Development of Organotitanium Reagents: Applications of Titanium Arylamine, Enolate and Enamine Derivatives in Organic Synthesis

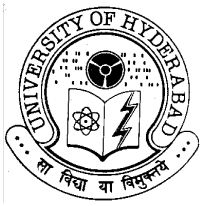
A Thesis

Submitted for the Degree of

DOCTOR OF PHILOSOPHY

By

Kishorebabu Neela



SCHOOL OF CHEMISTRY
UNIVERSITY OF HYDERABAD
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July 2006

To
My Teachers
&
Family members

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Statement

I hereby declare that the matter embodied in this thesis is the result of investigations carried out by me in the School of Chemistry, University of Hyderabad, Hyderabad, under the supervision of Professor M. Periasamy.

In keeping with the general practice of reporting scientific observations, due acknowledgement has been made wherever the work described is based on the findings of other investigators.

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Certificate

Certified that the work embodied in this thesis entitled '**Development of Organotitanium Reagents: Applications of Titanium Arylamine, Enolate and Enamine Derivatives in Organic Synthesis**' has been carried out by Mr. Kishorebabu Neela, under my supervision and the same has not been submitted elsewhere for a Degree.

PROFESSOR M. PERIASAMY

(THESIS SUPERVISOR)

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Acknowledgements

I wish to express my deep sense of gratitude with profound respect to my supervisor **Prof. M. Periasamy** for his inspiring guidance, constant encouragement and personal motivation throughout my tenure here. I will always be indebted to him for this.

I am grateful to Prof. M. Nagarajan, Prof. G. R. Desiraju and Prof. E. D. Jemmis, Deans, School of Chemistry, for providing all facilities to carry out my research work. I thank Prof. D. Basavaiah for his generous help in many ways. I would like to place on record my appreciation and gratitude to the faculty members of the School of Chemistry for their help throughout my stay here.

I would like to thank the Director, IICT, Hyderabad and Dr. M. Vairamani, Mass Spectroscopy group, IICT, for providing the mass spectra for some of the compounds.

I would like to thank my colleagues Dr. K. N. Jaya Kumar and Mr. P. Vairaprakash for their help and extreme cooperation during my thesis work. I extend my heartfelt thanks to my past and present labmates Dr. V. Dharma Rao, Dr. G. Srinivas, Dr. S. Sivakumar, Dr. N. Sampath Kumar, Mr. G. V. Karunakar, Dr. A. Mukkanti, Dr. M. Seenivasaperumal, Dr. M. Narsi Reddy, Dr. S. Suresh, Dr. M. Padmaja, Mr. D. Shyam Raj, Mr. G. P. Muthukumara Gopal, Mr. Shaik Anwar, Mr. S. Selva Ganesan, Mr. S. Sathish Kumar, Mr. M. Nagaraju, Mr. B. Mallesh and Mr. N. Sanjeeva Kumar for creating a pleasant work atmosphere.

All the research scholars of the School of Chemistry have been extremely helpful and I thank them all. A special note of thanks to Mr. Jorly and Mr. Prasad for their timely help regarding my research work. I also thank all of my friends in this campus that made my stay a memorable one.

I would like to thank Mr. Kishore, Mr. Praveen, Mr. Santhosh Kumar, Mr. Nataraj, Mr. Ravi Prakash, Mr. Shyam, Mr. Jaya Raju, Mr. Rama Krishna, Mr. Ravi, Mr. Masthan, Mr. Sudeep, Mr. Viswanathan, Mr. Joseph, Mr. Katema and all others for their prayers during my stay in this campus. I thank Mr. Dandamudi Lenin Babu, Mr. Nageswera Rao and Mr. Israel for their help and encouragement.

I wish to express my deep sense of gratitude to Pastor Abraham K. D. S. and all the church members (House of Prayer, Amberpet) for their heartfull prayers.

I thank Mr. Raghavaiah for his help in X-ray data collection. All the non-teaching staff of the School of Chemistry has been helpful, I thank them all. Mr. S. Satyanarayana, Mr. V. Bhaskar Rao, Mrs. Vijaya Lakshmi, Mrs. Asia Parwez, Mr. K. R. B. V. Prasad, Mr. Shetty, Mr. Vijay, Mr. Vijaya Bhaskar, Mr. Ramana, Mr. Joseph, Mr. Santosh and Mr. Rangaiah are a few to mention.

I should recall here, the kind of training I received from my elementary and high school teachers that laid a strong foundation for whatever I am today and I thank them all.

I thank all of my friends from my native place, 10^{th}, +2 classmates, B.Sc and M.Sc classmates for their encouragement.

I wish to extend my sincere thanks to the University authorities for providing all the necessary facilities for this work. The X-ray crystallographic data were collected in the National Single Crystal X-ray facility funded by DST, New Delhi.

Finally, I would like to thank the CSIR for the financial support during my tenure.

Kishorebabu Neela

Abbreviations

Ac	acetyl
acac	acetylacetonate
aq.	aqueous
Ar	aryl
ArM	arylmetal
binap	2,2’-bis(diphenylphosphino)-1,1’-binaphthyl
Bn	benzyl
BTMG	*t*-butyl 1,1,3,3-tetramethylguanidine
Bu	butyl
cat.	catalytic
COD	1,5-cyclooctadiene
Cp	cyclopentadienyl
dba	dibenzylideneacetone
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCA	9,10-dicyanoanthracene
DCM	dichloromethane
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DMAA	*N*,*N*-dimethylacetamide
DME	1,2-dimethoxyethane
DMF	*N*,*N*-dimethylformamide
dppb	1,2-bis(diphenylphosphino)benzene
dppe	1,2-bis(diphenylphosphino)ethane
dppf	1,2-bis(diphenylphosphino)ferrocene
dr	diastereomeric ratio
E	electrophile
ee	enantiomeric excess
EI	electron impact
eq.	equation

equiv.	equivalent
er	enantiomeric ratio
Et	ethyl
FG	Functional Group
HMPA	hexamethylphosphoric triamide
HQ-Cl	chlorohydroquinone
^{i}Pr	isopropyl
LiHMDS	lithium hexamethyldisilazane
liq.	liquid
Me	methyl
mp	melting point
M	metal
Ms	methanesulfonyl
n-	primary
NMP	*N*-methylpyrrolidone
NPMOV	molybdovanadophosphate
ORTEP	oak ridge thermal ellipsoid plot
Ph	phenyl
PPFA	*N*,*N*-dimethyl-1-[(*S*)-2-(diphenylphosphino)ferrocenyl]ethylamine
Py	pyridine
rt	room temperature
sec	secondary
t-	tertiary
TADDOL	α,α,α',α'-tetraaryl-2,2-dimethyl-1,3-dioxolan-4,5-dimethanol
TBAF	tetrabutylammonium fluoride
TBDMS	*t*-butyldimethylsilyl
TBDPS	*t*-butyldiphenylsilyl
Tf	trifluoromethanesulfonyl
tfp	tris(2-furyl)phosphine

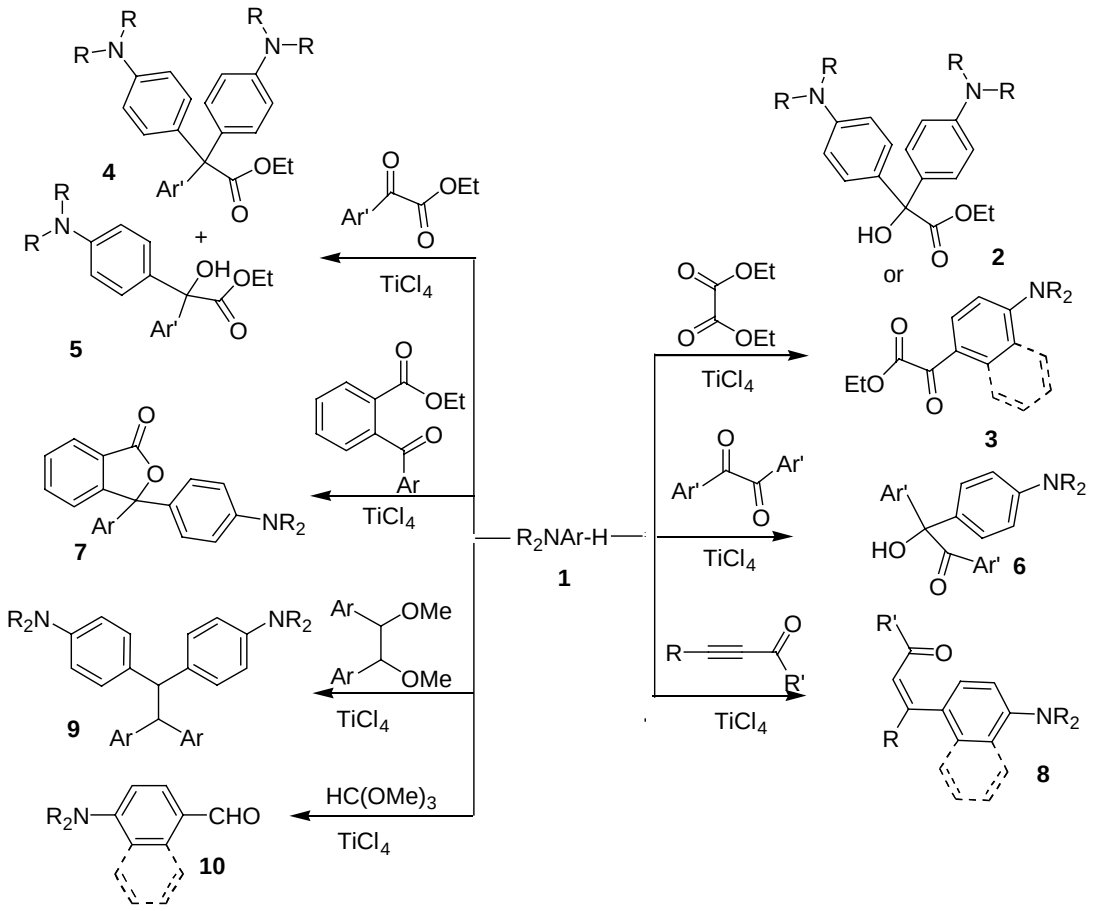
THF	tetrahydrofuran
TMEDA	*N*,*N*,*N'*,*N'*-tetramethyl-1,2-ethylenediamine
TMS	tetramethylsilane
TMSCl	trimethylsilyl chloride
TMU	1,1,3,3-tetramethylurea
Tol	tolyl
X	halide

ABSTRACT

This thesis describes, "**Development of Organotitanium Reagents: Applications of Titanium Arylamine, Enolate and Enamine Derivatives in Organic Synthesis''** comprises of three chapters. Each chapter is subdivided into four sections namely **Introduction**, **Results and Discussion**, **Conclusions** and **Experimental Section** along with **References**. The work described in this thesis is exploratory in nature.

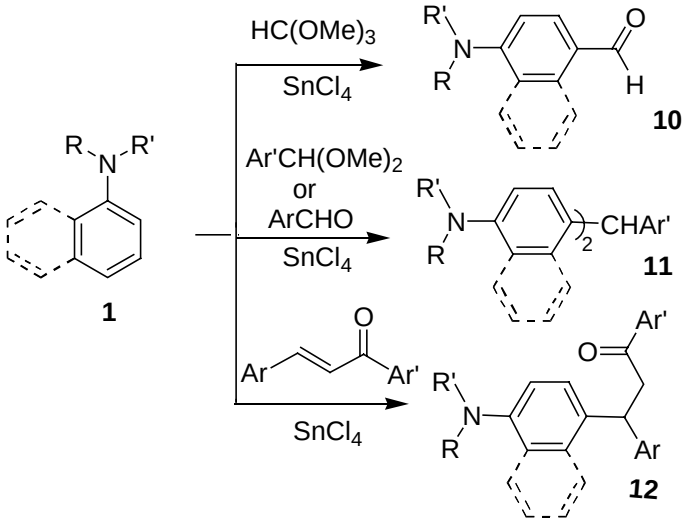
The first chapter describes a brief review on the preparation and applications of arylmetal reagents and aryltitanium reagents. The reaction of *N*,*N*-dialkylarylamines **1** in the presence of $TiCl_4$ was examined using electrophiles (Scheme 1). The reaction using *N*,*N*-dialkylarylamines and $TiCl_4$ with diethyl oxalate produced α-hydroxy esters **2** as well as α-ketoesters **3** by the addition of aryltitanium selectively at one carbonyl group. The aryltitanium species of *N*,*N*-dialkylanilines added to α-ketoester to produce diarylated acetic acid esters **4** as well as α-hydroxy esters **5** in good yields. The reaction with symmetrical α-dicarbonyl compounds like α-diketones produced α-hydroxy ketones **6** in good yields. The addition reaction of aryltitanium with unsymmetrical γ-dicarbonyl compounds like ethyl 2-benzoyl-benzoic acid ethyl esters give γ-lactones **7**. The reaction with α,β-unsaturated carbonyl compounds like alkynyl ketone gave the corresponding 1,4-addition product **8**. In the reactions with aryl ethers like 1,2-dimethoxy-1,2-diarylethane**,** the 1,1'- disubstistuted aryl product **9** were formed through rearrangement. The reaction with trimethyl orthoformate produced the corresponding formylated product **10** in good yields.

Scheme 1



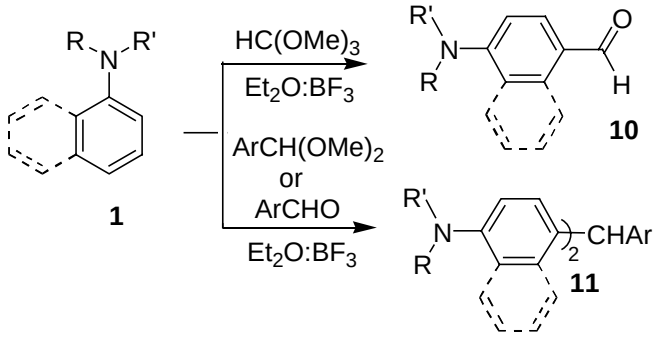
Several of these transformations can also rationalized considering $TiCl_4$ promoted activation of electrophiles without involving aryltitanium intermediates. In order to examine this possibility, we have carried out the reactions using other Lewis acids $SnCl_4$ and $Et_2O{:}BF_3$. The reactions of *N*,*N*-dialkylarylamines **1** and $SnCl_4$ with orthoformate, acetals or aldehyde as well as α,β-unsaturated carbonyl compounds give the corresponding arylated compounds **10-12** (Scheme 2).

Scheme 2



The *N,N*-dialkylarylamines **1** reacted with orthoformate, acetals or aryl aldehyde in the presence of $Et_2O{:}BF_3$. We have observed the reaction of *N,N*-dialkylarylamines with trimethyl orthoformate and $Et_2O{:}BF_3$. The expected formylated products **10** were obtained in good yields (Scheme 3).

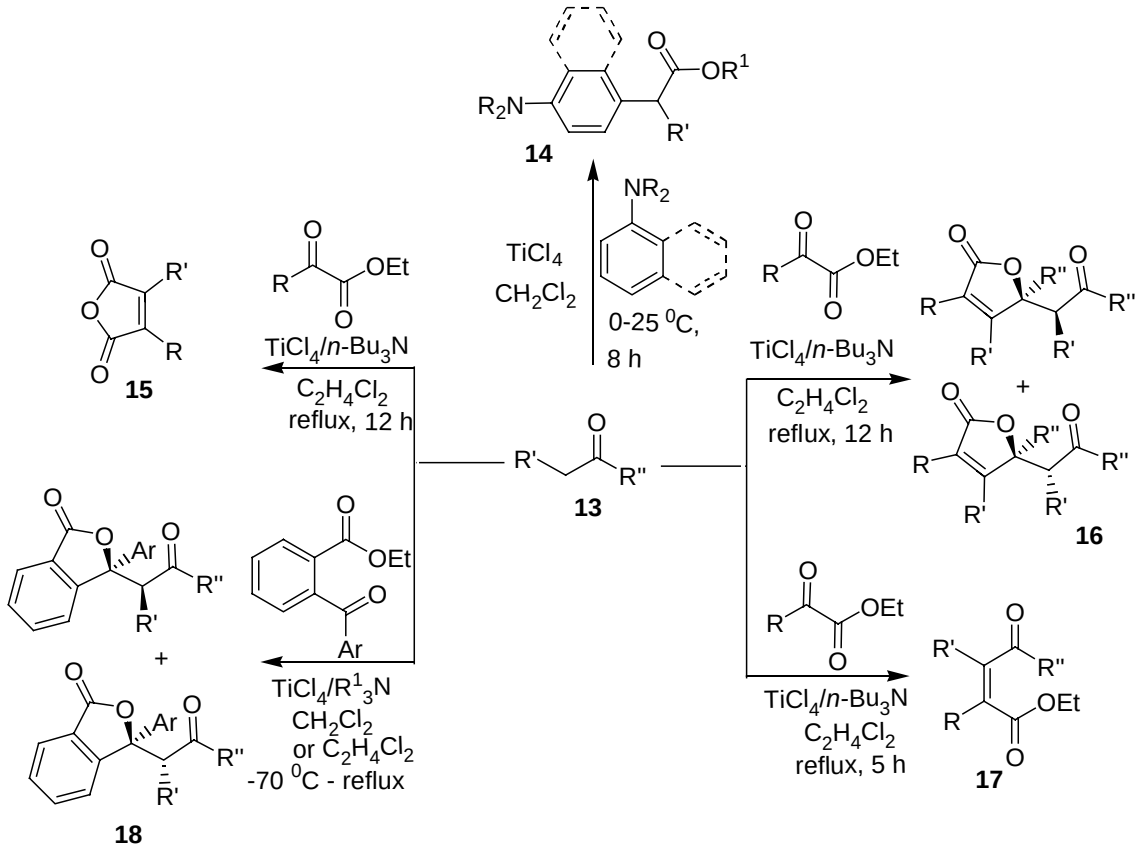
Scheme 3



In the second chapter, synthetic transformations of titanium enolates of esters and ketones with *N,N*-dialkylarylamines and dicarbonyl compounds are described. We have

observed that the reaction of aryltitanium species of *N,N*-dialkyl arylamines **1**, prepared *in situ* using $TiCl_4$, with arylacetic acid esters **13** (R''=OR') produces α-arylated products **14** in good yields (Scheme 4). α-Keto esters react with titanium enolate of alkanoic acid anhydrides **13** (R''= $OOCCH_2R'$) prepared *in situ* using the $TiCl_4$/*n*-Bu_3N reagent system to give maleic anhydrides **15** (Scheme 4). Diphenyl maleic anhydride was obtained by the reaction of phenylacetyl chloride and ethyl benzoylformate with the $TiCl_4$/*n*-Bu_3N reagent system.

Scheme 4

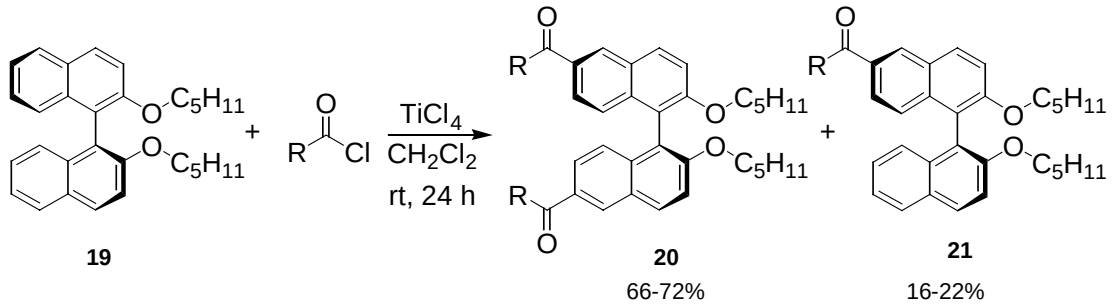


γ-Substituted γ-butenolides **16** were obtained in one step by the reaction of titanium enolates of ketones **13** (R''=aryl, alkyl) with α-keto esters in the presence of the $TiCl_4$/*n*-Bu_3N reagent system (Scheme 4). The intermediate **17** involved in this transformation was

isolated by changing the ratio of ethyl benzoylformate and ketone **13** to 1:1, respectively. In the reaction of ethyl 2-benzoylbenzoates and ketones **13** with the $TiCl_4$/*n*-Bu_3N reagent system, the γ-lactone **18** was obtained (Scheme 4). The ethyl-2-benzoylbenzoates react with esters **13** (R''=OR') in the presence of the $TiCl_4/Et_3N$ reagent system to give γ-lactones **18** (Scheme 4).

Efforts towards the synthesis of poly-1,1'-bi-2-naphthol pyrrole derivatives are discussed in chapter 3. We have developed a method for selective acylation of 1,1'-bi-2-naphthyl ether derivatives using $TiCl_4$ as well as with other Lewis acids $SnCl_4$ and $AlCl_3$. Initially, we have examined the acylation of 1,1'-bi-2-naphthol ether **19** using $TiCl_4$ and acid chlorides (Scheme 5). In this case, monoacyl derivative **20** and the diacyl derivative **21** were obtained.

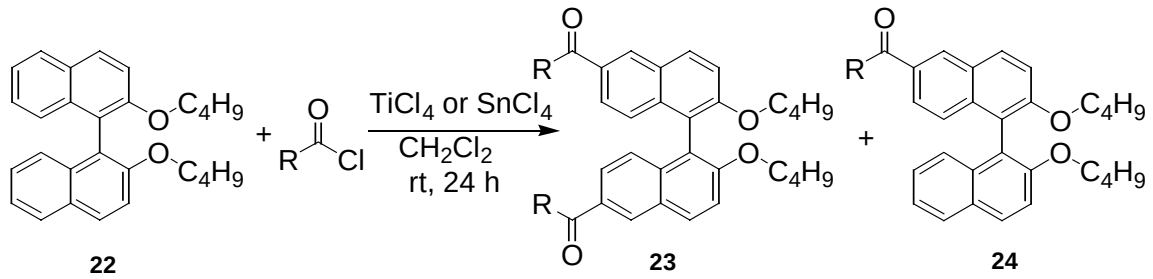
Scheme 5



19 **20** 66-72% **21** 16-22%

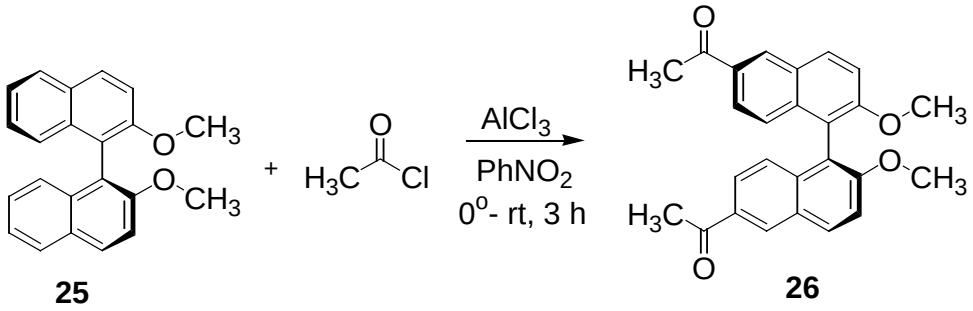
We have also examined the acylation of (±) 1,1'-bi-2-naphthol derived ether **22** with $TiCl_4$ as well as $SnCl_4$. The monoacyl and diacyl derivatives, **23** and **24**, were formed, in 15-21% and 66-71% yields, respectively (Scheme 6).

Scheme 6



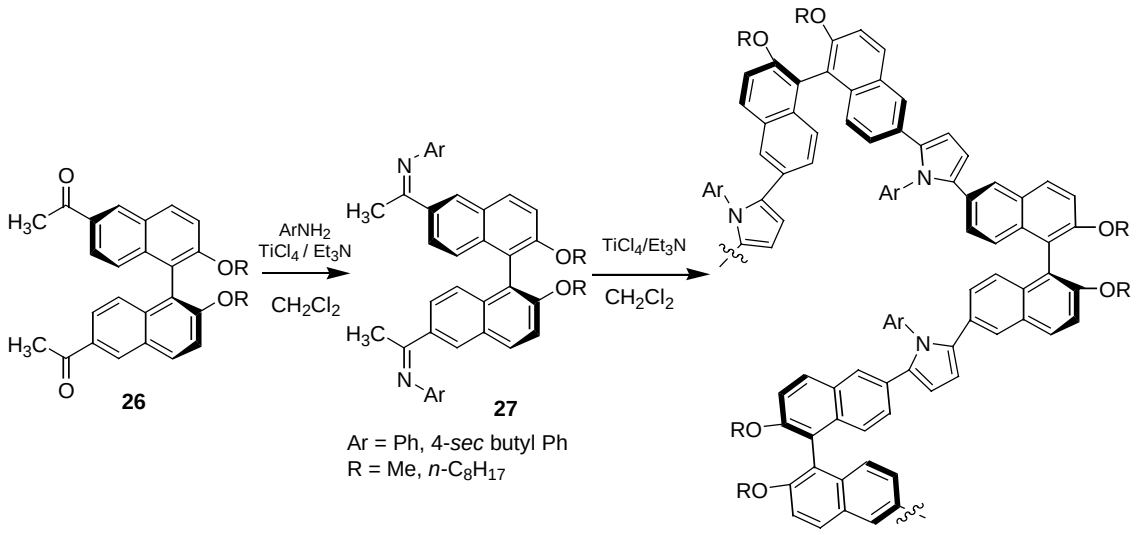
The acylation of methyl protected chiral 1,1'-bi-naphthol **25** was readily carried out using $AlCl_3$ to obtain the corresponding diacyl compound **26** (Scheme 7).

Scheme 7



The diacetyl derivative **26** was converted to ketimines **27** using arylamines and the $TiCl_4/Et_3N$ reagent system. The reaction of the diimine **27,** derivative of compound **26** was examined using the $TiCl_4/Et_3N$ reagent system to prepare poly-1,1'-bi-2-naphthyl derivatives containing pyrrole spacers following a procedure developed in this laboratory for the synthesis of diaryl pyrroles from certain ketimines (Scheme 8).

Scheme 8



Note: Scheme numbers and compound numbers given in this abstract are different from those given in the Chapters. Also, different set of numbers for Schemes, Tables, compounds, Figures and references etc. are given in different Chapters.

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Chapter 1

Synthetic Applications of the Tertiary Arylamine/$TiCl_4$ Reagent System

1. Introduction

Titanium, a very abundant, relatively inexpensive and generally nontoxic element, has been under utilized in organic synthesis. Although numerous compounds of titanium are known, only a handful of these reagents (eg.: $TiCl_4$, $TiCl_3$, $Ti(OR)_4$, $TiCl(OR)_3$, $TiCl_2(OR)_2$ and Cp_2TiCl_2) are widely used.[1] The titanium regents are by far the most versatile among the transition metal reagents used in the organic synthesis. Their applications range from use in attaining better selectivity in known organic transformations to the exploration of novel reactions.[1]

Discovery of Ziegler catalyst brought a new era to research in organometallic reactions as well as organotitanium chemistry.[2] Also, the $TiCl_4$/RMgX or RLi, Cp_2TiCl_2/RMgX or RLi or $LiAlH_4$ and $TiCl_4$/Li/TMSCl reagent combinations were found to be useful in fixation of molecular nitrogen under mild conditions.[3]

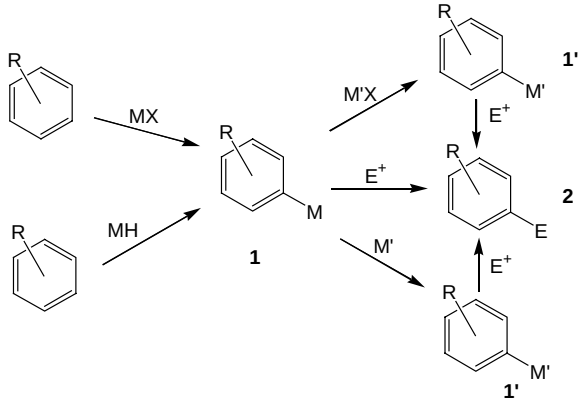
In recent years, the deoxygenative-reductive coupling reactions of carbonyl compounds (eg.: McMurry reaction) have been widely employed in synthesis using the low valent titanium (LVT) species, produced by the reduction of $TiCl_4$ with metals and metal hydrides.[4] The $Cp_2TiCl_2/(CH_3)_3Al$ (The Tebbe's reagent) and the $TiCl_4/CH_2Br_2$/Zn reagent systems have been used for the Wittig-type olefination of carbonyl compounds.[5] The Reetz reagent, Me_2TiCl_2, has been employed in *gem*-dimethylation of carbonyl compounds.[6] Several reports show that the transmetalation of organolithium or organomagnesium reagents with titanium reagents leads to better chemo-, regio- and stereoselectivities.[1,7]

Very recently, the $TiCl_4$/trialkylamine reagent system has been extensively employed in the preparation of titanium enolates for synthetic applications.[8] Also, the $TiCl_4$ has been used as Lewis acid for arylation as well as acylation of aromatic compounds.[9] We have undertaken research efforts on the development of aryltitanium reactions. Accordingly, it is of interest to briefly review the literature reports on these topics.

1.1 Preparation and reactions of arylmetal reagents

Generally, arylmetal reagents **1** and **1'** are prepared by metal-halogen[10] or metal-hydrogen exchange,[11] and transmetalation reaction between arymetal compound and a metal halide[12] or a metal.[13] (Scheme 1)

Scheme 1

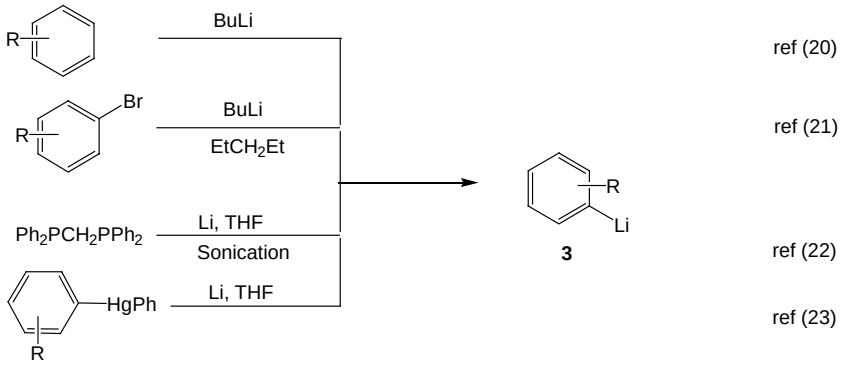


Arylmetal compounds are useful building blocks in synthetic organic chemistry (Scheme 1). In most cases, the addition of the arylmetal reagents to the electrophilic carbon-hetero atom double bonds in aldehydes[14] or imines[15], as well as the 1,4-addition to α,β-unsaturated carbonyl compounds and α-dicarbonyl compounds[16-18] occur chemo-, regioselectively (**2**). Moreover, aromatic metalation permits regioselective preparation of poly substituted aromatics and regiospecific construction of carbocyclic and heterocyclic systems,[17,19] which are not readily available by simple electrophilic substitution.

1.1.1 Aryllithium Reagents

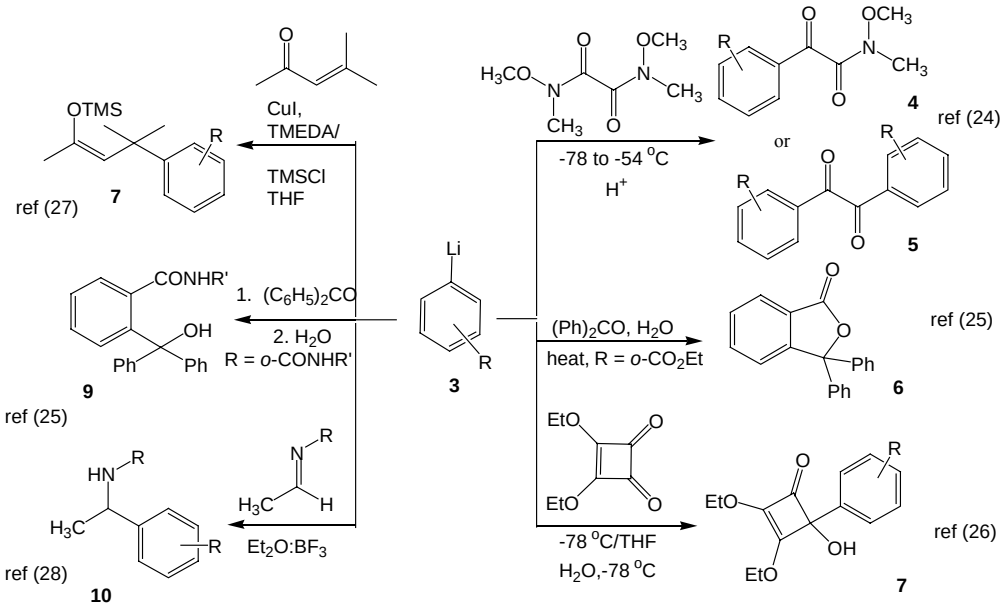
Among the alkali metals, aryl and heteroaryllithium compounds **3** were widely used for synthetic applications. They can be prepared by methods outlined in Chart 1.

Chart 1: Methods of Preparation of Aryllithium Compounds



These aryllithium compounds **3** are widely used for the synthesis of polyfunctionalized molecules (Chart 2).

Chart 2 : Synthetic Applications of Aryllithium Reagents



Addition of phenyllithium to *N,N'*-dimethoxy-*N,N'*-dimethylethanediamide provides α-keto amide **4** as well as 1,2-diketone **5** by nucleophilic displacement.[24] Condensation of

phenyldilithoamide (R=CONLiR) with benzophenone followed by thermal cyclization to afford the γ-lactone **6** was reported.[25] Phenyllithium addition in a clean 1,2-fashion to diisopropyl squarate produced 4-hydroxy-4-phenyl-2,3-bis(1-methylethoxy)-4-cyclobuten-1-one **7**.[26] 1,4-Addition of phenyllithium to enone in the presence of the CuI/TMEDA/TMSCl reagent system to give ketone **8** at –78 ^{o}C in THF was also reported.[27] Condensation of phenyldilithoamide (R=CONLiR) with benzophenone gave the γ-hydroxyamide **9**.[25] Addition reaction of aryllithium (R=H, OMe) reagents to oxime ethers in the presence of $F_3B{:}OEt_2$ gave compound **10** in 44% yield.[28]

In the last few years, aryllithium chemistry has also attracted the attention for use in the cross-coupling reactions catalyzed by transition metals,[29] since these reagents can participate in the preparation of other organometalics by the transmetallation.[30] Thus aryllithium chemistry is a very active field of investigation and several excellent reviews covering various aspects of this chemistry have appeared.[31]

Several other arylmetal reagents also have been widely used in organic reactions. Preparation and reactions of these reagents given in the charts and schemes outlined in next sections.

1.1.2 Arylmagnesium Reagents

Chart 3 : Preparation of Arylmagnesium Reagents

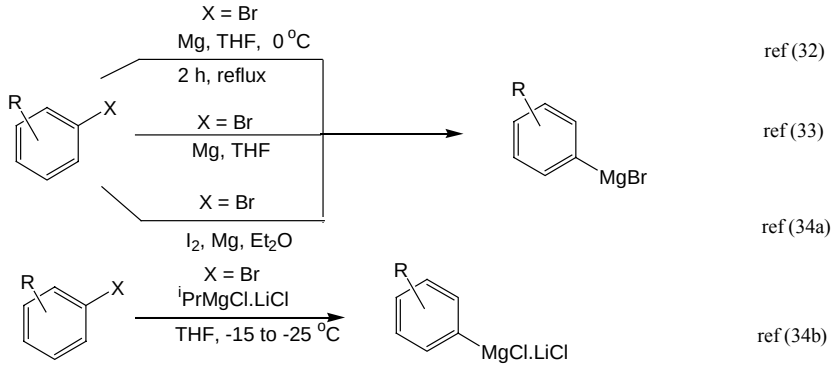
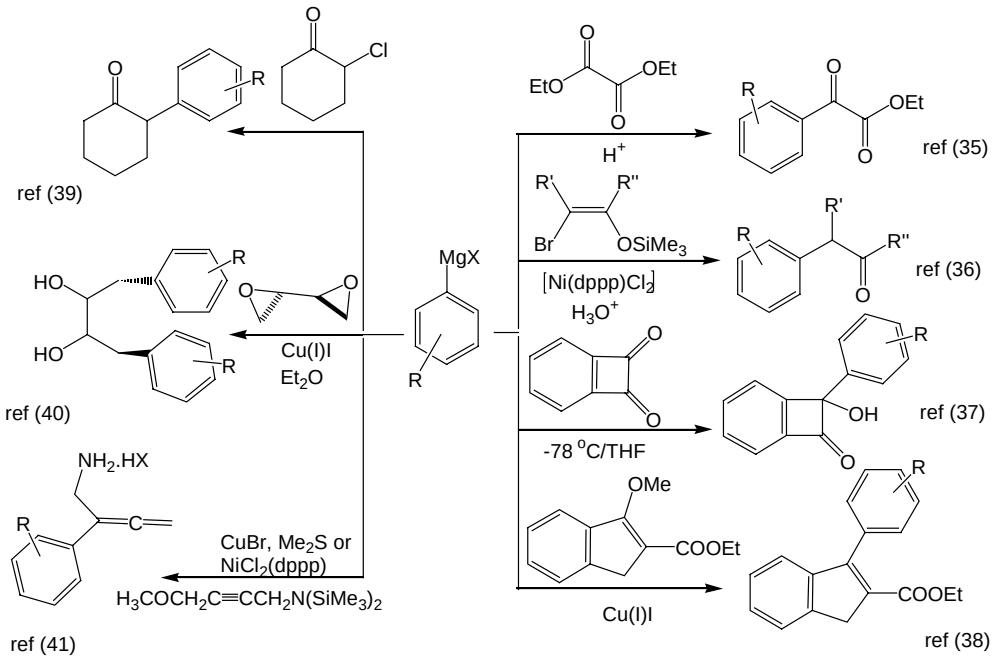


Chart 4 : Synthetic Applications of Arylmagnesium Reagents



1.1.3 Arylboron Reagents

Chart 5 : Preparation of Arylboron Reagents

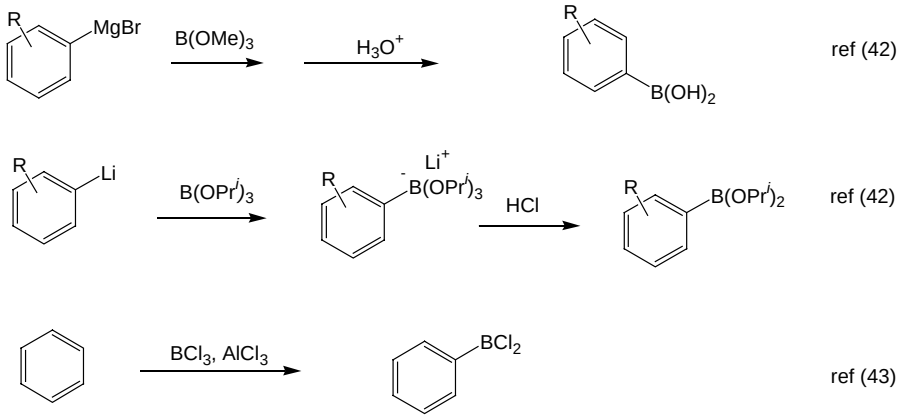
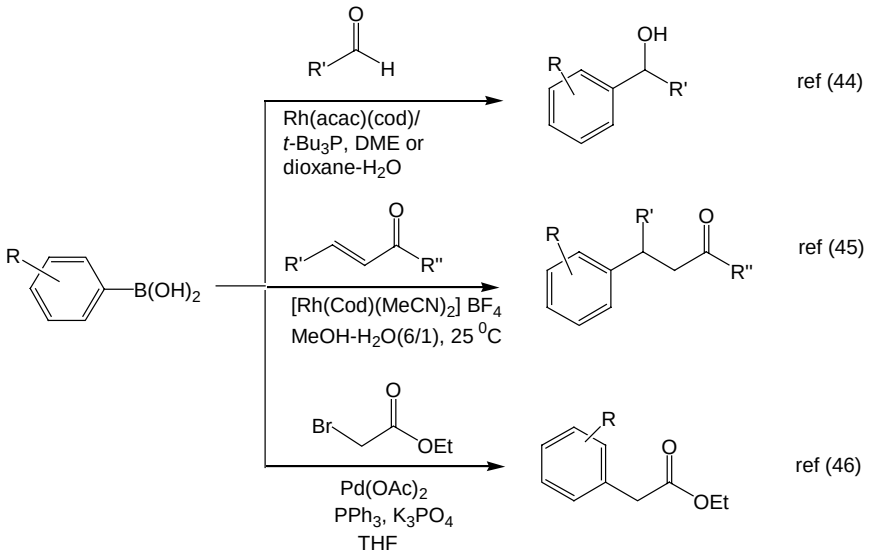


Chart 6 : Synthetic Applications of Arylboron Reagents



1.1.4 Arylsilicon Reagents

Chart 7 : Preparation of Arylsilicon Reagents

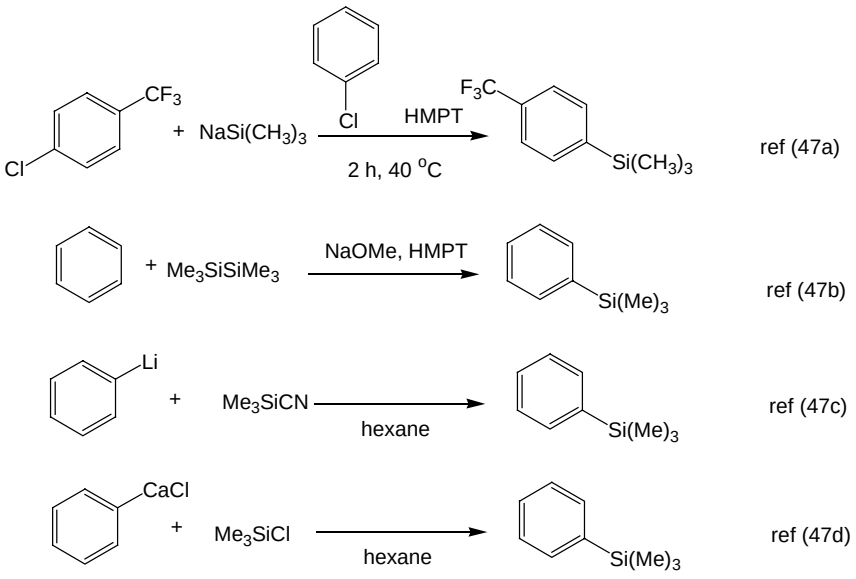
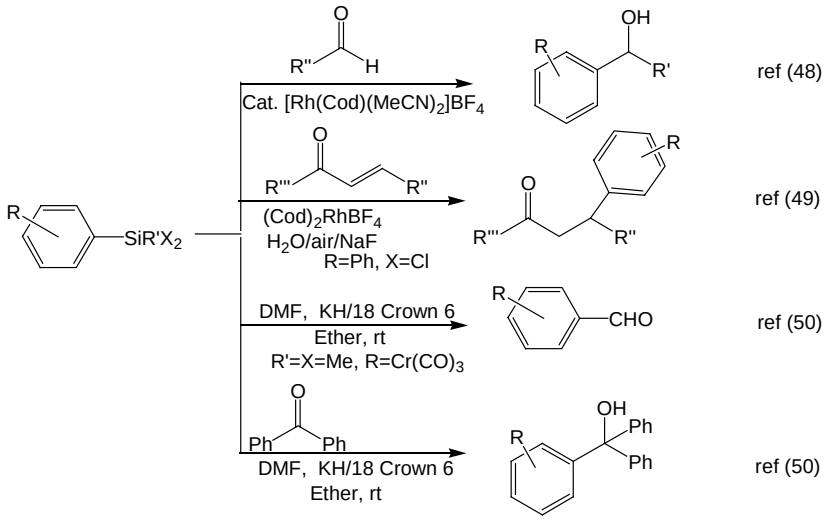


Chart 8 : Reactions of arylsilicon Reagents



1.1.5 Aryltin Reagents

Chart 9 : Preparation of Aryltin Reagents

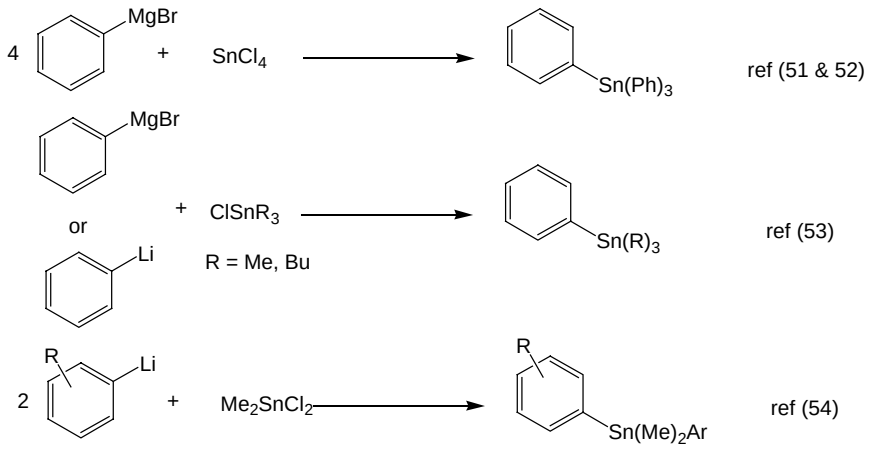
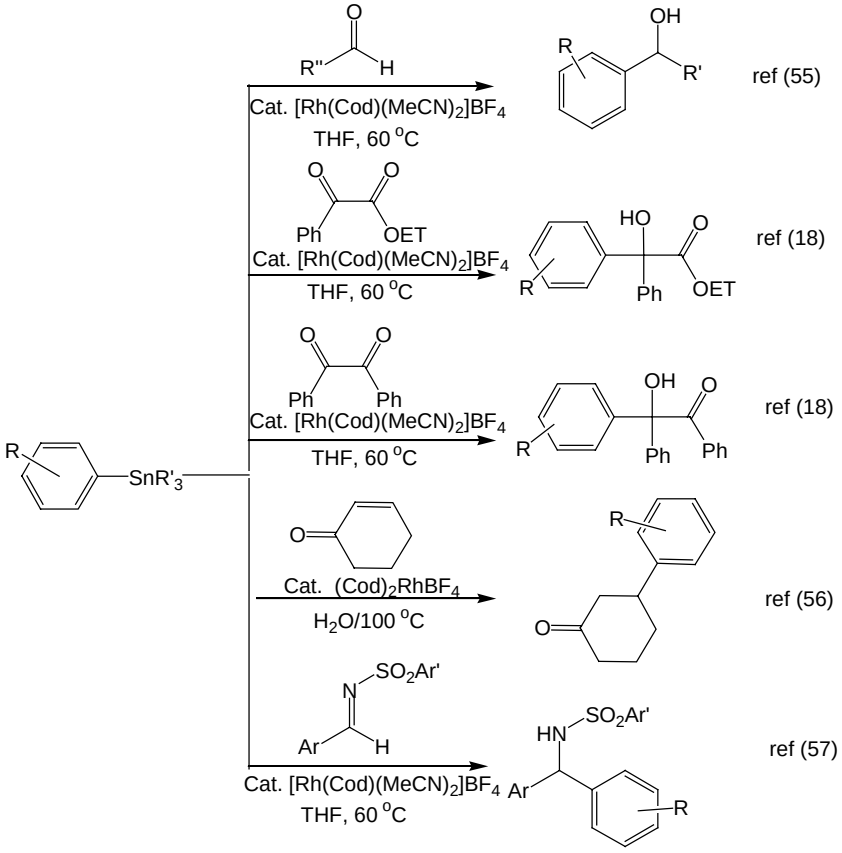


Chart 10 : Reactions of Aryltin Reagents



1.1.6 Aryllead reagents

Chart 11 : Preparation of Aryllead Reagents

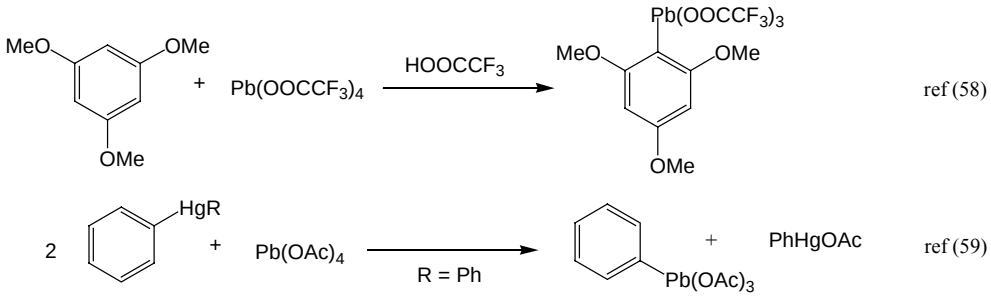


Chart 11 : (Continued)

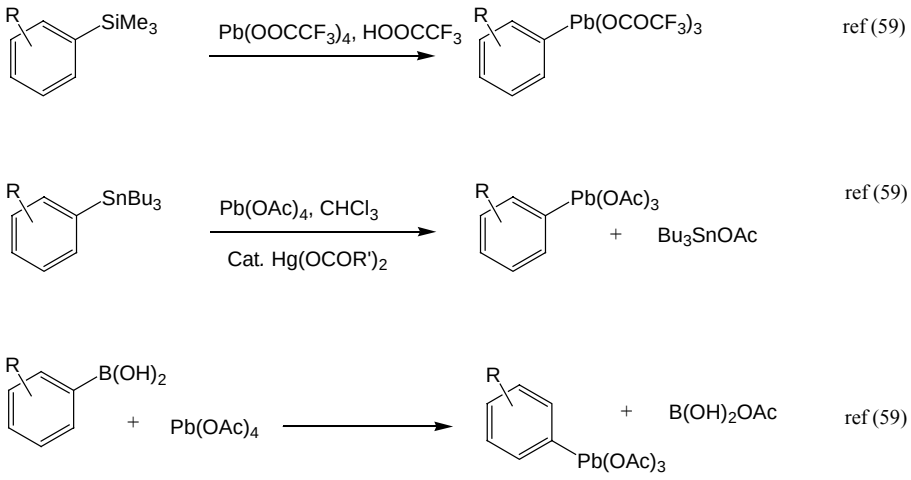
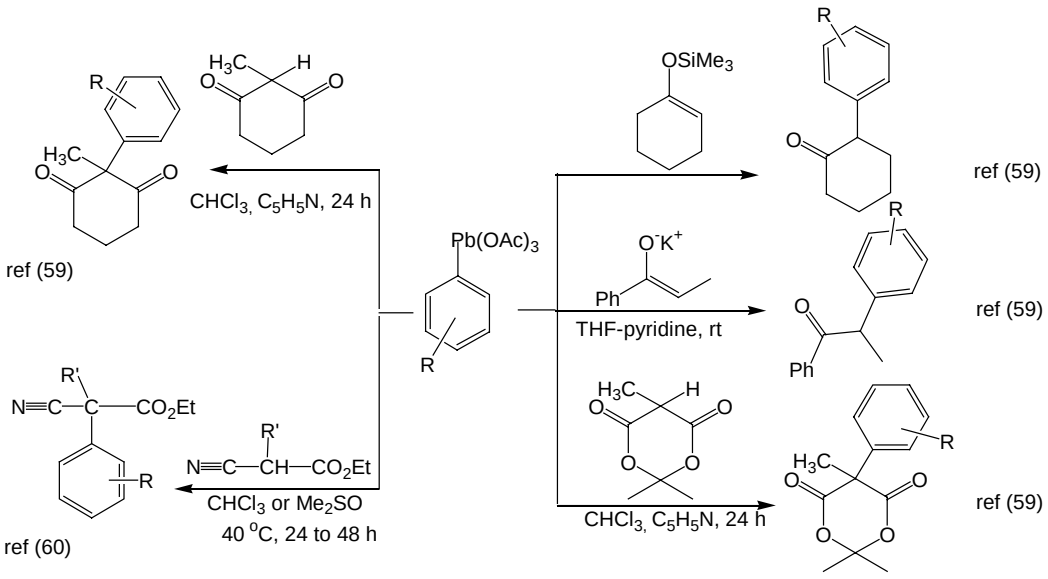


Chart 12 : Reactions of Aryllead Reagents



1.1.7 Arylbismuth Reagents

Chart 13 : Preparation of Arylbismuth Reagents

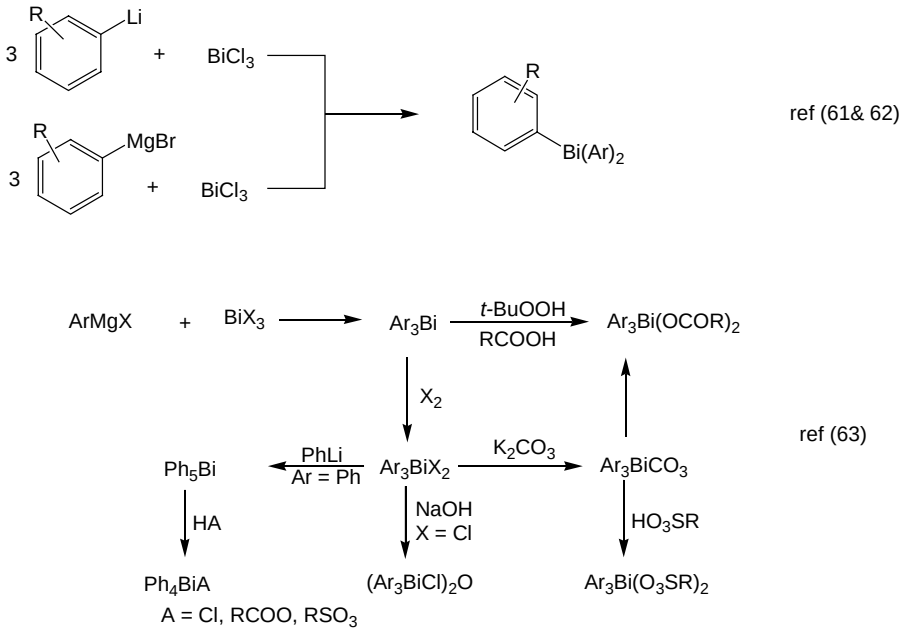
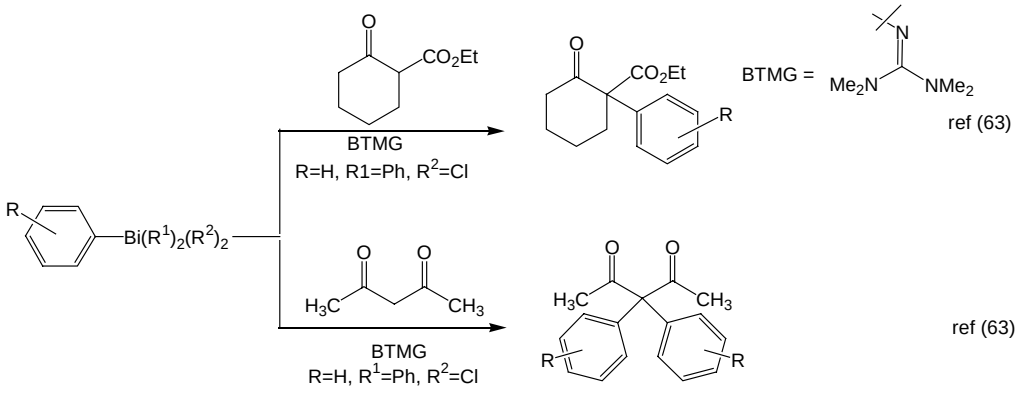


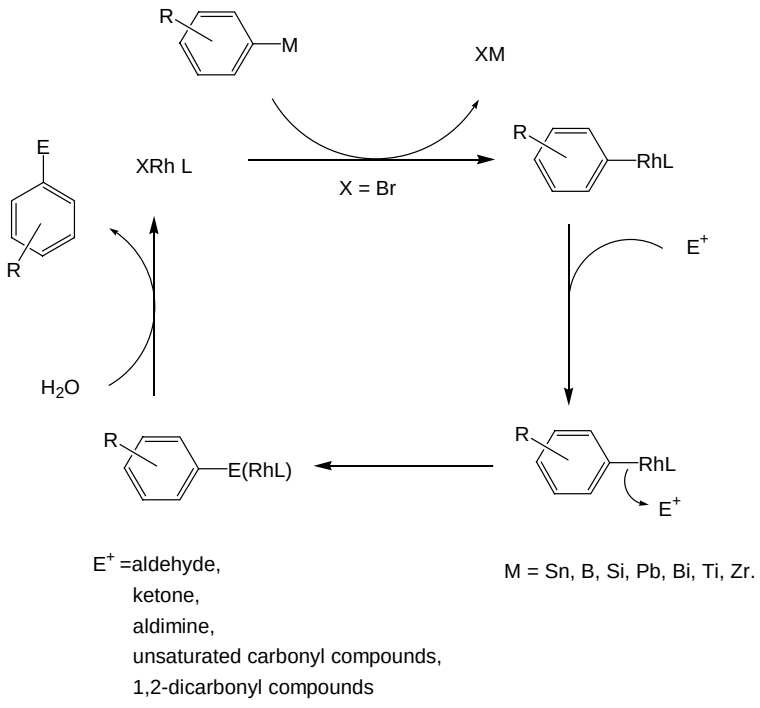
Chart 14 : Reactions of Arylbismuth Reagents



1.1.8 Preparation and reactions of arylrhodium reagents

Transition metal-catalyzed transformations using organometallic reagents are of great importance in modern organic chemistry. The rhodium-catalyzed addition of the organometallic reagents to the carbon-hetero atom double bond in such as aldehydes or imines, as well as the 1,4-addition to α,β-unsaturated carbonyl compounds and α-dicarbonyl compounds commonly involve organorhodium complexes as active species, produced *in situ* by the transmetalation with the organometallic reagents such as tin, boron, silicon, lead, bismuth, titanium and zirconium. In most cases, the reactions occur with chemo- and regioselectivity (Scheme 2).[18]

Scheme 2



1.1.9 Arylcopper Reagents

Chart 15 : Preparation of Arylcopper Reagents

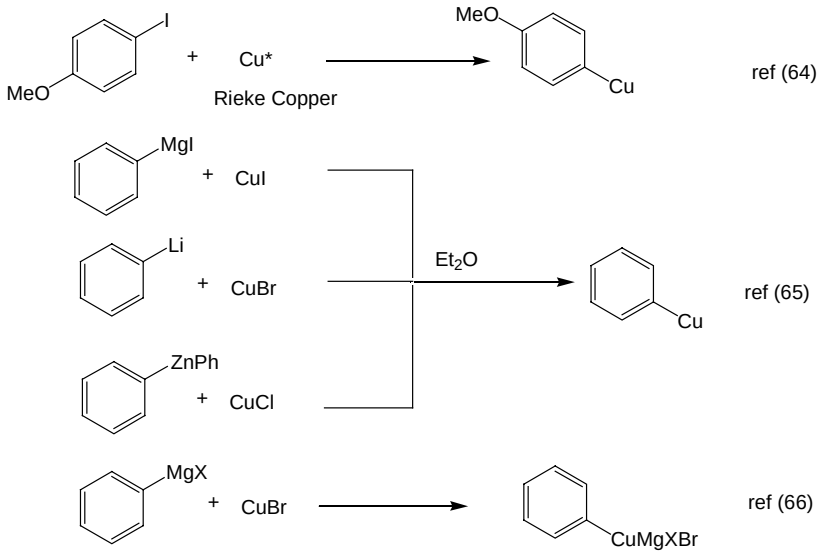
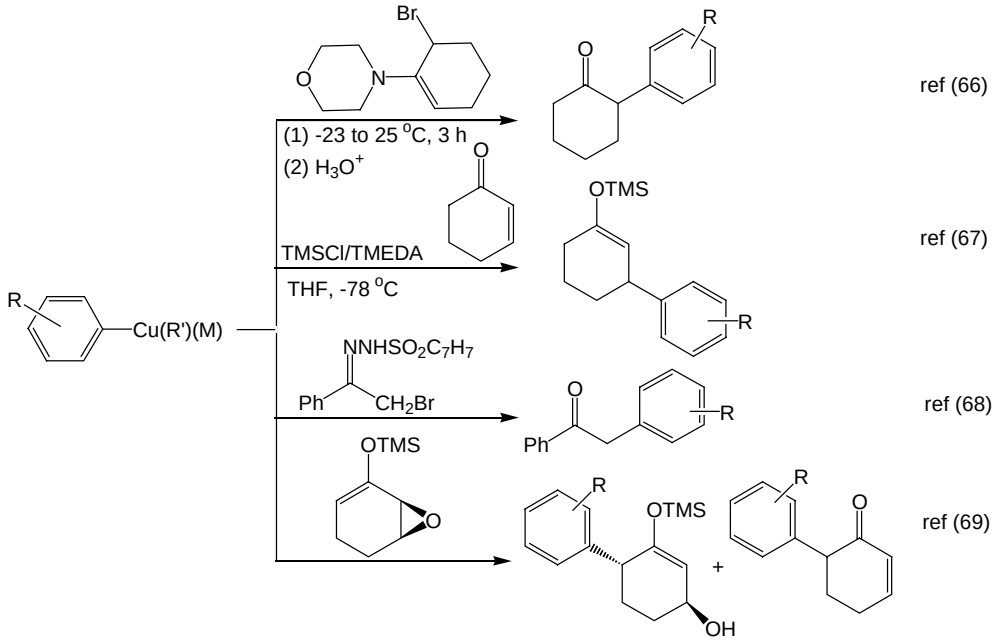
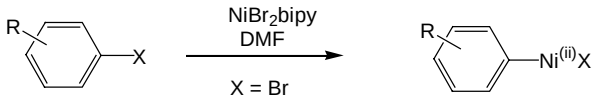


Chart 16 : Reactions of Arylcopper Reagents



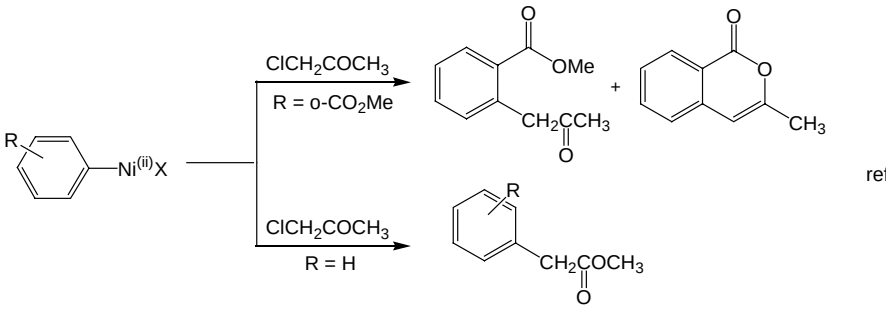
1.1.10 Arylnickel reagents

Scheme 3 : Preparation of Arylnickel Reagents



ref (70)

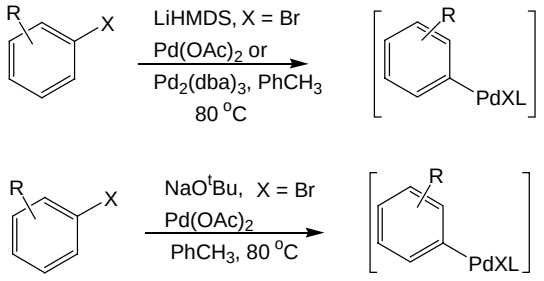
Scheme 4 : Reactions of Arylnickel Reagents



ref (70)

1.1.11 Arylpalladium Reagents

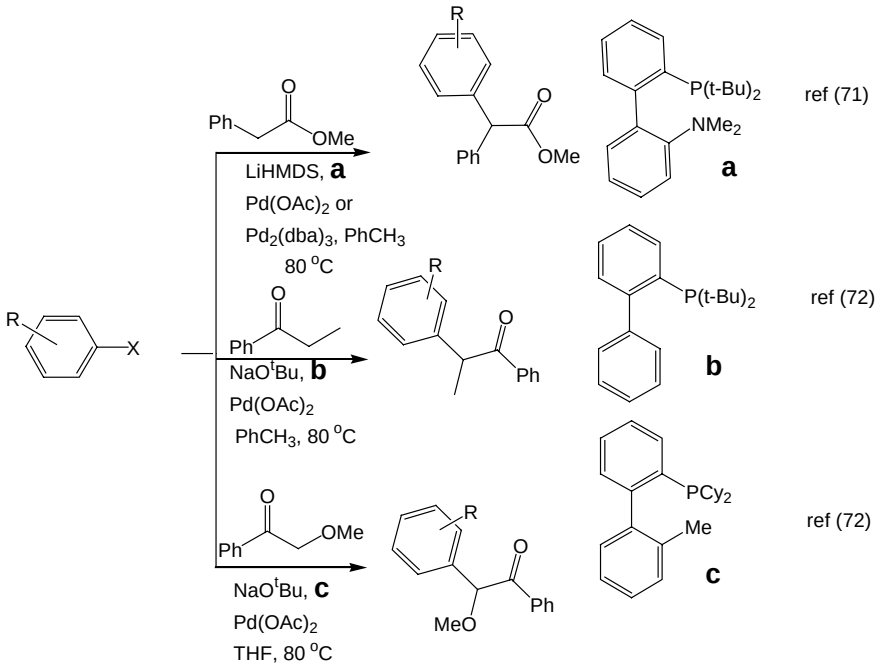
Chart 17 : Preparation of Arylpalladium Reagents

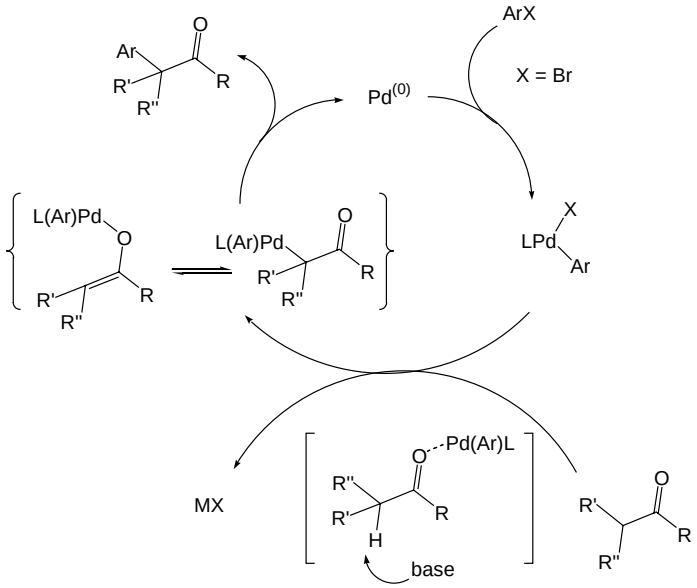


ref (71)

ref (72)

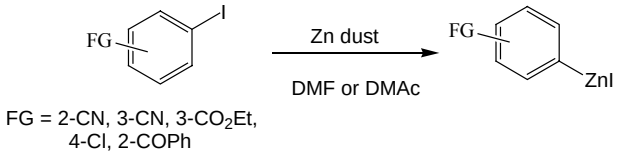
Chart 18: Reactions of Arylpalladium Reagents





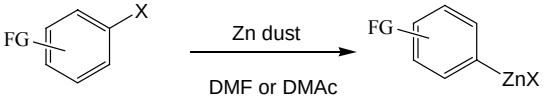
1.1.12. Arylzinc Reagents

Chart 19 : Preparation of Arylzinc Reagents



FG = 2-CN, 3-CN, 3-CO_2Et, 4-Cl, 2-COPh

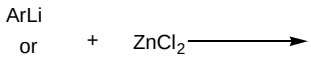
ref (73)



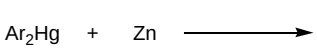
FG = 4-CO_2Et, X = I

ref (74)

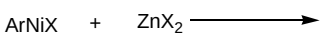
FG = 3-CO_2Et, 4-CN, 2-CN, X = I



ref (61a)

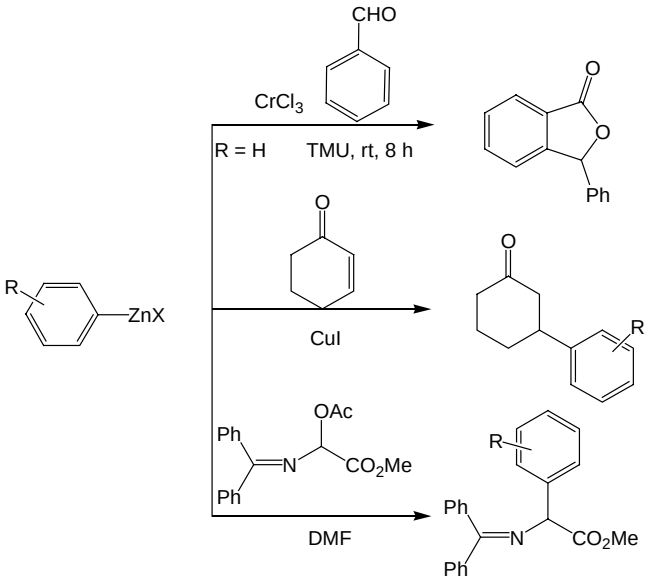


ref (75)



ref (76)

Chart 20 : Reactions of Arylzinc Reagents



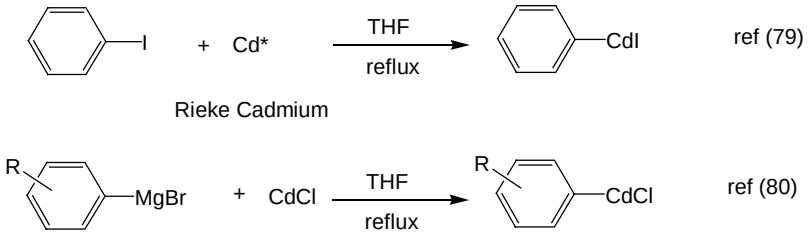
ref (77)

ref (76)

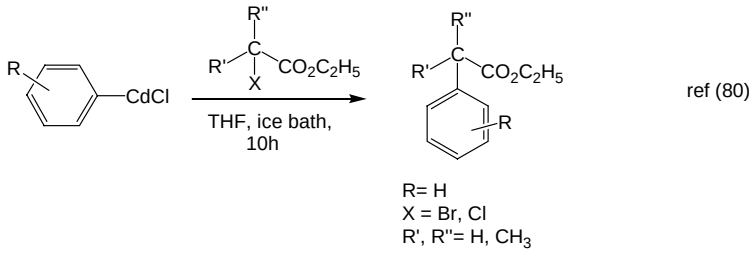
ref (78)

1.1.13 Arylcadmium Reagents

Chart 21 : Preparation of Arylcadmium Reagents

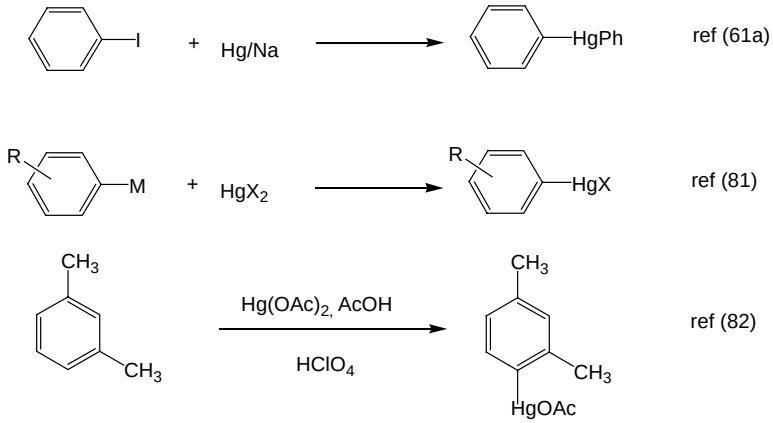


Scheme 5 : Reactions of Arylcadmium Reagents

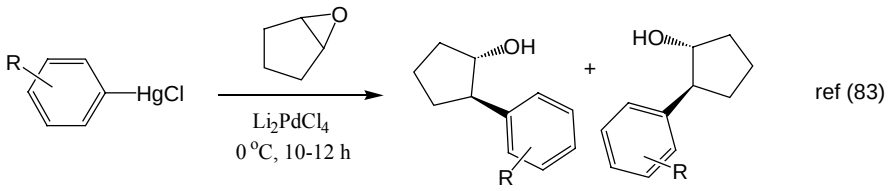


1.1.14 Arylmercury Reagents

Chart 22 : Preparation of Arylmercury Reagents



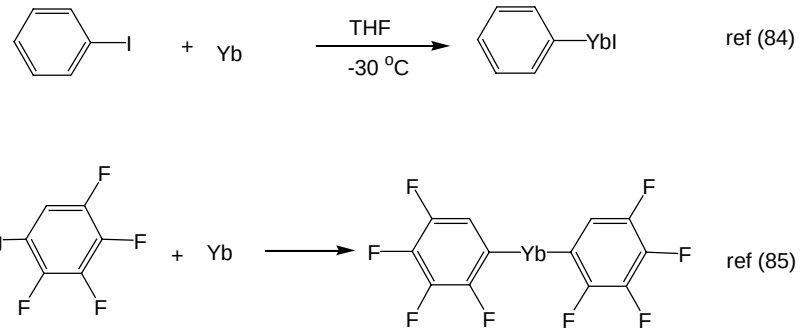
Scheme 6: Reactions of Arylmercury Reagents



ref (83)

1.1.15 Aryllanthanoide reagents

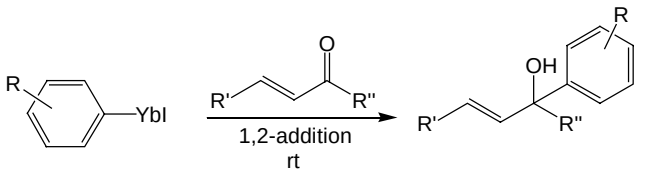
Chart 23 : Preparation of Aryllanthanoide Reagents



ref (84)

ref (85)

Scheme 7 : Reactions of Aryllanthanoide Reagents



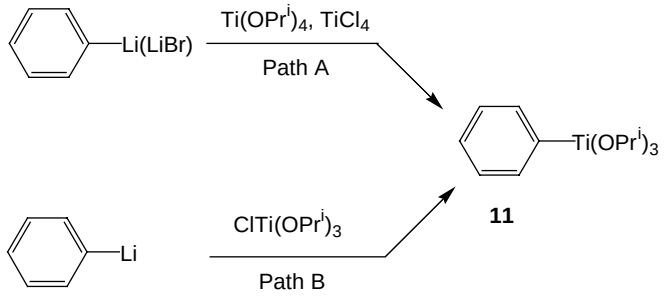
ref (86)

1.1.16 Preparation of aryltitanium reagents and their reactions

We have undertaken studies on the aryltitanium species. Accordingly, it is of interest to briefly review the reports on the preparation and applications of the aryltitanium reagents.

In 1953, the first unambiguous synthesis and characterization of an organotitanium compound **11** having a Ti-C σ-bond was reported.[87] The titanium tetraisopropoxide was reacted with phenyllithium (containing LiBr) and then with $TiCl_4$ to obtain the $PhTi(OPr^i)_3$ in an overall yield of 40% (Path A, Scheme 8).

Scheme 8

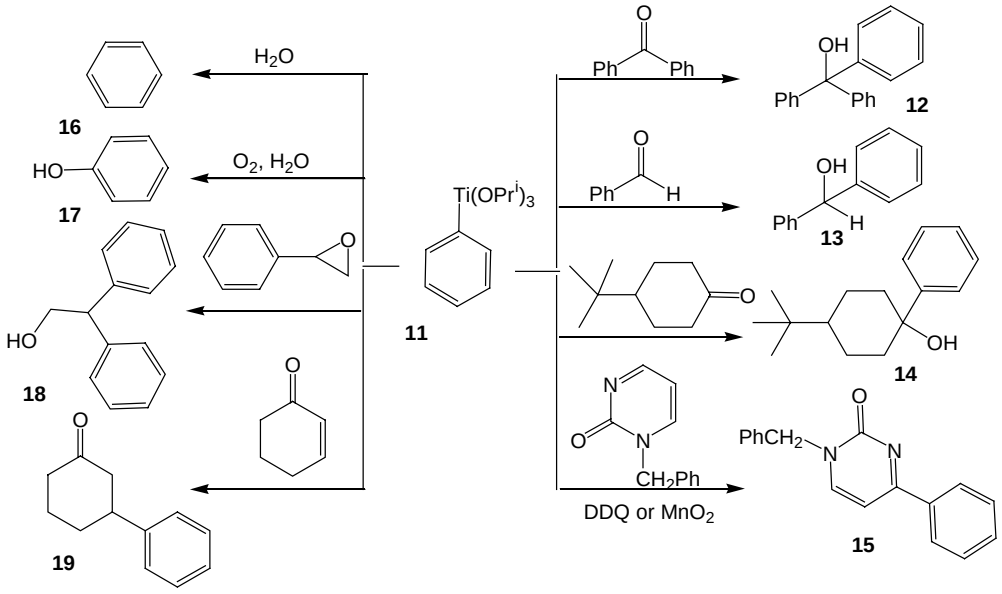


In 1962, an improved procedure was reported for preparing the $PhTi(OPr^i)_3$ **11** by the reaction of salt-free phenyllithium with chlorotriisopropoxytitanium at −10 °C (Path B, Scheme 8).[88] The $PhTi(OPr^i)_3$ is a yellow crystalline compound having a melting point of 88-90 °C and it is stable in the dark at 10 °C for months, but decomposes rapidly if heated above its melting point to form violet colored Ti(III) species and diphenyl.[88]

The phenyltitanium derivative **11** reacts with benzophenone to give the triphenylcarbinol **12** in 19% yield. The carbonation of the unisolated phenyltitanium derivative with excess dry ice gave a very small amount of benzoic acid (Chart 24).[87]

The reactions of organotitanium derivatives with carbonyl compounds were studied in detail (chart 24).[89]

Chart 24 : Reactions of Aryltitanium Reagents

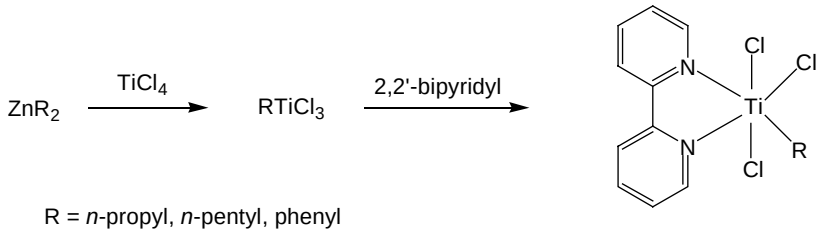


The phenyltitanium derivative **11** reacts with aryl aldehyde derivatives to give the corresponding alcohols **13** in good yields. Also, it reacts with 4-*t*-butylcyclohexanone to produce the corresponding alcohol **14** as a 1:1 *cis*/*trans* mixture (Chart 24). The reaction of aryltriisopropoxytitanium reagent with pyrimidin-2(1H)ones, produces the regioselective 1:1 adduct. Dehydrogenation of the adduct gives the arylated, fully conjugated heterocycle **15** (Chart 24).[90,91]

The aryltitanium derivative **11** is sensitive to air (oxygen) and moisture and gives phenol **17** and benzene **16** respectively.[92] The ring opening of unsymmetrical allylic, benzylic, propargylic and Si-substituted epoxides by titanium acetylides has been reported.[93] When the PhTi(OPr^i)$_3$ prepared from bromobenzene, ^{n}BuLi and ClTi(OPr^i)$_3$, (and without isolation) was treated with styrene oxide, regiospecific ring opening of the epoxide takes place to give the product **18** (Chart 24).[93] Recently, it has been reported that a rhodium catalyzed asymmetric 1,4-addition of aryltitanium reagents **11** to enones produced the β-ketone **19** through chiral titanium enolates generation (Chart 24).[94]

The alkyl and aryltitanium derivatives **20** were readily prepared by the reaction of zinc dialkyls or zinc diaryls and $TiCl_4$ or $TiBr_4$.[95] The aryltitanium species can be stabilized by bipyridyl adduct formation (Scheme 9).

Scheme 9



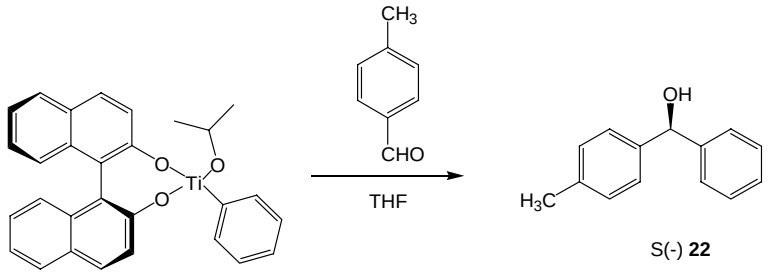
R = *n*-propyl, *n*-pentyl, phenyl

20

Tetraphenyltitanium was prepared in good yields by the reaction of phenylmagnesium bromide with the bipyridine adduct of $TiCl_4$ or similar complexes $TiCl_4L_2$ in ether.[96] In solution, $Ti(C_6H_5)_4$ is fairly stable, but in the solid state deterioration is rather rapid at room temperature.

An enantioselective addition of aryl groups to aromatic aldehydes using aryltitanium-binaphthol derivatives was developed. Chiral, non-racemic organotitanium reagents **21** were generated *in situ* from chiral-2-binaphthol, chlorotriisopropoxytitanium and ArMgX in THF. These reagents transfer aryl groups to aromatic aldehydes to produce the alcohol **22** with high enantioselectivity (Scheme 10).[97]

Scheme 10

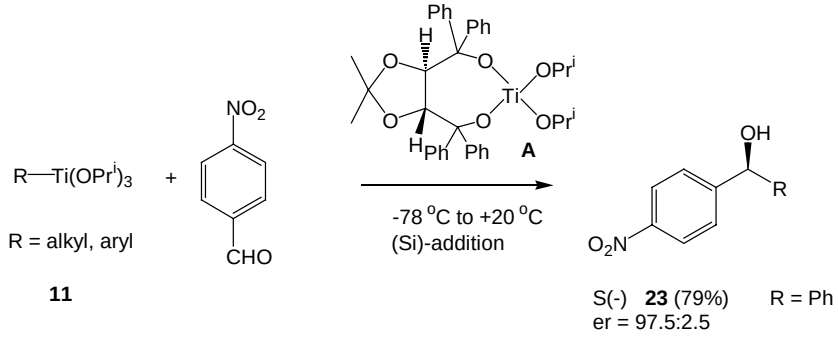


S(-) **21**

S(-) **22**

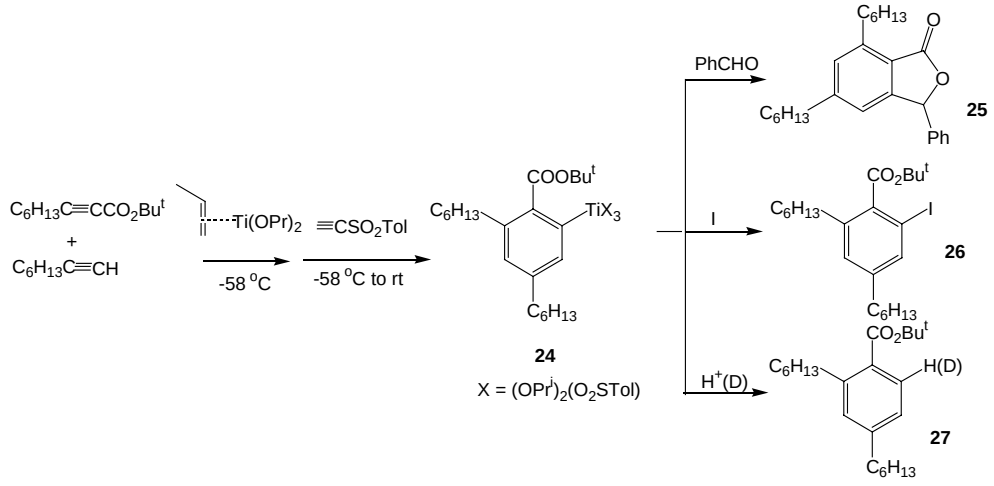
Also, the Ti-TADDOL complex **A** catalyzed the highly enantioselective (99.5:0.5) addition of alkyl and aryltitanium **11** derivatives to aldehydes.[98] Aryl and alkyl triisopropoxytitanium reagent **11** were prepared from the corresponding RLi or RMgX reagents and $ClTi(OPr^i)_3$ with careful removal of salts (Scheme 11).

Scheme 11



The first metalative Reppe reaction, in which direct preparation of aryltitanium compounds was reported (Scheme 12).[99] Three different unsymmetrical acetylenes and one molecule of titanium species are combined together in a highly controlled manner to give directly the aryltitanium compound **24**. The formation of aryltitanium compound was confirmed by subsequent reactions with electrophiles to obtain compounds **25**, **26** and **27** (Scheme 12).

Scheme 12



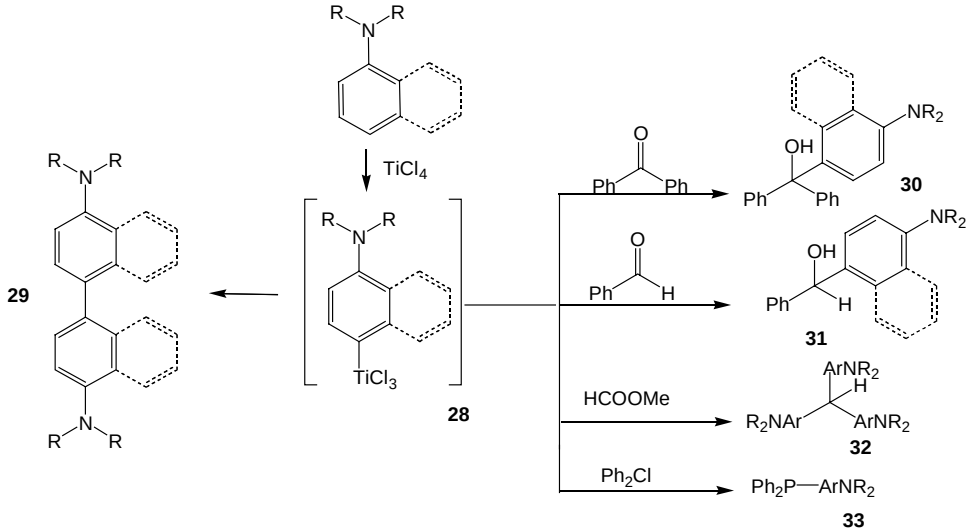
Generally, the alkyl and aryltitanium reagents $RTiX_3$ (X = $OCHMe_2$, Cl) react with α,β-unsaturated aldehydes and ketones in a 1,2–fashion.[86] However, the methyltitanium ate complexes and phenyltitanium complexes were reported to undergo nickel catalyzed 1,4-addition to enones.[100]

1.1.16.1 Previous work on aryltitanium reagents from this laboratory:

Aryltitanium species **28** can also generated by the direct metalation of *N*,*N*-dialkylarylamines with $TiCl_4$ without using another organometallic reagents. These species undergo oxidative coupling to produce *N*,*N*,*N'*,*N'*-tetraalkylbenzidines **29** in good yields.[101]

The reaction of aryltitanium species obtained *in situ* was examined with electrophiles (Scheme 13). In the reaction with diaryl ketones, the expected electrophilic addition products **30** were obtained. In the case of reactions using benzaldehyde, and methyl formate, the initially formed electrophilic addition products underwent further arylation to give compounds **31** and **32**. The chlorodiphenylphosphine gave the corresponding electrophilic substitution product **33** (Scheme 13).[101]

Scheme 13



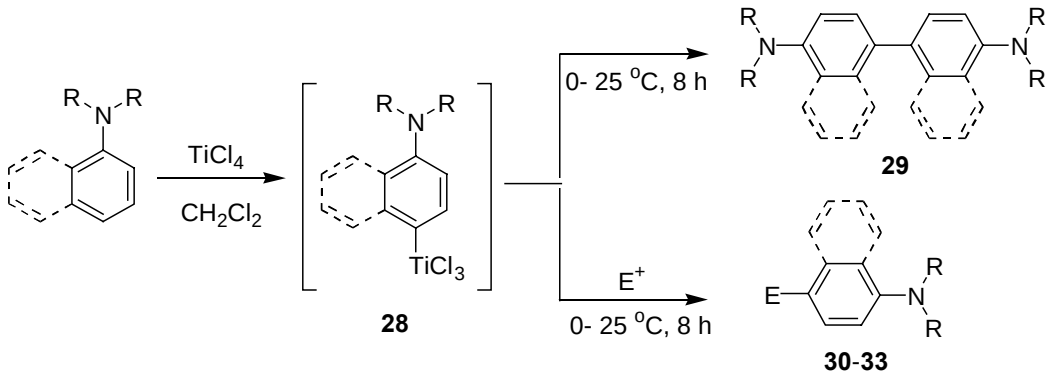
Further studies on the scope and limitations of the reactivity of aryltitanium species in the presence of other electrophiles are described in this chapter in the next section.

1.2 Results and Discussion

1.2 Reactions of the *N,N*-dialkylarylamines/$TiCl_4$ reagent system with various electrophiles

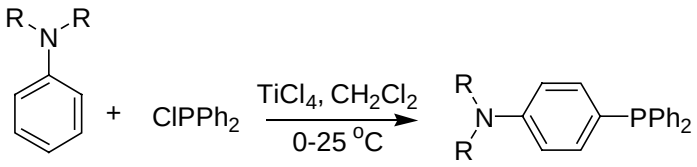
As discussed in the introductory section, it has been reported from this laboratory that the aryltitanium species **28** prepared *in situ* using *N,N*-dialkylarylamines and $TiCl_4$ reacts with simple electrophilies to produce arylated compounds **29**-**33** (Scheme 14).

Scheme 14



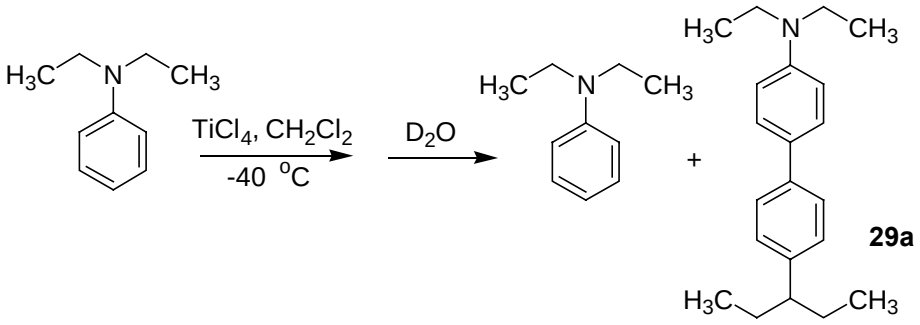
Though, the possibility of $TiCl_4$ playing the role of just activation of the electrophiles for reaction with arylamines cannot be ruled out, the formation of benzidine derivatives indicates the intermediacy of the aryltitanium species **28**. Moreover, the observation that the reaction of *N,N*-dialkylarylamines and $TiCl_4$ with compounds like $ClPPh_2$ (Scheme 15a) to give triaryl phosphine derivative is similar to the reaction of organometallic species, eg.: RLi or RMgX with phosphorous halides. The isolation of phosphorous derived compounds in organometallic reactions would also provide evidence for the presence of reactive C-M bonds.[101, 102]

Scheme 15a



To further examine the intermediacy of aryltitanium species, we have carried out an experiment (Scheme 15b) using *N,N*-diethylaniline at –40 °C for 6 h and quenched the reaction with D_2O at -40 °C. In this case, the corresponding benzidine was isolated in 10% yield and the recovered *N,N*-diethylaniline did not contain any deuterium in the *para*-position. Presumably, the reaction does not go through the arylamine intermediacy or the intermediate does not survive for 6h at -40 °C.

Scheme 15b



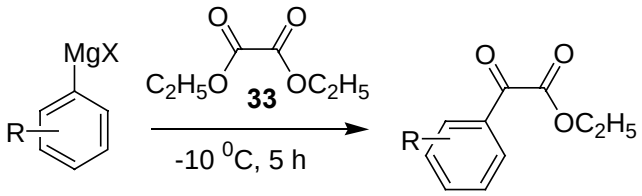
In continuation of these studies on the scope and limitations of the reactivity of the arylamines, we have further examined the reactions of $TiCl_4$/tertiary arylamine combination with dicarbonyl compounds of esters, keto esters and others electrophilies.

1.2.1 Reaction of *N,N*-dialkylarylamines and $TiCl_4$ with dicarbonyl compounds

1.2.1.1 Reaction of the tertiary arylamine/$TiCl_4$ reagent system with diethyl oxalate

We have examined the reaction of the *N,N*-dialkylanilines with diethyl oxalate **33** in the presence of $TiCl_4$, since it is well-known that the reaction of arylmagnesium reagents with diethyl oxalate produces α-keto esters (Scheme 16).[35]

Scheme 16



We have carried out the reaction between *N,N*-dialkylanilines and diethyl oxalate in the presence of $TiCl_4$ at 0-25 °C. Indeed, the expected reaction pattern was observed and corresponding *α*-hydroxy esters **34** were formed (Scheme 17). For example, the reaction of *N,N*-diethylaniline, $TiCl_4$ and diethyl oxalate at 0-25 °C for 5 h produced α-hydroxy ester **34a** in 54% yield. Whereas, *N*-phenyl piperidine gave the product **34b** in 52% yield. The results are summarized in Table 1.

Scheme 17

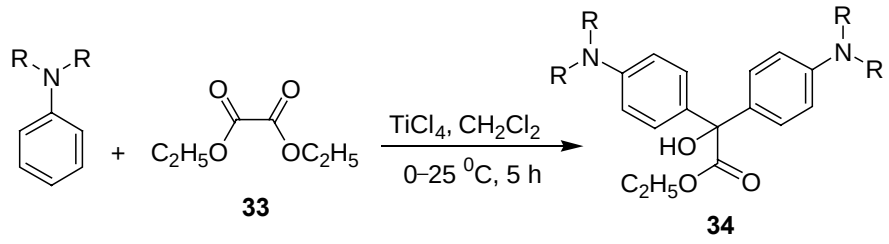
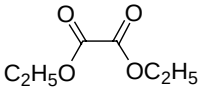
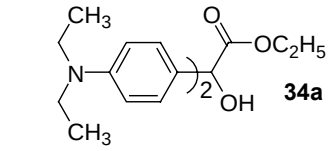
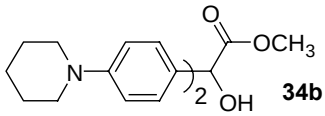
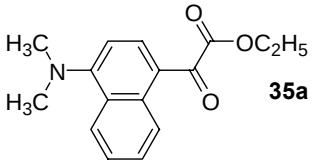
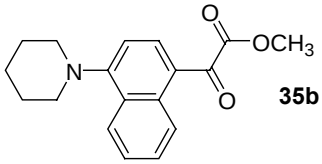


Table 1. Reaction of *N,N*-dialkylarylamines and $TiCl_4$ with diethyl oxalate.[a]

S.NO	$ArNR_2$	Ester	Product[b]	Yield[c] (%)
1	Ar = Ph, R = C_2H_5	 **33**	 **34a**	54
2	Ar = Ph, R = -C_5H_{10}-	**33**	 **34b**	52
3	Ar = 1-Naphthyl, R = CH_3	**33**	 **35a**	64
4	Ar = 1-Naphthyl, R = -C_5H_{10}-	**33**	 **35b**	61

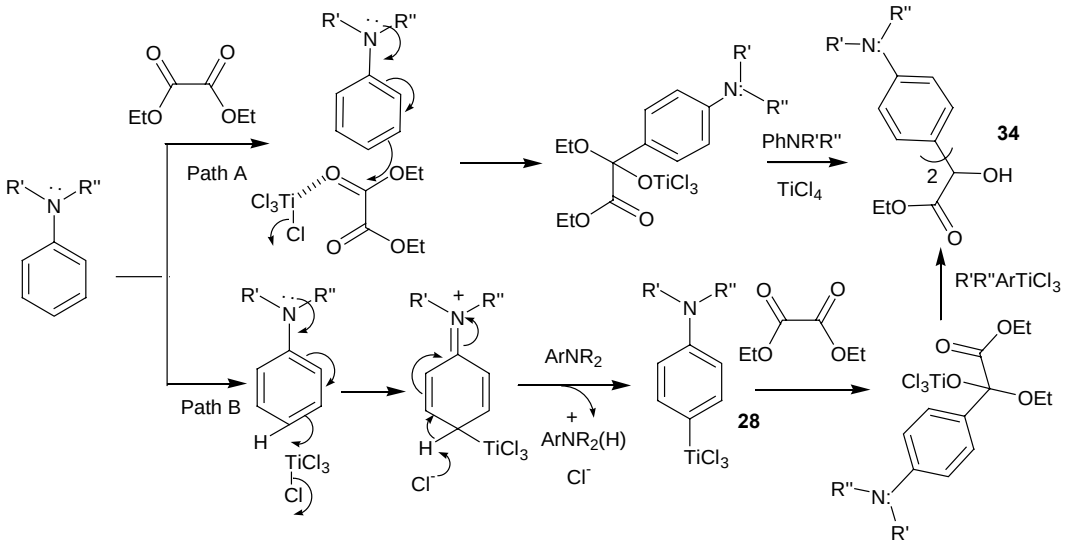
[a]The reactions were carried out using the amine (5 mmol), diethyl oxalate (2.5 mmol) and $TiCl_4$ (10 mmol, 2.2 mL of 1:1 solution of $TiCl_4/CH_2Cl_2$).

[b]The products were identified by ^1H, ^{13}C-NMR and mass spectral data.

[c]The isolated yields were based on the amount of diethyl oxalate used.

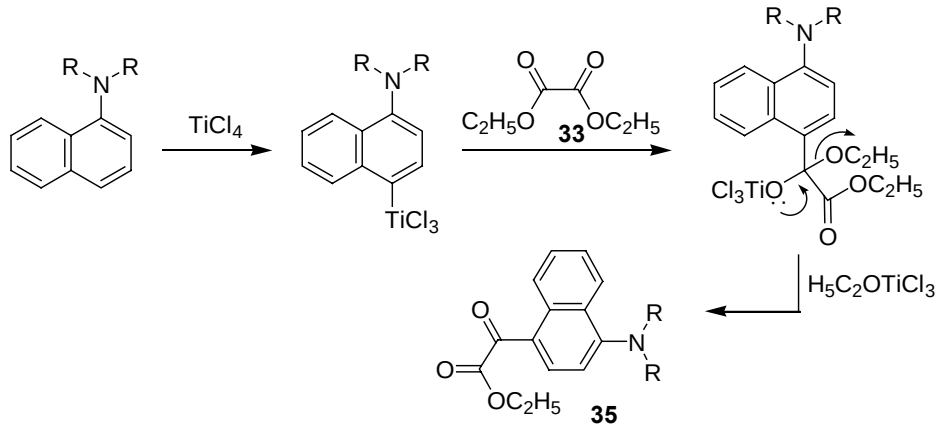
The reaction of *N,N*-dialkylaniline with diethyl oxalate can be visualized by two possible mechanistic pathways **A** or **B**. One is a simple addition reaction of *N,N*-dialkylaniline with diethyl oxalate activated by $TiCl_4$ (Path A). The other is the reaction between *in situ* formed aryltitanium species **28** and diethyl oxalate to give α-hydroxy esters **34** (Path B) as outlined in the Scheme 18.

Scheme 18



The reaction of diethyl oxalate **33** with the *N*,*N*-dialkyl-1-naphthylamine and $TiCl_4$ gave the α-keto ester **35** in 61-64% yields (Table 1, entries 3 and 4). The products and yields obtained with diethyl oxalate in the presence of other tertiary arylamines are summarized in Table 1. Presumably, in the case of *N*,*N*-dialkyl-1-naphthylamines the reaction stops at the α-keto ester stage due to steric hindrance (Scheme 19).

Scheme 19



1.2.1.2 Reaction of the tertiary arylamine/$TiCl_4$ reagent system with α-keto esters

We have examined the reaction of tertiary arylamine with unsymmetrical α-dicarbonyl compounds. Interestingly, the arylation takes place with selectivity at the keto carbonyl moiety of the α-keto ester **36** to produce the corresponding diarylated acetic acid esters **37** in 72-89% yields (Scheme 20). For example the reaction of *N*,*N*-diethylaniline gave the diarylated product **37a** in 89% yield with ethyl 4-methylbenzoylformate (Table 2, entry 1). Whereas, the reaction of ethyl benzoylformate with *N*,*N*-diethylaniline and $TiCl_4$ at 0-25 ºC for 5 h produced both the monoarylated **38a** as well as diarylated **37d** products in 22% and 68% yields, respectively (Table 2, entry 4). However, in the case of the transformation using *N*-ethyl,*N*-pentylaniline, the reaction stopped at the monoarylation stage to give exclusively the α-hydroxy ester **38b** in 78% yield (Table 2, entry 5). The transformation was generalized with various aryl α-keto esters as well as amines and the results are summarized in Table 2.

Scheme 20

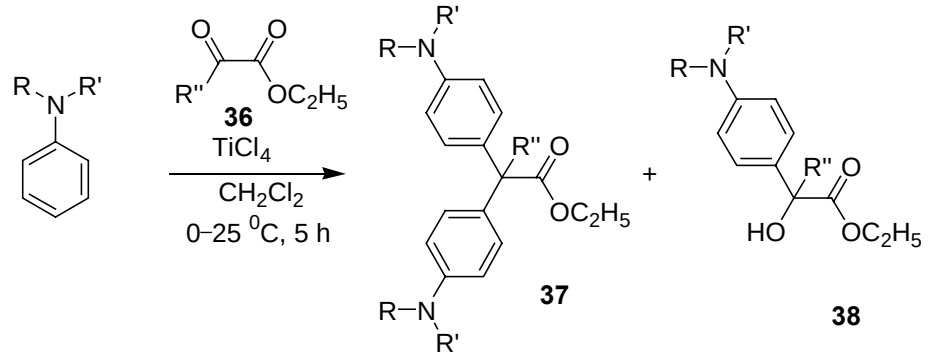
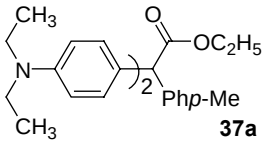
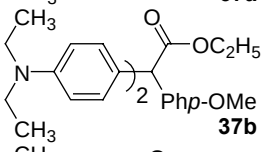
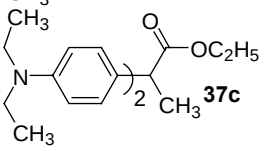
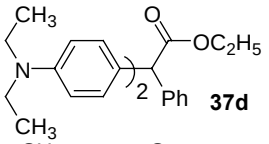
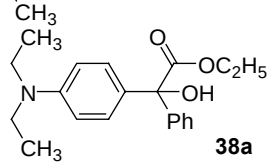
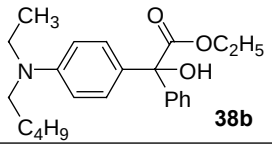


Table 2. Reaction of *N*,*N*-dialkyl arylamines and $TiCl_4$ with α-keto esters[a]

S.NO	PhNRR'	Keto ester	Product[b]	Yield[c] (%)
1	R, R' = C_2H_5	R'' = *p*-MePh	 **37a**	89
2	R, R' = C_2H_5	R'' = *p*-MeOPh	 **37b**	86
3	R, R' = C_2H_5	R'' = Me	 **37c**	81
4	R, R' = C_2H_5	R'' = Ph	 **37d**	68
			 **38a**	22
5	R = *n*-C_5H_{11} R' = C_2H_5	R'' = Ph	 **38b**	78

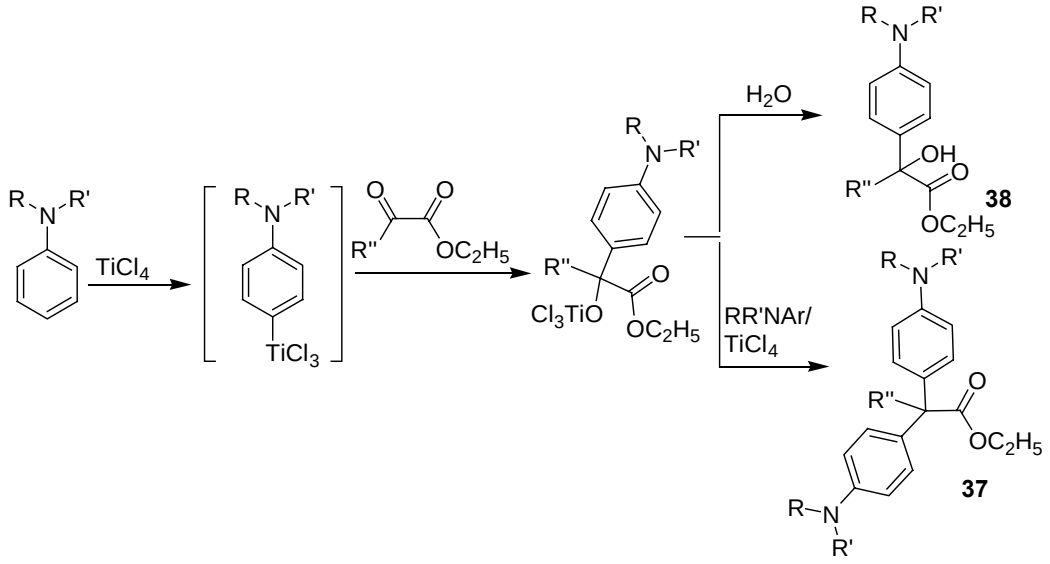
[a]The reactions were carried out using the amine (7.5 mmol), α-keto esters (2.5 mmol) and $TiCl_4$ (10 mmol, 2.2 mL of 1:1 solution of $TiCl_4/CH_2Cl_2$).

[b]The products were identified by ^1H, ^{13}C-NMR and mass spectral data.

[c]The isolated yields based on the amount of α-keto esters used.

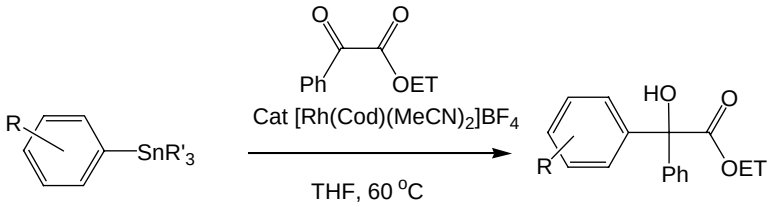
The addition of *N*,*N*-diethylaniline to α-keto ester can be visualized as outlined in the Scheme 21. Selective addition of *in situ* formed aryltitanium species to keto group of α-keto ester to give α-hydroxy esters **38**, followed by further addition of aryltitanium species to produce compound **37**.

Scheme 21



As outlined in the introductory section, arylmetal reagents such as aryltin reagents react with unsymmetrical α-dicarbonyl compounds to produce arylated products of type **38** under rhodium catalyst (Scheme 22).[18]

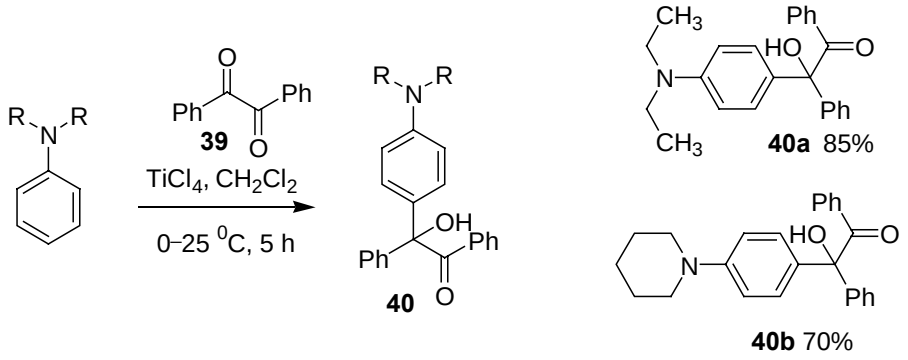
Scheme 22



1.2.1.3 Reaction of the tertiary arylamine/$TiCl_4$ reagent system with α-diketones

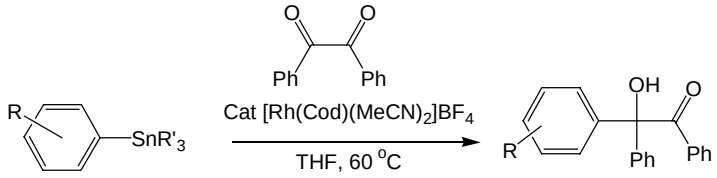
The reaction with symmetrical α-dicarbonyl compounds like benzil **39** was also examined. The corresponding monoarylated products were obtained in 70-85% yields. For example the reaction using *N*,*N*-diethylaniline gave α-hydroxy ketone **40a** in 85% yield and the use of *N*-phenylpiperidine gave **39b** in 70% yield (Scheme 23).

Scheme 23



This reaction pattern is also similar to that reported for rhodium catalyzed aryltin reagents as shown in Scheme 24.[18]

Scheme 24



1.2.1.4 Reaction of the tertiary arylamine/$TiCl_4$ reagent system with γ-dicarbonyl compounds

We have also examined the addition reaction of the arylamine/$TiCl_4$ reagent combination with unsymmetrical γ-dicarbonyl compounds. In the reaction using ethyl 2-benzoylbenzoates **41,** the γ-lactones **42** were obtained in 82-91% yields (Scheme 25). The results are summarized in Table 3.

Scheme 25

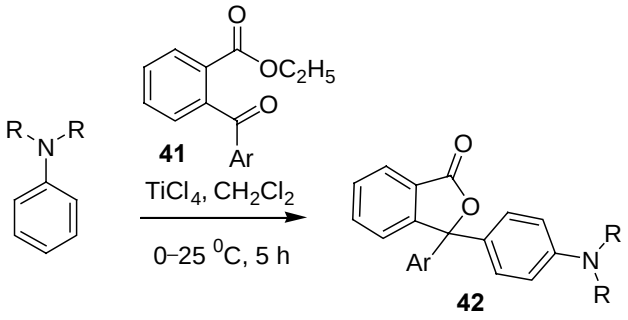
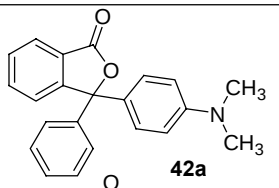
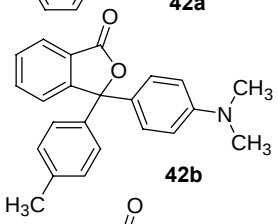
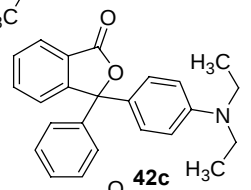
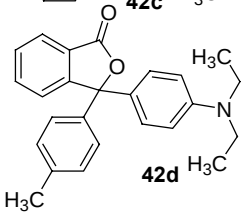


Table 3. Reaction of *N,N*-dialkyl arylamines with ethyl 2-benzoylbenzoates[a]

S.NO	$PhNR_2$	Keto ester **41**	Product[b]	Yield[c] (%)
1	R =CH_3	Ar = Ph	 **42a**	89
2	R = CH_3	Ar =*p*-CH_3Ph	 **42b**	86
3	R = C_2H_5	Ar = Ph	 **42c**	90
4	R = C_2H_5	Ar =*p*-CH_3	 **42d**	81

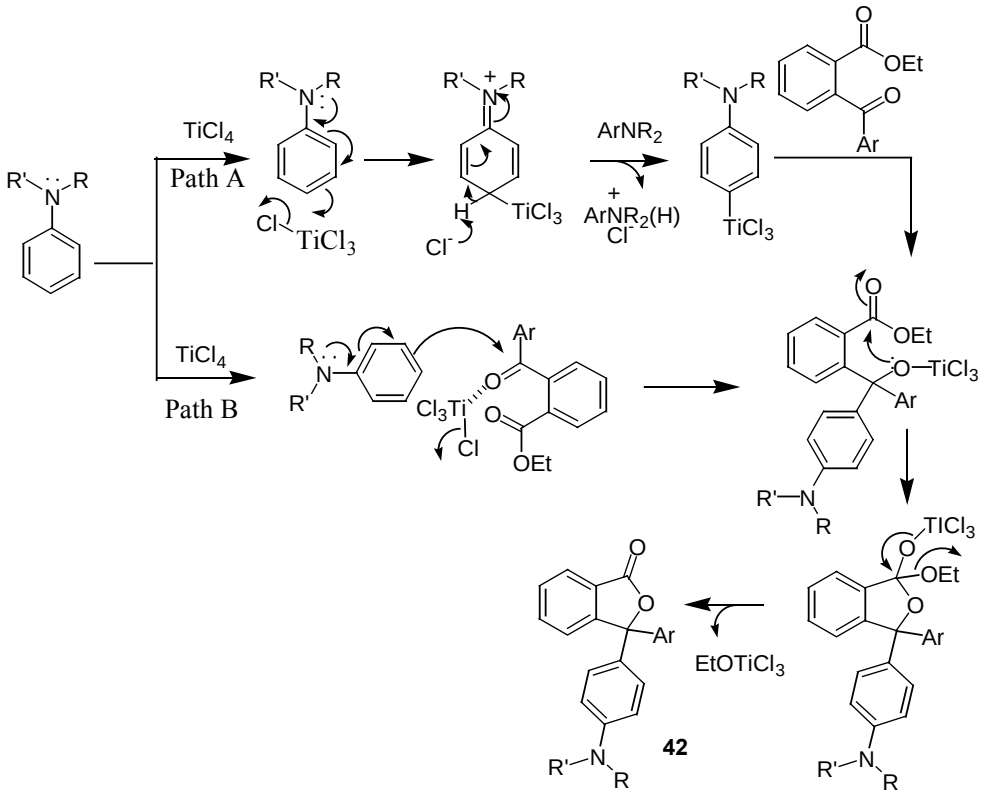
[a]The reactions were carried out using the amine (5 mmol), ethyl 2-benzoylbenzoate (2.5 mmol) and $TiCl_4$ (10 mmol, 2.2 mL of 1:1 solution of $TiCl_4/CH_2Cl_2$).

[b]The products were identified by ^1H, ^{13}C-NMR and mass spectral data.

[c]The isolated yields were based on the amount of carbonyl compound used.

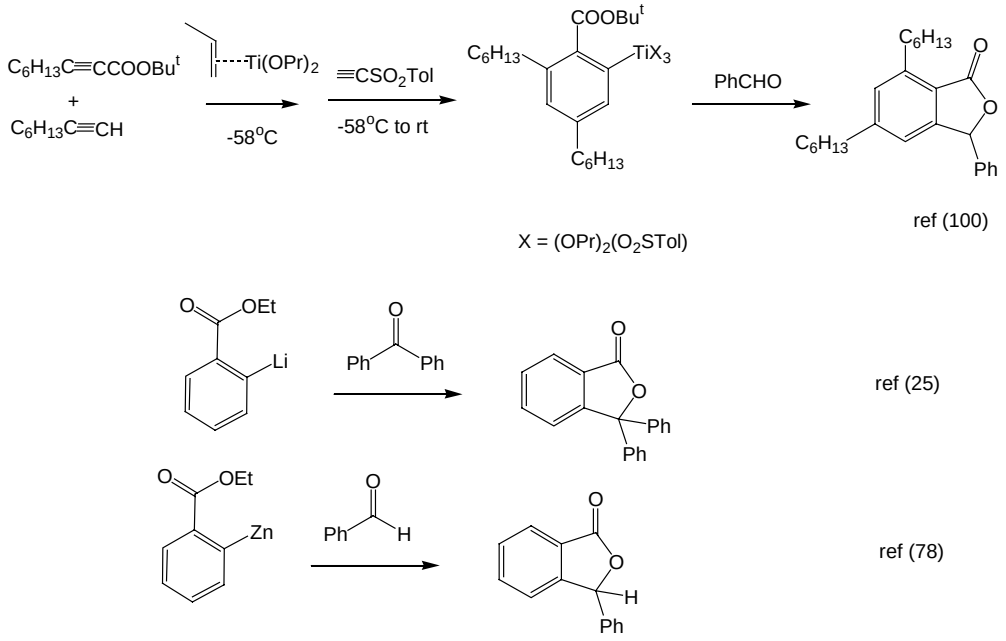
The selective addition of *N*,*N*-dialkylarylamines to ethyl 2-benzoylbenzoates **41** can be interpreted tentatively in terms of formation of aryltitanium species *in situ* as shown in (Path A) Scheme 26. However, the alternative pathway involving the activation of the ketocarbonyl by $TiCl_4$ followed by electrophilic substitution on the arylamine cannot be ruled out (Path B).

Scheme 26



Previously, the compounds of the type **42** were prepared using aryltitanium aryllithium, and arylzinc reagents as shown in Scheme 27.

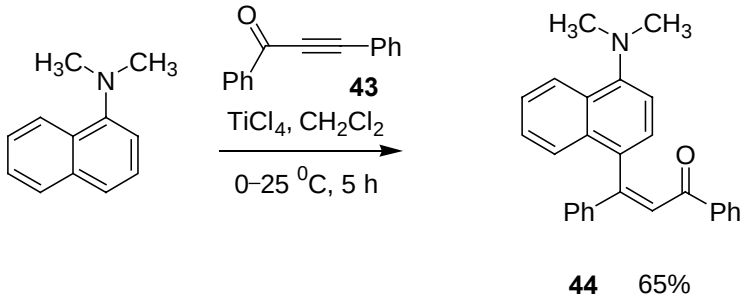
Scheme 27



1.2.1.5 Reaction of the tertiary arylamine/$TiCl_4$ reagent system with α,β-unsaturated carbonyl compounds

As outlined in introductory section,[94] aryltitanium reagents **11** undergoes 1,4-addition to enones, to give the ketone **19** (Chart 24)**.** We have observed that the reaction of the arylamine/$TiCl_4$ reagent system with α,β-unsaturated carbonyl compounds like alkynyl ketone gave the similar reactivity and the corresponding 1,4-addition product was formed. For example, in the reaction of *N*,*N*-dimethyl-1-naphthylamine and $TiCl_4$ with alkynyl ketone **43,** the ketone **44** was obtained in 65% yield (Scheme 28)**.**

Scheme 28

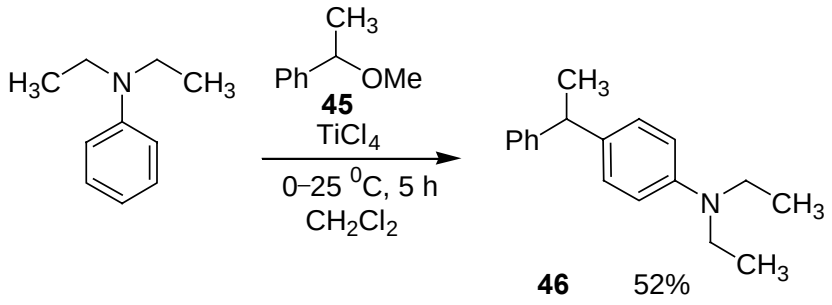


44 65%

1.2.2 Reaction of the tertiary arylamine/$TiCl_4$ reagent system with methoxy compounds

In the several of the above transformations, the $–OTiCl_3$ group is expected to be the leaving group. Accordingly, aryl ethers containing benzylic $-OCH_3$ groups would also undergo such transformation upon complexation with $TiCl_4$. Indeed, this was observed, the reaction of *N,N*-diethylaniline/$TiCl_4$ combination with 1-phenylethyl methyl ether **45** to produced *N,N*-diethylaniline derivative **46** in 52% yield (Scheme 29).

Scheme 29

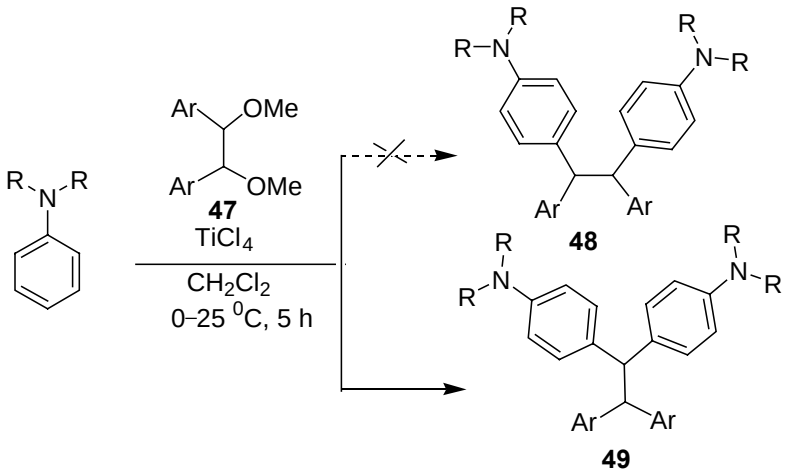


46 52%

Interestingly, in the reaction using aryl ethers like 1,2-dimethoxy-1,2-diarylethane **47,** the expected 1,2-disubstistuted product **48** was not formed. Instead, 1,1- disubstituted aryl product **49** was formed through rearrangement (Scheme 30). For example, the reaction

of the *N,N*-diethylaniline/$TiCl_4$ reagent system and 1,2-dimethoxy-1,2-diphenylethane produced the substituted product **49a** in 85% yield. The reaction was generalized using other 1,2-dimethoxy-1,2-diarylethane as well as amines. The results are summarized in Table 5.

Scheme 30



The product **49c** was also identified by X-ray crystal structure analysis.

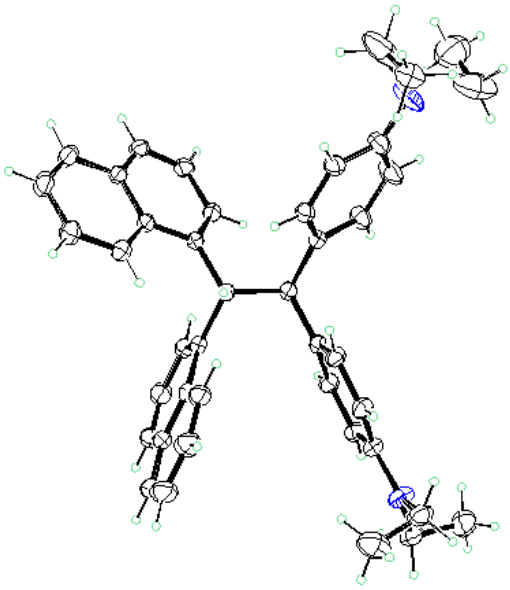
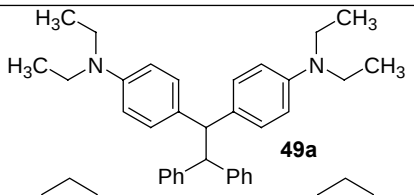
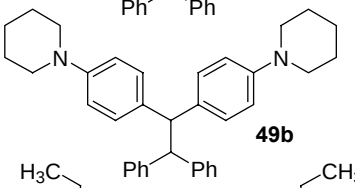
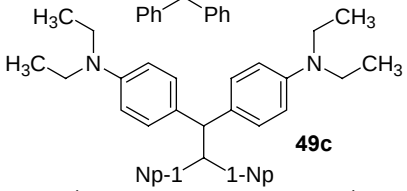
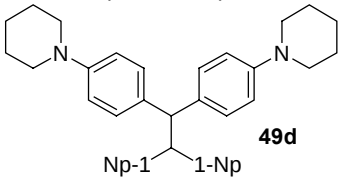


Fig. 1: ORTEP diagram of compound **49c**

Table 4: Crystal data and structure refinement for **49c**

Empirical formula	$C_{42} H_{44} N_2$
Formula weight	576.79
Temperature	298(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P-1
Unit cell dimensions	a = 11.2663(8) Å, α = 102.9260(10)°. b = 13.1471(9) Å, β = 111.8580(10)°. c = 13.8028(9) Å, γ = 08.1940(10)°.
Volume	1663.3(2) $Å^3$
Z	2
Density (calculated)	1.152 Mg/m^3
Absorption coefficient	0.066 mm^{-1}
F(000)	620
Crystal size	0.45 x 0.40 x 0.16 mm^3
Theta range for data collection	1.72 to 28.29°.
Index ranges	-14<=h<=14,-17<=k<=17, -18<=l<=18
Reflections collected	19581
Independent reflections	7789 [R(int) = 0.0415]
Completeness to theta = 25.00°	99.5 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.98 and 0.97
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	7789 / 0 / 397
Goodness-of-fit on F^2	1.029
Final R indices [I>2sigma(I)]	R1 = 0.0710, wR2 = 0.1950
R indices (all data)	R1 = 0.1222, wR2 = 0.2240
Largest diff. peak and hole	0.452 and -0.411 $e.Å^{-3}$

Table 5. Reaction of *N,N*-dialkyl arylamines and $TiCl_4$ with 1,2-dimethoxy-1,2-diarylethanes[a]

S.NO	$PhNR_2$	Ether **47**	Product[b]	Yield [c] (%)
1	R = C_2H_5	Ar' = Ph	 **49a**	89
2	R = -C_5H_{10}-	Ar' = Ph	 **49b**	86
3	R = C_2H_5	Ar' = 1-Naphthyl	 **49c**	90
4	R = -C_5H_{10}-	Ar' = 1-Naphthyl	 **49d**	81

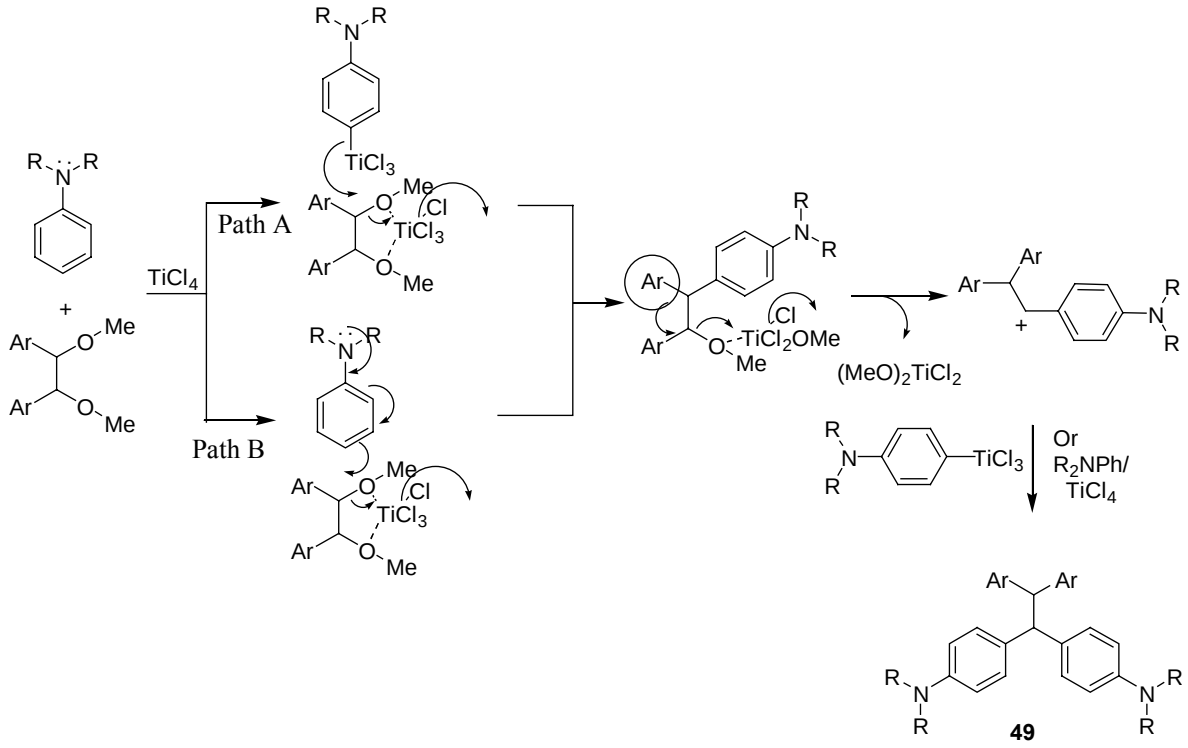
[a] The reactions were carried out using arylamine (7.5 mmol), 1,2-dimethoxy-1,2-diarylethane **47** (2.5 mmol) and $TiCl_4$ (10 mmol, 1:1 solutiom of $TiCl_4/CH_2Cl_2$).

[b]The products were identified by ^1H ,^{13}C-NMR and the product **49c** was identified by X-ray crystal structure.

[c]The isolated yields were based on the amount of ether **47** used.

The reaction of *N,N*-dialkylanilines to 1,2-dimethoxy-1,2-diarylethanes can be interpreted in terms of substitution of aryltitanium species formed *in situ* followed by the rearrangement of aryl group to give the carbocation and further arylation to produce product **49** as outlined in Scheme 31 (Path A). However, the alternative pathway involving the $TiCl_4$ promoted arylation by the amine cannot be ruled out (Path B).

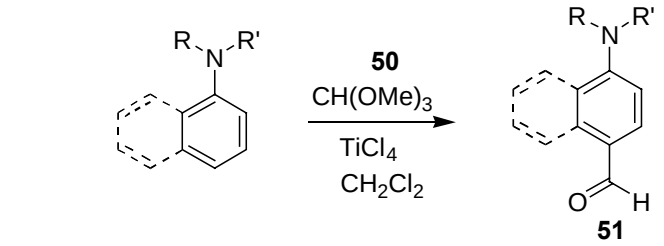
Scheme 31

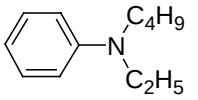
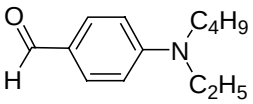
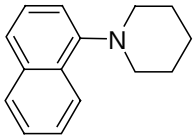
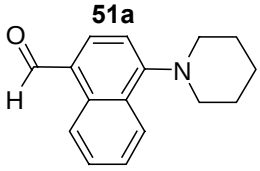


1.2.2.1 Reaction of the tertiary arylamine/$TiCl_4$ reagent system with trimethyl orthoformate

It was of interest to us to examine the reaction of *N*,*N*-dialkylarylamines with trimethyl orthoformate **50**. In this case, the corresponding formylated products **51** were obtained in good yields (Scheme 32). The reaction of *N*-ethyl, *N*-butylaniline with trimethyl orthoformate gave formylated product **51a** in 78% yield. Similarly, *N*-(1-naphthyl)piperidine gave corresponding aldehyde **51b** in 82% yield.

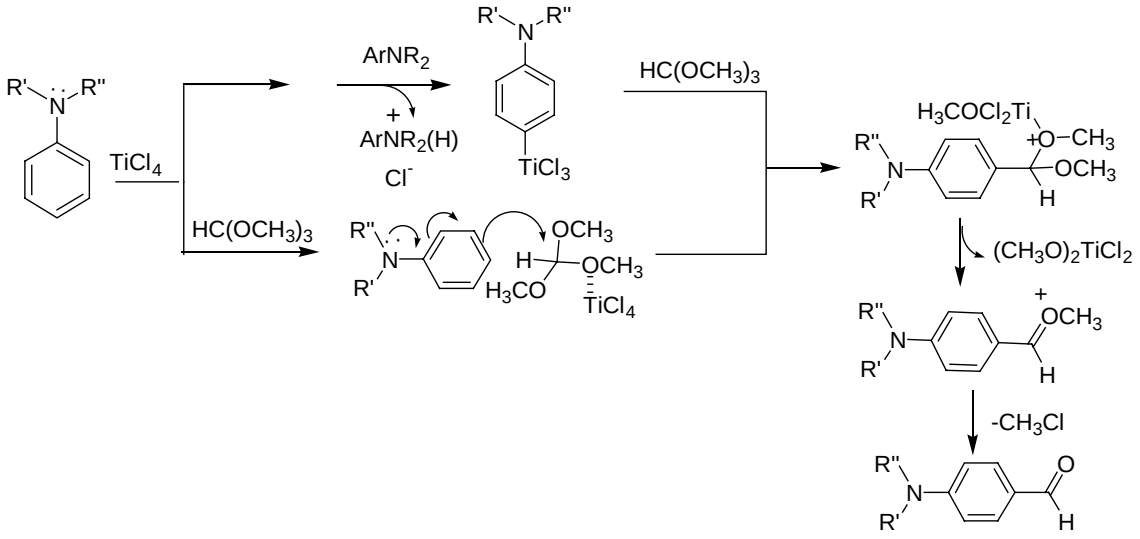
Scheme 32



Amine	Product	Yield%
	 **51a**	74
	 **51b**	82

Presumably, the monoarylated acetal intermediates are hydrolyzed upon work up to give the aldehyde products and the transformation can be visualized by the mechanistic pathway outlined in the Scheme 33. Again, the alternative pathway involving coordination of the -OCH_3 group in the orthoformate with $TiCl_4$ followed by arylation by amine cannot be ruled out.

Scheme 33



Formylation is a key process in organic synthesis. Not surprisingly, a large number of methods have been developed for this reaction. Reagents for electrophilic formylation [104] are mostly of the type Y-CH=X^+. Thus, the reaction attributed to Vilsmeier ($ClCH=NR_2^+$), Rieche (eg.: $MeOCHCl_2 \rightarrow MeO=CHCl^+$), Gatterman ($Zn[CN]_2/HCl \rightarrow HC=NH_2^{2+}$), Gatterman-Koch (CO/HCl/Lewis acid $\rightarrow HC=O^+$) and even Duff ($CH_2=NH_2^+$) followed by dehydrogenation of initially formed RCH_2NH_2 all fit this pattern.[103] Previously, $TiCl_4$ has been used in alliance with $MeOCHCl_2$ reagent system for the formylation of diphenols, 3-substituted thiophines and *O*-formylation of phenols.[104] The method described here is a good addition to these pool of the methods.

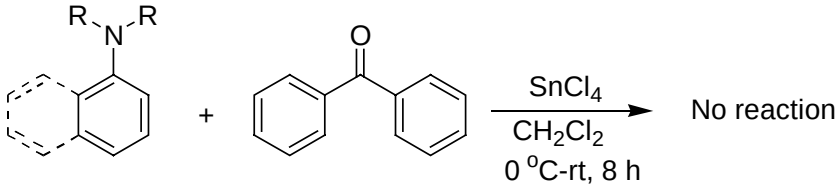
1.2.3 Reactions of *N,N*-dialkylarylamines in the presence of other Lewis acids with electrophiles

As discussed in the above sections, several transformations can be explained by initial complexation of the electrophiles by the Lewis acid $TiCl_4$ for reaction with arylamines. Accordingly, we became interested in examining some of these transformations using $SnCl_4$ and $F_3B{:}OEt_2$.

1.2.3.1 Reactions of the *N,N*-dialkylarylamines /$SnCl_4$ reagent system with electrophiles

Initially, we have used $SnCl_4$ as Lewis acid. The reactions of *N,N*-dialkylarylamines with aryl ketones like benzophenone was not observed (Scheme 34).

Scheme 34



However, *N*,*N*-dialkylarylamines reacted with methoxy compounds as well as α,β-unsaturated carbonyl compounds in the presence of $SnCl_4$ to give the corresponding arylated compounds.

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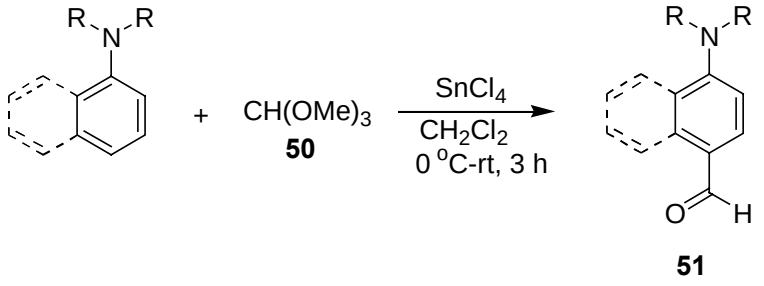
1.2.3.1.1 Reaction of the tertiary arylamine/$SnCl_4$ system with trimethyl orthoformate

We have observed that the reaction of *N*,*N*-dialkylarylamines with trimethyl orthoformate **50** and $SnCl_4$ produce the corresponding formylated products **51** in good yields (Scheme 35). The reaction of *N*,*N*-diethylaniline with trimethyl orthoformate gave formylated product **51c** in 64% yield. Whereas, *N*,*N*-dialkyl -1-naphthylamines produced better yields than *N*,*N*-dialkylanilines. In the case of *N*,*N*-dimethyl-1-naphthylamine, the corresponding aldehyde was obtained in 72% yield. The reaction was generalized with other amines and the results are summarized in Table 6.

Scheme 35



The reaction of *N*,*N*-dialkylarylamines with trimethyl orthoformate in the presence of $SnCl_4$ can be visualized by the mechanistic pathway outlined in the Scheme 36.

Scheme 36

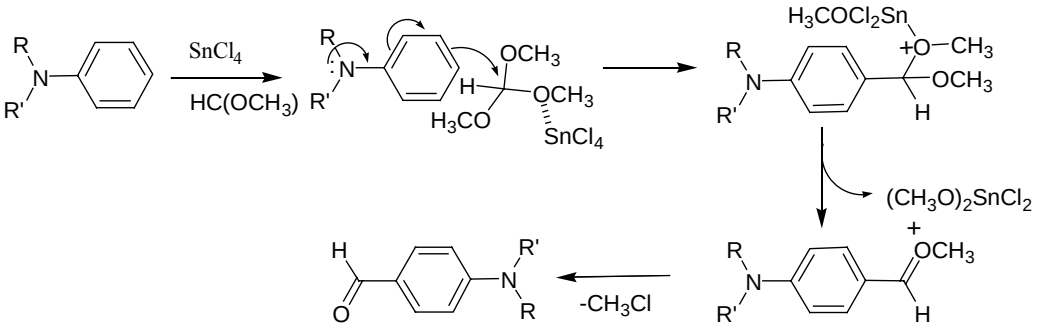
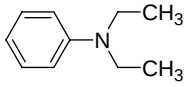
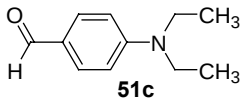
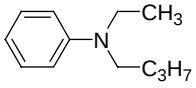
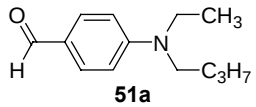
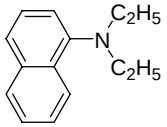
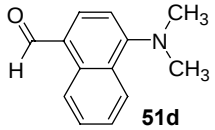
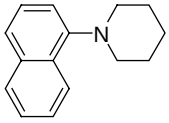
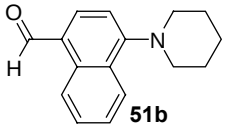


Table 6. Reaction of *N*,*N*-dialkyl arylamines with trimethyl orthoformate, acetals and $SnCl_4$[a]

S.NO	Amine	Electrophile (%)	Product[b]	Yield[c]
1		$HC(OCH_3)_3$	 **51c**	64
2		$HC(OCH_3)_3$	 **51a**	62
3		$HC(OCH_3)_3$	 **51d**	72
4		$HC(OCH_3)_3$	 **51b**	69

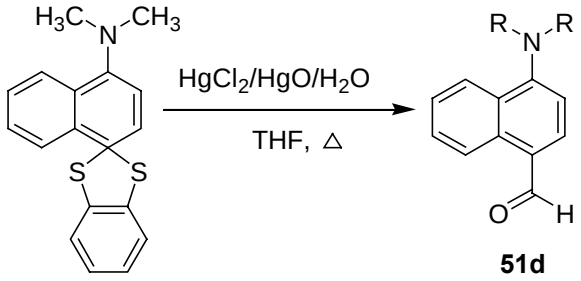
[a]The reactions were carried out using arylamine (5 mmol), trimthyl ortoformatethe (7.5 mmol), and $SnCl_4$ (10 mmol).

[b]The products were identified by ^1H, ^{13}C-NMR and mass spectral data.

[c]The yields were of isolated products.

Previously, it was reported that the hydrolysis of 2-arylbenzo-1,3-dithioles using mercury(II)chloride and mercury(II)oxide in boiling aqueous tetrahydrofuran produced 5**1d** in 37% yield (Scheme 37).[105]

Scheme 37

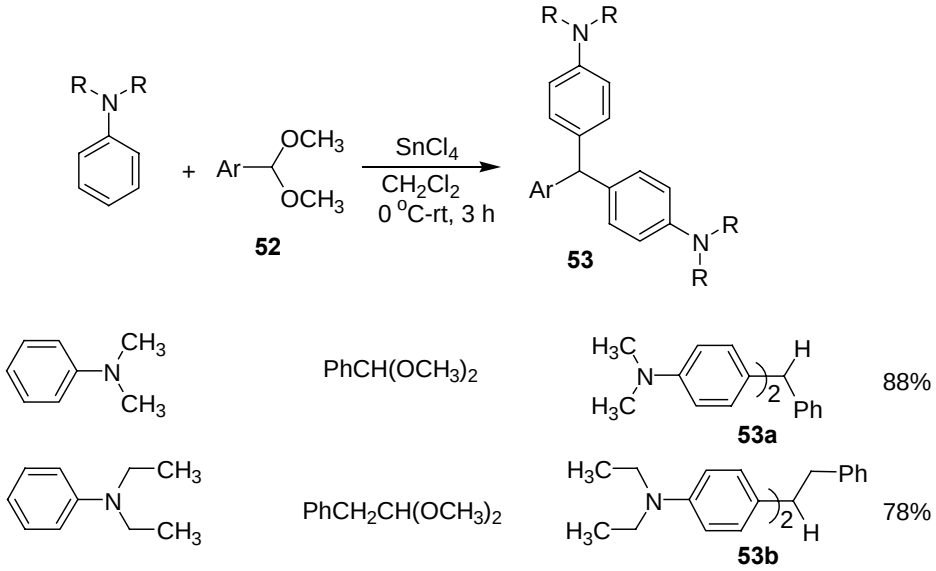


The present methods using $TiCl_4$ and $SnCl_4$ could serve as good alternative methods for this transformation.

1.2.3.1.2 Reaction of the tertiary arylamine /$SnCl_4$ system with acetals

We have also observed that in the reaction of *N*,*N*-dialkylanilines with acetals **52** gave the corresponding diarylated derivatives **53.** For example, the reaction of benzaldehyde dimethyl acetal and *N*,*N*-dimethylaniline with $SnCl_4$ produced triarylmethane derivative **53a** in 88% yield (Scheme 38). Similarly, phenylacetaldehyde dimethyl acetal gave diaryl substituted product **53b** in 78% yield.

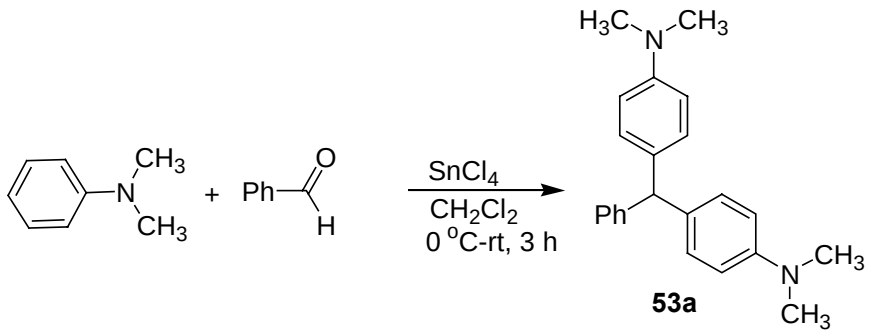
Scheme 38



1.2.3.1.3 Reaction of the tertiary arylamine/$SnCl_4$ system with benzaldehyde

The reaction of *N*,*N*-diethylaniline and benzaldehyde with $SnCl_4$ produced the triarylmethane derivative **53a** in 64% yield (Scheme 39). Presumably, this product would have formed through further arylation of the initially formed product.

Scheme 39

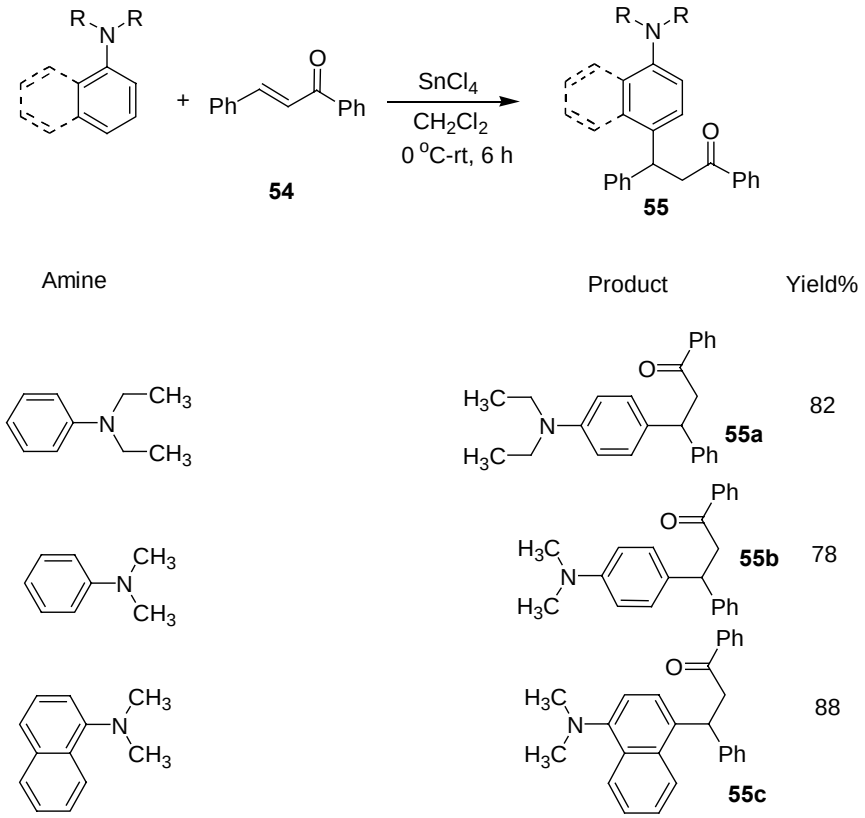


It is of interest to note here that aryl aldehydes have reported to react with $PhSn(Me)_3$ in the presence of a rhodium catalyst to produce the corresponding secondary alcohols.[55]

1.2.3.1.4 Reaction of the tertiary arylamine/$SnCl_4$ system with α,β-unsaturated carbonyl compounds

We have also examined the reaction of *N*,*N*-dialkylaniline with α,β-unsaturated carbonyl compounds like chalcone **54** in the presence of $SnCl_4$. In the reaction using, *N*,*N*-diethylaniline and chalcone, the corresponding 1,4-addition product **55a** was obtained in 82% yield. Whereas, with *N*,*N*-dimethylaniline and *N*,*N*-dimethyl-1-naphthylamine the corresponding 1,4-addition products **55b** and **55c** were produced in 78% and 88% yields, respectively (Scheme 40).

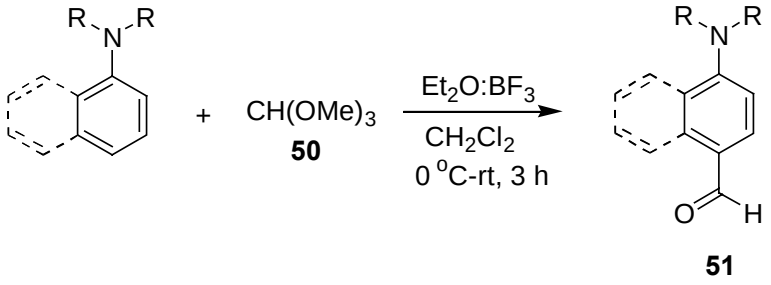
Scheme 40



1.2.3.2 Reactions of the *N,N*-dialkylarylamines/$Et_2O:BF_3$ reagent system with electrophiles

We have also examined the reaction of *N*,*N*-dialkylarylamines with methoxy compounds in the presence of $Et_2O:BF_3$. We have observed that the reaction of *N*,*N*-dialkylarylamines with trimethyl orthoformate **50** and $Et_2O:BF_3$. The corresponding formylated products **51** were obtained in good yields (Scheme 41). The reaction of *N*,*N*-diethylaniline with trimethyl orthoformate and $Et_2O:BF_3$ gave formylated product *N*,*N*-diethylaminobenzaldehyde **51c** in 61% yield. Whereas, in the case of, *N*,*N*-dimethyl-1-naphthylamine the corresponding aldehyde **51d** was obtained in 78% yield. The reaction was generalized with other amines and the results are summarized in Table 7.

Scheme 41



The reaction of acetals and *N*,*N*-dialkylanilines with $Et_2O:BF_3$ gave the corresponding arylated products **53** (Scheme 42). For example, the reaction of benzaldehyde dimethyl acetal and *N*,*N*-dimethylaniline with $Et_2O:BF_3$ produced triarylmethane derivative **53a** in 75% yield (entry 4, Table 7). Whereas, phenylacetaldehyde dimethyl acetal produced diarylmethane derivative **53b** in 80% yield (entry 5, Table 7).

Scheme 42

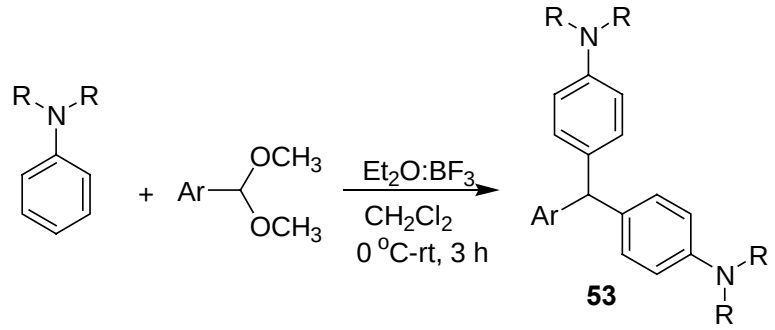
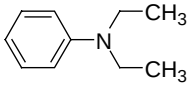
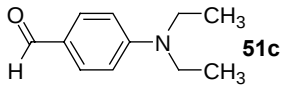
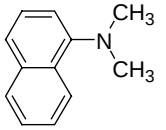
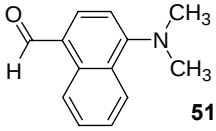
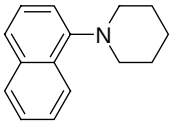
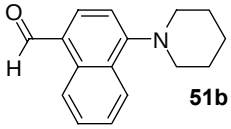
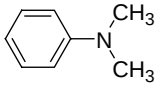
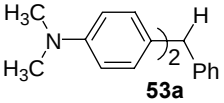
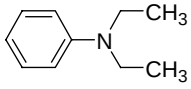
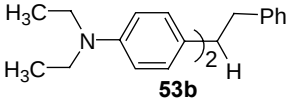


Table 7. Reaction of *N,N*-dialkyl aryl amines with trimethyl orthoformate, acetals and $Et_2O:BF_3$[a,b]

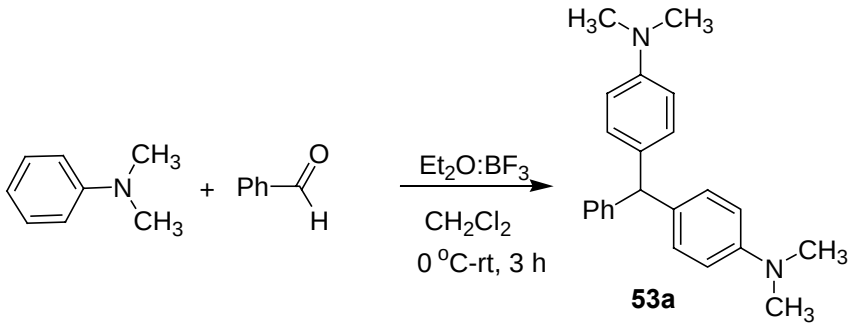
S.NO	Amine	Electrophile	Product	Yield (%)
1		$HC(OCH_3)_3$	 **51c**	61
2		$HC(OCH_3)_3$	 **51d**	78
3		$HC(OCH_3)_3$	 **51b**	64
4		$PhCH(OCH_3)_2$	 **53a**	75
5		$PhCH_2CH(OCH_3)_2$	 **53b**	80

[a] The reactions were carried out using arylamine (5 mmol), trimethyl orthoformate (7.5 mmol), and $Et_2O:BF_3$ (10 mmol).

[b]The reactions were carried out using acetals (2.5 mmol), amine (7.5 mmol) and $Et_2O:BF_3$ (10 mmol).

The product **53a** was obtained in 74% yield in the reaction of *N,N*-diethylaniline with benzaldehyde and $Et_2O{:}BF_3$ (Scheme 43).

Scheme 43



The formyl derivatives of *N,N*-dialkylarylamines have been used for the synthesis of dialkylaminostyryl dyes. Moreover, majority of naphthylidene dyes are found to be far better photographic sensitizers than the corresponding styryl dyes.[106] Accordingly, the new method described here for the synthesis of these derivatives has good synthetic potential.

1. 3 Conclusions

The reaction of reactive *N*,*N*-dialkyl arylamines and $TiCl_4$ was examined using electrophiles. The reaction using *N*,*N*-dialkylanilines and diethyl oxalate with $TiCl_4$ produced α-hydroxy esters as well as α-keto esters by the addition of arylamine moiety selectively at one carbonyl group. The reaction using *N*,*N*-dialkylanilines and α-keto ester produced the corresponding diarylated acetic acid esters as well as α-hydroxy esters in good yields. The reaction with symmetrical α-dicarbonyl compounds like α-diketones produced α-hydroxyketones in good yields. The addition reaction to unsymmetrical γ-dicarbonyl compounds like ethyl 2-benzoylbenzoates gave γ-lactones. The reaction using α,β-unsaturated carbonyl compounds like alkynyl ketone gave the corresponding 1,4-addition product. The reactions with aryl ethers like 1,2-dimethoxy-1,2-diarylethane gave 1,1-disubstituted aryl products through the rearrangement.

The reactivity of *N*,*N*-dialkyl arylamines with electrophiles were also examined using the Lewis acids $SnCl_4$ and $Et_2O{:}BF_3$. The reactivity pattern with benzylic $-OCH_3$ group is similar with all Lewis acids, $TiCl_4$, $SnCl_4$ and $F_3B{:}OEt_2$.

1.4 Experimental Section

General Information

Melting points reported in this thesis are uncorrected and were determined using a Superfit capillary point apparatus. IR (KBr) spectra were recorded on JASCO FT-IR spectrophotometer Model 5300. The neat IR spectra were recorded on JASCO FT-IR spectrophotometer Model 5300 and SHIMADZU FT-IR spectrophotometer Model 8300 with polystyrene as reference. ^{1}H-NMR (200 MHz), ^{13}C-NMR (50 MHz)) and ^{1}H-NMR (400 MHz), ^{13}C-NMR (100 MHz) spectra were recorded on Bruker-AC-200 and Bruker-Avance-400 spectrometer with chloroform-d as solvent and TMS as reference (δ = 0 ppm). The chemical shifts are expressed in δ downfield from the signal of internal TMS. Elemental analyses were carried out using a Perkin-Elmer elemental analyzer model-240C and Thermo Finnigan analyzer series Flash EA 1112. Mass spectral analyses were carried out on VG 7070H mass spectrometer using EI technique at 70 eV.

Analytical thin layer chromatographic tests were carried out on glass plates (3 x 10 cm) coated with 250 mμ acme's silica gel-G and GF_{254} containing 13% calcium sulfate as binder. The spots were visualized by short exposure to iodine vapour or UV light. Column chromatography was carried out using acme's silica gel (100-200 mesh).

All the glassware were pre-dried at 140 ^{o}C in an air-oven for 4 h, assembled in hot condition and cooled under a stream of dry nitrogen. Unless, otherwise mentioned, all the operations and transformations of reagents were carried out using standard syringe, septum technique recommended for handling air sensitive organometallic compounds. Reagents prepared *in situ* in solvents were transferred using a double-ended stainless steel (Aldrich) needle under a pressure of nitrogen whenever required.

In all experiments, a round bottom flask of appropriate size with a side arm, a side septum, a magnetic stirring bar, a condenser and a connecting tube attached to a mercury bubbler were used. The outlet of the mercury bubbler was connected by a long tube to the atmosphere. All dry solvents and reagents (liquids) used were distilled from appropriate

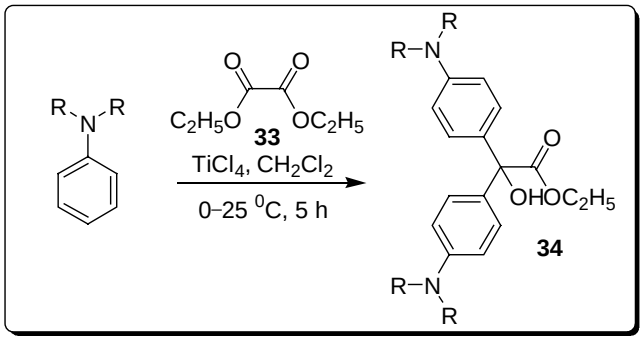
drying agents. As a routine practice, all organic extracts were washed with saturated sodium chloride solution (brine) and dried over anhydrous $MgSO_4$ or Na_2SO_4 and concentrated on Buchi-EL-rotary evaporator. All yields reported are of isolated materials adjudged homogeneous by TLC, IR and NMR spectroscopy. Dichloromethane, 1,2-dichloroethane and chloroform were distilled over CaH_2 and dried over molecular sieves. All the tertiary amines were distilled over CaH_2 and stored over KOH pellets. Titanium tetrachloride, supplied by Spectrochem Ltd., India was used. It was used as 1:1 $TiCl_4$:CH_2Cl_2 stock solution. *N*,*N*-Diethylaniline and *N*,*N*-dimethylaniline were supplied by Spectrochem Ltd., India. PhCHO was distilled before use. Trimethyl orthoformate were supplied by E. Merck (India).

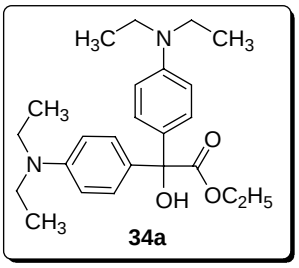
The X-ray diffraction measurements for the respective compounds were carried out at 293 K on an automated Enraf-Nonius MACH3 difractometer using graphite monochromated, Mo-Kα (λ = 0.71073 A^o) radiation with CAD4 software. Primary unit cell constants were determined with a set of 25 narrow frame scans. Intensity data were collected by the ω scan mode. Measuring the intensity of the three standard reflections after every one and half hour intervals monitored stability of the crystal during the measurement. No appreciable variation of the crystal was detected. X-ray diffraction measurements for the respective compounds were carried out at 293 K on Bruker-Nonius SMART APEX CCD area detector system. The data were reduced using XTAL 3.4 (or) SAINT programme,[107] without applying absorption correction. The refinement for structure was made by full-matrix least squares on F^2 (SHELX 97 or SHELXTL).[108]

1.4.1 Reaction of *N,N*-dialkyl arylamines and $TICl_4$ with electrophiles

1.4.1.1 Reaction of *N,N*-dialkyl arylamines and $TICl_4$ with diethyl oxalate

In CH_2Cl_2 (25 mL), *N,N*-diethylaniline (1.2 mL, 7.5 mmol) and diethyl oxalate (0.35 ml, 2.1 mmol) were taken at 0 °C under N_2. The $TiCl_4$ (2.2 mL of 1:1 solution of $TiCl_4/CH_2Cl_2$, 10 mmol) in 10 mL of CH_2Cl_2 was added drop wise for 15 minutes. The reaction mixture was stirred at 0 °C for 0.5 h and stirred further at 0-25 °C for 5 h. A saturated K_2CO_3 solution (10 mL) was added and stirred for 0.5 h. The contents were filtered through a Buchner funnel. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 25 mL). The combined organic extract was washed with brine solution (10 mL) and dried over anhydrous $MgSO_4$. The solvent was removed and the residue was chromatographed on a silica gel column. The unreacted amine and *N,N,N',N'*-tetramethylbenzidine were eluted using 2:98 EtOAc/hexane mixture. The α-hydroxy ester **34a** was next eluted.





34a

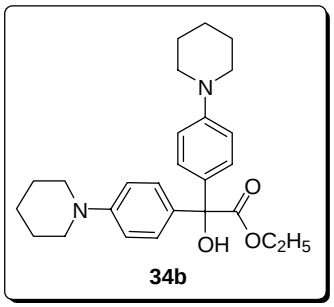
Yield 0.57 g (58%)

IR (Neat) (cm^{-1}) 3560, 2972, 1720, 1610, 1517, 1267, 1195, 812

^{1}H-NMR (δ ppm, $CDCl_3$) 7.27 (d, J=8.8 Hz, 4H), 6.53 (d, J=8.8 Hz, 4H), 4.30 (q, J=6.8 Hz, 2H), 3.37 (q, J=7.2 Hz, 8H), 1.32 (t, J=7.2 Hz, 3H), 1.18 (t, J=6.8 Hz, 12H) **(Spectrum No. 1)**

^{13}C-NMR (δ ppm, $CDCl_3$) 175.5, 147.4, 129.5, 128.5, 111.2, 80.5, 62.2, 44.3, 14.1, 12.7 **(Spectrum No. 2)**

MS (EI) m/z 398 (M^+, 37%) **(Spectrum No. 3)**



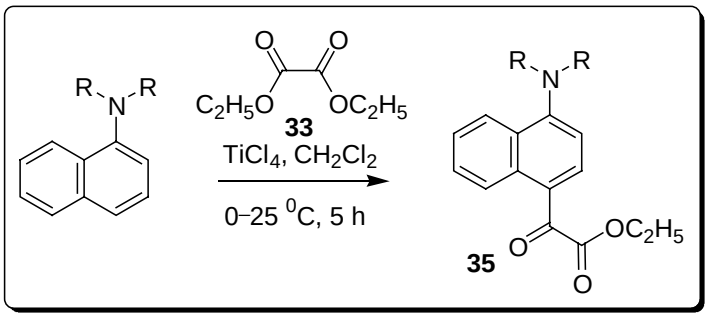
34b

Yield 0.59 g (57%)

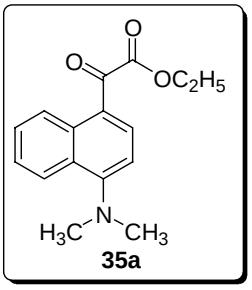
IR (Neat) (cm^{-1}) 3493, 2932, 1732, 748

^{1}H-NMR (δ ppm, $CDCl_3$) 7.31 (d, J=8.8 Hz, 4H), 6.88 (d, J=8.8 Hz, 4H), 4.29 (q, J=6.8 Hz, 2H), 3.18 (t, J=5.6 Hz, 8H), 1.85-1.52 (m, 12H), 1.27 (t, J=6.8 Hz, 3H)

^{13}C-NMR (δ ppm, $CDCl_3$) 172.7, 151.3, 131.3, 129.4, 115.1, 86.2, 60.6, 61.1, 50.2, 25.9, 24.3, 15.5, 14.1



Yield 0.46 g (69%)



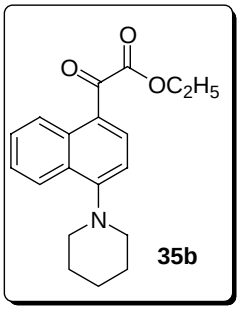
IR (Neat) (cm^{-1}) 2925, 2850, 1732, 1654, 1564, 1515, 1083, 771

^{1}H-NMR (δ ppm, $CDCl_3$) 9.30 (d, J=8.8 Hz, 1H), 8.13 (d, J=8.8 Hz, 1H), 7.88 (d, 1H), 7.72-7.48 (m, 2H), 6.91 (d, J=7.8 Hz, 1H), 4.46 (q, J=7.2 Hz, 2H), 3.05 (s, 6H), 1.43 (t, J=7.2 Hz, 3H)

^{13}C-NMR (δ ppm, $CDCl_3$) 187.4, 165.5, 157.8, 136.5, 133.4, 129.0, 127.5, 126.4, 125.4, 125.3, 120.5, 110.7, 61.9, 44.4, 14.1

MS (EI) m/z 271

Yield 0.47 g (62%)



IR (Neat) (cm^{-1}) 2935, 2850, 1732, 1658, 1566, 1512, 1207, 1080, 771

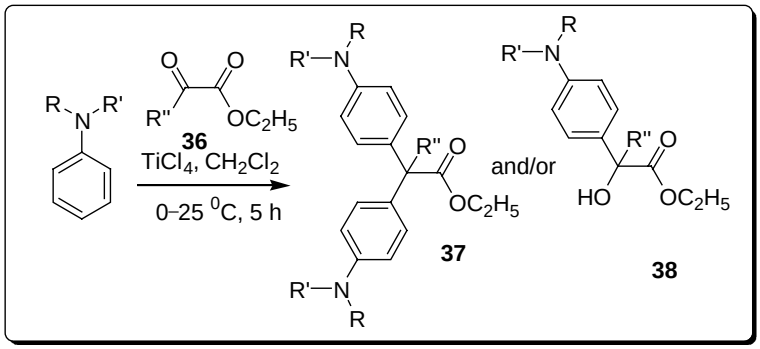
^{1}H-NMR (δ ppm, $CDCl_3$) 9.27 (d, J=8.8 Hz, 1H), 8.14 (d, J=8.8 Hz, 1H), 7.90 (d, J=8.8 Hz, 1H), 7.72-7.48 (m, 2H), 6.96 (d, J=8.8 Hz, 1H), 4.46 (q, J=6.8 Hz, 2H), 3.19 (t, J=5.6 Hz, 4H), 2.10-1.62 (m, 6H), 1.43 (t, J=6.8 Hz, 3H) **(Spectrum No. 4)**

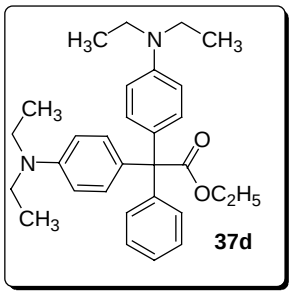
^{13}C-NMR (δ ppm, $CDCl_3$) 187.1, 165.4, 158.1, 136.5, 133.2, 129.0, 128.4, 126.4, 125.9, 124.7, 121.4, 112.0, 62.0, 54.2, 26.2, 24.4, 14.1 **(Spectrum No. 5)**

MS (EI) m/z 311 (M^+, 32%)

1.4.1.2 Reaction of the *N,N*-dialkyl arylamines/$TiCl_4$ reagent system with α-keto esters

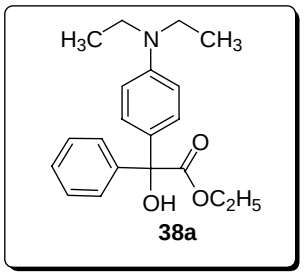
In CH_2Cl_2 (25 mL), *N,N*-diethylaniline (1.2 mL, 7.5 mmol) and ethyl benzoylformate (0.375 mL, 2.5 mmol) were taken at 0 °C under N_2. The $TiCl_4$ (2.2 mL of 1:1 solution of $TiCl_4/CH_2Cl_2$, 10 mmol) in 10 mL CH_2Cl_2 was added dropwise for 5 minutes. The reaction mixture was stirred at 0 °C for 0.5 h and stirred further at 0-25 °C for 8 h. A saturated K_2CO_3 solution (20 mL) was added and stirred for 0.5 h. The contents were filtered through a Buchner funnel. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 25 mL). The combined organic extract was washed with brine solution (10 mL) and dried over anhydrous $MgSO_4$. The solvent was removed and the residue was chromatographed on a silica gel column. The unreacted amine, benzidine derivative were eluted using 2:98 EtOAc/hexane. The arylated ester **37d** and α-hydroxy ester **38a** were then eluted with 4:96 EtOAc/hexane mixture.





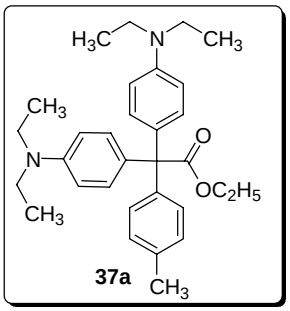
37d

Yield	0.77 g (68%)
mp	98-100 °C
IR (KBr)	(cm^{-1}) 2972, 2931, 1726, 1610, 1515, 1197, 700
^{1}H-NMR	(δ ppm, $CDCl_3$) 7.40-7.16 (m, 5H), 7.04 (d, J=8.8 Hz, 4H), 6.60 (d, J=8.8 Hz, 4H), 4.35 (q, J=6.8 Hz, 2H), 3.36 (q, J=7.2 Hz, 8H), 1.29-1.15 (m, 15H) **(Spectrum No. 11)**
^{13}C-NMR	(δ ppm, $CDCl_3$) 174.7, 146.4, 144.7, 131.3, 130.4, 127.6, 127.3, 126.3, 110.7, 65.8, 61.2, 44.5, 14.1, 12.7 **(Spectrum No. 12)**
MS (EI)`	m/z 458
Analysis	Calculated for $C_{30}H_{38}N_2O_2$: C, 78.56%; H, 8.35%; N, 6.11% Found : C, 78.61%; H, 8.30%; N, 6.40%



38a

Yield	0.17 g (22%)
IR (Neat)	(cm^{-1}) 3500, 2972, 2931, 2896, 1722, 1610, 1519, 1245, 1197, 698
^{1}H-NMR	(δ ppm, $CDCl_3$) 7.55-7.21 (m, 6H), 6.63 (d, J=8.8 Hz, 2H), 4.42 (q, J=6.8 Hz, 2H) 4.13 (s, 1H), 3.36 (q, J=7.2 Hz, 4H), 1.29 (t, J=7.2 Hz, 3H) 1.21 (t, J=6.8 Hz, 12H)
^{13}C-NMR	(δ ppm, $CDCl_3$) 175.0, 147.5, 142.6, 128.8, 128.4, 127.8, 127.7, 127.5, 111.0, 80.8, 62.6, 44.3, 14.1, 12.6



Yield 1.09 g (89%)

mp 100-102 °C

IR (KBr) (cm^{-1}) 2970, 2935, 1720, 1608, 1516, 1020, 814, 515

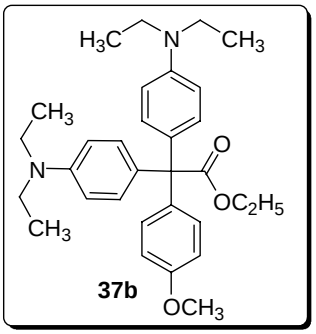
^{1}H-NMR (δ ppm, $CDCl_3$) 7.19-7.08 (m, 8H), 6.65 (d, J=8.8 Hz, 4H), 4.36 (q, J=6.8 Hz, 2H), 3.41 (q, J=7.2 Hz, 8H), 2.40 (s, 3H), 1.31 (t, J=7.2 Hz, 3H), 1.23 (t, J=6.8 Hz, 12H)

^{13}C-NMR (δ ppm, $CDCl_3$) 174.8, 146.3, 141.8, 135.8, 131.3, 130.4, 130.3, 128.1, 110.6, 65.5, 61.3, 44.3, 21.1, 14.2, 12.8

MS(EI) m/z 472

Analysis Calculated for $C_{25}H_{36}N_2O_2$: C, 75.72%; H, 9.15%; N, 7.06%

Found : C, 75.75%; H, 9.16%; N, 7.31%



Yield 1.0 g (82%)

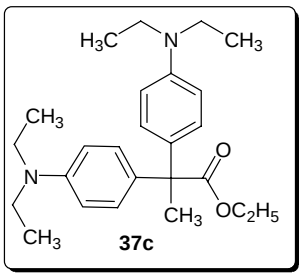
mp 101-103 °C

IR (KBr) (cm^{-1}) 2968, 2831, 1722, 1608, 1197, 1032, 814, 522

^{1}H-NMR (δ ppm, $CDCl_3$) 7.17 (d, J=9.2 Hz, 2H), 7.04 (d, J=8.8 Hz, 4H), 6.84 (d, J=8.8 Hz, 2H), 6.61 (d, J=9.2 Hz, 4H), 4.31 (q, J=7.2 Hz, 2H), 3.83 (s, 3H), 3.38 (q, J=6.8Hz, 8H), 1.28 (t, J= 7.2, 3H), 1.20 (t, J=6.8 Hz, 12H) **(Spectrum No. 6)**

^{13}C-NMR (δ ppm, $CDCl_3$) 174.9, 157.9, 146.3, 136.8, 131.5, 131.2, 130.4, 112.6, 110.6, 65.1, 61.3, 55.2, 44.3, 14.2, 12.7 **(Spectrum No. 7)**

MS (EI) m/z 488 (M^+, 11%) **(Spectrum No. 8)**



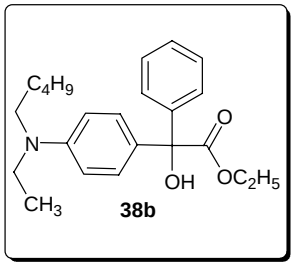
37c

Yield 0.81 g (82%)

IR (Neat) (cm^{-1}) 2972, 2930, 1724, 1621, 1518, 1199, 1091, 814

^{1}H-NMR (δ ppm, $CDCl_3$) 7.06 (d, 4H), 6.62 (d, 4H) 4.20 (q, J=6.8 Hz, 2H), 3.31 (q, J=7.2 Hz, 8H), 1.86 (s, 3H), 1.27-1.09 (m, 15H) **(Spectrum No. 9)**

^{13}C-NMR (δ ppm, $CDCl_3$) 176.3, 146.4, 131.9, 128.9, 111.2, 60.9, 54.7, 44.4, 27.3, 14.2, 12.7 **(Spectrum No. 10)**



38b

Yield 0.80 g (88%)

IR (Neat) (cm^{-1}) 3501, 2968, 2930, 2870, 1722, 1610, 1520, 1059, 767, 698

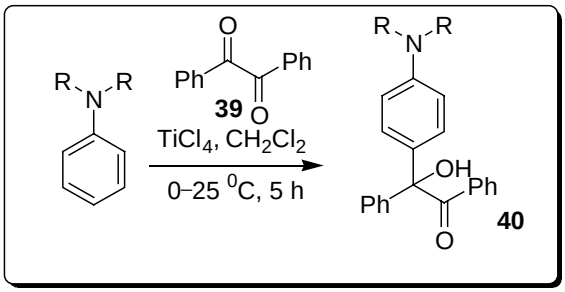
^{1}H-NMR (δ ppm, $CDCl_3$) 7.60-7.26 (m, 7H), 6.67 (d, J=8.8 Hz, 2H), 4.36-4.31 (m, 4H), 3.42-3.26 (m, 4H), 1.66-1.17 (m, 9H), 0.98 (t, J=6.8 Hz, 3H) **(Spectrum No. 13)**

^{13}C-NMR (δ ppm, $CDCl_3$) 174.8, 147.4, 142.5, 128.6, 128.2, 127.7, 127.5, 127.4, 110.8, 80.6, 62.4, 50.2, 44.7, 29.2, 27.1, 22.5, 14.0, 13.9, 12.2 **(Spectrum No. 14)**

MS (EI) m/z 369 (M^{+}, 23%) **(Spectrum No. 15)**

1.4.1.3 Reaction of the *N,N*-dialkyl arylamines/$TiCl_4$ reagent system with benzil

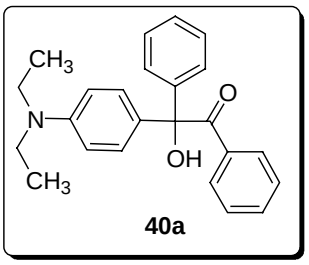
Dichloromethane (25 mL), *N,N*-diethylaniline (1.2 mL, 7.5 mmol) and benzil (0.22 g, 2.5 mmol) were taken at 0 °C under N_2. The $TiCl_4$ (2.2 mL of 1:1 solution of $TiCl_4/CH_2Cl_2$, 10mmol) in 10 mL CH_2Cl_2 was added dropwise for 5 minutes. The reaction mixture was stirred at 0 °C for 0.5 h and stirred further at 0-25 °C for 8 h. A saturated K_2CO_3 solution (20 mL) was added and stirred for 0.5 h. The contents were filtered through a Buchner funnel. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 25 mL). The combined organic extract was washed with brine solution (10 mL) and dried over anhydrous $MgSO_4$. The solvent was removed and the residue was chromatographed on a silica gel column. The unreacted amine and benzidine derivative (0.10 g, 12%) were eluted using 2:98 EtOAc/hexane mixture. The α-hydroxy ketone **40a** was eluted next.



Yield 0.85 g (85%)

IR (Neat) (cm^{-1}) 3423, 2970, 2929, 1674, 1608, 1517, 1267, 1197, 698

^{1}H-NMR (δ ppm, $CDCl_3$) 7.74 (d, J=7.8 Hz, 2H), 7.35-7.05

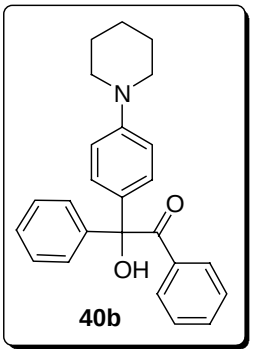


(m, 10H), 6.60 (s, 1H), 3.32 (q, J=6.8 Hz, 4H), 1.14 (t, J=6.8 Hz, 6H)

(Spectrum No. 16)

^{13}C-NMR (δ ppm, $CDCl_3$) 200.1, 146.2, 145.3, 138.4, 131.7, 131.1, 130.8, 129.9, 127.4, 127.3, 125.9, 110.9, 84.9, 44.2, 12.7 **(Spectrum No. 17)**

Yield 0.64 g (70%)



40b

IR (Neat) (cm^{-1}) 3456, 3059, 2934, 2854, 1672, 1608, 1512, 1238, 700

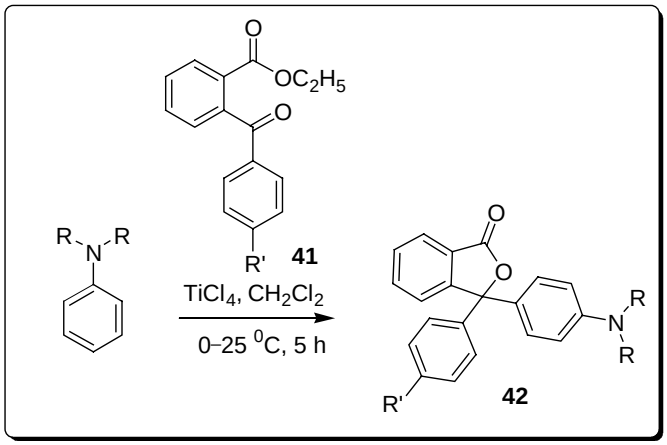
^{1}H-NMR (δ ppm, $CDCl_3$) 8.01-672 (m, 14H), 4.99 (s, 1H), 3.18 (t, J= 4.6 Hz, 4H), 2.15-1.45 (m, 6H)

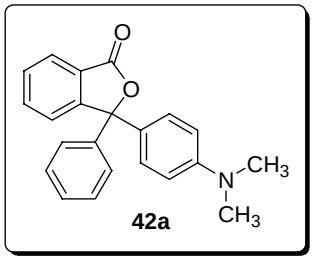
^{13}C-NMR (δ ppm, $CDCl_3$) 201.4, 151.8, 142.3, 135.5, 132.7, 130.8, 129.2, 128.4, 128.3, 128.1, 127.9, 115.7, 84.8, 50.2, 25.6, 24.2

1.4.1.4 Reaction of the *N,N*-dialkyl arylamines/$TiCl_4$ reagent system with ethyl 2-benzoyl benzoate

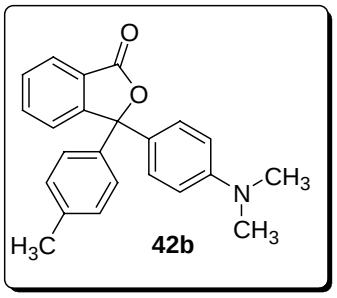
Dichloromethane (25 mL), *N,N*-diethylaniline (0.81 mL, 5 mmol) and Ethyl 2-benzoyl benzoate (0.63g, 2.5 mmol) were taken at 0 °C under N_2. The $TiCl_4$ (2.2 mL of 1:1 solution of $TiCl_4/CH_2Cl_2$, 10 mmol) in 10 mL CH_2Cl_2 was added dropwise for 5 minutes. The reaction mixture was stirred at 0 °C for 0.5 h and stirred further at 0-25 °C for 8 h. A saturated K_2CO_3 solution (20 mL) was added and stirred for 0.5 h. The contents were filtered through a Buchner funnel. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 25 mL). The combined organic extract was washed with brine solution (10 mL) and dried over anhydrous $MgSO_4$. The solvent was removed and the residue was chromatographed on a silica gel column. The unreacted amine and benzidine

derivative were eluted using 2:98 EtOAc/hexane mixture. The γ-lactone **42a** was isolated using 3:97 EtOAc/hexane mixture as eluent.





Yield	0.72 g (89%)
mp	52-54 °C
IR (KBr)	(cm^{-1}) 3057, 2891, 1757, 1610, 1521, 1356, 1259, 1109, 738, 696
^{1}H-NMR	(δ ppm, $CDCl_3$) 7.91-6.61 (m, 13H), 2.99 (s, 6H)
^{13}C-NMR	(δ ppm, $CDCl_3$) 170.1, 157.8, 150.5, 141.7, 134.1, 129.2, 128.6, 128.5, 128.3, 128.0, 127.0, 125.9, 124.2, 111.8, 92.3, 40.3
GCMS	m/z 329
Analysis	Calculated for $C_{22}H_{19}NO_2$: C, 80.22%; H, 5.81%; N, 4.25%
	Found : C, 80.01%; H, 5.82%; N, 4.05%



42b

Yield 0.73 g (86%)

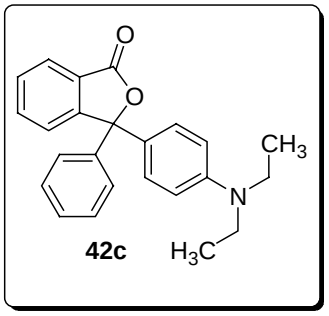
mp 98-100 °C

IR (KBr) (cm^{-1}) 3045, 2922, 2804, 1770, 1610, 1514, 1466, 1358, 1217, 1105, 1055, 925, 736, 692

^{1}H-NMR (δ ppm, $CDCl_3$) 7.93-7.11 (m, 10H), 6.64 (d, J=8.8 Hz, 2H), 2.93 (s, 6H), 2.33 (s, 3H)

^{13}C-NMR (δ ppm, $CDCl_3$) 170.2, 153.0, 150.5, 138.7, 138.1, 134.0, 129.1, 128.6, 127.0, 125.8, 124.2, 111.8, 92.4, 40.3, 21.1

GCMS m/z 343



42c

Yield 0.80 g (90%)

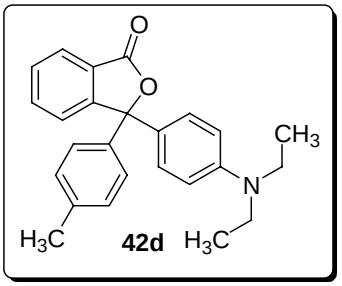
mp 108-110 °C

IR (KBr) (cm^{-1}) 3061, 2972, 1763, 1608, 1259, 1199, 699

^{1}H-NMR (δ ppm, $CDCl_3$) 7.92-6.55 (m, 13H), 3.32 (q, J=6.8 Hz, 4H), 1.13 (t, 6.8 Hz, 6H) **(Spectrum No. 18)**

^{13}C-NMR (δ ppm, $CDCl_3$) 169.9, 152.7, 147.7, 141.6, 133.8, 128.9, 128.2, 128.2, 126.7, 126.5, 125.6, 125.5, 124.0, 110.9, 92.2, 44.1, 12.4 **(Spectrum No. 19)**

MS (EI) m/z 357 (M^{+}, 83%) **(Spectrum No. 20)**



Yield 0.78 g (81%)

mp 101-103°C

IR (KBr) (cm^{-1}) 3045, 2970, 2928, 1759, 1610, 1521, 1466, 1402, 1375, 1259, 1199, 1105, 758, 733, 690

^{1}H-NMR (δ ppm, $CDCl_3$) 7.95-7.02 (m, 10H), 6.59 (d, J=9.8 Hz, 2H), 3.33 (q, J=6.8 Hz, 4H), 2.33 (s, 3H), 1.15 (t, J=6.8 Hz, 6H)

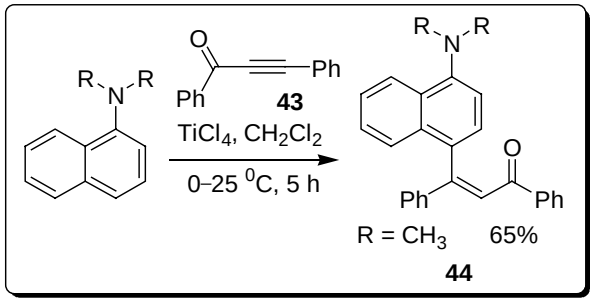
^{13}C-NMR (δ ppm, $CDCl_3$) 170.0, 153.0, 147.8, 138.7, 138.0, 133.9, 129.8, 127.7, 125.8, 124.1, 111.0, 92.4, 44.4, 21.1, 12.6

GCMS m/z 371

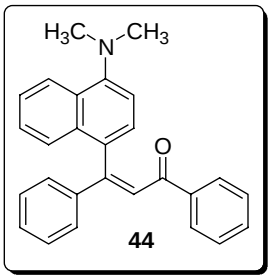
1.4.1.5 Reaction of the *N,N*-dialkyl arylamines/$TiCl_4$ reagent system with alkynyl ketone

In CH_2Cl_2 (25 mL), *N*,*N*-dimethyl-1-naphthylamine (0.8 mL, 5 mmol) and alkynyl ketone (0.52 g, 2.5 mmol) were taken at 0 °C under N_2. The $TiCl_4$ (1.65 mL of 1:1 solution of $TiCl_4/CH_2Cl_2$, 7.5 mmol) in 10 mL CH_2Cl_2 was added dropwise for 5 minutes. The reaction mixture was stirred at 0 °C for 0.5 h and stirred further at 0-25 °C for 5 h. A saturated K_2CO_3 solution (15 mL) was added and stirred for 0.5 h. The reaction mixture was filtered through a Buchner funnel. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2×20 mL). The combined organic extract was washed with brine solution (10 mL) and dried over anhydrous $MgSO_4$. The solvent was removed and the residue was chromatographed on a silica gel column. The unreacted amine and benzidine

derivative were eluted using 2:98 EtOAc/hexane mixture. The ketone **44** was isolated using 2:98 EtOAc/hexane mixture as eluent.



Yield 0.61 g (65%)



IR (Neat) (cm^{-1}) 3050, 2939, 2829, 1662, 1577, 1510, 1448, 1269, 1217, 1045, 1020, 765, 696

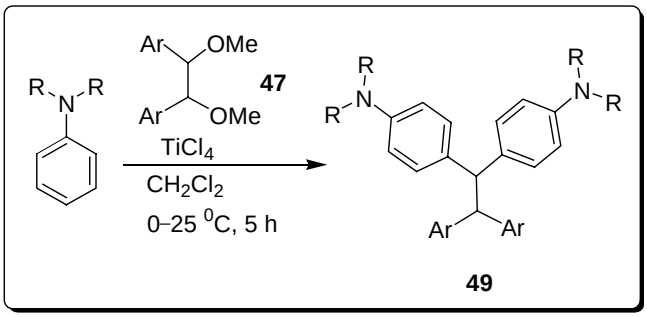
^{1}H-NMR (δ ppm, $CDCl_3$) 8.23-6.93 (m, 17H), 2.88 (s, 6H) **(Spectrum No. 21)**

^{13}C-NMR (δ ppm, $CDCl_3$) 193.0, 153.7, 151.4, 141.2, 138.7, 133.2, 132.0, 131.1, 129.4, 128.7, 128.3, 128.0, 127.8, 127.2, 126.6, 125.9, 125.7, 124.9, 124.6, 113.1, 45.1 **(Spectrum No. 22)**

GCMS m/z 377

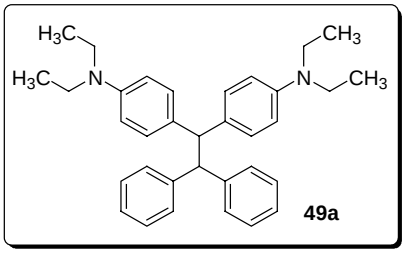
1.4.1.6 Reaction of the *N,N*-dialkyl arylamines/$TiCl_4$ reagent system with 1,2-dimethoxy-1,2-diaryl ethanes

In CH_2Cl_2 (25 mL), *N,N*-diethylaniline (1.2 mL, 7.5 mmol) and 1,2-dimethoxy-1,2-phenyl ethane (0.49 g, 2.5 mmol) were taken at 0 °C under N_2. The $TiCl_4$ (1.65 mL of 1:1 solution of $TiCl_4/CH_2Cl_2$, 7.5 mmol) in 10 mL CH_2Cl_2 was added dropwise for 5 minutes. The reaction mixture was stirred at 0 °C for 0.5 h and stirred further at 0-25 °C for 5 h. A saturated K_2CO_3 solution (15 mL) was added and stirred for 0.5 h. The reaction mixture was filtered through a Buchner funnel. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2×20 mL). The combined organic extract was washed with brine solution (10 mL) and dried over anhydrous $MgSO_4$. The solvent was removed and the residue was chromatographed on a silica gel column. The unreacted amine and benzidine derivative were eluted using 2:98 EtOAc/hexane mixture. The product 1,1',2,2'-tetra arylethane **49a** was isolated using 3:97 EtOAc/hexane mixture as eluent.



Yield 0.89 g (89%)

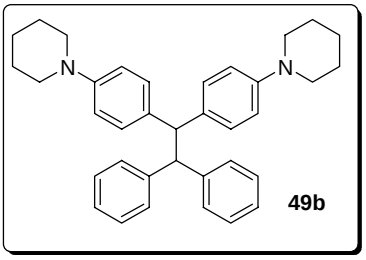
IR (Neat) (cm^{-1}) 3028, 2966, 2893, 1612, 1518, 1354, 1267,800, 742



^{1}H-NMR (δ ppm, $CDCl_3$) 7.32-7.06 (m, 14H), 6.56 (d, J=8.8 Hz, 4H), 4.73 (dd, J=11.7 Hz, 2H), 3.32 (q, J=6.8 Hz, 8H), 1.19 (t, J=6.8 Hz, 12H) **(Spectrum No. 25)**

^{13}C-NMR (δ ppm, $CDCl_3$) 148.9, 144.5, 131.9, 129.1, 128.7, 127.9, 125.4, 112.2, 56.9, 54.3, 44.3, 12.5 **(Spectrum No. 26)**

Yield 0.66 g (55%)



49b

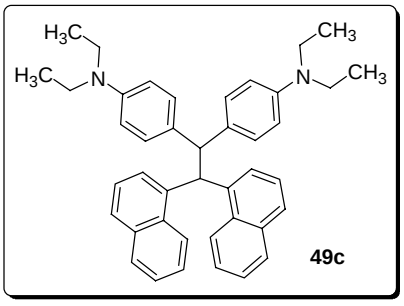
IR (Neat) (cm^{-1}) 3028, 2926, 2852, 1612, 1514, 1236, 804, 744, 698

^{1}H-NMR (δ ppm, $CDCl_3$) 6.36-6.08 (m, 14H), 5.78 (d, J=8.6 Hz, 4H), 3.78 (dd, J=11.7 Hz, 2H), 2.21 (t, J=5.0 Hz, 8H), 0.80-0.62 (m, 12H)

^{13}C-NMR (δ ppm, $CDCl_3$) 145.0, 144.1, 135.0, 128.9, 128.6, 128.0, 116.3, 56.7, 54.6, 50.7, 26.0, 24.2 **(Spectrum No. 27)**

Yield 1.0 g (72%)

mp 268-270 °C



49c

IR (KBr) (cm^{-1}) 3043, 2966, 1612, 1518, 775

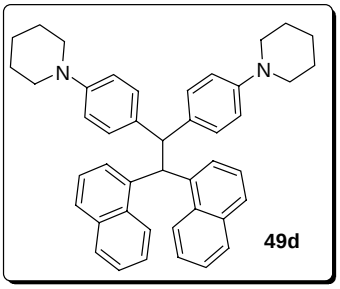
^{1}H-NMR (δ ppm, $CDCl_3$) 8.14-7.20 (m, 14H), 6.71 (d, J=8.4 Hz, 4H), 6.29 (d, J=8.4 Hz, 4H), 4.85 (d,J=11.0 Hz, 2H), 3.15 (q, J=6.8 Hz, 8H), 0.99 (t, J=6.8 Hz, 12H) **(Spectrum No. 28)**

^{13}C-NMR (δ ppm, $CDCl_3$) 140.4, 133.6, 132.3, 129.6, 128.4, 126.7, 126.4, 125.4, 125.1, 124.6, 123.7, 112.4, 55.9, 44.7, 12.4 **(Spectrum No. 29)**

The structure was also confirmed by single crystal X-ray data.

Analysis Calculated for $C_{42}H_{44}N_2$: C, 87.45%; H, 7.69%; N, 4.86%

Found : C, 87.63%; H, 7.65%; N, 4.81%



49d

Yield 0.63 g (42%)

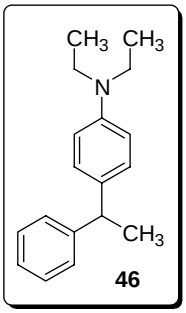
mp 248-250 °C

IR (KBr) (cm^{-1}) 2970, 2930, 2870, 1612, 1564, 1265, 808

^{1}H-NMR (δ ppm, $CDCl_3$) 8.06 (d, J=8.8 Hz, 2H), 7.66 (d, J=8.8 Hz, 2H), 7.55 (d, J=6.8 Hz, 2H), 7.31-7.17 (m, 4H), 6.71 (d J=8.6 Hz, 4H), 6.47 (d, J=8.8 Hz, 4H), 6.22 (d, J=8.8 Hz, 2H), 4.83 (d, J=11.0 Hz, 2H), 2.88 (t, J=6.0 Hz, 8H), 1.70-1.86 (m, 12H)

^{13}C-NMR (δ ppm, $CDCl_3$) 150.0, 140.1, 134.5, 133.6, 132.2, 129.3, 128.4, 126.5, 125.5, 125.1, 124.6, 123.5, 116.0, 56.2, 50.8, 25.7, 24.3

1.4.1.7 Reaction of the *N,N*-dialkyl arylamines/$TiCl_4$ reagent system with 1-methoxy-1-phenyl ethane



46

Yield 0.32 g (52%)

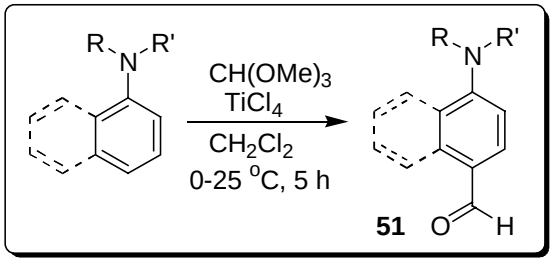
IR (Neat) (cm^{-1}) 2966, 2929, 2869, 1614, 1517, 1265, 815, 700

^{1}H-NMR (δ ppm, $CDCl_3$) 7.50-6.70 (m, 9H), 4.23 (q, J=7.2 Hz, 1H), 3.52 (q, J=6.8 Hz, 4H), 1.75 (d, J=7.2 Hz, 3H) 1.32 (t, J=6.8 Hz, 6H) **(Spectrum No. 23)**

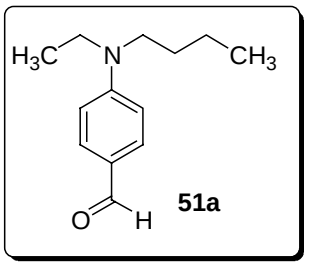
^{13}C-NMR (δ ppm, $CDCl_3$) 147.5, 146.3, 143.6, 128.5, 127.7, 126.3, 125.6, 112.2, 44.6, 44.0, 22.3, 12.8 **(Spectrum No. 24)**

1.4.1.8 Reaction of the *N,N*-dialkyl arylamines/$TiCl_4$ reagent system with trimethyl orthoformate

In CH_2Cl_2 (25 mL), *N*-ethyl,*N*-butylaniline (0.8 mL, 5 mmol) and trimethyl orthoformate (0.81 mL, 7.5 mmol) were taken at 0 °C under N_2. The $TiCl_4$ (2.2 mL of 1:1 solution of $TiCl_4/CH_2Cl_2$, 10 mmol) in 10 mL CH_2Cl_2 was added dropwise for 5 minutes. The reaction mixture was stirred at 0 °C for 0.5 h and stirred further at 0-25 °C for 5 h. A saturated K_2CO_3 solution (15 mL) was added and stirred for 0.5 h. The contents were filtered through a Buchner funnel. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 20 mL). The combined organic extract was washed with brine solution (10 mL) and dried over anhydrous $MgSO_4$. The solvent was removed and the residue was chromatographed on a silica gel column. The unreacted amine and benzidine derivative were eluted using 2:98 EtOAc/hexane mixture. The aldehyde derivative **51a** was eluted using 3:97 EtOAc/hexane mixture.



Yield 0.56 g (74%)



IR (Neat) (cm^{-1}) 2974, 2929, 2806, 2731, 1666, 1593, 1527, 1407, 1355, 817

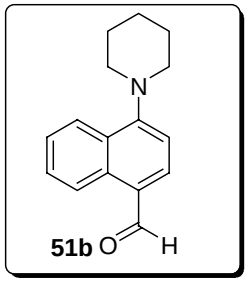
^{1}H-NMR (δ ppm, $CDCl_3$) 9.98 (s, 1H), 7.68 (d, J=9.0 Hz, 2H), 6.64 (d, J=8.8 Hz, 2H), 3.54-3.28 (m, 4H), 1.70-1.20 (m, 2H), 1.18 (t, J=6.8 Hz, 3H), 0.95 (t, J=7.2 Hz, 3H) **(Spectrum No. 30)**

^{13}C-NMR (δ ppm, $CDCl_3$) 189.9, 152.5, 132.2, 124.6, 110.7, 50.3, 45.2, 29.5, 20.3, 13.9, 12.2 **(Spectrum No. 31)**

GCMS m/z 205

The above procedure was followed for the reaction of *N*-(1-naphthyl) piperidine, trimethyl orthoformate and $TiCl_4$.

Yield 0.46 g (85%)



IR (Neat) (cm^{-1}) 3078, 3045, 2948, 2841, 2790, 2732, 1678, 1568, 1338, 1056, 767

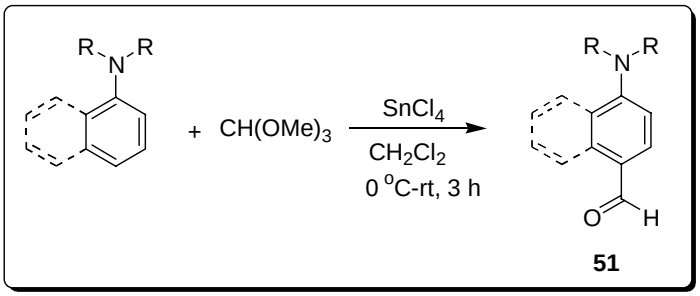
^{1}H-NMR (δ ppm, $CDCl_3$) 10.23 (s, 1H), 9.34 (d, J=8.8 Hz, 1H,), 8.18 (d, 1H, J=8.8 Hz), 7.67 (d, 1H, J=8.8 Hz), 7.90-7.55 (m, 2H), 7.10 (d, 1H, J=8.8 Hz), 3.21 (t, J=6.8 Hz, 4H), 1.95-1.87 (m, 4H), 1.76-1.72 (m, 2H)

^{13}C-NMR (δ ppm, $CDCl_3$) 192.3, 157.4, 138.7, 132.4, 128.7, 128.2, 126.0, 125.9, 125.5, 124.5, 112.7, 54.3, 24.3, 24.5

1.4.2 Reactions of *N,N*-dialkyl arylamines and $SnCl_4$ with electrophiles

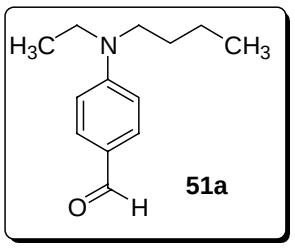
1.4.2.1 Reaction of *N,N*-dialkyl arylamines and $SnCl_4$ with trimethyl orthoformate

In CH_2Cl_2 (25 mL), *N,N*-diethylaniline (0.8 mL, 5 mmol) and trimethyl orthoformate (0.81 mL, 7.5 mmol) were taken at 0 °C under N_2. The $SnCl_4$ (1.1 mL, 10 mmol) was added dropwise for 5 minutes. The reaction mixture was stirred at 0 °C for 0.5 h and stirred further at 0-25 °C for 3 h. A saturated K_2CO_3 solution (15 mL) was added and stirred for 0.5 h. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2×20 mL). The combined organic extract was washed with brine solution (10 mL) and dried over anhydrous $MgSO_4$. The solvent was removed and the residue was chromatographed on a silica gel column. The unreacted amine was eluted using 2:98 EtOAc/hexane mixture. The aldehyde derivative **51c** was eluted using 3:97 EtOAc/hexane mixture.



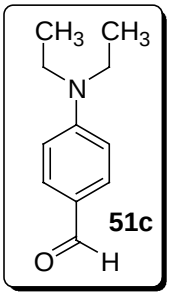
51

Yield 0.46 g (62%)



51a

Yield 0.43 g (64%)



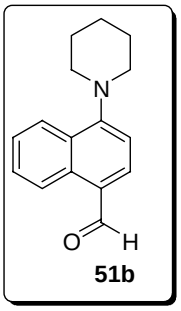
IR (Neat) (cm^{-1}) 2974, 2929, 2806, 2731, 1666, 1593, 1527, 1407, 1355, 817

^{1}H-NMR (δ ppm, $CDCl_3$) 9.70 (s, 1H), 7.70 (d, J=8.6 Hz, 2H), 6.65 (d, J=8.7 Hz, 2H), 3.45 (q, J=6.8 Hz, 4H), 1.25 (t, J=6.8 Hz, 6H)

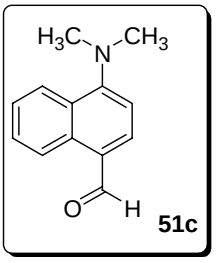
^{13}C-NMR (δ ppm, $CDCl_3$) 189.8, 152.2, 132.2, 124.6, 110.5, 44.6, 12.4

The above procedure was followed for the reaction of *N*,*N*-dialkyl-1-naphthylamine, trimethyl orthoformate and $SnCl_4$.

Yield 0.37 g (69%)



Yield 0.36 g (72%)



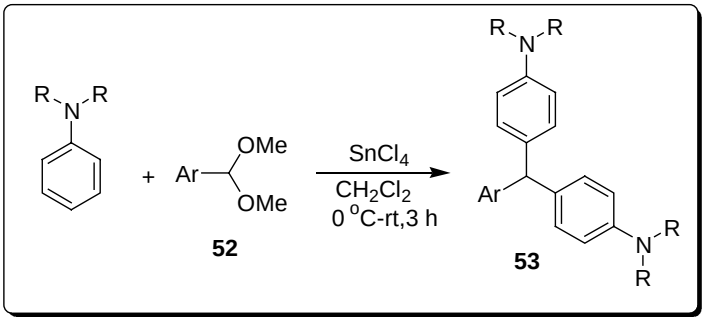
IR (Neat) (cm^{-1}) 3078, 3045, 2948, 2841, 2790, 2732, 1678, 1568, 1338, 1056, 767

^{1}H-NMR (δ ppm, $CDCl_3$) 10.11 (s, 1H), 9.37 (d, 1H, J=8.79 Hz), 8.13 (d, 1H, J=8.79 Hz), 7.73 (d, 1H, J=7.8 Hz), 7.67-7.42 (m, 2H), 6.90 (d, 1H, J=7.8 Hz), 2.94 (s, 6H)

^{13}C-NMR (δ ppm, $CDCl_3$) 192.1, 157.2, 138.9, 132.6, 128.7, 127.4, 125.5, 125.14, 111.51, 44.51

1.4.2.2 Reaction of *N,N*-dialkyl aniline and $SnCl_4$ with acetals

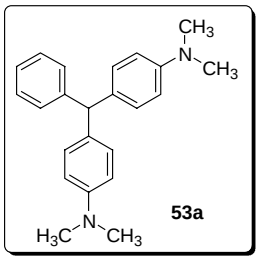
In CH_2Cl_2 (25 mL), *N,N*-diethylaniline (0.8 mL, 5 mmol) and benzaldehyde dimethyl acetal (0.42 mL, 2.5 mmol) were taken at 0 °C under N_2 and $SnCl_4$ (0.8 mL , 7.5 mmol) was added. The reaction mixture was stirred at 0 °C for 0.5 h and stirred further at 0-25 °C for 3 h. A saturated K_2CO_3 solution (15 mL) was added and stirred for 10 min. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2×20 mL). The combined organic extract was washed with brine solution (10 mL) and dried over anhydrous $MgSO_4$. The solvent was removed and the residue was chromatographed on a silica gel column. The unreacted amine was eluted using 2:98 EtOAc/hexane mixture. The product **53a** was eluted using 3:97 EtOAc/hexane mixture.



Yield 1.15 g (88%)

IR (Neat) (cm^{-1}) 3070, 3028, 2800, 1610, 1518, 1350, 1203, 1153, 1060, 788

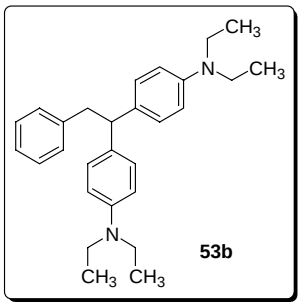
^{1}H-NMR (δ ppm, $CDCl_3$) 7.40-6.73 (m, 13H), 5.48 (s, 1H**)**, 2.99 (s, 12H)



^{13}C-NMR (δ ppm, $CDCl_3$) 149.1, 145.6, 133.0, 130.1, 129.5, 128.2, 125.9, 112.7, 55.2, 40.8

Analysis Calculated for $C_{23}H_{26}N_2$: C, 83.59%; H, 7.93%; N, 8.48%

Found : C, 86.66%; H, 7.92%; N, 8.55%



Yield 0.67 g (78%)

mp 64-66 °C

IR (KBr) (cm^{-1}) 2970, 2930, 2868, 1612, 1518, 1265, 704

^{1}H-NMR (δ ppm, $CDCl_3$) 7.30-6.60 (m, 13H), 4.15 (t, J=6.8 Hz, 1H), 3.45-3.25 (m, 10H), 1.25 (t, J=6.8 Hz, 12H)

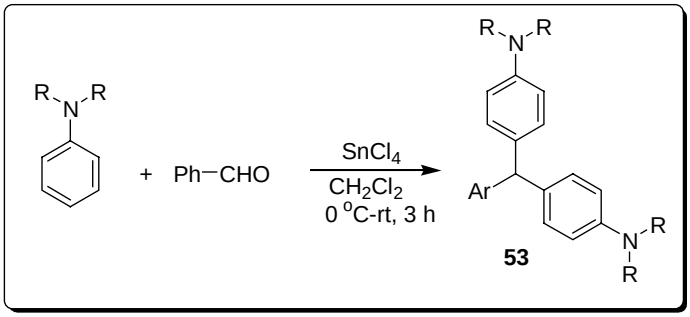
^{13}C-NMR (δ ppm, $CDCl_3$) 146.3, 141.5, 132.8, 129.3, 128.8, 128.0, 125.6, 112.3, 51.2, 44.5, 42.9, 12.8

MS(EI) m/z 400

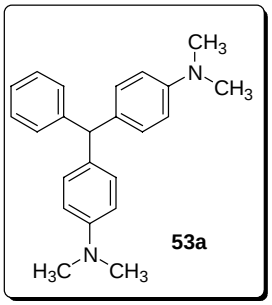
1.4.2.3 Reaction of *N,N*-dialkyl arylamines and $SnCl_4$ with benzaldehyde

In CH_2Cl_2 (25 mL), *N,N*-dimethylaniline (1.6 mL, 10 mmol) and benzaldehyde (0.5 mL, 5 mmol) were taken at 0 °C under N_2 and $SnCl_4$ (1.6 mL, 10 mmol) was added. The reaction mixture was stirred at 0 °C for 0.5 h and stirred further at 0-25 °C for 3 h. A saturated K_2CO_3 solution (20 mL) was added and stirred for 10 min. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2×25 mL). The combined organic extract was washed with brine solution (10 mL) and dried over anhydrous $MgSO_4$.

The solvent was removed and the residue was chromatographed on a silica gel column. The unreacted amine was eluted using 2:98 EtOAc/hexane mixture. The triarylmethane **53b** was next eluted.

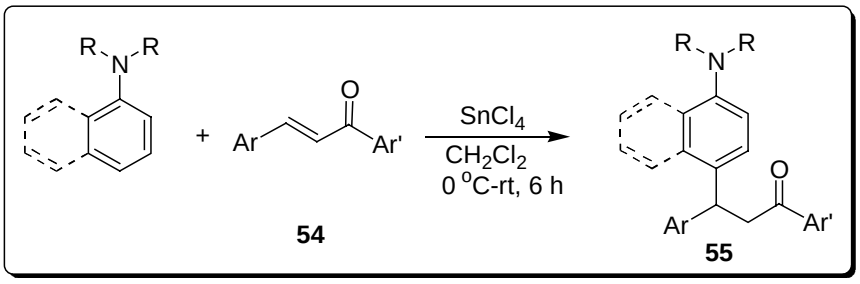


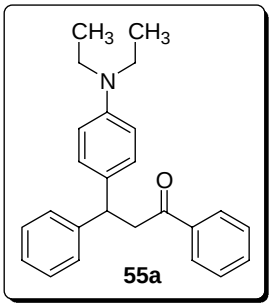
Yield 1.07 g (82%)



1.4.2.4 Reaction of *N,N*-dialkyl arylamines and $SnCl_4$ with α,β-unsaturated ketones

In CH_2Cl_2 (25 mL), *N,N*-diethylaniline (0.8 mL, 5 mmol) and chalcone (0.52 g, 2.5 mmol) were taken at 0 °C under N_2. The $SnCl_4$ (0.8 mL, 7.5 mmol) in 10 mL CH_2Cl_2 was added dropwise for 5 minutes. The reaction mixture was stirred at 0 °C for 0.5 h and stirred further at 0-25 °C for 6 h. A saturated K_2CO_3 solution (15 mL) was added and stirred for 0.5 h. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2×20 mL). The combined organic extract was washed with brine solution (10 mL) and dried over anhydrous $MgSO_4$. The solvent was removed and the residue was chromatographed on a silica gel column. The ketone **55a** was isolated using 2:98 EtOAc/hexane mixture as eluent.





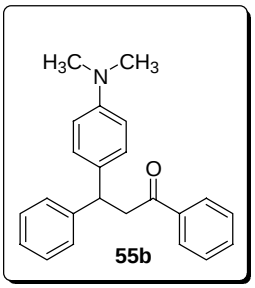
Yield 0.45 g (82%)

mp 62-64 °C

IR (KBr) (cm^{-1}) 3055, 2968, 2928, 2887, 1684, 1612, 1520, 1197, 752

^{1}H-NMR (δ ppm, $CDCl_3$) 8.03 (d, J=7.3 Hz, 2H), 7.70-7.15 (m, 10H), 6.70 (d, J=8.4 Hz, 2H), 4.85 (t, J=7.1 Hz, 1H), 3.80 (d, J=7.1 Hz, 2H), 3.40 (q, J=6.9 Hz, 4H), 1.21 (t, J=6.9 Hz, 6H)

^{13}C-NMR (δ ppm, $CDCl_3$) 198.50, 146.6, 145.2, 137.5, 133.0, 131.2, 128.7, 128.6, 128.5, 128.2, 128.0, 126.2, 112.2, 45.3, 44.4, 12.8



Yield 0.40 g (75%)

IR (Neat) (cm^{-1}) 3055, 2968, 2928, 2887, 1684, 1612, 1520, 1197, 752

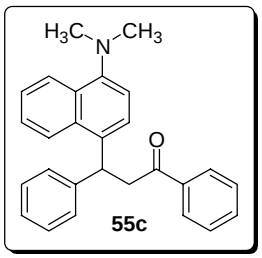
^{1}H-NMR 7.99-6.68 (m, 13H), 4.80 (t, J=6.9 Hz, 1H), 3.75 (d, J=6.8 Hz, 2H), 2.92 (s, 6H) **(Spectrum No. 32)**

^{13}C-NMR (δ ppm, $CDCl_3$) 198.4, 149.3, 145.0, 132.9, 132.2, 128.5, 128.1, 127.9, 126.2, 112.9, 45.3, 45.2, 40.7 **(Spectrum No. 33)**

Analysis Calculated for $C_{23}H_{23}NO$: C, 83.85%; H, 7.04%; N, 4.25%

Found : C, 83.69%; H, 7.10%; N, 4.15%

Yield 0.63 g (88 %)



55c

mp 154-156 °C

IR (KBr) (cm^{-1}) 3059, 3024, 2972, 2935, 2789, 1676, 1581, 1450, 763

^{1}H-NMR 8.46-7.06 (m, 16H), 5.71 (t, J=6.8 Hz, 1H), 3.92 (d, J=6.8 Hz, 2H), 2.95 (s, 6H)

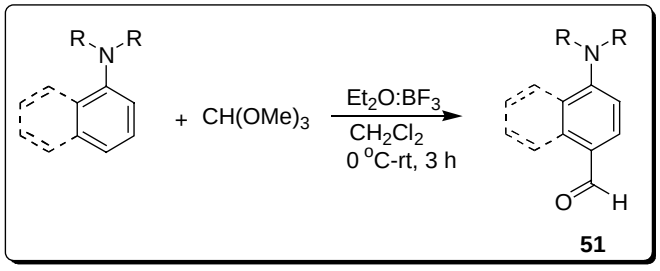
^{13}C-NMR (δ ppm, $CDCl_3$) 198.2, 150.1, 144.4, 137.3, 134.3, 133.1, 132.8, 129.6, 128.6, 128.1, 126.3, 126.1, 124.9, 124.5, 124.3, 113.5, 45.3, 41.4

1.4.3 Reactions of *N,N*-dialkyl arylamines and $Et_2O:BF_3$ with electerophiles

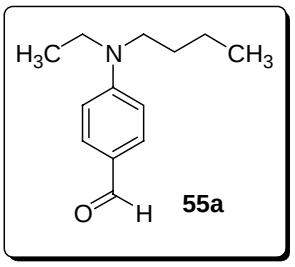
1.4.3.1 Reaction of *N,N*-dialkyl arylamines with trimethyl orthoformate and $Et_2O:BF_3$

In CH_2Cl_2 (25 mL), *N,N*-diethylaniline (0.8 mL, 5 mmol), trimethyl orthoformate (0.81 mL, 7.5 mmol) were taken at 0 °C under N_2 and $Et_2O:BF_3$ (1.1 mL, 10 mmol) was added. The reaction mixture was stirred at 0 °C for 0.5 h and stirred further at 0-25 °C for 3 h. A saturated K_2CO_3 solution (15 mL) was added and stirred for 0.5 h. The organic layer

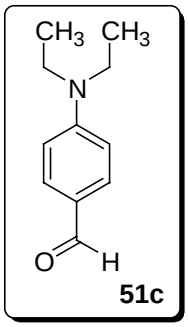
was separated, and the aqueous layer was extracted with CH_2Cl_2 (2×20 mL). The combined organic extract was washed with brine solution (10 mL) and dried over anhydrous $MgSO_4$. The solvent was removed and the residue was chromatographed on a silica gel column. The unreacted amine was eluted using 2:98 EtOAc/hexane mixture. The aldehyde derivative **51c** was eluted using 3:97 EtOAc/hexane mixture.



Yield 0.55 g (75%)

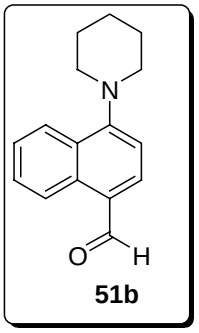


Yield 0.41 g (61%)



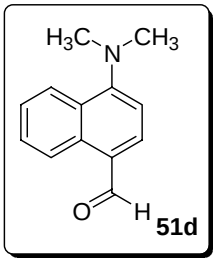
The above procedure was followed for the reaction of *N*,*N*-dimethyl-1-naphthylamine, trimethyl orthoformate and $Et_2O:BF_3$.

Yield 0.34 g (64%)



51b

Yield 0.39 g (78%)

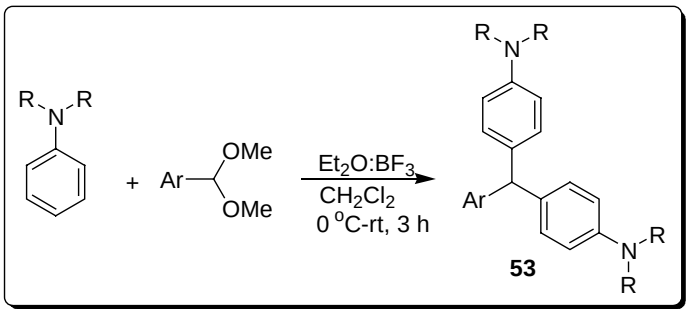


51d

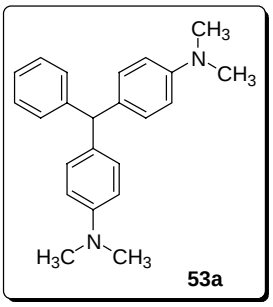
The spectral data were identified that of samples obtained in experiments using $TiCl_4$ or $SnCl_4$

1.4.3.2 Reaction of *N,N*-dialkyl arylamines and $Et_2O:BF_3$ with acetals

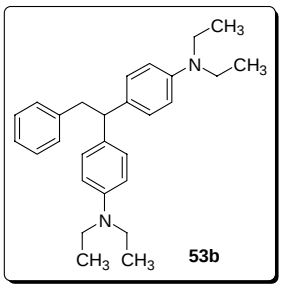
In CH_2Cl_2 (25 mL), *N,N*-diethylaniline (0.8 mL, 5 mmol), benzaldehyde dimethyl acetal (0.42 mL, 2.5 mmol) were taken at 0 °C under N_2 atmosphere and $Et_2O:BF_3$ (0.8 mL , 7.5 mmol) was added. The reaction mixture was stirred at 0 °C for 0.5 h and stirred further at 0-25 °C for 3 h. A saturated K_2CO_3 solution (15 mL) was added and stirred for 0.5 h. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2×20 mL). The combined organic extract was washed with brine solution (10 mL) and dried over anhydrous $MgSO_4$. The solvent was removed and the residue was chromatographed on a silica gel column. The unreacted amine were eluted using 2:98 EtOAc/hexane mixture. The product **53b** was eluted using 3:97 EtOAc/hexane mixture.



Yield 1.2 g (75%)



Yield 0.69 g (80%)

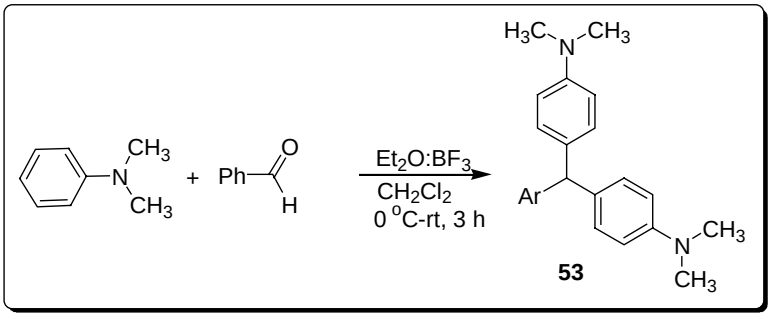


The spectral data were identified that of samples obtained in experiments using $SnCl_4$.

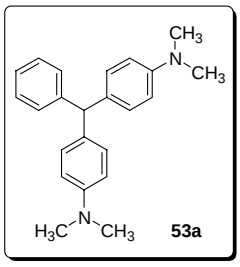
1.4.3.3 Reaction of *N,N*-dialkyl arylamines and $Et_2O:BF_3$ with benzaldehyde

In CH_2Cl_2 (25 mL), *N*,*N*-dimethylaniline (0.8 mL, 10 mmol) and benzaldehyde (0.25 mL, 2.5 mmol) were taken at 0 °C under N_2 and $Et_2O:BF_3$ (0.8 mL , 7.5 mmol) was added. The reaction mixture was stirred at 0 °C for 0.5 h and stirred further at 0-25 °C for 3 h. A

saturated K_2CO_3 solution (20 mL) was added and stirred for 0.5 h. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2×25 mL). The combined organic extract was washed with brine solution (10 mL) and dried over anhydrous $MgSO_4$. The solvent was removed and the residue was chromatographed on a silica gel column. The unreacted amine, benzidine derivative and unreacted benzaldehyde were eluted using 1:99 EtOAc/hexane mixture. The triarylmethane **53b** was next eluted.



Yield 1.4 g (88%)



The spectral data were identified that of samples obtained in experiments using $TiCl_4$ or $SnCl_4$

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Chapter 2

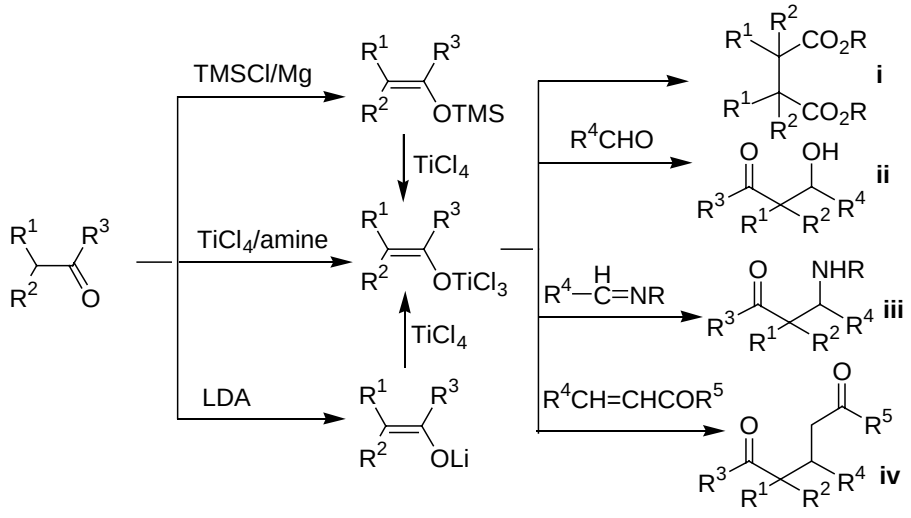
Synthetic Applications of Titanium Enolates

2.1 Reactions of metal enolates in the presence of titanium reagents.

One of the most fundamental reactions in organic chemistry is the C-C bond forming process. The most versatile approach for this transformation is the nucleophilic addition of metal enolates of α-hydrogen containing carbonyl compounds to various electrophiles. The metal ion associated with the enolate has pronounced effect on stereoselectivity.[1] Titanium enolates have been very successfully applied in this respect and there has been immense interest in this field. The titanium enolates are generally prepared by the transmetalation of the corresponding lithium enolates or silyl enol ethers. The titanium enolates can also be prepared directly by treating the α-hydrogen containing carbonyl compounds with the $TiCl_4$/tertiary amine reagent system (Chart 1).

The titanium enolates-mediated oxidative homocoupling, aldol, Mannich-type and Michael-type reactions to produce the corresponding products **i**, **ii**, **iii** and **iv** have tremendous synthetic potential for the construction of C-C bond in organic synthesis (Chart 1).

Chart 1.



We have undertaken research efforts on the development of directly prepared titanium enolates for C-C bond forming reactions. Accordingly, it is of interest to briefly review the literature reports on these C-C bond forming reactions mediated by titanium enolates.

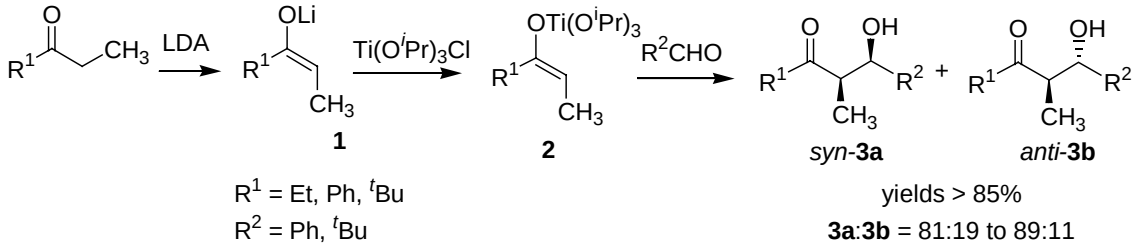
2.1.1 Titanium enolates in aldol reactions

Aldol reaction has been one of the powerful tool for the construction of C-C bond in organic synthesis, used in key steps in the syntheses of several complex and bioactive natural products.[2] Several metal enolate-based aldol transformations provided convenient access to aldol products in pure form. Among various metal enolates, the titanium enolate-mediated aldol reaction has tremendous synthetic potential, since the titanium reagents are readily available and inexpensive.[3]

2.1.1.1 Aldol reactions of titanium enolates prepared by the transmetalation of lithium enolates

Reetz *et al*.[4] reported that the lithium enolates of ketone **1**, prepared by the reaction of the corresponding ketone and LDA, react with aldehydes in the presence of $Ti(O^iPr)_3Cl$ or $Ti(NEt_2)_3Br$, to give *syn* **3a** and *anti* **3b**, respectively with high diastereoselectivity (Scheme 1). In this reaction, the titanium enolate **2** formed *in situ* is the reactive species.

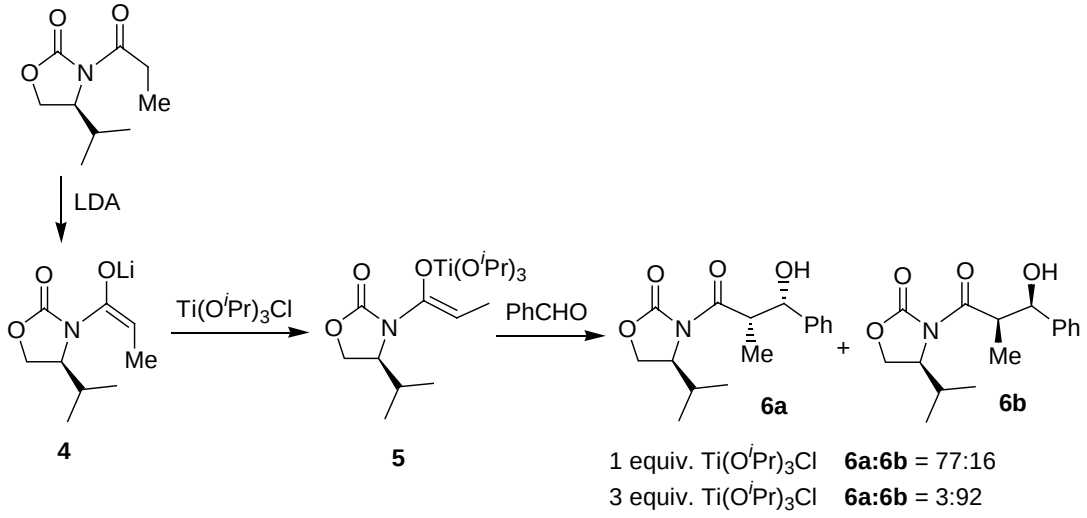
Scheme 1



Later, this methodology was extended by using the titanium enolates of aldehyde derivatives of *N*,*N*-dimethylhydrazones to obtain aldol type products in good yields with excellent selectivity.[4c]

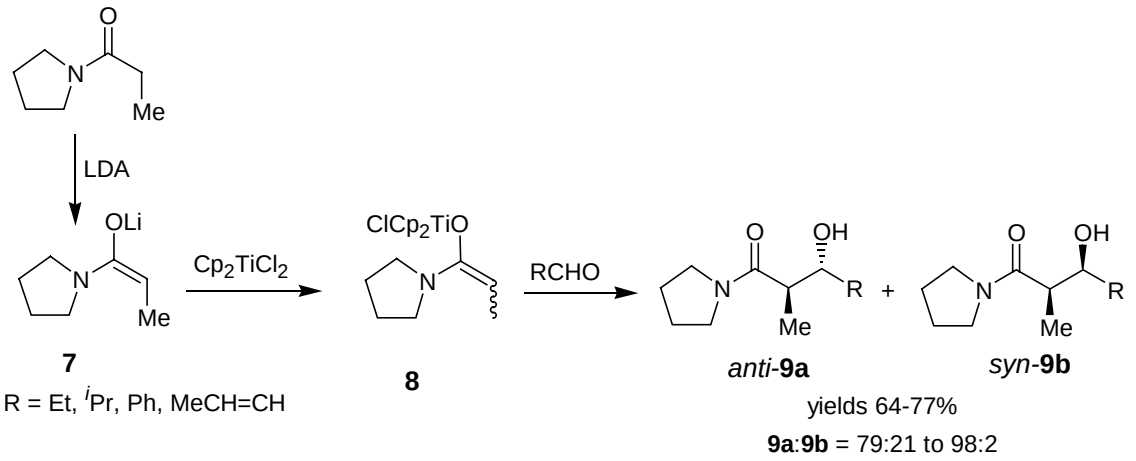
Lithium enolate of *N*-propanoyloxazolidinone **4** was treated with $Ti(O^iPr)_3Cl$ to produce titanium enolate **5** by the transmetalation for use in the aldol reaction with benzaldehyde to give **6**. The selectivities realized depended on the amount of the titanium reagent used (Scheme 2).[5]

Scheme 2



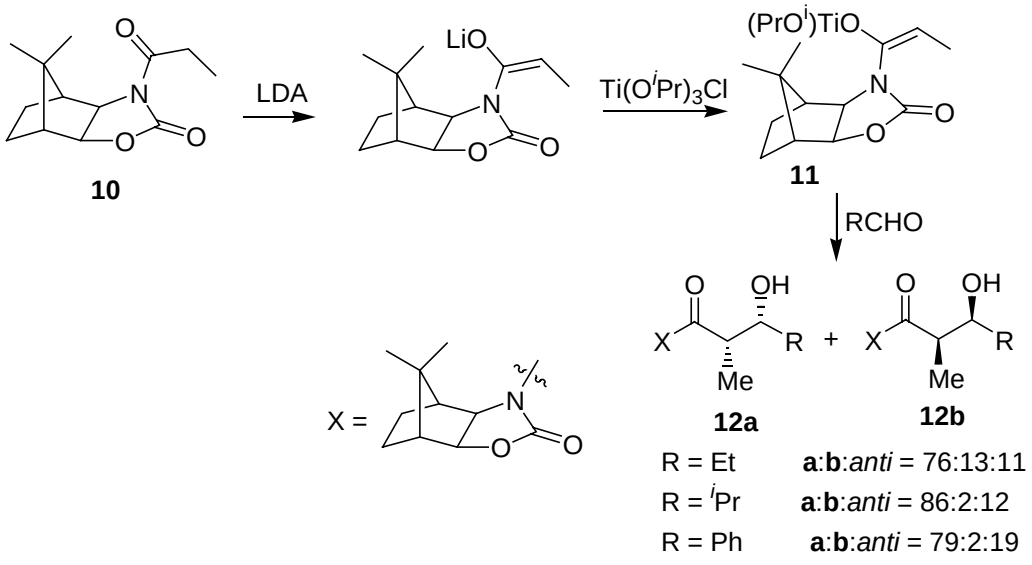
Murphy *et al*.[6] reported that the titanium enolate **8**, generated by the transmetalation of the corresponding lithium enolate of *N*-propionylpyrrolidine **7** with Cp_2TiCl_2, furnished the corresponding aldol adducts **9** in good yields with good to excellent selectivity through an *anti*-selective aldol process (Scheme 3).

Scheme 3



The *N*-propanoyloxazolidinone **10** readily accessed from camphorquinone, has been converted to the corresponding titanium enolate **11** via the lithium enolate using chlorotriisopropoxytitanium. Aldol reaction of the titanium enolate with a variety of aldehydes produces the products **12a** and **12b** with moderate to good selectivity (Scheme 4).[7]

Scheme 4

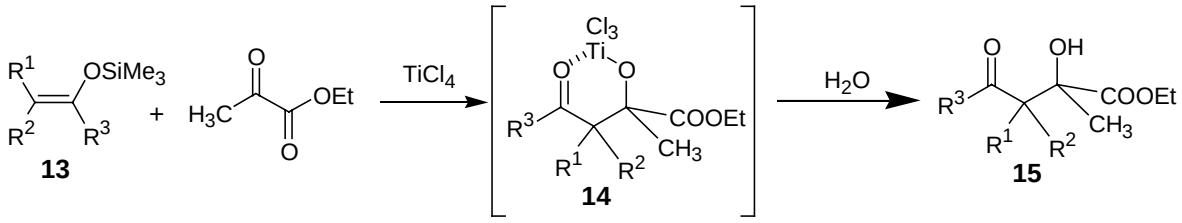


2.1.1.2 Aldol reactions of titanium enolates prepared by the transmetalation of enol silanes: (Mukaiyama aldol reaction)

The discovery of Mukaiyama and coworkers[8] that the aldehydes and acetals react with enol silanes in the presence of Lewis acids, provides an useful route for the construction of molecules via the crossed-aldol reaction. Stoichiometric quantities of Lewis acids like $TiCl_4$, $SnCl_4$, $AlCl_3$, BCl_3, BF_3:OEt_2 and $ZnCl_2$ were found to promote this reaction.

Mukaiyama and co-workers[9] also reported that the titanium complex **14** formed *in situ* by the reaction of $TiCl_4$ and trimethylsilyl enol ethers **13** react with aldehydes to give β-hydroxy carbonyl compounds **15** in good yields (Scheme 5).

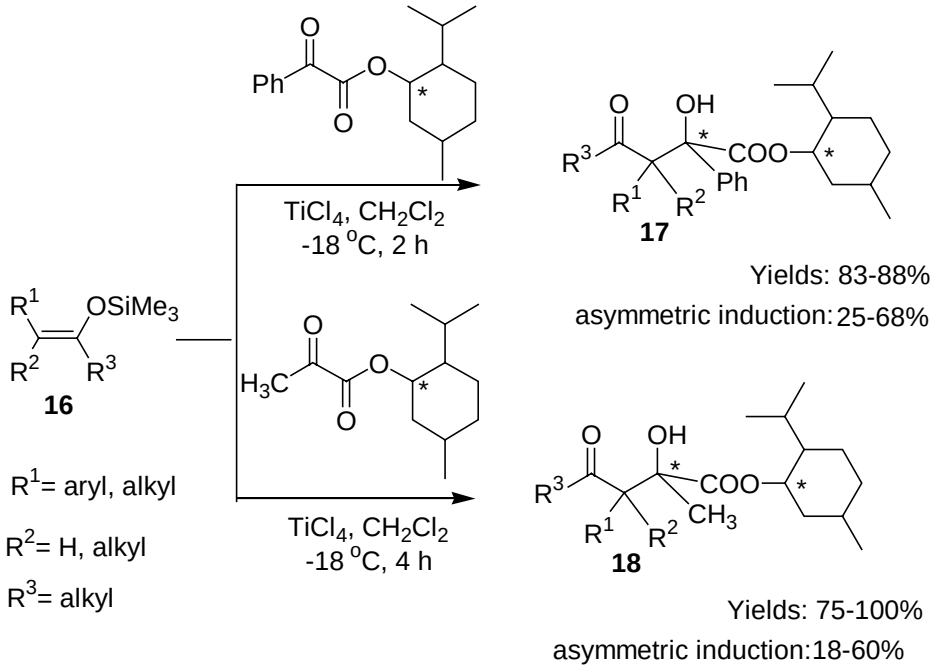
Scheme 5



R^1	R^2	Yields%
CH_3CH_2	CH_3	87
CH_3	H	55
C_6H_5	H	63

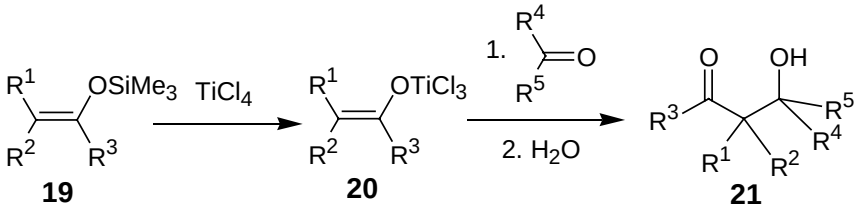
Ojima *et al.*[10] reported that the aldol synthesis mediated by $TiCl_4$ between silyl enol ethers and ketene silyl acetals **16** with (-) –methyl pyruvate and phenylglyoxalate gives the chiral β-hydroxy carbonyl compounds **17** and **18** in good yields (Scheme 6).

Scheme 6



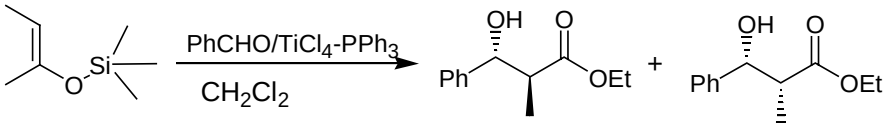
Mukaiyama *et al.*[11] reported that the titanium enolate **20** formed by the reaction of $TiCl_4$ and trimethylsilyl enol ethers **19** reacts smoothly with aldehydes or ketones to give the corresponding β-hydroxy carbonyl compounds **21** in good yields (Scheme 7).

Scheme 7



Gennari *et al.*[12] reported that the $TiCl_4$ in alliance with phosphines (PR_3) effectively catalyses the aldol addition of silyl ketene acetals **22** to aldehydes to produce **22a** and **22b** with improved *anti-syn* ratios (Scheme 8).

Scheme 8



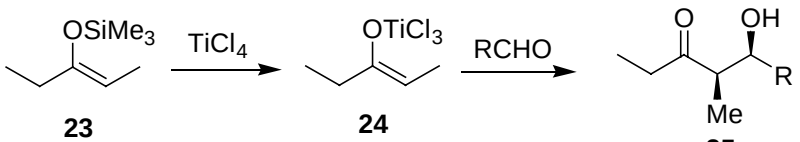
22 **22a** **22b**

95%

22a:22b 10.5 : 1

Addition of titanium enolate **24**, generated in the reaction of trimethylsilyl enol ether **23** of 3-pentanone and $TiCl_4$, to aldehydes delivered the corresponding *syn* aldol adducts **25** in good yields with moderate selectivity (Scheme 9).[13]

Scheme 9

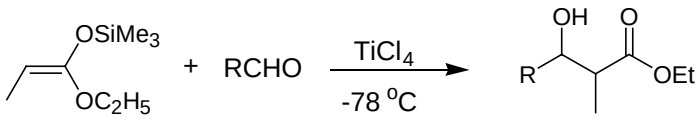


23 **24** **25**

R = ^{i}Pr	yield 63%	*syn*:*anti* = 75:25
R = Ph	yield 75%	*syn*:*anti* = 81:19

Chan *et al.*[14] reported that the condensation of the *E*-isomer of *O*-ethyl-*O*-trimethyl silylmethylketene acetal **26** with aldehyde promoted by titanium tetrachloride gives stereoselectively threo isomer of compound **27** (Scheme 10).

Scheme 10

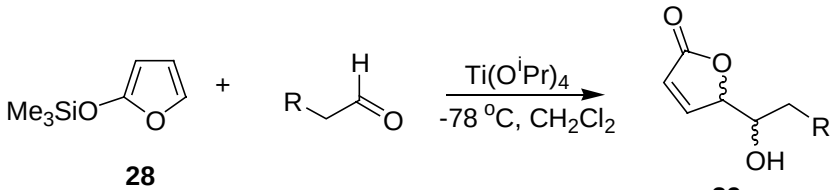


26 **27**

R	Yield%	threo/erythro
^{i}Pr	75	100/~0
Ph	79	75/25

The (TMSOF) 2-[(trimethylsilyl)oxy]furan **28** derivative has been used in an enantioselective aldol reaction by Figaderi *et al*. Indeed, addition of compound **28** to achiral aldehydes, in the presence of Ti(O^{i}Pr)$_4$ and (*R*)-1,1'-bi-2-napthol (BINOL), gave the corresponding butenolides **29** with moderate diastereomeric ratio (dr = 60%) and in 60-90% ee (Scheme 11).[15]

Scheme 11



28

R = $CH_3(CH_2)_6$-

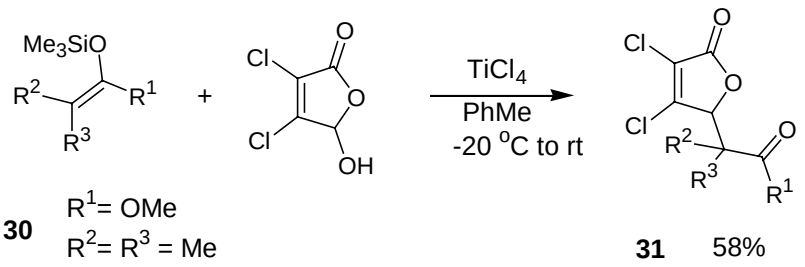
29

syn/*anti* ratio

79:21

Zhang *et al.*[16] reported the Mukaiyama aldol reaction on mucohalic acid. The reaction of mucohalic acid with various ketene silyl acetals or silyl enols ethers **30** in the presence of $TiCl_4$ produced the γ-substituted γ-butenolides **31** in good to excellent yields (Scheme 12).

Scheme 12



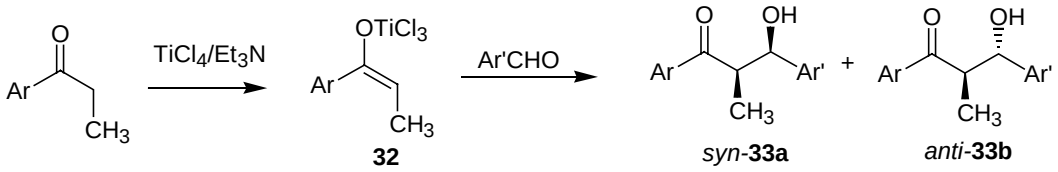
30 R^1= OMe; R^2= R^3 = Me

31 58%

2.1.1.3 Aldol reactions of titanium enolates prepared directly by using the $TiCl_4/R_3N$ reagent system

Harrison *et al.*[17] reported the first instances of titanium enolates **32**, generated directly by the reaction of carbonyl compounds using $TiCl_4$ and tertiary amine, exhibiting ability to promote stereoselective aldol reactions. It was reported that the reaction of propiophenone derived titanium enolates with aromatic aldehydes afforded the corresponding *syn* aldol adducts **33** with excellent selectivity and yields (Scheme 13).

Scheme 13



32

syn-**33a** *anti*-**33b**

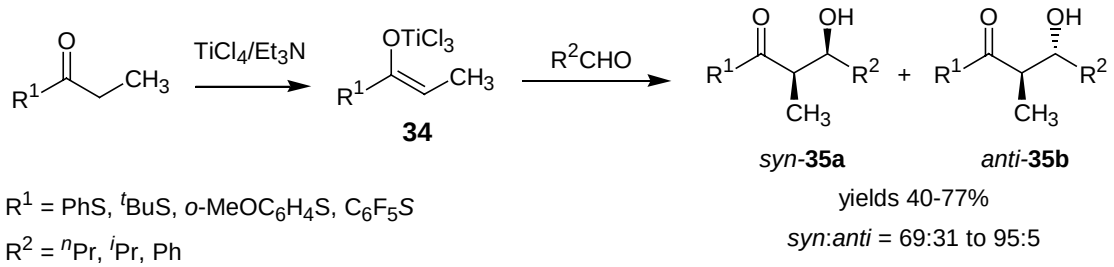
Ar = Ph, *o*-$MeOC_6H_4$, *p*-$NO_2C_6H_4$, *p*-MeC_6H_4, *p*-$MeOC_6H_4$

yields: 91-98%

33a:**33b** = 87:13 to 95:5

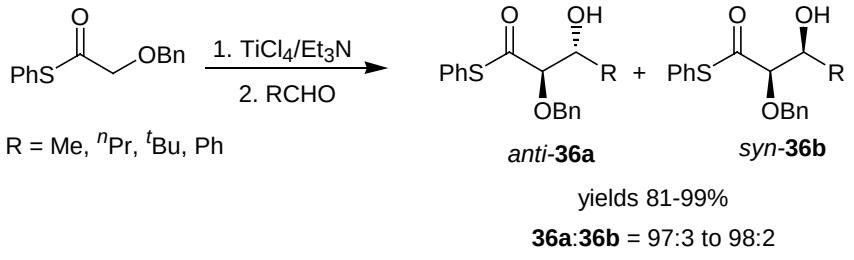
Aldol reactions involving thioester based titanium enolates **34**, generated directly using $TiCl_4$ and tertiary amine, were reported to give aldol adducts **35** in moderate yields with moderate to good *syn*-selectivity (Scheme 14).[18]

Scheme 14



Titanium enolates of α-benzyloxythioesters, generated using the $TiCl_4/Et_3N$ reagent system, were employed to obtain *anti*-α-benzyloxy-β-hydroxy thioesters **36** with excellent yields with high level of selectivity (Scheme 15).[19]

Scheme 15



Evans and other research groups[20] studied the asymmetric aldol processes by utilizing the reactions of several oxazolidinone-, oxazolidinethione-, oxazolidineselone-, thiazolidinethione-derived titanium enolates (generated directly by treating the respective carbonyl compound with chlorotitanium reagents and tertiary amines) with different

aldehydes. The selectivities realized in these reactions depend on the substrates, reagents and reaction conditions.

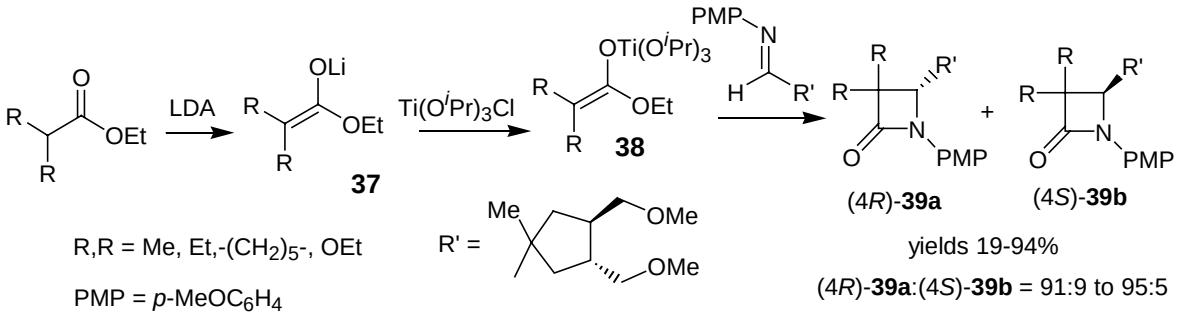
2.1.2 Titanium enolates in Mannich-type reactions

Mannich-type reactions afford convenient routes for the synthesis of β-amino carbonyl compounds.[21] Addition of titanium enolates to imines is a useful method to access the β-amino carbonyl compounds with one or two stereogenic centers depending upon the choice of enolate substituent and imine.

2.1.2.1 Mannich-type reactions of titanium enolates prepared by the transmetalation of lithium enolates

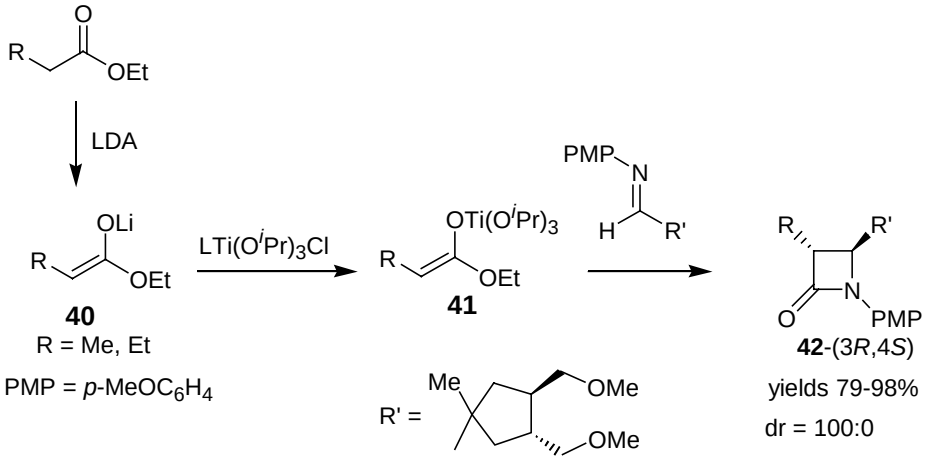
Fujisawa *et al.*[22] reported a diastereoselective addition of titanium enolates **38** of esters, prepared by the transmetalation of the corresponding lithium enolates **37** with the chlorotriisopropoxytitanium to a chiral imine that provided (4*R*)-β-lactams **39a** as major diastereomers while the use of lithium enolates gave (4*S*)-β-lactams **39b** as major products (Scheme 16).

Scheme 16



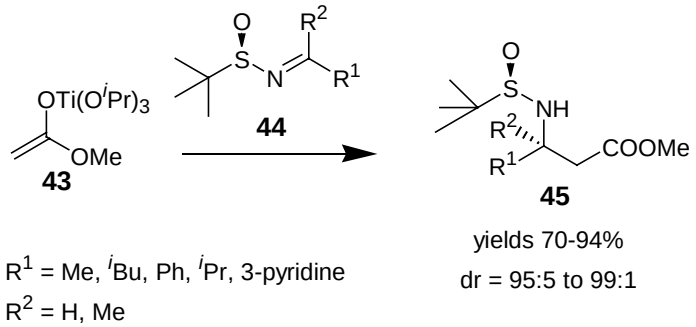
Later, two new stereogenic centers were introduced via the condensation reaction of the titanium enolates **41** of prochiral esters with the chiral imine to afford (3*R*,4*S*)-β-lactams **42** exclusively.[23] Whereas the use of lithium enolates **40** gave the corresponding (3*S*,4*S*)-β-lactams stereoselectively (Scheme 17).[23]

Scheme 17



Ellman and coworkers[24] reported the addition of titanium ester enolate **43**, prepared by the transmetalation of the corresponding lithium ester enolate, to enantiomerically pure *ter*-butanesulfinyl aldimines or ketimines **44** that provided optically active β-amino esters **45** in good yields with high diastereoselectivity (Scheme 18).

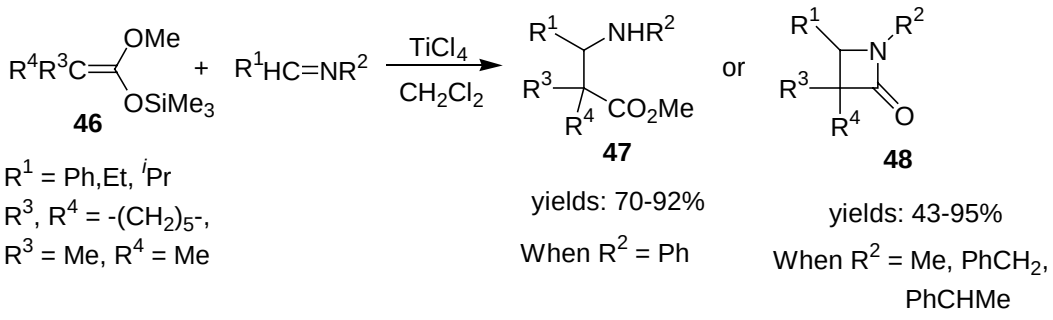
Scheme 18



2.1.2.2 Mannich-type reactions of titanium enolates prepared by the transmetalation of enol silanes

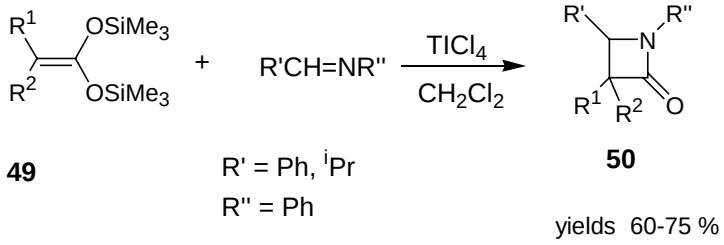
First instance for the synthesis of β-amino esters via $TiCl_4$-mediated reaction of enol silanes with imines, was reported by Ojima and coworkers[25] in 1977. These authors showed that *O*-methyl-*O*-trimethylsilyl ketene acetals **46** react with imines in the presence of $TiCl_4$ to afford β-amino esters or β-lactams depending on the nature of imine. Where as, *N*-arylimines afforded β-amino esters **47**, the *N*-alkylimines gave β-lactams **48** (Scheme 19).

Scheme 19



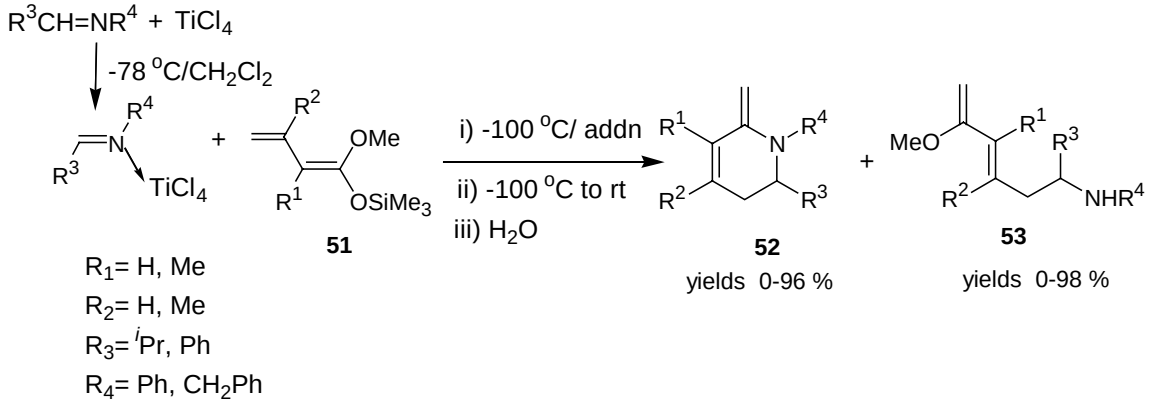
The use of the ketene bis(trimethylsilyl) acetals **49** with Schiff bases in the presence of $TiCl_4$ for the synthesis of β-lactams **50** was reported (Scheme 20)[26].

Scheme 20



Ojima and coworkers[27] reported that the reaction of vinylketene silyl acetals **51** with imine complex of $TiCl_4$ gives the corresponding 5,6-dihydro-2-pyridones **52** and/or 5-amino-2-alkenoates **53** in good to excellent yields (Scheme 21).

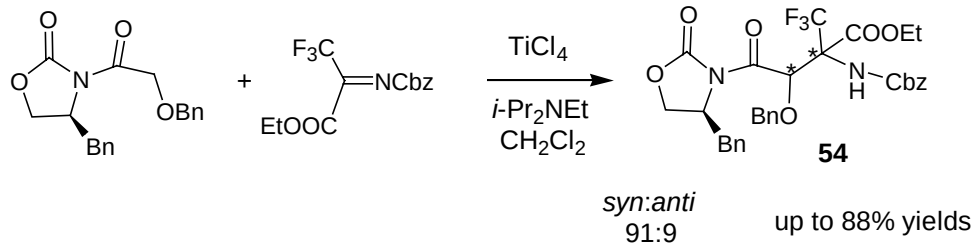
Scheme 21



2.1.2.3 Mannich-type reactions of titanium enolates generated directly from $TiCl_4$ and tertiary amines

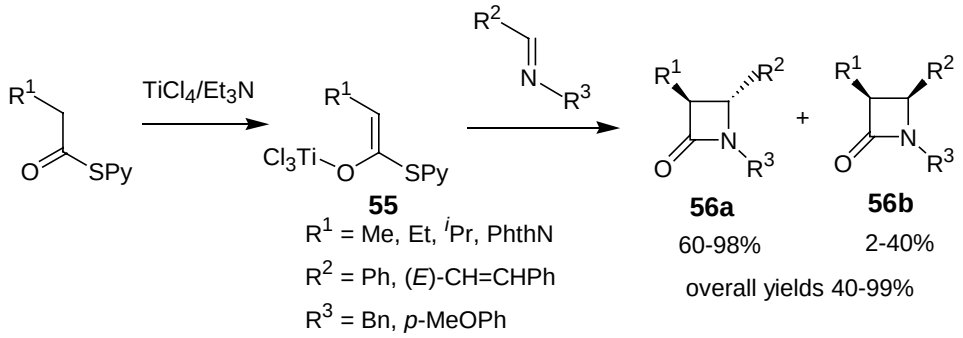
Zanda and co-workers[28] reported the stereoselective Mannich-Type reaction of an acyclic ketimine with a substituted chlorotitanium enolate for the efficient approach to D-erythro-α-trifluoromethyl-β-hydroxyaspartic units **54** (Scheme 22).

Scheme 22



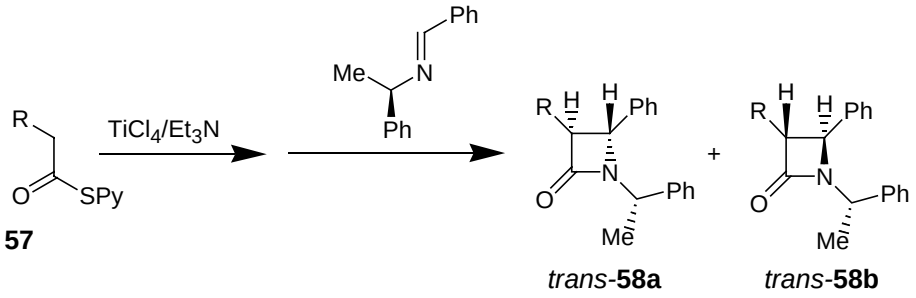
Cinquini *et al.*[29] reported that the reaction of titanium enolates **55**, generated by the treatment of 2-thiopyridyl esters using triethylamine and $TiCl_4$, with imines afforded *trans*-β-lactams **56** in good to excellent yields with moderate to good stereoselectivity (Scheme 23).

Scheme 23



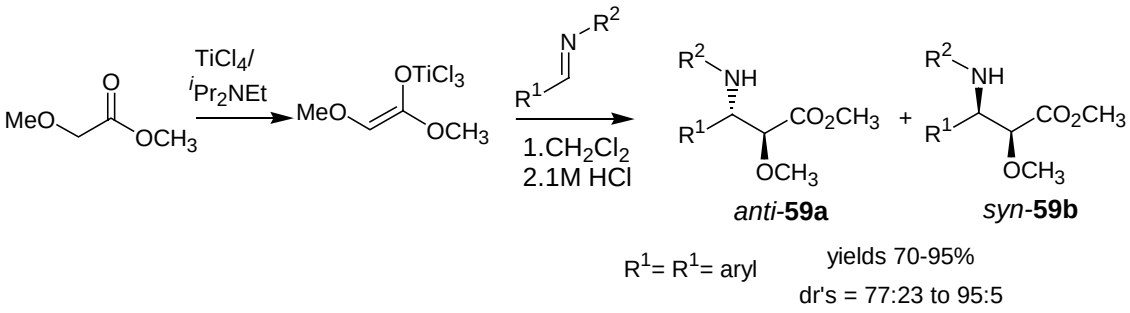
The *N*-benzylidene-(*R*)-α-methylbenzylamine was also employed in the stereo-selective synthesis of *trans*-β-lactams **58** using titanium enolates of 2-pyridyl thioesters **57** (Scheme 24).

Scheme 24



Andrian *et al.*[30] reported the synthesis of α-methoxy-β-substituted-β-amino esters **59** by an *anti* selective reaction of the titanium enolate of methyl methoxyacetate with imines (Scheme 25).

Scheme 25



2.1.3 Titanium enolates in Michael-type reactions

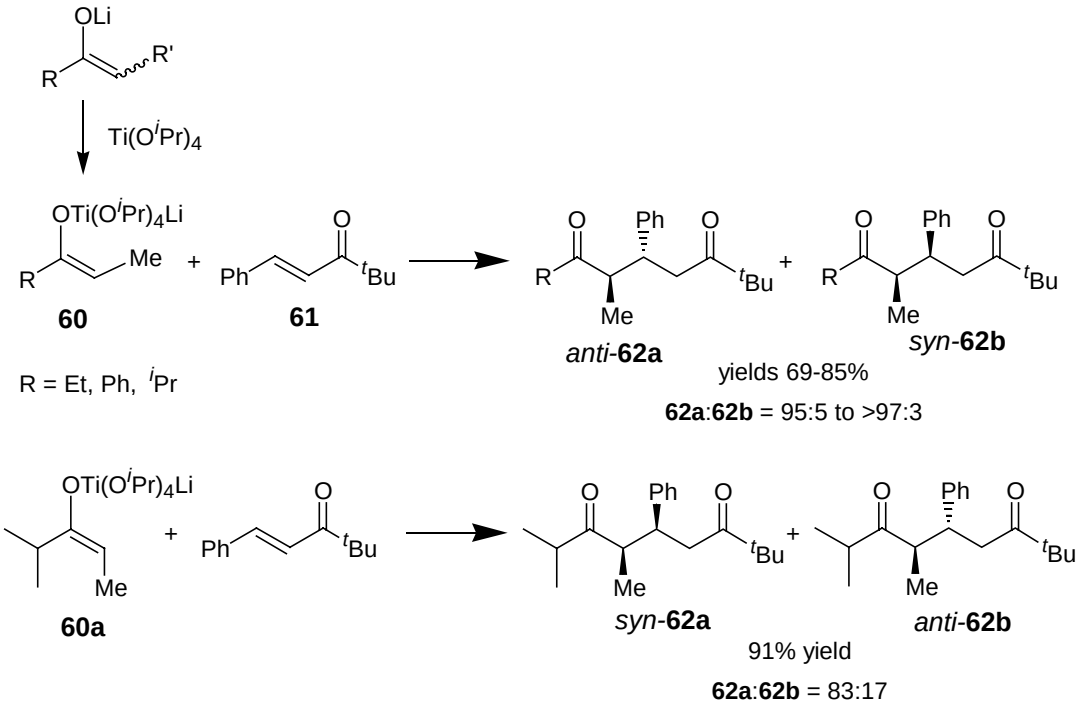
The Michael-type conjugate addition to α,β-unsaturated carbonyl systems has been established as one of the versatile functionalization methods in organic synthesis.[31] Generally, these reactions are promoted by strong bases such as alkali metal alkoxides or hydroxides or organoalkali metal reagents. The application of transition metal compounds as promoters is a mild and efficient alternative to strong base catalysis of the Michael reaction.[32] Accordingly, the utility of titanium enolates or titanium enolate complexes received considerable interest in the Michael-type reactions.

2.1.3.1 Michael-type reactions of titanium enolates prepared by the transmetalation of lithium enolates

Bernardi and coworkers[33] introduced the use of titanium enolate, prepared by treating the corresponding lithium enolates of carbonyl compounds with titanium(IV) isopropoxide, in conjugate addition (Michael-type) reactions. The reaction between *Z*-titanium ate

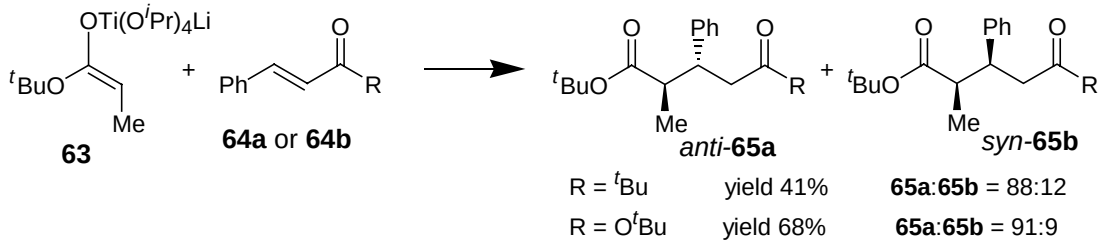
complexes **60** of ketones and benzalpinacolone **61** afforded the corresponding *anti*-Michael adducts **62a** in moderate to good yields with high selectivity. Whereas the addition of the *E*-titanium ate complex **60a** of isopropyl ethyl ketone furnished the *syn* adducts **62b** selectively (Scheme 26).[34]

Scheme 26



The *E*-titanium enolate complex **63** of the ^{t}butyl propionate was reacted with *E*-configured benzalpinacolone **64a** or ^{t}butyl *E*-cinnamate **64b** to obtain the respective Michael adducts **65a** with *anti*-selectivity (Scheme 27).

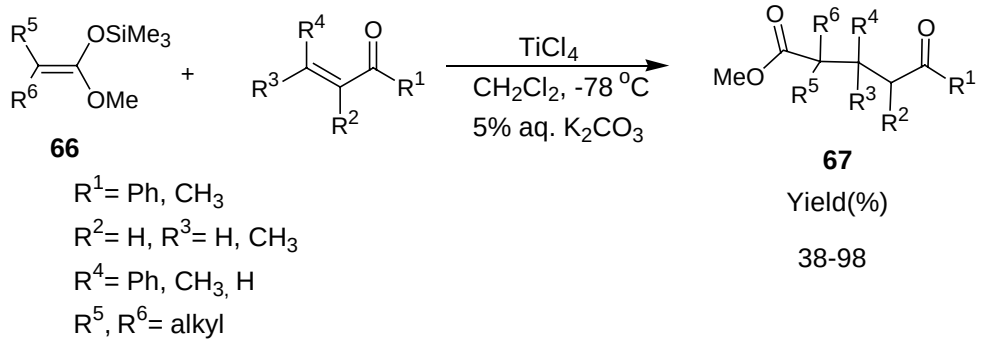
Scheme 27



2.1.3.2 Michael-type reactions of titanium enolates prepared by the transmetalation of silyl enolates

Mukaiyama *et al*.[35] reported the Michael type reaction of *O*-silylated ketene acetals **66** with α,β-unsaturated carbonyl compounds promoted by $TiCl_4$ to produce the adduct **67** (Scheme 28).

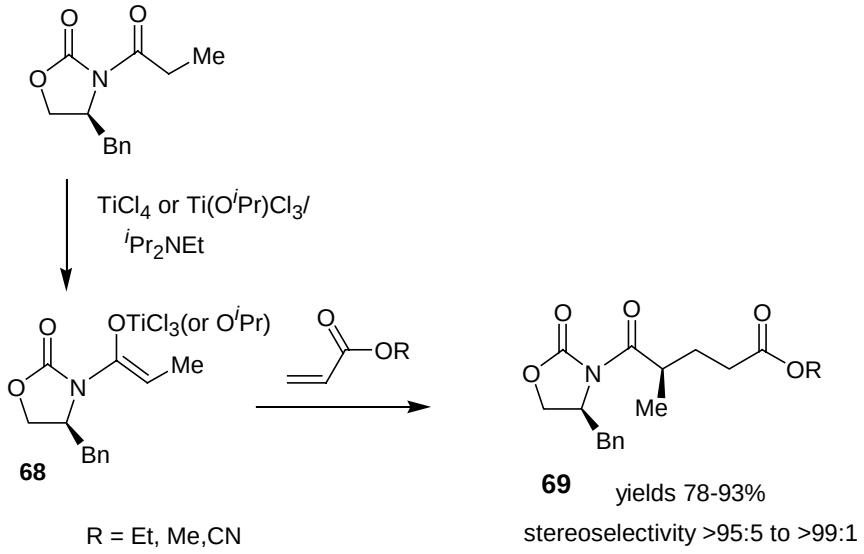
Scheme 28



2.1.3.3 Michael-type reactions of titanium enolates generated directly from chlorotitanium reagents and tertiary amines

Evans *et al.*[36] reported the diastereoselective addition of chlorotitanium enolate of chiral *N*-acyloxazolidinone **68** to Michael acceptors for obtaining the corresponding Michael adducts **69** in good yields with good selectivity (Scheme 29).

Scheme 29

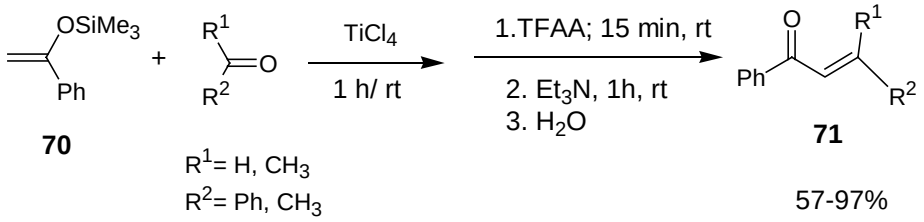


Different regio- and stereoselectivities were observed in the addition reactions of titanium dialkylamide or dialkylthioamide enolates and their lithium complexes with *E* or *Z* enones.[37] In these reactions, the regio- and stereochemical outcome depend on several factors such as the stoichiometry of the reagents, configurations of the substrates, and solvents.

2.1.4 Titanium enolate promoted alkylation reactions

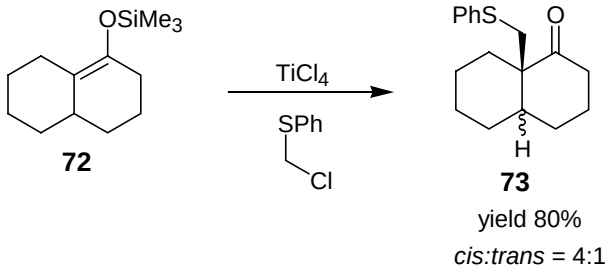
Hassine *et al.*[38] reported the one pot synthesis of α,β-unsaturated ketones **71** from trimethylsilylenol ethers **70** (Scheme 30).

Scheme 30



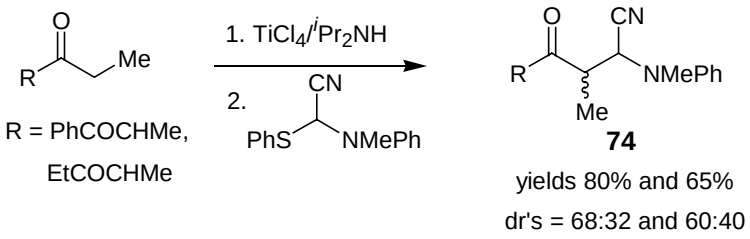
The phenylthiomethylation of *O*-silylated enolate **72** promoted by TiX_4 (X = Cl, Br) gave the corresponding thiomethylated product **73** in good yield with moderate stereoselection (Scheme 31).[39]

Scheme 31



Reaction of 2-(*N*-methylanilino)-2-phenylsulfonylacetonitrile and titanium enolates of ketones afforded the corresponding alkylated products **74** in moderate yields with low diastereoselectivity (Scheme 32).[40]

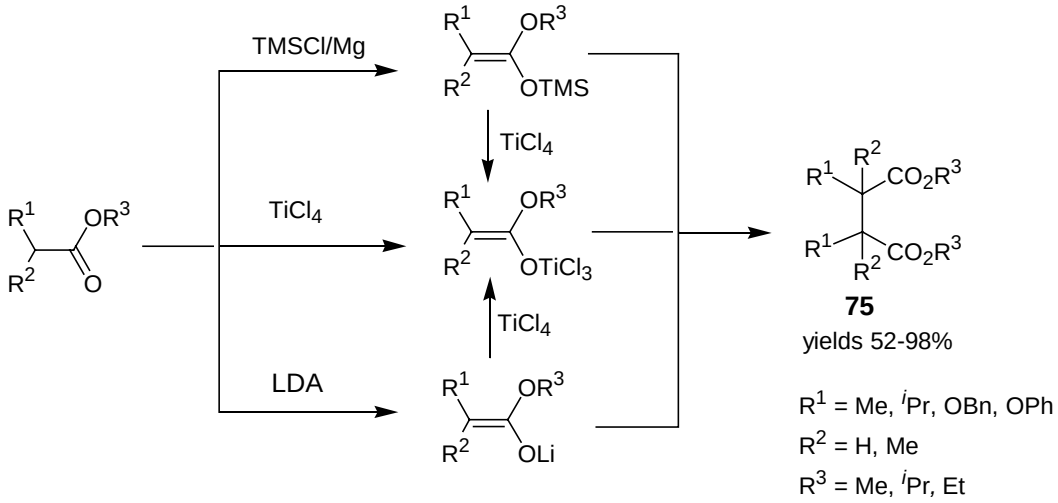
Scheme 32



2.1.5 Titanium enolate mediated oxidative coupling reactions

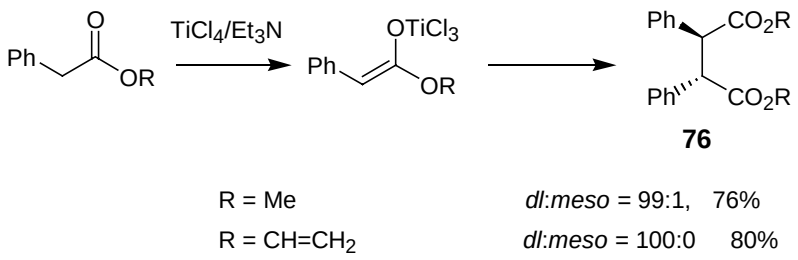
Ojima *et al.*[41] observed that the oxidative coupling of lithium ester enolates is effectively promoted by the use of $TiCl_4$. The homocoupled product **75** was obtained in this reaction in moderate to good yields (Scheme 33).

Scheme 33



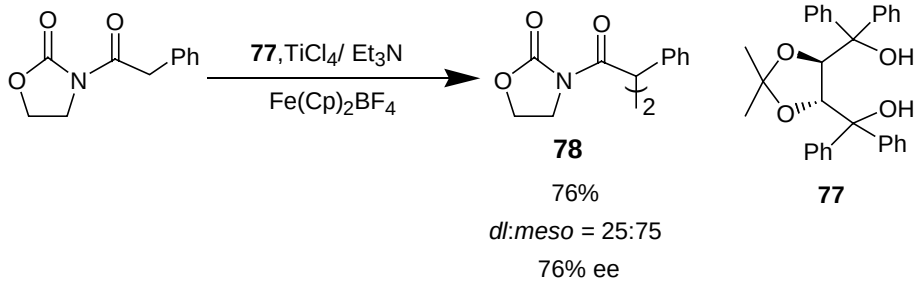
Titanium enolates of phenylacetic acid esters were used in the oxidative homocoupling to obtain 2,3-disubstituted succinic acid esters **76** in good yields with excellent diastereoselectivity (Scheme 34).[42]

Scheme 34



Enantioselective oxidative coupling of titanium enolates of *N*-phenylacetyl-oxazolidinones, in presence of a chiral ligand **77** and an oxidant, afforded the homodimer **78** (Scheme 35).[43]

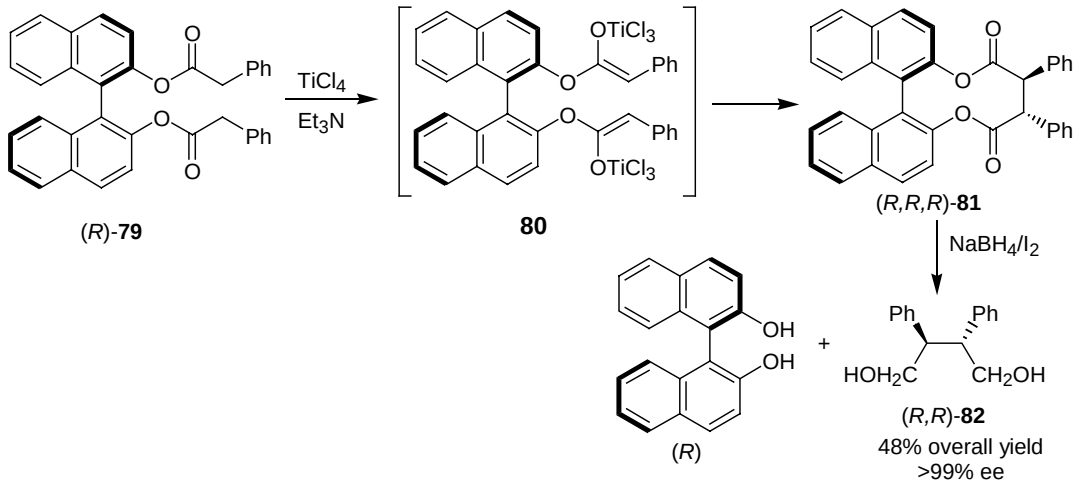
Scheme 35



2.1.6 Previous reports on reactions of titanium enolates from this laboratory

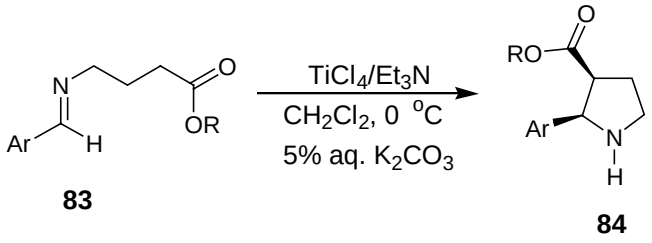
Intramolecular oxidative coupling of phenylacetic acid esters **79** of enantiomerically pure 1,1'-bi-2-naphthol was achieved by preparing the corresponding titanium ester enolates **80** *in situ* using the $TiCl_4/Et_3N$ reagent system. The coupled product **81** was reduced with the $NaBH_4/I_2$ reagent system to furnish the enantiomerically pure 2,3-diphenyl-1,4-butanediol **82** in good yields (Scheme 36).[44]

Scheme 36



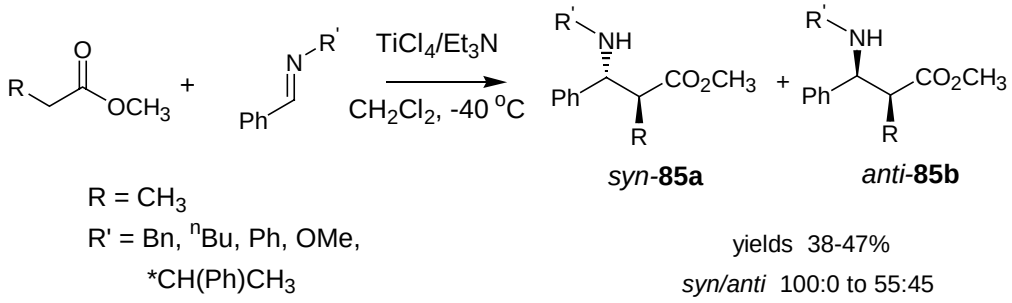
The γ-imino esters **83** cyclized diastereoselectively to produce the *cis*-2-aryl-3-pyrrolidine carboxylic esters **84** using the $TiCl_4/Et_3N$ reagent system (Scheme 37).[45]

Scheme 37



Stereoselective synthesis of *syn*-β-amino esters **85** was achieved by the reaction between the benzaldehyde imines and the titanium enolate generated from esters using the $TiCl_4/Et_3N$ reagent system (Scheme 38).[46]

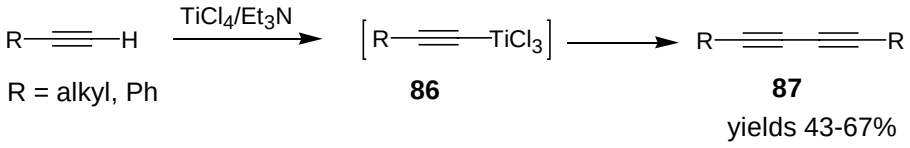
Scheme 38



2.1.7 Other reports on titanium reagents from this laboratory

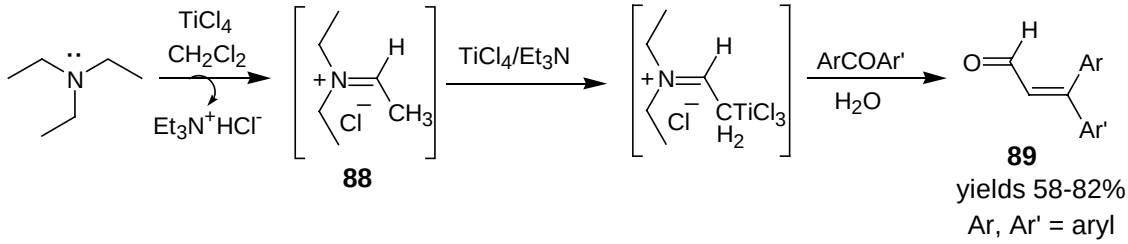
The titanium reagents were also used for several other organic transformations in this laboratory. Some of the transformations developed are described here. Terminal alkynes react with the $TiCl_4/Et_3N$ reagent system to produce the corresponding 1,3-diynes **87.** The reaction is considered to go through an alkynyl titanium intermediate **86** (Scheme 39).[47]

Scheme 39



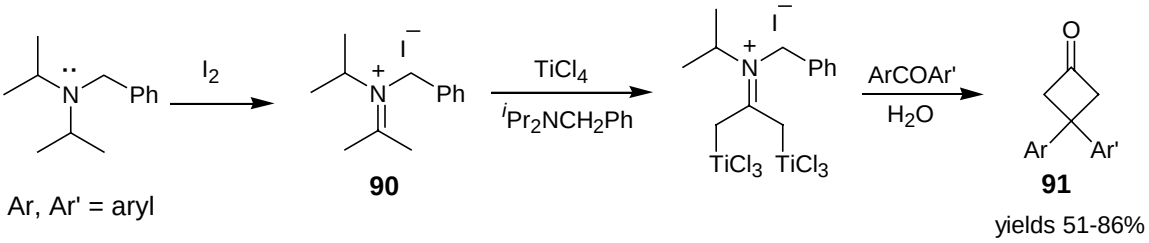
It was also reported from this laboratory that the trialkyl amines react with the $TiCl_4$ at 0-25 °C to give the corresponding iminium ions **88**, which undergo metalation followed by reaction with diaryl ketones to produce the corresponding α,β-unsaturated aldehydes **89** (Scheme 40).[48]

Scheme 40



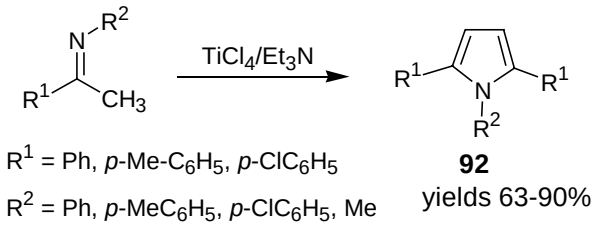
Recently, an interesting cyclobutanone synthesis was reported from this laboratory. The iminium ion **90** prepared using I_2 and diisopropylbenzylamine, upon reaction with $TiCl_4$ and excess amine produced the corresponding 3,3-diarylcyclobutanones **91** in moderate to good yields (Scheme 41).[49]

Scheme 41



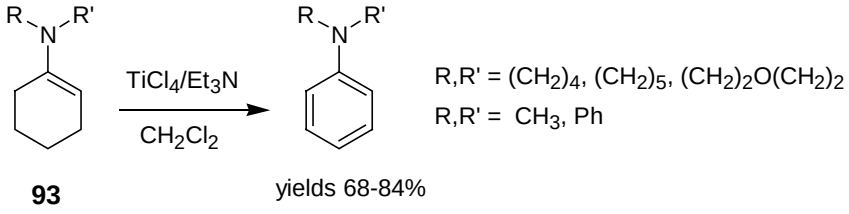
The reaction of the $TiCl_4/Et_3N$ reagent system with ketimines afforded the 1,2,5-trisubstituted pyrroles **92** in moderate to good yields (Scheme 42).[50]

Scheme 42



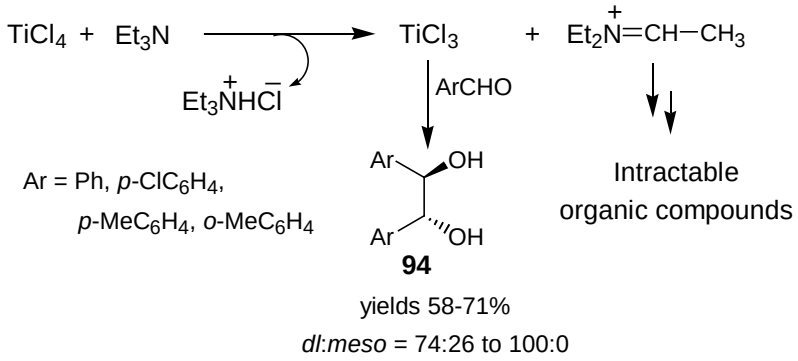
The $TiCl_4/Et_3N$ reagent system was used successfully for the aromatization of enamines **93** also reported (Scheme 43).[51]

Scheme 43



Low valent titanium species, Ti(III), prepared using $TiCl_4$ by oxidation of the trialkyl amines in the absence of electrophiles, is useful for the pinacol coupling of aryl aldehydes. The 1,2-diols **94** were obtained in moderate to good yields with moderate to excellent *dl*-selectivity (Scheme 44).[52]

Scheme 44



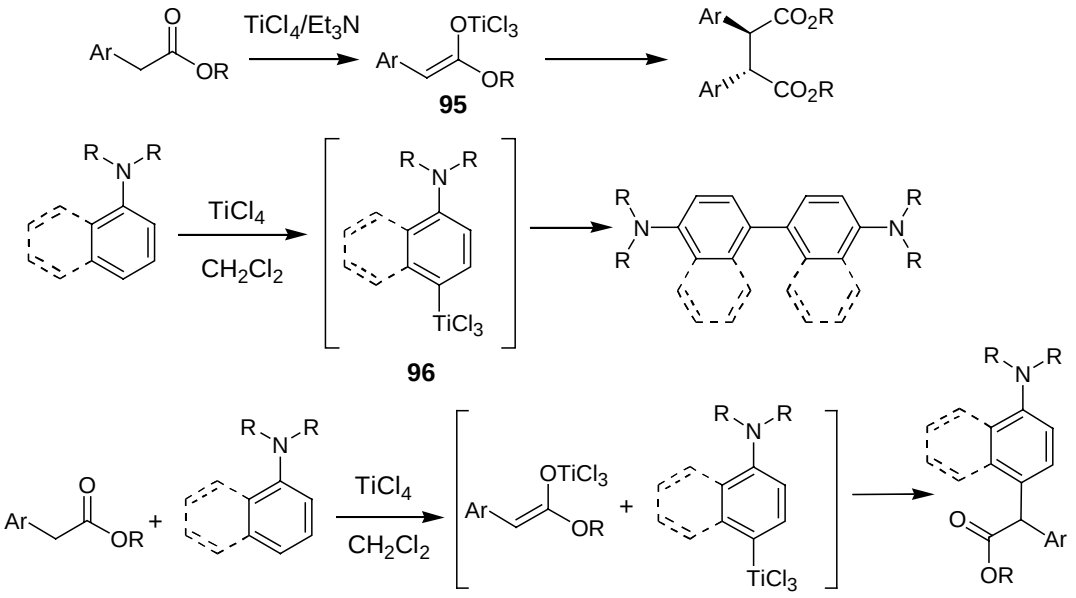
We have undertaken research efforts towards developing new methods for the C-C bond construction by exploiting the titanium enolates of carbonyl compounds, prepared *in situ* using the $TiCl_4/R_3N$ reagent system. The results are described in the next section.

2.2 Results and Discussion

2.2.1 Reaction of titanium enolates of esters with tertiary arylamines: α-arylation of esters

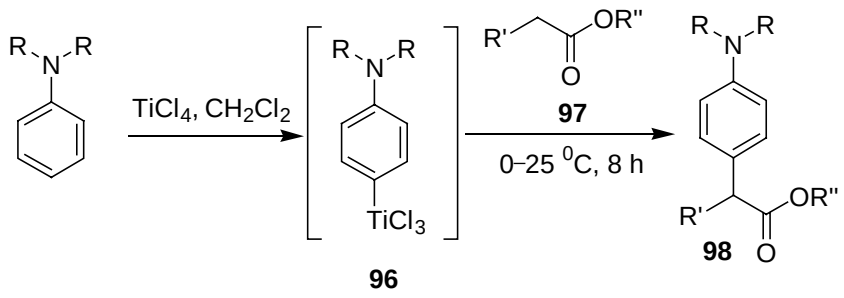
Previously, oxidative homocoupling of titanium enolates of phenylacetic acid esters **95** generated directly using $TiCl_4/R_3N$ reagent system[42] and oxidative homocoupling of *N,N*-dialkyl arylamines promoted by aryltitanium species[53] were reported from this laboratory. It was of interest to us to examine the cross-coupling between titanium enolates of arylacetic acid esters and aryltitanium species prepared *in situ* using *N,N*-dialkyl arylamines **96**. (Scheme 45)

Scheme 45



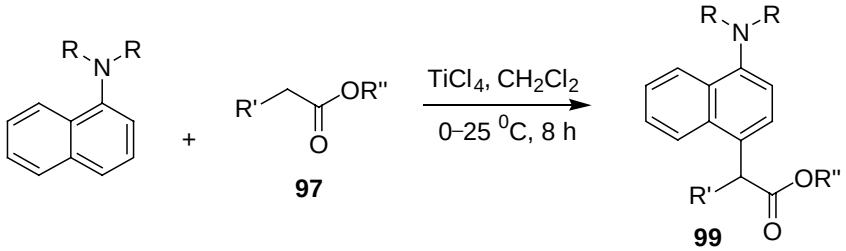
Indeed, the reaction of aryltitanium species **96** with alkyl arylacetates **97** produced the corresponding α-arylated products **98** in good yields (Scheme 46).

Scheme 46



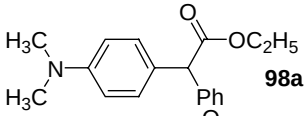
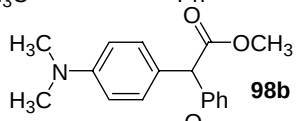
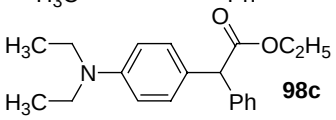
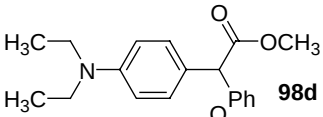
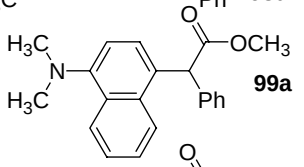
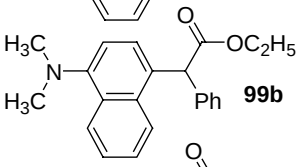
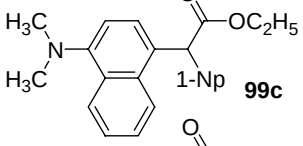
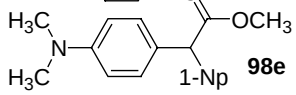
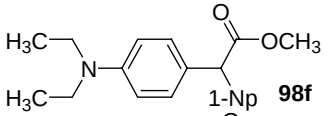
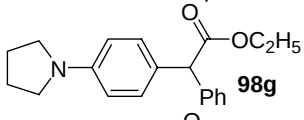
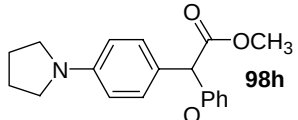
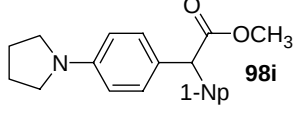
For example, the reaction of *N,N*-dimethylaniline and ethyl phenylacetate with $TiCl_4$ at 0-25 °C for 8 h produced **98a** in 89% yield, besides the corresponding benzidine derivative in 10% yield. Similarly, *N,N*-dialkyl-1-naphthylamines also reacted with alkyl arylacetates to give the corresponding α-arylated esters **99** in 65-75 % yields (Scheme 47).

Scheme 47



The transformation was examined using various esters as well as amines and the results are summarized in Table 1.

Table 1. Reaction of aryltitanium species with arylacetic acid esters

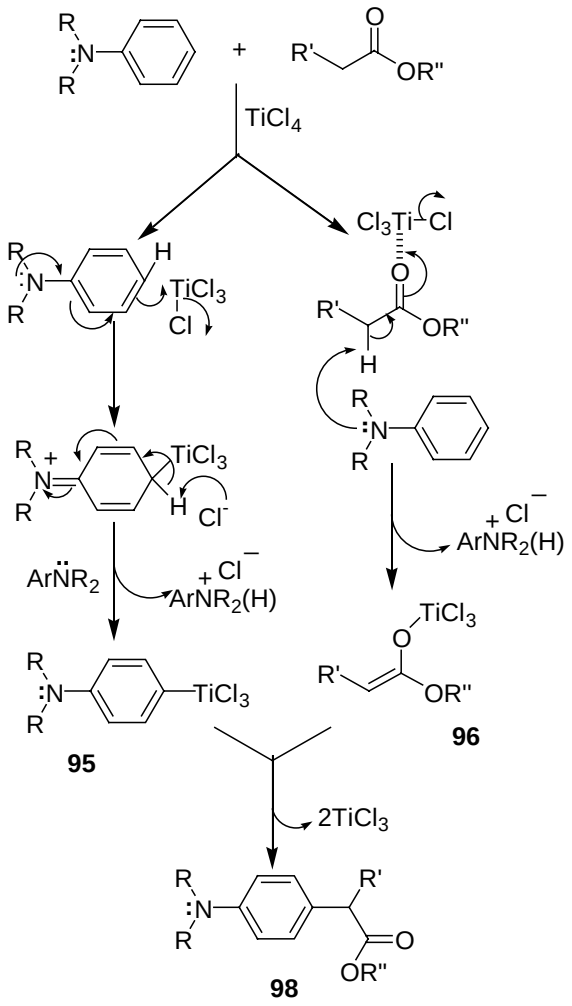
S.NO	$ArNR_2$	Ester	Product[a]	Yield[b] (%)
1	Ar = Ph, R = CH_3	R' = Ph, R'' = C_2H_5	 **98a**	89
2	Ar= Ph, R = CH_3	R' = Ph, R'' = CH_3	 **98b**	86
3	Ar = Ph, R = C_2H_5	R' = Ph, R'' = C_2H_5	 **98c**	90
4	Ar = Ph, R = C_2H_5	R' = Ph, R'' = CH_3	 **98d**	81
5	Ar = 1-Naphthyl, R = CH_3	R' = Ph, R'' = CH_3	 **99a**	65
6	Ar = 1-Naphthyl, R = CH_3	R' = Ph, R'' = C_2H_5	 **99b**	76
7	Ar =1-Naphthyl, R = CH_3	R' = 1-Naphthyl, R'' = CH_3	 **99c**	68
8	Ar = Ph, R = CH_3	R' = 1-Naphthyl, R '' = CH_3	 **98e**	65
9	Ar = Ph, R = C_2H_5	R' = 1-Naphthyl, R'' = CH_3	 **98f**	76
10	Ar = Ph, R = -C_4H_8-	R' = Ph, R'' = C_2H_5	 **98g**	62
11	Ar = Ph, R = -C_4H_8-	R' = Ph, R'' = CH_3	 **98h**	61
12	Ar = Ph, R = -C_4H_8-	R' =1-Naphthyl, R'' = CH_3	 **98i**	55

[a]The products were identified by ^1H, ^{13}C-NMR and mass spectral data and comparison with the data reported for compound **98a**.[54]

[b]The isolated yields were based on the amount of ester used.

The cross-coupled product formation can be explained considering cross coupling between the titanium enolate **95** of esters and aryltitanium species **96** formed *in situ* as shown in Scheme 48.

Scheme 48



Initially, the reaction of *N,N*-dialkylarylamines with $TiCl_4$ would produce aryltitanium intermediates (Scheme 48). The $TiCl_4$-ester complex could be deprotonated by the base *N,N*-dialkylarylamine which would lead to the formation of titanium enolates.

Finally, cross-coupling between aryltitanium and titanium enolates of ester lead to the formation of the α-arylated ester (Scheme 48).

In this reaction, the arylating agent *N,N*-dialkylarylamine itself is acting as a base for enolate formation. Here, $TiCl_4$ has the dual role of metalating the *N,N*-dialkylarylamine and producing the enolate from the ester. We have observed that some of the enolizable esters like methyl propionate did not react with aryltitanium under these reaction conditions, possibly due to weak basicity of the arylamines.

The product **98e** was also characterized by X-ray crystal structure analysis.

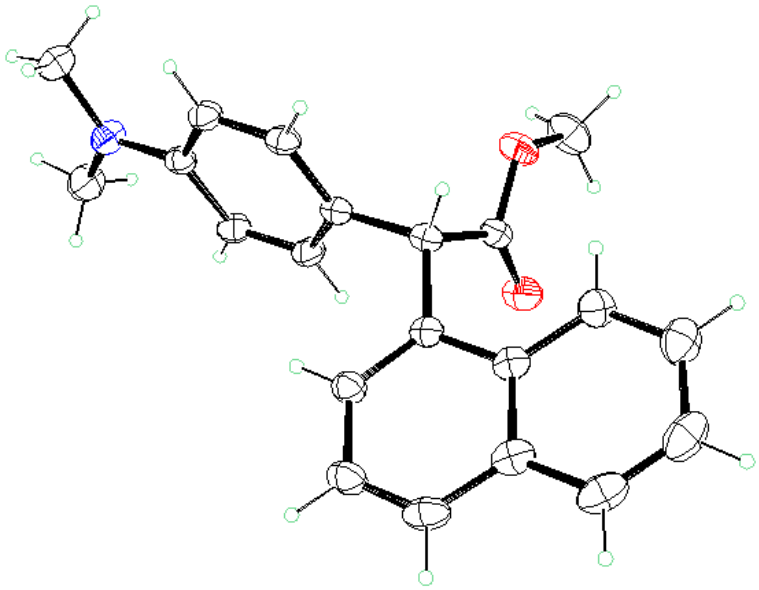


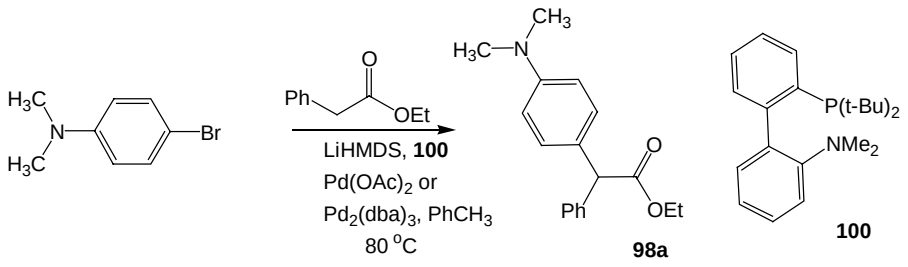
Fig 1. ORTEP diagram of compound **98e**

Table 2: Crystal data and structure refinement for compound **98e**

Empirical formula	C_{21} H_{21} N O_2	
Formula weight	319.39	
Temperature	293(2) K	
Wavelength	0.71073 A	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 8.4790(9) A	α = 89.811(2) º.
	b = 9.2843(10) A	β = 87.981(2) º.
	c = 11.9528(13) A	γ = 66.418(2) º.
Volume	861.77(16) $Å^3$	
Z	2	
Calculated density	1.231 Mg/m^3	
Absorption coefficient	0.079 mm^-1	
F(000)	340	
Theta range for data collection	1.70 to 25.97 º.	
Limiting indices	-10<=h<=10, -11<=k<=11, -14<=l<=14	
Reflections collected	8946	
Independent reflections	3348 [R(int) = 0.0200]	
Completeness to theta = 25.97	98.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1 and 0.914201	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3348 / 0 / 220	
Goodness-of-fit on F^2	1.040	
Final R indices [I>2sigma(I)]	R1 = 0.0464, wR2 = 0.1286	
R indices (all data)	R1 = 0.0586, wR2 = 0.1388	
Largest diff. Peak and hole	0.185 and -0.197 $e.Å^{-3}$	

Although, these reactions are limited to only *N,N*-dialkylarylamines, it is simple compared to the conventional ways of α-arylation of esters either starting from aryl halides using strong bases or involving transmetalation reactions. Generally, methods for the α-arylation of esters have a number of disadvantages like the need of special and toxic reagents, harsh reaction conditions, or multiple steps. For example, the compound **98a** was obtained in 80% yield by the reaction of ethyl phenylacetate with *N,N*-dimethyl-4-bromo benzene in the presence of 1.5 mol % $Pd_2(dba)_3$ and 6.3 mol% ligand **100** (Scheme 49).[54]

Scheme 49



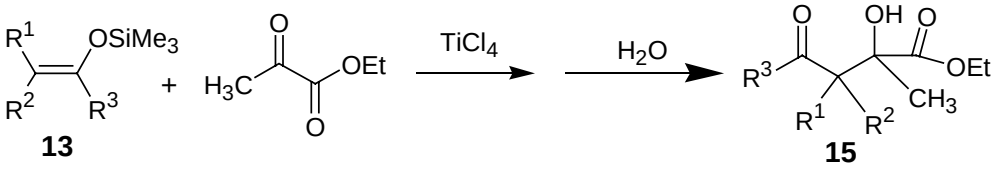
α-Aryl carbonyl compounds such as esters, ketones and their derivatives are important class of organic compounds.[55] In particular, α-aryl carboxylic acids are integral structural components of several pharmaceuticals with analgesic and anti-inflammatory properties, for example, ibuprofen, naproxen, ketoprofen, and flurbiprofen.[55,56] These compounds are able to reduce inflammation and pain by inhibition of the cycloxygenage system. Though the synthesis of *α*-aryl esters has been a field of active research for years,[57] the development of a reliable, economically reasonable, and general protocol remains elusive. Therefore, the synthesic method described here using readily accessible reagents has good potential for further exploitation,

2.2.2 Reactions of titanium enolates with dicarbonyl compounds

2.2.2.1 Reaction of titanium enolates of alkanoic acid anhydrides with α-keto esters: **Synthesis of maleic anhydrides**

During the investigations on the synthetic applications of the titanium enolates of ketone and esters, generated using the $TiCl_4/R_3N$ reagent system,[44-46] we became interested in the cross aldol condensation mediated by $TiCl_4$ with enolates and α-keto esters (Scheme 50).[9]

Scheme 50



It was of interest to examine the reaction pattern of titanium enolates of carbonyl compounds with α-keto esters. Initially, we have chosen alkanoic acid anhydrides as enolate source. We have observed that the α-keto esters **101** react with alkanoic acid anhydrides **102** in the presence of the $TiCl_4/n\text{-}Bu_3N$ reagent system to give maleic anhydrides **103** (Scheme 51). For example, ethyl benzoylformate reacts with acetic anhydride in 1,2-dichloroethane solvent at refluxing temperature to produce the phenylmaleic anhydride **103a** in 92% yield. This conversion of acyclic anhydrides to cyclic anhydrides was found to be general for aryl α-keto esters and alkyl anhydrides using the $TiCl_4/n\text{-}Bu_3N$ reagent system. The results are summarized in Table 3.

Scheme 51

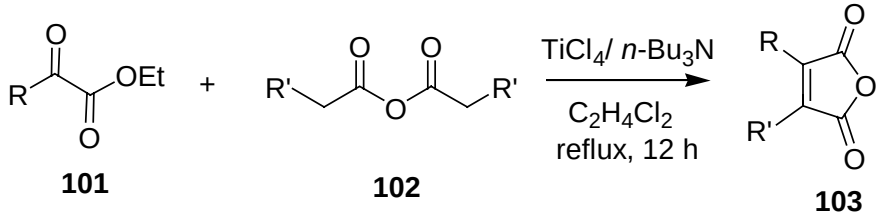
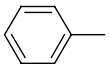
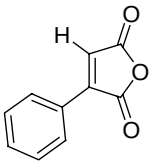
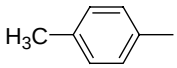
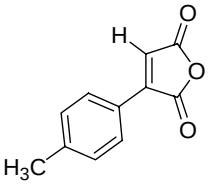
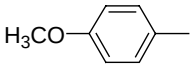
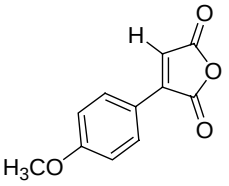
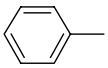
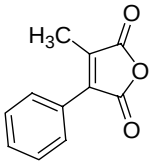
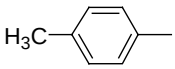
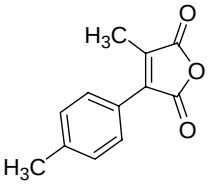
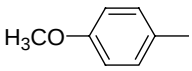
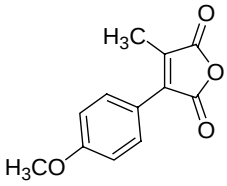


Table 3: Reaction of α-keto ester with anhydrides and $TiCl_4$/*n*-Bu_3N.[a]

S NO	R^1	R^2	Product[b]		Yield %[c]
1	H			**103a**	92
2	H			**103b**	84
3	H			**103c**	64[c]
4	CH_3			**103d**	81
5	CH_3			**103e**	76
6	CH_3			**103f**	62[c]

[a]The reactions were carried out using *α*-keto esters (5 mmol), acetic anhydride (10 mmol), $TiCl_4$ (3.3 mL of 1:1 solution of $TiCl_4/CH_2Cl_2$) (15 mmol) and *n*-Bu_3N (6 mmol).

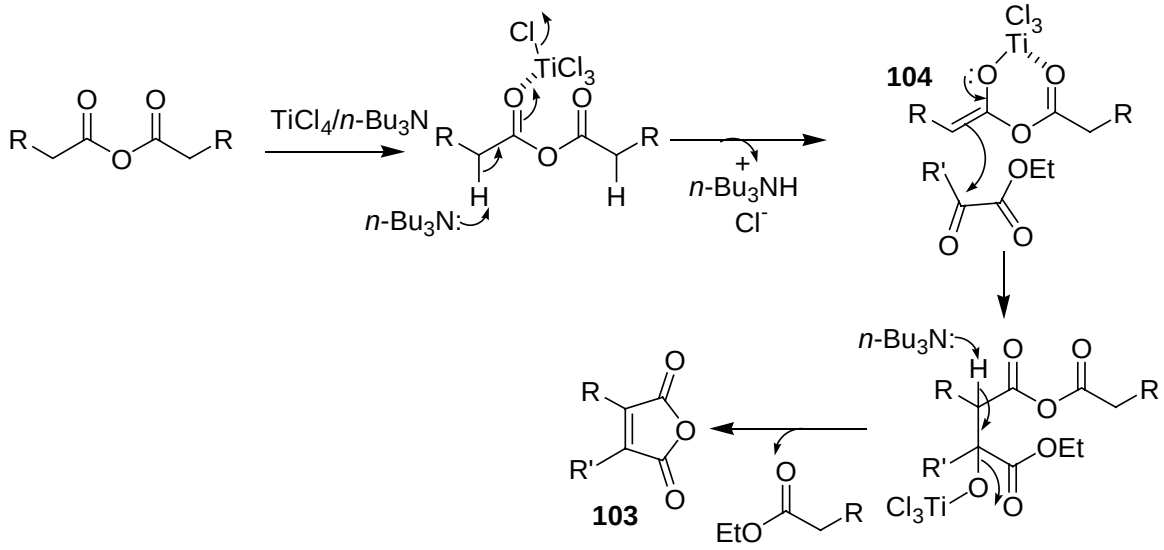
[b]The products were identified by ^1H, ^{13}C-NMR and mass spectral data and comparison of the data reported for compound **103a, 103b, 103c.**[62g]

[c]The isolated yields are based on the amount of keto ester used.

It was found that the use of acetic anhydride gave higher yields (entry 1-3) compared to that using propionic anhydride (entry 4-6). The reaction of acetic anhydride with benzoylformate gave **103a** in high yield 92% (entry 1). Whereas, with *p*-Me and *p*-OMe substituted benzoylformates produced **103b** and **103c** in 84% and 64% yields, respectively (entries 2 and 3). Similar variation of the yields with the substitution on the phenyl ring of α-keto esters was also observed with propionic anhydride.

The transformation can be rationalized by the mechanistic pathway outlined in Scheme 52, involving formation of titanium enolate of anhydride **104** and its aldol reaction with the α-keto esters followed by cyclization to give maleic anhydrides **103** (Scheme 52).

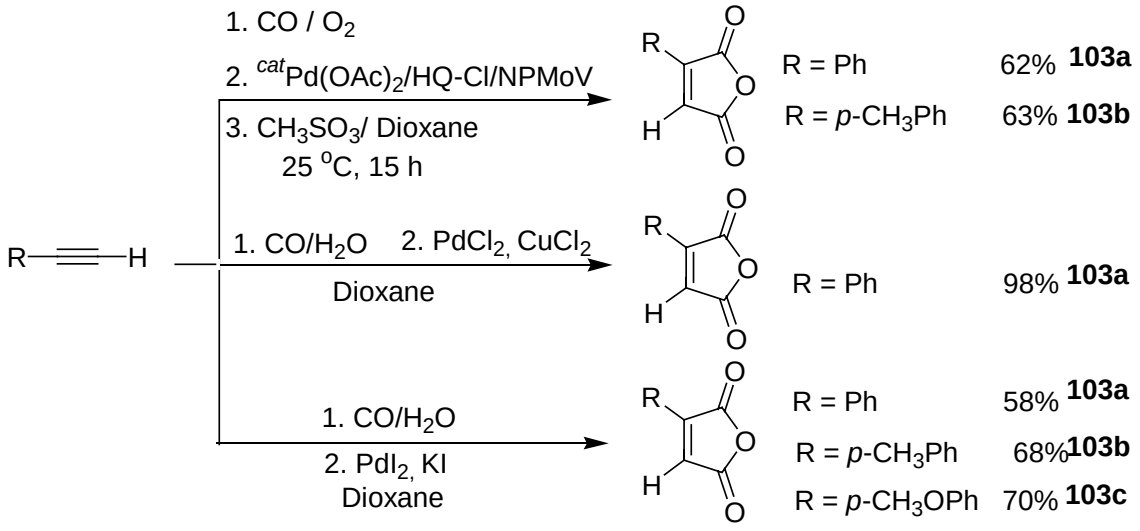
Scheme 52



Maleic anhydrides are important synthons widely used in the construction of new organic skeletons. These cyclic compounds have immense potential for application as dienophiles in Diels-Alder reactions[58] and as monomers in polymerization reactions.[59] Moreover, a large number of substituted maleic anhydrides were identified showing a range of biological activities,[60] including antibacterial activity.[61] However, only a very few general methods are available for the synthesis of the substituted maleic anhydrides.

Previously, synthesis of compounds **103a**, **103b** and **103c** were reported via Pd-catalyzed carbonylation of alk-1-ynes (Scheme 53).[62]

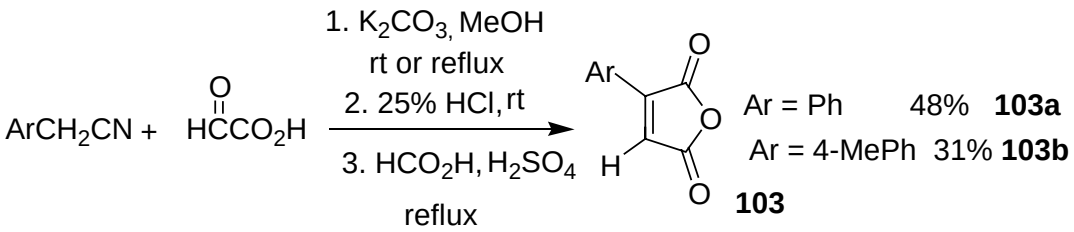
Scheme 53



More recently, it was reported that Pd catalyzed and CO_2 promoted oxidative carbonylation of the corresponding 1-alkynes in conjunction with excess of KI in water/dioxane gave the products **103a**, **103b** and **103c** in 54%, 68% and 70% yields, respectively.[62g] It has been reported from this laboratory that oxidative carbonylation of alk-1-ynes using metal carbonyls gives substituted maleic anhydrides.[63]

Dean *et al.*[64] reported the synthesis of compounds **103a** and **103b** by the condensation of aryl acetonitriles with glyoxylic acid in 48% and 31% yields, respectively (Scheme 54).

Scheme 54

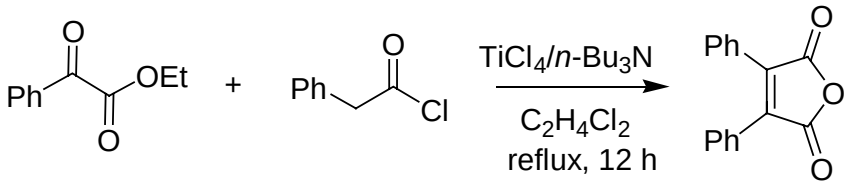


The method described here would serve as a simple alternative to these reported methods.

2.2.2.2 Reaction of phenylacetyl chloride with α-keto ester in the presence of the $TiCl_4$/*n*-Bu_3N reagent system

The diphenylmaleic anhydride **106** was obtained in 95% yield by the reaction of phenylacetyl chloride **105** and ethyl benzoylformate with the $TiCl_4$/*n*-Bu_3N reagent system under the refluxing temperature in 1,2-dichloroethane solvent (Scheme 55). Whereas, aliphatic acids and acid chlorides did not react with α-keto ester under the same reaction condition.

Scheme 55

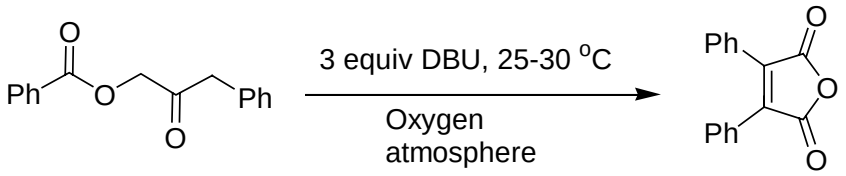


101a **105** **106**

Diarylmaleic anhydrides are known to be useful for controlling microbial growth in water as well as preventing slime formation in various industrial manufacturing processes. Diaryl substituted maleic anhydrides have been also used to prepare the corresponding photodimers as well as for the synthesis of biologically active derivatives.[65]

Recently, the synthesis of diarylsubstituted maleic anhydrides reported through tandem cyclization reaction as shown in Scheme 56.[66]

Scheme 56

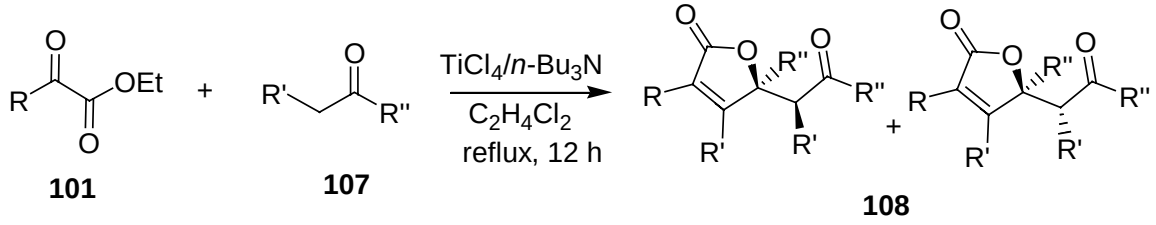


77% **106**

2.2.2.3 Reaction of titanium enolates of ketones with α-keto esters: Synthesis of γ-substituted γ-butenolides

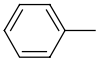
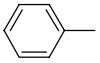
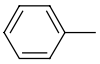
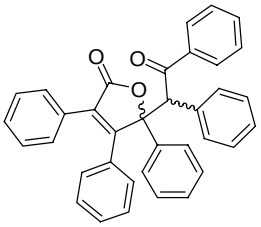
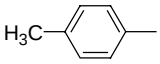
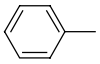
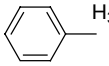
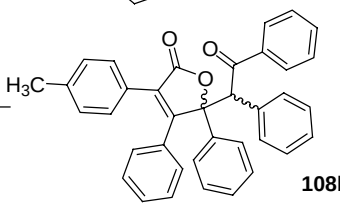
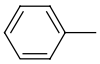
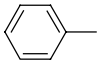
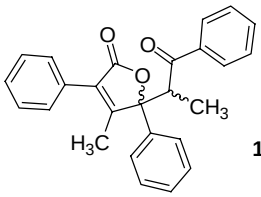
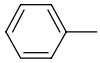
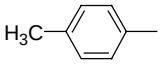
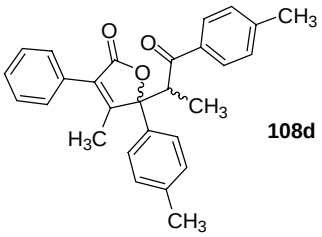
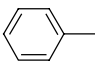
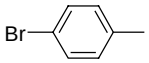
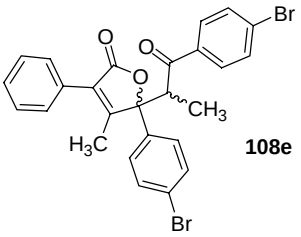
We have also examined the reaction of titanium enolates of ketones with α-keto esters. The titanium enolates of ketones were prepared directly by using the titanium tetrachloride and tertiary amines *in situ* in the presence of α-keto esters at 90-95 °C. Interestingly, the highly functionalized γ-substituted γ-butenolides **108** were obtained in one step by the reaction of ketones **107** and α-keto esters **101** in the presence of $TiCl_4$/*n*-Bu_3N (Scheme 57). For example, one equivalent ethyl benzoylformate reacts with two equivalence of deoxybenzoin in 1,2-dichloroethane solvent to produce the γ-butenolide (γ-lactone) **108a** in 82% yield. This transformation was found to be general for aryl α-keto esters and ketones using the $TiCl_4$/*n*-Bu_3N reagent system. The results are summarized in Table 4.

Scheme 57



101 **107** **108**

Table 4: Reaction of α-keto esters with ketones and $TiCl_4$/*n*-Bu_3N.[a]

S NO	R	R'	R''	Product[b]	Yield %[c]	dr%[d]
1				 **108a**	82	29:71[e]
2				 **108b**	84	0:100[e]
3				 **108c**	82	80:20[f]
4				 **108d**	61	51:49[f]
5				 **108e**	76	50:50[f]

[a]The reactions were carried out using *α*-keto esters (1.25 mmol), ketone (2.5 mmol), $TiCl_4$ (7.5 mmol, 1.65 mL of 1:1 solution of $TiCl_4/CH_2Cl_2$) and *n*-Bu_3N (1.43 mL, 7.5mmol).

[b]The products were identified by ^1H, ^{13}C-NMR spectral data.

[c]The isolated yields are based on the amount of ketone used.

[d]The diastereomeric ratio of compound are as determined by ^1H NMR.

[e]The diastereomeric ratio are for *syn*/*anti* as determined by ^1H NMR.

[f]Diastereomeric ratio and the configurations (*syn*/*anti*) could not be assigned with available data.

Generally, the yields are moderate to good for this transformation. Ethyl(4-methyl)benzoylformate gave butenolide **108b** in 84% yield with deoxybenzoin (Table 4 entry 2) and the reaction of deoxybenzoin with ethyl benzoylformate produced butenolide **108a** in 82% yield (Table 4 entry 2). In the case of propiophenones, yields of γ-butenolides were decreased compared to deoxybenzoin. The reaction of propiophenone with ethyl benzoylformate gave the lactone **108c** in 82% and 4-methyl propiophenone produced the butenolide **108d** in 61% yield, respectively, (Table 4 entries 3 and 4). Whereas, the product **108e** was obtained in 76% yield in the reaction of 4-bromo propiophenone with ethyl benzoylformate (Table 4 entry 5).

The structure of the major product **108b** was found to be *anti* by X-ray crystal structure analysis.

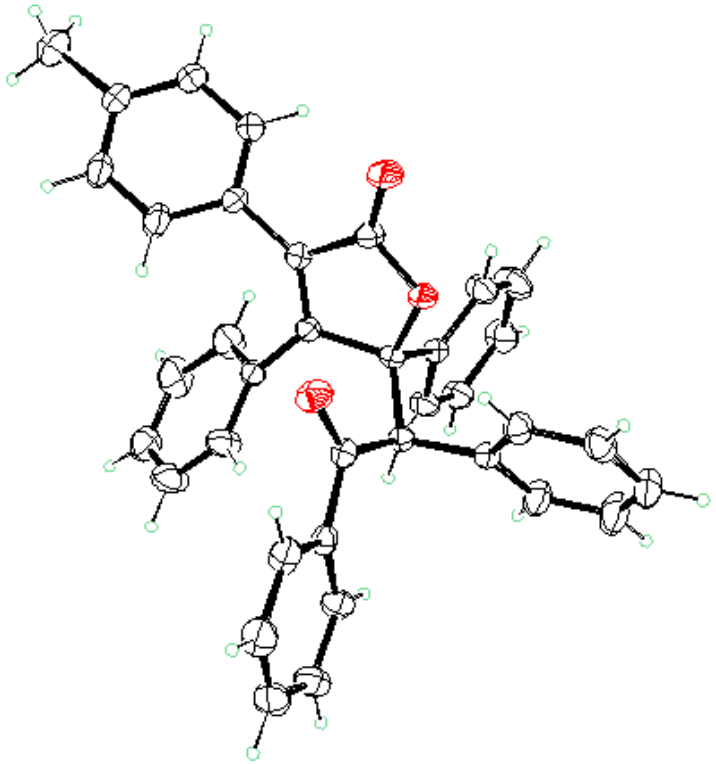


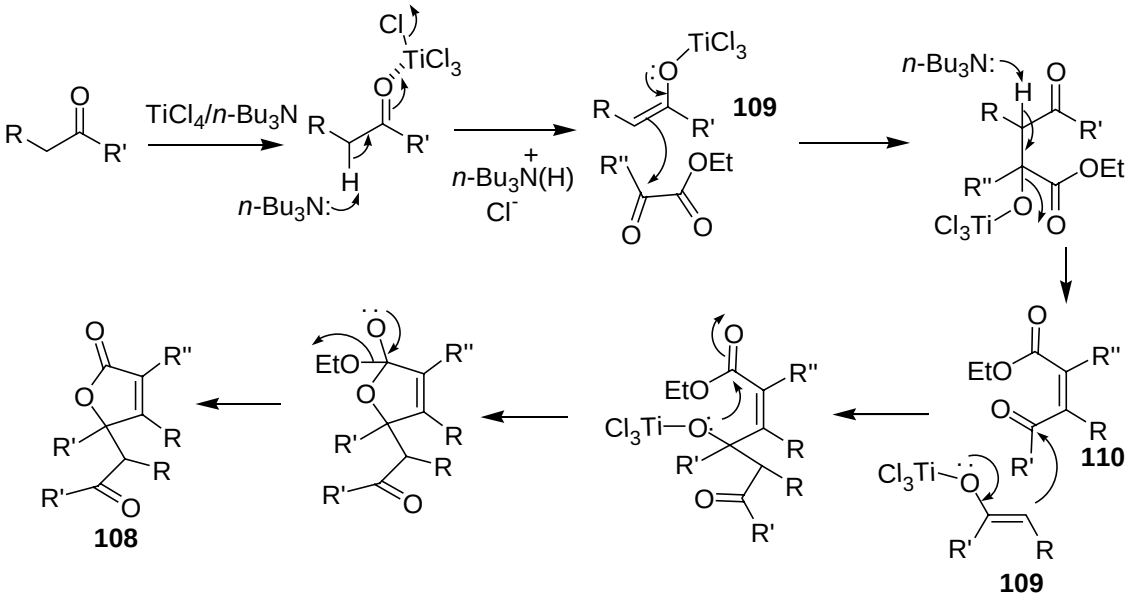
Fig 2. ORTEP diagram of compound **108b**

Table 5: Crystal data and structure refinement for **108b**

Empirical formula	$C_{37}H_{28}O_3$
Formula weight	520.59
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)/c
Unit cell dimensions	a = 10.212(4) Å β= 97.749(6)°.
	b = 18.516(7) Å
	c = 15.270(6) Å
Volume	2861.2(18) $Å^3$
Z	4
Density (calculated)	1.209 Mg/m^3
Absorption coefficient	0.076 mm^{-1}
F(000)	1096
Crystal size	0.42 x 0.27 x 0.12 mm^3
Theta range for data collection	1.74 to 28.36°.
Index ranges	-13<=h<=13, -24<=k<=24, -20<=l<=20
Reflections collected	31059
Independent reflections	6777 [R(int) = 0.0783]
Completeness to theta = 25.00°	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.991 and 0.952
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6777 / 0 / 362
Goodness-of-fit on F^2	0.879
Final R indices [I>2sigma(I)]	R1 = 0.0511, wR2 = 0.1350
R indices (all data)	R1 = 0.1324, wR2 = 0.1587
Largest diff. peak and hole	0.332 and -0.313 $e.Å^{-3}$

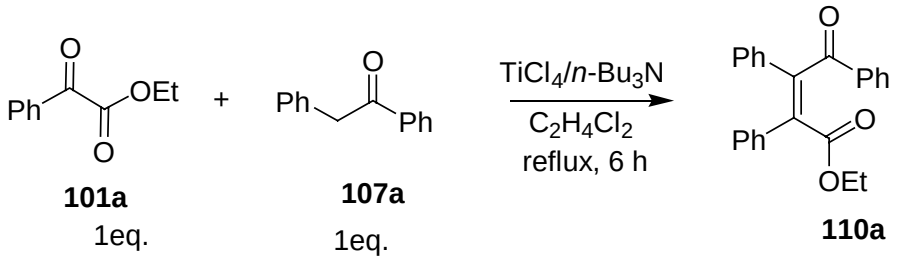
The transformation can be rationalized by the mechanistic pathway outlined in Scheme 58, involving formation of titanium enolate of ketone **109** and its aldol reaction with the α-keto esters followed by a second aldol reaction with intermediate **110** and then cyclization to give butenolide **108** as shown in Scheme 58.

Scheme 58



We have made efforts to isolate the intermediates involved in the above transformation. We have observed that the use of the ethyl benzoylformate and ketone in 1:1 ratio to produced the (*Z*)-γ-ketoester **110a** in 82% yield (Scheme 59).

Scheme 59



The configuration of the compound **110a** was assigned as (*Z*) by X-ray crystal structure analysis.

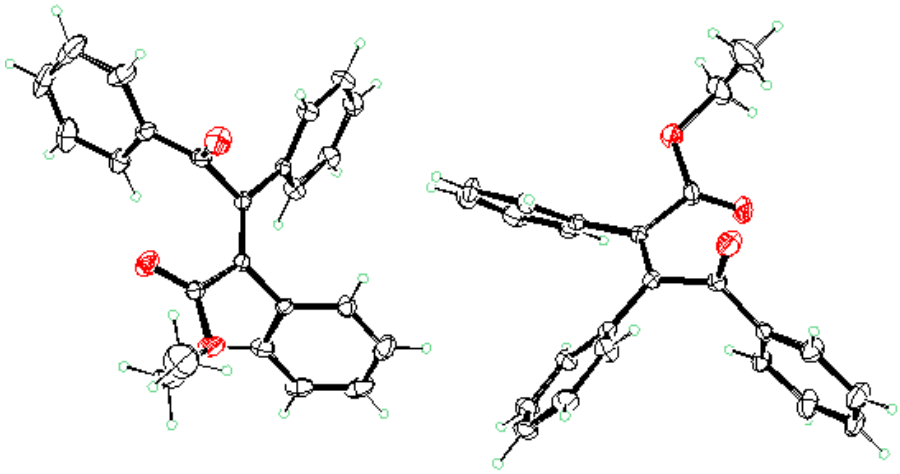


Fig 3. ORTEP diagram of compound **110a**

The transformation can be rationalized by the mechanistic pathway outlined in Scheme 60, involving formation of titanium enolate of ketone **109** and its aldol reaction with the α-keto esters followed by removal of second proton to give the γ-keto ester **110** as shown in Scheme 60.

Scheme 60

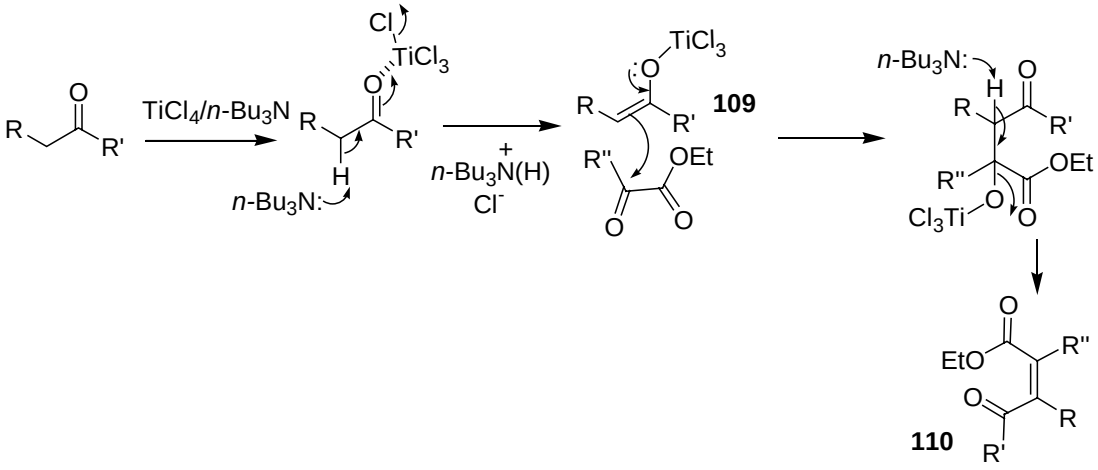


Table 5. Crystal data and structure refinement for **110a**

Empirical formula	$C_{24}\ H_{20}\ O_3$
Formula weight	356.40
Temperature	298(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	Pca2(1)
Unit cell dimensions	a = 18.168(4) Å $\alpha = \beta = \gamma = 90°$.
	b = 6.2483(12) Å
	c = 33.945(6) Å
Volume	3853.4(13) $Å^3$
Z	8
Density (calculated)	1.229 Mg/m^3
Absorption coefficient	0.080 mm^{-1}
F(000)	1504
Crystal size	0.42 x 0.32 x 0.20 mm^3
Theta range for data collection	2.24 to 26.03°.
Index ranges	-21<=h<=22, -7<=k<=7, -38<=l<=41
Reflections collected	18341
Independent reflections	3857 [R(int) = 0.0531]
Completeness to theta = 25.00°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9842 and 0.9321
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3857 / 1 / 489
Goodness-of-fit on F^2	1.082
Final R indices [I>2sigma(I)]	R1 = 0.0657, wR2 = 0.1474
R indices (all data)	R1 = 0.0869, wR2 = 0.1609
Absolute structure parameter	10(10)
Largest diff. peak and hole	0.324 and -0.176 $e.Å^{-3}$

In the present reaction of titanium enolates of ketones with α-ketoesters, *syn* and *anti* γ-substituted γ-butenolide adducts can be obtained with both (*E*)- and (*Z*)-enolates of ketones. The *anti* stereoselectivty for the transformation can be tentatively explained on the basis of the stereochemical model shown in Figure 5. The configuration of the intermediate **110** is expected to be (*Z*). The results can be explained considering that the *E*-titanium enolate of ketone would be in equilibrium with the *Z*-titanium enolate of ketone. The reaction of the *E*-titanium ketone enolate would give a lower-energy transition state **TS-1** leading to the major *anti* product. The *syn* product with *E*-titanium ketone enolate is not favored because it would give a higher-energy transition state **TS-2** due to the greater repulsions from the large group (X) of the intermediate **110.**

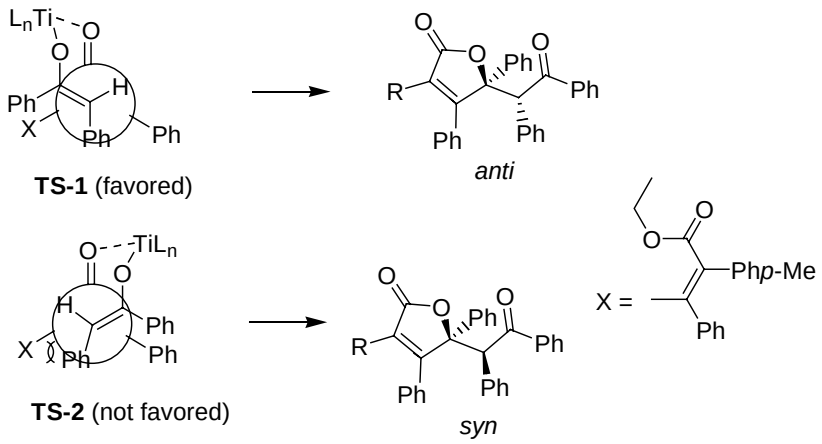
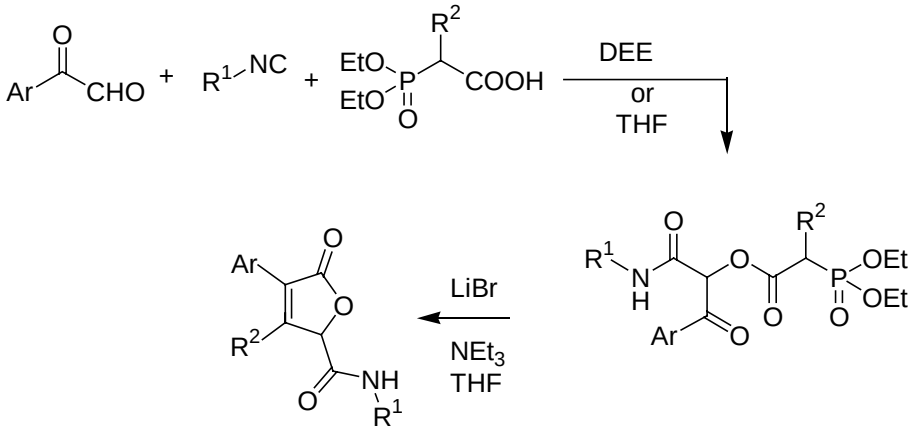


Fig 4: Stereochemical models

γ-Butenolides are ubiquitous chemical moieties found in various biologically active natural products. They have attracted the attention of synthetic organic and medicinal chemists.[67] The α,β-unsaturated γ-lactones are prominent moieties in the building of natural flavours and odors.[68] Moreover, certain functionalized open-chain molecules made by using γ-butenolides, such as 1,4-solfonylalcohols,[69] are found in fruits and vegetables and they have been the subject of intense research in flavor chemistry. Also, the butenolide is also a valuable synthon useful, in organic synthesis.[70]

There are many ways to synthesize the butenolide moiety.[71,72] Recently, Zhang *et al*.[73] reported a concise method for highly functionalized γ-substituted γ-butenolides by Mukaiyama aldol reaction on mucoholic acid catalyzed by Lewis acid. Domling *et al*.[74] have reported one-pot multi component approach for the synthesis of 5-acylamino butenolides using isocyanides, glyoxals and acetophosphonic acid diethyl esters through the Passerini three component reaction in the presence of DEE or THF followed by intramolecular Witting-type reaction (Scheme 61).

Scheme 61



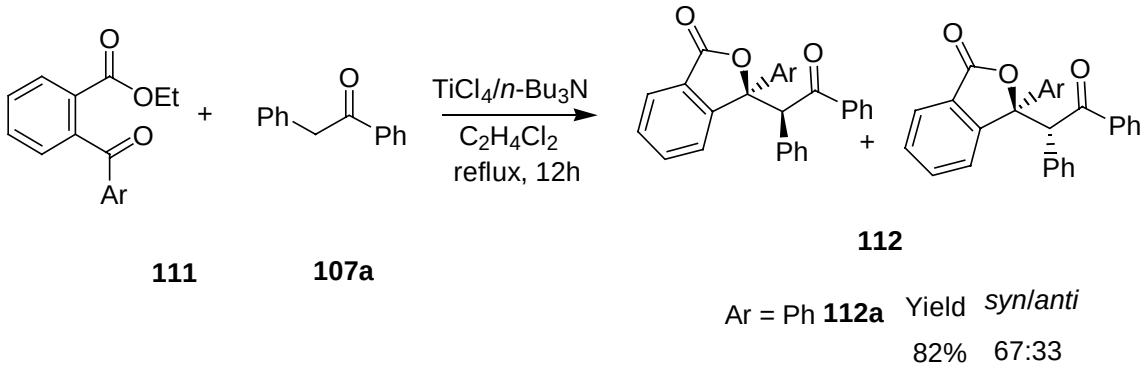
2.2.3 Reactions of titanium enolates with ethyl 2-benzoyl benzoates

2.2.3.1 Reaction of titanium enolates of ketones with ethyl 2-benzoylbenzoates: Synthesis of γ-lactones

It was of interest to us to examine the aldol reaction of ketones with γ-keto ester using the $TiCl_4/R_3N$ reagent system. We have examined the reaction of ethyl 2-benzoylbenzoates **111** with ketones **107** using the $TiCl_4/n\text{-}Bu_3N$ reagent system. In this case, corresponding γ-lactone **112** was obtained (Scheme 62). For example, ethyl 2-

benzoylbenzoate reacts with deoxybenzoin in 1,2-dichloroethane to produce the γ-lactones **112a** in 92% yield. The diastereomeric ratio of compound γ-lactones **112a** is 67:33 as determined by ^{1}H-NMR.

Scheme 62



111 **107a** **112**

Ar = Ph **112a**	Yield	*syn*/*anti*
	82%	67:33

The configuration of the major isomer of **112a** was found to be *syn* by X-ray crystal structure analysis.

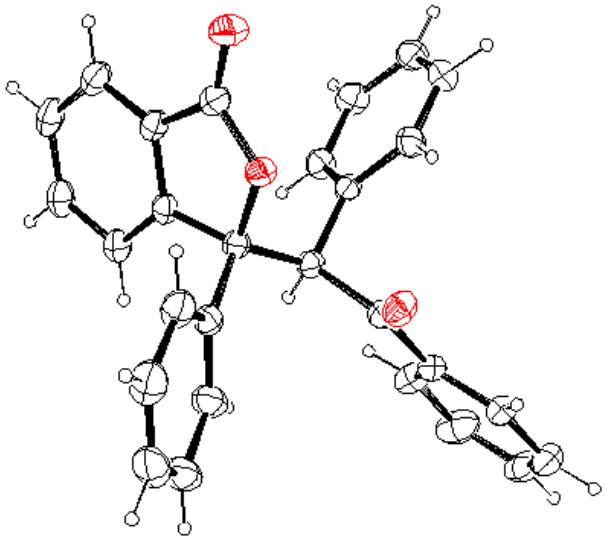


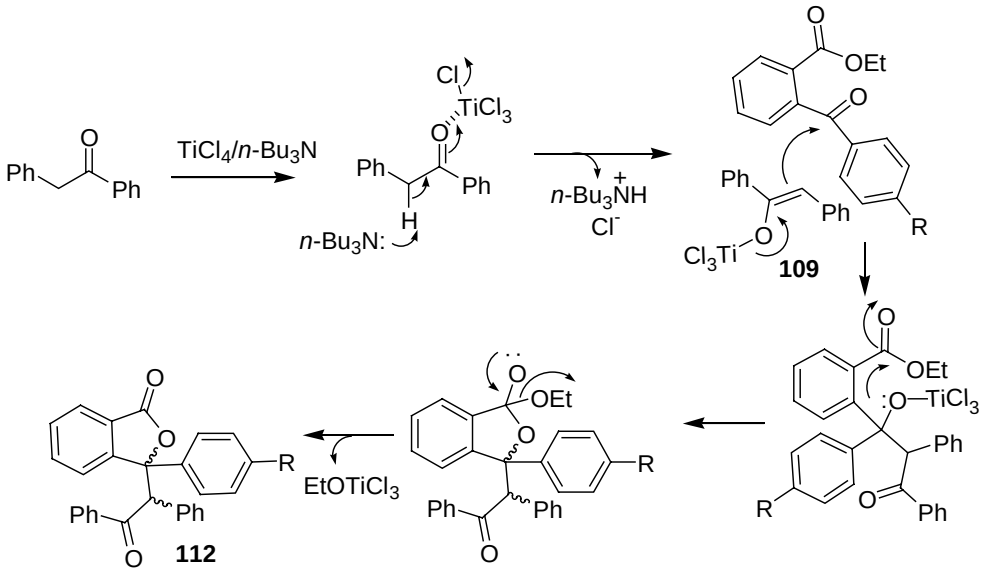
Fig 5. ORTEP diagram of compound **112a**

Table 6. Crystal data and structure refinement for **112a**

Empirical formula	$C_{28}\ H_{20}\ O_3$
Formula weight	404.44
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	Pbca
Unit cell dimensions	a = 12.9974(9) Å $\alpha=\beta=\gamma= 90°$.
	b = 16.4421(11) Å
	c = 20.1416(13) Å
Volume	4304.4(5) $Å^3$
Z	8
Density (calculated)	1.248 Mg/m^3
Absorption coefficient	0.080 mm^{-1}
F(000)	1696
Crystal size	0.32 x 0.22 x 0.20 mm^3
Theta range for data collection	2.02 to 26.03°.
Index ranges	-16<=h<=15, -20<=k<=20, -24<=l<=24
Reflections collected	42344
Independent reflections	4238 [R(int) = 0.0424]
Completeness to theta = 26.03°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.975 and 0.965
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4238 / 0 / 280
Goodness-of-fit on F^2	1.063
Final R indices [I>2sigma(I)]	R1 = 0.0519, wR2 = 0.1124
R indices (all data)	R1 = 0.0747, wR2 = 0.1232
Largest diff. peak and hole	0.147 and -0.135 $e.Å^{-3}$

The transformation can be rationalized by the mechanistic pathway involving the formation of titanium enolate of ketone **109** and its aldol reaction with the γ-keto esters followed by cyclization as outlined in scheme 63.

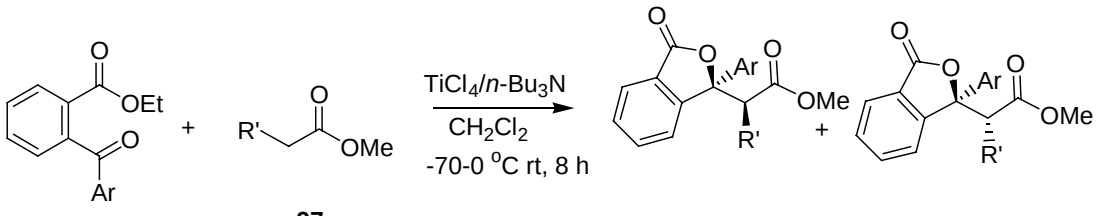
Scheme 63



2.2.3.2 Reaction of titanium enolates of esters with ethyl 2-benzoylbenzoates: Synthesis of γ-lactones

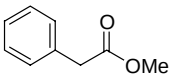
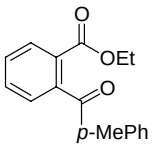
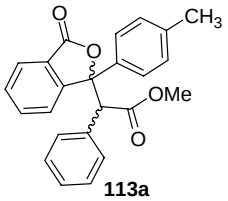
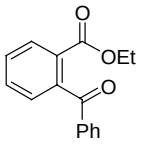
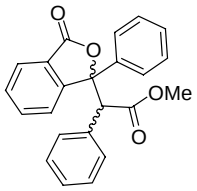
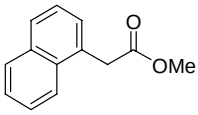
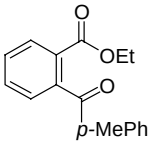
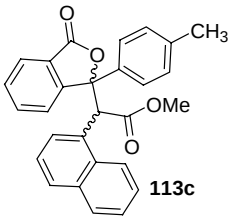
We have also examined the reaction of titanium enolates of arylaceticacid esters **97**. In this case, the γ-lactones **113** were isolated (Scheme 64). For example, ethyl 2-benzoylbenzoate reacts with methyl phenylacetate produced the corresponding γ-lactone **113b** in 92% yield. This transformation was found to be general for ethyl 2-benzoylbenzoates and esters using the $TiCl_4/Et_3N$ reagent system. The results are summarized in the Table 7.

Scheme 64



111 **97** **113**

Table 7: Reaction of ethyl 2-benzoylbenzoates with ester and $TiCl_4/Et_3N$.[a]

Entry	Ester	Substrate	T (°C)	Product[b]	Yield %[c]	dr %[d]
1			0-25	 **113a**	85	50:50
2	Ph		-40	**113a**	81	100:0[e]
3	Ph		-70	**113a**	76	100:0
4	Ph		0-25	 **113b**	92	52:48
5	Ph		-40	**113b**	74	73:27
6			0-25	 **113c**	78	53:47
7	1-Naphthyl		-40	**113c**	75	50:50

[a] The reactions were carried out using ethyl 2-benzoylbenzoates (5 mmol), ester (6 mmol), $TiCl_4$ (3.3 mL of 1:1 solution of $TiCl_4/CH_2Cl_2$) (12 mmol) and Et_3N (15mmol).

[b]The products were identified by ^1H, ^{13}C-NMR and mass spectral data.

[c]The isolated yields are based on the amount of keto ester used.

[d] The diastereomaric ratio of mixture are as determined by ^1H-NMR. The diastereomars could not be separated.

[e] The configuration was assigned as *syn* by X-ray crystal structure analysis.

It was found that the γ-lactones were obtained in higher yields at 0-25 °C (Table 8, entries 1,3 and 6) but the selectivity was better at -40 ^{o}C and –70 ^{o}C (Table 8, entries 2,4,5 and 7). The diastereomeric ratio of product **113a** formed at 0-25 ^{o}C was found to be 50:50, where as, at low temperatures –40 ^{o}C and –70 ^{o}C, it was identified as up to 100:0. Similarly, compound **113b** and **113c** gave higher selectivities 73:27 and 53:47 at –40 ^{o}C as determined by ^{1}H-NMR.

The product **113a** obtained in the case of entry 2 from Table 7 was identified by X-ray crystal structure analysis.

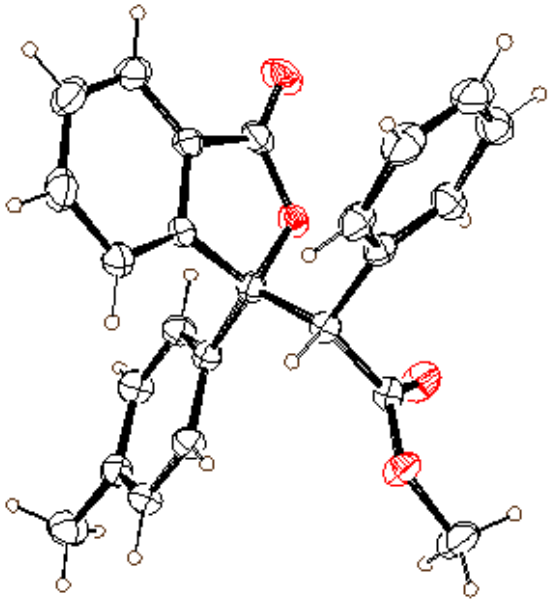


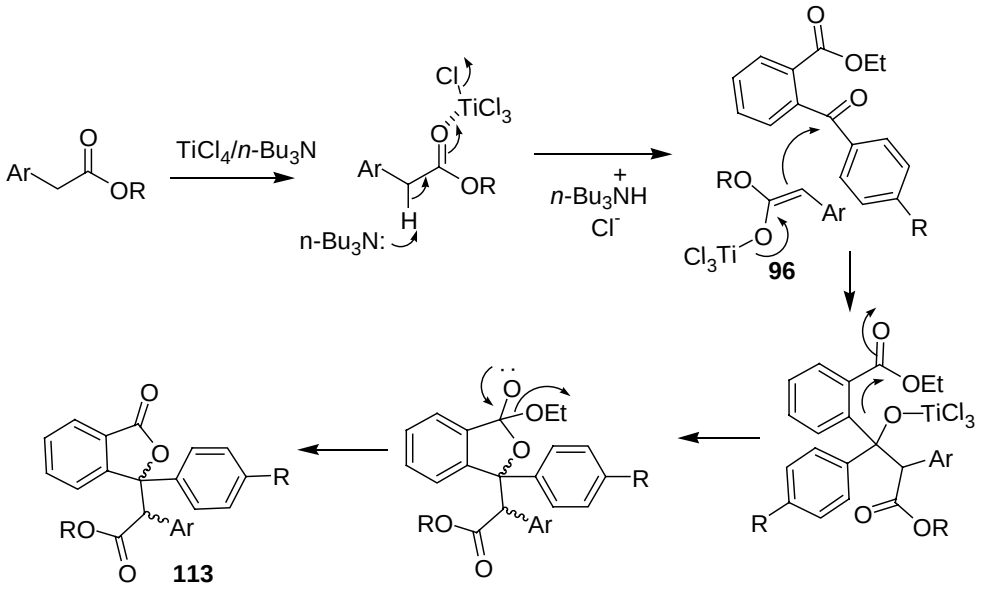
Fig 6: ORTEP diagram of compound **113a**

Table 8. Crystal data and structure refinement for **113a**

Empirical formula	$C_{24}H_{20}O_4$	
Formula weight	372.40	
Temperature	298(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/c	
Unit cell dimensions	a = 11.4052(14) Å	α = 90°.
	b = 10.6351(13) Å	β = 93.081(2)°.
	c = 16.450(2) Å	γ = 90°.
Volume	1992.4(4) $Å^3$	
Z	4	
Density (calculated)	1.241 Mg/m^3	
Absorption coefficient	0.084 mm^{-1}	
F(000)	784	
Crystal size	0.36 x 0.32 x 0.16 mm^3	
Theta range for data collection	1.79 to 26.01°.	
Index ranges	-14<=h<=14, -13<=k<=13, -19<=l<=20	
Reflections collected	14312	
Independent reflections	3915 [R(int) = 0.0289]	
Completeness to theta = 25.00°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9867 and 0.9204	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3915 / 0 / 255	
Goodness-of-fit on F^2	1.086	
Final R indices [I>2sigma(I)]	R1 = 0.0606, wR2 = 0.1294	
R indices (all data)	R1 = 0.0841, wR2 = 0.1408	
Largest diff. peak and hole	0.164 and -0.199 $e.Å^{-3}$	

This transformation can be rationalized by the mechanistic pathway involving formation of titanium enolate of ester **96** and its aldol reaction with the γ-keto esters followed by cyclization to give lactone **113** as shown in Scheme 65.

Scheme 65



In the present reaction of titanium enolates of ketones or esters with ethyl-2-benzoylbenzoates, *syn* and *anti* γ-lactone adducts can be obtained with both (*E*)- and (*Z*)-enolates. The *syn* stereoselectivty for the transformation can be tentatively explained on the basis of the stereochemical model shown in Figure 8. The results can be explained considering that the *E*-titanium ketone enolate would be in equilibrium with the *Z*-titanium ketone enolate. The reaction of the *E*-titanium ketone enolate would give a lower-energy transition state **TS-3** due to the lesser repulsions from the aryl group (X) leading to the major *syn* product. The *anti* product with *E*-titanium ketone enolate is not favored because it would give a higher-energy transition state **TS-4** due to greater repulsions from the large phenyl group (Ar).

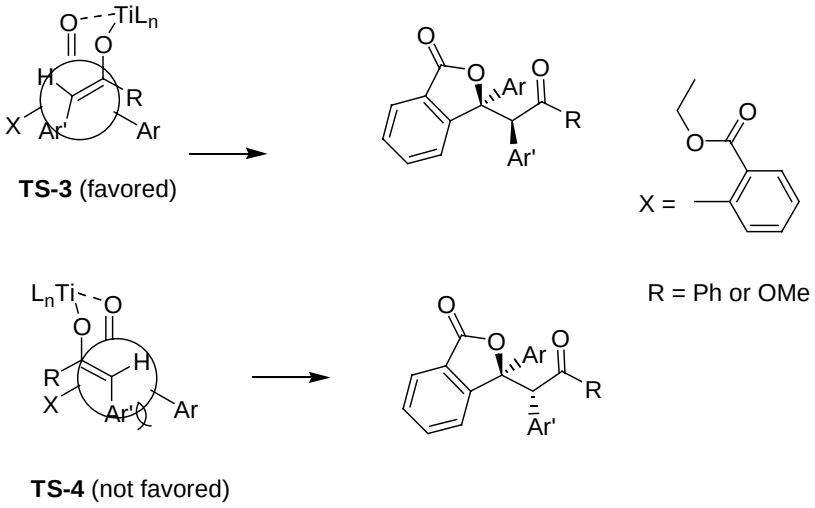


Fig 7: Stereochemical models

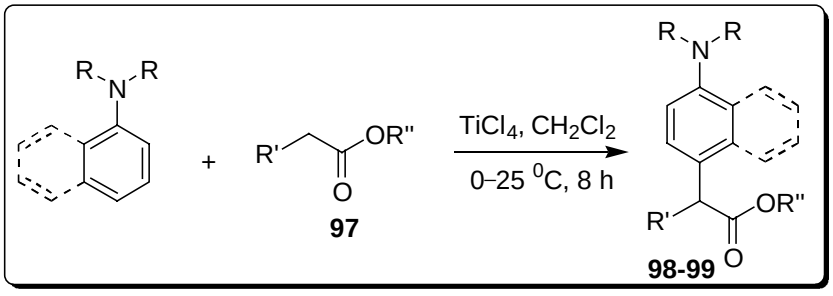
2. 3 Conclusions

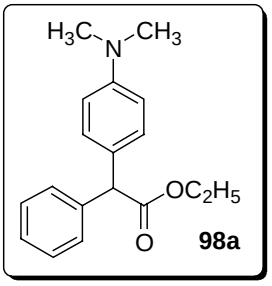
In conclusion, the aryltitanium species prepared *in situ* from *N*,*N*-dialkyl arylamines undergoes cross-coupling with titanium enolates of aryl acetic acid esters to give the corresponding α-diaryl acetic acid esters **98a-98i** and **99a-99c** in 55-90% yields. A simple and convenient method for the synthesis of maleic anhydrides **103a-103f** were achieved using the α-keto esters, alkanoic acid anhydrides and the $TiCl_4$/*n*-Bu_3N reagent system. Diphenylmaleic anhydride **106** was obtained in 95% yield by the reaction of phenylacetyl chloride and ethyl benzoylformate using the $TiCl_4$/*n*-Bu_3N reagent system. γ-Substituted γ-butenolides **108a-108e** with the diastereomeric ratio 0-100 were obtained in one step by the reaction of titanium enolates of ketones with α-keto esters, . The reaction of ethyl 2-benzoylbenzoates with ketones in the presence of the $TiCl_4$/*n*-Bu_3N reagent system gave the corresponding γ-lactone **112** with *syn*/*anti* ratio 67:33 in 82% yield. Also, ethyl 2-benzoylbenzoates react with titanium ester enolates prepared using the $TiCl_4$/Et_3N reagent system and esters to give γ-lactones **113a-113c** with diastereomeric ratio 0-100 in 74-92% yields.

2.4 Experimental Section

2.4.1 General procedure for the reaction of *N,N*-dialkylarylamines with arylacetic acid esters: α-Arylation of arylacetic acid esters

In CH_2Cl_2 (25 mL), *N,N*-dimethylaniline (1.2 mL, 7.5 mmol) and ethyl phenylacetate (0.35 ml, 2.1 mmol) were taken at 0 °C under N_2. The $TiCl_4$ (2.2 mL of 1:1 solution of $TiCl_4/CH_2Cl_2$, 10 mmol) in 10 mL CH_2Cl_2 was added drop wise for 5 minutes. The reaction mixture was stirred at 0 °C for 0.5 h and stirred further at 0-25 °C for 8 h. A saturated K_2CO_3 solution (10 mL) was added and stirred for 0.5 h. The reaction mixture was filtered through a Buchner funnel. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2×25 mL). The combined organic extract was washed with brine solution (10 mL) and dried over anhydrous $MgSO_4$. The solvent was removed and the residue was chromatographed on a silica gel column. The unreacted amine and *N,N,N',N'*-tetramethylbenzidine were eluted using 2:98 EtOAc/hexane mixture. The aminoester **98a** was next eluted.





Yield 0.52g (89%)[54]

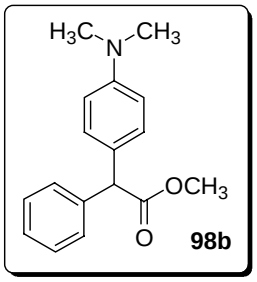
IR (Neat) (cm^{-1}) 2979, 2929, 2802, 1732, 1614, 1519, 1348, 1149, 721, 698

^{1}H-NMR (δ ppm, $CDCl_3$) 7.4-7.2 (m, 7H), 6.76 (d, J=8.8 Hz, 2H), 4.97 (s, 1H), 4.25 (q, J=7.2, 2H), 2.95 (s, 6H), 1.29 (t, J=7.2 Hz, 3H)

^{13}C-NMR (δ ppm, $CDCl_3$) 173.0, 149.8, 139.7, 129.3, 128.5, 128.5, 126.9, 126.8, 112.7, 60.9, 56.4, 40.6, 14.2

Analysis Calculated for $C_{18}H_{21}NO_2$: C, 76.29%; H, 7.49%; N, 4.94%

Found : C, 76.44%; H, 7.45%; N, 5.29%



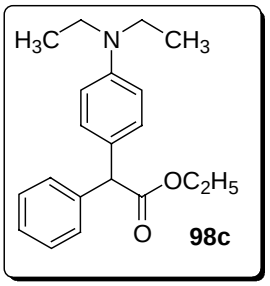
Yield 0.48 g (86%)

IR (Neat) (cm^{-1}) 2980, 2850, 2802, 1737, 1612, 1521, 1350, 1151, 719, 698

^{1}H-NMR (δ ppm, $CDCl_3$) 7.45-7.22 (m, 7H), 6.77 (d, J=8.8 Hz, 2H), 5.08 (s, 1H), 3.80 (s, 3H), 2.99 (s, 6H)

^{13}C-NMR (δ ppm, $CDCl_3$) 173.6, 149.9, 139.6, 129.4, 128.6, 127.4, 127.1, 126.5, 112.7, 56.3, 52.2, 40.6

MS (EI) m/z 269

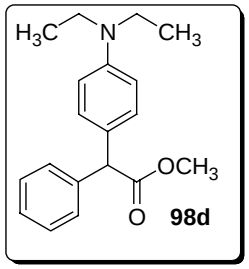


Yield 0.58 g (90%)

IR (Neat) (cm^{-1}) 2974, 2931, 2871, 1733, 1612, 1519, 1149, 698

^{1}H-NMR (δ ppm, $CDCl_3$) 7.4-7.15 (m, 7H), 6.66 (d, J=8.8 Hz, 2H), 4.92 (s, 1H), 4.22 (q, J=7.2 Hz, 2H), 3.35 (q, J=6.8 Hz, 4H), 1.28 (t, J=7.2 Hz, 3H), 1.17 (t, J=6.8 Hz, 6H) **(Spectrum No. 34)**

^{13}C-NMR (δ ppm, $CDCl_3$) 173.1, 147.0, 139.8, 129.5, 128.5, 128.4, 126.9, 125.5, 111.9, 60.9, 56.3, 44.4, 14.2, 12.6 **(Spectrum No. 35)**

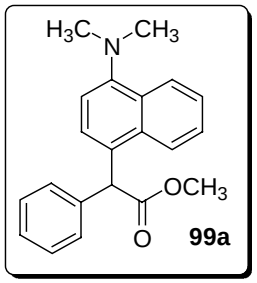


Yield 0.50 g (81%)

IR (Neat) (cm^{-1}) 2970, 2929, 2871, 1737, 1612, 1519, 1151, 806, 698

^{1}H-NMR (δ ppm, $CDCl_3$) 7.38-7.1 (m, 7H), 6.64 (d, J=8.8 Hz, 2H), 4.93 (s, 1H), 3.78 (s, 3H), 3.33 (q, J=7.2 Hz, 4H), 1.16 (t, J=7.2 Hz, 6H)

^{13}C-NMR (δ ppm, $CDCl_3$) 173.5, 147.1, 139.6, 129.5, 128.5, 128.5, 127.0, 125.2, 111.8, 56.2, 52.1, 44.3, 12.6



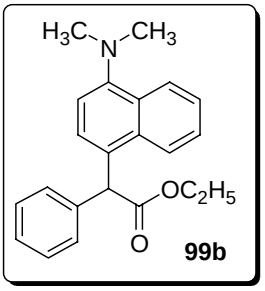
Yield 0.42 g (65%)

IR (Neat) (cm^{-1}) 2925, 2854, 2831, 1739, 1454, 1388, 1193, 1159, 769

^{1}H-NMR (δ ppm, $CDCl_3$) 8.38-7.23 (m, 10), 7.04 (d, J=8.8

Hz,1H), 5.75 (s, 1H), 3.78 (s, 3H), 2.90 (s, 6H)

^{13}C-NMR (δ ppm, $CDCl_3$) 173.5, 150.8, 138.3, 132.9, 129.3, 129.0, 128.6, 127.3, 126.3, 125.1, 124.9, 123.6, 113.5, 53.4, 52.4, 45.2 **(Spectrum No. 45)**



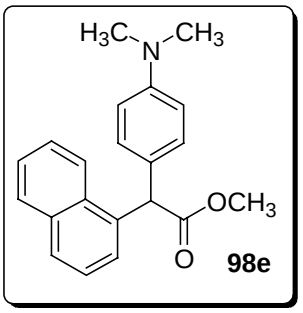
99b

Yield 0.52 g (76%)

IR (Neat) (cm^{-1}) 2935, 2860, 2829, 1735, 1454, 1390, 1172, 1147, 765, 700

^{1}H-NMR (δ ppm, $CDCl_3$) 8.38-7.25 (m, 10H), 7.08 (d, J=8.8 Hz, 1H), 5.73 (s, 1H), 4.26 (q, J=6.8 Hz, 2H), 2.90 (s, 6H), 1.27 (t, J=6.8 Hz, 3H)

^{13}C-NMR (δ ppm, $CDCl_3$) 173.0, 150.7, 138.4, 132.9, 129.3, 129.0, 128.6, 127.2, 126.3, 126.2, 125.0, 124.9, 123.6, 113.5, 61.2, 53.5, 45.2, 14.2 **(Spectrum No. 46)**



98e

Yield 0.42 g (65%)

mp 122-124 °C

IR (KBr) (cm^{-1}) 2949, 1737, 1612, 1521, 1352, 1191, 1061, 779

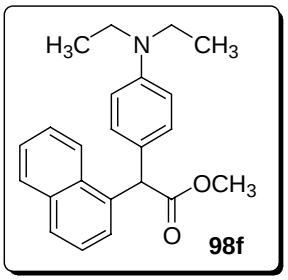
^{1}H-NMR (δ ppm, $CDCl_3$) 8.18-7.33 (m, 9H), 6.82 (d, J=8.8 Hz, 2H), 5.88 (s, 1H), 3.86 (s, 3H), 3.0 (s, 6H) **(Spectrum No. 36)**

^{13}C-NMR (δ ppm, $CDCl_3$) 173.9, 145.0, 135.5, 134.2, 131.9, 129.8, 129.1, 128.1, 126.6, 126.3, 125.7, 125.6, 123.5, 112.8, 53.0, 52.4, 40.6 **(Spectrum No. 37)**

MS (EI) m/z 319 **(Spectrum No. 38)**

` The structure **(98e)** was also confirmed by single crystal X-ray structure analysis)

Yield 0.54 g (76%)



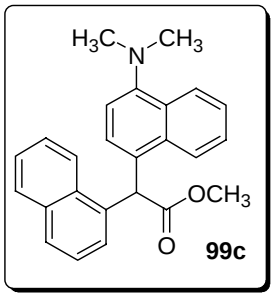
98f

IR (Neat) (cm^{-1}) 2970, 1735, 1610, 1517, 1353, 769

^{1}H-NMR (δ ppm, $CDCl_3$) 8.10-7.46 (m, 7H), 7.26 (d, J=8.4 Hz, 2H), 6.72 (d, J=8.8 Hz, 2H), 5.78 (s, 1H), 3.81 (s, 3H), 3.38 (q, J=7.2 Hz, 4H), 1.21 (t, J=7.2 Hz, 6H)

^{13}C-NMR (δ ppm, $CDCl_3$) 174.0, 147.2, 135.5, 134.1, 129.9, 129.0, 127.9, 126.5, 126.3, 125.6, 125.5, 124.4, 123.4, 112.0, 52.8, 52.3, 44.4, 12.7

Yield 0.52 g (68%)



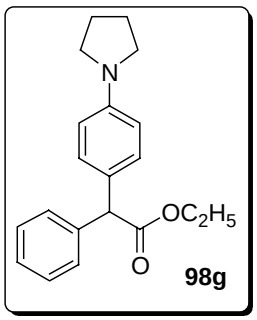
99c

IR (Neat) (cm^{-1}) 3062, 2925, 2854, 2385, 1741, 1581, 1450, 1390, 1190, 1157, 771

^{1}H-NMR (δ ppm, $CDCl_3$) 8.41-7.26 (m, 11H), 7.20 (d, J=8.8 Hz,1H), 7.00 (d, J=8.8 Hz,1H), 6.50 (s, 1H), 3.82 (s, 3H), 2.90 (s, 6H)

^{13}C-NMR (δ ppm, $CDCl_3$) 173.8, 150.8, 134.4, 134.1, 132.9, 131.8, 129.4, 129.0, 128.2, 127.7, 126.7, 125.7, 125.6, 125.2, 123.4, 123.1, 113.7, 52.5, 50.1, 45.3

Yield 0.37 g (62%)



98g

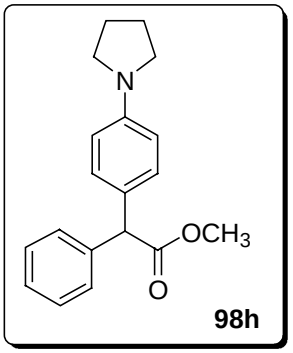
IR (Neat) (cm^{-1}) 2962, 2925, 2852, 1733, 1614, 1521, 1369, 1149, 692

^{1}H-NMR (δ ppm, $CDCl_3$) 7.6-7.2 (m, 7H), 6.54 (d, J=8.8 Hz, 2H), 4.93 (s, 1H), 4.21 (q, J=6.8 Hz, 2H), 3.27 (t, J=6.8 Hz, 4H), 2.25-1.92 (m, 4H), 1.28 (t, J=6.8 Hz, 3H) **(Spectrum No. 39)**

^{13}C-NMR (δ ppm, $CDCl_3$) 173.1, 147.1, 139.9, 129.4, 128.5, 128.4, 126.8, 60.9, 56.4, 47.7, 25.5, 14.2 **(Spectrum No. 40)**

Yield 0.39 g (61%)

IR (Neat) (cm^{-1}) 2949, 2839, 1737, 1614, 1521, 1375, 1151, 700



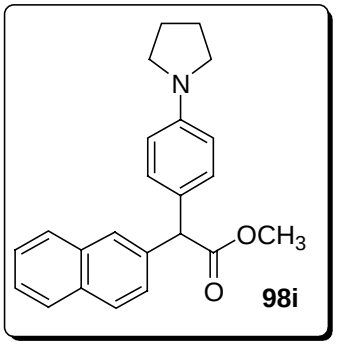
98h

^{1}H-NMR (δ ppm, $CDCl_3$) 7.40-7.10 (m, 7H), 6.65 (d, J=8.8 Hz, 2H), 4.97 (s, 1H), 3.75 (s, 6H), 3.28 (t, J=6.8 Hz, 4H), 2.25-1.95 (m, 4H) **(Spectrum No. 41)**

^{13}C-NMR (δ ppm, $CDCl_3$) 173.6, 147.1, 139.6, 129.4, 128.5, 126.9, 125.5, 111.4, 56.3, 52.1, 47.8, 25.5 **(Spectrum No. 42)**

Yield 0.28 g (55%)

IR (Neat) (cm^{-1}) 2925, 2923, 2850, 1735, 1612, 1519, 1163, 732



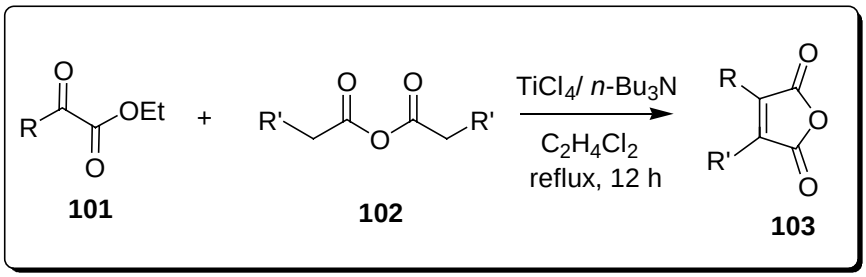
98i

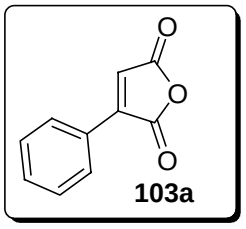
^{1}H-NMR (δ ppm, $CDCl_3$) 8.07-7.18 (m, 9H), 6.55 (d, J=8.8 Hz, 2H), 5.71 (s, 1H), 3.28 (t, J=6.8 Hz, 4H), 1.96-2.15 (m, 4H) **(Spectrum No. 43)**

^{13}C-NMR (δ ppm, $CDCl_3$) 173.8, 147.2, 135.4, 134.1, 131.9, 129.7, 128.9, 127.8, 126.3, 125.4, 123.3, 111.8, 52.9, 52.1, 47.7, 25.4 **(Spectrum No. 44)**

2.4.2 General procedure for the reaction of α-keto ester with alkanoic acid anhydrides using the $TiCl_4$/*n*-Bu_3N reagent system: Synthesis of substituted maleic anhydrides

Acetic anhydride (0.63 g, 2.5 mmol) and ethyl benzoylformate (0.96 g, 5 mmol) were taken in dichloroethane (25 mL) under N_2, and $TiCl_4$ (1.65 mL of 1:1 solution of $TiCl_4$-CH_2Cl_2, 7.5 mmol) was added at 0 °C followed by *N*,*N*,*N*-tributylamine (1.43 ml, 7.5 mmol). The contents were stirred at 0 °C for 10 min and then refluxed at 95-100 °C for 12 h. The mixture was brought to room temperature, saturated NH_4Cl solution (20 mL) was added and stirred for 0.5 h. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 25 mL). The combined organic extract was washed with 5N HCl (2 × 20 mL) to remove the unreacted amine, followed by water and brine solution (10 mL) and dried over anhydrous $MgSO_4$. The solvent was removed and the residue was chromatographed on a silica gel column. Unidentified less polar compounds and the unreacted ketone were eluted using 1:99 EtOAc/hexane mixture. The phenylmaleic anhydride **103a** (92%) was eluted using EtOAc/hexane (2:98) mixture.





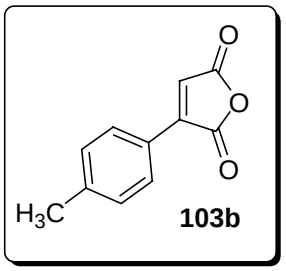
Yield 0.80 g (92%)

mp 117-118 (Lit [62g] 118-119) °C

IR (KBr) (cm^{-1}) 2966, 1766, 1724, 1606, 1514, 1248, 1028, 835, 738

^{1}H-NMR (δ ppm, $CDCl_3$) 7.96 (d, J=6.6 Hz, 2H), 7.72-7.40 (m, 3H), 7.00 (s, 1H) **(Spectrum No. 47)**

^{13}C-NMR (δ ppm, $CDCl_3$) 164.5, 163.6, 146.8, 132.7, 129.3, 129.0, 126.9, 124.5 **(Spectrum No. 48)**



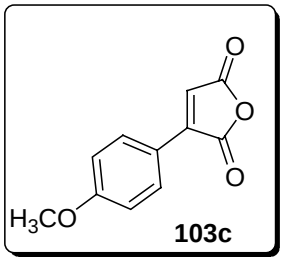
Yield 0.78 g (84%)

Mp 105-106 (Lit [62g] 106-108)°C

IR (KBr) (cm^{-1}) 3067, 2924, 1790, 1770, 1491, 1089, 831, 540

^{1}H-NMR (δ ppm, $CDCl_3$) 7.77 (d, J=8.0 Hz, 2H), 7.21 (d, J=8.0 Hz, 2H), 6.81 (s, 1H), 2.33 (s, 3H) **(Spectrum No. 49)**

^{13}C-NMR (δ ppm, $CDCl_3$) 164.6, 163.8, 146.6, 143.8, 130.1, 129.0, 124.2, 123.1, 21.6 **(Spectrum No. 50)**



103c

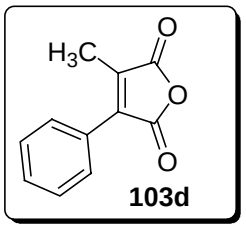
Yield 0.64 g (64%)

mp 141-143 (Lit [62g]142-143) °C

IR (KBr) (cm^{-1}) 3069, 2935, 1790, 1774, 1601, 1508, 1215, 831, 536

^{1}H-NMR (δ ppm, $CDCl_3$) 7.89 (d, J=8.2 Hz, 2H), 6.90 (d, J=8.2 Hz, 2H), 3.80 (s, 3H)

^{13}C-NMR (δ ppm, $CDCl_3$) 165.2, 163.3, 159.2, 146.4, 131.1, 128.6, 121.0, 114.9, 55.8



103d

Yield 0.76 g (81%)

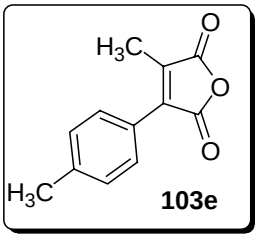
mp 98-100 °C

IR (KBr) (cm^{-1}) 2962, 2876, 1844, 1768, 1726, 1450, 1201, 916, 702

^{1}H-NMR (δ ppm, $CDCl_3$) 7.72-7.45 (m, 5H), 2.31 (s, 3H) **(Spectrum No. 51)**

^{13}C-NMR (δ ppm, $CDCl_3$) 166.1, 164.8, 139.9, 138.7, 130.9, 129.4, 128.9, 127.5, 10.7 **(Spectrum No. 52)**

MS (EI) m/z 188 (M^+, 62%) **(Spectrum No. 53)**



103e

Yield 0.76 g (76%)

mp 108-110 °C

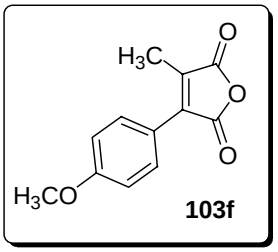
IR (KBr) (cm^{-1}) 2976, 2926, 1844, 1817, 1766, 1728, 1273, 1176, 920, 825, 734

^{1}H-NMR (δ ppm, $CDCl_3$) 7.57 (d, J=8.0 Hz, 2H), 7.32 (d, J=8.4 Hz, 2H), 2.42 (s, 3H), 2.30 (s, 3H)

^{13}C-NMR (δ ppm, $CDCl_3$) 166.4, 165.1, 141.7, 139.9, 137.657, 129.7, 129.4, 128.7, 21.5, 10.9

MS (EI) m/z 202 (M^+, 64%)

Yield 0.62 g (62%)



103f

mp 119-120 °C

IR (KBr) (cm^{-1}) 3059, 2916, 1786, 1450, 1371, 1105, 758, 731

^{1}H-NMR (δ ppm, $CDCl_3$) 7.68 (d, J=8.8 Hz, 2H), 6.92 (d, J=8.8 Hz, 2H), 3.87 (s, 3H), 2.29 (s, 3H)

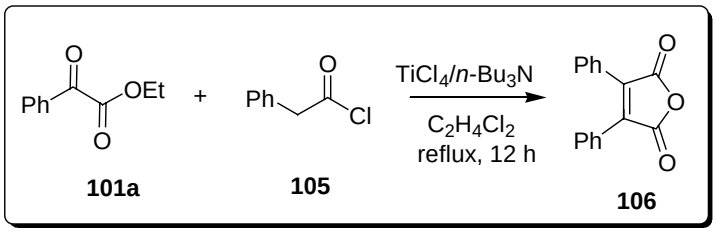
^{13}C-NMR (δ ppm, $CDCl_3$) 166.5, 164.7, 161.8, 139.7, 136.5 131.4, 128.9, 114.5, 55.5, 10.9

MS (EI) m/z 218 (M^+, 74%)

2.4.3 General procedure for the reaction of α-keto ester with phenylacetyl chloride using the $TiCl_4$/*n*-Bu_3N reagent system

Phenylacetyl chloride (0.66 mL, 5 mmol) and ethyl benzoylformate (0.36 mL, 2.5 mmol) were taken in dichloroethane (25 mL) under N_2, and $TiCl_4$ (1.65 mL of 1:1 solution of $TiCl_4$-CH_2Cl_2, 7.5 mmol) was added at 0 °C followed by *N*,*N*,*N*-tributylamine (1.43 mL, 7.5 mmol). The contents were stirred at 0 °C for 10 min and then refluxed at 95-

100 °C for 12 h. The mixture was brought to room temperature, saturated NH_4Cl solution (20 mL) was added and stirred for 0.5 h. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2×25 mL). The combined organic extract was washed with 5N HCl (2×20 mL) to remove the unreacted amine, followed by water and brine solution (10 mL) and dried over anhydrous $MgSO_4$. The solvent was removed and the residue was chromatographed on a silica gel column. The diphenylmaleic anhydride **106** was eluted using EtOAc/hexane (2:98) mixture.

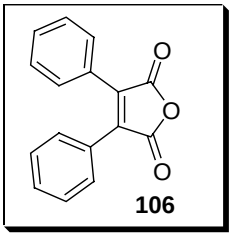


Yield 1.1 g (95%)

mp 157-159 °C (Lit[66] 159-162 °C)

IR (KBr) (cm^{-1}) 3063, 1822, 1757, 1637, 1352, 1273, 698

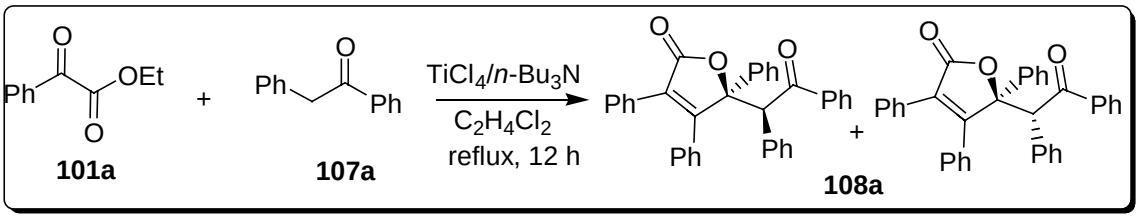
^{1}H-NMR (δ ppm, $CDCl_3$) 7.55-7.25 (m, 10H) **(Spectrum No. 54)**



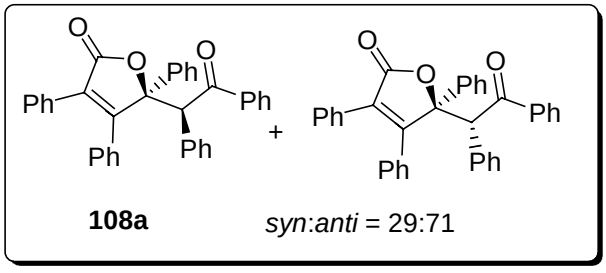
^{13}C-NMR (δ ppm, $CDCl_3$) 164.8, 138.1, 131.1, 129.7, 128.9, 127.1 **(Spectrum No. 55)**

2.4.4 General procedure for the reaction of α-keto esters with ketones using the $TiCl_4$/*n*-Bu_3N reagent system: Synthesis of γ-substituted γ-butenolides

Deoxybenzoin (0.49 g, 2.5 mmol) and ethyl benzoylformate (0.18 ml, 1.25 mmol) were taken in dichloroethane (20 mL) under N_2, and $TiCl_4$ (1.65 mL of 1:1 solution of $TiCl_4$-CH_2Cl_2, 7.5 mmol) was added at 0 °C followed by *N*,*N*,*N*-tributylamine (1.43 ml, 7.5 mmol). The contents were stirred at 0 °C for 10 min and then refluxed at 95-100 °C for 12 h. The mixture was brought to room temperature, saturated NH_4Cl solution (20 mL) was added and stirred for 0.5 h. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 25 mL). The combined organic extract was washed with 5N HCl (2 × 20 mL) to remove the amine, followed by water and brine solution (10 mL) and dried over anhydrous $MgSO_4$. The solvent was removed and the residue was chromatographed on a silica gel column. Unidentified less polar compounds and the unreacted ketone were eluted using 1:99 EtOAc/hexane mixture. The butenolide **108a** was eluted using EtOAc/hexane (10:90) mixture.



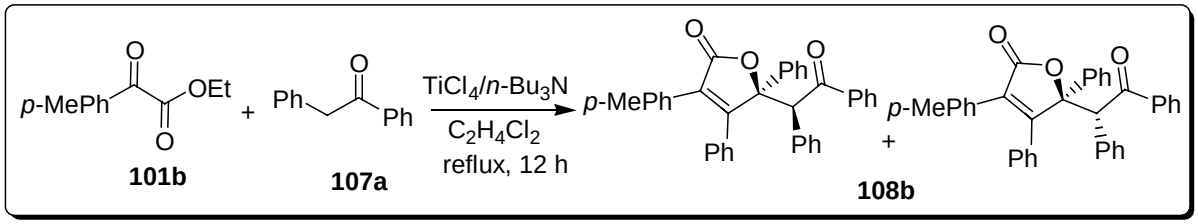
Yield	0.9 g (82%)
mp	216-218 °C
IR (KBr)	(cm^{-1}) 3059, 2924, 1761,



1685, 1597, 1514, 1493, 1448, 1346, 1248, 1174, 1076, 991, 827, 702, 652

^{1}H-NMR (δ ppm, $CDCl_3$) 7.83-6.61 (m, 25H), 5.62 (s, 1H), 5.45 (s, 1H) **(Spectrum No. 56)**

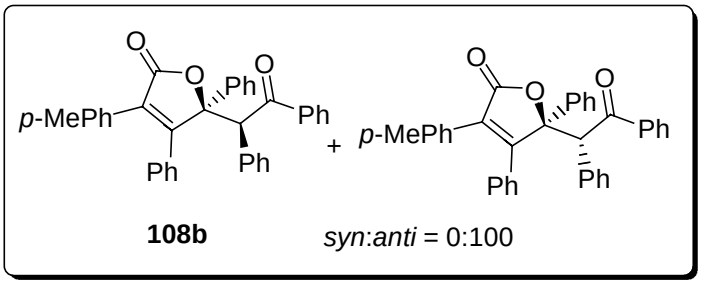
^{13}C-NMR (δ ppm, $CDCl_3$) 194.9, 193.1, 170.9, 170.8, 161.1, 160.1, 136.0, 135.8, 132.0, 131.9, 131.4, 131.1, 130.5, 130.2, 128.7, 128.5, 128.4, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.7, 127.6, 127.5 127.4, 127.4, 127.3, 127.2, 127.1, 127.1, 127.0, 126.7 125.5, 125.2, 89.0, 89.0, 55.6, 54.1 **(Spectrum No. 57)**



Yield 1.0 g (84%)

mp 197-199 °C

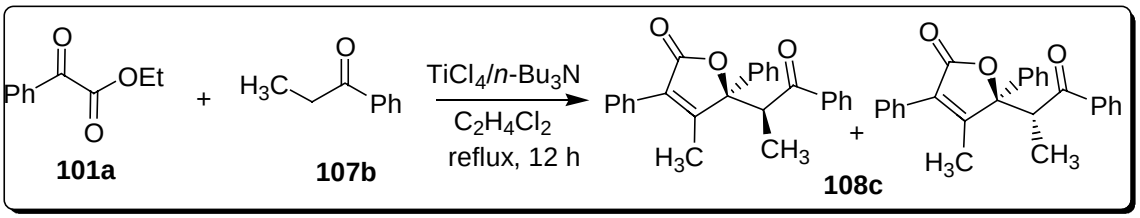
IR (KBr) (cm^{-1}) 3063, 1718, 1660, 1599, 1543, 1496, 1442, 1319, 1251, 1176, 1076, 1030, 964, 904, 754, 694



^{1}H-NMR (δ ppm, $CDCl_3$) 7.82-6.59 (m, 19H), 5.66 (s, 1H), 2.22 (s, 3H) **(Spectrum No. 58)**

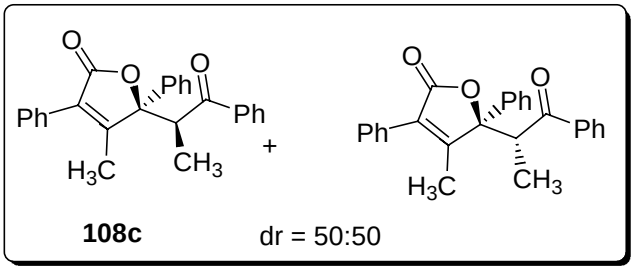
^{13}C-NMR (δ ppm, $CDCl_3$) 194.3, 172.2, 161.4, 138.3, 137.0, 133.0, 131.6, 131.4, 131.2, 129.6, 129.5, 129.4, 129.3, 129.2, 129.0, 128.9, 128.8, 128.8, 128.7, 128.6, 128.5, 128.5, 128.4, 126.5, 126.0, 90.0, 56.6, 21.4 **(Spectrum No. 59)**

(The structure was also confirmed by single crystal X-ray structure analysis)



Yield 0.7 g (78%)

IR (neat) (cm^{-1}) 3053, 2916, 1770, 1664, 1606, 1466, 1282, 1086, 943, 702

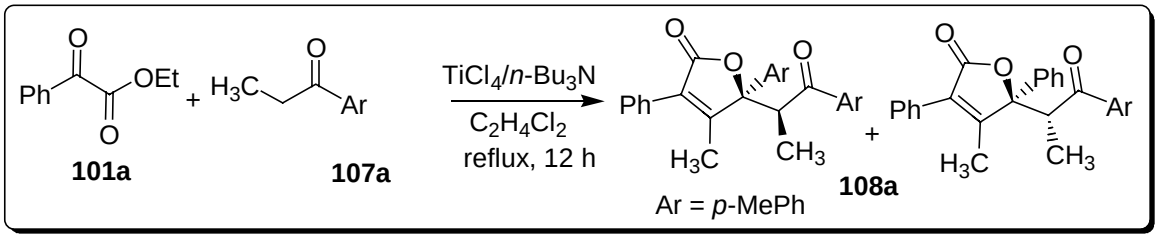


^{1}H-NMR (δ ppm, $CDCl_3$) 7.93-7.20 (m, 15H), 4.73 (q, J=6.8 Hz, 1H), 4.60 (q, J=6.8 Hz, 1H), 2.18 (s, 3H), 1.85 (s, 3H), 1.40 (d, J=6.8 Hz, 3H), 1.29 (d, J=6.8 Hz, 3H) **(Spectrum No. 60)**

^{13}C-NMR (δ ppm, $CDCl_3$) 199.7, 198.8, 172.3, 172.0, 162.7, 162.4, 138.1, 137.6, 137.0, 133.4, 133.2, 129.2, 129.1, 129.1, 129.0, 128.9, 128.8, 128.7, 128.5, 128.5, 128.4, 128.2, 128.1, 125.9, 125.3, 125.0, 90.3, 44.6, 44.1, 13.8, 13.3, 13.1, 12.9 **(Spectrum No. 61)**

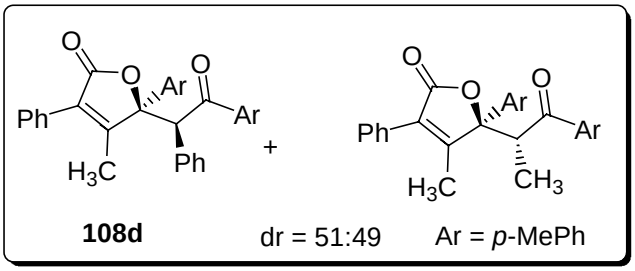
Analysis Calculated for $C_{26}H_{22}O_3$: C, 81.65%; H, 5.80%

Found : C, 81.72%; H, 5.83%



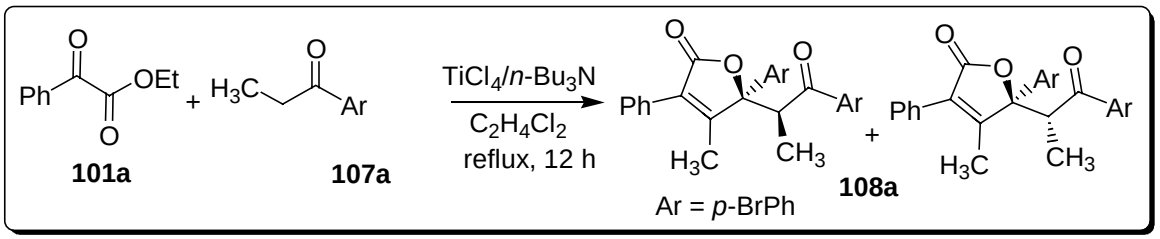
Yield 0.6 g (61%)

IR (neat) (cm^{-1}) 3059, 2928, 2854, 1751, 1687, 1597, 1494, 1448, 1381, 1350, 1265, 1188, 1080, 979, 700



^{1}H-NMR (δ ppm, $CDCl_3$) 7.93-7.16 (m, 15H), 4.73 (q, J=6.8 Hz, 1H), 4.60 (q, J=6.8 Hz, 1H), 2.37 (s, 3H), 2.32 (s, 3H), 2.17 (s, 3H), 1.84 (s, 3H), 1.39 (d, J=6.8 Hz, 3H), 1.29 (d, J=6.8 Hz, 3H)

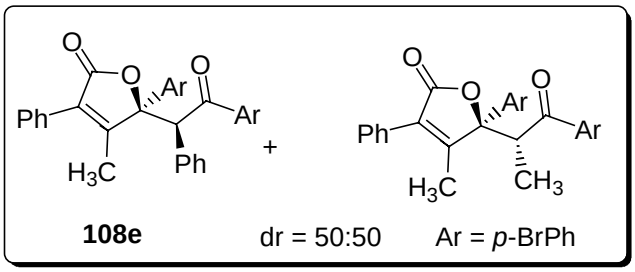
^{13}C-NMR (δ ppm, $CDCl_3$) 199.7, 198.8, 172.4, 172.0, 161.9, 160.5, 138.6, 138.3, 138.3, 137.7, 137.6, 133.3, 133.1, 129.2, 129.1, 129.0, 128.9, 128.9, 128.8, 128.8, 128.4, 128.2, 128.2, 128.1, 126.9, 126.9, 125.3, 125.0, 90.2, 90.2, 44.6, 44.2, 21.4, 21.3, 13.7, 13.3, 13.1, 12.6



Yield 1 g (78 %)

mp 124-126 °C

IR (KBr) (cm^{-1}) 2924, 1751, 1685, 1581, 1491, 1396, 1195, 1070, 695



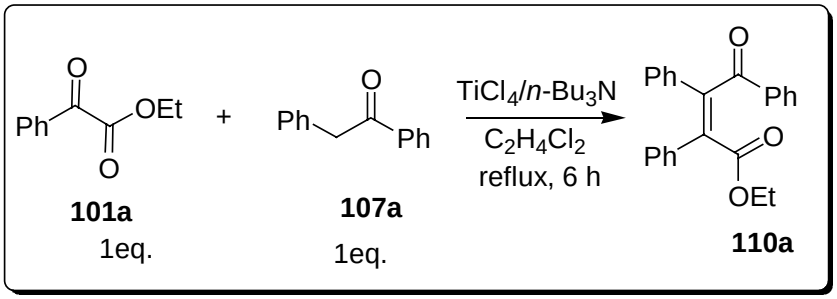
^{1}H-NMR (δ ppm, $CDCl_3$) 7.85-7.22 (m, 13H), 4.54 (q, J=6.8 Hz, 1H), 4.12(q, J=6.8 Hz, 1H), 2.16 (s, 3H), 2.04 (s, 3H), 1.29 (d, J=6.8 Hz, 3H), 1.25 (d, J=6.8 Hz, 3H)

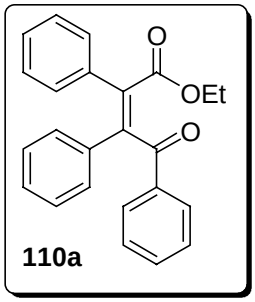
^{13}C-NMR (δ ppm, $CDCl_3$) 198.3, 198.1, 171.5, 169.8, 160.3, 159.8, 150.5, 139.2, 136.8, 135.8, 133.8, 132.3, 131.9, 131.6, 130.2, 129.7, 129.3, 129.1, 129.0, 128.7, 128.3, 128.2, 127.7, 127.1, 126.1, 125.6, 125.2, 122.8, 89.8, 88.6, 52.1, 13.8, 13.1, 11.7, 11.6

2.4.5 Procedure for the reaction of α-keto ester with ketone using the $TiCl_4$/*n*-Bu_3N reagent system: Synthesis of γ-keto ester

Deoxybenzoin (0.49 g, 2.5 mmol) and ethyl benzoylformate (0.375 ml, 2.5 mmol) were taken in dichloroethane (25 mL) under N_2, and $TiCl_4$ (1.65 mL of 1:1 solution of $TiCl_4$-CH_2Cl_2, 7.5 mmol) was added at 0 °C followed by *N*,*N*,*N*-tributylamine (1.43 ml, 7.5 mmol).

The contents were stirred at 0 °C for 10 min and then refluxed at 95-100 °C for 6 h. The mixture was brought to room temperature, saturated NH_4Cl solution (20 mL) was added and stirred for 0.5 h. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 25 mL). The combined organic extract was washed with 5N HCl (2 × 20 mL) to remove the amine, followed by water and brine solution (10 mL) and dried over anhydrous $MgSO_4$. The solvent was removed and the residue was chromatographed on a silica gel column. Unidentified less polar compounds and the unreacted ketone were eluted using 1:99 EtOAc/hexane mixture. The γ-keto ester **110a** was eluted using EtOAc/hexane (5:95) mixture.





Yield 0.8 g (92%)

mp 121-123 °C

IR (KBr) (cm^{-1}) 3053, 2976, 1720, 1672, 1610, 1520, 1448, 1267, 1064, 1020, 700

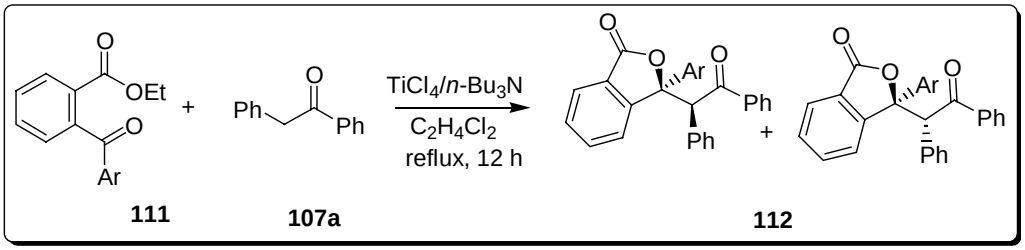
^{1}H-NMR (δ ppm, $CDCl_3$) 8.03-7.11 (m, 15H), 4.05 (q, J=7.2 Hz, 2H), 1.0 (t, J=7.2 Hz, 3H) **(Spectrum No. 62)**

^{13}C-NMR (δ ppm, $CDCl_3$) 195.9, 167.1, 150.6, 136.0, 135.1, 134.8, 133.7, 133.1, 130.7, 129.3, 129.3, 129.1, 128.8, 128.6, 128.5, 128.4, 128.1, 127.9, 61.6, 13.6 **(Spectrum No. 63)**

(The structure was also confirmed by single crystal X-ray structure analysis)

2.4.6 General procedure for the reaction of ethyl 2-benzoylbenzoate with ketone in the presence of the $TiCl_4$ *In*Bu_3N regent system: Synthesis of γ-lactones

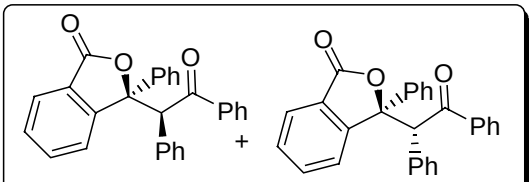
Ethyl 2-benzoyl benzoate (0.63 g, 2.5 mmol) and deoxybenzoin (0.96 g, 5 mmol) were taken in dichloroethane (25 mL) under N_2, $TiCl_4$ (1.65 mL of 1:1 solution of $TiCl_4/CH_2Cl_2$, 7.5 mmol) was added at 0 °C followed by *N*,*N*,*N*-tributylamine (1.43 mL, 7.5 mmol). It was stirred at 0 °C for 10 minutes and then refluxed at 95-100 °C for 6 h. The contents were brought to room temperature, then saturated NH_4Cl solution (20 mL) was added and stirred for 0.5 h. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 25 mL). The combined organic extract was washed with 5N HCl (2×20 mL) to remove the unreacted amine, followed by water and brine solution (10 mL) and dried over anhydrous $MgSO_4$. The solvent was removed and the residue was chromatographed on a silica gel column. The γ-lactone **112** was eluted using 8:92 EtOAc/hexane mixture.



111 **107a** **112**

Yield 0.92 g (92%)

mp 188-190 °C



112a *syn*/*anti* = 67:33

IR (KBr) (cm^{-1}) 3061, 2926, 1749, 1684, 1597, 1494, 1448, 1261, 1097, 974, 873, 700, 640

^{1}H-NMR (δ ppm, $CDCl_3$) 8.49-7.06 (m, 19H), 5.92 (s, 1H), 5.82 (s, 1H) **(Spectrum No. 64)**

^{13}C-NMR (δ ppm, $CDCl_3$) 196.6, 195.1, 169.7, 169.0, 151.2, 148.7, 138.9, 133.5, 133.2, 130.7, 130.3, 129.3, 128.7, 128.6, 128.6, 128.5, 128.5, 128.4, 128.3, 128.0, 126.7, 126.4, 125.3, 125.3, 91.4, 89.3, 62.0, 61.5 **(Spectrum No. 65)**

MS(EI) m/z 404

(The major product *syn* **112a** was also characterized by single crystal X-ray structure analysis)

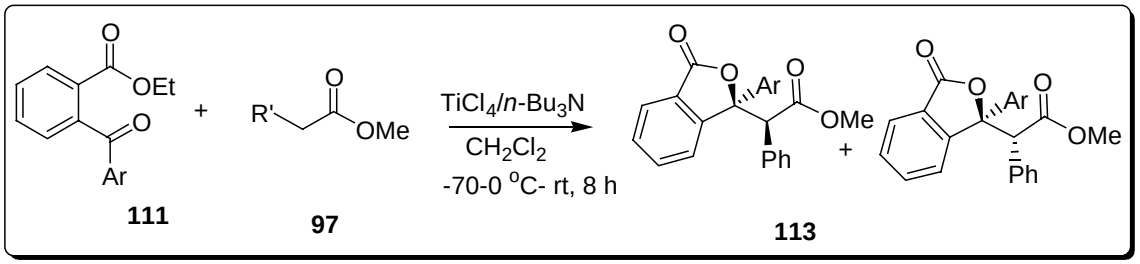
Analysis Calculated for $C_{28}H_{20}O_3$: C, 83.15%; H, 4.98%

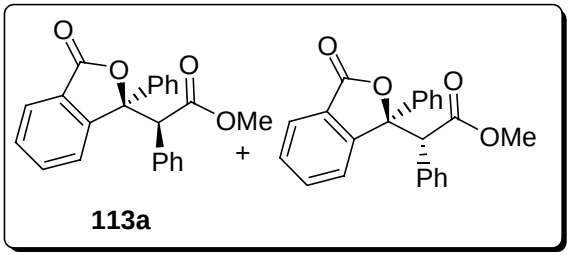
Found : C, 83.16%; H, 5.06%

2.4.7 General procedure for the reaction of ethyl 2-benzoylbenzoates with ester using the $TiCl_4/Et_3N$ reagent system: Synthesis of γ-lactones

In dichloromethane (25 mL), ethyl 2-benzoylbenzoate (0.63 mL, 2.5 mmol) and methyl phenylacetate (0.47 ml, 3 mmol) were taken under N_2. The $TiCl_4$ (2.2 mL of 1:1 solution of $TiCl_4/CH_2Cl_2$, 12 mmol) was added and mixture was stirred for 15 min, then added Et_3N (1.4 ml, 15mmol). The reaction mixture was stirred further 8 h. It was brought to 0 ^{o}C and a saturated NH_4Cl solution (10 mL) was added and the contents were stirred for 0.5 h. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2×

25 mL). The combined organic extract was washed with water (10 ml), brine solution (10 mL) and dried over anhydrous Na_2SO_4. The solvent was evaporated and the residue was chromatographed on a silica gel column. The γ-lactone **113b** (85% yield) was collected using EtOAc/hexane (5:95) mixture as eluent.





Yield 0.81g (92%), dr 52:48

mp 176-178 °C

IR (KBr) (cm^{-1}) 3055, 2949, 1768, 1743, 1599, 1466, 1199, 1089, 976, 731, 700

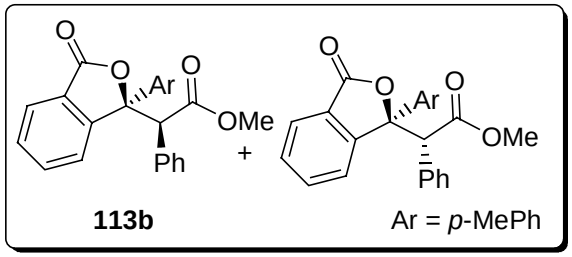
^{1}H-NMR (δ ppm, $CDCl_3$) 8.21-7.11 (m, 14H), 4.82 (s, 1H), 4.80 (s, 1H), 3.50 (s, 3H), 3.41 (s, 3H) **(Spectrum No. 66)**

^{13}C-NMR (δ ppm, $CDCl_3$) 170.2, 169.7, 150.4, 149.2, 139.3, 138.4, 133.7, 131.6, 130.2, 130.1, 129.5, 129.2, 128.7, 128.5, 128.3, 126.0, 125.6, 125.5, 125.1, 124.7, 122.9, 89.4, 88.6, 60.3, 60.0, 52.1, 52.0 **(Spectrum No. 67)**

MS (EI) m/z 358

Analysis Calculated for $C_{23}H_{18}O_4$: C, 77.08%; H, 5.06%

Found : C, 77.07%; H, 5.08%



Yield 0.69 g (76%), dr 50:50

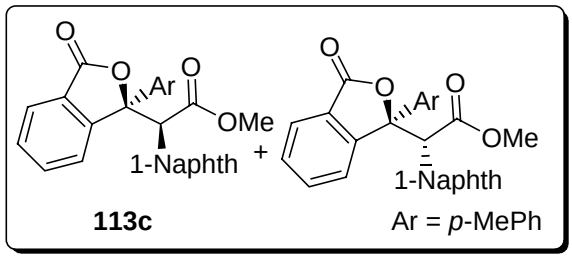
mp 160-162 °C

IR (KBr) (cm^{-1}) 3028, 2949, 1770, 1743, 1602, 1510, 1466, 1356, 1288, 1259, 1192, 1086, 760, 734, 692

^{1}H-NMR (δ ppm, $CDCl_3$) 8.22-7.11 (m, 13H), 4.78 (s, 1H), 3.53 (s, 3H), 3.43 (s, 3H), 2.33 (s, 3H), 2.29 (s, 3H)

^{13}C-NMR (δ ppm, $CDCl_3$) 170.4, 169.8, 150.6, 149.3, 138.3, 136.2, 133.7, 133.7, 131.59, 130.2, 130.1, 129.4, 129.2, 128.2, 128.1, 128.1, 128.0, 126.0, 125.6, 125.5, 125.0, 124.8, 122.8, 89.5, 88.6, 60.1, 59.9, 52.2, 52.1, 21.1

(The product was also characterized by single crystal X-ray structure analysis)



Yield 0.75 g (75%), dr 50:50

mp 161-163 °C

IR (KBr) (cm^{-1}) 3028, 2949, 1770, 1743, 1466, 1356, 1192, 1086, 815, 761, 734, 692

^{1}H-NMR (δ ppm, $CDCl_3$) 8.24-7.00 (m, 15H), 4.97 (s, 1H), 3.52 (s, 3H), 3.39 (s, 3H), 2.31 (s, 3H) **(Spectrum No. 68)**

^{13}C-NMR (δ ppm, $CDCl_3$) 170.6, 170.2, 169.7, 168.9, 150.4, 150.1, 138.3, 138.2, 133.8, 129.4, 129.2, 129.1, 129.0, 128.9, 128.9, 128.8, 126.6, 126.1, 125.8, 125.6, 125.2, 125.0, 124.9, 124.7, 123.2, 90.1, 88.7, 53.7, 53.5, 52.2, 52.2

(Spectrum No. 69)

Analysis Calculated for $C_{28}H_{22}O_4$: C, 79.60%; H, 5.25%

Found : C, 79.67%; H, 5.25%

2.5 References

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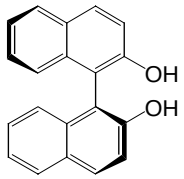
Chapter 3

Efforts Towards the Synthesis of Poly-1,1'-Bi-2-naphthyl Derivatives Containing Pyrrole Spacers

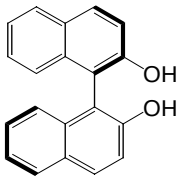
3.1 Introduction

The 2,2'-substituted 1,1'-binaphthyl derivatives exhibit outstanding chiral discrimination properties due to their highly stable chiral configuration. Reagents containing the binaphthyl moiety have been extensively used in many asymmetric syntheses.[1] The rigid structure and the C_2-symmetry of the chiral binaphthyl moiety play an important role in chiral induction. Asymmetric hydrogenation, hetero-Diels-Alder reaction, Claisen rearrangement and aldol condensation are some of the reactions in which optically active monomeric binaphthyl molecules have been used as asymmetric catalysts.[2]

The 1,1'-bi-2-naphthol (BINOL) **1**, often serve as the starting material for obtaining chiral binaphthyl derivatives. The 2,2'-hydroxyl groups of BINOL can be readily converted into other functional groups.



1
(*S*)-(-)



1
(*R*)-(+)

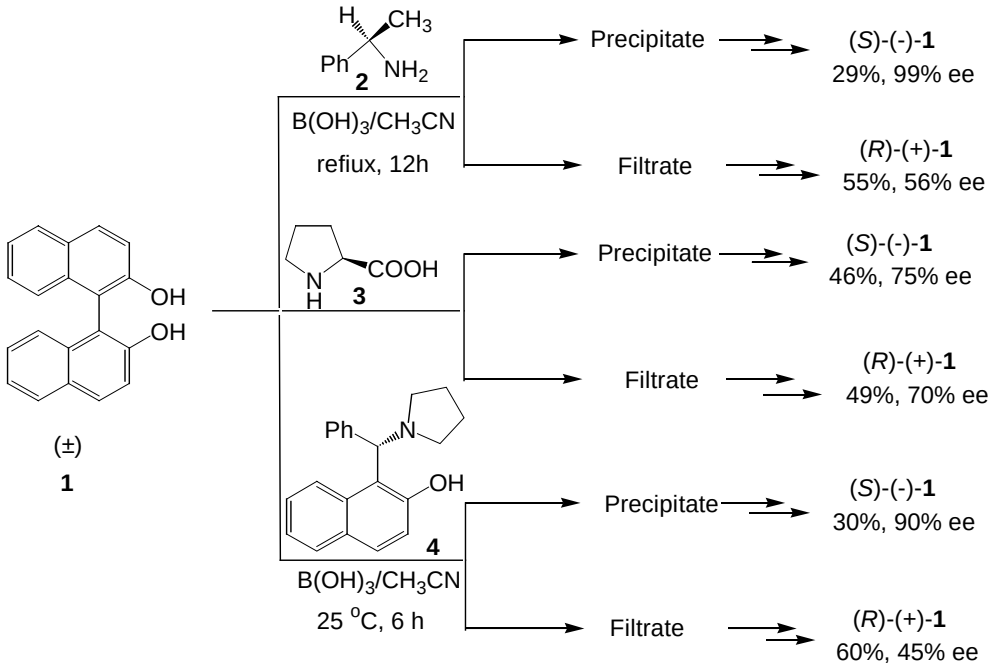
In addition, the 3,3', 4,4'and 6,6'-positions can be selectively functionalized to obtain a variety of binaphthyl derivatives. Also, molecules and polymers with unique structures and properties have been synthesized.[3]

3.1.1 Previous reports on 1,1'-bi-2-naphthol from this laboratory

As a part of research interests of this laboratory, methods have been developed to easily access chiral 1,1'-bi-2-naphthol in optically pure form.

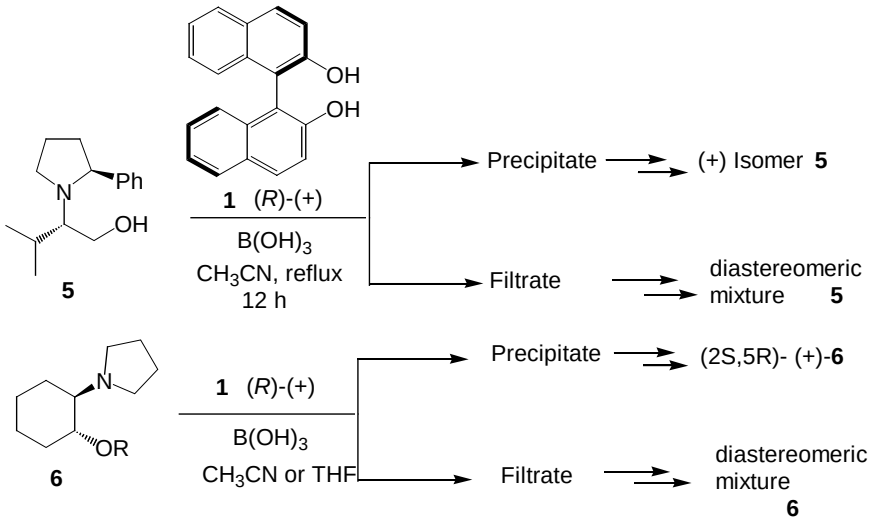
For example, the racemic 1,1'-bi-2-naphthol **1** was resolved using boric acid and (*R*)-(+)-α-methylbenzylamine **2** as well as (*S*)-proline **3** in this laboratory.[4] Very recently, racemic BINOL was resolved with (*S*)-amino naphthol **4** and boric acid in CH_3CN solvent (Scheme 1).[5]

Scheme 1



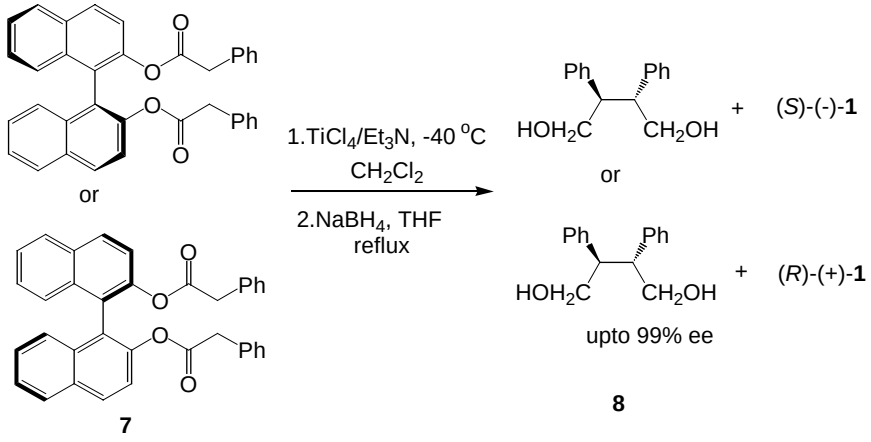
Chiral 1,1'-bi-2-naphthol **1** in alliance with boric acid was utilized for the purification of diastereomeric mixture **5** as well as for the resolution of trans-(±)-2-(pyrrolidinyl)cyclohexanol **6** and its methyl ether derivative (Scheme 2).[6]

Scheme 2

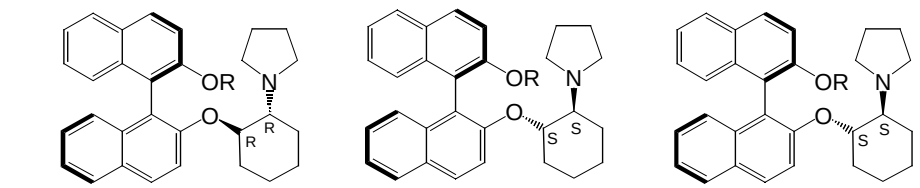


As outlined in chapter 2, enantiomerically pure 2,3-diphenyl-1,4-butanediol **8** was synthesized in good yields through intramolecular oxidative coupling of the titanium enolates of phenylacetic acid esters **7** of enantiomerically pure 1,1'-bi-2-naphthol followed by the reduction with the $NaBH_4/I_2$ reagent system (Scheme 3).[7]

Scheme 3



Convenient methods were developed for the preparation of chiral 1,1'-bi-2-naphthol derived amino ether derivatives **9**, **10** and **11** through opening of aziridinium ion intermediate derived from trans (±)-2-(1-pyrrolidinyl)cyclohexanol.[8]



R = H, CH_3, $COCH_3$ **9** **10** (*R*,*R*,*R*) -(-) **11**

diastereomeric mixture

In continuation of these research efforts on the synthesis and applications of chiral bi-2-naphthol derivatives, we became interested in the preparation of 6,6'-diacyl-1,1'-bi-2-naphthol derivatives for use in the synthesis of chiral polymers containing bi-2-naphthyl moiety. Accordingly, it is of interest to briefly review the literature reports on these topics.

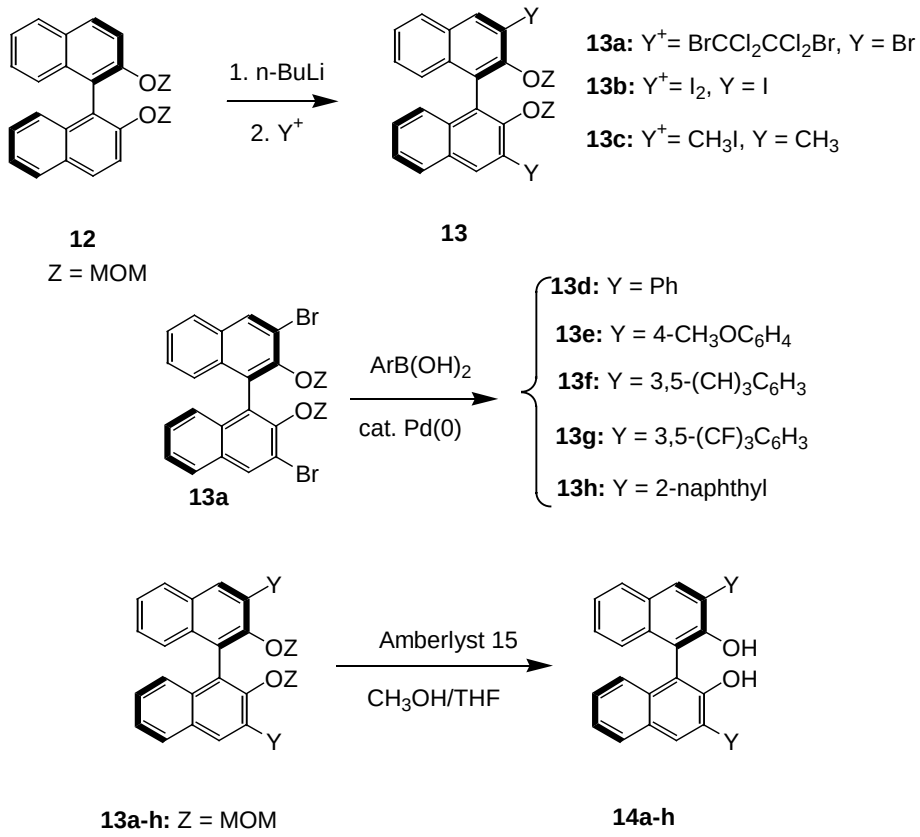
3.1.2 Synthesis and utility of 3,3'-poly-1,1'-bi-2-naphthol derivatives

Derivatives of BINOL, particularly 3,3'-disubstituted derivatives, have been used in the asymmetric synthesis. Dramatic increases in enantioselectivities were achieved using 3,3'-disubstituted BINOLs compared to BINOL itself.[9] Recently, 3,3'-disubstituted BINOLs have been also used to obtain greater enantioselectivities in 1,2-addition of diethylzinc to aldehydes,[10] conjugate addition of diethylzinc to enones, aldol reaction,[11] cyanation, silylation, olefin metathesis reactions and hetero-Diels-Alder reactions.[12]

Very recently, Chong *et al*.[13] reported that 3,3'-disubstituted BINOLs could be prepared from MOM derivative **12** (Scheme 4). Thus, lithiation of **12** followed by trapping of the aryllithium intermediate with appropriate electrophiles gave the compounds **13a**-**13c**.

The aryl dibromide **13a** underwent Suzuki cross-coupling with arylboric acids to afford the expected diaryl derivatives **13d-13h**.

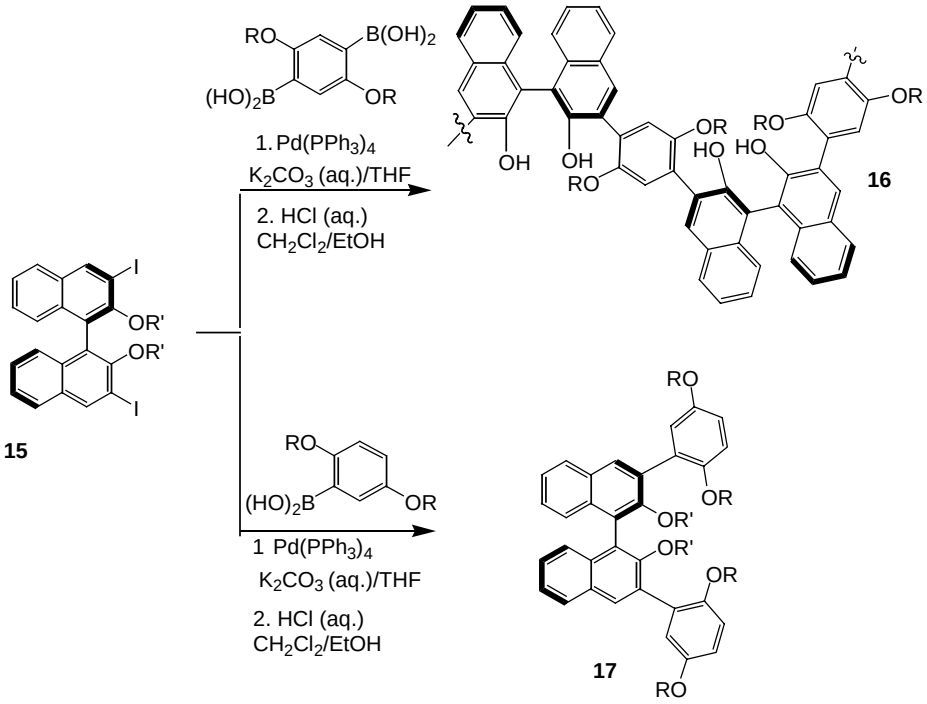
Scheme 4



Finally, each of the MOM derivatives could be deprotected using Amberlyst 15 in THF/MeOH to obtain the desired substituted BINOLs **14a-14h** in excellent yields.[13]

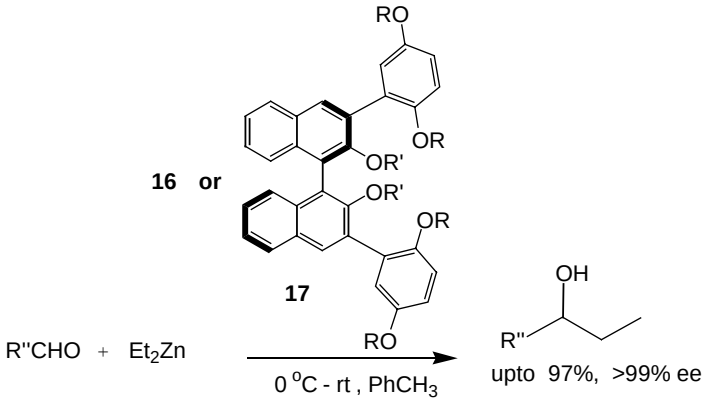
Pu *et al.*[14] used the 3,3'-diiodo-1,1'-bi-2-naphthol ether **15** for the Suzuki coupling with the arylboronic acids to synthesize monomer **17** as well as the polymers **16** (Scheme 5).

Scheme 5

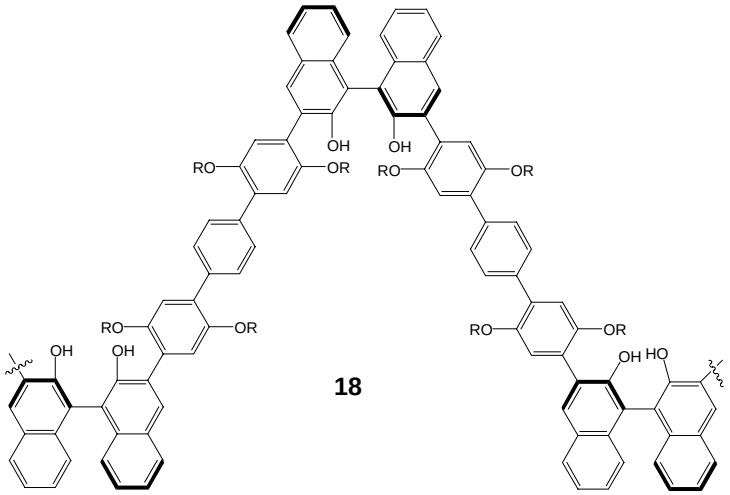


The 3,3'-diaryl-1,1'-bi-2-naphthol monomer **17** as well as the polymer **16** were used to catalyze the reaction of diethylzinc with benzaldehyde (Scheme 6).[14]

Scheme 6



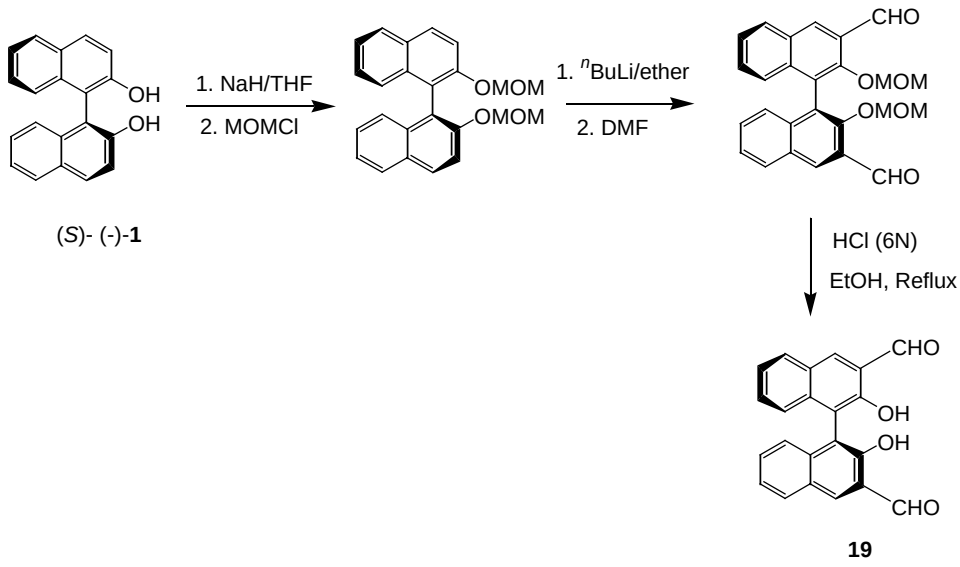
Several other 3,3'-poly-1,1'-bi-2-naphthol derivatives **18** obtained via Suzuki coupling were used in the reaction of diethylzinc with benzaldehyde as well as ketone reduction reactions. [3]



18

Zhang *et al*.[15] reported the synthesis of 3,3'-diformyl-2,2'-dihydroxy-1,1'-bi-naphthol **19** by starting with a MOM protected optically active (*S*)-BINOL **1** (Scheme7).

Scheme 7

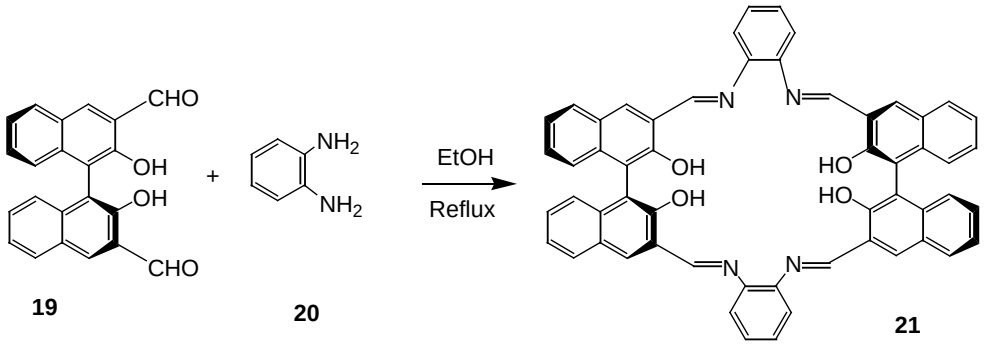


(*S*)- (-)-**1**

19

Macrocycle **21** was synthesized using 3,3'-diformyl-2,2'-dihydroxy-1,1'-bi-naphthol **19** and *O*-phenylenediamine **20** and used for UV spectral studies (Scheme 8).[15]

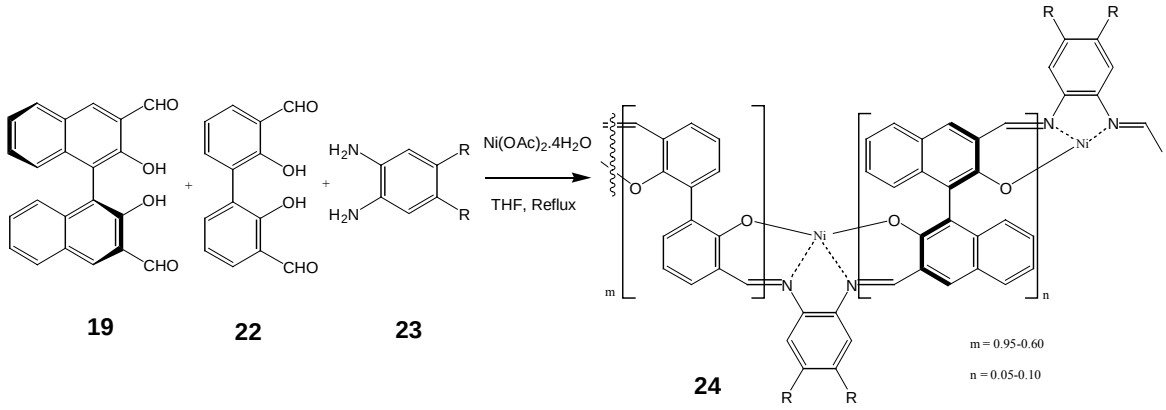
Scheme 8



19 **20** **21**

3,3'-Diformyl-1,1'-bi-2-naphthol **19** was also converted to polymer **24** in the presence of biphenyl dialdehyde monomer **22** and diamine derivative **23** using $Ni(OAc)_2.4H_2O$ (Scheme 9).[15]

Scheme 9

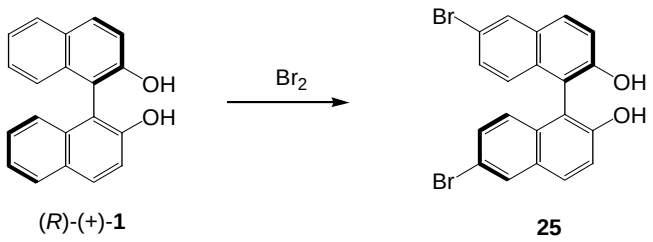


19 **22** **23** **24**

3.1.3 Synthesis and utility of 6,6'-poly-1,1'-bi-2-naphthol derivatives

The 6,6'-dibromo-1,1'-bi-2-naphthol **25** can be easily synthesized by the bromination of 1,1'-bi-2-naphthol (*R*)-(+)-**1** at low temperatures (Scheme 10).[16]

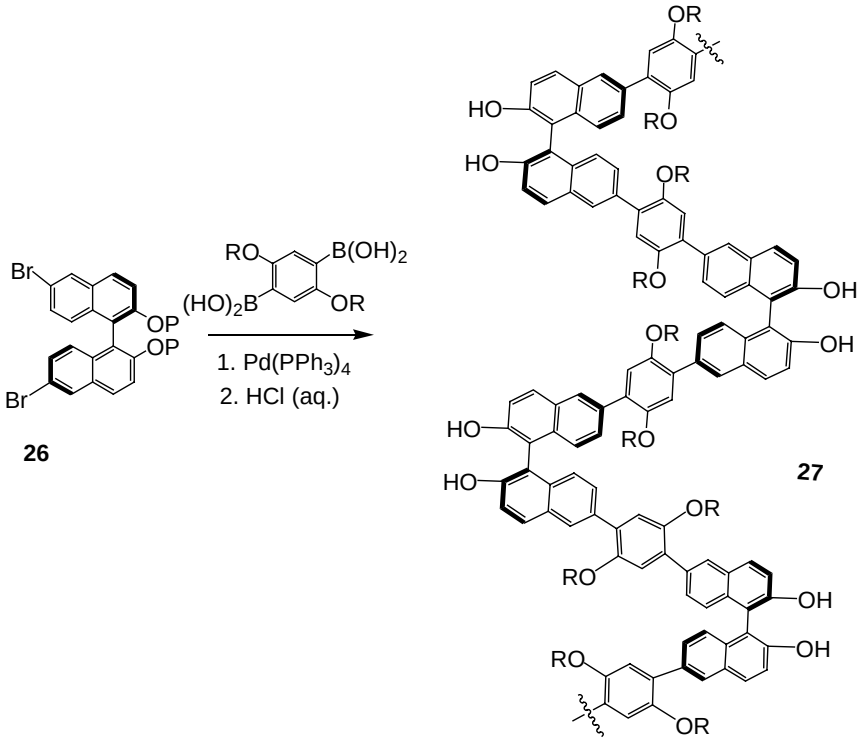
Scheme 10



(*R*)-(+)-**1** **25**

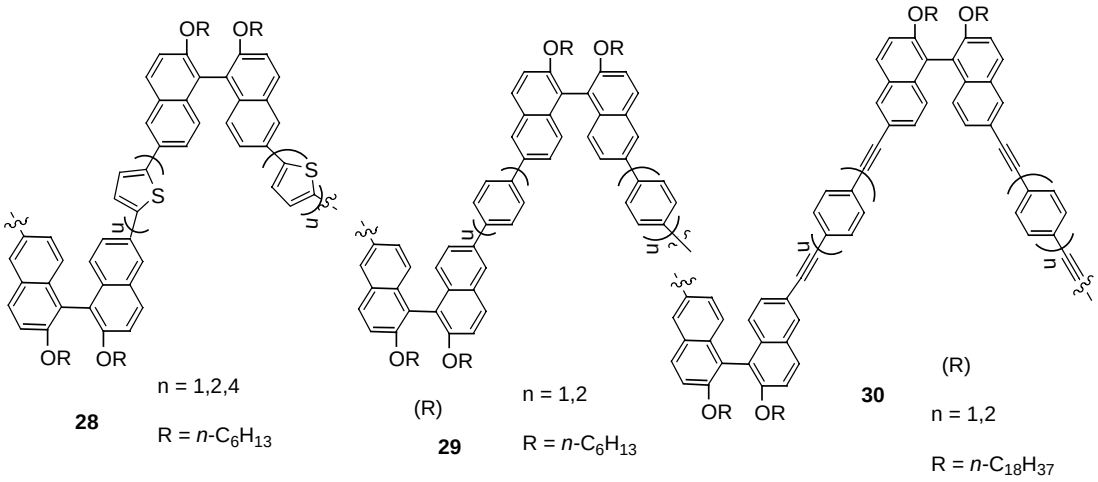
Pu *et al.*[17] used the 6,6'-dibromo-1,1'-bi-2-naphthol ether **26** for Suzuki coupling with the arylboronic acids to prepare the polymer **27** (Scheme 11).

Scheme 11



26 **27**

Also, Lin Pu *et al.* have reported a series of the syntheses and studies of binaphthyl polymers of various structures. Among them, polymers **28**, **29** and **30** synthesized by polymerization at the 6,6'-position of binaphthyl monomers have been found to be useful.[18-20]



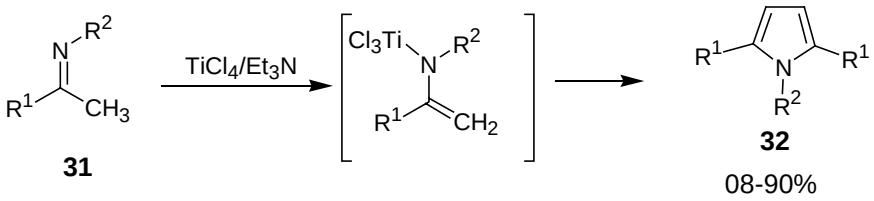
As outlined previously, we have undertaken efforts on the synthesis of chiral binaphthol polymers containing pyrrole spacers using synthetic methods developed in this laboratory. The results are discussed in the next section.

3.2 Results and Discussion

3.2 Efforts towards the synthesis of poly-1,1'-bi-2-naphthyl derivatives containing pyrrole spacers

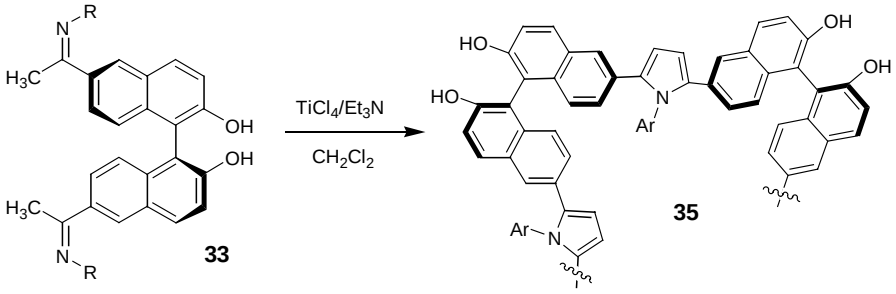
As a part of ongoing research program on the synthesis of chiral polymers, we have undertaken efforts towards the synthesis of chiral polymers containing 1,1'-bi-2-naphthyl moiety. It has been reported from this laboratory that the reaction of ketimines **31** with the $TiCl_4/R_3N$ reagent system gives the corresponding pyrroles **32** in 8-90% yields (Scheme 12).[21]

Scheme 12

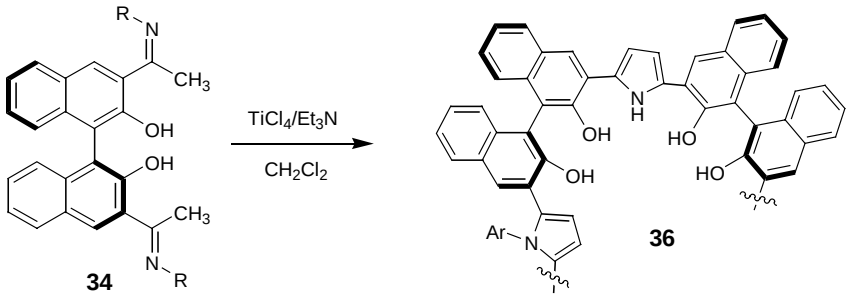


We have decided to use this transformation for the synthesis of poly-1,1'-bi-2-naphthol derivatives containing pyrrole spacers **35** and **36** from the corresponding diketimines **33** and **34** (Schemes 13a and 13b).

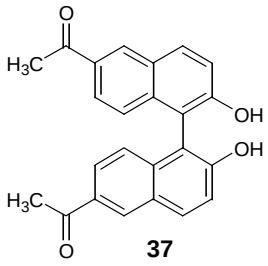
Scheme 13a



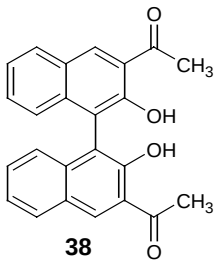
Scheme 13b



The chiral imines could be accessed using the diacyl derivatives of 1,1'-bi-2-naphthols **37** and **38**.



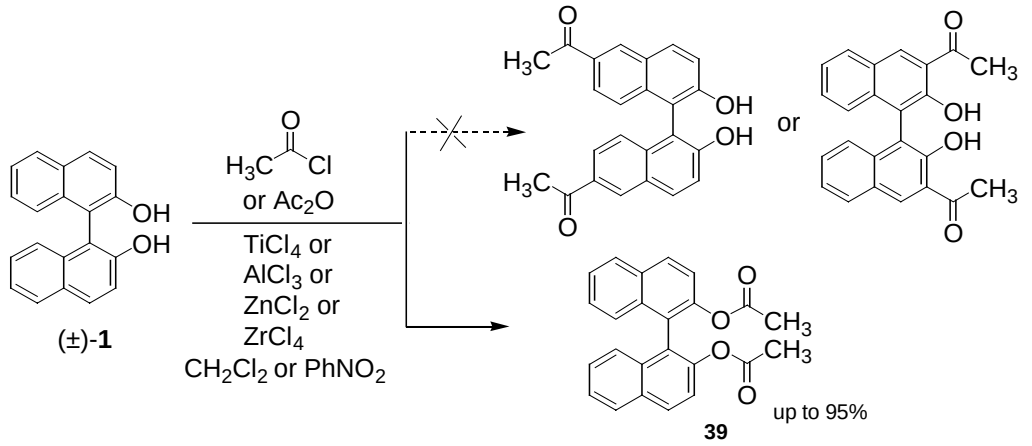
(*R*)-(+) and (*S*)-(-)



(*R*)-(+) and (*S*)-(-)

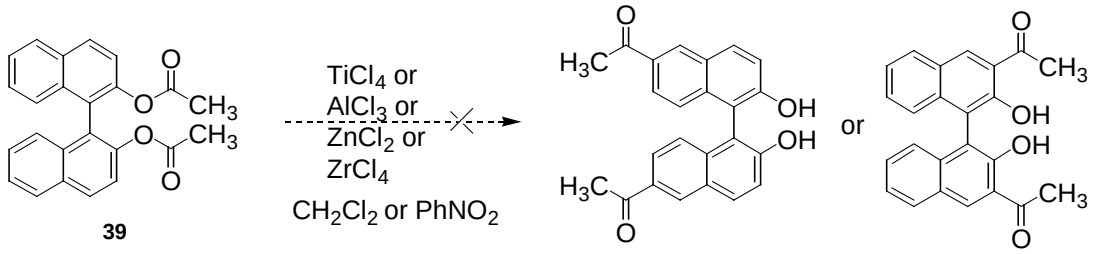
Initially, we have carried out the acylation of BINOL **1** using acetyl chloride as well as acetic anhydride in the presence of $TiCl_4$ in dichloromethane and nitrobenzene solvents. In these experiments, only the ester derivative **39** was obtained in 95% yield. Similar reactivity was also observed with other Lewis acids like $AlCl_3$, $ZnCl_2$, $ZrCl_4$ and $F_3B{:}OEt_2$ (Scheme 14).

Scheme 14



We have made efforts to carry out Fries rearrangement of the diester derivative **39** in a separate step using various Lewis acids like $TiCl_4$, $AlCl_3$, $ZnCl_2$ and $ZrCl_4$. Unfortunately, these efforts were unsuccessful (Scheme 15).

Scheme 15

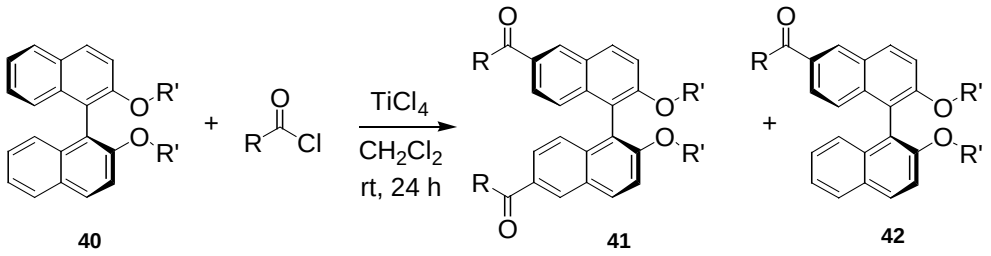


Therefore, we have undertaken studies on the acylation of BINOL derivatives. Eventually, it was observed that the hydroxy protected BINOL derivatives are suitable for acylation. The results are presented in the next section.

3.2.1 Acylation of 1,1'-bi-2-naphthyl alkyl ethers with $TiCl_4$ and acid chlorides

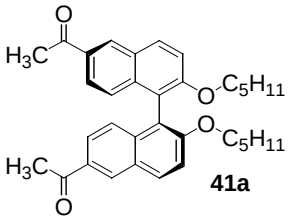
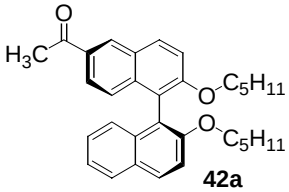
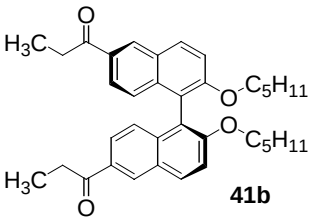
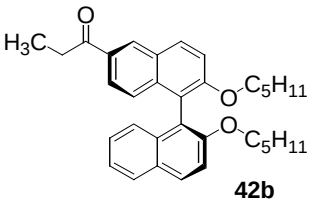
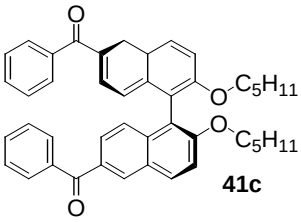
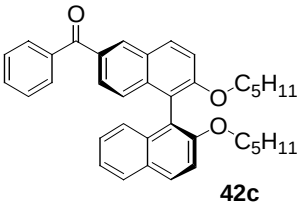
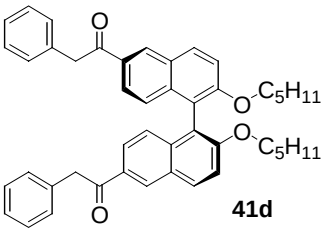
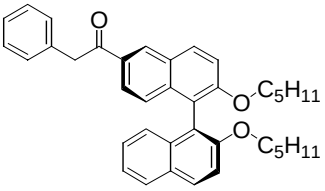
Initially, we have examined the acylation of 1,1'-bi-2-naphthol ether with $TiCl_4$ and acid chlorides We have observed the formation of both mono as well as diacylated products, selectively at the 6,6' positions. The acylation was generalized with various acid chlorides. For example, acylation of optically active 1,1'-bi-2-naphthol ether **40** using $TiCl_4$/acid chloride produced the diacylated compounds **41** as well as the monoacyl derivative **42** (Scheme 16). The use of acetic anhydride in the place of the acyl chloride did not give the acylated products.

Scheme 16



The acylation reaction was carried out using 2.2 equivalents of acetyl chloride and *n*-pentyl protected BINOL **40a** in dichloromethane solvent. The results are summarized in Table 1.

Table 1: Acylation of 1,1'-bi-2-naphthol ether derivative using $TiCl_4$ and acid chlorides[a]

S.No.	RCOCl	Substrate	Product[b]	Yield (%)[c]	Product[b]	Yield (%)[c]
1	R = Me	(*S*) (-) R' = C_5H_{11} **40a**	 **41a**	64	 **42a**	22
2	R = Et	**40a**	 **41b**	66	 **42b**	20
3	R = Ph	**40a**	 **41c**	62	 **42c**	21
4	R = Bn	**40a**	 **41d**	66	 **42d**	16

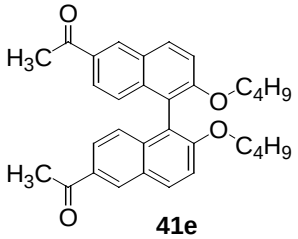
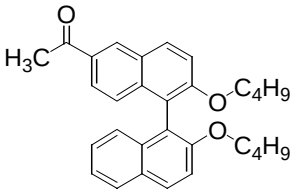
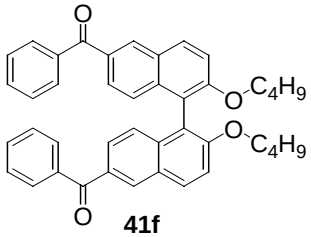
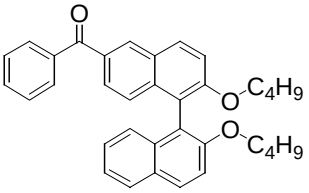
[a]The reactions were carried out using BINOL ether **40a** (5 mmol), acid chloride (12 mmol), $TiCl_4$ (3.3 mL of 1:1 solution of $TiCl_4/CH_2Cl_2$) (15 mmol)

[b]The products were identified by ^{1}H-NMR, ^{13}C-NMR and mass spectral data.

[c]The isolated yields are based on the amount of BINOL derivative used.

We have also examined the acylation of (±)-BINOL derived ether **40a** with $TiCl_4$. The results are summarized in Table 2.

Table 2: Acylation of (±)-1,1'-bi-2-napthol ether **40b** using $TiCl_4$/acid chlorides[a]

S.No.	RCOCl	Substrate	Product[b]	Yield (%)[c]	Product[b]	Yield (%)[c]
1	R = Me	**40b** (±) R '= *n*-butyl	 **41e**	60	 **42e**	17
2	R = Ph	**40b**	 **41f**	62	 **42f**	21

a The reactions were carried out using BINOL ether **40b** (5 mmol), acid chloride (12 mmol), TiCl4 (1.65 mL) (15 mmol)

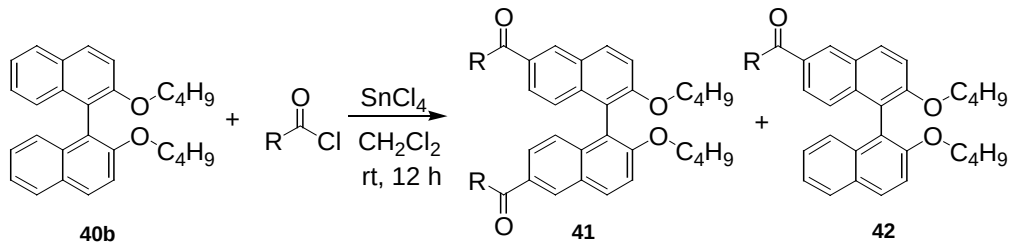
[b]The products were identified by ^{1}H-NMR and ^{13}C-NMR spectral data.

[c]The isolated yields are based on the amount of BINOL ether used.

3.2.2 Acylation of 1,1'-bi-2-naphthyl alkyl ethers using $SnCl_4$ and acid chlorides

We have also examined acylation of 1,1'-bi-2-naphthyl alkyl ethers **40b** using $SnCl_4$ as Lewis acid (Scheme 17). The products obtained were diacylated products **41e-f** and monoacylated derivatives **42e-f**.

Scheme 17

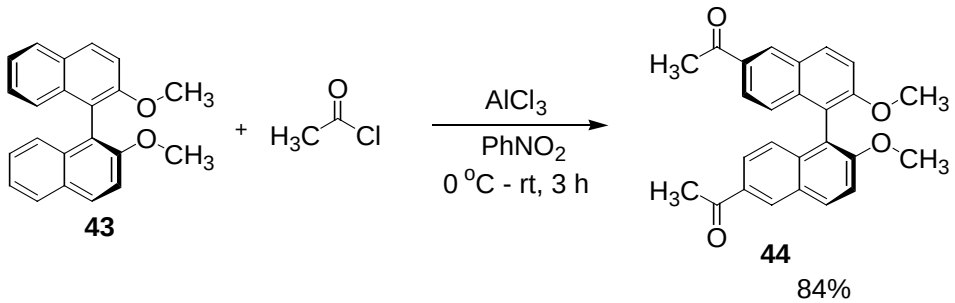


1	R = Me	**41e**	66%	**42e**	15%
2	R = Ph	**41f**	61%	**42f**	19%

3.2.3 Acylation of 1,1'-bi-2-naphthyl alkyl ethers with $AlCl_3$ and acid chlorides

Surprisingly, acylation reaction on methyl protected BINOL **43** did not give the desired product using $TiCl_4$ or $SnCl_4$ as Lewis acids. In these experiments only starting BINOL dimethyl ether **43** was recovered. Fortunately, the BINOL derivative **43** was successfully acylated using $AlCl_3$ (Scheme 18). For example, the acylation reaction of optically active (*S*)-(+)-BINOL methyl ether **43** with acetyl chloride in the presence of $AlCl_3$ in nitrobenzene gave 6,6'-diacyl-2,2'-dimethoxy-1,1'-bi-naphthalene **44** in 84% yield.

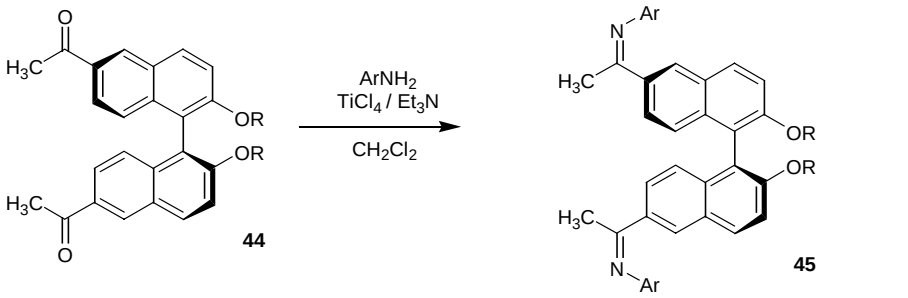
Scheme 18



3.2.4 Efforts towards the synthesis of chiral bi-2-naphthyl polymers containing pyrrole spacers using the ketimines of 6,6'-diacyl-1,1'-bi-2-naphthol methyl ethers and the $TiCl_4/Et_3N$ reagent system

The diacetyl derivatives **44** were converted to ketimines **45** using arylamines and the $TiCl_4/Et_3N$ reagent system by following the method developed in this laboratory (Scheme 19).[21]

Scheme 19



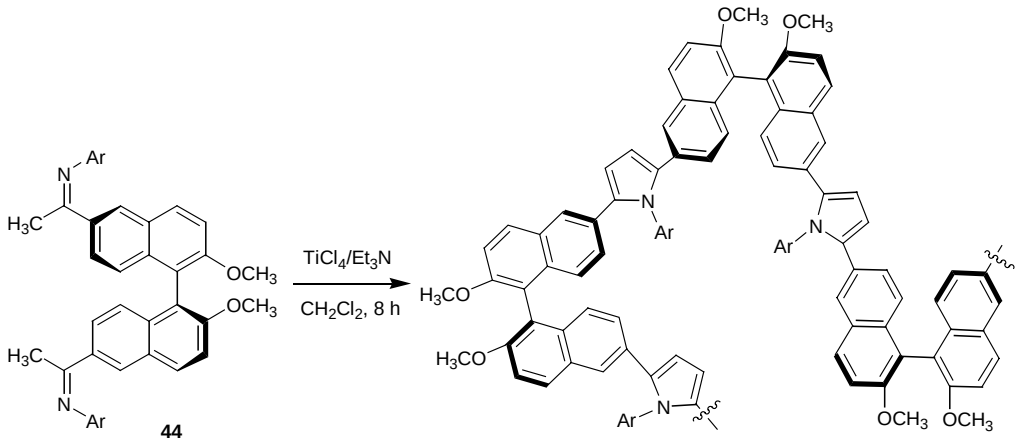
45a Ar = Ph, R = CH_3

45b Ar = 4-*sec*-butyl Ph, R = CH_3

45c Ar = Ph, R = *n*-C_8H_{17}

Conversion of the diimine **45a** derivative to the chiral polymers was carried out using the $TiCl_4/Et_3N$ reagent system. A light brown colored material was obtained (Scheme 20). Unfortunately, the material was insoluble in organic solvents as well as in water and HCl. We have also carried out the conversion of the diimine **45b** to polymers using the $TiCl_4/Et_3N$ reagent system under the same reaction conditions. Again, only insoluble light brown colored product was obtained.

Scheme 20



Ar = Ph, 4-*sec*-butyl Ph

We have also examined the reaction of the imine **45c** containing larger chain alkyl group under the same conditions. Surprisingly, these derivatives failed to react with the $TiCl_4/Et_3N$ reagent system under the same conditions. A more systematic investigation on the polymerization of these derivatives should give fruitful results.

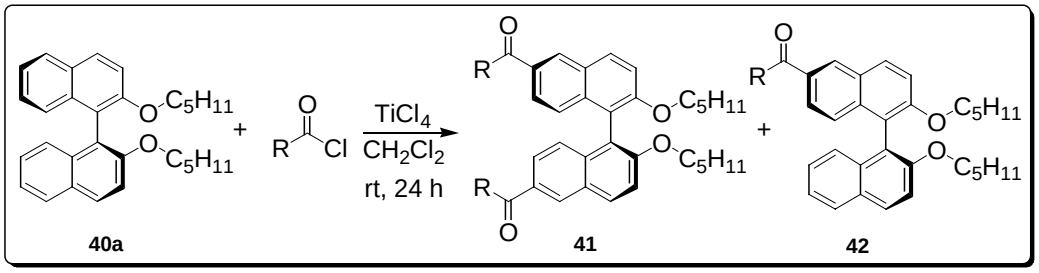
3.3 Conclusions

Acylation reaction was carried on alkyl protected 1,1'-bi-2-naphthol in the presence of $TiCl_4$. The acylation took place at 6 and 6,6' positions. The acylation reaction was also carried out using other Lewis acids like $SnCl_4$ and $AlCl_3$. Also, efforts toward the synthesis of chiral polymers containing bi-2-naphthyl moiety with pyrrole spacers was made using the diimine derivative of 6,6'-diacetyl-1,1'-bi-2-naphthol dialkyl ethers. The materials isolated were insoluble in organic as well as aqueous media. A more systematic studies using ketimines of BINOL ethers containing long chain alkyl groups should give chiral polymers useful for characterization and applications.

3.4 Experimental Section

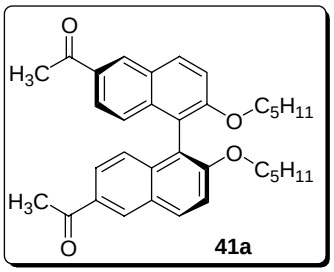
3.4.1 General procedure for the acylation of 1,1'-bi-2-naphthol ethers using acid chlorides and $TiCl_4$

Dichloromethane (25 mL), acid chloride (7.5 mmol), and $TiCl_4$ (1.1 mL, 10 mmol) were taken under N_2 atmosphere, at room temperature. The mixture was stirred for 20 min. To this mixture was added 1,1'-bi-2-naphthol ethers (*S*)-**40a** $[\alpha]_D^{25}$=-53.7 (*C* 0.6, $CHCl_3$) or **40b** (2.5 mmol) and stirred further for 24 h at 25 °C. It was quenched with water, the organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2×25 mL). The combined organic layer was washed with brine solution (10 mL) and dried over anhydrous Na_2SO_4. The solvent was removed and the residue was chromatographed on a silica gel column. The acylated compounds **41** and **42** were eluted using 4:96 EtOAc/hexane mixture as highly viscous materials.



Yield 0.8 g (64%)

IR (Neat) (cm^{-1}) 3063, 2953, 1682, 1618, 1466, 1356, 1273, 1051, 941, 866, 736, 698



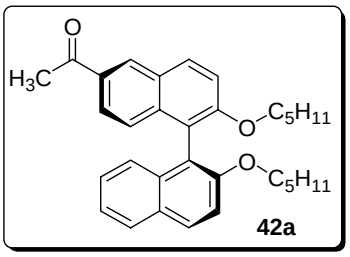
^{1}H-NMR (δ ppm, $CDCl_3$) 8.50 (s, 2H), 8.07 (d, J=8.8 Hz, 2H), 7.76 (d, J=8.8 Hz, 2H), 7.46 (d, J=8.8 Hz, 2H), 7.16 (d, J=8.8 Hz, 2H), 4.01-3.92 (m, 4H), 2.66 (s, 6H), 1.43-1.40 (t, J=7.2 Hz, 4H), 1.04 -0.88 (m, 8H), 0.63 (t, J=6.8 Hz, 6H) **(Spectrum No. 70)**

^{13}C-NMR (δ ppm, $CDCl_3$) 197.9, 156.7, 136.5, 132.3, 131.3, 130.6, 127.9, 125.5, 124.3, 119.6, 115.6, 69.2, 29.7, 28.9, 27.8, 26.6, 22.1, 13.0 **(Spectrum No. 71)**

LCMS m/z 511 (M+1)

$[\alpha]_D^{25}$ +14.3 (*c* 1, $CHCl_3$)

Yield 0.25 g (22%)



42a

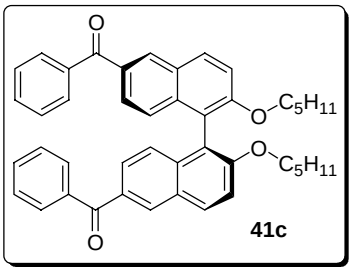
IR (Neat) (cm^{-1}) 3055, 2934, 2872, 1680, 1618, 1466, 1348, 1269, 1180, 1051, 736, 702

^{1}H-NMR (δ ppm, $CDCl_3$) 8.50-7.11 (m, 11H), 4.01-3.91 (m, 4H), 2.67 (s, 1H), 1.04-0.98 (m, 4H), 0.94-0.88 (m, 4H), 0.63 (t, J=6.8 Hz, 6H) **(Spectrum No. 72)**

^{13}C-NMR (δ ppm, $CDCl_3$) 198.0, 156.9, 154.6, 145.9, 136.8, 134.1, 132.4, 131.1, 130.53, 129.4, 129.3, 128.9, 128.0, 127.0, 126.3, 126.0, 125.2, 124.2, 123.5, 120.7, 119.9, 117.9, 117.2, 116.0, 115.6, 69.7, 29.1, 28.0, 26.6, 22.2, 13.9 **(Spectrum No. 73)**

LCMS m/z 469 (M+1

$[\alpha]_D^{25}$ -32.8 (*c* 1, $CHCl_3$)



41c

Yield 0.93 g (62%)

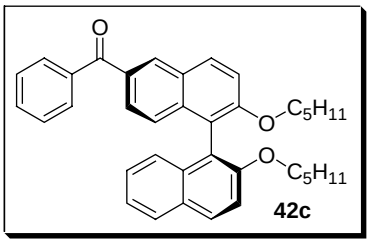
IR (Neat) (cm^{-1}) 3061, 2955, 2870, 1653, 1616, 1464, 1278,1140, 1051, 910, 729

^{1}H-NMR (δ ppm, $CDCl_3$) 8.35-7.26 (m, 20H), 4.04-3.97 (m, 4H), 1.46 (t, J=6.8 Hz, 4H), 1.09-0.95 (m, 8H), 0.68 (t, J=7.2 Hz, 6H) **(Spectrum No. 76)**

^{13}C-NMR (δ ppm, $CDCl_3$) 196.6, 156.7, 138.3, 136.3, 132.6, 132.5, 132.1, 130.0, 128.4, 127.8, 126.2, 125.5, 119.7, 115.7, 69.3, 29.7, 28.9, 27.9, 22.1, 13.9 **(Spectrum No. 77)**

LCMS m/z 635 (M+1)

$[\alpha]_D^{25}$ +10.0 (*c* 1, $CHCl_3$)



42c

Yield 0.27 g (21%)

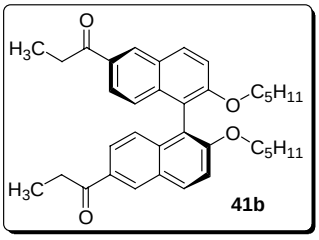
IR (Neat) (cm^{-1}) 3063, 2953, 2870, 2671, 2544, 1651, 1616, 1464, 1271, 1089, 728

^{1}H-NMR (δ ppm, $CDCl_3$) 8.33-7.30 (m, 16H), 4.02-3.91 (m, 4H), 1.43 (t, J=6.8 Hz, 4H), 1.27-0.92 (m, 8H), 0.67 (t, J=7.2 Hz, 6H)

^{13}C-NMR (δ ppm, $CDCl_3$) 196.7, 156.7, 154.5, 138.4, 136.5, 134.5, 134.1, 133.7, 132.5, 132.3, 132.0, 130.9, 130.6, 130.2, 130.0, 129.4, 129.3, 128.9, 128.5, 128.2, 127.9, 127.8, 127.3, 126.2, 126.0, 125.8, 123.5, 120.6, 19.8, 115.9, 115.6, 69.6, 69.3, 29.1, 28.9, 27.9, 27.8, 22.2, 22.1, 13.9

LCMS m/z 531 (M+1)

$[\alpha]_D^{25}$ -39.7 (*c* 1, $CHCl_3$)



41b

Yield 0.8 g (66%)

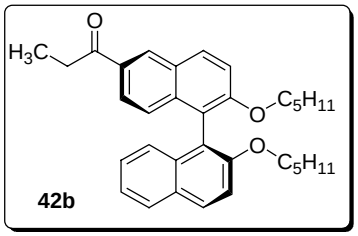
IR (Neat) (cm^{-1}) 3063, 2932, 2868, 1684, 1618, 1593, 1471, 1346, 1269, 1041, 736, 696

^{1}H-NMR (δ ppm, $CDCl_3$) 8.51 (s, 2H), 8.07 (d, J=8.8 Hz, 2H), 7.77 (d, J=8.8 Hz, 2H), 7.46 (d, J=8.8 Hz, 2H), 7.15(d, J=8.8 Hz, 2H), 4.01-3.92 (m, 4H), 3.09 (q, J=7.2 Hz, 2H), 1.43-1.40 (m, 4H), 1.26 (t, J=6.8 Hz, 6H), 1.03 - 0.88 (m, 8H), 0.63 (t, J=6.8 Hz, 6H) **(Spectrum No. 74)**

^{13}C-NMR (δ ppm, $CDCl_3$) 200.6, 156.6, 136.4, 132.0, 131.3, 129.9, 128.0, 125.5, 124.41, 119.4, 115.6, 69.3, 31.7, 28.9, 27.8, 22.1, 13.9, 8.5 **(Spectrum No. 75)**

LCMS m/z 541 (M+1)

$[\alpha]_D^{25}$ +18.2 (*c* 1, $CHCl_3$)



Yield 0.24 g (20%)

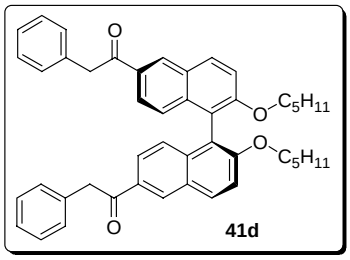
IR (Neat) (cm^{-1}) 3055, 2934, 2872, 1680, 1618, 1466, 1348, 1269, 1180, 1051, 736, 702

^{1}H-NMR (δ ppm, $CDCl_3$) 8.54-7.19 (m, 12H), 4.05-3.65 (m, 4H), 3.06 (q, J=7.2 Hz, 4H), 1.53-1.42 (m, 4H), 1.31 (t, J=6.8 Hz, 6H), 1.10-0.72 (m, 4H), 0.66 (t, J=6.8 Hz, 6H)

^{13}C-NMR (δ ppm, $CDCl_3$) 200.3, 156.6, 154.4, 136.6, 134.0, 131.9, 130.9, 129.7, 129.3, 129.2, 127.9, 127.8, 126.1, 125.8, 125.1, 124.0, 123.3, 120.4, 119.6, 115.7, 115.3, 69.4, 31.5, 29.0, 27.8, 22.0, 13.7, 8.4

LCMS m/z 483 (M+1)

$[\alpha]_D^{25}$ -41.2 (*c* 1, $CHCl_3$)



Yield 1.0 g (66%)

IR (Neat) (cm^{-1}) 3050, 2926, 2663, 1675, 1610, 1469, 939, 806, 698

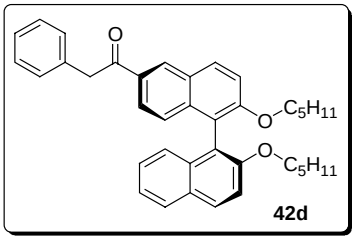
^{1}H-NMR (δ ppm, $CDCl_3$) 8.73-7.13 (m, 20H), 4.38 (s, 4H), 4.03-3.97 (m, 4H), 1.04 (t, J=6.0 Hz, 4H) 1.06-0.92 (m, 8H), 0.65 (t, J=7.2 Hz, 6H)

^{13}C-NMR (δ ppm, $CDCl_3$) 197.5, 156.8, 136.6, 135.0, 131.5, 129.8, 129.5, 129.0, 128.7, 128.0, 126.8, 125.7, 124.8, 119.6, 115.6, 69.2, 45.4, 28.9, 27.8, 22.1, 13.9

LCMS m/z 663 (M+1)

`$[\alpha]_D^{25}$ -33.7 (*c* 1, $CHCl_3$)

Yield 0.2 g (16%)



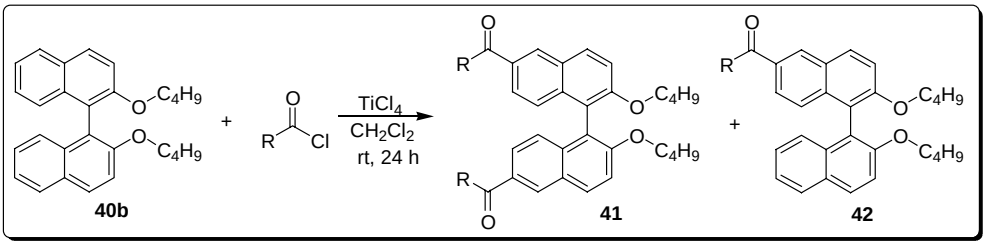
IR (Neat) (cm^{-1}) 3059, 2932, 2870, 1672, 1618, 1464, 1340, 1269, 1140, 1051, 746

^{1}H-NMR (δ ppm, $CDCl_3$) 8.22-8.66 (m, 15H), 4.40 (s, 2H), 4.08-3.94 (m, 4H), 1.47 (t, J=7.2 Hz, 4H), 0.96-1.09 (m, 8H), 0.71 (t, J=7.2 Hz, 6H)

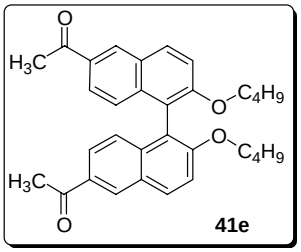
^{13}C-NMR (δ ppm, $CDCl_3$) 197.4, 157.0, 154.6, 144.5, 136.8, 135.2, 134.2, 131.8, 131.2, 130.9, 129,3, 129.3, 128.7, 128.6, 128.4, 128.01, 126.8, 126.3, 126.1, 125.2, 124.6, 123.6, 121.2, 115.9, 115.5, 69.4, 45.5, 29.0, 27.9, 22.2, 14.1

LCMS m/z 543 (M-1)

$[\alpha]_D^{25}$ -23.8 (*c* 0.6, $CHCl_3$)



Yield 0.72 g (60%)



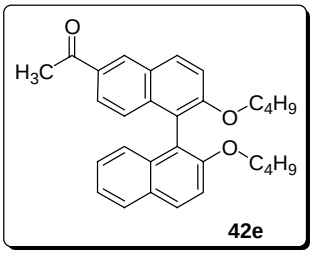
IR (Neat) (cm^{-1}) 2928, 2872, 1672, 1618, 1591, 1462, 1346, 1277, 1242, 1076, 1026, 947, 889, 800, 696

^{1}H-NMR (δ ppm, $CDCl_3$) 8.51 (s, 2H), 8.08-7.13 (m, 8H),

3.99 (t, J=6.8 Hz, 4H), 2.67 (s, 6H), 1.43-1.38 (m, 4H), 1.02-0.97 (m, 4H), 0.62 (t, J=7.2 Hz, 6H) **(Spectrum No. 78)**

^{13}C-NMR (δ ppm, $CDCl_3$) 197.9, 156.7, 136.5, 132.3, 131.4, 130.7, 127.9, 125.5, 124.3, 119.4, 115.6, 68.9, 31.2, 26.6, 18.7, 13.5 **(Spectrum No. 79)**

Yield 0.18 g (17%)



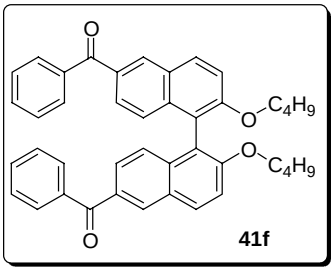
42e

IR (Neat) (cm^{-1}) 3063, 2928, 2874, 1662, 1618, 1458, 1354, 1273, 1091, 806, 748, 694

^{1}H-NMR (δ ppm, $CDCl_3$) 8.35 (s, 2H), 7.89-6.98 (m, 10H), 3.86-3.76 (m, 4H), 2.48 (s, 6H), 1.30-1.22 (m, 4H), 0.89-0.81 (m, 4H), 0.58-0.51 (m, 6H) **(Spectrum No. 80)**

^{13}C-NMR (δ ppm, $CDCl_3$) 197.0, 155.2, 153.4, 136.8, 134.1, 132.3, 131.1, 130.6, 130.2, 129.9, 128.0, 126.6, 126.5, 126.3, 126.3, 126.1, 124.2, 123.5, 119.7, 117.9, 69.0, 31.3, 26.6, 18.8, 13.2 **(Spectrum No. 81)**

Yield 0.93 g (62%)

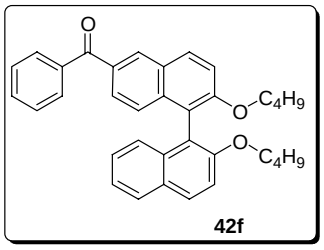


41f

IR (Neat) (cm^{-1}) 3072 2930, 1655, 1616, 1460, 1277, 719

^{1}H-NMR (δ ppm, $CDCl_3$) 8.21 (s, 2H), 8.11-7.23 (m, 10H), 4.01 (t, J=6.8 HZ, 4H), 1.52-1.44 (m, 4H), 1.16-0.98 (m, 4H), 0.69 (t, J=6.8 Hz, 6H) **(Spectrum No. 82)**

^{13}C-NMR (δ ppm, $CDCl_3$) 196.7, 156.7, 138.3, 136.3, 133.6, 132.6, 132.4, 132.1, 131.3, 130.2, 130.0, 128.5, 128.3, 127.7, 126.2, 125.5, 119.7, 115.7, 69.0, 31.2, 18.8, 13.6 **(Spectrum No. 83)**



42f

Yield 0.25 g (21%)

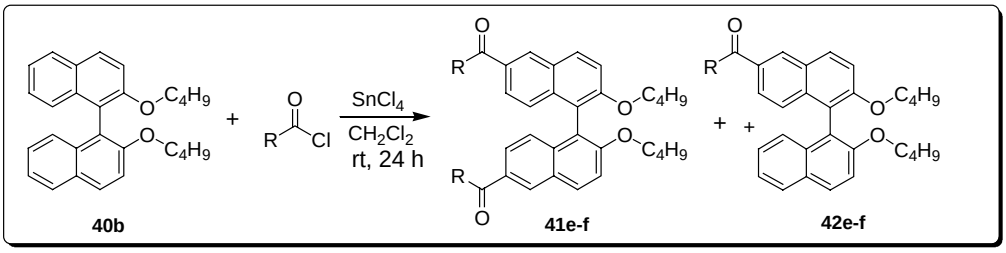
IR (Neat) (cm^{-1}) 3059, 2957, 2930, 1653, 1618, 1593, 1508, 1462, 1273, 1244, 723, 698

^{1}H-NMR (δ ppm, $CDCl_3$) 8.21 (s, 2H), 8.03-7.05 (m, 10H), 3.90-3.82 (m, 4H), 1.39-1.18 (m, 4H), 0.92-0.87 (m, 4H), 0.57-0.52 (m, 6H) **(Spectrum No. 84)**

^{13}C-NMR (δ ppm, $CDCl_3$) 200.7, 156.7, 154.6, 136.7, 134.1, 131.0, 129.6, 129.4, 129.3, 129.1,128.0, 126.2, 125.9, 125.1, 124.2, 123.5, 123.1, 120.5, 119.8, 115.6, 115.5, 69.3, 31.7, 31.3, 18.8, 13.6, 8.6 **(Spectrum No. 85)**

3.4.2 Acylation of 1,1'-bi-2-naphthol ethers using acid chlorides and $SnCl_4$

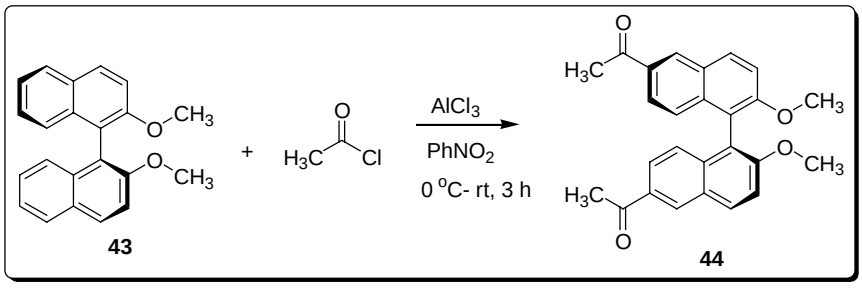
The above procedure was followed for the acylation of (±)1,1'-bi-2-naphthol ether **40b** using $SnCl_4$ and acid chlorides.



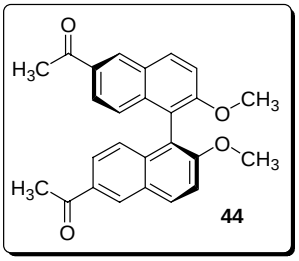
40b **41e-f** **42e-f**

3.4.3 General procedure for the acylation of 1,1'-bi-2-napthol ethers using $AlCl_3$

Anhydrous $AlCl_3$ (3.32 g, 25 mmol) and acetyl chloride (2 mL, 25 mmol) were added to 75 mL of nitrobenzene at 0 °C. The solution was stirred at 0 °C for 15 min, 2,2'-bis(methoxy)-1,1' –binaphthyl (10 mmol) was added, and the mixture was stirred for 3 h. The reaction mixture was pored into ice cold water, and was shaken with CH_2Cl_2. The water layer was extracted in CH_2Cl_2, and the combined organic phases were dried and evaporated (in vacuum). The residue was recrystallyzed in hexane/EtOAc mixture.to give 6,6'-bis(acetyl)-2,2'-bis(methoxy)-1,1'-binaphthyl **44** in 84% yield.



Yield 3.34 g (84%)



mp 190-192 °C

IR (KBr) (cm^{-1}) 3020, 2980, 1676, 1620, 1523, 1477, 1249, 1176, 1055, 891, 796, 707

^{1}H-NMR (δ ppm, $CDCl_3$) 8.25 (s, 2H), 8.13 (d, J=9.8Hz, 2H), 7.77 (d, J=8.8Hz, 2H), 7.52 (d, J=8.8Hz, 2H), 7.26 (d, J=8.8Hz, 2H), 7.11 (d, J=8.8Hz, 2H), 3.80 (s, 6H), 2.67 (s, 6H) **(Spectrum No. 86)**

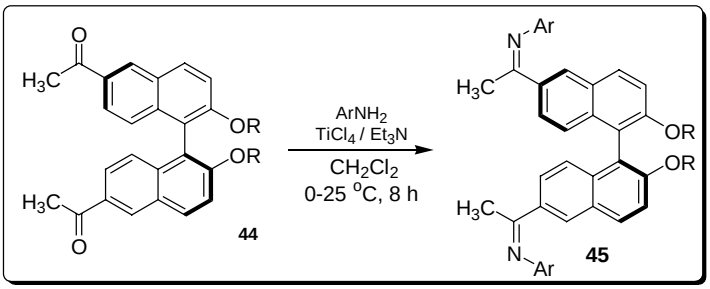
^{13}C-NMR (δ ppm, $CDCl_3$) 197.8, 157.1, 136.4, 132.6, 131.7, 130.6, 128.0, 125.3, 124.6, 118.9, 114.5, 56.5, 26.5 **(Spectrum No. 87)**

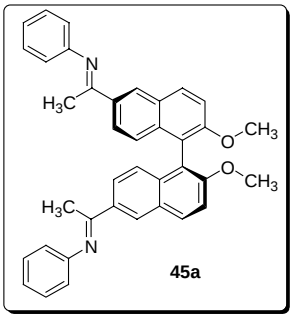
MS(EI) m/z 398 (M^+, 45%) **(Spectrum No. 88)**

$[\alpha]_D^{25}$ +96.6 (*c* 1, $CHCl_3$)

3.4.4 General procedure for the conversion of 6,6'-diacyl-1,1'-bi-2-naphthol ethers to the corresponding ketimines

Dichloromethane (25 mL), Et_3N (0.5 mL, 5 mmol), 6,6'-diacyl-1,1'-bi-2-naphthol ethers **44** (1.25 mmol), and amine (3 mmol) were taken under an N_2 atmosphere, $TiCl_4$ (1.25 mmol) in CH_2Cl_2 (10 ml) was added dropwise under N_2 at 0 °C for 15 min. The reaction mixture was stirred for 0.5 h at 0 °C and stirred further for 7-8 h at 25 °C. It was quenched with a saturated K_2CO_3 solution (30 mL), and the reaction mixture was filtered through a Buchner funnel. The organic layer was separated from the filtrate, and the remaining aqueous layer was extracted with CH_2Cl_2 (2×25 mL). The combined organic layer was washed with a brine solution (10 mL) and dried over anhydrous Na_2CO_3. The solvent was removed, and the ketimines **45** were isolated.





Yield 0.58 g (85%)

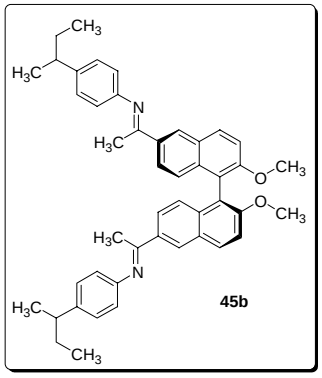
mp 125-127 °C

IR (KBr) (cm^{-1}) 3040, 2970, 1620, 1591, 1477, 1249, 802, 748, 694

^{1}H-NMR (δ ppm, $CDCl_3$) 8.45-6.83 (m, 20H), 3.81 (s, 6H), 2.35 (s, 6H) **(Spectrum No. 89)**

^{13}C-NMR (δ ppm, $CDCl_3$) 165.2, 156.2, 152.0, 135.2, 134.8, 130.8, 129.0, 128.6, 128.0, 125.4, 124.8, 123.1, 119.5, 119.4, 114.4, 56.7, 17.2 **(Spectrum No. 90)**

$[\alpha]_D^{25}$ +158.7 (*c* 1, $CHCl_3$)



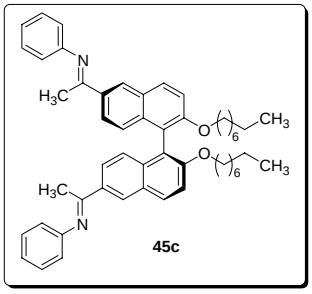
Yield 0.53 g (81%)

IR (Neat) (cm^{-1}) 2961, 2872, 1620, 1481, 1251, 1217, 831, 688

^{1}H-NMR (δ ppm, $CDCl_3$) 8.40 (s, 2H), 8.08 (d, 2H, J=8.8 Hz),7.95 (d, 2H, J=8.8 Hz), 7.50 (d, 2H, J=8.8 Hz), 7.15 (d, 4H, J=8.0 Hz), 6.97 (d, 2H J=8.8 Hz), 6.71 (d, 4H, J=8.0 Hz), 3.80 (s, 6H), 2.58-2.50 (m, 2H,), 2.34 (s, 6H), 1.62-1.56 (m, 4H), 1.25 (d, 6H, J=7.2), 0.84 (t, 6H, J=7.2 Hz)

^{13}C-NMR (δ ppm, $CDCl_3$) 165.0, 156.2, 149.7, 142.4, 135.2, 130.7, 128.7, 127.8, 127.5, 125.3, 124.9, 119.5, 115.3,114.4, 56.8, 41.2, 40.9, 31.4, 26.6, 22.0, 17.2, 12.3

$[\alpha]_D^{25}$ +86.25 (*c* 0.6, $CHCl_3$)



45c

Yield 0.58 g (83%)

IR (Neat) (cm^{-1}) 3065, 2926, 2856, 1620, 1593, 1466, 1363, 1280, 1246, 802, 698

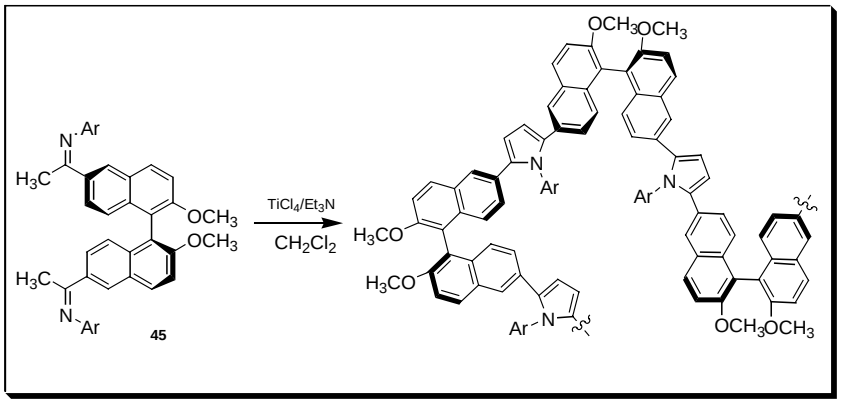
^{1}H-NMR (δ ppm, $CDCl_3$) 8.51-7.15 (m, 20H), 4.04-3.98 (m, 4H), 2.70 (s, 6H), 1.60-0.94 (m, 24H), 0.86 (t, J=7.2, 6H

^{13}C-NMR (δ ppm, $CDCl_3$) 165.1, 155.8, 152, 123.3, 134.5, 134.4, 128.9, 128.5, 127.8, 125.9,5 124.5, 123.0, 120.2, 119.5, 115.8, 69.5, 31.7, 29.4, 29.2, 25.7, 22.7, 17.2, 14.1

$[\alpha]_D^{25}$ +106 (*c* 1, $CHCl_3$)

3.4.5 General procedure for the reaction between 6,6'-diacetylimine –1,1'-bi-2-naphthol ethers and $TiCl_4$

Dichloromethane (25 mL), Et_3N (3 mmol) and ketimine **45** (1 mmol) were taken under an N_2 atmosphere. $TiCl_4$ (2.5 mmol) in CH_2Cl_2 (10 ml) was added drop wise under N_2 at 0 °C for 15 min. The reaction mixture was stirred for 0.5 h at 0 °C and stirred further for 7-8 h at 25 °C. It was quenched with a saturated K_2CO_3 solution (10 mL), and the reaction mixture was filtered through a Buchner funnel. Insoluble light brown color solid was washed with water and CH_2Cl_2.


N
Ar
H3C
OCH3
OCH3
H3C
N
Ar
45
TiCl4/Et3N
CH2Cl2
OCH3OCH3
N
Ar
H3CO
H3CO
N
Ar
N
Ar
OCH3OCH3

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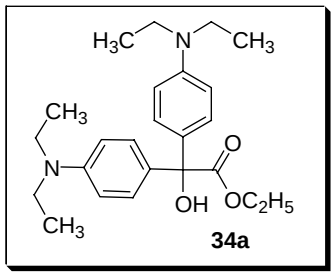
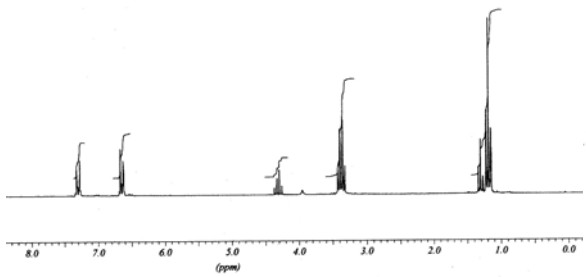
Appendix I

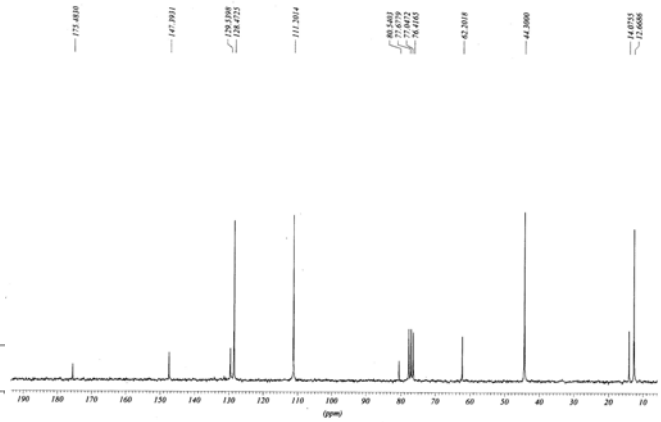
Representative Spectra

Spectrum No. 1 & 2 (Chapter 1, Section 1.4.1.1) ^{1}H NMR and ^{13}C Spectra (200 MHz, 50 MHz, $CDCl_3$)

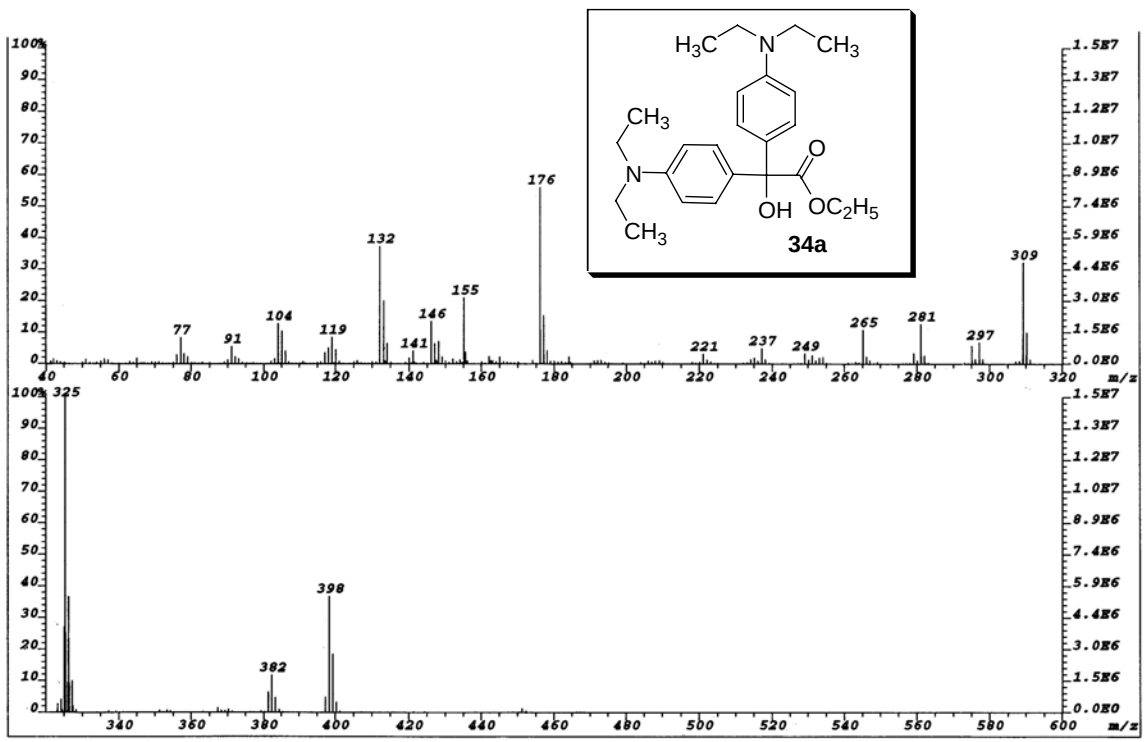


34a

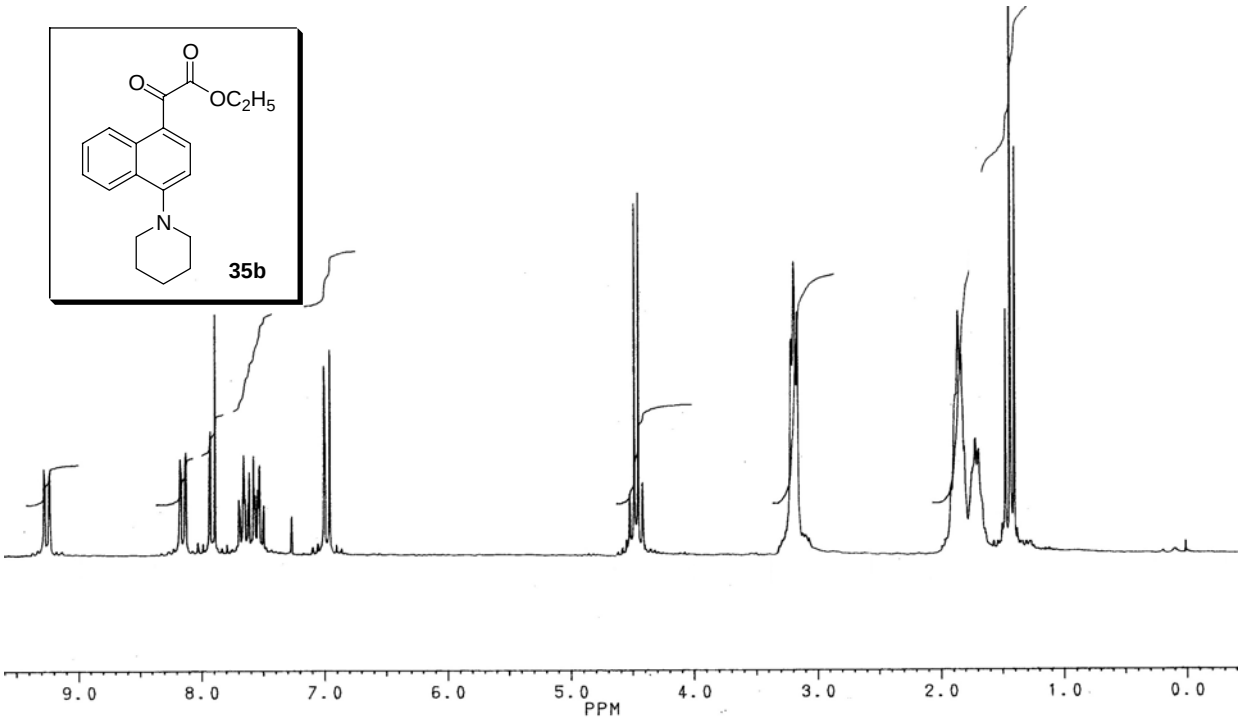




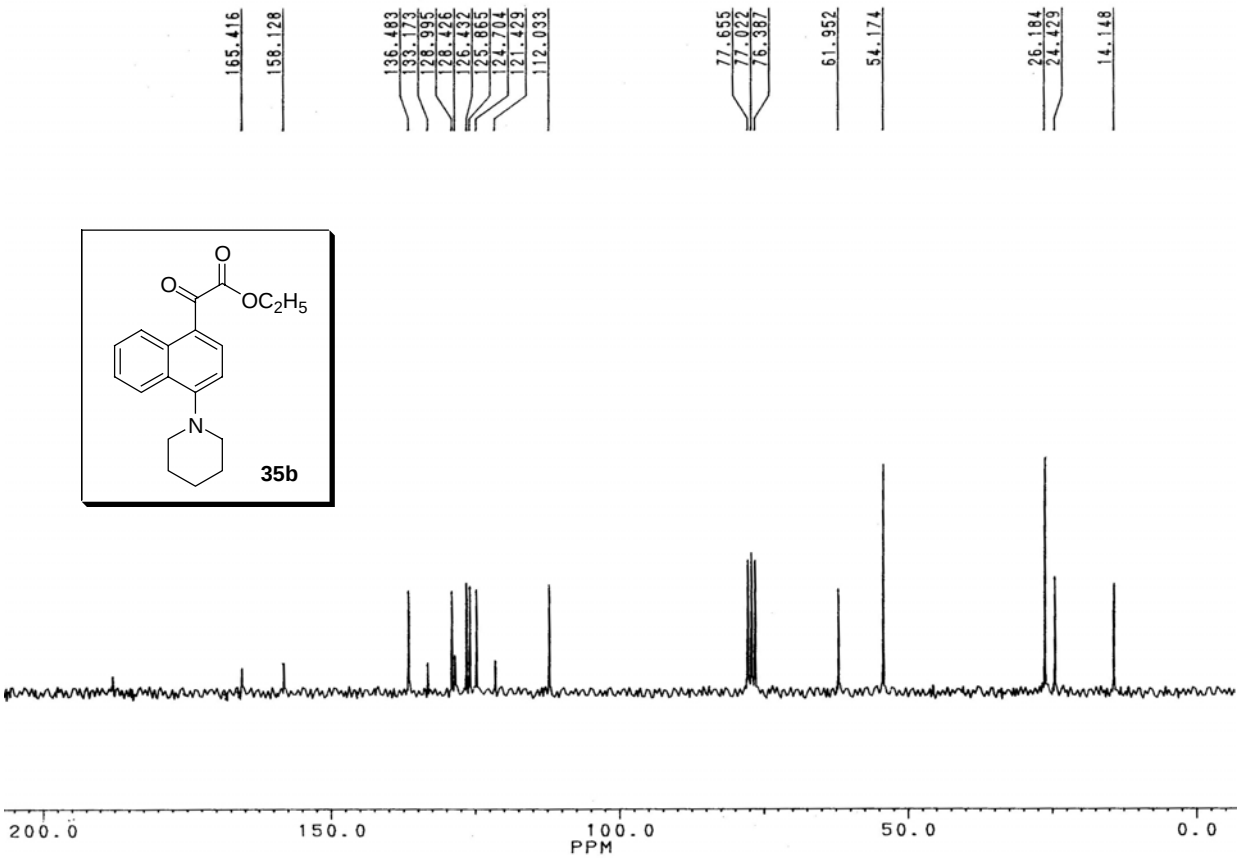
Spectrum No. 3 (Chapter 1, Section 1.4.1.1) Mass Spectrum (EI)



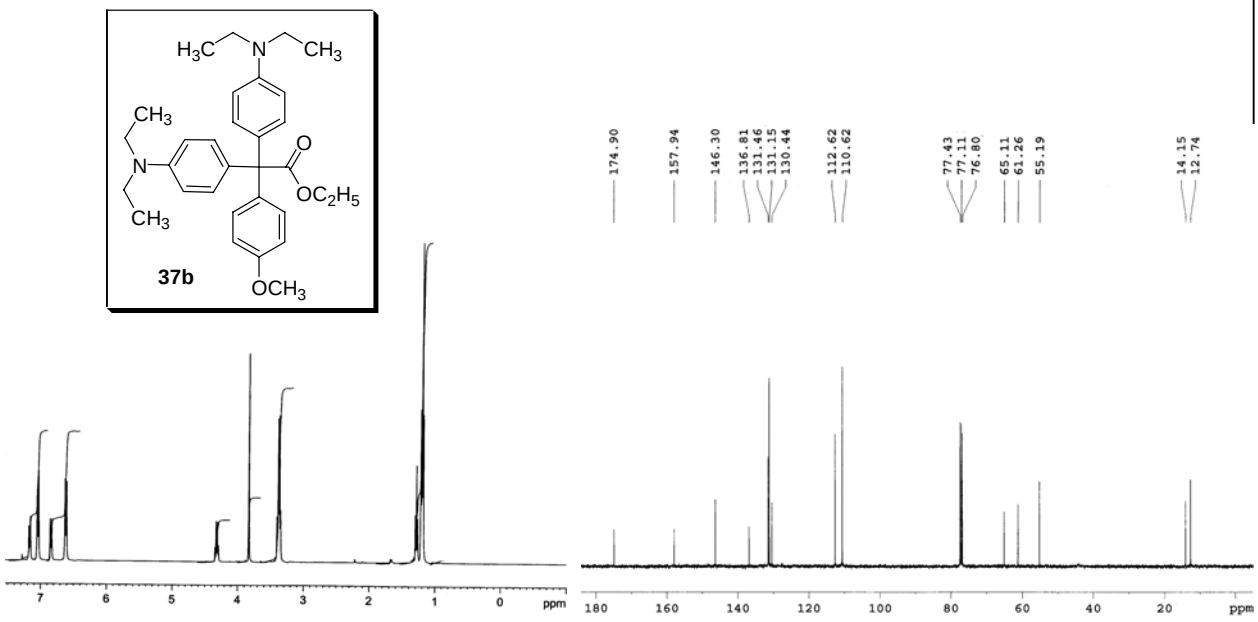
Spectrum No. 4 (Chapter 1, Section 1.4.1.1) ^{1}H NMR Spectrum (200 MHz, $CDCl_3$)



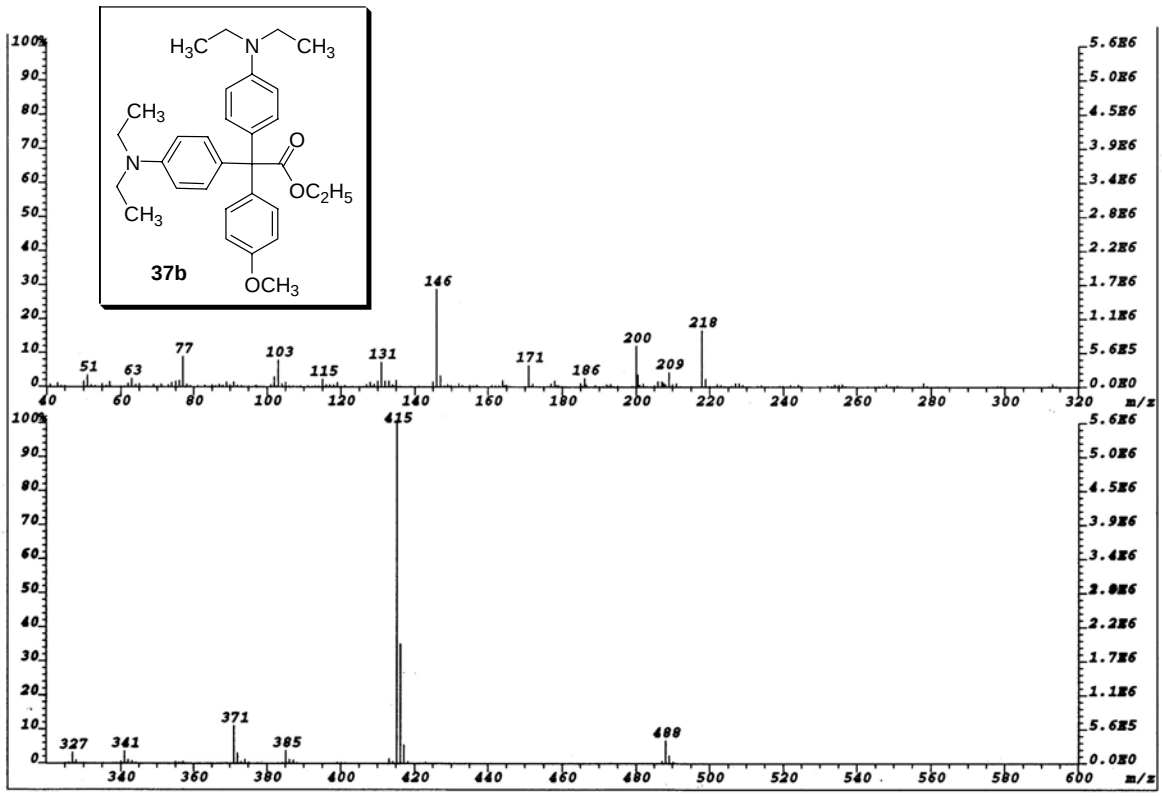
Spectrum No.5 (Chapter 1, Section 1.4.1.1) ^{13}C NMR Spectrum (50 MHz, $CDCl_3$)



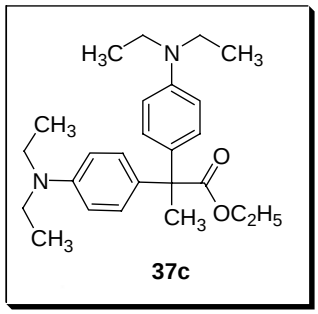
Spectrum No. 6 & 7 (Chapter 1, Section 1.4.1.2) ^{1}H and ^{13}C NMR Spectra (400 MHz and 100 MHz, $CDCl_3$)



Spectrum No. 8 (Chapter 1, Section 1.4.1.2) Mass Spectrum (EI)

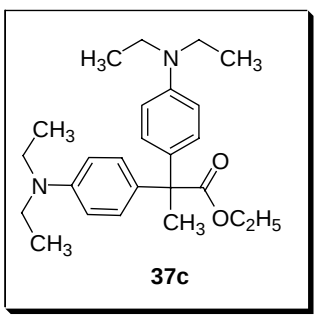


Spectrum No. 9 (Chapter 1, Section 1.4.1.2) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)

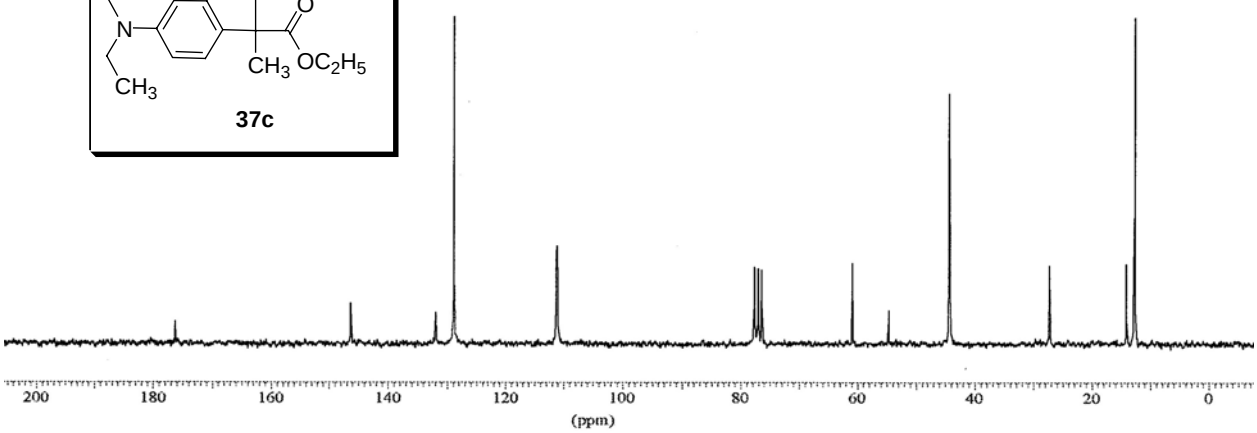


37c

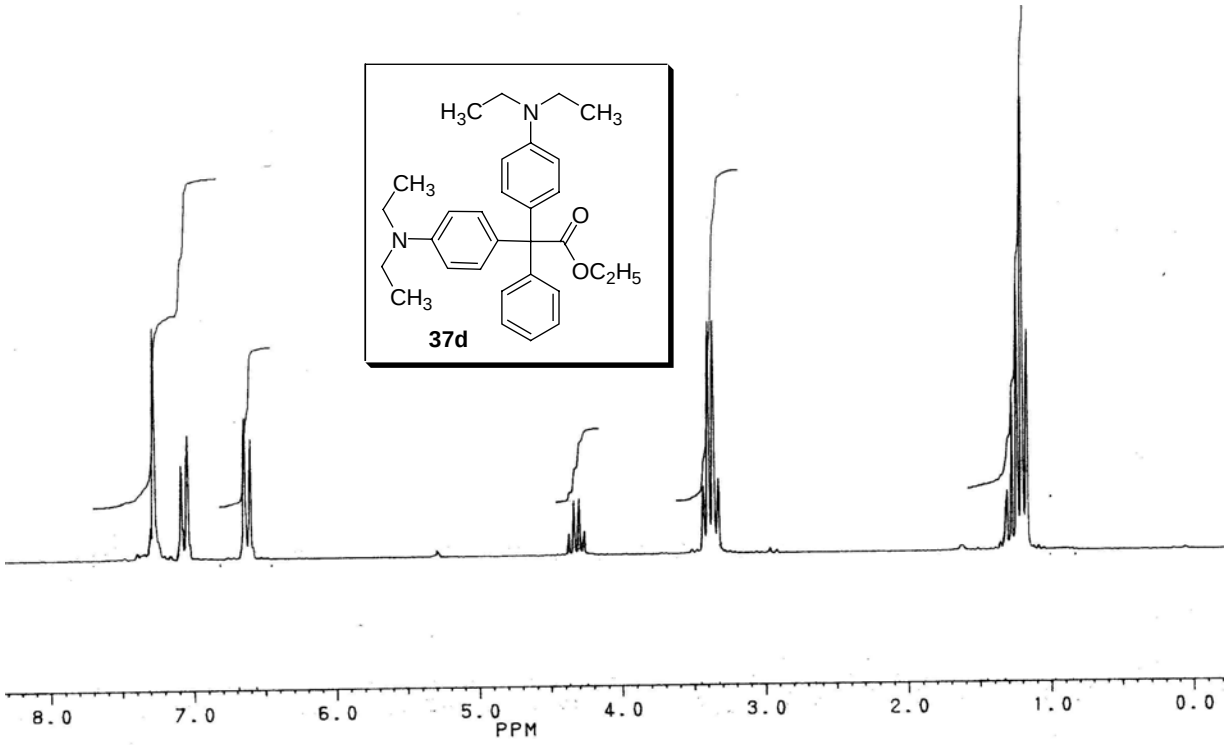
Spectrum No. 10 (Chapter 1, Section 1.4.1.2) ^{13}C NMR Spectrum (50 MHz, $CDCl_3$)



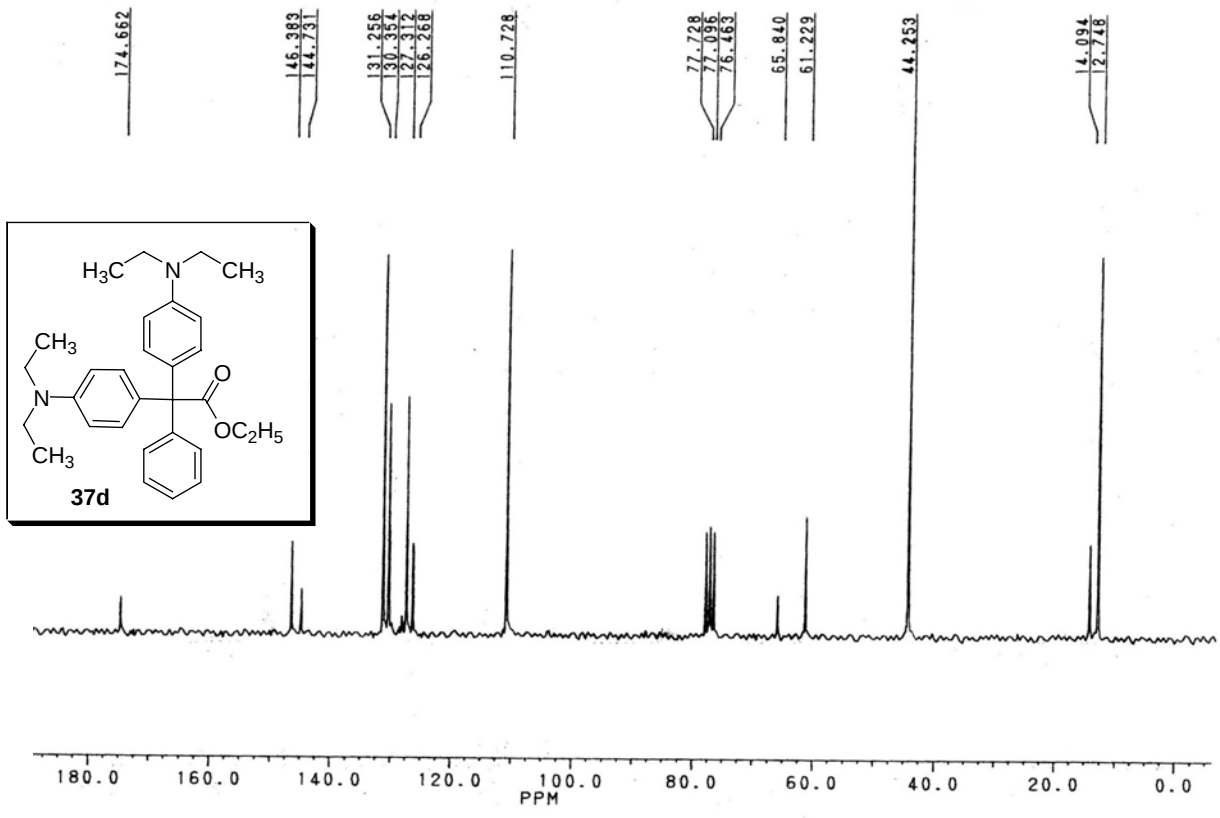
37c



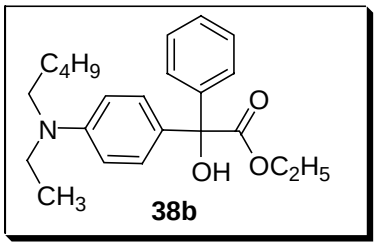
Spectrum No. 11 (Chapter 1, Section 1.4.1.2) ^{1}H NMR Spectrum (200 MHz, $CDCl_3$)



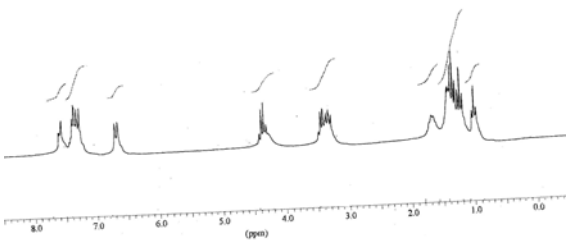
Spectrum No. 12 (Chapter 1, Section 1.4.1.2) ^{13}C NMR Spectrum (50 MHz, $CDCl_3$)

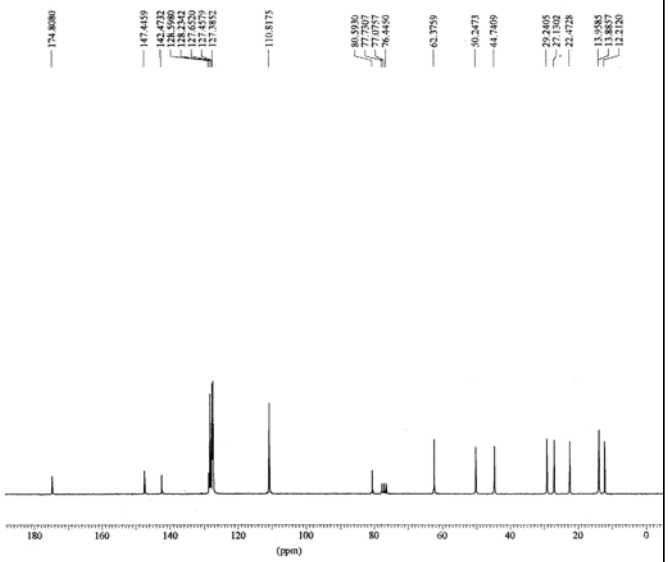


Spectrum No. 13 & 14 (Chapter 1, Section 1.4.1.2) ^{1}H and ^{13}C NMR Spectra (400 and 100 MHz, $CDCl_3$)

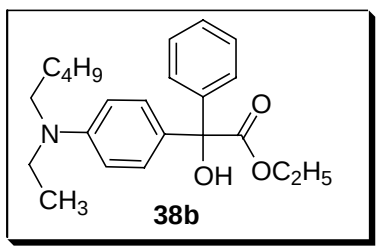


38b



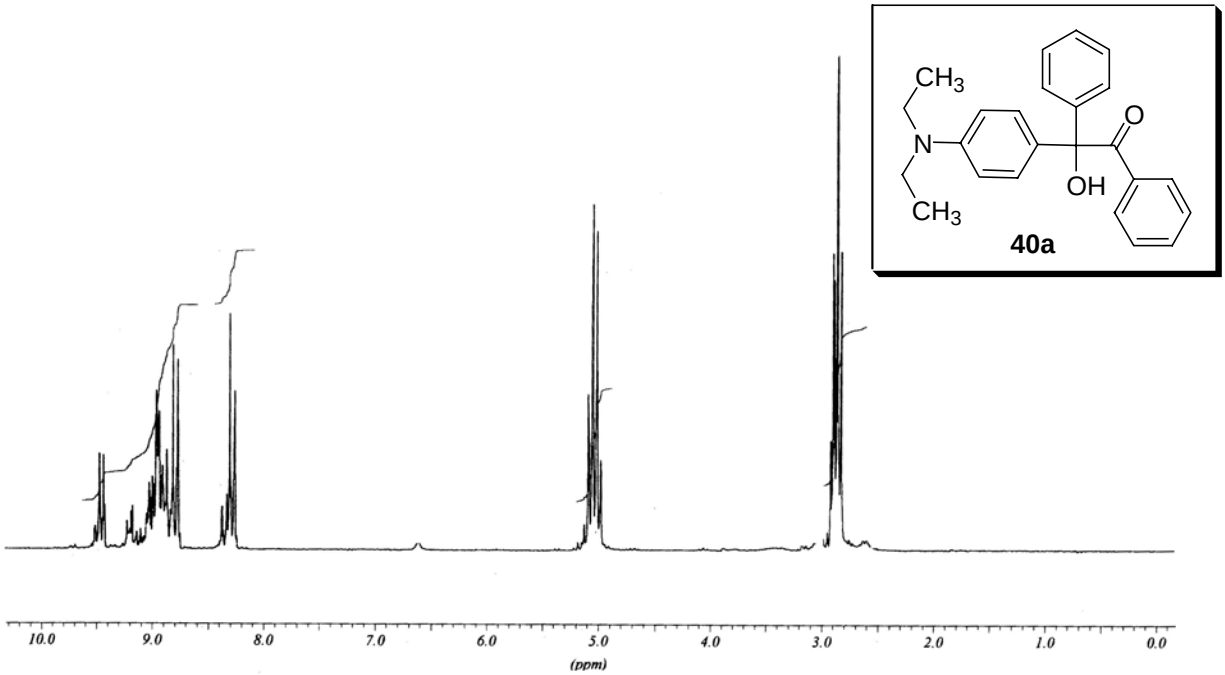


Spectrum No. 15 (Chapter 1, Section 1.4.1.2) Mass Spectrum (EI)

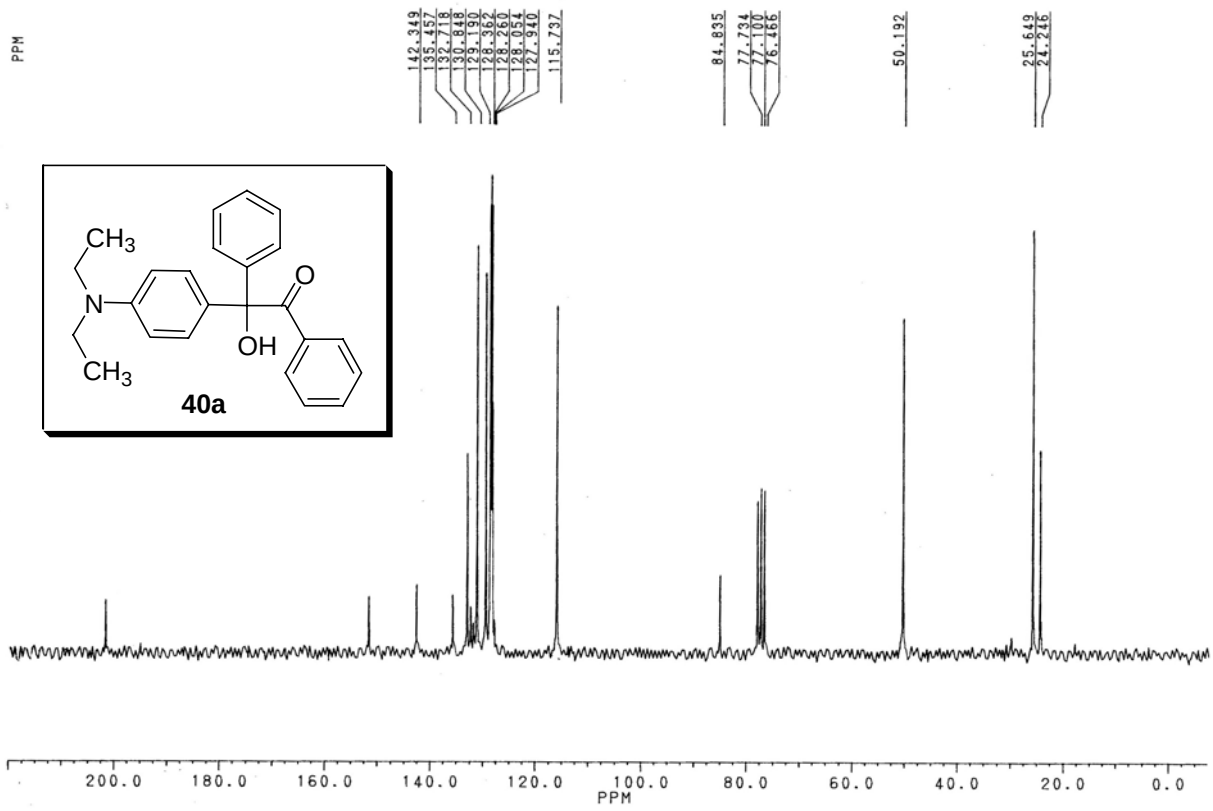


38b

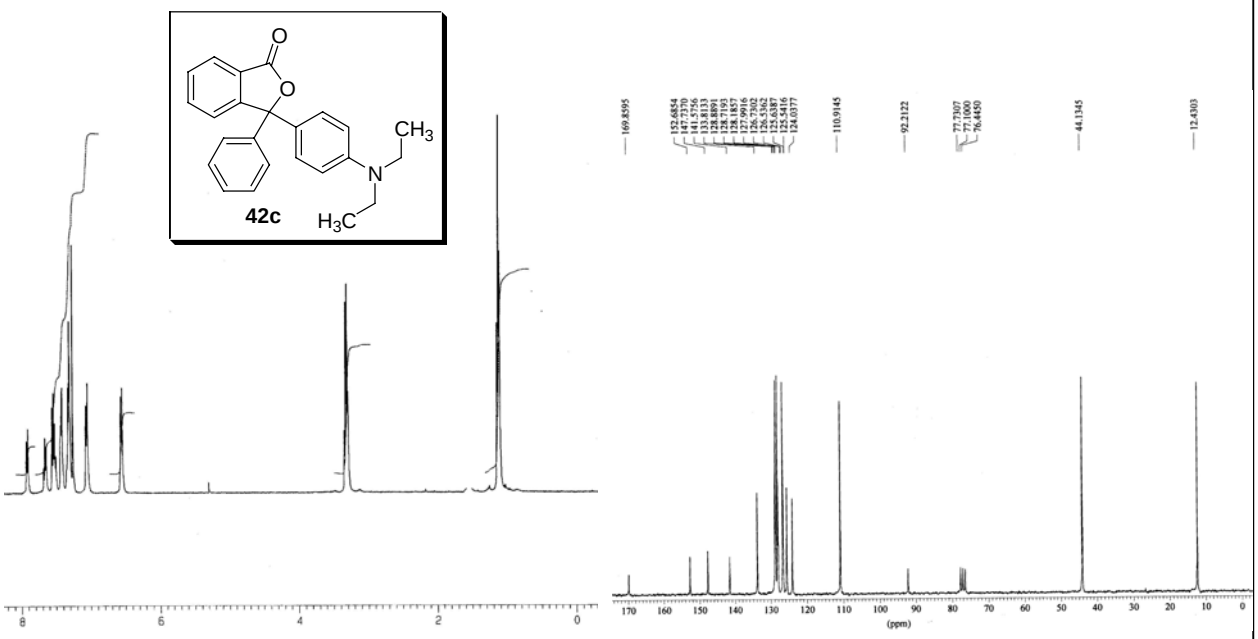
Spectrum No. 16 (Chapter 1, Section 1.4.1.3) ^{1}H NMR Spectrum (200 MHz, $CDCl_3$)



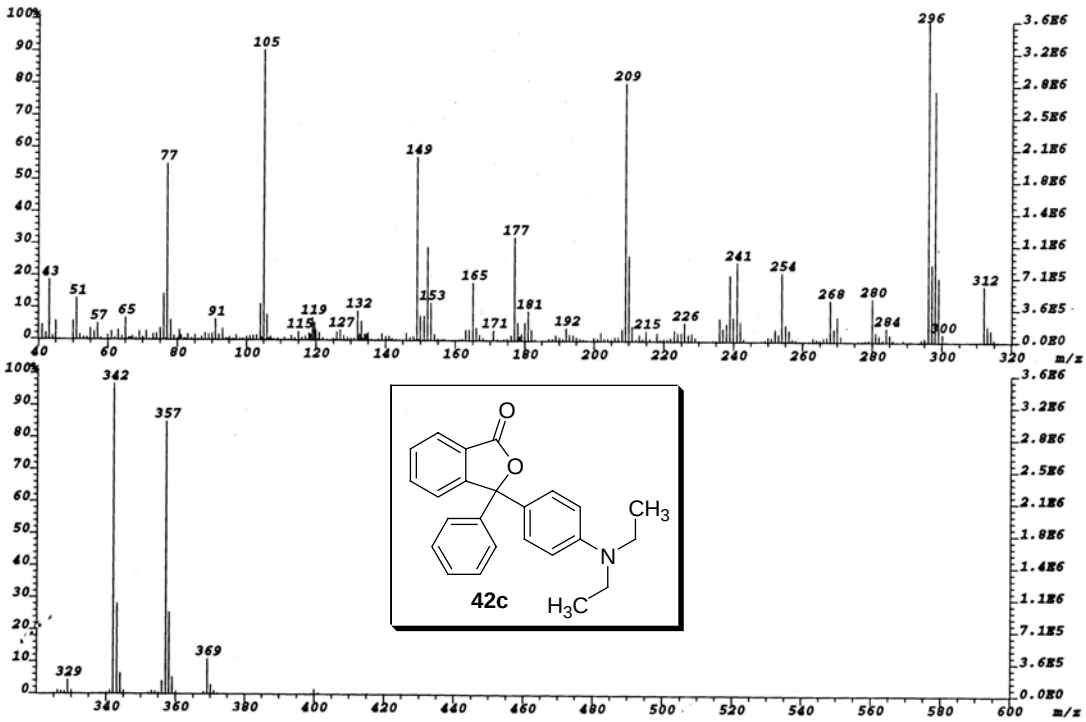
Spectrum No. 17 (Chapter 1, Section 1.4.1.3) ^{13}C NMR Spectrum (50 MHz, $CDCl_3$)



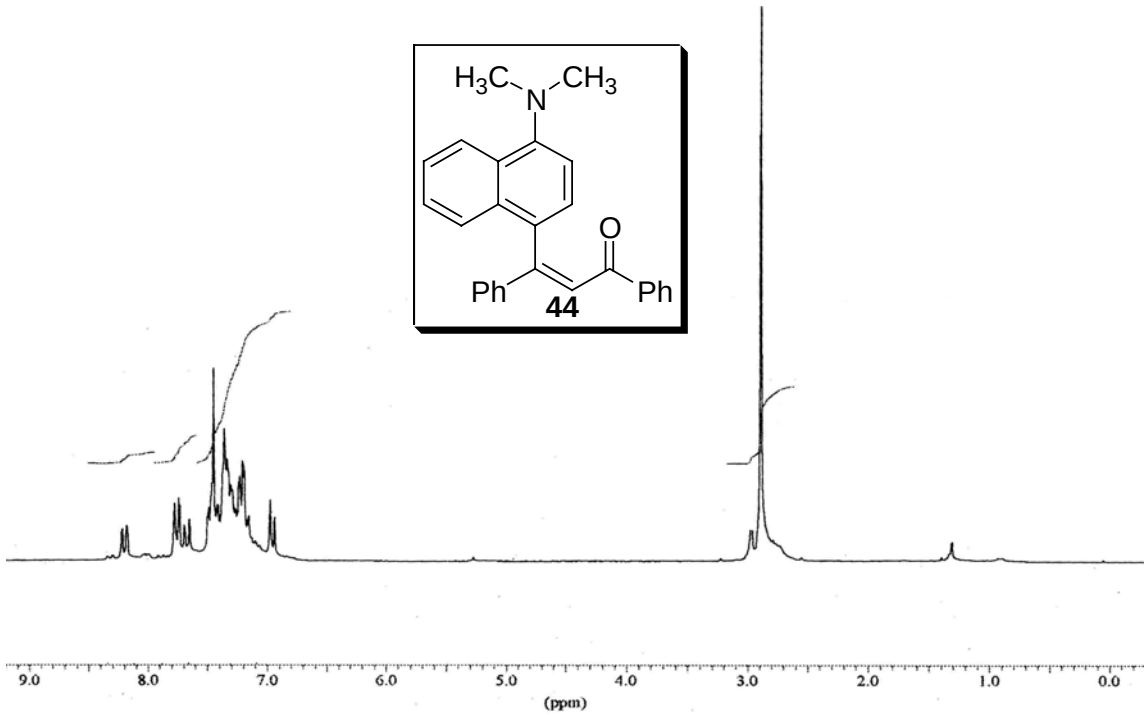
Spectrum No. 18 & 19 (Chapter 2, Section 1.4.1.4) ^{1}H and ^{13}C NMR Spectra (200 and 50 MHz, $CDCl_3$)



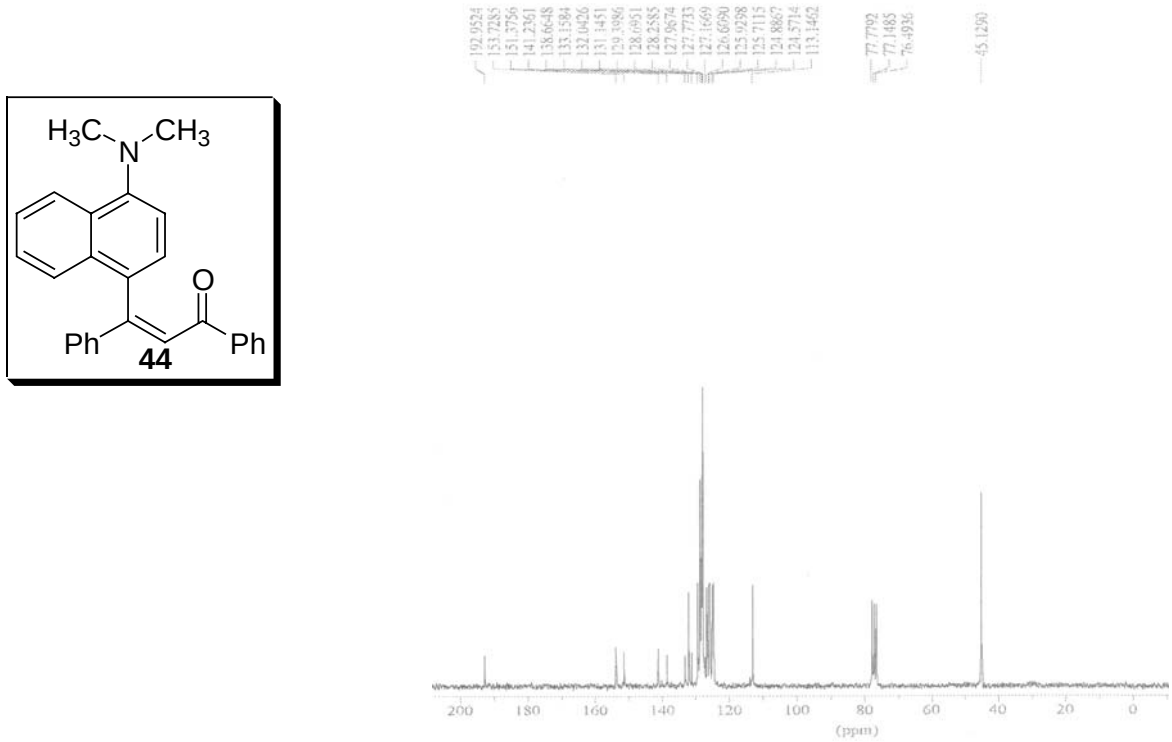
Spectrum No. 20 (Chapter 1, Section 1.4.1.4) Mass Spectrum (EI)



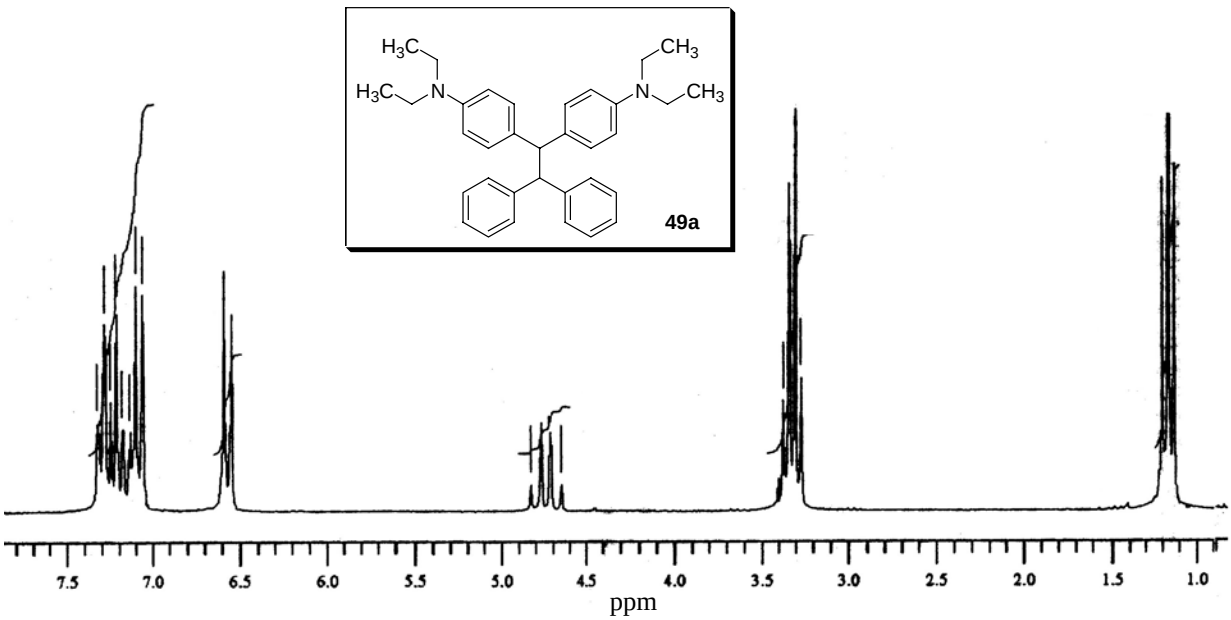
Spectrum No. 21 (Chapter 1, Section 1.4.1.5) ^{1}H NMR Spectrum (200 MHz, $CDCl_3$)



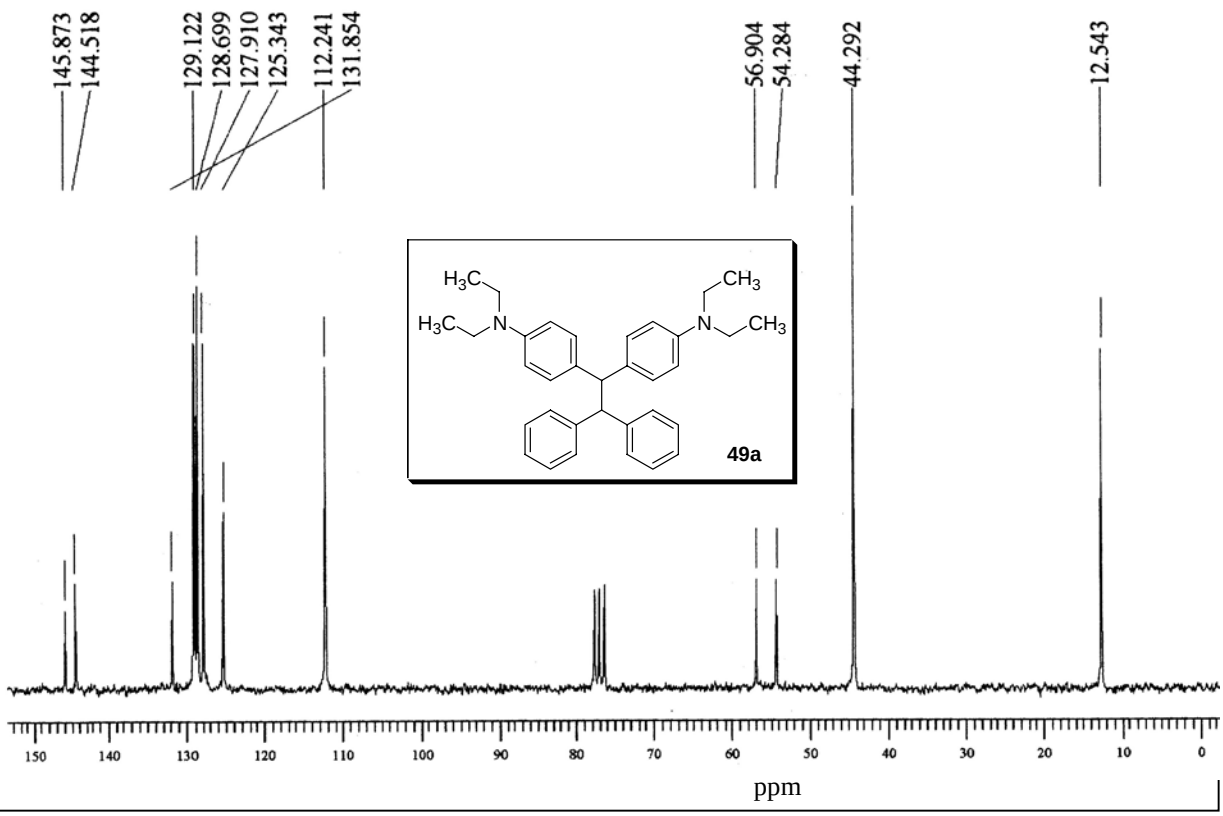
Spectrum No. 22 (Chapter 2, Section 1.4.1.5) ^{13}C NMR Spectrum (50 MHz, $CDCl_3$)



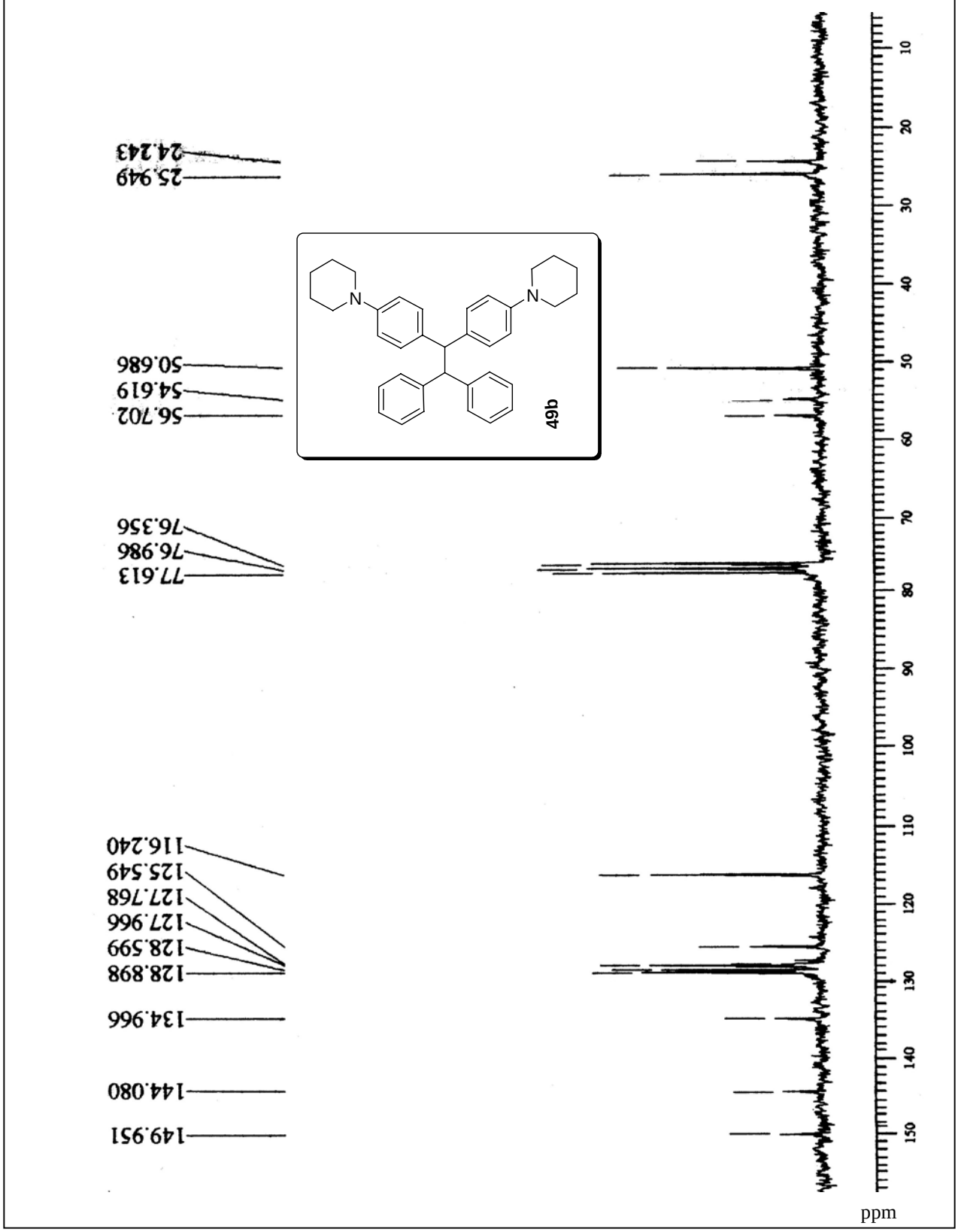
Spectrum No. 23 (Chapter 1, Section 1.4.1.6) ^{1}H NMR Spectrum (200 MHz, $CDCl_3$)



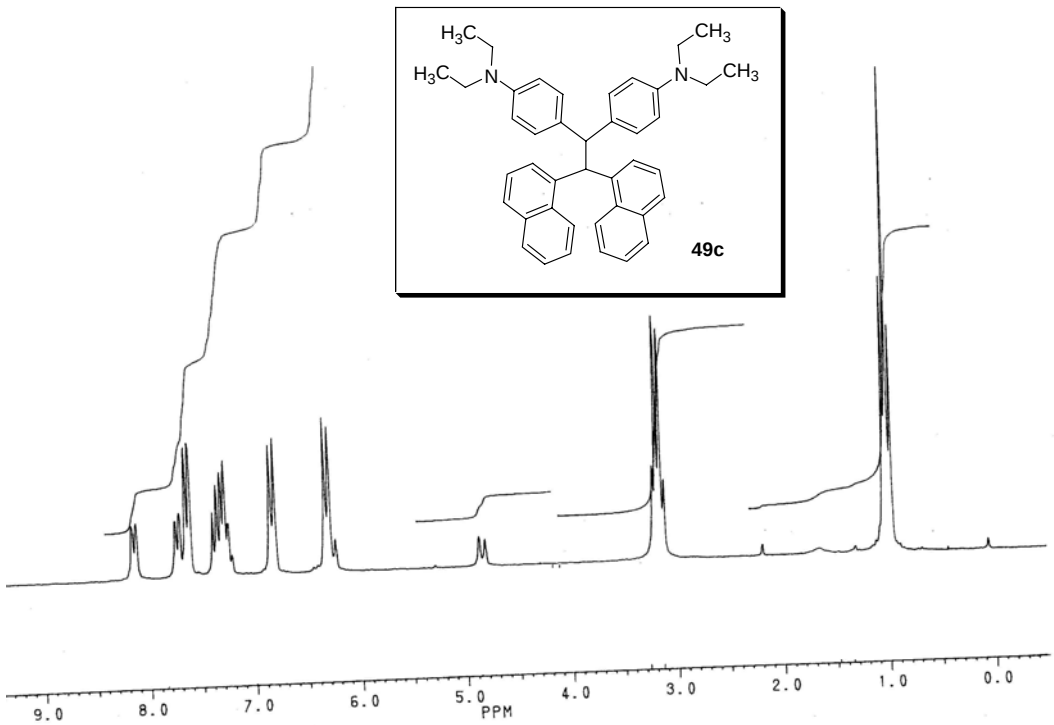
Spectrum No. 24 (Chapter 1, Section 1.4.1.6) ^{13}C NMR Spectrum (50 MHz, $CDCl_3$)



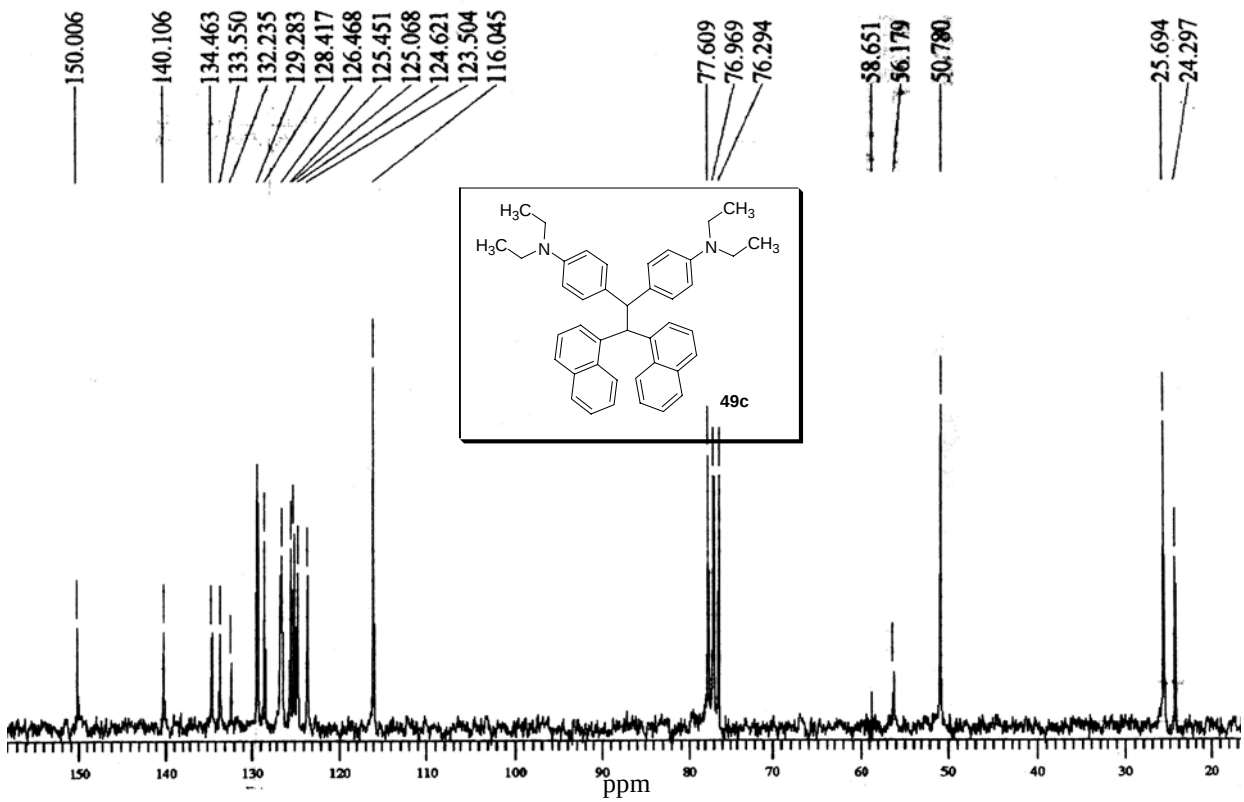
Spectrum No. 25 (Chapter 1, Section 1.4.1.6) ^{13}C NMR Spectrum (50 MHz, $CDCl_3$)



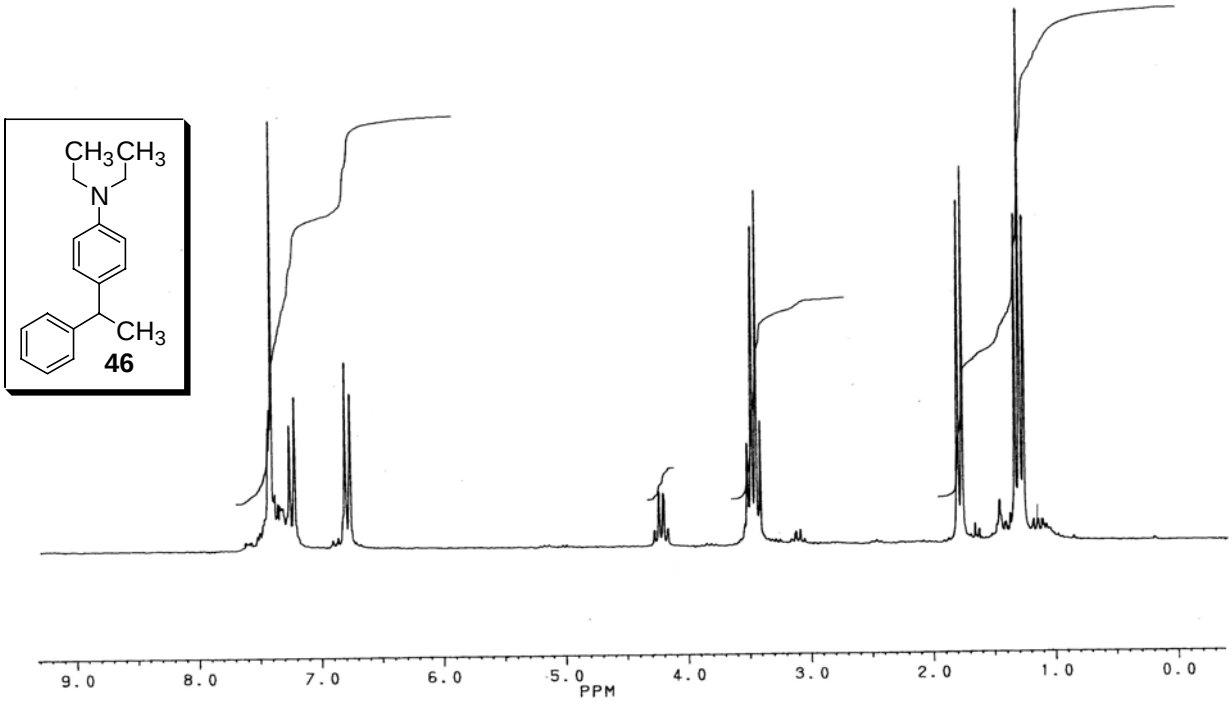
Spectrum No. 26 (Chapter 1, Section 1.4.1.6) ^{1}H NMR Spectrum (200 MHz, $CDCl_3$)



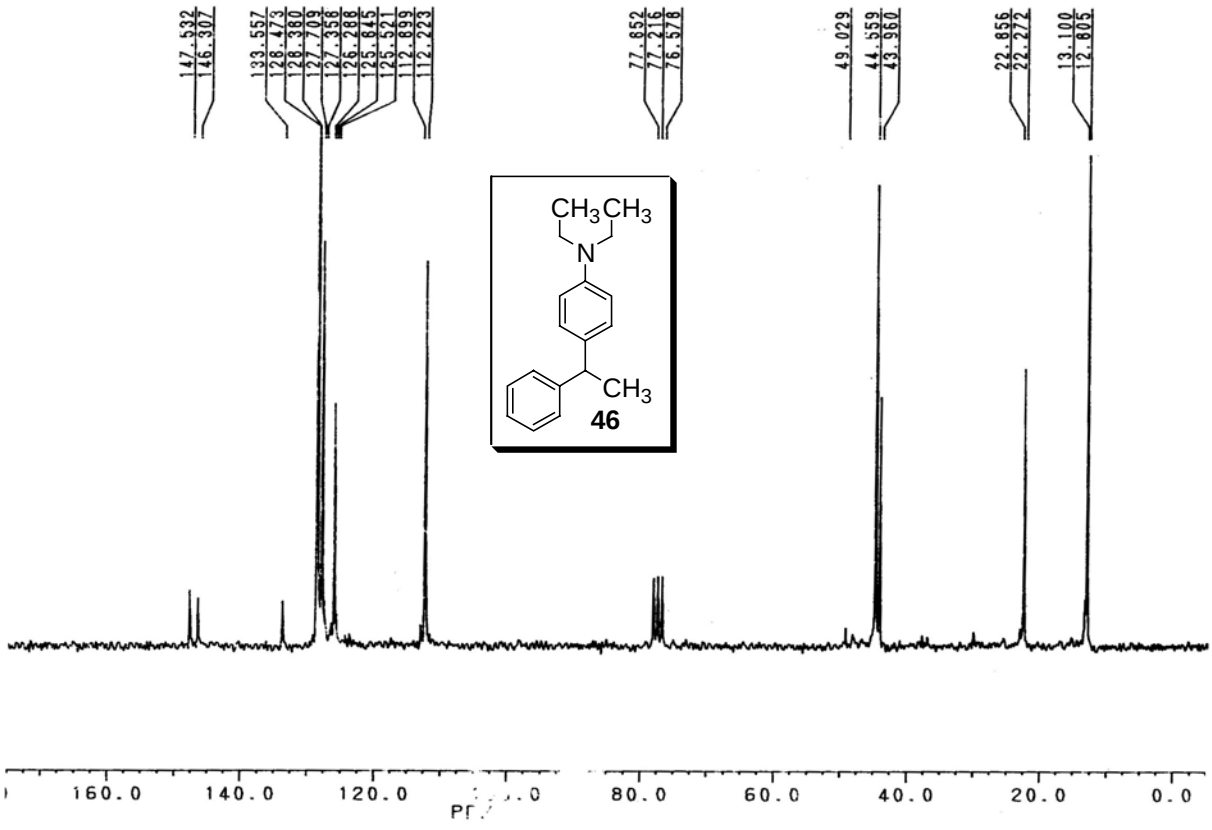
Spectrum No. 27 (Chapter 1, Section 1.4.1.6) ^{13}C NMR Spectrum (50 MHz, $CDCl_3$)



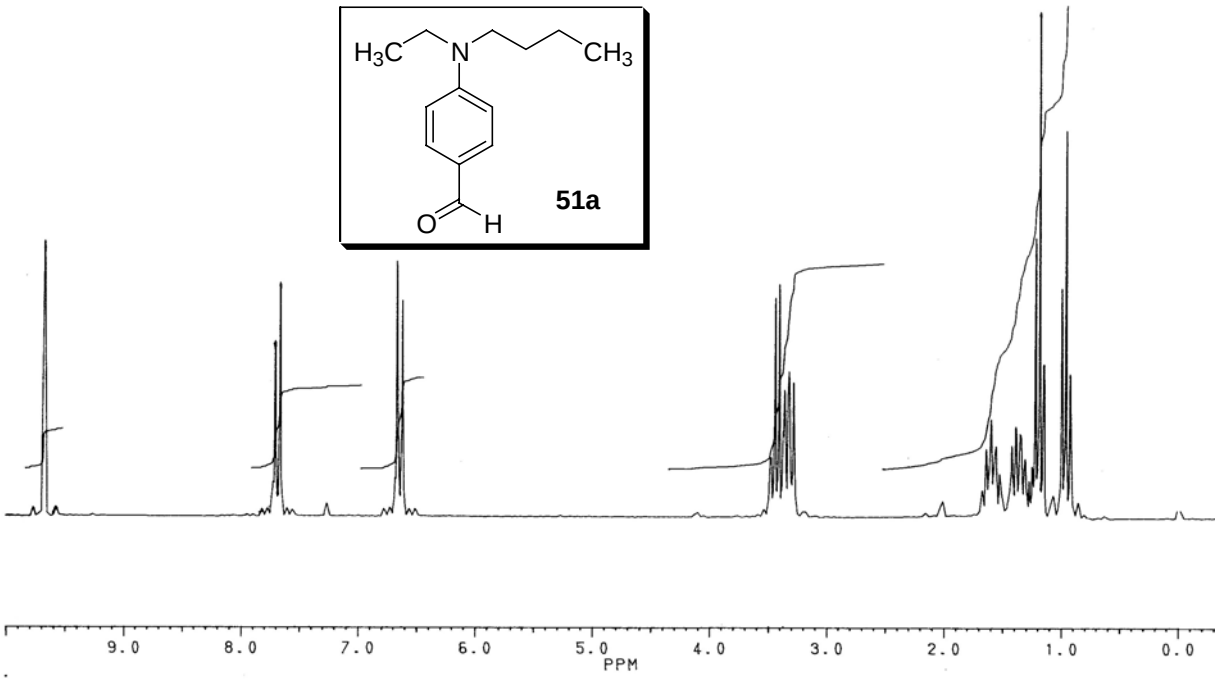
Spectrum No. 28 (Chapter 1, Section 1.4.1.7) ^{1}H NMR Spectrum (200 MHz, $CDCl_3$)



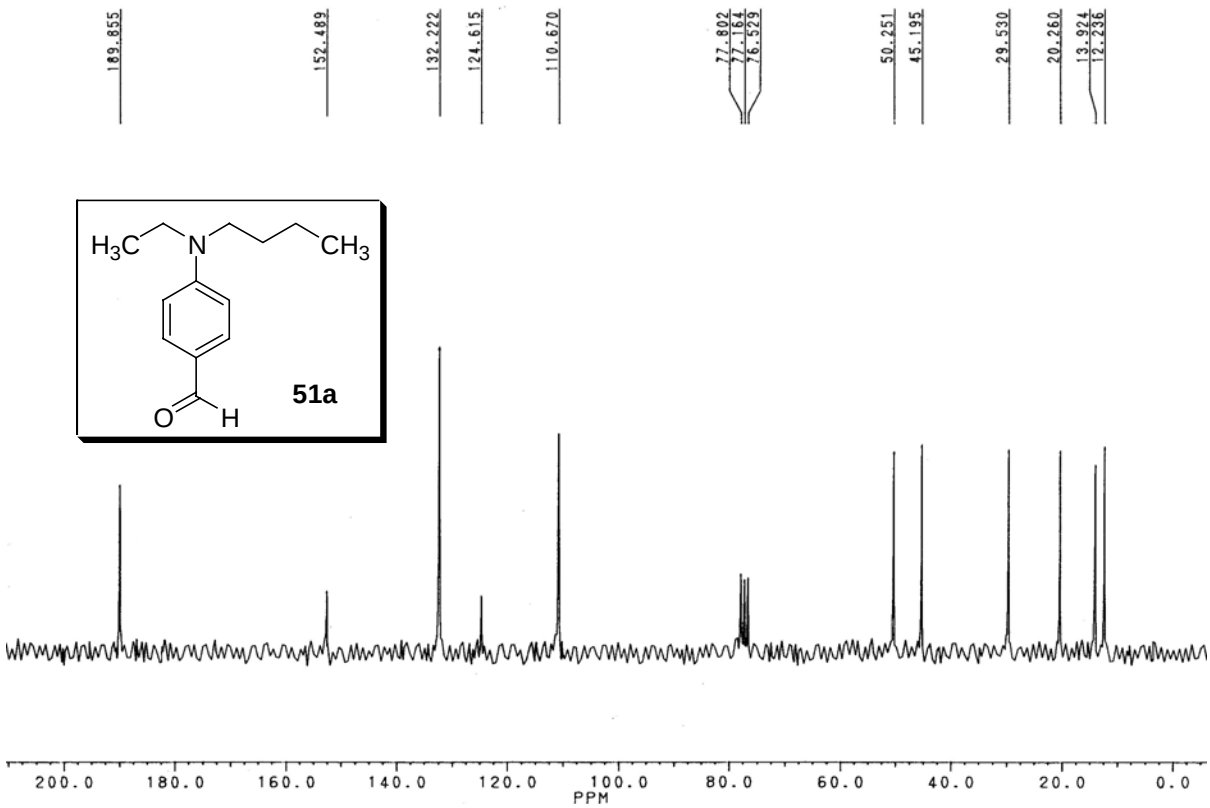
Spectrum No. 29 (Chapter 1, Section 1.4.1.7) ^{13}C NMR Spectrum (50 MHz, $CDCl_3$)



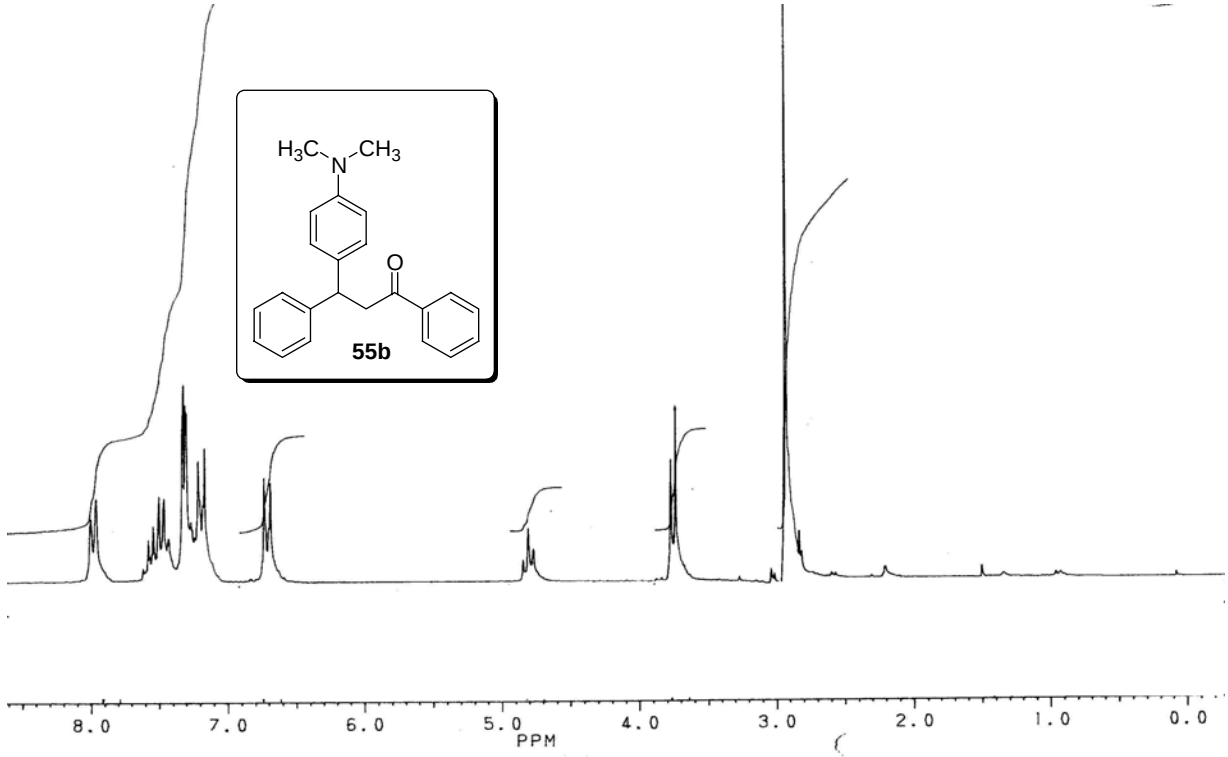
Spectrum No. 30 (Chapter 1, Section 1.4.1.8) ^{1}H NMR Spectrum (100 MHz, $CDCl_3$)



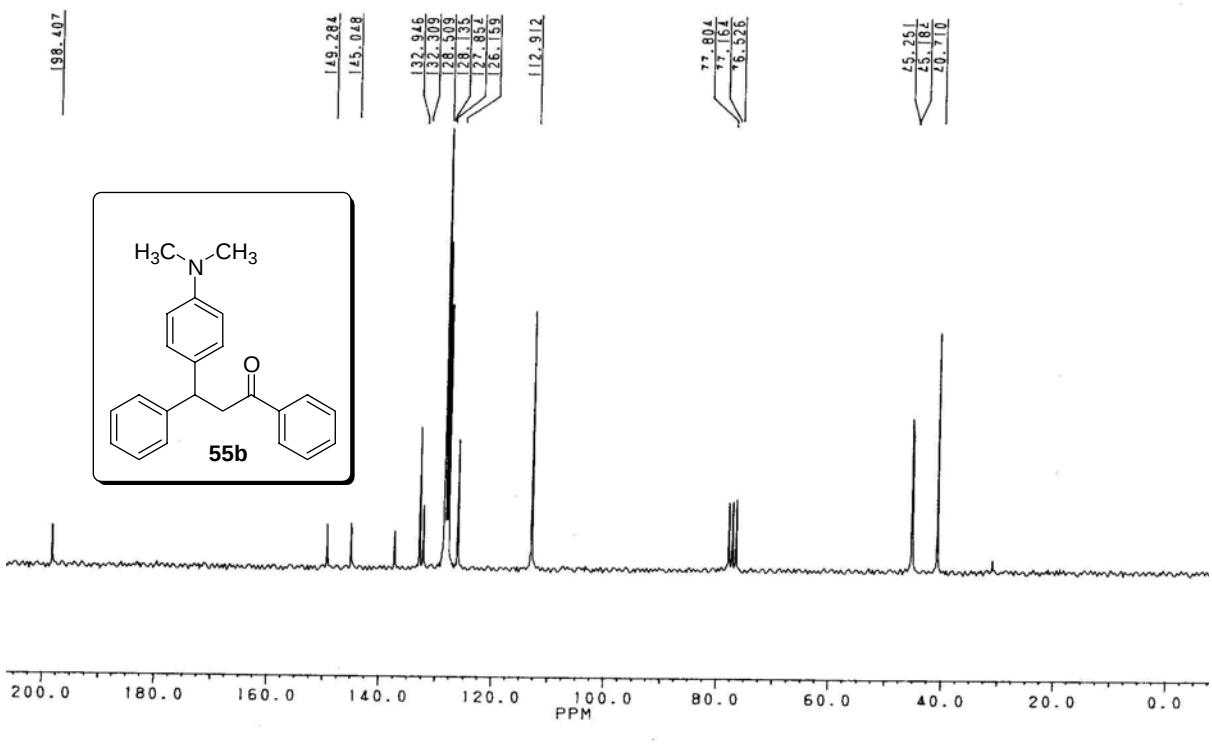
Spectrum No. 31 (Chapter 1, Section 1.4.1.8) ^{13}C NMR Spectrum (50 MHz, $CDCl_3$)



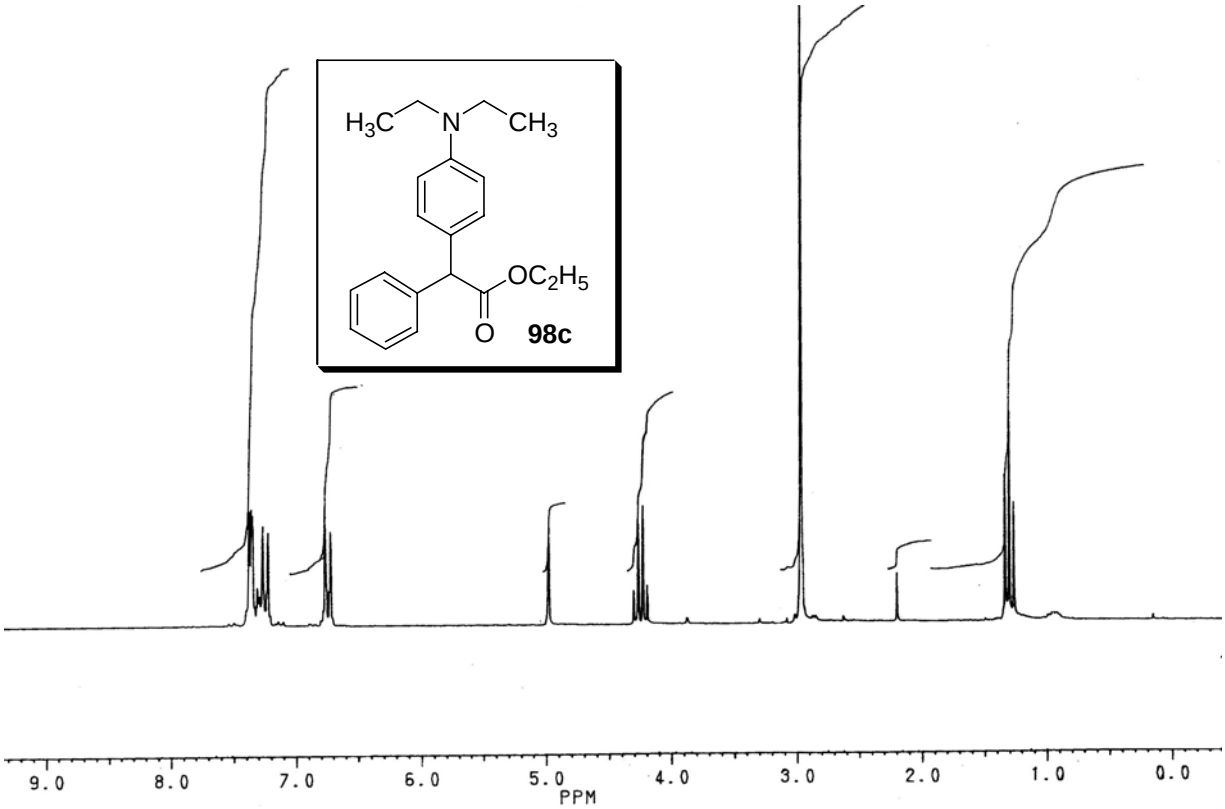
Spectrum No. 32 (Chapter 1, Section 1.4.2.4) ^{1}H NMR Spectrum (200 MHz, $CDCl_3$)



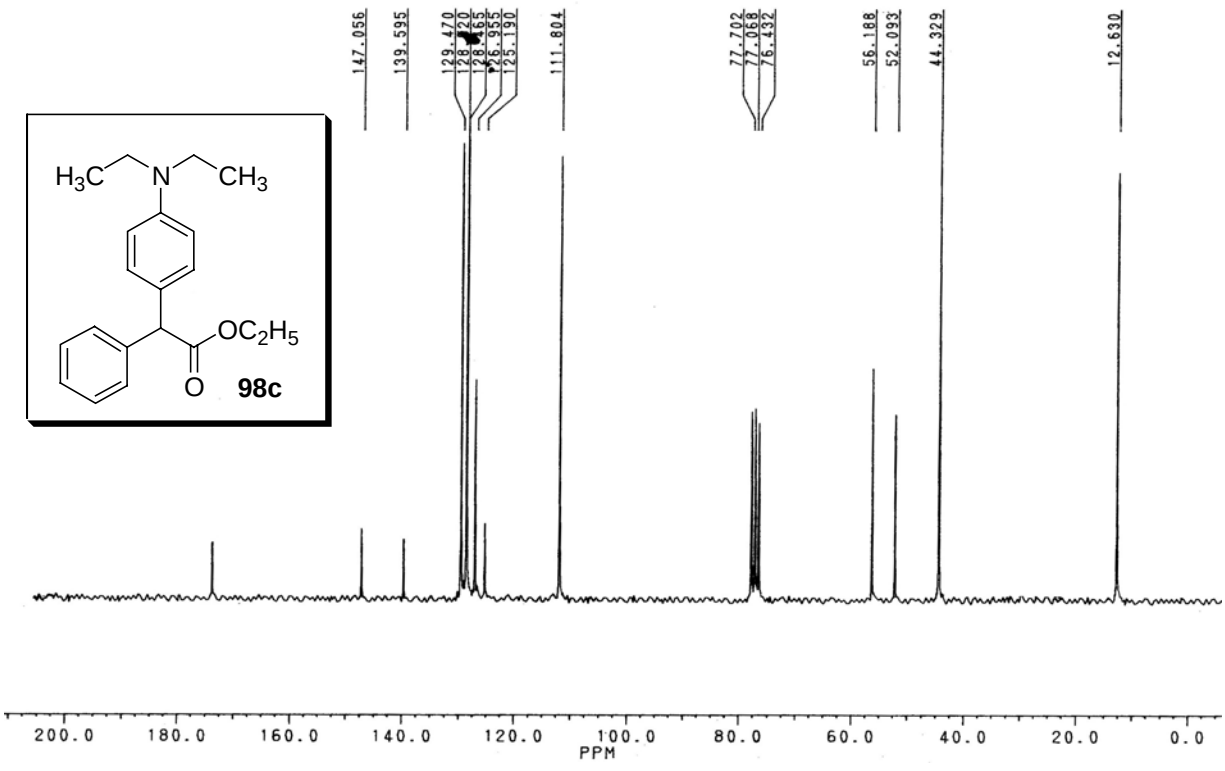
Spectrum No. 33 (Chapter 1, Section 1.4.2.4) ^{13}C NMR Spectrum (50 MHz, $CDCl_3$)



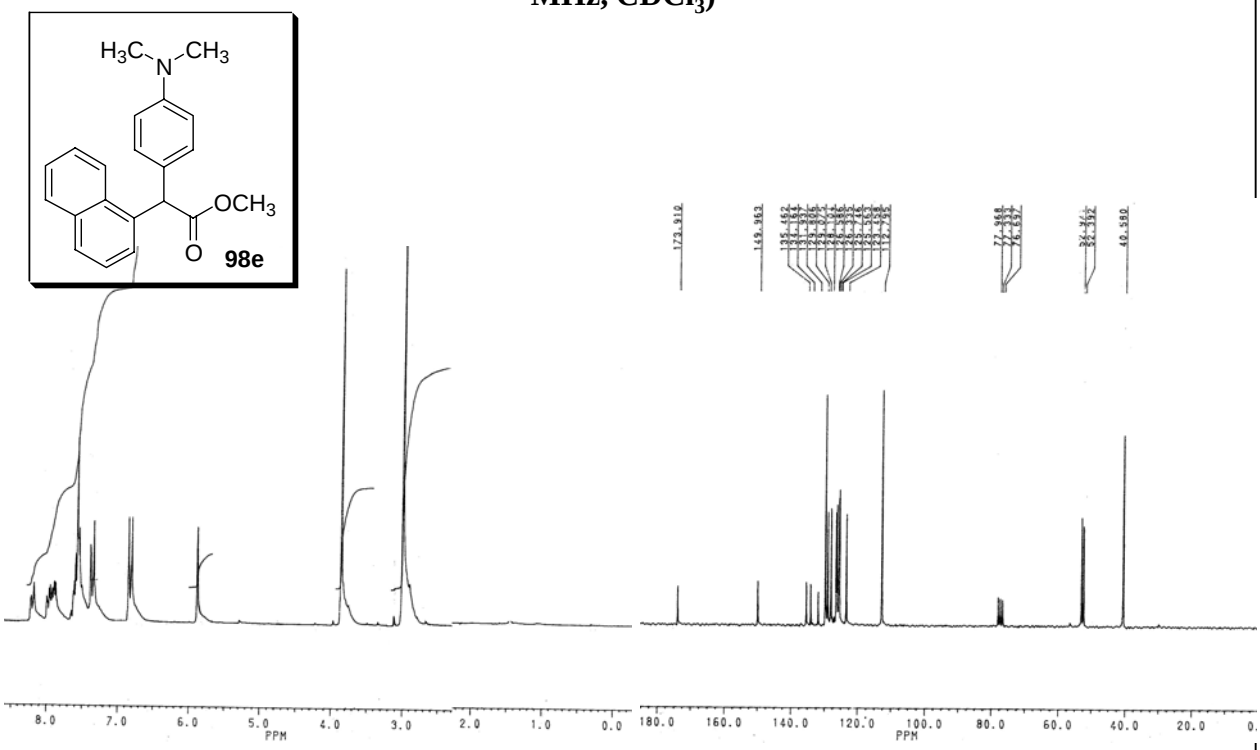
Spectrum No. 34 (Chapter 2, Section 2.4.1) ^{1}H NMR Spectrum (200 MHz, $CDCl_3$)



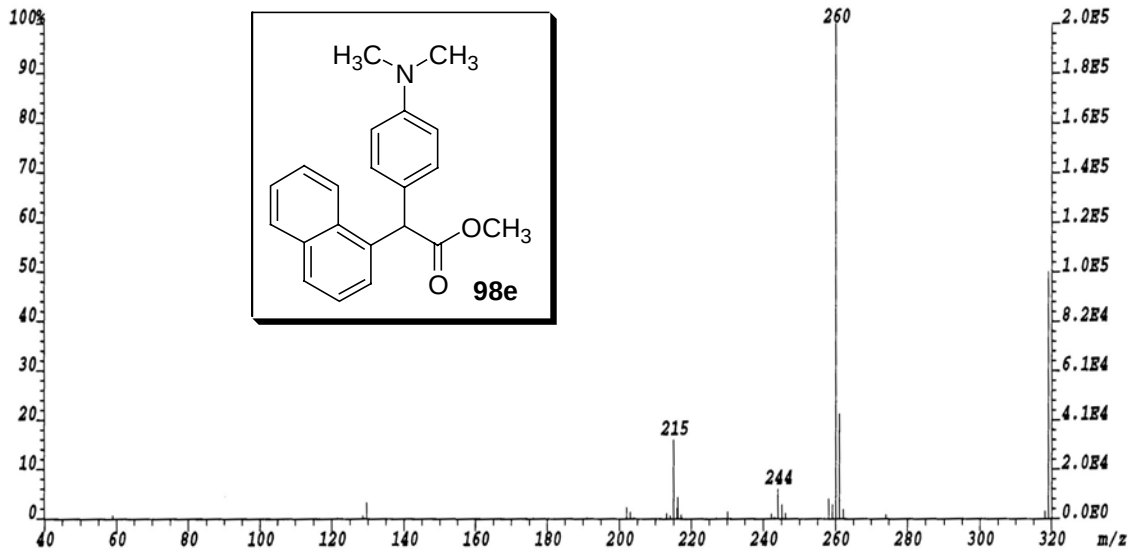
Spectrum No. 35 (Chapter 2, Section 2.4.1) ^{13}C NMR Spectrum (50 MHz, $CDCl_3$)



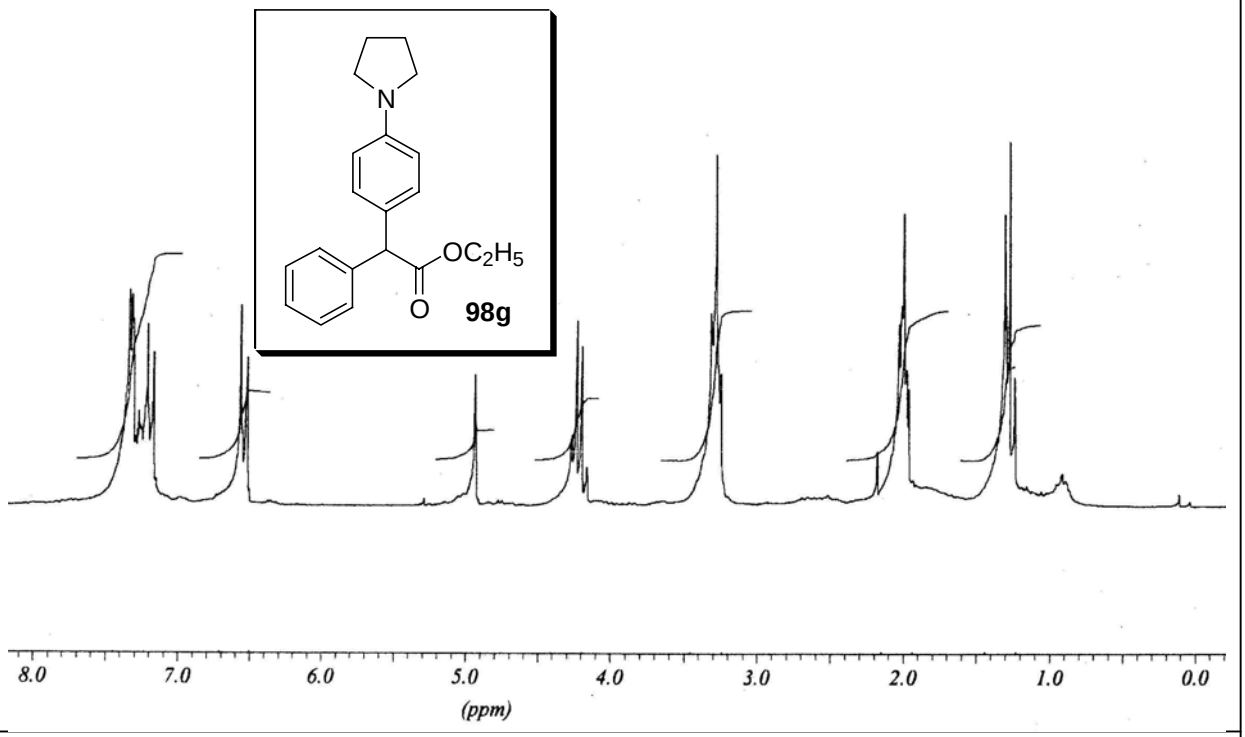
Spectrum No. 36 & 37 (Chapter 2, Section 2.4.1) ^{1}H and ^{13}C NMR Spectra (200 and 50 MHz, $CDCl_3$)



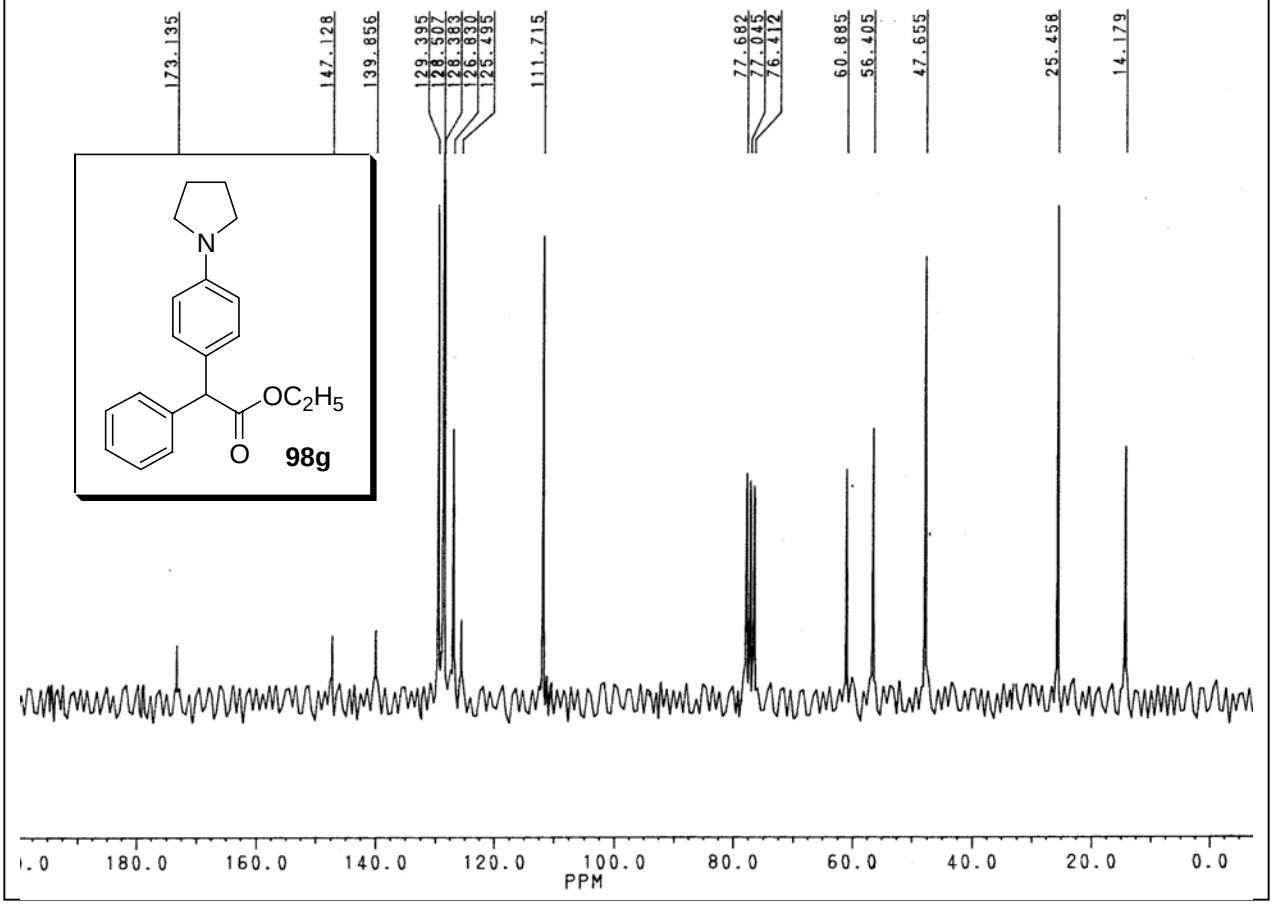
Spectrum No. 38 (Chapter 2, Section 2.4.1) Mass Spectrum (E I)



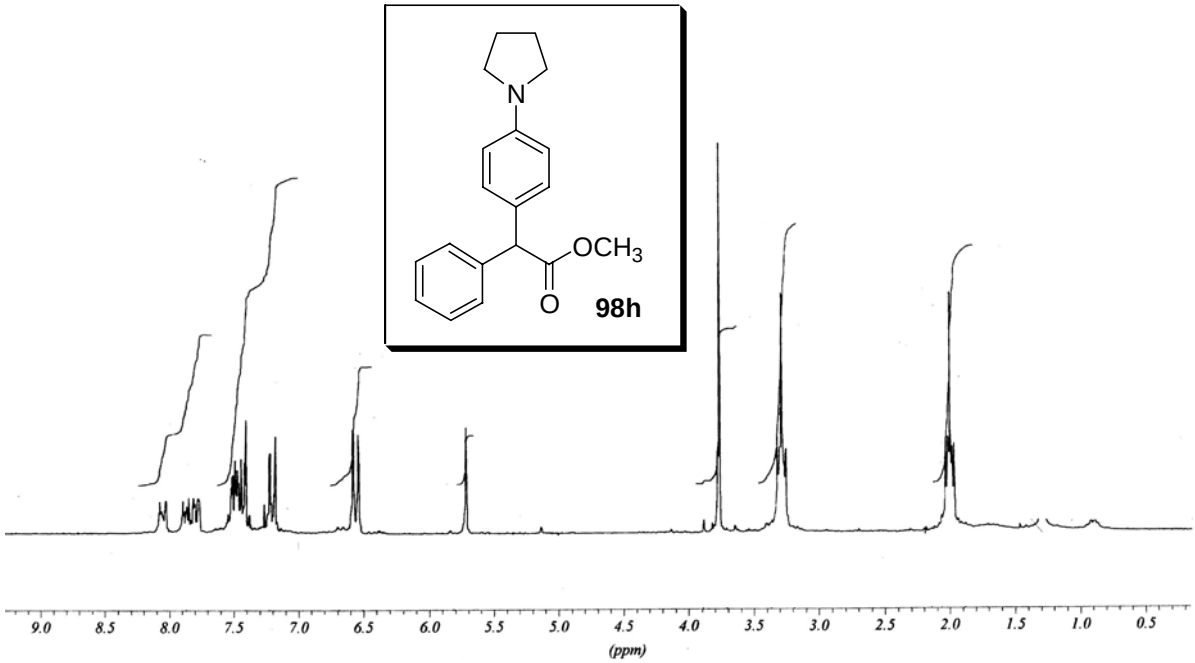
Spectrum No. 39 (Chapter 2, Section 2.4.1) ^{1}H NMR Spectrum (200 MHz, $CDCl_3$)



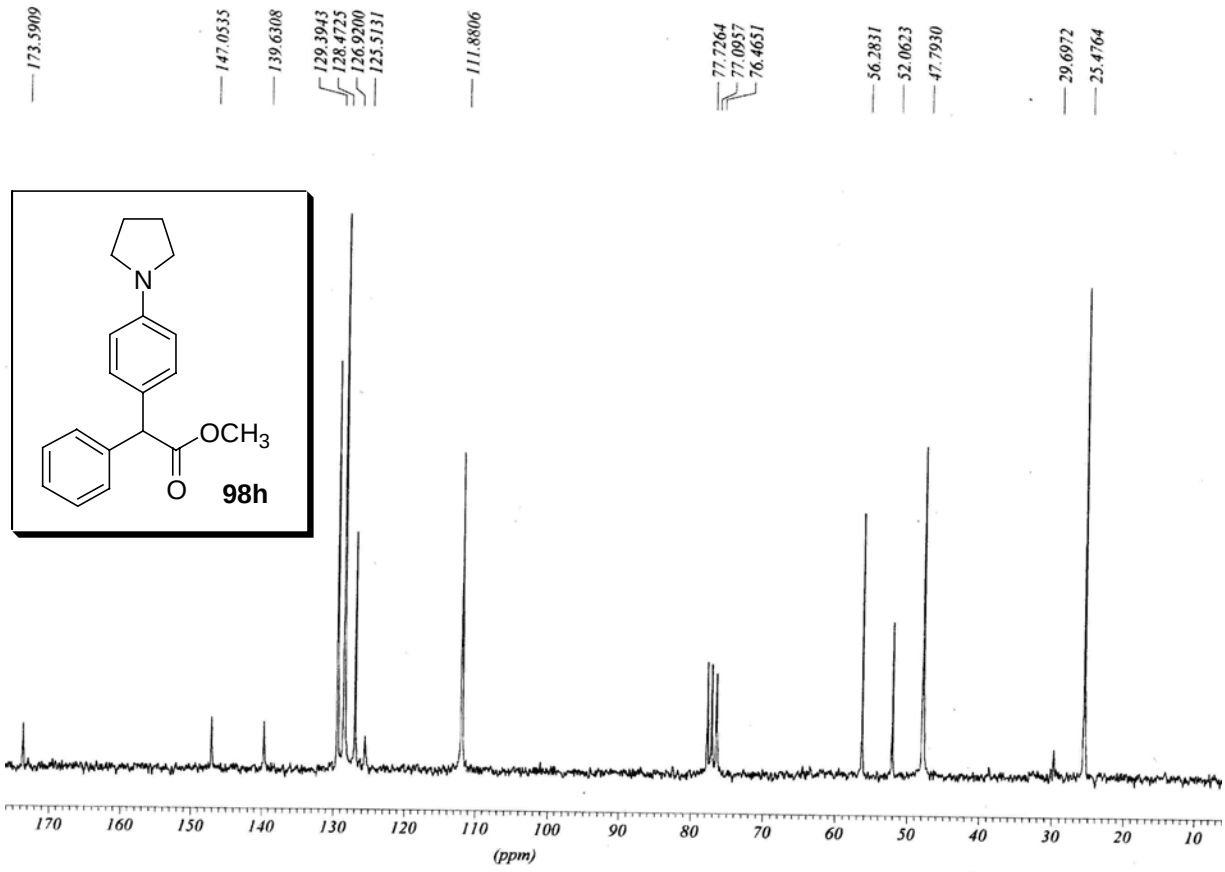
Spectrum No. 40 (Chapter 2, Section 2.4.1) ^{13}C NMR Spectrum (50 MHz, $CDCl_3$)



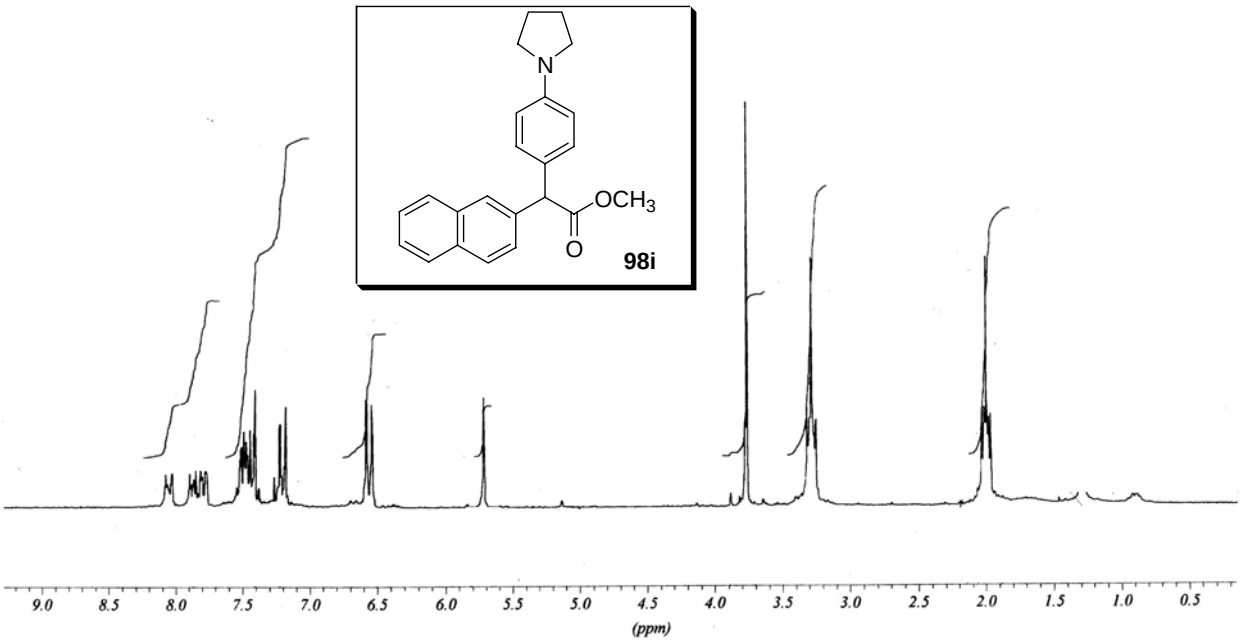
Spectrum No. 41 (Chapter 2, Section 2.4.1) ^{1}H NMR Spectrum (200 MHz, $CDCl_3$)



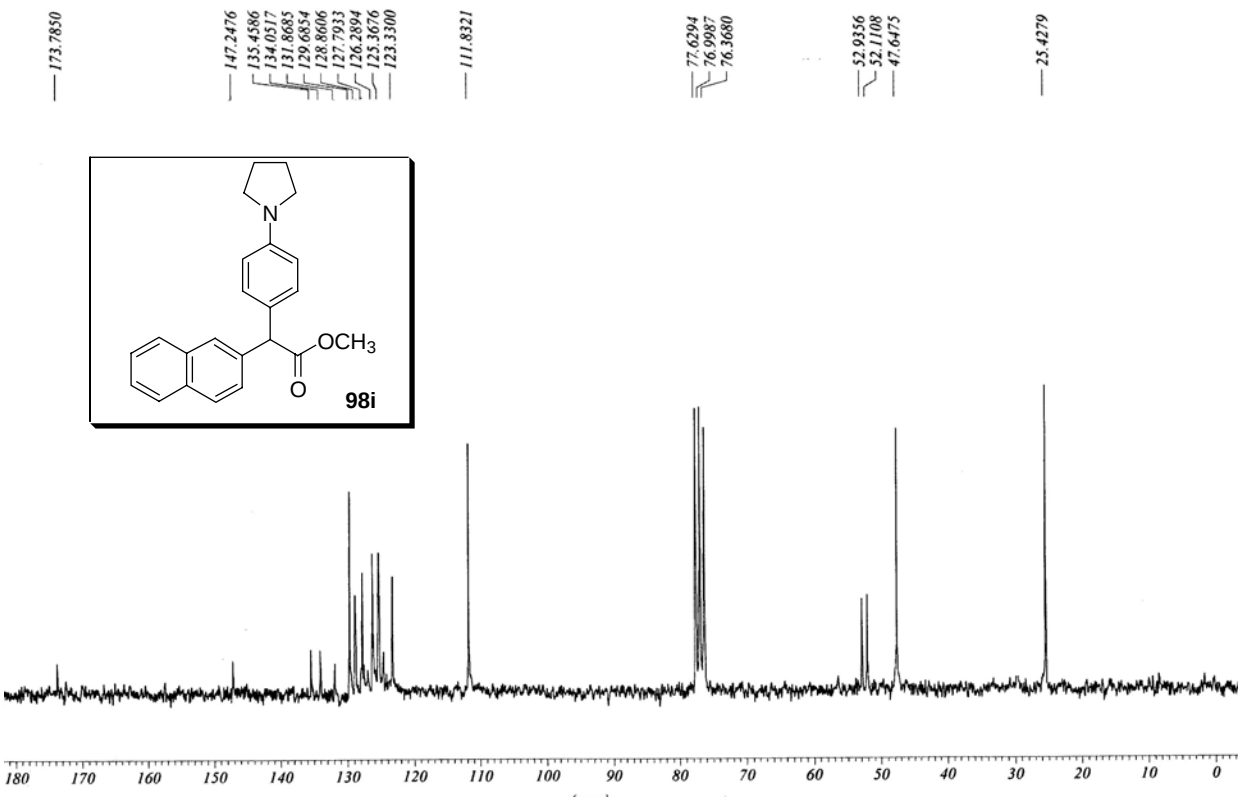
Spectrum No. 42 (Chapter 2, Section 2.4.1) ^{13}C NMR Spectrum (50 MHz, $CDCl_3$)



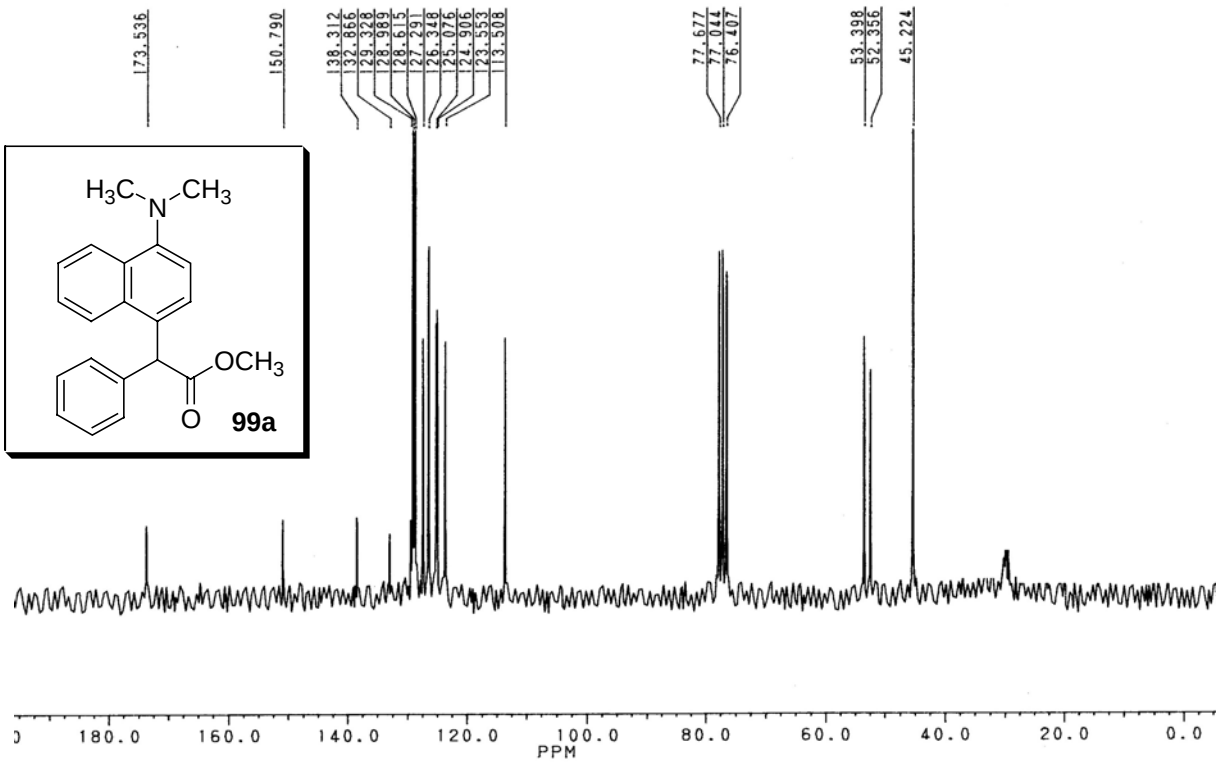
Spectrum No. 43 (Chapter 2, Section 2.4.1) ^{1}H NMR Spectrum (200 MHz, $CDCl_3$)



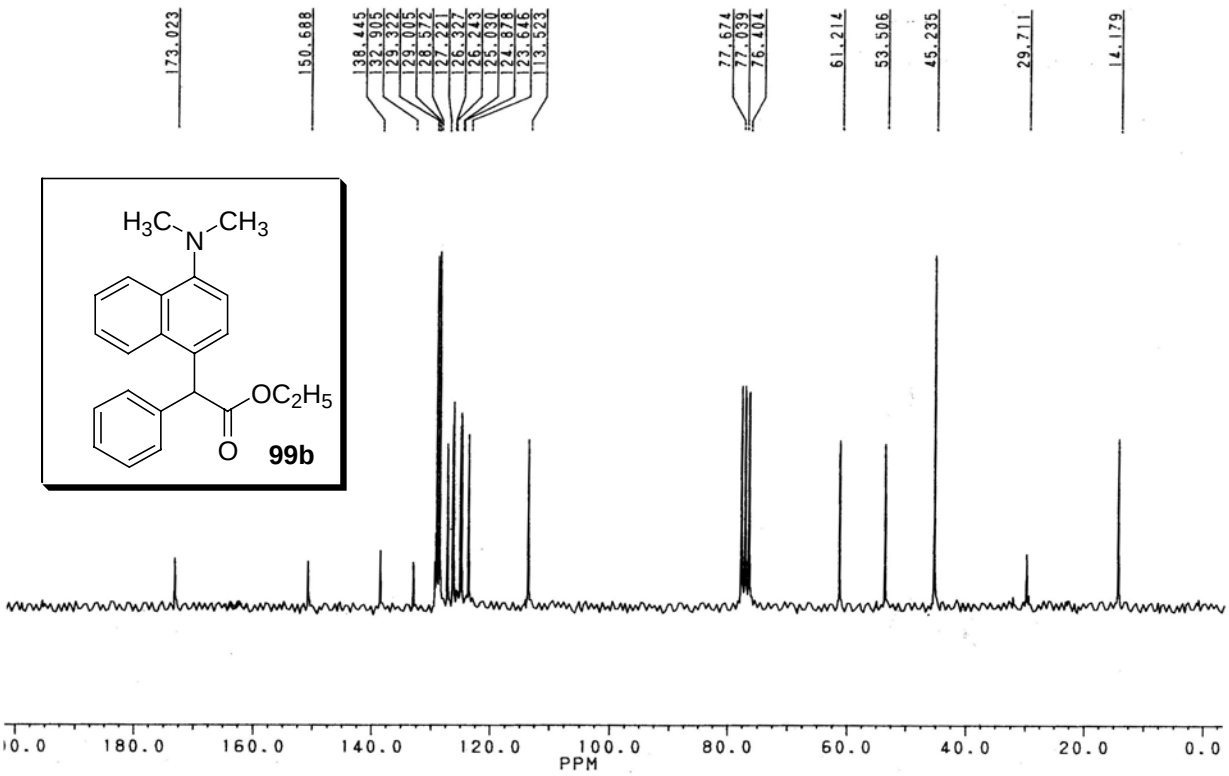
Spectrum No. 44 (Chapter 2, Section 2.4.1) ^{13}C NMR Spectrum (50 MHz,$CDCl_3$)



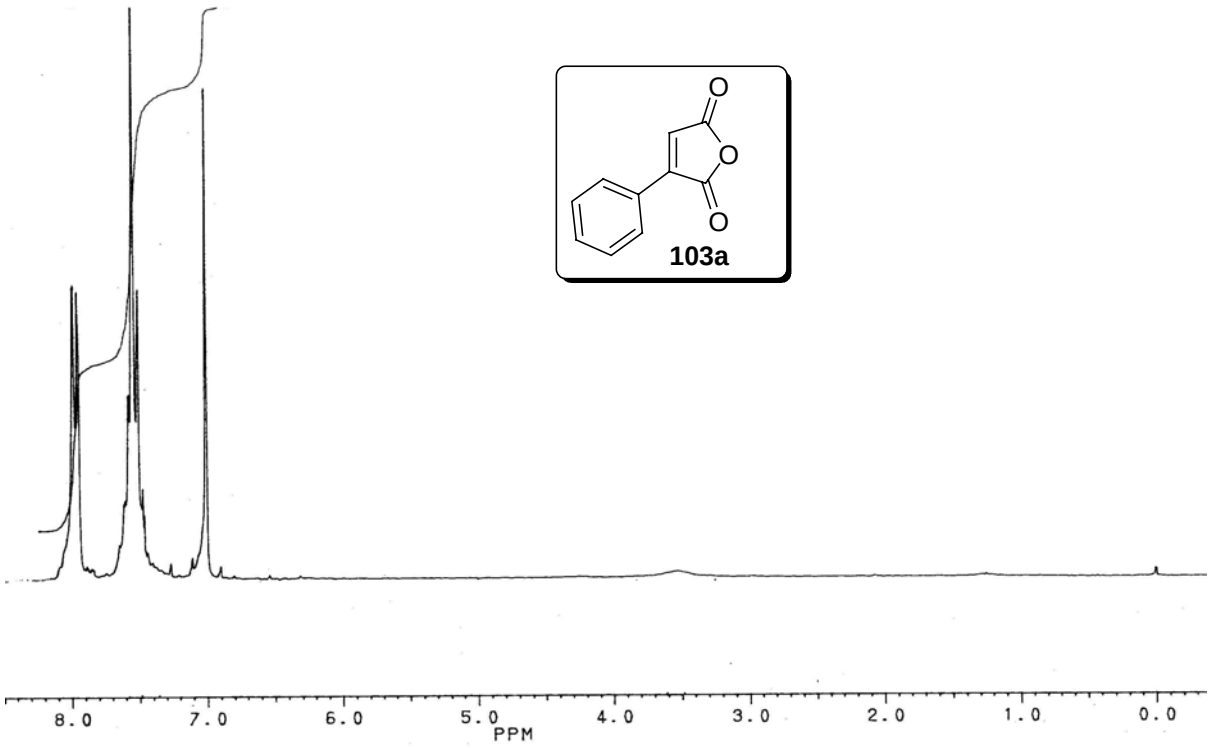
Spectrum No. 45 (Chapter 2, Section 2.4.1) ^{13}C NMR Spectrum (50 MHz, $CDCl_3$)



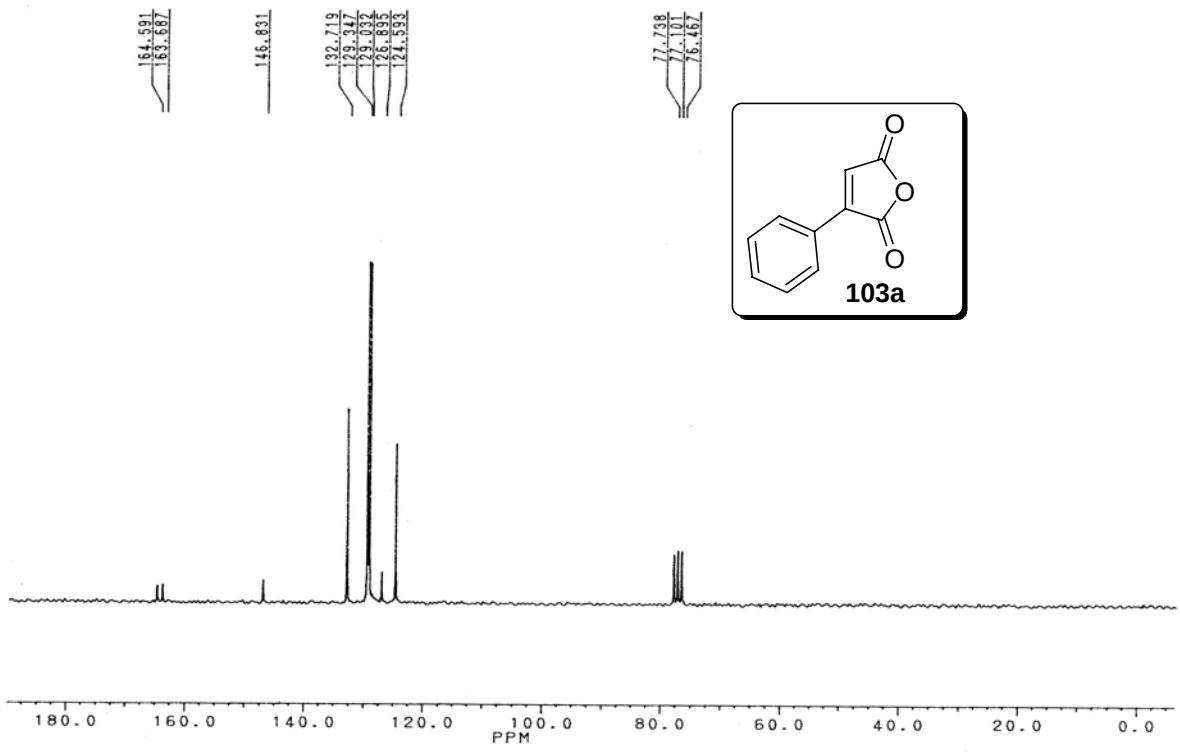
Spectrum No. 46 (Chapter 2, Section 2.4.1) ^{13}C NMR Spectrum (400 MHz, $CDCl_3$)



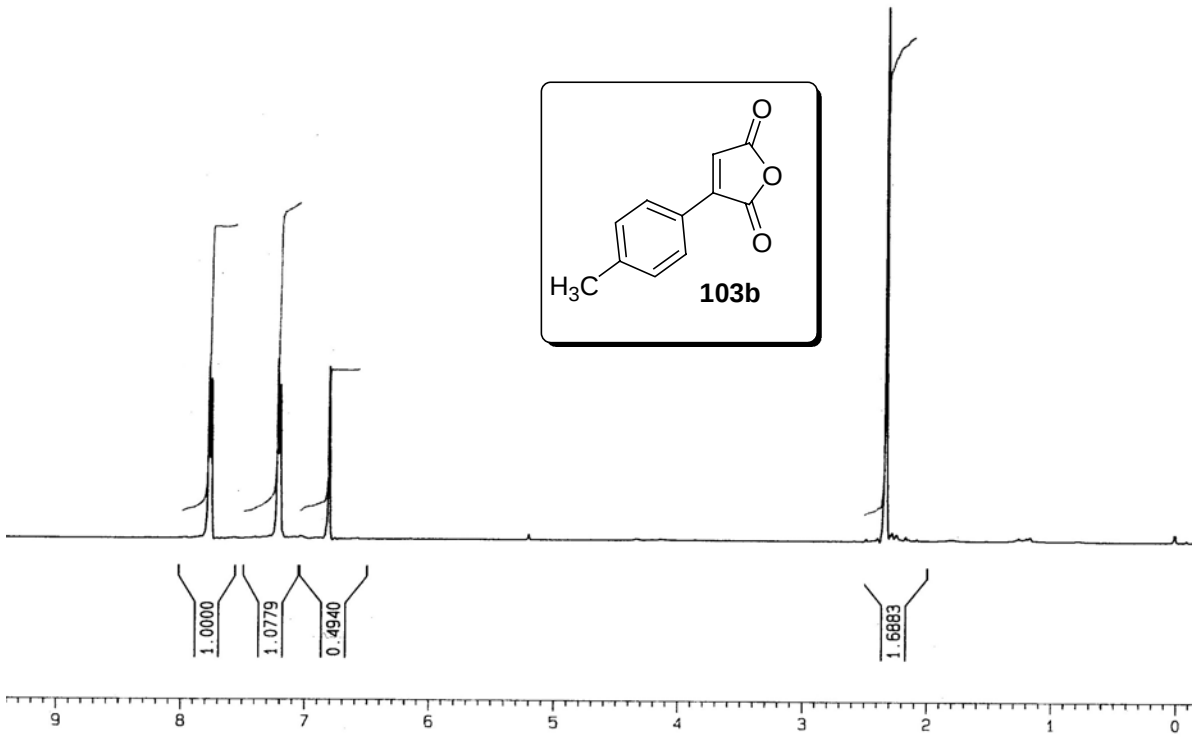
Spectrum No. 47 (Chapter 2, Section 2.4.2) ^{1}H NMR Spectrum (200 MHz, $CDCl_3$)



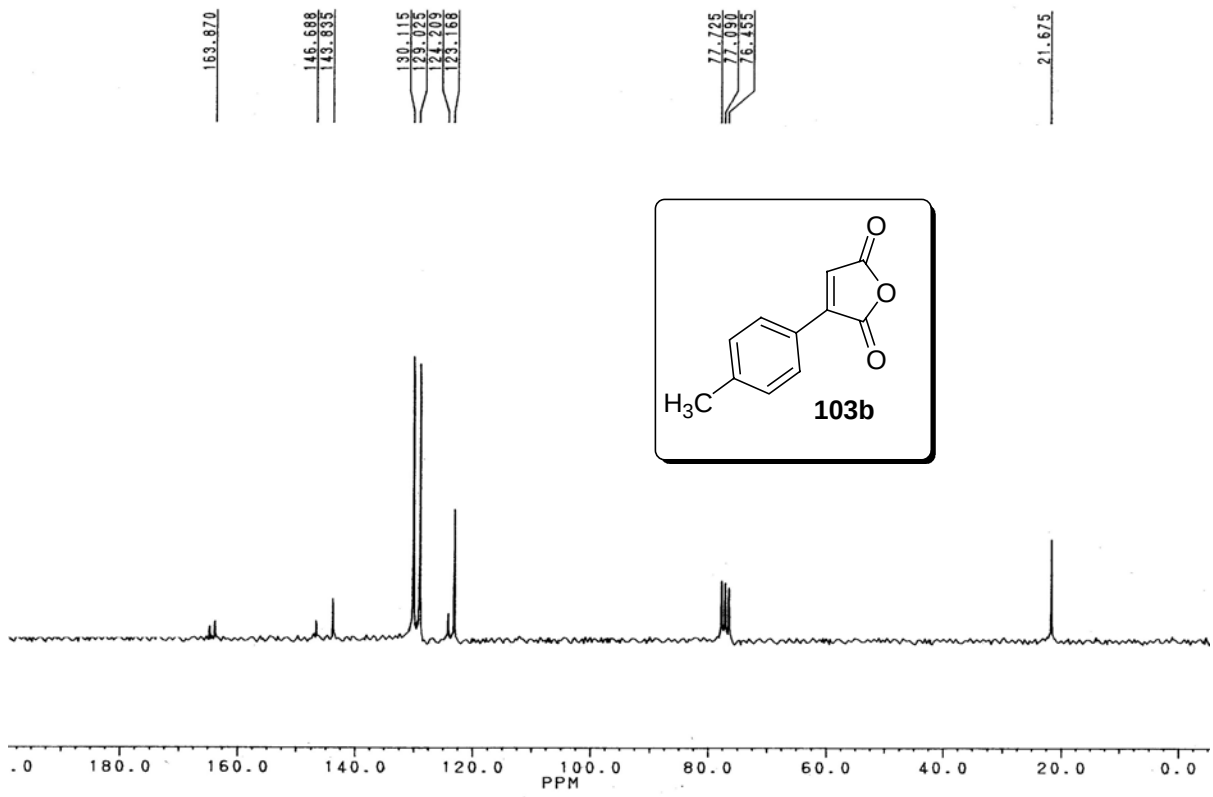
Spectrum No. 48 (Chapter 2, Section 2.4.2) ^{13}C NMR Spectrum (50 MHz, $CDCl_3$)



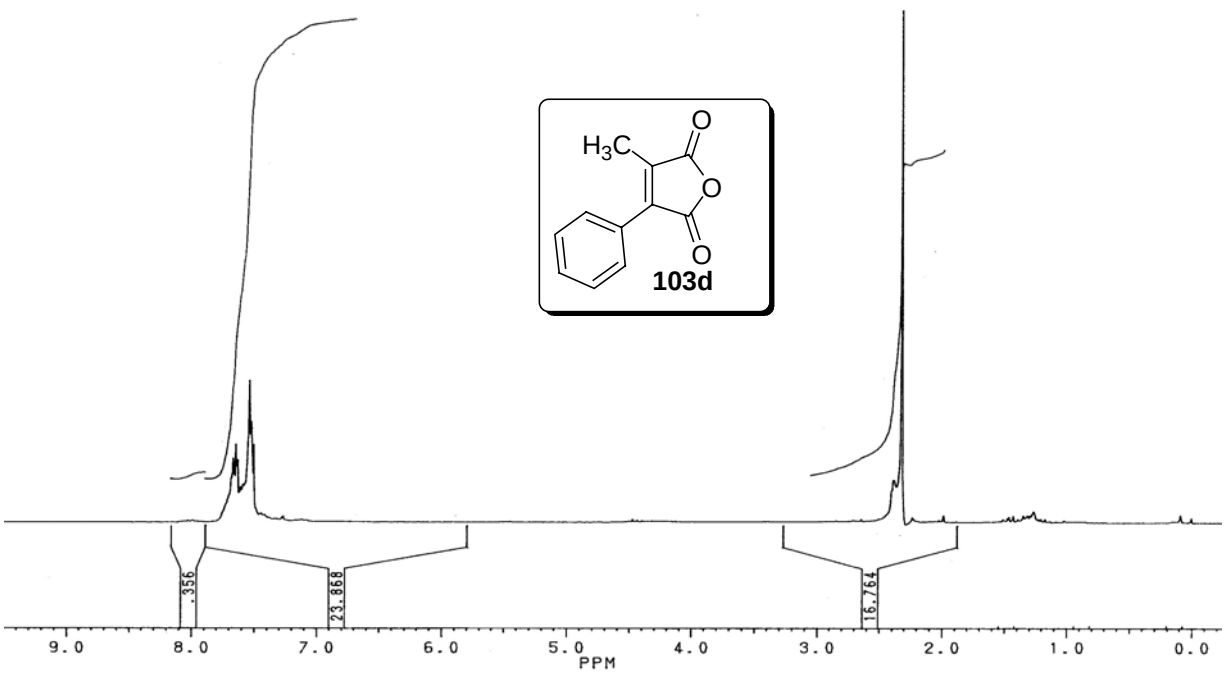
Spectrum No. 49 (Chapter 2, Section 2.4.2) ^{1}H NMR Spectrum (200 MHz, $CDCl_3$)



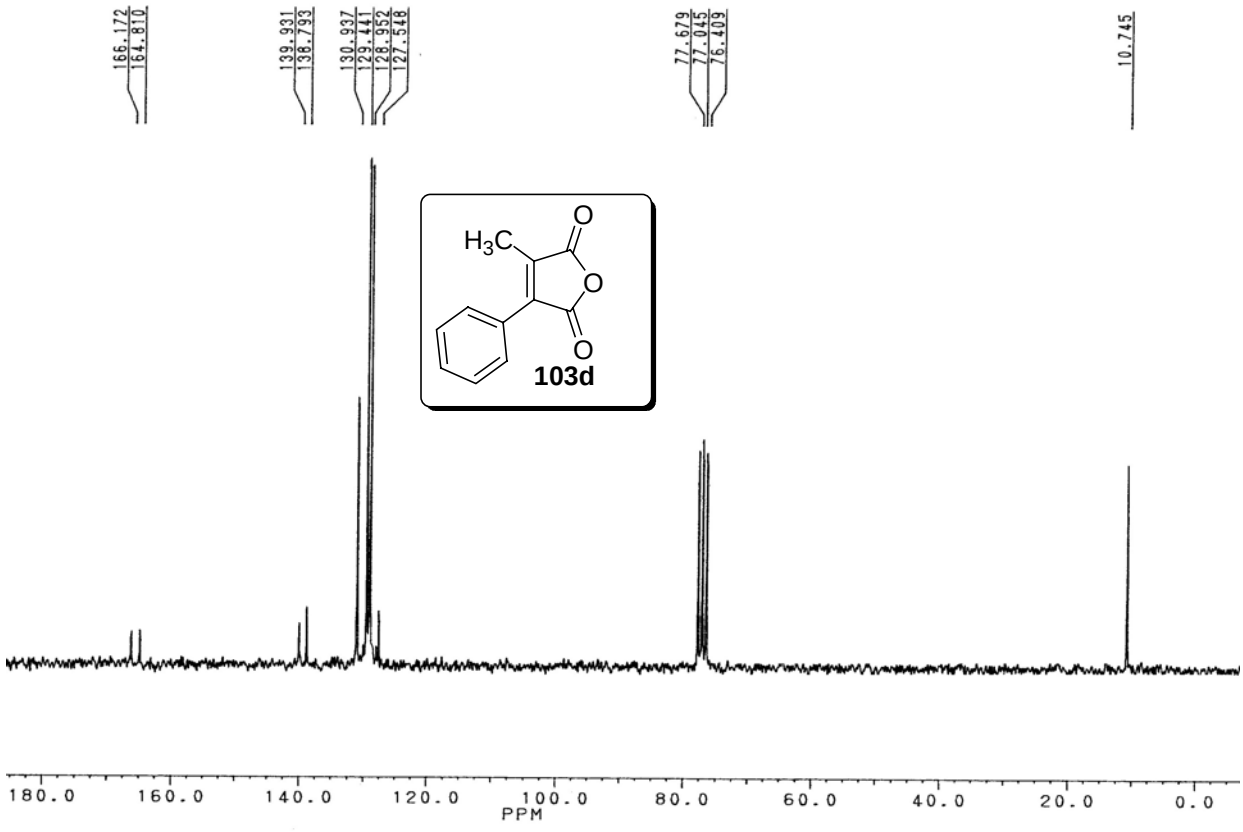
Spectrum No. 50 (Chapter 2, Section 2.4.2) ^{13}C NMR Spectrum 50 MHz, $CDCl_3$)



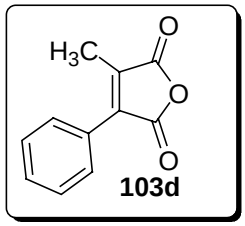
Spectrum No. 51 (Chapter 2, Section 2.4.2) ^{1}H NMR Spectrum 400 MHz, $CDCl_3$)



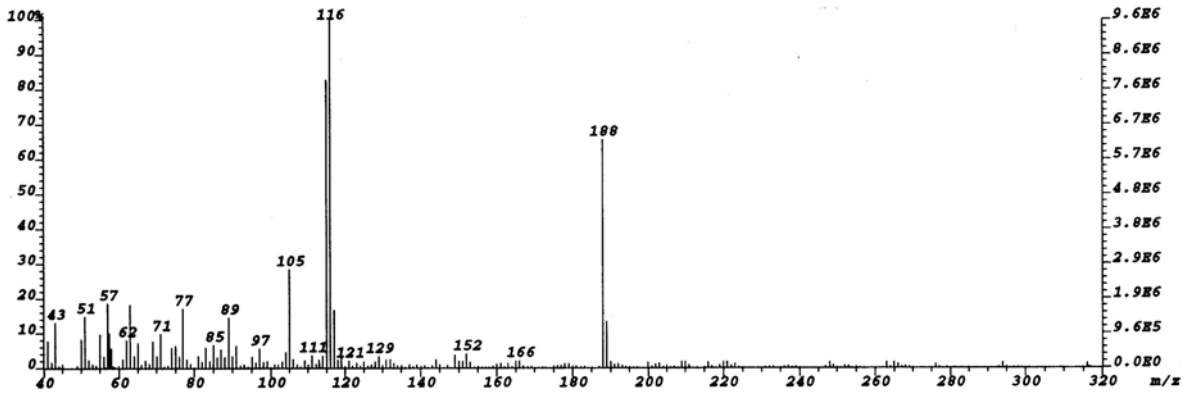
Spectrum No. 52 (Chapter 2, Section 2.4.2) ^{13}C NMR Spectrum (50 MHz, $CDCl_3$)



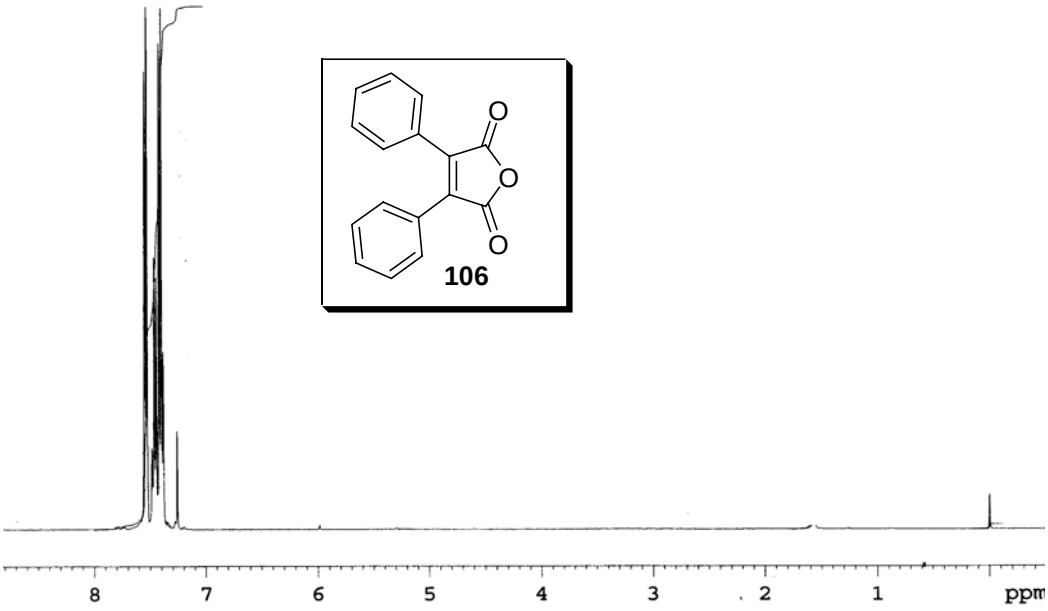
Spectrum No. 53 (Chapter 2, Section 2.4.2) Mass Spectrum (EI)



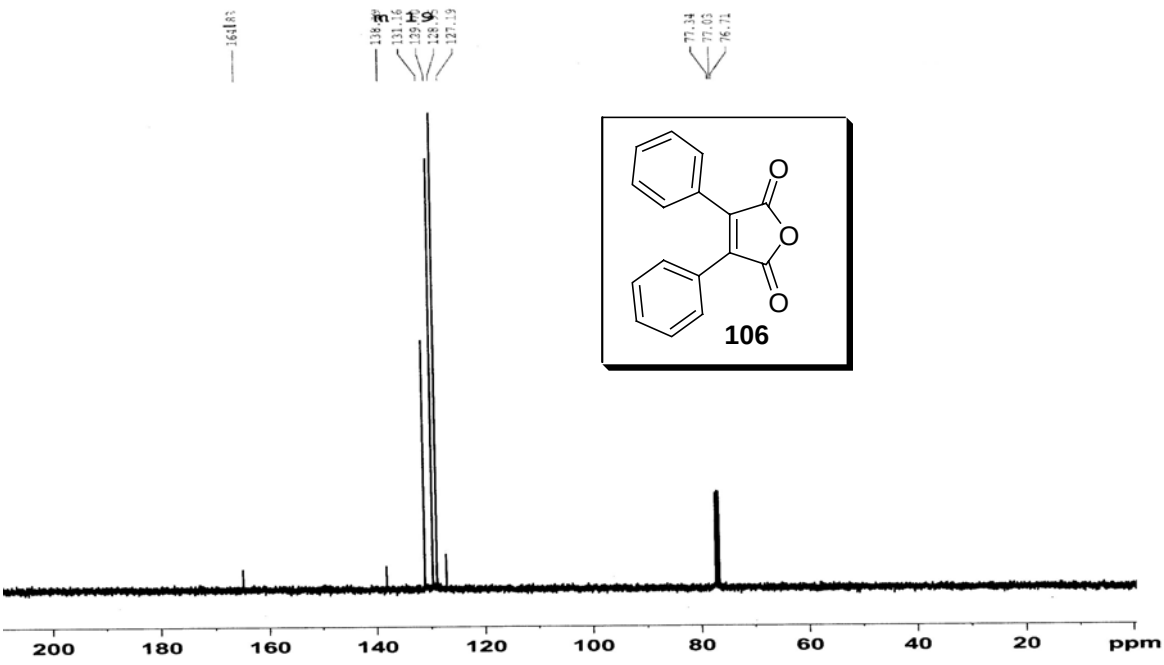
103d



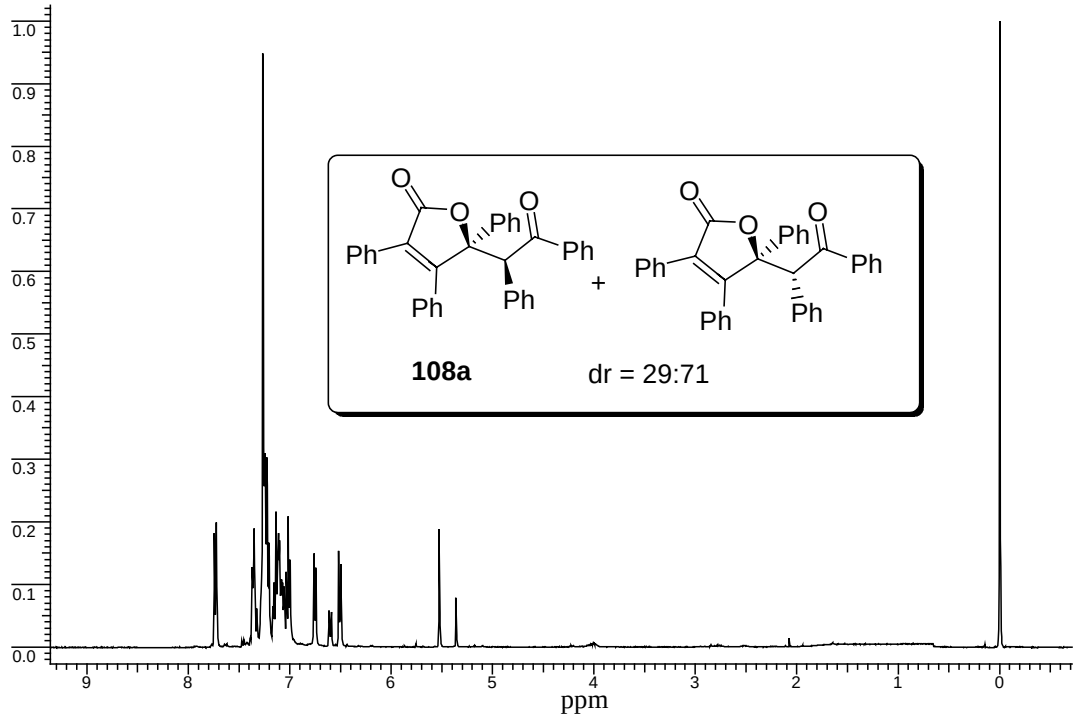
Spectrum No. 54 (Chapter 2, Section 2.4.3) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



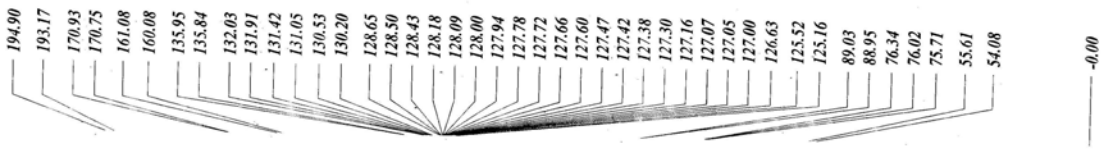
Spectrum No. 55 (Chapter 2, Section 2.4.3) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)

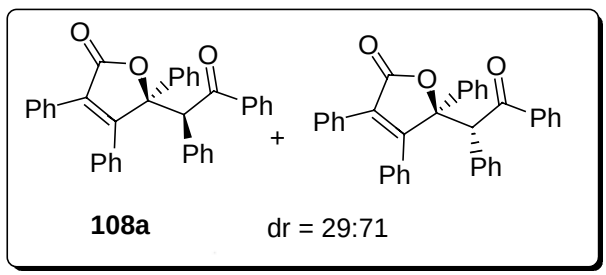


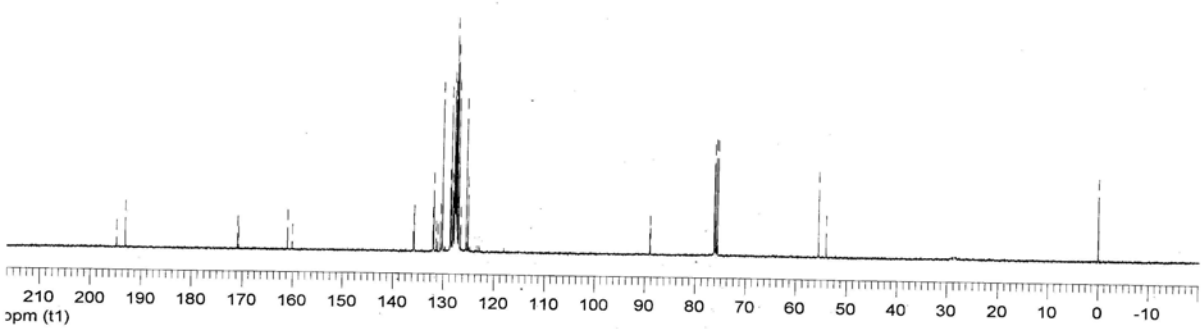
Spectrum No. 56 (Chapter 2, Section 2.4.4) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



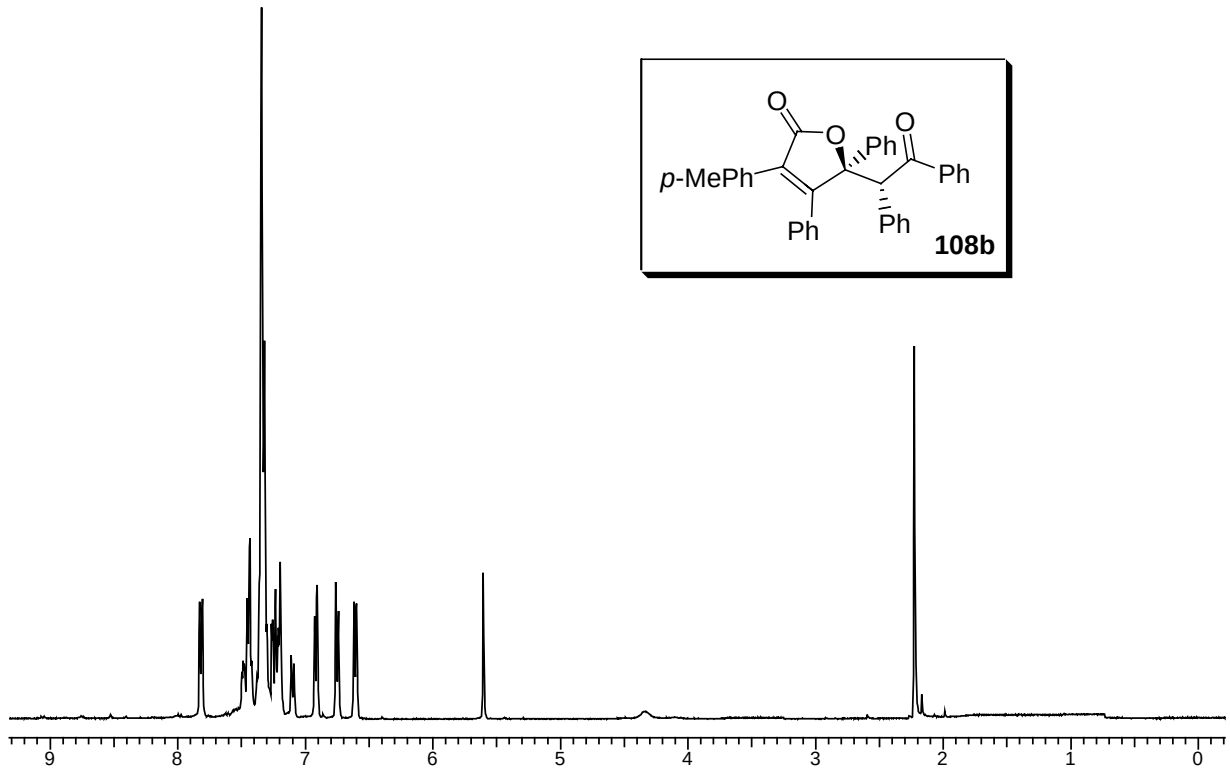
Spectrum No. 57 (Chapter 2, Section 2.4.4) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



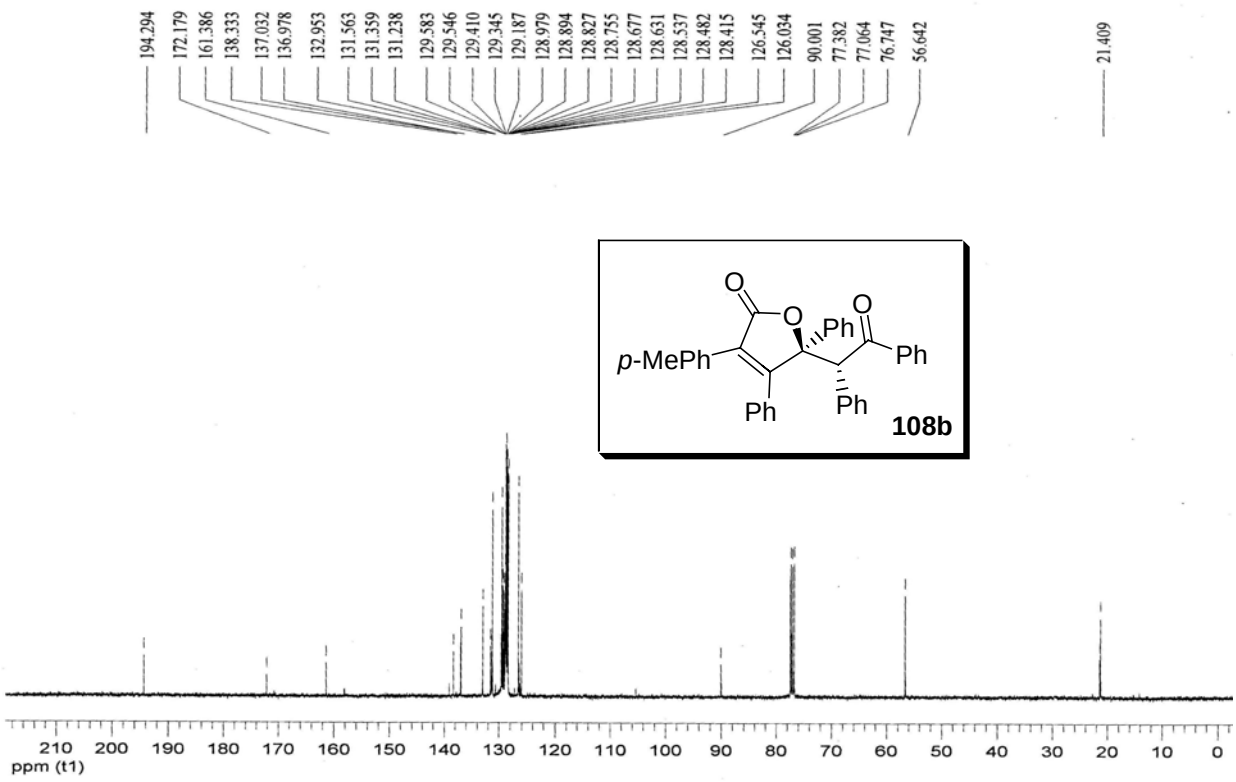




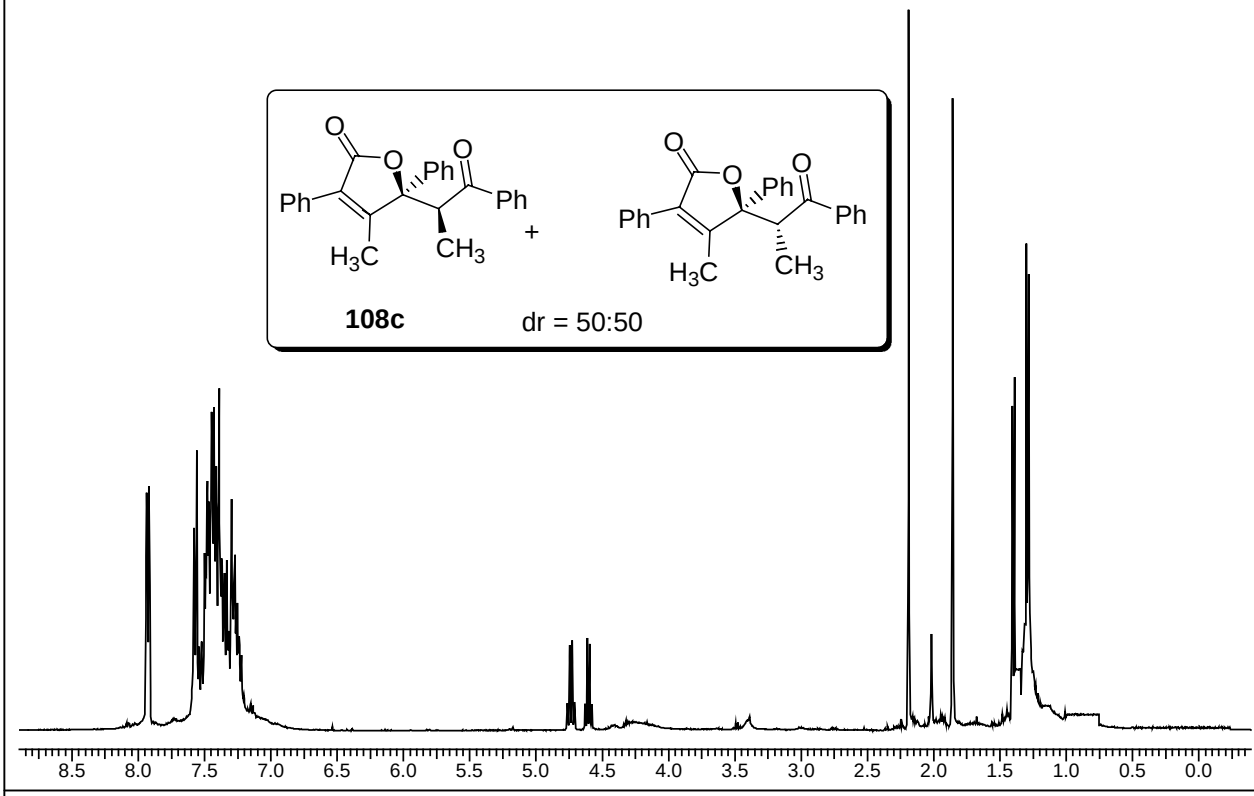
Spectrum No. 58 (Chapter 2, Section 2.4.4) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



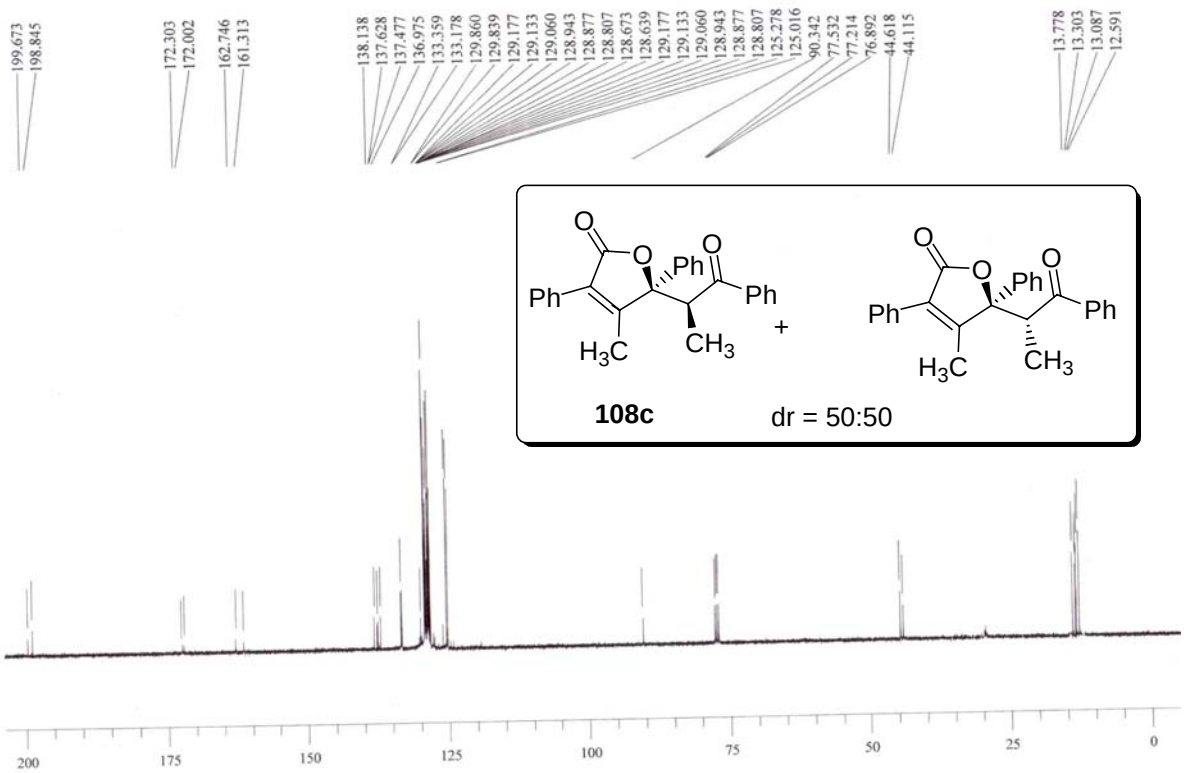
Spectrum No. 59 (Chapter 2, Section 2.4.4) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



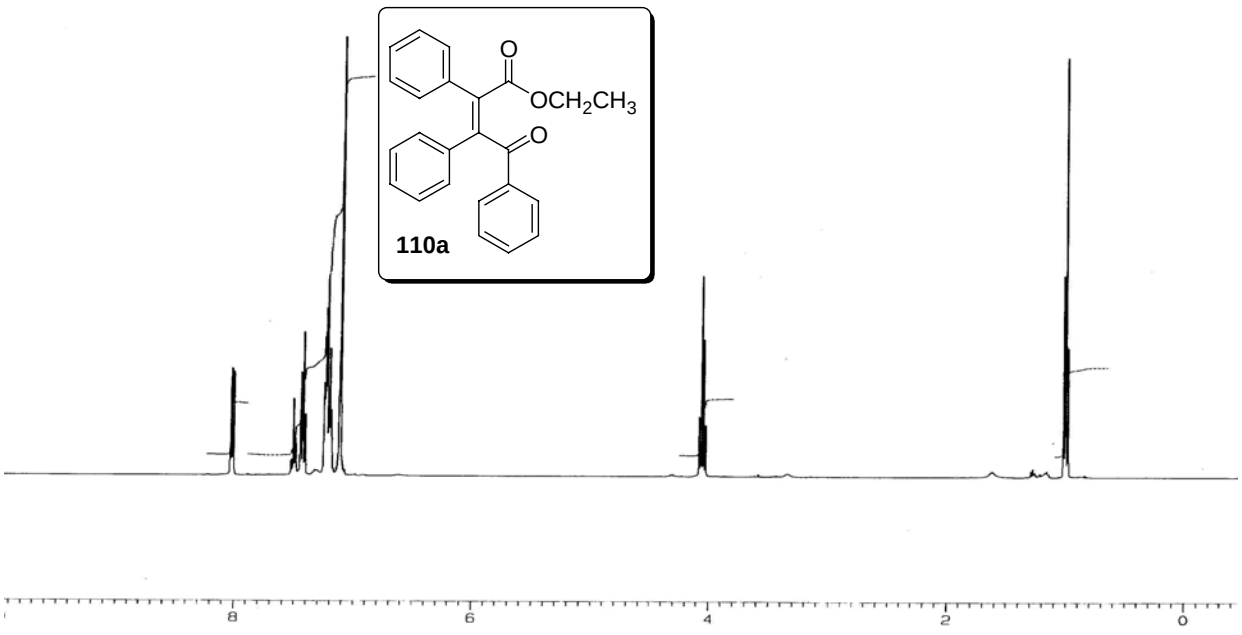
Spectrum No. 60 (Chapter 2, Section 2.4.4) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



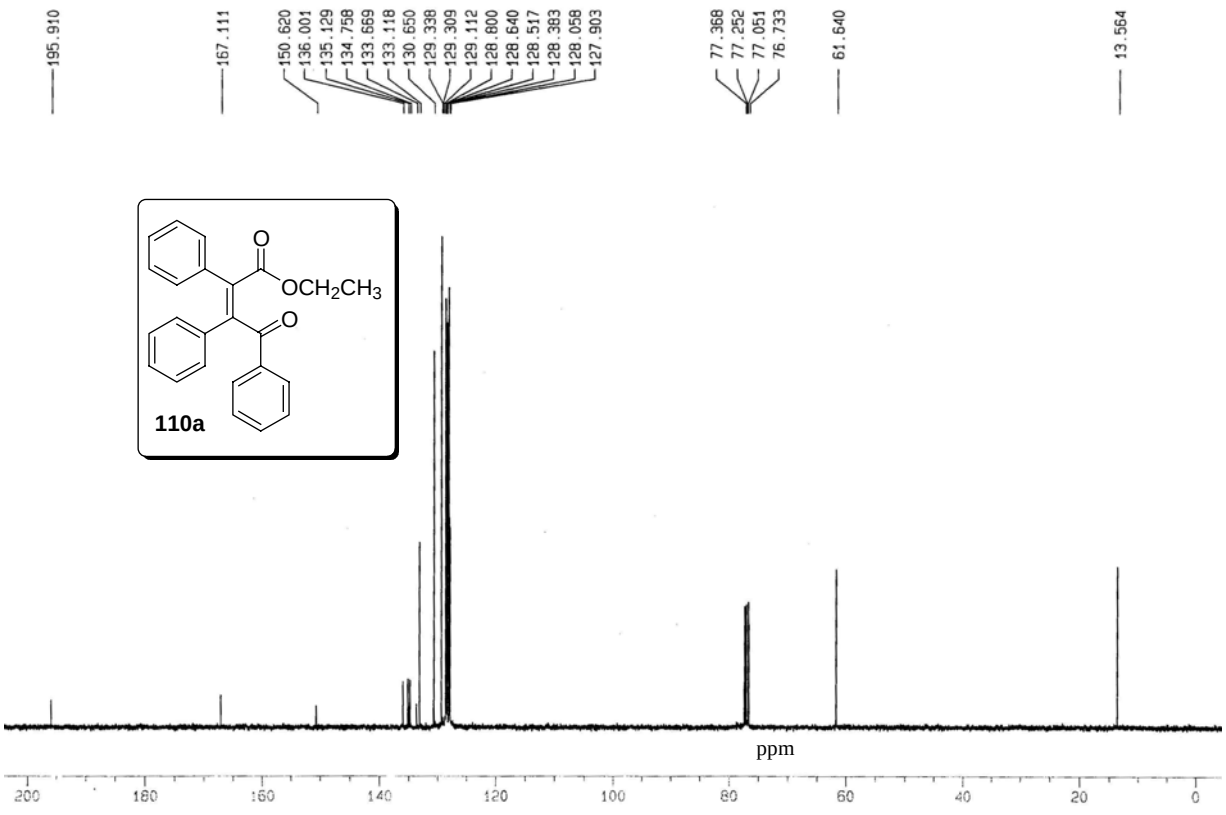
Spectrum No. 61 (Chapter 2, Section 2.4.4) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



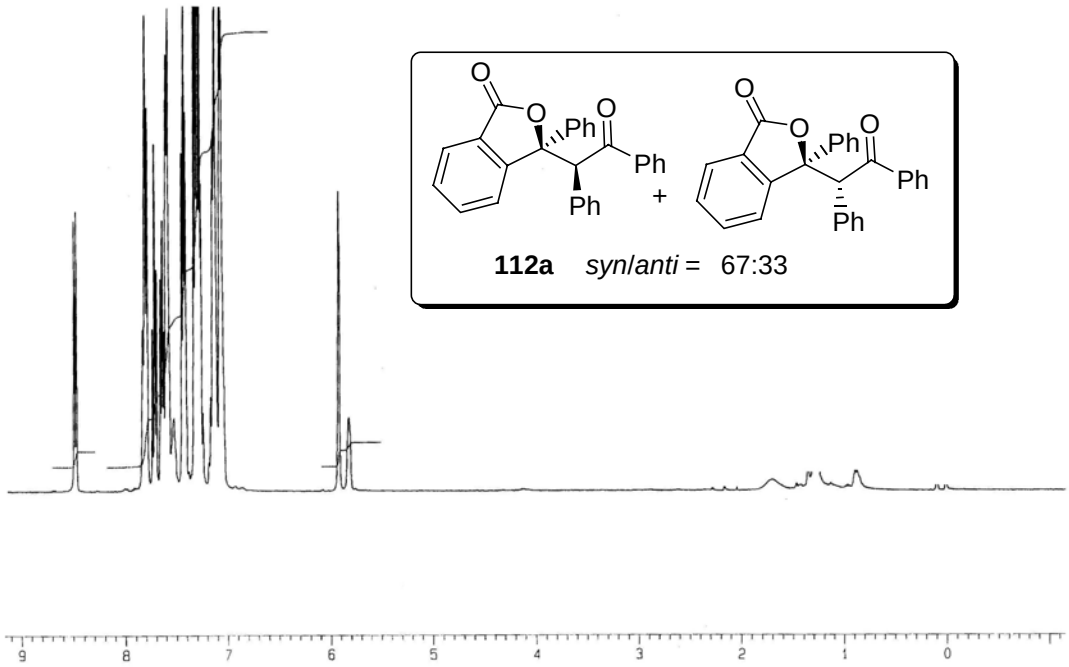
Spectrum No. 62 (Chapter 2, Section 2.4.5) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



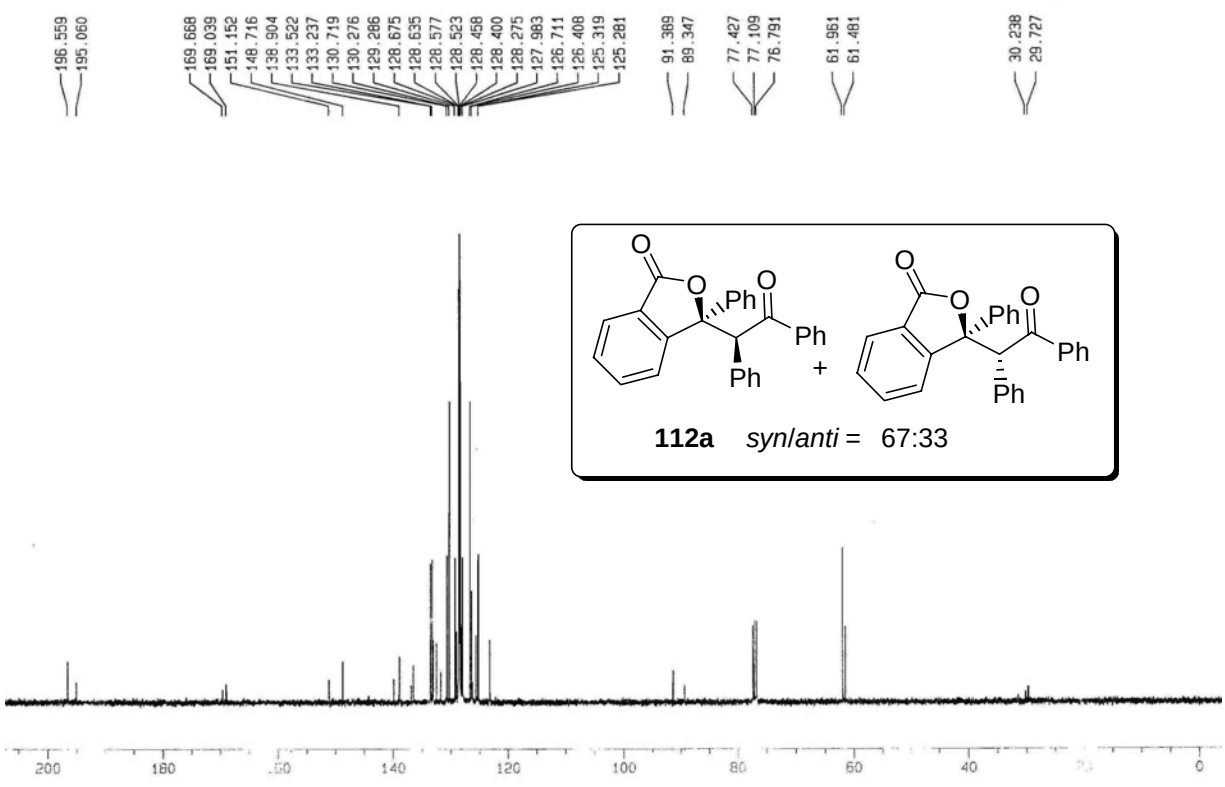
Spectrum No. 63 (Chapter 2, Section 2.4.5) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



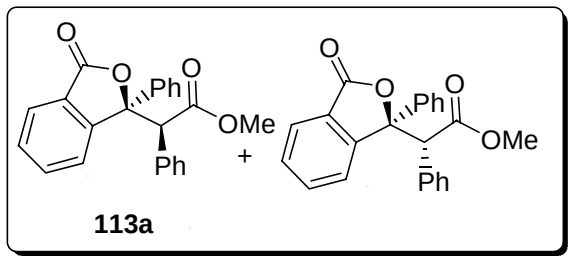
Spectrum No. 64 (Chapter 2, Section 2.4.6) ^{1}H NMR Spectrum (200 MHz, $CDCl_3$)



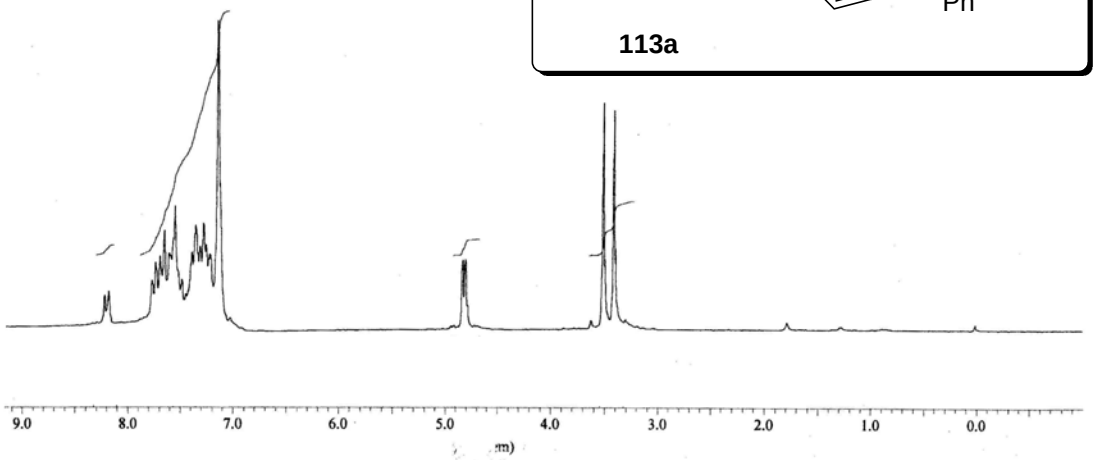
Spectrum No. 65 (Chapter 2, Section 2.4.6) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



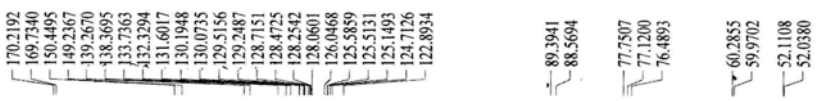
Spectrum No. 66 (Chapter 2, Section 2.4.7) ^{1}H NMR Spectrum (200 MHz, $CDCl_3$)

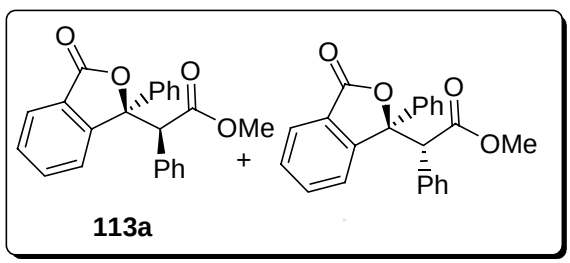


113a

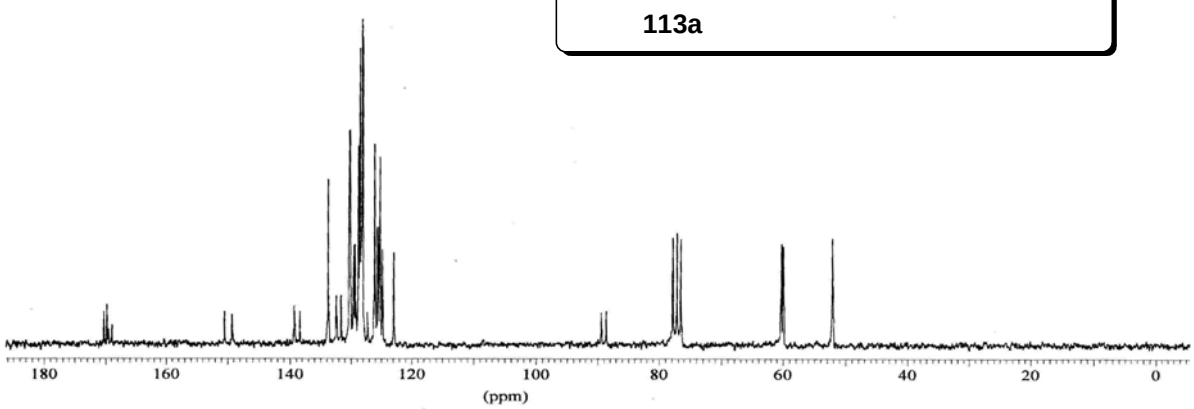


Spectrum No. 67 (Chapter 2, Section 2.4.7) ^{13}C NMR Spectrum (50 MHz, $CDCl_3$)

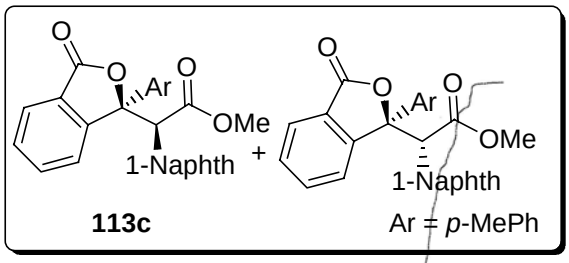




113a

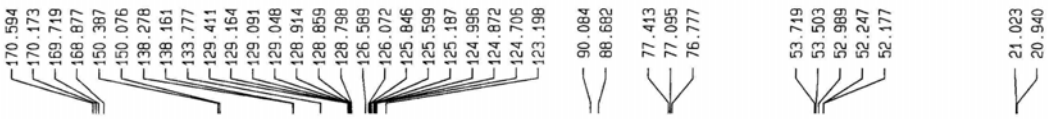


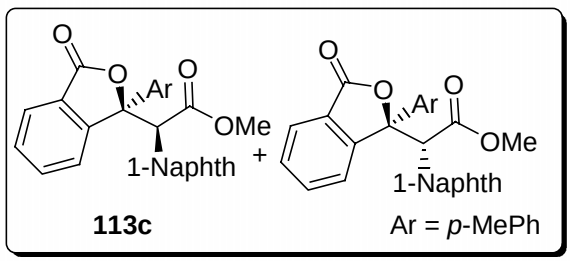
Spectrum No. 68 (Chapter 2, Section 2.4.7) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



113c Ar = *p*-MePh

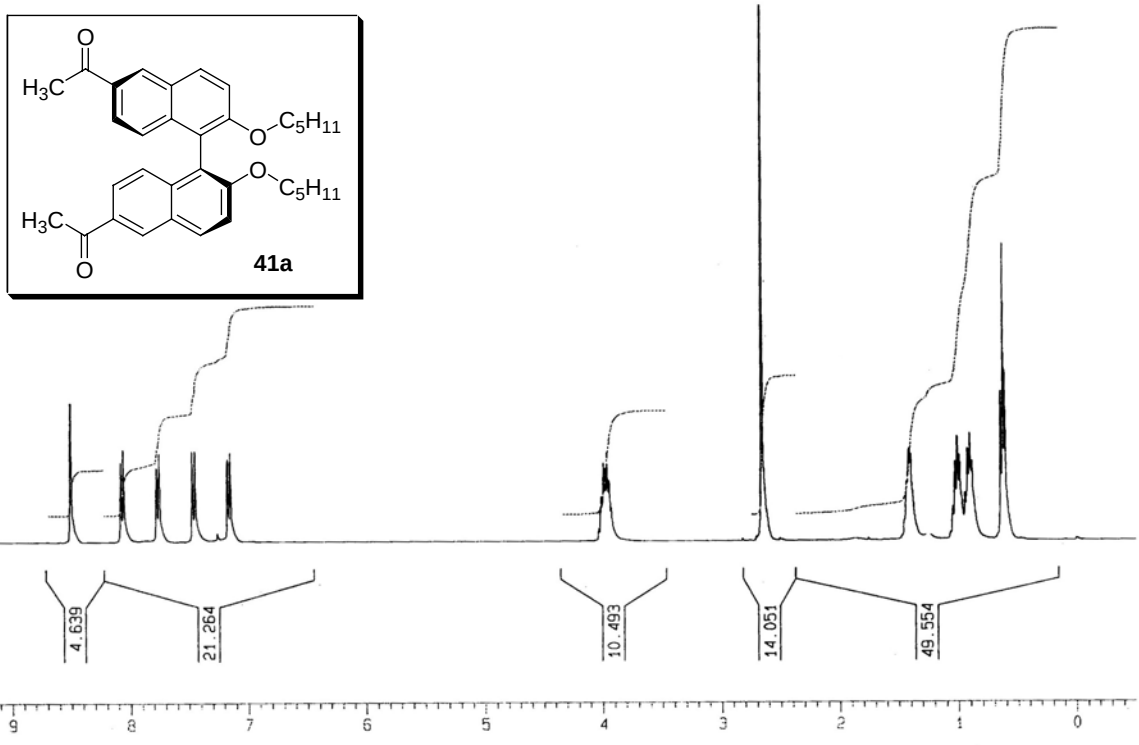
Spectrum No. 69 (Chapter 2, Section 2.4.7) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



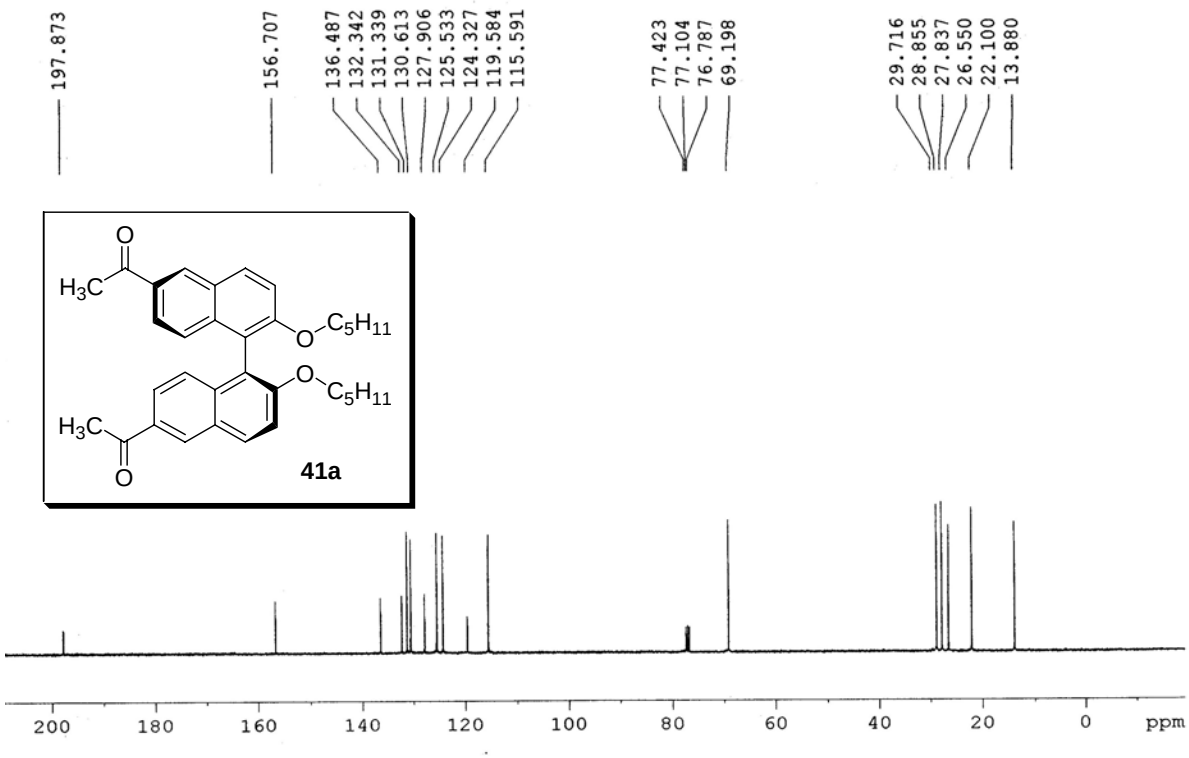


113c Ar = *p*-MePh

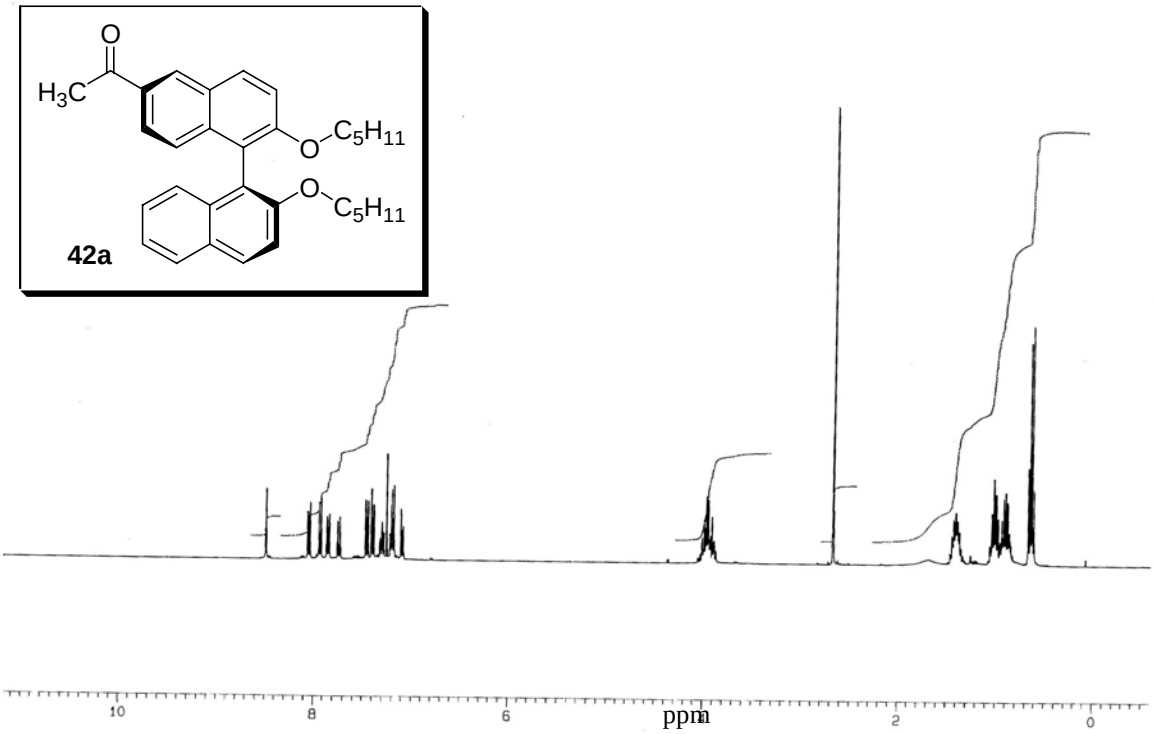
Spectrum No. 70 (Chapter 3, Section 3.4.1) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



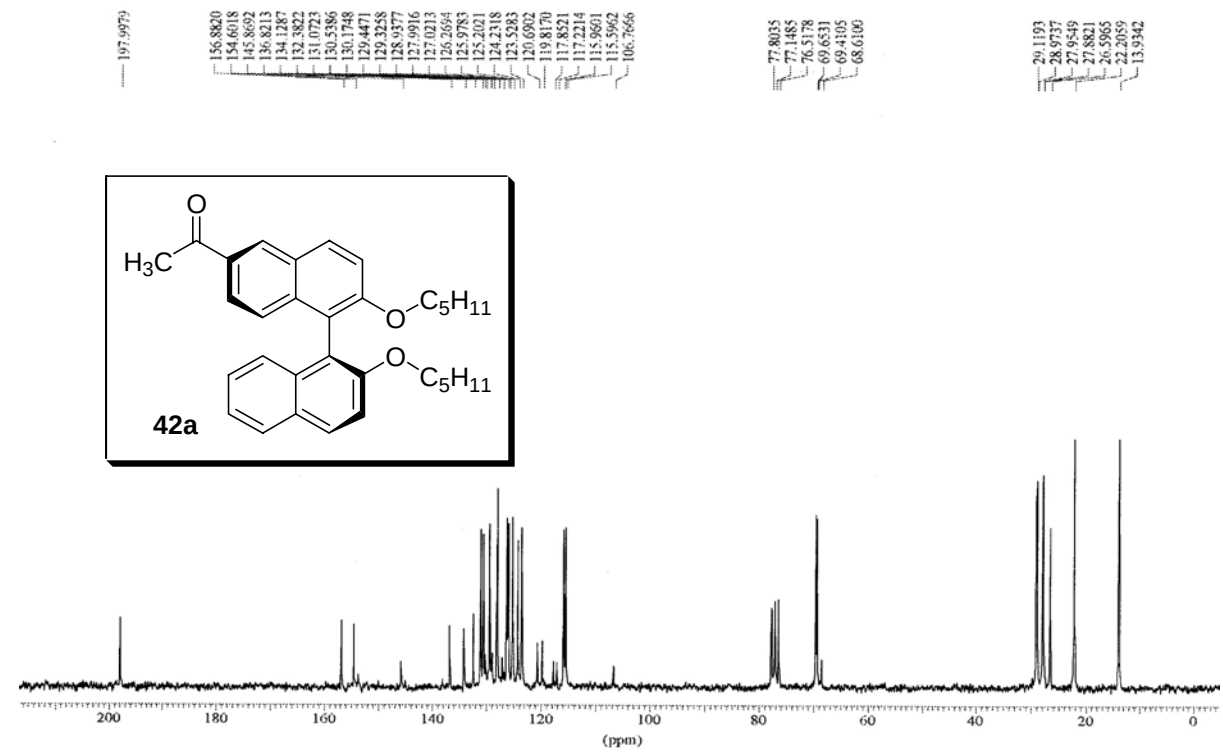
Spectrum No. 71 (Chapter 3, Section 3.4.1) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



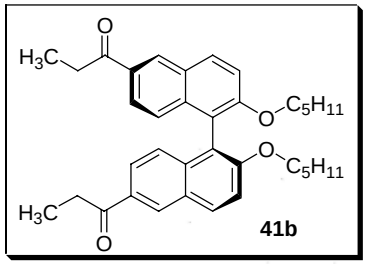
Spectrum No. 72 (Chapter 3, Section 3.4.1) ^{1}H NMR Spectrum (400MHz, $CDCl_3$)



Spectrum No. 73 (Chapter 3, Section 3.4.1) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)

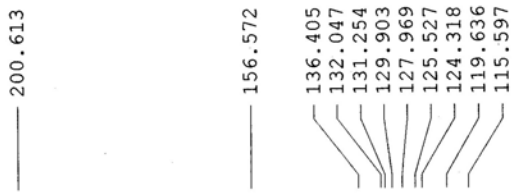


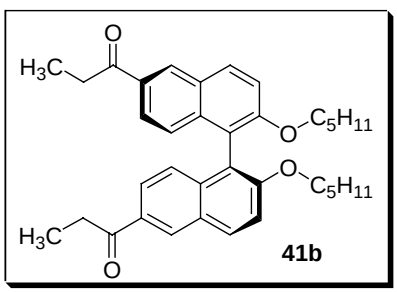
Spectrum No. 74 (Chapter 3, Section 3.4.1) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



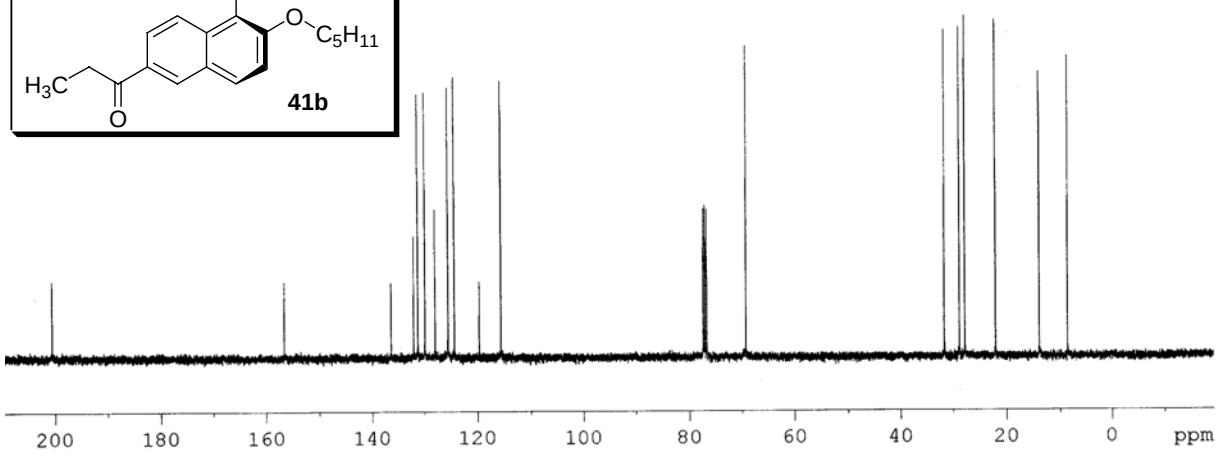
41b

Spectrum No. 75 (Chapter 3, Section 3.4.1) ^{13}C NMR Spectrum (100 MHz,$CDCl_3$)

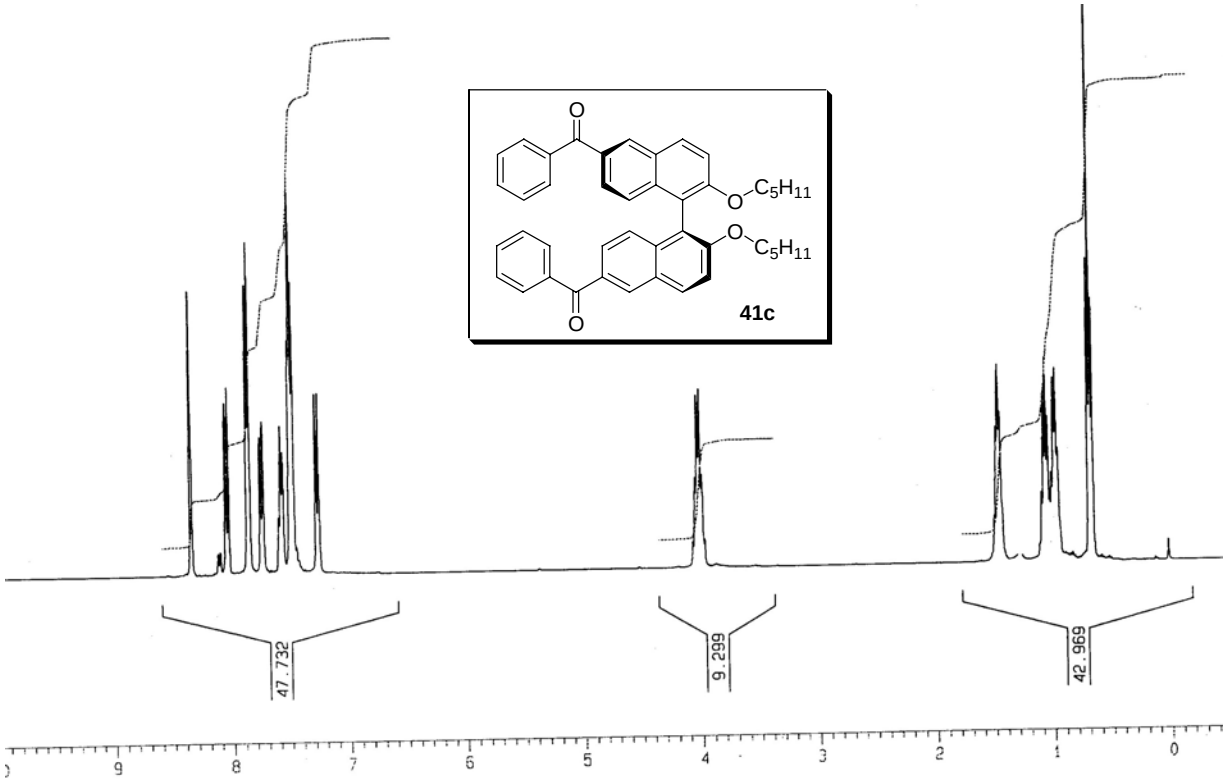




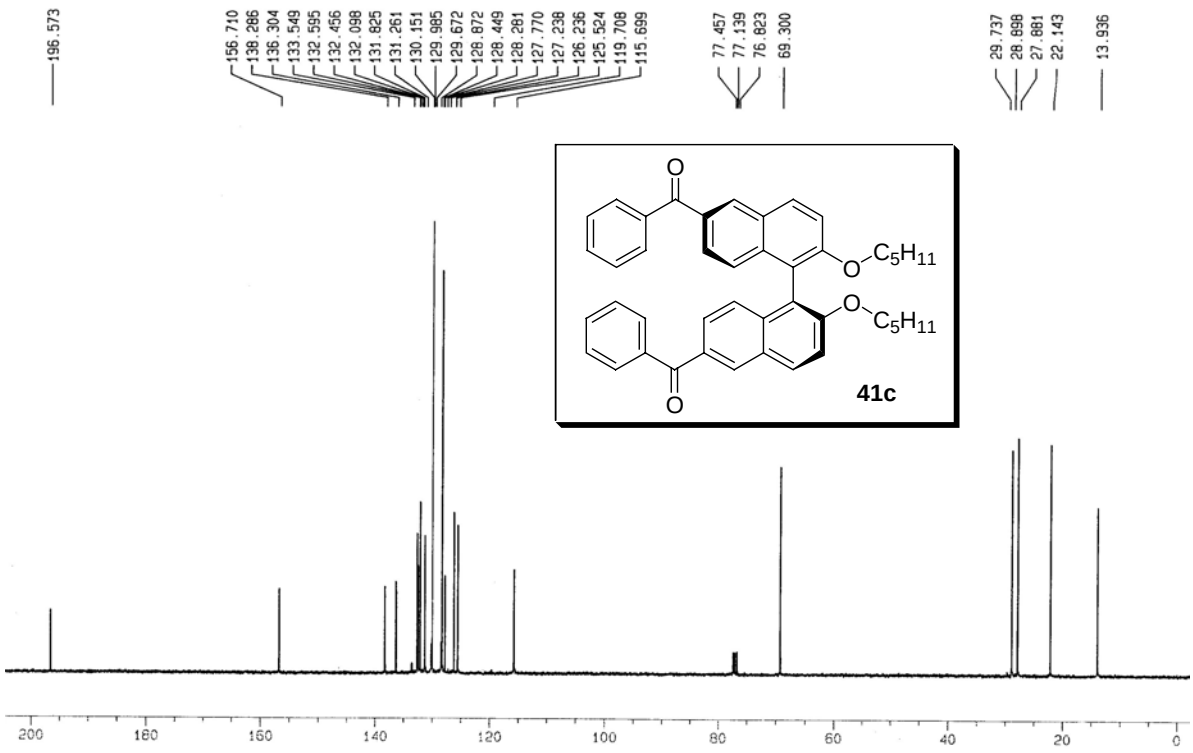
41b



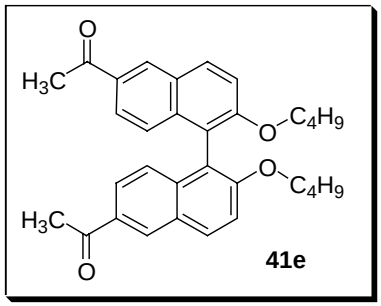
Spectrum No. 76 (Chapter 3, Section 3.4.1) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



Spectrum No. 77 (Chapter 3, Section 3.4.1) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)

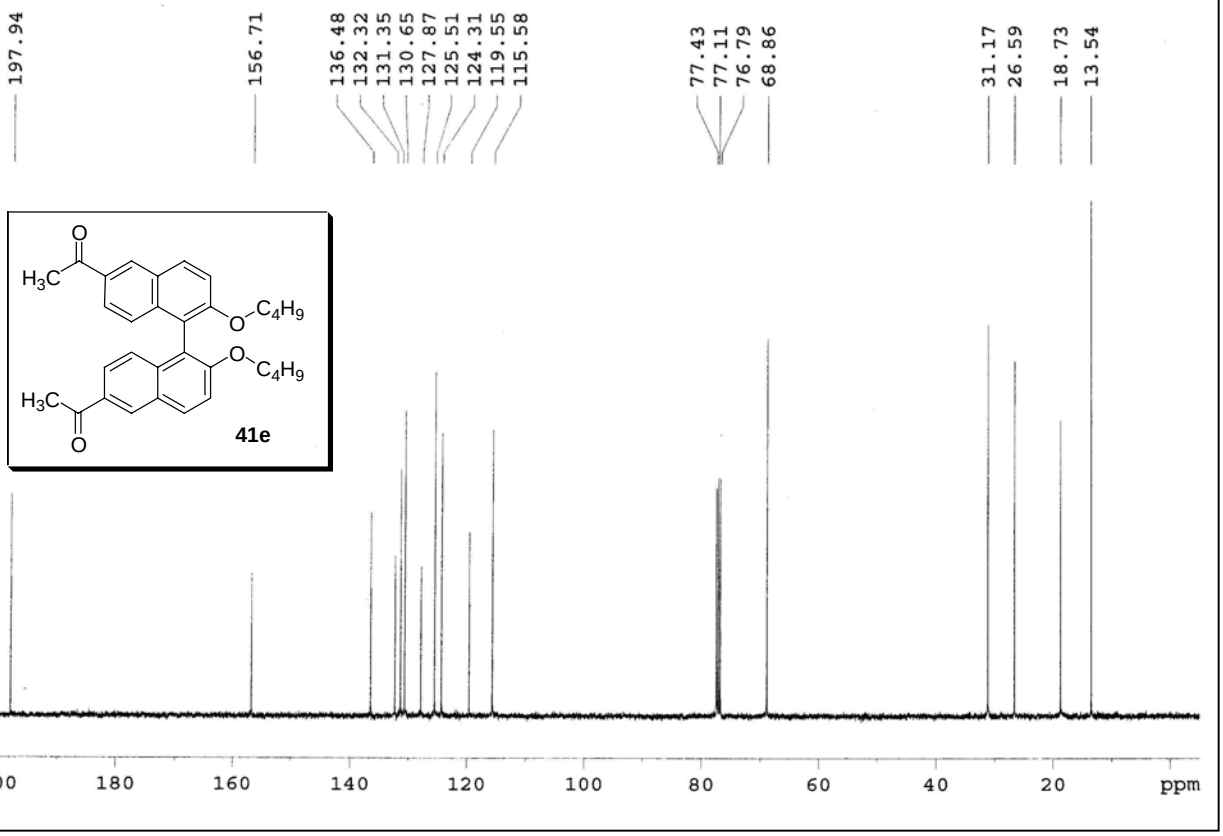


Spectrum No. 78 (Chapter 3, Section 3.4.1) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



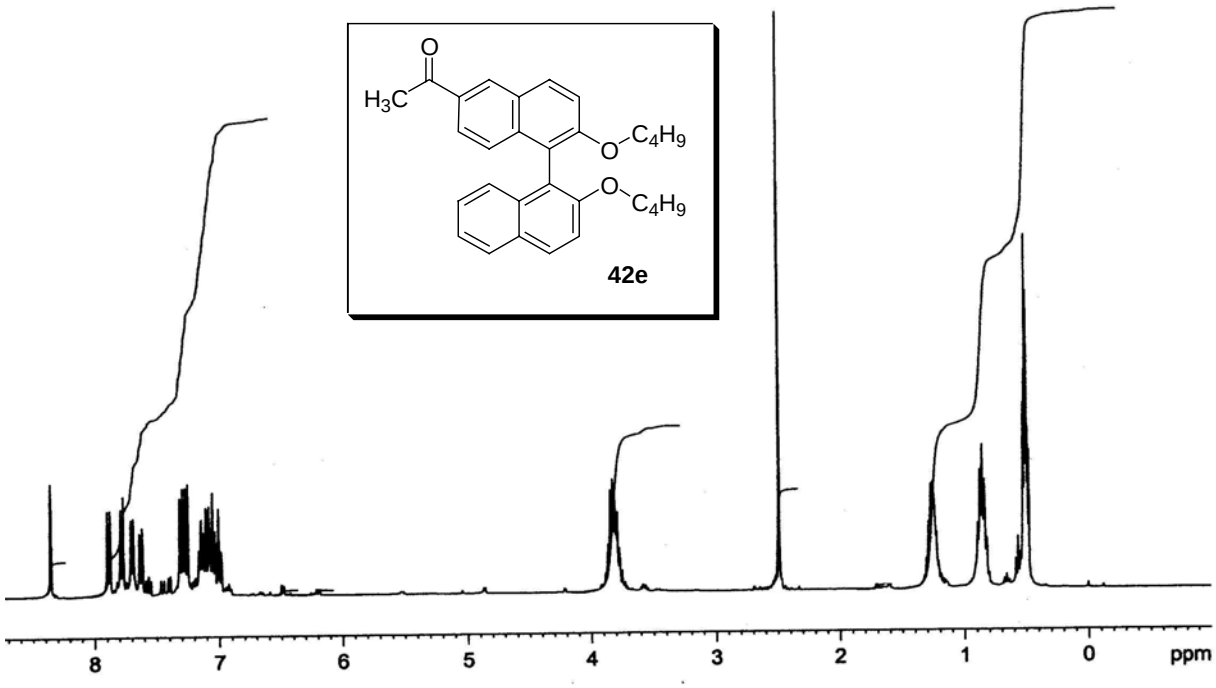
41e

Spectrum No. 79 (Chapter 3, Section 3.4.1) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)

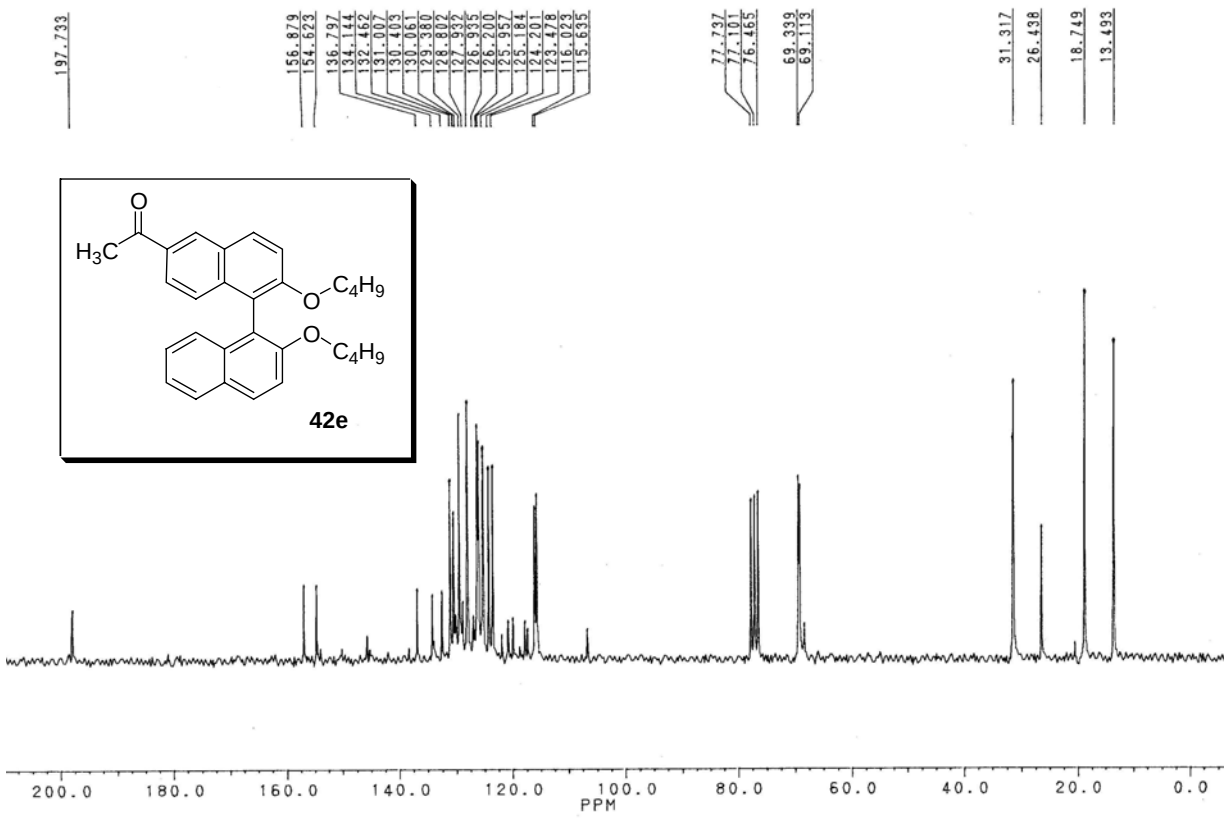


41e

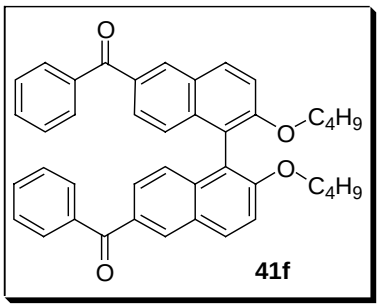
Spectrum No. 80 (Chapter 3, Section 3.4.1) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)

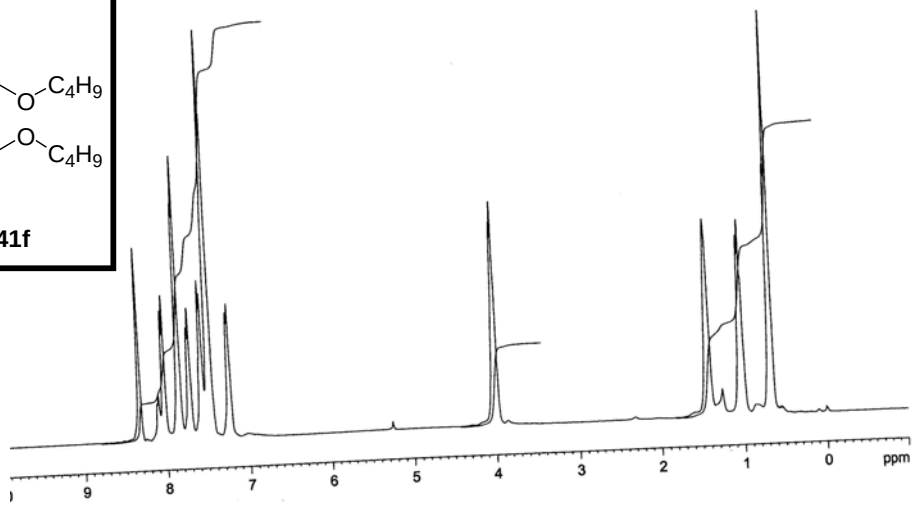


Spectrum No. 81 (Chapter 3, Section 3.4.1) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)

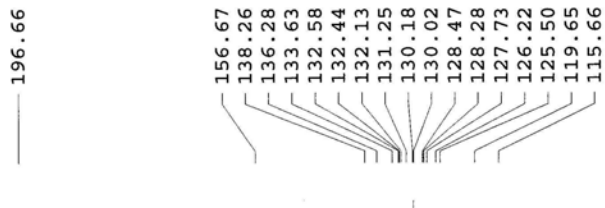


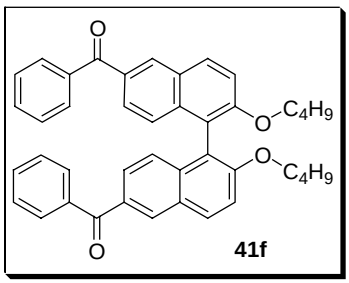
Spectrum No. 82 (Chapter 3, Section 3.4.1) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



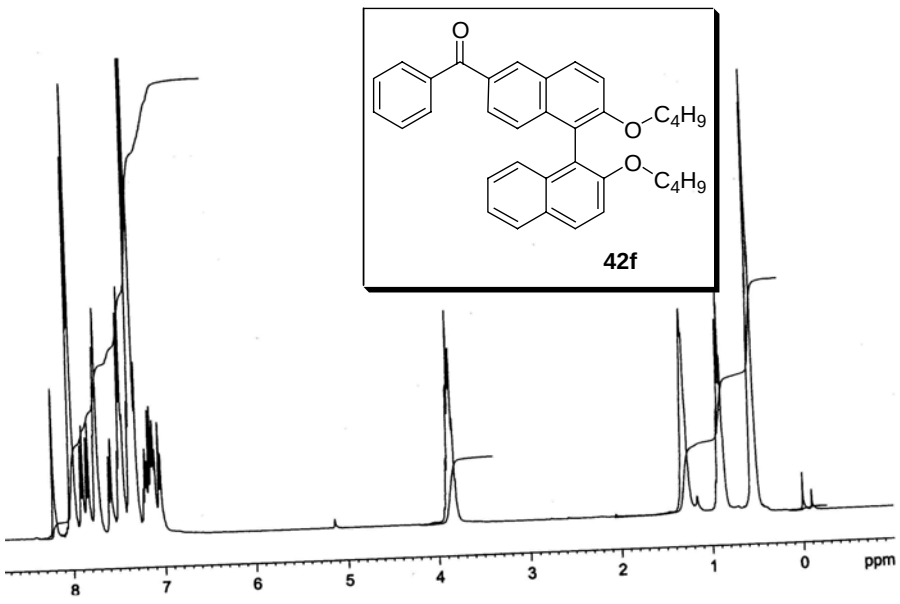


Spectrum No. 83 (Chapter 3, Section 3.4.1) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)

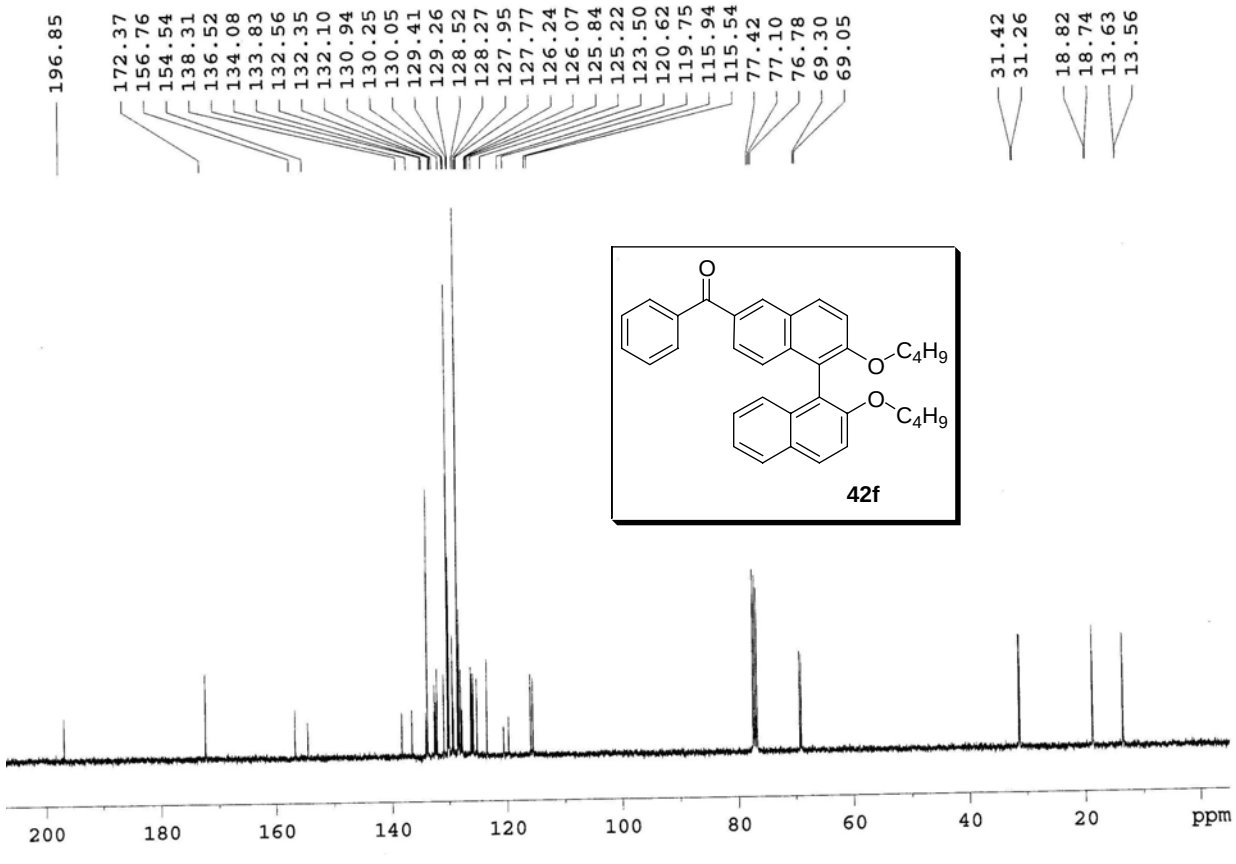




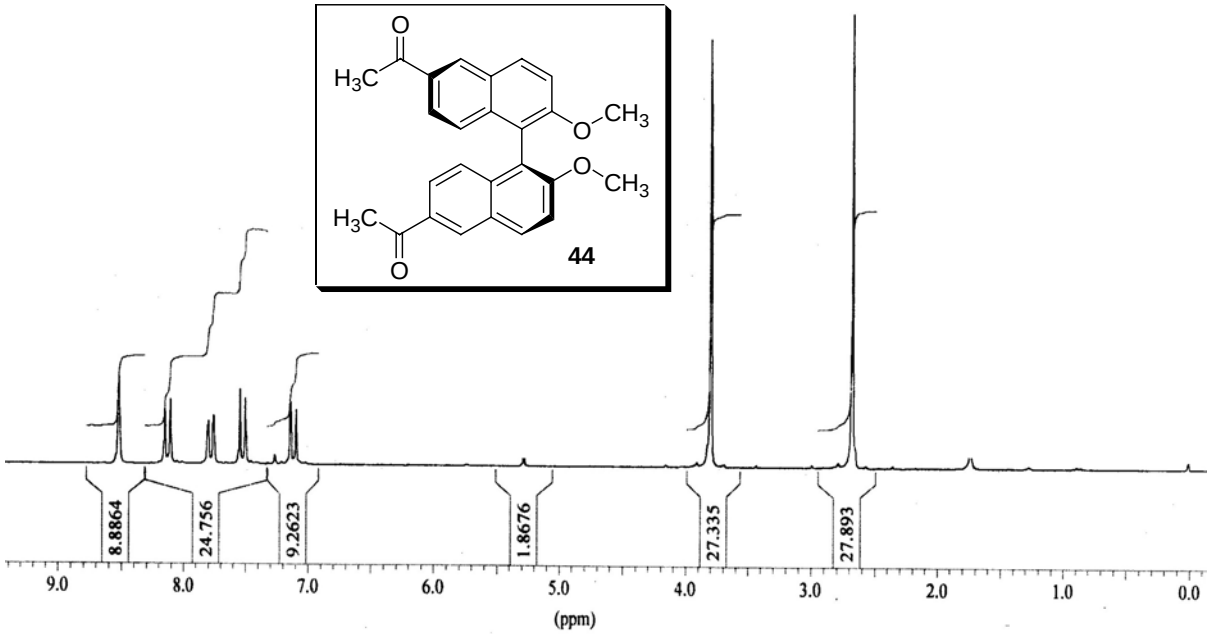
Spectrum No. 84 (Chapter 3, Section 3.4.1) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



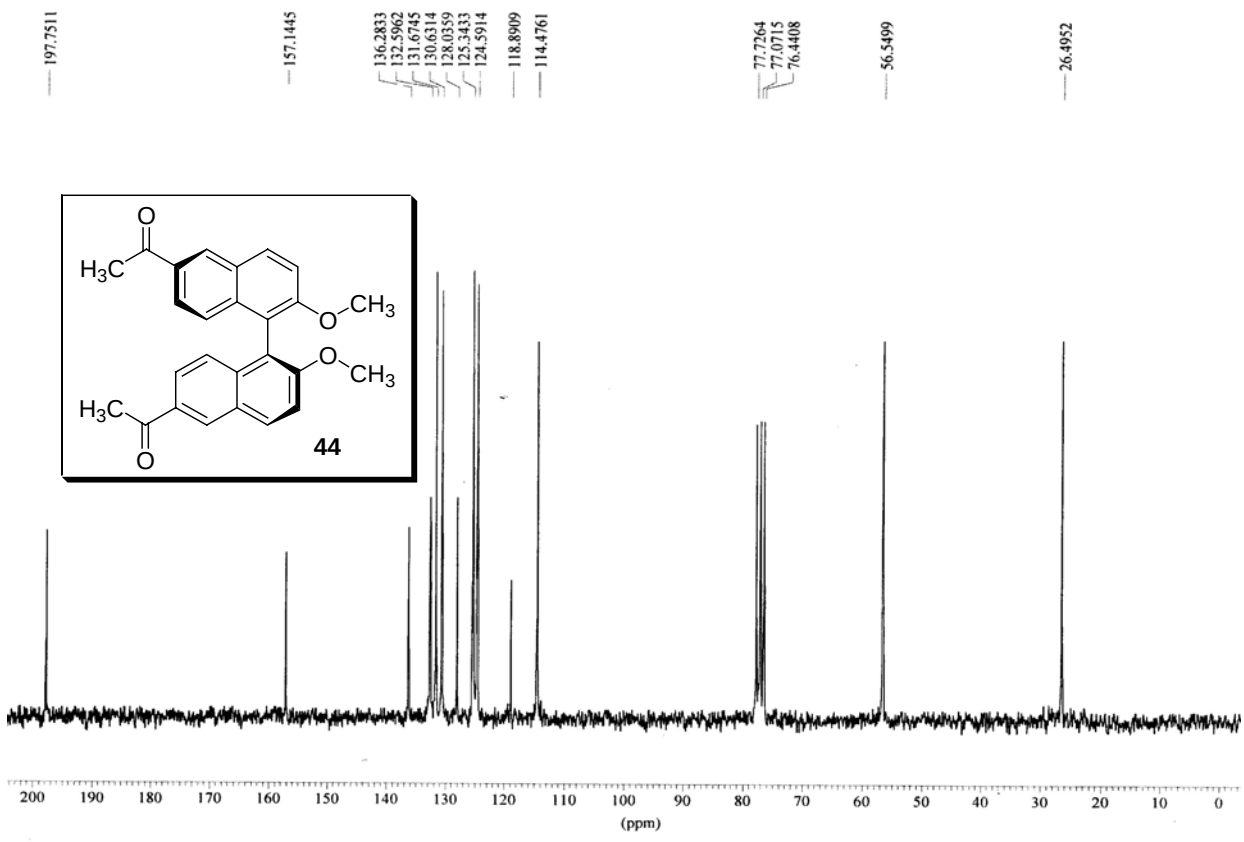
Spectrum No. 85 (Chapter 3, Section 3.4.1) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



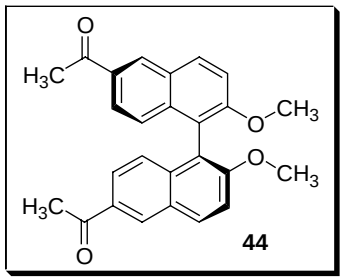
Spectrum No. 86 (Chapter 3, Section 3.4.3) ^{1}H NMR Spectrum (200 MHz, $CDCl_3$)



Spectrum No. 87 (Chapter 3, Section 3.4.3) ^{13}C NMR Spectrum (50 MHz, $CDCl_3$)



Spectrum No. 86 (Chapter 3, Section 3.4.3) EI Mass Spectrum



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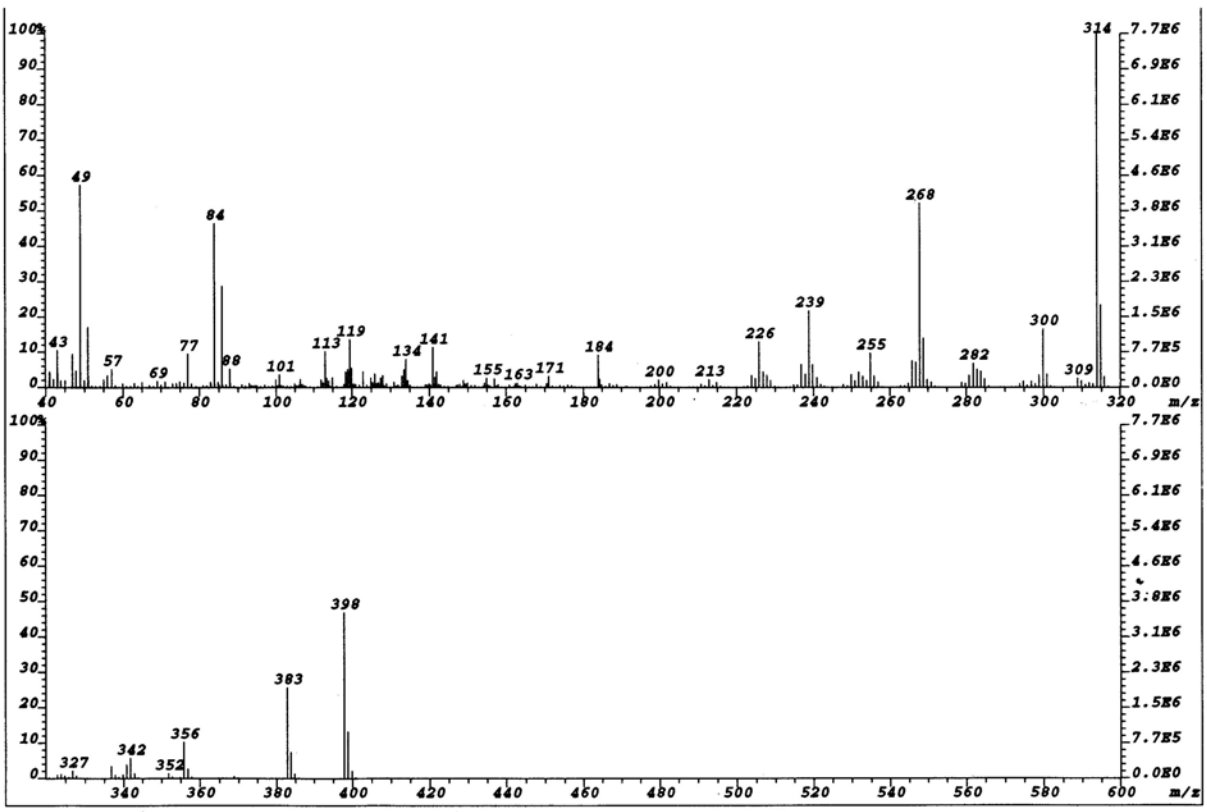
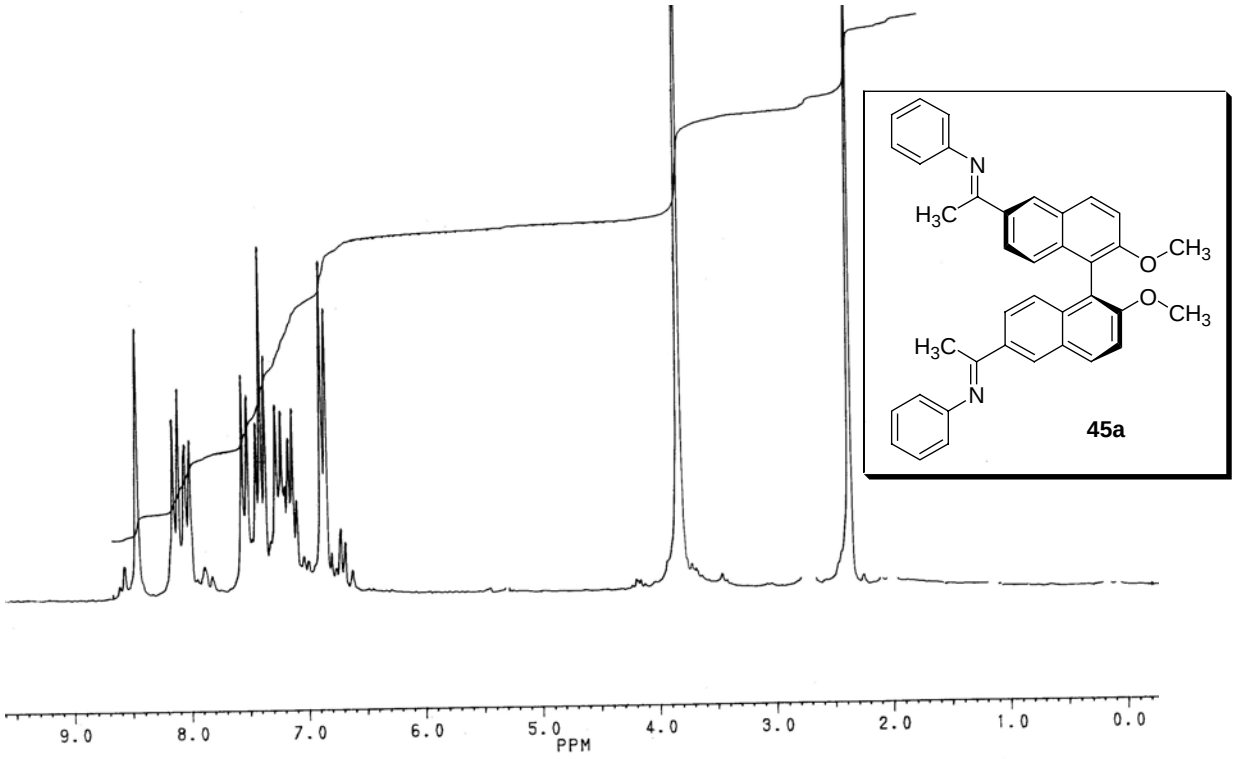
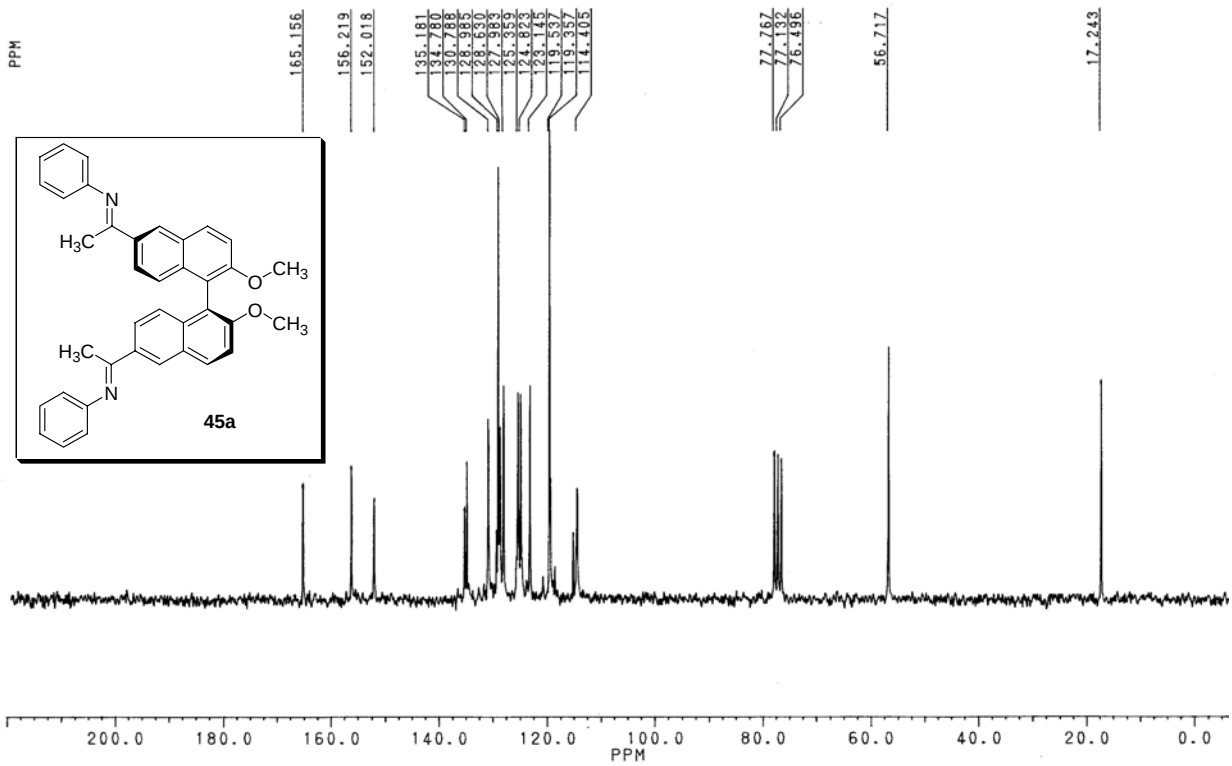


Spectrum No. 89 (Chapter 3, Section 3.4.4) ^{1}H NMR Spectrum (200 MHz, $CDCl_3$)



Spectrum No. 90 (Chapter 3, Section 3.4.4) ^{13}C NMR Spectrum (50 MHz, $CDCl_3$)



Appendix II

X-Ray Crystallographic Data

Table 1. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^2 x 10^3) for compound **49c (Chapter 1, section 1.2.2.1)**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

atom	x	y	z	U(eq)
C(1)	4811(2)	7447(2)	3853(2)	55(1)
C(2)	4966(3)	7067(2)	4754(2)	69(1)
C(3)	5727(3)	7835(3)	5856(2)	90(1)
C(4)	6371(3)	9015(3)	6120(3)	103(1)
C(5)	6261(3)	9427(3)	5292(3)	90(1)
C(6)	5494(2)	8664(2)	4142(2)	66(1)
C(7)	5379(3)	9084(2)	3283(3)	82(1)
C(8)	4644(3)	8360(2)	2190(3)	76(1)
C(9)	3961(2)	7157(2)	1891(2)	60(1)
C(10)	4021(2)	6686(2)	2682(2)	49(1)
C(11)	3235(2)	5369(2)	2296(2)	47(1)
C(12)	3532(2)	4723(2)	1411(2)	47(1)
C(13)	2609(2)	4283(2)	277(2)	56(1)
C(14)	2887(2)	3704(2)	-538(2)	61(1)
C(15)	4086(3)	3550(2)	-216(2)	62(1)
C(16)	5088(2)	3984(2)	939(2)	54(1)
C(17)	6371(3)	3875(2)	1293(3)	72(1)
C(18)	7371(3)	4359(2)	2389(3)	81(1)
C(19)	7135(3)	4966(2)	3209(2)	77(1)
C(20)	5885(2)	5064(2)	2908(2)	63(1)
C(21)	4824(2)	4597(2)	1767(2)	50(1)
C(22)	1615(2)	4967(2)	1893(2)	47(1)
C(23)	1337(2)	5671(2)	2747(2)	47(1)
C(24)	947(2)	6545(2)	2590(2)	55(1)
C(25)	709(2)	7204(2)	3352(2)	59(1)
C(26)	851(2)	7027(2)	4345(2)	58(1)
C(27)	1251(2)	6150(2)	4510(2)	60(1)
C(28)	1464(2)	5488(2)	3720(2)	54(1)
C(29)	775(3)	7503(2)	6147(2)	86(1)

C(30)	2282(4)	8152(3)	7087(3)	114(1)
C(31)	168(3)	8586(2)	4930(3)	84(1)
C(32)	-1404(4)	8142(3)	4246(4)	120(1)
C(33)	836(2)	3672(2)	1573(2)	49(1)
C(34)	1429(2)	3039(2)	2084(2)	57(1)
C(35)	678(2)	1870(2)	1801(2)	64(1)
C(36)	-738(3)	1259(2)	974(2)	75(1)
C(37)	-1343(3)	1892(2)	457(2)	87(1)
C(38)	-569(2)	3063(2)	755(2)	71(1)
C(39)	-641(6)	-687(4)	1004(3)	192(3)
C(40)	-733(5)	-541(3)	1927(5)	156(2)
C(41)	-3301(7)	-498(4)	52(4)	177(2)
C(42)	-3288(7)	-879(5)	-865(6)	201(3)
N(1)	596(2)	7672(2)	5115(2)	80(1)
N(2)	-1477(3)	113(2)	687(3)	128(1)

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for **98e (Chapter 2, section 2.2.1)**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

atom	x	y	z	U(eq)
C(15)	1332(2)	-1980(2)	1847(1)	51(1)
C(11)	3923(2)	786(2)	3229(1)	51(1)
C(12)	3035(2)	-182(2)	2732(1)	50(1)
C(13)	3742(2)	-1802(2)	2768(1)	54(1)
N(1)	502(2)	-2855(2)	1415(1)	68(1)
C(1)	4700(2)	1579(2)	2388(1)	51(1)
O(1)	2548(2)	1229(1)	4999(1)	73(1)
C(14)	2926(2)	-2687(2)	2343(1)	56(1)
C(9)	5650(2)	2434(2)	2781(1)	54(1)
O(2)	1756(2)	3293(1)	3875(1)	77(1)
C(16)	613(2)	-339(2)	1813(1)	58(1)
C(17)	1446(2)	520(2)	2247(1)	58(1)
C(2)	4548(2)	1451(2)	1263(1)	59(1)

C(20)	2627(2)	1953(2)	4046(1)	54(1)
C(4)	6151(2)	2996(2)	836(2)	75(1)
C(10)	6357(2)	3172(2)	1989(2)	64(1)
C(3)	5286(2)	2153(2)	484(1)	71(1)
C(8)	5934(2)	2581(2)	3927(2)	68(1)
C(5)	7270(2)	4042(2)	2383(2)	82(1)
C(19)	1183(2)	-4517(2)	1534(2)	77(1)
C(7)	6819(2)	3421(2)	4270(2)	86(1)
C(18)	-1097(3)	-2116(2)	883(2)	88(1)
C(6)	7489(2)	4167(2)	3485(2)	92(1)
C(21)	1191(3)	2088(3)	5802(2)	98(1)

Table 3. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for compound **108b (Chapter 2, section 2.2.2.3)**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

atom	x	y	z	U(eq)
C(1)	-579(3)	3316(1)	11075(2)	77(1)
C(2)	-1695(3)	3721(2)	10908(2)	106(1)
C(3)	-2663(3)	3541(2)	10238(2)	95(1)
C(4)	-2500(2)	2953(2)	9724(2)	80(1)
C(5)	-1356(2)	2541(1)	9890(2)	64(1)
C(6)	-380(2)	2720(1)	10569(1)	50(1)
C(7)	863(2)	2269(1)	10755(1)	46(1)
C(8)	1913(2)	2478(1)	10161(1)	47(1)
C(9)	2450(2)	3244(1)	10344(1)	49(1)
C(10)	2960(2)	3462(1)	11189(1)	60(1)
C(11)	3528(2)	4131(1)	11344(2)	69(1)
C(12)	3608(3)	4595(1)	10665(2)	84(1)
C(13)	3121(3)	4390(1)	9823(2)	96(1)
C(14)	2546(2)	3722(1)	9660(2)	72(1)
C(15)	486(2)	1465(1)	10702(1)	52(1)
C(16)	-114(2)	1139(1)	11447(1)	53(1)

C(17)	-720(2)	466(1)	11312(2)	71(1)
C(18)	-1203(3)	120(1)	12002(2)	89(1)
C(19)	-1079(3)	421(2)	12816(2)	89(1)
C(20)	-510(2)	1088(2)	12962(2)	78(1)
C(21)	-38(2)	1445(1)	12277(1)	64(1)
C(23)	3116(2)	1983(1)	10188(1)	48(1)
C(24)	4013(2)	1809(1)	10998(1)	50(1)
C(25)	3626(2)	1425(2)	11682(1)	78(1)
C(26)	4514(3)	1233(2)	12406(2)	96(1)
C(27)	5798(3)	1402(2)	12455(2)	89(1)
C(28)	6205(3)	1798(2)	11799(2)	104(1)
C(29)	5319(3)	2006(2)	11073(2)	89(1)
C(30)	2118(2)	2073(1)	8769(1)	58(1)
C(31)	3272(2)	1803(1)	9359(1)	54(1)
C(32)	4391(2)	1441(1)	9021(1)	61(1)
C(33)	4972(2)	1740(1)	8360(1)	67(1)
C(34)	6104(2)	1448(2)	8101(2)	77(1)
C(35)	6692(3)	856(2)	8495(2)	91(1)
C(36)	7972(3)	555(2)	8251(2)	132(1)
C(37)	6115(4)	563(2)	9151(2)	170(2)
C(38)	4987(4)	840(2)	9417(2)	147(2)
O(1)	1827(2)	2007(1)	7984(1)	81(1)
O(2)	1318(1)	2444(1)	9251(1)	56(1)
O(3)	667(2)	1109(1)	10066(1)	74(1)

Table 4. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for compound **110a (Chapter 2, section 2.2.2.3)**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

atom	x	y	z	U(eq)
C(1)	2633(3)	5835(6)	473(1)	47(1)
C(2)	2243(3)	6353(8)	134(2)	67(2)
C(3)	1851(3)	4834(8)	-65(2)	66(2)

C(4)	1861(3)	2755(10)	58(2)	74(2)
C(5)	2260(3)	2213(7)	388(2)	56(1)
C(6)	2650(2)	3727(6)	592(1)	38(1)
C(7)	3077(2)	3019(7)	943(1)	40(1)
C(8)	3253(2)	4628(6)	1266(1)	37(1)
C(9)	2612(2)	5088(5)	1522(1)	33(1)
C(10)	2488(3)	7142(6)	1673(1)	45(1)
C(11)	1883(3)	7563(8)	1896(2)	57(1)
C(12)	1381(3)	5982(8)	1978(2)	57(1)
C(13)	1491(3)	3963(9)	1836(2)	60(1)
C(14)	2112(3)	3523(7)	1608(1)	52(1)
C(15)	3937(2)	5333(7)	1316(1)	38(1)
C(16)	4206(2)	6633(6)	1653(1)	39(1)
C(17)	4202(3)	5796(8)	2031(1)	51(1)
C(18)	4484(3)	7017(11)	2338(2)	72(2)
C(19)	4751(3)	9020(12)	2276(2)	78(2)
C(20)	4743(3)	9879(9)	1907(2)	71(2)
C(21)	4476(2)	8669(8)	1594(2)	56(1)
C(22)	4493(3)	4843(8)	1002(2)	52(1)
C(23)	5737(3)	3872(15)	880(2)	106(3)
C(24)	5784(5)	1498(15)	850(3)	138(4)
C(25)	4886(3)	11054(7)	4504(2)	57(1)
C(26)	5253(4)	11754(11)	4846(2)	83(2)
C(27)	5690(4)	10367(16)	5051(2)	97(3)
C(28)	5768(4)	8306(15)	4927(2)	101(2)
C(29)	5397(3)	7593(9)	4608(2)	74(2)
C(30)	4952(2)	8956(7)	4393(1)	44(1)
C(31)	4557(2)	8061(7)	4049(1)	43(1)
C(32)	4340(2)	9614(6)	3719(1)	37(1)
C(33)	4968(3)	10174(6)	3458(1)	37(1)
C(34)	5069(3)	12219(7)	3314(1)	49(1)
C(35)	5667(3)	12690(8)	3077(2)	54(1)
C(36)	6177(3)	11147(9)	2991(2)	61(1)
C(37)	6094(3)	9133(9)	3137(2)	62(2)
C(38)	5497(2)	8627(8)	3371(1)	52(1)

C(39)	3646(2)	10246(6)	3679(1)	40(1)
C(40)	3365(2)	11570(6)	3341(1)	39(1)
C(41)	3101(3)	13604(7)	3405(2)	55(1)
C(42)	2831(3)	14832(9)	3102(2)	67(2)
C(43)	2816(3)	14034(11)	2728(2)	75(2)
C(44)	3071(3)	11972(11)	2654(2)	73(2)
C(45)	3349(3)	10754(8)	2963(1)	51(1)
C(46)	3092(2)	9600(7)	3976(2)	46(1)
C(47)	1848(3)	8962(17)	4111(2)	113(3)
C(48)	1732(4)	6616(18)	4091(3)	135(4)
O(1)	3252(2)	1160(5)	983(1)	72(1)
O(2)	4365(2)	4784(9)	664(1)	97(2)
O(3)	5150(2)	4495(8)	1154(1)	90(1)
O(4)	4469(2)	6170(5)	3997(1)	69(1)
O(5)	3253(2)	9020(7)	4303(1)	73(1)
O(6)	2425(2)	9661(8)	3845(1)	88(1)

Table 5. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^2 x 10^3) for compound **112a (Chapter 2, section 2.2.3.1)**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

atom	x	y	z	U(eq)
C(1)	1377(2)	241(1)	5954(1)	56(1)
C(2)	1047(2)	-363(1)	5524(1)	69(1)
C(3)	1735(3)	-850(2)	5199(1)	91(1)
C(4)	2762(3)	-740(2)	5297(1)	99(1)
C(5)	2424(2)	348(2)	6052(1)	77(1)
C(6)	3116(2)	-141(2)	5720(1)	100(1)
C(7)	580(2)	755(1)	6279(1)	53(1)
C(8)	923(1)	1381(1)	6791(1)	48(1)
C(9)	1080(1)	948(1)	7453(1)	47(1)
C(10)	410(2)	349(1)	7666(1)	61(1)
C(11)	581(2)	-46(1)	8261(1)	73(1)
C(12)	1399(2)	158(1)	8653(1)	74(1)

C(13)	2064(2)	752(1)	8449(1)	71(1)
C(14)	1911(1)	1141(1)	7848(1)	58(1)
C(15)	-170(2)	2445(1)	6174(1)	58(1)
C(16)	492(2)	2467(1)	5641(1)	76(1)
C(17)	173(3)	2769(2)	5030(1)	95(1)
C(18)	-813(3)	3062(2)	4959(2)	103(1)
C(19)	-1468(2)	3054(2)	5490(1)	96(1)
C(20)	-1155(2)	2746(1)	6095(1)	74(1)
C(22)	1828(2)	3796(1)	7643(1)	70(1)
C(23)	1539(2)	3255(1)	7151(1)	60(1)
C(24)	680(1)	2777(1)	7268(1)	50(1)
C(25)	143(1)	2845(1)	7850(1)	54(1)
C(26)	432(2)	3383(1)	8342(1)	69(1)
C(27)	1283(2)	3855(1)	8231(1)	76(1)
C(28)	188(1)	2122(1)	6844(1)	50(1)
C(29)	-720(2)	2274(1)	7832(1)	56(1)
O(1)	-325(1)	657(1)	6158(1)	69(1)
O(2)	-707(1)	1887(1)	7234(1)	54(1)
O(3)	-1377(1)	2128(1)	8237(1)	77(1)

Table 6. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for compound **113a (Chapter 2, section 2.2.3.2)**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

atom	x	y	z	U(eq)
C(1)	3516(2)	8191(2)	2903(1)	47(1)
C(2)	2232(2)	8361(2)	3087(1)	52(1)
C(3)	1798(2)	9506(2)	3328(1)	66(1)
C(4)	604(3)	9646(3)	3439(2)	83(1)
C(5)	-145(2)	8643(4)	3316(2)	92(1)
C(6)	286(2)	7507(3)	3090(2)	86(1)
C(7)	1459(2)	7362(2)	2973(1)	65(1)
C(8)	3774(2)	8724(2)	2049(1)	47(1)

C(9)	3054(2)	8004(2)	1407(1)	48(1)
C(10)	3094(2)	6748(2)	1198(1)	62(1)
C(11)	2284(2)	6337(3)	600(2)	79(1)
C(12)	1473(2)	7140(3)	226(2)	83(1)
C(13)	1450(2)	8383(3)	428(2)	74(1)
C(14)	2257(2)	8805(2)	1029(1)	55(1)
C(15)	2427(2)	10059(2)	1375(1)	62(1)
C(16)	5063(2)	8765(2)	1865(1)	46(1)
C(17)	5466(2)	9685(2)	1352(1)	58(1)
C(18)	6612(2)	9685(2)	1131(2)	64(1)
C(19)	7404(2)	8780(2)	1410(1)	59(1)
C(20)	7000(2)	7883(2)	1935(1)	60(1)
C(21)	5852(2)	7857(2)	2152(1)	55(1)
C(22)	4330(2)	8720(2)	3574(1)	51(1)
C(23)	5534(3)	8153(3)	4733(2)	88(1)
C(24)	8648(2)	8769(3)	1142(2)	85(1)
O(1)	1951(2)	11039(2)	1207(1)	92(1)
O(2)	3305(1)	9990(1)	1971(1)	55(1)
O(3)	4597(2)	9794(1)	3657(1)	75(1)
O(4)	4710(1)	7805(1)	4071(1)	64(1)

LIST OF PUBLICATIONS

1 A novel arylation of arylacetic acid esters using tertiary arylamines and $TiCl_4$; Periasamy, M.; **Kishorebabu, N.;** Jayakumar, K. N. *Tetrahedron Lett*. **2003**, *44,* 8939-8941.

2 A simple, convenient method for the synthesis of maleic anhydrides from *a*-keto esters and alkanoic acid anhydrides using the $TiCl_4$/*n*-Bu_3N reagent system; **Kishorebabu, N.;** Periasamy, M. *Tetrahedron Lett.* **2006,** *47,* 2107–2109.

3 A simple $TiCl_4$ promoted method of arylation of orthoformate and benzyl ethers by *N*,*N*-dialkylarylamines; Periasamy, M.; **Kishorebabu, N.** Jayakumar, K. N. *Communicated*.

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