

Chapter I

Part A: Introduction and development of benzannulation chemistry

1.1. Introduction to benzannulation reactions

Aromatic hydrocarbons constitute important building blocks in organic synthesis due to their extra stability, abundance and their ready reactivity in substitution reactions in comparison with non-aromatic hydrocarbons. The concept of aromaticity is important in order to understand the stability, bonding, structure, reaction and properties of conjugated cyclic molecules. Benzene is the quintessential aromatic hydrocarbon and can be transformed into various other aromatic hydrocarbons. Numerous electrophilic and nucleophilic aromatic substitutions reactions on phenyl ring form a significant chunk in organic chemistry literature. Due to their special properties, aromatic compounds find a variety of applications.^{1,2} As a consequences, a number of synthetic methods have been developed for construction of aromatic compounds and organic chemists continue to develop new strategies for their synthesis.

Substituted arenes are generally prepared from aromatic precursors *via* introduction of substituents on aromatic ring or by manipulating pre-installed functional groups. The pre-installed group alters the reactivity pattern of arene core and occasionally prevents the formation of desired regioisomers when syntheses of di-, tri- and tetra-substituted arenes are attempted. To overcome these issues alternate approaches for synthesis of poly-substituted arenes such as transition metal mediated coupling reactions³ and directed metallation reactions⁴ have been developed.

Benzannulation, a nonconventional approach, wherein arenes are constructed from acyclic precursors, addresses above mentioned challenges significantly. In benzannulation

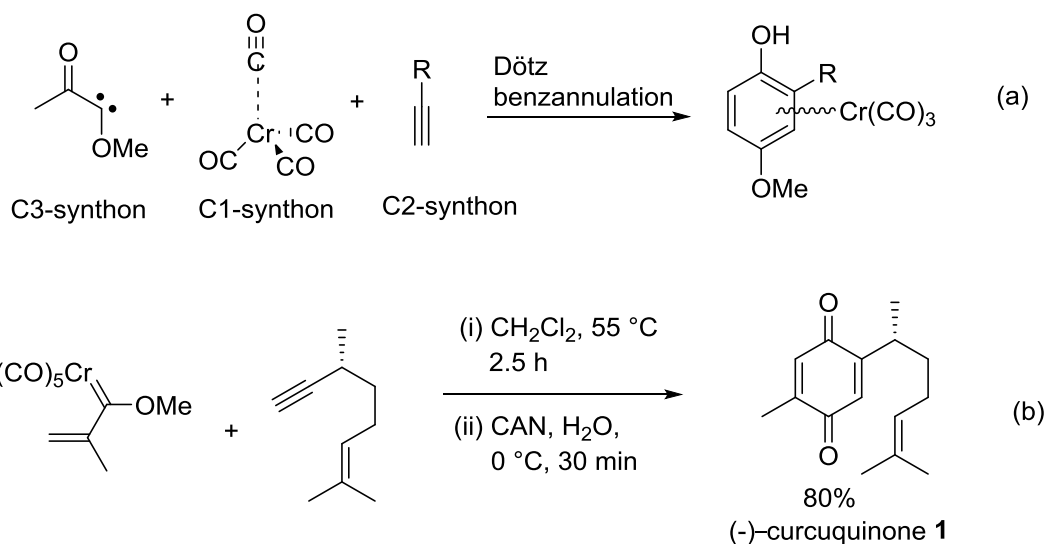
reactions a variety of acyclic components can be combined in various ways to afford a benzenoid aromatic product. These reactions can be either intramolecular (one-component) or intermolecular (two- or multi-component) in nature. The acyclic components can be of various sizes, nature and their union may be catalyzed or mediated by various catalysts, acid, base, light or metal complexes. Dotz reaction⁵ and Danheiser annulation⁶ are important and well known transformations which demonstrate the strength of benzannulation approach in synthesis. The availability of a diverse array of acyclic precursors, reaction conditions and different mechanistic types makes benzannulation strategy superior to aromatic substitution reactions for construction of substituted arenes.

The most general and common classification of benzannulation reactions is based on the number of carbon atoms contributed by each acyclic component to the final product. Accordingly, benzannulation reactions are categorized as [2+2+2], [3+2], [4+2], [5+1], [3+3], *etc* types. In addition, they can also be classified based on the mechanistic or type of reaction involved. Some of such categories include, cycloaddition, ring-closing metathesis, base mediated, Lewis acid catalyzed, light induced, transition-metal promoted, electrocyclic ring closure, *etc*. The work presented in the first two chapters of this thesis focuses on benzannulation reactions. Therefore, for presenting the work in proper context, a discussion on various benzannulation reactions is given below.

1.2. Various types of benzannulation reactions

1.2.1. Transition metal-mediated benzannulation reactions

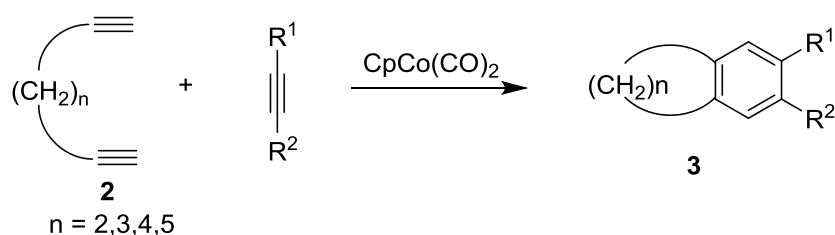
Dötz benzannulation is one of the most widely used transition metal-mediated benzannulation reaction for the construction of substituted arene derivatives.⁵



Scheme 1: (a) Schematic representation of Dötz benzannulation reaction (b) synthesis of (-)-curcuquinone via Dötz benzannulation reaction

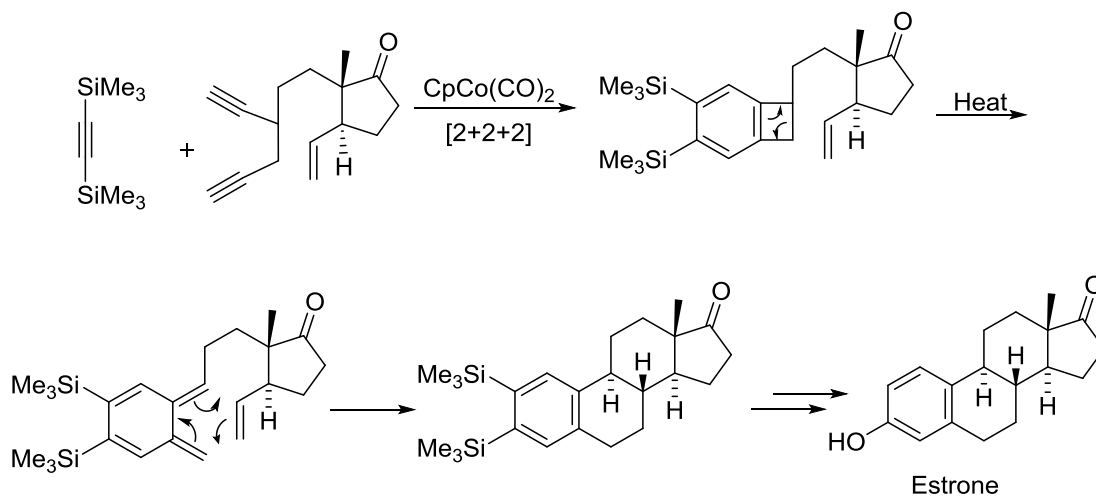
The reaction may be viewed as a [3+2+1] cycloaddition reaction which involves α,β -unsaturated Fischer carbene ligand, an alkyne and a carbon monoxide ligand on chromium (Scheme 1a). Dötz benzannulation reaction has found numerous applications in synthesis. For example, Dötz and co-workers reported a total synthesis of natural product (-)-curcuquinone **1** via chromium-mediated regioselective [3+2+1] benzannulation reaction (Scheme 1b).⁷

Vollhardt and co-workers found that cobalt complex $\text{CpCo}(\text{CO})_2$ have ability to catalyze [2+2+2] cyclisation of α,ω -diynes such as **2** and alkynes to generate benzene derivatives **3** (Scheme 2).



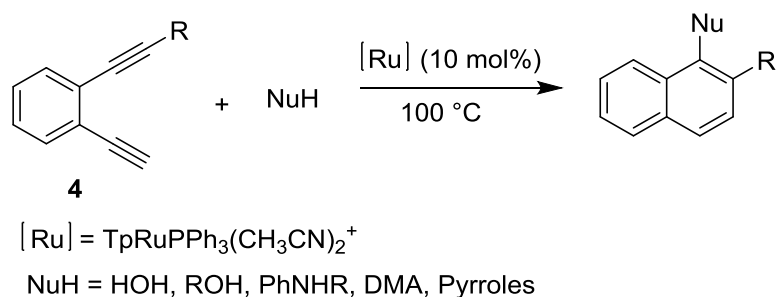
Scheme 2: Co-catalyzed cross-trimerisation of diyne with alkyne

This [2+2+2] cycloaddition reaction has wide scope and has been employed in synthesis of various natural products such as Estrone, as depicted in Scheme 3.⁸



Scheme 3: $\text{CpCo}(\text{CO})_2$ -catalysed steroid synthesis via [2+2+2] benzannulation

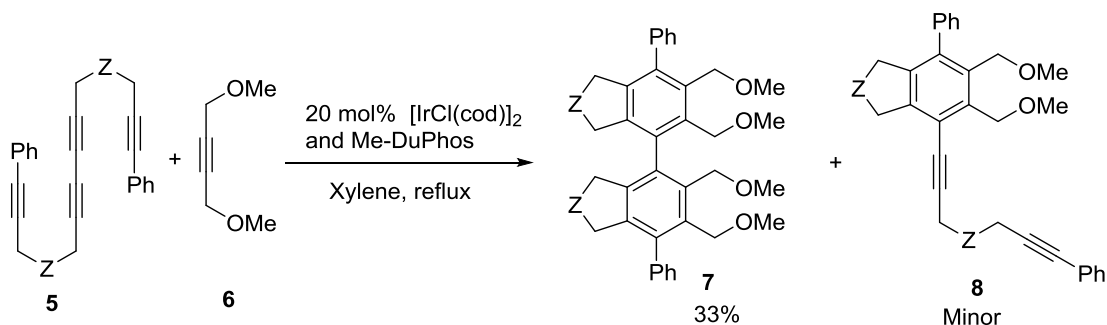
An efficient Ru-catalyzed cyclisation of enediyne system **4** with various nucleophiles affords naphthalene derivatives (Scheme 4). The reaction proceeds *via* regioselective addition of nucleophiles to the Ru-alkyne π -complex. The addition occurs regioselectively at the internal carbon of alkyne.⁹



Scheme 4: Ru-catalyzed regioselective aromatization of enediynes with nucleophiles

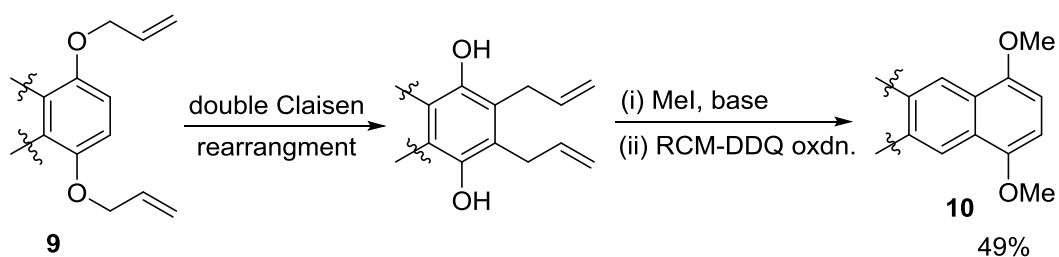
An enantioselective [2+2+2] cycloaddition reaction of carbon tethered tetrayene **5** and alkyne **6** catalyzed by a chiral iridium complex afforded axially chiral compound **7**

along with a mono-cyclized product **8** (Scheme 5).¹⁰ The catalytically active species is generated *in situ* from $[\text{IrCl}(\text{cod})]_2$ and the chiral ligand Me-DuPhos.



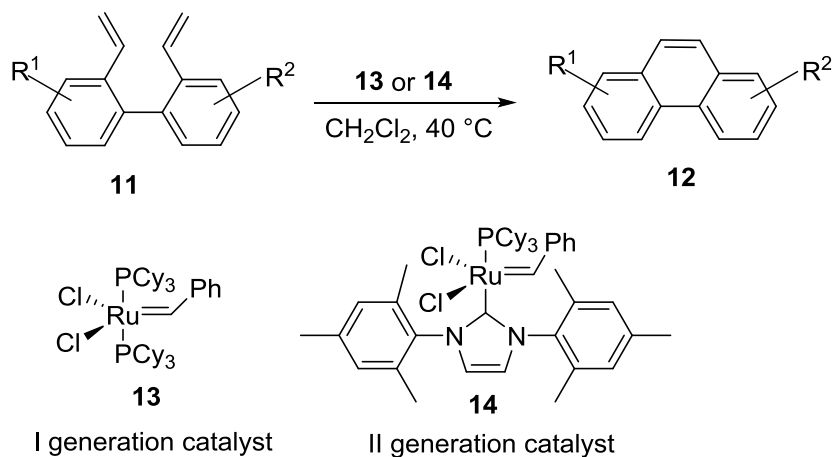
Scheme 5: Iridium-catalyzed [2+2+2] cycloaddition reaction

Ring-closing metathesis (RCM) constitutes a powerful tool for construction of carbocycles. The pioneering efforts of Grubbs, Hoveyda and Schrock, have led to the development of a wide variety of metathesis catalysts for promoting olefin metathesis of challenging substrates.¹¹ These reactions can be conveniently employed for the construction of aromatic carbocycles from suitable acyclic precursors such as terminal dienes. Kotha and co-workers have developed a methodology for the construction of hydroquinone derivative **10** from bis-allyl aryl ethers **9** *via* sequential double Claisen rearrangement, one pot RCM and DDQ oxidation as depicted in scheme 6.¹²



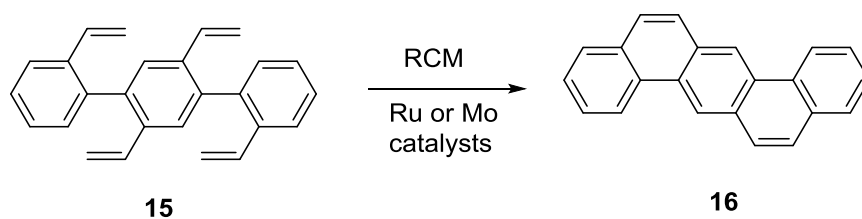
Scheme 6: Double Claisen rearrangement-RCM-oxidation sequence of bis-allyl phenyl ether

First and second generation ruthenium catalysts **13** and **14** promoted ring-closing metathesis of 2,2'-divinylbiphenyls **11** to afford substituted phenanthrenes **12** (Scheme 7). The reaction proceeds under very mild conditions and can tolerate a number of functional groups present on the biphenyl moiety.¹³



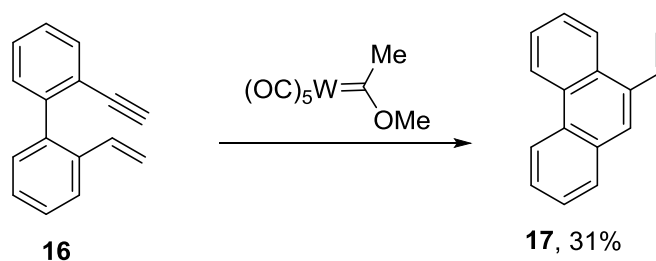
Scheme 7: RCM of 2,2'-divinylbiphenyls to generate phenanthrene derivatives

King and co-workers have developed a methodology for construction of polycyclic aromatic hydrocarbons (PAHs) *via* double ring closing metathesis of pendant olefins on a phenylene backbone. The ring closing metathesis of vinyl-substituted terphenyl derivatives **15** in presence of Grubbs I catalyst afforded dibenzanthracene derivative **16** (Scheme 8).¹⁴



Scheme 8: Synthesis of PAHs by ring closing metathesis of polyenes

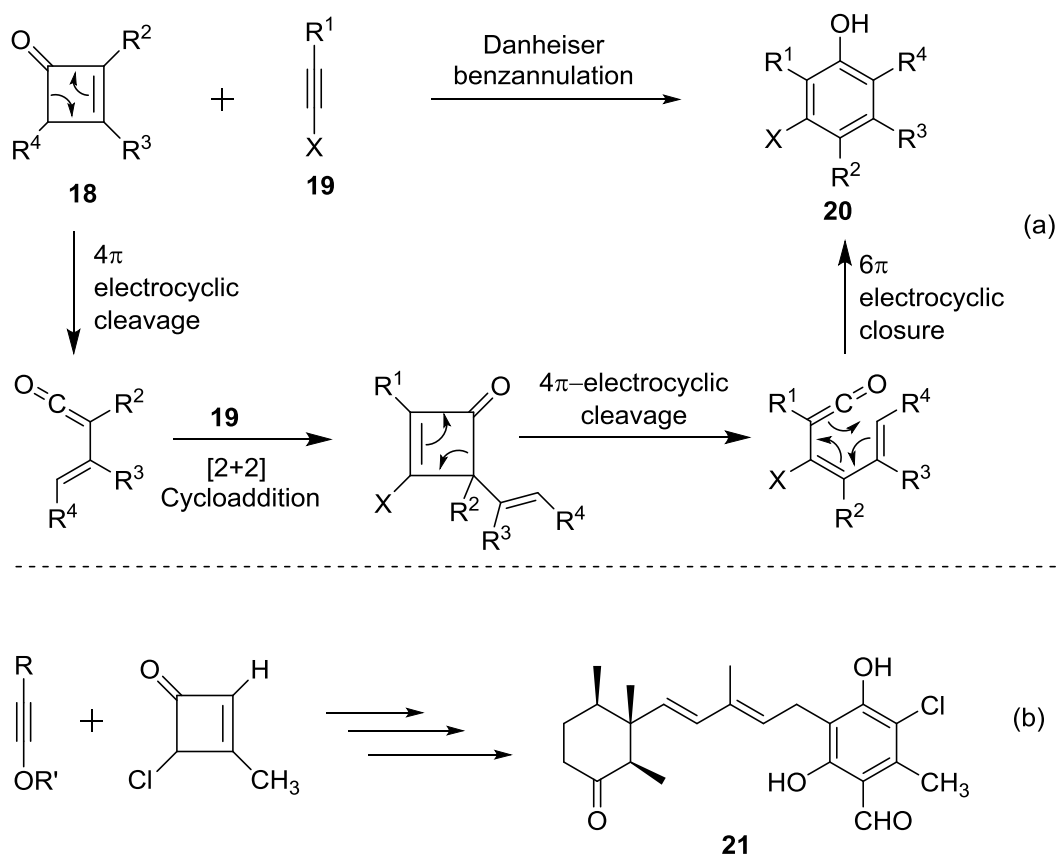
In addition to olefin metathesis, enyne metathesis strategy has also been found useful for synthesis of various aromatic hydrocarbons. In 1985, Katz has developed the first intramolecular enyne ring closing metathesis for construction of construction of 9-vinylphenanthrene **18** from enyne derivative **17** using a Fischer tungsten-carbene complex (Scheme 9).¹⁵



Scheme 9: Synthesis of phenanthrene by enyne ring closing metathesis

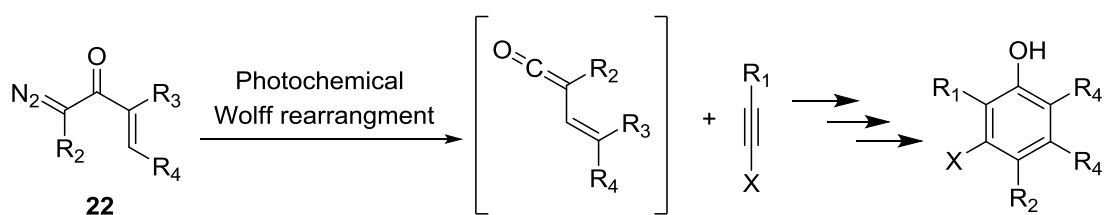
1.2.2. Electrocyclic benzannulation reaction

Danheiser has developed a regiocontrolled annulation wherein cyclobutenones **18** reacted with substituted acetylenes **19** to afford highly substituted phenol derivatives **20**.^{6a} The reaction involves sequential 4π electrocyclic cleavage, $[2+2]$ cycloaddition, 4π electrocyclic cleavage and 4π electron electrocyclic closure reactions as depicted in scheme 10. This reaction has wide applications for example used as key step for total synthesis of (-)-ascochlorin **21** (Scheme 10).¹⁶



Scheme 10: (a) Danheiser benzannulation reaction, (b) Synthesis of (-)-ascochlorin via Danheiser benzannulation

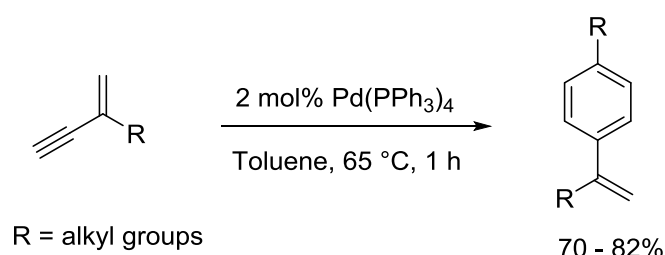
The modified Danheiser reaction involves the annulation of α -diazoketone **22** with acetylene derivatives to generate functionalized polycyclic aromatic and heteroaromatic compounds (Scheme 11).^{6b} The reaction proceeds via photochemical Wolff rearrangement of α -diazoketone **22** to generate a vinyl ketene, followed by cycloaddition and electrocyclic reactions.



Scheme 11: Modified Danheiser benzannulation reaction of α -diazoketone

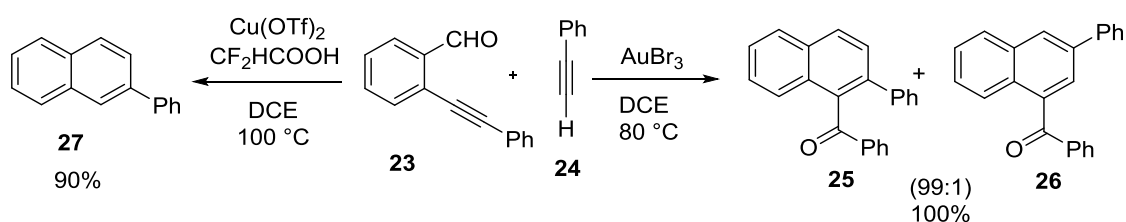
1.2.3. Dienes-Alder type benzannulation reactions

The Dienes-Alder [4+2] cycloaddition of suitably substituted dienes and a dienophiles has been widely used for synthesis of various polycyclic hydrocarbons. Many of the [4+2] cycloadditions are followed by an oxidative aromatization, either as spontaneous aerial oxidation or by the addition of oxidants such as DDQ. Yamamoto and co-workers has reported a palladium catalyzed benzannulation of conjugated enyne systems. The reaction proceeds *via* a [4+2] dimerisation of the enyne to generate 1,4-disubstituted benzenes (Scheme 12).¹⁷



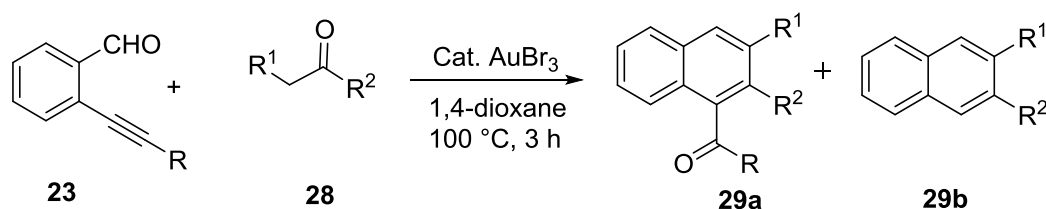
Scheme 12: [4+2] dimerization of conjugated enynes

Lewis acid-promoted [4+2] benzannulation reaction for the construction of polysubstituted aromatic compounds was developed by Asao and Yamamoto. For example, the cycloaddition reaction of *o*-(alkynyl)benzaldehyde **23** with alkyne **24** in presence of AuBr₃ produced naphthyl ketones **25** and **26**. On the other hand, the same pair of reactants combined in the presence of Cu(OTf)₂ and a Brønsted acid to afford a decarbonylated naphthalene derivative **27** (Scheme 13).¹⁸



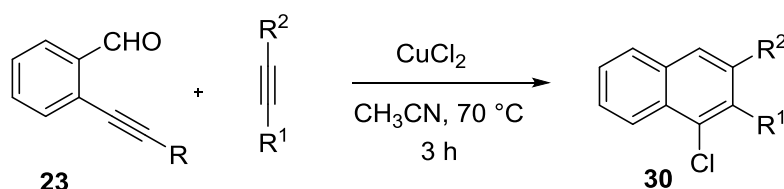
Scheme 13: [4+2] benzannulation of *o*-(alkynyl)benzaldehyde and alkyne

A gold-catalyzed [4+2] benzannulation of *o*-(alkynyl)benzaldehyde **23** and ketone **28** generated naphthalene derivative **29a-b** (Scheme 14).¹⁹ The transformation may be viewed as a Diels-Alder reaction of pyrylium species derived from *o*-(alkynyl)benzaldehyde under gold catalysis and the enol form of **28**.



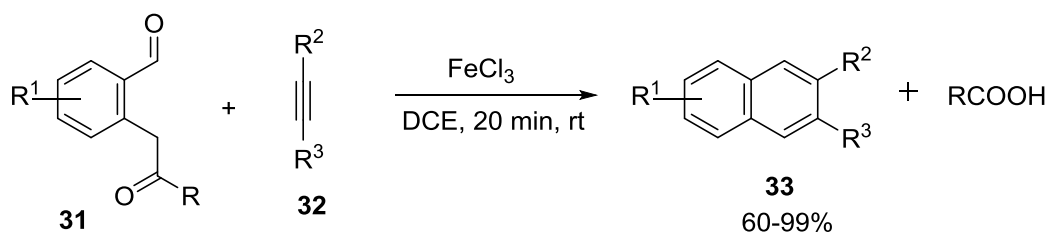
Scheme 14: Gold-catalyzed [4+2] benzannulation of *o*-(alkynyl)benzaldehyde and enol

Asao reported a CuCl₂-promoted [4+2] benzannulation of *o*-(alkynyl)benzaldehyde **23** with alkynes for the stereoselective synthesis naphthyl halides **30** (Scheme 15).²⁰



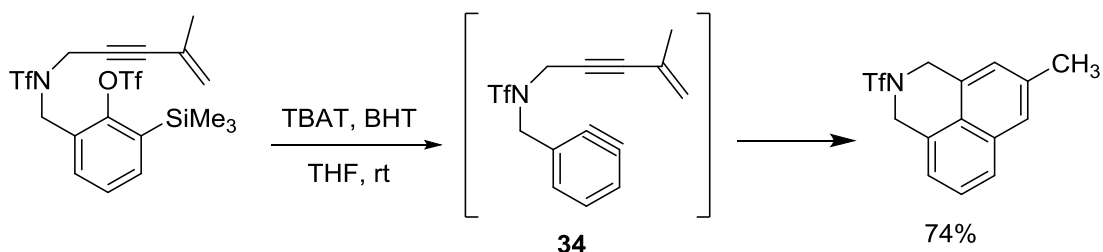
Scheme 15: Cu-catalyzed benzannulation of *o*-(alkynyl)benzaldehyde and alkynes

The iron-catalyzed benzannulation of 2-alkylbenzaldehyde with alkynes is another useful annulation reaction of *o*-substituted benzaldehyde for the synthesis of various aromatic compounds. For example, the reaction of 2-(2-oxoethyl)-benzaldehyde **31** with alkyne **32** in presence of FeCl₃ produced substituted naphthalene derivatives **33** (Scheme 16).²¹



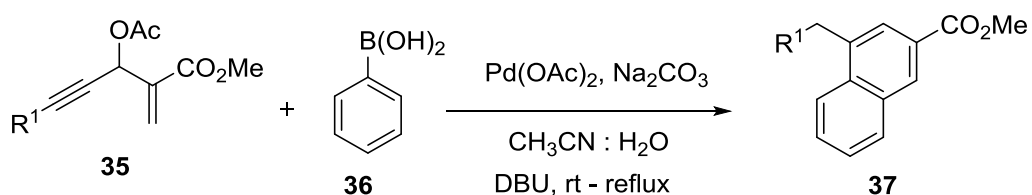
Scheme 16: Iron(III)-catalyzed cyclisation of 2-alkylbenzaldehyde

The intramolecular [4+2] cycloaddition of conjugated enynes with *in situ* generated benzyne furnished highly condensed polycyclic aromatic compounds. The benzyne intermediate **34** was generated *via* TBAT-promoted 1,2-elimination of *o*-(trimethylsilyl)aryl triflate (Scheme 17).²²



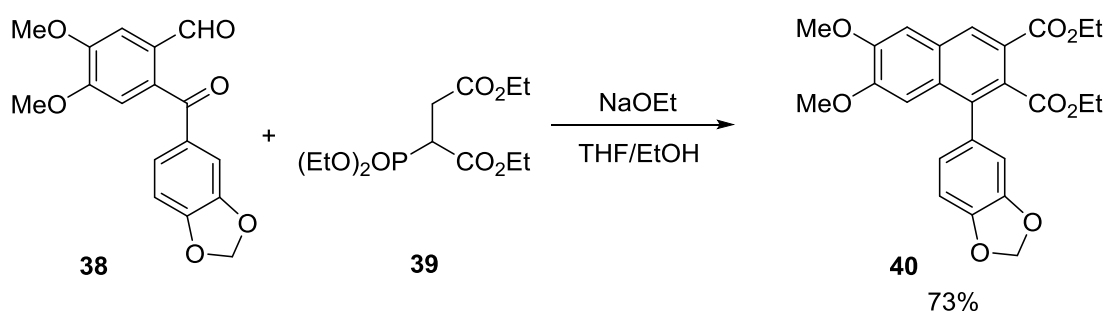
Scheme 17: Intramolecular [4+2] benzannulation of enynes with *in situ* generated benzyne

The reaction of Morita-Baylis-Hillman (MBH) acetate **35** derived from acetylenic aldehydes with boronic acid **36** to afford naphthalene derivative **37** was reported by Reddy and co-workers (Scheme 18).²³ This Pd(OAc)₂ catalysed [4+2] benzannulation proceeds via tandem allylic substitution/hydroarylation cycloisomerisation reactions.



Scheme 18: [4+2] benzannulation of MBH acetate with boronic acids

Base induced annulation reaction of ketoaldehyde **38** and phosphonate **39** was developed by Harrowven and co-workers. The reaction proceeded through sequential Wadsworth-Emmons and Claisen condensation reactions to afford substituted naphthalene derivative **40** that incorporated structural features of HIV-1 reverse transcriptase enzyme inhibiting natural products justicidine B and retrojusticidin B (Scheme 19).²⁴

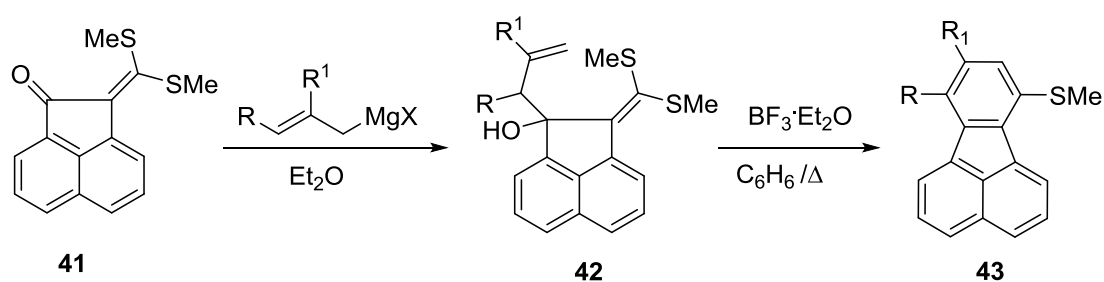


Scheme 19: Cyclisation of ketoaldehyde and phosphonate via Wadsworth-Emmons reaction

1.2.4. [3+3] benzannulation reactions

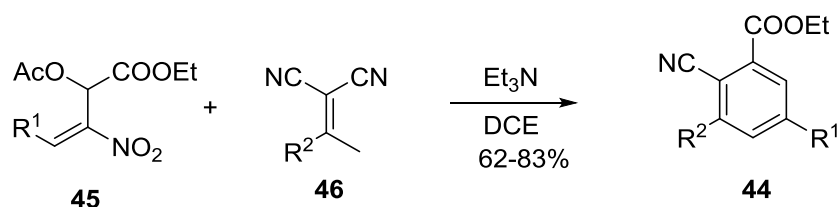
In [3+3] benzannulation approach, the union of two acyclic three-carbon components generates an arene product. The easy availability of a variety of precursors makes this strategy promising for construction of poly-substituted aromatic compounds, provided that the regiochemical challenges are overcome. Generally, [3+3] benzannulation reaction involves sequential nucleophilic attack on electrophilic partner, cyclisation and aromatization through elimination or oxidation.

Junjappa and co-workers have developed an efficient synthesis for the construction of fluoranthene derivatives **43** via a [3+3] benzannulation reaction of carbinol acetal **42**, which was derived by treatment of α -oxoketene dithioacetal **41** with allylic Grignard reagents (Scheme 20).²⁵



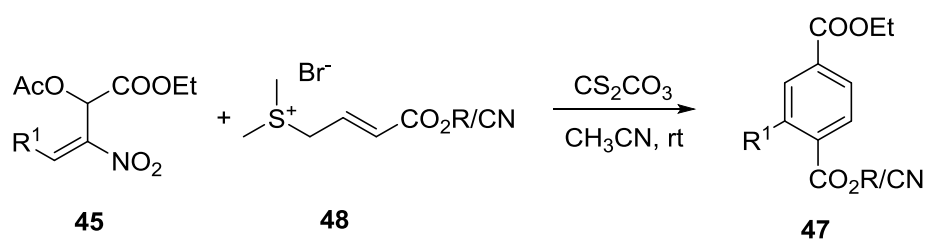
Scheme 20: Synthesis of fluoranthene via [3+3] benzannulation method

One-pot [3+3] benzannulation reaction for synthesis of *m*-terphenyls **44** has been developed by Namboothiri and co-workers. The reaction involves a base promoted regioselective cyclisation of Morita-Baylis-Hillman (MBH) acetates **45** of nitroalkenes and alkylidenemalononitriles **46** to afford a variety of polysubstituted meta-terphenyls **44** (Scheme 21).²⁶



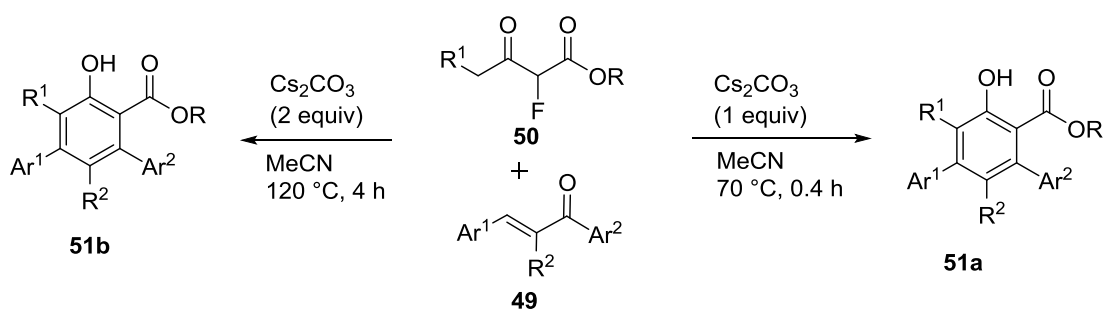
Scheme 21: [3+3] benzannulation for synthesis of *m*-terphenyls

Namboothiri's group also developed another interesting [3+3] benzannulation reaction for the synthesis of 2-aryl terephthalates **47** from MBH acetates **45** and stabilized sulfur ylides **48** (Scheme 22).²⁷ The products 2-aryl terephthalates **47** are useful precursors for the synthesis of many farnesyltransferase inhibitors.



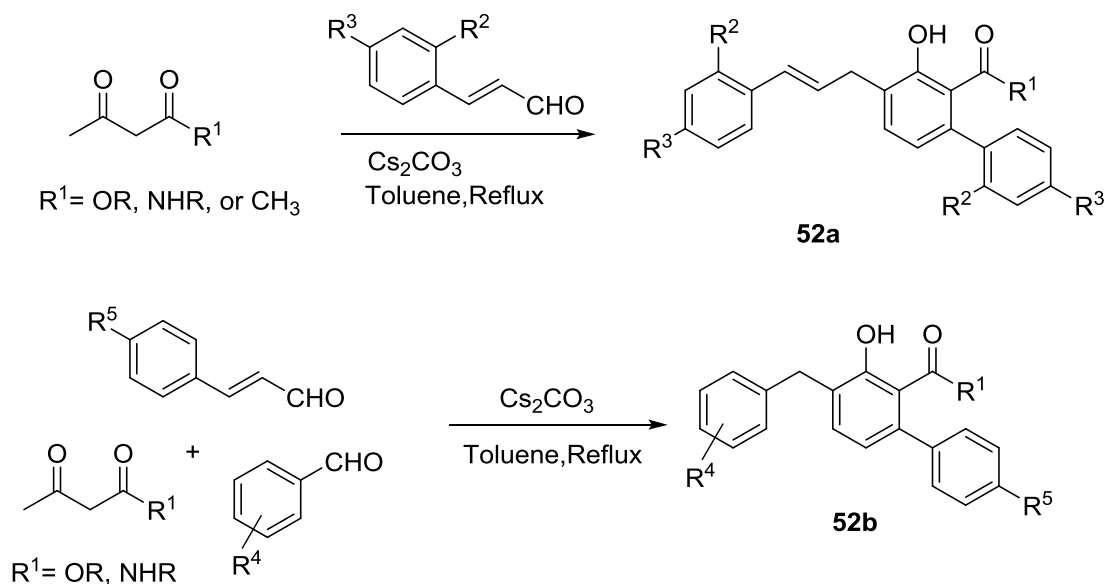
Scheme 22: [3+3] benzannulation for the synthesis of 2-aryl terephthalates

Polysubstituted phenols can be synthesized via the Robinson annulation reaction of α,β -unsaturated ketones **49** with α -fluoro- β -ketoesters **50**. The Robinson annulation is followed by a dehydrofluorination and subsequent tautomerization to afford substituted phenols **51a-b** (Scheme 23).²⁸



Scheme 23: Robinson annulations for synthesis of substituted phenols

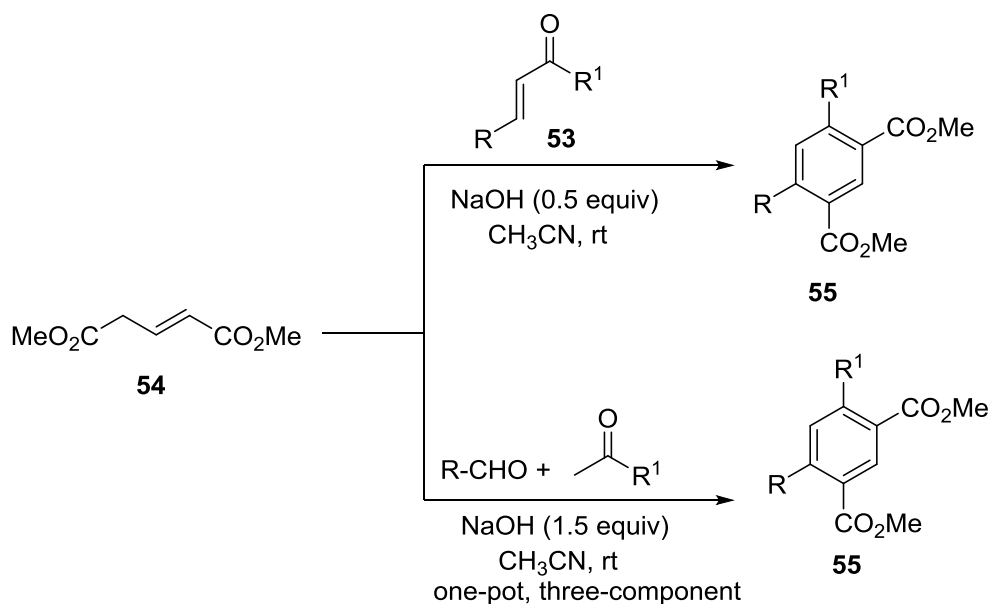
A transition-metal free benzannulation of readily available β -ketoester, β -ketoamides or 1,3-diketones with cinnamaldehyde or aryl aldehydes afforded polyfunctionalised biaryls **52a-b** (Scheme 24).²⁹ This base assisted cascade transformation involves the formation of three new bonds through multicomponent reactions.



Scheme 24: Transition metal free benzannulation reaction for synthesis of biaryl phenols

Zhao and Liu have developed a base-promoted, aerobic oxidative [3+3] benzannulation reaction of α,β -unsaturated carbonyls **53** with dimethylglutaconate **54**. The reaction afforded substituted benzene derivatives **55** in good yields. Furthermore, one-pot aromatization can also be carried out more conveniently through in situ generation of

α,β -unsaturated carbonyl compound from aldehyde and ketone via base-mediated aldol reaction prior to the benzannulation step (Scheme 25).³⁰



Scheme 25: Base mediated [3+3] benzannulation reaction of α,β -unsaturated carbonyls with dimethylglutaconate

1.3. Conclusion

From the above discussion, it is evident that the benzannulation approach is a highly diverse and powerful tool for generation of functionalized arenes. The availability of a variety of reaction components, reaction conditions, scope for catalysis, multitudes of mechanistic types, and possibility of multicomponent protocols are some of the features that make benzannulation reactions a highly useful method for the constructions of substituted arenes. Additionally, a number of benzannulation reactions can be carried out in aqueous reaction medium, in open-flasks and utilizes atmospheric air as an oxidant. The results of our investigations in this area are presented in detail in the following chapters of this thesis.

Part B: Introduction and synthetic applications of allenyl sulfones

1.4. Allenyl sulfones-An introduction

Allenes are cumulated dienes in which two double bonds share a single sp-hybridized carbon atom (Figure 1). The two double bonds of allene molecule are not conjugated and are less stable in comparison to either conjugated or isolated double bonds. Unlike conjugated dienes, allenes are often more reactive and the double bonds in substituted allenes may be differentiated in chemical reactions.

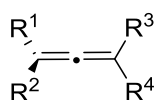


Figure 1: General structure of an allene

Substituted allenes may behave as electron deficient or electron rich entities depending on the nature of substituents. Allenes endowed with one or more electron withdrawing groups are known as electron deficient allenes. Allenates i.e., allenes possessing an ester substituent belongs to a well-studied class of electron deficient allenes and have been used in various addition and cyclisation reactions.³¹ A closely related class of allenes, viz., allenyl sulfones (or sulfonyl allene) constitute another important class of electron deficient allenes. Fuchs in a seminal *Chemical Reviews* article has summarized the unique features of sulfonyl, especially arylsulfonyl group.³² These include (i) tendency of vinyl sulfones to undergo base-catalyzed isomerisation to allyl sulfones (ii) leaving group capacity of sulfinate anions under both acidic and basic conditions (iii) capacity of sulfonyl group to stabilize negative charge adjacent to it. These features of allenyl sulfones influence the reactivity of allenyl framework and make it a unique class of electron deficient allenes. Generally, the addition of nucleophiles to electrophilic allenes

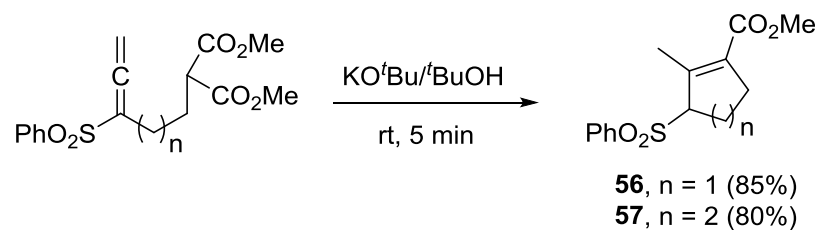
(electron deficient allenes) generates conjugated (vinyl) final products, however, in case of allenyl sulfones the nucleophilic addition proceeds *via* generation of stabilized α -sulfonyl carboanions which on protonation afford allyl sulfones as final products. The unique and highly unusual tendency of arylsulfoyl unit to *de-conjugate* the double bond adjacent to it combined with their leaving group ability make the sulfonyl group a versatile functional group. The work presented in last chapter of this thesis is based on allenyl sulfones. Therefore, for convenience and better understanding of the work, some important aspects of the chemistry of allenyl sulfones are presented below.

1.5. Reactions of allenyl sulfones

The sulfonyl group makes allenyl sulfones electrophilic in nature and majority of reactions involves addition of nucleophiles to the central carbon atom of allene. A number of nucleophiles undergo such conjugate addition reactions. Additionally, allenyl sulfones behave as dienophiles or dipolarophiles and readily engage in various cycloaddition reactions with dienes or dipoles. Other synthetic applications of allenyl sulfones such as electrophilic additions, transition-metal mediated processes and isomerisation reactions are also well investigated. A brief overview of important transformations of allenyl sulfones is presented in the following section.

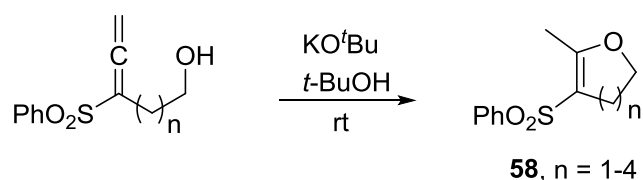
1.5.1. Conjugate addition reactions

Mukai and co-workers developed a method for construction for five- and six-membered carbocycles through endo-mode, Michael addition to allenyl sulfones. The base promoted intramolecular Michael addition of stabilized nucleophile to an allenyl sulfone moiety afforded tri-substituted cyclopentene and cyclohexene derivatives **56** and **57** (Scheme 26).³³



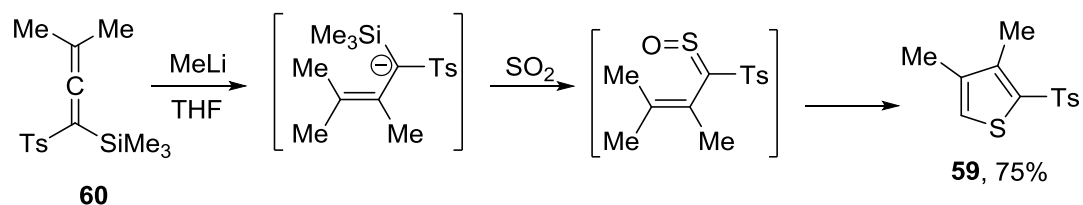
Scheme 26: Intramolecular conjugate addition of nucleophile to allenyl sulfones

Additionally, five to eight membered oxa-heterocycles **58** can also be synthesized via this route (Scheme 27). In presence of base, allenyl sulfones tethered to a terminal primary alcohol group, undergo oxa-Michael cyclisation to generate cyclic enol ethers **58** in high yields.³⁴



Scheme 27: Intramolecular oxa-Michael addition of alcohols to allenyl sulfones

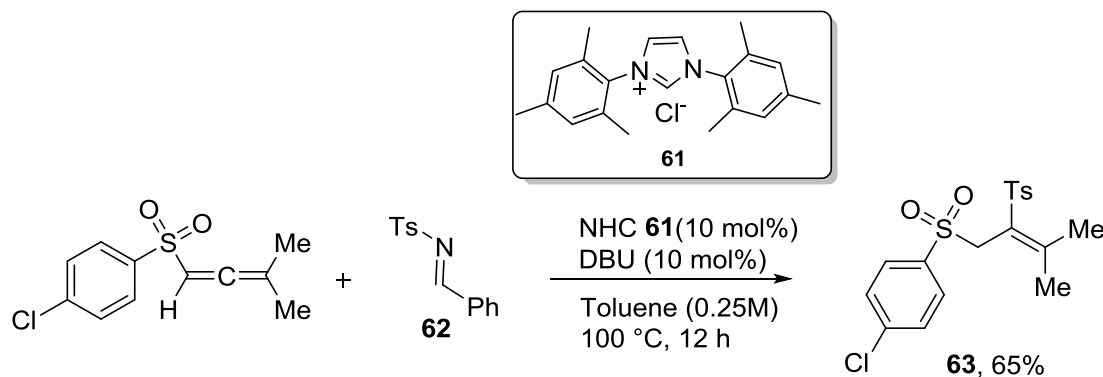
The thiophene derivative **59** can be synthesized from α -silylated allenyl sulfones **60** via a sequential Michael-type addition of an organolithium reagent to allenyl sulfone **60**, generation of α,β -unsaturated sulfine, and cyclisation as depicted in Scheme 28.³⁵



Scheme 28: Synthesis of thiophenes from allenyl sulfones

The N-heterocyclic carbene (NHC) **61** catalyzed reaction of allenyl sulfones with the aldimine derivative **62** in presence of DBU afforded tosylated allylic sulfones **63**

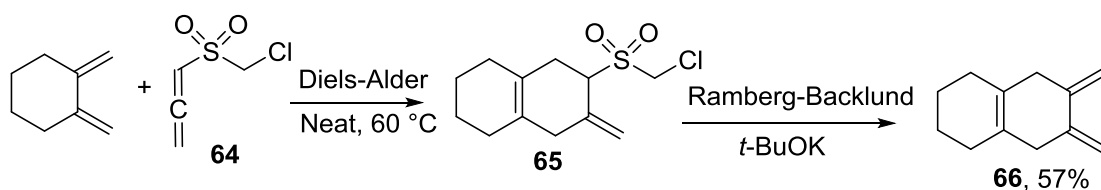
(Scheme 29).³⁶ The tosyl anion, generated from N-tosyl aldimine attacked selectively at the β -position of allenyl sulfones *via* sulfur atom to afford the final product.



Scheme 29: NHC catalyzed synthesis of allylic sulfones from allenyl sulfones

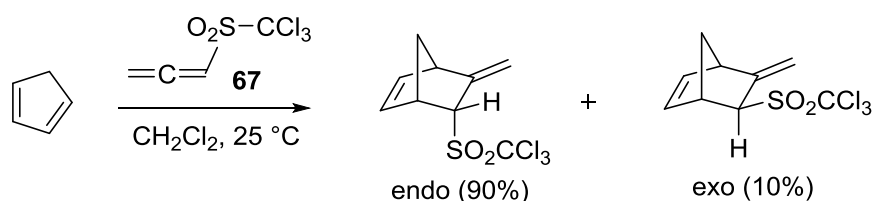
1.5.2. Cycloaddition reactions

Block and Putnam reported the [4+2] cycloaddition reaction of allenyl chloromethyl sulfones **64** with dienes.³⁷ The treatment of initial cycloadduct **65** with base generated a new 1,4-diene moiety **66** *via* Ramberg-Bäcklund rearrangement (Scheme 30). The overall reaction may be considered as a cyclo-homologation of the diene.



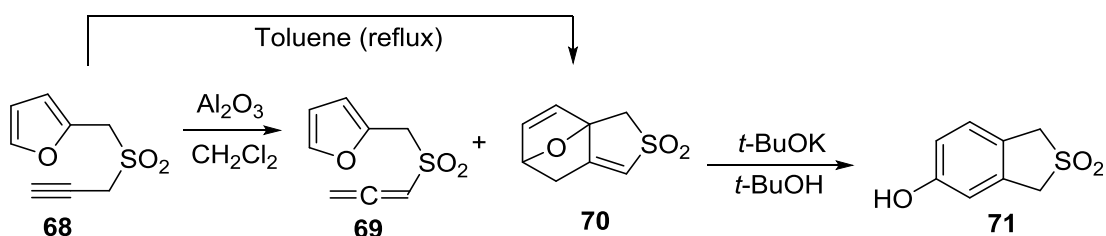
Scheme 30: Cyclo-homologation of diene via Diels-Alder reaction with allenyl sulfone

Diels-Alder reaction of allenyl trichloromethylsulfones **67** and cyclopentadiene were reported by Braverman. The cycloaddition reaction proceeded with good regio- and stereoselectivity (Scheme 31).³⁸ The trichloromethyl group enhanced the reactivity of allene and even less reactive dienes such as furan also underwent the cycloaddition reactions.



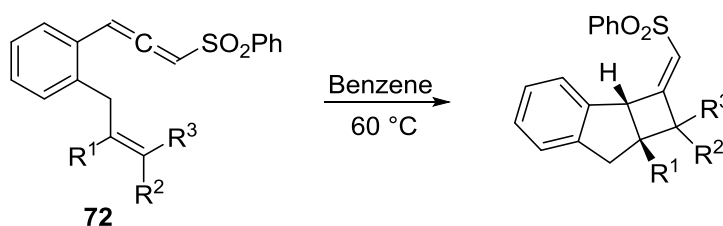
Scheme 31: [4+2] cycloaddition reaction of allenyl trichloromethylsulfones

The reaction of furfural propargyl sulfone **68** with catalytic amount of aluminium oxide produced allenyl furfural sulfone **69** along with cycloadduct **70**. When this mixture was refluxed in toluene, a single cycloadduct **70** was obtained. The cycloadduct **70**, on treatment with base afforded 5-hydroxy benzosulfolene **71** via base-mediated aromatization (Scheme 32).³⁹



Scheme 32: Intramolecular Diels-Alder reaction of allenyl sulfones

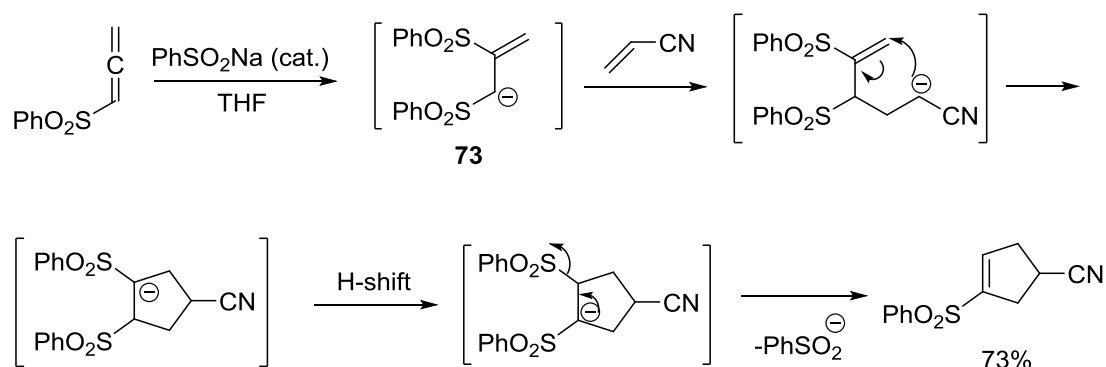
Padwa has extensively investigated the chemistry of allenyl sulfones. A highly regio- and stereospecific intramolecular [2+2] thermal cycloaddition reaction of ene-allenyl sulfones **72** was reported by Padwa. It may be noted that a non-activated double bond of allene participated in cycloaddition reaction (Scheme 33).⁴⁰



Scheme 33: Intramolecular [2+2] cycloaddition reaction of allenyl sulfones

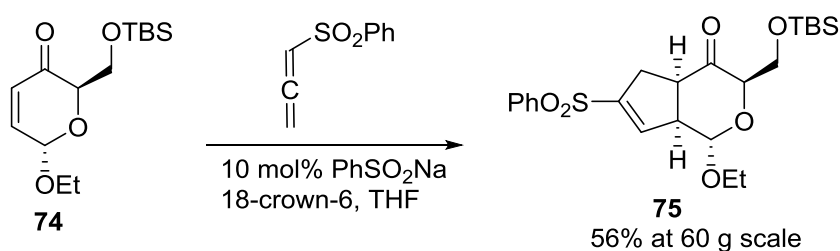
1.5.3. Sulfinate-triggered reactions

In addition to various cycloaddition reactions of allenyl sulfones, sulfinate anion-catalyzed [3+2] cycloaddition reactions of allenyl sulfones were also developed by Padwa.⁴¹ In these reactions allenyl sulfones functioned as three-atom components and sulfinate salts performed the role of catalysts. The reaction is initiated by addition of sulfinate anion to electrophilic carbon of allene to generate an α -sulfonyl carbanionic intermediate **73**, which undergoes cycloaddition reaction with electron deficient 2-atom component. A representative example of such cyclisation is presented in scheme 34.



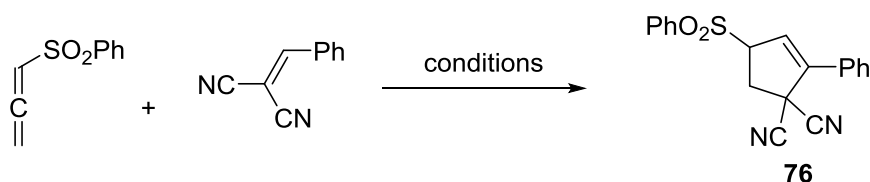
Scheme 34: Padwa anionic [3+2] cycloaddition of allenyl sulfones

Hale reported the total synthesis of (-)-echinosporin, 4-epi-brefeldin A and (+)-brefeldin A via Padwa anionic [3+2] cycloaddition.⁴² The sulfinate catalyzed cyclisation of allenyl sulfone with olefin **74** derived from D-glucal generated the desired bicyclic ketone **75**, which served as a common building block for synthesis of above mentioned natural products (Scheme 35).



Scheme 35: Padwa anionic [3+2] cycloaddition step in the total synthesis of (-)-echinosporin, 4-epi-brefeldin A and (+)-brefeldin A

The extension of this annulations reaction to other electron deficient components such as 1,1-dicyano olefins and other catalyst like NHCs was carried out by Perrio and Kuwano respectively (Scheme 36).^{43,44} Interestingly, these modified annulation reactions afforded allyl sulfones **76**, whereas, vinyl sulfones were formed in Padwa's [3+2] cycloaddition. (see, Scheme 34).

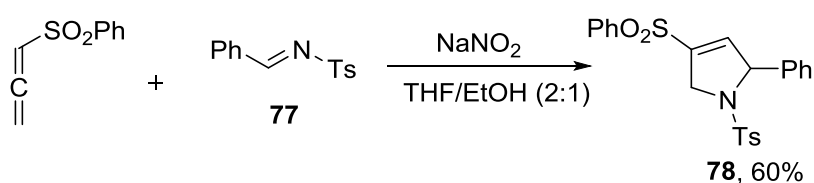


Perrio's method: PhSO₂Na, n-Bu₄NBr (10 mol% each), CH₃CN

Kuwano's method: Triphenyltriazolium salt (NHC precursor), Cs₂CO₃, THF

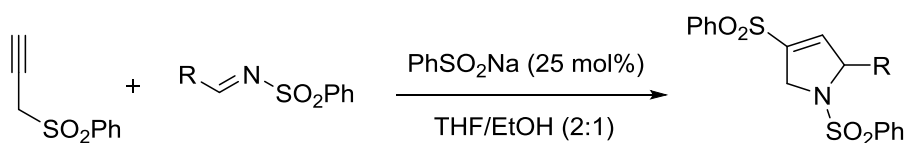
Scheme 36: Modification of Padwa's anionic [3+2] cycloaddition by Perrio and Kuwano

A [3+2] cyclisation reaction of electron deficient N-tosyl imine **77** and allenyl sulfone was developed by Robina (Scheme 37). This sodium nitrite promoted reaction afforded 3-pyrrolines **78**. However, controlled experiment revealed that in situ generated sulfinate anion was involved in the reaction and its addition increased the overall yield of reaction.⁴⁵



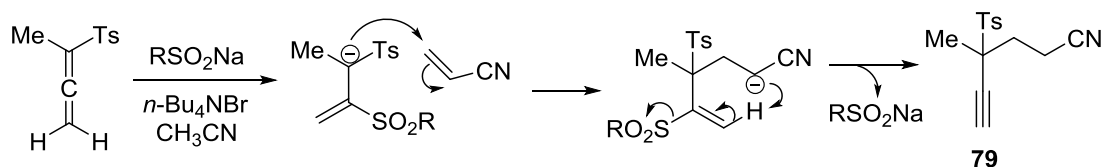
Scheme 37: [3+2] cyclisation of allenyl sulfones with N-tosyl imines

The same class of products can be synthesized from propargyl sulfones. Perrio and co-workers reported that allenyl sulfone was generated from propargyl sulfone *via* sulfinate anion promoted isomerisation (Scheme 39). The ensuing [3+2] cycloaddition proceeded as depicted in Scheme 38.⁴⁶



Scheme 38: Synthesis of 3-pyrrolines from propargyl sulfones

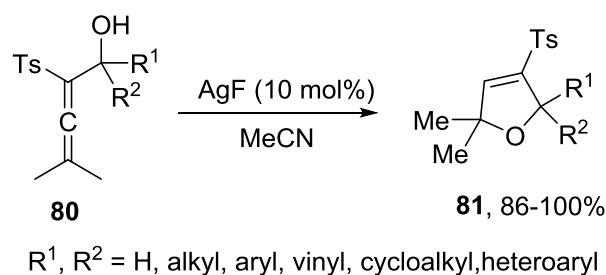
Same group have shown that the umpolung conjugate addition of α -substituted allenyl sulfones to Michael acceptors like acrylonitrile, acrylates and vinyl sulfones could catalyzed by sulfinate salt. In initial steps the process is similar to Padwa's [3+2] cyclisation, however, proton abstraction at later stage afforded alkyne derivatives **79** along with regeneration of sulfinate catalyst (Scheme 39).⁴⁷



Scheme 39: Sulfinate catalyzed umpolung conjugate addition of α -substituted allenyl sulfones

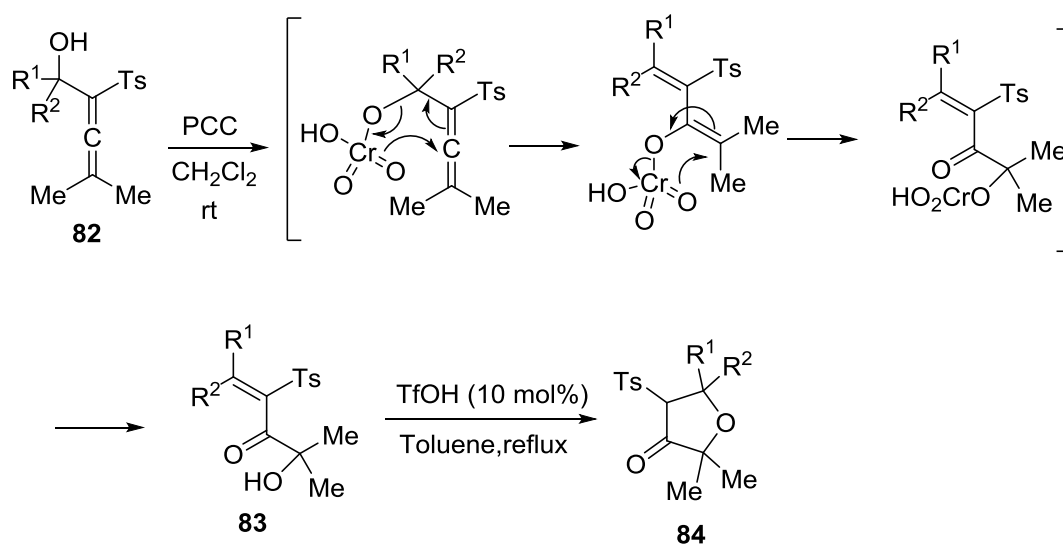
1.5.4. Miscellaneous reactions

Harmata has developed a number of important cyclisation and rearrangement reactions of functionalized allenyl sulfones. A facile Ag(I)-catalyzed 5-*endo*-trig cyclisation reaction of α -hydroxy allenyl sulfones **80** afforded dihydrofuran derivatives **81** (Scheme 40).⁴⁸



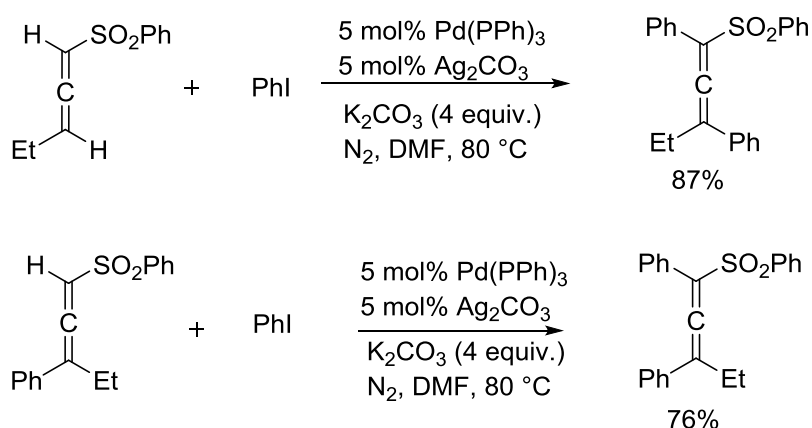
Scheme 40: Ag(I)-catalyzed cyclisation of α -hydroxy allenyl sulfones

A Cr(VI) triggered rearrangement reaction of sulfonyl allenols **82** was reported by same group in 2014. The reaction proceeded *via* a sequence of sigmatropic shifts to generate α^{\prime} -hydroxydienones **83** in moderate yields.⁴⁹ The acid catalyzed cyclisation of α^{\prime} -hydroxydienones **83** readily converted them into dihydrofuran-3(2H)-ones **84** (Scheme 41).⁵⁰



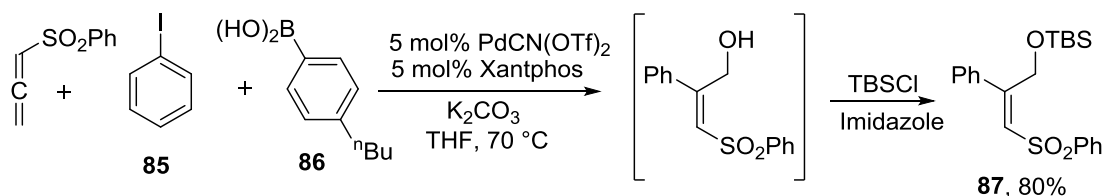
Scheme 41: Cr(VI) promoted rearrangement of sulfonyl allenols and subsequent acid catalyzed cyclisation

Recently, numerous transition metal catalyzed carbon-carbon bond forming reaction of allenyl sulfones have been developed. In 2005, the first Heck-type coupling of allenyl sulfones with aryl halides was reported by Fu and Ma.⁵¹ It was observed only terminal carbons of allenyl sulfones partake in coupling with aryl halides and allenic unit was left intact in the final product (Scheme 42).



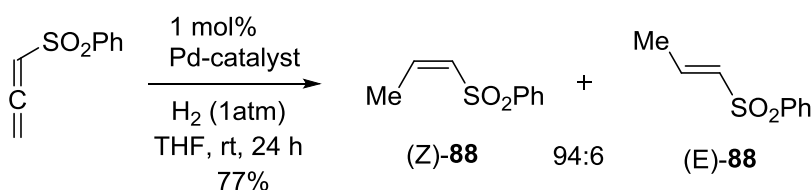
Scheme 42: Heck-type coupling of allenyl sulfones with aryl halides

Pd(0)-catalyzed reaction of allenyl sulfones with aryl iodides **85** and organoboronic acids **86** generated (*Z*)-allylic alcohols **87** in good regio- and stereoselectivity (Scheme 43).⁵² Here, boronic acid **86** acts as a source of hydroxide ion, which can be trapped by the π -allyl palladium complex to form a C-OH bond.



Scheme 43: Pd-catalyzed generation of (*Z*)-allylic alcohols from allenyl sulfones

Regio- and enantio-controlled reduction of conjugated unsaturated bonds is always challenging. The stereoselective palladium-catalyzed semi-hydrogenation of allenyl sulfones was reported to produce vinyl sulfones **88** (Scheme 44).⁵³



Scheme 44: Stereoselective semi-hydrogenation of allenyl sulfones

1.7. References

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