NOVEL REACTIONS OF TRIS(2-THIENYL)METHANE AND TRIS(2-FURYL)METHANE

THESIS SUBMITTED TO COCHIN UNIVERSITY OF SCIENCE AND TECHNOLOGY IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY UNDER THE FACULTY OF SCIENCE

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CERTIFICATE

This is to certify that the work embodied in the thesis entitled "**Novel Reactions of Tris(2-thienyl)methane and Tris(2-furyl)methane**" has been carried out by **Ms. Siji Thomas** under my supervision at the Organic Chemistry Division of the Regional Research Laboratory (CSIR), Trivandrum, and the same has not been submitted elsewhere for any other degree.

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CONTENTS

Part B

A Brief Introduction to Carbon Centered Radicals

CHAPTER 2

Novel Reactions of Tris(2-thienyl)methane 24-75

CHAPTER 3

Novel Reactions of Tris(2-furyl)methane 76-129

Preface

The history of organic free radicals dates back to Gomberg's monumental discovery of the triphenylmethyl radical in 1900. The heterocyclic analogs of triarylmethane are also interesting from the vantage point of their transformation to the corresponding radicals akin to Gomberg's triphenylmethyl radical and also they are prone to further transformation leading to three dimensionally elongated molecules such as dendrimers. Dendritic architectures are one of the most pervasive topologies observed in nature at the macro- and microdimensional length devices. Because of their ability to combine both organic and inorganic compounds and their propensity to either encapsulate or be engineered into unimolecular functional devices, dendrimers are versatile amongst existing nanoscale building blocks and materials.

A systematic investigation of the reactivity and functionalization of two heterocyclic analogs of triphenylmethane, namely tris(2-thienyl)methane and tris(2-furyl)methane have been carried out and the results are presented in this thesis entitled "NOVEL REACTIONS OF TRIS(2-THIENYL)METHANE AND TRIS(2-FURYL)METHANE."

The thesis is divided into three chapters. Relevant references are given at the end of each chapter.

A general introduction to dendrimers is presented in the first part of chapter 1 while the second part gives a brief indroduction on carbon centered radicals, giving special emphasis on Gomberg's triphenylmethyl radical. Definitions of the present research problems are also incorporated at the end of each section in chapter 1.

The second chapter deals with the reactions of tris(2-thienyl)methane. A brief description of the literature on tris(2-thienyl)methane is given at the beginning of the chapter. Results of the detailed investigation on the reactivity of tris(2-thienyl)methane and the preliminary results of our efforts towards the

synthesis of dendrimers based on this molecule are also presented in the second chapter.

The results of our investigation on tris(2-furyl)methane is disclosed in the third chapter. A brief account of the general reactions of furan is given as a prelude to this chapter. The reactivity of tris(2-furyl)methane towards various electrophilic reagents and the serendipitous synthesis of the furyl analog of Gomberg's hydrocarbon form the content of Chapter 3.

A summary of the work is given towards the end of the thesis.

ABBREVIATIONS

Ac	: acetyl
AIBN	: azobisisobutyronitrile
COSY	: correlation spectroscopy
bs	: broad singlet
d	: doublet
dd	: doublet of doublet
dba	: dibenzylidene acetone
DCE	: dichloroethane
DCM	: dichloromethane
DDQ	: 2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DMAD	: dimethyl acetylenedicarboxylate
DME	: 1,2-dimethoxyethane
DMF	: dimethyl formamide
DMSO	: dimethyl sulfoxide
EI	: electron impact
Et	: ethyl
FAB	: fast atom bombardment
HRMS	: high-resolution mass spectrum
Hz	: hertz
INDO	: Intermediate Neglect of Differential Overlap
IR	: infrared
J	: coupling constant
m	: multiplet
Me	: methyl
mg	: milligram
mL	: milliliter
m. p.	: melting point
NBS	: N-bromosuccinimide
NMR	: nuclear magnetic resonance
Ph	: phenyl
r.t.	: room temperature
s	: singlet
TBDMS	: tert-butyldimethylsilyl
TFA	: trifluoro acetic acid
THF	: tetrahydrofuran
TMEDA	: N,N, N',N'-tetramethylethylenediamine
TMS	: trimethylsilyl
Tr	: trityl
*p*TSA	: *p*-toluene sulfonic acid
^{t}Bu	: tertiary butyl

Chapter 1

A Brief Introduction to Dendrimers (Part A) and Carbon Centered Radicals (Part B)

INTRODUCTION

The thesis is mainly focused on an investigation aimed at gaining insight into the reactivity and functionalization of two symmetric molecules namely, tris(2-thienyl)methane and tris(2-furyl)methane. Two major themes, *viz.*, dendrimer synthesis based on a symmetric heterocycle core, tris(2-thienyl)methane and radical generation from the furan analog of Gomberg's triphenylmethyl system have been addressed and the results of the studies are discussed in detail. In order to put things in perspective, and to serve as a prelude to the work embodied in the Chapters 2 and 3 of the thesis, a brief account of dendrimers and carbon centered radicals is given in this chapter.

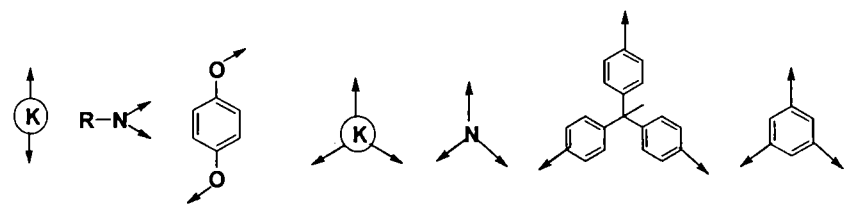
This chapter is divided into two parts. In the first part, a brief overview on the various aspects of dendrimer synthesis as well as their applications is given. A brief outline of carbon centered radicals with special emphasis on Gomberg's triphenylmethyl radical is discussed in the second part. Since the information available on the chemistry of tris(2-thienyl)methane is limited, it was considered more appropriate to include this in the introduction to the second chapter. Similarly, relevant background to the work on tris(2-furyl)methane is presented in the third chapter.

Part A

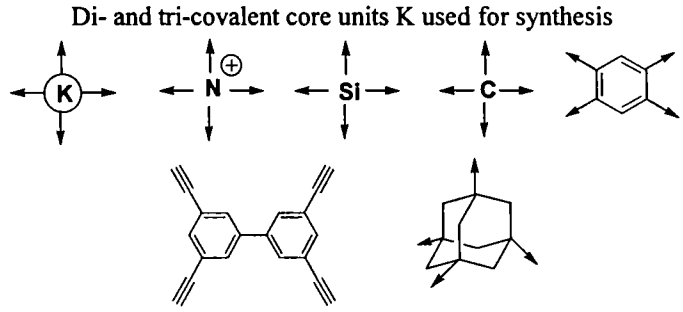
A Brief Introduction to Dendrimers

1.1 Introduction

Dendrimers are a new class of three-dimensional, man made molecules produced by an uncommon synthetic strategy which incorporates repetitive branching sequences to create a unique architecture.[1] The term dendrimer originates from Greek words 'dendron' which means 'tree' and 'meros' which means 'parts' and hence dendrimer chemistry deals with the architecture of such molecules. Dendrimers evolve from a core similar to a tree. They get more and more ramified with each subsequent branching units (generation). Variety of dendrimers with different core units K, branching units and end groups are reported in the literature (for selected examples, see Figure 1).[2] The first iterative synthetic procedure towards well-defined branched structures has been reported by Vögtle, who named this procedure a 'cascade synthesis'.[3]



Di- and tri-covalent core units K used for synthesis



Tetra covalent core units K used for synthesis

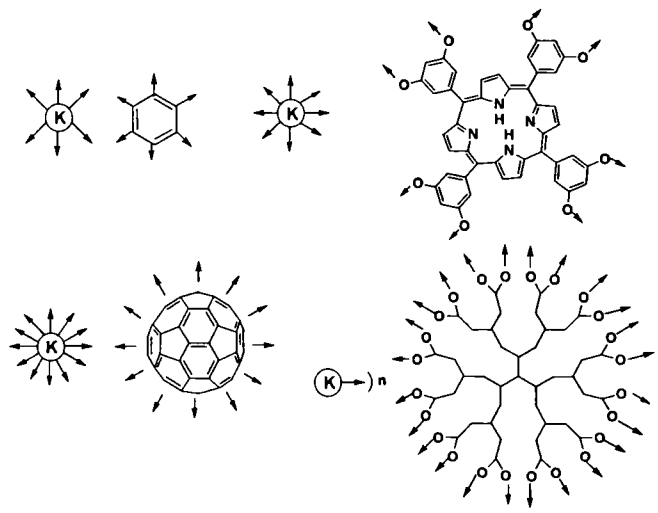


Figure 1. Hexa covalent and larger core units K used in synthesis

1.1.1 Construction Concepts

In contrast to the traditional polymers, dendrimers are unique core-shell structures possessing three basic architectural components: i) a core, ii) an interior of shells consisting of repeating branch cells-units, and iii) terminal functional groups. There are two fundamentally different construction concepts for the synthesis of high-generation dendrimers: the divergent approach and the convergent approach. Repetitive steps are needed in both approaches and each step adds one more generation to the previous generation.

1.1.1.1 Divergent Approach (Newkome Type) [4]

In divergent synthesis, numerous reactions have to be performed on a single molecule (core molecule), for the successive attachment of branching units (Figure 2). The number of building blocks that can be added is dependent upon the available sites on the peripheral core. A key feature of the divergent method is the exponentially increasing number of reactions that are required for the attachment of each subsequent layer. With the build-up of higher generations, accumulation of defects happens because of the incomplete reaction of the end groups. Since the side

products have physical properties similar to the dendritic products, chromatographic separation is extremely difficult.

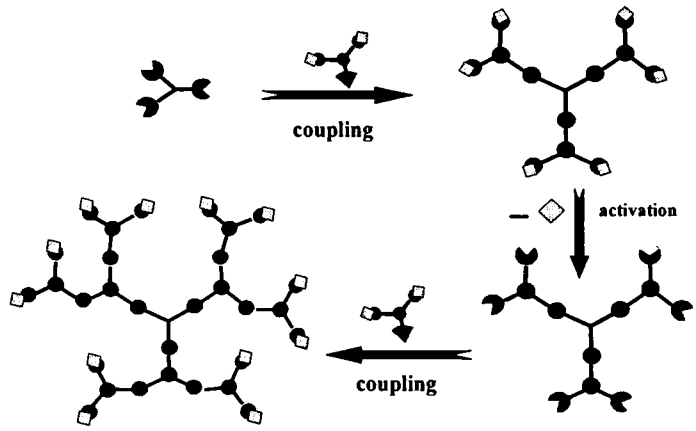
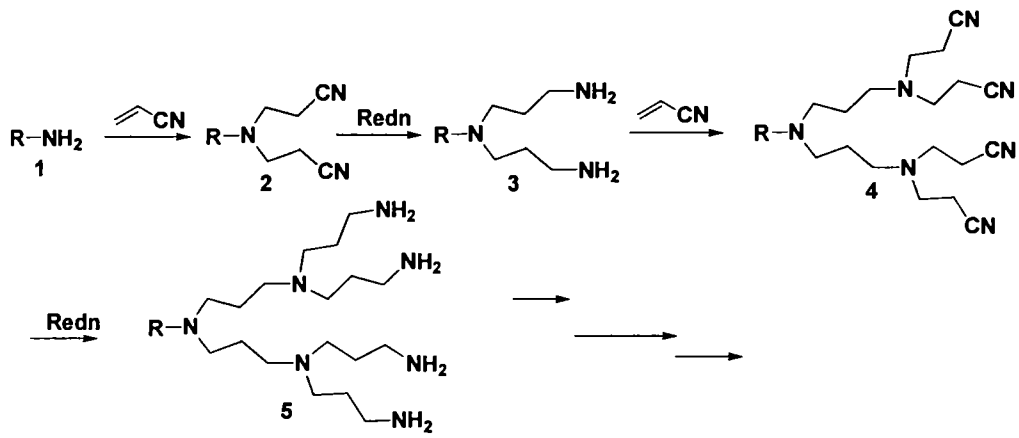


Figure 2

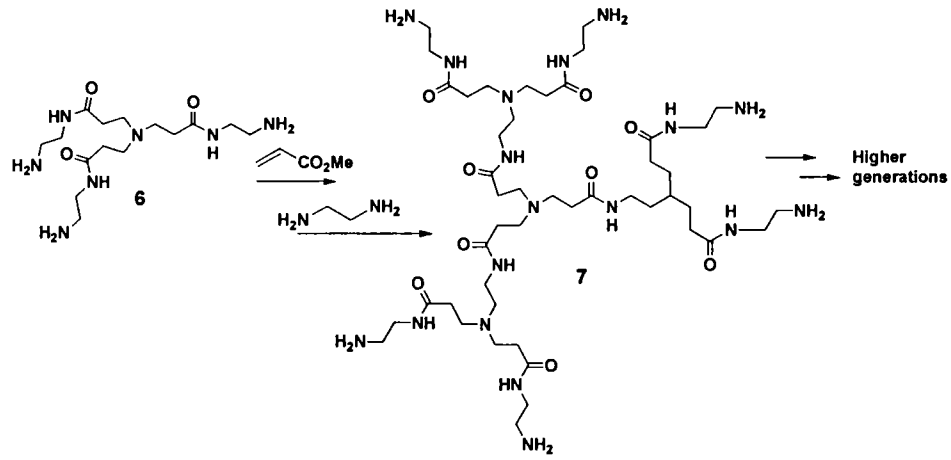
Vögtle and coworkers reported the first preparation, separation and characterization of simple fractal-like structures by synthetic methodology. The so called 'cascade synthesis' attempted by Vögtle[4a] is shown in Scheme 1. The reaction involves repetitive Michael addition followed by reduction.



Scheme 1

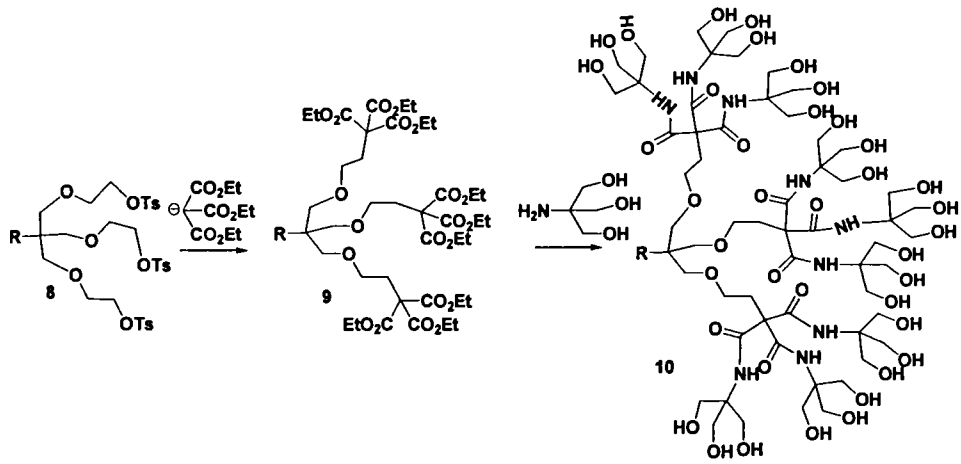
The first thoroughly investigated dendritic structures were Newkome's 'arborol' systems[4b] and Tomalia's PAMAM dendrimers.[5] In 1985 Tomalia *et al.* reported the preparation of polyamidoamines, which were generated from a three-dimensional core and possessed N-branching centers as well as amide connectivity.

Each generation was synthesized by Michael type addition of methyl acrylate to amine followed by amidation using ethylenediamine. The general procedure was repeated to obtain higher generations (Scheme 2).



Scheme 2

'Arborols' was synthesized using a strategy as shown in Scheme 3. The initial core, 1,1,1-tris(tosylmethyl)alkane was treated first with the sodium salt of the triester and then with tris(hydroxymethyl)aminomethane. The use of appropriate spacer between branching centers was found to be necessary due to the steric hindrance associated with quaternary carbon center. A three atom distance was demonstrated to be needed in between the branching point and the reaction center, to circumvent retardation of the S_N2 type transformations.



Scheme 3

1.1.1.2 Convergent Approach (Frèchet Approach)[6]

In convergent synthesis, the construction of dendrimers starts from the periphery towards inside. These branches are then finally treated with the core molecules giving rise to dendrimers (Figure 3).

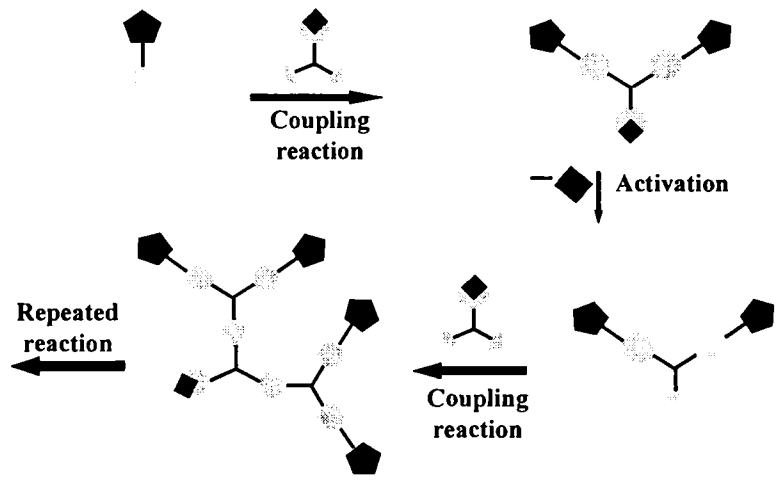
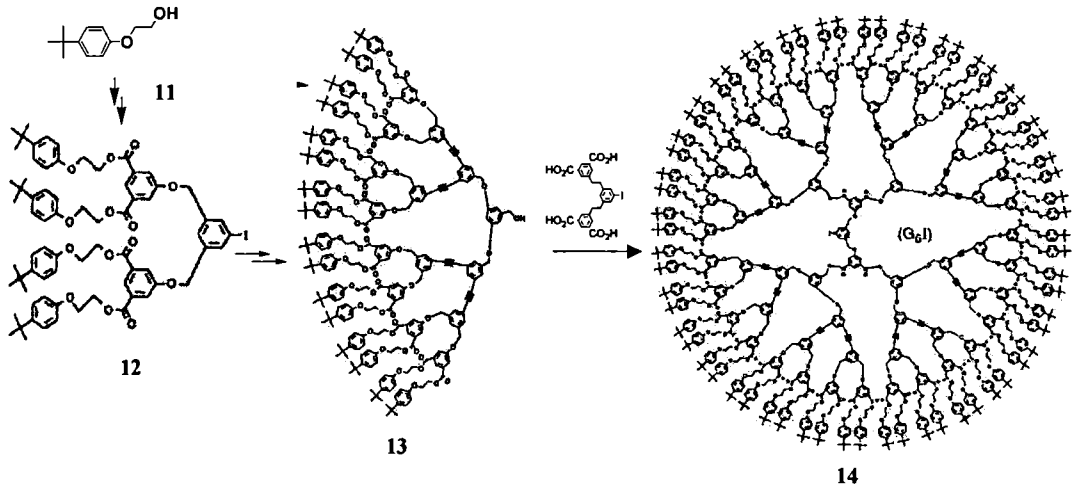


Figure 3

The advantage of this method is that, the number of reactions performed are fewer and only a small number of side products are formed. Moreover, purification is possible in each step and dendrimers prepared *via* this method can be ideally 'defect free'.

Zimmerman's group has reported the synthesis of a sixth generation dendrimer by convergent approach.[7] The monomer units were designed to couple by Mitsonobu esterification reaction or by Sonogashira reaction of a terminal acetylene with an aryl halide (Scheme 4).



Scheme 4

1.1.2 Structural Analysis

The three-dimensional structure of dendrimers is of great interest, since they have a three-dimensional covalently linked skeleton. It was postulated that dendrimers of lower generations take rather flat, ellipsoidal shape, according to some earlier studies.[8] The area of the end group was shown to become smaller with increasing number of generations until a critical branched state called 'starburst dense packing' is reached and prevents any further reaction. So these molecules are considered as spherical with a dense exterior and a loose interior with channels and cavities. Some experimental observations like inclusion of guest molecules and viscosity studies have confirmed this assumption.

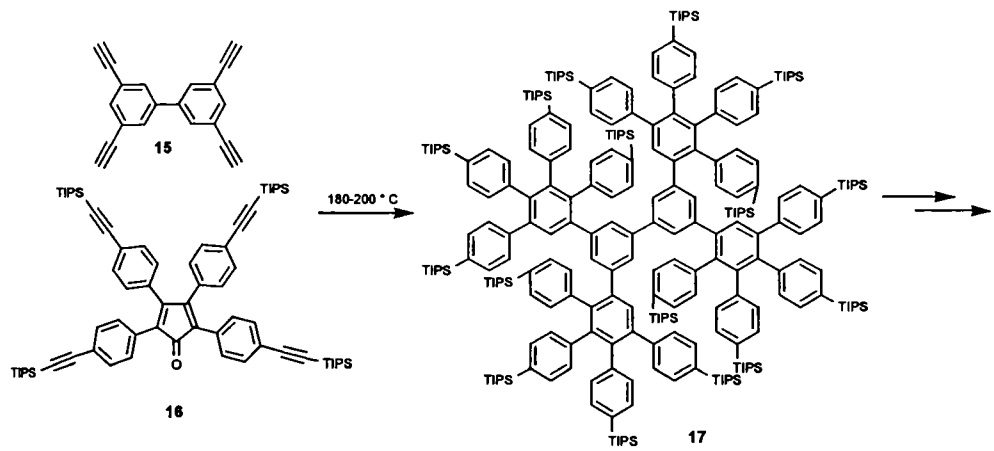
Recent methods for the structural analysis have added more information to the afore-mentioned concept in some respect. X-ray and neutron small angle scattering experiments have been done on higher generation of PAMAM (polyamidoamine) dendrimers which reveal its spherical structure and electron density distribution.[9] According to these experiments, electron density at the center is high and decreases continuously towards outside.

Experiments of Meijer *et al.* have shown that up to fifth generation, dendrimer is of comparatively high purity.[10] The structure of higher generation dendrimers cannot be regarded as absolutely perfect one, but rather as a highly ordered system with a high number of easily accessible functional groups.

1.1.3 Applications of Dendrimers

1.1.3.1 Nanostructures

Müllen *et al.* developed dendrimers consisting of only hydrocarbon skeleton in the nanometer size, wherein benzene rings act as linkages and these can act as interesting precursors to polycyclic aromatic systems.[11] These hydrocarbon dendrimers were constructed by Diels-Alder reaction of substituted cyclopentadiene derivatives and an acetylene unit. They were successful in the preparation of such dendrimers up to third generation with 142 benzene units (Scheme 5). Several other nanodimensional compounds like nanospheres, nanorods and nanocylinders were also synthesized.

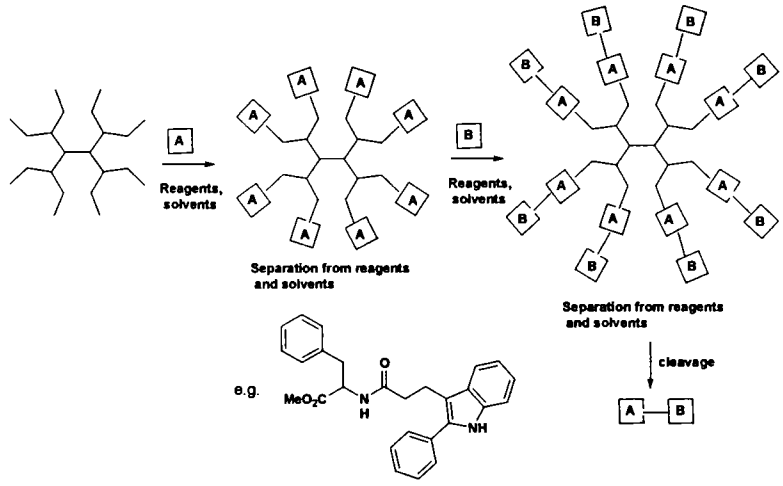


Scheme 5

1.1.3.2 Combinatorial Chemistry

Dendrimers have been known as homogeneous soluble carrier for combinatorial libraries. A schematic representation of amino acid synthesis using

this method is shown in Scheme 6. Newkome *et al.* have attached a triple branch juncture to poly(propyleneimine) dendrimers and they were able to graft on additional functionalities.[12]



Scheme 6

1.1.3.3 Surface Coating

The properties of surfaces can be manipulated by coating dendrimers on them. Crooks *et al.* have examined the sensory properties of such surfaces by covalently linking PAMAM dendrimers to the carboxyl groups of mercaptoundecanoic acid on gold surfaces and it was found that the surface gave the characteristics of an ideal sensor.[13]

1.1.3.4 Unconventional Photoactive Systems

Dendrimers with azobenzene unit as the initiator core and aryl ether branch junctures are photo-switchable and transformation from the *E*- to the *Z*- isomer has been performed under ultraviolet light irradiation.[14] Some modified azobenzene fused dendrimers are also found to be suitable materials for holographic data storage.

1.1.3.5 Redox-active Dendrimers

Austruc *et al.* have shown that the ferrocenyl dendrimers can serve as supramolecular redox sensors for inorganic anions. Using this technique, on addition of one equivalent of salt per ferrocene unit, it is possible to distinguish between four different anions.[15]

1.1.3.6 Dendrimers and Chirality

Chiral dendrimers known so far belong to one or other of the classes listed below.[16] Dendrimers with a) a chiral initiator core, b) a chiral branch juncture, c) chiral end groups, d) some of the characteristics mentioned above, e) constitutionally different segments anchored to an initiator core. It may be mentioned that dendrimers having a rigidly chiral conformation without possessing any stereo-centers or chiral moieties have not been synthesized so far. Studies on chiral dendrimers have revealed that the position and the number of chiral moieties strongly influence the resulting macroscopic optical properties of the dendrimer and also the optical properties are determined by the flexibility of the dendritic segments.[17]

1.1.3.7 Medicine and Diagnosis

Pioneering work in this area was the synthesis and study of lysine dendrimers which were found to be active in inhibiting the hemeagglutination of human erythrocytes by influenza viruses.[18] Dendrimers have been tested as therapeutic agents in boron neutron capture therapy which represents a potential method for the treatment of incurable forms of cancer.[19] PAMAM dendrimers have been tested in gene therapy,[20] and in pre-clinical studies like MRI[21] they have ensured a high signal-to-noise ratio.

1.1.3.8 Dendritic Catalysts

Because of the nanoscopic dimension and solubility of dendrimers, they combine the advantages of homo- and heterogeneous catalysts. Both catalytic systems, in which the active center is located at the core and at the periphery, have been studied in detail.[22]

1.1.4 Dendrimers Containing Rigid, Conjugated Backbone

Moore *et al.* have designed a series of rigid phenylacetylene derivatives in the nanoscale dimension and studied their energetic absorption and energy tunelling characteristics. Amphiphilic and water soluble poly(phenylacetylenes) have also been studied by the same group.[23] Müllen *et al.* have devised the synthesis of phenylene dendrimers *via* convergent methodology.[11b] Compared to their linear analogs, conjugated dendrimers could have a number of potential applications. eg. organic light emitting diodes (OLEDs).

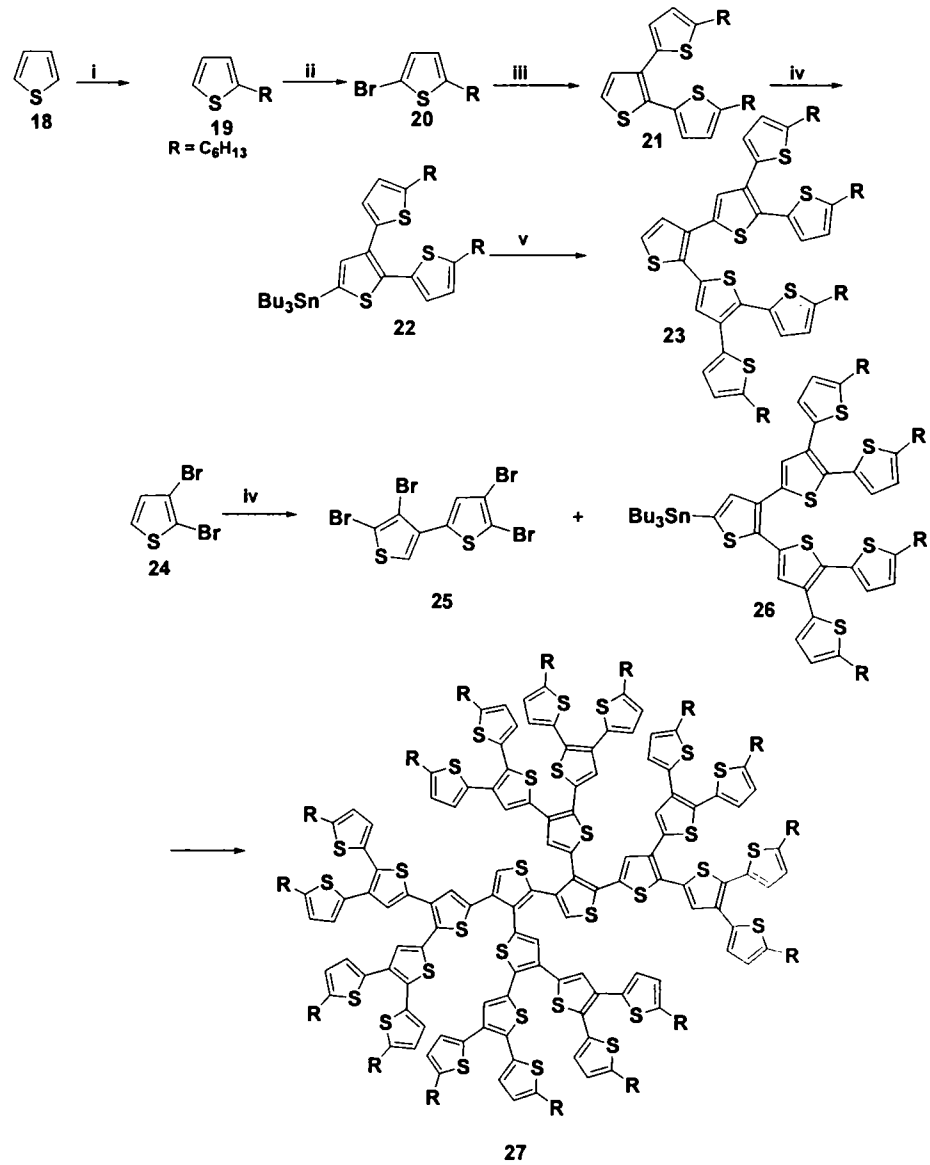
1.1.5 Heterocyclic Dendrimers

Dendrimers with heterocyclic subunits are relatively rare, although heterocyclics are a very important class of organic compounds. Most of the dendrimers with heterocyclic loci are from oligopyridine type.[24] Díez-Barra *et al.* have synthesized dendrons bearing pyrazole, imidazole and 1,2,4-triazole systems.[25] Later Verheyde *et al.* have synthesized the dendrimers of oxadiazole and the heterocyclic ring was formed by the condensation of acid chlorides and tetrazoles.[26] The same group has also synthesized triazole containing dendrimers using 1,3-dipolar cycloaddition strategy.[27]

1.1.5.1 Thiophene Dendrimers

In 2002, Advincula *et al.* have reported the synthesis of the first all-thiophene dendrimers *via* convergent methodology.[28] The synthetic route for thiophene

dendron is shown in Scheme 7. A number of metal mediated coupling reactions were performed on thiophene in order to attain the all-thiophene dendrimers.



I) BuLi, RX; ii) NBS/ DMF.; iii) Mg, 2,3-dibromothiophene, $NidpppCl_2$.; iv) BuLi, Bu_3SnCl.; v) 2,3-dibromothiophene, $Pd(PPh_3)_4$, DMF.; vi) $LDA/CuCl_2$.

Scheme 7

They carried out some investigations on the structural characterization, size information, optical properties and supramolecular assembly on different solid materials. It was observed that these materials exhibit both short-range and long-

range ordering through the influence of π-π stacking properties of the thiophene rings.[29]

1.1.6 Definition of the Problems

As already stated in the introduction, two problems which cover some common grounds are addressed in this thesis. The first one deals with dendrimers. Dendrimers represent a key stage in the ongoing evolution of macromolecular chemistry. From the literature survey it was revealed that although the synthesis and chemistry of benzene based dendrimers are well established,[5] very little is known about heterocycle based dendrimers.[24-29] The chemistry of the thiophene rings in tris(2-thienyl)methane has not been investigated so far, though the chemistry of tris(2-thienyl)methyl radical and the cation were studied in detail. Tris(2-thienyl)methane has attracted our attention since all the thiophene rings are susceptible to undergo the reactions that occur on thiophene. The propellar shape of the molecule would assist the formation of three dimensional architectures from the molecule. The second chapter of the thesis describes our detailed investigation on the reactivity of tris(2-thienyl)methane and our attempts on the synthesis of dendrons and few lower order dendrimers of tris(2-thienyl)methane molecule by divergent approaches.

Part B

A Brief Introduction to Carbon Centered Radicals

1.2 General

Radical is a neutral species that contains odd number of valence electrons and thus has a single unpaired electron in one of its orbitals. Much of the development in mechanistic organic chemistry during the 20th century is dependent on the trivalent carbon hypothesis, which was demonstrated experimentally by Gomberg.[30] He discovered the first stable trivalent carbon: triphenymethyl radical in 1900. A decade later Hey and Waters studied the mechanistic details of radical reactions.[31] Radical was regarded as an intermediate with limited synthetic potential, until the demonstration by Stork that controlled generation and addition of vinyl radicals to π-systems constitutes a powerful method for the construction of complex carbocycles.[32] Julia, Beckwith, Ingold and Giese have made noteworthy contributions by studying the structure and reactivity of radicals in detail.[33] The paradigm shift that lead to the general acceptance of radical methodology as a viable tool for the synthesis of biologically active natural and unnatural molecules can be attributed in large measure to the seminal contributions of Stork. A number of other groups, especially those of Curran and Pattenden have also made stellar contributions to this area.[34]

Most of the radicals have very short lifetimes and those radicals without stabilization can rapidly dimerize, disproportionate, or abstract hydrogen/other atoms from many of the solvents. In general, carbon-hydrogen bonds in R-H decrease in strength when R goes from primary to secondary and to tertiary. Moreover radicals are stabilized by both electron-withdrawing and electron-releasing groups and hence

radicals next to functional groups are even more stable than tertiary radicals. Some of the stable free radicals [35] are shown in Figure 4.

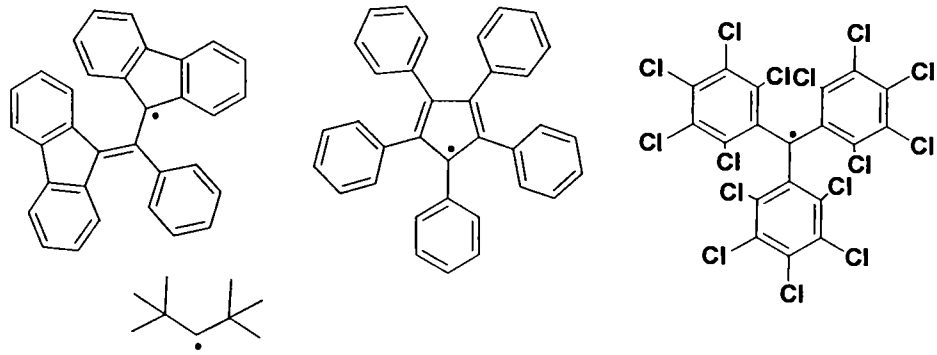
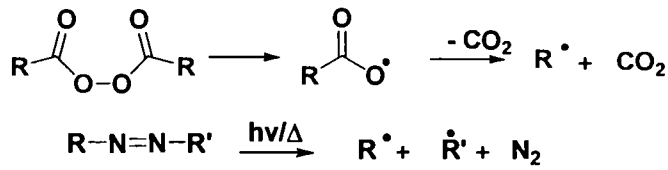


Figure 4. Some stable free radicals.

1.2.1 Generation of Free Radicals

There are several methods available in the literature for the generation of radicals. Some of them are discussed here.

One of the most generally used methods for the generation of radicals is the decomposition of peroxides and azo compounds (Scheme 8).[36] The energy source for the decomposition of azo compounds can be either thermal or photochemical.[37]



Scheme 8

The acyl derivative of *N*-hydroxypyridine-2-thione is another synthetically versatile source of free radicals.[38] Photolysis of a mixture of di-*t*-butyl peroxide, trimethylsilane and the alkyl bromide corresponding to the radical to be studied, is found to be a convenient technique for EPR studies of radicals.[39] In addition to the thermal and photochemical methods for the generation of radicals, electrochemical methods are also well established for generating radicals. Radicals generated by one

electron oxidants, such as metal salts, *viz.*, Mn(III), Co(II), Cu(II), Fe(III), V(V) and Ce(IV), with variable oxidation states have received considerable attention.[40]

1.2.2 Importance of Radicals in Organic Synthesis

Radical reactions offer a number of advantages over ionic processes, namely,

- Chemoselectivity can be achieved in reactions of compounds with unprotected functional groups such as –OH, –NHR *etc.*
- Can be used for the construction of quaternary and neopentyl centers.
- Regioselectivity can be achieved in the case of addition to α,β- unsaturated compounds.
- Many reactions involving cyclic radicals are stereoselective.
- Side reactions such as rearrangement, β- elimination and racemization of chiral centers at adjacent or remote carbon atoms are suppressed, since radical reactions are very fast.
- Carbon centered radicals can add to both electron rich and electron-deficient systems like alkenes, allenes and acetylenes.
- Reactions can be done under neutral conditions.
- Chirality at non-radical carbon atom can be preserved as this method employs mild reaction conditions and
- Radical reactions are not generally influenced by solvents.

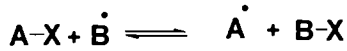
These characteristics along with the ability to accomplish many transformations which do not take place easily by conventional methods make radical reactions important in synthesis.

1.2.3 Carbon-Carbon Bond Forming Reactions Involving Radicals

For synthetic application, the selection of method for the generation of radical is important, since it will determine the fate of the intermediate radicals. Unlike anions and cations, they react with themselves by combination or disproportionation

and hence maintenance of a low concentration of the radicals throughout the reaction is desirable.

A variety of useful transformations can be accomplished by radical reactions and those can be divided mainly into two broad classes: (a) atom abstraction (Eq. 1) and (b) addition to multiple bonds (Eq. 2).

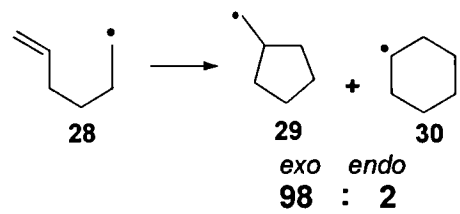


(1)

(2)

In the former case, the direction of the reaction is determined by the relative bond strengths of the forming and breaking bonds. The most commonly abstracted groups are univalent atoms like halogens and hydrogen, although other groups like -SR and -SeR can be quite useful. In the latter case, a radical adds to an unsaturated functional group and in principle it is reversible. The substituents located on both reaction partners determine the rate and regiochemistry of the reaction and the parameters are well established. The addition of carbon-centered radical to carbon-carbon multiple bond is favorable, since a carbon-carbon σ-bond is formed at the expense of a carbon-carbon π-bond.

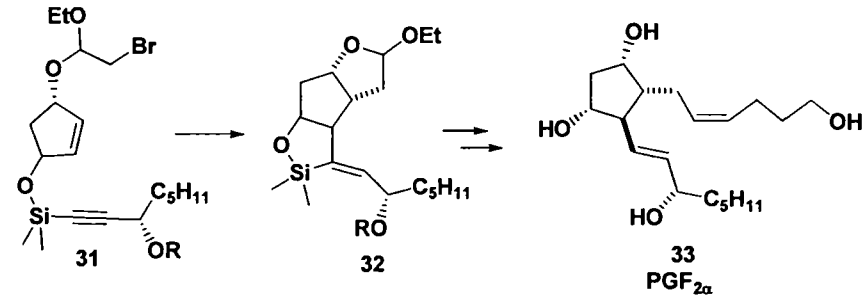
Intramolecular addition reactions are particularly useful in the construction of carbocycles. Cyclization follows Baldwin rules and smaller rings are formed (*exo* cyclization) though it would form less stable primary radical while steric and entropic effects favor *exo*-cyclization (Scheme 9).[33b]



Scheme 9

1.2.4 Applications in Natural Product Synthesis

Radical reactions now occupy an important position among the tools available to synthetic chemists for the construction of complex target molecules.[34a,41] In particular, radical cyclization has proven to be a very effective and expedient route to tetrahydrofurans, γ-lactones, fused bicyclic compounds, spirocyclic compounds, six membered ring systems and bridged systems.[42] Tandem reactions involving the cyclization of a haloacetal followed by an intermolecular reaction with a carbon trap are efficient methods to introduce two *trans* carbon residues at the vicinal alkene position of a cyclic allylic alcohol in a single step. This transformation represents the heart of the prostaglandin synthesis developed by Stork (Scheme 10).[43]

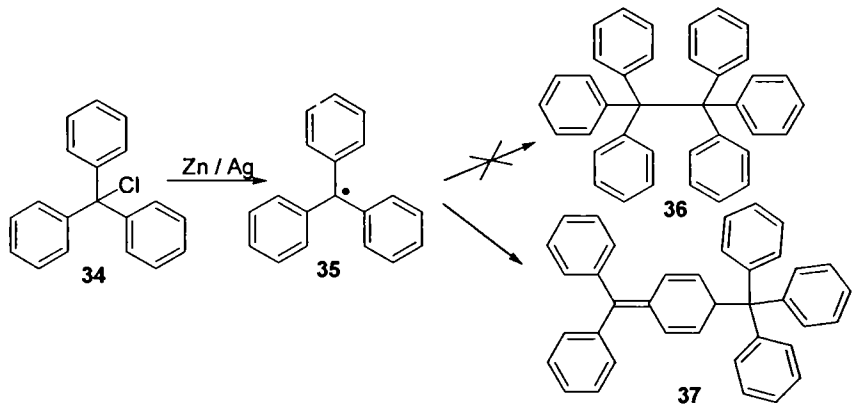


Scheme 10

1.2.5 Gomberg's Radical

The monumental development of structural organic chemistry in the latter half of the 19th century was based on Kekule's hypothesis of tetravalent carbon while most of the development in mechanistic organic chemistry in the 20th century is dependent on the trivalent carbon hypothesis, demonstrated experimentally by Gomberg.[30] He discovered the first stable trivalent carbon- triphenymethyl radical. This radical which was found to be stable and could be stored for weeks in dry crystalline state, was prepared by the action of zinc powder on triphenylchloromethane (Scheme 11). The isolated dimer of the radical, was thought to be the symmetrical hexaphenylethane (**36**). The discovery of triphenylmethyl

radical inaugurated the growth of free radical chemistry as a new branch of chemistry. Many of Gomberg's distinguished contemporaries started both experimental and theoretical investigations of such free radicals.[44]



Scheme 11

Until the determination of the correct structure of the dimer (**37**) by Lankamp, Nauta and MacLean, in 1968,[45] the hypothesis of an equilibrium between triphenymethyl radical and hexaphenylethane was almost certain. The quinoid structure of the dimer that Jacobson[46] had proposed in 1905 was later on proved using spectroscopic techniques.

1.2.6 Definition of the Problems

Triphenylmethyl radical as well as its chemistry has been thoroughly studied and established in the literature.[30,44-46] Two heterocyclic analogs, *viz.*, tri-2-thienylmethyl radical and tri-3-thienylmethyl radical, have been generated by the reduction of corresponding trithienylmethyl cation[47] and they are noteworthy in this context. Against the literature background of this area, it became clear that, no such work is known in the case of tris(2-furyl)methyl radical. We became interested in the generation of tris(2-furyl)methyl radical and the details of our efforts are presented in the third chapetr of the thesis. Although the synthesis of tris(2-furyl)methane was known, the chemistry of the molecule remained uninvestigated. Intrigued by the possibility of transforming it into a symmetrically growing three dimensional

macrostructure, a detailed investigation of the reactivity of tris(2-furyl)methane was carried out and the results obtained are also presented in the third chapter.

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Chapter 2

Novel Reactions of Tris(2-thienyl)methane

2.1 Introduction

Substituted thiophenes are valuable building blocks in the synthesis of many natural and non-natural products and have a number of applications in flavor and pharmaceutical industries. Thiophene containing drugs have been used in the therapy of disorders related to central nervous system, metabolic and infectious diseases.[1] In addition, desulfurization using Raney nickel has made thiophene an attractive surrogate for the synthesis of aliphatic compounds.[2] Also, a number of substituted thiophenes are known to undergo oxidation to sulfones which in turn can be used in Diels-Alder reaction to construct polycyclic compounds.[3] Since various functionalities can be easily built on thiophene molecule, a large number of poly- and oligothiophenes have been prepared and studied to date. Oligo- and polythiophenes have been investigated for their promising applications in the field of organic semiconductors[4] and are also studied extensively with regard to applications in organic electronic devices such as organic light emiting diodes (OLEDs)[5] and field-effect transistors (FETs).[6] Recently advanced materials based on oligo- and polythiophenes have found extensive use in optoelectronics,[7] chemosensor devices[8] and photovoltaics.[9] Some heterohelicenes containing thiophene rings were synthesized and their electronic and self-assembling properties were investigated in detail.[10]

Thiophene based dendrimers have also been investigated to some extent very recently, in view of their potential applications.[11] Macrocyclic and linear analogs of molecules containing thiophene have been synthesized. Their unusual spacial arrangement and macrostructure and the consequent electronic, optical and self-assembling properties have been investigated in detail.[12]

Triphenylmethyl derivatives represent an important class of dye stuffs as well as a family of protecting groups used widely in organic synthesis to transiently block various functional moieties.[13] On acidic treatment, tritanols or trityl esters easily give trityl cations which are stable because of the resonance effect of the three aryl rings. Triphenylmethyl based compounds which are capable of forming stable quinoid forms occupy an important niche in organic dye chemistry, representing an old and extensive class of dyes and fluorophores.[14] Compounds like xanthene fluorophore, rosilic acid, malachite green etc. are often available as functional derivatives, suitable for covalent fluorescent labeling of biomolecules. Tris(2-thienyl)methane **1** (Figure 1), like triphenylmethane has attracted the attention of several chemists because of its synthetic utility as well as potential applications.

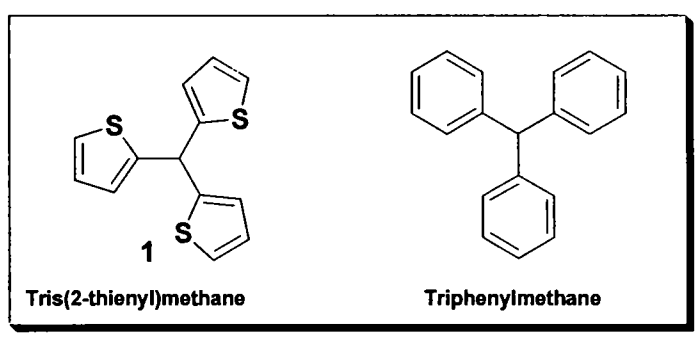


Figure 1

The heterocyclic analogs of the trityl cation, otherwise known as Crystal Violet analogs were studied extensively and used for various applications.[15] For application in non-linear optics and conducting polymers, series of thienylic and oligothienylic trityl analogs were prepared. In order to put things in perspective, a

brief literature survey on the various aspects of i) tristhienylmethyl radicals and ii) carbenium ions is presented in the following section.

2.1.1 Tristhienylmethyl Radicals

Although triphenylmethyl radical had attracted the attention of many leading organic chemists for several years since 1900, its heterocyclic analogs were brought to light only in 1968, by the detection of tris(2-thienyl) and tris(3-thienyl)methyl radicals **2** and **3** respectively (Figure 2).[16]

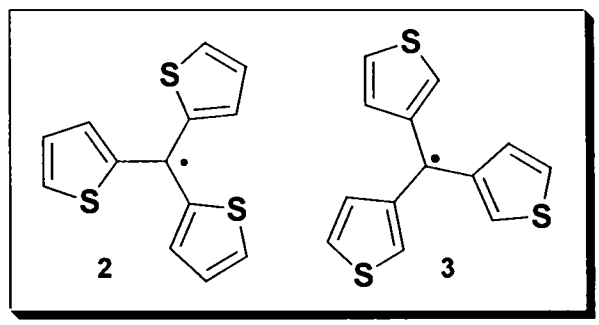


Figure 2

An INDO study of tris(2-thienyl)methyl radical has revealed the conformational properties and it has been shown that the radical exists in two diastereomeric propellar like conformations, a *cis* form with C_3 symmetry and a *trans* form with C_1 symmetry as represented in Figure 3.[17]

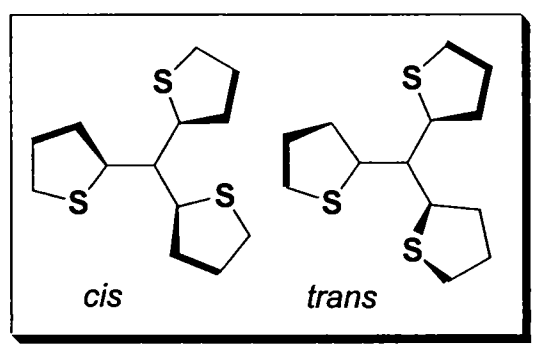
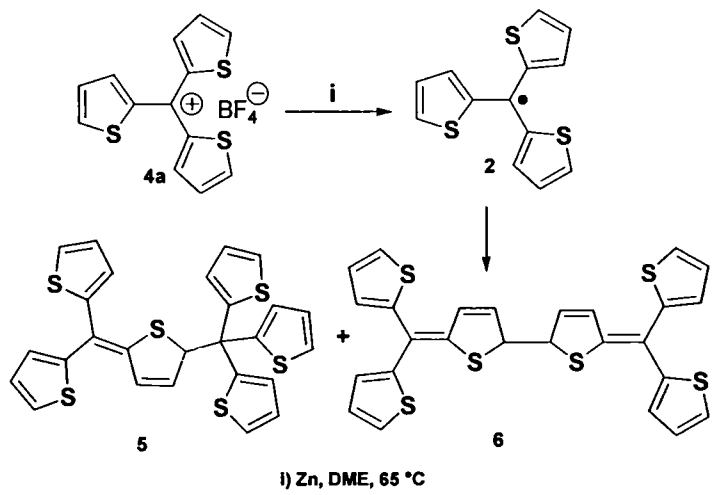


Figure 3

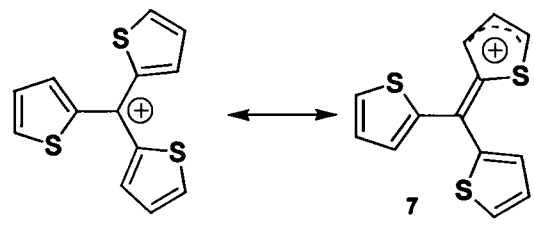
No structure proposal for the dimer of tris(2-thienyl)methyl radical was attempted until Nakayama *et al.* carried out some investigations on the dimerization of the radical in 1990. They reported the formation, structure elucidation and interconversion of the two isomeric dimers of **2** (Scheme 1).[18] Based on extensive studies, the authors have concluded that the dimerization of the radical between radical center and the sterically less hindered 5-position of 2-thienyl possessing a high spin density, initially afforded the kinetically favored product **5** which is then thermally equilibrated to another dimer **6**.



Scheme 1

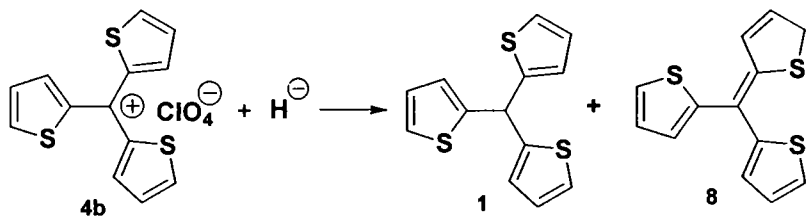
2.1.2 Reactions of Tris(2-thienyl)methyl cation and Tris(2-thienyl)methyl anion

Taddei *et al.*, in 1970, reported the proton NMR spectral parameters for the isomeric tristhienyl carbenium ions[19] while the ^{13}C NMR characteristics were investigated in some detail by Abarca *et al.* (Scheme 2).[20]



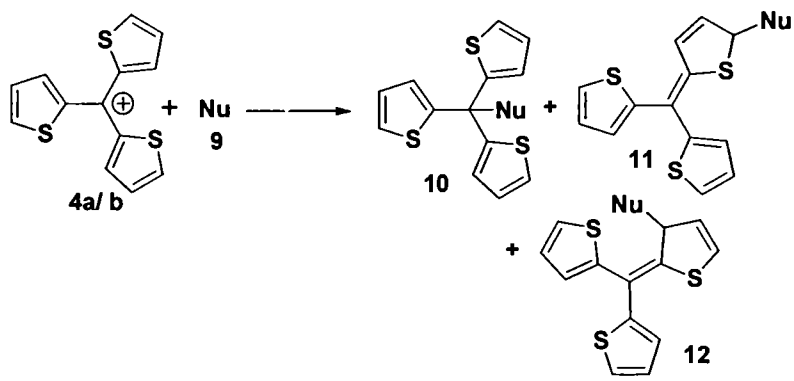
Scheme 2

The reactivity profile of the carbenium ion, towards hydride and carbon nucleophiles was studied by Nakayama *et al.* and it has been observed that addition occurs not only at the carbenium ion center but also on the thiophene ring.[21] Addition of $LiAlH_4$ to an ethereal solution of tris(2-thienyl)carbenium perchlorate **4b** at room temperature results in rapid hydride addition both at the carbenium ion center and at the 5-position of the thiophene ring affording compounds **1** and **8** (Scheme 3).



Scheme 3

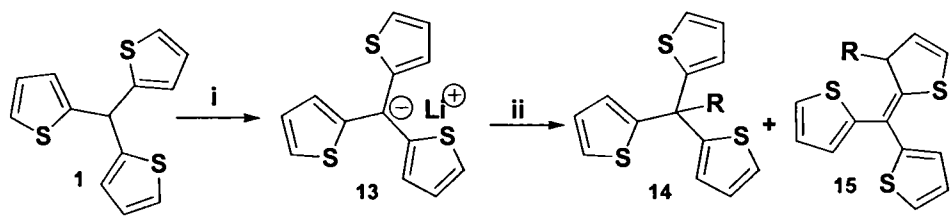
In order for the investigation of carbon nucleophiles towards **4** a variety of organometallic reagents have been employed. A typical schematic representation of this reaction, giving rise to compounds **10**, **11** and **12**, is shown in Scheme 4. When the alkyl group is bulky, **11** and **12** are the major products.



Scheme 4

Nakayama *et al.* explored the reactivity of the corresponding anion, tris(2-thienyl)methyl anion **13**, also towards carbon electrophiles.[22] They found that the optimum condition for addition of electrophiles to the methine carbon involves the use of butyllithium (1.3 eq) in the presence of TMEDA (1.5 eq) in THF at –78 °C

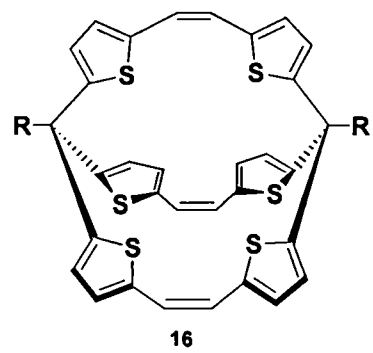
and subsequent addition of excess alkyl halide (5 eq) to the red suspension of the anion formed (Scheme 5). Although the reaction of tris(2-thienyl)methyl anion with primary alkyl halides occurs exclusively at the carbanion center, its reaction with bulkier tertiary alkyl halides occurs both on the carbanion center and at the less hindered thiophene ring as well.



i) BuLi, TMEDA, THF, -78 °C
ii) RX

Scheme 5

The synthesis of cage molecules (for example, compound **16** in Scheme 6) bicapped with tris(2-thienyl)methane was achieved by Oda *et al.* in 2001.[23] The target molecule was obtained *via* McMurry coupling reaction of tris(5-formyl-2-thienyl)methane. All the sulfur atoms of the six thienyl groups are directed inward and hence the molecule has a three dimensional cavity which might encapsulate metal ions (Figure 4). Corresponding monocation, dication and dianion of substantial stability were also synthesized.[24]



16

Figure 4

New octupolar non linear chromophores derived from oligothienylic crystal violet analogs **17** have been synthesized and their non linear optical properties were studied in detail (Figure 5).[25]

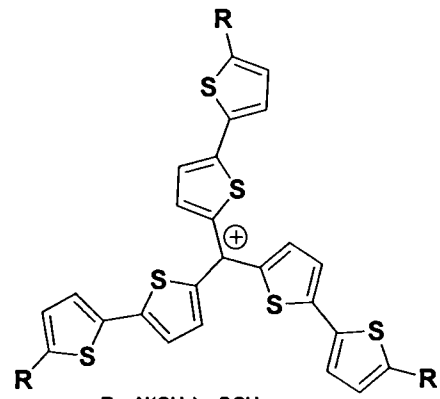
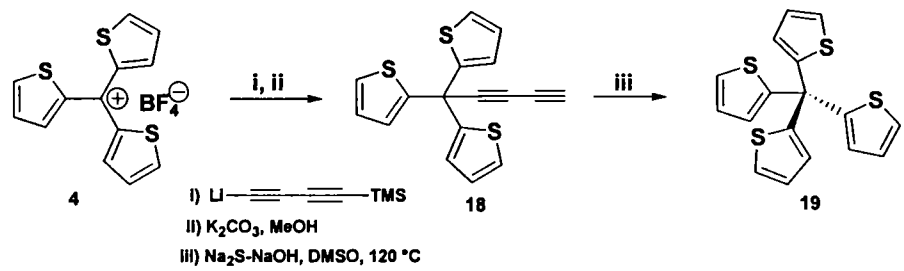


Figure 5

The synthetically and structurally important molecule, tetrakis(2-thienyl)methane **19**, was synthesized for the first time by Oda *et al.* using sodium sulfide induced cyclization of 5,5,5-tris(2-thienyl)pentadiyne which in turn was obtained from tris(2-thienyl)methyl cation **4**.[26] The synthesis of compound **19** is depicted in Scheme 6.



Scheme 6

2.2 Present Work

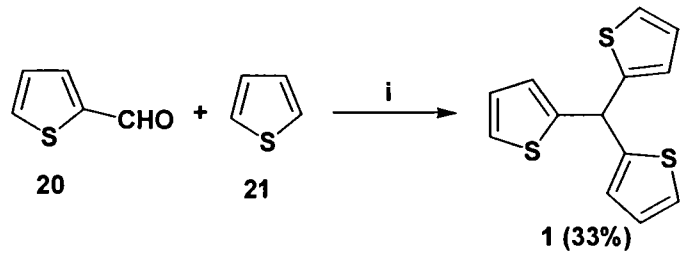
Tristhienylmethane has invoked considerable interest as a synthon for three dimensionally extended molecules or as building blocks for crystal engineering. It is expected to have wider applications in view of the ease of functionalization of

thiophene at C-2 position by either electrophilic substitution reaction or lithiation followed by reaction with electrophiles. The potential use of thiophene as synthon equivalent of n-butane *via* Raney nickel reduction is also noteworthy. The literature precedence presented here clearly indicates that, though the structure and the chemistry of tris(2-thienyl)methyl radicals and carbenium ions have been well established, the reactivity and functionalization of the parent tris(2-thienyl)methane has not been studied in detail. Therefore, we have undertaken an extensive investigation in this area, which includes electrophilic substitution reactions, reactions with carbenes and organometallic reagents. The results of our studies are presented in the first part of this chapter.

Dendritic architecture is one of the most pervasive topologies observed in Nature at the macro and micro-dimensional-length scales and hence dendrimers of controlled organic nanostructures represent a key stage in the ongoing evolution of macromolecular chemistry.[27] Although the synthesis and chemistry of benzene based dendrimers are well studied, there have been only very few attempts to synthesize heterocycle based dendrimers.[11] In view of this, we have attempted the synthesis of dendrons and a few lower order dendrimers of tris(2-thienyl)methane molecule by divergent approaches and the results are presented in the second part of this chapter.

2.3 Results and Discussion

Tris(2-thienyl)methane required for our studies was synthesized from thiophene-2-carbaldehyde and thiophene, *via* a condensation reaction, using P_2O_5 as the dehydrating agent (Scheme 7).[22]



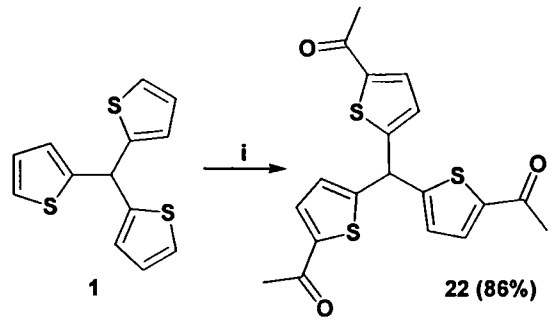
i) P_2O_5, Benzene, 1 h, 60 °C

Scheme 7

2.3.1 Electrophilic Substitution Reactions

i) Acetylation and Oximation Reactions

Friedel-Crafts acylation reaction of thiophene generally proceeds with good yield under controlled conditions. Usually α–substitution is observed in acylation reactions but occurs at β–position when the α–positions are blocked.[28] In order to explore the reactivity of tris(2-thienyl)methane in Friedel-Crafts reaction, it was reacted with acetyl chloride in presence of $AlCl_3$. Trisacetylated product **22** was formed exclusively as a viscous pale brown liquid in 86% yield (Scheme 8).



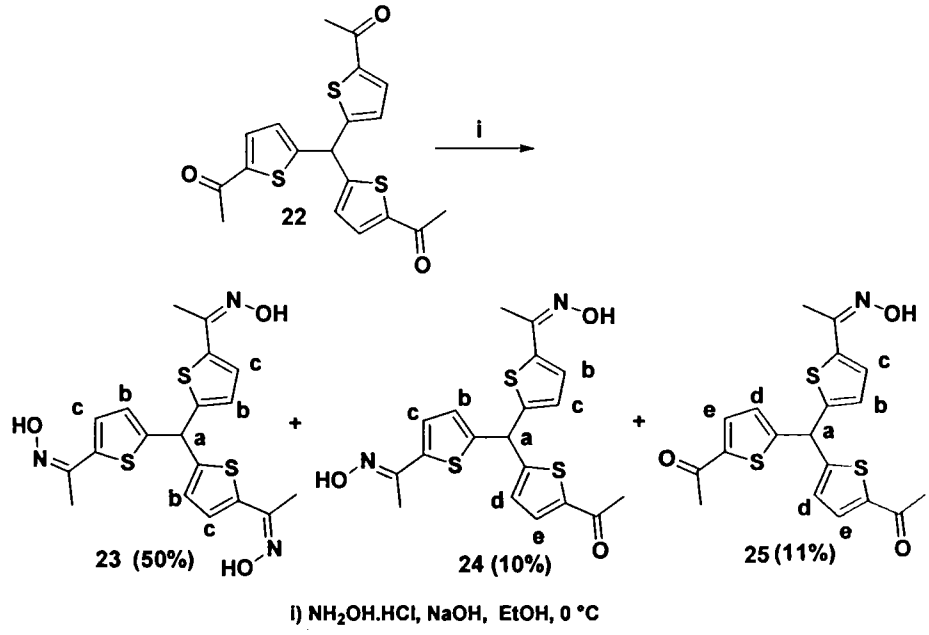
i) CH_3COCl, $AlCl_3$, CCl_4, 0 °C

Scheme 8

Structure of compound **22** was established by means of spectroscopic analysis. The IR spectrum of **22** exhibited a sharp signal at 1660 cm^{-1} corresponding to the carbonyl group absorption. In the ^1H NMR spectrum, the methyl group resonated as a singlet at δ 2.51. The central proton appeared as a singlet at δ 6.08 while the protons attached to thiophene rings were discernible as two sets of doublets

at δ6.97 (J = 3.8 Hz) and 7.54 (J = 3.8 Hz). ^{13}C NMR spectrum also supported the assigned structure. Signals due to the methyl carbons and the central carbon appeared at δ26.3 and 43.6 respectively. Carbons of the thiophene ring resonated at δ127.4, 132.1, 144.2, and 153.0 while the carbonyl group signal appeared at δ 190.0.

With the objective of preparing *H*-bonded supramolecular assemblies, the acetylated product was treated with hydroxylammonium chloride in presence of sodium hydroxide as base to get the corresponding oxime. As expected, the tris-oxime was obtained as the major product (50% yield) in the form of a viscous orange liquid along with small amounts of bis- (10%) and mono- (11%) oximes (Scheme 9).



Scheme 9

The structure of the tris-oxime **23** was assigned on the basis of spectroscopic analysis. In the IR spectrum, a broad band appeared around 3240 cm^{-1} indicating the presence of hydroxyl group. A peak seen at 1615 cm^{-1} corresponds to the C=N stretching of the imine functionality. ^{1}H NMR spectrum of **23** (Figure 6), taken in DMSO, exhibited a singlet corresponding to the methyl protons at δ2.19 and another

singlet corresponding to the central proton at δ 5.85. The aromatic protons were discernible at δ 6.80 (J = 3.7 Hz) and 6.98 (J = 3.7 Hz) in the form of doublets. N-OH peak was discernible at δ 10.15 as a singlet and was exchangeable with D_2O. In the ^{13}C NMR spectrum of the tris-oxime **23**, methyl carbons were seen at δ 10.5 and the central carbon signal was visible at δ 41.5. The signals corresponding to carbons of the thiophene ring were observed at δ 123.7, 124.7, 139.9 and 145.3, while the imine carbons resonated at δ 148.4.

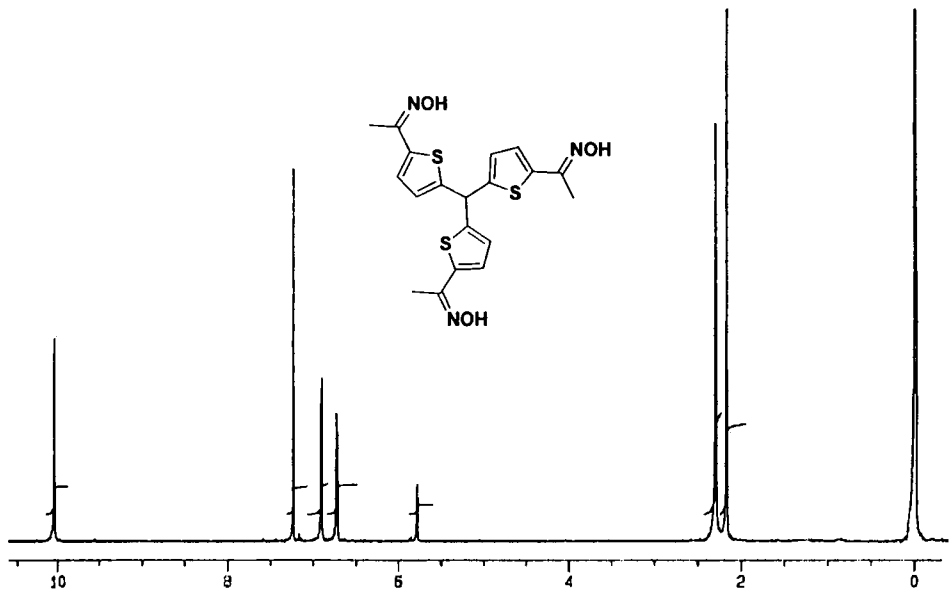


Figure 6. ^1H NMR spectrum of **23** in DMSO/$CDCl_3$

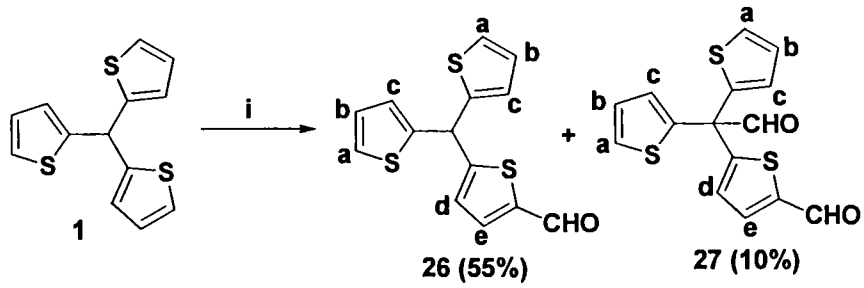
Satisfactory spectroscopic data were obtained for the bis- and mono-oximes also. IR spectrum of compound **24** showed peaks at 3241, 1659 and 1615 cm^{-1}, corresponding to the hydroxyl, carbonyl and imine functionalities. In the ^1H NMR spectrum, the methyl groups appeared at δ 2.17 and 2.59 as two separate singlets. The former value was due to the methyl group attached to the carbonyl group and the latter to imine functionality. The central proton labelled as **a** resonated at δ 5.91. Signals due to protons **d** and **e** were seen at δ 6.78 (J = 3.9 Hz) and 7.23 (J = 3.9 Hz) as two separate doublets while protons labelled **b** and **c** were discernible around δ

6.89 as a multiplet. The N-OH peak was seen at δ 10.21 as a singlet and was exchangeable with D_2O. In the ^{13}C NMR spectrum the signals corresponding to the imine functionalities were seen at δ 154.3 and 155.5 while that of the carbonyl group was discernible at δ 190.3.

The structure of compound **25** was also ascertained on the basis of spectroscopic analysis. IR spectrum exhibited a broad band around 3235 cm^{-1} indicating the presence of the hydroxyl group and the carbonyl and the imine stretching were visible at 1659 and 1615 cm^{-1}. In the ^1H NMR spectrum, signal due to the central proton, labelled **a**, appeared at δ 5.85. A doublet seen at δ 6.80 (J = 3.7 Hz) was assigned to the proton labelled **d** while a multiplet around δ 6.88 was due to the protons labelled **b** and **e**. The signal due to the proton **c** was discernible at δ 6.98 (J = 3.7 Hz) as a doublet. The hyroxyl group was seen as a singlet at δ 10.17 (exchangeable with D_2O). ^{13}C NMR spectrum of **25** showed the imine and the carbonyl carbons at δ 154.3 and 190.3.

ii) Formylation Reaction

Formylation of aromatic systems is an important process since the resulting aldehyde can function as a versatile synthon for the construction of many complex molecules. Formylation of tris(2-thienyl)methane using BuLi and DMF yielding tris(5-formyl-2-thienyl)methane, reported by Oda *et al.*, is noteworthy in this context.[23] We were interested in the reactivity profile of tris(2-thienyl)methane towards the classical Vilsmeier formylation conditions. When tris(2-thienyl)methane was treated with DMF and $POCl_3$ at 0 °C, two products were obtained. Compound **26**, with one of the thiophene rings formylated, was observed as the major product along with small quantities of compound **27** in which the central carbon is also substituted with formyl group (Scheme 10).



i) $POCl_3$, DMF, 1,2- DCE, 0 - 75 °C

Scheme 10

The structures of **26** and **27** were established on the basis of routine spectral analysis. IR spectrum of **26** exhibited a sharp signal at 1729 cm^{-1} corresponding to the formyl group. ^1H NMR spectrum of **26** (Figure 7) exhibited a singlet at δ 5.89 due to the central proton. The protons labelled **b** and **c** were seen together as a multiplet around δ 6.95. Proton **d** appeared at δ 7.02 (J = 3.7 Hz) as a doublet and protons **a** were discernible as a multiplet centered at δ 7.23. Proton **e** resonated at δ 7.60 (J = 3.8 Hz) as a doublet while the aldehydic proton was seen at δ 10.12 as a singlet. In the ^{13}C NMR spectrum, the central carbon was seen at δ 43.5. The aromatic carbons were observed at δ 125.8, 126.1, 127.0, 128.0, 135.9, 143.6, and 155.9. The aldehydic carbon was discernible at δ 182.3.

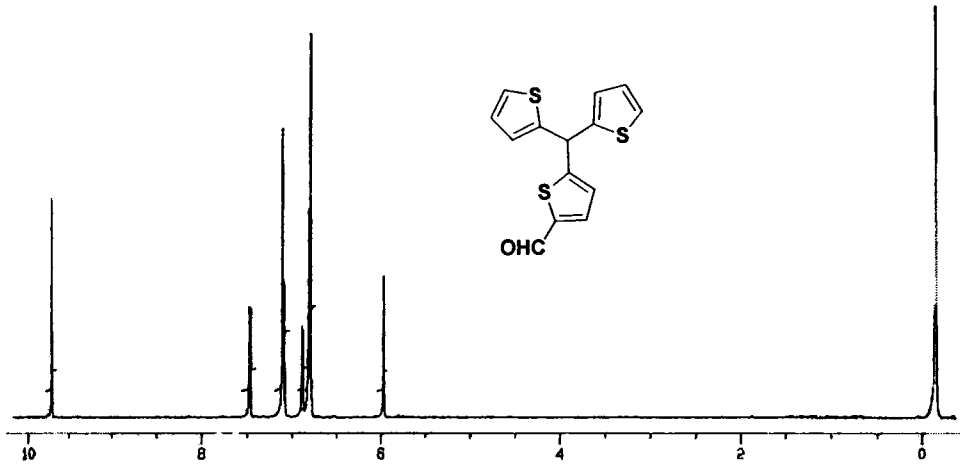


Figure 7. ^1H NMR spectrum of 26

The structure of the second compound **27** was also established by spectral analysis. In the IR spectrum the carbonyl stretching was seen at 1725 cm^{-1}. The characteristic signal (δ5.52) corresponding to the central proton was absent in the ^1H NMR spectrum (Figure 8), indicating substitution at the central carbon. Protons **c** appeared as a doublet at δ6.99 (J = 3.5 Hz) while protons **b** were seen as a multiplet around δ7.06. Proton **d** resonated at δ7.11 (J = 3.9 Hz) as a doublet. The signal due to protons **a** was discernible at δ7.37 (J = 5.1 Hz) as a doublet. Another doublet at δ 7.68 (J = 3.9 Hz) was assigned to the resonance of proton **e**. Two aldehydic protons were discernible in the form of very closely spaced singlets at δ9.93 and 9.98. In the ^{13}C NMR spectrum, the carbon at the center was seen at δ50.0, appearing at a lower field than that in the case of tris(2-thienyl)methane **1**, because of the attachment of formyl group. The two carbonyl carbons were observed separately at δ 182.5 and 189.8. All the other signals were in accordance with the assigned structure.

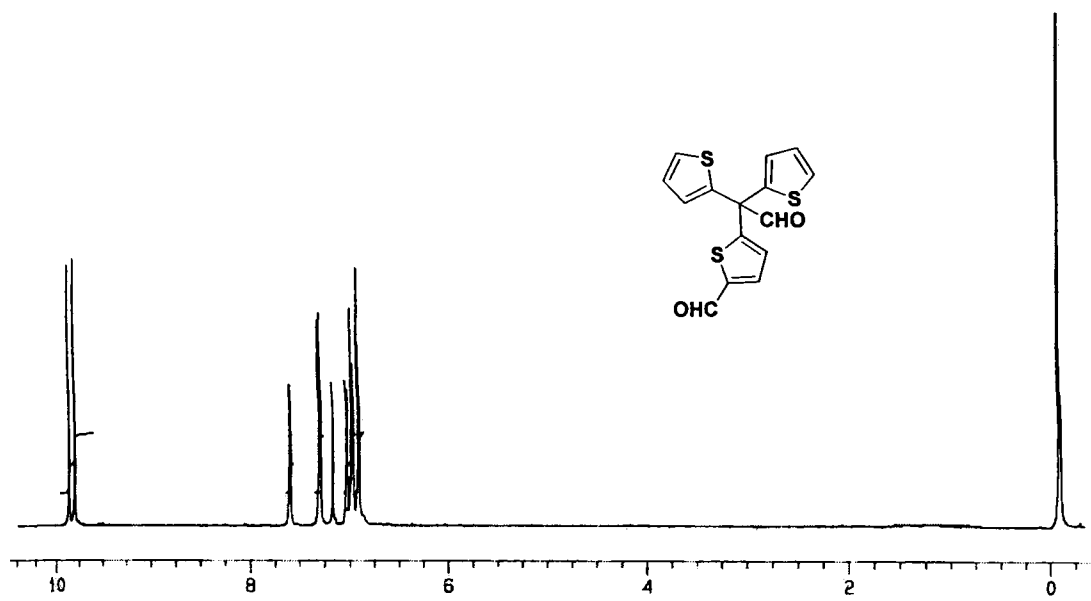
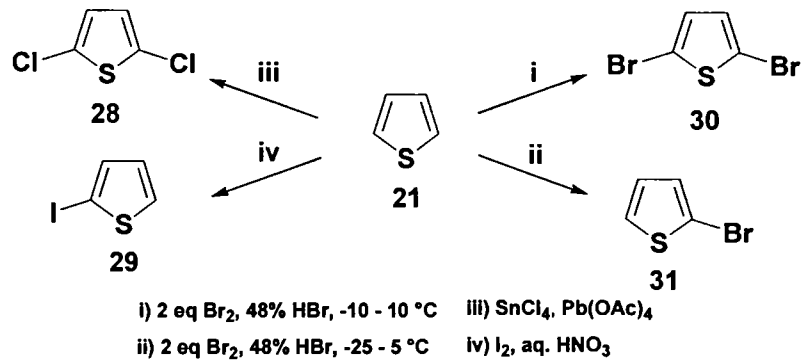


Figure 8. ^1H NMR spectrum of **27**

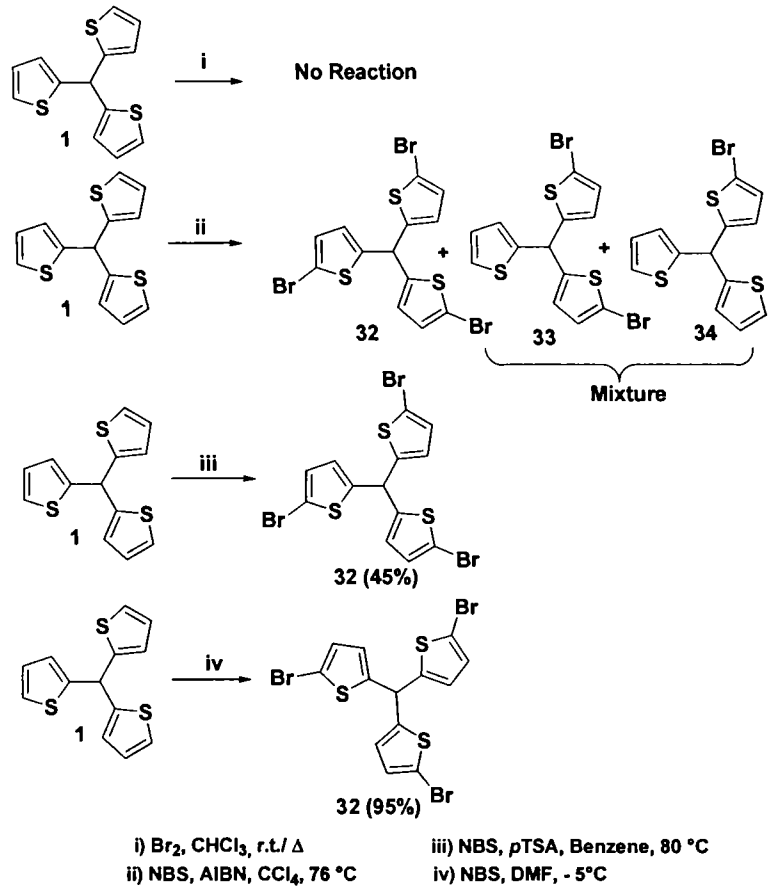
iii) Halogenation Reaction

The rate of halogenation of thiophene, at 25 °C, is known to be about 10^8 times that of benzene.[29] Various methods available for the preparation of 2- and 2,5-halosubstituted thiophenes are shown in Scheme 11.[30]



Scheme 11

With the objective to employ tris(2-thienyl)methane **1** as the core for dendrimer synthesis, we studied halogenation reactions of the same under various conditions. In an initial attempt, tris(2-thienyl)methane **1** was treated with Br_2 in $CHCl_3$ at room temperature. Since no product was formed, the reaction was carried out under reflux conditions, which also did not produce the desired product. It was then decided to resort to other brominating agents and NBS was selected. In an experiment with NBS using AIBN as the radical initiator, an inseparable mixture of mono-, bis- and tris- bromo derivatives of tris(2-thienyl)methane **1** was formed. In a modified procedure, tris(2-thienyl)methane **1** in refluxing benzene was treated with NBS in the presence of *p*TSA which afforded tris(5-bromo-2-thienyl)methane **32** in 45% yield. In order to improve the yield of the product tris(5-bromo-2-thienyl)methane **32**, another strategy was employed, wherein, to a stirred solution of tris(2-thienyl)methane **1** in DMF at –5 °C, a solution of NBS in DMF was added slowly. The reaction afforded tris(5-bromo-2-thienyl)methane **32** in 95% yield (Scheme 12).

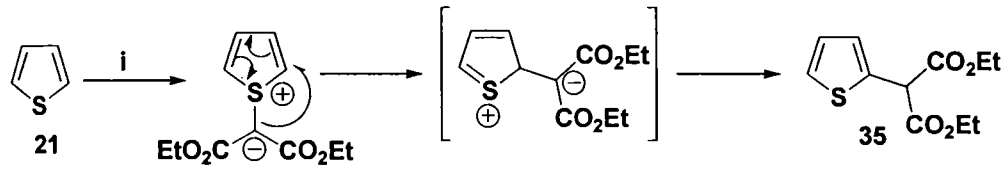


Scheme 12

The structure elucidation of tris(5-bromo-2-thienyl)methane **32** was done using spectroscopic techniques. The ^{1}H NMR spectrum of **32** exhibited a signal at δ 5.71 corresponding to the central proton, while the ring proton signals were seen as two separate doublets around δ 6.66 (J = 3.7 Hz) and δ 6.87 (J = 3.7 Hz). The ^{13}C NMR spectrum was also in agreement with the proposed structure.

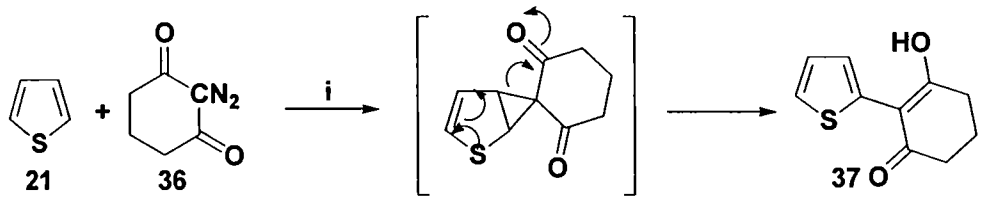
iv) Reaction with Electrophilic Carbenes

Thiophenium ylides, obtained from the reaction between thiophene and carbenes, on subsequent rearrangement yield 2-substituted thiophene (Scheme 13).[31]



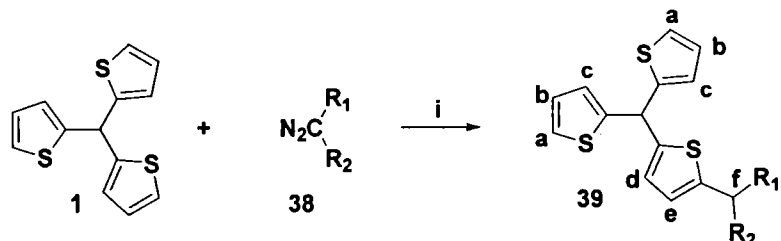
Scheme 13

Cyclic carbenes also react with thiophenes and the reaction is considered as involving a cyclopropane intermediate to form product (Scheme 14).[32]



Scheme 14

In order to exploit the reactivity of electrophilic carbenes towards tris(2-thienyl)methane **1**, some reactions with cyclic as well as acyclic carbenes were performed. In a typical experiment, tris(2-thienyl)methane **1** and the carbene precursor were taken in benzene to which rhodium(II) acetate was added under reflux conditions. In the case of acyclic carbenes, the reaction afforded products **39a-d** with only one of the rings participating in the reaction (Scheme 15).



a R_1 = R_2 = CO_2Et	37%
b R_1 = R_2 = CO_2Me	40%
c R_1 = H, R_2 = CO_2Et	45%
d R_1 = R_2 = COMe	39%

i) $Rh_2(OAc)_4$, Benzene, 80 °C

Scheme 15

The structure of the compound **39a** was ascertained by spectral analysis. IR spectrum exhibited a sharp absorption peak at 1733 cm^{-1} corresponding to the carbonyl group. In the ^1H NMR spectrum (Figure 9), protons of the carboethoxy group appeared at δ 1.29 as a triplet (3H) and around δ 4.23 as a multiplet (2H). The signal due to the resonance of protons **f** was seen at δ 4.76. The central proton appeared as a broad singlet at δ 6.07 while proton **e** was discernible at δ 6.76 (J = 3.4 Hz) as a doublet. Protons **b** and **d** resonated together as a multiplet centered at δ 6.93. Protons labelled **a** were seen as a multiplet around δ 7.19. Satisfactory ^{13}C NMR and HRMS values were also obtained for these compounds.

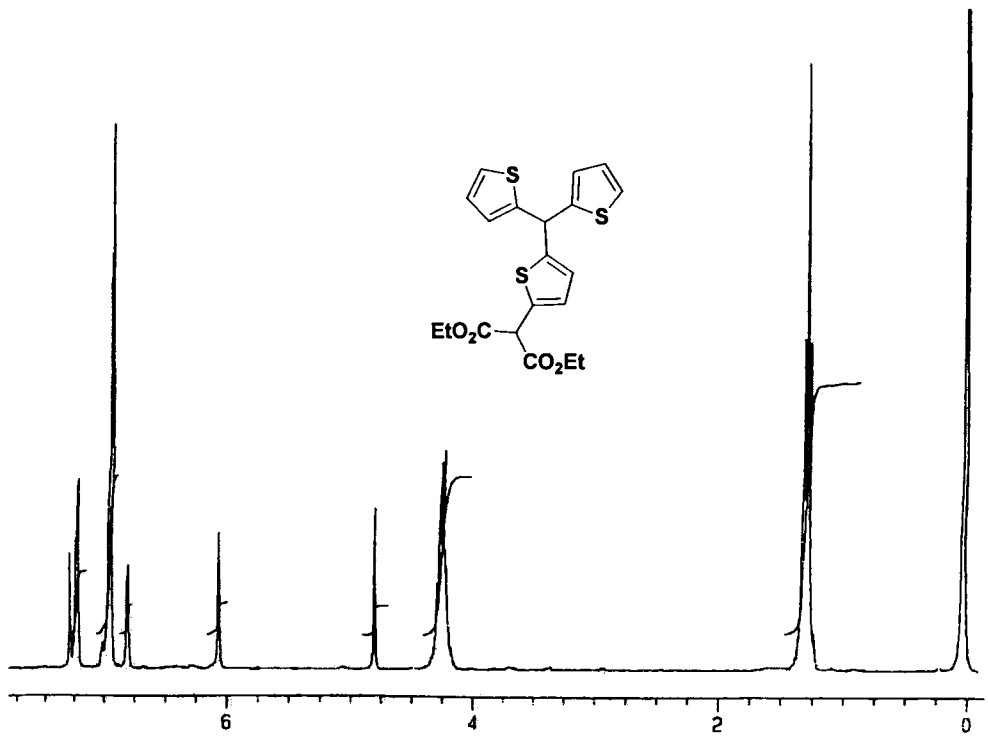
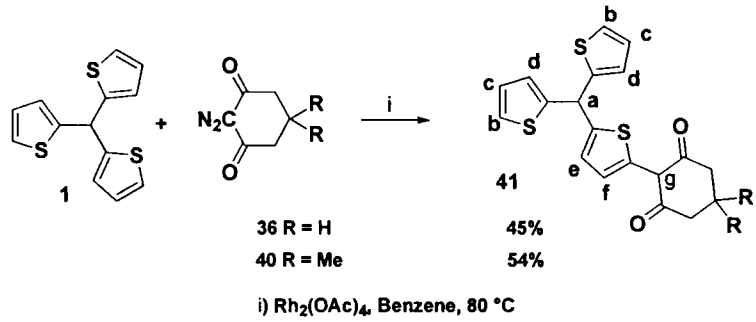


Figure 9. ^1H NMR spectrum of **39a**

Similar reactivity pattern was observed with cyclic carbenes **40a** and **b** also (Scheme 16). The reaction afforded products **41a** and **b** with only one of the rings participating in the reaction.



Scheme 16

The structure of the compound **41a** was elucidated on the basis of spectral analysis. A sharp peak displayed at 1740 cm^{-1} was attributed to the carbonyl absorption. In the ^1H NMR spectrum of **41a**, the methylene protons were seen together as a multiplet centered at δ 2.01. The proton labelled **g** and the central proton labelled **a** were discernible as two separate singlets at δ 4.20 and δ 6.05. The signal due to protons **e** and **f** were seen at δ 6.56 as a doublet (J = 3.4 Hz) and at δ 6.81 as a broad singlet. Protons **c** and **d** were together seen centered at δ 6.91 as a multiplet and the protons labelled **b** were discernible at δ 7.18 (m). In the ^{13}C NMR spectrum, the carbonyl peak appeared at δ 192.4. HRMS value was also in accordance with the assigned structure. Similar spectroscopic data were obtained for **41b** also.

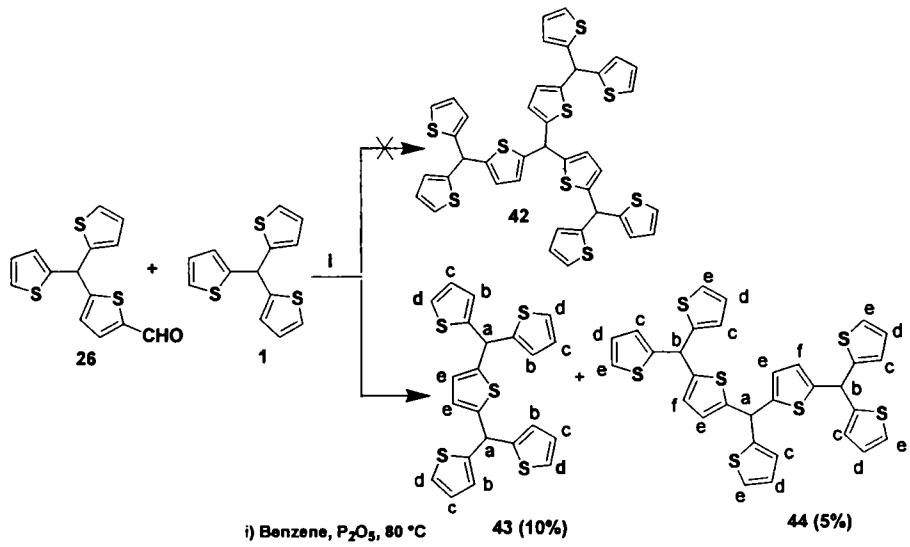
2.3.2 Synthetic Approaches Towards Dendrimers

Polyaryl ether and polyaryl alkyne based dendrimers are well-studied in the literature.[33] Some of the other functional core moieties used for the synthesis of dendrimers include crown ethers, calixarenes and cyclodextrins.[34] Because of the unique and well defined macromolecular structure, dendrimers are attractive tools for a variety of high end applications, *viz.* medicinal chemistry, supramolecular chemistry, catalysis etc.[35] Most of the well established dendrimers are comprised of benzene moieties whereas heteroaromatic compounds have found only limited application in dendrimer chemistry (Chapter 1, Section 1.2.5).[11]

In view of generating dendrimers from tris(2-thienyl)methane, we have undertaken some investigations wherein two types of divergent approaches were attempted *viz.*, i) nucleophilic addition reaction and ii) palladium-catalyzed reactions. Details of these investigations are discussed in the following sections.

2.3.2.1 Nucleophilic Addition Reactions

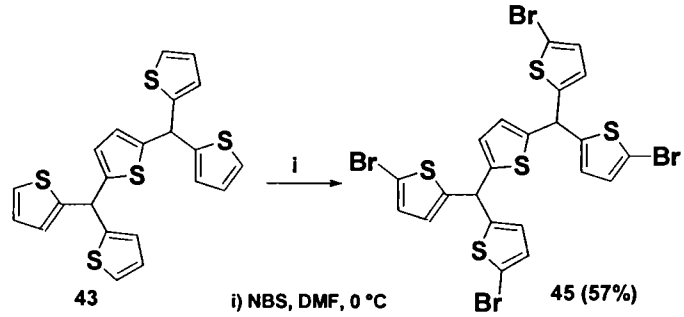
Tris(2-thienyl)methane was readily prepared from thiophene-2-carbaldehyde and thiophene *via*, a condensation reaction.[21] Intrigued by the possibility of adapting this reaction for the generation of dendrimers like **42**, the aldehyde **26** was heated with tris(2-thienyl)methane **1** in benzene in the presence of P_2O_5 at 80 °C. Interestingly, although **42** was not formed, two products **43** (10%) and **44** (5%) were obtained as shown in Scheme 17.



Scheme 17

The structure elucidation of compounds **43** and **44** was done using spectroscopic techniques. In the ^{1}H NMR spectrum of **43** (Figure 10), protons labelled **a** resonated together as a singlet at δ 5.98. The two protons **e** of thiophene at the center, were seen together at δ 6.70 as a broad singlet. Other aromatic protons were discernible at δ 6.88-6.91(m) and δ 7.17 (dd, J_1 = 1.4 Hz, J_2 = 3.4 Hz). The ^{13}C

NMR spectral data and HRMS value were also in agreement with the assigned structure. The structure of compound **43** was finally confirmed by single crystal X-ray analysis (Figure 11) of the corresponding bromoderivative **45** (Scheme 18).



Scheme 18

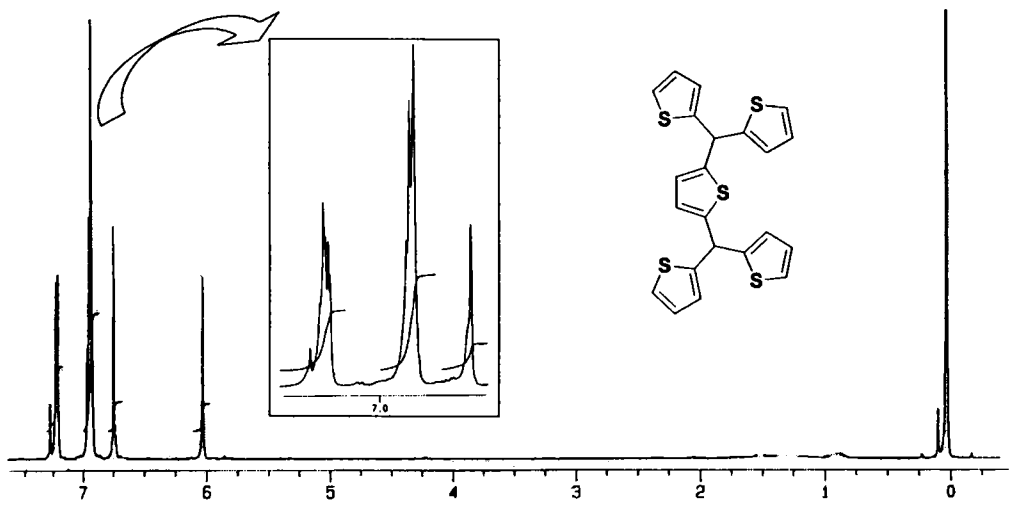


Figure 10. ^{1}H NMR spectrum of **43**

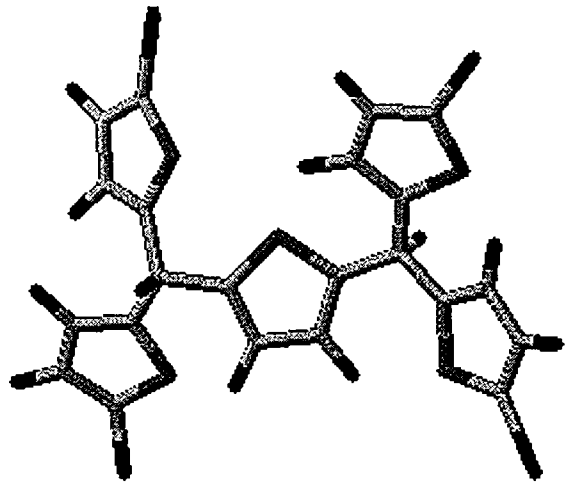


Figure 11. Single crystal X-ray structure of **45**

The structure of the second compound **44** was elucidated by comparing its spectral data with that of **43**. In the ^{1}H NMR spectrum (Figure 12), two singlets seen at δ 5.90 and δ 5.99 were assigned to the resonance of protons **a** and **b**. The signal due to protons **f** and **g** appeared as a broad singlet at δ 6.69 (4H). The signals of protons labelled **c** and **d** resonated together at δ 6.89-6.92 (m, 10H), while proton **e** was discernible at δ 7.18 (J_1 = 1.3 Hz, J_2 = 4.4 Hz, 5H). Satisfactory ^{13}C NMR spectrum and HRMS data were obtained for this compound also.

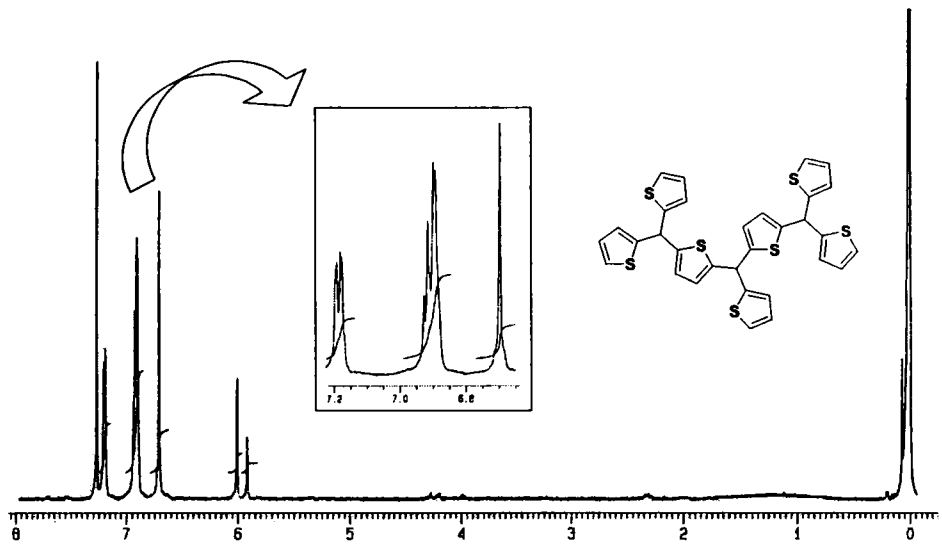
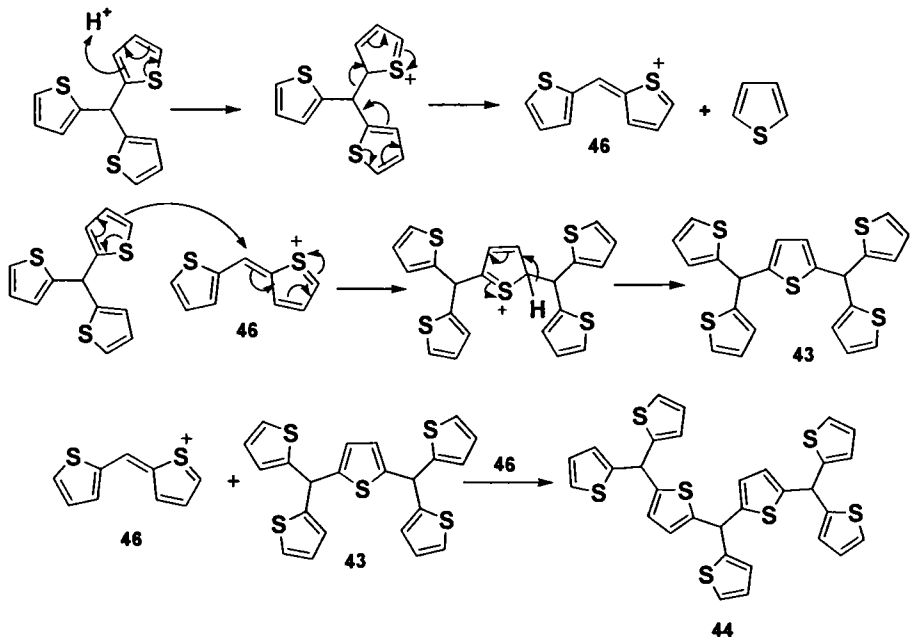


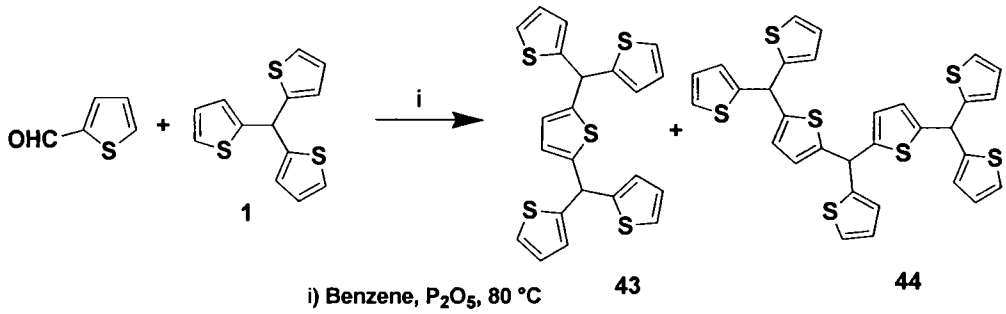
Figure 12. ^{1}H NMR spectrum of **44**

A probable mechanistic pathway for the formation of products can be as represented in Scheme 19. The initial event may be the acid catalyzed fragmentation of tris(2-thienyl)methane to an intermediate **46** as shown in the scheme 19. The species **46** can react with another molecule of the tris(2-thienyl)methane affording the product **43**. The other product **44** may be formed presumably *via* the reaction between the species **46** and product **43**. The monoaldehyde **26** used in the reaction can also fragment in a similar way.



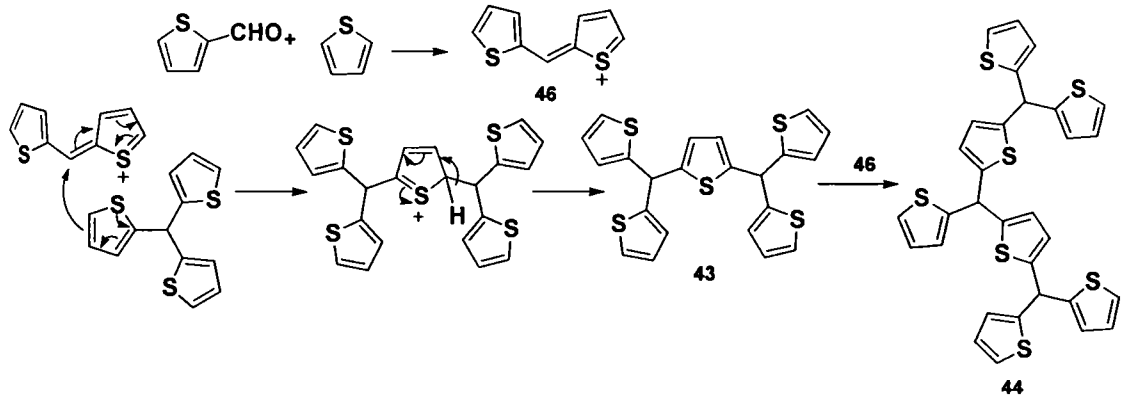
Scheme 19

The proposed mechanism implies that the compounds **43** and **44** would arise from a similar reaction between thiophene-2-carbaldehyde and tris(2-thienyl)methane **1**. This was attested by the formation of **43** and **44** in 18% and 9% yields respectively, when **1** and thiophene-2-carbaldehyde were treated with P_2O_5 in benzene (Scheme 20).



Scheme 20

Intrigued by these results, finally we revisited the synthesis of tris(2-thienyl)methane and surprisingly, we were able to isolate compound **43** from that reaction also. The following mechanism proposed, would rationalize the formation of all the three products from the reaction between thiophene-2-carbaldehyde and thiophene. The intermediate **46** initially formed, facilitates the formation of tris(2-thienyl)methane, **43** and **44** (Scheme 21).



Scheme 21

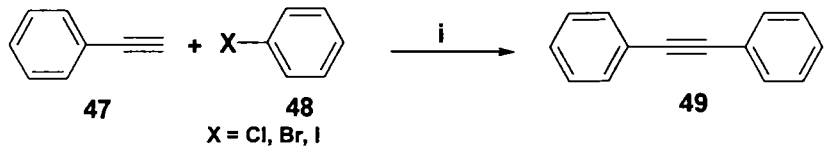
2.3.2.2 Palladium Catalyzed Reactions

i) Introduction

Reactions mediated by organometallic reagents play an important role in organic synthesis. Because of the high yields of the products and the tolerance towards various functional groups, they are superior to other reagents and hence these are used extensively in creating dendritic architecture. As there is not much

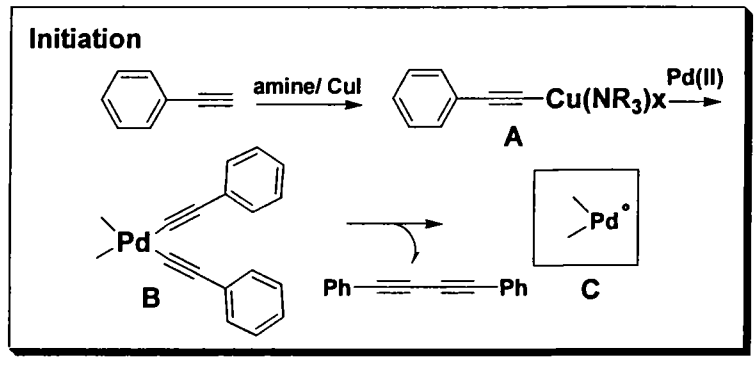
known about the synthesis and chemistry of thiophene based dendrimers, we have probed the feasibility of some reactions to prepare tris(2-thienyl)methane based dendrimers. During the various stages of the synthesis, different palladium reagents were used. Details of the work are presented in the following sections.

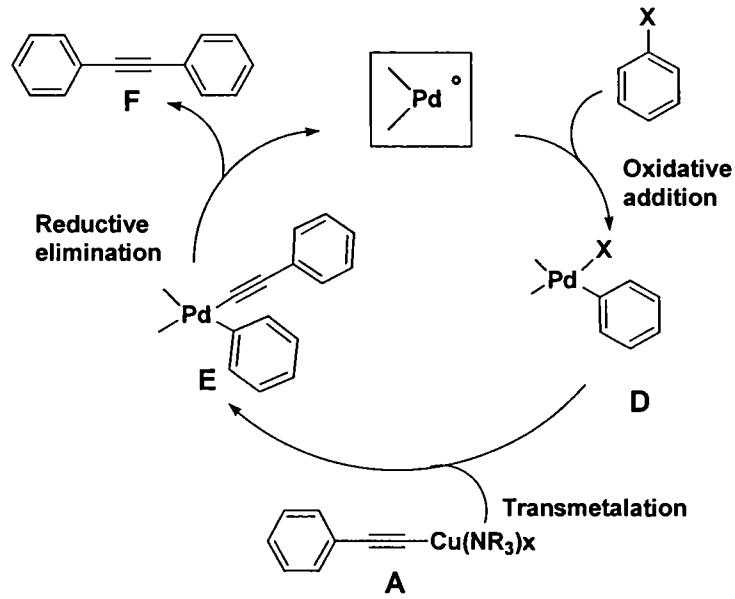
In the realm of alkyne chemistry, one of the most significant developments over the last 30 years is the palladium-catalyzed cross-coupling between vinyl/aryl halides and terminal acetylenes in the presence of Cu(I) generally known as the Sonogashira coupling reaction (Scheme 22).[36] This reaction also known as Heck-Cassar-Sonogashira-Hagihara reaction is an exceptionally powerful C-C bond forming reaction in organic chemistry. A carbon-carbon bond can be formed between an sp and an sp^2 center using this protocol.



Scheme 22

The generally accepted mechanism for the formation of the coupled product is shown in Scheme 23. In the initial step, two molecules of cuprate alkyne **A**, transmetalate the palladium catalyst precursor to form **B** which being highly unstable, reductively eliminates a symmetrical butadiyne and generates the active catalyst **C**.





Catalytic cycle

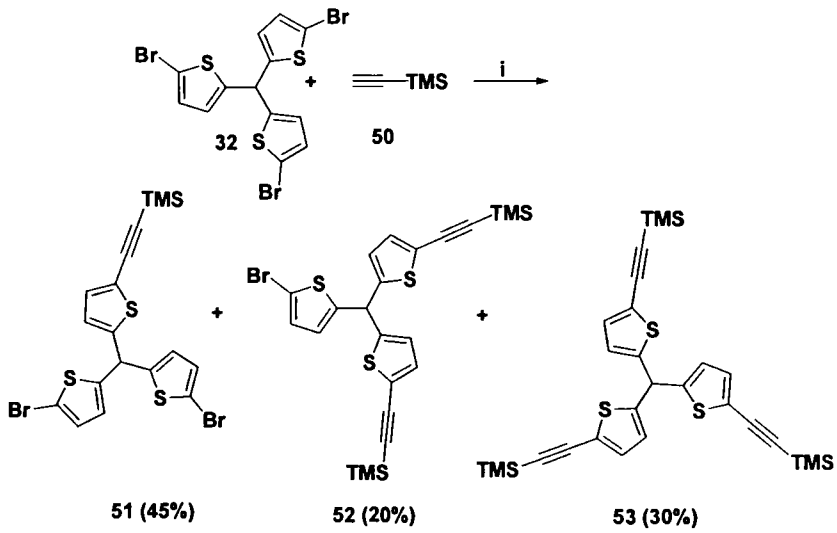
Scheme 23

In an oxidative addition, the aromatic halide forms the intermediate **D**, which in turn transmetalates with **A**, leading to a palladium species **E**. The latter on reductive elimination yields the product **F** and the active catalyst is regained to continue the catalytic cycle. Since 1975, extensive research has been going on in this area thus leading to new methodologies for more facile procedures, improved metal acetylide coupling partners and more active palladium catalysts for cross-coupling reactions.[37]

Heck-Cassar-Sonogashira-Hagihara reaction is used for the preparation of a large number of conjugated systems. Many of these systems find applications in semiconductor devices and in the design of materials for application in electronic and photonic devices.[4-6] Acetylene conjugated oligothiophenes are proposed as potential molecular wires in molecular scale devices.[38]

ii) Results and Discussion

Our attempts to synthesize thiophene dendrimers commenced by the palladium catalyzed coupling reaction between tris(5-bromo-2-thienyl)methane **32** and trimethylsilylacetylene **50** in presence of $Pd(PPh_3)_2Cl_2$, CuI and PPh_3. Di-isopropylamine was the base selected for the sp-sp^2 coupling reaction. The reaction afforded three products, mono- (**51**), bis- (**52**) and tris- (**53**) trimethylsilylacetylated derivatives in 45%, 20% and 30% yields respectively (Scheme 24).



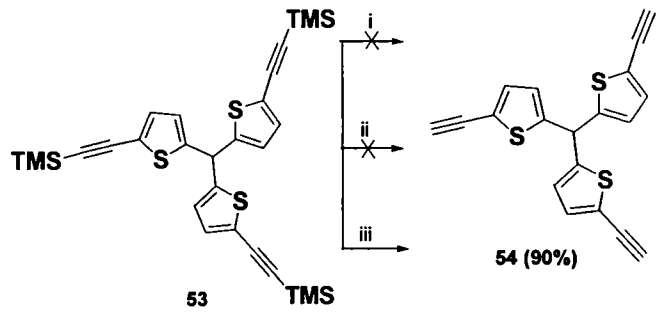
i) $PdCl_2(PPh)_3$, CuI, PPh_3, DIPA, Toluene, r.t.

Scheme 24

The structures of these compounds were confirmed using spectroscopic techniques. ^1H NMR spectrum of **53** exhibited a signal at δ 0.21 corresponding to the protons of TMS group; the central proton was discernible as a singlet at δ 5.88. Two sets of aromatic ring protons appeared as doublets at δ 6.73 (J = 3.5 Hz) and 7.02 (J = 3.5 Hz) respectively. ^{13}C NMR spectral values were also consistent with the assigned structure. Methyl carbon attached to silicon atom was discernible at δ −1.6 while the quaternary carbon at the center was seen at δ 43.0. The carbons of the triple bonds appeared at δ 89.4 and 97.4 respectively. The ring carbons were seen at

δ 123.4, 125.7, 132.1 and 147.5. The structures of the compounds **51** and **52** were also established on the basis of NMR spectral data. In the ^{1}H NMR spectrum of **52**, protons of the two TMS groups appeared together as a singlet at δ 0.21. The central proton signal was seen at δ 5.85 and the protons of the thiophene ring on which bromine is attached appeared at δ 6.64 (J = 3.7 Hz) and 6.86 (J = 3.7 Hz) as two sets of doublets while the protons of the ring carrying TMS group were observed at δ 6.75 (J = 3.6 Hz) and 7.03 (J = 3.6 Hz) as doublets.

The compound **54** appeared attractive from the vantage point of building more complexity *via* further coupling reactions. In view of this, and in order to activate the system for the contemplated coupling reactions, it was necessary to desilylate it. The reagents usually used for the deprotection of TMS groups are i) TBAF in THF[39] and ii) K_2CO_3 in methanol,[40] however these reagents failed to form the desired products. The expected product was obtained in excellent yields using the KF[41] mediated deprotection reaction carried out in methanol (Scheme 25).

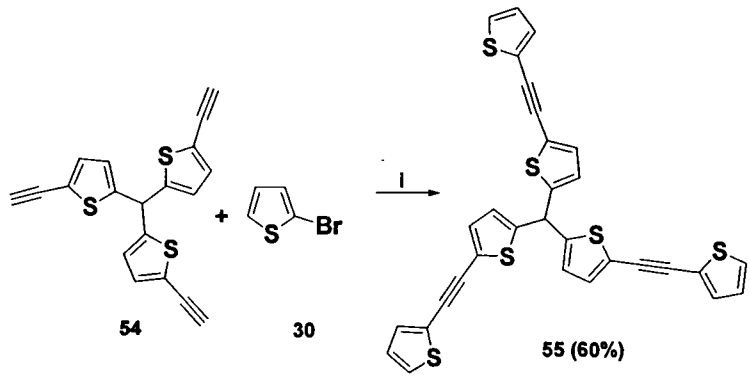


Scheme 25

Structure elucidation of **54** was based on spectral analysis. The IR spectrum exhibited a sharp signal at 3295 cm^{-1} due to the terminal acetylene C-H stretching. In the ^{1}H NMR spectrum, acetylenic protons were discernible as a singlet at δ 3.26 while another singlet at δ 5.90 corresponds to the central proton. Doublets which appeared at δ 6.77 (J = 3.6 Hz) and 7.09 (J = 3.6 Hz) were assigned to the ring

protons. In the ^{13}C NMR spectrum of **54**, a signal at δ 43.0 was attributed to the central carbon while signals at δ 81.8 and 109.7 were assigned to the resonance of the acetylenic carbons.

The three acetylenic groups of **54** were subjected to another Sonogashira coupling reaction with 2-bromothiophene. $Pd_2(dba)_3.CHCl_3$ was selected as the catalyst for this particular coupling reaction. The reaction afforded the product **55**, in which all the acetylenes were coupled to thiophene, in the form of a viscous liquid in 60% yield (Scheme 26).



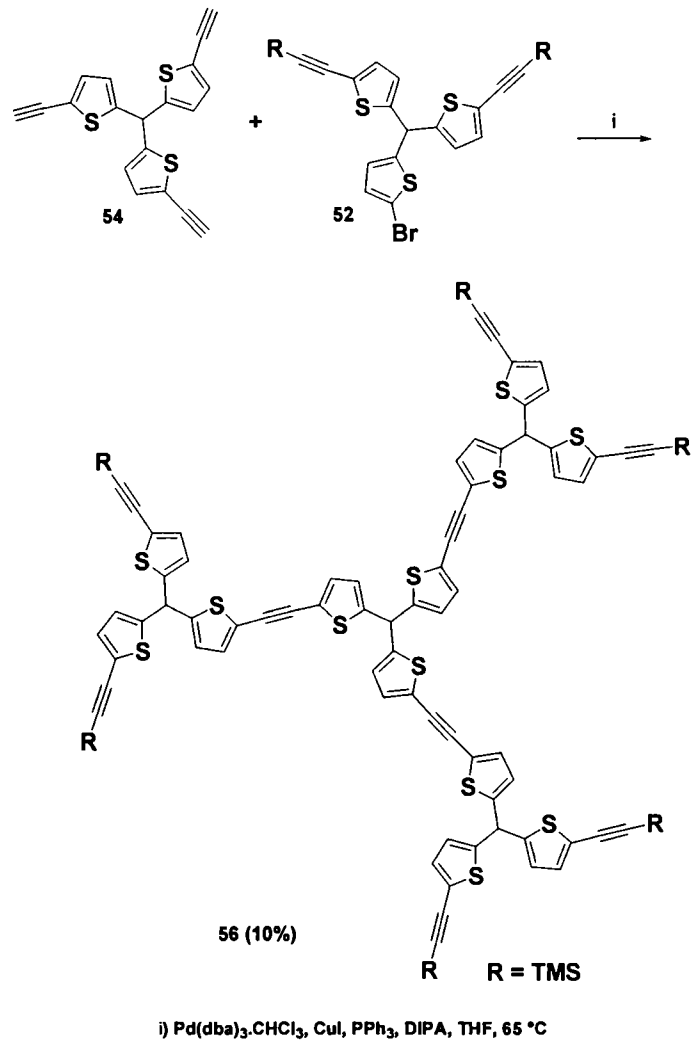
i) $Pd(dba)_3.CHCl_3$, CuI, PPh_3, DIPA, THF, 65 °C

Scheme 26

NMR spectral data of **55** was consistent with the proposed structure. In the ^1H NMR spectrum, the central proton appeared at δ 6.01 as a singlet. The ring protons were seen at δ 6.82 (d, J = 3.7 Hz, 2H), 6.94 (m, 5H), 7.01 (d, J = 3.8 Hz, 3H) and 7.23 (m, 5H). In the ^{13}C NMR spectrum, the central carbon was seen at δ 43.1 and the acetylenic carbons were discernible at δ 89.3 and 106.7. The signals at δ 113.2, 117.0 and 120.2 were attributed to the acetylene linked carbons of the thiophene rings. The other carbons of the thiophene rings were seen at δ 125.9, 126.1, 126.9, 127.4, 131.6, 131.9 and 133.0. HRMS data was also in agreement with the assigned structure.

Since the second Sonogashira coupling reaction was also successful, attempts were made to synthesize a dendrimer using **54** as the core moiety and **52** as the next

coupling unit. Under the usual conditions for the coupling reaction, the product **56** was obtained in 10% yield (Scheme 27).



Scheme 27

^{1}H NMR spectrum of **56** (Figure 13) was in agreement with the proposed structure. TMS protons were discernible at δ 0.21. The four methine protons of each tris(2-thienyl)methyl systems appeared as two singlets. The methine proton at the innermost system (core) appeared at δ 5.85 and the other three methine protons resonated together at δ 5.92. The protons of the thiophene rings were seen as multiplets centered around δ 6.74, 6.91, 7.03 and 7.21.

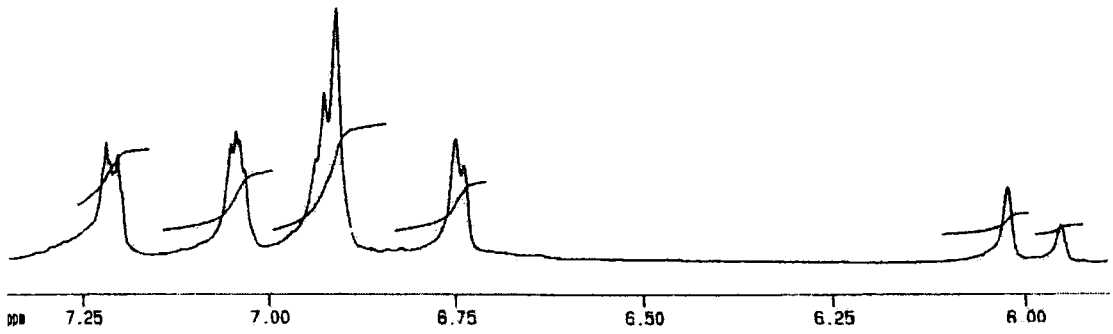
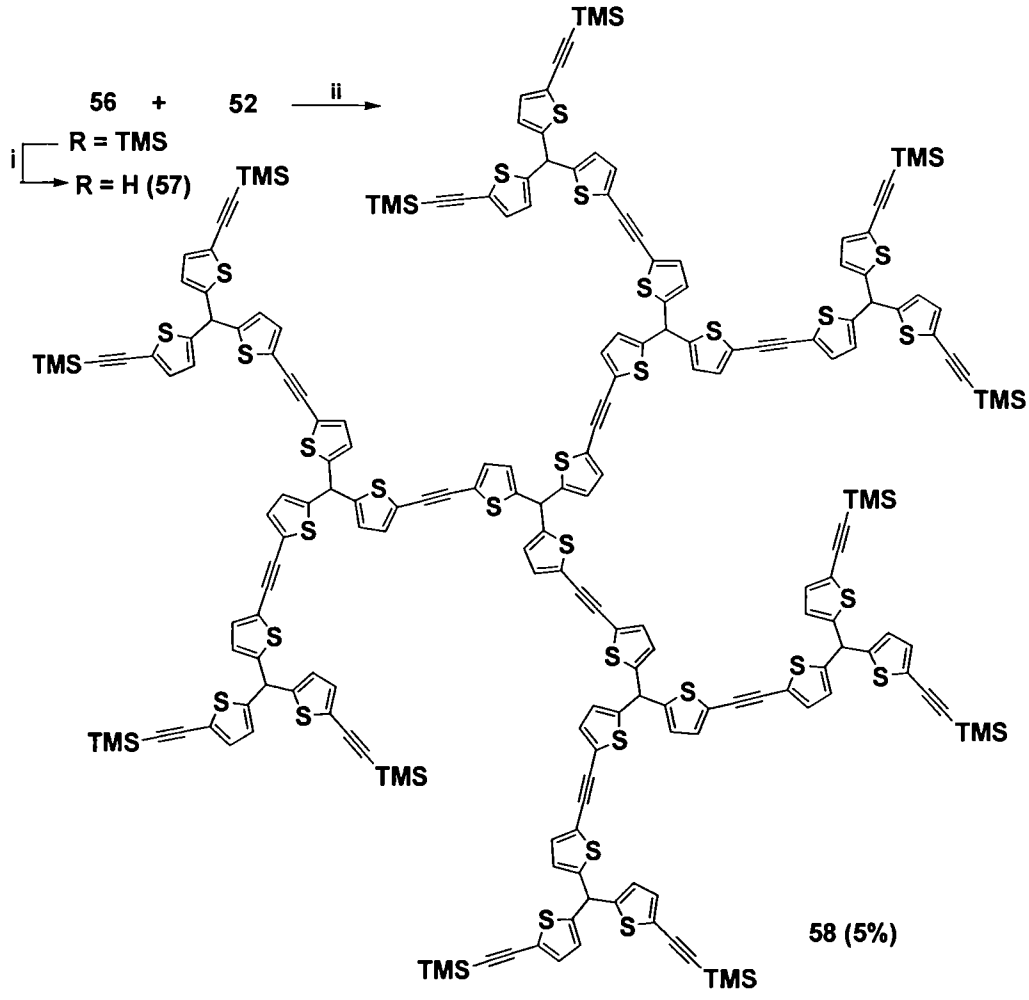


Figure 13. ^{1}H NMR spectrum of **56***

^{13}C NMR spectral signals were also in good agreement with the assigned dendritic structure. Carbons attached to the TMS moiety appeared at δ-0.1 while the central carbons were seen at δ42.7 and 42.8. Acetylenic carbons were discernible at δ96.1, 96.7, 97.5, 98.8 and 99.1. All the other signals were in accordance with the assigned structure.

After the successful synthesis of the first generation dendrimers, we extended this protocol to the next generation. The desilylated compound (**57**) corresponding to **56**, was treated with **52** in the presence of Pd(0) catalyst and as expected the reaction afforded the second generation dendrimer **58** in 5% yield (Scheme 28).

* The broadening of the peaks in the ^{1}H NMR may be due to the propellar shape of the tris(2-thienyl)methyl moeity.



Scheme 28

The structure of the compound **58** was assigned on the basis of ^{1}H NMR and ^{13}C NMR spectroscopic techniques. ^{1}H NMR spectrum of the compound is shown in Figure 14. The inner most methine proton was discernible at δ 6.09 and the other methine protons appeared together as a singlet at δ 5.92. The other ring protons resonated at δ 6.64 (d, J = 3.6 Hz), 6.75 (d, J = 3.6 Hz), 6.86 (d, J = 3.6 Hz), 6.91-

6.93 (m), 7.04 (d, J = 3.6 Hz), 7.18-7.23 (m). ^{13}C NMR spectral data obtained were also in good agreement with the proposed structure.‡

Figure 14. ^{1}H NMR spectrum of **58**

2.4 Conclusions

In conclusion, we have exploited the reactivity of tris(2-thienyl)methane towards various electrophilic substitution reactions. Acylation and bromination reactions afforded products in which all the three α- positions available for reaction are substituted. In contrast to these observations, Vilsmeier formylation reaction afforded two products; in the first one only one of the α- positions of tris(2-thienyl)methane got substituted with formyl group and in the second case, in addition to the substitution at one of the rings, the methine carbon also got substituted. Reaction with acyclic as well as cyclic carbenes afforded only the monoaddition products.

For the first time, tris(2-thienyl)methane dendrimers have been synthesized by means of two different divergent approaches, i) by nucleophilic addition reaction and ii) by palladium coupling reactions of the tris(5-bromo-2-thienyl)methane. Preliminary results show that we have been successful in generating some higher

‡ The structure assignment for **56** and **58** is entirely based on NMR analysis since mass analysis lead to the fragmentation of the products. The spectral values of the products were compared with that of their starting compounds and are found to be different.

generation dendrimers having highly conjugated thiophene rings *via* the palladium catalyzed reactions on various derivatives of tris(2-thienyl)methane.

2.5 Experimental

All reactions were conducted in oven-dried glassware under an atmosphere of argon with magnetic stirring unless otherwise noted. Solvents used for experiments were distilled and dried according to procedures given in standard manuals. NMR spectra were recorded on Bruker 300 MHz FT-NMR spectrometer with samples dissolved in $CDCl_3$ - CCl_4 mixtures (7/3 v/v). Chemical shifts are reported in δ (ppm) relative to Me_4Si (^1H NMR) or $CDCl_3$ (^{13}C NMR) as internal standards. Abbreviations for NMR multiplicities are as follows: s, singlet; d, doublet; m, multiplet; dd, doublet of doublet and bs, broad singlet. Coupling constants J are reported in Hertz (Hz). IR spectra were recorded on Bomem MB Series FT-IR spectrophotometer; absorbencies are reported in cm^{-1}. High-resolution mass spectra were recorded in EI/HRMS (at 5000 resolution) using JOEL JMS 600H mass spectrometer. Melting points were recorded on Melt-temp II apparatus (Laboratory Devices, USA) and are uncorrected. Analytical thin layer chromatography was performed on glass plates coated with silica gel containing calcium sulfate as the binder; visualization was effected with a UV lamp and/or by developing in iodine. Chromatography refers to open column chromatography on silica gel (100-200 mesh). Palladium catalysts mentioned here were prepared according to the reported procedures.[42]

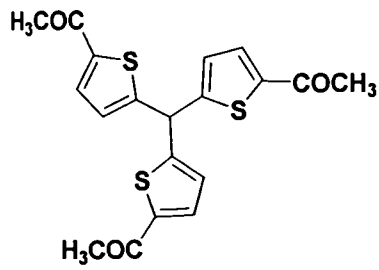
***Tris(2-thienyl)methane* 1**[22]

To a stirred solution of thiophene-2-carbaldehyde (5 g, 44.64 mmol) and thiophene (7.5 g, 89.28 mmol) in benzene (20 mL) was added P_2O_5 (15 g) in small portions. After stirring for 6 h, the crude tarry material was filtered and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel (100-200 mesh, hexane) to afford tris(2-

thienyl)methane **1** (3.85 g, 33%) as a colorless crystalline solid. m. p. 52-53 °C (lit. m. p. 50-51 °C).

***Tris(5-acetyl-2-thienyl)methane* 22**

To a solution of $AlCl_3$ (252 mg, 1.8 mmol) in CCl_4 (5 mL) was added CH_3COCl (148 mg, 1.8 mmol) slowly at 0 °C over 5 minutes. **1** (100 mg, 0.38 mmol) in CCl_4 (5 mL) was added dropwise to the reagent prepared as mentioned above. After stirring for further 30 minutes, the reaction mixture was allowed to stand *overnight and then poured into crushed ice. The organic layer was separated,* dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (20% ethylacetate in hexane) to afford pure **22** (127 mg, 86%) as a viscous pale brown liquid.



22

IR (Neat) ν_{max}: 1660, 1580, 1445, 1364, 1276, 1073, 1026, 932 cm^{-1}.

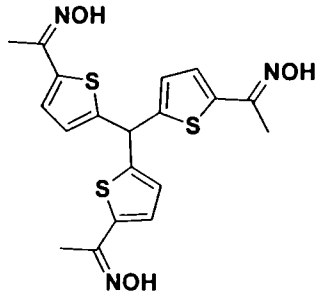
^{1}H NMR: δ 2.51 (s, 9H), 6.08 (s, 1H), 6.97 (d, J = 3.8 Hz, 3H), 7.54 (d, J = 3.8 Hz, 3H).

^{13}C NMR: δ 26.3, 43.6, 127.4, 132.1, 144.2, 153.0, 190.0.

***Oxime* 23, 24 and 25**

To a stirred solution of **22** (50 mg, 0.19 mmol) in ethanol (10 mL), sodium hydroxide (38 mg, 0.95 mmol) and hydroxylammonium hydrochloride (67 mg, 0.95 mmol) were added and refluxed for 1 h. The reaction mixture was poured into crushed ice, extracted with ethylacetate (2 X 50 mL) and processed as described previously. The crude product was purified by column chromatography on silica gel (40% ethylacetate in hexane) to afford **23** (viscous orange liquid, 41 mg, 50%). Further elution with 50% ethylacetate in hexane and 60% ethylacetate in hexane,

afforded **24** (viscous orange liquid, 8 mg, 10 %) and **25** (viscous red liquid, 9 mg, 11%).

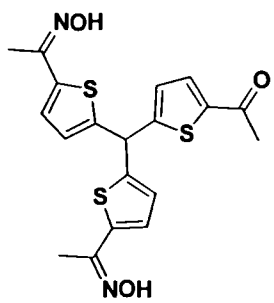


23

IR (Neat) ν_{max}: 3240, 1660, 1615, 1444, 1295, 993, 903, 818, 765 cm^{-1}.

^{1}H NMR: δ 2.19 (s, 9H), 5.85 (s, 1H), 6.80 (d, *J* = 3.7 Hz, 3H), 6.98 (d, *J* = 3.7 Hz, 3H), 10.15 (s, 3H, D_2O exchangeable).

^{13}C NMR: δ 10.5, 26.6, 41.5, 123.7, 124.7, 139.9, 145.3, 148.4.

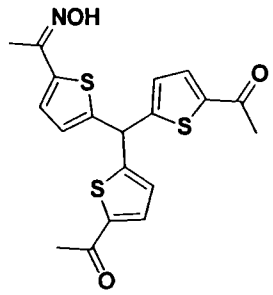


24

IR (Neat) ν_{max}: 3241, 1659, 1615, 1444, 1295, 993, 903, 818, 765 cm^{-1}.

^{1}H NMR: δ 2.17 (s, 6H), 2.59 (s, 3H), 5.91 (s, 1H), 6.78 (d, *J* = 3.9 Hz, 1H), 6.88-7.03 (m, 4H), 7.23 (d, *J* = 3.9 Hz, 1H), 10.21 (s, 2H, D_2O exchangeable).

^{13}C NMR: δ 26.4, 29.4, 124.5, 124.8, 125.0, 126.8, 127.2, 128.4, 132.3, 140.6, 145.6, 149.2, 154.3, 155.5, 190.3.



25

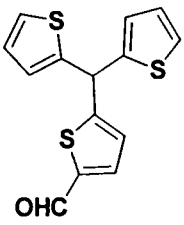
IR (Neat) ν_{max}: 3235, 1659, 1615, 1444, 1295, 993, 903, 818, 765 cm^{-1}.

^{1}H NMR: δ 2.18 (s, 3H), 2.58 (s, 6H), 5.85 (s, 1H), 6.80 (d, J = 3.7 Hz, 2H), 6.87-7.01(m, 3H), 6.98 (d, J = 3.7 Hz, 1H), 10.17 (s, 1H, D_2O exchangeable).

^{13}C NMR: δ 26.3, 30.1, 123.8, 124.8, 125.0, 126.8, 127.2, 128.4, 132.3, 140.6, 145.6, 149.2, 154.3, 190.3.

***1,1-Bis(2-thienyl)-1-(5-formyl-2-thienyl)methane* 26 and *2-{2,2-Bis(2-thienyl)}-2-(5-formyl-2-thienyl)-ethan-1-al* 27**

To a stirred solution of DMF (161 mg, 1.52 mmol) in 1,2-dichloroethane (3 mL) was added $POCl_3$ (232 mg, 1.52 mmol) at 0 °C. **1** (100 mg, 0.38 mmol) in 1,2-dichloroethane (3 mL) was introduced to the reaction mixture and stirred at room temperature for 2 h. It was then refluxed for further 2 h, cooled and poured into crushed ice. After neutralization with sodium acetate the compound was extracted using dichloromethane (2 X 50 mL). The organic layers were combined, dried over Na_2SO_4 and the solvent was removed on a rotary evaporator. The crude product was purified by column chromatography on silica gel (5% ethylacetate in hexane) to afford **26** (60 mg, 55%) as a viscous yellow liquid. Further elution with 10% ethylacetate in hexane afforded **27** (12 mg, 10%) as a viscous red liquid.

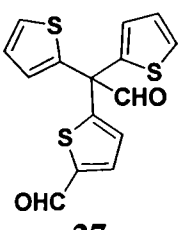


26

IR (Neat) ν_{max}: 1729, 1604, 1465, 1439, 1264, 1228, 1042 cm^{-1}.

^{1}H NMR: δ 5.89 (s, 1H), 6.94-6.96 (m, 4H), 7.02 (d, J = 3.7 Hz, 1H), 7.22-7.24 (m, 2H), 7.60 (d, J = 3.8 Hz, 1H), 10.12 (s, 1H).

^{13}C NMR: δ 43.5, 51.2, 125.8, 126.1, 127.0, 128.0, 135.9, 143.6, 155.9, 182.3.



27

IR (Neat) ν_{max}: 1725, 1665, 1522, 1444, 1221, 1053, 797 cm^{-1}.

^{1}H NMR: δ 6.99 (d, J = 3.5 Hz, 2H), 7.04-7.07 (m, 2H), 7.11 (d, J = 3.9 Hz, 1H), 7.37 (d, J = 5.1 Hz, 2H), 7.68 (d, J = 3.9 Hz, 1H), 9.93 (s, 1H), 9.98 (s, 1H)

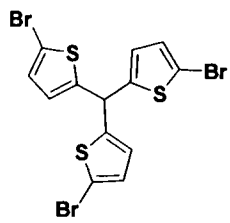
^{13}C NMR: δ 50.0, 127.1, 128.4, 129.2, 135.1, 142.7, 182.5, 189.8.

***Tris(5-bromo-2-thienyl)methane* 32**

a) To a stirred solution of **1** (50 mg, 0.19 mmol) in DMF (2 mL) was added NBS (135 mg, 0.76 mmol) in DMF (3 mL) and stirred for further 5 minutes. The reaction mixture was poured into crushed ice and the product was extracted using ethylacetate (2 X 20 mL). The organic layers were combined, dried over Na_2SO_4. The solvent was removed in vacuo and the residue was purified by column chromatography on silica gel (hexane) to afford **32** (90 mg, 95%) as a colorless crystalline solid. m. p. 72-74 °C.

b) To a stirred solution of **1** (50 mg, 0.19 mmol) and 10 mol % of PTSA in benzene (5 mL) was added NBS (135 mg, 0.76 mmol) and stirred for further 30 minutes. The solvent was removed in vacuo and the crude product was purified by

column chromatography as mentioned above to afford **32** (43 mg, 45%) as a colorless crystalline solid. m. p. 72-74 °C.



32

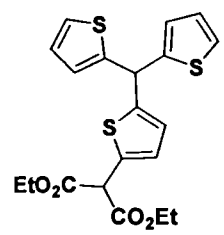
IR (KBr) ν_{max}: 3101, 2917, 2362, 1744, 1538, 1441, 1218, 1057, 971, 800, 702, 508 cm^{-1}.

^{1}H NMR: δ 5.71 (s, 1H), 6.66 (d, J = 3.7 Hz, 3H), 6.87 (d, J = 3.7 Hz, 3H).

^{13}C NMR: δ 43.3, 112.3, 126.8, 129.6, 146.8.

1,1-Bis(2-thienyl)-1-{5-diethoxycarbonyl methyl-(2-thienyl)}methane 39a

To a stirred solution of **1** (50 mg, 0.19 mmol) and **38a** (140 mg, 0.76 mmol) in benzene (5mL) was added 2 mol % of Rh(II) acetate and stirring was continued for 12 h. The solvent was removed in vacuo and the residue was purified by column chromatography on silica gel (10% ethylacetate in hexane) to afford **39a** (30 mg, 37%) as a viscous red liquid.



39a

IR (Neat) ν_{max}: 1733, 1548, 1444, 1362, 1218, 1023 cm^{-1}.

^{1}H NMR: δ 1.29 (t, J = 7.1 Hz, 6H), 4.20-4.25 (m, 4H), 4.76 (s, 1H), 6.07 (bs, 1H), 6.76 (d, J = 3.4 Hz, 1H), 6.91-6.95 (m, 5H), 7.18-7.20 (m, 2H).

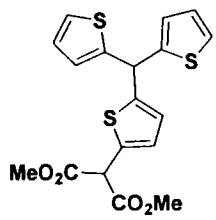
^{13}C NMR: δ 10.3, 38.0, 42.6, 52.8, 53.0, 62.0, 118.3, 124.8, 125.9, 126.5, 126.7, 127.9, 146.8, 147.8, 167.1.

HRMS (FAB, M+H): Calcd for $C_{20}H_{20}O_4S_3$: 421.06, Found: 420.42.

***1,1-Bis(2-thienyl)-1-{(5-dimethoxycarbonyl methyl)-2-thienyl}methane* 39b**

To a stirred solution of **1** (50 mg, 0.19 mmol) and **38b** (120 mg, 0.76 mmol) in benzene (5 mL) was added 2 mol % of Rh(II) acetate and stirring was continued

for 12 h. The solvent was removed in vacuo and the residue was purified by column chromatography on silica gel (5% ethylacetate in hexane) to afford **39b** (30 mg, 40%) as a viscous orange liquid.



39b

IR (Neat) ν_{max}: 1738, 1594, 1439, 1243, 1166, 1027 cm^{-1}.

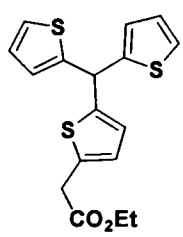
^{1}H NMR: δ 3.76 (s, 6H), 4.81 (s, 1H), 6.03 (s, 1H), 6.77 (d, J = 3.4 Hz), 7.18-7.20 (m, 5H), 7.50 (bs, 2H).

^{13}C NMR: δ 42.6, 52.8, 53.0, 118.3, 124.8, 125.9, 126.5, 126.6, 126.7, 127.4, 146.7, 148.2, 167.4.

HRMS (FAB, M+H): Calcd for $C_{18}H_{16}O_4S_3$: 393.03, Found: 392.02.

***1,1-Bis(2-thienyl)-1-{5-ethoxycarbonylmethyl-(2-thienyl)}methane* 39c**

To a stirred solution of **1** (50 mg, 0.19 mmol) and **38c** (86 mg, 0.76 mmol) in benzene (5 mL) was added 2 mol % of Rh(II) acetate and stirring was continued for 12 h. The solvent was removed in vacuo and the residue was purified by column chromatography on silica gel (5% ethylacetate in hexane) to afford **39c** (30 mg, 45%) as a viscous yellow liquid.



39c

IR (Neat) ν_{max}: 1740, 1599, 1518, 1430, 1240, 1164, 1025 cm^{-1}.

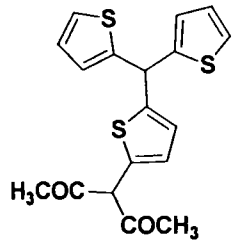
^{1}H NMR: δ 1.25-1.27 (m, 3H), 2.96-2.98 (m, 1H), 3.45-3.48 (m, 1H), 4.10-4.17 (m, 2H), 5.45 (s, 1H), 5.72 (s, 1H), 6.89-6.92 (m, 4 H), 7.20 (d, J = 4.7 Hz, 3H).

^{13}C NMR: δ 14.3, 33.5, 38.5, 42.7, 60.8, 124.7, 125.5, 125.8, 126.0, 126.2, 126.5, 126.7, 126.8, 133.6, 144.6, 144.7, 148.0, 173.0.

HRMS (FAB, M+H): Calcd for $C_{17}H_{16}O_2S_3$: 349.04, Found: 349.30.

***1,1-Bis(2-thienyl)-1-{5-diacetoxymethyl-(2-thienyl)}methane* 39d**

To a stirred solution of **1** (50 mg, 0.19 mmol) and **38d** (92 mg, 0.76 mmol) in benzene (5 mL) was added 2 mol % of Rh(II) acetate and stirring was continued for 12 h. The solvent was removed in vacuo and the residue was purified by column chromatography on silica gel (10% ethylacetate in hexane) to afford **39d** (27 mg, 39%) as a yellow viscous liquid.



39d

IR (Neat) ν_{max}: 1740, 1599, 1518, 1430, 1240, 1164, 1025 cm^{-1}.

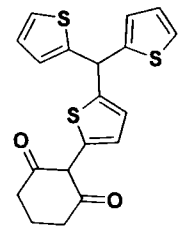
^{1}H NMR: δ 2.01 (s, 6H), 5.05 (s, 1H), 6.05 (s, 1H), 6.65 (d, J = 3.4 Hz, 1H), 6.81 (bs, 1H), 6.91-6.95 (m, 4H), 7.16-7.18 (m, 2H).

^{13}C NMR: δ 24.1, 42.8, 113.5, 124.8, 125.8, 126.1, 128.6, 192.4.

HRMS (FAB, M+H): Calcd for $C_{18}H_{16}O_2S_3$: 360.03, Found: 360.42.

***1,1-Bis(2-thienyl)-1-{5-cyclohex-2,6-dione-(2-thienyl)}methane* 41a**

To a stirred solution of **1** (50 mg, 0.19 mmol) and **36** (104 mg, 0.76 mmol) in benzene (5 mL) was added 2 mol % of Rh(II) acetate and stirring was continued for 12 h. The solvent was removed in vacuo and the residue was purified by column chromatography on silica gel (10% ethylacetate in hexane) to afford **41a** (31 mg, 45%) as a pink crystalline solid. m. p. 136-138 °C.



41a

IR (KBr) ν_{max}: 1740, 1599, 1518, 1430, 1240, 1164, 1025 cm^{-1}.

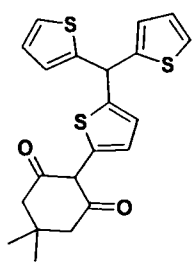
^{1}H NMR: δ 2.01 (s, 6H), 4.20 (s, 1H), 6.05 (s, 1H), 6.56 (d, J = 3.4 Hz, 1H), 6.81 (bs, 1H), 6.89-6.92 (m, 4H), 7.17-7.19 (m, 2H).

^{13}C NMR: δ 24.1, 42.8, 113.5, 124.8, 125.8, 126.1, 128.6, 192.4.

HRMS (FAB, M+H): Calcd for $C_{19}H_{16}O_2S_5$: 372.03, Found: 373.57.

***1,1-Bis(2-thienyl)-1-{5-(4-dimethyl-cyclohex-2,6-dione)-2-thienyl}methane* 41b**

To a stirred solution of **1** (50 mg, 0.19 mmol) and **40** (126 mg, 0.76 mmol) in benzene (5 mL) was added 2 mol % of Rh (II) acetate and stirred for further 12 h. The solvent was removed in vacuo and the residue was purified by column chromatography on silica gel (10% ethylacetate in hexane) to afford **58** (44 mg, 54%) as pink crystalline solid. m. p. 150-152 °C.



41b

IR (KBr) ν_{max}: 1722, 1604, 1377, 1243, 1166, 1027 cm^{-1}.

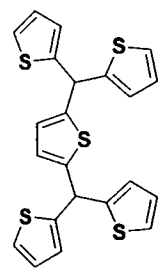
^{1}H NMR: δ 1.08 (s, 6H), 2.20 (s, 2H), 2.51 (s, 2H), 4.25 (s, 1H), 6.86 (s, 1H), 7.15-7.17 (m, 5H), 7.35 (d, J = 7.4 Hz, 1H), 7.38 (s, 2H).

^{13}C NMR: δ 28.4, 30.8, 52.5, 53.3, 68.1, 125.0, 126.9, 127.7, 127.8, 136.6, 137.6, 143.6, 203.8.

***Compounds* 43 and 44**

To a stirred solution of **26** (100 mg, 0.34 mmol) and **1** (180 mg, 0.69 mmol) in benzene (15 mL) was added P_2O_5 (10 g) in small portions over a period of 1h and refluxed for 12 h. The reaction mixture was filtered and the filtrate was concentrated

under reduced pressure. The residue was subjected to column chromatography on silica gel (hexane) to afford pure **43** (16 mg, 10%) as a red viscous liquid and **44** (10 mg, 5%) as an orange viscous liquid.



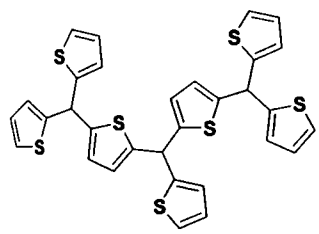
43

IR (Neat) ν_{max}: 1734, 1594, 1501, 1460, 1222, 1165, 1077, 1015, 777 cm^{-1}.

^{1}H NMR: δ 5.98 (s, 1H), 6.70 (bs, 1H), 6.88-6.89-6.91 (m, 4H), 7.17 (dd, J_1 = 1.4 Hz, J_2 = 3.4 Hz, 2H).

^{13}C NMR: δ 42.7, 124.7, 125.3, 125.8, 126.5, 146.5, 147.0.

HRMS (FAB, M+H): Calcd for $C_{22}H_{16}S_5$; 439.99, Found: 439.57.



44

IR (Neat) ν_{max}: 1736, 1590, 1505, 1466, 1220, 1165, 1077 cm^{-1}.

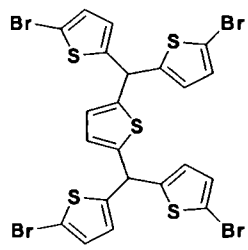
^{1}H NMR: δ 5.90 (s, 1H), 5.99 (s, 2H), 6.69 (s, 4H), 6.89-6.92 (m, 10H), 7.18 (dd, J_1 = 1.3 Hz, J_2 = 4.4 Hz, 5H).

^{13}C NMR: δ 42.9, 124.7, 125.3, 125.8, 126.5, 146.5, 147.0.

HRMS (FAB, M+H): Calcd for $C_{31}H_{22}S_7$: 617.98, Found: 618.53.

***Compound* 45**

To a stirred solution of **1** (40 mg, 0.09 mmol) in DMF (5 mL) was added NBS (80 mg, 0.45 mmol) in DMF slowly at 0 °C and stirred for 5 minutes. The product was extracted using ethylacetate (2 X 20 mL), dried over Na_2SO_4 and the solvent was removed in vacuo. The residue was purified by column chromatography on silica gel (hexane) to afford **45** (40 mg, 57%) as pale red crystalline solid. m. p. 152-154°C.



45

IR (KBr) ν_{max}: 2362, 1429, 1218, 1057, 960 cm^{-1}.

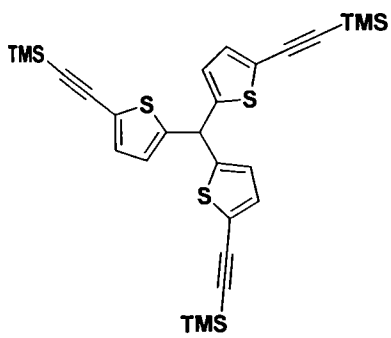
^{1}H NMR: δ 5.79 (s, 1H), 6.64 (d, J = 3.7 Hz, 2H), 6.74 (s, 1H), 6.87 (d, J = 3.7 Hz, 2H)

^{13}C NMR: δ 43.2, 125.7, 125.9, 126.2, 126.3, 129.5, 145.0, 145.8, 147.4.

HRMS (FAB): Calcd for $C_{22}H_{12}Br_4S_5$: 751.63, Found: 751.38.

***Tris{5-(2'-trimethylsilylethynyl)-2-thienyl}methane* 53, *1,1-Bis{[5-(2'-trimethylsilylethynyl)-2-thienyl]-1-5-bromo-2-thienyl}methane* 52 and *1,1-Bis{(5-bromo)-2-thienyl-1-(2'-trimethylsilylethynyl)-2-thienyl}methane* 51**

To a stirred and degassed solution of **32** (50 mg, 0.10 mmol) in toluene (4 mL), CuI (2 mol %), PPh_3 (2 mol %), and $PdCl_2(PPh_3)_2$ (10 mol %) were added followed by diisopropyl amine (40 mg, 0.4 mmol) and stirred at room temperature for 5 minutes. Trimethylsilylacetylene (40 mg, 0.40 mmol) was added to the complex formed and stirring continued for further 12 h. The reaction mixture was passed through a pad of silica gel (100-200 mesh) and the solvent was removed under reduced pressure. The residue was subjected to column chromatography on silica gel (hexane) to afford **51** (23 mg, 45%) and **52** (11 mg, 20%) a viscous yellow liquids, and **53** (15 mg, 30%) as a colorless crystalline solid. m. p. 72-74 °C.

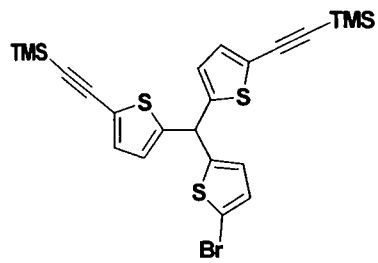


53

IR (KBr) ν_{max}: 2963, 2362, 2139, 1538, 1458, 1258, 1166, 1040, 1519 cm^{-1}.

^{1}H NMR: δ 0.21 (s, 27H), 5.88 (s, 1H), 6.73 (d, J = 3.5 Hz, 3H), 7.02 (d, J = 3.5 Hz, 3H).

^{13}C NMR: δ -1.6, 43.0, 89.4, 97.4, 99.3, 123.4, 125.7, 125.9, 132.1, 147.5.

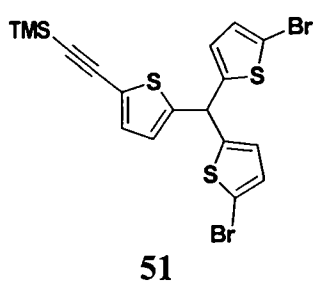


52

IR (Neat) ν_{max}: 2958, 2143, 1446, 1258, 1166, 1040, 851 cm^{-1}.

^{1}H NMR: δ 0.21 (s, 18H), 5.85 (s, 1H), 6.64 (d, J = 3.7 Hz, 1H), 6.75 (d, J = 3.6 Hz, 2H), 6.86 (d, J = 3.7 Hz, 1H), 7.03 (d, J = 3.6 Hz, 2H).

^{13}C NMR: δ -0.08, 43.1, 97.4, 116.5, 123.4, 125.9, 126.4, 129.4, 132.1, 147.2.



51

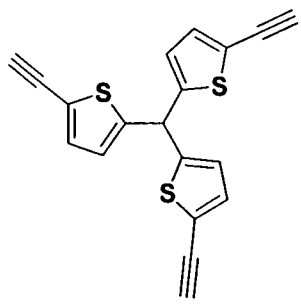
IR (Neat) ν_{max}: 2958, 2145, 2362, 1441, 1240, 1160, 966, 846, 508 cm^{-1}.

^{1}H NMR: δ 0.21 (s, 9H), 5.88 (s, 1H), 6.65 (d, J = 3.5 Hz, 2H), 6.72 (d, J = 3.5 Hz, 1H), 6.64 (d, J = 3.5 Hz, 2H), 7.02 (d, J = 3.5 Hz, 1H).

^{13}C NMR: δ -1.6, 43.0, 89.4, 97.4, 99.3, 123.4, 125.7, 125.9, 132.1, 147.5.

***Tris(5-ethynyl-2-thienyl)methane* 54**

To a solution of KF (22 mg, 0.36 mmol) in methanol (2 mL), was added a solution of **53** (50 mg, 0.09 mmol) in methanol (5 mL) and stirred for 3 h. The solvent was removed under reduced pressure and the product was extracted with ethylacetate (2 X 20 mL). The organic layers were combined, dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography on alumina (neutral, hexane) to afford **54** (27 mg, 90%) as a viscous brown liquid.



54

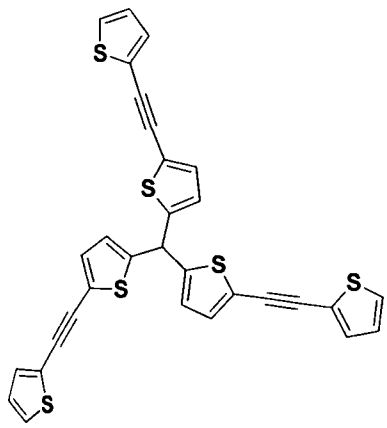
IR (Neat) ν_{max}: 3295, 1725, 1448, 1244, 1025, 806 cm^{-1}.

^{1}H NMR: δ 3.26 (s, 3H), 5.90 (s, 1H), 6.77 (d, *J* = 3.6 Hz, 3H), 7.09 (d, *J* = 3.6 Hz, 3H).

^{13}C NMR: δ -1.63, 43.0, 81.8, 89.4, 97.4, 99.3, 123.4, 125.7, 126.0, 132.1, 147.5.

***Tris{5-ethyn-2'-thienyl-2-thienyl}methane* 55**

To a degassed solution of **54** (30 mg, 0.08 mmol) in THF (4 mL), CuI (2 mol %), PPh_3 (2 mol %), and $Pd_2(dba)_3.CHCl_3$ (10 mol %) were added follwed by diisopropyl amine (8 mg, 0.08 mmol) and stirred at room temperature for 5 minutes. 2-Bromothiophene (21 mg, 0.08 mmol) was introduced to the stirred reaction mixture and it was allowed to stir for further 12 h. The reaction mixture was passed through a plug of silica gel (100-200 mesh) and the solvent was removed under reduced pressure. The residue was subjected to column chromatography on alumina (neutral, hexane) to afford **55** (28 mg, 60%) as a viscous brown liquid.



55

IR (Neat) ν_{max}: 1594, 1413, 1258, 1201,1103, 1015, 808 cm^{-1}.

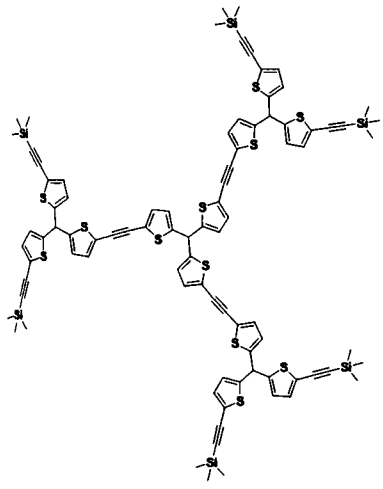
^{1}H NMR: δ 6.01 (s, 1H), 6.82 (d, J = 3.7 Hz, 2H), 6.94 (m, 5H), 7.01 (d, J = 3.8 Hz, 3H), 7.23-7.28 (m, 5H).

^{13}C NMR: δ 43.1, 89.3, 106.7, 113.2, 117.0, 120.2, 125.9, 126.1, 126.9, 127.4, 131.6, 131.9, 133.0.

HRMS (EI): Calcd for $C_{31}H_{16}S_6$: 578.9498, Found: 578.9685.

***Compound* 56**

To a degassed solution of **54** (30 mg, 0.08 mmol) in THF (4 mL), CuI (2 mol %), PPh_3 (2 mol %), and $Pd_2(dba)_3.CHCl_3$ (10 mol %) were added followed by diisopropyl amine (8 mg, 0.08 mmol) and stirred at room temperature for 5 minutes. **52** (128 mg, 0.24 mmol) was introduced into the stirred reaction mixture and it was allowed to stir for further 12 h. The reaction mixture was passed through a plug of silica gel (100-200 mesh) and the solvent was removed under reduced pressure. The residue was subjected to column chromatography on alumina (neutral, hexane) to afford **56** (13 mg, 10%) as a viscous brown liquid.



IR (Neat) ν_{max}: 2954, 2933, 2145, 1251, 1164, 1037, 850, 699, 530 cm^{-1}.

^{1}H NMR: δ 0.21 (s, 54H), 5.85 (s, 1H), 5.92 (s, 3H), 6.74-6.75 (m, 6H), 6.86-6.92 (m, 7H), 7.03-7.04 (m, 6H), 7.20-7.22 (m, 5H).

^{13}C NMR: δ - 0.4, -0.1, 42.7, 42.8, 96.1, 96.7, 97.5, 98.8, 99.1, 122.7, 123.0, 124.9, 125.1, 125.3, 125.6, 125.7, 126.0, 126.2, 126.6, 132.1, 132.2, 132.5, 146.4, 148.3, 149.2.

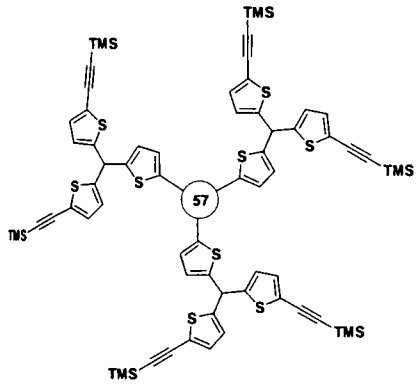
56

Compound **57**

To a solution of KF (17 mg, 0.29 mmol) in methanol (2 mL), was added a solution of **56** (50 mg, 0.03 mmol) in methanol (5 mL) and stirred for 3 h. The solvent was removed under reduced pressure and the product was extracted with ethylacetate (2 X 20 mL). The organic layers were combined, dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography on alumina (neutral, hexane) to afford **57** (32 mg, 84%) as a viscous brown liquid.

Compound **58**

To a degassed solution of **57** (30 mg, 0.02 mmol) in THF (4 mL), CuI (2 mol %), PPh_3 (2 mol %), and $Pd_2(dba)_3.CHCl_3$ (10 mol %) were added followed by diisopropyl amine (14 mg, 0.14 mmol) and stirred at room temperature for 5 minutes. **52** (74 mg, 0.14 mmol) in THF (1 mL) was introduced into the reaction mixture by a syrringe and was allowed to stir for further 12 h. The reaction mixture was passed through a plug of silica gel (100-200 mesh) and the solvent was removed under reduced pressure. The residue was subjected to column chromatography on alumina (neutral, hexane) to afford **58** (10 mg, 5%) as a viscous brown liquid.



58

IR (Neat) ν_{max}: 2953, 2932, 2143, 1250, 1161, 1030, 853, 699, 530 cm^{-1}.

^{1}H NMR: δ 0.21 (s, 108H), 5.92 (s, 10H), 6.09 (s, 1H), 6.64 (d, *J* = 3.6 Hz, 10H), 6.75 (d, *J* = 3.6 Hz, 10H), 6.86 (d, *J* = 3.6 Hz, 10H), 6.91-6.93 (m, 10H), 7.04 (d, *J* = 3.6 Hz, 10H), 7.18-7.23 (m, 10H).

^{13}C NMR: δ - 0.06, 42.9, 109.8, 111.9, 120.9, 124.7, 125.2, 125.8, 125.9, 126.2, 126.4, 126.5, 126.7, 129.3, 132.2. 146.4, 146.8, 149.2, 150.0.

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Chapter 3

Novel Reactions of Tris(2-furyl)methane

3.1 Introduction

Furan belongs to the family of five membered heterocyclic aromatic rings, and the chemistry of furan has long been an active field of research,[1] largely due to the presence of the ring system in many naturally occurring compounds, either in fully or partially reduced form. Also, furan and its derivatives have been employed as versatile building blocks in synthetic chemistry. Compounds incorporating the furan ring are of special importance in pharmaceutical, polymer and material sciences. The aromatic furan system, though not found in animal metabolism, occurs widely as a secondary plant metabolite especially in terpenoids; perilline **1** (Figure 1) is a simple example. Ascorbic acid **2** (Vitamin C), is at the level of a trihydroxyfuran, though it assumes an unsaturated lactone tautomeric form. Though thiols are normally associated with unpleasant odors, furfurylthiol **3** is present in the aroma of roasted coffee. An example of a nitroderivative which has important medicinal value is, nitrofurazone **4** (bactericide). Ranitidine **5**, used for the treatment of stomach ulcers is one of the most commercially successful drugs ever developed (Figure 1).

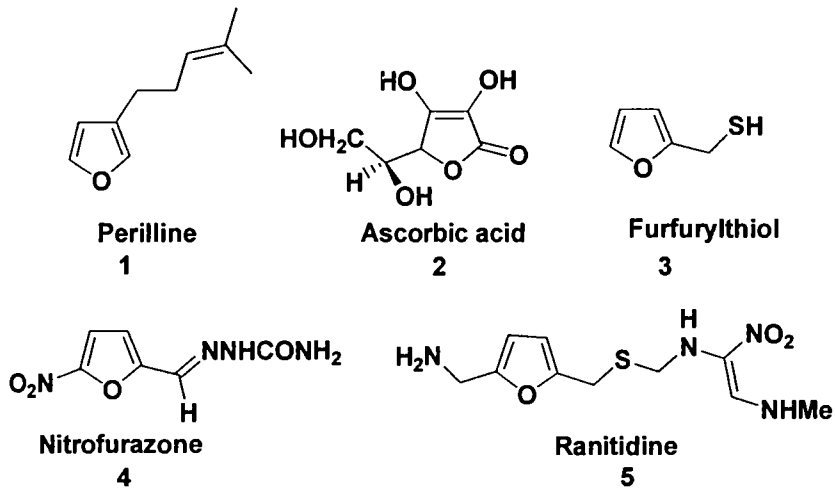


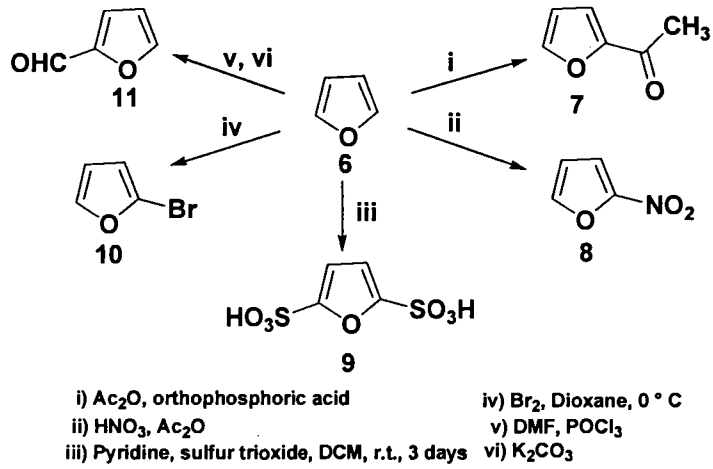
Figure 1

Since this chapter is concerned with our investigations aimed at uncovering the novel chemistry of furan and its covalent assemblies, a brief introduction to the reactions of furans in general and the synthetic strategy employed currently for the crafting of symmetric furans with relevant references are summarized as a prelude.

3.2 General Reactions of Furan

3.2.1 Electrophilic Substitution Reactions

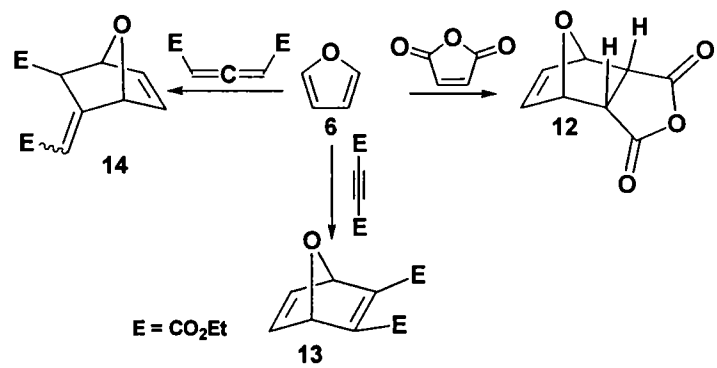
Among the five membered heteroaromatic systems with one heteroatom, *viz.*, thiophene, furan and pyrrole, furan is the 'least aromatic' and as such has the greatest tendency to react with electrophiles, preferably at the 2-position. It also undergoes facile Diels-Alder reactions. Some useful substitution reactions which can be performed easily on furan are Vilsmeier formylation,[2] acylation,[3] sulfonation,[4] halogenation[5] *etc.* (Scheme 1). On exposure to concentrated protic acids as well as Lewis acids, furan undergoes polymerization.



Scheme 1

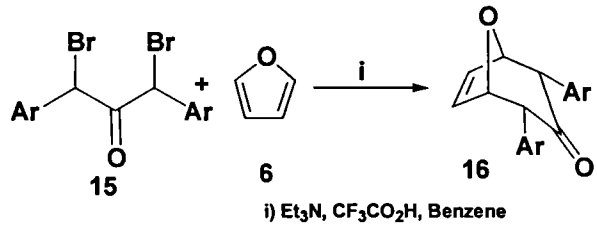
3.2.2 Cycloaddition Reactions

The proclivity of substituted furans to undergo Diels-Alder reaction presents an opportunity for rapid construction of valuable intermediates. One of the earliest examples of Diels-Alder reaction is the [4+2] cycloaddition reaction of furan with reactive dienophiles such as maleic anhydride, leading to the thermodynamically stable *exo*- isomer.[6] Notwithstanding the conclusions regarding the general mechanism of Diels-Alder reaction, inferred from furan- maleic anhydride cycloreversion kinetic data, the synthetic value of this intermolecular process is widely recognised as a means of carbon-carbon bond construction, ultimately leading to a variety of target molecules. Cycloaddition reactions of furan with allenes[7] and alkynes[8] are also well studied (Scheme 2).



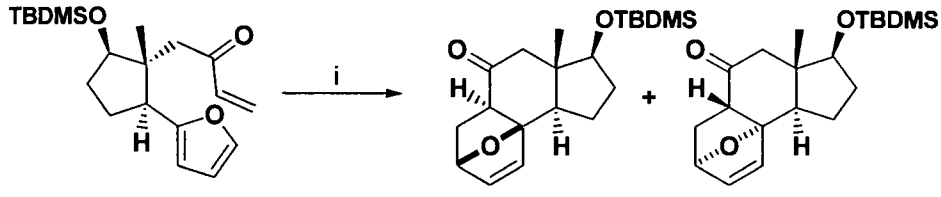
Scheme 2

Application of high pressure or the presence of Lewis acids accelerates the reaction.[9] High yields and stereoselectivity can be accomplished when ionic liquids are employed as the reaction medium.[10] Another useful protocol exploited for the synthesis of substituted furans and polycyclic materials is the [4+3] cycloaddition reaction of furan with oxyallyl cation (Scheme 3).[11] Compound **16** has been used as a precursor for the synthesis of nonactic acid, the building block of macrotetrolide antibiotic nonactin.



Scheme 3

The power of intramolecular [4+2] cycloaddition strategy has been applied to a variety of furan containing substrates.[12] De Clercq *et al.* have utilized intramolecular process to devise entries to both 11-keto steroids and functionalized gibbane skeletons. The targets were obtained *via* addition of enone **17** to the monosubstituted furan which afforded *exo*-products **18** and **19** as expected and the ratio of which was dependent on reaction conditions (Scheme 4).[13]

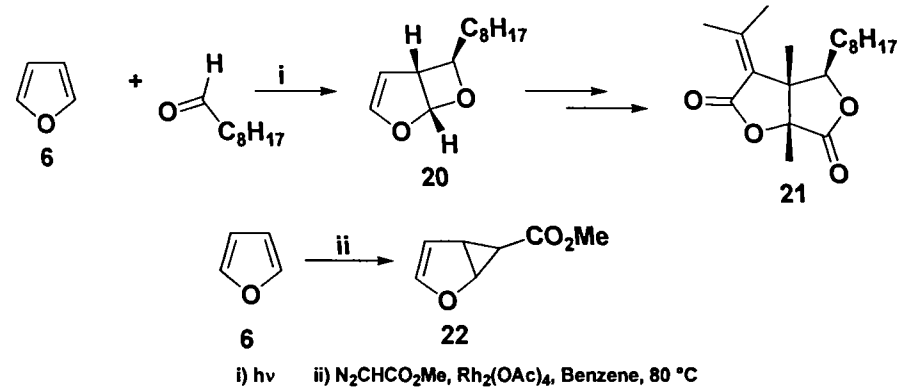


	i		
a	DCM, r.t.	1	8
b	PhH, 80° C	9	1

Scheme 4

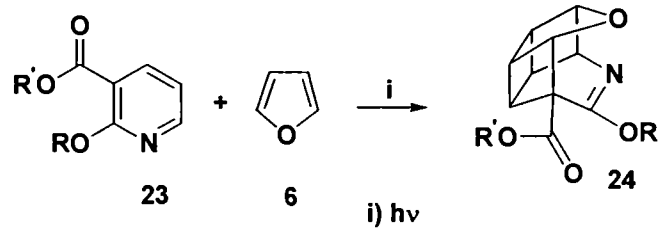
Furans occasionally act as electron-rich 2π component in cycloaddition reactions, an example being the 1,3-dipolar cycloaddition reaction of nitrile oxide to

furan.[14] The Paterno-Büchi reaction has been investigated using furan and a number of aldehydes which provide a method for the addition of enolate equivalent and thereby constitutes an easy access to *threo*-aldol products. This protocol was utilized in the synthesis of bistetrahydrofuran moiety **21**, of mycotoxin and asteltoxin.[15] The formation of cyclopropane derivatives of furan with carbenes is also a well studied reaction (e. g. compound **22** in Scheme 5).[16]



Scheme 5

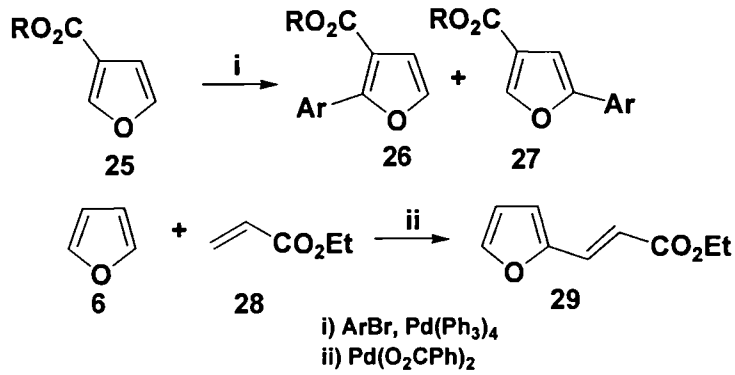
Recently Sakamoto *et al.* have shown that furan undergoes an interesting [4+4] photocycloaddition with nicotinic acid esters leading to the formation of a diastereomeric mixture of cage type adduct **24** in good yields (Scheme 6).[17]



Scheme 6

3.2.3 Metal Catalyzed Reactions

Palladium catalyzed reactions are employed to introduce aryl or alkenyl group on a furan ring at the 2-position. It has been achieved by different methods including direct substitution of hydrogen,[18] Suzuki type reactions,[19] or by Heck type reactions (Scheme 7).[20]



Scheme 7

3.3 Symmetric Furylmethanes

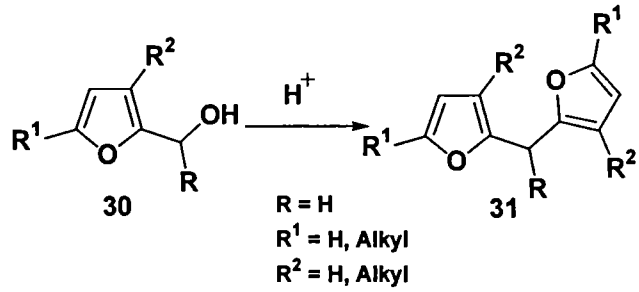
Difurylalkanes are useful as flavor agents and are important in perfume industry. They also constitute the base intermediates for macromolecular chemistry. Difurfuryl diamines can serve as curing agents for epoxy resins. In addition, they are readily converted to the corresponding difurfuryl diisocyanates, which can be used as a substitute for the petroleum-based compound diphenylmethane diisocyanate. They are excellent adhesives for the production of composite wood products.

Symmetric furans like bisfurylmethane and trisfurylmethane can be considered as potential synthons for various multi dimensional elaboration of methane, which cannot be achieved by conventional methods.

3.3.1 Bisfurylmethane

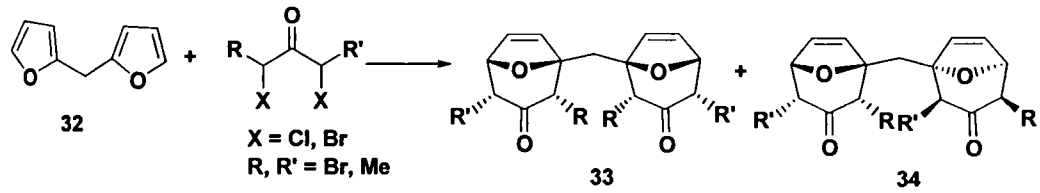
Bisfurylmethane **32** was first isolated from the mixture of products resulting from the oligomerization of furfurylalcohol in acidic medium.[21a] The diamine of bisfurylmethane series was formed as a minor product in the reaction of 5-hydroxymethylfurfurylamine with 5.1 M HCl. Hydrothermolysis of alkylfurylcarbinoles at 300 °C and at pH~7 also produced the corresponding bisfurylalkane.[21b-d] The formation of bisfurylmethane *via* these methods represent the side reaction and hence has no synthetic value. Later Stroganova *et al.* have synthesized symmetric bisfurylmethane *via* the self-condensation of furfuryl

alcohols, the most efficient method for the synthesis of symmetric bisfurylmethane.[22] Condensation was effected in the presence of acids like polyphosphoric acid, hydrochloric acid, Ag (I) ions or Cl_3CCO_2H (Scheme 8).



Scheme 8

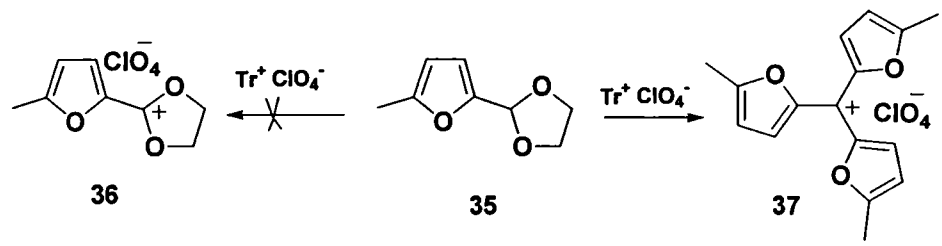
Recently, Vogel *et al.* have studied the scope and limitations of the double [4+3] cycloadditions of 2-oxyallyl cations to bisfurylmethane (Scheme 9).[23]



Scheme 9

3.3.2 Tris(2-furyl)methane

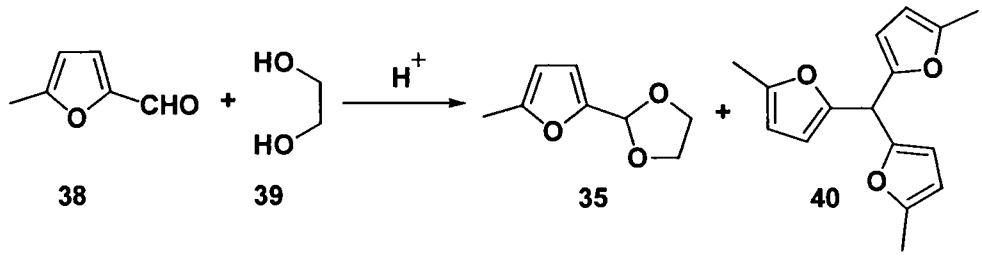
During the synthesis of dioxolanium salt **36** from 2-[5-methylfuryl 2-]-1,3-dioxolane **35**, accidently, Stroganova *et al.* have observed the formation of trifurylcarbenium perchlorate **37** in trace amounts (Scheme 10).[22]



Scheme 10

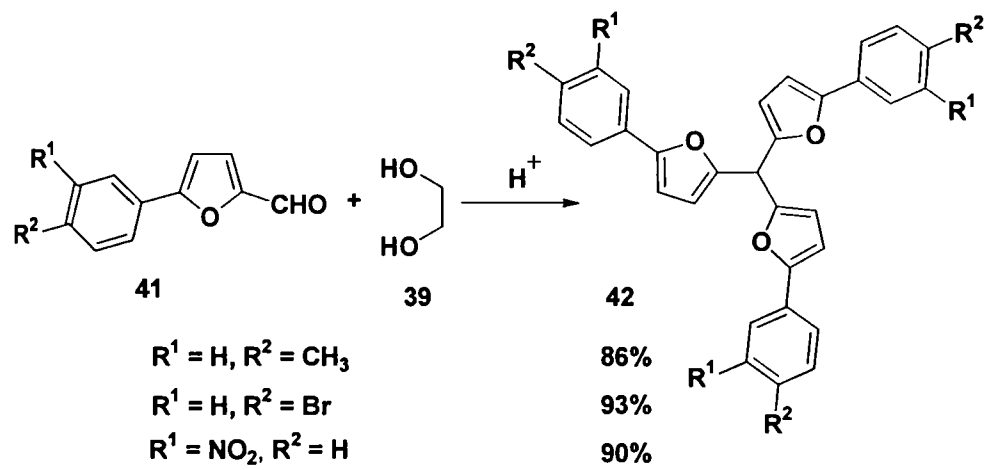
The influence of various acid catalysts on the selectivity of the reaction of furfural and ethylene glycol has been studied and it was concluded from the

experimental observations that weakly acidic catalysts like ion-exchange resins favor the formation of dioxolane **35** while strong catalysts favor the formation of trisfurylmethane **40** (Scheme 11).



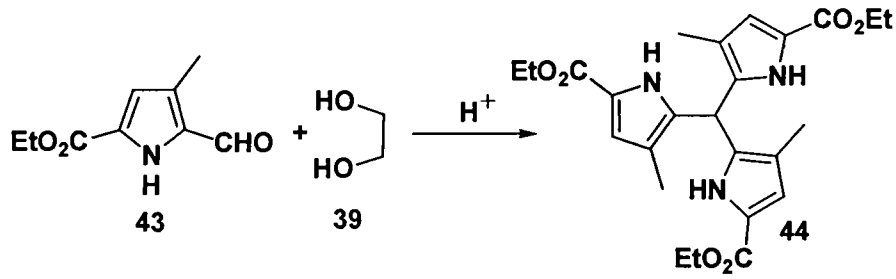
Scheme 11

Similar strategy was employed for the synthesis of tris(5-aryl-2-furyl)methane **42** which is important from the point that, 2-arylfurans are not easily accessible by traditional methods (Scheme 12). In another attempt, Riad *et al.* have synthesized tris(2-furyl)methane by the condensation of furfural with furan using macroporous ion exchange resins as catalysts.[24]



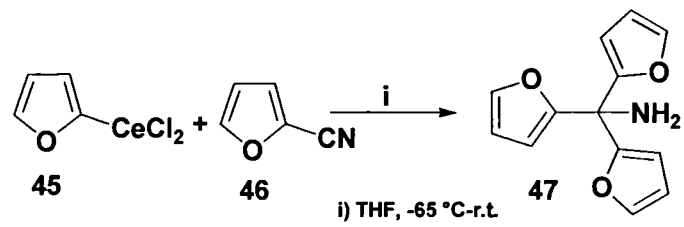
Scheme 12

Similar conversion of pyrrolic aldehyde is also known. When pyrrolic aldehyde was treated with ethylene glycol in the presence of catalytic amount of *p*-TsOH, the product obtained was tripyrrylmethane **44**, instead of the expected acetal (Scheme 13).[25]



Scheme 13

In 1992, Ciganek reported the preparation of tris(2-furyl)methylamine **47**, *via* the cerium-mediated addition to the 2-cyanofuran (Scheme 14).[26]



Scheme 14

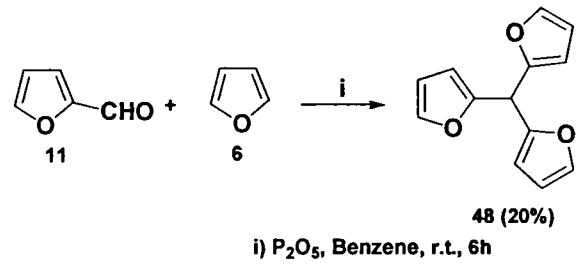
3.4 Present Work

It is clear from the literature survey that although the synthesis of tris(2-furyl)methane is known, its chemistry remains virtually uninvestigated. Intrigued by the possibility of synthesizing novel tris(2-furyl)methane derivatives, we have attempted some electrophilic substitution reactions, cycloaddition reactions, carbene reactions *etc.* Also, in the context of our ongoing research program for the synthesis of heterocycle based dendrimers, we have carried out some reactions aimed at the synthesis of furan based dendrimers.

In addition, tris(2-furyl)methane appeared interesting from the vantage point of its transformation to the corresponding radical, akin to Gomberg's triphenylmethyl radical. Although, the tris(2-thienyl)methyl radical has been generated by reduction of the corresponding cation, no such work is known in furan series. In this context, we attempted the synthesis of tris(2-furyl)methyl radical by various strategies. Details of these reactions are discussed in the following sections.

3.5 Results and Discussion

Tris(2-furyl)methane **48**, required for our studies was synthesized from furan 2-carbaldehyde and furan in benzene in presence of phosphorous pentoxide (Scheme 15).



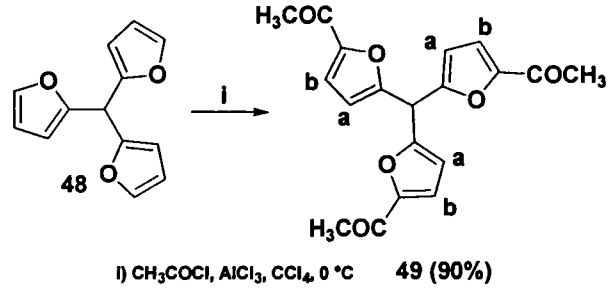
Scheme 15

3.5.1 Electrophilic Substitution Reactions

Furan is an electron rich heteroaromatic system and hence it can easily be substituted at the α-position by electrophilic reagents. In order to introduce functionality on tris(2-furyl)methane, a few electrophilic substitution reactions were carried out. These include a) acetylation followed by oximation, b) formylation c) bromination and d) iodination reactions and e) reaction with electrophilic carbenes.

3.5.1.1 Acetylation and Oximation Reactions

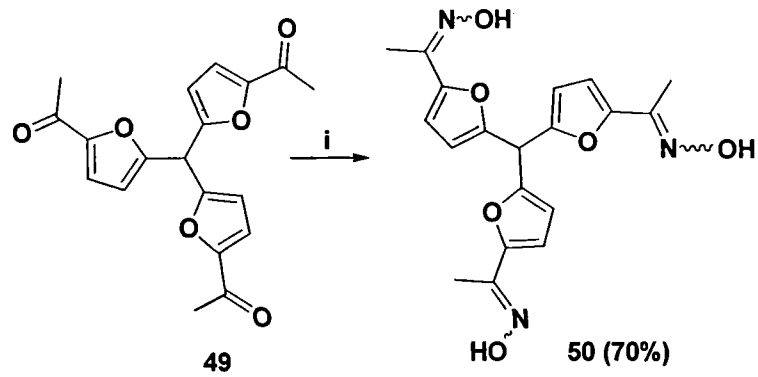
In the case of trisfurylmethane, we adopted the same acetylation procedure used in the case of tristhienylmethane.[3] We were successful in acetylating **48** at all α-positions and the reaction afforded **49** in 90% yield (Scheme 16).



Scheme 16

Structure of compound **49** was established by spectroscopic analysis. In the IR spectrum, the carbonyl stretching was seen at 1662 cm^{-1}. The ^1H NMR spectrum exhibited a singlet at δ 2.44 corresponding to the methyl group. The proton on the central carbon was discernible at δ5.74 while the ring protons labelled as **a** and **b** appeared as doublets at δ 6.37 (J = 3.4 Hz) and 7.12 (J = 3.4 Hz). In the ^{13}C NMR spectrum, methyl carbon appeared at δ 25.9 while the signal due to the central carbon was seen at δ39.6. The ring carbons resonated at δ 111.0 117.9, 152.8 and 153.6. A signal due to the carbonyl carbon manifested at δ185.9.

The tris-acetylated compound **49** on treatment with hydroxylamine in the presence of sodium hydroxide, afforded the oxime **50** in 70% yield (Scheme 17).



Scheme 17

The structure of **50** was ascertained by spectroscopic analysis. IR spectrum exhibited the characteristic C=N stretching at 1650 cm^{-1}. In the ^1H NMR spectrum (Figure 2), the methyl groups were discernible as two singlets at δ2.04 and δ2.12 and the central proton resonated at δ5.59. The values for the ring protons revealed that one of the furan rings is different from the other two. This is attributed to the existence of syn/anti isomers of the oxime functionalities. Hydrogens of the identical rings resonated at δ6.18 (d, J = 3.4 Hz) and 6.50 (d, J = 3.4 Hz), whereas the remaining ring hydrogens were seen at δ6.26 (d, J = 3.4 Hz) and 7.30 (d, J = 3.4

Hz). The broad signal at δ9.97 was due to the N-OH resonance. The ^{13}C NMR spectral values were also in agreement with the structure assigned.

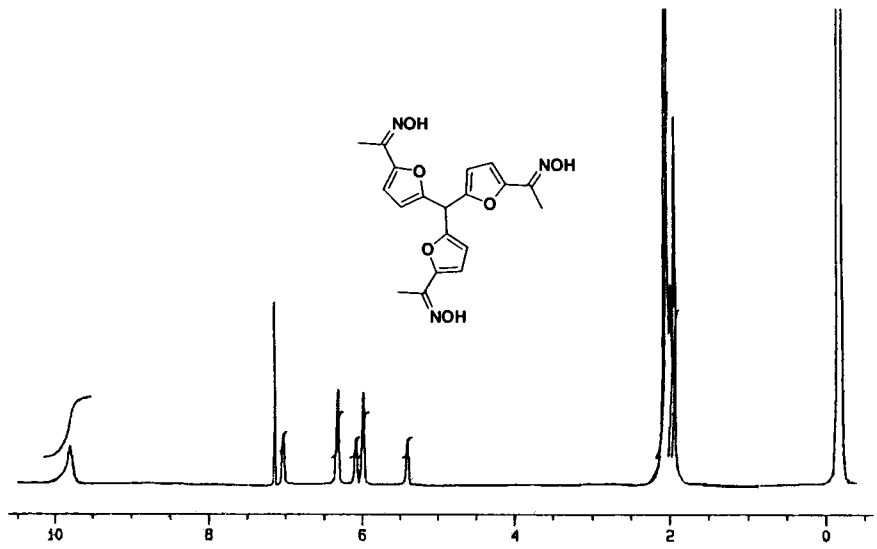
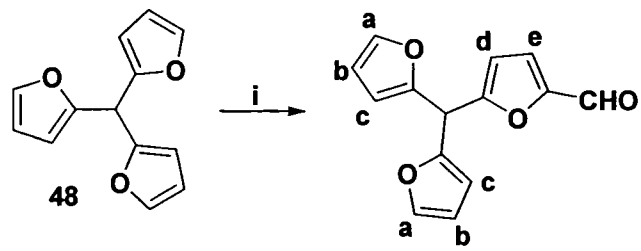


Figure 2. ^1H NMR spectrum of **50** in DMSO/$CDCl_3$

3.5.1.2 Formylation Reaction

Vilsmeier formylation reaction of furan is well known[2] and hence we performed it on tris(2-furyl)methane. When tris(2-furyl)methane was treated with the reagent prepared *in situ* from DMF and $POCl_3$ at 0 °C, monoaldehyde of tris(2-furyl)methane **51** was formed in 50% yield. It was found that even in the presence of excess reagents, only monoadduct was obtained (Scheme 18).



i) DMF, $POCl_3$, 1,2 DCE **51 (50%)**

Scheme 18

The structure of the aldehyde **51** was established with the help of spectroscopic data. In the IR spectrum, the carbonyl absorption appeared at

1729 cm^{-1}. The ^1H NMR spectral data (Figure 3) were also consistent with the proposed structure. The signal due to the central proton was seen as a singlet at δ5.61 and the protons labelled **c** were discernible as a doublet at δ6.09 (J = 3.2 Hz). Protons **b** and **d** appeared together as a multiplet centered at δ6.33 while proton **e** resonated as a doublet at δ7.16 (J = 3.5 Hz). The multiplet centered at δ7.37 was attributed to protons **a**. In the ^{13}C NMR spectrum, the signal due to carbonyl carbon was discernible at δ177.2. All other signals were also in accordance with the assigned structure.

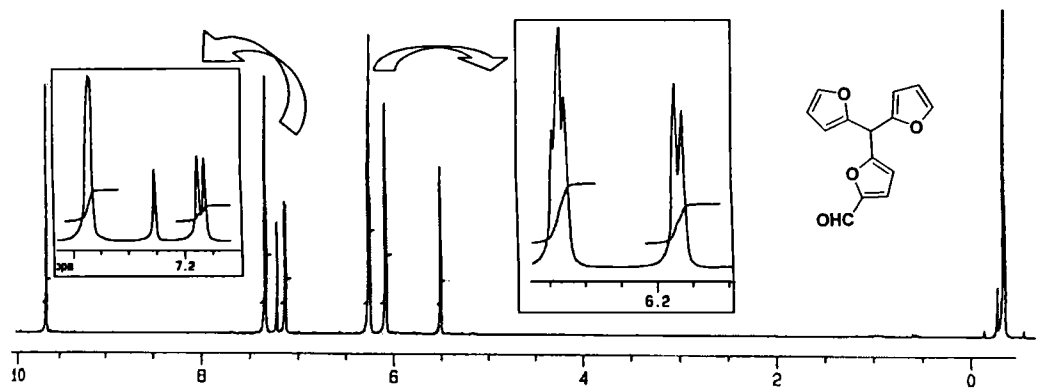
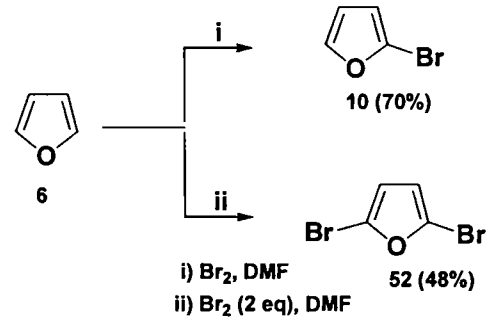


Figure 3. ^1H NMR spectrum of **51**

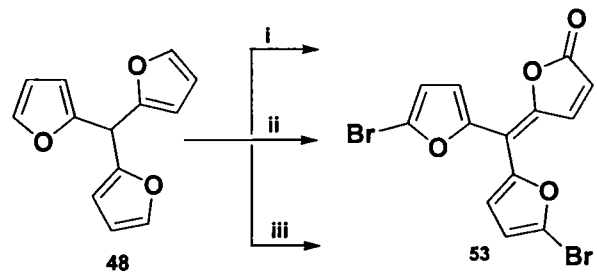
3.5.1.3 Bromination Reaction

Furan reacts vigorously with chlorine and bromine at room temperature to give polyhalogenated products, but it does not react at all with iodine. In 1987, Keegstra *et al.* have shown that under controlled conditions, 2-bromofuran can be formed from furan. One equivalent of bromine in DMF under carefully controlled conditions, such as temperature and addition rate, allowed the synthesis of 2-bromofuran. 2,5-Dibromofuran was formed with two equivalents of bromine in DMF under similar reaction conditions (Scheme 19).[5b]



Scheme 19

With the intention of crafting some dendritic architectures of tris(2-furyl)methane, *via* the bromo derivatives, various bromination reactions were attempted. The conditions employed include: i) Br_2 in DMF ii) NBS in DMF iii) NBS in the presence of catalytic amount of *p*TSA and iv) NBS in presence of AIBN. A polymer of tris(2-furyl)methane was the only product formed in the Br_2/DMF experiment. All the other methods mentioned above, yielded the butenolide **53** as the only product (Scheme 20).



Scheme 20

The structure of **53** was assigned by resorting to spectroscopic techniques. IR spectrum exhibited a sharp absorption peak at 1763 cm^{-1}, characteristic of a lactone carbonyl group. In the ^1H NMR (Figure 4), the central proton of tris(2-furyl)methane was absent and a doublet appeared at δ6.29 (J = 5.4 Hz), due to the proton α- to the lactone carbonyl group. Two of the protons of the furan rings resonated at δ6.50 as a multiplet and the other two were discernible as doublets at δ6.79 (J = 3.5 Hz) and

δ7.12 (J = 3.5 Hz). The protons β- to the lactone moiety resonated at δ8.01 (J = 5.4 Hz) as a doublet. The ^{13}C NMR spectral data was also in agreement with the assigned structure. The lactone carbonyl was discernible at δ195.0. Presumably due to the extended conjugation the resonance signal of the central carbon was shifted downfield to δ53.0 (Cf. δ39.1 for the central carbon in the tris(2-furyl)methane).

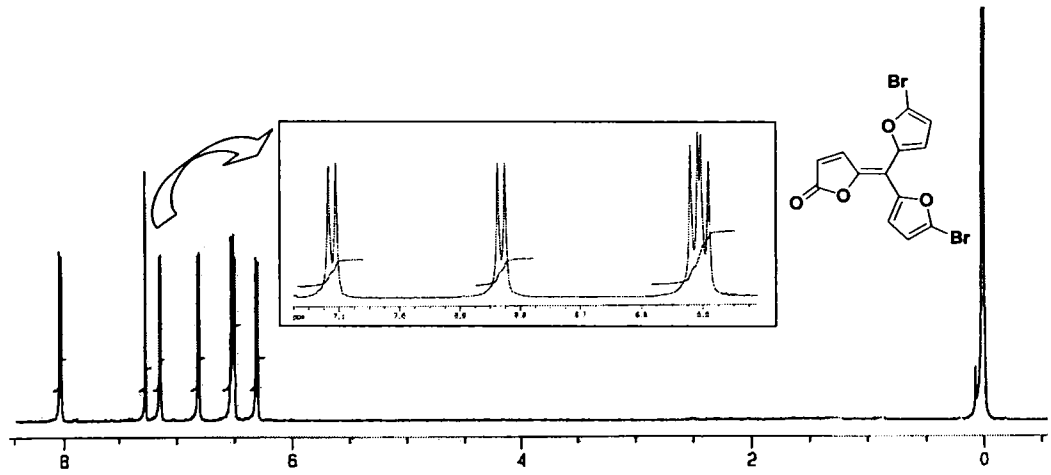
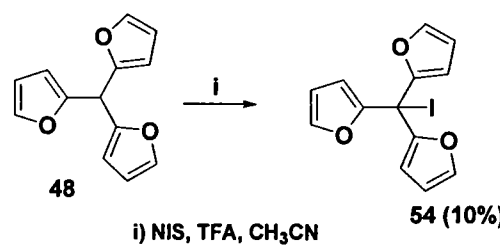


Figure 4. ^1H NMR spectrum of **53**

3.5.1.4 Iodination Reaction

Iodoarenes have assumed increasing importance in organic synthesis because they can be easily functionalized through metal catalyzed cross-coupling reactions. Recently, Colobert *et al.* have reported a mild and regioselective iodination of electron-rich aromatics with *N*-iodosuccinimide and catalytic amount of trifluoroacetic acid.[27] With the view to functionalize tris(2-furyl)methane **48** with iodine, it was treated with NIS in presence of TFA (Scheme 21).

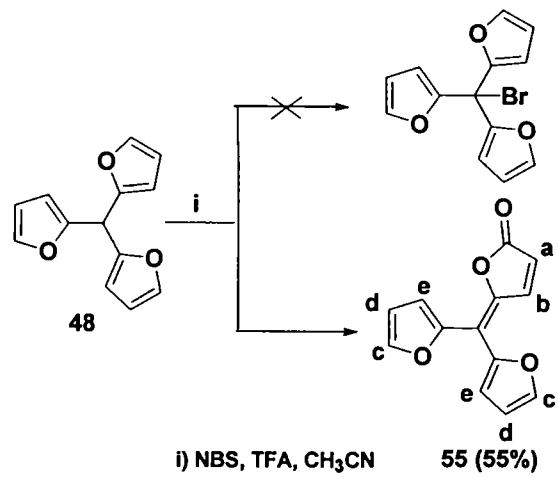


48 **54 (10%)**

i) NIS, TFA, CH_3CN

Scheme 21

The product formed was assigned the structure **54** based on spectral analysis. The signal due to the central proton, resonating at δ 5.52, characteristic of the starting compound **48**, was absent in the ^{1}H NMR spectrum. The three protons of the furan rings were seen at δ 6.60 (dd, J_1 = 1.9 Hz, J_2 = 3.5 Hz), 7.24 (d, J = 3.6 Hz) and 7.69 (bs). ^{13}C NMR spectrum was also in good agreement with the proposed structure. Contrary to this observation, no such brominated product was observed when tris(2-furyl)methane was treated with NBS under similar reaction conditions. We could isolate only the lactone **55** of tris(2-furyl)methane in this case (Scheme 22).



Scheme 22

Compound **55** was characterized by spectroscopic analysis. IR spectrum exhibited a sharp peak at 1784 cm^{-1}, characteristic of a lactone carbonyl absorption. The characteristic signal of the central proton (δ 5.52) was absent in the ^{1}H NMR spectrum (Figure 5). The proton labelled **a**, α- to the lactone carbonyl was discernible as a doublet at δ 6.23 (J = 5.4 Hz) and another doublet that appeared at δ 8.00 (J = 5.4 Hz) was assigned to the β-proton labelled **b**. Protons **d** resonated as a multiplet centered at δ 6.57 while the signal due to the protons **e** was discernible at δ 6.79 (d, J = 3.3 Hz) and δ 7.14 (d, J = 3.3 Hz). The signal due to protons **c** was

visible at δ7.57 as a broad singlet. In the ^{13}C NMR spectrum, the carbonyl peak was seen at δ185.2 and all other signals were in accordance with the assigned structure.

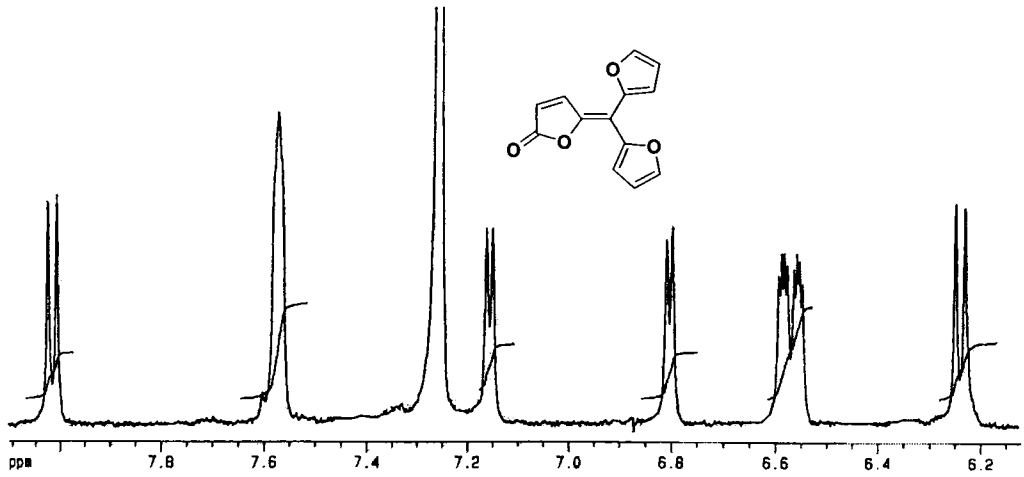
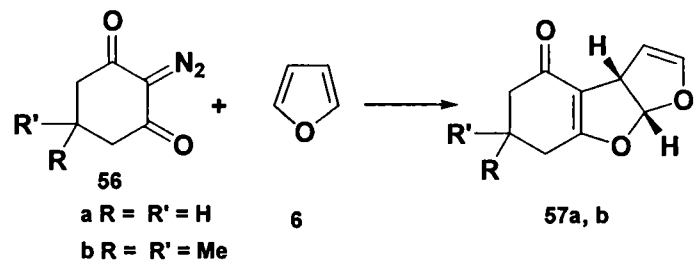


Figure 5. ^{1}H NMR spectrum of 55

3.5.1.5 Reaction with Electrophilic Carbenes

Both inter- and intramolecular metal catalyzed reactions of diazocompounds have attracted considerable attention. Furan reacts with electrophilic carbenes, generated in the presence of metal catalysts such as Rh(II) and Cu(II), forming cyclopropane derivatives, which in turn could rearrange according to the reaction conditions employed. Cyclic diazoketones, in presence of rhodium(II) catalysts, react with furan to afford the annulated product **57** (Scheme 23).[28]

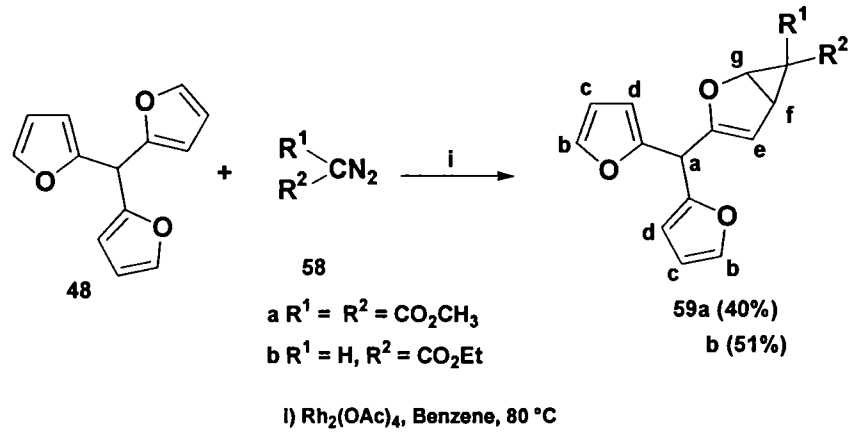


56
a R = R' = H
b R = R' = Me
6
57a, b

Scheme 23

In order to explore the reactivity of tris(2-furyl)methane towards electrophilic carbenes, some reactions were carried out with cyclic and acyclic carbenes in presence of Rh(II) acetate as catalyst. It can be observed that, with acyclic carbenes,

cyclopropanation took place only at one of the furan rings of the tris(2-furyl)methane system yielding the products **59a** and **b** (Scheme 24).



Scheme 24

The structure elucidation of the products was based on spectroscopic analysis. IR spectrum exhibited a sharp signal of the ester carbonyl at 1738 cm^{-1}. In the case of **59a**, the methoxy signals were seen as singlets at δ3.77 and 3.83 in the ^{1}H NMR spectrum (Figure 6). Proton **g** was seen as a doublet at δ3.61 (J = 8.9 Hz) while the signal due to proton **a** was seen as a multiplet centered at δ5.85. Proton **f** and **e** manifested doublet of a doublet at δ6.54 (J_1 = 2.1 Hz, J_2 = 6.2 Hz) and δ6.80 (J_1 = 1.8 Hz, J_2 = 6.0 Hz) as two separate sets of double doublets. Furan protons were seen centered at δ6.43 (m), 6.60 (d, J = 3.3 Hz), 7.34 (s) and 7.42 (s). Satisfactory ^{13}C NMR spectral values were also obtained.

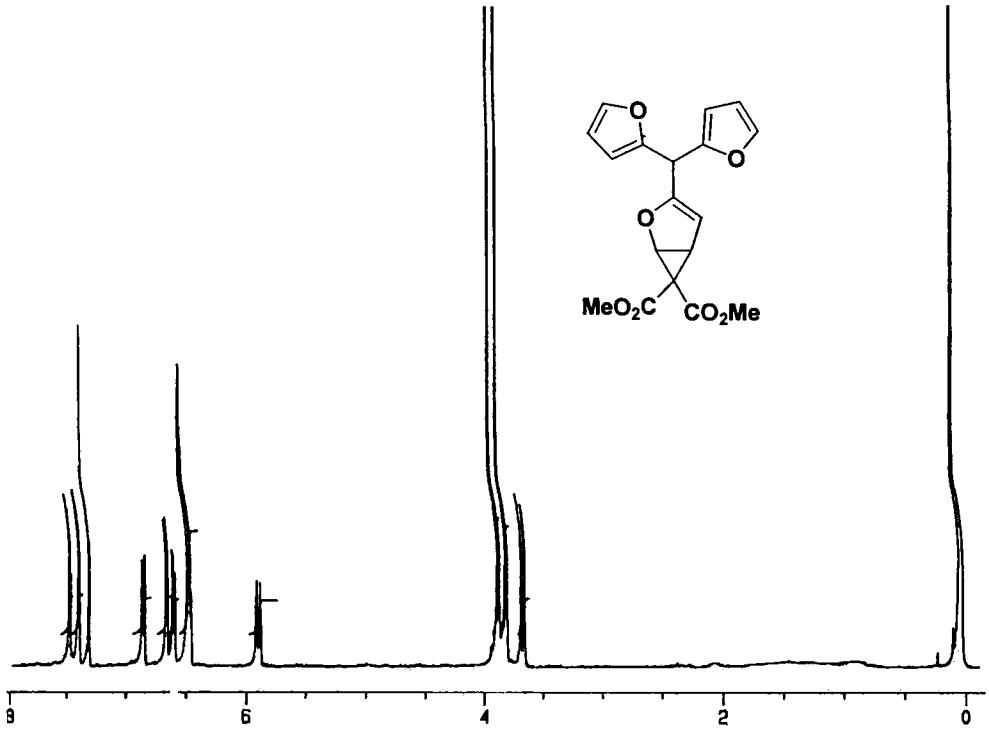
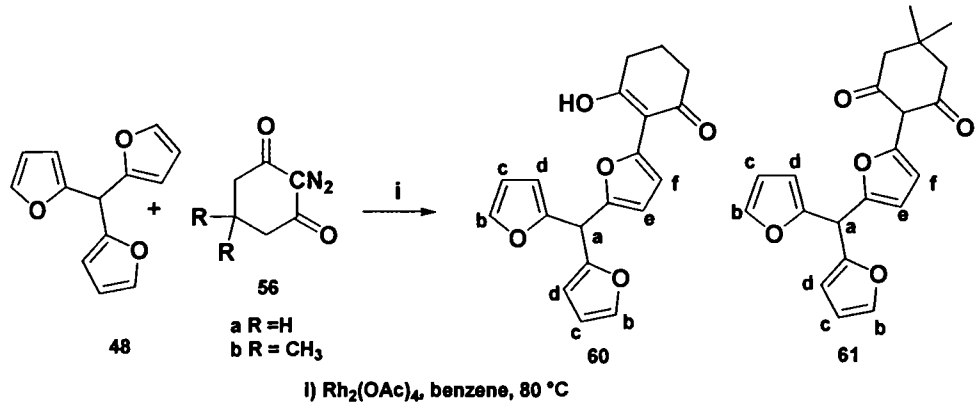


Figure 6. ^{1}H NMR spectrum of **59a**

The cyclic carbene precursors selected for the study were the diazocompounds **56a** and **b** (Scheme 25). The reactions of these under usual conditions afforded the rearranged products **60** and **61** respectively. It is noteworthy that the former was isolated exclusively in the enol form.



Scheme 25

The structure of **60** was elucidated by spectroscopic analysis. Its IR spectrum exhibited a broad absorption at 3407 cm^{-1} showing the presence of -OH group;

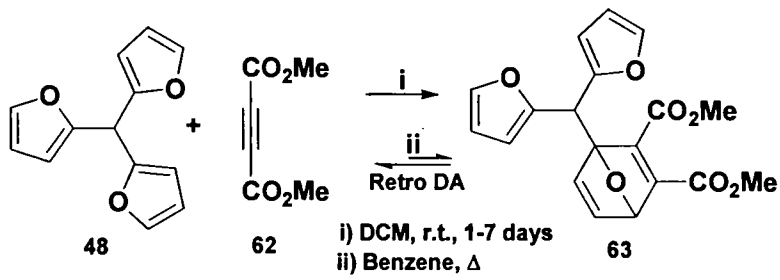
carbonyl absorption was seen at 1722 cm^{-1}. In the ^1H NMR spectrum, methylene groups were discernible as three sets of multiplets around δ1.96, 2.41 and 2.57. The central proton **a** appeared as a singlet at δ5.52. Protons labelled **b**, **c** and **d** were seen at δ6.13 (d, J = 3.0 Hz), 6.32 (m) and 7.37 (s). The protons **e** and **f** were seen as doublets at δ6.21 (J = 3.3 Hz) and 6.95 (J = 3.3 Hz) respectively. The -OH proton resonated at δ9.18 (D_2O exchangeable). Satisfactory ^{13}C NMR data were also obtained for compound **60**.

Compound **61** was also characterized by the usual spectroscopic techniques. In the IR spectrum, the peak at 1725 cm^{-1} is attributed to the carbonyl functionality. In the ^1H NMR spectrum, *gem*-dimethyl groups were discernible at δ1.08 and 1.11 as two singlets. Two methylene groups display their resonance signals at δ2.20 and 2.35. The singlet at δ4.31 corresponds to the methine proton in the cyclohexan-1,3-dione ring whereas the singlet at δ5.01 is attributed to the proton **a**. In the ^{13}C NMR spectrum, the signal due to the carbonyl functionality was seen at δ204.5.

3.5.2 Cycloaddition Reactions

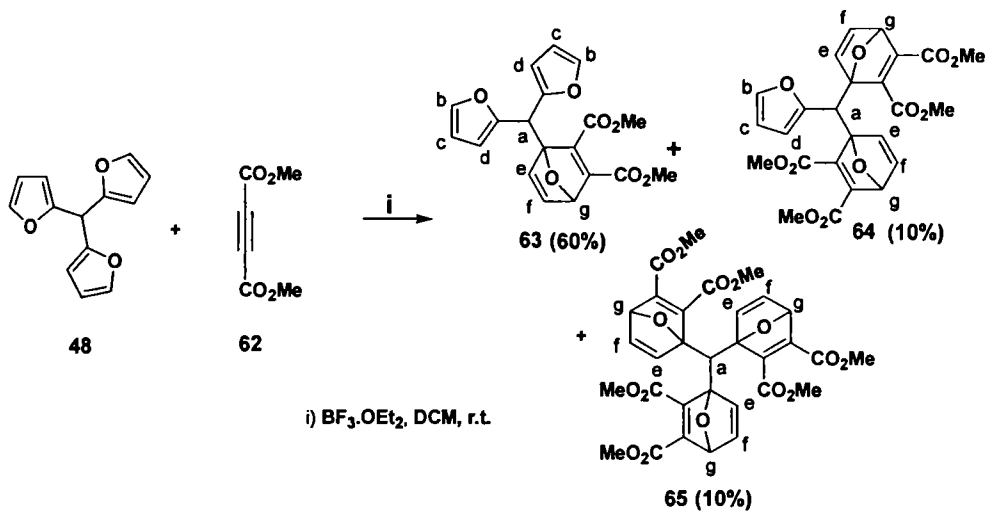
Diels-Alder reaction is a synthetically valuable process as it is widely recognized as a means to design and synthesis a wide variety of six membered ring target molecules in a stereoselective manner. With a view to elaborate three dimensional growth of systems based on tris(2-furyl)methane, we have carried out some cycloaddition reactions of the same. In a pilot experiment, tris(2-furyl)methane in dichloromethane was treated with DMAD at room temperature, and the reaction afforded the monocycloadduct **63** in 70% yield. Since only one of the furan rings of tris(2-furyl)methane underwent cycloaddition in the reaction mentioned above, the reaction was attempted at higher temperatures using benzene as well as toluene as solvents. But under these conditions, only 10% of the mono cycloadduct was formed and most of the starting compound remained unreacted. This may be attributed to the

propensity of the cycloadducts to undergo facile retro Diels-Alder reaction. Increasing the reaction time also did not show any appreciable enhancement of product formation (Scheme 26).



Scheme 26

Many Lewis acids are known to catalyze the Diels-Alder reaction of furan with dienophiles.[9] Hence the above mentioned reaction was carried out in presence of weak Lewis acids like $ZnCl_2$ and ZnI_2, but formation of bis- or tris-cycloadduct was not observed. Therefore the stronger Lewis acid $BF_3.OEt_2$ was employed as the catalyst. In this case, the reaction afforded all the three possible products *viz.*, mono-**63** (60%), bis- **64** (10%), and tris-**65** (10%) cycloadducts (Scheme 27). Later it was found that under neat conditions also at 120 °C, all the three products were formed in almost similar yields.



Scheme 27

Structures of the cycloadducts were assigned on the basis of spectral analysis. IR spectrum of **63** exhibited a sharp carbonyl absorption of the ester moiety at 1728 cm^{-1}. In the ^1H NMR spectrum (Figure 7), the methoxy signals were seen as singlets at δ3.73 and δ3.75 while the central proton **a** was discernible as a singlet at δ5.28. The bridgehead proton **g** was seen as a doublet at δ5.70 (J = 1.7 Hz). Two multiplets centered at δ6.21 and δ6.27 were attributable to the protons **c** and **d** of the unreacted furan rings. The protons **e** and **f** of the double bond appeared at δ7.10 (dd, J_1 = 1.8 Hz, J_2 = 5.2 Hz) and δ7.14 (d, J = 5.2 Hz). The remaining protons **b** of the furan rings resonated at δ7.30 and δ7.34 as broad singlets. ^{13}C NMR spectrum was also in good agreement with the proposed structure.

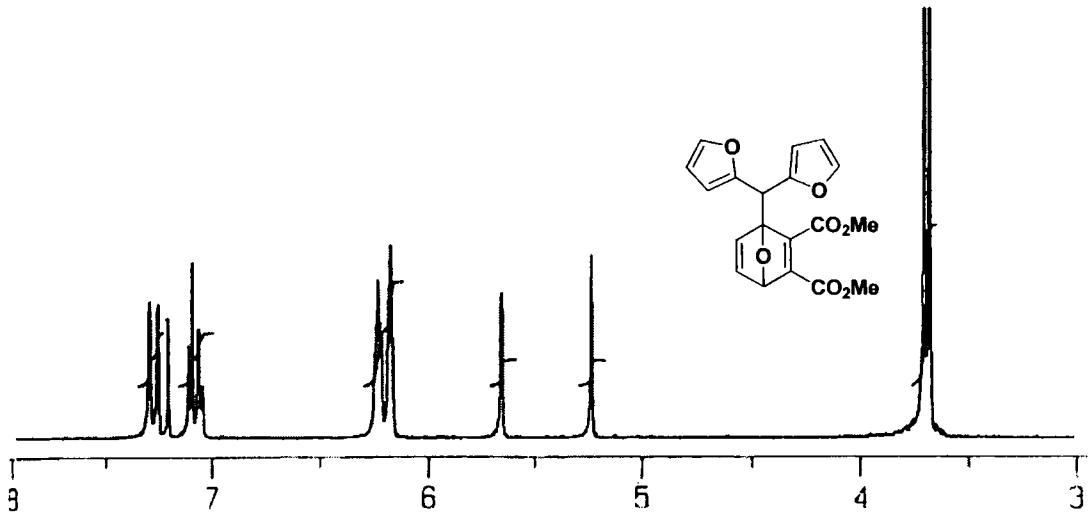


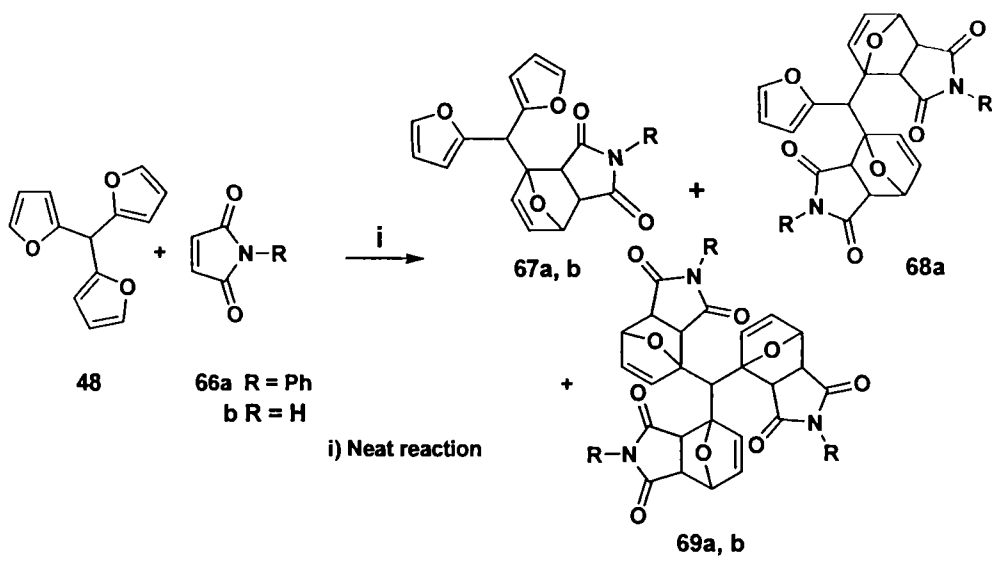
Figure 7. ^1H NMR spectrum of **63**

In the case of bis adduct **64**, ^1H NMR spectrum exhibited a singlet at δ4.93, and it was assigned to the central proton **a**. The bridgehead protons **g** resonated as a doublet at δ5.64 (J = 1.7 Hz). The protons **c** and **d** of the unreacted furan rings were seen at δ6.23 (d, J = 3.1 Hz) and 6.30 (d, J = 3.1 Hz). Protons **e** resonated at δ7.06 as doublet of a doublet (J_1 = 1.8 Hz, J_2 = 5.2 Hz). The other olefinic proton **f** gave signal at δ7.10 (d, J = 5.2 Hz). The proton **b** of the unreacted furan ring was

discernible at δ7.28 as a broad singlet. Satisfactory ^{13}C NMR data were also obtained for compound **64**.

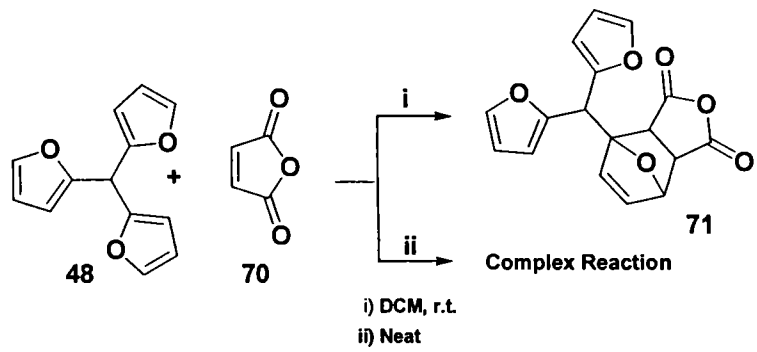
The structure of the tris cycloadduct **65** was also confirmed using spectroscopic analysis. In the ^{1}H NMR spectrum, methoxy protons appeared at δ3.64 and 3.74 as two singlets. The central proton was seen at δ5.60 (s) and the bridgehead protons appeared at different δvalues, *i.e.* at δ4.92 (d, J = 3.4 Hz), 5.65 (bs) and 6.34 (bs). The olefinic protons appeared as a multiplet around δ7.04 and a doublet at δ7.15 (J = 5.2 Hz). Satisfactory ^{13}C NMR spectral data and HRMS data were also obtained for **65** thereby confirming the structure.

The reaction was further extended to other dienophiles like *N*-phenyl maleimide, maleimide and maleic anhydride. Both *N*-phenyl maleimide and maleimide gave monocycloadduct in the absence of catalyst. *N*-Phenyl maleimide afforded mono- and bis-cycloadducts in the presence of $BF_3.OEt_2$ while under neat conditions it afforded all the three cycloadducts, *viz.* mono-, bis-, tris-cycloadducts (Scheme 28). In the case of maleimide, the reactions carried out both in the presence of catalyst and under neat conditions, afforded mono- and tris- cycloadducts.



Scheme 28

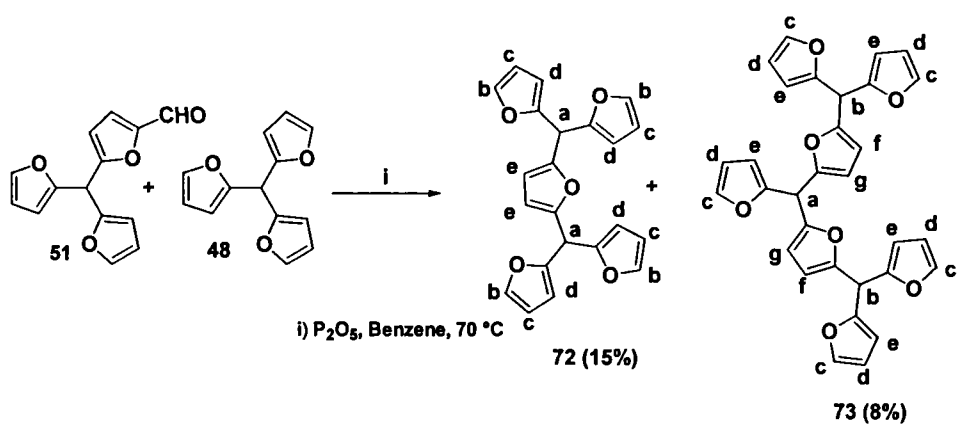
Reaction with maleic anhydride also resulted only in monocycloaddition in the absence of catalyst. Complex reactions resulted when maleic anhydride was treated with tris(2-furyl)methane both in the presence of $BF_3.OEt_2$ and under neat reaction conditions (Scheme 29). Attempts to isolate any of the products from the reaction mixture were unsuccessful.



Scheme 29

3.5.3 Dendritic Approach

Intrigued by the possibility of generating dendrimers from monoaldehyde **51** by the nucleophilic attack of tris(2-furyl)methane **48**, the following reaction was performed. P_2O_5 was added to a solution of **48** and **51** in benzene at 80 °C, and stirred for 12 h. Surprisingly two products **72** and **73**, the furan analogs of the products mentioned in section 2.3.2.1, were obtained in 15% and 8% yields respectively (Scheme 30).



Scheme 30

These compounds were characterized by spectroscopic techniques. The ^{1}H NMR spectrum of **72** (Figure 8) exhibited the signal of central protons **a** at δ 5.49. A singlet that appeared at δ 6.05 was attributed to proton **e** while the doublet at δ 6.29 (J = 3.1 Hz) and the multiplet centered at δ 6.09 accounted for protons **d** and **c** respectively. A broad singlet seen at δ 7.33 was assigned to proton **b**. The ^{13}C NMR spectral data and HRMS value were also in good agreement with the structure assigned.

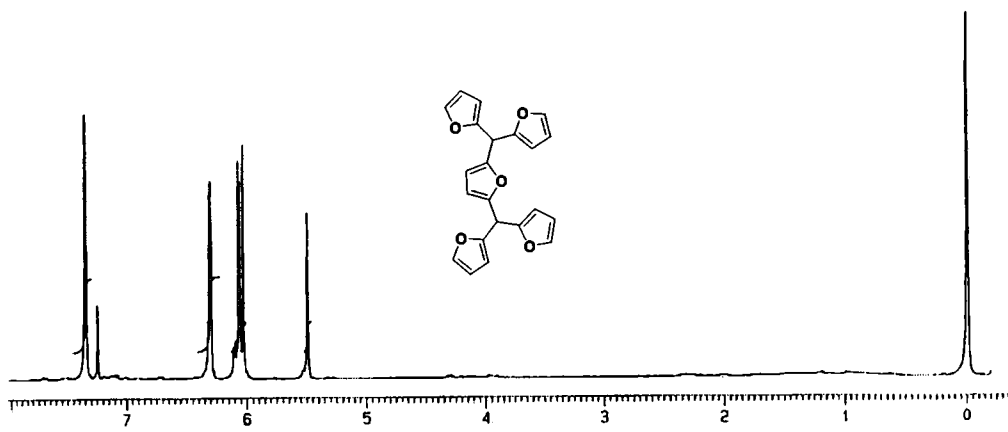


Figure 8. ^{1}H NMR spectrum of **72**

The structure of compound **73** was also established by spectroscopic techniques. In the ^{1}H NMR spectrum (Figure 9), signals due to the central protons **a** and **b** appeared at δ 5.45 (1H) and 5.47 (2H) as two separate singlets. Two sets of multiplets manifested around δ 6.02 (9H) and 6.29 (5H) were attributed to aromatic protons **e**, **f** and **g** (9H) and **d** (5H). Protons **c** were seen as a singlet at δ 7.34 (5H). ^{13}C NMR spectral data and HRMS value were also in good agreement with the proposed structure. A mechanistic analogy for the formation of **72** and **73** can be drawn from that presented for the thiophene series (Cf. Section 2.3.2.1, p. 45).

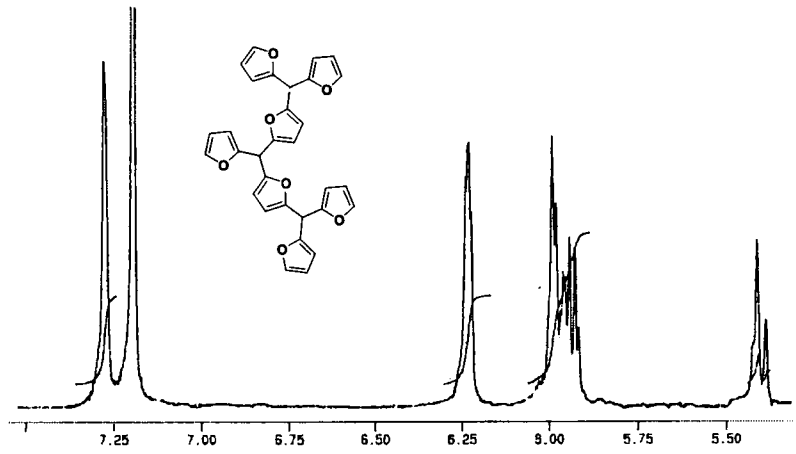


Figure 9. ^{1}H NMR spectrum of 73

3.5.4 Reactions on the Central Carbon of Tris(2-furyl)methane

The fundamental discovery of the triphenylmethyl radical by Gomberg in 1900[29] heralded a new era in organic chemistry. Gomberg's hypothesis of the equilibrium between triphenylmethyl radical and hexaphenyl ethane captured the imagination of leading organic chemists in the U.S. and Europe who engaged themselves in this new realm of chemistry *viz*, free radical chemistry. Although the original hexaphenyl ethane structure assigned for the dimer (**A** in Figure 10) was wrong and the correct quinoid structure was suggested by Jacobson as early as 1905,[30] the issue was settled only in 1968 by Nauta, MacLean and Lancamp who provided convincing evidence for the quinoid structure of the dimer (**B** in Figure 10).[31]

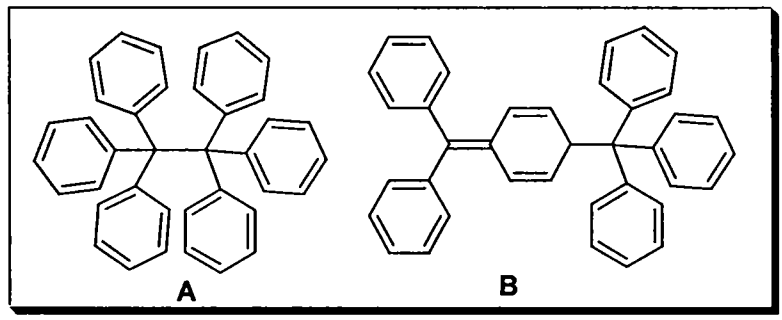
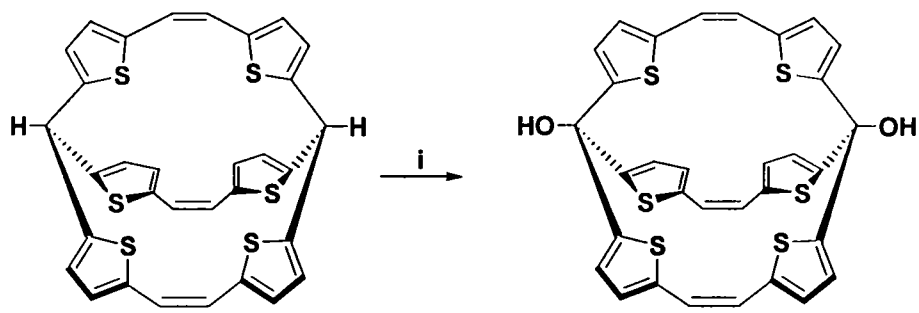


Figure 10

In spite of the universal interest shown on triphenylmethyl radical and its dimer,[31-33] surprisingly, there has been very little work on their heterocyclic analogs. The detection of tri-2-thienyl and tri-3-thienylmethyl radicals by Mangini[34] and the dimerization of tri-2-thienylmethyl radical generated by the reduction of the corresponding cation, studied in detail by Nakayama,[35] are noteworthy in this context. As already mentioned, in the context of an ongoing research program in our laboratory that is concerned with the synthesis of furan based dendrimers, we were intrigued by the possibility of generating a Gomberg type radical from **48**, and the results of our efforts are presented in the following section.

3.5.4.1 Reaction with DDQ and Bromide anion

Asao *et al.* have prepared various substituted trisazulenylmethyl cations employing DDQ as the hydride abstracting agent.[36] Later, for the preparation of carbinol **75**, Oda *et al.* also have used DDQ as the hydride abstraction reagent (Scheme 31).[37]

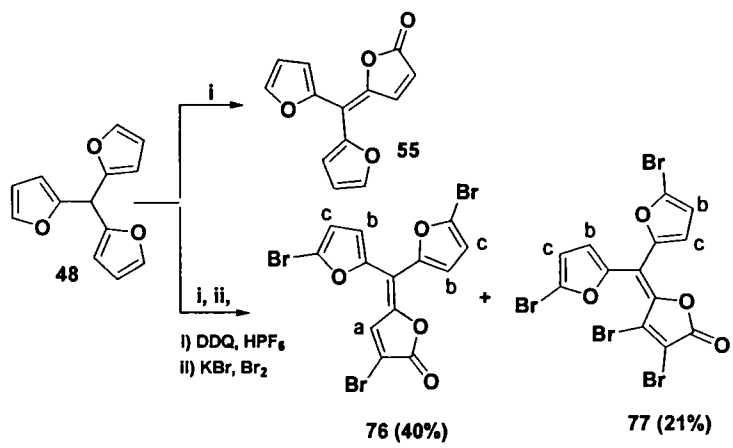


74 i) Excess DDQ, 5% wet benzene 75

Scheme 31

Against this literature precedence, attempts were made to synthesize tris(2-furyl)methyl cation using DDQ as the hydride abstracting agent. Conceivably the cation, in turn, could be used for the generation of the corresponding radical. Adopting similar experimental procedure employed by Asao *et al.* for the abstraction

of hydride, tris(2-furyl)methane **48** was stirred in dichloromethane with DDQ for 30 minutes. Surprisingly trisfurylmethane underwent oxidation to give the lactone **55**, instead of the expected cation. In another strategy, **48** was treated with DDQ and then with potassium bromide and bromine. In this case the reaction afforded the bromoderivatives of butenolide, **76** and **77**, instead of the expected bromoderivative. It may be noted that such lactones are synthetically important molecules (Scheme 32) since bromosubstituted butenolides have been used extensively in Pd-catalyzed coupling reactions.[38]



Scheme 32

The structure of the compounds **76** and **77** were ascertained using usual spectroscopic techniques. The IR spectrum of **76** showed the lactone carbonyl absorption at 1763 cm^{-1}. In the ^1H NMR spectrum (Figure 11), the single proton **a**, on the lactone ring resonated at δ8.08 as a singlet. The protons **b** and **c** of the furan rings were seen at different δvalues. These were discernible at δ6.50 (dd, J_1 = 3.5 Hz, J_2 = 5.1 Hz, 2H) and 6.82 (d, J = 3.5 Hz, 1H) and 7.10 (d, J = 3.6 Hz, 1H). The ^{13}C NMR spectrum of **77** also supported the assigned structure. The characteristic lactone carbonyl was seen at δ163.0. Conclusive proof for the structure of **76** was obtained by single crystal X-ray analysis (Figure 12).

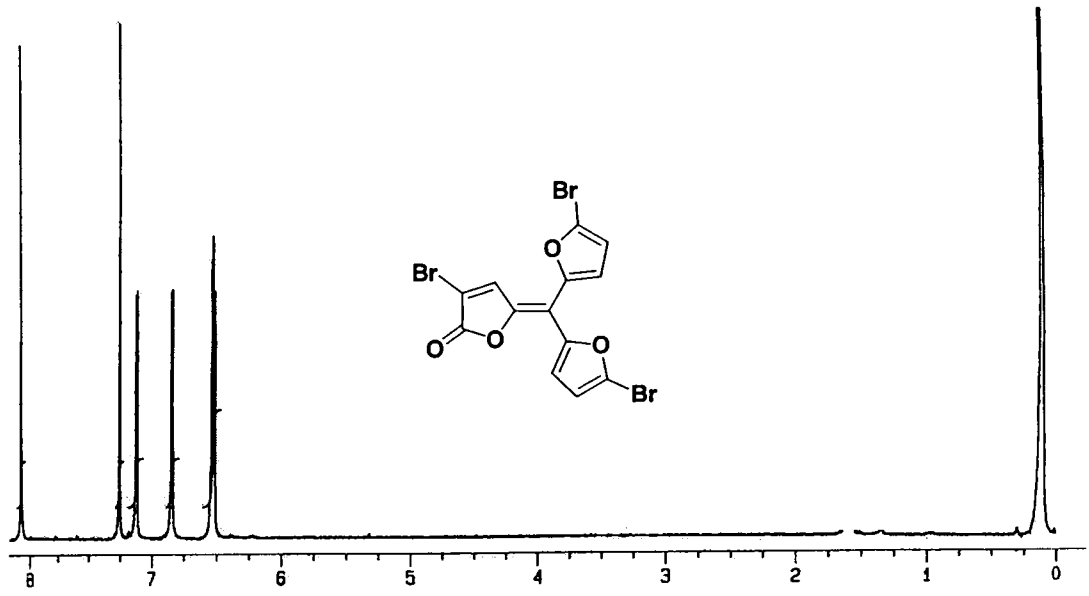


Figure 11. ^{1}H NMR spectrum of **76**

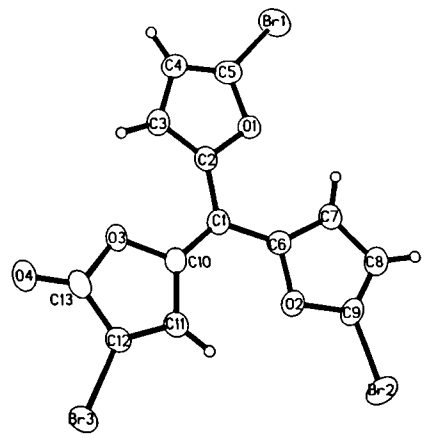


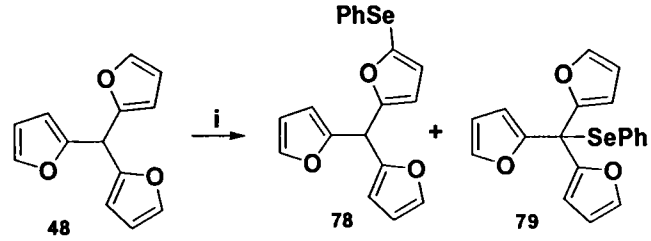
Figure 12. Single crystal X-ray structure of **76**

The structure of compound **77** was also established on the basis of spectroscopic data. Lactone carbonyl gave a sharp absorption peak at 1761 cm^{-1}, in the IR spectrum. In the ^{1}H NMR spectrum, four protons **b** and **c** of the two-furan rings were discernible as three separate signals. A doublet that appeared at δ6.39 (J = 5.4 Hz) was atributed to one of the protons labelled **b**. The other proton labelled **b** and one of the **c** protons were together seen as another doublet at δ6.50 (J = 6.1 Hz). The remaining proton **c** on the other ring was visible at δ 7.66 (d, J = 5.4 Hz). ^{13}C

NMR spectrum and HRMS data were also in good agreement with the structure assigned for **77**.

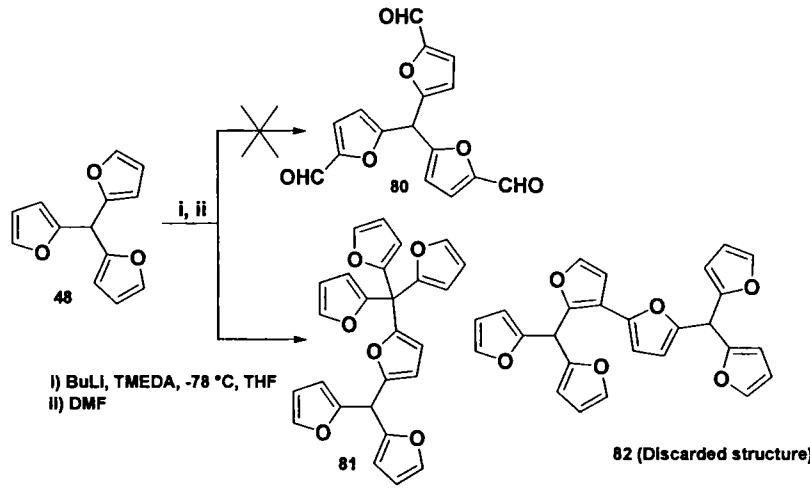
3.5.4.2 Selenenylation Reaction and Some Interesting Observations under Basic Reaction Conditions

Photolytic cleavage of carbon-selenium bonds is regarded as one of the best methods for the generation of carbon centered radicals.[39] In order to selenenylate the central carbon of tris(2-furyl)methane, a reaction was attempted with diphenyl diselenide in presence of BuLi, at –78 °C. The reaction afforded two products **78** and **80** along with various fractions which could possibly be the polymers of **48** (Scheme 33). Unfortunately the products obtained underwent rapid decomposition on exposure to light, thus hampering their proper characterization.



Scheme 33

Oda *et al.* have reported the introduction of carboxaldehyde group on tris(2-thienyl)methane by the reaction of BuLi and DMF. Adopting similar experimental conditions, and with the expectation of obtaining the trialdehyde **80**, compound **48** was treated with BuLi and DMF in presence of catalytic amounts of TMEDA. Surprisingly, however, the product obtained was the dimer of tris(2-furyl)methyl radical, in 40% yield, in the form of a very pale yellow liquid (Scheme 34). Any role of DMF in this reaction was discounted, since dimer was obtained in comparable yields, from experiments, which excluded DMF. Later experiments showed that **81** could be obtained more conveniently in 50% yield, by treating tris(2-furyl)methane with $KOBu^t$ (2 eq) in THF at r.t. for 30 min.



Scheme 34

The structure of the dimer was established using spectroscopic techniques. ^{1}H NMR spectrum of both tris(2-furyl)methane **48** and the dimer **81** are shown in Figure 13.

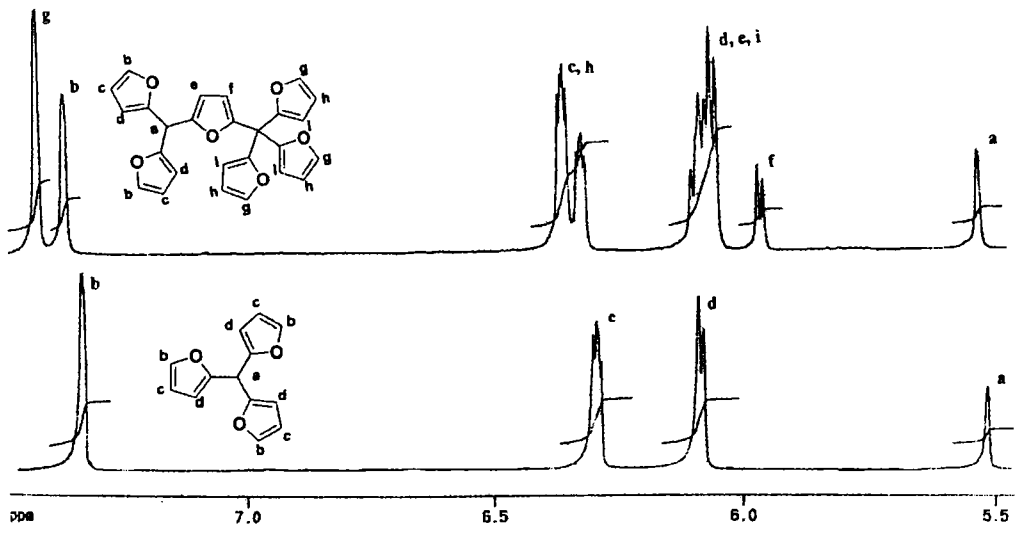


Figure 13. ^{1}H NMR spectrum of **48** and **81**

In the ^{1}H NMR spectrum, shown in Figure 13, the methine proton labelled **a** resonated as a singlet at δ 5.50. The identity of this proton was discernible from its chemical shift (δ 5.50) comparable to the methine proton (δ 5.52) of its precursor tris(2-furyl)methane. In both cases the methine protons were exchangeable with D_2O ($KOBu^t$, THF, r.t. 30 min.); no other protons were exchanged under these conditions.

Proton **f** appeared as a doublet around δ 5.92 (J = 3.2 Hz), while protons **d**, **e** and **i** appeared as a multiplet centered at δ 6.05. Two multiplets centered at δ 6.28 and δ 6.32 correspond to protons **c** and **h**. Protons **b** and **g** resonated as singlets at δ 7.30 and δ 7.39 respectively. Satisfactory ^{13}C NMR spectral data and HRMS data were also obtained for **81**.

Convincing evidence for the exclusion of **82** was obtained from ^{1}H NMR data. In the ^{1}H NMR spectrum, the signals for C-2 protons (labelled **b** and **g**) account for only five protons (agreeable to structure **81**) against the six such protons present in **82**. Further confirmation of the structure assignment came from a Gradient COSY experiment, which showed correlation between the protons resonating at δ 5.92 and δ 6.01 (Figure 14). These signals are assignable only to protons labelled **e** and **f** in **81**.

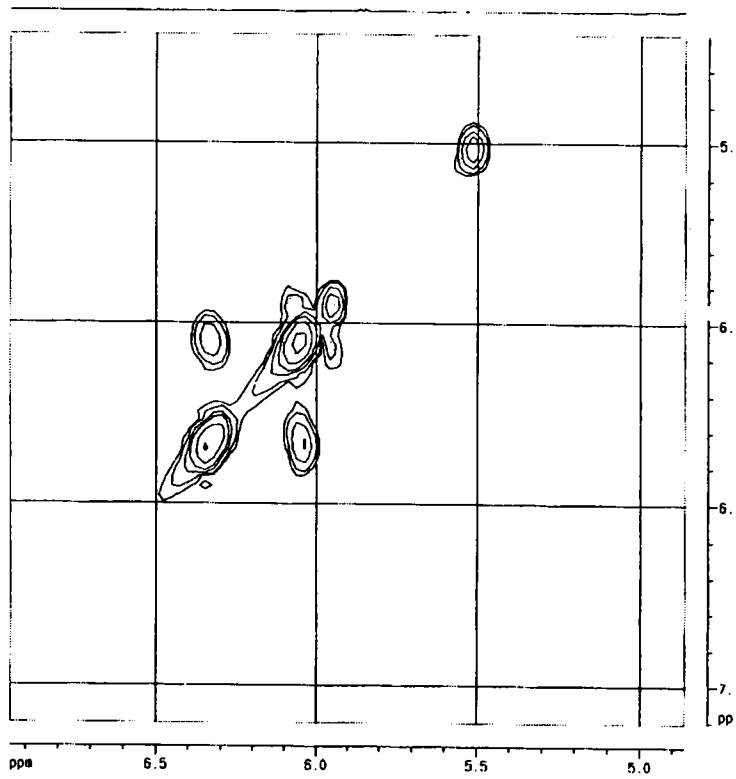
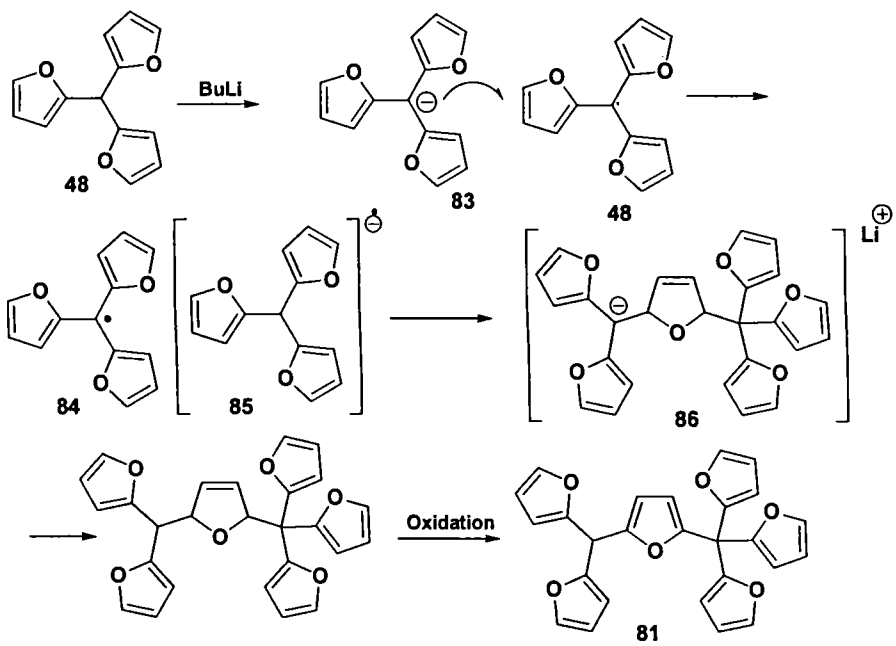


Figure 14. Expanded portion of Gradient COSY of **81** from δ 5.5 to 6.5

Although no definitive mechanistic pathway can be delineated for the reaction at the present time, the following rationalization can account for the formation of the product (Scheme 35). The initial event may be considered as the deprotonation of **48** by BuLi to generate tri-2-furylmethyl anion.* The latter then transfers an electron to a second molecule of **48** to generate a radical/radical anion pair.* Coupling of the radical and the radical anion leading to a species such as **86** followed by protonation of the latter and subsequent aromatization during work up can conceivably deliver **81**.



Scheme 35

3.6 Conclusions

In conclusion, it has been shown that, tris(2-furyl)methane shows reactivity patterns similar to that of simple furan, especially in electrophilic substitution

* The deep red color of the solution and the exchangeability of the methine hydrogen by deuterium (*vide supra*) lend credence to this assumption. For the record, furan itself is known to be deprotonated at the 2-position.[40] The situation in **48** is quite different and it is not surprising that the deprotonation is occuring exclusively at the sp^3 C-H.

* Addition of electrons to electron rich systems have precedent in the Birch reduction of phenols and anilines under very mild conditions.[41, 42]

reactions. Its reaction with diazocompounds yielded monoaddition products. Bromination reaction carried out in presence of NBS yielded bromoderivatives of butyrolactones while iodination in the presence of NIS afforded tris(2-furyl)iodomethane. Reaction of tris(2-furyl)methane with dienophiles in the presence of a strong Lewis acid catalyst such as $BF_3.OEt_2$ gave cycloaddition in the three rings, while in the absence of catalyst only monoadduct was formed. Thus, tris(2-furyl)methane shows diverse reactivity towards various reagents and reaction conditions.

In spite of the universal interest shown on triphenylmethyl radical and its dimer, surprisingly there has been very little work on their heterocyclic analogs. We have been successful in the facile synthesis of 1,1-bisfuryl-1-{5-[tris(2-furyl)methyl]}furylmethane, the dimer of the furan analog of triphenylmethane radical by the reaction of butyllithium with the tris(2-furyl)methane, presumably *via* an electron transfer process.

3.7 Experimental

General information about the experiments is given in section 2.5.

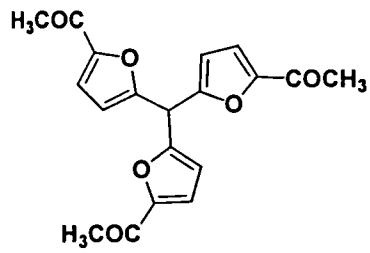
***Tris(2-furyl)methane* 48**

To a stirred solution of furfural (1 g, 10.4 mmol) and furan (1.77 g, 20.8 mmol) in benzene (10 mL) was added P_2O_5 (10 g) in small portions over a period of 1 h. After stirring for 6 h, the crude tarry material was filtered and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel (100-200 mesh, hexane) to afford tris(2-furyl)methane **48** (450 mg, 20%) as a colorless viscous liquid.

***Tris(5-acetyl-2-furyl)methane* 49**

To a stirred solution of $AlCl_3$ (248 mg, 1.8 mmol) in CCl_4 (5 mL), CH_3COCl (146 mg, 1.8 mmol) was added slowly at 0 °C over 5 minutes. After the reaction

mixture was stirred for additional 5 minutes at this temperature, **48** (100 mg, 0.47 mmol) in CCl_4 (5 mL) was added and stirred for further 30 minutes. The reaction mixture was allowed to stand overnight and then poured into crushed ice. The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (100-200 mesh, 20% ethylacetate in hexane) to afford pure **49** (142 mg, 90%) as a brown viscous liquid.



49

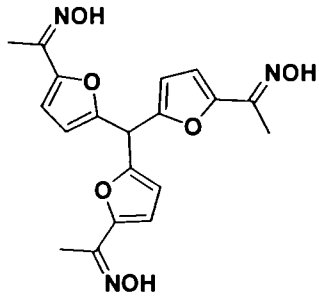
IR (Neat) ν_{max}: 1662, 1520, 1440, 1360, 1275, 1070, 1024, 930 cm^{-1}.

^{1}H NMR: δ 2.44 (s, 9H), 5.74 (s, 1H), 6.37 (d, *J* = 3.4 Hz, 3H), 7.12 (d, *J* = 3.4 Hz, 3H).

^{13}C NMR: δ 25.9, 39.6, 111.0, 117.9, 152.8, 153.6, 185.9.

Oxime **50**

To a stirred solution of **49** (50 mg, 0.23 mmol) in ethanol (10 mL) was added sodium hydroxide (38 mg, 0.93 mmol) and hydroxylammonium hydrochloride (65 mg, 0.93 mmols) and refluxed for 1 h. The reaction mixture was diluted with water and extracted with ethylacetate (2 X 25 mL). The organic layers were combined, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (40% ethylacetate in hexane) to afford **50** (63 mg, 70%) as a yellow viscous liquid.



50

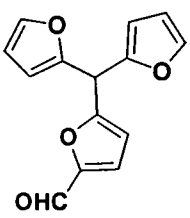
IR (Neat) ν_{max}: 1650, 1618, 1440, 1290, 993, 902, 818, 760 cm^{-1}.

^{1}H NMR: δ 2.04 (s, 6H), 2.12 (s, 3H), 5.59 (s, 1H), 6.18 (d, J = 3.4 Hz, 2H), 6.26 (d, J = 3.4 Hz, 1H), 6.50 (d, J = 3.4 Hz, 2H), 7.30 (d, J = 3.4 Hz, 1H), 9.97 (s, 3H).

^{13}C NMR: δ 10.4, 16.6, 39.9, 106.0, 108.5, 108.8, 109.4, 117.0, 126.5, 133.2, 145.5,150.1, 150.9.

***1,1-Bis(2-furyl)-1-(5-formyl-2-furyl)methane* 51**

To a stirred solution of DMF (99 mg, 0.93 mmol) in 1,2-dichloroethane (3 mL) was added $POCl_3$ (143 mg, 0.93 mmol) at 0 °C, and stirred for 5 minutes. **48** (50 mg, 0.23 mmol) in 1,2-dichloroethane (3 mL) was introduced into the reaction mixture and stirred at room temperature for 2 h. It was then refluxed for further 2 h, cooled and poured into crushed ice. After neutralization with sodium acetate the product was extracted with dichloromethane (2 X 20 mL). The organic layers were combined, dried over Na_2SO_4 and the solvent was removed on rotary evaporator. The crude product was purified by column chromatography on silica gel (5% ethylacetate in hexane) to afford **51** (28 mg, 50%) as a yellow viscous liquid.



51

IR (Neat) ν_{max}: 1729, 1603, 1460, 1435, 1260, 1222, 1042 cm^{-1}.

^{1}H NMR: δ 5.61 (s, 1H), 6.09 (d, J = 3.2 Hz, 2H), 6.33-6.34 (m, 3H), 7.16 (d, J = 3.5 Hz, 1H), 7.37 (m, 2H).

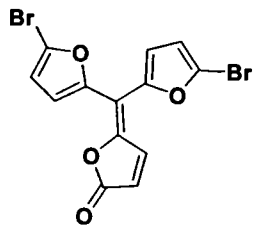
^{13}C NMR: δ 39.3, 108.0, 110.5, 121.0, 142.4, 150.4, 152.7, 158.5, 177.2.

***5-[Bis-(5-bromo-2-furyl)-methylene]-5H-furan-2-one* 53**

a) To a stirred solution of **48** (50 mg, 0.23 mmol) in DMF (2 mL), was added NBS (143 mg, 0.92 mmol) and stirred for further 30 minutes. The product was extracted with ethylacetate (2 X 20 mL), washed with sodium thiosulphate solution, dried over Na_2SO_4 and the solvent was removed in vacuo. The residue was purified by column chromatography on silica gel (100-200 mesh, 5% ethylacetate in hexane), to afford **53** (63 mg, 70%) in the form of a red crystalline soild. m. p. 170-172 °C.

b) To a stirred solution of **48** (50 mg, 0.23 mmol) and 10 mol% of AIBN, in CCl_4 (5 mL) was added NBS (143 mg, 0.92 mmol) and stirred for further 30 minutes. The solvent was removed in vacuo and the reaction mixture was purified by column chromatography as described earlier to afford **53** (68 mg, 75%) as a red crystalline soild. m. p. 170-172 °C.

c) To a stirred solution of **48** (50 mg, 0.23 mmol) and 10 mol% of *p*TSA, in benzene (5 mL) was added NBS (143 mg, 0.92 mmol) and stirred for further 30 minutes. The solvent was removed in vacuo and the reaction mixture was purified by column chromatography as described earlier to afford **53** (65 mg, 72%) in the form of a red crystalline soild. m. p. 170-172 °C.



53

IR (KBr) ν_{max} : 1763, 1472, 1457, 1352, 1240, 1210, 1139, 1117, 1035 cm^{-1}.

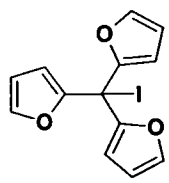
^{1}H NMR: δ 6.29 (d, J = 5.4 Hz, 1H), 6.50 (m 2H), 6.79 (d, J = 3.5 Hz, 1H), 7.12 (d, J = 3.5 Hz, 1H), 8.01 (d, J = 5.4 Hz, 1H).

^{13}C NMR: δ 53.0, 114.0, 114.6, 117.7, 119.1, 119.4, 120.6, 124.1, 124.5, 143.0, 164.2, 168.4, 195.0.

***Tris(2-furyl)iodomethane* 54**

To a stirred solution of **48** (50 mg, 0.23 mmol) and NIS (156 mg, 0.70 mmol) in acetonitrile (5 mL) was added TFA (10 mol %) at 0 °C and stirred for 30 minutes.

The solvent was concentrated and the product was extracted with ethylacetate (2 X 20 mL). The organic layers were combined, washed with sodium thiosulphate and sodium bicarbonate solutions, dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by column chromatography on silica gel (10 % ethylacetate in hexane) to afford **54** (5 mg, 10%) as a brown viscous liquid.



54

IR (Neat) ν_{max}: 1509, 1205, 1130, 1090, 1011, 811, 735 cm^{-1}.

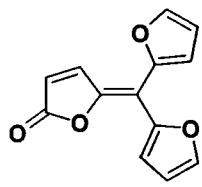
^{1}H NMR: δ 6.60 (dd, J = 1.9 Hz, J = 3.5 Hz, 3H), 7.24 (d, J = 3.6 Hz, 3H), 7.69 (bs, 3H).

^{13}C NMR: δ 112.4, 120.5, 147.8, 152.9, 177.5.

HRMS (FAB): Calcd for $C_{13}H_9IO_3$: 340.1132, Found: 340.2668

***5,5-[Bis-(2-furyl)-methylene]-furan-2-one* 55**

To a solution of **48** (50 mg, 0.23 mmol) and NBS (176 mg, 0.70 mmol) in acetonitrile (5 mL) was added TFA (10 mol %) at 0 °C and stirred for 30 minutes. The solvent was removed and the product was extracted with ethylacetate (2 X 20 mL). The organic layers were combined, washed with sodium thiosulphate and sodium bicarbonate solutions, dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by column chromatography on silica gel (10% ethylacetate in hexane) to afford **55** (29 mg, 55%) as a yellow crystalline solid. m.p. 110-112 °C.



55

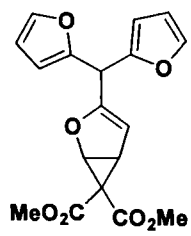
IR (KBr) ν_{max}: 1784, 1759, 1609, 1470, 1230, 1156, 1115, 1022 cm^{-1}.

^{1}H NMR: δ 6.23 (d, J = 5.4 Hz, 1H), 6.54-6.59 (m, 2H), 6.79 (d, J = 3.3 Hz, 1H), 7.14 (d, J = 3.3 Hz, 1H), 7.57 (bs, 2H), 8.00 (d, J = 5.4 Hz, 1H).

^{13}C NMR: δ 37.5, 106.1, 112.0, 112.6, 115.2, 117.0, 118.3, 143.3, 144.0, 185.2.

***1,1-Bis(2-furyl)-1-(4-oxa-5, 5-bismethoxycarbonyl [4.1.0] pent-2-enyl)methane* 59a**

To a stirred solution of **48** (50 mg, 0.23 mmol) and **58a** (147 mg, 0.93 mmol) in benzene (5 mL) was added 2 mol % of Rh(II) acetate under argon and stirred for 12 h. The solvent was removed under reduced pressure and the crude product was purified by column chromatography on silica gel (5% ethylacetate in hexane) to afford **59a** (32 mg, 40%) as an orange viscous liquid.



59a

IR (Neat) ν_{max}: 1738, 1594, 1439, 1243, 1166, 1027 cm^{-1}.

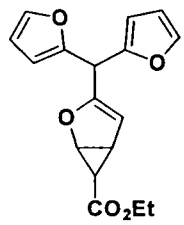
^{1}H NMR: δ 3.61 (d, J = 8.9 Hz, 1H), 3.77 (s, 3H), 3.83 (s, 3H), 5.83-5.87 (m, 1H), 6.40-6.44 (m, 2H), 6.53-6.56 (dd, J_1 = 2.1 Hz, J_2 = 6.2 Hz, 1H), 6.60 (d, J = 3.3 Hz, 1H), 6.80 (dd, J_1 = 1.8 Hz, J_2 = 6.0 Hz, 1H), 7.34 (s, 2H), 7.42 (s, 1H).

^{13}C NMR: δ 39.0, 51.7, 52.8, 53.0, 56.5, 78.2, 107.5, 108.7, 109.5, 110.8, 134.3, 140.6, 149.8, 151.2, 157.5, 166.3, 166.7.

HRMS (FAB, M+H): Calcd for $C_{22}H_{16}O_5$: 345.10, Found: 344.63.

***1,1-Bis(2-furyl)-1-(4-oxa-5-ethoxycarbonyl [4.1.0] pent-2-enyl)methane* 59b**

To a stirred solution of **48** (50 mg, 0.23 mmol) and **58b** (147 mg, 0.93 mmol) in benzene (5 mL) was added 2 mol % of Rh(II) acetate under argon and stirred for 12 h. The solvent was removed under reduced pressure and the crude product was purified by column chromatography on silica gel (5% ethylacetate in hexane) to afford **59b** (35 mg, 51%) as a viscous yellow liquid.



59b

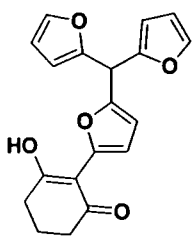
IR (Neat) ν_{max}: 1740, 1599, 1518, 1430, 1240, 1164, 1025 cm^{-1}.

^{1}H NMR: δ 1.06-1.07 (m, 1H), 1.26 (s, 3H), 2.73-2.77 (m, 1H), 4.07-4.14 (q, J = 7.1 Hz, 2H), 4.83 (d, J = 4.8 Hz, 1H), 4.98 (s, 1H), 5.20 (s, 1H), 6.10 (d, J = 3.12 Hz, 2H), 6.30-6.35 (m, 2H), 7.34 (s, 2H).

^{13}C NMR: δ 14.1, 22.2, 31.8, 38.4, 60.4, 67.2, 103.3, 107.3, 108.9, 109.4, 110.3, 112.0, 127.6, 141.9, 142.3, 150.8, 157.3.

***1,1-Bis(2-furyl)-1-{5-(6-hydroxy-cyclohex-6-en-2-one-2-furyl)}methane* 60**

To a stirred solution of **48** (50 mg, 0.23 mmol) and **56a** (147 mg, 0.93 mmol) benzene (5 mL) was added 2 mol % of Rh(II) acetate under argon and stirred for 12 h. The solvent was removed under reduced pressure and the crude product was purified by column chromatography on silica gel (10% ethylacetate in hexane) to afford **60** (45 mg, 60%) as a pink crystalline solid. m. p. 156-158°C.



60

IR (KBr) ν_{max} : 3407, 1722, 1650, 1624, 1594, 1548, 1383, 1336, 1171, 1135, 1012 cm^{-1}.

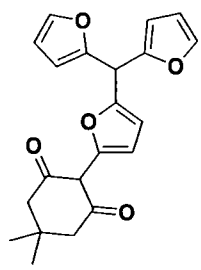
^{1}H NMR: δ 1.96-2.03 (m, 2H), 2.41-2.46 (m, 2H), 2.57-2.61 (m, 2H), 5.52 (s, 1H), 6.13 (d, J = 3.0 Hz, 2H), 6.21 (d, J = 3.3 Hz, 1H), 6.32-6.33 (m, 2H), 6.95 (d, J = 3.3 Hz, 1H), 7.37 (s, 2H), 9.18 (1H).

^{13}C NMR: δ 20.2, 29.7, 37.5, 38.7, 107.54, 109.0, 109.8, 110.5, 142.2, 147.7, 151.2, 171.6, 194.5.

HRMS (FAB, M+H): Calcd for $C_{22}H_{16}O_5$: 325.11, Found: 324.97.

***1,1-Bis(2-furyl)-1-{5-(4,4-dimethyl-cyclohex-2, 6-dione)-2-furyl)}methane* 61**

To a stirred solution of **48** (50 mg, 0.23 mmol) and **56b** (155 mg, 0.93 mmol) in benzene (5 mL) was added 2 mol % of Rh (II) acetate and stirred for 12 h. The solvent was removed under reduced pressure and the crude product was purified by column chromatography on silica gel (10% ethylacetate in hexane) to afford **61** (44 mg, 54%) as pink crystalline solid. m.p. 138-140 °C.



61

IR (KBr) ν_{max} : 1725, 1652, 1630, 1598, 1550, 1390, 1340, 1180, 1140 cm^{-1}.

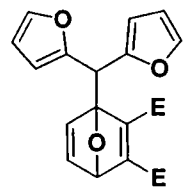
^{1}H NMR: δ 1.08 (s, 3H), 1.11 (s, 3H), 2.20 (s, 2H), 2.35 (s, 2H), 4.31 (s, 1H), 5.01 (s, 1H), 6.10-6.14 (m, 2H), 6.30 (bs, 3H), 6.60 (m, 1H), 7.38 (s, 2H).

^{13}C NMR: δ 28.2, 30.5, 39.8, 53.0, 67.5, 106.3, 109.3, 113.2, 141.5, 153.6, 153.9, 204.5.

***Cycloadducts* 63, 64 and 65**

a) A solution of DMAD (229 mg, 1.16 mmol) and **48** (50 mg, 0.23 mmols) in dichloromethane (5 mL) was stirred for 7 days at room temperature. The solvent was removed and the crude product was purified by column chromatography on silica gel (10% ethylacetate in hexane) to afford **63** (58 mg, 70%) as a viscous yellow liquid.

b) To a stirred solution of **48** (50 mg, 0.23 mmol) and DMAD (229 mg, 1.16 mmol) in dichloromethane (5 mL) was added $BF_3.OEt_2$ at –5 °C and stirred for 5 minutes. The reaction mixture was extracted with dichloromethane. The organic layers were combined, washed with bicarbonate solution, dried over Na_2SO_4 and the solvent was removed on rotary evaporator. The crude product was purified by column chromatography on silica gel (10% ethylacetate in hexane) to afford **63** (50 mg, 60%). Further elution with 15% and 30% ethylacetate in hexane solvent mixtures afforded **64** (11 mg, 10%) as a viscous yellow liquid and **65** (15 mg, 10%) as a white crystalline solid. m. p. 190-192 °C.

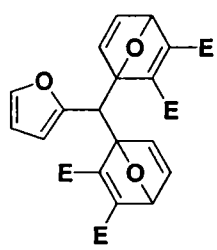


63

IR (Neat) ν_{max}: 1728, 1634, 1438, 1263, 1115, 1040 cm^{-1}.

^{1}H NMR: δ 3.73 (s, 3H), 3.75 (s, 3H), 5.28 (s, 1H), 5.70 (d, J = 1.7 Hz, 1H), 6.21-6.23 (m, 2H), 6.27-6.30 (m, 2H), 7.09 (dd, J_1 = 1.8 Hz, J_2 = 5.2 Hz, 1H), 7.14 (d, J = 5.2 Hz, 1H), 7.30 (bs, 1H), 7.34 (bs, 1H).

^{13}C NMR: δ 38.5, 52.0, 83.9, 98.1, 109.0, 109.1, 110.4, 141.8, 141.9, 143.5, 144.5, 150.0, 150.8, 151.1, 154.9, 162.4, 164.5.

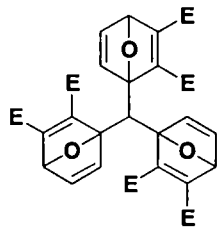


64

IR (Neat) ν_{max}: 1728, 1640, 1438, 1270, 1155 cm^{-1}.

^{1}H NMR: δ 3.65 (s, 12H), 4.93 (s, 1H), 5.64 (d, J = 1.7 Hz, 2H), 6.23 (d, J = 3.1 Hz, 1H), 6.30 (d, J = 3.1 Hz, 1H), 7.06 (dd, J_1 = 1.8 Hz, J_2 = 5.2 Hz, 2H), 7.10 (d, J = 5.2 Hz, 2H), 7.28 (bs, 1H).

^{13}C NMR: δ 38.2, 52.0, 52.1, 83.9, 98.0, 106.1, 110.0, 112.0, 141.3, 143.8, 145.0, 150.2, 162.3, 164.4.



65

IR (KBr) ν_{max} : 1728, 1634, 1438, 1263, 1115, 1040 cm^{-1}.

^{1}H NMR: δ 3.64 (s, 6H), 3.74 (s, 12H), 4.92 (d, *J* = 3.4 Hz, 1H), 5.60 (s, 1H), 5.65 (bs, 1H), 6.34 (bs, 1H), 7.03-7.06 (m, 3H), 7.15 (d, *J* = 5.2 Hz, 3H).

^{13}C NMR: δ 38.0, 51.9, 52.0, 52.1, 52.2, 53.2, 83.0, 83.1, 83.6, 96.7, 97.1, 97.9, 110.5, 110.9, 111.5, 142.0, 142.2, 142.4, 142.6, 144.9, 149.5, 151.0, 155.9, 158.2, 162.2, 162.4, 164.4, 164.7, 164.9.

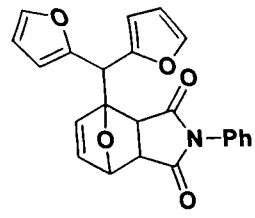
HRMS (FAB, M+H): Calcd for $C_{31}H_{28}O_{15}$: 641.11, Found: 640.11.

***Cycloadducts* 67a, 68a and 69a**

a) A solution of *N*-phenyl maleimide (199 mg, 1.16 mmol) and **48** (50 mg, 0.23 mmol) in dichloromethane (5 mL) was stirred for 7 days at room temperature. The solvent was removed and the crude product was purified by column chromatography on silica gel (10% ethylacetate in hexane) to afford **67a** (53 mg, 75%) as a viscous yellow liquid.

b) To a stirred solution of **48** (50 mg, 0.23 mmol) and *N*-phenyl maleimide (199 mg, 1.16 mmol) in dichloromethane (5 mL) was added $BF_3.OEt_2$ (10 mol %) at -5 °C and stirred for 5 minutes. The reaction mixture was extracted with dichloromethane (2 X 25 mL). The organic layers were combined, washed with bicarbonate solution, dried over Na_2SO_4 and the solvent was removed on rotary evaporator. The crude products were purified by column chromatography on silica gel (10% ethylacetate in hexane) to afford **67a** (64 mg, 72%) as a viscous yellow liquid. Further elution with 20% and 50% ethylacetate in hexane solvent mixtures

afforded **68a** (14 mg, 11%) as a white crystalline solid. m. p. 141-143 °C and 69a (17 mg, 10%) as a pale yellow crystalline solid. m. p. 198-200 °C.

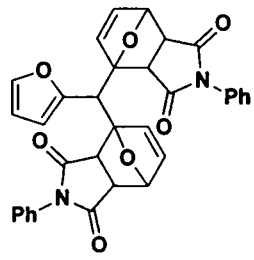


67a

IR (Neat) ν_{max}: 1715, 1595, 1499, 1384, 1189 cm^{-1}.

^{1}H NMR: δ 2.98 (d, *J* = 3.7 Hz, 2H), 5.08 (s, 1H), 5.40 (s, 1H), 6.24 (d, J = 3.0 Hz, 1H), 6.28 (d, *J* = 3.1 Hz, 1H), 6.39 (d, *J* = 1.8 Hz, 1H), 6.54-6.57 (m, 2H), 6.84-6.88 (m, 1H), 7.23-7.50 (m, 7H).

^{13}C NMR: δ 39.0, 48.7, 50.8, 81.4, 92.3, 107.4, 108.4, 109.9, 110.4, 110.7, 126.7, 128.5, 128.9, 131.9, 136.4, 138.7, 141.6, 142.0, 150.6, 150.9, 173.2, 174.1.

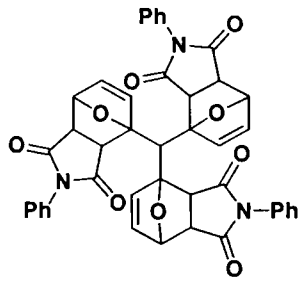


68a

IR (KBr) ν_{max} : 1705, 1595, 1497, 1382, 1191, 965, 720 cm^{-1}.

^{1}H NMR: δ 2.90 (d, *J* = 6.7 Hz, 1H), 2.98 (d, *J* = 6.7 Hz, 1H), 3.06 (d, *J* = 6.7 Hz, 1H), 3.31 (d, *J* = 6.7 Hz, 1H), 4.98 (s, 1H), 5.27 (d, *J* = 1.5 Hz, 1H), 5.39 (d, *J* = 1.5 Hz, 1H), 6.26-6.27 (m, 1H), 6.41 (d, *J* = 5.8 Hz, 1H), 6.48 (d, *J* = 5.7 Hz, 1H), 6.61 (d, *J* = 3.1 Hz, 1H), 6.68 (d, *J* = 5.7 Hz, 1H), 6.74 (d, *J* = 5.8 Hz, 1H), 7.18-7.38 (m, 10H), 7.50-7.53 (m, 1H).

^{13}C NMR: δ 37.4, 49.1, 49.8, 50.3, 50.6, 80.4, 81.3, 91.1, 92.1, 108.3, 110.5, 111.8, 126.2, 127.1, 128.2, 128.4, 128.6, 128.7, 129.0, 132.0, 135.6, 136.0, 137.9, 140.1, 142.3, 149.9, 173.2, 174.6.



69a

IR (KBr) ν_{max} : 1709, 1590, 1498, 1193, 754, 692 cm^{-1}.

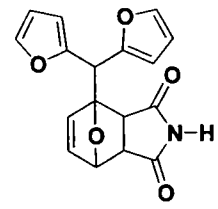
^{1}H NMR: δ 3.01 (d, *J* = 7.0 Hz, 3H), 3.25 (d, *J* = 7.0 Hz, 3H), 4.82 (s, 1H), 5.41 (s, 3H), 6.49 (d, *J* = 5.5 Hz, 3H), 6.76 (d, *J* = 5.7 Hz, 3H), 7.18-7.40 (m, 15H).

^{13}C NMR: δ 40.1, 50.0, 50.1, 79.6, 91.0, 95.6, 106.3, 126.3, 127.2, 127.5, 128.3, 128.6, 132.0, 135.0, 139.2, 172.0, 174.4.

***Cycloadduct* 67b and 69b**

a) A solution of maleimide (113 mg, 1.16 mmol) and **48** (50 mg, 0.23 mmol) in dichloromethane (5 mL) was stirred for 7 days at room temperature. The solvent was removed and the crude product was purified by column chromatography on silica gel (10% ethylacetate in hexane) to afford **67b** (47 mg, 65%) as a white crystaline solid. m. p. 202-204 °C.

b) To a dichloromethane solution of **48** (50 mg, 0.23 mmol) and maleimide (113 mg, 1.16 mmol) was added $BF_3.OEt_2$ (10 mmol %) at –5 °C and stirred for 5 minutes. The reaction mixture was extracted with dichloromethane (2 X 25 mL). The organic layers were combined, washed with bicarbonate solution, dried over Na_2SO_4 and the solvent was removed on rotary evaporator. The crude product was subjected to column chromatography on silica gel (10% ethylacetate in hexane) to afford **67b** (36 mg, 50%) as a yellow viscous liquid. Further elution with 60% ethylacetate in hexane afforded **69b** (17 mg, 15%) as a white crystalline solid. m. p. 120-122 °C.

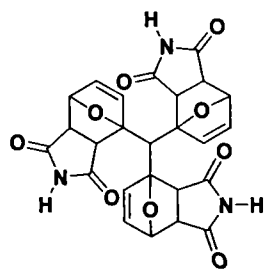


67b

IR (Neat) ν_{max}: 3216, 1769, 1712, 1635, 1362, 1197, 1032, 975, 780, 744 cm^{-1}.

^{1}H NMR: δ 2.96 (s, 2H), 5.07 (s, 1H), 5.26 (s, 1H), 6.25-6.28 (m, 2H), 6.34 (s, 1H), 6.39 (bs, 2H), 6.76 (d, J = 5.5 Hz, 1H), 7.32 (s, 1H), 7.42 (s, 1H), 8.20 (bs, 1H, D_2O exchangeable).

^{13}C NMR: δ 38.8, 49.9, 52.0, 81.1, 92.1, 108.4, 108.9, 109.7, 110.2, 110.6, 136.4, 138.3, 141.9, 142.2, 150.9.



69b

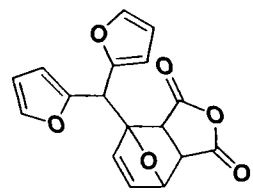
IR (KBr) ν_{max} : 3210, 1760, 1710, 1633, 1358, 1190, 1027, 965 cm^{-1}.

^{1}H NMR: δ 2.67 (d, J = 6.6 Hz, 2H), 2.82 (d, J = 6.5 Hz, 2H), 2.90 (d, J = 6.4 Hz, 2H), 4.83 (s, 1H), 5.05 (s, 1H), 5.38 (s, 1H), 6.23 (s, 1H), 6.31-6.84 (m, 6H), 7.31 (s, 1H), 7.38 (s, 1H), 4.43 (s, 1H).

^{13}C NMR: δ 38.7, 49.9, 50.3, 51.1, 51.5, 52.1, 81.0, 81.3, 90.7, 91.5, 108.4, 109.7, 110.2, 111.1, 135.0, 137.9, 139.7, 141.8, 150.0, 150.3.

***Cycloadduct* 71**

A solution of **48** (50 mg, 0.23 mmol) and maleic anhydride (114 mg, 1.16 mmol) in dichloromethane (5 mL) was stirred at room temperature for 7 days. The solvent was removed on rotary evaporator. The crude products were purified by column chromatography on silica gel (10% ethylacetate in hexane) to afford **71** (57 mg, 80%) as a white crystalline solid. m. p. 110-112 °C.



71

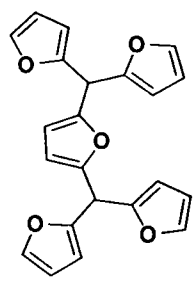
IR (KBr) ν_{max} : 1849, 1789, 1499, 1222, 1081, 926 cm^{-1}.

^{1}H NMR: δ 3.22 (d, *J* = 4.8 Hz, 2H), 5.01 (s, 1H), 5.38 (d, *J* = 1.6 Hz, 1H), 6.23 (d, *J* = 3.1 Hz, 1H), 6.28-6.31 (m, 1H), 6.39-6.41 (m, 1H), 6.49 (d, *J* = 3.1 Hz, 1H), 6.52 (d, *J* = 5.8 Hz, 1H), 6.82 (d, *J* = 5.8 Hz, 1H), 7.32 (s, 1H), 7.44 (s, 1H).

^{13}C NMR: δ 38.9, 50.4, 51.9, 82.1, 107.3, 108.6, 109.9, 110.4, 110.7, 136.4, 141.9, 151.9.

***Compounds* 72 and 73**

To a stirred solution of **51** (100 mg, 0.41 mmol) and **48** (176 mg, 0.82 mmol) in benzene (10 mL) was added P_2O_5 (10 g) in small portions at 70 °C and stirred for 12 h. The reaction mixture was filtered and the filtrate was concentrated in vacuo. The crude product was subjected to column chromatography on silica gel. Elution with 2% ethylacetate in hexane afforded **72** (22 mg, 15%) as a viscous red liquid and on further elution with 5% ethylacetate in hexane afforded **73** (16 mg, 8%) as a viscous orange liquid.



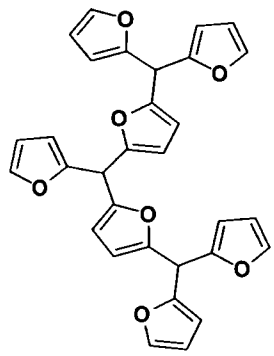
72

IR (Neat) ν_{max}: 1734, 1594, 1501, 1460, 1222, 1165, 1077, 1015, 777 cm^{-1}.

^{1}H NMR: δ 5.49 (s, 1H), 6.05 (s, 1H), 6.09 (m, 2H), 6.29 (d, *J* = 3.1 Hz, 2H), 7.33 (s, 2H).

^{13}C NMR: δ 39.0, 107.3, 108.2, 110.4, 141.9, 151.3, 151.9.

HRMS (FAB, Na): Calcd for $C_{22}H_{16}O_5$: 383, Found: 383.



73

IR (Neat) ν_{max}: 1729, 1597, 1504, 1232, 1168, 1076, 1012, 774 cm^{-1}.

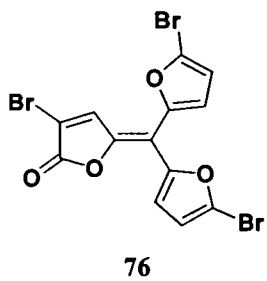
^{1}H NMR: δ 5.45 (s, 1H), 5.47 (s, 2H), 5.99 (m, 9H), 6.29 (m, 5H), 7.34 (bs, 5H).

^{13}C NMR: δ 39.0, 107.3, 108.2, 110.4, 141.9, 151.3, 151.9.

HRMS (FAB, Na): Calcd for $C_{31}H_{22}O_7$: 529, Found: 529.

Compounds 76 and 77

To a stirred solution of **48** (50 mg, 0.23 mmol) in dichloromethane (5 mL) was added DDQ (80 mg, 0.35 mmol) followed by aqueous HPF_6 (1 mL) and stirred for 10 minutes at room temperature. The solid formed was filtered, dried and used for further reaction without purification. To a stirred solution of the salt dissolved in dichloromethane (5 mL) was added KBr (63 mg, 0.46 mmol) and Br_2 (73 mg, 0.46 mmol). After stirring the reaction mixture for further 30 minutes, the solvent was removed and the crude products were purified by column chromatography on silica gel (5% ethylacetate in hexane) to afford **76** (42 mg, 40%) as a red crystalline solid. m.p. 164-166 °C. On further elution with 10% ethylacetate in hexane afforded **77** (26 mg, 21%) as a viscous red liquid.



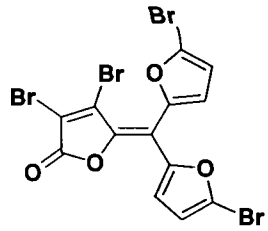
76

IR (KBr) ν_{max}: 1763, 1457, 1348, 1244, 1210, 1035, 982 cm^{-1}.

^{1}H NMR: δ 6.50 (dd, J_1 = 3.5 Hz, J_2 = 5.1 Hz, 2H), 6.82 (d, J = 3.5 Hz, 1H), 7.10 (d, J = 3.6 Hz, 1H), 8.08 (s, 1H).

^{13}C NMR: δ 114.2, 114.7, 118.2, 119.7, 124.6, 124.9, 140.7, 147.9, 148.3, 163.0.

HRMS (FAB, M+H): Calcd for $C_{13}H_5Br_3O_4$: 462.78, Found: 463.66.



77

IR (KBr) ν_{max} : 1784, 1760, 1537, 1485, 1336, 1300, 1233, 1166 cm^{-1}.

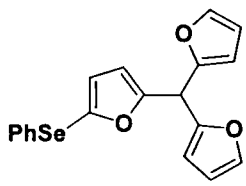
^{1}H NMR: δ 6.39 (d, J = 5.4 Hz, 1H), 6.50 (d, J = 6.1 Hz, 2H), 7.66 (d, J = 5.4 Hz, 1H).

^{13}C NMR: δ 88.9, 105.9, 106.3, 117.4, 121.5, 142.1, 161.3, 168.2.

HRMS (EI): Calcd for $C_{13}H_4Br_4O_4$: 543.78, Found: 543.69.

***1,1-Bis(2-furyl)-1-(5-phenylselenenyl-2-furyl)methane* 78 *and tris(2-furyl) pheneylselenenyl methane* 79**

To a degassed solution of **48** (100 mg, 0.46 mmol) in THF (10 mL) was added catalytic amount of TMEDA followed by BuLi (1.6 M solution in hexane, 1.15 mL (1.84 mmol) at -78 °C. After stirring the reaction mixture for 5 minutes, at -78 °C, diphenyldiselenide (433 mg, 1.38 mmol) in THF (5 mL) was added. The reaction mixture was alowed to stir at this temperature for further 30 minutes; the solvent was removed and extracted with ethylacetate (2 X 25 mL). The organic layers were combined, dried over Na_2SO_4 and the solvent was removed under reduced pressure. The crude product was subjected to column chromatography on silica gel (2% ethylacetate in hexane) to afford **78** (17 mg, 10%) as a pale yellow viscous liquid. Further elution using 5% ethylacetate in hexane afforded **79** (highly unstable).

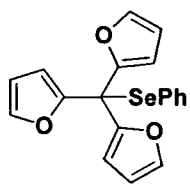


78

IR (Neat) ν_{max}: 1583, 1506, 1470, 1439, 1235, 1145, 1063, 1006 cm^{-1}.

^{1}H NMR: δ 5.48 (s, 1H), 6.01 (d, J = 3.14 Hz, 2H), 6.06 (d, J = 3.0 Hz, 1H), 6.22 (m, 2H), 6.59 (d, J = 3.1 Hz, 1H), 7.06 (m, 5H), 7.27 (bs, 2H).

^{13}C NMR: δ 39.2, 107.3, 107.6, 109.7, 110.4, 121.8, 126.7, 129.2, 130.1, 141.9, 142.0, 151.4, 156.0.



79

IR (Neat) ν_{max}: 1652, 1630, 1598, 1550, 1390, 1340, 1180, 1140 cm^{-1}.

^{1}H NMR: δ 6.02 (d, J = 3.14 Hz, 3H), 6.32-6.42 (m, 3H), 7.35-7.39 (m, 8H).

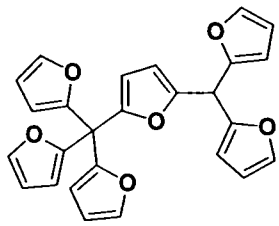
^{13}C NMR: δ 41.7, 107.3, 110.4, 127.7, 129.1, 129.2, 129.3, 131.5, 135.9, 137.3, 141.9.

***1,1-Bis(2-furyl)-1- [5-(tris-2-furylmethyl)]furylmethane* 81**

a) To a degassed solution of **48** (100 mg, 0.46 mmol) in THF (10 mL) was added catalytic amount of TMEDA followed by BuLi (1.6M solution in hexane, 1.15 mL (1.84 mmol) at -78 °C. After stirring the reaction for 30 min, the solvent was removed under reduced pressure and extracted with ethylacetate (2 X 25 mL). The organic layers were combined, dried over Na_2SO_4 and the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel (2% ethylacetate in hexane) to afford **81** (40 mg, 40%) as a viscous pale yellow liquid.

b) To a degassed solution of **48** (100 mg, 0.46 mmol) in THF (10 mL) was added $KOBu^t$ (110 mg, 1 mmol) and stirred for 30 min. The solvent was removed under reduced pressure and was extracted with ethylacetate (2 X 25 mL). The organic layers were combined, dried over Na_2SO_4 and the solvent was removed

under reduced pressure. The crude product was purified by column chromatography on silica gel (2% ethylacetate in hexane) to afford **81** (49 mg, 50%) as a viscous pale yellow liquid.



81

IR (Neat) ν_{max}: 1501, 1265, 1170, 1094, 1011, 811, 735 cm^{-1}.

^{1}H NMR: δ 5.50 (s, 1H,), 5.92 (d, J = 3.2 Hz, 1H), 6.01-6.10 (m, 6H), 6.28-6.29 (m, 2H), 6.32-6.33 (m, 3H), 7.34 (bs, 2H), 7.39 (bs, 3H).

^{13}C NMR: δ 31.9, 39.0, 107.3, 108.0, 108.8, 109.6, 110.3, 141.8, 142.2, 151.6, 151.8, 151.9, 152.6.

HRMS (EI): Calcd for $C_{26}H_{18}O_6$: 426.1103, Found: 426.1116.

3.8 References

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Summary

The thesis entitled "**Novel Reactions of Tris(2-theinyl)methane and Tris(2-furyl)methane**" embodies the results of investigations carried out to gain some insight into the reactivity of two trisheteroarylmethane moieties *viz.* tris(2-thienyl)methane and tris(2-furyl)methane.

The first part of Chapter 1 presents a brief account of the synthesis and applications of dendrimers. A general introduction to carbon centered radicals with some special emphasis on Gomberg's radical is presented in the second part of Chapter 1. A definition of the present research problem has also been incorporated at the end of each part.

The second chapter of the thesis deals with the results of our investigation on the reactivity of the heteroaromatic system, tris(2-thienyl)methane. It has been shown that the compound undergoes facile electrophilic substitution and reacts with electrophilic carbenes also. The facile formation of higher homologs of tris(2-thienyl)methane by nucleophilic addition reaction is also presented in this chapter. Palladium mediated coupling reaction of the bromoderivative of tris(2-thienyl)methane have been shown to be an efficient method for generating some lower order dendritic structures.

The third and the final chapter contains the results of our investigation on tris(2-furyl)methane. The furyl rings of the molecule underwent electrophilc substitution reactions and the reaction with cyclic and acyclic carbenes showed different reactivity patterns. Cycloaddition reaction with dienophiles afforded three cycloadducts in the presence of strong catalysts while in the absence of catalysts, exclusive formation of monoadduct was observed. Nucleophilic addition has been shown as a useful method for the generation of higher homologs of trifurylmethane systems. Our attempts towards the synthesis of tris(2-furyl)methyl

radical, the hetero analog of Gomberg's radical has also been described in Chapter 3.

In conclusion, we have uncovered some novel reactivity patterns of tris(2-thienyl)methane and tris(2-furyl)methane. It is worthy of note that this work has opened up efficient routes to the synthesis of some lower order dendrimers, higher homologs of trisheteroarylmethane systems and the dimer of tris(2-furyl)methyl radical. All these products are potentially amenable to further transformations leading to a variety of interesting compounds including unique three dimensional network systems.

List of Publications

1. Novel cycloadditions of *o*-thioquinones with acyclic dienes: Expeditious synthesis of benzoxathiins.
   Nair, V.; Mathew, B.; **Thomas, S.**; Vairamani, M.; Prabhakar, S.
   J. Chem., Soc. Perkin Trans. 1 **2001,** 3020.

2. An efficient bromination of alkenes using cerium(IV) ammonium nitrate (CAN) and potassium bromide.
   Nair, V.; Panicker, S. B.; Augustine, A.; George, T. G.; **Thomas, S.**; Vairamani, M.
   Tetrahedron **2001**, *57*, 7417.

3. Oxidative fragmentation of 1-aryl-1-cycloalkenes using cerium(IV) ammonium nitrate: some novel observations.
   Nair, V.; Panicker, S. B.; **Thomas, S.**; Santhi,V.; Mathai, S.; Vairamani, M.; Prabhakar, S.
   Tetrahedron **2002**, *58*, 3229.

4. Novel oxidative rearrangement of monoterpenes mediated by cerium(IV) ammonium nitrate.
   Nair, V.; Rajan, R.; Balagopal, L.; **Thomas, S.**; Narasimlu, K.
   Tetrahedron Lett. **2002**, *43*, 8971.

5. A serendipitious synthesis of 1,1-bisfuryl-1-[5-(tri-2-furylmethyl)]furylmethane by the reaction of tri-2-furylmethane with butyllithium.
   Nair, V.; **Thomas, S.**; Mathew, S. C.
   Org. Lett. **2004**, 3513.

6. A novel approach towards the synthesis of polyheterocyclic dendrimers using tri(2-thienyl)methane as the dendron.
   Nair, V.; **Thomas, S.** (manuscript to be communicated to *Org. Lett.*).

7. A one pot synthesis of higher generations of tris(2-thienyl)methane and tris(2-furyl)methane *via* nucleophilic addition reaction.
   Nair, V.; **Thomas, S.** (manuscript to be communicated).

POSTERS PRESENTED AT CONFERENCES

1. Novel Reactions of Phenylcycloalkenes with CAN in Methanol
   Siji Thomas, Sreeletha B. Panicker and Vijay Nair
   In the *"Fourth National Symposium in Chemistry"* by CRSI held at Pune, (India) February 7 – 9, 2002.
2. Novel Reactions of Activated *p*-Benzoquinones with Styrenes
   Siji Thomas and Vijay Nair
   In the *"Fifth National Symposium in Chemistry"* by CRSI held at Chennai, (India) February 7 – 9, 2003.