ORGANIC TRANSFORMATIONS USING CYCLOBUTENEDIONES

A Thesis

Submitted for the Degree of

DOCTOR OF PHILOSOPHY

By

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To the loving memory of my parents

Late Sri D. Raja Ram and Late Smt. D. Seetha

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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 "**Organic Transformations Using Cyclobutenediones"** has been carried out by **Mr. Shyam Raj Dharavath** under my supervision and the same has not been submitted elsewhere for a Degree.

PROFESSOR M. PERIASAMY
(THESIS SUPERVISOR)

DEAN
SCHOOL OF CHEMISTRY

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Shyam Raj Dharavath

Abbreviations

Ac	acetyl
aq.	aqueous
Ar	aryl
BINOL	1,1’-bi(2-naphthol)
Bn	benzyl
Boc	*tertiary*-butoxycarbonyl
br	broad (spectral)
Bu	butyl
Bz	benzoyl
cat.	catalytic
Cbz	benzyloxycarbonyl
d	doublet (spectral)
DABCO	1,4-diazabicyclo[2.2.2]octane
DCM	dichloromethane
de	diastereomeric excess
DEPT	distortionless enhancement by polarization transfer
DFT	density functional theory
DMAP	4-(*N*,*N*-dimethylamino)pyridine
DMF	*N*,*N*-dimethylformamide
DMSO	dimethylsulfoxide
dr	diastereomeric ratio
E	electrophile
ee	enantiomeric excess
EI	electron impact (in mass spectrometry)
equiv.	equivalent
er	enantiomeric ratio
Et	ethyl
EtOAc	ethyl acetate
HPLC	high-performance liquid chromatography
i	iso
i-Pr	isopropyl

J	coupling constant (in NMR spectroscopy)
LDA	lithium diisopropylamide
lit.	Literature
liq.	Liquid
LVT	low valent titanium
m	multiplet (spectral)
MALDI-tof	matrix assisted laser desorption/ionization--time-of-flight
Me	methyl
MO	molecular orbital
mp	melting point
n	primary
Nu	nucleophile
o	ortho
ORTEP	oak ridge thermal ellipsoid plot
Ph	phenyl
Pr	propyl
Py	pyridyl
q	quartlet (spectral)
R	alkyl
rt	room temperature
t	triplet (spectral)
t	tertiary
s	singlet (spectral)
TADDOL	α,α,α',α'-tetraaryl-2,2-dimethyl-1,3-dioxalan-4,5-dimethanol
TBS	tributylsilyl
THF	tetrahydrofuran
TMEDA	*N,N,N',N'*-tetramethylethylenediamine
TMS	trimethylsilyl
TMSCl	trimethylsilyl chloride
TS	transition state
X	halide

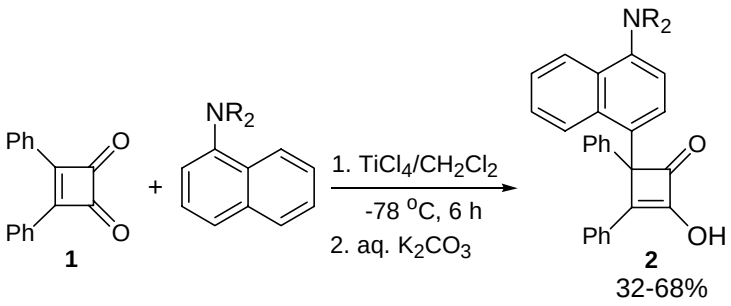
Abstract

This thesis entitled "**Organic Transformations Using Cyclobutenediones**" comprises of three chapters 1) **Introduction** 2) **Results and Discussion** and 3) **Experimental Section** along with references. The work described in this thesis is exploratory in nature.

The first chapter describes a brief review on the synthetic transformations of cyclobutenediones with various electrophiles and nucleophiles such as metal hydrides, organometallic reagents, amines, other C-C bond forming photochemical, thermal, substitution and addition reactions.

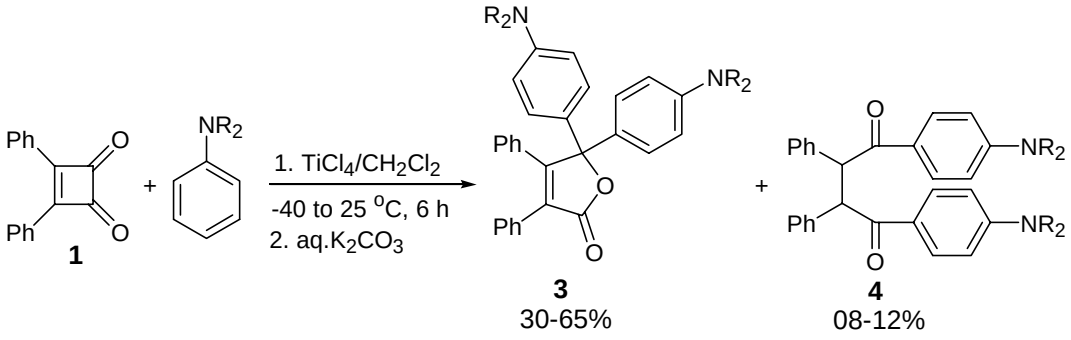
The second chapter deals with results and discussion of the studies undertaken towards the reactions of diphenylcyclobutenedione with *N,N*-dialkylarylamine/$TiCl_4$ or $SnCl_4$ and other Lewis acids reagent systems. It was observed that the reaction of *N,N*-dialkylarylamine/$TiCl_4$ system with diphenylcyclobutenedione **1** in dichloromethane at –78 ^oC leads to the formation of 4-(4-Dialkylamino-aryl)-2-hydroxy-3,4-diphenyl-cyclobut-2-enone **2** in moderate yields, 32-68% (**Scheme 1**). The 1,4-addition product **2** was identified by single crystal X-ray analysis.

Scheme 1



This is an interesting observation as the reaction at –40 to 25 ^{o}C gives the 5,5-bis-(4-dialkylamino-phenyl)-3,4-diphenyl-5*H*-furan-2-one **3** (butenolide) along with 1,4-bis-(4-dialkylamino-phenyl)-2,3-diphenyl-butane-1,4-dione (1,4-diketone) **4** (**Scheme 2**).

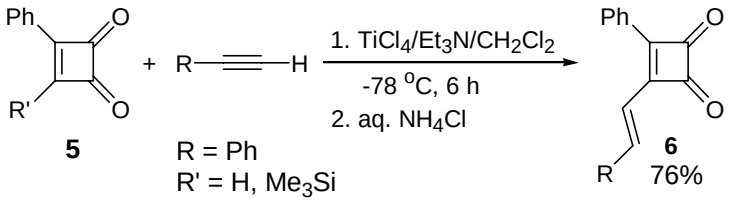
Scheme 2



Plausible reaction pathways and the intermediates that may be involved in these transformations are discussed.

The reaction of alkynyltitanium with 3-phenyl-cyclobut-3-ene-1,2-dione and 3-phenyl-4-trimethylsilanyl-cyclobut-3-ene-1,2-dione **5** in dichloromethane leads to the formation of alkenylcyclobutenedione **6** (**Scheme 3**).

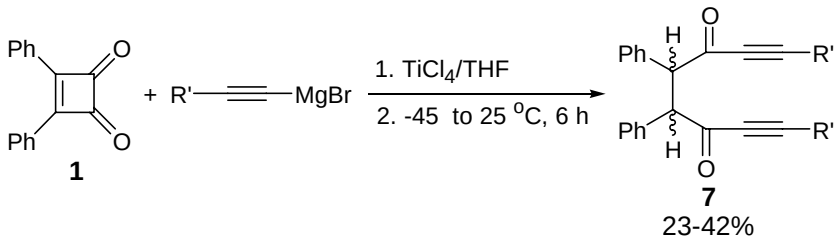
Scheme 3



We have examined the preparation of alkynyltitanium species *in situ via* transmetalation by the addition of $TiCl_4$ to alkynyl Grignard reagent at low temperature. The reaction of these alkynyltitanium species prepared in this way with 3,4-diphenyl-3-cyclobutene-1,2-dione **1** gave the corresponding *dl:meso* mixture of 1,4,5,8-tetraphenyl-

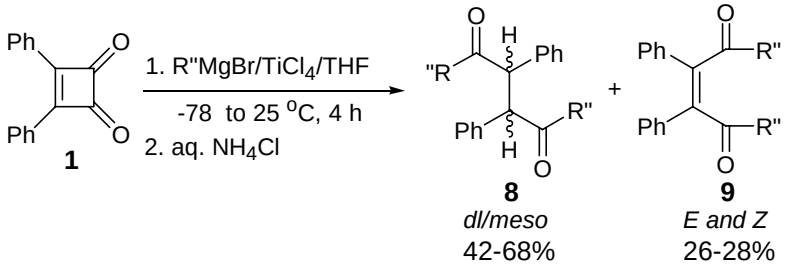
1,7-octadiyne-3,6-dione **7** in low yields (**Scheme 4**). The major isomer of **7** (R' = C_6H_5) was identified by single crystal X-ray analysis.

Scheme 4



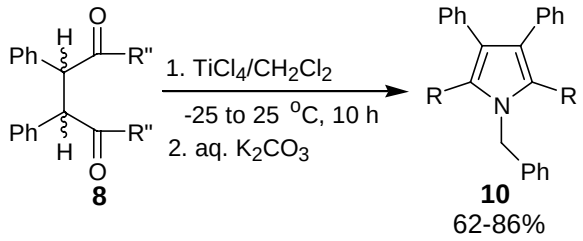
We have also examined the reactivity of alkyltitanium species prepared using RMgX and $TiCl_4$. The reaction of alkyltitanium reagents prepared in this way with 3,4-diphenyl-3-cyclobutene-1,2-dione **1** gave products **8** and **9** (**Scheme 5**). The compounds **8** (R" = C_2H_5), (R" = C_6H_5) and **9** (R" = PhOMe) were characterized by single crystal X-ray analysis.

Scheme 5



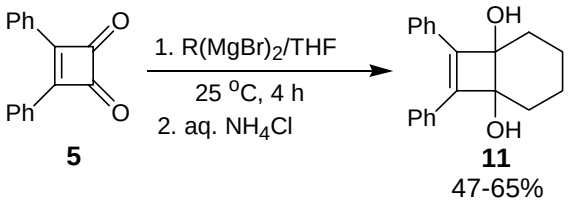
The 1,4-diketones **8** are readily converted to tetrasubstituted pyrroles **10** using $TiCl_4$ in dichloromethane at –25 to 25 °C (**Scheme 6**).

Scheme 6



We have also carried out the reaction of alkylmagnesium reagents, prepared using dibromoalkanes/magnesium reagent system, with diphenylcyclobutenedione. The corresponding bicyclic diols **11** were obtained as major products in moderate yields (**Scheme 7**). The product **11** (R = $^{-}CH_2^{-}CH_2^{-}CH_2^{-}CH_2^{-}$) was identified by single crystal X-ray analysis.

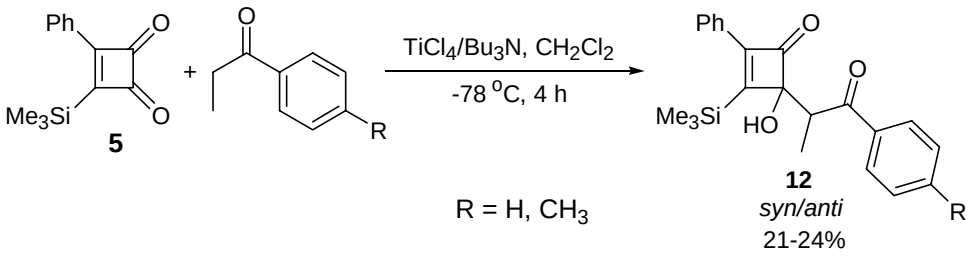
Scheme 7



5 **11**
47-65%

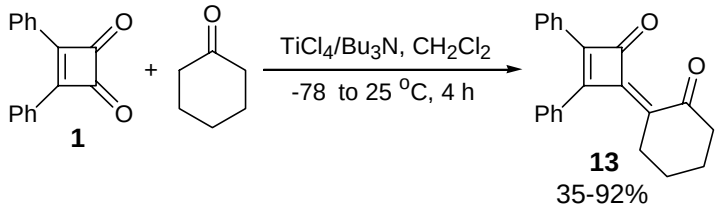
The aldol reaction was performed using acyclic and cyclic ketones and $TiCl_4/Bu_3N$ at –78 ºC, with a few cyclobutenediones. The corresponding aldol adducts were obtained in low yields (**Schemes 8**).

Scheme 8



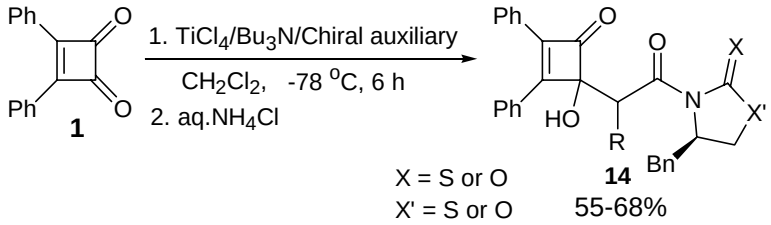
Whereas the reaction of cyclic ketones at –78 to 25 °C, with 3,4-diphenyl-3-cyclobutene-1,2-dione **1** provided the corresponding enones in good yields (**Scheme 9**). The product obtained in the reaction of indanone was characterized by single crystal X-ray analysis.

Scheme 9



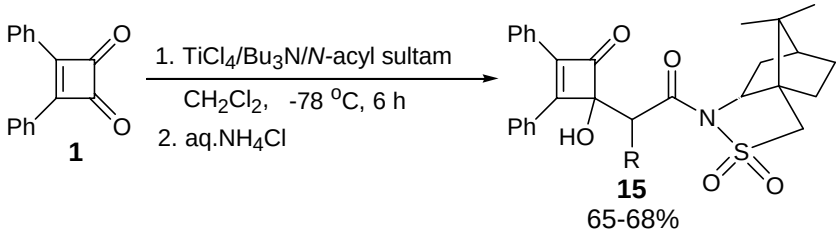
We have also examined some asymmetric transformations using diphenylcyclobutenedione. The reaction of *N*-acyl-oxazolidinethiones *N*-acyl-thiazolidinethiones and *N*-acyl-oxazolidinones and $TiCl_4/Bu_3N$ with 3,4-diphenyl-3-cyclobutene-1,2-dione **1** at –78 °C gave the corresponding 4-hydroxycyclobutenedione products **14** with good diastereoselectivity (**Scheme 10**).

Scheme 10



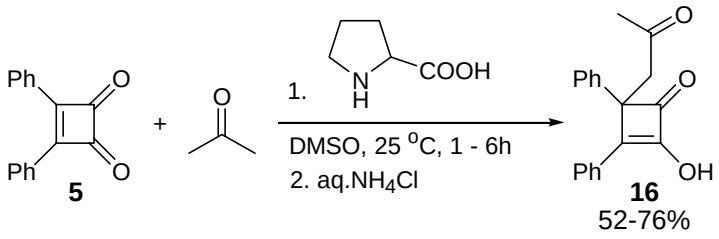
We have also carried out the reaction of titanium enolates, generated *in situ* using *N*-acyl-camphorsultam and $TiCl_4/Bu_3N$ at –78 °C, with diphenylcyclobutenedione **1**. The corresponding 4-hydroxy-4-acyl-camphorsultam-2-cyclobutenones **15** were obtained with good selectivity (**Scheme 11**).

Scheme 11



We have further examined the reaction of diphenylcyclobutenedione using L-proline in the presence of acetone. Only, the corresponding racemic 1,4-addition product was obtained (**Scheme 12**). The product **16** was also characterized by single crystal X-ray analysis.

Scheme 12



Mechanisms and intermediates involved in these transformations are discussed.

Note: Scheme numbers and compound numbers given in this abstract are different from those given in the Chapters. Thermal ellipsoids of ORTEP diagrams are drawn at 25% probability.

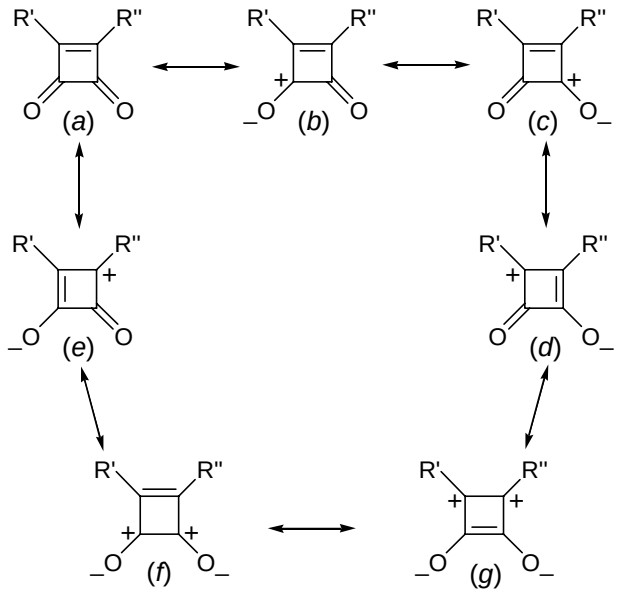
Contents

1. Introduction

1.1 Synthetic Applications of Cyclobutenedione Derivatives

The first cyclobutenedione was synthesized by *J. D. Roberts et al.*[1a] in 1955. Cyclobutenediones are considered as quinones of unstable cyclobutadienes because of their formal resemblance to cyclobutadienes by virtue of all sp^2 hybridized carbons in a four membered ring.[1] The initial studies on cyclobutenediones were limited primarily to their unusual stability,[1] vinylogous behaviour[2] and aromaticity of their oxoanions.[3] Extraction of moniliformin, a fungal toxin, from *Fusarium moniliforme* by *Cole et al.*[4] led to the synthesis and testing of a wide range of cyclobutenediones. Consequently, a number of biological and pharmaceutical applications of cyclobutenediones were discovered. For example, the di-*n*-butylsquarate is a potent allergen and has been used in the treatment of alopecia areata, and in immunotherapy for warts in children.[5,6] Squaric acid itself is an inhibitor of glyoxylase,[7] semisquaric acid is for pyruvate dehydrogenase and transketolase[8] is inhibitor for protein tyrosine phosphatases.[9]

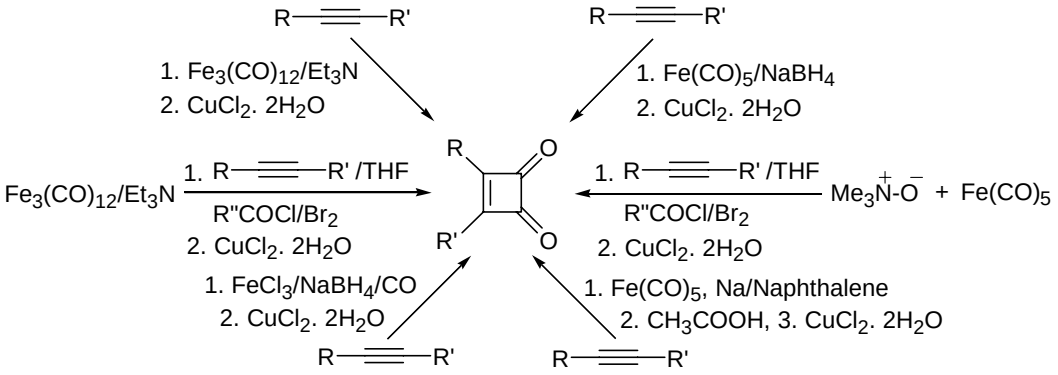
Synthetic investigations on cyclobutenediones have been concerned previously with three characteristic derivatives: i. Phenylcyclobutenedione, ii. Benzocyclobutenedione, iii. Squaric acid.[10] The cyclobutenediones can be considered as resonance hybrids of a series of dipolar structures. These characteristics make the cyclobutenediones as useful reactive intermediates.



Whereas several reactions, such as the Bayer-Villiger reaction, the Beckmann and Favorskii rearrangement and *cine*-substitution proceed in a manner specific to four-membered rings, other reactions such as the facile ring opening by nucleophiles, the rearrangement to tropolones, the thermal [2+2]-cycloreversion, the isomerisation to vinyl ketenes and the photochemical formation of oxacarbenes are rather specific to cyclobutenediones and cyclobutenones. The selectivity and the excellent yields of such transformations, which are favored or caused by ring strain as the driving force, offer the synthetic chemist interesting possibilities for the development of new strategies for the synthesis of natural products and biologically active compounds.[11]

The cyclobutenediones can be readily accessed following methods developed in this laboratory (**Chart 1**).[12-18]

Chart 1

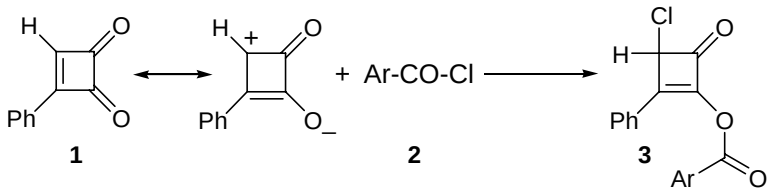


We have decided to explore the reactions of these useful intermediates. Accordingly, it may be of interest to review literature reports on various reactions of cyclobutenediones.

1.1.1 Reaction of Electrophiles with Cyclobutenedione Derivatives

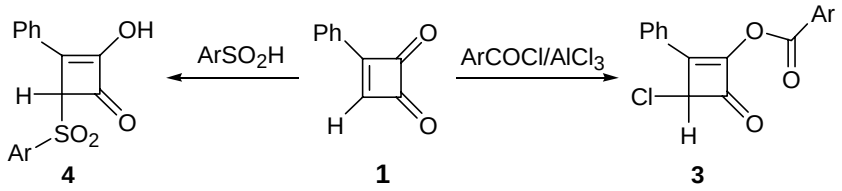
The reaction of aryl halides **2** with phenylcyclobutenedione **1** results in arylation of the carbonyl group adjacent to the phenyl residue to form the 2-aroyloxy-4-halo-3-phenyl-2-cyclobutene-1-ones **3** in good yields (**Scheme 1**).[19] Whereas, the reaction of 3,4-diphenylcyclobutenedione with benzoyl bromide in the presence of catalytic quantities of zinc chloride or with thionyl chloride in dimethylformamide leads to 2,2-dihalo-3,4-diphenylcyclobutenones.[19]

Scheme 1



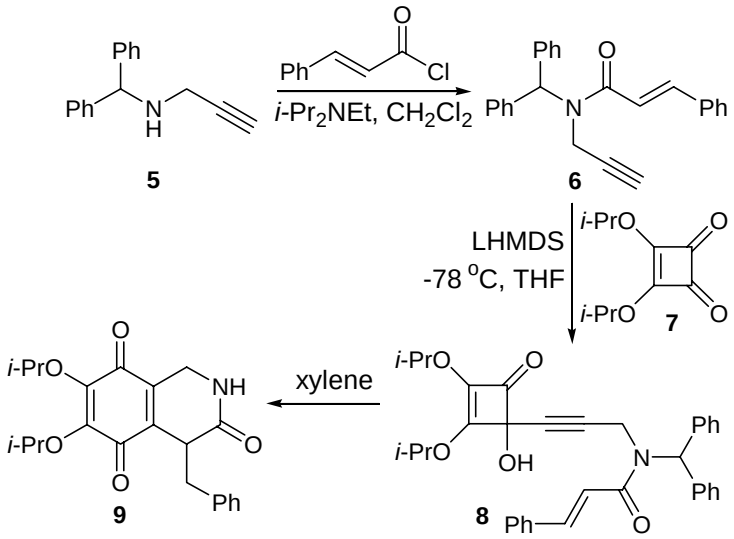
Acylation of phenylcyclobutenedione under Friedel Crafts reaction conditions provides the 1,4-addition product **4** (**Scheme 2**).[19]

Scheme 2



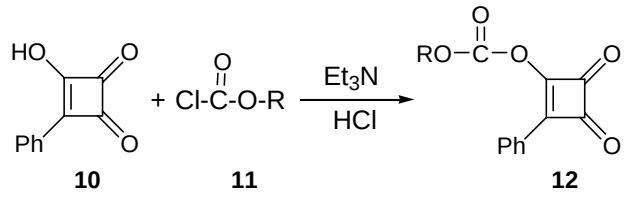
Acylation of amine **5** with cinnamoyl chloride gives the acylated product **6** which was further reacted with diisopropylcyclobutenedione **7** to obtain the adduct **8** that on further reaction proceeds in xylene to give the cyclized product **9** (**Scheme 3**).[20]

Scheme 3



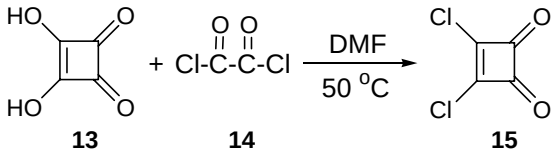
Reaction of 2-hydroxy-1-phenylcyclobutene-2-4-dione **10** in the presence of tertiary amine leads to the mixed anhydrides **12** (**Scheme 4**).[21]

Scheme 4



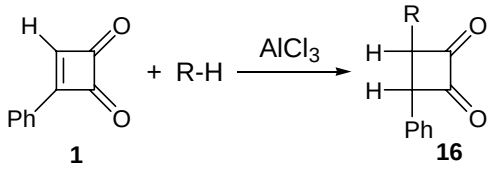
The 1,2-dichlorocyclobuten-3,4-dione, a useful synthon is obtained by the dimethylformamide catalyzed reaction of squaric acid and oxalyl chloride (**Scheme 5**).[22]

Scheme 5



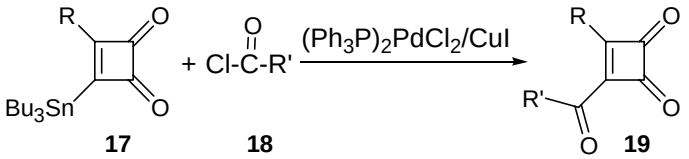
Aromatic compounds add readily to phenylcyclobutenedione **1** in the presence of an equimolar quantity of aluminum chloride to give the product **16** (**Scheme 6**).[23]

Scheme 6



Also, a variety of acyl substituted cyclobutenediones were prepared following a similar strategy (**Scheme 7**).[24]

Scheme 7

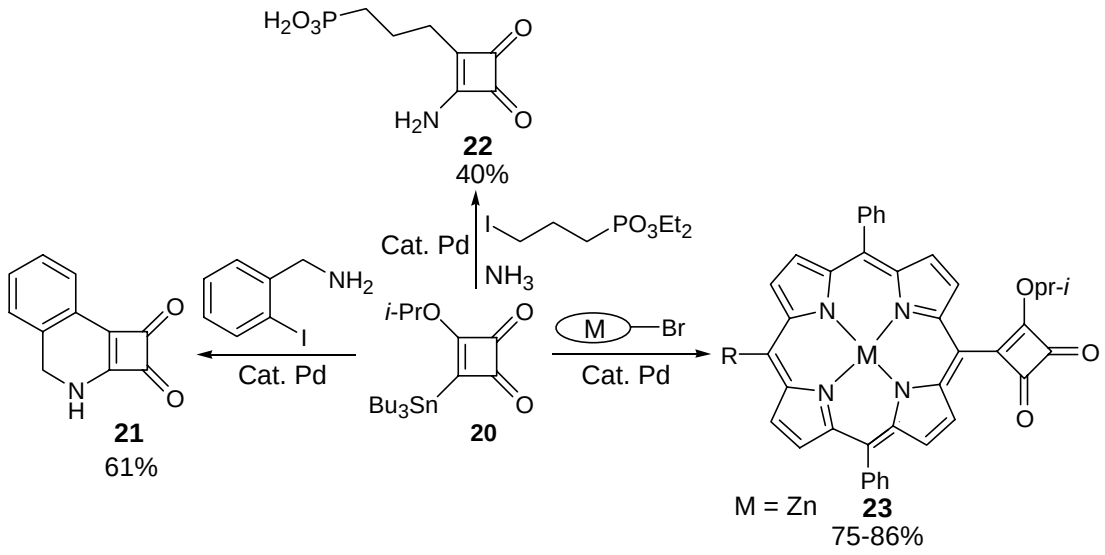


	R' = Ph	(E)-propenyl	*p*-OMeC$_6$H$_4$
R = NH_2	84%	93%	98%
O*i*-Pr	79%	68%	65%
N-piperidinyl	92%	83%	67%
N-morpholinyl	73%		

Stannylcyclobutenedione **20** undergoes cross-coupling with organic iodides attached to sp^3, sp^2 and sp-hybridized carbon atoms and with vinyltrifluoromethane-sulfonate esters in the presence of $PhCH_2Pd(PPh_3)_2Cl$/CuI catalyst to provide a wide

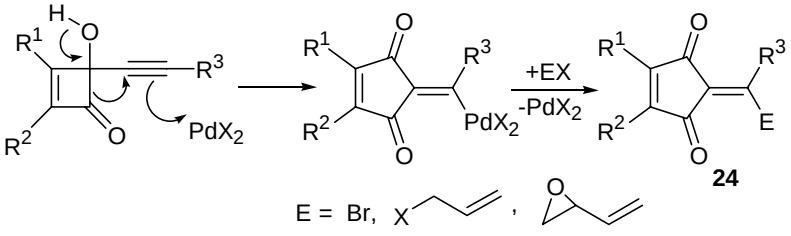
variety of substituted cyclobutenediones[24-26] including some porphyrin derivatives (**Chart 2**).[27]

Chart 2

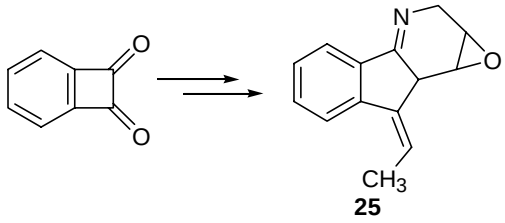


Liebeskind et al.[28] demonstrated that 4-alkynyl-4-hydroxycyclobutenones and their acetals undergo an efficient tandem ring expansion-functionalization sequences catalyzed by palladium(II) in the presence of suitable electrophiles such as H^+, NBS, and allyl bromide to give 2-alkylidene-4-cyclopentene-1,3-diones **24** with high stereoselectivity at the exocyclic double bond (**Scheme 8**).[12,29] Benzoabikoviromycin **25**, a potential antiviral agent has been synthesized following a similar strategy (**Scheme 9**).[30]

Scheme 8



Scheme 9



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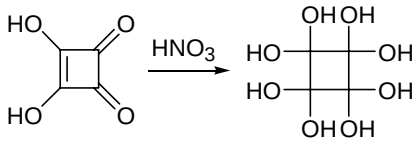
1.1.2 Oxidation Reactions of Cyclobutenedione Derivatives

Oxidation of squaric acid **13** under mild conditions affords octahydrocyclobutane **26** (**Scheme 10**).[31]

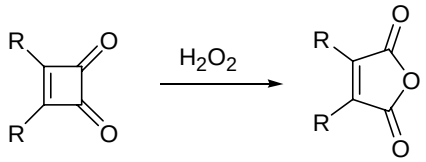
Scheme 10



13 **26**

It has been reported that cyclobutenediones undergo Bayer-Villiger type oxidation with hydrogen peroxide to give maleic anhydride derivatives (**Scheme 11**).[32]

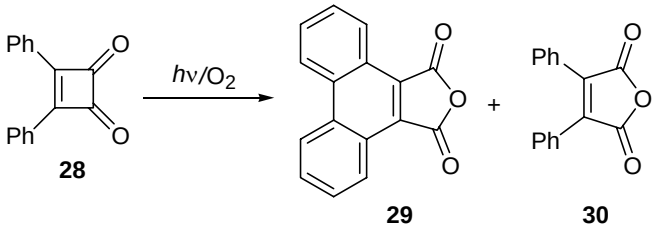
Scheme 11



27

Cyclobutenediones undergo facile ring expansion reaction to yield monomeric anhydrides under the influence of light (**Scheme 12**).[33]

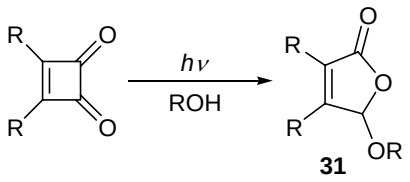
Scheme 12



28 **29** **30**

Irradiation of cyclobutenedione in the presence of methanol gives ring expanded product (**Scheme 13**).[34,35]

Scheme 13



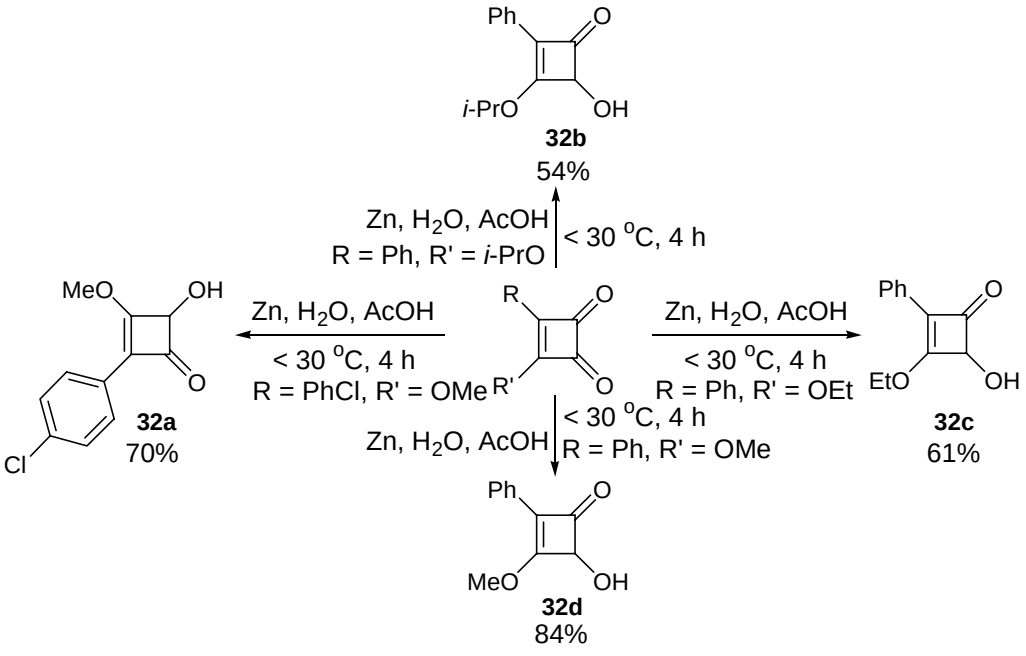
31

1.1.3 Reaction of Nucleophiles with Cyclobutenedione Derivatives

1.1.3.1 Reaction of Hydrides with Cyclobutenedione Derivatives

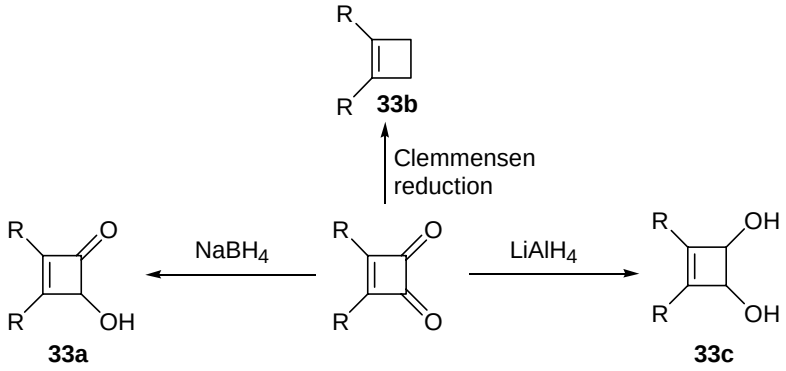
Recently, a new method was introduced to reduce cyclobutenedione derivatives using zinc to prepare 4-hydroxy-2-cyclobutennones (**Chart 3)**. The latter compounds gave new 5-halo-2(5*H*)-furanones by the reaction with halogenating agents *via* a cationic ring-opening-ring-closing mechanism.[36]

Chart 3



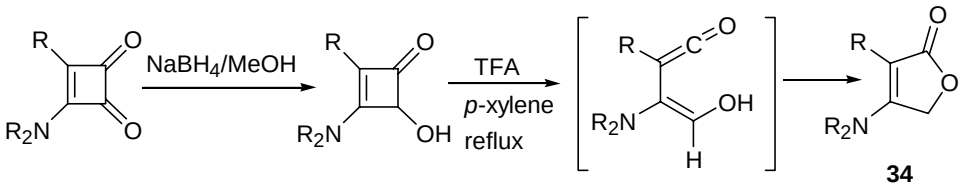
Cyclobutenediones are generally resistant to reducing agents and attempted catalytic hydrogenations were unsuccessful. However, under drastic conditions of the Clemmensen reduction, cyclobutene **33b** is obtained.[1b] Whereas, lithium aluminum hydride reduces both the carbonyls,[37] sodium borohydride reduces only one (**Chart 4**).[38]

Chart 4



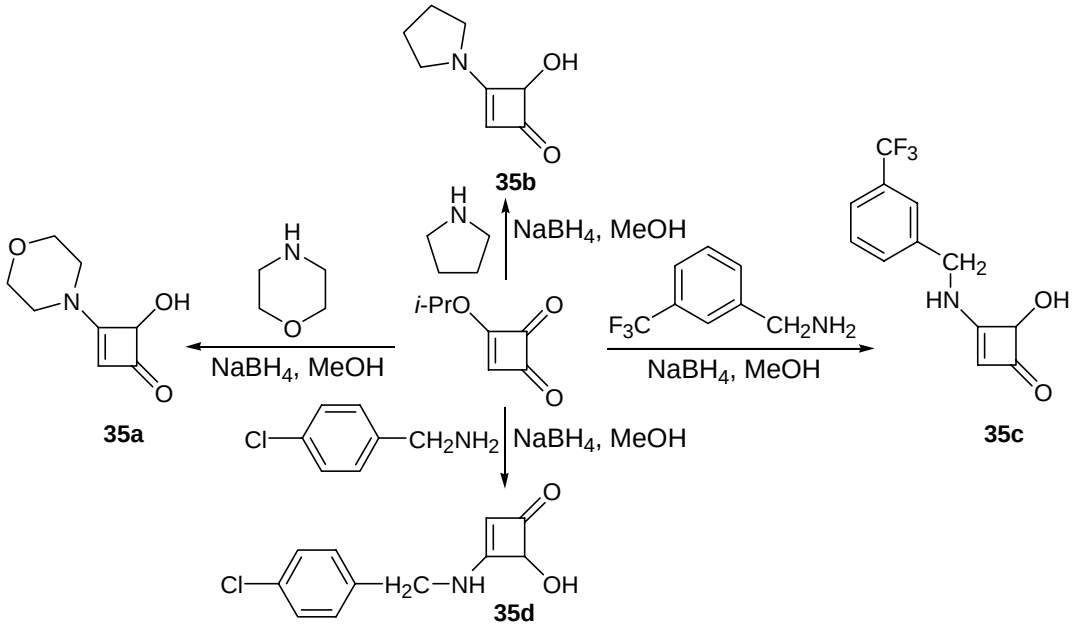
Similarly, 4-aminofuran-2(5H)-ones **34** were prepared *via* reduction followed by thermal ring expansion (**Scheme 14**).[38]

Scheme 14



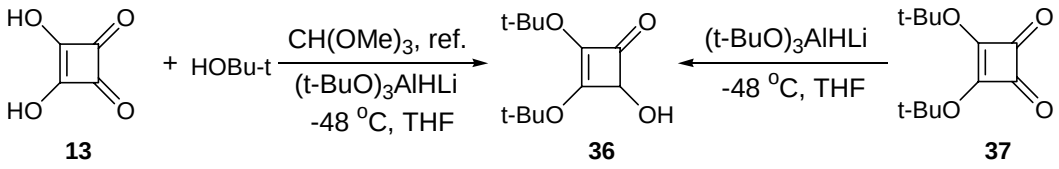
Several mono substituted reduced derivatives 3-amino-4-hydroxycyclobutene-diones **35a-d** of isopropyloxy cyclobutenedione were obtained using the $NaBH_4$/MeOH reagent system in high yields (**Chart 5**).[38]

Chart 5



Squaric acid **13** was reduced to the corresponding alcohol **36** in the presence of tertiary butyl alcohol and trimethoxymethane with LiAl(*t*-BuO)$_3$H under reflux conditions. Whereas, the tertiary butyl derivative of squaric acid **36** was reported to give the product at lower temperatures (**Scheme 15**).[39]

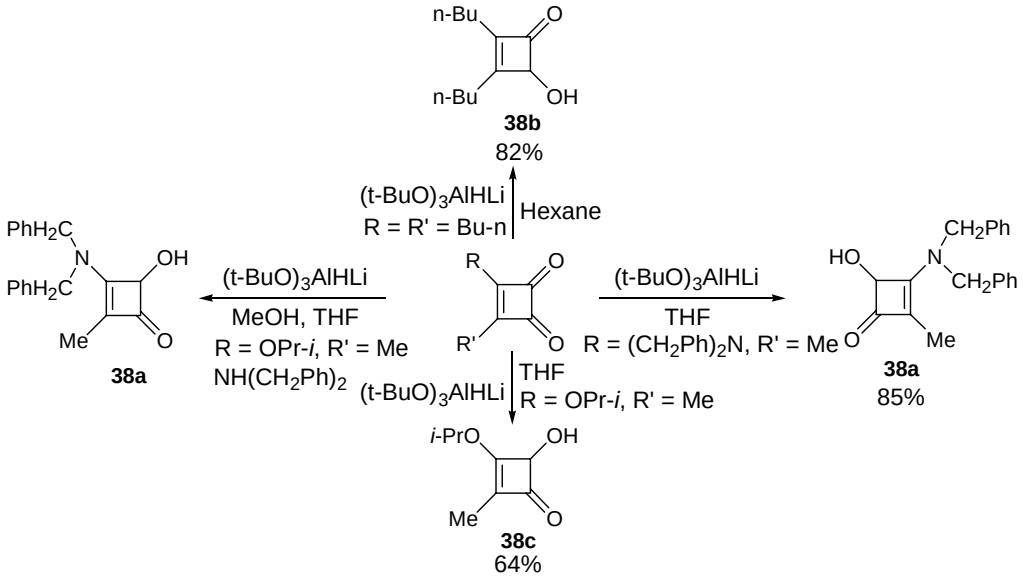
Scheme 15



Regiospecific construction of the desired substrates was achieved either directly from cyclobutenediones bearing one alkoxy or amino substituent (selective hydride reduction of more reactive carbonyl group with 1 equiv. of LiAl(*t*-BuO)$_3$H) or *via* the appropriate cyclobutenedione monoacetal (reduction of the unprotected carbonyl group with diisobutylaluminum hydride and hydrolysis to the corresponding 4-hydroxycyclobutenediones). In other words cyclobutenediones bearing on alkoxy or

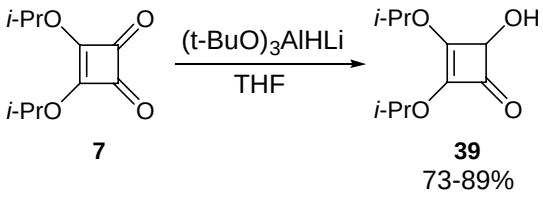
amino sbstituent react with nucleophiles exclusively at the non-vinylogous ester or non-vinylogous amide carbonyl group (**Chart 6**).[40]

Chart 6



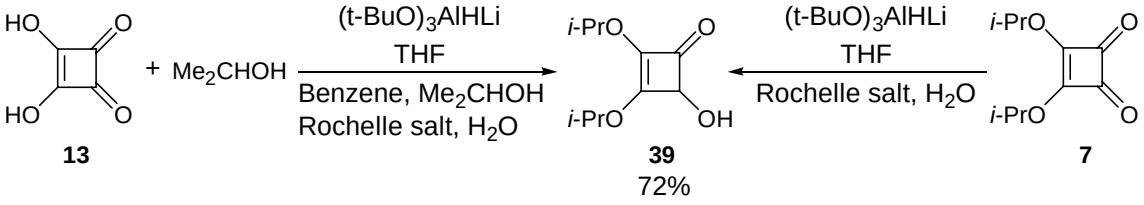
The 2,3-diisopropoxy-4-hydroxycyclobutene-1-one **39** was obtained by the reduction using LiAl(*t*-BuO)$_3$H) in good to excellent yields (**Scheme 16**).[41,42]

Scheme 16



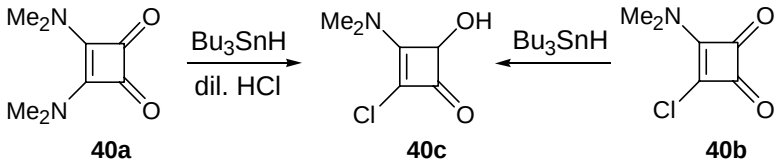
Diisopropylsquarate easily prepared by refluxing squaric acid **13** in 2-propanol or benzene with azeotropic removal of H_2O followed by reduction of carbonyl with LiAl(*t*-BuO)$_3$H) gives **27**. Whereas, the diisopropylsquarate **7** gives the adduct in the presence of Rochelle salt (isopropyl bromide and the bis (Ag salt) of squaric acid) and organolithium reagents (**Scheme 17**).[43]

Scheme 17



Regiospecific preparation of the 2-chloro-3-dimethylamino-4-hydroy-cyclobut-2-enone **40c** *via* selective reduction of carbonyl group of 3,4-bis-dimethylamino-cyclobut-3-ene-1,2-dione **40a** and 3-chloro-4-dimethylamino-cyclobut-3-ene-1,2-dione **40b** using Bu_3SnH has been reported (**Scheme 18)**.[44]

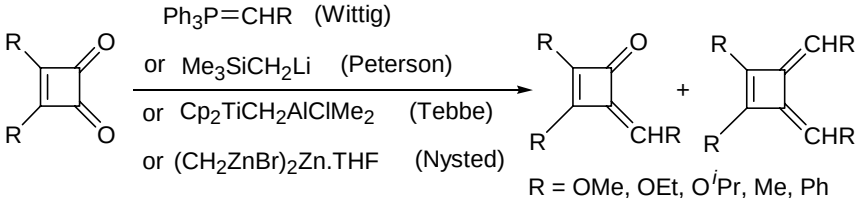
Scheme 18



1.1.3.2 Reaction of Organometallic Reagents with Cyclobutenedione Derivatives

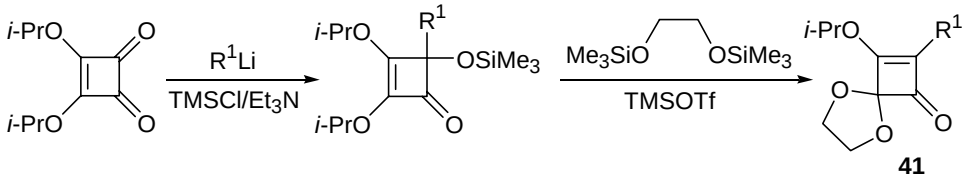
Methylenecyclobutenones were prepared by a variety of olefinating reagents and cyclobutenediones (**Scheme 19**).[45] Reaction of the dione with one equivalent of Wittig reagent is highly selective, giving only monoalkylidenation product, whereas with other olefination reagents bis(alkylidenation) product is also formed in lower yields. The use of two equiv. of Cp_2TiMe gives bis(methyledene)cyclobutene exclusively.

Scheme 19



Regioselective monoacetalisation of cylobutenediones was achieved (**Scheme 20**).[46] This sequence of reactions provides access to a wide range of isomeric cyclobutenedione monoacetals.

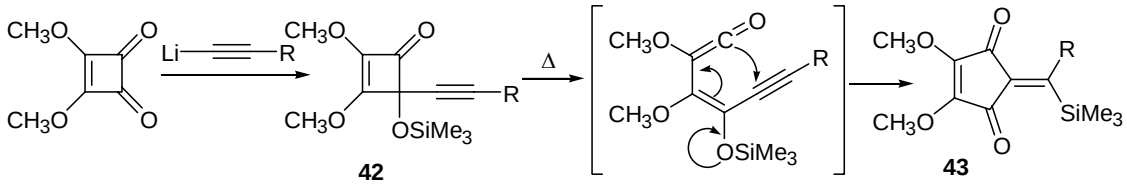
Scheme 20



Recently, monoehtylenedithioacetals **41** have been prepared by a similar method.[47] These compounds were shown to be valuable precursors for the synthesis of multifunctional molecules.

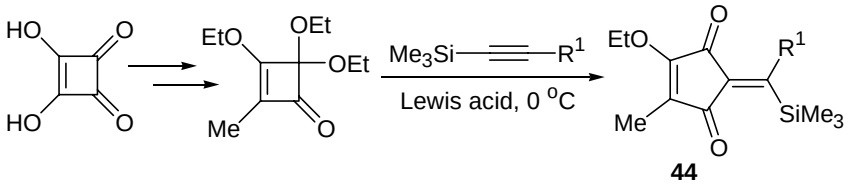
Thermolysis of 4-alkynyl-4-hydroxy or trimethylsilyloxy cyclobutenones **42** provides 2-alkylidene-4-cyclopentene-1,3-diones **43** (**Scheme 21**).[48,49] Presumably, these transformations proceed *via* electrocyclic ring opening of the cyclobutenone to an unsaturated vinylketene intermediate.

Scheme 21



Also, cyclobutenedione monoacetals react with silylacetylenes in the presence of Lewis acids as catalyst to form alkylidenecyclopentenediones **44** *via* cationic 1,2-silyl migration (**Scheme 22**).[50]

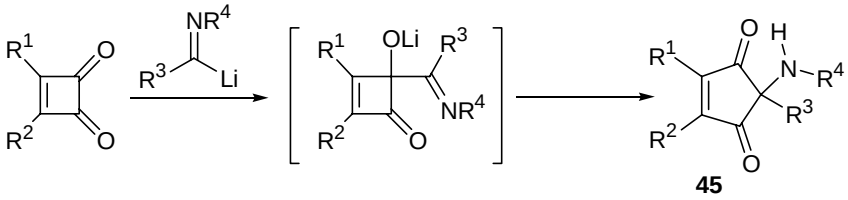
Scheme 22



44

The 2-(alkylamino)-4-cyclopentene-1,3-diones **45** could be prepared in good yields by the nucleophilic addition of imidoyl lithiates to cyclobutenediones (**Scheme 23**).[51]

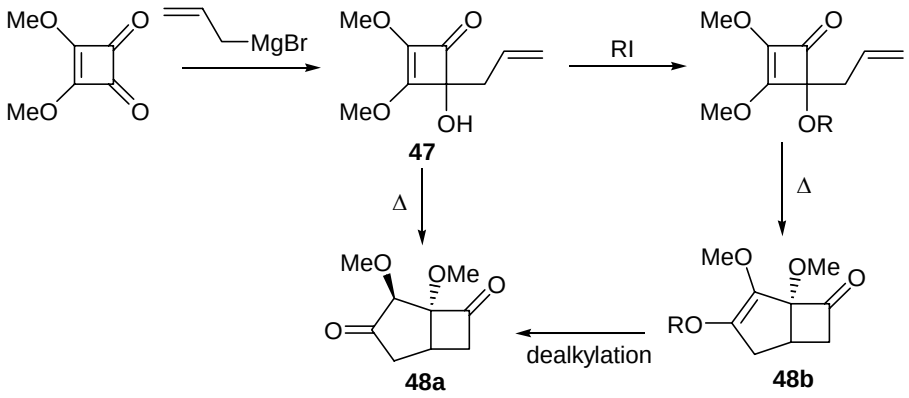
Scheme 23



45

It has been reported that 4-hydroxy-4-allyl-cyclobutenones **47**, prepared by the addition of allyl Grignard to dimethyl squarate, give functionalized bicyclic[3.2.0]heptane-3,7-diones **48a** or bicyclic[3.2.0]heptanones **48b** in good yields.[52] This transformation is envisaged to involve an electrocyclic ring opening of cyclobutenone and subsequent intramolecular [2+2] cycloaddition of the resulting vinylketene (**Scheme 24**).

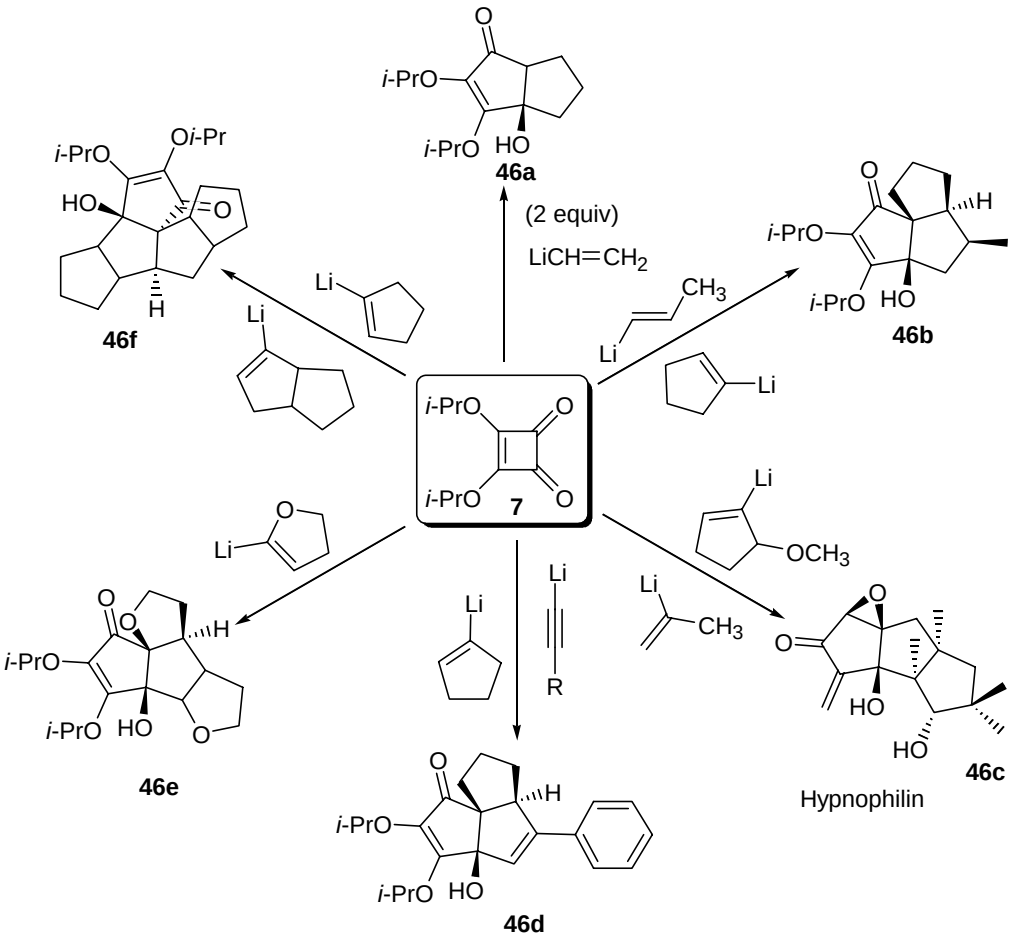
Scheme 24



47 **48a** **48b**

Two-fold addition of alkenyl anions (same or different) to a squarate ester initiates a cascade of chemical events that were exploited for the synthesis of highly functionalized polyquinanes (**Chart 7**).[53-62]

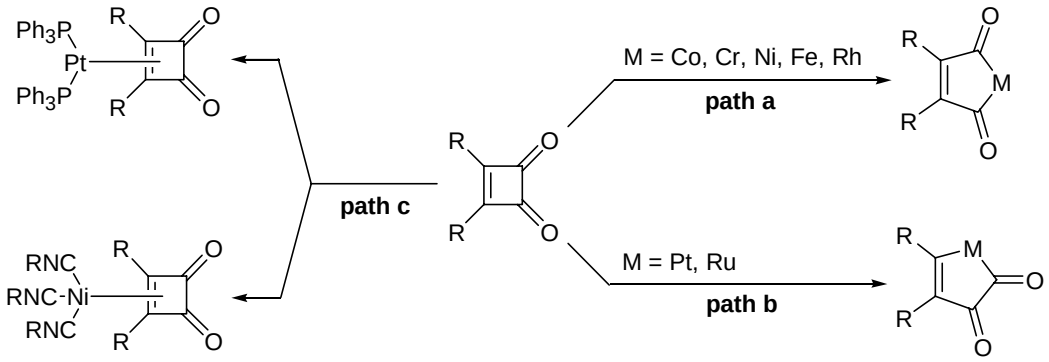
Chart 7



It has been reported that cyclobutenediones reacts with low-valent transition metal phosphine or carbonyl complexes to form stable metallocyclic complexes *via* C-C bond cleavage. The C-C single bond between a carbonyl and the α-carbon of cyclobutenedione is relatively weaker than other C-C single bonds. Moreover, carbonyl group kinetically facilitates the insertion of a transition metal into the α-C-C bond.[63] Activation of C-C bonds in cyclobutenediones by transition-metal complexes follows

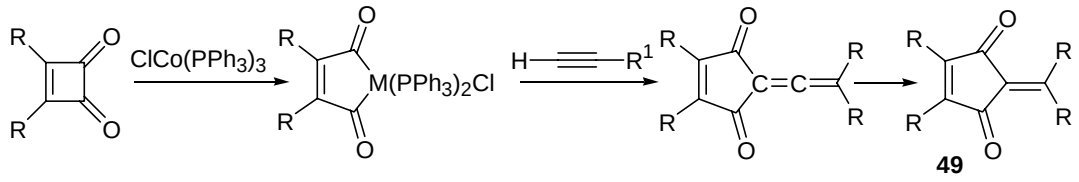
the two pathways illustrated in **Scheme 25**. Most transition-metal complexes, including those of rhodium, cobalt, iron, and nickel gave maleoyl metal complexes as a thermodynamic product resulting from insertion of the metal between two carbonyl groups in cyclobutenediones (**path a**),[64] while treatment of cyclobutenediones with platinum or ruthenium[65] complexes give unsymmetrical cleavage of the four membered ring to produce a kinetic product (**path b**). Some of the platinum and nickel complexes also form stable olefin complexes (**path c**).[66]

Scheme 25



Maleoyl metal complexes formed *via* **path a** can be selectively converted either to quinones or 5-alkylidene-2-cyclopentene-1,4-diones **49** using alkynes and under appropriate reaction conditions (**Scheme 26**).[67]

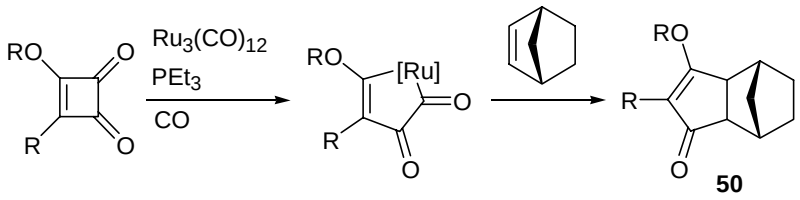
Scheme 26



Very recently, $Ru_3(CO)_{12}$ catalyzed unusual coupling of cyclobutenediones with alkenes was discovered for the preparation of cyclopentenone **50** with high

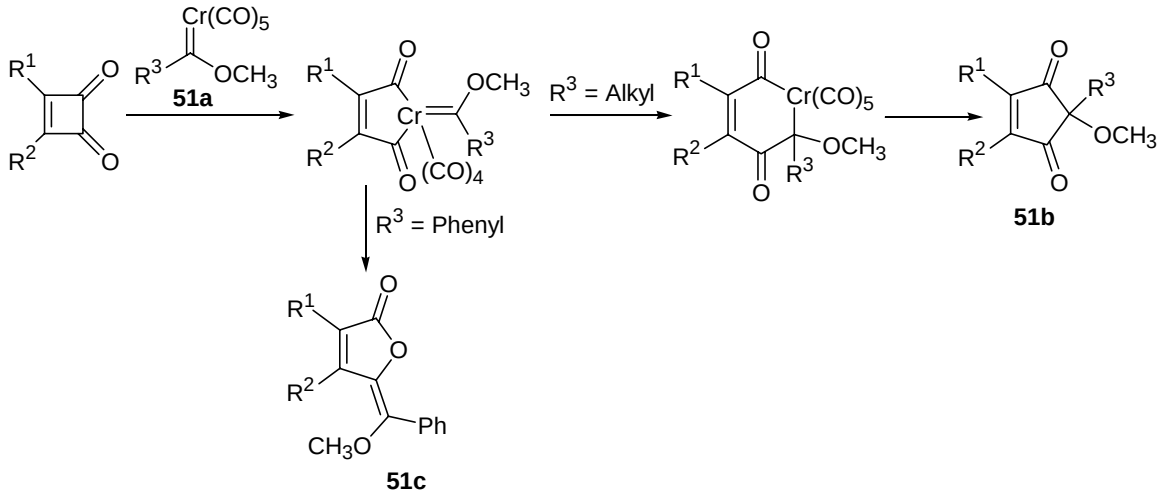
stereoselectivity (*exo* 100%) (**Scheme 27**).[68] The formation of cyclopentenones is believed to proceed *via* C-C bond cleavage (**path b**).

Scheme 27



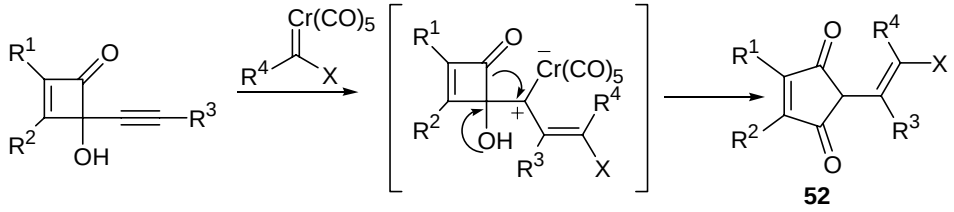
A novel C-C bond insertion reaction of Fisher carbenes **51a**, with cyclobutenediones has been discovered to produce 2-alkoxy-4-cyclopentene-1,3-diones **51b** as well as **51c**.[69] The proposed mechanism involves oxidative addition of the acyl-acyl C-C bond, followed by carbene insertion and reductive elimination (**Scheme 28**).

Scheme 28



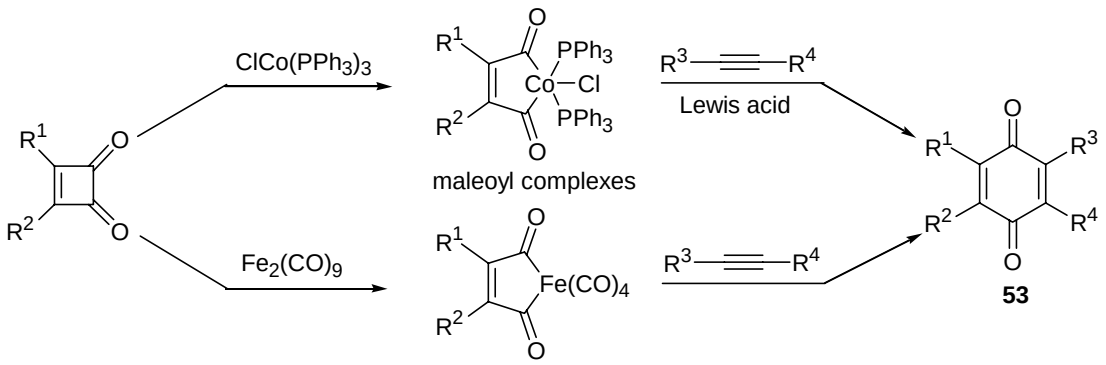
Chromium carbene complexes are also shown to react with 1-alkynylcyclobutenols to generate 2-alkenyl-4-cyclopentene-1,3-diones **52** (**Scheme 29**).[70]

Scheme 29



Quinone moiety is an important functionality present in many different classes of biologically active molecules including the K vitamins, ubiquinones, antibiotics and anticancer drugs.[71] Efficient synthesis of various quinones starting from cyclobutenediones have been developed. Cyclobutenediones undergo oxidative addition of the acyl-acyl C-C bond with low valent metal reagents to form maleoyl complexes, which reacts with alkynes by an insertion-elimination sequence to produce quinones (**Scheme 30**). Cobalt maleoyl complexes are superior to iron complexes and they generate quinones with a variety of alkynes from electron rich to electron deficient and to sterically demanding alkynes.[72]

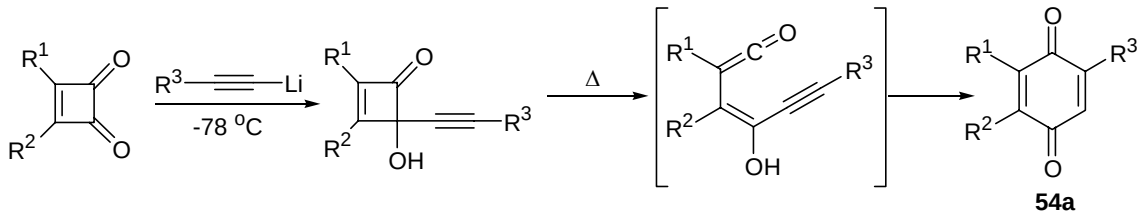
Scheme 30



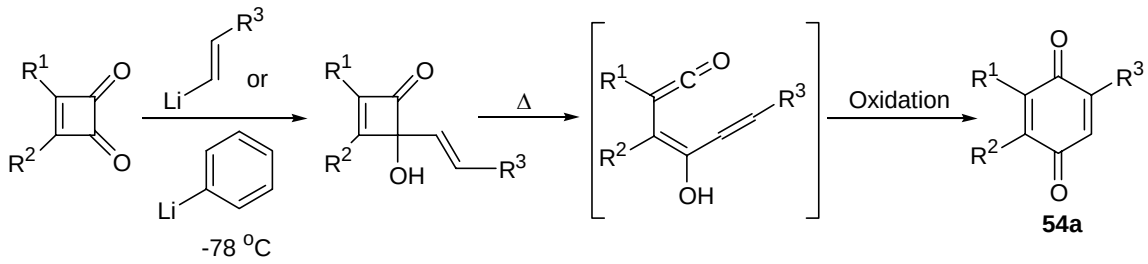
Powerful methodologies have been developed for the synthesis of quinones *via* electrocyclic ring opening of cyclobutenones, which may be accessed by addition of lithium nucleophiles to cyclobutenediones. Thermolysis of 4-alkynyl cyclobutenones

directly give substituted quinones *via* unsaturated ketenes (**Scheme 31**) while 4-aryl or 4-alkenyl cyclobutenones give quinones after oxidation (**Scheme 32**).[73]

Scheme 31

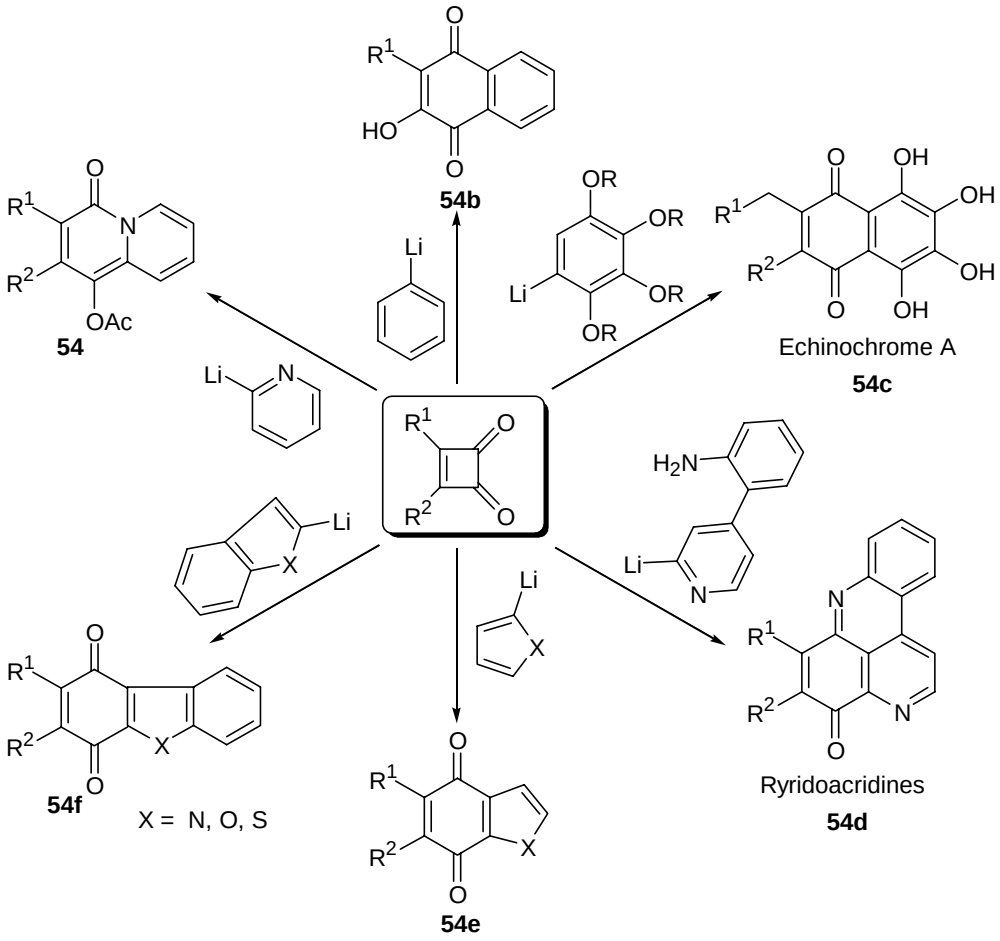


Scheme 32



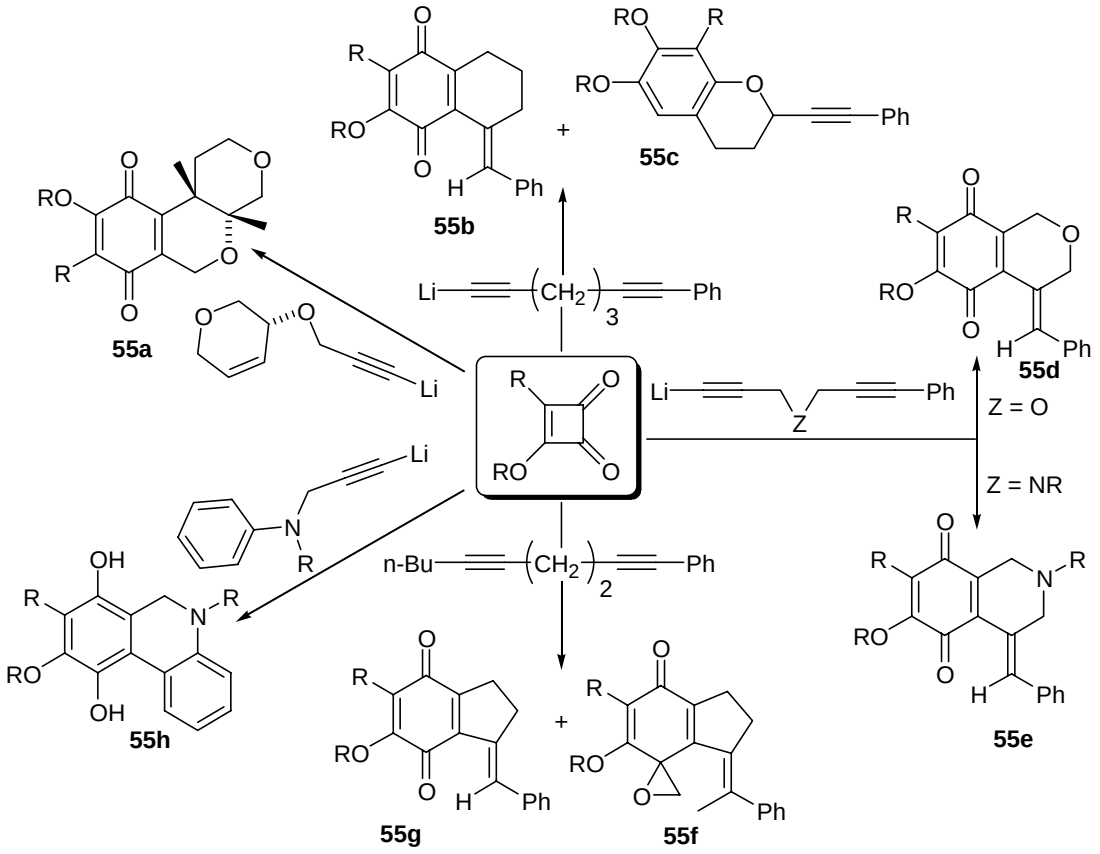
This chemistry has been extended to prepare a wide range of highly substituted quinones **54b-g** (**Chart 8**).[26a,49,74-77]

Chart 8



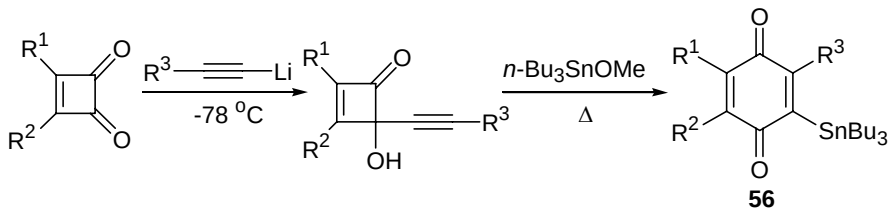
Also, it was observed that if the nucleophile is a diyne or enyne, further cyclization reactions results in the formation of highly functionalized molecules such as pyranoquinones **55a**, **55d**, piperidinoquinones **55e**, phenanthridinediols **55h**, annelated quinones, spiro epoxycyclohexadienones (**Chart 9**).[78]

Chart 9



Stannylquinone[79] **56**, a nucleophilic quinone and functionalized Stille cross coupling partner, has been synthesized by the thermolysis of 4-alkynyl-4-hydroxycyclobutenones in the presence of *n*-Bu_3SnOMe (**Scheme 33**).[79a]

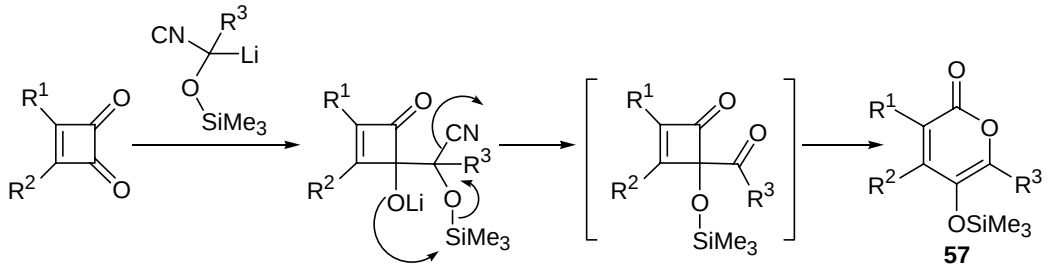
Scheme 33



The above versatile chemistry has been extended to the synthesis of substituted α-pyrones.[80] The addition of a lithiated *o*-silylated cyanohydrin to a cyclobutenedione with subsequent intramolecular 1,4-silyl migration and displacement of cyanide

generates 4-acylcyclobutenone which undergo facile rearrangement to form substituted α-pyrones **57** (**Scheme 34**).

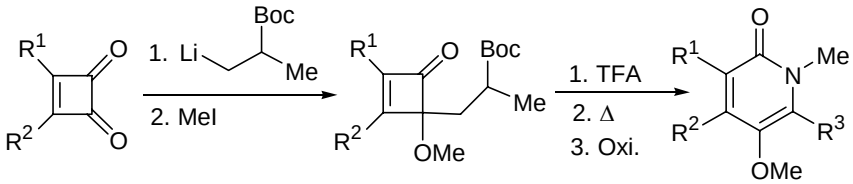
Scheme 34



57

Also, 2-pyridinones **58** were synthesized by the addition of N-protected α-amino carbanions to cyclobutenediones followed by deprotection and thermal ring expansion (**Scheme 35**).[81]

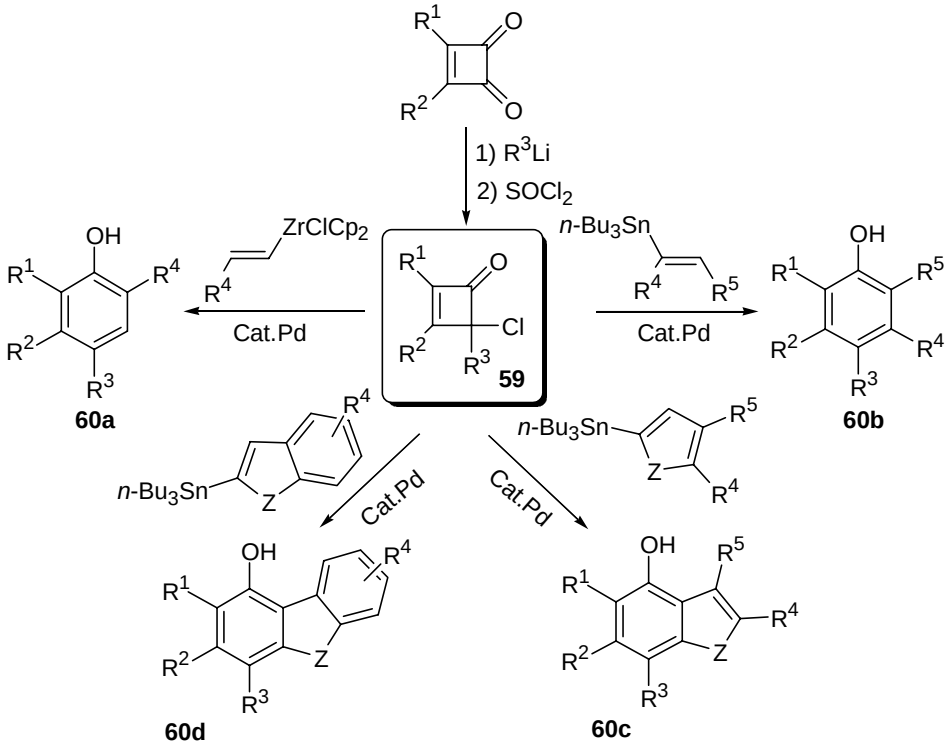
Scheme 35



58

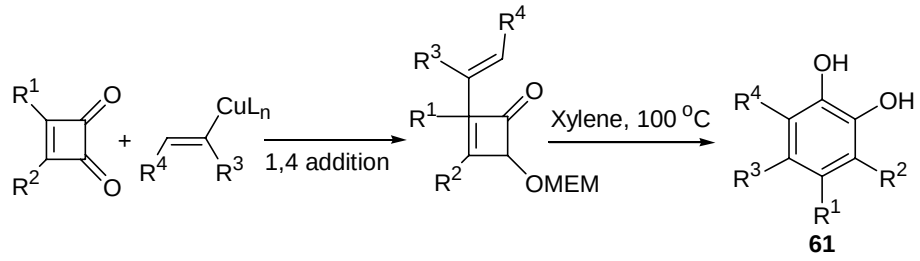
Thermolysis of 4-vinyl or 4-aryl-2-cyclobutenediones, prepared by the palladium catalyzed cross coupling of organotin or organozirconium reagents with 4-chloro-2-cyclobutenediones **59**, gives thermal-electrocyclic ring opening to provide highly substituted phenols **60a-d** (**Chart 10**).[82]

Chart 10

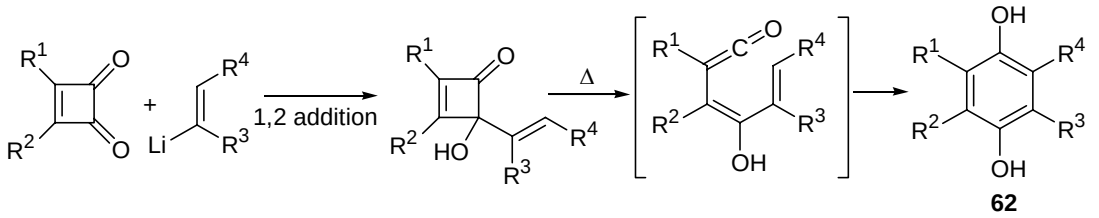


A general method for the synthesis of substituted catecols **61** were developed utilizing the 1,4-addition of vinyl, aryl and heteroarylcuprates to cyclobutenediones followed by thermal ring expansion (**Scheme 36**).[83] Similarly, 1,4 hydroquinones **62** have been prepared using lithium reagents (**Scheme 37**).

Scheme 36

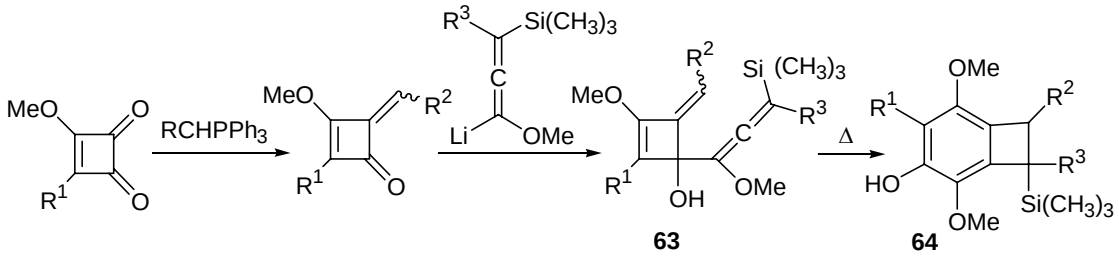


Scheme 37



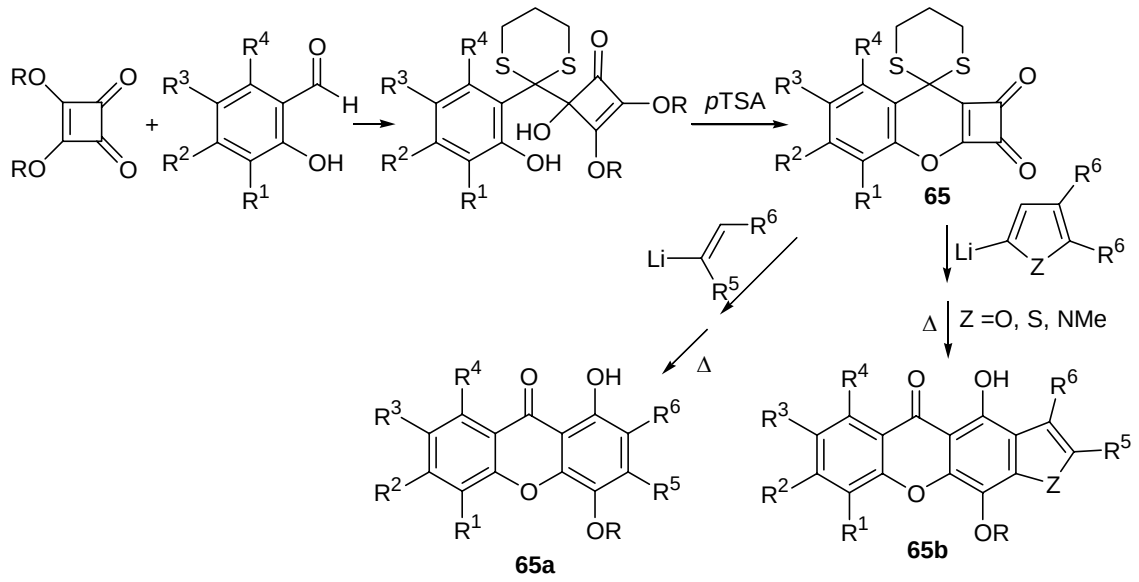
Also, some 3-alkylidene-4-alleylcyclobutenones **63** were shown to undergo unusual thermal ring expansion to highly functionalized benzocyclobutenes **64**. The formation of benzocyclobutenes is envisaged to involve ring opening of the starting cyclobutene to the corresponding octa-1,2,4,6,7,-pentenes that lead to the quinodimethanes upon electrocyclic ring closure (**Scheme 38**).[84]

Scheme 38



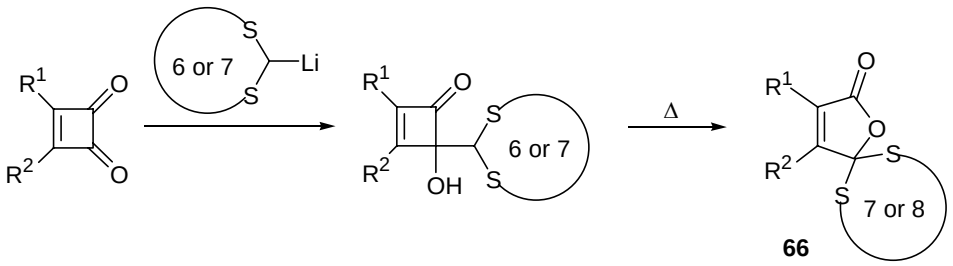
A novel approach to linearly-fused, highly functionalized xanthones **65a**, **65b** was recently discovered based on the benzannulation of alkenyl, aromatic or heteroaromatic lithiates with dithiate protected benzopyrone-fused cyclobutenediones **65** (**Scheme 39**).[85a] This demonstrates the versatility of cyclobutenediones as scaffolds for the construction of a diverse range of molecular structures. Also, similar cyclobutenedione based chemistry was employed to synthesize angularly fused xanthone from *o*-anisoyl substituted cyclobutenediones.[85b]

Scheme 39



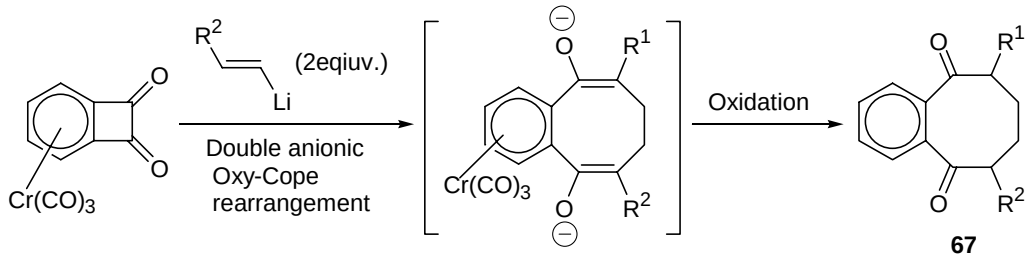
Recently, it was reported that the 4-alkyl-4-hydroxycylobutenones, in which the alkyl group bears sulphur atom at 2-position, undergoes an unusual thermal ring expansion to give spirobutenolide **66** (**Scheme 40**).[86]

Scheme 40



Benzocyclobutenedione coordinated to tricarbonylchromium moiety undergoes double anionic oxy-Cope rearrangement upon nucleophilic addition of vinyllithium reagents to form benzocyclooctan-1,4-diones **67** after oxidation of the metal carbonyl moiety (**Scheme 41**).[87]

Scheme 41

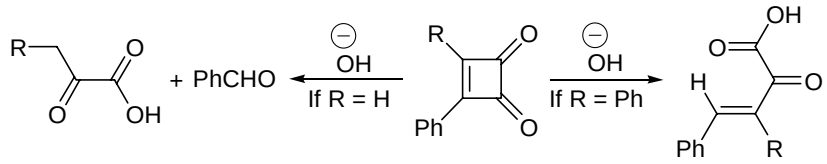


67

1.1.3.3 Reaction of Hydroxides and Azides with Cyclobutenedione Derivatives

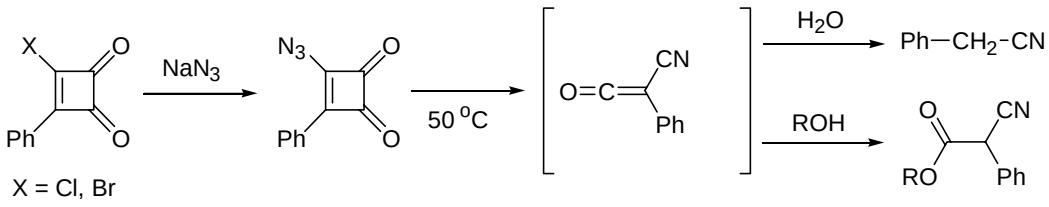
Cyclobutenediones undergo ring cleavage when heated in methanolic alkali solution to afford pyruvic acid derivatives as major decomposition products (**Scheme 42**).[32]

Scheme 42



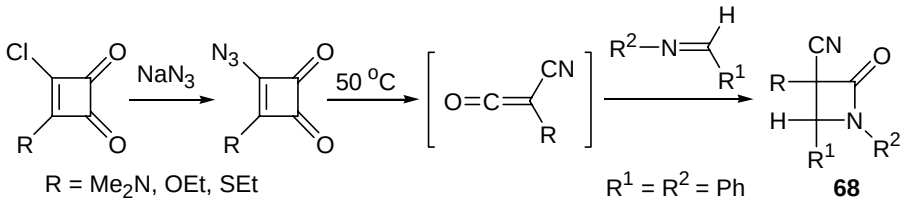
Halocyclobutenediones decomposes to cyanoketenes on sodium azide treatment with simultaneous evolution of N_2 and CO gas.[88] When the reaction is carried out in the presence of either water or alcohol the ring cleaved products such as 2-phenylacetonitrile and alkyl 2-cyano-2-phenylacetate are obtained, respectively (**Scheme 43**).

Scheme 43



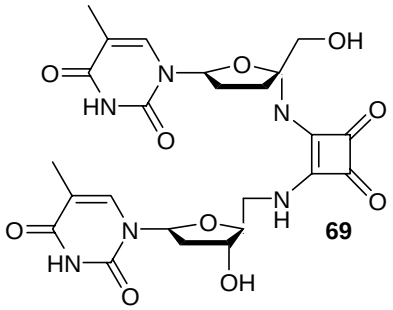
The reaction of sodium azide with chlorosubstituted cyclobutenediones generates cyanoketenes which are trapped by various aldimines to give 3-cyano β-lactams in **68** good yield (**Scheme 44**).[89]

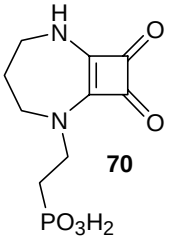
Scheme 44



1.1.3.4 Reaction of Amines with Cyclobutenedione Derivatives

Recently, the diamide of squaric acid **69** was used as a replacement for one of the phosphate diester linkages in an oligodeoxynucleotide,[90] while **70** as antagonist of the NMDA (*N*-methyl-D-aspartate) receptor.[91] Also, some of the cyclobutenedione derivatives are useful as high-affinity ligands for exitatory amino acid receptors[92] and anion recognition systems.[93]

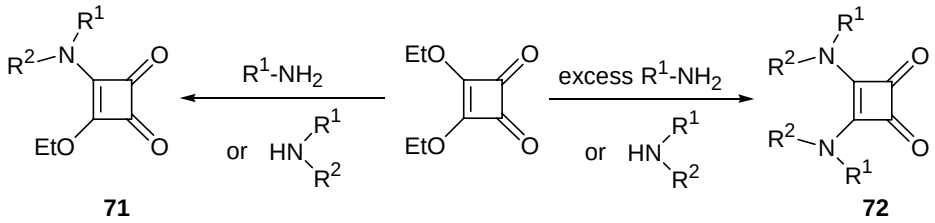




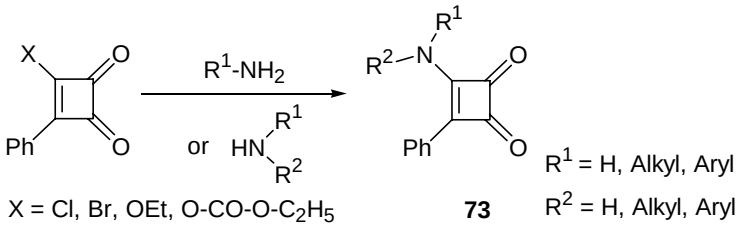
Amine derivatives of cyclobutenedione are known as amides of squaric acid. Reaction of slight excess of a primary or secondary amines with dialkylsquarate in CH_3OH or CH_2Cl_2 at room temperature give monoamide monoester **71** in excellent yield.[32,94] Diamides of squaric acid **72** are prepared under more basic conditions using large excess of amine or by adding triethylamine (**Scheme 45**). Also,

halocyclobutenediones react with amines but provide amides in lower yields **73** (**Scheme 46**).[95]

Scheme 45

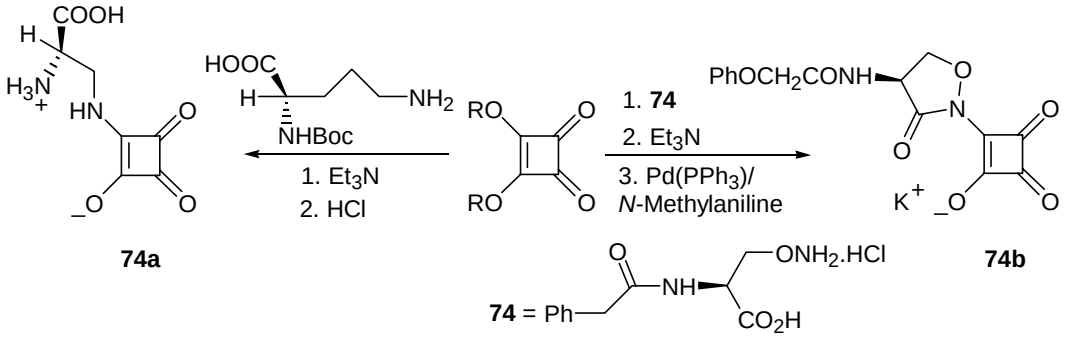


Scheme 46



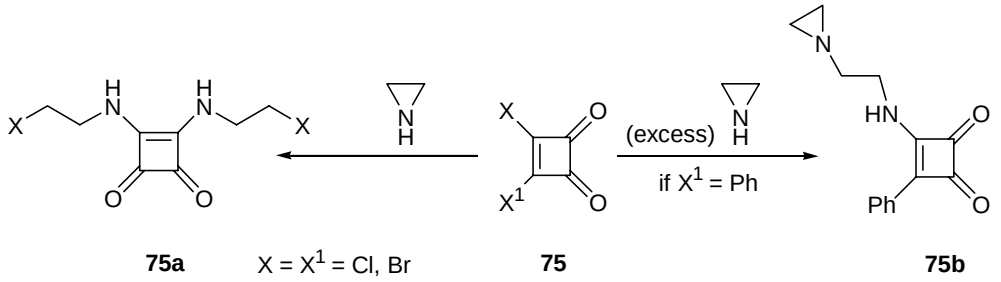
This reaction could also be performed in a buffered solution (pH 7), which is appropriate for biopolymers. Hence, this controlled nucleophilic substitution forms the basis for the use of diethyl squarate as a coupling reagent to conjugate oligosaccharides to proteins or polyazamacrocycles.[96] Several biologically active and drug molecules such as **74a** and **74b** have been developed following a similar method (**Scheme 47**).[25,97]

Scheme 47



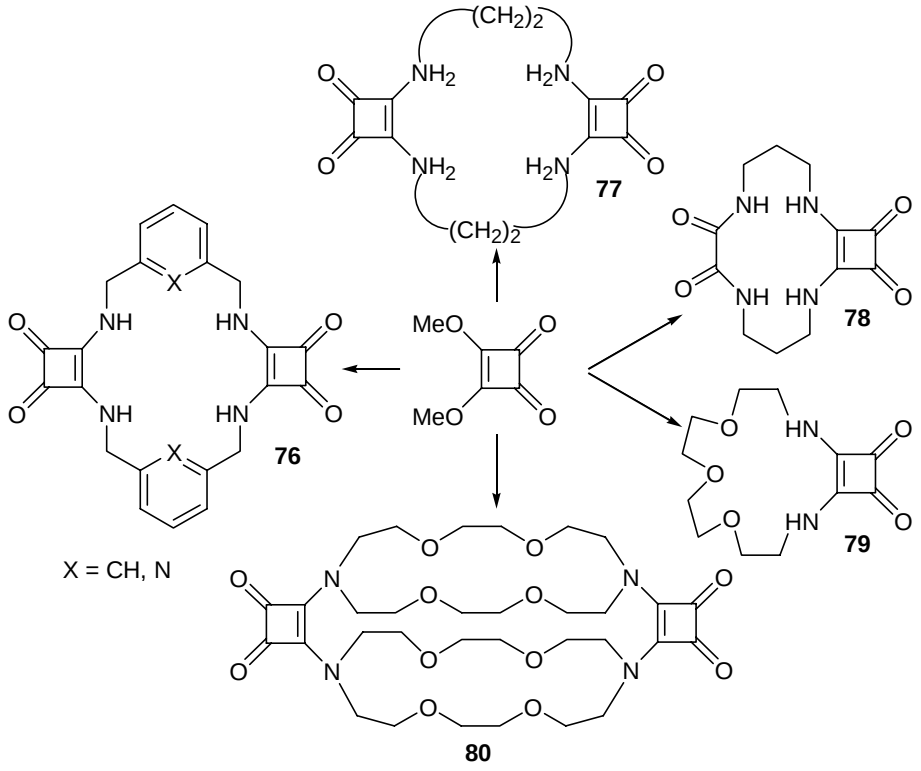
Also, it was found that aziridine reacts with dihalocyclobutenedione **75** under suitable conditions to generate either 1,2-diamides **75a** or (aziridinoethylamino) cyclobutenedione **75b** (**Scheme 48**).[98] Dichlorocyclobutenedione as well as bromophenylcyclobutenedione condense with electron rich olefins such as enamines, ketene acetals in the presence of triethylamine.[99]

Scheme 48



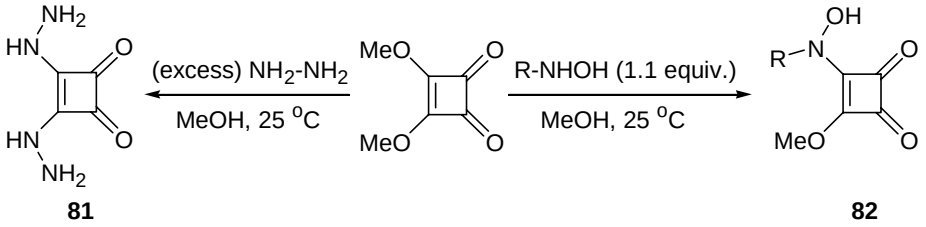
Macrocyclic bridged squaric acid diamides of type **76-80** have been synthesized in good yields by the reaction of 1,ω-diamines with 1,2-dimethoxycyclobutenedione under high dilution conditions (**Chart 11**).[100] Cryptands of type **80** are obtained from 1,2- dimethoxycyclobutenedione and monocyclic crown ether amines.

Chart 11



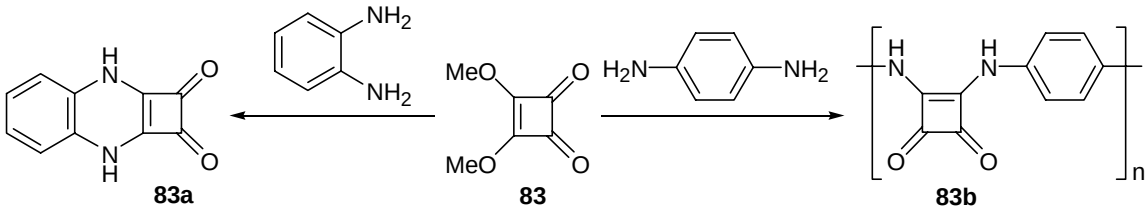
Dimethyl squarate reacts with hydrazine and hydroxylamines to form 3,4-dihydrazino-3-cyclobutenedione **81** and *N*-hydroxylamide methylesters **82** respectively (**Scheme 49**).[2d,101]

Scheme 49



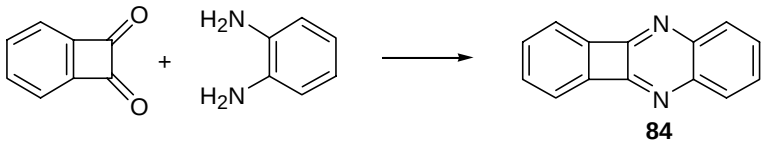
Also, dimethyl squarate **83** undergoes nucleophilic substitution reaction with *ortho* and *para*-phenylenediamine to provide **83a** and **83b** respectively (**Scheme 50**).[2d]

Scheme 50

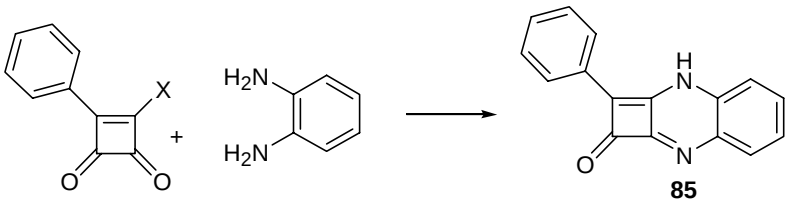


o-Phenylenediamine shows interesting reactivities with different cyclobutenediones. Substituents on dione have a large influence on course of reaction.[102] For example, benzocyclobutenedione[103] and halocyclobutenediones[1b,102a] give cyclobuta[b]quinoxalines **84** and **85**, a condensation product (**Scheme 51 and 52**).[102]

Scheme 51

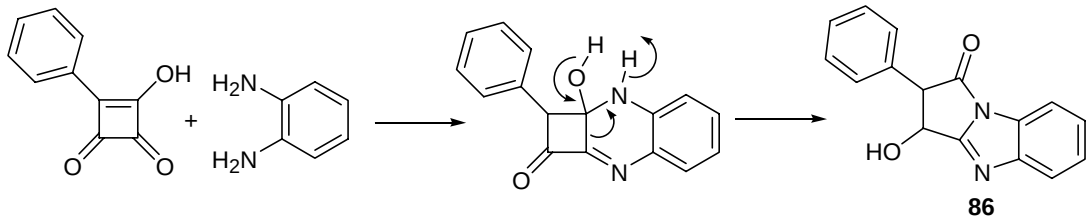


Scheme 52

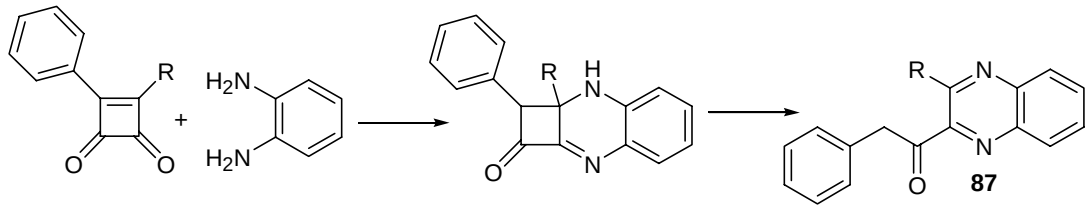


Hydroxyphenylcyclobutenedione,[102b] on the other hand, undergoes a novel ring expansion-oxidation reactions to give pyrrolobenzimidazole **86** (**Scheme 53**). Whereas some other disubstituted cyclobutenediones[102c] show entirely different reactivity and give the corresponding 2-phenylacetylquinoxalines **87**, a ring opened product (**Scheme 54**).

Scheme 53



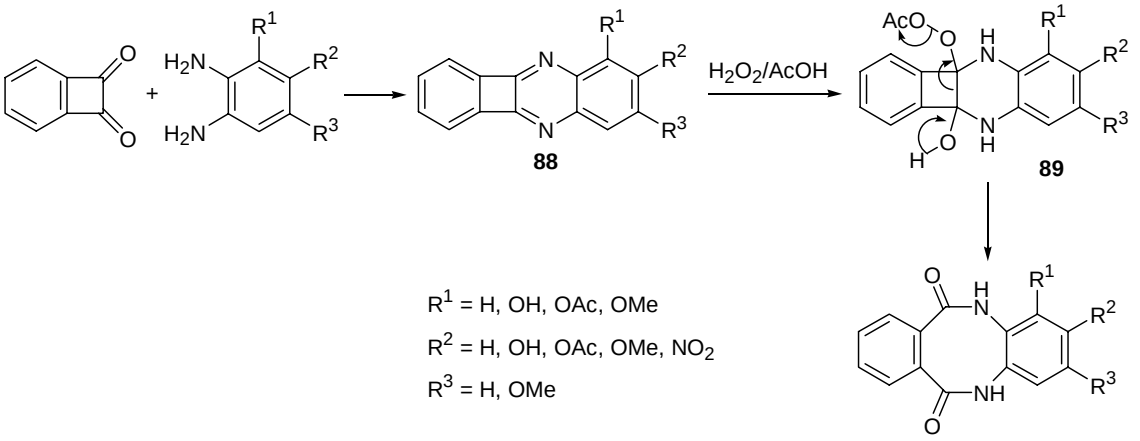
Scheme 54



R = H, Me, Ph

5,10-Diazabenzo[b]biphenylene **88**, a condensation product of benzocyclobutene 1,2-dione and *o*-phenylenediamines, undergoes ring expansion-reaction upon hydrogen peroxide oxidation in acetic acid to generate dibenzo-diazocine-5,12-dione **89** (**Scheme 55**).[104]

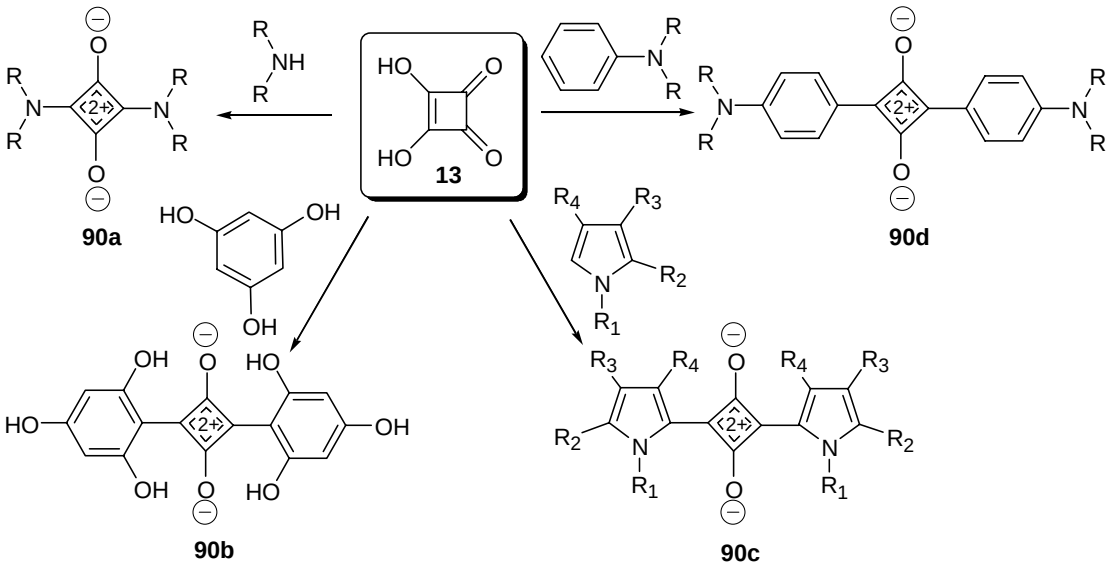
Scheme 55



It has been reported that secondary amines readily react with squaric acid to give 1,3-dianilides, a new class of zwitterions **90a-c**.[105] Also, certain phenols, pyrroles and arylamines were employed in this reaction (**Chart 12**). The condensation products of

squaric acid and *N,N*-dialkylanilines are known as squarines **90c** and they find applications as fluorescent dyes,[106] photoreceptors,[107] organic solar cells and NLO materials.[108]

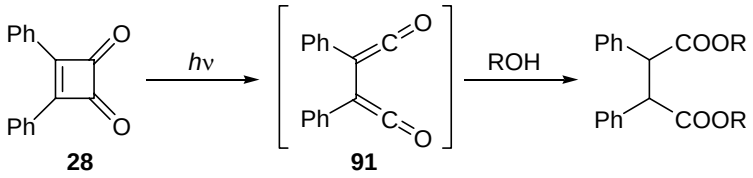
Chart 12



1.1.3.5 C-C bond Forming Reactions with Cyclobutenedione Derivatives

The photochemical ring opening of cyclobutene-1,2-diones (**28**) to 1,2-bisketenes (**91**) was discovered simultaneously by Mallory and Roberts[109] and by Blomquist and LaLancette[110] in 1961 (**Scheme 56**). The 1,2-bisketenes were not directly observed but were inferred as reactive intermediates on the basis of the products formed. Since that time, this technique has been utilized to generate several 1,2-bisketenes, but usually, these species have only been observed at low temperatures, often in matrices because of their facile thermal ring closure to give back cyclobutenedione **28**.[111]

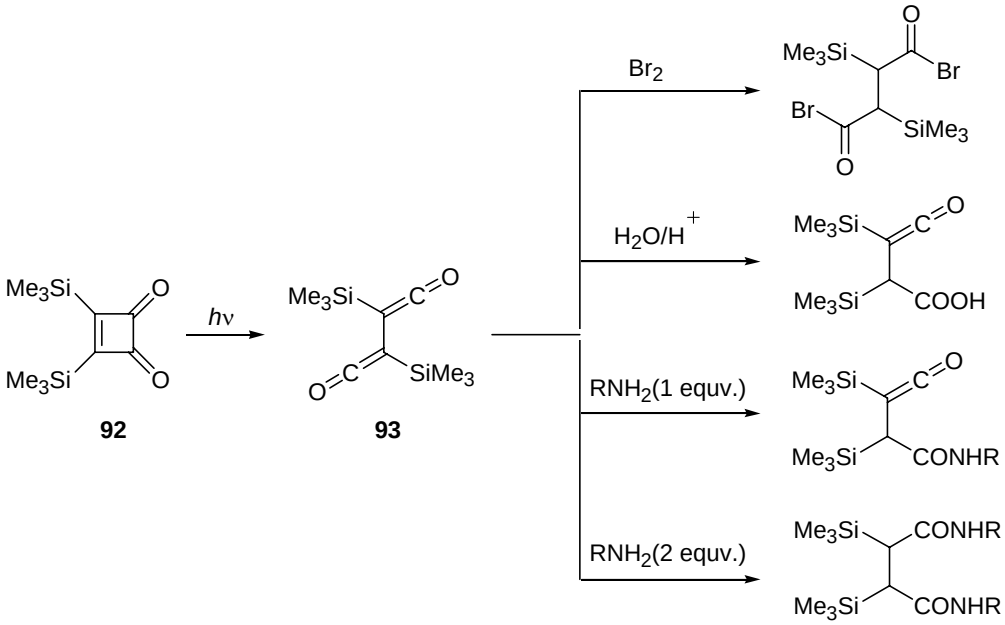
Scheme 56



28 **91**

Recently, *Tidwell et al.*[112,113] found that the Me_3Si substituted 1,2-bisketene **92** is thermodynamically stable compared to the corresponding cyclobutenedione **93**. Hence, it can be isolated at room temperature. This opened the way for extensive studies[112] of the spectroscopic and chemical properties of 1,2-bisketenes (**Scheme 57**), including an X-ray crystallographic structure determination.[112f]

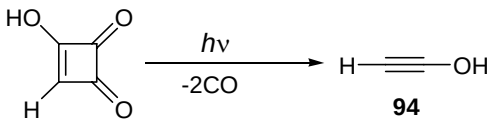
Scheme 57



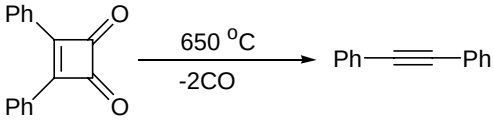
92 **93**

Ethynol **94**, a constituent of planetary atmosphere and interstellar clouds, was first synthesized by photolysis of semisquaric acid (**Scheme 58**).[114] Similarly, pyrolysis of diphenylcyclobutenedione gives diphenylacetylene (**Scheme 59**).[115]

Scheme 58

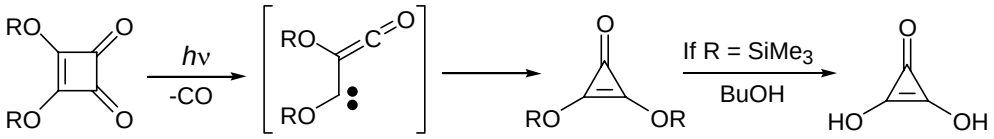


Scheme 59



It has been reported that irradiation of squaric acid esters yield ring contraction products.[116] For example, deltic acid **95**, dihydoxycyclopropenone, was first synthesized by *West et al.*[117] by photolytic decarbonylation of bis(trimethylsilyloxy) cyclobutenedione **95b** (**Scheme 60**).

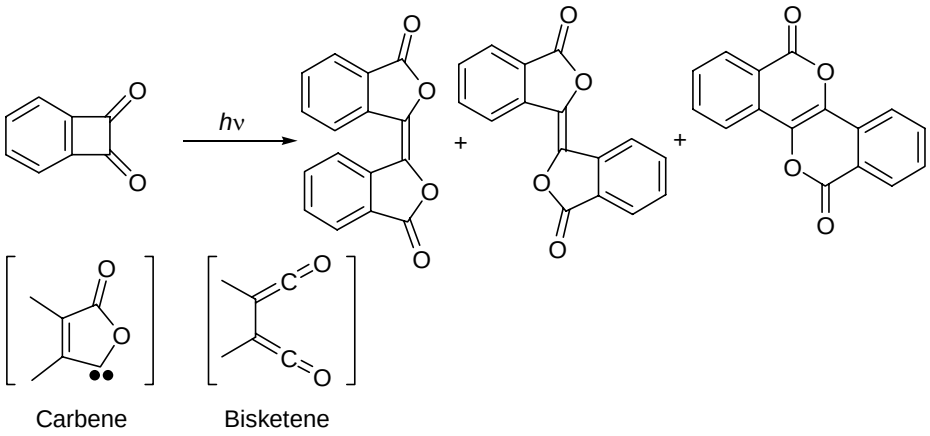
Scheme 60



95a = R = Et
95b = R = $SiMe_3$

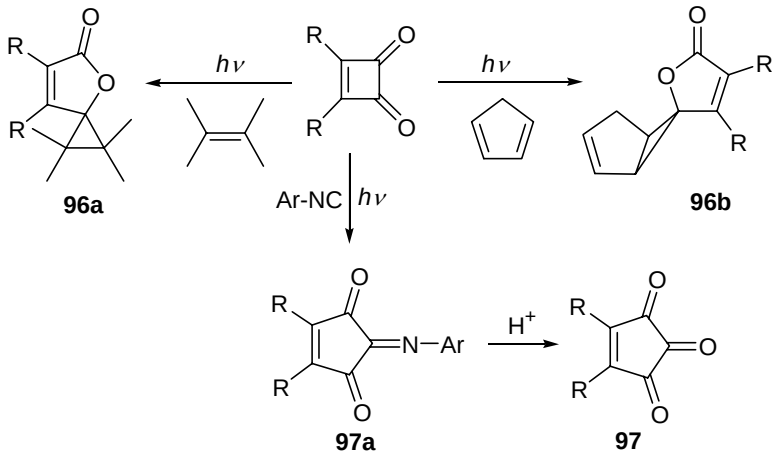
Cyclobutenediones undergo facile ring expansion reactions to yield dimers or monomeric anhydrides under the influence of light (**Schemes 61**).[118] The formation of these five membered ring compounds is believed to occur either through the carbene or the bisketene intermediates.

Scheme 61



Photolysis of diones in the presence of some ketene trapping agents produce 1:1 adducts (**Chart 13**). For example, olefins and dienes give 5-spirocyclopropyl $\Delta^{\alpha,\beta}$–butenolides **96a** and **96b**.[34] While the irradiation of diphenylcyclobutenedione in the presence of isonitriles gives ring expanded product **97a**, which may be converted to cylopentenetrione **97** by hydrolysis.[119]

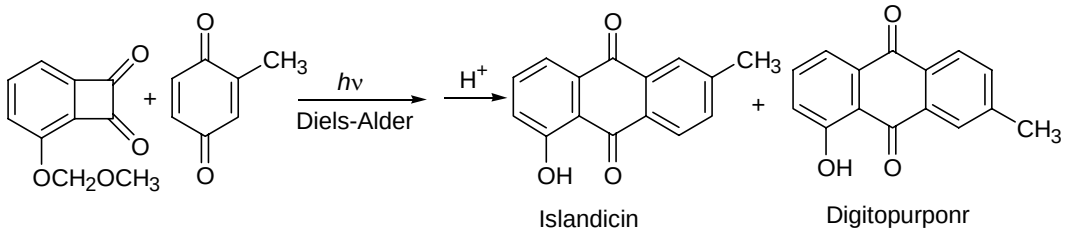
Chart 13



Bisketenes formed in photolysis of cyclobutenediones undergo *in situ* Diels-Alder reactions with maleic anhydride, benzoquinone or naphthoquinone. The use of 2-

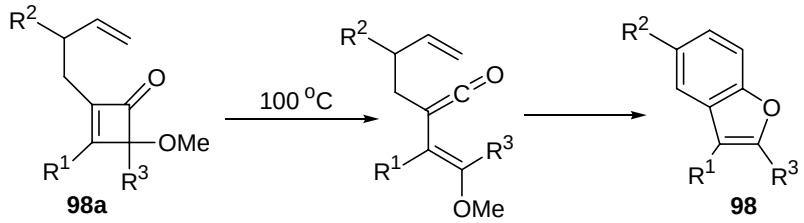
methoxybenzoquinone and 3-alkoxybenzocyclobutenediones permits a straightforward total synthesis of the natural products, islandicin and digitopurpone (**Scheme 62**).[120]

Scheme 62

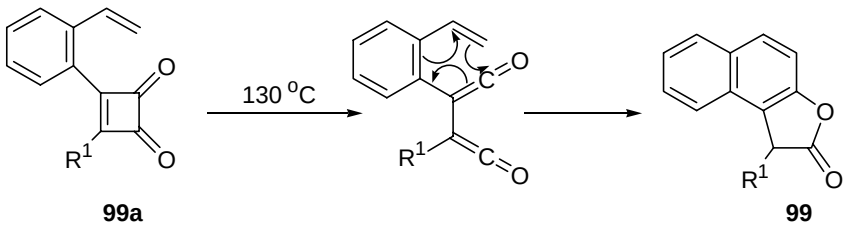


Thermolysis of 2-dienylcyclobutenones **98a** as well as 3-(2-ethynylphenyl)-cyclobutenediones **99a** undergo novel intramolecular cyclisation of bisketenes to furnish annulated furans **98** and naphthofuranones **99** respectively (**Schemes 63 and 64**).[121]

Scheme 63

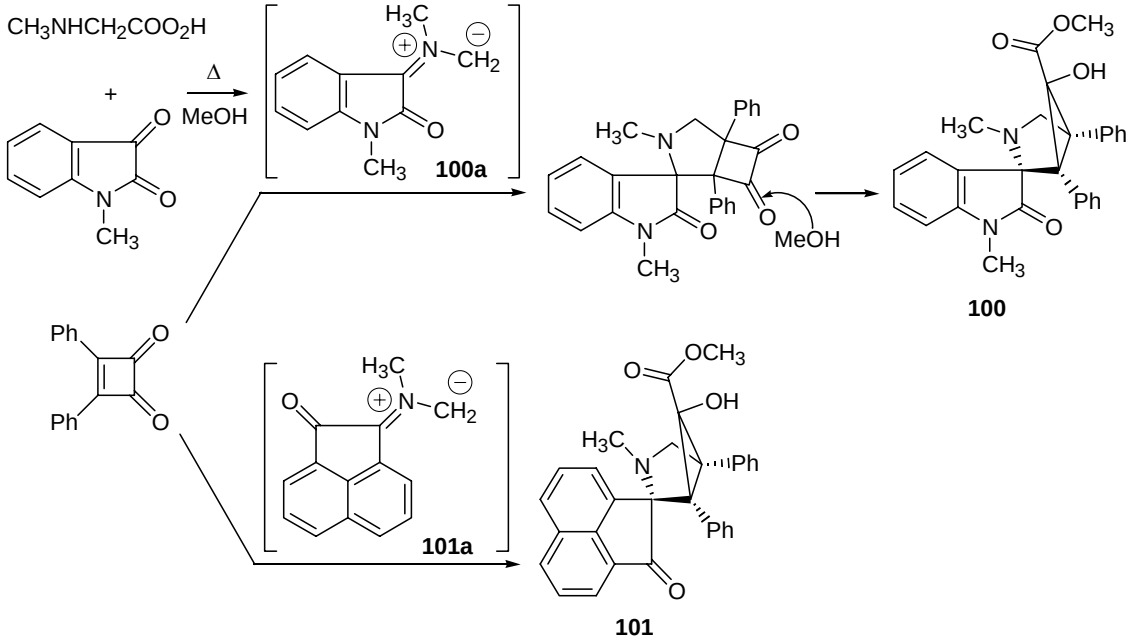


Scheme 64



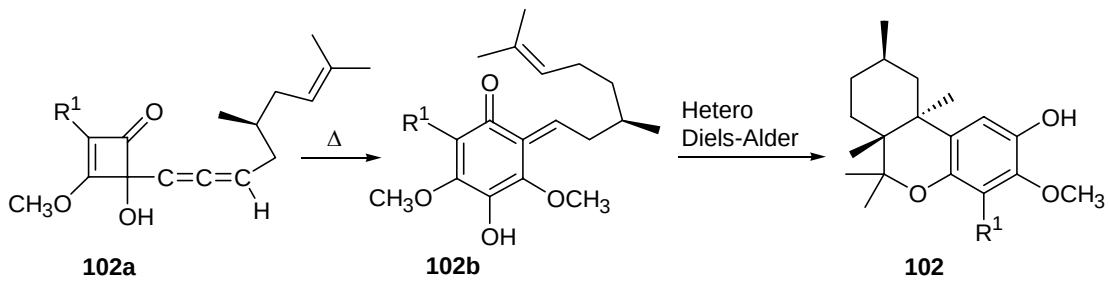
Recently, *Nair et al.*[122] observed the ring contraction of cyclobutenedione upon dipolar cycloaddition reactions. The reaction of 3,4-diphenylcyclobutene1,2-dione azomethine yields **100** and **101**, generated from isatins or acetonaphthenequinone, yields novel spiro[oxindole-3,2'-pyrrolidine] derivatives (**Chart 14**).

Chart 14



It has been reported that thermolysis of 4-allenylcyclobutenones **102a** prepared using cyclobutenedione and appropriate lithium reagents, leads to highly substituted *o*-quinone methides **102b**, a synthetically useful class of reactive intermediates that were not readily available by a general route. These *o*-quinone methides intermediates were exploited in total synthesis, for example, for the synthesis of hexahydrocannabinol **102** (HHC) (**Scheme 65**).[123]

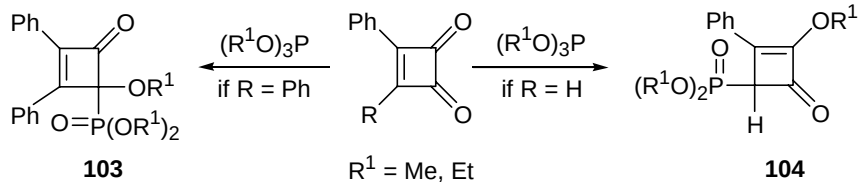
Scheme 65



It has been reported that the cyclobutenediones do not condense with phosphite esters in a manner analogous to simple diketones, but forms addition products.[33] For

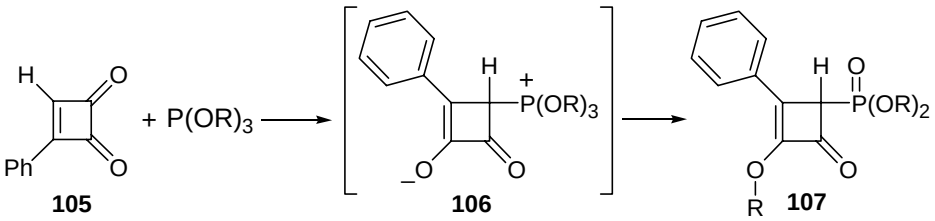
example, reaction of diphenylcyclobutenedione with trialkylphosphite gives 1,2 adduct **103**, while phenylcyclobutenedione yields 1,4 adduct **104** (**Scheme 66**).

Scheme 66



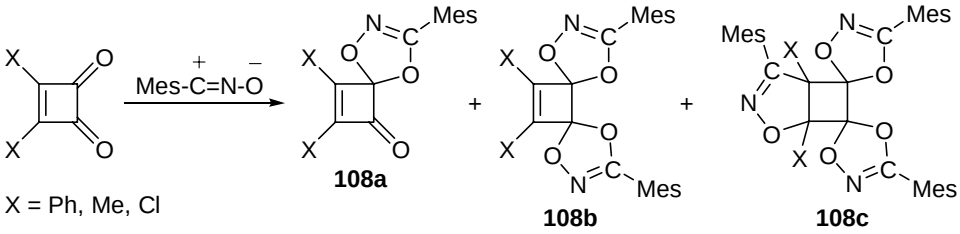
De Selms[88] showed that trialkylphosphites also add to phenylcyclobutenediones **105**. An alkyl group is transferred to the polarized carbonyl group of the hypothetical intermediate **106**, and the cyclobutenones **107** are formed (**Scheme 67**).

Scheme 67



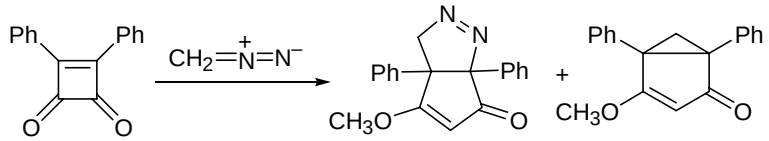
Also, cyclobutenediones have been reported to undergo 1,3 dipolar cycloadditions with mesitonirile oxide to give mono **108a**, bis **108b**, and tris **108c** adducts (**Scheme 68**).[120] As it is evident from reaction products that the 1,3-dipole attacks the carbonyl rather than the ethylene double bond, despite the usual low reactivity of C=O towards 1,3-dipoles.

Scheme 68



The action of excess diazomethane on diphenylcyclobutenedione leads to cyclopentapyrazole **109a** and bicyclo[3.1.0]hexanone **109b** in approximately 1:1 ratio (**Scheme 69**).[88] The reaction is thought to proceed through 1,3-dipolar addition of diazomethane to the double bond of the cyclobutenedione followed by CH_2 insertion between carbonyl groups, and then enolization followed by methylation.

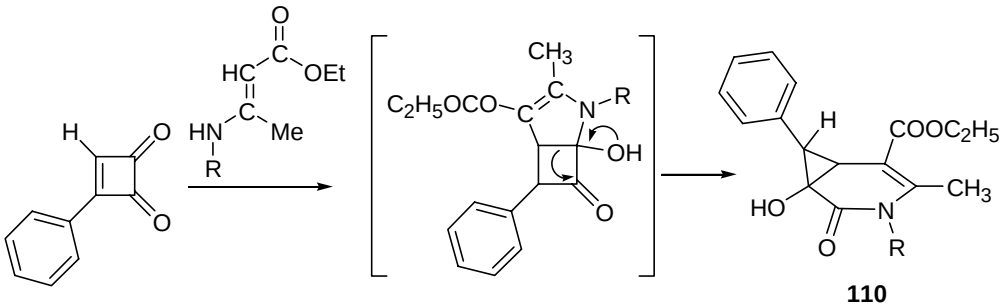
Scheme 69



109a **109b**

Simple stirring of a mixture of phenylcyclobutenedione and enamine in benzene at room temperature leads to ring enlargement of dione to generate a bicyclic compound, 1-hydroxy-3-azabicyclo[4.1.0]hept-4-en-2-one **110** (**Scheme 70**).[89]

Scheme 70

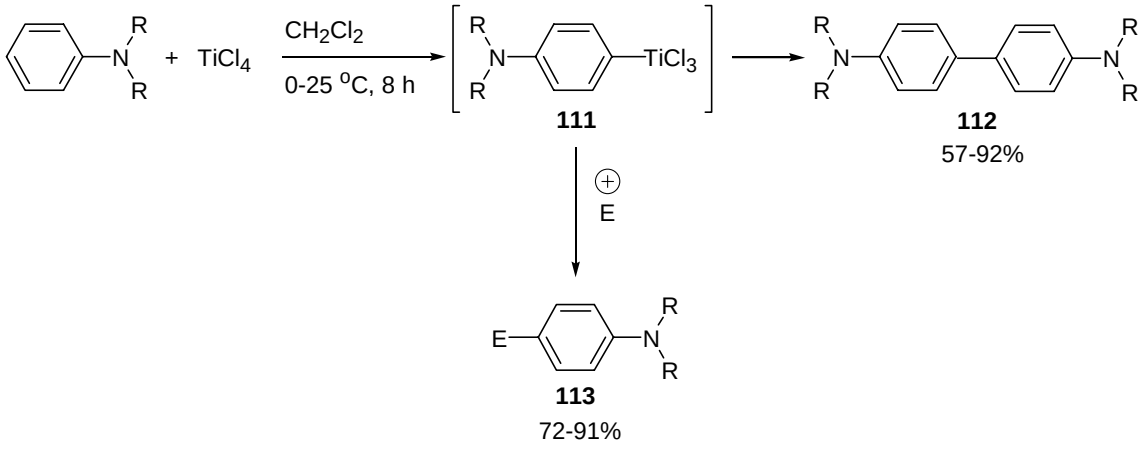


110

1.1.4 Previous work on $TiCl_4/ArNR_2$ Reagent System from this Laboratory

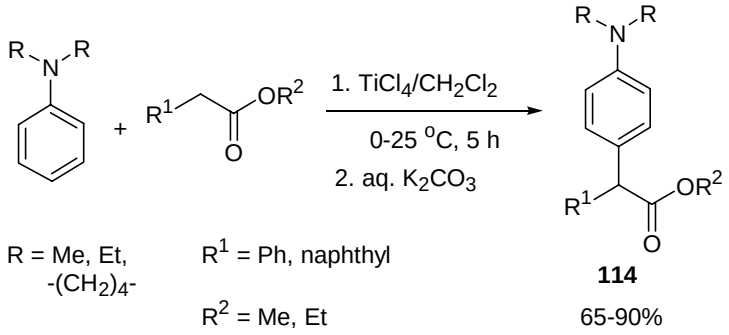
Previously, it was observed in this laboratory that $TiCl_4/Et_3N$ reagent system facilitates the direct metalation of organic compounds.[124-126] The *N*,*N*-dialkyl-arylamines/$TiCl_4$ reagent system produce, *N*,*N*,*N*',*N*'-tetraalkylbenzidines **112** in the absence of electrophiles (**Scheme 71**).[124] The possible intermediate can be trapped using various electrophiles.[124]

Scheme 71



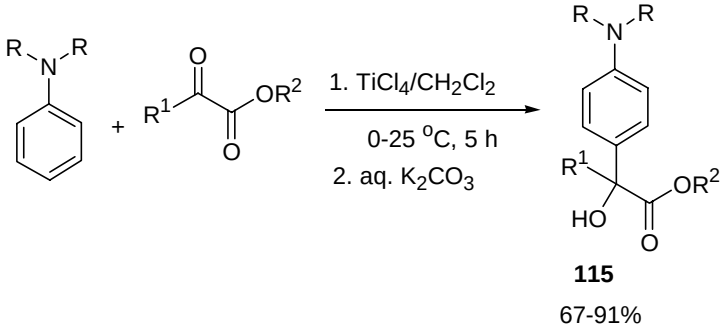
Recent studies on the reactions of $TiCl_4/ArNR_2$ reagent system gave some interesting results. For example, the reaction with enolizable esters like arylacetic acid esters produces the corresponding α-arylated products in good yields (**Scheme 72**).[126a]

Scheme 72

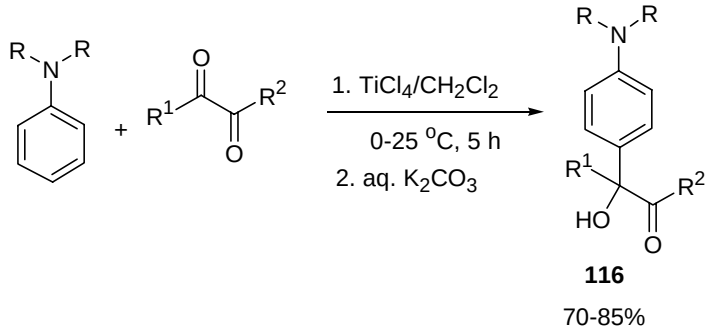


However, Grignard type nucleophilic addition reactions were realized using non-enolizable α-ketoesters and α-diketones (**Schemes 73 and 74**).

Scheme 73

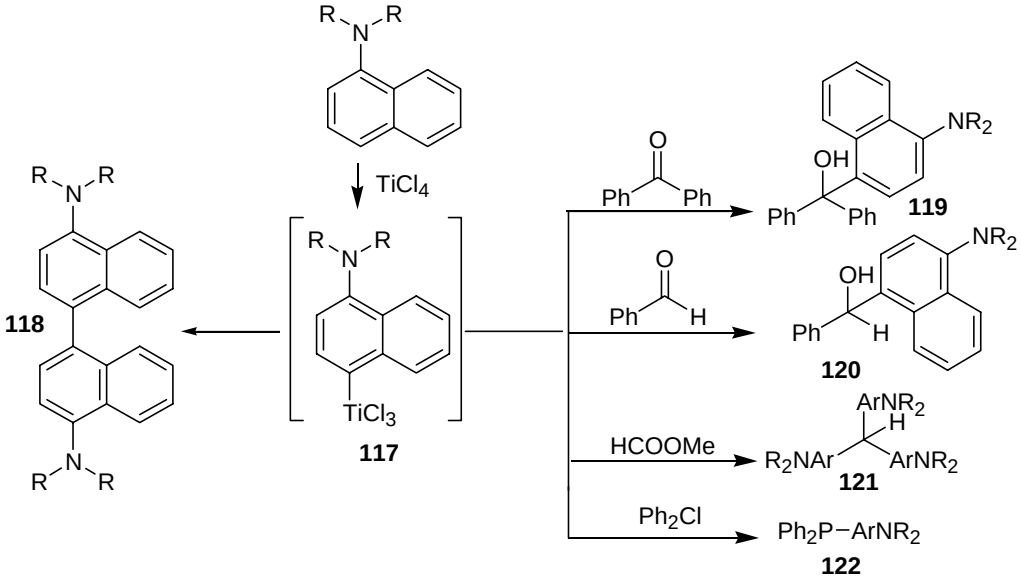


Scheme 74



The reaction of the $TiCl_4/ArNR_2$ system was examined with electrophiles (**Chart 15**). In the reaction with diaryl ketones, the expected electrophilic addition products **119** were obtained. In the case of reactions using benzaldehyde, and methyl formate, the initially formed electrophilic addition products underwent further arylation to give compounds **120** and **121**. The chlorodiphenylphosphine gave the corresponding electrophilic substitution product **122** (**Chart 15**).[126b]

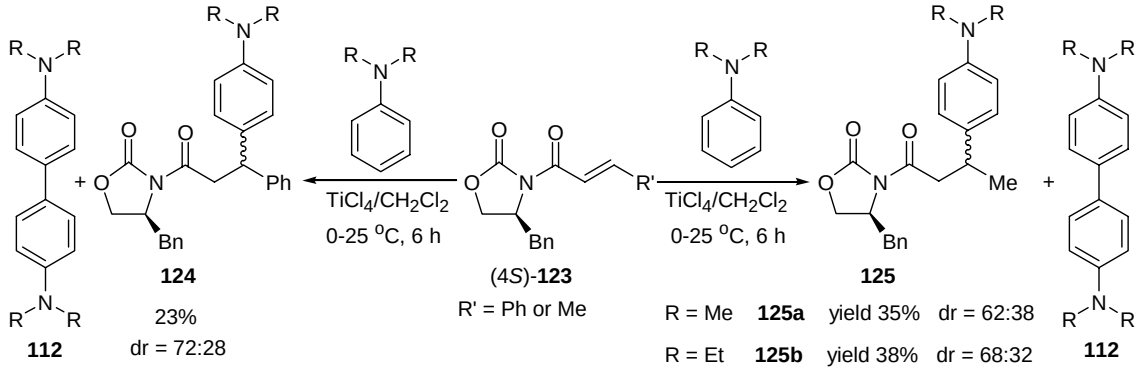
Chart 15



The reaction of oxazolidinone with diethylaniline in CH_2Cl_2 at 0 °C, give the corresponding 1,4-addition product **124** in 23% yield besides the benzidine **112** formed

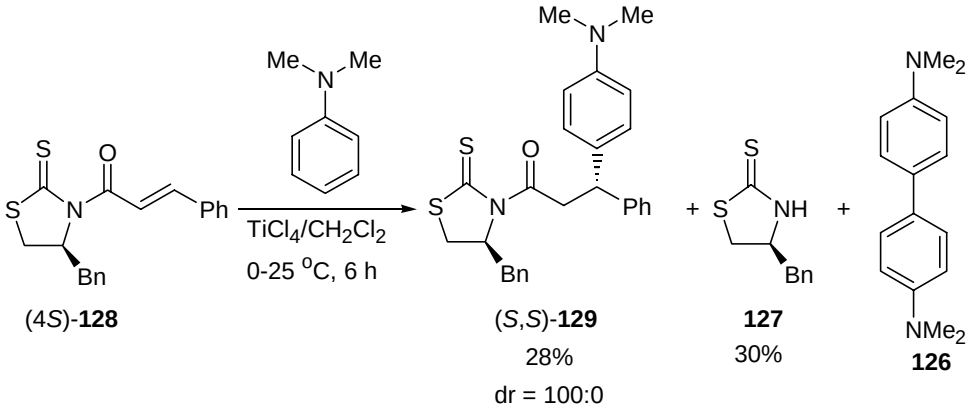
through coupling of $ArTiCl_3$ produced.[124] Whereas the reaction of *N*,*N*-diethylaniline with *N*-crotonoyl-oxazolidinone (4*S*)-**123** gave the corresponding adduct **125b** in 38% yield (dr = 68:32) (**Scheme 75**). Also, the corresponding benzidines **112** were obtained as side products in these reactions.[124]

Scheme 75



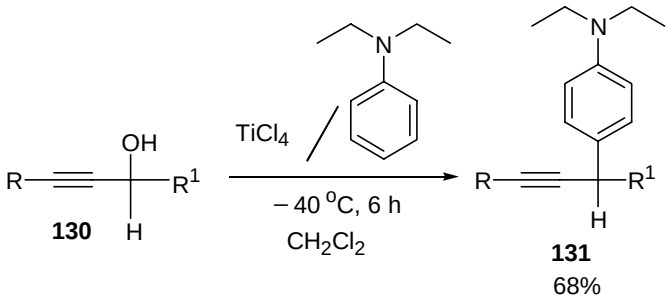
The chiral enone (4*S*)-**128** was reacted with *N*,*N*-dimethylaniline in the presence of $TiCl_4$. In this reaction, the corresponding 1,4-addition product **129** was isolated only in 28% yield besides the homocoupled benzidine product **126**.[124] Interestingly, only one of the diastereomers of the product **129** was formed in this reaction. The thiazolidinethione **127** (30%) was also isolated from the reaction mixture (**Scheme 76**).

Scheme 76



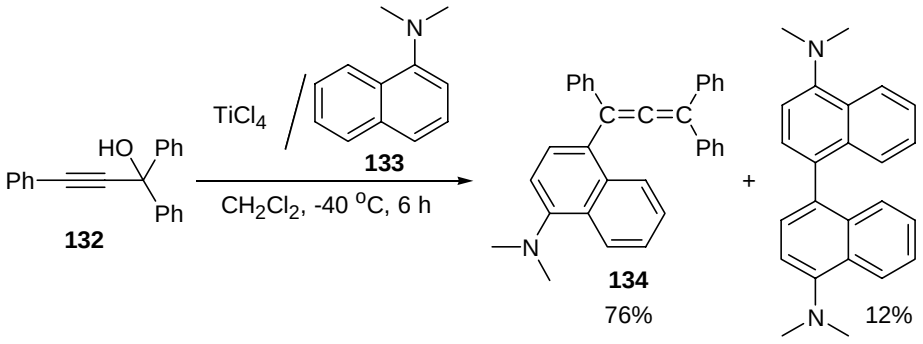
The 1-phenyl-2-octyn-1-ol **130** when reacted with *N*,*N*-diethylaniline and $TiCl_4$ gives the corresponding arylalkyne **131** in 68% yield (**Scheme 77**).[125]

Scheme 77



The reaction with 1,1,3-triphenyl-2-propyne-1-ol **132** with *N*,*N*-dimethylnapthylamine **133** at –40 °C gave the tetraarylallene **134** as a major product, besides 12% of the corresponding naphthadine (**Scheme 78**).[125]

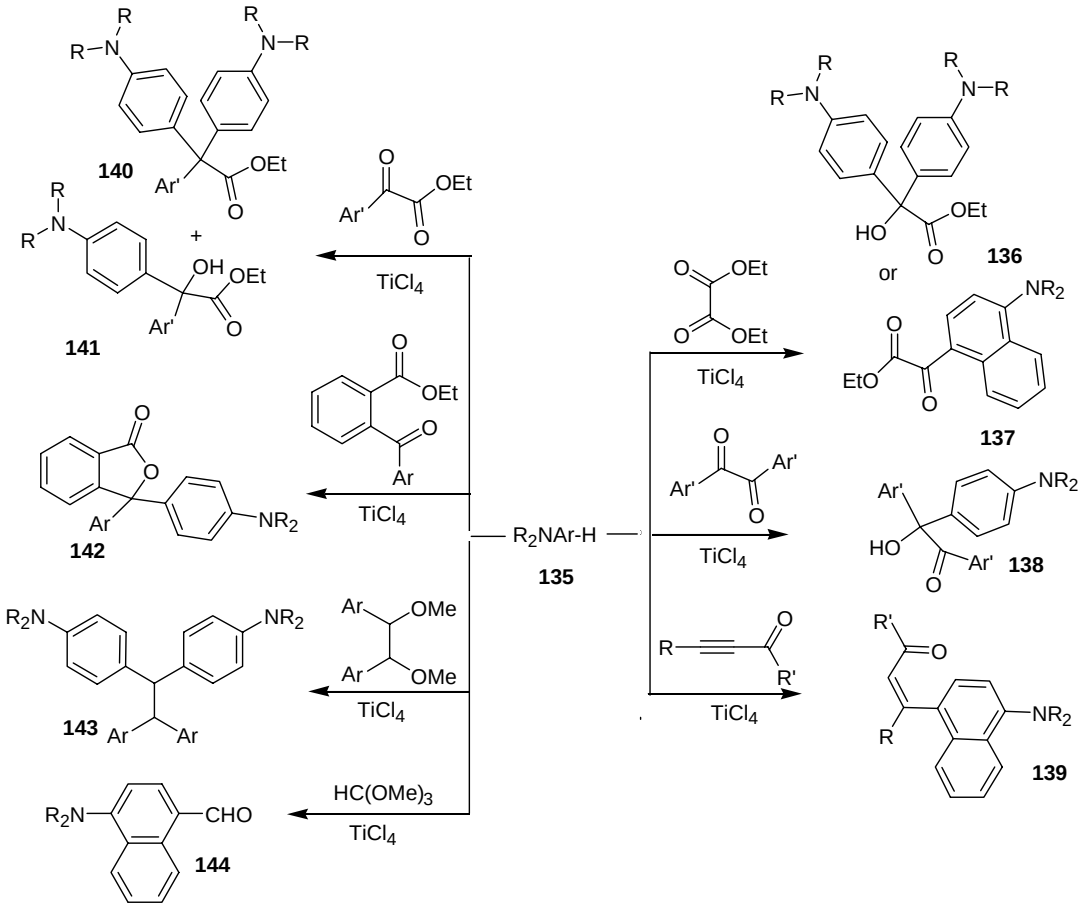
Scheme 78



The reaction of *N*,*N*-dialkylarylamines **135** in the presence of $TiCl_4$ was examined using electrophiles (**Chart 16**). The reaction using *N*,*N*-dialkylarylamines and $TiCl_4$ with diethyl oxalate produced α-hydroxy esters **136** as well as α-ketoesters **137** by the addition of aryltitanium selectively at one carbonyl group. The *N*,*N*-dialkylanilines added to α-ketoester in the presence of $TiCl_4$ to produce diarylated acetic acid esters **138** as well as α-hydroxy esters **139** in good yields. The reaction with

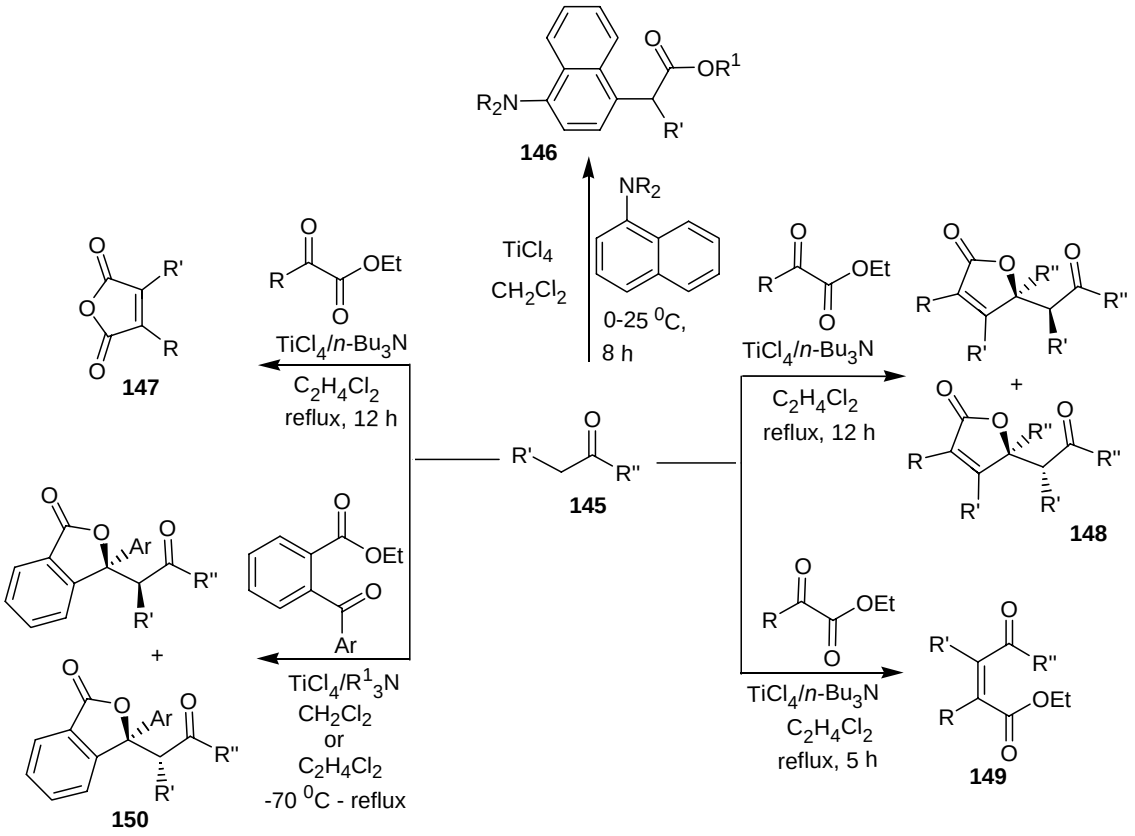
symmetrical α-dicarbonyl compounds like α-diketones produced α-hydroxy ketones **140** in good yields. The addition reaction of aryltitanium with unsymmetrical γ-dicarbonyl compounds like ethyl 2-benzoyl-benzoic acid ethyl esters give γ-lactones **141**. The reaction with α,β-unsaturated carbonyl compounds like alkynyl ketone gave the corresponding 1,4-addition product **142**. In the reactions with aryl ethers like 1,2-dimethoxy-1,2-diarylethane**,** the 1,1'-disubstistuted aryl product **143** were formed through rearrangement. The reaction with trimethyl orthoformate produced the corresponding formylated product **144** in good yields.[126]

Chart 16



The reaction of *N,N*-dialkyl arylamines/$TiCl_4$ system, with arylacetic acid esters **145** (R''=OR') produces α-arylated products **146** in good yields (**Chart 17**). α-Keto esters react with titanium enolate of alkanoic acid anhydrides **145** (R''= $OOCCH_2R'$) prepared *in situ* using the $TiCl_4$/*n*-Bu_3N reagent system to give maleic anhydrides **147** (**Chart 17**). Diphenyl maleic anhydride was obtained by the reaction of phenylacetyl chloride and ethyl benzoylformate with the $TiCl_4$/*n*-Bu_3N reagent system.[126]

Chart 17

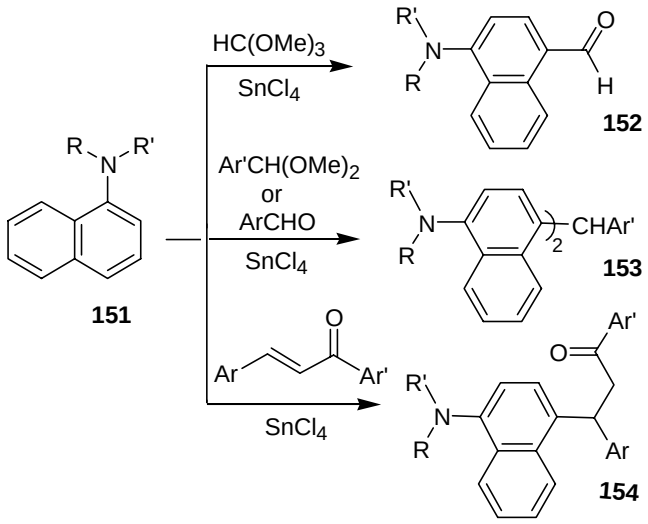


γ-Substituted γ-butenolides **148** were obtained in one step by the reaction of titanium enolates of ketones **145** (R''=aryl, alkyl) with α-keto esters in the presence of the $TiCl_4$/*n*-Bu_3N reagent system (**Chart 17**). The intermediate **149** involved in this transformation was isolated by changing the ratio of ethyl benzoylformate and ketone

145 to 1:1, respectively. In the reaction of ethyl 2-benzoylbenzoates and ketones **145** with the $TiCl_4$/*n*-Bu_3N reagent system, the γ-lactone **150** was obtained (**Chart 17**). The ethyl 2-benzoylbenzoates react with esters **145** (R'' = OR') in the presence of the $TiCl_4$/Et_3N reagent system to give γ-lactones **150** (**Chart 17**).

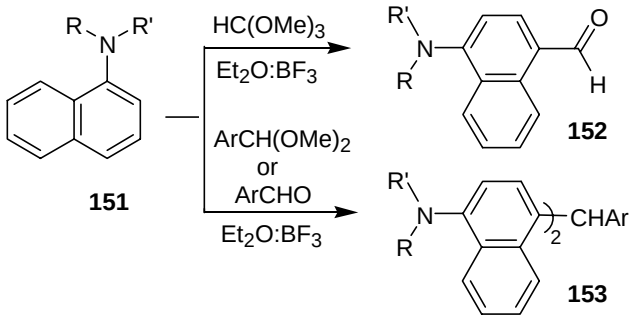
As discussed in the above sections, these transformations can be explained by initial complexation of the electrophiles by the Lewis acid $TiCl_4$ for reaction with arylamines. Several of these transformations can also rationalized considering $TiCl_4$ promoted activation of electrophiles without involving aryltitanium intermediates. The reactions of *N*,*N*-dialkylarylamines **151** and $SnCl_4$ with orthoformate, acetals or aldehyde as well as α,β-unsaturated carbonyl compounds give the corresponding arylated compounds **152-154** (**Chart 18**).

Chart 18



The *N*,*N*-dialkylarylamines **151** reacts with orthoformate, acetals or aryl aldehyde in the presence of Et_2O:BF_3. It was observed that the reaction of *N*,*N*-dialkylarylamines with trimethyl orthoformate and Et_2O:BF_3. The expected formylated products **152** were obtained in good yields (**Scheme 79**).

Scheme 79



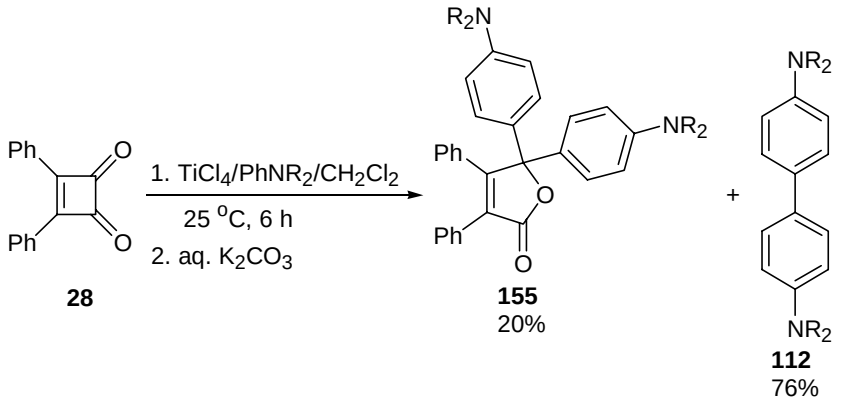
We have undertaken research efforts on the scope and limitations of the reactivity of arylamine/Lewis acid reagent systems, arylmagnesium, aryl and alkynyl titanium reagents with cyclobutenediones. The results of these studies are described in the next chapter. Other studies undertaken to explore the reactions of cyclobutenediones are also discussed in the next chapter.

2. Results and Discussion

2.1 Reaction of Cyclobutenedione and Tertiary Amines with $TiCl_4$

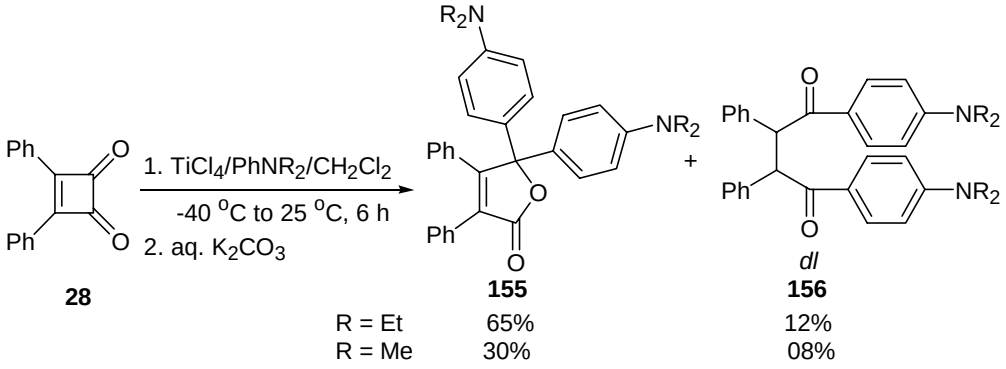
It was observed in this laboratory that the reaction with *N,N*-dialkylarylamines and $TiCl_4$ at room temperature, gives a small amount (20%) of butenolide **155** along with benzidine **112** (76%) and other highly coloured products (**Scheme 80**).[124,127]

Scheme 80



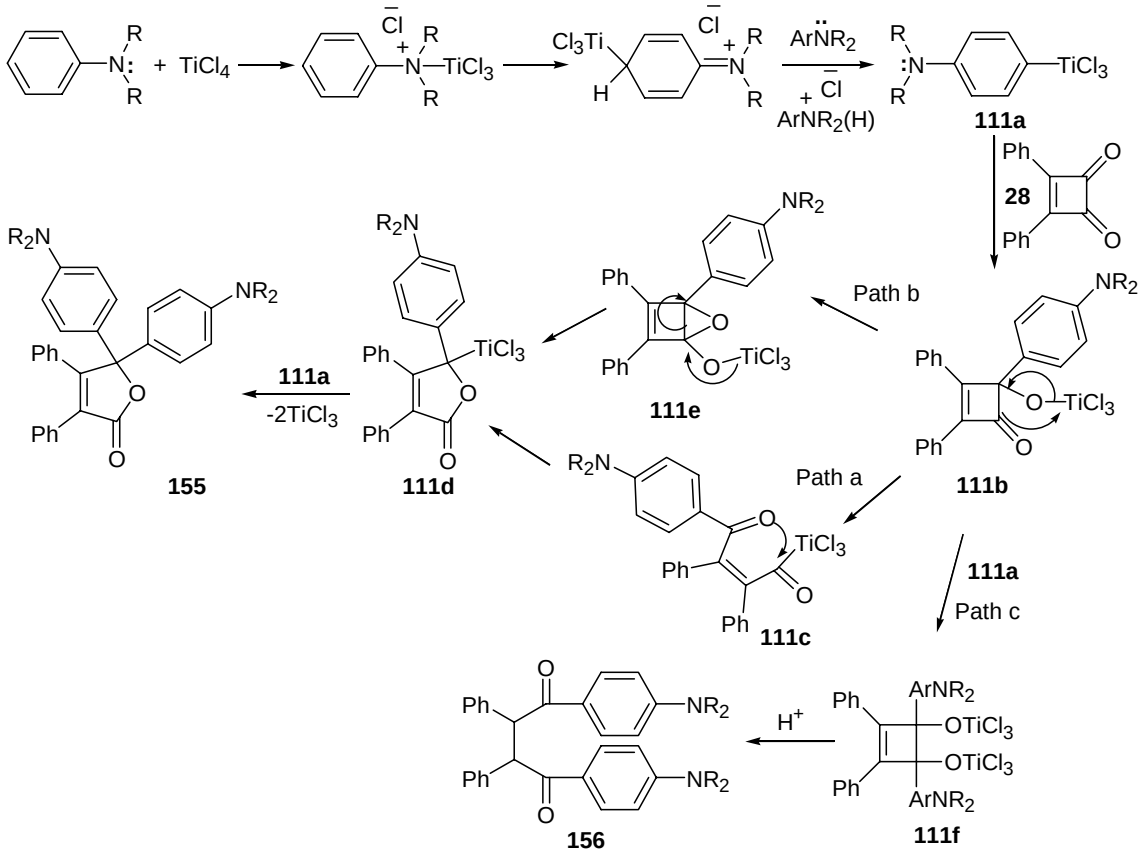
In a run using *N,N*-diethylaniline at –40 °C to 25 °C, the butenolide **155** was obtained in as high as 65% yield along with the 1,4-diketone **156**, a ring opened product (**Scheme 81**).[127] Only the racemic (±) diastereomer of **156** was obtained of the possible *dl* and *meso* isomers and the product was identified by comparison with the spectral data of closely related derivatives.[128-130] Whereas the *N,N*-dimethylaniline gave the corresponding butenolide in lower yields, as in this case the *N*-demethylated product *N*-methylaniline was also obtained in 26% yield.[124,127]

Scheme 81



The formation of butenolides[129,131] from diphenylcyclobutenedione using arylamines and $TiCl_4$ can be rationalized by considering a sequence of intermediates as depicted in **Scheme 82**.[127]

Scheme 82



Addition of one equivalent of aryltitanium reagent to the cyclobutenedione would give **111b**, which could undergo β-scission to produce the acyltitanium intermediate **111c**. Cyclization of **111c** to **111d** could then take place through the addition of the acyltitanium to carbonyl oxygen. The resulting intermediate could react with another equivalent of aryltitanium species to give the final product (**Path a**).[132] Alternatively, the intermediate **111b** could give the 5-oxabicyclo[2.1.0]pent-2-enyloxytitanium intermediate **111e** (**Path b**), which could then undergo ring opening to afford **111d** *via* the process demonstrated in the Dowd's ring-expansion reaction.[133] However, recent calculations revealed that the radical process similar the sequence **111a→111b→111c** is also energetically favorable.[134]

The formation of 1,4-diketone **156** can be rationalized by the reaction of two equivalents of aryltitanium reagents with the cyclobutenedione **28** to give **111f**. This intermediate upon electrocyclic ring opening could afford the final product **156** (**Path c**). Comparison of the ^{1}H NMR data indicate that the single diastereomer formed in these reactions could most probably be the thermodynamically more stable *meso* isomer.[129,130,135]

We have undertaken studies to examine the mechanism of this reaction by carrying out the reaction at lower temperatures. We have observed that the reaction at –78 ^{o}C, gave the corresponding 1,4-addition product in moderate yields (32-68%) (**Scheme 83**). This transformation was carried out with other *N,N*-dialkylarylamines and the reaction was found to be general in the presence of $TiCl_4$. The results are summarized in Table 1. The structure of **157e** was further characterized by single

crystal X-ray analysis (**Fig. 1**). The products **157a-d** were characterized by comparison with the spectral data of **157e**.

Scheme 83

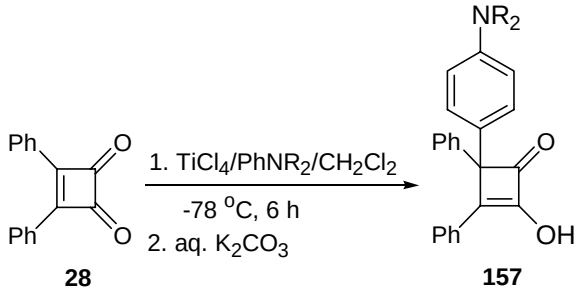
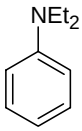
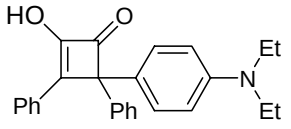
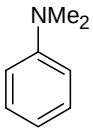
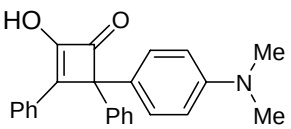
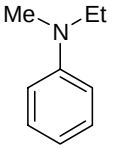
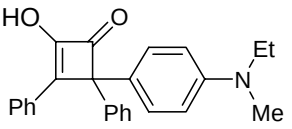
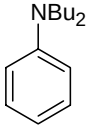
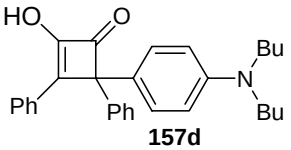
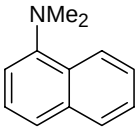
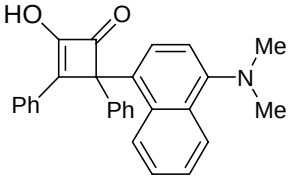


Table 1. Reaction of $TiCl_4$ and *N,N*-dialkylarylamines with cyclobutenedione

Entry	Arylamine	Product[a]	Yield (%)[b]
1		 **157a**	48
2		 **157b**	45
3		 **157c**	38
4		 **157d**	32
5		 **157e**	68

[a]The products were identified using spectral data (IR, ^{1}H NMR, ^{13}C NMR, Mass and CHN analysis).

[b]Yields are of the isolated products and based on the amount of cyclobutenedione used.

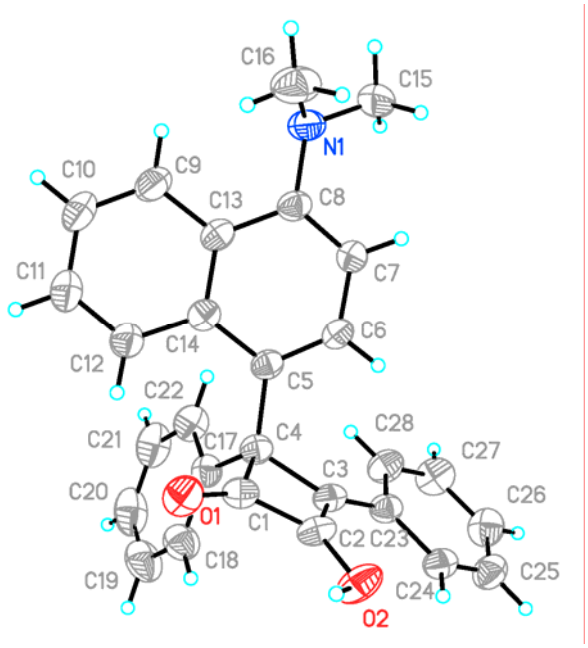
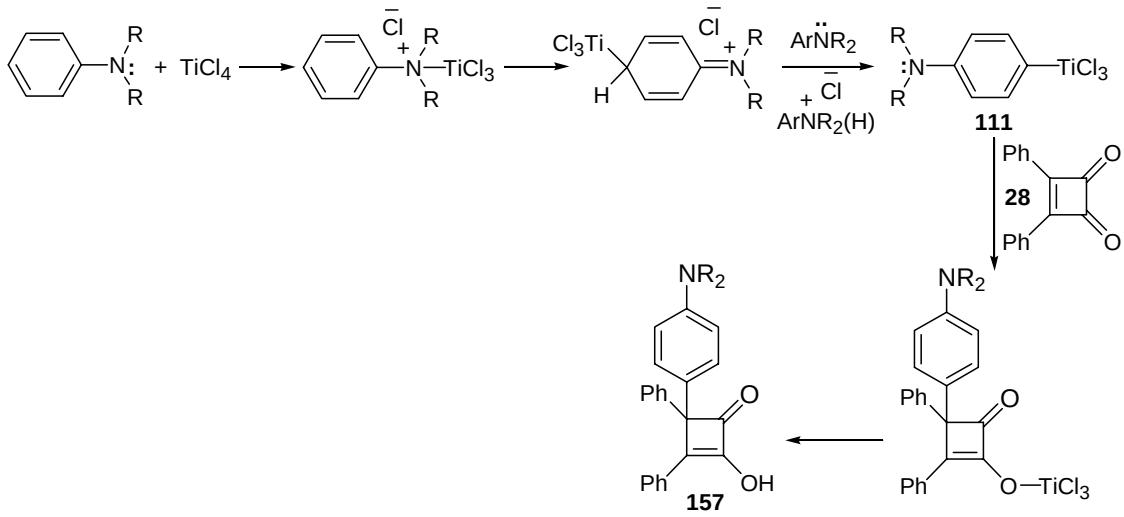


Fig. 1. ORTEP Diagram of Compound 157e

The formation of compounds **157a-e** using arylamines and $TiCl_4$ can be rationalized by considering a plausible sequence of reactions as depicted in **Scheme 84**.

Scheme 84

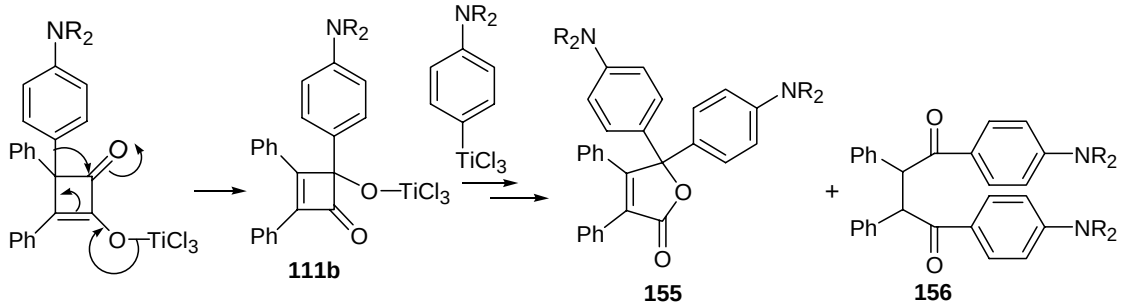


Presumably, this is the first intermediate that gives the butenolide derivatives **155** upon rearrangement (**Scheme 85**) followed by reaction of **111b** as depicted in **Scheme 82**.

Table 2. Crystal data and structure refinement for the Compound 157e.

Empirical Formula	C_{28} H_{23} N O_2
Formula weight F_w	405.47
Temperature T (K)	298(2)
Wavelength λ (Å)	0.71073
Crystal system, Space group	Triclinic, *P*-1
Unit cell dimensions	
a (Å), α (^{o})	9.0805(6), 106.4240(10)
b (Å), β (^{o})	10.9924(8), 103.3510(10)
c (Å), γ (^{o})	11.8409(8), 90.5230(10)
Volume V (Å^3)	1099.54(13)
Z	2
Calculated density ρ_{calcd} mg/M^3	1.225
Absorption coefficient μ (mm^{-1})	0.077
F (000)	428
Crystal Size (mm)	0.45 x 0.38 x 0.28
θ for data collection range/deg	1.85 to 26.07
Limiting indices	-11<=h<=11, -13<=k<=13, -14<=l<=14
Reflections collected/unique	11578 / 4328 [R(int) = 0.0215]
Completeness to θ	26.07, 99.2 %
Max. and min. transmission	0.9789 and 0.9664
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4328 / 0 / 283
Goodness-of-fit on GOF (F^2)	1.047
Final R indices *R1*, *wR2 [I>2σ(I)]*	*R1* = 0.0449 *wR2* = 0.1167
R indices (all data) *R1*, *wR2*	*R1* = 0.0596 *wR2* = 0.1258
Largest diff. Peak and hole (e·Å^{-3})	0.152 and -0.207

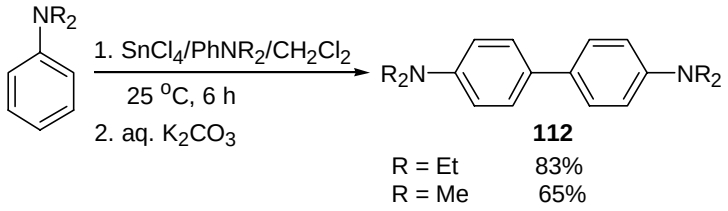
Scheme 85



2.2 Reaction of Cyclobutenedione and Tertiary Amines with $SnCl_4$ and $TiCl_4$

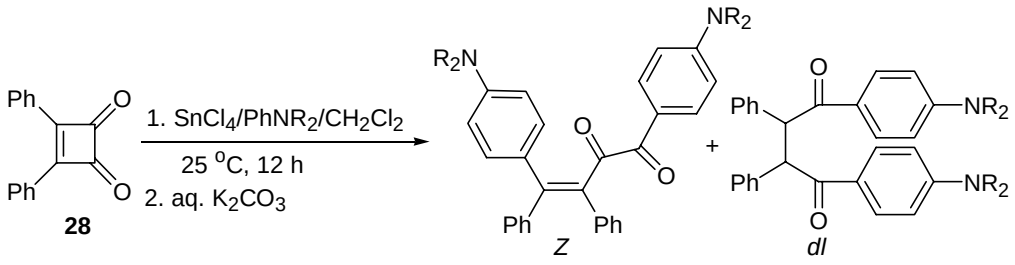
It was observed in this laboratory that the tertiary arylamine/$SnCl_4$ system upon reaction with gives corresponding benzidines in good yields ($ArNMe_2$ 65%; $ArNEt_2$ 83%) (**Scheme 86**).[124]

Scheme 86



The reactivity of arylamine with cyclobutenediones was also studied using $SnCl_4$. We have observed that the addition of $SnCl_4$ and *N,N*-diethylanilene to the 3,4-diphenyl-3-cyclobutene-1,2-dione **28** at room temperature gives a novel ring cleaved product, diaryl-3-butene-1,2-dione **158** (60%) along with the expected 1,4-diketone **156** (23%) (**Scheme 87**). The compound **158a** was identified as the *Z* isomer by single crystal X-ray analysis.

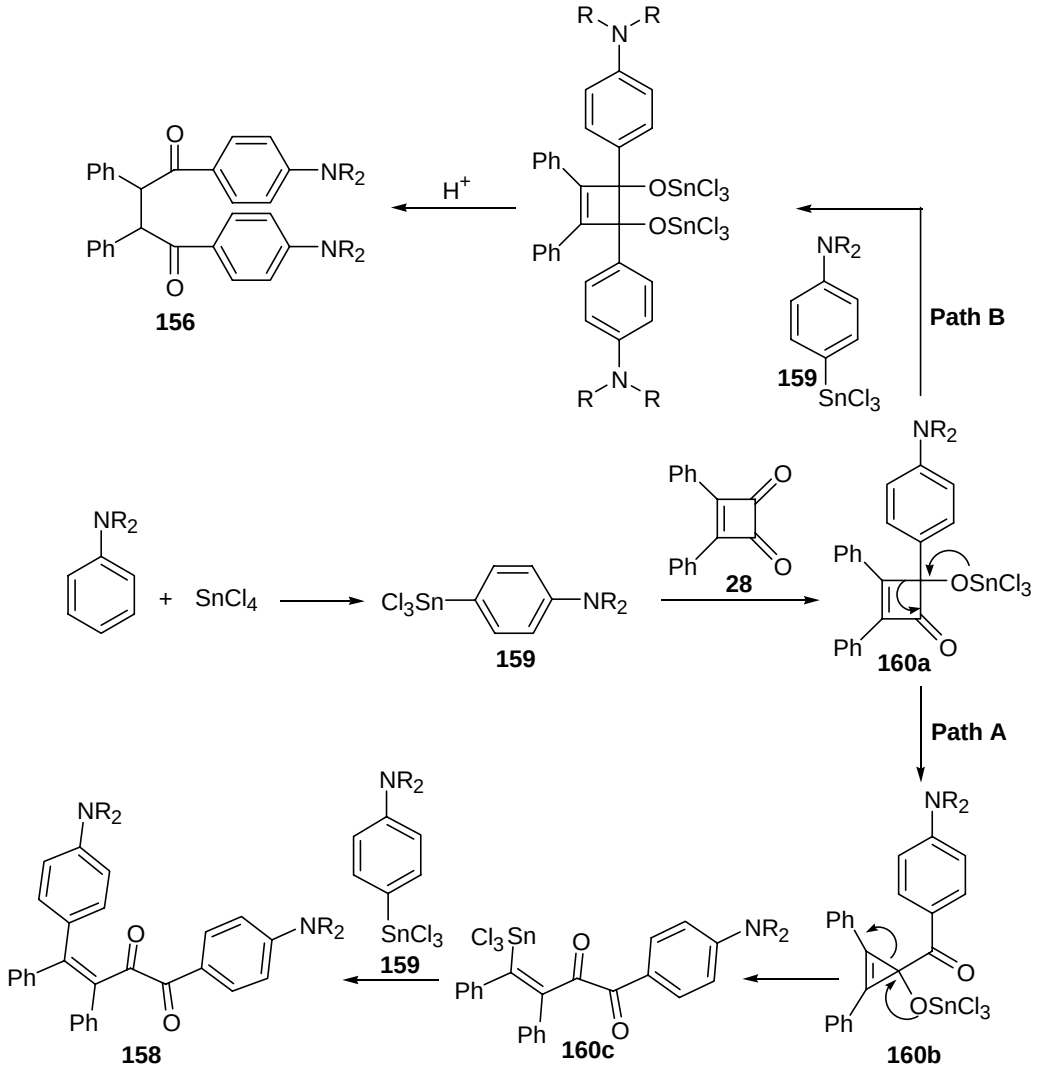
Scheme 87



R = Et	**158a** 60%	**156a** 20%
R = Me	**158b** 40%	**156b** 12%
R = Me, Et	**158c** 42%	**156c** 10%
R = *N,N-dimethylnaphthylaniline*	**158d** 38%	

A plausible route to the formation of **158** and **156** may involve an ionic mechanism as depicted in **Scheme 88**.

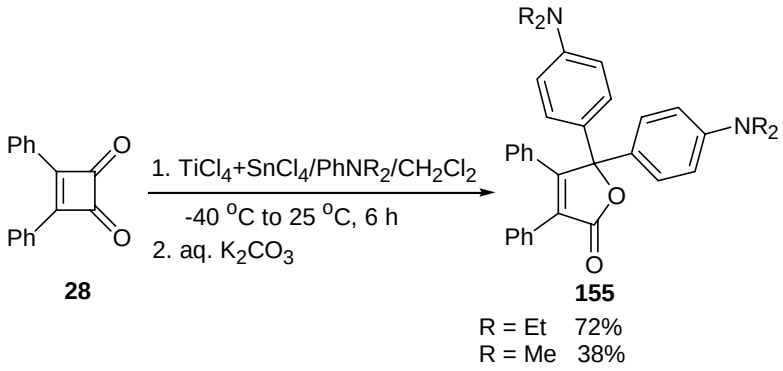
Scheme 88



Addition of one equivalent of aryltin species **159** to the cyclobutenedione **28** may lead to benzilic acid type rearrangement to generate cyclopropenol derivative **160b**. Ring opening would then give **160c**, which could undergo coupling with another aryltin species to afford the final product **158**. The compound **156 (Scheme 88)** could form through reaction with 2 equivalent of aryltin species similar to reaction realized in the case of aryltitanium species (**Scheme 82)**.

It was of interest to examine this reaction using the $TiCl_4$ and $SnCl_4$ mixture. Accordingly, we have examined the reaction of a 1:1 mixture of $TiCl_4$ and $SnCl_4$ with diphenylcyclobutenedione at -40 ^oC. Interestingly, in this run only the butenolide **155** was obtained in 38-72% yield. The 1,4-diketone **156** and the acyclic product **158** were not formed (**Scheme 89**).

Scheme 89



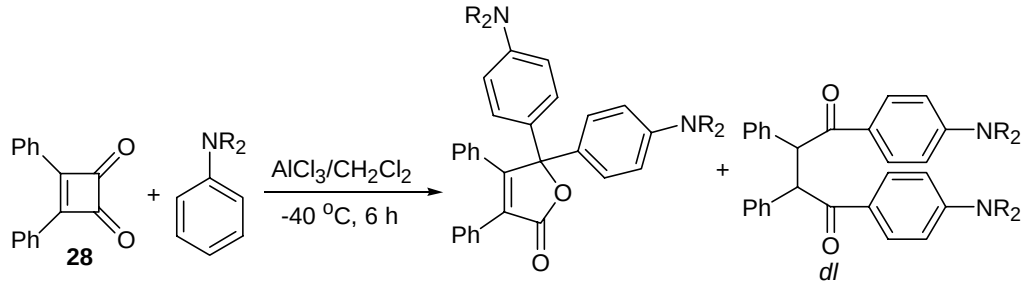
Presumably, the reactivity of $TiCl_4$ dominates in this case leading to the reaction characteristics of $TiCl_4$.

2.3 Reaction of Cyclobutenedione and Tertiary Amines with other Lewis Acids

Also, we have examined the reactivity of arylamines with diphenyl-cyclobutenediones in the presence of other Lewis acids such as $AlCl_3$, $BF_3.OEt_2$ and $ZnCl_2$. It was observed that, addition of $AlCl_3$ and *N,N*-dialkylarylamines to 3,4-

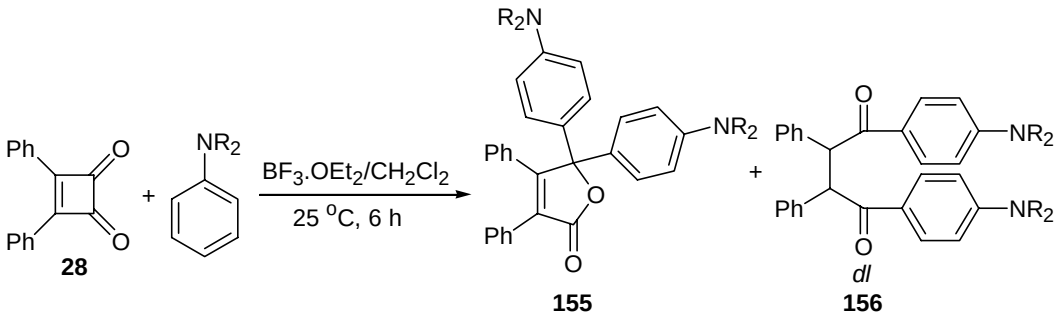
diphenyl-3-cyclobutene-1,2-dione at –40 ^{o}C leads to a butenolide **155** along with a small amount of expected 1,4-diketone **156** (**Scheme 90**). Whereas, the reactivity of arylamine/$BF_3.OEt_2$, at room temperature is similar to that of arylamine/$TiCl_4$ and the yields are moderate (**Scheme 91**). However, $ZnCl_2$ did not give the reaction.

Scheme 90



R = Et **155a** 60% **156a** 12%
R = Me **155b** 40% **156b** 08%

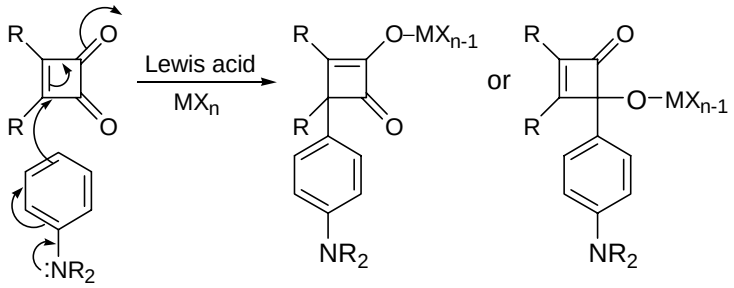
Scheme 91



R = Et **155a** 56% **156a** 12%
R = Me **155b** 36% **156b** 08%

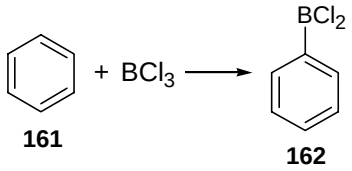
The above reactions take place only with highly activated arylamines and the reactions do not take place with activated rings like anisole. Accordingly, the reaction can be also explained by activation of the cyclobutenediones by the Lewis acids followed by reaction with amines, instead of formation of arylmetal reagents (**Scheme 92**).

Scheme 92



Generally, arylmetal reagents are prepared by metal-halogen or metal-hydrogen exchange, and transmetalation reaction between arylmetal compound and a metal halide or a metal. However, aromatic rings are known to react with Lewis acids to give the corresponding arylated products (**Scheme 93**).[136]

Scheme 93



161 **162**

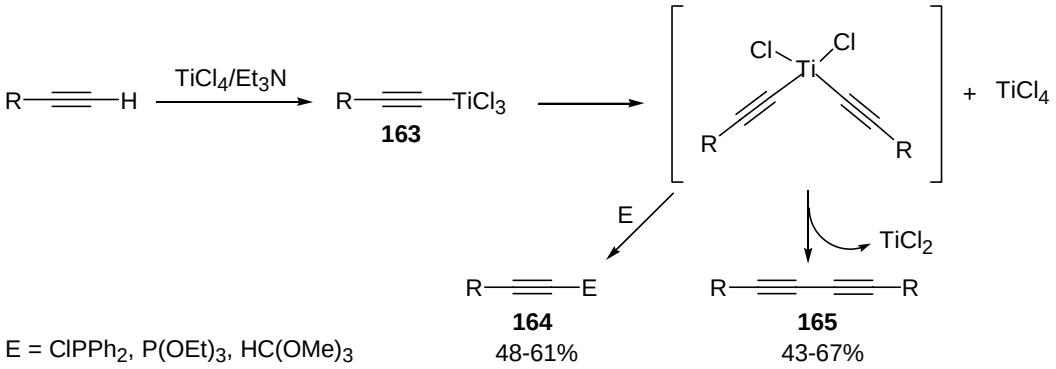
Accordingly, intermediacy of arylmetal species in the reactions of $ArNR_2$ with Lewis acids like $TiCl_4$ and $SnCl_4$ cannot be ruled out.

2.4 Reaction of Cylobutenedione with Alkynyltitanium Reagents

Recently, $TiCl_4/Et_3N$ reagent system was examined in this laboratory for the direct metalation of organic compounds.[137] For example, the direct preparation of alkynyltitanium reagents **163** has been achieved using 1-alkynes and the $TiCl_4/Et_3N$ reagent system for the first time, without using other organometallic reagents such as RLi or RMgX.[137] These alkynyltitanium species readily undergo dimerisation to give symmetrical 1,3 diynes **165** at room temperature in runs without electrophiles. Whereas

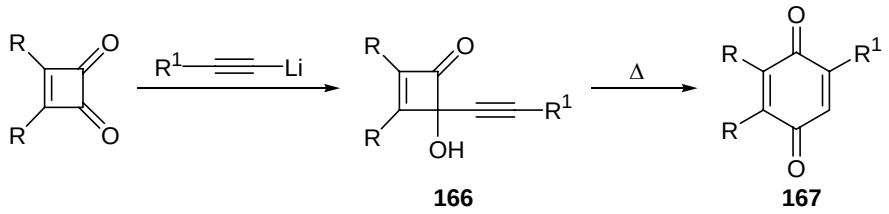
the corresponding addition or substitution products are obtained in the presence of electrophiles **164** (**Scheme 94**).

Scheme 94



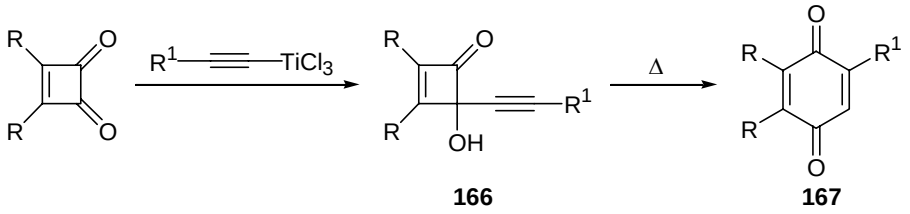
Previously, formation of quinones form cyclobutenediones was reported in the reaction of lithium reagents followed by rearrangement (**Scheme 95**).[26a,74-77]

Scheme 95



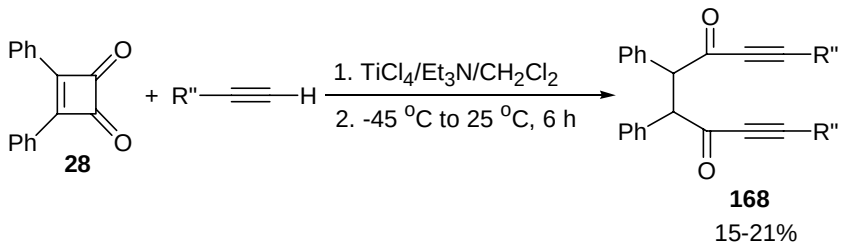
As all the reported methods for the synthesis of quinones from cyclobutenediones rely on the use of lithium reagents (**Scheme 95**), we have examined the reactivity of alkynyltitanium species produced using the 1-alkyne/$TiCl_4$/R_3N system and cyclobutenediones with a view to develop a convenient method for the synthesis of mixed quinones (**Scheme 96**).

Scheme 96



We have carried out the reaction of alkynyltitanium reagents **163**, prepared using phenylacetylene/$TiCl_4$/Et_3N reagent system, with 3,4-diphenyl-3-cyclobutene-1,2-dione **28** at room temperature. We have obtained the corresponding diyne as major isolable product along with a mixture of unidentified products. However, when the reaction was performed at –45 ˚C, a *dl:meso* mixture of 1,8 dialkyl-4,5-diphenyl-1,7-octadiyne-3,6-diones **168** were isolated along with unreacted cyclobutenedione (**Scheme 97**). Unfortunately, the yields are poor in the present method. Further optimization of reaction conditions to improve the yields is desirable.

Scheme 97



2.5 Alkynylation of Cyclobutenediones using $TiCl_4$/Et_3N Reagent System

We have also examined the reactivity of alkynyltitanium species at low temperature.[138] The reaction of these titanium reagents with diphenylcyclobutenedione gave product **169a** and **169b** (**Scheme 98**). Whereas the reaction with 3-phenyl-cyclobut-3-ene-1,2-dione and 3-phnyl-4-trimethylsilanyl-cyclobut-3-ene-1,2-dione gave

the alkenylcyclobutenedione **169c** product in moderate yield (**Scheme 98**). The product **169c** was also characterized by single crystal X-ray analysis (**Fig. 2**).

Scheme 98

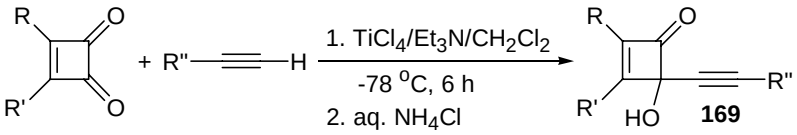
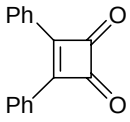
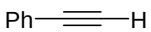
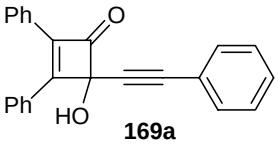
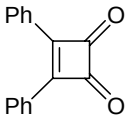
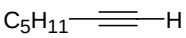
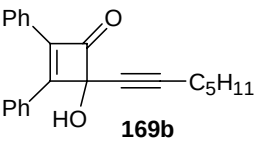
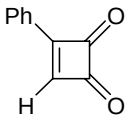
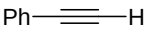
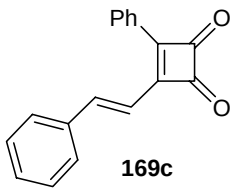
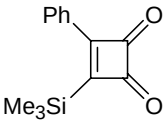
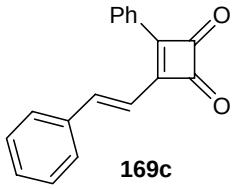


Table 3. Reaction of alkynes with cyclobutenediones

S. No.	Dione	Acetylene	Product[a]	Yield (%)[b]
1			 **169a**	62
2			 **169b**	58
3			 **169c**	64
4			 **169c**	76

[a]The products were identified by IR, ^{1}H NMR, ^{13}C NMR, Mass and CHN analysis.

[b]Yields are of the isolated products and based on the amount of cyclobutenedione used.

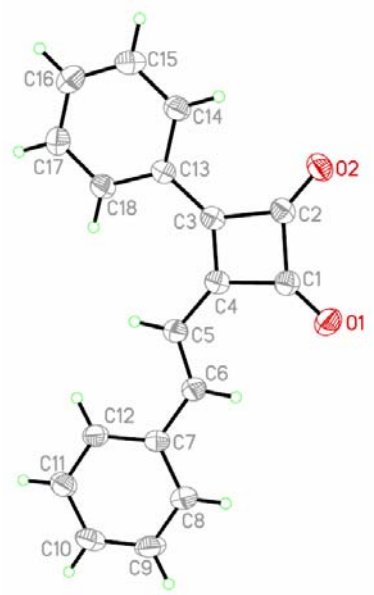
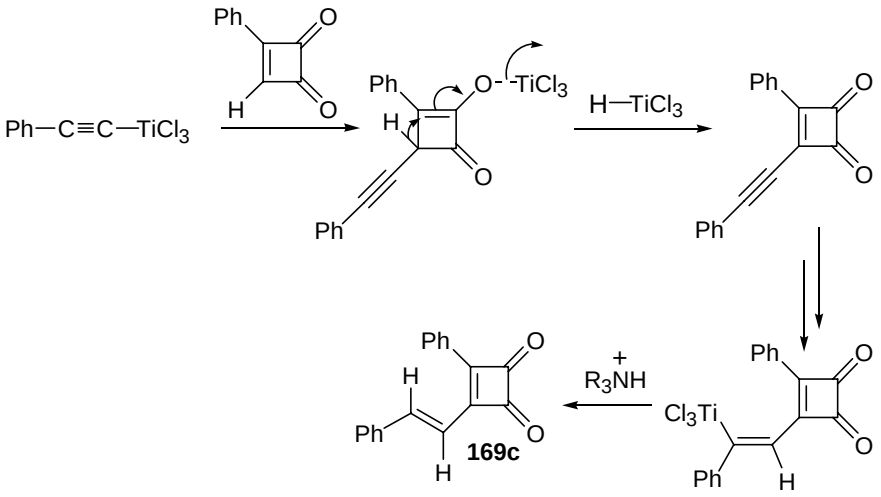


Figure 2. ORTEP Diagram of the product 169c.

A plausible reaction mechanism for formation of alkenylcyclobutenedione can be considered as depicted in **Scheme 99**.

Scheme 99

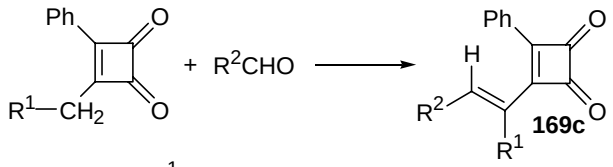


Previously, *Ried et al.*[139] reported that condensation of the 3-alkyl-4-phenyl-3-cyclobutene 1,2-dione with aromatic aldihydes produces the alkenylcyclobutenedione (**Scheme 100**).

Table 4. Crystal data and structure refinement for the Compound 169c.

Empirical Formula	$C_{18}\ H_{13}\ O_2$
Formula weight F_w	261.28
Temperature T (K)	293(2)
Wavelength λ (Å)	0.71073
Crystal system, Space group	Orthorhombic, pbca
Unit cell dimensions	
a (Å), α (°)	14.1854(10), 90
b (Å), β (°)	8.1184(6), 90
c (Å), γ (°)	23.8168(16), 90
Volume V ($Å^3$)	2742.8(3)
Z	8
Calculated density ρ_{calcd} mg/M^3	1.265
Absorption coefficient μ (mm^{-1})	0.082
F (000)	1096
Crystal Size (mm)	0.44 x 0.28 x 0.22
θ for data collection range/deg	1.71 to 28.29
Limiting indices	-18<=h<=18, -10<=k<=7, -31<=l<=28
Reflections collected/unique	15850 / 3302 [R(int) = 0.0327]
Completeness to θ	28.29, 96.9 %
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3302 / 0 / 181
Goodness-of-fit on GOF (F^2)	1.077
Final R indices *R1*, *wR2 [I>2σ(I)]*	*R1* = 0.0580 *wR2* = 0.1223
R indices (all data) *R1*, *wR2*	*R1* = 0.0879 *wR2* = 0.1362
Largest diff. Peak and hole ($e \cdot Å^{-3}$)	0.135 and -0.164

Scheme 100



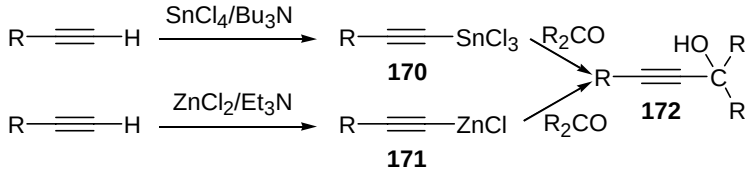
R^1 = H, CH_3, C_6H_5

R^2 = C_6H_5, $C_6H_4CH_3$ etc.

2.6 Alkynylation of Cyclobutenediones with Alkynes and other Lewis Acids

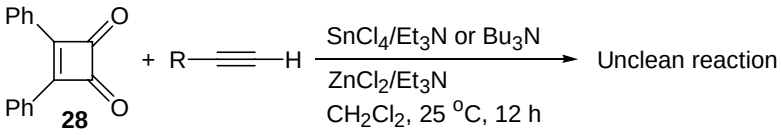
Previously, *Yamaguchi et al.*[140] reported the preparation of alkynyltin species using $SnCl_4/Bu_3N$ and alkynes **170**. Similarly, alkynylzinc species were prepared by the reaction of with $ZnCl_2/Et_3N$ **171**.[141] These alkynylmetal reagents have been utilized for the synthesis of various propargyl alcohols **172** (**Scheme 101**).

Scheme 101



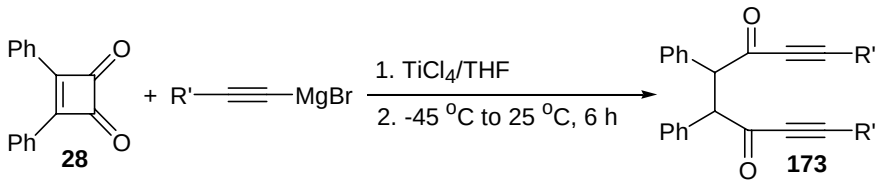
We have examined the use of these reagent systems with a view to improve the yields of the products, since the alkynyltin and zinc reagents would not undergo oxidative coupling to 1,3-diynes, which is a major side reaction in the case of $TiCl_4/Et_3N$/alkyne reagent systems. Accordingly, we have carried out the reaction of 1-alkynes with cyclobutenedione in the presence of $SnCl_4/Bu_3N$ or $ZnCl_2/Et_3N$, but the reaction was not clean in these runs (**Scheme 102**).

Scheme 102



Accordingly, we have examined the reactivity of alkynyltitanium species prepared *via* transmetalation by the addition of $TiCl_4$ to alkynyl Grignad reagent at –45 to 25 ^oC temperature. The reaction of these titanium reagents with cyclobutenedione gave *dl:meso* mixture of product **173** (**Scheme 103**) in moderate yields (**Table 5**). The compound 1,4,5,8-tetraphenyl-1,7-octadiyne-3,6-dione **173a** was further characterized by X-ray crystallographic analysis (**Fig. 3**).

Scheme 103



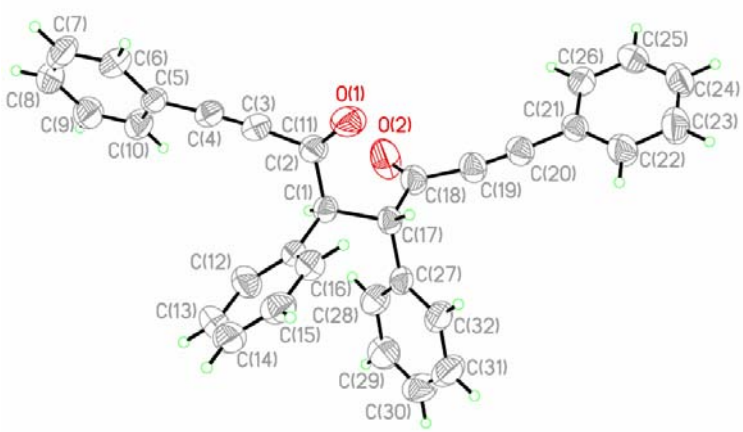
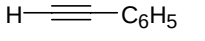
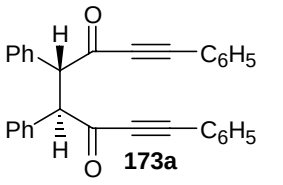
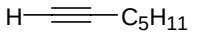
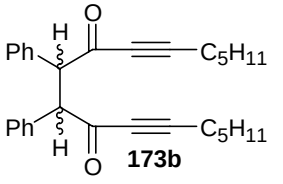
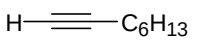
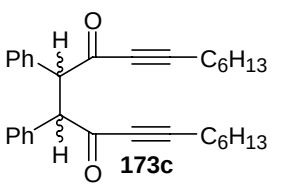
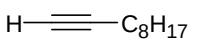
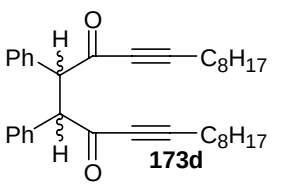
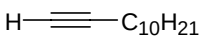
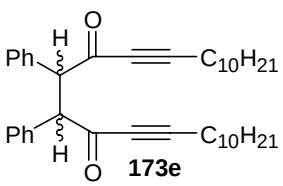


Figure 3. ORTEP Diagram of the product 173a.

The formation of 1,4,5,8-tetrasubstituted-1,7-octadiyne-3,6-dione **173** can be rationalized through a sequence of intermediates as depicted in **Scheme 104**. Nucleophilic addition of two equivalents of alkynyltitanium species to cyclobutenedione may lead to the intermediate **174a**, which could undergo [2+2] electrocyclic ring opening to give dienol **174c** after hydrolysis. The intermediate **174c** could tautomerize to the final product **173**.

Table 5. Reaction of alkynes with diphenylcyclobutenedione

S. No.	Alkyne	Product[a]	% of Yield[b]	*di:meso*[c]
1		 **173a**	32	100:00
2		 **173b**	35	60:40
3		 **173c**	42	70:30
4		 **173d**	23	75:25
5		 **173e**	28	75:25

[a]The products were identified using spectral data (IR, ^{1}H NMR, ^{13}C NMR, Mass and CHN analysis) and comparison with reported data for **173b**.[128]

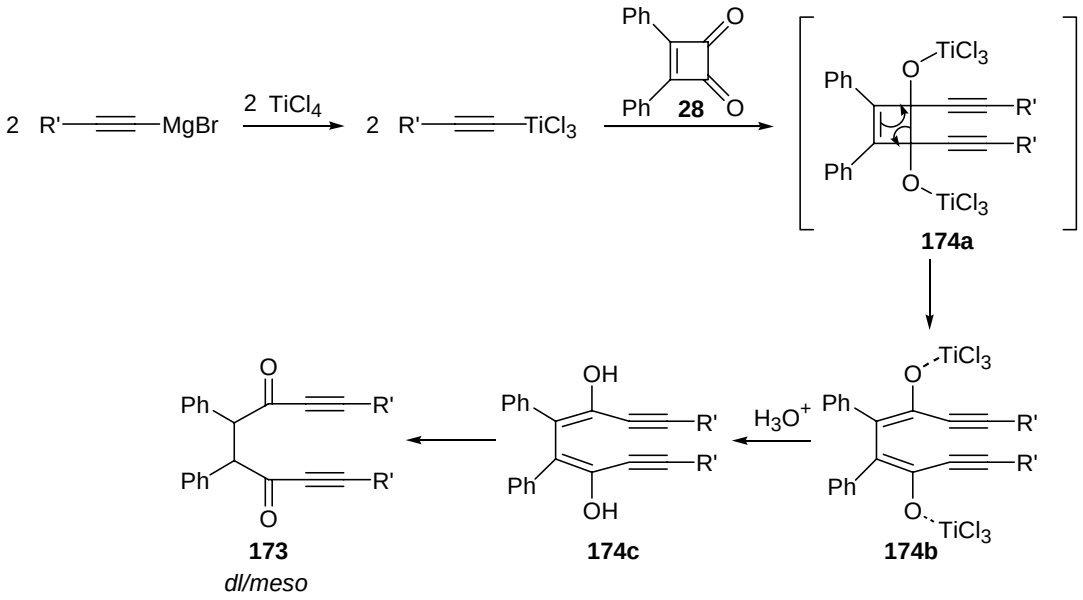
[b]Yields are of the isolated products and based on the amount of cyclobutenedione used.

[c]*dl:meso* ratios were determined by ^{1}H NMR intensities of the Ph-CH-CO signals.

Table 6. Crystal data and structure refinement for the Compound 173a.

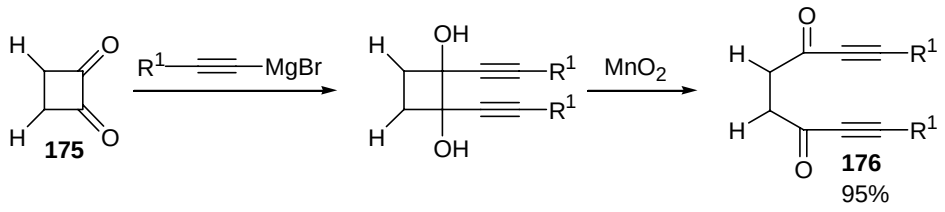
Empirical Formula	C_{32} H_{22} O_2
Formula weight F_w	438.50
Temperature T (K)	293(2)
Wavelength λ (Å)	0.71073
Crystal system, Space group	Monoclinic, $P2_1/c$
Unit cell dimensions	
a (Å), α (°)	12.8316(8), 90
b (Å), β (°)	18.2951(11), 93.2540(10)
c (Å), γ (°)	10.4748(6), 90
Volume V (Å^3)	2455.1(3)
Z	4
Calculated density ρ_{calcd} mg/M^3	1.186
Absorption coefficient μ (mm^{-1})	0.073
F (000)	920
Crystal Size (mm)	0.48 x 0.28 x 0.26
θ for data collection range/deg	1.59 to 28.30
Limiting indices	-17<=h<=17, -24<=k<=24, -13<=l<=13
Reflections collected/unique	28396 / 5942 [R(int) = 0.0415
Completeness to θ	28.30, 97.5 %
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5942 / 0 / 307
Goodness-of-fit on GOF (F^2)	1.038
Final R indices *R1*, *wR2 [I>2σ(I)]*	*R1* = 0.0618 *wR2* = 0.1207
R indices (all data) *R1*, *wR2*	*R1* = 0.1222 *wR2* = 0.1446
Largest diff. Peak and hole (e·Å^{-3})	0.192 and -0.194

Scheme 104



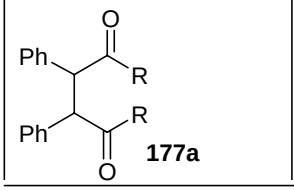
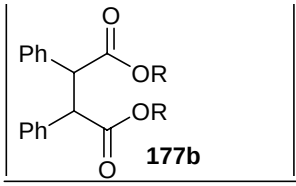
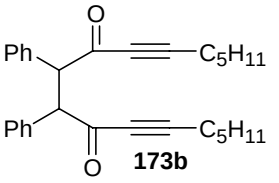
Similar compounds were isolated along with several other addition products in the reaction of Grignard reagents with cyclobutenedione.[128a] Also, addition of alkynyl Grignard to cyclobutanedione **175** yields a similar product after MnO_2 oxidation (**Scheme 105**).[128b]

Scheme 105

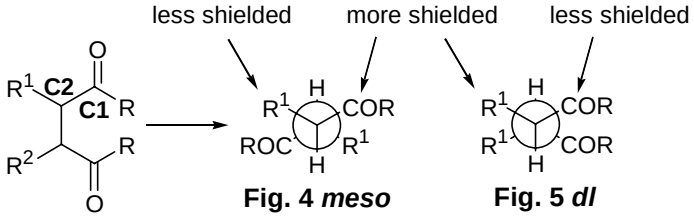


Previously, a few of this class of compounds have been reported[128] but the relative stereochemistry in these compounds was not assigned. We have identified the major diastereomer formed in the above reaction (**Scheme 103**) as *dl* isomer by comparison with the ^{1}H NMR data reported for the related molecules (**Table 7**).[129,130]

Table 7.

 **177a**	R = Me	*dl*	4.41 (s, 2H)
		meso	4.63 (s, 2H)
	R = Ph	*dl*	5.40 (s, 2H)
		meso	5.78 (s, 2H)
 **177b**	R = Me	*dl*	4.25 (s, 2H)
		meso	4.40 (s, 2H)
	R = Alkyl	*dl*	4.33 (s, 2H)
		meso	4.47 (s, 2H)
 **173b**		*dl*	4.57 (s, 2H)
		meso	4.77 (s, 2H)

Graham et al. proposed the following generation to identify *dl/meso* isomers of 3,4-disustituted-1,4-diones based on ^{13}C NMR chemical shifts.[135] In *meso* derivatives, (**Fig. 4**) the carbonyl groups are gauche to methyl (R^1), but in the *dl* isomer carbonyl groups are gauche to each other. The alkyl group would exert greater shielding than does the carbonyl group. Hence, the carbonyl carbon (C1) would be more shielded in the *meso* isomer and would appear at upfield. Whereas the C3 of R^1 would be more shielded in the *dl* isomer since the two R^1 groups are gauche to each other (**Fig. 5**). A similar pattern of chemical shift differences were observed for *dl:meso* isomers of compound **173b** (**Table 8**) (**Spectra 15 and 16**). Accordingly, the relative stereochemistry of the major isomer of compounds **173a-173e** may be assigned as *dl*.



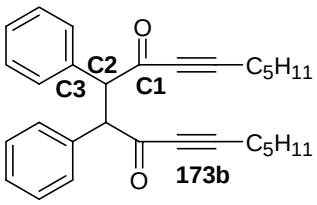


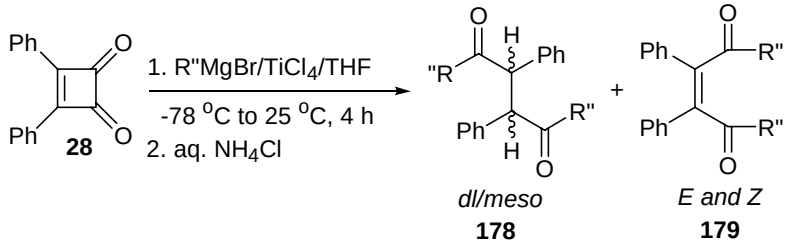
Table 8.

^{13}C NMR data of **173b**	
meso	**dl**
C1 184.3	**C1** 185.6
C2 62.1	**C2** 62.7
C3 135.2	**C3** 134.7

2.7 Alkylation of Cyclobutenedione using the R"MgBr/$TiCl_4$ Reagent System

In continuation of those efforts, we have also examined the reactivity of alkyltitanium species prepared *in situ via* transmetalation by the addition of $TiCl_4$ to alkyl Grignard reagents at low temperature. The reaction of these titanium reagents with cyclobutenedione gave products **178** and **179** (**Scheme 106**). The products **178a**, **178d** and **179b** were characterized by single crystal X-ray analysis (**Figs. 6, 7 and 8**).

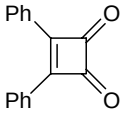
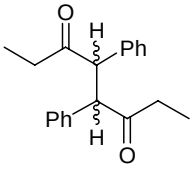
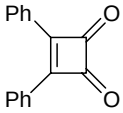
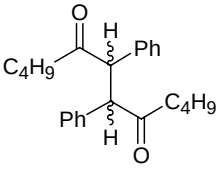
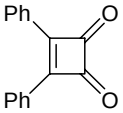
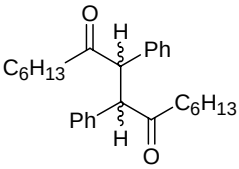
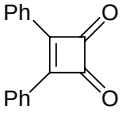
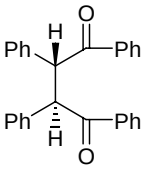
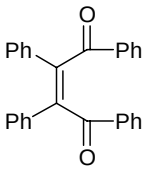
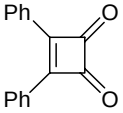
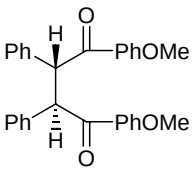
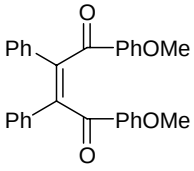
Scheme 106



The formation of *dl/meso* and *E/Z* 1,4-diketones can be rationalized through a sequence of reactions and intermediates as depicted in **Scheme 107**.

Nucleophilic addition of two equivalents of alkyltitanium species to 3,4-cyclobutene-1,2-dione **28** may lead to the intermediate **180a**, which could undergoes [2+2] electrocyclic ring opening to give **180b.** Rearrangement of the intermediate **180b**

Table 9. Reaction of alkyl and aryl Grignard reagents with diphenylcyclobutenedione

S. No.	Dione	R"MgBr	Product **178**[a]	Product **179**[a]	Yield (%)[b]		*dl:meso*[c]
					178	**179**	
1		C_2H_5MgBr	 dl/meso **178a**	–	68	–	05:95
2		C_4H_9MgBr	 dl/meso **178b**	–	63	–	58:42
3		$C_6H_{13}MgBr$	 dl/meso **178c**	–	48	–	56:44
4		PhMgBr	 dl **178d**	 E and Z **179a**	46	28	
5		MeOPhMgBr	 dl **178e**	 E and Z **179b**	42	26	

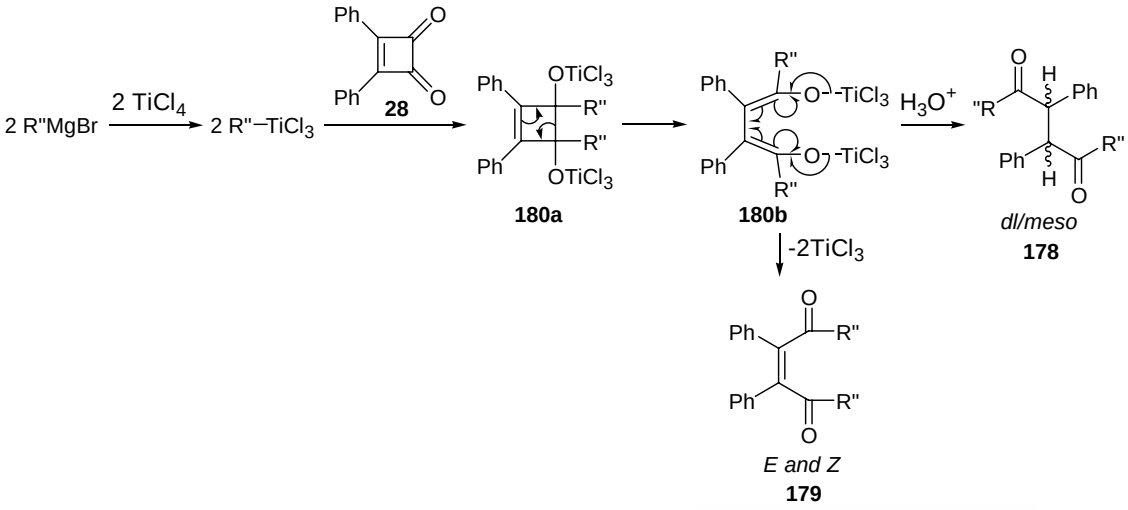
[a]The products were identified by IR, ^{1}H NMR, ^{13}C NMR, Mass and CHN analysis.

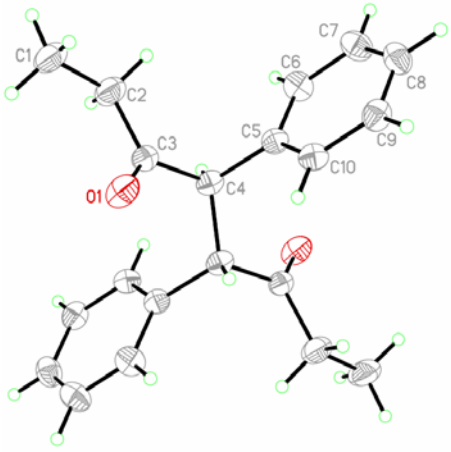
[b]Yields are of the isolated products and based on the amount of cyclobutenedione used.

[c]*dl:meso* ratios were determined by ^{1}H NMR intensities of the Ph-CH-CO signals.

leads to the formation of enedione **178** by loss of two equivalents of $TiCl_3$ and after hydrolysis, the intermediate **180b** tautomerizes to the final product **179**.

Scheme 107





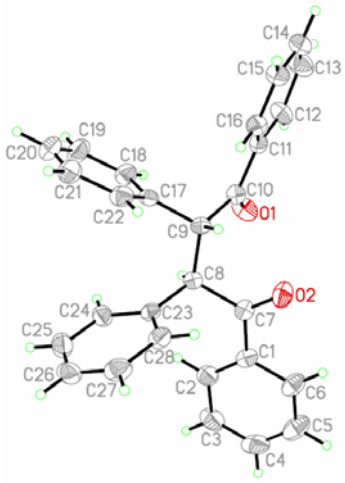


Fig. 6. ORTEP Diagram of the product 178a. Fig. 7. ORTEP Diagram of the product 178d.

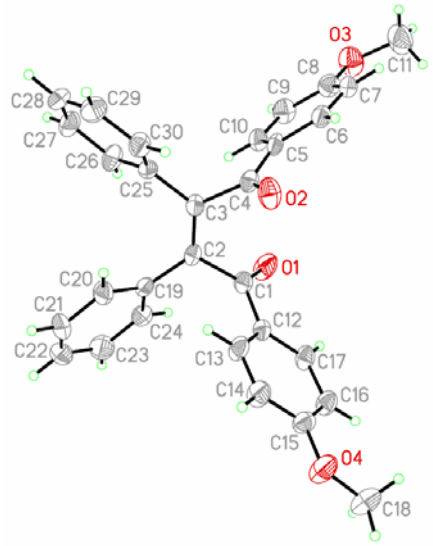


Figure 8. ORTEP Diagram of the product 179b.

Table 10. Crystal data and structure refinement for the Compound 178a.

Empirical Formula	$C_{20}\ H_{22}\ O_2$
Formula weight F_w	294.38
Temperature T (K)	273(2)
Wavelength λ (Å)	0.71073
Crystal system, Space group	Monoclinic, C_2/c
Unit cell dimensions	
a (Å), α (°)	23.172(2), 90
b (Å), β (°)	5.5978(5), 130.6990(10)
c (Å), γ (°)	16.7090(15), 90
Volume V ($Å^3$)	1643.2(3)
Z	4
Calculated density ρ_{calcd} mg/M^3	1.190
Absorption coefficient μ (mm^{-1})	0.075
F (000)	632
Crystal Size (mm)	0.38 x 0.2 x 0.18
θ for data collection range/deg	2.32 to 25.92
Limiting indices	-28<=h<=28, -6<=k<=6, -20<=l<=20
Reflections collected/unique	7972 / 1598 [R(int) = 0.0202]
Completeness to θ	25.92, 99.7 %
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1598 / 0 / 100
Goodness-of-fit on GOF (F^2)	1.053
Final R indices *R1*, *wR2 [I>2σ(I)]*	*R1* = 0.0538 *wR2* = 0.1378
R indices (all data) *R1*, *wR2*	*R1* = 0.0618 *wR2* = 0.1440
Largest diff. Peak and hole ($e \cdot Å^{-3}$)	0.275 and -0.145

Table 11. Crystal data and structure refinement for the Compound 178d.

Empirical Formula	$C_{28}\ H_{22}\ O_2$
Formula weight F_w	390.46
Temperature T (K)	273(2)
Wavelength λ (Å)	0.71073
Crystal system, Space group	Monoclinic, C_2/c
Unit cell dimensions	
a (Å), α (°)	24.179(3), 90
b (Å), β (°)	10.0074(12), 120.609(2)
c (Å), γ (°)	22.989(3), = 90
Volume V (Å^3)	4787.5(10)
Z	8
Calculated density ρ_{calcd} mg/M^3	1.083
Absorption coefficient μ (mm^{-1})	0.067
F (000)	1648
Crystal Size (mm)	0.42 x 0.36 x 0.22
θ for data collection range/deg	2.26 to 25.94
Limiting indices	-29<=h<=29, -12<=k<=12, -28<=l<=28
Reflections collected/unique	22376 / 4415 [R(int) = 0.0507]
Completeness to θ	25.94, 94.3 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9854 and 0.9724
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4415 / 0 / 271
Goodness-of-fit on GOF (F^2)	1.045
Final R indices $R1$, $wR2$ $[I>2\sigma(I)]$	$R1$ = 0.0745 $wR2$ = 0.1843
R indices (all data) $R1$, $wR2$	$R1$ = 0.1357 $wR2$ = 0.2705
Largest diff. Peak and hole (e·Å^{-3})	0.754 and -0.237

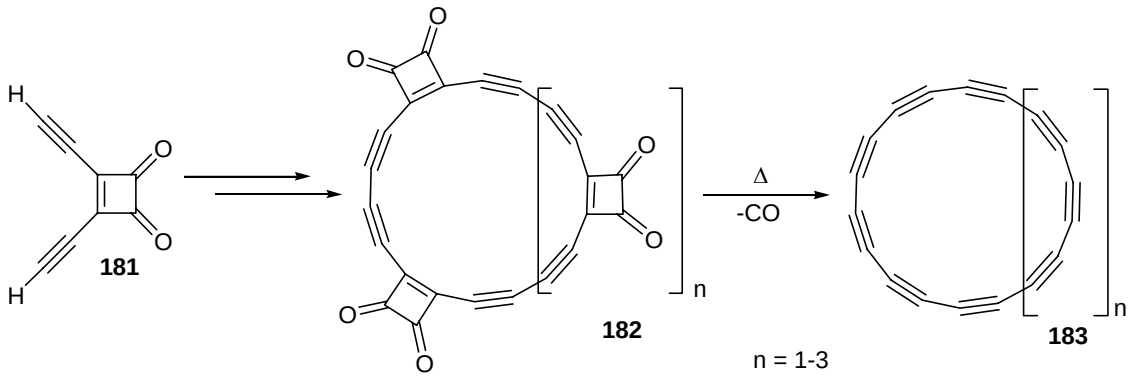
Table 12. Crystal data and structure refinement for the Compound 179b.

Empirical Formula	$C_{30}\ H_{24}\ O_4$
Formula weight F_w	448.49
Temperature T (K)	293(2)
Wavelength λ (Å)	0.71073
Crystal system, Space group	Monoclinic, $P2_{(1)}/c$
Unit cell dimensions	
a (Å), α (°)	11.586(3), 90
b (Å), β (°)	23.504(7), 109.652(6)
c (Å), γ (°)	9.499(3), 90
Volume V ($Å^3$)	2436.2(12)
Z	4
Calculated density ρ_{calcd} mg/M^3	1.223
Absorption coefficient μ (mm^{-1})	0.080
F (000)	944
Crystal Size (mm)	0.44 x 0.34 x 0.20
θ for data collection range/deg	1.73 to 28.26
Limiting indices	-14<=h<=14, -30<=k<=24, -12<=l<=12
Reflections collected/unique	16815 / 5568 [R(int) = 0.0480]
Completeness to θ	28.30, 97.5 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9841 and 0.9655
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5568 / 0 / 309
Goodness-of-fit on GOF (F^2)	1.351
Final R indices *R1*, *wR2 [I>2σ(I)]*	*R1* = 0.1553 *wR2* = 0.2544
R indices (all data) *R1*, *wR2*	*R1* = 0.2069 *wR2* = 0.2765
Largest diff. Peak and hole ($e \cdot Å^{-3}$)	0.257 and -0.151

2.8 Alkylation of Cyclobutenediones with the R"$(MgBr)_2$ Reagent System

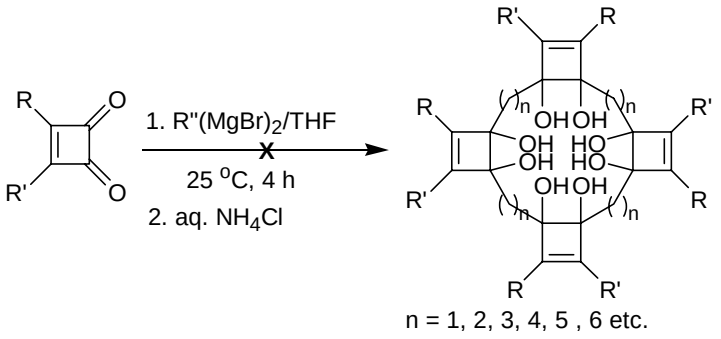
A recent review by *Diederich et al.*[115] gives an overview of the applications of cyclobutenediones in the synthesis of all carbon rods, rings and nets. Preparation of all carbon molecules rely on the use of 3-cyclobutene-1,2-dione, an acetylene synthon, which readily loses its two carbonyl groups in pyrolytic or photolytic reactions (**Scheme 108**).

Scheme 108



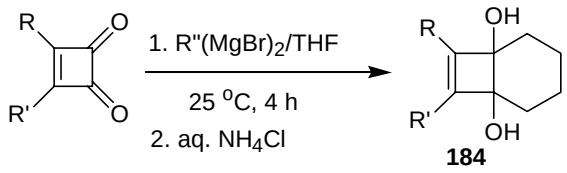
We have carried out the reactions using alkyldibromides with cyclobutenedione for the preparation of highly fused molecules. But the reaction was not clean (**Scheme 109**).

Scheme 109



Accordingly, we have carried out the reaction of alkylmagnesium reagents, prepared *in situ* using simple alkyldibromide and magnesium reagent system, with cyclobutenediones. The corresponding diols were obtained as major products (**Scheme 110**). However, the reaction using 1,2-dibromoethane, 1,3-dibromopropane, 1,2-dibromoxylene and 1,3-dibromoxylene did not give expected diol products and only unidentified products are obtained in these cases (**Table 13**).

Scheme 110



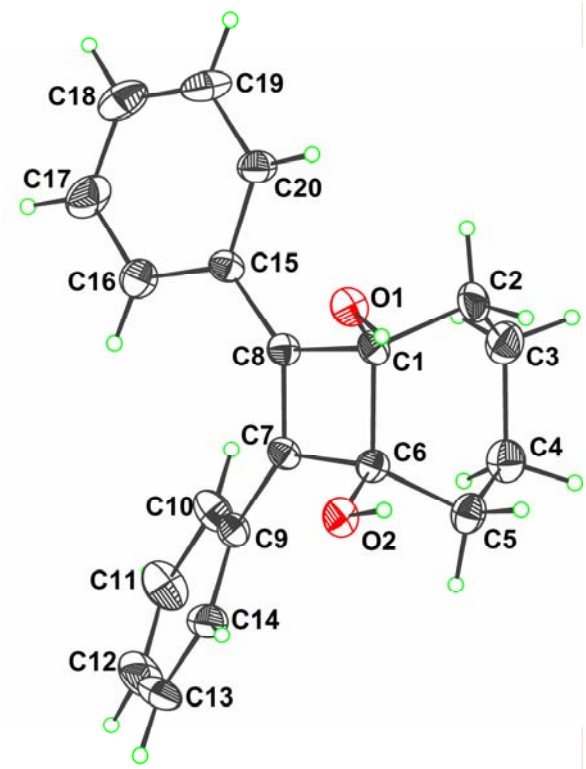
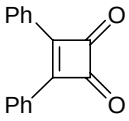
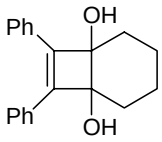
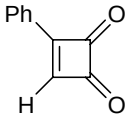
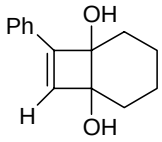
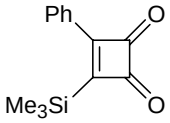
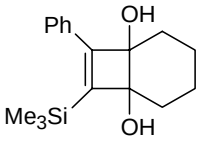
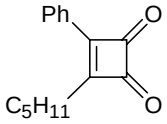
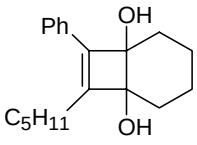
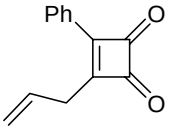
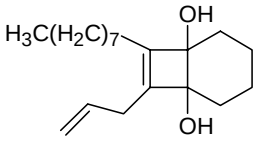
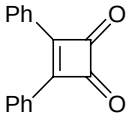
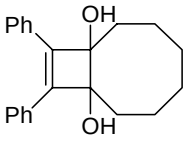


Figure 9. ORTEP Diagram of the product 184a.

Table 13. Reaction of alkyl Grignard reagents with cyclobutenediones

S. No.	Dione	R"(MgBr)$_2$	Product[a]	Yield (%)[b]
1		$C_4H_8(MgBr)_2$	 **184a**	65
2		$C_4H_8(MgBr)_2$	 **184b**	52
3		$C_4H_8(MgBr)_2$	 **184c**	58
4		$C_4H_8(MgBr)_2$	 **184d**	54
5		$C_4H_8(MgBr)_2$	 **184e**	55
6		$C_6H_{12}(MgBr)_2$	 **184f**	47

[a]The products were identified by IR, ^{1}H NMR, ^{13}C NMR, Mass and CHN analysis.

[b]Yields are of the isolated products and based on the amount of cyclobutenedione used.

2.9 Synthesis of Highly Substituted Pyrrole Derivatives from 1,4-diketones

The pyrrole moiety is present in a wide variety of molecules and materials like pharmaceuticals,[142] conducting polymers,[143] molecular optics,[144] electronic materials[145] and gas sensors,[146] in many physiologically interesting natural products, such as haeme,

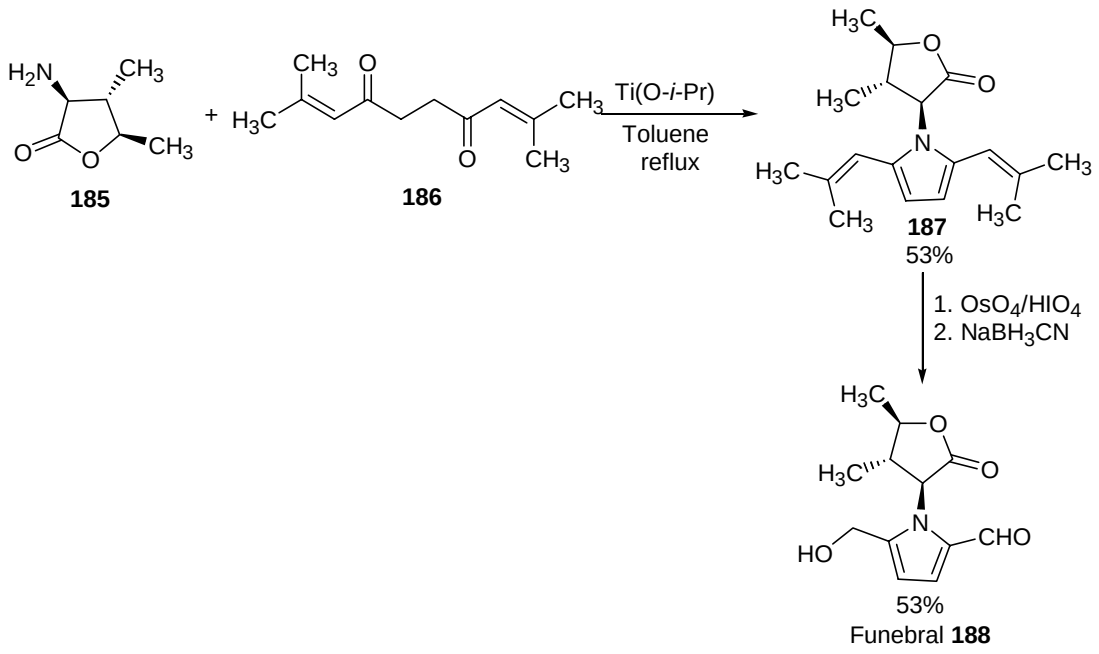
Table 14. Crystal data and structure refinement for the Compound 184a.

Empirical Formula	$C_{20}\ H_{20}\ O_2$
Formula weight F_w	292.37
Temperature T (K)	298(2)
Wavelength λ (Å)	0.71073
Crystal system, Space group	Monoclinic, $P2_1/c$
Unit cell dimensions	
a (Å), α (°)	15.075(2), 90
b (Å), β (°)	15.042(2), 103.565(2)
c (Å), γ (°)	31.879(5), 90
Volume V (Å^3)	7027.4(18)
Z	4
Calculated density ρ_{calcd} mg/M^3	1.105
Absorption coefficient μ (mm^{-1})	0.070
F (000)	2496
Crystal Size (mm)	0.44 x 0.32 x 0.28
θ for data collection range/deg	1.31 to 26.09
Limiting indices	-18<=h<=18, -18<=k<=18, -39<=l<=39
Reflections collected/unique	70695 / 13916 [R(int) = 0.0995]
Completeness to θ	26.09, 99.7 %
Max. and min. transmission	0.9807 and 0.9698
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	13916 / 0 / 801
Goodness-of-fit on GOF (F^2)	1.472
Final R indices *R1*, *wR2 [I>2σ(I)]*	*R1* = 0.0758 *wR2* = 0.1846
R indices (all data) *R1*, *wR2*	*R1* = 0.1444 *wR2* = 0.2443
Largest diff. Peak and hole (e·Å^{-3})	2.492 and -0.390

chlorophyll, bile pigments, pyrrolizidines, indolizidines alkaloids[147] and vitamin B_{12}.[148] Many substituted pyrroles show important biological activity. Halogenated pyrroles isolated from natural sources also represent the class of substituted pyrroles with important biological activities.[149,150] A number of alkaloids having the aryl or alkyl substituted pyrrole framework were isolated from marine sources.[151-155]

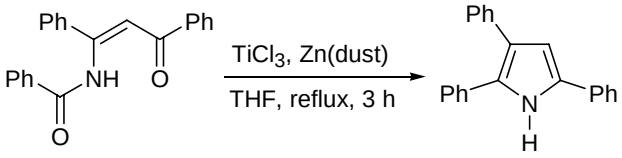
The Paal-Knorr pyrrole synthesis involves acid-catalyzed condensation of alkyl amines with 1,4-dicarbonyl compounds. Le Quesne *et al.*[156] employed Ti(O-*I*-Pr)$_4$ as a weak Lewis acid for the addition of amines **185** to doubly unsaturated 1,4-dicarbonyl derivative **186** (**Scheme 111**). Subsequent reaction of the adduct **187** with OsO_4/HIO_4 followed by reduction using $NaBH_3CN$ gave the (±)-Funebral **188** an alkaloid.

Scheme 111



Previously, a new procedure to transform oxoamides, acylated enaminones **189** or masked 1,3-dicarbonyl compounds, into several substituted pyrroles **190** by using low-valent titanium reagents was reported (**Scheme 112**).[157,158]

Scheme 112



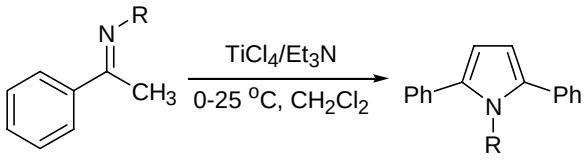
189 **190**

$R^1 = R^2 = R^3 = Ph$ 78%

$R^1 = R^2 = Me$, $R^3 = Ph$ 38%

A new protocol for pyrrole synthesis has also been reported from this laboratory. For example, arylmethyl ketimines **191** react with $TiCl_4/Et_3N$ at 0-25 ^oC in dichloromethane to give the corresponding 1,2,5-trisubstituted pyrroles **192** (**Scheme 113**).

Scheme 113



191 **192**

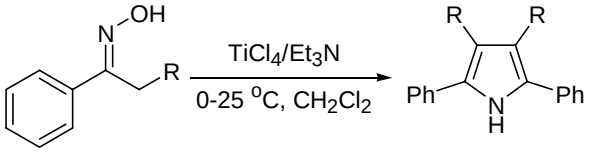
R = CH_3 78%

R = C_6H_5 90%

R = 4-ClC_6H_4 86%

It was also observed in this laboratory that the ketoximes **193** give corresponding 2,3,4,5-tetrasubstituted pyrroles **194** were obtained in moderate to good yields upon reaction with $TiCl_4/Et_3N$ at 0-25 ^oC (**Scheme 114**). Diketoxime **195** give corresponding 2,5-diphenylpyrrole **196** in 24% yield besides some unidentified products (**Scheme 115**).

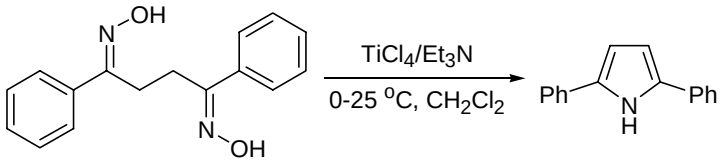
Scheme 114



193 **194**

R = CH_3 57%
R = C_6H_5 81%
R = C_2H_5 58%

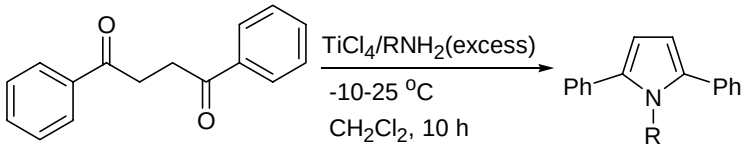
Scheme 115



195 **196**
24%

Recently, it was observed that the 1,4-diphenylbutane-1,4-dione **197** reacts with excess of primary amines in the presence of $TiCl_4$ at 25 °C for 10 h to give the corresponding 1,2,5-tirsubstituted pyrrole **198** in 64% yield (**Scheme 116**).

Scheme 116



197 **198**
50-64%

As we now have easy access to 1,4-diketones (**Scheme 106**), we were interested in the synthesis of substituted pyrroles. The 1,4-diketone was treated with $TiCl_4$ in dichloromethane at –25 °C, to produce the corresponding pentasubstituted pyrrole in good to excellent yields (**Scheme 117**). This transformation is found to be general for several primary amines and the results are summarized in Table 15. The crystals suitable for X-ray analysis were obtained in the case of the pyrrole **199b**. The crystal

structure data of **199b** are summarized Table A9 (Appendix II). The ORTEP diagram of the **199b** is shown in Figure 10.

Scheme 117

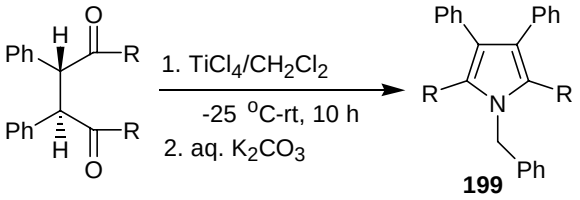
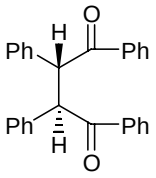
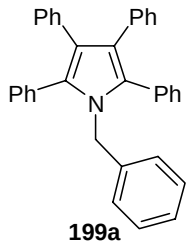
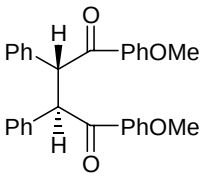
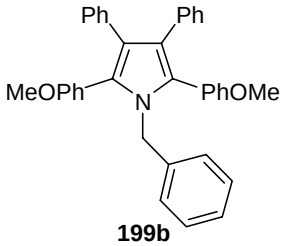
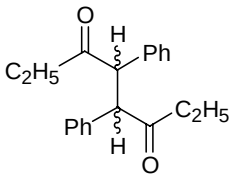
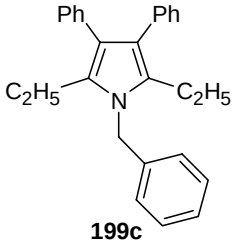
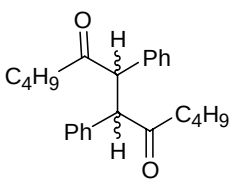
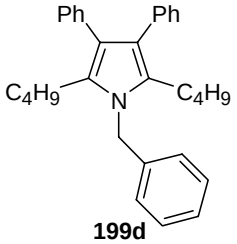


Table 15. Reaction of $TiCl_4$ and benzylamine with 1,4-diketones

S. No.	Diketone	Amine	Product[a]	Yield (%)[b]
1	 dl	$PhCH_2NH_2$	 **199a**	86
2	 dl	$PhCH_2NH_2$	 **199b**	82
3	 dl/meso	$PhCH_2NH_2$	 **199c**	75
4	 dl/meso	$PhCH_2NH_2$	 **199d**	62

[a]The products were identified by IR, ^{1}H NMR, ^{13}C NMR, Mass and CHN analysis.

[b]Yields are of the isolated products and based on the amount of 1,4-diketone used.

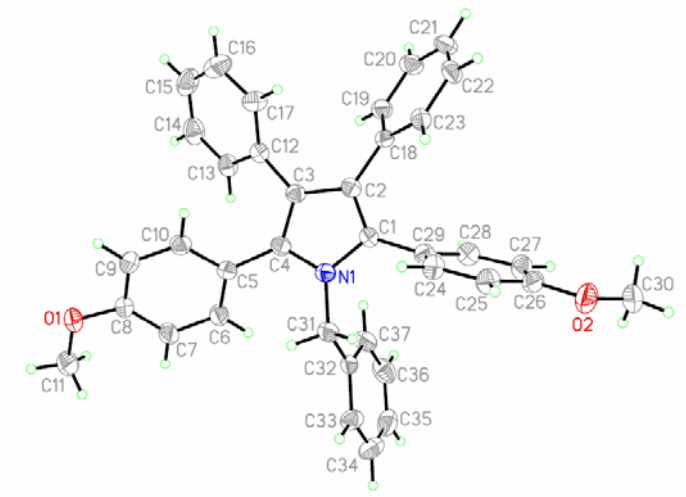


Figure 10. ORTEP Diagram of the product 199b.

Five-membered heterocycle derivatives with two aryl groups on adjacent positions include several class of natural and unnatural compounds that exhibit a variety of biological and biomedical properties.[159] These substances include unnatural compounds and a wide variety of substances isolated from natural sources that exhibit remarkable biological properties such as hypolipidemic, antimicrobial, anti-inflammatory and antitumour activity and are able to inhibit retroviral reverse transcriptases [i.e., human immunodeficiency virus type 1 (HIV-1)], cellular DNA polymerases and protein kinases. Further more, some of these compounds are useful intermediates in the synthesis of biologically important naturally occurring alkaloids and unnatural heterocycle derivatives.[160]

2.10 $TiCl_4/Bu_3N$ Promoted Aldol Reaction of Ketones with Cyclobutenedione

The aldol reaction is one of the fundamental and a widely exploited C-C bond forming reactions in organic synthesis.[161] The original method suffers from high reaction temperatures, poor yields and selectivity. However, the use of Lewis acids has revolutionized the classical method to be applicable as key reaction in the total synthesis

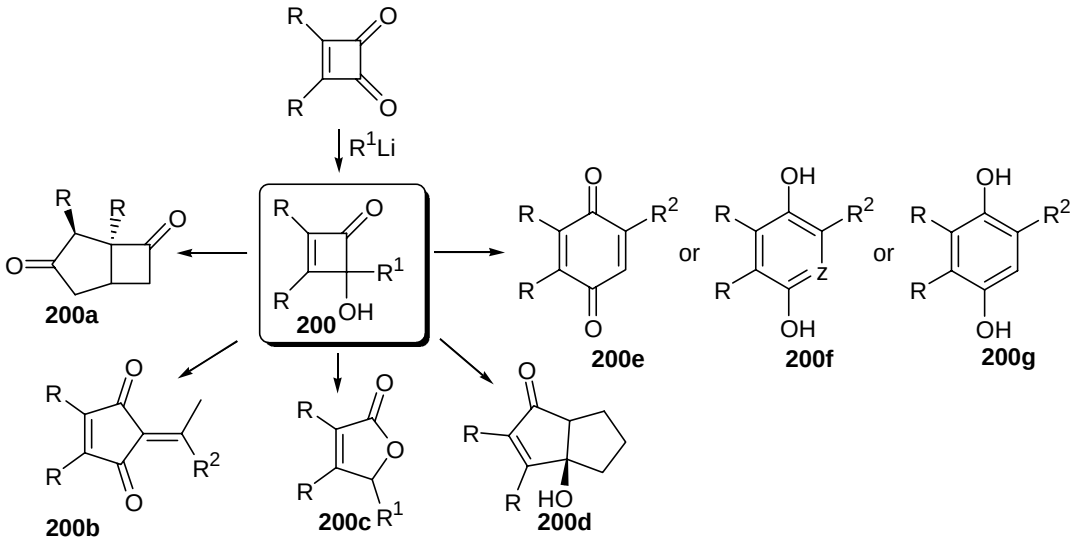
Table 16. Crystal data and structure refinement for the Compound 199b.

Empirical Formula	$C_{37}\ H_{31}\ N\ O_2$
Formula weight F_w	521.63
Temperature T (K)	293(2)
Wavelength λ (Å)	0.71073
Crystal system, Space group	Monoclinic, $P2_{(1)}/c$
Unit cell dimensions	
a (Å), α (°)	10.8742(16), 90
b (Å), β (°)	14.070(2), 109.072(7)
c (Å), γ (°)	19.660(3), 90
Volume V ($Å^3$)	2842.9(7)
Z	4
Calculated density ρ_{calcd} mg/M^3	1.219
Absorption coefficient μ (mm^{-1})	0.074
F (000)	1104
Crystal Size (mm)	0.42 x 0.36 x 0.21
θ for data collection range/deg	1.82 to 26.06
Limiting indices	-13<=h<=12, -17<=k<=16, -23<=l<=23
Reflections collected/unique	17460 / 5484 [R(int) = 0.0502]
Completeness to θ	26.06, 97.5 %
Max. and min. transmission	0.9845 and 0.9694
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5484 / 0 / 363
Goodness-of-fit on GOF (F^2)	1.066
Final R indices $R1$, $wR2$ $[I>2\sigma(I)]$	$R1$ = 0.0785 $wR2$ = 0.1450
R indices (all data) $R1$, $wR2$	$R1$ = 0.1396 $wR2$ = 0.1678
Largest diff. Peak and hole ($e \cdot Å^{-3}$)	0.212 and -0.146

of complex target molecules[162] and to achieve high enantio and diastereoselectivities.[163] Aldehydes are most generally used as the electrophiles in aldol reactions and relatively very few reports are available with ketones or diketones.[164]

Extensive studies over last 15 years, primarily by *Liebeskind, Moore and Paquette,* illustrated that the 4-subsituted-4-hydroxycyclobutenones **200**, are versatile C_4 synthons useful for the synthesis of highly functionalized carbocyclic compounds (**Scheme 118**).[59a,76g,165] The general strategy adopted for the synthesis of **200** involves addition of alkyllithium reagents to cyclobutenediones, which requires dry and inert conditions.

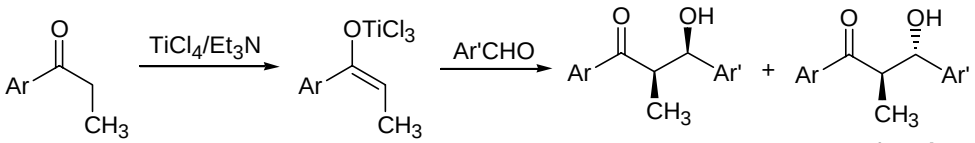
Scheme 118



Harrison *et al.*[163a] reported the first instances of stereoselective aldol reactions mediated by titanium enolates, generated directly by the reaction of carbonyl compounds using $TiCl_4$ and tertiary amine. It was reported that the reaction of propiophenone-derived titanium enolate **201** with aromatic aldehydes afforded the

corresponding *syn* aldol adducts **202a** with excellent selectivity and yields (**Scheme 119**).

Scheme 119



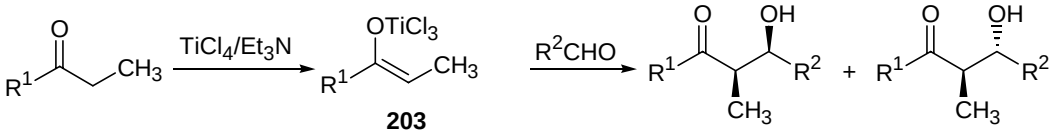
Ar = Ph, *o*-$MeOC_6H_4$, *p*-$NO_2C_6H_4$, *p*-MeC_6H_4, *p*-$MeOC_6H_4$

yields: 91-98%

202a:**202b** = 87:13 to 95:5

Aldol reactions involving directly generated thioester based titanium enolates **203** were reported to give aldol adducts **204** in moderate yields with moderate to good *syn*-selectivity (**Scheme 120**).[166]

Scheme 120



R^1 = PhS, ^{t}BuS, *o*-$MeOC_6H_4S$, C_6F_5S

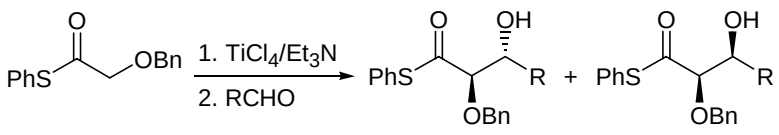
R^2 = ^{n}Pr, ^{i}Pr, Ph

yields 40-77%

syn:*anti* = 69:31 to 95:5

Titanium enolates of α-benzyloxythioester, generated using the $TiCl_4/Et_3N$ reagent system, were employed in the synthesis of *anti*-α-benzyloxy-β-hydroxy thioesters **205**. The products were obtained in excellent yields with high level of selectivity (**Scheme 121**).[167]

Scheme 121



R = Me, ^{n}Pr, ^{t}Bu, Ph

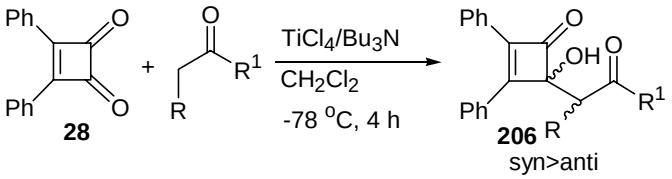
yields 81-99%

205a:**205b** = 97:3 to 98:2

Recent reports from this laboratory and elsewhere illustrate the versatile reactivity patterns of the $TiCl_4/R_3N$ reagent system for applications in organic synthesis.[163b,168-176] These reactions involve deprotonation of the organic substrates to yield the corresponding titanium species.

It was found in this laboratory that the Bu_3N is a superior base for the present transformation among various commonly used nitrogen bases in combination with $TiCl_4$. The use of other amine bases like Et_3N, *i*-Pr_2NEt and TMEDA for the aldol reaction of propiophenone with diphenylcyclobutenedione gave poor yields (**Scheme 122**).[127]

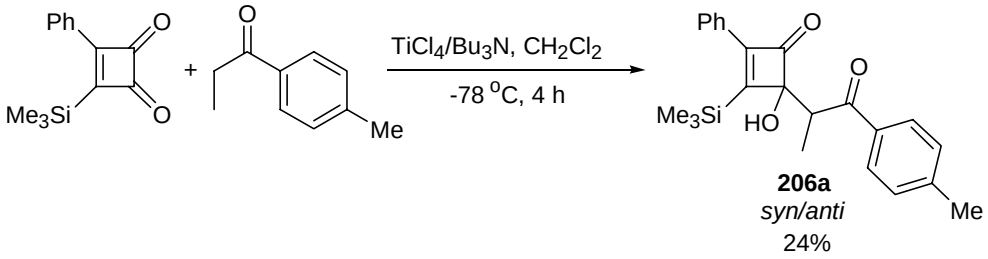
Scheme 122



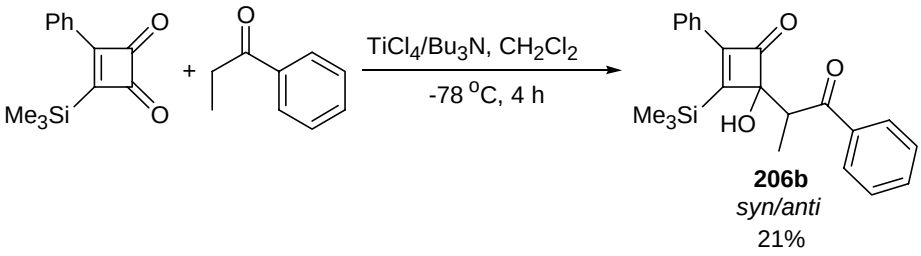
R_3N	yield
Et_3N	10%
i-Pr_2NEt	48%
TMEDA	10%
Bu_3N	94%

The reaction was also performed using acyclic and cyclic ketones and $TiCl_4/Bu_3N$ at –78 ºC, with various cyclobutenediones. Though, the reaction of these titanium enolates with cyclobutenedines gave a complex mixture of products, we are able to isolate the products in some cases in poor yields (**Schemes 123 and 124**).[127]

Scheme 123

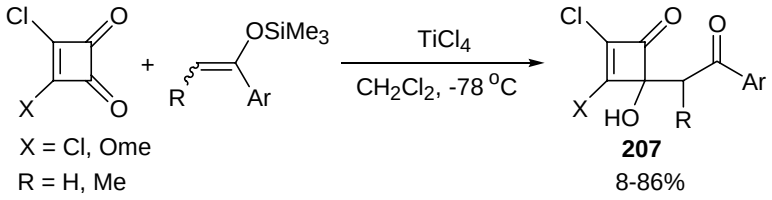


Scheme 124



Previously, derivatives of 4-hydroxycyclobutenones have been synthesized by titanium mediated addition of silylenol ethers to cyclobutenediones (**Scheme 125**).[177] However, the diastereomeric ratio and the relative stereochemistry of the products were not disclosed.

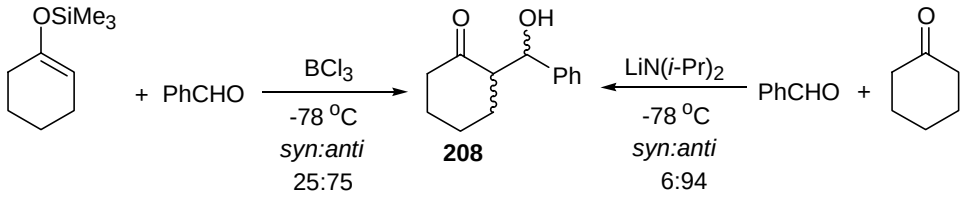
Scheme 125



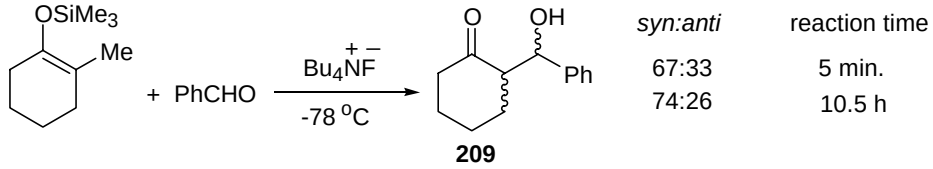
We have identified the relative stereochemistry of acyclic ketones at the newly formed chiral centers of the major product 4-hydroxy-4-alkyl-2-cyclobutenones **206** as *syn* using single crystal X-ray analysis.[127] The relative configuration of the major diastereomer of products were assigned as "*syn*". Whereas with cyclic ketones as "*anti*" by comparison of the spectral data.

Generally, cyclic ketones give *anti* aldols *via E*-enolates (**Scheme 126**).[178] However, in some cases *syn* aldol adducts were obtained as major products even with cyclic ketones (**Schemes 127 and 128**).[131,179]

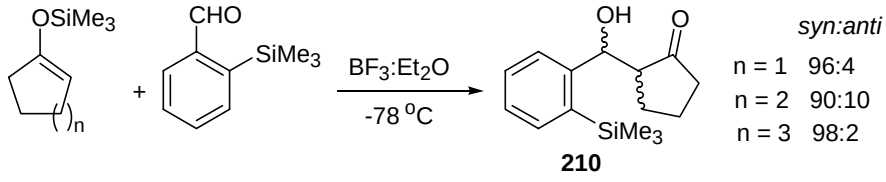
Scheme 126



Scheme 127



Scheme 128



Accordingly, it was of interest to examine the reaction of cyclobutenedione with cyclic ketones. We have carried out the reaction of ketones at –78 to 25 °C, with diphenylcyclobutenedione. However, only the corresponding condensed α, β-unsaturated products were isolated (**Scheme 129**). This transformation was found to be general and the results are summarized in Table 17. The structure was further characterized by single crystal X-ray analysis in the case of product **211c** (**Fig. 11**).

Scheme 129

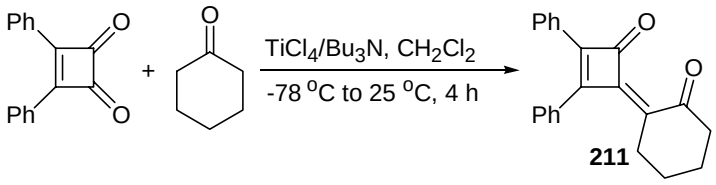
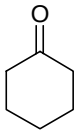
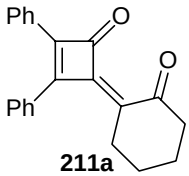
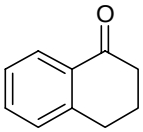
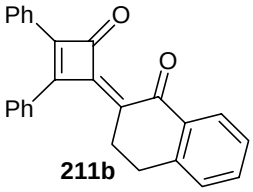
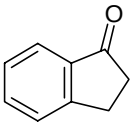
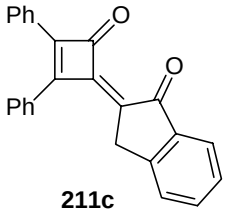
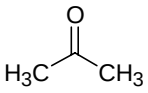
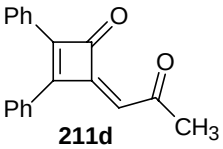
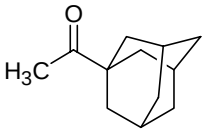
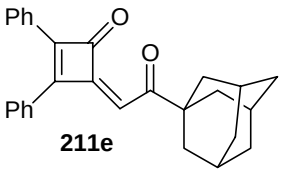


Table 17. $TiCl_4/Bu_3N$ promoted reaction of ketones with cyclobutenedione

S. No.	Ketone	Product[a]	Yield[b]
1		 **211a**	83
2		 **211b**	92
3		 **211c**	84
4		 **211d**	35
5		 **211e**	42

[a]Products were identified by IR, ^{1}H NMR, ^{13}C NMR, Mass Spectral data and CHN analysis.

[b]Yields are of the isolated products and based on the amount of cyclobutenedione used.

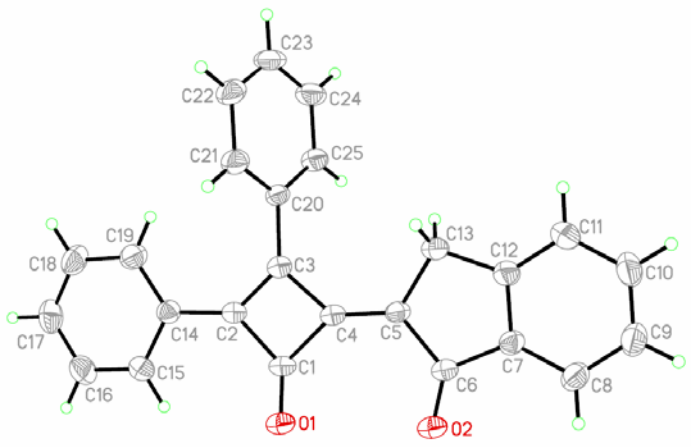
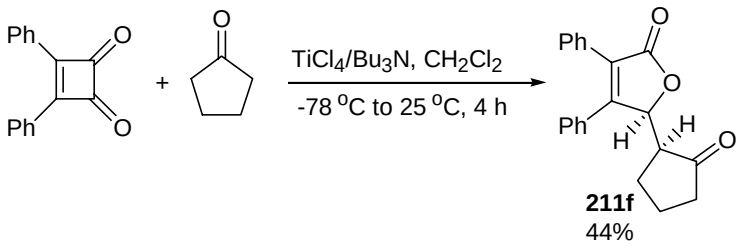


Fig. 11. ORTEP Diagram of Adduct 211c

In the case of cyclopentanone, interestingly, a 5-membered cyclic lactone was obtained in 44% yield (**Scheme 130**). This product was characterized by single crystal X-ray analysis (**Fig. 12**).

Scheme 130



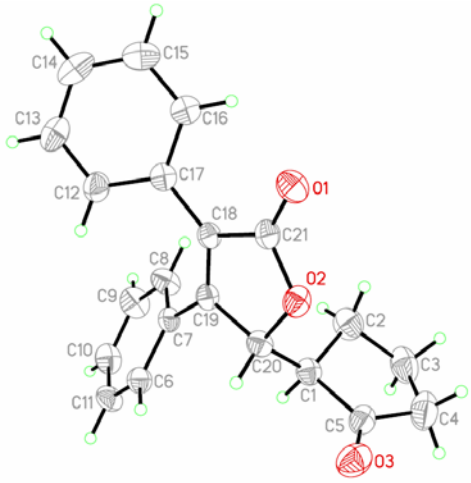


Fig. 12. ORTEP Diagram of Adduct 211f

Table 18. Crystal data and structure refinement for the Compound 211c.

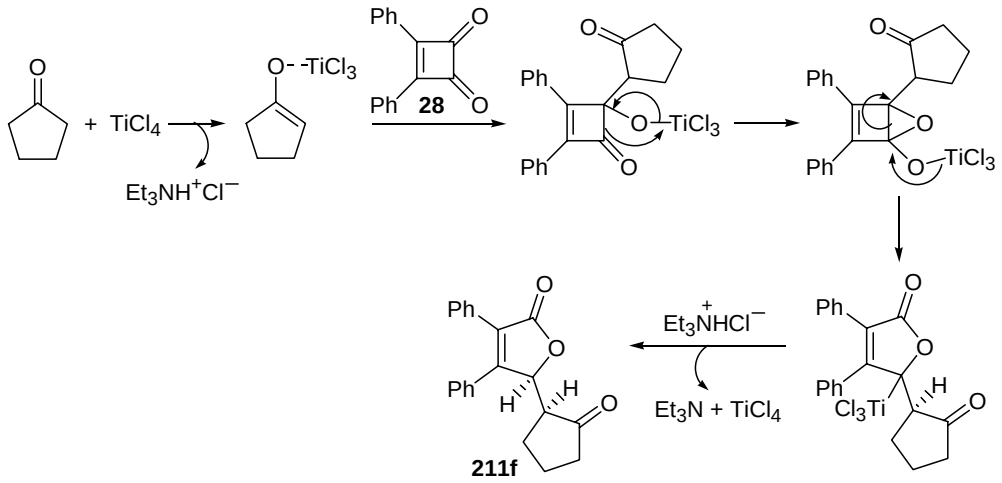
Empirical Formula	$C_{25}\ H_{16}\ O_2$
Formula weight F_w	348.38
Temperature T (K)	293(2)
Wavelength λ (Å)	0.71073
Crystal system, Space group	Monoclinic, $P2_1/c$
Unit cell dimensions	
a (Å), α (°)	14.322(3), 90
b (Å), β (°)	6.9271(12), 127.488(8)
c (Å), γ (°)	22.089(3), 90
Volume V (Å^3)	1738.9(5)
Z	4
Calculated density ρ_{calcd} mg/M^3	1.331
Absorption coefficient μ (mm^{-1})	0.083
F (000)	728
Crystal Size (mm)	0.44 x 0.39 x 0.28
θ for data collection range/deg	1.79 to 25.88
Limiting indices	-17<=h<=17, -8<=k<=8, -27<=l<=27
Reflections collected/unique	16999 / 3373 [R(int) = 0.0426]
Completeness to θ	25.88, 99.6 %
Max. and min. transmission	0.9770 and 0.9642
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3373 / 0 / 244
Goodness-of-fit on GOF (F^2)	1.125
Final R indices *R1*, *wR2 [I>2σ(I)]*	*R1* = 0.0722 *wR2* = 0.1550
R indices (all data) *R1*, *wR2*	*R1* = 0.1084 *wR2* = 0.1728
Largest diff. Peak and hole (e·Å^{-3})	0.336 and -0.147

Table 19. Crystal data and structure refinement for the Compound 211f.

Empirical Formula	$C_{21}\ H_{18}\ O_3$
Formula weight F_w	318.35
Temperature T (K)	273(2)
Wavelength λ (Å)	0.71073
Crystal system, Space group	Orthorhombic, $P2_12_12_1$
Unit cell dimensions	
a (Å), α (^{o})	9.2958(14), 90
b (Å), β (^{o})	9.4943(15), 90
c (Å), γ (^{o})	19.379(3), 90
Volume V (Å^3)	1710.3(4)
Z	4
Calculated density ρ_{calcd} mg/M^3	1.236
Absorption coefficient μ (mm^{-1})	0.082
F (000)	672
Crystal Size (mm)	0.5 x 0.4 x 0.3
θ for data collection range/deg	2.10 to 26.00
Limiting indices	-11<=h<=11, -11<=k<=8, -21<=l<=19
Reflections collected/unique	4472 / 2756 [R(int) = 0.0483]
Completeness to θ	26.00, 91.6 %
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2756 / 0 / 217
Goodness-of-fit on GOF (F^2)	1.003
Final R indices *R1*, *wR2 [I>2σ(I)]*	*R1* = 0.0611 *wR2* = 0.1036
R indices (all data) *R1*, *wR2*	*R1* = 0.1186 *wR2* = 0.1239
Largest diff. Peak and hole (e·Å^{-3})	0.153 and -0.117

The formation of lactone **211f** using cyclopentanone and $TiCl_4$ can be rationalized by a plausible mechanism considering a sequence of reactions as depicted in **Scheme 131**.

Scheme 131

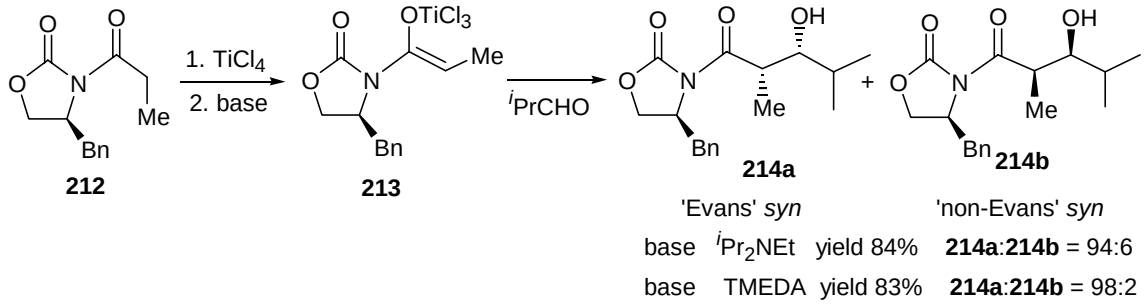


2.11 $TiCl_4/Bu_3N$ Promoted Reaction of Acylthio and Acyloxazolidinones with Diphenylcyclobutenedione

Evans and several other research groups studied the asymmetric aldol processes by utilizing the reactions of several oxazolidinone-, oxazolidinethione-, oxazolidineselone-, thiazolidinethione-derived titanium enolates (generated directly by treating the respective carbonyl compound with chlorotitanium reagents and tertiary amines) with different aldehydes.[180] The selectivities realized in these reactions depend on the substrates, reagents and reaction conditions. Accordingly, we have undertaken efforts to examine the use of *N*-acyl-oxazolidinethione **221** or *N*-acyl-thiazolidinethione **222** as chiral auxiliaries in the Aldol reactions with cyclobutenediones.

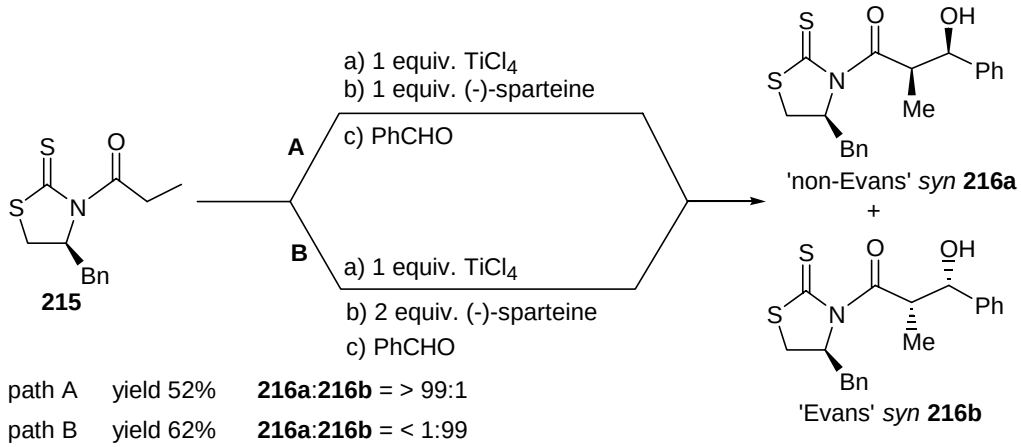
Evans et al.[180] reported the addition of enantiomerically pure oxazolidinone **212**-derived titanium enolate **213** to isobutyraldehyde for obtaining the corresponding 'Evans' *syn* aldol product **214a** in good yield with excellent selectivity (**Scheme 132**).

Scheme 132



It was also found that the amount of base has tremendous effect in the titanium-mediated aldol reaction of *N*-propanoylthiazolidinethione **215** with benzaldehyde. For example, use of 1 equiv. of (-)-sparteine afforded 'non-Evans' *syn* aldol product **216a**, whereas 2 equiv. of (-)-sparteine delivered 'Evans' *syn* aldol product **216b** (**Scheme 133**).[181]

Scheme 133

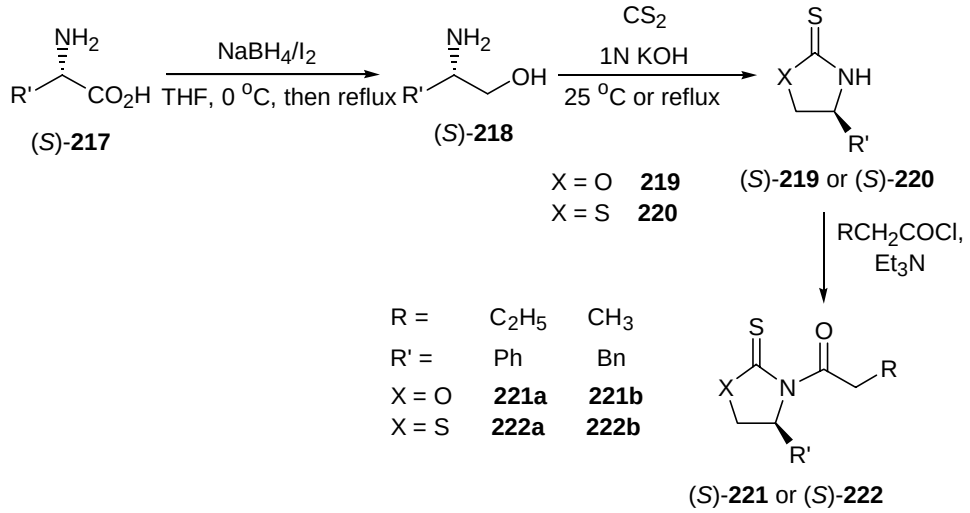


We have prepared the corresponding chiral auxiliaries starting from (*S*)-phenylalanine following reported procedures.[182,183] (*S*)-Phenylalanine **217** was reduced

to give (*S*)-phenylalaninol **218** using the $NaBH_4/I_2$ reagent system.[184] The amino alcohol (*S*)-**218** was then reacted with CS_2 in 1N KOH to obtain the corresponding 5-membered cyclic product. It was found that the oxazolidinethione (*S*)-**219** was formed at room temperature and under reflux condition the thiazolidinethione (*S*)-**220** was obtained (**Scheme 134**).[183]

The chiral heterocycles (*S*)-**219** or (*S*)-**220** were reacted with acid chlorides (*n*-butyryl chloride or acetyl chloride) in the presence of Et_3N to obtain the corresponding *N*-acyloxazolidinethiones (*S*)-**221** or *N*-acylthiazolidinethiones (*S*)-**222** (**Scheme 134**).[184]

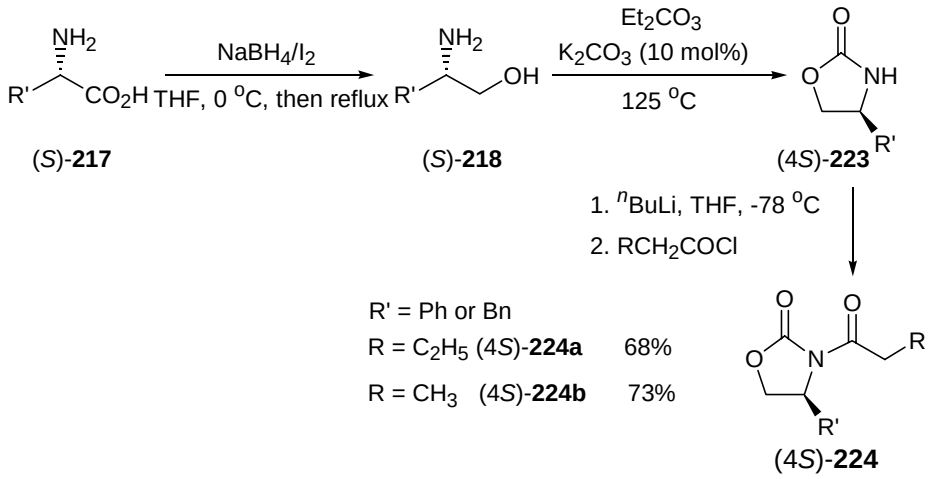
Scheme 134



Similarly, *N*-acyl-oxazolidinones **224** were prepared by following the literature procedures. (*S*)-Phenylalanine **217** was reduced to give (*S*)-phenylalaninol **218** using the $NaBH_4/I_2$ reagent system.[182] The reaction of (*S*)-phenylalaninol **218** with diethyl carbonate in the presence of catalytic amount of K_2CO_3 resulted in the formation of the corresponding oxazolidinone (4*S*)-**223** in good yields.[185a] The product (4*S*)-**223** was

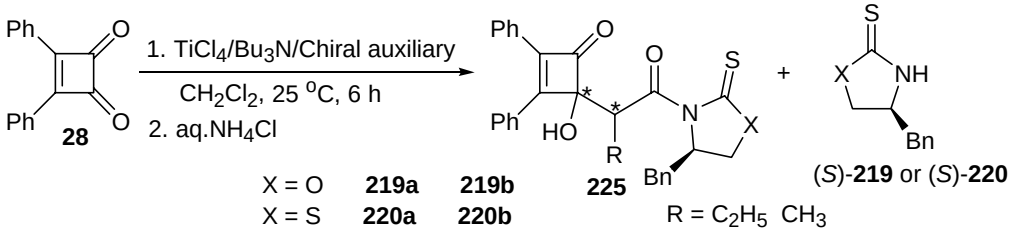
reacted with acid chlorides in the presence of *n*-butyllithium to obtain the corresponding *N*-acyl-oxazolidinones (4*S*)-**224a** or (4*S*)-**224b**, respectively (**Scheme 135**).[185b]

Scheme 135



The Aldol reactions of (*S*)-**221** or (*S*)-**222** with cyclobutenediones were run using $TiCl_4/Bu_3N$ or $TiCl_4/Et_3N$ reagent systems (**Scheme 136**). Unfortunately, the reactions were not clean. The corresponding *N*-acyloxazolidinethiones (*S*)-**221** or *N*-acylthiazolidinethiones (*S*)-**222** gave deacylation to oxazolidinethiones (*S*)-**219** or thiazolidinethiones(*S*)-**220**.

Scheme 136



Accordingly, we have examined the reaction of *N*-acyl-oxazolidinethiones (*S*)-**221**, *N*-acyl-thiazolidinethiones (*S*)-**222** and *N*-acyl-oxazolidinones (4*S*)-**224** with diphenylcyclobutenedione **28** at –78 °C, to obtain the corresponding 4-hydroxy-cyclobutenedione products in moderate yields (**Scheme 137**). The results are

summarized in Table 20. The diasteriomeric ratios are only approximate values as they are estimated only by ^{13}C-NMR data. Also, the configuration of the new asymmetric centers could not be assigned from the available data.

Scheme 137

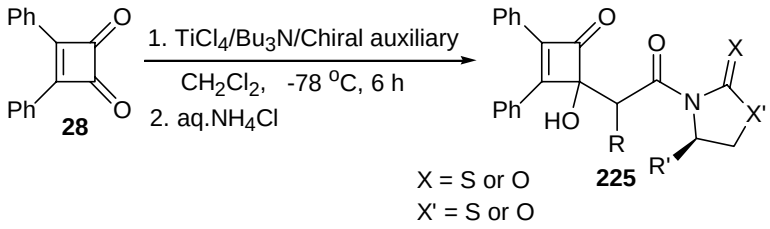
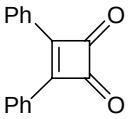
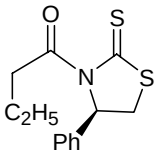
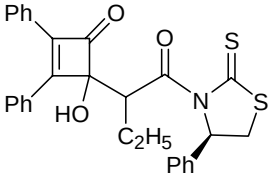
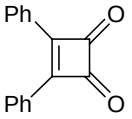
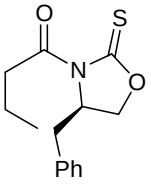
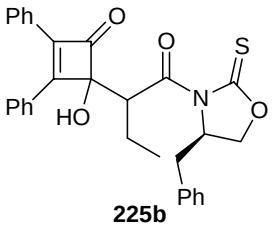
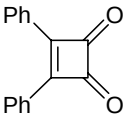
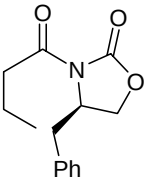
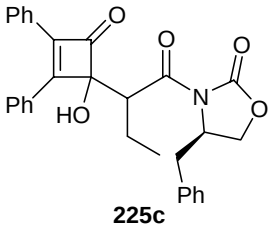


Table 20. $TiCl_4/Bu_3N$ promoted reaction of chiral auxiliaries with cyclobutenedione

S. No.	Dione	Chiral auxiliary	Product[a]	Yield (%)[b]	dr[c]
1			 **225a**	68	93:7
2			 **225b**	56	100:0
3			 **225c**	55	95:5

[a]Products were identified by IR, ^{1}H NMR, ^{13}C NMR, Mass Spectral data and CHN analysis.

[b]Yields are of the isolated products and based on the amount of cyclobutenedione used.

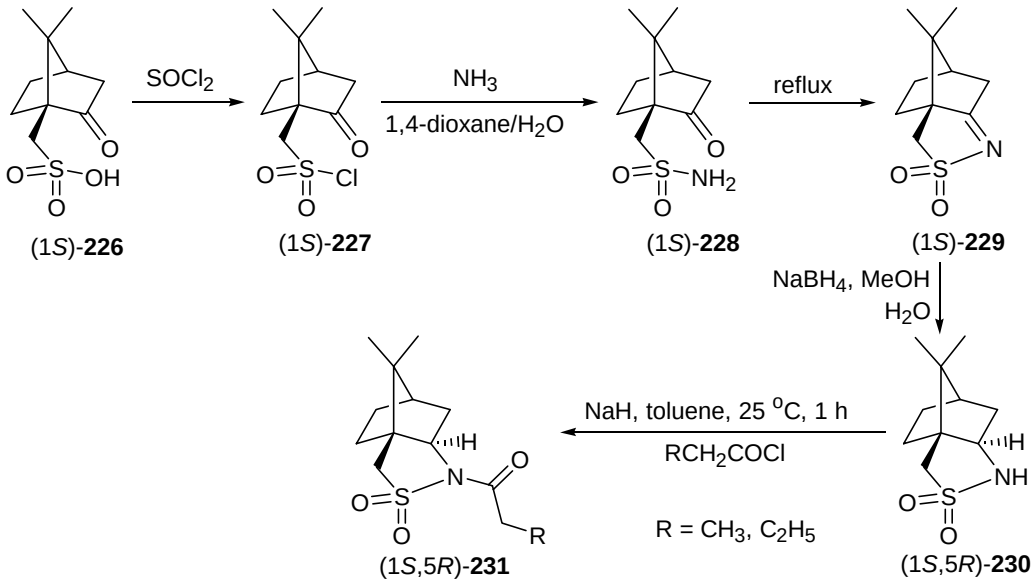
[c]Diasteriomeric ratios were determined by ^{13}C NMR spectral data.

2.12 $TiCl_4/Bu_3N$ Promoted Reaction of Acylcamphorsultam with diphenylcyclobutenedione

The Oppolzer camphorsultam **230** is a versatile chiral auxiliary that is known to mediate several diastereoselective C-C bond forming reactions.[186] We became interested to carry out investigations on the asymmetric additions of camphorsultam-derived enolates using cyclobutenediones.

Accordingly, we have prepared the *N*-acyl-camphorsultam **231** by following the literature reports.[187,188] The synthetic protocol followed for the preparation of *N*-acylcamphorsultam (1*S*,5*R*)-6 is given in Scheme 138.

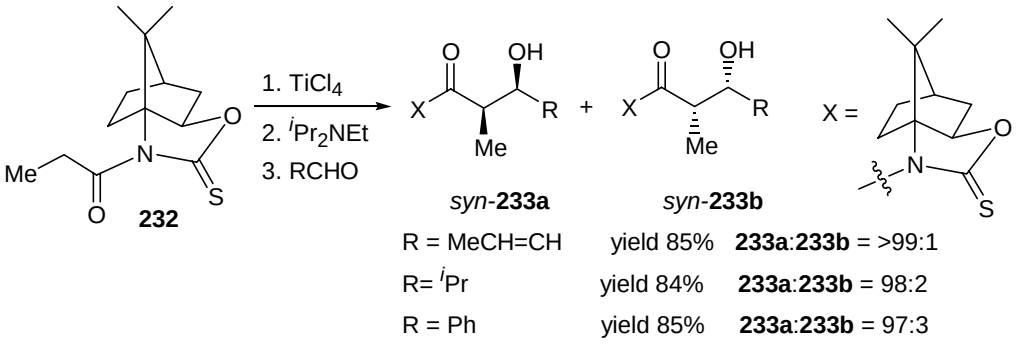
Scheme 138



Yan and coworkers[163e,189] developed titanium enolate mediated aldol reaction as an extension of their boron enolate methodology. Good yields and *syn* diastereoselectivity were reported using the camphor-derived *N*-acyloxazolidinethione **232** (**Scheme 139**). The high selectivities were attributed to additional chelation afforded by the thiocarbonyl of the chiral auxiliary. The reactions with the

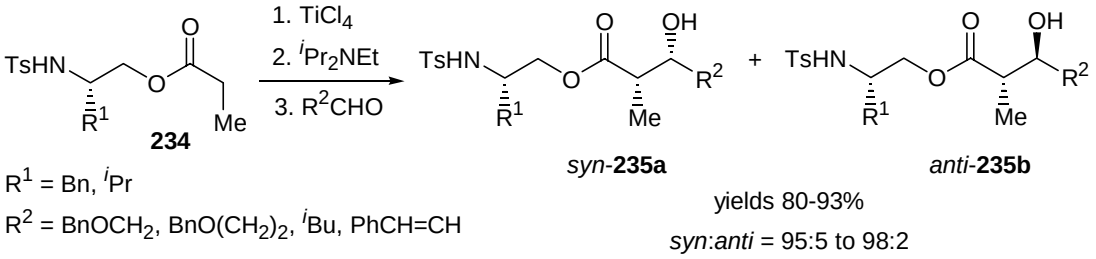
corresponding *N*-bromoacyl derivatives also provided the products in excellent isolated yields and stereoselectivity.[189b,c]

Scheme 139



Excellent *syn* selectivity was realized in the titanium enolate-mediated asymmetric aldol reactions by utilizing the chiral auxiliaries **234** derived from enantiomerically pure 1,2-amino alcohols (**Scheme 140**).[190]

Scheme 140



We have carried out the reaction of titanium enolates, generated *in situ* using *N*-acyl-camphorsultam and $TiCl_4/Bu_3N$ at –78 °C, with diphenylcyclobutenedione **28**, and found that the corresponding 4-hydroxy-4-acyl-camphorsultam-2-cyclobutenones are formed in moderate yields (**Scheme 141**).

Scheme 141

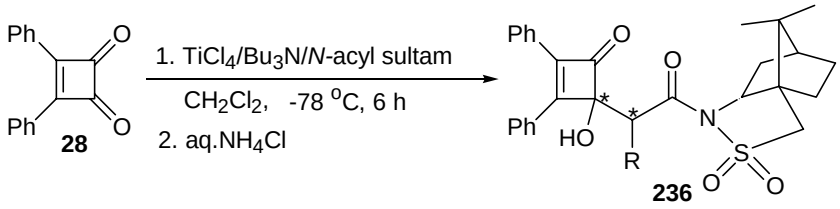
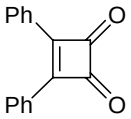
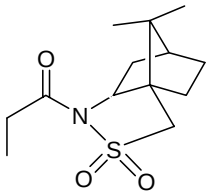
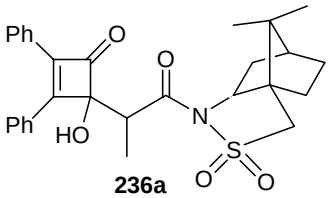
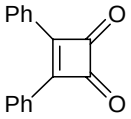
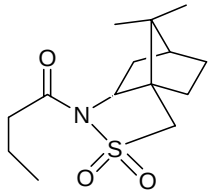
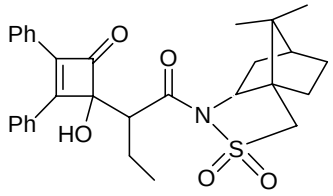


Table 21. $TiCl_4/Bu_3N$ promoted reaction of *N*-acyl sultam with cyclobutenedione

S. No.	Dione	*N*-acyl sultam	Product[a]	Yield (%)[b]	dr[c]
1			 **236a**	68	96:4
2			 **236b**	65	97:3

[a]Products were identified by IR, ^{1}H NMR, ^{13}C NMR, Mass Spectral data and CHN analysis.

[b]Yields are of the isolated products and based on the amount of cyclobutenedione used.

[c]Diasteriomeric ratios were determined by ^{13}C NMR spectral data.

The diasterioeric ratios given in the Table 21 are only approximate values as they are estimated only by ^{13}C-NMR data. The configuration of the new asymmetric centers in compounds **236** could not be assigned from the available data.

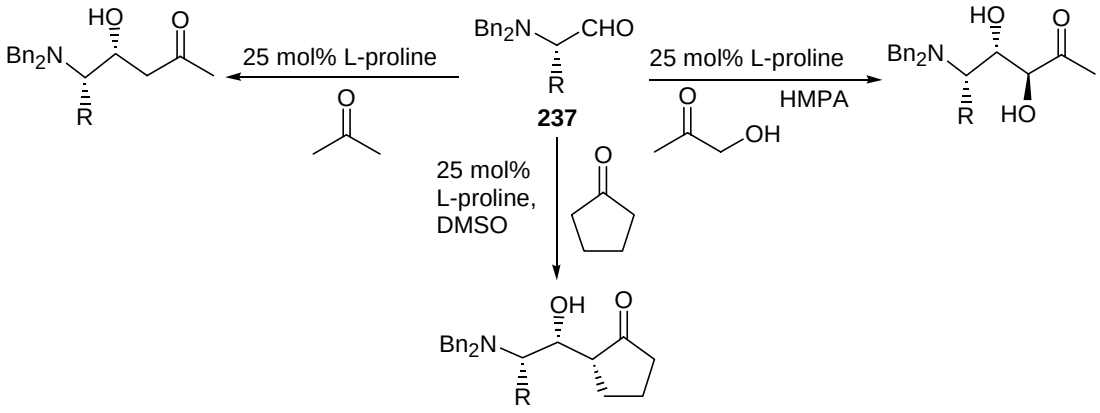
Though, the chemical yields are moderate, the results may be helpful in screening for the asymmetric chiral auxiliary-derived enones using organotitanium reagents.

2.13 Proline Catalyzed Reaction of Acetone with Cyclobutenediones

The development of new asymmetric C-C formation reactions is one of the most important problems of contemporary chemistry. Among recent achievements, proline-catalyzed direct enantioselective aldol reaction between aldehydes and ketones is more attractive because of its operational simplicity and cheaper catalytic system. However, the scope of this catalytic reaction is still narrow and more substrates, especially functionalized aldehydes and ketones, need to be explored in order to expand its application in the synthesis of highly functionalized useful molecules.

L-Proline-catalyzed direct aldol reaction of L-amino acid-derived *N,N*-dibenzyl aldehydes **237** with acetone, cyclopentanone, or hydroxyacetone provides *γ*-amino-*β*-hydroxy- or *γ*-amino-*α,β*-dihydroxy-ketones with moderate to excellent yields and diasterioselectivities (**Scheme 142**).[191]

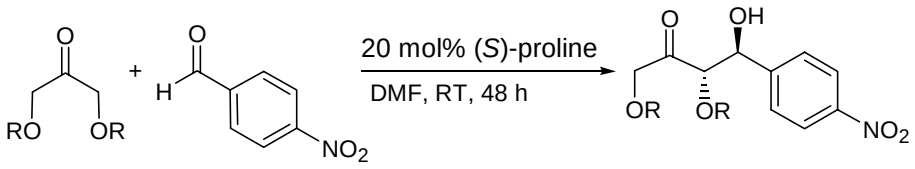
Scheme 142



A practical and environmentally friendly organocatalytic strategy to mimic the DHAP (dihydroxy acetone phosphate) aldolases has been developed and shown to be effective in the preparation of carbohydrates and aminosugars. (*S*)-Proline and (*S*)-2-pyrrolidine-tetraole catalyzed the aldol reaction between dihydroxy acetone variants

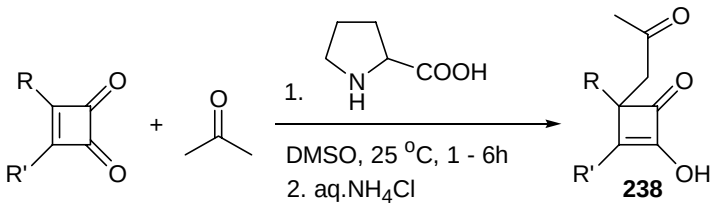
such as 1,3-dioxan-5-one and 2,2-dimethyl-1,3-dioxan-5-one to give the corresponding polyols in good yields (**Scheme 143**).[192]

Scheme 143



We have examined the organocatalyzed reaction with cyclobutenediones. The reaction was carried out at 25 ^{o}C using L-proline in the presence of acetone. The corresponding 1,4-addition products **238** were obtained in good yields (**Scheme 144**). Compound **238a** was further characterized by single crystal X-ray analysis (**Fig. 13**). However, the product obtained was found to be racemic.

Scheme 144



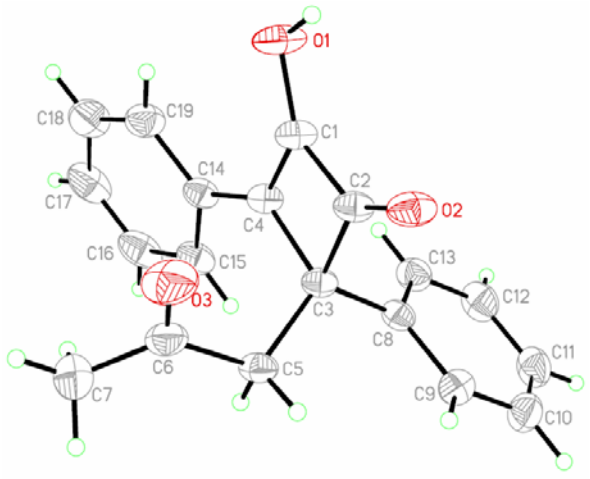


Figure 13. ORTEP Diagram of the product 238a

A plausible reaction mechanism can be rationalized through the formation of enamine with acetone and proline followed by 1,4-addition to the cyclobutenedione as depicted in **Scheme 145**.

Scheme 145

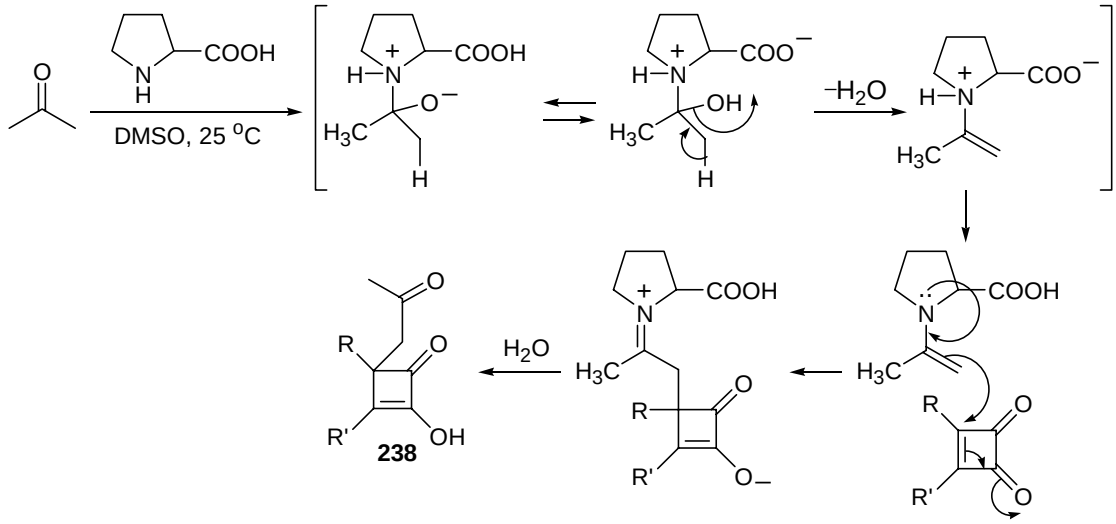
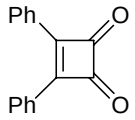
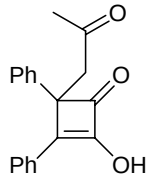
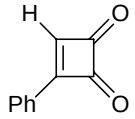
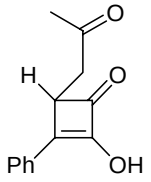
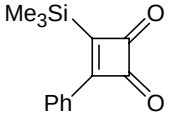
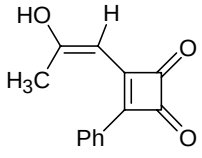


Table 22. Proline catalyzed reaction of acetone with cyclobutenediones

S. No.	Dione	Ketone	Product[a]	Yield (%)[b]
1			 **238a**	76
2			 **238b**	52
3			 **238c**	65

[a]Products were identified by IR, ^{1}H NMR, ^{13}C NMR, Mass Spectral data and CHN analysis.

[b]Yields are of the isolated products and based on the amount of cyclobutenedione used.

Table 23. Crystal data and structure refinement for the Compound 238a.

Empirical Formula	$C_{19}\ H_{16}\ O_3$
Formula weight F_w	292.32
Temperature T (K)	273(2)
Wavelength λ (Å)	0.71073
Crystal system, Space group	Monoclinic, $P2_1/c$
Unit cell dimensions	
a (Å), α (°)	10.932(4), 90
b (Å), β (°)	8.455(3), 104.283(6)
c (Å), γ (°)	18.084(6), 90
Volume V (Å^3)	1619.7(10)
Z	4
Calculated density ρ_{calcd} mg/M^3	1.199
Absorption coefficient μ (mm^{-1})	0.081
F (000)	616
Crystal Size (mm)	0.42 x 0.36 x 0.28
θ for data collection range/deg	1.99 to 28.38
Limiting indices	-13<=h<=14, -11<=k<=11, -23<=l<=23
Reflections collected/unique	17941 / 3874 [R(int) = 0.0281]
Completeness to θ	28.38, 95.3 %
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3874 / 0 / 201
Goodness-of-fit on GOF (F^2)	1.028
Final R indices *R1*, *wR2 [I>2σ(I)]*	*R1* = 0.0548 *wR2* = 0.1401
R indices (all data) *R1*, *wR2*	*R1* = 0.0713 *wR2* = 0.1523
Largest diff. Peak and hole (e·Å^{-3})	0.268 and -0.222

We have also examined the reaction using some other ketones (ethyl methyl ketone, diethyl ketone, isopropyl methyl ketone, cyclohexanone and cyclopentanone) but these efforts were not successful. Use of more reactive aldehyde substrates may give more fruitful results.

Conclusions

The arylamine/$TiCl_4$ reagent system react with diphenylcyclobutenedione to provide the corresponding butenolides and 1,4-diketones. Whereas, the reaction of arylamine/$SnCl_4$ reagent system with diphenylcyclobutenedione gives a novel ring opening product 1,4-bis(4-dimethylaminophenyl)-3,4-diphenyl-3-butene-1,2-dione. Though, the differences in reactions in these cases are not clearly understood, the methods have good potential for further synthetic exploitation, since the products are important class of organic synthons.

Studies were carried out to examine the reactivity of organotitanium reagents prepared *in situ* with cyclobutenediones. Reaction of alkynyltitanium reagents prepared *in situ* using Grignard reagents with diphenylcyclobutenedione gave the corresponding 4,5-diphenyl-1,7-octadiyne-3,6-dione. Whereas, the alkyltitanium reagents prepared in a similar way provides the corresponding 1,4-diketones. We have also prepared 4-6 and 4-8 bicyclic diols using substituted cyclobutenediones. A novel one-pot synthesis of 1,2,3,4,5-pentasubstituted pyrroles were developed using 1,2,3,4-tetrasubstituted-1,4-diones and the $TiCl_4/Et_3N$ reagent system.

An efficient $TiCl_4/Bu_3N$ mediated diasterioselective cross aldol reaction between ketones and cyclobutenediones was accomplished to obtain the corresponding 4-hydroxy-4-substituted-2-cyclobutenone derivatives that are versatile C_4 synthons for the synthesis of a variety of carbo and heterocycles. The present method has advantage over the reported methods for synthesis of similar compounds using silylenol ethers as this facilitates the direct addition of ketones to cyclobutenediones.

The chiral auxiliary mediated C-C bond forming reactions using thiazolidenones, oxazolidenones and camphorsultam involving diphenylcyclobutene-diones were also examined. L-Proline mediated organocatalysis reactions using acetone provided novel 1,4-addition products. The results reported here have considerable potential for further synthetic exploitations.

3. Experimental Section

3.1 General Information

Melting points reported in this thesis are uncorrected and were determined using a Superfit and Buchi-510 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 spectrometers, respectively with chloroform-D and dimethylsulfoxide-D as solvents and TMS as reference (δ = 0 *ppm*). Liquid Chromatography (LC) and mass analysis (LC-MS) were performed on SHIMADZU-LCMS-2010A. Mass spectral analyses for some of the compounds were carried out on VG 7070H mass spectrometer using EI technique at 70 eV. Elemental analyses were carried out using a Perkin-Elmer elemental analyzer model-240C and Thermo Finnigan analyzer series Flash EA 1112. Analytical Column chromatography was carried out using acme's silica gel (100-200 mesh). Thin layer chromatographic tests were carried out on glass plates (3 x 10 cm) coated with 250 mμ acme's silica gel-G and GF_{254} containing 13% calcium sulfate as binder. The spots were visualized by short exposure to iodine vapor or UV light.

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 to the atmosphere. All dry solvents and reagents (liquids) used were distilled from appropriate drying agents just before use. 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 isolated yields of material judged homogeneous by TLC, IR and NMR spectroscopy.

Iron pentacarbonyl supplied by Fluka, Switzerland and Aldrich, USA was used. $NaBH_4$ supplied by Aldrich, USA was used. THF supplied by E-Merck, India was distilled over sodium benzophenone ketyl system. Titanium tetrachloride was supplied by E-Merck, India. Triethylamine, tributylamine, *N,N*-diethylaniline and *N,N*-dimethylaniline supplied by Spectrochem Ltd., India, were distilled and stored over KOH. Dichloromethane was distilled over CaH_2 and dried over molecular sieves. $Fe_3(CO)_{12}$ was prepared following a reported procedure starting from $Fe(CO)_5$.[193] Alkynes except 1-heptyne, used in the reaction were prepared following a reported procedure.[194] 1-Heptyne was supplied by Fluka, Switzerland. Mg metal turnings supplied by Ranbaxy fine chemicals limited, India. Bromobenzene, *p*-anisylbromide, *n*-ethylbromide, *n*-butylbromide, *n*-hexylbromide, 1,2-dibromoethane 1,3-dibromopropane, 1,4-dibromobutane, 1,6-dibromohexane were supplied by Loba

Chemie (P) Ltd., India. Acetone, acetophenone, *p*-methylacetophenone, propeophenone, diethylketone, isopropylethylketone, cyclopentanone, cyclohexanone, tetralone and indanone were supplied by Loba Chemie (P) Ltd., India. (*S*)-Phenylalanine, (*S*)-valine and (*1S*)-camphorsulfonic acid were purchased from Lancaster Synthesis Ltd., UK. Diethyl carbonate, carbon disulfide, ^{n}butyllithium (1.6 M in hexane) and sodium hydride (60% dispersion in mineral oil) were obtained from E-Merck, India. Methanoyl chloride, ethanoyl chloride and propenoyl chloride supplied by E-Merck, India. DL-proline, D-proline and L-proline were purchased from Lancaster Synthesis Ltd., UK.

Optical rotations were measured on Rudolph Research Analytical AUTOPOL-II (readability $\pm 0.01^{o}$) and AUTOPOL-IV (readability $\pm 0.001^{o}$) automatic polarimeters. 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.

The X-ray diffraction measurements for the respective compounds were carried out on an automated Enraf-Nonius MACH 3 difractometer using graphite monochromated, Mo-Kα (λ = 0.71073 Å) 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 and the data was corrected for absorption

effects using the multiscan technique (SADABS). The data were reduced using XTAL 3.4 (or) SAINT program,[195] without applying absorption correction. The refinement for structure was made by full-matrix least squares on F^2 (SHELX 97 or SHELXTL).[196]

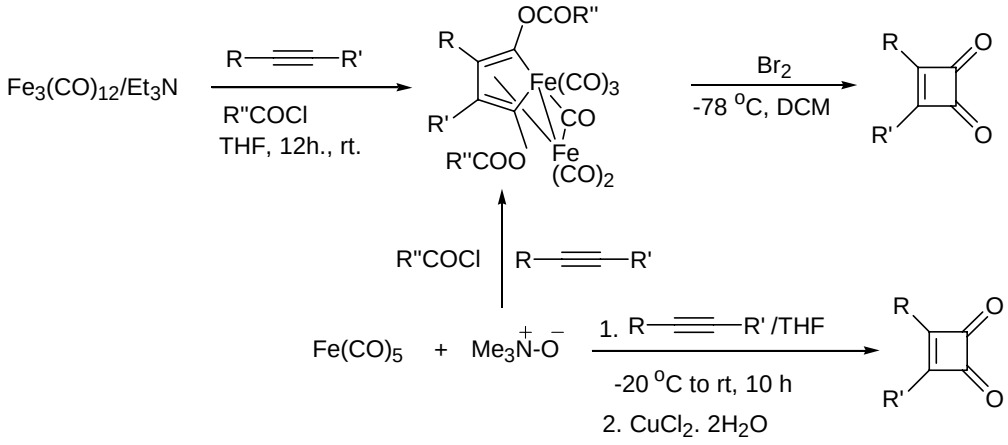
3.2 Preparation of $Fe_3(CO)_{12}$

A reported procedure involving MnO_2 oxidation of $NaHFe(CO)_4$ was followed.[133] The $Fe(CO)_5$ (30 g, 0.015 mol) and methanol (85 mL) were placed in a three necked 1 lit. flask fitted with a stirrer, nitrogen inlet and a refluxing condenser. The reaction mixture was treated with a solution of NaOH (22.5 g) in H_2O (45 mL). The mixture was stirred for 30 min. and then treated with saturated NH_4Cl solution (70 mL) to obtain $NaHFe(CO)_4$ in solution.

Meanwhile the MnO_2 was prepared by cautiously adding $KmnO_4$ (32.3 g) in water (150 mL) with of 95% ethanol (50 mL) under stirring in a large beaker covered with a watch glass. Stirring was continued further to get a brown precipitate of MnO_2. The suspension of MnO_2 thus obtained was added to the $HFe(CO)_4^-/NH_4Cl$ solution. The reaction mixture was stirred for 2-3 h. The excess MnO_2 was then decomposed by gradual addition of a solution of $FeSO_4.7H_2O$ (20 g) dissolved in dil. H_2SO_4 (~2N, 125 mL). The mixture was then treated with 1:1 H_2SO_4: H_2O (150 mL). The black precipitate of $Fe_3(CO)_{12}$ was then filtered and washed successively with hot dil. H_2SO_4 (~2N, 200 mL), 95% ethanol (100 mL) and pentane (75 mL) and dried under pressure. Yield 18 g (70%).

3.3 General Procedure for the Preparation of Cyclobutenediones

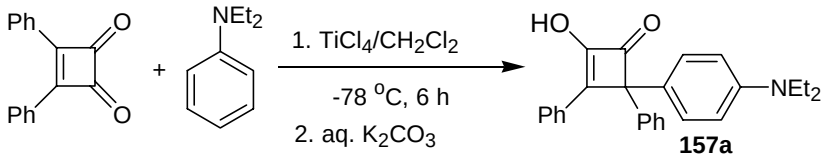
To a solution of anhydrous Me_3NO (0.9 g, 12 mmol) in THF (30 mL) was drop wise added $Fe(CO)_5$ (294 g, 15 mmol) in THF over a period of 30 minutes at –20 ^oC under dry nitrogen. The reaction starts with immediate evolution of CO_2 and the colour of the reaction mixture changes from yellow to dark brown. The reaction mixture was stirred for another 1 h and the contents were slowly brought to room temperature. Diphenylacetylene (0.44 g, 2.5 mmol) was added and the contents were further stirred for 10 h 20 ^oC. The metal carbonyl complexes were oxidized using $CuCl_2.2H_2O$ (4.2 g, 25mol) in acetone (15 mL). Saturated NaCl solution (50 mL) was added and the contents were extracted with ether (2X75 mL) dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was subjected to column chromatography (silica gel, hexane-EtOAc). Ethyl acetate (1.5%) in hexane eluted the cyclobutenedione.[17,18]



3.4 Reaction of Diphenylcyclobutenedione with $TiCl_4$/*N,N*-dialkylaniline at -78 ^oC

To a mixture of 3,4-diphenyl-3-cyclobutene-1,2-dione (0.234 g, 1 mmol) and *N,N*-diethylaniline (0.37 g, 2.5 mmol) in CH_2Cl_2 (20 mL), $TiCl_4$ (0.13 mL of 1:1 solution of $TiCl_4/CH_2Cl_2$, 1.2 mmol) in CH_2Cl_2 (5 mL) was added drop-wise at –78 ºC under N_2

atmosphere. The contents were stirred for 6 h at the same temperature, quenched with 5 mL of saturated K_2CO_3 solution and extracted with CH_2Cl_2 (2X50 mL). The combined organic extract was washed with brine solution and dried over anhydrous Na_2SO_4. The solvent was removed and the residue was chromatographed on a silica gel column. The product was eluted using hexane/ethyl acetate 96:4.



157a

Yield : 48% (0.18 g)

IR (neat) : $\tilde{\nu}$ = 3439, 3061, 2930, 1747, 1606 cm^{-1}

^{1}H NMR : (200 MHz, $CDCl_3$) δ = 7.44-7.31 (m, 10H), 6.86-6.79 (m, 4H), 3.52-3.45 (q, 4H), 2.45 (s, 1H), 1.33 (t, J = 7.4 Hz, 6H) *ppm* **(Spectrum No. 1)**

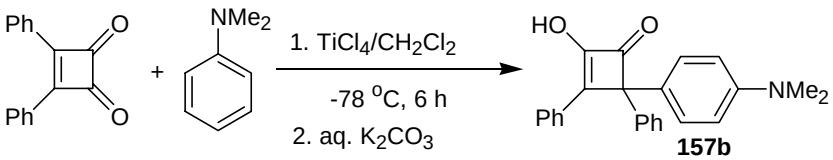
^{13}C NMR : (50 MHz, $CDCl_3$) δ = 185.8, 147.0, 139.8, 139.3, 134.3, 131.4, 130.6, 130.1, 129.5, 129.0, 128.9, 128.6, 128.4, 111.7, 70.7, 44.4, 12.6 *ppm* **(Spectrum No. 2)**

Analysis : for $C_{26}H_{25}NO_2$

Calculated: C, 81.43%; H, 6.57%; N, 3.65%; O, 8.34%

Found: C, 81.38%; H, 6.48%; N, 3.58%

GCMS : *m/z* = 383



157b

Yield : 45% (0.16 g)

IR (neat) : $\tilde{\nu}$ = 3393, 3055, 2926, 1749, 1610 cm^{-1}

^{1}H NMR : (400 MHz, $CDCl_3$) δ = 7.79-7.19 (m, 10H), 6.73-6.64 (m, 4H), 2.98 (s, 6H), 2.66 (s, 1H) *ppm*

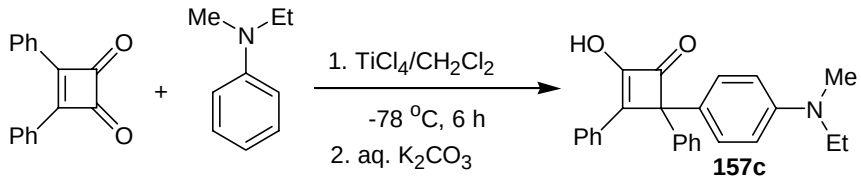
^{13}C NMR : (100 MHz, $CDCl_3$) δ = 185.4, 147.1, 140.6, 139.7, 133.9, 131.6, 130.4, 129.7, 129.1, 128.9, 128.7, 128.6, 128.3, 112.2, 76.7, 40.7, 40.6 *ppm*

Analysis : for $C_{24}H_{21}NO_2$

Calculated: C, 81.10%; H, 5.96%; N, 3.94%; O, 9.00%

Found: 81.06%; H, 5.89%; N, 3.98%

GCMS : *m/z* = 355



157c

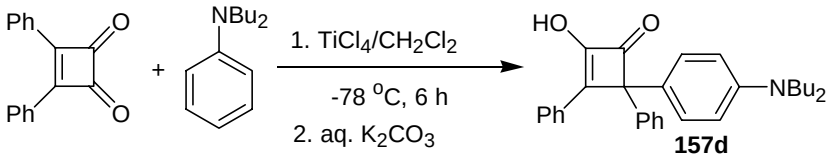
Yield : 38% (0.14 g)

IR (neat) : $\tilde{\nu}$ = 3433, 2922, 1743, 1610 cm^{-1}

^{1}H NMR : (400 MHz, $CDCl_3$) δ = 7.56-7.29 (m, 10H), 6.95-6.42 (m, 4H), 4.10 (q, *J* = 7.0 Hz, 2H), 2.99 (s, 3H), 2.15 (s, 1H), 1.25 (t, *J* = 6.8 Hz, 3H) *ppm*

^{13}C NMR : (100 MHz, $CDCl_3$) δ = 185.7, 147.3, 140.5, 139.2, 138.8, 132.4, 130.4, 129.8, 129.6, 128.7, 128.6, 128.4, 128.2, 111.7, 78.7, 43.3, 36.7, 14.2 *ppm*

GCMS : *m/z* = 369



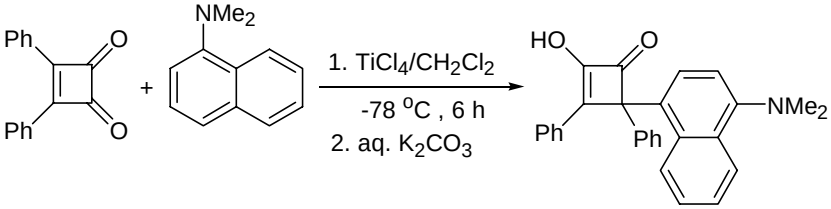
157d

Yield **:** 32% (0.14 g)

IR (neat) **:** $\tilde{\nu}$ = 3435, 3057, 2926, 1749, 1608 cm^{-1}

^{1}H NMR **:** (400 MHz, $CDCl_3$) δ = 8.12-6.96 (m, 10H), 6.60-6.52 (m, 4H), 3.36 (t, *J* = 7.2 Hz, 4H), 2.95 (s, 1H), 1.37-1.25 (m, 8H), 0.98 (t, *J* = 6.9 Hz, 6H) *ppm*

^{13}C NMR **:** (100 MHz, $CDCl_3$) δ = 185.9, 147.9, 140.8, 139.0, 134.9, 130.6, 129.9, 129.5, 129.3, 129.0, 128.6, 128.3, 128.2, 128.2, 110.9, 71.9, 50.1, 50.0, 44.9, 44.8, 20.3, 12.3 *ppm*



157e

Yield **:** 68% (0.27 g)

Mp **:** 163-165 °C

IR (KBr) **:** $\tilde{\nu}$ = 3425, 3061, 2924, 1747 cm^{-1}

^{1}H NMR **:** (400 MHz, DMSO) δ = 8.14–6.89 (m, 16H), 3.72 (s, 1H), 2.76 (s, 6H) *ppm* **(Spectrum No. 3)**

^{13}C NMR **:** (100 MHz, DMSO) δ = 184.7, 148.7, 147.4, 144.2, 140.0, 131.0, 130.1, 129.1, 127.6, 127.2, 127.1, 126.7, 126.6, 126.0, 125.2, 124.7, 122.9, 122.7, 122.2, 111.6, 69.7, 43.2 *ppm* **(Spectrum No. 4)**

Analysis : for $C_{28}H_{23}NO_2$

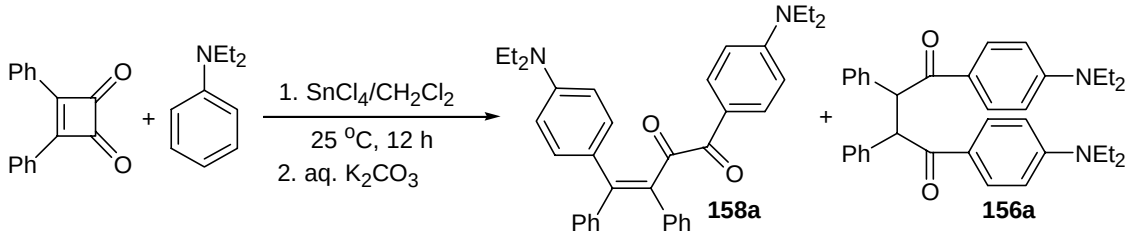
Calculated: C, 82.94%; H, 5.72%; N, 3.45%; O, 7.89%

Found: C, 82.89%; H, 5.74%; N, 3.36%

GCMS : *m/z* = 405

3.5 Reaction of Diphenylcyclobutenedione with $SnCl_4$/*N,N*-dialkylaniline

A mixture of 3,4-diphenyl-3-cyclobutene-1,2-dione (0.234 g, 1 mmol) $SnCl_4$ (0.31 g, 1. 2 mmol) in CH_2Cl_2 (20 mL) was stirred for 10 min. and *N,N*-diethylaniline (2.5 mmol), added at 25 ºC under N_2 atmosphere. The contents were stirred for 12 h at the same temperature. The reaction was quenched with 5 mL of saturated K_2CO_3 solution and extracted with CH_2Cl_2 (2X50 mL). The combined organic extract was washed with brine solution and dried over anhydrous Na_2SO_4. The solvent was removed and the residue was chromatographed on a silica gel column. The compound **158a** was eluted using hexane/ethyl acetate 95:5 while the compound **156a** was eluted using hexane/ethyl acetate 97:3



Compound 158a

Yield : 60% (0.32 g)

Mp : 138-140 °C

IR (KBr) : $\tilde{\nu}$ = 3042, 2972, 1625 cm^{-1}

^{1}H NMR : (200 MHz, $CDCl_3$) δ = 7.72 (d, *J* = 9.2 Hz, 2H), 7.28-6.97 (m, 10H), 6.96 (d, *J* = 8.8 Hz, 2H), 6.47(d, *J* = 9.2 Hz, 2H), 6.26 (d, *J*

= 8.8 Hz, 2H), 3.40 (q, *J* = 6.8 Hz, 4H), 3.20 (q, *J* = 7.2 Hz, 2H), 3.15 (q, *J* = 7.2 Hz, 2H), 1.16 (t, *J* = 6.8 Hz, 6H), 1.10 (t, *J* = 7.2 Hz, 3H) 0.99 (t, *J* = 7.2 Hz, 3H) *ppm* **(Spectrum No. 5)**

^{13}C NMR : (50 MHz, $CDCl_3$) δ = 198.4, 190.0, 155.0, 151.2, 148.6, 141.3, 140.3, 140.0, 137.1, 133.5, 133.4, 132.5, 131.9, 131.8, 131.7, 131.6, 131.3, 128.6, 128.2, 127.9, 127.8, 127.5, 126.8, 121.0, 110.8, 110.1, 109.6, 109.3, 44.4, 44.1, 12.6 *ppm* **(Spectrum No. 6)**

Analysis : for $C_{36}H_{38}N_2O_2$

Calculated: C, 81.48 %; H, 7.22 %; N, 5.28 %; O, 6.03 %

Found: C, 81.41 %; H, 7.24 %; N, 5.22 %

LCMS : *m/z* = 530

Compound 156a

Yield : 20% (0.12 g)

Mp : 107-108 ºC

IR (KBr) : $\tilde{\nu}$ = 3032, 2972, 1683 cm^{-1}

^{1}H NMR : (200 MHz, $CDCl_3$) δ = 8.01-7.28 (m, 14H), 6.67 (d, *J* = 9.2 Hz, 4H), 4.31 (s, 2H), 3.46 (q, *J* = 7.2 Hz, 8H), 1.24 (t, *J* = 7.2 Hz, 12H) *ppm* **(Spectrum No. 7)**

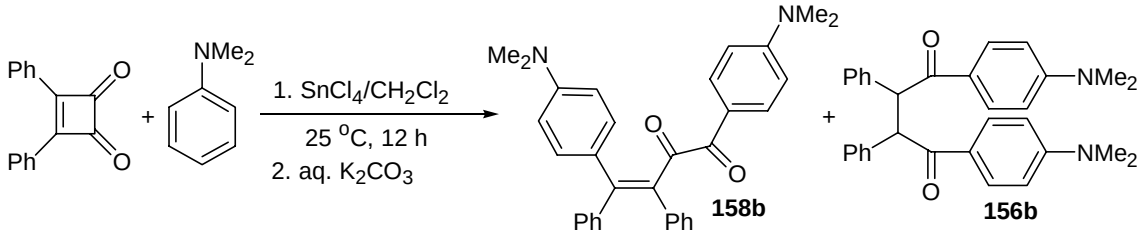
^{13}C NMR : (50 MHz, $CDCl_3$) δ = 218.2, 148.1, 134.8, 133.1, 130.9, 129.9, 129.0, 128.6, 128.0, 126.9, 110.1, 45.5, 44.5, 12.5 *ppm* **(Spectrum No. 8)**

Analysis : for $C_{36}H_{40}N_2O_2$

Calculated: C, 81.17%; H, 7.57%; N, 5.26%; O, 6.01%

Found: C, 81.09%; H, 7.6%; N, 5.32%

GCMS : *m/z* = 532



Compound 158b

Yield : 40% (0.19 g)

IR (KBr) : $\tilde{\nu}$ = 3057, 2916, 1655 cm^{-1}

Mp : 170-171 ^{o}C

^{1}H NMR : (200 MHz, $CDCl_3$) δ = 7.89 (d, *J* = 9.1 Hz, 2H), 7.28-6.84 (m, 10H), 6.65 (d, *J* = 8.9 Hz, 2H), 6.42 (d, *J* = 9.1 Hz, 2H), 6.26 (d, *J* = 8.9 Hz, 2H), 2.93 (s, 6H), 2.85 (s, 6H) *ppm*

^{13}C NMR : (50 MHz, $CDCl_3$) δ = 198.6, 190.1, 154.6, 151.3, 148.6, 141.3, 140.3, 139.8, 137.0, 33.5, 133.4, 132.5, 131.9, 131.8, 131.7, 131.6, 131.3, 128.6, 128.2, 127.9, 127.8, 127.5, 126.8, 121.0, 112.7, 112.3, 111.8, 111.5, 40.6, 40.4 *ppm*

Analysis : for $C_{32}H_{30}N_2O_2$

Calculated: C, 80.98%; H, 6.37%; N, 5.90%; O, 6.74%

Found: C, 80.83%; H, 6.24%; N, 5.82%

LCMS : *m/z* = 474

Compound 156b

Yield : 12% (0.07 g)

Mp : 150-153 ^{o}C

IR (KBr) : $\tilde{\nu}$ = 3032, 2983, 1690 cm^{-1}

^{1}H NMR : (200 MHz, $CDCl_3$) δ = 8.02-7.26 (m, 14H), 6.78 (d, J = 8.9 Hz, 4H), 4.31 (s, 2H), 3.05 (s, 12H) *ppm*

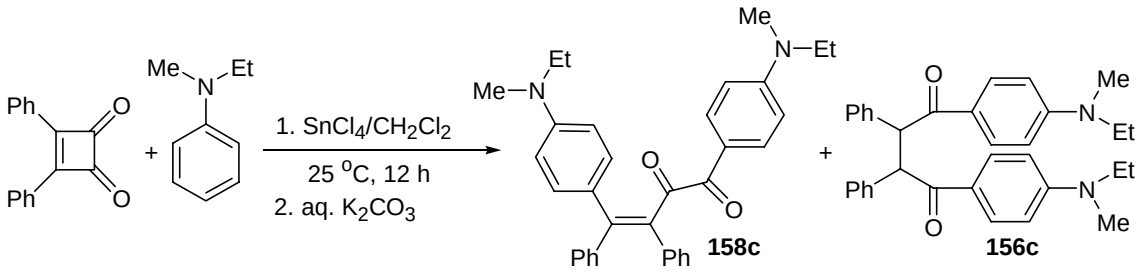
^{13}C NMR : (50 MHz, $CDCl_3$) δ = 218.2, 148.6, 134.8, 133.1, 130.0, 129.3, 128.6, 127.8, 112.1, 46.0, 40.7 *ppm*

Analysis : for $C_{32}H_{32}N_2O_2$

Calculated: C, 80.64%; H, 6.77%; N, 5.88%; O, 6.71%

Found: C, 79.95%; H, 6.77%; N, 5.9%

GCMS : *m/z* = 476



Compound 158c

Yield : 42% (0.21 g)

Mp : 176-177 ^{o}C

IR (KBr) : $\tilde{\nu}$ = 3059, 2942, 1652 cm^{-1}

^{1}H NMR : (200 MH, $CDCl_3$) δ = 7.82 (d, J = 9.2 Hz, 2H), 7.34-6.88 (m, 10H), 6.72 (d, J = 8.9 Hz, 2H), 6.45 (d, J = 9.1 Hz, 2H), 6.26 (d, J

= 8.9 Hz, 2H), 3.8 (q, *J* = 6.7 Hz, 4H), 2.91 (s, 6H), 2.86 (s, 6H) *ppm*

^{13}C NMR **:** (50 MHz, $CDCl_3$) δ = 198.5, 190.3, 154.0, 152.3, 148.8, 141.6, 141.3, 140.7, 137.0, 133.6, 133.4, 132.5, 131.9, 131.7, 131.6, 131.4, 131.3, 128.8, 128.5, 127.6, 127.5, 127.2, 126.8, 121.5, 110.5, 110.3, 109.6, 109.2, 44.7, 44.2, 36.4, 12.9 *ppm*

LCMS **:** *m/z* = 502

Compound 156c

Yield **:** 10% (0.05 g)

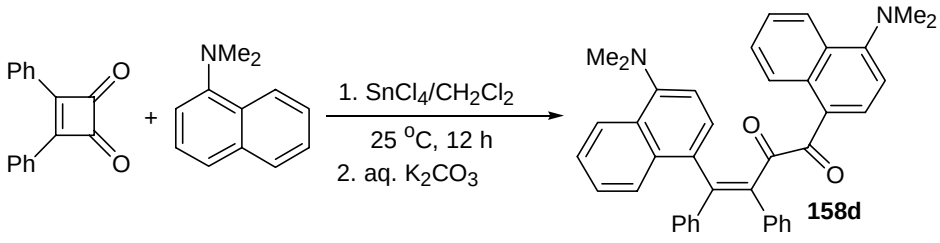
Mp **:** 112-115 ^{o}C

IR (KBr) **:** $\tilde{\nu}$ = 3036, 2978, 1686 cm^{-1}

^{1}H NMR **:** (400 MHz, $CDCl_3$) δ = 7.82-7.28 (m, 14H), 6.66 (d, *J* = 9.1 Hz, 4H), 4.34 (s, 2H), 3.37-3.42 (q, *J* = 7.2 Hz, 4H), 1.28-1.14 (m, 12H) *ppm*

^{13}C NMR **:** (50 MHz, $CDCl_3$) δ = 218.8, 148.5, 134.7, 133.5, 129.3, 129.4, 128.3, 128.7, 110.1, 46.5, 46.4, 38.7, 12.5 *ppm*

LCMS **:** *m/z* = 504



158d

Yield **:** 38% (0.21 g)

Mp **:** 182-184 ^{o}C

IR (KBr) **:** $\tilde{\nu}$ = 3057, 2924, 1636 cm^{-1}

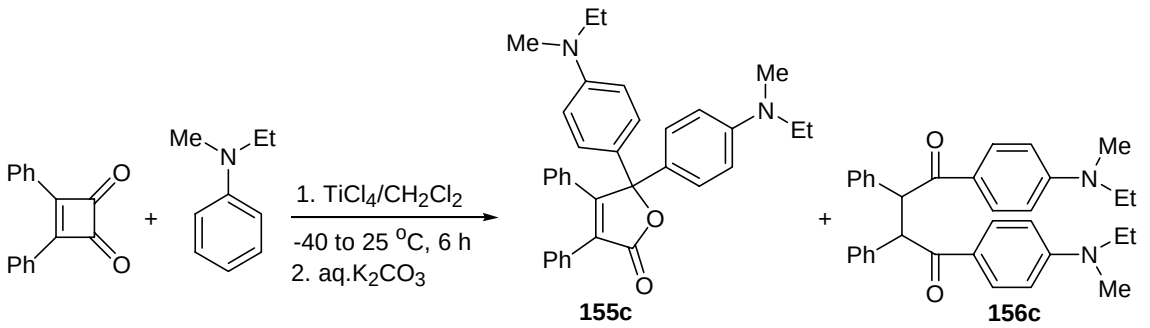
^{1}H NMR **:** (200 MHz, $CDCl_3$) δ = 7.82 (d, J = 9.2 Hz, 3H), 7.43-6.66 (m, 10H), 6.64 (d, J = 8.9 Hz, 3H), 6.24 (d, J = 9.2 Hz, 3H), 6.08 (d, J = 8.9 Hz, 3H), 2.93 (s, 6H), 2.84 (s, 6H) *ppm*

^{13}C NMR **:** (50 MHz, $CDCl_3$) δ = 187.3, 183.3, 173.4, 163.7, 161.7, 131.9, 131.4, 129.9, 129.3, 129.0, 128.9, 128.9, 128.8, 128.6, 128.5, 128.4, 128.2, 128.0, 127.9, 127.7, 127.6, 122.3, 116.3, 114.9, 109.9, 109.8, 45.0, 44.8 *ppm*

LCMS **:** *m/z* = 574

3.6 Reaction of Diphenylcyclobutenedione with $TiCl_4$/*N,N*-dialkylaniline

To a mixture of 3,4-diphenyl-3-cyclobutene-1,2-dione (0.234 g, 1 mmol) and *N,N*-ethylmethylaniline (0.34 g, 2.5 mmol) in CH_2Cl_2 (20 mL), $TiCl_4$ (0.13 mL, 1.2 mmol) in CH_2Cl_2 5mL was added drop-wise at –40 ºC under N_2 atmosphere. The contents were stirred for 6 h at the same temperature. Then, the reaction mixture was brought to room temperature and quenched with 5 mL of saturated K_2CO_3 solution and extracted with CH_2Cl_2 (2X50 mL). The combined organic extract was washed with brine solution and dried over anhydrous Na_2SO_4. The solvent was removed and the residue was chromatographed on a silica gel column. The products **155c** and **156c** were eluted using hexane/ethyl acetate 97:3.



Compound 155c

Yield **:** 38% (0.19 g)

Mp **:** 123-125 ^{o}C

IR (KBr) **:** $\tilde{\nu}$ = 3055, 2926, 1749 cm^{-1}

^{1}H NMR **:** (200 MHz, $CDCl_3$) δ = 7.82-7.19 (m, 14H), 6.65 (d, J = 8.4 Hz, 4H), 3.41-3.38 (q, J = 7.2 Hz, 2H), 3.02-2.88 (q, J = 7.2 Hz, 2H), 1.43-0.85 (m, 12H) *ppm*

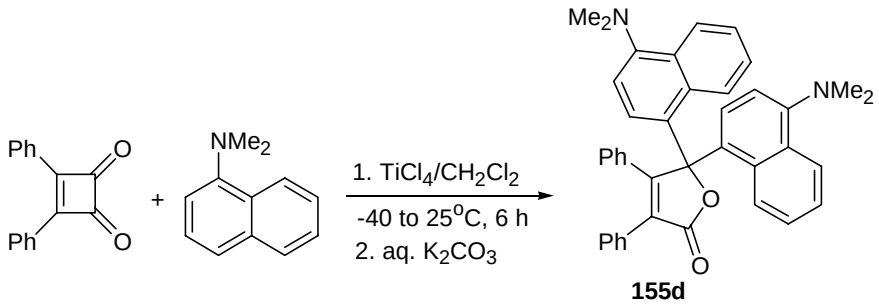
^{13}C NMR **:** (50 MHz, $CDCl_3$) δ = 191.7, 168.2, 162.6, 149.4, 148.1, 143.2,140.9 133.7, 132.9, 130.7, 129.2, 128.7, 128.3, 127.9, 116.8, 112.2, 111.6, 46.8, 46.6, 37.4, 11.4 *ppm*

LCMS **:** *m/z* = 502

Compound 156c

Yield **:** 08% (0.04 g)

The IR, ^{1}H NMR and ^{13}C data show 1:1 correspondence with the data of the compound obtained using $SnCl_4$/*N,N*-ethylmethylaniline.



155d

Yield **:** 32% (0.18 g)

Mp **:** 134-135 ^{o}C

IR (KBr) **:** $\tilde{\nu}$ = 3057, 2924, 1743 cm^{-1}

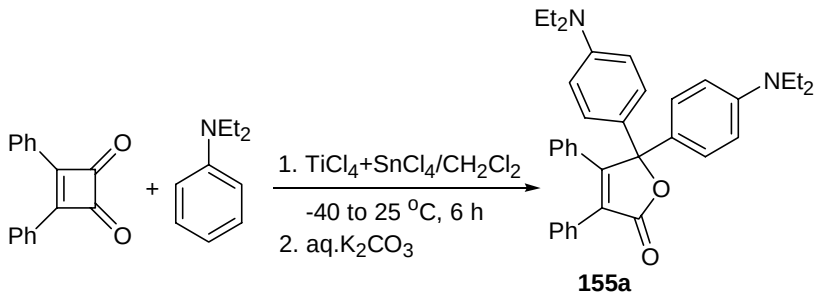
^{1}H NMR **:** (200 MHz, $CDCl_3$) δ = 7.79-7.28 (m, 16H), 6.70-6.66 (m, 6H), 2.97 (s, 6H), 2.94 (s, 6H) *ppm*

^{13}C NMR **:** (50 MHz, $CDCl_3$) δ = 187.8, 171.3, 150.7, 148.0, 147.9, 141.3, 136.0, 133.2, 129.6, 129.4, 129.2, 128.9, 128.8, 128.6, 128.7, 128.5, 128.2, 128.1, 126.9, 126.7, 126.0, 124.8, 113.6, 113.4, 113.2, 45.2, 45.2 *ppm*

LCMS **:** *m/z* = 574

3.7 Reaction of Diphenylcyclobutenedione with $TiCl_4$+$SnCl_4$/*N,N*-dialkylaniline

To a mixture of 3,4-diphenyl-3-cyclobutene-1,2-dione (0.234 g, 1 mmol) and *N,N*-diethylaniline (0.37 g, 2.5 mmol) in CH_2Cl_2 (20 mL), $TiCl_4$+$SnCl_4$ (0.54 g, 1.2 mmol) in CH_2Cl_2 5mL was added drop-wise at –40 ºC under N_2 atmosphere. The contents were stirred for 6 h at the same temperature. Then, the reaction mixture was brought to room temperature and quenched with 5 mL of saturated K_2CO_3 solution and extracted with CH_2Cl_2 (2X50 mL). The combined organic extract was washed with brine solution and dried over anhydrous Na_2SO_4. The solvent was removed and the residue was chromatographed on a silica gel column. The products **155a** and **156a** were eluted using hexane/ethyl acetate 97:3.



155a

Yield **:** 72% (0.38 g)

Mp **:** 81-83 ^oC

IR (KBr) **:** $\tilde{\nu}$ = 3050, 2974, 1743 cm^{-1}

^{1}H NMR **:** (200 MHz, $CDCl_3$) δ = 7.81-7.24 (m, 14H), 6.70 (d, *J* = 7.6 Hz, 2H), 6.60 (d, *J* = 8.6 Hz, 2H), 3.43 (q, *J* = 7.0 Hz, 4H), 3.36 (q, *J* = 7.0 Hz, 4H), 1.23 (t, *J* = 7.0 Hz, 12H) *ppm* **(Spectrum No. 9)**

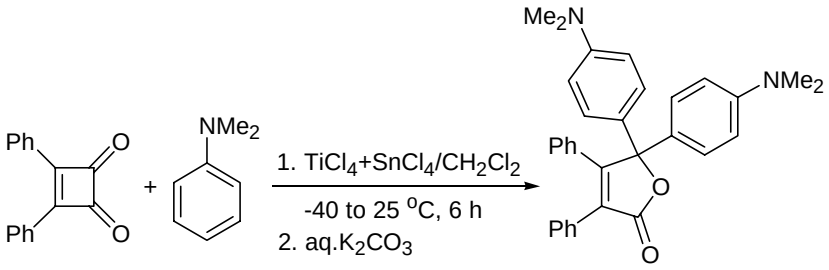
^{13}C NMR **:** (50 MHz, $CDCl_3$) δ = 191.5, 162.3, 148.3, 146.9, 143.9, 141.1, 133.9, 129.9, 129.3, 128.7, 128.6, 128.3, 128.2, 127.0, 126.8, 116.4, 111.7, 111.2, 44.4, 44.3, 12.7 *ppm* **(Spectrum No. 10)**

Analysis **:** for $C_{36}H_{38}N_2O_2$

Calculated: C, 81.48%; H, 7.22%; N, 5.28%; O, 6.03%

Found: C, 81.43%; H, 7.29%; N, 5.14%

GCMS **:** *m/z* = 530



155b

Yield **:** 38% (0.18 g)

Mp **:** 126-129 ^{o}C

IR (KBr) **:** $\tilde{\nu}$ = 3047, 2982, 1747 cm^{-1}

^{1}H NMR **:** (200 MHz, $CDCl_3$) δ = 7.79-7.26 (m, 14H), 6.79 (d, *J* = 9.2 Hz, 2H), 6.68 (d, *J* = 8.7 Hz, 2H), 2.97 (s, 6H), 2.88 (s, 6H) *ppm*

^{13}C NMR **:** (50 MHz, $CDCl_3$) δ = 191.6, 162.3, 148.3, 147.0, 141.3, 133.9, 130.2, 129.2, 128.8, 128.7, 128.6, 128.3, 127.9, 127.2, 127.0, 116.7, 112.6, 112.4, 40.2, 40.1 *ppm*

Analysis : for $C_{32}H_{30}N_2O_2$

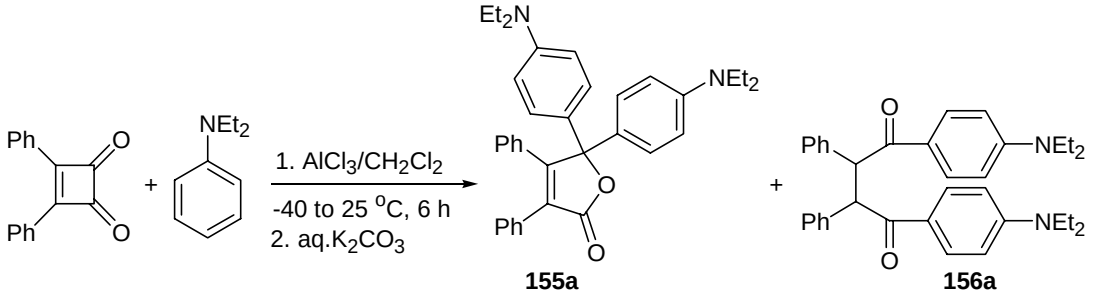
Calculated: C, 80.98%; H, 6.37%; N, 5.90%; O, 6.74%

Found: C, 80.67%; H, 6.10%; N, 5.92%

GCMS : *m/z* = 474

3.8 Reaction of Diphenylcyclobutenedione with $AlCl_3$/*N,N*-dialkylaniline

To a mixture of 3,4-diphenyl-3-cyclobutene-1,2-dione (0.234 g, 1 mmol) and *N,N*-diethylaniline (0.37 g, 2.5 mmol) in CH_2Cl_2 (20 mL), $AlCl_3$ (0.16 g, 1.2 mmol) in CH_2Cl_2 5mL was added drop-wise at –40 ºC under N_2 atmosphere. The contents were stirred for 6 h at the same temperature. Then, the reaction mixture was brought to room temperature and quenched with 5 mL of saturated K_2CO_3 solution and extracted with CH_2Cl_2 (2X50 mL). The combined organic extract was washed with brine solution and dried over anhydrous Na_2SO_4. The solvent was removed and the residue was chromatographed on a silica gel column. The products **155a** and **156a** were eluted using hexane/ethyl acetate 97:3.



Compound 155a

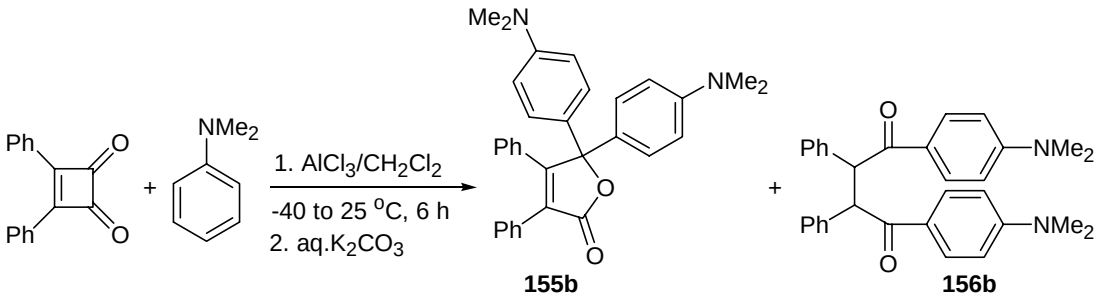
Yield : 60% (0.32 g)

The IR, ^{1}H NMR and ^{13}C data show 1:1 correspondence with the data of the compound obtained using $TiCl_4$+$SnCl_4$/*N,N*-diethylaniline.

Compound 156a

Yield **:** 12% (0.06 g)

The IR, ^{1}H NMR and ^{13}C data show 1:1 correspondence with the data of the compound obtained using $SnCl_4$/*N,N*-diethylaniline.



Compound 155b

Yield **:** 40% (0.19 g)

The IR, ^{1}H NMR and ^{13}C data show 1:1 correspondence with the data of the compound obtained using $TiCl_4$+$SnCl_4$/*N,N*-dimethylaniline.

Compound 156b

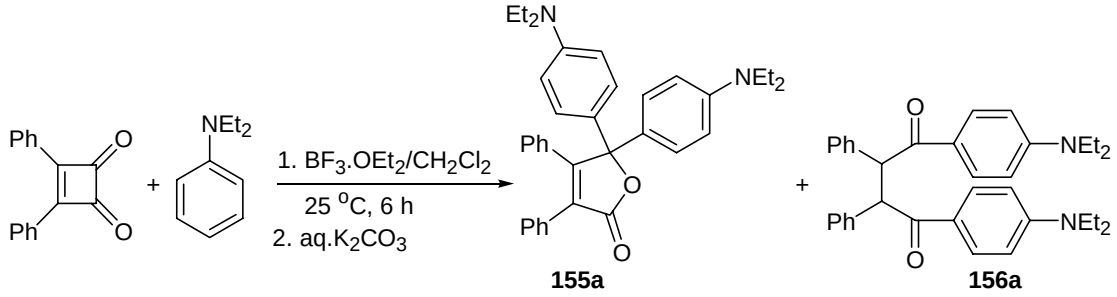
Yield **:** 08% (0.04 g)

The IR, ^{1}H NMR and ^{13}C data show 1:1 correspondence with the data of the compound obtained using $SnCl_4$/*N,N*-dimethylaniline.

3.9 Reaction of Diphenylcyclobutenedione with BF_3OEt_2/*N,N*-dialkylaniline

To a mixture of 3,4-diphenyl-3-cyclobutene-1,2-dione (0.234 g, 1 mmol) and *N,N*-diethylaniline (0.37 g, 2.5 mmol) in CH_2Cl_2 (20 mL), BF_3OEt_2 (0.17 g, 1.2 mmol) in CH_2Cl_2 5mL was added drop-wise at 25 ºC under N_2 atmosphere. The contents were stirred for 6 h at the same temperature. Reaction was quenched with 5 mL of saturated K_2CO_3 solution and extracted with CH_2Cl_2 (2X50 mL). The combined organic extract was washed with brine solution and dried over anhydrous Na_2SO_4. The solvent was

removed and the residue was chromatographed on a silica gel column. The products **155a** and **156a** were eluted using hexane/ethyl acetate 97:3.



Compound 155a

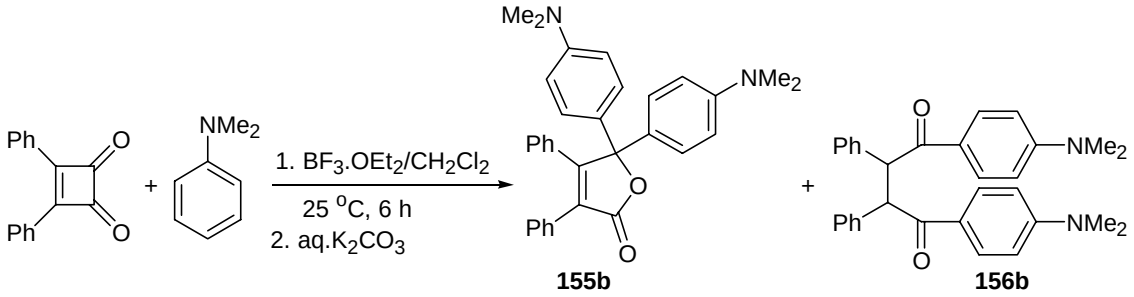
Yield **:** 56% (0.30 g)

The IR, ^{1}H NMR and ^{13}C data show 1:1 correspondence with the data of the compound obtained using $TiCl_4$+$SnCl_4$/*N,N*-diethylaniline.

Compound 156a

Yield **:** 12% (0.06 g)

The IR, ^{1}H NMR and ^{13}C data show 1:1 correspondence with the data of the compound obtained using $SnCl_4$/*N,N*-diethylaniline.



Compound 155b

Yield **:** 36% (0.17 g)

The IR, ^{1}H NMR and ^{13}C data show 1:1 correspondence with the data of the compound obtained using $TiCl_4$+$SnCl_4$/*N,N*-dimethylaniline.

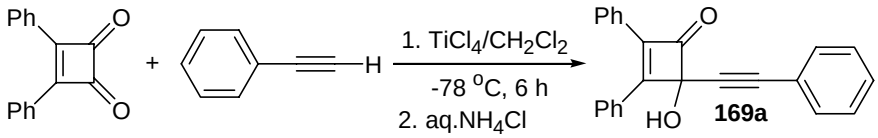
Compound 156b

Yield **:** 08% (0.04 g)

The IR, ^{1}H NMR and ^{13}C data show 1:1 correspondence with the data of the compound obtained using $SnCl_4$/*N,N*-dimethylaniline.

3.10 General Procedure for Alkynylation of Cyclobutenediones using $TiCl_4/Et_3N$ Reagent System

To a mixture of 3,4-diphenyl-3-cyclobutene-1,2-dione (0.234 g, 1 mmol), triethylamine (0.35 g, 3.5 mmol) and alkyne (3mmol) in CH_2Cl_2 (20 mL), $TiCl_4$ (0.66 mL of 1:1 solution of $TiCl_4/CH_2Cl_2$, 3mmol) in CH_2Cl_2 (5 mL) was added drop-wise at –78 ^{o}C under N_2 atmosphere. The contents were stirred for 6 h at same temperature and quenched with 5 mL of saturated NH_4Cl. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (3x30 ml). The combined organic extract was washed successively with brine solution and dried over anhydrous Na_2SO_4, concentrated at reduced pressure and the residue was subjected to chromatographed on a silica gel column. The products **169** were separated with hexane/ethyl acetate 97:3 as eluent.



Yield **:** 62% (0.20 g)

IR (neat) **:** $\tilde{\nu}$ = 3368, 3046, 2939, 2216, 1765 cm^{-1}

^{1}H NMR **:** (200 MHz, $CDCl_3$) δ = 7.34-7.12 (m, 15H) 4.17 (s, 1H) *ppm*

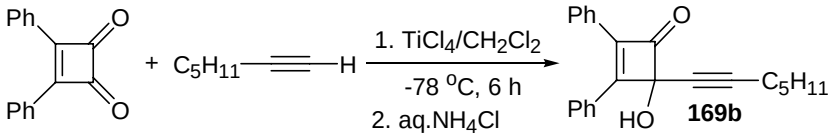
^{13}C NMR **:** (50 MHz, $CDCl_3$) δ = 186.9, 145.6, 133.2, 132.3, 131.8, 130.9, 130.1, 129.7, 129.4, 128.6, 128.2, 71.8, 68.7, 67.9 *ppm*

Analysis **:** for $C_{24}H_{16}O_2$

Calculated: C, 85.69%; H, 4.79%; O, 9.51%

Found: C, 85.72%; H, 4.75%

GCMS **:** *m/z* = 336



169b

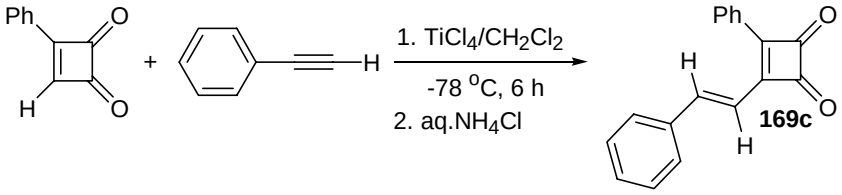
Yield **:** 58% (0.19 g)

IR (neat) **:** $\tilde{\nu}$ = 3347, 3052, 2936, 2212, 1767 cm^{-1}

^{1}H NMR **:** (200 MHz, $CDCl_3$) δ = 7.28-7.13 (m, 10H), 3.97 (s, 1H), 2.44 (t, *J* = 6.9 Hz, 2H), 1.48-1.36 (m, 6H), 1.17 (t, *J* = 7.1 Hz, 3H) *ppm*

^{13}C NMR **:** (50 MHz, $CDCl_3$) δ = 186.0, 142.7, 135.3, 134.2, 129.2, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 128.2, 128.0, 127.6, 80.5, 63.5, 53.3, 30.9, 27.2, 22.1, 18.9, 13.9 *ppm*

GCMS **:** *m/z* = 330



169c

Yield **:** 64% (0.16 g)

Mp **:** 160-162 °C

IR (KBr) **:** $\tilde{\nu}$ = 3056, 2968, 1765, 1602 cm^{-1}

^{1}H NMR **:** (200 MHz, $CDCl_3$) δ = 8.37-7.26 (m, 12H) *ppm* **(Spectrum No. 11)**

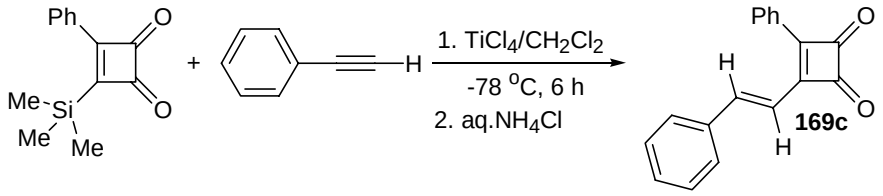
^{13}C NMR **:** (50 MHz, $CDCl_3$) δ = 196.8, 195.9, 184.3, 183.4, 146.2, 134.9, 133.2, 131.4, 129.5, 129.2, 129.0, 128.8, 128.4 115.3 *ppm* **(Spectrum No. 12)**

Analysis **:** for $C_{18}H_{12}O_2$

Calculated: C, 83.06%; H, 4.65%; O, 12.29%

Found: C, 82.86%; H, 4.58%

LCMS **:** *m/z* = 260



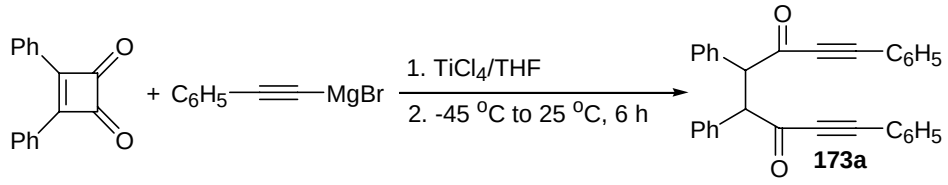
Yield **:** 76% (0.19 g)

The IR, ^{1}H NMR and ^{13}C data show 1:1 correspondence with the data of the compound obtained with phenylcyclobutenedione and phenyl acetylene.

3.11 Preparation of Alkynyldiketones using the RMgBr/$TiCl_4$ Reagent System

Magnesium turnings (3 mmol, 0.075 g) were treated with bromoethane (3mmol, 0.3 mL) in THF (5 mL) for 0.5 h at 25 ^oC, and then 1-heptyne (0.29 g, 3 mmol) was added, after the formation of the Grignard reagent, $TiCl_4$ (0.66 mL of 1:1 solution of $TiCl_4/CH_2Cl_2$, 3 mmol) in CH_2Cl_2 5 mL was added drop-wise at -45 ºC under N_2 atmosphere. 3,4-Diphenyl-3-cyclobutene-1,2-dione (0.234 g, 1 mmol) in THF (5 mL) was added to the reaction mixture and the contents were stirred for 5 h at the same temperature. The reaction mixture was brought to room temperature and quenched with 5 mL of saturated NH_4Cl solution and extracted with ether (2X50 mL). The combined organic extract was washed with brine solution and dried over anhydrous Na_2SO_4. The

solvent was removed and the residue was chromatographed on a silica gel column. The product was eluted using hexane/ethyl acetate 99:1.



173a

Yield 32% (0.14 g)

Mp **:** 211-213 °C

IR (KBr) **:** $\tilde{\nu}$ = 3032, 2180, 1660 cm^{-1}

^{1}H NMR **:** (200 MHz, $CDCl_3$) δ = (*dl*) 7.48-7.15 (m, 20H), 4.81 (s, 2H) *ppm* **(Spectrum No. 13)**

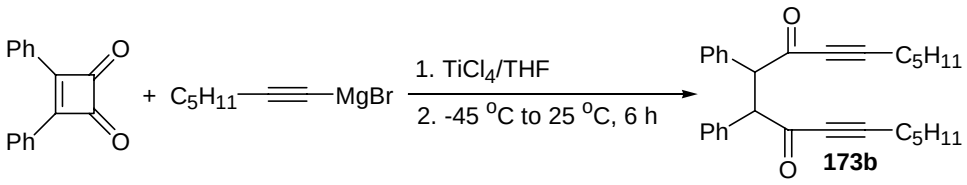
^{13}C NMR **:** (50 MHz, $CDCl_3$) δ = 185.6, 134.5, 133.0, 130.7, 130.3, 129.3, 128.7, 128.5, 127.7, 120.0, 93.1, 87.9, 62.7.*ppm* **(Spectrum No. 14)**

Analysis **:** for $C_{32}H_{22}O_2$

Calculated: C, 87.65%; H, 5.06%; O, 7.3 %

Found: C, 87.68%; H, 5.06%

GCMS **:** *m/z* = 438



173b

Yield **:** 35% (0.15 g)

Mp **:** 76-78 °C

IR (KBr) **:** $\tilde{\nu}$ = 3030, 2933, 2210, 1668 cm^{-1}

^{1}H NMR **:** (200 MHz, $CDCl_3$) δ = 7.45-6.97 (m, 10H), (*meso*) 4.77 (s, 2H), (*dl*) 4.57 (s, 2H), 2.21 (t, *J* = 6.8 Hz, 4H), 1.46-1.21 (m, 12H), 0.85 (t, *J* = 7.1 Hz, 6H) *ppm* **(Spectrum No. 15)**

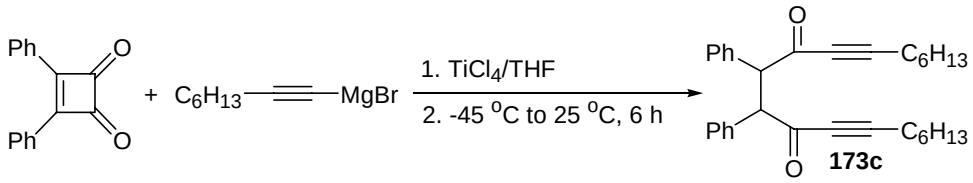
^{13}C NMR **:** (50 MHz, $CDCl_3$) δ = (*dl*) 185.6, 134.7, 128.8, 128.5, 127.4, 96.5, 80.8, 62.7, 30.8, 27.2, 22.0, 18.9, 13.7, (*meso*) 184.3, 135.2, 96.7, 62.1, 30.7 *ppm* **(Spectrum No. 16)**

Analysis **:** for $C_{30}H_{34}O_2$

Calculated: C, 84.47%; H, 8.03%; O, 7.50%

Found: C, 84.61%; H, 8.05%

GCMS **:** *m/z* = 426



173c

Yield **:** 42% (0.19 g)

Mp **:** 77-79 ^oC

IR (KBr) **:** $\tilde{\nu}$ = 3030, 2929, 2212, 1669 cm^{-1}

^{1}H NMR **:** (200 MHz, $CDCl_3$) δ = 7.38-6.99 (m, 10H), (*meso*) 4.77 (s, 2H), (*dl*) 4.57 (s, 2H), 2.72 (t, *J* = 7.1 Hz, 4H), 1.46-1.21 (m, 16H), 0.85 (t, *J* = 7.3 Hz, 6H) *ppm*

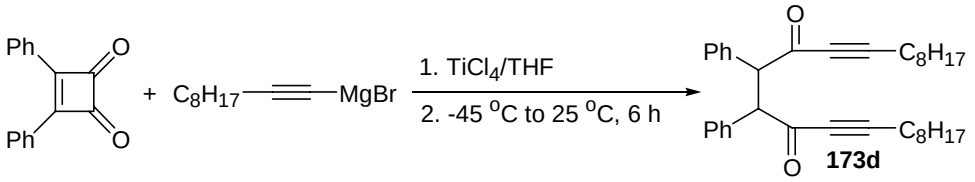
^{13}C NMR **:** (50 MHz, $CDCl_3$) δ = (*dl*) 185.7, 134.7, 128.6, 128.5, 127.4, 96.6, 80.8, 62.7, 31.1, 27.4, 21.9, 18.9, 13.8, (*meso*) 184.4, 135.2, 96.7, 80.8 *ppm*

Analysis **:** for $C_{32}H_{38}O_2$

Calculated: C, 84.54%; H, 8.42%; O, 7.04 %

Found: C, 84.50%; H, 8.42%

GCMS **:** *m/z* = 454



173d

Yield **:** 23% (0.11 g)

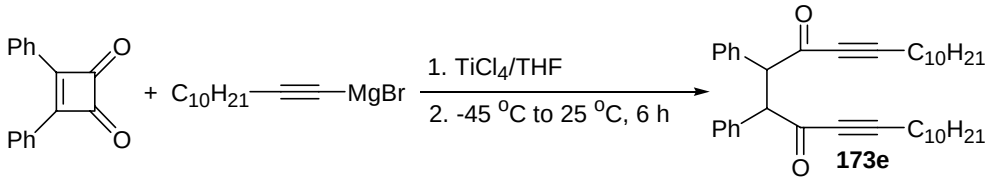
Mp **:** 81-82 °C

IR (KBr) **:** $\tilde{\nu}$ = 3030, 2925, 2212, 1674 cm^{-1}

^{1}H NMR **:** (200 MHz, $CDCl_3$) δ = 7.28-6.99 (m, 10H), (*meso*) 4.83 (s, 2H), (*dl*) 4.58 (s, 2H), 2.29 (t, *J* = 7.5 Hz, 4H), 1.49-1.24 (m, 24H), 0.92 (t, *J* = 7.4 Hz, 6H) *ppm* **(Spectrum No. 17)**

^{13}C NMR **:** (50 MHz, $CDCl_3$) δ = (*dl*) 185.9, 134.6, 129.2, 128.5, 127.5, 96.8, 80.7, 62.7, 31.8, 29, 28.9, 28.7, 27.5, 22.6, 19.0, 14.0, (*meso*) 184.8, 134.4, 96.9, 80.7, 62.2 *ppm* **(Spectrum No. 18)**

GCMS **:** *m/z* = 510



173e

Yield **:** 28% (0.15 g)

Mp **:** 81-82 °C

IR (KBr) **:** $\tilde{\nu}$ = 3030, 2925, 2214, 1672 cm^{-1}

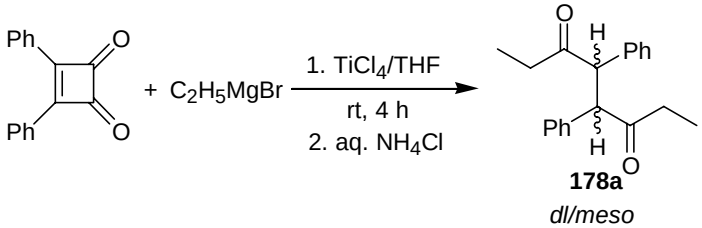
^{1}H NMR **:** (200 MHz, $CDCl_3$) δ = 8.01-7.0 (m, 10H), (*meso*) 4.80 (s, 2H), (*dl*) 4.58 (s, 2H), 2.27 (t, *J* = 7.5 Hz, 4H), 1.48-1.27 (m, 32H), 0.89 (t, *J* = 7.3 Hz, 6H) *ppm*

^{13}C NMR **:** (50 MHz, $CDCl_3$) δ = (*dl*) 185.8, 134.6, 129.2, 128.8, 127.9, 96.9, 80.7, 62.6, 31.9, 29.5, 29.4, 29.3, 29.0, 28.8, 27.5, 22.7, 19.0, 14.0, (*meso*) 184.6, 135.1, 96.8, 62.0 *ppm*

GCMS **:** *m/z* = 566

3.12 Preparation of Diketones using the RMgBr/$TiCl_4$ Reagent System

Magnesium turnings (4 mmol, 0.10 g) were treated with bromoethane (4mmol, 0.4 mL) in THF (15 mL) for 0.5 h at 25 ^oC, after the formation of the Grignard reagent, $TiCl_4$ (0.88 mL of 1:1 solution of $TiCl_4/CH_2Cl_2$, 4 mmol) added drop-wise at –45 ^oC and further allowed to stirr for 0.5 h and then diphenylcyclobutenedione (1 mmol, 234 mg), dissolved in THF (5 mL), was added and the stirring was continued for 3 h at room temperature. The reaction mixture was quenched with saturated NH_4Cl. The organic phase was separated and the aqueous phase was extracted with ether (3x30 ml). The combined organic extract was washed successively with brine solution and dried over anhydrous Na_2SO_4, concentrated at reduced pressure and the residue was subjected to chromatography on a silica gel column and the compounds **178** and **179** were separated with hexane/ethyl acetate 97:3 and 98:2 as eluent.



178a
dl/meso

Yield **:** 68% (0.20 g)

Mp : 72-74 ^{o}C

IR (KBr) : $\tilde{\nu}$ = 3056, 2978, 1703, 1597 cm^{-1}

^{1}H NMR : (400 MHz, $CDCl_3$) δ = 7.42-7.24 (m, 10H), (*meso*) 4.64 (s, 2H), (*dl*) 4.42 (s, 2H), 2.31-2.40 (m, 4H), 0.73 (t, *J* = 7.2 Hz, 6H) *ppm* **(Spectrum No. 19)**

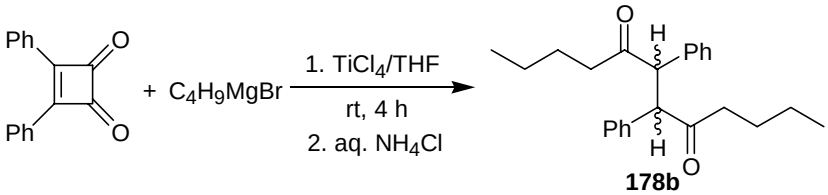
^{13}C NMR : (100 MHz, $CDCl_3$) δ = (*dl*) 209.1, 136.7, 128.8, 128.8, 128.7, 128.5, 127.6, 127.2, 60.4, 36.7, 7.4, (*meso*) 61.2, 35.1, 7.8 *ppm* **(Spectrum No. 20)**

Analysis : for $C_{20}H_{22}O_2$

Calculated: C, 81.60%; H, 7.53%; O, 10.87%

Found: C, 81.45%; H, 7.51%

GCMS : *m/z* = 294



178b
dl/meso

Yield : 63% (0.22 g)

Mp : 76-78 ^{o}C

IR (KBr) : $\tilde{\nu}$ = 3061, 2957, 2934, 1705, 1599 cm^{-1}

^{1}H NMR : (400 MHz, $CDCl_3$) δ = 7.42-6.93 (m, 10H), (*dl*) 4.63 (s, 2H), (*meso*) 4.42 (s, 2H), 2.53 (m, 4H), 2.29-2.23 (m, 4H), 0.94-0.88 (m, 4H), 0.65 (t, *J* = 7.3 Hz, 6H) *ppm* **(Spectrum No. 21)**

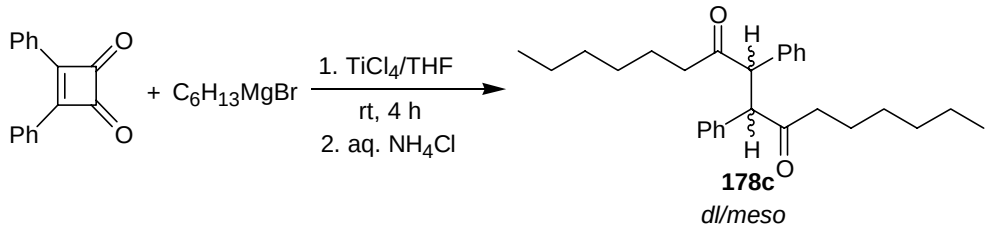
^{13}C NMR **:** (100 MHz, $CDCl_3$) δ = (*dl*) 210.2, 208.6, 136.7, 136.5, 128.9, 128.8, 128.6, 127.5, 127.2, 60.6, 43.1, 25.3, 21.7, 13.6, (*meso*) 61.5, 41.7, 25.7, 22.1, 13.8 *ppm* **(Spectrum No. 22)**

Analysis **:** for $C_{24}H_{30}O_2$

Calculated: C, 82.24; H, 8.63%; O, 9.13%

Found: C, 82.16%; H, 8.58%

GCMS **:** *m/z* = 350



178c
dl/meso

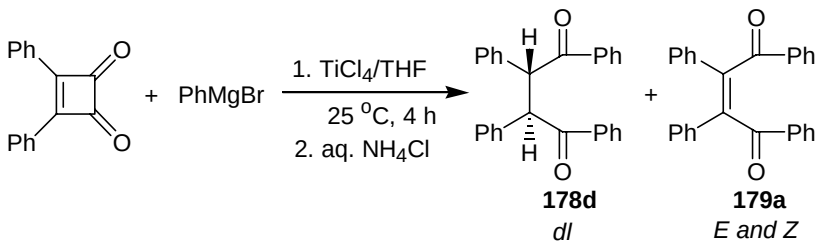
Yield **:** 48% (0.19 g)

IR (neat) **:** $\tilde{\nu}$ = 3061, 2957, 2934, 1705, 1599 cm^{-1}

^{1}H NMR **:** (400 MHz, $CDCl_3$) δ = 7.37-6.95 (m, 10H), (*dl*) 4.58 (s, 2H), (*meso*) 4.46 (s, 2H), 2.58 (t, *J* = 7.0 Hz, 4H), 2.16-2.13 (m, 4H), 1.43-1.28 (m, 12H), 0.95 (t, *J* = 7.3 Hz, 6H) *ppm*

^{13}C NMR **:** (100 MHz, $CDCl_3$) δ = (*dl*) 196.2, 191.6, 147.1, 146.2, 141.2, 133.4, 131.7, 131.4, 131.2, 131.0, 129.9, 129.8, 129.4, 129.0, 128.9, 128.5, 128.3,127.9, 127.1, 126.7, 34.1, 24.9, 83.5, 65.9, 31.7, 29.8, 26.1, 22.7, (*meso*) 81.3, 60.5, 32.1, 30.2, 27.0, 21.0, 14.1 *ppm*

GCMS **:** *m/z* = 406



178d *dl* **179a** *E and Z*

Compound 178d

Yield **:** 46% (0.18 g)

Mp **:** 216-218 °C

IR (KBr) **:** $\tilde{\nu}$ = 3063, 2976, 1662,1595 cm^{-1}

^{1}H NMR **:** (400 MHz, $CDCl_3$) δ = (*dl*) 7.90-7.12 (m, 20H), 5.81 (s, 2H) *ppm* **(Spectrum No. 23)**

^{13}C NMR **:** (100 MHz, $CDCl_3$) δ = (*dl*) 198.4, 144.6, 136.9, 136.4,135.3, 132.9, 132.9, 130.0, 129.8, 129.1, 128.8, 128.6, 128.5, 128.5, 128.4, 128.3, 127.4, 56.2 *ppm* **(Spectrum No. 24)**

Analysis **:** for $C_{28}H_{22}O_2$

Calculated: C, 86.13%; H, 5.68%; O, 8.19%

Found: C, 86.08%; H, 5.62%

GCMS **:** *m/z* = 390

Compound 179a

Yield **:** 28% (0.10 g)

Mp **:** 209-212 °C

IR (KBr) **:** $\tilde{\nu}$ = 3057, 2978, 1662, 1560 cm^{-1}

^{1}H NMR **:** (400 MHz, $CDCl_3$) δ = (*E and Z*) 7.80-6.97 (m, 20H) *ppm* **(Spectrum No. 25)**

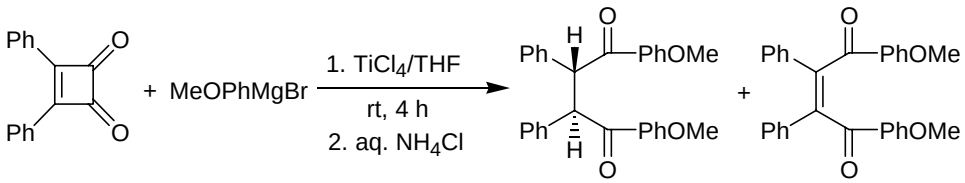
^{13}C NMR **:** (100 MHz, $CDCl_3$) δ = (*E and Z*) 196.9, 191.4, 153.8, 140.9, 140.3, 138.7, 138.6, 133.6, 132.6, 131.5, 131.1, 129.8, 129.8, 128.5, 128.4, 128.3, 127.8, 127.7, 127.6 *ppm* **(Spectrum No. 26)**

Analysis **:** for $C_{28}H_{20}O_2$

Calculated: C, 86.57%; H, 5.19%; O, 8.24%

Found: C, 86.49%; H, 5.17%

GCMS **:** *m/z* = 388



178e *dl* **179b** *E and Z*

Compound 178e

Yield **:** 42% (0.19 g)

Mp **:** 223-225 ^{o}C

IR (KBr) **:** $\tilde{\nu}$ = 3059, 2959, 1662, 1599 cm^{-1}

^{1}H NMR **:** (400 MHz, $CDCl_3$) δ = (*dl*) 7.91-6.81 (m, 18H), 5.76 (s, 2H), 3.80 (s, 6H) *ppm*

^{13}C NMR **:** (100 MHz, $CDCl_3$) δ = (*dl*) 196.9, 163.4, 137.4, 132.3, 131.2, 131.1, 130.8, 129.9, 129.7, 128.9, 128.7, 128.5, 127.2, 113.7, 113.6, 55.6, 55.4 *ppm*

Analysis **:** for $C_{30}H_{26}O_4$

Calculated: C, 79.98%; H, 5.82%; O, 14.21%

Found: C, 79.85%; H, 5.76%

GCMS **:** *m/z* = 450

Compound 179b

Yield **:** 26% (0.11 g)

Mp **:** 213-215 ^{o}C

IR (KBr) **:** $\tilde{v}$ = 3058, 2926, 1653, 1601 cm^{-1}

^{1}H NMR **:** (400 MHz, $CDCl_3$) δ = (*E and Z*) 8.05-6.50 (m, 18H), 3.86 (s, 6H) *ppm*

^{13}C NMR **:** (100 MHz, $CDCl_3$) δ = (*E and Z*) 197.6, 190.5, 163.8, 160.6, 159.8, 153.9, 140.4, 139.0, 133.3, 132.9, 132.3, 132.2, 131.7, 131.3, 131.3, 131.2, 129.2, 129.2, 128.5, 128.4, 128.3, 128.3, 127.8, 127.5, 127.4, 113.0, 112.9, 55.5, 55.3 *ppm*

Analysis **:** for $C_{30}H_{24}O_4$

Calculated: C, 80.34%; H, 5.39%; O, 14.27%

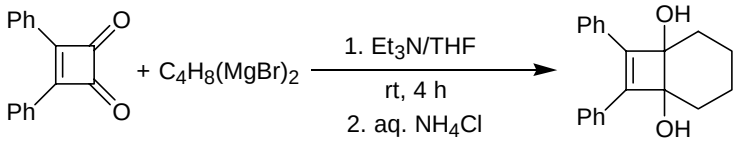
Found: C, 80.22%; H, 5.35%

GCMS **:** *m/z* = 448

3.13 Preparation of Diols using the R(MgBr)$_2$ Reagent System

Magnesium turnings (3 mmol, 0.075 g) in THF (10 mL) were treated with dibromobutane (3mmol, 0.64 mL) for 0.5 h at 25 ^{o}C under N_2 atmosphere. After the formation of the Grignard reagent, diphenylcyclobutenedione (1 mmol, 0.234 g), dissolved in THF (5 mL), was added and the stirring was continued for 3 h at room temperature. The reaction mixture was quenched with saturated NH_4Cl. The organic phase was separated and the aqueous phase was extracted with ether (3x30 ml). The combined organic extract was washed successively with brine solution and dried over anhydrous Na_2SO_4, concentrated at reduced pressure and the residue was subjected to

chromatography on a silica gel column. The compound **184** was separated with hexane/ethyl acetate 96:4 as eluent.



184a

Yield : 65% (0.19 g)

Mp : 246 ^{o}C

IR (KBr) : $\tilde{\nu}$ = 3441, 3061, 2928, 1712 cm^{-1}

^{1}H NMR : (400 MHz, $CDCl_3$) δ = 7.65-7.28 (m, 10H), 3.02 (s, 2H), 2.14 (t, J = 12.2 Hz, 4H), 1.96 (t, J = 4.9 Hz, 4H) *ppm* **(Spectrum No. 27)**

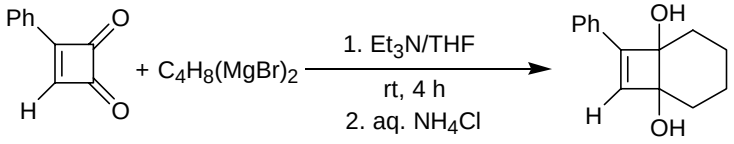
^{13}C NMR : (100 MHz, $CDCl_3$) δ = 144.4, 133.0, 128.6, 128.5, 127.4, 79.6, 29.3, 17.8 *ppm* **(Spectrum No. 28)**

Analysis : for $C_{20}H_{20}O_2$

Calculated: C, 82.16%; H, 6.89%; O, 10.94%

Found: C, 82.18%; H, 6.89%

GCMS : m/z = 292



184b

Yield : 52% (0.11 g)

IR (neat) : $\tilde{\nu}$ = 3429, 3065, 2918, 1721 cm^{-1}

^{1}H NMR : (400 MHz, $CDCl_3$) δ = 7.18-7.13 (m, 5H), 6.52 (s, 1H), 2.86 (s, 2H), 1.71 (t, J = 12.1 Hz, 2H), 1.69 (t, J = 4.8 Hz, 2H), 1.27 (m, 4H) *ppm*

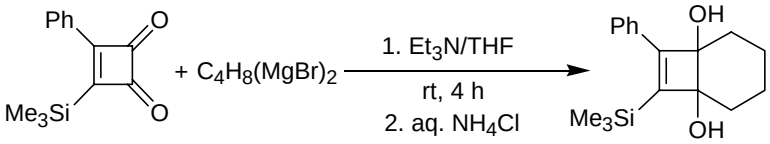
^{13}C NMR **:** (100 MHz, $CDCl_3$) δ = 143.8, 132.6, 128.7, 128.4, 127.3, 122.6, 79.5, 76.3, 28.4, 28.2, 18.2, 17.8 *ppm*

Analysis **:** for $C_{14}H_{16}O_2$

Calculated: C, 77.75%; H, 7.46%; O, 14.80%

Found: C, 77.67%; H, 7.44%

LCMS: *m/z* = 216



184c

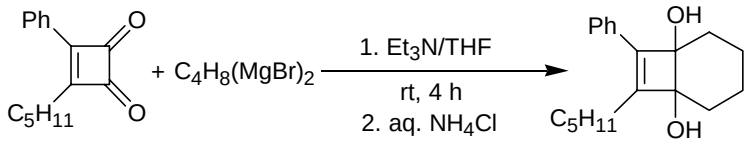
Yield **:** 58% (0.16 g)

IR (neat) **:** $\tilde{\nu}$ = 3435, 3061, 2938, 1713 cm^{-1}

^{1}H NMR **:** (400 MHz, $CDCl_3$) δ = 7.28-7.19 (m, 5H), 2.65 (s, 2H), 1.58 (t, *J* = 11.9 Hz, 4H), 1.29 (t, *J* = 4.8 Hz, 4H), 0.27 (s, 9H) *ppm*

^{13}C NMR **:** (100 MHz, $CDCl_3$) δ = 146.2, 137.3, 135.8, 128.6, 127.4, 126.7, 81.3, 79.6, 28.6, 27.4, 17.7, 17.5, -0.97 *ppm*

GCMS **:** *m/z* = 288



184d

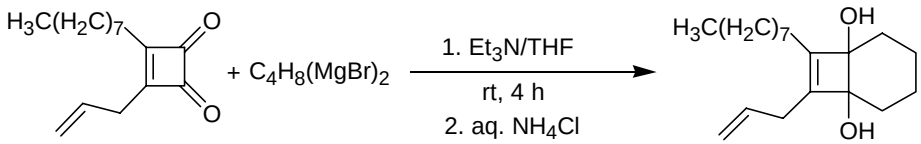
Yield **:** 54% (0.15 g)

IR (neat) **:** $\tilde{\nu}$ = 3425, 3059, 2938, 1716 cm^{-1}

^{1}H NMR **:** (400 MHz, $CDCl_3$) δ = 7.23-7.18 (m, 5H), 2.63 (s, 2H), 2.13-2.11(m, 4H), 1.94-1.93 (m, 4H), 1.65 (t, *J* = 6.9 Hz, 4H), 1.29 (t, *J* = 12.3 Hz, 4H) 1.09 (t, *J* = 4.9 Hz, 3H) *ppm*

^{13}C NMR **:** (100 MHz, $CDCl_3$) δ = 142.3, 136.6, 134.7, 128.3, 127.5, 126.7, 78.5, 77.8. 32.5, 31.3, 29.7, 28.4, 26.5, 26.1, 19.7, 19.6, 14.5 *ppm*

GCMS **:** *m/z* = 286



184e

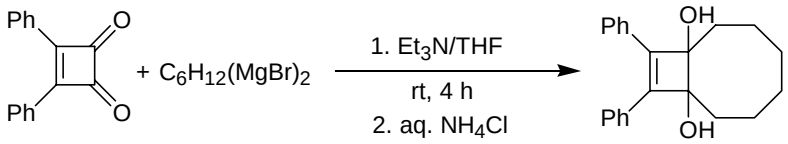
Yield **:** 55% (0.15 g)

IR (neat) **:** $\tilde{\nu}$ = 3423, 3069, 2946, 1709 cm^{-1}

^{1}H NMR **:** (400 MHz, $CDCl_3$) δ = 6.63 (t, *J* = 7.5 Hz,1H), 5.83 (d, 2H), 5.14-4.90 (m, 2H), 3.02 (s, 2H), 2.03 (t, *J* = 6.8 Hz, 2H), 1.53-1.52 (m, 2H), 1.43-1.39 (m, 8H), 1.27 (t, *J* = 12.1 Hz, 4H), 0.99 (t, *J* = 7.2 Hz, 4H), 0.88 (t, *J* = 4.9 Hz, 3H) *ppm*

^{13}C NMR **:** (100 MHz, $CDCl_3$) δ = 139.2, 130.9, 128.8, 123.9, 123.4, 115.8, 114.1, 71.8, 66.1, 62.9, 33.8, 31.9, 31.6, 29.7, 29.4, 22.7, 19.1, 15.6, 15.5, 14.1 *ppm*

LCMS: *m/z* = 278



184f

Yield **:** 47% (0.15 g)

IR (neat) **:** $\tilde{\nu}$ = 3412, 3063, 2928, 1714 cm^{-1}

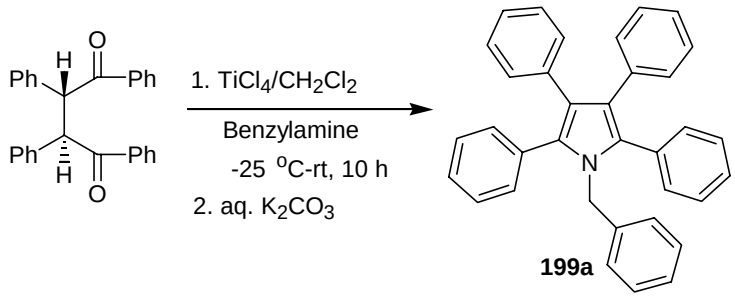
^{1}H NMR **:** (200 MHz, $CDCl_3$) δ = 7.34-7.27 (m, 10H), 2.27 (s, 2H), 1.58 (t, *J* = 11.9 Hz, 4H), 1.28-1.27 (m, 4H), 0.92 (t, *J* = 4.7 Hz, 4H) *ppm*

^{13}C NMR : (50 MHz, $CDCl_3$) δ = 167.7, 134.2, 130.9, 128.8, 128.5, 128.0, 127.2, 125.7, 71.8, 32.7, 29.7, 19.2 *ppm*

LCMS: *m/z* = 320

3.14 Preparation *N*-substituted Pyrroles from 1,4-diketones

Dichloromethane (25 mL), 1,2,3,4-tetraphenylbutane-1,4-dione (3 mmol) and benzylamine (2 mL, 18 mmol) were taken under N_2 atmosphere. $TiCl_4$ (3.3 mmol, 0.68 mL, of 1:1 (Volume/volume) solution of $TiCl_4/CH_2Cl_2$) in CH_2Cl_2 (5 mL) was added under N_2 at –10 ^oC for 10 min. The reaction mixture was stirred for 2 h at –10 ^oC and stirred further for 8-10 h at 25 ^oC. The reaction was quenched with saturated K_2CO_3 solution (10 mL) and filtered through a Buchner funnel. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2X25 mL). The combined organic extract was washed with brine (10 mL) and dried over anhydrous sodium sulphate. The solvent was removed and the residue was chromatographed on a silica gel column. Hexane/ethyl acetate 99:1 eluted the pyrrole.



199a

Yield : 86% (0.39 g)

Mp : 187-189 ^oC

IR (KBr) : $\tilde{\nu}$ = 3063, 3030, 2928, 1601, 1494 cm^{-1}

^{1}H NMR : (400 MHz, $CDCl_3$) δ = 7.28-7.01 (m, 20H), 6.80-6.78 (m, 5H), 5.12 (s, 2H) *ppm* **(Spectrum No. 29)**

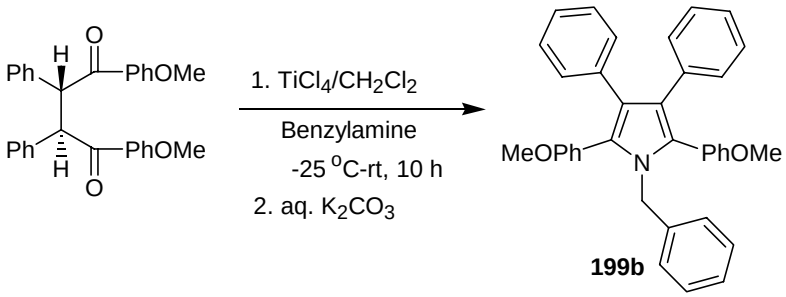
^{13}C NMR **:** (100 MHz, $CDCl_3$) δ = 139.2, 135.6, 132.8, 131.9, 131.6, 130.9, 129.2, 128.5, 128.3, 128.2, 127.9, 127.8, 127.4, 127.4, 126.7, 126.0, 125.1, 122.7 *ppm* **(Spectrum No. 30)**

Analysis **:** for $C_{35}H_{27}N$

Calculated: C, 91.07%; H, 5.90%; N, 3.30%

Found: C, 91.02%; H, 5.89%; N, 3.27%

GCMS **:** *m/z* = 461



199b

Yield **:** 82% (0.42 g)

Mp : 182-184 ^{o}C

IR (KBr) **:** $\tilde{\nu}$ = 3065, 3032, 2932, 1660, 1458 cm^{-1}

^{1}H NMR **:** (400 MHz, $CDCl_3$) δ = 7.23-7.17 (m, 18H), 6.73-6.98 (m, 5H), 5.14 (s, 2H), 1.3 (s, 6H) *ppm* **(Spectrum No. 31)**

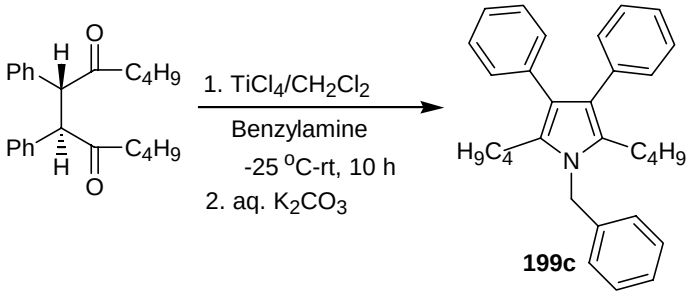
^{13}C NMR **:** (100 MHz, $CDCl_3$) δ = 158.9, 141.5, 139.5, 135.9, 132.8, 131.5, 130.9, 128.8, 128.6, 128.5, 128.4, 128.3, 128.2, 127.5, 127.2, 127.0, 126.7, 126.0, 125.1, 125.0, 122.4, 118.9, 113.5, 55.1, 48.1 *ppm* **(Spectrum No. 32)**

Analysis **:** for $C_{37}H_{31}NO_2$

Calculated: C, 85.19%; H, 5.99%; N, 2.69%; O, 6.13%

Found: C, 85.18%; H, 5.93%; N, 2.67%

LCMS : *m/z* = 521



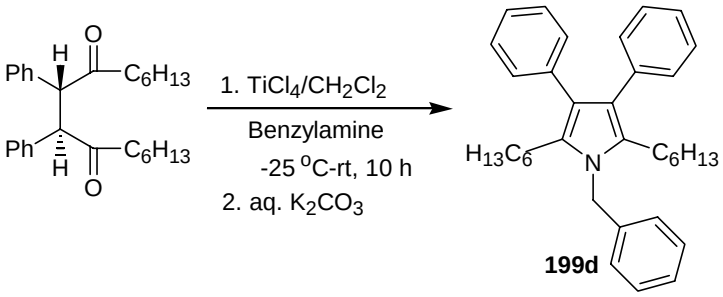
199c

Yield **:** 75% (0.31 g)

IR (neat) **:** $\tilde{\nu}$ = 3065, 3037, 2928, 1665, 1462 cm^{-1}

^{1}H NMR **:** (400 MHz, $CDCl_3$) δ = 7.48-7.32 (m, 10H), 6.22 (m, 5H), 5.12 (s, 2H), 3.12 (t, *J* = 6.7 Hz, 4H), 1.67-1.63 (m, 4H), 1.35-1.33 (m, 4H), 1.12 (t, *J* = 7.6 Hz, 6H) *ppm*

^{13}C NMR **:** (100 MHz, $CDCl_3$) δ = 138.6, 137.5, 132.4, 130.5, 129.7, 129.3, 128.5, 128.3, 127.4, 124.7, 54.8, 36.5, 24.5, 19.3, 14.6 *ppm*



199d

Yield **:** 62% (0.29 g)

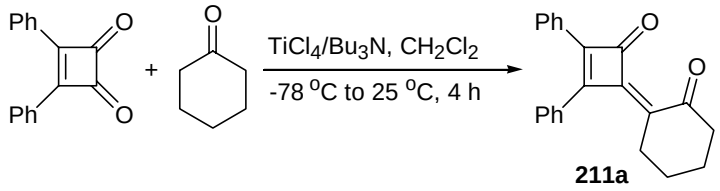
IR (neat) **:** $\tilde{\nu}$ = 3048, 3036, 2933, 1666, 1467 cm^{-1}

^{1}H NMR **:** (400 MHz, $CDCl_3$) δ = 7.45-7.31 (m, 10H), 6.25 (m, 5H), 5.09 (s, 2H), 3.17 (t, *J* = 6.8 Hz, 4H), 2.35 (m, 8H), 1.66-1.64 (m, 4H), 1.34-1.31 (m, 4H), 1.11 (t, *J* = 7.5 Hz, 6H) *ppm*

^{13}C NMR **:** (100 MHz, $CDCl_3$) δ = 138.9, 137.2, 132.5, 130.7, 129.6, 129.5, 128.7, 128.4, 127.2, 124.8, 54.7, 36.5, 24.5, 22.9, 21.7, 19.3, 14.6 *ppm*

3.15 $TiCl_4/Bu_3N$ Promoted Reaction of Ketones with Diphenylcycobutenedione

$TiCl_4$ (0.13 mL of 1:1 solution of $TiCl_4/CH_2Cl_2$, 1.2 mmol) was added drop-wise to a solution of cyclohexanone (0.10 g, 1.1 mmol) in CH_2Cl_2 (5 mL) at –78 ºC under N_2 atmosphere (the contents become yellow slurry). After 5 min. of stirring, Bu_3N (0.28 g, 1.5 mmol) was added drop-wise and the resulting deep red solution was stirred at –78 ºC under N_2 for 1.5 h. After the drop-wise addition of 3,4-diphenylcyclobutenedione (0.234 g, 1 mmol) in CH_2Cl_2 (2 mL), stirring was continued at the same temperature for 3 h. The reaction mixture was brought to 25 ^oC, quenched by addition of 2 mL water and the solvent was removed under reduced pressure. The crude mixture was washed with dilute HCl and aqueous layer was extracted with ether. The product **211** was isolated using column chromatography (silica gel, hexane/ethyl acetate 97:3).



211a

Yield **:** 83% (0.26 g)

Mp **:** 214-216 ^oC

IR (KBr) **:** $\tilde{\nu}$ = 3059, 2939, 1759, 1697 cm^{-1}

^{1}H NMR **:** (400 MHz, $CDCl_3$) δ = 7.74-7.28 (m, 10H), 3.08 (t, J = 6.6 Hz, 2H), 2.43 (t, J = 7.3 Hz, 2H), 1.94-1.85 (m, 4H) *ppm* **(Spectrum No. 33)**

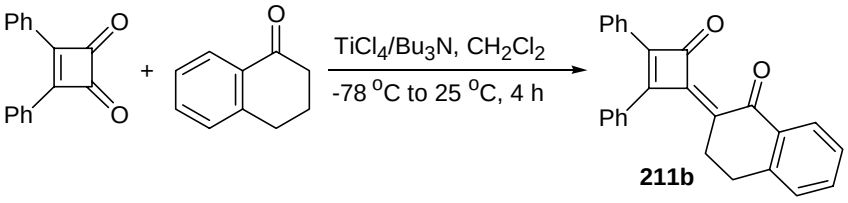
^{13}C NMR **:** (50 MHz, $CDCl_3$) δ = 200.0, 188.5, 176.3, 161.6, 151.4, 132.7, 130.7, 129.8, 128.8, 128.1, 127.8, 126.8, 125.6, 42.2, 42.0, 29.5, 29.1, 24.6 *ppm* **(Spectrum No. 34)**

Analysis **:** for $C_{22}H_{18}O_2$

Calculated: C, 84.05%; H, 5.77%; O, 10.18%

Found: C, 84.02%; H, 5.73%

GCMS **:** *m/z* = 314



211b

Yield **:** 92% (0.33 g)

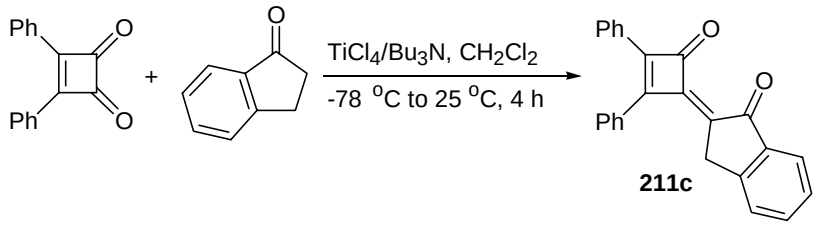
Mp **:** 235-237 ^{o}C

IR (KBr) **:** $\tilde{\nu}$ = 3067, 2926, 1778, 1687 cm^{-1}

^{1}H NMR **:** (400 MHz, $CDCl_3$) δ = 7.89-7.32 (m, 14H), 3.27 (t, *J* = 6.7 Hz, 2H), 2.59 (t, *J* = 7.2 Hz, 2H) *ppm*

^{13}C NMR **:** (100 MHz, $CDCl_3$) δ = 196.4, 187.6, 158.7, 153.5, 148.6, 140.6, 138.4, 133.7, 133.2, 130.8, 129.7, 129.3, 128.6, 128.5, 128.4, 127.6, 127.2, 126.7, 126.6, 126.8, 125.5, 125.3, 123.9, 30.9, 28.6 *ppm*

GCMS **:** *m/z* = 362



Yield **:** 84% (0.29 g)

Mp **:** 226-228 ^{o}C

IR (KBr) **:** $\tilde{\nu}$ = 3069, 2914, 1778, 1676 cm^{-1}

^{1}H NMR **:** (400 MHz, $CDCl_3$) δ = 8.07-7.32 (m, 14H), 3.96 (s, 2H) *ppm* **(Spectrum No. 35)**

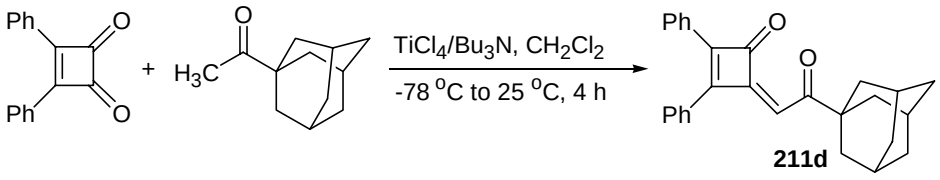
^{13}C NMR **:** (100 MHz, $CDCl_3$) δ = 195.2, 187.4, 155.0, 151.7, 148.6, 140.8, 139.5, 133.6, 133.4, 130.4, 129.7, 129.3, 128.9, 128.2, 128.1, 127.9, 127.3, 126.9, 126.3, 125.9, 125.9, 125.7, 123.6, 30.9 *ppm* **(Spectrum No. 36)**

Analysis **:** for $C_{25}H_{16}O_2$

Calculated: C, 86.19%; H, 4.63%; O, 9.18%

Found: C, 86.16%; H, 4.62%

GCMS **:** *m/z* = 348



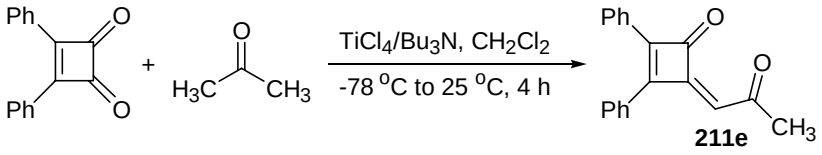
Yield **:** 38% (0.15 g)

IR (neat) **:** $\tilde{\nu}$ = 3058, 2908, 2850, 1770, 1639 cm^{-1}

^{1}H NMR **:** (200 MHz, $CDCl_3$) δ = 7.72-7.30 (m, 10H), 6.27 (s, 1H), 2.04-1.26 (m, 15H) *ppm*

^{13}C NMR **:** (50 MHz, $CDCl_3$) δ = 202.7, 182.4, 172.2, 164.4, 162.5, 131.5, 131.2, 128.9, 128.1, 108.4, 46.1, 38.3, 36.6, 28.0 *ppm*

GCMS **:** *m/z* = 394



211e

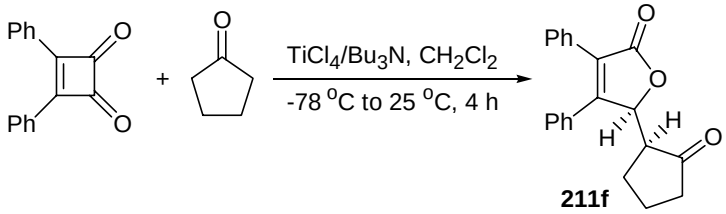
Yield **:** 42% (0.11 g)

IR (neat) **:** $\tilde{\nu}$ = 3061, 2961, 2860, 1770, 1674 cm^{-1}

^{1}H NMR **:** (200 MHz, $CDCl_3$) δ = 7.47-7.12 (m, 10H), 6.79 (s, 1H), 2.38 (s, 3H) *ppm*

^{13}C NMR **:** (50 MHz, $CDCl_3$) δ = 201.7, 189.4, 172.2, 165.4, 163.2, 138.3, 133.5, 130.6, 128.9, 128.6, 109.9, 48.8, 29.7 *ppm*

GCMS **:** *m/z* = 274



211f

Yield **:** 48% (0.16 g)

Mp **:** 212-215 °C

IR (KBr) **:** $\tilde{\nu}$ = 3059, 2957, 1765, 1703, 1645 cm^{-1}

^{1}H NMR **:** (200 MHz, $CDCl_3$) δ = 7.75–7.22 (m, 10H), 5.28 (d, *J* = 4.8 Hz, 1H), 3.23 (d, *J* = 4.9 Hz, 1H), 3.09 (t, *J* = 7.3 Hz, 2H), 2.35–2.23 (m, 2H), 1.88-1.86 (m, 2H) *ppm*

^{13}C NMR **:** (50 MHz, $CDCl_3$) δ = 206.5, 186.7, 148.9, 148.2, 139.0, 131.0, 130.4, 130.2, 129.6, 129.4, 128.9, 128.7, 128.3, 127.8, 127.7, 127.5, 127.1, 126.9, 123.1, 68.7, 54.2, 38.9, 30.4, 24.9 *ppm*

Analysis **:** for $C_{21}H_{18}O_3$

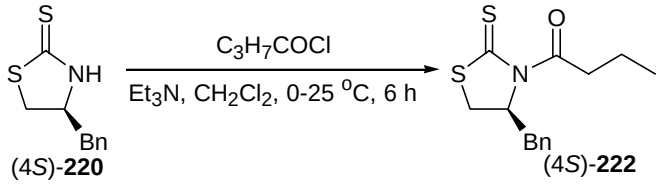
Calculated: 79.22%; H, 5.70%; O, 15.08%

Found: 79.18%; H, 5.58%

GCMS **:** *m/z* = 318

3.16 Procedure for the Synthesis of *N*-butanoylthiazolidinethione

To a solution of thiazolidinethione (4*S*)-**220** (2.09 g, 10 mmol) in CH_2Cl_2 (30 mL) was added freshly distilled butanoyl chloride (1.17g, 11 mmol) at 0 ^oC under N_2 atmosphere. Triethylamine (1.2 g, 1.7 mL, 12 mmol) in CH_2Cl_2 (10 mL) was added drop-wise over 10 min at 0 ^oC and the reaction was stirred at 25 ^oC for 6 h. The contents were diluted with CH_2Cl_2 (40 mL) and washed successively with saturated aq. sodium bicarbonate (20 mL) and then brine (15 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated in vacuum. The crude product was purified on a silica column using hexane/ethyl acetate (90:10) mixture as eluent.



(4*S*)-**220** (4*S*)-**222**

Yield **:** 78% (2.17 g)

IR (neat) **:** $\tilde{\nu}$ = 3028, 2964, 1757, 1697, 1602 cm^{-1}

^{1}H NMR **:** (400 MHz, $CDCl_3$) δ = 7.36-7.26 (m, 5H), 5.40-5.34 (m, 1H), 3.35 (d, *J* = 3.2 Hz, 2H), 3.22 (d, *J* = 3.6 Hz, 2H), 3.13 (t, *J* = 6.0 Hz, 2H), 1.77-1.70 (m, 2H), 0.98 (t, *J* = 7.2 Hz, 3H) *ppm*

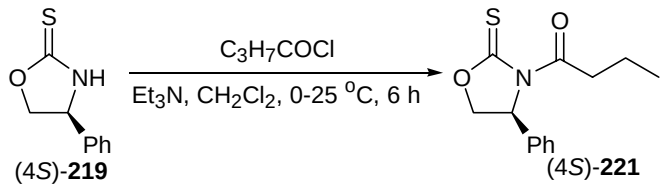
^{13}C NMR **:** (100 MHz, $CDCl_3$) δ = 201.1, 174.0, 136.6, 129.5, 128.9, 127.2, 68.6, 40.4, 36.8, 31.9, 18.2, 13.7 *ppm*

Analysis **:** for $C_{14}H_{17}NOS_2$

Calculated: C, 60.18%; H, 6.13%; N, 5.01%; O, 5.73%; S, 22.95%

Found: C, 60.16%; H, 6.12%; N, 4.98%

GCMS **:** *m/z* = 279



(4*S*)-**219** (4*S*)-**221**

Yield **:** 82% (2.04 g)

IR (neat) **:** $\tilde{\nu}$ = 2964, 2874, 1778, 1705 cm^{-1}

^{1}H NMR **:** (400 MHz, $CDCl_3$) δ = 7.44-7.28 (m, 5H), 4.82-4.77 (t, *J* = 3.2 Hz, 1H), 4.46-4.43 (d, *J* = 3.7 Hz, 2H), 1.69-1.62 (m, 2H), 1.30-1.27 (t, *J* = 5.9 Hz, 2H), 0.96-0.94 (t, *J* = 7.3 Hz, 2H) *ppm*

^{13}C NMR **:** (50 MHz, $CDCl_3$) δ = 173.5, 138.8, 129.2, 128.8, 127.6, 125.9, 73.9, 62.1, 39.4, 17.8, 13.4 *ppm*

Analysis **:** for $C_{13}H_{15}NO_2S$

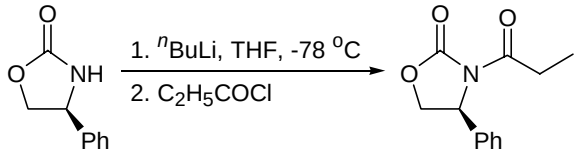
Calculated: C, 62.62%; H, 6.06%; N, 5.62%; O, 12.83%; S, 12.86 %

Found: C, 62.64%; H, 6.04%; N, 5.64%

GCMS **:** *m/z* = 249

3.17 Procedure for the Synthesis of *N*-propenoyloxazolidinone

To a solution of oxazolidinone (4*S*)-**223** (1.77 g, 10 mmol) in anhydrous THF (30 mmol) was added *n*-butyllithium (6.2 mL, 1.6 M solution in hexane, 10 mmol) at –78 ^{o}C under N_2 atmosphere. After 15 min, freshly distilled propenoyl chloride (1.0 g, 11 mmol) was added. The reaction mixture was stirred at –78 ^{o}C for 30 min and at 0 ^{o}C for 15 min. It was quenched with excess saturated aqueous ammonium chloride (15 mL), and the resultant slurry was concentrated in vacuum. The residue was diluted with ether (60 mL) and washed successively with saturated aqueous sodium bicarbonate (20 mL) and then saturated aqueous sodium chloride (15 mL). The organic extract was dried over Na_2SO_4, filtered and concentrated in vacuum. The crude product was purified on a silica column using hexane/ethyl acetate (90:10) mixture as eluent.



(4*S*)-**223** (4*S*)-**224**

Yield : 72% (1.57 g)

IR (neat) : $\tilde{\nu}$ = 3034, 2982, 1784, 1712 cm^{-1}

^{1}H NMR : (400 MHz, $CDCl_3$) δ = 7.38-7.27 (m, 5H), 5.44-5.37 (t, *J* = 3.3 Hz, 1H), 4.70 (d, *J* = 3.7 Hz, 2H), 12.94-12.91 (m, 2H), 1.12 (t, *J* = 7.1 Hz, 3H) *ppm*

^{13}C NMR : (50 MHz, $CDCl_3$) δ = 173.4, 153.8, 139.3, 129.1, 128.6, 125.9, 70.0, 57.5, 29.1, 8.1 *ppm*

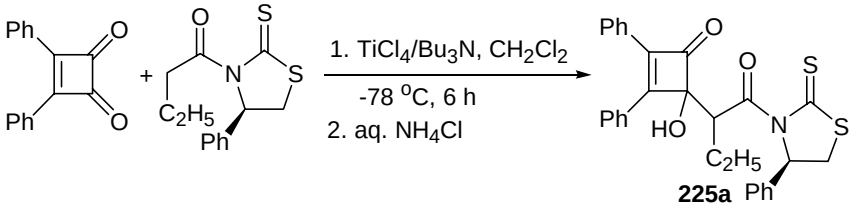
Analysis : for $C_{12}H_{13}NO_3$

Calculated: C, 65.74%; H, 5.98%; N, 6.39%; O, 21.89%

Found: C, 65.76%; H, 5.96%; N, 6.35%

3.18 $TiCl_4/Bu_3N$ Promoted Reaction of Acylthiazolidinonethione, Acyloxazolidinonethione and Acyloxazolidinone with Diphenylcyclobutenedione

$TiCl_4$ (0.13 mL of 1:1 solution of $TiCl_4/CH_2Cl_2$, 1.2 mmol) was added drop-wise to a solution of *N*-acyl-(4*S*)-phenyl-2-thiazolidinethione (0.30 g, 1.1 mmol) in CH_2Cl_2 (5 mL) at –78 ºC under N_2 atmosphere. After 5 min. of stirring, Bu_3N (0.28 g, 1.5 mmol) was added drop-wise and the resulting deep red solution is stirred at –78 ºC under N_2 for 1.5 h. After the drop-wise addition of 3,4-diphenylcyclobutenedione (0.234 g, 1 mmol) in CH_2Cl_2 (2 mL), stirring was continued at the same temperature for 3 h. The reaction was quenched by addition of 2 mL aq. NH_4Cl at low temperature and the solvent was removed under reduced pressure. The crude mixture was washed with dilute HCl and aqueous layer was extracted with ether. The product was isolated using column chromatography (silica gel, hexane/ethyl acetate 94:6).



225a

Yield : 68% (0.34 g)

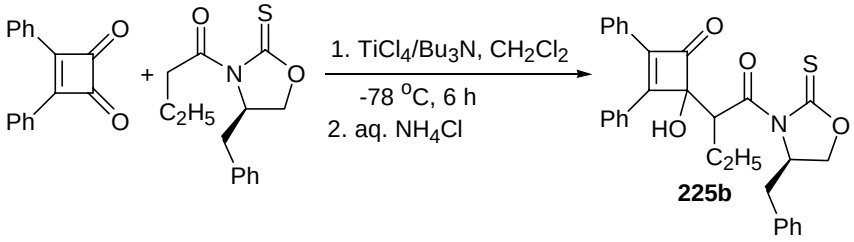
IR (neat) : $\tilde{\nu}$ = 3308, 2966, 1736, 1647 cm^{-1}

^{1}H NMR : (200 MHz, $CDCl_3$) δ = 7.46-6.93 (m, 15H), 3.75 (t, *J* = 7.6 Hz, 1H), 2.81 (s, 1H), 2.31 (t, *J* = 7.7 Hz, 1H), 2.15-1.98 (m, 4H), 1.21 (t, *J* = 7.8 Hz, 3H) *ppm*

^{13}C NMR : (50 MHz, $CDCl_3$) δ = 203.6, 191.9, 174.5, 171.1, 167.2, 147.0, 138.2, 131.4, 130.9, 129.5, 129.2, 128.8, 128.6, 128.4, 127.8,

126.1, 125.4, 95.6 (major) 69.8, 60.4, 48.2, 36.7, 24.0, 11.72 (minor) 67.6, 54.8, 41.2, 30.2, 20.9, 14.1 *ppm*

GCMS : *m/z* = 499



225b

Yield : 56% (0.28 g)

IR (neat) : $\tilde{\nu}$ = 3416, 2961, 1755, 1697 cm^{-1}

^{1}H NMR : (200 MHz, $CDCl_3$) δ = 8.26-6.98 (m, 15H), 3.35 (t, *J* = 7.7 Hz, 1H), 2.81 (s, 1H), 2.33 (t, *J* = 8.1 Hz, 1H), 2.02-1.98 (m, 5H), 1.23 (t, *J* = 7.8, Hz, 3H) *ppm* **(Spectrum No. 37)**

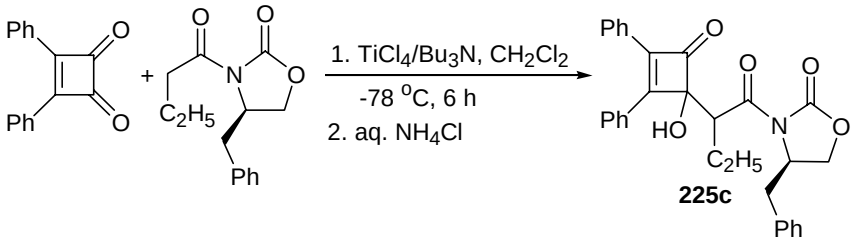
^{13}C NMR : (50 MHz, $CDCl_3$) δ = 201.1, 187.5, 173.9, 158.4, 149.9, 136.6, 133.4, 130.9, 130.7, 129.9, 129.5, 129.3, 129.0, 128.9, 128.5, 128.2, 127.2, 125.3, 86.6, 68.6, 40.3, 36.8, 31.9, 18.2, 13.6 *ppm* **(Spectrum No. 38)**

Analysis : for $C_{30}H_{27}NO_4S$

Calculated: C, 72.41%; H, 5.47%; N, 2.81%; O, 12.86%; S, 6.44%

Found: C, 72.12%; H, 5.32%; N, 2.68%

GCMS : *m/z* = 497



225c

Yield : 55% (0.27 g)

IR (neat) : $\tilde{\nu}$ = 3416, 2961, 1755, 1697 cm^{-1}

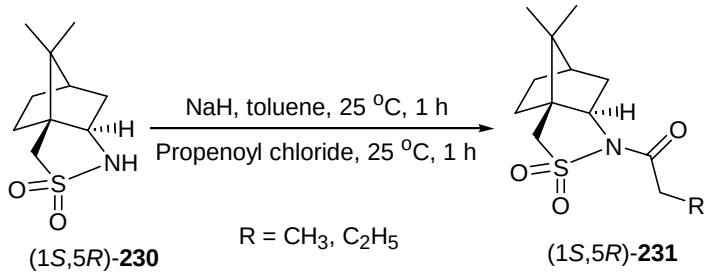
^{1}H NMR : (200 MHz, $CDCl_3$) δ = 8.19-6.70 (m, 15H), 4.11 (t, J = 7.6 Hz, 1H), 2.28 (m, 1H), 2.03 (s, 1H), 1.30-1.24 (m, 4H), 1.12 (t, J = 7.8 Hz, 3H) *ppm*

^{13}C NMR : (50 MHz, $CDCl_3$) δ = 203.6, 191.9, 174.5, 167.2, 147.0, 138.2, 131.2, 130.8, 129.7, 129.3, 129.0, 128.8, 128.5, 127.9, 127.7,127.3, 126.4, 126.2, 125.9, 125.7, 96.4, 73.9, 60.1, 43.2, 32.7, 21.4, 14.5 *ppm*

GCMS : *m/z* = 481

3.19 Procedure for the Synthesis of (1*S*,5*R*)-*N*-Propenoylcamphorsultam

A solution of camphorsultam (1*S*,5*R*)-**230** (0.86 g, 4 mmol) in toluene (20 mL) was added drop-wise at 25 ^oC to a stirred suspension of NaH (0.24 g, 60% dispersion in mineral oil, 6 mmol). After 1 h a solution of propenoyl chloride (0.74 g, 8 mmol) in toluene (20 mL) was added slowly and the mixture was stirred at room temperature for 3 h. The reaction was quenched with water and the organic phase was separated. The aqueous phase was extracted with CH_2Cl_2 (2 x 10 mL). The combined organic extract was dried over Na_2SO_4, filtered and concentrated. The crude product was purified on a silica column using hexane/ethyl acetate (88:12) mixture as eluent.



(1*S*,5*R*)-**230** (1*S*,5*R*)-**231**

Yield **:** 42% (0.45 g)

IR (KBr) **:** $\tilde{\nu}$ = 2964, 2887, 1765, 1709 cm^{-1}

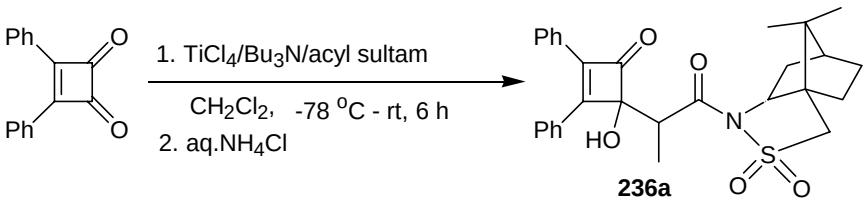
^{1}H NMR **:** (400 MHz, $CDCl_3$) δ = 3.85-3.82 (t, J = 7.2 Hz, 1H), 3.48-3.38 (q, J_1 = 13.8 Hz, J_2 = 12.5 Hz, 1H), 2.72 (q, J_1 = 7.2 Hz, J_2 = 5.8 Hz, 2H), 2.12 (s, 1H), 2.09-2.04 (m, 2H),1.87 (t, J = 7.5 Hz, 2H), 1.36 (d, J = 8.0 Hz, 2H),1.15 (s, 6H), 0.94 (s, 3H) *ppm*

^{13}C NMR **:** (50 MHz, $CDCl_3$) δ = 172.7, 65.3, 52.9, 48.47, 47.7, 44.7, 38.5, 32.8, 30.8, 28.9, 26.4, 20.8, 19.9, 8.4 *ppm*

GCMS **:** *m/z* = 271

3.20 $TiCl_4/Bu_3N$ Promoted Reaction of Acylcamphorsultam with Diphenylcyclobutenedione

$TiCl_4$ (0.13 mL of 1:1 solution of $TiCl_4/CH_2Cl_2$, 1.2 mmol) was added drop-wise to a solution of *N*-acylcamphorsultam (0.29 g, 1.1 mmol) in CH_2Cl_2 5 mL at –78 ºC under N_2 atmosphere (the contents become yellow slurry). After 5 min. of stirring, Bu_3N (0.28 g, 1.5 mmol) was added-drop wise and the resulting deep red solution was stirred at –78 ºC under N_2 for 1.5 h. After the drop-wise addition of 3,4-diphenylcyclobutenedione (0.234 g, 1 mmol) in CH_2Cl_2 (2 mL), stirring was continued at the same temperature for 3 h. The reaction was quenched by addition of 2 mL water at low temperature and the solvent was removed under reduced pressure. The crude mixture was washed with dilute HCl and aqueous layer was extracted with ether. The product was isolated using column chromatography (silica gel, hexane/ethyl acetate 94:6).



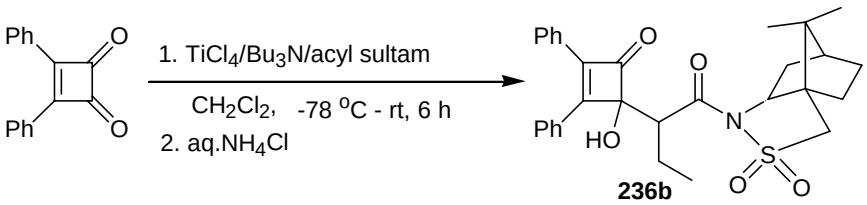
236a

Yield **:** 68% (0.35 g)

IR (neat) **:** $\tilde{\nu}$ = 3328, 3037, 2968, 1758, 1707 cm^{-1}

^{1}H NMR **:** (200 MHz, $CDCl_3$) δ = 7.36-7.11 (m, 10H), 3.84-3.26 (m, 8H), 2.22-1.86 (m, 10H), 1.24-0.97 (m, 7H) *ppm* **(Spectrum No. 39)**

^{13}C NMR **:** (50 MHz, $CDCl_3$) δ = 191.8, 173.6, 167.3, 146.4, 131.3, 129.6, 128.9, 128.7, 128.5, 128.1, 127.9, 95.0, 65.3, 53.0, 48.3, 47.7, 44.7, 44.0, 38.0, 32.9, 26.4, 20.5, 19.9, 13.5 *ppm* **(Spectrum No. 40)**



236b

Yield **:** 65% (0.34 g)

IR (neat) **:** $\tilde{\nu}$ = 3323, 3034, 2964, 1761, 1709 cm^{-1}

^{1}H NMR **:** (200 MHz, $CDCl_3$) δ = 7.83-7.26 (m, 10H), 3.82-3.06 (m, 8H), 2.01-1.8 (m, 10H), 1.34-1.0 (m, 6H), 0.97 (t, J = 5.8 Hz, 3H) *ppm*

^{13}C NMR **:** (50 MHz, $CDCl_3$) δ = 191.8, 173.7, 167.5, 146.4, 131.1, 129.6, 129.2, 128.9, 128.8, 128.6, 128.4, 127.8, 95.0, 65.3, 53.1, 48.3, 47.7, 44.7, 43.8, 38.0, 32.9, 26.4, 20.9, 20.5, 19.9, 13.4 *ppm*

Analysis **:** for $C_{31}H_{37}NO_5S$

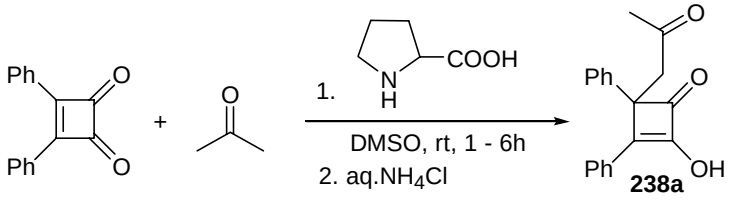
Calculated: C, 69.50%; H, 6.96%; N, 2.61%, O, 14.93%, S, 5.99%

Found: C, 69.52%; H, 6.94%; N, 2.62%

GCMS : *m/z* = 535

3.21 Proline Catalyzed Reaction of Acetone with Cyclobutenediones

To a solution of L-proline (0.46 g, 4 mmol) in DMSO (5 mL), acetone (0.23 g, 4 mmol) was added and stirred for 1 h at 25 ^{o}C under N_2 atmosphere. The 3,4-diphenylcyclobutenedione (0.234 g, 1 mmol) dissolved in DMSO (2 mL) and added to the reaction mixture. The reaction was allowed to stirr for 5 h at 25 ^{o}C and quenched with saturated NH_4Cl, the organic layer was extracted with ethyl acetate, washed with brine solution, dried over $MgSO_4$ and concentrated at reduced pressure. The residue was subjected to column chromatography on silica gel and the product was eluted using hexane/ethyl acetate 94:6.



238a

Yield : 76% (0.20 g)

Mp : 148-150 ^{o}C

IR (KBr) : $\tilde{\nu}$ = 3163, 1743, 1645 cm^{-1}

^{1}H NMR : (200 MHz, $CDCl_3$) δ = 9.18 (s, 1H), 7.73-7.28 (m, 10H), 3.47 (d, *J* = 9.8 Hz, 2H), 2.06 (d, *J* = 8.8 Hz, 3H) *ppm* **(Spectrum No. 41)**

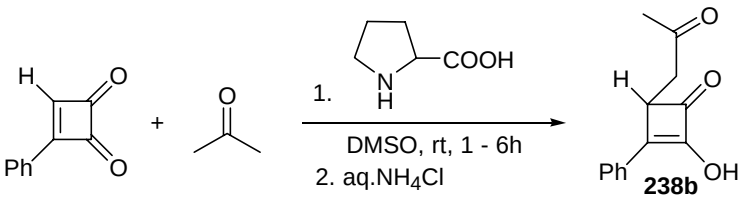
^{13}C NMR : (50 MHz, $CDCl_3$) δ = 206.6, 188.9, 147.9, 143.5, 139.6, 133.5, 129.8, 129.0, 128.8, 128.6, 128.4, 127.4, 126.4, 62.9, 45.3, 31.7, **(Spectrum No. 42)**

Analysis : for $C_{19}H_{16}O_3$

Calculated: C, 78.06%; H, 5.52%; O, 16.42%

Found: C, 77.99%; H, 5.52%

LCMS **:** *m/z* = 293

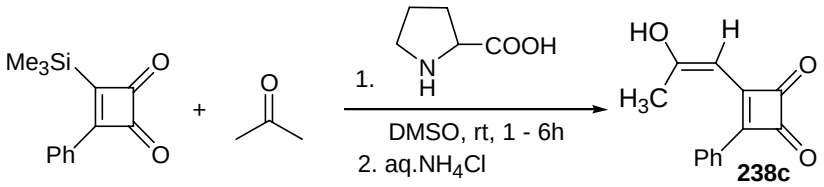


Yield **:** 52% (0.11 g)

IR (neat) **:** $\tilde{\nu}$ = 3286, 1748, 1642 cm^{-1}

^{1}H NMR **:** (400 MHz, $CDCl_3$) δ = 9.05 (s, 1H), 7.61-7.15 (m, 5H), 3.37 (t, *J* = 9.6 Hz, 1H), 3.19 (d, *J* = 8.9 Hz, 2H), 1.97 (s, 3H) *ppm*

^{13}C NMR **:** (100 MHz, $CDCl_3$) δ = 207.4, 189.6, 153.7, 138.5, 112.7, 129.5, 128.3, 127.7, 57.5, 46.3, 29.7 *ppm*



Yield **:** 65% (0.18 g)

IR (neat) **:** $\tilde{\nu}$ = 3243, 1745, 1647 cm^{-1}

^{1}H NMR **:** (400 MHz, $CDCl_3$) δ = 11.44 (s, 1H), 8.02-7.53 (m, 5H), 5.84 (s, 1H), 2.23 (s, 3H) *ppm*

^{13}C NMR **:** (100 MHz, $CDCl_3$) δ = 202.8, 188.6, 182.4, 178.5, 176.9, 134.1, 132.9, 129.5, 129.4, 129.3, 128.8, 128.3, 92.9, 23.2 *ppm*

LCMS **:** *m/z* = 214

References

1. (a) Smutny, E. J.; Roberts, J. D. *J. Am. Chem. Soc.* **1955**, *77*, 3420. (b) Smutny, E. J.; Caserio, M. C.; Roberts, J. D. *J. Am. Chem. Soc.* **1960**, *82*, 1793. (c) Cava, M. P.; Mitchel, M. J. *Cyclobutadiene and Related Compounds*, Academic Press, New York, **1967**.

2. (a) Schmidt, A. H.; Ried, W. *Synthesis* **1978**, 1. (b) Knorr, H.; Ried, W. *Synthesis* **1978**, 649. (c) Schmidt, A. H.; Ried, W. *Synthesis* **1978**, 869. (d) Schmidt, A. H. *Synthesis* **1980**, 961.

3. (a) West, R.; Niu, J. *Non-Benzenoid Aromatics*, Academic Press, New York, **1969**, Vol. *1*, p132. (b) West, R.; Niu, H. Y.; Powell, D. L.; Evans, M. V. *J. Am. Chem. Soc.* **1960**, *82*, 6204. (c) West, R.; Powell, D. L. *J. Am. Chem. Soc.* **1963**, *85*, 2577. (d) Ito, M.; West, R. *J. Am. Chem. Soc.* **1963**, *85*, 2580.

4. Cole, R. J.; Kirksey, J. W.; Cutlar, H. G.; Doupnik, B. L.; Peckham, J. C. *Science* **1973**, *179*, 1324. (b) Sringer, J. P.; Clardy, J.; Cole, R. J.; Kirksey, J. W.; Hill, R. K.; Carlson, R. M.; Isidor, J. *J. Am. Chem. Soc.* **1974**, *96*, 2267. (c) Pirrung, M. C.; Nauhaus, S. K.; Sing, B. *J. Org. Chem.* **1996**, *61*, 2592.

5. Tietze, L. F.; Arlt, M.; Beller, M.; Glusenkamp, K. H.; Jahde, E.; Rajewsky, M. F. *Chem. Ber.* **1991**, *124*, 1215.

6. (a) Gardner, S. H.; Freyschmidt-paul, P.; Hoffman, R.; Sundberg, J. P.; Happle, R.; Nigel, J.; Tobin, D. J. *Eur. J. Dermatol.* **2000**, *10*, 443. (b) Freyschmidt-paul, P.; Sundberg, J. P.; Happle, R.; McElwee, K. J.; Metz, S.; Boggess, D.; Hoffman, R. J. *Investigative Dermatol.* **1999**, *113*, 61. (c) Kazumasa, M.;

Motonobu, N.; Miyako, N.; Tatsuo, K.; Yoshiki, M. *J. Dermatol.* **2002**, *29*, 661. (d) Silverberg, N. B.; Lim, J. K.; Paller, A. S.; Mancini, A. J. *J. Acad. Dermatol.* **2000**, *42*, 803.

7. Douglas, K. T.; Nadvi, I. N. *FEBS Lett.* **1979**, *106*, 393.
8. Burka, L. T.; Doran, J.; Wilson, B. *J. Biochem. Pharmacol.* **1982**, *31*, 79.
9. Xie, J.; Comeau, A. B.; Seto, C. T. *Org. Lett.* **2004**, *6*, 83.
10. Hinshaw, J. C. *Chem. Commun.* **1971**, 630.
11. Bellus, D.; Ernst, B. *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 797.
12. Periasamy, M.; Radhakrishnan, U.; Brunet, J. J.; Chauvin, R.; Elzaizi, A. *Chem. Commun*. **1996**, 1499.
13. Periasamy, M.; Rameshkumar, C.; Radhakrishnan, U. *Tetrahedron Lett*. **1997**, *38*, 7229.
14. Periasamy, M.; Rameshkumar, C. *Organometallics* **2000**, *19*, 4200.
15. Periasamy, M.; Rameshkumar, C. *Tetrahedron Lett.* **2000**, *41*, 2719.
16. Periasamy, M.; Rameshkumar, C.; Mukkanti A. *J. Organomet. Chem.* **2002,** *649*, 209.
17. Periasamy, M.; Mukkanti, A.; Shyam Raj, D. *Organometallics* **2004**, *23*, 619.
18. Periasamy, M.; Mukkanti, A.; Shyam Raj, D. *Organometallics* **2004**, *23*, 6323.
19. Ried, W.; Schmidt, A. H. *Tetrahedron Lett.* **1969**, *19*, 1443.
20. Peter, W.; Corey, R. H. *J. Org. Chem.* **1999**, *64*, 6881.
21. Ried, W.; Schmidt, A. H. *Liebigs Ann. Chem.* **1970**, *742*, 116.
22. Lunelli, B. *Tetrahedron Lett.* **2007**, *48*, 3595.
23. Ried, W.; Dietrich, P. S. *Chem. Ber.* **1969**, *102*, 4193.

24. Liebeskind, L. S.; Yu, M. S.; Fengl, R. W. *J. Org. Chem.* **1993**, *58*, 3543.

25. Kinney, W. A. *Tetrahedron Lett.* **1993**, *34*, 2715.

26. (a) Liebeskind, L. S.; Zhang, J. *J. Org. Chem.* **1991**, *56*, 6379. (b) Liebeskind, L. S.; Yu, M. S.; Yu, R. H.; Wang, J.; Hagen, K. S. *J. Am. Chem. Soc.* **1993**, *115*, 9048.

27. Shi, X.; Amin, Sk. R.; Liebeskind, L. S. *J. Org. Chem.* **2000**, *65*, 1650.

28. (a) Liebeskind, L. S.; Mitchell, D.; Foster, B. S. *J. Am. Chem. Soc*. **1987**, *109*, 7908. (b) Liebeskind, L. S.; Bombrun, A. *J. Org. Chem*. **1994**, *59*, 1149.

29. Periasamy, M.; Rameshkumar, C.; Radhakrishnan, U.; Brunet, J. J. *J. Org. Chem***. 1998**, *63*, 4930.

30. Mitchell, D.; Liebeskind, L. S. *J. Am. Chem. Soc*. **1990**, *112*, 291.

31. West, R.; Niu, H. Y.; Ito, M. *J. Am. Chem. Soc.* **1963**, *85*, 2584.

32. Maahs, G.; Hegenberg, P. *Angew. Chem. Int. Ed. Engl.* **1966**, *5*, 888.

33. Chapman, O. L.; McIntosh, C. L.; Barber, L. L. *Chem. Commun.* **1971**, 1162.

34. Miller, R. D.; Kirchmeyer, S. *J. Org. Chem*. **1993**, *58*, 90.

35. Obata, N.; Takizawa, T. *Chem. Commun*. **1971**, 587.

36. Verniest, G.; Kimpe, N. D. *Synlett* **2005**, *6*, 947.

37. Blomquist, A. T.; LaLancette, E. A. *J. Org. Chem*. **1964**, *29*, 2331.

38. Wang, J.; Jiang, X.; Chen, M.; Ge, Z.; Hu, Y.; Hu, H. *J. Chem. Soc., Perkin Trans*. *1*, **2001**, 66.

39. Jian, X.; Anthony, B.; Comeau; Seto, C. T. *Org. Lett.* **2004**, *6(1)*, 83.

40. Krysan, D. J.; Gurski, A.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1992**, *114(4)*, 1412.

41. Liebeskind, L. S.; Wirtz, K. R. *J. Org. Chem.* **1990**, *55(19)*, 5350.

42. Liebeskind, L. S. *Tetrahedron* **1989**, *45(10)*, 3053.

43. Liebeskind, L. S.; Fengl, R. W.; Wirtz, K. R.; shawe, T. T. *J. Org. Chem.* **1988**, *53(11)*, 2482.

44. Seitz, G.; Morck, H.; Schmiedel, R.; Sutrisno, R. *Synthesis* **1979**, *5*, 361.

45. Huang, W.; Tidwell, T. T. *Synthesis* **2000**, 457.

46. Liebeskind, L. S.; Wirtz, K. R. *J. Org. Chem*. **1990**, *55*, 5350.

47. Regenhardt, W.; Schaumann, E.; Moore, H. W. *Synthesis* **2001**, 1076.

48. Karlsson, J. O.; Nguyen, N. V.; Foland, L. D.; Moore, H. W. *J. Am. Chem. Soc*. **1985**, *107*, 3392.

49. Foland, L. D.; Karlsson, J. O.; Perri, S. T.; Schwabe, R.; Xu, S. L.; Patil, S.; Moore, H. W. *J. Am. Chem. Soc*. **1989**, *111*, 975.

50. Yamamoto, Y.; Noda, M.; Ohno, M.; Eguchi, S. *J. Org. Chem*. **1997**, *62*, 1292.

51. Sun, L.; Liebeskind, L. S. *J. Org. Chem*. **1994**, *59*, 6856.

52. (a) Xu, S. L.; Moore, H. W. *J. Org. Chem.* **1989**, *54*, 6018. (b) Xu, S. L.; Xia, H.; Moore, H. W. *J. Org. Chem.* **1991**, *56*, 6094. (c) Tiedemann, R.; Turnbull, P.; Moore, H. W. *J. Org. Chem.* **1999**, *64*, 4030.

53. (a) Negri, J. T.; Morwick, T.; Doyon, J.; Wilson, P. D.; Hickey, E. R.; Paquette, L. A. *J. Am. Chem. Soc*. **1993**, *115*, 12189. (b) Paquette, L. A.; Morwick, T. *J. Am. Chem. Soc*. **1995**, *117*, 1451.

54. (a) Paquette, L. A.; Kuo, L. H.; Doyon, J. *Tetrahedron* **1996**, *52*, 11625. (b) Paquette, L. A.; Kuo, L. H.; Doyon, J. *J. Am. Chem. Soc*. **1997**, *119*, 3038. (c) Paquette, L. A.; Kuo, L. H.; Tae, J. *J. Org. Chem*. **1998**, *63*, 2010.

55. Paquette, L. A. *Eur. J. Org. Chem*. **1998**, 1709.

56. Paquette, L. A.; Morwick, T. M. *J. Am. Chem. Soc*. **1997**, *119*, 1230.

57. Paquette, L. A.; Kuo, L. H.; Hamme, A. T.; II; Kreuzholz, R.; Doyon, J. *J. Org. Chem*. **1997**, *62*, 1730.

58. (a) Morwick, T.; Doyon, J.; Paquette, L. A. *Tetrahedron Lett*. **1995**, *36*, 2369. (b) Morwick, T. M.; Paquette, L. A. *J. Org. Chem*. **1997**, *62*, 627.

59. (a) Paquette, L. A.; Morwick, T. M.; Negri, J. T.; Rogers, R. D. *Tetrahedron* **1996**, *52*, 3075. (b) Tae, J.; Paquette, L. A. *Can. J. Chem*. **2000**, *78*, 689.

60. Paquette, L. A.; Tae, J. *J. Org. Chem*. **1998**, *63*, 2022.

61. (a) Paquette, L. A.; Doyon, J.; Kuo, L. H. *Tetrahedron Lett*. **1996**, *37*, 3299. (b) Paquette, L. A.; Hamme, A. T.; II; Kuo, L. H.; Doyon, J.; Kreuzholz, R. *J. Am. Chem. Soc*. **1997**, *119*, 1242.

62. Geng, F.; Liu, J.; Paquette, L. A. *Org. Lett.* **2002**, *4*, 71.

63. (a) Murakami, M.; Ito, Y. In *"Activation of Unreactive Bonds and Organic Synthesis"*; Murai, S. Ed.; Springer: New York, **1999**; p 97 (b) Murakami, M.; Amii, H.; Shigeto, K.; Ito, Y. *J. Am. Chem. Soc*. **1996**, *118*, 8285.

64. (a) Liebeskind, L. S.; Baysdon, S. L.; South, M. S.; Iyer, S.; Leeds, J. P. *Tetrahedron* **1985**, *41*, 5839.

65. (a) Burgess, J.; Haines, R. I.; Hamner, E. R.; Kemmitt, R. D. W.; Smith, M. A. R. *J. Chem. Soc., Dalton Trans.* **1975**, 2579 and references therein. (b) Liebeskind, L. S.; Baysdon, S. L.; South, M. S.; Blount, J. F. *J. Organomet. Chem*. **1980**, *202*, 73.

66. (a) Russel, D. R.; Tucker, P. A. *J. Chem. Soc., Dalton Trans*. **1976**, 2181. (b) Litaka, Y.; Oohama, T.; Shiina, M.; Takizawa, T. *J. Chem. Soc., Dalton Trans*. **1987**, 853.

67. Liebeskind, L. S.; Chidambaram, R. *J. Am. Chem. Soc*. **1987**, *109*, 5025.

68. Kondo, T.; Nakamura, A.; Okada, T.; Suzuki, N.; Wada, K.; Mitsudo, T.-a. *J. Am. Chem. Soc* **2000**, *122*, 6319.

69. Zora, M.; Herndon, J. W. *Organometallics* **1993**, *12*, 248.

70. Zora, M.; Herndon, J. W. *J. Org. Chem.* **1994**, *59*, 699.

71. Thompson, R. H. "*Naturally Occurring Quinones*", 2nd ed., Academic Press: New York, **1971** ; p 340. (b) Thompson, R. H. *ibid p* 172. (c) Morton, R. A. "*Biochemistry of Quinones*", 1st Ed., Academic Press: New York, **1965**.

72. (a) Liebeskind, L. S.; Baysdon, S. L.; South, M. S. *J. Am. Chem. Soc*. **1980**, *102*, 7397. (b) Liebeskind, L. S.; Leeds, J. P.; Baysdon, S. L.; Suresh, I. *J. Am. Chem. Soc*. **1984**, *106*, 6451. (c) Iyer, S.; Liebeskind, L. S. *J. Am. Chem. Soc*. **1987**, *109*, 2759.

73. Jung, M. E.; Lowe, J. A. *J. Org. Chem.* **1977**, *42*, 2371.

74. (a) Liebeskind, L. S.; Iyer, S.; Jewell, C. F., Jr. *J. Org. Chem.* **1986**, *51*, 3065. (b) Birchler, A. G.; Lin, F.; Liebeskind, L. S. *J. Org. Chem.* **1994**, *59*, 7737. (c) Liebeskind, L. S.; Granberg, K. L.; Zhang, J. *J. Org. Chem*. **1992**, *57*, 4345. (d) Zhang, D.; Llorente, I.; Liebeskind, L. S. *J. Org. Chem*. **1997**, *62*, 4330. (e) Liu, F.; Liebeskind, L. S. *J. Org. Chem*. **1998**, *63*, 2835.

75. Cabrera, E. P.; Liebeskind, L. S. *J. Org. Chem*. **2002**, *67*, 1689.

76. (a) Perri, S. T.; Foland, L. D.; Decker, O. H. W.; Moore, H. W. *J. Org. Chem.* **1986**, *51*, 3067. (b) Moore, H. W.; Perri, S. T. *J. Org. Chem.* **1988**, *53*, 996. (c) Enhsen, A.; Karabelas, K. Heerding, J. M.; Moore, H. W. *J. Org. Chem.* **1990**, *55*, 1177. (d) Heerding, J. M.; Moore, H. W. *J. Org. Chem.* **1991**, *56*, 4048. (e) Gayo, L. M.; Winters, M. P.; Moore, H. W. *J. Org. Chem.* **1992**, *57*, 6896. (f) Enhsen, A.; Karabelas, K.; Heerding, J. M.; Moore, H W. *J. Org. Chem.* **1990**, *55*, 1177. (g) Moore, H. W.; Yerxa, B. R. *Adv. Strain Org. Chem.* **1995**, *4*, 81. (h) Perri, S. T.; Moore, H. W. *J. Am. Chem. Soc.* **1990**, *112*, 1897. (i) Heileman, M. J.; Tiedemann, R.; Moore, H W. *J. Am. Chem. Soc.* **1998**, *120*, 3801. (j) Moore, H. W.; Yerxa, B. R. *Chemtracts: Org. Chem.* **1992**, *5*, 273.

77. Selwood, D. L.; Jandu, K. S. *Heterocycles* **1988**, *27*, 1191.

78. (a) Xia, H.; Moore, H. W. *J. Org. Chem.* **1992**, *57*, 3765. (b) Xiong, Y.; Xia, H.; Moore, H. W. *J. Org. Chem.* **1995**, *60*, 6460. (c) Xiong, Y.; Moore, H W. *J. Org. Chem.* **1996**, *61*, 9168.

79. (a) Liebeskind, L. S.; Foster, B. S. *J. Am. Chem. Soc.* **1990**, *112*, 8612. (b) Edwards, J. P.; Krysan, D. J.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1993**, *115*, 9868. (c) Liebeskind, L. S.; Riesinger, S. W. *J. Org. Chem.* **1993**, *58*, 408.

80. Mingo, P.; Zhang, S.; Liebeskind, L. S. *J. Org. Chem.* **1999**, *64*, 2145.

81. Zhang, S.; Liebeskind, L. S. *J. Org. Chem.* **1999**, *64*, 4042.

82. (a) Krysan, D. J.; Gurski, A.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1992**, *114*, 1412. (b) Liebeskind, L. S.; Wang, J. *J. Org. Chem.* **1993**, *58*, 3550.

83. Gurski, A.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1993**, *115*, 6101.

84. Ezcurra, J. E.; Moore, H. W. *Tetrahedron Lett.* **1993**, *34*, 6177.

85. (a) Sun, L.; Liebeskind, L. S. *J. Am. Chem. Soc*. **1996**, *118*, 12473. (b) Sun, L.; Liebeskind, L. S. *Tetrahedron Lett*. **1997,** *38*, 3663.

86. Lee, K. H.; Moore, H. W. *J. Org. Chem.* **1995**, *60*, 735.

87. Branda, M.; Goddard, R.; Wey, H. G.; Butenschon, H. *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 267.

88. De Selms, R. C. *Tetrahedron Lett*. **1969**, *10*, 1179.

89. Labille, M. C.; Janousek, Z.; Viehe, H. G. *Tetrahedron* **1991**, *47*, 8161.

90. (a) Sato, K.; Seio, K.; Sekine, M. *J. Am. Chem. Soc.* **2002**, *124*, 12715. (b) Beaulieu, P. L.; Cameron, D. R.; Ferland, J. –M.; Gauthier, J.; Ghiro, E.; Gillard, J.; Gorys; Poirier, M.; Rancourt, J.; Wernic, D.; Llinas-Brunet, M.; Betageri, R.; Cardozo, M.; Hickey, E. R.; Ingraham, R.; Jakes, S.; Kabcenell, A.; Kirrane, T.; Lukas, S.; Patel, U.; Proudfoot, J.; Sharma, R.; Tong, L.; Moss, *J. Med. Chem.* **1999**, *42*, 1757.

91. Kinny, W. A.; Abou-Gharbia, M.; Garrison, D. T.; Schmidt, J.; Kowal, D. M.; Bramlett, D. R.; Millar, T. L.; Tasse, R. P.; Zaleska, M. M.; Moyer, J. A. *J. Med. Chem.* **1998**, *41*, 236.

92. Chan, P. C. M.; Roon, R. J.; Koerner, J. F.; Taylor, N. J.; Honek, J. F. *J. Med. Chem.* **1995**, *38*, 4433.

93. (a) Tomas, S.; Rotger, M. C.; Gonzalez, J. F.; Deya, P. M.; Ballester, P.; Costa, A. *Tetrahedron Lett.* **1995**, *36*, 2523. (b) Tomas, S.; Prohens, R.; Deslongchamps, G.; Ballester, P.; Costa, A. *Angew. Chem. Int. Ed. Eng.* **1999**, *38*, 2208. (c) Prohens, R.; Martorell, G.; Ballester, P.; Costa, A. *Chem. Commun.* **2001**, 1456.

94. (a) P. Cohen, S.; Cohen, S. G. *J. Am. Chem. Soc*. **1966**, *88*, 1533. (b) Thrope, J. E. *J. Chem. Soc*. *(B)* **1968**, 435. (c) Neuse, E.; Green, B. *Justus Liebigs Ann. Chem.* **1973**, 619.

95. Ried, W.; Kunstmann, W. *Chem. Ber*. **1969**, *102*, 1431.

96. (a) Vermeer, H. J.; Halkes, K. M.; van Kuik, A.; Kamerling, J. P.; Vliegenthart, J. F. G. *J. Chem. Soc., Perkin Trans. 1,* **2000**, 2249. (b) Corsi, D. M.; Elst, L. V.; Muller, R. N.; van Bekkum, H.; Peters, J. A. *Chem. Eur. J.* **2001**, *7*, 64. (c) Kitov, P. I.; Bundle, D. R. *J. Chem. Soc., Perkin Trans. 1,* **2001**, 838. (d) Chernyak, A.; Karavanov, A.; Ogawa, Y.; Kovac, P. *Carbohydr. Res.* **2001**, *330*, 479.

97. Ueda, Y.; Crast, L. B.; Jr.; Mikilineni, A. B.; Partyka, R. A. *Tetrahedron Lett*. **1991**, *32*, 3767.

98. (a) Schmidt, A. H.; Ried, W. *Justus Liebigs Ann. Chem.* **1975**, 1863. (b) Ried, W.; Schmidt, A. H. *Tetrahedron Lett*. **1969**, 2435. (c) Ried, W.; Schmidt, A. H. *Tetrahedron Lett*. **1969**, 3007. (d) Ried, W.; Schmidt, A. H. *Tetrahedron Lett*. **1969**, 4115.

99. Ried, W.; Batz, F. *Justus Liebigs Ann. Chem.* **1972**, *755*, 32.

100. Vogtle, F.; Dix, P. *Justus Liebigs Ann. Chem.* **1977**, 1698.

101. Lim, N. C.; Morton, M. D.; Jenkins, H. A; Bruckner, C. *J. Org. Chem*. **2003**, *68*, 9233.

102. (a) Ried, W.; Kunstmann, W. *Angew. Chem. Int. Ed. Engl.* **1968**, *7*,135. (b) Blomquist, A. T.; LaLancette, E. A. *J. Am. Chem. Soc.* **1962**, *84*, 220. (c) Ooms, P. H. J.; Scheeren, J. W.; Nivard, R. J. F. *Synthesis* **1975**, 639.

103. Cava, M. P.; Napier, D. R. *J. Am. Chem. Soc.* **1957**, *79*, 3606.

104. Barton, J. W.; Goodland, M. C.; Gould, K. J.; Hadley, J.; McOmie, J. F. W. *Tetrahedron* **1978,** *34*, 495.

105. (a) Treibs, A.; Jacob, D.–c. K. *Angew. Chem. Int. Ed. Engl.* **1965**, *4,* 694. (b) Sprenger, H. E.; Ziegenbein, W. *Angew. Chem. Int. Ed. Engl.* **1966**, *5*, 894. (c) Sprenger, H. E.; Ziegenbein, W. *Angew. Chem. Int. Ed. Engl.* **1968**, *7*, 530. (d) Neuse, E. W.; Green, B. R. *J. Org. Chem.* **1974,** *39,* 3881.

106. Oguz, U.; Akkaya, E. U. *Tetrahedron Lett.* **1997**, *38*, 4509.

107. (a) Tam, A. C.; Balanson, R. D. IBM *J. Res. Dev.* **1982**, *26,* 186. (b) Wingard, R. E. IEEE *Trans. Ind. Appl.* **1982**, 1251. (c) Tam, A. C. *Appl. Phys. Lett.* **1980**, *37,* 978.

108. (a) Loutfy, R. O.; Hsiao, C. K.; Kazmaier, P. M. *Photogr. Sci. Eng.* **1983**, *27,* 5. (b) Piechowski, A. P.; Bird, G. R.; Morel, D. L.; Stogryn, E. L. *J. Phys. Chem.* **1984**, *88,* 934. (c) Meeritt, V. Y.; Hovel, H. *J. Appl. Phys. Lett.* **1976**, *29,* 414.

109. Mallory, F. B.; Roberts, J. D. *J. Am. Chem. Soc.* **1961**, *83*, 393.

110. Blomquist, A. T.; LaLancette, E. A. *J. Am. Chem. Soc*. **1961**, *83*, 1387.

111. (a) Staab, H. A.; Ipaktschi, J. *Chem. Ber*. **1968**, *101,* 1457. (b) Kasai, M.; Oda, M.; Kitahara, Y. *Chem. Lett*. **1978**, 217. (c) Maier, G.; Reisenauer, H. P.; Sayrac, T. *Chem. Ber.* **1982**, *115*, 2192. (d) Obata, N.; Takizawa, T. *Bull. Chem. Soc. Jpn*. **1977**, *50*, 2017. (e) Diederich, F.; Rubin, Y.; Chapman, O. L.; Goroff, N. S. *Helv. Chim. Acta* **1994**, *77*, 1441. (f) Adam, W.; Patterson, W. S. *J. Org. Chem*. **1995**, *60*, 7769.

112. (a) Zhao, D.-c.; Allen, A. D.; Tidwell, T. T. *J. Am. Chem. Soc*. **1993**, *115*, 10097. (b) Allen, A. D.; Lai, W.-Y.; Ma, J.; Tidwell, T. T. *J. Am. Chem. Soc.* **1994**, *116*, 2625. (c) McAllister, M. A.; Tidwell, T. T. *J. Am. Chem. Soc*. **1994**, *116*, 7233. (d) Allen, A. D.; Colomvakos, J. D.; Egle, I.; Lusztyk, J.; McAllister, M. A.; Tidwell, T. T.; Wagner, B. D.; Zhao, D.-c. *J. Am. Chem. Soc.* **1995**, *117*, 7552. (e) Tidwell, T. T. *Ketenes*; Wiley: New York, **1995**. (f) Allen, A. D.; Ma, J.; McAllister, M. A.; Tidwell, T. T.; Zhao, D.-c. *Acc. Chem. Res.* **1995**, *28*, 265.

113. (a) Allen, A. D.; Egle, I.; Janoschek, R.; Liu, H. W.; Ma, J.; Marra, R. M.; Tidwell, T. T. *Chem. Lett.* **1996**, 45. (b) Liu, R.; Tidwell, T. T. *J. Chem. Soc., Perkin Trans. 2* **1996**, 2757. (c) Colomvakos, J. D.; Egle, I.; Ma, J.; Pole, D. L.; Tidwell, T. T.; Warkentin, J. *J. Org. Chem*. **1996**, *61*, 9522. (d) Egle, I.; Lai, W.-Y.; Renton, P.; Tidwell, T. T.; Zhao, D.-c. *J. Org. Chem.* **1997**, *62*, 18. (e) Allen, A. D.; Ma, J.; McAllister, M. A.; Tidwell, T. T.; Zhao, D-c. *J. Chem. Soc., Perkin Trans. 2* **1995**, 847. (f) Allen, A. D.; Lough, A. J.; Tidwell, T. T. *Chem. Commun.* **1996**, 2171. (g) Huang, W.-w.; Moore, P. A.; Far. A. F.; Tidwell, T. T. *J. Org. Chem.* **2000**, *65*, 3877.

114. Hochstrasser, R.; Wirz, J. *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 181.

115. Diederich, F.; Rubin, Y. *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1101.

116. (a) Dehmlow, E. V. *Tetrahedron Lett.* **1972**, 1271. (b) Dehmlow, E. V. *Angew. Chem. Int. Ed. Engl.* **1974**, *13*, 209.

117. Eggerding, D.; West, R. *J. Am. Chem. Soc.* **1975**, *97*, 207.

118. (a) De Selms, R. C. *Tetrahedron Lett.* **1968**, 5545. (b) Ortiz de Montellano, P. R.; Thorstenson, P. C. *Tetrahedron Lett*. **1972**, 787.

119. Ried, W.; Schomann, P. *Justus Liebigs Ann. Chem*. **1968**, *714*, 140.

120. Argyropoulos, N. G.; Alexandrou, N. E.; Nicolaides, D. N. *Tetrahedron Lett*. **1976**, *17*, 83.

121. Heileman, M. J.; Moore, H. W. *Tetrahedron Lett*. **1998,** *39*, 3643.

122. (a) Nair, V.; Sheela, K. C.; Rath, N. P.; Eigendorf, G. K. *Tetrahedron Lett*. **2000,** *41*, 6217. (b) Nair, V.; Sheela, K. C.; Rath, N. P. *Chem. Lett*. **2000**, 980.

123. Taing, M.; Moor, H. W. *J. Org. Chem.* **1996**, *61*, 329.

124. Periasamy, M.; Jayakumar, K. N.; Bharathi, P. *J. Org. Chem*. **2000**, *65*, 3548.

125. Periasamy, M.; Karunakar, G. V. *J. Org. Chem*. **2006**, *71*, 7463.

126. (a) Periasamy, M.; KishoreBabu, N.; Jayakumar, K. N. *Tetrahedron Lett.* **2003**, *44*, 8939. (b) Periasamy, M.; Kishorebabu, N.; Jayakumar, K. N. *Tetrahedron Lett.* **2007**, *48*, 1955.

127. Mukkanti, A. Thesis, University of Hyderabad, **2004**.

128. (a) Hambrecht, J.; Straub, H.; Muller, E. *Chem. Ber*. **1974**, *107*, 3962. (b) Hambrecht, J.; Straub, H. *Tetrahedron Lett.* **1976**, 1079.

129. (a) Jin, S.-J.; Arora, A. K.; Sayre, L. M. *J. Org. Chem.* **1990**, *55*, 3011. (b) Sayre, L. M.; Jin, S.-J. *J. Org. Chem.* **1984**, *49*, 3498.

130. (a) Matsumura, Y.; Nishimura, M.; Hiu, H.; Watanabe, M.; Kise, N. *J. Org. Chem.* **1996**, *61*, 2809. (b) Junggebauer, J.; Neumann, W. P. *Tetrahedron* **1997**, *53*, 1301.

131. Mukai, C.; Cho, W.-J.; Hanaoka, M. *Tetrahedron Lett.* **1989**, *30*, 7435.

132. Yamamoto, Y.; Ohno, M.; Eguchi, S. *J. Org. Chem*. **1994**, *59*, 4707.

133. Dowd, P.; Zhang, W. *Chem. Rev.* **1993**, *93*, 2091.

134. Mendenhall, G. D.; Protasiewicz, J. D.; Brown, C. E.; Ingold, K. U.; Lusztyk, J. *J. Am. Chem. Soc*. **1994**, *116*, 1718.

135. Szakal-Quin, G.; Graham, D. G.; Millington, D. S.; Maltby, D. A.; McPhail, A. T. *J. Org. Chem.* **1986**, *51*, 621.

136. (a) Bujwid, Z. J.; Gerrard, W.; Lappert, M. F. *Chem. Ind. (London)*, **1959**, 1091. (b) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457.

137. Bharathi, P.; Periasamy, M. *Organometallics* **2000**, *19*, 5511.

138. Inoue, A.; Kitagawa, K.; Shinokubo, H.; Oshima, K. *Tetrahedron* **2000**, *56*, 9601.

139. Ried, W.; Manfred, V. *Chem. Ber*. **1982**, *115*, 402.

140. Yamaguchi, M.; Hayashi, A.; Himara, *Chem. Lett.* **1992**, 2479.

141. Biao, J.; Yu-Gui, S. *Tetrahedron Lett.* **2002**, *43*, 8323.

142. (a) Magnus, P.; Or, Y. S. *J. Am. Chem. Soc., Chem. Commun.* **1983**, 26. (b) Carter P.; Fitzjohn, S.; Halazy, S.; Magnus, P. *J. Am. Chem. Soc.* **1987**, *107*, 2711.

143. (a) Gimenez, I. F.; Alves, O. L. *J. Braz. Chem. Soc.* **1999**, *10*, 167. (b) Reynolds, J. R.; Poropatic, P. A.; Toyooka, R. L. *Macromolecules* **1987**, *20*, 958.

144. (a) Nizurski-Mann, R. E.; Cava, M. P. *Heterocycles* **1992**, *34*, 2003. (b) Chou, S. S.P.; Yeh, Y. H. *Tetrahedron Lett.* **2001**, *42*, 1309.

145. D'Silva, C.; Walker, D. A. *J. Org. Chem.* **1998**, *63*, 6715.

146. Evans, P.; de Lacy, B. P. J.; Guernion, N.; Ratcliffe, N. M.; Sivanand, P. S.; Teare, G. C. *Synth. Met.* **2000**, *114*, 181.

147. (a) Casiraghi, G.; Zanardi, F.; Rassu, G.; Pinna, L. *Org. Prep. Proced. Int.* **1996**, *28*, 641. (b) Takohata, H.; Momose, T. *The alkaloids*; Cordell, G. A. Ed.; Academic Press, San Diego **1993**.

148. *Comprehensive Organic Chemistry*: Sammes. P. G., Ed.; Pergamon: Oxford, **1979**: Vol. 4 Chapter 17.

149. Pudleiner, H.; Laatsch, H. *Liebigs Ann. Chem.* **1990**, 423.

150. Davies, D. G.; Hodge, P. *Tetrahedron Lett.* **1970**, *11*, 1673.

151. (a) Spivey, A. C.; Frampton, C. S.; Battersby, A. R. *J. Chem. Soc., Perkin Trans. 1*, **1996**, 2103. (b) Jacobi, P. A.; Buddhu, S. C.; Fry, D.; Rajeswari, S. *J. Org. Chem.* **1997**, *62*, 2894. (c) Leung, S. H.; Nguyen, L. T.; Smith, K. M. *Heterocycl. Commun.* **1996**, *2*, 9.

152. Furstner, A.; Weintritt, H.; Hupperts, A. *J. Org. Chem.* **1995**, *60*, 6637.

153. Gupton, J. T.; Krumpe, K. E.; Burnham, B. S.; Dwornik, K. A.; Petrich, A.; Du, K. X.; Bruce, M. A.; Vu, P.; Vargas, M.; Keerbkar, K. M.; Hoseinclaude, K. N.; Jones, R.; Sikorski, J. A. *Tetrahedron* **1998**, *54*, 5075.

154. Khanna, I. K.; Weier, R. M.; Yu, Y.; Collins, P. W.; Miyashiro, J. M.; Koboldt, C. M.; Veenhuizen, A. W.; Currie, J. L.; Seibert, K.; Isakson, P.C. *J. Med. Chem.* **1997**, *40*, 1619.

155. Ferreira, V. F.; Cecilia, M.; De Souza, B. V.; Cunha, A. C.; Pereira, L. O. R.; Ferreira, M. L.G. *Org. Prep. Proced. Int.* **2001**, *33*, 411.

156. Yu, S. X.; Le Quesne, P. W. *Tetrahedron Lett.* **1995**, *36*, 6205.

157. Periasamy, M.; Srinivas, G.; Suresh, S. *Tetrahedron Lett.* **2001**, *42*, 7123.

158. Furstner, A.; Bogdanovic, B. *Angew. Chem., Int. Ed.* **1996**, *35*, 2442.

159. (a) Fry, A. J.; Little, R. D.; Leonetti, J. *J. Org. Chem.* **1994**, *59*, 5017. (b) Molander, G. A.; Kenny, C. *J. Am. Chem. Soc.* **1989**, *111*, 8236. (c) Leonard, E.; Dunach, E.; Perichon, J. *J. Chem. Soc. Chem. Commun.* **1989**, 276. (d) Furstner, A.; Csuk, R.; Rohrer, C.; Wiedmann, H. *J. Chem. Soc. Perkin Trans. I* **1988**, 1729. (e) Nonaka, T.; Asai, M. *Bull. Chem. Soc. Jpn.* **1978,** *51*, 2976.

160. Renzo, R.; Bellina, F. *Tetrahedron* **2006**, *62*, 7213.

161. Heathcock, C. H. *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; **1991**; Vol. 2, p 181.

162. (a) Northrup A. B.; MacMillan, D. W. C. *Science*, **2004**, *305*, 1752. (b) *Modern Aldol Reactions* Mahrwald, R. Vol 1 and 2 VCH July **2004**.

163. (a) Harrison, C. R. *Tetrahedron Lett.* **1987**, *28*, 4135. (b) Evans, D. A.; Urpi, F.; Somers, T. C.; Clark, J. S.; Bilodeau, M. T. *J. Am. Chem. Soc.* **1990**, *112*, 8215. (c) Evans, D. A.; Rieger, D. L.; Bilodeau, M. T.; Urpi, F. *J. Am. Chem. Soc.* **1991**, *113*, 1047. (d) Xiang, Y.; Olivier, E.; Ouimet, N. *Tetrahedron Lett.* **1992**, *33*, 457. (e) Yan, T.-H.; Lee, H-C.; Tan, C-W. *Tetrahedron Lett.* **1993**, *34*, 3559. (f) Mahrwald, R.; Costisella, B.; Gundogan, B. *Tetrahedron Lett.* **1997**, *38*, 4543. (g) Crimmins, M. T.; King, B. W.; Tabet, E. A. *J. Am. Chem. Soc.* **1997**, *119*, 7883. (h) Ghosh, A. K.; Onishi, M. *J. Am. Chem. Soc.* **1996**, *118*, 2527.

164. (a) Tanabe, Y.; Matsumoto, N.; Higashi, T.; Misaki, T.; Itoh, T.; Yamamoto, M.; Mitarai, K.; Nishii, Y. *Tetrahedron* **2002,** 58, 8269. (b) Yoshida, Y.; Hayashi, R.; Sumihara, H.; Tanabe, Y. *Tetrahedron Lett.* **1997**, *38*, 8727.

165. (a) Liebeskind, L. S. *Tetrahedron* **1989**, *45*, 3053. (b) Perri, S. T.; Rice, P.; Moore, H. W. *Org. Synth.* **1990**, *69*, 220.

166. Annunziata, R.; Cinquini, M.; Cozzi, F.; Cozzi, P. G.; Coslandi, E. *Tetrahedron* **1991**, *47*, 7897.

167. Annunziata, R.; Cinquini, M.; Cozzi, F.; Borgia, A. L. *J. Org. Chem.* **1992**, *57*, 6339.

168. (a) Mukaiyama, T. *Organic Reactions*; Wiley: New York, **1982**; Vol. *28*, p. 203. (b) Heathcock, C. H. in *Comprehensive Organic Synthesis*, Trost, B. M.; Fleming I. Eds.; Pergamon: Oxford, **1991**; Vol. *2*, p 181. (c) Heathcock, C. H. In *Asymmetric Synthesis*, Morrison, J. D., Ed.; Academic Press: New York, **1984**, p. 111. (d) Masamune, S.; Choy, W.; Peterson, J. S.; Rita, L. R. *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 1.

169. (a) Evans, D. A.; Clark, J. S.; Metternich, R., Novack, V. J.; Sheppard, G. S. *J. Am. Chem. Soc.* **1990**, *112*, 866. (b) Mahrwald, R. *Chem. Ber.* **1995**, *128*, 919.

170. Yoshida, Y.; Hayashi, R.; Sumihara, H.; Tanabe, Y. *Tetrahedron Lett.* **1997**, *38*, 8727.

171. Bharathi, P.; Periasamy, M. *Org. Lett.* **1999**, *1*, 857.

172. (a) Periasamy, M.; Jayakumar, K. N.; Bharathi, P. *Chem. Commun.* **2001**, 1728. (b) Periasamy, M.; Jayakumar, K. N.; Bharathi, P. *J. Org. Chem.* **2005**, *70*, 5420.

173. Periasamy, M.; Srinivas, G.; Bharathi, P. *J. Org. Chem*. **1999**, *64*, 4204.

174. (a) Srinivas, G.; Periasamy, M. *Tetrahedron Lett.* **2002**, *43*, 2785. (b) Suresh, S.; Periasamy, M. *Tetrahedron Lett.* **2004**, 45, 6291.

175. Rao, V. D.; Periasamy, M. *Tetrahedron*: *Asymmetry* **2000**, *11*, 1151.

176. Periasamy, M.; Srinivas, G.; Karunakar, G. V.; Bharathi, P. *Tetrahedron Lett.* **1999**, *40*, 7577.

177. (a) Ohno, M.; Yamamoto, Y.; Eguchi, S. *J. Chem. Soc., Perkin Trans. 1,* **1991**, 2772. (b) Ohno, M.; Yamamoto, Y.; Shirasaki, Y.; Eguchi, S. *J. Chem. Soc., Perkin Trans. 1,* **1993**, 263. (c) Ohno, M.; Yamamoto, Y.; Eguchi, S. *Tetrahedron Lett*. **1993**, *34*, 4807.

178. (a) Mukayama, T.; Narasaka, K.; Banno, K. *Chem. Lett*. **1973**, 1011. (b) Ohki, H.; Wada, M.; Akiba, K.-Y. *Tetrahedron Lett.* **1988**, *29*, 4719. (b) Majewski, M.; Gleave, D. M. *Tetrahedron Lett.* **1989**, *30*, 5681.

179. (a) Nayori, R.; Yokoyama, K.; Sakata, J.; Kuwajima, I.; Nakamura, E.; Shimizu, M. *J. Am. Chem. Soc*. **1977**, *99*, 1265. (b) Ooki, T.; Doda, K.; Maruoka, K. *Org. Lett.* **2001**, *3*, 1273.

180. Evans, D. A.; Rieger, D. L.; Bilodeau, M. T.; Urpí, F. *J. Am Chem. Soc.* **1991**, *113*, 1047.

181. Crimmins, M. T.; Chaudhary, K. *Org. Lett.* **2000**, *2*, 775.

182. McKennon, M. J.; Meyers, A. I.; Drauz, K.; Schwarm, M. *J. Org. Chem.* **1993**, *58*, 3568.

183. Delaunay, D.; Toupet, L.; Corre, M. L. *J. Org. Chem.* **1995**, *60*, 6604.

184. Evans, D. A.; Downey, C. W.; Shaw, J. T.; Tedrow, J. S. *Org. Lett.* **2002**, *4*, 1127.

185. (a) Evans, D. A.; Mathre, D. J.; Scott, W. L. *J. Org. Chem.* **1985**, *50*, 1830. (b) Evans, D. A.; Chapman, K. T.; Bisaha, J. *J. Am. Chem. Soc.* **1988**, *110*, 1238.

186. (a) Oppolzer, W.; Moretti, R.; Thomi, S. *Tetrahedron Lett.* **1989**, *30*, 5603. (b) Hanessian, S.; Yang, R. –Y. *Tetrahedron Lett.* **1996**, *37*, 5273. (c) Oppolzer, W.; Rosset, S.; DeBrabander, J. *Tetrahedron Lett.* **1997**, *38*, 1593. (d) Cusk, R.;

Schröder, C.; Hutter, S.; Mohr, K. *Tetrahedron: Asymmetry* **1997**, *8*, 1411. (e) Jezewski, A. Chajewska, K.; Wielogórski, Z.; Jurczak, J.; *Tetrahedron: Asymmetry* **1997**, *8*, 1741. (f) Bond, S.; Perlmutter, P. *J. Org. Chem.* **1997**, *62*, 6397. (g) Brzezinski, L. J.; Rafel, S.; Leahy, J. W. *J. Am. Chem. Soc.* **1997**, *117*, 4317.

187. Capet, M.; David, G.; Bertin, L.; Hardy, J. C. *Synth. Commun.* **1995**, 25, 3123.

188. Vandewalle, M.; vander Eychen, J. *Tetrahedron* **1986**, *42*, 4035.

189. (a) Yan, T.; Tan, C.; Lee, H.; Lo, H.; Huang, T. *J. Am. Chem. Soc.* **1993**, *115*, 2613. (b) Wang, Y.; Su, D.; Lin, C.; Tseng, H.; Li, C.; Yan, T. *Tetrahedron Lett.* **1999**, *40*, 3577. (c) Wang, Y.; Su, D.; Lin, C.; Tseng, H.; Li, C.; Yan, T. *J. Org. Chem.* **1999**, *64*, 6495.

190. Ghosh, A. K.; Kim, J. *Tetrahedron Lett.* **2002**, *43*, 5621.

191. Qiangbiao, P., Benli, Z., Yuji, W., Dawei, M. *Org. Lett.* **2004**, *6*, 1009.

192. Barbas III, C. F., Suri, J. T., Ramachary, D. B. *Org. Lett.* **2005**, *7*, 1383.

193. King, R. B.; Stone, F. G. A. *Inorg. Synth.* **1963**, *7*, 193.

194. (a) Dehmlow, E. V.; Lissel, M. *Tetrahedron* **1981**, *37*, 1653. (b) Brandsma, L.; Verkruijsse, H. D. *Synthesis of Acytylenes, Allenes and Cumulenes*; Elsevier, New York, **1974**.

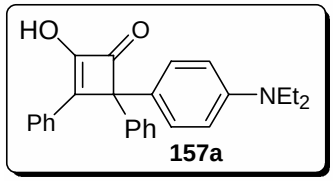
195. (a) Hall, S. R., King, G. S. D., Stewart, J. M., Eds.; *Xtal 3.4 Users manual;* Xtal system, University of Western Australia, 1995. (b) *SAINT* Version 6.2.

196. (a) Sheldrick, G. M. *SHELX-97*, University of Göttingen, Göttingen, Germany,1997. (b) *SHELXTL* Version 6.14, Bruker AXS.

Appendix I

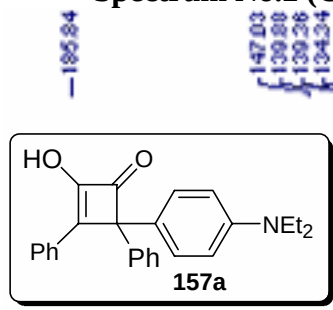
(Representative Spectra)

Spectrum No. 1 (Chapter 3, Section 3.4) ^{1}H NMR Spectrum (200 MHz, $CDCl_3$)



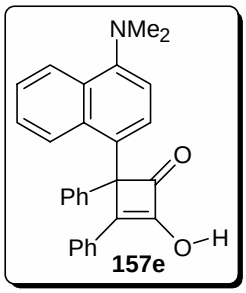
157a

Spectrum No.2 (Chapter 3, Section 3.4) ^{13}C NMR Spectrum (50 MHz, $CDCl_3$)



157a

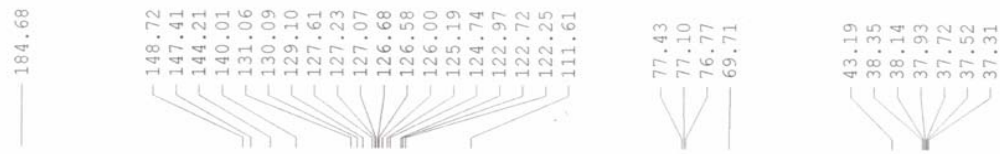
Spectrum No. 3 (Chapter 3, Section 3.4) ^{1}H NMR Spectrum (400 MHz, DMSO)

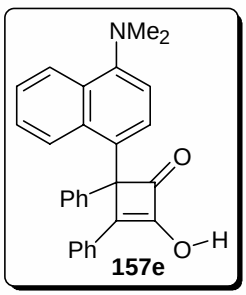


157e

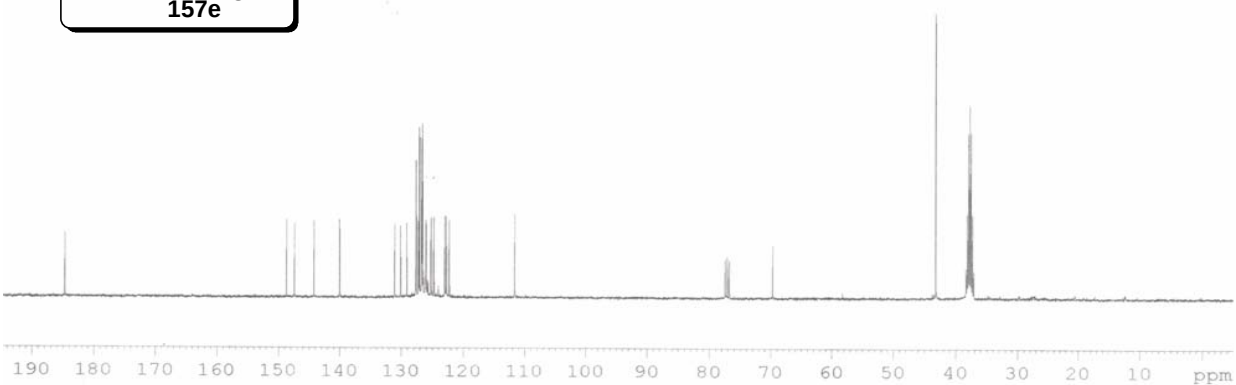
ppm

Spectrum No. 4 (Chapter 3, Section 3.4) ^{13}C NMR Spectrum (100 MHz, DMSO)

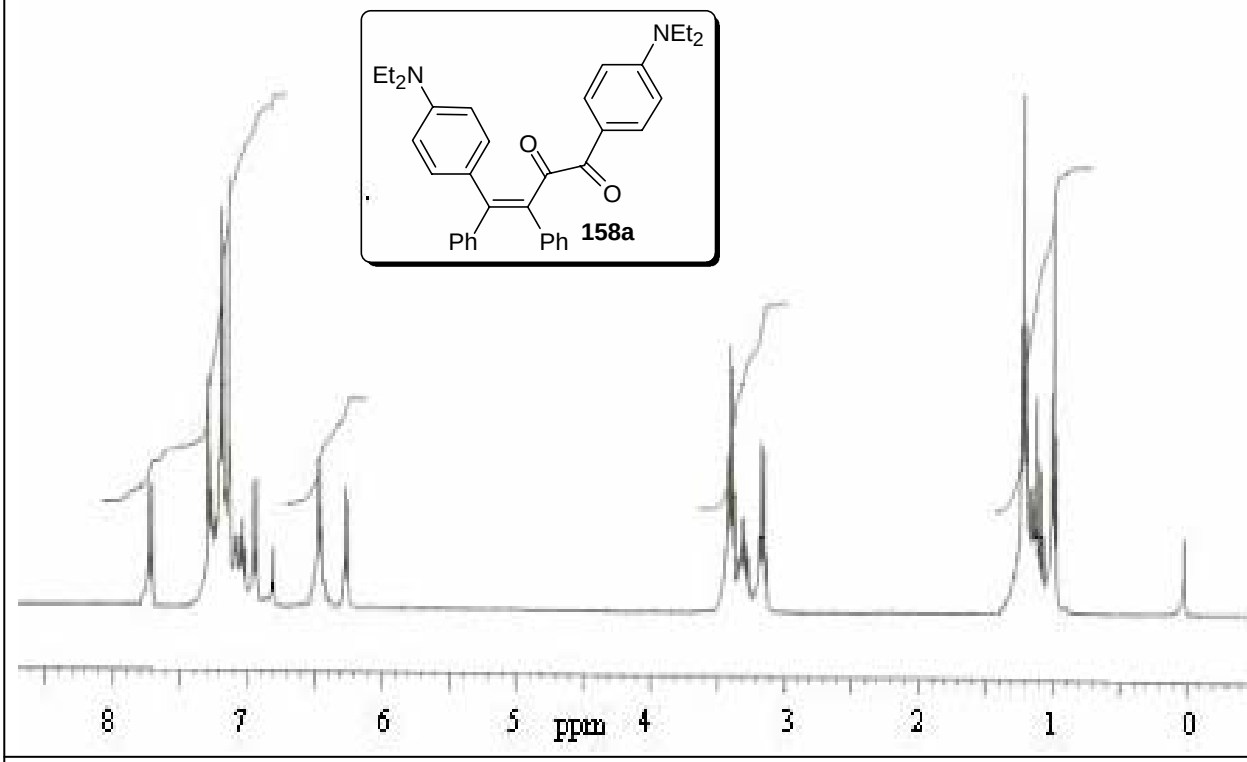




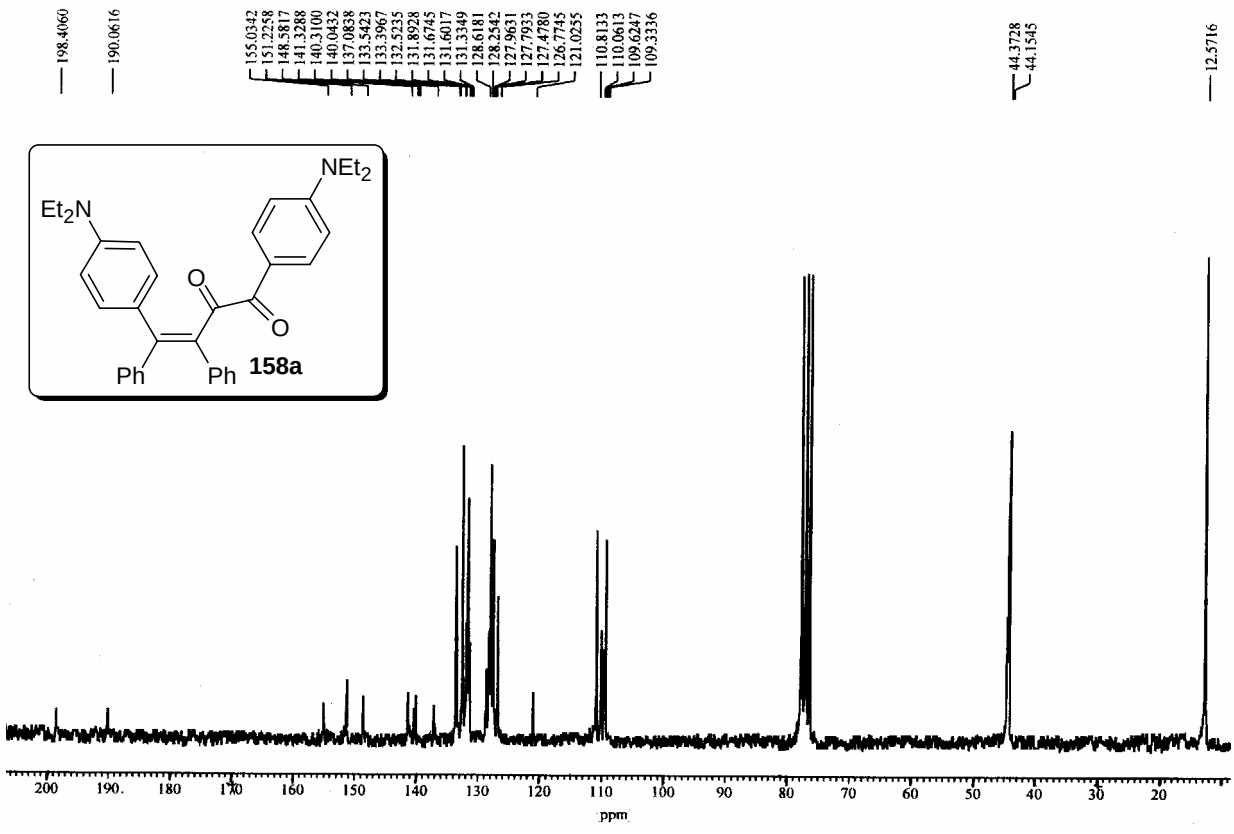
157e



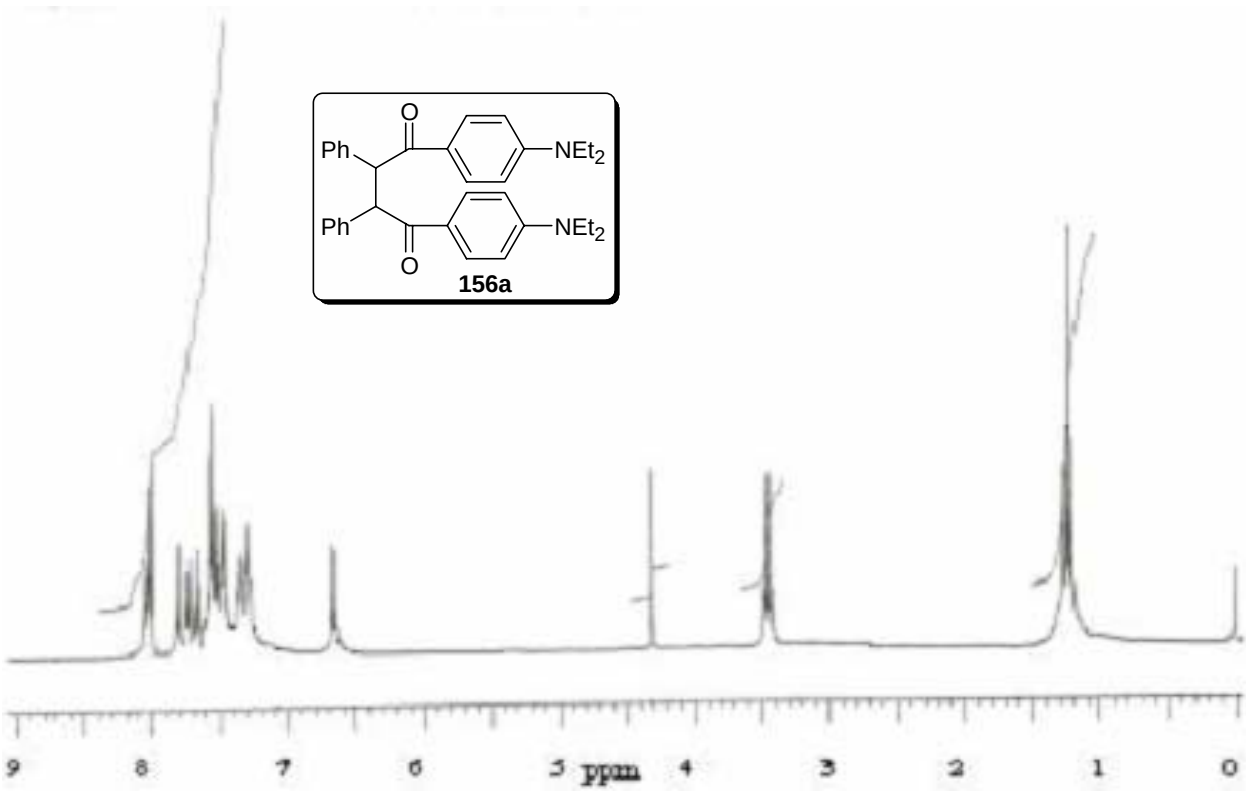
Spectrum No. 5 (Chapter 3, Section 3.5) ^{1}H NMR Spectrum (200 MHz, $CDCl_3$)



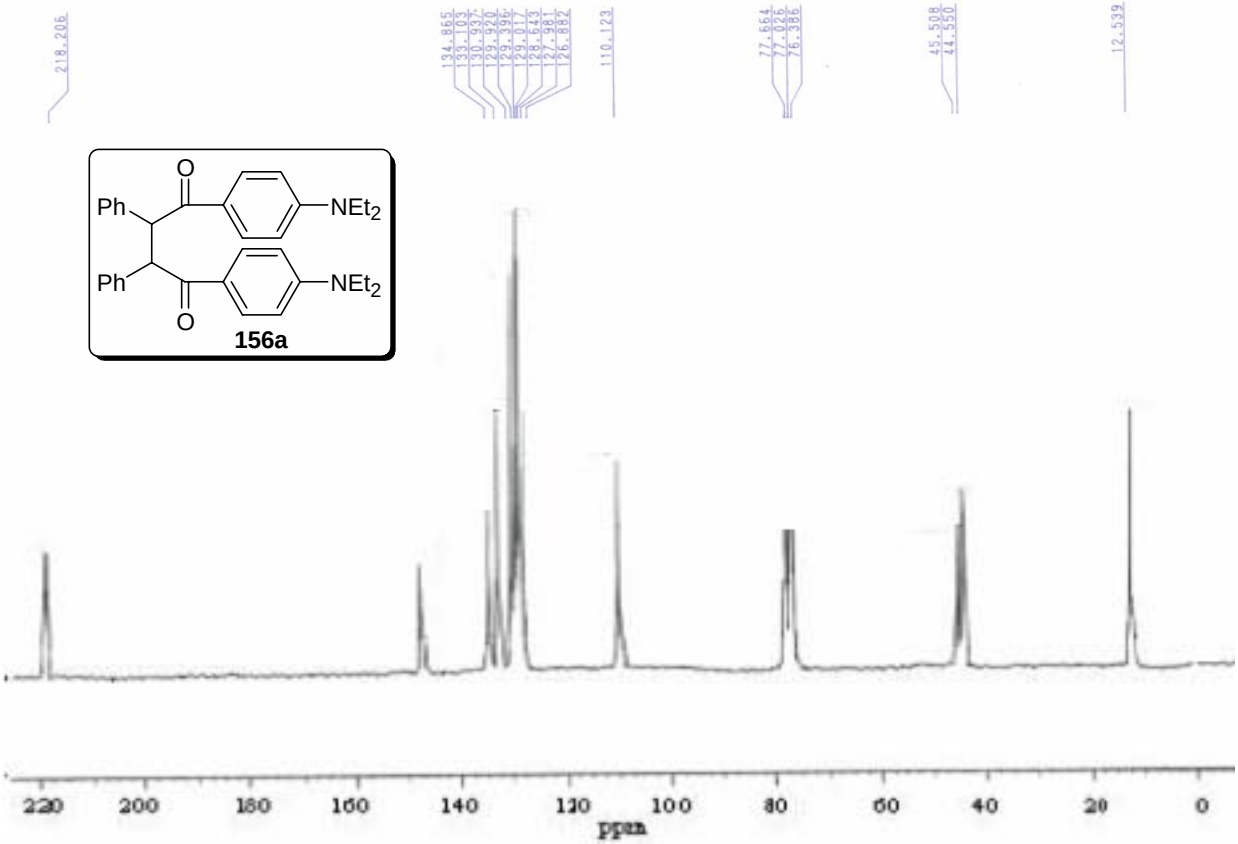
Spectrum No. 6 (Chapter 3, Section 3.5) ^{13}C NMR Spectrum (50 MHz, $CDCl_3$)



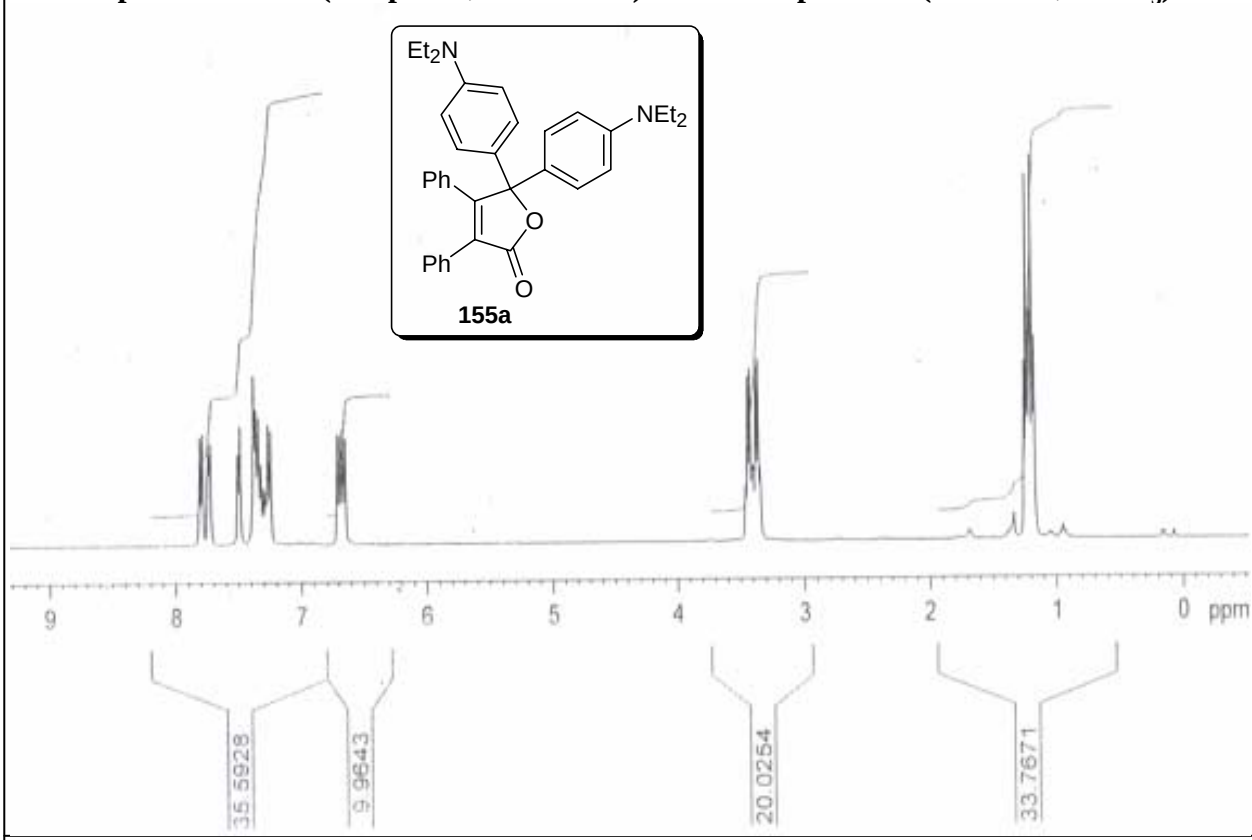
Spectrum No. 7 (Chapter 3, Section 3.5) ^{1}H NMR Spectrum (200 MHz, $CDCl_3$)



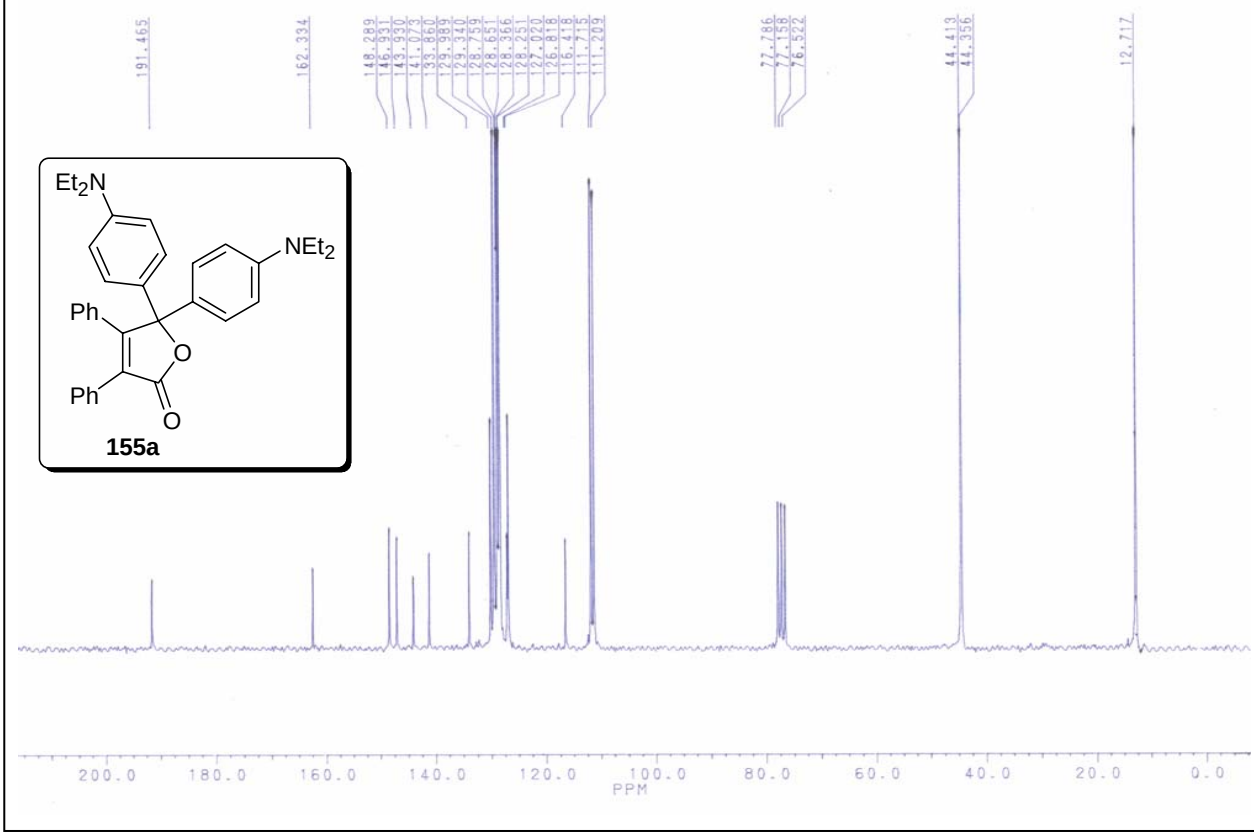
Spectrum No. 8 (Chapter 3, Section 3.5) ^{13}C NMR Spectrum (50 MHz, $CDCl_3$)



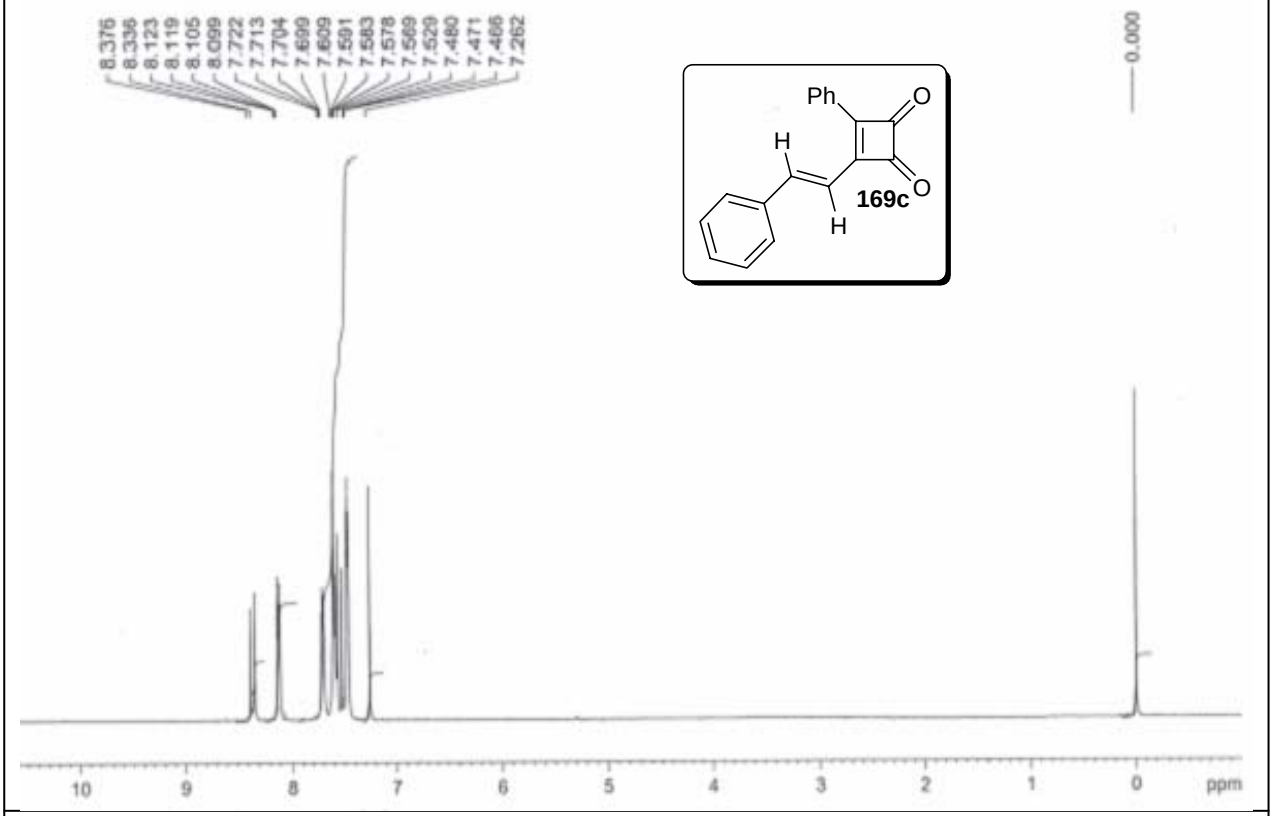
Spectrum No. 9 (Chapter 3, Section 3.7) ^{1}H NMR Spectrum (200 MHz, $CDCl_3$)



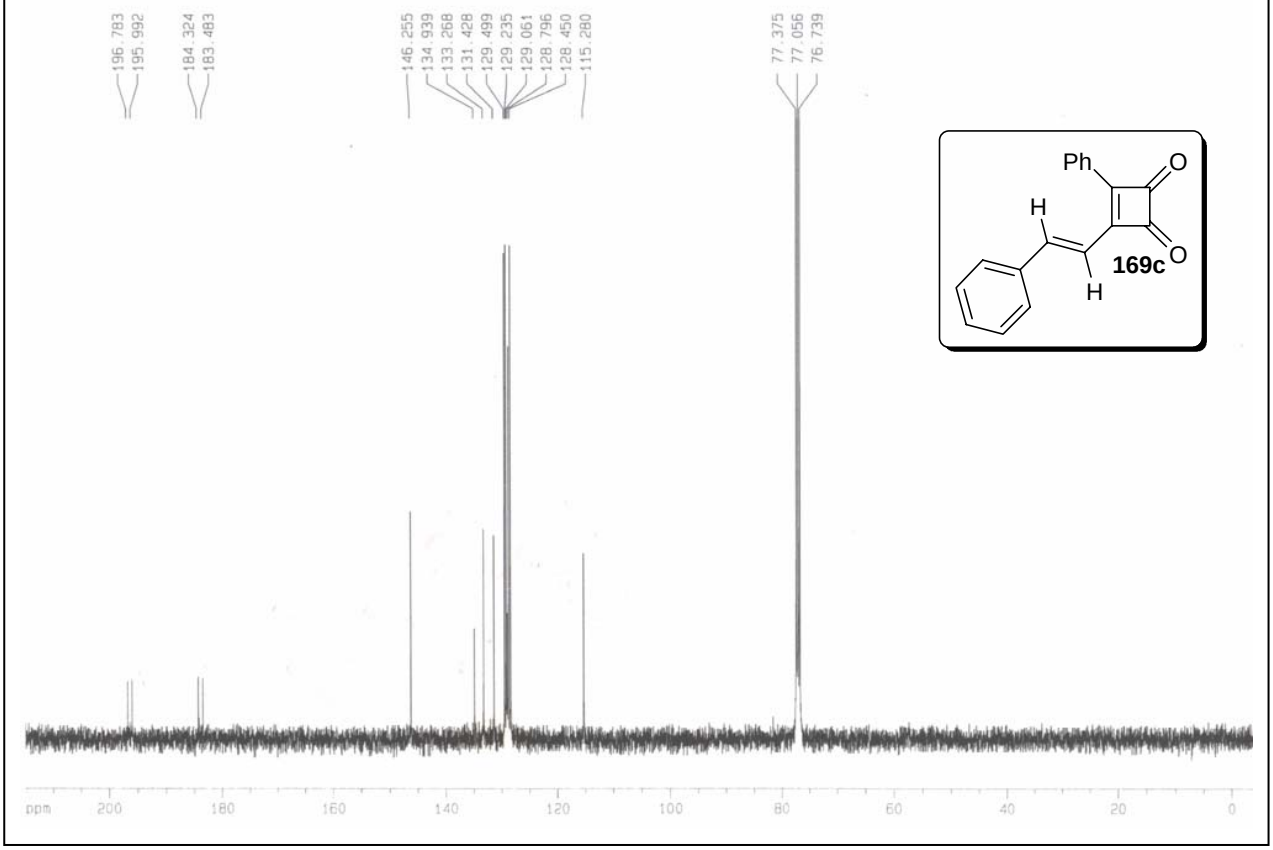
Spectrum No. 10 (Chapter 3, Section 3.7) ^{13}C NMR Spectrum (50 MHz, $CDCl_3$)



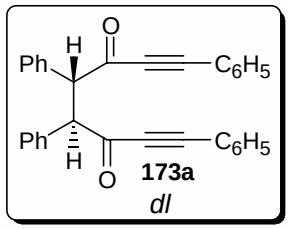
Spectrum No. 11 (Chapter 3, Section 3.10) ^{1}H NMR Spectrum (200 MHz, $CDCl_3$)



Spectrum No. 12 (Chapter 3, Section 3.10) ^{13}C NMR Spectrum (50 MHz, $CDCl_3$)

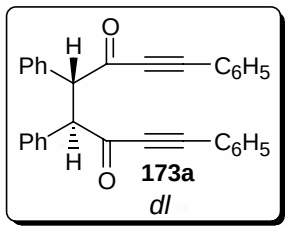


Spectrum No. 13 (Chapter 3, Section 3.11) ^{1}H NMR Spectrum (200 MHz, $CDCl_3$)



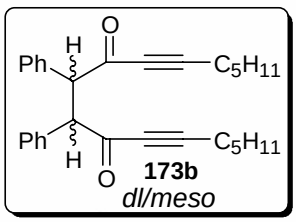
173a
dl

Spectrum No. 14 (Chapter 3, Section 3.11) ^{13}C NMR Spectrum (50 MHz, $CDCl_3$)

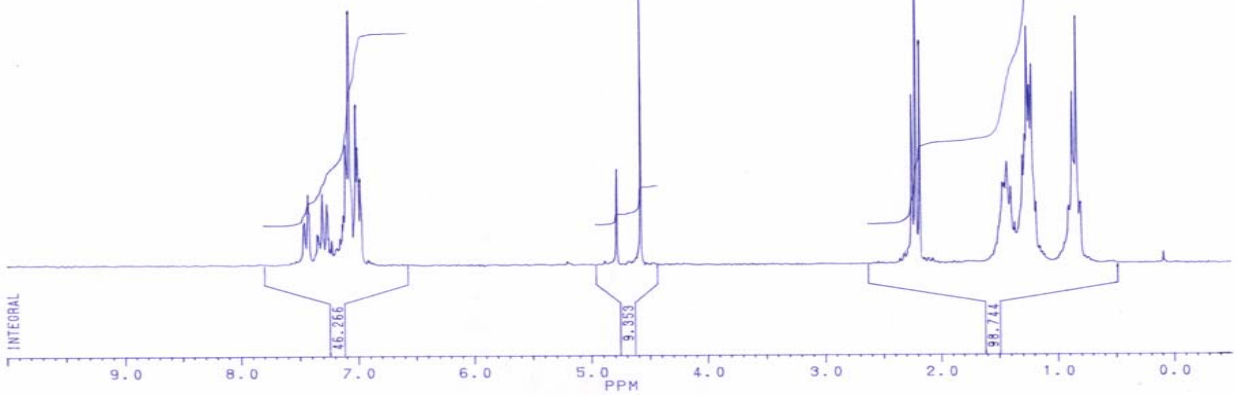


173a
dl

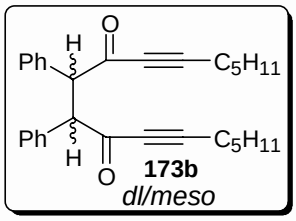
Spectrum No. 15 (Chapter 3, Section 3.11) ^{1}H NMR Spectrum (200 MHz, $CDCl_3$)



173b
dl/meso

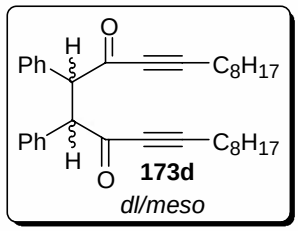


Spectrum No. 16 (Chapter 3, Section 3.11) ^{13}C NMR Spectrum (50 MHz, $CDCl_3$)



173b
dl/meso

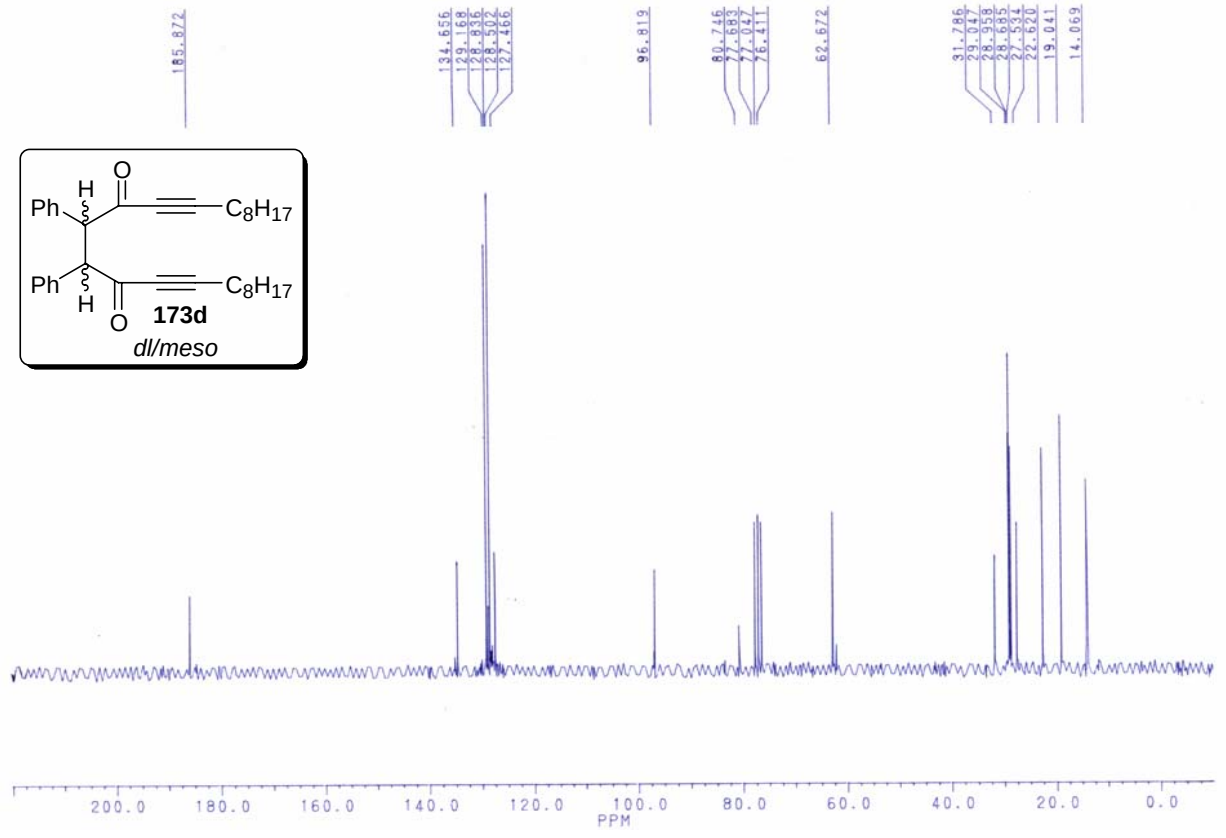
Spectrum No. 17 (Chapter 3, Section 3.11) ^{1}H NMR Spectrum (200MHz, $CDCl_3$)



173d

dl/meso

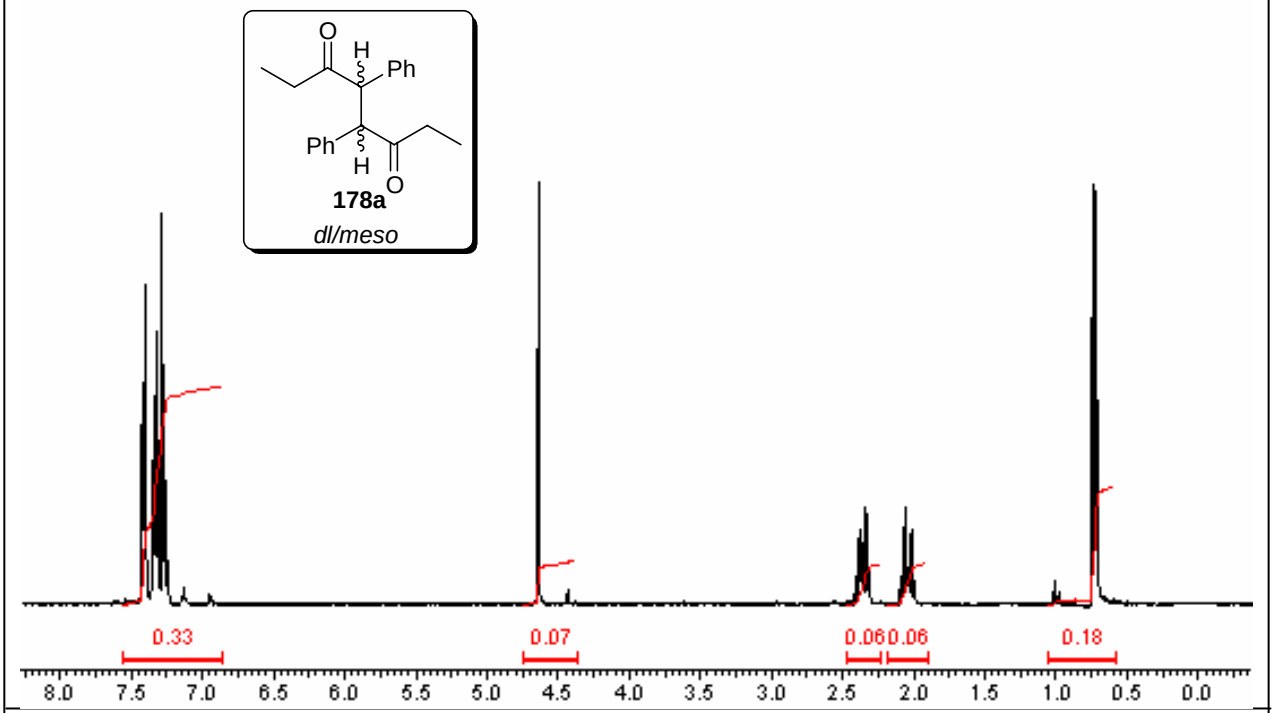
Spectrum No. 18 (Chapter 3, Section 3.11) ^{13}C NMR Spectrum (50 MHz, $CDCl_3$)



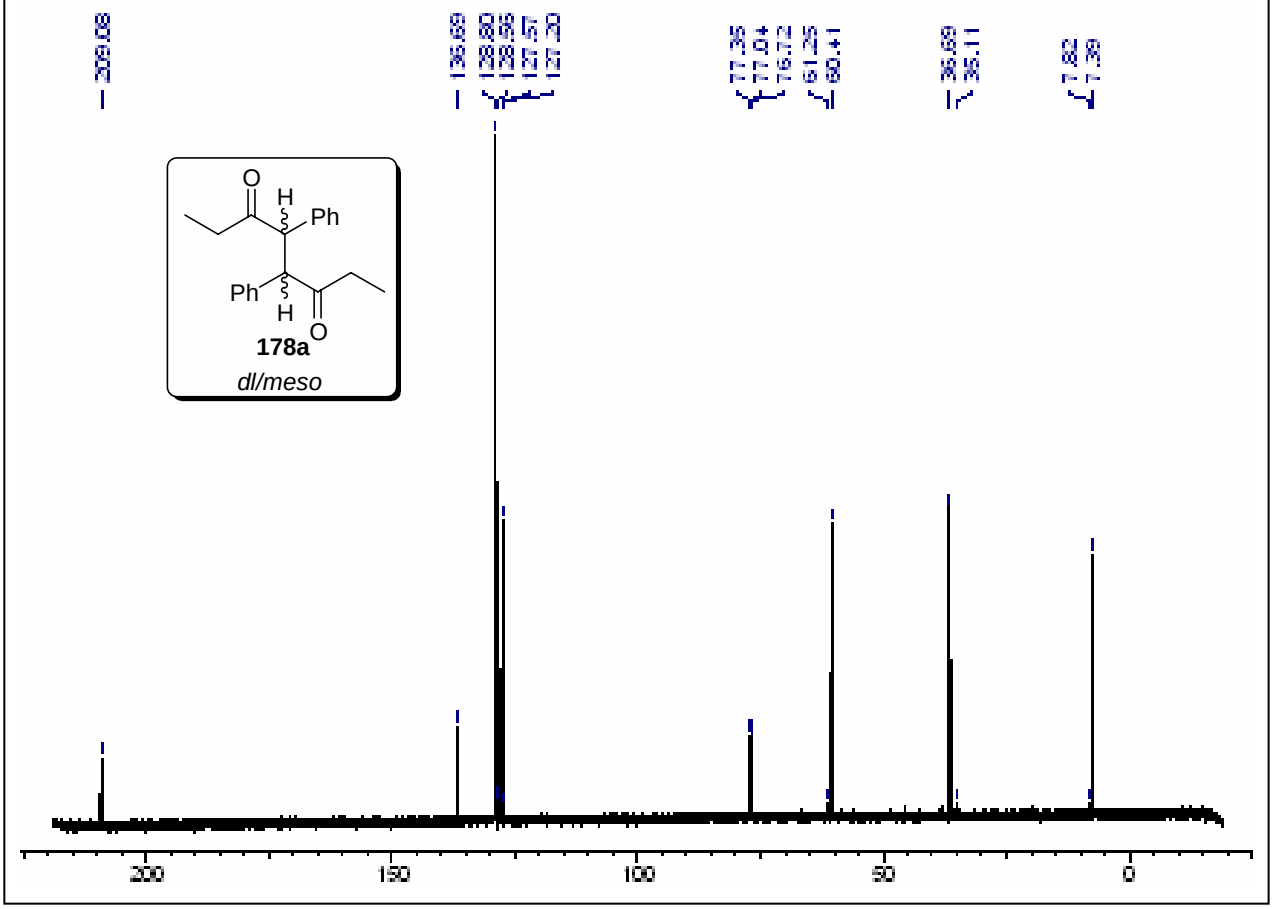
173d

dl/meso

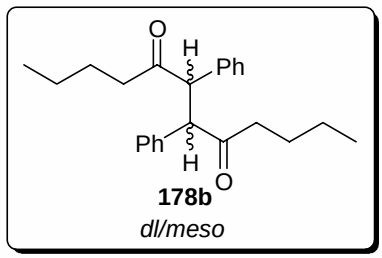
Spectrum No. 19 (Chapter 3, Section 3.12) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



Spectrum No. 20 (Chapter 3, Section 3.12) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)

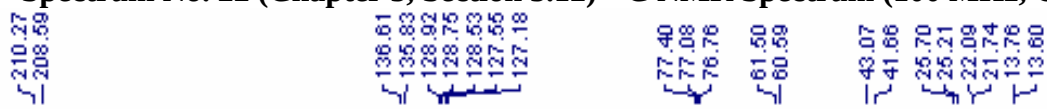


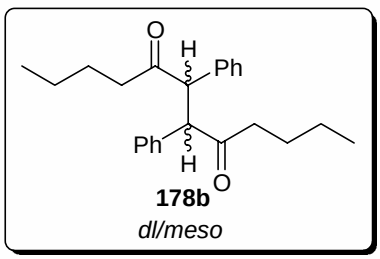
Spectrum No. 21 (Chapter 3, Section 3.12) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



178b
dl/meso

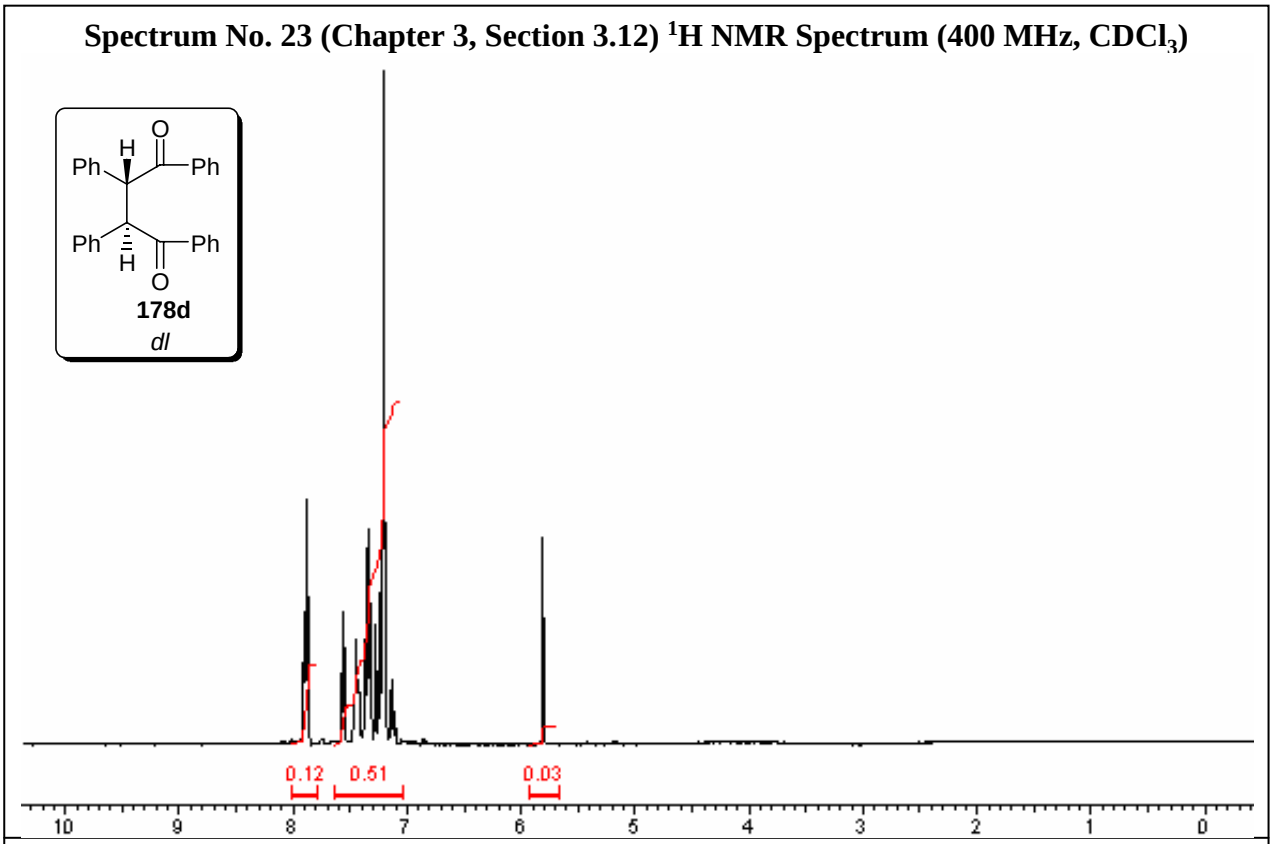
Spectrum No. 22 (Chapter 3, Section 3.12) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



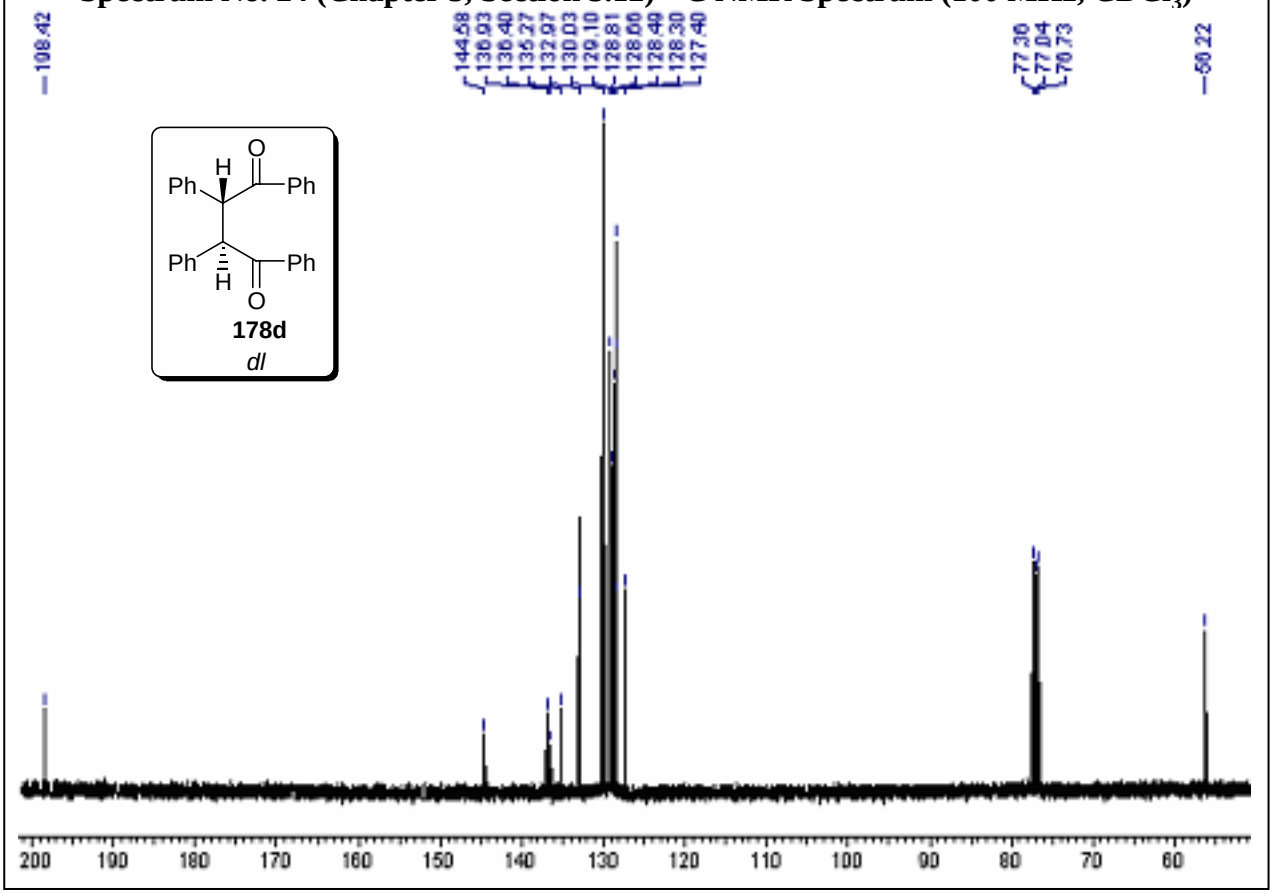


178b
dl/meso

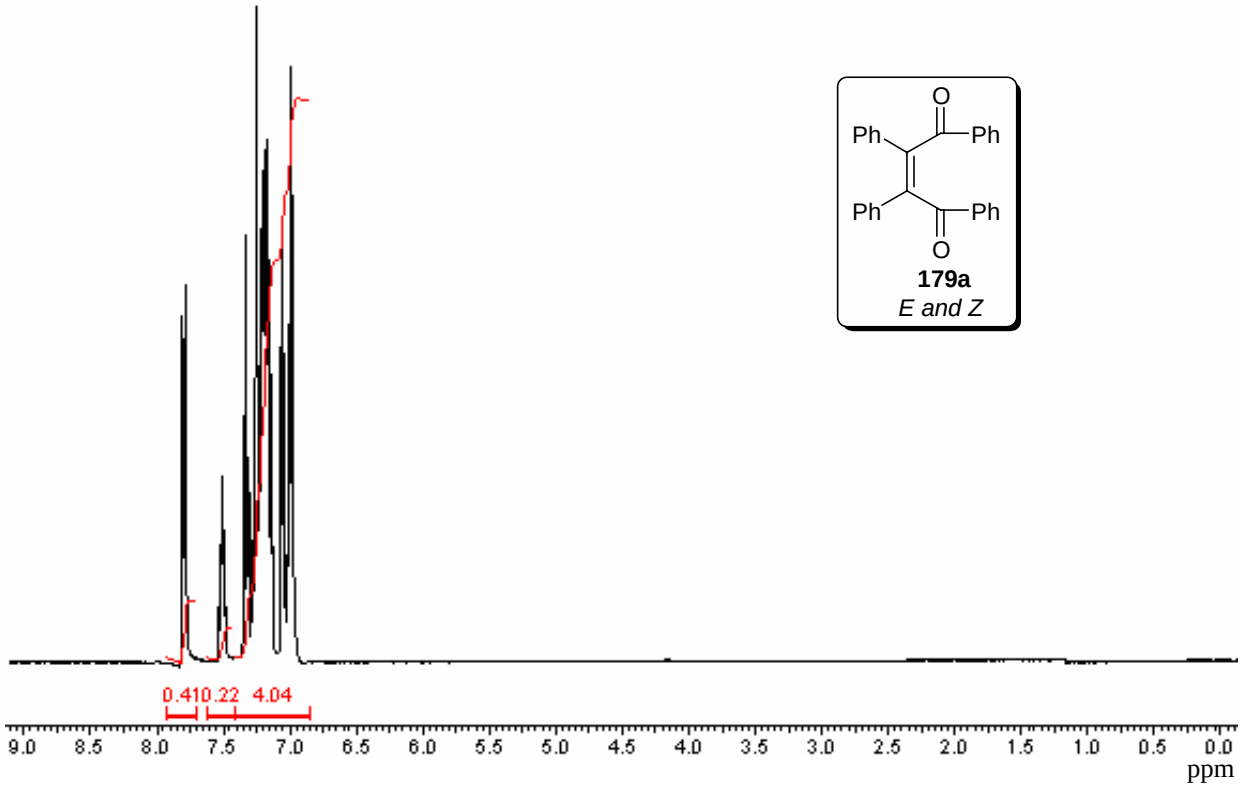
Spectrum No. 23 (Chapter 3, Section 3.12) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



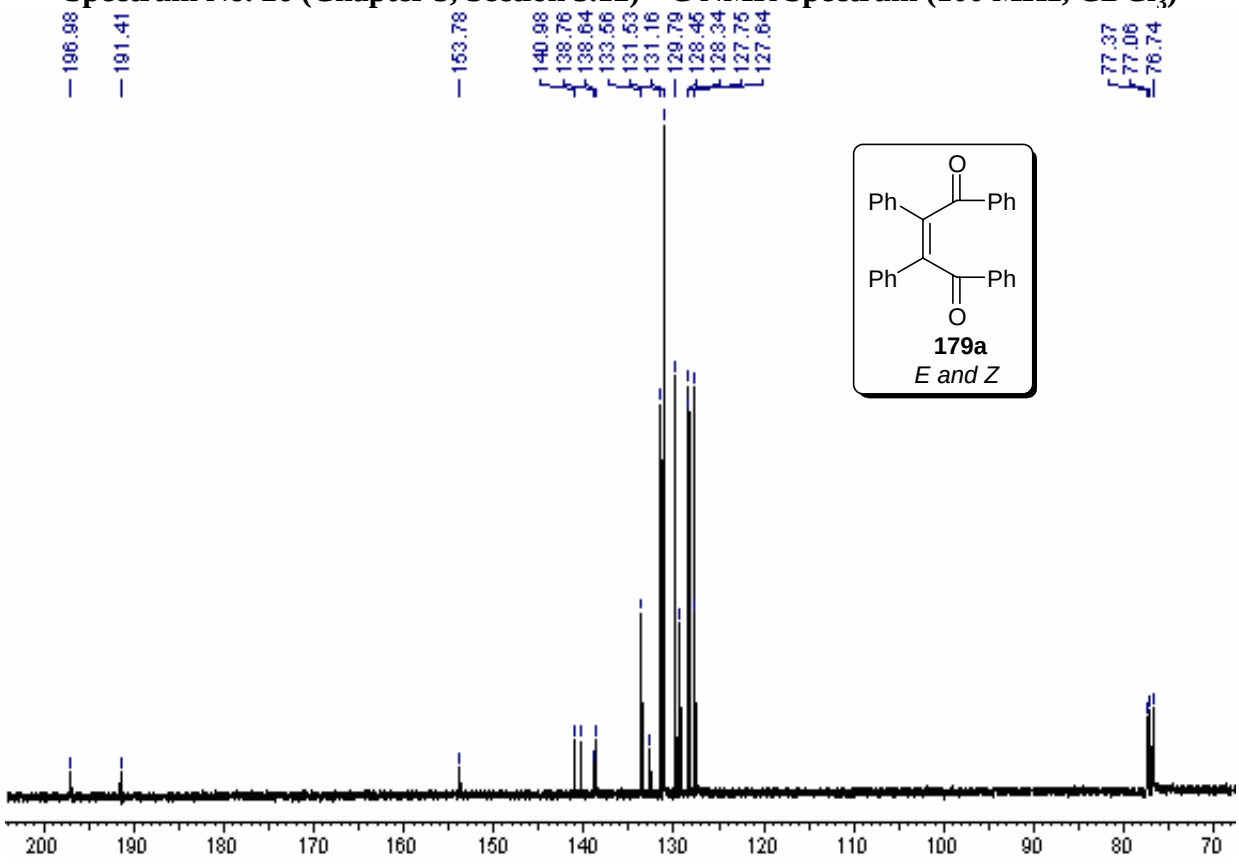
Spectrum No. 24 (Chapter 3, Section 3.12) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



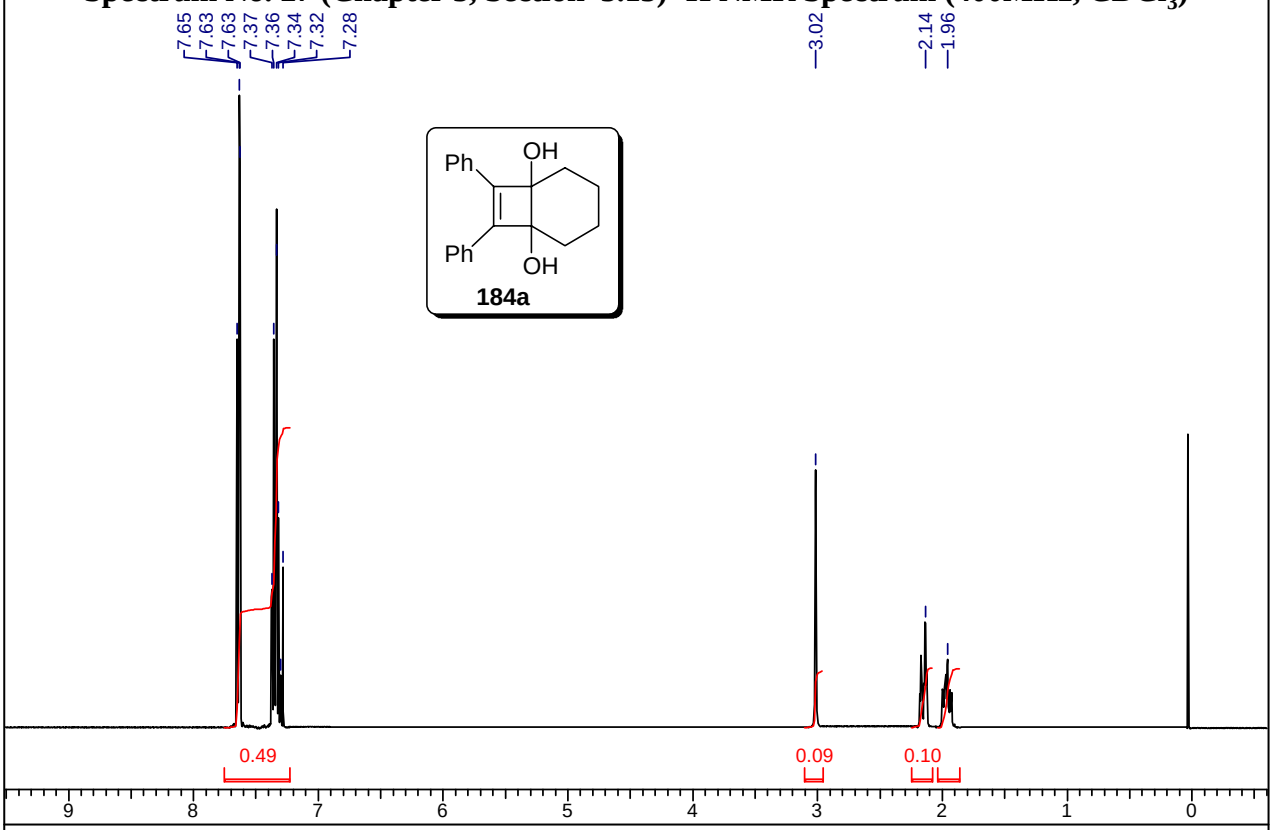
Spectrum No. 25 (Chapter 3, Section 3.12) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



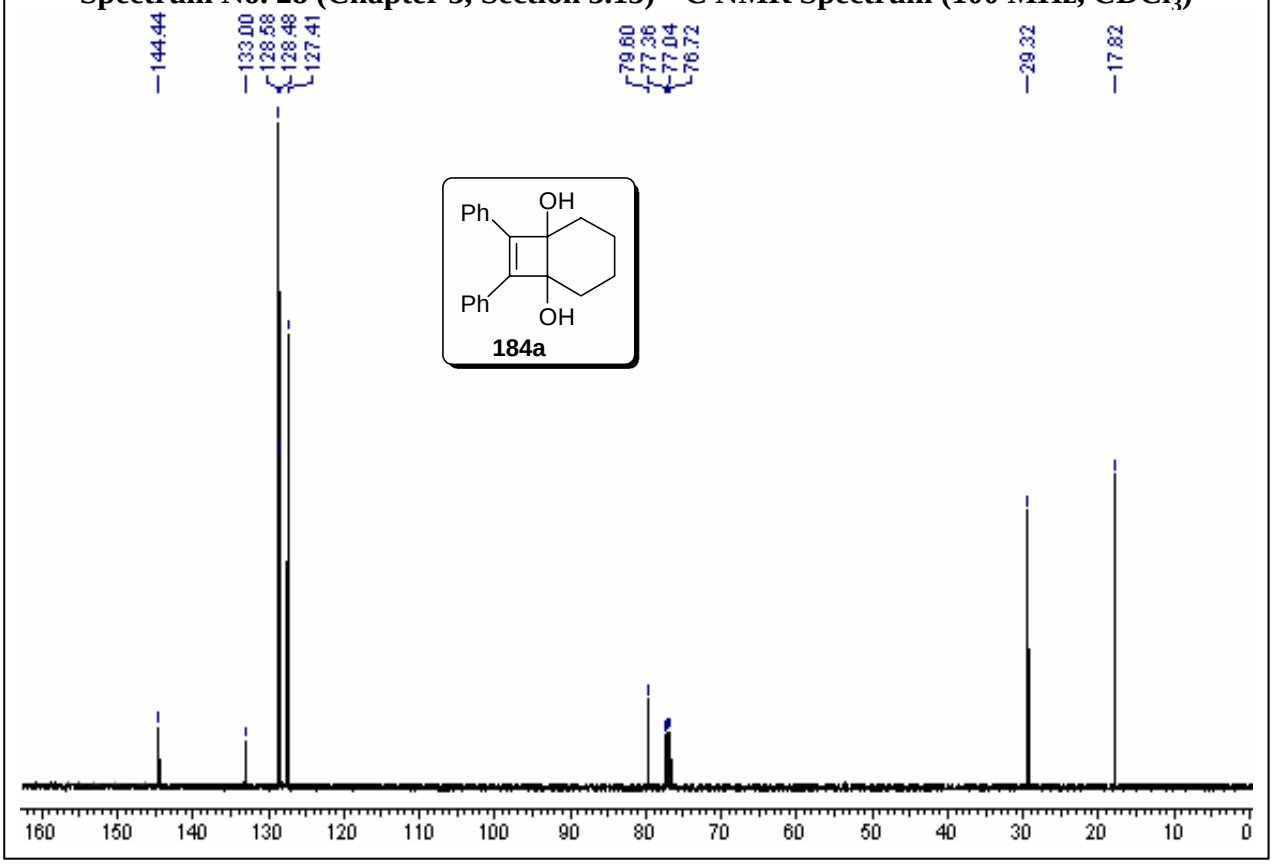
Spectrum No. 26 (Chapter 3, Section 3.12) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



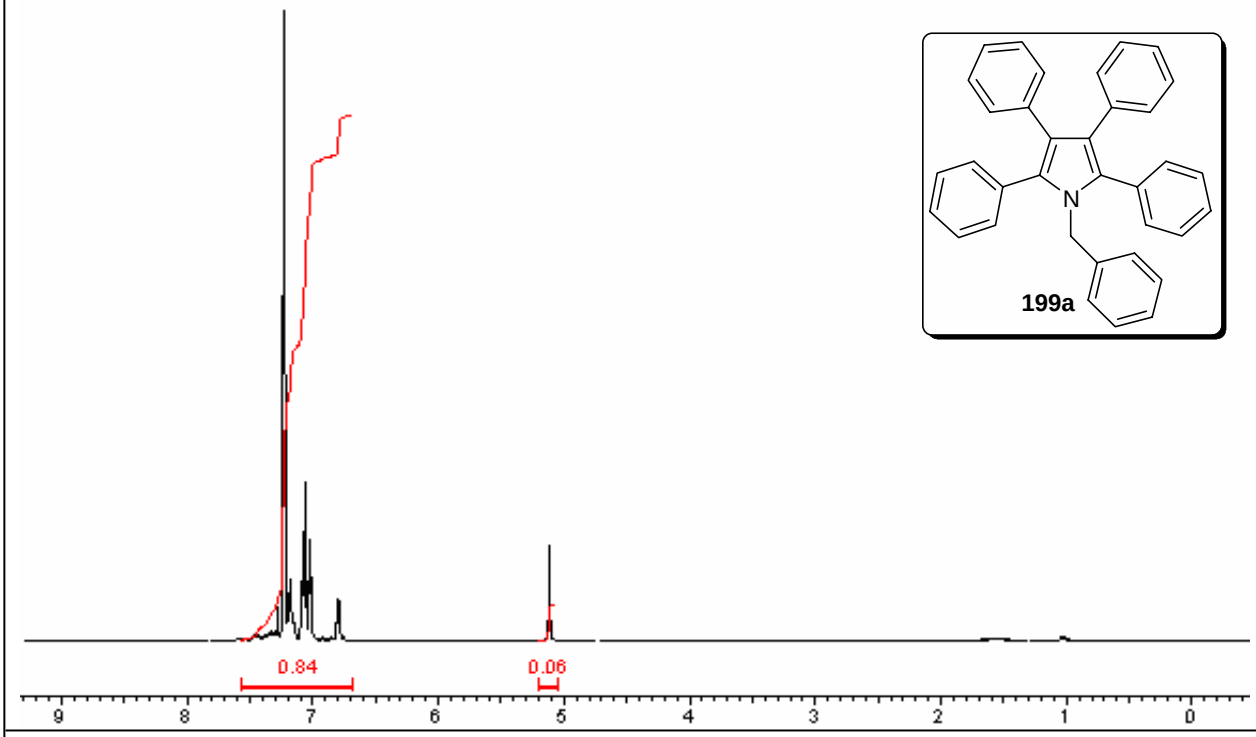
Spectrum No. 27 (Chapter 3, Section 3.13) ^{1}H NMR Spectrum (400MHz, $CDCl_3$)



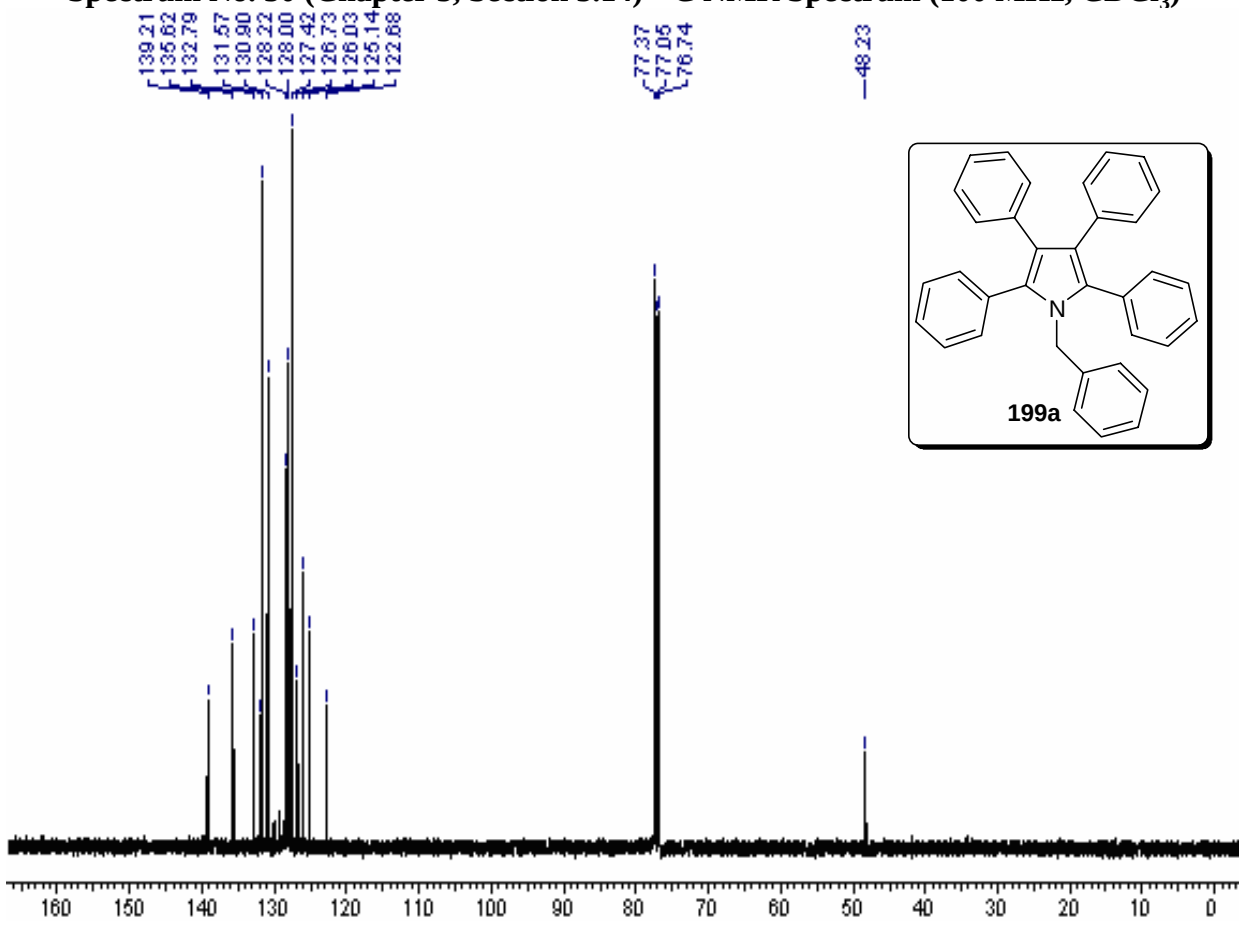
Spectrum No. 28 (Chapter 3, Section 3.13) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



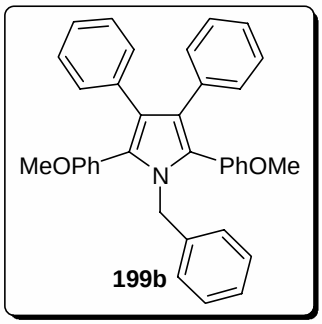
Spectrum No. 29 (Chapter 3, Section 3.14) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



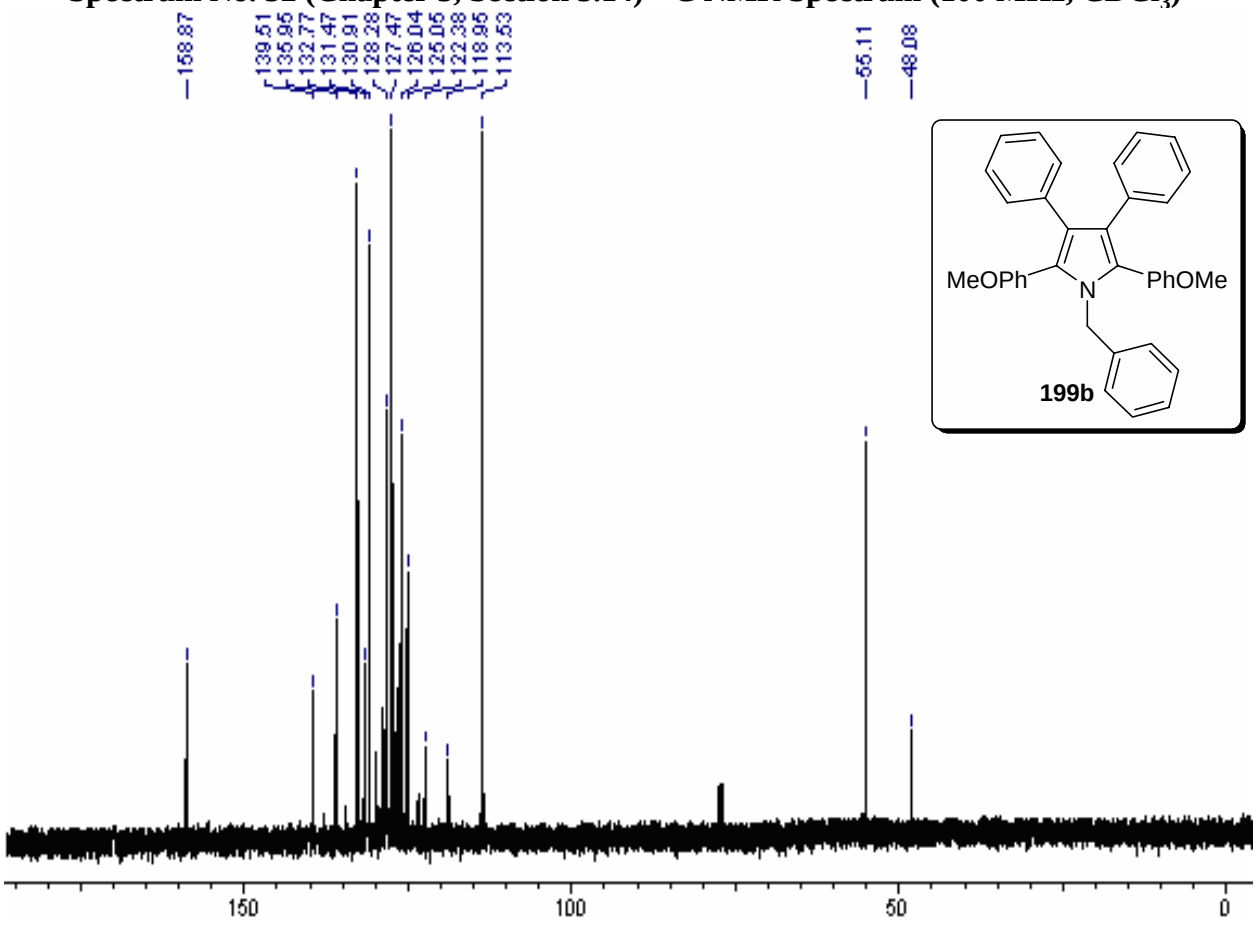
Spectrum No. 30 (Chapter 3, Section 3.14) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



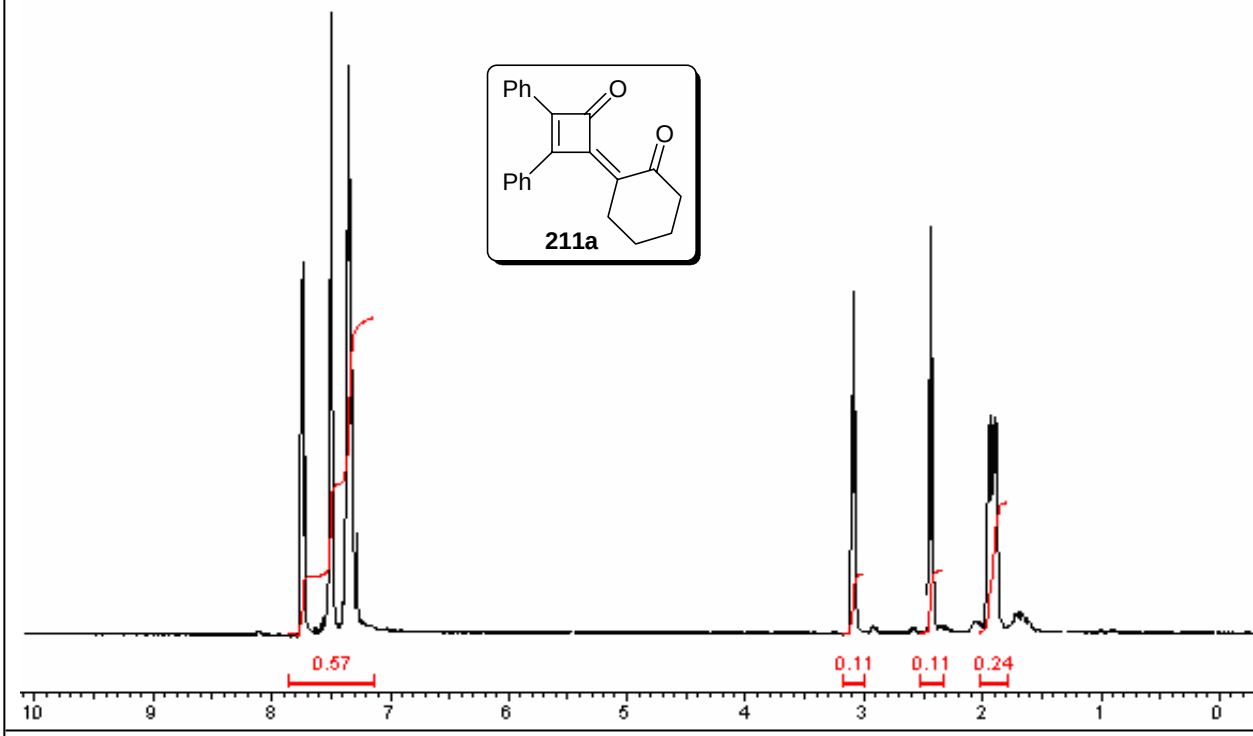
Spectrum No. 31 (Chapter 3, Section 3.14) ^{1}H NMR Spectrum (200 MHz, $CDCl_3$)



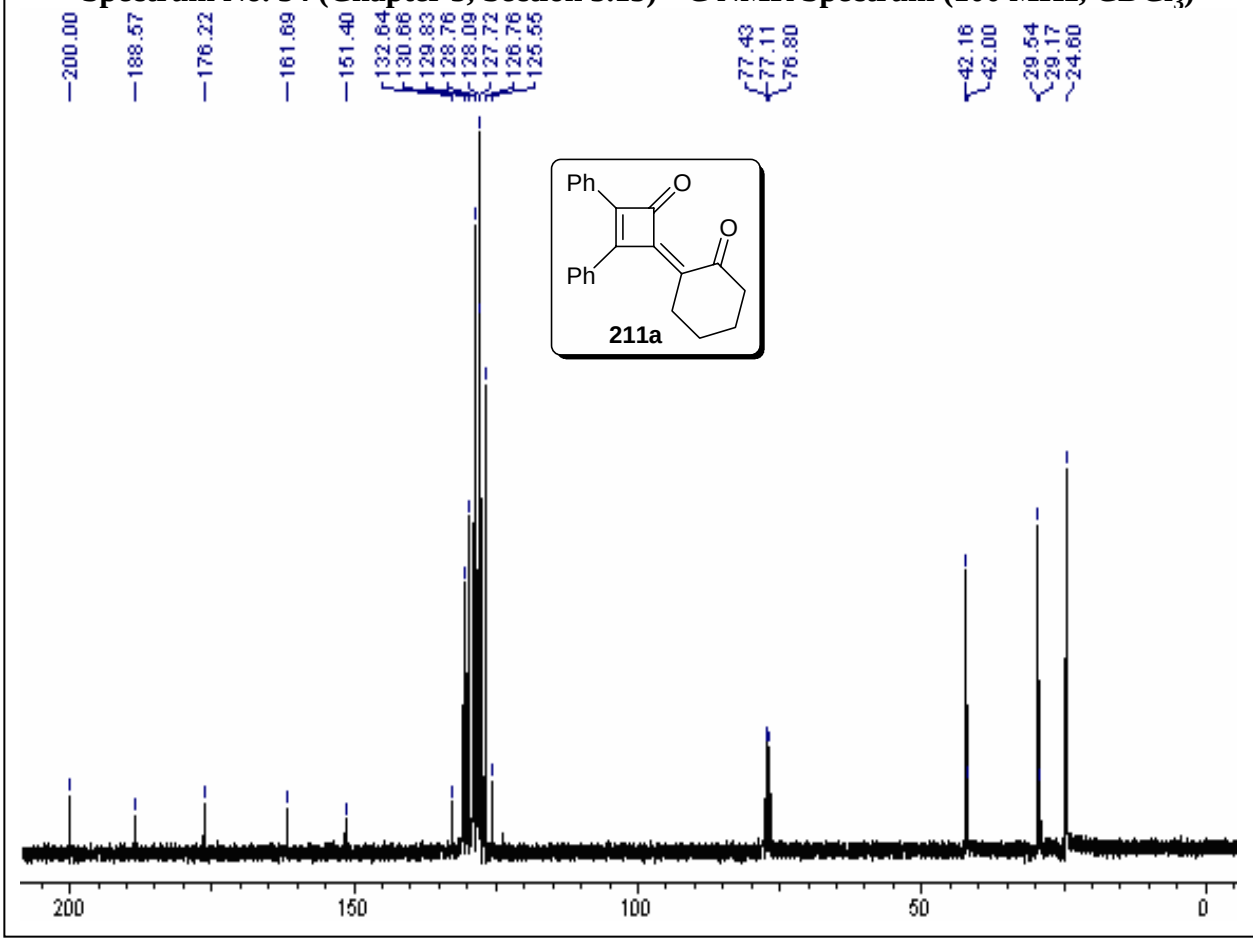
Spectrum No. 32 (Chapter 3, Section 3.14) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



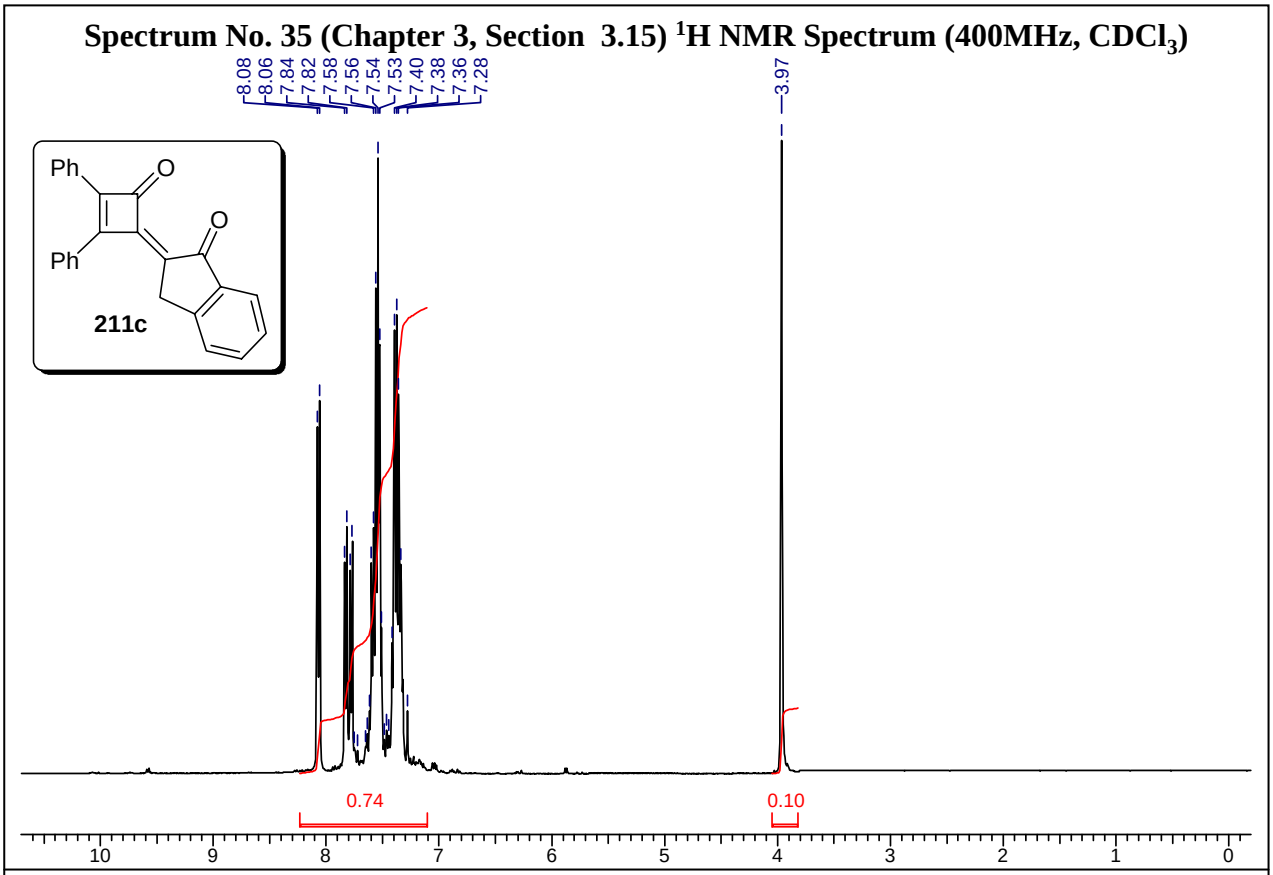
Spectrum No. 33 (Chapter 3, Section 3.15) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



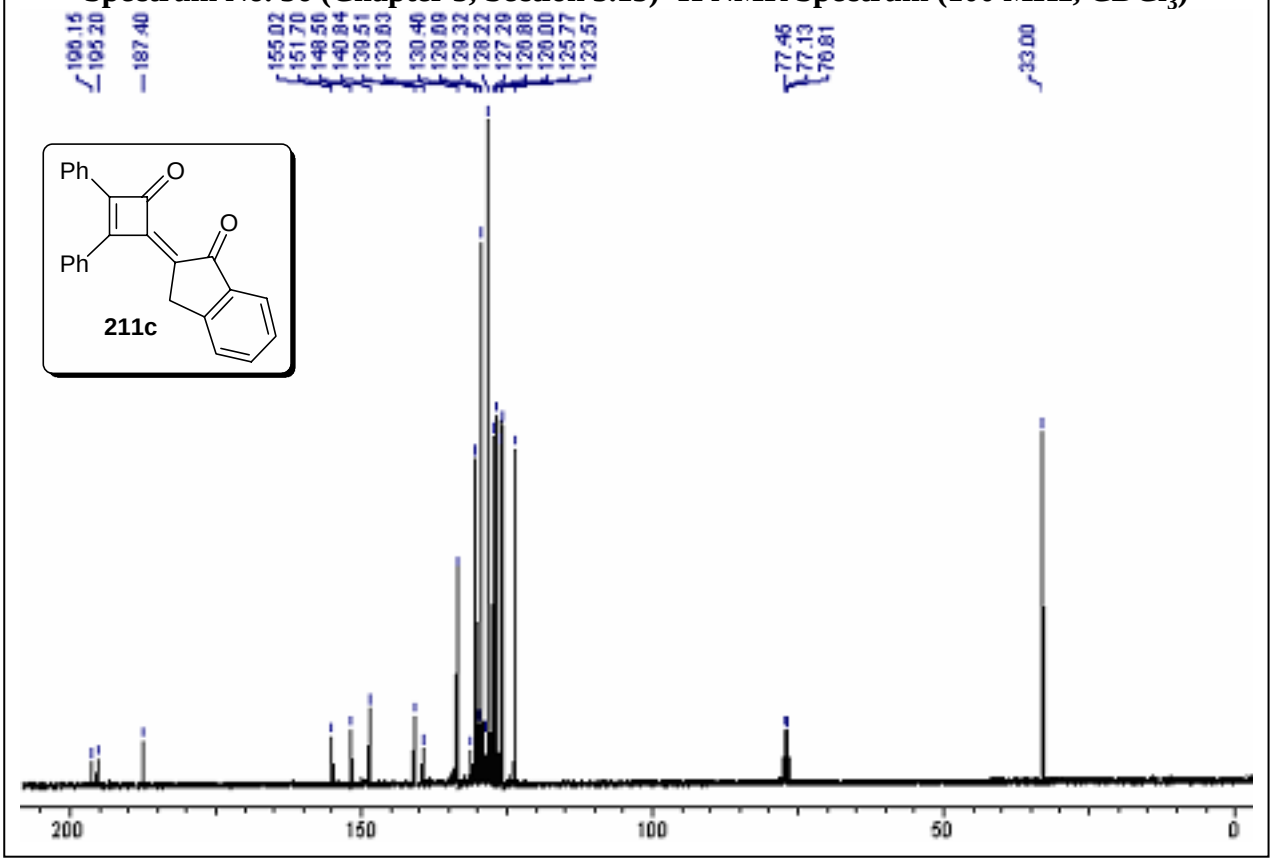
Spectrum No. 34 (Chapter 3, Section 3.15) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



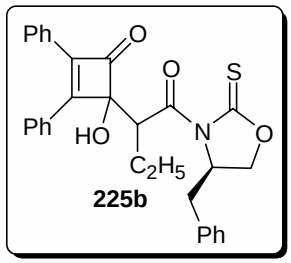
Spectrum No. 35 (Chapter 3, Section 3.15) ^{1}H NMR Spectrum (400MHz, $CDCl_3$)



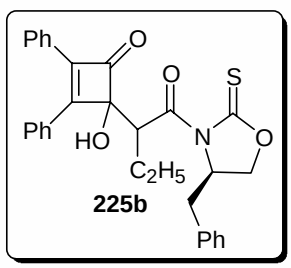
Spectrum No. 36 (Chapter 3, Section 3.15) ^{1}H NMR Spectrum (100 MHz, $CDCl_3$)



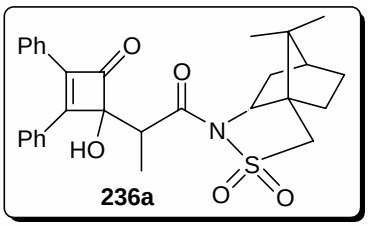
Spectrum No. 37 (Chapter 3, Section 3.18) ^{1}H NMR Spectrum (200 MHz, $CDCl_3$)



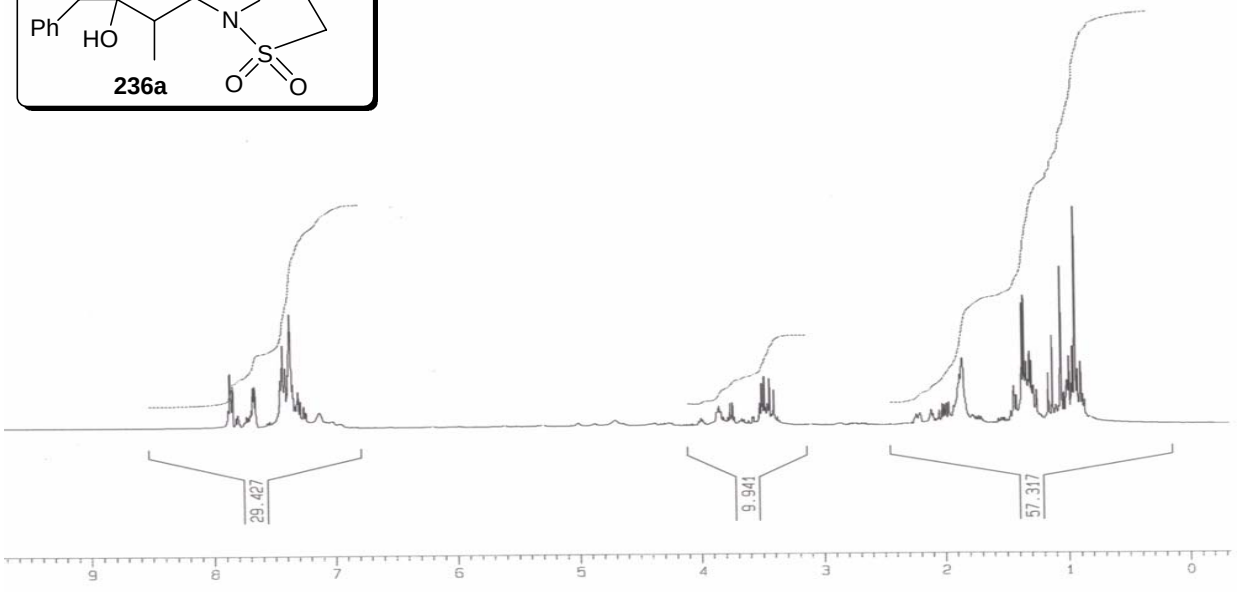
Spectrum No. 38 (Chapter 3, Section 3.18) ^{13}C NMR Spectrum (50 MHz, $CDCl_3$)



Spectrum No. 39 (Chapter 3, Section 3.20) ^{1}H NMR Spectrum (200 MHz, $CDCl_3$)

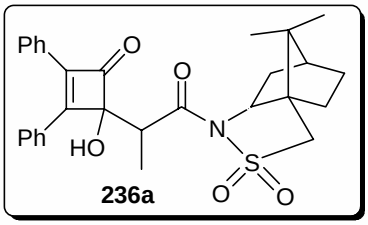


236a



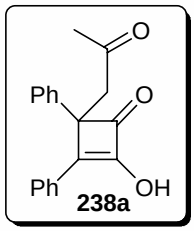
Spectrum No. 40 (Chapter 3, Section 3.20) ^{13}C NMR Spectrum (50 MHz, $CDCl_3$)

191.88
173.57
167.36
146.37
131.19
129.56
129.35
128.89
128.67
128.47
128.11
127.89
95.05
77.87
77.22
76.59
65.28
53.08
48.33
47.67
44.71
44.01
38.07
32.90
26.42
20.99
20.50
19.92
13.54

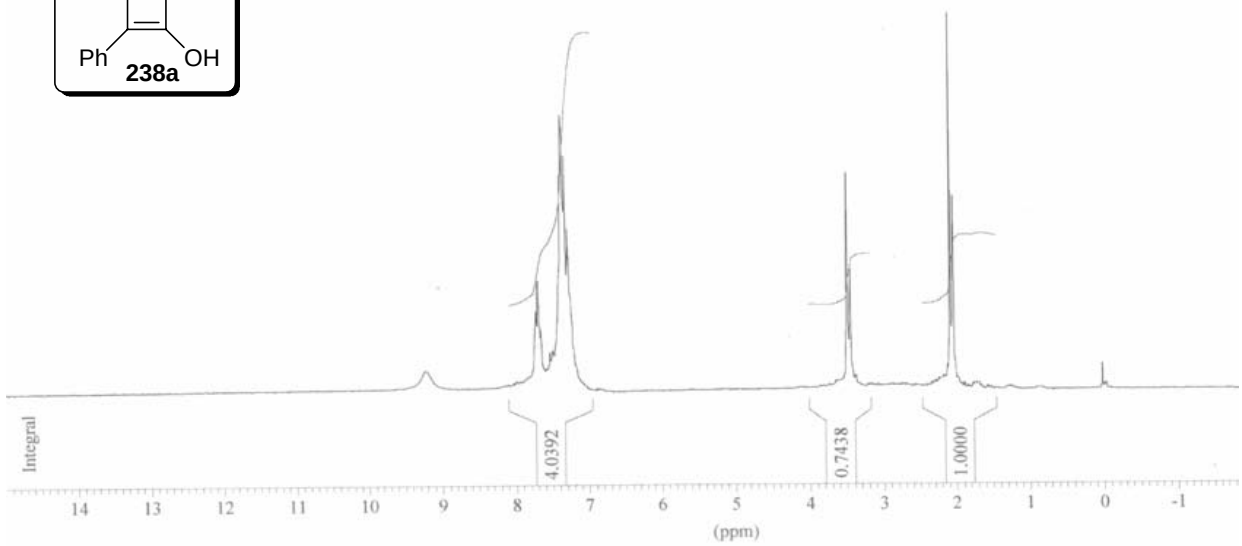


236a

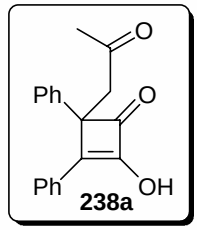
Spectrum No. 41 (Chapter 3, Section 3.21) ^{1}H NMR Spectrum (200 MHz, $CDCl_3$)



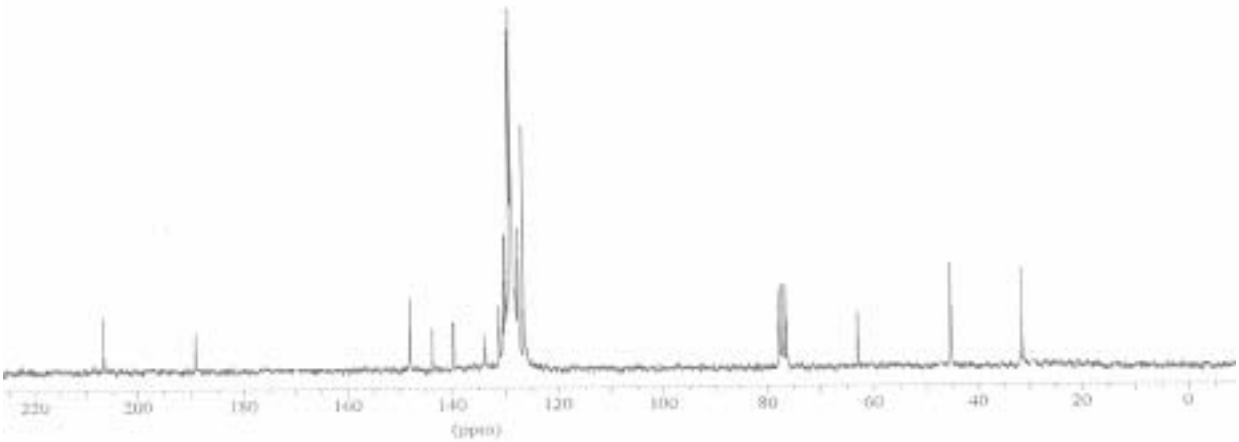
238a



Spectrum No. 42 (Chapter 3, Section 3.21) ^{13}C NMR Spectrum (50 MHz, $CDCl_3$)



238a



Appendix II

(X-Ray Crystallographic Data)

Table A1. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for **157e (Chapter 2, Section 2.1)**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	X	Y	Z	U(eq)
N(1)	480(2)	7360(1)	8462(1)	58(1)
O(1)	1409(1)	1343(1)	5123(1)	64(1)
O(2)	657(1)	-201(1)	6928(1)	70(1)
C(1)	1828(2)	1485(1)	6204(1)	48(1)
C(2)	1560(2)	818(1)	7036(1)	50(1)
C(3)	2615(2)	1575(1)	7987(1)	46(1)
C(4)	2986(2)	2471(1)	7267(1)	45(1)
C(5)	2358(2)	3772(1)	7565(1)	44(1)
C(6)	1827(2)	4200(1)	8582(1)	51(1)
C(7)	1199(2)	5373(1)	8887(1)	53(1)
C(8)	1080(2)	6159(1)	8165(1)	47(1)
C(9)	1725(2)	6610(2)	6391(2)	63(1)
C(10)	2321(2)	6263(2)	5406(2)	77(1)
C(11)	2868(2)	5068(2)	5066(2)	73(1)
C(12)	2845(2)	4243(2)	5731(1)	57(1)
C(13)	2277(2)	4573(1)	6786(1)	45(1)
C(14)	1653(2)	5776(1)	7099(1)	47(1)
C(15)	437(2)	7880(2)	9722(2)	78(1)
C(16)	-966(2)	7458(2)	7652(2)	83(1)
C(17)	4640(2)	2458(1)	7186(1)	49(1)
C(18)	5207(2)	1321(2)	6668(2)	66(1)
C(19)	6726(2)	1270(2)	6656(2)	82(1)
C(20)	7696(2)	2353(3)	7150(2)	85(1)
C(21)	7156(2)	3484(2)	7656(2)	77(1)
C(22)	5641(2)	3540(2)	7682(2)	61(1)
C(23)	3272(2)	1532(1)	9212(1)	47(1)
C(24)	2893(2)	502(1)	9588(1)	53(1)
C(25)	3520(2)	463(2)	10752(2)	64(1)
C(26)	4512(2)	1439(2)	11558(2)	70(1)
C(27)	4907(2)	2456(2)	11203(2)	71(1)
C(28)	4307(2)	2502(2)	10041(1)	60(1)

Table A2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for **169c (Chapter 2, Section 2.5)**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	X	Y	Z	U(eq)
O(1)	4889(1)	4443(2)	6095(1)	76(1)
O(2)	4165(1)	3115(2)	4864(1)	74(1)
C(1)	5205(1)	3627(2)	5720(1)	57(1)
C(2)	4864(1)	2983(2)	5146(1)	55(1)
C(3)	5801(1)	2169(2)	5088(1)	51(1)
C(4)	6116(1)	2772(2)	5599(1)	53(1)
C(5)	6963(1)	2677(2)	5921(1)	61(1)
C(6)	7034(1)	3338(2)	6431(1)	57(1)
C(7)	7852(1)	3323(2)	6799(1)	55(1)
C(8)	7800(1)	4079(3)	7323(1)	70(1)
C(9)	8558(2)	4063(3)	7682(1)	81(1)
C(10)	9378(2)	3298(3)	7532(1)	77(1)
C(11)	9447(1)	2541(3)	7015(1)	72(1)
C(12)	8693(1)	2556(2)	6652(1)	61(1)
C(13)	6175(1)	1154(2)	4644(1)	49(1)
C(14)	5590(1)	696(2)	4203(1)	63(1)
C(15)	5927(2)	-267(3)	3772(1)	75(1)
C(16)	6849(2)	-766(3)	3769(1)	73(1)
C(17)	7444(1)	-307(2)	4195(1)	68(1)
C(18)	7112(1)	638(2)	4631(1)	60(1)

Table A3. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for **173a (Chapter 2, Section 2.6)**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	X	Y	Z	U(eq)
O(1)	7280(1)	3184(1)	4969(2)	91(1)
O(2)	5679(1)	3160(1)	7540(2)	104(1)
C(1)	7004(1)	2192(1)	6415(2)	49(1)
C(2)	7582(2)	2846(1)	5909(2)	57(1)
C(3)	8559(2)	3010(1)	6601(2)	58(1)
C(4)	9343(2)	3099(1)	7256(2)	56(1)
C(5)	10259(1)	3181(1)	8084(2)	53(1)
C(6)	11174(2)	3465(1)	7654(2)	67(1)
C(7)	12044(2)	3521(1)	8478(2)	81(1)
C(8)	12012(2)	3306(1)	9721(2)	79(1)

C(9)	11111(2)	3033(1)	10160(2)	79(1)
C(10)	10238(2)	2966(1)	9350(2)	70(1)
C(11)	7561(1)	1512(1)	5992(2)	49(1)
C(12)	8118(2)	1086(1)	6873(2)	74(1)
C(13)	8641(2)	475(1)	6484(3)	95(1)
C(14)	8620(2)	283(1)	5223(3)	84(1)
C(15)	8075(2)	705(1)	4340(2)	72(1)
C(16)	7551(1)	1316(1)	4719(2)	59(1)
C(17)	5837(1)	2212(1)	6000(2)	51(1)
C(18)	5328(2)	2873(1)	6571(2)	62(1)
C(19)	4384(2)	3161(1)	5943(2)	64(1)
C(20)	3657(2)	3477(1)	5442(2)	63(1)
C(21)	2809(1)	3904(1)	4897(2)	56(1)
C(22)	2155(2)	3642(1)	3912(2)	79(1)
C(23)	1344(2)	4071(2)	3419(2)	96(1)
C(24)	1196(2)	4757(1)	3879(2)	85(1)
C(25)	1842(2)	5022(1)	4836(2)	77(1)
C(26)	2645(2)	4601(1)	5352(2)	68(1)
C(27)	5272(1)	1527(1)	6392(2)	52(1)
C(28)	5336(2)	1291(1)	7647(2)	68(1)
C(29)	4856(2)	648(1)	7987(2)	82(1)
C(30)	4286(2)	251(1)	7082(3)	88(1)
C(31)	4204(2)	487(1)	5841(3)	86(1)
C(32)	4703(1)	1118(1)	5492(2)	67(1)

Table A4. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for **178a (Chapter 2, Section 2.7)**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	X	Y	Z	U(eq)
O(1)	1712(1)	10974(2)	4740(1)	68(1)
C(1)	237(1)	9754(6)	3868(2)	97(1)
C(2)	803(1)	7930(4)	4099(2)	70(1)
C(3)	1552(1)	8908(3)	4507(1)	47(1)
C(4)	2084(1)	7142(3)	4569(1)	47(1)
C(5)	1850(1)	6996(3)	3478(1)	47(1)
C(6)	1441(1)	5053(3)	2838(2)	59(1)
C(7)	1208(1)	4902(4)	1845(2)	67(1)
C(8)	1391(1)	6682(4)	1477(2)	64(1)
C(9)	1798(1)	8618(4)	2100(2)	59(1)
C(10)	2025(1)	8789(3)	3095(1)	52(1)

Table A5. Atomic coordinates (x 10^4) a5nd equivalent isotropic displacement parameters (A^2 x 10^3) for **178d (Chapter 2, Section 2.7)**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	X	Y	Z	U(eq)
O(1)	10067(1)	1237(3)	4413(1)	77(1)
O(2)	10641(1)	3803(2)	5342(1)	72(1)
C(1)	11146(1)	2517(3)	6329(2)	54(1)
C(2)	11113(2)	1545(4)	6730(2)	66(1)
C(3)	11653(2)	1225(6)	7354(2)	92(1)
C(4)	12217(2)	1885(6)	7554(2)	96(2)
C(5)	12262(2)	2838(5)	7154(3)	89(1)
C(6)	11734(2)	3164(4)	6552(2)	70(1)
C(7)	10586(1)	2931(3)	5671(2)	51(1)
C(8)	9931(1)	2285(3)	5434(1)	46(1)
C(9)	9453(1)	2677(3)	4695(1)	46(1)
C(10)	9665(1)	2114(3)	4227(2)	51(1)
C(11)	9349(1)	2600(3)	3517(2)	51(1)
C(12)	9461(2)	1925(4)	3059(2)	72(1)
C(13)	9157(2)	2322(5)	2391(2)	90(1)
C(14)	8766(2)	3410(4)	2183(2)	77(1)
C(15)	8662(2)	4115(4)	2629(2)	70(1)
C(16)	8949(2)	3710(3)	3290(2)	57(1)
C(17)	8777(1)	2209(3)	4476(1)	49(1)
C(18)	8588(2)	905(3)	4269(2)	65(1)
C(19)	7986(2)	483(5)	4095(2)	85(1)
C(20)	7559(2)	1329(5)	4121(2)	90(1)
C(21)	7738(2)	2618(5)	4327(2)	79(1)
C(22)	8342(2)	3059(4)	4498(2)	61(1)
C(23)	9684(1)	2647(3)	5898(1)	48(1)
C(24)	9426(2)	1672(3)	6121(2)	61(1)
C(25)	9204(2)	2007(5)	6549(2)	80(1)
C(26)	9241(2)	3310(5)	6763(2)	84(1)
C(27)	9493(2)	4258(5)	6545(2)	83(1)
C(28)	9711(2)	3958(3)	6111(2)	62(1)

Table A6. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for **179b (Chapter 2, Section 2.7)**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	X	Y	Z	U(eq)
O(1)	6557(3)	1595(1)	-216(5)	89(1)
O(2)	9070(3)	1073(2)	3286(4)	81(1)
O(3)	4404(4)	1907(2)	4737(5)	103(1)
O(4)	11412(3)	2362(2)	-1345(5)	92(1)
C(1)	7449(4)	1327(2)	-216(5)	58(1)
C(2)	7503(4)	691(2)	93(5)	49(1)
C(3)	7652(4)	512(2)	1467(5)	50(1)
C(4)	8014(4)	934(2)	2762(5)	51(1)
C(5)	7062(4)	1151(2)	3344(5)	52(1)
C(6)	7401(4)	1476(2)	4632(5)	57(1)
C(7)	6542(5)	1733(2)	5148(6)	65(1)
C(8)	5315(5)	1666(2)	4358(6)	71(1)
C(9)	4961(5)	1326(2)	3086(6)	74(2)
C(10)	5828(5)	1077(2)	2588(5)	64(1)
C(11)	4726(7)	2311(3)	5946(9)	120(3)
C(12)	8488(4)	1592(2)	-555(5)	51(1)
C(13)	9558(4)	1306(2)	-441(6)	66(1)
C(14)	10503(5)	1564(2)	-702(7)	75(2)
C(15)	10406(4)	2136(2)	-1127(6)	63(1)
C(16)	9355(4)	2437(2)	-1256(6)	65(1)
C(17)	8406(4)	2161(2)	-963(5)	60(1)
C(18)	11339(5)	2926(3)	-1882(7)	96(2)
C(19)	7371(4)	331(2)	-1239(5)	48(1)
C(20)	8145(5)	-127(2)	-1183(6)	65(1)
C(21)	8071(6)	-419(2)	-2453(7)	83(2)
C(22)	7240(7)	-266(3)	-3806(7)	92(2)
C(23)	6489(6)	186(3)	-3871(7)	90(2)
C(24)	6549(4)	481(2)	-2612(6)	64(1)
C(25)	7607(4)	-93(2)	1937(4)	47(1)
C(26)	8576(5)	-325(2)	3055(5)	67(1)
C(27)	8534(6)	-887(2)	3488(6)	80(2)
C(28)	7517(6)	-1212(2)	2839(6)	76(2)
C(29)	6553(5)	-984(2)	1732(7)	73(2)
C(30)	6598(4)	-430(2)	1275(6)	67(1)

Table A7. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for **184a (Chapter 2, Section 2.8)**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	X	Y	Z	U(eq)
O(1)	7355(3)	8822(3)	9590(1)	54(1)
O(2)	8378(3)	7341(3)	9486(1)	52(1)
C(1)	8044(4)	8968(4)	9364(2)	44(1)
C(2)	8605(5)	9761(4)	9564(2)	63(2)
C(3)	9359(5)	9957(5)	9338(2)	73(2)
C(4)	9979(5)	9150(5)	9295(2)	69(2)
C(5)	9664(4)	8293(4)	9465(2)	58(2)
C(6)	8647(4)	8151(4)	9315(2)	46(1)
C(7)	8237(4)	8217(4)	8828(2)	43(1)
C(8)	7697(4)	8926(4)	8869(2)	42(1)
C(9)	8486(4)	7731(4)	8473(2)	46(1)
C(10)	8598(5)	8179(5)	8105(2)	63(2)
C(11)	8832(6)	7690(6)	7777(2)	81(2)
C(12)	8977(6)	6824(7)	7810(3)	95(3)
C(13)	8856(6)	6381(5)	8169(3)	86(2)
C(14)	8624(5)	6840(5)	8503(2)	65(2)
C(15)	7048(4)	9491(4)	8581(2)	45(1)
C(16)	6709(5)	9320(5)	8144(2)	64(2)
C(17)	6091(5)	9869(6)	7897(2)	84(2)
C(18)	5804(6)	10630(6)	8056(3)	84(2)
C(19)	6106(5)	10807(5)	8474(3)	84(2)
C(20)	6701(4)	10237(4)	8745(2)	58(2)

Table A8. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for **199b (Chapter 2, Section 2.9)**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	X	Y	Z	U(eq)
O(1)	802(2)	-5510(2)	-5682(1)	78(1)
O(2)	9674(3)	-3720(2)	378(1)	91(1)
N(1)	5673(2)	-4086(2)	-2873(1)	50(1)
C(1)	6581(3)	-3410(2)	-2533(1)	46(1)
C(2)	6471(3)	-2667(2)	-3006(1)	45(1)
C(3)	5461(3)	-2899(2)	-3657(1)	46(1)
C(4)	4987(3)	-3778(2)	-3559(1)	48(1)
C(5)	3883(3)	-4301(2)	-4063(1)	48(1)
C(6)	3974(3)	-5218(2)	-4284(2)	63(1)
C(7)	2949(3)	-5660(2)	-4806(2)	69(1)
C(8)	1833(3)	-5166(2)	-5134(2)	58(1)
C(9)	1707(3)	-4253(2)	-4910(2)	63(1)

C(10)	2708(3)	-3837(2)	-4380(2)	56(1)
C(11)	896(4)	-6441(2)	-5929(2)	96(1)
C(12)	4928(3)	-2308(2)	-4311(1)	45(1)
C(13)	4676(3)	-2717(2)	-4985(1)	58(1)
C(14)	4123(3)	-2209(3)	-5596(2)	79(1)
C(15)	3791(4)	-1278(3)	-5567(2)	90(1)
C(16)	4029(4)	-857(3)	-4906(2)	87(1)
C(17)	4614(3)	-1364(2)	-4282(2)	63(1)
C(18)	7262(3)	-1787(2)	-2847(1)	45(1)
C(19)	7782(3)	-1405(2)	-3344(2)	57(1)
C(20)	8504(3)	-579(2)	-3203(2)	67(1)
C(21)	8702(3)	-109(2)	-2566(2)	70(1)
C(22)	8210(3)	-473(2)	-2063(2)	63(1)
C(23)	7498(3)	-1302(2)	-2200(2)	52(1)
C(24)	7422(3)	-3517(2)	-1777(1)	48(1)
C(25)	8750(3)	-3580(2)	-1594(2)	60(1)
C(26)	9550(3)	-3635(2)	-880(2)	69(1)
C(27)	9000(4)	-3636(2)	-339(2)	64(1)
C(28)	7673(3)	-3562(2)	-516(2)	64(1)
C(29)	6903(3)	-3502(2)	-1222(2)	59(1)
C(30)	11052(4)	-3785(3)	596(2)	111(2)
C(31)	5551(3)	-5020(2)	-2578(2)	55(1)
C(32)	6492(3)	-5764(2)	-2661(1)	47(1)
C(33)	6416(3)	-6675(2)	-2417(1)	61(1)
C(34)	7274(4)	-7371(3)	-2454(2)	79(1)
C(35)	8219(4)	-7168(3)	-2742(2)	83(1)
C(36)	8298(3)	-6280(3)	-3008(2)	79(1)
C(37)	7434(3)	-5581(2)	-2965(2)	66(1)

Table A9. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for **211c (Chapter 2, Section 2.10)**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	X	Y	Z	U(eq)
O(1)	4212(2)	7670(3)	3985(1)	65(1)
O(2)	2576(2)	6807(3)	4459(1)	68(1)
C(1)	5011(2)	7670(4)	4649(1)	49(1)
C(2)	6298(2)	7968(4)	5099(1)	46(1)
C(3)	6451(2)	7709(4)	5768(1)	47(1)
C(4)	5194(2)	7394(3)	5396(1)	46(1)
C(5)	4549(2)	7074(4)	5640(1)	47(1)

C(6)	3252(2)	6823(4)	5149(2)	50(1)
C(7)	2948(2)	6597(4)	5673(2)	52(1)
C(8)	1853(3)	6320(4)	5505(2)	68(1)
C(9)	1788(3)	6147(5)	6093(2)	82(1)
C(10)	2773(3)	6285(6)	6830(2)	87(1)
C(11)	3859(3)	6560(6)	7005(2)	83(1)
C(12)	3948(2)	6707(4)	6418(2)	58(1)
C(13)	5031(2)	6959(5)	6464(2)	61(1)
C(14)	7054(2)	8253(4)	4877(2)	50(1)
C(15)	6546(3)	8341(4)	4109(2)	66(1)
C(16)	7214(3)	8545(5)	3861(2)	80(1)
C(17)	8398(3)	8664(5)	4374(2)	79(1)
C(18)	8926(3)	8602(5)	5137(2)	78(1)
C(19)	8269(2)	8386(4)	5394(2)	66(1)
C(20)	7489(2)	7704(4)	6574(1)	49(1)
C(21)	8177(2)	9337(5)	6905(2)	63(1)
C(22)	9185(3)	9284(6)	7649(2)	75(1)
C(23)	9501(3)	7596(6)	8061(2)	80(1)
C(24)	8811(3)	5988(6)	7741(2)	76(1)
C(25)	7806(2)	6033(5)	6998(2)	63(1)

Table A10. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for **211f (Chapter 2, Section 2.10)**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	X	Y	Z	U(eq)
O(1)	5128(4)	1639(3)	-696(2)	74(1)
O(2)	5806(3)	2109(2)	385(2)	61(1)
O(3)	6389(4)	1593(4)	1996(2)	88(1)
C(1)	5342(5)	3559(4)	1380(2)	55(1)
C(2)	3755(5)	3827(5)	1256(3)	81(2)
C(3)	3057(6)	3462(6)	1948(3)	92(2)
C(4)	3909(6)	2208(6)	2198(3)	99(2)
C(5)	5356(6)	2337(5)	1887(2)	62(1)
C(6)	7792(5)	6237(4)	907(2)	57(1)
C(7)	6652(4)	5944(4)	470(2)	48(1)
C(8)	5771(5)	7038(4)	262(2)	66(1)
C(9)	6043(6)	8405(5)	487(3)	77(1)
C(10)	7167(6)	8664(5)	924(2)	71(1)
C(11)	8043(5)	7588(5)	1134(2)	65(1)

C(12)	6991(5)	5745(5)	-1193(2)	67(1)
C(13)	7044(6)	6375(5)	-1825(3)	81(2)
C(14)	6157(7)	5934(6)	-2348(3)	84(2)
C(15)	5189(6)	4879(5)	-2226(3)	77(2)
C(16)	5107(5)	4238(4)	-1582(2)	59(1)
C(17)	6012(5)	4671(4)	-1055(2)	51(1)
C(18)	5969(4)	3983(4)	-374(2)	48(1)
C(19)	6336(4)	4484(4)	245(2)	46(1)
C(20)	6299(5)	3322(4)	769(2)	51(1)
C(21)	5581(4)	2481(4)	-294(3)	55(1)

Table A11. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for **238a (Chapter 2, Section 2.13)**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	X	Y	Z	U(eq)
O(1)	3256(1)	4796(1)	457(1)	73(1)
O(2)	5683(1)	7036(1)	409(1)	63(1)
O(3)	3153(2)	9196(2)	-273(1)	93(1)
C(1)	3749(2)	6158(2)	774(1)	51(1)
C(2)	4835(1)	7113(2)	728(1)	47(1)
C(3)	4485(1)	8330(2)	1298(1)	43(1)
C(4)	3374(1)	7181(2)	1252(1)	45(1)
C(5)	4114(2)	10001(2)	981(1)	50(1)
C(6)	3065(2)	10011(2)	266(1)	63(1)
C(7)	1946(2)	11021(3)	254(2)	102(1)
C(8)	5487(1)	8393(2)	2046(1)	45(1)
C(9)	6559(1)	9314(2)	2112(1)	56(1)
C(10)	7486(2)	9345(2)	2792(1)	68(1)
C(11)	7367(2)	8447(2)	3404(1)	71(1)
C(12)	6319(2)	7533(2)	3346(1)	71(1)
C(13)	5381(2)	7498(2)	2670(1)	58(1)
C(14)	2256(1)	7272(2)	1550(1)	49(1)
C(15)	2185(2)	8321(2)	2135(1)	62(1)
C(16)	1106(2)	8387(2)	2399(1)	81(1)
C(17)	93(2)	7457(3)	2089(1)	89(1)
C(18)	142(2)	6426(3)	1509(1)	85(1)
C(19)	1217(2)	6321(2)	1242(1)	66(1)

LIST OF PUBLICATIONS

1. Convenient Methods of Synthesis of Cyclobutenediones and Anhydrides from Alkynes Using the $Fe(CO)_5/Me_3NO$ Reagent System, Periasamy, M.; Mukkanti, A.; **Shyam Raj, D.** *Organometallics* **2004**, *23*, 6323.
2. Novel Synthesis of Acyloxyferrole Complexes from Alkynes and their Conversion to Cyclobutenediones, Periasamy, M.; Mukkanti, A.; **Shyam Raj, D.** *Organometallics* **2004**, *23,* 619.
3. Diasterioselective Cross Aldol Reaction of Ketones with Diphenylcyclobutenedione Promoted by the $TiCl_4/Bu_3N$ Reagent, Periasamy, M.; Mukkanti, A.; **Shyam Raj, D.** *Communicated.*
4. Novel Reactions of Dyphenylcyclobutenedione and Tertiary Arylamines with $TiCl_4$ and $SnCl_4$, Periasamy, M.; **Shyam Raj, D.**; Mukkanti, A. *Communicated.*
5. Conversion of 1-Alkynes to Benzoquinones Using the $Fe(CO)_5/TiCl_4$ Reagent System, Periasamy, M.; Mukkanti, A.; **Shyam Raj, D.** *Manuscript under preparation.*
6. Conversion of Cyclobutenediones to 1,4-Diketones Using the $RMgBr/TiCl_4$ Reagent System, Periasamy, M.; **Shyam Raj, D**.; Mallesh, B. *Manuscript under preparation.*
7. Synthesis of Bicyclic Diols with Cyclobutenediones Using the Grignard Reagent, Periasamy, M.; **Shyam Raj, D**. *Manuscript under preparation.*
8. Proline Catalyzed 1,4-addition Reactions of Cyclobutenediones with Ketones, Periasamy, M.; **Shyam Raj, D**.; Mallesh, B. *Manuscript under preparation.*
9. Diasterioselective Cross Aldol Reaction of Chiral Auxiliaries with Diphenyl-cyclobutenedione Promoted by the $TiCl_4/Bu_3N$ Reagent, Periasamy, M.; **Shyam Raj, D**.; Mallesh, B. *Manuscript under preparation.*

POSTERS/PAPERS PRESENTED IN SYMPOSIA

1. Poster and Oral presentation in the *"Chemfest 2007"* in house symposium held at University of Hyderabad, Hyderabad, India, April 09, **2007**; Title: "Reactivity, Mechanistic Studies and Applications of Cylobutenediones" Periasamy, M. and **Shyam Raj, D.**
2. Presented a poster in the *"Chemfest 2006"* in house symposium held at University of Hyderabad, Hyderabad, India, March 07, **2006**; Title: "Applications of Cyclobutenediones" Periasamy, M. and **Shyam Raj, D.**
3. Presented a poster in the *"**NOST-National Organic Symposium Trust**"* held at IACS Jadhavpur, Kolkata, India, February 04-06, **2005;** Title: "Synthetic Methods and Applications of Cyclobutenediones" Periasamy, M. and **Shyam Raj, D.**
4. Presented a poster in the *"Chemfest 2004"* in house symposium held at University of Hyderabad, Hyderabad, India, March 12, **2004**; Title: "Synthetic Applications of Cyclobutenediones" Periasamy, M. and **Shyam Raj, D.**