

Summary

The thesis entitled “**Unsaturated sulfones as versatile building blocks for carbocyclic and heterocyclic construction**” is divided into four chapters.

Chapter I

This chapter is divided into two parts *i.e.* Part-A and Part-B.

Part A of chapter I entitled “*Introduction and development of benzannulation chemistry*” provide an overview about the importance and methods of synthesis of substituted aromatic hydrocarbons. Substituted aromatic hydrocarbons find various applications in pharmaceuticals, agrochemicals, materials and synthesis. The transformations of quintessential aromatic hydrocarbon benzene into various other aromatic hydrocarbons and numerous aromatic substitution reactions on phenyl ring form a significant chunk in organic chemistry literature. As a consequence, organic chemists continue to develop new strategies for the construction of substituted aromatic hydrocarbons. Their construction conventionally relies on synthetic methods involving introduction of substituents on aromatic ring or by manipulating pre-installed functional groups. In this approach the control of regiochemistry is a major challenge hence the alternative strategy of *benzannulation*, a nonconventional approach becomes attractive. The various type benzannulation reactions are described in this chapter. In benzannulation reactions the union of simple and cheap acyclic precursors affords substituted arenes. In these reactions a variety of acyclic components are combined in various ways with excellent control of regiochemistry. Of late, this area has been growing continuously due its versatility, convenience, and economical viability.

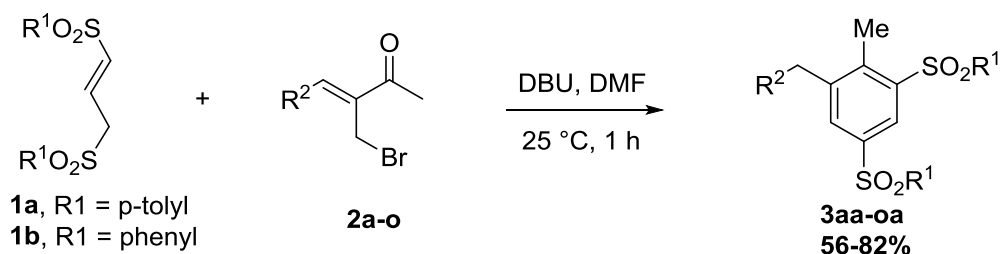
Part B entitled “*Introduction and synthetic applications of allenyl sulfones*” provides an account on electron deficient allenyl sulfones (or sulfonyl allene). The unusual features of sulfonyl, especially arylsulfonyl groups, such as tendency of vinyl sulfones undergo base-catalyzed isomerisation to allyl sulfones, leaving group capacity of sulfinate anions under both acidic and basic conditions influence the reactivity of allenyl framework and make it a special class of electron deficient allenes. Generally, the addition of nucleophiles to electron deficient allenes generates conjugated (vinyl) final products, however, in case of allenyl sulfones the nucleophilic addition afford allyl sulfones as final products. Other than addition of nucleophiles to the central atom of allene, allenyl sulfones also behave as dienophiles or dipolarophiles and readily engage in various cycloaddition reactions with dienes or dipoles. A variety of important transformation of allenyl sulfones are described in this chapter.

Chapter II: Base-mediated [3+3] benzannulation reactions of bis-sulfonyl propenes and Morita-Baylis-Hillman (MBH) bromides for the synthesis of highly substituted arenes

This chapter provides a brief overview about aryl sulfones. The construction of aryl sulfones is an important area of work due to their synthetic utility and favorable properties. The synthetic methods for construction of aryl sulfones are oxidation of aryl sulfides, sulfonylation of arenes and coupling of sulfonates with aryl halides or tosylates. Each of these methods is described in this chapter. The sulfonylation of pre-functionalised arene allows the synthesis of simple aryl sulfones, however, synthesis of more substituted aryl sulfones would be difficult by using these methods. Also, the already present functional group on arene will influence the regiochemistry and reactivity of sulfonylation reaction. *Benzannulation strategy*, in which an acyclic sulfone moiety can be converted

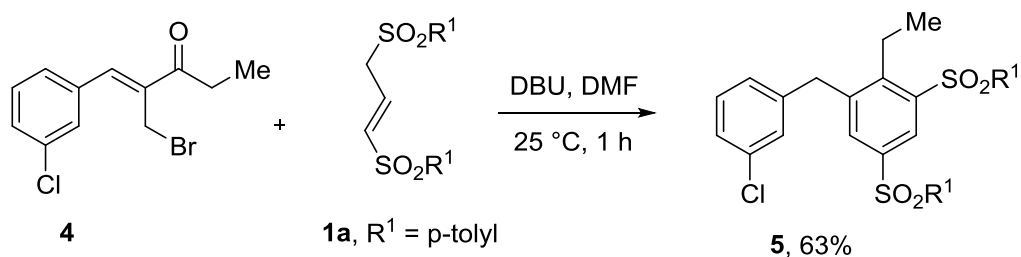
into arene (aryl sulfone) *via* annulation reaction with another suitable precursor, appears highly attractive. A highly substituted aryl sulfone with deactivating groups can be readily synthesized via benzannulation method, still this approach has been applied only rarely and the available examples are presented in this chapter.

The work presented in this chapter describes a [3+3] benzannulation for synthesis of highly substituted aryl sulfones. The building blocks of this benzannulation reaction are bis-sulfonyl propenes **1** and Morita-Baylis-Hillman (MBH) bromides **2** (Scheme 1). The reactions conditions involve the use of DBU as a base and DMF as the solvent. A variety of bis-sulfonyl propenes and MBH bromides afford highly substituted arene products **3**.



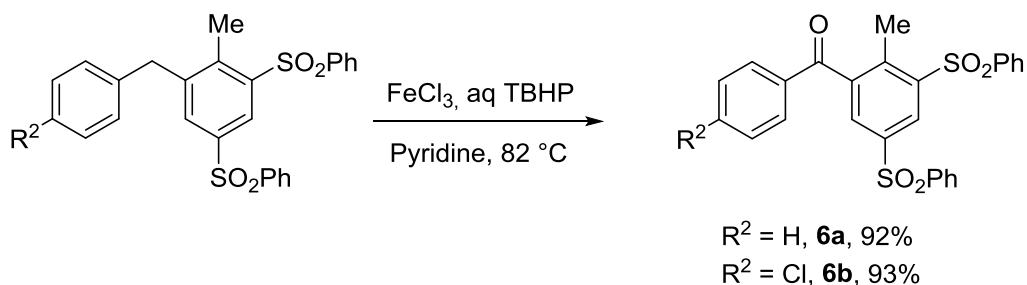
Scheme 1: [3+3] Benzannulation reaction of **1** and **2**

The benzannulation reaction of MBH bromide **4** derived from ethyl vinyl ketone with **1a** under the conditions of benzannulation reaction afforded ethyl-substituted bis-sulfonylarene **5** (Scheme 2).



Scheme 2: Benzannulation reaction with MBH bromide derived from ethyl vinyl ketone

The selective oxidation of methylene group of biarylmethane product by *tert*-butyl hydroperoxide (TBHP) and FeCl₃ afforded corresponding benzophenone derivatives **6** (Scheme 3).



Scheme 3: Site-selective oxidation of biarylmethanes

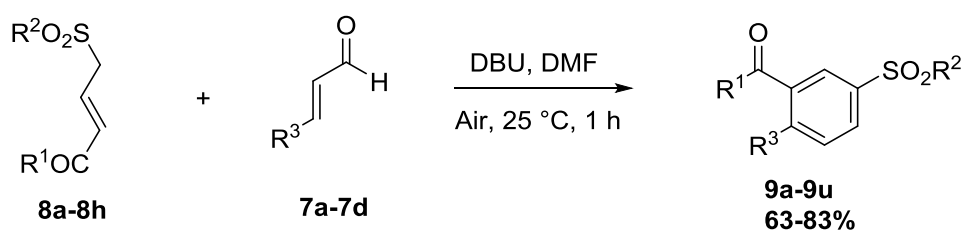
It is important to mention here that all the bis-sulfonylarene products are novel molecules. Also, the bis-sulfonylarene products may assume special importance in view of utility as pincer-type ligands.

Chapter III: Regioselective and oxidative [3+3] benzannulation reactions for the synthesis of highly Substituted benzophenone derivatives

Benzophenone is a privileged structural motif that is present in numerous biologically active natural products and pharmaceuticals. Many benzophenone containing naturally occurring molecules exhibits a wide range of biological activities. Additionally, benzophenone show a significant absorption of ultra-violet (UV) light and represents one of the important classes of compounds in photochemical applications. As a consequence, a number of synthetic methods have been developed for the construction of benzophenones and a brief discussion on the various methods for the synthesis of benzophenone derivatives is provided as an introduction.

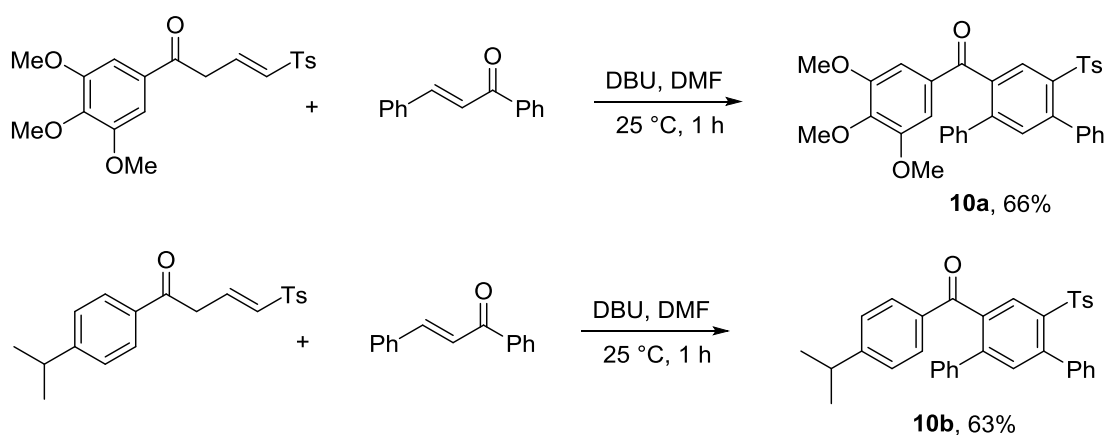
In this chapter, a novel regioselective and oxidative [3+3] benzannulation reaction for the synthesis of substituted benzophenone is described. In view of the successful

development of the [3+3] benzannulation reaction described in the previous chapter and a [3+3] benzannulation reaction of α,β -unsaturated carbonyl compounds with 4-sulfonyl crotonates developed by our group, it was of interest to explore the further application of benzannulation strategy in synthesis of highly substituted arenes. For this purpose we attempted a benzannulation reaction of α,β -unsaturated carbonyl compounds **7** with 1,3-bis-nucleophile **8**. Our investigation along this direction led to the discovery novel regioselective and oxidative [3+3] benzannulation reaction for the synthesis of arylsulfonyl containing benzophenone **9** (Scheme 4).



Scheme 4: [3+3] benzannulation reaction of α,β -unsaturated carbonyl compounds with 1,3-bis-nucleophile **8**

It is important to note that a heterocyclic residue can also be easily incorporated into final product **9** by using the corresponding 1,3-bis-nucleophile. Also, the reaction is not limited to aryl 1,3-bis-nucleophile. The alkyl ketone derivative of **8** reacted smoothly with various enals in the benzannulation reaction to generate the corresponding substituted isobutyl aryl ketones. The structure and regiochemistry of product was assigned on the basis of single crystal X-ray analysis of a crystalline derivative. Further benzannulation reaction of 1,3-bis-nucleophile with enones affords highly substituted benzophenone **10** (Scheme 5). The newly installed benzene ring is endowed with four substituents at well defined positions.

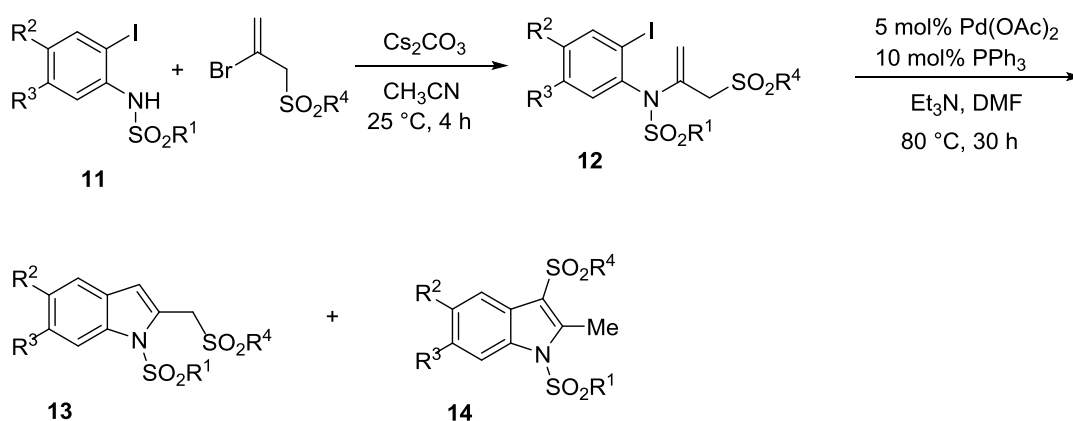


Scheme 5: Benzannulation reaction of trans-chalcone and enals

The regioselectivity is thought to arise from steric interactions that favor the bonding of carbonyl carrying carbon with the β -carbon of enal. The reaction is metal free, utilizes atmospheric oxygen for oxidation and proceeds at room temperature in an open flask, in presence of DBU under mild conditions. The benzannulation reaction described here afforded sulfonyl containing highly substituted benzophenone derivatives which are difficult to synthesize via conventional methods.

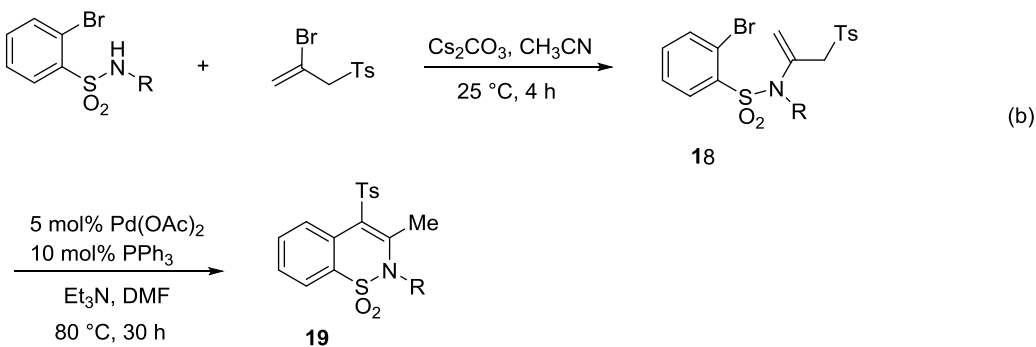
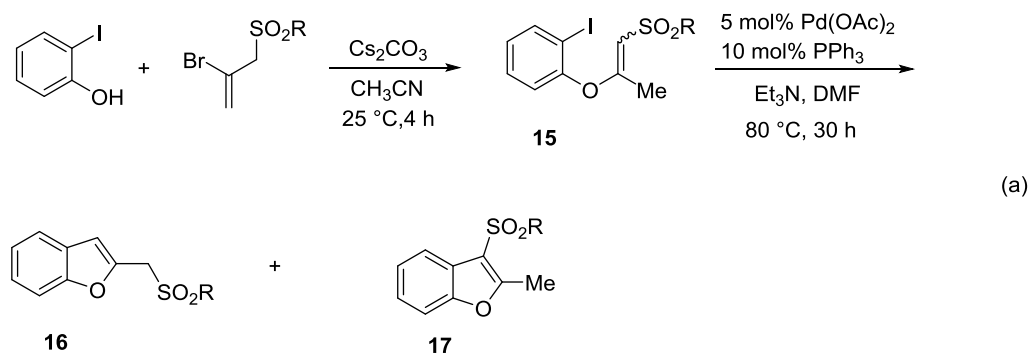
Chapter IV: Facile synthesis of sulfone-bearing indoles and related heterocycles via a sequential formal vinylic substitution and intramolecular Heck coupling reaction

Indole motif form core unit of valuable natural products, drug molecules and agrochemicals. A majority among the numerous naturally occurring indole derivatives exhibit important pharmacological activities. In this chapter a facile synthesis of arylsulfonyl group-bearing indoles is described. The reaction proceeds in two steps. Initially, ortho-halogenated sulfonamides **11** reacted with 2-bromoallyl sulfones in presence of cesium carbonate to furnish products **12** resulting from a formal vinylic substitution reaction. The intramolecular Heck cyclisation of these adducts furnished sulfonylated indoles **13** and **14** (Scheme 6).



Scheme 6: Synthesis and intramolecular Heck cyclisation of N-sulfonyl-N-vinyl-o-iodo sulfonamides **12**

Isomerisation of the double bond participating in the Heck reaction under basic conditions used in reaction led to the formation of two isomeric products of indole. It is important to mention here that conditions for selectively accessing each of the regioisomers were developed and the details are described in this chapter.



Scheme 7: (a) Synthesis of sulfonyl benzofurans **16** and **17** from *o*-iodophenol. (b) Synthesis of benzosultam derivatives **19** via regioselective Heck cyclization

We tested the applicability of this method for construction of other related hetrocycles. Our efforts along this direction led to the formation of benzofurans (Scheme 7a) and benzosultams (Scheme 7b) endowed with arylsulfonyl groups.

Benzosultams derivatives are well-known for their favorable biological activities. The reaction described here shows the synthetic utility of bromoallyl sulfones and afforded sulfonyl containing indoles, benzofurans and benzosultams derivatives.

Conclusion

In this section salient feature of newly developed reactions, their concise description and application are explained. The potential future applications of these methods and product classes are also described.