Studies on Synthesis of Bicyclic Acetals from Epoxyalkynes and α-Diarylacetic Esters from Benzoins *via in Situ* Generated Acetals

DOCTOR OF PHILOSOPHY

by

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Studies on Synthesis of Bicyclic Acetals from Epoxyalkynes and α-Diarylacetic Esters from Benzoins *via in Situ* Generated Acetals

A Thesis Submitted for the Degree of

DOCTOR OF PHILOSOPHY

In Chemistry

by

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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 **Dr. Rengarajan Balamurugan**.

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. Any omission, which might have occurred by oversight or error, is regretted.

University of Hyderabad
November, 2014

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Certificate

Certified that the work embodied in this thesis entitled "**Studies on Synthesis of Bicyclic Acetals from Epoxyalkynes and α-Diarylacetic Esters from Benzoins *via in Situ* Generated Acetals**" has been carried out by **Mr. RAVEENDRA BABU KOTHAPALLI** under my supervision and the same has not been submitted elsewhere for a degree.

Dr. R. BALAMURUGAN
(THESIS SUPERVISOR)

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…Dedicated to my Parents

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List of acronyms used

[α]	Specific rotation [expressed without units; the actual units are deg $dm^{-1}cm^3$ g^{-1}]
Å	Angstrom
Ac	Acetyl
Anal. Calc'd	Analytically calculated
Aq.	Aqueous
Ar	Aryl
Bn	Benzyl
br s	Broad singlet (spectral)
t-Bu	*tert*-Butyl
^oC	Degree Celsius
Cacld	Calculated
Cat.	Catalytic
CBS	Corey-Bakshi-Shibata
cm^{-1}	Wavenumber(s)
conc.	Concentrated
m-CPBA	*m*-Chloroperbenzoic acid
CSA	Camphorsulfonicacid
Cy	Cyclohexyl
δ	Chemical shift in parts per million
d	Doublet
DCE	Dichloroethane
DCM	Dichloromethane
dd	Doublet of doublets (spectral)
DDQ	2,3-Dichloro-4,6-dicyano-1,4-benzoquinone
ddd	Doublet of doublet of doublets
DET	Diethyl tartrate
DIBAL-H	Diisobutylaluminium hydride
dil.	Dilute
DMF	N,N-Dimethylformamide
DMG	Directed metalation group
DMSO	Dimethylsulfoxide
DoL	Directed *ortho*-lithiation
DoM	Directed *ortho*-metalation

DPP	*α*,*α*-diphenylprolinol
dr	Diastereomeric ratio
dt	Doublet of triplets (Spectral)
EA	Elemental analysis
ee	Enantiomeric excess
equiv	Equivalent
ESI	Electron spin ionisation
Et	Ethyl
EtOAc	Ethyl acetate
EtOH	Ethyl alcohol
FT	Fourier transformation
g	Gram(s)
h	Hour(s)
HPLC	High performance liquid chromatography
HRMS	High resolution mass spectrometry
Hz	Hertz
i-Pr	Isopropyl
IR	Infrared
J	Coupling constant (in NMR Spectroscopy)
K	Kelvin (Temperature)
LA	Lewis acid
LCMS	Liquid chromatography-mass spectrometry
Lit.	Literature
M	Molar (Solution concentration)
m	Multiplet (spectral)
Me	Methyl
MeCN	Acetonitrile
mg	Milligram(s)
MHz	Megahertz
min	Minute(s)
mL	Millilitre (s)
mmol	Millimole(s)
mp	Melting point
MS	Molecular sieves
μL	microlitre
NCS	N-Chlorosuccinimide

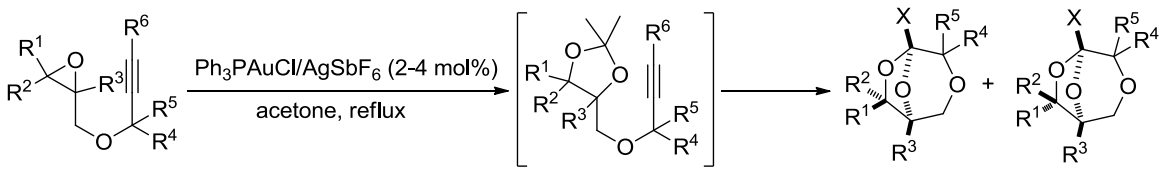
NMR	Nuclear magnetic resonance
ORTEP	Oak ridge thermal ellipsoid plot
OTf	Trifluoromethanesulfonate
PCC	Pyridinium chlorochromate
PDC	Pyridinium dichromate
Ph	Phenyl
PMA	Phosphomolybdic acid
PTSA/*p*-TsOH	*p*-Toluenesulfonic acid
q	Quartet (spectral)
R_f	Retardation factor
rt	Room temperature
s	Singlet (spectral)
t	Triplet (spectral)
TBAF	Tetrabutylammonium fluoride
TBDMS	*tert*-Butyldimethylsilyl ether
TBDPS	*tert*-Butyldiphenylsilyl ether
TBHP	*tert*-Butyl hydroperoxide
td	Triplet of doublets(spectral)
TFA	Trifluoroacetic acid
TfOH	Triflic acid
THF	Tetrahydrofuran
TLC	Thin layer chromatography
TMEDA	*N*,*N*,*N'*,*N'*-Tetramethylethane-1,2-diamine
TMP	2,2,6,6-Tetramethylpiperidinato
TMSCl	Trimethylsilyl chloride
UV	Ultraviolet
w/w	Weight/weight

SYNOPSIS

This thesis entitled "**Studies on Synthesis of Bicyclic Acetals from Epoxyalkynes and α-Diarylacetic Esters from Benzoins *via in Situ* Generated Acetals**" consists of three chapters. Each chapter is subdivided into six sections namely Introduction, Results and Discussion, Conclusions, Experimental section, References and Representative spectra. The summary of each chapter is depicted here briefly.

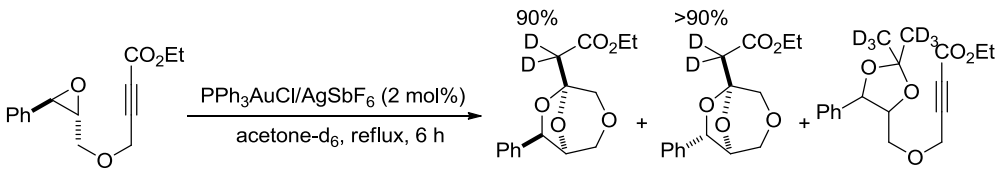
Chapter 1: Gold(I)-Catalyzed Synthesis of Bicyclic Acetals form Epoxyalkynes

Chapter 1 describes the synthesis of bicyclic acetals from epoxyalkynes using gold(I) catalyst. In the present reaction, gold catalyst utilizes its oxo- and alkynophilicities in tandem. A diol equivalent (acetonide) is generated when epoxyalkynes are treated with Gold(I) catalyst in acetone. The acetonide cyclizes intramoleculary on the gold-activated triple bond to generate bicyclic acetal. While *cis*-acetonide gives *endo* bicyclic acetal, the *trans*-acetonide furnishes *exo* bicyclic acetal. Substituents on the epoxide ring decide the stereochemical outcome in the product.



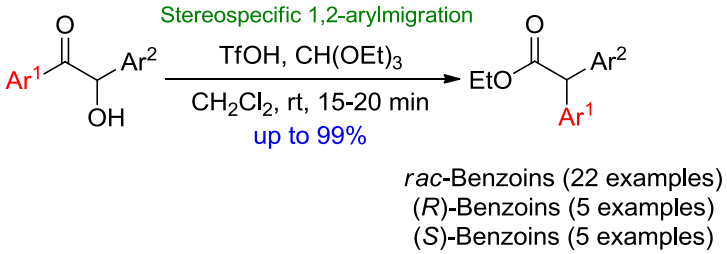
Scheme 1. Au(I)-catalyzed synthesis of bicyclic acetals

The mechanism of this reaction was systematically evaluated. Using deuterium incorporation studies, it has been established that water is formed under the reaction condition by aldol self-condensation of solvent acetone. It was found to play a crucial role in the cyclization of the acetonide on the triple bond.



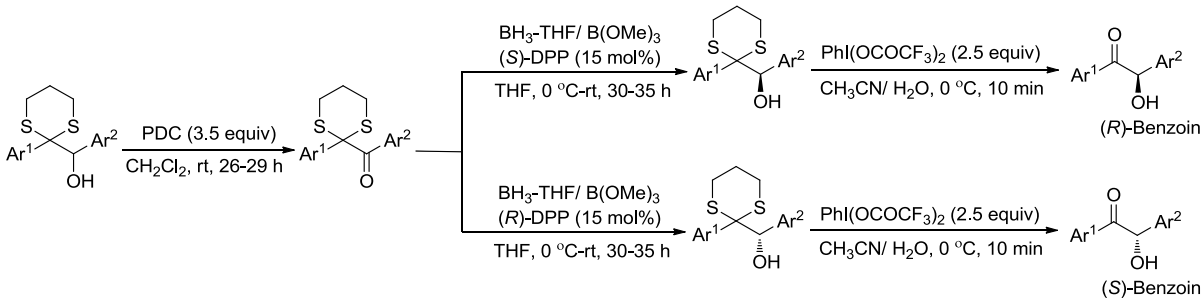
Scheme 2. Deuterium incorporation studies

Chapter 2: Synthesis of *α*-Diarylacetic Esters *via in Situ* Formed Acetals by Stereospecific 1,2-Aryl Migration



Scheme 3. Synthesis of *α*-diarylacetic esters by 1,2-aryl migration

Chapter 2 presents a simple and efficient method for the synthesis of *α*-diarylacetic esters from benzoins on treatment with TfOH and triethyl orthoformate. The *in situ* generated acetal assists the 1,2-aryl migration. Importantly this aryl migration occurs in a highly stereospecific manner (Scheme 3). A new methodology for the synthesis of chiral benzoins with high enantiomeric excess by applying CBS reduction has been developed (Scheme 4). When (*S*)-DPP was used as chiral ligand, (*R*)-benzoins is obtained while (*R*)-DPP gives (*S*)-benzoins. This is a very straight forward and new protocol for the synthesis of enantiopure benzoins. Using *in situ* generated acetal-assisted 1,2-aryl migration, enantioenriched *α*-diaryl acetates could be obtained from enantiomerically pure benzoins. Optically active *α*-diaryl acetates could serve as valuable building blocks for the synthesis of many biologically active compounds.

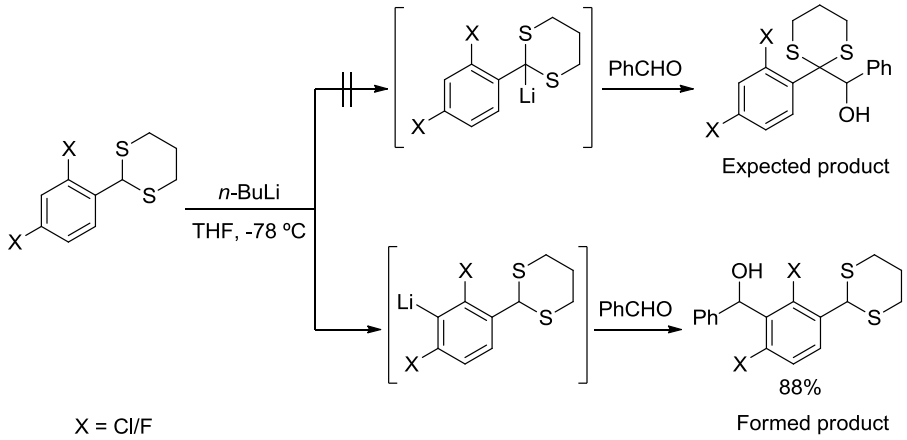


Scheme 4. Synthesis of chiral (*R*) and (*S*)-benzoins

Chapter 3: Regioselective Lithiation of Dithiane Protected 2,4-Dichloro/Difluoro Substituted Benzaldehydes

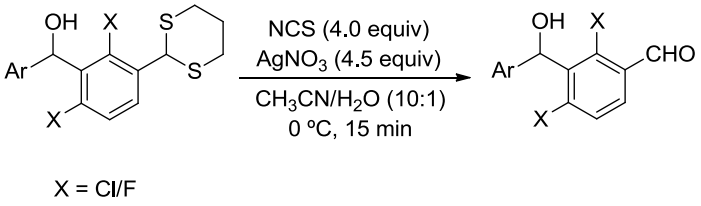
In chapter 3 a regioselective lithiation in dithiane protected 2,4-dichloro/difluoro substituted benzaldehydes using *n*-BuLi is described. The lithiated intermediates were treated with different electrophiles to furnish 1,2,3,4-tetrasubstituted aromatic compounds. Strictly, there are two sites present in dithiane protected 2,4-dichloro/difluoro substituted benzaldehydes for lithiation. Although the hydrogen at dithiane carbon and the C3-position on aromatic ring might have similar pK_a values, lithiation occurs only at C3-position on aromatic ring, which upon

treatment with electrophiles result in polysubstituted aromatic compounds (Scheme 5). It is demonstrated that inductive and coordination effects of halogen atoms cooperatively increase the acidity of the C3-H of aromatic ring over hydrogen present in dithiane carbon for the lithiation to occur regioselectively.



Scheme 5. Regioselective lithiation to produce 1,2,3,4-tetrasubstituted aromatic compounds

The products upon deprotection using NCS/$AgNO_3$ reagent system afford 1,2,3,4-tetrasubstituted aromatic aldehydes (Scheme 6).



Scheme 6. Deprotection of dithianes to polysubstituted aromatic aldehydes

Chapter-1

Gold(I)-Catalyzed Synthesis of Bicyclic Acetals from Epoxyalkynes

1.1 Introduction to gold catalysis

Transition metal catalysis plays an important role in organic synthesis and industrial applications. From last decade onwards gold-catalyzed reactions have been used in many synthetic strategies due to their efficiency and simplicity. Gold catalysts uniquely act as soft carbophilic Lewis acids for the efficient activation of C-C multiple bonds and thus allow the formation of new C-C, C-O, C-N and C-S bonds by nucleophilic attack on the activated C-C multiple bonds. Many reports have been published so far on gold catalysis and are covered by several review articles.[1] Among gold-catalyzed reactions, homogeneous gold catalysis has received much attention than heterogeneous gold catalysis.[1] Atomic number of gold is 79 and its electronic configuration is [Xe] $4f^{14}$ $5d^{10}$ $6s^{1}$. Although gold can exhibit -1 to +5 oxidation states theoretically, gold compounds in +1 and +3 oxidation states are fairly stable and are widely used as catalysts in organic synthesis.[2] Gold(I) species is superior Lewis acid than other group 11 metals owing to high relativistic effects associated with gold(I). The high electronegativity of Au (2.4, compared with 1.9 for Ag) is due to relativistic contraction of 6s orbital of gold.[3] In most of the reported reactions, gold catalysts act as carbophilic Lewis acids. Yamamoto has shown, from the computed heats of formation values, that the gold catalysts possess considerable oxophilicity also in addition to carbophilicity in both +1 and +3 oxidation states.[4] If the functional groups are suitably placed in substrate, both the alkynophilic and oxophilic activations could be achieved under gold-catalysis. Many reactions using the oxo and alkynophilicities of gold are cascade in nature.

1.1.1 Carbophilicity of gold catalysts

Most of the gold-catalyzed reactions reported in the literature exploit the carbophilicity of gold catalysts.[2] In these reactions, gold activates the C-C multiple bonds first to assist further transformations to take place (Scheme 1.1).[5] Gold(I) or gold(III) coordinates to alkynes orthogonally in the same fashion as halogens react with alkynes or alkenes. Gold catalyst coordinates to C-C π-bond of alkynes/allenes/olefins towards the attack of nucleophile. Here the nucleophiles can be based on carbon ( ,  ,), nitrogen (-NH_2, -NHR), oxygen (-OH) and sulphur (-SH). After the

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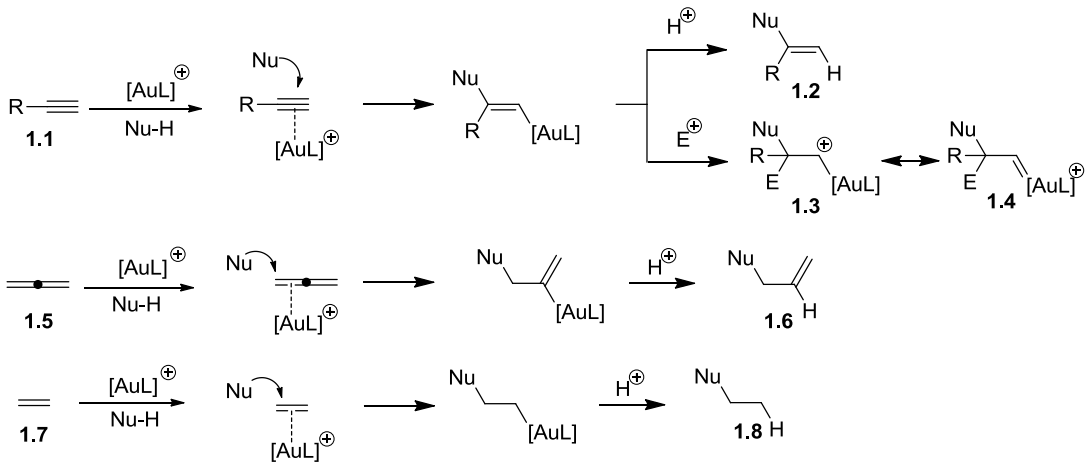
attack of nucleophile, the intermediate species undergo protodemetalation to give the respective products.

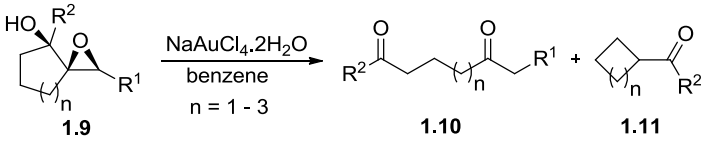


Scheme 1.1. Activation of alkynes, allenes and alkenes by gold catalysts (carbophilicity)

1.1.2 Oxophilicity of gold catalysts

As mentioned earlier, recent advances showed that gold has significant oxophilicity.[4] However it has not explored much. Although Au(III) possesses greater oxophilicity than Au(I) due to its hard nature, Au(I) species also have considerable amount of oxophilicity.[4] Most of the oxophilic gold-catalyzed reactions involve the activation of carbonyl and epoxide functional groups.[6]

Xiao *et al.* reported the rearrangement of *α*-hydroxy epoxides **1.9** into 1,5- or 1,6- or 1,7-diketones **1.10** and monoketones **1.11** (Scheme 1.2).[6c] In this reaction Au(III) activate epoxide ring of **1.9** and further isomerizations occured to form **1.10** and **1.11**.



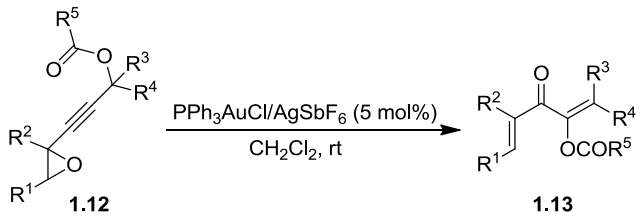
Scheme 1.2. Rearrangement of *α*-hydroxy epoxides

1.1.3 Tandem activation by gold catalysts

In most of the gold catalyzed organic transformations where its oxophilicity is utilized, gold plays dual role involving tandem activation of C-C multiple bonds and oxygen functionalities. The reactions could either be intermolecular or intramolecular. The reactions can take place in either ways

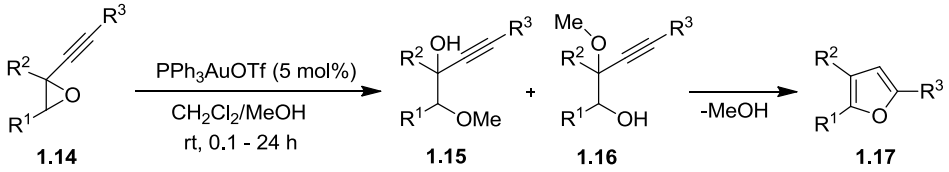
i.e. the gold catalyst first acts as carbophilic catalyst and then as oxophilic catalyst or *vice versa*. The order of activation by gold catalysts depends on the nature of functional groups present in the substrate.

Pale and co-workers reported the synthesis of functionalized divinyl ketones **1.13** through an Au(I)-catalyzed rearrangement of (3-acyloxyprop-1-ynyl)oxiranes **1.12** (Scheme 1.3). In this reaction gold activates alkyne and epoxide functions simultaneously due to its multifaceted coordination character.[7]



Scheme 1.3. Au(I)-Catalyzed rearrangement of **1.12** to divinyl ketones **1.13**

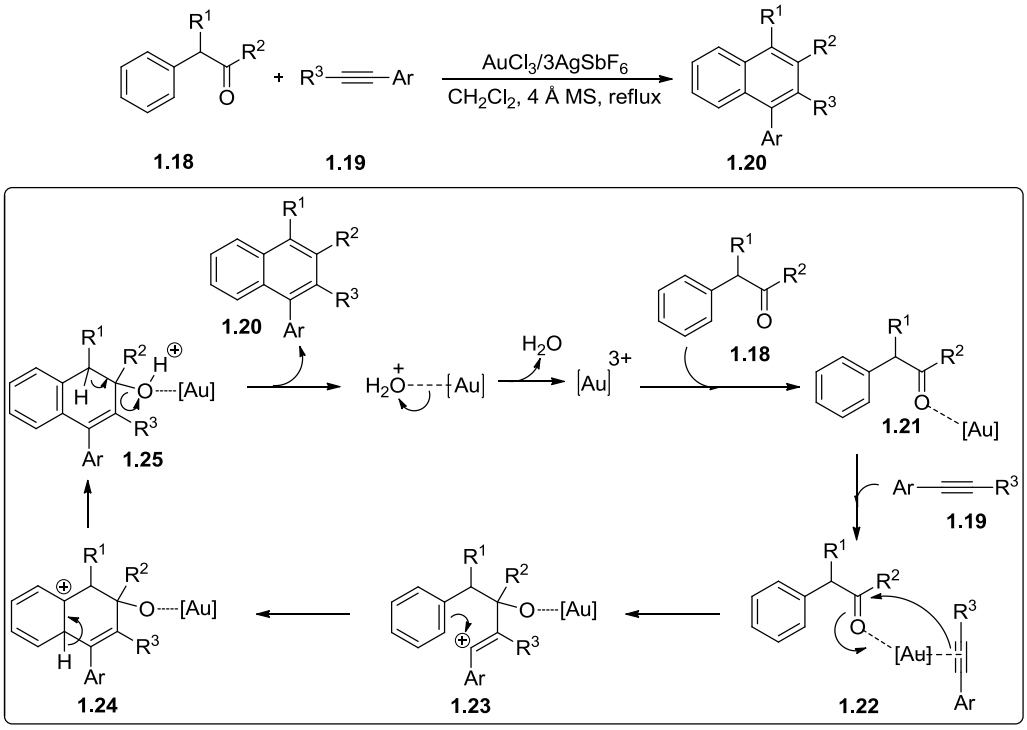
Later, in 2009, the same group reported that Au(I) or Ag(I) salts can catalyze the isomerisation of alkynyloxiranes of type **1.14** to generate highly substituted furans **1.17** in a cascade manner (Scheme 1.4). Au(I) coordinates to both oxirane and alkyne functionalities in **1.14**. Mechanistic studies revealed that the reaction takes place in cascade manner involving oxirane ring-opening by nucleophilic attack of methanol followed by cyclization and elimination of methanol to produce **1.17**.[8]



Scheme 1.4. Au(I)-Catalyzed cascade transformation of alkynyloxiranes to furans

In the context of utilizing the multifaceted qualities of gold catalysts, our research group has developed the gold-catalyzed naphthalenes synthesis, epoxide rearrangement, transglycosylation on per-*O*-acetylglycals and methylene bridged bis-1,3-dicarbonyls synthesis by exploiting the oxo- and alkynophilicities of gold catalysts.[9] The synthesis of substituted naphthalene derivatives by gold-catalyzed electrophilic addition on C-C triple bond followed by benzannulation is described in Scheme 1.5. Au(III) coordinates with carbonyl oxygen of **1.18** as the oxophilic Lewis acid. At the same time gold coordinates to alkyne **1.19** using its carbophilic nature. Electrophilic attack of the

carbonyl carbon takes place to form new C-C bond to result benzylic vinyl carbocation **1.23**. Here gold catalyst holds both the carbonyl and alkyne to facilitate the electrophilic addition. Later, SbF_6^- counter ion promoted aromatic electrophilic substitution takes place to form the bicyclic intermediate **1.24** which subsequently aromatizes to give substituted naphthalene product **1.20**.[9a]



Scheme 1.5. Gold(III)-catalyzed synthesis of 1-arylnaphthalenes

1.1.4 Synthesis of bicyclic acetals using transition metal catalysts

Bicyclic acetal moiety is present in many natural products especially in marine natural products. These compounds show various biological activities like anticancer activity.[10] Some of the natural products having bicyclic acetal core in their structure are shown in figure 1.1. Because of their potential biological activities, many synthetic methodologies were developed for the synthesis of compounds consisting bicyclic acetal moiety.[11-13]

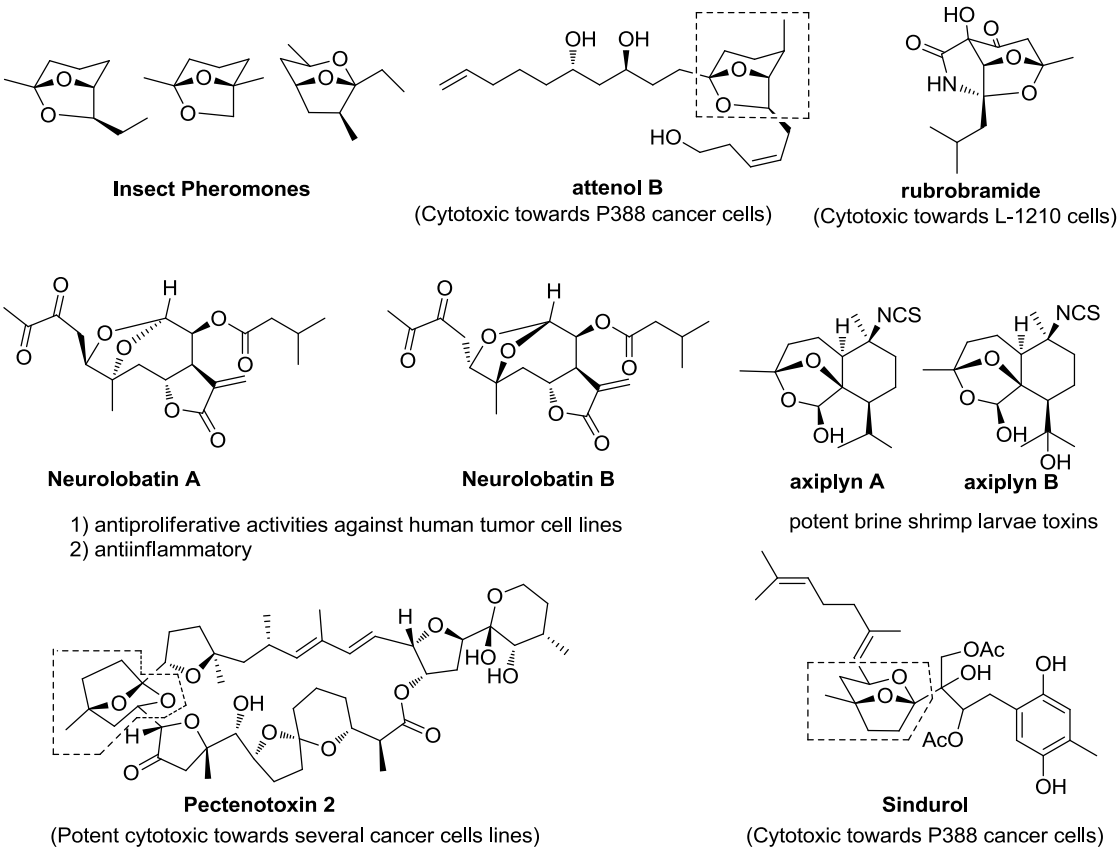
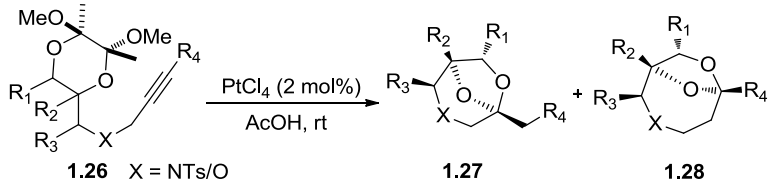


Figure 1.1. Natural products having bicyclic acetal scaffold

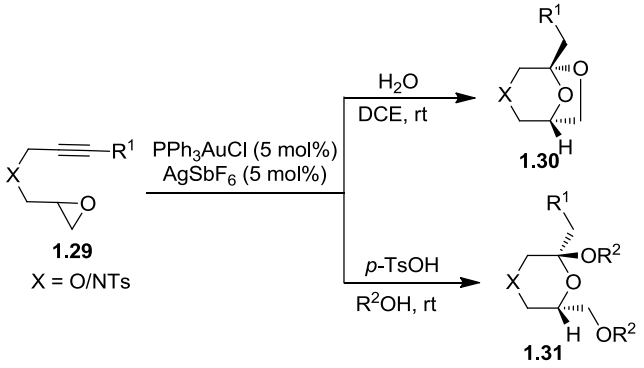
Ley and co-workers reported the $PtCl_4$-catalyzed synthesis of complex bicyclic acetals **1.27** and **1.28** from simple butane-2,3-diacetal (BDA) protected diols **1.26** as starting material (Scheme 1.6). This reaction is a regioselective reaction based on the nature of alkyne. If the alkyne **1.26** is terminal alkyne, it will give [3.2.1]bicyclic acetal **1.27** by a 6-*exo* cyclization pathway on the other hand if **1.26** is aryl-substituted alkyne it will yield [4.2.1]bicyclic acetal **1.28** through a 7-*endo* cyclization.[11]



Scheme 1.6. $PtCl_4$-catalyzed bicyclic acetals synthesis

Shi and co-workers reported the Au(I)-catalyzed highly regio- and diastereoselective intermolecular addition of water and alcohols on epoxyalkynes **1.29** to give bicyclic acetals **1.30** and

acetals **1.31** respectively (Scheme 1.7). This reaction proceeds in a domino fashion through epoxide ring-opening, 6-*exo*-cycloisomerization and intra- or intermolecular nucleophilic addition to alkene.[12]



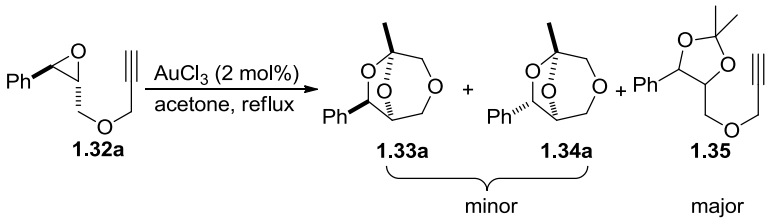
Scheme 1.7. Au(I)-catalyzed bicyclic acetal **1.30** and acetal **1.31** synthesis from epoxyalkynes

Knowing the importance of bicyclic acetal core structure and their synthetic importance we thought to utilize the multifaceted coordination character of gold catalyst for the synthesis of these bicyclic acetals. In this way we wanted to develop a methodology for the synthesis of bicyclic acetals using oxirane ring attached to a suitably placed alkyne by gold catalysis.

1.2 Results and discussion

1.2.1 Background of the reaction

While working on developing reactions based on gold catalysis, it was found in our lab that epoxides, upon treatment with $AuCl_3$ in acetone, can be efficiently transformed into corresponding acetonide derivatives in high yields.[14] We wished to explore the intramolecular cyclization of the acetonide on a tethered alkyne moiety under the reaction conditions. For this purpose we prepared the epoxyalkyne derivative **1.32a**. When we treated **1.32a** with $AuCl_3$ in acetone solvent at room temperature it ended up in acetonide **1.35** as a mixture of *cis* and *trans* isomers. Later we subjected the reaction to reflux condition. Interestingly, we found the formation of bicylcic acetal **1.33a** and **1.34a** in poor yield along with the acetonide derivative **1.35** (Scheme 1.8). Although the reaction resulted in poor yield of the desired product, it encouraged us to optimize the reaction conditions to get better yield of the bicyclic acetal derivatives. The results are presented in Table 1.1.

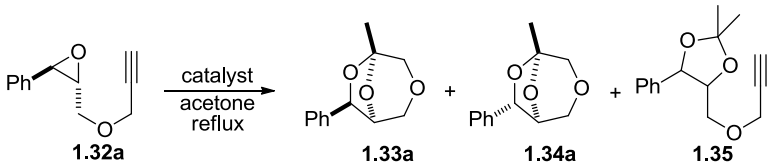


Scheme 1.8. Bicyclic acetal formation from epoxyalkyne under gold catalysis

1.2.2 Optimization of reaction conditions

To find out the best condition and suitable gold catalyst for the formation of bicyclic acetal, we performed several reactions. In this respect, when $AgSbF_6$ was added to $AuCl_3$, improvement in the yield of bicyclic acetal was noticed. However, the result was not impressive from synthetic perspectives (Table 1.1, entry 2). While there was no reaction with Ph_3PAuCl, cationic gold(I) generated from Ph_3PAuCl and $AgSbF_6$ combination worked well for the formation of bicyclic acetal and resulted **1.33a** and **1.34a** in good yields (Table1.1, entry 4). It is important to note that with $AgSbF_6$ alone, the epoxyalkyne **1.32a** gave its corresponding acetonide **1.35** only (entry 5). It was found that some of the reported gold-catalyzed reactions were actually occurred due to Brønsted acid catalysis, which might operate under certain reaction conditions.[15] For example, alcohol addition to carbon-carbon double bonds, which has been carried out using gold-catalysis could be carried out using Brønsted acid TfOH as catalyst.[16] Similarly hydration and alcohol addition on unsymmetrical arylalkynes using catalytic *p*-TSA has been reported by Brion and co-workers.[17] Hence, we felt that it is wise to check whether Brønsted acid catalysis played any role in the present reaction. Reflux of **1.32a** with TfOH in acetone resulted in a mixture of *cis* and *trans* acetonides only along with some decomposed materials (entry 6). Thus it was confirmed that the formation of bicyclic acetal can not be achieved by Brønsted acid catalysis in the present transformation. We then proceeded to study the scope of Au(I)-catalyzed bicyclic acetal formation.

Table 1.1. Optimization of reaction conditions for the bicyclic acetal formation

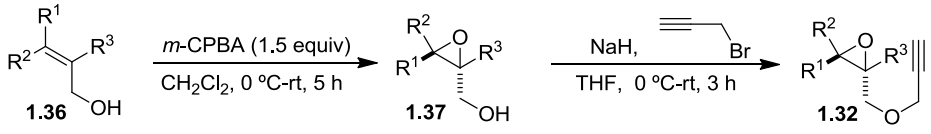


Entry	Catalyst	Time	Yield **1.33a**:**1.34a**:**1.35**[a,b]
1	$AuCl_3$ (2 mol%)	11 h	6: 0: 85 (1:1.4)
2	$AuCl_3$ /3$AgSbF_6$ (2 mol%)	12 h	20: 7: 30 (1:13)
3	Ph_3PAuCl (2 mol%)	11 h	0: 0: 0
4	**Ph_3PAuCl /$AgSbF_6$ (2 mol%)**	**6 h**	**46: 30: 3 (0:1)**
5	$AgSbF_6$ (2 mol%)	8 h	0: 0: 82 (1.2:1)
6	TfOH (5 mol%)	5 h	0: 0: 56 (1:1.9)

[a] Isolated yield. [b] Values in the paranthesis correspond to the *cis*/*trans* ratio of **1.35**.

1.2.3 Preparation of starting materials

A series of epoxyalkyne substrates were synthesized with different substitution pattern and subjected to cascade cyclization using $Ph_3PAuCl/AgSbF_6$ in acetone under reflux conditions. The epoxyalkynes **1.32a-1.32e** were prepared by following the strategy shown in Scheme 1.9. Allyl alcohols **1.36a-1.36e** were subjected to epoxidation using *m*-CPBA to get epoxy alcohols **1.37a-1.37e** which upon treatment with propargyl bromide under strong basic conditions resulted in required epoxyalkynes **1.32a-1.32e**.



1.36a: $R^1 = C_6H_5$, R^2 = H, R^3 = H
1.36b: R^1 = 4-ClC_6H_4, R^2 = H, R^3 = H
1.36c: R^1 = 4-$NO_2C_6H_4$, R^2 = H, R^3 = H
1.36d: $R^1 = C_6H_5$, R^2 = H, $R^3 = CH_3$
1.36e: $R^1 = CH_2CH_2CHC(CH_3)_2$, $R^2 = CH_3$, R^3 = H

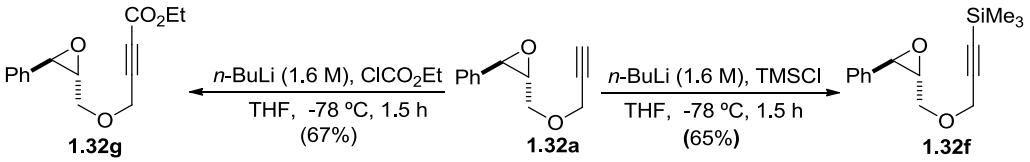
1.37a: $R^1 = C_6H_5$, R^2 = H, R^3 = H (98%)
1.37b: R^1 = 4-ClC_6H_4, R^2 = H, R^3 = H (80%)
1.37c: R^1 = 4-$NO_2C_6H_4$, R^2 = H, R^3 = H (87%)
1.37d: $R^1 = C_6H_5$, R^2 = H, $R^3 = CH_3$ (85%)
1.37e: $R^1 = CH_2CH_2CHC(CH_3)_2$, $R^2 = CH_3$, R^3 = H (70%)

1.32a: $R^1 = C_6H_5$, R^2 = H, R^3 = H (80%)
1.32b: R^1 = 4-ClC_6H_4, R^2 = H, R^3 = H (94%)
1.32c: R^1 = 4-$NO_2C_6H_4$, R^2 = H, R^3 = H (82%)
1.32d: $R^1 = C_6H_5$, R^2 = H, $R^3 = CH_3$ (70%)
1.32e: $R^1 = CH_2CH_2CHC(CH_3)_2$, $R^2 = CH_3$, R^3 = H (60%)

Scheme 1.9. Synthesis of epoxyalkynes **1.32a-1.32e**

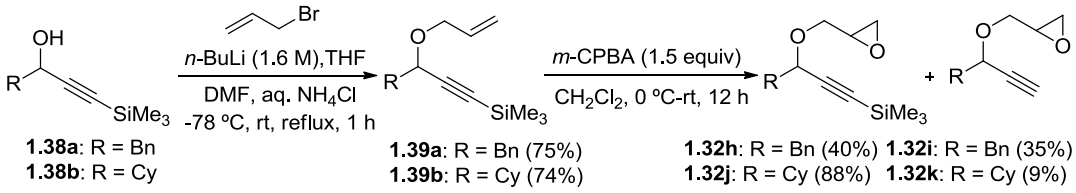
Substrates **1.32f** and **1.32g** were prepared from epoxyalkyne **1.32a** in one step each as depicted in Scheme 1.10. The epoxyalkyne **1.32a** was lithiated using *n*-BuLi at -78 ºC and the

resulting anoin was treated with TMSCl and ethyl chloroformate ($ClCO_2Et$) separately to obtain substrates **1.32f** and **1.32g** respectively.



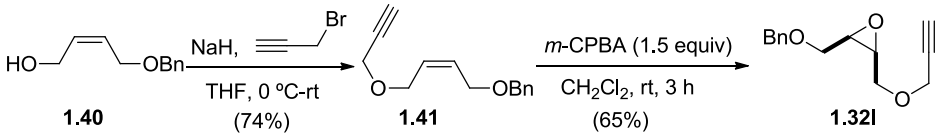
Scheme 1.10. Synthesis of epoxyalkynes **1.32f** and **1.32g**

The substrates **1.32h-1.32k** were synthesized by following the Scheme 1.11. Propargyl alcohols **1.38a** and **1.38b** were allylated using allyl bromide in presence of *n*-BuLi. The products of the above reactions **1.39a** and **1.39b** were subjected to epoxidation using *m*-CPBA to get the desired starting materials **1.32h-1.32k**.



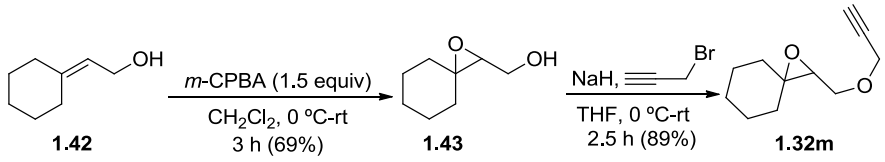
Scheme 1.11. Synthesis of epoxyalkynes **1.32h-1.32k**

Epoxyalkyne **1.32l** was prepared by following a two step protocol outlined in the Scheme 1.12. The mono-benzylated *cis*-but-2-ene-1,4-diol **1.40** was propargylated first to get the enyne **1.41** which on epoxidation resulted in **1.32l**.



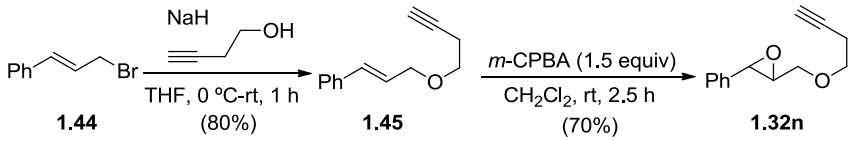
Scheme 1.12. Synthesis of epoxyalkyne **1.32l**

The epoxyalkyne **1.32m** was prepared from allyl alcohol **1.42**. Epoxidation on **1.42** using *m*-CPBA resulted in epoxyalcohol **1.43** which on subsequent propargylation using NaH and propargyl bromide gave the epoxyalkyne **1.32m** (Scheme 1.13).



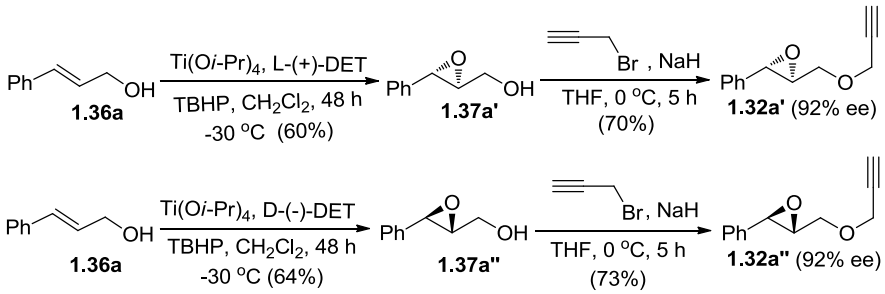
Scheme 1.13. Synthesis of epoxyalkyne **1.32m**

The epoxyalkyne **1.32n** was prepared by following the synthetic procedure shown in Scheme 1.14. Cinnamyl bromide **1.44** was treated with homopropargyl alcohol to give cinnamyl homopropargyl ether **1.45** which was further treated with *m*-CPBA to obtain **1.32n** in which the ether oxygen and the alkyne carbon are separated by two methylene units.



Scheme 1.14. Synthesis of epoxyalkyne **1.32n**

Optically active epoxyalkynes **1.32a'** and **1.32a''** were prepared starting from **1.36a** by performing Sharpless asymmetric epoxidations using (+)-DET and (-)-DET. The obtained optically pure epoxyalochols **1.37a'** and **1.37a''** were propargylated using propargyl bromide to get, respectively, enantioenriched **1.32a'** and **1.32a''** in good yields.



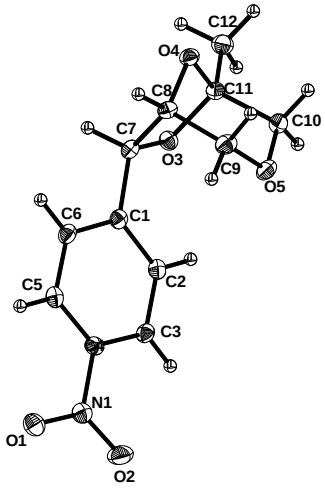
Scheme 1.15. Synthesis of optically active epoxyalkynes **1.32a'** and **1.32a''**

1.2.4 Substrate scope for gold-catalyzed bicyclic acetal formation

The synthesized epoxyalkyne derivatives were subjected to Au(I)-catalyzed bicyclic acetal formation in acetone. The results are presented in Table 1.3. When the epoxide ring has an aryl substitution, a mixture of *endo* and *exo* products were obtained which can easily be separated by column chromatography. The epoxyalkyne derivative **1.32l** which bears two alkyl substituents on the oxirane ring in *cis* fashion gave the *exo* product **1.34i** exclusively *via* a S_N2 attack of acetone on oxirane ring during the acetonide formation. On the other hand, substrates containing aryl groups or *gem*-dialkyl substituents on epoxide gave a mixture of *exo* and *endo* products. This is because the aryl/*gem*-dialkyl substituent on the oxirane ring will stabilize the carbocation generated upon ring-opening of epoxide which is eventually attacked by acetone from either sides.[18] Trimethylsilyl group on alkyne did not survive under the reaction condition as the corresponding desilylated products were obtained (entries

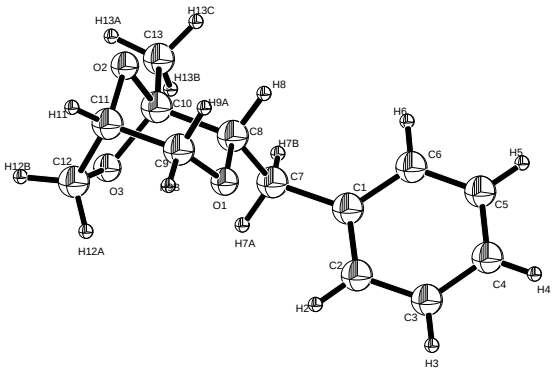
6, 8 and 10, Table 1.3). The reaction of **1.32f** with $Ph_3PAuCl/AgSbF_6$ in acetone-d_6 revealed that the desilylation occurred before the formation of bicyclic acetal. This was confirmed by analysing the reaction mixture after 1 h which showed considerable amount of deuterium incorporation in the place of $SiMe_3$ of the intermediate acetonides. Further, the bicyclic acetals formed in 1 h of reaction did not contain $SiMe_3$ group. The [4.2.1]bicyclic acetal **1.33k** and **1.34k** could also be prepared using this strategy (entry 14, Table 1.3). The stereochemistry of substituents in the bicyclic acetal products were assigned based on X-ray crystal structure analysis and comparing the spectral data with similar compounds reported in literature.[11] X-ray structure analysis of **1.33c** and **1.33g** revealed that the *p*-nitrophenyl and benzyl substituents are present in *endo* orientation (Figures 1.2 and 1.3).

Figure 1.2. ORTEP diagram of compound **1.33c**



Thermal ellipsoidal plot of the compound **1.33c** asymmetric unit. (40% probability).

Figure 1.3. ORTEP diagram of compound **1.33g**

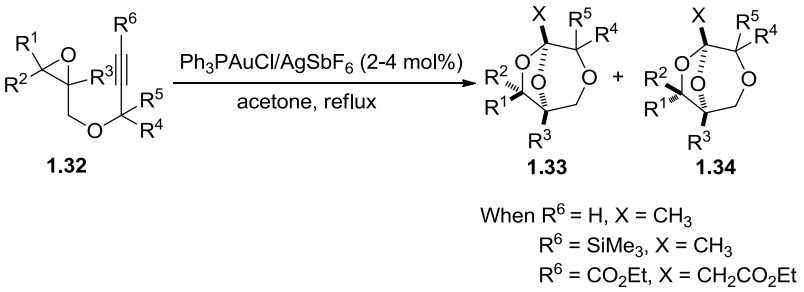


Thermal ellipsoidal plot of the compound **1.33g** asymmetric unit. (40% probability).

Table 1.2. Important crystal parameters

Parameter	**Compound 1.33c**	**Compound 1.33g**
Empirical formula	$C_{12}\,H_{13}\,N\,O_5$	$C_{13}\,H_{16}\,O_3$
Formula weight	251.23	220.26
Temperature (K)	100K	298K
Crystal size (mm)	0.40 x 0.32 x 0.20	0.40 x0.30 x 0.20
Crystal system	Monoclinic	Triclinic
space group	P2(1)/n	p-1
Z	4	2
Wavelength (Å)	0.7107	0.7107
a [Å]	11.5989(6)	5.9391(15)
b [Å]	5.7251(3)	9.790(3)
c [Å]	17.8093(9)	10.911(3)
α [°]	90.00	64.859(3)
β [°]	108.6050(10)	87.354(4)
γ [°]	90.00	80.846(4)
Volume [$Å^3$]	1120.82(10)	566.9(3)
Calculated density (Mg/m^{-3})	1.489	1.290
Reflections collected/ unique	10212 / 1983	3870/1953
R(int)	0.0241	0.0309
F(000)	528	236
Max. and min. transmission	0.9770 and 0.9546	0.9821 and 0.9646
θ range for data collection(deg.)	1.86 to 25.00	2.06 to 24.99
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data / restraints / parameters	1983 / 0 / 164	1953 / 0 / 147
Goodness-of-fit on F^2	1.082	1.279
R_1/wR_2 [I>2sigma(I)]	0.0367/ 0.0874	0.1042/ 0.3371
R_1/wR_2 (all data)	0.0380/ 0.0832	0.1090/ 0.3386
Largest diff. peak and hole [$e.Å^{-3}$]	0.239 and -0.294	0.371 and -0.315

Table 1.3. Au(I)-catalyzed formation of bicyclic acetal derivatives from epoxyalkynes.[(a)]



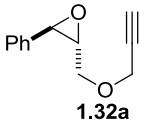
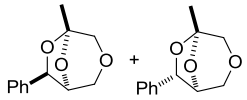
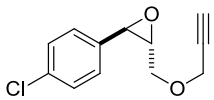
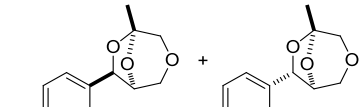
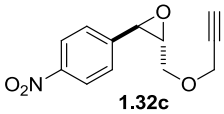
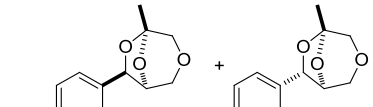
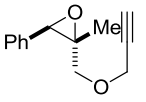
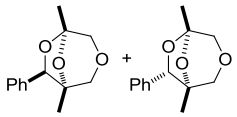
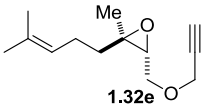
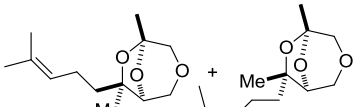
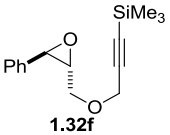
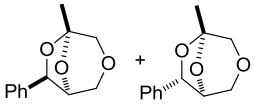
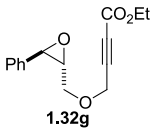
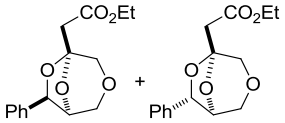
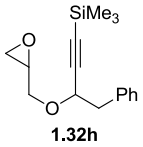
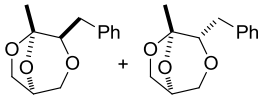
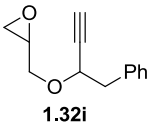
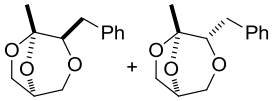
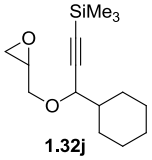
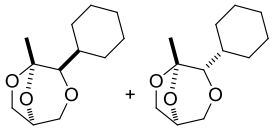
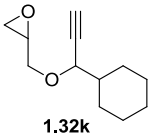
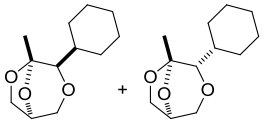
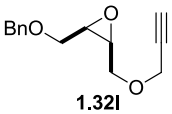
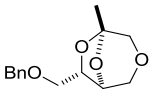
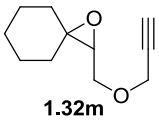
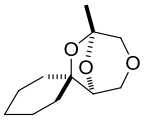
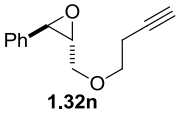
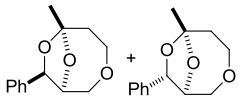
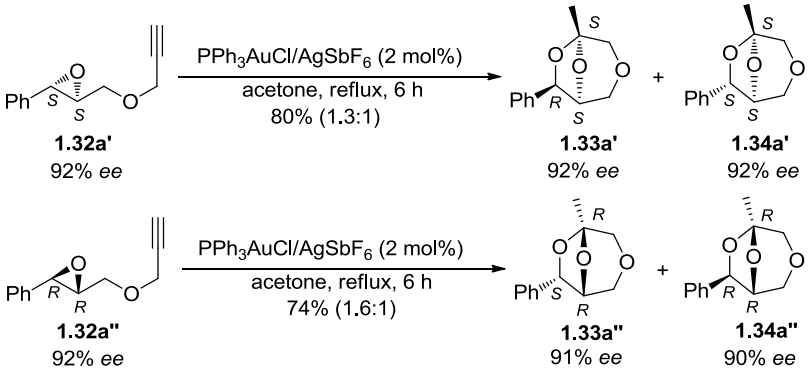
Entry	Epoxyalkyne **1.32**	Time (h)	Products[(b)] **1.33** (*endo*) + **1.34** (*exo*)
1	 **1.32a**	6[(c)]	 **1.33a** (46%) **1.34a** (30%)
2	 **1.32b**	4[(c)]	 **1.33b** (45%) **1.34b** (20%)
3	 **1.32c**	3[(c)]	 **1.33c** (64%) **1.34c** (5%)
4	 **1.32d**	2[(e)]	 **1.33d** (44%) **1.34d** (15%)
5	 **1.32e**	4[(e)]	 **1.33e** (22%) **1.34e** (15%)
6	 **1.32f**	6[(c)]	 **1.33a** (42%) **1.34a** (25%)

Table 1.3 contd…

Entry	Epoxyalkyne **1.32**	Time (h)	Products[(b)] **1.33** (*endo*) + **1.34** (*exo*)
7	 **1.32g**	2[(c)]	 **1.33f** (47%) **1.34f** (38%)
8	 **1.32h**	5[(d)]	 **1.33g** (31%) **1.34g** (25%)
9	 **1.32i**	5[(d)]	 **1.33g** (35%) **1.34g** (29%)
10	 **1.32j**	3[(d)]	 **1.33h** (49%) **1.34h** (16%)
11	 **1.32k**	3[(d)]	 **1.33h** (55%) **1.34h** (11%)
12	 **1.32l**	4[(e)]	 **1.34i** (73%)
13	 **1.32m**	9[(c)]	 **1.33j** (21%)
14	 **1.32n**	5[(d)]	 **1.33k** (25%) **1.34k** (10%)

[a]All the reactions were carried out in acetone under refluxion. [b] Isolated yields. [c] 2 mol% catalyst. [d] 3 mol% catalyst. [e] 4 mol% catalyst.

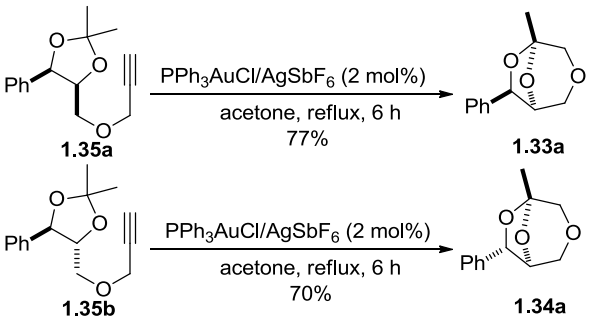
To evaluate the scope of our gold-catalyzed bicyclic acetal formation further, enantiomerically pure epoxyalkyne derivatives of **1.32a'** and **1.32a''** prepared using Sharpless asymmetric epoxidation were reacted under the established optimized condition.[19] Cascade cyclization of **1.32a'** under the reaction conditions resulted in the formation of two separable diastereomers of the corresponding bicyclic acetals **1.33a'**and **1.34a'**. Both the products maintained the enantiomeric excess of that of the starting epoxyalkyne **1.32a'** (Scheme 1.16). Similarly, the reaction of **1.32a''** resulted in the formation of the corresponding separable diastereomers **1.33a''** and **1.34a''**. The enantiomeric excess values of these products were found to be slightly lower than that of the starting epoxyalkyne **1.32a''** which may be due to experimental error and is in acceptable range. These results clearly reveal that the epoxide opening occurred at the benzylic carbon. Thus, this methodology could be used to access all possible diastereomers of the bicyclic acetal derivative.



Scheme 1.16. Synthesis of enantiomerically pure bicyclic acetals

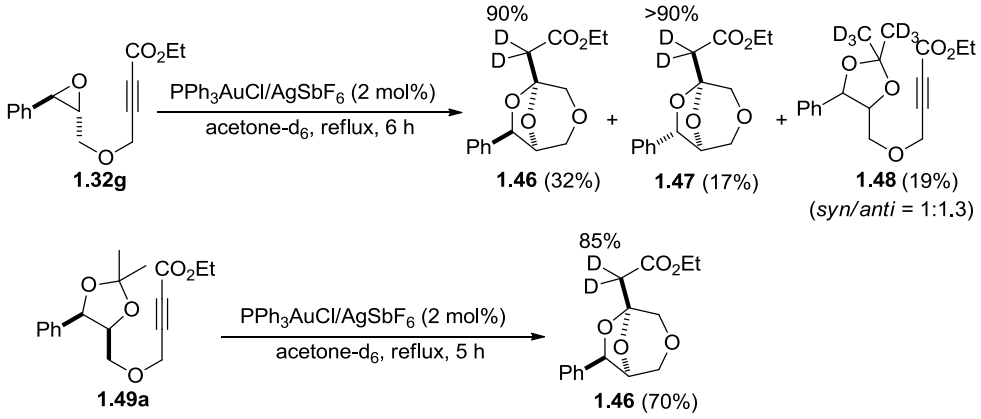
1.2.5 Mechanistic studies

TLC analysis of the present gold-catalyzed bicyclic acetal formation from epoxyalkynes revealed the formation of acetonide derivatives first which subsequently transformed into the corresponding bicyclic acetal derivatives. Hence gold activates the epoxide ring first and then alkyne in a sequential fashion and not in a simultaneous fashion. To confirm the above proposal further, *cis* and *trans* 1,3-dioxalane derivatives, **1.35a** and **1.35b** were prepared from epoxyalkyne **1.32a** and refluxed separately in acetone with $Ph_3PAuCl/AgSbF_6$ (Scheme 1.17).[20] It was found that the *cis* dioxalane **1.35a** gave the *endo* bicyclic acetal **1.33a** and the corresponding *trans* counterpart **1.35b** gave the *exo* product **1.34a**. These observations clearly rules out the possibility of simultaneous coordination of gold to epoxide and alkyne. From these experiments we conclude that gold first converts the oxirane into acetonide and then the cyclization takes place to form the bicyclic acetal.



Scheme 1.17. Formation of bicyclic acetals from acetonide tethered alkynes

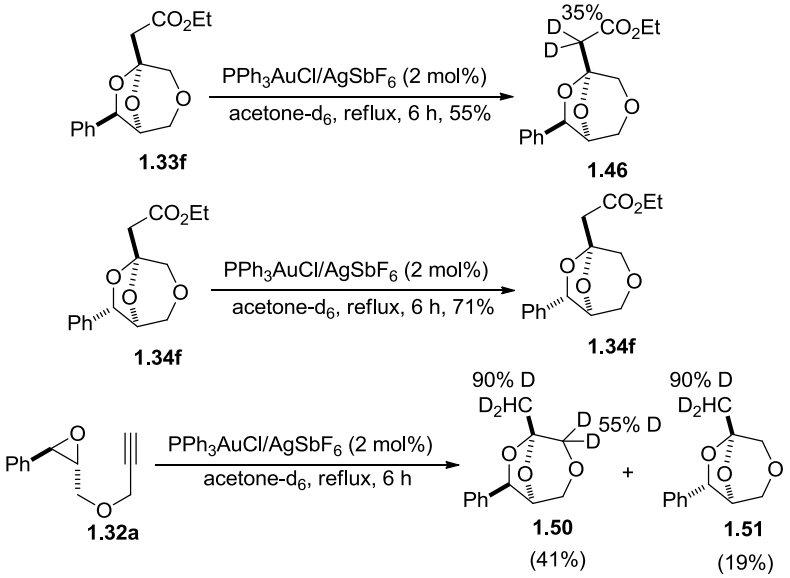
In order to establish the mechanism of the cyclization, two different experiments were performed. In the first experiment, the epoxyalkyne **1.32g** was treated with $PPh_3AuCl/AgSbF_6$ in deuterated acetone which resulted in bicyclic acetals **1.46** and **1.47** with ≥90% deuterium incorporation at methylene carbon α to ester.[21] In the second experiment, the acetonide **1.49a** derived from **1.32g** was subjected to the same reaction condition which resulted in the product **1.46** with slightly less deuterium incorporation (85%) at the methylene carbon α to ester. The reactions in acetone-d_6 were slow, hinting at a possible isotope effect. These results emphasize the involvement of solvent acetone in the protodemetallation steps.



Scheme 1.18. Deuterium incorporation studies

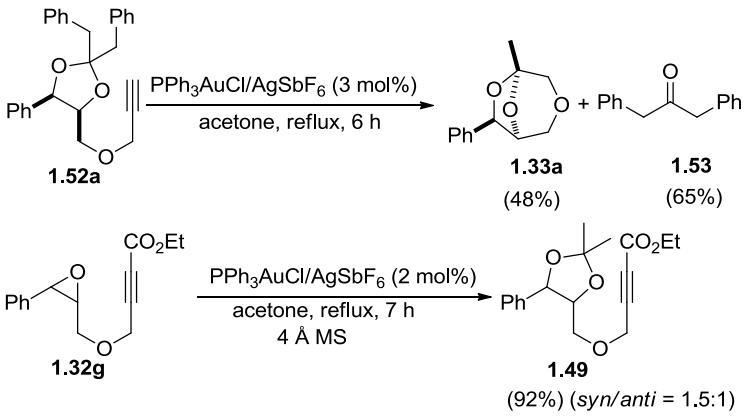
In control experiments, the bicyclic acetals **1.33f** and **1.34f** were treated separately with 2 mol% of $Ph_3PAuCl/AgSbF_6$ in refluxing acetone-d_6 (Scheme 1.19). While the substrate **1.33f** showed 35% of α-deuterium incorporation at methylene carbon α to ester, substrate **1.34f** did not respond so. A possible explanation could be the acetal in bicyclic substrate **1.33f** can open up and set-up an equilibrium with diol keto ester. The ring-opened species can incorporate deuterium at the active methylene site. In another experiment, compound **1.32a** was treated with catalytic $Ph_3PAuCl/AgSbF_6$ in acetone-d_6 under reflux. Good amount of deuterium incorporation was noticed at the methyl

substituent of the bicyclic acetals. Interestingly, in the *endo* isomer **1.50**, considerable amount of deuterium incorporation was noticed at the ring methylene. This deuterium incorporation, as occured with the *endo* bicyclic acetal **1.33f**, might have taken place when the bicyclic acetal opens under the reaction conditions. Surprisingly, such deuterium incorporation did not occur in the *exo* isomer **1.51**.



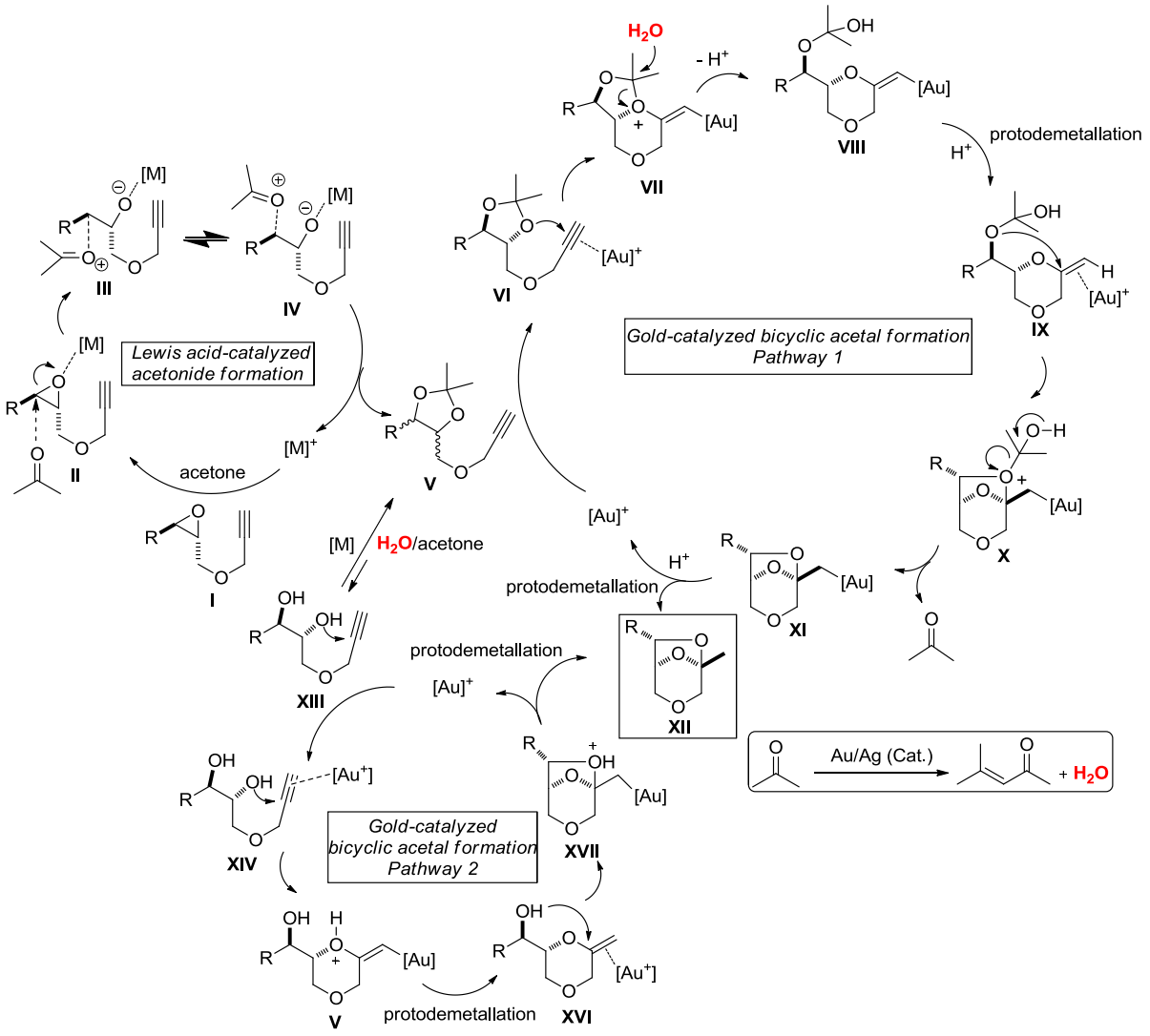
Scheme 1.19. Control experiments for deuterium incorporation studies

After realizing clearly the involvement of acetone during protodemetallation, the fate of initially formed acetonide was studied. For that, the reaction of substrate **1.52a** was studied. Reaction of **1.52a** gave the bicyclic acetal **1.33a** and 1,3-diphenylpropan-2-one **1.53** in 48% and 65% respectively (Scheme 1.20). The compound **1.52a** was prepared from the corresponding diol **1.54**[22] and 1,3-diphenylpropan-2-one **1.53**.[23] Hence attack of water at the dioxalane ring is the realistic way to explain the formation of **1.53** from **1.52a**. Presence of adventitious water in solvent acetone to play the role could be excluded since deuterium incorporation was noticed in the reactions which were carried out in acetone-d_6. Moreover, it points out that the water should have come from acetone. Under the Lewis acidic condition there is a great possibility for the solvent acetone to undergo aldol self-condensation to generate water. The slowness of the reactions in acetone-d_6 could have arisen from the isotopic effects involved in aldol reaction (Scheme 1.18). Further when **1.32g** was treated with $AuCl(PPh_3)/AgSbF_6$ in acetone in the presence of 4 Å molecular sieves, the reaction stopped at the acetonide formation stage itself. In this experiment water formed was trapped by molecular sieves. These experiments clearly indicate that water which was formed slowly from acetone by aldol self-condensation plays a vital role in the cyclisation.

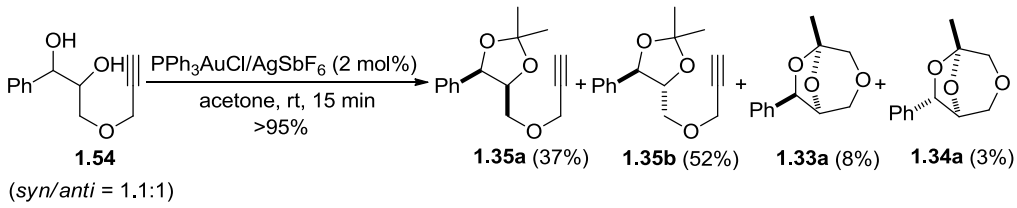


Scheme 1.20. Experimental support for the formation of water under the reaction conditions

Based on the above observations, a mechanism as shown in Scheme 1.21 could be proposed. Initially the oxirane ring of the epoxyalkyne **I** is opened by the Lewis acid (gold catalyst) with the nucleophilic assistance of the solvent acetone. The ring-opened species **III** and **IV** give a mixture of *cis* and *trans* acetonides **V**. The intermediate **V** can, in principle, take either pathway 1 or pathway 2 to give the bicyclic acetal. To demonstrate the stereospecificity involved in the bicyclic acetal formation from acetonide, the *trans* isomer of the acetonide **V** is shown in the cyclization pathways 1 and 2. It is known that oxygen of acetonide can act as nucleophile.[24] Hence the acetonide oxygen can attack the gold activated triple bond to give the intermediate **VII** as given in the pathway 1. Water generated under the reaction condition can attack at this stage and subsequent protodemetallation will give **IX**. One more intramolecular oxy-cyclization on the gold-activated double bond followed by acetone exclusion generates **XI**, which on protodemetallation would furnish the exo bicyclic acetal **XII**. On the other hand (pathway 2), the acetonide **V** could set up an equilibrium with the diol **XIII** by the assistance of Lewis acid and water generated from solvent acetone.[25] Now the diol can cyclize intramolecularly on the triple bond under gold-catalysis.[26] This pathway (pathway 2) is more feasible than the pathway 1 as the diol **1.54** in the presence of $AuCl(PPh_3)/AgSbF_6$ in acetone resulted in small amounts of bicyclic acetals **1.33a** and **1.34a** in 15 minutes although the major products were the acetonides **1.35a** and **1.35b** (Scheme 1.22). In a similar manner the *cis* isomer of **V** would give the *endo* bicyclic acetal.



Scheme 1.21. Tentative mechanism for the formation of bicyclic acetal



Scheme 1.22. Au(I)-catalyzed bicyclic acetal formation from diol **1.54**

1.3 Conclusions

Gold catalysis has become an important tool in the hands of synthetic organic chemists for the activation of C-C multiple bonds. Gold catalysts have both carbophilic and oxophilic nature. In presence of gold catalysts epoxides can be converted to acetonides. We have utilized this reaction for the synthesis of bicyclic acetals from epoxyalkynes in a cascade manner using Au(I)-catalyst. Gold(I) catalyst initially interacts with epoxide to form acetonide which generates diol to cyclize on the gold activated alkyne to result in bicyclic acetal. The mechanism of this reaction was systematically evaluated and water formed under the reaction conditions by aldol self-condensation of solvent acetone was found to play a crucial role in the cyclization of the acetonide on triple bond. This method is simple and efficient. Hence it might be used to build a small library of compounds to evaluate their biological activities.

1.4 Experimental section

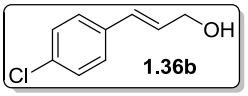
1.4.1 General information

Chemicals and solvents were purchased from various commercial sources. All starting materials were prepared by following known literature procedures. Ph_3PAuCl, $AgSbF_6$, *n*-BuLi (1.6 M in Hexanes), NaH (60% dispersed in mineral oil) and *m*-CPBA (75%) were purchased from Aldrich Chemical Co. Acetone was dried over $KMnO_4$ and stored over 4 Å type molecular sieves. THF was dried over sodium-benzophenone and freshly distilled from a still before use. ^1H and ^{13}C spectra were recorded on a Bruker Avance 400 MHz machine using solutions in $CDCl_3$ with tetramethylsilane (TMS) as an internal standard. IR spectra were recorded on JASCO FT/IR-5300 spectrometer. Elemental (C, H, N) analysis were done using Thermo Finnigan Flash EA 1112 analyser. The X-ray diffraction measurements were carried out at 100 K and 298 K on an automated diffractometer using graphite monochromated, Mo-Kα (λ = 0.71073 Å) radiation with CAD4 software or the X-ray intensity data were measured at 100 K and 298 K on a CCD area detector system equipped with a graphite monochromator and a Mo-Kα fine-focus sealed tube (λ = 0.71073 Å). For TLC, silica gel plates 60 F254 were used and compounds were visualized by UV light and/or by treatment with Seebach solution (phosphomolibdic acid (2.5 g), $Ce(SO_4)_2$ (1 g), Conc. H_2SO_4 (6 mL), H_2O (94 mL)) followed by heating. Column chromatography was performed on silicagel 100-200 mesh, using ethyl acetate and hexanes mixture as eluent. HPLC analysis of the samples was performed using Daicel Chiralcel OD-H column, hexanes/*i*-PrOH as eluent, flow rate = 0.5 mL/min at λ_{max} = 220 nm.

1.4.2 Experimental procedures, spectral and analytical data

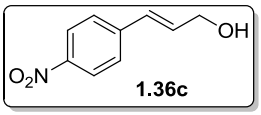
Compounds **1.36a** and **1.36e** are commercially available.

(*E*)-3-(4-Chlorophenyl)prop-2-en-1-ol (1.36b)



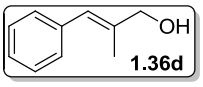
Compound **1.36b** was synthesized by following a known procedure.[27] To a solution of (*E*)-ethyl 3-(4-chlorophenyl)acrylate (500 mg, 2.37 mmol) in dry CH_2Cl_2 (15 mL), DIBAL-H (1M solution in cyclohexane, 5.7 mmol, 5.7 mL) was added at 0 ^oC under N_2 atmosphere and stirred at the same temperature for 1 h. After that, excess DIBAL-H was quenched by adding few drops of MeOH followed by few drops of aqueous NH_4Cl. Stirring was continued for another 15 min. Then the reaction mixture was filtered, dried over Na_2SO_4 and concentrated. The crude product (yield = 384 mg, 96%) was used for the next step without further purification. ^1H NMR (400 MHz, $CDCl_3$): δ 7.32-7.27 (m, 4H), 6.58 (d, J = 16.0 Hz, 1H), 6.34 (dt, J = 15.6, 5.6 Hz, 1H), 4.33 (d, J = 4.8 Hz, 2H), 1.65 (bs, 1H).

(*E*)-3-(4-Nitrophenyl)prop-2-en-1-ol (1.36c)



Compound **1.36c** was synthesized from the (*E*)-ethyl 3-(4-nitrophenyl)acrylate by following the same procedure employed to **1.36b**.[28] ^1H NMR (400 MHz, $CDCl_3$): δ 8.19 (d, J = 8.8 Hz, 2H), 7.52 (d, J = 8.8 Hz, 2H), 6.73 (d, J = 16.0 Hz, 1H), 6.55 (dt, J = 16.0, 4.8 Hz, 1H), 4.41 (d, J = 4.0 Hz, 2H), 1.62 (s, 1H).

(*E*)-2-Methyl-3-phenylprop-2-en-1-ol (1.36d)

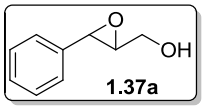


Compound **1.36d** was synthesized by following the reported procedure.[29] ^1H NMR (400 MHz, $CDCl_3$): δ 7.36-7.21 (m, 5H), 6.52 (s, 1H), 4.68 (s, 1H), 4.18 (s, 2H), 1.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.6, 128.8, 128.1, 127.0, 126.4, 125.0, 68.9, 65.3, 15.2.

General procedure for epoxidation to prepare compounds 1.37a-1.37e

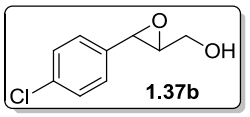
To a solution of allylic alcohol **1.36** (1 equiv) in CH_2Cl_2 (4 mL/mmol), *m*-CPBA (1.5 equiv) was added slowly at 0 ºC and the reaction was allowed to stir at room temperature. After completion of the reaction, 10 mL of saturated Na_2SO_3 solution was added and stirred for 15 min. Then the reaction mixture was taken in a separating funnel and washed two times each with saturated aqueous $NaHCO_3$ solution and brine solution, dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexanes) to get the pure epoxy alcohol product **1.37**.

(3-Phenyloxiran-2-yl)methanol (1.37a)



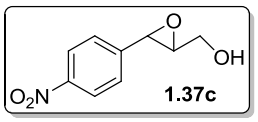
Compound **1.37a** was synthesized from cinnamyl alcohol **1.36a** by following the general epoxydation procedure. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.27 (m, 5H), 4.04 (dd, J = 12.8, 2.4 Hz, 1H), 3.93 (s, 1H), 3.82-3.76 (m, 1H), 3.23 (br d, J = 1.6 Hz, 1H), 2.16 (t, J = 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.6, 128.5, 128.3, 125.7, 62.5, 61.2, 55.6.

(3-(4-Chlorophenyl)oxiran-2-yl)methanol (1.37b)



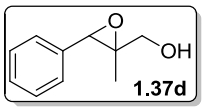
Compound **1.37b** was prepared from **1.36b** by following the general epoxidation procedure.[30] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (d, J = 8.4 Hz, 2H), 7.21 (d, J = 8.4 Hz, 2H), 4.04 (bd, J = 12.8 Hz, 1H), 3.91 (d, J = 1.6 Hz, 1H), 3.80 (bd, J = 12.8 Hz. 1H), 3.18 (dt, J = 4.0, 2.4 Hz, 1H), 2.20 (bs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 135.3, 134.1, 128.8, 127.1, 62.6, 61.0, 55.0.

(3-(4-Nitrophenyl)oxiran-2-yl)methanol (1.37c)



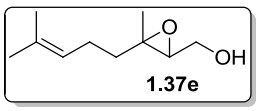
Compound **1.37c** was prepared from **1.36c** by following the general procedure for epoxydation.[30] ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.20 (d, J = 8.8 Hz, 2H), 7.46 (d, J = 8.8 Hz, 2H), 4.06 (s, 2H), 3.87 (dd, J = 12.8, 3.2 Hz, 1H), 3.20 (s, 1H), 2.11 (bs, 1H).

(2-Methyl-3-phenyloxiran-2-yl)methanol (1.37d)



Compound **1.37d** was synthesized from **1.37c** according to the general epoxydation procedure.[31] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38-7.34 (m, 2H), 7.31-7.28 (m, 3H), 4.21 (s, 1H), 3.85 (d, J = 12.4 Hz, 1H), 3.78-3.73 (m, 1H), 1.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 135.6, 128.1, 127.6, 126.4, 65.0, 63.7, 60.2, 13.4.

(3-Methyl-3-(4-methylpent-3-en-1-yl)oxiran-2-yl)methanol (1.37e)



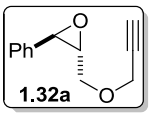
To a stirred solution of geraniol (0.5 g, 3.24 mmol) and vanadium oxy acetylacetonate (0.45 g, 1.70 mmol) in toluene, *tert*-butyl hydroperoxide (5.5 M in decane, 0.2 mL) were added. After 15 minutes, another portion of tert-butyl hydroperoxide (10.2 mmol, 1.65 mL) was added and stirred at room temperature for 1 h. When TBHP was added dark green colored solution turned to dark brown colored solution. Then the reaction was quenched with saturated aquous $Na_2S_2O_3$ solution and stirred for few more minutes. It was extracted with ether (3 x 20 mL), dried over anhydrous Na_2SO_4, concentrated and purified by column chromatography (1:5 EtOAc/hexanes) to get the epoxy alcohol as pale yellow colored liquid (0.386 g, 70%).[32] ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.09 (t, J = 7.0 Hz, 1H), 3.83 (bd, J = 12.0 Hz, 1H),

3.69 (dd, *J* = 12.0, 6.7 Hz, 1H), 2.98 (dd, *J* = 6.7, 4.3 Hz, 1H), 2.11 (d, *J* = 7.7 Hz, 1H), 2.07 (d, *J* = 7.2 Hz, 1H), 1.72-1.65 (m, 4H), 1.61 (s, 3H), 1.51-1.44 (m, 1H), 1.30 (s, 3H).

General procedure for propargylation to synthesize compounds 1.32a-1.32e

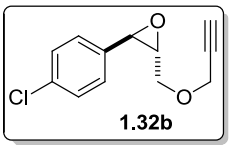
To the epoxy alcohol **1.37** (1 equiv) dissolved in dry THF (5 mL/mmol), NaH (60% dispersed in mineral oil, 1.5 equiv) was added slowly at 0 ^{o}C under N_2 atmosphere and stirred for 45 minutes. At the same temperature propargyl bromide (80% in toluene, 1.3 equiv) was added slowly and the stirring was continued at room temperature. After completion of the reaction, saturated aqueous NH_4Cl solution was added to quench the reaction. Solvent was evaporated under reduced pressure. The residue was dissolved in ethyl acetate, washed with water, brine solution, dried over anhydrous Na_2SO_4, concentrated and the residue was purified by column chromatography on silica gel (eluent: EtOAc/hexanes) to get the pure product.

2-Phenyl-3-((prop-2-yn-1-yloxy)methyl)oxirane (**1.32a**)



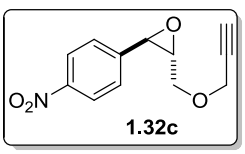
Compound **1.32a** was synthesized from **1.37a** by following the general propargylation procedure. Colorless liquid; R_f = 0.52 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.28 (m, 5H), 4.27 (s, 2H), 3.93 (dd, *J* = 11.6, 2.8 Hz, 1H), 3.83 (s, 1H), 3.71 (dd, *J* =11.2, 5.2 Hz, 1H), 3.25-3.24 (m, 1H), 2.48 (br d, *J* = 0.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.4, 128.1, 127.9, 125.4, 79.1, 74.9, 69.0, 60.3, 58.1, 55.4; IR (neat): υ 3287, 2920, 2118, 1721, 1454, 1099 cm^{-1}; Anal. calc'd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43; Found: C, 76.65; H, 6.48.

2-(4-Chlorophenyl)-3-((prop-2-yn-1-yloxy)methyl)oxirane (1.32b)



Compound **1.32b** was prepared from **1.37b** by following the general procedure for propargylation. Colorless liquid; R_f = 0.50 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 4.25 (d, *J* = 2.0 Hz, 2H), 3.90 (dd, *J* = 11.6, 3.2 Hz, 1H), 3.80 (s, 1H), 3.70 (dd, *J* = 11.6, 5.2 Hz, 1H), 3.19 (dt, *J* = 5.2, 2.4 Hz, 1H), 2.47 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 135.3, 134.1, 128.7, 127.1, 79.2, 75.1, 69.1, 60.8, 58.6, 55.3; IR (neat): υ 3297, 2859, 2118, 1495, 1092, 826 cm^{-1}; Anal. Calc'd for $C_{12}H_{11}ClO_2$: C, 64.73; H, 4.98; Found: C, 64.85; H, 4.91.

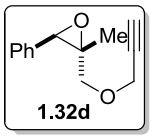
2-(4-Nitrophenyl)-3-((prop-2-yn-1-yloxy)methyl)oxirane (1.32c)



Compound **1.32c** was prepared from **1.37c** by following the general propargylation procedure. Yellow color liquid; R_f = 0.5 in 1:5 EtOAc/hexanes (three elutions); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 (d, *J* = 8.0 Hz, 2H), 7.45

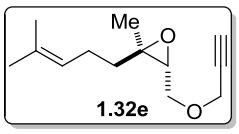
(d, *J* = 8.0 Hz, 2H), 4.26 (s, 2H), 3.95 (s, 1H), 3.91 (d, *J* = 11.6 Hz, 1H), 3.76 (dd, *J* = 11.6, 4.8 Hz, 1H), 3.21 (bs, 1H), 2.48 (br d, 1.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.9, 144.4, 126.5, 123.8, 79.0, 75.2, 68.7, 61.2, 58.7, 54.8; IR (neat): υ 3293, 2120, 1522, 1348, 1101 cm^{-1}; Anal. Calc'd for $C_{12}H_{11}NO_4$: C, 61.80; H, 4.75; N, 6.01; Found: C, 61.72; H, 4.81; N, 6.12.

2-Methyl-3-phenyl-2-((prop-2-yn-1-yloxy)methyl)oxirane (1.32d)



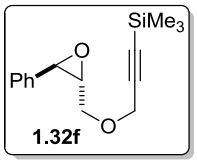
Compound **1.32d** was synthesized from **1.37d** by following the general propargylation procedure. Colorless liquid; R_f = 0.71 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.26 (m, 5H), 4.26 (d, *J* = 2.4 Hz, 2H), 4.06 (s, 1H), 3.73 (d, *J* = 11.2 Hz, 1H), 3.68 (d, *J* = 11.2 Hz, 1H), 2.48 (t, *J* = 2.4 Hz, 1H), 1.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 135.5, 128.0, 127.5, 126.4, 79.3, 74.8, 73.5, 62.2, 61.0, 58.4, 13.6; IR (neat): υ 3293, 2932, 2118, 1604, 1451, 1254, 1107, 1026 cm^{-1}; Anal. Calc'd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98; Found: C, 77.35; H, 6.90.

2-Methyl-2-(4-methylpent-3-en-1-yl)-3-((prop-2-yn-1-yloxy)methyl)oxirane (1.32e)



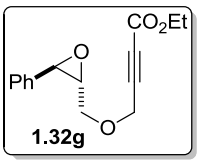
Compound **1.32e** was synthesized from **1.37e** by following the general propargylation procedure. Colorless liquid; R_f = 0.58 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.08 (t, *J* = 7.1 Hz, 1H), 4.25 (dd, *J* = 15.8, 2.2 Hz, 1H), 4.18 (dd, *J* = 15.8, 2.2 Hz, 1H), 3.75 (dd, *J* = 11.1, 4.5 Hz, 1H), 3.59 (dd, *J* = 11.1, 6.2 Hz, 1H), 2.98 (dd, *J* = 5.9, 4.8 Hz, 1H) 2.46 (t, *J* = 2.3 Hz, 1H), 2.10 (d, *J* = 7.7 Hz, 1H), 2.06 (d, *J* = 7.5 Hz, 1H), 1.72-1.63 (m, 4H), 1.61 (s, 3H), 1.52-1.44 (m, 1H), 1.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 132.0, 123.4, 79.3, 74.7, 68.4, 60.7, 60.0, 58.2, 38.3, 25.6, 23.6, 17.6, 16.7; IR (neat): υ 2974, 2930, 2118, 1454, 1383, 1094 cm^{-1}; Anal. Calc'd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68; Found: C, 74.85; H, 9.71.

Trimethyl(3-((-3-phenyloxiran-2-yl)methoxy)prop-1-yn-1-yl)silane (1.32f)



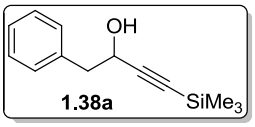
Compound **1.32f** was prepared according to the known procedure from compound **1.32a.**[33] Colorless liquid; R_f = 0.55 in 1:10 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36-7.27 (m, 5H), 4.28 (d, *J* = 15.2 Hz, 1H), 4.23 (d, *J* = 15.2 Hz, 1H), 3.89 (dd, *J* = 11.6, 3.2 Hz, 1H), 3.81 (d, *J* = 2.0 Hz, 1H), 3.69 (dd, *J* = 11.2, 5.2 Hz, 1H), 3.24 (dt, *J* = 5.2, 3.2 Hz, 1H), 0.18 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.8, 128.5, 128.3, 125.7, 100.9, 92.1, 69.4, 60.8, 59.4, 56.0, -0.2; IR (neat): υ 2959, 2174, 1603, 1458, 1250, 1101, 845 cm^{-1}; Anal. Calc'd for $C_{15}H_{20}O_2Si$: C, 69.19; H, 7.74, Found: C, 69.25; H, 7.70.

Ethyl 4-((-3-phenyloxiran-2-yl)methoxy)but-2-ynoate (1.32g)



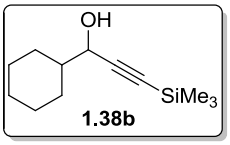
Compound **1.32g** was prepared according to the known procedure from compound **1.32a**.[33] Pale yellow color liquid; R_f = 0.60 in 1:3 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.28 (m, 5H), 4.39 (s, 2H), 4.24 (q, J = 7.2 Hz, 2H), 3.94 (dd, J = 11.6, 2.8 Hz, 1H), 3.82 (d, J = 2.0 Hz, 1H), 3.70 (dd, J = 11.6, 5.2 Hz, 1H), 3.24 (dt, J = 5.2, 2.8 Hz, 1H), 1.32 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153, 136.4, 128.5, 128.3, 125.6, 82.5, 78.5, 69.7, 62.2, 60.5, 58.2, 55.7, 13.9; IR (neat): υ 2984, 2237, 1715, 1464, 1254, 1107, 750 cm^{-1}; Anal. Calc'd for $C_{15}H_{16}O_4$: C, 69.22; H, 6.20, Found: C, 69.12; H, 6.25.

1-Phenyl-4-(trimethylsilyl)but-3-yn-2-ol (1.38a)



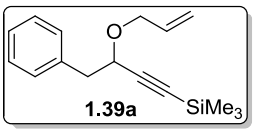
Compound **1.38a** was synthesized from phenylacetaldehyde and trimethylsilylacetylene by following the known procedure.[34] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.24 (m, 5H), 4.55 (t, J = 6.4 Hz, 1H), 3.0 (d, J = 6.4 Hz, 2H), 0.18 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.4, 129.9, 128.3, 126.8, 105.9, 90.5, 63.5, 44.0, -0.26.

1-Cyclohexyl-3-(trimethylsilyl)prop-2-yn-1-ol (1.38b)



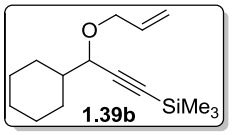
Compound **1.38b** was prepared from cyclohexanal and trimethylsilylacetylene following the reported procedure.[35] ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.13 (t, J = 5.8 Hz, 1H), 1.87-1.75 (m, 5H), 1.69-1.66 (m, 1H), 1.57-1.48 (m, 1H), 1.34-0.99 (m, 5H), 0.17 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 106.0, 90.3, 67.7, 44.1, 28.6, 28.2, 26.5, 25.99, 25.97, 0.01.

(3-(Allyloxy)-4-phenylbut-1-yn-1-yl)trimethylsilane (1.39a)



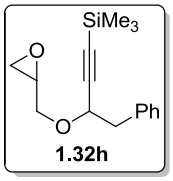
Compound **1.39a** was synthesized from **1.38a** following reported procedure.[36] Colorless liquid; R_f = 0.54 in 1:20 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29-7.21 (m, 5H), 5.93-5.83 (m, 1H), 5.26 (dd, J = 17.2, 1.6 Hz, 1H), 5.17 (dd, J = 10.4, 1.2 Hz, 1H), 4.29-4.24 (m, 2H), 3.97 (dd, J = 12.8, 6.0 Hz, 1H), 3.07 (dd, J = 13.6, 6.8 Hz, 1H), 2.99 (dd, J = 13.2, 6.8 Hz, 1H), 0.17 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.3, 134.4, 129.9, 128.1, 126.6, 117.3, 104.3, 91.5, 70.4, 69.7, 42.3, -0.1; IR (neat): υ 3030, 2959, 2859, 2170, 1497, 1454, 1335, 1252, 1080, 843 cm^{-1}; Anal. Calc'd for $C_{16}H_{22}OSi$: C, 74.36; H, 8.58; Found: C, 74.45; H, 8.51.

(3-(Allyloxy)-3-cyclohexylprop-1-yn-1-yl)trimethylsilane (1.39b)



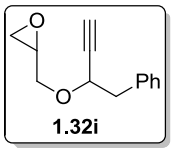
Compound **1.39b** was prepared from **1.38a** following the known literature procedure.[36] Pale yellow liquid; R_f = 0.59 in 1:20 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.96-5.86 (m, 1H), 5.30 (dd, *J* = 17.2, 1.6 Hz, 1H), 5.17 (d, *J* = 9.6 Hz, 1H), 4.25 (dd, *J* = 12.8, 4.8 Hz, 1H), 3.94 (dd, *J* = 12.8, 6.4 Hz, 1H), 3.84 (d, *J* = 6.4 Hz, 1H), 1.87-1.43 (m, 5H), 1.26-1.02 (m, 6H), 0.18 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 134.7, 117.0, 104.0, 91.1, 74.1, 69.6, 42.5, 29.0, 28.5, 26.5, 25.99, 25.95, 0.01.

Trimethyl(3-(oxiran-2-ylmethoxy)-4-phenylbut-1-yn-1-yl)silane (1.32h)



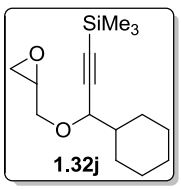
Compound **1.32h** was prepared from **1.39a** following the general epoxydation procedure. Colorless liquid; R_f = 0.65 in 1:10 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): (dr = 1:1.32) δ 7.30-7.22 (m, 10H), 4.28 (t, *J* = 6.8 Hz, 2H), 3.95 (dd, *J* = 11.2, 3.2 Hz, 1H), 3.78 (dd, *J* = 11.6, 4.8 Hz, 1H), 3.63 (dd, *J* = 11.2, 3.2 Hz, 1H), 3.36 (dd, *J* = 11.6, 6.4 Hz, 1H), 3.13-3.09 (m, 2H), 3.08-2.94 (m, 4H), 2.78-2.74 (m, 2H), 2.60 (dd, *J* = 4.8, 2.8 Hz, 1H), 2.56 (dd, *J* = 4.8, 2.8 Hz, 1H), 0.15 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.1, 129.9, 128.2, 126.7, 103.8, 103.7, 92.04, 92.00, 71.64, 71.62, 69.9, 68.6, 50.8, 50.6, 44.8, 44.6, 42.2, 42.1, -0.1; IR (neat): υ 2959, 2170, 1492, 1454, 1337, 1250, 1094, 843, 700 cm^{-1}; Anal. Calc'd for $C_{16}H_{22}O_2Si$: C, 70.03; H, 8.08; Found: C, 70.12; H, 8.11.

2-(((1-Phenylbut-3-yn-2-yl)oxy)methyl)oxirane (1.32i)



Compound **1.32i** was synthesized from **1.39a** following general epoxidation procedure. Colorless liquid; R_f = 0.59 in 1:3 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): (dr = 1:1.45) δ 7.32-7.22 (m, 10 H), 4.35-4.28 (m, 2H), 3.99 (dd, *J* = 11.2, 2.8 Hz, 1H), 3.76 (dd, *J* = 11.6, 5.2 Hz, 1H), 3.67 (dd, *J* = 11.6, 3.2 Hz, 1H), 3.37 (dd, *J* = 11.6, 6.4 Hz, 1H), 3.15-3.11 (m, 2H), 3.09 (dd, *J* = 6.8, 2.4 Hz, 1H), 3.05 (dd, *J* = 10.8, 2.4 Hz, 1H), 3.02-2.97 (m, 2H), 2.76 (dd, *J* = 10.8, 5.6 Hz, 2H), 2.60 (dd, *J* = 5.2, 2.8 Hz, 1H), 2.56 (dd, *J* = 4.8, 2.8 Hz, 1H), 2.45 (t, *J* = 2.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.9, 129.7, 128.3, 126.7, 81.9, 74.99, 74.96, 71.0, 70.8, 69.8, 68.7, 50.8, 50.5, 44.6, 44.3, 42.1, 42.0; IR (neat): υ 3289, 2926, 2112, 1719, 1497, 1454, 1333, 1254, 1094, 847 cm^{-1}; Anal. Calc'd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98; Found: C, 77.32; H, 6.91.

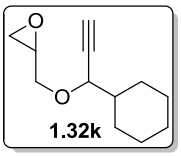
(3-Cyclohexyl-3-(oxiran-2-ylmethoxy)prop-1-yn-1-yl)trimethylsilane (1.32j)



Compound **1.32j** was prepared from **1.39b** following the general epoxydation procedure. Light yellow color liquid; R_f = 0.38 in 1:20 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): (dr = 1:1.37) δ 3.94 (dd, *J* = 11.2, 3.2 Hz, 1H), 3.873 (d, *J* = 6.4 Hz, 1H), 3.870 (d, *J* = 6.0 Hz, 1H), 3.79 (dd, *J* = 11.6, 4.8 Hz, 1H), 3.61 (dd, *J* =

11.2, 3.6 Hz, 1H), 3.34 (dd, *J* = 11.6, 6.4 Hz, 1H), 3.19-3.14 (m, 2H), 2.80 (t, *J* = 4.8 Hz, 2H), 2.70 (dd, *J* = 5.2, 2.8 Hz, 1H), 2.59 (dd, *J* = 5.2, 2.8 Hz, 1H), 1.88-1.82 (m, 4H), 1.76-1.73 (m, 4H), 1.68-1.57 (m, 6H), 1.24-1.02 (m, 8H), 0.18 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 103.7, 103.6, 91.7, 91.6, 75.63, 75.60, 70.1, 68.7, 51.0, 50.6, 44.9, 44.6, 42.6, 42.5, 29.1, 29.0, 28.5, 28.38, 28.37, 26.5, 26.02, 25.9, -0.03; IR (neat): υ 2926.3, 2849.1, 2168.2, 1645.1, 1452.5, 1249.9, 844.9 cm^{-1}; Anal. Calc'd for $C_{15}H_{26}O_2Si$: C, 67.61; H, 9.84; Found: C, 67.72; H, 9.78.

2-(((1-Cyclohexylprop-2-yn-1-yl)oxy)methyl)oxirane (1.32k)

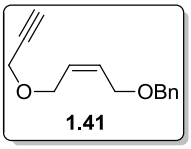


Compound **1.32k** was prepared from compound **1.32j** by following the reported desilylation procedure.[37] Colorless liquid; R_f = 0.28 in 1:20 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): (dr = 1:1.33) δ 3.98 (dd, *J* = 11.2, 3.2 Hz, 1H), 3.91 (dd, *J* = 6.2, 2.0 Hz, 1H), 3.88 (dd, *J* = 6.4, 2.0 Hz, 1H), 3.77 (dd, *J* = 11.2, 4.8 Hz, 1H), 3.65 (dd, *J* = 11.2, 6.3 Hz, 1H), 3.35 (dd, *J* = 11.6, 6.4 Hz, 1H), 3.19-3.14 (m, 2H), 2.80 (t, *J* = 4.8 Hz, 2H), 2.69 (dd, *J* = 5.2, 2.8 Hz, 1H), 2.59 (dd, *J* = 5.2, 2.8 Hz, 1H), 2.43 (t, *J* = 2.4 Hz, 2H), 1.87-1.84 (m, 4H), 1.77-1.74 (m, 4H), 1.68-1.62 (m, 4H), 1.27-1.07 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 81.7, 81.6, 74.9, 74.8, 74.7, 74.6, 70.1, 68.8, 50.9, 50.5, 44.6, 44.3, 42.5, 42.4, 28.82, 28.80, 28.29, 28.27, 26.4, 25.88, 25.84; IR (neat): υ 3289, 2928, 2855, 2104, 1452, 1327, 1253, 1088, 843 cm^{-1}; Anal. Calc'd for $C_{12}H_{18}O_2$: C, 74.19, H, 9.34; Found; C, 74.12; H, 9.38.

(*Z*)-4-(Benzyloxy)but-2-en-1-ol (1.40)

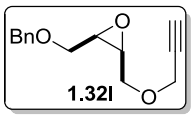
Compound **1.40** was prepared according to the reported procedure.[38] Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38-7.27 (m, 5H), 5.81 (dt, *J* = 11.2, 6.0 Hz, 1H), 5.73 (dt, *J* = 11.2, 6.0 Hz, 1H), 4.52 (s, 2H), 4.16 (d, *J* = 6.8 Hz, 2H), 4.09 (d, *J* = 6.0 Hz, 2H), 2.21 (bs, 1H).

(*Z*)-(((4-(Prop-2-yn-1-yloxy)but-2-en-1-yl)oxy)methyl)benzene (1.41)



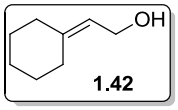
Compound **1.41** was synthesized from **1.40** following the general procedure for propargylation. Pale yellow liquid; R_f = 0.45 in 1:10 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36-7.28 (m, 5H), 5.83 (dt, *J* = 11.2, 6.2 Hz, 1H), 5.73 (dt, *J* = 11.2, 6.4 Hz, 1H), 4.52 (s, 2H), 4.13 (m, 6H), 2.41 (t, *J* = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.2, 130.4, 128.6, 128.4, 127.8, 127.7, 79.6, 74.6, 72.3, 65.7, 65.2, 57.2; IR (neat): υ 3289, 3030, 2857, 2116, 1454, 1362, 1076, 739 cm^{-1}; Anal. Calc'd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46, Found: C, 77.65; H, 7.45.

2-((Benzyloxy)methyl)-3-((prop-2-yn-1-yloxy)methyl)oxirane (1.32l)



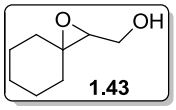
Compound **1.32l** was synthesized from **1.41** following the general procedure for epoxydation. Yellow color liquid; R_f = 0.45 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36-7.28 (m, 5H), 4.63 (d, *J* = 12.0 Hz, 1H), 4.54 (d, *J* = 12.0 Hz, 1H), 4.23 (dd, *J* = 16.0, 1.6 Hz, 1H), 4.16 (dd, *J* = 16.0, 1.6 Hz, 1H), 3.76 (dd, *J* = 11.2, 4.0 Hz, 1H), 3.72 (dd, *J* = 11.6, 4.0 Hz, 1H), 3.61-3.55 (m, 2H), 3.29-3.22 (m, 2H), 2.45 (t, *J* = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.8, 128.5, 127.85, 127.84, 79.2, 75.0, 73.3, 68.0, 67.7, 58.4, 54.4, 54.0; IR (neat): υ 3287, 2861, 2116, 1454, 1361, 1096, 741 cm^{-1}; Anal. Calc'd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94, Found: C, 72.45; H, 6.88.

2-Cyclohexylideneethanol (1.42)



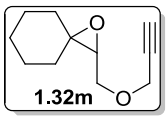
Compound **1.42** was prepared from ethyl 2-cyclohexylideneacetate following the reported procedure.[39] ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.36 (t, *J* = 7.2 Hz, 1H), 4.14 (d, *J* = 7.2 Hz, 2H), 2.19 (t, *J* = 5.6 Hz, 2H), 2.11 (bs, 2H), 1.55 (bs, 6H).

1-Oxaspiro[2.5]octan-2-ylmethanol (1.43)



Compound **1.43** was prepared from **1.42** following the general epoxidation procedure.[40] ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.84 (d, *J* = 11.6 Hz, 1H), 3.69 (dd, *J* = 11.6, 6.4 Hz, 1H), 2.96 (dd, *J* = 6.4, 4.0 Hz, 1H), 1.94 (bs, 1H), 1.79-1.67 (m, 2H), 1.61-1.52 (m, 8H).

2-((Prop-2-yn-1-yloxy)methyl)-1-oxaspiro[2.5]octane (1.32m)

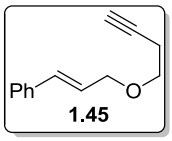


Compound **1.32m** was prepared from **1.43** following the general propargylation procedure. Colorless liquid; R_f = 0.48 (1:3 EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.25 (dd, *J* = 15.6, 2.4 Hz, 1H), 4.18 (dd, *J* = 16.0, 2.4 Hz, 1H), 3.77 (dd, *J* = 11.2, 4.8 Hz, 1H), 3.60 (dd, *J* = 11.2, 6.0 Hz, 1H), 2.96 (dd, *J* = 6.0, 4.8 Hz, 1H)), 2.45 (t, *J* = 2.4 Hz, 1H), 1.75-1.69 (m, 2H), 1.60-1.49 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 79.4, 74.8, 68.0, 62.3, 61.9, 58.3, 35.3, 29.5, 25.6, 24.9, 24.8; IR (neat): υ 3264, 2936, 2859, 2116, 1721, 1449, 1360, 1096, 897 cm^{-1}; Anal. Calc'd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95; Found: C, 73.45; H, 8.85.

(*E*)-(3-Bromoprop-1-en-1-yl)benzene (1.44)

Compound**1.44** is commercially available.

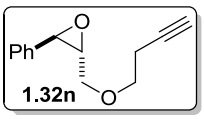
(*E*)-(3-(But-3-yn-1-yloxy)prop-1-en-1-yl)benzene (1.45)



To a solution of homopropargyl alcohol (0.5 g, 7.2 mmol) in dry THF (25 mL), NaH (0.6 g, 14 mmol, 60% dispersion in mineral oil) was added slowly at 0 ºC and stirred at the same temperature for 45 min. To this mixture cinnamyl bromide **1.44** (1.8 g,

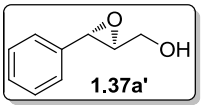
9.3 mmol) was added slowly and the reaction was continued for 1 h. Then excess NaH was quenched by slow addition of methanol. Solvents were evaporated and the crude reaction mixture was dissolved in ethyl acetate. It was washed with saturated brine solution and the organic layer was dried over anhydrous sodium sulphate. Solvents were removed at reduced pressure. The crude product was purified by column chromatography (8% EtOAc in hexanes) as yellow colored liquid (1.07 g, 80%). R_f = 0.42 in 1:10 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 (d, *J* = 7.2 Hz, 2H), 7.31 (t, *J* = 7.2 Hz, 2H), 7.24 (d, *J* = 7.2 Hz, 1H), 6.61 (d, *J* = 15.6 Hz, 1H), 6.28 (dt, *J* = 16.0, 6.0 Hz, 1H), 4.18 (d, *J* = 6.0 Hz, 2H), 3.61 (t, *J* = 6.8 Hz, 2H), 2.50 (dt, *J* = 7.2, 2.8 Hz, 2H), 2.00 (t, *J* = 2.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.5, 132.6, 128.5, 127.7, 126.4, 125.7, 81.3, 71.5, 69.3, 68.1, 19.8; IR (neat): υ 3297, 2919, 2120, 1728, 1452, 1113, 750, 698 cm^{-1}; Anal. Calc'd for $C_{13}H_{14}O$: C, 83.83; H, 7.58; Found: C, 83.75; H, 7.61.

2-((But-3-yn-1-yloxy)methyl)-3-phenyloxirane (1.32n)



Compound **1.32n** was synthesized from **1.45** following the general epoxydation procedure. Light yellow colored liquid; R_f = 0.54 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.26 (m, 5H), 3.88 (dd, *J* = 11.6, 2.8 Hz, 1H), 3.80 (d, *J* = 2.0 Hz, 1H), 3.70 (dd, *J* = 6.8, 1.6 Hz, 1H), 3.67 (dd, *J* = 6.8, 2.0 Hz, 1H), 3.62 (dd, *J* = 11.6, 5.2 Hz, 1H), 3.22 (dt, *J* = 4.8, 2.8 Hz, 1H), 2.51 (td, *J* = 6.8, 2.8 Hz, 2H), 2.00 (t, *J* = 2.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.7, 128.4, 128.2, 125.6, 81.1, 70.1, 69.5, 69.4, 61.0, 55.7, 19.8; IR (neat): υ 3291, 2872, 2120, 1604, 1115, 882 cm^{-1}; Anal.Calc'd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98; Found: C, 77.32; H, 6.85.

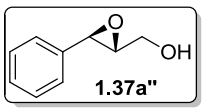
((2*S*,3*S*)-3-Phenyloxiran-2-yl)methanol (1.37a')



Compound **1.37a'** was prepared by following known procedure.[19] To a suspension of 4 Å molecular sieves (0.3 g, 30 % w/w based on cinnamyl alcohol) in CH_2Cl_2 (20 mL), $Ti(O^iPr)_4$ (2.12 g 7.46 mmol) was added. The mixture was cooled to -30 ºC and L-(+)-diethyl tartrate (1.86 g, 8.95 mmol) in CH_2Cl_2 (5 mL) was added followed by cinnamyl alcohol (1 g, 7.46 mmol) in CH_2Cl_2 (5 mL) and the resulting suspension was stirred for 40 min. Then anhydrous *tert*-butyl hydroperoxide in hexane (5.5 M, 4.1 mL, 22.38 mmol) was added dropwise and the stirring was continued for two days at -30 ºC. After warming the reaction mixture to 0 ºC, H_2O (45 mL) was added and the mixture was stirred for 1 h. 30% Aqueous NaOH saturated with NaCl (7.5 mL) was added and the stirring was continued for another 1.5 h during which the slurry changed color from yellow to white, the white slurry was filtered through a plug of Celite 545, which was rinsed thoroughly with CH_2Cl_2. The filtrate was washed with saturated aqueous NaCl, dried over Na_2SO_4 and concentrated. The resulting light yellow liquid was purified by column chromatography (1:5

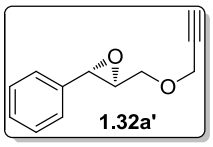
EtOAc/hexanes) as colorless liquid (0.672 g, 60%). $[\alpha]_D^{25}$ = -40.6º (*c* 0.225, $CHCl_3$) (*lit*: [41] -46.4º, *c* 1.32, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.27 (m, 5H), 4.04 (d, *J* = 12.6 Hz, 1H), 3.93 (s, 1H), 3.79 (d, *J* = 12.5 Hz, 1H), 3.24-3.23 (m, 1H), 2.43 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.6, 128.5, 128.3, 125.7, 62.5, 61.2, 55.6.

((2*R*,3*R*)-3-Phenyloxiran-2-yl)methanol (1.37a'')



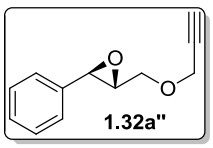
Compound **1.37a''** prepared by following the above described procedure (procedure employed for **1.37a'**) using D-(-)-diethyl tartrate in place of L-(+)-diethyl tartrate. White semisolid; $[\alpha]_D^{25}$ = +41.1º (*c* 1.5, $CHCl_3$) (*lit*:[30] +57.3º, *c* 1.5, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41-7.28 (m, 5H), 4.08 (ddd, *J* = 12.8, 5.2, 2.0 Hz, 1H), 3.96 (d, *J* = 2.4 Hz, 1H), 3.83 (ddd, *J* = 12.8, 7.6, 4.0 Hz, 1H), 3.26 (dt, *J* = 3.6, 2.4 Hz, 1H), 2.22-2.06 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.6, 128.5, 128.3, 125.7, 62.5, 61.2, 55.6.

(2*S*,3*S*)-2-Phenyl-3-((prop-2-yn-1-yloxy)methyl)oxirane (1.32a')



Compound **1.32a'** prepared from **1.37a'** following the general propargylation procedure. Colorless liquid; $[\alpha]_D^{25}$ = - 41.8º (*c* 2.1, $CHCl_3$, 92.2% *ee*); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.27 (m, 5H), 4.26 (d, *J* = 2.3 Hz, 2H), 3.92 (dd, *J* = 11.4, 3.1 Hz, 1H), 3.82 (d, *J* = 2.0 Hz, 1H), 3.70 (dd, *J* =11.4, 5.3 Hz, 1H), 3.24 (dt, *J* = 5.1, 2.7 Hz, 1H), 2.47(t, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.7, 128.5, 128.3, 125.7, 79.2, 75.0, 69.4, 60.7, 58.6, 55.9; IR (neat): υ 3287, 2920, 2118, 1721, 1454, 1099 cm^{-1}; Anal. Calc'd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43, Found: C, 76.45; H, 6.48.

(2*R*,3*R*)-2-Phenyl-3-((prop-2-yn-1-yloxy)methyl)oxirane (1.32a'')



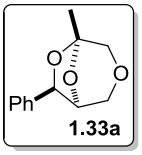
Compound **1.32a''** synthesized from **1.37a''** following the general propargylation procedure. Colorless liquid; $[\alpha]_D^{25}$ = +39.3º (*c* 1.98, $CHCl_3$, 91.6% ee); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.28 (m, 5H), 4.27 (s, 2H), 3.93 (dd, *J* = 11.6, 2.8 Hz, 1H), 3.83 (s,1H), 3.71 (dd, *J* =11.2, 5.2 Hz, 1H), 3.25-3.24 (m, 1H), 2.48 (bs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.7, 128.5, 128.3, 125.7, 79.2, 75.0, 69.4, 60.7, 58.6, 55.9; IR (neat): υ 3287, 2920, 2118, 1721, 1454, 1099 cm^{-1}; Anal. Calc'd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43, Found: C, 76.45; H, 6.41.

General procedure for $(Ph_3P)AuCl/AgSbF_6$ catalyzed bicyclic acetal formation (1.33 and 1.34)

To a solution of epoxyalkyne **1.32** (0.532 mmol) in dry acetone (2.5 mL) was added $(PPh_3)AuCl$ (0.0106 mmol, 2 mol%) and $AgSbF_6$ (2 mol%) consecutively. Precipitation of AgCl as white solid was noticed. The mixture was stirred at 60 ºC. After the completion of the reaction, solvent was removed

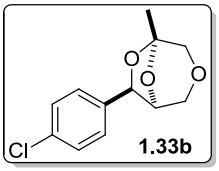
under reduced pressure and the residue was subjected to column chromatography (eluent: 6-10% EtOAc in hexanes) to get the pure products **1.33** and **1.34**.

5-Methyl-7-phenyl-3,6,8-trioxabicyclo[3.2.1]octane (1.33a)



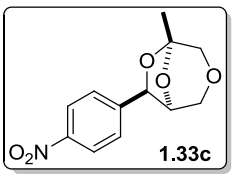
Compound **1.33a** was obtained from two substrates **1.32a** and **1.32f** (Table 2, entry 1 and 6) by separately following the general bicyclic acetal formation procedure. Colorless semisolid; R_f = 0.46 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (d, J = 7.2 Hz, 2H), 7.36 (t, J = 7.2 Hz, 2H), 7.29 (d, J = 7.2 Hz, 1H), 5.29 (d, J = 4.8 Hz, 1H), 4.43 (d, J = 4.4 Hz, 1H), 3.70 (d, J = 12.0 Hz, 1H), 3.68 (d, J = 10.8 Hz, 1H), 3.63 (d, J = 11.2 Hz, 1H), 3.31 (d, J = 12.0 Hz, 1H), 1.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.1, 128.2, 127.5, 126.1, 105.8, 81.1, 78.5, 71.8, 64.3, 20.2; IR (neat): υ 2963, 1494, 1452, 1302, 1233, 1063, 876, 700 cm^{-1}; Anal. Calc′d for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84; Found: C, 69.95; H, 6.81.

7-(4-Chlorophenyl)-5-methyl-3,6,8-trioxabicyclo[3.2.1]octane (1.33b)



Compound **1.33b** was synthesized from **1.32b** by following the general bicyclic acetal formation procedure. Colorless solid, mp 172-174 ºC; R_f = 0.39 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H), 5.24 (d, J = 5.2 Hz, 1H), 4.42 (d, J = 4.8 Hz, 1H), 3.70 (d, J = 11.6 Hz, 1H), 3.65 (d, J = 11.2 Hz, 1H), 3.62 (d, J = 11.2 Hz, 1H), 3.28 (d, J = 11.6 Hz, 1H), 1.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 135.6, 133.2, 128.3, 127.6, 105.9, 80.4, 78.3, 71.7, 64.2, 20.1; IR (neat): υ 2961, 2920, 2856, 1490, 1068, 834, 648 cm^{-1}; Anal. Calc′d for $C_{12}H_{13}ClO_3$: C, 59.88; H, 5.44; Found: C, 59.75; H, 5.41.

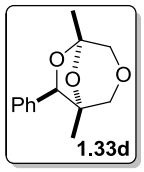
5-Methyl-7-(4-nitrophenyl)-3,6,8-trioxabicyclo[3.2.1]octane (1.33c)



Compound **1.33c** was synthesized from **1.32c** by following the general bicyclic acetal formation procedure.Yellow colored solid, mp 135-137 ºC; R_f = 0.47 in 1:5 EtOAc/hexanes (tripple elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 (d, J = 8.0 Hz, 2H), 7.68 (d, J = 8.0 Hz, 2H), 5.35 (d, J = 4.8 Hz, 1H), 4.56 (d, J = 4.4 Hz, 1H), 3.73 (d, J = 12.0 Hz, 1H), 3.67 (d, J = 11.2 Hz, 1H), 3.63 (d, J = 11.2 Hz, 1H), 3.21 (d, J = 12.0 Hz, 1H), 1.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.2, 144.8, 127.0, 123.4, 106.4, 80.1, 78.3, 71.6, 64.3, 19.9; IR (neat): υ 3293, 2922, 1728, 1520, 1346, 1074, 856 cm^{-1}; Anal. Calc′d for $C_{12}H_{13}NO_5$: C, 57.37; H, 5.22; N, 5.58; Found: C, 57.25; H, 5.26; N, 5.71.

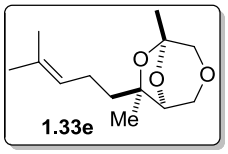
1,5-Dimethyl-7-phenyl-3,6,8-trioxabicyclo[3.2.1]octane (1.33d)

Compound **1.33d** was synthesized from **1.32d** following the general bicyclic acetal formation procedure. Colorless liquid; R_f = 0.67 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz,



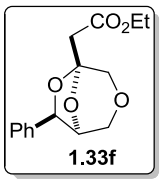
$CDCl_3$): δ 7.57 (d, J = 7.6 Hz, 2H), 7.35 (t, J = 7.6 Hz, 2H), 7.30 (d, J = 7.2 Hz, 1H), 4.78 (s, 1H), 3.7 0 (d, J = 10.8 Hz, 1H), 3.58 (d, J = 10.8 Hz, 1H), 3.41 (d, J = 11.6 Hz, 1H), 3.24 (d, J = 11.6 Hz, 1H), 1.48 (s, 3H), 1.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.5, 128.1, 127.7, 126.5, 105.0, 86.6, 82.3, 70.7, 68.5, 20.3, 17.8; IR (neat): υ 2978, 2853, 1605, 1452, 1379, 1223, 1103, 824, 700 cm^{-1}; Anal. Calc′d for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32; Found: C, 70.92; H, 7.33.

5,7-Dimethyl-7-(4-methylpent-3-en-1-yl)-3,6,8-trioxabicyclo[3.2.1]octane (1.33e)



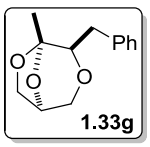
Compound **1.33e** was synthesized from **1.32e** following the general bicyclic acetal formation procedure. Colorless liquid; Colorless liquid; R_f = 0.52 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.15 (t, J = 6.8 Hz, 1H), 3.84 (d, J = 14.4 Hz, 1H), 3.80 (d, J = 14.4 Hz, 1H), 3.77 (s, 1H), 3.52 (d, J = 10.8 Hz, 1H), 3.44 (d, J = 10.8 Hz, 1H), 2.20 – 2.13 (m, 1H), 2.11-1.99 (m, 2H), 1.90-1.84 (m, 1H), 1.69 (s, 3H), 1.62 (s, 3H), 1.36 (s, 3H), 1.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 131.7, 124.2, 105.0, 83.1, 80.7, 71.8, 64.8, 34.9, 25.6, 25.4, 23.9, 20.8, 17.7; IR (neat): υ 2965, 2922, 1454, 1373, 1259, 864 cm^{-1}; Anal. Calc′d for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80; Found: C, 69.05; H, 9.96.

Ethyl 2-(7-phenyl-3,6,8-trioxabicyclo[3.2.1]octan-5-yl)acetate (1.33f)



Compound **1.33f** was synthesized from **1.32g** following the general bicyclic acetal formation procedure. Colorless solid, mp 56-58 ºC; R_f = 0.53 in 1:3 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 (d, J = 7.2 Hz, 2H), 7.35 (t, J = 7.2 Hz, 2H), 7.28 (d, J = 7.6 Hz, 1H), 5.29 (d, J = 4.4 Hz, 1H), 4.48 (d, J = 4.0 Hz, 1H), 4.21 (q, J = 7.2 Hz, 2H), 3.87 (d, J = 11.2 Hz, 1H), 3.78 (d, J = 11.2 Hz, 1H), 3.73 (d, J = 11.6 Hz, 1H), 3.32 (d, J = 11.6 Hz, 1H), 2.86 (d, J = 14.8 Hz, 1H), 2.82 (d, J = 14.8 Hz, 1H), 1.30 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.2, 136.5, 128.2, 127.6, 126.2, 104.8, 81.3, 78.7, 70.6, 64.4, 61.0, 40.4, 14.2; IR (neat): υ 2964, 2866, 1730, 1452, 1190, 1055, 966, 658 cm^{-1}; Anal. Calc′d for $C_{15}H_{18}O_5$: C, 64.74; H, 6.52; Found: C, 64.63; H, 6.42.

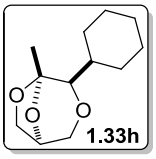
4-Benzyl-5-methyl-3,6,8-trioxabicyclo[3.2.1]octane (1.33g)



Compound **1.33g** was obtained from two substrates **1.32h** (Table 2, entry 8) and **1.32i** (Table 2, entry 9) following the general bicyclic acetal formation procedure. Colorless solid, mp 68-70 ºC; R_f = 0.43 in 1:3 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29 (t, J = 7.2 Hz, 2H), 7.23 (d, J = 6.8 Hz, 2H), 7.20 (d, J = 7.2 Hz, 1H), 4.42 (d, J = 4.8 Hz, 1H), 4.23 (d, J = 6.4 Hz, 1H), 3.94 (dd, J = 6.0, 5.6 Hz, 1H), 3.85 (d, J = 11.6 Hz, 1H), 3.76 (dd, J = 9.6, 4.0 Hz, 1H), 3.62 (d, J = 11.2 Hz, 1H), 2.81 (dd, J = 14.4, 4.0 Hz, 1H), 2.75 (dd, J = 14.4, 9.6 Hz, 1H), 1.41 (s, 3H);

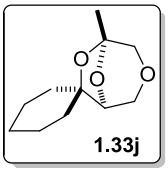
^{13}C NMR (100 MHz, $CDCl_3$): δ 138.5, 129.2, 128.3, 126.3, 106.9, 81.2, 74.5, 69.6, 68.2, 37.3, 20.2; IR (neat): υ 2928, 1732, 1460, 1121, 824, 700, 563 cm^{-1}; Anal. Calc′d for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32; Found: C, 70.80; H, 7.22.

4-Cyclohexyl-5-methyl-3,6,8-trioxabicyclo[3.2.1]octane (1.33h)



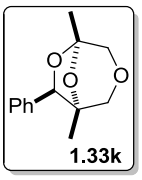
Compound **1.33h** was obtained from two substrates **1.32j** (Table 2, entry 10) and **1.32k** (Table 2, entry 11) following the general bicyclic acetal formation procedure. Colorless heavy liquid; R_f = 0.45 in 1:10 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.38 (d, J = 4.0 Hz, 1H), 4.14 (d, J = 4.0 Hz, 1H), 3.89-3.86 (m, 2H), 3.64 (d, J = 12.0 Hz, 1H), 3.31 (s, 1H), 1.92 (bd, J = 12.0 Hz, 1H), 1.75-1.73 (m, 2H), 1.62-1.61 (m, 1H), 1.49-1.42 (m, 2H), 1.37 (s, 3H), 1.27-1.10 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 107.4, 85.0, 74.4, 70.1, 68.2, 39.2, 30.9, 27.0, 26.6, 26.4, 25.8, 20.2; IR (neat): υ 2936, 1722, 1453, 1382, 1227, 1098, 700 cm^{-1}; Anal. Calc′d for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50; Found: C, 67.95; H, 9.46.

5-Methyl-3,6,8-trioxaspiro[bicyclo[3.2.1]octane-7,1'-cyclohexane] (1.33j)



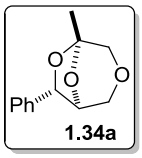
Compound **1.33j** was synthesized from **1.32m** following the general bicyclic acetal formation procedure. Colorless semisolid; R_f = 0.33 in 1:3 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.89 (s, 1H), 3.86-3.77 (m, 2H), 3.53 (d, J = 10.8 Hz, 1H), 3.45 (d, J = 10.8 Hz, 1H), 2.00-1.97 (m, 2H), 1.79-1.68 (m, 2H), 1.62 (t, J = 3.2 Hz, 2H), 1.45-1.39 (m, 4H), 1.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 104.6, 82.8, 78.8, 72.0, 64.6, 37.5, 31.4, 25.6, 24.2, 23.8, 21.0; IR (neat): υ 3397, 2932, 2859, 1726, 1451, 1377, 1161, 860 cm^{-1}; Anal. Calc′d for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15; Found: C, 66.56; H, 9.21.

1,5-Dimethyl-7-phenyl-3,6,8-trioxabicyclo[3.2.1]octane (1.33k)



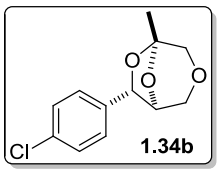
Compound **1.33k** was synthesized from **1.32n** following the general bicyclic acetal formation procedure. Colorless liquid; R_f = 0.46 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (d, J = 7.2 Hz, 2H), 7.36 (t, J = 7.6 Hz, 2H), 7.28 (d, J = 7.2 Hz, 1H), 5.18 (d, J = 5.2 Hz, 1H), 4.38 (dd, J = 5.6, 2.4 Hz, 1H), 3.97 (dd, J = 12.4, 6.4 Hz, 1H), 3.75 (td, J = 12.4, 4.4 Hz, 1H), 3.45 (d, J = 13.2 Hz, 1H), 3.39 (dd, J = 13.2, 2.4 Hz, 1H), 2.49 (ddd, J = 14.4, 12.0, 6.4 Hz, 1H), 1.90 (dd, J = 14.4, 4.0 Hz, 1H), 1.59 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.4, 128.2, 127.6, 126.8, 110.7, 82.0, 79.6, 70.7, 68.2, 42.3, 27.5; IR (neat): υ 3412, 2930, 1715, 1452, 1377, 1173, 700 cm^{-1}; Anal. Calc′d for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32; Found: C, 70.85; H, 7.36.

5-Methyl-7-phenyl-3,6,8-trioxabicyclo[3.2.1]octane (1.34a)



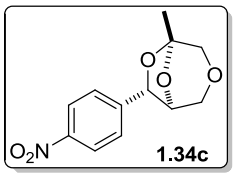
Compound **1.34a** was obtained from two substrates **1.32a** (Table 2, entry 1) and **1.32f** (Table 2, entry 6) separately following the general bicyclic acetal formation procedure. Colorless liquid; R_f = 0.33 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39-7.26 (m, 5H), 5.38 (s, 1H), 4.22 (s, 1H), 3.88 (d, *J* = 11.6 Hz, 1H), 3.79 (d, *J* = 11.6 Hz, 1H), 3.64 (s, 2H), 1.55 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.9, 128.5, 127.8, 126.0, 106.3, 81.5, 80.4, 72.2, 68.3, 19.6; IR (neat): υ 2965, 2916, 2855, 1605, 1495, 1452, 1393, 1238, 1074, 980, 754 cm^{-1}; Anal. Calc′d for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84; Found: C, 69.95; H, 6.81.

7-(4-Chlorophenyl)-5-methyl-3,6,8-trioxabicyclo[3.2.1]octane (1.34b)



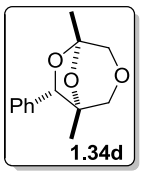
Compound **1.34b** was synthesized from **1.32b** following the general bicyclic acetal formation procedure. Colorless semisolid; R_f = 0.25 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (d, *J* = 9.2 Hz, 2H), 7.30 (d, *J* = 9.2 Hz, 2H), 5.34 (s, 1H), 4.18 (s, 1H), 3.87 (d, *J* = 11.6, 1H), 3.78 (d, *J* = 11.6 Hz, 1H), 3.62 (s, 2H), 1.53 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.4, 133.7, 128.6, 127.4, 106.5, 81.5, 79.8, 72.2, 68.2, 19.6; IR (neat): υ 2924, 1734, 1493, 1238, 826 cm^{-1}; Anal. Calc′d for $C_{12}H_{13}ClO_3$: C, 59.88; H, 5.44; Found: C, 59.65; H, 5.41.

5-Methyl-7-(4-nitrophenyl)-3,6,8-trioxabicyclo[3.2.1]octane (1.34c)



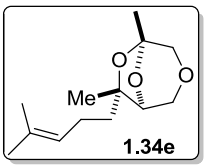
Compound **1.34c** was synthesized from **1.32c** following the general bicyclic acetal formation procedure. Yellow colored semisolid; R_f = 0.37 in 1:5 EtOAc/hexanes (tripple elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 (d, *J* = 8.4 Hz, 2H), 7.54 (d, *J* = 8.4 Hz, 2H), 5.47 (s, 1H), 4.22 (s, 1H), 3.91 (d, *J* = 11.2 Hz, 1H), 3.82 (d, *J* = 11.6 Hz, 1H), 3.65 (s, 2H), 1.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.2, 147.7, 126.8, 123.7, 107.1, 81.5, 79.4, 72.1, 68.2, 19.5; IR (neat): υ 3293, 2859, 1601, 1520, 1346, 1111, 857 cm^{-1}; Anal. Calc′d for $C_{12}H_{13}NO_5$: C, 57.37; H, 5.22; N, 5.58; Found: C, 57.45; H, 5.16; N, 5.51.

1,5-Dimethyl-7-phenyl-3,6,8-trioxabicyclo[3.2.1]octane (1.34d)



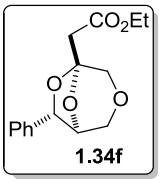
Compound **1.34d** was synthesized from **1.32d** following the general bicyclic acetal formation procedure. Colorless liquid; R_f = 0.58 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36-7.28 (m, 5H), 5.25 (s, 1H), 3.70 (d, *J* = 10.8 Hz, 1H), 3.65 (d, *J* = 11.2 Hz, 1H), 3.64 (d, *J* = 11.2 Hz, 1H), 3.56 (d, *J* = 11.2 Hz, 1H), 1.56 (s, 3H), 0.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.1, 128.2, 128.0, 127.2, 105.3, 83.5, 82.5, 73.7, 71.4, 19.6, 17.5; IR (neat): υ 2934, 2851, 1716, 1454, 1227, 1098, 1018, 868 cm^{-1}; Anal. Calc′d for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32; Found: C, 70.83; H, 7.41.

5,7-Dimethyl-7-(4-methylpent-3-en-1-yl)-3,6,8-trioxabicyclo[3.2.1]octane (1.34e)



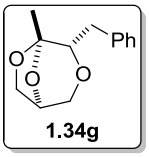
Compound **1.34e** was synthesized from **1.32e** following the general bicyclic acetal formation procedure. Colorless liquid; R_f = 0.44 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.11 (t, J = 5.6 Hz, 1H), 3.85 (s, 1H), 3.84 (d, J = 10.0 Hz, 1H), 3.80 (d, J = 12.0 Hz, 1H), 3.54 (d, J = 10.8 Hz, 1H), 3.47 (d, J = 10.8 Hz, 1H), 2.10-1.98 (m, 2H), 1.68 (s, 3H), 1.62 (s, 3H), 1.60-1.58 (m, 2H), 1.36 (s, 3H), 1.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 131.7, 124.2, 105.0, 83.0, 79.5, 71.8, 65.7, 31.9, 25.6, 23.2, 20.5, 19.1, 14.1; IR (neat): υ 2965, 2922, 1454, 1373, 1259, 864 cm^{-1}; Anal. Calc′d for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80; Found: C, 68.91; H, 9.85.

Ethyl 2-(-7-phenyl-3,6,8-trioxabicyclo[3.2.1]octan-5-yl)acetate (1.34f)



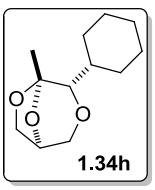
Compound **1.34f** was synthesized from **1.32g** following the general bicyclic acetal formation procedure. Colorless heavy liquid; R_f = 0.45 in 1:3 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38-7.27 (m, 5H), 5.41 (s, 1H), 4.31 (s, 1H), 4.24-4.12 (m, 2H), 3.91 (d, J = 11.6 Hz, 1H), 3.90 (d, J = 11.2 Hz, 1H), 3.82 (d, J = 11.2 Hz, 1H), 3.80 (d, J = 11.2 Hz, 1H), 2.91 (d, J = 14.8 Hz, 1H), 2.87 (d, J = 14.8 Hz, 1H), 1.26 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.3, 141.4, 128.6, 128.1, 126.2, 105.5, 81.8, 80.6, 71.2, 68.5, 61.2, 40.4, 14.2; IR (neat): υ 2913, 2854, 1728, 1452, 1204, 1074, 870, 700 cm^{-1}; Anal. Calc′d for $C_{15}H_{18}O_5$: C, 64.74; H, 6.52, Found: C, 64.47; H, 6.47.

4-Benzyl-5-methyl-3,6,8-trioxabicyclo[3.2.1]octane (1.34g)



Compound **1.34g** was obtained from two substrates **1.32h** (Table 1.2, entry 8) and **1.32i** (Table 1.2, entry 9) following the general bicyclic acetal formation. White solid, mp 66-68 ºC; R_f = 0.32 in 1:3 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 (t, J = 7.2 Hz, 2H), 7.22-7.20 (m, 3H), 4.48 (d, J = 4.8 Hz, 1H), 4.17 (d, J = 6.4 Hz, 1H), 4.10 (d, J = 11.6 Hz, 1H), 3.91 (dd, J = 6.0, 5.6 Hz, 1H), 3.74 (dd, J = 10.8, 3.6 Hz, 1H), 3.41 (d, J = 11.6 Hz, 1H), 3.17 (dd, J = 14.4, 10.8 Hz, 1H), 2.77 (dd, J = 14.4, 3.6 Hz, 1H), 1.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.5, 128.9, 128.4, 126.3, 106.9, 79.5, 75.4, 67.4, 63.4, 34.1, 20.7; IR (neat): υ 2926, 1732, 1454, 1240, 860, 554 cm^{-1}; Anal. Calc′d for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32; Found: C, 70.91; H, 7.29.

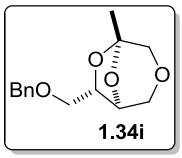
4-Cyclohexyl-5-methyl-3,6,8-trioxabicyclo[3.2.1]octane (1.34h)



Compound **1.34h** was obtained from two substrates **1.32j** (Table 1.2, entry 10) and **1.32k** (Table 1.2, entry 11) following the general bicyclic acetal formation procedure. Colorless liquid; R_f = 0.30 in 1:10 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.44 (d, J = 5.2 Hz, 1H), 4.14 (d, J = 6.4 Hz, 1H), 4.01 (d, J = 11.6 Hz, 1H), 3.87 (dd, J = 6.4,

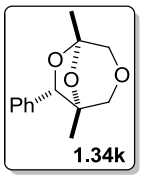
5.2 Hz, 1H), 3.50 (d, *J* = 11.6 Hz, 1H), 3.23 (d, *J* = 4.8 Hz, 1H), 2.03 (bd, *J* = 8.0 Hz, 1H), 1.80-1.72 (m, 2H), 1.67-1.62 (m, 3H), 1.44 (s, 3H), 1.34-1.26 (m, 2H), 1.24-1.16 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 107.4, 82.3, 74.9, 67.0, 66.4, 39.6, 31.9, 28.8, 26.7, 26.6, 26.4, 21.6; IR (neat): υ 2926, 1732, 1451, 1373, 1014 cm^{-1}; Anal. Calc′d for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50; Found: C, 67.83; H, 9.56.

7-((Benzyloxy)methyl)-5-methyl-3,6,8-trioxabicyclo[3.2.1]octane (1.34i)



Compound **1.34i** was synthesized from **1.32l** following the general bicyclic acetal formation procedure.[11] Colorless heavy liquid; R_f = 0.35 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36-7.25 (m, 5H), 4.54 (s, 2H), 4.51 (dd, *J* = 8.4, 5.6 Hz, 1H), 4.24 (s, 1H), 3.82 (d, *J* = 11.2 Hz, 1H), 3.61 (d, *J* = 11.2 Hz, 1H), 3.54-3.48 (m, 3H), 3.35 (dd, *J* = 9.2, 8.4 Hz, 1H), 1.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.0, 128.5, 127.84, 127.82, 105.6, 77.1, 76.8, 73.5, 72.3, 71.2, 68.2, 19.9; IR (neat): υ 2861, 1723, 1452, 1381, 1236, 1115, 739 cm^{-1}; Anal. Calc′d for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25, Found: C, 67.22; H, 7.21.

1,5-Dimethyl-7-phenyl-3,6,8-trioxabicyclo[3.2.1]octane (1.34k)

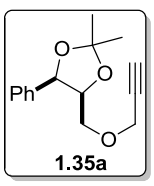


Compound **1.34k** was synthesized from **1.32n** following the general bicyclic acetal formation procedure. Colorless liquid; R_f = 0.38 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39-7.27 (m, 5H), 5.09 (d, *J* = 3.2 Hz, 1H), 4.26 (d, *J* = 3.2 Hz, 1H), 3.95-3.91 (m, 1H), 3.89 (d, *J* = 12.4 Hz, 1H), 3.72 (dd, *J* = 12.8, 1.6 Hz, 1H), 3.66 (td, *J* = 12.4, 3.2 Hz, 1H), 2.36 (ddd, *J* = 15.2, 12.0, 5.2 Hz, 1H), 2.00 (dt, *J* = 15.2, 3.6 Hz, 1H), 1.67 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.9, 128.6, 127.9, 126.1, 111.2, 85.8, 78.4, 73.7, 67.9, 44.1, 27.5; IR (neat): υ 2920, 1736, 1456, 1379, 1196, 698 cm^{-1}; Anal. Calc′d for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32; Found: C, 70.93; H, 7.25.

Preparation of acetonides (1.35a and 1.35b)

To a solution of epoxyalkyne **1.32a** (400 mg, 2.13 mmol) in acetone (10 mL), $AuCl_3$ (13 mg, 2 mol%) was added under N_2 atmosphere. The reaction mixture was allowed to stir at room temperature for 15 min. Solvent was removed from the reaction mixture after completion of reaction and the crude product was purified by column chromatography using EtOAc/hexanes (1:12) as eluent to separate **1.35a** (241 mg, 46%) and **1.35b** (225 mg, 43%).

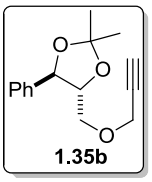
2,2-Aimethyl-4-phenyl-5-((prop-2-yn-1-yloxy)methyl)-1,3-dioxolane (1.35a)



Colorless liquid; R_f = 0.41 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36-7.27 (m, 5H), 5.26 (d, *J* = 7.2 Hz, 1H), 4.57 (dt, *J* = 10.8, 4.4 Hz, 1H), 3.92 (dd, *J* = 15.6, 2.4 Hz, 1H), 3.86 (dd, *J* = 16.0, 2.4 Hz, 1H), 3.16 (dd, *J* = 10.0, 8.0 Hz, 1H), 3.00 (dd, *J* = 10.4, 4.4 Hz, 1H), 2.32 (t, *J* = 2.4 Hz, 1H), 1.66 (s, 3H), 1.47 (s,

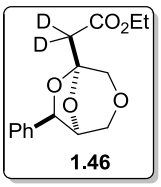
3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.0, 128.2, 128.0, 126.7, 109.0, 79.3, 78.6, 77.4, 74.5, 70.0, 58.3, 27.2, 24.7; IR (neat): 3287, 2861, 2118, 1721, 1462, 1101, 879 cm^{-1}; Anal. Calc′d for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37; Found: C, 73.17; H, 7.42.

2,2-Dimethyl-4-phenyl-5-((prop-2-yn-1-yloxy)methyl)-1,3-dioxolane (1.35b)



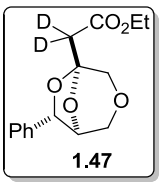
Colorless liquid; R_f = 0.54 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42-7.30 (m, 5H), 4.83 (d, J = 8.8 Hz, 1H), 4.26 (dd, J = 16.0, 2.4 Hz, 1H), 4.20 (dd, J = 16.0 , 2.4 Hz, 1H), 3.99 (ddd, J = 8.4, 5.2, 2.8 Hz, 1H), 3.74 (dd, J = 10.4, 2.8 Hz, 1H), 3.69 (dd, J = 10.4, 5.2 Hz, 1H), 2.43 (t, J = 2.4 Hz, 1H), 1.58 (s, 3H), 1.54 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.8, 128.6, 128.3, 126.6, 109.6, 82.4, 79.6, 79.4, 74.9, 68.4, 58.8, 27.1; IR (neat): υ 3289, 2986, 2934, 2116, 1604, 1454, 1090, 756 cm^{-1}; Anal. Calc′d for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37; Found: C, 73.22; H, 7.32.

Compound 1.46



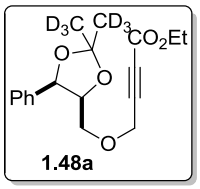
Compound **1.46** was prepared from **1.32g** following the general bicyclic acetal formation procedure, the solvent in the reaction was acetone-d_6. Colorless liquid; R_f = 0.38 in 1:5 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 (d, J = 7.6 Hz, 2H), 7.36 (t, J = 7.6 Hz, 2H), 7.29 (d, J = 7.2 Hz, 1H), 5.29 (d, J = 4.4 Hz, 1H), 4.48 (d, J = 4.4 Hz, 1H), 4.21 (q, J = 7.2 Hz, 2H), 3.87 (d, J = 11.2 Hz, 1H), 3.78 (d, J = 11.2 Hz, 1H), 3.73 (d, J = 12.0 Hz, 1H), 3.32 (d, J = 12.0 Hz, 1H), 1.30 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.2, 136.4, 128.2, 127.5, 126.1, 104.7, 81.2, 78.6, 70.5, 64.3, 61.0, 40.0-39.5 (m, -CD_2), 14.2; IR (neat): υ 2984, 1730, 1451, 1271, 849, 700 cm^{-1}; Anal. Calc′d for $C_{15}H_{16}D_2O_5$; C, 64.27; H, 7.19; Found: C, 64.32; H, 7.21.

Compound 1.47



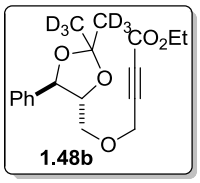
Compound **1.47** was prepared from **1.32g** following the general bicyclic acetal formation procedure, the solvent in the reaction was acetone-d_6. Colorless liquid; R_f = 0.24 in 1:5 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36-7.29 (m, 5H), 5.41 (s, 1H), 4.31 (s, 1H), 4.22-4.15 (m, 2H), 3.91 (d, J = 11.6 Hz, 1H), 3.89 (d, J = 11.6 Hz, 1H), 3.81 (d, J = 11.2 Hz, 1H), 3.80 (d, J = 11.6 Hz, 1H), 1.28 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.2, 141.2, 128.5, 128.0, 126.1, 105.3, 81.7, 80.5, 71.1, 68.3, 61.1, 40.2-39.3 (m, -CD_2), 14.1; IR (neat): υ 2984, 2054, 1734, 1452, 1267, 1061, 739 cm^{-1}; Anal. Calc′d for $C_{15}H_{16}D_2O_5$; C, 64.27; H, 7.19; Found: C, 64.15; H, 7.22.

Compound 1.48a



Compound **1.48a** fromed from **1.32g**. *cis* isomer; Colorless liquid; R_f = 0.70 in 1:10 EtOAc/hexanes (four elutions); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39-7.27 (m, 5H), 5.28 (d, *J* = 7.2 Hz, 1H), 4.58-4.54 (m, 1H), 4.22 (q, *J* = 7.2 Hz, 2H), 4.01 (s, 2H), 3.18 (dd, *J* = 9.2, 8.4 Hz, 1H), 3.02 (dd, *J* = 9.6, 3.6 Hz, 1H), 1.29 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.0, 136.8, 128.2, 128.0, 126.6, 108.9, 82.7, 78.5, 78.0, 77.3, 70.5, 62.0, 58.0, 26.2 (septet, *J* = 20.0 Hz, -CD_3), 23.8 (sept, *J* = 20.0 Hz, -CD_3), 13.9; IR (neat): υ 2910, 2240, 1715, 1454, 1366, 1250, 750 cm^{-1}; Anal. Calc′d for $C_{18}H_{16}D_6O_5$: C, 66.64; H, 8.70; Found: C, 66.75; H, 8.75.

Compound 1.48b

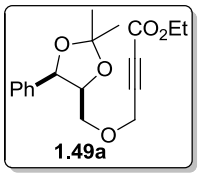


Compound **1.48b** formed from **1.32g**. *trans* isomer; Colorless liquid; R_f = 0.74 in 1:10 EtOAc/hexanes (four elutions); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41-7.31 (m, 5H), 4.83 (d, *J* = 8.4 Hz, 1H), 4.41 (d, *J* = 16.8 Hz, 1H), 4.32 (d, *J* = 16.8 Hz, 1H), 4.25 (q, *J* = 7.2 Hz, 2H), 3.98 (dt, *J* = 8.4, 4.0 Hz, 1H), 3.75-3.68 (m, 2H), 1.32 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.0, 137.5, 128.6, 128.3, 126.5, 109.4, 82.7, 82.2, 79.3, 78.4, 68.7, 62.1, 58.5, 26.6-25.5 (m,(-CD_3)$_2$), 14.0; IR (neat): υ 2905, 2239, 1715, 1454, 1366, 1252, 1068, 750 cm^{-1}; Anal. Calc′d for $C_{18}H_{16}D_6O_5$: C, 66.64; H, 8.70; Found: C, 66.75; H, 8.67.

Preparation of acetonides 1.49a and 1.49b

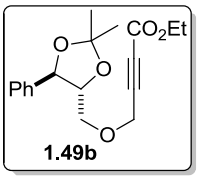
To a solution of epoxyalkyne **1.32g** (374 mg, 1.437 mmol) in acetone (10 mL), $AuCl_3$ (9 mg, 2 mol%) was added under N_2 atmosphere. After stirring for 10 min. at room temperature, solvent was removed. The crude product was purified by column chromatography using EtOAc/hexanes (1:13) as eluent to separate **1.49a** (*cis* isomer, 206 mg, 45%) and **1.49b** (*trans* isomer, 192 mg, 42%).

Ethyl 4-((2,2-dimethyl-5-phenyl-1,3-dioxolan-4-yl)methoxy)but-2-ynoate (1.49a)



Colorless liquid; R_f = 0.48 in 1:10 EtOAc/hexanes (three elutions); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.29 (m, 5H), 5.28 (d, *J* = 7.2 Hz, 1H), 4.59-4.54 (m, 1H), 4.22 (q, *J* = 7.2 Hz, 2H), 4.01 (s, 2H), 3.18 (dd, *J* = 9.6, 8.0 Hz, 1H), 3.02 (dd, *J* = 10.0, 4.0 Hz, 1H), 1.66 (s, 3H), 1.48 (s, 3H), 1.30 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.0, 136.7, 128.2, 128.0, 126.6, 109.1, 82.7, 78.5, 78.1, 77.2, 70.5, 62.0, 58.0, 27.1, 24.7, 13.9; IR (neat): υ 2988, 2936, 2238, 1713, 1454, 1379, 864, 741 cm^{-1}; Anal. Calc′d for $C_{18}H_{22}O_5$: C, 67.91; H, 6.97; Found: C, 68.12; H, 6.91.

Ethyl 4-((2,2-dimethyl-5-phenyl-1,3-dioxolan-4-yl)methoxy)but-2-ynoate (1.49b)

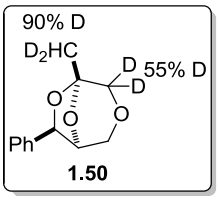


Colorless liquid; R_f = 0.56 in 1:10 EtOAc/hexanes (three elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41-7.32 (m, 5H), 4.83 (d, *J* = 8.4 Hz, 1H), 4.40 (d, *J* = 16.8 Hz, 1H), 4.32 (d, *J* = 16.8 Hz, 1H), 4.24 (q, *J* = 7.2 Hz, 2H), 3.93-3.95 (m, 1H), 3.75-3.68 (m, 2H), 1.57 (s, 3H), 1.53 (s, 3H), 1.31 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.0, 137.5, 128.6, 128.3, 126.5, 109.6, 82.7, 82.2, 79.3, 78.4, 68.7, 62.1, 58.5, 27.0, 13.9; IR (neat): υ 2986, 2934, 2238, 1714, 1454, 1371, 1252, 868, 752 cm^{-1}; Anal. Calc′d for $C_{18}H_{22}O_5$: C, 67.91; H, 6.97; Found: C, 67.85; H, 7.05.

Formation of 1.50 and 1.51

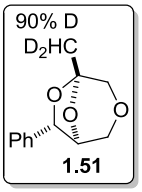
Compound **1.50** and **1.51** obtained from **1.32a** performing bicyclic acetal formation general procedure, but solvent used in this reaction was acetone-d_6.

Compound 1.50



Colorless semisolid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (d, *J* = 7.6 Hz, 2H), 7.36 (t, *J* = 7.2 Hz, 2H), 7.29 (d, *J* = 7.2 Hz, 1H), 5.29 (d, *J* = 4.8 Hz, 1H), 4.44 (d, *J* = 4.8 Hz, 1H), 3.71 (d, *J* = 11.6 Hz, 1H), 3.66-6.61 (m, 1H), 3.31 (d, *J* = 11.6 Hz, 1H), 1.50-1.47 (m, 1H, -C*H*D$_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.0, 128.2, 127.4, 126.1, 105.7, 81.0, 78.4, 71.7, 71.6 (m), 64.2, 20.1-19.6 (m); IR (neat): υ 2963, 2857, 1605, 1495, 1059, 1233 cm^{-1}.

Compound 1.51

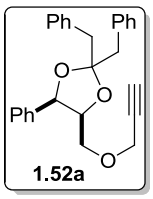


Colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.30 (m, 5H), 5.38 (s, 1H), 4.22 (s, 1H), 3.88 (d, *J* = 11.2 Hz, 1H), 3.79 (d, *J* = 11.6 Hz, 1H), 3.64 (s, 2H), 1.55-1.52 (m, 1H, -C*H*D$_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.0, 128.5, 128.0, 126.1, 106.4, 81.6, 80.5, 72.3, 68.4, 19.6-19.1 (m); IR (neat): υ 3436, 2911, 1452, 1240, 1009, 872 cm^{-1}.

Preparation of acetonides 1.52a and 1.52b

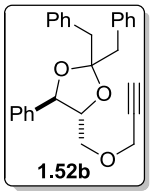
To a solution of diol **1.54** (300 mg, 1.587 mmol) in dichloromethane (10 mL) *p*-TsOH (120 mg, 40 mol%) was added. Then triethyl orthoformate (0.39 mL, 2.38 mmol) was added slowly. After stirring for 0.5 h at room temperature, 1,3-diphenylpropan-2-one **1.53** (267 mg, 1.27 mmol) was added and the stirring was continued at room temperature for 3 h. Then the reaction mixture was washed with aqueous sodium bicarbonate solution, saturated brine solution, dried over anhydrous Na_2SO_4, concentrated and purified by column chromatography (1:20 EtOAc/hexanes) as colorless liquid (*trans*, 156 mg; *cis*, 246 mg; 80%; *cis*/ *trans* = 1.58:1).

2,2-Dibenzyl-4-phenyl-5-((prop-2-yn-1-yloxy)methyl)-1,3-dioxolane (1.52a)



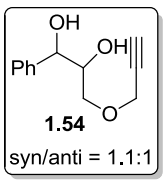
Compound **1.52a** prepared from **1.54** following the above described procedure. Colorless liquid; R_f = 0.50 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34-7.20 (m, 13H), 6.88-6.86 (m, 2H), 4.84 (d, *J* = 7.6 Hz, 1H), 4.34 (dt, *J* = 11.2, 4.4 Hz, 1H), 3.71 (d, *J* = 15.6 Hz, 1H), 3.63 (d, *J* = 15.6 Hz, 1H), 3.12-3.04 (m, 3H), 2.98 (d, *J* = 14.0 Hz, 1H), 2.60 (dd, *J* = 9.2, 8.4 Hz, 1H), 2.46 (dd, *J* = 9.6, 4.0 Hz, 1H), 2.24 (bs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.6, 136.04, 136.00, 131.4, 130.6, 128.1, 128.0, 127.8, 127.7, 126.5, 111.3, 79.3, 79.0, 77.8, 74.2, 70.0, 58.0, 44.14, 44.10; IR (neat): υ 3293, 2926, 2117, 1721, 1601, 1454 cm^{-1}; Anal. Calc′d for $C_{27}H_{26}O_3$: C, 81.38; H, 6.58; Found: C, 81.22; H, 6.67.

2,2-Dibenzyl-4-phenyl-5-((prop-2-yn-1-yloxy)methyl)-1,3-dioxolane (1.52b)



Compound **1.52b** prepared from **1.54** following the above described procedure. Colorless liquid; R_f = 0.64 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38-7.18 (m, 13H), 6.84 (d, *J* = 7.2 Hz, 2H), 4.17 (d, *J* = 16.0 Hz, 1H), 4.12 (d, *J* = 16.0 Hz, 1H), 3.98 (d, *J* = 9.2 Hz, 1H), 3.55 (dt, *J* = 9.2, 3.2 Hz, 1H), 3.35-3.31 (m, 2H), 3.18 (d, *J* = 14.0 Hz, 1H), 3.10-3.04 (m, 3H), 2.41 (bs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.6, 136.4, 136.3, 131.24, 131.20, 129.5, 128.4, 128.3, 128.0, 127.9, 127.2, 126.5, 111.6, 82.3, 80.2, 79.4, 74.7, 68.3, 58.4, 45.5, 45.0; IR (neat): υ 3057, 2924, 2117, 1716, 1495, 1454, 1265, 748 cm^{-1}; Anal. Calc′d for $C_{27}H_{26}O_3$: C, 81.38; H, 6.58; Found: C, 81.56; H, 6.67.

Preparation of 1.54



Epoxyalkyne **1.32a** (1900 mg, 10.1 mmol) in distilled water was heated at 60 ºC for 3 h.[22] Then the product was extracted in ethyl acetate and purified by column chromatography (1:3 EtOAc/hexanes) as colorless heavy liquid (yield 98%, *cis*/*trans* = 1:1.1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38-7.31 (m, 10H), 4.88 (t, *J* = 4.8 Hz, 1H), 4.73 (dd, *J* = 6.8, 2.8 Hz, 1H), 4.18 (d, *J* = 2.4 Hz, 1H), 4.17 (d, *J* = 2.0 Hz, 1H), 4.160 (d, *J* = 2.0 Hz, 1H), 4.157 (d, *J* = 2.4 Hz, 1H), 4.02-3.98 (m, 1H), 3.88-3.83 (m, 1H), 3.63 (dd, *J* = 9.6, 6.4 Hz, 1H), 3.55 (dd, *J* = 5.2, 3.6 Hz, 1H), 3.53 (dd, *J* = 5.2, 3.6 Hz, 1H), 3.49 (dd, *J* = 9.6, 5.2 Hz, 1H), 2.92 (d, *J* = 2.8 Hz, 1H), 2.82 (d, *J* = 4.4 Hz, 1H), 2.70 (d, *J* = 5.2 Hz, 1H), 2.56 (d, *J* = 4.8 Hz, 1H), 2.44 (t, *J* = 2.0 Hz, 1H), 2.436 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.3, 140.0, 128.37, 128.36, 127.9, 127.7, 126.7, 126.2, 79.1, 75.01, 75.00, 74.8, 74.6, 74.4, 73.4, 70.5, 70.2, 58.6, 58.5; IR (neat): υ 3453, 2915, 2116, 1495, 1454, 1099 cm^{-1}; Anal. Calc′d for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84; Found: C, 69.75; H, 6.91.

1.5 References

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1.6 Representative spectra

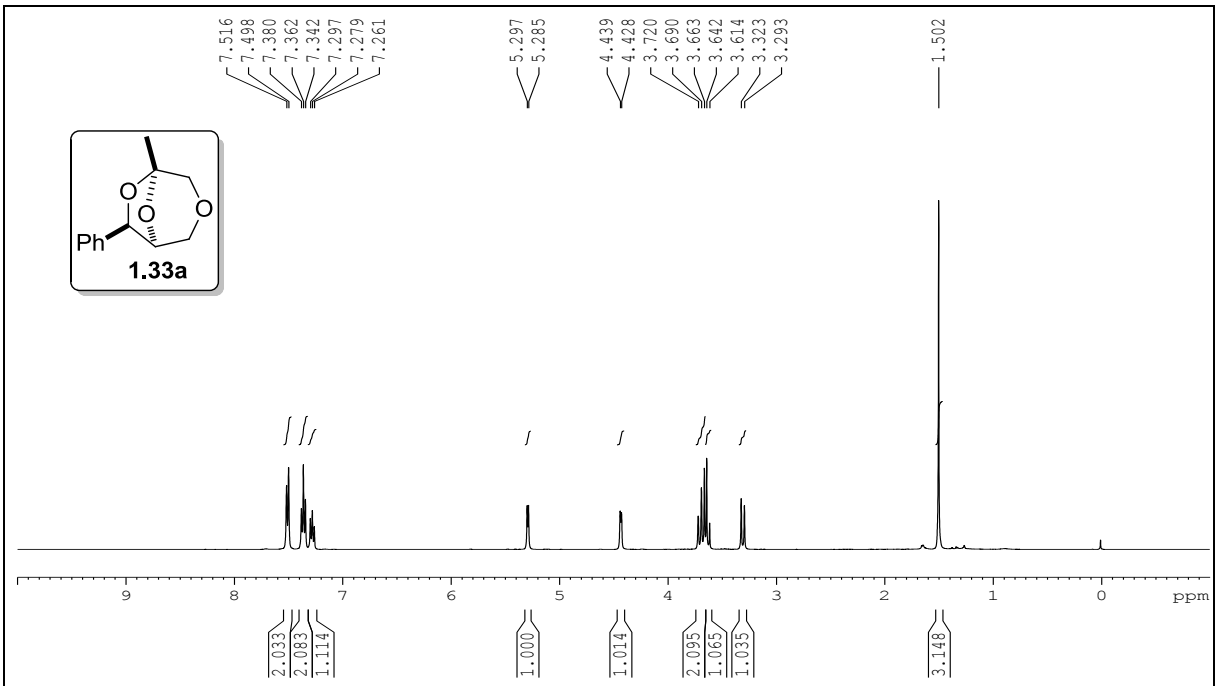


Figure 1.4. ^{1}H NMR spectrum of **1.33a**

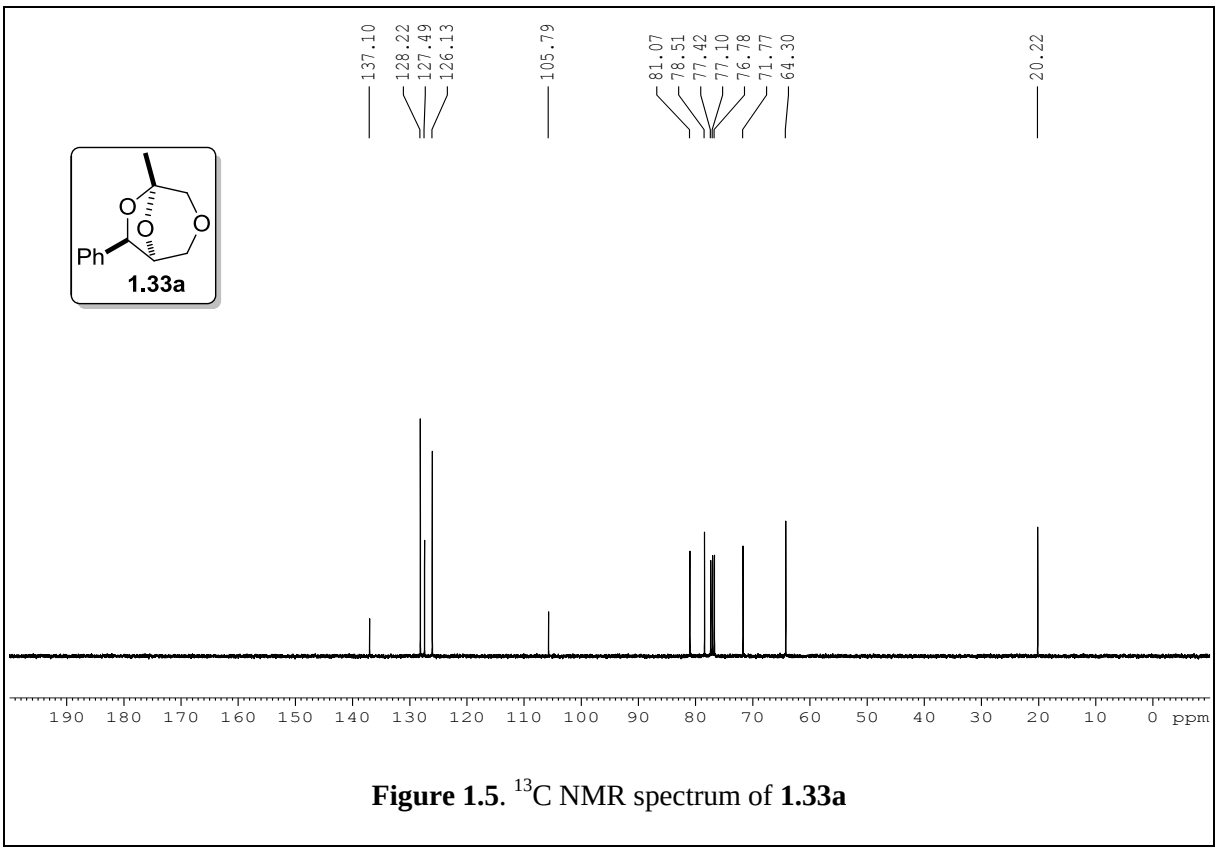


Figure 1.5. ^{13}C NMR spectrum of **1.33a**

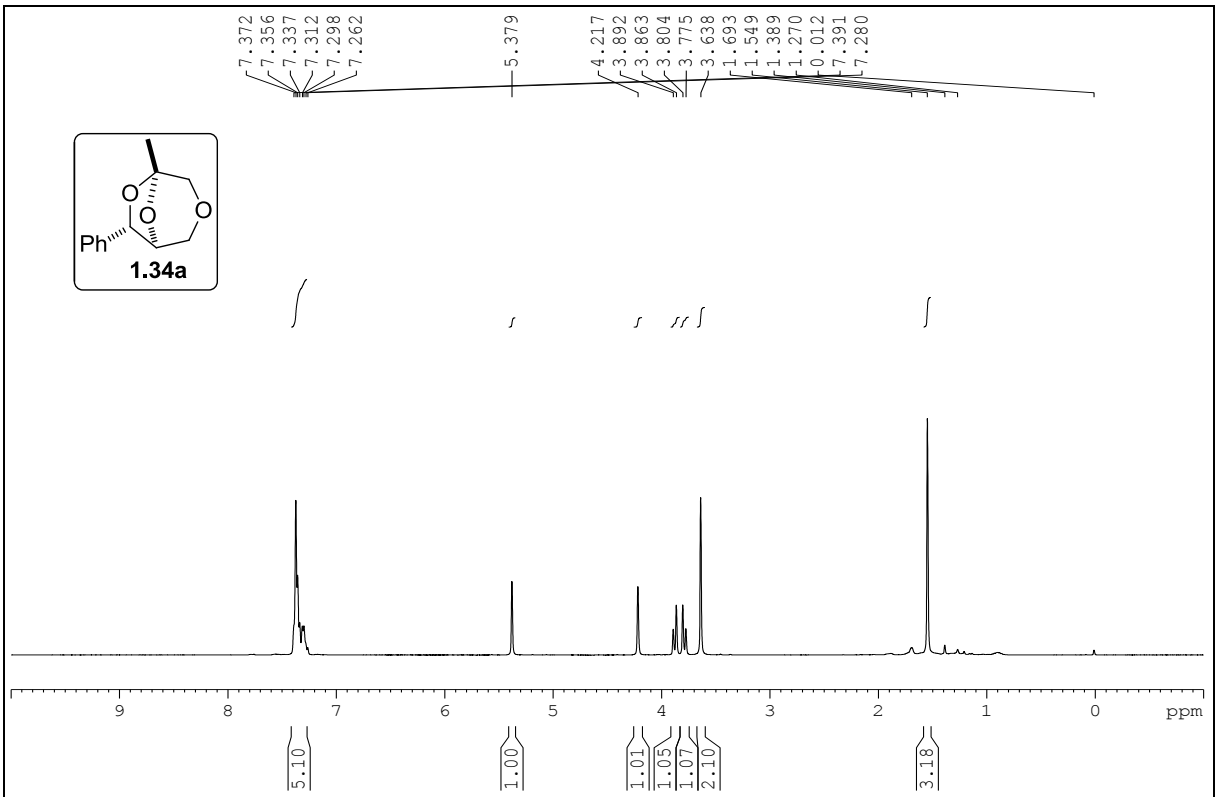


Figure 1.6. ^{1}H NMR spectrum of **1.34a**

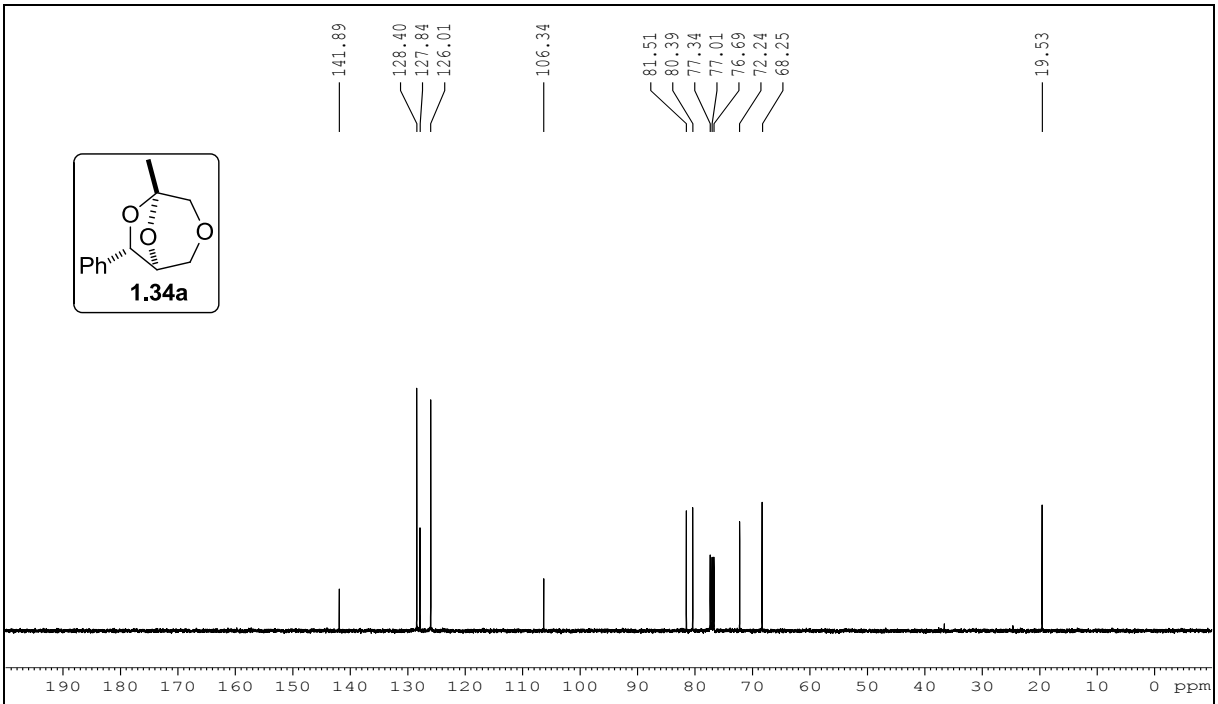


Figure 1.7. ^{13}C NMR spectrum of **1.34a**

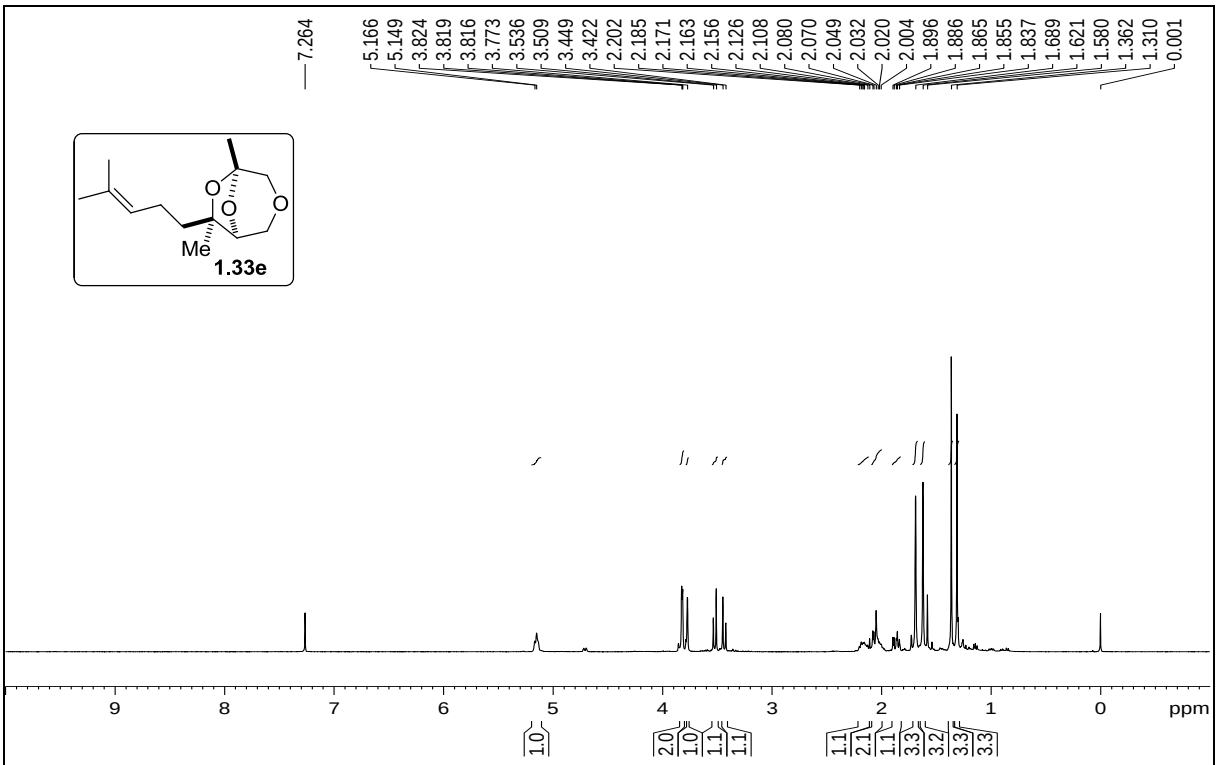


Figure 1.8. ^{1}H NMR spectrum of **1.33e**

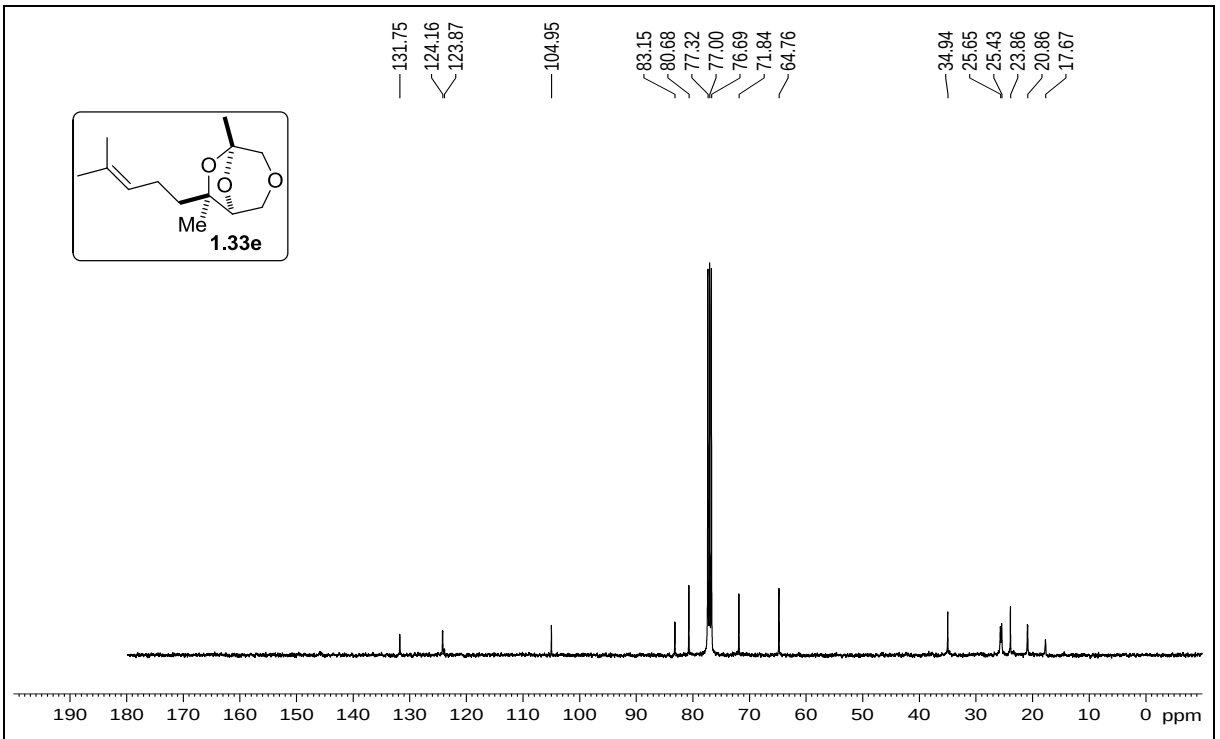


Figure 1.9. ^{13}C NMR spectrum of **1.33e**

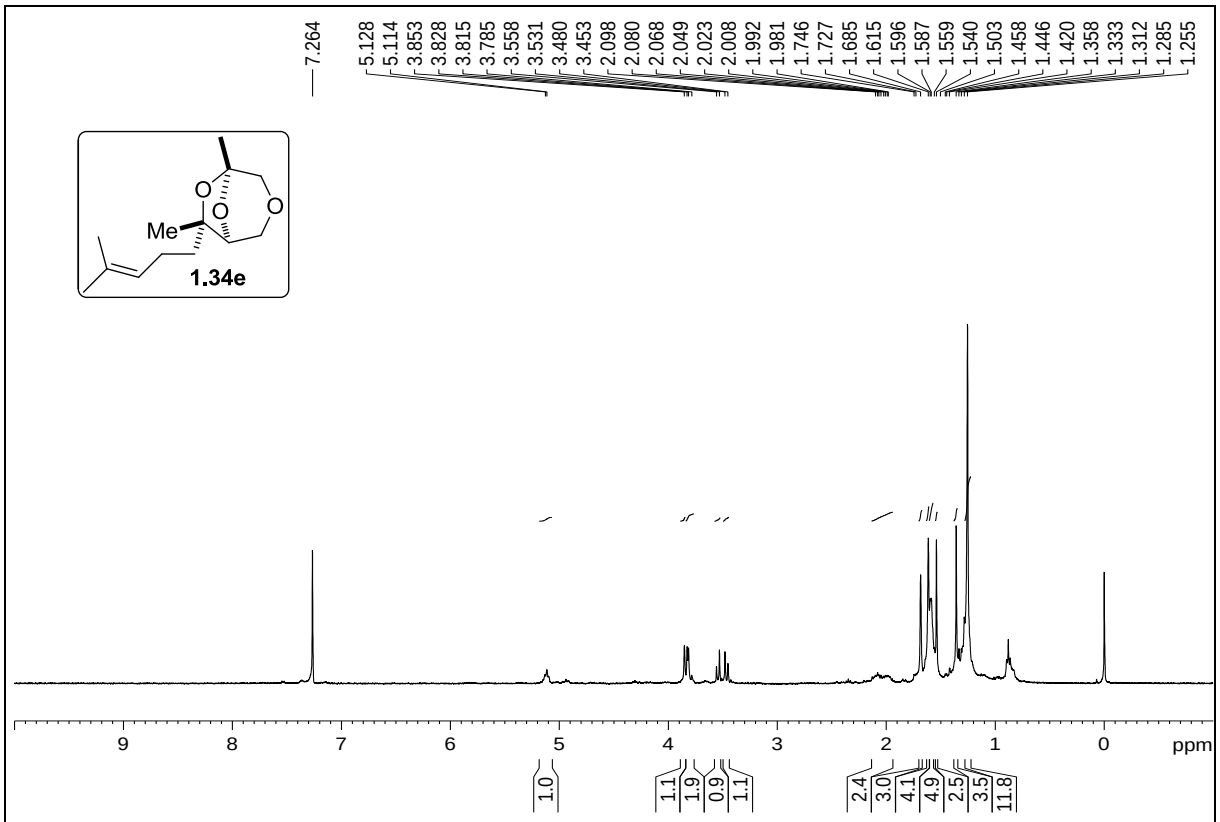


Figure 1.10. ^{1}H NMR spectrum of **1.34e**

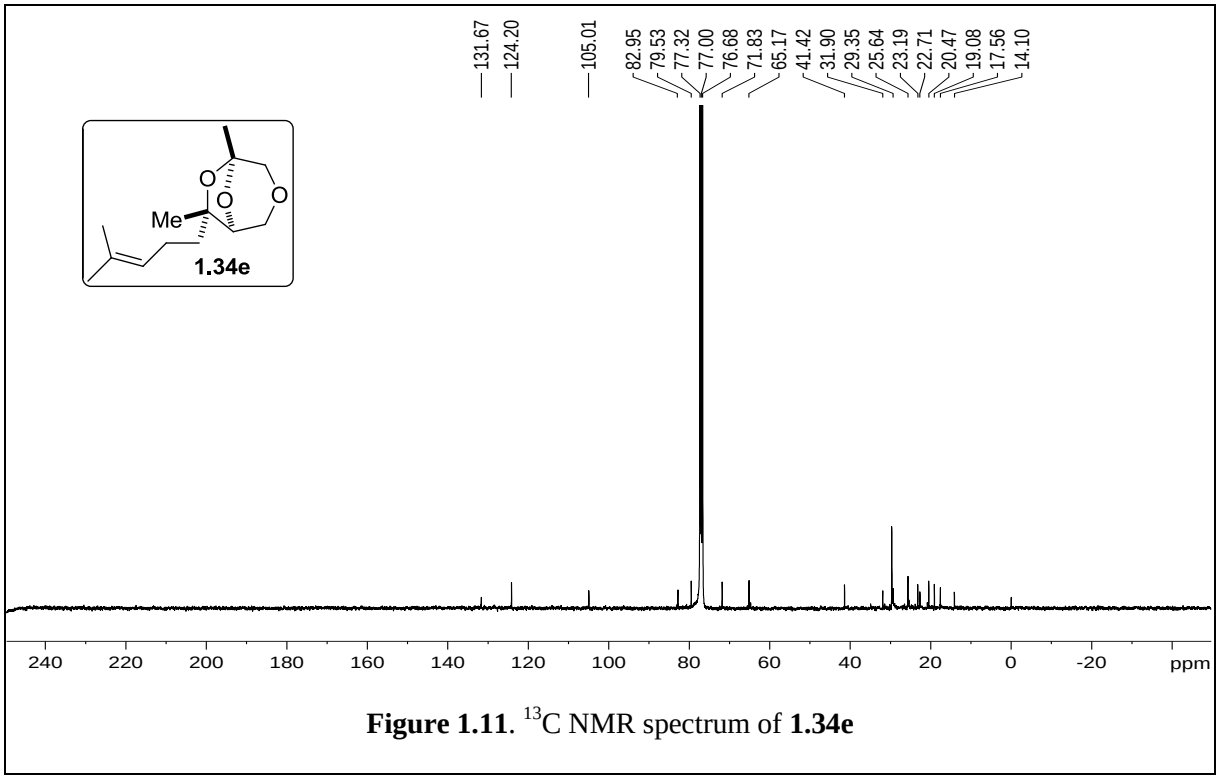


Figure 1.11. ^{13}C NMR spectrum of **1.34e**

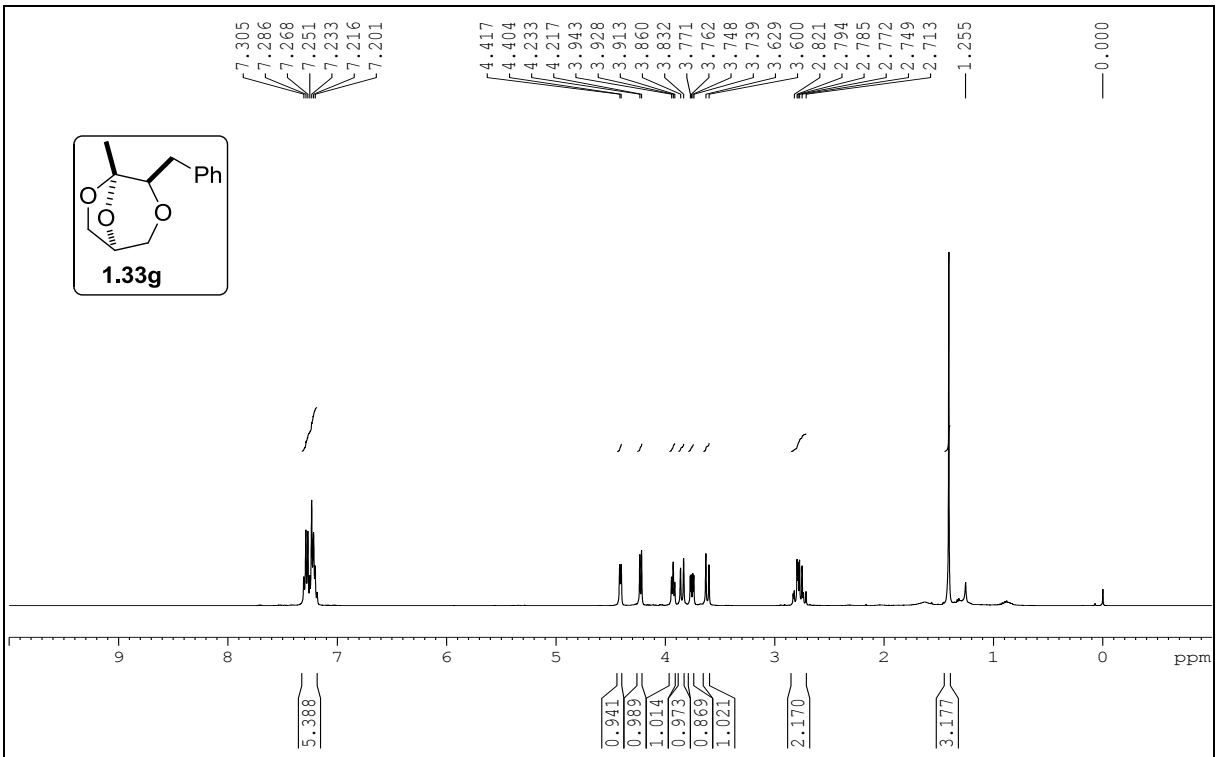


Figure 1.12. ^{1}H NMR spectrum of **1.33g**

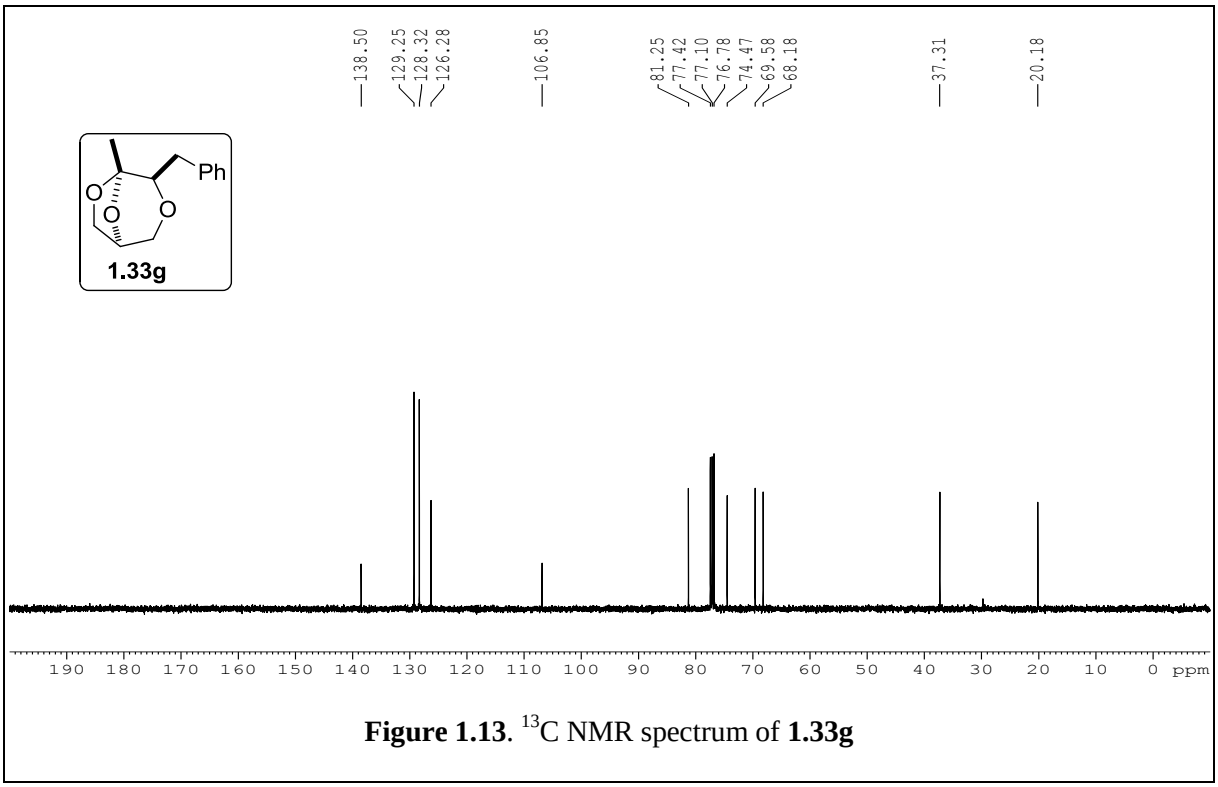


Figure 1.13. ^{13}C NMR spectrum of **1.33g**

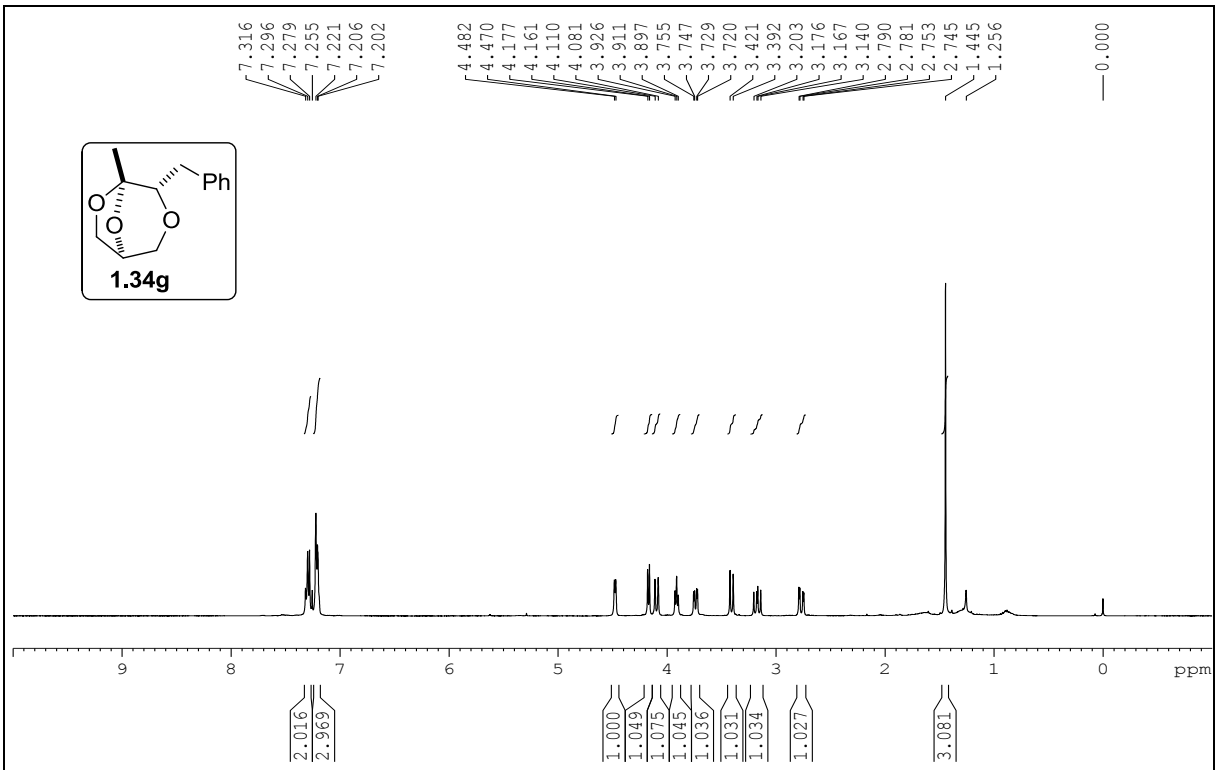


Figure 1.14. ^{1}H NMR spectrum of **1.34g**

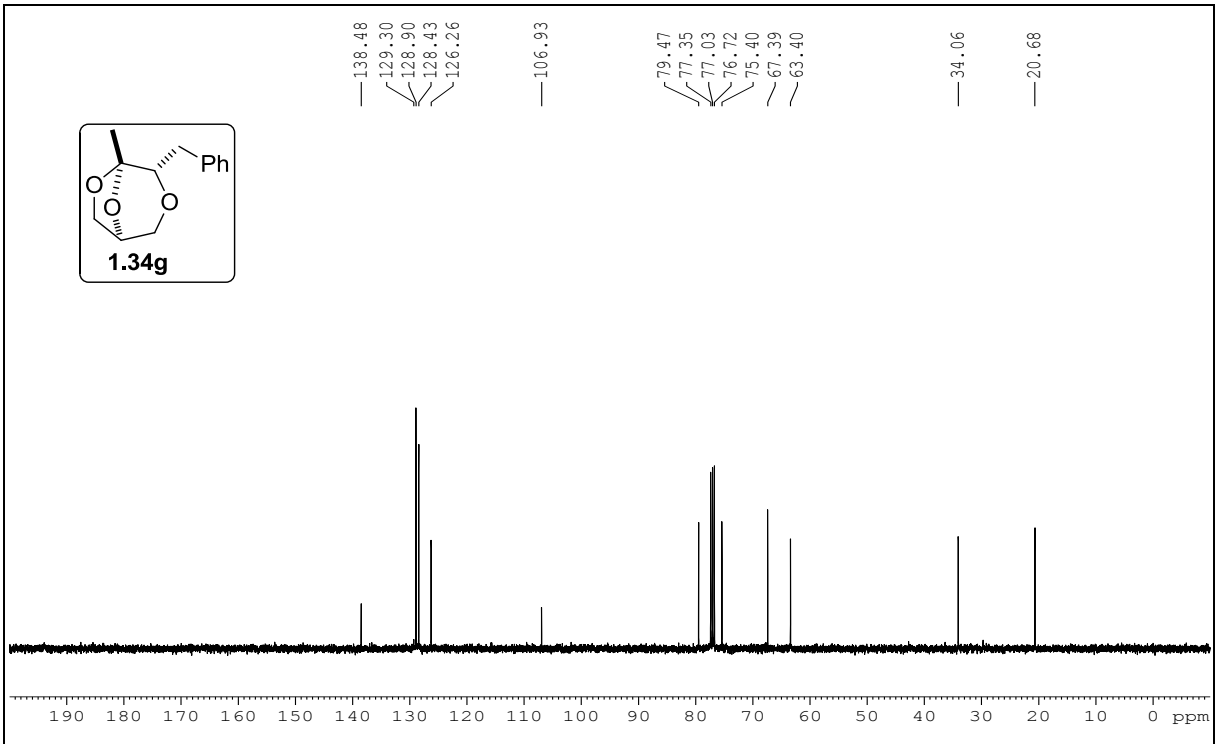


Figure 1.15. ^{13}C NMR spectrum of **1.34g**

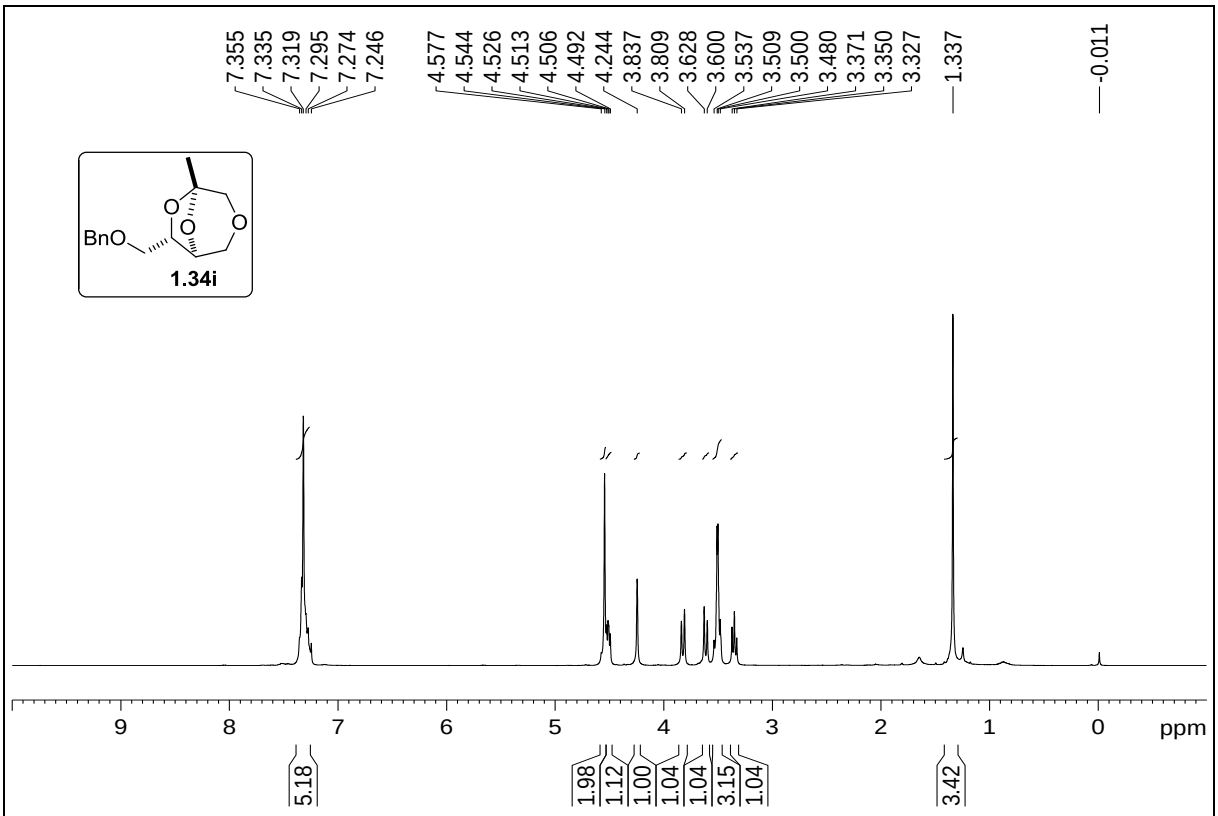


Figure 1.16. ^{1}H NMR spectrum of **1.34i**

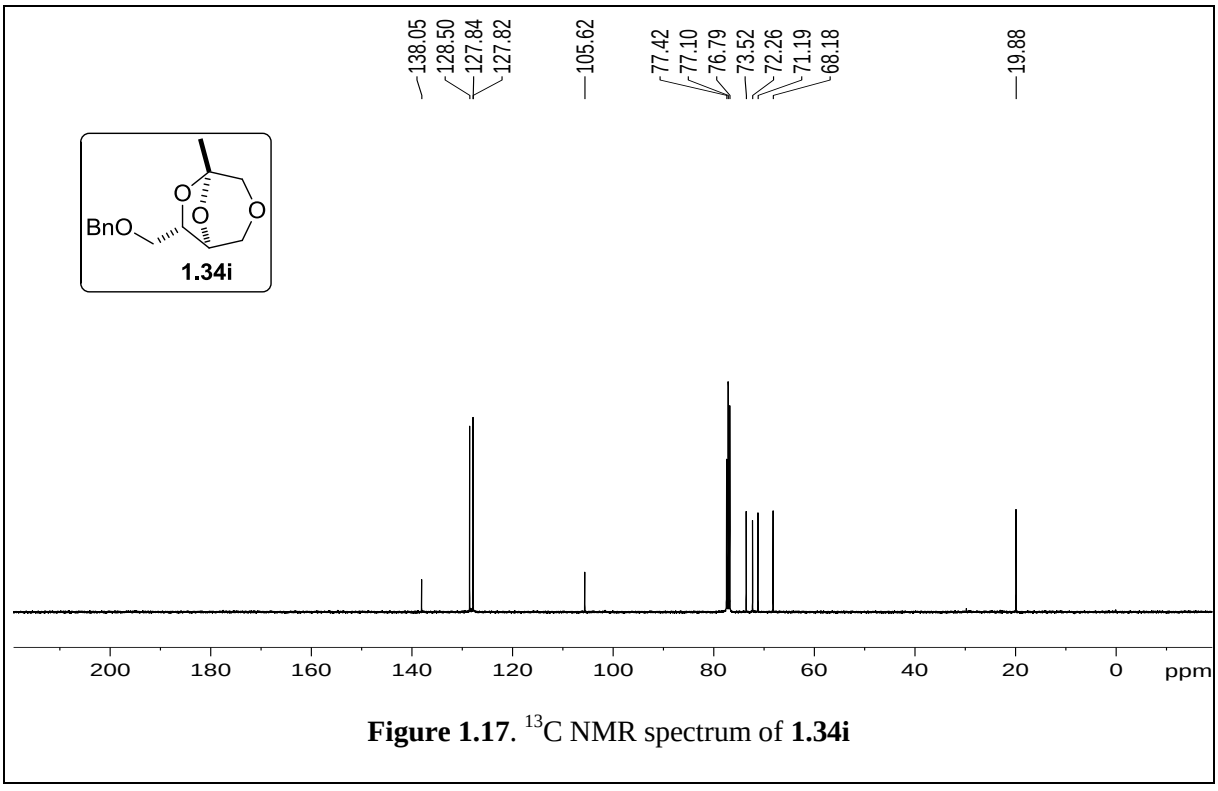


Figure 1.17. ^{13}C NMR spectrum of **1.34i**

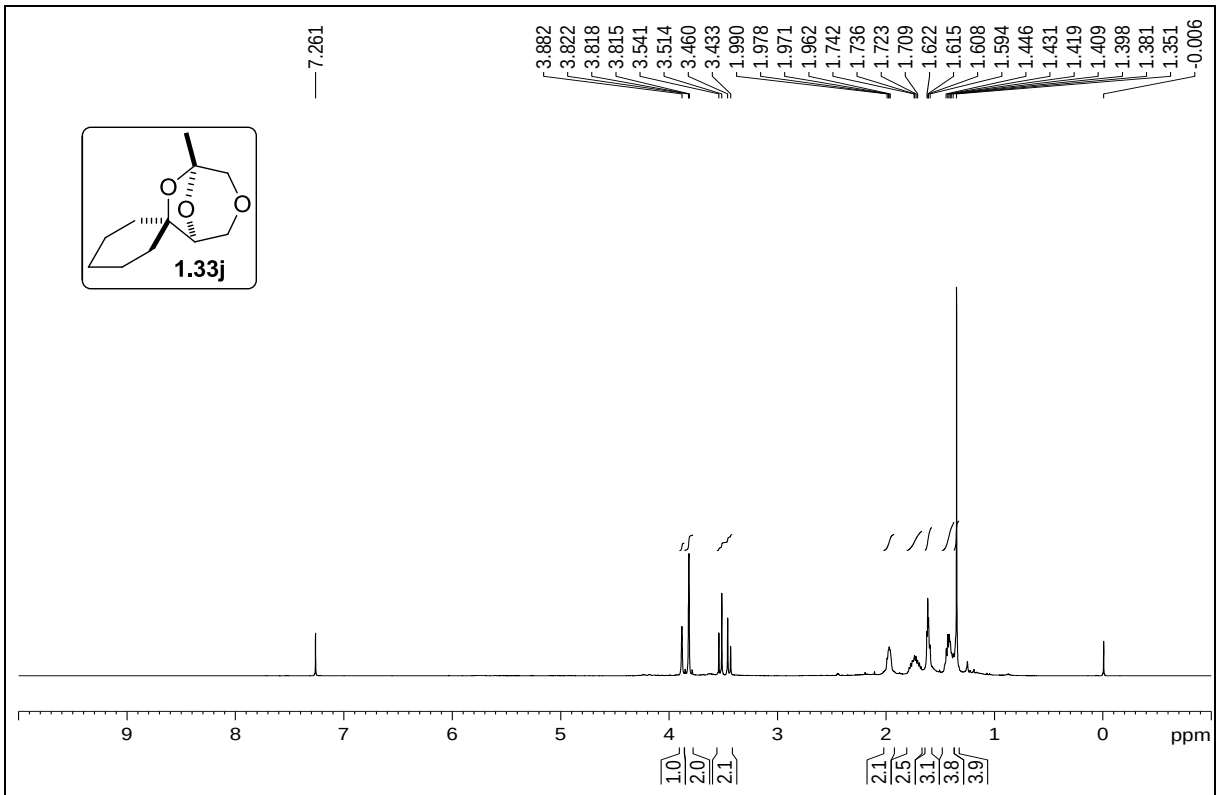


Figure 1.18. ^{1}H NMR spectrum of **1.34j**

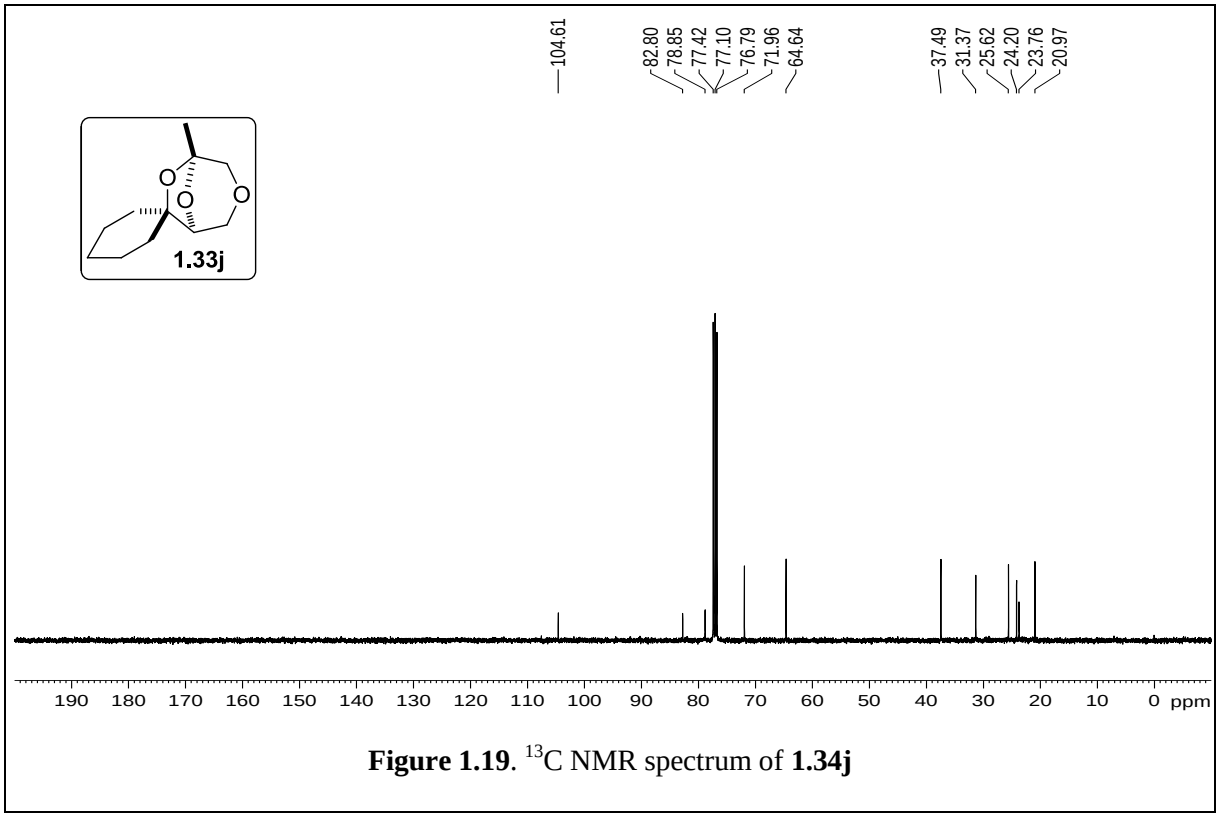


Figure 1.19. ^{13}C NMR spectrum of **1.34j**

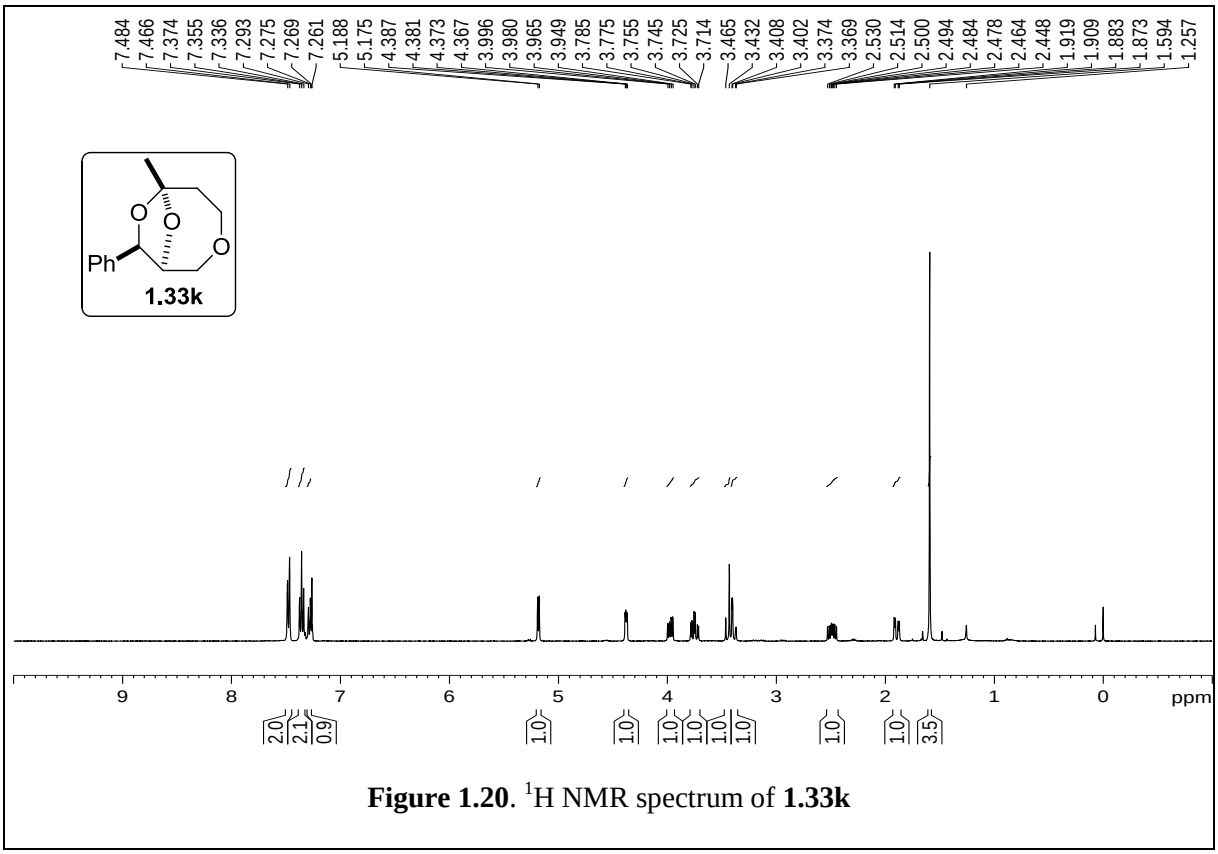


Figure 1.20. ^{1}H NMR spectrum of **1.33k**

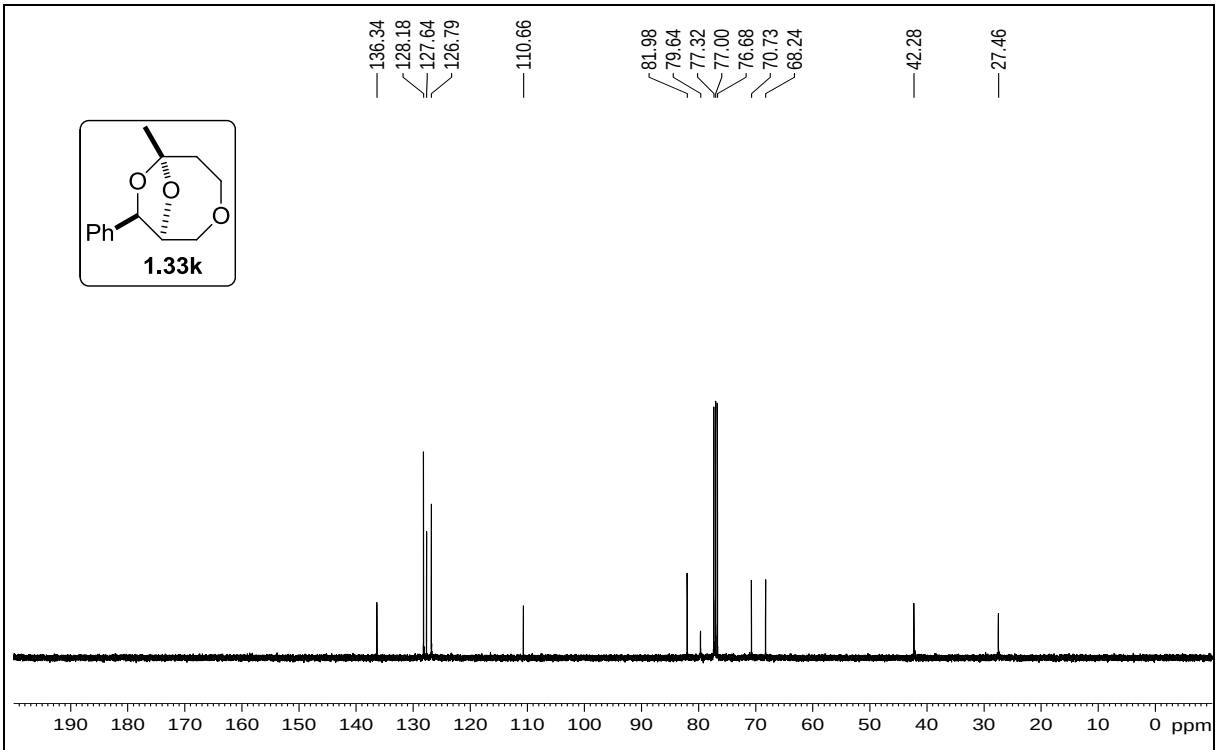


Figure 1.21. ^{13}C NMR spectrum of **1.34k**

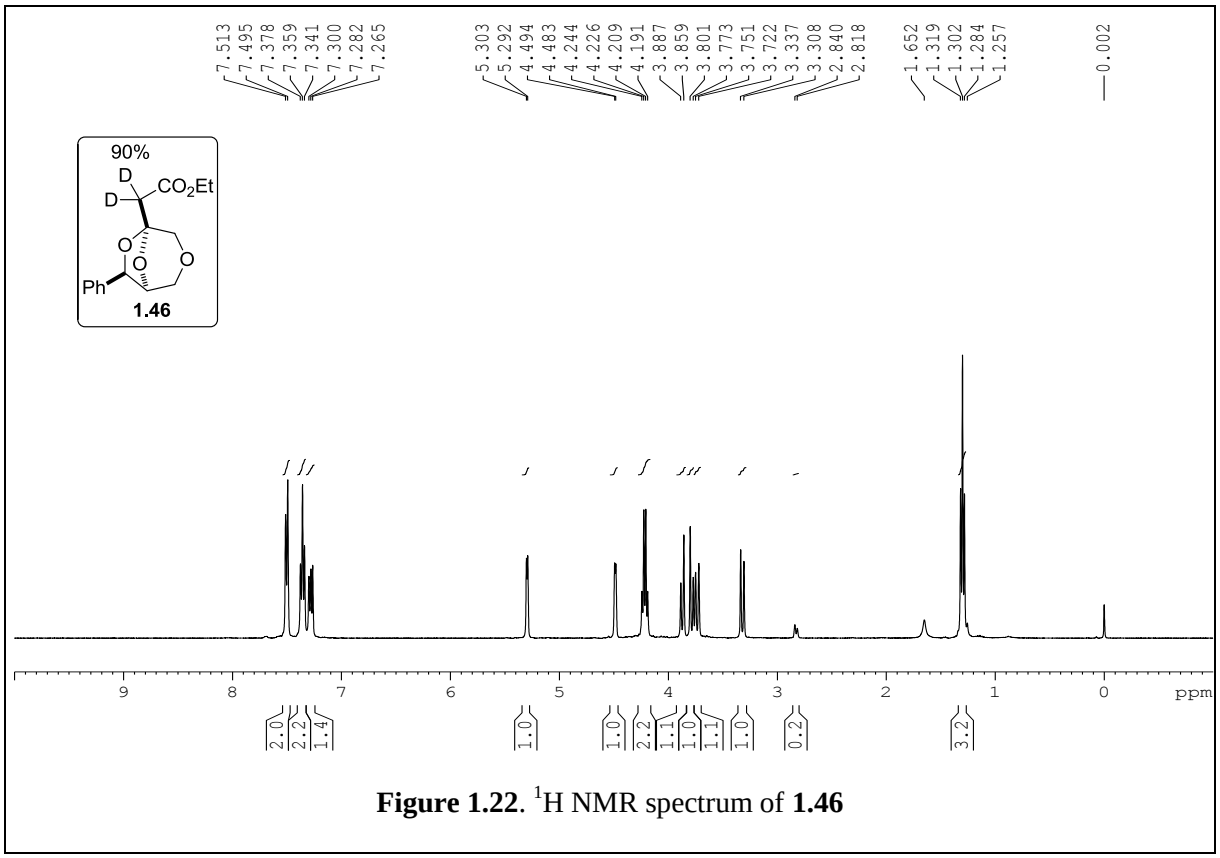


Figure 1.22. ^{1}H NMR spectrum of **1.46**

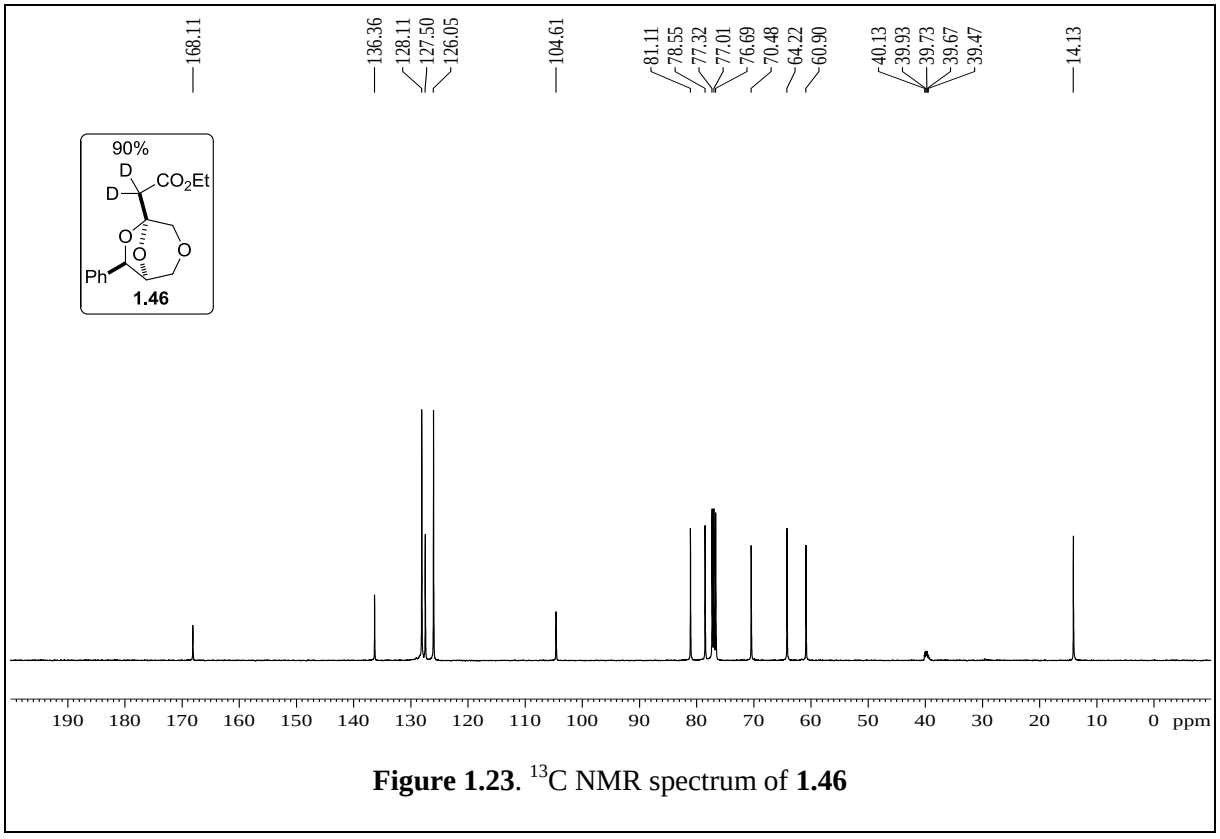


Figure 1.23. ^{13}C NMR spectrum of **1.46**

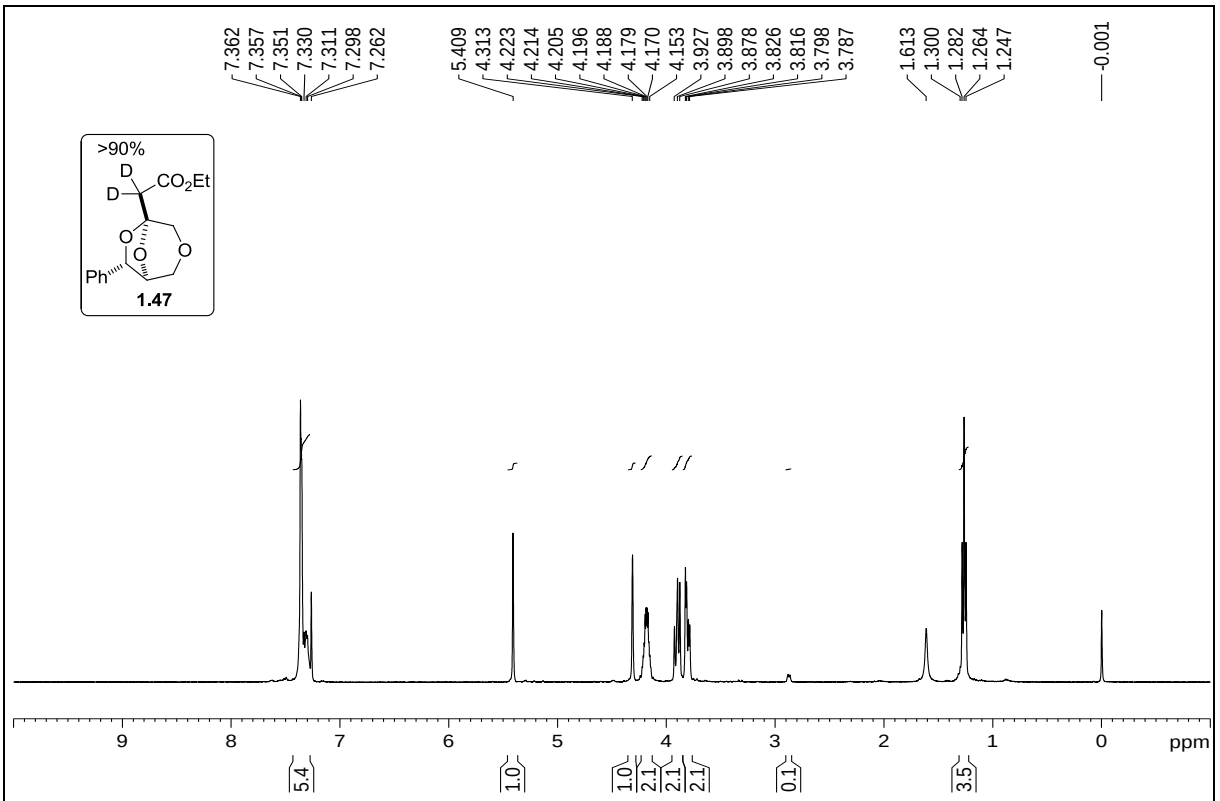


Figure 1.24. ^{1}H NMR spectrum of **1.47**

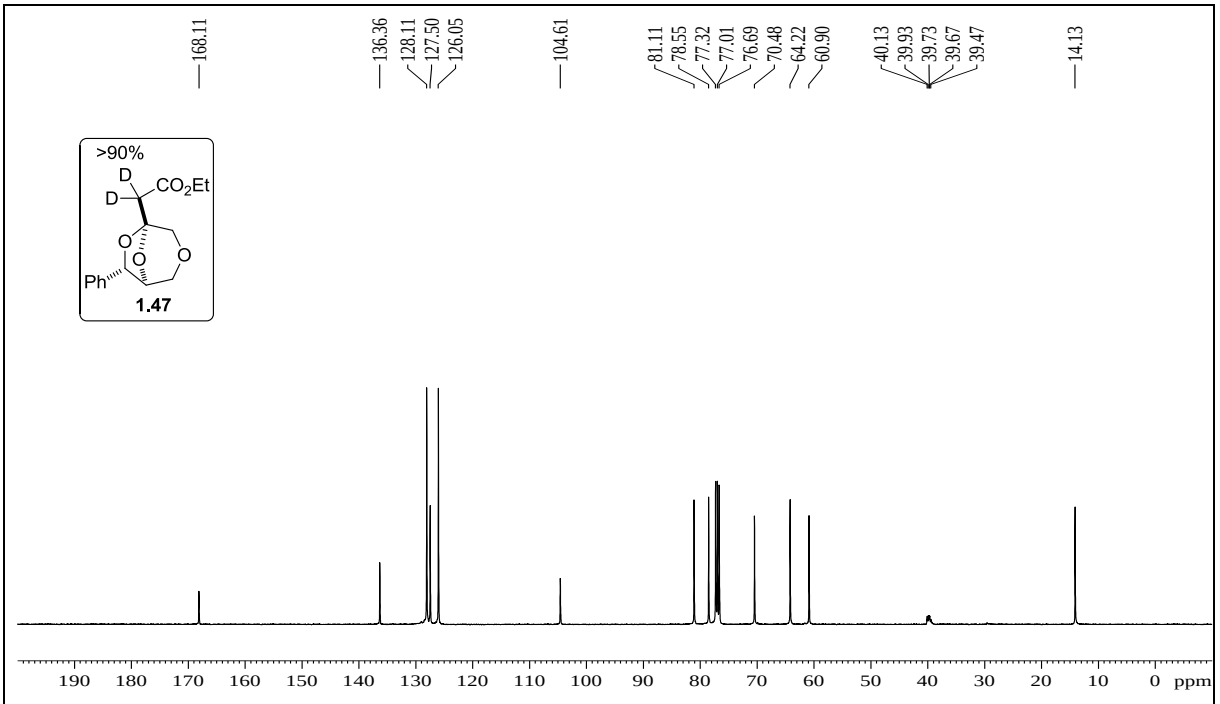
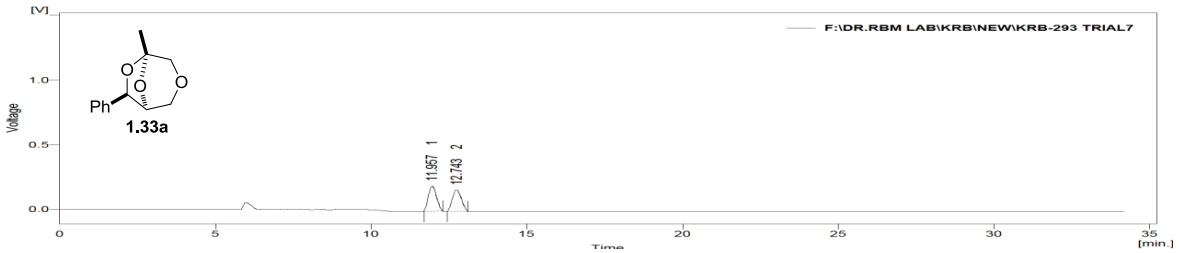


Figure 1.25. ^{13}C NMR spectrum of **1.47**

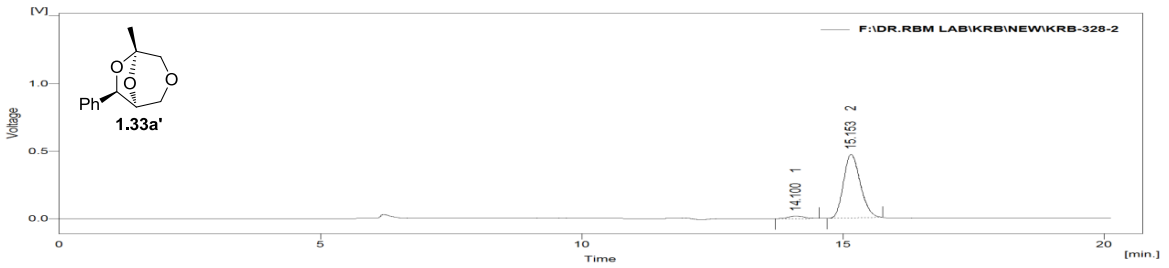


Result Table (Uncal - F:\DR.RBM LAB\KRB\NEW\KRB-293 TRIAL7)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	11.957	2341.615	129.527	51.3	53.9	0.30
2	12.743	2220.967	110.620	48.7	46.1	0.33
	Total	4562.582	240.147	100.0	100.0	

CHIRALCEL OD-H, FLOW RATE 0.5 mL/min, HEX:IPA=95:5, 220 nm.

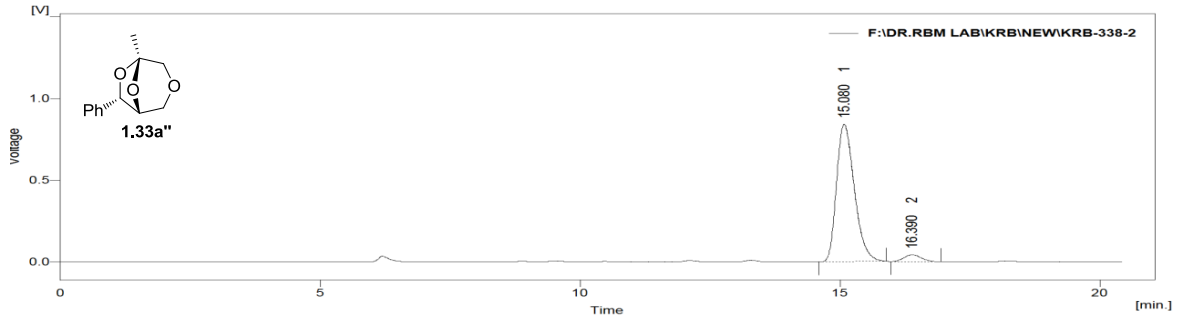
Figure 1.26. HPLC spectrum of racemic compound **1.33a**



Result Table (Uncal - F:\DR.RBM LAB\KRB\NEW\KRB-328-2)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	14.100	254.597	12.769	3.5	3.9	0.32
2	15.153	7048.964	314.262	96.5	96.1	0.35
	Total	7303.562	327.031	100.0	100.0	

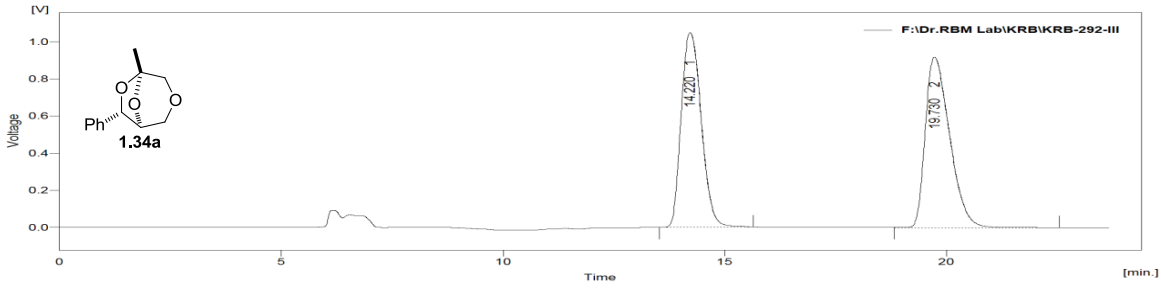
Fig 1.27. HPLC spectrum of chiral compound **1.33a'**



Result Table (Uncal - F:\DR.RBM LAB\KRB\NEW\KRB-338-2)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	15.080	13328.752	561.066	95.5	95.3	0.37
2	16.390	623.263	27.595	4.5	4.7	0.36
	Total	13952.015	588.661	100.0	100.0	

Fig 1.28. HPLC spectrum of chiral compound **1.33a''**

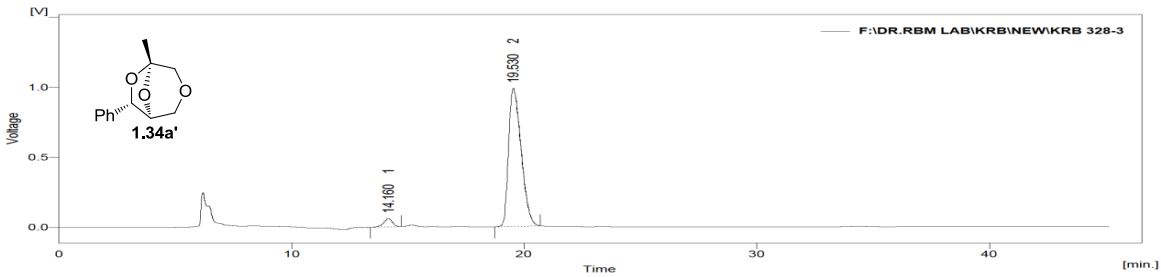


Result Table (Uncal - F:\Dr.RBM Lab\KRB\KRB-292-III)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	14.220	21987.386	700.017	48.5	53.3	0.50
2	19.730	23342.337	612.586	51.5	46.7	0.60
	Total	45329.723	1312.604	100.0	100.0	

CHIRALCEL OD-H, FLOW RATE 0.5 mL/min, HEX:IPA=95:5, 220 nm.

Figure 1.29. HPLC spectrum of racemic compound **1.34a**



Result Table (Uncal - F:\DR.RBM LAB\KRB\NEW\KRB 328-3)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	14.160	1047.021	40.963	4.1	5.9	0.39
2	19.530	24713.946	657.210	95.9	94.1	0.60
	Total	25760.968	698.173	100.0	100.0	

Fig 1.30. HPLC spectrum of chiral compound **1.34a'**

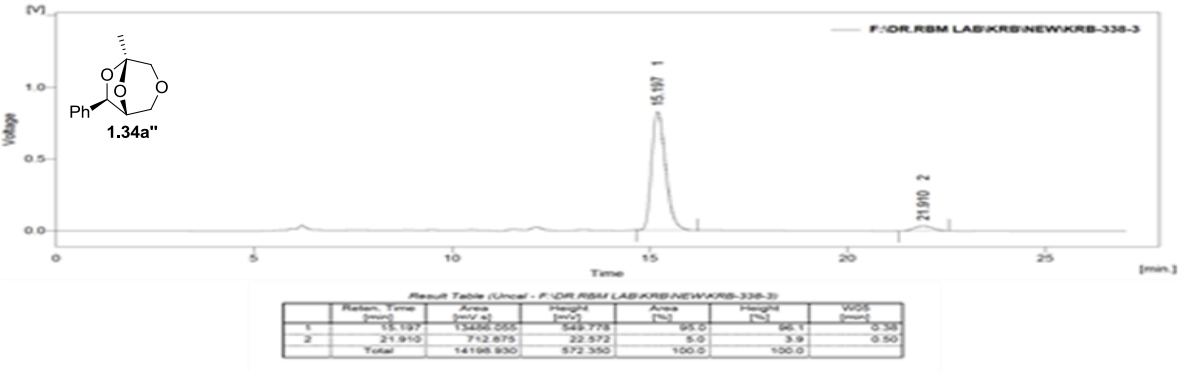


Fig 1.31. HPLC spectrum of chiral compound **1.34a''**

Chapter 2

Synthesis of α-Diarylacetic Esters *via in Situ* Formed Acetals by Stereospecific 1,2-Aryl Migration

2.1 Introduction

The *gem*-diarylalkyl moiety is often present in many biologically active natural products.[1] Several commercially available drugs contain *gem*-diarylalkyl structural unit.[1, 11a] This motif is the key unit in certain antidepressant, anti-inflammatory and analgesic drugs. Among the *gem*-diarylalkyl compounds, α-diaryl carbonyl compounds are interesting as the carbonyl can be manipulated in further synthetic transformations. Quite a few methods have been developed for the synthesis of racemic unsymmetrical α-diaryl carbonyl compounds.[2] Most of these reported methods are based on transition metal-catalyzed α-arylation of α-aryl carbonyl compounds. The α-diaryl carbonyl compounds can be synthesized by 1,2-aryl migration as well.

2.1.1 α-Arylation of α-aryl carbonyl compounds

The α-diaryl carbonyl compounds can be synthesized from α-aryl carbonyl compounds by α-arylation.[2] These transformations are generally performed by using transition metal catalysts especially Pd-catalysts. Several factors determine the success of a metal-catalyzed α-arylation reaction. In order to be active in these transformations, Pd-catalyst should be pre-coordinated to bulky ligands which are generally expensive. The ligands can influence the rate of oxidative addition and reductive elimination steps. Generally, in cross-coupling reactions the steric and electronic characters of ligands are important. More electron-rich ligands tend to stabilize the Pd(II) intermediate, hence facilitate the initial oxidative addition of aryl halide. On the other hand sterically hindered ligands facilitate the reductive elimination by pushing the aryl and enolate group at the palladium center closer together in space to coordinate in a *cis* mode (Scheme 2.1).[2m] In addition, the nature of aryl halide, the strength of base and reaction temperature also play important roles in these reactions. Buchwald and Hartwig have contributed significantly for the development of α-arylation reactions.[2i-k, 2o-p] All these methods are simple and efficient but these reactions are to be carried out under strong basic conditions. Hence, base-sensitive functional groups if present in reactants may affect the reaction and lead to undesired products.

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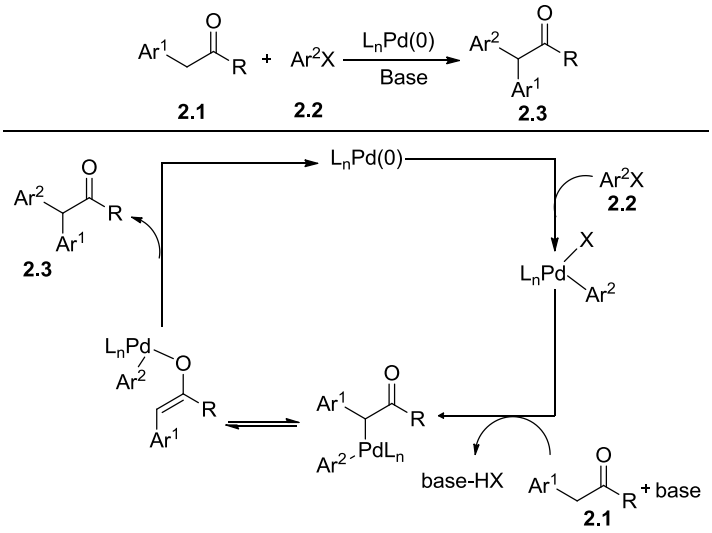
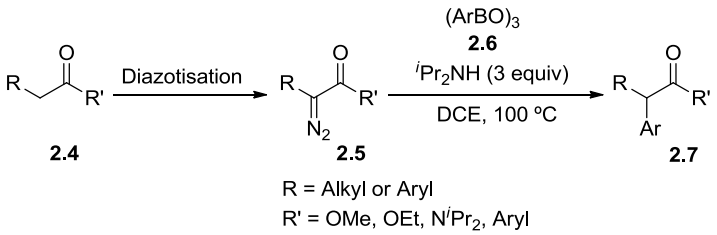


Scheme 2.1. Pd-catalyzed α-arylation of α-aryl carbonyl compounds

In 2009, Wang and co-workers have reported an alternate method for the α-arylation of carbonyl compounds.[2h] In this method, the carbonyl compound **2.4** is initially converted into the corresponding α-diazocarbonyl compound **2.5** and treated with easily accessible arylboroxines **2.6** to get the *gem*-diarylalkyl carbonyl compound **2.7** (Scheme 2.2). The reaction is initiated by the nucleophilic attack of diazo substrate to the boron atom of arylboroxine **2.6**, followed by 1,2-migration from boron to carbon which upon hydrolysis results in the product **2.7**. The acidic species generated during the course of the reaction could decompose the diazo substrate. In order to prevent this decomposition diisopropylamine is added. This can be understood from the remarkable increase of product yield upon the addition of additive diisopropylamine.

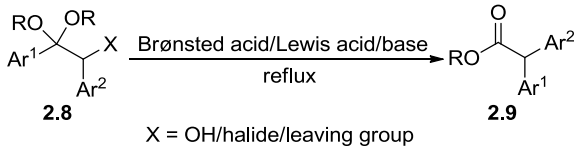


Scheme 2.2. α-Arylation of α-diazocarbonyl compounds using arylboroxines **2.6**

2.1.2 1,2-aryl migrations

1,2-Aryl migration reactions are important rearrangements in the carbocation chemistry. 1,2-Aryl migration in alkyl aryl ketones and their derivatives have proven to be very useful.[3] Generally, 1,2-aryl migrations take place in compounds containing halo/hydroxyl/suitable leaving group at the α-position of the aryl acetals in the presence of Brønsted acid/Lewis acid/base catalysts (Scheme 2.3).[3]

Many soft and borderline Lewis acids such as salts of Zn, Sn, Co, Hg, Pd, Sb, Bi, and Fe (MXn) can promote the 1,2-aryl shift in *α*-haloalkylaryl acetals to *α*-arylalkanoic acids at reflux temperatures.[3g] Aldehydes and ketones can be converted into the corresponding acetals in the presence of trialkyl orthoformates under Brønsted/Lewis acidic conditions.[4] The *α*-bromo acetals are more reactive than their chloro counterparts. This indicates that the breaking of carbon-halogen bond of acetal is an irreversible step. Secondary *α*-bromo acetals are more reactive than primary *α*-bromo acetals owing to the energy difference of C-Br bond. In the case of metal-catalyzed reactions, preformed acetals are employed and the affinity of metal towards halide boost the 1,2-aryl migration. The higher affinity of metal ion towards the halogen than oxygen of the acetal, more facile is this 1,2-aryl migration with complete inversion of configuration at the carbon bearing the halogen.[3e] The driving force for this migration is the stabilization of positive charge by the acetal oxygens in the intermediate species generated upon 1,2-aryl migration. In all these reported methods acetals were preformed and reacted. But none of them have generated acetals *in situ* to employ in the reaction. Miroslav and co-workers have used *in situ* formed acetal for the preparation of methyl-2-(4-ethylphenyl)-2-methylpropionate from 1-(4-ethylphenyl)-2-hydroxy-2-methylpropan-1-one.[3a] In another report also *in situ* formed acetals were employed. But they did not try any reaction on the benzoin type substrates to prepare *α*-diarylacetic esters.[3f] 1,2-Aryl migration has also been known to provide ample opportunities to synthesize compounds which are difficult to make otherwise.[5]



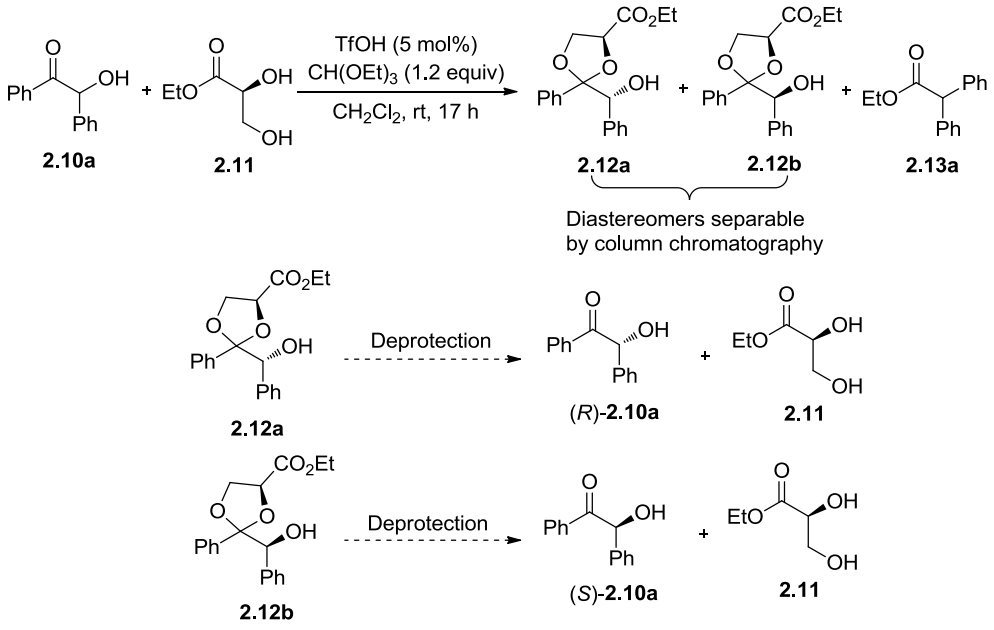
Scheme 2.3. *α*-Diarylalkyl esters formation by 1,2-aryl migration

2.2 Results and discussion

2.2.1 Background of the work

While working on the gold-catalyzed synthesis of bicyclic acetals, we observed that the optically active diastereomers of bicyclic acetals can be separated by simple column chromatography (Chapter 1, Scheme 1.16).[6] From this result we thought that racemic *α*-hydroxy ketones can be resolved if they are converted into *α*-hydroxy acetals using chiral diols which have some groups to make hydrogen bond with the hydroxy of the *α*-hydroxy ketones. Having this idea in mind, we attempted the resolution of benzoin **2.10a** as chiral benzoins are useful compounds but are expensive. For that our first task was to protect the carbonyl group of benzoin with a chiral diol ester like **2.11**

(which can easily be accessed from D-mannitol) or diethyl tartrate to get the two acetal diastereomers **2.12a** and **2.12b** which are expected to be separated by column chromatography. If the diastereomers are separated they can easily be deprotected to get both the enantiomers of benzoin (Scheme 2.4). At the same time the diol can also be recovered. In this contest, when we attempted the reaction of **2.10a** with **2.11**[7] using different Brønsted acids no acetal formation was observed. However, we succeeded a bit when we used triethyl orthoformate. But the yields of the diastereomers **2.12a** and **2.12b** were very poor. For the protection of benzoin with diol, we have attempted using many Brønsted and Lewis acids. During the investigation of the reaction, we isolated the 1,2-phenyl migrated product ethyl diphenylacetate **2.13a** in poor yield when we used TfOH (5 mol%)/triethyl orthoformate (1.2 equiv). Compound **2.13a** is expected to be formed by the 1,2-migration of the phenyl group in the *in situ* formed acetal. Knowing the importance of the *gem*-diarylalkyl derivatives we turned our attention to develop a methodology for the synthesis of *gem*-diarylalkyl compounds from *in situ* formed acetals of benzoins by 1,2-aryl migration. Then we proceeded to optimize the reaction condition.



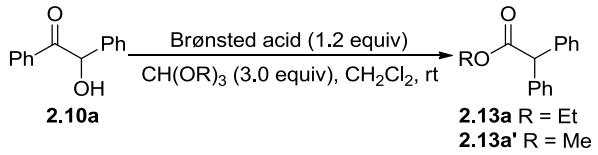
Scheme 2.4. Attempted resolution of benzoin

2.2.2 Optimization of reaction conditions

Benzoin **2.10a** was reacted with triethyl orthoformate in the presence of different Brønsted acids separately in dichloromethane to find out the condition that result the highest yield of the rearranged product. Table 2.1 summarizes the results of these experiments. Among the Brønsted acids studied, triflic acid was found to be the best in the presence of 3 equivalents of triethyl orthoformate

and the reaction completed in 15 min at room temperature to furnish **2.13a** in 97% of yield (Table 2.1, entry 9). Methanesulfonic acid also worked well resulting in 89% of the product. However the reaction was slower and less efficient than that of the one involving triflic acid (Table 2.1, entry 1). The reaction was tested with (+)-camphorsulfonic acid also and found to result in 49% of the expected product (Table 2.1, entry 5). Reactions using mineral acids were sluggish and the yields were poor (Table 2.1, entry 4 and 6). Importantly, this 1,2-phenyl migration did not occur in the presence of mild acids such as amberlyst 15 and amberlite IR 120 (Table 2.1, entry 7 and 8). When triflic acid was used in sub-stoichiometric amount, the reaction resulted in poor yields of the product **2.13a** (Table 2.1, entries 11 and 12). Reactions utlizing triethyl orthoformate resulted in good yields of the product than that employing trimethyl orthoformate. This may be due to diethyl acetals undergo elimination more readily than dimethyl acetals.[4a]

Table 2.1. Screening of different Brønsted acids for the conversion of benzoin **2.10a** into α-diphenyl acetate derivative **2.13**



2.10a

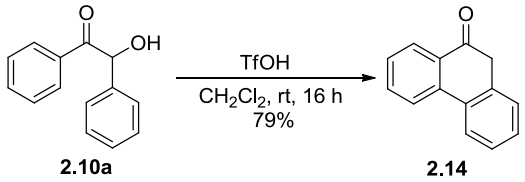
2.13a R = Et
2.13a' R = Me

Entry	Brønsted acid	R	time	yield (%)[a]
1	CH_3SO_3H	Et	1 h	89
2	TFA	Et	24 h	79
3	PTSA	Et	24 h	70
4	$HClO_4$	Et	24 h	11
5	(+)-CSA	Et	24 h	49
6	HCl	Et	24 h	trace
7	Amberlyst 15	Et	24 h	NR
8	Amberlite IR 120	Et	24 h	NR
9	**TfOH**	**Et**	**15 min**	**97**
10	TfOH	Me	15 min	95
11	TfOH[b]	Me	4 h	6
12	TfOH[c]	Me	27 h	61

[a] Isolated yield. [b] 10 mol %. [c] 50 mol %. NR: no reaction.

We presumed that the *in situ* formed acetal is the key intermediate in this reaction for 1,2-phenyl migration. Olah and co-workers have reported that, in the absence of triethyl orthoformate, benzoin **2.10a** undergoes benzannulation to furnish phenanthren-9(10H)-one **2.14** (Scheme 2.15).[8] So, it is clear that triethyl orthoformate is very important in this reaction to generate acetal *in situ* for the

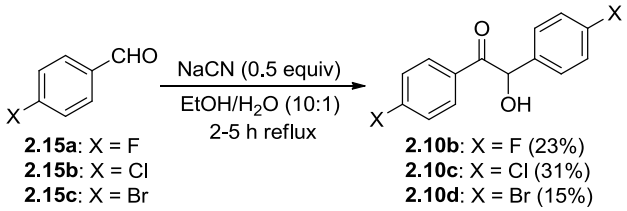
1,2-aryl migration to take place. To evaluate the scope of this method we started to prepare various substituted benzoins.



Scheme 2.5. Benzannulation of benzoin promoted by TfOH

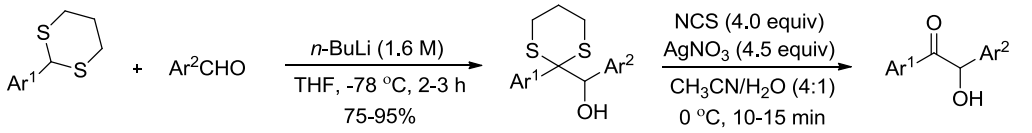
2.2.3 Synthesis of racemic benzoins

A variety of benzoins and *α*-hydroxy ketones were synthesized to study the *in situ* acetal-assisted 1,2-aryl migration. Symmetrical benzoins **2.10b**-**2.10d** were prepared by classical benzoin condensation from aromatic aldehydes **2.15a**-**2.15c** in presence of sodium cyanide under reflux condition (Scheme 2.6).[9, 10]



Scheme 2.6. Synthesis of benzoins **2.10b** – **2.10d** by benzoin condensation

Unsymmetrical benzoins **2.10e**-**2.10t** were prepared by following the strategy outlined in the Scheme 2.7. The dithiane protected aryl aldehydes **2.16a**-**2.16h** were prepared by treating corresponding aryl aldehydes with propane-1,3-dithiol in presence of BF_3·etherate. The dithiane protected aryl aldehydes **2.16a**-**2.16h** were lithiated using *n*-BuLi at -78 ºC and the generated anions were treated separately with aryl aldehydes **2.15a, 2.15b, 2.15d**-**2.15g** at the same temperature to get the corresponding dithiane protected benzoins **2.17a**-**2.17p**. The dithianes **2.17a**-**2.17p** were deprotected using *N*-chlorosuccinimide and $AgNO_3$ reagent system to yield the desired benzoins **2.10e**-**2.10t**.



2.16a-2.16h **2.15a, 2.15b, 2.15d-g** **2.17a-2.17p** **2.10e-2.10t**

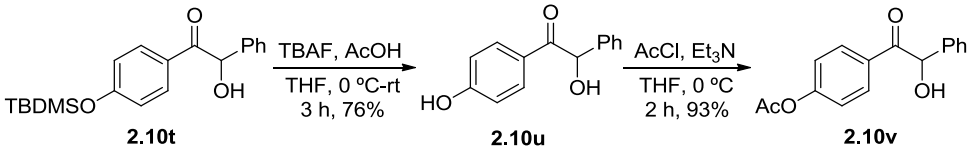
2.16a: Ar^1 = Ph
2.16b: Ar^1 = 4-MeC_6H_4
2.16c: Ar^1 = 4-$OMeC_6H_4$
2.16d: Ar^1 = 4-ClC_6H_4
2.16e: Ar^1 = 3,4-$(OMe)_2C_6H_3$
2.16f: Ar^1 = 3,4-$(OCH_2O)C_6H_3$
2.16g: Ar^1 = 4-(OTBDPS)C_6H_4
2.16h: Ar^1 = 4-(OTBDMS)C_6H_4

2.15a: Ar^2 = 4-FC_6H_4
2.15b: Ar^2 = 4-ClC_6H_4
2.15d: Ar^2 = 2,4-$Cl_2C_6H_3$
2.15e: Ar^2 = C_6H_5
2.15f: Ar^2 = 3-FC_6H_4
2.15g: Ar^2 = 2-ClC_6H_4

2.17a, 2.10e: Ar^1 = Ph, Ar^2 = 2-ClC_6H_4
2.17b, 2.10f: Ar^1 = Ph, Ar^2 = 4-ClC_6H_4
2.17c, 2.10g: Ar^1 = Ph, Ar^2 = 2,4-$Cl_2C_6H_3$
2.17d, 2.10h: Ar^1 = 4-MeC_6H_4, Ar^2 = Ph
2.17e, 2.10i: Ar^1 = 4-MeC_6H_4, Ar^2 = 4-ClC_6H_4
2.17f, 2.10j: Ar^1 = 4-MeC_6H_4, Ar^2 = 3-FC_6H_4
2.17g, 2.10k: Ar^1 = 4-$OMeC_6H_4$, Ar^2 = 4-ClC_6H_4
2.17h, 2.10l: Ar^1 = 4-$OMeC_6H_4$, Ar^2 = 4-FC_6H_4
2.17i, 2.10m: Ar^1 = 4-ClC_6H_4, Ar^2 = 4-FC_6H_4
2.17j, 2.10n: Ar^1 = 3,4-$(OMe)_2C_6H_3$, Ar^2 = Ph
2.17k, 2.10o: Ar^1 = 3,4-$(OMe)_2C_6H_3$, Ar^2 = 4-ClC_6H_4
2.17l, 2.10p: Ar^1 = 3,4-$(OCH_2O)C_6H_3$, Ar^2 = Ph
2.17m, 2.10q: Ar^1 = 3,4-$(OCH_2O)C_6H_3$, Ar^2 = 4-FC_6H_4
2.17n, 2.10r: Ar^1 = 3,4-$(OCH_2O)C_6H_3$, Ar^2 = 4-ClC_6H_4
2.17o, 2.10s: Ar^1 = 4-(OTBDPS)C_6H_4,Ar^2 = C_6H_5
2.17p, 2.10t: Ar^1 = 4-(OTBDMS)C_6H_4, Ar^2 = C_6H_5

Scheme 2.7. Synthesis of unsymmetrical benzoins **2.10e**-**2.10t**

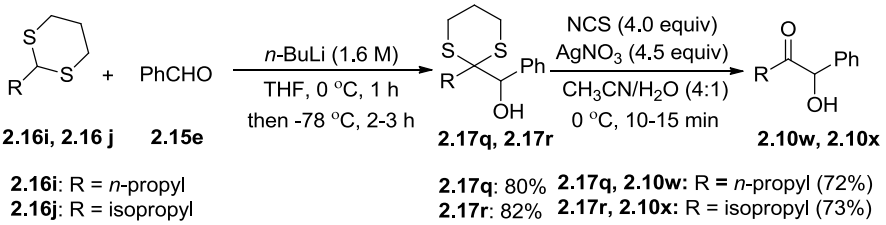
The benzoins **2.10u** and **2.10v** were prepared from benzoin **2.10t**. The TBDMS protected benzoin **2.10t** was deprotected by using TBAF to furnish benzoin **2.10u**, which upon acetylation yielded the benzoin **2.10v** (Scheme 2.8).



2.10t **2.10u** **2.10v**

Scheme 2.8. Synthesis of unsymmetrical benzoins **2.10u** and **2.10v**

To check whether 1,2-alkyl migration is possible under the reaction condition, alkyl aryl substituted *α*-hydroxy ketones **2.10w** and **2.10x** were prepared by following the Scheme 2.9. Dithiane protected aliphatic aldehydes **2.16i** and **2.16j** were prepared from the corresponding aldehydes by following the trivial dithiane protection procedure. Dithianes **2.16i** and **2.16j** were lithiated using *n*-BuLi and the lithiated derivatives were reacted with benzaldehyde to yield dithiane protected alcohols **2.17q** and **2.17r**. Dithiane deprotection in **2.17q** and **2.17r** was performed with NCS/$AgNO_3$ to get the *α*-hydroxy ketones **2.10w** and **2.10x**.



Scheme 2.9. Synthesis of α-hydroxy ketones **2.10w** and **2.10x**

2.2.4 Synthesis of α-diarylacetic esters

After preparing several substituted symmetric and unsymmetric benzoins, they were subjected to triflic acid/triethyl orthoformate mediated 1,2-aryl migration and results are shown in Figure 2.1. Benzoins having different substituents including electron withdrawing and electron donating groups like F, Cl, Br, Me, OMe, OCH_2O, OTBDPS, OTBDMS, OH, and OAc on aryl rings were subjected to the reaction condition presented in the entry 9 of Table 2.1. Both the less sensitive (Cl, F, Me, OMe, OCH_2O) and highly sensitive (OTBDMS, OTBDPS, OH, OAc) groups survived under the reaction conditions. We did not observe any significant electronic and steric effects in the formation of α-diarylacetic esters. All these reactions were fast and completed in less than 20 min. All the reactions studied were clean and the yields were generally excellent.

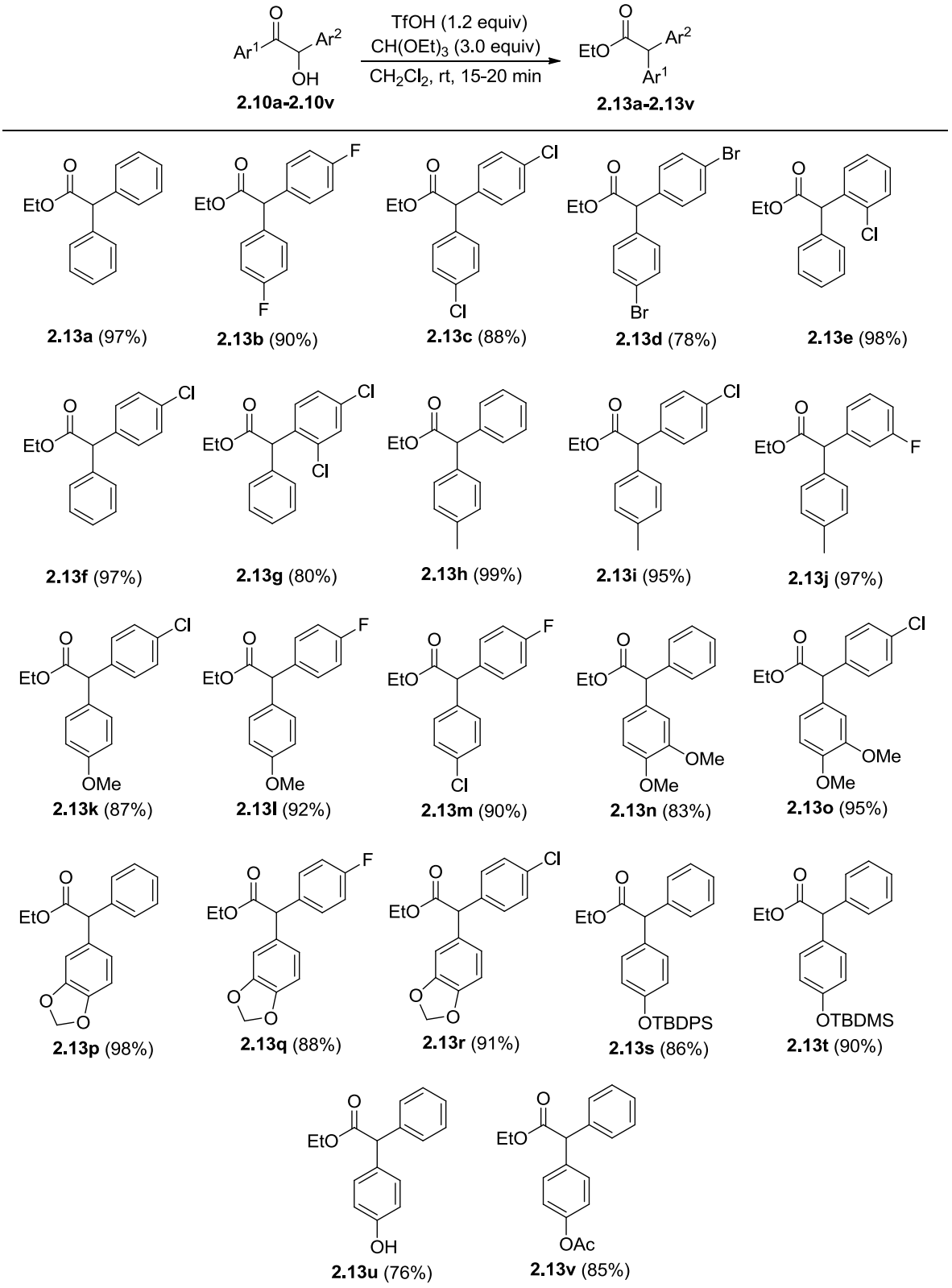
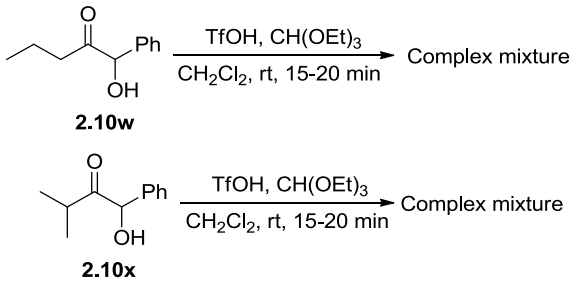


Figure 2.1. Substrate scope for 1,2-aryl migration of benzoins

To extend this methodology, 1,2-alkyl migration was tested using the substrates 1-hydroxy-1-phenylpentan-2-one **2.10w** and 1-hydroxy-3-methyl-1-phenylbutan-2-one **2.10x**. By choosing these substrates, we wished to study the migration abilities of primary and secondary alkyl groups. Unfortunately, both the reactions resulted in complex product mixtures (Scheme 2.10). So, from these reactions it is understood that the 1,2-alkyl migration can not be performed under these reaction conditions.



Scheme 2.10. Attempts for 1,2-alkyl migration

We then proceeded to study the stereospecificity of the 1,2-aryl migration. There are two situations possible in this reaction. Upon protonation, a carbocation can be generated at the carbinol carbon which will be followed by the 1,2-aryl migration. On the other hand, 1,2-aryl migration can occur as the water molecule leaves in the protonated species in a concerted manner.

2.2.5 Stereospecific 1,2-aryl migration and its application in the synthesis of enantioenriched α-diarylacetic esters from chiral benzoins

2.2.5.1 Literature on the synthesis of chiral α-diarylacetic esters

The chiral *gem*-diarylalkyl moiety is present in many pharmaceutically and biologically important compounds.[11, 1b] For example, this moiety is the key structural feature of muscarinic antagonists like fesoterodine,[11b] tolterodine (Detrol®),[11c, d] antidepressants such as sertraline (Zoloft®),[11e] nomifensine[11f] and phosphodiesterase type 4 inhibitor CDP-840[11g] (Fig. 2.2). Making enantiomerically pure α-diaryl carbonyl compounds is really a challenging task due to the associated epimerization issues. Straightforward enantioselective protonation of enolates which is used to introduce chirality at the α-position of a carbonyl function cannot be applied in these substrates as it is difficult to differentiate the faces of their enolates. Although the asymmetric version of transition metal-catalyzed α-arylation[12] has seen remarkable development in recent times, it is limited to the synthesis of enantiopure α-monoaryl carbonyl compounds only.

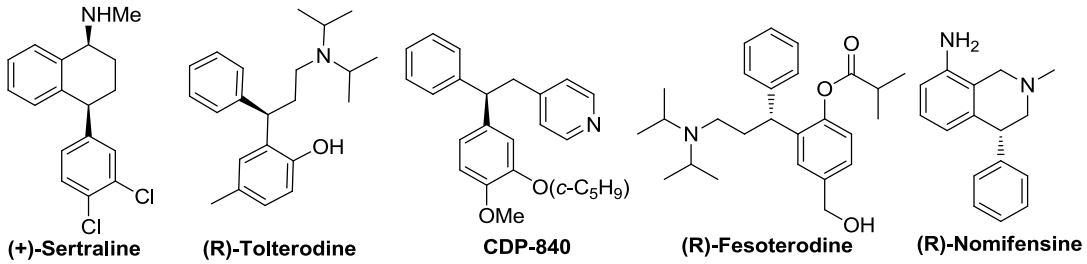
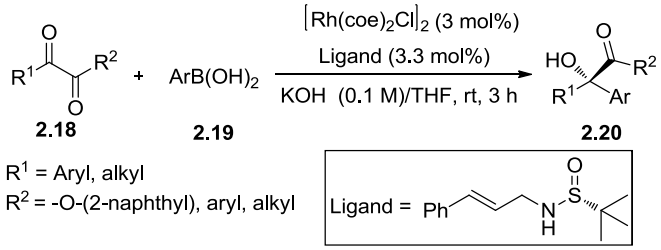


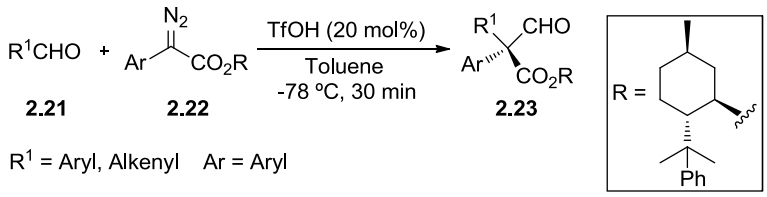
Figure 2.2. Important pharmaceutical compounds having chiral *gem*-diaryl moiety

Very few reports are available for the synthesis of enantioenriched *α*-diaryl carbonyl compounds.[13-15] Among them, majorly explored method is the 1,2-addition of aryl boronic acids to *α*-ketoesters or *α*-diketones using chiral rhodium or ruthenium catalysts.[13] Using chiral *N*-(sulfinyl)cinnamylamine ligand, Xu and co-workers have developed a highly efficient Rh-catalyzed asymmetric 1,2-addition of aryl boronic acids **2.19** to *α*-ketoesters or *α*-diketones **2.18** (Scheme 2.11).[13a] It is an easy, practical and high yielding method to access highly enantioenriched tertiary *α*-hydroxy carbonyl compounds **2.20**.



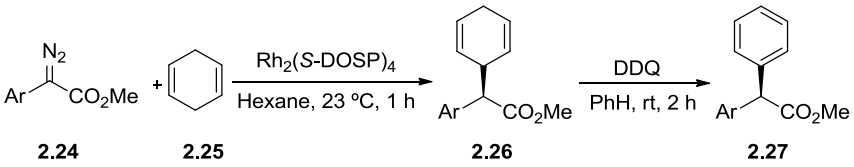
Scheme 2.11. Asymmetric 1,2-addition of arylboronic acids to *α*-ketoesters and *α*-diketones

Maruoka and co-workers have developed an excellent strategy for generating chiral all carbon quaternary center *α* to carbonyl by TfOH-catalyzed insertion of aryldiazoacetate **2.22** to aldehydes **2.21** (Scheme 2.12).[14] In this reaction the chirality is transferred through (–)-phenylmenthyl chiral auxillary attached to the aryldiazo substrate. In this reaction the undesired *β*-keto ester is formed in less than 10% yield by 1,2-hydride shift. But this side reaction could be suppressed by careful selection of acid catalyst used for aldehyde activation.



Scheme 2.12. Stereoselective insertion of (–)-phenylmenthyl aryldiazoacetates to aldehydes

Davies and co-workers have reported a rhodium-catalyzed asymmetric insertion of aryldiazoacetate **2.24** into C-H bond of 1,4-cyclohexadiene **2.25** and subsequent oxidation of the product **2.26** using DDQ to chiral *gem*-diaryl acetates **2.27**.[15] However, this method is applicable to make enantioenriched α-diaryl acetates in which one of the aryl groups is compulsorily phenyl (Scheme 2.13). They have demonstrated the synthetic utility of this transformation by utilizing it in a formal asymmetric synthesis of (+)-sertraline.



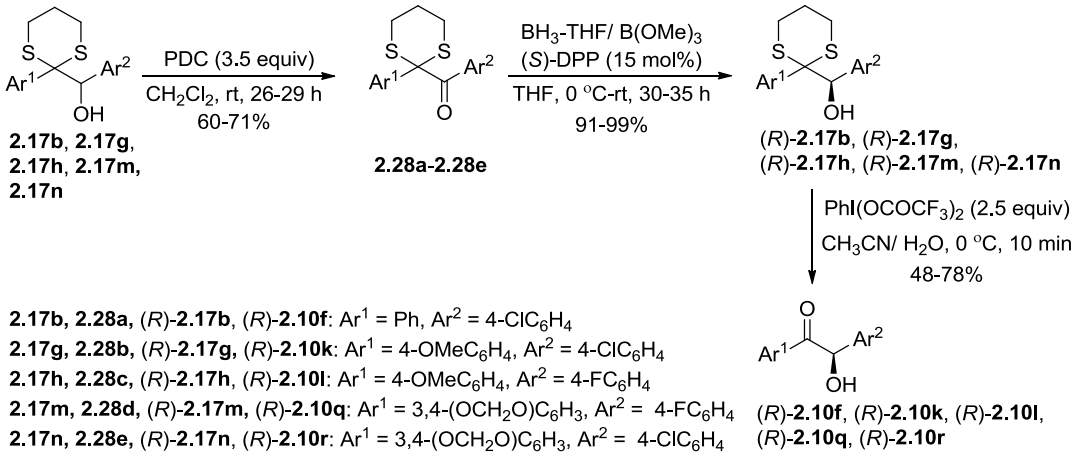
Scheme 2.13. Synthesis of α-diarylacetates from diazoacetates

It is known that the 1,2-aryl migration in chiral acetals of 1-aryl-2-sulfonyloxyl-1-alkanones proceeds with complete inversion of the configuration at the sulfonyloxy carbon center,[3f, 3e] *i.e.* in the chiral substrates 1,2-aryl migration occur in streospecific manner. We then focused our attention to synthesize enantiomerically pure benzoins to evaluate the stereospecificity of the 1,2-aryl migration. If the migration is stereospecific, it can be applied in the synthesis of enantioenriched α-diaryacetates.

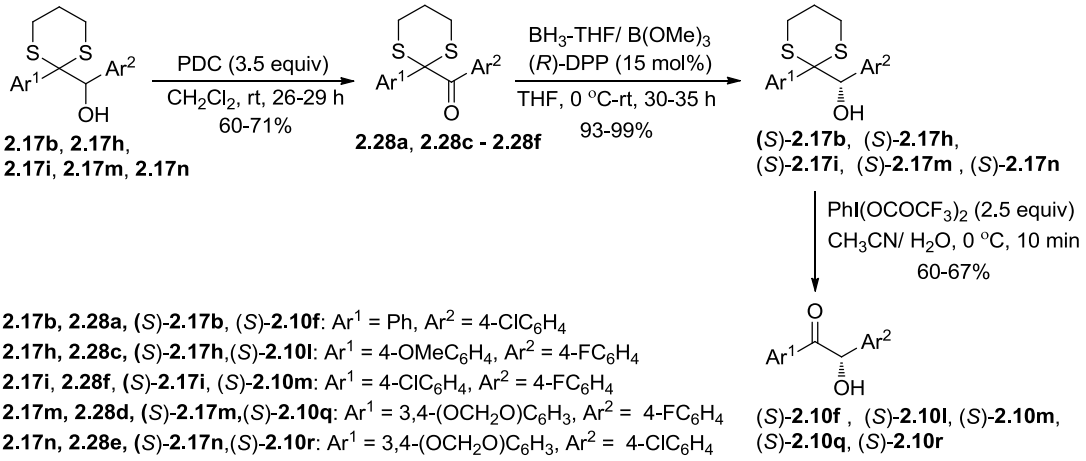
2.2.5.2 Synthesis of chiral benzoins

For the synthesis of optically pure benzoins we have developed a new protocol. The dithiane protected benzylic alcohol derivatives **2.17** were oxidized to their corresponding ketones **2.28**. For the oxidation of **2.17** PDC only worked well. Other oxidation methods such as Swern oxidation, PCC oxidation and Dess-Martin periodinane oxidation were not suitable and resulted in undesired products. CBS reduction was carried out on the ketones **2.28**. Deprotection of chiral dithianes (*R*)/(*S*)-**2.17** yielded the optically active benzoins (*R*)/(*S*)-**2.10** with high enantiomeric excess (Schemes 2.14 and 2.15). By following this procedure, both enantiomers of benzoins were obtained in high enantiomeric excess using ligands (*S*)-DPP/(*R*)-DPP in the CBS reduction step.[16] When (*S*)-DPP was

used as chiral ligand, (*R*)-benzoins were obtained and when (*R*)-DPP was used, (*S*)-benzoins were attained. This is a very straight forward and new protocol for the synthesis of enantiopure benzoins. DeNinno and co-workers reported the enantioselective reduction of 2-acyl-1,3-dithianes using oxazaborolidine (B-Ph) catalyst.[17] However they did not apply this methodology for the synthesis of chiral benzoins. In their substrates, the bulkiness is imparted by the dithiane moiety and good enantioselectivities were obtained only when the acyl group is less bulky like acetyl. When the acyl group is propanoyl the enantioselectivity reduced considerably. However, using classical B-Me oxazaborolidine as catalyst, we were delighted to observe very good enantioselectivities with our substrates. After performing asymmetric reduction, dithiane was deprotected using hypervalent iodine reagent bis(trifluoroacetoxy)iodobenzene. In the deprotection step, only moderate yields of chiral benzoins were obtained. This may be due to the formation of over oxidized products such as benzils. Benzoins (*R*)-**2.10f**, (*R*)-**2.10k** and (*S*)-**2.10f** are already reported.[18] The absolute configurations of other chiral benzoins were assigned by analogy of the reported literature. Following this way we accessed chiral benzoins having electron-withdrawing and electron-donating substituents on any of the aromatic rings.



Scheme 2.14. Synthesis of chiral benzoins (*R*)-**2.10**

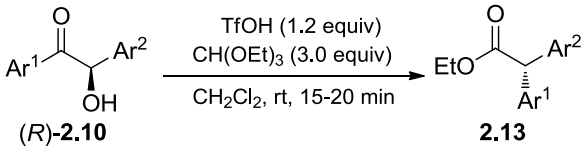


Scheme 2.15. Synthesis of chiral benzoins (*S*)-**2.10**

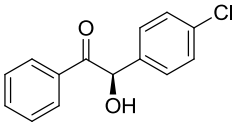
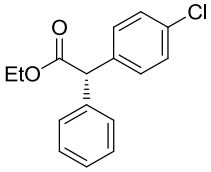
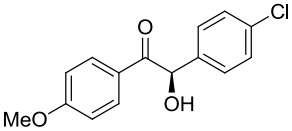
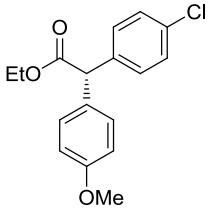
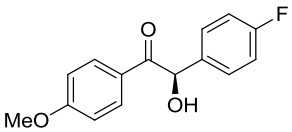
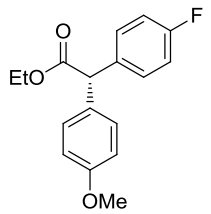
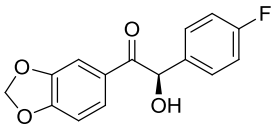
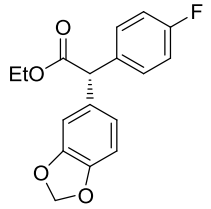
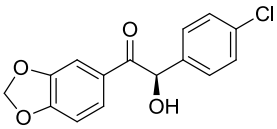
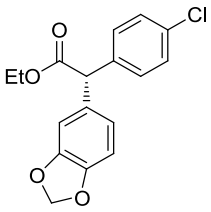
2.2.5.3 Synthesis of enantioenriched α-diarylacetic esters

After synthesizing chiral benzoins in a successful way, both (*R*) and (*S*)-benzoins were subjected to *in situ* formed acetal-assisted 1,2-aryl migration reactions separately. The aryl migration took place from back side of the leaving group OH in a concerted manner[19, 20] and resulted enantioenriched α-diarylacetic esters in excellent yields (Tables 2.2 and 2.3). The anchimeric assistance of the aryl group and stabilization of positive charge generated at carbon center by acetal function favor this stereospecific 1,2-aryl migration. Except in the reaction of (*S*)-**2.10m**, the *ee* of the products are the same or slightly less than that of the starting benzoins. Whenever there was an electron withdrawing fluoro substituent present in the aryl ring, the *ee* slightly reduced. This effect was more in substrate (*S*)-**2.10m** which contains 4-F-phenyl and 4-Cl-phenyl groups in it (Table 2.3, entry 3). The configuration of the products chiral α-diarylacetic esters was assigned based on the configuration of staring chiral benzoins. Also the analogous methyl α-diaryl acetate of (*R*)-**2.13f** is already reported in the literature.[15]

Table 2.2. Synthesis of enantiopure *α*-diarylacetic esters from (*R*)-benzoins

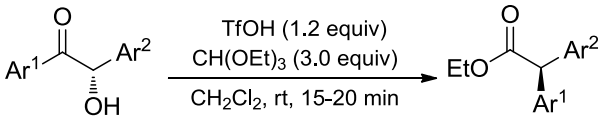


(*R*)-**2.10** → **2.13**

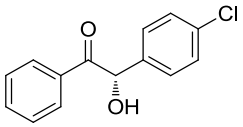
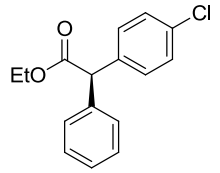
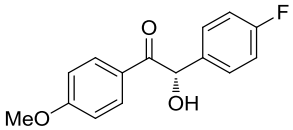
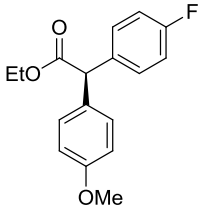
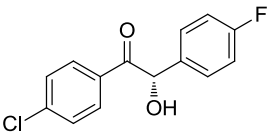
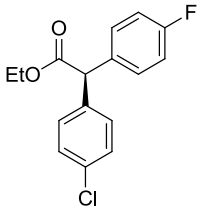
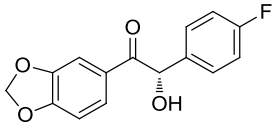
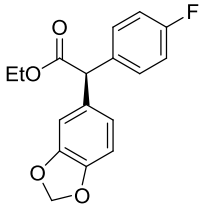
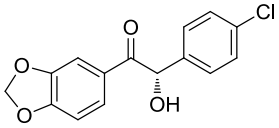
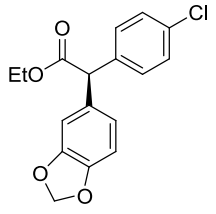
Entry	(*R*)-**2.10**	**2.13**[a]
1	 (*R*)-**2.10f** (91% *ee*)	 (*S*)-**2.13f** 87% (88% *ee*)
2	 (*R*)-**2.10k** (87% *ee*)	 (*S*)-**2.13k** 90% (87% *ee*)
3	 (*R*)-**2.10l** (92% *ee*)	 (*S*)-**2.13l** 88% (90% *ee*)
4	 (*R*)-**2.10q** (98% *ee*)	 (*R*)-**2.13q** 87% (93% *ee*)
5	 (*R*)-**2.10r** (95% *ee*)	 (*R*)-**2.13r** 88% (93% *ee*)

[a] Isolated yield.

Table 2.3. Synthesis of enantiopure α-diarylacetic esters from (*S*)-benzoins

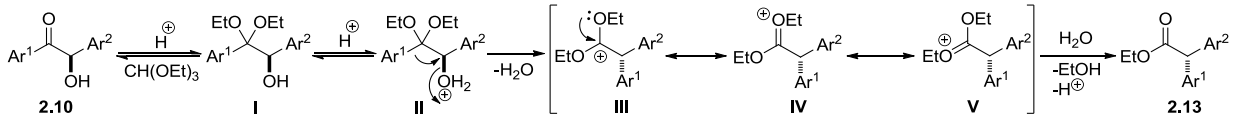


(*S*)-**2.10** → **2.13**

Entry	(*S*)-**2.10**	**2.13**[a]
1	 (*S*)-**2.10f** (99% *ee*)	 (*R*)-**2.13f** 96% (93% *ee*)
2	 (*S*)-**2.10l** (96% *ee*)	 (*R*)-**2.13l** 93% (91% *ee*)
3	 (*S*)-**2.10m** (99% *ee*)	 (*S*)-**2.13m** 93% (85% *ee*)
4	 (*S*)-**2.10q** (98% *ee*)	 (*S*)-**2.13q** 96% (92% *ee*)
5	 (*S*)-**2.10r** (97% *ee*)	 (*S*)-**2.13r** 85% (96% *ee*)

[a] Isolated yield.

Regarding mechanism, this reaction follows a well-established 1,2-aryl migration. Under triflic acid conditions, benzoins **2.10** are converted into corresponding acetals **I** in the presence of triethyl orthoformate.[4] The *in situ* formed acetals facilitate the 1,2-aryl migration. The aryl migration takes place from back side of the leaving OH group in a concerted process to form **2.13** (Scheme 2.16).



Scheme 2.16. Plausible mechanism for the formation of *α*-diarylacetic esters by 1,2-aryl migration

2.3 Conclusions

In conclusion, we have developed a simple and efficient protocol for the synthesis of *α*-diarylacetic esters **2.13** involving *in situ* generated acetal-assisted 1,2-aryl migration. We have demonstrated a new methodology for the synthesis of chiral benzoins with high enantiomeric excess by applying CBS reduction. Using *in situ* generated acetal-assisted 1,2-aryl migration enantioenriched *α*-diaryl acetates which are otherwise difficult to make could be prepared from enantiomerically pure benzoins by stereospecific 1,2-aryl migration. Optically active *α*-diaryl acetates could serve as valuable building blocks for the synthesis of many biologically active compounds.

2.4 Experimental section

2.4.1 General information

Chemicals and solvents were purchased from various commercially available sources. The starting materials were prepared by following known and standard literature procedures. Dichloromethane solvent dried over CaH_2 and used as freshly distilled from the still. THF was dried over sodium metal and freshly distilled from the still before use. ^{1}H and ^{13}C spectra were recorded on Brucker 400 MHz or 500 MHz NMR spectrometer using solutions in $CDCl_3$ with tetramethylsilane (TMS) as internal standard. IR spectra were recorded on JASCO FT/IR spectrometer. Elemental (C, H, N) analysis were done by flash combustion method in a CHN analyzer. HRMS (Brucker) were recorded using electron spray ionization. Column chromatography was performed on silicagel 100-200 mesh, using ethyl acetate and hexanes mixture as eluent. HPLC analysis of the samples was performed using Chiralcel OD-H/AS-H/AD-H/OJ-H columns, hexanes/*i*-PrOH as eluent, flow rate = 1.0 mL/min or 0.8 mL/min at λ_{max} = 220 nm. Melting points were found using a melting point range apparatus.

2.4.2 Experimental procedures, spectral and analytical data

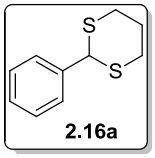
Benzoin **2.10a** is commercially available.

Symmetrical benzoins **2.10b**-**2**.**10d** were prepared by classical benzoin condensation.[8, 9]

General procedure for synthesis of dithianes 2.16a-2.16j

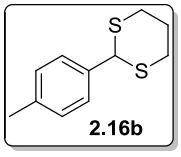
To a solution of corrresponding aryl aldehyde (1 equiv) and propane-1,3-dithiol (1.1 equiv) in dichloromethane (4 mL per mmol), $BF_3 \cdot OEt_2$ (30 mol%) was added at room temperature. Reaction was monitered by TLC. Aqueous $NaHCO_3$ was added after completion of reaction (3-5 h). Organic layer was washed with saturated brine solution, concentrated to get the corresponding dithiane derivatives **2.16a-2.16j** in quantitative yield. The crude solid dithiane material was washed with hexane and was sufficiently pure to be used for next step without column purification.

2-Phenyl-1,3-dithiane (2.16a)



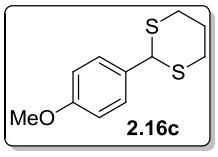
Compound **2.16a** was synthesized from benzaldehyde by following general dithine protection procedure.[21] ^{1}H NMR (400 MHz, CDCl3): δ 7.48 (d, J = 7.6 Hz, 2H), 7.37-7.29 (m, 3H), 5.18 (s, 1H), 3.07 (dt, J = 14.4, 2.0 Hz, 2H), 2.92 (td, J = 14.4, 3.6 Hz, 2H), 2.20-2.16 (m, 1H), 2.00-1.89 (m, 1H); 13C NMR (100 MHz, CDCl3): δ 139.1, 128.7, 128.4, 127.7, 51.4, 32.1, 25.1.

2-*p*-Tolyl-1,3-dithiane (2.16b)



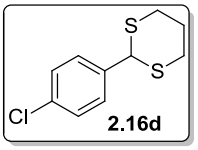
Compound **2.16b** was synthesized from 4-methylbenzaldehyde by following general dithine protection procedure.[21] White solid, mp 86-87 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 (d, J = 8.0 Hz, 2H), 7.16 (d, J = 8.0 Hz, 2H), 5.16 (s, 1H), 3.06 (dt, J = 14.4, 2.0 Hz, 2H), 2.90 (td, J = 14.4, 3.6 Hz, 2H), 2.35 (s, 3H), 2.19-2.14 (m, 1H), 1.98-1.87 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.2, 136.1, 129.3, 127.5, 51.1, 32.0, 25.0, 21.1.

2-(4-Methoxyphenyl)-1,3-dithiane (2.16c)



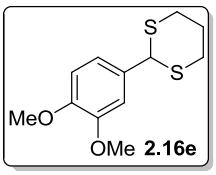
Compound **2.16c** was synthesized from 4-methoxybenzaldehyde by following general dithine protection procedure.[21] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (d, J = 8.8 Hz, 2H), 6.86 (d, J = 8.8 Hz, 2H), 5.13 (s, 1H), 3.78 (s, 3H), 3.04 (td, J = 14.4, 2.4 Hz, 2H), 2.89 (dt, J = 14.0, 3.6 Hz, 2H), 2.18-2.12 (m, 1H), 1.97-1.84 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.5, 131.2, 128.9, 114.0, 55.2, 50.7, 32.1, 25.0.

2-(4-Chlorophenyl)-1,3-dithiane (2.16d)



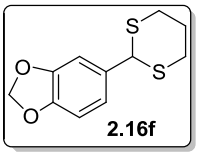
Compound **2.16d** was synthesized from 4-chlorobenzaldehyde by following general dithine protection procedure.[21] White solid, mp 90-91 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (d, J = 8.8 Hz, 2H), 7.31 (d, J = 8.8 Hz, 2H), 5.14 (s, 1H), 3.05 (dt, J = 14.4, 2.4 Hz, 2H), 2.90 (td, J = 14.4, 4.0 Hz, 2H), 2.20-2.13 (m, 1H), 1.98-1.86 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.6, 134.1, 129.1, 128.9, 50.5, 31.9, 24.9.

2-(3,4-Dimethoxyphenyl)-1,3-dithiane (2.16e)



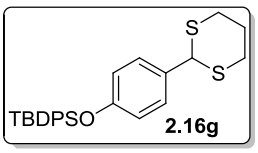
Compound **2.16e** was synthesized from 3,4-dimethoxybenzaldehyde by following general dithine protection procedure.[22] White solid, mp 95-96 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.02-7.00 (m, 2H), 6.80 (d, J = 8.0 Hz, 1H), 5.12 (s, 1H), 3.88 (s, 3H), 3.84 (s, 3H), 3.07-3.00 (m, 2H), 2.88 (td, J = 14.4, 3.2 Hz, 2H), 2.16-2.12 (m, 1H), 1.95-1.85 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.9, 131.5, 119.9, 110.9, 110.6, 55.8, 51.1, 32.1, 24.9.

5-(1,3-Dithian-2-yl)benzo[*d*][1,3]dioxole (2.16f)



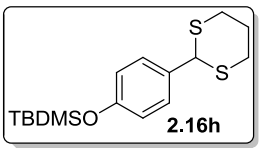
Compound **2.16f** was synthesized from benzo[d][1,3]dioxole-5-carbaldehyde by following general dithine protection procedure.[22] White solid, mp 93-94 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.99 (d, J = 1.6 Hz, 1H), 6.95 (dd, J = 8.0, 1.6 Hz, 1H), 6.88 (d, J = 8.0 Hz, 1H) 5.96 (s, 2H), 5.10 (s, 1H), 3.05 (dt, J = 14.4, 2.4 Hz, 2H), 2.90 (td, J = 14.4, 4.0 Hz, 2H), 2.19-2.14 (m, 1H), 1.96-1.90 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ147.6, 147.4, 132.8, 121.1, 108.2, 101.1, 51.0, 32.0, 24.8.

(4-(1,3-Dithian-2-yl)phenoxy)(tert-butyl)diphenylsilane (2.16g)



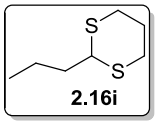
Compound **2.16g** was synthesized following a published procedure.[23] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, J = 7.2 Hz, 4H), 7.42-7.32 (m, 6H), 7.18 (d, J = 8.4 Hz, 2H), 6.71(d, J = 8.4 Hz, 2H), 5.04 (s, 1H), 3.00-2.94 (m, 2H), 2.83-2.79 (m, 2H), 2.09-2.05 (m, 1H), 1.88-1.79 (m, 1H), 1.08 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.5, 135.4, 134.7, 132.6, 131.5, 129.8, 128.6, 127.7, 119.7, 50.7, 32.0, 26.4, 24.9, 19.3.

(4-(1,3-Dithian-2-yl)phenoxy)(tert-butyl)dimethylsilane (2.16h)



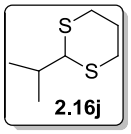
Compound **2.16h** was synthesized following a reprorted procedure.[24] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 (d, J = 8.4 Hz, 2H), 6.79 (d, J = 8.4 Hz, 2H), 5.13 (s, 1H), 3.08-3.02 (m, 2H), 2.91-2.88 (m, 2H), 2.15 (t, J = 7.2 Hz, 1H), 1.96-1.86 (m, 1H), 0.98 (s, 9H), 0.20 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.7, 131.8, 128.8, 120.1, 50.8, 32.1, 25.6, 25.0, 18.1, -4.5.

2-Propyl-1,3-dithiane (2.16i)



Compound **2.16i** was synthesized following general dithine protection procedure.[25] ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.08-4.03 (m, 1H), 2.90-2.80 (m, 4H), 2.15–2.09 (m, 1H), 1.89-1.82 (m, 1H), 1.77-1.67 (m, 2H), 1.57-1.48 (m, 2H), 0.93 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 46.7, 37.1, 30.1, 25.7, 19.5, 13.4.

2-Isopropyl-1,3-dithiane (2.16j)

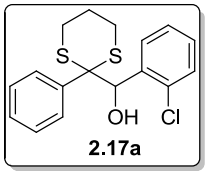


Compound **2.16j** was synthesized following general dithine protection procedure.[26] ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.05 (dd, J = 5.2, 1.6 Hz, 1H), 2.93-2.83 (m, 4H), 2.13-2.01 (m, 2H), 1.86-1.81 (m, 1H), 1.11 (d, J = 1.6 Hz, 3H), 1.09 (d, J = 1.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 56.2, 33.4, 30.7, 26.1, 19.8.

General procedure for synthesis of 2.17a-2.17p

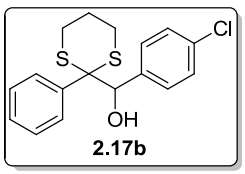
To a solution of dithiane **2.16a-2.16h** (1 equiv) in dry THF, *n*-BuLi (1.6 M) (1.1 equiv) was added at -78 ºC. After stirring at the same temperature for 2 h, aromatic aldehyde **2.15** (1.1 equiv) was added slowly and the reaction was continued for 1 h. After completion of the reaction, aquous NH_4Cl was added to the reaction mixture. Solvent THF was evaporated and the residue was extracted with ethyl acetate. The organic layer was dried over anhydrous Na_2SO_4, concentrated and purified by column chromatography using mixture of ethyl acetate and hexanes.

(2-Chlorophenyl)(2-phenyl-1,3-dithian-2-yl)methanol (2.17a)



Compound **2.17a** was synthesized from **2.16a** and **2.15g** by following the above general procedure. White solid, mp 91-92 °C; Yield: 99%; R_f = 0.5 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74-7.72 (m, 2H), 7.28-7.26 (m, 3H), 7.16-7.08 (m, 4H), 5.55 (s, 1H), 3.04 (bs, 1H), 2.79-2.69 (m, 3H), 2.61-2.54 (m, 1H), 1.95-1.86 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.9, 135.3, 134.2, 130.6, 130.4, 129.0, 128.5, 128.0, 127.5, 75.7, 66.6, 27.3, 26.7, 24.5; IR (KBr): υ 3447, 1478, 1065, 1034, 748 cm^{-1}; $C_{17}H_{17}ClOS_2$: calcd. C 60.61, H 5.09; found C 60.56, H 5.15.

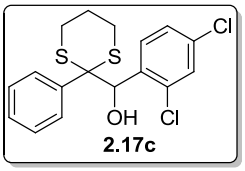
(4-Chlorophenyl)(2-phenyl-1,3-dithian-2-yl)methanol (2.17b)



Compound **2.17b** was synthesized from **2.16a** and **2.15b** by following the above general procedure. White solid, mp 83-86 ºC; Yield: 90%; R_f = 0.34 in 1:5 EtOAc/hexanes; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.66 (d, J = 8.0 Hz, 2H), 7.32-7.26 (m, 3H), 7.09 (d, J = 8.5 Hz, 2H), 6.78 (d, J = 8.0 Hz, 2H), 4.95 (s,

1H), 3.03 (s, 1H), 2.76-2.62 (m, 4H), 1.94-1.91 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.2, 135.7, 133.8, 130.3, 129.5, 128.3, 127.7, 127.1, 80.3, 66.3, 27.2, 26.9, 24.6; IR (neat): υ 3445, 3057, 1593, 1489, 1053, 698 cm^{-1}; $C_{17}H_{17}ClOS_2$: calcd. C 60.61, H 5.09; found C 60.76, H 5.15.

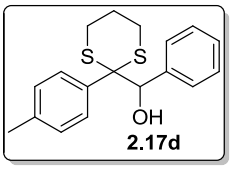
(2,4-Dichlorophenyl)(2-phenyl-1,3-dithian-2-yl)methanol (2.17c)



2.17c

Compound **2.17c** was synthesized from **2.16a** and **2.15d** by following the above general procedure. White solid, mp 105-107 ºC; Yield: 88%; R_f = 0.52 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74-7.72 (m, 2H), 7.33-7.29 (m, 3H), 7.20 (s, 1H), 7.09 (s, 2H), 5.49 (d, *J* = 3.2 Hz, 1H), 3.10 (d, *J* = 3.2 Hz, 1H), 2.81-2.71 (m, 3H), 2.63-2.56 (m, 1H), 1.97-1.88 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.8, 135.1, 134.3, 134.0, 131.4, 130.5, 128.4, 128.3, 127.8, 126.0, 75.4, 66.6, 27.5, 26.8, 24.6; IR (KBr): υ 3515, 2953, 1586, 1470, 1275, 1044, 822 cm^{-1}; $C_{17}H_{16}Cl_2OS_2$: calcd. C 54.98, H 4.34; found 54.85, H 4.31.

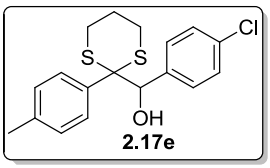
Phenyl(2-*p*-tolyl-1,3-dithian-2-yl)methanol (2.17d)



2.17d

Compound **2.17d** was synthesized from **2.16b** and **2.15e** by following the above general procedure. White solid, mp 96-97 °C; Yield: 81%; R_f = 0.29 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, *J* = 8.0 Hz, 2H), 7.21 (t, *J* = 7.2 Hz, 1H), 7.14 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 8.4 Hz, 2H), 6.89 (d, *J* = 7.2 Hz, 2H), 4.97 (s, 1H), 2.74-2.60 (m, 4H), 2.35 (s, 3H), 1.93-1.87 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.3, 137.2, 134.2, 130.4, 128.9, 128.2, 128.0, 126.9, 81.0, 66.3, 27.2, 26.9, 24.8, 20.9; IR (KBr): υ 3376, 1502, 1039, 696 cm^{-1}; $C_{18}H_{20}OS_2$: calcd. C 68.31, H 6.37; found C 68.17, H 6.45.

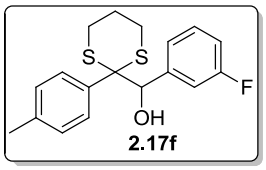
(4-Chlorophenyl)(2-p-tolyl-1,3-dithian-2-yl)methanol (2.17e)



2.17e

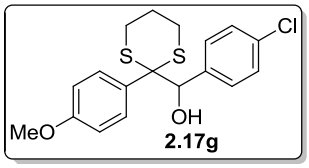
Compound **2.17e** was synthesized from **2.16b** and **2.15b** by following the general procedure. White solid, mp 112-114 °C; Yield: 84%; R_f = 0.29 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53 (d, *J* = 8.0 Hz, 2H), 7.12-7.07 (m, 4H), 6.79 (d, *J* = 8.0 Hz, 2H), 4.91 (s, 1H), 3.18 (s, 1H,), 2.72-2.60 (m, 4H), 2.36 (s, 3H), 1.91-1.89 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.3, 135.7, 133.8, 133.5, 130.2, 129.4, 128.8, 126.9, 80.1, 65.9, 27.0, 26.7, 24.6, 20.8; IR (KBr): υ 3431, 2909, 1680, 1505, 1277, 1038, 773 cm^{-1}; $C_{18}H_{19}ClOS_2$: calcd. C 61.61, H 5.46; found C 61.72, H 5.56.

(3-Fluorophenyl)(2-*p*-tolyl-1,3-dithian-2-yl)methanol (2.17f)



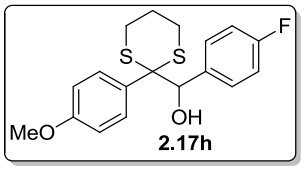
Compound **2.17f** was synthesized from **2.16b** and **2.15f** by following the general procedure. White solid, mp 94-95 °C; Yield: 95%; R_f = 0.28 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (d, J = 8.4 Hz, 2H), 7.12-7.07 (m, 3H), 6.92-6.88 (m, 1H), 6.68 (d, J = 7.6 Hz, 1H), 6.62-6.59 (m, 1H), 4.95 (s, 1H), 3.02 (s, 1H), 2.73-2.65 (m, 4H), 2.36 (s, 3H), 1.94-1.91 (m,2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.8 (d, J = 243.2 Hz), 139.9 (d, J = 7.8 Hz), 137.5, 134.1, 130.2, 129.0, 128.2 (d, J = 8.1 Hz), 123.9, 115.2 (d, J = 22.5 Hz), 114.8 (d, J = 20.9 Hz), 80.4, 66.2, 27.2, 26.9, 24.7, 20.9; IR (KBr): υ 3364, 2909, 1613, 1590, 1487, 1452, 1244, 1051, 872, 696 cm^{-1}; $C_{18}H_{19}FOS_2$: calcd. C 64.64, H 5.73; found C 64.53, H 5.81.

(4-Chlorophenyl)(2-(4-methoxyphenyl)-1,3-dithian-2-yl)methanol (2.17g)



Compound **2.17g** was synthesized from **2.16c** and **2.15b** by following the general procedure. Colorless gummy liquid; Yield: 95%; R_f = 0.18 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (d, J = 8.8 Hz, 2H), 7.09 (d, J = 8.8 Hz, 2H), 6.82 (d, J = 8.8 Hz, 2H), 6.79 (d, J = 8.8 Hz, 2H), 4.92 (s, 1H), 3.81 (s, 3H), 3.10-3.08 (m, 1H), 2.74-2.64 (m, 3H), 1.91-1.89 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.9, 135.8, 133.7, 131.7, 129.5, 128.8, 127.1, 113.4, 80.3, 65.8, 55.2, 27.1, 26.8, 24.7; IR (neat): υ 3436, 2928, 1605, 1505, 1250, 1034, 835 cm^{-1}; $C_{18}H_{19}ClO_2S_2$: calcd. C 58.92, H 5.22; found C 58.79, H 5.32.

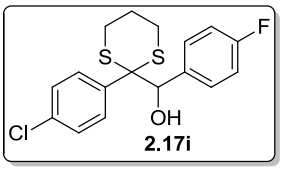
(4-Fluorophenyl)(2-(4-methoxyphenyl)-1,3-dithian-2-yl)methanol (2.17h)



Compound **2.17h** was synthesized from **2.16c** and **2.15a** by following the general procedure. White solid, mp 103-104 °C; Yield: 99%; R_f = 0.45 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (d, J = 9.2 Hz, 2H), 6.83-6.80 (m, 6H), 4.93 (s, 1H), 3.81 (s, 3H), 2.74-2.59 (m, 4H), 1.90-1.89 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.3 (d, J = 245 Hz), 158.8, 133.0, 131.7, 129.7 (d, J = 8.0 Hz), 128.8, 113.7 (d, J = 21.0 Hz), 113.2, 80.2, 65.80, 55.1, 27.0, 26.7, 24.6; IR (KBr): υ 3443, 2911, 1603, 1506, 1294, 1250, 1038, 833 cm^{-1}; $C_{18}H_{19}FO_2S_2$: calcd. C 61.69, H 5.46; found: C 61.75, H 4.38.

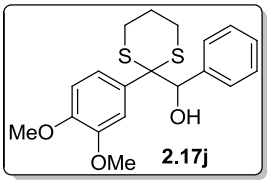
(2-(4-Chlorophenyl)-1,3-dithian-2-yl)(4-fluorophenyl)methanol (2.17i)

Compound **2.17i** was synthesized from **2.16d** and **2.15a** by following the general procedure. White solid, mp 94-95 ºC; Yield: 95%; R_f = 0.52 in 1:5 EdtOAc/hexanes (double elution); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.60 (d, J = 7.0 Hz, 2H), 7.27 (d, J = 7.0 Hz, 2H), 6.85-6.83 (m, 4H), 4.96 (d, J = 1.5



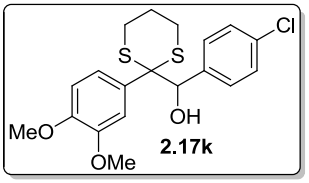
Hz, 1H), 2.76-2.72 (m, 2H), 2.68-2.59 (m, 2H), 1.95-1.90 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.6 (d, J = 245.4 Hz), 136.0, 133.7, 132.8, 132.1, 129.8 (d, J = 8.1 Hz), 128.2, 114.0 (d, J = 21.2 Hz), 80.2, 65.7, 27.2, 26.9, 24.6; IR (KBr): υ 3436, 2911, 1904, 1603, 1510, 1223 cm^{-1}; $C_{17}H_{16}ClFOS_2$: calcd. C 57.53, H 4.54; found C 57.65, H 4.51.

(2-(3,4-Dimethoxyphenyl)-1,3-dithian-2-yl)(phenyl)methanol (2.17j)



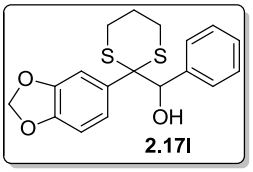
Compound **2.17j** was synthesized from **2.16e** and **2.15e** by following the general procedure. White solid, mp 138-140 ºC; Yield: 85% ; R_f = 0.36 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55 (d, J = 8.4, 2.0 Hz, 1H), 7.21 (t, J = 7.6 Hz, 1H), 7.14 (t, J = 7.6 Hz, 2H), 7.05 (d, J = 2.0 Hz, 1H), 6.90 (d, J = 7.2 Hz, 2H), 6.81 (d, J = 8.4 Hz, 1H), 4.95 (s, 1H), 3.89 (s, 3H), 3.63 (s, 3H), 2.74-2.63 (m, 4H), 1.96-1.88 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 148.21, 148.20, 137.3, 129.3, 128.2, 127.9, 126.9, 123.0, 113.8, 110.2, 81.0, 66.4, 55.72, 55.66, 27.3, 26.9, 24.7; IR (KBr): υ 3497, 1601, 1510, 1257, 1028, 768 cm^{-1};$C_{19}H_{22}O_3S_2$: calcd. C 62.95, H 6.12; found C 62.85, H 6.18.

(4-Chlorophenyl)(2-(3,4-dimethoxyphenyl)-1,3-dithian-2-yl)methanol (2.17k)



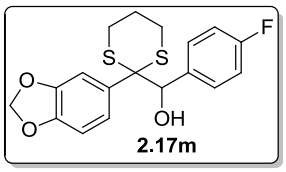
Compound **2.17k** was synthesized from **2.16e** and **2.15b** by following the general procedure. White semisolid; Yield: 70%; R_f = 0.48 in 1:3 EtOAc/hexanes (triple elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29 (dd, J = 8.4, 2.0 Hz, 1H), 7.11 (d, J = 8.4 Hz, 2H), 7.07 (d, J = 2.0 Hz, 1H), 6.83-6.79 (m, 3H), 4.90 (d, J = 3.2 Hz, 1H), 3.90 (s, 3H), 3.68 (s, 3H), 3.07 (d, J = 3.2 Hz, 1H), 2.76-2.66 (m, 4H), 1.94-1.88 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.39, 148.35, 135.8, 133.8, 129.5, 129.2, 127.1, 123.0, 113.6, 110.4, 80.4, 66.3, 55.79, 55.75, 27.3, 26.9, 24.6; IR (neat): υ 3447.0, 1645.4, 1508.5, 1257.7, 1024.3 cm^{-1}; $C_{19}H_{21}ClO_3S_2$: calcd. C 57.49, H 5.33; found C 57.41, H 5.28.

(2-(Benzo[*d*][1,3]dioxol-5-yl)-1,3-dithian-2-yl)(phenyl)methanol (2.17l)



Compound **2.17l** was synthesized from **2.16f** and **2.15e** by following the general procedure. White solid, mp 108-109 ºC; Yield: 95%; R_f = 0.21 in 1:5 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26 (s, 1H), 7.20 (d, J = 7.2 Hz, 1H), 7.17-7.16 (m, 3H), 6.93 (d, J = 7.6 Hz, 2H), 6.70 (d, J = 8.0 Hz, 1H), 5.97 (d, J = 4.4 Hz, 2H), 4.93 (s, 1H), 2.95 (bs, 1H), 2.71-2.62 (m, 4H), 1.92-1.87 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.7, 146.8, 137.3, 131.2, 128.12, 128.10, 127.0, 124.5, 110.9, 107.5, 101.2, 81.1, 66.2, 27.2, 27.0, 24.7; IR (KBr): υ 3397, 1481, 1236, 1034, 698 cm^{-1}; $C_{18}H_{18}O_3S_2$: calcd. C 62.40, H 5.24; found C 62.56, H 5.16.

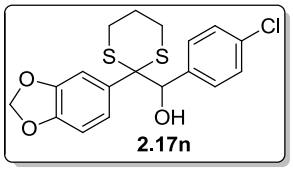
(2-(Benzo[*d*][1,3]dioxol-5-yl)-1,3-dithian-2-yl)(4-fluorophenyl)methanol (2.17m)



2.17m

Compound **2.17m** was synthesized from **2.16f** and **2.15a** by following the general procedure. White gummy solid; Yield: 96%; R_f = 0.36 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24 (d, *J* = 2.0 Hz, 1H), 7.12 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.90-6.80 (m, 4H), 6.70 (d, *J* = 8.0 Hz, 1H), 5.97 (d, *J* = 1.2 Hz, 1H), 5.96 (d, *J* = 1.2 Hz, 1H), 4.89 (s, 1H), 3.10 (bs, 1H), 2.72-2.64 (m, 4H), 1.92-1.87 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.5 (d, *J* = 244.5 Hz), 147.9, 147.0, 133.2, 131.2, 129.8 (d, *J* = 8.0 Hz), 124.5, 113.9 (d, *J* = 21.2 Hz), 110.8, 107.6, 101.4, 80.4, 66.2, 27.3, 27.0, 24.7; IR (KBr): υ 3428, 2915, 1603, 1483, 1238, 1042, 806 cm^{-1}; $C_{18}H_{17}FO_3S_2$: calcd. C 59.32, H 4.70; found C 59.45, H 4.61.

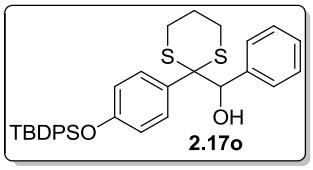
(2-(Benzo[*d*][1,3]dioxol-5-yl)-1,3-dithian-2-yl)(4-chlorophenyl)methanol (2.17n)



2.17n

Compound **2.17n** was synthesized from **2.16f** and **2.15b** by following the general procedure. White solid, mp 104-106 ºC; Yield: 90%; R_f = 0.17 in 1:5 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26 (d, *J* = 8.0 Hz, 1H), 7.11-7.09 (m, 3H), 6.83 (d, *J* = 8.0 Hz, 2H), 6.69 (d, *J* = 8.4 Hz, 1H), 5.97 (s, 2H), 4.87 (s, 1H), 3.16 (s, 1H), 2.69-2.63 (m, 4H), 1.89-1.84 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.7, 146.8, 135.8, 133.6, 130.9, 129.4, 127.0, 124.3, 110.6, 107.4, 101.2, 80.2, 65.9, 27.1, 26.8, 24.5; IR (neat): υ 3468, 2907, 1482, 1429, 1238, 1040, 934 cm^{-1}; $C_{18}H_{17}ClO_3S_2$: calcd. C 56.76, H 4.50; found C 56.65, H 4.58.

(2-(4-((Tert-butyldiphenylsilyl)oxy)phenyl)-1,3-dithian-2-yl)(phenyl)methanol (2.17o)

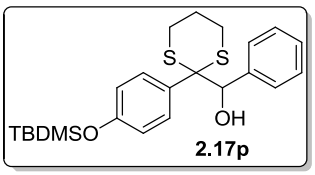


2.17o

Compound **2.17o** was synthesized from **2.16g** and **2.15e** by following the general procedure. Yellow liquid; Yield: 75%; R_f = 0.20 in 1:5 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73-7.72 (m, 4H), 7.45-7.34 (m, 9H), 7.07-7.03 (m, 2H), 6.77 (d, *J* = 7.6 Hz, 2H), 6.68 (d, *J* = 8.8 Hz, 2H), 4.99 (d, *J* = 3.6 Hz, 1H), 2.89 (d, *J* = 4.0 Hz, 1H), 2.67-2.60 (m, 4H) 1.91-1.89 (m, 2H), 1.12 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.1, 137.2, 135.5, 132.9, 132.8, 131.6, 129.9, 129.4, 128.1, 127.8, 127.7, 126.8, 119.3, 80.8, 66.0, 27.1, 26.8, 26.5, 24.8, 19.5, 14.1; IR (neat): υ 2953, 1506, 1249, 920, 701 cm^{-1}; HRMS (ESI): calcd for $C_{33}H_{36}O_2S_2Si$ $(M+Na)^+$ 579.1824; found 579.1824.

(2-(4-((Tert-butyldimethylsilyl)oxy)phenyl)-1,3-dithian-2-yl)(phenyl)methanol (2.17p)

Compound **2.17p** was synthesized from **2.16h** and **2.15e** by following the general procedure. Gummy liquid; Yield: 85%; R_f = 0.26 in 1:5 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (d, *J* = 8.8 Hz, 2H), 7.21-7.18 (m, 1H), 7.11 (t, *J* = 7.6 Hz, 2H), 6.85 (d, *J* = 7.6 Hz, 2H), 6.74 (d, *J* = 8.8 Hz,

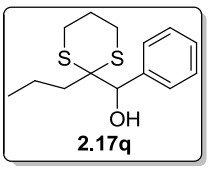


2H), 4.95 (s, 1H), 3.02 (bs, 1H), 2.74-2.62 (m, 4H), 1.93-1.91 (m, 2H), 0.99 (s, 9H), 0.21 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.1, 137.3, 131.7, 129.8, 128.4, 128.2, 127.9, 126.9, 125.9, 119.6, 80.9, 66.1, 27.2, 26.9, 25.7, 18.3, -4.4; IR (neat): υ 3446, 2926, 1605, 1496, 1266, 909, 696 cm^{-1}; HRMS (ESI): calcd for $C_{23}H_{32}O_2S_2Si$ $(M+Na)^+$ 455.1511; found 455.1512.

Procedure for synthesis of 2.17q and 2.17r

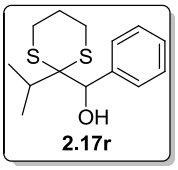
To a solution of dithiane **2.16i**/**2.16j** (1 equiv) in dry THF (5 mL/ 1 mmol), *n*-BuLi (1.6 M, 1.1 equiv) was added at 0 °C. After stirring at the same temperature for 2 h, reaction mixture was cooled to -78 ºC. Aromatic aldehyde **2.15** (1.1 equiv) was added slowly and reaction continued for 1 h. After completion of the reaction, aquous NH_4Cl was added to the reaction mixture. Solvent THF was evaporated and the residue was extracted with ethyl acetate. The organic layer was dried over anhydrous Na_2SO_4, concentrated and purified by column chromatography using mixture of ethyl acetate and hexanes.

Phenyl(2-propyl-1,3-dithian-2-yl)methanol (2.17q)



Compound **2.17q** was synthesized from **2.16i** and **2.15e** by following the general procedure. Pale yellow solid, mp 96-98 °C; Yield: 80%; R_f = 0.35 in 1:10 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 (d, J = 6.4 Hz, 2H), 7.34-7.28 (m, 3H), 5.14 (s, 1H), 3.37 (s, 1H), 3.15 (td, J = 14.4, 2.8 Hz, 1H), 2.98 (td, J = 14.4, 2.8 Hz, 1H), 2.70-2.61 (m, 2H), 2.10-2.07 (m, 1H), 1.89–1.75 (m, 2H), 1.63-1.48 (m, 2H), 1.31-1.24 (m, 1H), 0.83 (t, J = 7.6 Hz, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.7, 128.5, 127.6, 127.1, 73.6, 59.1, 36.6, 26.4, 25.3, 24.1, 17.6, 14.3; IR (KBr): υ 3430, 2958, 2904, 1496, 1425, 1282, 1041, 904, 767 cm^{-1}; HRMS (ESI): calcd for $C_{14}H_{20}OS_2$ $(M+Na)^+$ 291.0853; found 291.0854.

(2-Isopropyl-1,3-dithian-2-yl)(phenyl)methanol (2.17r)

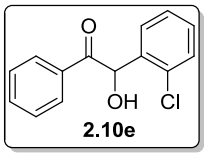


Compound **2.17r** was synthesized from **2.16j** and **2.15e** by following the general procedure. White solid, mp 70-72 °C; Yield: 82%; R_f = 0.36 in 1:10 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (d, J = 7.2 Hz, 2H), 7.34-7.25 (m, 3H), 5.22 (s, 1H), 3.45 (bs, 1H), 3.03-2.96 (m, 1H), 2.72-2.56 (m, 3H), 2.05-1.99 (m, 1H), 1.94-1.81 (m, 2H), 1.17 (d, J = 6.4 Hz, 3H), 1.10 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.1, 128.6, 127.6, 127.3, 75.1, 63.4, 34.4, 26.9, 25.2, 24.2, 19.4, 18.6; IR (KBr): υ 3430, 2920, 2893, 1457, 1391, 1189, 1041, 756, 701 cm^{-1}; HRMS (ESI): calcd for $C_{14}H_{20}OS_2$ $(M+Na)^+$ 291.0853; found 291.0854.

General dithiane deprotection procedure for synthesis of 2.10e- 2.10x

To a solution of *N*-chlorosuccinimide (4.0 equiv) and $AgNO_3$ (4.5 equiv) in acetonitrile/water (4:1) dithiane alcohol **2.17a-2.17r** (1 equiv) was added at room temperature. The mixture was stirred at room temperature. After completion of the reaction, aqueous $Na_2S_2O_3$ solution was added. Compound was extracted with EtOAc, dried over anhydrous Na_2SO_4, concentrated and purified by column chromatography.

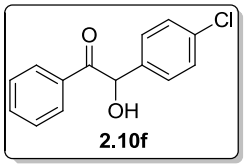
2-(2-Chlorophenyl)-2-hydroxy-1-phenylethanone (2.10e)



2.10e

Compound **2.10e** was synthesized from **2.17a** by following the general dithiane deprotection procedure.[27] Pale yellow solid, mp 79-80 ºC; Yield: 52%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (d, J = 8.0 Hz, 2H), 7.53 (t, J = 8.0 Hz, 1H), 7.43-7.38 (m, 3H), 7.24-7.16 (m, 2H), 7.13-7.10 (m, 1H), 6.39 (d, J = 5.6 Hz, 1H), 4.59 (d, J = 5.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.7, 136.7, 134.1, 133.6, 133.1, 130.3, 130.0, 129.2, 128.85, 128.80, 127.7, 72.8.

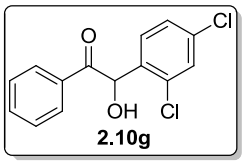
2-(4-Chlorophenyl)-2-hydroxy-1-phenylethanone (2.10f)



2.10f

Compound **2.10f** was synthesized from **2.17b** by following the general dithiane deprotection procedure.[28] White solid, mp 115-117 ºC; Yield 60%; R_f = 0.54 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 (d, J = 8.0 Hz, 2H), 7.55 (t, J = 7.2 Hz, 1H), 7.42 (t, J = 8.0 Hz, 2H), 7.31-7.29 (m, 4H), 5.94 (s, 1H), 4.57 (s, 1H).

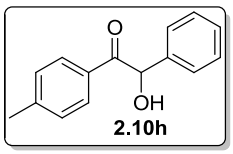
2-(2,4-Dichlorophenyl)-2-hydroxy-1-phenylethanone (2.10g)



2.10g

Compound **2.10g** was synthesized from **2.17c** by following the general dithiane deprotection procedure. White solid, mp 69-71 ºC; Yield 71%; R_f = 0.50 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, J = 7.6 Hz, 2H), 7.52 (t, J = 7.6 Hz, 1H), 7.41-7.37 (m, 3H), 7.13 (dd, J = 8.4, 2.0 Hz, 1H), 7.04 (d, J = 8.4 Hz, 1H), 6.32 (s, 1H), 4.64 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.2, 135.3, 135.1, 134.2, 132.9, 130.01, 130.00, 128.77, 128.72, 128.0, 72.1; IR (KBr): υ 3428, 1682, 1590, 1244, 972, 748, 687 cm^{-1}; $C_{14}H_{10}Cl_2O_2$: calcd. C 59.81, H 3.59; found C 59.73, H 3.65.

2-Hydroxy-2-phenyl-1-(*p*-tolyl)ethanone (2.10h)

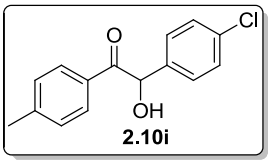


2.10h

Compound **2.10h** was synthesized from **2.17d** by following the general dithiane deprotection procedure.[29] White solid, mp 114-115 ºC; Yield: 49%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, J = 8.0 Hz, 2H), 7.34-7.24 (m, 5H), 7.17 (d, J= 8.0 Hz, 2H), 5.92 (d, J = 5.6 Hz, 1H), 4.61 (d, J = 5.6 Hz, 1H), 2.33 (s, 3H); ^{13}C NMR (100 MHz,

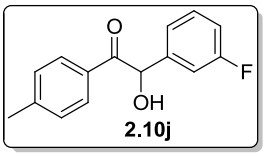
$CDCl_3$): δ 198.4, 145.0, 139.2, 130.8, 129.3, 129.0, 128.4, 127.7, 76.0, 21.7.

2-(4-Chlorophenyl)-2-hydroxy-1-*p*-tolylethanone (2.10i)



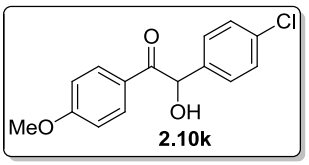
Compound **2.10i** was synthesized from **2.17e** by following the general dithiane deprotection procedure. White solid, mp 86-88 ºC; Yield 60%; R_f = 0.62 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, J = 8.0 Hz, 2H), 7.27 (s, 4H), 7.20 (d, J = 8.0 Hz, 2H), 5.91 (d, J = 4.4 Hz, 1H), 4.61 (d, J = 5.2 Hz, 1H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.1, 145.3, 137.8, 134.4, 130.6, 129.5, 129.23, 129.20, 129.0, 75.2, 21.7; IR (neat): υ 3443, 1672, 1608, 1489, 1258, 1087, 812, 737 cm^{-1}; $C_{15}H_{13}ClO_2$: calcd. C 69.10, H 5.03; found C 68.91, H 5.12.

2-(3-Fluorophenyl)-2-hydroxy-1-(*p*-tolyl)ethanone (2.10j)



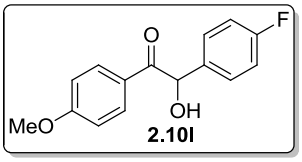
Compound **2.10j** was synthesized from **2.17f** by following the general dithiane deprotection procedure. White semisolid; Yield: 65%; R_f = 0.33 in 1:5 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, J = 8.0 Hz, 2H), 7.32-7.28 (m, 1H), 7.23 (d, J = 8.0 Hz, 2H), 7.15 (d, J = 8.0 Hz, 1H), 7.08-7.04 (m, 1H), 6.99-6.94 (m, 1H), 5.94 (s, 1H), 4.66 (bs, 1H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.0, 163.0 (d, J = 246.1 Hz), 145.3, 141.6 (d, J = 6.8 Hz), 130.7, 130.6 (d, J = 8.1 Hz), 129.5, 129.3, 123.4 (d, J = 32.7 Hz), 115.5 (d, J = 21.0 Hz), 114.7 (d, J = 21.9 Hz), 75.3 (d, J = 1.4 Hz), 21.7; IR (KBr): υ 3416, 1674, 1609, 1240, 920 cm^{-1}; $C_{15}H_{13}FO_2$: calcd. C 73.76, H 5.36; found C 73.61, H 5.31.

2-(4-Chlorophenyl)-2-hydroxy-1-(4-methoxyphenyl)ethanone (2.10k)



Compound **2.10k** was synthesized from **2.17g** by following the general dithiane deprotection procedure.[30] White solid, mp 89-90 ºC; Yield: 90%; R_f = 0.38 in 1:10 EtOAc/hexanes (triple elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (d, J = 8.8 Hz, 2H), 7.26 (s, 4H), 6.85 (d, J = 8.8 Hz, 2H), 5.88 (s, 1H), 4.75 (bs, 1H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.6, 164.1, 138.0, 134.2, 131.4, 129.1, 128.9, 125.8, 113.9, 74.8, 55.3; IR (neat): υ 3441, 2926, 1669, 1603, 1256, 1173, 1087 cm^{-1}; $C_{15}H_{13}ClO_3$: calcd. C 65.11, H 4.74; found C 65.26, H 4.71.

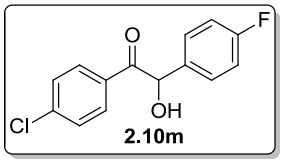
2-(4-Fluorophenyl)-2-hydroxy-1-(4-methoxyphenyl)ethanone (2.10l)



Compound **2.10l** was synthesized from **2.17h** by following the general dithiane deprotection procedure. White solid, mp 76-77 ºC; Yield: 75%; R_f = 0.36 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, J = 8.8 Hz, 2H), 7.31 (dd, J = 8.4 Hz, 5.6 Hz, 2H), 7.00 (t, J = 8.4 Hz, 2H), 6.87 (d, J = 8.8 Hz, 2H), 5.88 (s, 1H), 4.66 (s, 1H), 3.81 (s, 3H); ^{13}C NMR (100

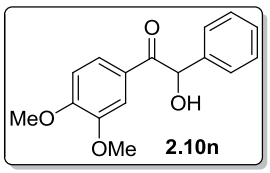
MHz, $CDCl_3$): δ 196.9, 164.1, 162.6 (d, J = 246.0 Hz), 135.5, 131.5, 129.4 (d, J = 8.2 Hz), 126.0, 116.0 (d, J = 21.6 Hz), 114.0, 74.9, 55.4; IR (neat): υ 3461, 1678, 1605, 1509, 1427, 1263, 1026 cm^{-1}; $C_{15}H_{13}FO_3$: calcd. C 69.22, H 5.03; found C 69.11, H 5.12.

1-(4-Chlorophenyl)-2-(4-fluorophenyl)-2-hydroxyethanone (2.10m)



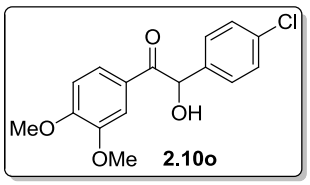
Compound **2.10m** was synthesized from **2.17i** by following the general dithiane deprotection procedure. White solid, mp 87-89 ºC; Yield: 53%; R_f = 0.21 in 1:10 EtOAc/hexanes (triple elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (d, J = 8.4 Hz, 2H), 7.35 (d, J = 8.4 Hz, 2H), 7.31-7.28 (m, 2H), 7.00 (d, J = 8.4 Hz, 2H), 5.91 (s, 1H), 4.46 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.6, 162.6 (d, J = 246.8 Hz), 140.4, 134.5, 131.6, 130.4, 129.4 (d, J = 8.3 Hz), 129.0, 116.1 (d, J = 21.7 Hz), 75.3; IR (neat): υ 3416, 1690, 1674, 1591, 1507, 1230, 1087, 816 cm^{-1};$C_{14}H_{10}ClFO_2$: calcd. C 63.53, H 3.81; found C 63.71, H 3.76.

1-(3,4-Dimethoxyphenyl)-2-hydroxy-2-phenylethanone (2.10n)



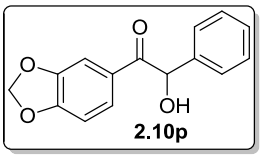
Compound **2.10n** was synthesized from **2.17j** by following the general dithiane deprotection procedure. White gummy semisolid; Yield: 90%; R_f = 0.25 in 1:5 EtOAc/hexanes (triple elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 (d, J = 8.4 Hz, 1H), 7.48 (d, J = 1.6 Hz, 1H), 7.35-7.24 (m, 5H), 6.77 (d, J = 8.4 Hz, 1H), 5.90 (d, J = 5.6 Hz, 1H), 4.67 (d, J = 6.0 Hz, 1H), 3.85 (s, 3H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.1, 153.7, 148.9, 139.6, 129.0, 128.3, 127.5, 126.2, 124.1, 111.0, 110.0, 75.7, 56.0, 55.8; IR (neat): υ 3414, 1665, 1586, 1516, 1271, 1020, 766 cm^{-1}; $C_{16}H_{16}O_4$: calcd. C 70.57, H 5.92; found C 70.65, H 5.88.

2-(4-Chlorophenyl)-1-(3,4-dimethoxyphenyl)-2-hydroxyethanone (2.10o)



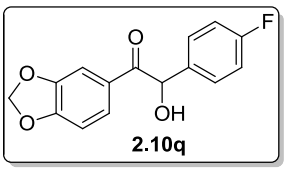
Compound **2.10o** was synthesized from **2.17k** by following the general dithiane deprotection procedure. White solid, mp 115-117 ºC; Yield: 65%; R_f = 0.25 in 1:3 EtOAc/hexanes (double elution); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.50-7.48 (m, 2H), 7.29-7.27 (m, 4H), 6.80 (d, J = 9.0 Hz, 1H), 5.89 (d, J = 5.5 Hz, 1H), 4.64 (d, J = 6.0 Hz, 1H), 3.90 (s, 3H), 3.88 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 196.8, 154.1, 149.2, 138.2, 134.3, 129.2, 128.9, 126.1, 124.1, 111.1, 110.1, 74.9, 56.0, 55.9; IR (KBr): υ 3426, 2934, 1659, 1586, 1275, 1009, 891 cm^{-1};$C_{16}H_{15}ClO_4$: calcd. C 62.65, H 4.93; found C 62.79, H 4.85.

(2-(Benzo[*d*][1,3]dioxol-5-yl)-2-hydroxy-2-phenylethanone (2.10p)



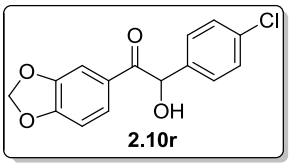
Compound **2.10p** was synthesized from **2.17l** by following the general dithiane deprotection procedure. White solid, mp 119-121 ºC; Yield: 68%; R_f = 0.37 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (d, *J* = 8.0 Hz, 1H), 7.39 (s, 1H), 7.32-7.26 (m, 5H), 6.76 (d, *J* = 8.0 Hz, 1H), 5.98 (s, 2H), 5.85 (d, *J* = 1.2Hz, 1H), 4.60 (bs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.8, 152.4, 148.1, 139.4, 129.1, 128.5, 127.9, 127.6, 125.9, 108.6, 108.0, 102.0, 75.8; IR (KBr): υ 3432, 1668, 1601, 1447, 1032, 802 cm^{-1}; $C_{15}H_{12}O_4$: calcd. C 70.31, H 4.72; found C 70.25, H 4.79.

1-(Benzo[*d*][1,3]dioxol-5-yl)-2-(4-fluorophenyl)-2-hydroxyethanone (2.10q)



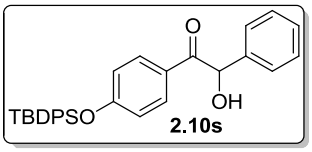
Compound **2.10q** was synthesized from **2.17m** by following the general dithiane deprotection procedure. White solid, mp 114-116 ºC; Yield: 71%; R_f = 0.31 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (d, *J* = 8.4 Hz, 1H), 7.37 (s, 1H), 7.31-7.27 (m, 2H), 7.00 (t, *J* = 8.4 Hz, 2H), 6.77 (d, *J* = 8.4 Hz, 1H), 6.00 (s, 2H), 5.85 (d, *J* = 5.6 Hz, 1H), 4.62-4.60 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.6, 162.6 (d, *J* = 246.1 Hz), 152.5, 148.2, 135.3, 129.4 (d, *J* = 8.3 Hz), 127.7, 125.8, 116.0 (d, *J* = 21.6 Hz), 108.6, 108.1, 102.0, 75.0; IR (KBr): υ 3422, 1665, 1603, 1505, 1447, 1260, 1034, 787 cm^{-1}; $C_{15}H_{11}FO_4$: calcd. C 65.69, H 4.04; found C 65.58, H 4.12.

1-(Benzo[*d*][1,3]dioxol-5-yl)-2-(4-chlorophenyl)-2-hydroxyethanone (2.10r)



Compound **2.10r** was synthesized from **2.17n** by following the general dithiane deprotection procedure. White foamysolid, mp 119-121 ºC; Yield: 95%; R_f = 0.25 in 1:5 EtOAc/hexanes(double elution); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.49 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.36 (d, *J* = 1.5 Hz, 1H), 7.30 (d, *J* = 8.5 Hz, 2H), 7.25 (d, *J* = 8.5 Hz, 2H), 6.78 (d, *J* = 8.0 Hz, 1H), 6.02 (s, 2H), 5.83 (d, *J* = 5.0 Hz, 1H), 4.59 (d, *J* = 5.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 196.5, 152.7, 148.3, 138.0, 134.5, 129.3, 129.0, 127.8, 125.9, 108.6, 108.2, 102.1, 75.1; IR (neat): υ 3468, 2907, 1665, 1482, 1238, 1040, 824 cm^{-1}; $C_{15}H_{11}ClO_4$: calcd. C 61.98, H 3.81; found C 61.88, H 3.75.

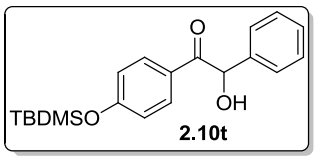
1-(4-((Tert-butyldiphenylsilyl)oxy)phenyl)-2-hydroxy-2-phenylethanone (2.10s)



Compound **2.10s** was synthesized from **2.17o** by following the general dithiane deprotection procedure. Yellow liquid; Yield: 70%; R_f = 0.61 in 1:3 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, *J* = 8.4 Hz, 2H), 7.64 (d, *J* = 8.0 Hz, 4H), 7.42 (d, *J* = 7.2 Hz, 2H), 7.33 (m, 4H), 7.28-7.22 (m, 5H), 6.71 (d, *J* = 8.8 Hz, 2H), 5.80 (d, *J* = 5.6 Hz, 1H), 4.60 (d, *J* = 6.0 Hz, 1H), 1.07 (s, 9H); ^{13}C NMR (100 MHz,

$CDCl_3$): δ 197.2, 160.6, 139.4, 135.5, 131.8, 131.3, 130.2, 129.0, 128.4, 127.9, 127.6, 126.6, 119.8, 75.7, 26.3, 19.4; IR (neat): υ 3441, 2931, 1666, 1600, 1271, 915, 827, 701 cm^{-1}; HRMS (ESI): calcd for $C_{30}H_{30}O_3Si$ $(M+Na)^+$ 489.1862; found 489.1864.

1-(4-((Tert-butyldimethylsilyl)oxy)phenyl)-2-hydroxy-2-phenylethanone (2.10t)

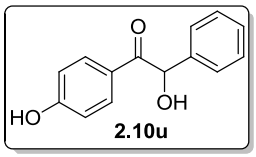


2.10t

Compound **2.10t** was synthesized from **2.17p** by following the general dithiane deprotection procedure. Gummy liquid; Yield: 69%; R_f = 0.57 in 1:5 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, J = 8.4 Hz, 2H), 7.38-7.26 (m, 5H), 6.82 (d, J = 8.8 Hz, 2H), 5.91 (d, J = 6.0 Hz, 1H), 4.74 (q, J = 6.0 Hz, 1H), 1.01 (s, 9H), 0.23 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.1, 160.8, 139.4, 131.4, 128.9, 128.2, 127.6, 126.6, 125.8, 119.8, 75.6, 25.3, 18.0, -4.6; IR (neat): υ 3452, 2926, 1671, 1600, 1277, 915, 838, 701 cm^{-1}; HRMS (ESI): calcd for $C_{20}H_{26}O_3Si$ $(M+Na)^+$ 365.1549; found 365.1550.

2-Hydroxy-1-(4-hydroxyphenyl)-2-phenylethanone (2.10u)

To a solution of the substrate **2.10t** (128 mg, 0.37 mmol) in THF (4 mL), TBAF in 1 M THF solution (0.41 mmol) and AcOH (26 µL) were added at 0 °C. The reaction mixture was allowed to stir at room temperature for 3 h. After completion of reaction brine solution was added and the product extracted with ethyl acetate and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure and the crude product was purified by column chromatography using mixture of ethyl acetate and hexanes to get pure benzoin **2.10u** (65 mg, 76%).[31]

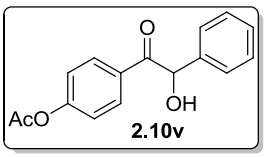


2.10u

White semisolid, mp 192-194 °C; Yield: 76%; R_f = 0.33 in 1:1 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$ + CD_3OD): δ 7.84 (d, J = 8.8 Hz, 2H), 7.40-7.27 (m, 5H), 6.78 (d, J = 8.4 Hz, 2H), 5.91 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.9, 162.4, 139.2, 131.6, 128.8, 128.2, 127.4, 125.0, 115.2, 75.3; IR (KBr): υ 3260, 2953, 1726, 1605, 1293, 975, 860, 701 cm^{-1}; HRMS (ESI): calcd for $C_{14}H_{12}O_3$ $(M+Na)^+$ 251.0684; found 251.0684.

4-(2-Hydroxy-2-phenylacetyl)phenyl acetate (2.10v)

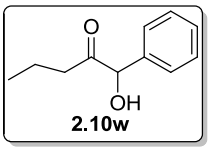
To a stirred solution of benzoin **2.10u** (44 mg, 0.19 mmol) and triethylamine (27 µL, 0.19 mmol) in dry THF (2 mL) at 0 °C, acetyl chloride (15 µL, 0.21 mmol) was added and maintained at the same temprature for 2 h. The precipitate was removed by filtration and the solvent was evoporated. The crude product was diluted with dichloromethane, washed with saturated sodium carbonate solution and water. The organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The crude product was purified by column chromatography using mixture of ethyl acetate and hexanes to get pure benzoin **2.10v** (49 mg, 93%).[32]



2.10v

Gummy liquid; Yield: 93%; R_f = 0.60 in 1:1 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, J = 8.4 Hz, 2H), 7.33-7.27 (m, 5H), 7.12 (d, J = 8.8 Hz, 2H), 5.91(d, J = 5.6 Hz, 1H), 4.56 (d, J = 6.0 Hz, 1H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.5, 168.6, 154.7, 138.7, 130.8, 129.2, 128.7, 127.7, 121.9, 76.2, 21.0; IR (neat): υ 3463, 2909, 1764, 1605, 1200, 975, 915, 701 cm^{-1}; HRMS (ESI): calcd for $C_{16}H_{14}O_4$ $(M+Na)^+$ 293.0790; found 293.0790.

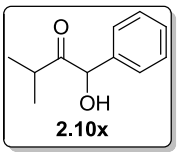
1-Hydroxy-1-phenylpentan-2-one (2.10w)



2.10w

Compound **2.10w** was synthesized from **2.17q** by following the general dithiane deprotection procedure.[33] Yellow liquid; yield: 72%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 – 7.26 (m, 5H), 5.07 (s, 1H), 4.40 (bs, 1H), 2.40-2.23 (m, 2H), 1.16 - 1.47 (m, 2H), 0.79 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 209.4, 138.0, 128.8, 128.5, 127.3, 79.6, 39.6, 17.0, 13.4.

1-Hydroxy-3-methyl-1-phenylbutan-2-one (2.10x)



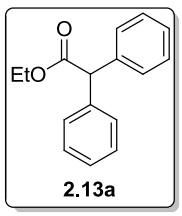
2.10x

Compound **2.10x** was synthesized from **2.17r** by following the general dithiane deprotection procedure.[34] White foamy solid; yield: 73%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 –7.26 (m, 5H), 5.22 (s, 1H), 4.40 (bs, 1H), 2.73-2.66 (m, 1H), 1.13 (d, J = 6.8 Hz, 3H), 0.83 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 213.5, 137.9, 128.9, 128.6, 127.6, 78.3, 35.9, 19.3, 17.9.

General procedure for the synthesis of α-diarylacetic esters 2.13a-2.13v

To a solution benzoin **2.10** (1 equiv) and triethyl orthoformate (3 equiv) in dry dichloromethane, triflic acid (1.2 equiv) was added at room temperature. Colorless solution turns into dark brown color. After completion of reaction (15-20 min), aqueous $NaHCO_3$ solution was added, the reaction mixture turns into colorless solution. Organic layer was washed with brine solution, dried over anhydrous Na_2SO_4, concentrated under reduced pressure. Crude residue was purified by column chromatography (silica gel, hexanes/ EtOAc) to get the pure product **2.13**.

Ethyl 2,2-diphenylacetate (2.13a)

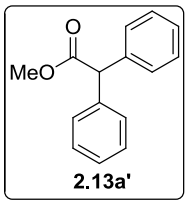


2.13a

Compound **2.13a** was obtained from **2.10a** by following the general procedure for the synthesis of α-diarylacetic esters.[35] White solid, mp 51-52 °C; Yield: 97%; R_f = 0.65 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32-7.25 (m, 10H), 5.01 (s, 1H), 4.21 (q, J = 7.2 Hz, 2H), 1.25 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.4, 138.7, 128.5, 127.2, 61.2, 57.1, 14.1; IR

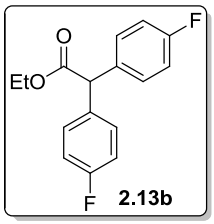
(neat): υ 2978, 1730, 1491, 1454, 1153, 1022, 704 cm^{-1}; $C_{16}H_{16}O_2$: calcd. C 79.97, H 6.71; found C 79.85, H 6.65.

Methyl 2,2-diphenylacetate (2.13a')



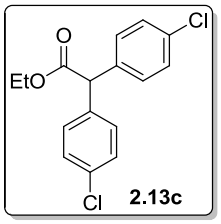
Compound **2.13a'** (Table 2.1, entry 10, 11, 12) obtained when α-diarylacetic esters formation reaction performed using trimethyl orthoformate instead of triethyl orthoformate.[36] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.29 (m, 10H), 5.09 (s, 1H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.9, 138.6, 128.6, 127.2, 57.0, 52.2.

Ethyl 2,2-bis(4-fluorophenyl)acetate (2.13b)



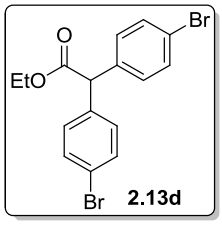
Compound **2.13b** was obtained from **2.10b** by following the general procedure for the synthesis of α-diarylacetic esters.[35] Colorless liquid; Yield: 90%; R_f = 0.6 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27 (d, J = 8.4 Hz, 2H), 7.25 (d, J = 8.4 Hz, 2H), 7.02 (d, J = 8.4 Hz, 2H), 7.00 (d, J = 8.4 Hz, 2H), 4.96 (s, 1H), 4.20 (q, J = 7.2 Hz, 2H), 1.25 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.2, 162.0 (d, J = 245.0), 134.4, 130.0 (d, J = 8.0 Hz), 115.5 (d, J = 22.0 Hz), 61.4, 55.4, 14.1; IR (neat): υ 3046, 2984, 1890, 1732, 1605, 1506, 1370, 1028, 837 cm^{-1}; $C_{16}H_{14}F_2O_2$: calcd. C 69.56, H 5.11; found C 69.45, H 5.19.

Ethyl 2,2-bis(4-chlorophenyl)acetate (2.13c)



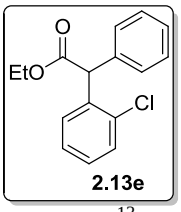
Compound **2.13c** was obtained from **2.10c** by following the general procedure for the synthesis of α-diarylacetic esters.[35] Pale yellow solid, mp 87-88 ºC; Yield: 88%; R_f = 0.6 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29 (d, J = 8.8 Hz, 4H), 7.22 (d, J = 8.8 Hz, 4H), 4.94 (s, 1H), 4.20 (q, J = 7.2 Hz, 2H), 1.25 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.7, 136.8, 133.4, 129.8, 128.8, 61.5, 55.7, 14.0; IR (neat): υ 2982, 1732, 1489, 1190, 1092, 1015 cm^{-1}; $C_{16}H_{14}Cl_2O_2$: calcd. C 62.15, H 4.56; found C 62.25, H 4.49.

Ethyl 2,2-bis(4-bromophenyl)acetate (2.13d)



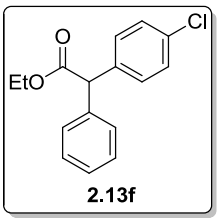
Compound **2.13d** was obtained from **2.10d** by following the general procedure for the synthesis of α-diarylacetic esters. White solid, mp 78-80 ºC; Yield: 78%; R_f = 0.6 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 (d, J = 8.0 Hz, 4H), 7.17 (d, J = 8.0 Hz, 4H), 4.91 (s, 1H), 4.21 (q, J = 7.2 Hz, 2H), 1.26 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.6, 137.2, 131.8, 131.3, 130.2, 121.6, 61.5, 55.8, 14.1; IR (neat): υ 1730, 1485, 1154, 1011, 772 cm^{-1}; $C_{16}H_{14}Br_2O_2$: calcd. C 48.27, H 3.54; found C 48.36, H 3.61.

Ethyl 2-(2-chlorophenyl)-2-phenylacetate (2.13e)



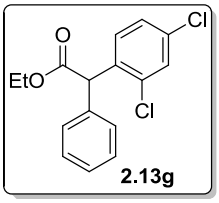
Compound **2.13e** was obtained from **2.10e** by following the general procedure for the synthesis of α-diarylacetic esters. Pale yellow liquid; Yield: 98%; R_f = 0.57 in 1:5 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39-7.33 (m, 3H), 7.30-7.28 (m, 3H), 7.23-7.18 (m, 3H), 5.46 (s, 1H), 4.22 (q, J = 7.2 Hz, 2H), 1.25 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.9, 137.1, 136.7, 134.2, 130.0, 129.5, 128.9, 128.7, 128.5, 127.4, 126.9, 61.4, 53.9, 141; IR (neat): υ 2924, 1736, 1468, 1190, 1015 cm^{-1}; $C_{16}H_{15}ClO_2$: calcd. C 69.95, H 5.50; found C 69.85, H 5.58.

Ethyl 2-(4-chlorophenyl)-2-phenylacetate (2.13f)



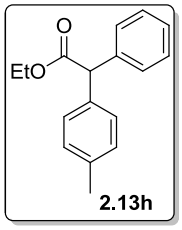
Compound **2.13f** was obtained from **2.10f** by following the general procedure for the synthesis of α-diarylacetic esters. White solid, mp 63-64 ºC; Yield: 97%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33-7.22 (m, 9H), 4.97 (s, 1H), 4.20 (q, J = 7.2 Hz, 2H), 1.24 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.1, 138.3, 137.2, 133.1, 130.0, 128.6, 128.4, 127.4, 61.3, 56.4, 14.0; IR (neat): υ 2982, 1734, 1489, 1453, 1190, 1155 cm^{-1}; $C_{16}H_{15}ClO_2$: calcd. C 69.95, H 5.50; found C 69.85, H 5.43.

Ethyl 2-(2,4-dichlorophenyl)-2-phenylacetate (2.13g)



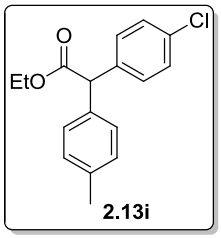
Compound **2.13g** was obtained from **2.10g** by following the general procedure for the synthesis of α-diarylacetic esters. Pale yellow liquid; Yield: 80 %; R_f = 0.79 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, J = 2.0 Hz, 1H), 7.37-7.30 (m, 3H), 7.28-7.26 (m, 2H), 7.17-7.16 (m, 2H), 5.40 (s, 1H), 4.22 (q, J = 7.2 Hz, 2H), 1.25 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.5, 136.8, 135.5, 134.9, 133.7, 131.0, 129.3, 128.9, 127.7, 127.2, 61.6, 53.4, 14.1; IR (neat): υ 2982, 1736, 1472, 1194, 1026, 698 cm^{-1}; $C_{16}H_{14}Cl_2O_2$:calcd. C 62.15, H4.56; found 62.27, H 4.51.

Ethyl 2-phenyl-2-(*p*-tolyl)acetate (2.13h)



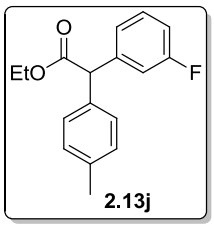
Compound **2.13h** was obtained from **2.10h** by following the general procedure for the synthesis of α-diarylacetic esters.[37] Colorless liquid; Yield: 99%; R_f = 0.62 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31-7.23 (m, 5H), 7.20 (d, J = 7.6 Hz, 2H), 7.12 (d, J = 7.6 Hz, 2H), 4.97 (s, 1H), 4.19 (q, J = 7.2 Hz, 2H), 2.30 (s, 3H), 1.24 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.6, 138.9, 136.8, 135.7, 129.2, 128.5, 128.4, 127.1, 61.1, 56.7, 21.0, 14.1; IR (neat): υ 2982, 1736, 1514, 1454, 1152, 1028, 731 cm^{-1}.

Ethyl 2-(4-chlorophenyl)-2-*p*-tolylacetate (2.13i)



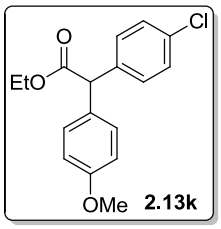
Compound **2.13i** was obtained from **2.10i** by following the general procedure for the synthesis of α-diarylacetic esters. White solid, mp 71-72 ºC; Yield: 95%; R_f = 0.7 in 1:5 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27 (d, J = 8.4 Hz, 2H), 7.24 (d, J = 8.4 Hz, 2H), 7.17 (d, J = 8.0 Hz, 2H), 7.13 (d, J = 8.0 Hz, 2H), 4.93 (s, 1H), 4.20 (q, J = 7.2 Hz, 2H), 2.32 (s, 3H), 1.24 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.3, 137.5, 137.1, 135.2, 133.0, 129.9, 129.4, 128.6, 128.3, 61.3, 56.0, 21.0, 14.1; IR (neat): υ 2980, 1732, 1487, 1154, 770 cm^{-1}; $C_{17}H_{17}ClO_2$: calcd. C 70.71, H 5.93; found 70.65, H 5.86.

Ethyl 2-(3-fluorophenyl)-2-(*p*-tolyl)acetate (2.13j)



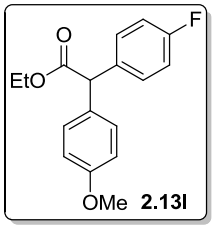
Compound **2.13j** was obtained from **2.10j** by following the general procedure for the synthesis of α-diarylacetic esters. Colorless liquid; Yield: 97%; R_f = 0.45 in 1:5 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32-7.26 (m, 1H), 7.23 (d, J = 7.6 Hz, 2H), 7.16 (d, J = 8.0 Hz, 2H), 7.12-7.05 (m, 2H), 6.99-6.94 (m, 1H), 4.98 (s, 1H), 4.23 (q, J = 7.2 Hz, 2H), 2.35 (s, 3H), 1.28 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.1, 162.8 (d, J = 244.5 Hz), 141.4 (d, J = 7.3 Hz), 137.2, 135.1, 129.9 (d, J = 8.2 Hz), 129.4, 128.3, 124.2, 115.6 (d, J = 22.1 Hz), 114.1 (d, J = 20.9 Hz), 61.3, 56.3, 21.0, 14.1; IR (neat): υ 2982, 1736, 1591, 1487, 1258, 1028 cm^{-1}; $C_{17}H_{17}FO_2$: calcd. C 74.98, H, 6.29; found: C 74.86, H 6.15.

Ethyl 2-(4-chlorophenyl)-2-(4-methoxyphenyl)acetate (2.13k)



Compound **2.13k** was obtained from **2.10k** by following the general procedure for the synthesis of α-diarylacetic esters. Colorless liquid; Yield: 87%; R_f = 0.61 in 1:5 EtOAc/hexanes (two elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28- 7.19 (m, 6H), 6.85 (d, J = 8.4 Hz, 2H), 4.92 (s, 1H), 4.19 (q, J = 7.2 Hz, 2H), 3.76 (s, 3H), 1.24 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.3, 158.8, 137.6, 133.0, 129.8, 129.5, 128.6, 114.0, 61.2, 55.6, 55.2, 14.1; IR (neat): υ 3445.2, 1732.2, 1647.4, 1251.9 cm^{-1}; $C_{17}H_{17}ClO_3$: calcd. C 67.00, H 5.62; found C 67.12, H 5.56.

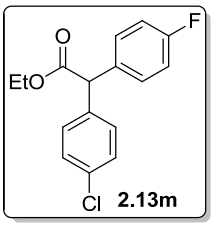
Ethyl 2-(4-fluorophenyl)-2-(4-methoxyphenyl)acetate (2.13l)



Compound **2.13l** was obtained from **2.10l** by following the general procedure for the synthesis of α-diarylacetic esters. Pale yellow liquid; Yield: 92%; R_f = 0.57 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28-7.25 (m, 2H), 7.21 (d, J = 8.8 Hz, 2H), 6.98 (t, J = 8.8 Hz, 2H), 6.90 (d, J = 8.4 Hz,

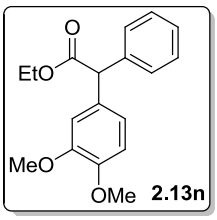
2H), 4.93 (s, 1H), 4.19 (q, *J* = 7.2 Hz, 2H), 3.76 (s, 3H), 1.24 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.6, 161.9 (d, *J* = 244.5 Hz), 158.8, 134.9, 130.7, 130.0 (d, *J* = 8.0 Hz), 129.5, 115.3 (d, *J* = 21.4 Hz), 114.0, 61.2, 55.4, 55.2, 14.1; IR (neat): υ 2982, 1736, 1609, 1510, 1032, 835 cm^{-1}; $C_{17}H_{17}FO_3$: calcd. C 70.82, H 5.94; found C 70.91, H 5.89.

Ethyl 2-(4-chlorophenyl)-2-(4-fluorophenyl)acetate (2.13m)



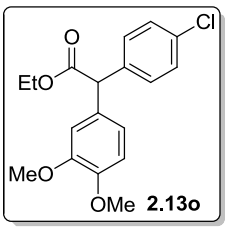
Compound **2.13m** was obtained from **2.10m** by following the general procedure for the synthesis of α-diarylacetic esters. White solid, mp 67-68 ºC; Yield: 90%; R_f = 0.69 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34-7.25 (m, 6H), 7.06-7.02 (m, 2H), 4.99 (s, 1H), 4.24 (q, *J* = 7.2 Hz, 2H), 1.28 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.0, 162.1 (d, *J* = 245 Hz), 137.1, 134.1 (d, *J* = 3.5 Hz), 133.4, 130.1 (d, *J* = 8 Hz), 129.9, 128.8, 115.6 (d, *J* = 21.3 Hz), 61.5, 55.6, 14.1; IR (neat): υ 2982, 1734, 1602, 1510, 1151, 824 cm^{-1}; $C_{16}H_{14}ClFO_2$: calcd. C 65.65, H 4.82; found C 65.48, H 4.75.

Ethyl 2-(3,4-dimethoxyphenyl)-2-phenylacetate (2.13n)



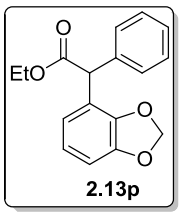
Compound **2.13n** was obtained from **2.10n** by following the general procedure for the synthesis of α-diarylacetic esters. Colorless liquid; Yield: 83%; R_f = 0.56 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31-7.25 (m, 5H), 6.88-6.86 (m, 2H), 6.81 (d, *J* = 8.4 Hz, 1H), 4.96 (s, 1H), 4.20 (q, *J* = 7.2 Hz, 2H), 3.84 (s, 3H), 3.82 (s, 3H), 1.25 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.6, 148.8, 148.1, 138.9, 131.0, 128.4, 128.3, 127.1, 120.7, 11.7, 110.9, 61.0, 56.5, 55.7, 14.1; IR (neat): υ 2936, 1734, 1591, 1518, 1459, 1263, 1026, 700 cm^{-1}; $C_{18}H_{20}O_4$: calcd. C 71.98, H 6.71; found C 71.85, H 6.67.

Ethyl 2-(4-chlorophenyl)-2-(3,4-dimethoxyphenyl)acetate (2.13o)



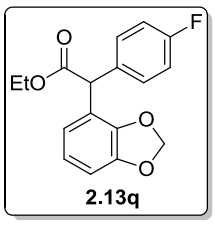
Compound **2.13o** was obtained from **2.10o** by following the general procedure for the synthesis of α-diarylacetic esters. Pale yellow liquid; Yield: 95%; R_f = 0.45 in 1:3 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29 (d, *J* = 8.8 Hz, 2H), 7.24 (d, *J* = 8.4 Hz, 2H), 6.86-6.81 (m, 3H), 4.92 (s, 1H), 4.21 (q, *J* = 7.2 Hz, 2H), 3.86 (s, 3H), 3.84 (s, 3H), 1.26 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.2, 149.0, 148.3, 137.4, 133.0, 130.6, 129.7, 128.6, 120.6, 111.6, 111.1, 61.2, 55.8, 14.0; IR (neat): υ 2936, 1732, 1591, 1516, 1264, 1028, 804 cm^{-1}; $C_{18}H_{19}ClO_4$: calcd C 64.57, H 5.72; found C 64.47, H 5.68.

Ethyl 2-(benzo[*d*][1,3]dioxol-4-yl)-2-phenylacetate (2.13p)



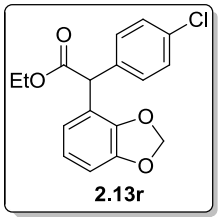
Compound **2.13p** was obtained from **2.10p** by following the general procedure for the synthesis of α-diarylacetic esters. Colorless liquid; Yield: 98%; R_f = 0.50 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35-7.27 (m, 5H), 6.87 (s, 1H), 6.80 (d, J = 8.0 Hz, 1H), 6.78 (d, J = 8.0 Hz, 1H), 5.94 (s, 2H), 4.96 (s, 1H), 4.24 (q, J = 7.2 Hz, 2H), 1.29 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.4, 147.8, 146.7, 138.8, 132.5, 128.5, 128.3, 127.2, 121.8, 109.1, 108.1, 101.0, 61.1, 56.6, 14.1; IR (neat): υ 2982, 2901, 1732, 1605, 1489, 1445, 1036, 932, 810 cm^{-1}; $C_{17}H_{16}O_4$: calcd. C 71.82, H, 5.67; found C 71.75, H 5.61.

Ethyl 2-(benzo[d][1,3]dioxol-4-yl)-2-(4-fluorophenyl)acetate (2.13q)



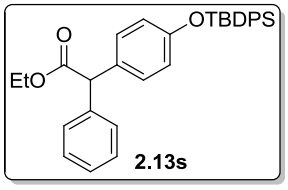
Compound **2.13q** was obtained from **2.10q** by following the general procedure for the synthesis of α-diarylacetic esters. Colorless liquid; Yield: 88%; R_f = 0.48 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28-7.25 (m, 2H), 6.99 (t, J = 8.4 Hz, 2H), 6.80 (s, 1H), 6.74 (s, 2H), 5.91 (s, 2H), 4.89 (s, 1H), 4.20 (q, J = 7.2 Hz, 2H), 1.25 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.3, 161.9 (d, J = 244.5 Hz), 147.9, 146.8, 134.6, 132.3, 130.0 (d, J = 8.0 Hz), 121.7, 115.4 (d, J = 21.3 Hz), 108.9, 108.2, 101.1, 61.2, 55.8, 14.1; IR (neat): υ 2984, 1732, 1506, 1250, 1038, 814 cm^{-1}; $C_{17}H_{15}FO_4$: calcd. C 67.54; H 5.00; found C 67.48, H 5.08.

Ethyl 2-(benzo[*d*][1,3]dioxol-4-yl)-2-(4-chlorophenyl)acetate (2.13r)



Compound **2.13r** was obtained from **2.10r** by following the general procedure for the synthesis of α-diarylacetic esters. Colorless liquid; Yield: 91%; R_f = 0.46 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (d, J = 8.8 Hz, 2H), 7.27 (d, J = 8.8 Hz, 2H), 6.83 (s, 1H), 6.78-6.77 (m, 2H), 5.95 (s, 2H), 4.92 (s, 1H), 4.23 (q, J = 7.2 Hz, 2H), 1.28 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.2, 148.0, 147.0, 137.4, 133.2, 132.1, 129.8, 128.7, 121.8, 109.0, 108.3, 101.2, 61.4, 56.0, 14.1; IR (neat): υ 2982, 1734, 1489, 1442, 1248, 1038, 932 cm^{-1}; $C_{17}H_{15}ClO_4$: calcd. C 64.06, H 4.74; found C 64.12, H 4.85.

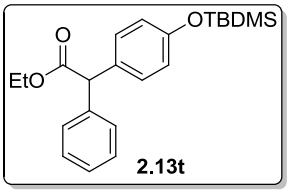
Ethyl 2-(4-((tert-butyldiphenylsilyl)oxy)phenyl)-2-phenylacetate (2.13s)



Compound **2.13s** was obtained from **2.10s** following the general procedure for the synthesis of α-diarylacetic esters. Colourless liquid; Yield: 86%; R_f = 0.65 in 1:5 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, J = 6.4 Hz, 4H), 7.42-7.32 (m, 6H), 7.29-7.21 (m, 5H), 7.02 (d, J = 8.4 Hz,

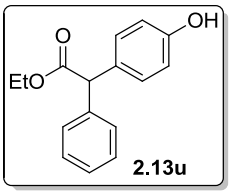
2H), 6.70 (d, *J* = 8.8 Hz, 2H), 4.87 (s, 1H), 4.13 (q, *J* = 7.2 Hz, 2H) 1.20 (t, *J* = 7.2 Hz, 3H), 1.08 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.7, 154.7, 139.0, 135.5, 132.8, 131.1, 129.8, 129.4, 128.5, 128.4, 127.7, 127.0, 119.6, 61.0, 56.3, 26.5, 19.4, 14.1; IR (neat): υ 3074, 2926, 1731, 1512, 1430, 1260, 1151, 926, 701 cm^{-1}; HRMS (ESI): calcd for $C_{32}H_{34}O_3Si$ $(M+Na)^+$ 517.2175; found 517.2173.

Ethyl 2-(4-((tert-butyldimethylsilyl)oxy)phenyl)-2-phenylacetate (2.13t)



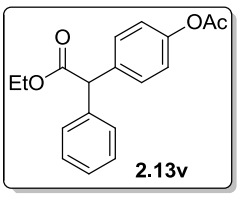
Compound **2.13t** was obtained from **2.10t** by following the general procedure for the synthesis of α-diarylacetic esters. Colourless liquid; Yield: 90%; R_f = 0.85 in 1:5 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30-7.23 (m, 5H), 7.16 (d, *J* = 8.4 Hz, 2H), 6.77 (d, *J* = 8.4 Hz, 2H), 4.94 (s, 1H), 4.17 (q, *J* = 6.8 Hz, 2H) 1.24 (t, *J* = 7.2 Hz, 3H), 0.96 (s, 9H), 0.18 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.7, 154.8, 139.1, 131.4, 129.6, 128.5, 127.1, 120.0, 61.0, 56.3, 25.6, 198.1, 14.1, -4.4; HRMS (ESI): calcd for $C_{22}H_{30}O_3Si$ $(M+Na)^+$ 393.1862; found 393.1861.

Ethyl 2-(4-hydroxyphenyl)-2-phenylacetate (2.13u)



Compound **2.13u** was obtained from **2.10u** by following the general procedure for the synthesis of α-diarylacetic esters. Light yellow liquid; Yield: 76%; R_f = 0.69 in 1:1 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31-7.26 (m, 5H), 7.16 (d, *J* = 8.4 Hz, 2H), 6.75 (d, *J* = 8.4 Hz, 2H), 5.11 (s, 1H), 4.95 (s, 1H), 4.20 (q, *J* = 7.2 Hz, 2H) 1.25 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.9, 154.8, 139.0, 130.9, 129.8, 128.5, 128.4, 127.1, 115.4, 61.2, 56.3, 29.7, 14.1; IR (neat): υ 3097, 2926, 1715, 1512, 1441, 1189, 843, 701 cm^{-1}; HRMS (ESI): calcd for $C_{16}H_{16}O_3$ $(M+Na)^+$ 279.0997; found 279.1000.

Ethyl 2-(4-acetoxyphenyl)-2-phenylacetate (2.13v)



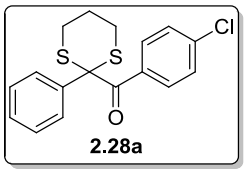
Compound **2.13v** was obtained from **2.10v** by following the general procedure for the synthesis of α-diarylacetic esters. Colourless liquid; Yield: 85%; R_f = 0.76 in 1:1 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34-7.24 (m, 7H), 7.03 (d, *J* = 8.8 Hz, 2H), 5.00 (s, 1H), 4.19 (q, *J* = 6.8 Hz, 2H), 2.27 (s, 3H) 1.25 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.2, 169.4,149.7, 138.4, 136.2, 129.6, 128.6, 128.5, 127.3, 121.5, 61.2, 56.4, 21.1, 14.1; IR (neat): υ 3057, 1770, 1507, 1452, 1194, 1019, 915, 696 cm^{-1}; HRMS (ESI): calcd for $C_{18}H_{18}O_4$ $(M+Na)^+$ 321.1103; found 321.1104.

General PDC oxidation procedure for synthesis of ketones 2.28a-2.28f

To a solution of corresponding benzoin **2.17** in dry dichloromethane, 3.5 equiv of PDC reagent was added at room temperature. Reaction was continued at room temperature till TLC showed the

disappearance of starting material (26-29 h). After completion of the reaction, crude product was extracted in ether and decanted. The organic layer was washed with aqueous $NaHCO_3$, concentrated and purified by silica gel column chromatography using hexane/EtOAc as eluent.

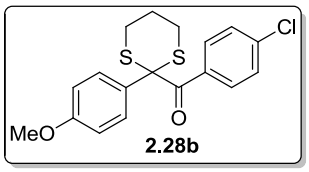
(4-Chlorophenyl)(2-phenyl-1,3-dithian-2-yl)methanone (2. 28a)



2.28a

Compound **2.28a** was synthesized from **2.17b** by following the PDC oxidation procedure. Yellow foamy solid, mp 116-117 ºC; Yield: 62%; R_f = 0.62 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (d, J = 8.8 Hz, 2H), 7.56-7.53 (m, 2H), 7.38-7.31 (m, 3H), 7.17 (d, J = 8.4 Hz, 2H), 3.25 (dt, J = 14.4, 2.4 Hz, 2H), 2.78 (td, J = 14.4, 3.2 Hz, 2H), 2.16-2.12 (m, 1H), 1.99-1.93 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.5, 138.7, 138.4, 132.6, 132.2, 129.2, 127.9, 127.3, 63.1, 29.2, 23.9; IR (KBr): υ 2911, 1672, 1586, 1209, 748 cm^{-1}; $C_{17}H_{15}ClOS_2$: calcd. C 60.97, H 4.51; found C 60.90, H 4.45.

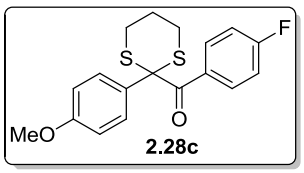
(4-Chlorophenyl)(2-(4-methoxyphenyl)-1,3-dithian-2-yl)methanone (2.28b)



2.28b

Compound **2.28b** was synthesized from **2.17g** by following the PDC oxidation procedure. White solid; mp 128-130 ºC; Yield: 71%; R_f = 0.4 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (d, J = 8.8 Hz, 2H), 7.44 (d, J = 8.8 Hz, 2H), 7.17 (d, J = 8.8 Hz, 2H), 6.87 (d, J = 8.8 Hz, 2H), 3.78 (s, 3H), 3.21 (dt, J = 14.0, 2.0 Hz, 2H), 2.75 (td, J = 14.0, 3.6 Hz, 2H), 2.13-2.09 (m, 1H), 1.96-1.87 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.6, 159.7, 138.2, 132.6, 132.2, 130.4, 128.5, 127.8, 114.5, 62.6, 55.2, 29.2, 23.8; IR (KBr): υ 2957, 1676, 1510, 1258, 1173, 781 cm^{-1}; $C_{18}H_{17}ClO_2S_2$: calcd. C 59.25, H 4.70; found C 59.12, H 4.78.

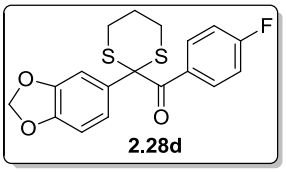
(4-Fluorophenyl)(2-(4-methoxyphenyl)-1,3-dithian-2-yl)methanone (2.28c)



2.28c

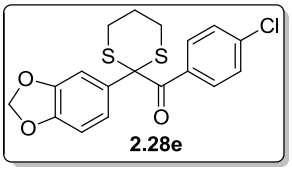
Compound **2.28c** was synthesized from **2.17h** by following the PDC oxidation procedure. Yellow foamy solid, mp 108-109 ºC; Yield: 62%; R_f = 0.50 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76-7.73 (m, 2H), 7.46 (d, J = 8.8 Hz, 2H), 6.90-6.86 (m, 4H), 3.80 (s, 3H), 3.26-3.20 (m, 2H), 2.78-2.74 (m, 2H), 2.14-2.10 (m, 1H), 1.98-1.89 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.4, 164.7 (d, J = 252.9 Hz), 159.7, 133.5 (d, J = 8.8 Hz), 130.7, 130.5, 128.6, 114.6 (d, J = 21.6 Hz), 114.5, 62.7, 55.2, 29.3, 23.9; IR (neat): υ 2901, 1674, 1588, 1487, 1244, 1039, 779 cm^{-1}; $C_{18}H_{17}FO_2S_2$: calcd. C 62.04, H 4.92; Found C, 62.12, H, 4.85.

(2-(Benzo[*d*][1,3]dioxol-5-yl)-1,3-dithian-2-yl)(4-fluorophenyl)methanone (2.28d)



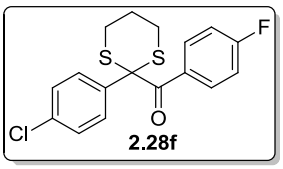
Compound **2.28d** was synthesized from **2.17m** by following the PDC oxidation procedure. White solid, mp 99-100 ºC; Yield: 66%; R_f = 0.48 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79-7.75 (m, 2H), 7.06 (d, *J* = 2.0 Hz, 1H), 7.00 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.89 (t, *J* = 8.4 Hz, 2H), 6.76 (d, *J* = 8.4 Hz, 1H), 5.96 (s, 2H), 3.20 (dt, *J* = 14.4, 2.8 Hz, 2H), 2.74 (td, *J* = 14.4, 4.4 Hz, 2H), 2.12-2.07 (m, 1H), 1.96-1.85 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.9, 164.6 (d, *J* = 253.3 Hz), 148.2, 147.8, 133.4 (d, *J* = 8.3 Hz), 132.4, 130.3 (d, *J* = 2.0 Hz), 121.2, 114.6 (d, *J* = 21.6 Hz), 108.6, 107.6, 101.4, 62.9, 29.2, 23.8; IR (KBr): υ 3329, 2893, 1674, 1595, 1503, 1244, 1038, 615 cm^{-1}; $C_{18}H_{15}FO_3S_2$: calcd. C 59.65, H 4.17; found 59.56, H 4.25.

(2-(Benzo[*d*][1,3]dioxol-5-yl)-1,3-dithian-2-yl)(4-chlorophenyl)methanone (2.28e)



Compound **2.28e** was synthesized from **2.17n** by following the PDC oxidation procedure. Yellow solid, mp 116-117 ºC; Yield: 66%; R_f = 0.50 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49-7.48 (m, 2H), 7.22-7.19 (m, 2H), 7.07 (d, *J* = 1.6 Hz, 1H), 7.00 (dd, *J* = 8.0, 1.6 Hz, 1H), 6.77 (dd, *J* = 8.0, 1.6 Hz, 1H), 5.97 (s, 2H), 3.24-3.17 (m, 2H), 2.77-2.73 (m, 2H), 2.13-2.09 (m, 1H), 1.96-1.86 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.3, 148.3, 148.0, 138.4, 132.6, 132.3, 132.2, 128.0, 121.3, 108.8, 107.7, 101.6, 62.9, 29.3, 23.9; IR (neat): υ 2901, 1676, 1597, 1501, 1483, 1242, 1213, 1034, 773 cm^{-1}; $C_{18}H_{15}ClO_3S_2$: calcd. C 57.06, H 3.99; found C 57.16, H 3.91.

(2-(4-Chlorophenyl)-1,3-dithian-2-yl)(4-fluorophenyl)methanone (2.28f)



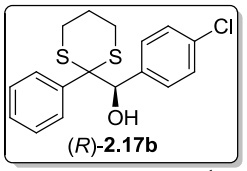
Compound **2.28f** was synthesized from **2.17i** by following the PDC oxidation procedure. White solid, mp 102-103 °C; Yield: 60%; R_f = 0.45 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75-7.72 (m, 2H), 7.49 (d, *J* = 8.5 Hz, 2H), 7.33 (d, *J* = 8.5 Hz, 2H), 6.89 (t, *J* = 8.5 Hz, 2H), 3.24 (td, *J* = 14.0 Hz, 2.5 Hz, 2H), 2.78 (dt, *J* = 14.0 Hz, 4.0 Hz, 2H), 2.16-2.10 (m, 1H), 1.98-1.89 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ190.9, 164.8 (d, *J* = 262.5 Hz), 137.6, 134.8, 133.4 (d, *J* = 8.8 Hz), 130.3, 129.3, 128.8, 114.8 (d, *J* = 21.2 Hz), 62.7, 29.2, 23.8; IR (neat): υ2905, 1672, 1593, 1489, 1012, 833; $C_{17}H_{14}ClFOS_2$: calcd C 57.86, H 4.00; found C 57.71, 4.08.

CBS asymmetric reduction procedure for the synthesis of ((*R*)-2.17)

To a solution of (*S*)-DPP (0.15 equiv) in dry THF, trimethylborate (0.15 equiv) was added at room temperature. After stirring for 30 minutes, BH_3-THF (1.1 equiv) solution was added slowly at 0 ºC

and stirred. After 10 minutes, the solution of ketone **2.28** in THF was added drop wise at 0 ºC and the reaction mixture was brought to room temperature and continued. Reaction was monitored by TLC, after completion of reaction few drops of water was added to quench the reaction. THF was evaporated; product was extracted with ethyl acetate, concentrated and purified by silica gel column chromatography using hexane/EtOAc as eluent.

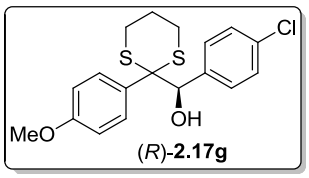
(*R*)-(4-chlorophenyl)(2-phenyl-1,3-dithian-2-yl)methanol ((*R*)-2.17b)



(*R*)-**2.17b**

Compound (*R*)-**2.17b** was synthesized from **2.28a** following the above asymmetric reduction procedure. White foamy solid, mp 84-85 °C; Yield: 99%; $[\alpha]_D^{25}$ = -14.8º (*c* 2.87, $CHCl_3$, 98% *ee*); R_f = 0.63 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83-7.65 (m, 2H), 7.34-7.27 (m, 3H), 7.09 (d, *J* = 8.4 Hz, 2H), 6.79 (d, *J* = 8.4 Hz, 2H), 4.95 (s, 1H), 2.78-2.62 (m, 4H), 1.96-1.90 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.2, 135.7, 133.9, 130.4, 129.5, 128.3, 127.7, 127.2, 80.4, 66.4, 27.3, 26.9, 24.7; IR (neat): υ 3447, 2907, 1595, 1489, 1188, 823 cm^{-1}; $C_{17}H_{17}ClOS_2$: calcd. C 60.61, H 5.09; found C 60.52, H 5.14.

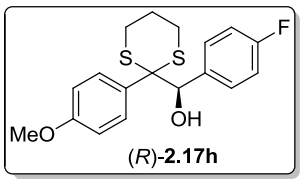
(*R*)-(4-chlorophenyl)(2-(4-methoxyphenyl)-1,3-dithian-2-yl)methanol ((*R*)-2.17g):



(*R*)-**2.17g**

Compound (*R*)-**2.17g** was synthesized from **2.28b** following the above asymmetric reduction procedure. White solid, mp 94-95 °C; Yield: 99%; $[\alpha]_D^{25}$ = -14.2º (*c* 4.17, $CHCl_3$, 93% *ee*); R_f = 0.38 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (d, *J* = 8.8 Hz, 2H), 7.10 (d, *J* = 8.8 Hz, 2H), 6.81 (t, *J* = 9.2 Hz, 4H), 4.92 (s, 1H), 3.82 (s, 3H), 3.10 (bs, 1H), 2.75-2.65 (m, 4H), 1.92-1.90 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.9, 135.7, 133.7, 131.7, 129.5, 128.7, 127.1, 113.4, 80.2, 65.8, 55.2, 27.1, 26.8, 24.7; IR (neat): υ 3445, 2903, 1605, 1505, 1250, 1034, 835 cm^{-1}; $C_{18}H_{19}ClO_2S_2$: calcd. C 58.92, H 5.22; found C 58.79, H 5.28.

(*R*)-(4-fluorophenyl)(2-(4-methoxyphenyl)-1,3-dithian-2-yl)methanol ((*R*)-2.17h)

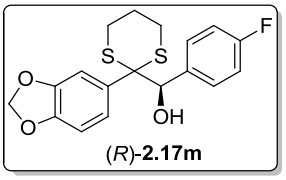


(*R*)-**2.17h**

Compound (*R*)-**2.17h** was synthesized from **2.28c** following the above asymmetric reduction procedure. White solid, mp 100-101 °C; Yield: 95%; $[\alpha]_D^{25}$ = -15.7º (*c* 5.4, $CHCl_3$, 93% *ee*); R_f = 0.33 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53 (d, *J* = 8.0 Hz, 2H), 6.84-6.77 (m, 6H), 4.92 (s, 1H), 3.80 (s, 3H), 3.19 (bs, 1H), 2.72-2.60 (m, 4H), 1.90-1.88 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.3 (d, *J* = 244.7 Hz), 158.8, 133.1, 131.6, 129.7 (d, *J* = 8.0 Hz), 128.8, 113.6 (d, *J* = 21.2 Hz), 113.2, 80.1, 65.8, 55.1, 27.0, 26.7, 24.6; IR

(neat): υ 3457, 2907, 1605, 1506, 1294, 1250, 1034, 835 cm^{-1}; $C_{18}H_{19}FO_2S_2$: calcd. C 61.69, H 5.46; found C 61.85, H 5.39.

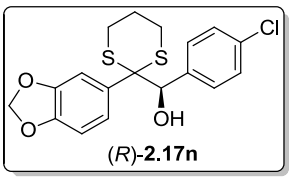
(*R*)-(2-(benzo[*d*][1,3]dioxol-5-yl)-1,3-dithian-2-yl)(4-fluorophenyl)methanol ((*R*)-2.17m)



(*R*)-**2.17m**

Compound (*R*)-**2.17m** was synthesized from **2.28d** following the above asymmetric reduction procedure. White foamy semisolid; Yield: 91%; $[\alpha]_D^{25}$ = -14.1º (*c* 3.25, $CHCl_3$, 98% *ee*); R_f = 0.38 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25 (d, *J* = 2.0 Hz, 1H), 7.15 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.92-6.82 (m, 4H), 6.72 (d, *J* = 8.0 Hz, 1H), 6.00 (d, *J* = 1.2 Hz, 1H), 5.99 (d, *J* = 1.6 Hz, 1H), 4.91 (d, *J* = 2.4 Hz, 1H), 3.04 (bs, 1H), 2.74-2.62 (m, 4H), 1.94-1.87 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.6 (d, *J* = 245.0 Hz), 147.9, 147.0, 133.1 (d, *J* = 3.2 Hz), 131.2, 129.8 (d, *J* = 8.1 Hz), 124.5, 113.9 (d, *J* = 21.2 Hz), 110.8, 107.6, 101.3, 80.5, 66.3, 27.3, 27.0, 24.7; IR (neat): υ 3468, 2905, 1603, 1508, 1481, 1238, 1040, 737 cm^{-1}; $C_{18}H_{17}FO_3S_2$: calcd. C 59.32, H 4.70; found C 59.45, H 4.75.

(*R*)-(2-(benzo[*d*][1,3]dioxol-5-yl)-1,3-dithian-2-yl)(4-chlorophenyl)methanol ((*R*)-2.17n)



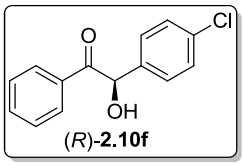
(*R*)-**2.17n**

Compound (*R*)-**2.17n** was synthesized from **2.28e** following the above asymmetric reduction procedure. White solid, mp 142-144 °C; Yield: 95%; $[\alpha]_D^{25}$ = -9.6º (*c* 4.83, $CHCl_3$, 98% *ee*); R_f = 0.34 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27 (s, 1H), 7.14-7.12 (m, 3H), 6.87 (d, *J* = 8.4 Hz, 2H), 6.72 (d, *J* = 8.4 Hz, 1H), 6.02-5.99 (m, 2H), 4.90 (s, 1H), 3.03 (bs, 1H), 2.74-2.67 (m, 4H), 1.94-1.88 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.9, 147.0, 135.8, 133.9, 131.1, 129.5, 127.2, 124.4, 110.7, 107.6, 101.3, 80.4, 66.1, 27.2, 26.9, 24.6; IR (neat): υ 3440, 2903, 1482, 1238, 1039 cm^{-1}; $C_{18}H_{17}ClO_3S_2$: calcd. C 56.76, H 4.50; found C 56.85, H 4.41.

General procedure for dithiane deprotection to synthesize chiral benzoins (*R*)-2.10

To a solution of dithiane protected chiral benzoin (*R*)-**2.17** (1.0 equiv) in acetonitrile/water (4:1) bis(trifluroacetoxy)iodobenzene (2.5 equiv) was added at 0 ºC. After stirring for 10 min aqueous $Na_2S_2O_3$ was added and stirred. The crude benzoin compound was extracted with ethyl acetate, concentrated and purified by silica gel column chromatography using hexane/EtOAc as eluent.

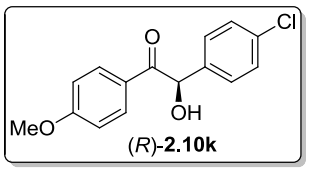
(*R*)-2-(4-Chlorophenyl)-2-hydroxy-1-phenylethanone ((*R*)-2.10f)



(*R*)-**2.10f**

Compound (*R*)-**2.10f** was synthesized from (*R*)-**2.17b** following the general dithiane deprotection procedure.[18a] White solid, mp 87-88 ºC; Yield: 48%; $[\alpha]_D^{25}$ = -115.7º (*c* 0.83, $CHCl_3$, 91% *ee*); R_f = 0.32 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (d, *J* = 7.2 Hz, 2H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.31-7.27 (m, 4H), 5.94 (d, *J* = 4.8 Hz, 1H), 4.54 (d, *J* = 5.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.6, 137.5, 134.6, 134.1, 133.3, 129.3, 129.1, 128.8, 75.4; IR (KBR): υ 3410, 1674, 1595, 1491, 1258, 1088, 812 cm^{-1}; $C_{14}H_{11}ClO_2$: calcd. C 68.16, H 4.49; found C 68.26, H 4.41.

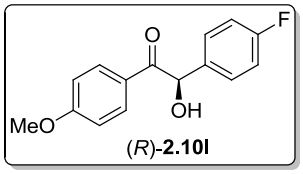
(*R*)-2-(4-Chlorophenyl)-2-hydroxy-1-(4-methoxyphenyl)ethanone ((*R*)-2.10k)



(*R*)-**2.10k**

Compound (*R*)-**2.10k** was synthesized from (*R*)-**2.17g** following the general dithiane deprotection procedure.[19c] White solid, mp 89-90 ºC; Yield: 59%; $[\alpha]_D^{25}$ = -52.1º (*c* 1.58, $CHCl_3$, 87% *ee*); R_f = 0.38 in 1:10 EtOAc/hexanes (triple elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, *J* = 8.8 Hz, 2H), 7.28 (s, 4H), 6.87 (d, *J* = 8.8 Hz, 2H), 5.88 (s, 1H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ196.7, 164.2, 138.0, 134.3, 131.5, 129.2, 129.0, 125.9, 114.0, 74.9, 55.4; IR (neat): υ 3437, 1674, 1599, 1512, 1264, 1170, 976 cm^{-1}; $C_{15}H_{13}ClO_3$: calcd. C 65.11, H 4.74; found C 65.28, H 4.86.

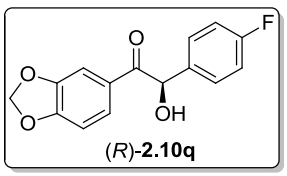
(*R*)-2-(4-Fluorophenyl)-2-hydroxy-1-(4-methoxyphenyl)ethanone ((*R*)-2.10l)



(*R*)-**2.10l**

Compound (*R*)-**2.10l** was synthesized from (*R*)-**2.17h** following the general dithiane deprotection procedure. Colorless heavy liquid; Yield: 78%; $[\alpha]_D^{25}$ = -83.2º (*c* 1.98, $CHCl_3$, 92% *ee*); R_f = 0.34 in 1:10 EtOAc/hexanes (triple elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (d, *J* = 8.8 Hz, 2H), 7.33-7.29 (m, 2H), 6.99 (t, *J* = 8.4 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 2H), 5.90 (s, 1H), 3.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.9, 164.1, 162.5 (d, *J* = 246.0 Hz), 135.5, 131.5, 129.4 (d, *J* = 8.0 Hz), 126.0, 115.9 (d, *J* = 22.0 Hz), 113.9, 74.8, 55.4; IR (neat): υ 3441, 2937, 1671, 1600, 1507, 1260, 1173, 975 cm^{-1}; $C_{15}H_{13}FO_3$: calcd. C 69.22, H 5.03; Found C, 69.35, H, 5.12.

(*R*)-1-(Benzo[*d*][1,3]dioxol-5-yl)-2-(4-fluorophenyl)-2-hydroxyethanone ((*R*)-2.10q)

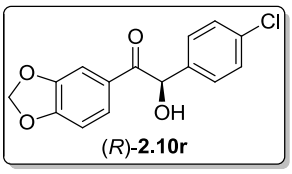


(*R*)-**2.10q**

Compound (*R*)-**2.10q** was synthesized from (*R*)-**2.17m** following the general dithiane deprotection procedure.White solid, mp 90-92 °C; Yield: 94%; $[\alpha]_D^{25}$ = -104.1º (*c* 1.42, $CHCl_3$, 98% *ee*); R_f = 0.31 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (dd,

J = 8.4, 1.6 Hz, 1H), 7.37 (d, *J* = 1.6 Hz, 1H), 7.31-7.28 (m, 2H), 7.01 (d, *J* = 8.8 Hz, 2H), 6.78 (d, *J* = 8.0 Hz, 1H), 6.02 (s, 2H), 5.84 (s, 1H), 4.57 (bs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.7, 162.7 (d, *J* = 246.3 Hz), 152.6, 148.3, 135.4 (d, *J* = 3.2 Hz), 129.4 (d, *J* = 8.3 Hz), 125.9, 118.9, 116.1 (d, *J* = 21.7 Hz), 108.6, 108.1, 102.1, 75.0; IR (KBr): υ 3401, 2924, 1669, 1506, 1264, 831 cm^{-1}; $C_{15}H_{11}FO_4$: calcd. C 65.69, H 4.04; found C 65.86, H 4.12.

(*R*)-1-(Benzo[*d*][1,3]dioxol-5-yl)-2-(4-chlorophenyl)-2-hydroxyethanone ((*R*)-2.10r)



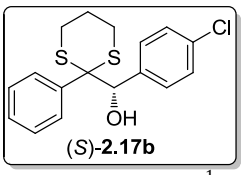
(*R*)-**2.10r**

Compound (*R*)-**2.10r** was synthesized from (*R*)-**2.17n** following the general dithiane deprotection procedure. White foamy solid, mp 93-94 °C; Yield: 61%; $[\alpha]_D^{25}$ = -80.4º (*c* 1.5, $CHCl_3$, 95% *ee*); R_f = 0.31 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (d, *J* = 8.0, 1H), 7.36 (s, 1H), 7.29 (d, *J* = 8.4 Hz, 2H), 7.25 (d, *J* = 8.4 Hz, 2H), 6.78 (d, *J* = 8.4 Hz, 1H), 6.01 (s, 2H), 5.83 (s, 1H), 4.61 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.4, 152.6, 148.2, 137.9, 134.4, 129.2, 129.0, 127.7, 125.8, 108.6, 108.1, 102.1, 75.0; IR (KBr): υ 3468, 1655, 1451, 1267, 1036, 738 cm^{-1}; $C_{15}H_{11}ClO_4$: calcd. C 61.98, H 3.81; found C 61.85, H 3.85.

CBS asymmetric reduction procedure for the synthesis of ((*S*)-2.17)

To a solution of (*R*)-DPP (0.15 equiv) in dry THF, trimethylborate (0.15 equiv) was added at room temperature. After stirring for 30 minutes, BH_3-THF (1.1 equiv) solution was added slowly at 0 ºC and the stirring was continued. After 10 minutes, the solution of ketone **2.28** in THF was added drop wise at 0 ºC and reaction mixture was brought to room temperature. Reaction was monitored by TLC. After completion of reaction, few drops of water were added to quench the reaction, THF was evaporated, and the compound was extracted with ethyl acetate, concentrated and purified by silica gel column chromatography using hexane/EtOAc as eluent.

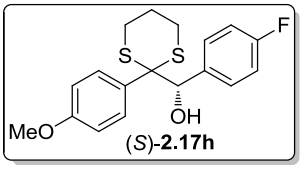
(*S*)-(4-Chlorophenyl)(2-phenyl-1,3-dithian-2-yl)methanol ((*S*)-2.17b)



(*S*)-**2.17b**

Compound (*S*)-**2.17b** was synthesized from **2.28a** by following above asymmetric reduction procedure. White solid, mp 83-85 °C; Yield: 95%; $[\alpha]_D^{25}$ = +15.0º (*c* 4.3, $CHCl_3$, 97% *ee*); R_f = 0.59 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67-7.65 (m, 2H), 7.31-7.26 (m, 3H), 7.08 (d, *J* = 8.4 Hz, 2H), 6.78 (d, *J* = 8.4 Hz, 2H), 4.95 (s, 1H), 3.04 (s, 1H), 2.77-2.62 (m, 4H), 1.95-1.91 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.0, 135.7, 133.6, 130.2, 129.4, 128.1, 127.5, 126.9, 80.1, 66.1, 27.1, 26.8, 24.5; IR (neat): υ 3459, 2909, 1491, 1014, 824 cm^{-1}; $C_{17}H_{17}ClOS_2$: calcd. C 60.61, H, 5.09; found C 60.48, H 5.15.

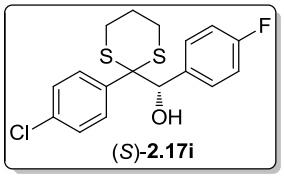
(*S*)-(4-Fluorophenyl)(2-(4-methoxyphenyl)-1,3-dithian-2-yl)methanol ((*S*)-2.17h)



(*S*)-**2.17h**

Compound (*S*)-**2.17h** was synthesized from **2.28c** following the above asymmetric reduction procedure. White solid, mp 100-101 °C; Yield: 94%; $[\alpha]_D^{25}$ = +18.9º (*c* 4.6, $CHCl_3$, 97% *ee*); R_f = 0.34 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (d, *J* = 9.2 Hz, 2H), 6.83-6.80 (m, 6H), 4.93 (s, 1H), 3.81 (s, 3H), 2.74-2.59 (m, 4H), 1.92-1.87 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.5 (d, *J* = 244.7 Hz), 159.0, 133.2, 131.8, 129.9 (d, *J* = 8.0 Hz), 128.9, 113.8 (d, *J* = 21.3 Hz), 113.4, 80.4, 66.0, 55.3, 27.2, 26.9, 24.8; IR (KBr): υ 3466, 1601, 1503, 1217, 1026, 790 cm^{-1}; $C_{18}H_{19}FO_2S_2$: calcd. C 61.69, H 5.46; found C 61.78, H 5.39.

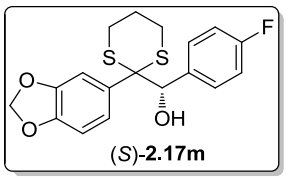
(*S*)-(2-(4-Chlorophenyl)-1,3-dithian-2-yl)(4-fluorophenyl)methanol ((*S*)-2.17i)



(*S*)-**2.17i**

Compound (*S*)-**2.17i** was synthesized from **2.28f** following the above asymmetric reduction procedure. Pale yellow semisolid; Yield: 99%; $[\alpha]_D^{25}$ = +26.8º (*c* 5.8, $CHCl_3$, 99% *ee*); R_f = 0.48 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, *J* = 8.8 Hz, 2H), 7.27 (d, *J* = 8.8 Hz, 2H), 6.85-6.83 (m, 4H), 4.96 (d, *J* = 3.2 Hz, 1H), 3.02-3.01 (m, 1H), 2.76-2.72(m, 2H), 2.69-2.60 (m, 2H), 1.95-1.92 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.6 (d, *J* = 245.4 Hz), 135.9, 133.7, 132.7, 132.1, 129.8 (d, *J* = 8.1 Hz), 128.2, 114.0 (d, *J* = 21.4 Hz), 80.2, 65.7, 27.2, 26.9, 24.5; IR (neat): υ 3453, 2907, 1603, 1510, 1225, 1157, 835 cm^{-1}; $C_{17}H_{16}ClFOS_2$:calcd. C 57.53, H 4.54; found C 57.42, H 4.51.

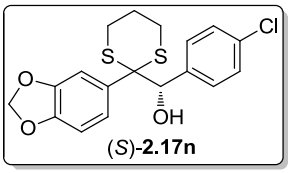
(*S*)-(2-(Benzo[*d*][1,3]dioxol-5-yl)-1,3-dithian-2-yl)(4-fluorophenyl)methanol ((*S*)-2.17m)



(*S*)-**2.17m**

Compound (*S*)-**2.17m** was synthesized from **2.28d** following the above asymmetric reduction procedure. White foamy semisolid; Yield: 93%; $[\alpha]_D^{25}$ = +24.2º (*c* 2.2, $CHCl_3$, 98% *ee*); R_f = 0.34 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25 (d, *J* = 1.6 Hz, 1H), 7.14 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.92-6.82 (m, 4H), 6.71 (d, *J* = 8.4 Hz, 1H), 5.99 (d, *J* = 1.2 Hz, 1H), 5.98 (d, *J* = 1.6 Hz, 1H), 4.91 (s, 1H), 3.00 (bs, 1H), 2.73-2.67 (m, 4H), 1.94-1.91 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.6 (d, *J* = 245.0 Hz), 147.9, 147.0, 133.1 (d, *J* = 3.0 Hz), 131.2, 129.9 (d, *J* = 8.1 Hz), 124.5, 114.0 (d, *J* = 21.2 Hz), 110.8, 107.6, 101.4, 80.5, 66.3, 27.3, 27.0, 24.7; IR (KBr): υ 3543, 2905, 1482, 1236, 829 cm^{-1}; $C_{18}H_{17}FO_3S_2$: calcd. C 59.32, H 4.70; found C 59.18, H 4.75.

(*S*)-(2-(Benzo[*d*][1,3]dioxol-5-yl)-1,3-dithian-2-yl)(4-chlorophenyl)methanol ((*S*)-2.17n)



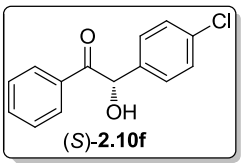
(*S*)-**2.17n**

Compound (*S*)-**2.17n** was synthesized from **2.28e** following the above asymmetric reduction procedure. White foamy solid, mp 141-142 °C; Yield: 95%; $[\alpha]_D^{25}$ = +7.8º (*c* 4.9, $CHCl_3$, 98% *ee*); R_f = 0.34 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27-7.26 (m, 1H), 7.14-7.11 (m, 3H), 6.85 (d, *J* = 8.4 Hz, 2H), 6.71 (d, *J* = 8.0 Hz, 1H), 5.98 (d, *J* = 2.4 Hz, 2H), 4.89 (s, 1H), 3.09 (bs, 1H), 2.72-2.62 (m, 4H), 1.93-1.86 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.8, 146.9, 135.7, 133.8, 131.0, 129.4, 127.1, 124.4, 110.7, 107.5, 101.3, 80.3, 66.0, 27.2, 26.9, 24.6; IR (neat): υ 3450, 2903, 1482, 1238, 1040 cm^{-1}; $C_{18}H_{17}ClO_3S_2$: calcd: C 56.76, H 4.50; found: C 56.65, H 4.43.

Synthesis of chiral benzoins (*S*)-2.10

Deprotection procedure employed for the synthesis of chiral (*R*)-benzoins ((*R*)-**2.10**) was followed.

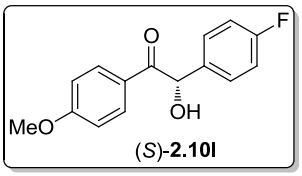
(*S*)-2-(4-Chlorophenyl)-2-hydroxy-1-phenylethanone ((*S*)-2.10f)



(*S*)-**2.10f**

Compound (*S*)-**2.10f** was synthesized from (*S*)-**2.17b** following the above described deprotection procedure.[19b] White foamy solid, mp 88-89 °C; Yield: 61%; $[\alpha]_D^{25}$ = +119.3º (*c* 1.55, $CHCl_3$, 99% *ee*); R_f = 0.48 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.91 (d, *J* = 7.5 Hz, 2H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 2H), 7.34-7.28 (m, 4H), 5.96 (d, *J* = 5.5 Hz, 1H), 4.59 (d, *J* = 5.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 198.6, 137.5, 134.5, 134.1, 133.3, 129.3, 129.1, 128.8, 75.4; IR (neat): υ 3378, 1680, 1591, 1237, 974 cm^{-1}.

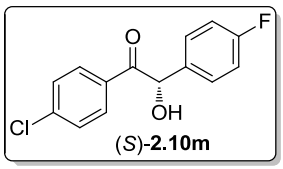
(*S*)-2-(4-Fluorophenyl)-2-hydroxy-1-(4-methoxyphenyl)ethanone ((*S*)-2.10l)



(*S*)-**2.10l**

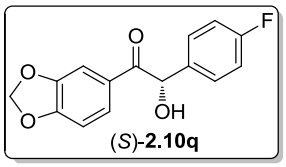
Compound (*S*)-**2.10l** was synthesized from (*S*)-**2.17h** following the above described deprotection procedure. Pale yellow liquid; Yield: 60%; $[\alpha]_D^{25}$ = +79.0º (*c* 1.43, $CHCl_3$, 96% *ee*); R_f = 0.30 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (d, *J* = 8.8 Hz, 2H), 7.33-7.30 (m, 2H), 7.00 (t, *J* = 8.8 Hz, 2H), 6.87 (d, *J* = 8.8 Hz, 2H), 5.89 (s, 1H), 4.68 (bs, 1H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.0, 164.2, 162.7 (d, *J* = 246.0 Hz), 135.6, 131.6, 129.5 (d, *J* = 8.3 Hz), 126.1, 116.1 (d, *J* = 21.6 Hz), 114.0, 74.9, 55.5; IR (neat): υ 3455, 1672, 1601, 1510, 1258, 1173, 976, 837 cm^{-1}; $C_{15}H_{13}FO_3$: calcd. C 69.22, H 5.03; found C 69.45, H 5.12.

(*S*)-1-(4-Chlorophenyl)-2-(4-fluorophenyl)-2-hydroxyethanone ((*S*)-2.10m)



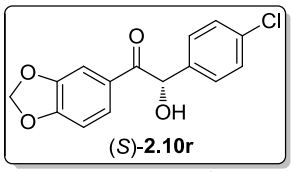
Compound (*S*)-**2.10m** was synthesized from (*S*)-**2.17i** following the above described deprotection procedure. White solid, mp 80-81 °C; Yield: 61%; $[\alpha]_D^{25}$ = +89.8º (*c* 1.72, $CHCl_3$, 99% *ee*); R_f = 0.48 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, *J* = 8.0 Hz, 2H), 7.39 (d, *J* = 8.0 Hz, 2H), 7.31-7.27 (m, 2H), 7.02 (t, *J* = 8.0 Hz, 2H), 5.90 (d, *J* = 4.4 Hz, 1H), 4.49 (d, *J* = 5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.6, 162.8 (d, *J* = 247.0 Hz), 140.6, 134.6, 131.6, 130.4, 129.5 (d, *J* = 8.4 Hz), 129.2, 116.3 (d, *J* = 21.7 Hz), 75.4; IR (neat): υ 3378, 1680, 1591, 1509, 1237, 1082, 974 cm^{-1}; $C_{14}H_{10}ClFO_2$: C 63.53, H 3.81; Found C 63.45, H 3.76.

(*S*)-1-(Benzo[*d*][1,3]dioxol-5-yl)-2-(4-fluorophenyl)-2-hydroxyethanone ((*S*)-2.10q)



Compound (*S*)-**2.10q** was synthesized from (*S*)-**2.17m** following the above described deprotection procedure. White solid, mp 91-93 °C; Yield: 67%; $[\alpha]_D^{25}$ = +106.2º (*c* 1.0, $CHCl_3$, 98% *ee*); R_f = 0.31 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (d, *J* = 8.0 Hz, 1H), 7.38 (s, 1H), 7.31-7.28 (m, 2H), 7.01 (t, 8.4 Hz, 2H), 6.78 (d, *J* = 8.0 Hz, 1H), 6.01 (s, 2H), 5.85 (s, 1H), 4.61 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.7, 162.7 (d, *J* = 246.3 Hz, 152.6, 148.3, 135.4, 129.5 (d, *J* = 8.3 Hz), 127.8, 125.9, 116.1 (d, *J* = 21.6 Hz), 108.7, 108.2, 102.1, 75.0; IR (KBr): υ 3399, 2897, 1667, 1603, 1505, 1451, 1263, 1067, 831 cm^{-1}; $C_{15}H_{11}FO_4$: calcd. C 65.69, H 4.04; found: C 65.79, H 4.15.

(*S*)-1-(Benzo[*d*][1,3]dioxol-5-yl)-2-(4-chlorophenyl)-2-hydroxyethanone ((*S*)-2.10r)

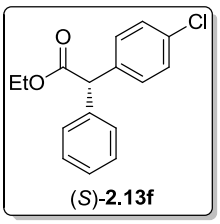


Compound (*S*)-**2.10r** was synthesized from (*S*)-**2.17n** following the above described deprotection procedure. White solid, mp 97-98 °C; Yield: 60%; $[\alpha]_D^{25}$ = +73.3º (*c* 1.63, $CHCl_3$, 97% *ee*); R_f = 0.31 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.37 (d, *J* = 1.6 Hz, 1H), 7.29 (d, *J* = 8.4 Hz, 2H), 7.25 (d, *J* = 8.4 Hz, 2H), 6.78 (d, *J* = 8.4 Hz, 1H), 6.01 (s, 2H), 5.83 (s, 1H), 4.61 (bd, *J* = 4.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.4, 152.6, 148.2, 137.9, 134.4, 129.3, 129.0, 127.7, 125.8, 108.6, 108.1, 102.1, 75.0;IR (neat): υ 3470, 2922, 1657, 1600, 1453, 1267, 1036 cm^{-1}; $C_{15}H_{11}ClO_4$: calcd. C 61.98, H 3.81; found: C 61.85, H 3.76.

Synthesis of chiral α-diarylacetic esters from (*R*)-benzoins

The procedure followed for racemic α-diarylacetic esters synthesis was employed.

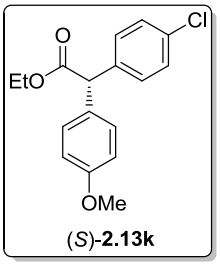
(*S*)-Ethyl 2-(4-chlorophenyl)-2-phenylacetate ((*S*)-2.13f)



(*S*)-**2.13f**

Compound (*S*)-**2.13f** obtained from (*R*)-**2.10f** following the general procedure for the synthesis of α-diarylacetic esters. White solid, mp 89-90 °C; Yield: 87%; $[\alpha]_D^{25}$ = -11.3º (*c* 0.63, $CHCl_3$, 88% *ee*); R_f = 0.61 in 1:10 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36-7.26 (m, 9H), 4.99 (s, 1H), 4.23 (q, *J* = 7.2 Hz, 2H), 1.27 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.1, 138.3, 137.3, 133.2, 130.0, 128.7, 128.4, 127.4, 61.3, 56.4, 14.1;IR (neat): υ 2956, 1732, 1485, 1194, 1085, 1014cm^{-1}; $C_{16}H_{15}ClO_2$: calcd. C 69.95, H 5.50; found C 70.11, H 5.41.

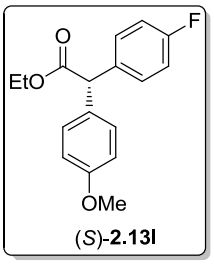
(*S*)-Ethyl 2-(4-chlorophenyl)-2-(4-methoxyphenyl)acetate ((*S*)-2.13k)



(*S*)-**2.13k**

Compound (*S*)-**2.13k** obtained from (*R*)-**2.10k** following the general procedure for the synthesis of α-diarylacetic esters. Colorless liquid; Yield: 90%; $[\alpha]_D^{25}$ = -10.2º (*c* 1.23, $CHCl_3$, 87% *ee*); R_f = 0.46 in 1:3 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31-7.22 (m, 6H), 6.88 (d, *J* = 8.4 Hz, 2H), 4.95 (s, 1H), 4.22 (q, *J* = 7.2 Hz, 2H), 3.80 (s, 3H), 1.27 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.3, 158.8, 137.6, 133.0, 130.4, 129.8, 129.5, 128.6, 114.0, 61.2, 55.5, 55.2, 14.1; IR (neat): υ 2934, 1734, 1512, 1252, 1032 cm^{-1}; $C_{17}H_{17}ClO_3$: calcd. C 67.00, H 5.62; found C 67.12, H 5.56.

(*S*)-Ethyl 2-(4-fluorophenyl)-2-(4-methoxyphenyl)acetate ((*S*)-2.13l)

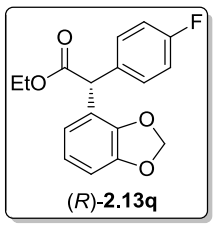


(*S*)-**2.13l**

Compound (*S*)-**2.13l** obtained from (*R*)-**2.10l** following the general procedure for the synthesis of α-diarylacetic esters. Colorless liquid; Yield: 88%; $[\alpha]_D^{25}$ = -13.3º (*c* 1.17, $CHCl_3$, 90% *ee*); R_f = 0.57 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33-7.29 (m, 2H), 7.26 (d, *J* = 8.8 Hz, 2H), 7.03 (t, *J* = 8.8 Hz, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 4.98 (s, 1H), 4.24 (q, *J* = 7.2 Hz, 2H), 3.81 (s, 3H), 1.29 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.7, 162.0 (d, *J* = 244.3 Hz), 158.8, 135.0 (d, *J* = 3.4 Hz), 130.8, 130.1 (d, *J* = 8.0 Hz), 129.5, 115.4 (d, *J* = 21.3 Hz), 114.1, 61.2, 55.5, 55.2, 14.1; IR (neat): υ 2982, 1734, 1609, 1510, 1252, 1032, 835 cm^{-1}; $C_{17}H_{17}FO_3$: calcd. C 70.82, H 5.94; found C 70.96, H 5.88.

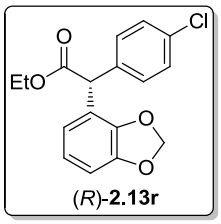
(*R*)-Ethyl 2-(benzo[*d*][1,3]dioxol-4-yl)-2-(4-fluorophenyl)acetate ((*R*)-2.13q)

Compound (*R*)-**2.13q** obtained from (*R*)-**2.10q** following the general procedure for the synthesis of α-diarylacetic esters. Colorless liquid; Yield: 87%; $[\alpha]_D^{25}$ = -9.8º (*c* 1.18, $CHCl_3$, 93% *ee*); R_f = 0.52 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32-7.28 (m, 2H), 7.03 (t, *J* =



8.8 Hz, 2H), 6.83 (s, 1H), 6.78 (s, 2H), 5.96 (s, 2H), 4.92 (s, 1H), 4.23 (q, *J* = 7.2 Hz, 2H), 1.28 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.4, 162.0 (d, *J* = 244.6 Hz), 147.9, 146.9, 134.6 (d, *J* = 3.2 Hz), 132.4, 130.0 (d, *J* = 8.0 Hz), 121.8, 115.4 (d, *J* = 21.3 Hz), 109.0, 108.3, 101.2, 61.3, 55.8, 14.1; IR (neat): υ 2903, 1732, 1604, 1506, 1489, 1443, 1231, 1038, 932, 814 cm^{-1}; $C_{17}H_{15}FO_4$: calcd. C 67.54, H 5.00; found C 67.39, H 4.89.

(*R*)-Ethyl 2-(benzo[*d*][1,3]dioxol-4-yl)-2-(4-chlorophenyl)acetate ((*R*)-2.13r)

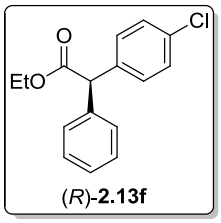


Compound (*R*)-**2.13r** obtained from (*R*)-**2.10r** following the general procedure for the synthesis of α-diarylacetic esters. Colorless liquid; Yield: 88%; $[\alpha]_D^{25}$ = -9.0º (*c* 1.13, $CHCl_3$, 93% *ee*); R_f = 0.46 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (d, *J* = 8.0 Hz, 2H), 7.23 (d, *J* = 8.8 Hz, 2H), 6.79 (s, 1H), 6.74 (s, 2H), 5.92 (s, 2H), 4.88 (s, 1H), 4.20 (q, *J* = 7.2 Hz, 2H), 1.25 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.1, 147.9, 146.9, 137.3, 133.2, 132.0, 129.8, 128.7, 121.8, 108.9, 108.2, 101.1, 61.3, 55.9, 14.1; IR (neat): υ 2982, 1732, 1491, 1443, 1250, 1155, 1038, 932 cm^{-1}; $C_{17}H_{15}ClO_4$: calcd. C 64.06, H 4.74; found: C 64.12, H 4.68.

Synthesis of chiral α-diarylacetic esters from (S)-benzoins

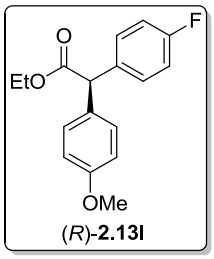
The procedure followed for racemic α-diarylacetic esters synthesis was employed.

(*R*)-Ethyl 2-(4-chlorophenyl)-2-phenylacetate ((*R*)-2.13f)



Compound (*R*)-**2.13f** obtained from (*S*)-**2.10f** following the general procedure for the synthesis of α-diarylacetic esters.[14] Light yellow liquid; Yield: 96%; $[\alpha]_D^{25}$ = +11.2º (*c* 1.47, $CHCl_3$, 93% *ee*); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33-7.22 (m, 9H), 4.97 (s, 1H), 4.20 (q, *J* = 7.2 Hz, 2H), 1.24 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.1, 138.3, 137.2, 133.1, 130.0, 128.6, 128.4, 127.4, 61.3, 56.4, 14.1;IR (neat): υ 2980, 1735, 1489, 1456, 1193, 1158, 880 cm^{-1}; $C_{16}H_{15}ClO_2$: calcd. C 69.95, H 5.50; found C 69.85, H 5.56.

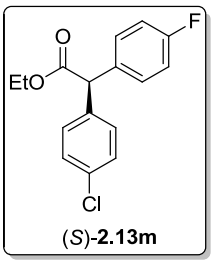
(*R*)-Ethyl 2-(4-fluorophenyl)-2-(4-methoxyphenyl)acetate ((*R*)-2.13l)



Compound (*R*)-**2.13l** obtained from (*S*)-**2.10l** following the general procedure for the synthesis of α-diarylacetic esters. Colorless liquid; Yield: 93%; $[\alpha]_D^{25}$ = +12.2º (*c* 0.88, $CHCl_3$, 91% *ee*); R_f = 0.57 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28-7.24 (m, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 6.99 (t, *J* = 8.4 Hz, 2H), 6.85 (d, *J* = 8.8 Hz, 2H), 4.93 (s, 1H), 4.19 (q, *J* =

7.2 Hz, 2H), 3.77 (s, 3H), 1.24 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.6, 161.9 (d, *J* = 244.1 Hz), 158.8, 134.9, 130.7, 130.0 (d, *J* = 7.8 Hz), 129.5, 115.3 (d, *J* = 21.3 Hz), 114.0, 61.2, 55.4, 55.2, 14.1; IR (neat): υ 2976, 1732, 1609, 1510, 1252, 1152, 1032, 835 cm^{-1}; $C_{17}H_{17}FO_3$: calcd. C 70.82, H 5.94; found C 70.91, H 5.85.

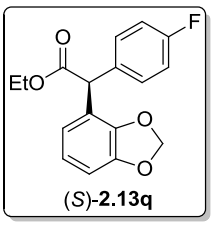
(*S*)-Ethyl 2-(4-chlorophenyl)-2-(4-fluorophenyl)acetate ((*S*)-2m)



(*S*)-**2.13m**

Compound (*S*)-**2.13m** obtained from (*S*)-**2.10m** following the general procedure for the synthesis of α-diarylacetic esters. Colorless liquid; Yield: 93%; $[\alpha]_D^{25}$ = +8.4º (*c* 1.12, $CHCl_3$, 85% *ee*); R_f = 0.69 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32-7.24 (m, 6H), 7.03 (t, *J* = 8.4 Hz, 2H), 4.97 (s, 1H), 4.23 (q, *J* = 7.2 Hz, 2H), 1.27 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.0, 162.0 (d, *J* = 245.0 Hz), 137.1, 134.0, 133.0, 130.1 (d, *J* = 8.0 Hz), 129.8, 128.8, 115.5 (d, *J* = 21.0 Hz), 61.4, 55.6, 14.0; IR (neat): υ 2982, 1734, 1508, 1152, 824 cm^{-1}; $C_{16}H_{14}ClFO_2$: calcd. C 65.65, H, 4.82; found C 65.51, H 4.89.

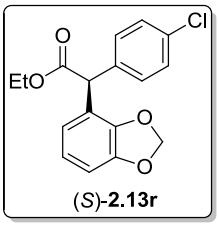
(*S*)-Ethyl 2-(benzo[*d*][1,3]dioxol-4-yl)-2-(4-fluorophenyl)acetate ((*S*)-2.13q)



(*S*)-**2.13q**

Compound (*S*)-**2.13q** obtained from (*S*)-**2.10q** following the general procedure for the synthesis of α-diarylacetic esters. Colorless liquid; Yield: 96%; $[\alpha]_D^{25}$ = +9.2º (*c* 1.43, $CHCl_3$, 92% *ee*); R_f = 0.53 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33-7.29 (m, 2H), 7.03 (t, *J* = 8.8 Hz, 2H), 6.84 (s, 1H), 6.78 (s, 2H), 5.95 (s, 2H), 4.93 (s, 1H), 4.24 (q, *J* = 7.2 Hz, 2H), 1.29 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.4, 162.0 (d, *J*= 244.7 Hz), 148.0, 146.9, 134.70, 134.66, 132.4, 130.1 (d, *J* = 8.0 Hz), 121.8, 115.4 (d, *J* = 21.4 Hz), 109.0, 108.3, 101.2, 61.3, 55.8, 14.1; IR (neat): υ 2984, 2901, 1726, 1605, 1485, 1248, 1039, 932, 814 cm^{-1}; $C_{17}H_{15}FO_4$: calcd. C 67.54, H 5.00; Found C 67.32, H 5.08.

(*S*)-Ethyl 2-(benzo[*d*][1,3]dioxol-4-yl)-2-(4-chlorophenyl)acetate ((*S*)-2.13r)



(*S*)-**2.13r**

Compound (*S*)-**2.13r** obtained from (*S*)-**2.10r** following the general procedure for the synthesis of α-diarylacetic esters. Colorless liquid; Yield: 85%; $[\alpha]_D^{25}$ = +9.5º (*c* 1.1, $CHCl_3$, 96% *ee*); R_f = 0.46 in 1:5 EtOAc/hexanes (double elution); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (d, *J* = 8.0 Hz, 2H), 7.23 (d, *J* = 8.8 Hz, 2H), 6.79 (s, 1H), 6.74 (d,*J* = 8.0 Hz, 2H), 5.92 (s, 2H), 4.88 (s, 1H), 4.20 (q, *J* = 7.2 Hz, 2H), 1.25 (t, *J* =

7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.1, 147.9, 146.9, 137.3, 133.1, 132.0, 129.8, 128.7, 121.7, 108.9, 108.2, 101.1, 61.3, 55.9; IR (neat): υ 2980, 1736, 1489, 1250, 932, 802cm^{-1}; $C_{17}H_{15}ClO_4$: calcd. C 64.06, H 4.74; found C 64.21, H 4.81.

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2.6 Representative spectra

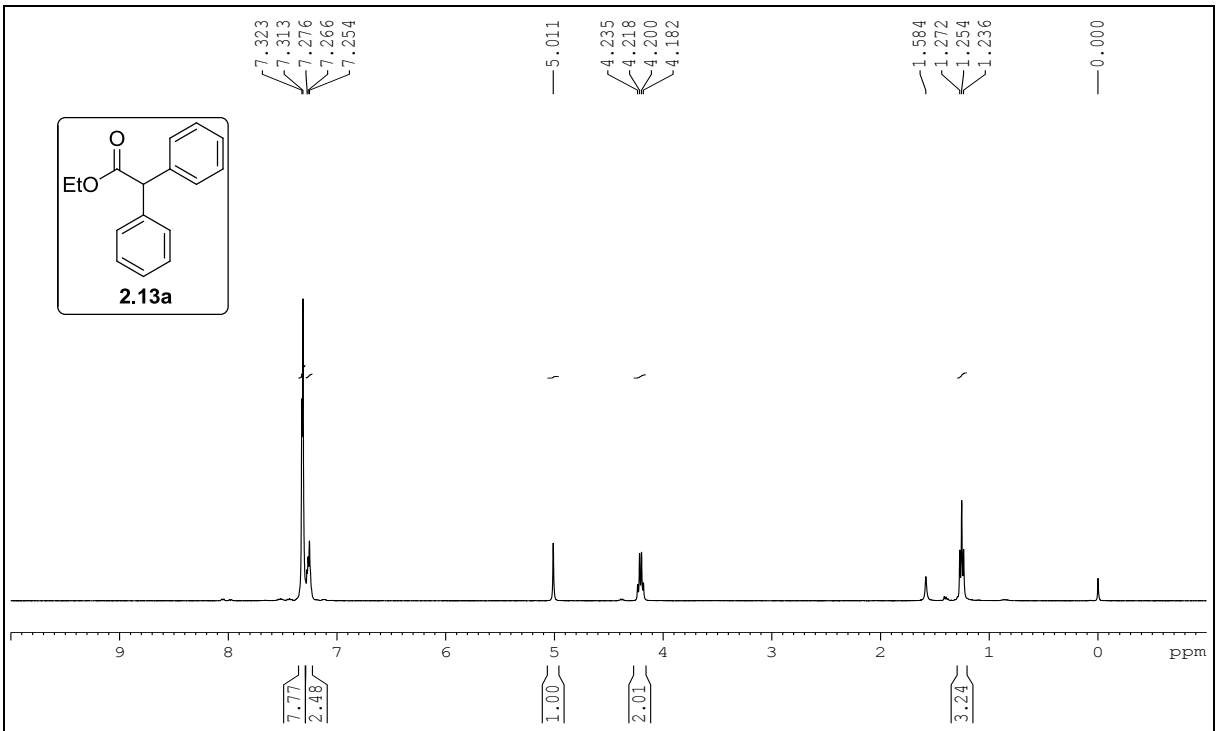


Fig 2.3. ^{1}H NMR spectrum of compound **2.13a**

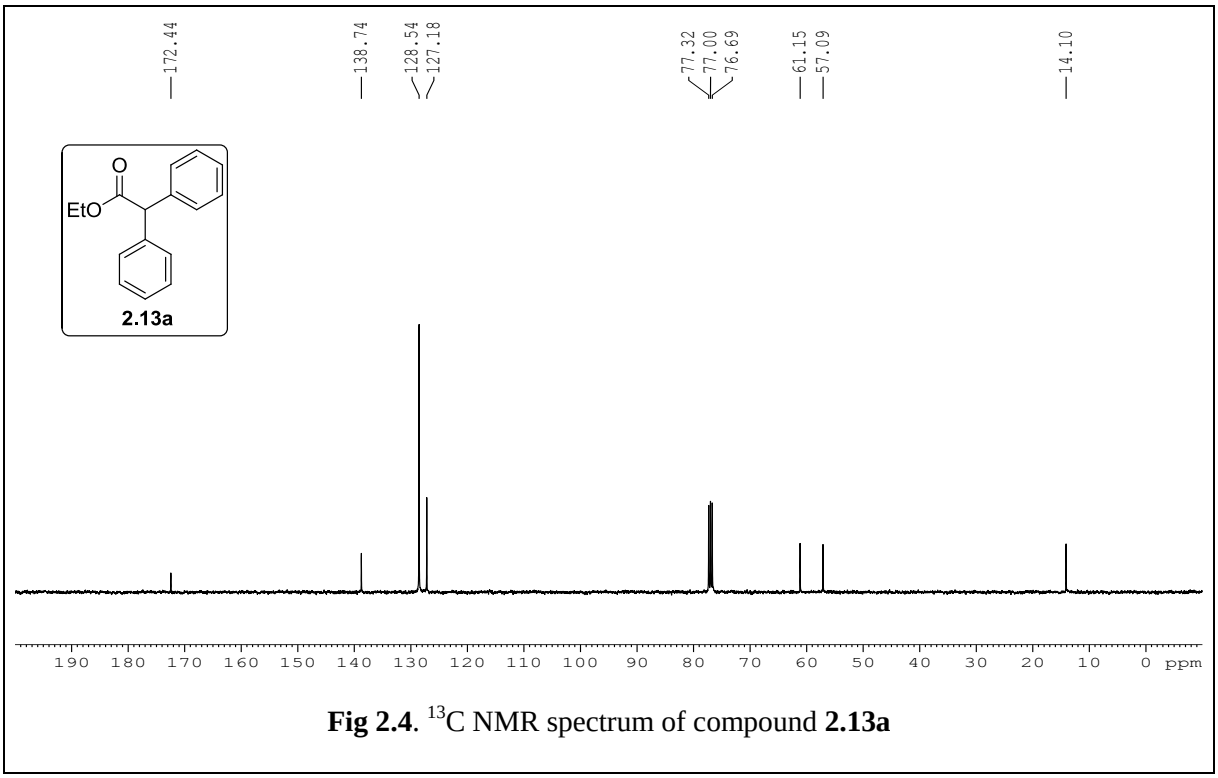


Fig 2.4. ^{13}C NMR spectrum of compound **2.13a**

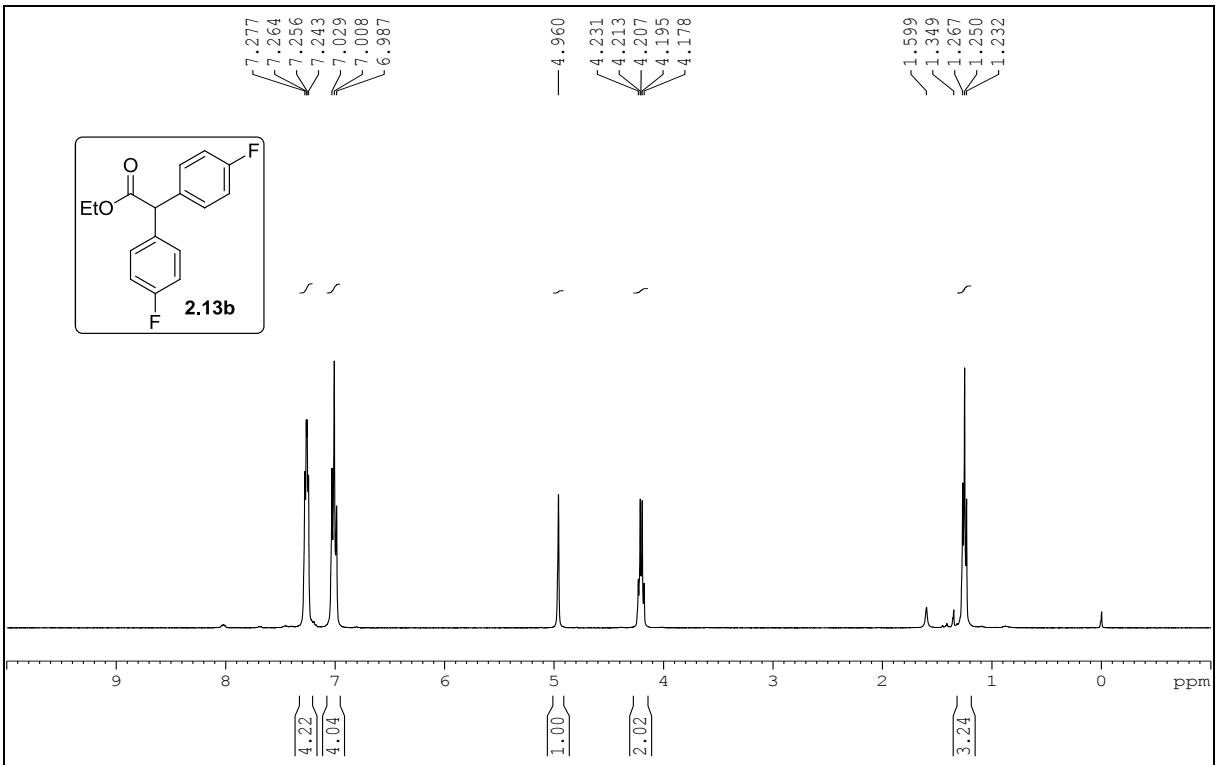


Fig 2.5. ^{1}H NMR spectrum of compound **2.13b**

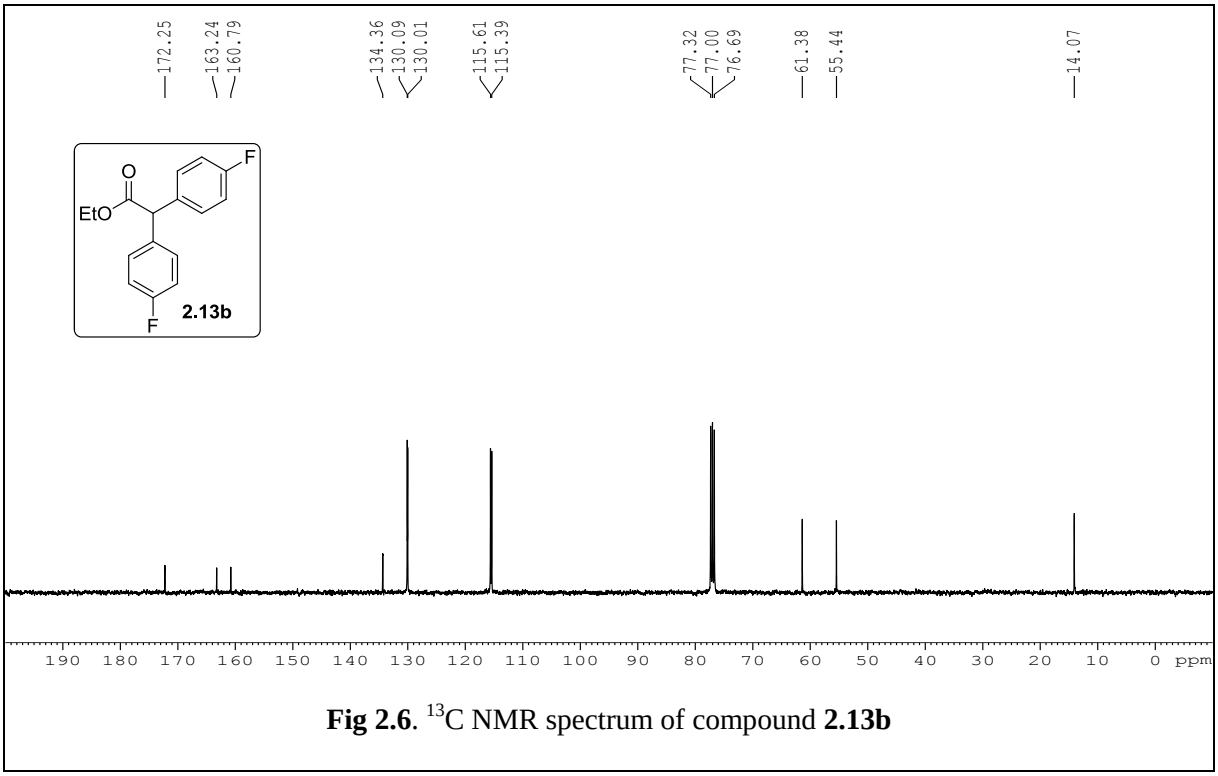


Fig 2.6. ^{13}C NMR spectrum of compound **2.13b**

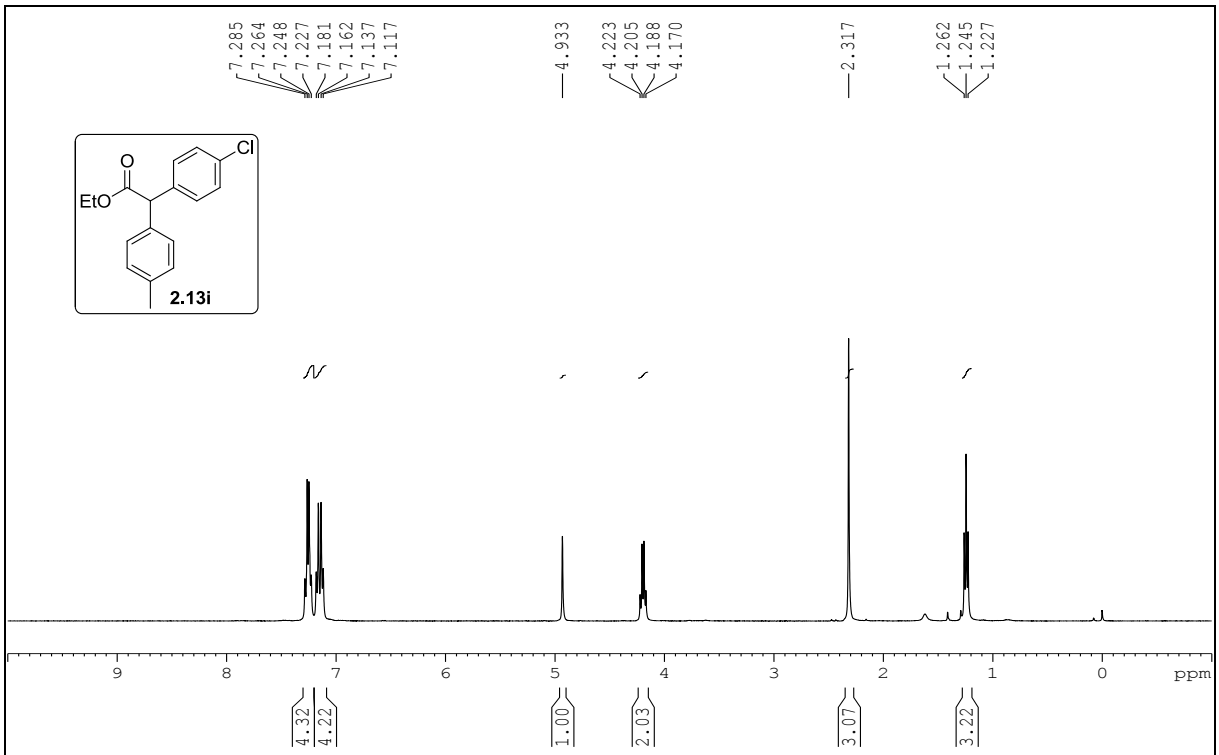


Fig 2.7. ^{1}H NMR spectrum of compound **2.13i**

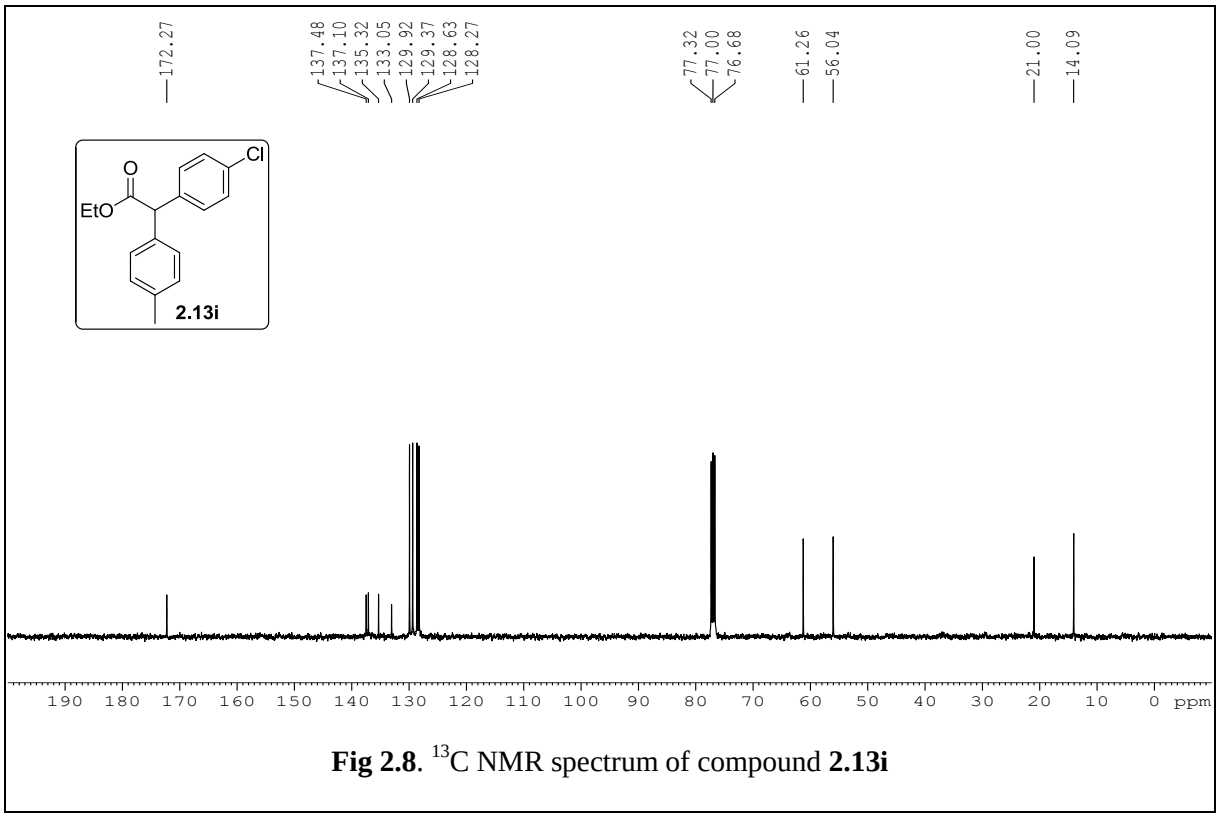


Fig 2.8. ^{13}C NMR spectrum of compound **2.13i**

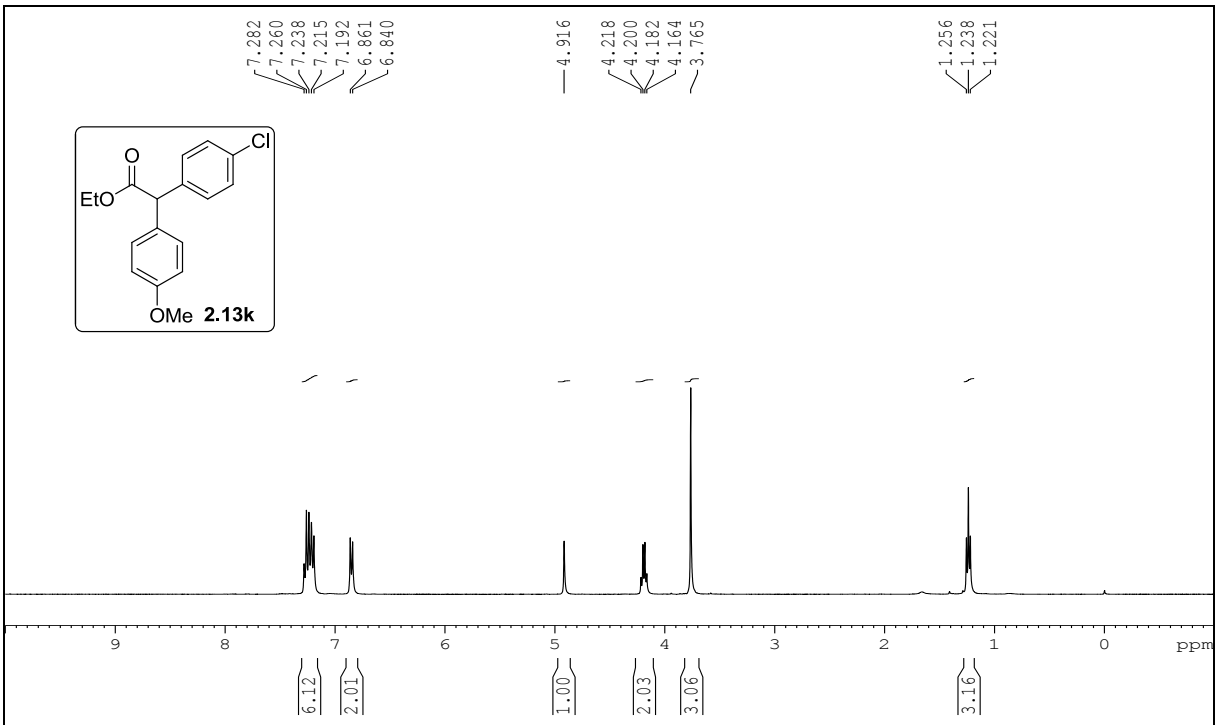


Fig 2.9. ^{1}H NMR spectrum of compound **2.13k**

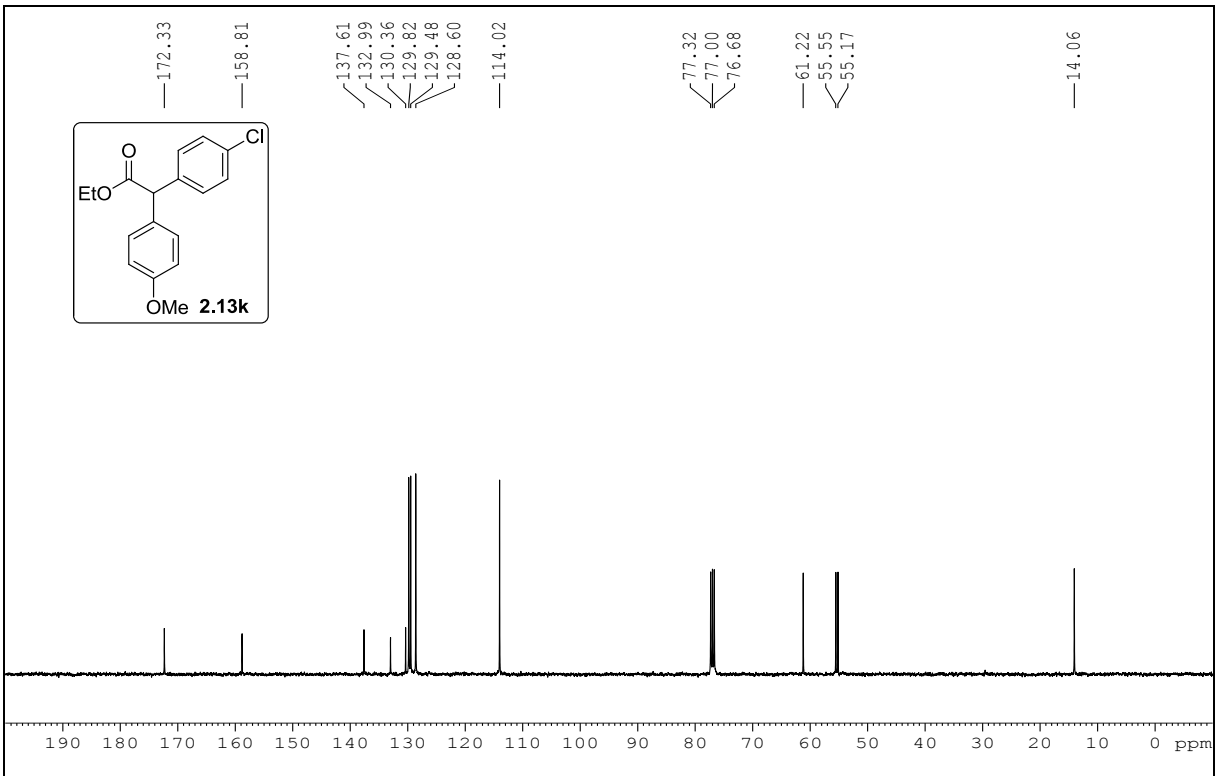


Fig 2.10. ^{13}C NMR spectrum of compound **2.13k**

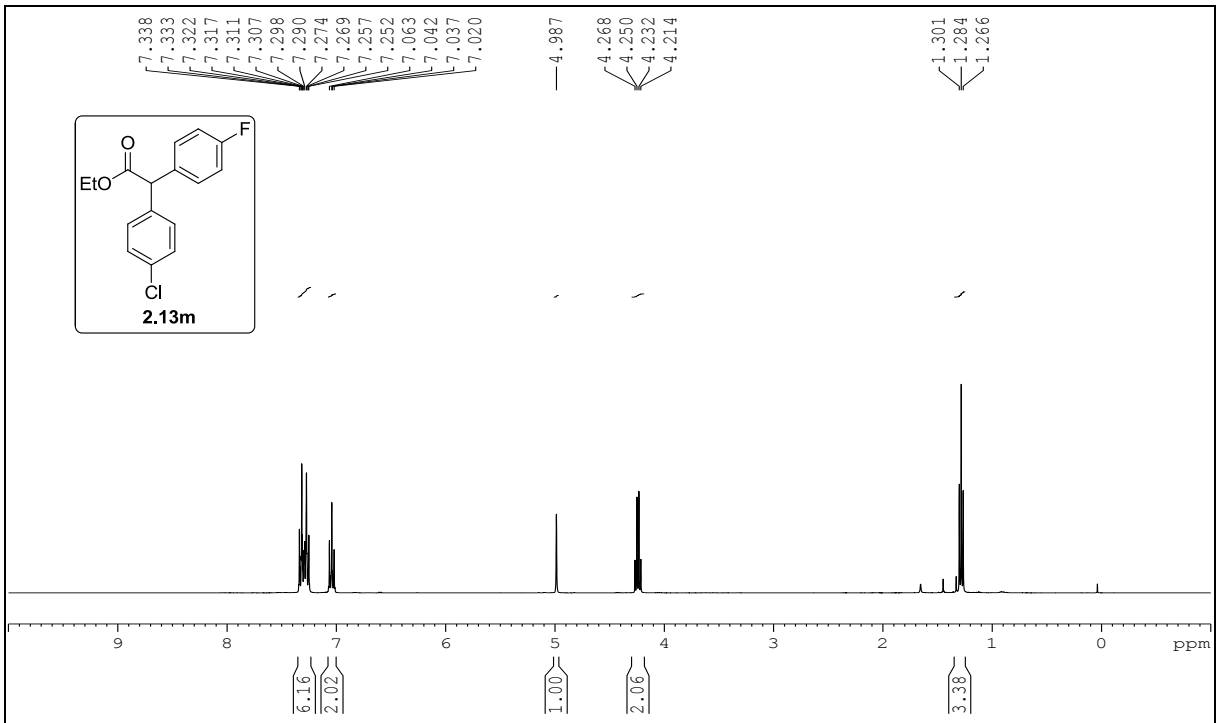


Fig 2.11. ^{1}H NMR spectrum of compound **2.13m**

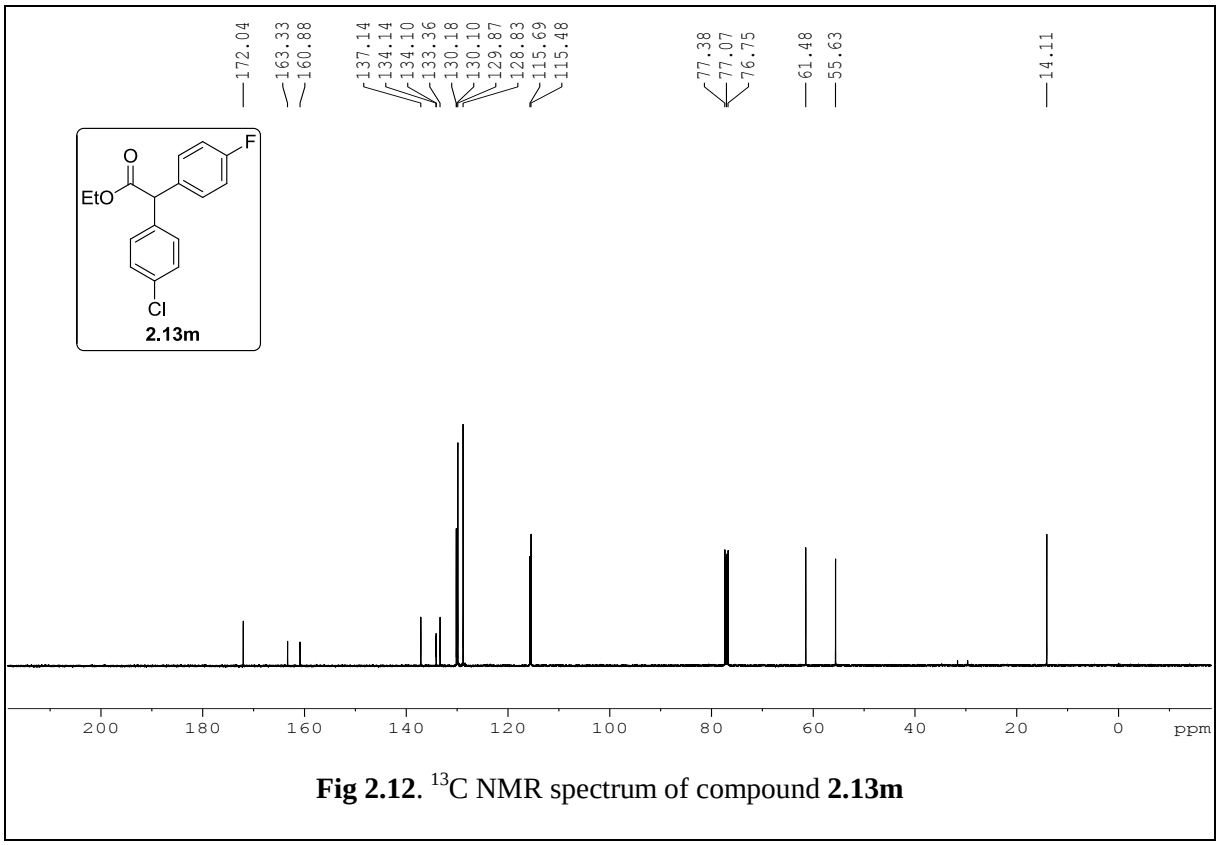


Fig 2.12. ^{13}C NMR spectrum of compound **2.13m**

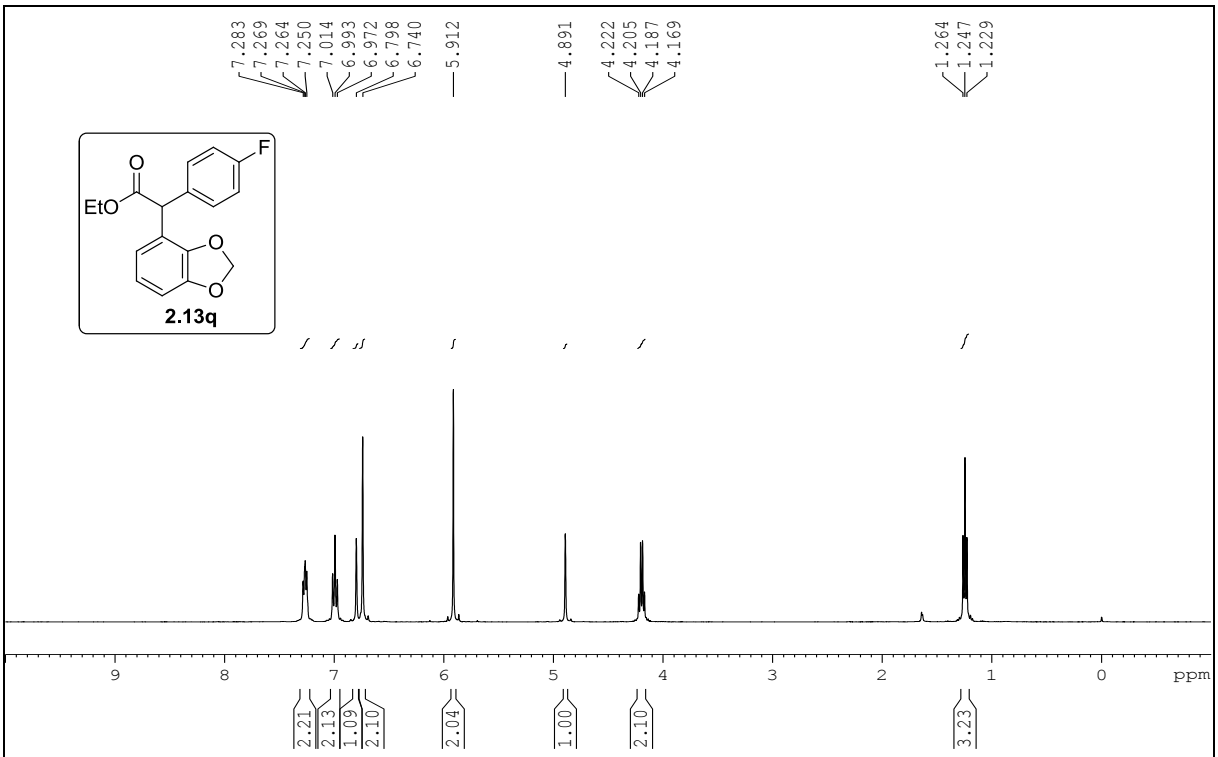


Fig 2.13. ^{1}H NMR spectrum of compound **2.13q**

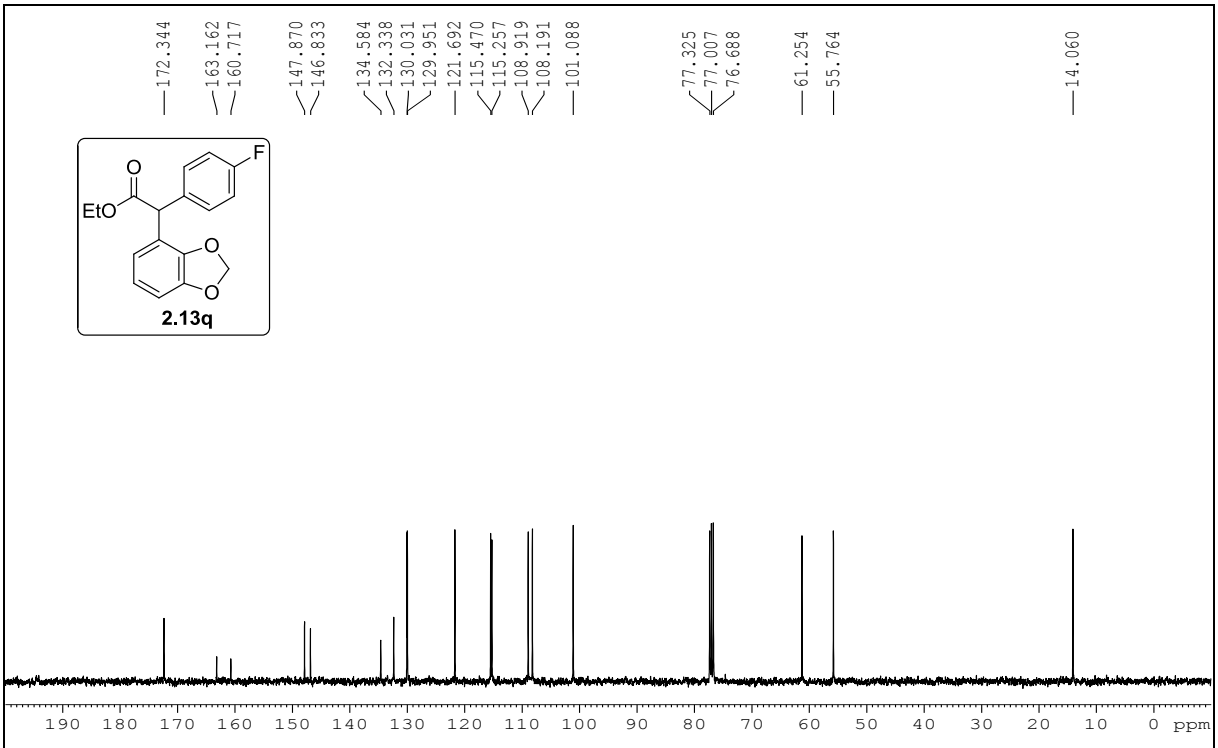
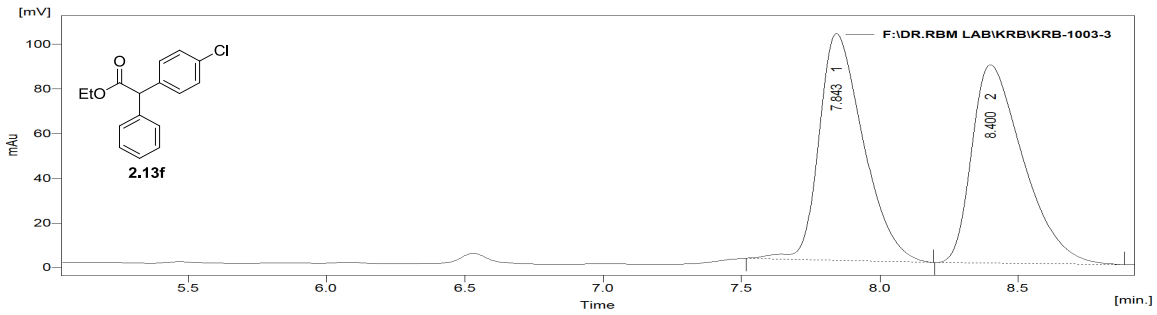


Fig 2.14. ^{13}C NMR spectrum of compound **2.13q**

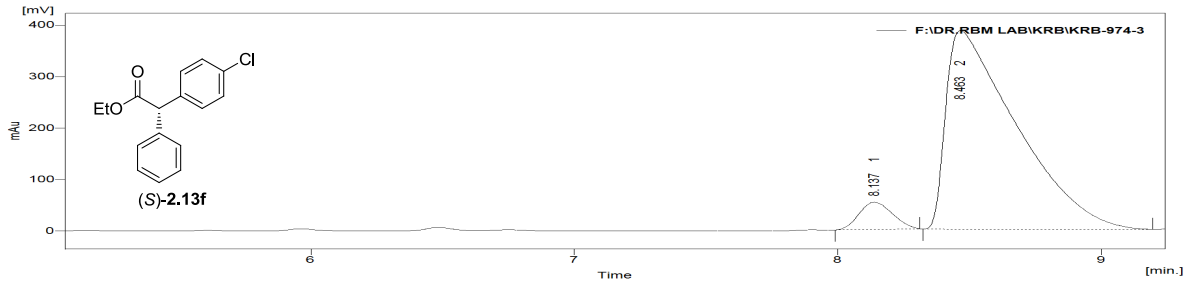


Result Table (Uncal - F:\DR.RBM LAB\KRB\KRB-1003-3)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	7.843	755.852	67.632	49.7	53.4	0.17
2	8.400	763.682	59.124	50.3	46.6	0.20
	Total	1519.535	126.756	100.0	100.0	

CHIRALCEL OJ-H, FLOW RATE 1.0 mL/min, HEX:IPA= 90:10, 254

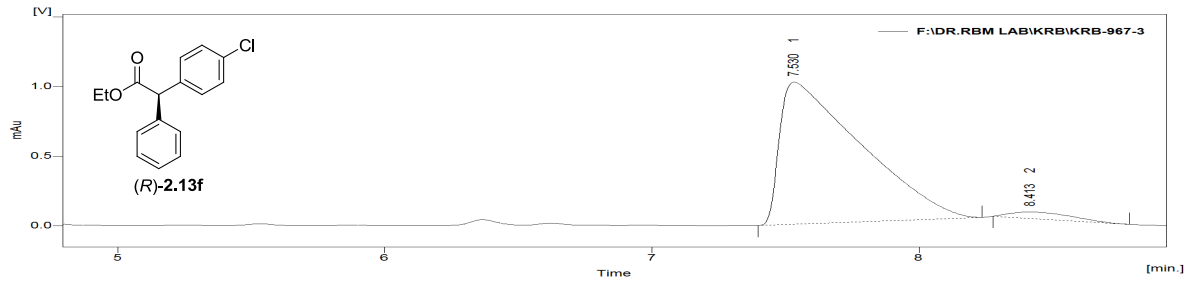
Fig 2.15. HPLC spectrum of racimic compound **2.13f**



Result Table (Uncal - F:\DR.RBM LAB\KRB\KRB-974-3)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	8.137	308.747	35.222	6.1	12.0	0.14
2	8.463	4773.502	257.232	93.9	88.0	0.29
	Total	5082.248	292.453	100.0	100.0	

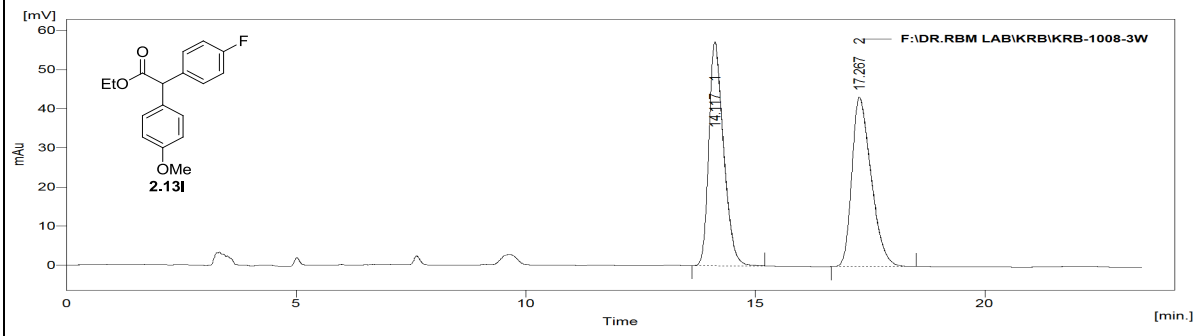
Fig 2.16. HPLC spectrum of compound (*S*)-**2.13f**



Result Table (Uncal - F:\DR.RBM LAB\KRB\KRB-967-3)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	7.530	14352.757	680.138	96.5	95.7	0.35
2	8.413	525.027	30.522	3.5	4.3	0.25
	Total	14877.783	710.660	100.0	100.0	

Fig 2.17. HPLC spectrum of compound (*R*)-**2.13f**

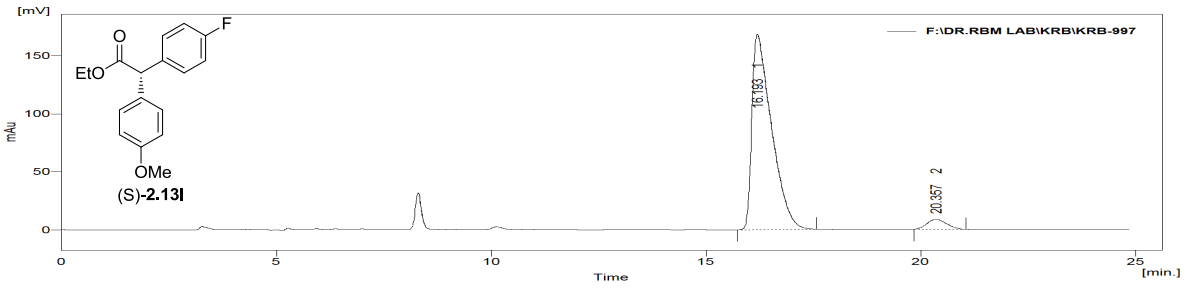


Result Table (Uncal - F:\DR.RBM LAB\KRB\KRB-1008-3W)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	14.117	849.250	38.116	50.1	56.9	0.34
2	17.267	845.074	28.913	49.9	43.1	0.45
	Total	1694.324	67.029	100.0	100.0	

CHIRALCEL OJ-H. FLOW RATE 1.0 mL/min. HEX:IPA= 90:10. 254 nm

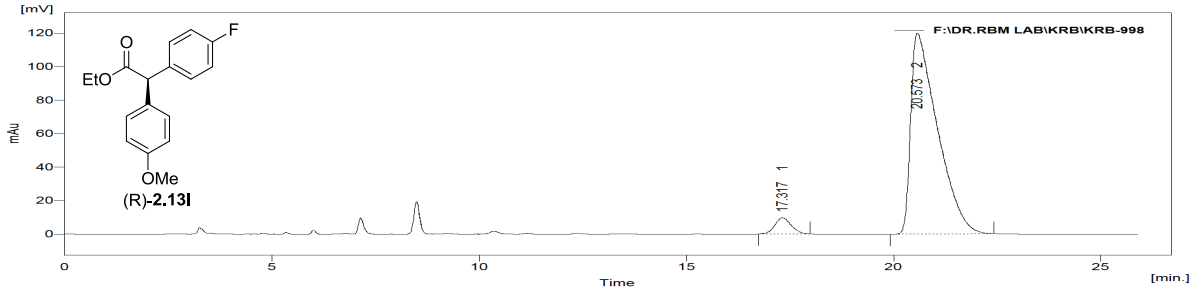
Fig 2.18. HPLC spectrum of racimic compound **2.13l**



Result Table (Uncal - F:\DR.RBM LAB\KRB\KRB-997)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	16.193	3564.296	112.338	95.1	95.2	0.49
2	20.357	182.131	5.686	4.9	4.8	0.51
	Total	3746.427	118.024	100.0	100.0	

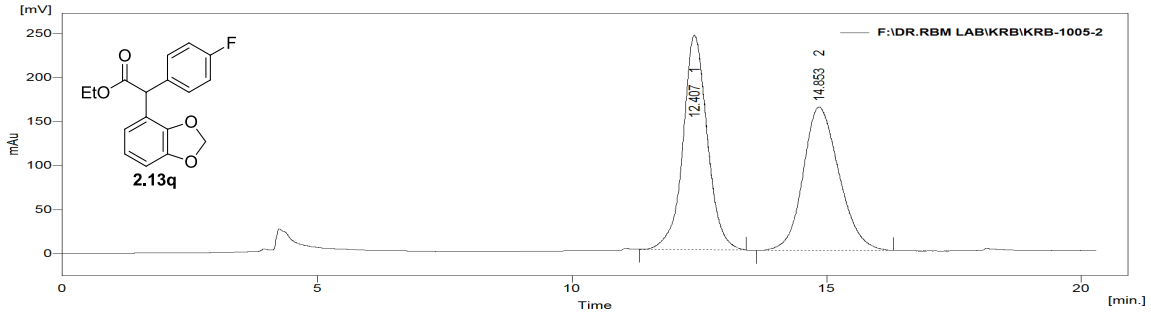
Fig 2.19. HPLC spectrum of compound (*S*)-**2.13l**



Result Table (Uncal - F:\DR.RBM LAB\KRB\KRB-998)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	17.317	177.149	6.436	4.7	7.4	0.43
2	20.573	3579.045	80.026	95.3	92.6	0.69
	Total	3756.194	86.461	100.0	100.0	

Fig 2.20. HPLC spectrum of compound (*R*)-**2.13l**

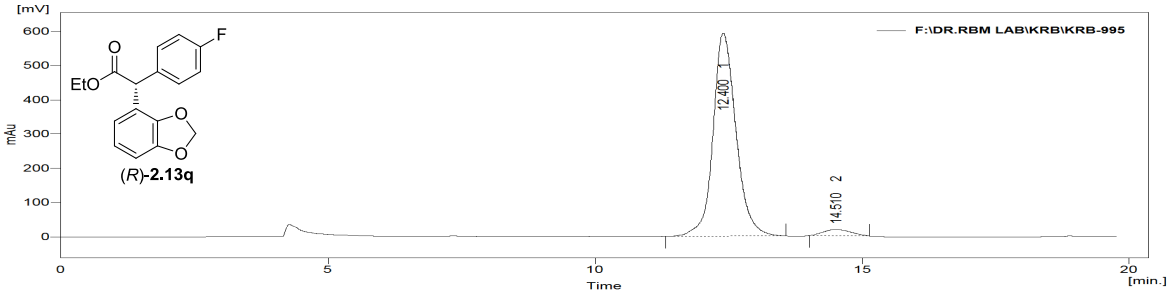


Result Table (Uncal - F:\DR.RBM LAB\KRB\KRB-1005-2)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	12.407	5391.827	162.383	50.3	59.9	0.49
2	14.853	5330.956	108.712	49.7	40.1	0.75
	Total	10722.783	271.095	100.0	100.0	

CHIRALCEL OD-H, FLOW RATE 0.8 mL/min, HEX:IPA= 99.2:0.8, 254 nm

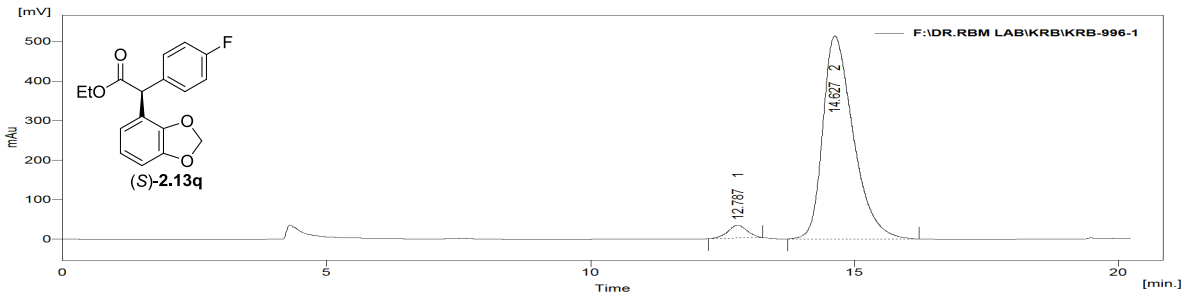
Fig 2.21. HPLC spectrum of racimic compound **2.13q**



Result Table (Uncal - F:\DR.RBM LAB\KRB\KRB-995)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	12.400	11782.353	395.052	96.5	97.0	0.44
2	14.510	424.842	12.042	3.5	3.0	0.58
	Total	12207.195	407.095	100.0	100.0	

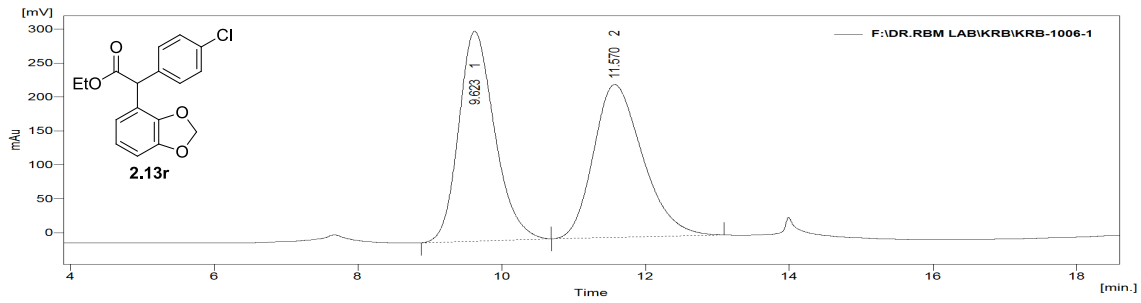
Fig 2.22. HPLC spectrum of compound (*R*)-**2.13q**



Result Table (Uncal - F:\DR.RBM LAB\KRB\KRB-996-1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	12.787	552.381	21.512	3.9	5.9	0.40
2	14.627	13715.313	342.461	96.1	94.1	0.60
	Total	14267.694	363.973	100.0	100.0	

Fig 2.23. HPLC spectrum of compound (*S*)-**2.13q**

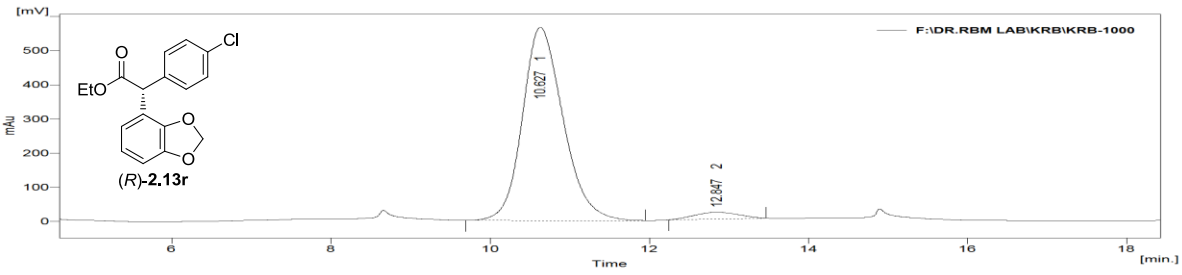


Result Table (Uncal - F:\DR.RBM LAB\KRB\KRB-1006-1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	9.623	7156.373	206.068	50.1	57.8	0.53
2	11.570	7118.784	150.150	49.9	42.2	0.73
	Total	14275.157	356.218	100.0	100.0	

CHIRALCEL OD-H, FLOW RATE 1.0 mL/min, HEX:IPA= 99.2:0.8, 254 nm

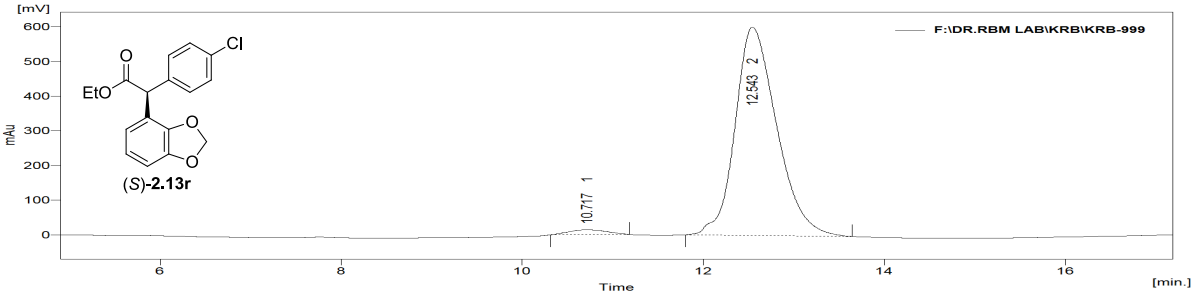
Fig 2.24. HPLC spectrum of racimic compound **2.13r**



Result Table (Uncal - F:\DR.RBM LAB\KRB\KRB-1000)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	10.627	13361.613	376.346	96.3	96.6	0.54
2	12.847	507.984	13.246	3.7	3.4	0.64
	Total	13869.596	389.591	100.0	100.0	

Fig 2.25. HPLC spectrum of compound (*R*)-**2.13r**



Result Table (Uncal - F:\DR.RBM LAB\KRB\KRB-999)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	10.717	272.573	9.484	2.1	2.3	0.49
2	12.543	12781.682	400.443	97.9	97.7	0.48
	Total	13054.255	409.927	100.0	100.0	

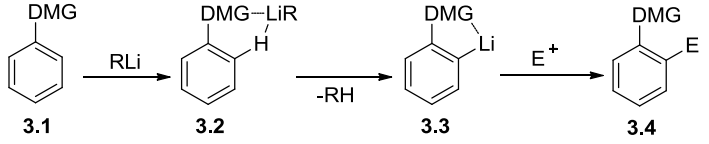
Fig 2.26. HPLC spectrum of compound (*S*)-**2.13r**

Chapter 3

Regioselective Lithiation of Dithiane Protected 2,4-Dichloro/Difluoro Substituted Benzaldehydes

3.1 Introduction

Directed metalation using complex-induced proximity effect (CIPE) is an useful approach in the regioselective functionalization of organic compounds. Gilman and Wittig were the first to observe the directed *ortho*-metalation (DoM) facilitated by a coordinating group.[1a, b] In their initial work, anisole was treated with *n*-butyllithium to generate an *ortho*-lithiated anisole that could be reacted with electrophiles to make *o*-functionalized compounds exclusively (Scheme 3.1). They ascribed the selective lithiation was due to the increased acidity of *ortho* hydrogens due to the presence of the coordinating group (directed metalation group (DMG)). Around the same time complementary metal-halogen exchange in aromatic compounds was discovered by the same groups.[1c, d] This finding gave further scope in the field of metalation chemistry. Extensive amount of work has been developed based on this metalation chemistry.[2] In particular, the research groups of Snieckus and Beak have contributed a lot.[2-5] In direct *ortho*-metalation step, the proton close to the DMG will be abstracted by a strong base, generally an alkyllithium reagent and leads to the formation of *ortho*-lithiated species **3.3**, which upon treatment with electrophile furnish the product **3.4** (Scheme 3.1).



Scheme 3.1. Directed *ortho*-lithiation (DoL)

Alkyllithium bases exist as aggregates in hydrocarbon solvents. In basic solvents like ethers, amines and phosphines, these alkyllithium aggregates dissociate due to acid-base interactions. In THF or ether, *n*-butyllithium exists as tetramer $(n\text{-BuLi})_4$. Addition of Et_3N makes it as a dimer $(n\text{-BuLi})_2$. In the presence of bidentate ligand additives, especially TMEDA (*N*,*N*,*N'*,*N'*-tetramethylethylenediamine), alkyllithium exists as monomers (when the concentration is low, less than 0.1M) and dimers (when the concentration is high) and thus, its basicity increases significantly.[3] The *s*-BuLi-TMEDA reagent works as more powerful lithiation agent than *n*-BuLi-TMEDA.

A good DMG must have a good coordinating atom to bind with the base alkyllithium. At the same time the DMG should be less electrophilic so that it is not attacked by this strong base. Therefore a DMG must possess a heteroatom. Gschwend and Rodrigue suggested that, the directed *ortho*-metalation can be achieved in two ways by DMGs: one is coordination mechanism and the second is acid-base mechanism (inductive).[4a] The relative significance of coordination and inductive effects of DMGs have not been systematically correlated with fundamental Lewis acid-base and electronic principles. A list of directing groups classified based on their directing abilities is presented in Figure 3.1.When the DMG is F, Br, CN or CF_3, inductive factors influence the deprotonation whereas coordination effect dominates to effect deprotonation when DMG is OMe or NMe_2.[4]

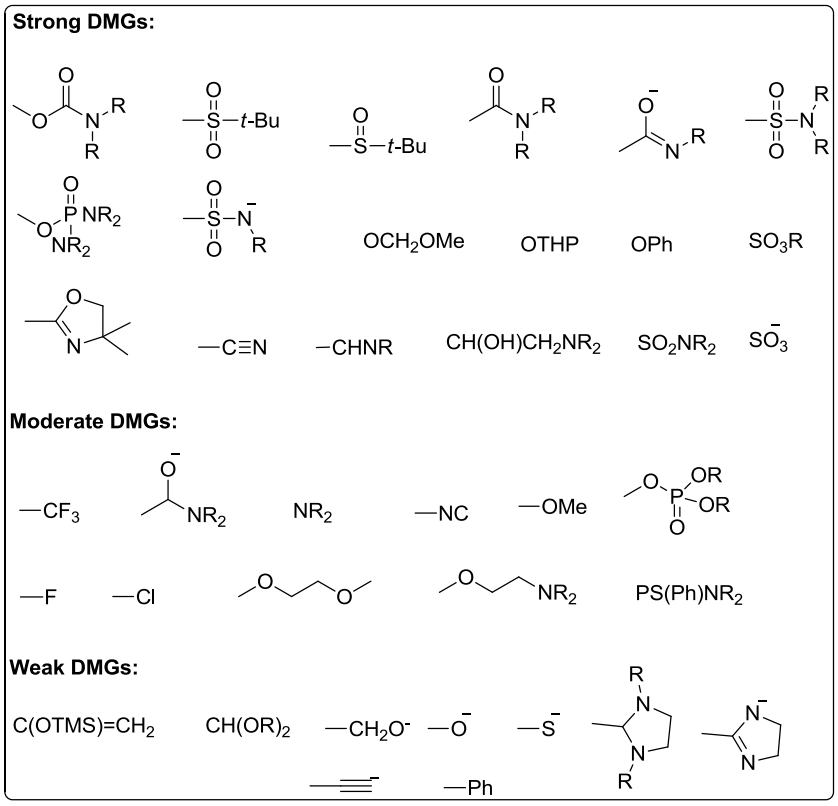
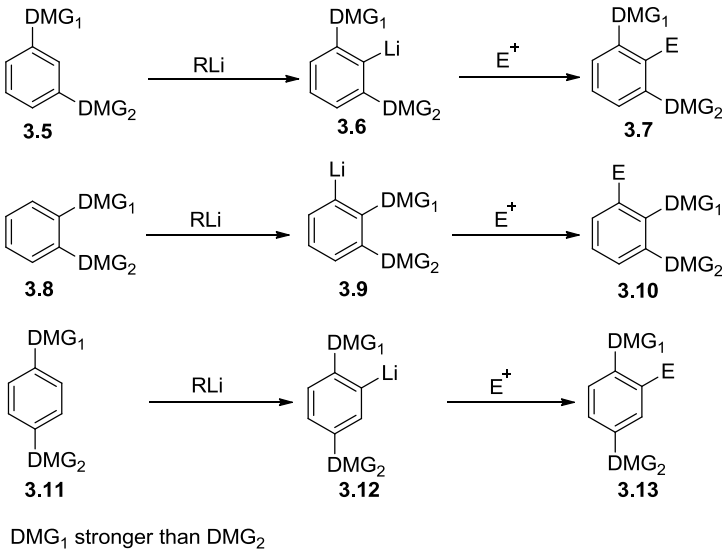


Figure 3.1. Common directed metalation groups (DMGs)

The same proposal was reiterated after thorough mechanistic studies by Snieckus and Beak that the lithiation could occur in two steps. First lithium coordinates with the DMG to form prelithiation complex, which will bring the reactive groups close for directed lithiation.[5] This phenomenon is known as complex-induced proximity effect (CIPE). Schlosser correlated the acidities of few substrates with the rate of lithiation.[6] These studies were harmonious with the Collum's results

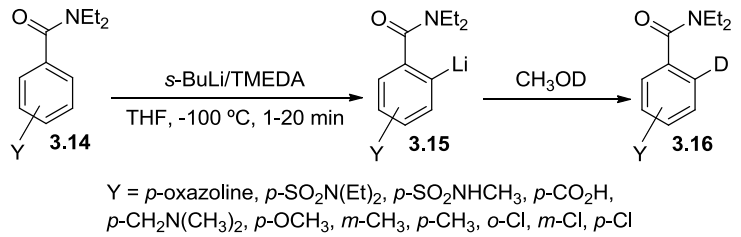
on lithiation of benzene, anisole and several alkoxy-substituted aromatic compounds by *n*-BuLi/TMEDA reagent.[7]

With two DMGs present on a benzene ring, there are three ways that the two DMGs may exist, *i.e*, 1,2-, 1,3- and 1,4- positions. When the DMGs are in 1 and 3 positions, the two DMGs will direct the lithiation to occur at the C2-position through a cooperative coordination to *n*-alkyllithium base. In this case, the steric factors of the DMGs have to be considered. When the DMGs are in 1,2- or 1,4- positions on the benzene ring, the lithiation will occur at *ortho* position to the stronger DMG. If the strengths of DMGs are similar a mixture of products may result (Scheme 3.2). Many electrophiles can be used to react with lithiated aromatic compounds. Common electrophiles used are ArCHO, RCHO, RX, RCOX, Ac_2O, RCN, X_2, XCO_2Et, BnX, DMF, CO_2, $(RS)_2$, TMSCl, $B(OR)_3$, Bu_3SnCl, TsN_3, BnX, RNCO, terminal epoxides etc..



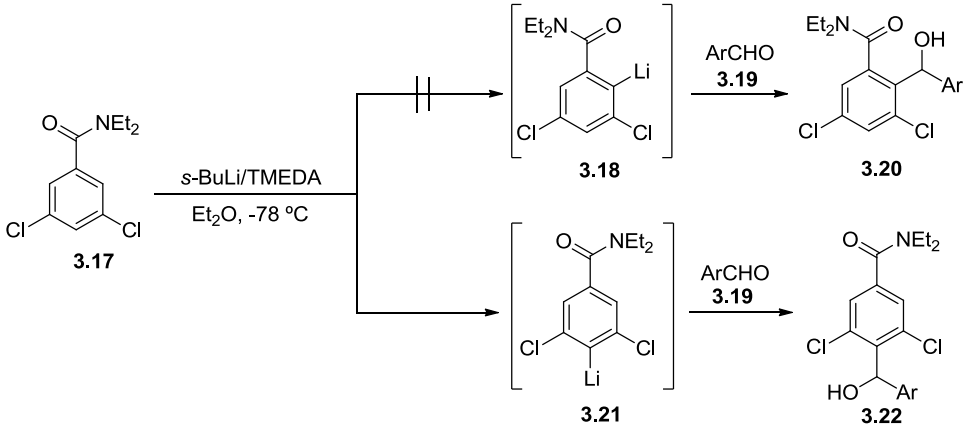
Scheme 3.2. General considerations in directed *ortho*-lithiation

After a systematic investigation on directing ability of different DMGs, Beak and co-workers have found that the tertiary carboxamide group showed a superior directing ability than oxazoline, sulfonamide, methoxy, (dimethylamino)methyl, chloro, carboxyl, and methyl groups. When benzene ring has another DMG in addition to carboxamide, the lithiation was directed to the *ortho* position of carboxamide to form the aryllithium **3.15**, which upon quenching with CH_3OD resulted in **3.16** (Scheme 3.3).[8]



Scheme 3.3. Superior directing ability of tertiary carboxamide DMG

Bradley and co-workers have reported an unusual regioselective lithiation on 3,5-dichloro-*N*,*N*-diethylbenzamide **3.17** using *s*-BuLi/TMEDA at -78 ºC. The directing capability is associated with the electronic effects, steric effects or combination of both. In principle, two sites are available for metalation in 3,5-dichloro-*N*,*N*-diethylbenzamide **3.17**. By predictable classical knowledge, lithiation was thought to occur at C2- or C6- position with respect to carboxamide DMG due to the cumulative directing ability of carboxamide and chloro DMGs. But lithiation occured, regioselectively, at C4- position with respect to carboxamide. Upon treatment of the lithiated species with an electrophile **3.19**, the reaction resulted in the product **3.22** (Scheme 3.4). The lithiated intermediate **3.21** is obtained due to the complex formed between chlorines and *s*-BuLi is less bulky than the complex formed between carboxamide and chlorine with *s*-BuLi. Moreover, the acidity of the C4-hydrogen increases as a result of both additive effect of complexation between the two chlorines with lithium and cumulative inductive effect of two the chlorine atoms.[9a] Recently, Knochel and co-workers have reported a directed magnesiation of polyhaloaromatic compounds using $TMP_2Mg{\cdot}2LiCl$ or TMPMgCl·LiCl. The metalated species were treated with a variety of electrophiles to obtain highly functionalised building blocks in good to excellent yields.[9b]

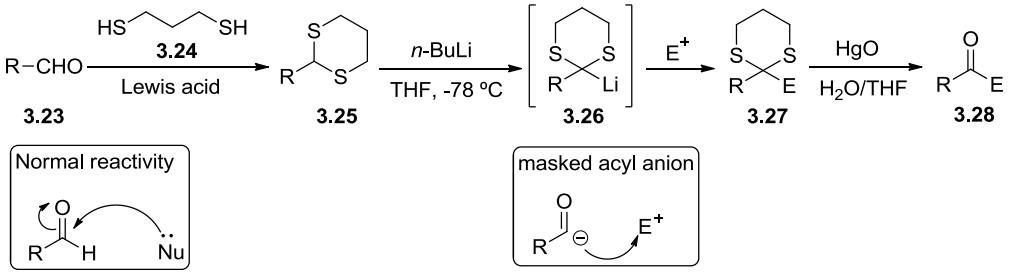


Scheme 3.4. Unusual regioselectivity of directed lithiation

3.2 Results and discussion

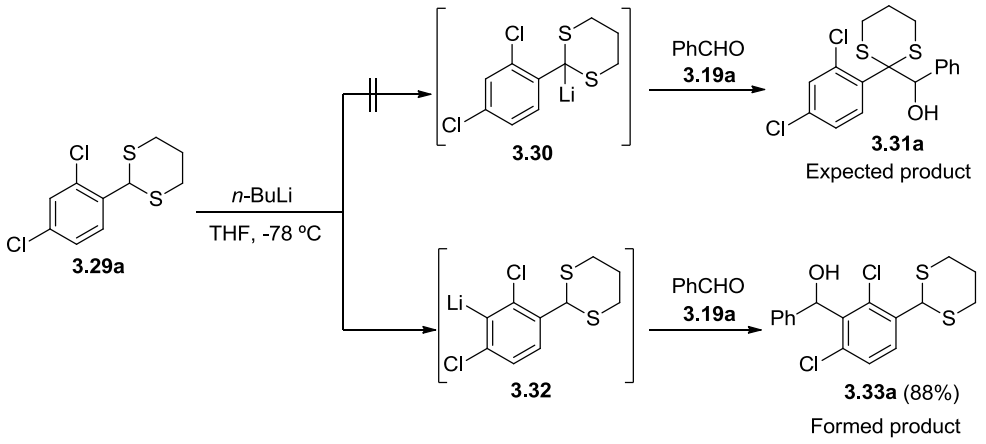
3.2.1 Background of the reaction

Inversion of polarity at a functional carbon atom is known as umpolung. Umpolung reagents are very useful in organic synthesis. Dithiane is one of the important umpolung reagents. By converting into dithianes, the electrophilic carbon in aldehydes changes to nucleophilic. These can be lithiated using strong bases such as alkyllithiums to furnish lithiated 1,3-dithianes **3.26**, which can be viewed as a masked acyl anion and can react with electrophiles to result **3.27**. Deprotection of dithiane will regenerate the carbonyl functionality (Scheme 3.5).[10]



Scheme 3.5. Umpolung reactivity of carbonyl functional group

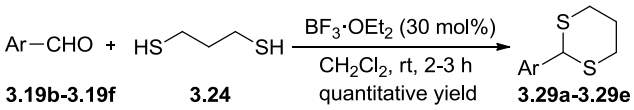
While preparing benzoins to employ in the 1,2-aryl migration reaction in *in situ* formed acetals (2nd chapter),[11a] we observed an unexpected lithiation with 2-(2,4-dichlorophenyl)-1,3-dithiane **3.29a**. The substrate **3.29a** was treated with *n*-BuLi at –78 ºC to lithiate at the dithiane carbon to obtain **3.31a** *via* **3.30**. But, to our surprise, lithiation took place at arene ring by directed *ortho*-metalation effect of two chlorine atoms and upon quenching with benzaldehyde **3.19a** compound **3.33a** was obtained in good yield (88%) (Scheme 3.6). Even minor amount of **3.31a** was also not detected in this reaction. This interesting observation motivated us to study this lithiation in detail.



Scheme 3.6. Observed regioselective lithiation

3.2.2 Preparation of starting materials

Starting materials used in this study are dithiane protected aromatic aldehydes **3.29**. These were prepared from corresponding aromatic aldehydes **3.19** on treatment with 1,3-propanedithiol **3.24** under Lewis acid $BF_3{\cdot}OEt_2$ conditions (Scheme 3.7). Reactions were clean, completed in 2-3 h to get the dithianes **3.29a-3.29e** in quantitative yields. Column purification was also not required for these products. The prepared dithianes were used in the study of regioselective lithiation.



3.19b, **3.29a**: Ar = 2,4-$Cl_2C_6H_3$
3.19c, **3.29b**: Ar = 2,4-$F_2C_6H_3$
3.19d, **3.29c**: Ar = 2-ClC_6H_4
3.19e, **3.29d**: Ar = 4-ClC_6H_4
3.19f, **3.29e**: Ar = 2,4-$(OMe)_2C_6H_3$

Scheme 3.7. Synthesis of dithianes **3.29a-3.29e**

3.2.3 Regioselective lithiation

The dithiane substrates **3.29a** and **3.29b** contain two acidic protons H_a and H_b as shown in Figure 3.2. The reported pK_a of dithiane hydrogen in 2-phenyl-1,3-dithiane **3.35** is 30.7 and the hydrogen at the 2nd position of 1,3-difluorobenzene **3.34** is 28.7. So it is expected that the pK_a of dithiane hydrogen in **3.29a** and **3.29b** to be much lower than 30.7 due to the presence of two electron withdrawing groups in the aryl ring. Also it is expected that the pK_a of H_b increases due to the electron donating nature of dithiane ring. Hence theoretically H_a is expected to be more acidic than H_b. Hence it is expected that lithiation to occur at the dithiane when **3.29a** or **3.29b** is treated with *n*-BuLi. But, in the present reaction condition lithiation occurred exclusively at the aromatic ring carbon and furnished **3.33** upon treatment with an electrophile. Surprisingly, even minor amount of **3.31** was not detected. Here, Cl/F are moderate *ortho*-directing groups only. However if they are present in 1,3-positions in an aromatic ring, the acidity of the C2-hydrogen H_b increases significantly. This might be due to the combination of coordination effect (between Li and two F/Cl) and inductive effect of electronegative halogen atoms. Therefore the regioselective lithiation occurred may be because of the more pronounced coordination effect of Li with F/Cl rather than acidity of the dithiane hydrogen. This observation is parallel to Beak's observation of kinetically controlled regioselectivity due to complex-induced proximity effect (CIPE).[5, 2c] Directed *ortho*-lithiation performed on 2-(2,4-dichlorophenyl)-1,3-dithiane **3.29a** and 2-(2,4-difluorophenyl)-1,3-dithiane **3.29b** followed by electrophile addition results good to excellent yields of products **3.33**. The results are shown in Table

3.1. When aromatic aldehydes were used as electrophiles secondary alcohols were formed **3.33a-g, 3.33i**. When ethyl chloroformate **3.37** was used as electrophile aromatic ester **3.33h** was formed in good yield. With DMF **3.38** as electrophile, we obtained aldehyde **3.33j**. All these compounds are 1,2,3,4-tetrasubstituted aromatic compounds. It is worth mentioning that polysubstituted aromatic compounds are useful agrochemicals.[13]

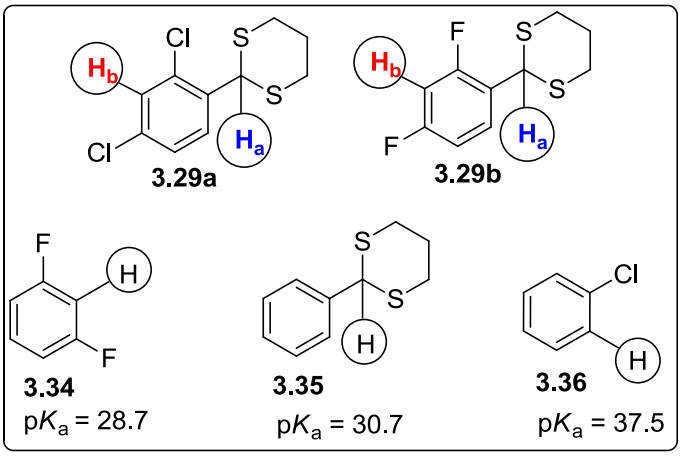
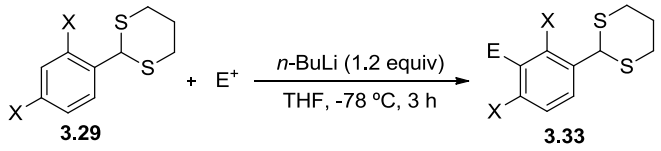


Figure 3.2. pK_a values of related substrates

Table 3.1. Regioselective lithiation to synthesize highly substituted aromatic compounds



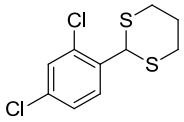
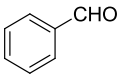
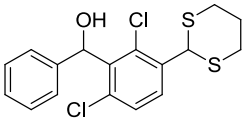
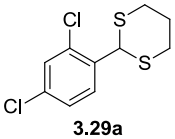
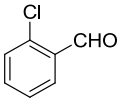
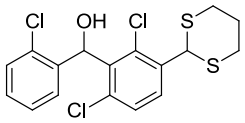
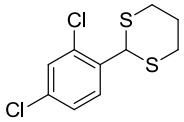
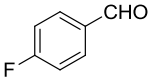
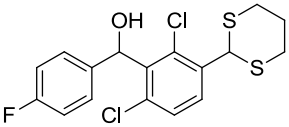
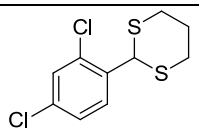
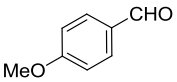
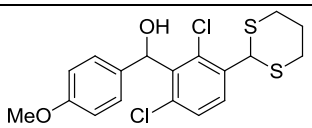
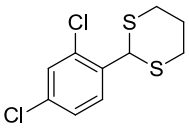
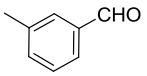
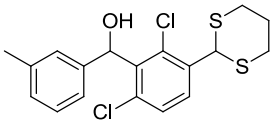
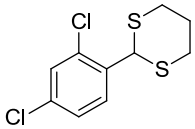
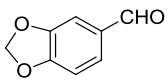
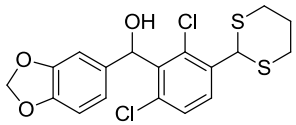
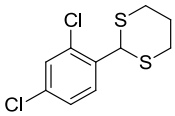
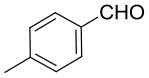
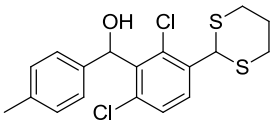
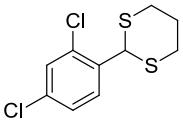
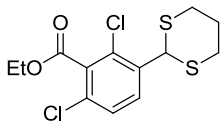
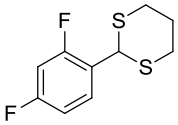
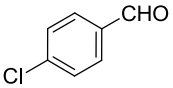
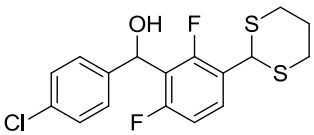
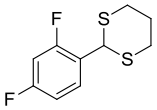
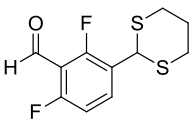
Entry	Dithiane	E^+	Product (Yield %)[a]
1	 **3.29a**	 **3.19a**	 **3.33a** (88%)
2	 **3.29a**	 **3.19d**	 **3.33b** (90%)
3	 **3.29a**	 **3.19g**	 **3.33c** (99%)

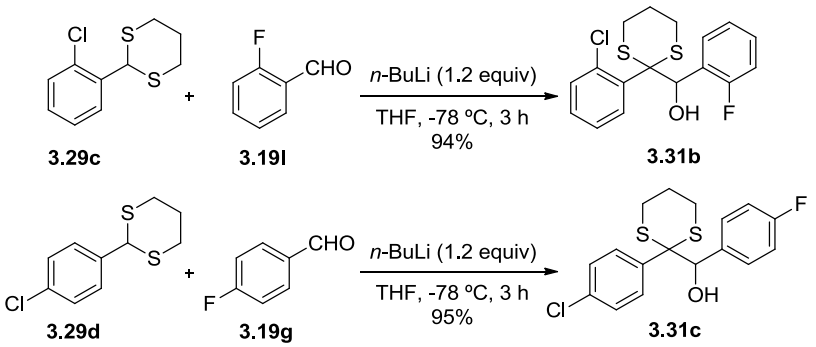
Table 3.1 contd…

Entry	Dithiane	E^+	Product (Yield %)[a]
4	 **3.29a**	 **3.19h**	 **3.33d** (98%)
5	 **3.29a**	 **3.19i**	 **3.33e** (95%)
6	 **3.29a**	 **3.19j**	 **3.33f** (84%)
7	 **3.29a**	 **3.19k**	 **3.33g** (83%)
8	 **3.29a**	 **3.37**	 **3.33h** (82%)
9	 **3.29b**	 **3.19e**	 **3.33i** (89%)
10	 **3.29b**	DMF **3.38**	 **3.33j** (80%)

[a] Isolated yield.

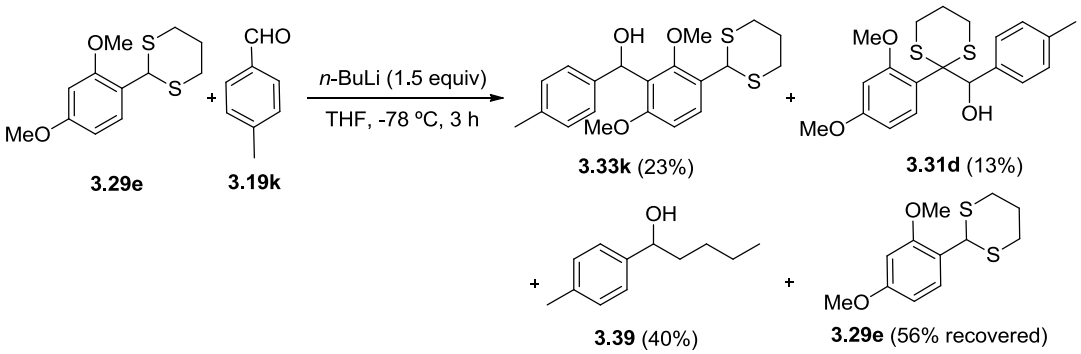
Further, to evaluate the importance of presence of two DMGs in 1,3-position in the substrate for regioselective lithiation, we conducted the following two experiments (Scheme 3.8). When dithiane substrates **3.29c** and **3.29d**, containing a moderately *ortho*-directing group such as chloro were lithiated using *n*-BuLi, lithiation took place at the dithiane carbon centre only. The compounds **3.31b** and **3.31c** were obtained upon treatment of the lithiated species with aromatic aldehydes **3.19l** and **3.19g** respectively. In these substrates, the difference between the pK_a values of two acidic hydrogens is more and the more acidic dithiane hydrogen is deprotonated to result in only **3.31**(Figure

3.2). In other words, lithiation occurred according to more pronounced acidity of dithiane than the less pronounced coordination effect of single chlorine atom.



Scheme 3.8. Reactions of mono chloro-substituted aromatic dithianes

Later, we performed a reaction to know whether coordination effect alone caused *ortho*-lithiation or DMG's inductive effect also plays an important role in the lithiation step. For this purpose compound **3.29e** which has two moderately *ortho*-directing -OMe groups was chosen. This substrate is less reactive and good amount of the starting material was recovered back (Scheme 3.9). Interestingly, we obtained 13% of **3.31d** (formed by lithiation at the dithiane ring), 23% of **3.33k** (formed by lithiation at the arene ring), and 40% of **3.39** (formed by addition of *n*-BuLi at the carbonyl carbon of the aldehyde **3.19k**). This result shows that both arene and dithiane rings are susceptible for lithiation, the former being more effective. The moderately *ortho*-directing methoxy groups in aromatic ring direct the lithiation to occur at the arene carbon due to coordination effect. It has to be kept in mind that OMe group exhibits strong mesomeric effect also. So the pK_a value of the arene hydrogen will be higher than that of the dichloro and difluoro analogues. Therefore, coordination effect shows greater influence in effecting the lithiation at the arene ring despite the less acidity of the arene hydrogen. The dithiane ring also got lithiated due to its acidic hydrogen. The substrate **3.29e** is on a whole less reactive as the dimethoxy substituent on the aryl ring would make both the dithiane and arene hydrogens less acidic.

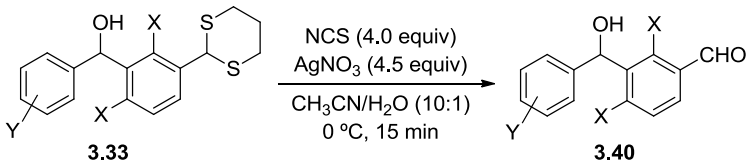


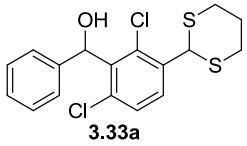
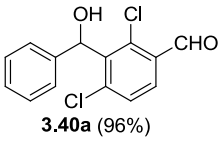
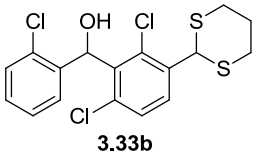
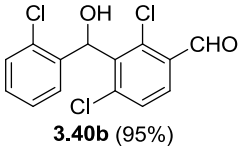
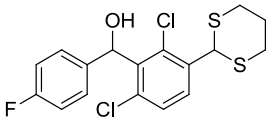
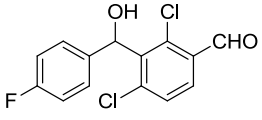
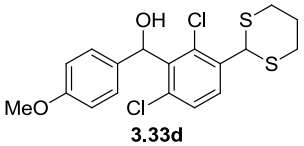
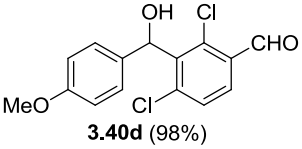
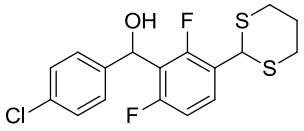
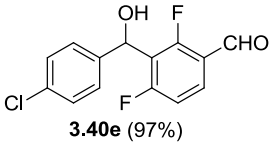
Scheme 3.9. Lithiation studies on **3.29e**

3.2.4 Synthesis of polysubstituted aromatic aldehydes

Dithiane compounds **3.33**, which were obtained from **3.29** by lithiation followed by electrophile addition, can be transformed into 1,2,3,4-tetrasubstituted aromatic aldehydes **3.40**. The deprotection of dithiane was achieved by treating dithiane compounds **3.33** with NCS/$AgNO_3$ reagent system. These reactions were very clean and high yielding (Table 3.2). The resulted compound **3.40** contains alcohol and aldehyde functional groups which can be synthetically elaborated.

Table 3.2. Deprotection of dithianes **3.33** to polysubstituted aromatic aldehydes **3.40**



Entry	Dithiane (**3.33**)	Product (Yield %)[a]
1	 **3.33a**	 **3.40a** (96%)
2	 **3.33b**	 **3.40b** (95%)
3	 **3.33c**	 **3.40c** (73%)
4	 **3.33d**	 **3.40d** (98%)
5	 **3.33i**	 **3.40e** (97%)

[a] Isolated yield.

3.3 Conclusions

A regioselective lithiation of dithiane protected 2,4-dichloro/difluoro substituted benzaldehydes **3.29** using *n*-BuLi was studied. The formed lithiated derivatives were treated with different electrophiles to furnish 1,2,3,4-tetrasubstituted aromatic compounds **3.33**. Strictly, there are two lithiation sites present in 2,4-dichloro/difluoro substituted benzaldehydes **3.29**. However, lithiation occurred only at the arene ring, which upon treatment with electrophiles resulted polysubstituted aromatic compounds **3.33**. It is demonstrated that the inductive effect and coordination effect of halogen atoms cooperatively increase the acidity of the C3-H of aromatic ring over hydrogen present at dithiane carbon atom. Hence, it is shown that besides pK_a value of acidic hydrogen, the inductive effect and coordination effect of DMGs play important roles in the regioselective lithiation. A detailed study on computational calculation of pK_a values of the arene and dithiane hydrogens will give a better picture of the relative contribution of these two effects (inductive effect and coordination effect).

3.4 Experimental section

3.4.1 General information

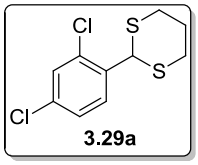
Chemicals and solvents were purchased from commercial sources. The starting materials were prepared by following known and standard literature procedures. Dichloromethane solvent dried over CaH_2 was freshly distilled before use. THF was dried over sodium metal and freshly distilled from the still before use. ^1H and ^{13}C spectra were recorded on Brucker 400 MHz or 500 MHz NMR spectrometer using solutions in $CDCl_3$ with tetramethylsilane (TMS) as internal standard. IR spectra were recorded on JASCO FT/IR spectrometer. HRMS (Brucker) was recorded using electron spray ionization. Column chromatography was performed on silicagel 100-200 mesh, using ethyl acetate and hexanes mixture as eluent.

3.4.2 Experimental procedures, spectral and analytical data

General procedure for synthesis of 3.29a-3.29e

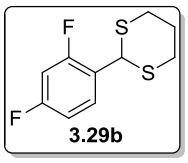
To a solution of corrresponding aryl aldehyde **3.19** (1 equiv) and propane-1,3-dithiol **3.24** (1.1 equiv) in dichloromethane (4 mL per mmol), $BF_3{\cdot}OEt_2$ (30 mol%) was added at room temperature. Reaction was monitered by TLC. Aqueous $NaHCO_3$ was added after completion of reaction (3-5 h). Organic layer was washed with saturated brine solution, concentrated to get the corresponding dithiane derivative in quantitative yield. The crude solid dithiane **3.29** material was washed with hexane and was sufficiently pure to be used for next step without column purification.

2-(2,4-Dichlorophenyl)-1,3-dithiane (3.29a)



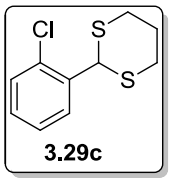
Compound **3.29a** was prepared from **3.19b** and **3.24** following general dithiol protection procedure.[14] Quantitative yield; White solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61(d, J = 8.4 Hz, 1H), 7.38 (d, J = 2.0 Hz, 1H), 7.26 (dd, J = 8.4, 2.0 Hz, 1H), 5.57 (s, 1H), 3.14-3.08 (m, 2H), 2.94-2.89 (m, 2H), 2.20-2.16 (m, 1H), 1.94-1.90 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 135.2, 134.5, 133.2, 130.5, 129.4, 127.8, 46.8, 32.2, 25.0.

2-(2,4-Difluorophenyl)-1,3-dithiane (3.29b)



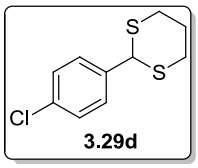
Compound **3.29b** was prepared from **3.19b** and **3.24** following general dithiol protection procedure. Quantitative yield; White solid, mp 85-87 ºC; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62-7.56 (m, 1H), 6.91-6.86 (m, 1H), 6.83-6.77 (m, 1H), 5.48 (s, 1H), 3.14-3.07 (m, 2H), 2.93-2.88 (m, 2H), 2.19-2.15 (m, 1H), 1.97-1.91 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.6 (dd, J = 248.0, 12.0 Hz), 158.7 (dd, J = 249.0, 12.0 Hz), 130.6-130.5 (m, 1C), 122.4 (dd, J = 14.0, 3.0 Hz), 111.9 (dd, J = 21.0, 3.0 Hz), 103.9 (t, J = 26.0 Hz), 42.4, 32.2, 25.0.

2-(2-Chlorophenyl)-1,3-dithiane (3.29c)



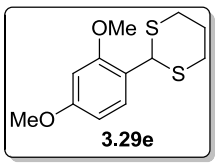
Compound **3.29c** was prepared from **3.19d** and **3.24** following general dithiol protection procedure.[14] Quantitative yield; White solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (dd, J = 7.6, 1.6 Hz, 1H), 7.35 (dd, J = 8.0, 1.6 Hz, 1H), 7.27 (td, J = 7.6, 1.6 Hz, 1H), 7.21 (td, J = 7.6, 1.6 Hz, 1H), 5.64 (s, 1H), 3.10 (td, J = 14.4, 2.4 Hz, 2H), 2.90 (dt, J = 14.4, 3.2 Hz, 2H), 2.18-2.13 (m, 1H), 1.97-1.87 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.5, 132.3, 129.6, 129.5, 129.3, 127.4, 47.5, 32.2, 25.0.

2-(4-Chlorophenyl)-1,3-dithiane (3.29d)



Compound **3.29d** was prepared from **3.19b** and **3.24** following general dithiol protection procedure.[15] Quantitative yield; White solid, mp 90-91 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (d, J = 8.8 Hz, 2H), 7.31 (d, J = 8.8 Hz, 2H), 5.14 (s, 1H), 3.05 (dt, J = 14.4, 2.4 Hz, 2H), 2.90 (td, J = 14.4, 4.0 Hz, 2H), 2.20-2.13 (m, 1H), 1.98-1.86 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.6, 134.1, 129.1, 128.9, 50.5, 31.9, 24.9.

2-(2,4-Dimethoxyphenyl)-1,3-dithiane (3.29e)

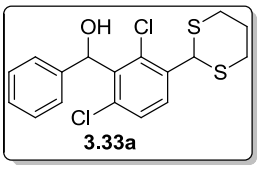


Compound **3.29e** was prepared from **3.19f** and **3.24** following general dithiol protection procedure.[15] Quantitative yield; White solid, mp 107-108 ºC; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (d, J = 8.4 Hz, 1H), 6.49 (d, J = 8.4 Hz, 1H), 6.43 (s, 1H), 5.62 (s, 1H), 3.84 (s, 3H), 3.79 (s, 3H), 3.13-3.07 (m, 2H), 2.90-2.86 (m, 2H), 2.17-2.14 (m, 1H), 1.96-1.89 (m, 1H).

General procedure for regioselective synthesis of 3.33a-3.33k, 3.31b-3.31d

To a solution of dithiane **3.29** (1 equiv) in dry THF, *n*-BuLi (1.6 M) (1.1 equiv) was added at -78 ºC. After stirring at the same temperature for 2 h, electrophile **3.19/3.37/3.38** (1.1 equiv) was added slowly and the reaction was continued for 1 h. After completion of the reaction, aquous NH_4Cl was added to the reaction mixture. Solvent THF was evaporated and the residue was extracted with ethyl acetate. The organic layer was dried over anhydrous Na_2SO_4, concentrated and purified by column chromatography using mixture of ethyl acetate and hexanes.

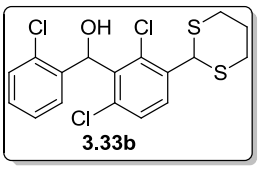
(2,6-Dichloro-3-(1,3-dithian-2-yl)phenyl)(phenyl)methanol (3.33a)



3.33a

Compound **3.33a** was synthesized from **3.29a** and **3.19a** following general lithiation procedure. White solid, mp 149-150 °C; Yield: 88%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (d, J = 8.4 Hz, 1H), 7.36 (d, J = 8.4 Hz, 1H), 7.34-7.25 (m, 5H), 6.70 (d, J = 10.8 Hz, 1H), 5.63 (s, 1H), 3.43 (dd, J = 10.6, 2.4 Hz, 1H), 3.14-3.05 (m, 2H), 2.93-2.89 (m, 2H), 2.19-2.14 (m, 1H), 1.97-1.87 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.2, 138.1, 136.9, 134.9, 133.4, 129.7, 129.6, 128.2, 127.1, 125.2, 72.7, 47.6, 32.1, 24.9; IR (KBR): υ 3545, 3063, 2937, 1577, 1501, 1451, 1276, 1183, 1084, 909, 772, 700 cm^{-1}; HRMS Cacld for $C_{17}H_{16}Cl_2NaOS_2$ $(M + Na)^+$ 392.9917, Found 392.9918.

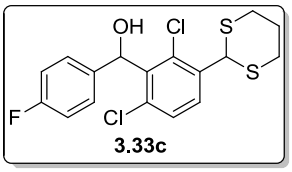
(2-Chlorophenyl)(2,6-dichloro-3-(1,3-dithian-2-yl)phenyl)methanol (3.33b)



3.33b

Compound **3.33b** was synthesized from **3.29a** and **3.19d** following general lithiation procedure. White solid, mp 64-66 °C; Yield: 90%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63 (d, J = 8.4 Hz, 1H), 7.59-7.57 (m, 1H), 7.36-7.33 (m, 2H), 7.28-7.22 (m, 2H), 6.76 (d, J = 6.4 Hz, 1H), 5.64 (s, 1H), 3.14-3.07 (m, 3H), 2.94-2.90 (m, 2H), 2.20-2.16 (m, 1H), 1.98-1.88 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.0, 136.8, 136.4, 135.3, 133.9, 132.7, 129.8, 129.7, 129.2, 128.9, 126.2, 71.5, 47.7, 32.2, 24.9; IR (KBR): υ 3375, 2926 1572, 1451, 1380, 1274, 1188, 1079,1035, 761 cm^{-1}; HRMS Cacld for $C_{17}H_{15}Cl_3NaOS_2$ $(M + Na)^+$ 426.9528, Found 426.9528.

(2,6-Dichloro-3-(1,3-dithian-2-yl)phenyl)(4-fluorophenyl)methanol (3.33c)

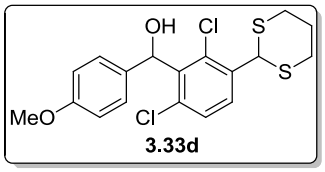


3.33c

Compound **3.33c** was synthesized from **3.29a** and **3.19g** following general lithiation procedure. Pale yellow solid, mp 99-100 °C; Yield: 99%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, J = 8.4 Hz, 1H), 7.38 (d, J = 8.4 Hz, 1H), 7.27-7.22 (m, 2H), 7.02 (t, J = 8.4 Hz, 2H), 6.66 (d, J = 10.4 Hz, 1H), 5.64 (s, 1H), 3.40 (d, J = 10.4 Hz, 1H), 3.16-3.08 (m, 2H), 2.95-2.92 (m, 2H), 2.22-2.18 (m, 1H), 1.99-1.93 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.0 (d, J = 244.0 Hz), 143.0, 137.2, 133.5,

132.5, 129.4, 127.0 (d, *J* = 8.0 Hz), 115.1 (d, *J* = 21.0 Hz), 72.1, 70.5, 37.4, 27.8, 22.4, 14.0; IR (KBR): υ 3545, 2937, 1610, 1512, 1440, 1221, 1054, 838, 772 cm^{-1}; HRMS Cacld for $C_{17}H_{15}Cl_2FNaOS_2$ $(M + Na)^+$ 410.9823, Found 410.9822.

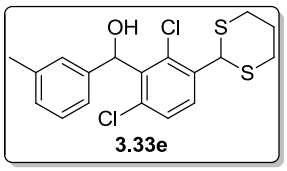
(2,6-Dichloro-3-(1,3-dithian-2-yl)phenyl)(4-methoxyphenyl)methanol (3.33d)



3.33d

Compound **3.33d** was synthesized from **3.29a** and **3.19h** following general lithiation procedure. Gummy yellow liquid; Yield: 98%; ^1H NMR (400 MHz, $CDCl_3$): δ 7.64 (d, *J* = 8.4 Hz, 1H), 7.37 (d, *J* = 8.8 Hz, 1H), 7.19 (d, *J* = 8.4 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 2H), 6.65 (d, *J* = 9.6 Hz, 1H), 5.64 (s, 1H), 3.79 (s, 3H), 3.44 (d, *J* = 10.8 Hz, 1H), 3.15-3.07 (m, 2H), 2.94-2.90 (m, 2H), 2.20-2.16 (m, 1H), 1.98-1.88 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.7, 138.1, 136.9, 134.8, 133.4, 133.2, 129.6, 126.6, 113.6, 72.6, 55.2, 47.6, 32.2, 24.9; IR (neat): υ 3457, 2955, 2903, 2830, 1609, 1583, 1511, 1443, 1247, 1180, 1081, 1029, 838, 776, 740 cm^{-1}.

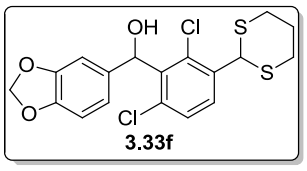
(2,6-Dichloro-3-(1,3-dithian-2-yl)phenyl)(*m*-tolyl)methanol (3.33e)



3.33e

Compound **3.33e** was synthesized from **3.29a** and **3.19i** following general lithiation procedure. White solid, mp 118-120 °C; Yield: 95%; ^1H NMR (400 MHz, $CDCl_3$): δ 7.64 (d, *J* = 8.4 Hz, 1H), 7.37 (d, *J* = 8.4 Hz, 1H), 7.20 (t, *J* = 7.6 Hz, 1H), 7.11 (s, 1H), 7.07 (d, *J* = 8.0 Hz, 1H), 7.02 (d, *J* = 7.6 Hz, 1H), 6.66 (s, 1H), 5.64 (s, 1H), 3.15-3.06 (m, 2H), 2.94-2.90 (m, 2H), 2.33 (s, 3H), 2.20-2.16 (m, 1H), 1.99-1.88 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.2, 138.2, 138.0, 136.9, 134.9, 133.5, 129.7, 129.6, 128.2, 128.0, 126.0, 122.3, 72.8, 47.6, 32.2, 24.9, 21.5; IR (neat): υ 3430, 2898, 1577, 1451, 1276, 1150, 1073, 1035, 909, 750, 701 cm^{-1}; HRMS Cacld for $C_{18}H_{18}Cl_2NaOS_2$ $(M + Na)^+$ 407.0074, Found 407.0075.

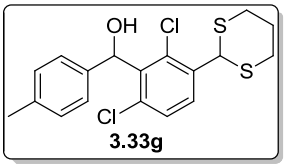
Benzo[*d*][1,3]dioxol-5-yl(2,6-dichloro-3-(1,3-dithian-2-yl)phenyl)methanol (3.33f)



3.33f

Compound **3.33f** was synthesized from **3.29a** and **3.19j** following general lithiation procedure. Yellow solid, mp 109-110 °C; Yield: 84%; ^1H NMR (400 MHz, $CDCl_3$): δ 7.64 (d, *J* = 8.4 Hz, 1H), 7.37 (d, *J* = 8.8 Hz, 1H), 6.80 (s, 1H), 6.75 (d, *J* = 8.0 Hz, 1H), 6.67 (d, *J* = 8.4 Hz, 1H), 6.59 (s, 1H), 5.94 (s, 2H), 5.63 (s, 1H), 3.42 (bs, 1H), 3.14-3.07 (m, 2H), 2.94-2.91 (m, 2H), 2.20-2.17 (m, 1H), 1.98-1.92 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.8, 146.7, 138.0, 137.0, 135.2, 134.8, 133.4, 129.8, 129.7, 118.6, 108.0, 106.3, 101.0, 72.7, 47.6; IR (KBR): υ 3425, 2882, 1682, 1501, 1485, 1441, 1238, 1041, 920, 762 cm^{-1}; HRMS Cacld for $C_{18}H_{16}Cl_2NaO_3S_2$ $(M + Na)^+$ 436.9816, Found 436.9816.

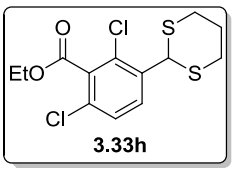
(2,6-Dichloro-3-(1,3-dithian-2-yl)phenyl)(*p*-tolyl)methanol (3.33g)



3.33g

Compound **3.33g** was synthesized from **3.29a** and **3.19k** following general lithiation procedure. Yellow liquid; Yield: 83%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, J = 8.4 Hz, 1H), 7.37 (d, J = 8.4 Hz, 1H), 7.18 (d, J = 8.4 Hz, 2H), 7.14 (d, J = 8.4 Hz, 2H), 6.69 (d, J = 10.4 Hz, 1H), 5.65 (s, 1H), 3.46 (dd, J = 10.4, 4.4 Hz, 1H), 3.15-3.07 (m, 2H), 2.94-2.91 (m, 2H), 2.35 (s, 3H), 2.20-2.16 (m, 1H), 1.99-1.89 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.2, 138.1, 136.82, 136.80, 134.8, 133.4, 129.59, 129.55, 128.9, 125.2, 72.7, 47.6, 32.1, 24.9, 21.0; IR (neat): υ 3572, 3457, 2898, 1906, 1572, 1506, 1440, 1276, 1079, 903, 733 cm^{-1}; HRMS Cacld for $C_{18}H_{18}NaCl_2OS_2$ $(M + Na)^+$ 407.0074, Found 407.0074.

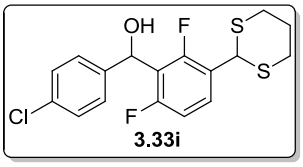
Ethyl 2,6-dichloro-3-(1,3-dithian-2-yl)benzoate (3.33h)



3.33h

Compound **3.33h** was synthesized from **3.29a** and ethyl chloroformate **3.37** following general lithiation procedure. White solid, mp 136-138 °C; Yield: 82%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, J = 8.4 Hz, 1H), 7.34 (d, J = 8.4 Hz, 1H), 5.57 (s, 1H), 4.46 (q, J = 7.2 Hz, 2H), 3.13-3.07 (m, 2H), 2.93-2.89 (m, 2H), 2.19-2.16 (m, 1H), 1.97-1.87 (m, 1H), 1.41 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ.164.4, 136.0, 134.2, 131.2, 130.8, 129.9, 128.4, 62.3, 46.7, 32.0, 24.8, 14.0; IR (KBR): υ 2887, 1742, 1567, 1447, 1266, 1156, 1014, 904, 778 cm^{-1}; HRMS Cacld for $C_{13}H_{15}Cl_2O_2S_2$ $(M + H)^+$ 336.9891, Found 336.9887.

(3-(1,3-Dithian-2-yl)-2,6-difluorophenyl)(4-chlorophenyl)methanol (3.33i)

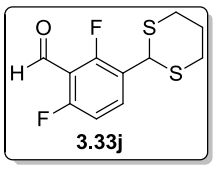


3.33i

Compound **3.33i** was synthesized from **3.29b** and **3.19e** following general lithiation procedure. Yellow liquid; Yield: 89%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58-7.53 (m, 1H), 7.32-7.27 (m, 4H), 6.92-6.88 (m, 1H), 6.18 (d, J = 7.6 Hz, 1H), 5.44 (s, 1H), 3.09-3.02 (m, 2H), 2.96 (d, J = 8.0 Hz, 1H), 2.87 (dt, J = 14.0, 3.6 Hz, 2H), 2.16-2.11 (m, 1H), 1.94-1.83 (m ,1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.2 (dd, J = 250.0, 8.0 Hz), 156.8 (dd, J = 249.0, 8.0 Hz), 140.2, 133.3, 129.8(d, J = 10.0, 5.0 Hz), 128.5, 126.9, 123.1 (d, J = 15.0 Hz), 118.9 (t, J = 17.0 Hz), 112.4 (d, J = 23.0 Hz), 66.8, 42.4 (d, J = 4.0 Hz), 32.1, 24.8; IR (neat): υ 3435, 2909, 1901, 1621, 1599, 1490, 1276, 1177, 1013, 777, 733 cm^{-1}; HRMS Cacld for $C_{17}H_{15}ClF_2OS_2$ $(M + Na)^+$ 395.0119, Found 395.0120.

3-(1,3-Dithian-2-yl)-2,6-difluorobenzaldehyde (3.33j)

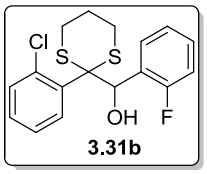
Compound **3.33j** was synthesized from **3.29b** and DMF **3.38** following general lithiation procedure. White solid, mp 100-101 °C; Yield: 80%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.31 (s, 1H), 7.83 (dd, J = 14.4, 8.0 Hz, 1H), 6.99 (t, J = 9.2 Hz, 1H), 5.48 (s, 1H), 3.13-3.06 (m, 2H)2.91-2.88 (m, 2H), 2.19-



3.33j

2.15 (m, 1H), 1.94-1.84 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.0, 162.4 (d, J = 269.0 Hz), 159.2 (d, J = 268.0 Hz), 136.1-135.9 (m, 1C), 123.7 (dd, J = 14.0, 4.0 Hz), 113.9-113.7 (m, 1C), 112.8 (d, J = 24.0 Hz), 41.6, 31.9, 24.6; IR (KBR): υ 2920, 2849, 2783, 1709, 1621, 1479, 1276, 1226, 1193, 1035, 920, 772, 712 cm^{-1}; HRMS Cacld for $C_{11}H_{11}F_2OS_2$ $(M + H)^+$ 261.0219, Found 261.0214.

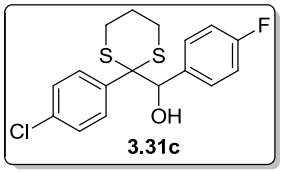
(2-(2-Chlorophenyl)-1,3-dithian-2-yl)(2-fluorophenyl)methanol (3.31b)



3.31b

Compound **3.31b** was obtained from **3.29c** and **3.19d** following general lithiation procedure. Pale yellow liquid; Yield: 94%; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.87 (d, J = 6.4 Hz, 1H), 7.64 (t, J = 6.0 Hz, 1H), 7.44 (d, J = 6.0 Hz, 1H), 7.20 (t, J = 6.0 Hz, 1H), 7.17-7.14 (m, 1H), 7.11 (t, J = 6.0 Hz, 1H), 7.06 (t, J = 6.0 Hz, 1H), 6.72 (t, J = 7.2 Hz, 1H), 6.09 (s, 1H), 3.42 (s, 1H), 2.99-2.96 (m, 1H), 2.68-2.56 (m, 3H), 1.94-1.86 (m, 1H), 1.82-1.77 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.0 (d, J = 246.2 Hz), 135.8, 134.5, 133.1, 132.6, 130.0 (d, J = 2.5 Hz), 129.4 (d, J = 8.8 Hz), 129.1, 126.2, 124.9 (d, J = 12.5 Hz), 122.8 (d, J = 3.8 Hz), 114.6 (d, J = 22.5 Hz), 70.6, 68.4, 27.5, 26.5, 23.3; IR (neat): υ 3436, 3058, 2953, 2926, 1616, 1589, 1490, 1463, 1227, 1047, 751 cm^{-1}; HRMS Cacld for $C_{17}H_{17}ClFOS_2$ $(M + H)^+$ 355.0393, Found 355.0393.

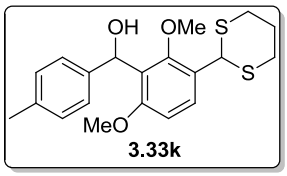
(2-(4-Chlorophenyl)-1,3-dithian-2-yl)(4-fluorophenyl)methanol (3.31c)



3.31c

Compound **3.31c** was obtained from **3.29d** and **3.19e** following general lithiation procedure. White solid, mp 94-95 ºC; Yield: 95%; R_f = 0.52 in 1:5 EtOAc/hexanes (double elutions); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.60 (d, J = 7.5 Hz, 2H), 7.27 (d, J = 9.0 Hz, 2H), 6.85-6.83 (m, 4H), 4.96 (d, J = 1.5 Hz, 1H), 2.76-2.72 (m, 2H), 2.68-2.59 (m, 2H), 1.95-1.90 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.6 (d, J = 245.4 Hz), 136.0, 133.7, 132.8, 132.1, 129.8 (d, J = 8.1 Hz), 128.2, 114.0 (d, J = 21.2 Hz), 80.2, 65.7, 27.2, 26.9, 24.6; IR (KBR): υ 3436, 2911, 1904, 1603, 1510, 1223 cm^{-1}; $C_{17}H_{16}ClFOS_2$: Cacld. C 57.53, H 4.54; Found C 57.65, H 4.51.

(3-(1,3-Dithian-2-yl)-2,6-dimethoxyphenyl)(*p*-tolyl)methanol (3.33k)

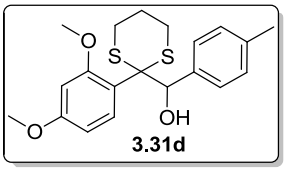


3.33k

Compound **3.33k** was obtained from **3.29e** and **3.19k** following general lithiation procedure. Colorless liquid; Yield: 23%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (d, J = 8.8 Hz, 1H), 7.22 (d, J = 8.0 Hz, 2H), 7.10 (d, J = 8.0 Hz, 2H), 6.76 (d, J = 8.8 Hz, 1H), 6.19 (d, J = 11.2 Hz, 1H), 5.49 (s, 1H), 4.13 (d, J = 11.6 Hz, 1H), 3.75 (s, 3H), 3.68 (s, 3H), 3.14-3.07 (m, 2H), 2.92-2.88 (m, 2H), 2.32 (s, 3H), 2.20-2.16 (m, 1H), 1.98-1.88 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.0, 155.2, 141.4, 136.2, 129.6, 128.7, 125.6, 125.5, 125.0, 108.1, 69.0, 63.3, 55.8, 44.0, 32.5, 25.1, 21.0; IR (neat): υ

3534, 2937, 2899, 1600, 1485, 1419, 1271, 1227, 1085, 1041, 740 cm^{-1}; HRMS Cacld for $C_{20}H_{24}NaO_3S_2$ $(M + Na)^+$ 399.1065, Found 399.1069.

(2-(2,4-Dimethoxyphenyl)-1,3-dithian-2-yl)(*p*-tolyl)methanol (3.31d)



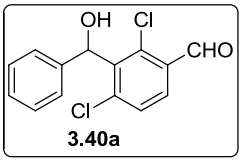
3.31d

Compound **3.31d** was obtained from **3.29e** and **3.19k** following general lithiation procedure. Colorless liquid; Yield: 13%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (d, J = 8.8 Hz, 1H), 6.94 (d, J = 8.0 Hz, 2H), 6.89 (d, J = 8.0 Hz, 2H), 6.58 (d, J = 2.4 Hz, 1H), 6.36 (dd, J = 8.8, 2.4 Hz, 1H), 5.53 (d, J = 3.2 Hz, 1H), 3.93 (s, 3H), 3.82 (s, 3H), 3.75 (d, J = 3.6 Hz, 1H), 3.06-3.00 (m, 1H), 2.68-2.61 (m, 3H), 2.26 (s, 3H), 1.98-1.91 (m, 1H), 1.88-1.80 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.6, 158.7, 137.0, 135.2, 132.7, 127.63, 127.60, 120.4, 104.0, 100.6, 67.4, 55.9, 55.3, 27.2, 26.1, 23.8, 21.2; IR (neat): υ 3474, 2921, 2838, 1611, 1578, 1490, 1463, 1414, 1304, 1205, 1052, 931, 734 cm^{-1}; HRMS Cacld for $C_{20}H_{24}NaO_3S_2$ $(M + Na)^+$ 399.1065, Found 399.1067.

General dithiane deprotection procedure for synthesis of 3.40a-3.40e

To a solution of *N*-chlorosuccinimide (4.0 equiv) and $AgNO_3$ (4.5 equiv) in acetonitrile/water (4:1), compound **3.33** (1 equiv) was added at room temperature. The reaction mixture was stirred at room temperature for 15 min. After completion of reaction, aqueous $Na_2S_2O_3$ solution was added. Crude product was extracted with EtOAc, dried over anhydrous Na_2SO_4, concentrated and purified by column chromatography hexanes/EtOAc as eluent.

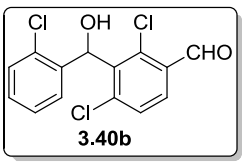
2,4-Dichloro-3-(hydroxy(phenyl)methyl)benzaldehyde (3.40a)



3.40a

Compound **3.40a** was prepared from **3.33a** by following general dithiane deprotection procedure. Colorless liquid; Yield: 96%; ^{1}H NMR (400 MHz, CDCl3): δ 10.50 (s, 1H), 7.86 (d, J = 8.4 Hz, 1H), 7.48 (d, J = 8.4 Hz, 1H), 7.38-7.29 (m, 5H), 6.78 (d, J = 6.4 Hz, 1H), 3.48 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, CDCl3): δ 190.0, 141.2, 140.7, 139.2, 138.7, 132.2, 129.8, 129.3, 128.4, 127.4, 125.2, 71.9; IR (neat): υ 3446, 3057, 3030, 2876, 1698, 1572, 1490, 1446, 1369, 1237, 1084, 931, 827, 695 cm^{-1}; HRMS Cacld for $C_{14}H_{11}Cl_2O_2$ $(M + H)^+$ 281.0136, Found 281.0139.

2,4-Dichloro-3-((2-chlorophenyl)(hydroxy)methyl)benzaldehyde (3.40b)

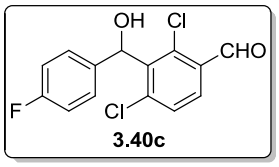


3.40b

Compound **3.40b** was prepared from **3.33b** by following general dithiane deprotection procedure. Pale yellow liquid; Yield: 95%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.45 (s, 1H), 7.82 (d, J = 8.0 Hz, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.43 (d, J = 8.0 Hz, 1H), 7.36-7.28 (m, 3H), 6.79 (s, 1H), 3.32 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.3, 141.8, 139.3, 137.9, 137.5, 132.2, 132.1, 129.9, 129.8, 129.3,

129.2, 129.1, 126.3, 70.4; IR (neat): υ 3402, 3068, 2926, 2876, 1693, 1577, 1435, 1380, 1238, 1089, 1029, 827, 750 cm^{-1}; HRMS Cacld for $C_{14}H_9Cl_3NaO_2$ $(M + Na)^+$ 336.9566, Found 336.9563.

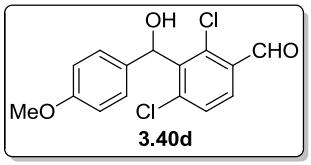
2,4-Dichloro-3-((4-fluorophenyl)(hydroxy)methyl)benzaldehyde (3.40c)



3.40c

Compound **3.40c** was prepared from **3.33c** by following general dithiane deprotection procedure. Gummy yellow solid; mp 79-81 °C; Yield: 73%; ^1H NMR (400 MHz, $CDCl_3$): δ 10.47 (s, 1H), 7.86 (d, J = 8.4 Hz, 1H), 7.48 (d, J = 8.4 Hz, 1H), 7.49-7.25 (m, 2H), 7.03 (t, J = 8.8 Hz, 2H), 6.73 (s, 1H), 3.44 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.9, 162.1 (d, J = 245 Hz), 141.1, 138.9, 138.6, 136.4, 132.3, 129.9, 129.4, 127.0 (d, J = 8.0 Hz), 115.3 (d, J = 21.0 Hz), 71.4; IR (KBR): υ 3441, 3041, 2926, 2888, 1699, 1600, 1578, 1507, 1375, 1216, 1090, 838 cm^{-1}; HRMS Cacld for $C_{14}H_{10}Cl_2FO_2$ $(M + H)^+$ 299.0042, Found 299.0038.

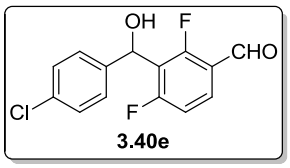
2,4-Dichloro-3-(hydroxy(4-methoxyphenyl)methyl)benzaldehyde (3.40d)



3.40d

Compound **3.40d** was prepared from **3.33d** following general dithiane deprotection procedure. Yellow liquid; Yield: 98%; ^1H NMR (400 MHz, $CDCl_3$): δ 10.48 (s, 1H), 7.85 (d, J = 8.4 Hz, 1H), 7.47 (d, J = 8.4 Hz, 1H), 7.20 (d, J = 8.4 Hz, 2H), 6.88 (d, J = 8.8 Hz, 2H), 6.71 (s, 1H), 3.80 (s, 3H), 3.42 (bs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.0, 158.9, 141.1, 139.2, 138.6, 132.6, 132.2, 129.8, 129.2, 126.6, 113.8, 71.7, 55.2; IR (neat): υ 3463, 2997, 2958, 2931, 2898, 2838, 1693, 1615, 1577, 1512, 1446, 1243, 1177, 1084, 1034, 928, 843, 733 cm^{-1}; HRMS Cacld for $C_{15}H_{12}Cl_2NaO_3$ $(M + Na)^+$ 333.0061, Found 333.0033.

3-((4-Chlorophenyl)(hydroxy)methyl)-2,4-difluorobenzaldehyde (3.40e)



3.40e

Compound **3.40e** was prepared from **3.33i** following general dithiane deprotection procedure. White solid; mp 88-90 °C; Yield: 97%; ^1H NMR (400 MHz, $CDCl_3$): δ 10.22 (s, 1H), 7.84 (dd, J = 14.8, 8.4 Hz, 1H), 7.35 (d, J = 8.8 Hz, 2H), 7.32 (d, J = 8.8 Hz, 2H), 7.02 (t, J = 8.8 Hz, 1H), 6.26 (s, 1H), 3.13 (bs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.6 (d, J = 7.0 Hz), 164.5 (dd, J = 258.0, 9.0 Hz), 163.2 (dd, J = 261.0, 9.0 Hz), 139.7, 133.7, 129.6 (d, J = 11.0 Hz), 128.7, 126.8, 121.4 (d, J = 9.0 Hz), 120.0 (t, J = 16.0 Hz), 113.1 (d, J = 23.0 Hz), 66.4; IR (KBR): υ 3485, 3074, 2926, 1912, 1682, 1616, 1594, 1496, 1441, 1266, 1057, 1008, 816, 608 cm^{-1}; HRMS Cacld for $C_{14}H_{10}ClF_2O_2$ $(M + H)^+$ 283.0337, Found 283.0333.

3.5 References

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3.6 Representative spectra

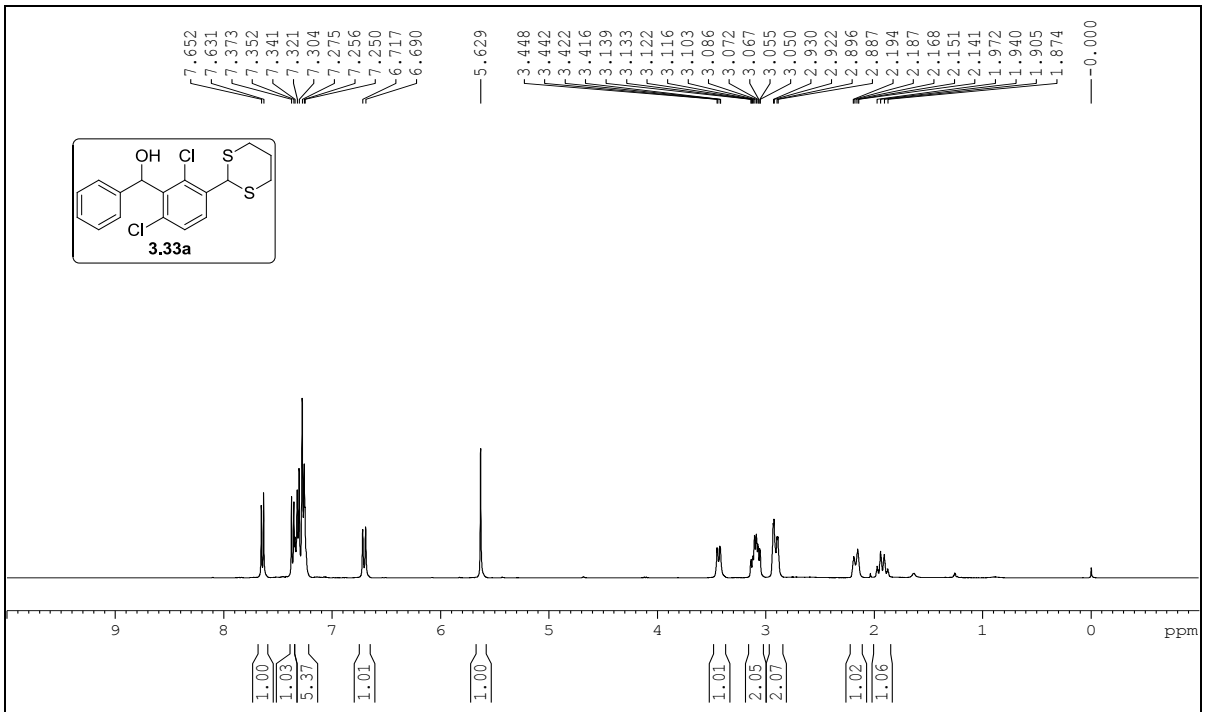

Figure 3.3. ^{1}H NMR spectrum of compound **3.33a**

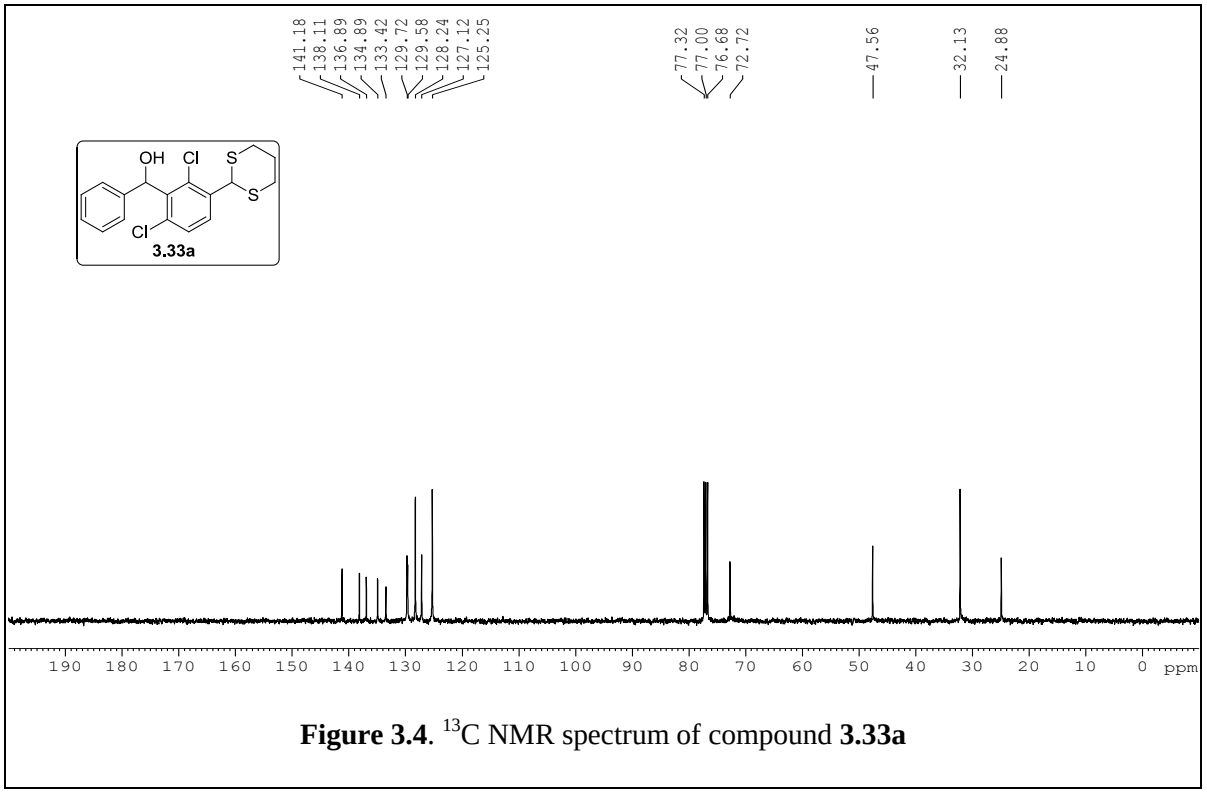

Figure 3.4. ^{13}C NMR spectrum of compound **3.33a**

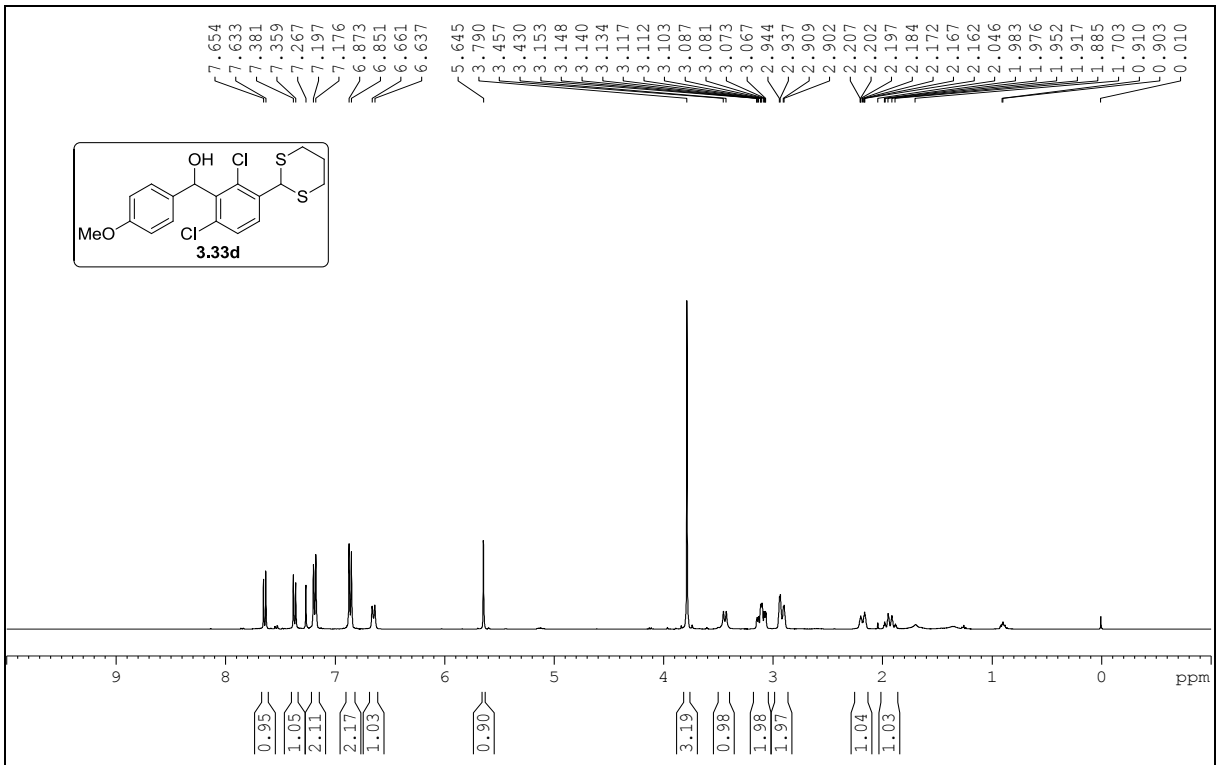

Figure 3.5. ^{1}H NMR spectrum of compound **3.33d**

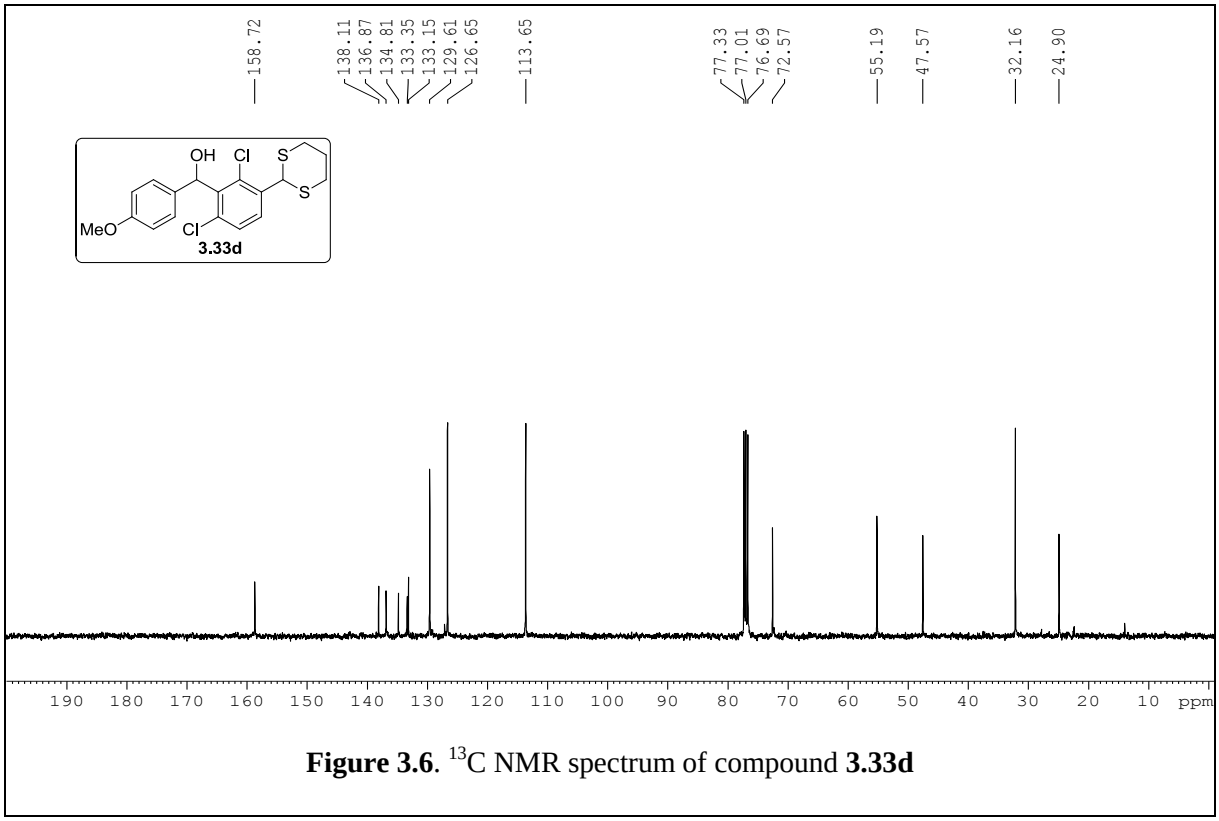

Figure 3.6. ^{13}C NMR spectrum of compound **3.33d**

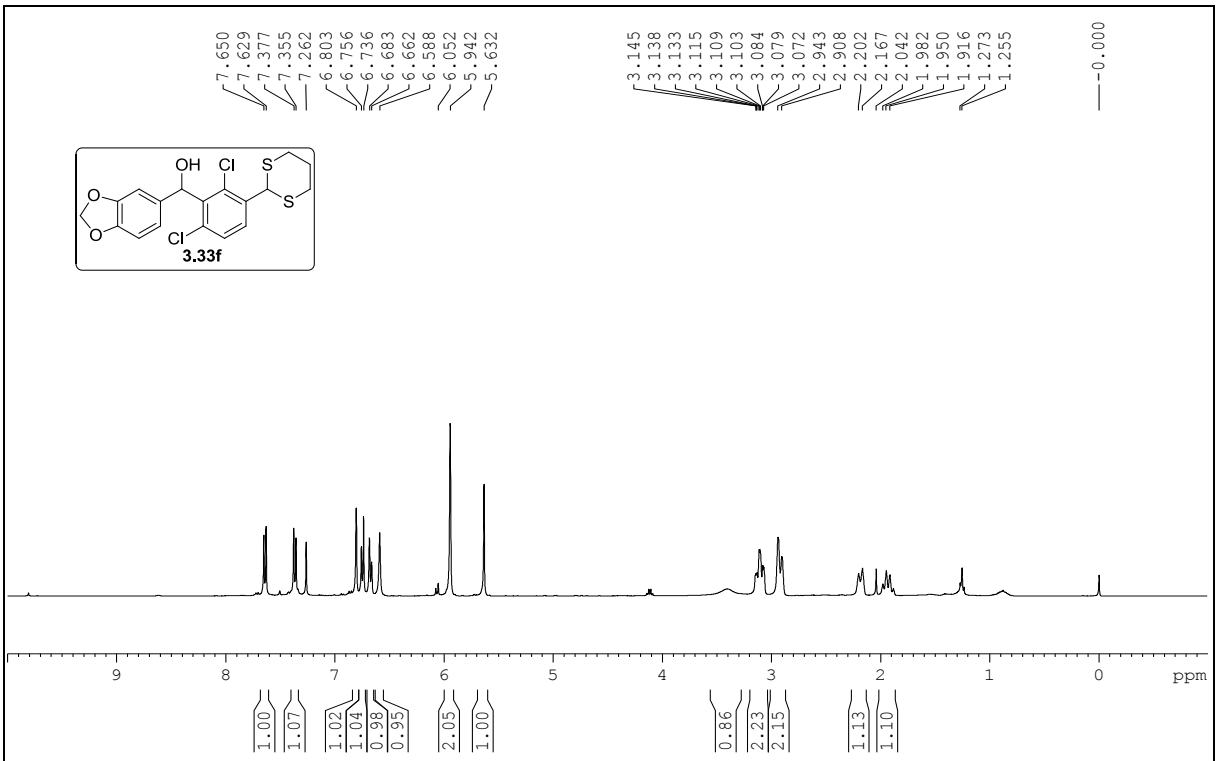

Figure 3.7. ^{1}H NMR spectrum of compound **3.33f**

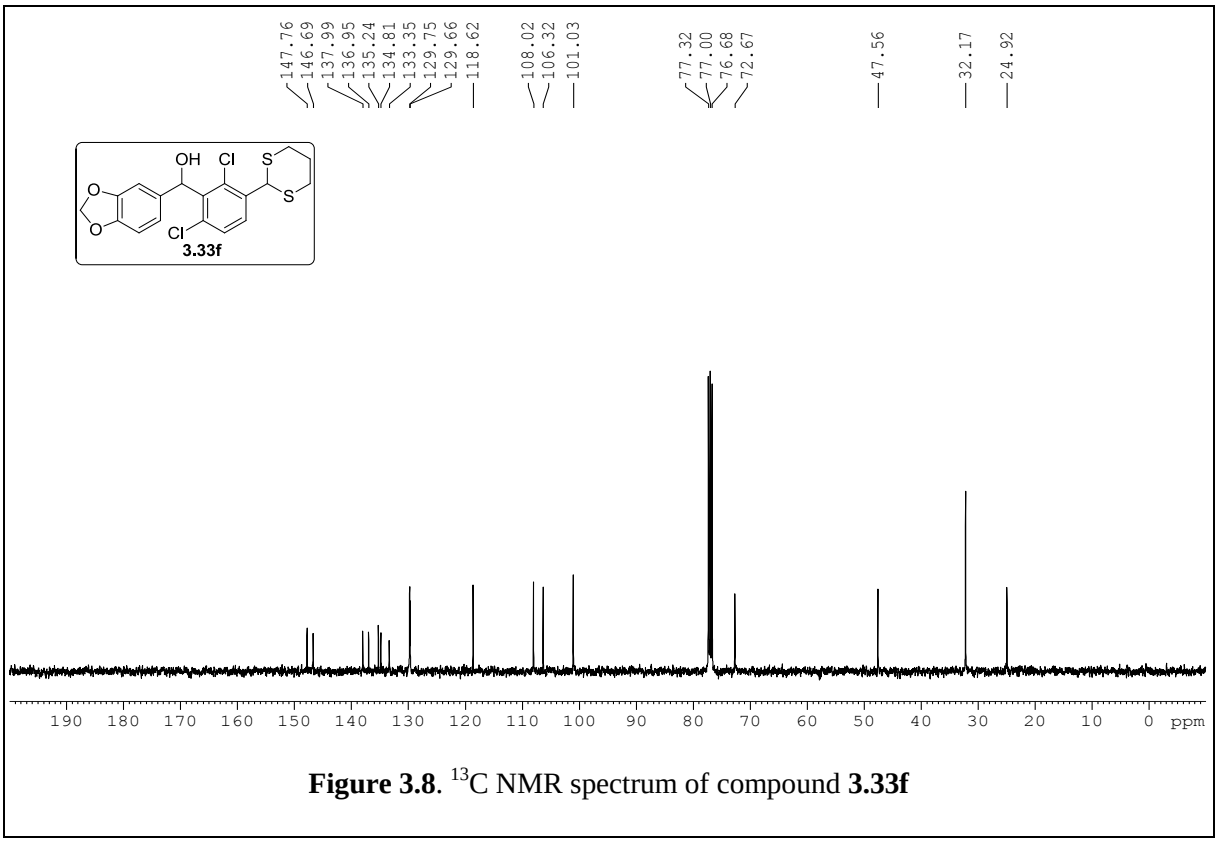

Figure 3.8. ^{13}C NMR spectrum of compound **3.33f**

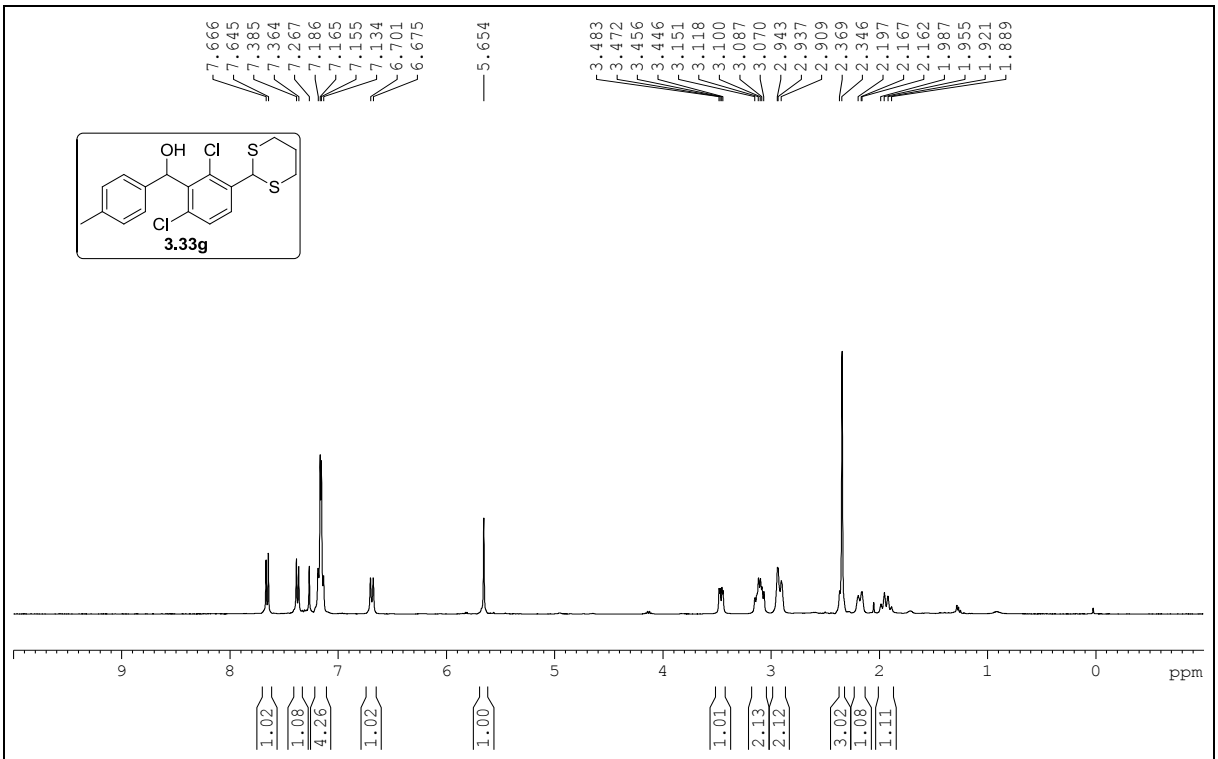

Figure 3.9. ^{1}H NMR spectrum of compound **3.33g**

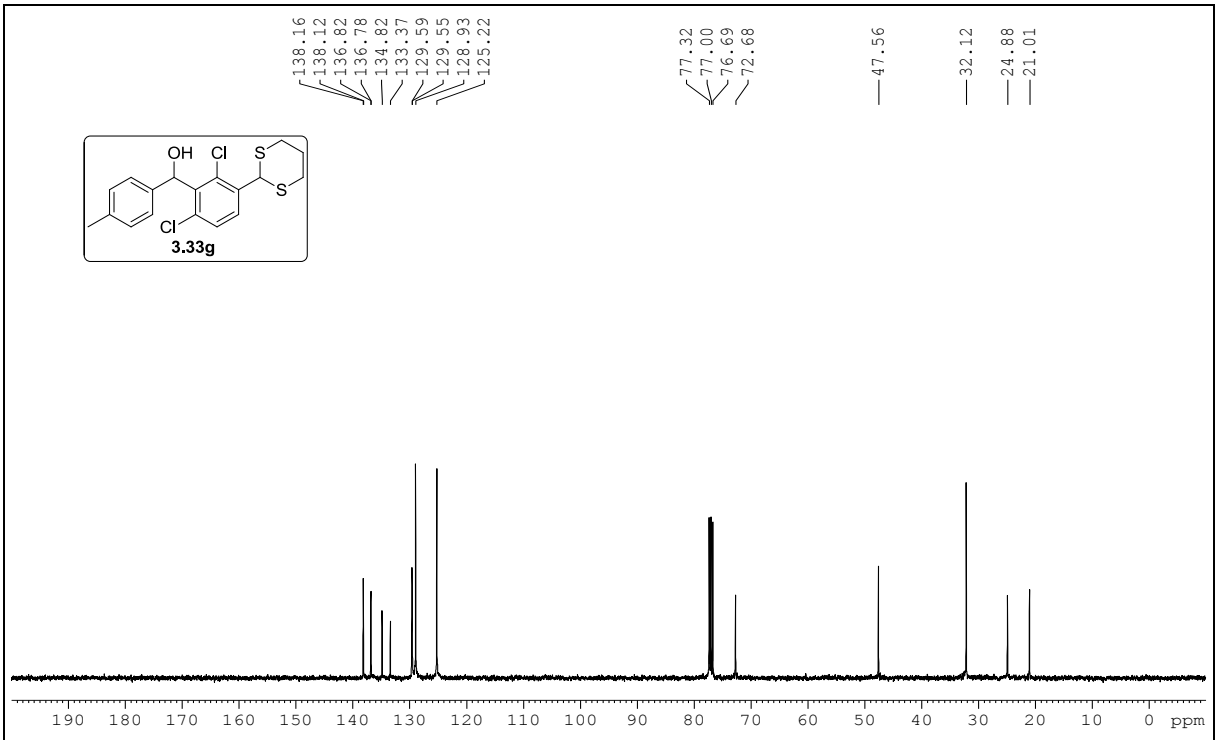

Figure 3.10. ^{13}C NMR spectrum of compound **3.33g**

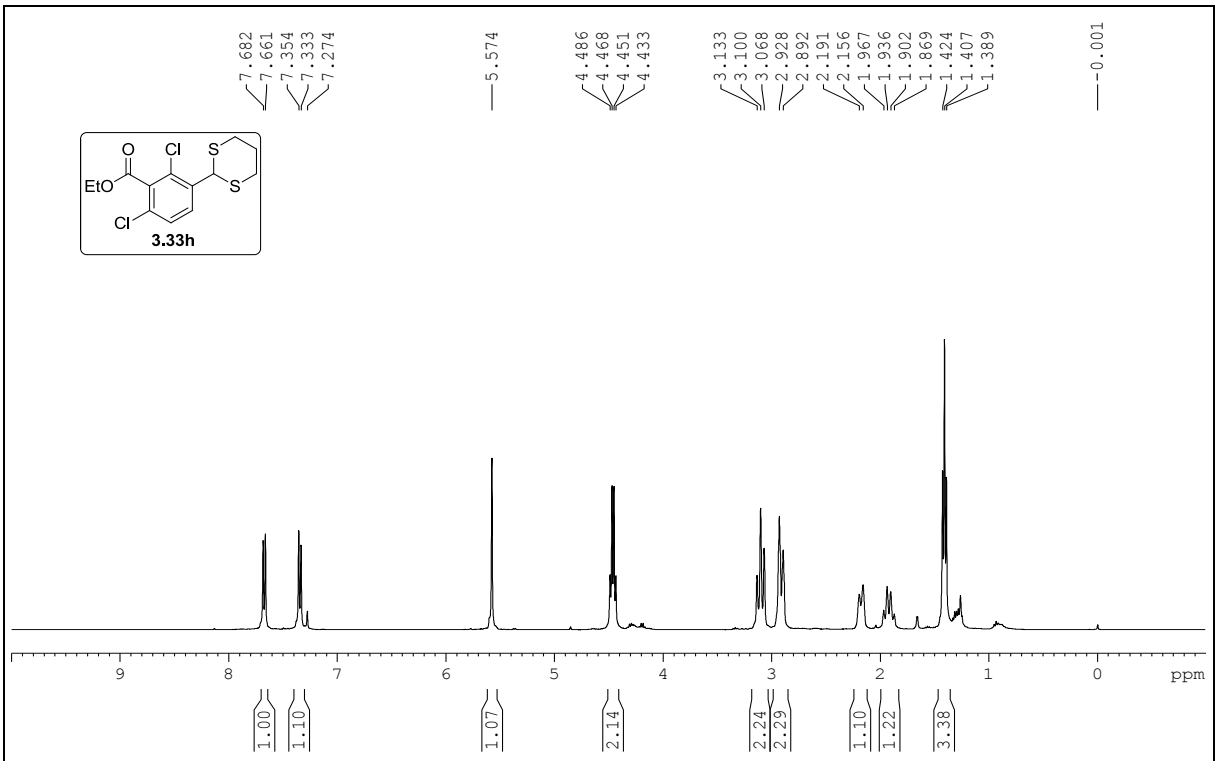

Figure 3.11. ^{1}H NMR spectrum of compound **3.33h**

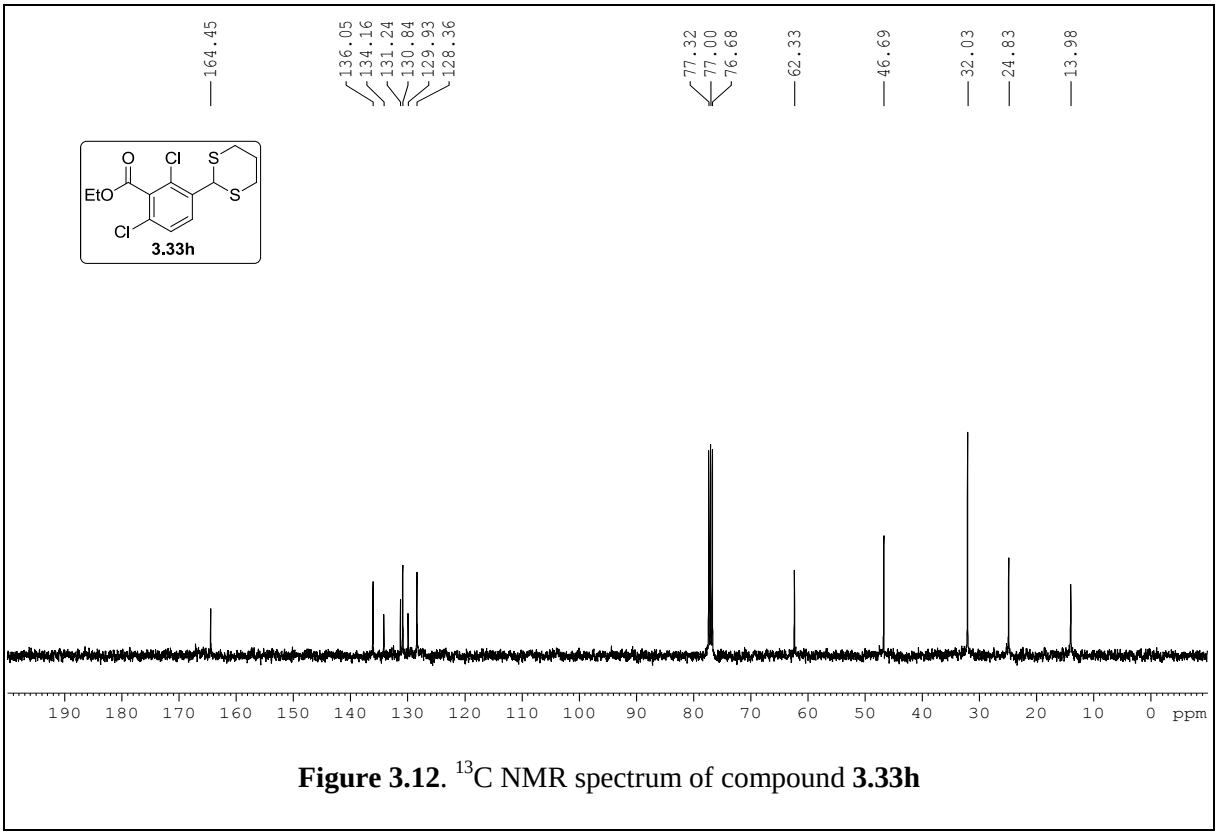

Figure 3.12. ^{13}C NMR spectrum of compound **3.33h**

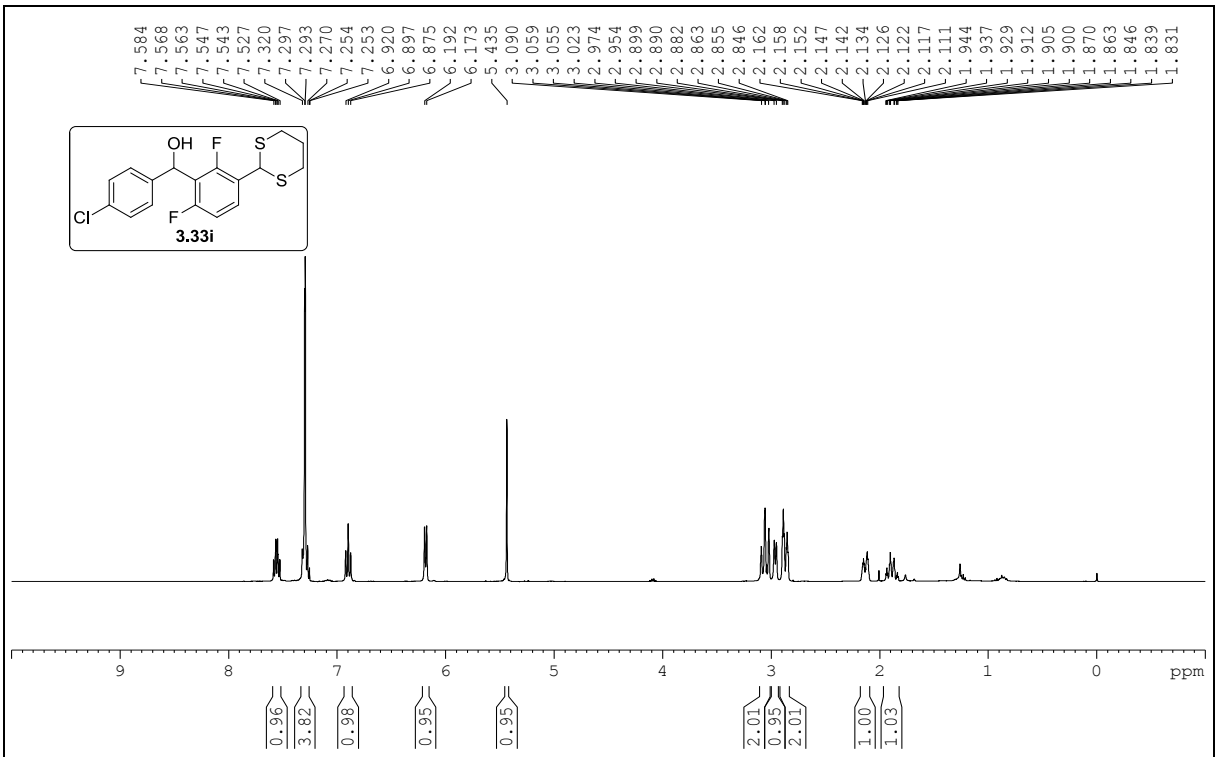

Figure 3.13. ^{1}H NMR spectrum of compound **3.33i**

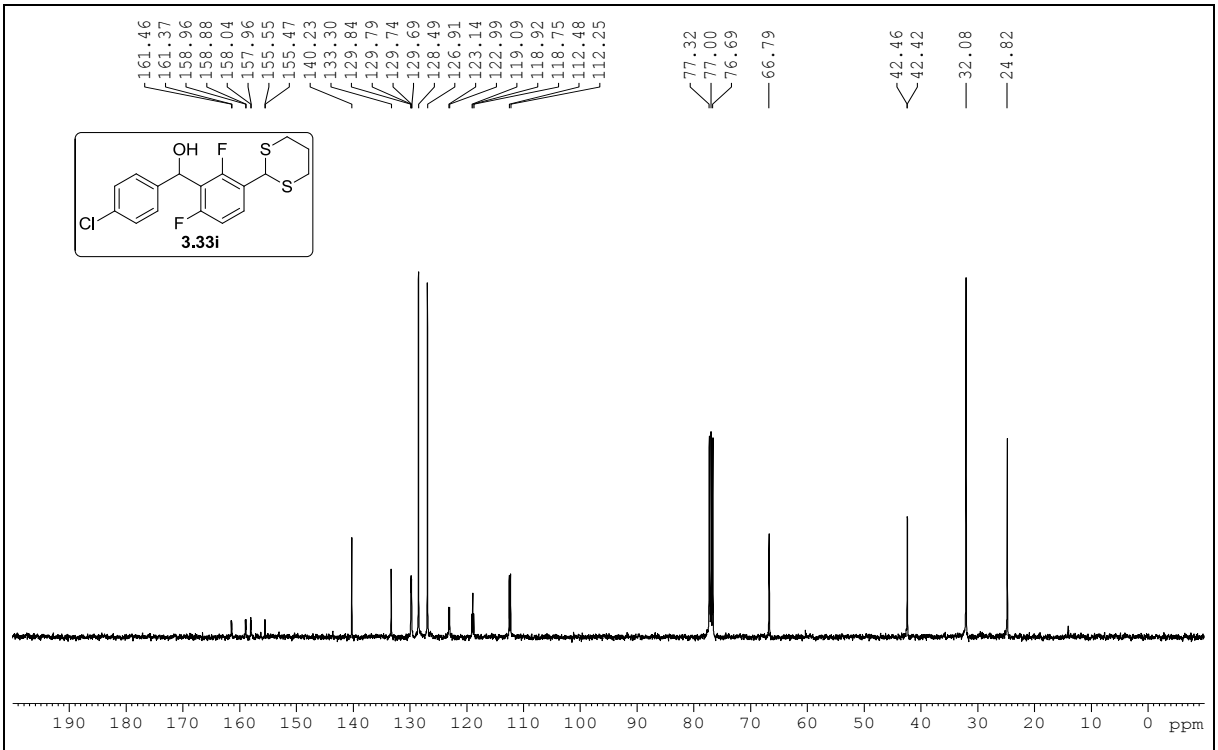

Figure 3.14. ^{13}C NMR spectrum of compound **3.33i**

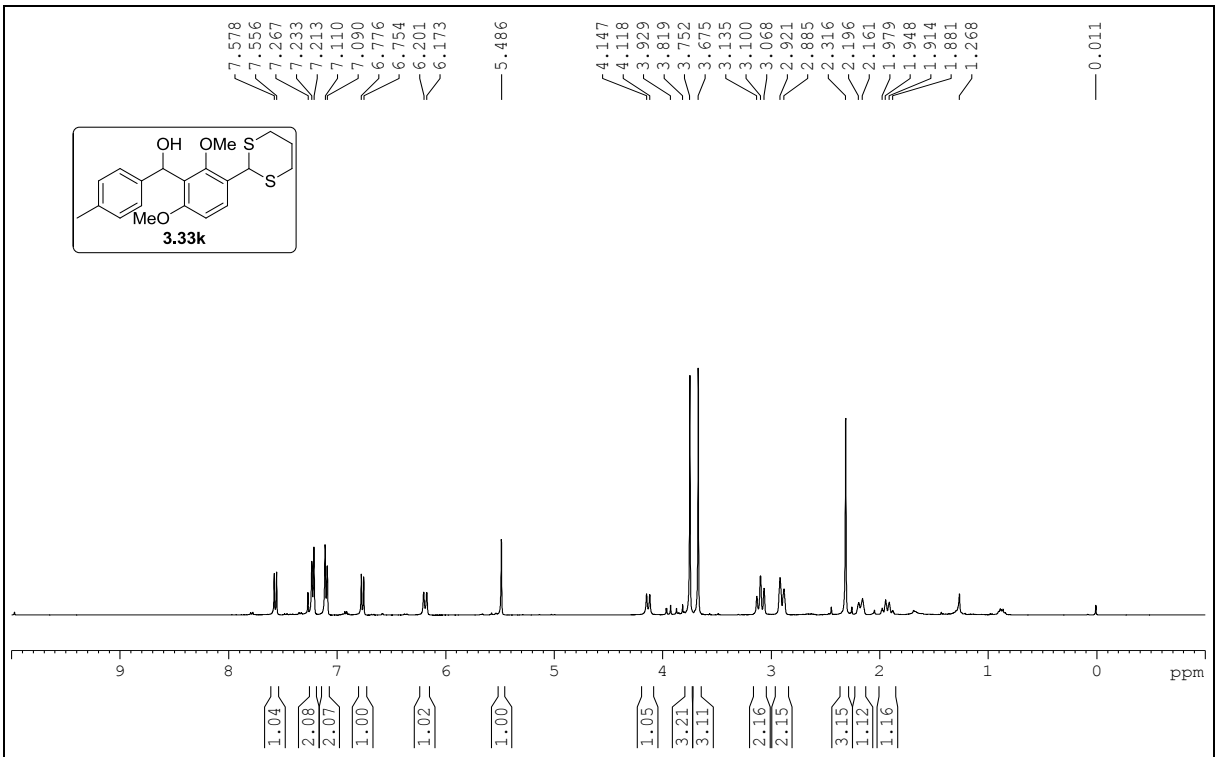

Figure 3.15. ^{1}H NMR spectrum of compound **3.33k**

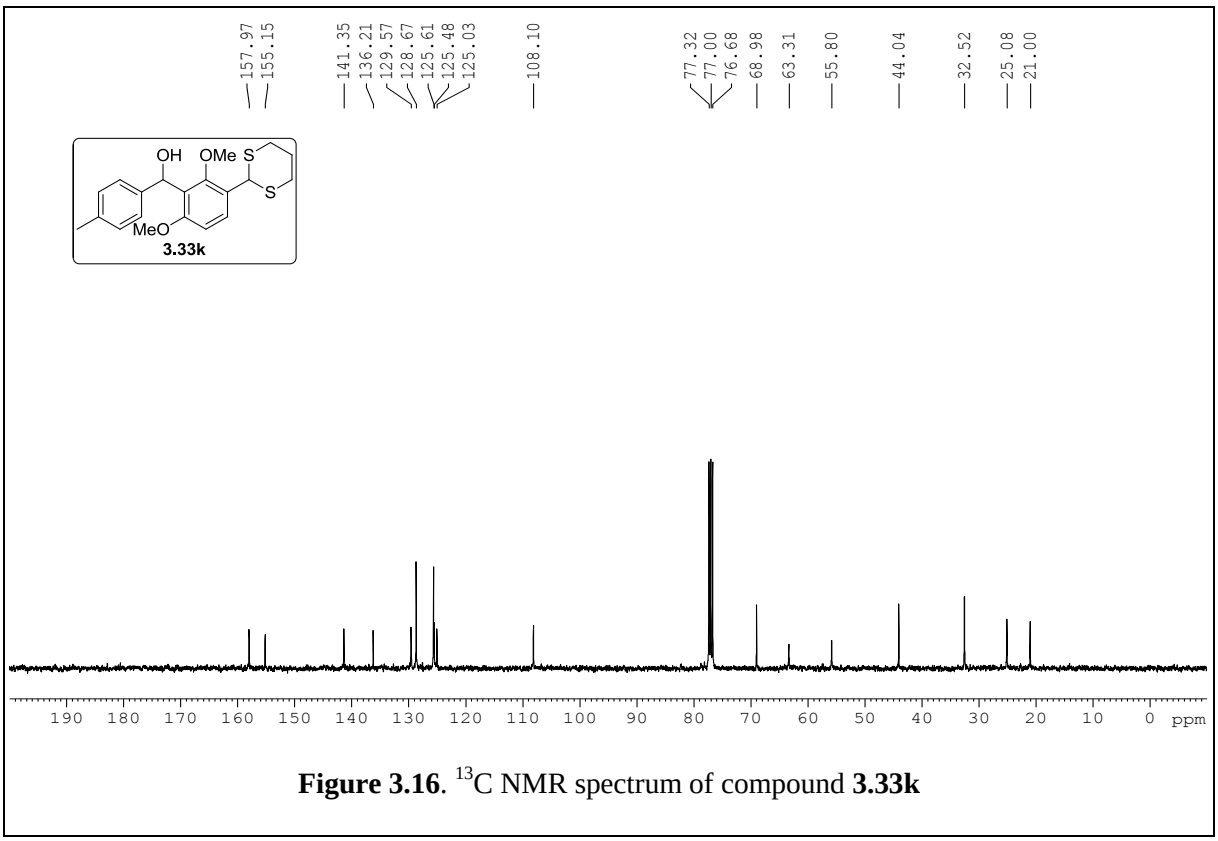

Figure 3.16. ^{13}C NMR spectrum of compound **3.33k**

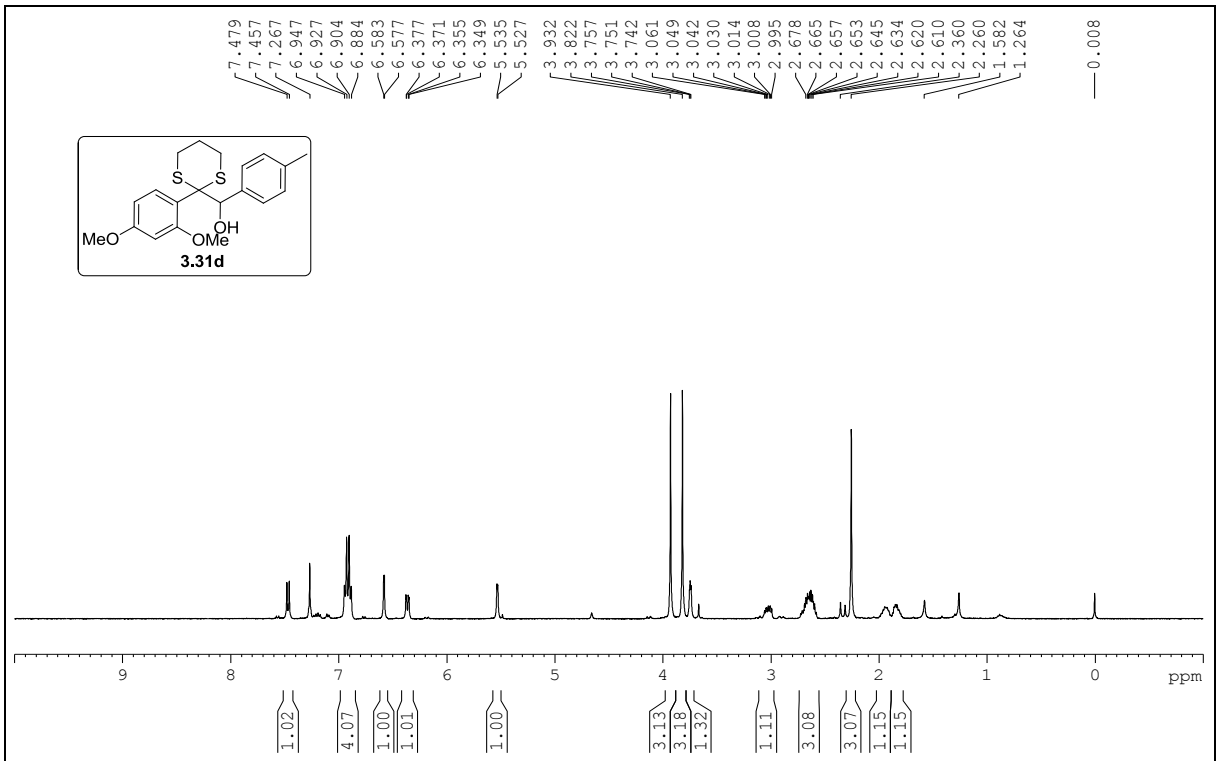

Figure 3.17. ^{1}H NMR spectrum of compound **3.31d**

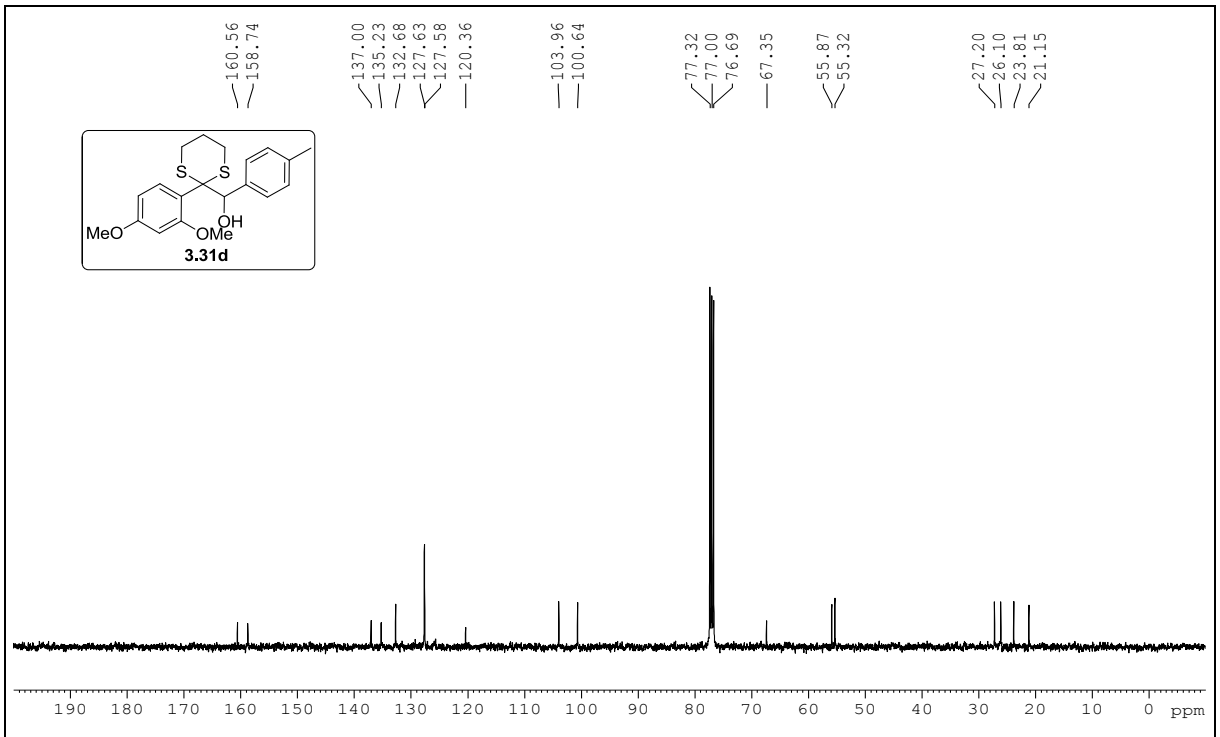

Figure 3.18. ^{13}C NMR spectrum of compound **3.31d**

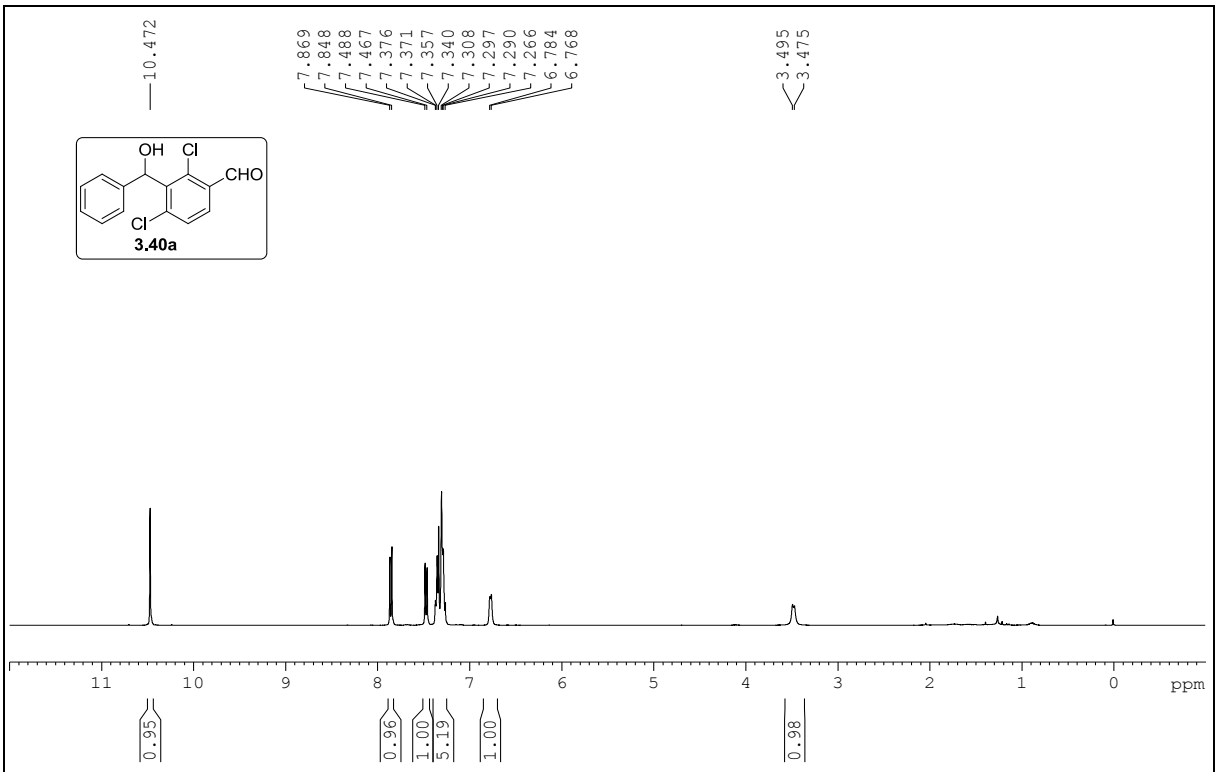

Figure 3.19. ^{1}H NMR spectrum of compound **3.40a**

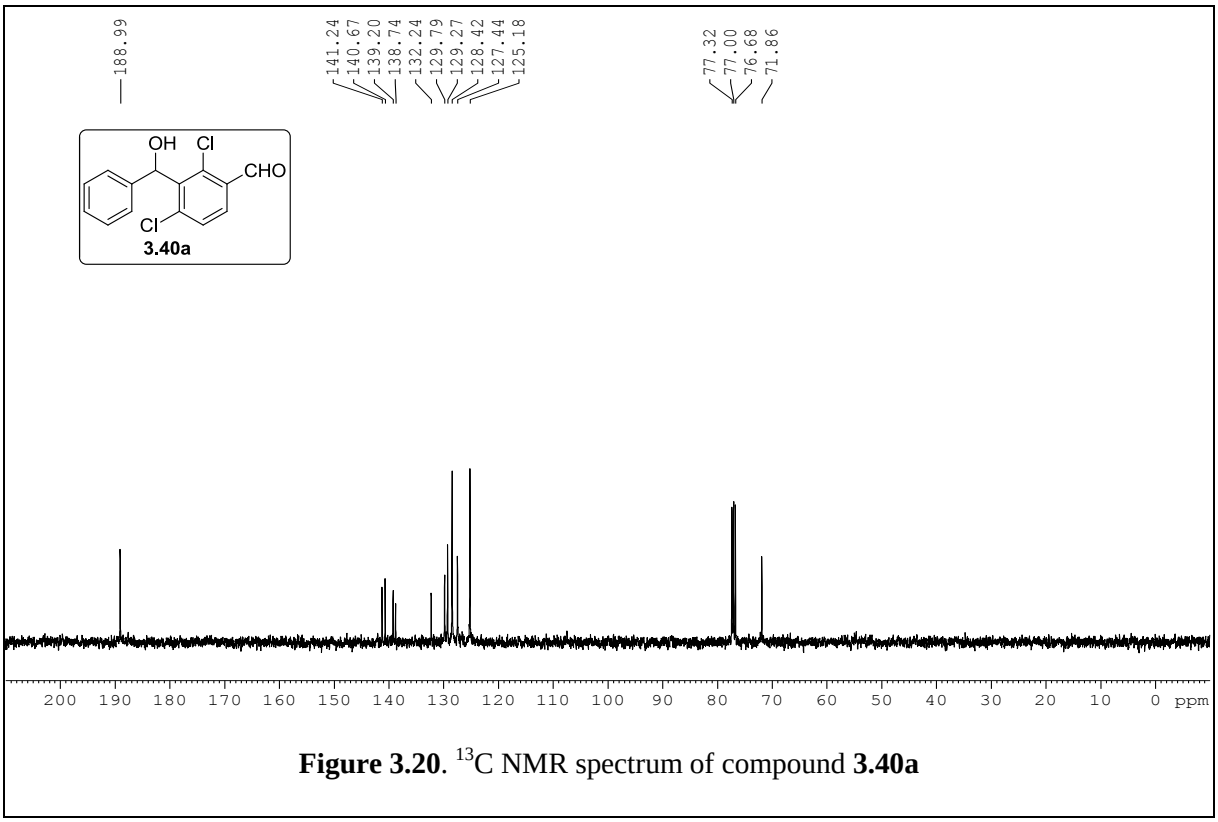

Figure 3.20. ^{13}C NMR spectrum of compound **3.40a**

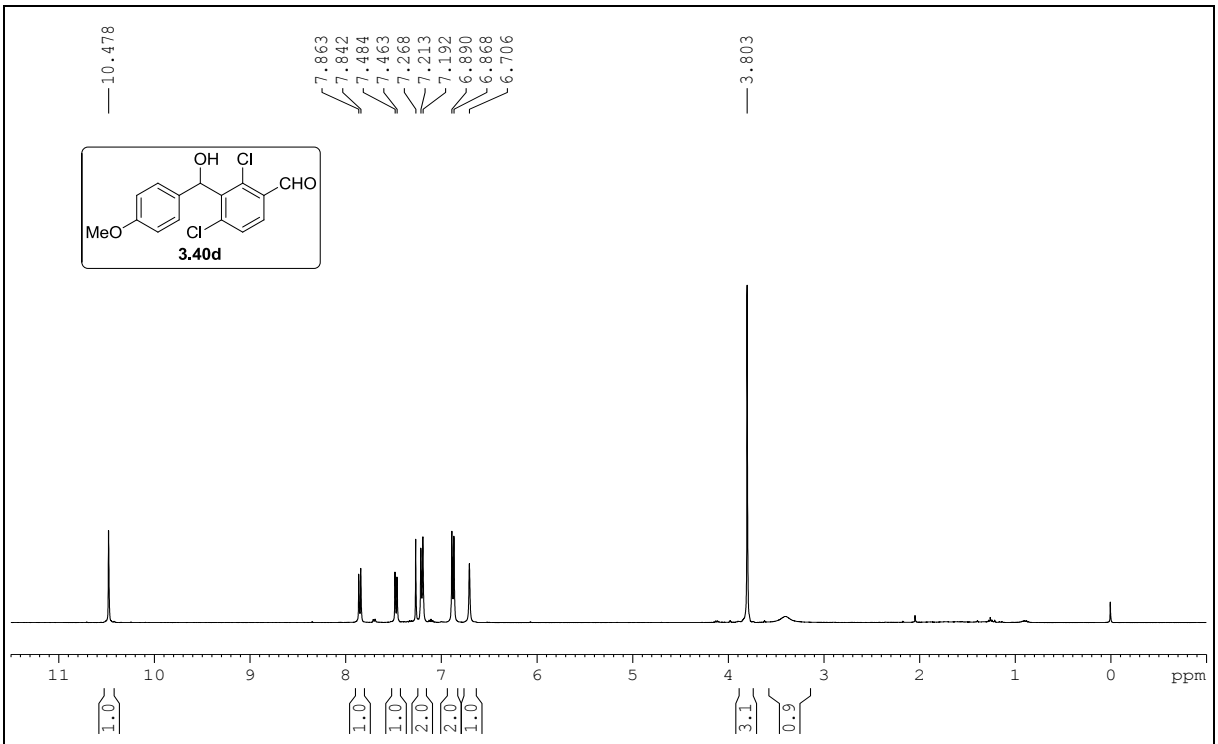

Figure 3.21. ^{1}H NMR spectrum of compound **3.40d**

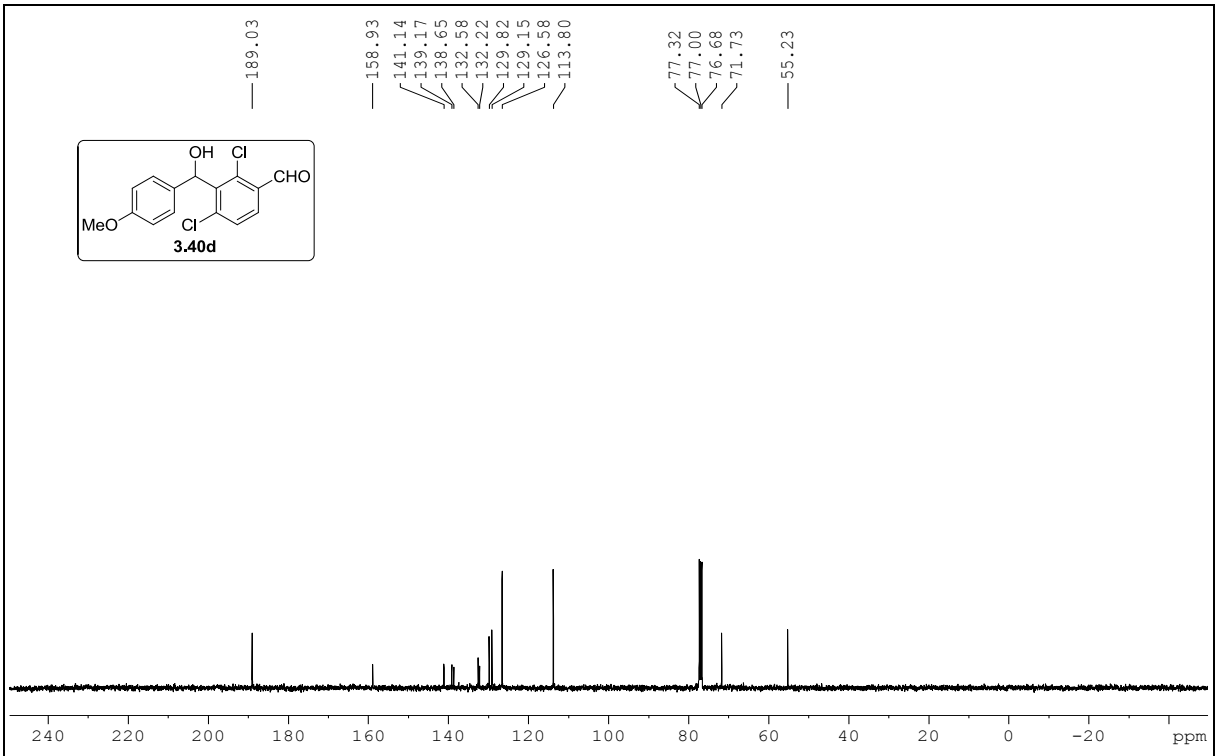

Figure 3.22. ^{13}C NMR spectrum of compound **3.40d**

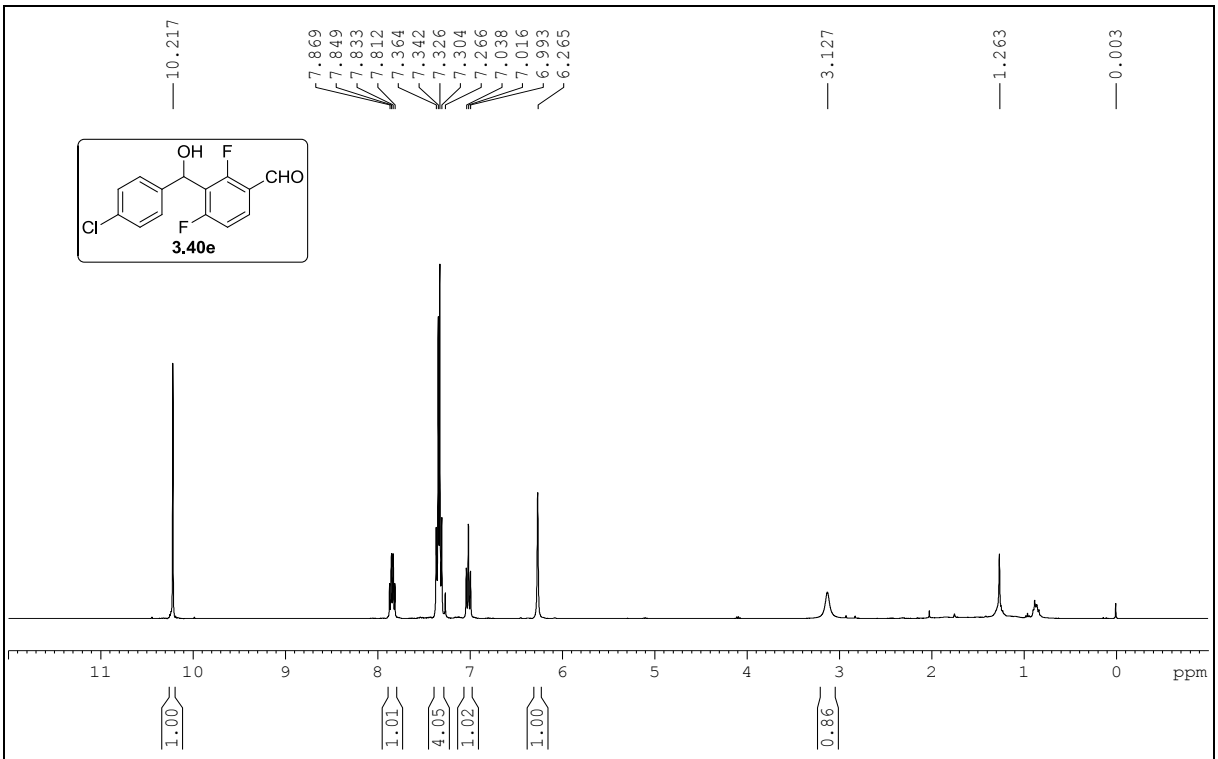

Figure 3.23. ^{1}H NMR spectrum of compound **3.40e**

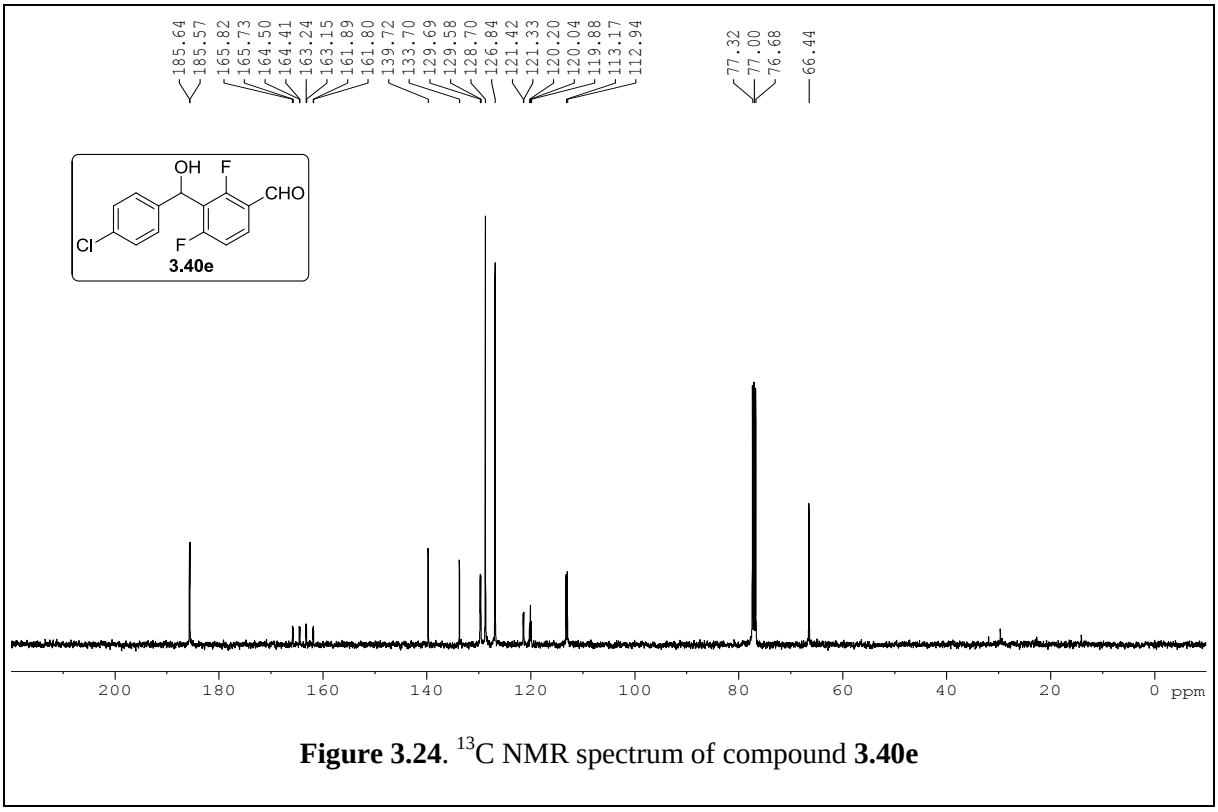

Figure 3.24. ^{13}C NMR spectrum of compound **3.40e**

List of Publications

1. Gold(I)-Catalyzed Activation of Epoxides: Application in the Synthesis of Bicyclic Ketals.

   Balamurugan, R.; Kothapalli, R. B.; Thota, G. K. *Eur. J. Org. Chem.* **2011**, 1557.

2. Synthesis of Chiral α-Diarylacetic Esters by Stereospecific 1,2-Aryl Migration Promoted by *in Situ* Generated Acetals from Benzoins.

   Kothapalli, R. B.; Niddana, R.; Balamurugan, R. *Org. Lett.* **2014**, *16*, 1278.

3. Regioselective Lithiation of Dithiane Protected 2,4-Dichloro/Difluoro Substituted Benzaldehydes.

   Balamurugan, R.; Kothapalli, R. B.; Sakthivel, S. *Manuscript to be communicated.*

Oral and Poster Presentations

1. Oral presentation was given on "**Synthesis of *α*-Diarylacetic esters from *in situ* formed acetals by stereospecific 1,2-aryl migration**" at 7th J-NOST (Junior National Organic Symposium Trust) held at Indian Institute of Science Education and Research (IISER) Mohali, India.

2. A poster was presented on "**Gold-catalyzed organic reactions**" at CHEMFEST-2010, 7th in-house symposium held at University of Hyderabad, Hyderabad.