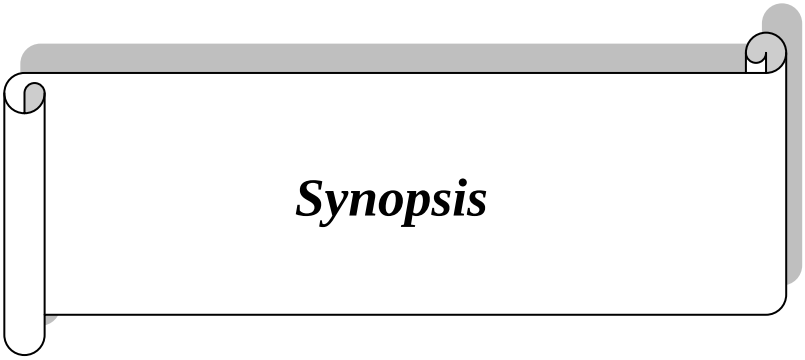

Synopsis

SYNOPSIS

The thesis entitled "**TOTAL SYNTHESIS OF BIOACTIVE MACROLIDES, SEIMATOPOLIDE B & (+)-CLADOSPOLIDE D AND DEVELOPMENT OF NOVEL [4+2]-BENZANNULATION REACTIONS**" has been divided into four chapters.

CHAPTER-I : Chapter **I** describes the "Total synthesis and revision of the absolute configuration of Seimatopolide B"

CHAPTER-II : Chapter **II** describes the "Total synthesis of (+)-Cladospolide D".

CHAPTER-III : Chapter **III** describes "A novel [4+2]-benzannulation to access substituted benzenes, polycyclic aromatic and benzene-fused heteroaromatic compounds from MBH-acetates of acetylenic aldehydes".

CHAPTER-IV : Chapter **IV** describes the "Atom- and Pot-Economical Consecutive Multi-Step Reaction Approach to Polycyclic Aromatic Hydrocarbons (PAHs)".

CHAPTER-I: **"Total synthesis and revision of the absolute configuration of Seimatopolide B"**

Nonanolides (decanolides or 10-membered macrolides) constitute an important class of bio-active secondary metabolites due to their notable diverse biological and pharmocoligical properties such as anti-bacterial, anti-fungal, anti-malarial, cytotoxic, phytotoxic, anti-microfilament, etc. In 2012, Lee and co-workers have isolated two new polyhydroxylated 10-membered macrolides, Seimatopolide A (**1**) and B (**2**, Figure 1.1) from an ethyl acetate extract of *Seimatosporium discosioides* culture medium.

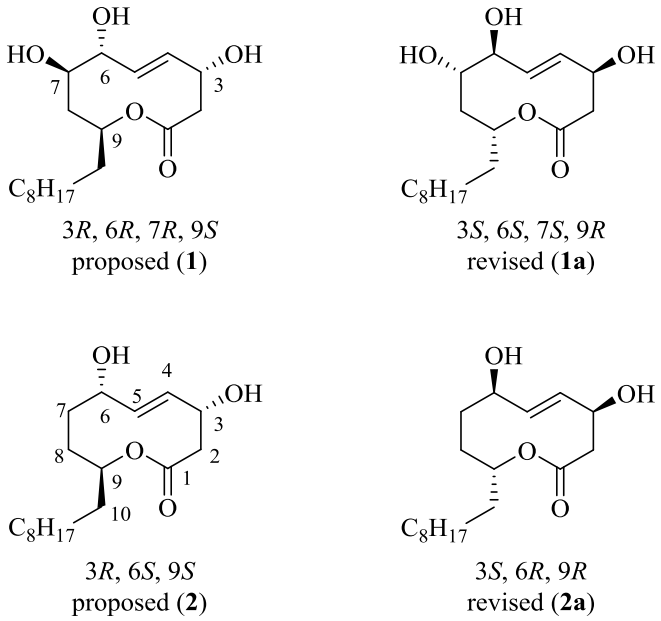


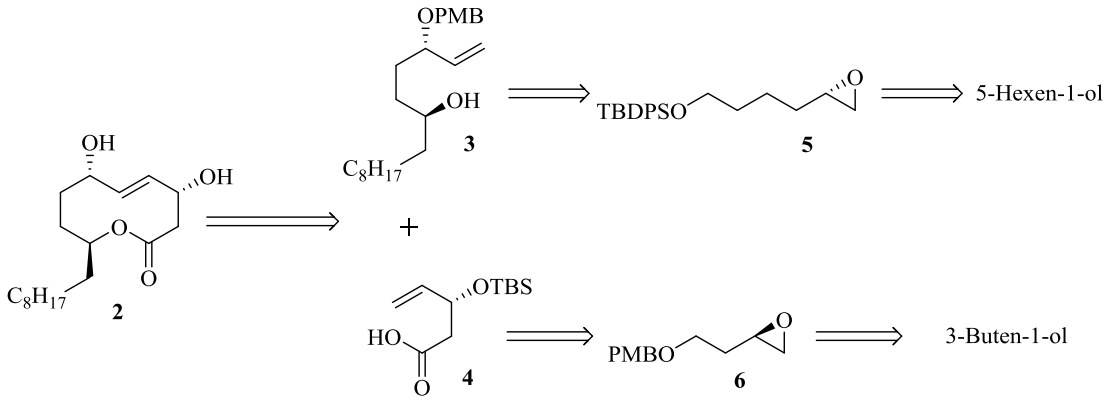
Figure 1.1: Structures of Seimatopolide A (**1**), B (**2**) and their enantiomers **1a** & **2a**.

The structural features combined with interesting biological profile of both compounds attracted the synthetic organic chemists towards their total synthesis. In this direction, we completed the total synthesis of (+)-Seimatopolide A (**1**) wherein we found that the absolute configuration of the natural product was misassigned and should be revised as 3*S*, 6*S*, 7*S*, 9*R* (**1a**, Figure 1.1).

With this results, we wanted to analyze the reported Mosher ester data for **2**, which revealed that it might also be another case of misassigned natural product. To prove this ambiguity and confirmation of absolute stereochemistry, we started the

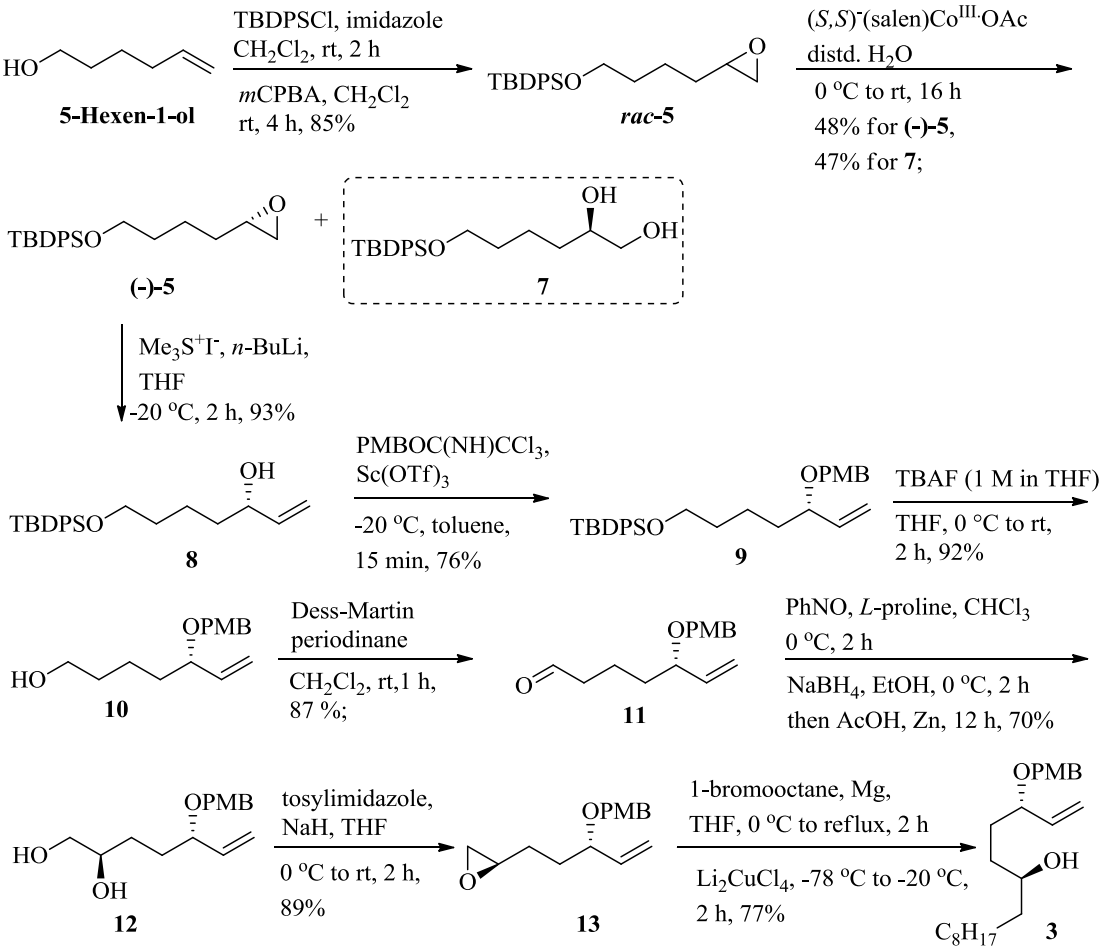
total synthesis of **2** in a stereo flexible manner, wherein both isomers could be synthesized.

Synthesis of **2** was planned from the alcohol **3** and the acid **4**, which could be coupled *via* Yamaguchi esterification followed by ring-closing metathesis. Alcohol **3** was synthesized from the epoxide **5**, which was planned from commercially available 5-hexen-1-ol. Synthesis of acid fragment **4** was considered from 3-buten-1-ol through the epoxide **6** using Jacobson epoxide resolution. (**Scheme 1.1**)



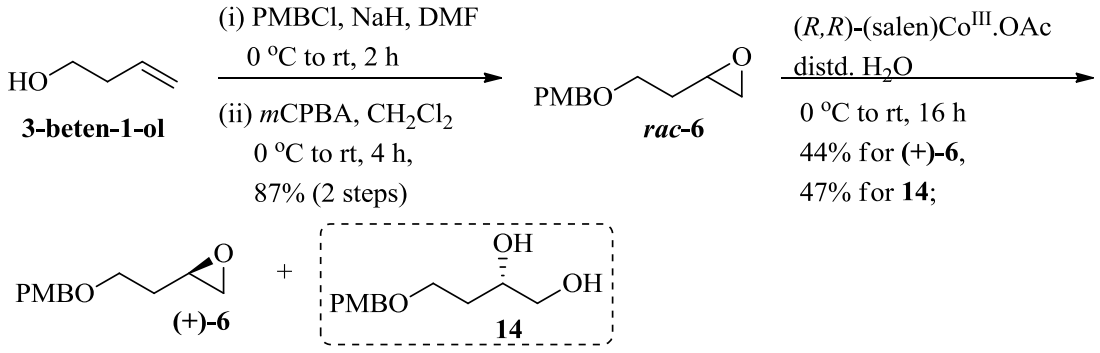
Scheme 1.1 Retrosynthesis of Seimatopolide B (**2**).

Initially the racemic epoxide **5** was obtained from 5-hexen-1-ol. Resolution of *rac*-**5** with (*S,S*)-(salen)Co^{III}.OAc Jacobson catalyst provided the desired epoxide **(-)-5** along with the diol **7**. Epoxide (-)-**5** was opened with trimethylsulfonium iodide in the presence of *n*-BuLi in THF at -20 ^oC provided the alcohol **8**. Subsequent PMB ether formation using the PMB-trichloroacetimidate in presence of $Sc(OTf)_3$ in toluene at -20 ^oC provided **9**. Desilylation compound **9** using TBAF in THF gave the alcohol **10**. Alcohol **10** was subjected to Dess-Martin periodinane oxidation to furnish the aldehyde **11**, which was exposed to asymmetric α-hydroxylation using *L*-proline and nitrosobenzene in chloroform at 0 ^oC followed by the *in situ* reduction of the resulting anilinoxy aldehyde with $NaBH_4$ in ethanol at 0 ^oC and treatment with Zn to get the diol **12**. Treatment of the diol **12** with tosylimidazole in the presence of NaH in THF at 0 ^oC to room temperature furnished the epoxide **13**. Then, the epoxide **13** was treated with *n*-octyl magnesium bromide in the presence of Li_2CuCl_4 at -78 ^oC to give the desired alcohol fragment **3**. (**Scheme 1.2**)



Scheme 1.2

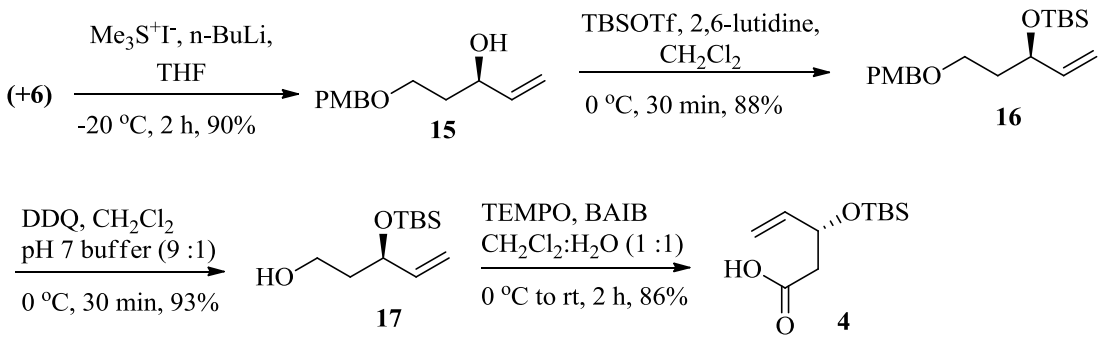
3-buten-1-ol was protected as PMB ether with PMBCl and NaH followed by epoxidation with *m*CPBA gave the racemic epoxide **6**, which was subjected Jacobson resolution to give chiral epoxide (+)-**6** and diol **14**. (**Scheme 1.3**)



Scheme 1.3

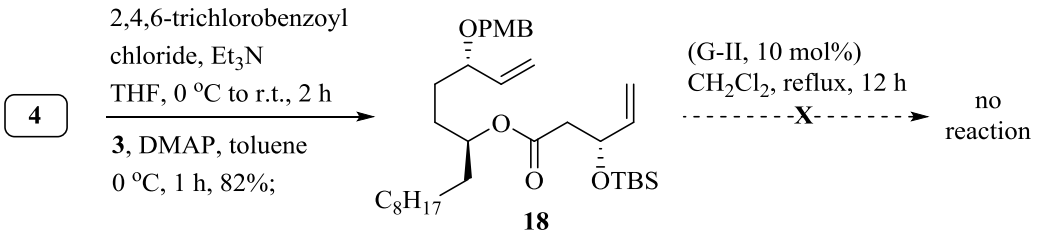
The chiral epoxide (+)-**6** was opened with trimethylsulfonium iodide in the presence of *n*-BuLi in THF at -20 °C provided the alcohol **15**, which was protected

with TBS triflate in the presence of 2,6-lutidine to provide compound **16**. PMB group of compound **16** was deprotected with DDQ and gave the alcohol **17**. The desired acid **4** has been accomplished by BAIB, TEMPO oxidation of alcohol **17** in dichloromethane and water. (**Scheme 1.4**)



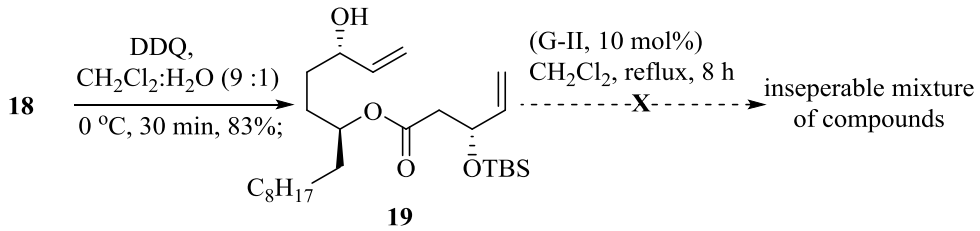
Scheme 1.4

Having both the alcohol **3** and the acid **4** in hand, construction of macrocyclic framework was achieved. Esterification reaction of **3** with the acid **4** was carried out under Yamaguchi conditions to furnish the RCM precursor **18**. Towards the ring-closing metathesis (RCM), initially **18** was treated with Grubbs second generation catalyst (G-II, 10 mol%). But, there is no progress in reaction and the starting material was recovered. (**Scheme 1.5**)



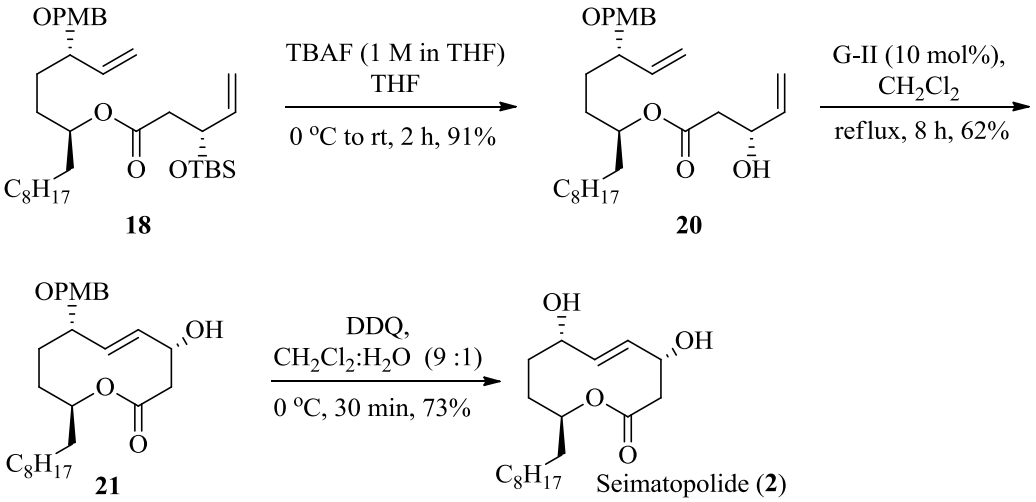
Scheme 1.5

Then, we tried the RCM reaction in two different ways. Firstly, PMB group in compound **18** was deprotected using DDQ in CH_2Cl_2:H_2O (9:1) to obtain **19**, which was then subjected to RCM reaction using G-II, (10 mol%). However, the reaction failed to give the desired pure product, instead the formation of an inseparable mixture of compounds was observed. (**Scheme 1.6**)



Scheme 1.6

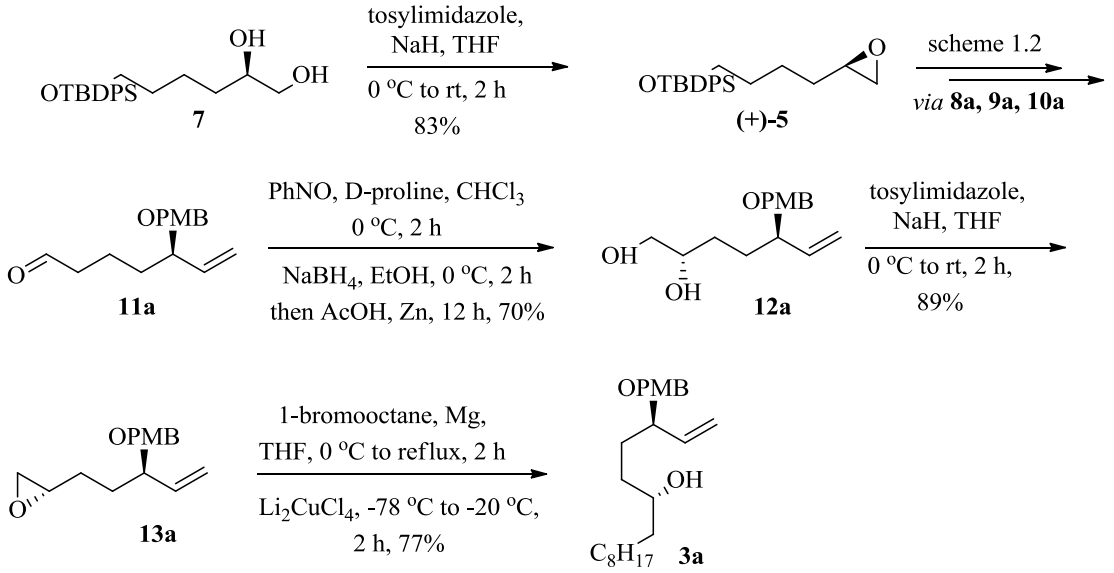
Subsequently, desilylation of the TBS group of **18** using TBAF in THF provided the alcohol **20**. Treatment of the diene **20** with G-II (10 mol%) offered clear formation of the macrolide **21**. Lastly, deprotection of the PMB group of **21** with DDQ in CH_2Cl_2:H_2O (9:1) completed the synthesis of the target compound, Seimatopolide B (**2**). (**Scheme 1.7**)



Scheme 1.7

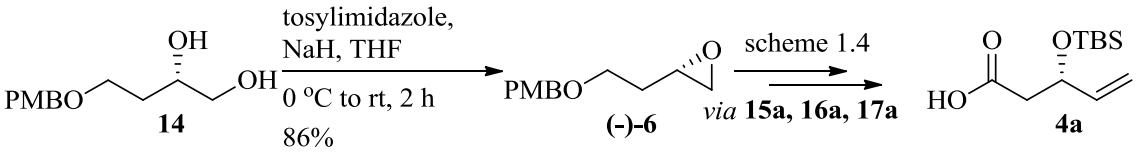
All the spectroscopic data (^{1}H, ^{13}C NMR, mass and IR) including NOE analysis for synthetic **2** were in full agreement to those reported for the natural product. However, the specific rotation for synthetic **2** was observed as $[\alpha]^{20}_D$ = +16.6 (*c* = 0.03, MeOH), whereas for isolated compound it is reported as $[\alpha]^{26}_D$ = -125.4 (*c* = 0.03, MeOH). The observation of opposite sign for synthetic **2** supports misassingment of the absolute configuration for reported compound. To further confirm this, based on the observations for Seimatopolide A, we decided to synthesize the enantiomer (**2a**) of the proposed structure (**2**).

The synthetic route for the enantiomer of alcohol subunit **3a** is depicted from the requisite epoxide (+)-**5**, obtained from the diol **7**. Thus, the treatment of diol **7** with tosylimidazole/NaH in THF at 0 ^{o}C provided (+)-**5**. The epoxide (+)-**5** was then converted to **3a** following the sequence of reactions used for the conversion of (-)-**5** to **3**. (**Scheme 1.8**)



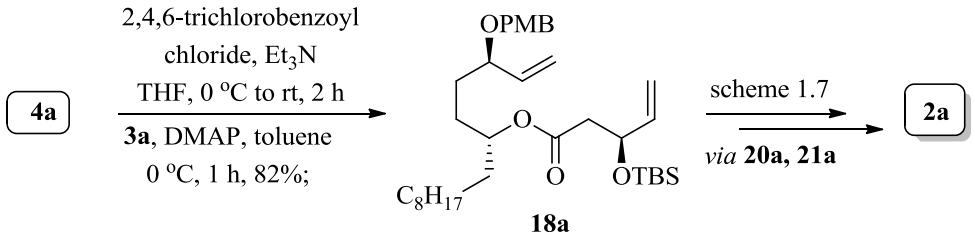
Scheme 1.8

The enantiomer of acid fragment (**4a**) was synthesized from the diol **14**. Treatment of diol **14** with tosylimidazole/NaH in THF at 0 ^{o}C provided (-)-**6**, which was transformed to **4a** following the sequence of reactions used for the conversion of (+)-**6** to **4**. (**Scheme 1.9**)



Scheme 1.9

Next phase was to complete the synthesis of **2a** from the alcohol **3a** and acid **4a**, which was sucessfully attained by following the similar sequence of reactions used for **2**. (**Scheme 1.10**)



Scheme 1.10

All the spectral data (^{1}H, ^{13}C NMR, mass and IR) of **2a** were in full agreement to those reported for the natural product. The specific rotation for **2a** was observed {$[\alpha]^{20}_{D}$ = -13.4 (*c* = 0.03, MeOH)} with identical sign of isolated compound {$[\alpha]^{26}_{D}$ = -125.4 (*c* = 0.03, MeOH)}. specific rotation values for natural and synthetic Seimatopolide B as well as the analysis of Mosher ester data for reported compound, suggests that the absolute configuration of natural Seimatopolide B should be revised as 3*S*, 6*R*, 9*R* represented by structure **2a** (enantiomer of **2**).

In summary, we have successfully accomplished the total synthesis of the initially proposed structure of Seimatopolide B (**2**) in 14 linear steps with 4.2% overall yield. The specific rotations of the synthesized compound and the natural product displayed opposite signs. This observation supports the misassignment of the absolute configuration for the natural product, which was further confirmed through total synthesis of the enantiomer **2a**. These results suggest that the absolute configuration in the natural product should be 3*S*, 6*R*, 9*R* which is in accordance with the natural product revised data.

CHAPTER-II: **"Total synthesis of (+)-Cladospolide D".**

In 2001, Satoshi Omura and co-workers have isolated a new 12-membered oxo-lactone, namely Cladospolide D, along with known Cladospolides A, B and C *Cladosporium* sp. FT-0012 (Figure 2.1). The absolute and relative stereochemistry as well as the stereo chemical assignment of the C2-C3 double bond were correctly determined only after it's total synthesis independently by Hou and O'Doherty research groups. In continuation of our research program on total synthesis of bioactive natural macrolides, in particular Cladospolides, we started the total synthesis of (+)-Cladospolide D.

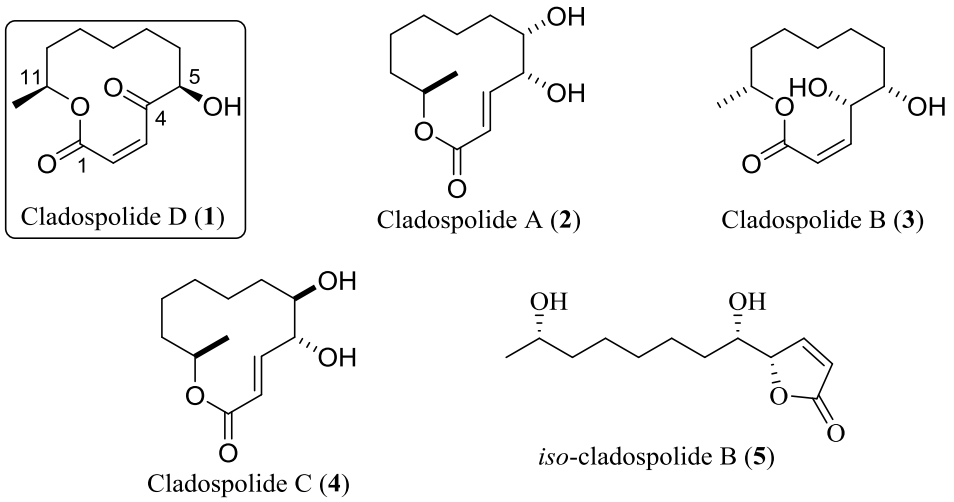
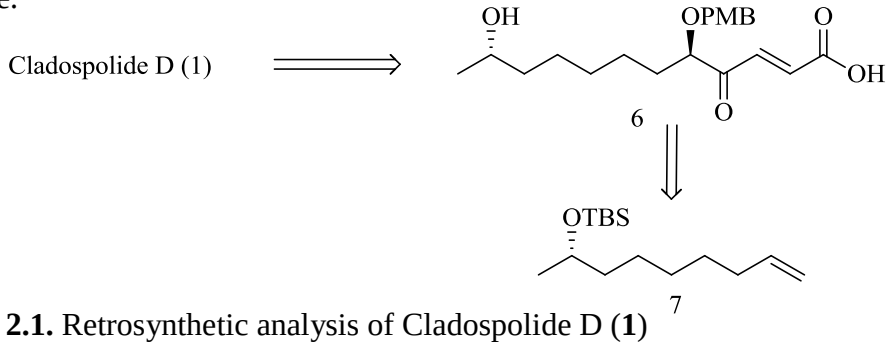


Figure 2.1. Structures of Cladospolides A-D and *iso*-Cladospolide B

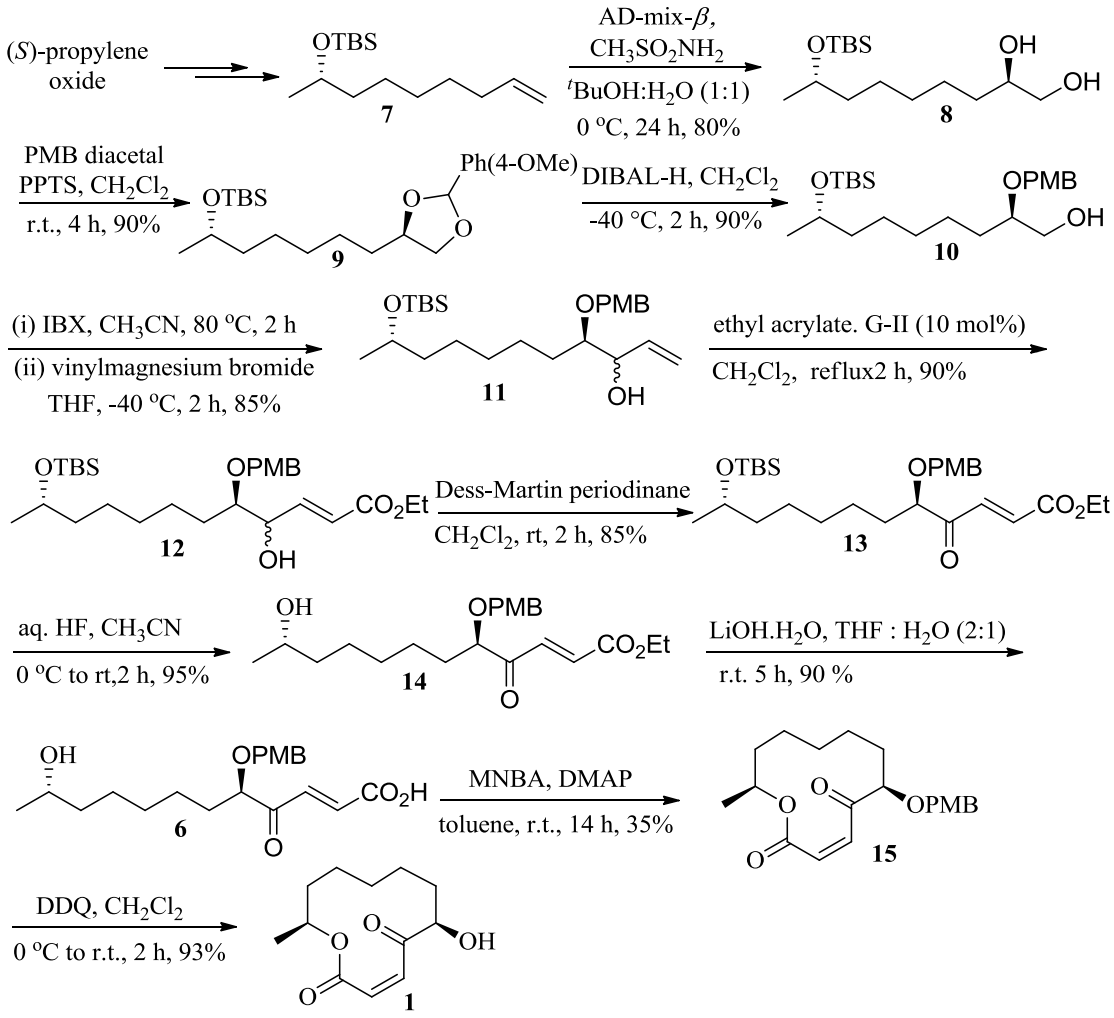
The retrosynthetic analysis suggests TBS-protected alkenol **7** to be a suitable starting material. Cladospolide D (**1**) should be prepared by Shiina lactonization of hydroxy acid **6**, which could be obtained from alkenol **7** involving Sharpless asymmetric dihydroxylation for the installation of C5-hydroxyl group and Grubbs olefin metathesis to have the desired C2-C3 olefin functionality of the target molecule.



Scheme 2.1. Retrosynthetic analysis of Cladospolide D (**1**)

The synthesis of Cladospolide D (**1**) began from the known alkenyl *tert*-butyldimethylsilyl ether **7**, which was obtained readily in two-steps from (*S*)-propylene oxide. Sharpless asymmetric dihydroxylation of alkene **7** with AD-mix *β*, $CH_3SO_2NH_2$, *t*BuOH/H_2O (1:1) gave the diol **8**. The diol **8** was protected as its *para*-methoxybenzylidene acetal **9**, which was subjected to reductive opening under DIBAL-H in CH_2Cl_2 at -78 ^oC to provide the primary alcohol **10**. Primary alcohol **10** was oxidized using IBX in CH_3CN to aldehyde, which upon treatment with vinylmagnesium bromide afforded the allylic alcohol **11**. Allylic alcohol **11** was subjected to cross-metathesis reaction with ethyl acrylate using Grubb's second-generation catalyst (G-II), which provided **12**. Hydroxyl group of **12** was oxidized

with Dess-Martin periodinane to keto-ester **13**. Than *tert*-butyldimethyl silyl (TBS) was deprotected with *aq*. HF in CH_3CN to obtain hydroxy keto-ester **14**. Subsequently, hydrolysis of ester group of **14** using LiOH in THF:H_2O gave the hydroxy-acid **6**. Treatment of **6** under Shiina lactonization using 2-methyl-6-nitrobenzoic anhydride (MNBA) in the presence of DMAP in toluene provided the keto-lactone **15**. Finally, DDQ-mediated deprotection of PMB group of **15** provided the target molecule, Cladospolide D. The spectral data (IR, ^1H and ^{13}C NMR) of obtained **1** was identical and the optical rotation observed for **1**, $[\alpha]_D^{20}$ = +55.53 (*c* 0.8, CH_3OH), is comparable with the reported data ($[\alpha]_D$ = +56.0 (*c* 1.00, CH_3OH).[1]

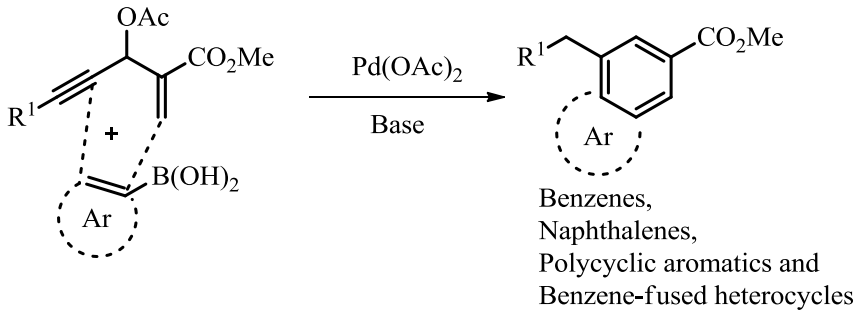


Scheme 2.2

In summary, the chemistry described in this chapter defines an asymmetric approach for the construction of natural Cladospolide D based on Shiina lactonization strategy involving Sharpless asymmetric dihydroxylation and Grubb's olefin cross metathesis reactions as key steps.

CHAPTER-III: **"A novel [4+2]-benzannulation to access substituted benzenes, polycyclic aromatic and benzene-fused heteroaromatic compounds from MBH-acetates of acetylenic aldehydes".**

The development of new synthetic methods to substituted aromatic, polycyclic aromatic and heteroaromatic compounds continues to command extensive interest due to their wide range of applications. Benzannulation is one of the important reactions for the construction of substituted benzene ring. In this chapter, we report a novel [4+2]-benzannulation using Morita-Baylis-Hillman acetates of acetylenic aldehydes as C4 precursor and aryl or vinyl boronic acids as C2 synthon. This approach offers a significant advantage over the known enyne-based [4+2]-benzannulation methods by giving an access to substituted benzenes, as well as to polycyclic aromatic hydrocarbons and benzene-fused heterocyclic compounds from easily accessible substrates.

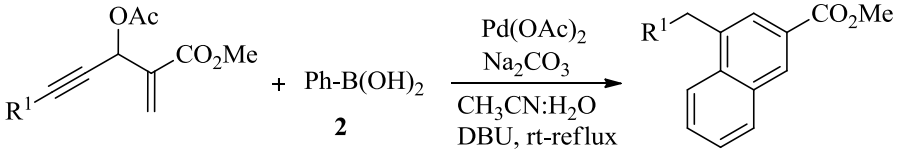


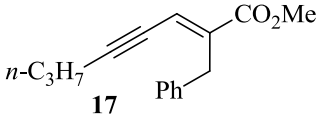
Scheme 3.1. [4+2]-Benzannulation reaction of enynes.

To test the hypothesis MBH-acetate **1** and phenyl boronic acid (**2**) were chosen as model substrates. From the optimization studies, we were pleased to found that the [4+2]-benzannulation product, naphthalene **3**, was accomplished in 89% yield using 5 mol% of $Pd(OAc)_2$, Na_2CO_3 in acetonitrile:H_2O and DBU reaction conditions.

With the optimized reaction conditions, we tested the substrate scope of this reaction by using variety of MBH acetates of acetylenic aldehydes with phenylboronic acid (**2**) to obtain naphthalenes with a variety of substituents and results are summarised in **Table 3.1**. However, the reaction of MBH-acetate **16** having an *n*-propyl group on the alkyne functionality with **2** provided the enyne intermediate **17**, instead of the expected naphthalene.

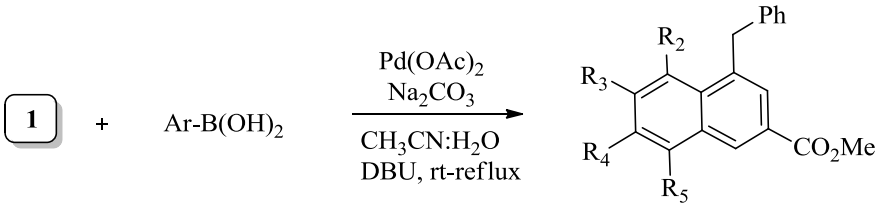
Table 3.1. [4+2]-Benzannulation of MBH-acetates of acetylenic aldehydes with **2**.

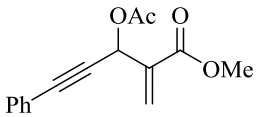
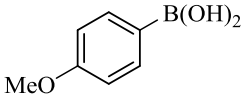
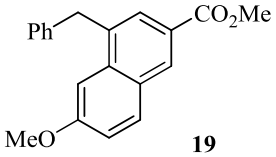
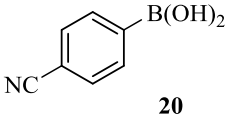
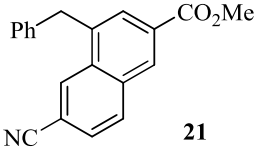
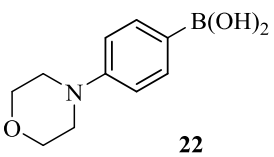
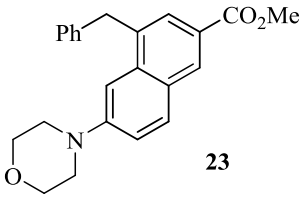


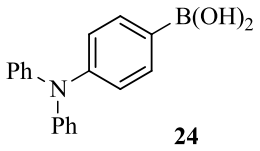
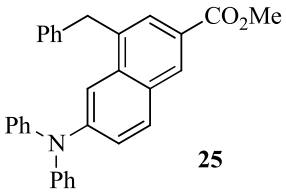
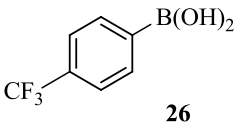
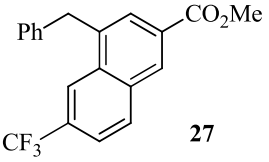
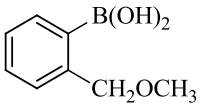
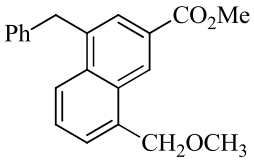
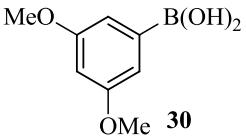
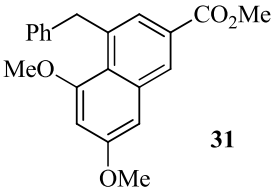
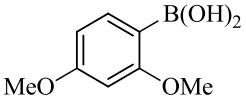
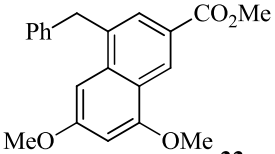
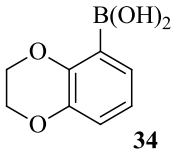
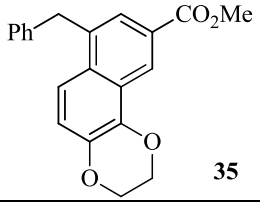
Entry	MBH-acetate	Time (h)	Naphthlene	Yield (%)
1	R^1 = Ph, **1**	5	**3**	89
2	R^1 = 1-Napthyl, **4**	6	**5**	88
3	R^1 = 2-Thiophenyl, **6**	4	**7**	86
4	R^1 = 4-Me-Ph, **8**	5	**9**	84
5	R^1 = 4-Cl-Ph, **10**	6	**11**	87
6	R^1 = 3-CF_3-Ph, **12**	8	**13**	75
7	R^1 = Ph-CH=CH-, **14**	5	**15**	60
8	R^1 = *n*-C_3H_7-, **16**	5	 **17**	95

We next evaluated the reactivity of diversely substituted phenylboronic acids and the results are summarized in **Table 3.2**.

Table 3.2. Substituted arylboronic acids for benzannulation reaction

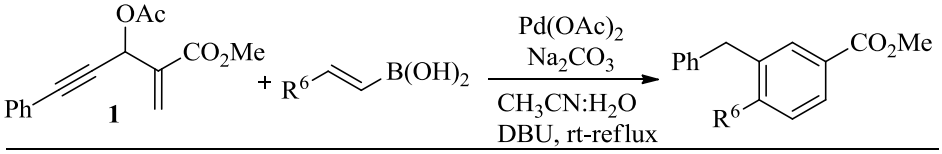


S.No	MBH acetate	Boronic Acid	Time (h)	Product	Yield (%)
1	 **1**	 **18**	4	 **19**	89
2	**1**	 **20**	6	 **21**	88
3	**1**	 **22**	4	 **23**	86

4	**1**	 **24**	5	 **25**	84
5	**1**	 **26**	6	 **27**	87
6	**1**	 **28**	8	 **29**	75
7	**1**	 **30**	5	 **31**	60
8	**1**	 **32**	6	 **33**	70
9	**1**	 **34**	3	 **35**	82

Next, we tested the reactivity of vinylic boronic acids with MBH-acetate **1** in the present annulation reaction is also feasible, which allows the synthesis of substituted benzenes. (**Table 3.3**).

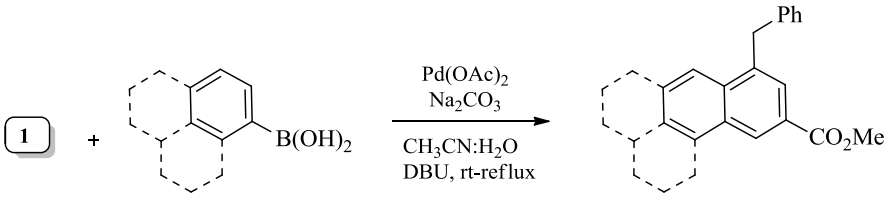
Table 3.3. Synthesis of substituted benzenes using vinyl boronic acids.

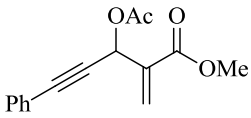
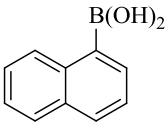
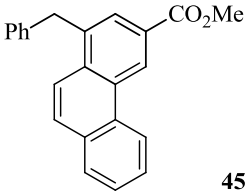
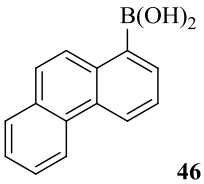
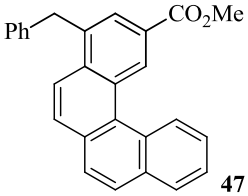
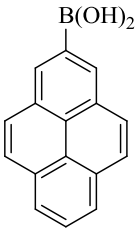
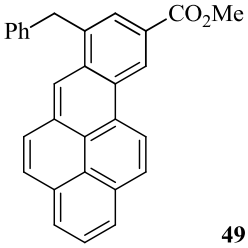
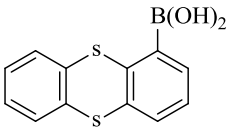
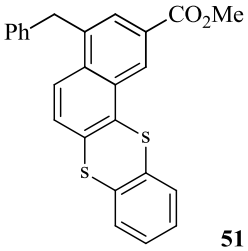
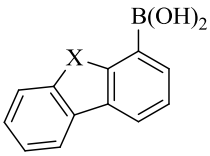
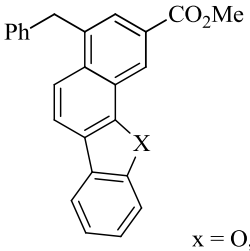


Entry	Boronic acid (4)	Time (h)	Benzene (5)[b]	Yield (%)[c]
1	R^6 = Ph, **36**	5	**37**	80
2	R^6 = 4-F-C_6H_4-, **38**	4	**39**	72
3	R^6 = *n*-C_6H_{13}, **40**	6	**41**	80
4	R^6 = *t*-Bu-, **42**	5	**43**	78

The reaction scope was further extended by exploring the one-pot [4+2]-benzannulation approach to the synthesis of polycyclic aromatic hydrocarbons (**Table 3.4**).

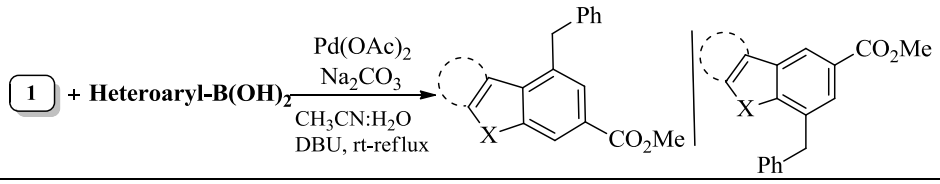
Table 3.4. Polycyclic aromatic compounds using [4+2]-benzannulation reaction.

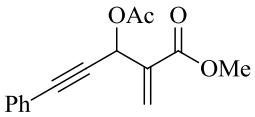
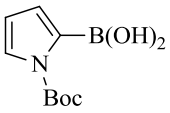
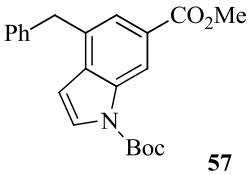
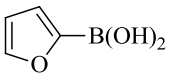
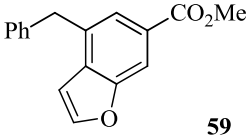
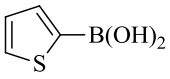
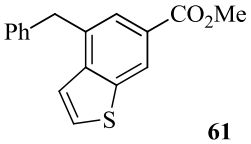
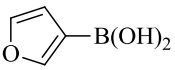
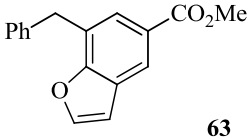
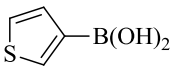
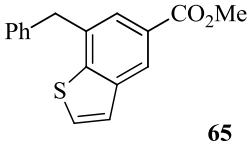
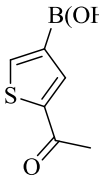
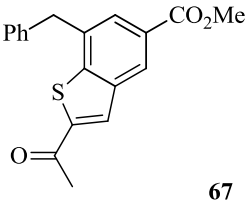


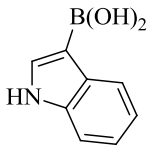
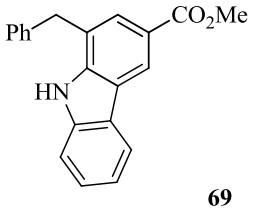
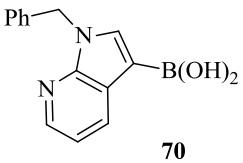
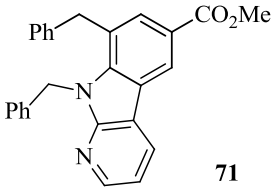
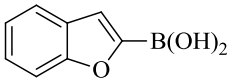
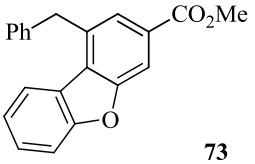
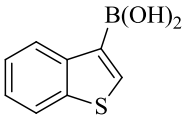
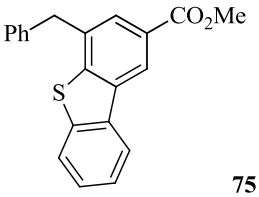
S.No	MBH acetate	Boronic Acid	Time (h)	Product	Yield (%)
1	 **1**	 **44**	8	 **45**	82
2	**1**	 **46**	5	 **47**	83
3	**1**	 **48**	7	 **49**	81
4	**1**	 **50**	6	 **51**	71
5	**1**	 x = O, **52**	6	 x = O, **53**	67
6	**1**	x = S, **54**	8	x = S, **55**	65

Having the above success in using the MBH-acetates of acetylenic aldehydes for the synthesis of polycyclic aromatic hydrocarbons *via* [4+2]-benzannulation, we next embarked on the synthesis of bicyclic or tricyclic benzene-fused heterocycles. These results clearly demonstrate the application of MBH acetates of acetylenic aldehydes in [4+2]-benzannulation towards the synthesis of a diverse range of heterocyclic frameworks. (**Table 3.5**)

Table 3.5. Benzene-fused heteroaromatics *via* [4+2]-benzannulation.

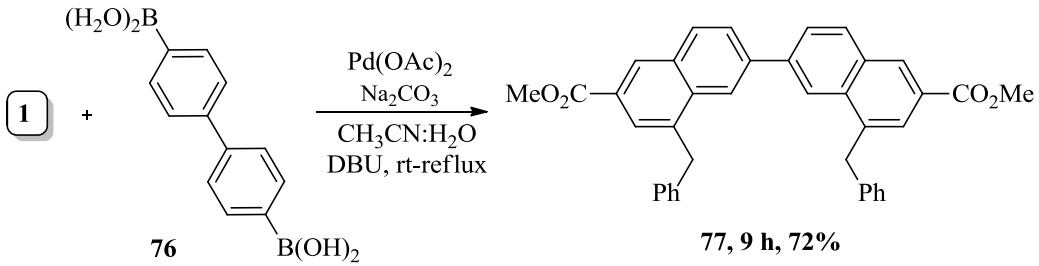


S.No	MBH acetate	Boronic Acid	Time (h)	Product	Yield (%)
1	 **1**	 **56**	6	 **57**	79
2	**1**	 **58**	5	 **59**	72
3	**1**	 **60**	5	 **61**	68
4	**1**	 **62**	5	 **63**	78
5	**1**	 **64**	5	 **65**	73
6	**1**	 **66**	7	 **67**	70

7	**1**	 **68**	5	 **69**	72
8	**1**	 **70**	6	 **71**	62
9	**1**	 **72**	5	 **73**	75
10	**1**	 **74**	6	 **75**	79

Interestingly, benzannulation of [1,1'-biphenyl]-4,4'-diyldiboronic acid (**76**) with **1** gave the resultant 2,2'-binaphthalene **77** in 72% yield (**Scheme 3.1**).

Scheme 3.2. Synthesis of bis-naphthlene derivative.

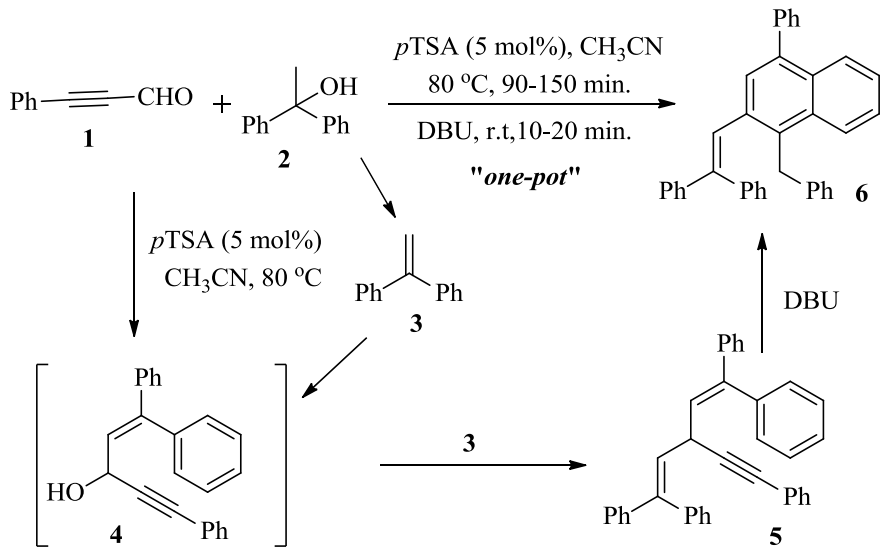


In summary, a general strategy for the synthesis of substituted benzenes, polycyclic aromatic hydrocarbons as well as benzene-fused heterocycles has been developed, starting from the reaction of MBH acetates of acetylenic aldehydes with aryl/heteroaryl or vinyl boronic acid.

CHAPTER-IV: **"Atom- and Pot-Economical Consecutive Multi-Step Reaction Approach to Polycyclic Aromatic Hydrocarbons (PAHs)".**

Functionalized Polycyclic aromatic hydrocarbons are important motifs in pharmaceutical chemistry, bio-active molecules and advanced organic materials. The properties of PAHs attracted the chemist for synthesis. There are few methods are developed for construction of PAHs. Everyone are metal mediated reactions and multistep synthesis. These drawbacks encouraged us to develop a ene-yne based cycloisomerisation for construction of substituted PAHs in one pot under metal-free conditions.

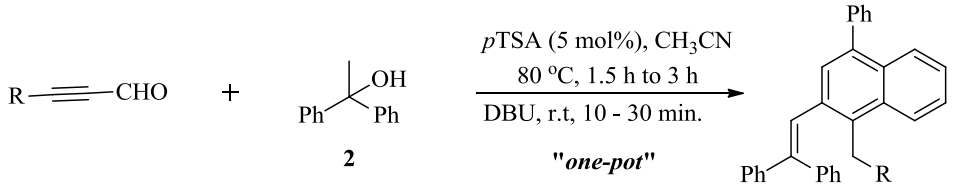
Initially, 1,1-diphenylethanol (**2**) and propargylic aldehyde **1** were treated with $Cu(OTf)_2$ for the formation of ene-yne through dehydration of **2** to give **3** followed by nucleophilic addition at aldehyde (with **3**) to give **4**. Interestingly, it gave the di-alkenyl product **5** at room temperature. The three step reaction (dehydration, nucleophilic addition and substitution) was evaluated using various acid catalysts ($FeCl_3$, *p*TSA and $ZnCl_2$). Among these *p*TSA was fond to give **4** in 94% yield. Based on our previous work on DBU cycloisomerization reactions, we treated the compound **5** with DBU and found that the reaction progressed smoothly to give vinylated naphthalene **6** in 92% yield. Next, the reaction of **1** with **2** was carried out in one pot by the sequential addition of 5 mol% *p*TSA followed by DBU and to our delight, the target product **6** was obtained in 90% yield. (**Scheme 4.1**)

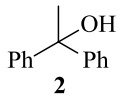
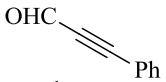
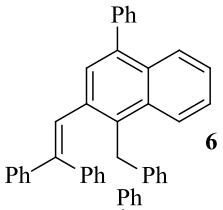
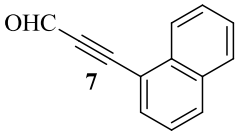
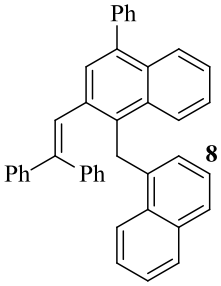
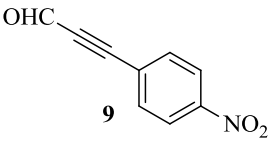
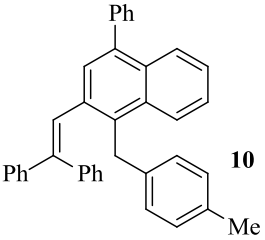
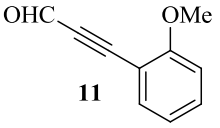
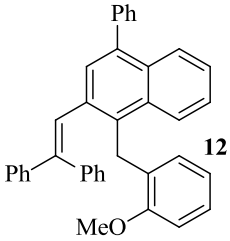
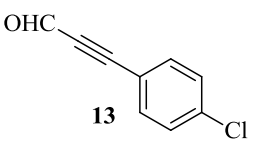
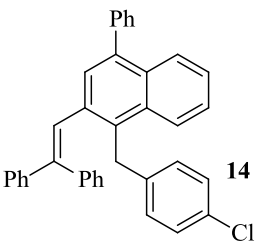


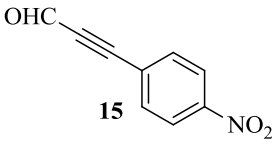
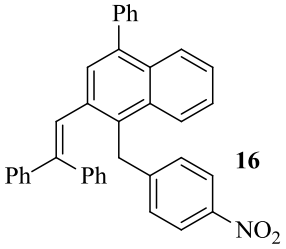
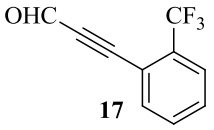
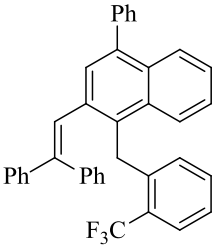
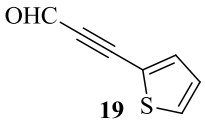
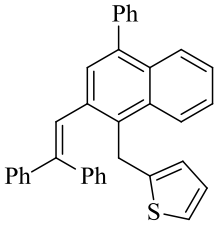
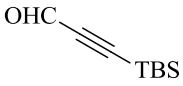
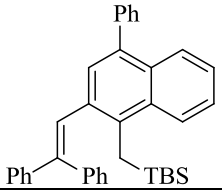
Scheme 4.1

Having established optimal conditions, the generality of the domino [4+2] annulation was explored. Initially, we study the reactivity of **2** with several propargylic aldehydes in construction of different substituted naphthalenes and results are summarized in **Table 4.1**.

Table 4.1: Reaction of **2** with propargylic aldehydes

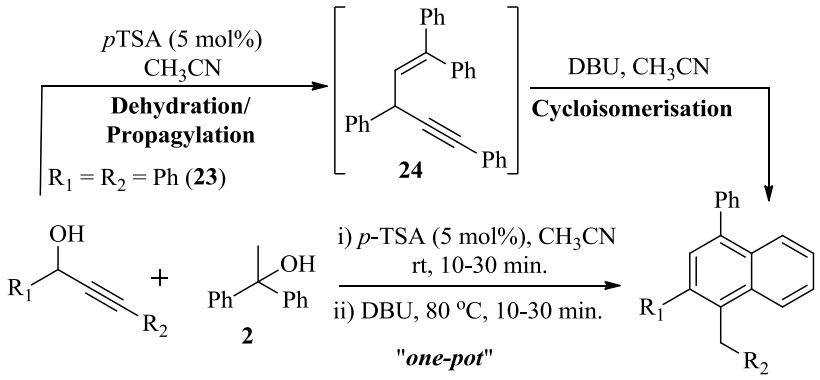


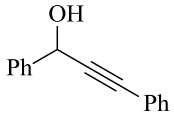
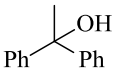
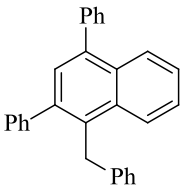
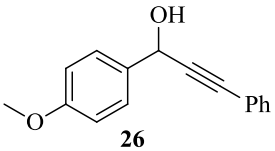
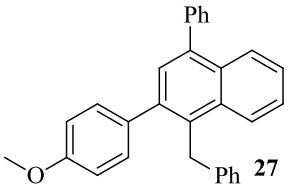
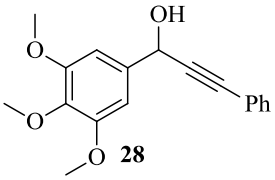
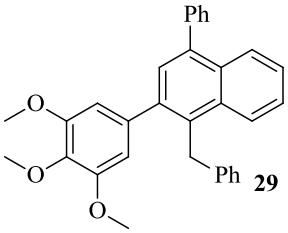
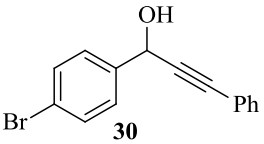
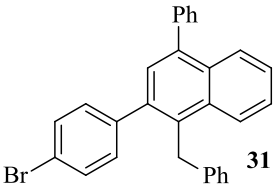
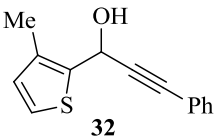
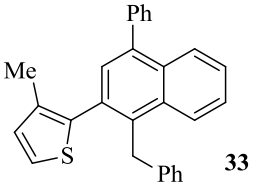
S.No	1,1-diphenyl ethan-2-ol	propargyl aldehyde	Time (min)	Product	Yield (%)
1	 **2**	 **1**	120/10	 **6**	85
2	**2**	 **7**	150/20	 **8**	83
3	**2**	 **9**	120/10	 **10**	88
4	**2**	 **11**	150/20	 **12**	82
5	**2**	 **13**	90/15	 **14**	92

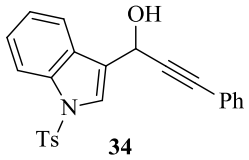
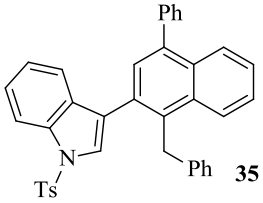
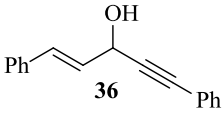
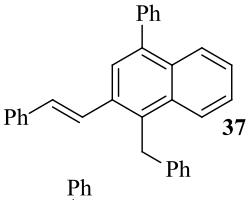
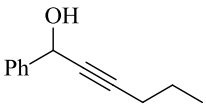
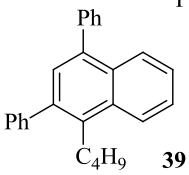
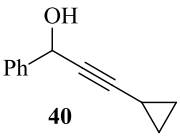
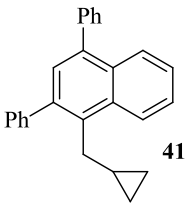
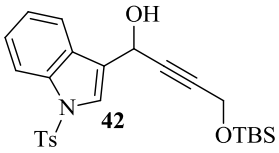
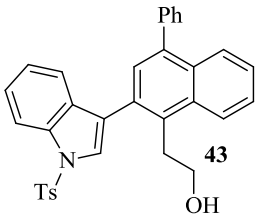
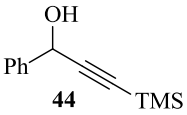
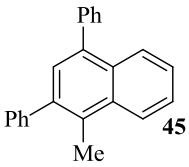
6	**2**	 **15**	120/10	 **16**	95
7	**2**	 **17**	120/10	 **18**	95
8	**2**	 **19**	120/10	 **20**	95
9	**2**	 **21**	120/10	 **22**	95

As the formation of intermediate **5** from propargylic aldehyde is assumed through the nucleophilic substitution of propargylic alcohol **4** with insitu generated nucleophile **3**, we next tested the possibility of propargylic alcohols as an alternative reaction partners in the place of propargylic aldehydes. Initially, 1,1-diphenylethanol (**2**) was reacted with propargylic alcohol **23** under the optimal reaction conditions. To our delight, reaction was proceeded smoothly in one pot to offer the naphthalene **25** in 89% yield *via* the enyne **24**, which was isolated and fully characterized. In this case both reactions (dehydration/ propargylation) were proceeded at room temperature, while the cycloisomerization required 80 ^{o}C for faster reaction (at room temperature the reaction time was more than 8 h). Then, we explored the reactivity of propargylic alcohols with 1,1-diphenylethanol (**2**) was investigated and synthesized various substituted naphthalenes in good yields. The results are showed in **Table 4.2**.

Table 4.2: Scope of propargylic alcohols in [4+2]-benzannulation with **2**

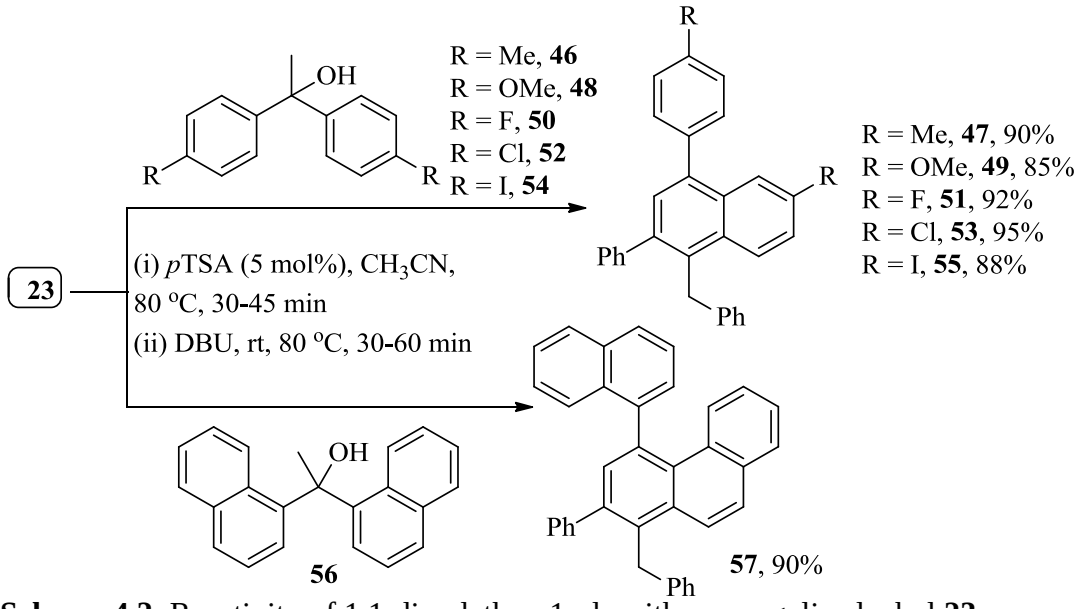


S.No	propargyl alcohol	1,1-diphenyl ethan-2-ol	Time (min)	Product	Yield (%)
1	 **23**	 **2**	10/30	 **25**	89
2	 **26**	**2**	15/30	 **27**	90
3	 **28**	**2**	10/30	 **29**	90
4	 **30**	**2**	10/30	 **31**	92
5	 **32**	**2**	30/60	 **33**	89

6	 **34**	**2**	10/30	 **35**	90
7	 **36**	**2**	10/30	 **37**	85
8	 **38**	**2**	15/30	 **39**	88
9	 **40**	**2**	10/30	 **41**	88
10	 **42**	**2**	15/30	 **43**	90
11	 **44**	**2**	10/30	 **45**	83

Next, our study was designed for the 1,1-diarylethan-1-ols **2** in the present [4+2] benzannulation reaction. These substrates having both of the electron- donating (*p*-Me, *p*-OMe) as well as electron-withdrawing (*p*-F, *p*-Cl, *p*-I) substitution, were compatible for the developed method in providing the corresponding naphthalenes.

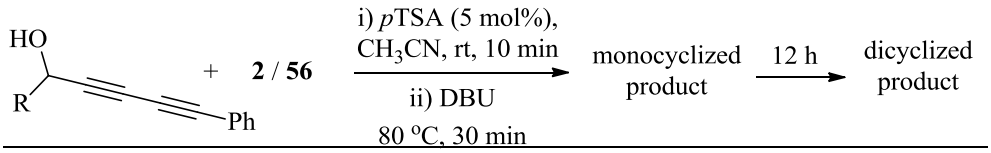
Also, 1,1-di(naphthalene-1-yl)ethan-1-ol (**56**) was reacted with **23** and gave the substituted phenanthrene **57** in 87% yield.

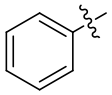
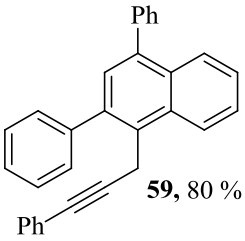
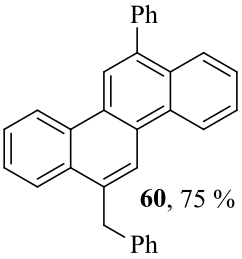
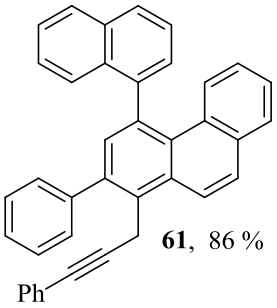
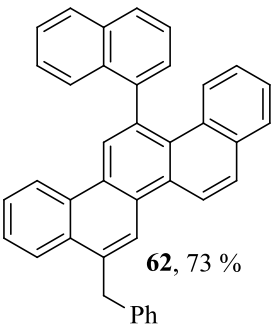


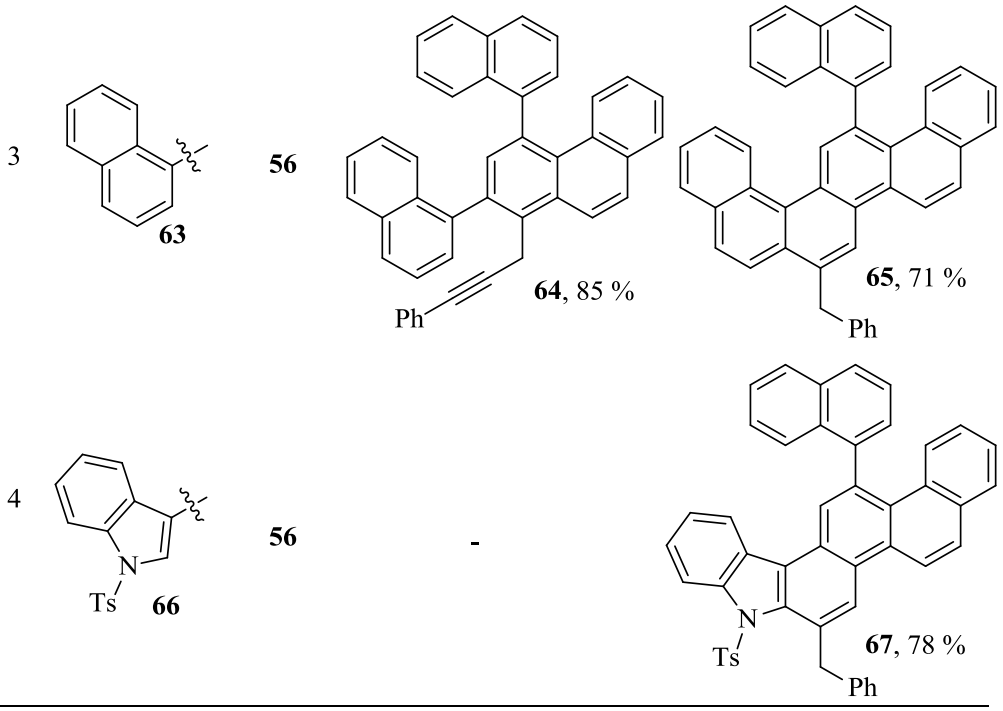
Scheme 4.2: Reactivity of 1,1-diarylethan-1-ols with propargylic alcohol **23**

Further, we extended this domino process towards the synthesis of polycyclic aromatic hydrocarbons such as chrysene, picene and benzopicene. 1,1-diarylethan-1-ols with 2,4-diyn-1-ols in this domino reaction conditions involved 4 steps (dehydration and propargylation followed double cycloisomerization) in one pot to construct the higher-membered aromatic hydrocarbons.

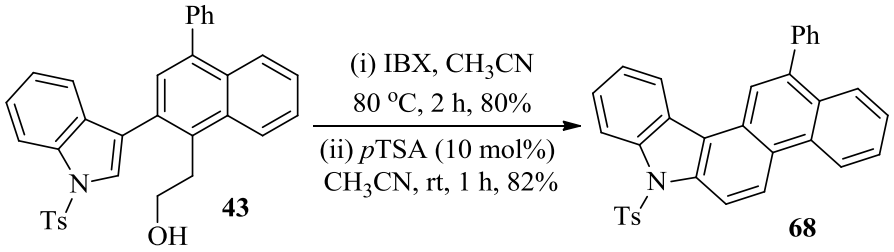
Table 4.3. Synthesis of PAHs *via* double cycloisomerization (di-benzannulation)



entry	R	3°-alcohol	monocyclized product	dicyclized product
1	 **58**	**2**	 **59,** 80 %	 **60**, 75 %
2	**58**	**56**	 **61**, 86 %	 **62**, 73 %



In addition, naphthalene **43** was conveniently utilized for the synthesis of 13-phenyl-7-tosyl-7*H*-naphtho[1,2-*c*]carbazoles **68** in 82% yield through IBX oxidation and *p*TSA mediated cyclization (**Scheme 4.3**).



Scheme 4.3. Conversion of **43** to naphtho[1,2-*c*] carbazole **68**

In conclusion, a simple and metal-free novel domino reaction was developed for the synthesis of diverse aromatic hydrocarbons from readily accessible propargylic aldehydes/alcohols and diaryl ethanols. This domino [4+2]-benzannulation involves an uninterrupted sequence of dehydration/addition-substitution (propargylic aldehydes) or nucleophilic substitution (propargylic alcohols)/cycloisomerization. This method is useful for the rapid construction of various polycyclic aromatic hydrocarbons such as chrysene, picene, benzopicene and phenanthrocarbazole through the dibenzannulation reaction.