New Organic Synthetic Methods Using Titanium Reagents:

Synthetic Transformations of Alkynes, Propargyl Alcohols and Pinacols

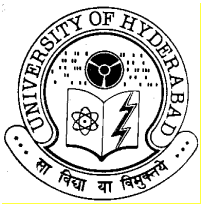
A Thesis

Submitted for the Degree of

DOCTOR OF PHILOSOPHY

By

GALLA V. KARUNAKAR



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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 "**New Organic Synthetic Methods Using Titanium Reagents: Synthetic Transformations of Alkynes, Propargyl Alcohols and Pinacols**" has been carried out by Mr. **Galla V. Karunakar** under my supervision and the same has not been submitted elsewhere for a Degree.

PROFESSOR M. PERIASAMY
(THESIS SUPERVISOR)

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□□□□□□□□□ □. □.

Abbreviations

[α]	specific rotation [expressed without units; the actual units, deg.mL/g.dm, are understood]
AIBN	2,2'-azobisisobutyronitrile
aq.	aqueous
Ar	aryl
BINOL	1,1'-bi(2-naphthol)
br	broad (spectral)
Bu	butyl
Bz	benzoyl
cat.	catalytic
COD	1,5-cyclooctadiene
CSA	camphorsulfonic acid
DABCO	1,4-diazabicyclo[2.2.2]octane
de	diastereomeric excess
$(DHQD)_2PHAL$	hydroquinidine 1,4-phthalazinediyl diether
(+)DIPT	diisopropyltartrate
DPPM	α,α-diphenyl-2-pyrrolidinemethanol
dr	diastereomeric ratio
ee	enantiomeric excess
EI	electron impact (in mass spectrometry)
equiv.	equivalent
er	enantiomeric ratio
Et	ethyl
HPLC	high-performance liquid chromatography
i	iso
J	coupling constant (in NMR spectroscopy)
KAPA	potassium 3-aminopropylamide
Lit.	literature
m	multiplet (spectral)

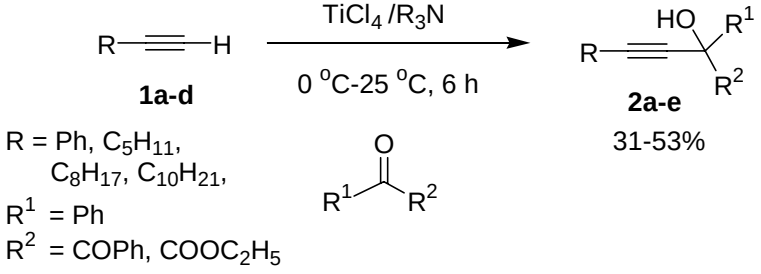
Me	methyl
mp	melting point
n	primary
Nu	nucleophile
ORTEP	oak ridge thermal ellipsoid plot
Ph	phenyl
Pr	propyl
PPSE	polyphosphoricacid trimethylsilyl ester
q	quartet (spectral)
rt	room temperature
t	triplet (spectral)
t	tertiary
s	singlet (spectral)
TIP	titaniumtetraisopropoxide
THF	tetrahydrofuran
TMEDA	*N*,*N*,*N*',*N*'-tetramethylethylenediamine
TMS	trimethylsilyl
X	halide

Abstract

This thesis entitled "**New Organic Synthetic Methods Using Titanium Reagents: Synthetic transformations of Alkynes, Propargyl Alcohols and Pinacols"** 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.

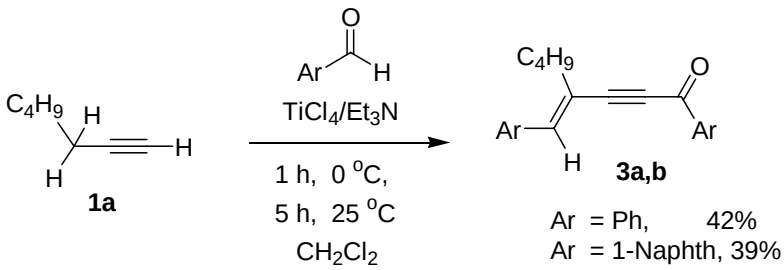
The first chapter describes the studies on the synthesis of the propargyl alcohols, enynones and 1,2-diaryl-1,2-diones. Synthetic applications of the $TiCl_4/R_3N$ reagent system are briefly reviewed in the introduction. We have carried out systematic investigations on the reactions of alkynes with aromatic aldehydes. Propargyl alcohols **2a-2e** were prepared in the reaction of alkynes **1a-d** and certain ketones using the $TiCl_4/Et_3N$ reagent system (Scheme 1).

Scheme 1



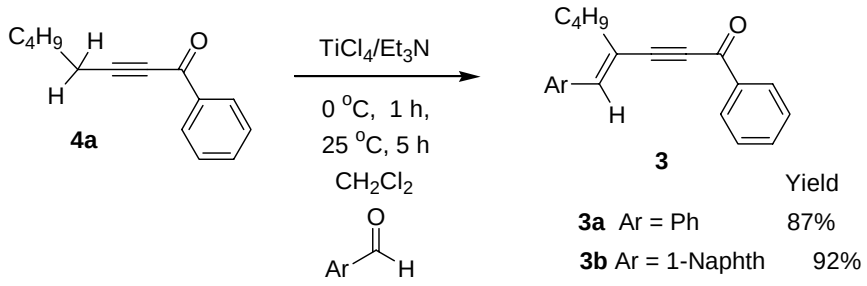
E-Enynones **3a**,**b** are produced in the reaction of alkynes **1** and aldehydes using the $TiCl_4/Et_3N$ reagent system (Scheme 2).

Scheme 2



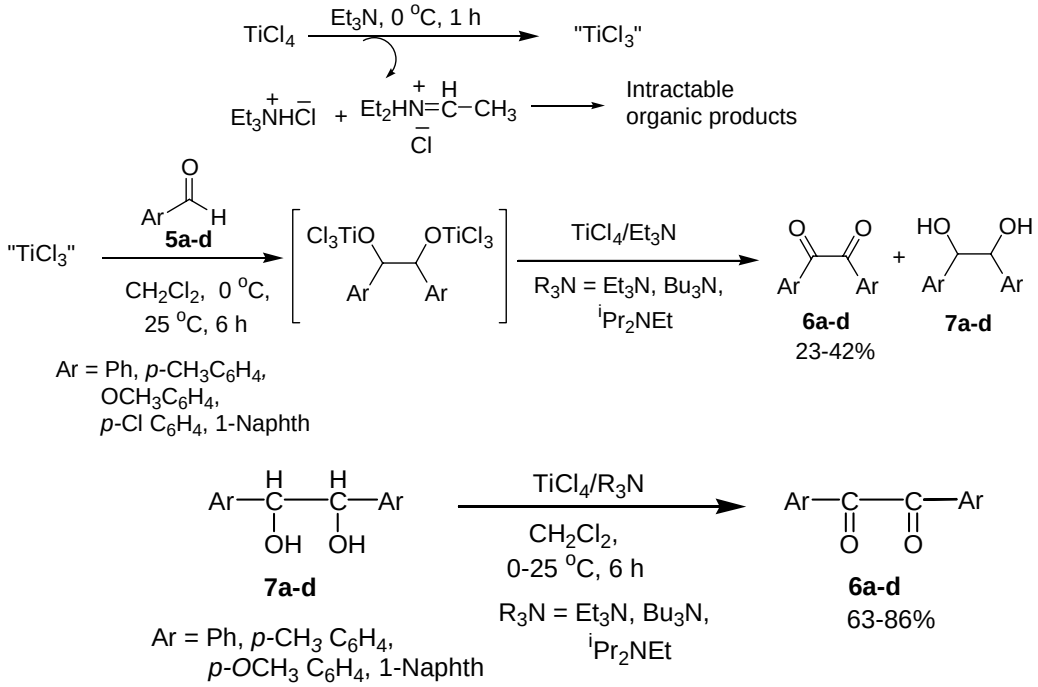
The alkynyl ketone **4a** reacts with $TiCl_4$/ Et_3N reagent and aromatic aldehydes to give the enynones **3a, 3b** in good yields (Scheme 3).

Scheme 3



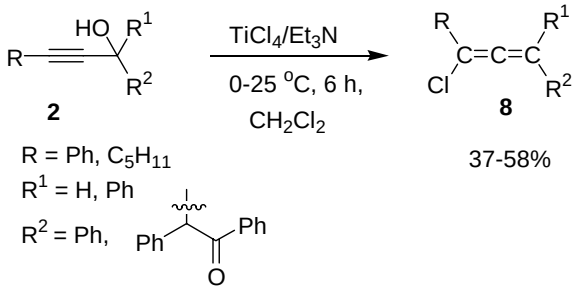
We have also examined the reactivity of the different aromatic aldehydes **5a-d** with the Ti(III)/Ti(IV) species produced using the $TiCl_4/Et_3N$ reagent in CH_2Cl_2 at 0-25 ^oC. The corresponding 1,2-diketones **6a-d** are obtained in 23-42% yields. In the reaction of 1,2-diphenylethane-1,2-diols **7a-d** with the $TiCl_4/Et_3N$ reagent in CH_2Cl_2 at 0-25 ^oC, the corresponding 1,2-diketones **6a-d** are obtained in 63-86% yields (Scheme 4).

Scheme 4



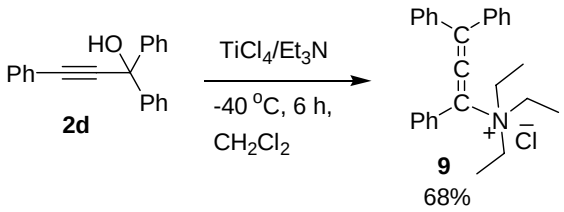
In the second chapter, synthetic transformations of propargyl alcohols using the $TiCl_4/Et_3N$ reagent system are described. Reactions of propargyl alcohol using various reagents are briefly reviewed in the introductory section. We have observed that the propargyl alcohols **2** derived from aromatic aldehydes and ketones are converted to the corresponding chloroallenes **8** using the $TiCl_4/Et_3N$ reagent system (Scheme 5).

Scheme 5



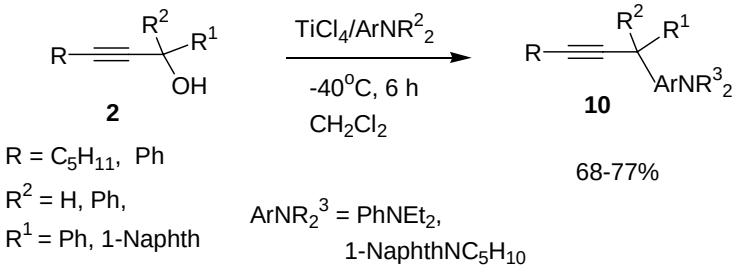
The propargyl alcohol **2d** on reaction with the $TiCl_4/Et_3N$ reagent system at –40 ^oC produces the allene derived triethylamine salt **9**. The product **9** was further characterized by single crystal X-ray studies (Scheme 6).

Scheme 6



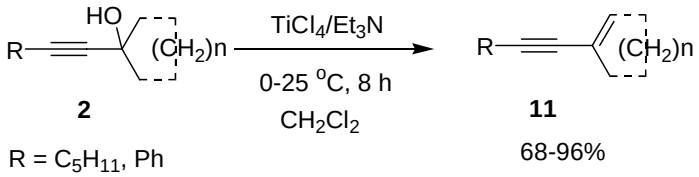
The propargyl alcohols **2** react with $TiCl_4$/aryl amines to give the corresponding aryl alkyne products **10** at -40^oC (Scheme 7).

Scheme 7



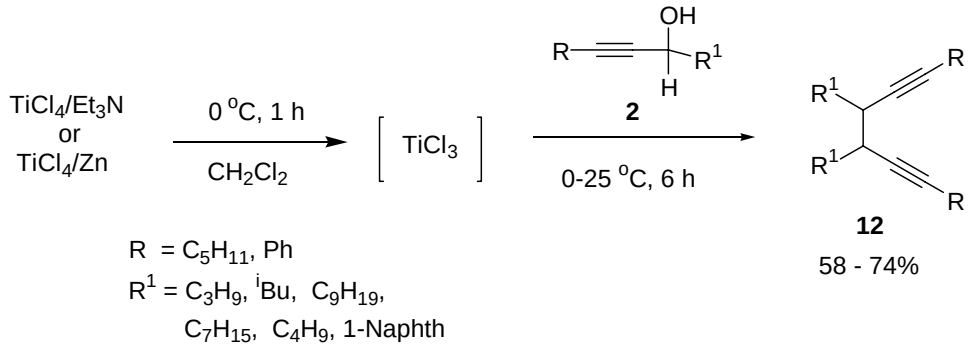
The propargyl alcohols **2** derived from aliphatic ketones are converted to the corresponding 1,3-enynes **11** using the $TiCl_4/Et_3N$ reagent system (Scheme 8).

Scheme 8



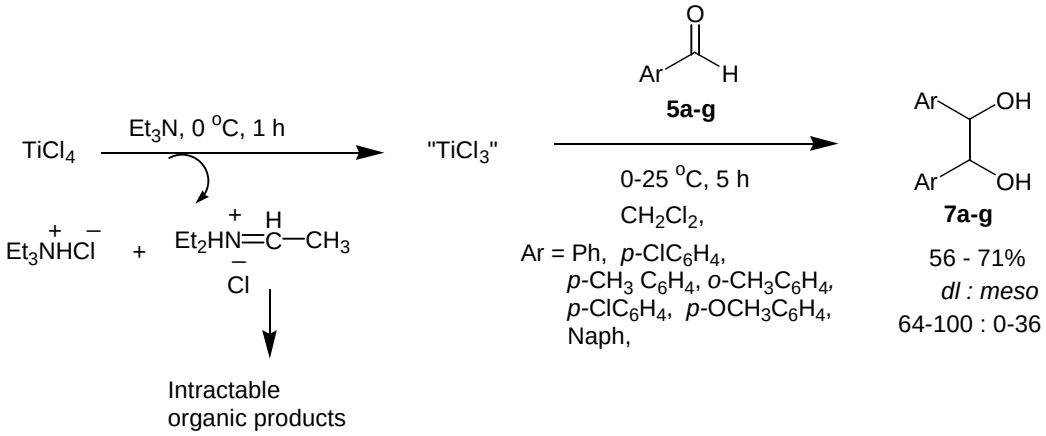
Low-valent titanium species prepared using $TiCl_4/Et_3N$ or $TiCl_4/Zn$ react with propargyl alcohols **2** to the corresponding 1,5-diynes **12**. The structure of 1,5-diyne **12f** (R = Ph, R^1 = Naphth) was characterized by the single crystal X-ray data (Scheme 9).

Scheme 9



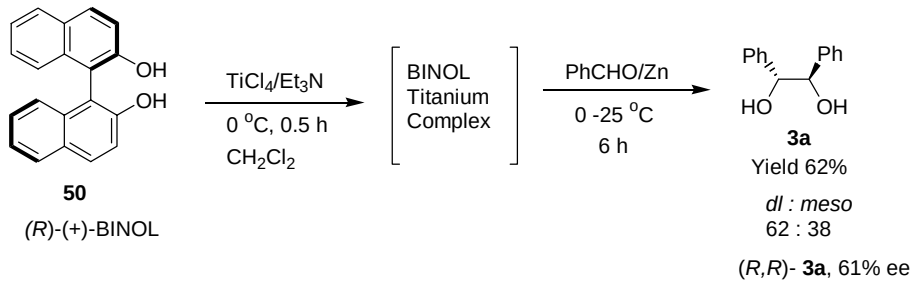
Synthesis of 1,2-diaryl-1,2-diols and attempts towards studies on the chiral duplication of 1,2-diaryl-1,2-diols via pinacol coupling are discussed in the third chapter. Low-valent titanium species generated using the $TiCl_4/Et_3N$ reagent system reacts with aromatic aldehydes **5a-g** to give the corresponding 1,2-diarylethane-1,2-diols **7a-g** (Scheme 10).

Scheme 10



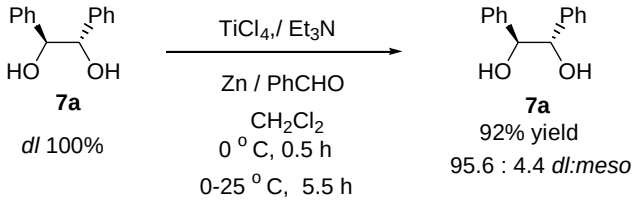
Also, the low-valent titanium species generated in this way reduces the aromatic nitro compounds to the corresponding aromatic amines in moderate yields (27-42%). Asymmetric pinacol coupling of benzaldehyde gave poor selectivity using the (*R*)-(+)-BINOL(**14**)/$TiCl_4$/Et_3N/Zn reagent system (Scheme 11)

Scheme 11



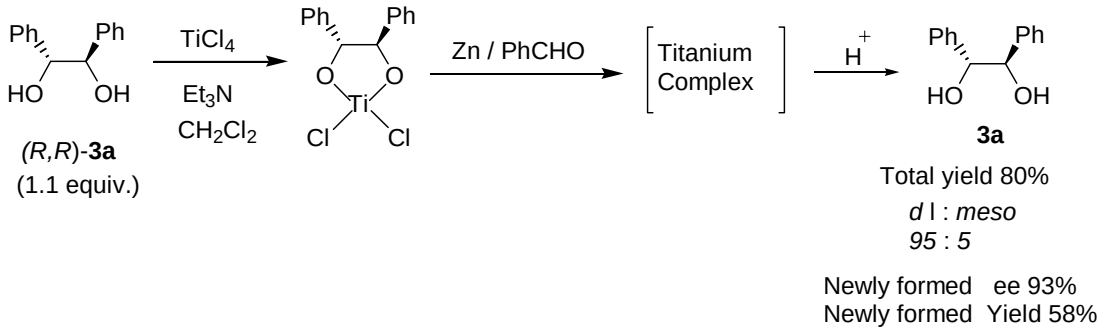
Diastereoselective duplication of chirality in the pinacol coupling of benzaldehyde to 1,2-diphenylethane-1,2-diols **7a** using $TiCl_4$/R_3N/1,2-diphenylethane-1,2-diol (**7a**) system gave good selectivity (Scheme 12).

Scheme 12



Enantioselective duplication of chirality was briefly studied using the (*R*,*R*)-1,2-diphenylethane-1,2-diol/benzaldehyde/$TiCl_4$/Et_3N/Zn reagent system (Scheme 13).

Scheme 13



The results are discussed by considering the intermediates and mechanisms involved in all these transformations.

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.

Contents

Chapter 2

Synthetic transformations of propargyl alcohols using the $TiCl_4/Et_3N$ reagent system

Chapter 3

Synthetic applications of low-valent titanium species generated using the $TiCl_4/R_3N$ and $TiCl_4/Zn$ reagent system

Chapter 1

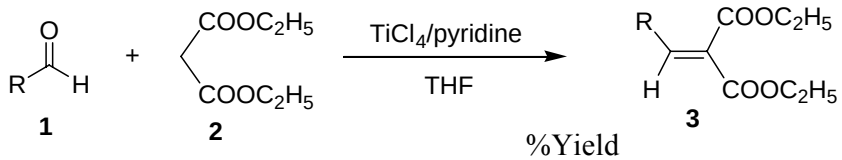
Synthetic Applications of the $TiCl_4/R_3N$ Reagent System

1.1 Introduction

Organotitanium reagents are well known for utilization in the C-C bond forming reactions.[1] Among the various transition metal reagents, titanium reagents are widely used, because they are more selective than the other transition metal reagents.[2] Within the titanium reagents, $TiCl_4$ has vast applications in organic synthesis.[3] It has been used as such or in combination with an additive. In the last twenty years, several useful synthetic transformations have been reported involving the use of $TiCl_4$ along with a tertiary amine R_3N. In continuation of our research efforts towards the development of new synthetic methods using the $TiCl_4/R_3N$ reagent system, we have observed several new transformations. A brief review of the literature on this topic will be helpful for discussion.

The $TiCl_4/R_3N$ reagent system has been widely used for the preparation of titanium enolates for applications in aldol and related reactions in organic synthesis.[4] For example, it has been reported that the aldehydes **1** and diester **2** react in the presence of $TiCl_4$/pyridine reagent to give the Knoevenagel condensation products **3** (Scheme 1).[5]

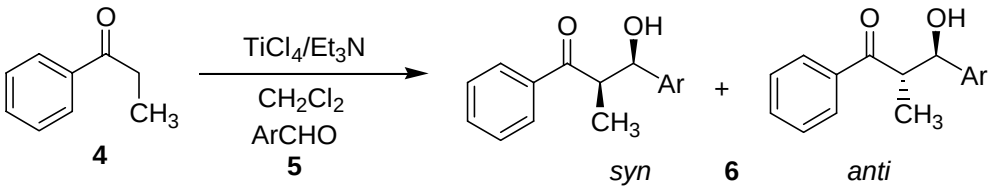
Scheme 1



	%Yield
R = CH_3	86
R = *n*-C_4H_9	81
R = Ph	97

It was reported that propiophenone **4** reacts with arylaldehydes **5** in the presence of $TiCl_4/Et_3N$ to give the corresponding aldol condensation products **6** with very high *syn* selectivity (Scheme 2).[6]

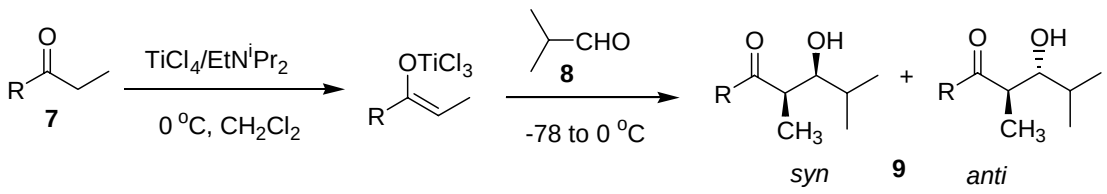
Scheme 2



	%Yield	*syn* : *anti*
Ar = Ph	91	95 : 5
Ar = *p*-$OCH_3C_6H_4$	95	89 : 11
Ar = *p*-$CH_3C_6H_4$	94	96 : 4
Ar = *p*-$NO_2C_6H_4$	98	87 : 13

A similar reactivity pattern has also been observed in the reaction of aliphatic ketones. For example, isopropyl ethyl ketone **7**-derived chlorotitanium enolate generated by the sequential addition of $TiCl_4$ and diisopropylethyl amine reacts with aldehyde **8** to give the corresponding aldol products **9** with *syn* selectivity (Scheme 3).[7]

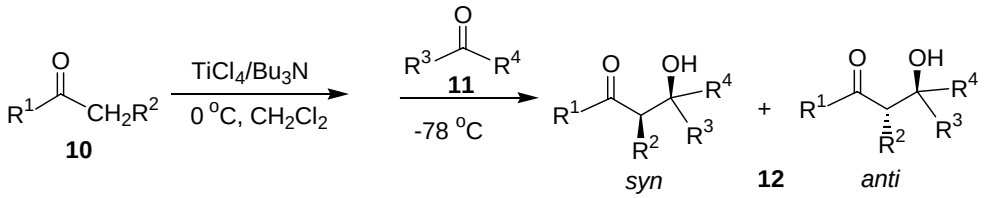
Scheme 3



	%Yield	*syn : anti*
R = C_2H_5	95	92 : 8
R = C_3H_7	95	93 : 7

The titanium enolate prepared using a ketone **10** and $TiCl_4/Bu_3N$ reagent reacts with other ketones **11** to give the aldol product **12** stereoselectively (Scheme 4).[8]

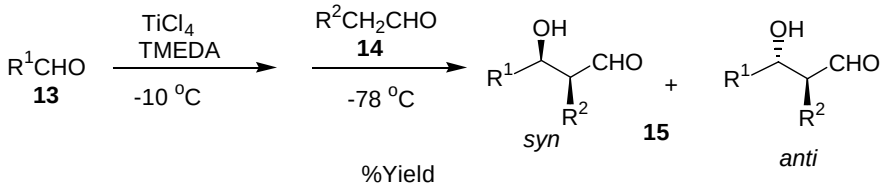
Scheme 4



	%Yield	*syn* : *anti*
R^1 = Ph, R^2 = CH_3, R^3 = Ph, R^4 = CH_3	95	>99 : <1
R^1 = Ph, R^2 = CH_3, R^3 = Ph, R^4 = CH_2Cl	91	>99 : <1

Aldehydes **13** form complexes of $TiCl_4$ that react with other aldehydes **14** in the presence of TMEDA to give the corresponding aldol products **15** with high *syn* selectivity (Scheme 5).[9]

Scheme 5

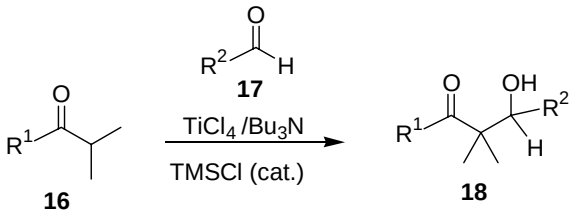


	%Yield
R^1 = Ph, R^2 = CH_3	72
R^1 = Ph, R^2 = CH_3CH_2	78

syn : *anti*
>96 : <4

The reaction of $TiCl_4/Bu_3N$, α,α-dimethylketone **16** and aldehydes **17** in the presence of TMSCl produces the aldol adducts **18** (Scheme 6).[10]

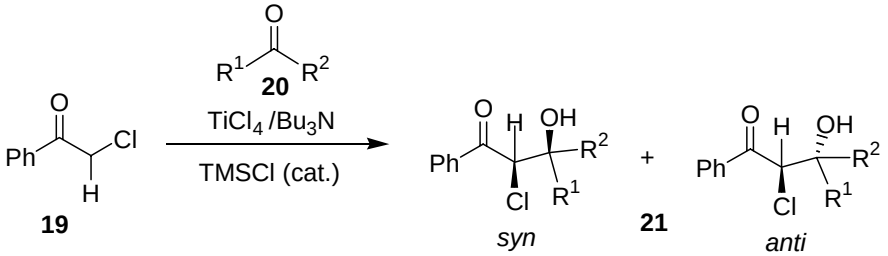
Scheme 6



	%Yield
R^1 = ^{i}Pr, R^2 = ^{i}Pr	87
R^1 = ^{i}Pr R^2 = Ph	51

Stereoselective synthesis of aldol products **21** was achieved by the reaction of α-chloroketones **19** with ketones **20** in the presence of $TiCl_4/Bu_3N$/TMSCl (Scheme 7).[10]

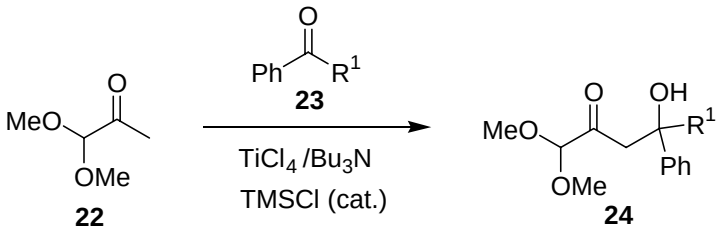
Scheme 7



R^1	R^2	%Yield	*syn : anti*
Ph	H	81	>94 : <6
Bu	H	71	
Et	Et	15	

In the presence of $TiCl_4/Bu_3N$/TMSCl, α-oxyketones **22** react with ketones **23** to produce the aldol product **24** (Scheme 8).[10]

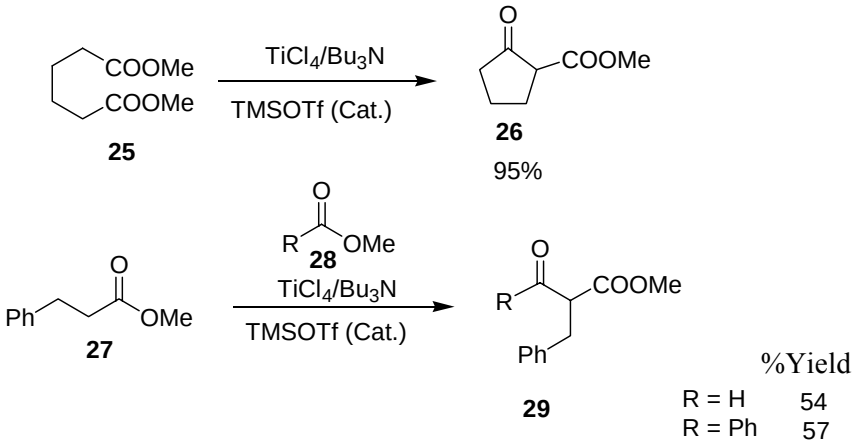
Scheme 8



R^1	%Yield
H	80
CH_2Cl	63

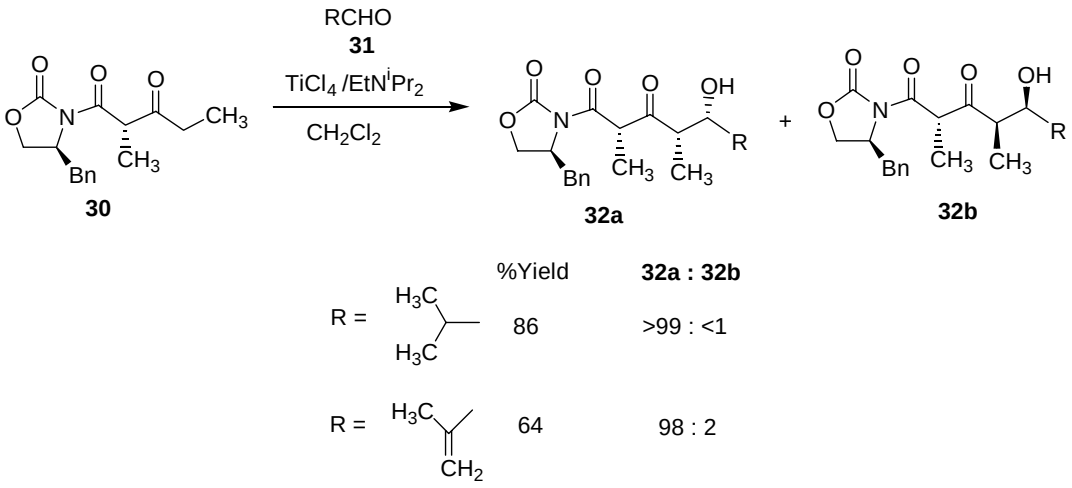
It was also reported that the direct Claisen condensation product **26** was isolated from **25** and **29** was obtained from **27** and **28** using the $TiCl_4/Bu_3N$/TMSOTf reagent system (Scheme 9).[10]

Scheme 9



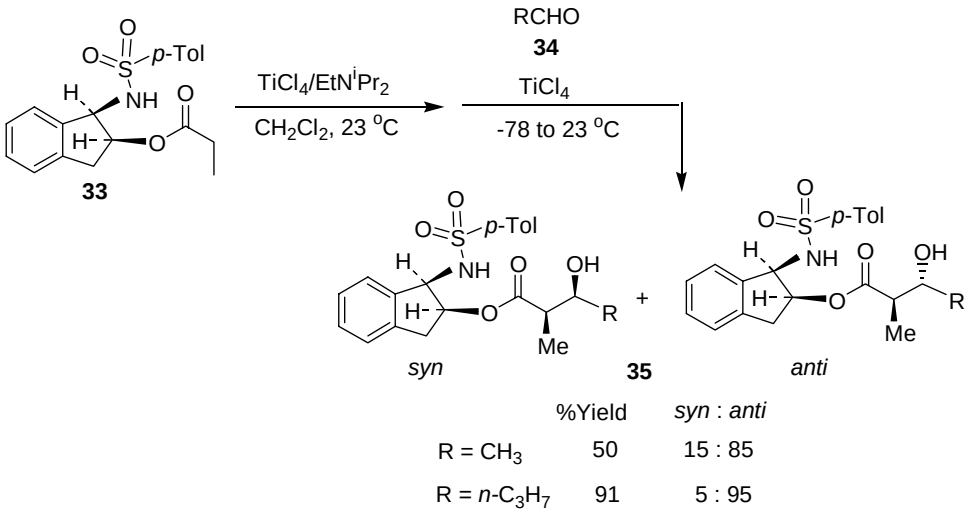
In the presence of $TiCl_4/EtN^iPr_2$ reagent system, β-keto imide **30** reacts with aldehydes **31** to produce the aldol products **32** with very high diastereoselectivity (Scheme 10).[11]

Scheme 10



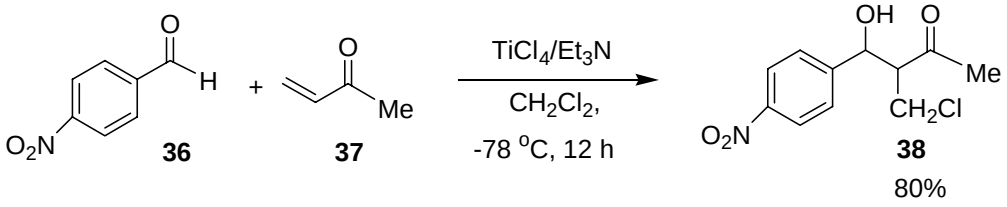
The chiral amino indanol **33** reacts with aldehydes **34** in the presence of the $TiCl_4/EtN^iPr_2$ reagent system to form **35** with high level of *anti* selectivity (Scheme 11).[12]

Scheme 11



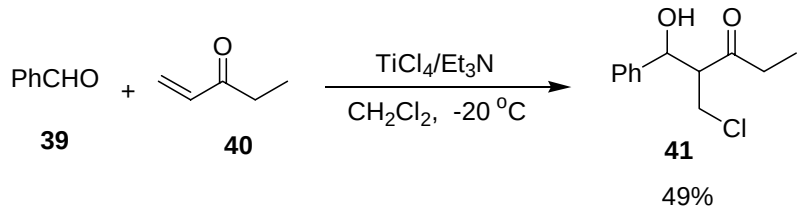
It was reported that non-enolizable aldehyde **36** reacts with α,β-unsaturated carbonyl compound **37** in the presence of $TiCl_4/Et_3N$ reagent to give the corresponding Baylis-Hillmann type product **38** (Scheme 12).[13]

Scheme 12



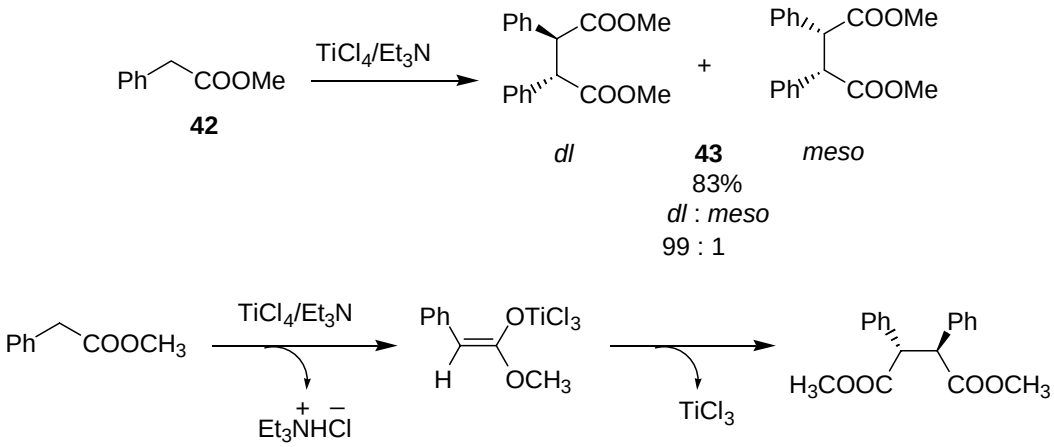
It was reported that the $TiCl_4/Et_3N$ reagent system reacts with the aldehyde **39** and methyl vinylketone **40** to give the corresponding chlorinated adduct **41** (Scheme 13).[14]

Scheme 13



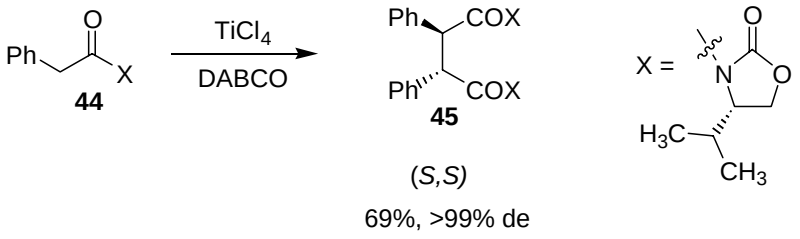
It was reported that the $TiCl_4/Et_3N$ reagent system is useful in the preparation of the (*dl*)-C_2 symmetric 2,3-diphenylsuccinic acid esters **43** from methyl phenylacetate **42**. The reaction is highly chemo- and diastereoselective (Scheme 14).[15] The reaction proceeds through the formation of the corresponding titanium enolate, followed by oxidative coupling with concomitant formation of the titanium (III) species.

Scheme 14



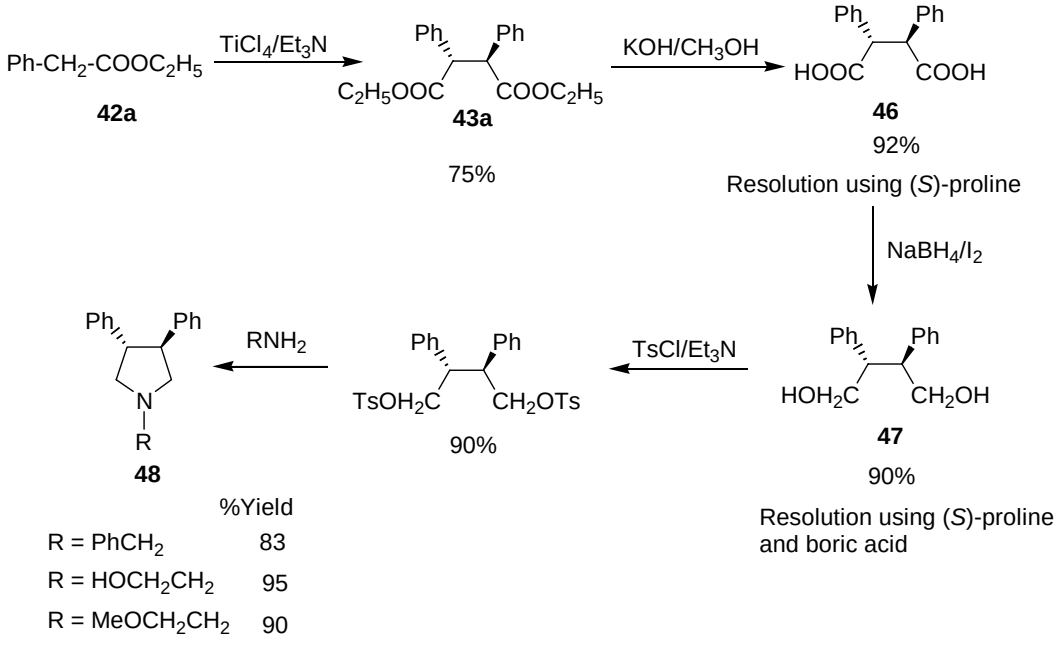
Also, it was observed that the asymmetric version of oxidative coupling of **44** using the $TiCl_4$/DABCO reagent system gives the homocoupled product **45** with high selectivity (Scheme 15).[16]

Scheme 15



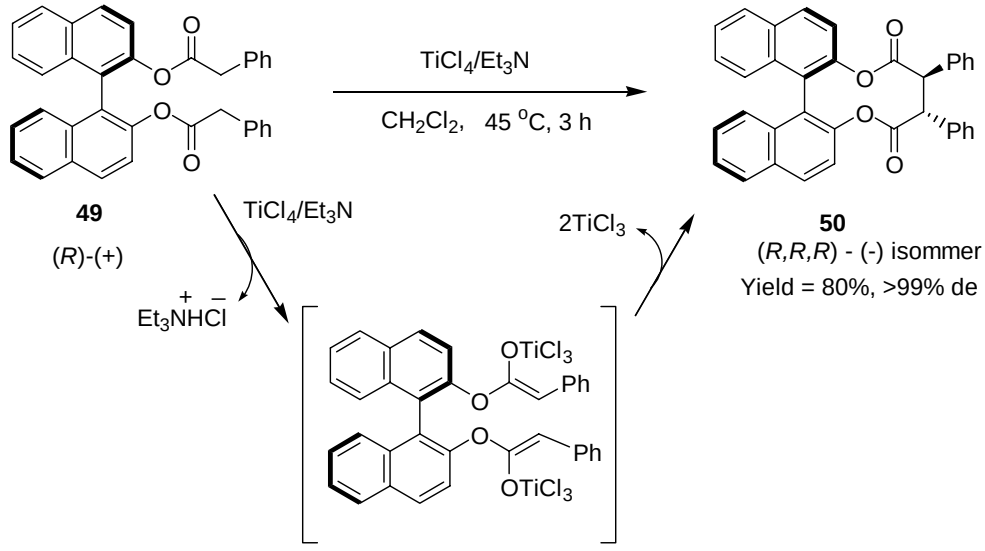
The dicarboxylic acid **46**, formed in the oxidative coupling reaction was further used for the synthesis of chiral 3,4-diphenylpyrrolidine **48** system (Scheme 16).[17]

Scheme 16



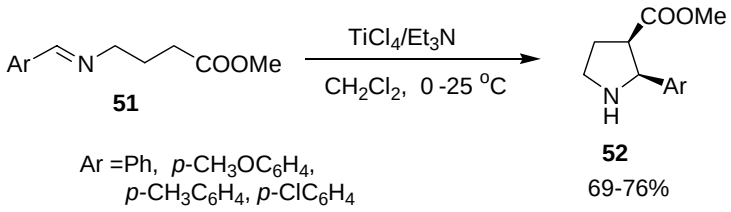
It was reported that the chiral binaphthyl phenyl acetate **49** on reaction with $TiCl_4/Et_3N$ reagent gives the corresponding diastereoselective cyclic compound **50** (Scheme 17).[18]

Scheme 17



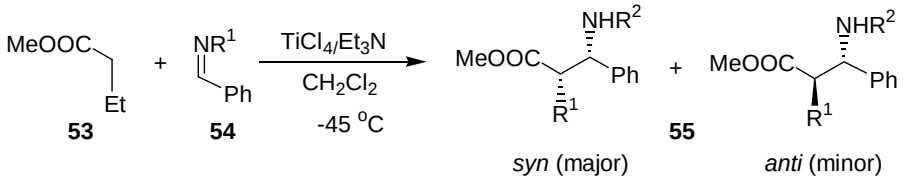
Facile synthesis of the 2-aryl-3-pyrrolidine carboxylates **52** from readily accessible γ-imino esters **51** was achieved by intramolecular cyclization mediated by the $TiCl_4/Et_3N$ reagent system (Schem18).[19]

Scheme 18



Reaction of benzaldehyde imines **54** and esters **53** with the $TiCl_4/Et_3N$ reagent system produced the *syn*-β-amino esters **55** stereoselectively (Scheme 19).[20]

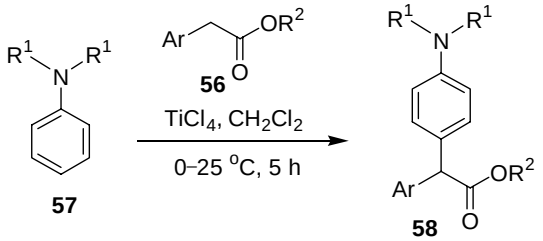
Scheme 19



	R^1	%Yield	*syn* : *anti*
1	Bn	87	100 : 0
2	*n*-Bu	78	95 : 5

The reaction of arylacetic acid esters **56** with tertiary arylamines **57** in the presence of $TiCl_4$ gives α,α-diarylated products **58** (Scheme 20).[21]

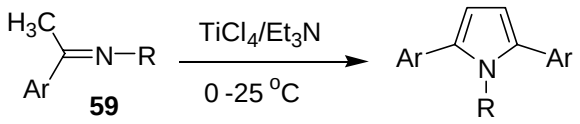
Scheme 20



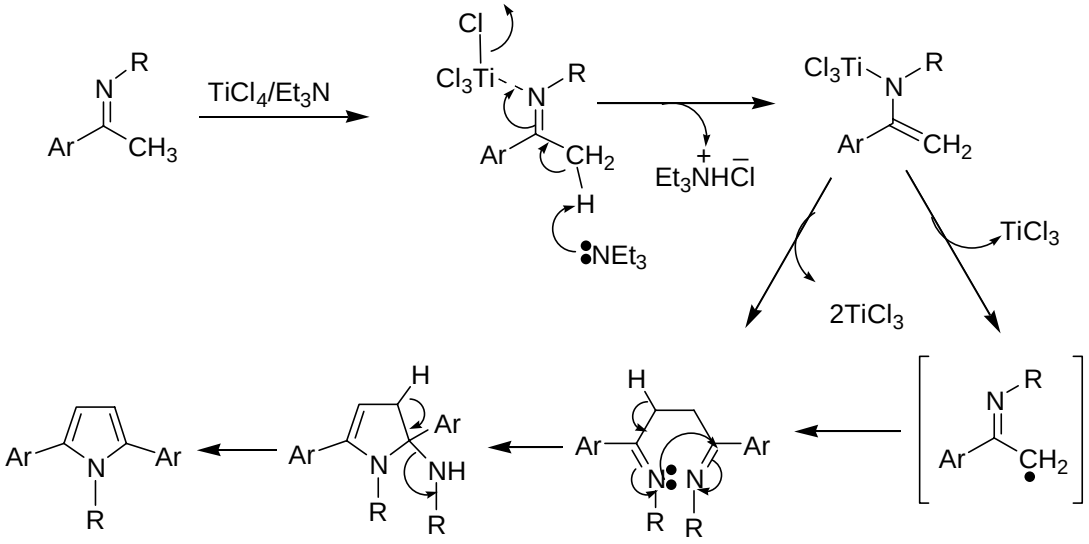
	$PhNR_2^1$	Ester	%Yield
1	$R^1 = CH_3$	Ar = Ph, $R^2 = C_2H_5$	89
2	$R^1 = C_2H_5$	Ar = Ph, $R^2 = C_2H_5$	90
3	$R^1 = CH_3$	Ar = 1-Naph, $R^2 = CH_3$	88

The reactivity pattern of the $TiCl_4/Et_3N$ reagent system with other organic substrates containing acidic hydrogen has been also reported. For instance, reaction of aromatic ketimines **59** with $TiCl_4/Et_3N$ produced the corresponding 2,5-disubstituted pyrroles **60** through oxidative coupling and aromatization reactions (Scheme 21). The results can be rationalized by the mechanism shown below.[22]

Scheme 21

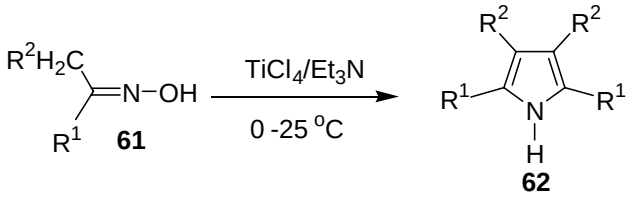


	%Yield
Ar = Ph, R = Ph	81
Ar = Ph, R = *p*-$OMeC_6H_4$	62
Ar = 2-Naph, R = Ph	55



Certain ketoximes **61** react with the $TiCl_4/Et_3N$ reagent system to give the corresponding tetra substituted pyrroles **62** (Scheme 22).[23]

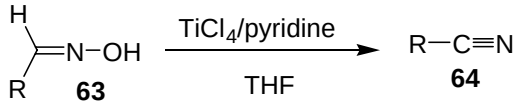
Scheme 22



	%Yield
R^1 = Ph, R^2 = Ph	81
R^1 = CH_2Ph, R^2 = Ph	62
R^1 = *p*-$CH_3C_4H_6$, R^2 = CH_3	55

Aldoximes **63** give the corresponding nitriles **64** on reaction with the $TiCl_4$/pyridine reagent system (Scheme 23).[24]

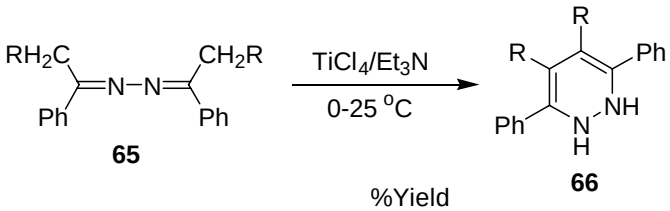
Scheme 23



	%Yield
R = $CH_3CH_2CH_2$	80
R = Ph	97

The reaction of hydrazones **65** with the $TiCl_4/Et_3N$ reagent system gives the corresponding 1,2-dihydropyridazines **66** (Scheme 24).[25]

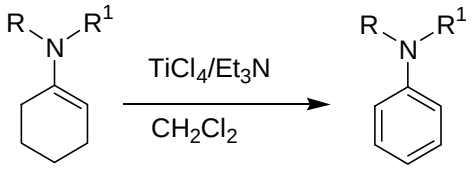
Scheme 24



	%Yield
R = H	50
R = CH_3	55

Certain enamines **67** react with the $TiCl_4/Et_3N$ reagent system to give the corresponding aromatized products **68** (Scheme 25).[26]

Scheme 25



67 **68**

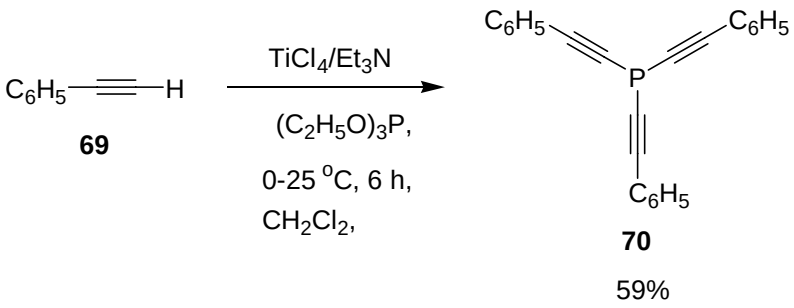
68-84%

$R,R^1 = (CH_2)_4,\ (CH_2)_5,\ (CH_2)_2O(CH_2)_2$

$R,R^1 = CH_3,\ Ph$

It has been observed that the $TiCl_4/Et_3N$ reagent system reacts with 1-alkyne **69** to give titanium acetylide, which on reaction with triethyl phosphate produce the trialkynyl phosphine **70** (Scheme 26).[27]

Scheme 26

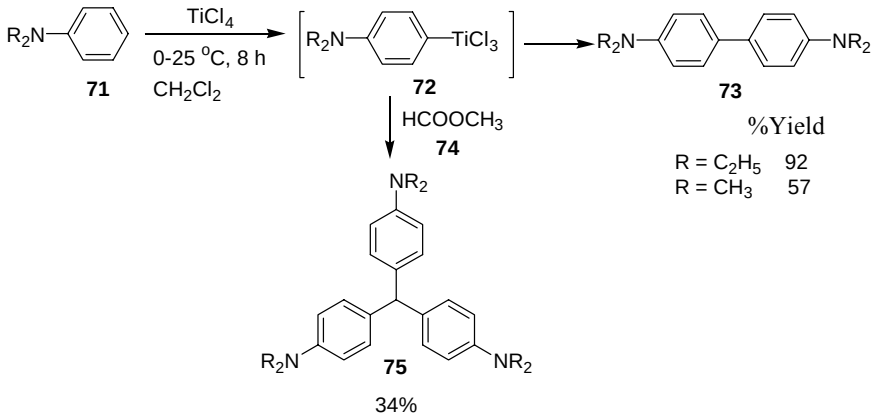


69 **70**

59%

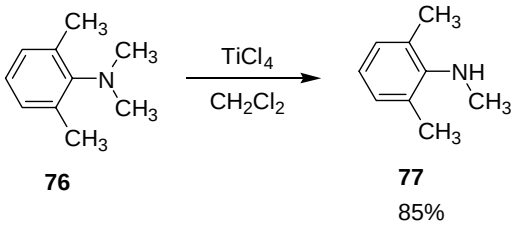
In the presence of $TiCl_4$, oxidative coupling reactions are also observed with *N, N*-dialkylaniline **71** derivatives. The corresponding benzidine products **73** are formed. This transformation can be rationalized considering the intermediacy of the corresponding aryl titanium species **72**. The aryl titanium species prepared *in situ* in this way react with $HCOOCH_3$ **74** electrophile to produce the coupled product **75** (Scheme 27).[28]

Scheme 27



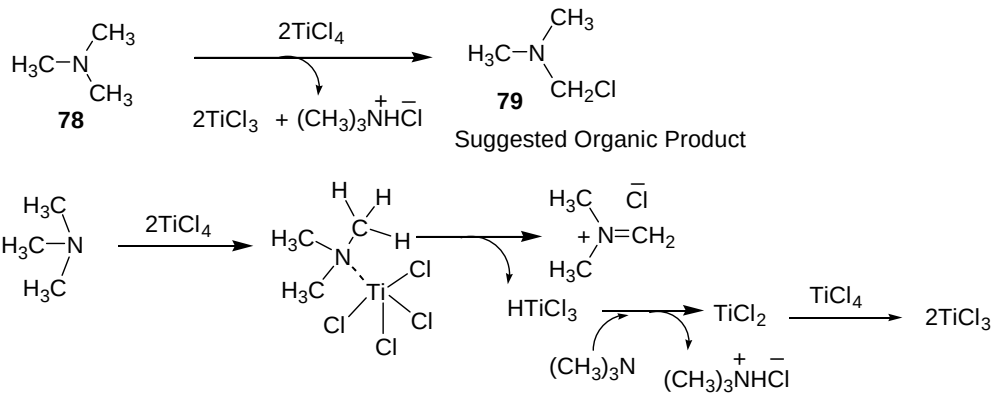
Also, it was observed that arylamine substrate like **76** undergoes *N*-demethylation to give the product **77** (Scheme 28).[28]

Scheme 28



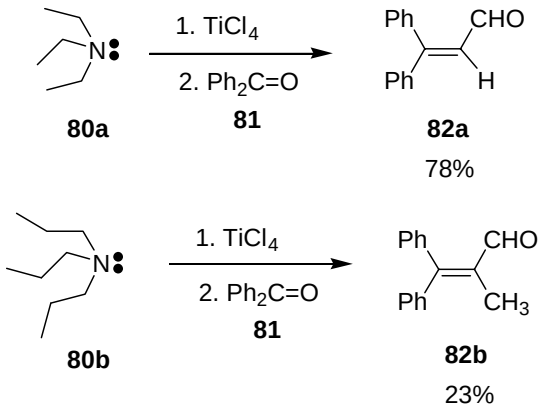
It was reported that the $TiCl_4$ oxidizes tertiary amines **78**. Presumably, the corresponding iminium ions would be the organic product **79** and the reaction can be rationalized by the intermediates shown in the Scheme 29.[29]

Scheme 29



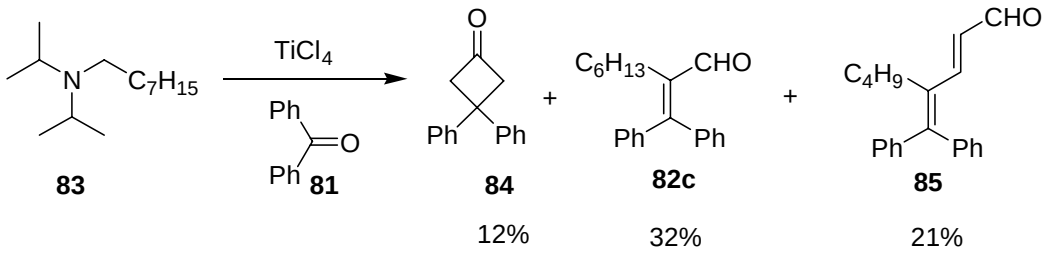
The iminium ions produced *in situ* in this way from trialkylamines **80** react with $TiCl_4$ and diaryl ketones **81** to produce the corresponding α,β-unsaturated aldehydes **82** (Scheme 30).[30]

Scheme 30



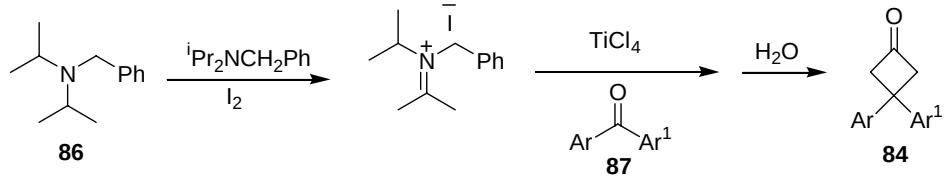
Also, it was found that the reaction of *N*,*N*-diisopropylalkylamine **83**, benzophenone and $TiCl_4$ leads to the formation of the corresponding cyclobutanone **84** in low yield (12%) in addition to the aldehydic products **82c** and **85** (Scheme 31).[31]

Scheme 31



The iminium ion generated from I_2 and trialkylamine **86** undergoes metalation with $TiCl_4$ followed by reaction with diaryl ketones **87** to produce the corresponding 3,3-diarylcyclobutanones **84** (Scheme 32).

Scheme 32

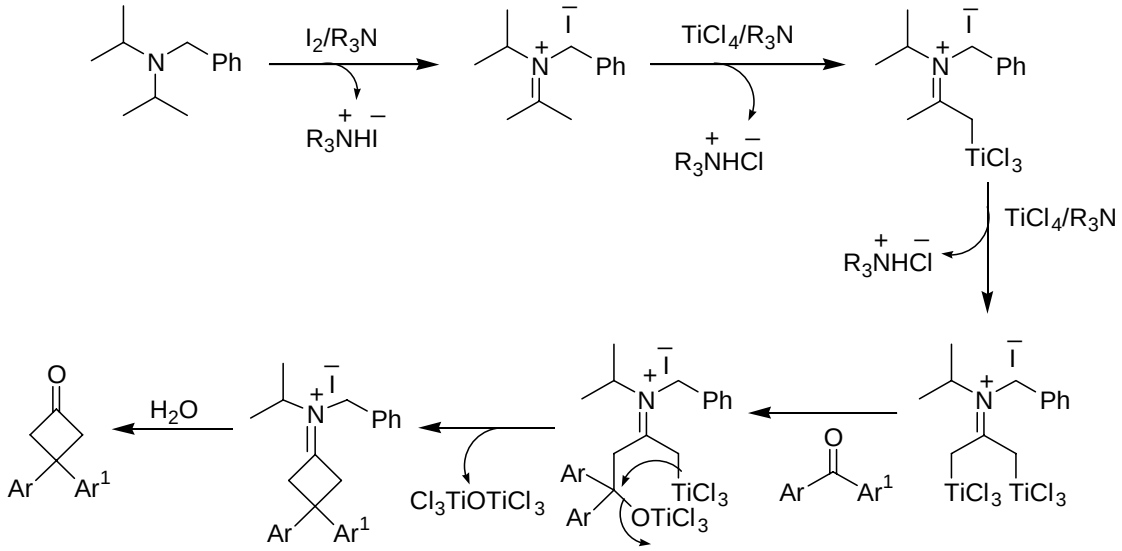


86 **87** **84**

	%Yield
Ar = Ar^1 = Ph	76
Ar = Ar^1= *p*-MeC_6H_4	71
Ar = Ph, Ar^1 = *p*-MeC_6H_4	73
Ar =Ph, Ar^1 = Ferrocenyl	76

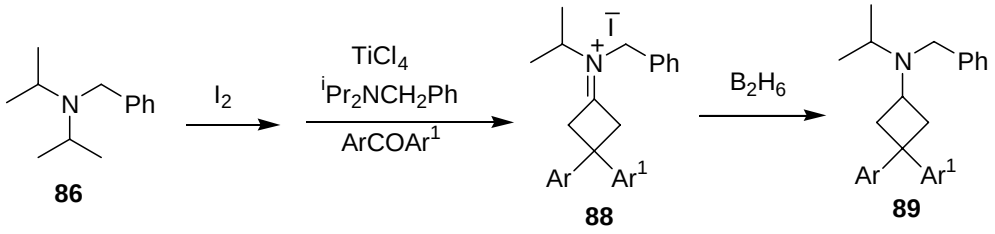
The results can be rationalized by the mechanism and the intermediates outlined in Scheme 33.[31]

Scheme 33



Synthesis of cyclobutylamine derivatives **89** was achieved by carrying out the reduction of the iminium ion intermediates **88** using B_2H_6 (Scheme 34).[32]

Scheme 34

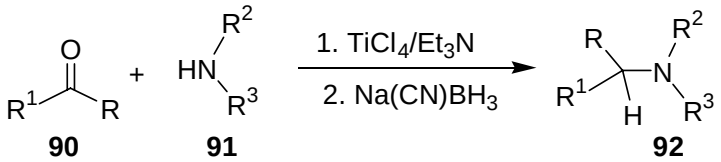


86 **88** **89**

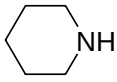
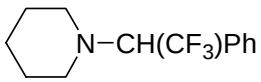
	%Yield
Ar = Ar^1 = Ph	73
Ar = Ar^1 = *p*-MeC_6H_4	61
Ar = Ph, Ar^1 = *p*-MeC_6H_4	51

It was reported that the reductive amination of carbonyl compounds **90** with amines **91** gives the hindered amines **92** *via* the reaction with $TiCl_4/Et_3N$ followed by $Na(CN)BH_3$ reduction (Scheme 35).[33]

Scheme 35

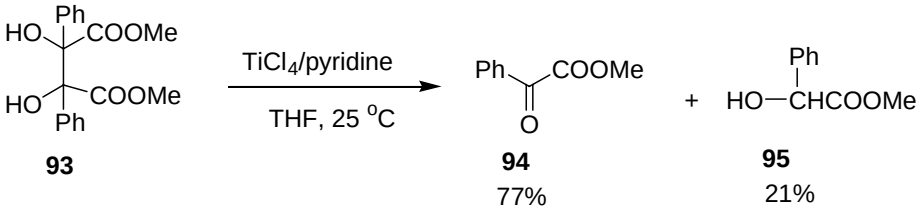


90 **91** **92**

Ketone	Amine	Product	%Yield
$PhCOCH_3$	$C_6H_5NH_2$	$Ph(CH_3)CHNHPh$	94
$PhCOCH(CH_3)_2$	$(CH_3)_2NH$	$PhCHN(CH_3)_2$ $CH(CH_3)_2$	54
$PhCOCF_3$			60

The $TiCl_4$/amine reagent system has been also used in the oxidation of certain alcohols. For example, the $TiCl_4$/pyridine reagent combination is useful for the oxidative cleavage of methyl diphenyltartrate **93** gives the products **94** and **95** (Scheme 36).[34]

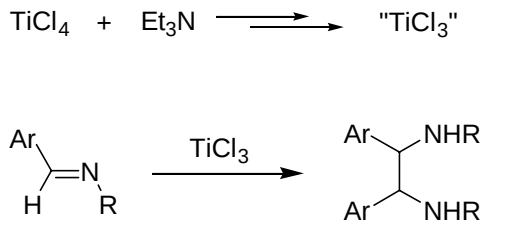
Scheme 36



93 **94** 77% **95** 21%

As discussed earlier, oxidation of the amines by $TiCl_4$ should produce '$TiCl_3$' species. Reductive coupling of aldimines **96** to the corresponding diamines **97** was achieved by the '$TiCl_3$' species produced in this way (Scheme 37).[35]

Scheme 37

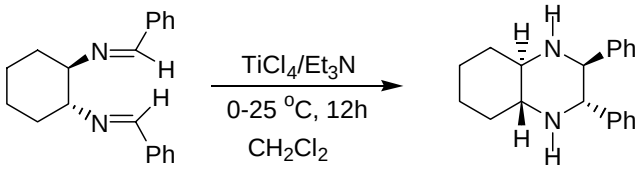


96 **97**

	%Yield	*dl* : *meso*
Ar = Ph, R = Ph	65	90 : 20
Ar = *p*-ClC_6H_4, R = Ph	60	85 : 15
Ar = Ph, R = $(CH_3)_3C$	51	33 : 77

Reaction of chiral diimines **98** derived from chiral 1,2-diaminocyclohexane with the $TiCl_4/Et_3N$ reagent system produced the corresponding chiral 3,4-disubstituted-2,5-diazabicyclo[4.4.0] decanes **99** via intramolecular reductive coupling path way (Scheme 38).[36]

Scheme 38



98
(1*R*,2*R*)

99
(1*R*,3*S*,4*S*,6*R*)

	%Yield
$TiCl_4/Et_3N$	28
$TiCl_4/Mg$	54
$TiCl_4/Zn$	75

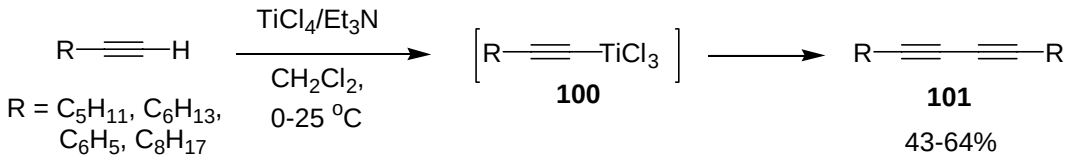
We have examined several new synthetic applications of the $TiCl_4/R_3N$ reagent system for organic transformations. The transformations exploiting the Ti(IV) character of this reagent system is presented in this Chapter.

1.2 Results and Discussion

1.2.1 Reaction of alkynes with $TiCl_4/Et_3N$ reagent system

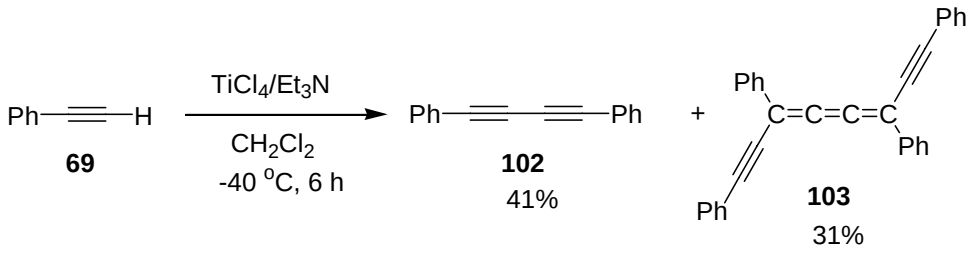
It has been reported from this laboratory that 1-alkynes react with $TiCl_4/Et_3N$ reagent system to give reactive $RC{\equiv}CTiCl_3$ species **100**, which dimerizes to the corresponding 1,3-diynes **101** (Scheme 39).[27]

Scheme 39



We have observed that when the reaction was carried at –40 °C, the 1,3-diyne **102** was isolated in 41% yield besides the corresponding cumulenediyne **103** in 31% yield (Scheme 40). Also, the use of Bu_3N gave better yields compared to Et_3N and $^iPr_2NEt$.

Scheme 40

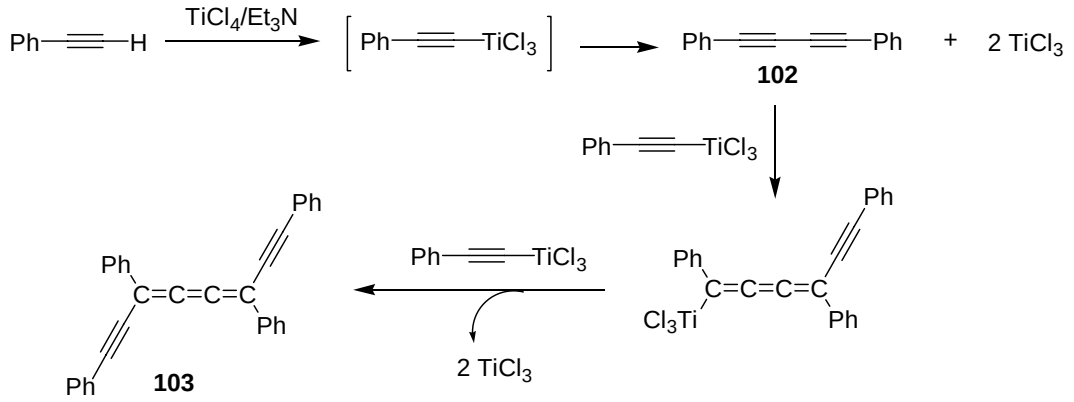


% Yield

	102	**103**
$TiCl_4/Bu_3N$	34	42
$TiCl_4/^iPr_2NEt$	43	28

This transformation can be explained by the sequence of reactions shown in Scheme 41.

Scheme 41



We have also examined this reaction using 1-heptyne. In this case, only the corresponding 1,3-diyne was obtained as outlined in Scheme 39.

The crystal structure data of the cumulenediyne **103** are summarized in Table 1 and Table A1 (Appendix II). The ORTEP diagram of cumulenediyne **103** is shown in Figure 1.

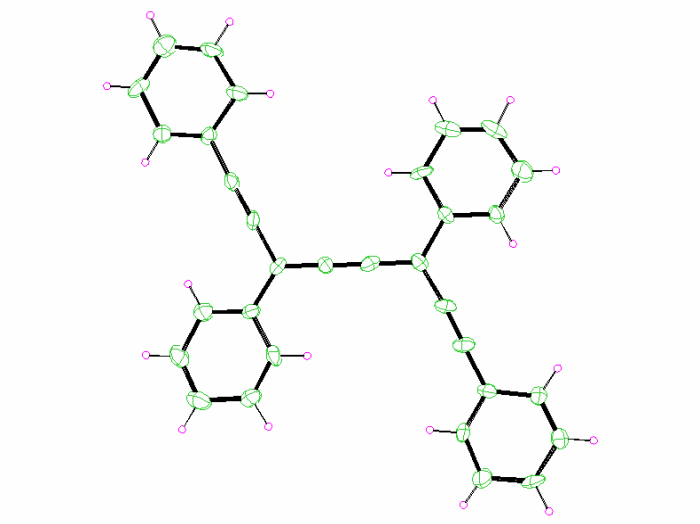


Figure 1: ORTEP diagram of the cumulenediyne 103

(Thermal ellipsoids are drawn at 20% probability)

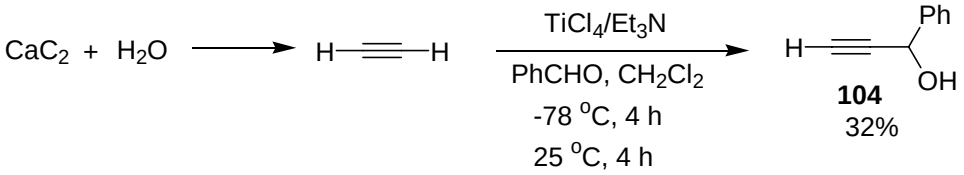
Table 1: X-ray data and structure refinement for cumulenediyne 103

Empirical formula	$C_{32}\ H_{20}$
Formula weight	404.48
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	$P\ 2_1/c$
Unit cell dimensions	a = 6.151(4) Å, α=90˚
	b = 15.583(2) Å, β = 95.19(4)˚
	c = 11.946(2) Å, γ = 90˚
Volume	1140.3(8) $Å^3$
Z	4
Calculated density	1.178 Mg/m^3
Absorption coefficient	0.067 mm^{-1}
F(000)	424
Crystal size	0.4 x 0.3 x 0.3 mm
θ Range for data collection	1.71 to 24.96 ˚
Limiting indices	$0 \le h \le 7, 0 \le k \le 18, -14 \le l \le 14$
Reflections collected/unique	2279 / 2088 [R(int) = 0.0293]
Completeness to θ = 27.47	100 %
Refinement method	full-matrix least-square on F^2
Data / restraints / parameters	2088 / 1 / 290
Goodness-of-fit on F^2	0.959
Final *R* indices [I> 2σ (I)]	R1 = 0.0529, wR2 = 0.0741
R indices (all data)	R1 = 0.1919, wR2 = 0.1106
Largest diff. Peak and hole	0.110 and -0.146 $eÅ^{-3}$

1.2.2 Reaction of acetylene gas and benzaldehyde with $TiCl_4/Et_3N$ reagent system

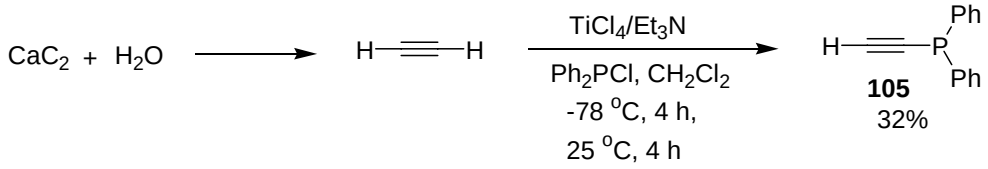
As outlined in the introductory section, the alkynyl titanium produced *in situ* react with certain electrophiles (Scheme 26). It was of interest to examine the reactivity of unsubstituted acetylene. The acetylene gas generated using CaC_2 and H_2O was passed through DCM containing $TiCl_4$, Et_3N and benzaldehyde at –78 ^oC. In this case, the corresponding propargyl alcohol **104** was isolated in 32% yield along with some unidentified polar compounds (Scheme 42).

Scheme 42



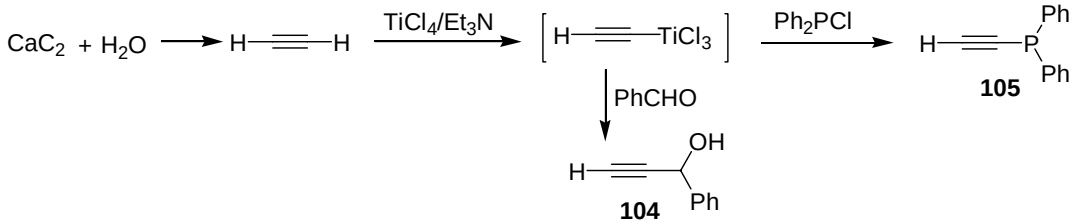
Under these conditions, the reaction of chlorodiphenylphosphine gave the 1-ethynyl (diphenyl) phosphine **105** in 32% yield (Scheme 43).

Scheme 43



Presumably, the corresponding organotitanium intermediate is trapped in the presence of electrophiles.

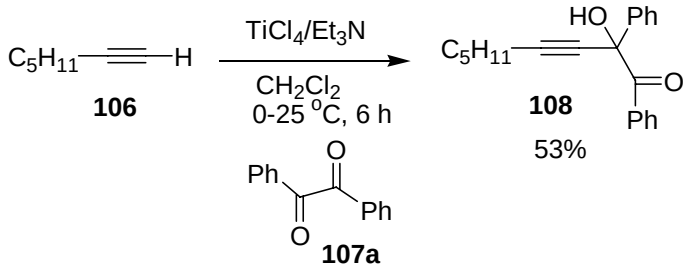
Scheme 44



1.2.3 Synthesis of propargyl alcohols from alkynes and ketones using the $TiCl_4/R_3N$ reagent system

We have also examined the alkynyl titanium intermediates for the synthesis of propargyl alcohols using certain non-enolizable ketones. The propargyl alcohol derivative **108** was obtained in 53% yield in the reaction of benzil **107a** and 1-heptyne **106** (Scheme 45).

Scheme 45



We have then examined the reactivity of the different ketones using the $TiCl_4/Et_3N$ in DCM at 0-25 ^oC. The corresponding propargyl alcohols were obtained in 31-53% yields. The results are summarized in Table 2.

Previously, it has been reported that ketones react with organotitanium species prepared using *n*-BuLi and $ClTi(O^iPr)_3$ to give the corresponding propargyl alcohols (Scheme 46).[37]

Scheme 46

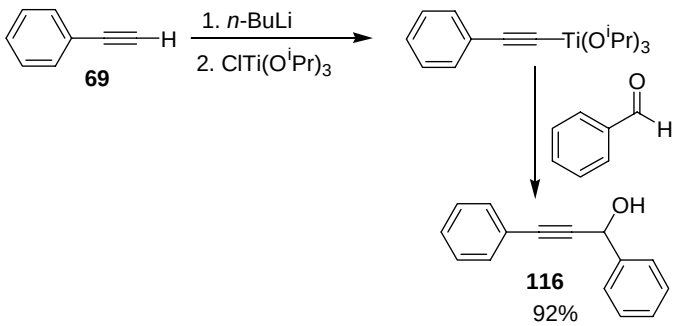
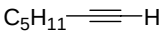
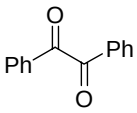
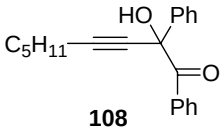
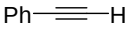
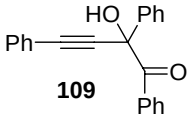
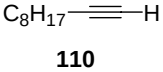
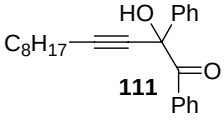
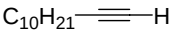
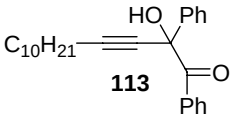
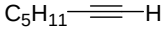
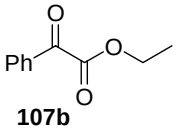
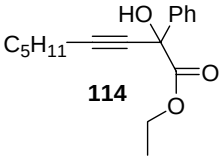
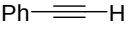
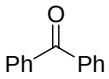
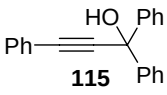


Table 2: Reaction of alkynes with ketones in the presence of $TiCl_4/R_3N$ reagent system[a]

entry	alkyne	ketone	amine	product[b]	%Yield[c]
1	 **106**	 **107a**	Et_3N	 **108**	53
2	**106**	**107a**	Bu_3N	**108**	43
3	**106**	**107a**	$^{i}Pr_2NEt$	**108**	31
4	 **69**	**107a**	Et_3N	 **109**	51
5	 **110**	**107a**	Et_3N	 **111**	46
6	 **112**	**107a**	Et_3N	 **113**	50
7	 **106**	 **107b**	Et_3N	 **114**	51
8	 **69**	 **81**	Et_3N	 **115**	49

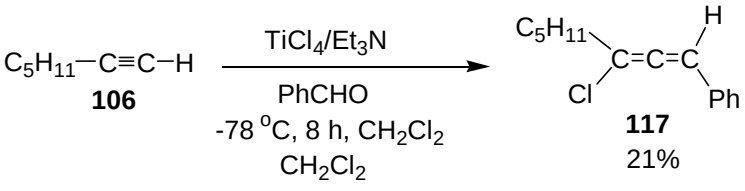
[a]Reactions were carried out using of 1-alkynes (10 mmol), Et_3N (15 mmol) and $TiCl_4$ (10 mmol).
[b]The products were identified by spectral data (IR, ^{1}H-NMR, ^{13}C-NMR and mass spectral analysis).
[c]The yields are based on the alkynes used.

The readily accessible propargyl alcohols have a very rich chemistry.[38] They are versatile building blocks in the synthesis of many natural products such as prostaglandins, steroids, carotenoids and synthesis of α-tocopherol (vitamin-E) and related isoprenoids, biologically active prostacyclin mimetics,[39] and in the synthesis of some important molecules like cytostation, 11-α-hydroxyprogesterone, vitamin K, insect sex phermones, fatty acids, enediynes (Taxamycins), (*Z*)-Tamoxifen, AB-Taxane ring with enone, Taxol and Taxotere, Vitamin A, β-Lactones, (+)-Parviflorin and (+)-5*S*-hydroxyparviflorin.[40] Though, several methods are available for the synthesis of propargyl alcohols,[41] the new method described here involving the $TiCl_4/R_3N$ reagent system is a good addition to this pool of reagents.

1.2.4 Reaction of 1-heptyne and benzaldehyde with the $TiCl_4/Et_3N$ reagent system

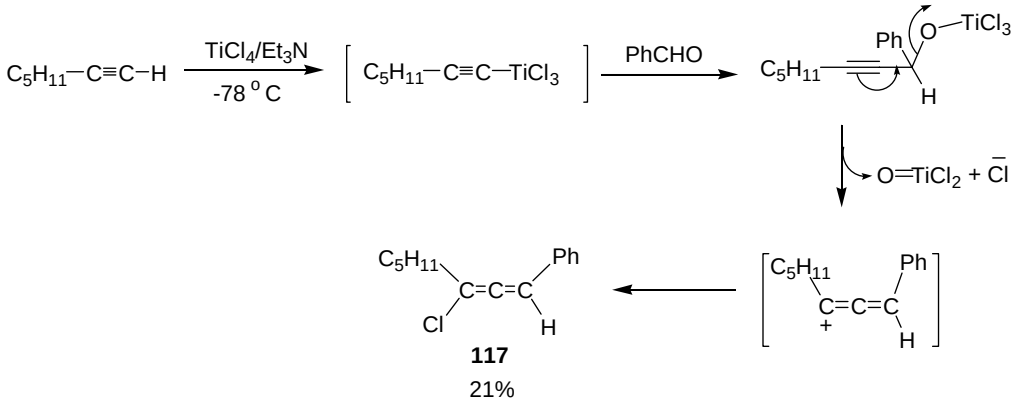
We have observed that when benzaldehyde was used as electrophile in the reaction of 1-heptyne **106** and $TiCl_4/Et_3N$ at -78 ^oC, corresponding chloroallene **117** was isolated in 21% yields besides some unidentified products (Scheme 47).

Scheme 47



Most probably, this reaction may go through the intermediacy of the corresponding propargyl alcohol (Scheme 48).

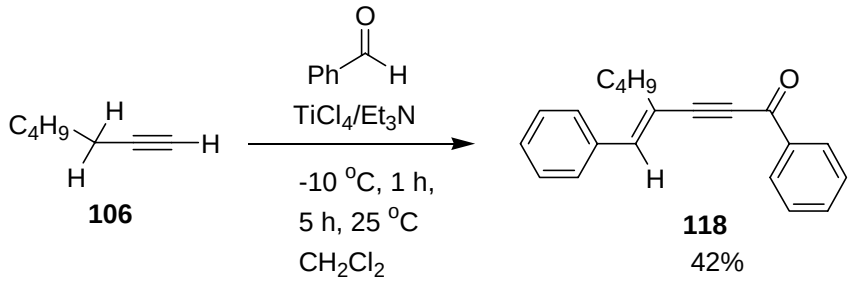
Scheme 48



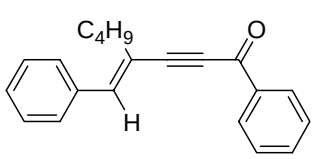
We have examined this reactivity pattern of propargyl alcohol derivatives in detail and the results are discussed in Chapter 2.

Previously, it was observed in this laboratory that the reaction of 1-heptyne **106,** $TiCl_4$, Et_3N and benzaldehyde gave the corresponding enynone **118** in 42% yield (Scheme 49).

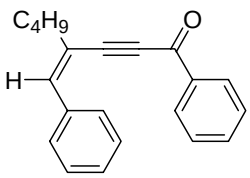
Scheme 49



However, the stereochemistry of the products **118a** and **118b** was not established. Accordingly, we have carried out further investigations to establish the stereochemistry.



118a

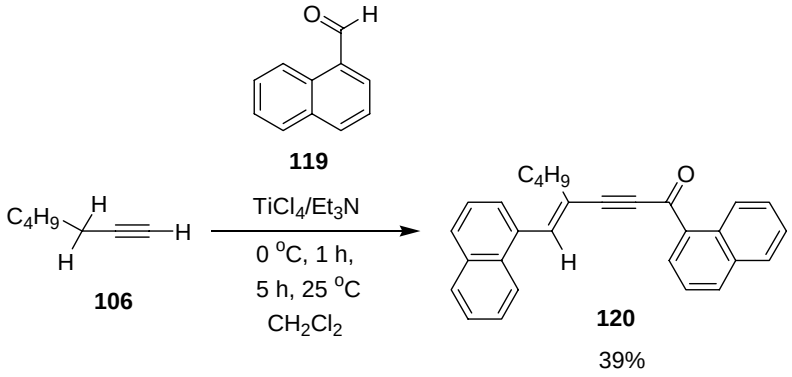


118b

In this reaction, two isomeric products **118a** and **118b** are possible. Among these two isomers *E*- isomer **118a** was found to be the major product. This structure of the major product was confirmed by the ^{1}H-NMR and the NOESY experiments.

The reaction of 1-naphthaldehyde **119** with 1-heptyne in the presence of the $TiCl_4/Et_3N$ reagent system gave the corresponding enynone **120** in 39% yield (Scheme 50). In this case also, the ^{1}H NMR and the NOESY experiments revealed that the major product is the *E*- isomer.

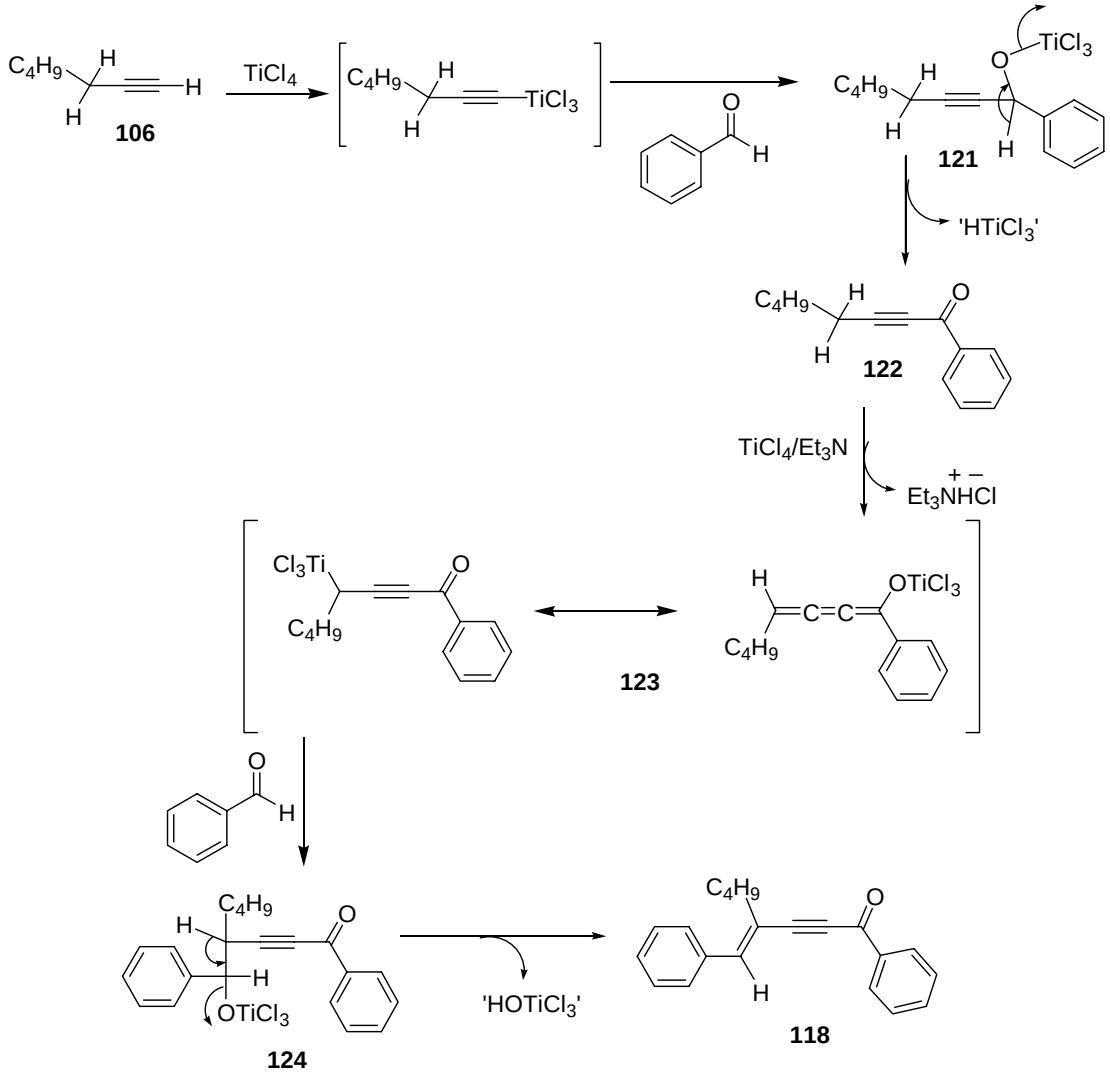
Scheme 50



A tentative reaction mechanism for the formation of enynone is given in Scheme 51. The reaction of alkynyltitanium with benzaldehyde would involve the corresponding alkoxy intermediate **121**, which could eliminate '$HTiCl_3$' species giving the ketone **122** that on further metalation by $TiCl_4/Et_3N$ would give the organotitanium

intermediate **123** that could give the enynone **118** on reaction with benzaldehyde through the intermediate **124**.

Scheme 51

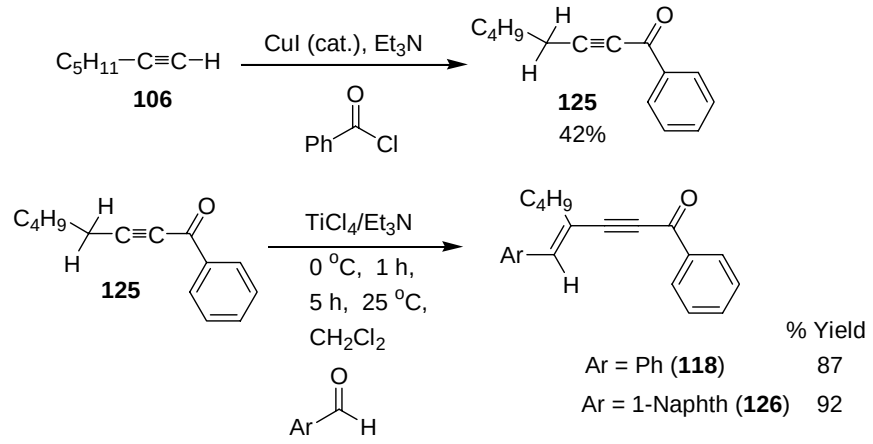


In the reaction mechanism outlined in scheme 51, the intermediacy of the alkynone is proposed. Accordingly, it was of interest to carry out the reaction starting from the alkynone.

1.2.5 Reaction of alkynyl ketone in the presence of $TiCl_4/Et_3N$ reagent system

We have observed that the alkynyl ketone **125** reacts with $TiCl_4/Et_3N$ and benzaldehyde to give the enynone **118** in 87% yield. The alkynyl ketone was prepared following a known procedure (Scheme 52).[42] The enynone **126** was obtained in 92% yield using 1-napthaldehyde as electrophile under the same reaction conditions.

Scheme 52

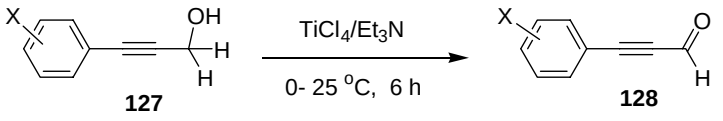


Some enynone derivatives were previously used for the preparation of Red Ginseng a biologically active molecule.[43] Some enynones were used as intermediate precursors for the total synthesis of Pumiliotoxin B,[44a] pomactin,[44b] (-)-Borrelidin,[44c] anti-helicobacter pylori agent,[44d] vitamin D (Calciferol),[44e] and methylenomycin B,[44f] furanoid fatty ethers,[44g] neocarzinostation.[44h] methylenecyclopentenones.[44i] Though a few methods have been reported for the synthesis of this class of compounds,[45] the method described here would serve as a good alternative to the pool of methods available for the synthesis of enynones.

1 2.6 Reaction of aromatic aldehydes with the $TiCl_4/Et_3N$ reagent system

As outlined in the introductory section, the reaction of $TiCl_4$ with tertiary amines gives "$TiCl_3$" and intractable organic products in the absence of electrophiles. Previously, it was reported that propargyl alcohols **127** react with $TiCl_4/Et_3N$ to give the corresponding propargyl ketones **128** (Scheme 53).[46]

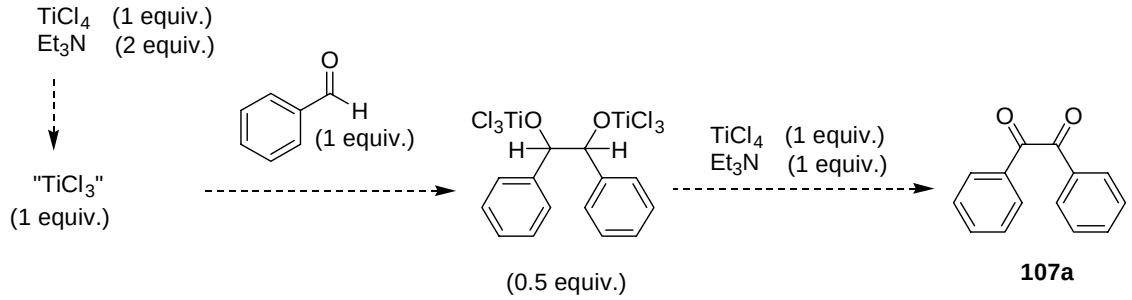
Scheme 53



	% Yield
X = *p*-Br	73
X = *p*-Cl	61
X = *o*-Br	76

The $TiCl_3$ is known to react with carbonyl compounds to give the corresponding pinacol derivatives (This transformation is discussed in detail in the Chapter 3). Accordingly, the $TiCl_4$ and $TiCl_3$ reagent combination is expected to give pinacol coupling followed by oxidation to diketones as envisaged in Scheme 54.

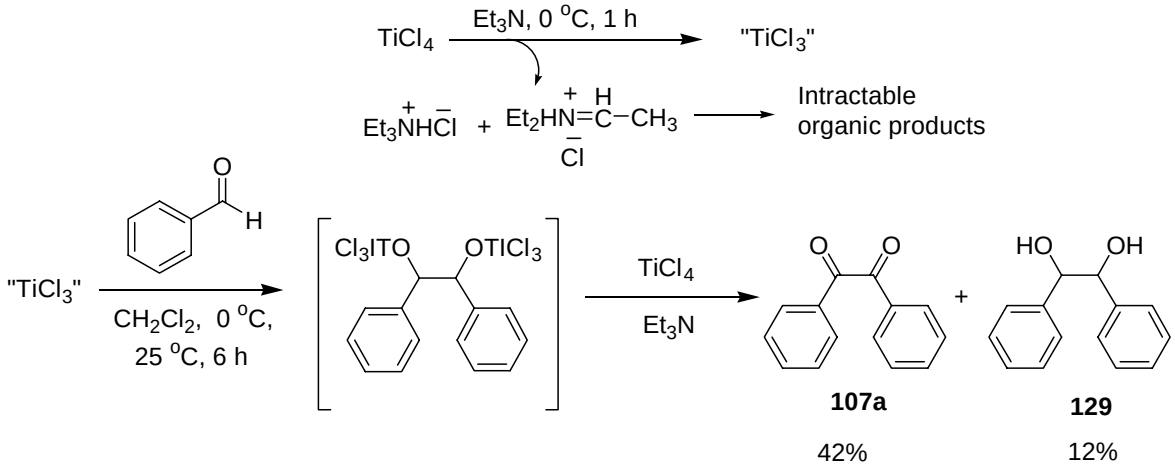
Scheme 54



To examine this possibility, we have carried out the reaction using $TiCl_4$ (20 mmol) and Et_3N (30 mmol) by sequential addition as outlined in Scheme 54.

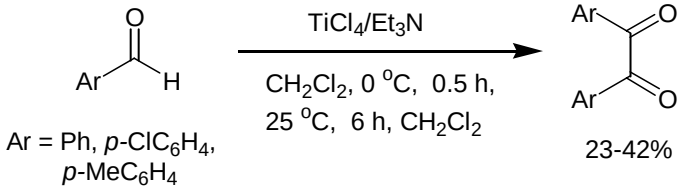
Indeed the 1,2-diketone **107a** was formed in 42%yield besides the corresponding 1,2-diol (12%) (Scheme 55). Several other aldehydes were also converted to the corresponding diones in this way (Table1).

Scheme 55



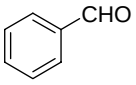
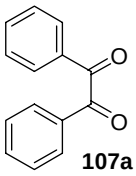
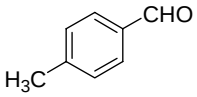
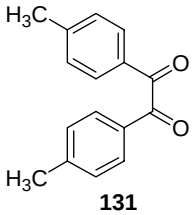
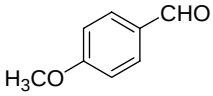
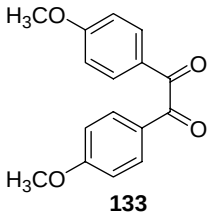
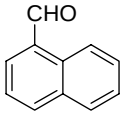
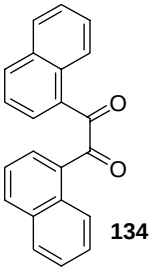
We have then examined the reactivity of different aromatic aldehydes using the $TiCl_4/Et_3N$ reagent system (Scheme 56). The 1,2-diketones were obtained in 23-42% yields besides the corresponding 1,2-diaryl-1,2-diols (~10%).

Scheme 56



This indicates that the initially formed 1,2-diarylethane-1,2-diol is oxidized to the corresponding diketone in the presence of excess of $TiCl_4$. We have also carried out the reaction with *p*-anisaldehyde and 1-naphthaldehyde and isolated the corresponding 1,2-diketones. The results are summarized in Table 3.

Table 3: Reaction of aromatic aldehydes with the $TiCl_4/Et_3N$ reagent system[a]

Entry	Substrate	Reducing agent	Product[b]	Yield[c] (%)
1		Et_3N	 **107a**	42
2	do	Bu_3N	**107a**	31
3	do	$^iPr_2NEt$	**107a**	23
4	 **130**	Et_3N	 **131**	36
5	 **132**	Et_3N	 **133**	28
6	 **119**	Et_3N	 **134**	34

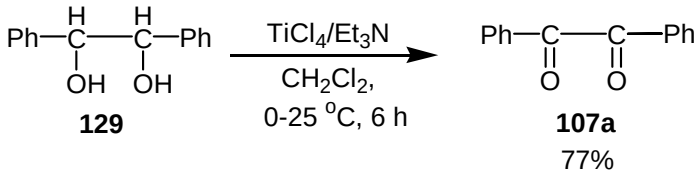
[a]Reactions were carried out using of aromatic aldehydes (10 mmol), Et_3N (40 mmol) and $TiCl_4$(20 mmol).
[b]All the products were characterized by spectral data and comparison with the reported data.
[c]Yield refers to pure product isolated by chromatography over silica gel column, corresponding pinacols were also isolated in (~12%).

Benzil **107a** was isolated in 42% yield using benzaldehyde and the $TiCl_4/Et_3N$ reagent system. In the case of 4-methoxybenzaldehyde and naphthaldehyde, we have isolated the 1,2-diones **133** and **134** in 28% and 34% yields, respectively.

1.2.7 Reaction of 1,2-diaryl-1,2-diols with the $TiCl_4/Et_3N$ reagent system

We have further examined the oxidation of 1,2-diphenylethane-1,2-diol **129** as a reactant using $TiCl_4/Et_3N$. In this case, the benzil **107a** was isolated in 77% yield (Scheme 57).

Scheme 57



This transformation was also studied using various amines. The use of Et_3N gave good yields. We have then examined the reactivity of the different 1,2-diaryl-1,2-diols using the $TiCl_4/Et_3N$ reagent in DCM at 0-25 °C. The corresponding 1,2-diketones were obtained (Scheme 58). The yields are in the range of 63-86%. The results are summarized in Table 4.

Scheme 58

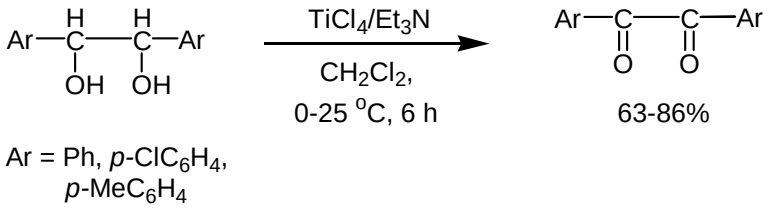
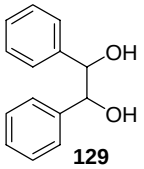
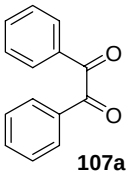
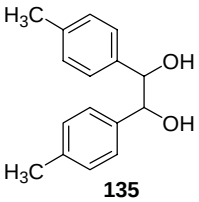
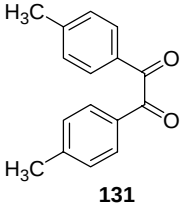
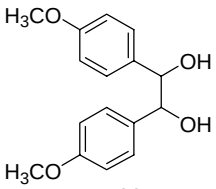
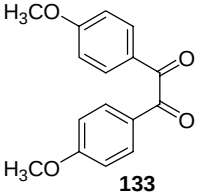
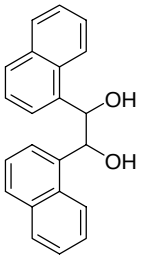
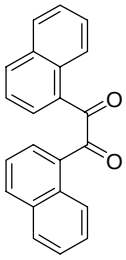


Table 4: Oxidation of 1,2-diaryl-1,2-diols to 1,2-diketones using $TiCl_4/Et_3N$ reagent system[a]

Entry	Substrate	Reducing agent	Product[b]	Yield[c] (%)
1	 **129**	Et_3N	 **107a**	77
2	**129**	Bu_3N	**107a**	73
3	**129**	$^{i}Pr_2NEt$	**107a**	71
4	 **135**	Et_3N	 **131**	83
5	 **136**	Et_3N	 **133**	86
6[d]	 **137**	Et_3N	 **134**	63

[a]Reactions were carried out using 1,2-diphenylethane-1,2-diol (2 mmol), Et_3N (8 mmol) and $TiCl_4$ (8 mmol).

[b]All the products were characterized by spectral data and comparison with the reported data.

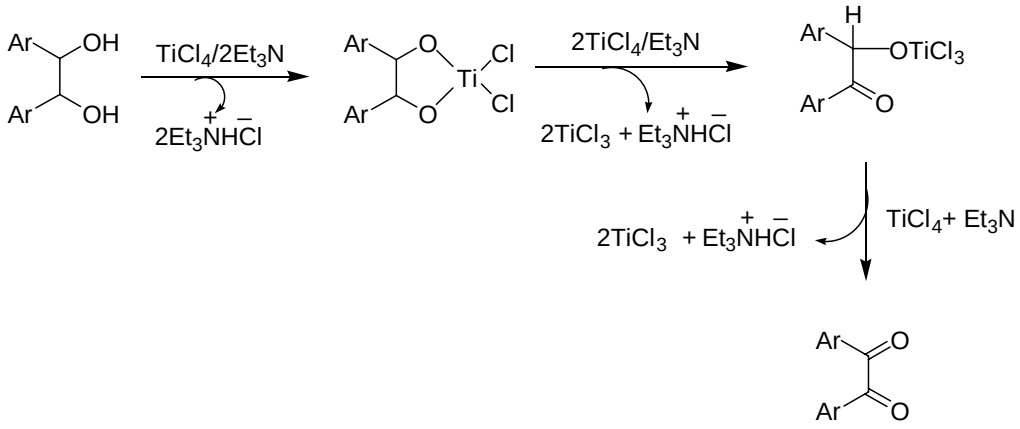
[c]Yield refers to pure products isolated by chromatography over silica gel column.

[d]Reaction was carried out for 10 h.

It was observed that 1,2-di(4-methylphenyl)-1,2-ethanediol **135** gave 1,2-di(4-methylphenyl)-1,2-ethanedione **131** in 83% yield. Similarly, 1,2-di(4-methoxyphenyl)-1,2-ethanediol **136** gave 1,2-di(4-methoxyphenyl)-1,2-ethanedione **133** in 86% yield. Also, it was observed that 1,2-di(1-naphthyl)-1,2-ethanediol **137** gave the 1,2-di(1-naphthyl)-1,2-ethanedione **134** in 63% yield (Table 4).

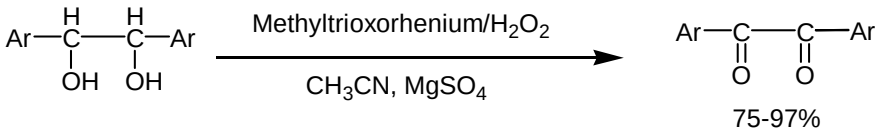
This transformation can be visualized by a tentative mechanism involving complexation, oxidation and deprotonation sequence as outlined in Scheme 59.

Scheme 59



The 1,2-diarylethane-1,2-diones are useful as starting materials in the synthesis of biologically active molecules and pharmaceuticals.[47] Accordingly, several synthetic methods have been reported.[48] For example, the reaction of 1,2-diaryl-1,2-diols with methyltrioxorhenium/H_2O_2 under refluxing condition gave 1,2-diaryl-1,2-diketones in 75-97% yields (Scheme 60).[49]

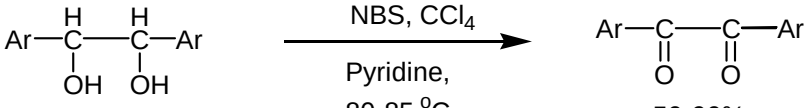
Scheme 60



Ar = Ph, *p*-$CH_3C_6H_4$, *p*-$OCH_3C_6H_4$

Recently, the conversion of 1,2-diaryl-1,2-diols to the corresponding 1,2-diaryl-1,2-diketones using NBS, pyridine in CCl_4 under refluxing conditions was reported (Scheme 61).[50]

Scheme 61



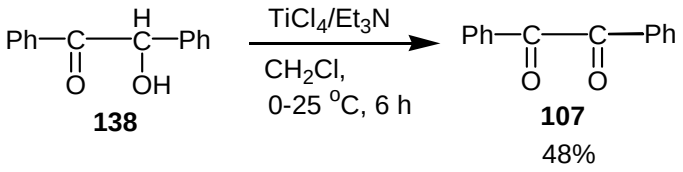
Ar = Ph, *p*-$CH_3C_6H_4$, *p*-$OCH_3C_6H_4$

The method of conversion of 1,2-diarylethane-1,2-diols to 1,2-diarylethane-1,2-diones described here by using $TiCl_4/Et_3N$ under mild conditions would serve as a simple alternative to the pool of reagents available in the literature.

1.2.8 Reaction of benzoin, cyclohexanol and benzhydrol with $TiCl_4/Et_3N$ reagent system

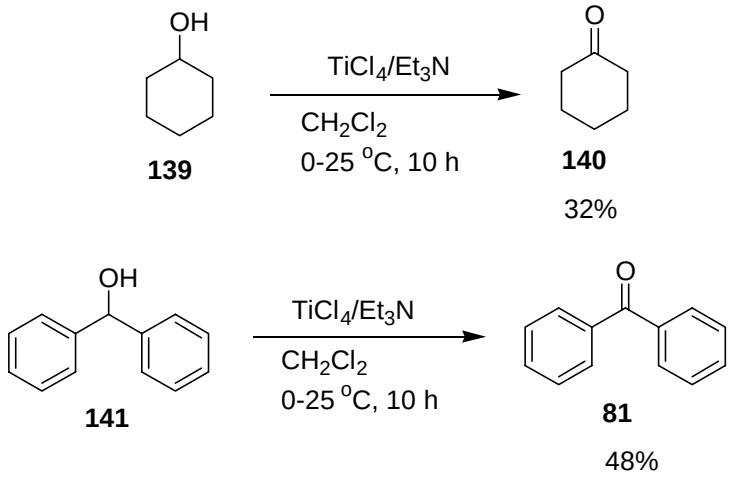
We have also observed when benzoin **138** was treated with $TiCl_4/Et_3N$, benzil **107a** was isolated in 48% yield (Scheme 62).

Scheme 62



We have also examined the oxidation of simple alcohols such as cyclohexanol and benzhydrol. It was observed that the reaction of cyclohexanol **139** with $TiCl_4/Et_3N$ gave cyclohexanone **140** in 32% yield, whereas benzhydrol **141** gave benzophenone **81** in 48% yield under the reaction conditions (Scheme 63).

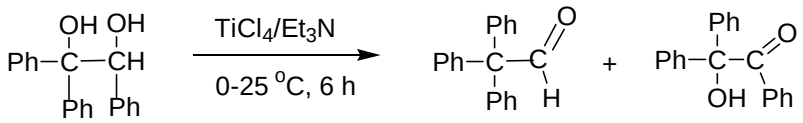
Scheme 63



1.2.9 Rearrangement of 1,1,2-triphenylethane-1,2-diol by using the $TiCl_4/Et_3N$ reagent system

Interestingly, when the 1,1,2-triphenylethane-1,2-diol **142** was reacted with the $TiCl_4/Et_3N$ reagent system, the rearranged products 2,2,2-triphenyl acetaldehyde **143** **(**32%), and diphenylacetophenone **144** (28%) were obtained (Scheme 64).

Scheme 64



142 **143** 32% **144** 28%

Presumably, deprotonation-oxidation becomes difficult due to steric hindrance in this system (Scheme 64).

1. 3 Conclusions

Whereas propargyl alcohols were formed in the reaction of alkynes and carbonyl compounds using the $TiCl_4/Et_3N$ reagent system, *E*-enynones were produced in the reaction of 1-heptyne, benzaldehyde and the $TiCl_4/Et_3N$ reagent system. *E*-Enynones were also synthesized from certain alkynyl ketones, benzaldehyde and 1-naphthaldehyde using the $TiCl_4/Et_3N$ reagent system. Aromatic aldehydes were converted to the corresponding 1,2-diaryl-1,2-diones in the presence of $TiCl_4/Et_3N$ reagent system and the 1,2-diaryl-1,2-diols are converted to the corresponding 1,2-diaryl-1,2-diones using the $TiCl_4/Et_3N$ reagent system.

1.4 Experimental Section

1.4.1 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 Finnegan 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 250mμ acme's silica gel-G and GF_{254} containing 13% calcium sulfate as binder. The spots were visualized by short exposure to iodine vapor or UV light. Column chromatography was carried out using acme's silica gel (100-200 mesh) neutral alumina, and basic alumina.

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 transfer of reagents were carried out using standard syringe, septum technique recommended for handling air sensitive reagents and 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.

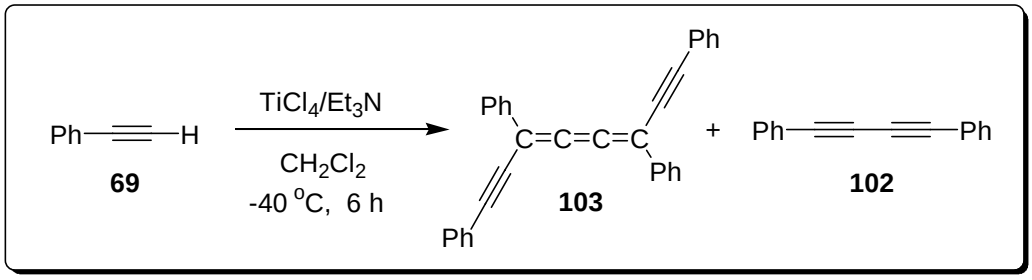
In all experiments, a round bottom flask of appropriate size with a side arm, a side septum, a magnetic stirring bar, a condenser and a connecting tube attached to a mercury bubbler were used. The outlet of the mercury bubbler was connected to the atmosphere by a long tube. All dry solvents and reagents (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 or K_2CO_3 and concentrated on Heidolph-EL-rotary evaporator. All yields reported are of isolated materials judged homogeneous by TLC, IR and NMR spectroscopy.

Dichloromethane, dichloroethane and chloroform were distilled over CaH_2 and dried over molecular sieves. Methanol and ethanol supplied by Ranbaxy were distilled over CaO before use. Titanium tetrachloride was supplied by E-Merck, India. Triethylamine, tributylamine, diisopropylethylamine supplied by Lancaster Synthesis, Ltd., England was distilled over CaH_2 and stored over KOH pellets. Cyclohexanol, phenylacetylene, 1-heptyne, 1-decyne, 1-dodecyne, 1-octyne, ethylphenylglyoxalate were supplied by E-Merck, India. Benzophenone, Benzhydrol and all aldehydes supplied by Loba Chemicals (P) Ltd., India were distilled or recrystallized from the appropriate solvents before use. 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

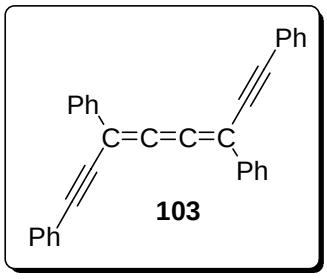
frame scans. Intensity data were collected by the ω scan mode. Measuring the intensity of the three standard reflections after every one and half hour intervals monitored stability of the crystal during the measurement. No appreciable variation of the crystal was detected. X-ray diffraction measurements 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,[51a] without applying absorption correction. The refinement for structure was made by full-matrix least squares on F^2 (SHELX 97 or SHELXTL).[51b]

1.4.2 Typical procedure for the preparation of cummulenediyne 103 from phenylacetylene using the $TiCl_4/Et_3N$ reagent system

In dichloromethane (35 mL), phenylacetylene **69** (1.0 g, 1 mL, 10 mmol), $TiCl_4$ (1.9 g, 1.1 mL, 10 mmol) and Et_3N (1.5 g, 2.1 mL, 15 mmol) were taken at – 40 ^oC under N_2. The reaction mixture was stirred for 6 h at – 40 ^oC. Saturated NH_4Cl solution (20 mL) was added and stirred for 10 min. The organic layer was separated and the aqueous layer was extracted with dichloromethane (2 X 15 mL). The combined organic extract 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 with ethyl acetate/hexane (1:99) mixture. The cumulenediyne **103** was isolated in 31% yield.



Yield 1.33 g (31%)



103

IR (KBr) (cm^{-1}) 3055, 2307, 2187, 1491, 1265

^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm): 7.27-8.15 (m, 20H)

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 88.1, 91.2, 123.0, 125.0, 127.2, 127.5, 127.9, 128.4, 129.7, 131.7, 136.6, 137.1, 147.7

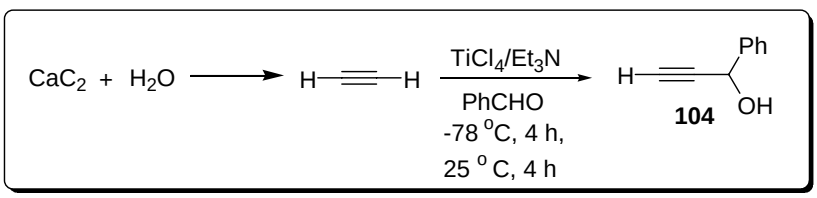
MS (EI) *m/z* 404 (M^+)

Analysis Calculated for $C_{32}H_{20}$: C, 95.02%; H, 4.98%

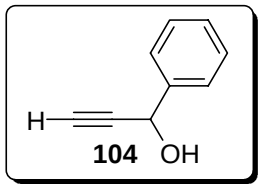
Found : C, 95.12%; H, 4.91%

1.4.3 Typical procedure for the synthesis of propargylalcohols with acetylene gas and benzaldehyde using the $TiCl_4/Et_3N$ reagent system

Acetylene gas, generated using CaC_2 and water was passed through dichloromethane (35 mL) containing $TiCl_4$ (1.9 g, 1 mL, 10 mmol), Et_3N (1.5 g, 2.1 mL, 15 mmol) and benzaldehyde (1.1 g, 1.1 mL, 10 mmol) at –78 ^oC under N_2. The reaction mixture was stirred for 4 h at – 78 ^oC, and further stirred for 4 h at 25 ^oC. Saturated NH_4Cl solution (20 mL) was added and stirred for 10 min. The organic layer was separated and the aqueous layer was extracted with dichloromethane (2 X 15 mL). The combined organic extract 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 with ethyl acetate/hexane (97:3) mixture. The propargyl alcohol **104** was isolated in 32% yield.



104



104

Yield 0.42 g (32%)

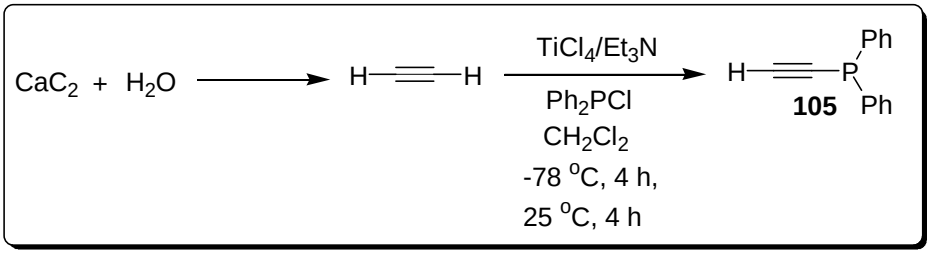
IR (Neat) (cm^{-1}) 3439, 2198, 1452, 1265

^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm): 2.41 (d, 1H *J* = 6.5Hz), 2.85 (s, 1H), 5.42 (s, 1H), 7.17-7.46 (m, 5H)

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 47.6, 73.7, 78.0, 126.8, 127.9, 128.5, 128.9, 137.3

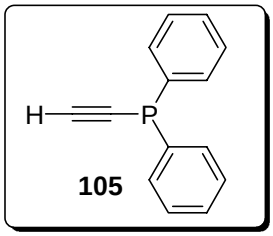
1.4.4 Typical procedure for the reaction of acetylene gas with chlorodiphenylphosphine using the $TiCl_4/Et_3N$ reagent system

Acetylene gas, generated using CaC_2 and water. It was passed through dichloromethane (35 mL) containing $TiCl_4$ (1.9 g, 1 mL, 10 mmol), Et_3N (1.5 g, 2.1mL, 15 mmol) and diphenylchlorophosphine (2.2 g, 10 mmol) at –78 ^{o}C under N_2. The reaction mixture was stirred for 4 h at –78 ^{o}C and further stirred for 4 h at 25 ^{o}C. Saturated NH_4Cl solution (20 mL) was added and stirred for 10 min. The organic layer was separated and the aqueous layer was extracted with dichloromethane (2 X 15 mL). The combined organic extract 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 with ethyl acetate/hexane (95:5) mixture. The phosphine **105** was isolated in 32% yield.



105

Yield 0.67 g (32%)



IR (KBr) (cm^{-1}) 3055, 2109, 1437, 1132, 1016, 731

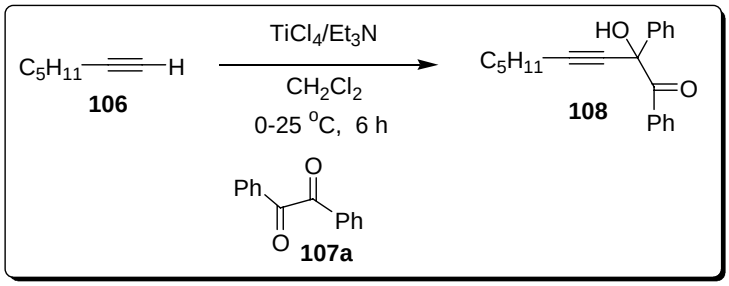
^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm): 3.34 (s, 1H), 7.32-7.83 (m, 10H)

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 94.4, 96.0, 128.5,128.7, 129.2, 132.3, 132.4, 135.4, 137.2

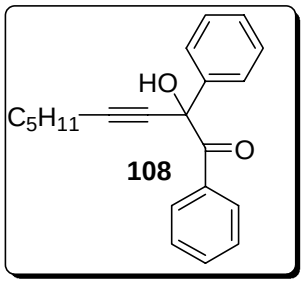
MS (EI) *m/z* 210 (M^+)

1.4.5 Typical procedure for the synthesis of propargyl alcohols from alkynes and carbonyl compounds using $TiCl_4/Et_3N$ reagent system

In dichloromethane (35 mL), 1-heptyne (0.96 g, 10 mmol), $TiCl_4$ (1.9 g, 10 mmol), Et_3N (1.5 g, 2.1 mL, 15 mmol) and benzophenone (2.2 g, 10 mmol) were taken at 0 ^oC under N_2. The reaction mixture was stirred for 1h at 0 ^oC and further stirred for 4 h at 25 ^oC. Saturated NH_4Cl solution (20 mL) was added and stirred for 10 min. The organic layer was separated and the aqueous layer was extracted with dichloromethane (2 X 15 mL). The combined organic extract 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 with ethyl acetate/hexane (97:3) mixture. The propargyl alcohol **108** was isolated in1.62 g (53%) yield.



Yield 1.62 g (53%)



IR (Neat) (cm^{-1}) 3385, 2962, 2219, 1438, 1178, 997

^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm): 0.86 (t, 3H, *J* = 7.2 Hz), 1.27-1.34 (m, 4H), 1.53-1.56 (m, 2H), 2.31-2.36 (m, 2H), 5.52 (s, 1H), 7.29-7.45 (6H), 7.63-7.65 (d, 2H, *J* = 7.4 Hz), 8.04-8.07 (d, 2H, *J* = 7.2 Hz)

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 13.9, 18.99, 22.1, 27.9, 31.0, 76.0, 78.7, 92.1, 126.83, 128.0, 128.6, 128.8, 131.1, 131.6, 133.6, 140.5, 195.5

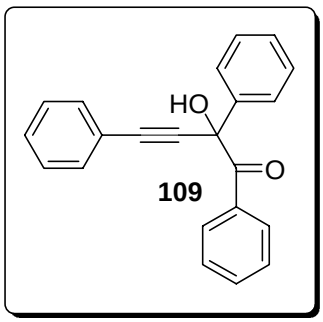
MS (EI) *m/z* 306 (M^+)

Analysis Calculated for $C_{14}H_{17}Cl$: C, 82.32%; H, 7.24%

Found : C, 82.39%; H, 7.19%

The same procedure was followed for other alkynes. The data are given below.

Propargyl alcohol 109



Yield 1.59 g (51%)

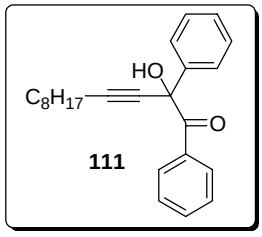
IR (Neat) (cm^{-1}) 3379, 2955, 2226, 1454, 1192, 997

^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm): 5.63 (s, 1H), 7.32-7.52 (m, 11H), 7.70-7.73 (d, 2H, *J* = 6.8 Hz), 8.12-8.14 (d, 2H, *J* = 6.7 Hz)

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 76.4, 87.3, 90.4, 121.9, 126.8, 128.2, 128.4, 128.9, 129.0, 129.9, 131.1, 131.7, 133.8, 140.2, 195.0

MS (EI) *m/z* 312 (M^+)

Propargyl alcohol 111



Yield 1.6 g (46%)

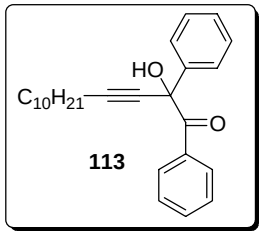
IR (Neat) (cm^{-1}) 3431, 2928, 2235, 1448, 1143, 1060

^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm): 0.90 (t, 3H, *J* = 6.8 Hz),1.20-1.42 (9H), 1.49-1.63 (m, 2H), 2.32 (t, 3H, *J* = 7 Hz), 5.47 (s, 1H), 7.28-7.55 (m, 6H), 7.63 (d, 2H, *J* =7.6 Hz), 8.04 (d, 2H, *J* = 7.8 Hz) **(Spectrum No. 1)**

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm):14.0, 18.9, 22.6, 28.2, 29.02, 29.09, 31.7, 76.1, 77.7, 92.0, 126.8, 127.9, 128.5, 128.9, 131.0, 131.8, 133.4, 140.6, 195.6 **(Spectrum No. 2)**

MS (EI) *m/z* 348 (M^+)

Propargyl alcohol 113



Yield 1.88 g (50%)

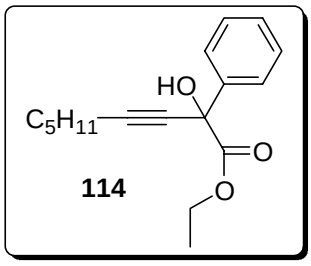
IR (Neat) (cm^{-1}) 3331, 2235, 1682, 1597, 1448, 1211

^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm): 0.90 (t, 3H, *J* = 7.2 Hz), 1.16-1.45 (14H), 1.48-1.60 (2H), 2.32 (t, 2H, *J* = 7.1 Hz), 5.47 (s, 1H), 7.28-7.61 (6H), 7.90-8.02 (m, 4H)

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 14.0, 19.0, 22.6, 28.2, 28.8, 29.0, 29.3, 29.5, 31.8, 76.1, 78.8, 92.0, 126.8, 127.9, 128.6, 128.8, 129.0, 129.8, 131.0, 131.8, 133.1, 133.4, 134.8, 140.6, 195.6

MS (EI) *m/z* 376 (M^+)

Propargyl alcohol 114



Yield 1.4 g (51%)

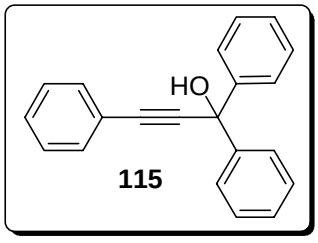
IR (Neat) (cm^{-1}) 3337, 2224, 1722, 1681

^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm): 0.92 (t, 3H, *J* = 6.9 Hz), 1.20 (t, 3H, *J* =7 Hz), 1.27-1.69 (m, 6H), 2.32 (t, 3H, *J* = 6.8 Hz), 4.12-4.45 (2H), 7.62-7.78.(m, 5H) **(Spectrum No. 3)**

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 13.8, 18.7, 22.1, 28.0, 30.9, 63.1, 72.9, 78.6, 87.4, 126.2, 117.3, 128.1, 128.3, 140.0, 172.2 **(Spectrum No. 4)**

MS (EI) *m/z* 274 (M^+)

Propargyl alcohol 115



Yield 1.39 g (49%)

IR (KBr) (cm^{-1}) 3547, 3055, 2220, 1487, 1334

^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm): 2.91 (s, 1H), 7.28-7.41 (10H), 7.56-7.57 (2H), 7.72-7.74 (3H) **(Spectrum No. 5)**

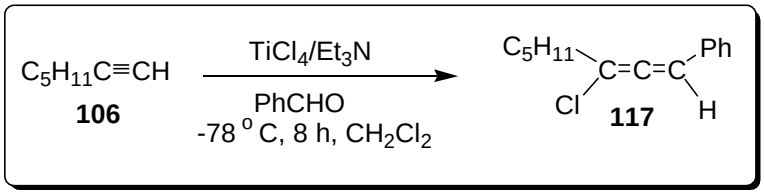
^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 74.8, 87.2, 91.7, 122.4, 126.1, 127.7, 128.3, 128.7, 131.8, 145.0 **(Spectrum No. 6)**

MS (EI) *m/z* 284 (M^+)

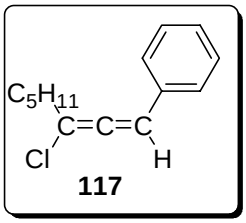
1.4.6 Procedure for the synthesis of chloroallenes from 1-heptyne and benzaldehyde using $TiCl_4/Et_3N$ reagent system

In DCM (35 mL), 1-heptyne (0.96 g, 1 mL, 10 mmol), $TiCl_4$ (1.9 g, 1.1 mL, 10 mmol), Et_3N (1.5 g, 2.1 mL, 15 mmol) and benzaldehyde (1.1 g, 1 mL, 10 mmol) were taken at –78 ^{o}C under N_2. The reaction mixture was stirred for 8 h at –78 ^{o}C. Saturated

NH_4Cl 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 X 15 mL). The combined organic extract 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 with pure hexane. The chloroallene **117** was isolated in 21% yield.



Yield 0.46 g (21%)

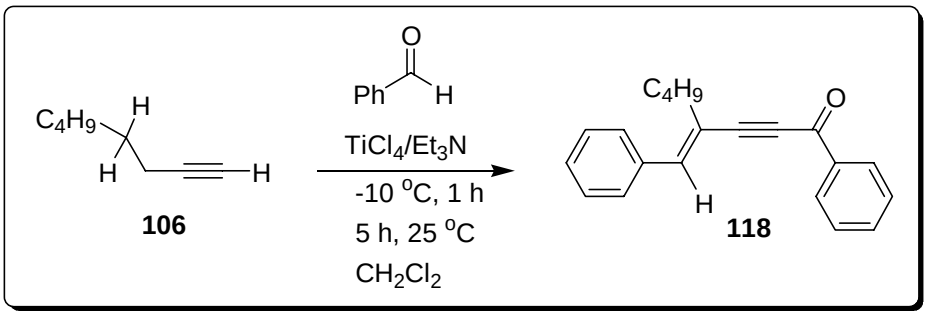


The spectral data were identical to those obtained in the experiment described in Chapter 2 section **2.4.2**.

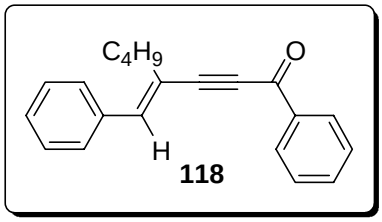
1.4.7 Typical procedure for the synthesis of enynones from benzaldehyde and 1-heptyne using the $TiCl_4/Et_3N$ reagent system

In dichloromethane (35 mL), 1-heptyne (0.48 g, 0.5 mL, 5 mmol), $TiCl_4$ (1.9 g, 1 mL, 10 mmol), triethylamine (1.2 g, 1.7 mL, 12 mmol) and benzaldehyde (1.1 g, 1 mL, 10 mmol) were taken at 0 ^oC under N_2. The reaction mixture was stirred for 1 h at -10 ^oC and further stirred for 5 h at 25 ^oC. Saturated NH_4Cl solution (20 mL) was added and stirred for 10 min. The organic layer was separated and the aqueous layer was extracted with dichloromethane (2 X 15 mL). The combined organic extract 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 with ethyl acetate/hexane (99:1) mixture. The enynone **118**, 0.54 g was isolated in 42% yield.



Yield 0.54 g (42%)



IR (Neat) (cm^{-1}) 3061, 2957, 2932, 2214, 1664, 1597

^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm) 1.02 (t, 3H, *J* = 6.7 Hz), 1.41-1.72 (m, 4H), 2.52 (t, 2H, *J* =6.88 Hz), 7.40-8.21 (m, 11H) **(Spectrum No. 7)**

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 13.5, 19.7, 21.9, 30.2, 78.1, 103.1, 121.8, 128.0, 128.4, 129.7, 130.0, 130.2, 132.3, 134.9, 137.3, 143.9, 194.2 **(Spectrum No. 8)**

We have recorded the carbon-proton correlation spectrum (COSY) and proton-proton correlation spectrum (NOESY) to identify the *E*-stereochemistry. **(COSY Spectrum No. 9) (NOESY Spectrum No. 10)**

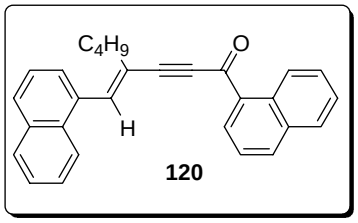
MS (EI) *m/z* 288 (M^+)

Analysis Calculated for $C_{21}H_{20}O$: C, 87.46%; H, 6.99%

Found : C, 87.52%; H, 6.87%

The same procedure was followed for the synthesis of enynone **120**. The data are given below.

Enynone 120



120

Yield 0.75 g (39%)

IR (KBr) (cm^{-1}) 3059, 2957, 2930, 2218, 1664

^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm): 0.89 (t, 3H, *J* = 8.1 Hz), 1.28-1.36 (2H), 1.46-1.55 (2H), 2.22-2.26 (2H), 6.90-8.02 (13H), 8.16 (d, 1H, *J* = 7.8 Hz), 8.31 (d, 1H, *J* = 7.8 Hz)

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 13.6, 19.6, 21.9, 30.2, 77.7, 101.9, 123.4, 125.0, 126.0, 126.7, 127.2, 128.1, 128.8, 129.8, 130.3, 132.4, 137.4, 141.2, 194.7

MS (EI) *m/z* 388 (M^+)

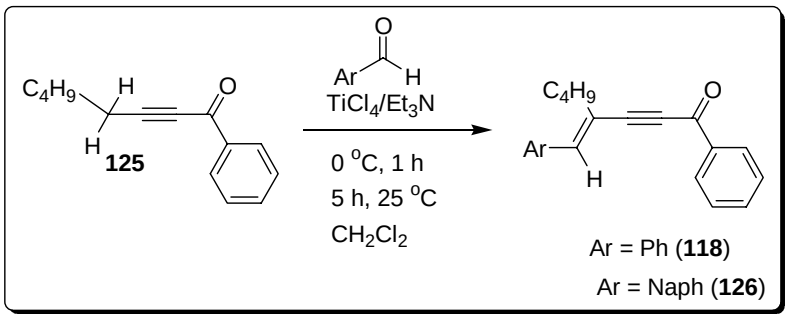
Analysis Calculated for $C_{29}H_{24}O$: C, 89.66%; H, 6.23%

Found : C, 89.54%; H, 6.37%

1.4.8 Typical procedure for the synthesis of enynones from alkynyl ketones using $TiCl_4/Et_3N$ reagent system

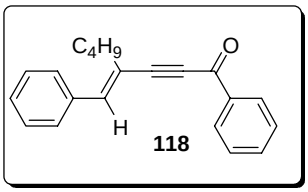
In dichloromethane (35 mL), alkynyl ketone **5** (0.4 g, 2 mmol), $TiCl_4$ (0.38 g, 0.22 mL, 2 mmol) and triethylamine (0.4 g, 0.56 mL, 4 mmol) were taken at 0 ^oC under N_2 atmosphere, to this benzaldehyde (0.21 g, 0.2 mL, 2 mmol) was added. The reaction mixture was stirred for 1 h at 0 ^oC. This was further stirred for 6 h at 25 ^oC. Saturated NH_4Cl solution (20 mL) was added and stirred for 10 min. The organic layer was separated and the aqueous layer was extracted with dichloromethane (2 X 15 mL). The

combined organic extract 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 with ethyl acetate/hexane (99:1) mixture to isolate the enynone **118** (0.25 g, 87%).

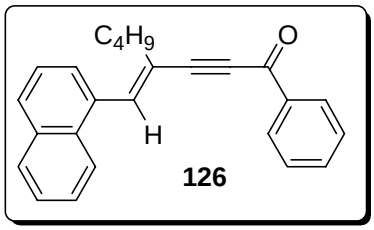


Yield 0.25 g (87%)

(Spectral data was given in section **1.4.7**)



Enynone 126



Yield 0.60 g (89%)

IR (Neat) (cm^{-1}) 3059, 2930, 2251, 1676, 1574

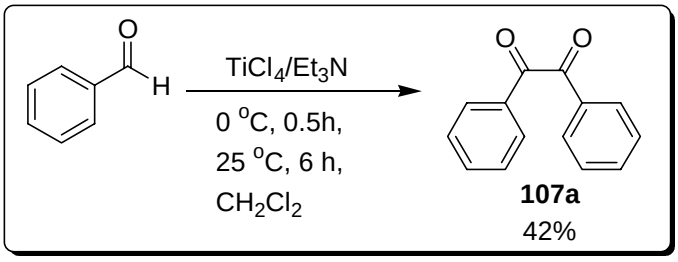
^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm): 0.87 (t, 3H, *J* =7.2 Hz), 1.22-1.27 (m, 2H), 1.27-1.33 (2H), 1.47-1.53 (2H), 6.89 (1H), 7.28-7.73 (m, 10H), 7.82 (d, 1H, *J* = 7.2 Hz), 7.99 (d, 1H, *J* = 7.3 Hz)

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 13.83, 18.73, 22.0, 28.1, 30.9, 77.7, 102.1, 122.6, 124.1, 125.2, 126.2, 127.0, 128.4, 128.7, 130.9, 131.3, 133.5, 148.8, 193.3

MS (EI) *m/z* 338 (M^+)

1.4.9 Typical procedure for the synthesis of 1,2-diaryl-1,2-diones from aromatic aldehydes using $TiCl_4/Et_3N$ reagent system

In dichloromethane (35 mL), $TiCl_4$ (3.7 g, 2.2 mL, 20 mmol), Et_3N (3.0 g, 4.2 mL, 30 mmol) and benzaldehyde (1.1 g, 1 mL, 10 mmol) were taken at 0 ^oC under N_2 and stirred for 0.5 h and stirred further at 25 ^oC for 6 h. Saturated NH_4Cl 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 X 15 mL). The combined organic extract 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 with pure hexane. The benzil **107a** was isolated in 42% yield.



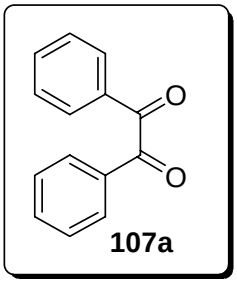
Yield 0.44 g (42%)

IR (KBr) (cm^{-1}) 3428, 1656, 1048, 658

mp 94-96 ^oC, Lit[53a] mp 94-96 ^oC

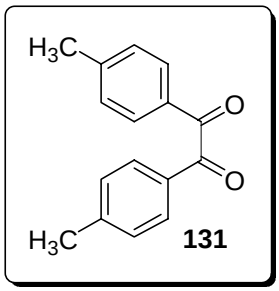
^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm): 7.53-7.48 (m, 4H), 7.69-7.63 (m, 2H), 7.99-7.97 (m, 4H)

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 128.5, 129.91, 133.0, 134.9, 194.6



The same procedure was followed for other aromatic aldehydes. The data are given below.

Dione 131



Yield 0.43 g (36%)

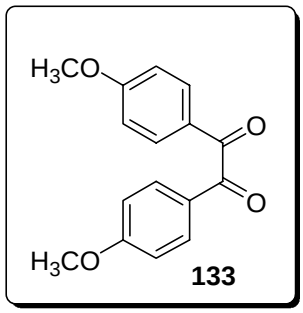
IR (KBr) (cm^{-1}) 3427, 1657, 1046, 679

mp 103-105 °C Lit[53b]mp 104–105 °C

^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm) 2.43 (6H, s), 7.31 (4H, d, *J* = 7.9 Hz), 7.86 (4H, d, *J* = 7.8 Hz)

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 16.4, 123.6, 124.9, 129.9, 137.6, 191.0

Dione 133



Yield 0.38 g (28%)

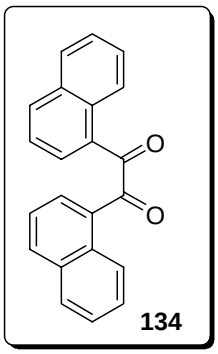
IR (KBr) (cm^{-1}) 3432, 1662, 1572, 1051, 684

mp 132-134 °C, Lit[53c] mp 132-133 °C

^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm) 3.12 (s, 6H, *J* = 8.2 Hz), 6.96-7.7 (8H)

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 55.4, 113.4, 130.8, 132.1, 165.3, 194.3

Dione 134



Yield 0.53 g (34%)

mp 192-194 °C, Lit[53d] mp 192-194 °C

IR (KBr) (cm^{-1}) 3431, 1654, 1063

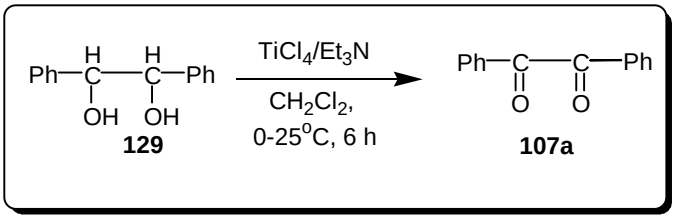
^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm): 7.63-8.04 (m, 12H), 8.32 (2H)

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 123.3, 125.4, 126.4, 126.9, 127.2, 128.2, 129.1, 131.9, 132.6, 134.2, 199.2

1.4.10 Typical procedure for the synthesis of 1,2-diaryl-1,2-diones from 1,2-diaryl-1,2-diols using $TiCl_4/Et_3N$ reagent system

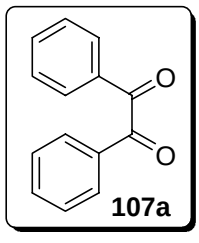
Dichloromethane (25 mL), 1,2-diphenylethane-1,2-diol **129** (0.43 g, 2 mmol) and Et_3N (0.81 g, 1.1 mL, 8 mmol) were taken in a reaction flask under N_2 atmosphere. $TiCl_4$ (1.5 g, 0.8 mL, 8 mmol) was added under N_2 at 0 ^oC. The reaction mixture was stirred for 6 h at 0-25 ^oC. It was quenched with saturated NH_4Cl solution (20 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2 X 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 product 1,2-diphenylethane-1,2-dione **107a** was isolated in 77% yield using hexane/ethyl acetate (90:10) mixture as eluent.



Yield 0.32 g (77%)

(Spectral data was given in section **1.4.9**)

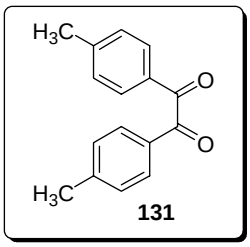


The same procedure was followed for synthesis of other 1,2-diols. The spectral data are identical to the 1,2-diketone samples obtained in previous experiments.

Dione 131

Yield 0.4 g (83%)

(Spectral data was given in section **1.4.9**)

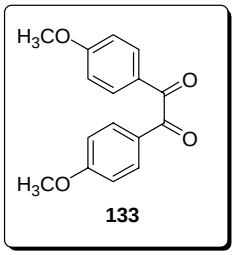


131

Dione 133

Yield 0.46 g (86%)

(Spectral data was given in section **1.4.9**)

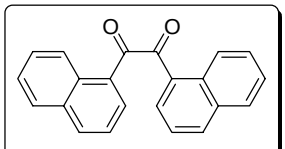


133

Dione 134

Yield 0.41 g (63%)

(Spectral data was given in section **1.4.9**)

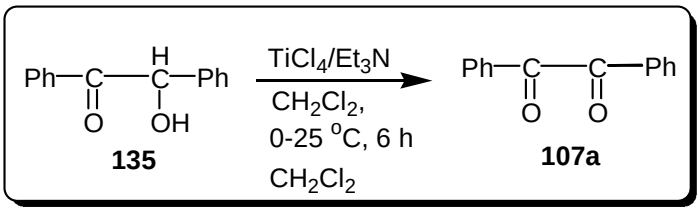


134

1.1.11 Procedure for the synthesis of benzil from benzoin using the $TiCl_4/Et_3N$ reagent system

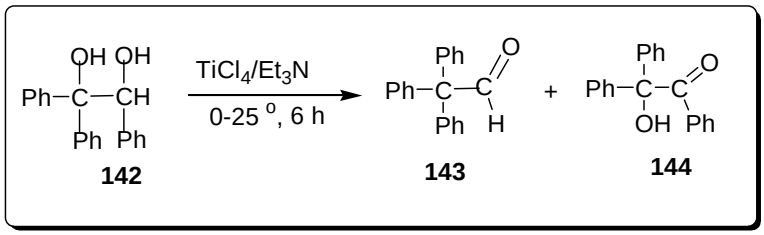
Dichloromethane (25 mL), benzoin **135** (0.42 g, 2 mmol) and Et_3N (0.81 g, 1.1 mL, 8 mmol) were taken in a reaction flask under N_2 atmosphere, to this $TiCl_4$ (1.5 g, 0.8 mL, 8 mmol) was added under N_2 at 0 ^oC. The reaction mixture was stirred for 0.5 h at 0 ^oC and stirred further for 5.5 h at 0-25 ^oC. It was quenched with saturated NH_4Cl solution (20 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2 X 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 product 1,2-diphenylethane-1,2-dione

was isolated using hexane/ethyl acetate (90:10) mixture as eluent. Benzil **107a** was isolated in 77% yields.

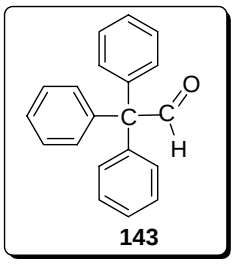


1.4.12 Reaction of 1,1,2-triphenylethane1,2-diol with the $TiCl_4/Et_3N$ reagent system

Dichloromethane (25 ml), Et_3N (0.81 g, 1.1 mL, 8 mmol), $TiCl_4$ (0.76 g, 0.43 mL, 4 mmol) and 1,1,2-triphenyl-1,2-ethane-diol (0.58 g, 2 mmol) added under N_2 at 0 ^oC. The reaction mixture was stirred for 10 h at 0-25 ^oC. It was quenched with saturated NH_4Cl solution (20 ml). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2 X 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 products 2,2,2-triphenyl-acetaldehyde **143** (32%) and 1,2,2-triphenyl-1-ethanone **144** (28%) were isolated using ethyl acetate/hexane (95:5) mixture as eluent.



Aldehyde 143



143

Yield 0.17 g (32%)

mp 104-106 °C, Lit[53e] mp 104-105 °C

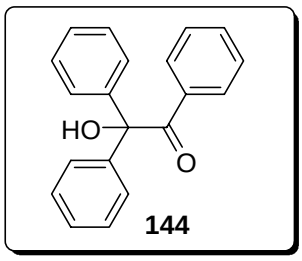
IR (KBr) (cm^{-1}) 3412, 1681,1037

^{1}H-NMR 7.14-7.56 (m, 15H), 9.1 (s, 1H)

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 70.1, 127.4, 128.4, 130.4, 140.6, 198.1

MS (EI) *m/z* 272 (M^+)

Ethanone 144



144

Yield 0.16 g (28%)

mp 82-84 °C, Lit [53f] mp 82-84 °C

IR (KBr) (cm^{-1}) 3334, 1657, 1034

^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm): 4.42 (s, 1H), 6.97-7.55 (13H), 7.71 (d, 2H, *J* = 6.8 Hz)

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 59.4, 127.1, 128.7, 128.9, 129.2, 133.0, 137.01, 139.1, 198.2

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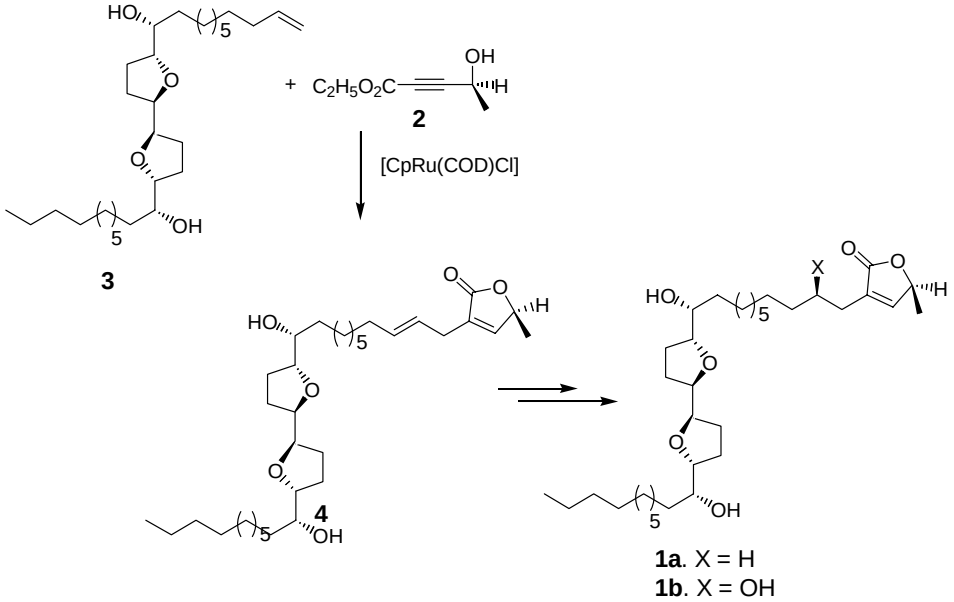
Chapter 2

Synthetic Transformations of Propargyl Alcohols using the $TiCl_4/R_3N$ Reagent System

2.1 Introduction

The propargyl alcohols are useful, reactive organic synthons. In recent years, synthetic applications of propargyl alcohols received increased attention due to their wide applications in the synthesis of many biologically active molecules, drug molecules and natural products. For example, a propargyl alcohol **2** was used for the total synthesis of (+)-*parviflorin* **1a** and (+)-(5*S*)-*hydroxyparviflorin* **1b** (Scheme 1).[1a,b] The propargyl alcohol **2** was reacted with bis(tetrahydrofuran) **3** in the presence of [CpRu(COD)Cl] to give the corresponding butenolide **4,** which has been transformed to **1** in several steps (Scheme 1).

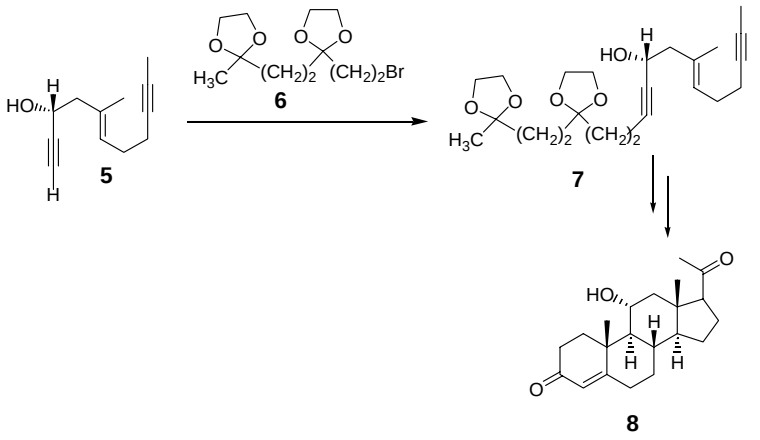
Scheme 1



Propargyl alcohol **5** reacts with bis(tetrahydrofuran)-derived bromide **6** to produce bis(tetrahydrofuran)-derived propargylalcohol **7**, which is used for the synthesis of 11α-

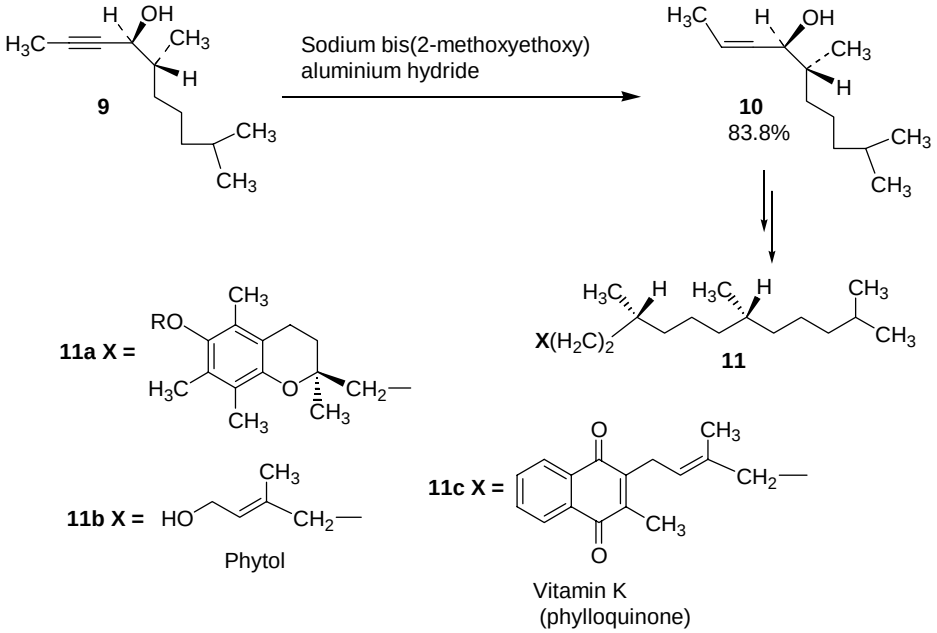
hydroxyprogesterone **8**, the key intermediate in the commercial production of hydrocortisone acetate (Scheme 2).[1c]

Scheme 2



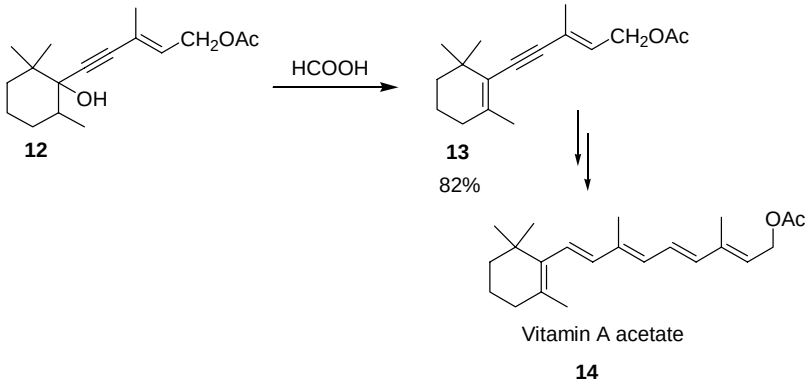
The propargyl alcohol **9** has been used for the synthesis of (2*R*,4'*R*,8'*R*)-α-tocopheryl acetate (Vitamin E acetate) **11a**, Phytol **11b** and Vitamin K **11c** (Chart 1).[2]

Chart 1



The propargyl alcohol **12** has been used for the synthesis of Vitamin A acetate **14** (Scheme 3).[2]

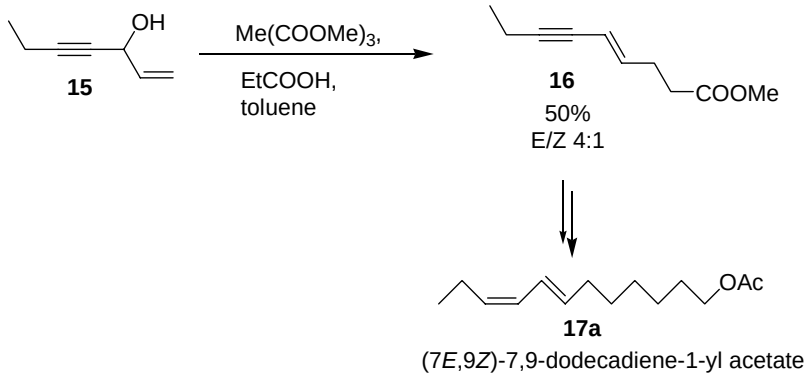
Scheme 3



12 **13** 82% Vitamin A acetate **14**

Propargyl alcohol intermediates were used in crucial steps in the synthesis of several insect sex pheromones.[3] The (7*E*, 9*Z*)-7,9- dodecadien-1-yl acetate **17a** a European grapvine moth,[4a] (9*Z*,11*E*)-9,11-tetradecadien-1-yl-acetate **17b** related Egyptian cotton leaf worm, [4b] (7*Z*,11*E*) –7,11-hexadecadiene-1-yl acetate **17c** a pink bollworm moth destructive pest of cotton in many places of the world, [4c] (-)-methyl(*E*)-2,4,5-tetradecartienoate **17d**[4d] a pheromone of male bean weevil were prepared starting from propargyl alcohols (Chart 2).

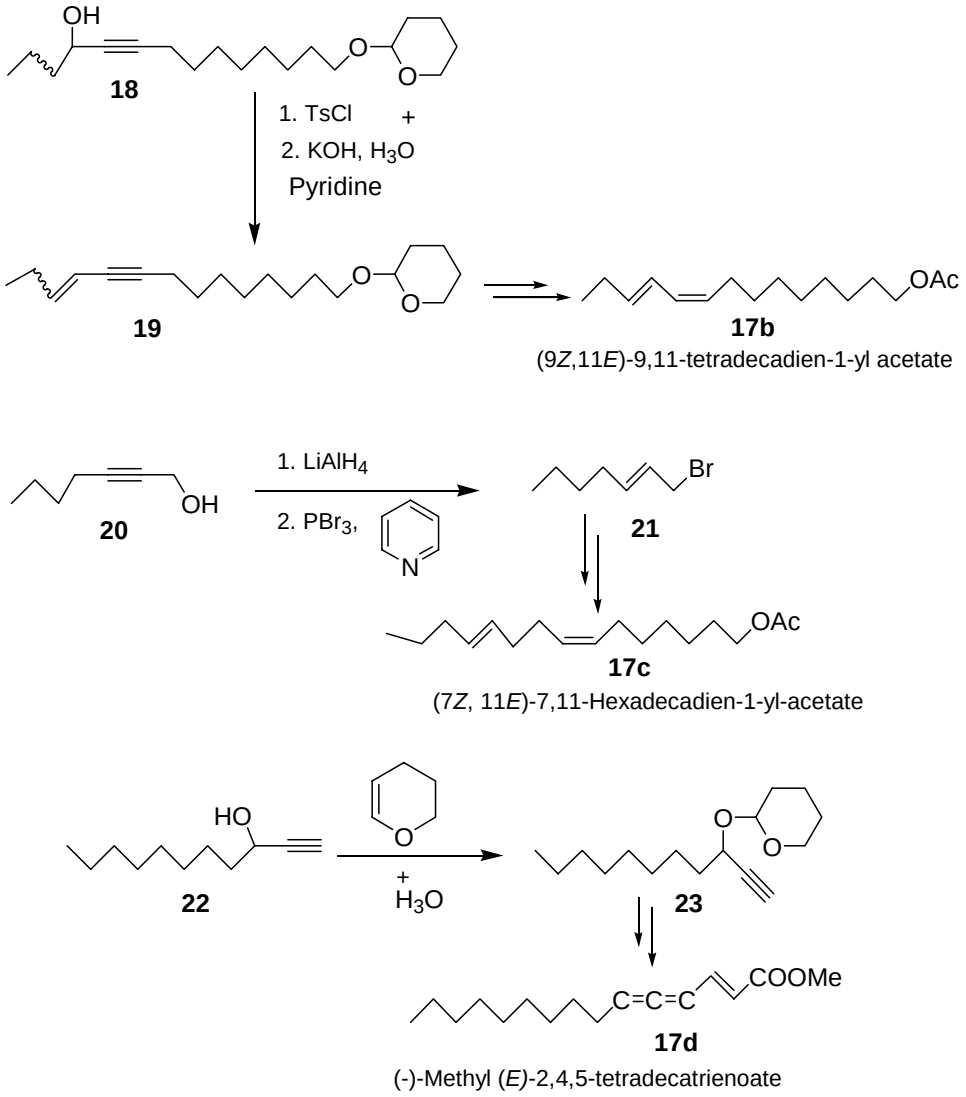
Chart 2



15 **16** 50% E/Z 4:1 **17a** (7*E*,9*Z*)-7,9-dodecadiene-1-yl acetate

(continued…)

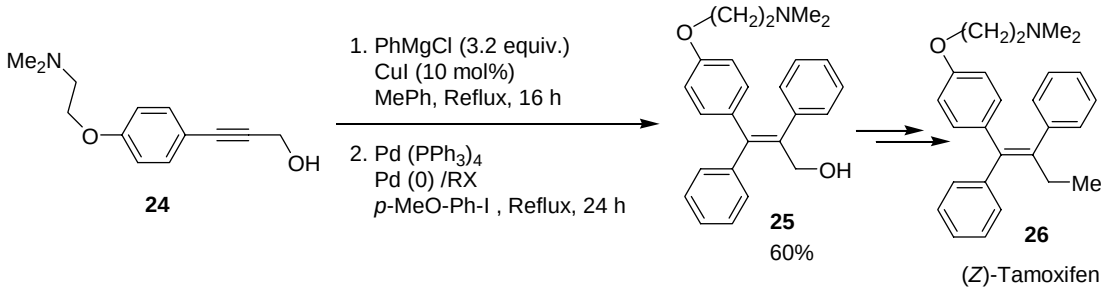
(continued…Chart 2)



Fallis *et al*.[5] reported the synthesis of tetra substituted alkenes and dienes in a regio and stereo controlled manner via magnesium-mediated carbometalation. For example, propargyl alcohol **24** was treated with PhMgCl, CuI and $Pd(PPh_3)_4$ under refluxing

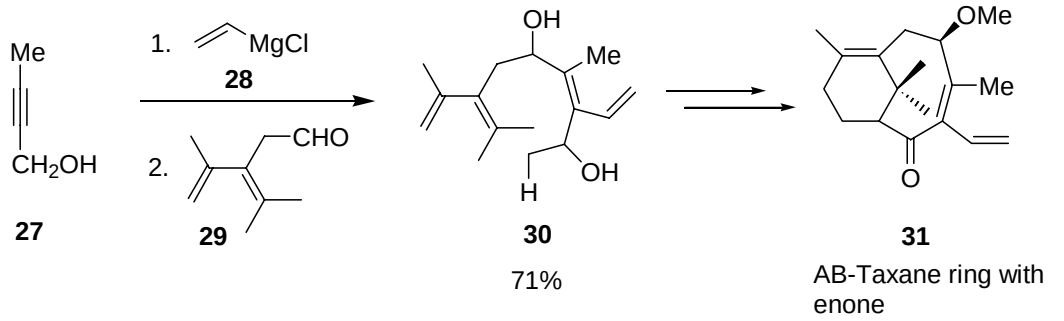
condition to provide alkenol **25** which is the key intermediate for the synthesis of (*Z*)-tomoxaifen, useful as breast cancer drug (Scheme 4).

Scheme 4



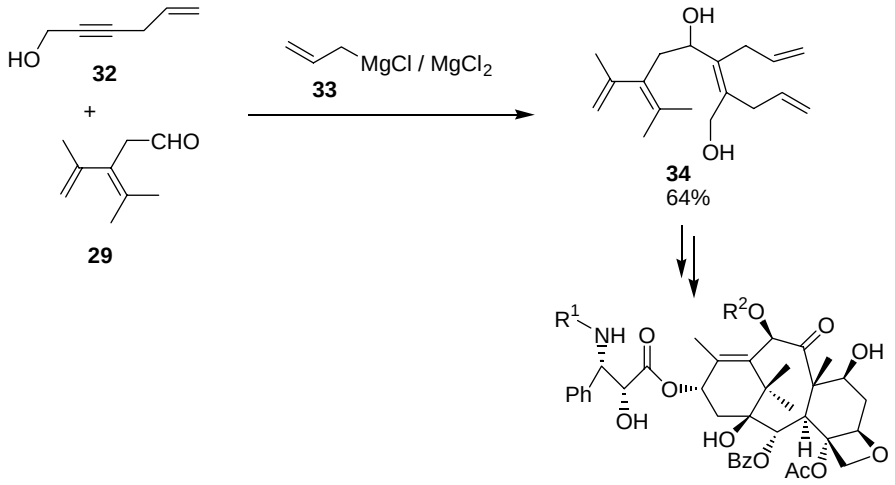
The construction of taxane ring **31**, which is a precursor for the synthesis of the Taxol®(paclitaxel) and Taxotere® (docetaxel) involves propargyl alcohol in a crucial step.[6] In this system, propargyl alcohol **27** was reacted with vinyl magnesium chloride **28** and aldehyde **29** to produce **30**, which was transformed to the taxane ring **31** in several steps (Scheme 5).

Scheme 5



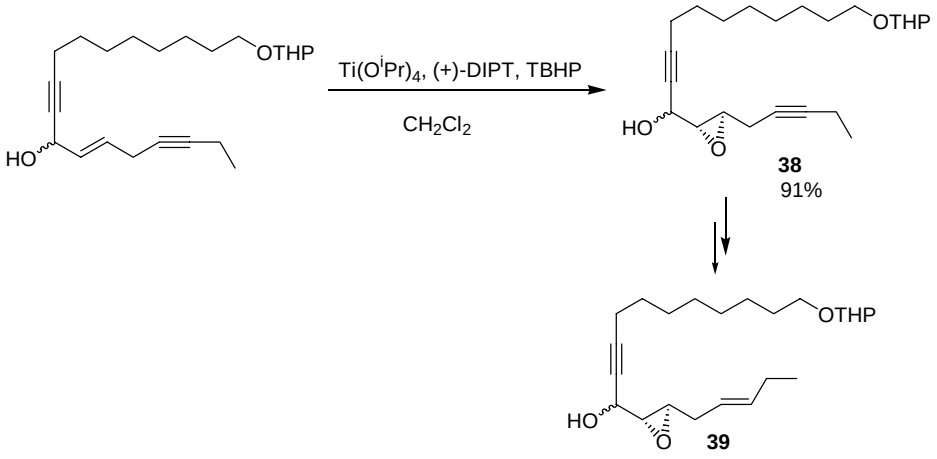
It was reported that propargyl alcohol **32** reacts with aldehyde **29** and allyl magnesium chloride **33** to produce the diol derivative **34**. This is one of the key steps in the synthesis of the tricyclic ABC core taxoids **35** and **36** (Scheme 6).[7]

Scheme 6



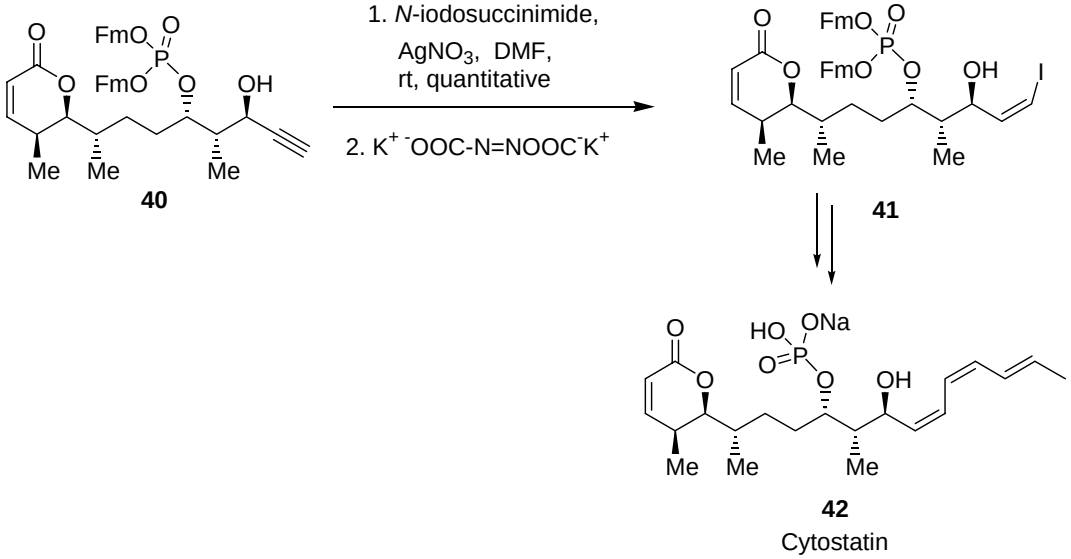
One of the most important class of compounds in biological systems is unsaturated oxygenated fatty acids. Enantioselective total synthesis of the fatty acid **39** was achieved through a propargyl alcohol intermediate.[8] It was reported that propargyl alcohol **37** reacts with titanium tetraisopropoxide and diisopropyl tartrate to produce the corresponding product **38**, which was converted to the fatty acid **39** in several steps (Scheme 7).

Scheme 7



Propargyl alcohol **40** has been used in a key intermediate step in the synthesis of the polyketide natural products of the cytostatin family.[9] It was reported that propargyl alcohol **40** reacts with *N*-iodosuccinimide, $AgNO_3$ and potassium salt to give the iodo alcohol derived product **41**, a precursor for the synthesis of cytostatin **42** in several steps (Scheme 8).

Scheme 8



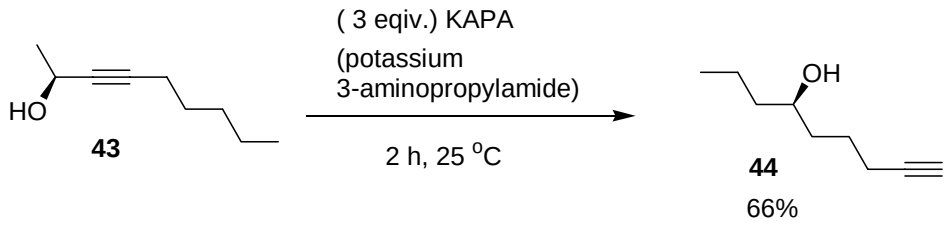
In this chapter we describe the reactions of propargyl alcohols with titanium reagents. Accordingly, it will be helpful for the discussion to briefly review the synthetic transformations of propargyl alcohols with various main group and transition metal reagents.

2.1.1 Reaction of propargyl alcohols with potassium reagents

Midland and coworkers[10] reported the isomerization of optically-active secondary alcohols to terminal secondary alcohols using potassium(3-amino)propylamide (KAPA),

which proceeds without loss of configuration at the hydroxy center. For example, it was observed that the isomerization of enatiomerically pure (*R*)-3-octyn-2-ol **43** with 3 equiv. of KAPA for 2 h at 25 ^{o}C gives (*R*)-1-octyn-7-ol **44** with out racemization (Scheme 9).

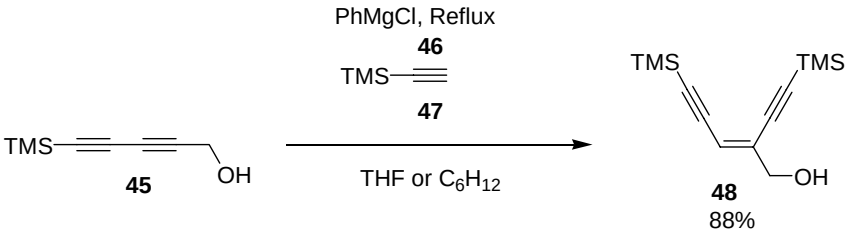
Scheme 9



2.1.2 Transformation of propargyl alcohols using RMgX

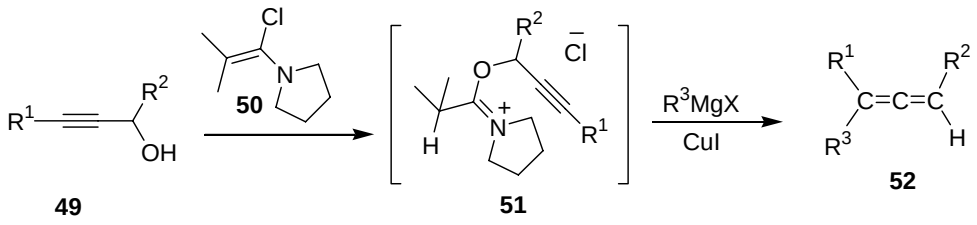
It was reported that propargyl alcohol **45** reacts with trimethylsilylalkyne **47** in the presence of Grignard reagent **46**, to gives the enediyne **48** (Scheme 10).[11]

Scheme 10



Fujisawa and coworkers[12] reported that propargyl alcohols **49** react with α-chloroenamine **50** to produce the propargyloxyiminium salt **51**, which on further reaction with Grignard reagent produce allenes **52** (Scheme 11).

Scheme 11

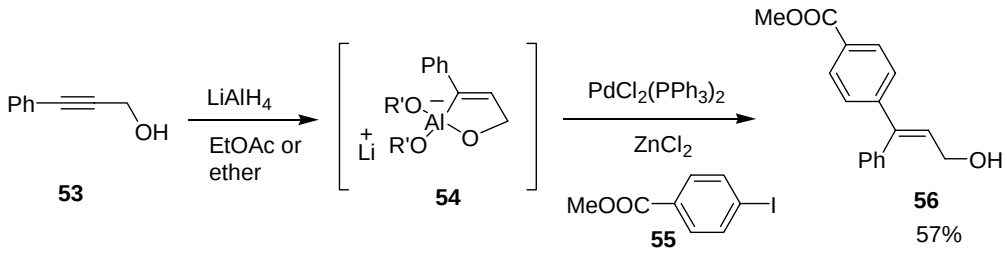


R^1	R^2	R^3	%Yield
H	H	$PhCH_2CH_2$	96
CH_3	Ph	$PhCH_2CH_2$	85
CH_3	Ph	$H_2C=CH_2$	41

2.1.3 Reaction of propargyl alcohols with $LiAlH_4$

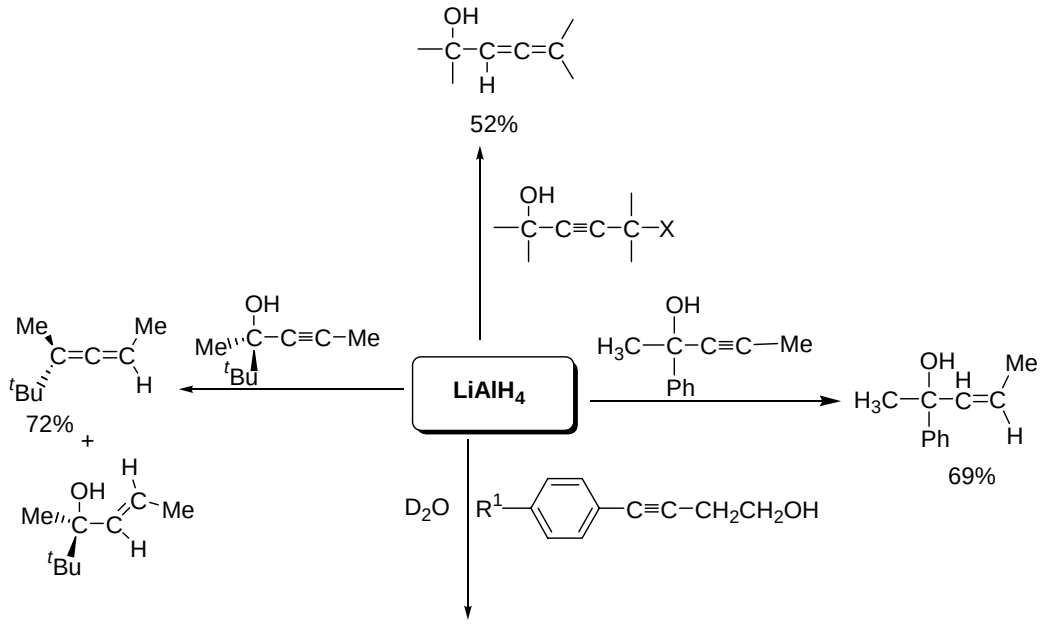
Dvořak and coworkers[13] reported that the 3-phenyl-2-propyn-1-ol **53** forms hydroaluminated intermediates **54** on reaction with $LiAlH_4$. This was further reacted with $PdCl_2(PPh_3)_2$, $ZnCl_2$ and iodoaryl ester **55** to produce the corresponding 3,3-disubstituted aryl alcohol **56** (Scheme 12).

Scheme 12



Substituted propargyl alcohols when reacted with lithium aluminum hydride give a variety of compounds as shown in Scheme 13.[14]

Scheme 13

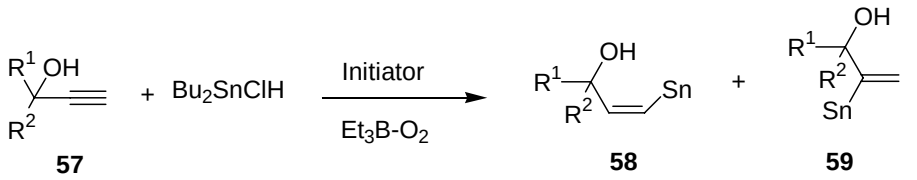


R^1	% Yield	A	B	C
CH_3O	92	59	-	38
CH_3	93	100	-	-
H	100	65	-	34

2.1.4 Reaction of propargyl alcohols with tin derivatives

Miura and coworkers[15] reported the Et_3B initiated reaction of γ-unsubstituted propargyl alcohols **57** with dibutylchlorostannane (Bu_2SnClH). In the presence of initiator at low temperature, (*Z*)-vinylstannanes **58** and **59** were obtained with high level of regio- and stereoselectivities (Scheme 14).

Scheme 14

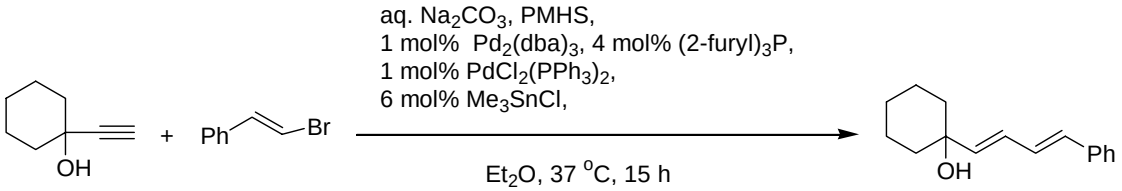


57 **58** **59**

R^1	R^2	%Yield	(**58:59**)
n-C_8H_{17}	H	81	98:2
H	H	71	99:1

It was reported that syringe pump addition of Stille electrophile **61** to the propargyl alcohol **60**, aqueous Na_2CO_3, PMHS, Pd_2dba_3, trifurylphosphine, $PdCl_2(PPh_3)_2$, and Me_3SnCl over a period of 15 hours afforded the corresponding cross-coupled product **62** (Scheme 15).[16]

Scheme 15

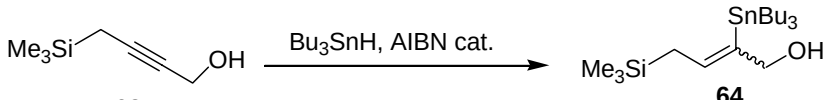


60 **61** **62**

90%

Reaction of tri-*n*-butylstannyl hydride with substituted propargyl alcohol **63** gives a mixture of *Z/E* isomeric product **64** (Scheme 16).[17]

Scheme 16

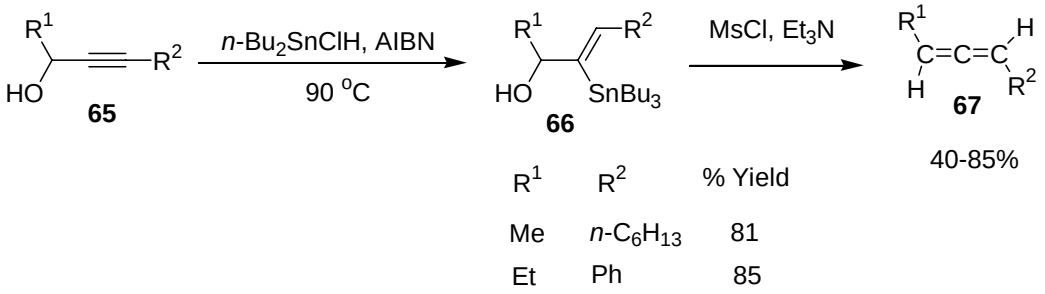


63 **64**

Yield 71%
Z : *E*
1 : 1

Konoike and coworkers[18] reported that the propargyl alcohols **65** are converted to the corresponding allenes **67**, through the intermediate **66** using *n*-Bu_3SnClH and AIBN (Scheme 17).

Scheme 17

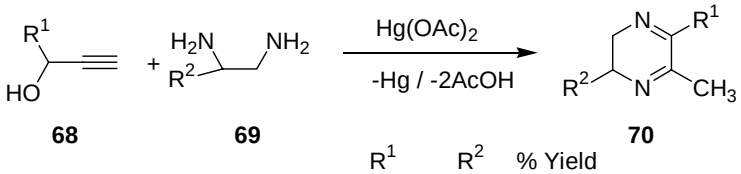


R^1	R^2	% Yield
Me	*n*-C_6H_{13}	81
Et	Ph	85

2.1.5 Reaction of propargyl alcohols with $Hg(OAc)_2$

It was reported that 5-methyl-2,3-dihydropyrazines **70** are obtained by the reaction of a propargyl alcohols **68** with mercury(II) acetate and excess of aliphatic 1,2-diamines **69** (Scheme 18).[19]

Scheme 18



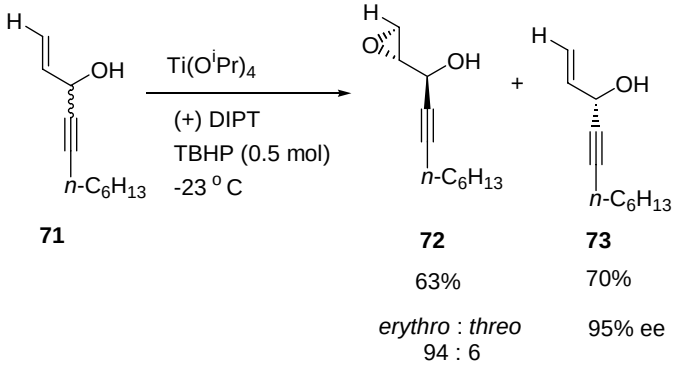
R^1	R^2	% Yield
CH_3	CH_3	46
C_6H_5	H	64

2.1.6 Reaction of propargyl alcohols with titanium

A complex prepared from titanium tetraisoipropoxide in CH_2Cl_2 and (+) diisopropyl tartrate [(+)DIPT] reacts with the propargyl alcohol **71** and tertiary butylhydroperoxide in

dichloromethane at –23 ^{o}C to produce the corresponding asymmetric epoxy propargyl alcohol **72** and propargyl alcohol **73** (Scheme 19).[20]

Scheme 19



71 **72** **73**

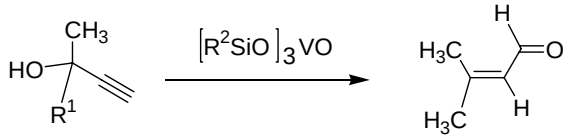
63% 70%

erythro : *threo* 94 : 6 95% ee

2.1.7 Reaction of propargyl alcohols with vanadium complexes

Pauling and coworkers[21] reported that the $[R_3SiO]_3VO$ catalyst reacts with propargyl alcohol **74** to produce the corresponding α,β-unsaturated carbonyl compounds **75** (Scheme 20).

Scheme 20

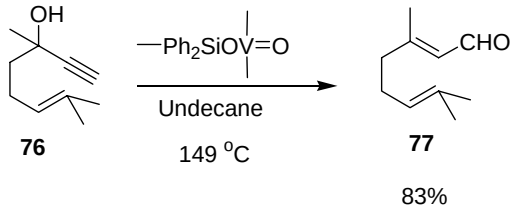


74 **75**

R^1	R^2	% Yield
C_6H_5	C_6H_5	90

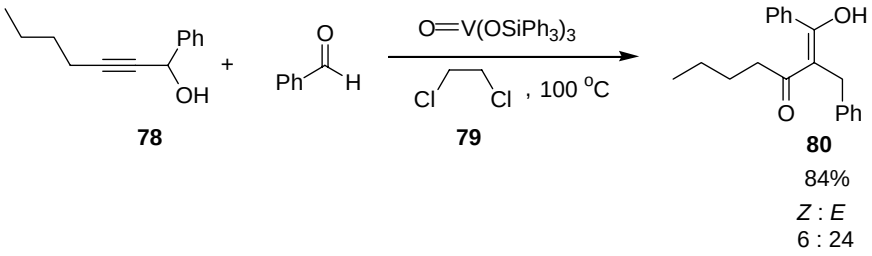
It was reported that tertiary propargyl alcohol **76** rearranges to the corresponding α, β-unsaturated aldehyde **77** when heated in the presence of organosilylvanadates (Scheme 21).[22]

Scheme 21



Trost *et al.*[23] reported that the reaction of propargyl alcohol **78** with benzaldehyde and 1,2-dichloroethane **79** in the presence of tris(triphenylsilyl)vanadate at 100 °C gives the corresponding adduct **80** (Scheme 22).

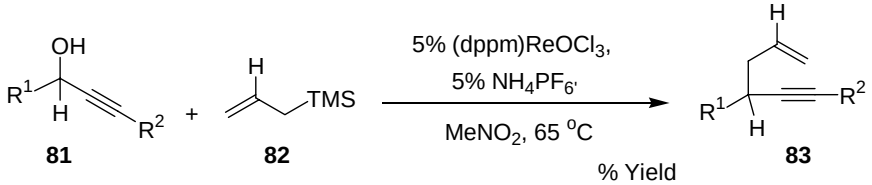
Scheme 22



2.1.8 Reaction of propargyl alcohols with rhenium complexes

Toste and coworkers[24] reported the rhenium-catalyzed coupling of propargyl alcohols and allyltrimethylsilane. For example, the propargyl alcohol **81** and trimethylsilylallyl compound **82** react with (dppm)$ReOCl_3$ (5 mol%) and $AgSbF_6$ (5 mol%) in nitromethane at 65 °C to produce the 1,5-enyne **83** (Scheme 23).

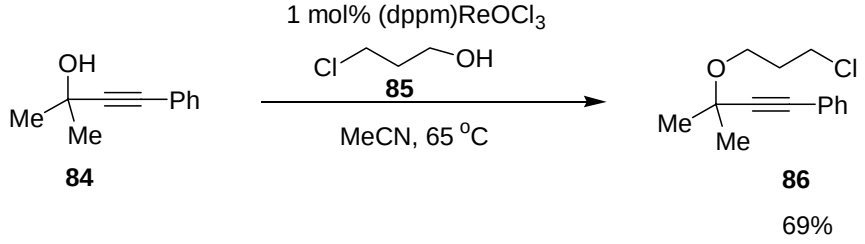
Scheme 23



	% Yield
$R^1 = R^2 =$ Ph	79
$R^1 = p$-$OMeC_6H_4$, $R^2 =$ Me	95

Reaction of the propargyl alcohol **84** with 1 mol% (dppm)$ReOCl_3$ and chloro alcohol **85** produces the propargylic ethers **86** (Scheme 24).[25]

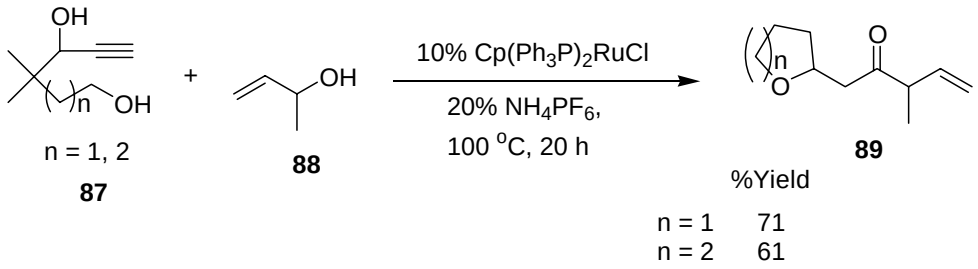
Scheme 24



2.1.9 Reaction of propargyl alcohols with ruthenium complexes

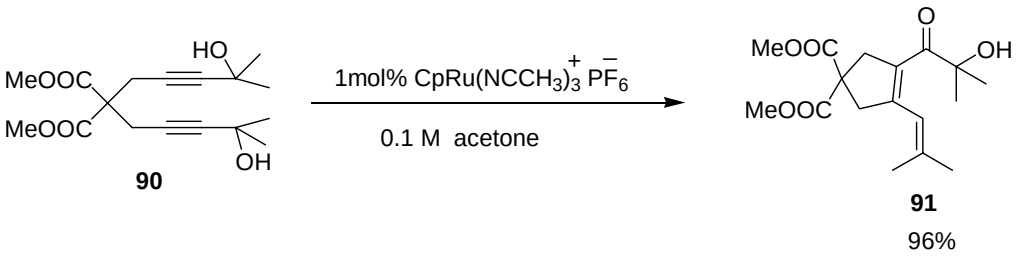
Trost *et al.*[26] reported a novel ruthenium-catalyzed tandem cyclization-reconstitutive addition of propargyl alcohols with allyl alcohols. A neat mixture of propargyl alcohol **87** and 3-buten-2-ol **88** containing 10 mol% $Cp(Ph_3P)_2RuCl$ and 20 mol% NH_4PF_6 was heated at 100 °C for 8 hours to obtain the tetrahydropyranyl ketone **89** (Scheme 25).

Scheme 25



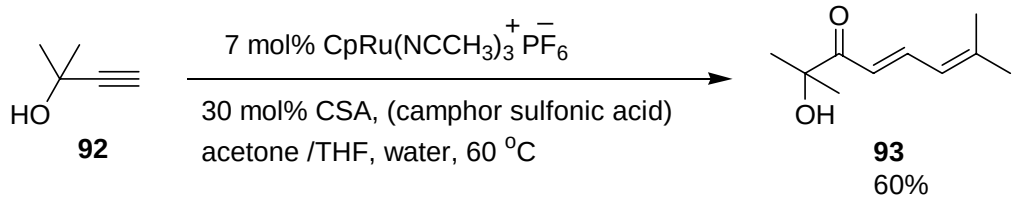
Also, ruthenium-catalyzed cycloisomerization of bis propargyl alcohol **90** gives the α-hydroxydienone **91** (Scheme 26). [27]

Scheme 26



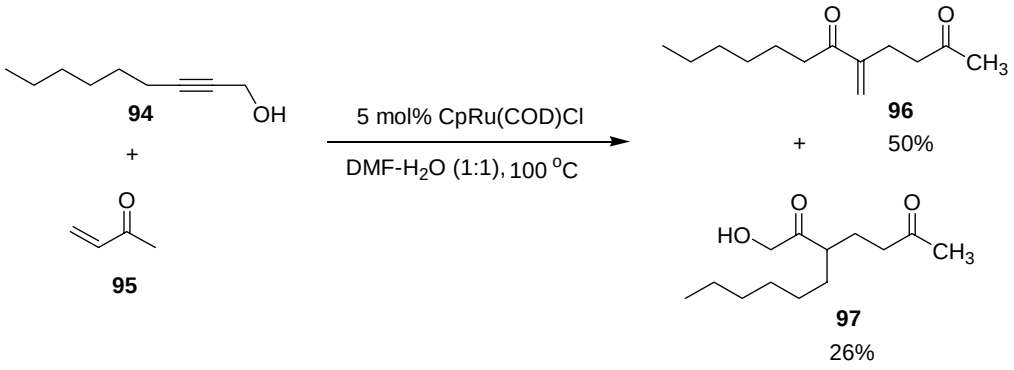
3,3-Dimethyl propargyl alcohol **92** reacts with the ruthenium reagent to give the corresponding product **93** in 60% yield (Scheme 27).[28]

Scheme 27



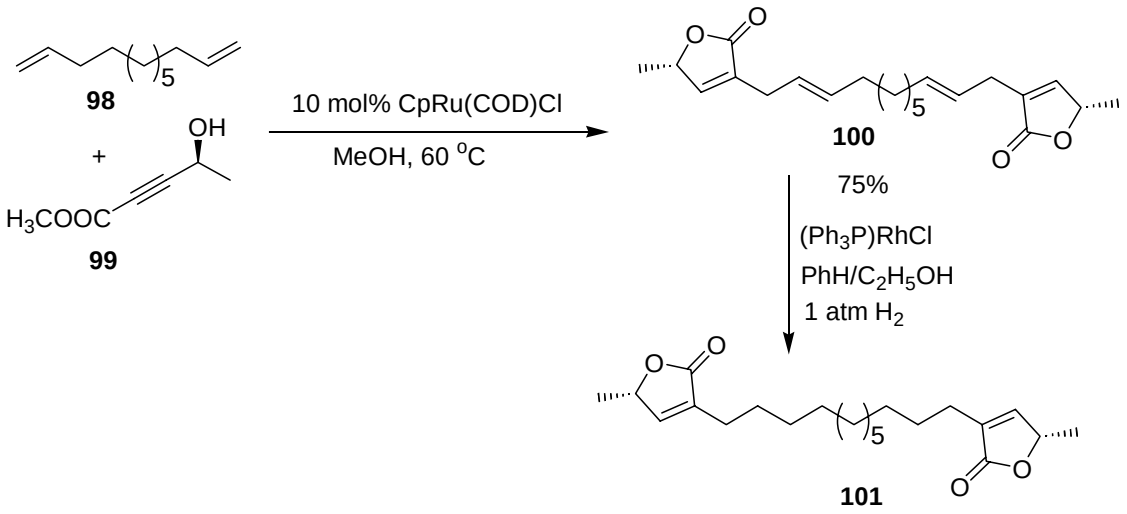
Also, the reaction of propargyl alcohol **94** and methyl vinyl ketone **95** in the presence of CpRu(COD)Cl in DMF-H_2O (1:1) produces the desired product **96** in 50% yield along with the product **97** in 26% yield (Scheme 28).[29]

Scheme 28



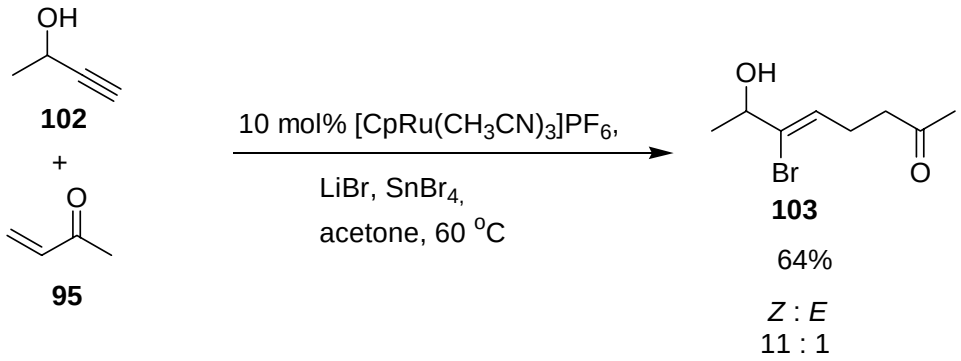
Ruthenium catalyzed reaction of 1,11-dodecadiene **98** with alkynoate **99** produces tetraene **100** in 75% yield (Scheme 29).[30] Chemoselective hydrogenation of the unconjugated olefins produced the naturally occurring acetogenin, (+)-ancepsenolide **101**.

Scheme 29



The 3-butyn-2-ol **102** reacts with methyl vinyl ketone **95** in the presence of 10 mol% $CpRu(CH_3CN)_3PF_6$ to form vinyl bromide **103** in 64% yield (Scheme 30).[31]

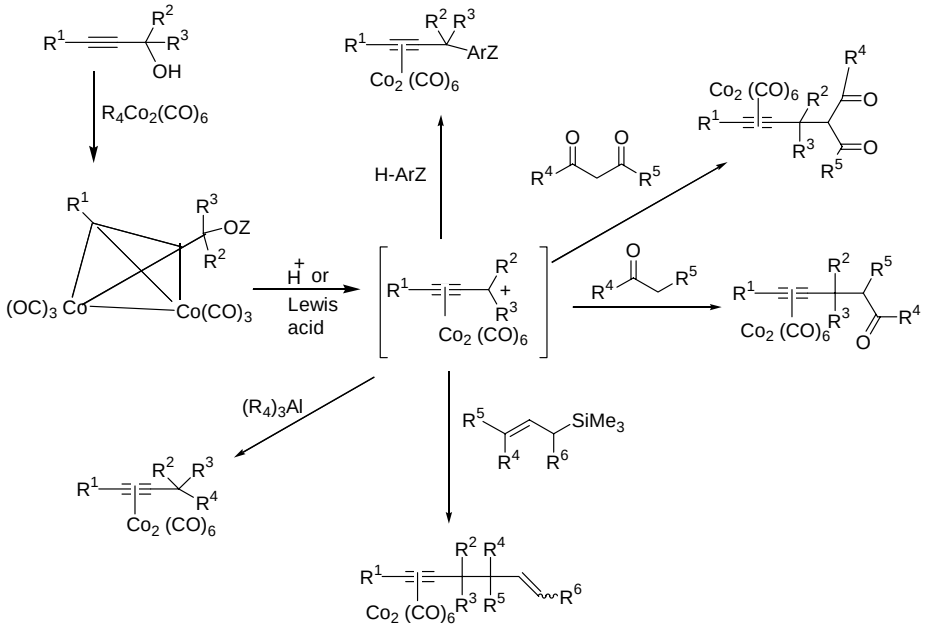
Scheme 30



2.1.10 Reaction of propargyl alcohols with cobalt complexes

The extraordinary stabilization of carbocations by adjacent organotransition metal groups provided in the α-(alkynyl)$Co_2(CO)_6$ system is the basis for a highly versatile method of C-C bond formation. The results are outlined in the Scheme 31.[32]

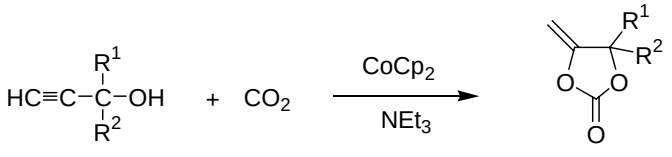
Scheme 31



2.1.11 Reaction of propargyl alcohols with rhodium complexes

It was reported that the reaction of CO_2 with propargyl alcohol **104** catalyzed by cobaltocene ($CoCp_2$) gives α-methylene cyclic carbonates **105** in the presence of triethylamine (Scheme 32).[33]

Scheme 32



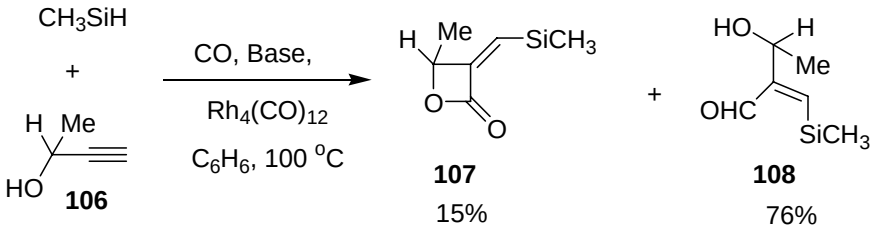
104 **105**

Cp = cyclopentadienyl

R^1	R^2	% Yield
CH_3	$CH_2CH(CH_3)_2$	87
C_6H_5	H	82
C_2H_5	C_2H_5	83

Access to α-(triorganosilyl)methylene β-lactones have been reported using propargyl alcohols in the presence of rhodium catalysts. For example, carbonylation of a mixture of 2-methyl-3-butyn-2-ol **106**, CH_3SiH using $Rh_4(CO)_{12}$ catalyst produce the α-silylmethylene β-lactone **107** and 3-silylpropenal **108** in the presence of a catalytic amount of $Rh_4(CO)_{12}$ (Scheme 33).[34]

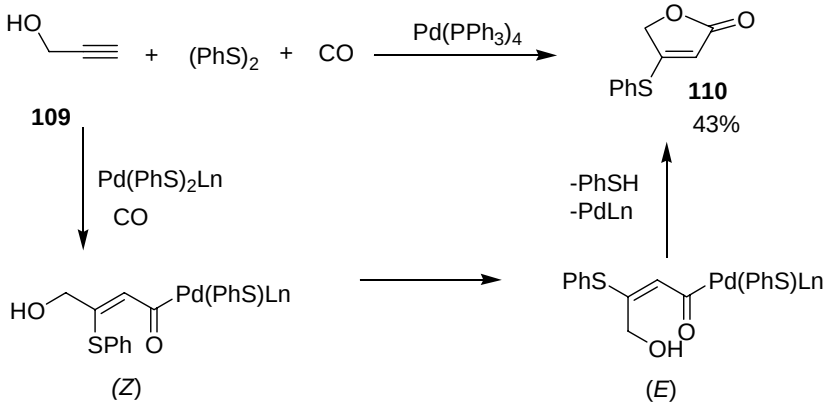
Scheme 33



2.1.12 Reaction of propargyl alcohols with palladium complexes

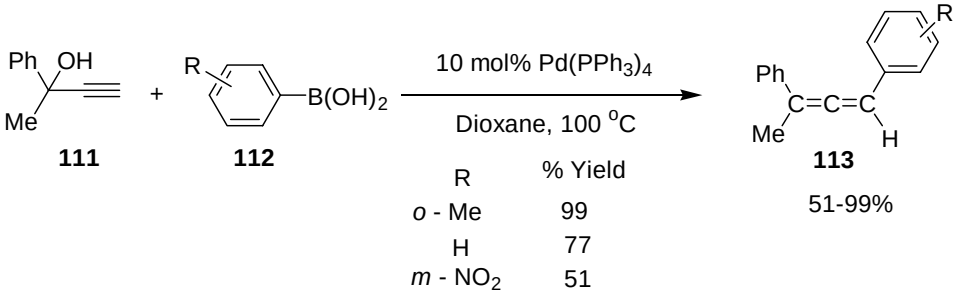
Reaction of 2-propyn-1-ol **109** with diphenyl disulfide and carbon monoxide in the presence of tetrakis(triphenylphosphine)palladium at 100 °C for 50 h provides **110** (Scheme 34).[35]

Scheme 34



The direct coupling of propargyl alcohols with aryl boronic acids has been achieved using a palladium catalyst. For example, 2-phenyl-3-butyn-2-ol **111** and 2-arylboronic acid **112** react in the presence of $Pd(PPh_3)_4$ in dioxane at 100 ^oC to afford allene **113** in up to 99% yield (Scheme 35).[36]

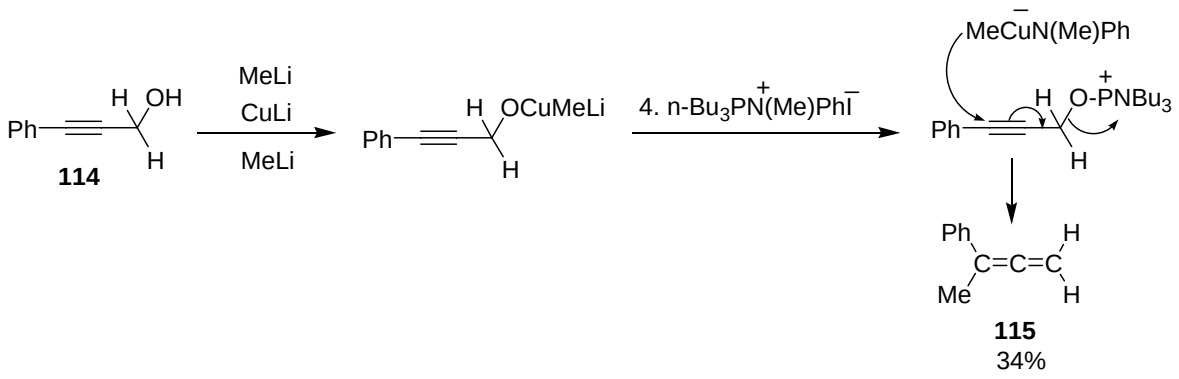
Scheme 35



2.1.13 Reaction of propargyl alcohols with copper reagents

It was reported that the organocuprate induced coupling of propargyl alcohols **114** using (methylphenylamino)tributylphosphoniumiodide gives allenes **115** (Scheme 36).[37]

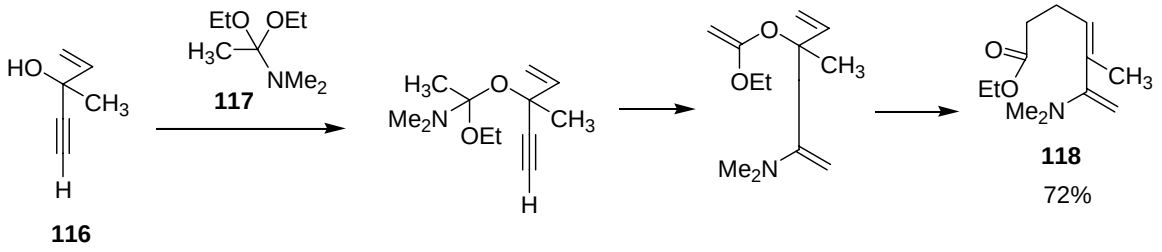
Scheme 36



2.1.14 Reaction of propargyl alcohols with amide acetals

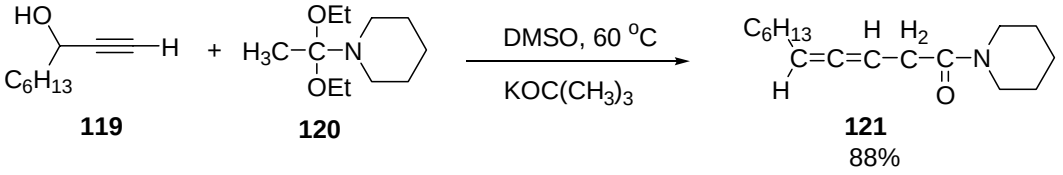
Parker and coworkers[38] reported that the 3-methyl-4-penten-1-yn-3-ol **116** undergoes the ester Claisen rearrangement with the diethyl acetal **117** (DMA-DEA) to afford the enamine **118** (Scheme 37).

Scheme 37



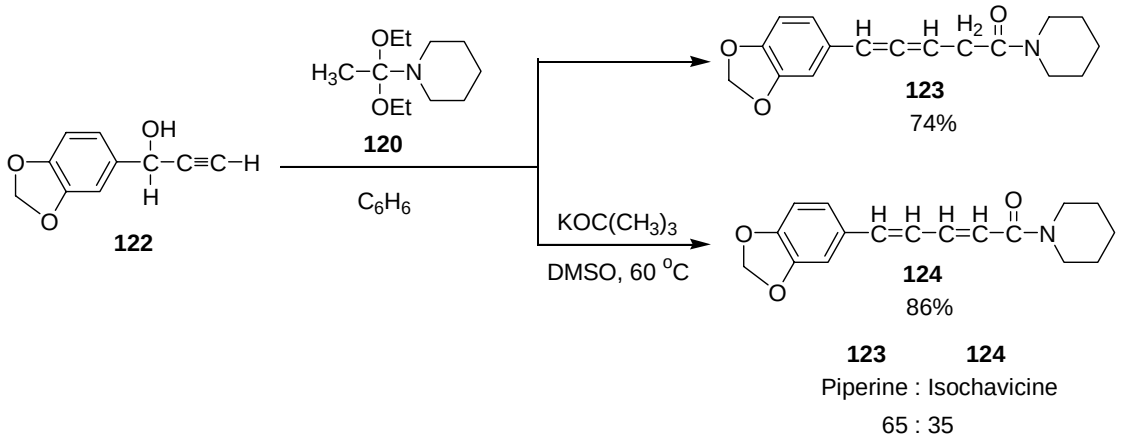
Thermal condensation of propargyl alcohols **119** with amide acetals **120** gives the 3,4-dienamides **121** (Scheme 38).[39]

Scheme 38



The thermal condensation of propargyl alcohol **122** with acetal **120** with a base in benzene at refluxing condition produces allene amide of piperine **123** and isochavicine **124** (65:35) (Scheme 39).[40]

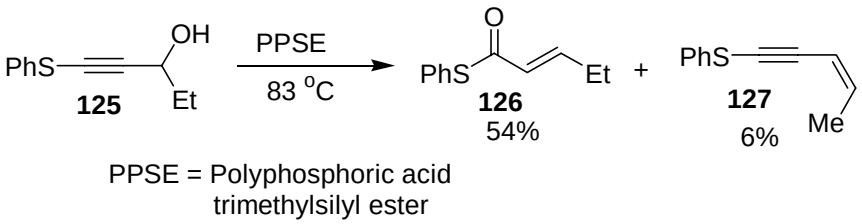
Scheme 39



2.1.15 Reaction of propargyl alcohols with phosphorus

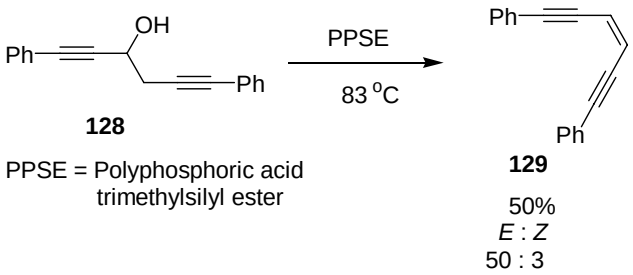
Yoshimatsu and coworkers[41] reported that the γ-sulfur-substituted propargyl alcohol **125** reacts with PPSE at 83 °C to give the (*E*)-S-phenyl-2-pentenethioate **126** (54%) and (*Z*)-enyne sulfide **127** (6%) (Scheme 40).

Scheme 40



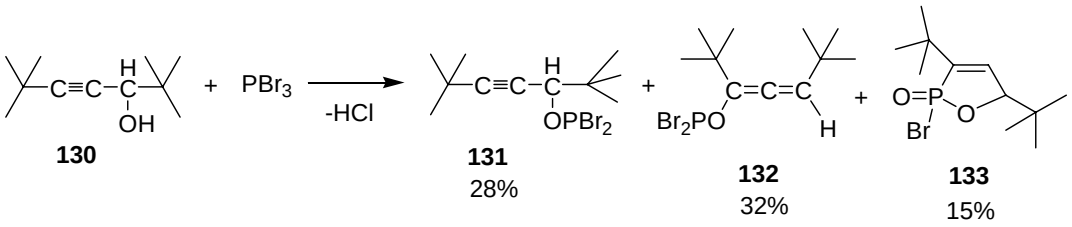
It has been reported that propargyl alcohol **128** reacts with polyphosphoric acid trimethylsilyl ester to afford enediyne **129** (*E:Z* = 50:3) (Scheme 41).[42]

Scheme 41



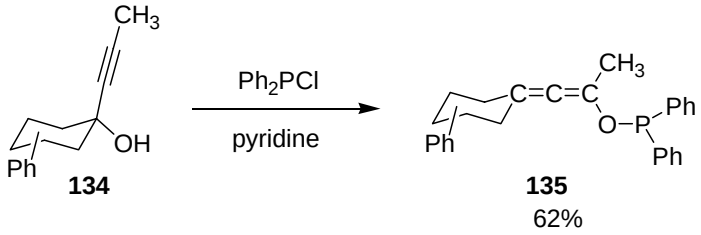
Macomber and coworkers[43] reported that the reaction of propargyl alcohol **130** with phosphorus tribromide afforded crystalline phosphorus containing compounds **131, 132** and **133** (Scheme 42).

Scheme 42



It has been reported that propargyl alcohol **134** react with diphenyl chlorophosphine to produce allenic phosphorus derived product **135** (Scheme 43).[44]

Scheme 43



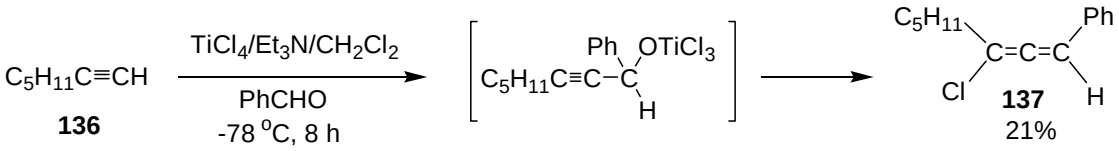
We have examined the reaction of substituted propargyl alcohols with the $TiCl_4/Et_3N$ reagent system. The results are discussed in the next section.

2.2 Results and Discussion

2.2.1 Reaction of propargyl alcohols prepared from aryl aldehydes and ketones using the $TiCl_4/Et_3N$ reagent system

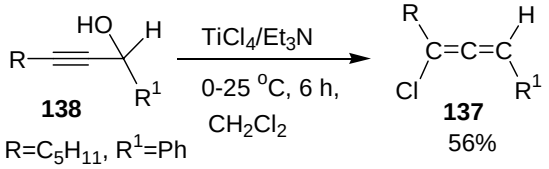
We have observed that when benzaldehyde was used as electrophile in the reaction of 1-heptyne **136** and $TiCl_4/Et_3N$ at -78 ^oC, gave the corresponding chloroallene **137** was isolated in 21% yield (Scheme 43).

Scheme 43



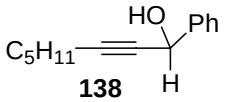
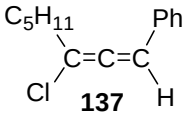
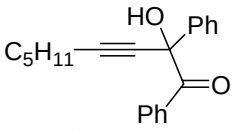
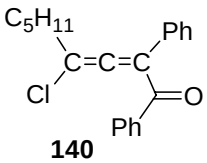
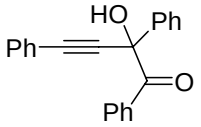
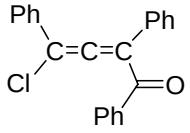
Presumably, this reaction may go through the corresponding propargyl alcohol intermediate. Accordingly, we decided to examine the reaction of propargyl alcohols under various conditions. At 0-25 ^oC, the propargyl alcohol (1-phenyl-2-octyn-1-ol) **138** is reacted with triethylamine and $TiCl_4$ to give the corresponding chloroallene **137** in 56% yield (Scheme 44).

Scheme 44



We have then examined the reactivity of different propargyl alcohols, using the $TiCl_4/Et_3N$, in DCM at 0-25 ^oC. The corresponding chloroallenes were obtained in 44-58% yields. The results are summarized in Table 1.

Table 1: **Conversion of propargyl alcohols to chloroallenes using the $TiCl_4/Et_3N$ reagent system**[a]

Entry	Substrate	Amine	Product[b]	Yield (%)[c]
1	 **138**	Et_3N	 **137**	56
2	**138**	Bu_3N	**137**	45
3	**138**	$^{i}Pr_2NEt$	**137**	37
4	 **139**	Et_3N	 **140**	54
5	 **141**	Et_3N	 **142**	58

[a]The reagents were used in the following quantities: propargyl alcohol (1 mmol), $TiCl_4$ (1 mmol),and alkylamine (2 mmol).

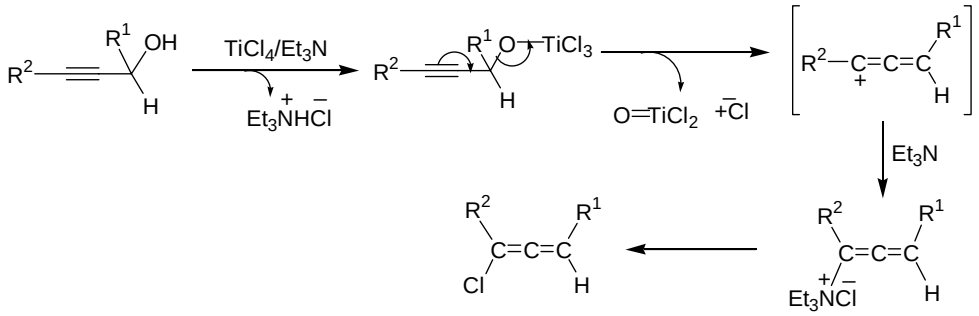
[b]The products were identified by IR, ^{1}H-NMR, ^{13}C-NMR, mass spectral data and elemental analysis.

[c]Yield of isolated products.

We have also examined this transformation using different amines, and found that triethylamine gave better yields (Table 1, entry 1). The propargyl alcohol **138** reacts with $TiCl_4$ in the presence of tributylamine and *N,N*-diisopropylethylamine to give the corresponding chloroallene **137** in 45% and 37% yields, respectively (Table 1, entries 2 and 3). The chloroallenes **140**, **142** were also isolated in 54% and 58% yields from the propargyl alcohols **139** and **141**, respectively (Table 1, entries 4 and 5).

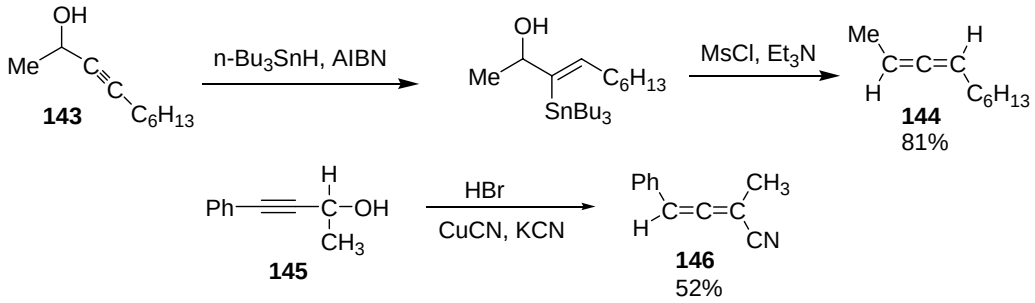
However, the propargyl alcohols derived from aliphatic aldehydes and ketones (e.g. butyraldehyde, acetophenone and cyclohexanone) led to unclean reaction and the corresponding chloroallenes were not formed in these cases. A tentative reaction mechanism can be considered as shown in the Scheme 45.

Scheme 45



Allenes are important class of organic compounds and are useful for the synthesis of important molecules like (+)-Aphanamol, (+)-Dictamnol, Astenine, Antoxin, Dysidiolide.[45] In recent years, several methods have been reported for the preparation of allene derivatives from propargyl alcohols.[14,18,36,37] For example, it was reported that the propargyl alcohol **143** gives the corresponding allenes **144** in the presence of *n*-Bu_3SnH, followed by the reaction with MsCl. Similarly, CuCN/KCN reacts with propargyl alcohols **145** to give cyano substituted allene **146** (Scheme 46).[46]

Scheme 46

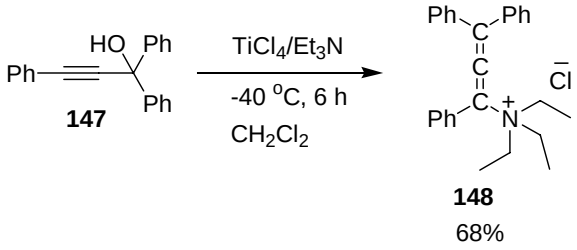


The simple method of synthesis of chloroallenes described here is a good addition to this pool of procedures.

2.2.2 Isolation of allenyl quaternary salt in the reaction of propargyl alcohol with the $TiCl_4/Et_3N$ reagent system

We have observed that in the reaction of 1,1,3-triphenyl-2-propyn-1-ol **147** with the $TiCl_4/Et_3N$ reagent system at –40 °C, the triphenylallene ammonium salt **148** was isolated in 68% yield (Scheme 47).

Scheme 47



The crystal structure data of the triethylamine salt **148** are summarized in Table 2 and Table A2 (Appendix II). The ORTEP diagram of **148** is shown in Figure 1.

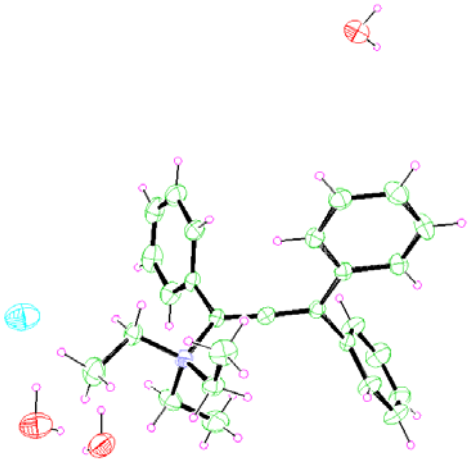


Figure 1: ORTEP diagram of the triethyl amine salt 148
(Thermal ellipsoids are drawn at 20% probability)

The asymmetric unit consists of allenyl cation, chloride anion and three water molecules. These water clusters form a cubane (Figure 2a). The three water molecules interacting with chloride anion via non-covelent interactions to form a discrete cyclic hexameric, chair form water clusters Figure 2b.

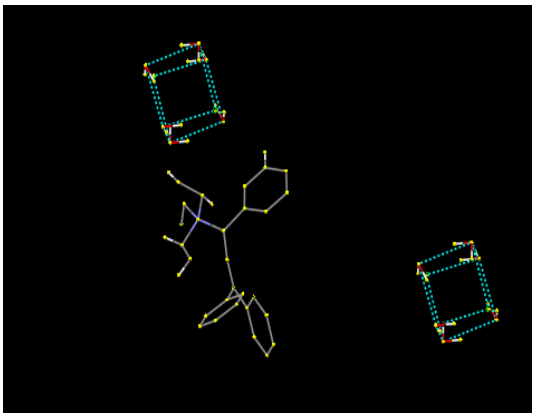


Figure 2a. Cubane formation of water cluster of allenyl triethylamine salt **148**.

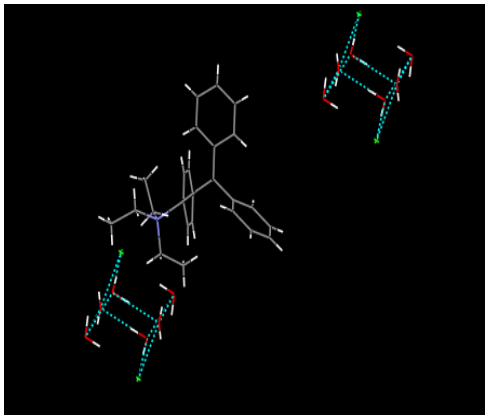


Figure 2b. Chair form of the water cluster of allenyl triethylamine salt **148**.

Single water cluster is surrounded by the triphenyl allene moiety as shown in Figure 3a, and the packing is shown in the Figure 3b.

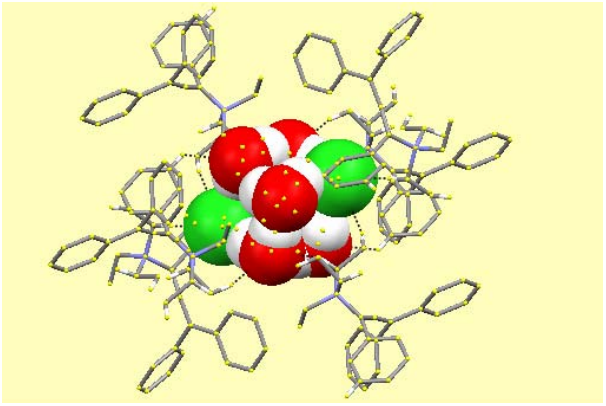


Figure 3a. Water cluster formation by two chloride ions in allenyl triethylamine salt **148**.

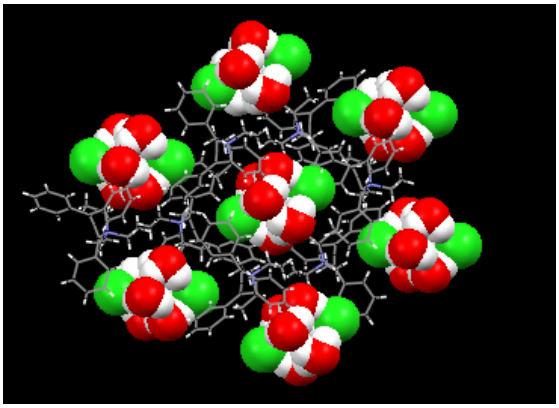


Figure 3b. Water clusters formation in allenyl triethylamine salt **148**.

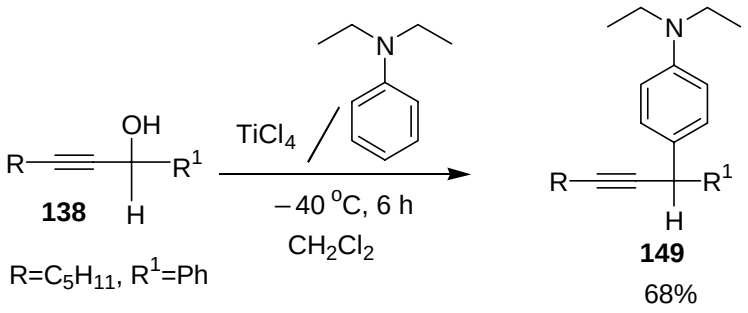
Table 2: X-ray data and structure refinement for triphenylallene ammonium salt 148

Empirical formula	$C_{27}H_{36}ClNO_3$
Formula weight	458.02
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	*P*21/n
Unit cell dimensions	a = 16.2829(9) Å, α = 90˚
	b = 9.8672(5) Å, β = 107.8470(10)˚
	c = 17.0435(9) Å, γ = 90˚
Volume	2606.5(2) Å ^{3}
Z	4
Calculated density	1.167 Mg/m^3
Absorption coefficient	0.173 mm^{-1}
F(000)	984.0
Crystal size	0.48 x 0.40 x 0.22 mm
θ Range for data collection	1.51 to 25.00˚
Limiting indices	$-19 \leq h \leq 19$, $-11 \leq k \leq 11$, $-20 \leq l \leq 20$
Reflections collected/unique	24177 / 4574 [R(int) = 0.0401]
Completeness to θ = 27.47	96.5 %
Refinement method	full-matrix least-square on F^2
Data / restraints / parameters	4574 / 10 / 313
Goodness-of-fit on F^2	1.070
Final *R* indices [I> 2σ (I)]	R_1 =0.0821, wR_2 = 0.2610
R indices (all data)	R_1 = 0.1143, wR_2 = 0.2959
Largest diff. Peak and hole	0.539 and -0.667 eÅ^{-3}

2.2.3 Reaction of propargyl alcohols with aryl amines and $TiCl_4$ reagent system

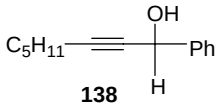
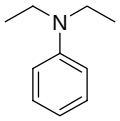
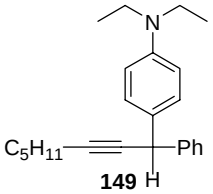
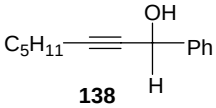
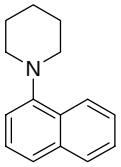
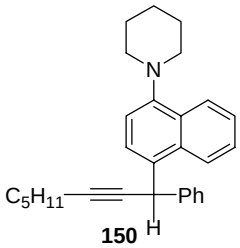
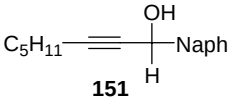
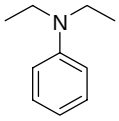
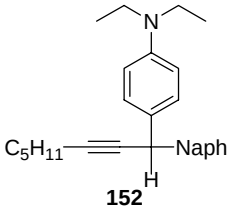
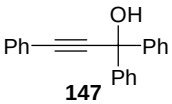
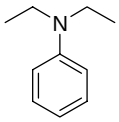
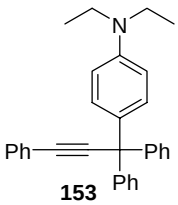
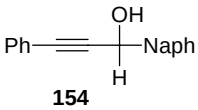
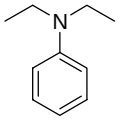
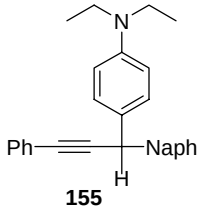
We have also noticed some interesting reactivity pattern in the reaction of propargyl alcohols with $TiCl_4$ using aryl amines at –40 ^oC. For example, the 1-phenyl-2-octyn-1-ol **138** when reacted with *N,N*-diethylaniline and $TiCl_4$ gives the corresponding aryl alkyne **149** in 68% yield (Scheme 48).

Scheme 48



We have then examined the reaction of the propargyl alcohols with different aryl amines using the $TiCl_4$, in DCM at -40 ^oC. The corresponding aryl alkynes were obtained and the yields are in the range of 68-77%. The results are summarized in Table 3. The propargyl alcohol **138** reacts with cyclohexyl napthylamine to give the corresponding arylated alkyne **150** in 71% yield (entry 2). The propargyl alcohols **151, 147** and **154** react with *N,N*-diethyl aniline to give the corresponding aryl alkynes **152, 153** and **155** in 73%, 77% and 73% yields, respectively (entry 3,4, and 5). In all these cases the corresponding benzidines were obtained as minor products (~10%).

Table 3: Arylation of propargyl alcohols using the $TiCl_4/R_2NAr$ reagent system[a]

Entry	Substrate	Aryl amine	Product[b]	Yield (%)[c,d]
1	 **138**		 **149**	68
2	 **138**		 **150**	71
3	 **151**		 **152**	73
4	 **147**		 **153**	77
5	 **154**		 **155**	73

[a]The reagents were used in the following quantities: propargyl alcohol (1 mmol), $TiCl_4$ (1 mmol) and aryl amine (1.5 mmol).

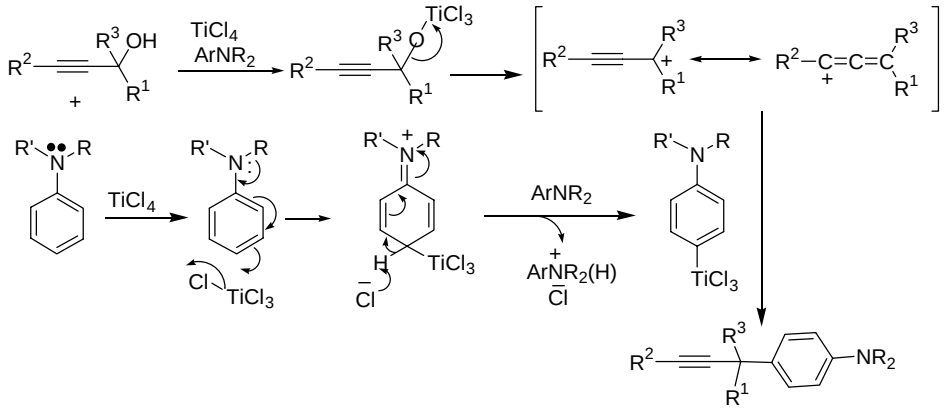
[b]The products were identified by ^{1}H-NMR, ^{13}C-NMR, mass spectral data and elemental analysis.

[c]Yield of isolated products.

[d]The corresponding benzidine was obtained with 10% yield in all cases.

A tentative reaction mechanism can be considered to explain this transformation as shown in the Scheme 49. The initial step would be the formation of the titanium complex of the propargyl alcohol, which could be attacked by the arylamine or aryltitanium derivative to give the arylalkyne product.

Scheme 49

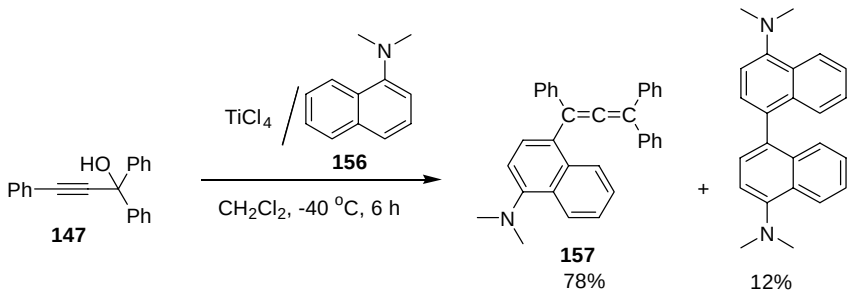


To the best of our knowledge, there is no method available for the synthesis of such α-arylalkyne derivatives. Accordingly, this interesting reactivity uncovered for the $TiCl_4$/tertiaryaryl amine reagent system should be useful for further synthetic exploitations.

2.2.4 Formation of tertiary aryl allene product

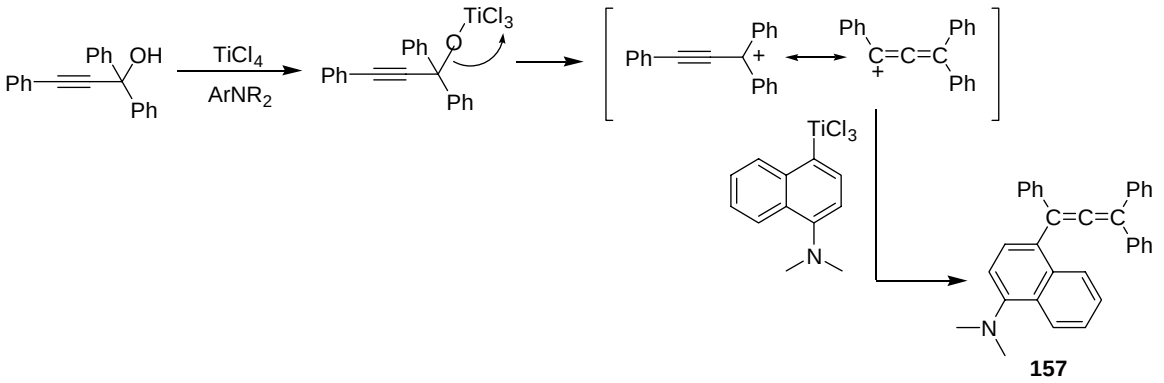
Surprisingly, the reaction of 1,1,3-triphenyl-2-propyne-1-ol **147** with *N,N*-dimethylnapthylamine **156** at –40 ^{o}C gave the tetraarylallene **157** as a major product, besides 12% of the corresponding benzidine derivative (Scheme 50).

Scheme 50



Presumably, in this case the allene is formed as there would be tremendous steric hindrance toward attack on the propargylic cation compared to the attack on the allenic cation that would be formed *in situ* as shown in Scheme 51.

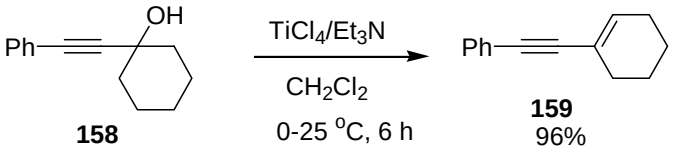
Scheme 51



2.2.5 Reaction of propargyl alcohols prepared from alkyl ketones with the $TiCl_4/Et_3N$ reagent system

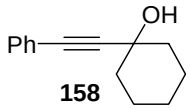
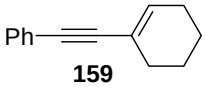
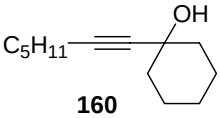
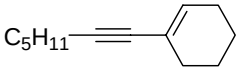
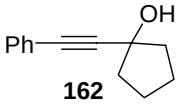
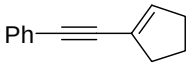
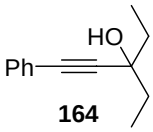
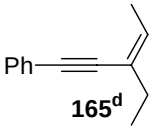
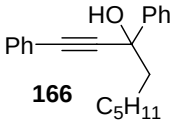
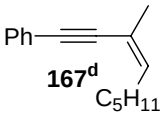
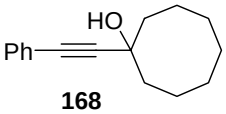
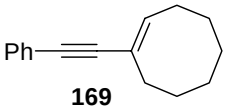
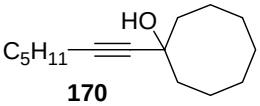
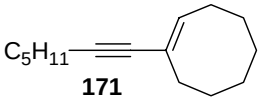
We have also examined the reaction of propargyl alcohols prepared from aliphatic ketones. We have observed that the reaction of 1-(2-phenyl-1-ethynyl)-1-cyclohexanol **158** in the presence of $TiCl_4/Et_3N$ reagent system gave the corresponding 1-(2-phenyl-1-ethynyl)-1-cyclohexene **159** in 96% yield (Scheme 52).

Scheme 52



Different substituted propargyl alcohols were synthesized and the reaction with $TiCl_4/Et_3N$ was examined. The corresponding 1,3-enyne products were isolated. The yields are in the range of 68-96%. The results are summarized in Table 4.

Table 4: Conversion of propargyl alcohols to 1,3-enynes using the $TiCl_4/R_3N$[a]

Entry	Substrate	Amine	Product[b]	Yield (%)[c]
1	 **158**	Et_3N	 **159**	96
2	**158**	Bu_3N	**159**	92
3	**158**	$^iPr_2NEt$	**159**	68
4	 **160**	Et_3N	 **161**	91
5	 **162**	Et_3N	 **163**	87
6	 **164**	Et_3N	 **165**[d]	82
7	 **166**	Et_3N	 **167**[d]	81
8	 **168**	Et_3N	 **169**	71
9	 **170**	Et_3N	 **171**	68

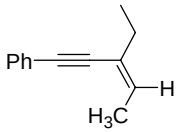
[a]The reagents were used in the following quantities: propargyl alcohol (1 mmol), $TiCl_4$ (1 mmol)and alkyl amines (1.5 mmol).

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

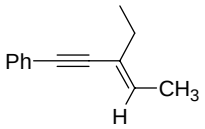
[c]Yield are based on the product isolated.

[d]The ^{1}H-NMR and NOESY (400 MHz) spectral analysis indicate that the products have *E*-stereochemistry.

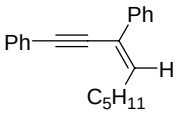
The reaction of propargyl alcohol **158** was examined with different amines. The use of tributylamine gave the enyne **159** in 92% yield and the use of *N,N*-diisopropylethylamine gave 68% yield. When the propargyl alcohol **164** was reacted with the $TiCl_4/Et_3N$ reagent system, the corresponding 1,3-enyne **165** product was obtained in 82% yield (Table 4, entry 7).



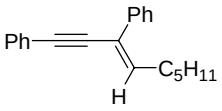
165a



165b



167a

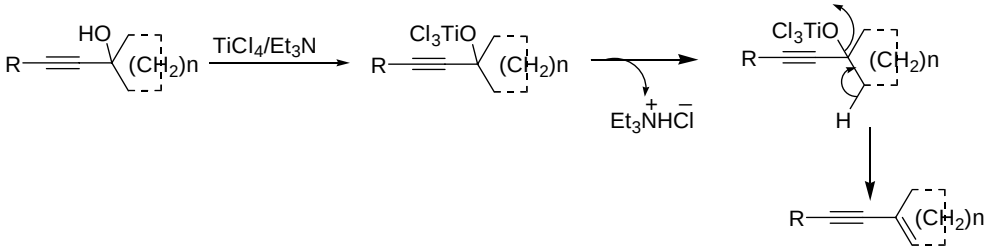


167b

In the case of **164** and **165** the corresponding *E*-isomers **165** and **167**, respectively were formed and the configuration of the isomers was assigned by ^{1}H NMR and NOESY experiments.

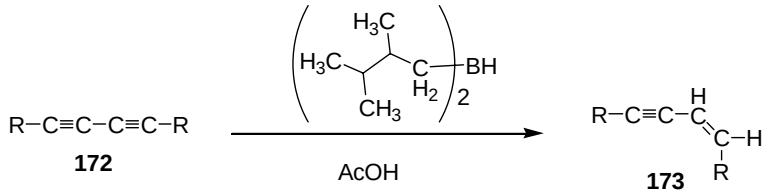
The transformation can be explained by tentative reaction mechanism shown in Scheme 53. The oxytitanium complex produced *in situ* form with propargyl alcohol helps in the elimination to give the 1,3-enyne.

Scheme 53



As mentioned in the introductory section, 1,3-enyne moiety is present in certain pheromones.[4,47] Previously, such enynes **173** were prepared through hydroboration and protonalysis starting from the corresponding 1,3-diynes **172** (Scheme 54).[48]

Scheme 54

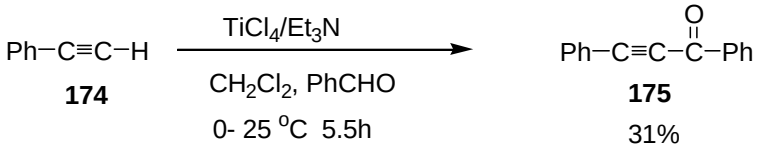


The simple method for the synthesis of 1,3-enynes described here is a good addition for the preparation of 1,3-enyne derivatives.

2.2.6 Reaction of propargyl alcohol with low-valent titanium species

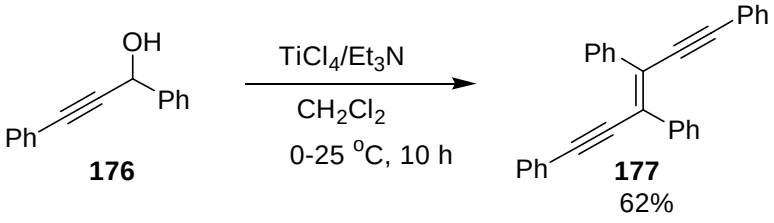
Previously, it was observed in this laboratory that phenyl acetylene **174** reacts with benzaldehyde to give benzoylphenyl acetylene **175** (Scheme 55).[49]

Scheme 55



We have observed that the reaction of propargyl alcohol **176** with the $TiCl_4/Et_3N$ reagent system at 0-25 ^oC gives the product **177** in 62% yield (Scheme 56).

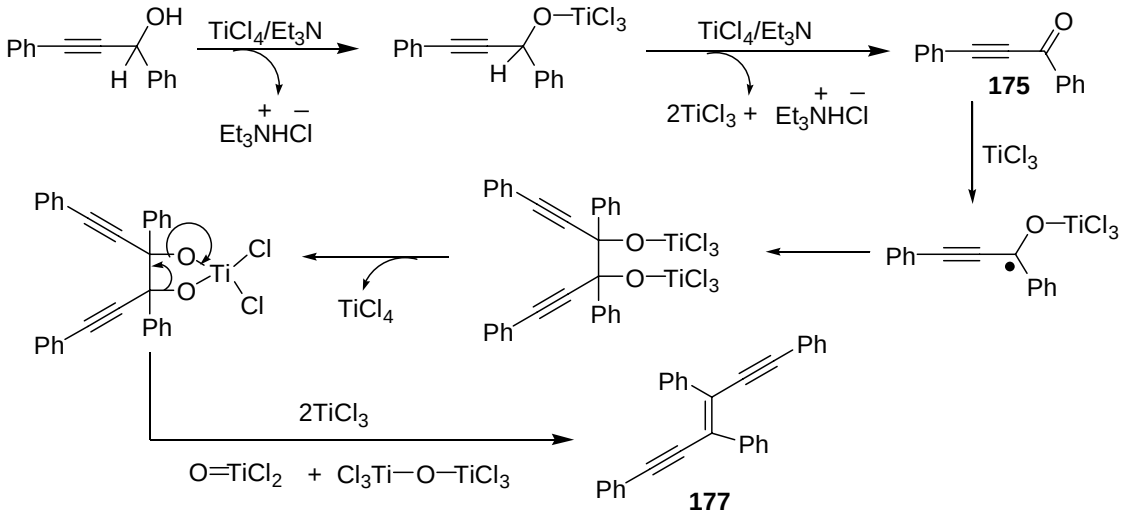
Scheme 56



Presumably, the reaction may go through initial formation of the alkoxy titanium intermediate followed by oxidation by the $TiCl_4/Et_3N$ reagent (Scheme 52, Chapter 1) to

give $TiCl_3$ and the ketone **175** which could then further undergo pinacol coupling followed by elimination similar to the McMurry coupling reaction (Scheme 57).

Scheme 57



The crystal structure data of the enediyne are summarized in Table 5 and Table A3 (Appendix II). The ORTEP diagram of **177** is shown in Figure 4.

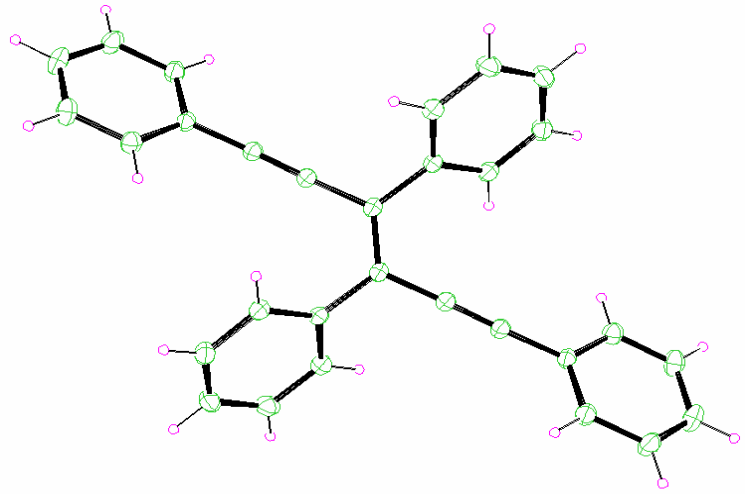


Figure 4: ORTEP diagram of the enediyne 177.

(Thermal ellipsoids are drawn at 20% probability)

Table 5: X-ray data and structure refinement for enediyne 177

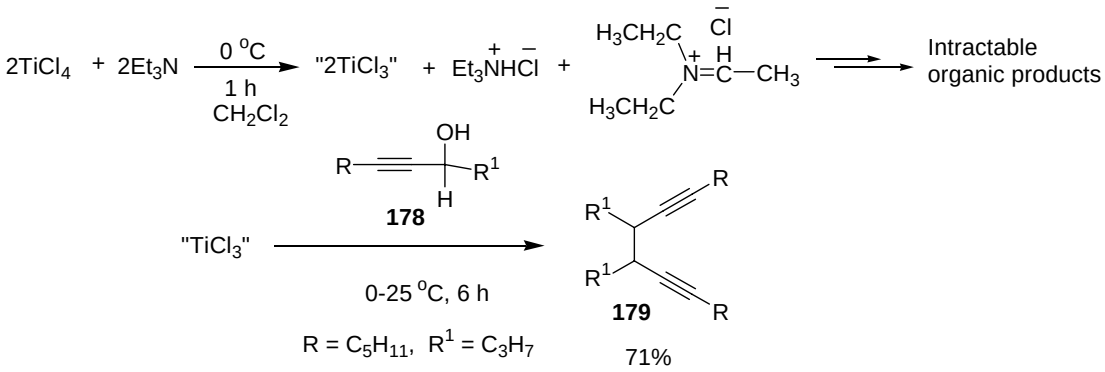
Empirical formula	$C_{30}H_{20}$
Formula weight	380.46
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system	monoclinc
Space group	$P2_1/n$
Unit cell dimensions	a = 9.1453(18) Å, α = 90˚
	b = 9.1141(18) Å, β = 99.15(3)˚
	c = 12.567(3) Å, γ = 90˚
Volume	1034.1(4) Å ^{3}
Z	4
Calculated density	1.222 Mg/m^3
Absorption coefficient	0.069 mm^{-1}
F(000)	400
θ Range for data collection	2.57 to 28.23˚
Limiting indices	$-12 \leq h \leq 11$, $-12 \leq k \leq 12$, $-16 \leq l \leq 16$
Reflections collected/unique	11647 / 2467 [R(int) = 0.0217]
Completeness to θ = 27.47	96.5 %
Refinement method	full-matrix least-square on F^2
Data / restraints / parameters	2467 / 0 / 136
Goodness-of-fit on F^2	1.031
Final *R* indices [I> 2σ (I)]	$R_1 = 0.0458$, $wR_2 = 0.1173$
R indices (all data)	$R_1 = 0.0579$, $wR_2 = 0.1260$
Largest diff. Peak and hole	0.193 and -0.239 $eÅ^{-3}$

The enediynes are an important class of compounds. In recent years, several enediyne derivatives were reported to be useful as DNA cleaving agents.[50] Several procedures were reported for the preparation of enediynes.[51] The synthesis of enediyne described here is a good addition to this pool of procedures.

2.2.7 Reaction of propargyl alcohols with the low valent titanium formed in the reaction of $TiCl_4$ with Et_3N

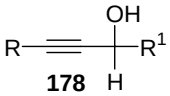
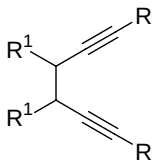
We have also examined the reaction of propargyl alcohols using low valent titanium species produced *in situ* using $TiCl_4$ and R_3N reagents. Accordingly, we have examined the reaction of propargyl alcohol **178** (R = C_5H_{11}, R^1 = C_3H_7) with the low-valent titanium species produced *in situ* and isolated the corresponding diastereomeric mixture of 1,5-diyne **179** in 71% yield (Scheme 58).

Scheme 58



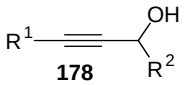
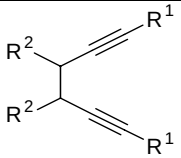
We have examined the reaction of 1-propyl-2-octynyl alcohol **178** using the titanium reagent prepared using various amines like Bu_3N, $^iPr_2NEt$ and Et_3N. The corresponding 1,5-diyne **179** (R^1 = C_5H_{11}, R^2 = C_3H_7) was isolated in 66%, 61% and 71% yields, respectively. Among these amines the Et_3N is found to be the best. The results are summarized in Table 6.

Table 6: **Conversion of propargyl alcohols to symmetrical 1,5-diynes using $TiCl_4/Et_3N$ reagent system**[a]

Entry	Substrate	Reducing agent	Product[b]	Diastereomeric ratio[c]	Yield(%)[d]
1	 **178**	Et_3N	 R = C_5H_{11} R' = C_3H_7 **179**	100:0	71
2	**178**	Bu_3N	R = C_5H_{11} R^1 = C_3H_7 **179**	100:0	66
3	**178**	$^iPr_2NEt$	R = C_5H_{11} R^1 = C_3H_7 **179**	100:0	61
4	R = C_5H_{11} R^1 = ^{i}Bu **180**	Et_3N	R = C_5H_{11}, R^1 = ^{i}Bu **181**	86:14	68
5	R = C_5H_{11}, R^1 = C_7H_{15} **182**	Et_3N	R = C_5H_{11}, R^1 = C_7H_{15} **183**	100:0	69
6	R = C_5H_{11}, R^1 = C_9H_{19} **184**	Et_3N	R = C_5H_{11}, R^1 = C_9H_{19} **185**	100:0	74
7	R = Ph, R^1 = C_4H_9 **186**	Et_3N	R = Ph, R^1 = C_4H_9 **187**	100:0	68
8	R = Ph, R^1 = C_7H_{15} **188**	Et_3N	R = Ph, R^1 = C_7H_{15} **189**	100:0	58
9	R = Ph, R^1 = C_9H_{19} **190**	Et_3N	R = Ph, R^1 = C_9H_{19} **191**	100:0	63
10	R = Ph, R^1 = 1-Naphth **154**	Et_3N	R = Ph, R^1 = 1-Naphth **192**	87:13	61

[a]The reagents were used in the following quantities: $TiCl_4$ (2 mmol), Et_3N (4 mmol) and propargyl alcohol (2 mmol) were used.
[b]Products were identified by IR, ^{1}H-NMR, ^{13}C-NMR, mass spectral data and elemental analysis.
[c]Diastereomeric ratios were estimated by ^{1}H-NMR (400 MHz) data.
[d]Yield are based on the product isolated.

Table 7: Synthesis of symmetrical 1,5-diynes from propargyl alcohols through low valent titanium species generated from $TiCl_4$/Zn reagent system[a]

Entry	Substrate	Product[b]	Diastereomeric ratio[c]	Yield(%)[d]
1	 **178**	 $R^1 = C_5H_{11}$ $R^2 = C_3H_7$ **179**	100:0	63
2	$R^1 = C_5H_{11}$, $R^2 = C_9H_{19}$ **184**	$R^1 = C_5H_{11}$, $R^2 = C_9H_{19}$ **185**	100:0	58
3	R^1 = Ph, $R^2 = C_4H_9$ **186**	R^1 = Ph, $R^2 = C_4H_9$ **187**	100:0	68
4	R^1 = Ph, R^2 = 1-Naph **154**	R^1 = Ph, R^2 = 1-Naph **192**	84:16	71
5	$R^1 = C_5H_{11}$, R^2 = Ph **138**	$R^1 = C_5H_{11}$, R^2 = Ph **193**	87:13	56

[a]The reagents were used in the following quantities; $TiCl_4$ (2 mmol), Zn (4 mmol) and propargyl alcohol (2 mmol) were used.

[b]Products were identified by IR, ^{1}H-NMR, ^{13}C-NMR, mass spectral data and elemental analysis.

[c]Diastereomeric ratios were estimated by ^{1}H-NMR (400 MHz) data.

[d]Yield are based on the product isolated.

We have also examined this transformation using the titanium reagent prepared by reducing $TiCl_4$ with Zn, since this system gives the $TiCl_3$ as major species.[52] The titanium reagent prepared by reducing $TiCl_4$ with Zn reacted with propargyl alcohol 178 to give 1,5-diynes 179 in 63% yields (entry 1, Table 7).

The propargyl alcohol 154 was converted to the corresponding 1,5-diyne 192 in 71% yield (Table 7). Crystallization of the product mixture in the case of the 1,5-diyne 192 from hexane gave crystals suitable for X-ray structure analysis. The crystal data 192 are

summarized in Table 9 and Table A4 (Appendix II). The ORTEP representation of the crystal structure is given in the figure 5.

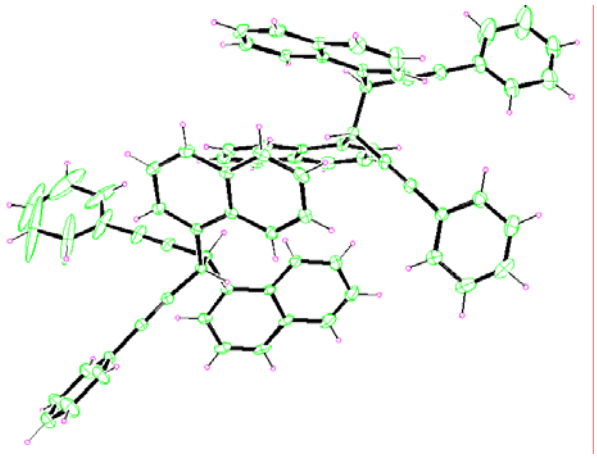


Figure 5: ORTEP diagram of the 1,5-diyne 192.
(Thermal ellipsoids are drawn at 15% probability)

The crystal structure analysis of **192** revealed that the major isomer in this case is *dl*. The chemical shift of the ^{1}H-NMR signals of the CH adjacent to the triple bond for compounds **192**, **193**,**179** and **187** are given in Table 8.

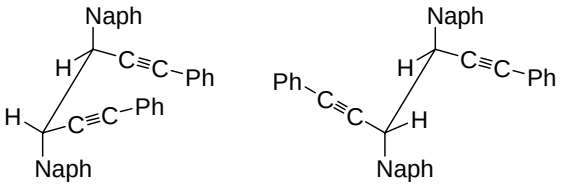
Table 8: 1,5-Diynes ^{1}H NMR signals of the CH adjacent to the triple bond

Compound	Major isomer		Minor isomer	
	%	δ	%	δ
192	87	5.21	13	5.92
193	87	5.64	13	5.23
179	100	4.56	0	-
187	100	4.81	0	-

Table 9: X-ray data and structure refinement for 1,5-diyne 192

Empirical formula	$C_{76}H_{52}$
Formula weight	965.18
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P_1
Unit cell dimensions	a = 10.1221(8) Å, α = 90.8400(10)˚
	b = 14.9303(12) (18) Å, β = 103.840(2)˚
	c = 18.7341(15) (3) Å, γ = 90.520(2)˚
Volume	2748.5(4) $Å^3$
Z	2
Calculated density	1.166 Mg/m^3
Absorption coefficient	0.066 mm^{-1}
F(000)	1016
Crystal size	0.22 x 0.18 x 0.16 mm
θ Range for data collection	1.12 to 22.50˚
Limiting indices	$-10 \le h \le 10$, $-16 \le k \le 16$, $-20 \le l \le 20$
Reflections collected/unique	21406 / 7174 [R(int) = 0.0563]
Completeness to θ = 27.47	100%
Refinement method	full-matrix least-square on F^2
Data / restraints / parameters	7174 / 0 / 685
Goodness-of-fit on F^2	1.003
Final *R* indices [I> 2σ (I)]	$R_1 = 0.0734$, $wR_2 = 0.2016$
R indices (all data)	$R_1 = 0.1437$, $wR_2 = 0.2372$
Largest diff. Peak and hole	0.483 and -0.336 $eÅ^{-3}$

The expected conformations of the *dl* and *meso* **192** are given below.

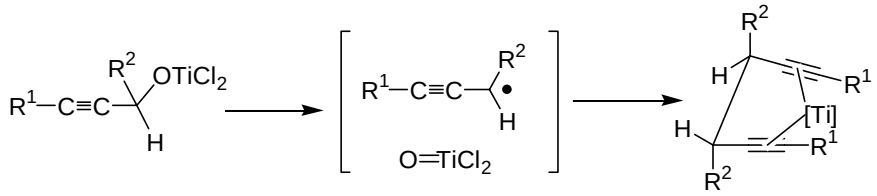


dl-**192**
Major

meso-**192**
Minor

On the basis of only steric ground the *meso* compound is expected to be the more stable. Accordingly, it is surprising that the *dl* isomer was obtained as a major product in the case of **192**. Presumably, the radical species may be still bound to titanium and the *dl* product is expected to be formed to more extent if the 1,5-diyne is formed in a complexed form with titanium species (Scheme 59).

Scheme 59

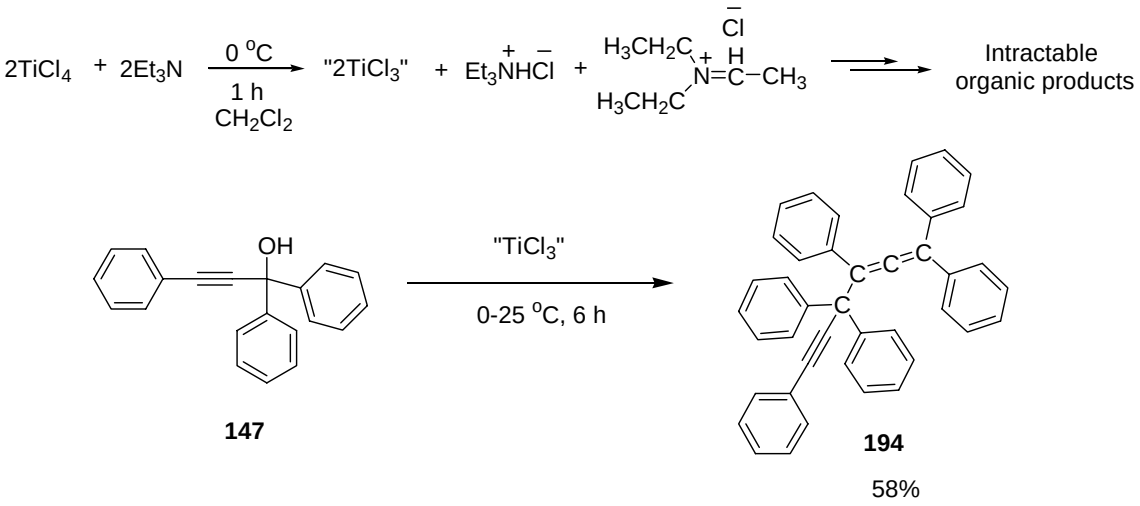


If this is true, then for other 1,5-diynes also the major isomer would be the corresponding *dl* compound. However, this speculation cannot be confirmed on the basis of available data.

2.2.8 Formation of allenynes in the reaction of propargyl alcohols and the $TiCl_4/Et_3N$ reagent system

The reaction of the propargyl alcohol **147** gave the corresponding allenyne **194** under these conditions. It is expected that the reaction goes through the "$TiCl_3$" species formed *in situ* in the reaction of $TiCl_4$ and Et_3N (Scheme 60).

Scheme 60



The crystal structure data of the allenyne **194** are summarized in Table 10 and Table A5 (Appendix II). The ORTEP diagram of **194** is shown in Figure 6.

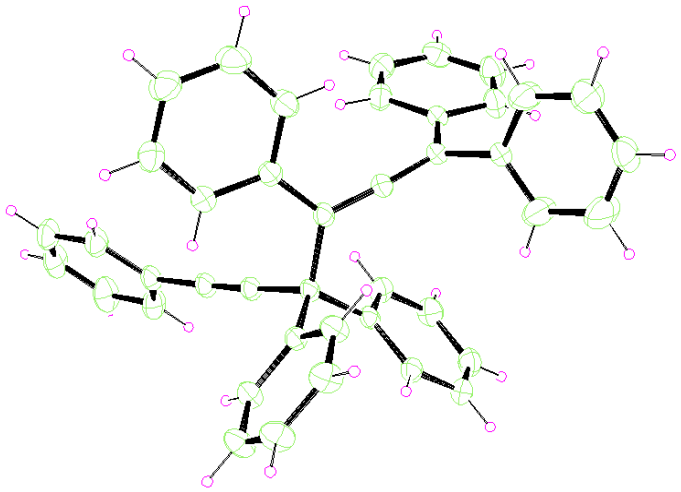


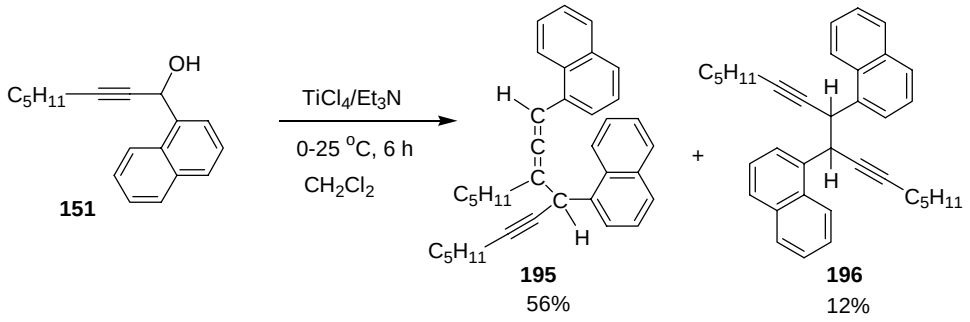
Figure 6: ORTEP diagram of the allenyne 194.
(Thermal ellipsoids are drawn at 20% probability)

Table 10: X-ray data and structure refinement for allenyne 194

Empirical formula	$C_{42}H_{30}$
Formula weight	534.66
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P_1
Unit cell dimensions	a = 9.3743(6) Å, α = 86.6500(10)˚
	b = 10.2376(7)Å, β = 89.4930(10)˚
	c = 16.0252(10)Å, γ = 78.4450(10)˚
Volume	1504.19(17)Å ^{3}
Z	2
Calculated density	1.180 Mg/m^3
Absorption coefficient	0.067 mm^{-1}
F(000)	564
Crystal size	0.24 x 0.22 x 0.18 mm
θ Range for data collection	2.03 to 28.29˚
Limiting indices	$-12 \le h \le 12$, $-13 \le k \le 13$, $-21 \le l \le 21$
Reflections collected/unique	17711 / 7064 [R(int) = 0.0485]
Completeness to θ = 27.47	94.3 %
Refinement method	full-matrix least-square on F^2
Data / restraints / parameters	7064 / 0 / 379
Goodness-of-fit on F^2	1.070
Final *R* indices [I> 2σ (I)]	$R_1 = 0.0564$, $wR_2 = 0.1612$
R indices (all data)	$R_1 = 0.0808$, $wR_2 = 0.1756$
Largest diff. Peak and hole	0.206 and -0.234 eÅ^{-3}

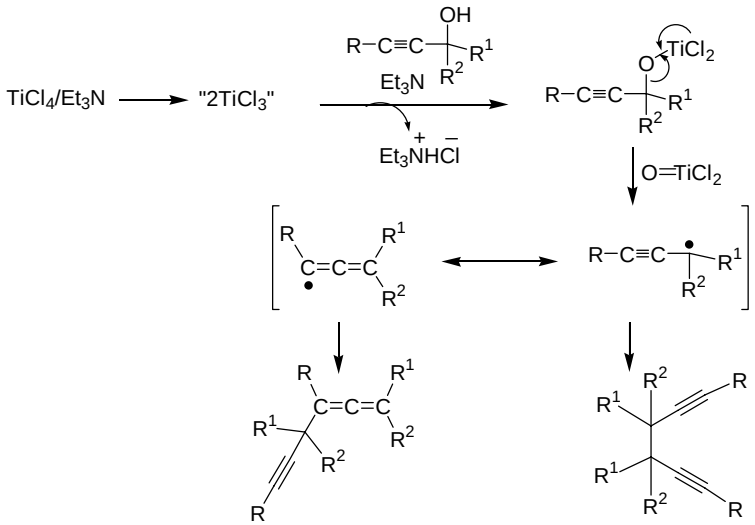
Similar allenyne product **195** was obtained in 56% yield besides the corresponding 1,5-diyne**196** in the reaction of the propargyl alcohol **151** with the $TiCl_4/Et_3N$ reagent system (Scheme 61).

Scheme 61



A tentative mechanism involving the reaction of Ti(III) species with propargyl alcohol followed by homolysis of the carbon-oxygen bond to give $OTiCl_2$ and propargyl radical species may be considered for these transformations. The propargyl radical would then couple to give the 1,5-diyne or allenyne depending on the steric requirements (Scheme 62).

Scheme 62



The 1,5-diynes are important intermediate precursors for the synthesis of biologically active enediynes[53] and other important molecules.[54] Very few methods were reported for the synthesis of 1,5-diynes.[55] Accordingly, the one-pot synthesis of 1,5-diynes described here has considerable synthetic potential.

2. 3 Conclusions

The propargyl alcohols derived from aromatic aldehydes and ketones are converted to the corresponding chloroallenes using the $TiCl_4/Et_3N$ reagent system and the reactions using $TiCl_4$/aryltertiaryamines gave the corresponding arylated alkynes. The propargyl alcohols derived from aliphatic ketones are converted to the corresponding 1,3-enynes using the $TiCl_4/Et_3N$ reagent system. Low-valent titanium reagents prepared using $TiCl_4/Et_3N$ or $TiCl_4$/Zn react with propargyl alcohols to give the corresponding symmetrical 1,5-diynes or allenyne.

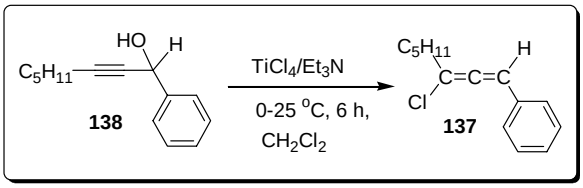
2.4 Experimental section

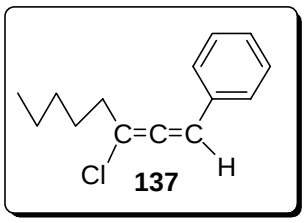
2.4.1 General Information

Several informations given in the section 1.4 are also applicable to the experiments outlined in this section. Cyclopentanone, 3-pentanone, cycloctanone, butyraldehyde, iso-valeraldehyde, heptaldehyde, decyl aldehyde were supplied by E-Merck, India, *N,N*-Diethylaniline supplied by Lancaster Synthesis, Ltd., England were used as purchased.

2.4.2 Typical procedure for the preparation of chloroallenes from propargyl alcohols using the $TiCl_4/Et_3N$ reagent system

In dichloromethane (35 mL), 1-phenyl-2-octyn-1-ol **138** (0.20 g, 1 mmol), $TiCl_4$ (0.19 g, 0.1 mL, 1 mmol) and Et_3N (0.15 g, 0.21 mL, 1.5 mmol) were taken at 0 ^oC under N_2. The reaction mixture was stirred for 6 h at 0-25 ^oC. Saturated NH_4Cl solution (20 mL) was added and stirred for 10 min. The organic layer was separated and the aqueous layer was extracted with dichloromethane (2 X 15 mL). The combined organic extract 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 with pure hexane. The chloroallene **137** was isolated 56% yield.





Yield 0.12 g (56%)

IR (Neat) (cm^{-1}) 2957, 2930, 1936, 1658, 1597, 1493

^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm): 0.95 (t, 3H, *J* = 6.8 Hz), 1.67-1.38 (m, 6H), 2.53 (t, 2H, *J* = 6.8 Hz), 6.48 (s, 1H), 7.5-7.2 (m, 5H) **(Spectrum No. 11)**

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 14.0, 22.3, 26.8, 30.9, 36.5, 101.7, 108.8, 127.7, 128.1, 128.7, 133.3, 200.4 **(Spectrum No. 12)**

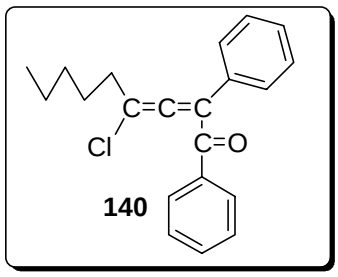
MS (EI) *m/z* 220 (M^+) **(Spectrum No. 13)**

Analysis Calculated for $C_{14}H_{17}Cl$: C, 76.18%; H, 7.76%

Found: C, 76.21%; H, 7.78%

The same procedure was followed for other ketones. The data of the chloro allenes are given below.

Chloro allene 140



Yield 0.17 g (54%)

IR (Neat) (cm^{-1}) 2951, 2932, 1939, 1655, 1591, 1499, 1441, 1272, 1176

^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm): 0.85 (t, 3H, *J* = 7.2 Hz), 1.43-1.24 (m, 6H), 2.21 (t, 2H, *J* = 5.6 Hz), 8.11-7.25 (m, 10H) **(Spectrum No. 14)**

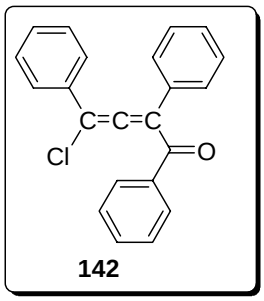
^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 13.9, 22.3, 28.6, 31.2, 97.3, 108.9,128.0,128.1, 128.4, 129.4, 132.5, 133.9, 138.0, 194.1, 211.1 **(Spectrum No. 15)**

MS (EI) *m/z* 324 (M^+)

Analysis Calculated for $C_{21}H_{21}ClO$: C, 77.29%; H, 6.16%

Found: C, 77.30%; H, 6.18%

Chloro allene 142



142

Yield 0.19 g (58%)

IR (Neat) (cm^{-1}) 2974, 1963, 1597, 1491, 1446, 1263

^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm): 7.82-7.21 (m, 15H)

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 100.6, 112.3, 127.5, 128, 128.1, 128.3,128.7, 129, 129.4, 129.9, 132.1, 132.9, 133.1, 138, 192.8, 212.4 **(Spectrum No. 16)**

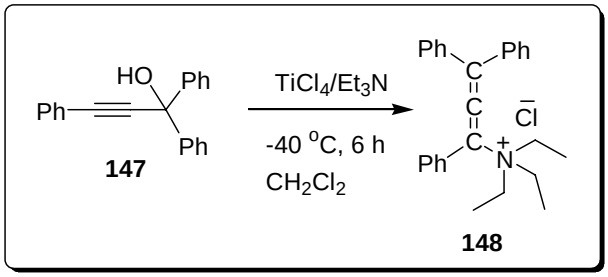
MS (EI) *m/z* 330 (M^+)

Analysis Calculated for $C_{22}H_{15}ClO$: C, 79.88%; H, 4.57%

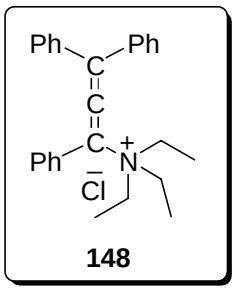
Found: C, 77.93%; H, 4.56%

2.4.3 Typical procedure for the preparation of triethylamine salt of triphenylallene with $TiCl_4/Et_3N$ reagent system

In dichloromethane (35 mL), 1,1,3-triphenyl-2-propyn-1-ol **147**, (0.28 g, 1 mmol), $TiCl_4$ (0.19 g, 0.1 mL, 1 mmol) and Et_3N (0.3 g, 0.42 mL, 3 mmol) were taken at –40 ^{o}C under N_2. The reaction mixture was stirred for 6 h at - 40 ^{o}C. Water (10 mL) was added to the reaction mixture. The organic layer was separated and the aqueous layer was extracted with dichloromethane (2 X 15 mL). The solvent was removed and the colorless solid was recrystallized from ethyl acetate to obtain the triphenyl allene triethylamine salt **148** in 68% yield.



Yield 0.27 g (68%)



IR (KBr) (cm^{-1}) 3393, 1946, 1651, 1454, 1001

^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm): 1.48 (t, 9H, *J* = 6.8 Hz), 3.75-3.7 (q, 6H, *J* = 6.8 Hz), 7.56-7.29 (m, 15H) **(Spectrum No. 17)**

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 8.78,53.14, 115.1, 121.6, 126.1, 127.4, 128.2, 128.6, 129.2, 129.7, 130.1, 131.2, 133.4, 201.1 **(Spectrum No. 18)**

MS (EI) *m/z* 403 (M^+)

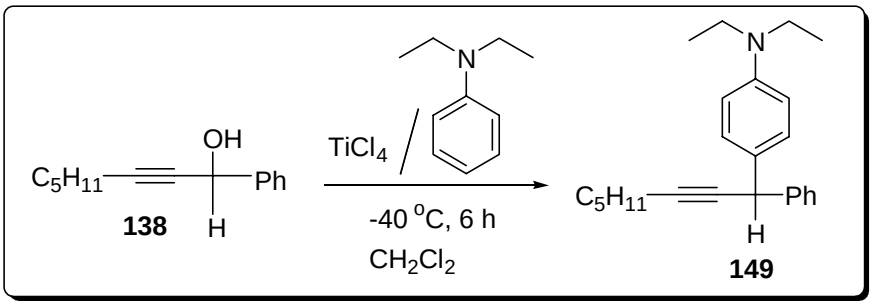
Analysis Calculated for $C_{27}H_{30}ClN$: C, 80.27%; H, 7.48%; N, 3.47%

Found: C, 80.31%; H, 7.25%; N, 3.56%

2.4.4 Typical procedure for the preparation of aryl alkynes with $TiCl_4$/arylamine reagent system

In dichloromethane (35 mL), 1-phenyl-2-octyn-1-ol **138** (0.20 g, 1 mmol), $TiCl_4$ (0.19 g, 0.1 mL, 1 mmol) and *N*,*N*-diethylaniline (0.3 g, 0.32 mL, 2 mmol) were taken at –40 °C under N_2. The reaction mixture was stirred for 6 h at -40 °C. 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 dichloromethane (2 X 15 mL). The combined organic extract was washed with brine solution (10 mL) and dried over

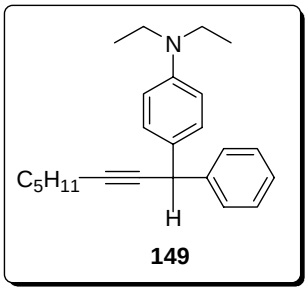
anhydrous Na_2SO_4. The solvent was removed residue was chromatographed on a silica gel column with ethyl acetate/hexane (2:98) mixture. The aryl alkyne **149** was isolated in 68% yield.



Yield 0.26 g (68%)

IR (Neat) (cm^{-1}) 3412, 3067, 2069, 1634

^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm): 0.92 (t, 3H, *J* =7.2 Hz), 1.41 (t, 6H, *J* = 7.3 Hz), 1.48-1.56 (6H), 3.12-3.32 (2H), 2.2-2.24 (4H), 4.48 (s, 1H), 7.13-7.39 (m, 9H) **(Spectrum No. 19)**



^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 12.5, 14.0, 18.9, 22.2, 28.7, 30.9, 42.2, 44.3, 84.4, 96.0, 111.8, 123.3, 126.3, 128.0, 129.1, 133.2, 143.3, 146.5 **(Spectrum No. 20)**

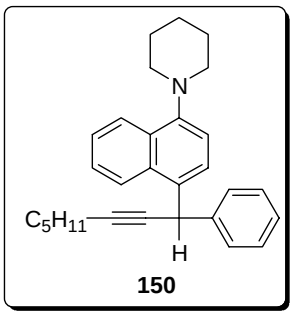
MS (EI) *m/z* 333 (M^+) **(Spectrum No. 21)**

Analysis Calculated for $C_{24}H_{31}N$: C, 86.43%; H, 9.37%; N, 4.27%

Found: C, 86.45%; H, 9.39%; N, 4.25%

The same procedure was followed for other aryl amines and propargyl alcohols. The data of the aryl alkyne products are given below.

Aryl alkyne 150



150

Yield 0.28 g (71%)

IR (Neat) (cm^{-1}) 3450, 2930, 2858, 2057, 1583, 1450

^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm): 0.93 (t, *J* = 7.1 Hz, 3H), 1.46-1.33 (m, 6H), 1.57 (t, *J* = 7.1 Hz, 2H), 1.88 (m, 6H), 2.3 (t, *J* =6.3 Hz, 4H), 5.66 (s, 1H), 7.56-7.07 (m, 9H), 8.1 (d, *J* =8.1 Hz, 1H), 8.31 (d, *J* = 7.9 Hz, 1H) **(Spectrum No. 22)**

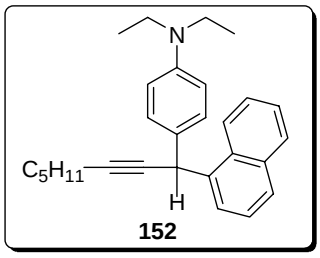
^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): ^{13}C-NMR: 14, 19, 22.2, 24.6, 26.6, 28.7, 31.1, 40.1, 54.7, 81, 85.3, 114.2, 123.8, 124.4, 124.7, 124.8, 125.2, 125.9, 126.5, 128, 128.3, 129.6, 132.1, 142.1, 150.5 **(Spectrum No. 23)**

MS (EI) *m/z* 395 (M^+) **(Spectrum No. 24)**

Analysis Calculated for $C_{29}H_{33}N$: C, 88.05%; H, 8.41%; N, 3.54%

Found: C, 88.11%; H, 8.44%; N, 3.54%

Aryl alkyne 152



152

Yield 0.28 g (73%)

IR (Neat) (cm^{-1}) 3403, 3051, 2071, 1641, 779

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm) 0.94 (t, 3H, *J* = 7.8 Hz), 1.18 (t, 6H, *J* = 7.8 Hz), 1.62-1.33 (m, 6H), 2.32-2.29 (t, 2H, *J* = 6.8 Hz), 3.36-3.31 (q, 4H, *J* = 6.9 Hz), 5.67 (s, 1H), 6.55 (d, 2H, *J* = 7.8 Hz), 8.22-7.26 (m, 8H), 8.23 (d, 1H, *J* = 4.3 Hz)

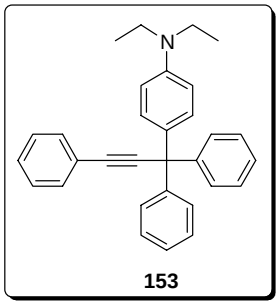
^{13}C-NMR: (100 MHz, $CDCl_3$, δ ppm): 12.6, 14, 19, 22.2, 28.7, 31.2, 39.3, 44.3, 81.5, 84.7, 112.4, 124.5, 125.5, 125.8, 126.2, 127.5, 128.6, 128.8, 129.3, 131.2, 134.1, 138.5, 146.5 **(Spectrum No. 25)**

MS (EI) *m/z* 383 (M^+) **(Spectrum No. 26)**

Analysis Calculated for $C_{28}H_{33}N$: C, 87.67%, H, 8.41%, N, 3.65%

Found: C, 87.59%, H, 8.65%, N, 3.70%

Aryl alkyne 153



153

Yield 0.32 g (77%)

IR (KBr) (cm^{-1}) 2970, 2928, 2032, 1657, 1608, 1516

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 1.22 (t, 6H, *J* = 5.8), 3.42-3.4 (q, 4H, *J* = 5.8 Hz), 6.67 (d, 2H, *J* = 7.1 Hz), 7.58-7.18 (m, 17H) **(Spectrum No. 27)**

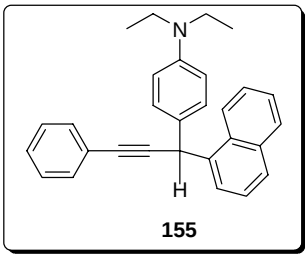
^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 12.7, 44.3, 55.2, 84.5, 96.4, 111, 124, 126.5, 127.8, 127.9, 128.2, 129.2, 130, 131.6, 131.8, 146.5, 146.2 **(Spectrum No. 28)**

MS (EI) *m/z* 415 (M^+) **(Spectrum No. 29)**

Analysis Calculated for $C_{31}H_{29}N$: C, 89.60%;H, 7.03%; N, 3.07%

Found: C, 89.57%; H,6.99%; N, 3.04%

Aryl alkyne 155



155

Yield 0.29 g (73%)

IR (KBr) (cm^{-1}) 2978, 2097, 1598, 1506, 1375, 1197

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 1.01 (t, 6H, *J* = 6.8 Hz,), 3.19 (q, 4H, *J* = 6.8 Hz), 5.75 (s, 1H), 6.52 (d, 2H, *J* = 8.8 Hz), 7.30-7.14 (m, 13H), 8.13 (d, 1H, *J* = 1.6 Hz)

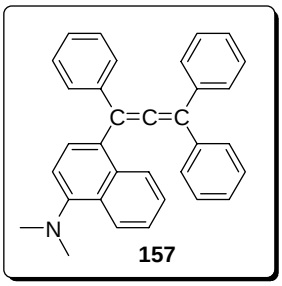
^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 10.9, 38.0, 42.6, 82.7, 89.6, 110.1, 122.1, 122.6, 123.7, 123.8, 124.2, 124.6, 125.8, 126, 126.1, 126.4, 127, 127.1, 129.4, 129.9, 132.4, 136, 144.9 **(Spectrum No. 30)**

MS (EI) *m/z* 389 (M^+) **(Spectrum No. 31)**

Analysis Calculated for $C_{29}H_{27}N$: C, 89.42%; H, 6.99%; N, 3.60%

Found: C, 89.47%; H, 6.99%; N, 3.62%

Aryl allene 157



157

Yield 0.34 g (78%)

IR (KBr) (cm^{-1}) 3429, 2930, 1968, 1574, 1489, 1442, 1386, 1051

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 2.81 (s, 6H), 7.40-7.01 (m,17H), 7.79 (d, 2H, *J* = 8.4 Hz), 8.19 (d, 2H, *J* = 8.8 Hz)

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 45.3, 110, 112.1, 113.8, 124.4, 125.1, 125.8, 126.9, 127, 127.1, 127.4, 127.6, 128.1, 128.3, 128.6, 129.1, 129.3, 133.8, 136.9, 151, 208.1 **(Spectrum No. 32)**

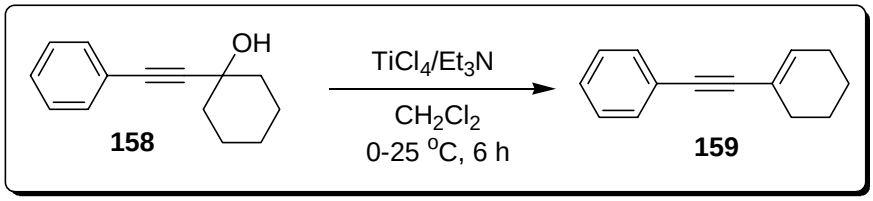
MS (EI) *m/z* 437 (M^+)

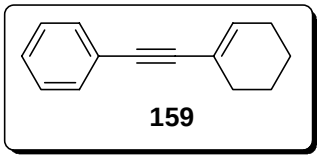
Analysis Calculated for $C_{33}H_{27}N$: C, 90.58%, H, 6.22%, N, 3.20%

Found: C, 90.63%, H, 6.20%, N, 3.24%

2.4.5 Typical procedure for the preparation of 1,3-enynes with $TiCl_4/Et_3N$ reagent system

In dichloromethane (35 mL), 1-(2-phenyl-1-ethynyl)-1-cyclohexanol **158**, (0.2 g, 1 mmol), $TiCl_4$ (0.19 g, 0.1 mL, 1 mmol) and Et_3N (0.2 g, 0.28 mL, 2 mmol) were taken at 0 ^oC under N_2. The reaction mixture was stirred for 6 h at 0-25 ^oC. It was quenched with saturated NH_4Cl solution (10 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2 X 15 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 using hexane as eluent. The 1,3-enyne **159** was isolated in 96% yield.





Yield 0.17 g (96%)

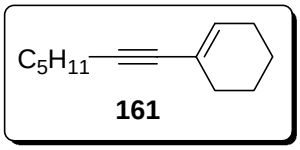
IR (Neat) (cm^{-1}) 2930, 2858, 2202, 1595, 1489, 1440

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): Lit[56] 1.65-1.74 (6H), 2.17-2.29 (2H), 6.26-6.28 (m, 1H), 7.28-7.49 (m, 5H) **(Spectrum No. 33)**

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 21.5, 22.4, 25.8, 29.2, 86.8, 91.3, 120.7, 123.8, 127.7, 128.5, 131.4, 135.1 **(Spectrum No. 34)**

The same procedure was followed for other propargyl alcohols. The data are given below.

1,3-Enyne 161



Yield 0.16 g (91%)

IR (Neat) (cm^{-1}) 2932, 2858, 2216, 1678, 1458, 1346

^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm): 0.83-0.90 (5H), 1.19-1.33 (m, 4H), 1.46-1.54 (m, 4H), 1.80-2.08 (m, 4H), 2.17-2.28 (m, 2H), 5.85-6.00 (m, 1H) **(Spectrum No. 35)**

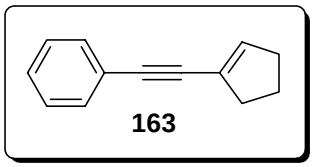
^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 13.9, 19.2, 21.6, 21.9, 22.1, 25.5, 29.4, 29.6, 31.0, 82.2, 87.2, 121.1, 132.8; MS (EI) m/z 176 **(Spectrum No. 36)**

MS (EI) *m/z* 176 (M^+)

Analysis Calculated for $C_{13}H_{20}$: C, 88.57%; H, 11.43%

Found: C, 88.60%; H, 11.47%

1,3-Enyne 163



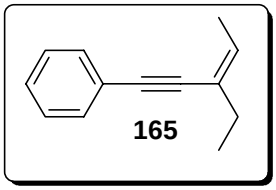
Yield 0.15 g (87%)

IR (Neat) (cm^{-1}) 2931, 2212, 1459, 1345

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): Lit[57] 1.95-2.06 (4H), 2.47-2.59 (m, 2H), 6.16-6.17 (m, 1H), 7.28-7.60 (m, 5H) **(Spectrum No. 37)**

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 23.3, 33.4, 36.5, 86.8, 90.4, 123.6, 124.6, 128.5, 128.6, 130.1, 138.2 **(Spectrum No. 38)**

1,3-Enyne 165



Yield 0.14 g (82%)

IR (Neat) (cm^{-1}) 2968, 2932, 2199, 1489, 1440, 1358, 1068

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm) 1.12-1.46 (m, 3H), 1.92-1.97 (m, 3H), 2.21-2.32 (2H), 5.70-5.84 (m, 1H), 7.28-7.54 (m, 5H) **(Spectrum No. 39)**

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 13.4, 16.1, 29.7, 30.3, 88.1, 94.1, 124.0, 125.6, 127.9, 128.3, 131.1, 131.5; MS (EI) m/z 170 **(Spectrum No. 40)**

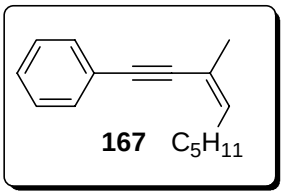
We have recorded the proton-proton correlation spectrum (NOESY) to identify the stereochemistry of the compound **165**. **(NOESY Spectrum No. 41)**

MS (EI) *m/z* 170 (M^+)

Analysis Calculated for $C_{13}H_{14}$: C, 91.71%; H, 8.29%

Found: C, 91.78%; H, 8.34%

1,3-Enyne 167



Yield 0.17 g (81%)

IR (Neat) (cm^{-1}) 2961, 2927, 2189, 1492, 1447

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 0.84 (t, 3H, *J* = 7.8 Hz), 1.21-1.25 (4H), 1.37-1.43 (2H), 1.89 (t, 3H, *J* = 7.6 Hz), 2.1-2.16 (m, 2H), 5.05 (1H), 7.27-7.34 (m, 5H)

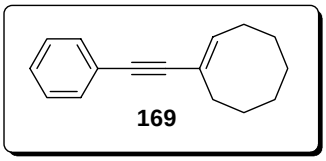
^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 11.5, 20.0. 20.1, 26.3, 27.6, 28.2, 86.5, 90.0, 118.4, 125.5, 125.7, 128.8, 129.0, 136.8

MS (EI) *m/z* 212 (M^+)

Analysis Calculated for $C_{16}H_{20}$: C, 90.51%; H, 9.49%

Found: C, 910.59%; H, 9.518%

1,3-Enyne 169



Yield 0.15 g (71%)

IR (Neat) (cm^{-1}) 2926, 2852, 2200, 1489, 1307

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm) 1.46-1.50 (6H), 1.61-1.65 (m, 2H), 2.18-2.20 (m, 2H), 2.38 (t, 2H, *J* = 6.4 Hz), 6.18 (t, 1H, *J* = 8.4 Hz), 7.21-7.29 (m, 3H), 7.39-7.44 (m, 2H) **(Spectrum No. 42)**

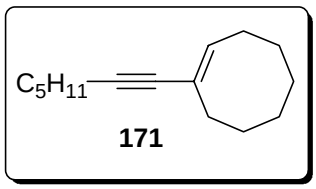
^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 25,9, 26.4, 27.1, 28.5, 29.7, 30.1, 86.4, 92.1, 122.5, 122.7, 123.9, 124.0, 132.4, 137.8 **(Spectrum No. 43)**

MS (EI) *m/z* 210 (M^+)

Analysis Calculated for $C_{16}H_{18}$: C, 91.37%; H, 8.63%

Found: C, 91.39%; H, 8.64%

1,3-Enyne 171



171

Yield 0.14 g (68%)

IR (Neat) (cm^{-1}) 2930, 2858, 2210, 1716, 1680, 1466, 1265, 1022

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm) 0.87-0.95 (5H), 1.41-1.18 (2H), 1.35-1.38 (2H), 1.39-1.70 (m, 10H), 2.42-2.50 (2H), 3.32-3.37 (2H), 6.67-6.69 (m, 1H)

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 13.8, 18.6, 22.1, 25.2, 25.9,26.1, 26.4, 27.2, 28.2, 30.8, 30.9, 79.7, 83.5, 132.7, 136.2

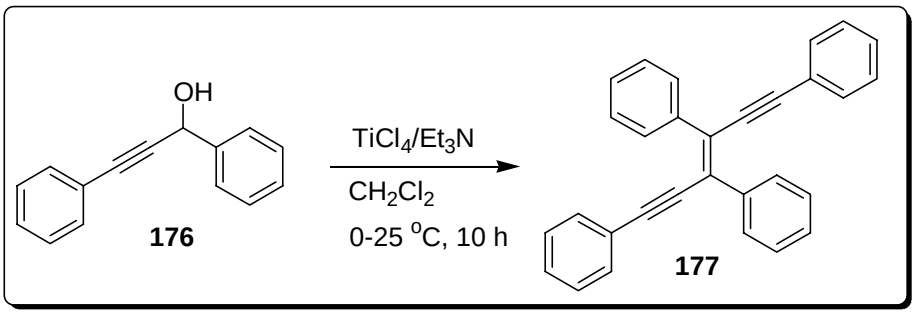
MS (EI) *m/z* 204 (M^+)

Analysis Calculated for $C_{15}H_{24}$: C, 88.16%; H, 11.84%

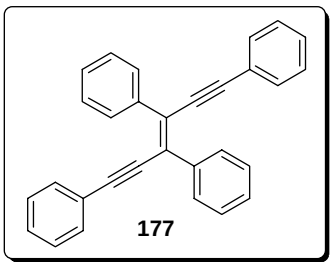
Found: C, 88.17%; H, 11.86%

2.4.6 Procedure for the preparation of enediyne with the $TiCl_4/Et_3N$ reagent system

In dichloromethane (35 mL), $TiCl_4$ (0.38 g, 0.22 mL, 2 mmol) and Et_3N (0.3 g, 0.42 mL, 3 mmol) were taken at 0 ^oC under N_2. To this 1,3-diphenyl-2-propyn-1-ol **176** (0.42 g, 2 mmol) was added and allow to stir for 10 h at 25 ^oC. Saturated NH_4Cl solution (10 mL) was added and stirred for 10 min. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2 X 15 mL). The combined organic extract was washed with brine solution (5 mL) and dried over anhydrous Na_2SO_4. The solvent was removed and the residue was chromatographed on a silica gel column using hexane. The enediyne **177** was isolated in 62% yield.



Yield 0.24 g (62%)



IR (KBr) (cm^{-1}) 2961, 2219, 1379, 1205

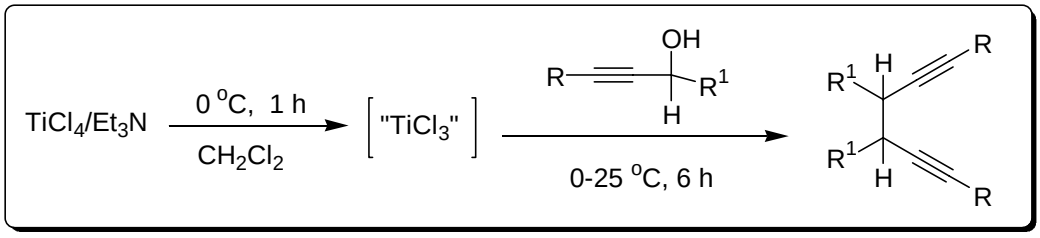
^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 7.21-7.48 (m, 20H)

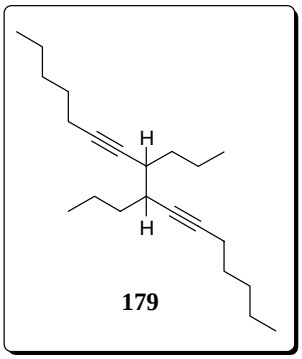
^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 139.14, 131.44. 129.29, 128.71, 128.47, 128.32, 127.88, 123.33, 98.68, 90.99 Lit[58]

MS(EI) *m/z* 380 (M^+)

2.4.7 Typical procedure for the preparation of 1,5-diynes using the $TiCl_4/Et_3N$ reagent system

In dichloromethane (35 mL), $TiCl_4$ (0.38 g, 0.2 mL, 2 mmol) and Et_3N (0.3 g, 0.42 mL, 3 mmol) were taken at 0 ^oC under N_2. The reaction mixture was stirred for 1h at 0 ^oC. To this 1-propyl-2-octynyl alcohol **178** (0.34 g, 2mmol) was added and stirred for another 6 h at 25 ^oC. Saturated NH_4Cl solution (10 mL) was added and stirred for 10 min. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2 X 15 mL). The combined organic extract was washed with brine solution (5 mL) and dried over anhydrous Na_2SO_4. The solvent was removed and the residue was chromatographed on a silica gel column using hexane as eluent to isolate the 1,5-diyne **179** [Yield 0.22g, (71%)].





179

Yield 0.22 g (71%)

dr 100:0

IR (Neat) (cm^{-1}) 2961, 2930, 2235, 1460, 1379, 1205

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 0.89-0.97 (m, 12H), 1.21-1.36 (8H), 1.50-1.57 (8H), 1.88-1.92 (4H), 2.21-2.24 (4H), 4.54-4.58 (m, 2H) **(Spectrum No. 44)**

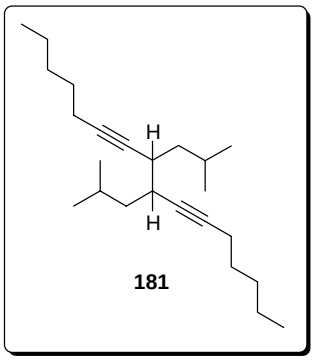
^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 13.3, 13.9, 18.7, 19.5, 22.1, 28.1, 31.0, 41.6, 49.4, 78.7, 87.2 **(Spectrum No. 45)**

MS (EI) *m/z* 302 (M^+)

Analysis Calculated for $C_{22}H_{38}$: C, 87.34%; H, 12.66%

Found: C, 87.37%; H, 12.63%

The same procedure was followed with other propargyl alcohols. The data are given below.



181

1,5-Diynes 181

Yield 0.22 g (68%)

dr 86:14

IR (Neat) (cm^{-1}) 2959, 2872, 2237, 1467, 1369, 1255

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm) 0.82-1.00 (14H), 1.29-1.42 (10H), 1,48-1.61 (4H), 1.78-1.85 (4H), 1.78-1.85 (4H), 2.17-2.24 (4H), 4.54-4.57 (2H) **(Spectrum No. 46)**

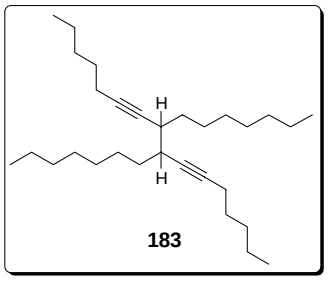
^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 13.4, 18.7, 21.9, 22.3, 25.7, 28.1, 30.8, 48.2, 48.6, 87.2, 98.5 **(Spectrum No. 47)**

MS (EI) *m/z* 331 (M+1)

Analysis Calculated for $C_{24}H_{42}$: C, 87.19%; H, 12.81%

Found: C, 87.17%; H, 12.83%

1,5-Diyne 183



183

Yield 0.28 g (69%)

dr 100:0

IR (Neat) (cm^{-1}) 2928, 2233, 1458, 1377, 1107

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 1.88-1.67 (m,

12H), 1.23-1.32 (m, 24H), 1.43-1.49 (8H), 1.81-1.86 (4H), 2.14-1.18 (4H), 4.45-4.49 (2H) **(Spectrum No. 48)**

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 14.1, 18.7, 22.6, 26.2, 28.1, 28.8, 29.1, 29.4, 31.0, 31.6, 31.9, 39.7, 49.7, 78.7, 87.3 **(Spectrum No. 49)**

MS (EI) *m/z* 414 (M^+)

Analysis Calculated for $C_{30}H_{54}$: C, 86.88%; H, 13.12%

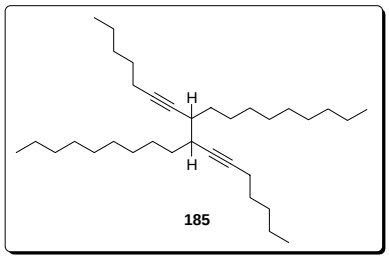
Found: C, 86.81%; H, 13.19%

1,5-Diyne 185

Yield 0.35 g (74%)

dr 100:0

IR (Neat) (cm^{-1}) 2931, 2228, 1461, 1367.



^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm) 1.67-1.88 (m, 12H), 1.23-1.32 (m, 24H), 1.43-1.49 (m, 8H), 1.81-1.86 (m, 8H), 2.14-2.18 (m, 8H), 4.45-4.49 (2H)

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 14.1, 18.7, 22.2, 22.6, 24.5, 25.7, 26.2, 28.1, 28.8, 29.1, 31.0, 31.6, 31.9, 39.7, 49.7, 78.7, 87.3

MS (EI) *m/z* 470 (M^+)

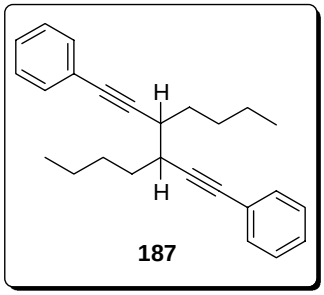
Analysis Calculated for $C_{34}H_{62}$: C, 86.73%; H, 13.27%

Found: C, 86.71%; H, 13.29%

1,5-Diyne 187

Yield 0.23 g (68%)

dr 100:0



187

IR (Neat) (cm^{-1}) 2931, 2212, 1462

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm) 1.02 (t, 6H, *J* = 7 Hz), 1.40-1.47 (m, 4H), 1.59-1.66 (m, 4H), 2.06-2.12 (m, 4H), 4.82 (t, 2H, *J* = 6.4 Hz), 7.34-7.50 (m, 10H) **(Spectrum No. 50)**

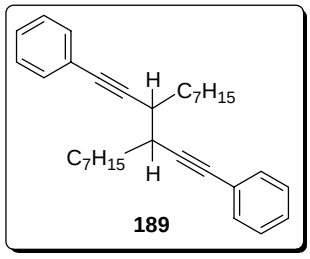
^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 13.9, 22.0, 28.4, 39.1, 49.3, 86.0, 87.5, 122.2, 128.3, 128.7, 131.8 **(Spectrum No. 51)**

MS (EI) *m/z* 343 (M+1) **(Spectrum No. 52)**

Analysis Calculated for $C_{26}H_{30}$: C, 91.17%; H, 8.83%

Found: C, 91.21%; H, 8.79%

1,5-Diyne 189



189

Yield 0.25 g (58%)

dr 100:0

IR (Neat) (cm^{-1}) 2926, 2207, 1464.

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 0.85 (t, *J* =7.1 Hz 6H), 1.22-1.51 (m, 10H), 1.62-1.73 (m, 4H), 1.18-1.46 (m, 6H) 2.06-2.15 (m, 4H), 4.84 (t, 2H, *J* = 7.0 Hz), 7.10-7.21 (m, 10H) **(Spectrum No. 53)**

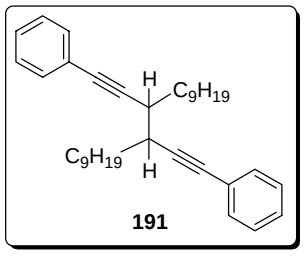
^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 14.1, 22.7, 26.3, 28.9, 29.1, 31.8, 39.4, 49.4, 86.1, 87.6, 122.3, 128.4, 128.7, 131.8 **(Spectrum No. 54)**

MS (EI) *m/z* 426 (M^+)

Analysis Calculated for $C_{32}H_{42}$: C, 90.08%; H, 9.92%

Found: C, 90.11%; H, 9.89%

1,5-Diyne 191



191

Yield 0.30 g (63%)

dr 100:0

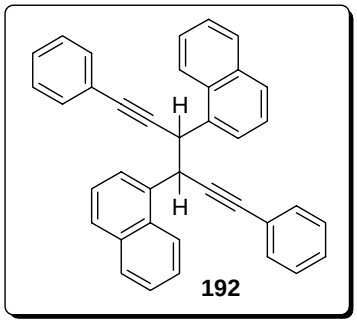
IR (Neat) (cm^{-1}) 2926, 2207, 1491, 1464, 1028

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm) 0.92 (t, 6H, *J* = 6.8 Hz), 1.25-1.42 (m, 24 H), 1.59-1.68 (m, 4H), 2.04-2.10 (m, 4H), 4.80 (t, 2H, *J* = 6.7 Hz), 7.33-7.48 (m, 10H) **(Spectrum No. 55**

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 14.1, 22.7, 26.3, 29.3, 29.5, 29.6, 29.7, 31.9, 39.4, 49.4, 86.0, 87.5, 122.3, 127.8, 127.9, 131.8 **(Spectrum No. 56)**

MS (EI) *m/z* 483 (M+1) **(Spectrum No. 57)**

1,5-Diyne 192



192

Yield 0.29 g (61%)

dr 87:13

IR (KBr) (cm^{-1}) 2937, 2204,1590, 1498, 1028

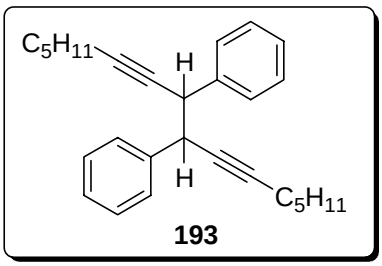
^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 5.21 (s, 1H, *dl*), 5.92 (s, 1H, *meso*), 7.18-7.90 (m, 24H) **(Spectrum No. 58)**

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 63.6, 68.4, 69.7, 87.0, 88.7, 124.2, 125.1, 125.2, 125.5, 126.2, 126.7, 127.9, 128.3, 128.9, 129.4, 130.5, 131.8, 132.9, 133.8 **(Spectrum No. 59)**

MS (EI) *m/z* 482 (M^+)

A similar procedure was followed for the synthesis of 1,5-diynes using the $TiCl_4$/Zn reagent system. In this reaction, Zn (2 mmol) was taken in the place of Et_3N.

1,5-Diyne 193



193

Yield 0.21 g (56%)

dr 87:13

IR (Neat) (cm^{-1}) 2932, 2207, 1498

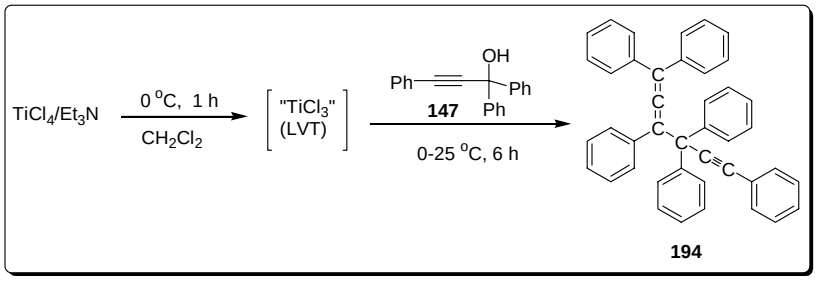
^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 0.91 (t, 6H, *J* = 7 Hz), 1.22-1.46 (m, 8H), 1.60-1.74 (m, 4H), 2.30-2.34 (m, 4H),5.23 (s,1H), 5.64 (s, 1H), 7.26-7.37 (m, 6H), 7.37-7.58 (m, 4H)

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 13.9, 18.9, 22.2, 28.3, 31.1, 69.6, 78.2, 88.7, 127.6, 127.9, 128.2, 139.4

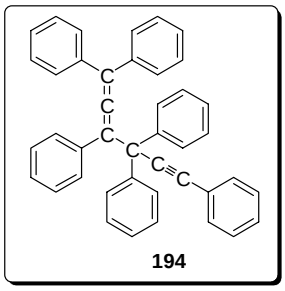
MS (EI) *m/z* 370 (M^+)

2.4.8 Procedure for the preparation of allenynes using the $TiCl_4/Et_3N$ reagent system

In dichloromethane (35 mL), $TiCl_4$ (0.19 g, 0.1 mL, 1 mmol) and Et_3N (0.15 g, 0.21 mL, 1.5 mmol) were taken at 0 ^oC under N_2. The reaction mixture was stirred for 1 h at 0 ^oC. To this 1,1,3-triphenyl-2-propyn-1-ol **89**, (0. 568 g, 2 mmol) was added and stirred for another 10 h at 25 ^oC. Saturated NH_4Cl solution (10 mL) was added and stirred for 10 min. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2 X 15 mL). The combined organic extract was washed with brine solution (5 mL) and dried over anhydrous Na_2SO_4. The solvent was removed and the residue was chromatographed on a silica gel column in hexane to isolate allenyne **194** (0.34 g, 64%).



Yield 0.31 g (58%)



IR (KBr) (cm^{-1}) 3079, 2920, 1595, 1489, 1442, 1178

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm) 6.82-7.78 (m, 30H)

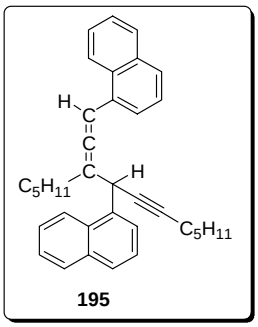
^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 54.8, 87.2, 93.5, 115.8, 123.5, 126.9, 127.0, 127.4, 127.8, 128.0, 128.1, 128.2, 128.3, 128.7, 128.8, 131.6, 135.0, 136.2, 143.8, 209.3 **(Spectrum No. 60)**

MS (EI) *m/z* 534(M^{+})

Analysis Calculated for $C_{42}H_{30}$: C, 94.34%; H, 5.66%

Found: C, 94.38%; H, 5.65%

The same procedure was followed for the propargyl alcohol **151** and the allenyne **195** and 1,5-diyne **196** was isolated.



Allenyne 195

Yield 0.26 g (56%)

IR (KBr) (cm^{-1}) 3049, 2959, 2197, 1946, 1967, 1593

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm) 0.79-0.91 (6H), 1.24-1.54 (12H), 2.19-2.32 (m, 4H), 5.25 (2H), 6.95-7.0 (8H), 7.30-7.62 (8H), 7.68-7.93 (4H), 8.05-8.30 (2H) **(Spectrum No. 61)**

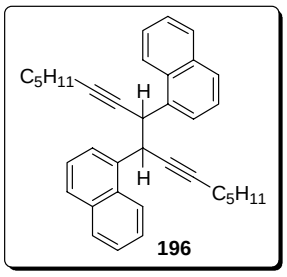
^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 14.2, 19.0, 22.5, 27.4, 28.7, 29.8, 30.1, 31.2, 31.7, 39.6, 79.7, 85.2, 93.9, 94.23, 109.3, 123.8, 125.3, 125.4, 125.5, 125.6, 125.8, 125.9, 126.4, 127.1,127.2,127.8, 127.9, 128.55, 128.58, 128.68, 128.72, 131.3, 135.6, 204.8 **(Spectrum No. 62)**

MS (EI) *m/z* 470 (M^+)

Analysis Calculated for $C_{36}H_{38}$: C, 91.86%; H, 8.14%

Found: C, 91.89%, H; 8.10%

1,5-Diyne 196



196

Yield 0.06 g (12%)

dr 83:17

IR (KBr) (cm^{-1}) 2920, 2231,1456, 1032

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm) 0.85-0.96 (t, 6H, *J* = 8.4 Hz), 1.19-1.57 (12H), 1.57-2.26 (4H), 4.87 (s, 1H), 5.05 (s, 1H), 7.31-8.19 (m, 14H) **(Spectrum No. 63)**

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 14.0, 18.2, 22.2, 28.3, 28.7, 30.9, 40.9, 80.5, 85.0, 123.3, 125.3, 125.4, 125.8, 127.1, 127.6, 129.1, 133.7, 136.0 **(Spectrum No. 64)**

MS (EI) *m/z* 470 (M^+)

2.5 References

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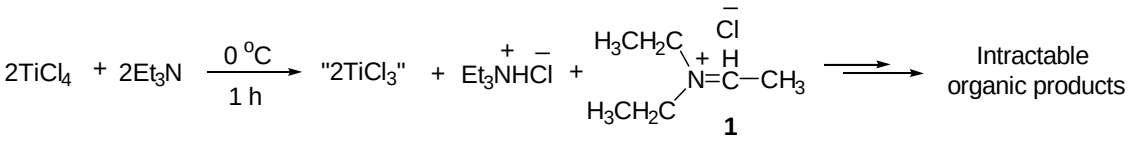
Chapter 3

Synthetic Applications of Low-Valent Titanium Species Prepared using $TiCl_4/R_3N$ and $TiCl_4/Zn$ Reagent Systems

3.1 Introduction

As discussed in Chapters 1 and 2, the $TiCl_4$ readily oxidizes tertiary amines in the absence of compounds containing acidic hydrogens leading to the formation of $TiCl_3$ species and iminium salt **1** (Scheme 1).[1]

Scheme 1

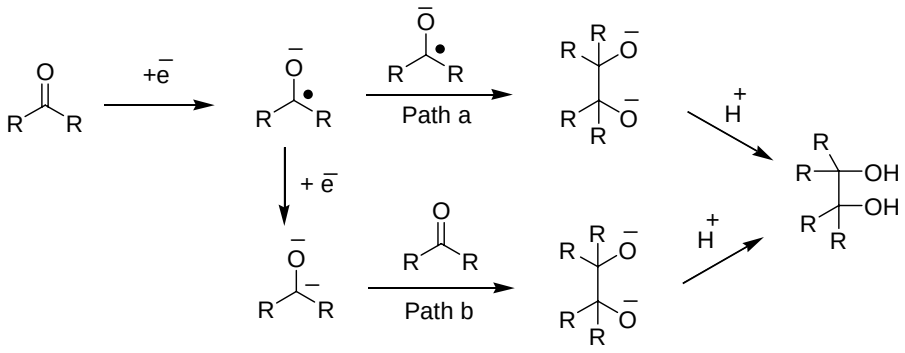


In the absence of electrophiles such as benzaldehyde and benzophenone, the iminium ions produced in this way give intractable organic compounds.[2] It was of interest to examine the reactivity pattern of the $TiCl_3$ prepared in this way as it is produced here without using metal or metal hydride reducing agents. Also, it was of interest to examine the use of low-valent titanium species prepared in this way for pinacol coupling and other reactions. Accordingly, a brief review on the synthetic applications of low-valent titanium reagents will be helpful for the discussion.

3.1 Pinacol coupling reactions using $TiCl_4$/metals or metal hydrides

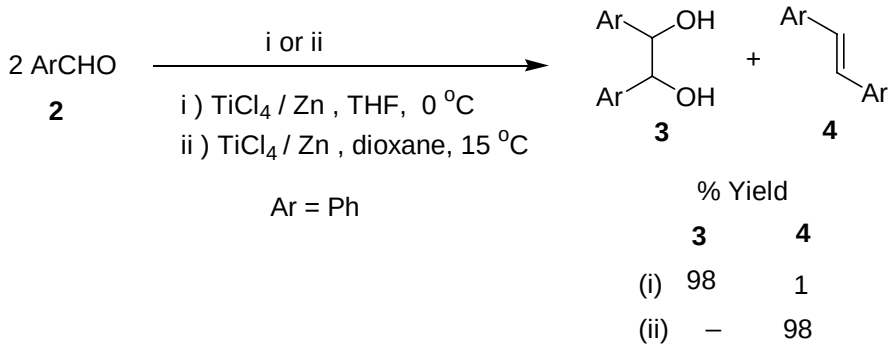
The intermolecular pinacol coupling of carbonyl compounds was first discovered in 1859.[3] A general reaction pathway is shown in Scheme 2.

Scheme 2



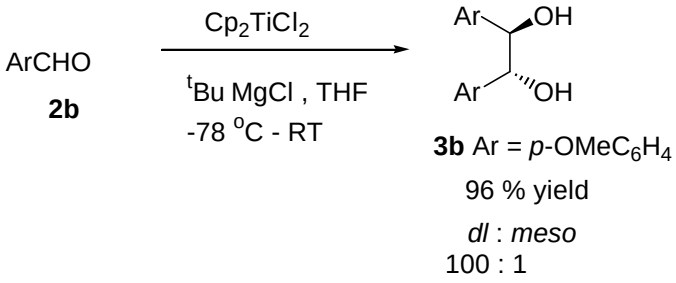
Pinacol coupling can be initiated photo chemically, electrochemically or with a range of metal reducing agents. Mukaiyama *et al.* [4] demonstrated that titanium species, prepared using $TiCl_4$/Zn, selectively coupled both aromatic and aliphatic aldehydes **2** and ketones to either pinacols **3** or alkenes **4** (Scheme 3).

Scheme 3



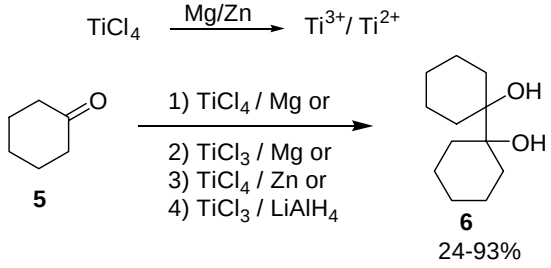
It was reported that the titanium species, produced using Cp_2TiCl_2 and t-BuMgCl, react with *para*-methoxy benzaldehyde **2b** to give the corresponding 1,2-diol **3b** in excellent yields with high diastereoselectivity (Scheme 4).[5]

Scheme 4



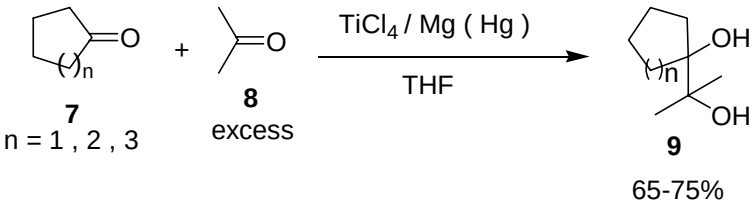
The $TiCl_4$ is reduced by Mg, Zn, $LiAlH_4$ and the resulting low-valent titanium (mainly Ti^{2+}) species react with cyclohexanone **5** to give the corresponding pinacol **6** (Scheme 5).[6]

Scheme 5



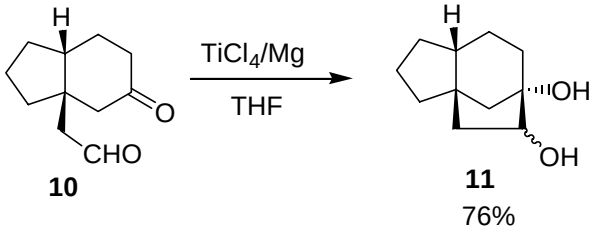
It was also reported that the ketones **7** and excess of **8** are efficiently coupled by titanium species prepared in the reduction of $TiCl_4$ with Mg-Hg to give the corresponding mixed 1,2-diol **9** (Scheme 6).[7]

Scheme 6



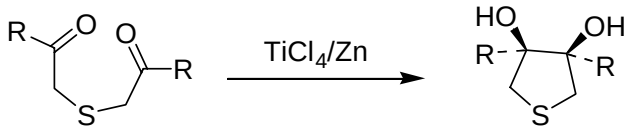
The titanium species produced using $TiCl_4$/Mg is useful for the preparation of intramolecular pinacolic product **11** from **10** (Scheme 7).[8]

Scheme 7



Stereoselective cyclization of 1,5-diketones **12** to *cis*-cyclopentane 1,2-diols **13** was observed using titanium species prepared using the $TiCl_4$/Zn reagent system. This method has been used to prepare stereo defined sterically hindered acyclic 1,2-diols when a removable heteroatom such as sulfur is included in the linking chain (Scheme 8).[9]

Scheme 8

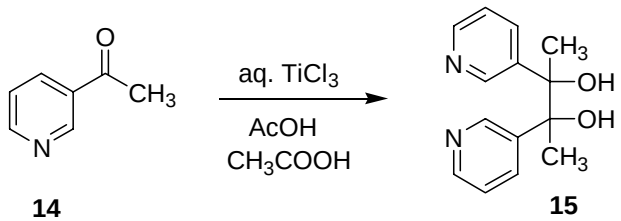


12
R = CH_3, C_2H_5

13
56-87%

3-Acetyl pyridine **14** reacts with $TiCl_3/CH_3COOH$ reagent system to produce the corresponding 1,2-diol **15**. It was shown that the reducing power of Ti ^{III} redox system is strongly pH dependent (Scheme 9).[10]

Scheme 9

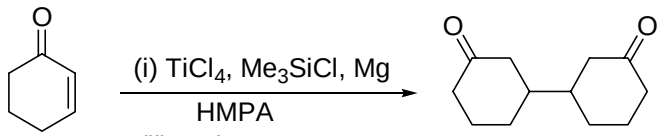


14

15
72%

Cyclohexenone **16** is selectively coupled at the β-position using a TMSCl, $TiCl_4$, Mg, HMPA reagent system to obtain the product **17** (Scheme 10).[11]

Scheme 10

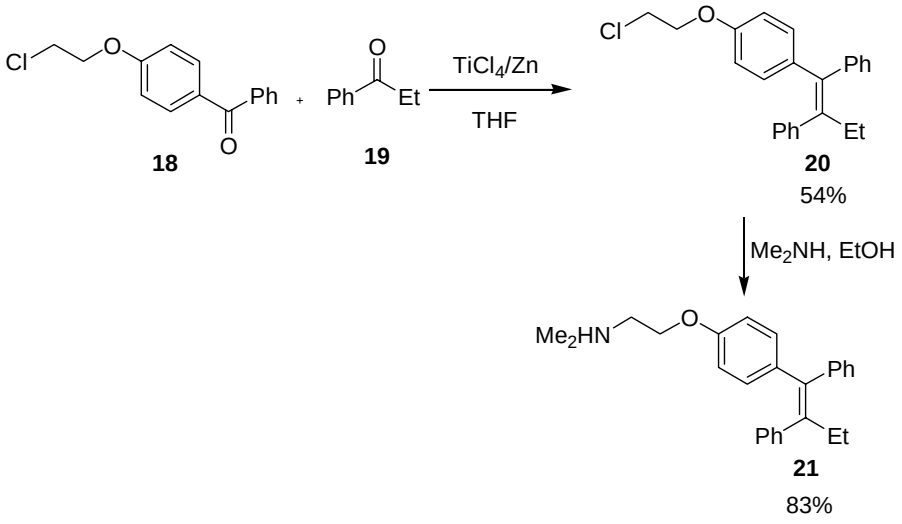


16

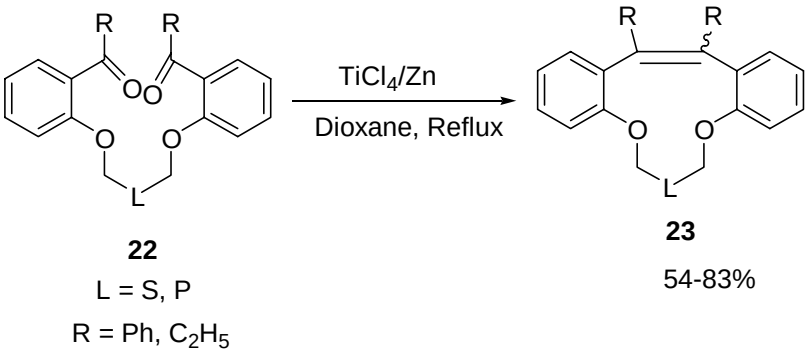
17
65%

The reaction of ketones **18** and **22** with the $TiCl_4/Zn$ reagent system under refluxing conditions gives the biologically active olefins **21** and **23**, respectively (Schemes 11 and 12).[12,13]

Scheme 11



Scheme 12

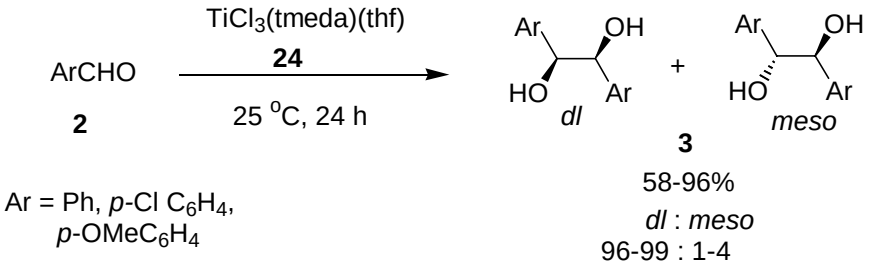


3.2 Stereoselective pinacol coupling reactions

3.2.1 Diastereoselective pinacol coupling reactions

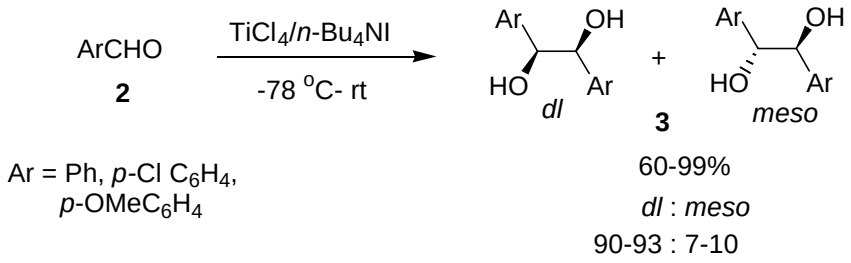
It was reported that a monomeric titanium(III) complex, $TiCl_3$(tmeda)(thf) **24**, prepared using $TiCl_4$ with TMEDA, Zn and catalytic amount of $PbCl_2$ in THF, reacts with aromatic aldehydes to produce the corresponding stereoselective pinacol products **3** in moderate to good yields (Scheme 13).[14]

Scheme 13



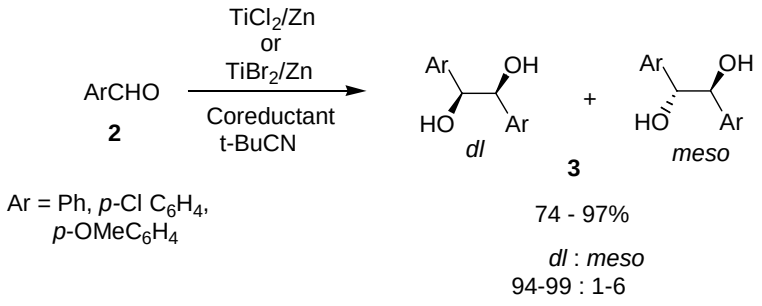
The $TiCl_4$/*n*-Bu_4NI reagent system was used for the stereoselective synthesis of pinacol coupling product **3** (Scheme 14).[15]

Scheme 14



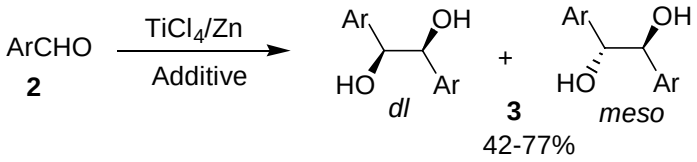
It was reported that the $TiCl_2$/Zn or $TiBr_2$/Zn is useful in diastereoselective pinacol coupling reactions (Scheme 15).[16]

Scheme 15



A highly *dl*-stereoselective pinacolization of aromatic aldehydes mediated by titanium reagents prepared using $TiCl_4$/Zn reagent system has been reported.[17] Effect of some of the additives on the selectivity was also reported (Scheme 16).

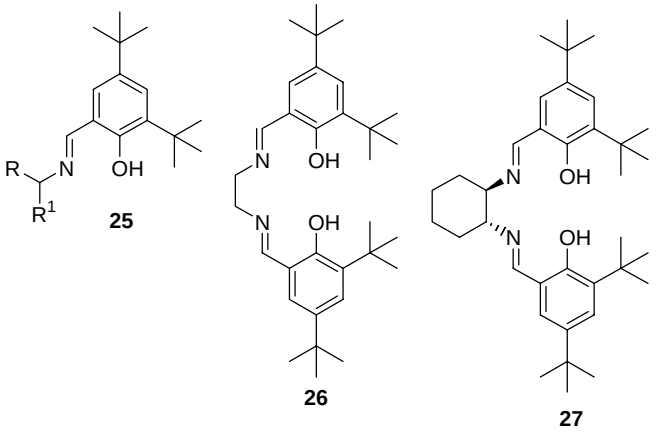
Scheme 16

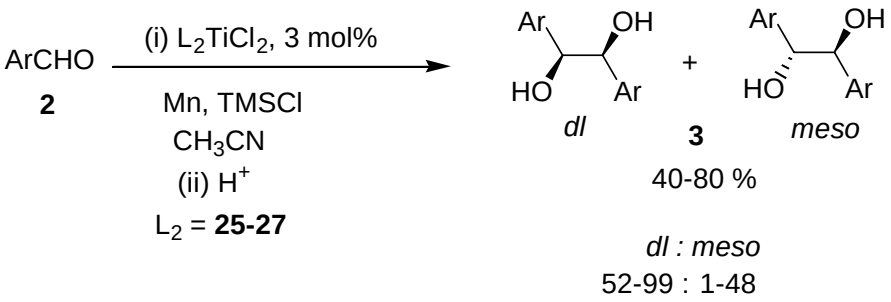


Additive	% Yield	*dl* : *meso*
Pyridine	42	5.2 : 1
DME	58	129 : 1
TMEDA	77	100 : 0

Titanium species prepared by the reduction of titanium Schiff base complex give highly diastereoselective pinacol coupling of aldehydes (Scheme 17).[18]

Scheme 17

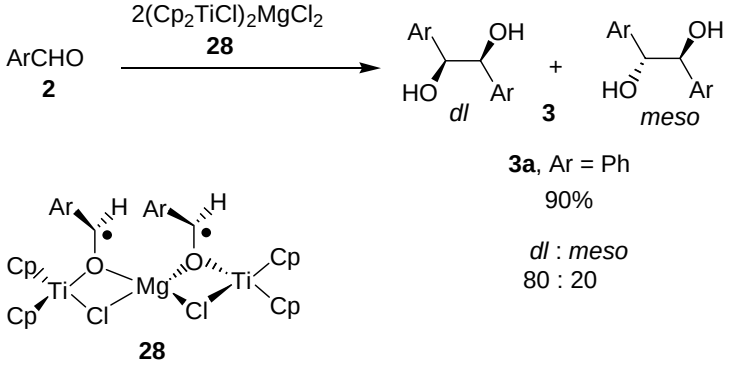




It was reported that the reaction of titanocene dichloride with Grignard reagents lead to a green trinuclear titanium(III) reagent formulated as $(Cp_2TiCl)_2MgCl_2$ **28**. This

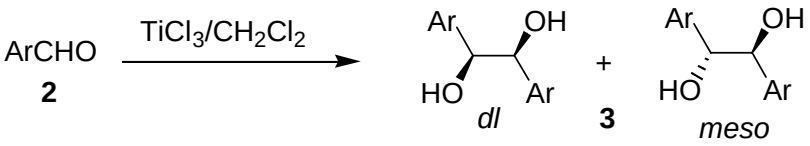
reagent reacts with aldehydes to give the racemic C_2-symmetrical 1,2-diols in high yields with high diastereoselectivities (Scheme 18).[19]

Scheme 18



Aromatic aldehydes are stereoselectively coupled to *dl*-hydrobenzoins upon reaction with anhydrous $TiCl_3$ in CH_2Cl_2 solvent (Scheme 19).[20]

Scheme 19



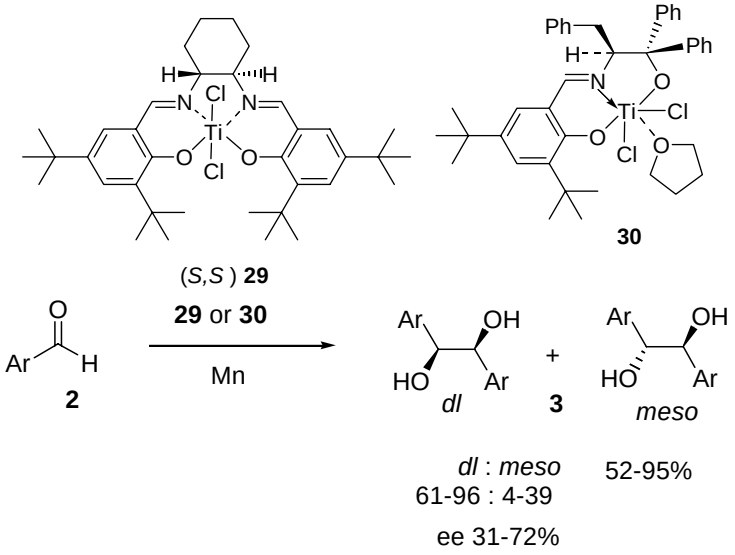
Ar	% Yield	*dl* : *meso*
p-MeC_6H_4	35	>100 : 0
p-ClC_6H_4	>90	>100 : 1

dl : *meso*
200 : 1

3.2.2 Enantioselective pinacol coupling reactions

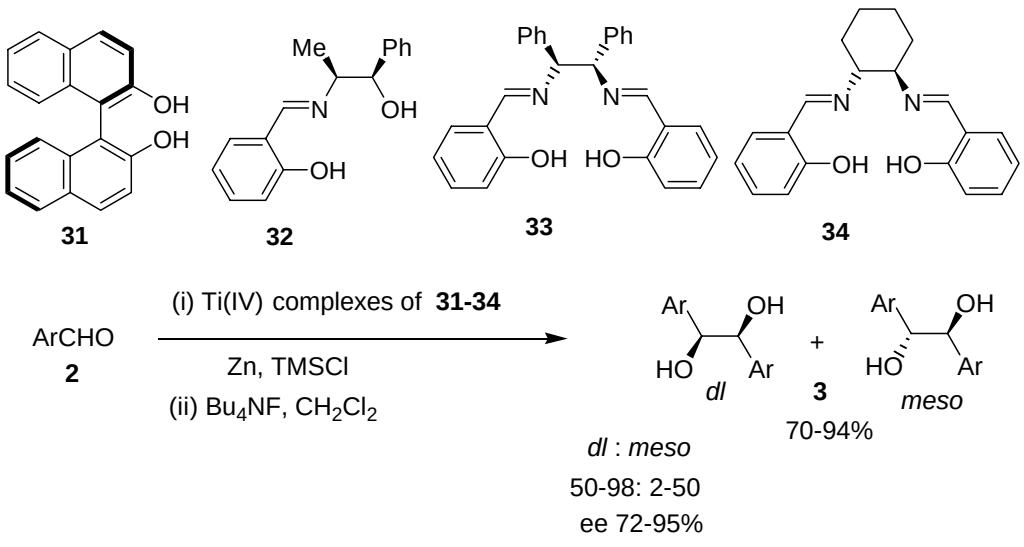
Enantioselective pinacol coupling of aldehydes was reported using chiral low-valent titanium complexes prepared by the reduction of Ti(IV) complexes with manganese (Scheme 20).[21]

Scheme 20



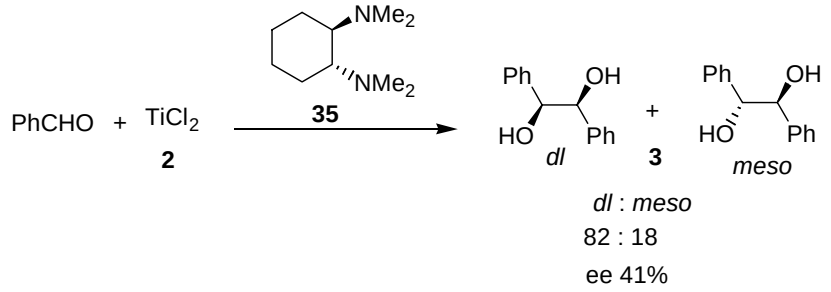
Chiral titanium complexes of the ligands **31-34** were also prepared using different solvents and additives. These complexes were used for enantioselective coupling of aldehydes to the corresponding 1,2-diols **3** (Scheme 21). The Ti(IV)-SALEN complexes prepared using **32-34** gave better yields and selectivities.[22]

Scheme 21



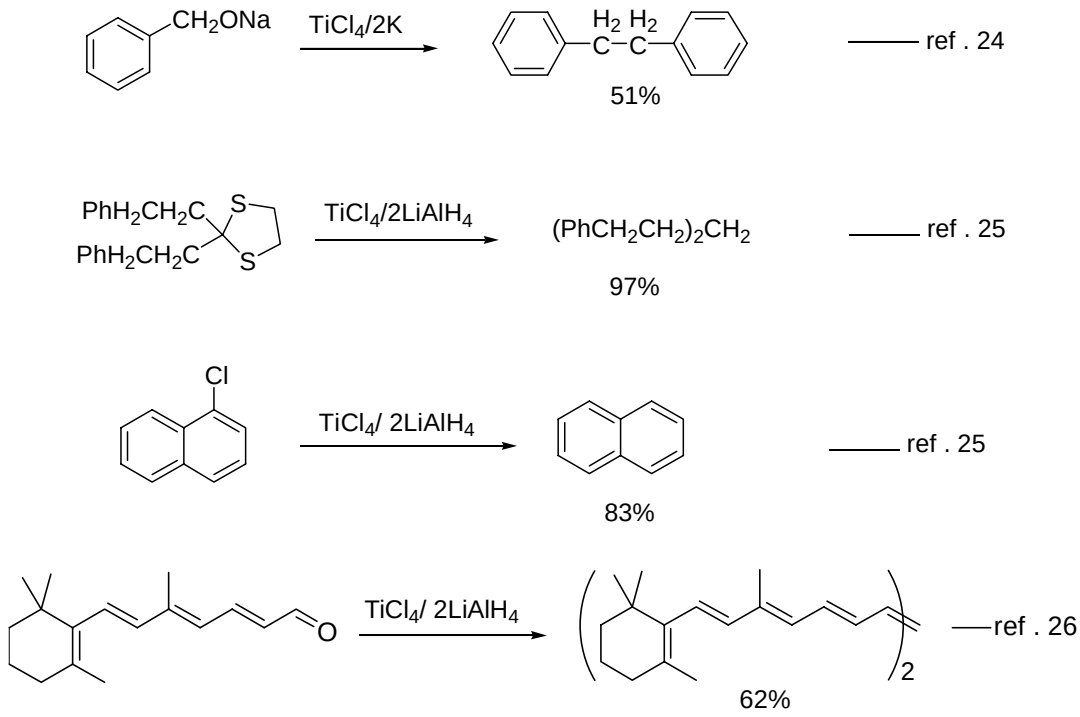
The Ti(II) complex of chiral amine **35** was used for the conversion of benzaldehyde to the corresponding 1,2-diols **3** with moderate enantioselectivity (Scheme 22).[23]

Scheme 22



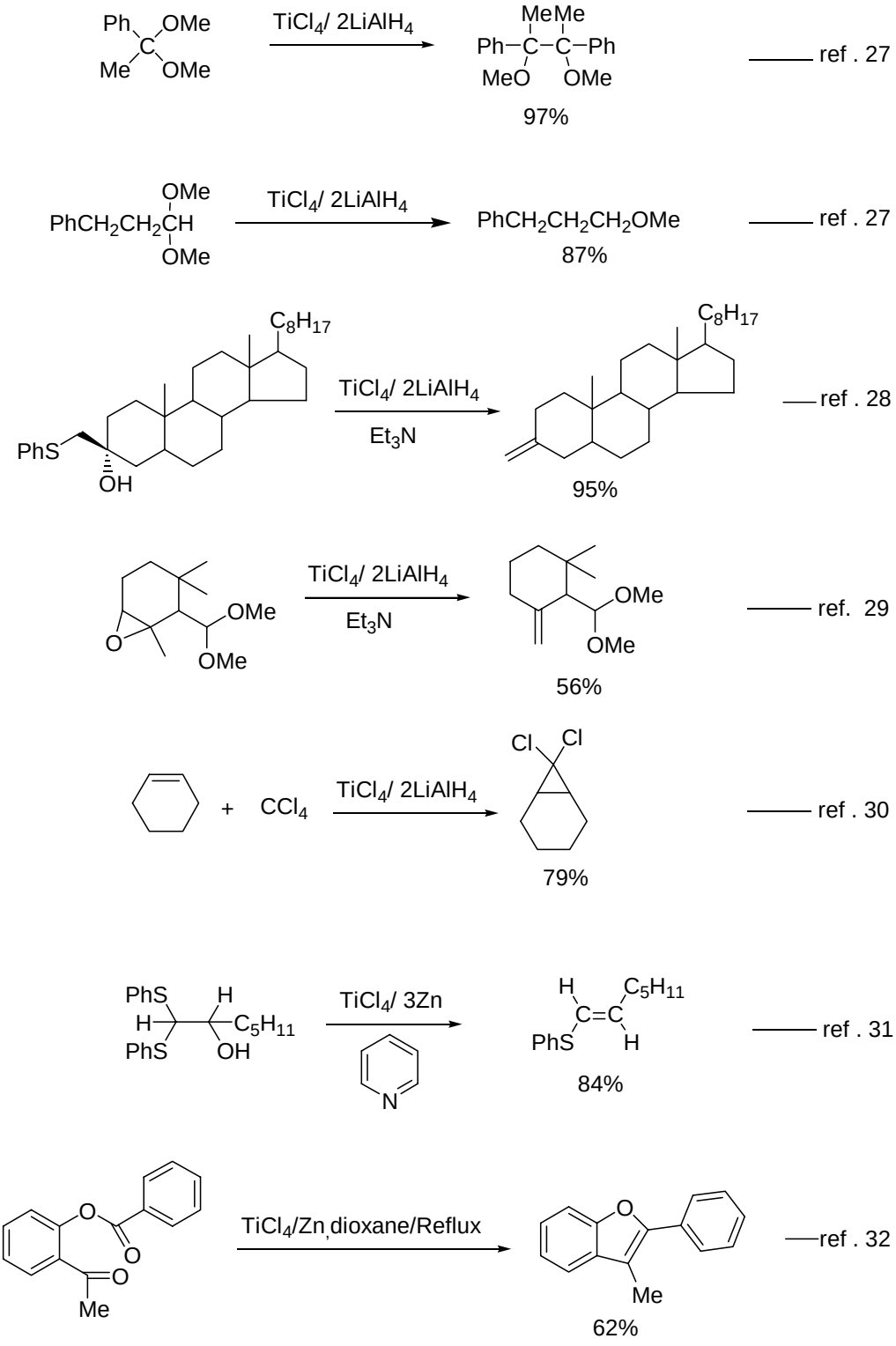
The low-valent titanium reagents have been also used for several other synthetic transformations. These transformations are summarized in Chart 1.

Chart 1



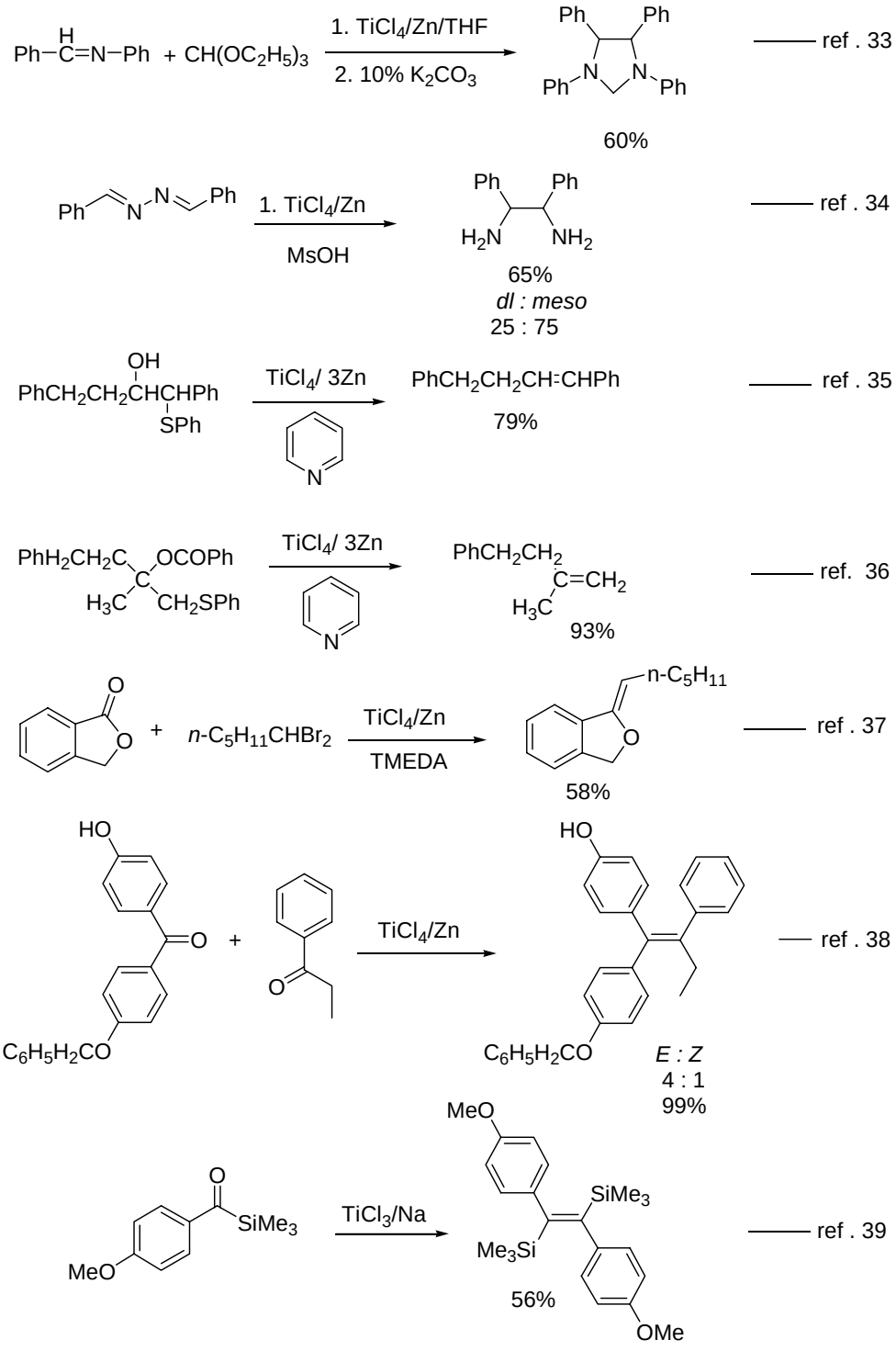
(continued…)

(….continued Chart 1)



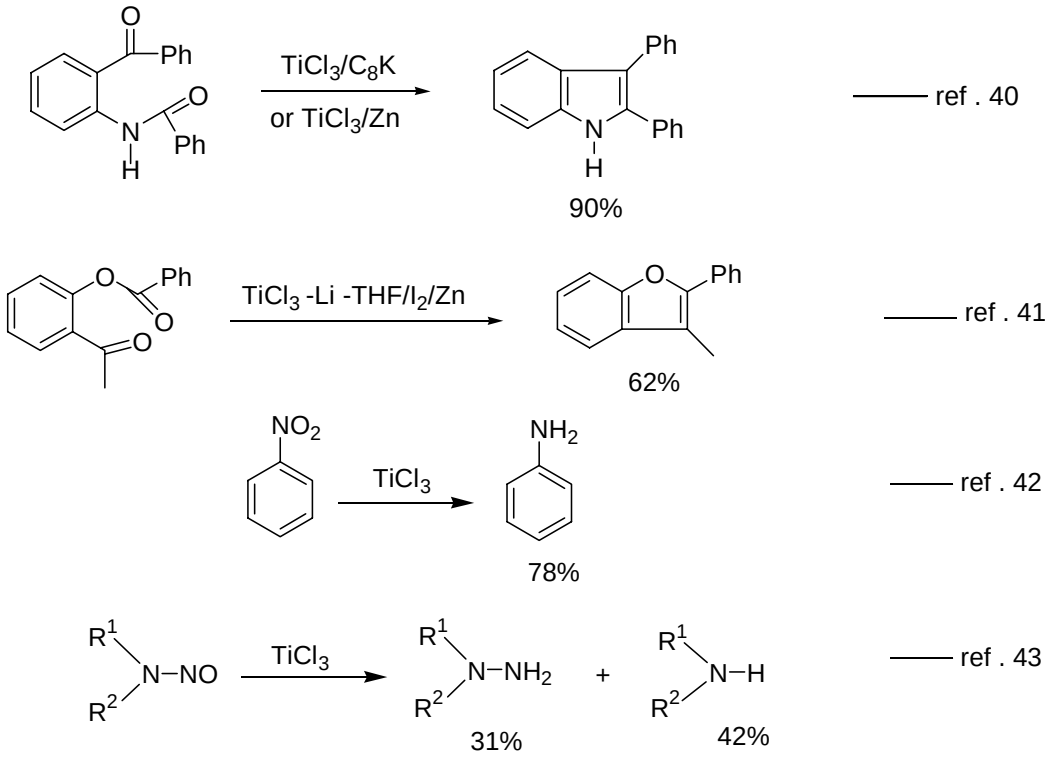
(continued…)

(….continued Chart 1)



(continued…)

(….continued Chart 1)



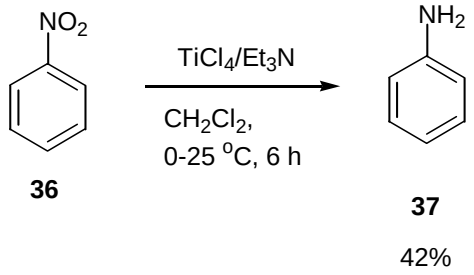
We describe the results of studies on the applications of the low-violent titanium species prepared using the $TiCl_4/Et_3N$ reagent system for pinacol coupling reactions and reduction of aromatic nitro compounds in the next section.

3.2 Results and Discussion

3.2.1 Reduction of nitroarenes with the low-valent titanium species formed in the reaction of the $TiCl_4$ and Et_3N reagent system

We have observed that nitrobenzene **36** reacts with $TiCl_3$, prepared *in situ* using $TiCl_4/Et_3N$ system, to give aniline **37** in 42% yield besides some unidentified polar compounds (Scheme 23). We have examined the reactivity of different nitroarenes using the $TiCl_3$ produced in this way. The corresponding amines were obtained in 27-42% yields. The results are summarized in Table 1.

Scheme 23



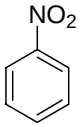
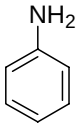
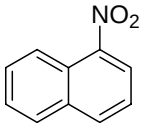
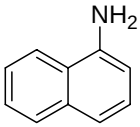
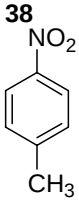
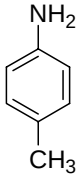
36 **37**

42%

In the case of 1-nitronaphthalene **38**, 1-napthylamine **39** was isolated in 32% yield. *p*-Nitrotoluene **40** gave the corresponding amine **41** in 28% yield.

As outlined in the introductory section, previously nitroarenes were reduced to arylamines using aqueous $TiCl_3$. Since the yields are poor with the $TiCl_3$ produced using the $TiCl_4/Et_3N$ system, we did not pursue these studies further.

Table 1. Reaction of aromatic nitro compounds with the $TiCl_4/Et_3N$ reagent system[a]

Entry	Substrate	Reducing agent	Product[b]	Yield (%)
1	 **36**	Et_3N	 **37**	42
2	**36**	Bu_3N	**37**	31
3	**36**	$^iPr_2NEt$	**37**	27
4	 **38**	Et_3N	 **39**	32
5	 **40**	Et_3N	 **41**	28

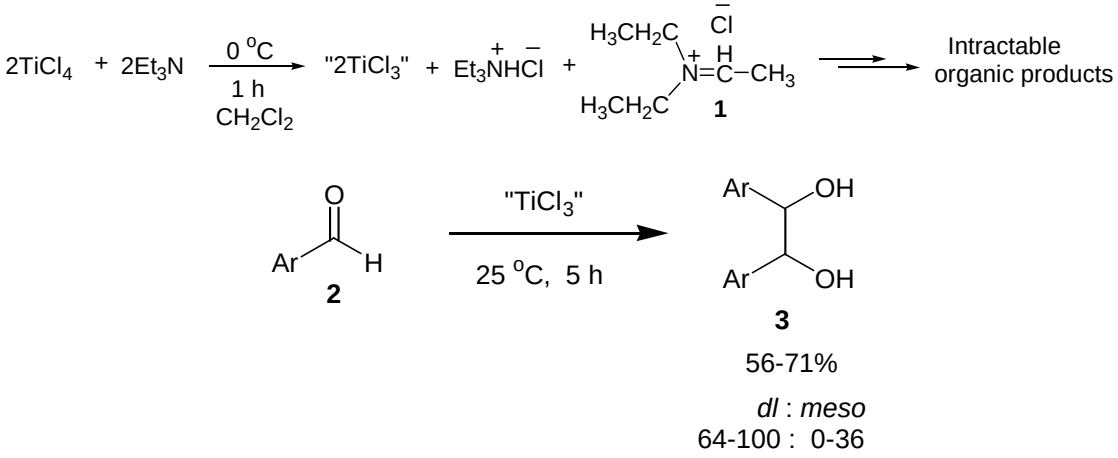
[a]Reactions were carried out using of Et_3N (7 mmol) and $TiCl_4$ (5 mmol) and nitroarenes (5 mmol) at 0-25 ^oC for 6 h.

[b]The products were identified by spectral (IR, ^{1}H-NMR, ^{13} C-NMR) and physical constant data.

3.2.2 Applications of low-valent titanium species generated by the reaction of $TiCl_4$ and Et_3N for pinacol coupling reactions

The low-valent titanium reagents were prepared *in situ* using $TiCl_4$ and Et_3N would be $TiCl_3$ species.[44] We have observed that these species react with benzaldehyde to give the corresponding 1,2-diphenylethane-1,2-diol (Scheme 24).

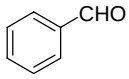
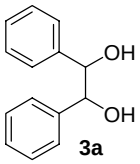
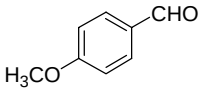
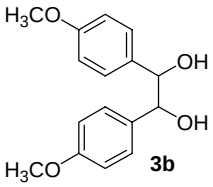
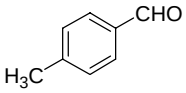
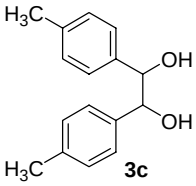
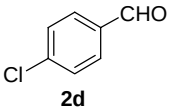
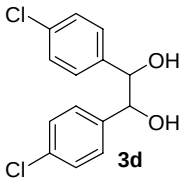
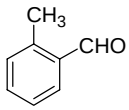
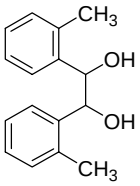
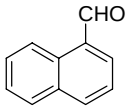
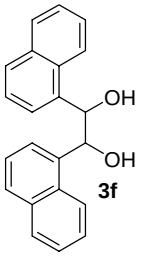
Scheme 24



We have examined the reactivity of different aromatic aldehydes using the $TiCl_3$ produced in this way. The corresponding 1,2-diaryl-1,2-diols were obtained. The yields are in the range of 56-71%. The results are summarized in Table 2. The 4-methoxy benzaldehyde **2b** gave the corresponding 1,2-diol **3b** 62% yield with 67:33 *dl:meso* ratio (entry 5). In the case of 4-chloro benzaldehyde **2d**, the corresponding 1,2-diol **3d** was obtained in 58% yield with *dl:meso* ratio of 83:17 (entry 7). 3-Methyl benzaldehyde **2e** and 1-napthaldehyde **2f** gave the corresponding 1,2-diols **3e** and **3f** in 63% and 58% yields with the *dl:meso* ratios of 75:25 and 72:28, respectively. Interestingly, in the case of tolualdehyde **2c**, only the *dl* isomer of 1,2-diol **3c** was isolated in 61% yield.

We have also examined the preparation of the low-valent titanium species using different reducing reagents. The reagents prepared using $TiCl_4$ and Bu_3N, $^{i}Pr_2NEt$ and Zn reacted with benzaldehyde to give the corresponding 1,2-diols in 62%, 56% and 67% with the *dl:meso* ratios of 68:32, 64:36, 72:28, respectively.

Table 2 Reductive coupling of aromatic aldehydes in the presence of low-valent titanium reactive species[a]

Entry	Substrate	Reducing agent	Product[b]	Yield (%)[c]	*dl:meso*[d]
1	 **2a**	Et_3N	 **3a**	71	74:26
2	**2a**	Bu_3N	**3a**	62	68:32
3	**2a**	$(^iPr)_2NEt$	**3a**	56	64:36
4	**2a**	Zn	**3a**	67	72:28
5	 **2b**	Et_3N	 **3b**	62	67:33
6	 **2c**	Et_3N	 **3c**	61	100:0[e]
7	 **2d**	Et_3N	 **3d**	58	83:17
8	 **2e**	Et_3N	 **3e**	63	75:25
9	 **2f**	Et_3N	 **3f**	58[f]	72:28

[a]Reactions were carried out using of Et_3N (15 mmol) and $TiCl_4$ (10 mmol) and aromatic aldehydes (5 mmol) at 0 ^oC for 0.5 h and for 6 h at 25 ^oC.

[b]The products were identified by spectral and physical constant data (IR, ^{1}H-NMR, ^{13} C-NMR) and comparison with reported data.[50]

[c]The *dl:meso* ratio in the mixture was determined by comparision with reported ^{1}H-NMR data.[50]

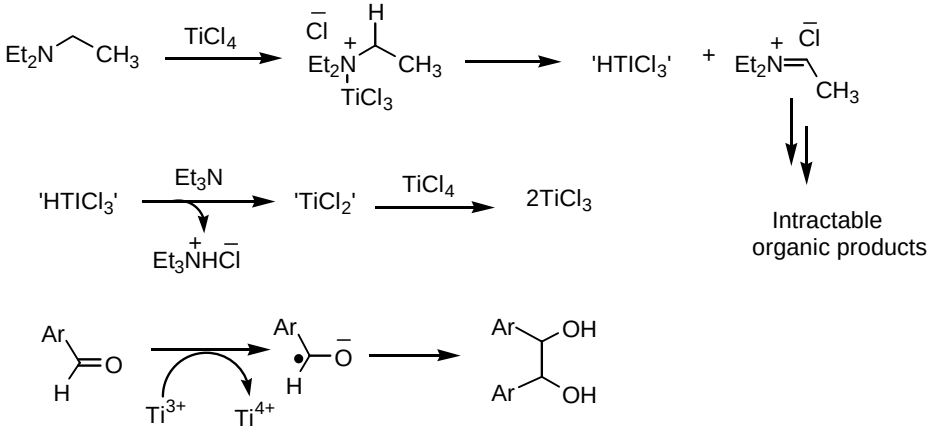
[d]The yields are based on the aldehyde used.

[e] Only *dl* isomer was isolated.

[f] The reaction was carried out for 12 h.

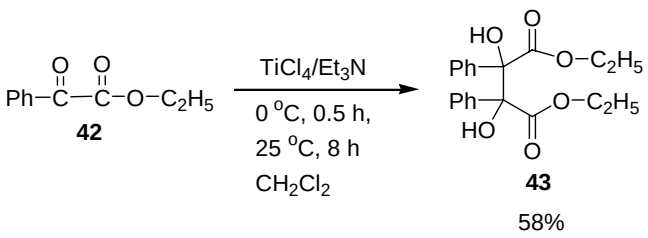
The order of addition of the reagents affected the course of the reaction. The Ti^{3+} species needs to be produced by the reaction of $TiCl_4$ with Et_3N before reaction with aromatic aldehyde. Accordingly, the transformation described here can be explained by the sequence of reactions outlined in Scheme 25.

Scheme 25



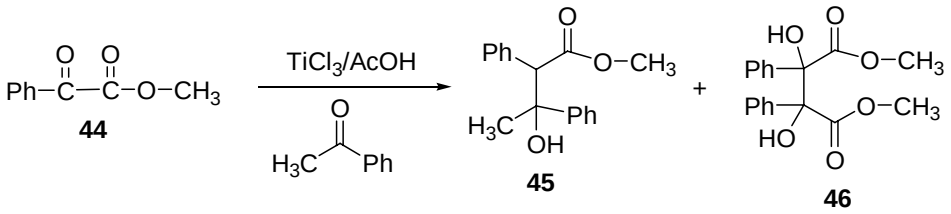
We have observed that the $TiCl_3$ species prepared in this way reacts with ethyl phenylglyoxalate **42,** to give the corresponding pinacol product **43** in 48% yield (Scheme 26).

Scheme 26



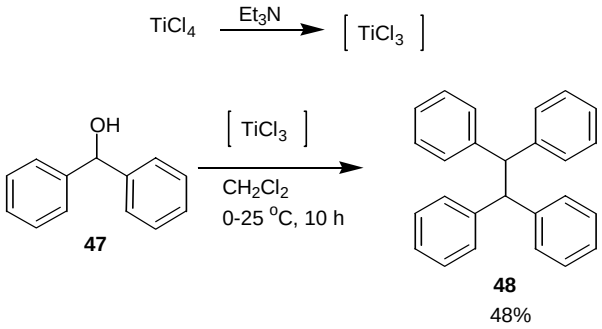
Previously, it has been reported that the $TiCl_3$ reacts with methyl phenylglyoxalate and a ketone in acetic acid to produce the corresponding unsymmetrical pinacol and dimer (Scheme 27).[45]

Scheme 27



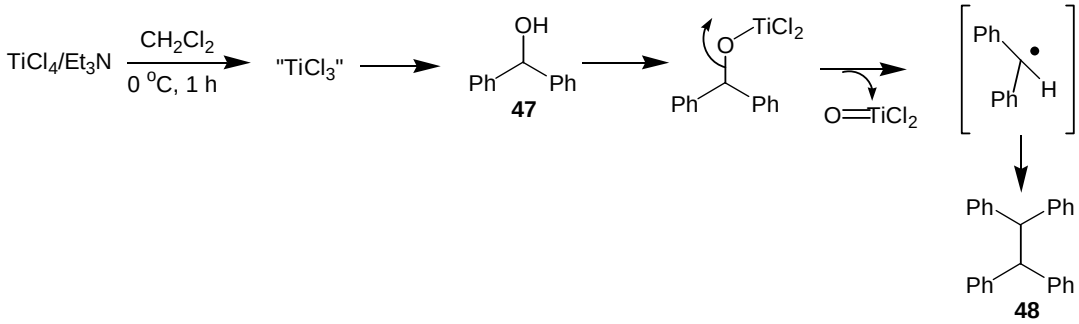
We have also examined the reaction of benzhydrol **47** with the $TiCl_3$ species prepared using the $TiCl_4/Et_3N$ reagent system. In this case the tetraphenylethane **48** was obtained in 48% yield (Scheme 28).

Scheme 28



This transformation may be explained by the mechanism outlined in Scheme 29. The Ti(II) or Ti(III) species could lead to coupling reactions described here (Scheme 24). However, the Ti(II) species is likely to react with the $TiCl_4$ present in the medium to give $TiCl_3$. The $TiCl_3$ produced in this way would form oxytitanium complex with benzhydrol, which could give a radical intermediate that further dimerizes to give the tetraphenyl ethane.

Scheme 29

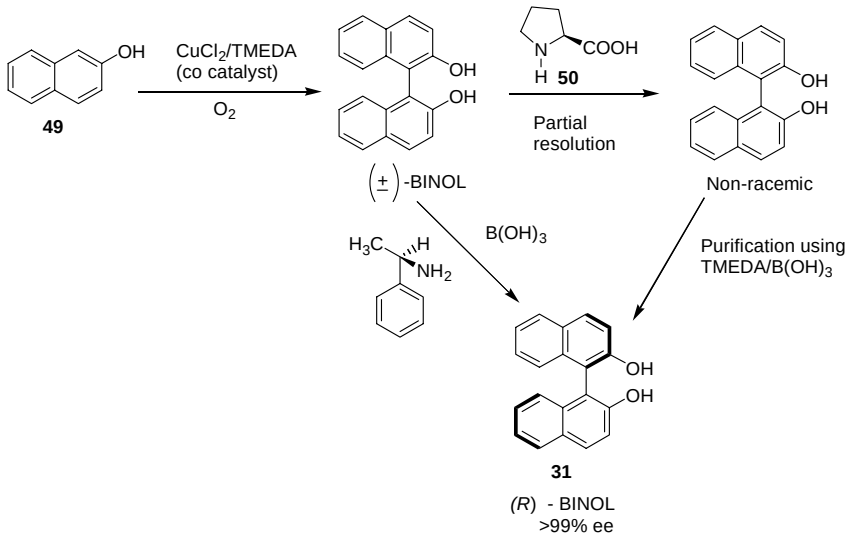


As discussed in the introductory section, such transformations have been observed with low-valent titanium species generated from $TiCl_4$ and different metal reducing agents like Mg, Zn, Li, Pb-Te and $LiAlH_4$.[46] Here, the low-valent titanium species was generated using $TiCl_4$ and Et_3N without using metal or metal hydrides. Accordingly, this reagent system has considerable synthetic potential.

3.2.3 Studies on the asymmetric pinacol coupling of benzaldehyde using (*R*)-(+)-bi 2-napthol (BINOL) and the $TiCl_4/Et_3N$ reagent system

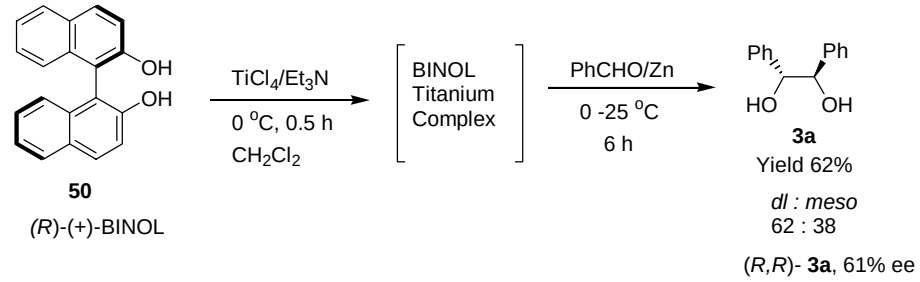
The chiral bi-2-napthol (BINOL) **50** is readily accessible through methods developed in this laboratory (Scheme 30).[47]

Scheme 30



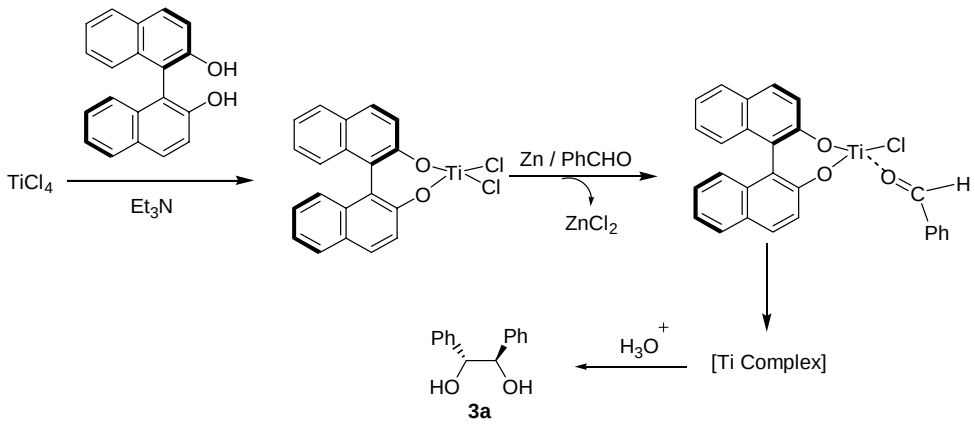
Accordingly, it was of interest to examine the applications of the Ti complex prepared using chiral BINOL/$TiCl_4$/Zn for asymmetric pinacol coupling. We have carried out several experiments to examine this possibility (Scheme 31). Unfortunately, the enantioselectivities realized were poor.

Scheme 31



The anticipated intermediates and a tentative reaction mechanism are given in Scheme 32.

Scheme 32

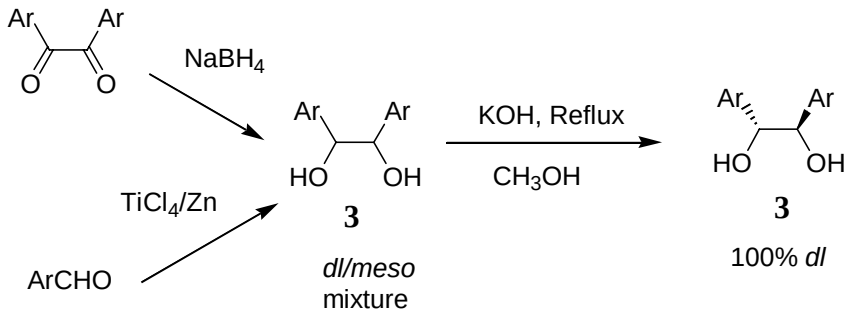


Since the selectivities realized were poor, we did not pursue these studies further.

3.2.4 Diastereoselective duplication of 1,2-diphenylethane-1,2-diol via pinacol coupling of benzaldehyde using $TiCl_4$ with various amines and metals

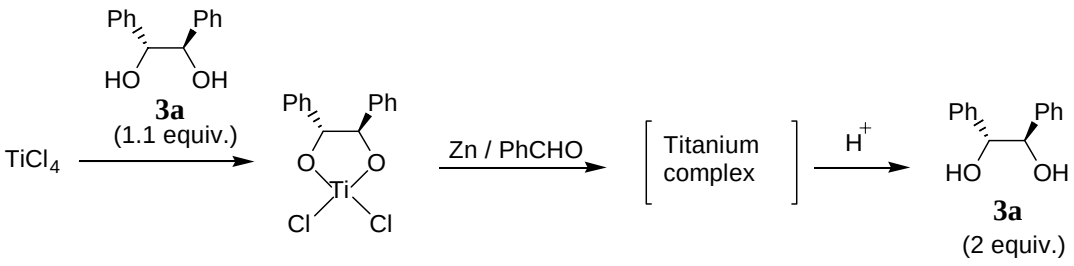
As described earlier, the reductive coupling of aromatic aldehydes with titanium species produced using $TiCl_4/Et_3N$ reagent gives 1,2-diarylethane-1,2-diols. In the case of *p*-methyl benzaldehyde, only the *dl* isomer was isolated. Also, the *dl*-1,2-diarylethane-1,2-diols are readily accessible. For example, the readily accessible *dl:meso* 1,2-diols mixture can be easily converted to the corresponding *dl*-1,2-diols using KOH, under reduced pressure and refluxing conditions (Scheme 33).[48]

Scheme 33



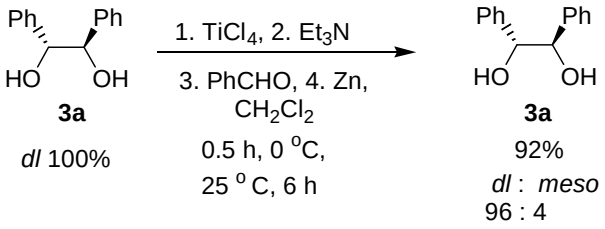
Accordingly, we became interested in the possibility of duplication of chirality via the pinacol coupling of benzaldehyde as outlined in the Scheme 34.

Scheme 34



To examine this possibility, we have carried out the reaction under several conditions (Scheme 35).

Scheme 35



We have observed that the recemic mixture of 1,2-diphenylethane-1,2-diol with *dl*:*meso* ratio of 96:4 was obtained in 92% yield in the reductive coupling of benzaldehyde with titanium species prepared by reducing $TiCl_4/Et_3N$ and *dl*-1,2-diol complex with Zn.

We have carried out this reaction with different amines using the $TiCl_4$ in DCM at 0-25 ^oC. The corresponding 1,2-diols were obtained. The yields are in the range of 58-92%. The results are summarized in Table 3.

We have examined the use of various bases such as Et_3N, pyridine, DABCO, TMEDA, $^nPr_3N$ and $^iPr_2NEt$ in this reaction. The reaction is highly diastereoselective using the Et_3N, 92% yield, *dl:meso* ratio 96:4 (entry 1, Table 3). The amines, pyridine and $^iPr_2NEt$ give the 1,2-diol in comparable yields with slightly lower de (entries 3 and 7 in Table 3). Whereas the use of DABCO, Pr_3N and TMEDA gave poor yields (entries 4, 5 and 6 in Table 3). Presumably, in addition to removing the HCl moiety to form the titanium complex of the diol, the amines may also play a role in the reductive coupling step. As for the solvent effects, the reaction gives poor diastereoselectivity in THF solvent compared to dichloromethane. Also, it was observed that the reaction takes

longer time using reducing agents like Mn and Fe in the place of Zn (entries 8 and 9 in Table 3) and the yields are also moderate with these reagents.

Table 3 Diastereoselective pinacol coupling of benzaldehyde in presence of $TiCl_4$, *dl*-1,2-diphenylethane-1,2-diol with various amines and reducing agents[a]

Entry	Solvent	Amine	Reducing Agent	Time	Product **3a** Yield (%)	*dl:meso*
1	DCM	Et_3N	Zn	6h	92	96:4
2	THF	Et_3N	Zn	6h	82	91:8
3	DCM	Pyridine	Zn	6h	90	78:22
4	DCM	DABCO	Zn	6h	58	92:8
5	DCM	Pr_3N	Zn	6h	62	91:9
6	DCM	TMEDA	Zn	6h	60	89:11
7	DCM	$(^iPr)_2NEt$	Zn	6h	92	90:10
8	DCM	Et_3N	Mn	18h	75	93:7
9	DCM	Et_3N	Fe	18h	62	91:9

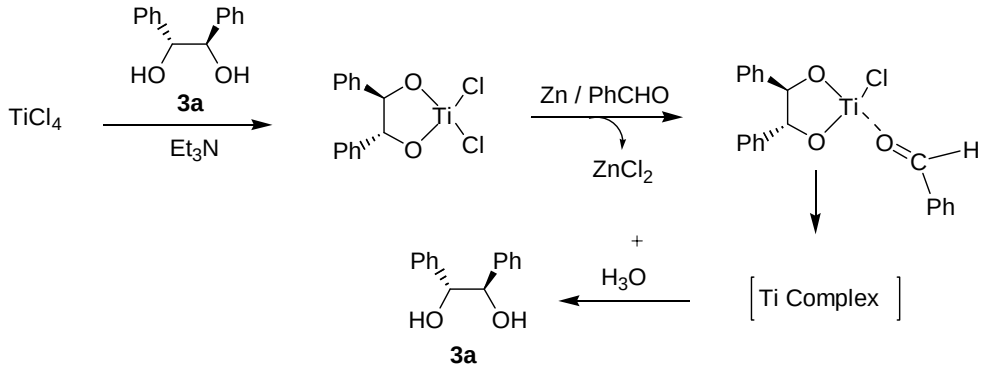
[a]The reagents were used in the following quantities: 1,2-diol (*dl*) (1 mmol), $TiCl_4$ (1mmol), triethylamine (3 mmol), benzaldehyde (4 mmol) and Zn (4 mmol).

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

[c]The *dl:meso* ratio was estimated using ^{1}H NMR data.

Presumably, the reaction may go through the initial formation of titanium(III) species (Scheme 36).

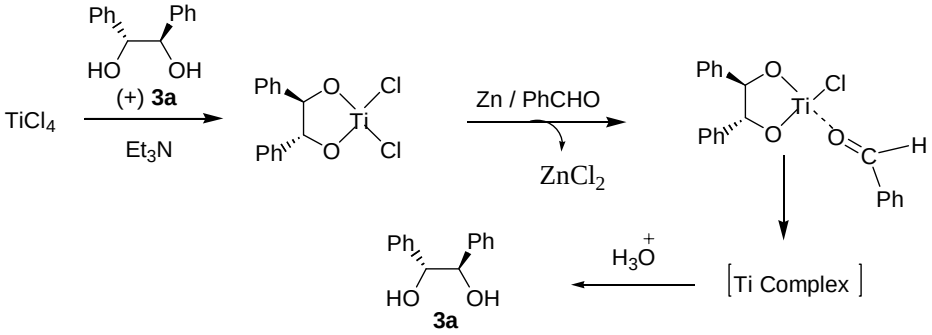
Scheme 36



3.2.5 Enantioselective duplication of chirality in the pinacol coupling of benzaldehyde to 1,2-diphenylethane-1,2-diol

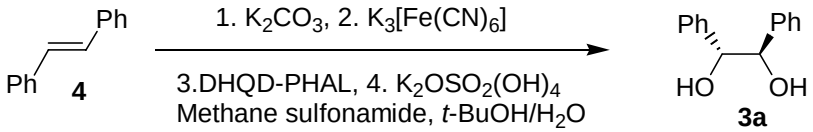
We became interested in the synthesis of the optically active 1,2-diols by following the reaction outlined in Scheme 37.

Scheme 37



The (*R,R*)-(+)-1,2-diphenylethane-1,2-diol **3a** is easily accessed following the reported Sharpless asymmetric dihydroxylation process (Scheme 38).[49]

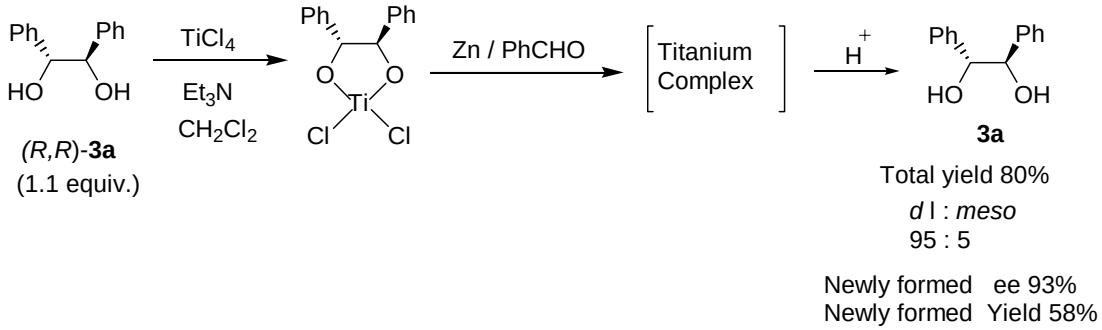
Scheme 38



(R,R)-(+)-1,2-diphenylethane-1,2-diol

We have briefly investigated the possibility of duplication of chirality as outlined in Scheme 37. We have carried out this transformation under various conditions and found that the newly formed (*R,R*)-(+)-1,2-diphenylethane-1,2-diol is obtained in 58% yield with 93% ee (Scheme 39).

Scheme 39



Further studies using different 1,2-diarylethane-1,2-diols should be helpful in standardizing conditions to realize optimum results.

3.3 Conclusions

Low-valent titanium species generated using the $TiCl_4/R_3N$ reagent system is useful in the reduction of the aromatic nitro compounds to obtain the corresponding aromatic amines in moderate yields. These titanium species are also useful in pinacol coupling reactions. Enantioselective duplication of 1,2-diphenylethane-1,2-diol via coupling of benzaldehyde gave poor selectivity using the (*R*)-(+)-BINOL/$TiCl_4$/Et_3N/Zn reagent system. Diastereoselective duplication of chirality in the pinacol coupling of benzaldehyde to 1,2-diphenylethane-1,2-diols using $TiCl_4/R_3N$/(±)-1,2-diphenylethane-1,2-diol system gave good selectivity. Enantioselective duplication of chirality using chiral 1,2-diphenylethane-1,2-diol under these conditions gave the newly formed diol in 58% yield and 93% ee.

3.4 Experimental Section

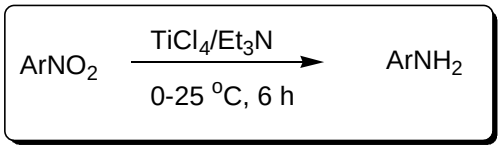
3.4.1 General Information

Optical rotations were measured in an AUTOPOL-II automatic polarimeter (readability ± 0.01^{o}). The condition of the polarimeter was checked by measuring the optical rotation of a standard solution of (*R)*-(+)-α-methylbenzylamine $[\alpha]_D^{25}$ =+30.2 (c 10, EtOH) supplied by Fluka. Toluene and THF supplied by E-Merck, India were distilled over sodium-benzophenone ketyl and freshly distilled before use. Ethylphenylgyloxalate, benzhydrol, nitrobenzene, nitronapthalene and 4-methyl nitrobenzene were supplied by Fluka. Potassium carbonate, potassium hydroxide, potassium Ferro cyanide, sodium sulfate, methanol and ethanol were supplied by E-Merck, India. Potassium osmate dihydrate, methane sulfonamide were supplied by Aldrich USA. BINOL was supplied by Gerchem Labs, India Limited. Zinc, magnesium and iron were supplied by SISCO, India (P) Ltd.

3.4.2 Typical procedure for the preparation of aniline from nitrobenzene using the $TiCl_4/Et_3N$ reagent system

Dichloromethane (25 mL), nitroarene **36** (0.61 g, 0.51 mL, 5 mmol) and Et_3N (0.71 g, 0.97 mL, 7 mmol) were taken in a reaction flask under N_2 atmosphere. $TiCl_4$ (0.95 g, 0.5 mL, 5 mmol) was added under N_2 at 0 ^{o}C. The reaction mixture was stirred for 6 h at 0-25 ^{o}C. It was quenched with saturated NH_4Cl solution (20 mL). The organic layer was

separated and the aqueous layer was extracted with CH_2Cl_2 (2 X 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 amine **37** was isolated using hexane as eluent.



Yield 0.2 g (42%)

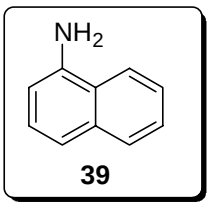
IR (Neat) (cm^{-1}) 3356, 3312, 1278

^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm): 4.29 (s, 2H), 6.41-7.01(m, 5H).

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 114.1, 117.4, 128.6, 149.7

The same procedure was followed for the reaction of nitroarenes and the data are given below.

Compound 39



39

Yield 0.23 g (32%)

IR (Neat) (cm^{-1}) 3362, 3307, 1267

^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm): 4.41 (s,2H), 6.82-7.41 (m, 7H)

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 108.3, 116.3, 121.5, 123.7, 124.7, 125.2, 127.2, 129.1, 132.6, 143.2

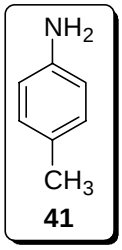
Compound 41

Yield 0.15 g (28%)

IR (Neat) (cm^{-1}) 3371, 3292, 1257

^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm): 2.21 (s, 3H), 4.29 (s, 2H), 6.51-6.98 (m, 4H)

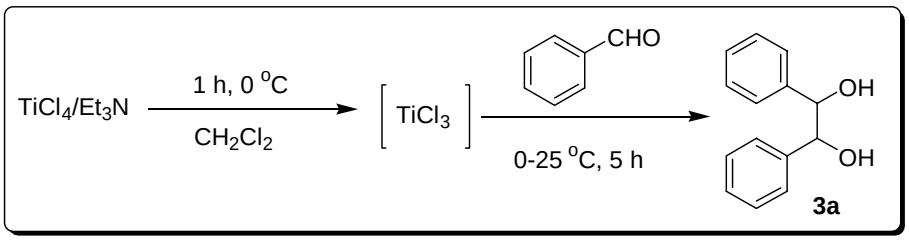
^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 17.3, 116.3, 127.8, 129.3, 147.4



41

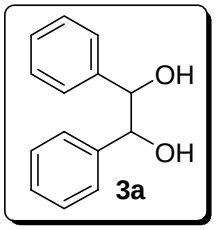
3.4.3 Procedure for the preparation of 1,2-diaryl 1,2-diols from aromatic aldehydes using the $TiCl_4/Et_3N$ reagent system

In dichloromethane (35 mL), $TiCl_4$ (1.9 g, 1 mL, 10 mmol) and Et_3N (1.5 g, 2.1 mL, 15 mmol) were taken at 0 ^{o}C under N_2 and stirred for 1 h. To this benzaldehyde **2a** (0.52 g, 0.5 mL, 5 mmol) was added and the reaction mixture was stirred further at 25 ^{o}C for 5 h. Saturated NH_4Cl 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 X 15 mL). The combined organic extract 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 using ethyl acetate/hexane (85:15) as eluent. The 1,2-diphenylethane-1,2-diol **3a** was isolated in 71% yield.



3a

Compound 3a



Yield 0.15 g (71%)

mp 118 ^{o}C[50]

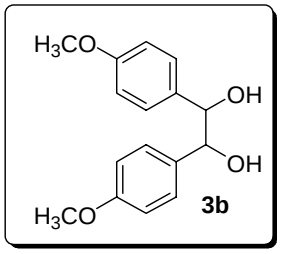
IR (KBr) (cm^{-1}) 3416, 3051, 3028, 2916

^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm): 2.91 (s, broad, 2H), 4.72 (s, 2H, *dl*), 4.8 (s, 2H, *meso*), 7.11-7.35 (m, 10H)

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 78.2, 127.3, 127.4, 128. 7, 139.8

The same procedure was followed using other aromatic aldehydes. The results are given below.

Compound 3b



Yield 0.16 g (62%)

dl:*meso* 67:33[50]

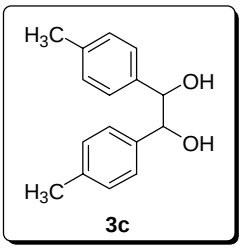
IR (KBr) 3375, 29591720, 1602, 1510

^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm): 2.82 (s, 2H), 3.73 (6H), 4.72 (s, 2H, *dl*), 4.89 (s, 2H, *meso*), 7.06-7.32 (m, 8H)

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 56.7, 84.5, 114.6, 128.7, 133.3, 158.7

dl:*meso* 63:27

Compound 3c



Yield 0.15 g (61%)

dl:*meso* 100:0

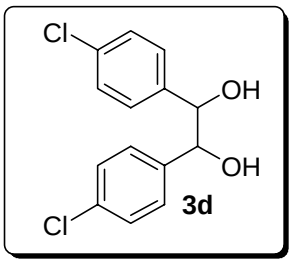
mp 160-161 ^{o}C[50]

IR (KBr) (cm^{-1}) 3368, 3037,1618, 1467, 1021, 694

^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm) 2.30 (s, 6H), 2.8 (s, 2H), 4.68 (s, 2H, *dl*), 7.10-7.25 (m, 8H)

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 20.9, 82.3, 128.9, 131.8, 136.9, 138.6

Compound 3d



Yield 0.16 g (58%)

dl:*meso* 83:17

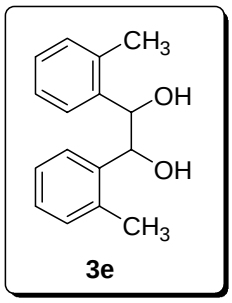
mp 152-154 ^{o}C Lit[50]

IR (KBr) (cm^{-1}) 3323, 3060, 3029, 2912

^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm) 3.05 (s, broad, 2H), 4.60 (s, 2H, *dl*), 4. 85 (s, 2H, *meso*), 7.12-7.32 (m, 8H)

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 82.3, 128.5, 130.8, 134.3, 137.4

Compound 3e



Yield 0. 15 g (63%)

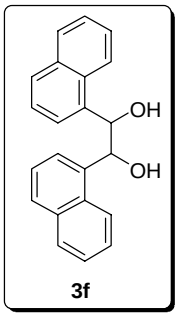
dl:*meso* 75:25

IR (KBr) (cm^{-1}) 3366, 3032, 1621,1459, 1021, 678

^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm): 1.71 (s, 6H), 2.92 (s, broad, 2H), 5.0 (s, 2H, *dl*), 5.15 (s, 2H, *meso*), 6.81-7.71 (m, 8H)

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 21.3, 87.3, 126.6, 128.2, 129.1, 129.9, 137.3, 138.6

Compound 3f



3f

Yield 0.18 g (58%)

dl:*meso* 83:17

IR (KBr) (cm^{-1}) 3414, 3317, 1618, 1402, 1060, 773, 613.

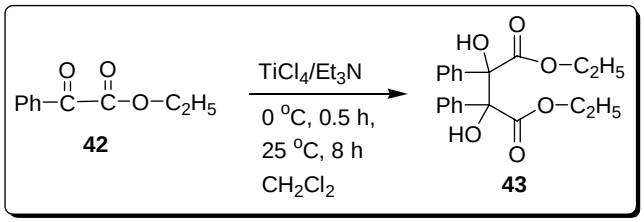
^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm): 3.74 (2H), 5.39 (2H), 6.87 (t, 1H, J = 7.2 Hz), 7.12-7.65 (10H), 7.87-7.89 (2H), 7.96-7.99 (2H)

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 82.3, 123.7, 123.9, 124.6, 126.7, 127.2, 127.3, 129.7, 135.5, 137.6, 147.9

3.4.4 Procedure for the pinacol coupling of α-ketoester using the $TiCl_4/Et_3N$ reagent system

Dichloromethane (25 mL), α-ketoester **42** (0.9 g, 0.79 mL, 5 mmol) and Et_3N (0.7 g, 0.98 mL, 7 mmol) were taken in a reaction flask under N_2 atmosphere. $TiCl_4$ (0.7 g, 0.98 mL, 5 mmol) was added under N_2 at 0 ^oC. The reaction mixture was stirred for 0.5 h at 0 ^oC and stirred further for 8 h at 25 ^oC. It was quenched with saturated NH_4Cl solution (20 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2 X 25 mL). The combined organic extract was washed with brine solution (10 mL) and dried over anhydrous $MgSO_4$. Solvent was removed and the residue was chromatographed

on a silica gel column using ethyl acetate/hexane (2:98) as eluent to isolate the couple product **43** in 58% yield.



Yield 0.21 g (58%)

IR (KBr) (cm^{-1}) 3468, 2982, 1701, 1496,1452, 1371, 1302, 1259, 1197,856

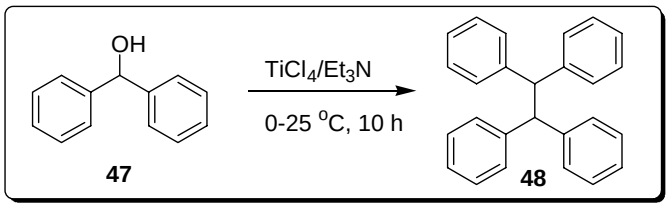
^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm) 1.26-1.33 (m, 6H), 4.34 (m, 4H), 4.91 (s, 2H), 7.12-7.24 (m, 10H) **(Spectrum No. 70)**

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 13.92, 62.7, 82.0, 126.9, 127.31, 128.5, 135.0, 175.5 Lit.[51] **(Spectrum No. 71)**

3.4.5 Procedure for the preparation of tetraphenylethane from diphenylmethanol using the $TiCl_4/Et_3N$ reagent system

Dichloromethane (25 mL) diphenylmethanol **47** (0.37 g, 2 mmol) and Et_3N (0.4 g, 0.55 mL, 4 mmol) were taken in a reaction flask under N_2 atmosphere. $TiCl_4$ (0.76 g, 0.4 mL, 4 mmol) was added under N_2 at 0 ^{o}C. The reaction mixture was stirred for 10 h at 0-25 ^{o}C. It was quenched with saturated NH_4Cl solution (20 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2 X 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 using hexane as eluent to isolate the product tetraphenylethane **48** in 48% yield.



Yield 0.17 g (48%)

IR (Neat) (cm^{-1}) 3714, 1789,789

^{1}H-NMR (200 MHz, $CDCl_3$, δ ppm): 4.69 (s, 2H), 6.70-7.29 (m, 20H)

^{13}C-NMR (50 MHz, $CDCl_3$, δ ppm): 56.4, 125.8, 128.3, 18.41, 143.5. Lit[52] **(Spectrum No. 72)**

3.4.6 Asymmetric pinacol coupling of benzaldehyde using (*R*)-(+)-BINOL in the presence of the $TiCl_4/Et_3N$ reagent system

To a DCM solution (25 mL) of (*R*)-(+)-BINOL **50** (0.27 g, 1.1 mmol) and $TiCl_4$ (0.2 mL of 1:1 solution of $TiCl_4$/toluene, 1 mmol) at 0 °C was added under nitrogen atmosphere. Et_3N (0.3 g, 0.4 mL, 3 mmol) was added and stirred for 15 min. Benzaldehyde **2a** (0.4 g, 0.4 mL, 4 mmol) was added and the mixture was stirred for another 15 min at 0 °C. Zinc dust (0.24 g, 4 mmol) was added and the mixture was brought to room temperature and stirred for 6 h. It was filtered to remove the insoluble materials and the filtrate was added to the 20 mL of 2N HCl, ether (50 mL) and THF (5 mL). After stirring for 30 min the organic layer was separated and the aqueous layer was extracted with ether (2 X 50 mL). The combined organic layer was washed with brine solution, dried over anhydrous Na_2SO_4,

concentrated and subjected to chromatography using on a silica gel column. A 0.33 g of **3a** was obtained using ethyl acetate/hexane (15:85) as eluent.

Yield 0.132 g (62%)

dl : meso 62 : 38

$[\alpha]_D^{25}$ (+) 57.7 (*c* 0.26*, EtOH) {lit.[53] for 100% ee $[\alpha]_D^{25}$: +94.5. (*c* 0.998, EtOH)}

The ee is 61% (approx,* excluding the meso isomer present in the mixture).

3.4.7 Procedure for the preparation of diastereoselective 1,2-diphenylethane-1,2-diol

A reported procedure was followed.[48]

(a) Reduction of benzil using $NaBH_4$/MeOH

Benzil (21 g, 100 mmol) was taken in methanol (150 mL) and cooled to 0 ^oC. Sodium borohydride (4.6 g, 120 mmol) was added in portions to the reaction mixture. The contents were refluxed for 12 h. Methanol was evaporated and the residue was extracted with ethyl acetate (3 X 30 mL). The organic extracts were washed with 3N HCl (5 mL), water, brine and dried over $MgSO_4$. Upon evaporation of the solvent, recemic-1,2-diphenylethane-1,2-diol was obtained.

Yield 18.6 g (87%)

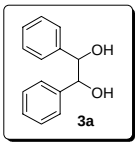
(b) Conversion of the *meso-dl* mixture to *dl* 1,2-diphenylethane-1,2-diol

Finely powdered mixture of 1,2-diphenylthane-1,2-diol (16.6 g, 77 mmol) and potassium hydroxide (60 g) were taken in a round bottom flask. Methanol (15 mL) was added to make a paste. The reaction mixture was rapidly heated at 100-110 ^oC. The pressure was gradually reduced to 15-20 mm of Hg. These conditions (110-115 ^oC/15-

20mm Hg) were maintained for 1 h. The temperature was then raised to 170-180 ^{o}C and heating was continued for another 1 h. The reaction mixture was cooled under vacuum and brought to room temperature and water (30 mL) was added. It was extracted with ether (3 X 30 mL) and the combined ether extract was washed successively with 3N HCl (5 mL), water, brine and dried over $MgSO_4$. Upon evaporation of the solvent and recrystallization from water/MeOH mixture (4:1), *dl* 1,2-diphenylethane-1,2-diol was isolated.

Yield 13.1 g (79.1%)

dl:meso 100:0



3a

3.4.8 Procedure for the diastereoselective duplication of (±)-1,2-diphenylethane-1,2-diol from benzaldehyde using the $TiCl_4/Et_3N/Zn$ reagent system

To a solution of (±)-1,2-diphenylethane-1,2-diol (0.24 g, 1.1 mmol) and $TiCl_4$ {(0.2 mL of 1:1 solution of $TiCl_4$/toluene (1 mmol)} in 25 ml of dichloromethane at 0 ^{o}C was added Et_3N (0.32 mL, 3 mmol) for 15 min under nitrogen atmosphere. Benzaldehyde (0.4 mL, 4 mmol) was added to the reaction mixture and stirred for another 15 min at 0 ^{o}C. Zinc dust (0.24 g, 4 mmol) was added and the mixture was allowed to come to 25 ^{o}C and stirred for further 6 h. The reaction mixture was filtered to remove the insoluble materials and the filtrate was added to the 20 mL of 10% HCl, ether (50 mL) and THF (5 mL). After stirring for 30 min, the organic layer was separated and the aqueous layer was washed with ether (2 X 50 mL) and the combined organic layer was washed with brine solution. The organic layer was dried over anhydrous Na_2SO_4, concentrated and subjected to column chromatography using EtOAc/hexane (15:85) as eluent to isolate 1,2-diol **3a**.

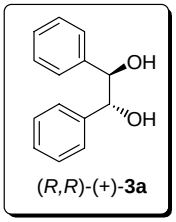
Yield 0.41 g, (92%)

3.4.9 Procedure for the preparation of optically active (*R,R*)-(+)-1,2-diphenylethane-1,2-diol from *trans*-stilbene using the Sharpless asymmetric dihydroxylation process

To a solution of K_2CO_3 (6.2 g, 45 mmol), $K_3Fe(CN)_6$ (14.7 g, 45 mmol), $CH_3SO_2NH_2$ (1.42 g, 15 mmol) in 50 mL of water was added and stirred for 20 min (all the solids completely dissolved). A potassium osmatedihydride [$K_2OSO_2(OH)_4$] (0.011 g, 0.03 mmol) solution in 25 mL of water added to the reaction mixture. To this *trans*-stilbene (2.7g, 15 mmol) dissolved in 55 mL of ^{t}BuOH and added. The mixture was stirred vigorously at 0 ^{o}C for 18 h. Sodium sulfate anhydrous (20 g) was added and the mixture was allowed to warm to room temperature and stirred for 3 h. Ethyl acetate (100 mL) was added to the reaction mixture. After separation of the layers, the aqueous layer was further extracted with ethyl acetate (2 X 50 mL) and the combined organic layer was washed with 2N KOH (20 mL). It was dried over anhydrous $MgSO_4$, concentrated and subjected to column chromatography using silica gel. The (*R,R*)-(+)- 1,2-diphenylethane-1,2-diol was isolated using EtOAc/hexane (15:85) as eluent. The yield of the corresponding 1,2-diol was obtained in 77% yield and 99.9% ee.

Yield 2.47g (77%)

$[\alpha]_D^{25}$ (+) 94.44 (*c* 1.1, EtOH) {lit.[53] for 100% ee $[\alpha]_D^{25}$: +94.5. (*c* 0.998, EtOH)}



(*R,R*)-(+)-**3a**

3.4.10 Procedure for the duplication of (*R,R*)-(+)-1,2-diphenylethane-1,2-diol 3a from benzaldehyde using the $TiCl_4/Et_3N$ reagent system

In DCM (25 mL) solution (*R,R*)-(+)-1,2-diphenylethane-1,2-diol **3a** (0.24 g, 1.1 mmol) and $TiCl_4$ (0.2 mL of 1:1 solution of $TiCl_4$/toluene, 1 mmol) and Et_3N (0.32 mL, 3 mmol) was added under nitrogen atmosphere, stirred for 15 min. Benzaldehyde (0.4 g, 0.4 mL, 4 mmol) was added to reaction mixture and stirred for another 15 min at 0 ^oC. Zinc dust (0.24 g, 4 mml) was added to the reaction mixture, stirred for further 6 h while allowing the reaction mixture to come to the room temperature. The reaction mixture was filtered to remove the insoluble materials and the filtrate was added to the 20 mL of 10% HCl, ether (50 mL) and THF (5 mL). After stirring for 30 min, the organic layer was separated and the aqueous layer was extracted with ether (2 ×50 mL) and the combined organic layer was washed with brine solution. The organic layer was dried over anhydrous $MgSO_4$, concentrated and subjected to column chromatography using silica gel. The (*R,R*)-(+)- 1,2-diphenylethane-1,2-diol was isolated using EtOAc/hexane (15:85) as eluent. The yield of the corresponding 1,2-diol was obtained in 80% yield.

Yield	0.363 g (80%)
dl : meso	95 : 5
$[\alpha]_D^{25}$	(+) 92.5 (*c* 0.38,* EtOH) {lit.[53] for 100% ee $[\alpha]_D^{25}$: +94.5. (*c* 0.998, EtOH)} The ee is 98% (approx,* excluding the meso isomer present in the mixture). The newly formed product (R,R)-1,2-diol yield is 58% with 93% ee.

3.5 References

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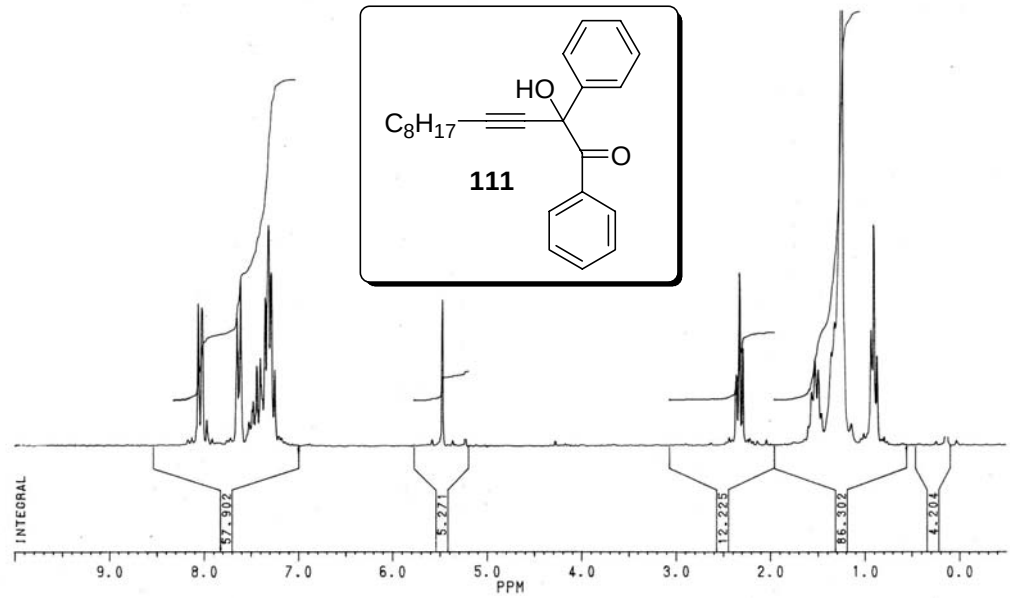
Appendix I

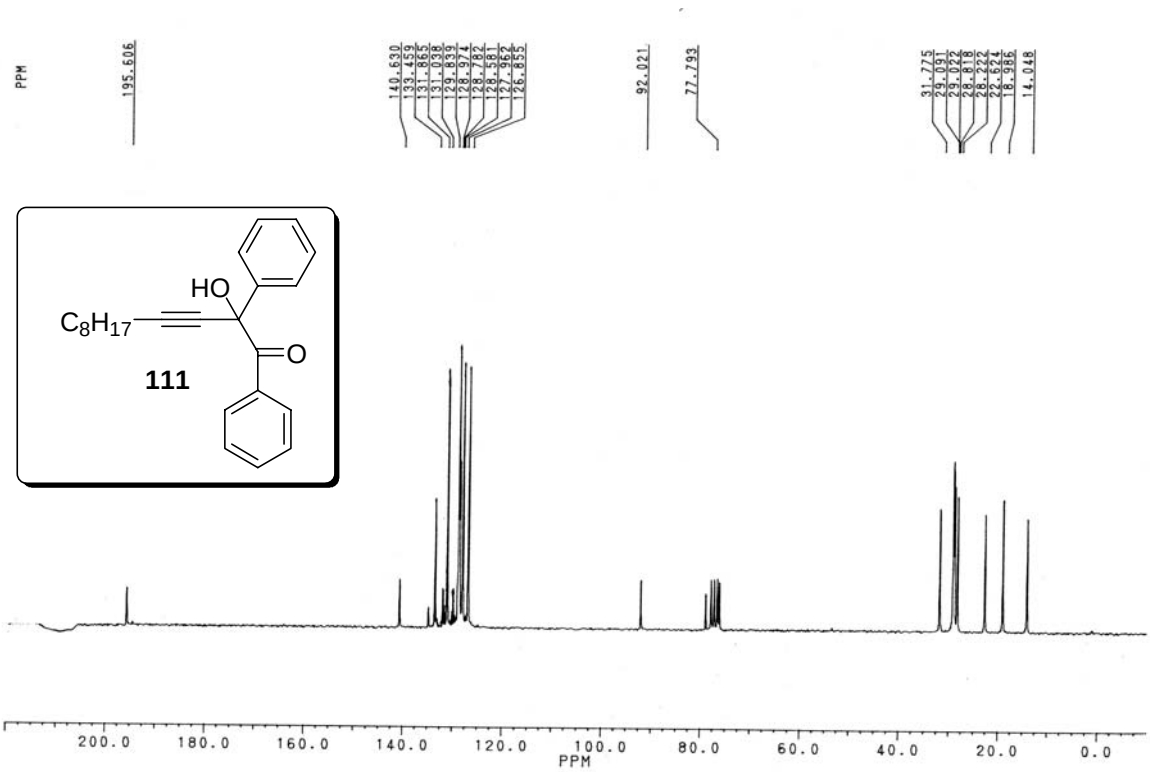
Representative Spectra

Spectrum No. 1 (Chapter 1, Section 1.4.5) ^{1}H NMR Spectrum (200MHz, $CDCl_3$)



ppm

Spectrum No. 2 (Chapter 1, Section 1.4.5) ^{13}C NMR Spectrum (50 MHz,$CDCl_3$)



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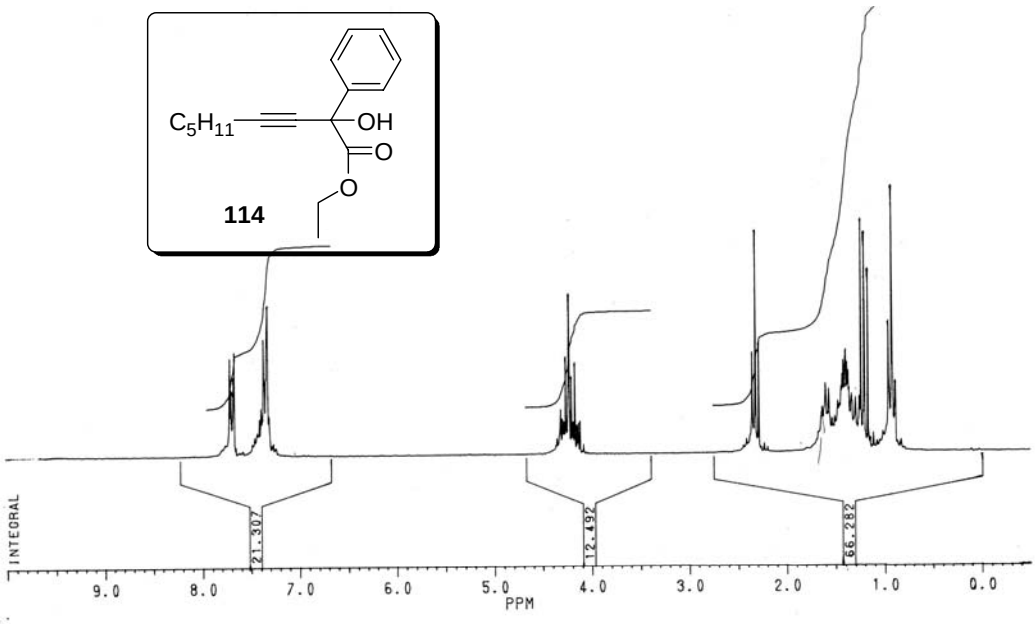
Spectrum No. 3 (Chapter 1, Section 1.4.5) ^{1}H NMR Spectrum (200 MHz, $CDCl_3$)



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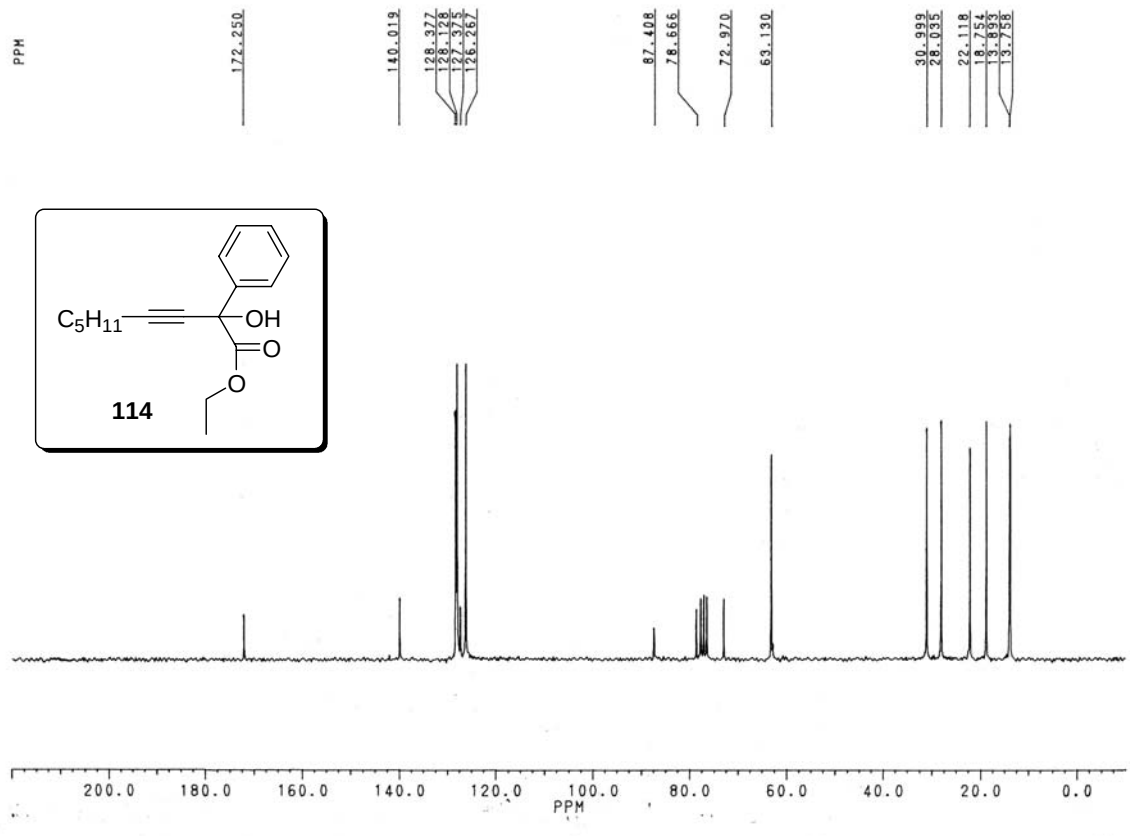
Spectrum No. 4 (Chapter 1, Section 1.4.5) ^{13}C NMR Spectrum (50 MHz,$CDCl_3$)



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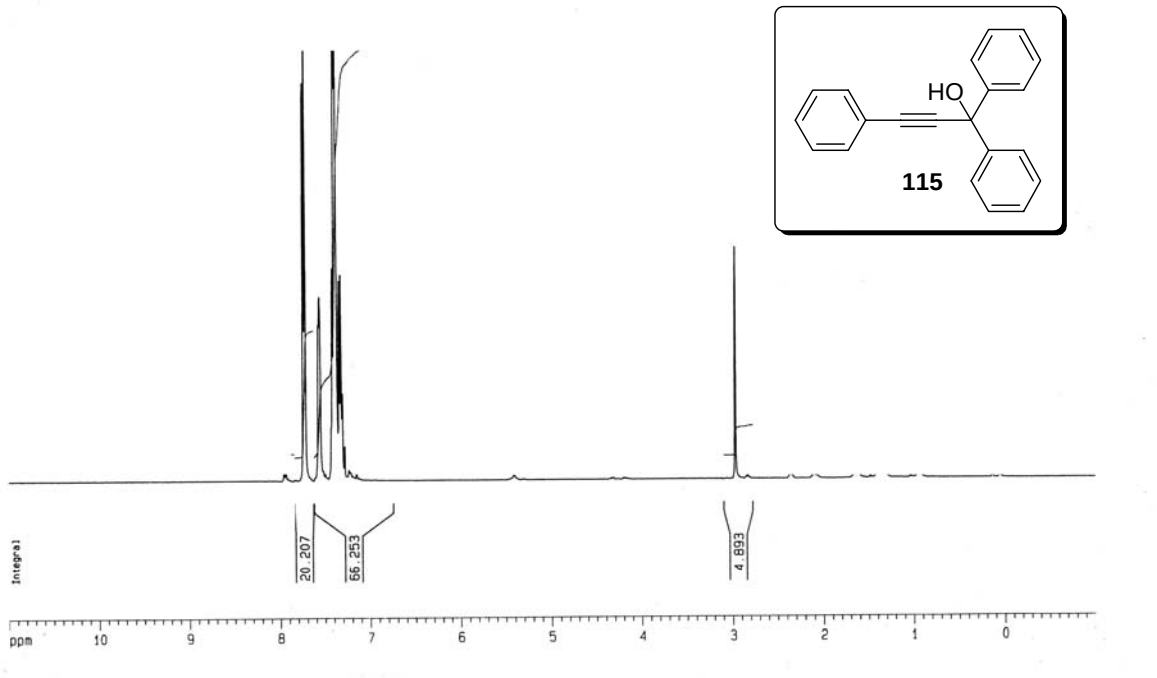
Spectrum No. 5 (Chapter 1, Section 1.4.5) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



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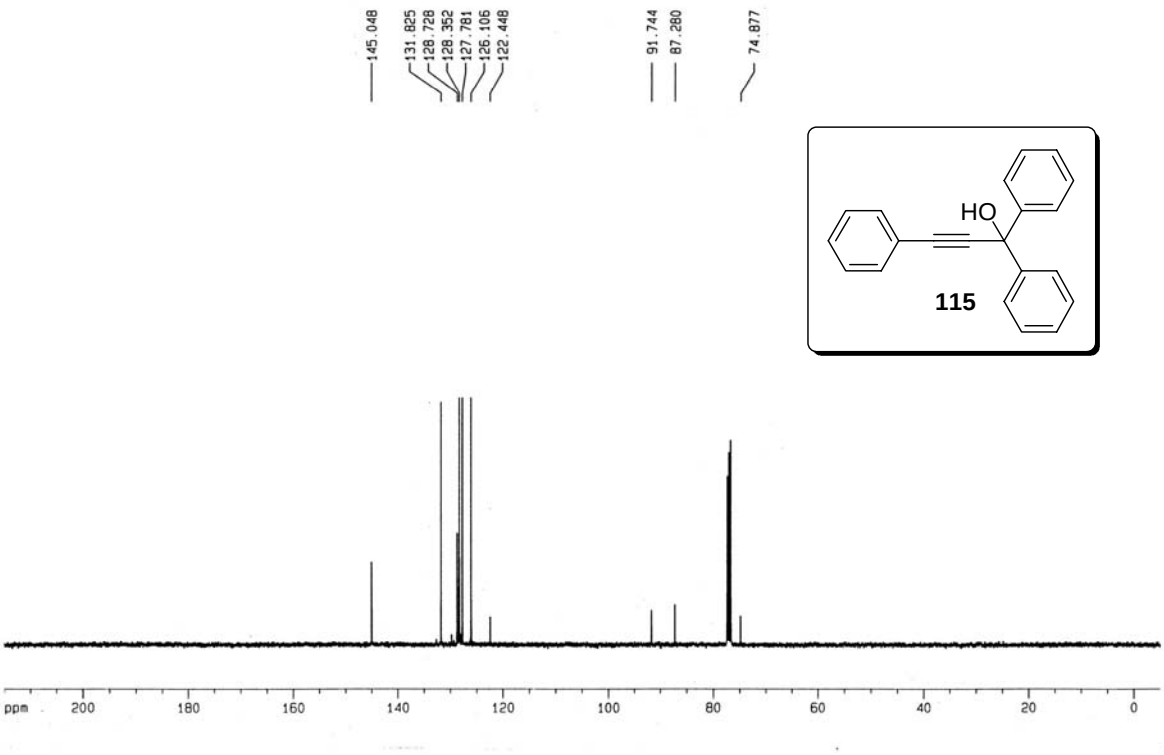
Spectrum No. 6 (Chapter 1, Section 1.4.5) ^{13}C NMR Spectrum (100 MHz,$CDCl_3$)



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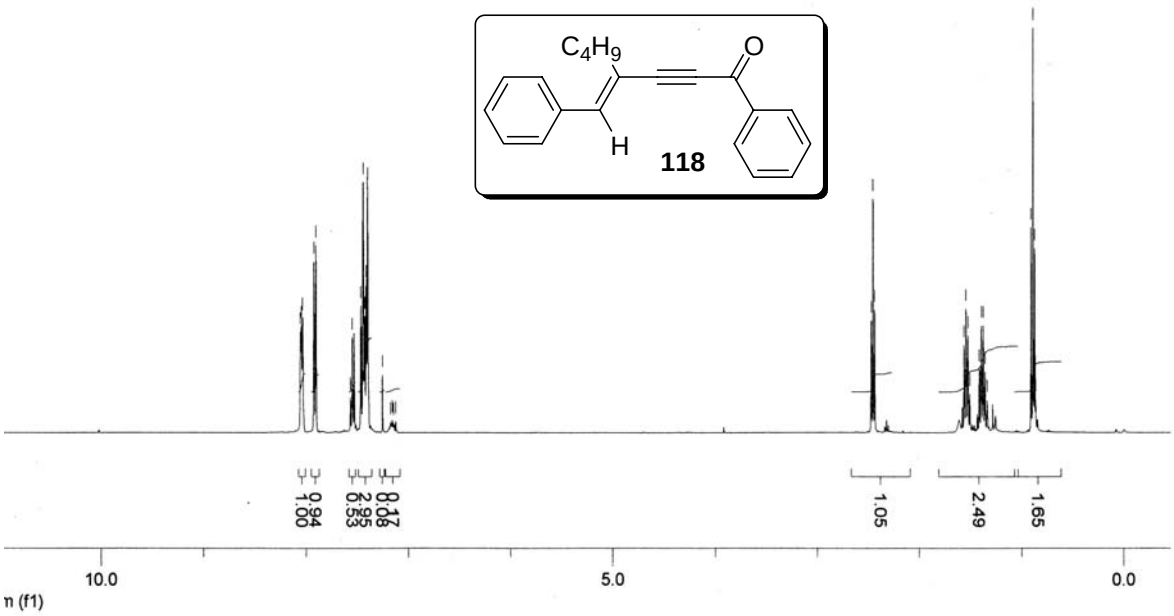
Spectrum No. 7 (Chapter 1, Section 1.4.7) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



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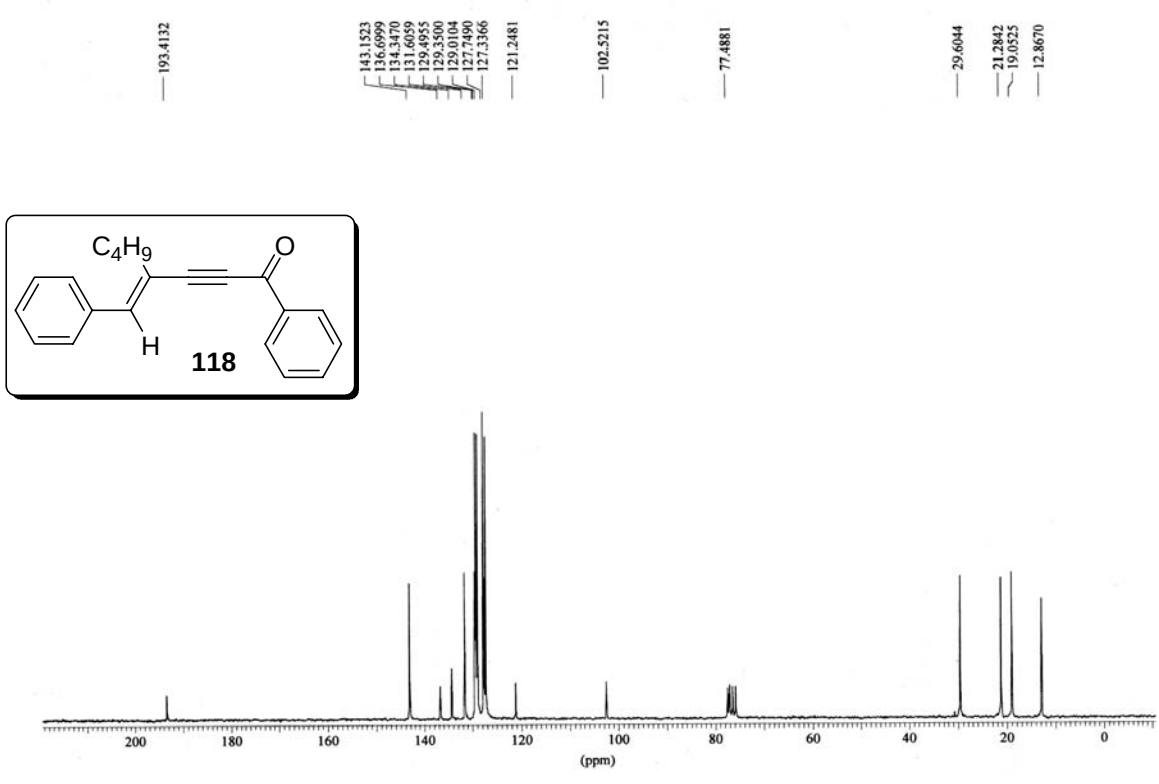
Spectrum No. 8 (Chapter 1, Section 1.4.7) ^{13}C NMR Spectrum (100 MHz,$CDCl_3$)



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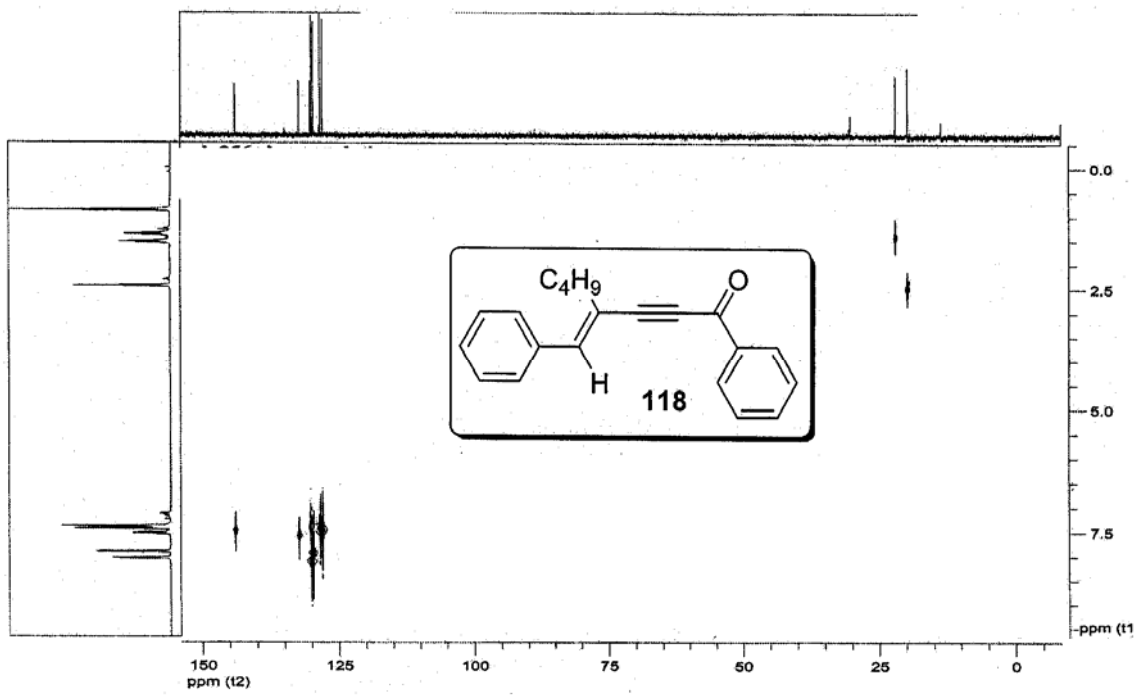
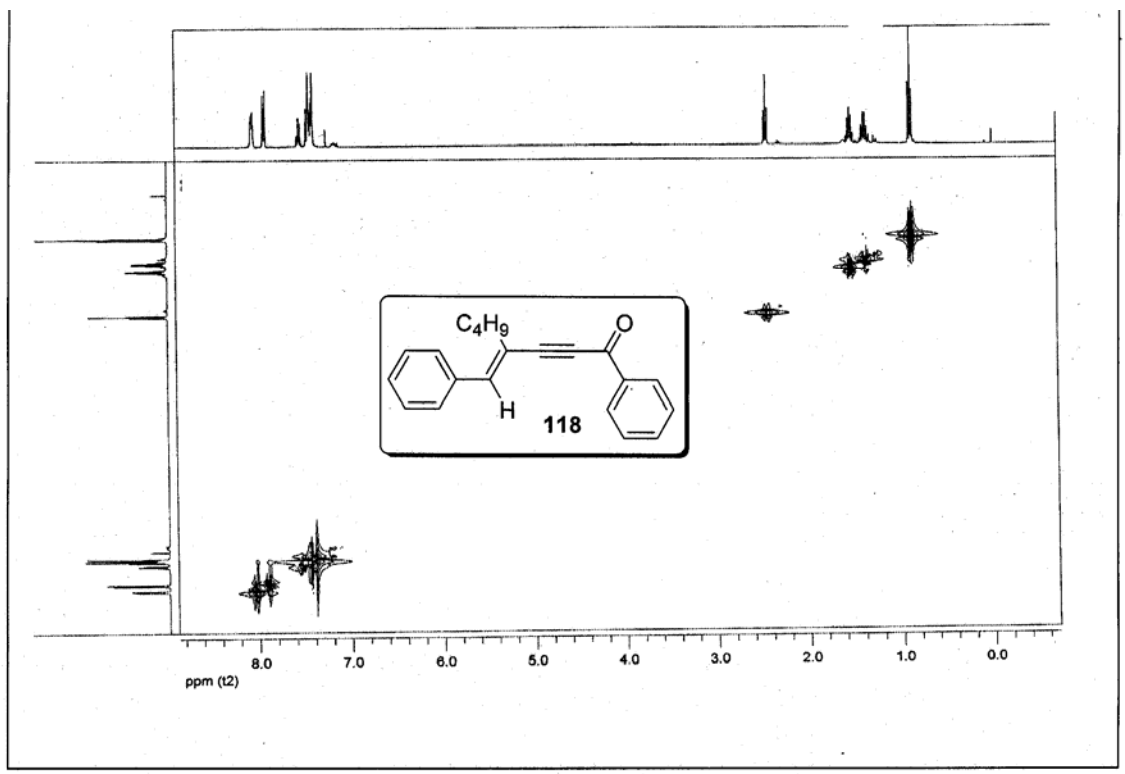
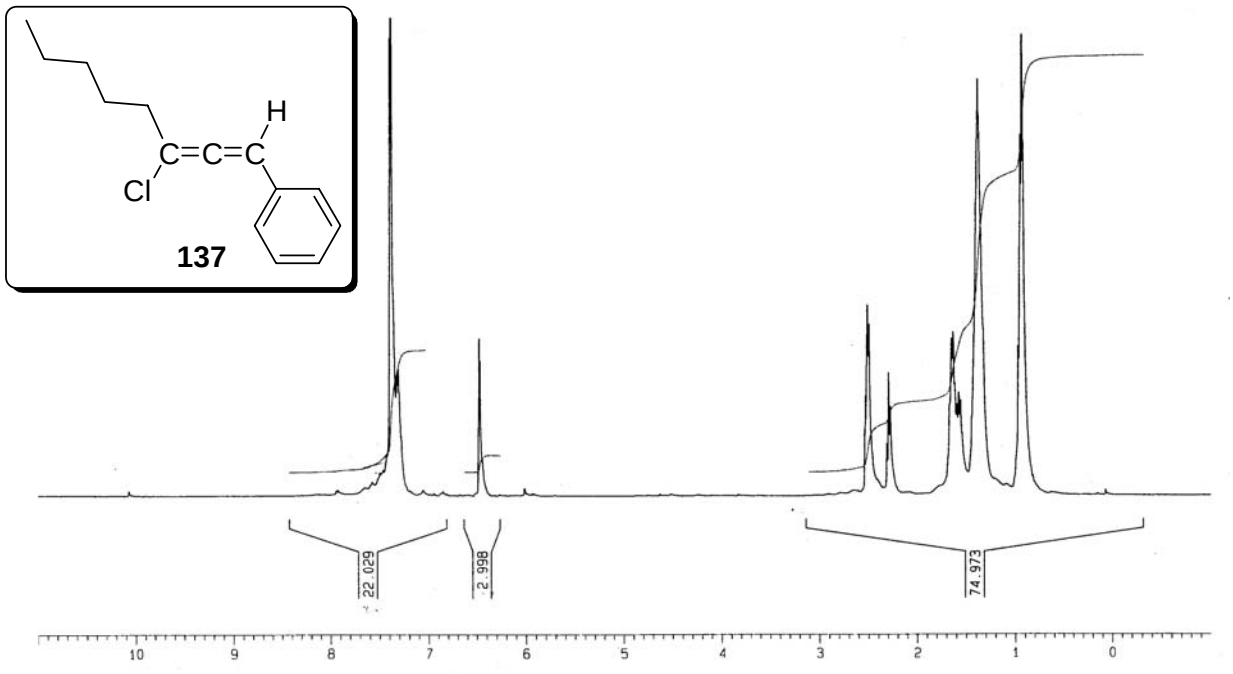
Spectrum No. 9 (Chapter 1, Section 1.4.7) C-H Co-relation COSY NMR Spectrum



Spectrum No. 10 (Chapter 1, Section 1.4.7) NOESY NMR Spectrum (400 MHz,$CDCl_3$)



Spectrum No. 11 (Chapter 2, Section 2.4.2) ^{1}H NMR Spectrum 400 MHz,$CDCl_3$)



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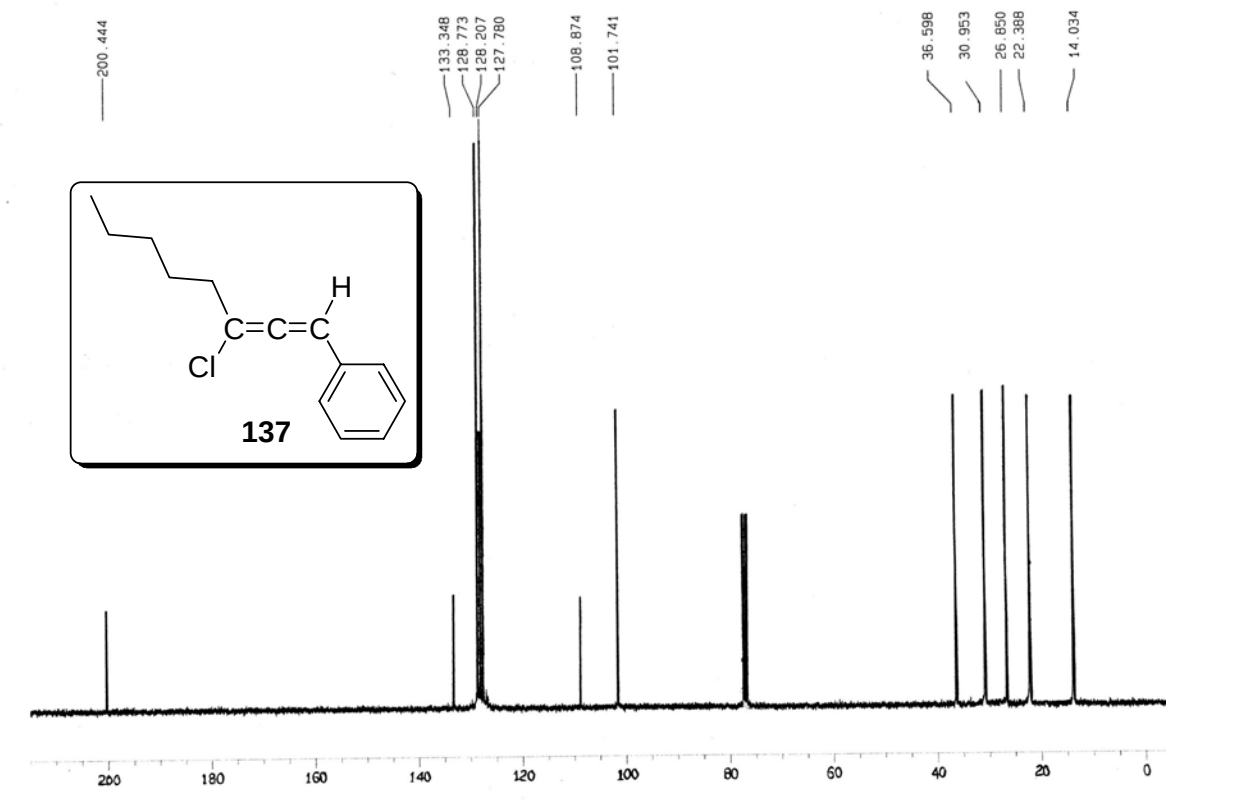
Spectrum No. 12 (Chapter 1, Section 2.4.2) ^{13}C NMR Spectrum (100 MHz,$CDCl_3$)



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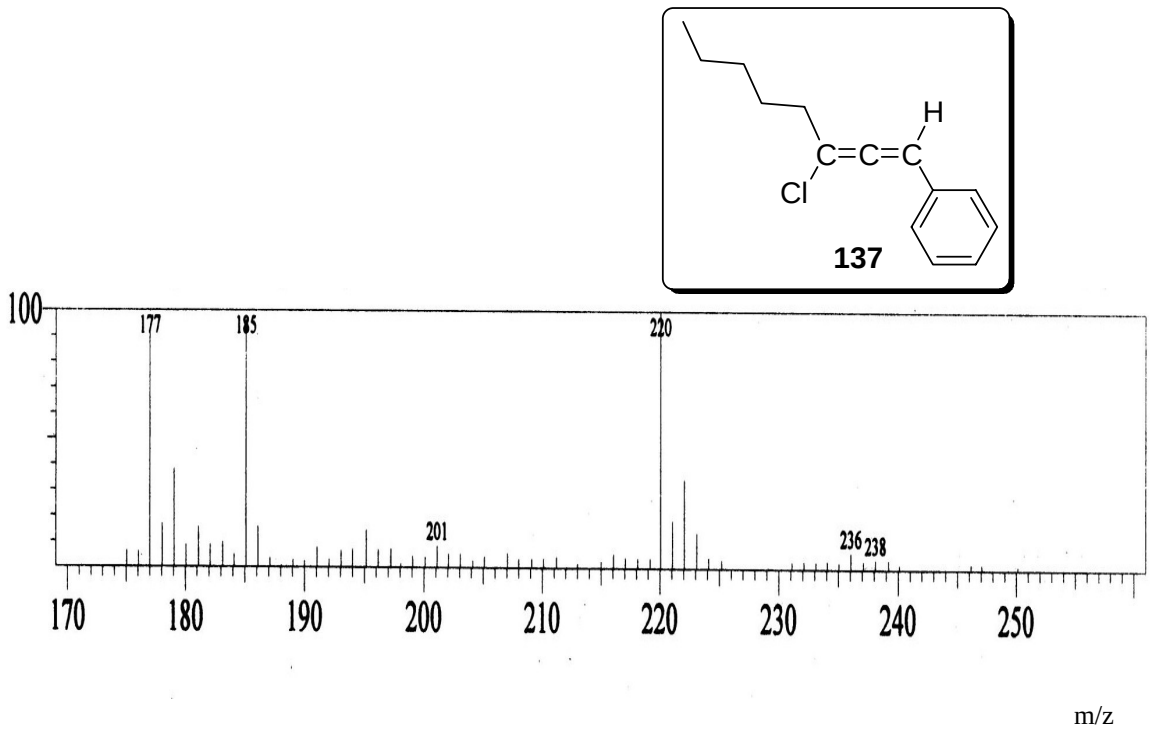
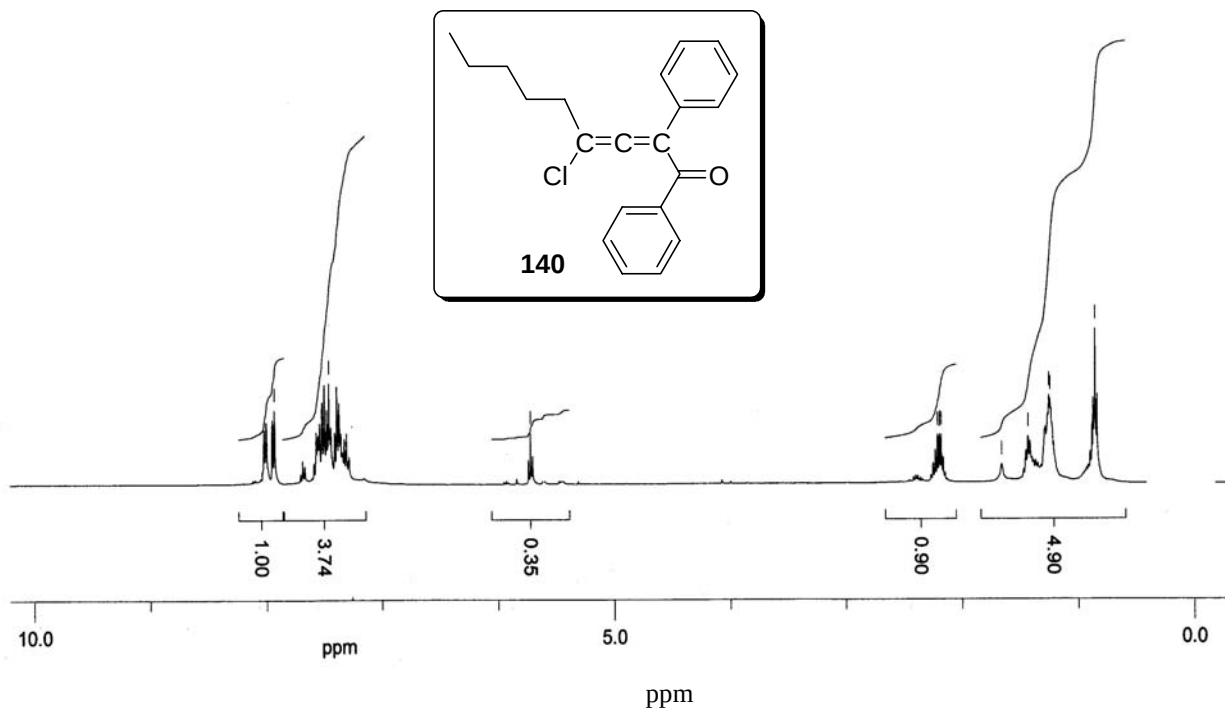
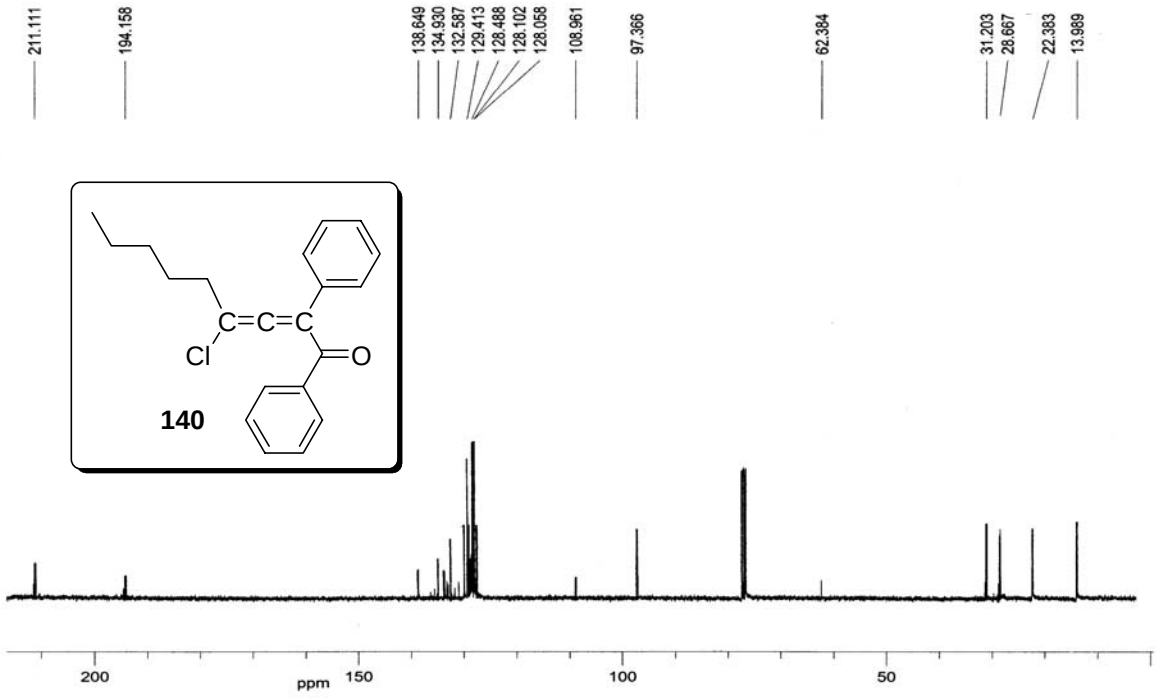
Spectrum No. 13 (Chapter 2, Section 2.4.2) EI Mass Spectrum



Spectrum No. 14 (Chapter 2, Section 2.4.2) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



Spectrum No. 15 (Chapter 2, Section 2.4.2) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



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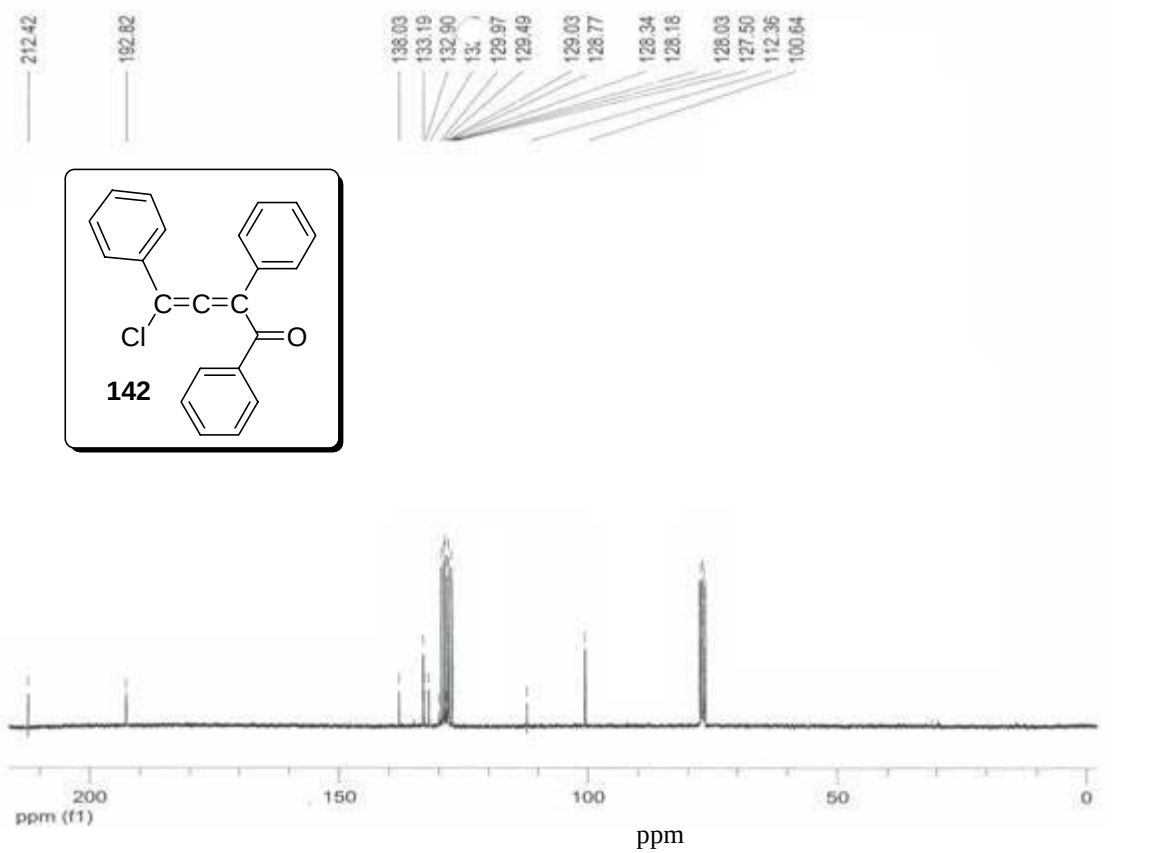
Spectrum No.16 (Chapter 2, Section 2.4.2) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



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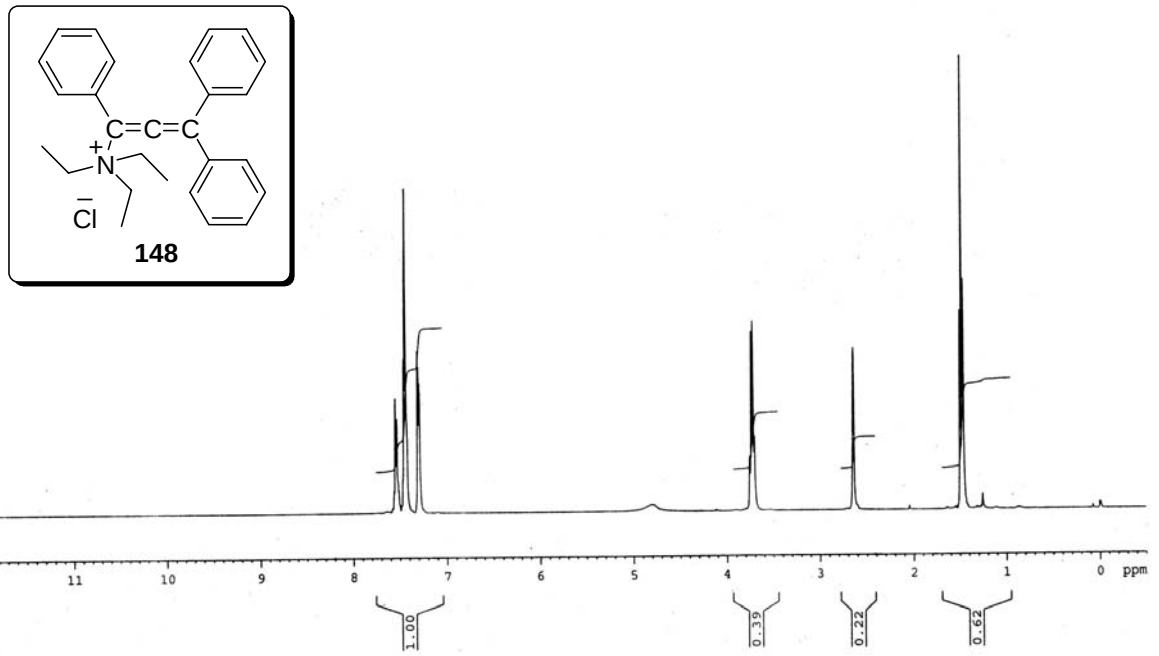
Spectrum No. 17 (Chapter 2, Section 2.4.3) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



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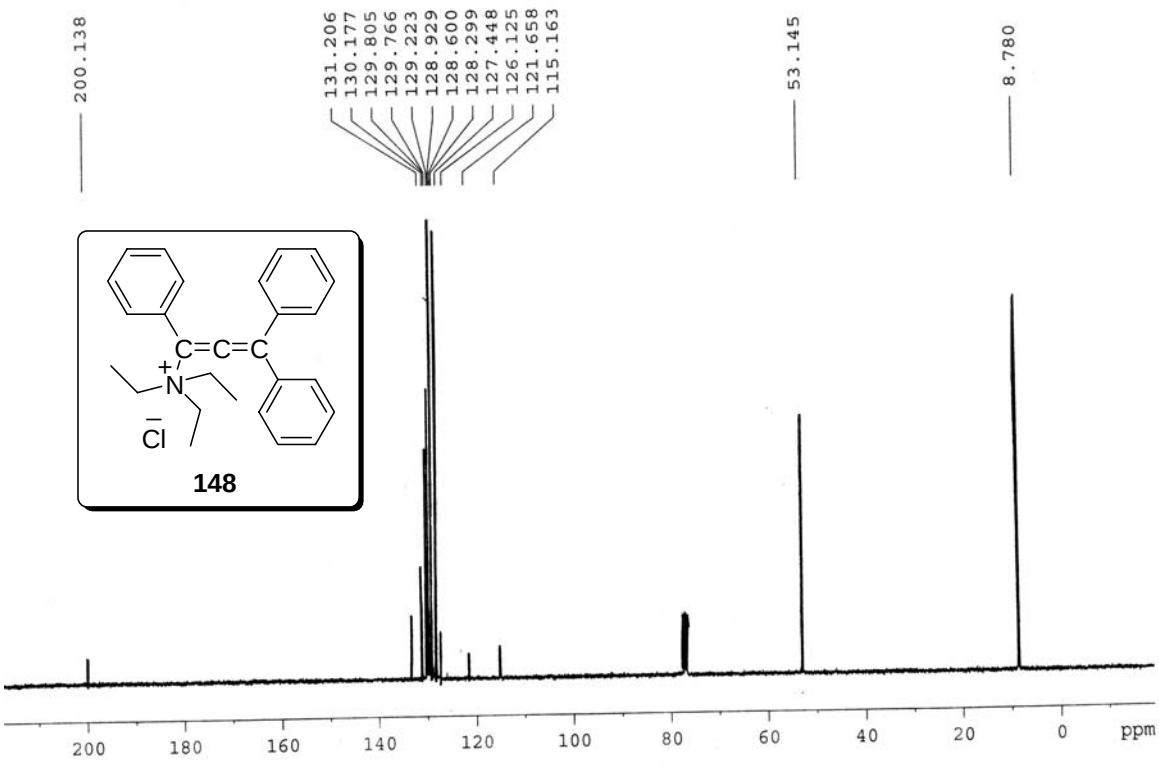
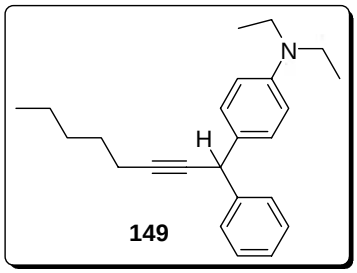
Spectrum No. 18 (Chapter 2, Section 2.4.3) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



Spectrum No. 19 (Chapter 2, Section 2.4.4) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



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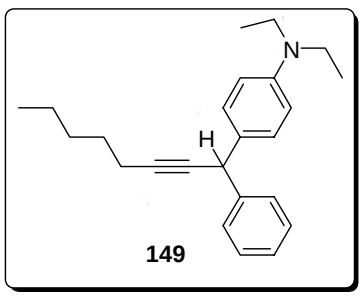
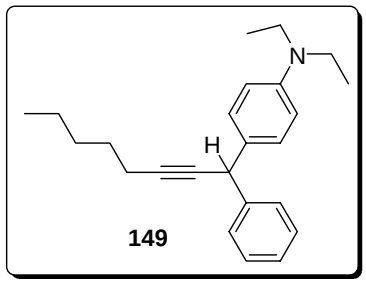
ppm

Spectrum No. 20 (Chapter 2, Section 2.4.4) ^{13}C NMR Spectrum (100 MHz,$CDCl_3$)

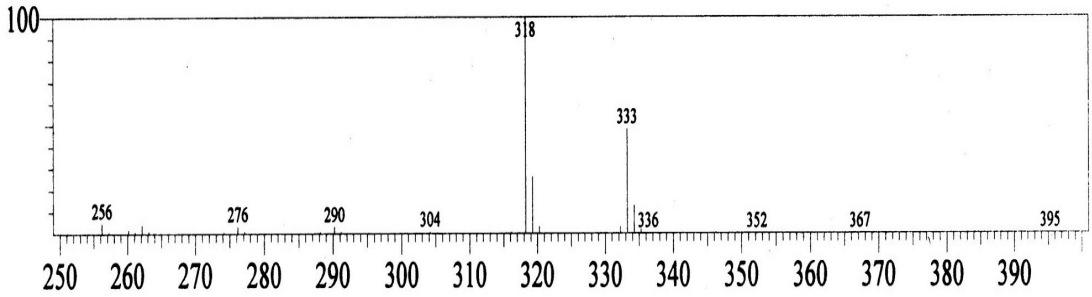


149

Spectrum No. 21 (Chapter 2, Section 2.4.4) EI Mass Spectrum

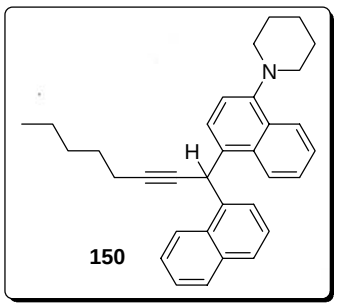


149



m/z

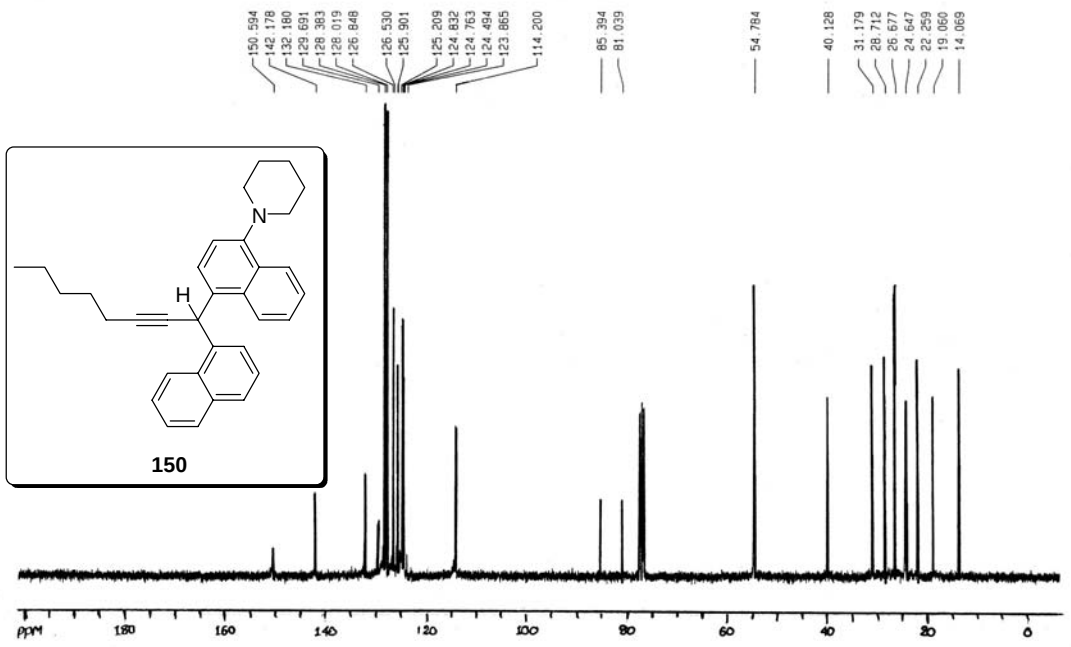
Spectrum No. 22 (Chapter 2, Section 2.4.4) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



150

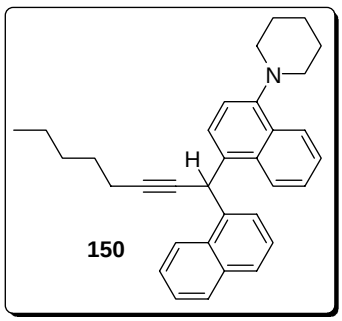
ppm

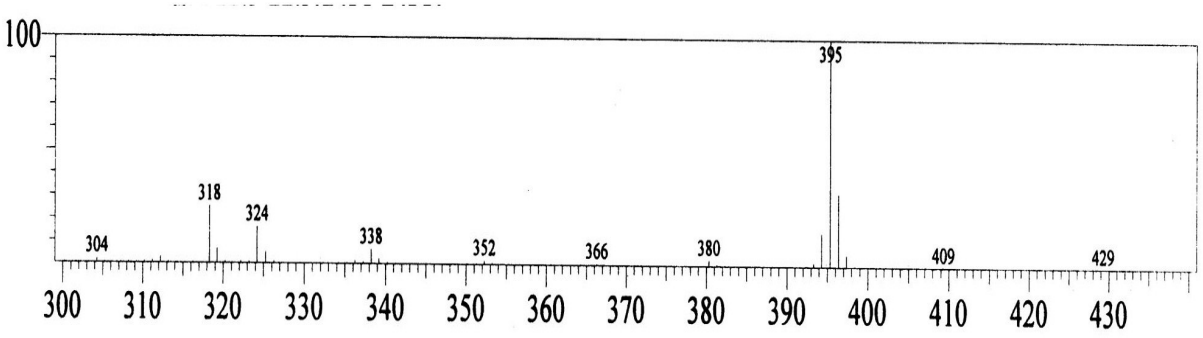
Spectrum No. 23 (Chapter 2, Section 2.4.4) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



ppm

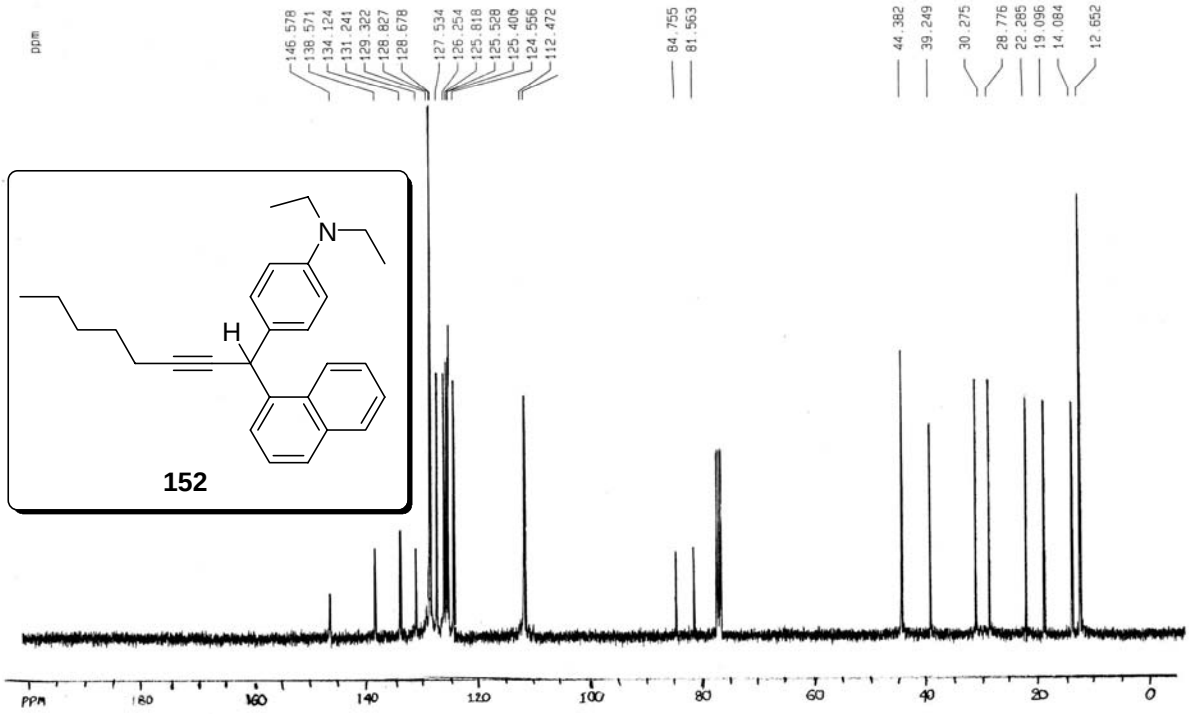
Spectrum No. 24 (Chapter 2, Section 2.4.4) EI Mass Spectrum





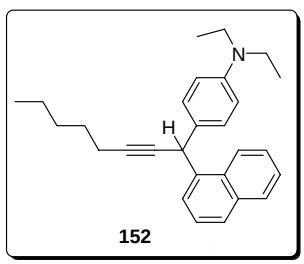
m/z

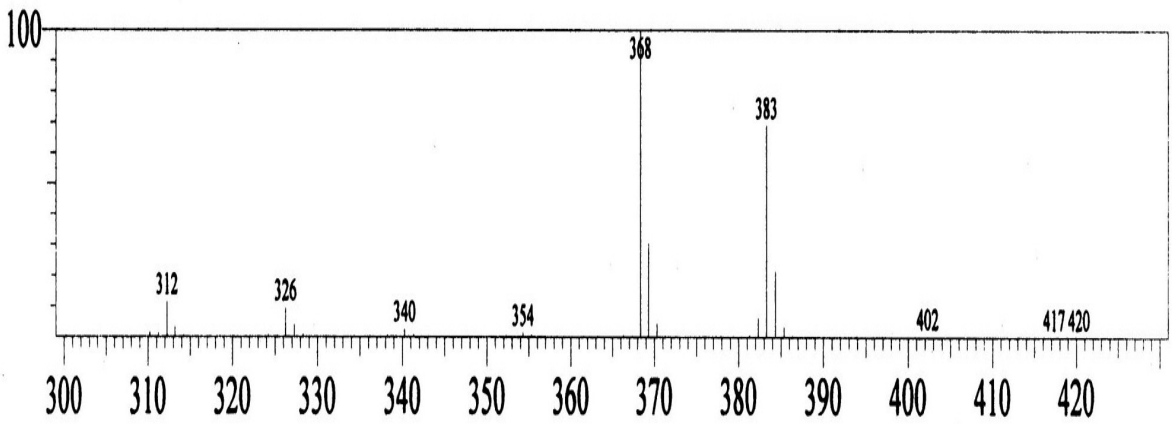
Spectrum No. 25 (Chapter 2, Section 2.4.4) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



ppm

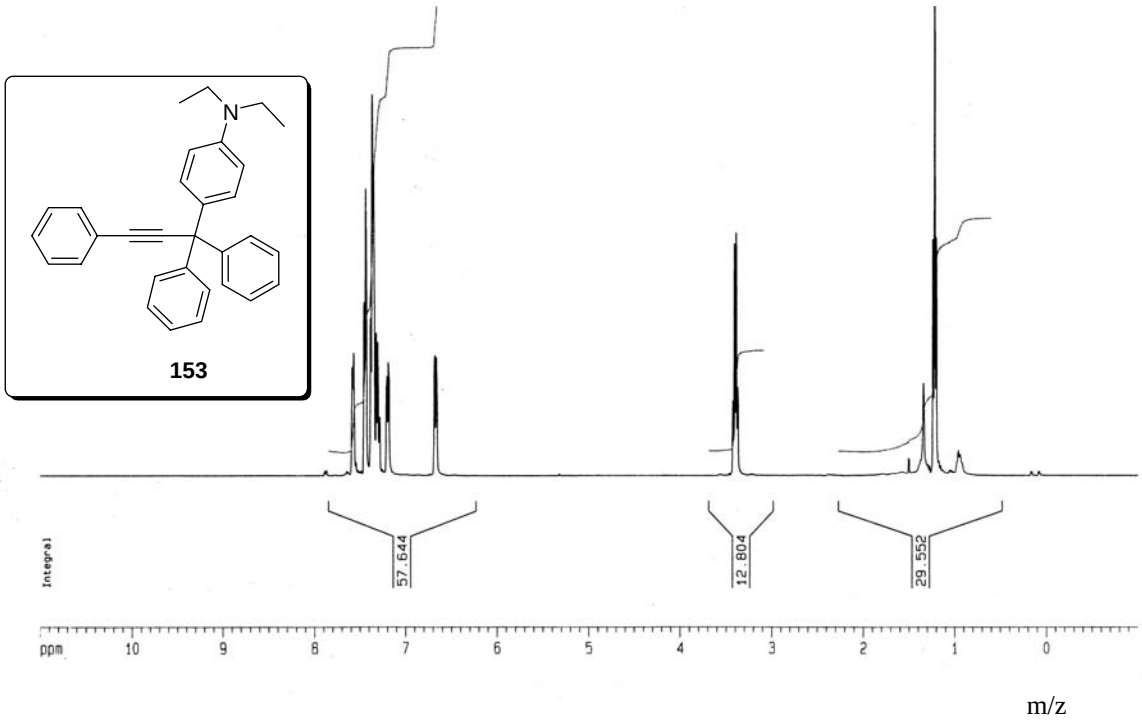
Spectrum No. 26 (Chapter 2, Section 2.4.4) EI Mass Spectrum





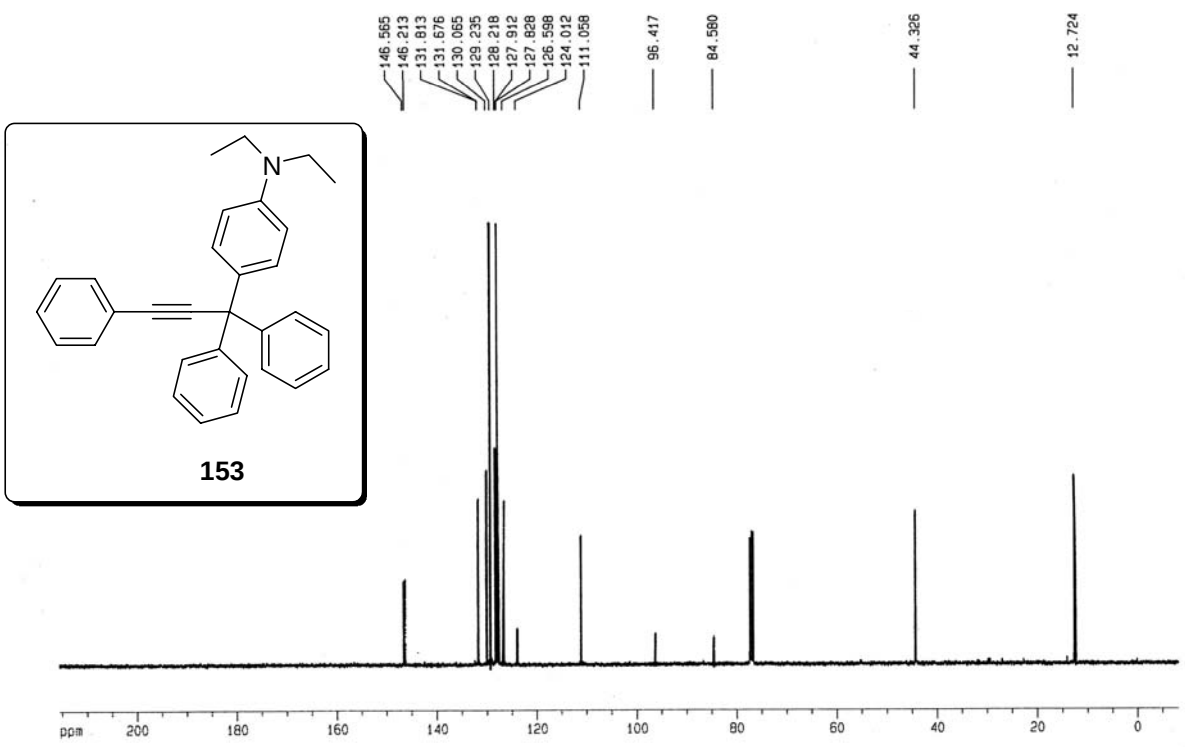
m/z

Spectrum No. 27 (Chapter 2, Section 2.4.4) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



m/z

Spectrum No. 28 (Chapter 1, Section 2.4.4) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



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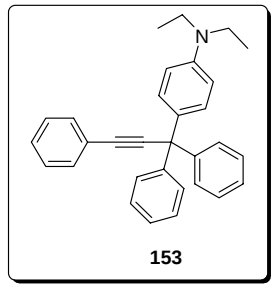
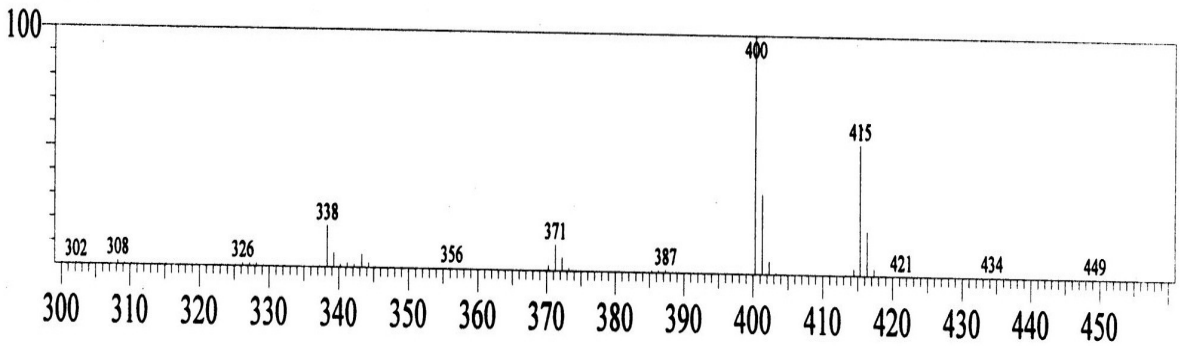
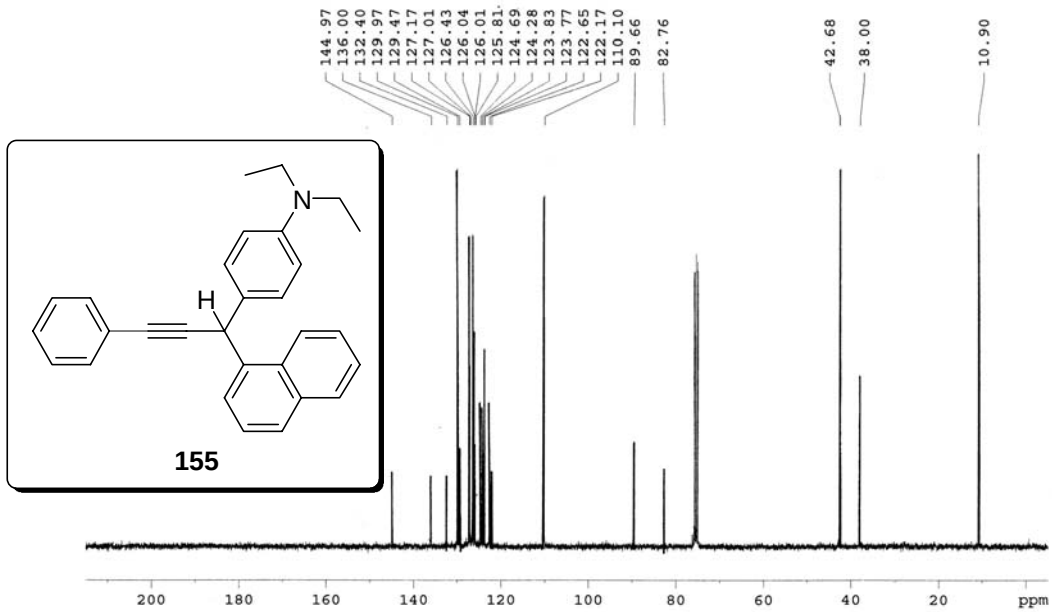
Spectrum No. 29 (Chapter 1, Section 1.4.12) EI Mass Spectrum





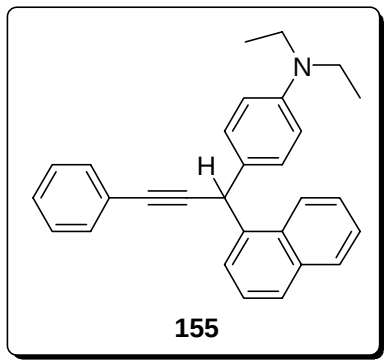
m/z

Spectrum No.30 (Chapter 1, Section 1.4.12) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)

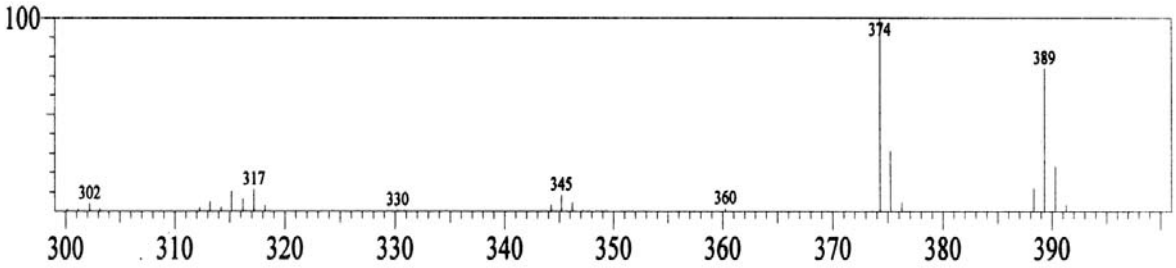


ppm

Spectrum No. 31 (Chapter 2, Section 2.4.4) EI Mass Spectrum

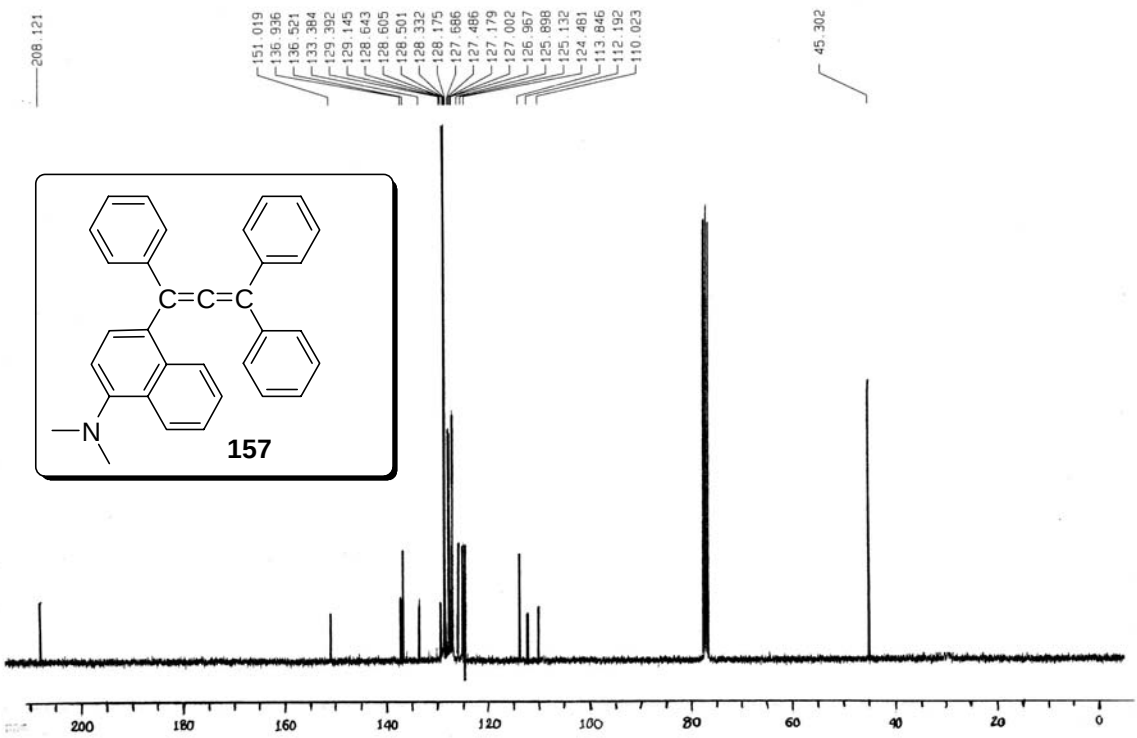


155



m/z

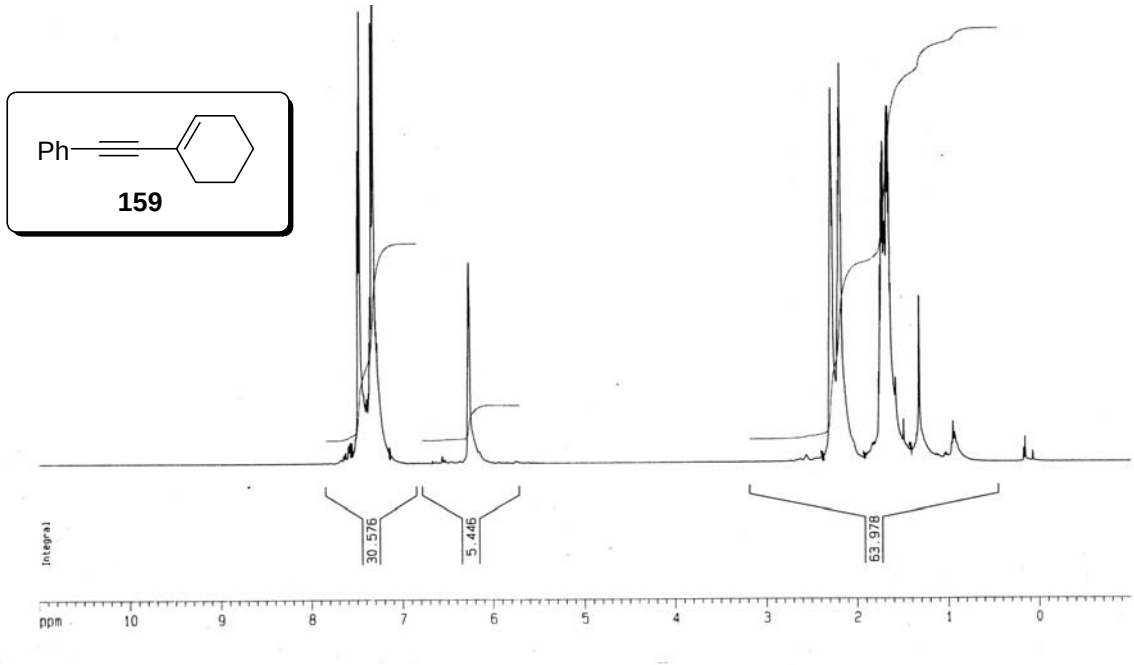
Spectrum No. 32 (Chapter 2, Section 2.4.4) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



157

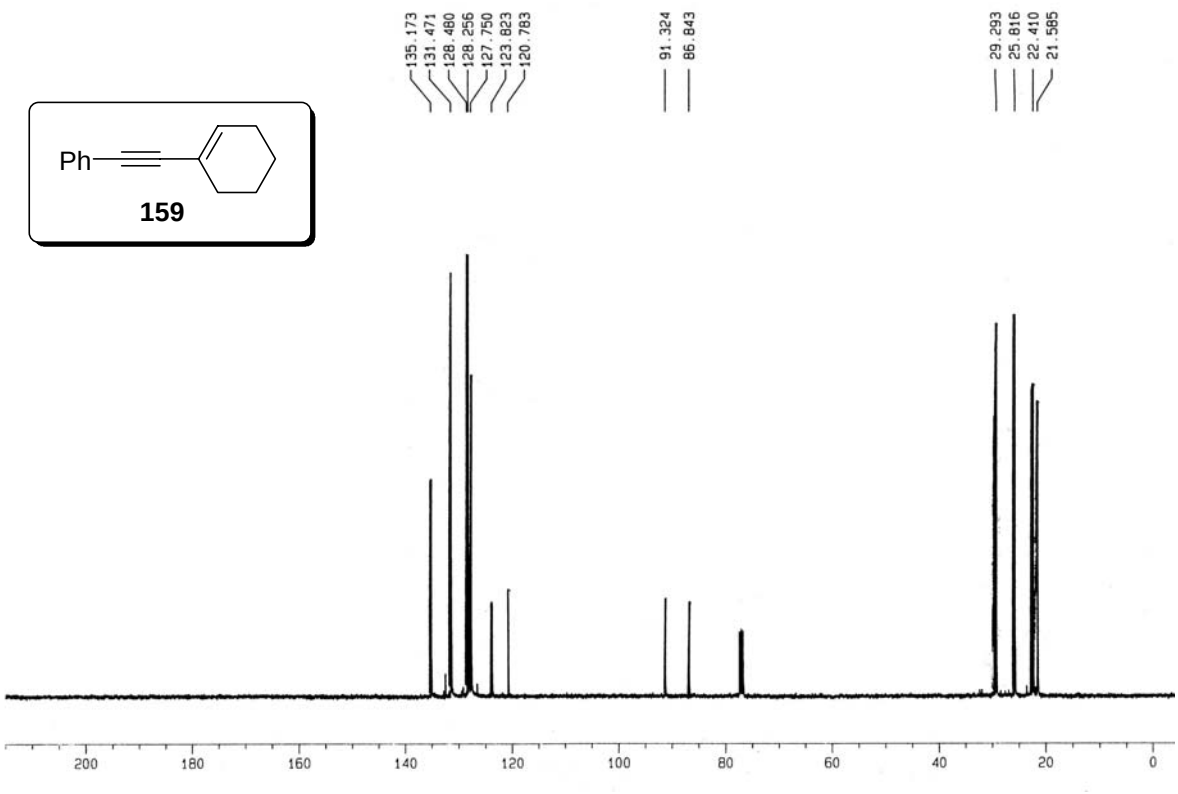
ppm

Spectrum No. 33 (Chapter 2, Section 2.4.4) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



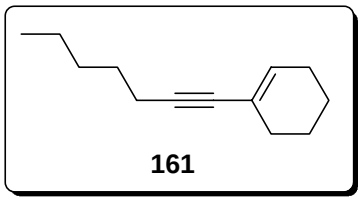
ppm

Spectrum No. 34 (Chapter 2, Section 2.4.4) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



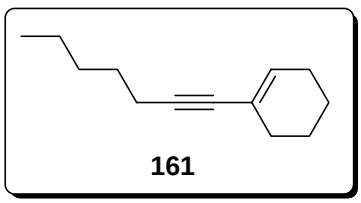
ppm

Spectrum No. 35 (Chapter 2, Section 2.4.5) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



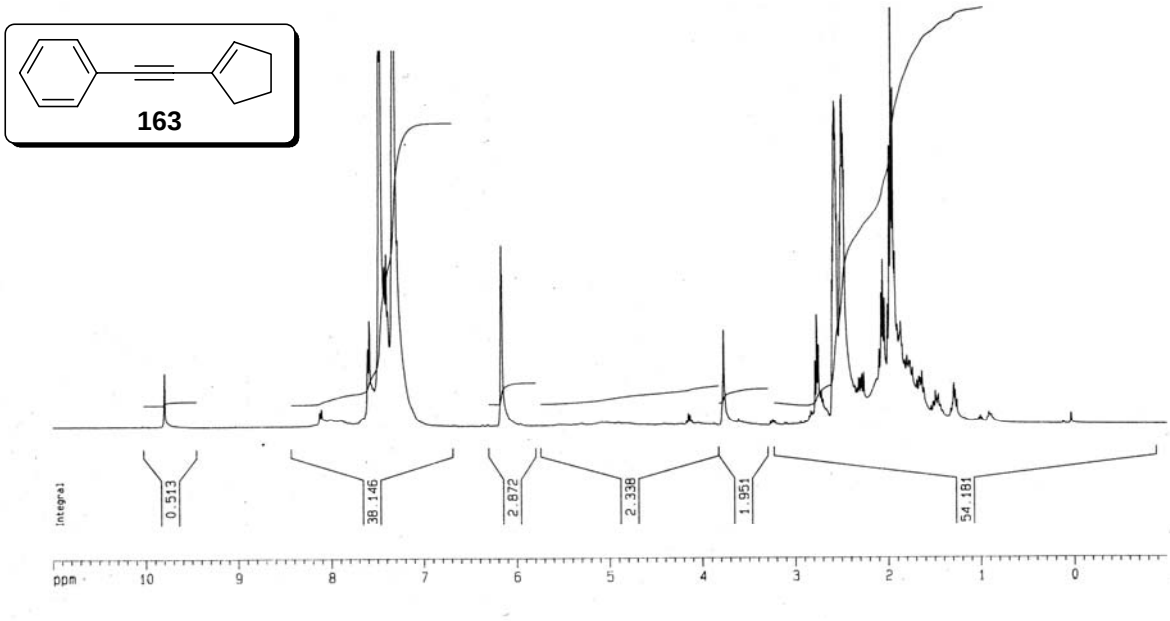
ppm

Spectrum No. 36 (Chapter 2, Section 2.4.5) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



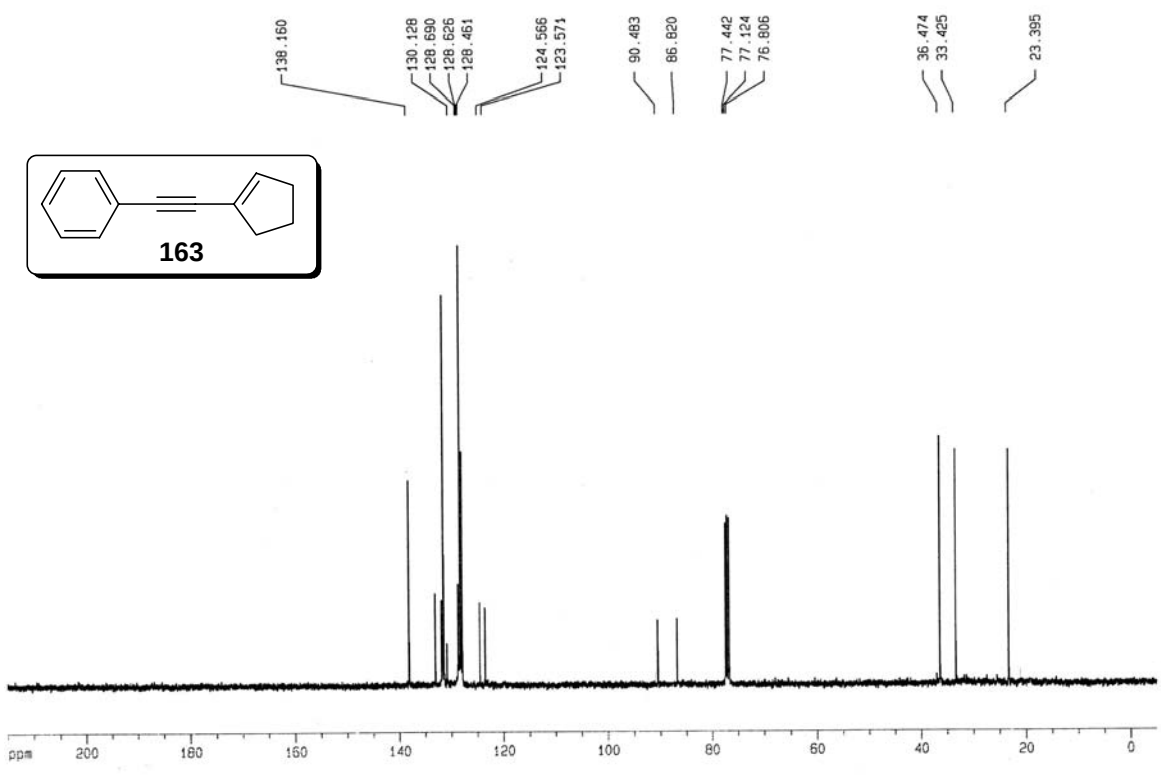
ppm

Spectrum No. 37 (Chapter 2, Section 2.4.5) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



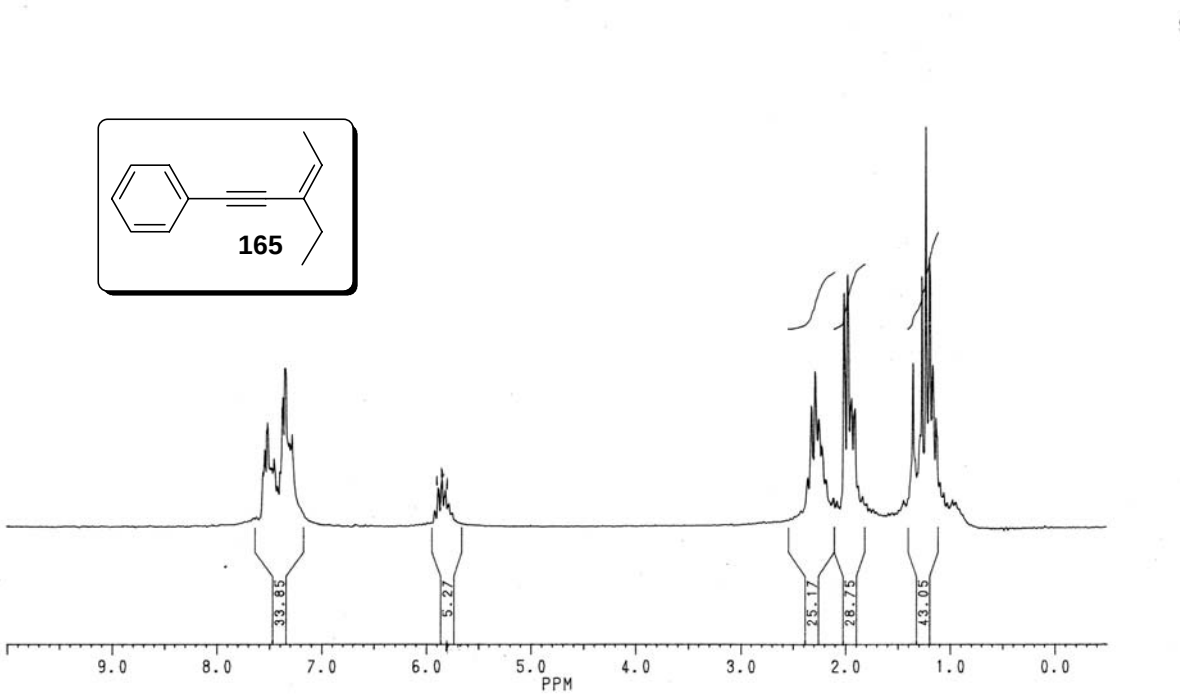
ppm

Spectrum No. 38 (Chapter 2, Section 2.4.5) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



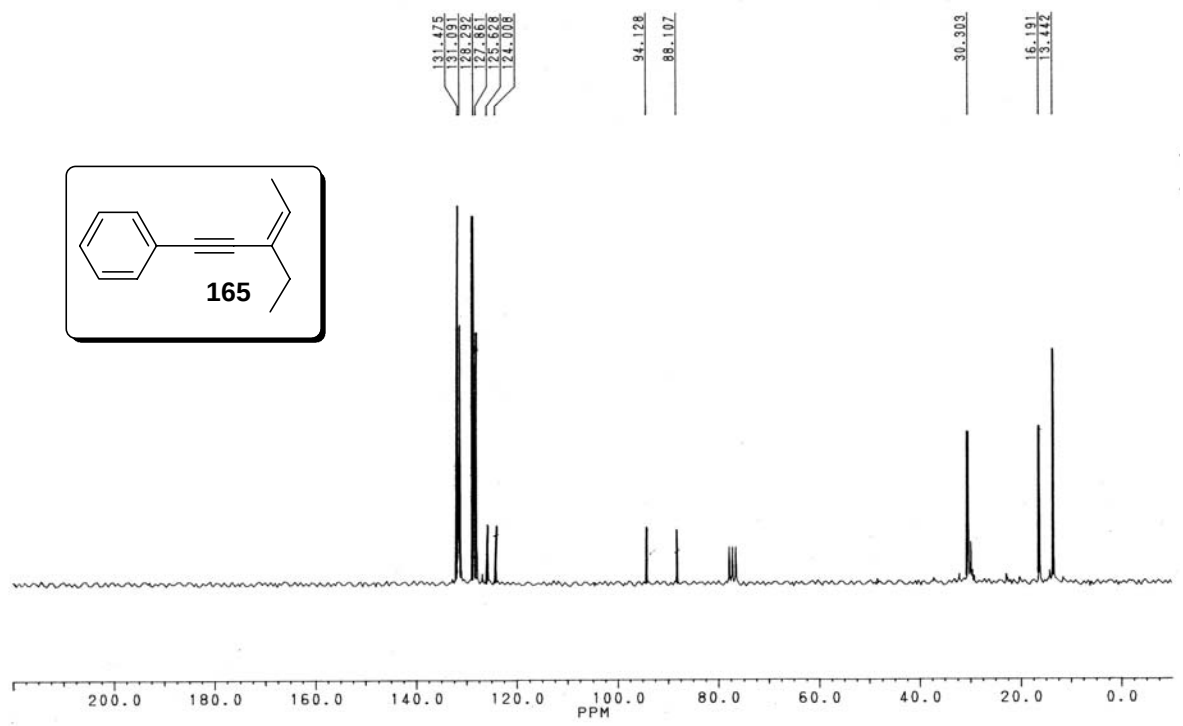
ppm

Spectrum No. 39 (Chapter 2, Section 2.4.5) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



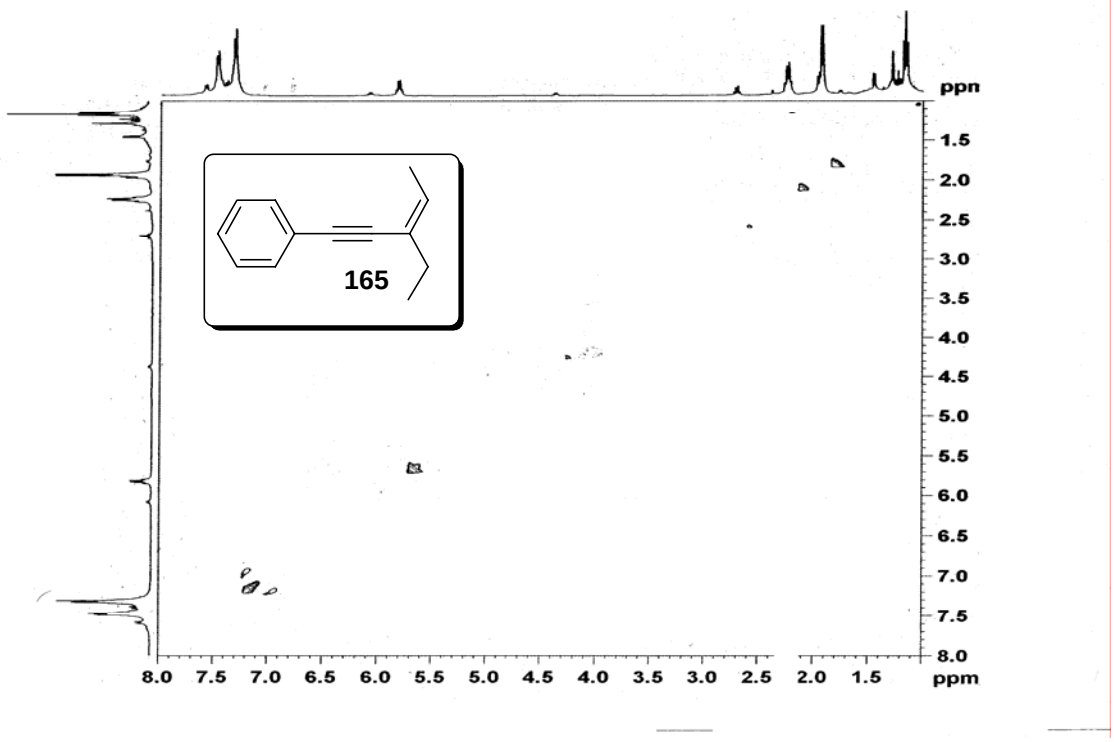
ppm

Spectrum No. 40 (Chapter 2, Section 2.4.5) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



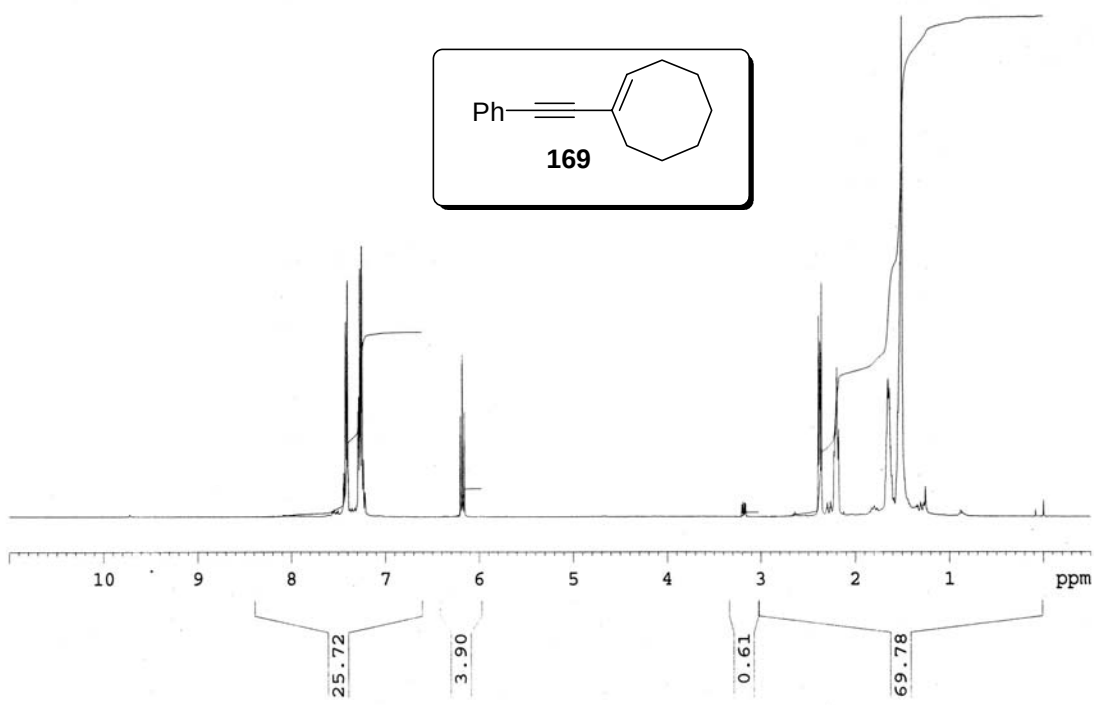
ppm

Spectrum No. 41 (Chapter 2, Section 2.4.5) NOESY Spectrum (400 MHz, $CDCl_3$)



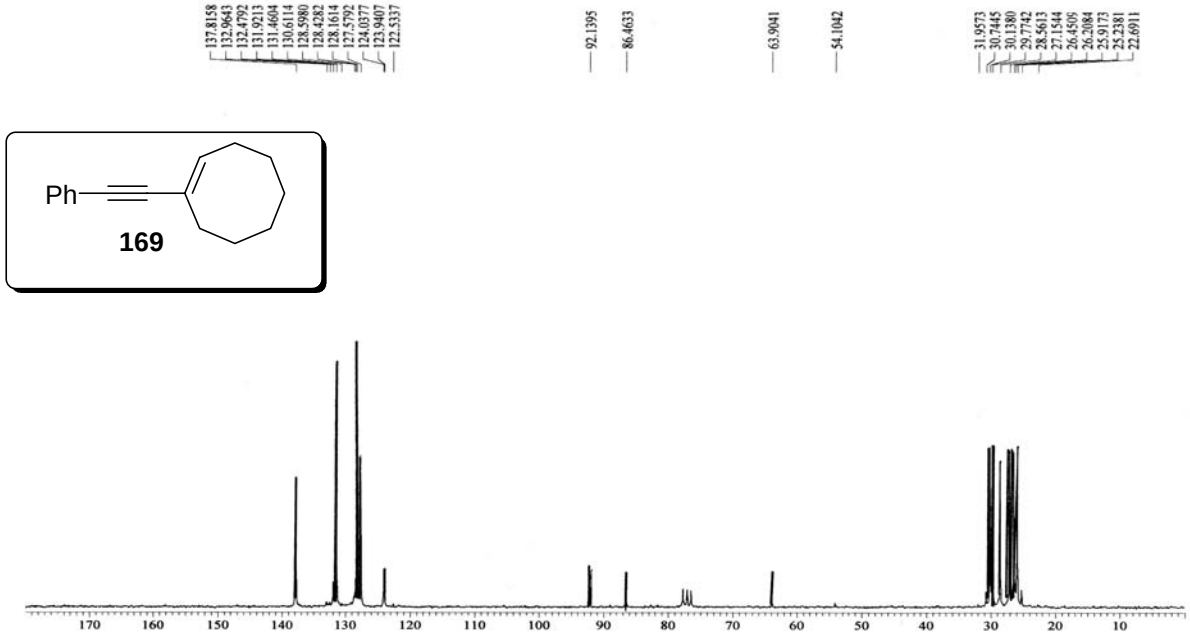
ppm

Spectrum No. 42 (Chapter 2, Section 2.4.5) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)

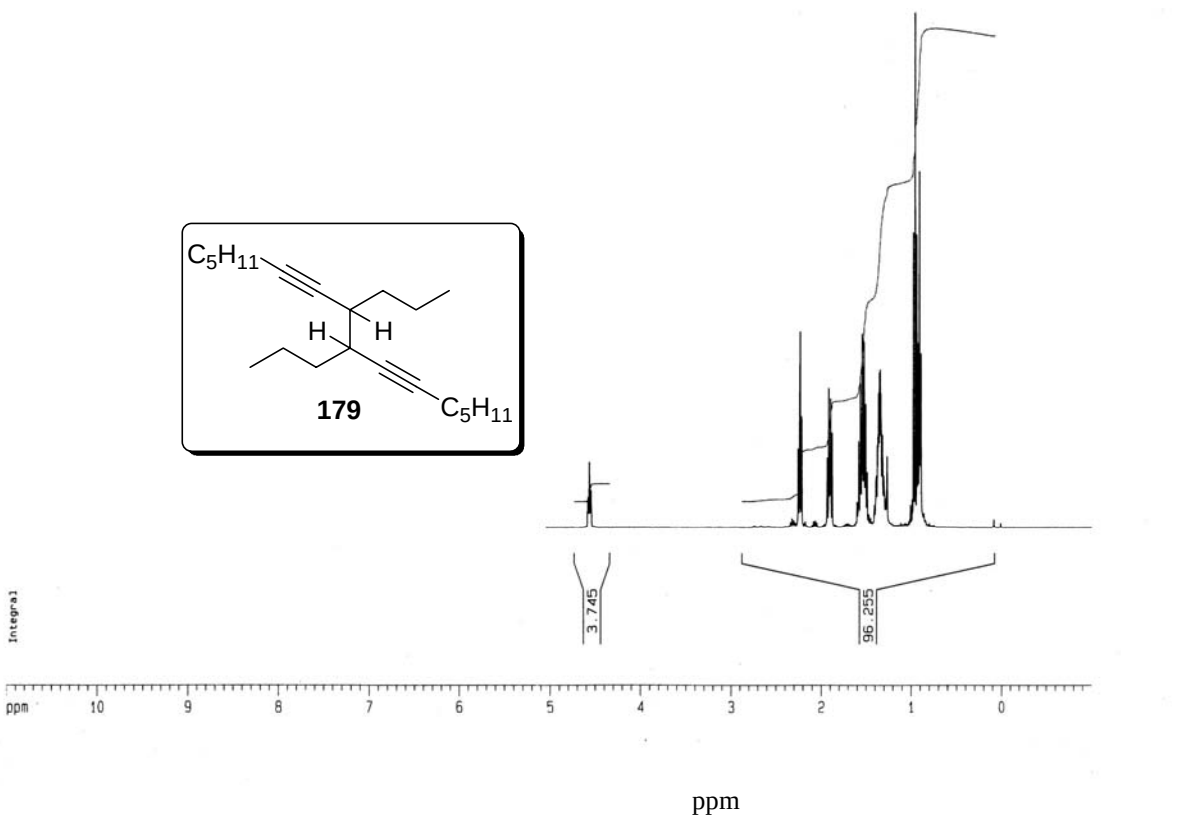


ppm

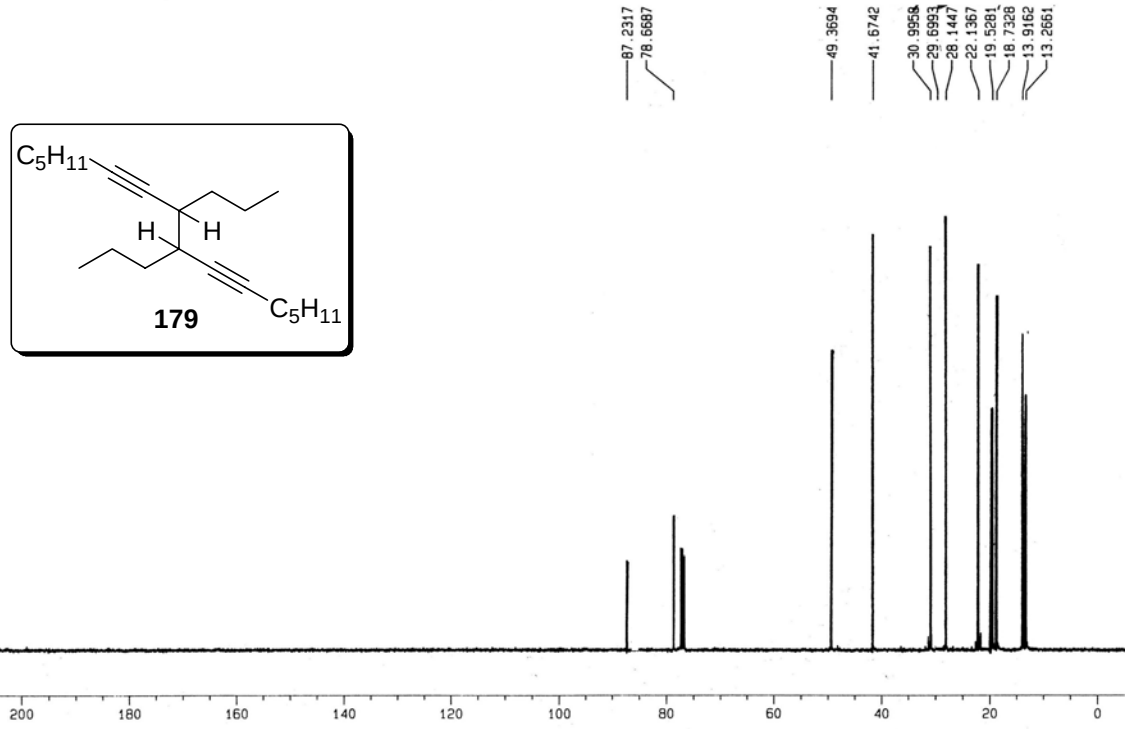
Spectrum No. 43 (Chapter 2, Section 2.4.5) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



Spectrum No. 44 (Chapter 2, Section 2.4.7) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)

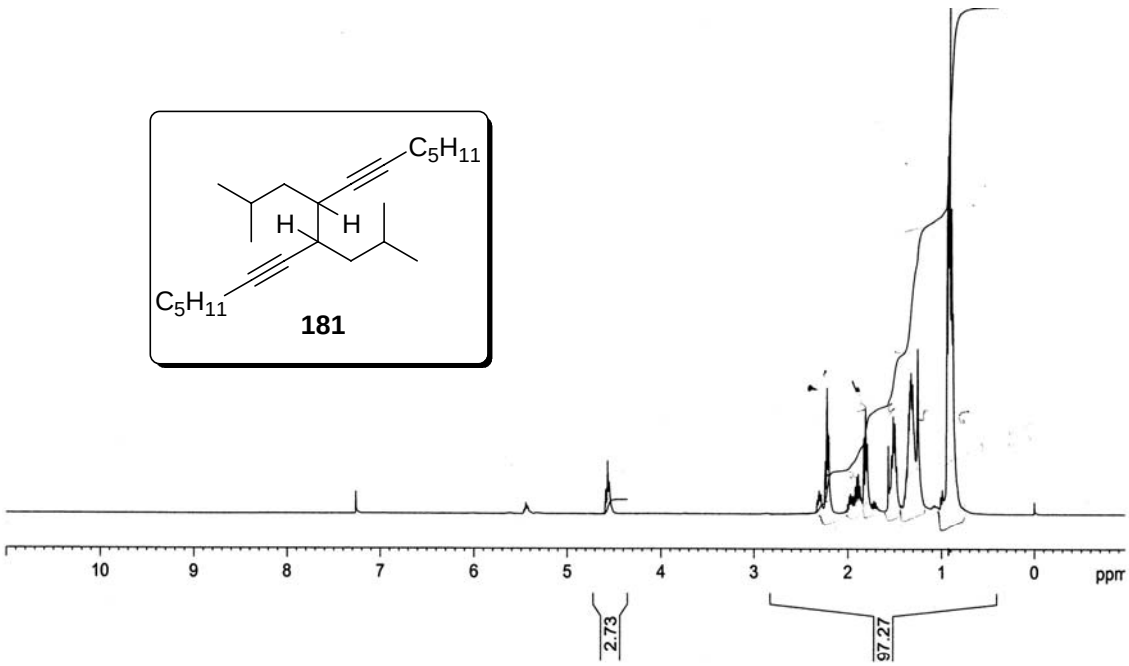


Spectrum No. 45 (Chapter 2, Section 2.4.7) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



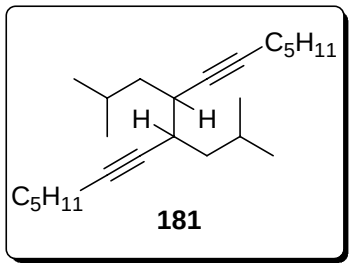
ppm

Spectrum No. 46 (Chapter 2, Section 2.4.7) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



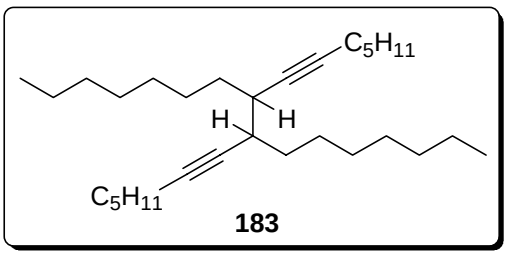
ppm

Spectrum No. 47 (Chapter 2, Section 2.4.7) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



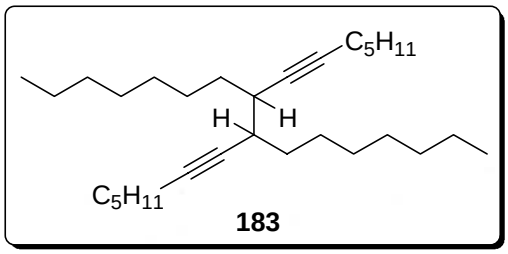
181

Spectrum No. 48 (Chapter 2, Section 2.4.7) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



183

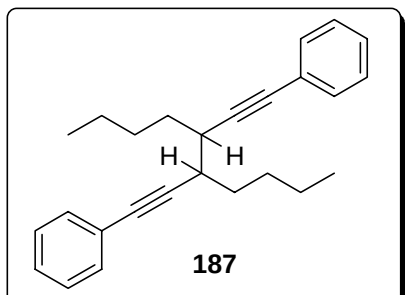
Spectrum No. 49 (Chapter 2, Section 2.4.7) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



183

ppm

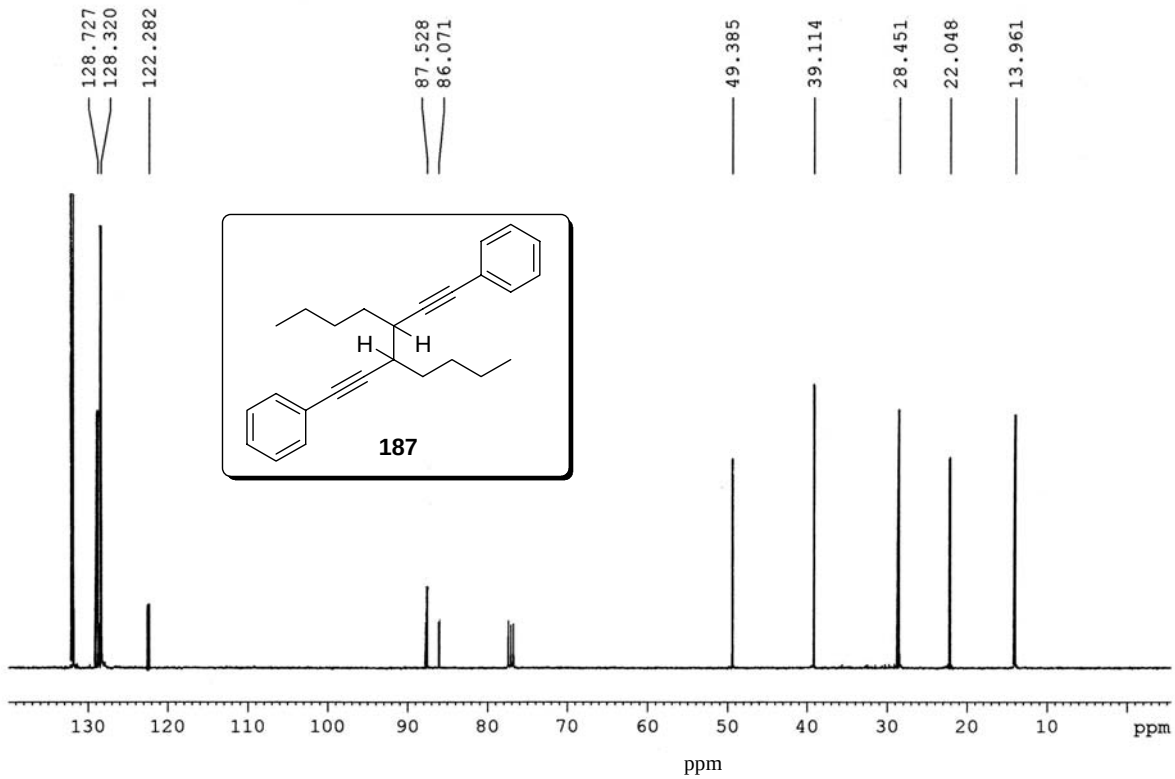
Spectrum No. 50 (Chapter 2, Section 2.4.7) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



187

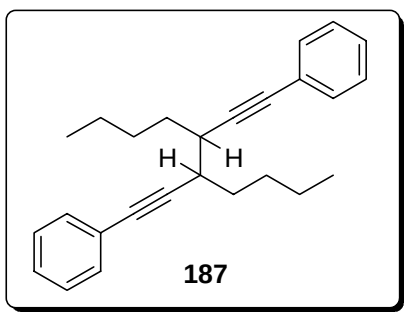
ppm

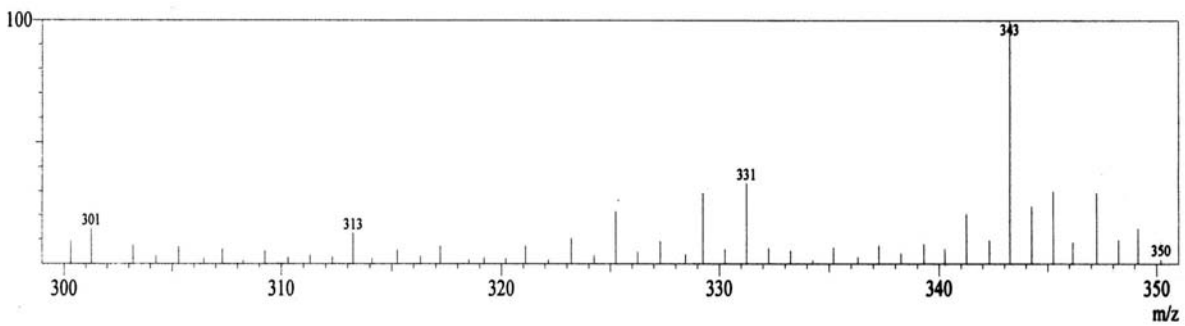
Spectrum No. 51 (Chapter 2, Section 2.4.7) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



ppm

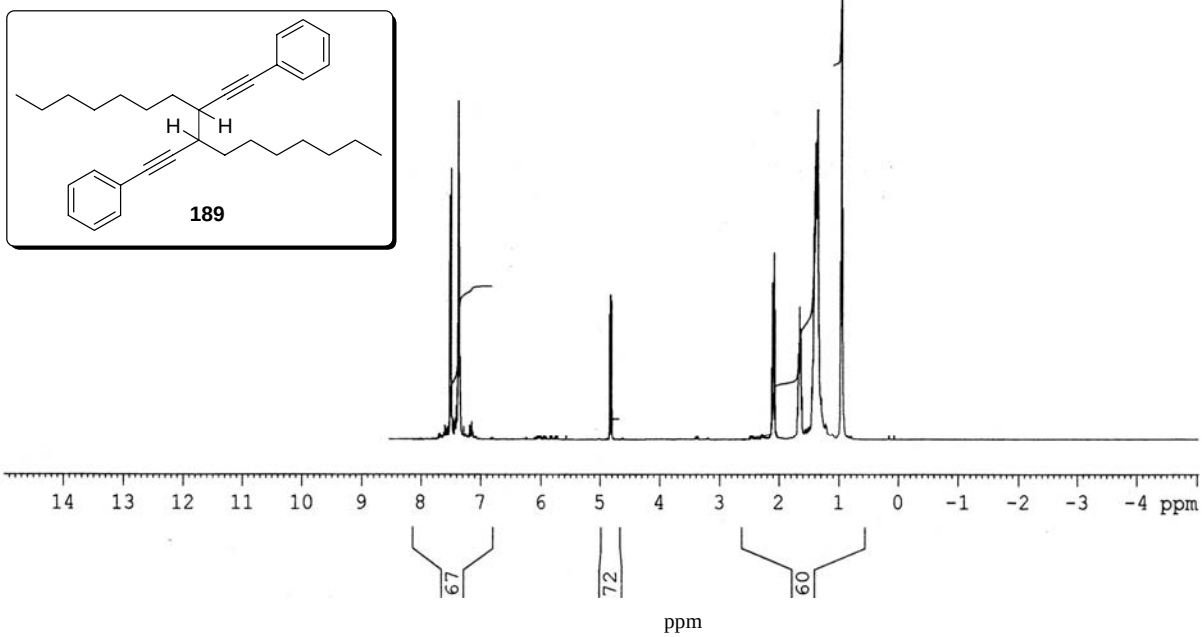
Spectrum No. 52 (Chapter 2, Section 2.4.7) EI Mass Spectrum



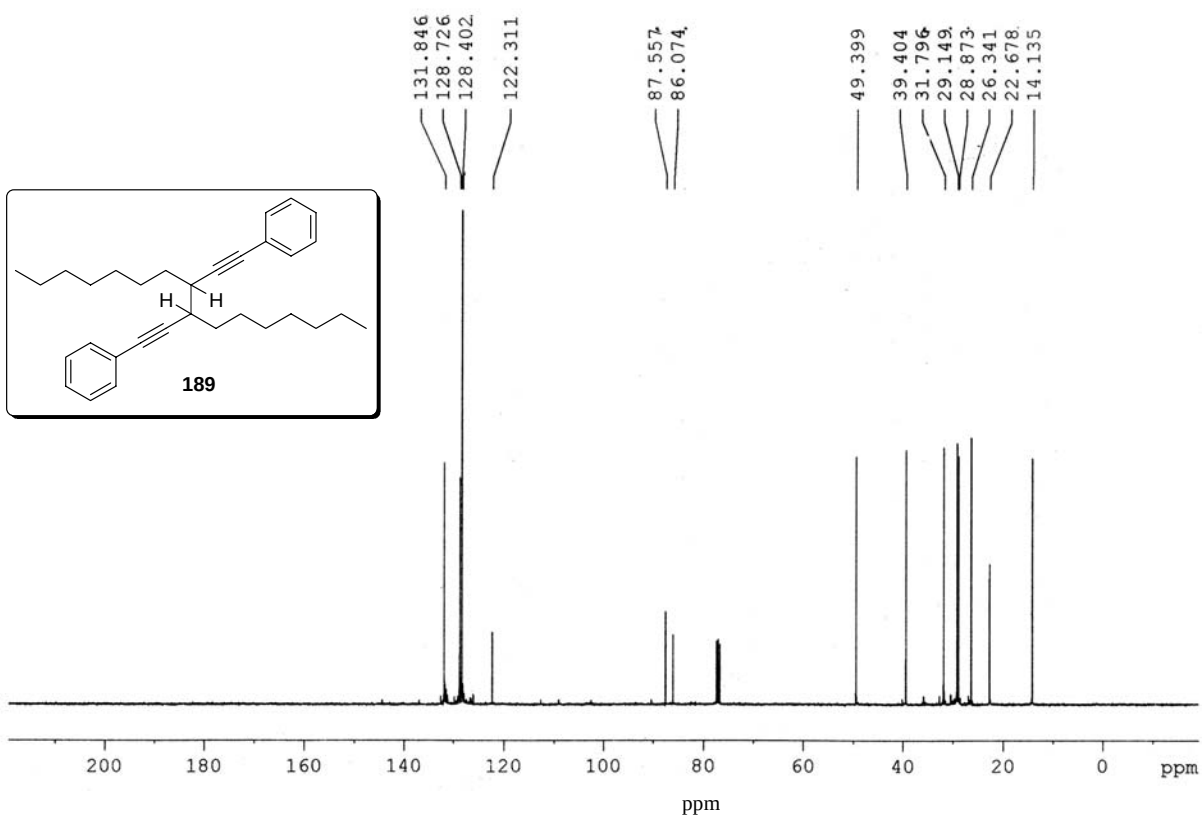


m/z

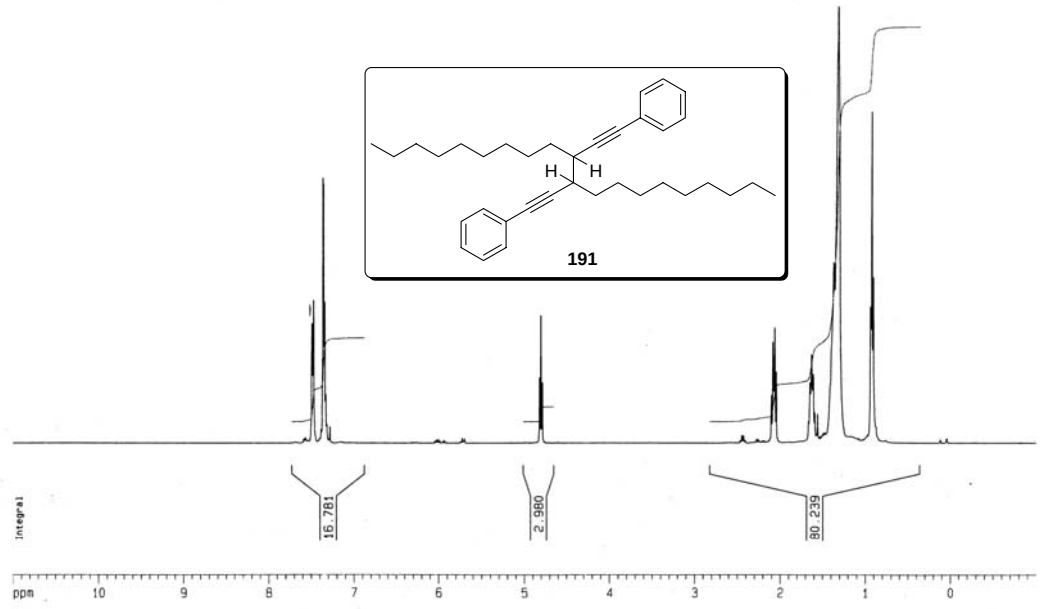
Spectrum No. 53 (Chapter 2, Section 2.4.7) ^{1}H NMR Spectrum(400 MHz, $CDCl_3$)



Spectrum No. 54 (Chapter 2, Section 2.4.7) ^{13}C NMR Spectrum (100MHz,$CDCl_3$)

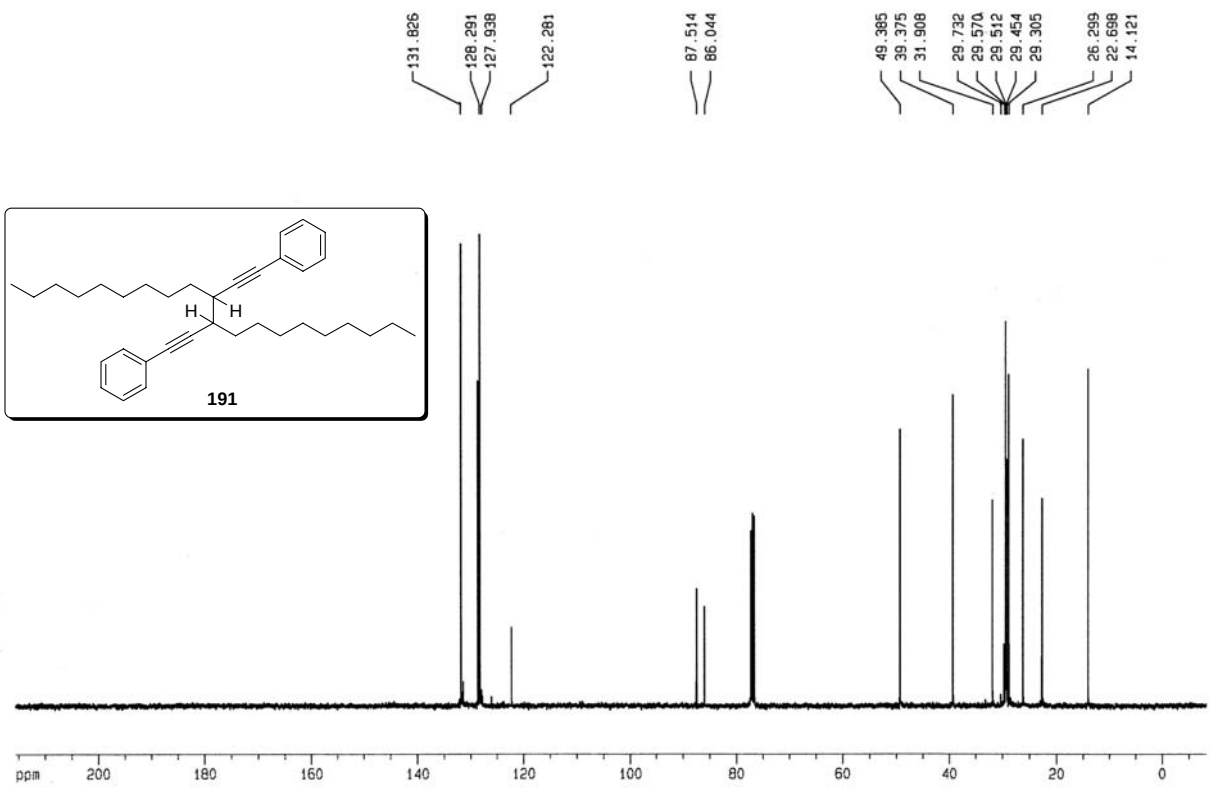


Spectrum No. 55 (Chapter 2, Section 2.4.7) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



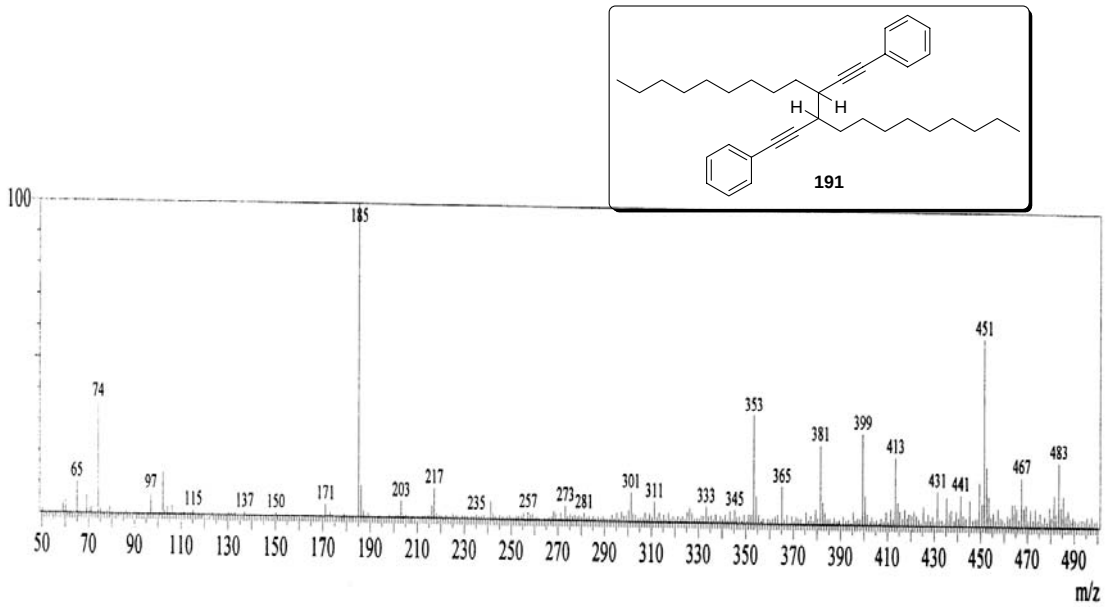
ppm

Spectrum No. 56 (Chapter 2, Section 2.4.7) ^{13}C NMR Spectrum (100 MHz,$CDCl_3$)



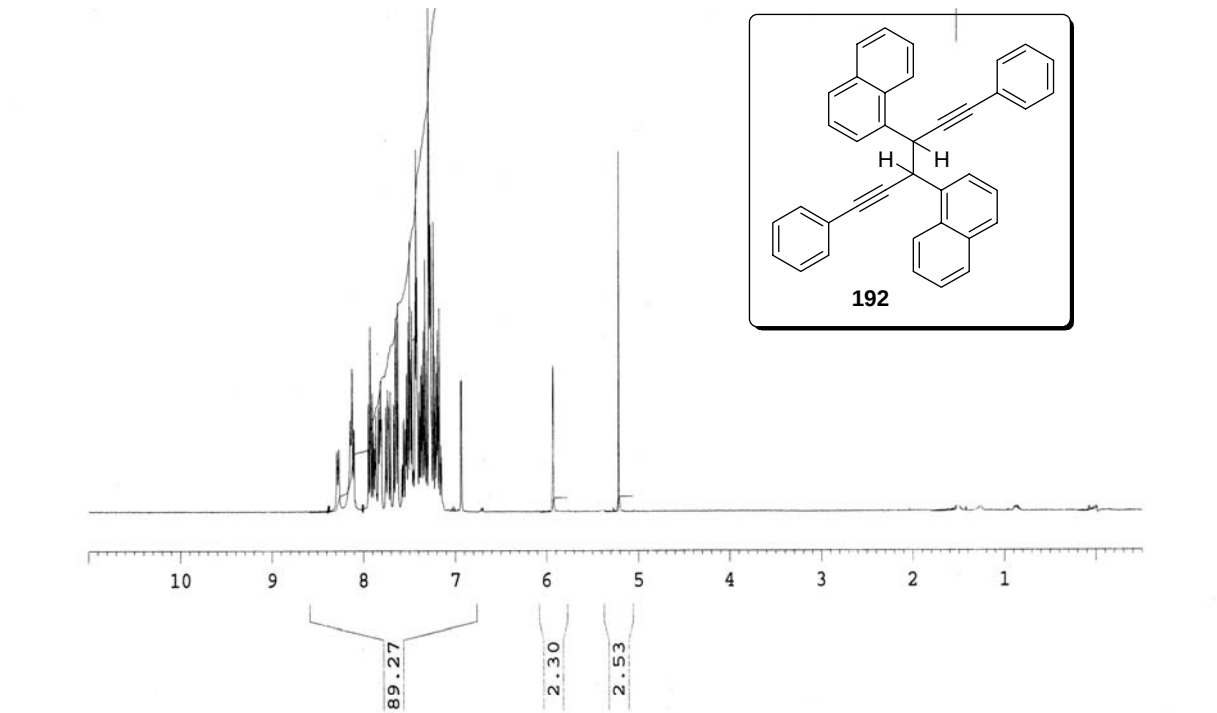
ppm

Spectrum No. 57 (Chapter 2, Section 2.4.7) EI Mass Spectrum



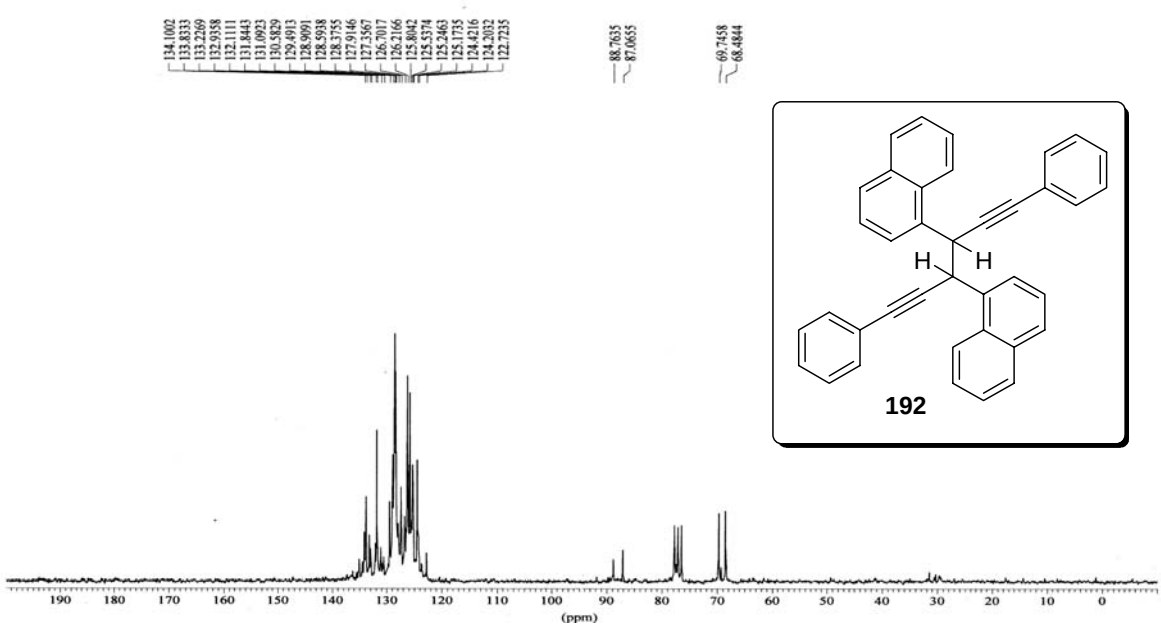
m/z

Spectrum No. 58 (Chapter 2, Section 2.4.7) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



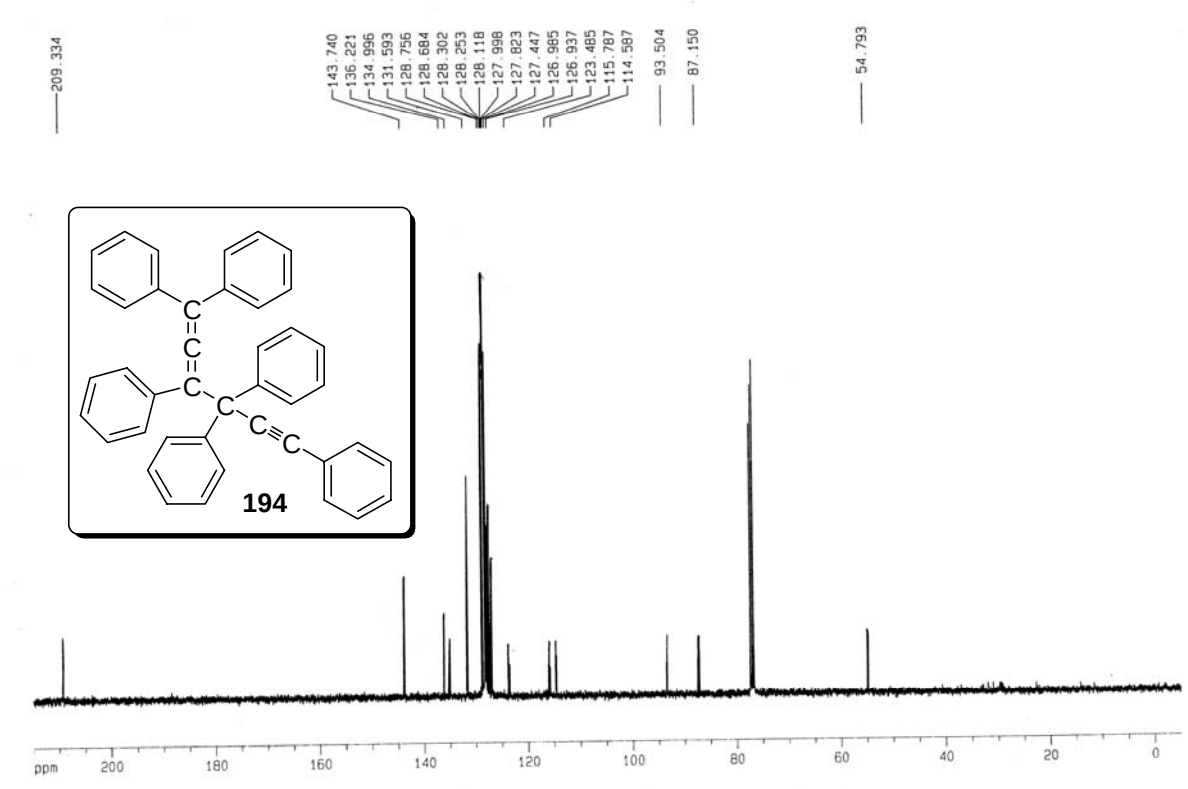
ppm

Spectrum No. 59 (Chapter 2, Section 2.4.7) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



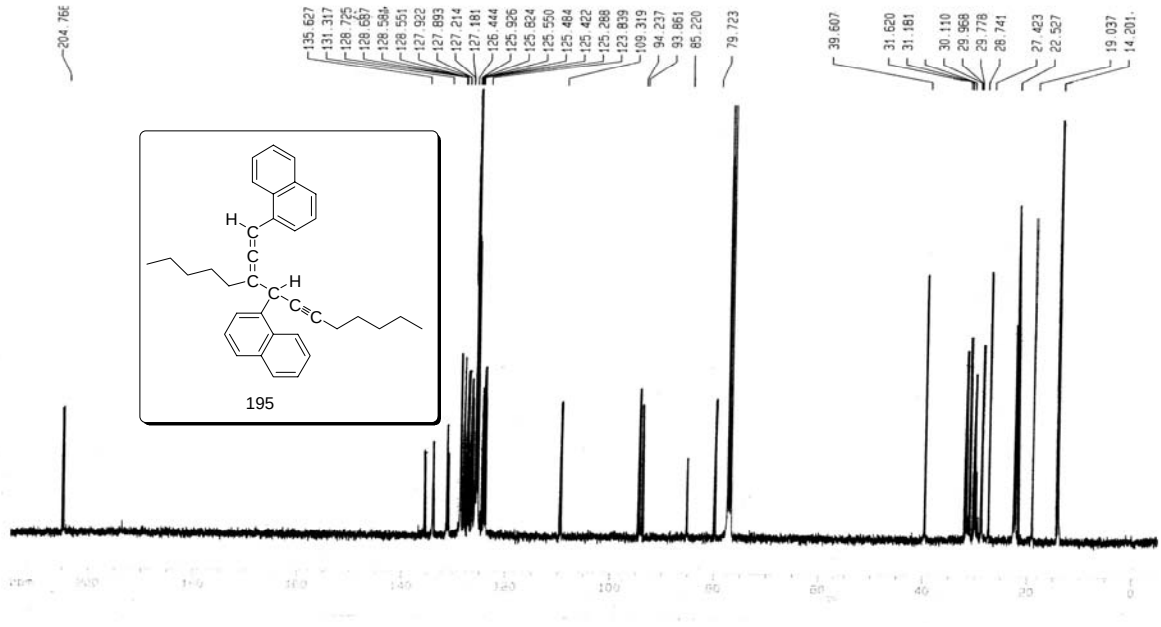
ppm

Spectrum No. 60 (Chapter 2, Section 2.4.8) ^{13}C NMR Spectrum (100 MHz,$CDCl_3$)



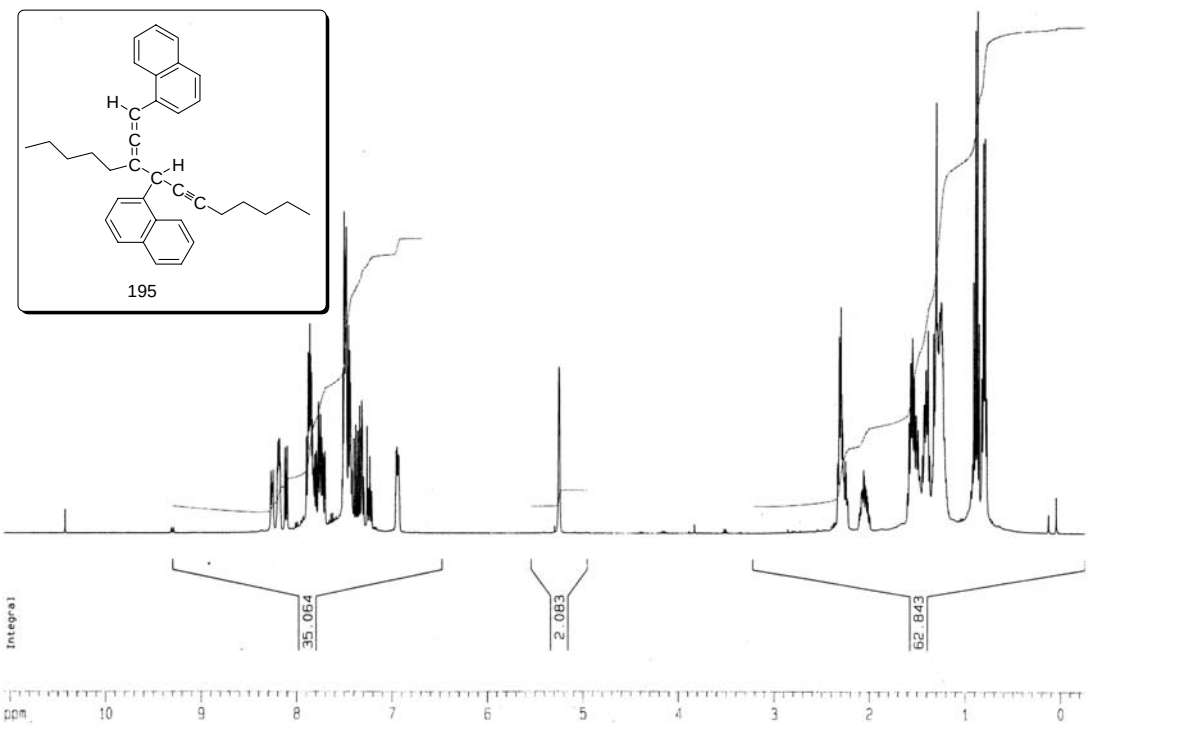
ppm

Spectrum No. 61 (Chapter 2, Section 2.4.8) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



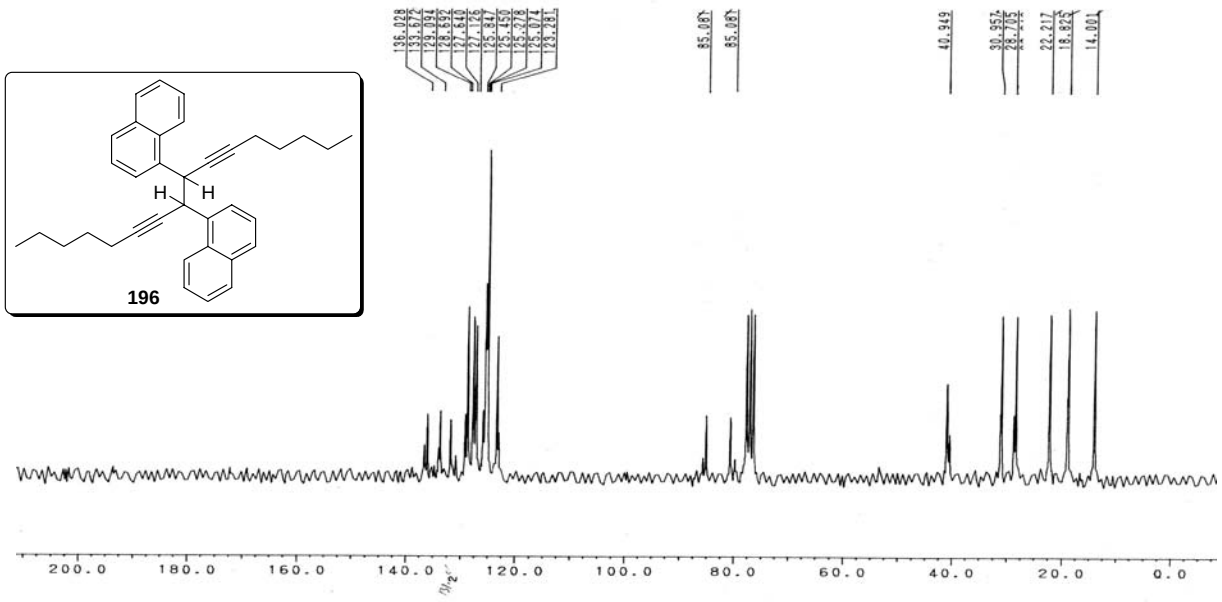
ppm

Spectrum No. 62 (Chapter 2, Section 2.4.7) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)

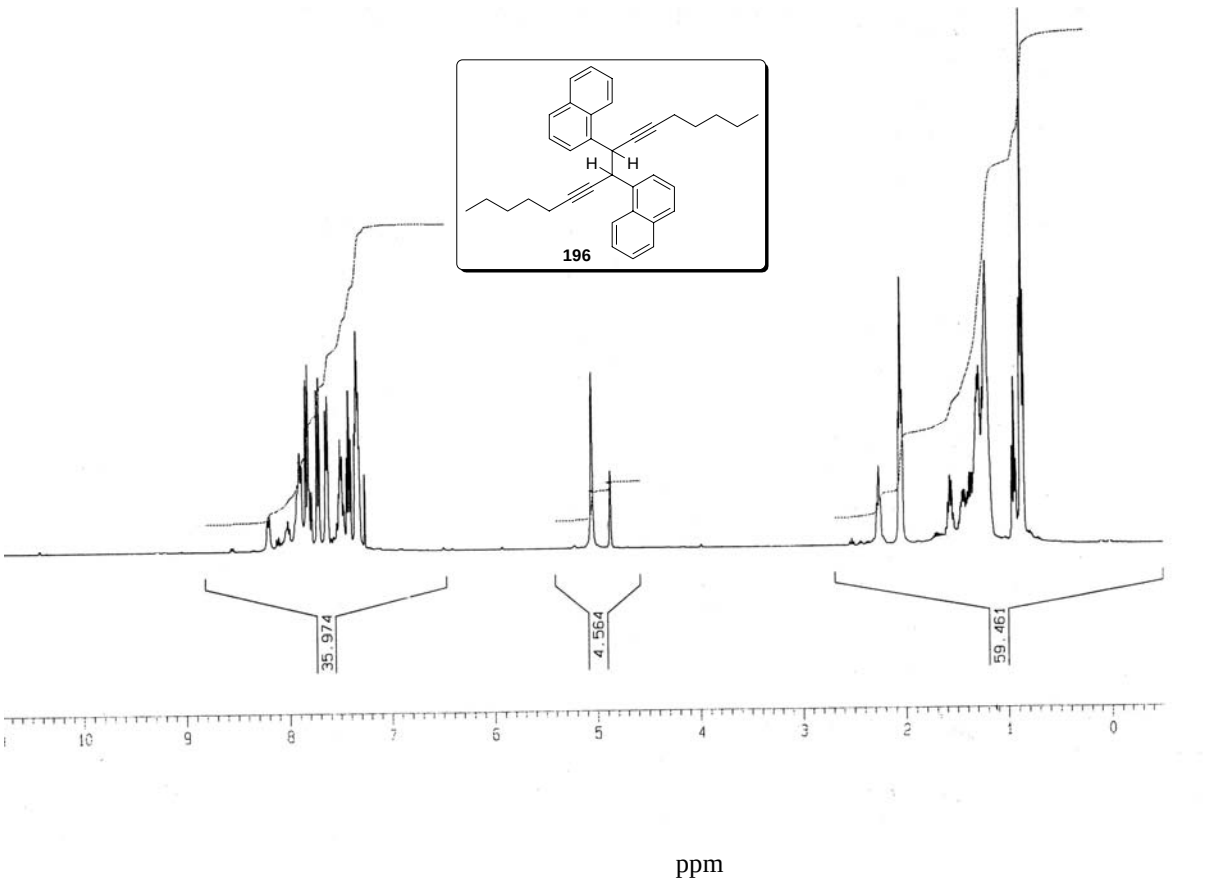


ppm

Spectrum No. 63 (Chapter 2, Section 2.4.8) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



Spectrum No. 64 (Chapter 2, Section 2.4.8) ^{1}H NMR Spectrum (400 MHz,$CDCl_3$)



Appendix II

X-Ray Crystallographic Data

Table A1. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for compound number **103 (Chapter 1, section 1.2.1)**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	**x**	**y**	**z**	**U(eq)**
C(1)	1190(20)	3290(9)	3339(12)	62(4)
C(2)	-390(20)	3594(10)	2464(15)	75(5)
C(3)	180(30)	3601(12)	1374(16)	93(6)
C(4)	2070(30)	3261(11)	1174(11)	83(5)
C(5)	3710(30)	2981(10)	1959(11)	81(5)
C(6)	3150(20)	3024(8)	3088(11)	50(4)
C(7)	4710(20)	2735(10)	3952(11	58(4)
C(8)	6020(20)	2435(8)	4669(11)	60(4)
C(9)	7540(20)	2069(8)	5523(11)	49(4)
C(10)	7220(30)	2180(9)	6704(11)	56(4)
C(11)	5290(30)	2443(10)	7039(13)	77(5)
C(12)	5120(30)	2575(12)	8184(14)	86(5)
C(13)	6600(30)	2353(12)	9028(13)	97(6)
C(14)	8580(30)	2010(11)	8618(13)	75(5)
C(15)	8820(20)	1942(9)	7526(11)	65(4)
C(16)	9220(20)	1652(9)	5185(9)	55(4)
C(17)	10750(30)	1226(10)	4854(11)	58(4)
C(18)	12450(20)	759(9)	4501(10)	54(4)
C(19)	12750(20)	684(9)	3269(11)	51(4)
C(20)	11090(20)	903(9)	2479(10)	(5)
C(21)	11430(40)	802(12)	1330(13)	98(6)
C(22)	13320(40)	552(12)	1060(13)	98(6)
C(23)	15090(30)	308(11)	1815(14)	92(6)
C(24)	14670(20)	338(8)	2931(11)	56(4)
C(25)	14000(20)	397(8)	5307(10)	54(4)
C(26)	15260(20)	154(9)	6043(11)	61(4)
C(27)	16830(20)	-135(9)	6910(11)	59(4)
C(28)	16450(20)	-138(8)	8006(11)	59(4)
C(29)	17820(30)	-420(11)	8890(13)	87(5)
C(30)	19900(30)	-708(10)	8607(12)	78(5)
C(31)	20320(20)	-737(10)	7482(14)	73(4)
C(32)	18900(20)	-472(9)	6681(12)	63(4)

Table A2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for compound number **148 (Chapter 2, section 2.2.2)**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	x	y	z	U(eq)
Cl(1)	6553(1)	598(2)	1302(1)	152(1)
O(1)	5481(3)	270(5)	8650(2)	142(1)
O(3)	3861(3)	1804(4)	48(3)	127(1)
O(2)	5544(3)	2270(4)	104(3)	137(1)
N(1)	5732(1)	5044(2)	2036(1)	53(1)
C(1)	3748(2)	7657(4)	3146(3)	78(1)
C(2)	2857(3)	7772(5)	2973(3)	97(1)
(3)	2409(2)	6852(5)	3265(3)	89(1)
C(4)	2836(3)	5797(5)	3716(3)	98(1)
C(5)	3701(2)	5677(4)	3887(3)	79(1)
C(6)	4172(2)	6599(3)	3596(2)	53(1)
C(7)	5132(2)	6448(3)	3782(2)	49(1)
C(8)	5735(2)	7171(3)	4478(2)	51(1)
C(9)	5432(2)	7991(3)	4998(2)	63(1)
C(10)	5997(3)	8635(4)	5655(2)	81(1)
C(11)	6867(3)	8482(4)	5827(2)	83(1)
C(12)	7184(2)	7671(4)	5322(2)	73(1)
C(13)	6630(2)	7031(3)	4666(2)	61(1)
C(14)	5395(2)	5638(3)	3287(2)	53(1)
C(15)	5632(2)	4707(3)	2868(2)	47(1)
C(16)	5820(2)	3312(3)	3196(2)	54(1)
C(17)	5359(2)	2173(3)	2865(3)	75(1)
C(18)	5556(3)	919(4)	3236(4)	95(1)
C(19)	6206(3)	795(4)	3952(3)	92(1)
C(20)	6677(3)	1901(4)	4308(3)	88(1)
C(21)	6488(2)	3151(3)	3930(2)	70(1)
C(22)	4964(2)	4447(4)	1349(2)	77(1)
C(23)	4099(2)	4864(6)	1394(3)	101(1)
C(24)	6556(2)	4399(3)	1981(2)	66(1)
C(25)	6755(3)	4676(5)	1184(3)	99(1)
C(26)	5743(2)	6556(3)	1908(2)	70(1)
C(27)	6530(3)	7300(4)	2426(3)	92(1)

Table A3. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for compound number **177 (Chapter 2, section 2.2.6)**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	x	y	z	U(eq)
C(1)	6181(2)	1022(1)	1212(1)	46(1)
C(2)	6578(2)	-1164(2)	204(1)	56(1)
C(3)	7457(2)	-122(2)	-170(1)	60(1)
C(4)	7924(2)	1084(2)	452(1)	57(1)
C(5)	7532(2)	1241(2)	1463(1)	48(1)
C(6)	6670(1)	178(1)	1860(1)	38(1)
C(7)	6316(1)	267(1)	2930(1)	41(1)
C(8)	6002(1)	222(1)	3818(1)	40(1)
C(9)	5689(1)	183(1)	4899(1)	37(1)
C(10)	6953(1)	539(1)	5766(1)	38(1)
C(11)	8320(1)	-119(1)	5753(1)	45(1)
C(12)	9519(2)	201(2)	6538(1)	54(1)
C(13)	9376(2)	1207(2)	7332(1)	57(1)
C(14)	8035(2)	1890(2)	7346(1)	54(1)
C(15)	6826(1)	1554(1)	6573(1)	45(1)

Table A4. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for compound number **192 (Chapter 2, section 2.2.7)**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	x	y	z	U(eq)
C(1)	2315(5)	6189(4)	1499(3)	78(2)
C(2)	1037(6)	5857(5)	1142(3)	99(2)
C(3)	863(6)	4982(6)	957(3)	96(2)
C(4)	1959(6)	4395(5)	1129(3)	(2)
C(5)	1805(8)	3467(6)	946(3)	115(2)
C(6)	2847(10)	2900(6)	1124(5)	130(3)
C(7)	4128(8)	3229(5)	1490(4)	118(2)
C(8)	4329(6)	4107(4)	1675(3)	81(2)
C(9)	3265(5)	4719(4)	1506(2)	64(1)
C(10)	3417(5)	5648(4)	1680(2)	60(1)

C(11)	4794(4)	6044(3)	2088(2)	60(1)
C(12)	5024(5)	6938(4)	1836(3)	75(2)
C(13)	5227(7)	7647(5)	1641(3)	116(2)
C(14)	5435(15)	8519(8)	1403(7)	239(8)
C(15)	5140(30)	9240(8)	1719(7)	480(20)
C(16)	5340(40)	10083(11)	1479(9)	800(40)
C(17)	5750(30)	10268(13)	965(16)	570(30)
C(18)	6312(17)	9514(16)	635(16)	550(30)
C(19)	6034(10)	8658(12)	887(10)	370(16)
C(20)	4993(4)	6012(3)	2939(2)	55(1)
C(21)	4226(5)	6708(3)	3214(3)	61(1)
C(22)	3560(5)	7241(4)	3445(3)	70(1)
C(23)	2748(5)	7875(3)	3740(3)	68(1)
C(24)	2751(7)	7897(5)	4452(4)	117(2)
C(25)	1971(8)	8503(6)	4728(4)	139(3)
C(26)	1197(8)	9090(5)	4281(6)	127(3)
C(27)	1190(7)	9085(5)	3564(5)	130(3)
C(28)	1962(7)	8476(4)	3283(4)	104(2)
C(29)	6494(4)	6033(3)	3326(2)	57(1)
C(30)	7216(5)	6824(4)	3385(3)	74(1)
C(31)	8631(6)	6858(4)	3683(3)	85(2)
C(32)	9302(5)	6110(5)	3938(3)	80(2)
C(33)	8613(5)	5282(4)	3902(2)	65(1)
C(34)	9309(6)	4503(5)	4166(3)	79(2)
C(35)	8651(7)	3700(5)	4149(3)	87(2)
C(36)	7237(6)	3659(4)	3865(3)	82(2)
C(37)	6538(5)	4396(4)	3597(3)	68(1)
C(38)	7179(5)	5240(3)	3597(2)	58(1)
C(39)	11436(6)	1722(4)	3580(3)	97(2)
C(40)	12209(8)	1727(5)	4316(4)	120(2)
C(41)	12788(6)	2494(5)	4634(3)	99(2)
C(42)	12652(5)	3292(4)	4239(3)	73(1)
C(43)	13221(5)	4106(5)	4575(3)	86(2)
C(44)	13060(5)	4880(5)	4202(3)	90(2)
C(45)	12312(5)	4889(4)	3469(3)	78(2)
C(46)	11761(4)	4109(4)	3126(3)	66(1)
C(47)	11893(4)	3294(4)	3498(3)	61(1)
C(48)	11278(5)	2478(3)	3177(3)	65(1)
C(49)	10386(5)	2461(3)	2392(3)	68(1)
C(50)	10424(5)	1593(4)	2024(3)	78(2)
C(51)	10471(6)	890(4)	1737(3)	89(2)
C(52)	10532(8)	32(5)	1394(4)	107(2)
C(53)	9780(10)	670(6)	1483(5)	163(3)
C(54)	9877(12)	-1501(7)	1142(8)	189(5)
C(55)	10699(14)	-1608(7)	724(6)	176(4)
C(56)	11480(20)	-960(9)	658(10)	422(16)

C(57)	11364(17)	-146(7)	1010(9)	366(12)
C(58)	8909(5)	2752(3)	2392(2)	64(1)
C(59)	8167(6)	2056(4)	2691(3)	71(1)
C(60)	7557(5)	1504(4)	2934(3)	75(2)
C(61)	6853(6)	841(4)	3260(3)	74(1)
C(62)	5599(7)	1002(5)	3385(4)	137(3)
C(63)	4950(9)	339(8)	3704(6)	178(4)
C(64)	5611(12)	-435(8)	3916(5)	153(4)
C(65)	6822(12)	-594(5)	3806(4)	129(3)
C(66)	7439(7)	48(5)	3475(3)	99(2)
C(67)	8117(5)	3042(4)	1633(3)	63(1)
C(68)	7619(5)	2417(4)	1102(3)	87(2)
C(69)	6907(6)	2641(5)	392(3)	98(2)
C(70)	6678(6)	3498(6)	213(3)	95(2)
C(71)	7163(5)	4197(5)	738(3)	75(2)
C(72)	6942(5)	5110(5)	563(3)	90(2)
C(73)	7404(6)	5773(5)	1076(4)	94(2)
C(74)	8088(5)	5545(4)	1784(3)	81(2)
C(75)	8319(4)	4679(4)	1969(3)	65(1)
C(76)	7890(4)	3964(4)	1458(3)	62(1)

Table A5. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for compound number **194 (Chapter 2, section 2.2.8)**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	x	y	z	U(eq)
C(1)	582(2)	2988(2)	3763(1)	82(1)
C(2)	-105(2)	2246(2)	328(2)	98(1)
C(3)	65(2)	2331(2)	5154(2)	101(1)
C(4)	937(3)	3129(2)	5443(1)	95(1)
C(5)	1635(2)	3879(2)	4892(1)	78(1)
C(6)	1449(2)	3814(2)	4036(1)	61(1)
C(7)	2113(2)	4638(2)	3453(1)	58(1)
C(8)	2660(2)	5353(1)	3002(1)	53(1)
C(9)	3319(1)	6289(1)	2451(1)	47(1)
C(10)	4988(1)	5851(1)	2426(1)	49(1)
C(11)	5838(2)	6779(2)	2221(1)	63(1)
C(12)	7330(2)	6393(2)	2147(1)	75(1)
C(13)	7985(2)	5073(2)	2279(1)	80(1)
C(14)	7154(2)	4147(2)	2482(1)	76(1)
C(15)	5665(2)	4524(2)	2552(1)	60(1)

C(16)	2668(1)	6311(1)	1564(1)	48(1)
C(17)	1173(2)	6478(2)	1470(1)	62(1)
C(18)	552(2)	6489(2)	694(1)	74(1)
C(19)	1411(2)	6319(2)	-4(1)	74(1)
C(20)	2891(2)	6158(2)	78(1)	70(1)
C(21)	3517(2)	6153(1)	852(1)	57(1)
C(22)	2897(1)	7694(1)	2807(1)	50(1)
C(23)	3357(2)	7923(1)	3665(1)	53(1)
C(24)	3005(2)	9193(2)	3967(1)	73(1)
C(25)	3344(3)	9427(2)	4768(2)	96(1)
C(26)	4050(2)	8410(2)	5296(1)	92(1)
C(27)	4432(2)	7160(2)	5014(1)	82(1)
C(28)	4096(2)	6916(2)	4209(1)	68(1)
C(29)	2103(2)	8682(1)	2351(1)	56(1)
C(30)	1279(2)	9698(1)	1943(1)	54(1)
C(31)	-335(2)	9968(1)	2034(1)	55(1)
C(32)	-1238(2)	10724(2)	1435(1)	78(1)
C(33)	-2736(2)	10943(2)	1530(2)	93(1)
C(34)	-3353(2)	10431(2)	2207(1)	83(1)
C(35)	-2471(2)	9679(2)	2804(1)	85(1)
C(36)	-984(2)	9459(2)	2722(1)	75(1)
C(37)	1978(2)	10608(1)	1382(1)	55(1)
C(38)	2601(4)	10238(2)	665(2)	143(1)
C(39)	3236(5)	11103(3)	154(2)	170(2)
C(40)	3281(2)	12318(2)	366(2)	89(1)
C(41)	2672(4)	12699(2)	1062(2)	128(1)
C(42)	2003(4)	11863(2)	1569(2)	129(1)

LIST OF PUBLICATIONS

1 Reductive coupling of aromatic aldehydes and imines by the low-valent titanium species generated in the reaction of $TiCl_4$ with Et_3N; Periasamy, M.; Srinivas, G.; **Karunakar, G. V.**; Bharathi, P. *Tetrahedron Lett*. **1999**, *40*, 7577.

2 Nickle(II) complexes of tridentate N,N,O-donor ligands: synthesis, structures and redox properties; **Karunakar, G. V.**; Sangeetha, N. R.; Susila, V.; Pal, S. *J. Coord. Chem*. **2000**, *50*, 51.

3 A simple method for the conversion of propargyl alcohols to symmetrical 1,5-diynes using low valent titanium reagents; **Karunakar, G. V.**; Periasamy, M. *Tetrahedron Lett*. **2006**, *47*, 0000.

4 A novel, simple method for the conversion of aromatic aldehydes and 1,2-diarylethane-1,2-diols to 1,2-diarylethane –1,2-diones using $TiCl_4/Et_3N$ reagent system; Periasamy, M.; **Karunakar, G. V.**; Bharathi, P. *Communicated*.

5 Synthesis of enynones from alkynes and alkynyl ketones using the $TiCl_4/Et_3N$ reagent system; Periasamy, M.; **Karunakar, G. V.**; Bharathi, P. *Communicated*.

6 Conversion of propargyl alcohols to chloroallenes and aryl alkynes using the $TiCl_4/Et_3N$ reagent system; **Karunakar, G. V.**; Periasamy, M. *Communicated*.

7 Synthesis of enynes from propargyl alcohols using $TiCl_4/Et_3N$ reagent system; **Karunakar, G. V.**; Periasamy, M. (to be communicated).

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9 Effect of substituents on the catalytic asymmetric dihydroxylation of *trans*-stilbene derivatives: relationship to the mechanism of ligand accelerated catalysis of OsO_4 addition to olefins; Periasamy, M.; Kumar, N. S.; Ramanathan, C. R.; **Karunakar, G. V.** (to be communicated).

10 Reaction of alkynes with ketones and tertiary halides using $TiCl_4/Et_3N$ reagent system; Periasamy, M.; **Karunakar, G. V.**; Kamalababu, B. (*manuscript under preparation*)

POSTERS PRESENTED IN SYMPOSIA

1 Synthetic transformations of propargyl alcohols using using $TiCl_4/Et_3N$ reagent system; Karunakar, G. V.; Periasamy, M. *Chemfest 2005*, School of Chemistry, University of Hyderabad, Hyderabad, February 19, **2005**.

2 A simple method for the conversion of propargyl alcohols to symmetrical 1,5-diynes using low valent titanium reagents; **Karunakar, G. V.**; Periasamy, M. *Chemfest 2006*, School of Chemistry, University of Hyderabad, Hyderabad, March 4, **2006**