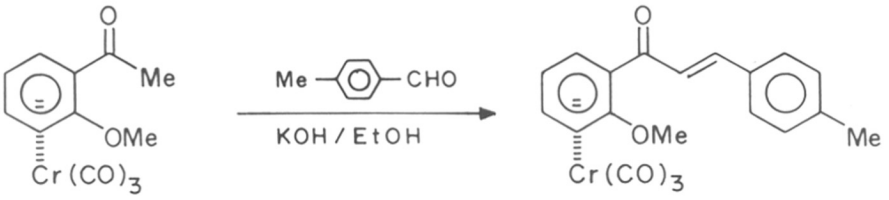
A singlet at 7.85 and the doublets at 7.6 (J=9Hz) and 8.3 (J=9Hz) in the ^1H NMR spectrum was consistent with the *para*-substituted benzene ring containing electron withdrawing NO_2 group. The complexed aromatic ring protons appeared as doublet, triplet, triplet and doublet at 5.15 (J=9Hz), 5.4 (J=6 Hz), 5.7 (J=6Hz), 6.3 (J=7Hz) respectively. The tetralone ring protons appeared as multiplet between 2.62 - 2.8 and 2.9 - 3.3.

^{13}C NMR spectrum of this compound showed a signal at 147.3 corresponding to the aromatic carbon attached to NO_2 group. The olefinic carbon [=C(H)(Ar)] appeared at 147.3 and [=C=C(H)(Ar)] appeared at 141.5, while rest of the signals appeared at the usual region.

The uncomplexed enone **2e** was prepared following a reported procedure and the spectral characteristics were found to be in tune with the reported values[8].

The enones **3a - c** were prepared for the first time by condensation of aromatic aldehydes with *o*-methoxyacetophenone-$Cr(CO)_3$ in ethanol using KOH as the base.

Using the above reaction condition, the complex **3a** was prepared in excellent yield (94%).



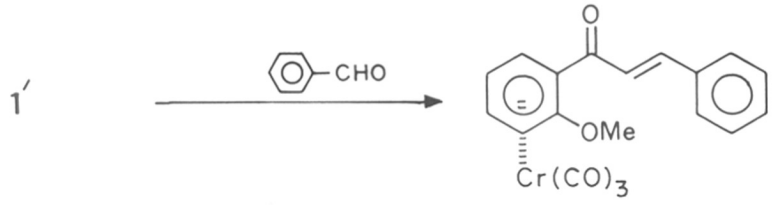
1′ 3a

The complex was also found to be analytically pure. The IR spectrum exhibited bands at 1980, 1910 for Cr-CO and 1660, 1600 corresponding to -CO-C=C(H)(Ar).

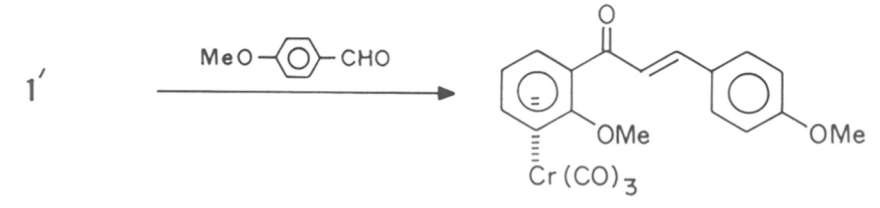
The ^{1}H NMR spectrum of this compound showed downfield signals at 7.75 (J=16Hz) corresponding to the olefinic proton while the other olefinic proton resonated at 7.45 (J=16Hz). The coupling constant observed between the olefinic protons in this case clearly establishes the *trans*- stereochemistry of the olefin. The aromatic protons appeared as a pair of doublets at 7.55 and 7.2 (J=9Hz). The protons of the complexed aromatic ring appeared in the usual region, at 5.0, 5.1, 5.8 and 6.2. The singlet at 3.9 was assigned to the methoxy group while the singlet at 2.4 was assigned to the methyl group.

The ^{13}C NMR spectrum exhibited downfield signals at 231.4 (Cr-CO) and 186.8 (-CO-). The olefinic carbons appeared at 143.9 and 143.0. The uncomplexed aromatic carbon signals resonated between 140.9 and 123.7. The complexed aromatic carbon signals appeared in the region 95.9 to 72.5. The signal at 55.95 was assigned to the methoxy group and the signal at 21.34 was assigned to the methyl group.

The complexes **3b** and **3c** exhibited similar spectral pattern as observed in the case of **3a**. The complexes were isolated in excellent yield and were found to be analytically pure.



3b



3c

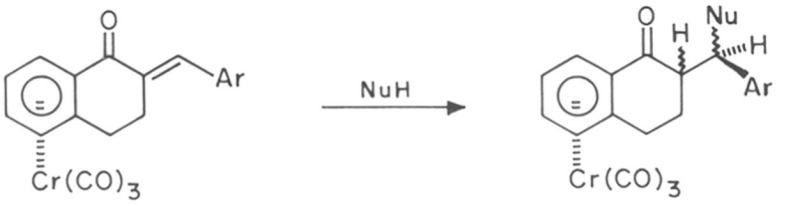
Conjugate Addition of Nitromethane :

It was decided to perform Michael reaction on the arylidene substrates **2a-d** with readily available nucleophiles. Nitromethane was chosen as a nucleophile for the initial experiments since its small size and high reactivity was expected to contribute minimally with respect to steric discrimination.

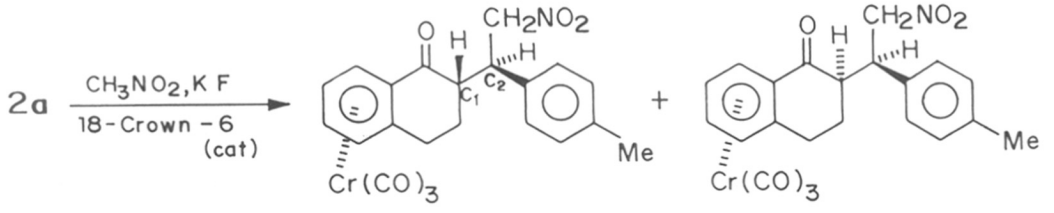
The reaction was carried out at room temperature in nitromethane as solvent using equimolar amount of KF[10] as the base in the presence of 18-crown-6 (5% by weight of the enone) as catalyst. While the reaction of the uncomplexed 2-benzylidene-1-tetralone **2e** was very slow (2 days), the reaction of the complex **2b** was complete in 2h. The reaction was monitored by TLC and worked up after all the starting material had been consumed.

Two product fractions were isolated by chromatography, which were later found to be two diastereomers of the expected Michael adduct. In all the cases the more polar product was the major isomer.

Of the possible four pair of diastereomers (due to the presence of two chiral centres and $Cr(CO)_3$) isolation of only two were immediately indicative of a high degree of diastereoselectivity.



From the reaction of **2a** with nitromethane (12 h) the major fraction **4a** and minor fraction **5a** were separated (diast. ratio 87:13) using flash chromatography. They were identified as two diastereomeric Michael adducts from their spectral data as discussed below.



4a (Major) **5a** (Minor)

The bands in the IR spectrum of **4a** appeared in the characteristic regions 1990, 1920 [$Cr(CO)_3$], 1680 (-CO-) and 1560 (NO_2).

Absence of the strong C=C absorption in the IR spectrum and the olefinic singlet at 7.83 in the ^{1}H NMR spectrum clearly indicated that conjugate addition had taken place. The nitromethane protons CH_2NO_2 were geminally coupled (diastereotopic) and appeared as separate multiplets in the region 5.2 to 5.05 and 4.9 to 4.75, as confirmed from the COSY spectrum.

Resonances corresponding to the protons on the uncomplexed aromatic ring appeared at 7.1 as a broad singlet. The protons of the complexed aromatic ring appeared in the usual region 6.25-5.0. The benzylic methine proton appeared as a multiplet at 4.2. Assignment of this signal was supported by the COSY spectrum which showed coupling relationship of this signal with the nitromethane protons as well as the -CH-CO- . The proton on the carbon adjacent to the ketone and the benzylic methylene protons of the tetralone appeared in the region 2.8-2.6 and 3.05-2.8 as multiplets. A singlet at 2.3 corresponded to the methyl group on the aromatic ring. The other methylene protons of the tetralone ring appeared as multiplet between 2.0-1.6.

The ^{13}C NMR spectrum showed characteristic signals at 230.1 (Cr-CO) and 196.0 (-CO-) in the downfield region. The complexed and the uncomplexed aromatic carbons appeared in the characteristic regions at 114.2 - 88.7 and 137.6 - 127.9 respectively.

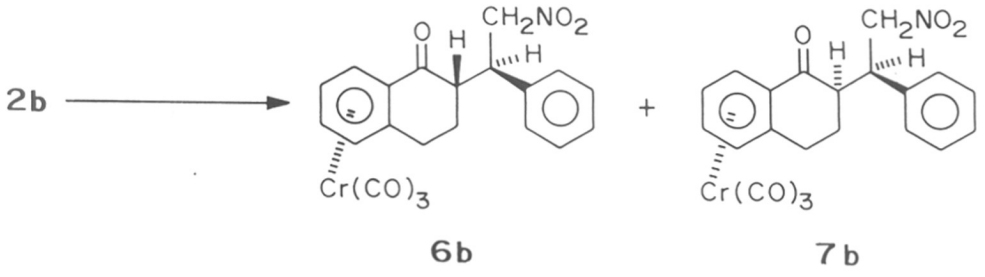
The nitromethane signal appeared at 78.3, while the carbon α to the ketone appeared at 48.8. The signal at 43.0 corresponded to the benzylic carbon, while the signals corresponding to the tetralone ring appeared at 27.4 and 24.8. The methyl group resonated at 20.8. Hetero-correlation spectroscopy served as an important tool to correlate the proton signals with the corresponding carbon signals. The geminally coupled nitromethane protons correlated with the carbon peak at 78.3. The multiplet at 4.2 correlated with the carbon signal at 43.0. The carbon signal at 48.8 was assigned to the carbon adjacent to the ketone from correlation with the proton signal at 2.8. The tetralone protons in the region 2-1.6 and 3.05-2.6 showed the corresponding carbon signals at 27.4 and 24.8.

The minor fraction provided the complex **5a**, which showed characteristic IR bands at 1990, 1920 [Cr-(CO_3)], 1680 (-CO-) and 1560 (NO_2).

The ^1H NMR spectrum exhibited a broad signal for the aromatic group between 7.35-7.1. The complexed aromatic protons appeared in the usual region 6.25-5. The nitromethane protons appeared as multiplet between 5.15 to 4.95. Consistently throughout the series, the chemical shift difference between the two non-equivalent nitromethane protons was found to be 0.3 ppm for the major isomers and 0.2 ppm for the minor isomers. The multiplet corresponding to the benzylic proton appeared at 4.2. The proton on the carbon next to the ketone and the benzylic CH_2 appeared as a multiplet at 3.1-2.6. The other CH_2 of the tetralone ring appeared at 2.15 to 1.75. A singlet at 2.3 was observed for the methyl group.

Due to the paucity of this compound, the ^{13}C NMR was not recorded. The compound was found to be analytically pure.

The complex **2b** afforded two isomeric products **6b** (major) and **7b** (minor)(diast. ratio 90:10).



6b **7b**

The compound **6b** showed IR bands at 1980, 1920 (Cr-CO), 1680 (-CO-) and 1560 (NO_2).

The protons of the uncomplexed aromatic ring appeared in the usual region as a multiplet between 7.45-7.2. The protons of the complexed aromatic ring appeared at higher field at 6.2-5.3. One of these signals was superimposed on one of the CH_2-NO_2 protons at around 5.2, where a multiplet was observed due to geminal coupling of the nitromethane proton; the other proton appeared as a multiplet at 4.8. At 4.3, a multiplet was observed due to the benzylic methine. The tetralone protons appeared as separate multiplets in the region 3.05 to 2.85, 2.8 to 2.62, 2.05 to 1.85 and 1.8 to 1.6.

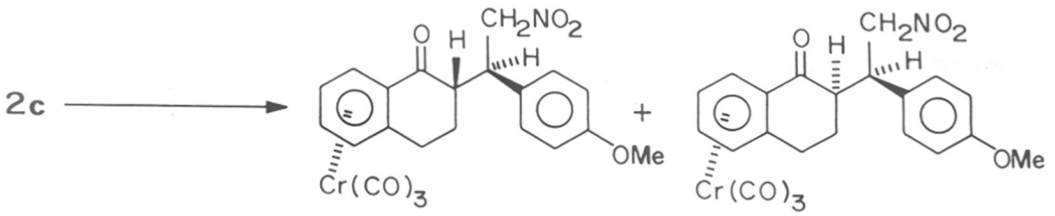
The ^{13}C NMR spectrum showed two downfield signals at 230 (Cr-CO) and 195.8 (-CO-). The uncomplexed aromatic ring carbons appeared between 127.86 to 136.6. The complexed aromatic ring carbons appeared in the region between 114.2 to 88.8. The carbon adjacent to the ketone resonated at 48.8 while the benzylic carbon appeared at 43.2. The methylene carbons of tetralone appeared at 27.4 and 24.7.

The other product **7b** obtained as a minor fraction exhibited characteristic bands in the IR spectrum at 1980, 1920 (Cr-CO), 1680 (-CO-) and 1560 (NO_2).

In the ^1H NMR spectrum of **7b** the resonances due to the protons of the uncomplexed aromatic ring appeared in the region 7.15 - 7.45 while the protons of the complexed aromatic ring appeared in the characteristic region. The protons of CH_2NO_2 which are geminally coupled appeared as multiplet between 4.9 - 5.35. A multiplet at 4.1 corresponding to the benzylic proton was observed. The methine and benzylic methylene protons of the tetralone ring appeared at 2.6 - 3.1 as multiplet. The other CH_2 protons of the tetralone ring appeared as separate multiplets between 1.6 - 2.05 and 2.15 - 2.4.

The downfield signals in the ^{13}C NMR spectrum were assigned to (Cr-CO) at 230 and (-CO-) at 195.3. The carbon signals of the uncomplexed ring appeared in the usual region 127.1 - 136.7, while the complexed ring carbons were in the region 88.5 - 114.9. The nitromethane carbon signal appeared at 77.1. The carbon adjacent to the ketone appeared at 48.1 and the benzylic carbon signal was observed at 45.1. The tetralone (CH_2) carbon signals appeared at 25.6 and 26.5.

The complex **2c** reacted with nitromethane in 24 h, to provide the major isomer **8c** and minor isomer **9c**(diast. ratio 89:11).



8c **9c**

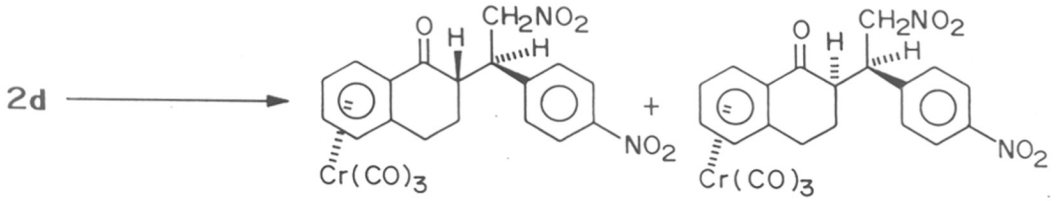
The IR spectrum of **8c** showed characteristic bands at 1980, 1910 (Cr-CO), 1680 (-CO-) and 1560 (NO_2).

The ^1H NMR spectrum was quite similar to those of **4a** and **5a** as far as the pattern of signals were concerned. The uncomplexed aromatic carbons appeared as doublets at 6.9 (J=9Hz) and 7.2 (J=9Hz), typical of 1,4 disubstituted aromatic ring. The signals due to the complexed aromatic ring protons appeared between 5-6.2. The nitromethane protons appeared as separate multiplets in the region 4.75-4.9 and 5.05-5.2. The multiplet at 4.2 was assigned to the benzylic methine. A singlet at 3.85 was assigned to the methoxy group on the uncomplexed aromatic ring. The multiplet in the region 2.6-3.05 was attributed to the ketomethine proton and the benzylic (CH_2) of the tetralone, while the other (CH_2) appeared in the region 1.65-2.05 as multiplet.

The ^{13}C NMR spectra exhibited downfield signals at 230.2 (Cr-CO) and 196 (-CO-). The *ipso* carbon bearing the methoxy group appeared at 158.9, while the rest of the aromatic carbon signals were in the region 129.1 to 114.4. The complexed aromatic carbon signals were in the usual region 88.9 to 114.1. The nitromethane signal appeared at 78.3. The methoxy signal was observed at 55.0. The carbon adjacent to the ketone displayed a signal at 48.8 while the benzylic carbon appeared at 42.5. The tetralone (CH_2) appeared at 27.2 and 24.1.

The minor diastereoisomer **9c** exhibited characteristic IR bands. The ^{1}H and ^{13}C NMR spectra were also consistent with the structure of the complex.

Reaction of **2d** with nitromethane in 36 h provided the products **10d** and **11d**, major and minor isomers respectively(diast. ratio 95:5).



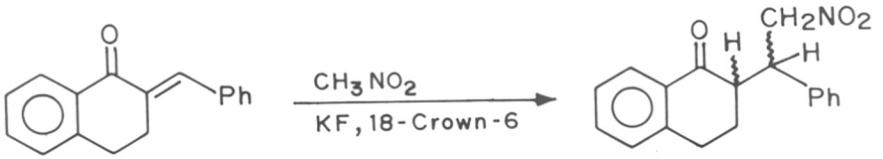
10d **11d**

The complex **10d** exhibited characteristic bands in the IR spectrum 1980, 1910 (Cr-CO), 1680 (-CO-) and 1560 (NO_2).

The protons of the uncomplexed aromatic carbons appeared downfield as a pair of doublets at 7.5 (J=9Hz) and 8.25 (J=9Hz). Rest of the signals appeared at the expected position.

The minor isomer **11d** displayed resonances in the expected region in ^{1}H NMR spectrum. The ^{13}C NMR spectrum could not be scanned due to paucity of compound. However, the compound was found to be analytically pure.

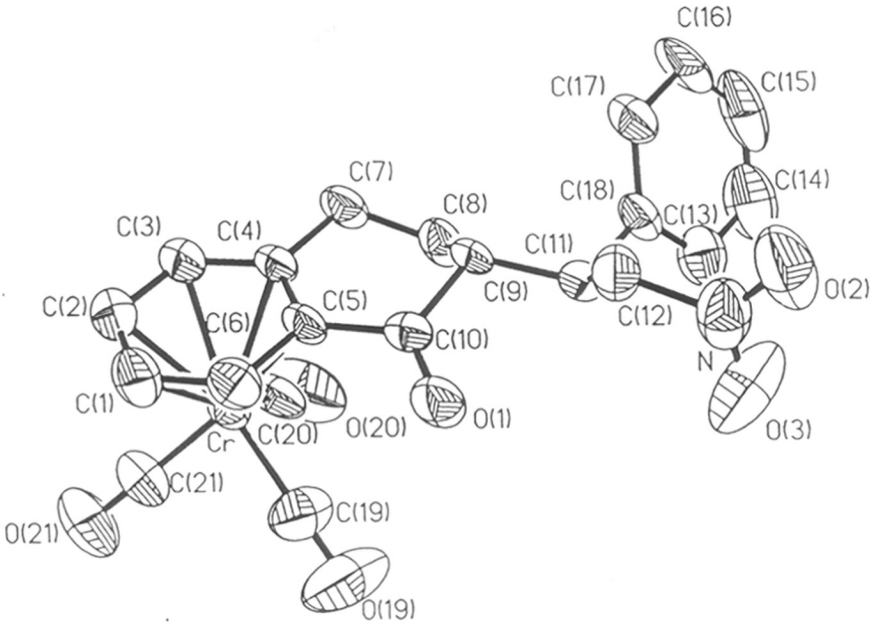
Reaction of uncomplexed enone 2e: The enone **2e** took two days to react completely, to afford a diastereomeric mixture (50:50) in 90% yield.



2e

Discussion on Stereochemistry of the products / X-ray Crystal Structure :

Although the spectral data for the nitromethane adducts were consistent with the expected structures, the stereochemical relationship between the stereoisomers was not resolved. There are two chiral centres, namely C-2 and C-3. To find out whether any of these centres were epimeric, equilibration was carried out in nitromethane in the presence of KF/18Crown 6. The progress was monitored by TLC. While the complex **2d** required 48h for the completion of the reaction, the major diastereomer **10d** underwent equilibration to afford a diastereomeric mixture in 2h. The same mixture was also obtained from the minor diastereomer **11d** under the same condition. The ratio of diastereomers was the same as obtained in the original Michael reaction. The equilibration was equally effective in dichloromethane as solvent. This clearly established that the isomers were epimeric at the carbon adjacent to the ketone (C-2), and they were not formed as a result of retro-Michael reaction. Therefore, the addition of nitromethane at C-3 must have been completely stereospecific. In order to determine the relative stereochemistry of different centres the major diastereomer **5b** was subjected to X-Ray crystal structure analysis. The **ORTEP** diagram as shown below revealed that the nitromethane attacked from the *anti* face, and protonation at C-2 also ocurred from the same face with respect to the metal. Thus, *the steric inhibition to reagent approach, exerted by the bulky Cr(CO)3 was found to be effective even three carbons away from the aromatic ring.*

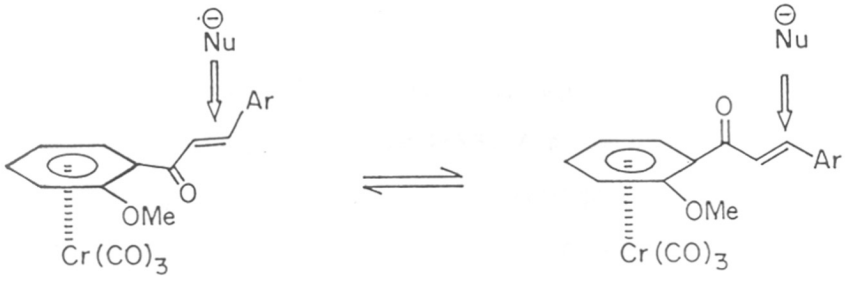


Monoclinic space group $P2_1/n$; a = 12.385(6) $\mathring{A}$, b = 12.185(6) $\mathring{A}$, C = 13.958(7) $\mathring{A}$, β = 111.47(3)° $\mathring{A}$, V = 1960.2(17) $\mathring{A}^3$, D_c = 1.462 Mg/m^3, Z = 4, μ(Mo - K_α) = 0.604mm^{-1} 2013 unique reflections, R = 4.68 for 1668 observed reflections. The structure was solved by Prof. R.D. Willett of Washington State University, USA.

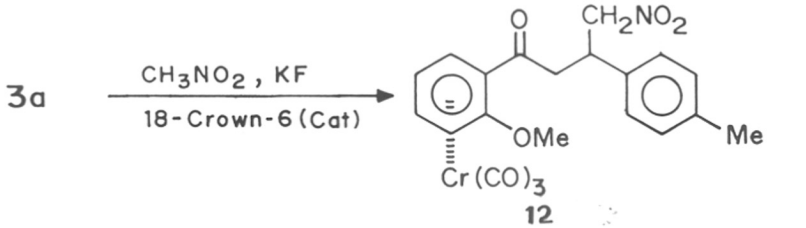
Conjugate addition of nitromethane on acyclic enones:

Encouraged by the high degree of stereocontrol in the addition of nitromethane three carbons away from the complexed aromatic ring, it was thought appropriate to investigate such stereocontrol in an analogous acyclic enone system. Current literature records numerous application of *o*-OMe substituted benzene derivatives where excellent diastereoface discrimination was observed for nucleophilic addition[11]. Thus *o*-methoxyacetophenone-$Cr(CO)_3$ complex was prepared and condensed with three aromatic aldehydes to obtain the required enones.

These acyclic enones provide an additional advantage that only two diastereomeric products can now result from a conjugate addition as compared to four possible isomers from the tetralone derivatives. It was recognized at the same time that the diastereomers can arise from exclusive *exo*-attack with respect to the metal, by virtue of the following conformational equilibrium.



Conjugate addition of nitromethane on the acyclic enone **3a**, at room temperature overnight in the presence of KF/18-crown-6, afforded the addition product **12** in high yield (93%).



12

(Diastereoisomeric mixture)

IR spectrum of the complex exhibited bands at 1980, 1900 (Cr-CO), 1670 (-CO-) and 1540 (NO_2).

The ^1H NMR spectrum showed an intense signal at 7.2, assigned to the protons of the uncomplexed aromatic ring. Two sets of signals at 6.2 and 6.3 as well as 3.85 and 3.9 indicated that the product consisted of a mixture of two diastereomers. Attempts to separate the isomers by chromatography were not successful.

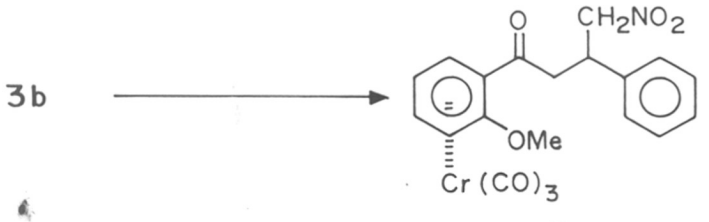
The diastereomeric ratio (60:40) could be estimated from the integration of the pair of *peri* proton signals of the complexed aromatic ring, which appeared at 6.3 (d) and 6.2 (d). This ratio was consistent for the acyclic enones studied. There was a multiplet between 5.75-6.0 corresponding to another proton on the complexed ring. The other two protons of the complexed ring appeared as complex multiplet between 4.85-5.2. The nitromethane protons appeared between 4.55-5.2. A multiplet between 4.3-4.1 was assigned to the benzylic proton. Two singlets were observed for methoxy groups, at 3.9 and 3.85. The multiplet between 3.2-3.6 corresponded to the protons on the carbon adjacent to ketone. A broad singlet is observed at 2.35 assigned as the methyl signal.

The ^{13}C NMR spectrum exhibited two downfield signals at 230.8 and 230.6 (Cr-CO). The carbonyl carbon resonance appeared at 194.4 and 194.1. The uncomplexed aromatic ring carbons appeared in the region 144.0 to 127.4. The complexed aromatic carbons resonated in the region 95.4-84.0. The nitromethane carbons appeared at 79.8 and 79.4.

The signals appearing at 72.7 and 72.3 were assigned to the carbon adjacent to (OMe) in the ring

complexed to $Cr(CO)_3$. At 55.8 the signal corresponding to methoxy carbon was observed. Twin signals corresponding to diastereomers were observed for the carbon adjacent to ketone (45.8 and 45.5) as well as the benzylic carbon (39.1 and 39). The methyl signal was observed at 20.7.

Under similar conditions the complex **3b** afforded the addition product in excellent yield (91%).



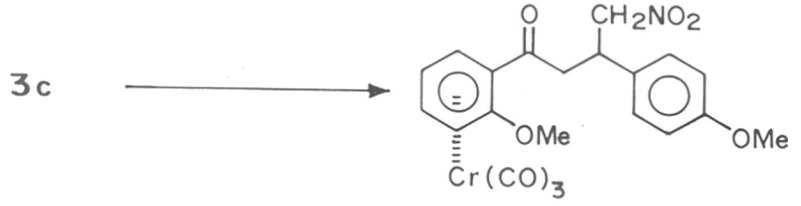
13

The IR spectrum showed characteristic bands at 1970, 1900 (Cr-CO), 1670 (-CO-), and 1550 (NO_2).

The ^1H NMR spectroscopy exhibited peaks at the expected region. The diastereomeric ratio was calculated from the integration of the *peri* proton and was found to be 60:40.

The ^{13}C NMR spectrum showed resonances in the expected regions. Except for the absence of the signal corresponding to methyl group, the spectral characteristics were quite similar to that of **12**.

The complex **3c** was obtained in high yield under similar reaction condition as above.



14

The IR spectrum exhibited bands at 1980, 1900 (Cr-CO), 1670 (-CO-) and 1540 (NO_2).

The ^1H NMR spectrum showed signals at the expected position. The diastereomeric ratio was observed to be 59:41. Peaks corresponding to methoxy groups were observed at 3.85, 3.86, 3.80 and 3.75.

The ^{13}C NMR spectrum exhibited signals at the expected position. The signal due to the *para* methoxy group appeared at 55.3.

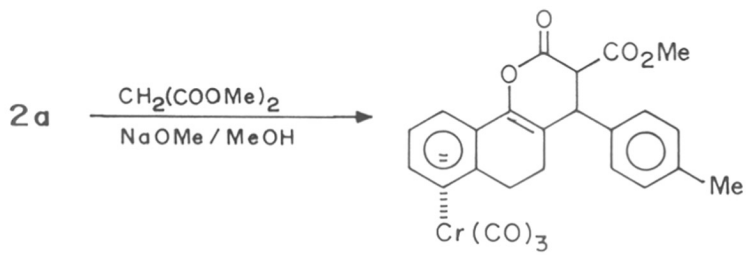
Conjugate Addition of Dimethyl malonate on the cyclic enones:

Encouraged by the diastereoselectivity in the conjugate addition of nitromethane, it was decided to use dimethylmalonate as the nucleophile in the Michael reaction.

Following a reported procedure[12ab], to 10 equiv. dimethylmalonate and 10 equiv. of sodium methoxide in methanol, the enone was added followed by diethyl ether. The reaction was followed by TLC. The deep red colour of the reaction mixture turned pale orange as the reaction progressed. The reaction was complete in 2 to 4h depending on the substrate. The product was more polar than the starting material. After usual work up the product was dissolved in minimum amount of CH_2Cl_2. Pet ether was added to it and the solution was refrigerated overnight. The product was precipitated as a yellow powder, leaving only trace

impurities in the mother liquor.

The complex **2a** afforded the product **15** as yellow powder in 89% yield.



15

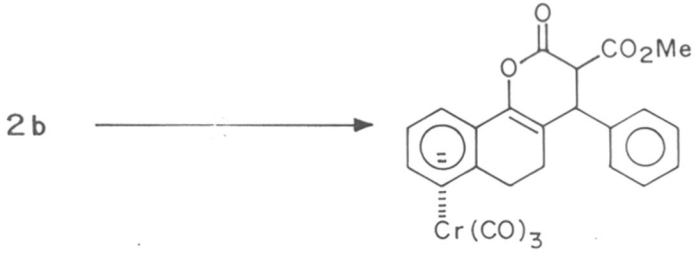
The IR spectrum of the compound **15** exhibited strong bands at 1980 and 1900, indicating the presence of $Cr(CO)_3$ moiety. But the carbonyl absorption around 1680 was absent. Instead, two bands were observed at 1770 and 1730. While the band at 1730 could be assigned to the COOMe group, the band at 1770 was assigned to the enol lactone, the structure of which was supported by ^1H NMR spectrum.

An AB quartet at 7.15 was observed for the protons on the 1,4 disubstituted aromatic ring. At 5.98 a doublet was observed corresponding to the proton in the complexed ring. The signals due to the protons on the complexed aromatic ring were observed in the usual region between 5.9 to 5.25. A doublet (J = 6.2Hz) at 4.2 was assigned to the methine proton on the carbon bearing the ester group and the lactone moiety. This proton was coupled with the adjacent benzylic methine proton, which also appeared as a doublet at 3.85 (J = 6.2Hz). The singlet at 3.75 was assigned to the methoxy group. The multiplet between 2.95-2.25 was due to the methylene protons of the tetralone. The singlet at 2.38 was assigned to the methyl group. The other methylene protons appeared as multiplet in the region 2.05-2.2. From the proton NMR spectrum it was inferred that a single diastereomer had been obtained.

The assignment of the two doublets at 4.2 and 3.85 was further confirmed from the COSY spectrum, which showed cross peaks for both signals indicating mutual coupling.

The complex **15**, exhibited the most downfield ^{13}C signal at 232.6 ppm corresponding to (Cr-CO). The signal at 195 due to the tetralone -CO- was absent. Two new signals at 167.1 and 162.6 were observed, which could be assigned to the ester and the lactone respectively. The olefin carbon appeared at 140.7. The uncomplexed aromatic ring carbons appeared in the characteristic region, 138. 0 to 127.5. The signal at 106.5 corresponded to the other olefin carbon. The complexed aromatic carbons appeared in the region 86.8 to 115.3. The ($COOCH_3$) signal appeared at 54, while the signal at 53 corresponds to (-CO-CH-COOMe). The benzylic carbon signal appeared at 45.0. The methylenes of the tetralone ring appeared at 26.2 and 24.6. The methyl group appeared at 20.9.

The complex **16** was obtained in 2h in excellent yield (88%) under similar reaction conditions.



16

The IR spectrum showed characteristic bands at 1980, 1900 (Cr-CO), 1770 (enol lactone) and 1730 (COOMe).

The ^1H NMR spectrum showed similar spectral characteristics as in **15**. The uncomplexed aromatic ring protons appeared as a multiplet between 7.5 to 7.2. The product was obtained as a single diastereomer as confirmed from the proton NMR spectrum. The ^{13}C NMR spectrum exhibited signals in the expected region.

The coupling constant between the contiguous methine protons in the lactone ring was 6.2 Hz. Of the two possible stereochemical relationships between the two substituents at those centres, the *cis* relationship was ruled out on grounds of severe steric interaction on perusal of the Drieding model.

In the *trans* compound, the stereocentre at the benzylic position was fixed based on precedences (*cf.* nitromethane adducts). If a flattened lactone ring results from delocalisation of the oxygen lone pair, the dihedral angle between the protons under discussion would approach 60° and be consistent with the observed coupling constant.

Summary:

The conjugate addition of nitromethane on conformationally rigid (2-arylidene1-tetralone) $Cr(CO)_3$ proceeded with complete stereospecificity at a carbon centre three atoms removed from the chromium complexed aromatic ring, at room temperature. Such stereoselectivity at a remote centre was observed for the first time. However, the acyclic complexes being flexible, exhibited only a modest selectivity. Conjugate addition of dimethylmalonate yielded an enol lactone as a single diastereomer despite the presence of an acidic proton four carbons away from the complexed aromatic ring.

GENERAL REMARKS

1. All melting points (recorded on Thermonik Cambell melting point apparatus) and boiling points (bath temperature) are recorded on Celsius scale (and are uncorrected).

2. IR spectra were recorded in chloroform, on a Perkin-Elmer Infracord Spectrophotometer Model 599-B. IR bands are expressed in frequency (cm^{-1}).

3. ^1H NMR spectra were recorded using tetramethylsilane/chloroform signal as reference on Varian FT - 80, (Varian 80 MHz FT NMR Spectrometer), Bruker WH - 90 (Bruker 90 MHz FT NMR Spectrometer) and Burker AC - 200 (Bruker 200 MHz FT NMR Spectrometer). ^{13}C NMR were recorded on AC - 200 Bruker NMR Spectrometer at 50 MHz frequency, MSL 300 MHz (Bruker) FT NMR Spectrometer at 75 MHz frequency. Chemical Shifts are recorded in parts per million (δ). Standard abbreviations have been used for signal multiplicity.

4. Microanalysis (C, H, N) was carried out on a Carbo-Erba 1100 automatic analyser by Dr. S.Y. Kulkarni and his group at NCL.

5. All known compounds were characterized by their IR & ^1H NMR spectra and duly cited.

6. Silica gel (LOBA/SD Chemicals, 60-120 mesh) was used for normal column chromatography. Flash column chromatography was carried out with silica gel, grade 60, Merck 9385, mesh size 230 - 400.

7. Solvents were purified as follows : Benzene, toluene were distilled over sodium-benzophenone ketyl under argon freshly before use. Tetrahydrofuran was distilled over potassium-benzophenone ketyl under argon freshly before use. EDC and methylene chloride were distilled over phosphorus pentoxide under argon; diethyl ether was distilled successively over phosphorous pentoxide and LAH under argon. Pet ether (60 - 80°C) LR grade, was used as received. Ethylacetate was dried over anhydrous calcium chloride and distilled. n-Dibutyl ether was distilled over LAH under argon freshly before use.

8. Chromium hexacarbonyl and 18-Crown-6 were purchased from Aldrich/Fluka and used as such. Allyl chloride, methallyl chloride, cinnamyl chloride, salicylaldehyde, KOH, NaOH pellets, anhyd. sodium sulphate, ammonium chloride, ethyl alcohol (LR grade), methanol (AR grade) were purchased from SD Chemicals. Nitromethane and trimethylsilyl chloride (Fluka) were purchased and distilled before use. Tetrabutylammonium bromide (FLUKA) was used as such.

9. All the reactions were carried out under argon atmosphere. The usual work up procedure involves extraction with appropriate organic solvent, washing with water and brine and drying over anhydrous sodium sulphate, unless otherwise mentioned. The solutions were concentrated in a Buchi rotary evaporator connected to water aspirator.

EXPERIMENTAL :

Preparation of 1-tetralone : Following a reported procedure, benzene (500ml) was treated with γ-butyrolactone (52g, 0.6moles) in the presence of $AlCl_3$ (300g, 2.26moles) to afford 1-tetralone (83g, 88%) (b.p.100°/2mm).

Preparation of 2-Methoxybenzaldehyde : Following a reported procedure, from 2-hydroxybenzaldehyde (12.2g, 0.1mole), potassium carbonate (15.4g, 0.11mole) and dimethyl sulphate (13.8g, 0.11mole), 2-methoxybenzaldehyde (12.8g, 94%) was obtained as a pale yellow liquid, which was used as such for subsequent reaction.

Preparation of 2-Methoxyalphamethyl benzylalcohol : In a dry two necked flash flushed with argon, were placed Mg turnings (3.6g, 0.15mol) a small crystal of iodine and dry ether (35ml). Methyl iodide (9.3ml, 0.15mol) was added dropwise. Initially 2ml was added and thereafter the addition was continued at a rate sufficient to maintain gentle reflux. Heating was continued for one hour after the addition was complete. The reaction mixture was cooled below 0°C in an ice salt bath and a solution of the aldehyde (13.6g, 0.1mol) in dry ether (20ml) was added dropwise with stirring. Stirring was continued at room temperature overnight (10 to 12h). The reaction mixture was then cooled below 0°C in ice salt bath and saturated aqueous ammonium chloride solution (15ml) was added dropwise. The organic layer was extracted in ether and worked up as usual. The product (12g) was used as such for the next reaction.

Preparation of 2-Methoxyacetophenone : To a solution of 2-methoxyalphamethyl benzyl alcohol (12g, 0.9moles) in acetone (75ml), Jones reagent [prepared by adding a solution of H_2SO_4 (5.8ml) in distilled water (3ml) to CrO_3 (6.7g) in distilled water (12.5ml)] was added dropwise at room temperature until complete consumption of the alcohol (TLC) was observed. Excess reagent was destroyed by dropwise addition of isopropanol. The acetone solution was decanted, and the dark green residue was washed with acetone. The combined acetone extract was concentrated under reduced pressure to provide a residue. It was distilled under reduced pressure (b.p. 80°C / 2mm) to afford the product (10g, 85 %) as a colourless liquid.

Preparation of 1-tetralone chromium tricarbonyl : To a solution of 1-tetralone (7ml, 54mmol) in n-dibutyl ether (100ml), $Cr(CO)_6$ (3g, 13.7mmol) and THF (5ml) were added and the reaction mixture was heated under reflux at 150°C (oil bath temp). After 12h, the reaction mixture was allowed to cool to room temperature and filtered through celite. The filtrate was refrigerated to provide a red crystalline solid and unreacted $Cr(CO)_6$ (800mg). The chromium complex was dissolved in benzene while the $Cr(CO)_6$ remained insoluble. Concentration of the benzene solution provided the product (1.4g, 64%), based on consumed $Cr(CO)_6$.

Preparation of 2-methoxyacetophenone chromium tricarbonyl : To a solution of 2-methoxyacetophenone (4ml, 30mmol) in n-dibutyl ether (50ml), $Cr(C0)_6$ (2g, 10mmol) and THF (2ml) were added and the reaction mixture was heated under reflux at 150°C for 10h. The reaction mixture was allowed to cool to room temperature and filtered through celite. The filtrate was refrigerated to provide crystals of 2-methoxyacetophenone chromium complex and $Cr(CO)_6$ (500mg). As above, the product was isolated (1.4g, 72%), based on consumed $Cr(C0)_6$.

General method for the preparation of enones (2a - d) :

A solution of aromatic aldehyde (2.64-5.34mmol) and 1-tetralone chromium tricarbonyl complex **1** (1.76-3.56mmol) in ethanol (10ml) was cooled in ice salt bath. An ethanolic solution of KOH (1.76mmol - 3.56mmol in 10ml ethanol) was added dropwise *via* syringe. The reaction was monitored by TLC. After complete disappearance of starting material the reaction mixture was worked up as usual to provide orange to red solid products **2a - d**. The crude products were washed with pet ether (3x20ml) and recrystallized from dichloromethane/pet ether to afford analytically pure complexes.

Preparation of 2a : From the reaction of the complex **1** (494mg, 1.76mmol) and p-tolualdehyde (316mg, 2.64mmol) the complex **2a** was isolated (641mg, 95%) as an orange crystalline solid.

m.p. : 164 - 165°C

IR : 1980, 1910 (b), 1660, 1600

^{1}H NMR : 2.40 (s, 3H), 2.56 - 2.58 (m, 1H), 2.59 - 3.15 (m, 2H), 3.25 - 3.50 (m, 1H), 5.20 (d, 1H, J = 7Hz), 5.40 (t, 1H, J = 6Hz), 5.70 (t, 1H, J = 6Hz), 6.30 (d, 1H, J = 7Hz), 7.27 (d, 2H, J = 9Hz), 7.38 (d, 2H, J = 9Hz), 7.85 (s, 1H).

^{13}C NMR : 21.2, 25.5, 27.0, 84.6, 89.8, 91.4, 94.2, 114.6, 129.1, 129.8, 130.0, 131.3, 132.1, 138.3, 139.2, 185.7, 230.9.

Analysis : Calc : C = 65.79, H = 4.17

Obs : C = 65.56, H = 4.74

Preparation of 2b : From the reaction of complex **1** (983mg, 3.5mmol) and benzaldehyde (557mg, 5.25mmol) the complex **2b** (1.26g, 97%) was obtained as a red crystalline solid.

m.p. : 150 - 151°C

IR : 1980, 1910, 1670, 1610

^{1}H NMR : 2.50 - 2.80 (m, 1H), 2.85 - 3.15 (m, 2H), 3.20 - 3.40 (m, 1H), 5.15 (d, 1H, J = 7Hz), 5.40 (t, 1H, J = 6Hz), 5.65 (t, 1H, J = 6Hz), 6.25 (d, 1H, J = 7Hz), 7.30 - 7.55 (bs, 5H), 7.85 (s, 1H).

^{13}C NMR : 25.4, 26.9, 89.6, 89.8, 91.4, 93.9, 94.2, 114.7, 128.3, 128.8, 129.9, 132.1, 134.9, 138.0, 185.7, 230.8.

Analysis : Calcd : C = 65.04, H = 3.79

: Obsd. : C = 65.19, H = 4.15

Reaction of 2c : The reaction of the complex **1** (900mg, 3.2mmol) and p-anisaldehyde (652.5mg, 4.8mmol) afforded the complex **2c** (1.24mg, 96.8%) as a red solid.

m.p. : 154 - 155°C

I.R. : 1980, 1920 (b), 1660, 1620

^{1}H NMR : 2.62 - 2.75 (m, 1H), 2.85 - 3.15 (m, 2H), 3.2 - 3.35 (m, 1H), 3.85 (s, 3H), 5.15 (d, 1H, J = 7Hz), 5.40 (t, 1H, J = 6Hz), 5.65 (t, 1H, J = 6Hz), 6.25 (d, 1H, J = 7Hz), 6.95 (d, 2H, J = 9Hz), 7.45 (d, 2H, J = 9Hz), 7.85 (S, 1H).

^{13}C NMR : 25.5, 26.8, 55.1, 89.6, 89.8, 91.4, 94.2, 113.9, 114.6, 127.5, 130.0, 131.9, 138.0, 160.2, 185.5, 230.9.

Analysis : Calc : C = 63.15, H = 4.01

Obs : C = 62.91, H = 4.37

Preparation of 2d : The reaction of the complex **1** (1.0g, 3.56mmol) and p-nitrobenzaldehyde (806mg, 5.34mmol) yielded the product **2d** (1.44g, 97%) as a red solid.

m.p. : decomposed at 200°C

IR : 1980, 1900 (b), 1660, 1600

^{1}H NMR : 2.62 - 2.85 (m, 1H), 2.92 - 3.30 (m, 3H), 5.15 (d, 1H, J = 7Hz), 5.40 (t, 1H, J = 6Hz), 5.70 (t, 1H, J = 6Hz), 6.30 (d, 1H, J = 7Hz), 7.60 (d, 2H, J = 9Hz), 7.85 (S, 1H), 8.30 (d, 2H, J = 9Hz).

^{13}C NMR : 25.5, 26.7, 89.6, 91.4, 93.1, 94.3, 114.3, 123.5, 124.1, 126.6, 127.8, 128.1, 130.4, 135.0, 135.1, 141.5, 147.3, 185.2, 230.5.

Analysis : Calc : C = 57.97 H = 3.14, N = 3.38

Obs : C = 57.63, H = 3.14, N = 3.3

Preparation of 2-Benzylidene-1-tetralone (2e): From the reaction of 1-tetralone (4.38g, 30mmol) and benzaldehyde (3.18g, 30mmol) under similar conditions the product (6.7g, 95%) was isolated.

General procedure for the preparation of acyclic enones 3a - c :

A solution of the aromatic aldehyde (2.64 - 45mmol) and 2-methoxy acetophenone chromium tricarbonyl (1.76-3mmol) in ethanol (10ml - 15ml) was cooled in ice salt bath and KOH (1.76-3.00mmol) in ethanol (10ml) was added dropwise *via* syringe. The reaction mixture was allowed to stir at room temperature overnight. After complete disappearance of starting material (TLC) the reaction mixture was worked up to provide a solid residue. It was washed with pet ether (3 x 15 ml) and recrystallized from dichloromethane/pet ether.

Preparation of 3a : From the reaction of the complex **3a** (500mg, 1.76mmol) and p-tolualdehyde (316g, 2.64mmol), the complex **5a** (640mg, 94%) was isolated as an orange crystalline solid.

m.p. : 127 - 129°C

IR : 1980, 1920, 1660, 1600

^{1}H NMR : 2.40 (s, 3H), 3.90 (s, 3H), 5.00 (t, 1H, J = 6Hz), 5.10 (d, 1H, J = 7Hz), 5.80 (t, 1H, J = 6Hz), 6.20 (d, 1H, J = 7Hz), 7.20 (d, 2H, J = 9Hz), 7.45 (d, 2H, J = 16Hz), 7.55 (d, 2H, J = 9Hz), 7.75 (d, 2H, J = 16Hz).

^{13}C NMR : 21.3, 55.9, 72.5, 84.2, 92.5, 95.1, 95.9, 123.7, 128.4, 129.5, 132.0, 140.9, 143.0, 143.9, 186.8, 231.4.

Analysis : Calc : C = 62.0, H = 4.13

: Obs : C = 61.6, H = 4.50

Preparation of 3b : From the reaction of the complex **3b** (500mg, 1.76mmol) and benzaldehyde (280mg, 2.64mmol), the complex **5b** (628mg, 96%) was obtained as a red crystalline solid.

m.p. : 135 - 136°C

IR : 1980, 1900, 1660, 1600

^{1}H NMR : 3.95 (s, 3H), 4.95 - 5.15 (m, 2H), 5.85 (t, 1H, J = 6Hz), 6.25 (d, 1H, J = 7Hz), 7.42 - 7.95 (m, 7H).

^{13}C : 55.9, 72.6, 84.2, 92.4, 94.9, 95.7, 124.9, 128.3, 128.7, 130.2, 134.9, 142.8, 143.8, 186.7, 231.2.

Analysis : Calc : C = 61.1, H = 3.75

Obs : C = 60.48, H = 4.10

Preparation of 3c : From the reaction of the complex **3c** (855mg, 3mmol) and anisaldehyde (612mg, 4.5mmol), the complex **5c** (1.1g, 92 %) was obtained as an orange crystalline solid.

m.p. : 115 - 116°C

IR : 1980, 1910, 1660, 1600 and 1580

^{1}H NMR : 3.85 (s, 3H), 3.95 (s, 3H), 5.00 (t, 1H, J = 6Hz), 5.10 (d, 1H, J = 7Hz), 5.80 (t, 1H, J = 6Hz), 6.20 (d, 1H, J = 7Hz), 6.95 (d, 2H, J = 9Hz), 7.35 (d, 2H, J = 16Hz), 7.60 (d, 2H, J = 9Hz), 7.80 (d, 2H, J = 16Hz).

^{13}C : 55.2, 55.9, 72.5, 84.2, 92.8, 95.1, 95.9, 144.3, 122.4, 127.5, 130.1, 142.8, 143.9, 161.6, 186.7, 231.4.

Analysis : Calc : C = 59.5, H = 3.97

Obs : C = 58.99, H = 4.18

General procedure for the addition of nitromethane to the complexes (2a - d)

Nitromethane (5 to 7ml) was added to a flask containing the complex **2a-d** (1-1.36mmol), KF (1-1.36mmol) and 18-Crown-6 (5% by weight of the complex) and the solution was stirred at room temperature (2h to 30h). The solvent was removed under reduced pressure and the reaction mixture was worked up as usual. The crude semisolid residue was subjected to flash column chromatography. Gradient elution (10% EtoAc - pet ether to 50% EtoAc - pet ether) led to the separation of diastereomers. The residue was loaded on the column with 10% EtoAc - pet ether. The less polar fraction provided the minor isomer while the polar fraction contained the major isomer in each case. The combined yield is reported.

Reaction of 2b : Nitromethane (7ml), complex **2b** (500mg, 1.36mmol), KF (79mg, 1.36 mmol) and 18-Crown-6 (25mg) were stirred at room temperature for 2h. After usual workup the residue was chromatographed with 30% EtoAc - pet ether, minor diastereomer (50mg, **7b**) and major diastereomer (430mg, **6b**) were isolated (yield = 83%).

Compound **6b**

m.p. : 169-170°C

IR : 1980, 1920, 1680, 1560

^{1}H NMR : 1.60 - 1.85 (m, 1H), 1.85 - 2.05 (m, 1H), 2.62 - 2.80 (m, 2H), 2.85 - 3.05 (m, 1H), 4.30 (m, 1H), 4.75 - 4.85 (m, 1H), 5.00 - 5.20 (m, 2H), 5.30 (t, 1H, J = 6Hz), 5.65 (t, 1H, J = 6Hz), 6.15 (d, 1H, J = 7Hz), 7.20 - 7.45 (m, 5H).

^{13}C NMR : 24.7, 27.4, 43.2, 48.8, 78.1, 88.8, 89.0, 91.6, 94.7, 114.2, 127.8, 128.1, 128.8, 136.6, 195.8, 230.1.

Analysis : Calc : C = 58.6, H = 3.95, N = 3.79

Obs : C = 59.0, H = 4.35, N = 3.62

compound **7b**

m.p. : 161 - 162°C

IR : 1980, 1920, 1680, 1560

^{1}H NMR : 1.60 - 2.05 (m, 1H), 2.15 - 2.40 (m, 1H), 2.60 - 3.10(m, 3H), 4.10(m, 1h), 4.90 - 5.35(m, 3H), 5.70 (t, 1H), 6.25 (d, 1H), 7.15 - 7.45 (m, 5H).

^{13}C NMR : 25.6, 26.5, 45.1, 48.1, 88.5, 77.1, 88.5, 89.1, 91.7, 92.0, 94.9, 114.9, 127.1, 128.0, 128.3, 128.8, 129.0, 136.7, 195.3, 230.4.

Analysis : Calc : C = 58.6, H = 3.95, N = 3.79

Obs : C = 57.95, H = 3.81, N = 3.19

Reaction of 2a : Nitromethane (5ml), complex **2a** (383mg, 1mmol), KF (58mg, 1mmol) and 18-Crown-6 (19mg) were stirred at room temperature for 12h and worked up as usual. With 30% EtoAc - pet ether, minor diastereomer (53mg, **5a**) and major diastereomers (342 mg, **4a**) were separated (yield = 89%).

Compound **4a**

m.p. : 178 - 179°C

IR : 1990, 1920, 1680, 1560

^{1}H NMR : 1.60 - 2.00 (m, 2H), 2.30 (s, 3H), 2.60 - 2.80 (m, 2H), 2.80 - 3.05 (m, 1H), 4.20 (m, 1H), 4.75 - 4.90 (m, 1H), 5.05 - 5.20 (m, 2H), 5.30 (t, 1H, J = 6Hz), 5.65 (t, 1H, J = 6Hz), 6.15 (d, 1H, J = 7Hz), 7.10 (bs, 4H).

^{13}C NMR : 20.8, 24.8, 27.4, 43.0, 48.8, 78.3, 88.7, 89.0, 91.6, 92.0, 94.7, 114.2, 127.9, 129.5, 133.4, 137.6, 196.0, 230.1.

Analysis : Calc : C = 59.45, H = 4.27, N = 3.15

: Obs : C = 59.16, H = 4.36, N = 3.27

compound **5a**

m.p. : 161 - 162°C

IR : 1990, 1920, 1680, 1560

^{1}H NMR : 1.75 - 2.15 (m, 2H), 2.40 (s, 3H), 2.60 - 3.10 (m, 3H), 4.20 (m, 1H), 4.90 - 5.20 (m, 3H), 5.30 (t, 1H, J = 6Hz), 5.65 (t, 1H, J = 6Hz), 6.20 (d, 1H, J = 7Hz), 7.20 (s, 2H), 7.30 (s, 2H).

Analysis : Calc : C = 59.45, H = 4.27, N = 3.15

: Obs : C = 59.51, H = 3.91, N = 3.05

Reaction of 2c : Nitromethane (5ml), the complex **2c** (399mg, 1mmol), KF (58mg, 1mmol) and 18-Crown-6 (20mg) were stirred at room temperature for 24h. The reaction mixture was worked up as usual to provide crude mixture of products. With 40% EtoAc - pet ether, minor diastereomer (41mg, **9c**) and major diastereomer (338mg, **8c**) was obtained (yield = 82%).

Compound **8c**

m.p. : 128-129°C

IR : 1980, 1910, 1680, 1610, 1560

^{1}H NMR : 1.65 - 2.05 (m, 2H), 2.62 - 2.80 (m, 2H), 2.85 - 3.05 (m, 1H), 3.85 (s, 3H), 4.25 (m, 1H), 4.75 - 4.90 (m, 1H), 5.05 - 5.20 (m, 2H), 5.30 (t, 1H, J = 6Hz), 5.65 (t, 1H, J = 6Hz), 6.20 (d, 1H, J = 7Hz), 6.90 (d, 2H, J = 9Hz), 7.20 (d, 2H, J = 9Hz).

^{13}C NMR : 24.1, 27.2, 42.5, 48.8, 55.0, 78.3, 88.9, 89.2, 91.6, 92.0, 94.8, 114.1, 114.4, 128.3, 129.1, 158.9, 196.0, 230.3.

Analysis	:	Calc	:	C = 57.39, H = 4.13, N = 3.04
	:	Obs	:	C = 58.17, H = 4.41, N = 2.97

compound **9c**

m.p. : 81 - 82°C

IR : 1980, 1910, 1680, 1610, 1560

^{1}H NMR : 1.75 - 2.20 (m, 2H), 2.65 - 3.10 (m, 4H), 3.80 (s, 3H), 4.10 (m, 1H), 5.10 (d, 3H, J = 9Hz), 5.30 (t, 1H, J = 6Hz), 5.65(t, 1H, J = 6Hz), 6.20 (d, 1H, J = 7Hz), 6.90 (d, 2H, J = 9Hz), 7.20 (d, 2H, J = 9Hz).

^{13}C : 24.4, 24.6, 41.8, 47.7, 55.1, 79.1, 88.9, 89.2, 91.9, 94.9, 114.6, 128.9, 159.4, 195.5, 230.3.

Analysis	:	Calc	:	C = 57.39, H = 4.13, N = 3.04
	:	Obs	:	C = 58.03, H = 4.53, N = 3.00

Reaction of 2d : Nitromethane (5ml), the complex **2d** (414mg, 1mmol), KF (58mg, 1mmol) and 18-Crown-6 (21mg) were stirred at room temperature for 30 hrs. The reaction mixture was worked up as usual. With 50% EtoAc - pet ether, minor diastereomer (19mg, **11d**) and major diastereomer (379mg, **10d**) could be separated (yield = 84 %).

Compound **10d**

m.p. : 165 - 166°C

IR : 1980, 1910, 1680, 1610, 1560

^{1}H NMR : 1.70 - 1.95 (m, 1H), 1.95 - 2.15 (m, 1H), 2.62 - 2.85 (m, 2H), 2.90 - 3.20 (m, 1H), 4.75 (m, 1H), 4.45 - 4.60 (m, 1H), 4.85 - 5.00 (m, 1H), 5.05 - 5.20 (m, 2H), 5.25 - 5.40 (m, 1H), 5.65 (t, 1H, J = 6Hz), 6.15 (d, 1H, J = 7Hz), 7.50 (d, 2H, J = 9Hz), 8.25 (d, 2H, J = 9Hz).

^{13}C NMR : 24.5, 27.5, 42.7, 48.8, 89.0, 89.1, 91.4, 94.7, 113.6, 123.9, 129.4, 143.8, 147.5, 195.0, 229.9.

Analysis : Calc : C = 53.05, H = 3.36, N = 5.89

: Obs : C = 52.91, H = 3.40, N = 5.65

compound **11d**

m.p. : 100 - 101°C

IR : 1980, 1910, 1680, 1560

^{1}H NMR : 1.70 - 2.15 (m, 2H), 2.60 - 3.15 (m, 3H), 4.20 (m, 1H), 4.95 - 5.40 (m, 4H), 5.65 (t, 1H, J = 6Hz), 6.15 (d, 1H, J = 7Hz), 7.50 (d, 2H, J = 9Hz), 8.20 (d, 2H, J = 9Hz).

Analysis : Calc : C = 53.05, H = 3.36, N = 5.89

: Obs : C = 53.10, H = 3.51, N = 5.83

Reaction of 2e: Using similar conditions as above the uncomplexed enone **2e** was reacted with nitromethane. The reaction was observed to be complete after three days. After usual workup and column chromatography (10% EtOAc - Pet ether) the addition product was obtained in 90% yield.

m.p. : 108-110°C

IR : 1680, 1560

^{1}H NMR : 1.65 - 2.30 (m, 2H), 2.70 - 3.10 (m, 3H), 4.00 - 4.35 (m, 1H), 4.70 - 4.90 (m, 1H), 4.95 - 5.25 (m, 2H), 7.20 - 7.60 (m, 9H).

^{13}C NMR : Two sets of signals were observed which correspond to the dia stereomeric mixture are given below

26.2, 26.3, 27.5, 29.1, 43.0, 44.2, 49.2, 51.2, 76.7, 78.9, 126.6, 127.3, 127.5, 127.6, 128.1, 128.3, 128.4, 128.5, 128.7, 132.0, 132.4, 133.5, 133.6, 137.4, 137.6, 143.2, 143.3, 197.4, 198.1.

General procedure for the addition of nitromethane to the complexes (5a - c): Nitromethane (5ml) was added to the complex **5a-c** (0.5mmol), KF (29mg, 0.5mmol) and 18-Crown-6 (5% by weight of the complex) and stirred overnight at room temperature to afford a residue. It was subjected to flash column chromatography with 30% EtOAc - pet ether, to afford the desired product as a diastereomeric mixture (semisolid). The semisolid was dissolved in minimum amount of dichloromethane and diluted with pet ether. On refrigeration, red solid product was obtained. The diastereomeric ratio was determined from the ^{1}H NMR spectra.

Reaction of 5a : From the complex **5a** (186.5mg, 0.5mmol), Nitromethane (5ml), KF (29mg, 0.5mmol). Michael adduct **13** was obtained (198mg, 91%) as a diastereomeric mixture (Ratio 57:43).

Compound No. **13**

IR : 1980, 1900, 1670, 1540

^{1}H NMR : The signals given below correspond to the major dia stereomer

3.30 - 3.65 (m, 2H), 3.85 (s, 3H), 4.25 (m, 1H), 4.60 - 5.10 (m, 4H), 5.85 (m, 1H), 6.30 (d, 1H, J = 6Hz), 7.20 - 7.50 (m, 5H).

Some of the signals due to the minor diastereomer which could be seen are given below

3.90 (s, 3H), 6.20 (d, 1H, J = 6Hz).

^{13}C NMR : The signals given below correspond to the major dia stereomer

39.3, 45.3, 45.7, 55.8, 72.1, 72.4, 79.2, 79.8, 84.0, 84.4, 88.5, 95.2, 95.4, 127.3, 127.6, 128.8, 138.5, 139.1, 144.1, 193.8, 194.2, 230.6, 230.8.

Some of the signals due to the minor diastereomer which could be seen are given below

39.1, 45.5, 72.3, 79.8, 84.0, 89.2, 95.3, 127.7, 130.1, 135.6, 194.1, 230.6.

Analysis : Calc : C = 56.25, H = 4.24, N = 3.12

: Obs : C = 55.98, H = 4.32, N = 3.34

Reaction of 5b : Following the above procedure, complex **5b** (194mg, 0.5mmol.) afforded the product (210mg, 93 %)

Compound No. **12**

IR : 1980, 1900, 1670, 1540

^{1}H NMR : The signals given below correspond to the major diastereomer

2.35 (s, 6H), 3.20 - 3.60 (m, 4H), 3.85 (s, 3H), 3.90 (s, 3H), 4.10 - 4.30 (m, 2H), 4.55 - 4.85 (m, 2H), 4.85 - 5.20 (m, 6H), 5.75 - 6.00 (m, 2H), 6.20 (d, 1H), 6.30 (d, 1H, J = 6Hz), 7.10 - 7.30 (bs, 4H).

Some of the signals due to the minor diastereomer which could be seen are given below

3.80 (s, 3H), 6.25 (d, 1H, J = 6Hz).

^{13}C NMR : The signals given below correspond to the major dia stereomer

20.7, 39.0, 39.1, 45.5, 45.8, 55.8, 72.3, 72.7, 79.4, 79.8, 84.0, 84.4, 89.0, 89.2, 95.2, 95.4, 127.1, 129.4, 135.6, 136.2, 137.1, 143.9, 194.1, 194.4, 230.6, 230.8.

Some of the signals due to the minor diastereomer which could be seen are given below

48.6, 55.8, 72.4, 83.9, 90.9, 116.4, 127.5, 135.2, 143.6, 196.4, 230.9.

Analysis : Calc : C = 55.29, H = 3.91, N = 3.22

: Obs : C = 55.32, H = 4.13, N = 3.34

Reaction of 5c : Nitromethane (5ml), the complex (201.5mg, 0.5mmol) KF (29mg, 0.5mmol) and 18-Crown-6 (10mg) were stirred at room temperature overnight. After usual workup and column chromatography, the desired product was obtained (218 mg, 94%).

Compound No. **14**

IR : 1970, 1900, 1660, 1540

^{1}H NMR : The signals given below correspond to the major dia stereomer

3.15 - 3.60 (m, 2H), 3.80 (s, 3H), 3.82 (s, 3H), 4.05 - 4.30 (m, 1H), 4.55 - 4.85 (m, 2H), 4.85 - 5.15 (m, 2H), 5.75 - 5.90 (m, 1H), 6.25 (d, 1H, J = 6Hz), 6.85 (bd, 2H), 7.20 (bd, 2H).

Some of the signals due to the minor diastereomer which could be seen are given below

3.75 (s, 3H), 3.85 (s, 3H), 6.15 (d, 1H, J = 6Hz).

^{13}C NMR : The signals given below correspond to the major dia stereomer

38.6, 45.8, 55.0, 72.7, 79.5, 84.4, 89.0, 95.2, 114.3, 120.5, 128.3, 130.6, 131.1, 144.1, 159.0, 194.4, 230.8.

Some of the signals due to the minor diastereomer which could be seen are given below

38.7, 45.6, 55.8, 72.3, 79.9, 89.2, 95.3, 128.3, 130.0, 133.6, 194.0, 230.6.

Analysis : Calc : C = 54.30, H = 4.09, N = 3.01

: Obs : C = 53.91, H = 3.91, N = 2.65

General procedure for the reaction of dimethylmalonate with the complexes 2a - b : Dimethylmalonate (1.58 g,12 mmol) was added to NaOMe (276 mg,12 mmol of Na in 5ml of methanol) at 0°C. After 10 minutes, the complexed substrate **2a-b** (1.2 mmol) was added as solid followed by diethyl ether (15ml). After 10 minutes, the reaction was allowed to warm to room temperature and stirred for 2 - 3.5h. The reaction was worked up as usual and the product was crystallized from dichloromethane/pet ether.

Reaction of 2b : From complex **2b** (442 mg, 1.2 mmol) during a reaction period of 2h, the product was obtained (492 mg, 88%) as an yellow solid.

Compound No. **16**

m.p. : 188 - 189°C

IR : 1970, 1900, 1770, 1740

^{1}H NMR : 2.05 - 2.30 (m, 1H), 2.35 - 2.70 (m, 2H), 2.75 - 3.00 (m, 1H), 3.85 (s, 3H), 3.90 (d, 1H, J = 5Hz), 4.20 (d, 1H, J = 5Hz), 5.30 - 5.60 (m, 3H), 5.90 (d, 1H, J = 6Hz), 7.20 - 7.50 (m, 5H).

^{13}C NMR : 24.7, 26.2, 45.5, 53.0, 53.9, 86.7, 90.9, 91.1, 92.2, 96.1, 106.5, 115.1, 127.7, 128.2, 129.3, 136.5, 140.9, 162.5, 167.2, 232.6.

Analysis : Calc : C = 61.4, H = 3.83

: Obs : C = 61.07, H = 4.76

Reaction of 2a : From complex **2a** (580 mg, 1.2 mmol) during a reaction period of 3h and 30 minutes, the product was obtained (678 mg, 89%) as an yellow solid.

Compound No. **15**

m.p. : 170 - 172°C

IR : 1970, 1900, 1770, 1740.

^{1}H NMR : 2.05 - 2.20 (m, 1H), 2.30 (s, 3H), 2.35 - 2.70 (m, 2H), 2.70 - 2.95 (m, 1H), 3.75 (s, 3H), 3.85 (d, 1H, J = 6.3Hz), 4.15 (d, 1 H, J = 6.3Hz), 5.25 - 5.35 (m, 2H), 5.40 - 5.50 (m, 1H), 5.85 (d, 1H, J = 6Hz), 7.10 (d, 2H, J =9Hz), 7.15 (d, 2H, J = 9Hz).

^{13}C NMR : 20.9, 24.6, 26.2, 45.0, 53.0, 54.0, 86.8, 90.9, 91.2, 92.2, 96.2, 106.5, 115.3, 127.5, 129.9, 133.3, 138.0, 140.7, 162.6, 167.2, 232.7.

Analysis : Calc : C = 62.1, H = 4.14

: Obs : C = 61.8, H = 4.35

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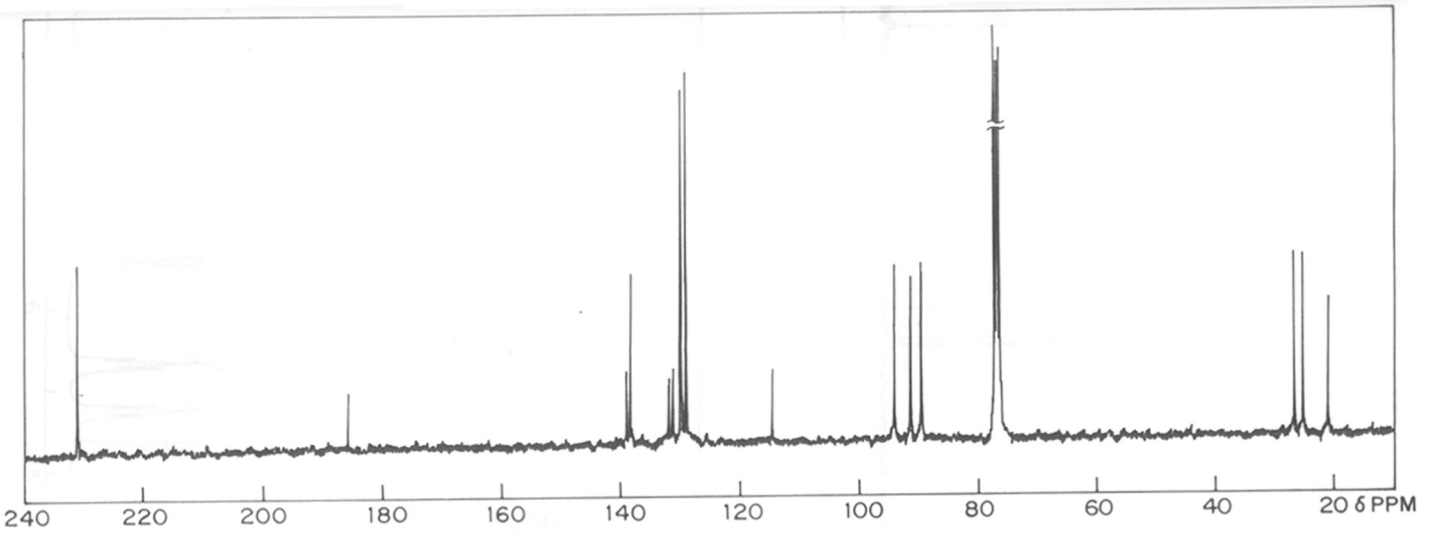
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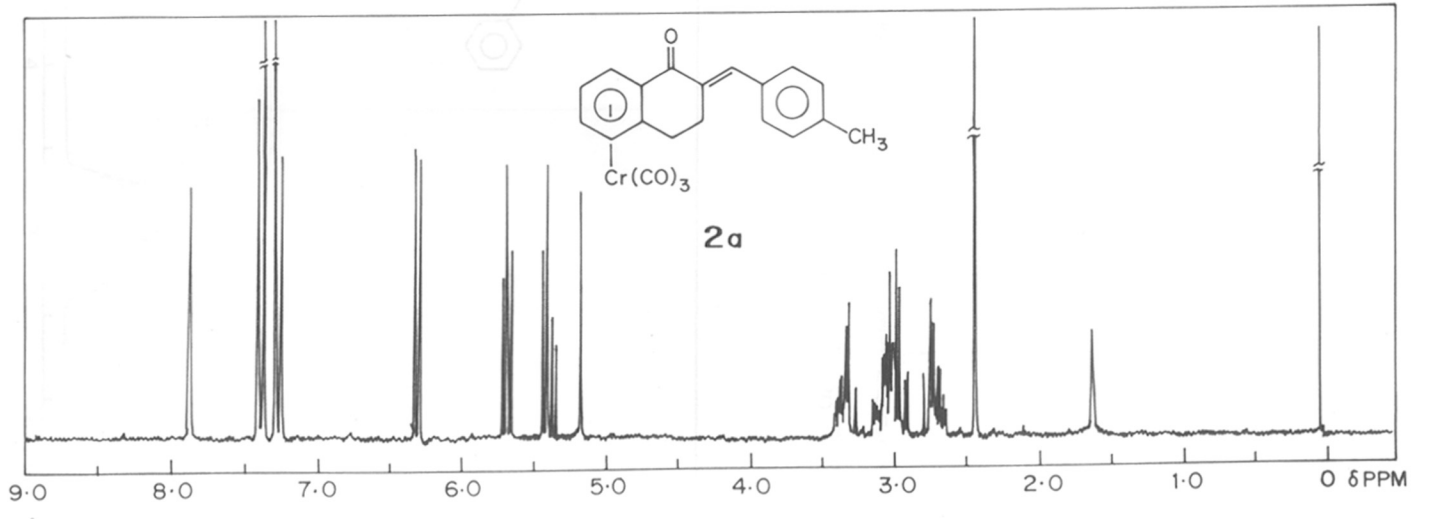
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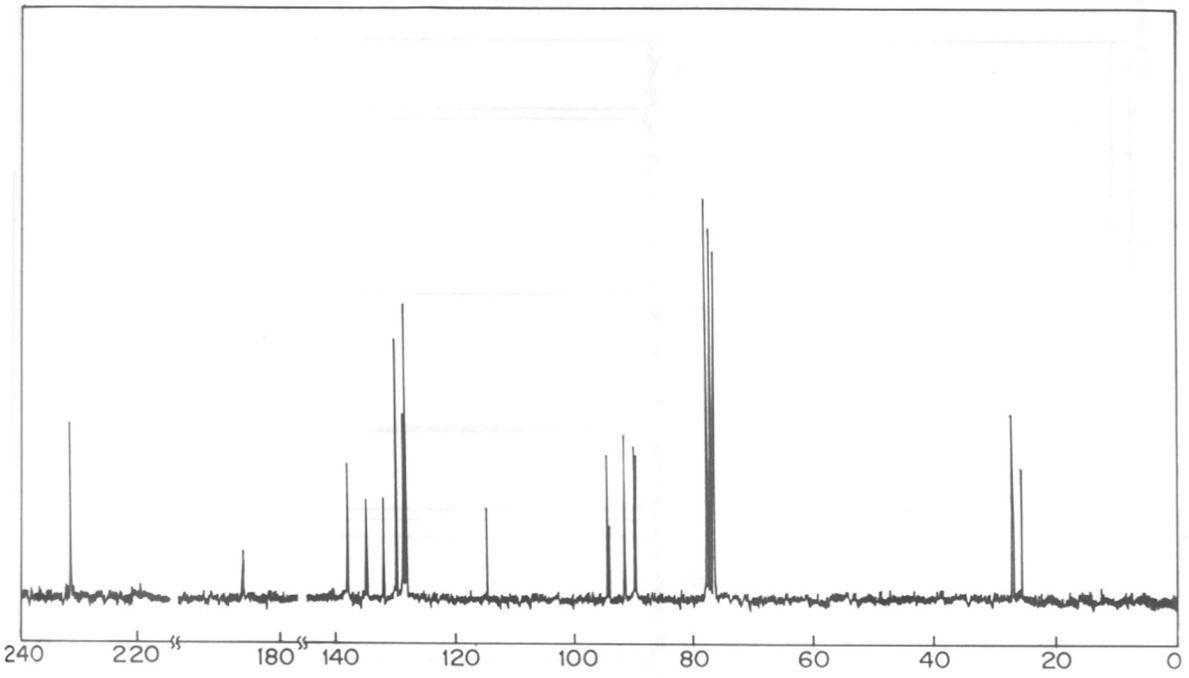

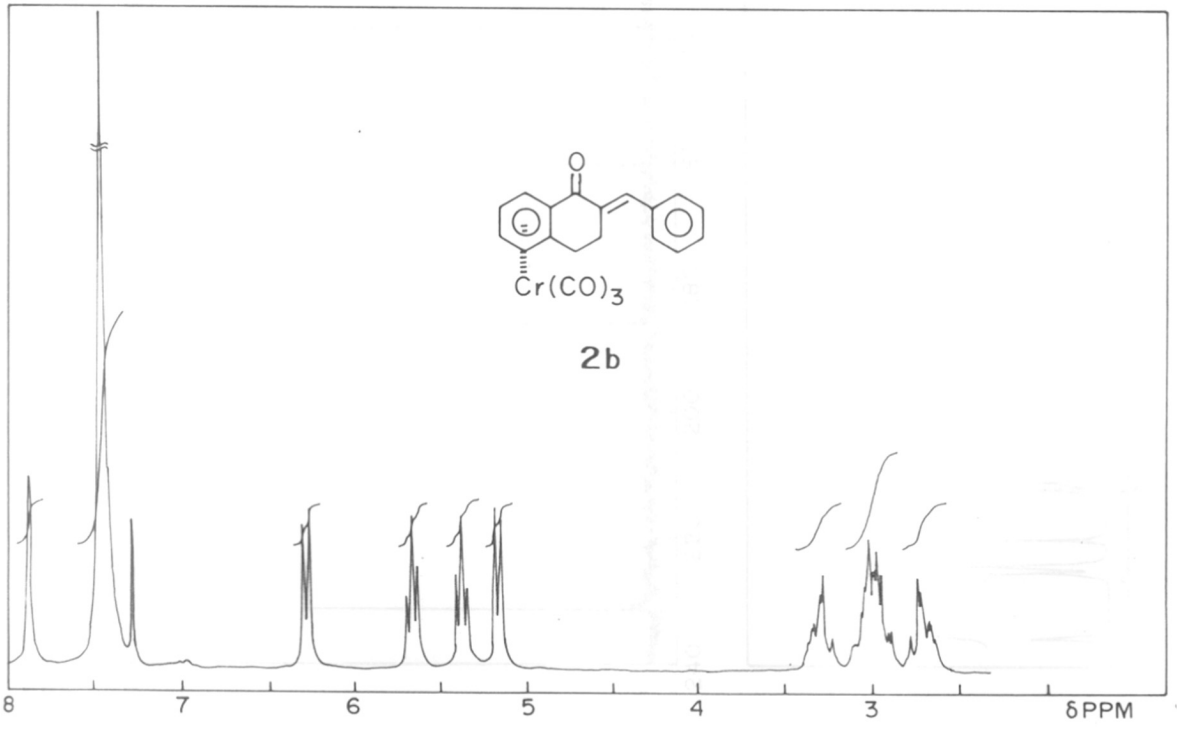

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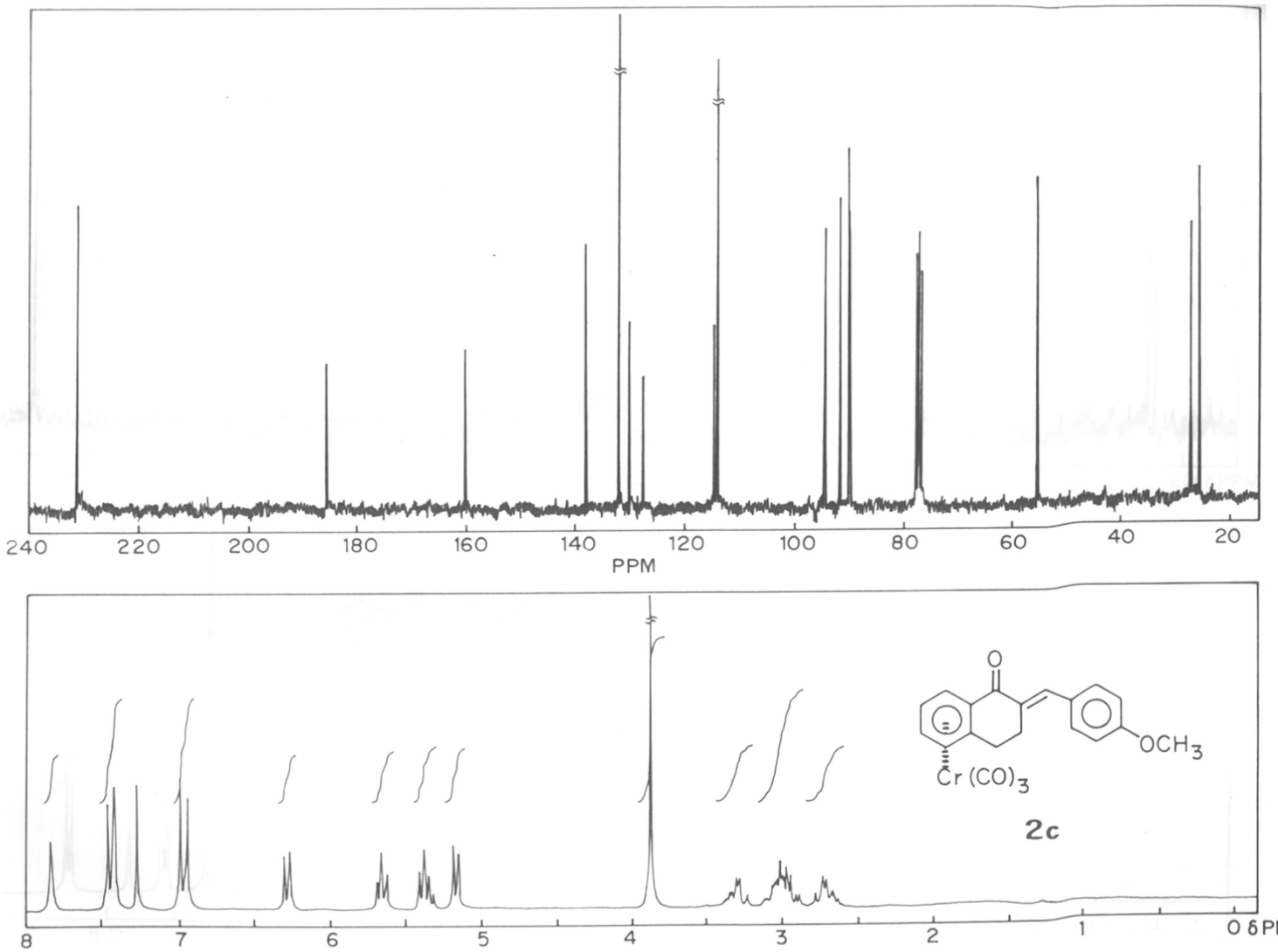
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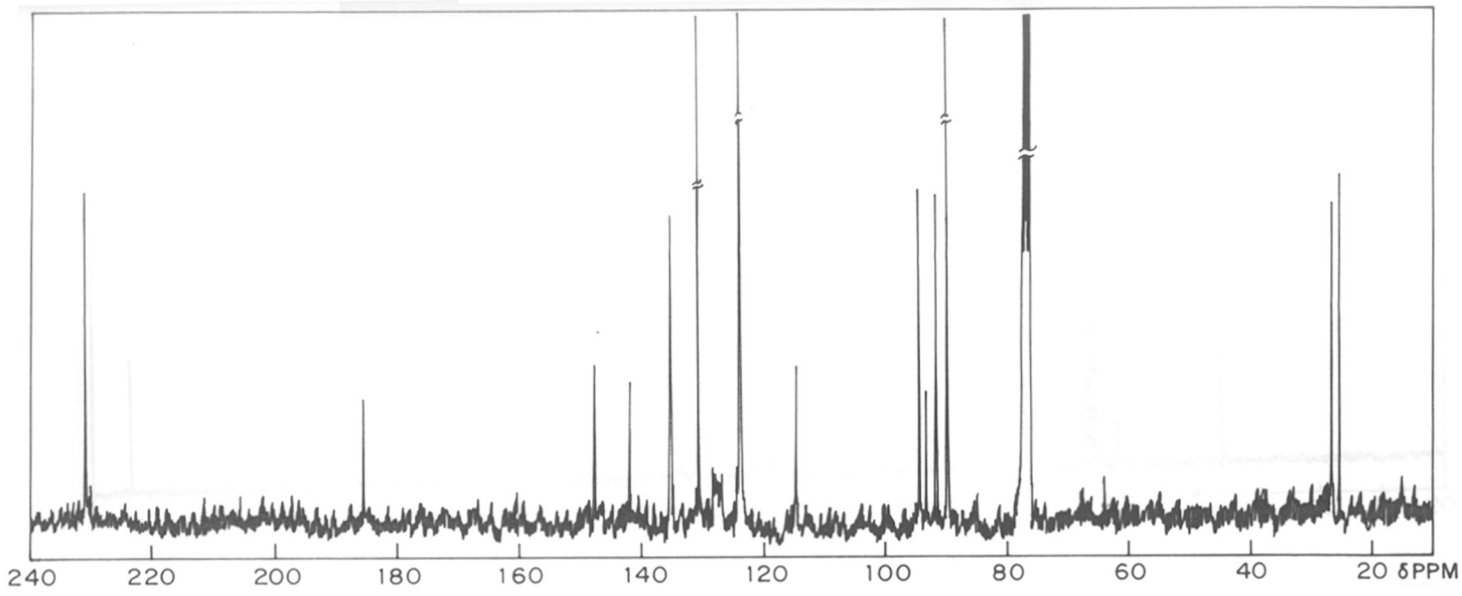
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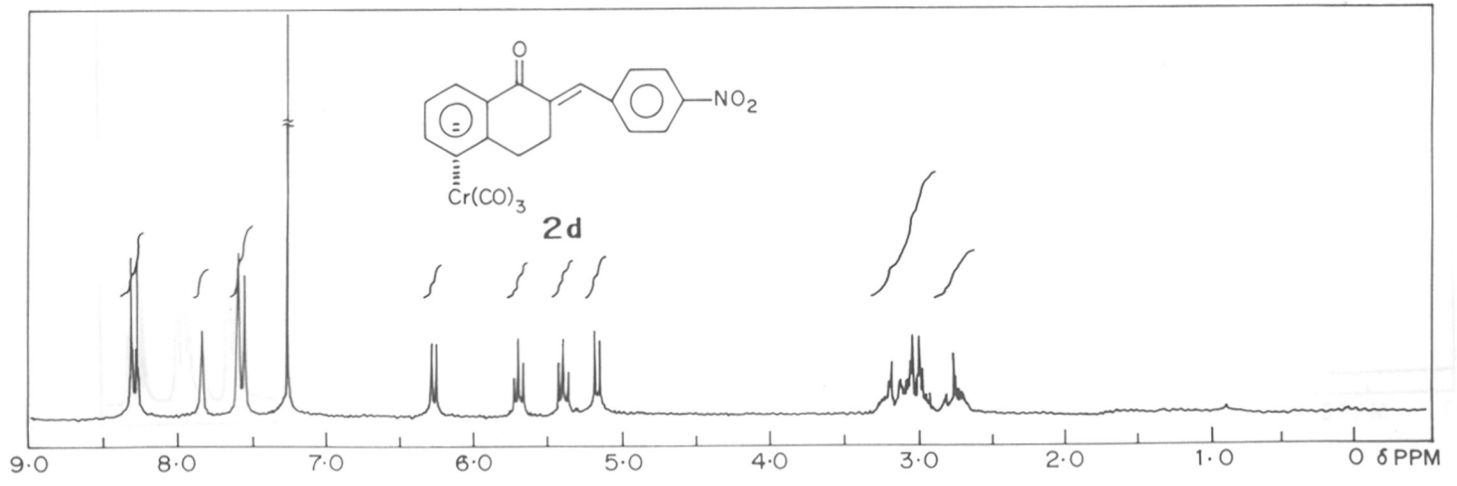
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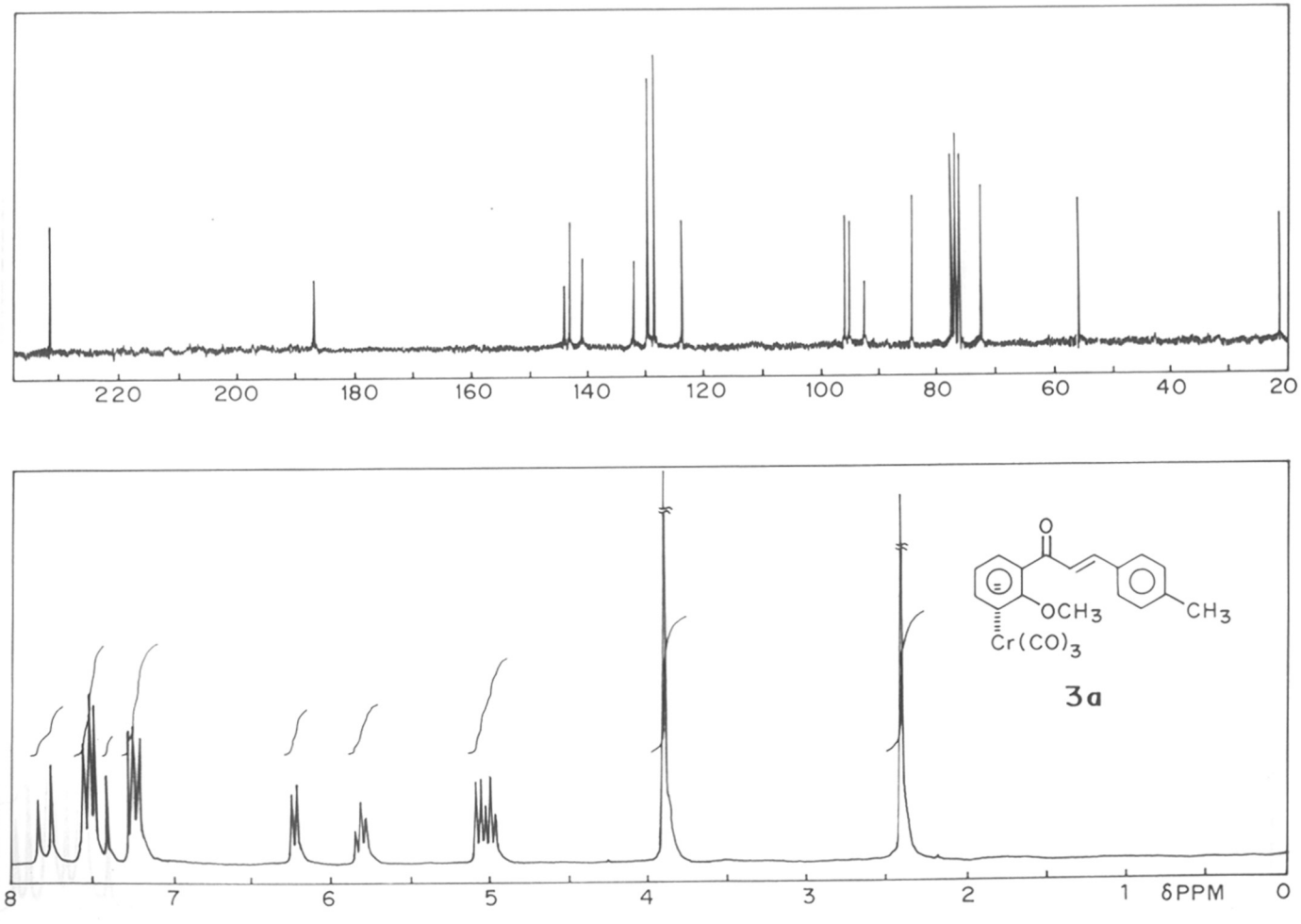
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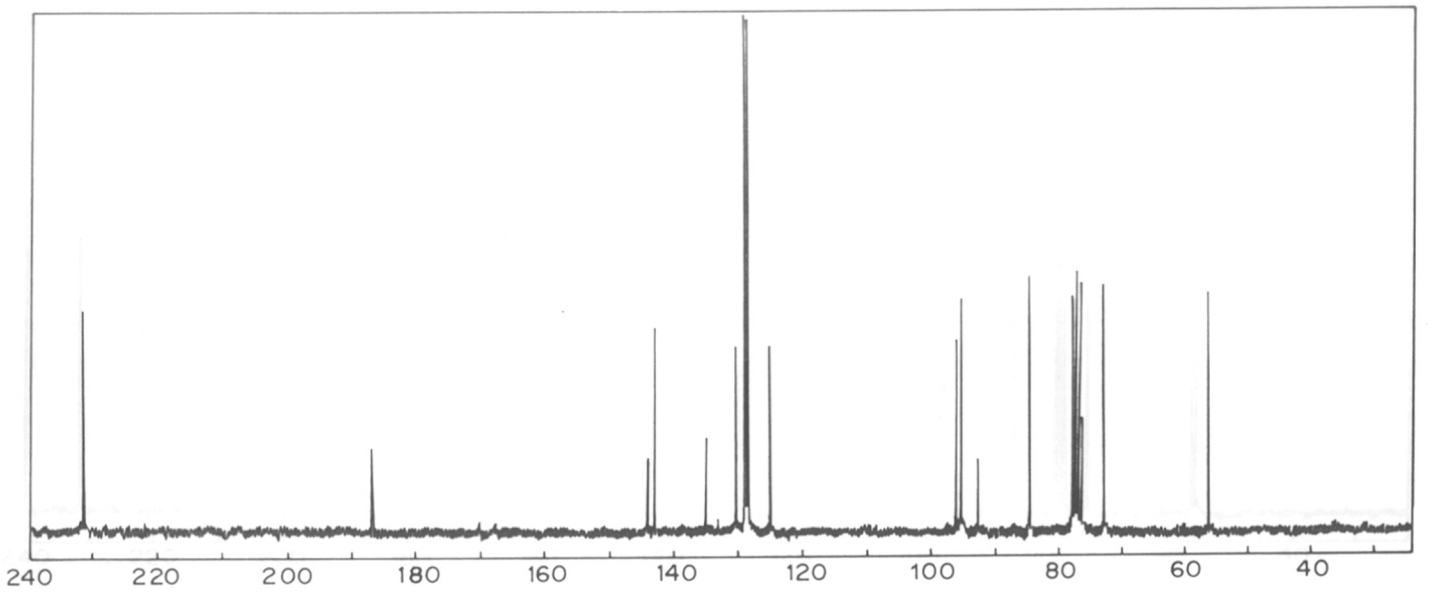
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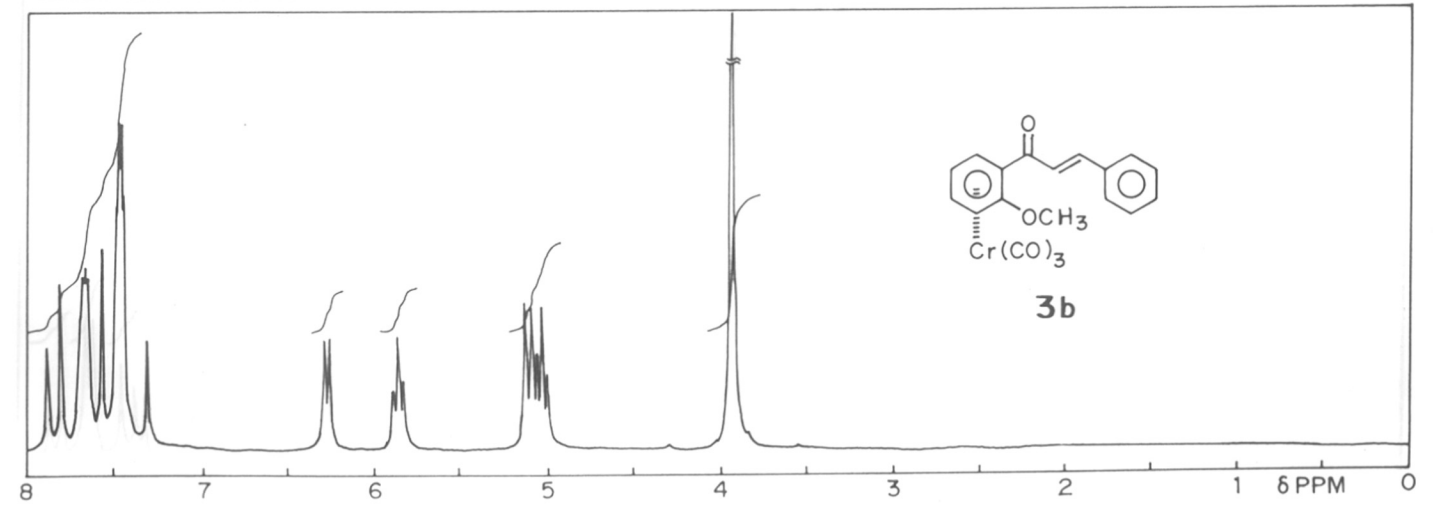
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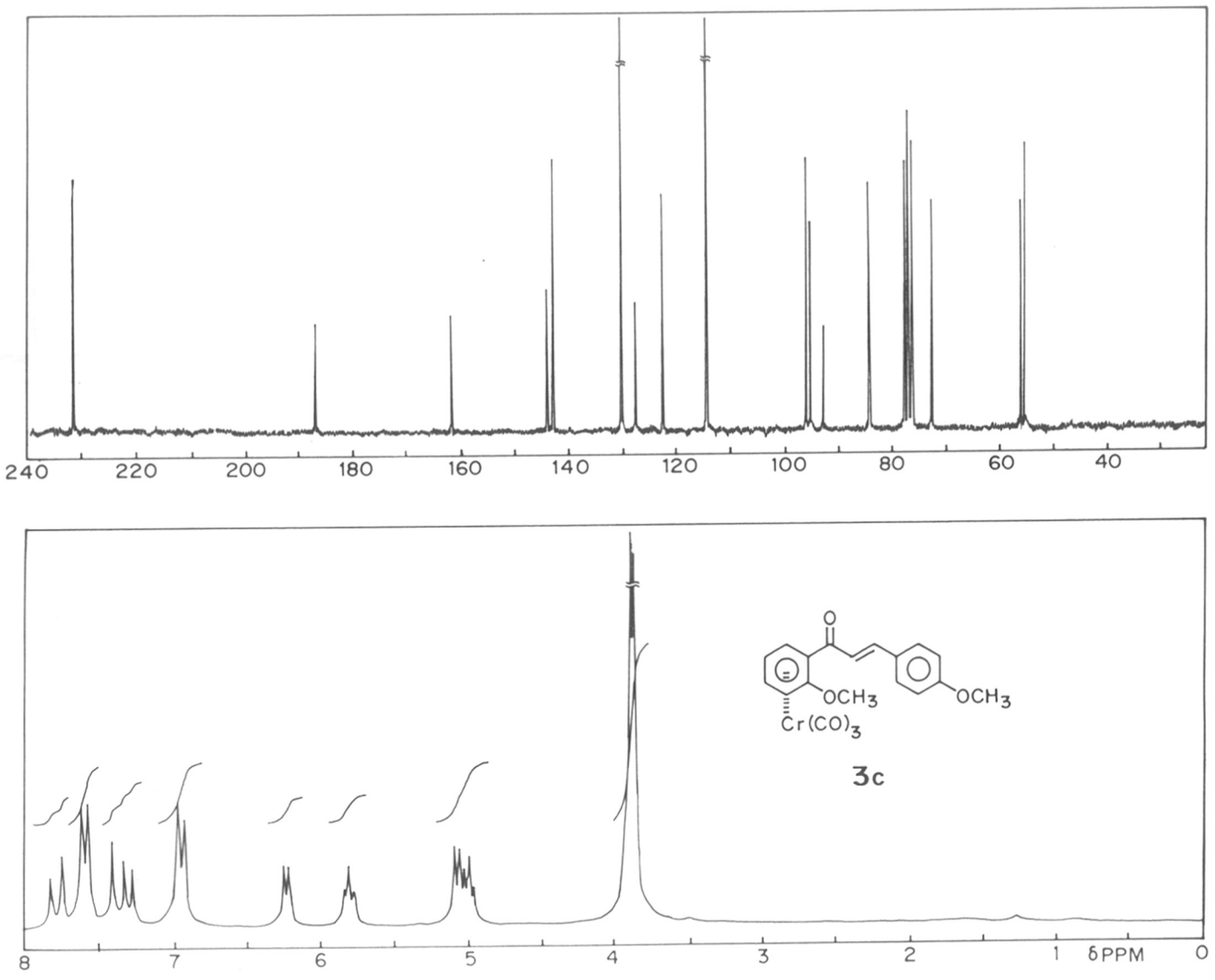
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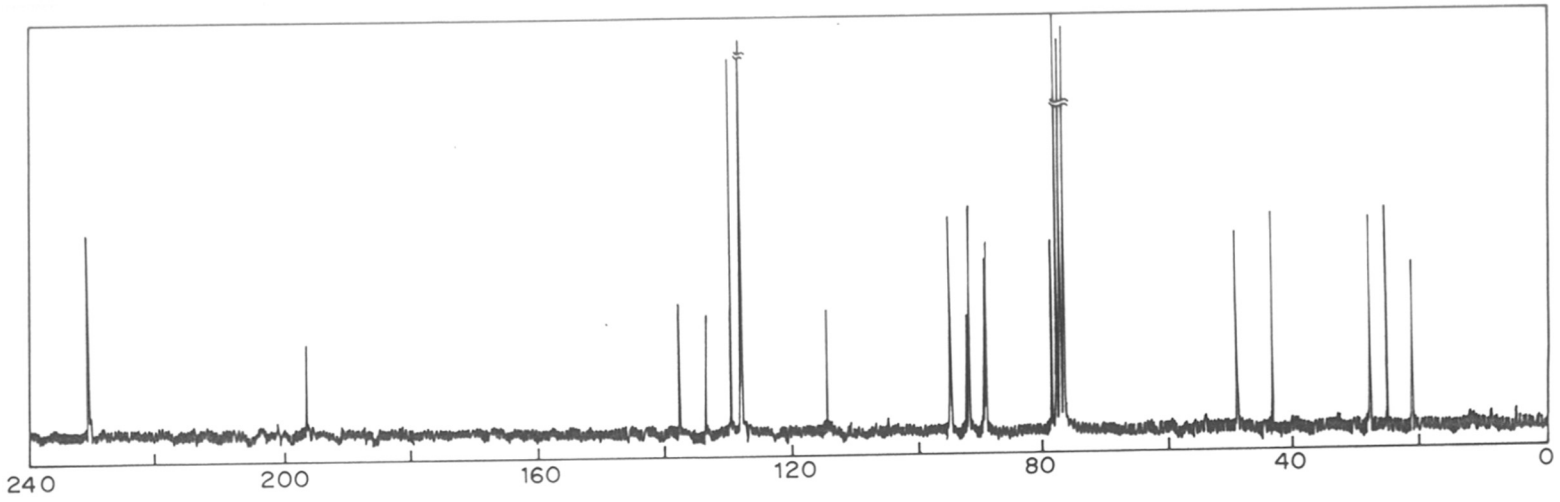
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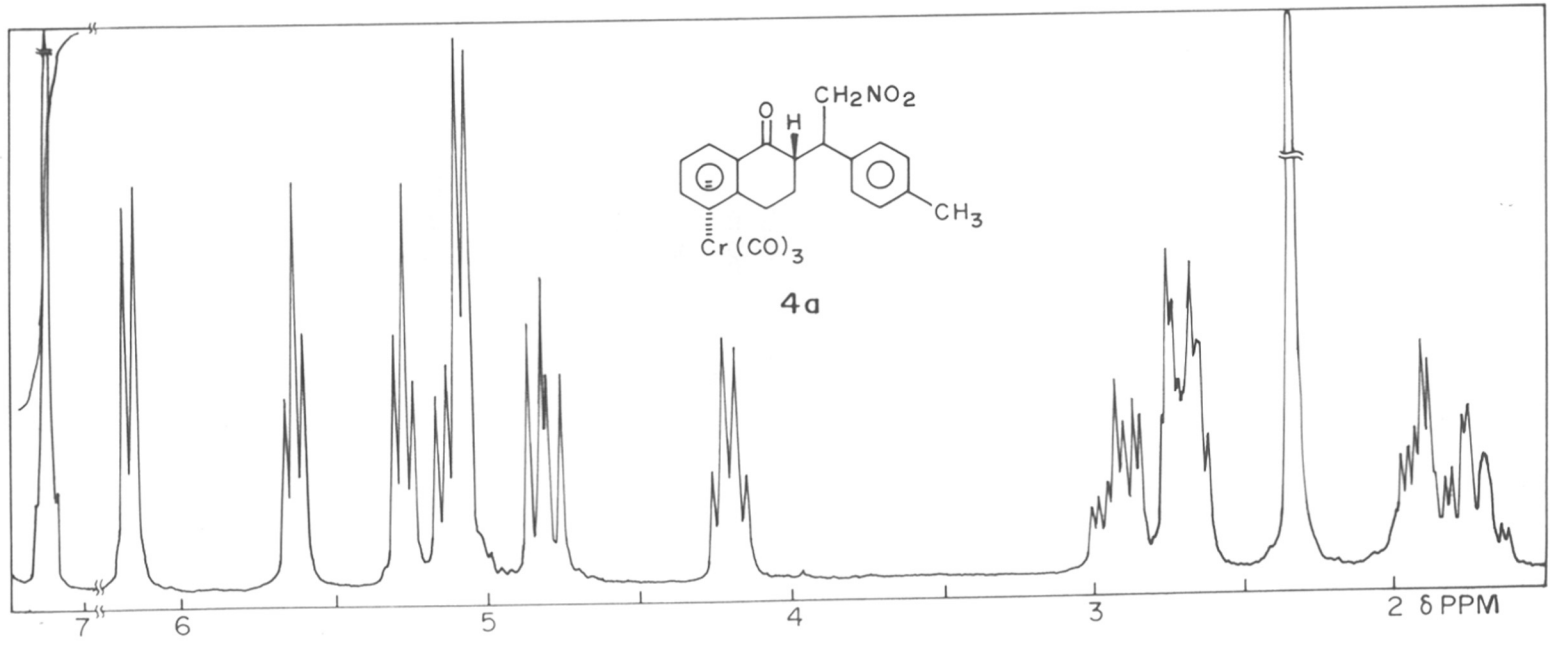
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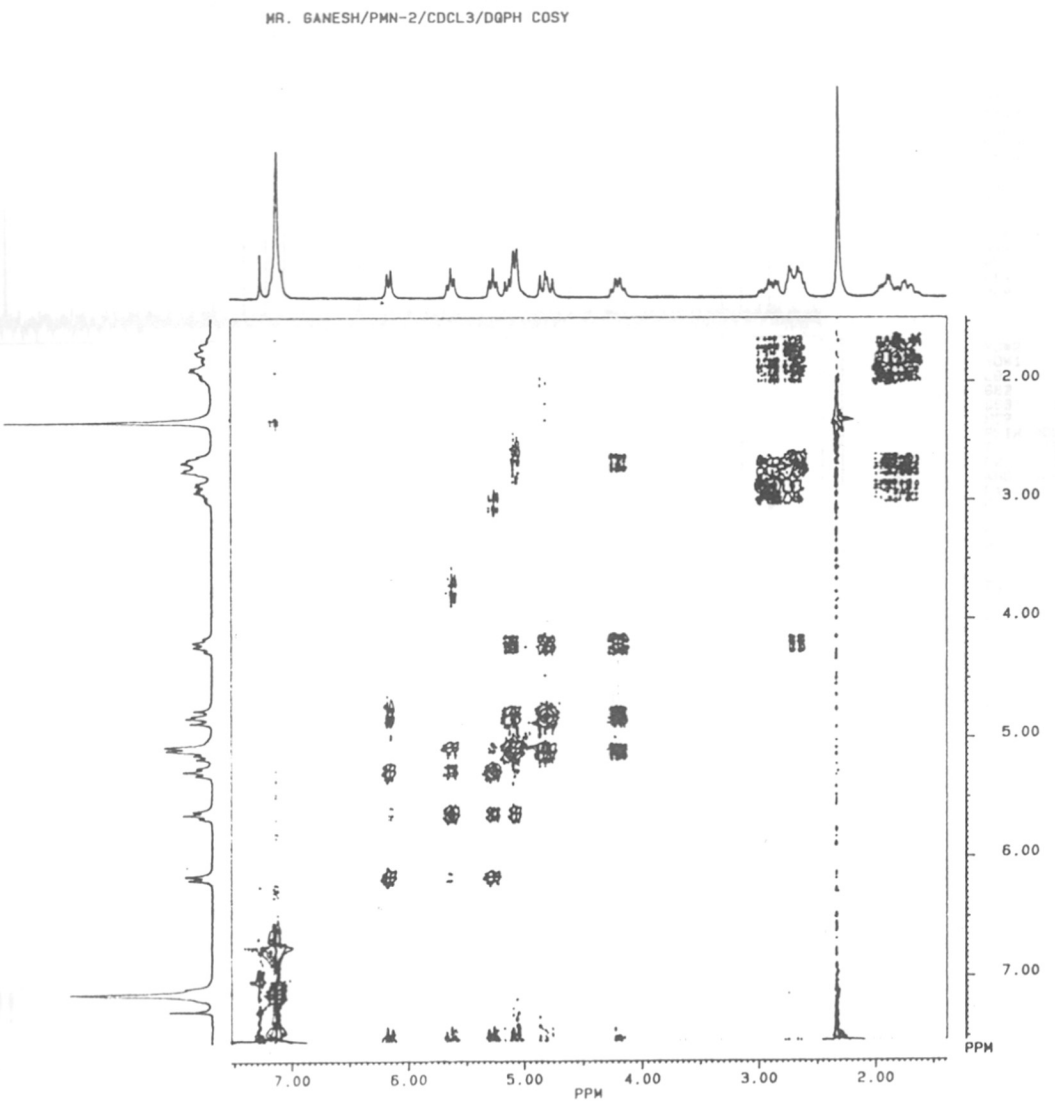
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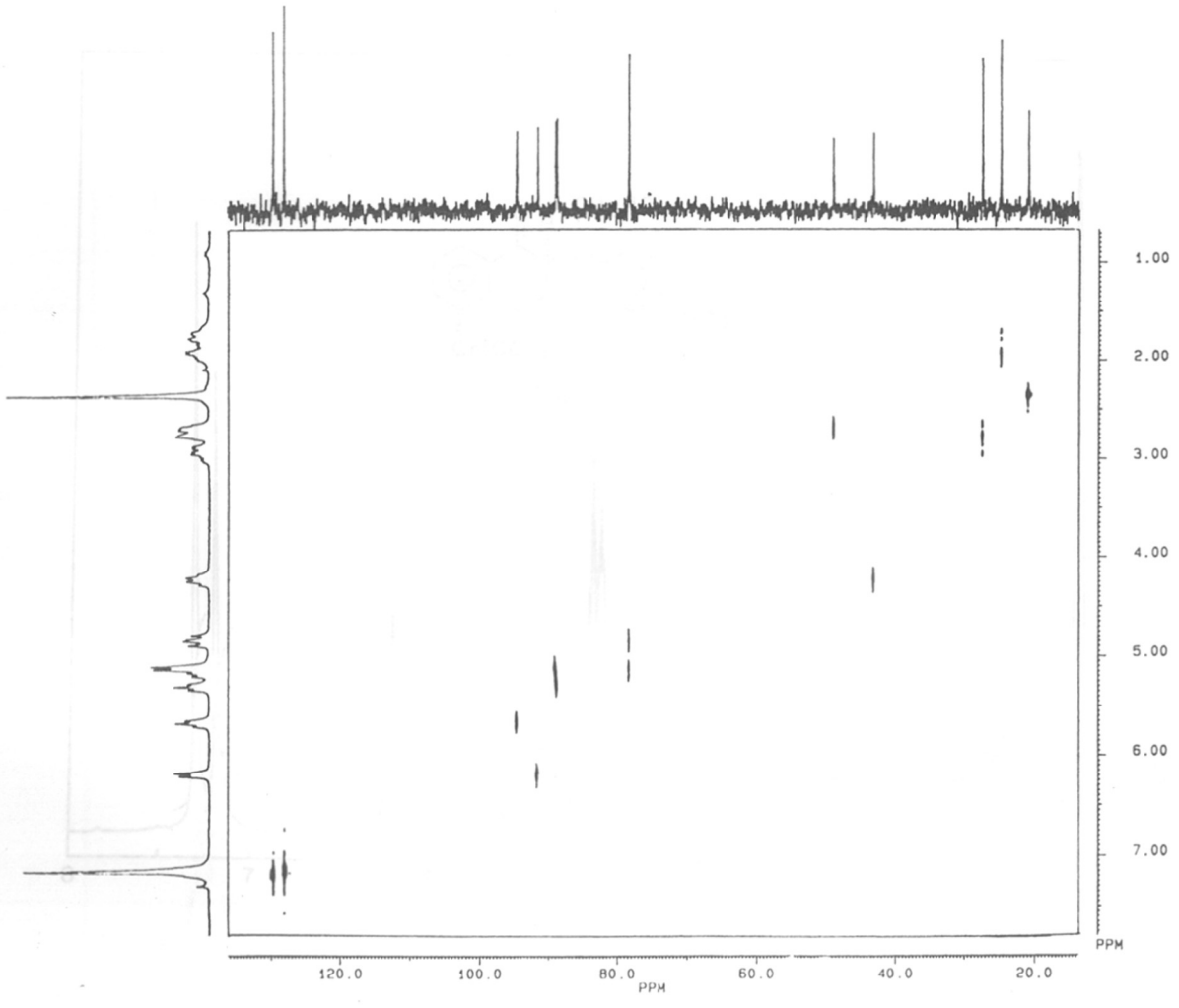

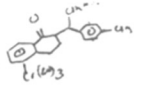

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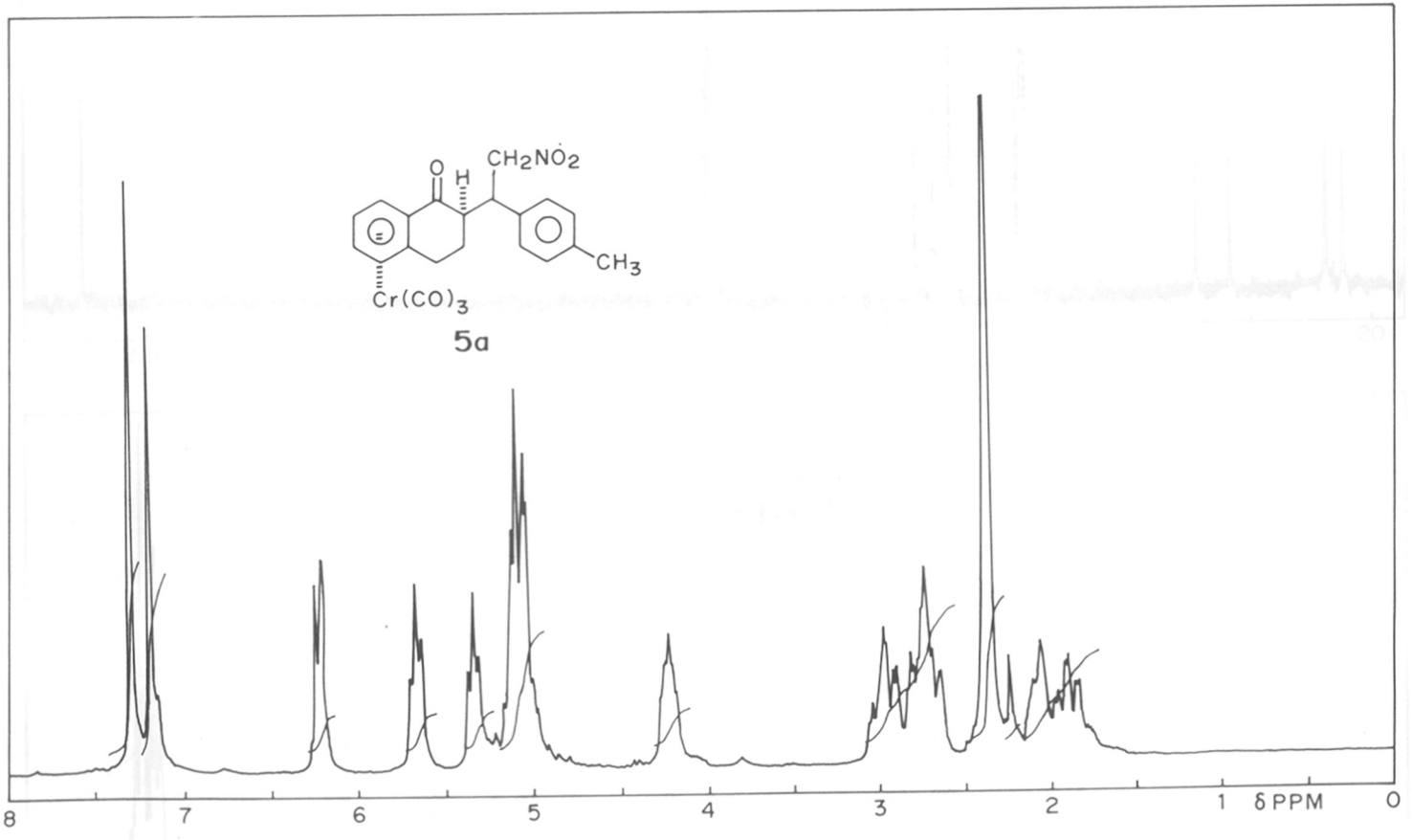
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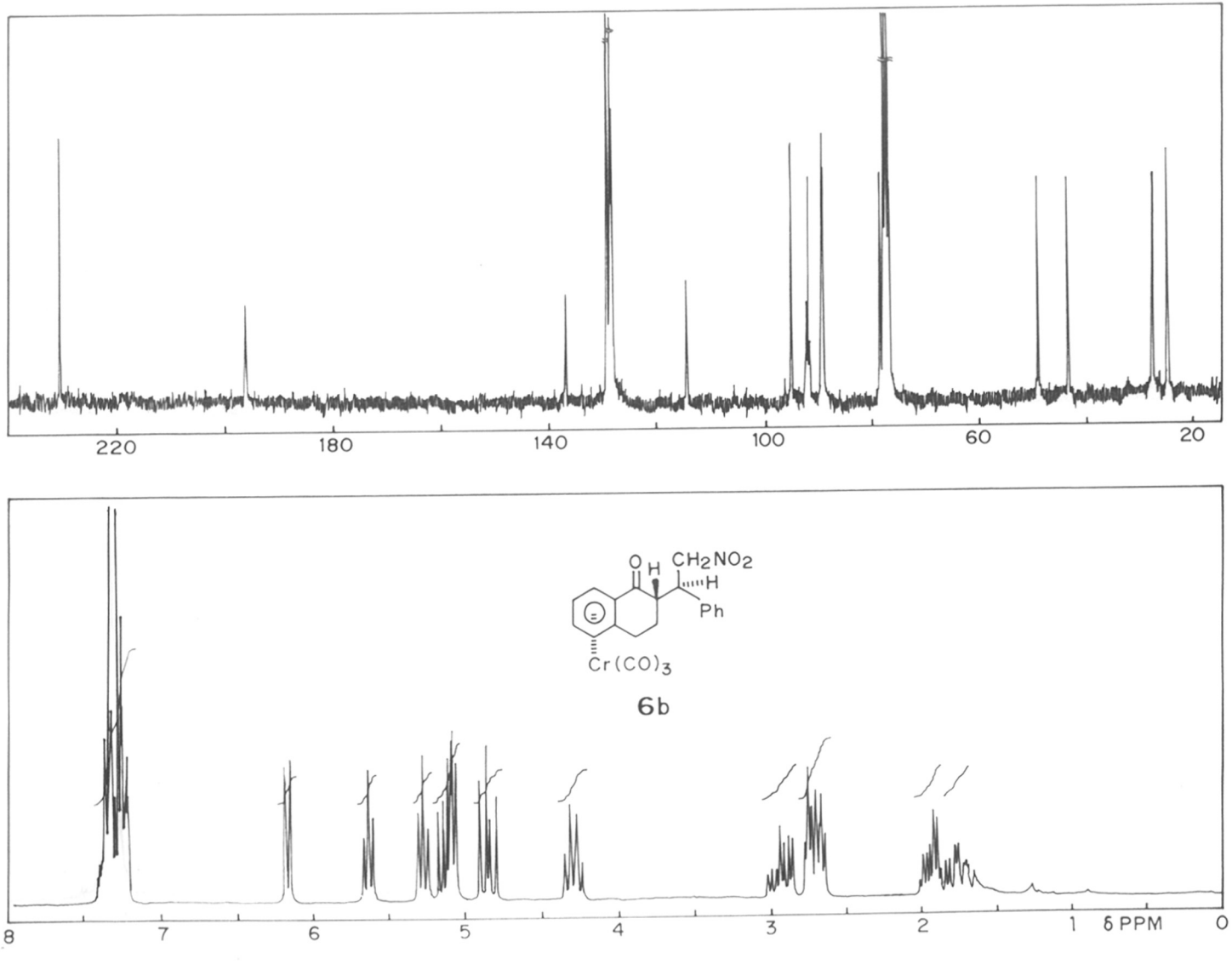
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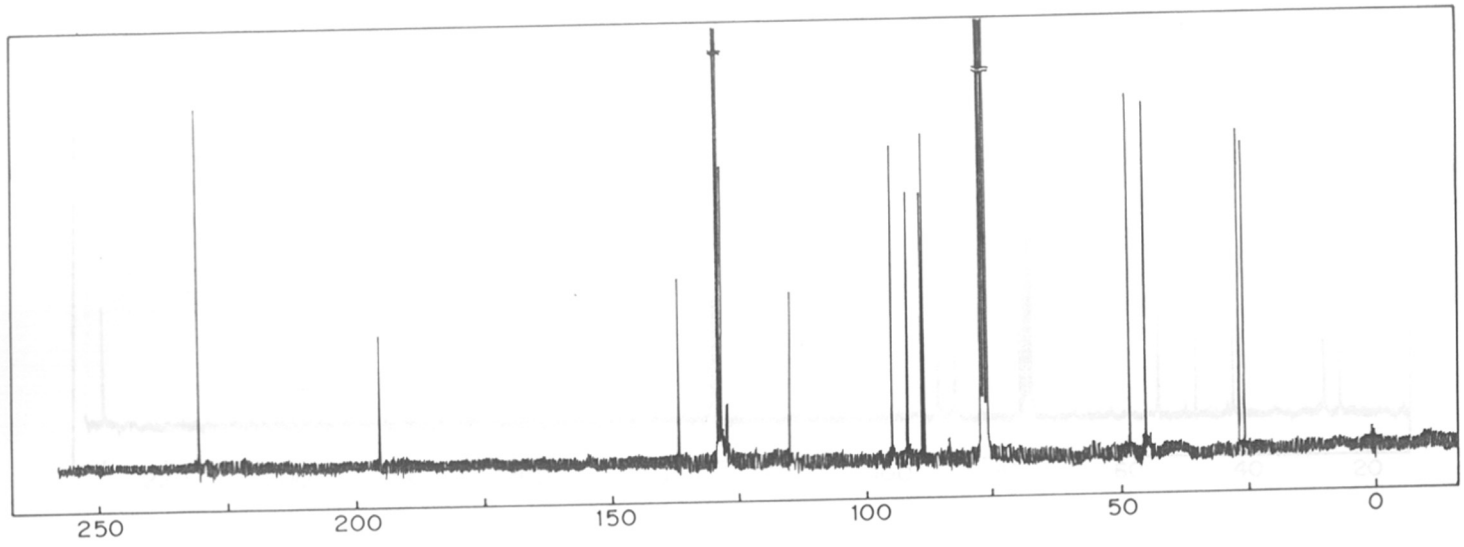

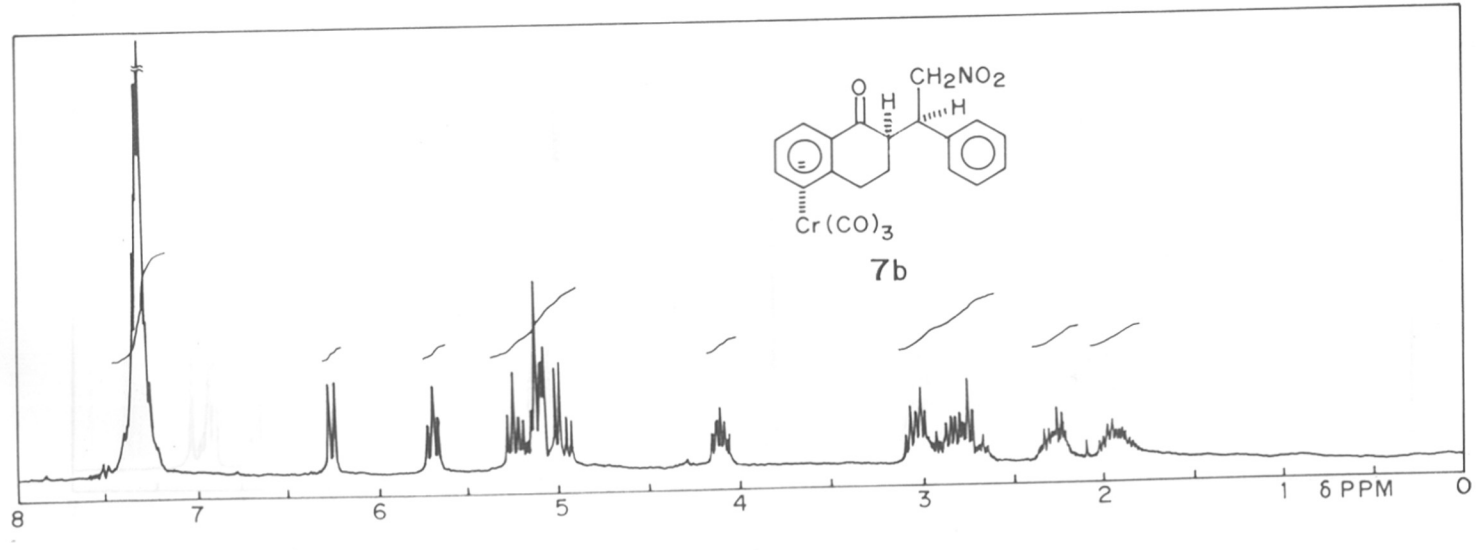

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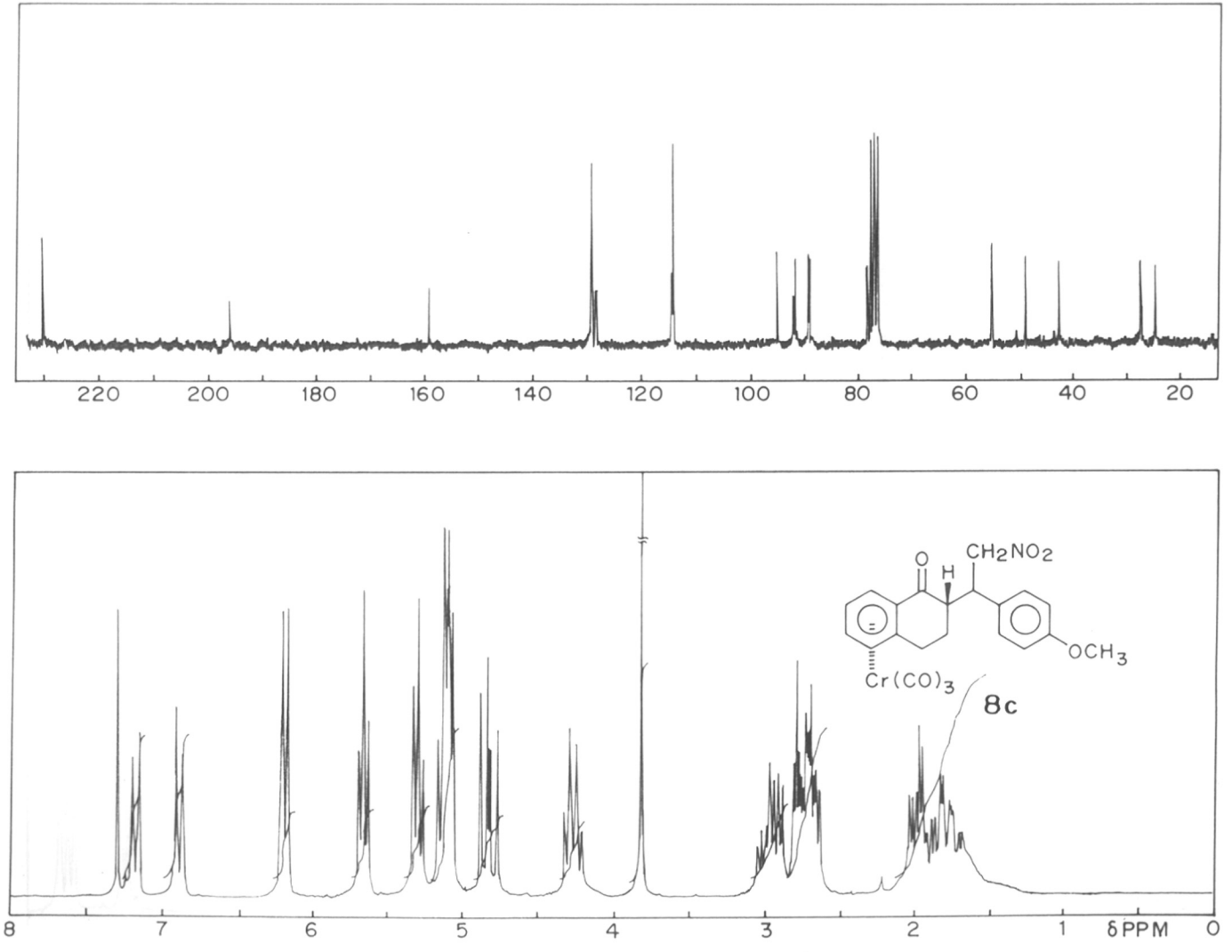
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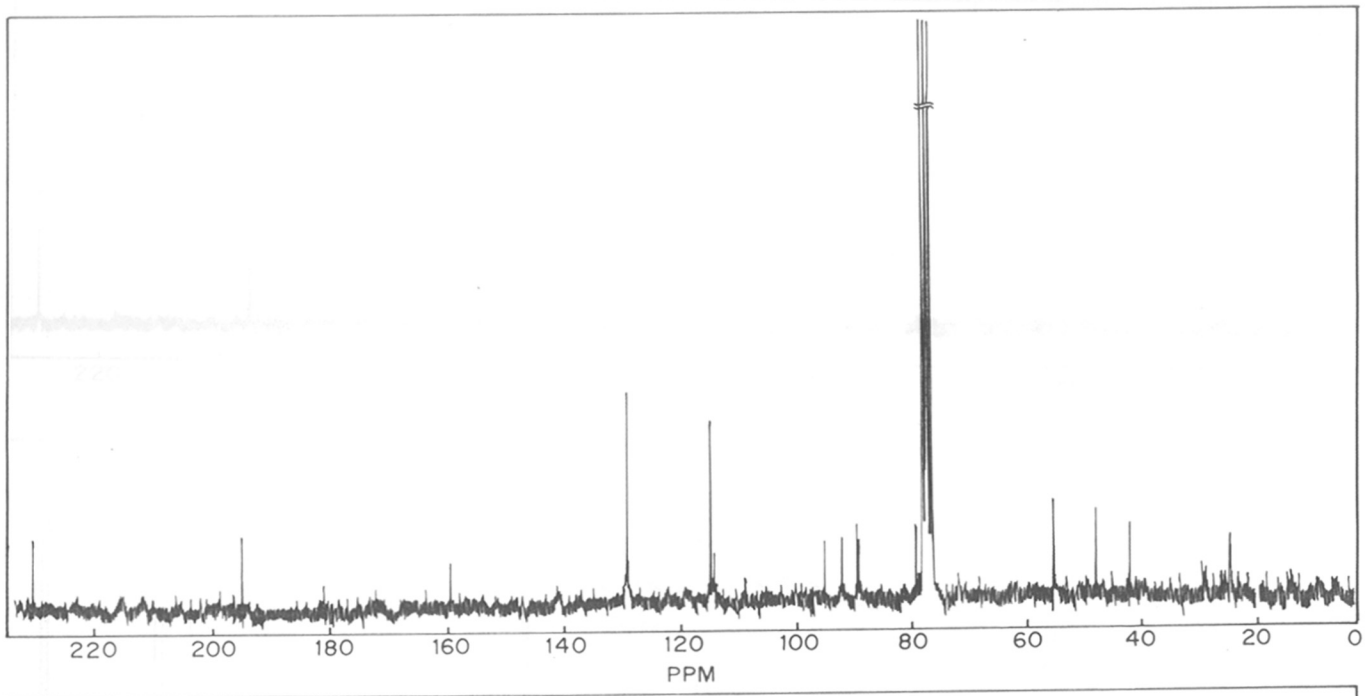
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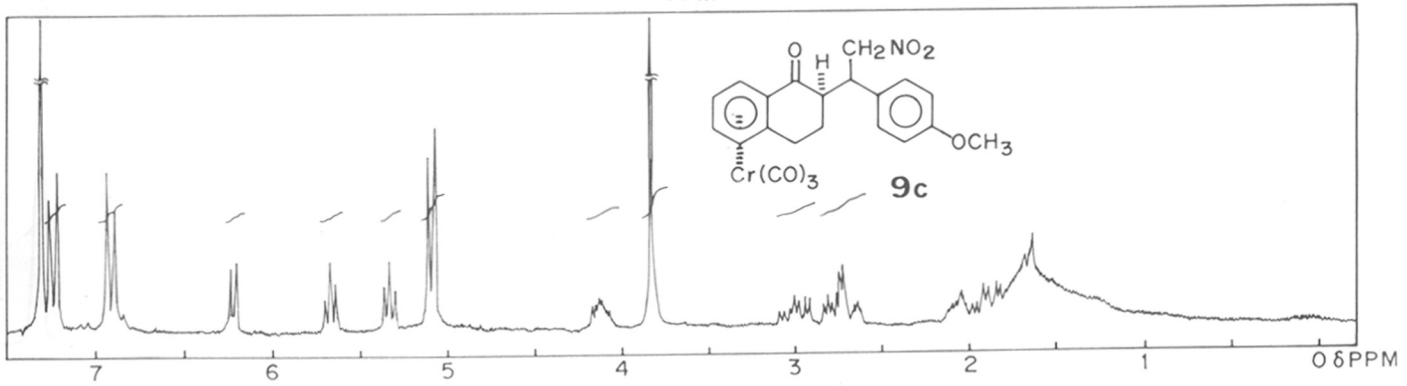
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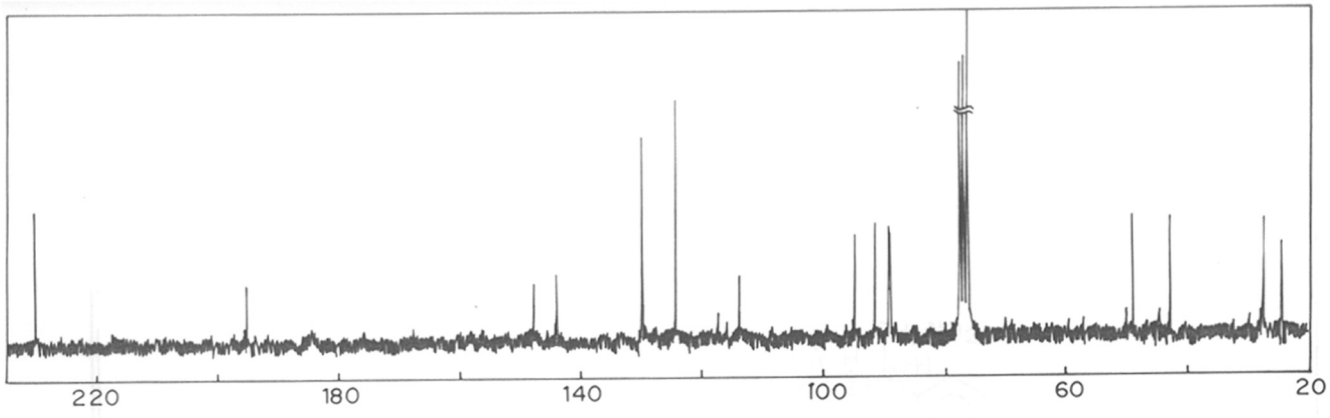
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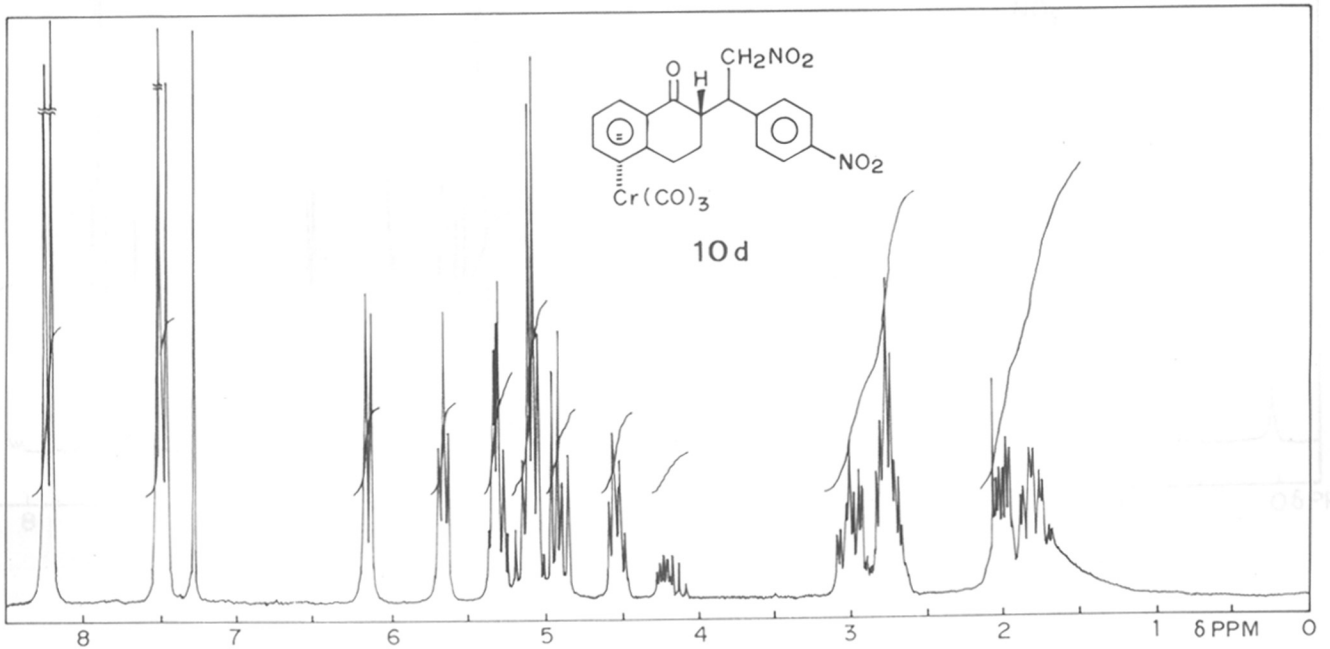
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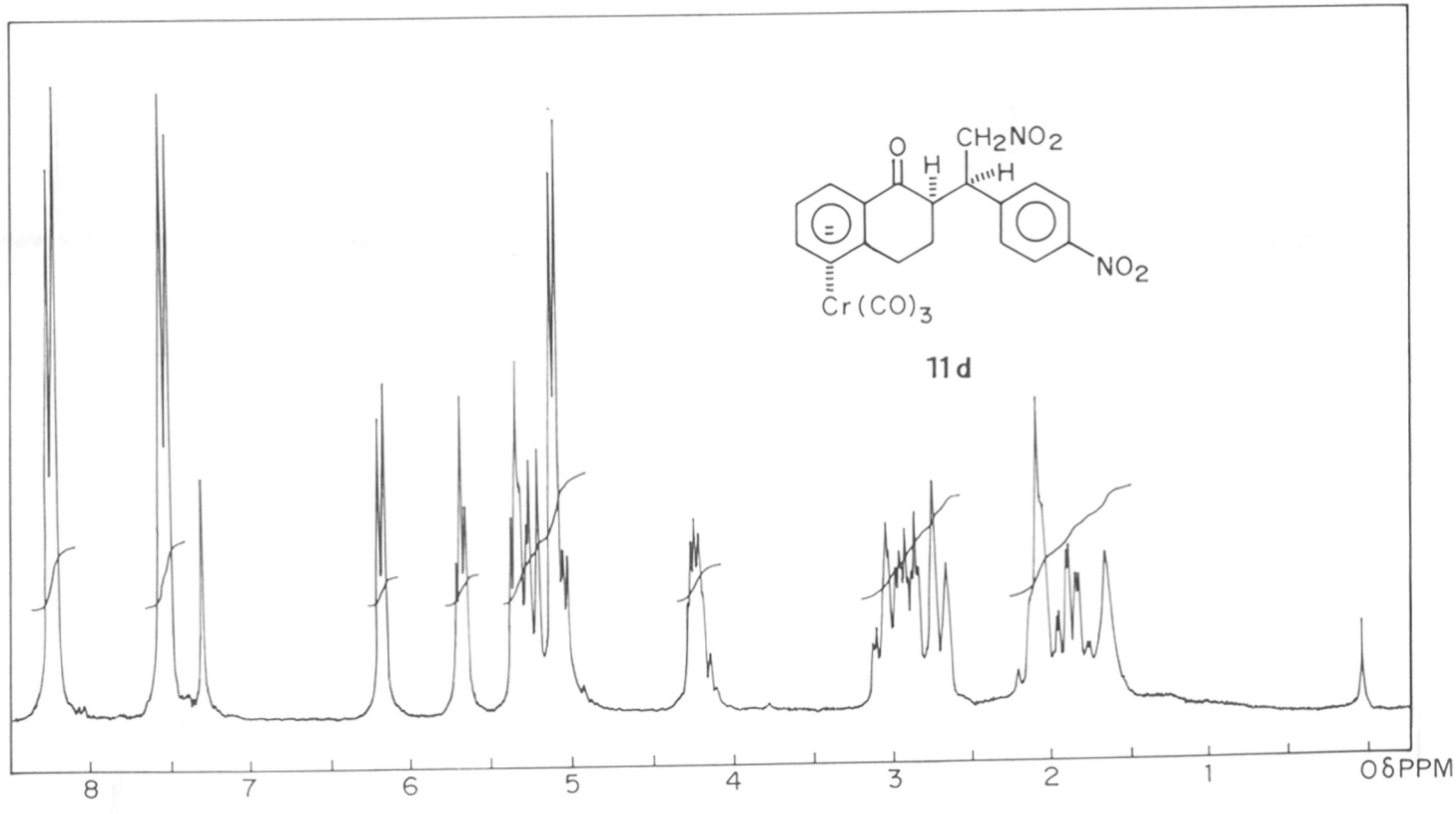
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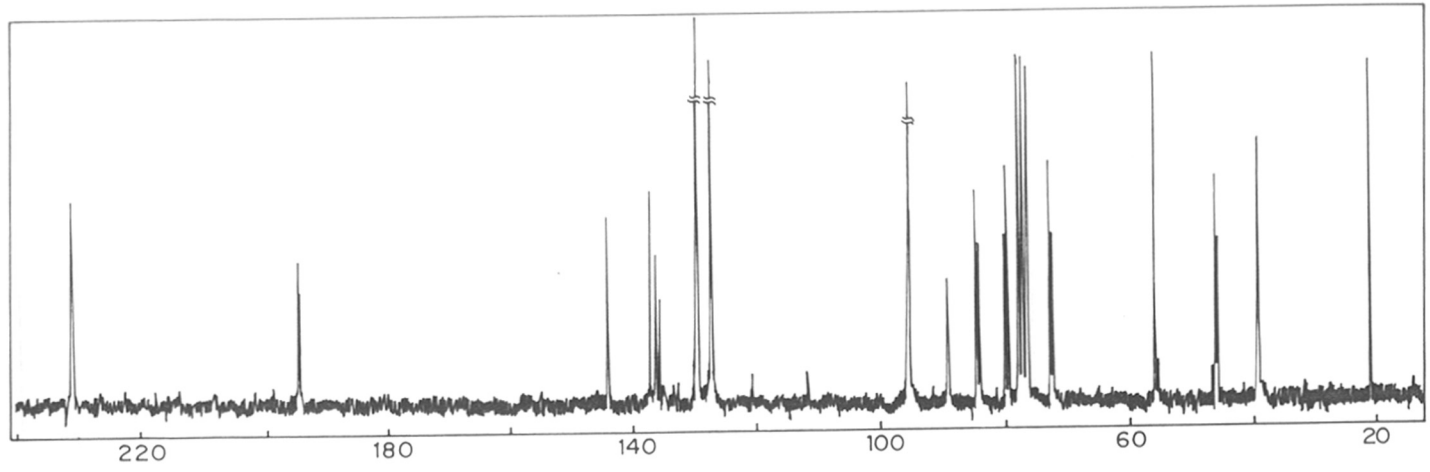

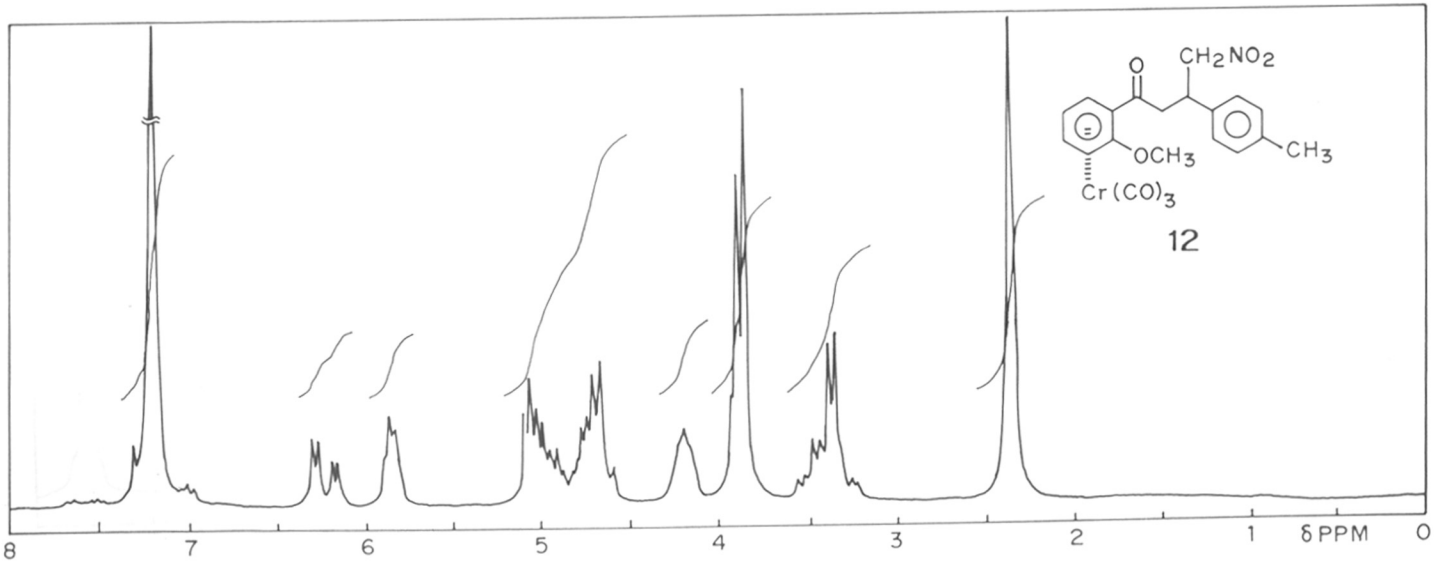

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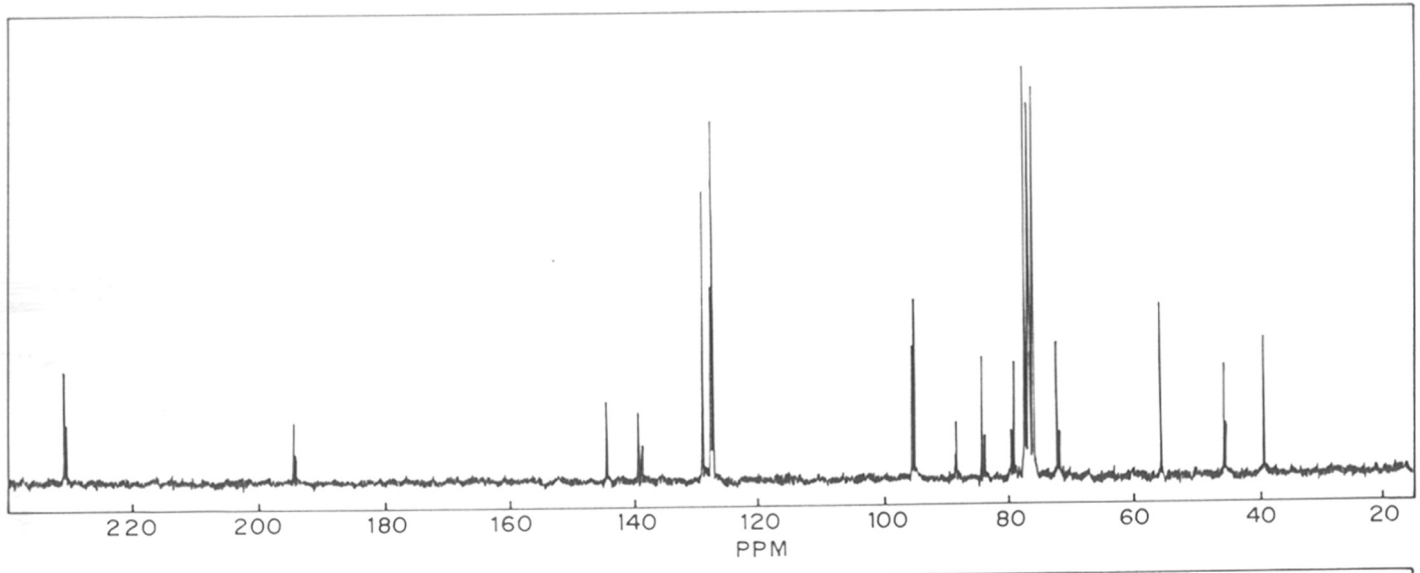
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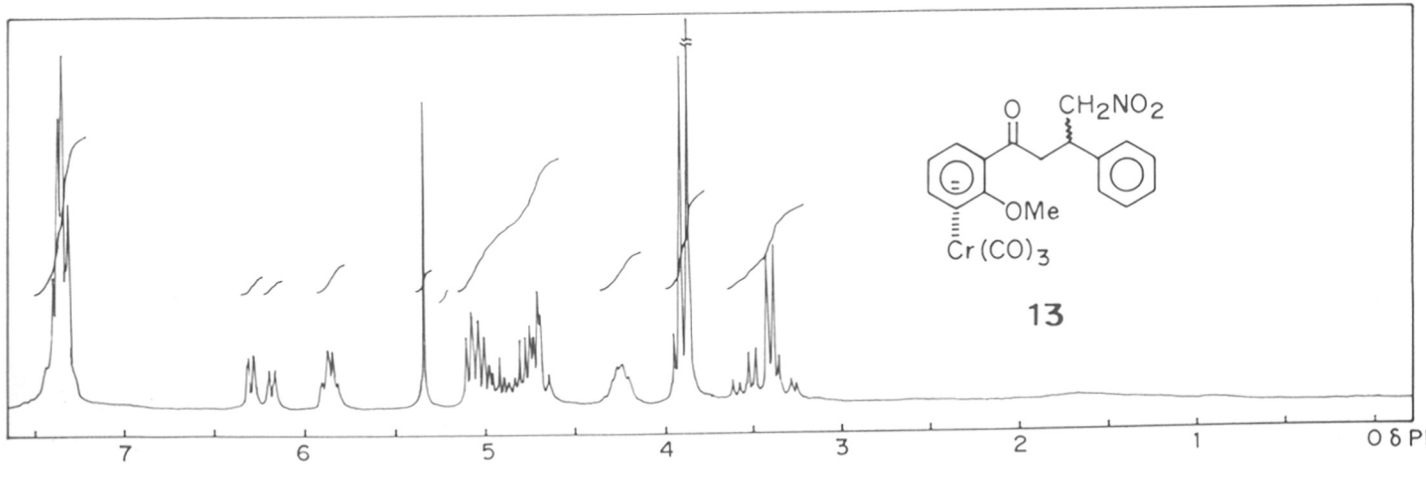
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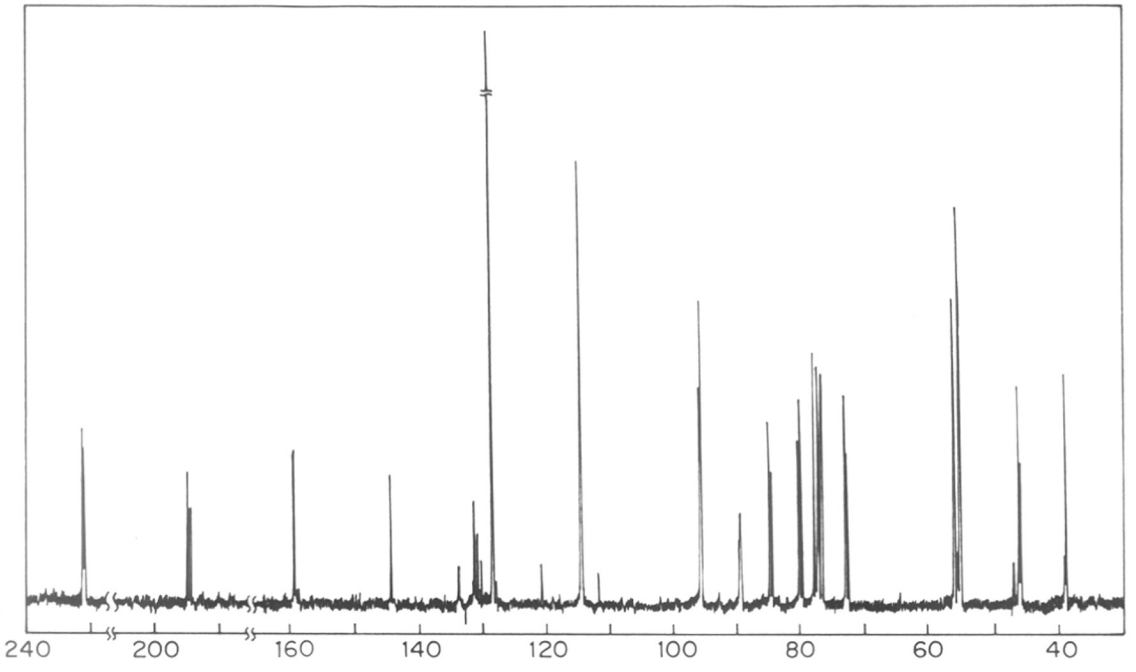
13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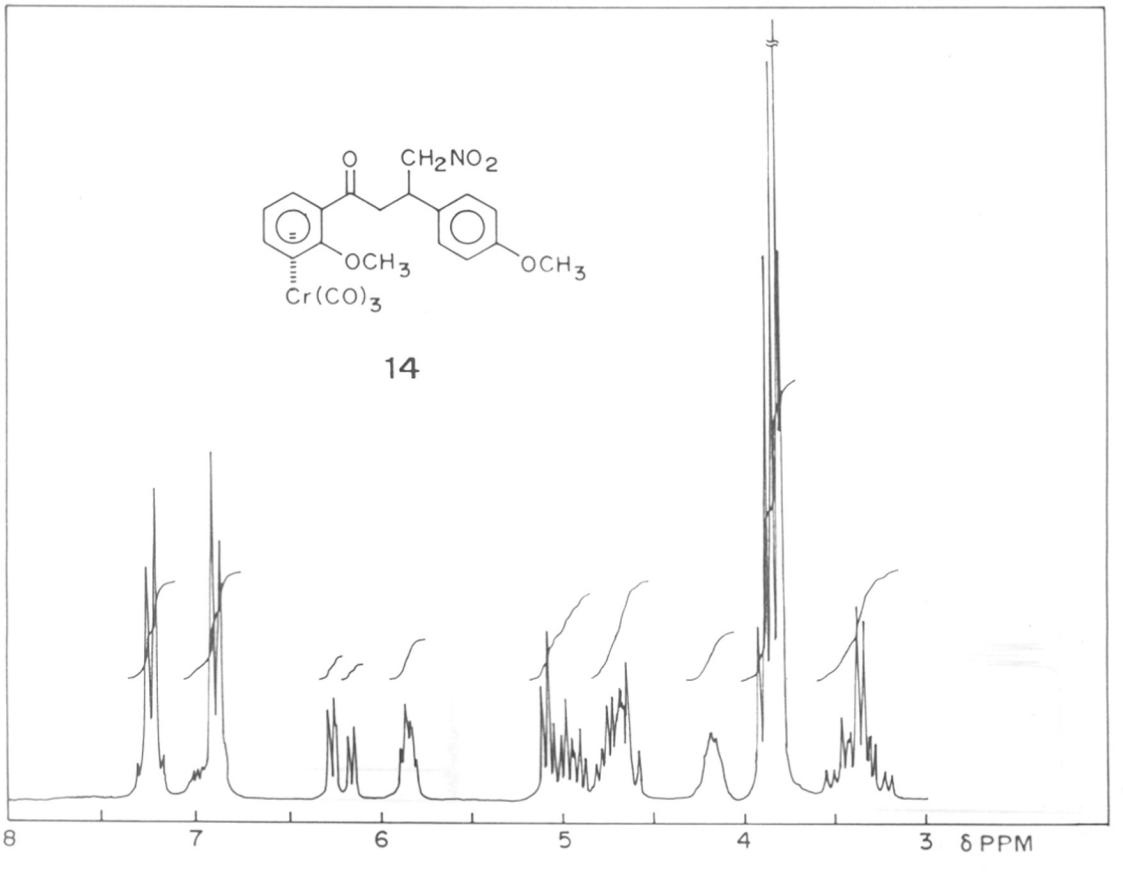
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δ PPM

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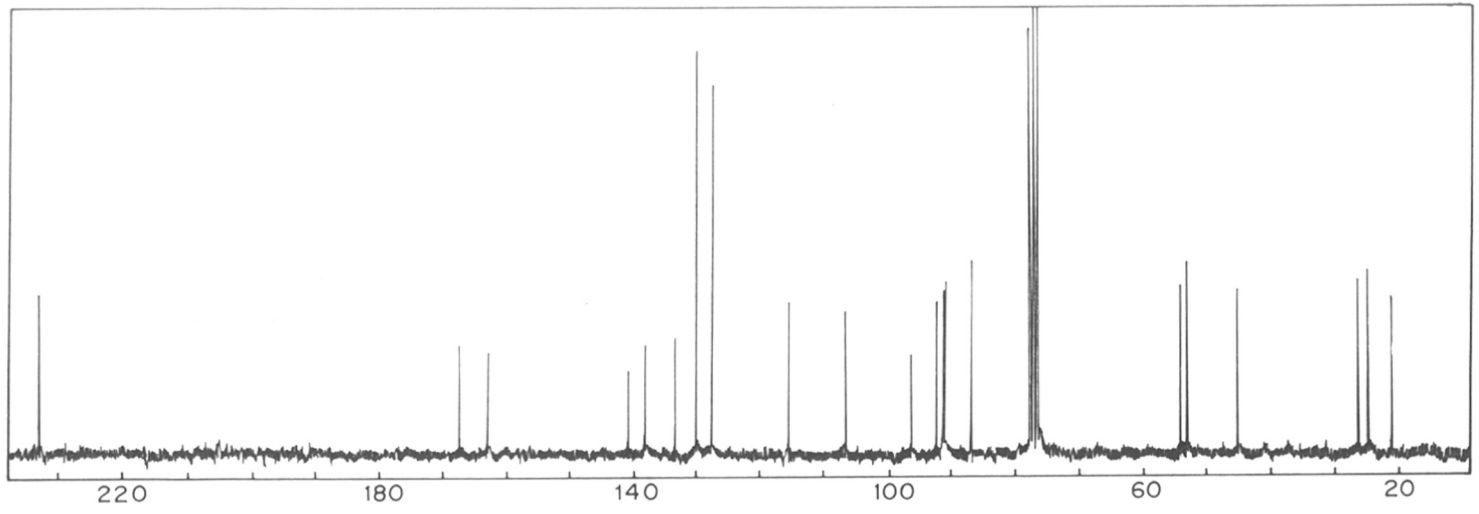

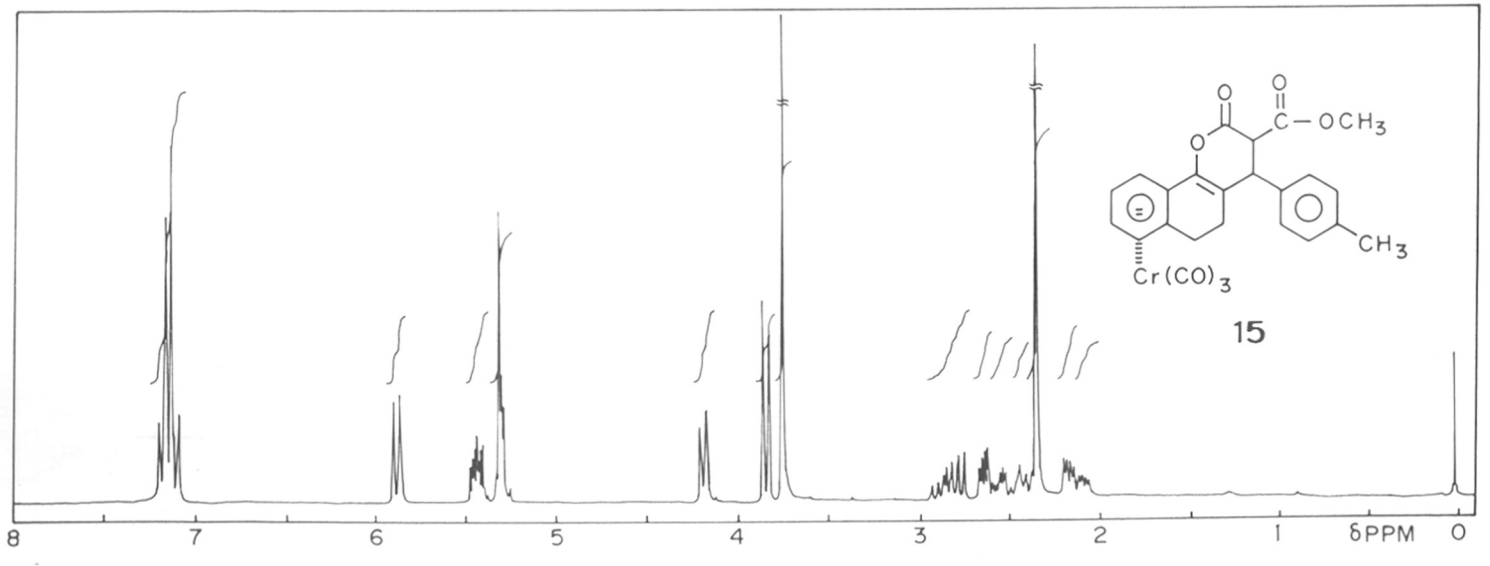

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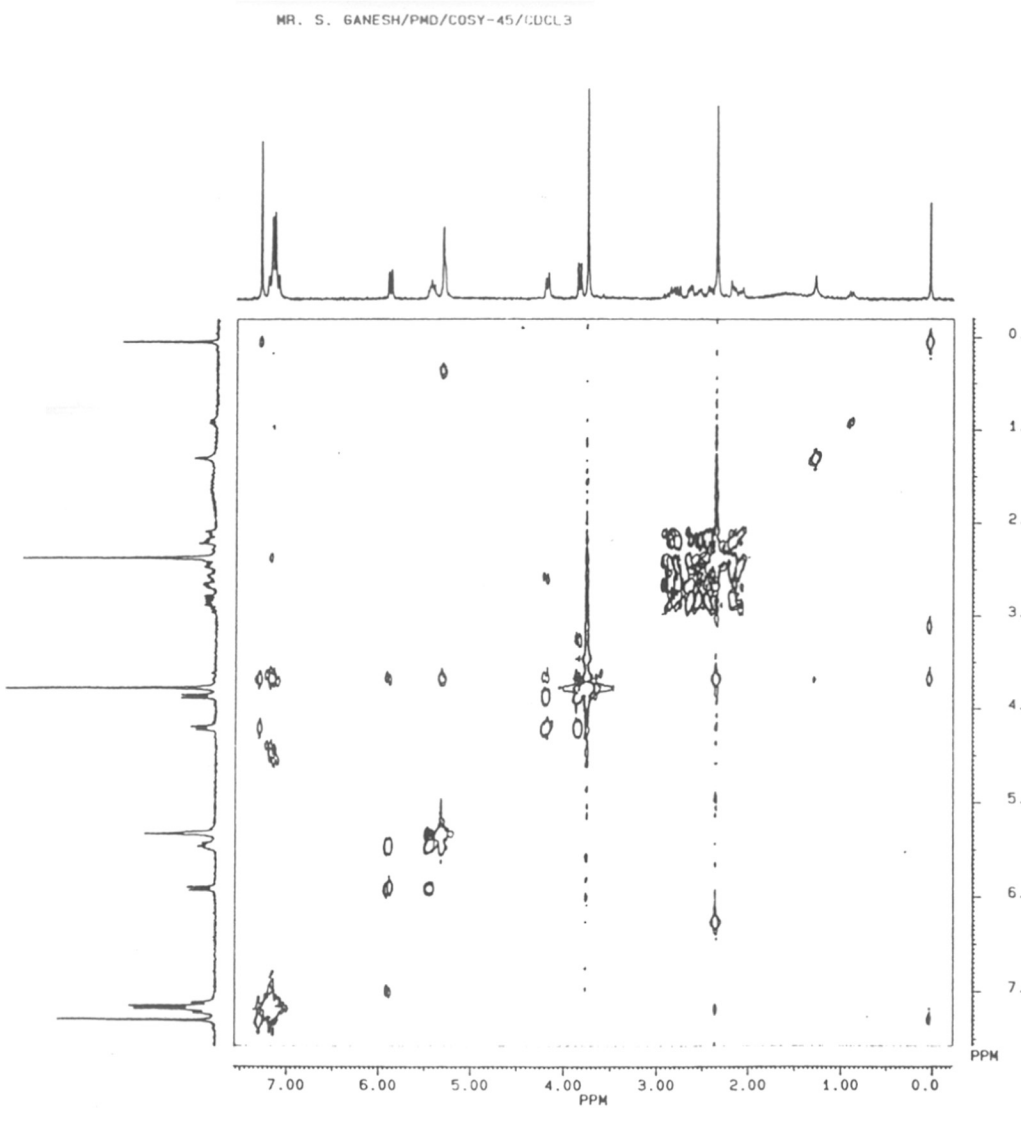

BRUKER

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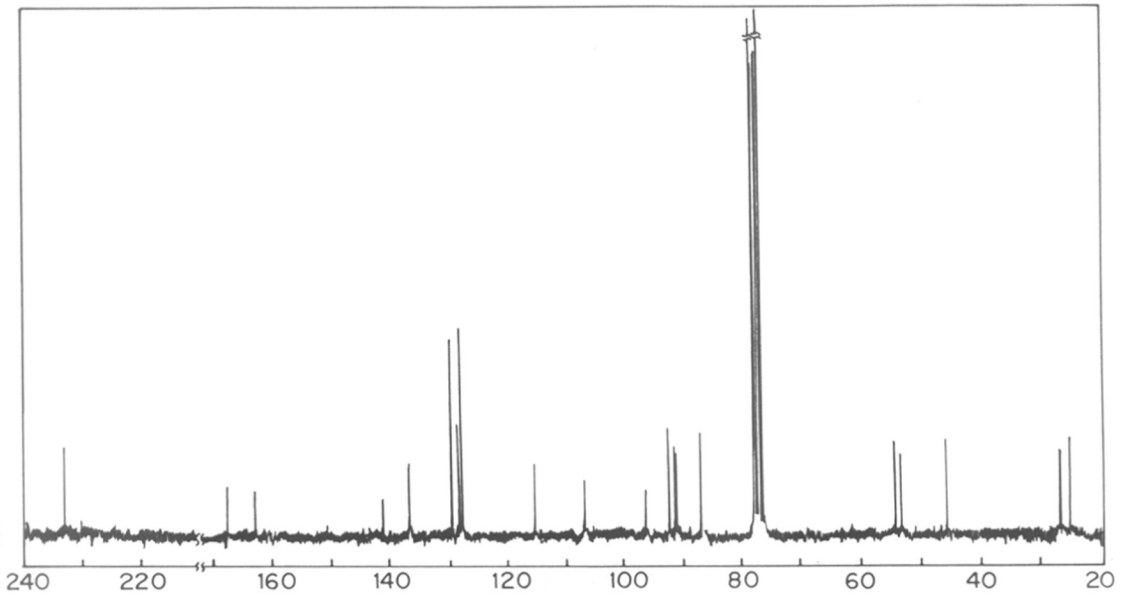
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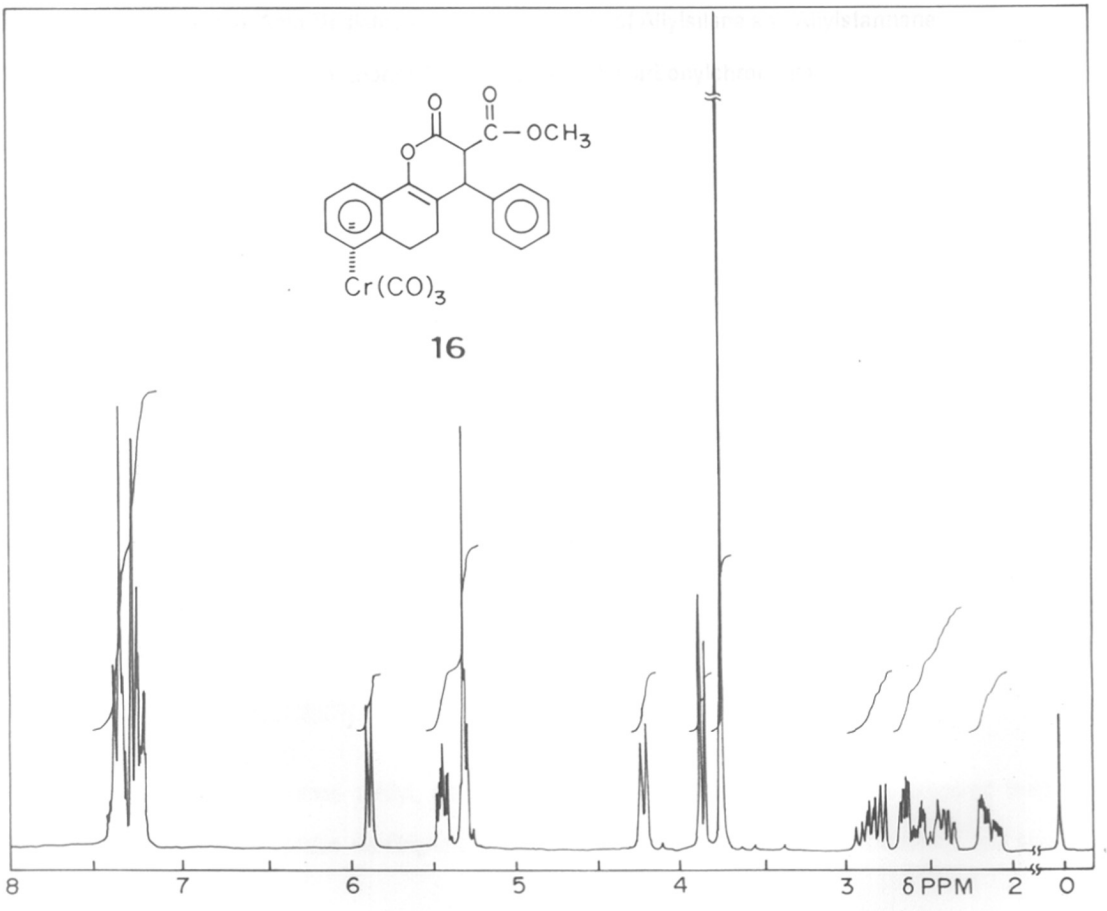
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CHAPTER - 3

Lewis Acid Mediated Conjugate Addition of Allylsilane and Allylstannane to Enones Complexed with Tricarbonylchromium

INTRODUCTION :

Allylsilanes are useful synthetic intermediates with highly nucleophilic double bonds[1]. The reaction of allylsilanes with an electrophile may be represented as shown below:

The electrophile attacks the γ carbon of the allyl system to generate a cation stabilised by a neighbouring C-Si bond. Nucleophilic desilylation results in allylation of the electrophile. Enones can be used as electrophiles[2]. In such a case, it would lead to 1,4-addition to enones. Such a reaction is usually carried out in the presence of a Lewis acid. Difunctionalisation of α-β-unsaturated carbonyl substrates has also been reported[1b,3].

The 2-arylidene-1-tetralone $Cr(CO)_3$ complex is sufficiently electrophilic as a result of complexation with metal. Thus, it was of interest to study the diastereoselectivity in Lewis acid mediated conjugate addition of allylsilane to these compounds **2a-c**. Since this reaction is usually conducted at a low temperature (-78°C), a proton quench at that temperature was expected to be stereoselective as well. During addition of nitromethane, as described in the previous chapter, the major product resulted from *exo* protonation even at room temperature.

RESULTS AND DISCUSSION :

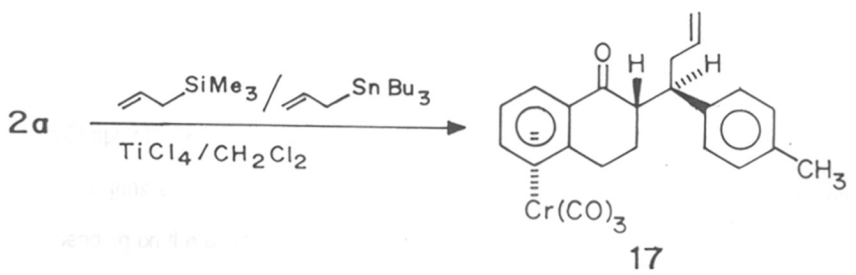
Preparation of allylsilanes : Allyl, methallyl and cinnamyl trimethyl silanes were prepared from the corresponding allyl chlorides *via* Grignard reaction[4]. The silanes were purified by distillation and spectral

comparison (NMR) indicated that they were > 95% pure. Allytributylstannane was prepared from allyl bromide and tributyltin chloride *via* Grignard reaction following a reported procedure[5] and purified by distillation. Triphenylallyltin was prepared similarly from triphenyltin chloride and allyl choride.

Reaction with Enones :

The complex **2a** was dissolved in dichloromethane and the solution was cooled to -78°C. To the stirred solution, $TiCl_4$ in dichloromethane was added dropwise. Addition of $TiCl_4$ resulted in an immediate change of colour of the reaction mixture from deep red to violet. After stirring the solution at low temperature for 30 minutes, allyltrimethylsilane in dichloromethane was added dropwise. The temperature of the reaction mixture was then raised to -50°C and maintained at that temperature for 8h. The colour of the reaction mixture gradually changed to brown during this period. The reaction was monitored by TLC. After completion of the reaction, the temperature was lowered to -78°C, and quenched by dropwise addition of methanol. White fumes of HCl was observed while quenching and it was carefully removed under vacuum. The reaction mixture was then allowed to attain room temperature. It was poured into a flask containing saturated ammonium chloride solution and dichloromethane.

After usual work up and flash column chromatography, the product **17** could be isolated (refrigeration overnight in CH_2Cl_2/pet ether) as an orange solid.



17

The IR spectrum exhibited bands at 1980, 1910 (Cr-CO) and 1670 (-CO-).In the ^1H NMR spectrum,

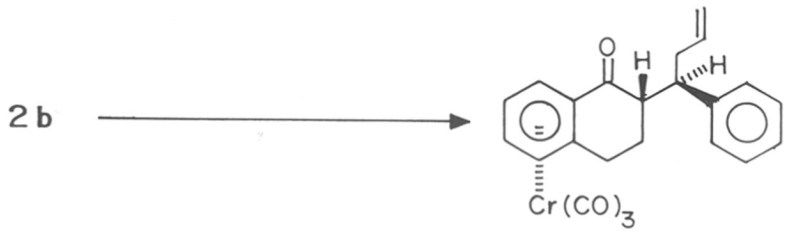
the uncomplexed aromatic ring proton signals were the most deshielded (7.2 - 7.1). The signals due to the complexed aromatic ring protons as well as the olefinic protons of the allyl group had considerable overlap. However, the peaks were well-resolved to permit assignment. The signal at 6.2 was assigned to the *peri* proton of the complexed aromatic ring. The signal due to the olefinic proton ($\underline{H}C=CH_2$) had overlapped with the aromatic proton signal between 5.8 - 5.5. A triplet at 5.3 was assigned to an aromatic proton signal. The signal due to the olefinic protons ($HC=C\underline{H}_2$) superimposed on the signal of another proton of the complexed aromatic ring in the region 5.15 - 4.85. The benzylic methine signal resonated as a multiplet at 3.85. The benzylic methylene, the proton on the carbon adjacent to ketone and the allylic methylene appeared as a multiplet between 2.9 - 2.25. The singlet corresponding to methyl group was observed at 2.35. The other methylene of the tetralone ring appeared in the region 2.15 - 1.9 as multiplet.

In the ^{13}C NMR spectrum the downfield signals at 230.6 and 196.2 were assigned to (Cr-CO) and (-CO-) respectively. The uncomplexed aromatic ring carbons resonated in the region 128 - 136.6. The olefin carbon signal were observed at 138.9 and 116.2. The complexed aromatic ring carbon resonances appeared in the region 89.0 - 114.9. The carbon adjacent to carbonyl resonated at 54.0. The benzylic carbon appeared at 42.4. The tetralone ring methylenes resonated at 32.6 and 28.2. The allylic methylene was observed at 21.7. The signal at 20.8 was assigned to the methyl group.

From the NMR spectrum it was clear that the allylated product was obtained as a single diastereomer, the low temperature proton quench being 100% stereospecific.

The NMR spectrum was also compared with the major isomer obtained in nitromethane addition (compound **4a** in Chapter 2). The configuration of the proton at the epimeric centre affects the coupling pattern of the methylene protons of tetralone ring. As a result, the spectral pattern in the upfield region differs considerably depending on the proton C$\underline{H}$-CO being α-H or β-H. The pattern was similar in the case of all major isomers (β-H) while the minor isomers (α-H) exhibited a different but consistent pattern. The relevant region of the allylated product spectrum was found to be similar to that of the major isomer (β-H) of the former series and the relative configuration of the stereocentres was thus assigned.

Under similar reaction condition the complex **2b** reacted in 6h to afford the product **18** in 76% yield.



18

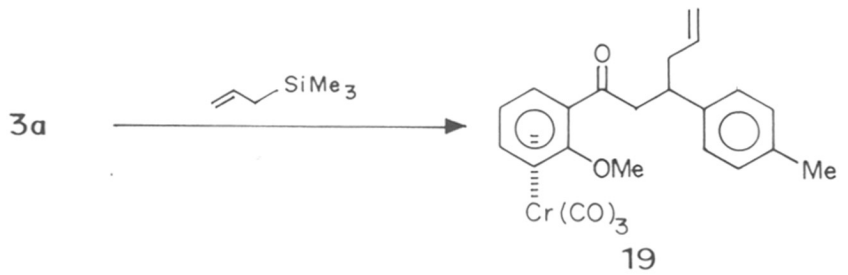
The IR spectrum exhibited bands at 1980, 1910 (Cr-CO) and 1670 (-CO-). In the ^{1}H NMR spectrum, the uncomplexed aromatic ring protons were the most deshielded. The signals due to the complexed aromatic ring as well as the olefinic protons of the allyl group had considerable overlap. The ^{13}C NMR of the complex exhibited signals in the usual region and could be assigned without ambiguity.

The complex **2b** was found to react in 6h with allylstannane under similar condition in 73% yield. The ^{1}H NMR of the product was identical with that of compound **18**.

For reasons unknown the complex **2c** did not undergo allylation under similar condition even after 10h. The enone **2c** was recovered in 87% yield.

Encouraged with the level of stereoselectivity attained in this reaction, we proceeded to explore stereoselectivity with corresponding acyclic substrates **3a-c**. In this case, the low temperature quench was not crucial, since there no longer existed a chiral centre at C-2. But, the low temperature of the reaction was expected to arrest conformational equilibrium illustrated below and improve stereoselectivity at C-3.

The complex **3a-c** was subjected to similar reaction condition as the cyclic substrates. The complex **3a** reacted completely in 3h. After usual work up and flash chromatography, a thick, orange liquid was obtained, which solidified on refrigeration overnight (91%).



19

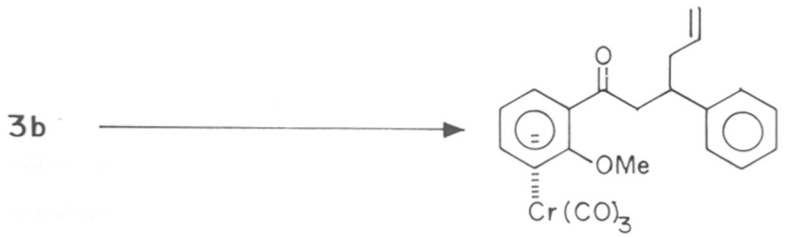
The IR spectrum of the complex **19** had characteristic bands at 1980, 1900 (Cr-CO) and 1670 (-CO-).From the appearance of the ^1H spectral pattern one could clearly discern that the product consisted of a diastereoisomeric mixture, since some signals appeared as two sets (this trend was observed for the allylated products **20** and **21** also). The downfield signals were of the uncomplexed aromatic ring protons, which appeared as a singlet at 7.15. The *peri* proton of the complexed ring appeared as two doublets corresponding to the two diastereomers. The integration of these two signals provided the ratio of diastereomers as 71:29. The olefinic protons resonate in the same region as the complexed aromatic ring protons and appeared as multiplets between 5.9 - 5.6 and 5.15 - 4.80. The diastereomers exhibited two singlets for methoxy groups at

3.88 and 3.83. The methyl group also appeared as two singlets at 2.35 and 2.33. The benzylic proton and the protons on carbon adjacent to ketone appeared between 3.55 - 3.1. The allylic methylene protons appeared as a broad multiplet in the region 2.55 - 2.40.

Pair of signals due to the two diastereomers were also observed for some of the carbons in the ^{13}C NMR spectrum. It showed a pair of downfield signals at 231.1 and 230.9 (Cr-CO). The carbonyl carbons appeared at 196.2 and 196.1. The *ipso* carbon attached to methyl group appeared at 140.8. The olefinic carbons appeared at 143.8 and 141.4. The rest of the uncomplexed aromatic carbons resonated at 136.4, 136.1, 135.5, 128.9, 127.2. The complexed aromatic carbons appeared at 116.2, 116.3, 95.6, 95.1, 90.8, 84.0, 83.7, 72.4 and 72.1. The methoxy carbon signal appeared at 55.7. The signals due to carbon adjacent to the carbonyl appeared at 48.9 and 48.6. The allylic methylene appeared at 40.3. The benzylic carbon resonated at 40.0. The methyl signal appeared at 20.7.

The diastereomers could not be separated by chromatography, but they provided satisfactory elemental analysis.

The complex **3b** was allowed to react under similar conditions for 4h to afford the product **20** (92%).

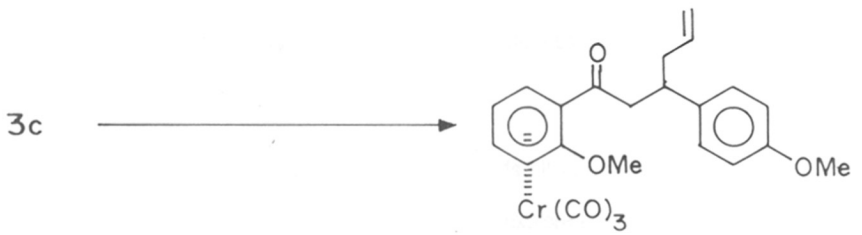


20

The IR spectrum and ^{1}H NMR spectral features were consistent with the structure of the complex. The diastereomeric ratio of 70:30 was determined from the integration of resolved signals due to identical

protons in the two diastereomers. The ^{13}C NMR spectrum was unexceptional in the characteristic regions.

The complex **3c** under similar reaction conditions for 4h, provided the product **21** (82%).



21

The IR spectrum exhibited bands at 1980, 1900 (Cr-CO) and 1670 (-CO-). The ^{1}H NMR spectrum indicated resonances at the expected region. The ^{13}C NMR spectrum showed signals in the characteristic region.

The diastereomeric ratio for the products (71:29) were calculated based on the integration for the *peri* proton of the complexed aromatic ring. Thus the low temperature was indeed conducive to stereodifferentiation in the reaction with acyclic substrates. Concurrent to our investigations, a report had appeared where low temperature cuprate addition on structurally related complexes proceeded with considerable diastereoselectivity (50:50 to 8:92)[6].

Attempted reactions with complex 2b : Using similar reaction conditions, trimethyl methallylsilane was added to the reaction mixture. The reaction was maintained at -50°C for 5h and during this time the colour of the reaction mixture gradually changed from violet to dark green. The reaction was monitored by TLC and since no reaction was observed even after 5h, the reaction was warmed to O°C and maintained at this temperature for 1h. Since no product was observed even then, it was worked up as usual and the starting material was recovered in 88% yield.

Under similar reaction conditions, the complex **2b** was treated with cinnamyltrimethylsilane. Since no observable product was formed, it was worked up as usual when the starting material was recovered in 85% yield.

Attempted reaction of 2b with triphenylallyltin : Similar reaction condition as above proved futile and the starting material was recovered in 88% yield.

Attempted reaction of complex 2b with different Lewis acids : It was of interest to study the compatibility of other Lewis acid with our substrate. Therefore, in order to explore the role of Lewis acid in this allylation reaction, different Lewis acids were used to bring about this transformation.

Attempted reaction with $SnCl_4$: Similar reaction condition failed to induce any reaction. The starting material was recovered in 91% yield.

Attempted reaction with $AlCl_3$: Following a reported procedure[1b,3], the reaction was carried out -50°C. The reaction was monitored by TLC. Since no change was observed for 6h, the temperature was raised to O°C. After 1h, the reaction was worked up as there was no observable change, to recover the starting material in 85% yield.

Attempted reaction with $BF_3.OEt_2$[7] : The reaction was conducted under similar condition as above but at -15°C. The reaction mixture was warmed to room temperature after observing the reaction at low temperature for 5h. It was maintained at this temperature for about an hour. As no visible reaction took place as followed by TLC, it was worked up as usual to provide the starting material in 93 % yield.

Summary :

$TiCl_4$ mediated allylation and proton quench at -78°C in the case of complexed cyclic enones afforded a single diastereoisomer of the product. The acyclic enones, on the other hand, were less selective and provided a diastereomeric mixture in the ratio 70:30. Allyltributylstannane yielded the same result. Substituted allylsilanes did not undergo any reaction within similar reaction period.

EXPERIMENTAL:

General procedure for the reaction of allylsilane/stannane with the complexes 2a-b :

For the sake of convenience in transferring measurable quantity of $TiCl_4$ by syringe, a stock solution of $TiCl_4$ in dichloromethane (0.3ml in 10ml dichloromethane) was prepared before use.

Dichloromethane (2ml) was added to the complex (**2a-b**, 0.25mmol) and the solution cooled to -78°C. After 10 minutes, $TiCl_4$ in dichloromethane (2ml of the stock solution, *ca* 0.5mmol) was added dropwise. The reaction mixture was allowed to stir at this temperature for 30min. Allylsilane (0.2ml, 1.25mmol) or allylstannane (0.4ml, 1.25mmol) in dichloromethane (1ml) was added at the same temperature. The reaction was maintained at -50°C for 6 - 8h. Once the reaction was complete (TLC : 20% benzene - pet ether) the temperature was lowered to -78°C and methanol (3ml) was added dropwise. The reaction mixture was allowed to warm to room temperature and then poured into a flask containing saturated ammonium chloride solution (15ml) and dichloromethane (20ml). After extraction with dichloromethane and usual work up the crude product obtained was subjected to flash column chromatography. Elution with 20% benzene - pet ether afforded the desired product.

Preparation of allyltrimethylsilane : Following a reported procedure, from trimethylchlorosilane (31.7ml, 250mmol), allyl chloride (24.3ml, 299mmol) and Mg turnings (8g, 329mmol) in diethylether (180ml), allyltrimethylsilane was obtained (15g, 52.5%).

Preparation of methallyltrimethylsilane : From trimethylchlorosilane (21.7g, 200mmol), methylallyl chloride (21.7g, 240mmol) and Mg turnings (6.4g, 263mmol) in diethylether (90ml), methallyltrimethylsilane was obtained (15.7g, 61.3%).

Preparation of cinnamyltrimethylsilane : Following the same method, from trimethylchlorosilane (11.9g, 109.8mmol), cinnamyl chloride (14.0g, 92mmol) and Mg turnings (3.2g, 131.6mmol) in diethylether (120ml), cinnamyltrimethylsilane was obtained (6g, 27%).

Preparation of allyltriphenylstannane : Following a reported procedure, from triphenylchlorotin (21.1g, 55mmol), allyl chloride (6.1ml, 74.9mmol) and Mg turnings in diethylether (300ml), allyltriphenylstannane (10g, 46.6%) was obtained.

Preparation of allyltributylstannane : From tributyltin chloride (20g, 62mmol), allyl bromide (7.15ml, 83mmol) and Mg turnings (7g, 300mmol) in THF (120ml), allyltributylstannane was obtained (15g, 74%).

Reaction of 2a : From the reaction of the complex **2a** (96mg) with allyltrimethylsilane for 8h, the product **17** (91mg, 86%) was obtained as an orange crstalline solid.

With allyltributylstannane, under similar reaction conditions for about 9h, the same product **17** was obtained (86mg, 81%).

m.p. : 160 - 162°C

IR : 1980, 1910, 1670.

^{1}H NMR : 1.90 - 2.10 (m, 2H), 2.40 (s, 3H), 2.45 - 2.90 (m, 5H), 3.80 - 3.90 (m, 1H), 4.85 - 5.15 (m, 3H), 5.30 (t, 1H, J = 7Hz), 5.55 - 5.80 (m, 2H), 6.20 (d, 1H, J = 6Hz), 7.10 - 7.20 (s, 4H).

^{13}C NMR : 20.8, 21.7, 28.2, 32.6, 42.4, 54.0, 89.0, 89.4, 91.3, 93.0, 94.4, 114.9, 116.2, 128.0, 129.0, 135.9, 136.6, 138.9, 196.2, 230.6.

Analysis : Calc : C = 67.7, H = 5.17

Obs : C = 67.39, H = 5.35

Reaction of 2b : From the reaction of the complex **2b** (92.5mg) with allyltrimethylsilane for 6h, the product **18** (78mg, 76%) was obtained as an orange crstalline solid.

With allyltributylstannane, under same reaction conditions a comparable yield of the product **18** (74mg, 73%) was obtained.

m.p. : 118 - 119°C

IR : 1980, 1910, 1670.

^{1}H NMR : 1.85 - 2.20 (m, 2H), 2.30 - 2.90 (m, 5H), 3.80 - 3.95 (m, 1H), 4.85 - 5.10 (m, 3H), 5.30 (t, 1H, J = 7Hz), 5.55 - 5.80 (m, 2H), 6.20 (d, 1H, J = 6Hz), 7.15 - 7.35 (m, 5H).

^{13}C NMR : 21.9, 28.2, 32.7, 43.1, 53.8, 89.0, 89.3, 91.3, 94.4, 116.2, 126.3, 128.3, 128.5, 136.5, 142.1, 196.0, 230.5.

Analysis : Calc : C = 67.10, H = 4.86

Obs : C = 66.47, H = 5.05

General procedure for the reaction of allyltrimethylsilane with acyclic enone complexes 5a - c :

A stock solution of $TiCl_4$ in dichloromethane (1ml of $TiCl_4$ in 20ml of dichloromethane) was prepared before use.

A solution of the complex **5a - c** (0.5mmol) in dichloromethane (2ml) was cooled to -78°C. The $TiCl_4$ solution (2ml, *ca.* 1mmol of $TiCl_4$) was added dropwise with stirring. The reaction mixture was allowed to stir at this temperature for 30min. Allyltrimethylsilane (0.4ml, 1.25mmol, in dichloromethane [2ml]) was added at the same temperature. The reaction was maintained at -50°C for 3 - 4h. Once the reaction was complete (TLC, 20% benzene - pet ether) the temperature was lowered to -78°C and methanol (5ml) was added dropwise. The reaction mixture was allowed to warm to room temperature (40min.) and then worked up as before. The residue was subjected to column chromatography with 20% benzene- pet ether, to provide the desired product as a diastereomeric mixture. The diastereomeric ratio was determined from the ^{1}H NMR spectra.

Reaction of 5a : From the reaction of the complex **5a** (194mg, 0.5mmol) with allyltrimethylsilane for 3h, the product **19** was obtained (196mg, 91%) as an orange crystalline solid.

IR : 1970, 1900, 1680

^{1}H NMR : The signals given below correspond to the major diastereomer

2.33 (s,3H), 2.40 - 2.55 (m,2H), 3.15 - 3.55 (m,3H), 3.88 (s,3H), 4.80 - 5.15 (m, 5H), 5.60 - 5.90 (m, 2H), 6.15 (d, 1H, J= 6Hz), 7.15 (m,4H).

Some signals corresponding to the minor diastereomer were observed as given below

2.35 (s, 3H), 3.83 (s, 3H), 6.25 (d, 1H, J = 6Hz).

^{13}C NMR : The signals given below correspond to the major diastereomer

20.7, 40.3, 48.6, 55.7, 72.1, 83.7, 90.8, 95.6, 116.2, 127.2, 128.9, 135.5, 136.4, 140.8, 143.8, 196.1, 230.9.

Some signals corresponding to the minor diastereomer were observed as given below

40.1, 48.9, 72.4, 84.0, 95.1, 116.3, 127.4, 136.1, 141.3, 196.2, 231.1.

Analysis : Calc : C = 64.30, H = 5.10

Obs : C = 64.75, H = 4.46

Reaction of 5b : From the reaction of the complex **5b** (187mg, 0.5mmol) with allyltrimethylsilane for 4h, the product **20** (190 mg, 92%) was obtained as an orange crystalline solid.

IR : 1970, 1900, 1670

^{1}H NMR : The signals given below correspond to the major diastereomer

2.35 - 2.60 (m, 2H), 3.10 - 3.60 (m, 3H), 3.90 (s, 3H), 4.75 - 5.15 (m, 5H), 5.55 - 5.90 (m, 2H), 6.10 (d, 1H, J = 6Hz), 7.10 - 7.45 (m, 5H).

Some signals corresponding to the minor diastereomer were observed as given below 3.85 (s, 3H), 6.25 (d, 1H, J = 6Hz).

^{13}C NMR : The signals given below correspond to the major diastereomer 40.7, 48.5, 55.7, 72.1, 83.7, 90.7, 95.0, 95.5, 116.3, 126.1, 127.4, 128.2, 136.3, 143.9, 196.0, 230.8.

Some signals corresponding to the minor diastereomer were observed as given below 48.6, 72.2, 83.8, 90.9, 116.4, 127.6, 136.2, 143.7, 196.1, 231.0.

Analysis : Calc : C = 63.60, H = 4.81

Obs : C = 63.13, H = 5.04

Reaction of 5c : The reaction of the complex **5c** (200mg,0.5mmol) with allyltrimethylsilane, for 4h, afforded the product **21** (180mg, 82%) as an orange solid.

IR : 1980, 1900, 1670

^{1}H NMR : The signals given below correspond to the major diastereomer 2.35 - 2.55 (m, 2H), 3.10 - 3.55 (m, 3H), 3.80 (s, 3H), 3.90 (s, 3H), 4.80 - 5.15 (m, 5H), 5.55 - 5.90 (m, 2H), 6.10 (d, 1H, J = 6Hz), 6.85 (d, 2H, J = 9Hz), 7.25 (d, 2H, J = 9Hz).

Some signals corresponding to the minor diastereomer were observed as given below 3.82 (s, 3H), 3.85 (s, 3H), 6.25 (d, 1H, J = 6Hz).

^{13}C NMR : The signals given below correspond to the major diastereomer 40.0, 40.8, 48.8, 55.7, 72.0, 83.7, 91.1, 95.5, 113.9, 116.2, 128.3, 136.2, 143.8, 158.1, 196.1, 230.8.

Some signals corresponding to the minor diastereomer were observed as given below 39.9, 40.4, 49.1, 55.1, 72.3, 84.0, 94.9, 113.8, 128.5, 136.1, 196.3, 231.0.

Analysis : Calc : C = 62.00, H = 4.90

Obs : C = 62.64, H = 4.45

Attempted reaction with complex 2c : Following similar reaction conditions as in cyclic enone case, allyltrimethylsilane was added to the complex **2c** (100mg, 0.25mmol). Since the reaction did not proceed even after 8h, it was worked up as usual to afford the starting material (87mg) in 87% yield.

Attempted reactions with complex 2b : Using similar reaction conditions, trimethyl methallylsilane was added to the reaction mixture. The reaction was maintained at -50°C for 5h and during this time the colour of the reaction mixture gradually changed from violet to dark green. The reaction was monitored by TLC and since no reaction was observed even after 5h, the reaction was warmed to O°C and maintained at this temperature for 1h. Since no reaction was observed even then, it was worked up as usual and the starting material was recovered (81mg) in 88% yield.

Under similar reaction conditions, the complex **2b** was treated with cinnamyltrimethylsilane. Since no observable product was formed, it was worked up as usual and the starting material was recovered (78mg) in 85 % yield.

Attempted reaction of 2b with triphenylallyltin : Similar reaction conditions as above proved futile and the starting material was recovered (81mg) in 88% yield.

Attempted reaction of complex 2b with different Lewis acids : It was of interest to study the compatibility of other Lewis acid with our substrate. Therefore, in order to explore the role of Lewis acid in this allylation reaction, different Lewis acids were used to bring about this transformation.

Attempted reaction with $SnCl_4$: Similar reaction condition failed to induce any reaction. Therefore, the starting material was recovered (84mg) in 91% yield.

Attempted reaction with $AlCl_3$: Following a reported procedure, the reaction was carried out at -50°C. The reaction was monitored by TLC and as no change was observed, the temperature was raised to O°C. After 1h, the reaction was worked up as there was no observable change, to afford the starting material (78mg) in 85% yield.

Attempted reaction with $BF_3.OEt_2$: The reaction was conducted under similar conditions as above but at -15°C. The reaction mixture was warmed to room temperature after observing the reaction at low temperature for 5h. It was maintained at this temperature for about an hour. As no visible reaction took place as followed by TLC, it was worked up as usual to provide the starting material (86mg) in 93 % yield.

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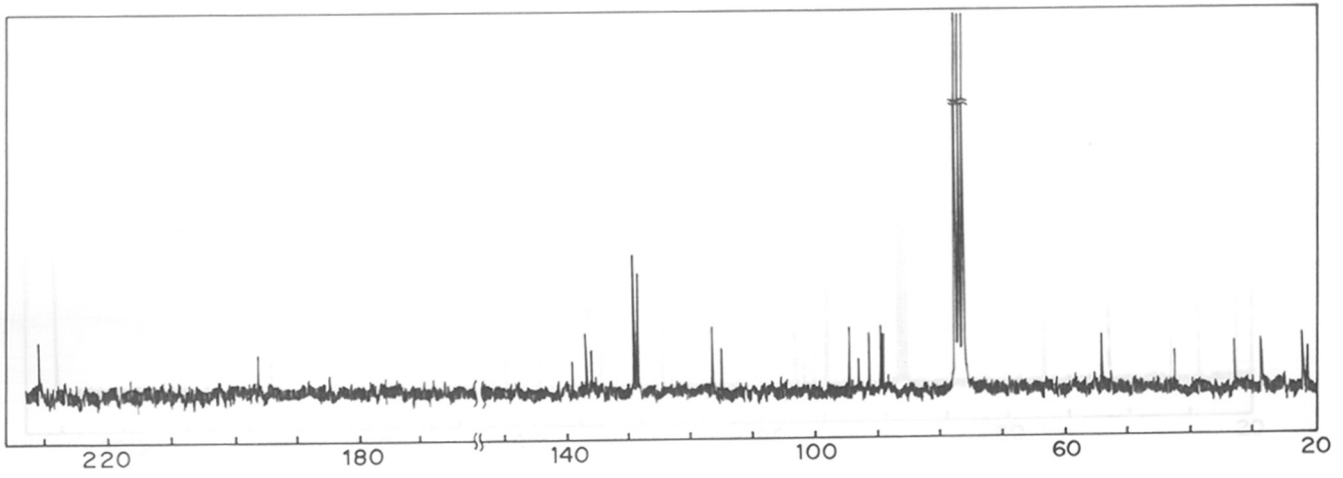

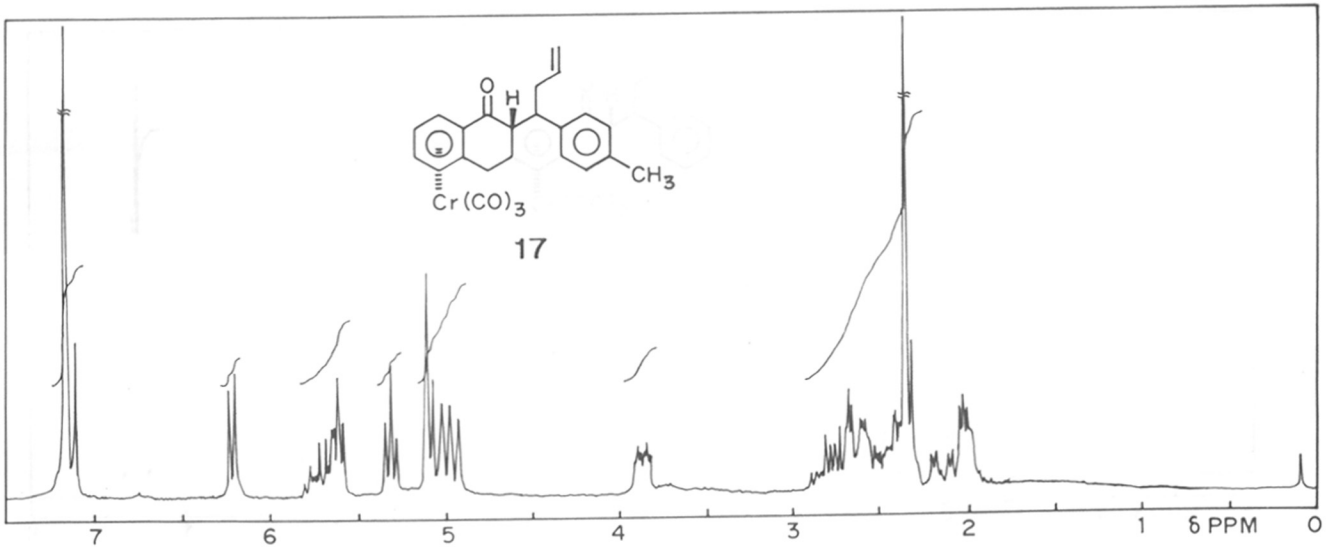

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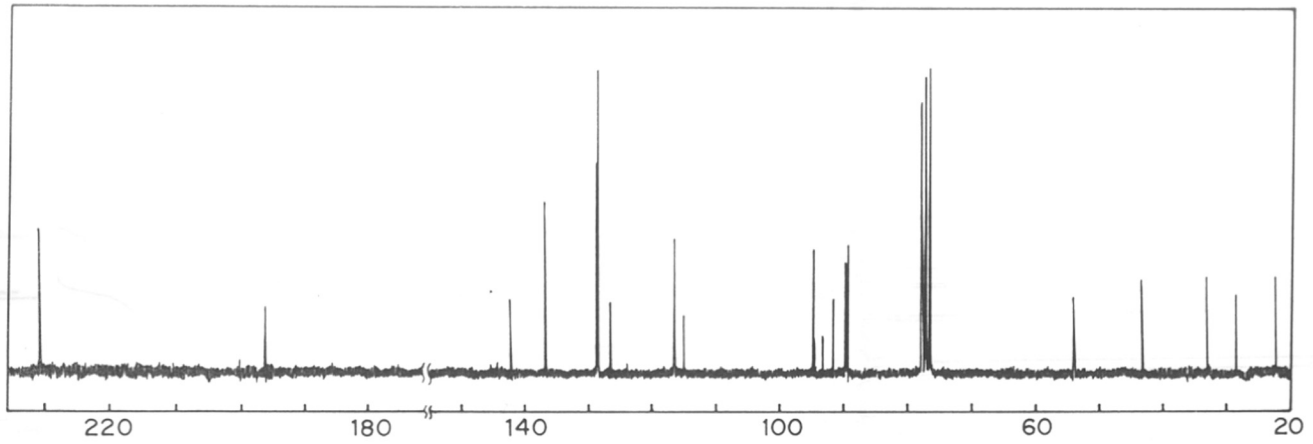

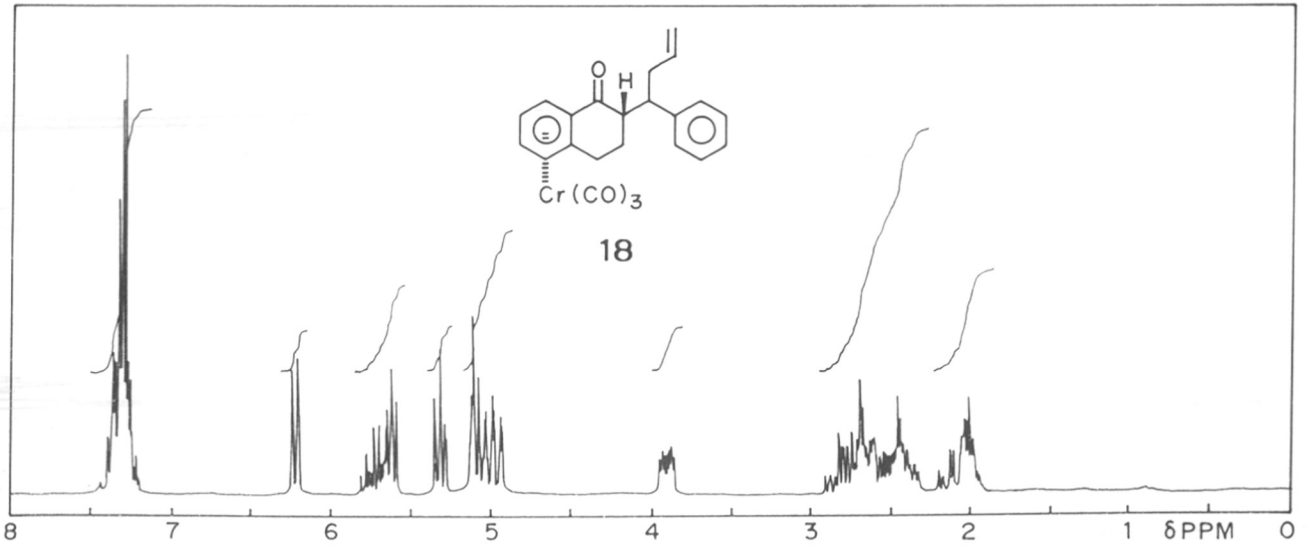

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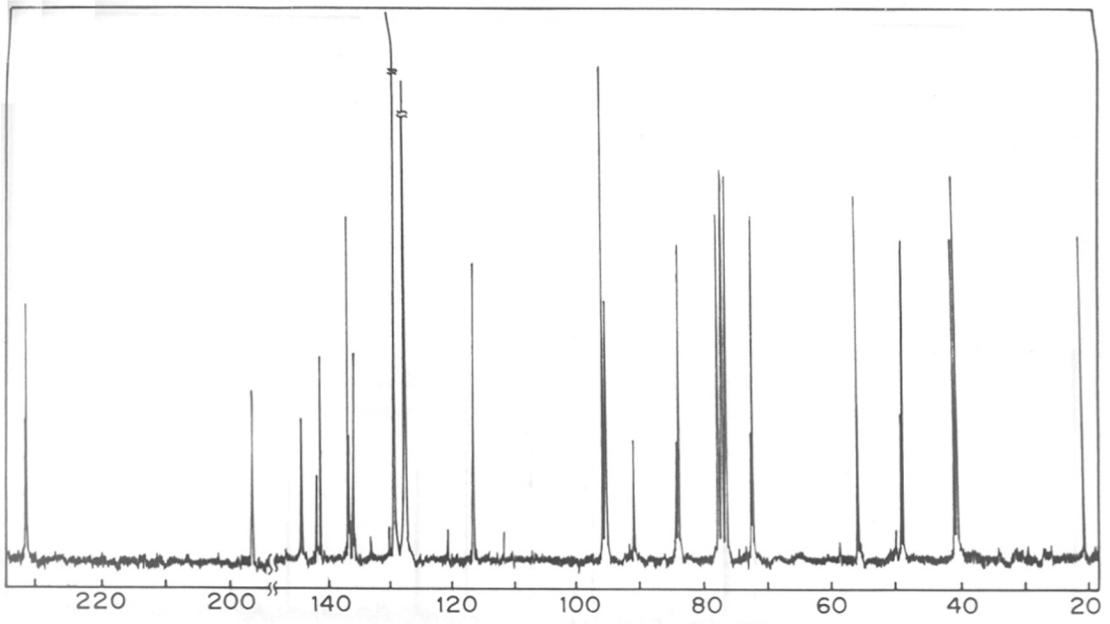

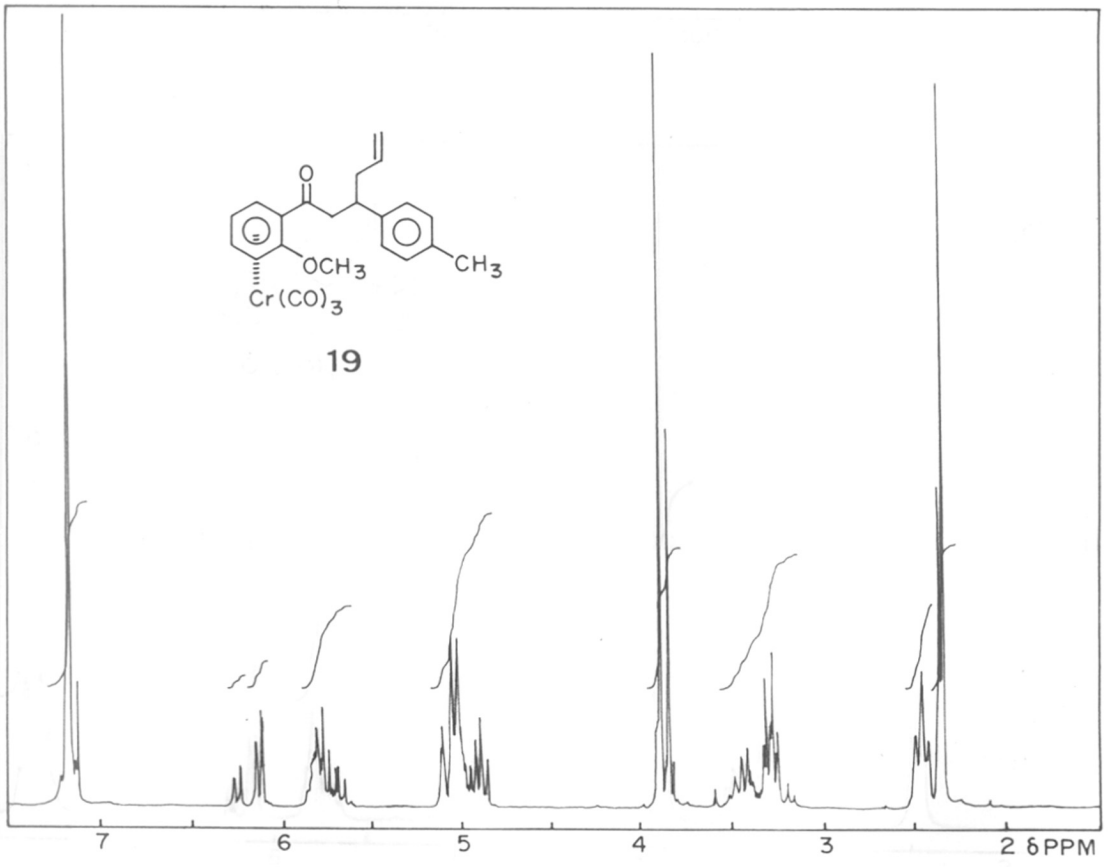

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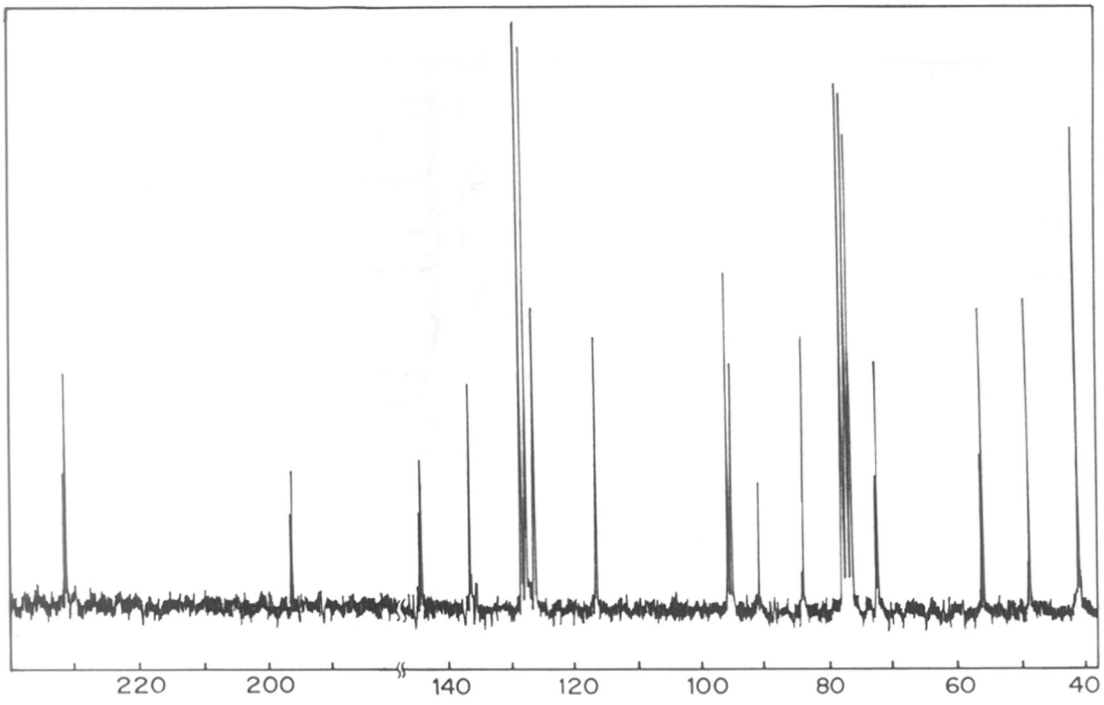
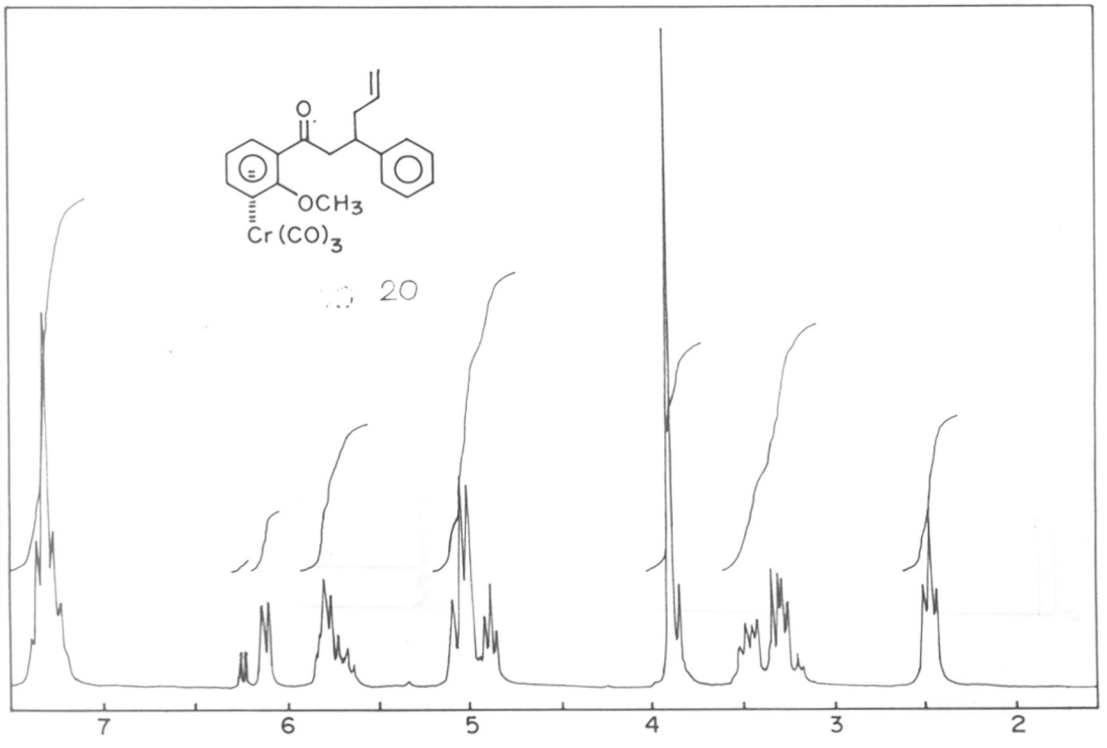
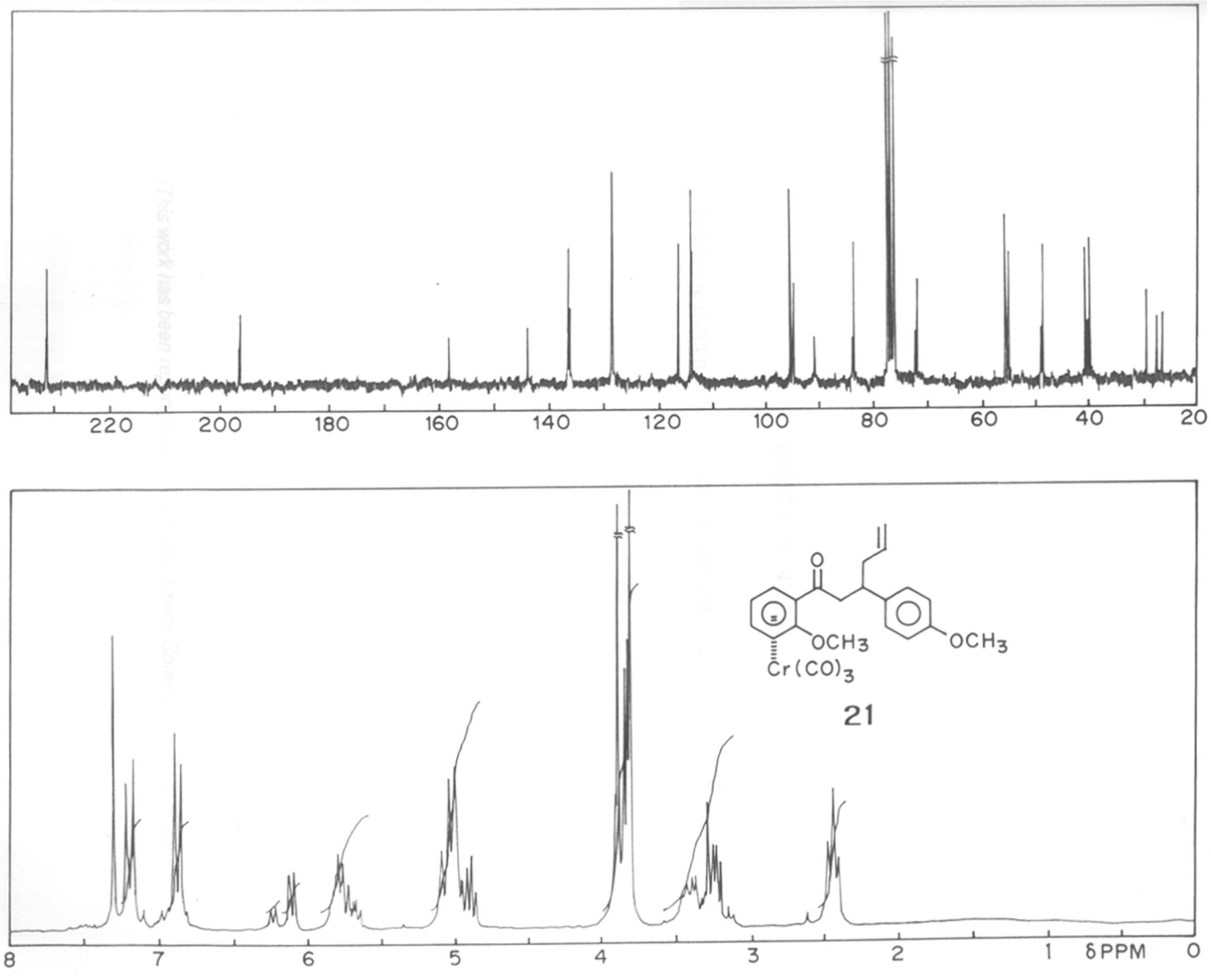

220
200
140
120
100
80
60
40


O
OCH3
Cr(CO)3
20
7
6
5
4
3
2


220
200
180
160
140
120
100
80
60
40
20
8
7
6
5
4
3
2
1
δPPM
0
O
OCH3
OCH3
Cr(CO)3
21

CHAPTER - 4

Cyclopropanation of Enones Complexed with Tricarbonylchromium

(This work has been reported in J. Chem. Soc. Chem. Commun., 1993, 224-226)

INTRODUCTION

So far we have discussed two types of reactions : (i) conjugate addition of nitromethane, and, (ii) Lewis acid mediated addition of allylsilane to 2-arylidene-1-tetralones complexed with $Cr(CO)_3$. In the former reaction, it was established that the conjugate addition at the β-carbon of the enone was 100% stereospecific. It was also realised that protonation at the epimeric centre was stereoselective even at room temperature, and the major product resulted from protonation from the *exo* face. The latter reaction described the addition of allyltrimethylsilane in the presence of $TiCl_4$ at C-3 with complete stereospecificity. This time the proton quench was carried out at low temperature, which ensured total selectivity of protonation at C-2 from the *exo* face.

Therefore, if a reagent was selected such that the enolate generated by nucleophilic addition could be trapped by an intramolecular electrophile, stereoselectivity at both the centres, C-3 and C-2 could be simultaneously controlled.

It is generally accepted that sulfoxonium ylides react with a double bond activated by an electron withdrawing group in a manner similar to conjugate addition and lead to a cyclopropane by intramolecular displacement of dimethyl sulfoxide[1]. Such cyclopropanation would satisfy the criteria described above.

RESULTS AND DISCUSSION

The cyclopropanation was carried out using dimethylsulfoxonium methylide generated *in situ*, with 2-arylidene-1-tetralone-$Cr(CO)_3$ complexes.

Preparation of the Sulfoxonium salt :

The trimethylsulfoxonium iodide was prepared following a reported procedure[2], by gentle reflux of dimethylsulfoxide and methyl iodide to provide a white solid in 50% yield. The generation of the ylide and cyclopropanation was carried out under PTC conditions[3].

Reaction of trimethyl sulfoxonium ylide with enones (2a - 2c) (PTC condition): The complex **2b** was dissolved in CH_2Cl_2 to which trimethylsulfoxonium iodide and tetrabutylammonium bromide (catalytic amount) were added. To this solution, 50% aqueous NaOH (10ml) was added and the mixture was heated under reflux for 16h. The reaction was monitored by TLC. The product was less polar than the starting material. It was observed that even after 16h, trace amount of starting material persisted in the reaction medium. The reaction was stopped at this stage and worked up as usual. The product **23** was separated from the starting material by flash column chromatography and isolated in 87% yield, as orange crystals.

23

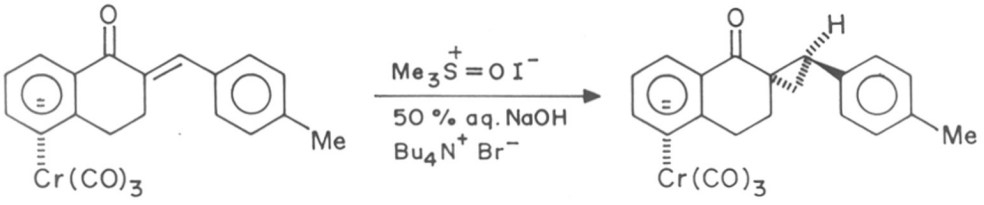
The IR spectrum of the complex exhibited bands at 1990, 1920 (Cr-CO) and 1670 (-CO-).

The ^{1}H NMR spectrum showed the downfield signals which were assigned to the uncomplexed phenyl ring protons at 7.3. The complexed aromatic ring protons appeared as doublet of doublet due to *ortho* coupling (J = 6.8Hz) and *meta* coupling (1Hz) at 6.2. Unsymmetrical triplets were observed due to two *ortho* couplings and one *meta* coupling at 5.6 and 5.3. A doublet with a coupling J = 7Hz resonated at 5.1.

The benzylic methylene, the cyclopropane methylene and the benzylic methine appeared as a multiplet between 2.8-2.15. The other methylene protons of the tetralone ring appeared in the region 1.55-1.35.

The ^{13}C NMR spectrum showed downfield resonances at 230.9 and 195.8 corresponding to Cr-CO and -CO- respectively. The signals of uncomplexed aromatic ring carbon appeared in the region 136.0 to 127.1. The complexed ring carbons resonated between 115.2 to 89.4. The carbon adjacent to ketone appeared at 37.1. The benzylic carbon signal resonated at 33.1. The methylene signals of the tetralone ring appeared at 26.4 and 24.6. The signal at 18.3 was assigned to the methylene of the cyclopropane ring.

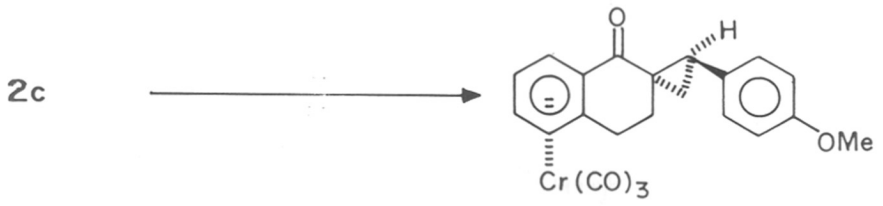
From the NMR spectra, it was apparent that a single diastereomer of the product was obtained. The complex **2a** under similar reactions provided the product **22** in 84% yield, as orange crystals of a single diastereomer.



2a **22**

The IR spectrum of the complex had characteristic bands. The $^{1}HNMR$ spectrum showed signals in the expected region. The methyl signal appeared at 2.4 as a singlet. In the $^{13}CNMR$ spectrum the resonances appeared as expected. The methyl carbon signal resonated at 20.9.

The complex **2c** also afforded the product, **24** as orange crystals in 77% yield under similar reaction conditions. Only one diastereoisomer of the product was obtainedThe IR spectrum exhibited bands at 1980, 1910 (Cr-CO) and 1660 (-CO-). The resonances in the $^{1}HNMR$ were as expected. The protons of the methoxy group appeared as a singlet at 3.8. The ^{13}C NMR spectrum of the complex exhibited signals in the expected region. The methoxy signal was observed at 55.1..



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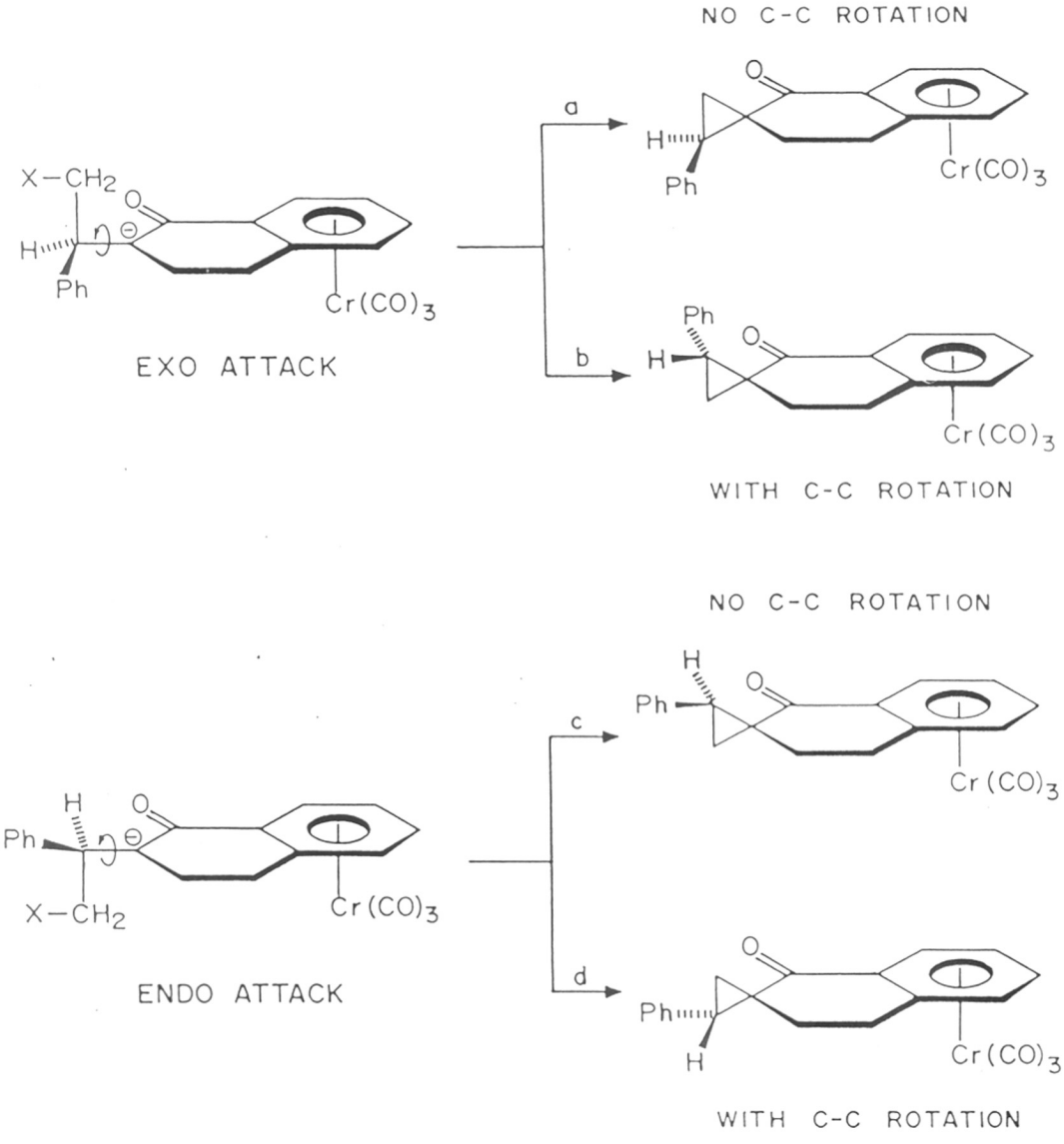
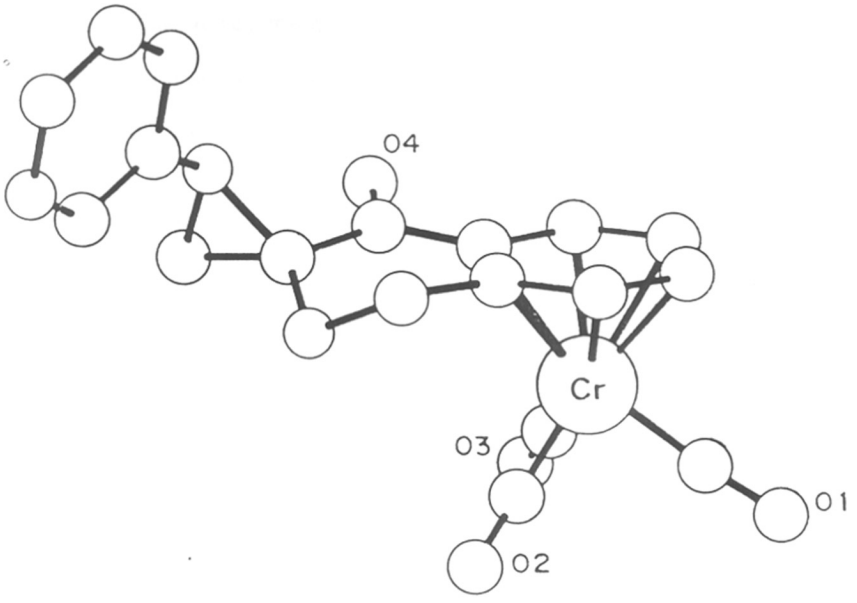
The formation of a single diastereomer of the product indicated excellent stereocontrol in the cyclopropanation reaction. Similarity in the ^{1}H NMR spectral pattern suggested that the stereochemical relationships in all three products were the same. The stereochemistry of the cyclopropane ring, however, could not be established from the spectral data alone.

Thus, four possible diastereoisomeric products may be formed as depicted in Scheme-1, as a result of *exo* or *endo* attack on the enone system.

It can be clearly seen that the pathway leading to the product would determine the stereochemical relationship between the phenyl, carbonyl and methylene groups.

In order to establish such spatial relationship without ambiguity, the structure of the compound **23** was determined by single crystal *X*-ray diffraction. The *X*-ray diffraction analysis revealed that the cyclopropane was appended from the same face of the molecule as occupied by the $Cr(CO)_3$ group. The PLUTO diagram of **23** is shown below. The product has resulted from an unusual *endo*-attack (path *c* in Scheme 1).

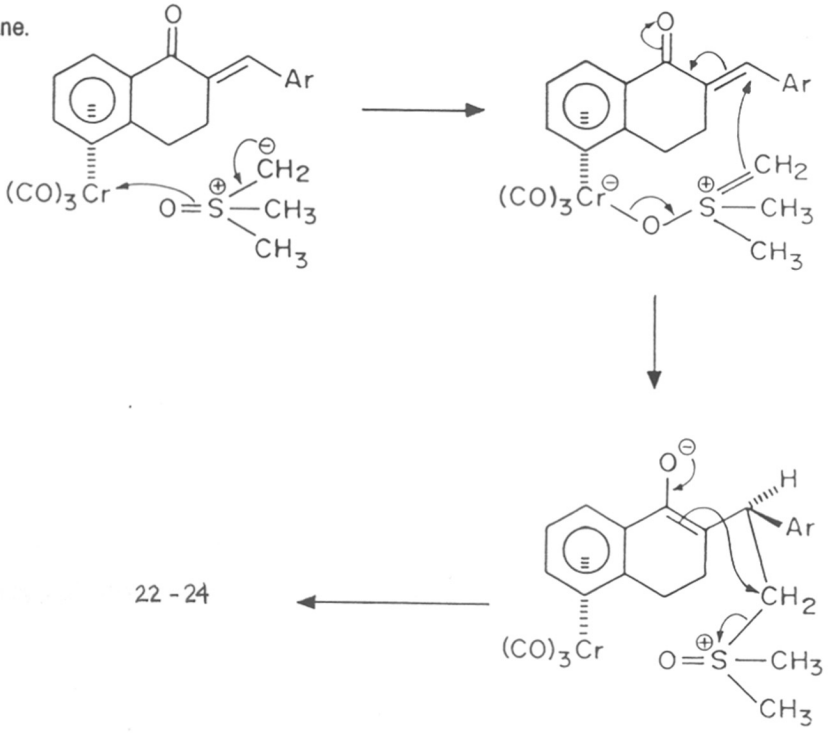

NO C-C ROTATION
X−CH2
O
H
Ph
Cr(CO)3
a
b
EXO ATTACK
WITH C-C ROTATION
NO C-C ROTATION
H
Ph
X−CH2
c
d
ENDO ATTACK
WITH C-C ROTATION



Monoclinic space group $P2_1/n$; a = 7.616(2) $\mathring{A}$, b = 10.100(2) $\mathring{A}$, C = 22.916(2) $\mathring{A}$, β = 95.92(1)° $\mathring{A}$, V = 1753.4 $\mathring{A}^3$, D_c = 1.456 Mg/m^3, Z = 4, μ(Mo - K_α) = 0.66mm^{-1} 2809 unique reflections, R = 0.038 for 1723 observed reflections.

We may recall that conjugate addition to 2-arylidene-tetralones complexed with $Cr(CO)_3$ was found to proceed (Chapter-2) with exclusive *exo*-attack. The reason for the exclusive *endo*-selectivity in the present case is not obvious.

A possible mechanism can be invoked which would involve participation of the metal in the delivery of the reagent. The sulfoxonium methylide may coordinate with $Cr(CO)_3$ moiety, which will necessitate ring slippage[4] from η^6 to η^4-arene in order to maintain 18 electron configuration around the metal. Electron reorganisation could lead to the *endo* attack at the enone terminus. A fast ring closure would afford the *endo* cyclopropane.



An alternative explanation for this unusual stereochemical result, which does not involve participation by the metal, may be based on the following two premises: (i) the attack of the sulfur ylide is reversible[1] and (ii) the ring closure of the *endo* adduct is fast enough to shift the equilibrium in its favour. Thus, the cyclopropanes **22**, **23** and **24** could be kinetic products.

The uncomplexed 2-benzylidene-1-tetralone did not undergo any reaction under identical condition.

Reaction of trimethylsulfonium ylide with 2b (Homogeneous conditions) :

Following a reported procedure[2], the ylide was generated in THF, using NaH as base. A solution of the complex **2b** in THF was added to the ylide and allowed to react at room temperature overnight. The product was isolated by flash column chromatography in 82.5% yield.

The ^{1}H NMR spectrum of this product was found to be identical with that of **23**. Thus, no change in stereoslectivity was observed.

Attempted reaction :

Use of triphenylphosphine isopropylidene ylide was investigated as the cyclopropanating reagent for the same substrates. Following a reported procedure[5], isopropyltriphenylphosphonium bromide was prepared from triphenylphosphine and isopropyl bromide by heating at 150°C in a pressure bottle for one day. The product was recrystallised from a small amount of ethanol and diethyl ether in 89% yield. Isopropylidenetriphenylphosphine was generated from isopropyl triphenylphosphonium bromide (1.1mmol) and n-BuLi (1mmol) in THF at 0°C. A solution of the complex **2a** in THF was added dropwise. After addition of the complex, the reaction mixture was allowed to stir overnight at room temperature. The reaction was monitored by TLC. The reaction did not proceed even after 12h and the starting material was recovered in 94% yield.

Summary :

An unprecedented, completely stereospecific *endo* cyclopropanation of 2-arylidene-1-tetralone $Cr(CO)_3$ complex by dimethylsulfoxonium methylide has been observed. Although the factors responsible for such reversal of stereoselectivity remain unclear, this result is likely to initiate search for other possible *endo*-selective transformations.

EXPERIMENTAL:

General procedure for cyclopropanation :

Preparation of trimethyl sulfoxonium iodide : Following a reported procedure dimethyl sulphoxide (8ml.,1.1moles) and methyl iodide (16ml.) were refluxed under nitrogen for three days to provide the salt (10g,45%).

Phase Transfer Catalysis(PTC) method: To a solution of the complex **2a-c** (0.4mmol. to 1mmol), trimethyl sulfoxonium iodide(0.4mmol. to 1mmol.) and tetrabutylammonium bromide (2 mol% of iodide) in deaerated dichloromethane (7 to 10ml) was added 50% aqueous NaOH (5 to 10ml). The reaction was heated under reflux for 16h under argon. It was cooled to room temperature and worked up as usual. The residue thus obtained was subjected to flash column chromatography. The starting material and the product could be separated using solvent gradient(10% EtOAc-pet ether to 30% EtOAc-pet ether). The less polar fraction was identified as the starting material. The polar fraction afforded the desired product. The yields were calculated based on consumed starting material.

Reaction of 2b: From the complex **2b** (369mg, 1mmol), Trimethyl sulfoxonium iodide (220mg, 1mmol) and tetrabutylammonium bromide (4mg) and 50% aqueous NaOH (10ml) in dichloromethane (10ml), a residue was obtained after usual work up. The starting material (60mg) and the product (285mg, 89%) could be separated by flash chromatography using 20% EtOAc-pet ether as eluant.

m.p. : 127 - 128°C

IR : 1990, 1920, 1670

^{1}H NMR : 1.35 - 1.55 (m, 2H), 2.15 - 2.80 (m, 5H), 5.10 (d, 1H, J = 6Hz), 5.30 (t, 1H, J = 7Hz), 5.60 (dt, 1H, J = 6.1Hz), 6.20 (dd, 1H, J = 6.8Hz), 7.30 (m, 5H).

^{13}C NMR : 18.3, 24.6, 26.4, 33.3, 37.1, 89.4, 90.2, 90.6, 93.1, 94.0, 115.2, 127.1, 128.2, 128.9, 136.0, 195.8, 230.9.

Analysis : Calc : C = 65.79, H = 4.17

Obs : C = 65.93, H = 4.37

Reaction of 2a : From the complex **2a** (153mg, 0.4mmol), trimethyl sulfoxonium iodide (88mg, 0.4mmol) and tetrabutylammonium bromide (2mg) and 50% aqueous NaOH (7ml) in dichloromethane (10ml) a crude residue was obtained. Flash column chromatoraphy with 20% EtOAc-pet ether provided the starting material (15mg) and the product (120mg, 84%).

m.p. : 162 - 164°C

IR : 1970, 1900, 1660.

^{1}H NMR : 1.25 - 1.50 (m, 2H), 2.10 - 2.30 (m, 2H), 2.40 (s, 3H), 2.45 - 2.75 (m, 2H), 5.10 (d, 1H, J = 6Hz), 5.35 (t, 1H, J = 7Hz), 5.60 (t, 1H, J = 7Hz), 6.15 (d, 1H, J = 6Hz), 7.10 (s, 4H).

^{13}C NMR : 18.2, 20.9, 24.5, 26.4, 37.2, 89.3, 90.2, 90.6, 93.0, 94.1, 115.3, 128.7, 128.9, 132.7, 136.8, 195.9, 230.9.

Analysis : Calc : C = 66.49, H = 4.53

Obs : C = 66.22, H = 4.67

Reaction of 2c : Using similar condition as in **2b**, the complex **2c** (159mg, 0.4mmol) afforded a residue, which on chromatography with 30% EtOAc-pet ether furnished the desired product (116mg, 77%) as well as some starting material (13mg).

m.p. : 134 - 136°C

IR : 1980, 1910, 1660

^{1}H NMR : 1.25 - 1.50 (m, 2H), 2.15 - 2.75 (m, 5H), 3.80 (s, 3H), 5.10 (d, 1H, J = 6Hz), 5.35 (t, 1H, J = 7Hz), 5.60 (t, 1H, J = 7Hz), 6.20 (d, 1H, J = 6Hz), 6.90 (d, 2H, J = 9Hz), 7.15 (d, 2H, J = 9Hz).

^{13}C NMR : 18.5, 24.6, 26.5, 33.3, 37.0, 55.1, 89.4, 90.2, 90.6, 94.0, 94.1, 113.7, 115.2, 127.9, 129.9, 158.8, 195.8, 230.9.

Analysis : Calc : C = 63.92, H = 4.35

Obs : C = 63.30, H = 4.46

Reaction of 2-benzylidene-1-tetralone : The enone (234 mg, 1mmol) under similar conditions did not yield any product and starting material (216mg, 92%) was recovered.

Homogeneous Condition : NaH (48mg, 50% dispersion in oil, 2mmol) was washed with pet-ether (3 x 10ml) and dried. THF (10ml) and the salt (220mg, 1mmol) was added to the dried NaH and the flask was cooled in an ice bath (15min). The complex **2a** (332mg, 0.9mmol) in THF (109ml) was added to it dropwise *via* siringe. After 16h the reaction was observed to have progressed as usual. With 20% EtOAc - pet ether, starting material (41mg) and product (222mg, 82.5%) could be seperated.

Attempted Reaction: Preparation of isopropyltriphenylphosphonium bromide : Following a reported procedure, triphenylphosphine (13.1g, 0.05mol) and isopropyl bromide (4.7ml, 0.05mol) were taken in a pressure bottle and heated at 150°C for one day. It was recrystallised from a small amount of ethanol and diethyl ether, m.p. 238-239°C (17 gm, 89%).

Triphenylphosphineisopropylidene reagent : The reagent was prepared from isopropyltriphenylphosphonium bromide (423mg, 1.1mmol) and n-BuLi (1ml, 1mmol) in THF (8ml) at 0°C. After stirring for 30min, a solution of the complex **2a** (383mg, 1mmol) in THF (7ml) was added at the same

temperature. After 10min the reaction mixture was allowed to warm to room temperature. The reaction did not proceed even after 16h. After workup and flash column chromatography with 20% EtOAc - pet ether, starting material (361 mg, 94%) was recovered.

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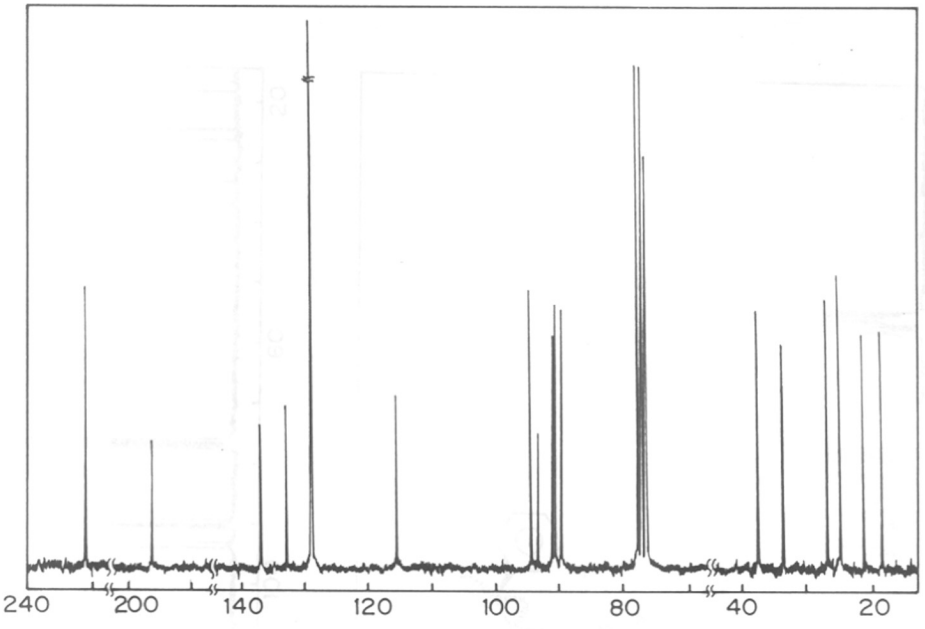
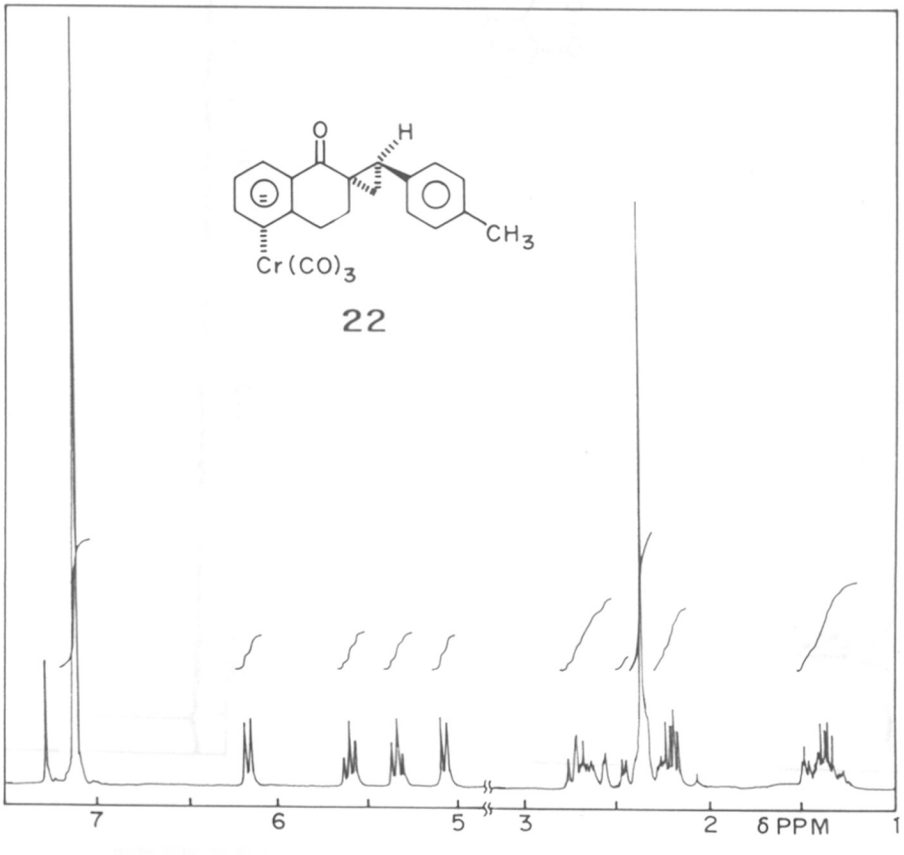
5. U. H. M. Fagerlund and D. R. Idler, *J. Am. Chem. Soc.*, 1957, **79**, 6473.





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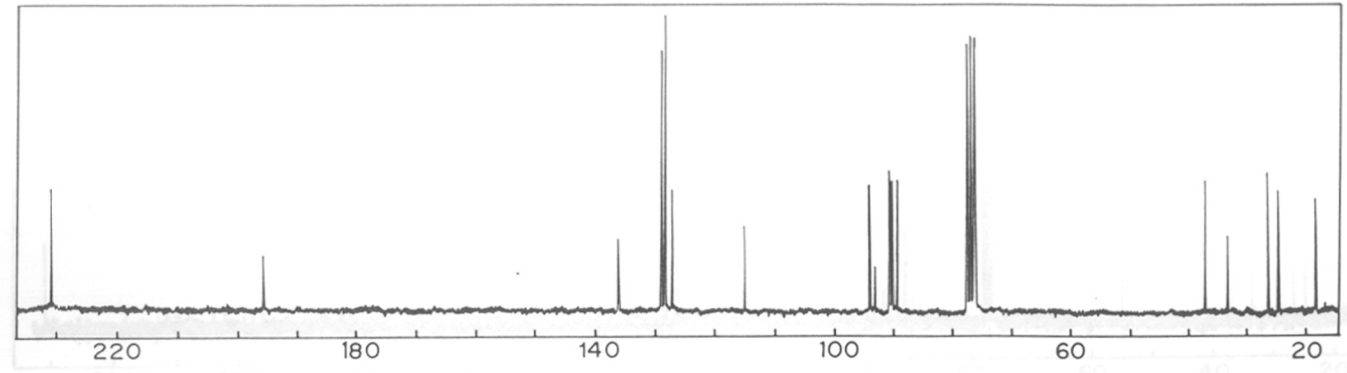

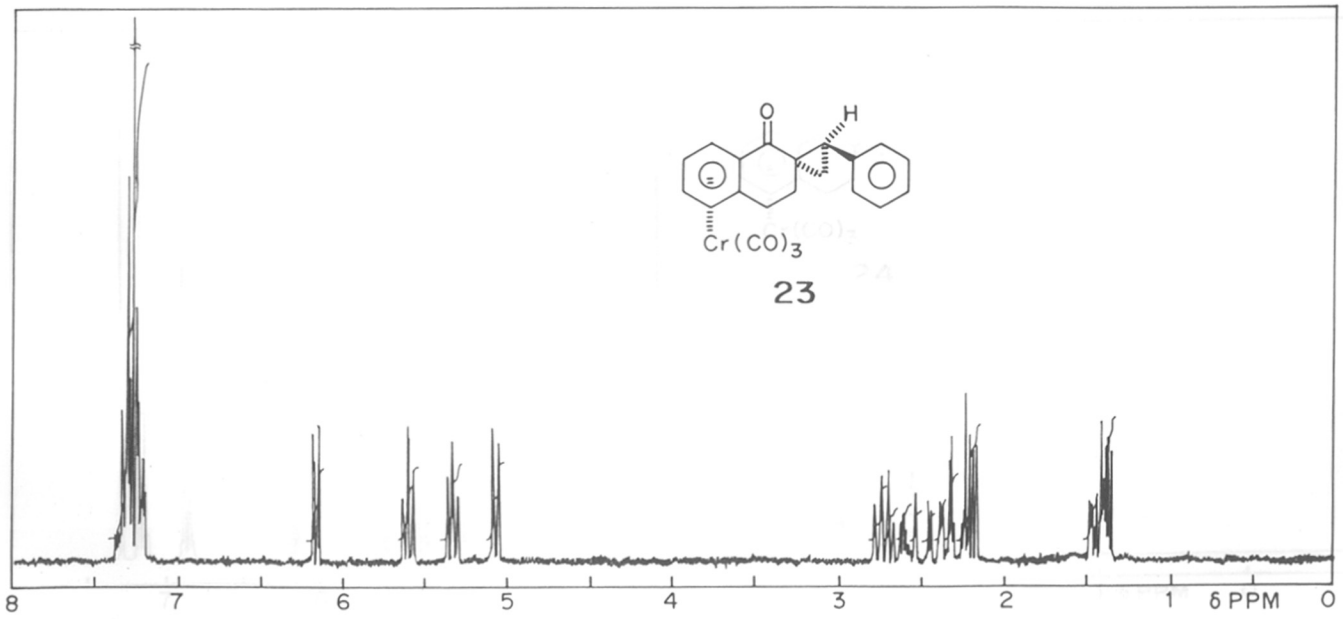

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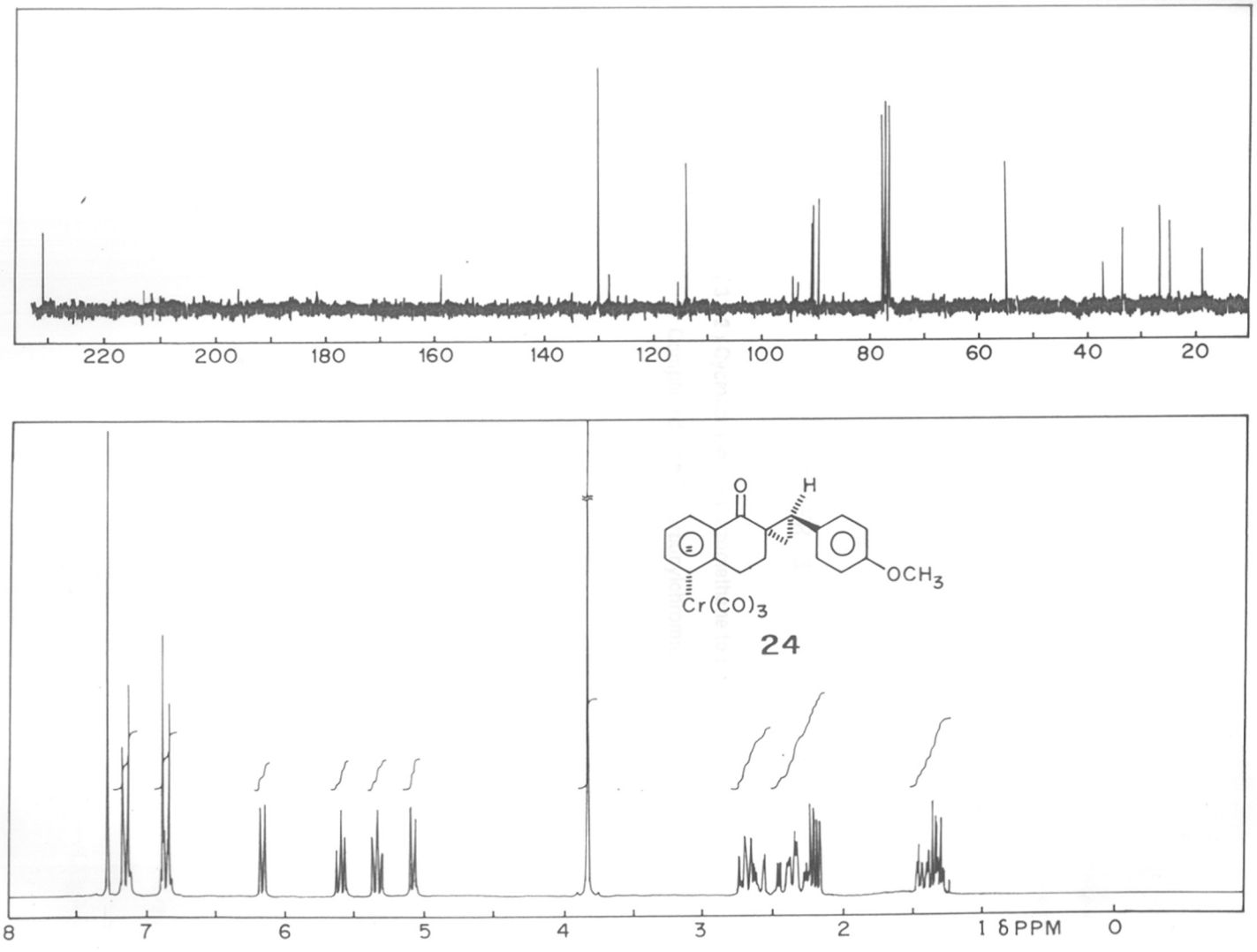
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CHAPTER - 5

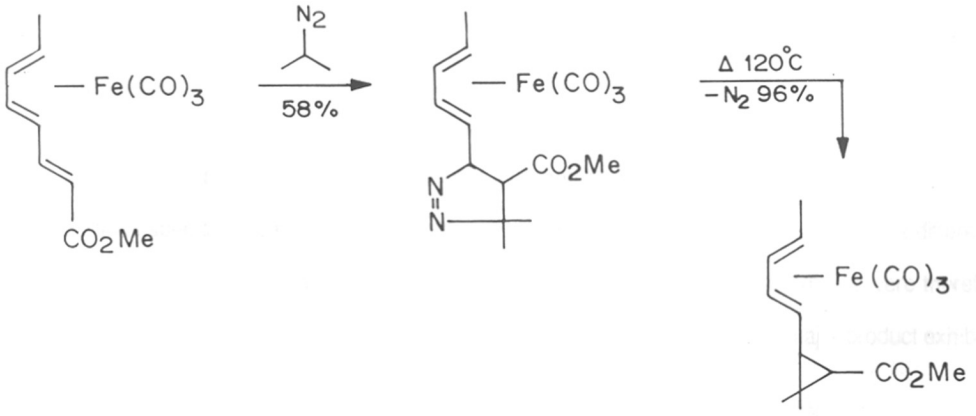
(3 + 2) Cycloaddition of Diazomethane to Enones Complexed with Tricarbonylchromium

INTRODUCTION

Cycloaddition reactions generally proceed *via* an organized transition state. The steric interaction which come into play in the transition state dictate the product stereochemistry[1]. As described previously, stepwise conjugate addition of nucleophilc reagents were demonstrated to be stereospecific on the 2-arylidene-1-tetralone $Cr(CO)_3$ complexes (**2a-d**). Therefore, it was of interest to study such selectivity in 1,3 dipolar cycloaddition reactions involving the electron deficient double bond of such substrates. Diazomethane was chosen as the 1,3-dipolar reagent for our preliminary study. Owing to its small size, the transition state would be expected to have minimal steric requirement. The diastereofacial selectivity of this cycloaddition would thus reflect the lowest limit of steric interaction of the 1,3-dipolarophile with the pendant $Cr(CO)_3$ group.

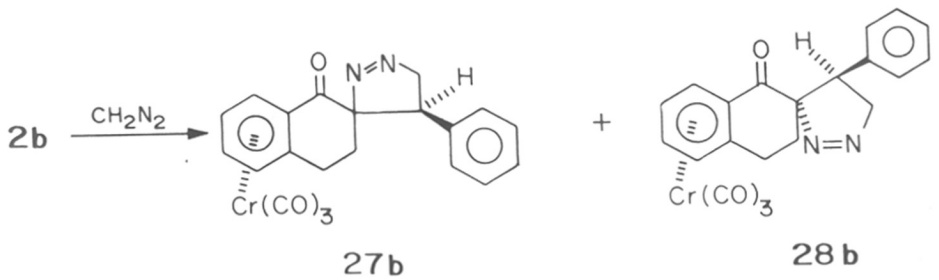
The pyrazoline products, on thermolysis, often extrude nitrogen and afford cyclopropanes. If such thermal extrusion of nitrogen can be realized in the present case, the orientation of the product cyclopropane would immediately indicate the disposition of the parent pyrazoline. Orientation of the cyclopropane can be deduced by direct comparison with those described in Chapter 4.

A related transformation on $Fe(CO)_3$-diene template has been reported[2].



RESULTS AND DISCUSSION :

The diazomethane addition reaction was carried out following a reported procedure[3] with minor modification. Diazomethane was generated from N-nitrosomethylurea and 50% aqueous potassium hydroxide at 0°C and extracted into ether. The ether extract containing diazomethane was added to the complex in diethyl ether at the same temperature, in one portion. The complex **2b** was partially soluble in diethyl ether. After addition of diazomethane, the reaction mixture was allowed to warm up to room temperature. After about 30 min. a homogeneous solution was obtained. The reaction went to completion by stirring overnight (TLC). Excess diazomethane was destroyed with acetic acid and the reaction mixture was worked up as usual. The product consisted of two components, which were separated using flash column chromatography (major component **27b : 28b** minor component, combined yield 84%). From the colour of the bands, it appeared that both were arene $Cr(CO)_3$ complexes.



27b 28b

The structures of these compounds were assigned as diastereomeric pyrazolines (80:20) based on their ^1H NMR spectra. The two isomers display significantly different spectral pattern, and this difference is consistent throughout the series of three pair of product compounds. The assignments were therefore based on COSY spectra for one pair of the series. The IR spectrum of the less polar major product exhibited bands at 1980, 1910 (Cr-CO), 1670 (-CO-) and 1520 (-N=N-).

In the ^{1}H NMR spectrum of the complex **27b**, the uncomplexed aromatic proton signals appeared as two separate multiplets between 7.4-7.2 and 7.0-6.9. The complexed aromatic ring protons resonated as a doublet at 6.2 (J=6Hz), a triplet at 5.7 (J=6Hz) and 5.4 (J=6Hz) and a doublet at 5.2 (J=6Hz). The methylene group of the pyrazoline ring was coupled with the benzylic methine proton and appeared as a doublet at 5.1 (J=6Hz). The methine proton resonated as a triplet at 4.0 (J=6Hz). The benzylic protons of the tetralone ring appeared as two separate multiplets in the region 3.8 - 3.6 and 2.7 - 2.5. The other methylene protons of the tetralone ring resonated as a multiplet between 1.9 - 1.5.

In the COSY spectrum the coupling between the methylene and the methine protons of the pyrazoline ring could be immediately identified. The spectral pattern was similar for all the major isomers in this series.

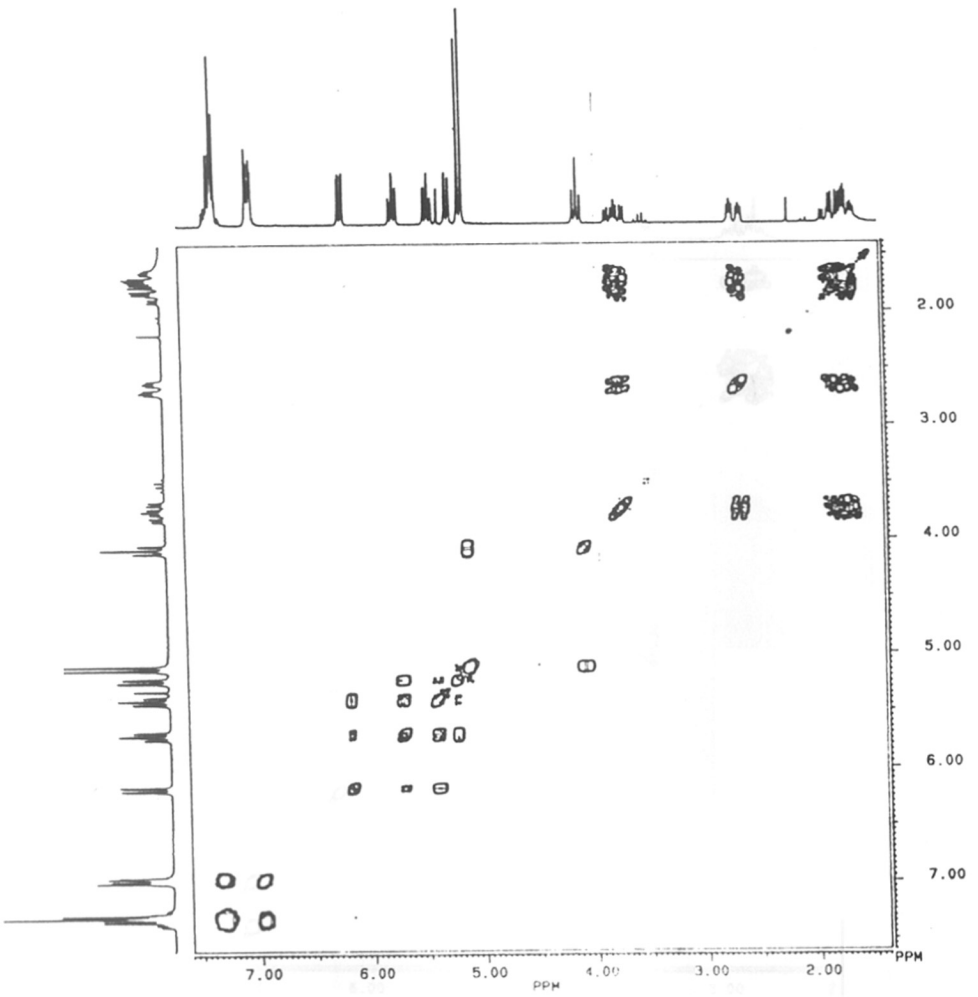
The downfield signal at 230 in the ^{13}C NMR spectrum was assigned to (Cr-CO). The (-CO-) resonated at 190. The aromatic carbon signals of the uncomplexed ring appeared in the region 126.7 to 136.7. The C-2 signal appeared rather downfield at 100. The complexed aromatic carbon signals resonated in the region 89.1 to 114.2. The methylene carbon signal of the pyrazoline ring resonated at 84. The signal at 42 was assigned to C-3 of the pyrazoline ring. The benzylic carbon of the tetralone ring appeared at 28.1, while the other methylene resonated at 25.1.

The IR spectrum of the complex **28b** had characteristic bands at 1980, 1990 (Cr-CO), 1670 (-CO-) and 1520 (-N=N-).

The downfield resonances in the ^{1}H NMR spectrum were assigned to the uncomplexed aromatic ring protons which appeared as two separate multiplets between 7.4 - 7.2 and 7 - 6.85 in the ratio 2:3. The complexed aromatic protons appeared in the expected region. The signals of N-CH_2-C protons of the pyrazoline ring presented a complex patttern compared to the other diastereomer. They appeared as a multiplet centred at 4.95. The methine proton of the pyrazoline ring also appeared as a multiplet at 3.55. The assignments were

MR. S. GANESH/SG(DIB)/COSY-45

27b



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SGDIBPR.001
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COSY.AU
DATE 27-5-92

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SI1 512
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SW1 621.891
NDO 1

WDW2 S
WDW1 S
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SSB1 0
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F2 1.396P
AND COLUMN:
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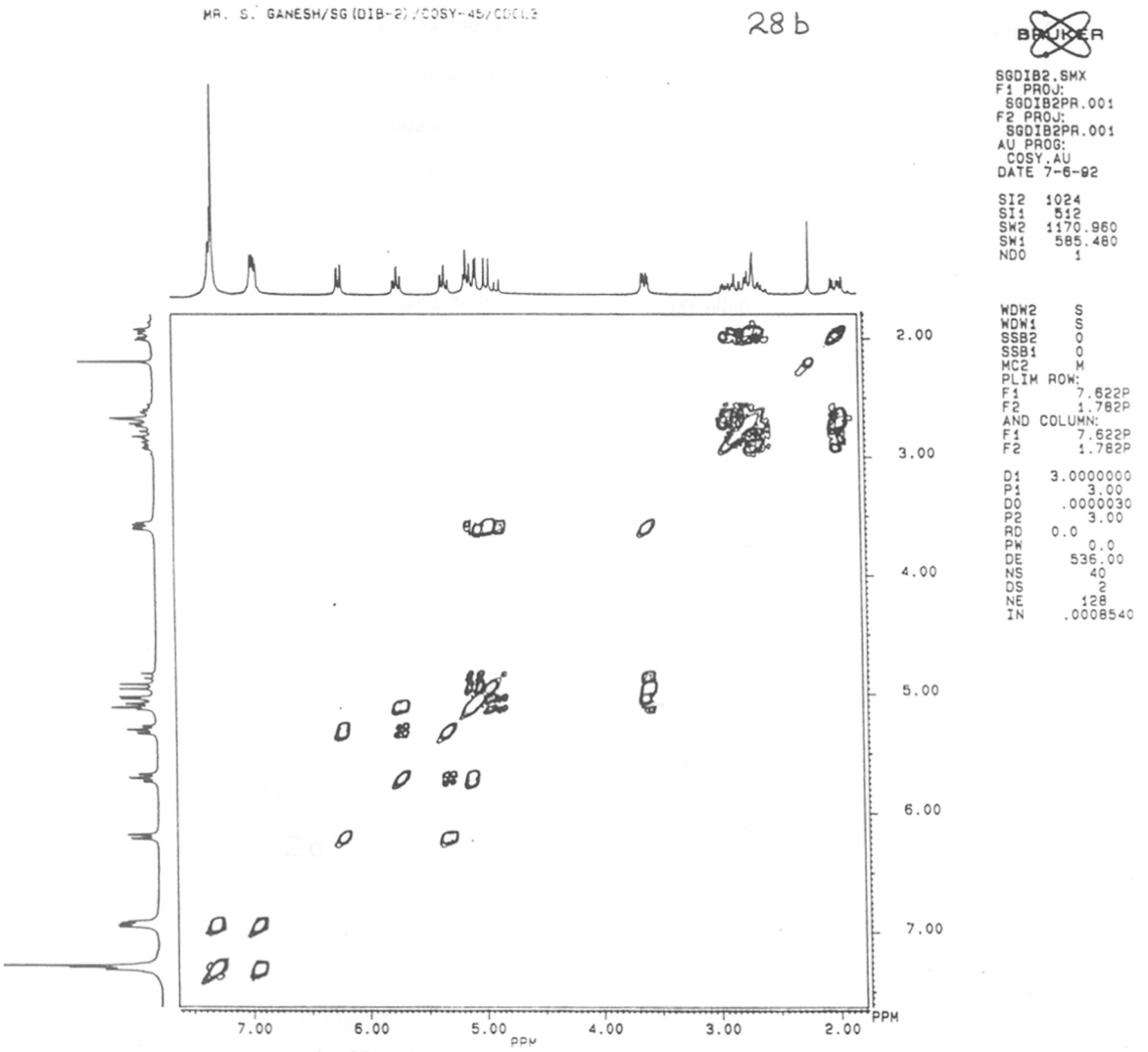
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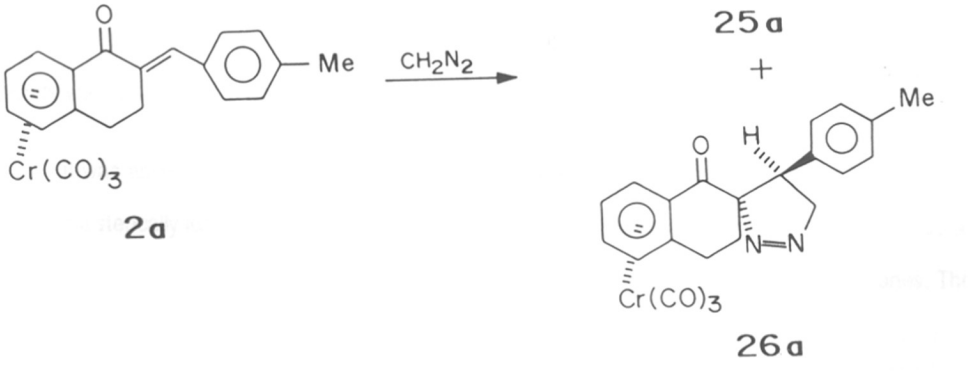
based on the COSY spectrum. The benzylic protons of the tetralone ring and one of the protons of the other methylene appeared as a multiplet together in the region 2.95 - 2.5. The other methylene proton resonated as a multiplet between 2.0 - 1.9.

The ^{13}C NMR of the complex exhibited downfield signals corresponding to (Cr-CO) and (-CO-) at 230.0 and 190.0 respectively. The uncomplexed aromatic carbons resonated between 138.2 to 128. The complexed aromatic signals appeared in the usual region 88.6 - 114.7. The signal at 99 was assigned to the C-2 centre, while CH_2 of the pyrazoline ring appeared at 85.0. The C-3 carbon signal resonated at 45. The tetralone methylenes appeared at 27 and 24.7.

The complex **2a** under similar reaction conditions provided the products **25a** and **26a** respectively, in combined yield of 82%, the ratio of diastereomers being 77:23.

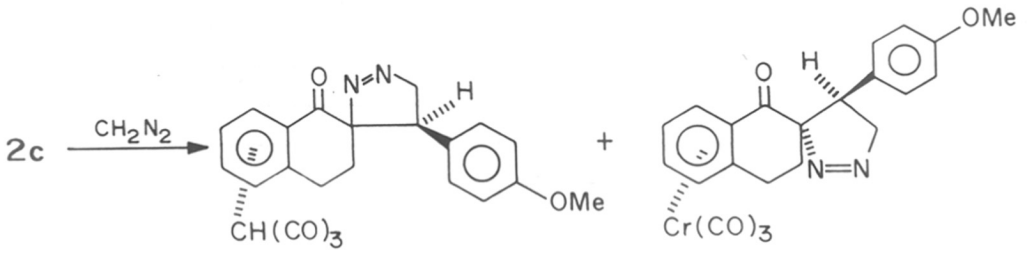


The complex **25a** exhibited characteristic IR bands. The spectral pattern was very similar to **27b**. The uncomplexed aromatic ring being 1,4 disubstituted showed the characteristic AB quartet at 7.1 and 6.85.

The ^{13}C NMR spectrum showed resonances in the expected region. The signal at 20.8 was assigned to the methyl group.

The complex **26a** had spectral features that resembled the spectrum of compound **28b**.

The complex **2c** was treated with diazomethane using similar reaction condition as before. The products **29c** and **30c** could be separated (combined yield 88%) using flash chromatography. The diastereomeric ratio was found to be 79:21.



29c **30c**

The spectral pattern of the compound **29c** and **30c** matched well with the previous compounds obtained for both the series (major and minor). All the signals could be assigned unambiguously. The compounds were also found to be analytically pure.

It was assumed at this point that the major isomer was the *exo* adduct while the minor isomer resulted from a sterically less favourable *endo* addition. If these compounds would provide cyclopropanes on thermolysis, attempts could be made to correlate their stereochemistry with those of the cyclopropanes. The *endo* cyclopropanes have been described in the previous chapter.

In order to explore this possibility, the diasteroisomeric complexes were individually heated under reflux in a solvent mixture containing EtOAc and Isooctane (1:15) (Ethyl acetate was necessary to ensure dissolution of the complexes). The results are summarised in Table 1 and 2. It was observed that each

diastereoisomeric pair provided the same product, which was identified as β-methyl-2-arylidene-1-tetralone with *E* configuration of the olefin. To investigate whether a change in solvent polarity would lead to new decomposition pathway, different solvents, viz. benzene, toluene, ethylene dichloride were used. The complex **25a** was used for this study and the results are summarised in Table 2.

Table 1

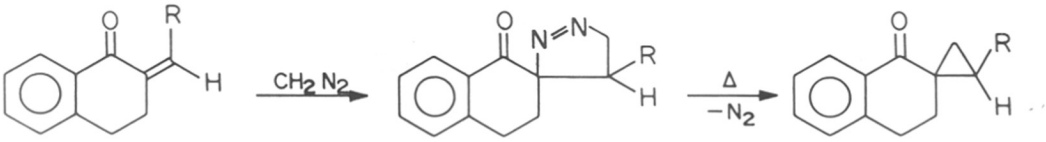
Substrate	Solvent	Temperature	Time	Product	% of Product
27 b	EtoAc (1 ml) Isooctane (15 ml)	100°C	8h	32	88.5
28 b	"	100°C	8h	32	85
25 a	"	"	"	31	81
26 a	"	"	"	31	75
29 c	"	"	"	33	80
30 c	"	"	"	33	85

Table 2

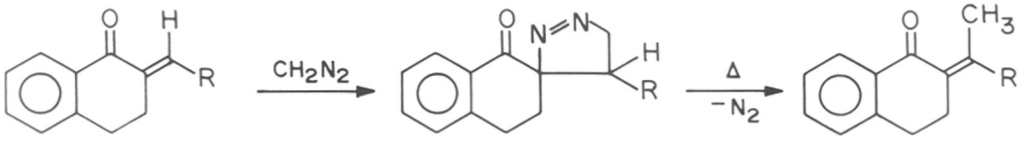
Substrate	Solvent	Temperature	Time	% of product
25a	Benzene	80°C	8 h	76
25a	Toluene	110°C	3 h	84
25a	Ethylene dichloride	83°C	8 h	81

The ^{1}H NMR spectra of the enone complexes (**31-33**) were simpler than the parent pyrazoline complexes. The two tetralone methylenes appeared between 2.5 - 3.00 and the β-methyl singlet at 2.45 were the common features in all of them. Additional signals corresponding to the aromatic substituents were observed in the usual region. The ^{13}C NMR spectra were also consistent with the structures. Formation of olefins from pyrolysis of pyrazolines are well documented[4]. Concurrent to the present work, a Hungarian research group was investigating the chemistry of similar spiro pyrazoline[5,6] and made similar observations.

According to this report, from *E*-olefins cyclopropanes were also observed as minor products (6-18%). We could not detect any trace of cyclopropane in our reaction mixture.



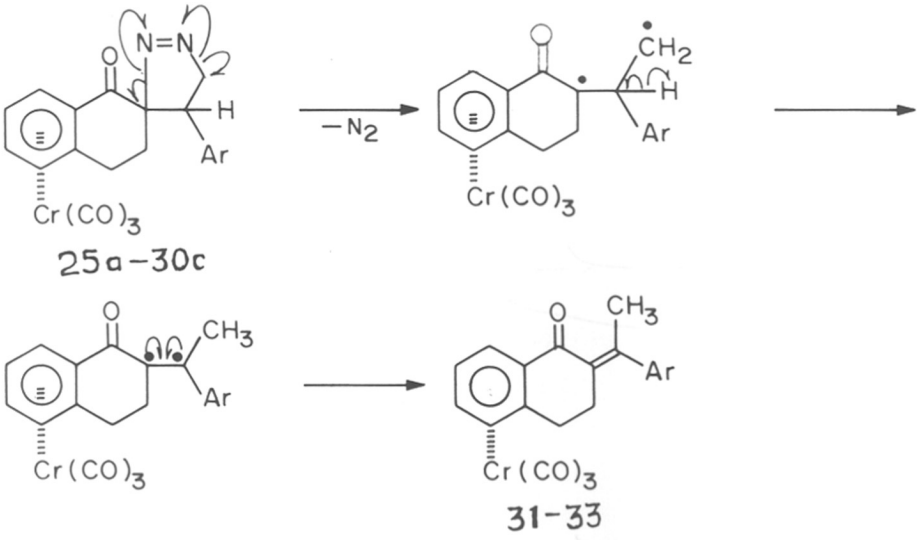
Z - Olefin



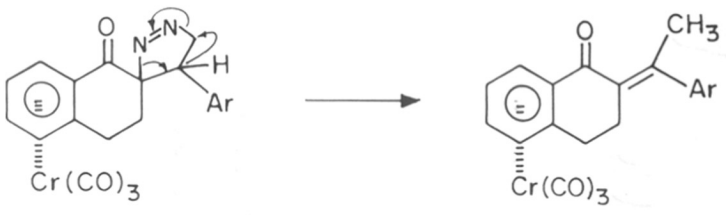
E - Olefin

Major

Biradical intermediates have been frequently proposed for the extrusion of N_2 from the spiro pyrazolines[5].



The benzylic stabilization of the intermediate radical could facilitate the rearrangement. The radicals, if formed in the present case, remained carbon-centered and did not interfere with the complexed metal. In an attempt to trap the proposed radical, thermolysis was carried out in toluene-d^8. No deuterium incorporation was observed in the product. This would indicate either a) the radicals were extremely short-lived, or b) the rearrangement occurred by a synchronous process. Alternatively, an ionic mechanism could be envisaged as follows:

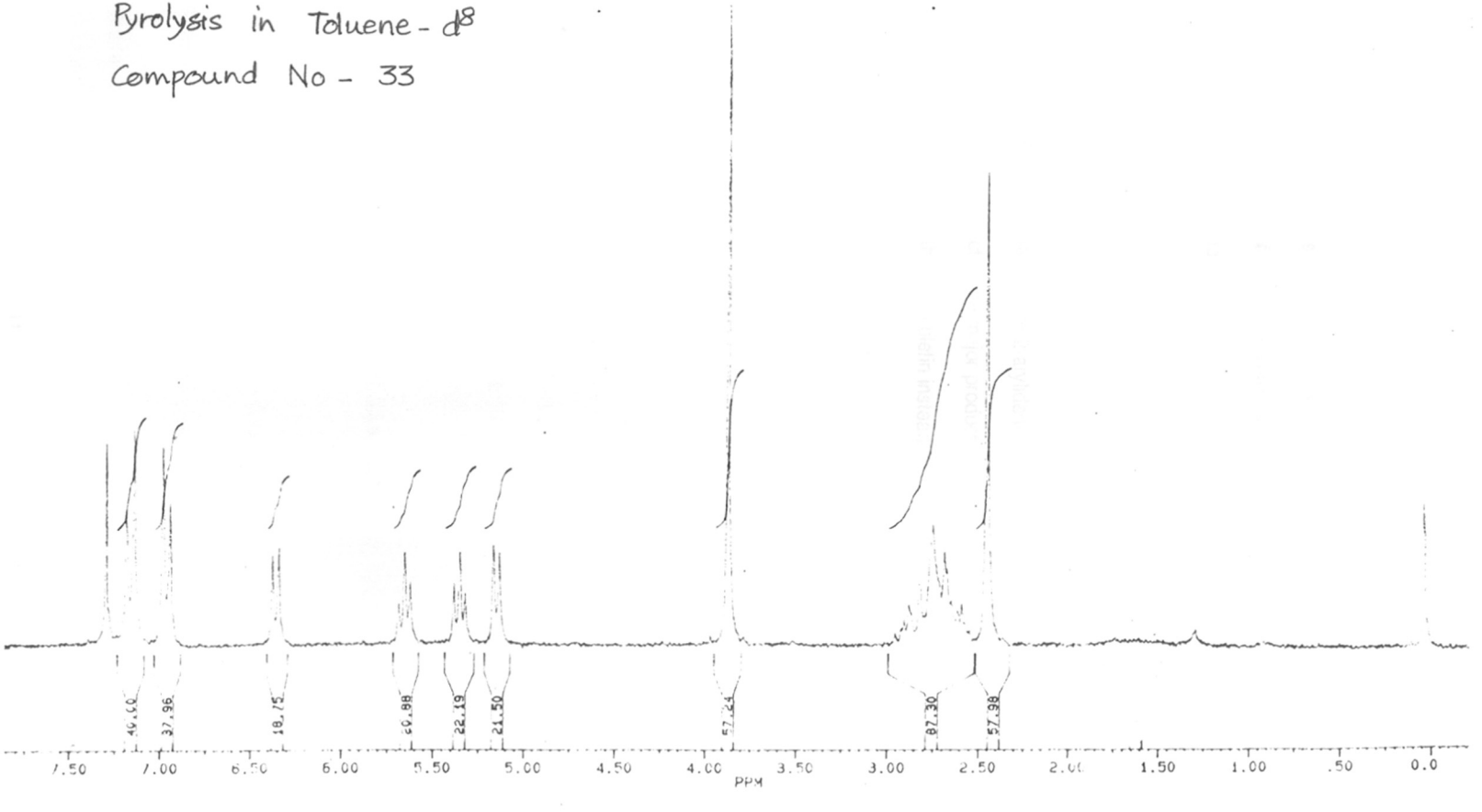


(Deuterium)

MR. GANESH/DIPOMD/CDCL3

Pyrolysis in Toluene-d^8

Compound No - 33



However, ionic intermediates are less likely in such reactions. Solvents too did not have any significant effect on the thermolysis. Formation of the same olefinic product from different stereoisomeric pyrazolines is more consistent with a radical mechanism.

SUMMARY

1,3-Dipolar cycloaddition of diazomethane to the 2-arylidene-1-tetralone $Cr(CO)_3$ complexes led to an unequal mixture of diastereoisomeric products. The major product has been proposed to be the *exo* adduct. Both the isomers, on thermolysis, yielded the same olefin instead of a cyclopropane.

EXPERIMENTAL :

General procedure for diazomethane addition to the complexes 2a - c :

To a solution of the complex **2a - c** (1mmol) in diethyl ether (10ml) cooled in an ice bath, diazomethane [generated in diethyl ether (15ml) from nitrosomethyl urea (8mmol) and 50% aqueous KOH (6ml)] was added in a portion. The solution was stirred at room temperature overnight. After usual work up, the crude solid product obtained as a diasteromeric mixture, was subjected to flash column chromatography using gradient elution (10% EtoAc - pet ether to 40% EtOAc - pet ether). The less polar fraction provided the major isomer while the polar fraction afforded the minor isomer.

Reaction of 2b : From the reaction of diazomethane with the complex **2b** (369mg, 1mmol) a crude semisolid was obtained. With 20% EtoAc - pet ether, the major isomer **27b** (276mg) and minor isomer **28b** (70mg), were isolated (84%).

Spectral data for the major diastereomer

m.p. : 140°C

IR : 1980, 1910, 1670, 1530

^{1}H NMR : 1.55 - 1.90 (m, 2H), 2.55 - 2.70 (m, 1H), 3.60 - 3.80 (m, 1H), 4.07 (t, 1H, J = 7Hz), 5.10 (d, 1H, J = 6Hz), 5.22 (d, 1H, J = 6Hz), 5.40 (t, 1H, J = 6Hz), 5.70 (t, 1H, J = 6Hz), 6.95 - 7.05 (m, 2H), 7.25 - 7.4 (m, 3H).

^{13}C NMR : 25.1, 28.1, 41.9, 83.9, 89.1, 89.3, 90.7, 90.9, 93.9, 99.7, 114.2, 126.7, 127.4, 128.0, 136.7, 190.1, 229.7.

Analysis : Calc : C = 61.30, H = 3.89, N = 6.81

: Obs : C = 60.99, H = 3.72, N = 6.69

Spectral data for the minor diastereomer

m.p. : 145 - 146°C

IR : 1980, 1910, 1670, 1530

^{1}H NMR : 1.90 - 2.00 (m, 1H), 2.50 - 2.95 (m, 3H), 3.50 - 3.60 (m, 1H), 4.80 - 5.05 (m, 2H), 5.10 (d, 1H, J = 6Hz), 5.30 (t, 1H, J = 6Hz), 5.70 (t, 1H, J = 6Hz), 6.20 (d, 1H, J = 6Hz), 6.85 - 7.00 (m, 2H), 7.20 - 7.40 (m, 3H).

^{13}C NMR : 24.7, 26.9, 44.9, 84.9, 88.6, 90.1, 91.4, 94.2, 98.9, 114.7, 127.7, 128.0, 128.7, 138.2, 190.0, 229.9.

Analysis : Calc : C = 61.30, H = 3.89, N = 6.81

: Obs : C = 60.70, H = 3.90, N = 7.05

Reaction of 2a : Complex **2a** (383mg, 1mmol) under similar conditions afforded the major isomer **25a** (269mg) and minor isomer **26a** (79mg), in 82% combined yield.

Spectral data for the major diastereomer

m.p. : 109°C

IR : 1980, 1920, 1670, 1520

^{1}H NMR : 1.55 - 1.90 (m, 3H), 2.30 (s, 3H), 2.50 - 2.70 (m, 1H), 3.60 - 3.80 (m, 1H), 4.00 (t, 1H, J = 6Hz), 5.07 (d, 2H, J = 6Hz), 5.20 (d, 1H, J = 6Hz), 5.40 (t, 1H, J = 6Hz), 5.70 (t, 1H, J = 6Hz), 6.15 (d, 1H, J = 6Hz), 6.82 (d, 2H, J = 9Hz), 7.15 (d, 2H, J = 9Hz).

^{13}C NMR : 20.8, 25.8, 28.7, 42.2, 84.8, 89.7, 89.9, 91.5, 94.5, 100.3, 114.8, 127.9, 129.3, 134.3, 137.0, 190.9, 230.3.

Analysis : Calc : C = 62.10, H = 4.23, N = 6.58

: Obs : C = 62.41, H = 4.35, N = 6.72

Spectral data for the minor diastereomer

m.p. : 141°C

IR : 1980, 1910, 1670, 1520

^{1}H NMR : 1.90 - 2.05 (m, 1H), 2.30 (s, 3H), 2.55 - 2.90 (m, 3H), 3.45 - 3.55 (m, 1H), 4.75 - 5.05 (m, 2H), 5.10 (d, 1H, J = 6Hz), 5.3 (t, 1H, J = 6Hz), 5.70 (t, 1H, J = 6Hz), 6.20 (d, 1H, J = 6Hz), 6.80 (d, 2H, J = 9Hz), 7.10 (d, 2H, J = 9Hz).

^{13}C NMR : 20.8, 24.6, 26.7, 44.7, 84.9, 88.7, 88.8, 90.1, 91.5, 94.5, 98.6, 114.8, 127.8, 129.3, 134.9, 137.5, 190.1, 230.0.

Analysis : Calc : C = 62.10, H = 4.23, N = 6.58

: Obs : C = 62.48, H = 4.37, N = 6.76

Reaction of 2c : From the reaction of complex **2c** (399mg, 1mmol) a semisolid residue was isolated. With 90% EtoAc - pet ether, the major isomer **29c** (310mg) and minor isomer **30c** (82mg) were separated (88%).

Spectral data for the major diastereomer

m.p. : 122°C

IR : 1990, 1910,1670, 1520

^{1}H NMR : 1.55 - 1.95 (m, 3H), 2.55 - 2.70 (m, 1H), 3.60 - 3.75 (m, 1H), 3.80 (s, 3H), 4.00 (t, 1H, J = 6Hz), 5.05 (d, 2H, J = 6Hz), 5.22 (d, 1H, J = 6Hz), 5.40 (t, 1H, J = 6Hz), 5.70 (t, 1H, J = 6Hz), 6.15 (d, 1H, J = 6Hz), 6.80 - 6.90 (bs, 4H).

^{13}C NMR : 24.7, 26.7, 44.4, 55.1, 85.0, 88.6, 88.7, 90.1, 91.5, 94.3, 98.7, 114.1, 114.8, 129.0, 130.0, 159.0, 190.0, 230.0.

Analysis : Calc : C = 59.86, H = 4.08, N = 6.34

: Obs : C = 59.89, H = 3.82, N = 6.60

Spectral data for the minor diastereomer

m.p. : 140°C

IR : 1980, 1910, 1670, 1520

^{1}H NMR : 1.90 - 2.05 (m, 1H), 2.50 - 2.90 (m, 3H), 3.45 - 3.55 (m, 1H), 3.80 (s, 3H), 4.75 - 5.00 (m, 2H), 5.10 (d, 1H, J = 6Hz), 5.30 (t, 1H, J = 6Hz), 5.70 (t, 1H, J = 6Hz), 6.20 (d, 1H, J = 6Hz), 6.75 - 6.85 (bs, 4H).

^{13}C NMR : 25.7, 28.6, 41.9, 55.0, 84.8, 89.7, 90.0, 91.4, 94.5, 100.3, 114.1, 114.9, 129.0, 129.3, 158.8, 190.9, 230.3.

Analysis : Calc : C = 59.86, H = 4.08, N = 6.34

: Obs : C = 59.65, H = 3.90, N = 6.60

Reaction of 2-benzylidene 1-tetralone : Following the above procedure, reaction of the enone **2e** (234mg, 1mmol) and diazomethane was completed by overnight. After usual workup, the semisolid residue was loaded on a silica gel (60 - 120mesh) column. Elution with 20% EtoAc - pet ether afforded the product (248mg, 90%), as a white crystalline solid. The spectral characteristics were similar to the reported values.

General procedure for pyrolysis of pyrazolines : The diastereomers of the chromium complexed pyrazolines **(25a,26a)**, **(27b,28b)**, and **(29c,30c)** (0.1mmol) dissolved in a solvent mixture [EtoAc (1ml) and

Isooctane (15ml] were individually heated under reflux for 8h. The product and starting material were separated on a flash column using 20% EtoAc - pet ether. The less polar fraction afforded the product while the polar fraction furnished the starting material. The yields are based on consumed starting material.

Reaction of 25a : The complex **25a** (42mg, 0.1mmol) on reflux for 8h provided the product **31** (31mg) (88.5%) and the starting material (4mg).

Reaction of 26a : Under similar conditions **26a** afforded the product **31** (29mg) (85%) and the starting material (4.8mg).

m.p. : 138°C

IR 1970, 1900, 1660, 1610

^{1}H NMR : 2.45 (s, 3H), 2.50 (s, 3H), 2.55 - 3.00 (m, 4H), 5.15 (d, 1H, J = 6Hz), 5.35 (t, 1H, J = 7Hz), 5.65 (t, 1H, J = 7Hz), 6.35 (d, 1H, J = 6Hz), 7.1 (d, 2H, J = 9Hz), 7.25 (d, 1H, J = 9Hz).

^{13}C NMR : 21.0, 23.5, 28.6, 29.0, 89.1, 89.6, 92.0, 94.4, 114.7, 127.0, 129.0, 137.4, 140.0, 151.0, 188.0, 231.0.

Analysis : Calc : C = 66.49, H = 4.53

: Obs : C = 66.84, H = 4.59

Reaction of 27b : The complex **27b** (41mg, 0.1mmol) furnished the product **32** (27.6mg, 81%) and the starting material (4mg).

Reaction of 28b : The complex **28b** (41mg, 0.1mmol) provided the product **32** (25mg) (75%) and the starting material (5mg)

m.p. : 159 - 160°C

IR 1980, 1900, 1670, 1610

^{1}H NMR : 2.45 (s, 3H), 2.55 - 3.00 (m, 4H), 5.15 (d, 1H, J = 6Hz), 5.35 (t, 1H, J = 6Hz), 5.65 (t, 1H, J = 6Hz), 6.35 (d, 1H, J = 6Hz), 7.10 - 7.20 (m, 5H).

^{13}C NMR : 23.5, 28.5, 29.0, 89.0, 89.5, 92.0, 94.5, 95.3, 114.7, 127.0, 127.4, 127.8, 128.4, 129.1, 143.0, 150.6, 188.0, 231.0.

Analysis : Calc : C = 65.79, H = 4.17

: Obs : C = 65.93, H = 4.26

Reaction of 29c : The complex **29c** (44mg, 0.1mmol) afforded the product **33** (30mg, 80%) and the starting material (3.5mg).

Reaction of 30c : The complex **30c** (44mg, 0.1mmol) yielded the product **33** (32mg, 85%) and the starting material (4.1mg).

m.p. : 120 - 122°C

IR : 1970, 1900, 1650, 1600

^{1}H NMR : 2.45 (s, 3H), 2.55 - 2.95 (m, 4H), 3.85 (s, 3H), 5.15 (d, 1H, J = 6Hz), 5.35 (t, 1H, J = 7Hz), 5.65 (t, 1H, J = 7Hz), 6.35 (d, 1H, J = 6Hz), 6.95 (d, 2H, J = 9Hz), 7.20 (d, 2H, J = 9Hz).

^{13}C NMR : 20.8, 24.8, 27.5, 49.0, 88.7, 89.0, 91.5, 92.1, 94.6, 114.2, 128.0, 129.5, 133.6, 137.6, 196.0, 230.0.

Analysis : Calc : C = 63.90, H = 4.35

: Obs : C = 63.54, H = 4.67

General procedure for pyrolysis of the complex 25a in different solvents : A solution of the complex 10b (0.1mmol) in various solvents (C_6H_6, EDC, toluene, toluene-d^8) was heated under reflux for 3 - 8h (monitored by TLC) the semisolid residue, obtained after removal of solvent, was subjected to flash column chromatography (20% EtoAc - pet ether) to separate the product and the starting material. The results are summarised in Table **1** and **2**.

Pyrolysis in benzene as solvent : Solution of the complex **25a** (42mg, 0.2mmol) in benzene (15ml) was heated under reflux for 8h to afford starting material (5 mg) and product (26mg, 76%).

Pyrolysis in Toluene-d^8 : A solution of the complex (22mg) in toluene (2.0ml) heated under reflux for 3h to afford the product (15mg, 90%) and traces of starting material was obtained.

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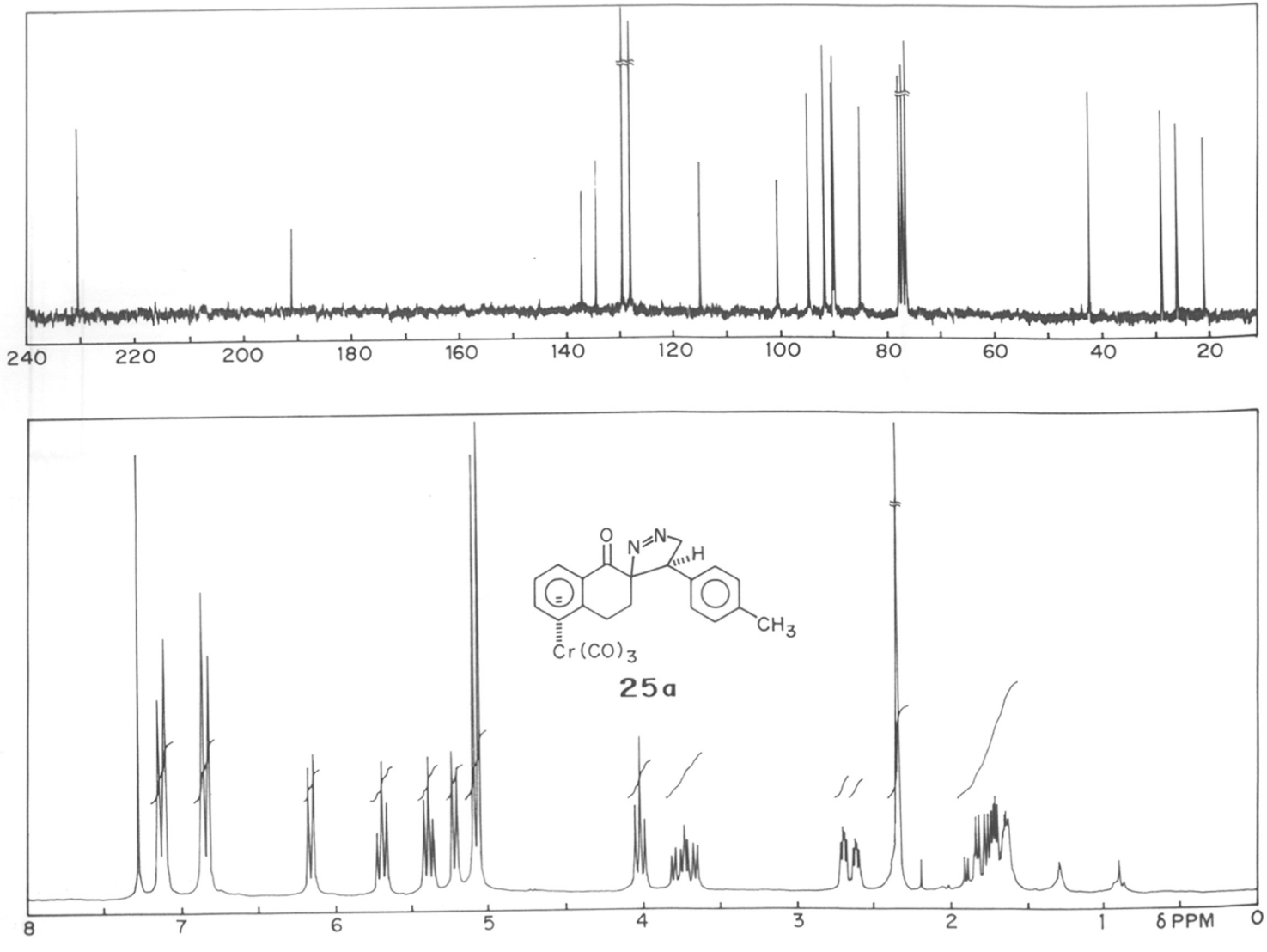
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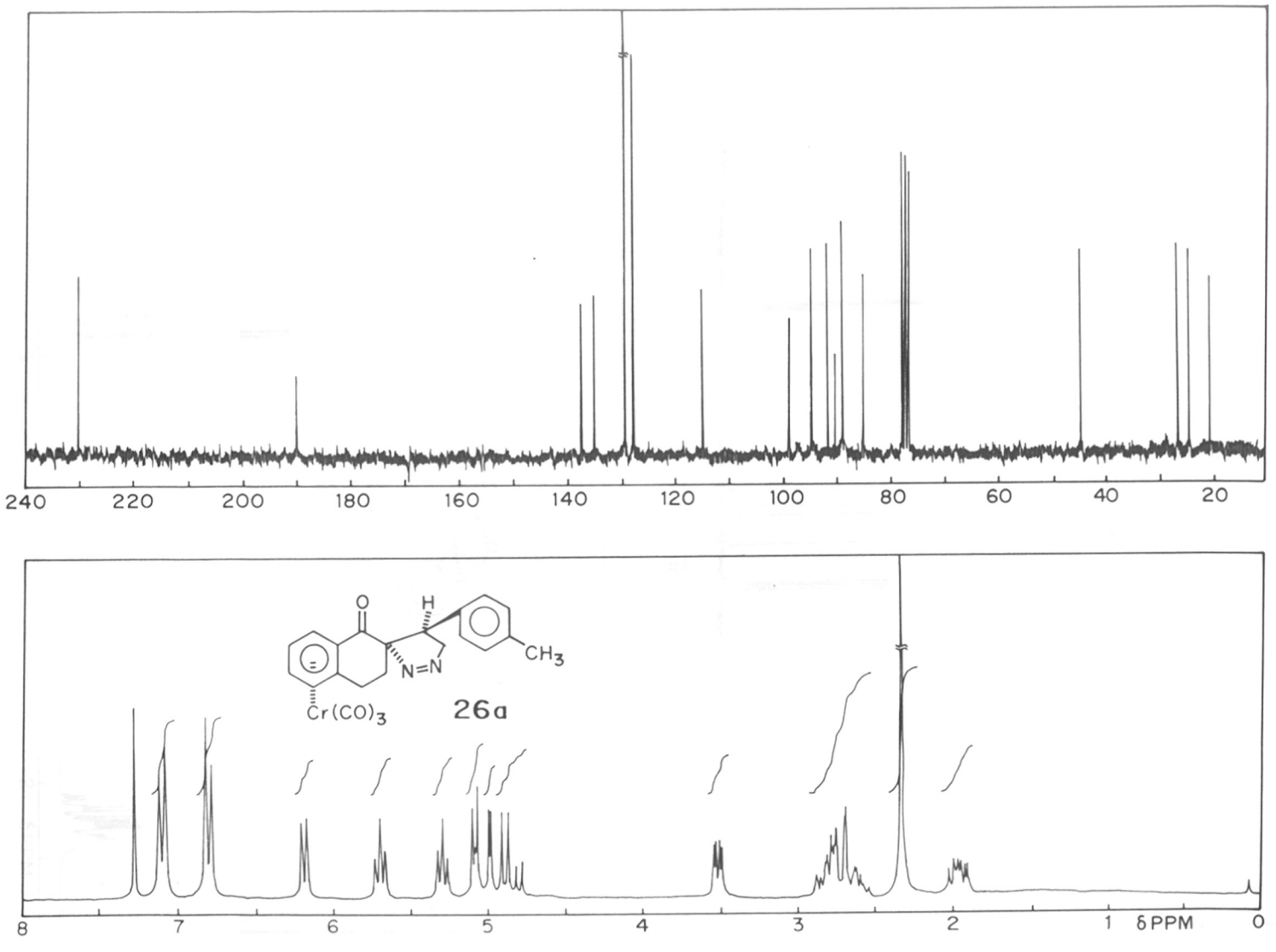
25a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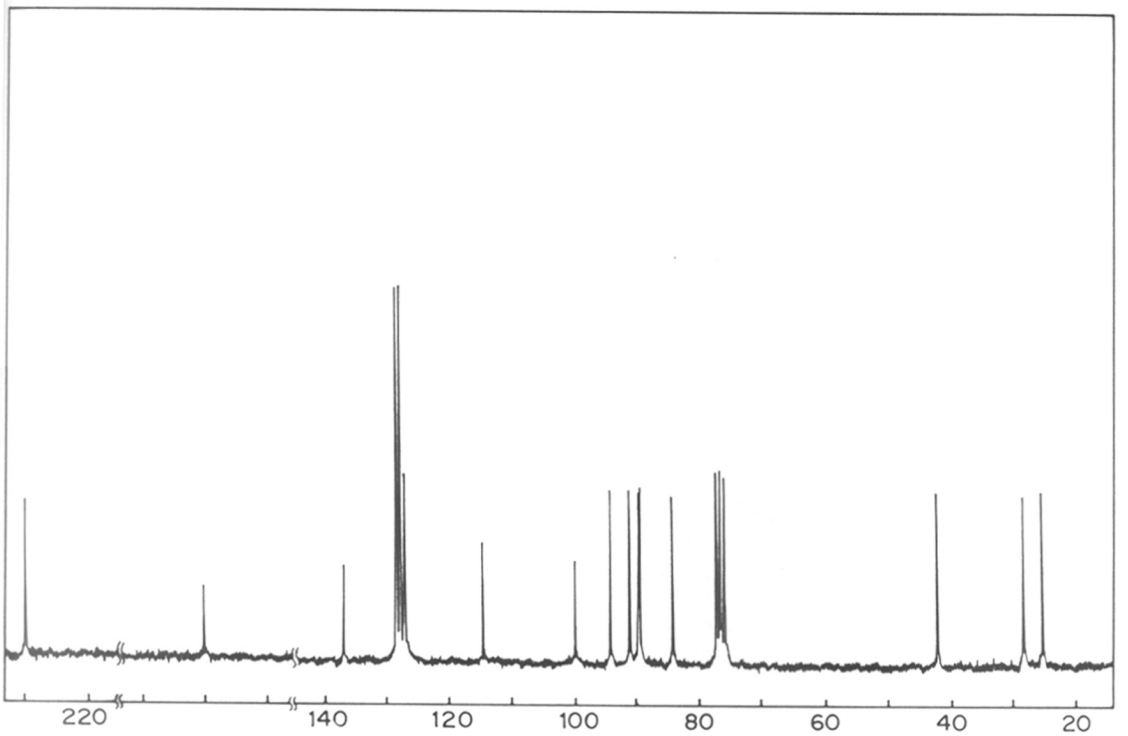

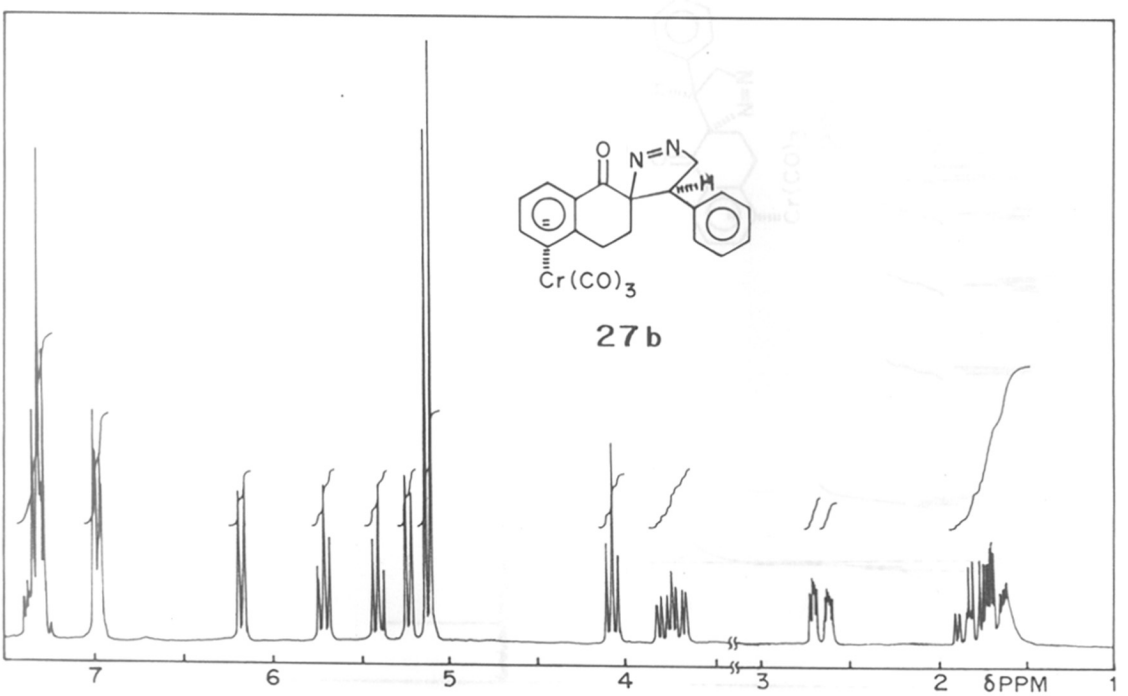

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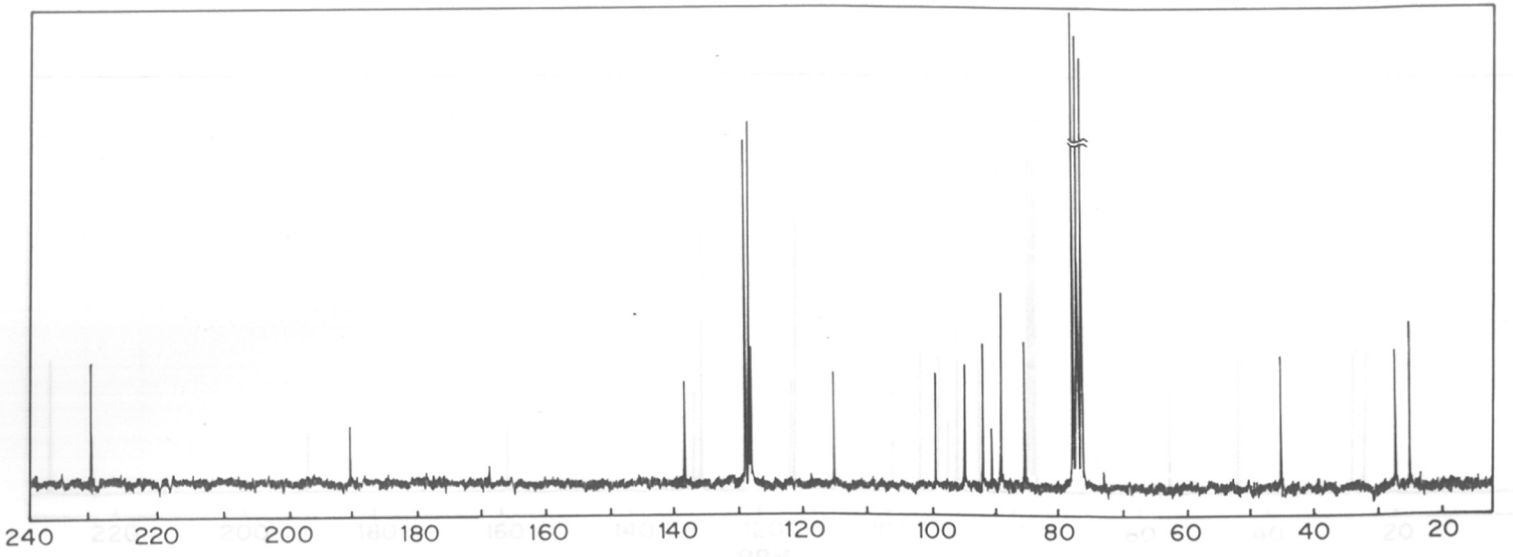
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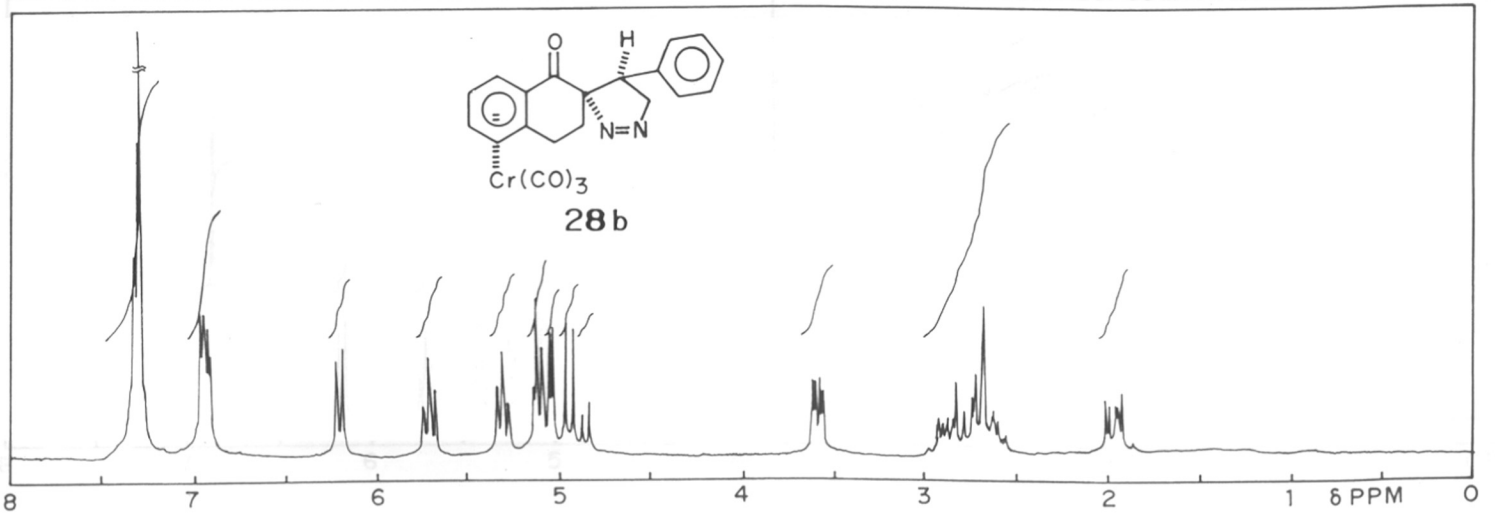
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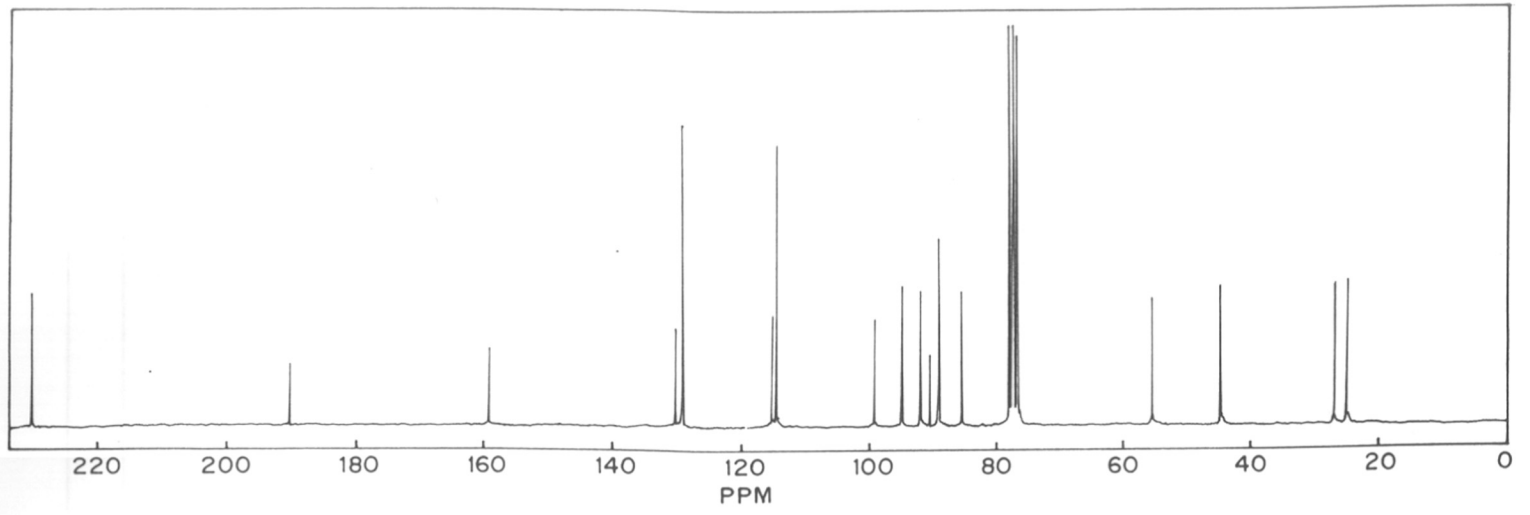
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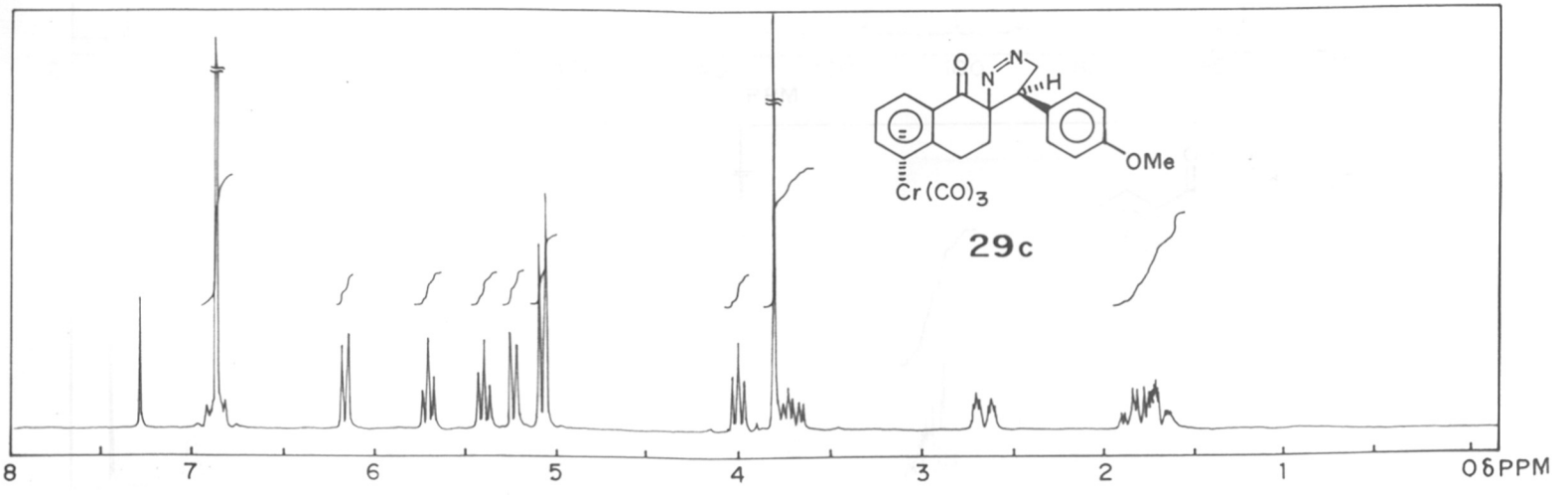
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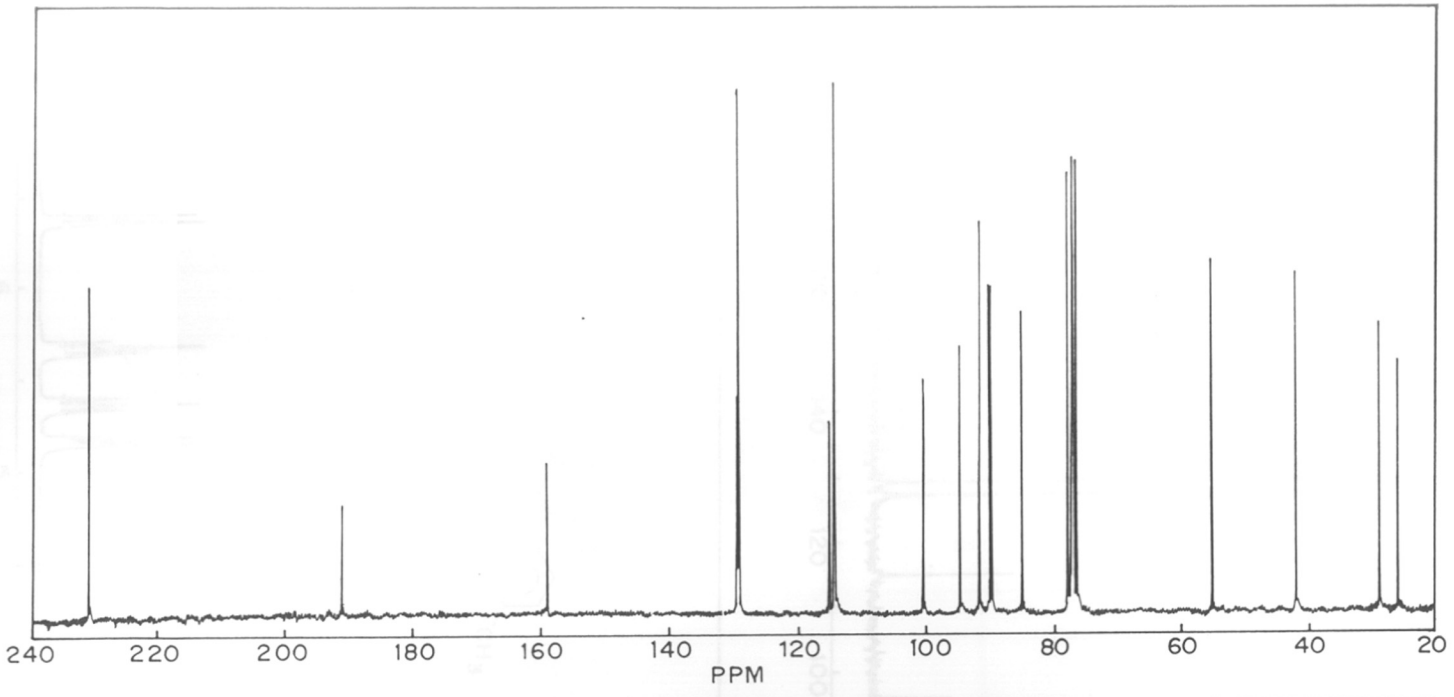
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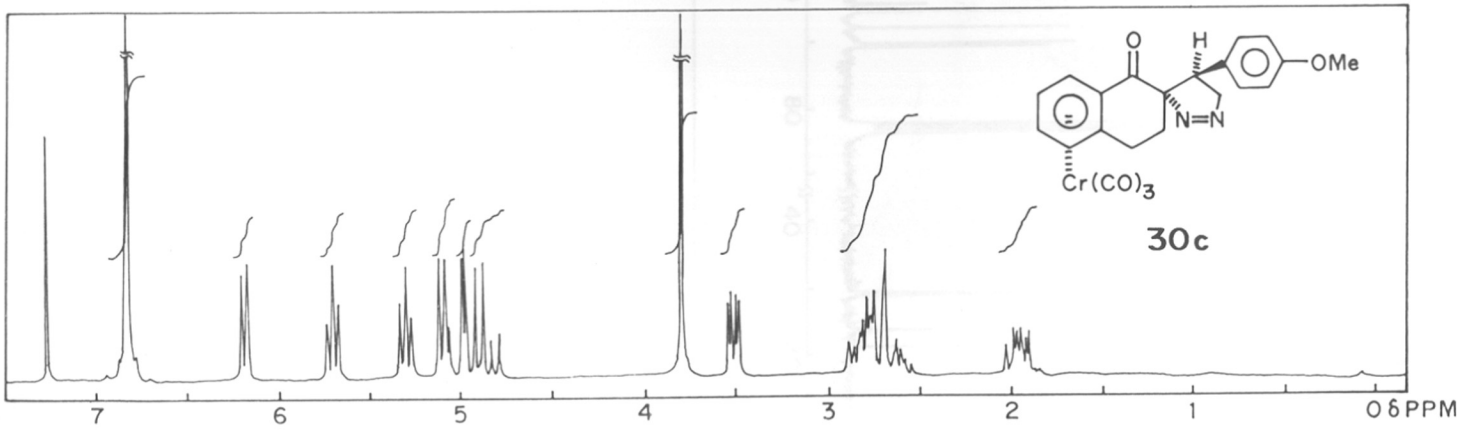
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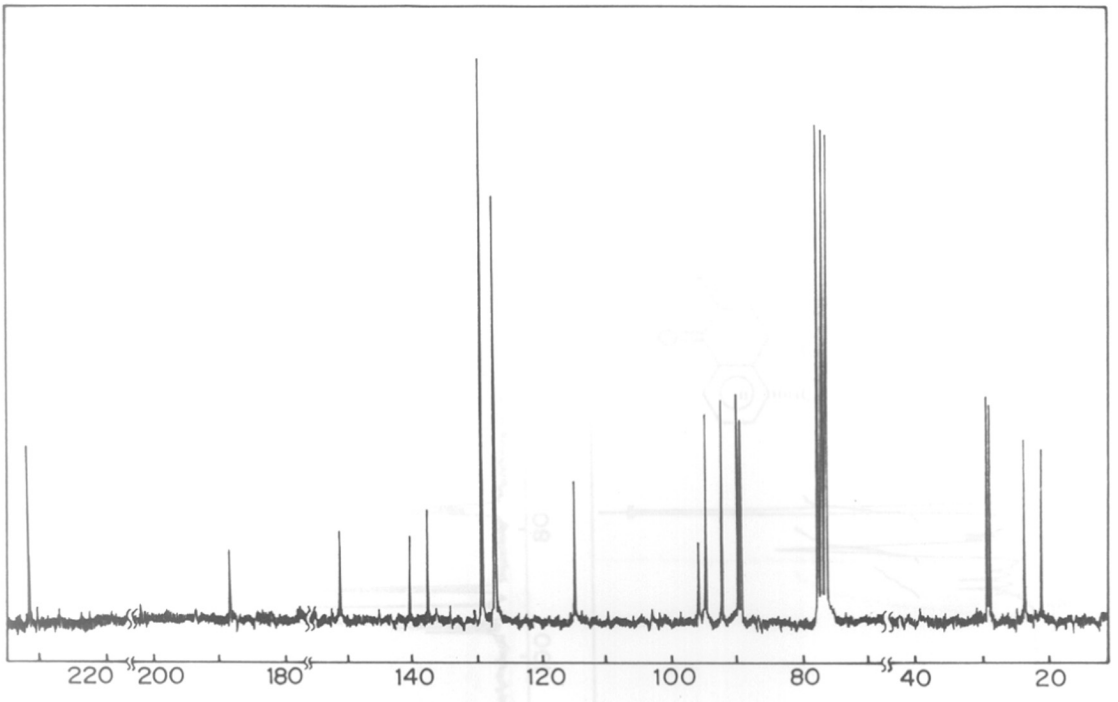

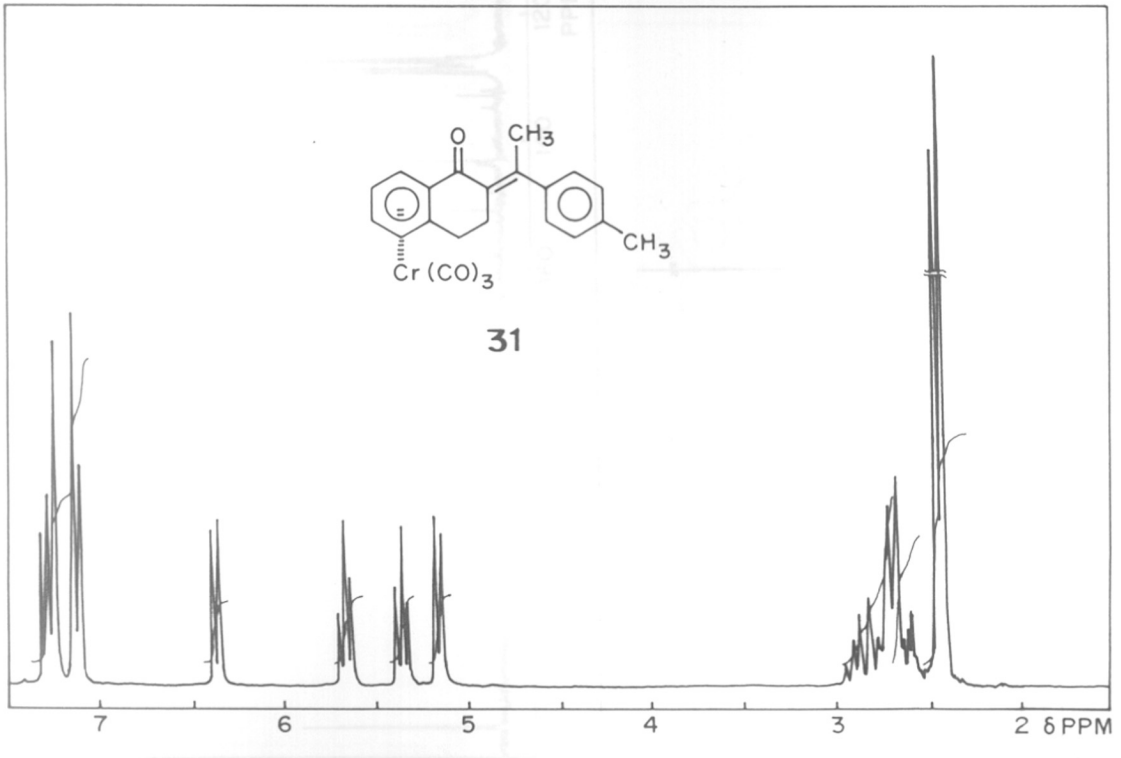

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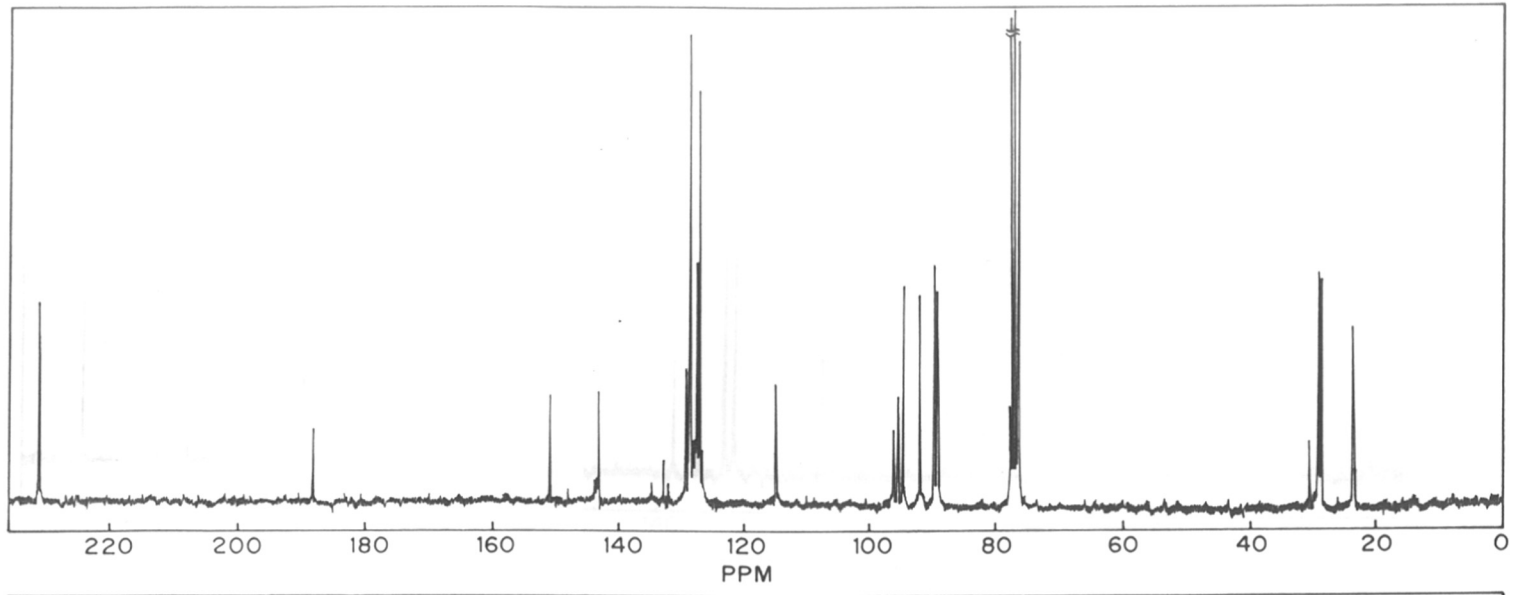
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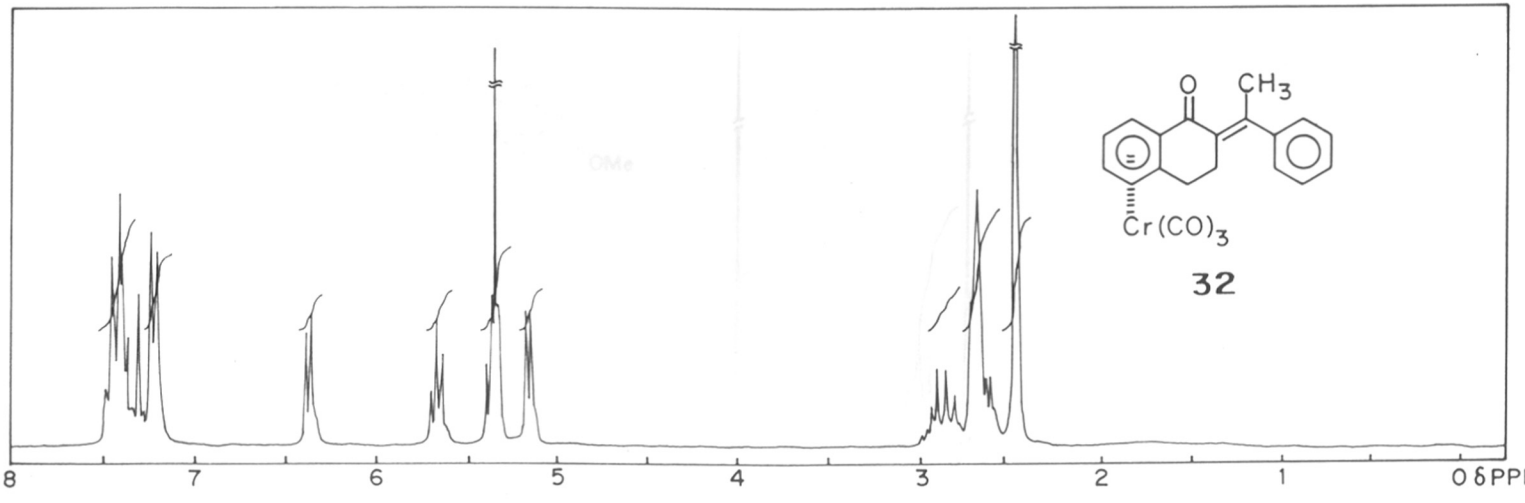
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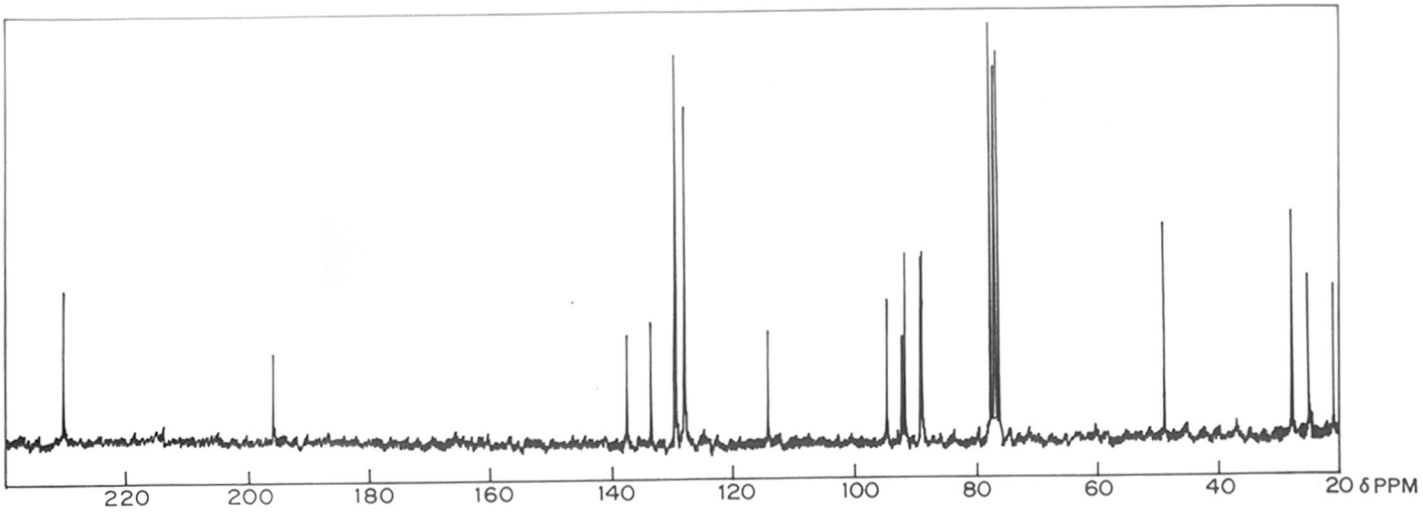
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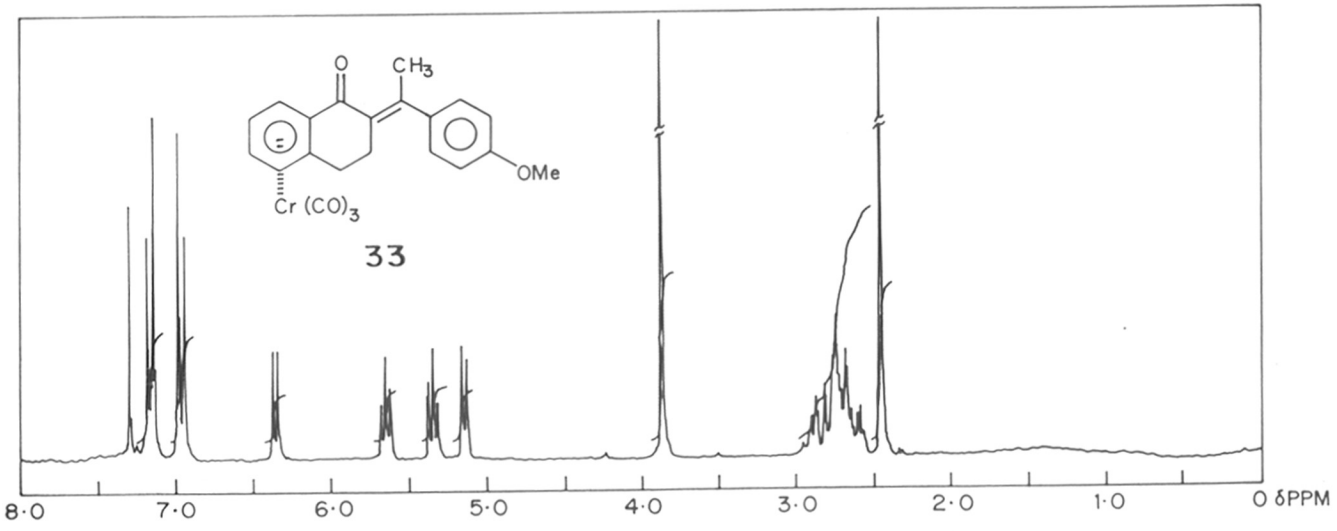
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33