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ANNELATED BIPHENYLENES - SYNTHESES AND INVESTIGATION

By

GHISLAIN REAUSSEL MANDOUMA

A dissertation submitted to the Graduate Faculty in Chemistry in partial fulfillment of the requirements for the degree of Doctor of Philosophy, The City University of New York

2002

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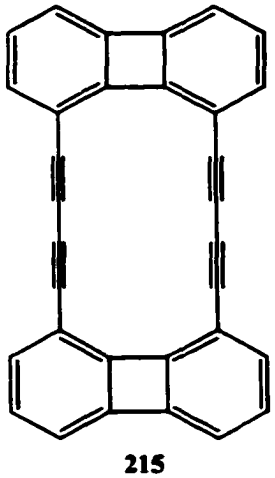
BIPHENYLENE ANNELATED COMPOUNDS: SYNTHESES AND INVESTIGATION

By Ghislain Reaussel Mandouma

Advisor: Professor Klaus G. Grohmann



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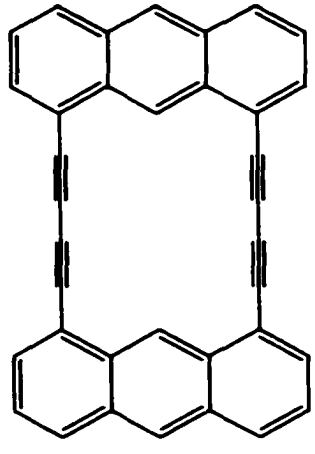

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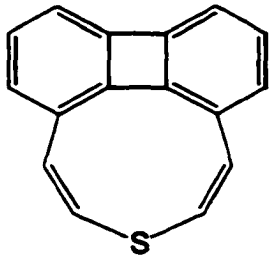

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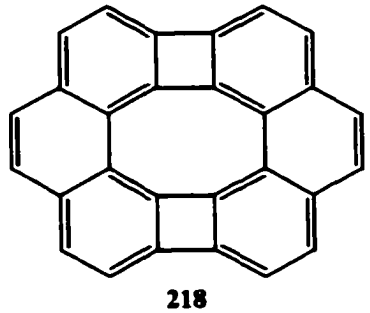

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Abstract

The aim of the dissertation was to develop synthetic routes to bis(diacetylene)biphenylene **215**, 4,5:6,7-dibenzocyclobutathionin (biphenylenothionin) **217** and biscyclobuta[*c,g*]phenanthrene (bi-3,4:5,6-phenanthrylene) **218** as well as the study of their physical and chemical properties. Bis(diacetylene)anthracene **216**, the dimer of 1,8-diethynylanthracene **213**, prepared 40 years ago by the group of Nakagawa, was more efficiently synthesized as a model compound to **215**. Molecules **215** and **216** are considered as precursors to carbon-rich materials and were synthesized by oxidative alkyne-alkyne coupling reaction.

The first part of this dissertation introduces the initial concepts for synthesizing biphenylene and its dialkyl and dihalo derivatives as the basis to the successful total syntheses of **215** and **216**, through similar protocoles: palladium/nickel-mediated couplings of protected acetylene to dihaloarenes (biphenylene and anthracene) followed by copper(II)-mediated oxidative coupling of the terminal acetylenes to afford the dimers **215** and **216** (second part). Attempts to synthesize the annelated thionin **217** through nucleophilic addition of sulfide ion to 1,8-diethynylbiphenylene will be presented.

Preliminary results (GCMS) suggest a facile and expected extrusion of sulfur atom to give cycloocta[*def*]biphenylene.

This is followed by a theoretical discussion predicting the formation of bis(cyclobuta)phenanthrene **218** and our synthetic efforts directed towards the target are presented in the final part.

Acknowledgements

Give thanks with a grateful heart...

I would like to thank a host of people. In fact, too many so that, in advance, I apologize to those whose names won't appear in the following lines. I want to thank all those who contributed to my education in general and this dissertation in particular. Starting with the latter, I am grateful to the wonderful colleagues I've met and known in and around the "Grohmann lab". From Ronnie Benshafrut and Shu Ya Hsu who welcomed me into the lab to those whom I am leaving behind, Jelena Zivkovic and Kaifan Cheng, Stewart Hung and colleagues from the "Matsui group". I've greatly enjoyed their friendship, collaboration and support. Thanks!

Thanks that I gladly extend to the graduate and undergraduate students in the chemistry department with whom I had friendly interactions and laughs with special mention to Darren Dabbiden (my groom's man), Janice Thai and John Zambrano.

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Emmanuel Bolimba

Louise Massiko

Sydrac Mandouma

Gilesi Mongelo-Bokelo

Barthelémy Olandzobo

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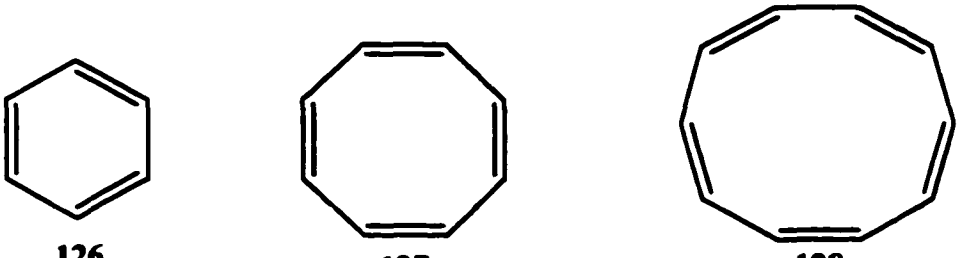
Historical Background

1.1. From Benzene to Annulenes



126 C_6H_6

127 C_8H_8

128 $C_{10}H_{10}$

Figure 1: benzene, cyclooctatetraene and cyclodecapentaene

Soon after the structure of benzene **126** was proposed by Kekulé[1] in 1865, chemists began to suspect that this C_6H_6 hydrocarbon might not be unique in its properties, but rather the first-discovered member in a series of cyclic, conjugated polyenes similarly endowed with stability. The synthesis of the next higher vinylog, cyclooctatetraene C_8H_8 **127** became the focus of researchers in order to test this hypothesis. This was achieved in 1911 by Willstätter and Waser[2], but just to reveal that this homolog exhibited chemical reactivity like that expected of a linear polyene, hence, making

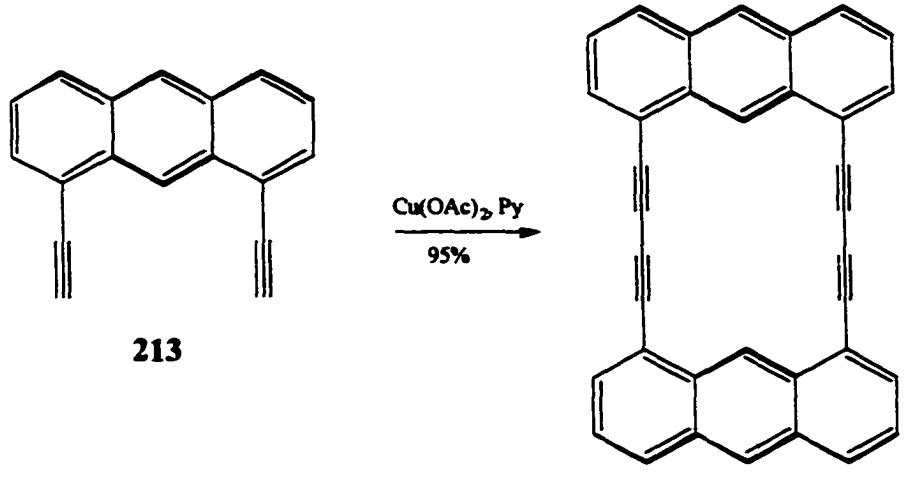
benzene a special case. The "aromatic sextet" of electrons theory -among many others- was developed to rationalize the inordinate stability of the formal triene, including the tendency to retain its structural type during reaction. In 1932, Hückel[3], employing a quantum mechanical approach, developed a theoretical treatment that repositioned benzene as one member of a series of structures expected to be stable by virtue of a closed shell of $4n+2$ π-electrons. Hückel's theory was stated to be valid only for monocyclic polyolefins which were fully conjugated. The extent to which Hückel's rule has succeeded in permitting predictions of aromaticity or the absence thereof is now general knowledge.

Cyclodecapentaene **128**, with its closed shell of 10 π-electrons was to be considered next. It was hypothesized to exist in various cis-trans isomers[4] to relieve the bond angle strain and/or nonbonded atomic repulsion in the interior of the carbocyclic structure. The synthetic efforts towards this annulene and its higher homologues were to become critical in the definition of criteria for aromaticity[5-12]. This era witnessed the emergence of NMR spectroscopy as one of the most direct criteria[13] for aromaticity, along with determination of heats of hydrogenation or combustion and diminished bond alternation in the conjugated cyclic system, NMR being used to established the presence of a magnetically induced diamagnetic ring current.

1.2. The dehydrobenzoannulenes and the aromaticity era

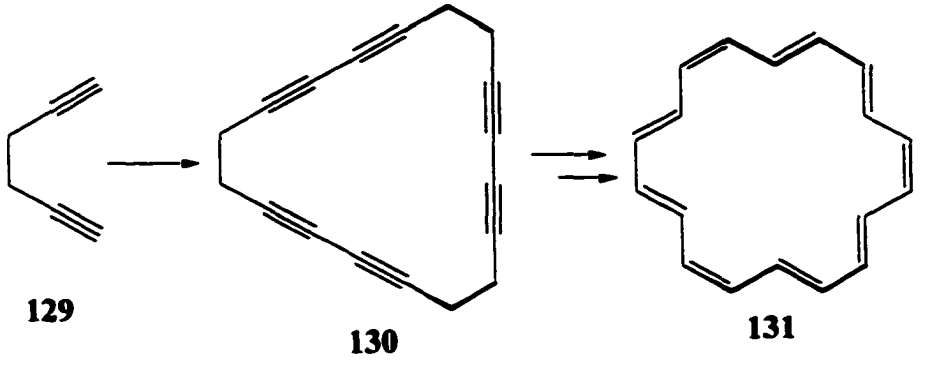
Back in the 1960s and 1970s, led by the groups of Nakagawa[47], Sondheimer[48], and Staab[49], acetylene chemistry saw a tremendous expansion in the area of dehydrobenzoannulenes (DBAs). They prepared an impressive array of DBA structures in connection to the dominating question of ring currents in the DBA macrocycles. Nakagawa and coworkers applied the copper acetate-mediated oxidative coupling reaction to 1,8-diethynylanthracene to synthesize the resultant cyclic dimer in very high yield[50].

Scheme 1: *Synthesis of* ***216*** *by the Eglinton oxidative acetylene coupling by Nakagawa et al.*[47]



213 **216**

Starting in the mid-1950s Sondheimer and co-workers began to develop an approach to the *annulenes* (from the latin word for ring). The numerous annulenes prepared by the Sondheimer group are part of chemistry textbooks today and many reviews have appeared[51]. A prototypical synthesis is that of the [18]annulene **131**, in three steps including an oxidative trimerization of 1,5-hexadiyne **129** by the Eglinton coupling process.

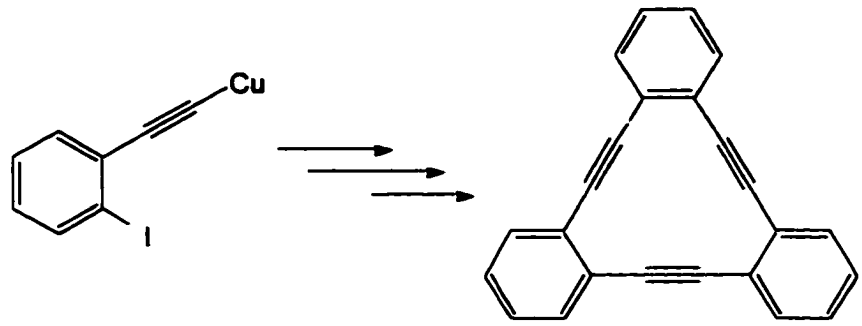


129 **130** **131**

Scheme 2:*Sondheimer's synthesis*[48] *of [18]annulene* **131** *via oxidative alkyne coupling of 1,5-hexadiyne* **129** *to* **130**

Eglinton and Raphael[52] had previously used the copper acetate route, while Staab *et al.*[53] employed a Wittig reaction to arrive almost simultaneously to 5,11,17-tris-dehydro-tribenzo-[*a,e,i*]-[12]annulene **133**, a precursor to graphyne.

***Scheme 3**: Synthesis of graphyne monomer* **133** *by Eglinton et al.*[52]



132 **133**

When one extra alkyne unit was included between the aromatic rings of graphyne, the macromolecular unit for the network of graphdiyne resulted.

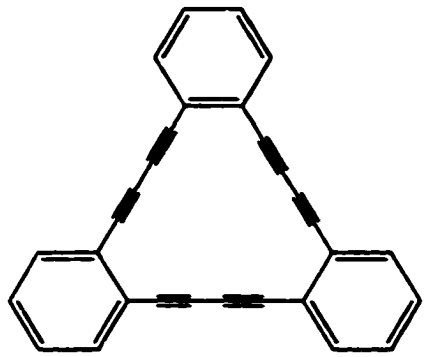


Figure 2: Graphdiyne monomer unit

1.3. From Annelated Annulenes to Novel Carbon Networks

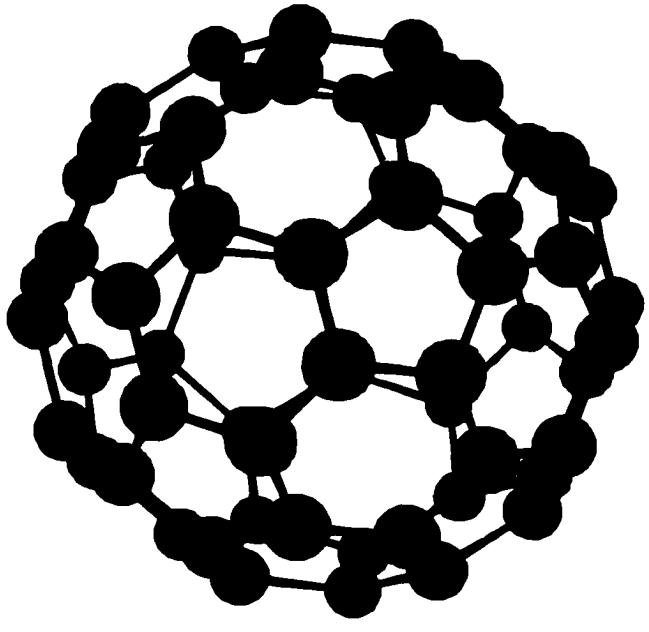


Figure 3: Buckminsterfullerene (ball and stick model)

The properties of annulenes annelated with a 6π ring system are of considerable interest with respect to the participation of benzenoid π–electrons in the macrocyclic π–electron system. The chemistry of dehydrobenzoannulenes (DBAs)[14] initiated in the 1960s by the groups of Nakagawa, Staab, and Sondheimer was then driven by the question of ring currents in the DBA macrocycles and how diatropic, paratropic or atropic each of these systems were. It was found[15] that annelation of one 6π ring onto a dehydro [4n]- or dehydro[4n+2]annulene ring strongly suppressed the tropicity of the macrocyclic ring as compared with that of the corresponding

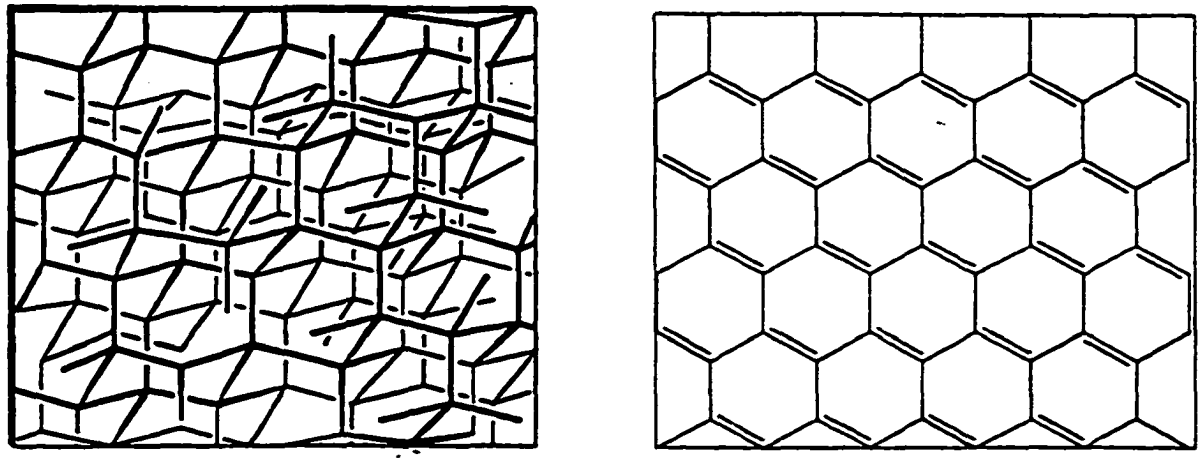
non-annelated dehydroannulene. However, an interestingly strong diatropicity was found in annelated dehydroannulenes fused with two aromatic rings. We were intrigued by the prospect of annelating a different system, namely biphenylene, to the dehydroannulene cores and studying the properties of such a system. Hence, the compounds **215**, **217** and **218** are illustrative of biphenylene annelation to [16], [10] and [8]annulenes respectively which may serve as the latest frontiers in the theory of aromaticity, as well as novel materials with interesting properties.

With the discovery of molecular allotropes of carbon, epitomized by buckminsterfullerene (C_{60}) and the corresponding elongated structures called buckytubes with their exceptional physico-chemical and material properties, research on all-carbon and carbon-rich molecular and polymeric systems, of which DBAs are a prime example, has become of actuality.

Long before the discovery of buckminsterfullerene and the subsequent development of fullerene chemistry, the assembly of carbon atoms into all-carbon molecules and polymers had already been the subject of a large body of experimental and theoretical work[16]. With the advent of laser vaporization techniques in the early 1980s, all-carbon molecules and ions became the subject of intensive experimental and theoretical studies[17]. Ion cyclotron resonance experiments have been particularly valuable for generating mass-

selected ion beams of significant lifetime, allowing the study of both physical and chemical properties of these ions. The consensus among the theoreticians is that the larger molecules C_{10} through C_{29} should have monocyclic structures[18] while above C_{40}, fullerene structures should become abundant[19]. A variety of imaginative and practical structures for two-dimensional and three-dimensional all-carbon networks that differ from graphite and diamond were proposed in the literature[20-22].

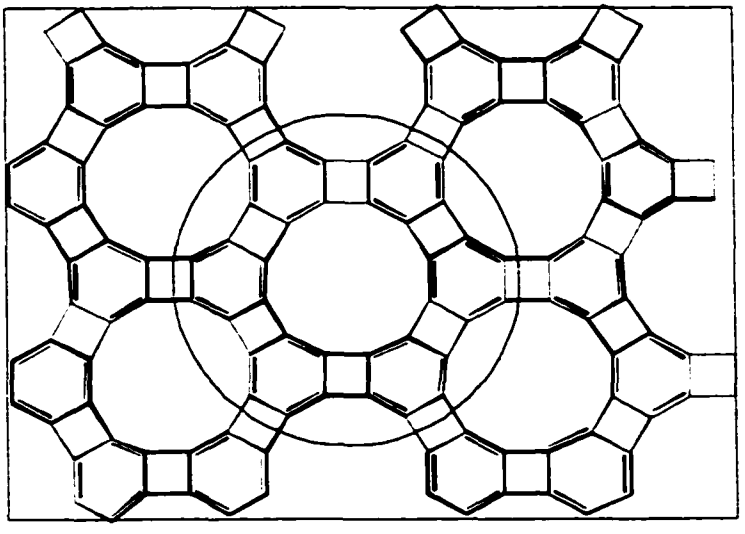
Figure 4: Diamond and graphite all-carbon networks



called karbin were thought to have a structure which contained carbon in alkyne or cumulene needles (see Polyynes: Precursors to Molecular Carbon Rods). These theoretical studies on hypothetical carbon systems have been reviewed by Stankevich and others[24-26].

Balaban and Hoffmann were among the first to suggest two and three dimensional carbon networks based on a repetitive unit or monomer. Thus Balaban's net based on the putative compound antikekulene:

Figure 5: Carbon network suggested by Balaban et al[27].



The most significant early efforts towards the synthesis of all-carbon molecules were initiated by Chapman[28], quickly followed by Diederich *et al*[29].who have prepared a variety of perethynylated monomers such as

tetraethynylethene[30], tetraethynylbutatriene[31], and hexaethynyl[3]radialene[32]. Copper-mediated oxidative oligomerization of *cis* doubly deprotected tetraethynylethene derivatives produced remarkable annulenic substructures[33], which were potential precursors to additional networks. Whereas removal of the protecting group and subsequent oxidative dimerization of the perethynylated molecules should lead to the desired diacetylenic carbon allotropes, the deprotected polyynes unstability, even in dilute solutions at subzero temperatures has significantly restricted oligomerization or polymerization studies of these systems.

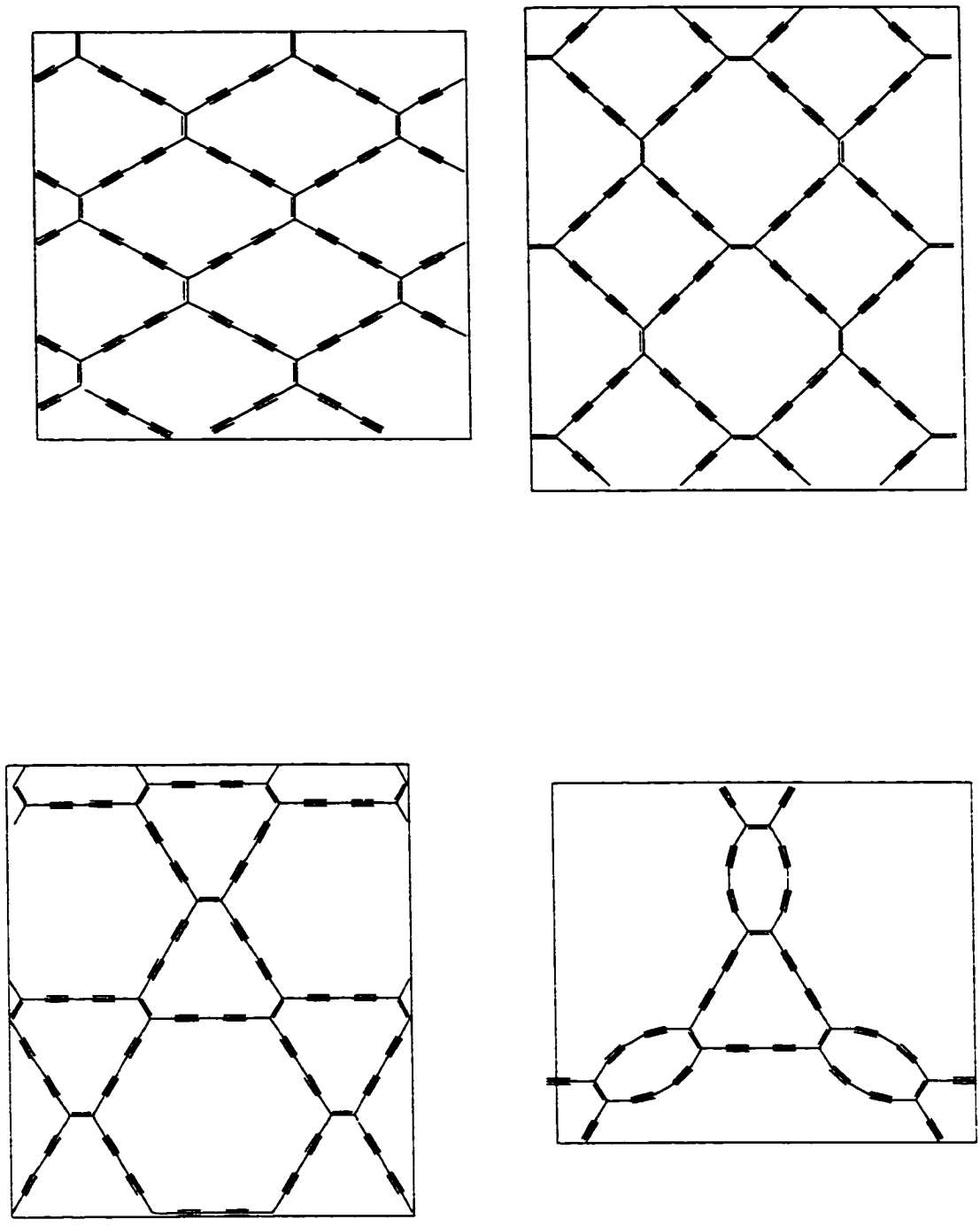


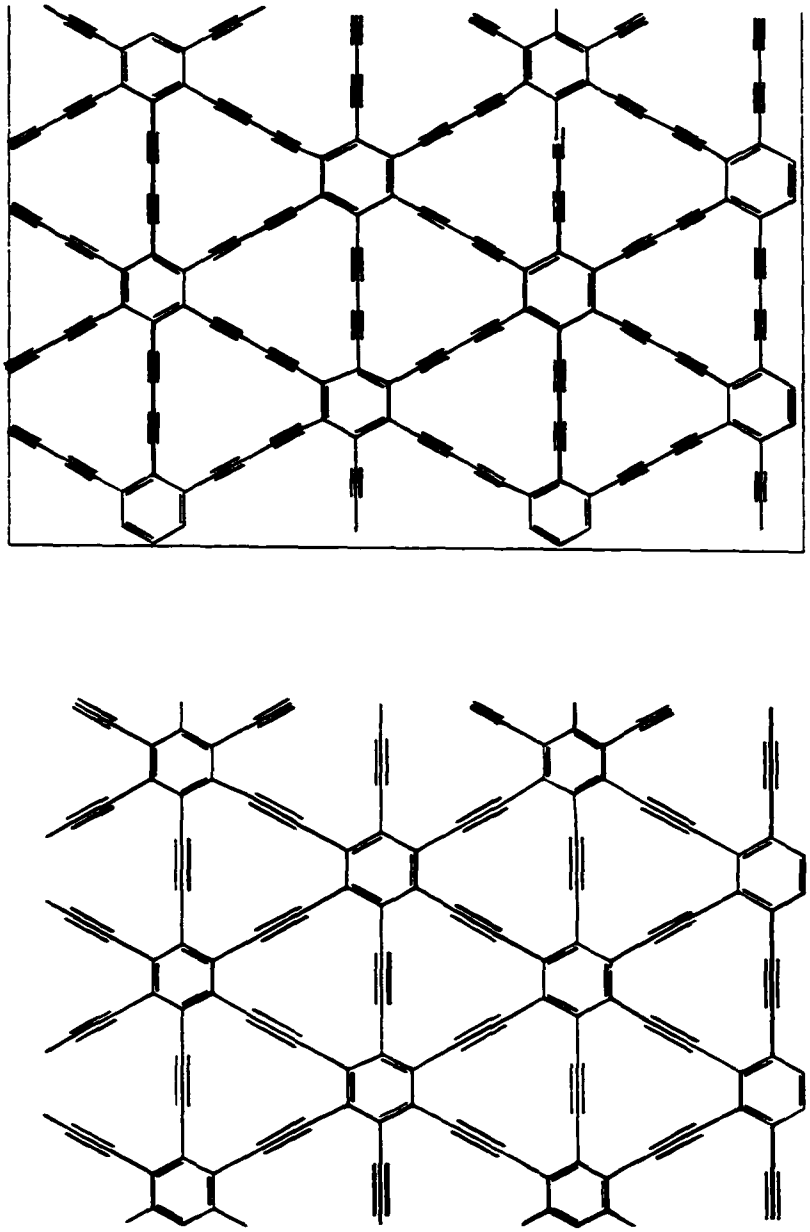
Figure 6: Hypothetical novel carbon networks[29] based on perethynylated molecules

Strained diacetylenes have been shown to polymerize below 200 °C and over a relative narrow range by Swager *et al*[34]. Vollhardt and Youngs[35], while pyrolysing strained diacetylene, observed a topochemical polymerization as a tube-like structure with a polydiacetylene backbone.

Topochemical polymerization of diacetylenes creates single crystals of organic polymers with conjugated backbones[36]. The resultant polydiacetylenes are known to exhibit NonLinearOptical (NLO) properties and are photogenerated carriers with mobilities much higher than the organic polymers[37].

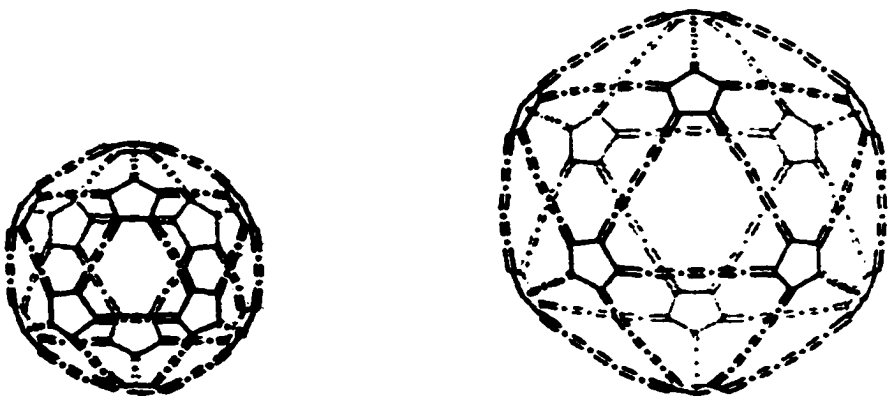
Incorporation of a stabilizing aromatic ring into the network backbone made preparation and isolation of larger substructures feasible. Thus, replacement of the ethene units in a polymer with benzene moieties leads to the all-carbon network of graphdiyne (**Fig.7**), the most stable carbon allotrope containing diacetylenic linkages. It was predicted to exhibit fascinating properties such as high, third-order nonlinear optical susceptibility, conductivity or superconductivity when doped with alkali metals, and enhanced redox activity. In addition, graphdiyne could provide a method of dopant storage that is not available to graphite, namely intrasheet intercalation. Work by Haley and coworkers is rapidly progressing towards syntheses of graphdiyne[38] and graphyne (with a monoacetylenic linkage)[39].

Figure 7: Graphdiyne (top) and graphyne (bottom) networks



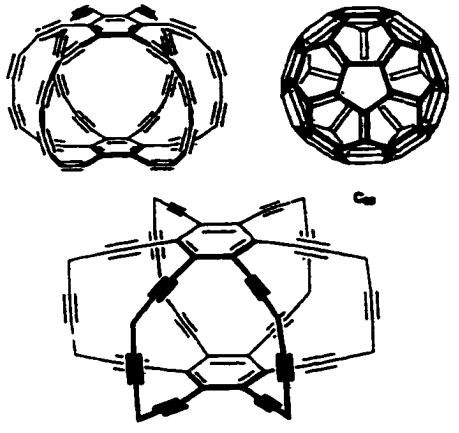
In addition to the formation of planar carbon networks, the linkage of pentagonal scaffolds can give three-dimensional cages such as C_{120} termed fullereneyne[40] and the more extended structure C_{180} which was coined fullerenediyne[41], in analogy to the structure of fullerene C_{60}.

Figure 8: Fullereneyne[40] (left) and fullerenediyne[41] (right)



Hexaethynylbenzene, already a motif for planar graphitic networks, has been proposed as a bridgehead scaffold for polyyne bridged all-carbon cage molecules such as D_{6h}-C_{60}, an isomer of I_h-C_{60}. This high-energy cage molecule has been proposed as a potential synthetic precursor to the fullerene C_{60}..

Figure 9: High energy cage structures[40] precursors to C_{60}



and its endohedral metal complexes[40].

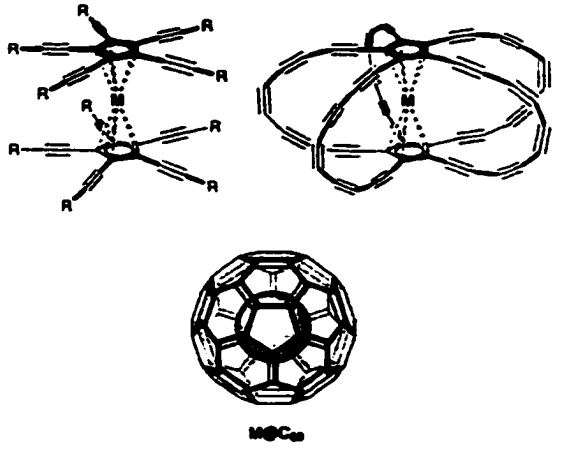
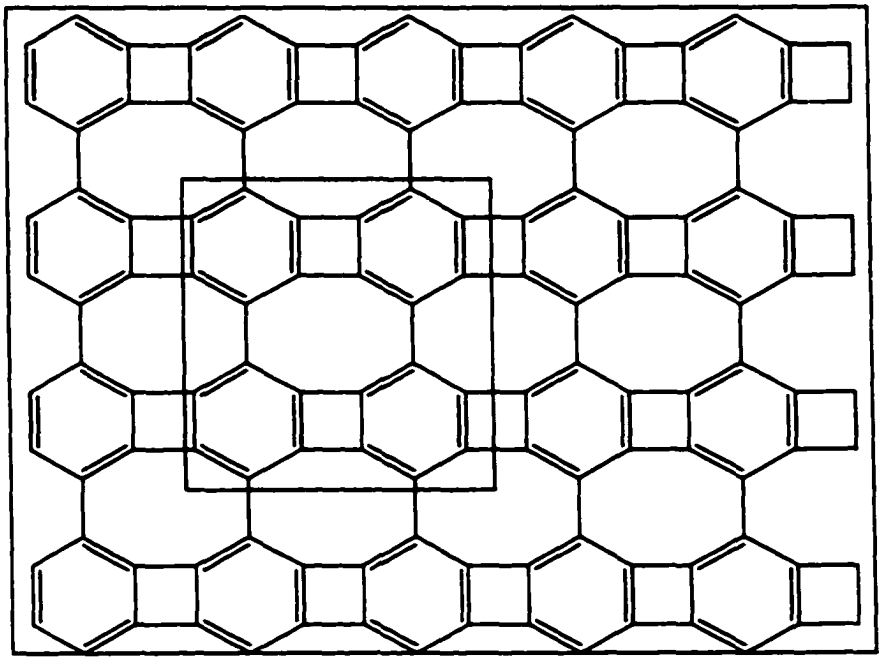


Figure 10: Encapsulated metal and endohedral fullerene[40]

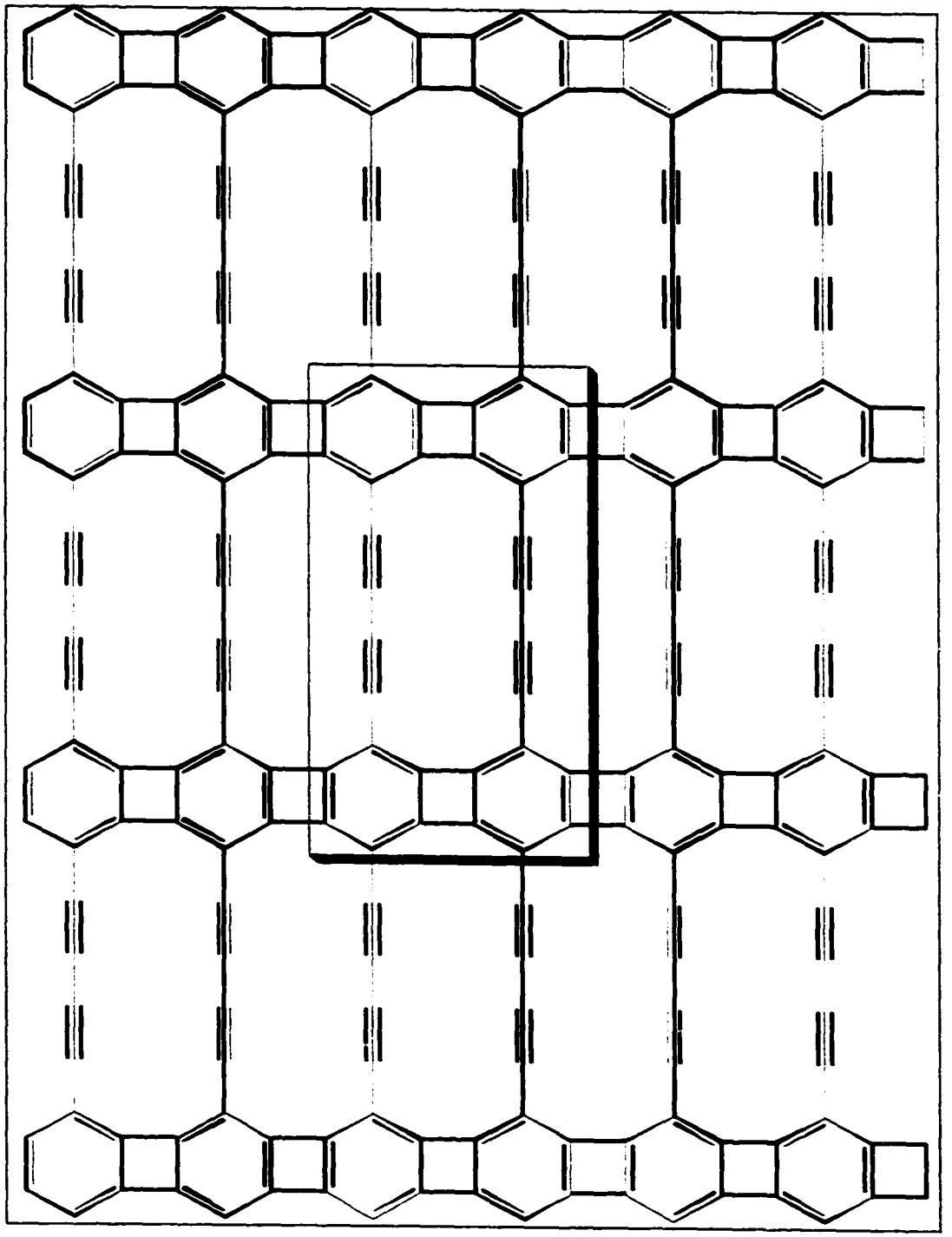
It was, however, the synthesis by Rajca *et al*[42].of the first biphenylene-based oligomer in 1996 that prompted us into consideration of the biphenylene nucleus as a versatile replacement of ethene or benzene in the network backbone.

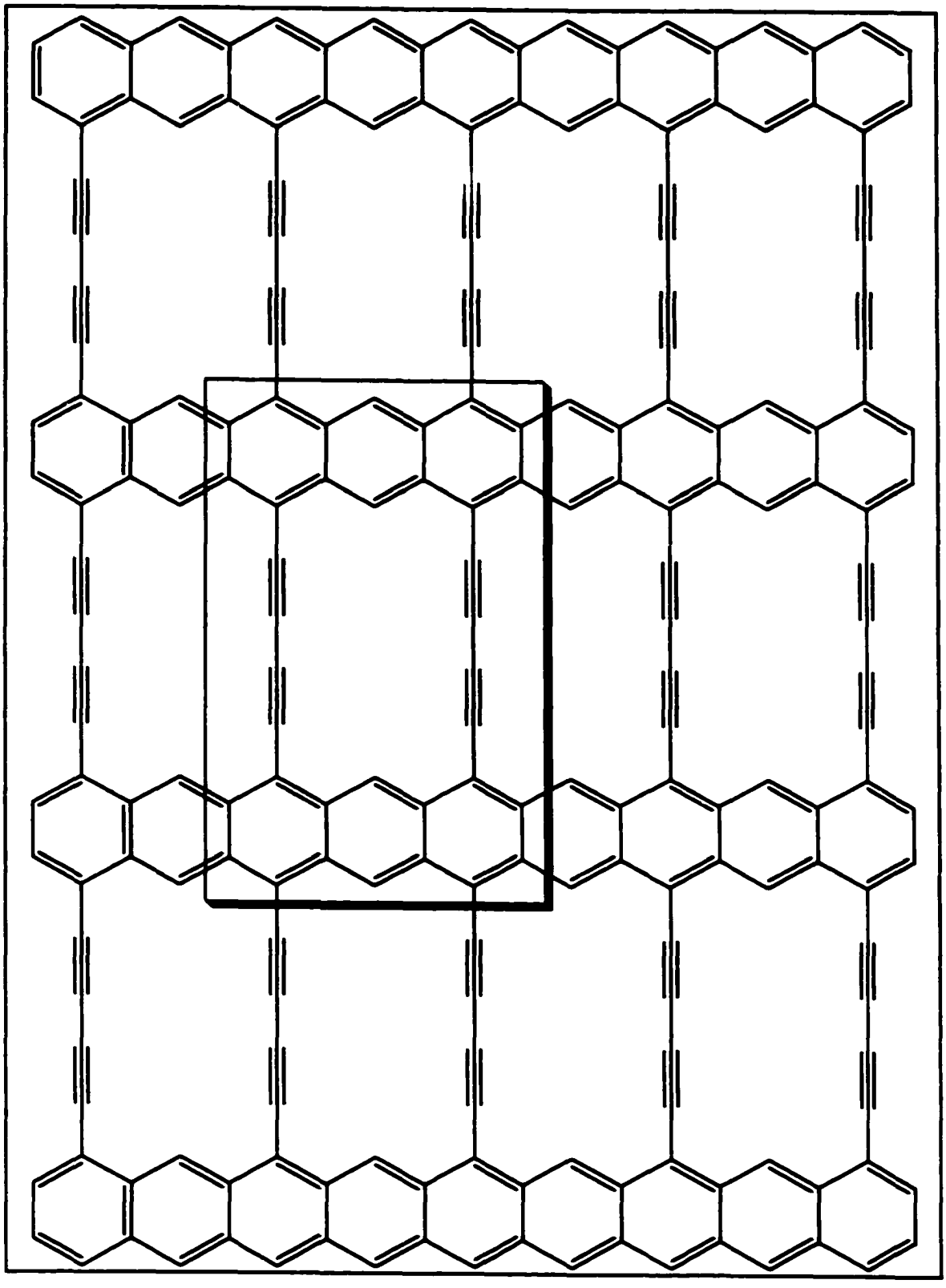
Figure 11: Rajca' s all-carbon net based on biphenylene-dimer



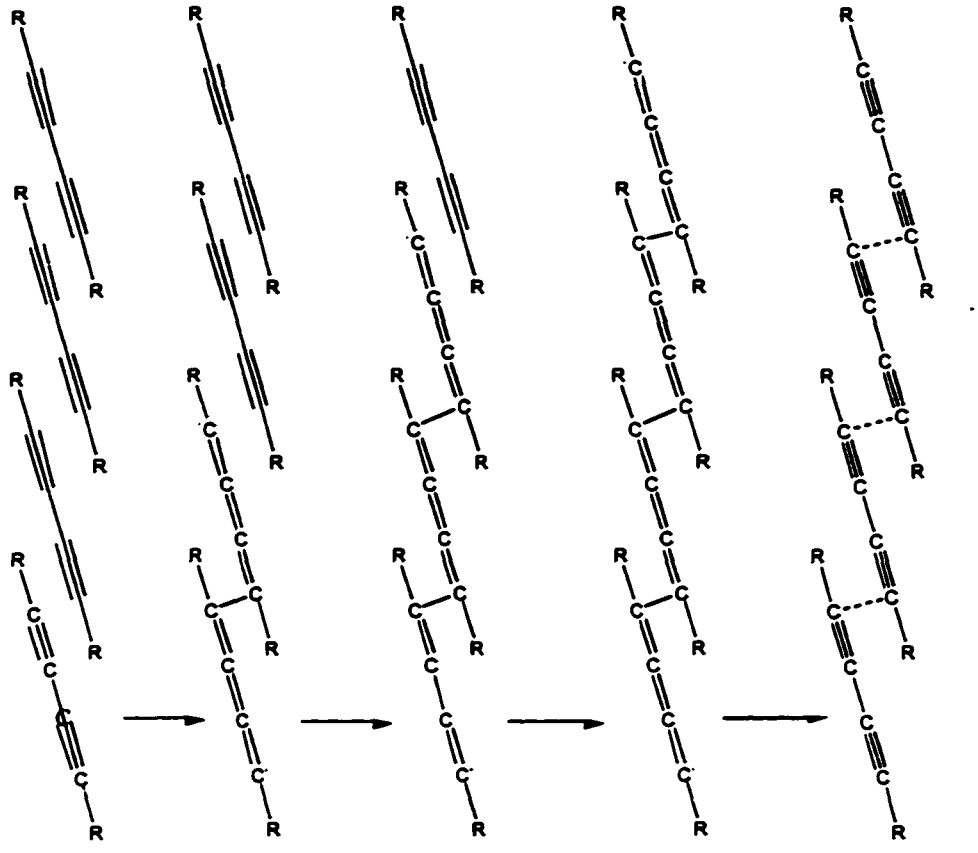
The precedent, by Rajca *et al.* established biphenylene as stabilizing in an all-carbon net, thus the assumption was made that not only "biphenylenediyne" would be stable but also that it would exhibit perhaps some of the attractive electronic properties exhibited by graphdiyne which is, after all, quite a close analog. In the same vein, consideration was also given to an anthracene analog.

Figure 12: The proposed 'biphenylenediyne' (below) and 'anthracenediyne' networks (the following page)





1.4. Solid-state Polymerization

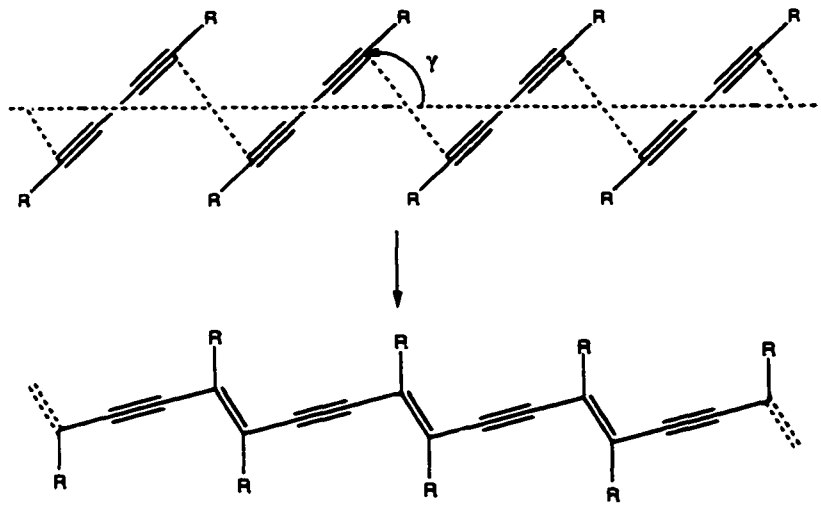


Scheme 4: *Polymerization of diacetylenes*

Polymerization of acetylene units has been used for generating annulenes by Reppe as early as 1948[43]. Recent efforts by Wegner[44] and others[45,46] have established the technique as one of the most reliable for topochemical polymerization from a monomeric unit. Substituted 1,3-diacetylenes undergo smooth topochemical polymerization in their crystalline states by heat, UV-light, γ-ray irradiation or pressure.

The resulting polydiacetylene polymer displays a quasi-one-dimensional structure with a long effective conjugation length.

The crystal of a monomer 1,3-butadiyne acts as a preformed lattice for the polymer crystal. Thus the monomer molecules should stack with the repeating unit of 4.9-5.1 A to form a one-dimensional chain in which the bond-forming carbons in the adjacent molecules are situated in proximity with the molecular axis being slanted by an angle of 45 ° from the direction of the one-dimensional chain.



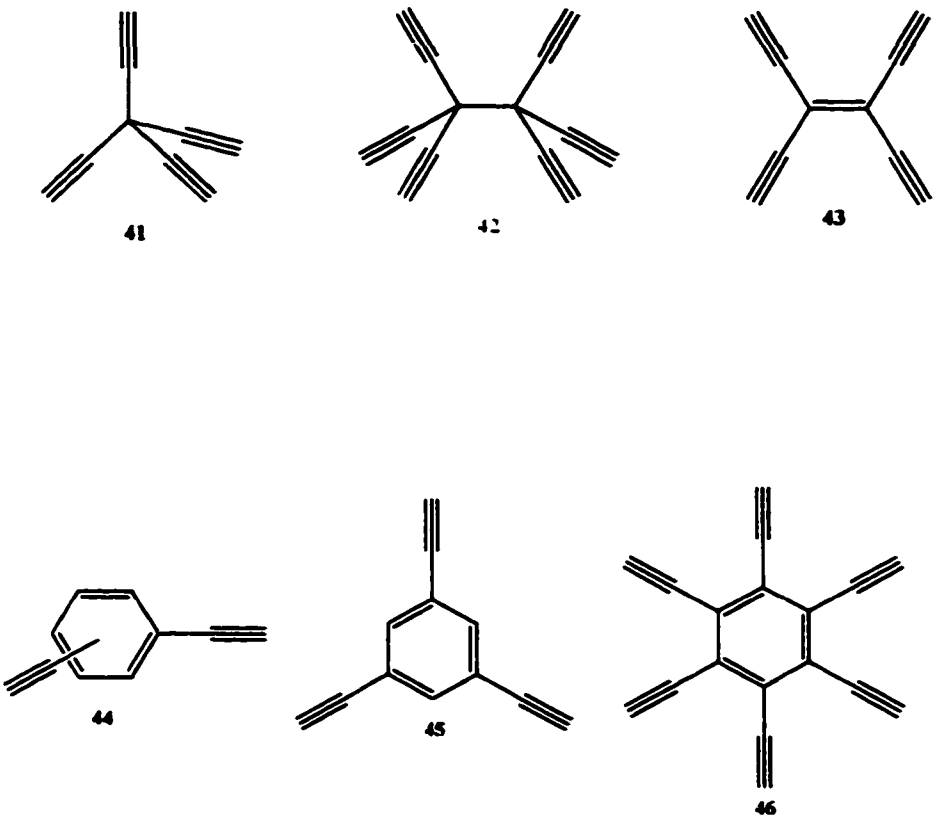
Scheme 5: *Geometric requirements for polymerization*

1.5. Fullerene and the era of novel carbon allotropes

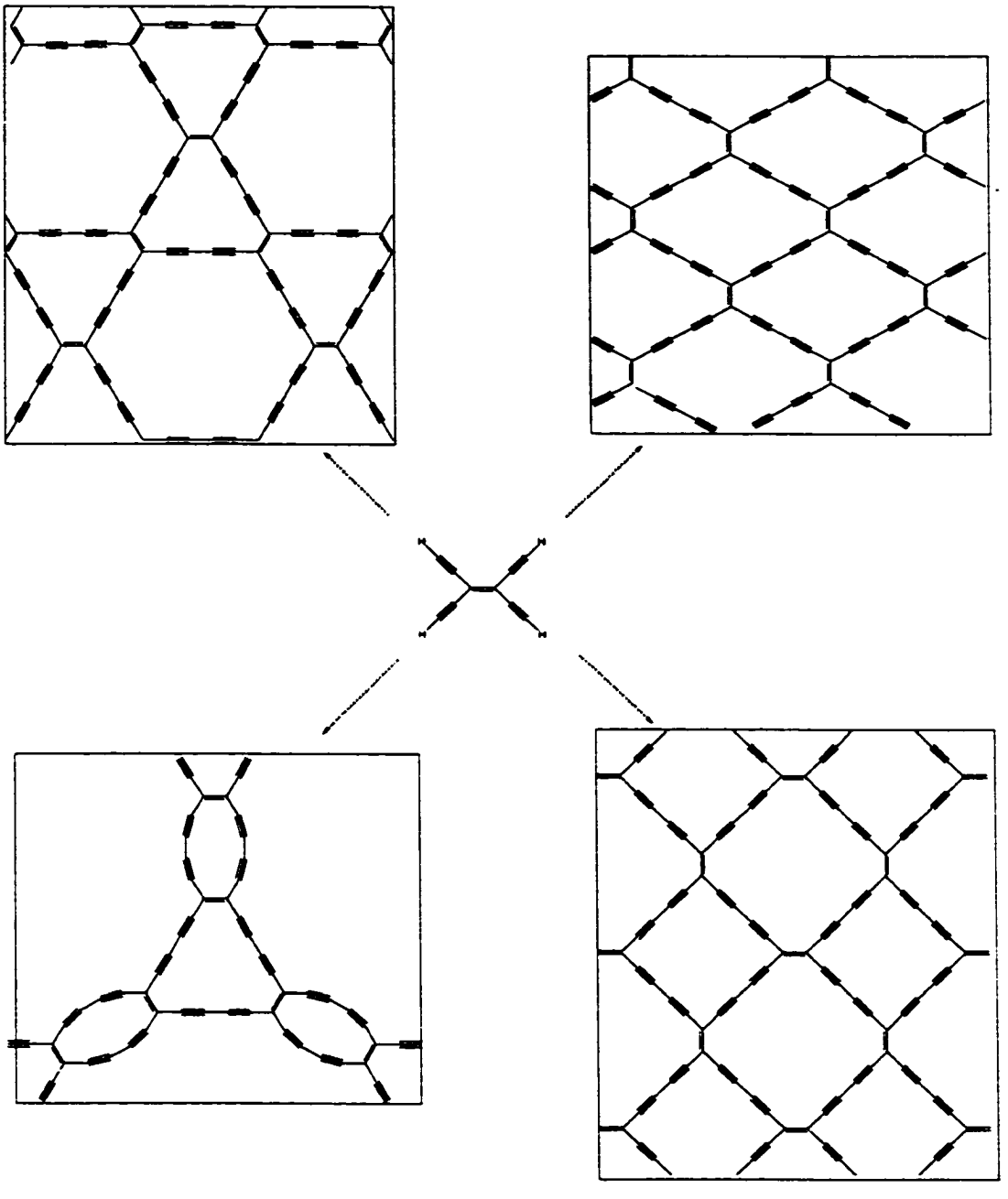
With the advent of fullerene chemistry[54], reinvigorated by the recent rational synthesis of C_{60} by Scott *et al*[55]., research on all-carbon and carbon-rich molecular and polymeric systems, continues to be of intense interest[56]. The properties of these novel systems are of great relevance in the search for organic conductors, electrochromic display materials, liquid crystals, synthetic ferromagnets, and non-linear optical substances.[57]

Because of the availability of both the acetylenes and the method for acetylene dimerization, namely the oxidative coupling of terminal alkynes as the first stage of elongation, constructions of extended hydrocarbon systems were to utilize the alkyne building block. Among the large number of potential acetylenic 'monomers' for the dimerization and/or oligomerization, those listed below have been most used:

Figure 13: Acetylenic building 'blocks' for extended all-carbon networks



From tetraethynylmethane[58] **41**, oxidative coupling should lead to graphyne, derived from graphite by replacing single bonds with acetylenic linkages between every other hexagon. It was proposed to exhibit unusual NLO and metallic properties when doped with an alkali metal.[59] Graphyne has sizable pores within its dehydro[12]annulene units and can conceivably lead to transition metal complexes/intercalation compounds analogous to "sandwich" structures.[60]



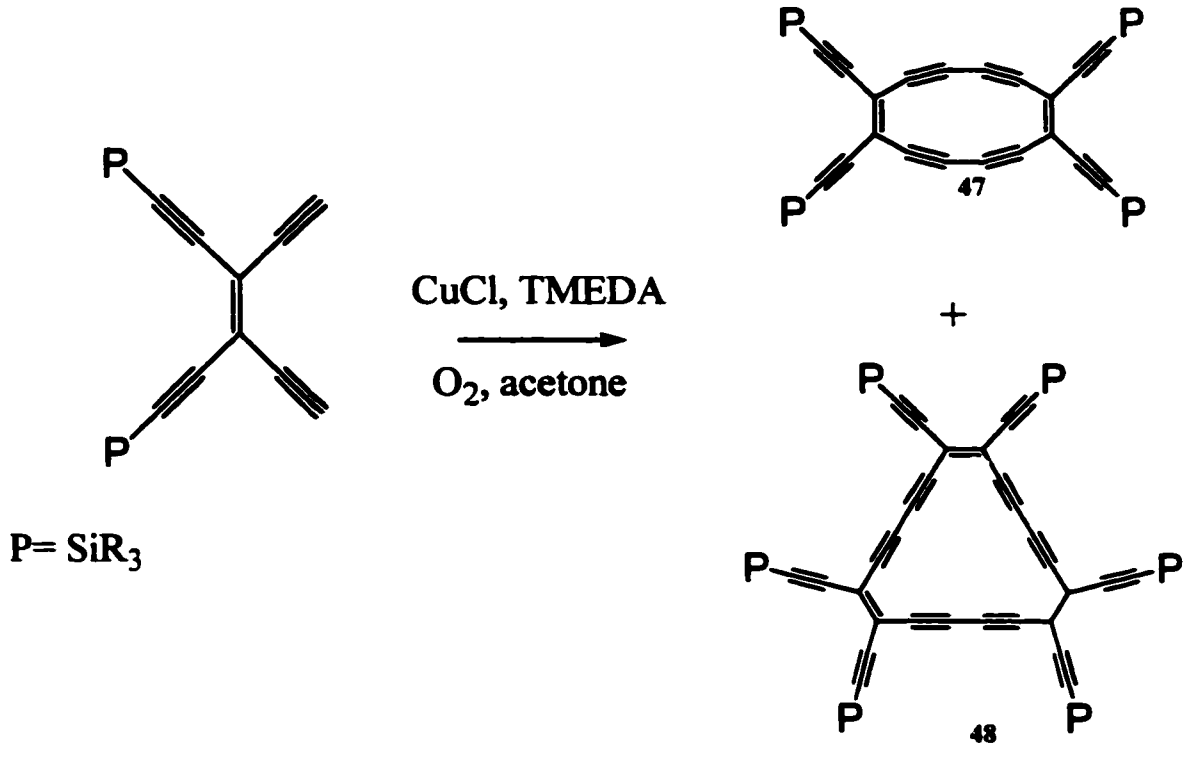
Scheme 6: *Hypothetical novel carbon networks*[29] *from tetraethynylethene* **42**

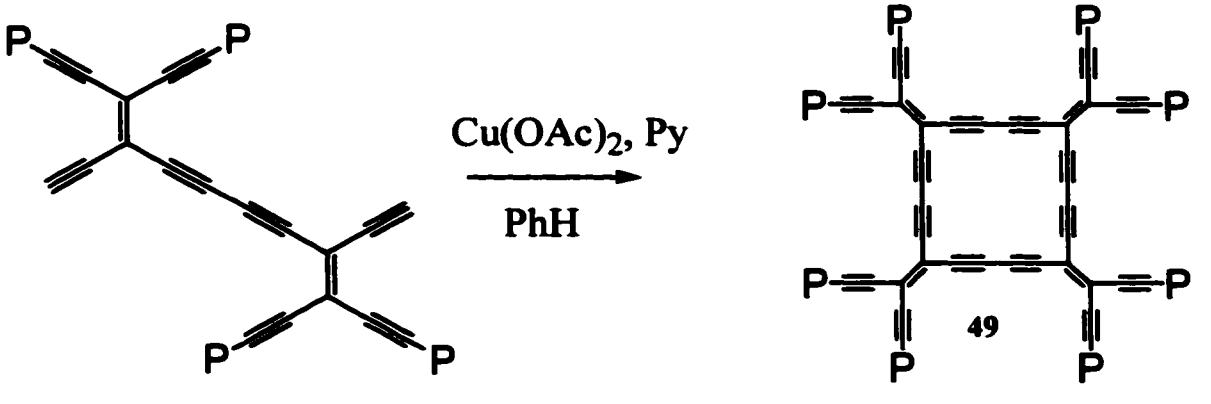
Tetraethynylethene[61] **42** and its differentially protected derivatives are versatile building blocks for two-dimensional all-carbon networks and

carbon-rich nanomaterials. They exhibit a fully cross-conjugated π-electron system. Hori and co-workers[62] reported the first synthesis of tetraethynylethene derivative in 1969, and the subsequent development in this area has been reviewed by Hopf *et al.*[63], where the authors have suggested substituted tetraethynylethenes as monomers for new polymers. In 1991, Rubin *et al.* reported the first synthesis[64] of the unsubstituted tetraethynylethene, which is also a precursor to numerous two-dimensional all-carbon networks and carbon-rich nanomaterials.[65]

The preparation of a specific network could not be accomplished by simple oxidative polymerization of tetraethynylethene, a repeat unit in many two-dimensional carbon networks, but required some macrocyclic precursors in order to attain the extended carbon sheets. These are the perethynylated dehydroannulenes **47**, **48** and the expanded radialenes **49** and **50**, novel carbon-rich materials exhibiting unusual and interesting structures and functions.

***Scheme** 7: Oxidative coupling reactions: Hay(top) and Eglinton (bottom)*





The yields of these oxidative Hay/Eglinton coupling reactions have been found[66] to be highly concentration-dependent with the dimer being formed

preferentially at lower concentrations while the trimeric cycle would be favoured at higher concentrations.

According to X-ray crystal studies[67] of these structures, the dimer shows a highly strained 12-membered ring with the butadiyne fragments significantly bent (angle: 164.5°) while the trimer is a perfectly planar carbon frame with linear (angle: 180°) butadiyne fragments in the [18]annulenes ring. The electronic absorption spectra[68] characterized the former as antiaromatic [12]annulenes while the latter is clearly a stable Hückel-aromatic [18]annulenes.

Recently, Grohmann and Benshafrut[69] observed only the trimer in an

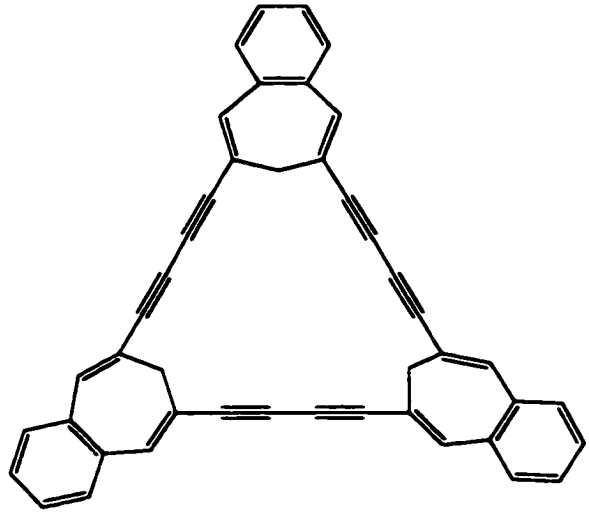
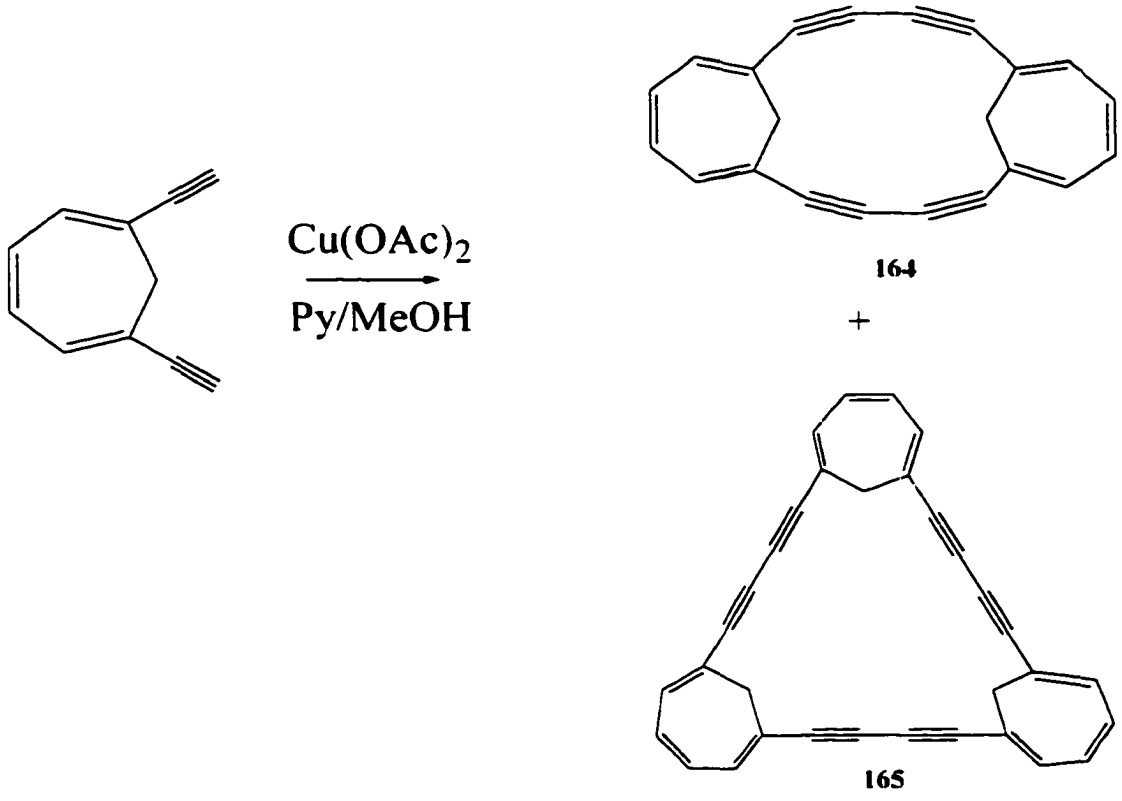


Figure 14: Grohmann' s 'benzocycloheptatrienediyne' unit

Eglinton-type coupling of 1,6-diethynyl-3,4-benzcycloheptatriene while Ojima,[70] working with 1,6-diethynylcycloheptatriene isolated both the dimer and the trimer.



Scheme 8: *Ojima's synthesis of dimer* **164** *and trimer* **165**

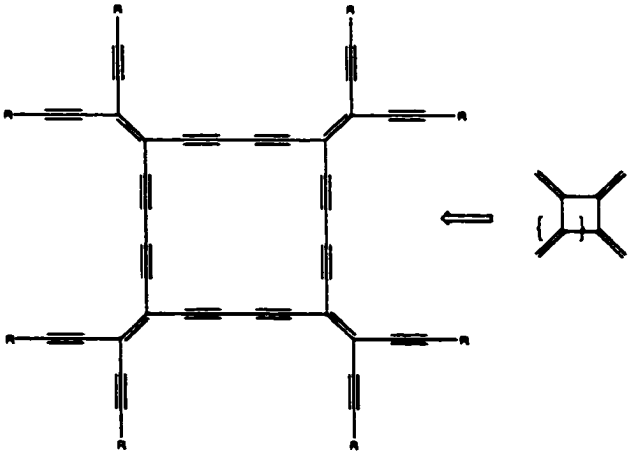
1.6. Radialenes

Radialenes are homologous series of all-*exo*-methylenecycloalkanes of molecular formula C_nH_n .

Carbon-rich expanded radialenes $C_{3n}H_n$ are obtained upon insertion of butadiynyl moieties into the cyclic framework between each pair of

vicinal *exo*-methylene units. The diameters of these large carbon-rich molecules are in the nanometer range with values of *ca* 17 to 22 Å

Figure 15: [3] and [4] radialenes.

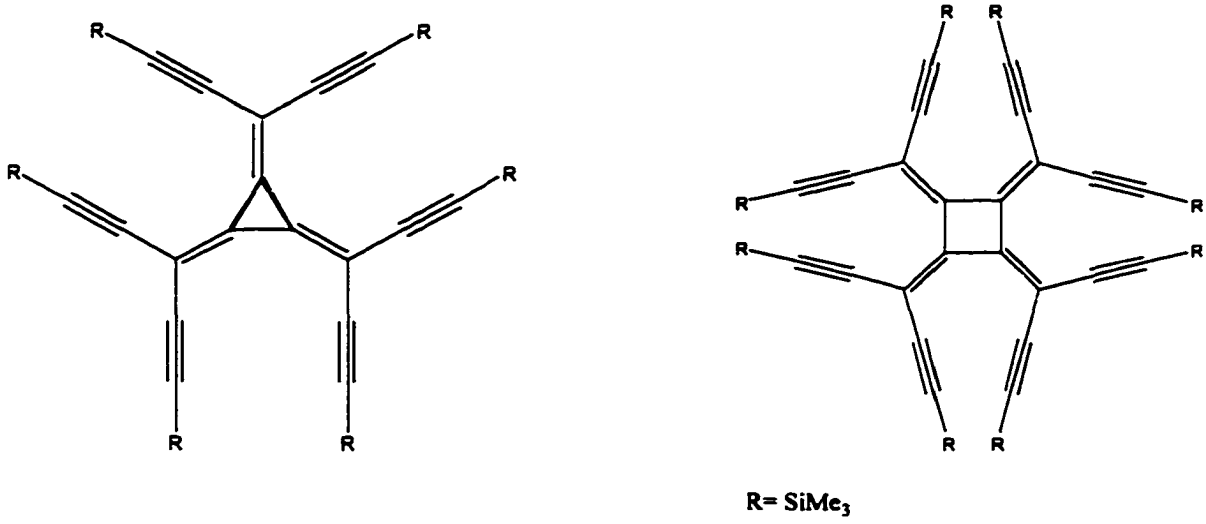


***Scheme 9**:Expanded radialene from insertion of butadiynyl moiety.*

In these [n]radialenes series, it is the corresponding hexaethynyl[n]radialenes that would be the choice precursors to carbon-rich

materials, via the oxidative alkyne-alkyne coupling of partially or fully desilylated derivatives.

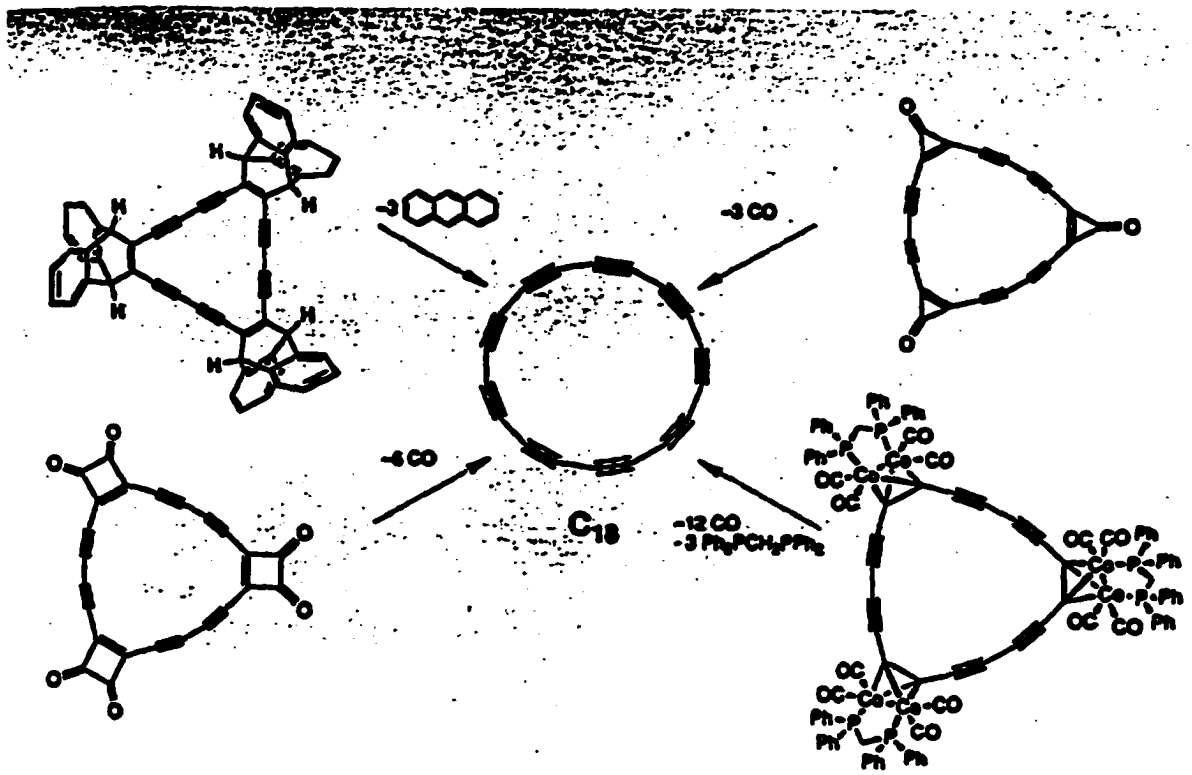
Figure 16 : Hexaethynyl[n]radialenes for n= 3 and 4



Diederich and coworkers,[71] have synthesized the hexaethynyl[3]radialene monomer which is believed to polymerize into an all-carbon network.[72]

1.7. Polyynes: Precursors to Molecular Carbon Rods

The preparation of infinite one-dimensional rods constituted of alkyne units has been pursued for many years because the resulting infinite linear polyynes, called "chaoite" or "karbyne"[73-74] are expected to be one-dimensional conductors, and calculations predict an unusual variety of soliton and polaron states. Walton made an initial synthesis of materials approaching carbyne with his preparation of extended linear polyynes incorporating up to 16 conjugated acetylene units.[75] Longer polyynes where only stable when protected with bulky Et_3Si end-groups. Since, Diederich and coworkers[76] have developped a general method for the preparation of symmetrically and unsymmetrically substituted polyynes starting from 3,4-dichloro-3-cyclobutene-1,2-diones and the acetylene synthon. The resultant, thermally sensitive 3,4-dialkynyl-3-cyclobutene-1,2-diones were subjected to Solution-Spray Flash vacuum Pyrolysis (SS-FVP) to generate triynes and pentaynes by extrusion of two CO groups. This, and other approaches (scheme) were to provide an entry into the study of linear Cyclo[n]carbons or Cx species of various sizes.



Scheme 10: C_{18} can be synthesized[76, 81] from four different precursors

1.8. Cyclo[*n*]carbons: The Molecular Wires

As in the [*n*]annulenes,[77] *n* defines the number of carbon atoms that are connected to form the monocyclic structure of this novel class of compounds.[78] Among the candidates for synthesis, C_{18} or cyclo[*18*]carbon was predicted to show a distinctive aromatic stabilization since two perpendicular systems of conjugated π-orbitals would exist, one in-plane and the other out-of-plane, with [4n+2] π–electrons each. Building by analogy

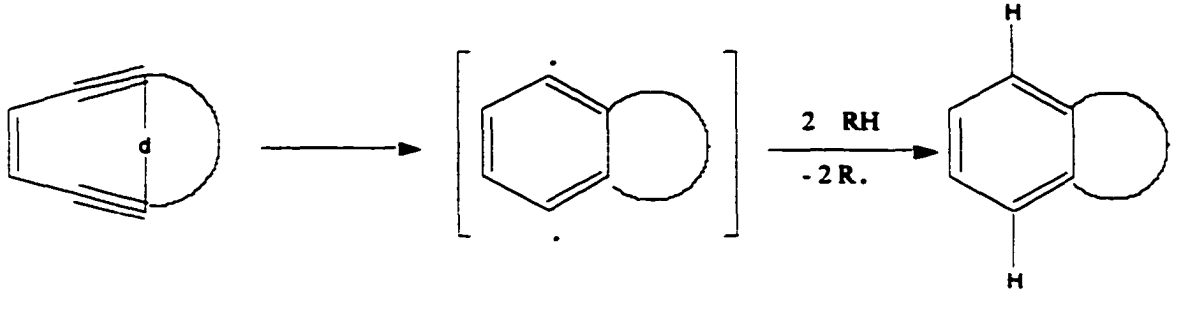
from earlier work by Sondheimer et al. on the synthesis of hexadehydro[18]annulene, it was excepted that strained cycles bearing suitable leaving groups could be fused to the ene-ends of the [18]annulene. Diederich and Tobe' s groups expected C_{18} to be generated in the final step of the synthesis by extrusion of those leaving groups. Cyclopropenones, like 3-cyclobutenediones, were expected to eliminate carbon monoxide in pyrolytic[79] and photolytic processes[80] to form acetylenes. Loss of anthracene molecules under thermolytic conditions was envisioned from the macrocyclic propellane-annelated dehydroannulenes of Tobe[81] and Diederich.[82] Finally, alkyne liberation from its hexacarbonyl dicobalt complex under flash vacuum pyrolysis conditions was expected when the leaving groups were chosen to be hexacarbonyl dicobalt fragments.

1.9. Organic Reactions of Cyclic Alkynes

A characteristic feature of the reactions of cyclic alkynes is the tendency to release ring strain by changing the hybridization at the alkyne carbons from sp to sp^2. This is achieved either by rearrangement reactions or by intra- or intermolecular addition reactions.

The equilibrium between the allenic system and the acetylenic system tends to shift towards the former whenever an acetylenic unit -which requires two bond angles of 180°- is part of a decreasing ring size.

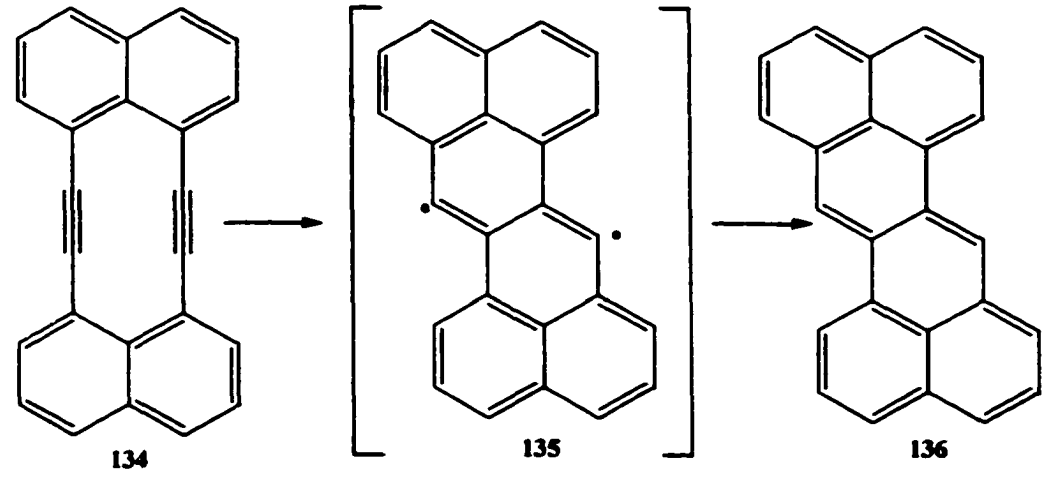
Transannular reactions are observed when, in cyclic systems, proximity of functional groups is the cause of unusual effects. One of the most important transannular reactions of cyclic alkynes is the Bergman cyclization[83] of enediynes, which takes place when the distance between the termini of the enediyne system is in the range of d= 3.1 - 3.2 Å.[84]

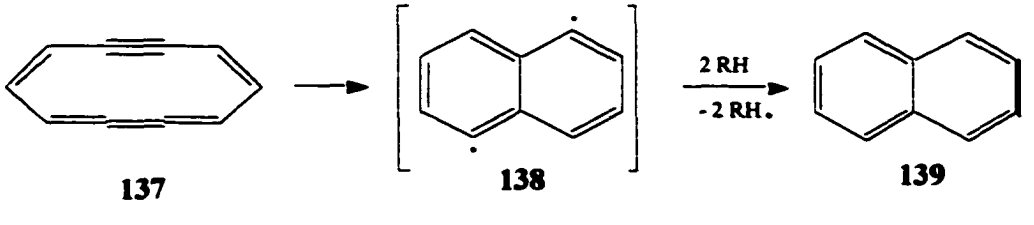


***Scheme 11**: The Bergman cyclization of enediynes*

This was first reported by Sondheimer[85] and Staab[86] whose attempts to prepare a cyclic diyne annulated to naphthalene nuclei **134** led only to the isolation of zethrene **136** and by the observation that 1,6-dehydro[10]annulene **137** spontaneously cyclized to give naphthalene **139** via 1,5-dehydronaphthalene **138** at low temperature.

***Scheme 12**: The first observed[85, 86] example Bergman cyclization*



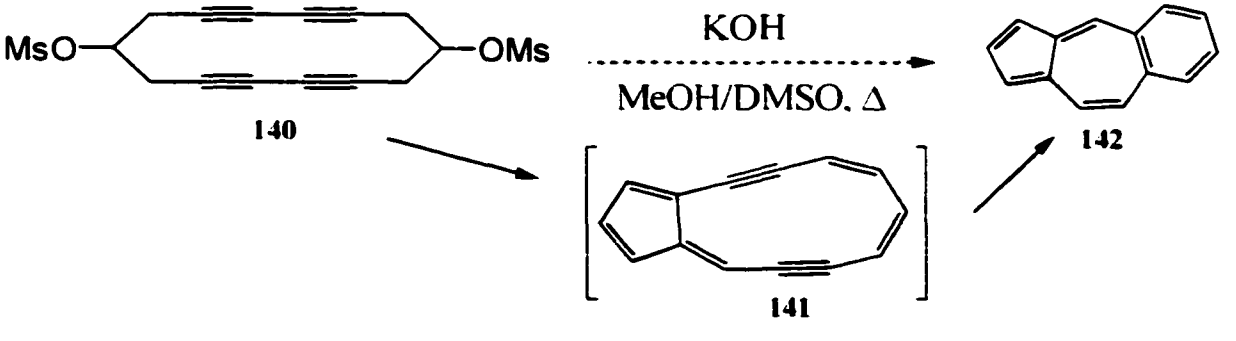


The diyne cyclizations involve the formation of an aromatic system together with the biradical. Subsequently the mode of action of this diradical in newly discovered naturally occuring molecules termed enediynes, was to revolutionize the medicinal chemistry community. Indeed, the diradical intermediate is a powerful weapon used by these antibiotics to cleave a DNA strand by abstracting a critical hydrogen atom from the DNA' s sugar phosphate backbone.

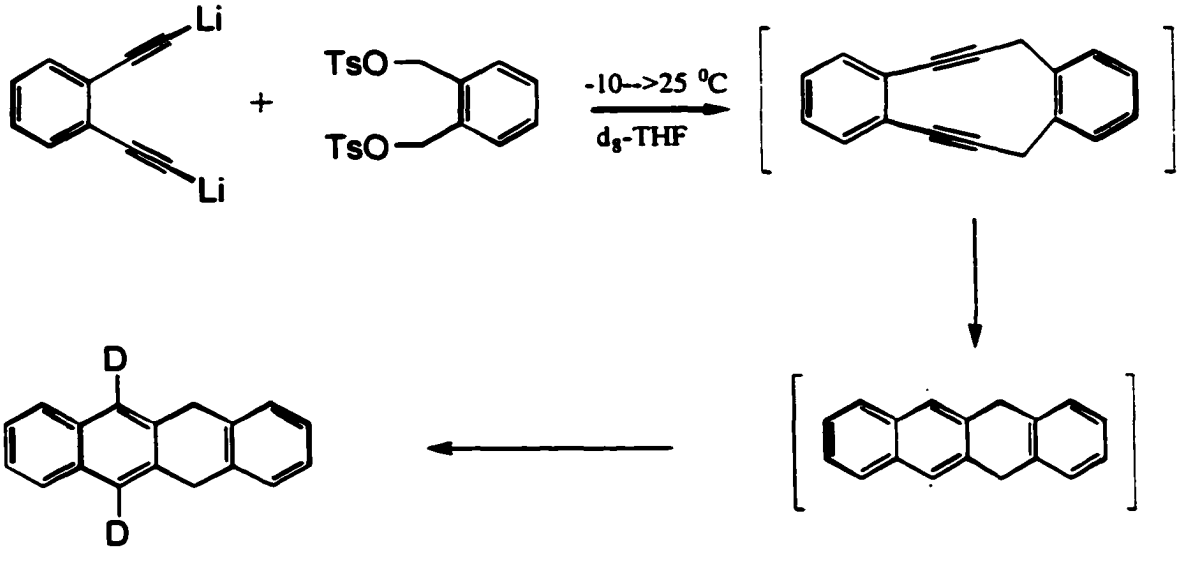
1.10. Chemistry of the Enediynes: Cycloaromatization of Didehydro[10]annulenes

The seminal observation by Sondheimer and Mayer[87] of the first cycloaromatization, in 1966, set the stage for the development and the study of the scope/conditions of this important reaction (scheme 10).

***Scheme 13**: Cycloaromatization of tetrayne* **140** *by Sondheimer et al.*



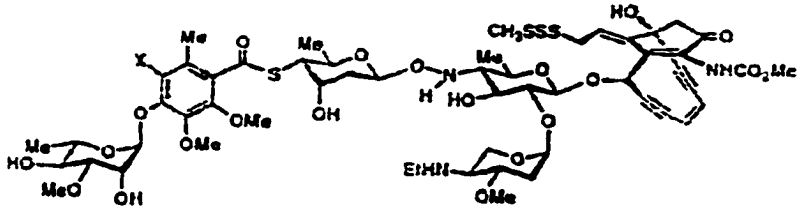
Later work by Sondheimer with Garratt, Wolovsky, Grohmann, Mitchell and Wong produced a vast array of strained cyclic "enediynes" or didehydroannulenes which were shown to undergo facile cycloaromatization with incorporation of deuterium in the product when the reaction was carried out in the presence of d_8-THF (scheme 14).



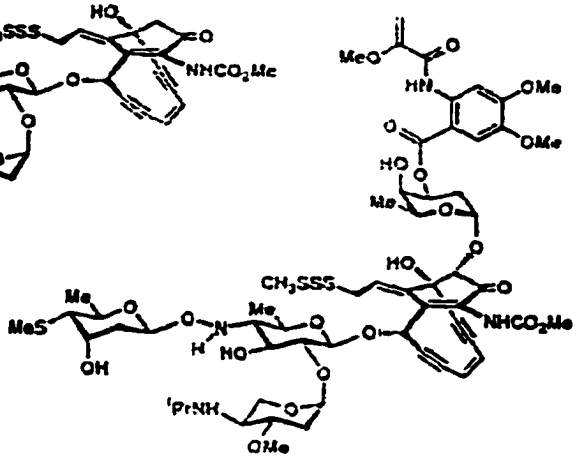
***Scheme 14**: Further example of cycloaromatization in enediyne intermediate*

1.11. Enediyne Antibiotics

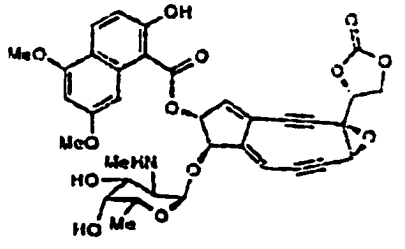
Fig.17: Some naturally occuring enediyne antibiotics (reproduced, ref. 187)



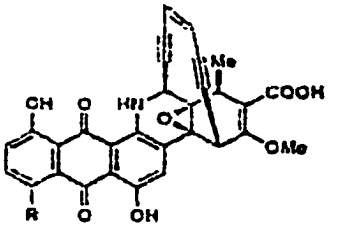
Calicheamicin γ_1^I (2)



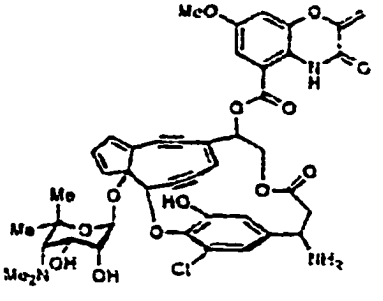
Esperamicin A_1 (3)



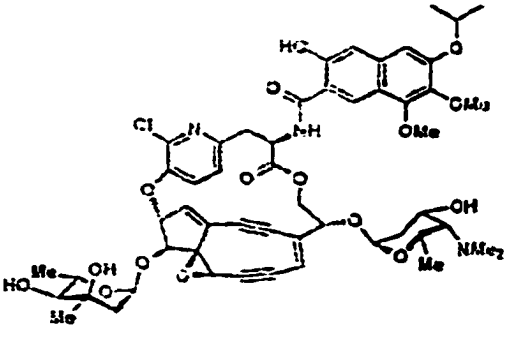
Neocarzinostatin chromophore (1)



Dynemicin A (4)



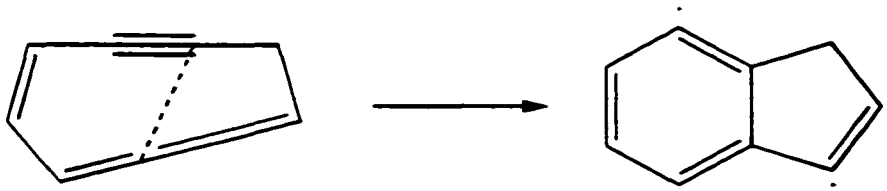
C-1027 chromophore (6)



Kedarcidin chromophore (5)

The cycloaromatization reaction was to be visited with the publication in 1987 of the structures of two closely related new classes of potent antitumor antibiotics exhibiting an enediyne unit embedded within their complex architectural frameworks. These are the calicheamicins[88] and esperamicins[89] whose mechanism of action involves a cumulene-ene-yne **143** cycloaromatization to generate the DNA-damaging diradical **144**.

***Scheme 15**: Cycloaromatization in cumulene-ene-yne system* **143**

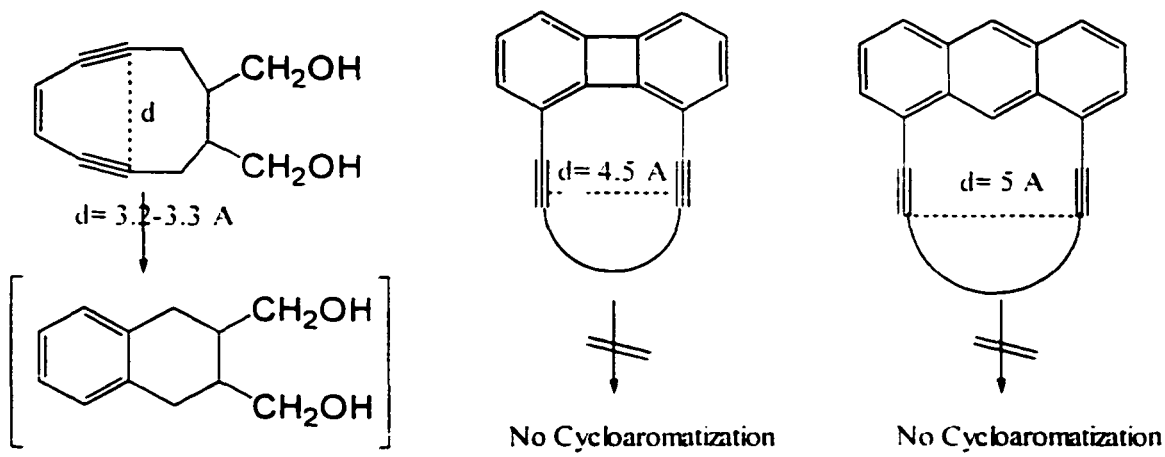


143 **144**

The reaction has a half-life of ca. 25 min at –51 °C and is, thus, one of the most rapid diradical-forming reactions known.[90]

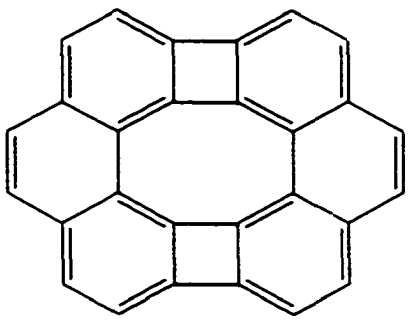
It was subsequently shown that ten-membered ring enediyne readily underwent the Bergman cycloaromatization reaction at room temperature while the larger ring enediynes were found to be stable. Comparison of the distances between the termini of the enediyne moiety of these systems and the ease with which cyclization took place established the critical distance needed for predicting transannular aromatization in these enediyne systems.

The distance was found to be around 3.2- 3.3 Å. It was therefore necessary for us to use spacers larger than 3.2-3.3 Å in order to avoid cycloaromatization during the research described in chapter 3. Thus, our selection of biphenylene (d equal ca. 4.5 Å) and anthracene (d equal ca. 5.0 Å) proved justified.



Scheme 16: *Comparison of the distance d critical for cycloaromatization in an enediyne. 1,8-diethynylbiphenylene and 1,8-diethynylanthracene*

1.12. Bis-cyclobutaphenanthrene 218, A Kind of Kekulene



218

Polyarenes exhibit extraordinary structural diversity.[91] The most familiar classes are the regular cata-condensed and peri-condensed alternant hydrocarbons, such as anthracene, chrysene and pyrene that contain only fused benzenoid rings. However, numerous other classes of alternant polycyclic aromatic hydrocarbons (PAH) are known.

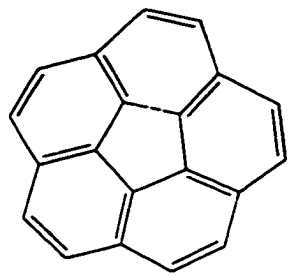
a) *The helicenes*

b) The chain-linked polyarenes such as *biphenyls*, *terphenyl* and their higher analogs such as *binaphthyls*, *bipyrenyls*, *ternaphthalene* etc. which consist of assemblies of single or fused benzenoid rings linked together like sausages.

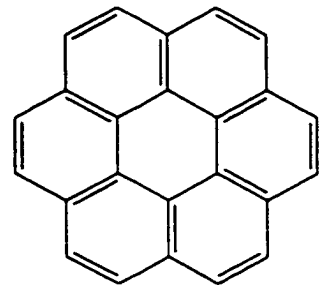
c) Benzenoid rings may also be linked together in macrocyclic systems, such as *penta-m-phenylene* and *hexa-m-phenylene*.

d) Another interesting class of PAHs is the *circulenes*, notably corannulene **160**, coronene **120** and kekulene **118**, which are characterized by fusion of rings in a macrocyclic arrangement.

Fig. Corannulene or [5]-circulene (left) and coronene [6]-circulene (right)



160



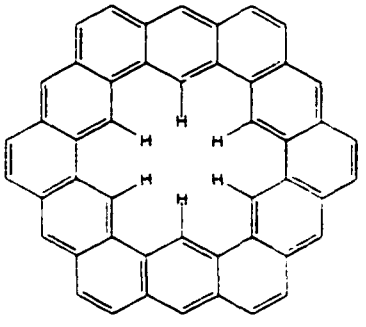
120

e) The nonalternant PAHs contribute even greater structural diversity to the family of polyarenes due to the large number and range of their structural variety which include polycyclic derivatives of biphenylene, fluorene, naphthene, cyclopenta[*def*]phenanthrene, dibenzopentalene and phenalene. Biphenylene is the prototype for nonalternant PAHs that contain one or more four membered-rings. Remarkable for their reactivity are the angular [*N*]phenylenes.

Biphenylene is the parent compound of the [*N*]phenylenes comprised of alternating benzene and cyclobutadiene rings. Their interior benzene rings can be substituted in a linear or angular manner, as in the [*3*]phenylenes or a branched manner, as in [*4*]phenylene. This gives rise to a rapidly increasing

number of isomers, e.g. five [*4*]phenylenes, twelve [*5*]phenylenes, thirty-seven [*6*]phenylenes, etc. Phenylenes can also form or contain cyclic structures such as the cyc[*6*]phenylene (antikekulene), cyc[*5*]phenylene and much larger systems.

Kekulene **118** and antikekulene are two very interesting structures, representative of alternant and nonalternant PAHs.



118

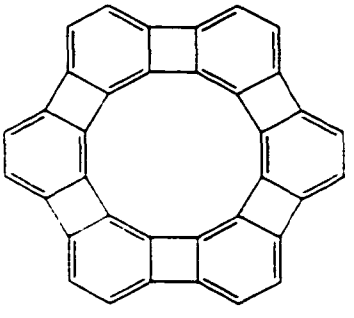
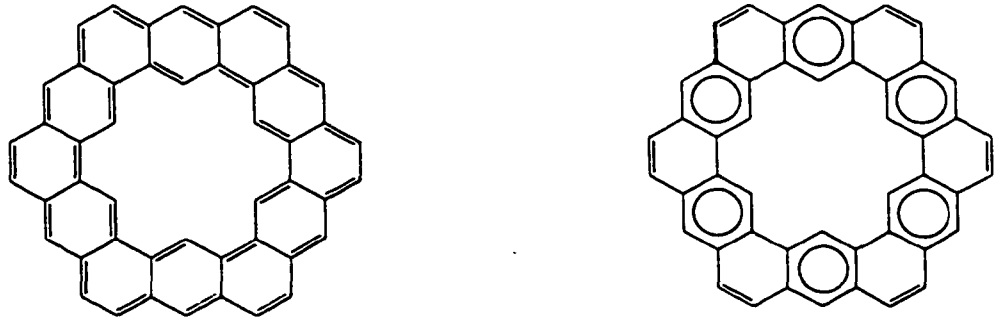


Fig.18: Kekulene (left) and Antikekulene (right)

Kekulene is considered an 'extended circulene' and was first synthesized by Staab and Diederich in 1983.[92] Kekulene is of interest because it can be regarded as a combination of two annulene perimeters (see **Fig.18:** the outer is a [30]annulene and the inner, an [18]annulene) connected by radial single bonds (see structures in **Fig.19**) and that it is also

illustrative of the Clar' s "Sextet concept"[93] as there could be localization of the π–electrons into benzene rings. Moreover, because kekulene has both external and internal hydrogen atoms substituents, ^{1}H NMR spectroscopy should enable a decision about the extent to which the diatropicity in the macrocyclic system can compete with ring-current induction within the benzenoid subunits.

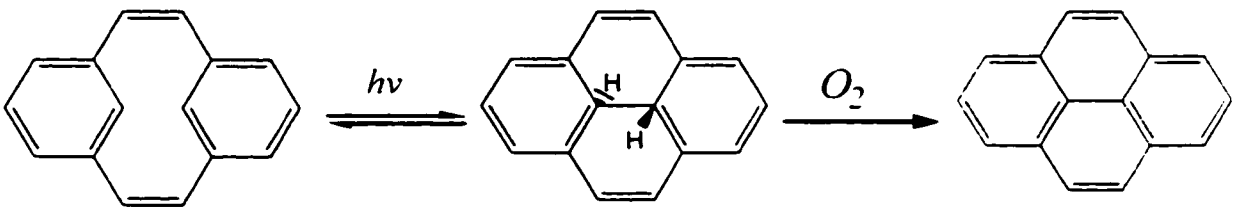
Fig.19: Kekulene: two annulene perimeters (left) and localized π-electrons (right)



Antikekulene on the other hand displays an empty internal cavity ([12]annulene) and a perimeter that can be viewed as a [24]annulene. Its synthesis is in progress (Vollhardt *et al.*) as it is being targeted as the prototype for 'superdelocalization'.[94]

1.13. Ring Closing Oxidative Photocyclization

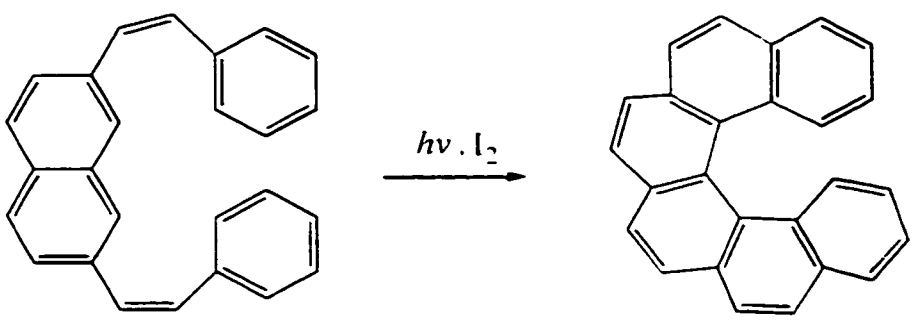
An impressive array of circulene structures were obtained by, a ring-closing oxidative photocyclization (inter and/or intramolecular).[95] Thus, irradiation of metacyclophane **145** in solution under nonoxidizing conditions yields the dihydropyrene **146**, which upon exposure to air produced pyrene **147**.[96]



145 **146** **147**

Scheme 17: *Synthesis of pyrene* **147** *by oxidative photocyclization*

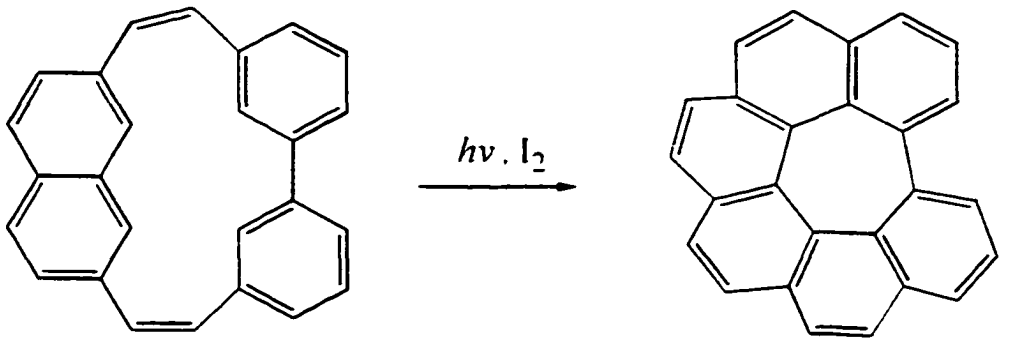
2,7-distyrylnaphthalene **124** gives [6]helicene[97] **125** while its cyclic analog **122** gives the circulene **123**.[98]



124 **125**

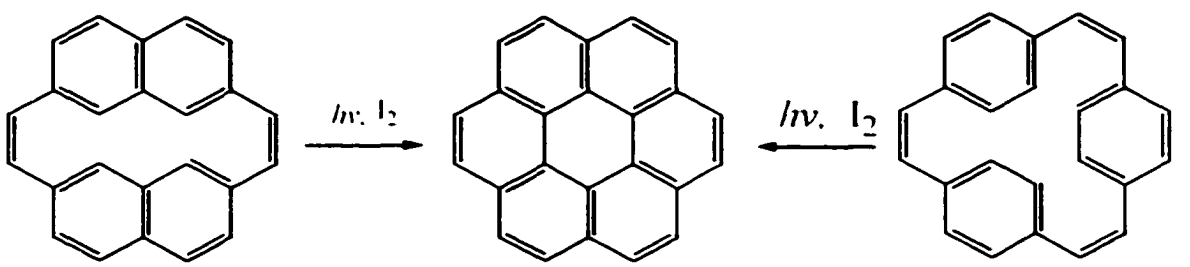
Scheme 18: *Synthesis of [6]helicene* **125** *by oxidative photocyclization*

***Scheme 19**: Synthesis of circulene* **123** *by oxidative photocyclization*



122 123

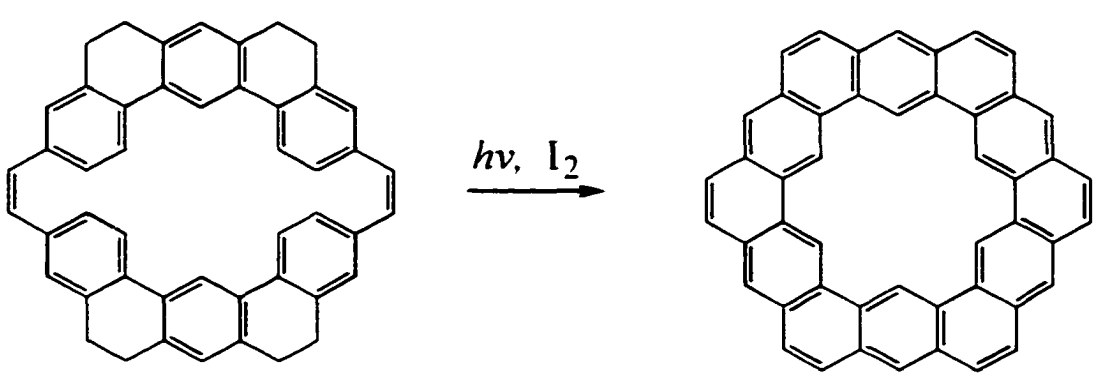
Coronene **120** was synthesized, from two differents substrates, the diene **119**[99] and the triene **121**[100] by oxidative photocyclization.



119 120 121

Scheme 20**: Similar routes to coronene* **120** *(top) and kekulene* **118(bottom)*

Kekulene **118** was prepared under similar conditions.[92]



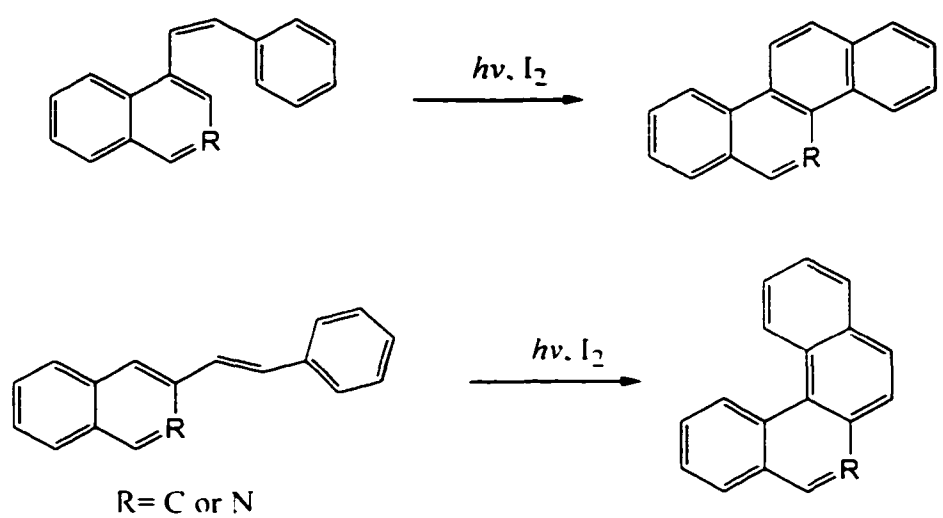
117 118

We, therefore proposed to apply this method to bisvinylbiphenylene **105** in order to synthesize the title compound biscyclobutaphenanthrene **218** (see scheme 22 below).

Background:

As a precedent, the photocyclisations of both 1- and 2-styrylnaphthalene (R= C) and their isoquinoline (R= N) counterparts have been reported by Mallory[101] and Timmons[102] respectively.

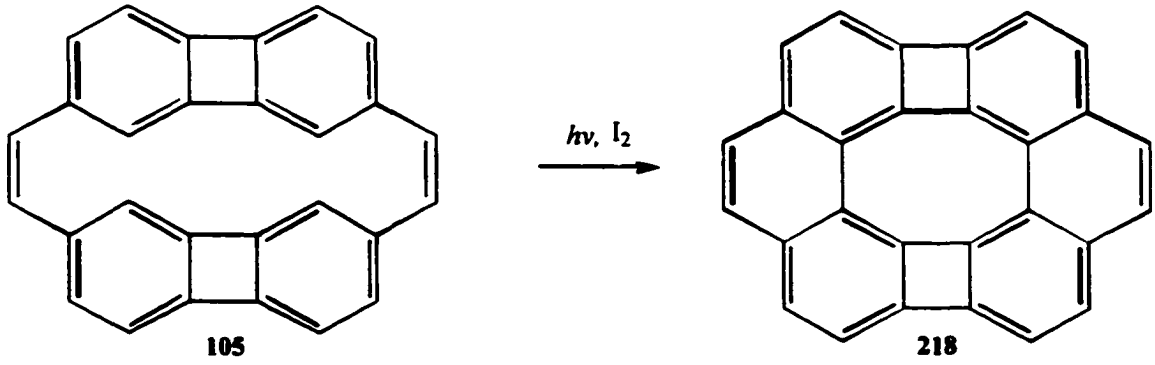
***Scheme 21**: Oxidative photocyclization of non –and- heterocarbocycles*



1.14. Retrosynthesis of bis-cyclobutaphenanthrene 218

Retrosynthetic consideration for compound **218** suggests a double oxidative photocyclization of the type stilbene to phenanthrene -as documented by Mallory *et al.*[95]- on the precursor **105** in order to obtain the final product. Interest in this polycyclic unsaturated hydrocarbon is multifold.

***Scheme 22**:Proposed double oxidative photocyclization route to* **218**



The study of benzobiphenylenes by Wilcox, Grohmann[103] Garrat[104] and others[105] have contributed to the redefinition of the concepts of aromaticity since these compounds exhibit, to varying degrees, properties normally associated with antiaromaticity, yet are generally long-lived enough to permit detailed study. Compound **218** would be the ultimate

annulene model having a [28]annulene outer perimeter and an [8]annulene inner core (both antiaromatic) while being planar or nearly planar. In addition, the central cyclooctatetraene would adopt a unique planar conformation. The consequences would be of great interest for the theory of aromaticity and therefore NMR studies of such a system are equally important. Finally, synthetic accessibility to the precursor annulene **105** is feasible by various coupling methodologies, among them the Mc Murry coupling[106] and the Wittig reaction.[107]

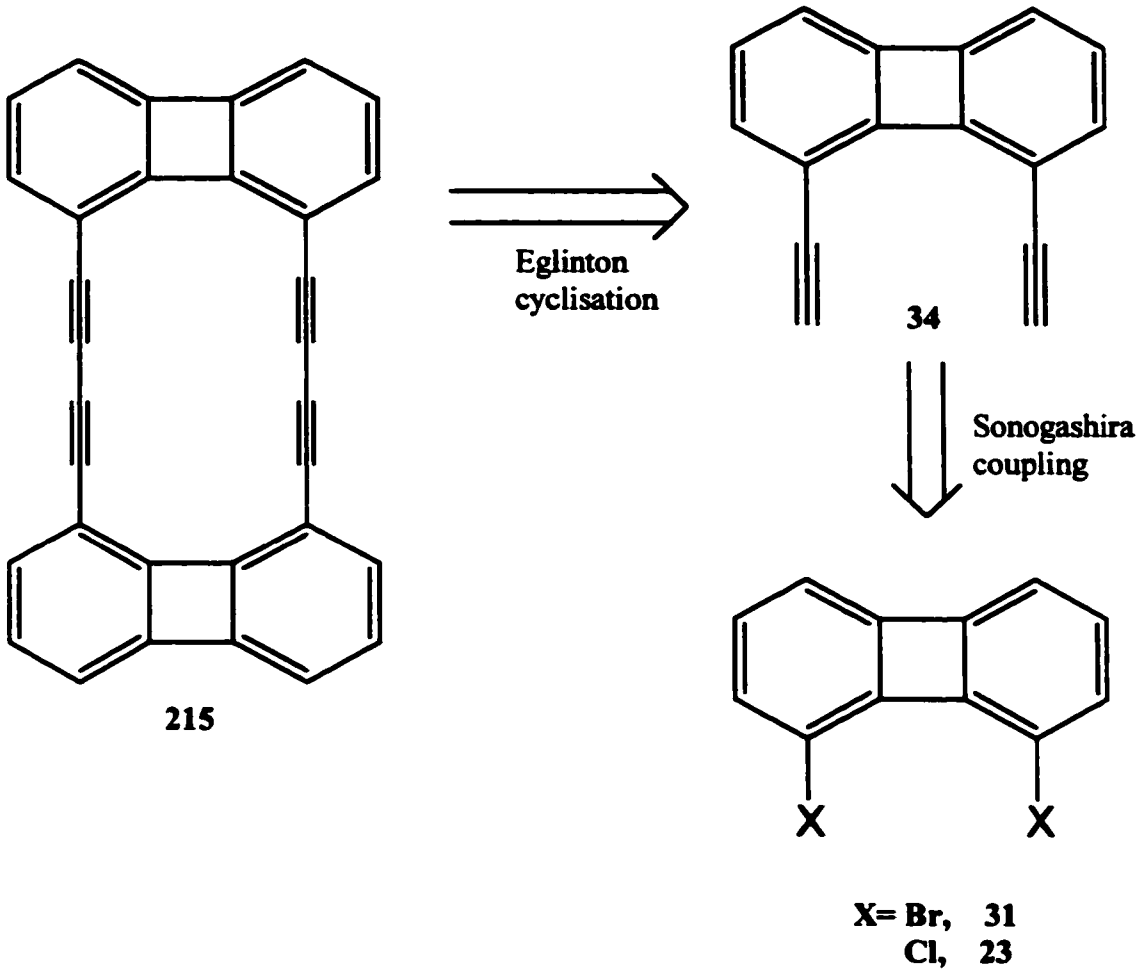
CHAPTER 2

2.0. Synthesis and Investigation of 'Biphenylenediyne'

Biphenylenediyne or the 1,8-annelated dibiphenyleno-octadehydro[16]annulene **215,** a tetrayne, is a novel all-carbon polymer precursor which is formed of biphenylene nuclei fused to the [16]annulene core. The compound was sought for its aromatic as well as material properties. The syntheses of **215**, and its close analog anthracenediyne **216,** involved a thorough reinvestigation of the chemistry of biphenylene **8** and acetylene building blocks.

2.1.0. Retrosynthetic Analysis

The ideal retrosynthetic steps would include an Eglinton-Glaser[106] alkyne-alkyne coupling reaction following a Sonogashira[107] coupling reaction of dihalobiphenylene and trimethylsilylacetylene.



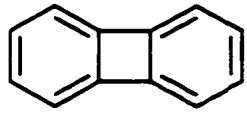
Scheme 21: *Retrosynthetic analysis of biphenylenediyne* ***215***

In order to implement the retrosynthetic scheme above, it was necessary to synthesize the appropriate 1,8-dihalobiphenylene in sufficient quantity for the subsequent steps. While 1,8-diiodobiphenylene has yet to be prepared, the synthesis of 1,8-dibromobiphenylene by the reported method[108]

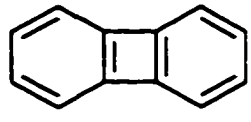
is not amenable to preparative scale. However, 1,8-dichlorobiphenylene was prepared in higher yields and, was used, not in a formal Sonogashira coupling reaction, but rather in a nickel(0)-catalyzed coupling reaction[109] with trimethylsilylethynylmagnesium bromide. We, therefore anticipate to use and modify the above retrosynthetic scheme by using both methods. In the course of synthesizing these and other much needed disubstituted biphenylenes, we have reviewed and, at times, improved on the published methods/results. An analysis of the preparative methods and the results obtained will, first, be treated in what follows.

2.1.1. Biphenylene, Dialkyl- and Dihalo-biphenylenes

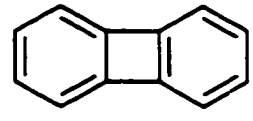
2.1.1.0. Biphenylene



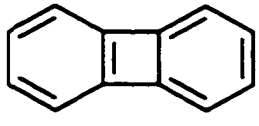
8a



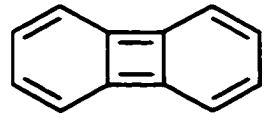
8b



8c



8d



8e

Scheme 22: Resonance structures of biphenylene 8

Biphenylene **8** forms pale yellow crystals which melt in the range 110-111°C. It is steam volatile, can be distilled without decomposition at 190°C. It is inert towards aerial oxidation and behaves in most respects as a typical tricyclic aromatic hydrocarbon. Five canonical forms can be drawn for biphenylene (*scheme 22*) but the chemistry is dominated by that of (**8a**) in which cyclobutadienoid character is reduced to a minimum. It undergoes substitution in preference to addition, showing reactivity comparable to that of naphthalene, and does not readily participate in the Diels-Alder reaction. However, the four-membered ring significantly affects the regiochemistry of substitution in (**8a**) so that the system cannot merely be regarded as an ortho-bridged biaryl.

The molecular geometry of biphenylene has been determined in the solid state by X-ray crystallography[110] and in the vapor phase by electron diffraction.[111] Both results indicate a limited degree of bond fixation in the benzenoid rings, best represented in (**8a**). Molecular Orbital (MO) calculations are in qualitative accord in predicting this to be the dominant contributor. The 'bridge' σ–bonds are weak as a result of poor orbital overlap and, at *ca.* 1.52 _, indicate that they have virtually no double bond character. The system can be regarded as consisting of two weakly interacting 6π-units which repel one another.

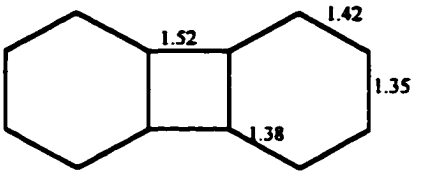


Fig.20: Crystallographic data of biphenylene

The heat of combustion of biphenylene was determined to be 1483.0 kcal mol^{-1},[112] giving a standard heat of formation for (**8**) of *ca.* 84 kcal mol^{-1}.[113] The standard heat of formation of biphenylene is in the range 100-108 kcal mol^{-1}.[114]

Although predictions of the resonance energy of biphenylene vary in magnitude, most are unanimous in classifying the molecule as weakly aromatic. It is predicted by PMO theory and SCF calculations to have lower delocalization energy than biphenyl.[115] The residual destabilization of biphenylene can be attributed to the limited degree of (4n) character in the central ring and the associated bond-fixation in the benzenoid rings. This has a significant effect on its chemical behavior in that 'cyclobutadienoid' intermediates are strongly disfavored and substitution at the β–position is consequently preferred over the α–position.

The ^1H nmr spectrum of biphenylene in $CDCl_3$ consists of an AA'BB' system centered at δ6.72 and 6,62ppm. Deuterium labelling experiments

have established that the high field portion of this multiplet is due to the protons adjacent to the four-membered ring and this points to an induced paramagnetic current in the central ring.[116] The overall shielding experienced by biphenylene relative to that observed in benzene is consistent with a reduction in diatropism in the two benzenoid rings and/or enhanced paratropism associated with the contributing 4π, 8π and 12π-circuits.[117]

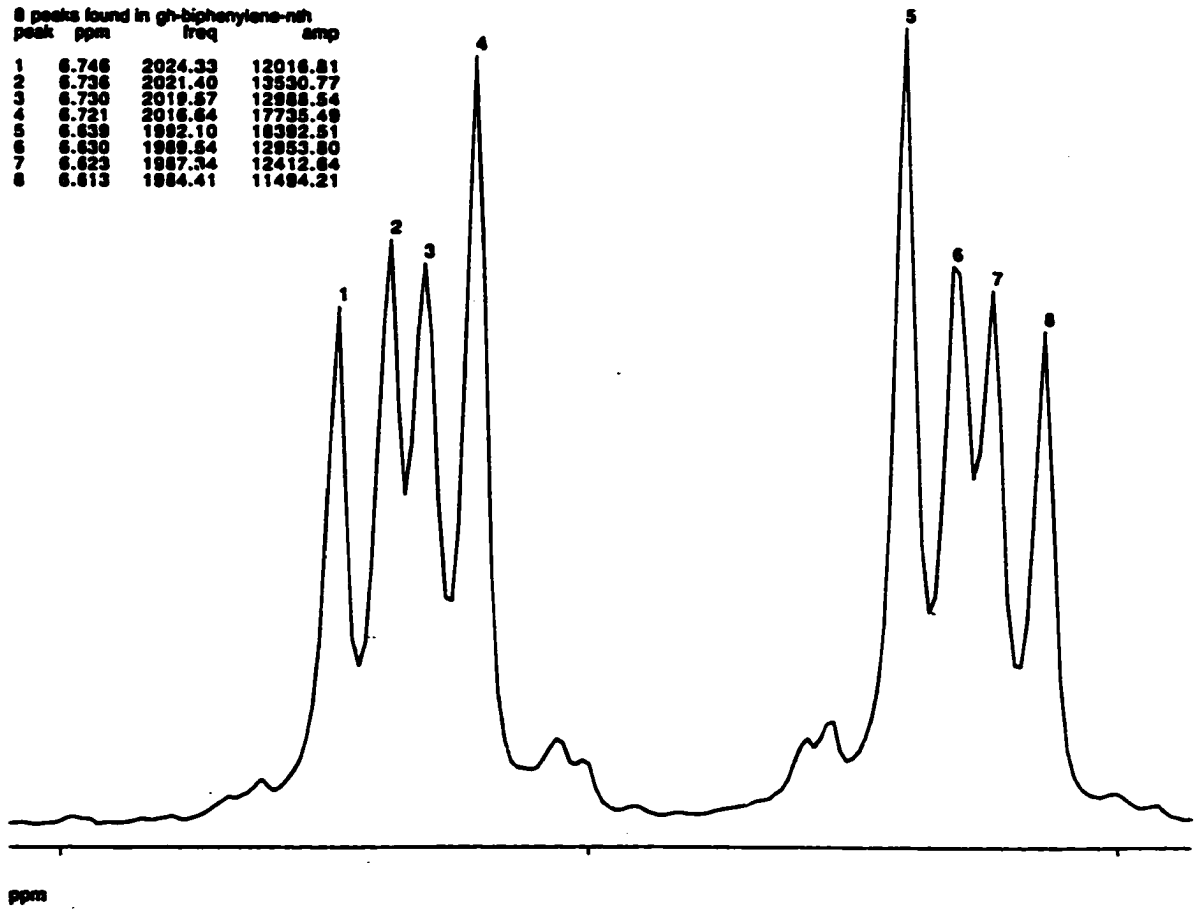
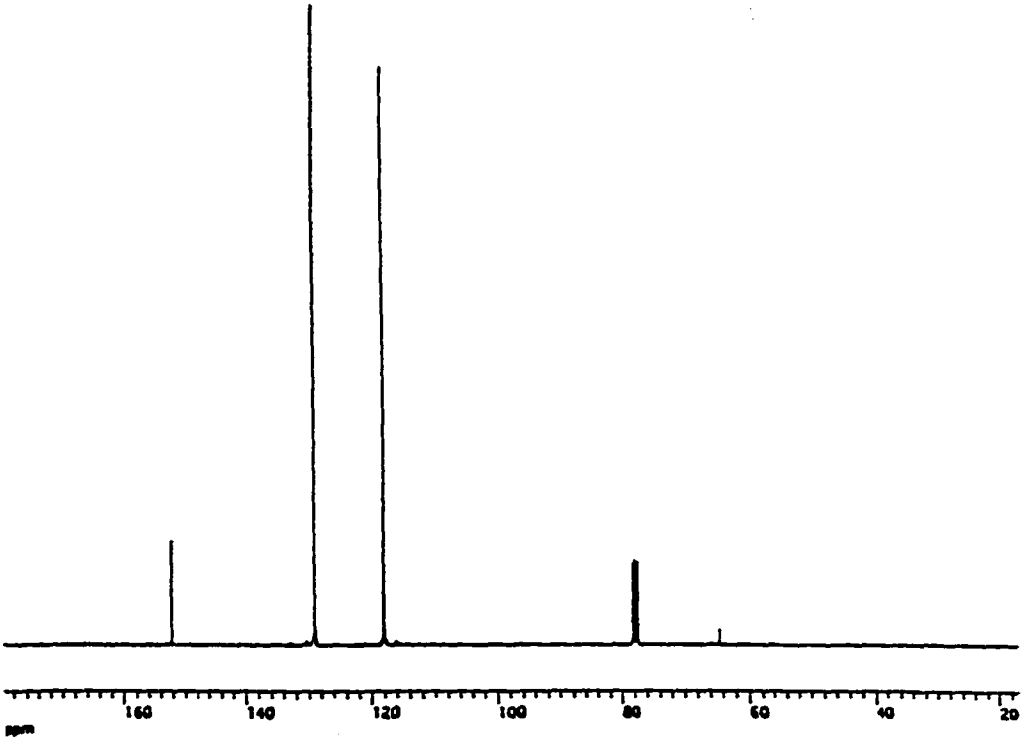


Fig.21: H NMR of biphenylene (6.55 – 6.8 ppm region)

^{13}C nmr data for biphenylene is presented below. The low-field position of the quaternary carbons (151.7ppm) is largely due to rehybridisation effects rather than a paratropic current.[118]

Fig.22: ^{13}C NMR of biphenylene (CDCl3 78 ppm)



Biphenylene has been referred to as diphenylene in the literature prior to 1960. Another name for biphenylene, cyclobutadibenzene, never gained

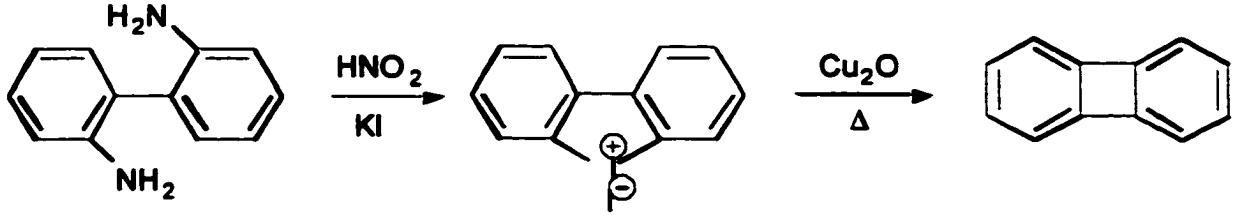
widespread acceptance. The first unambiguous synthesis of biphenylene was reported by Lothrop in 1941,[119] who pyrolysed 2,2'-diiodobiphenyl in the presence of cuprous oxide.

2.2.1.0. Methods of Preparation of Biphenylene

2.2.1.1. Using Cuprous Oxide:The Lothrop Cyclization

Mills-Nixon effects, that is, the localization of double bonds in aromatic systems as a result of strain caused by annelation to small rings, provided the incentive for biphenylene synthesis at the turn of the 20th century. Niementowsky[120] suggested the possibility of preparing biphenylene by the action of copper on 2,2'-dichlorobiphenyl. After many attempts, which were either unsuccessful immediately or later shown to have led to products with different structures, Lothrop[121] eventually succeeded in obtaining traces of biphenylene using a partially oxidised sample of copper as the dehalogenating agent. The yield of biphenylene obtained from the reaction between 2,2'-dibromobiphenyl and cuprous oxide at 350 °C was about 5%, increased to 15% when 2,2'-diiodobiphenyl was used.[122] Diazotization of the diamine **52** using nitrous acid followed by addition of

potassium iodide produced the intermediate iodonium iodide **53** which, on pyrolysis with cuprous oxide, gave biphenylene.



52 **53** **8**

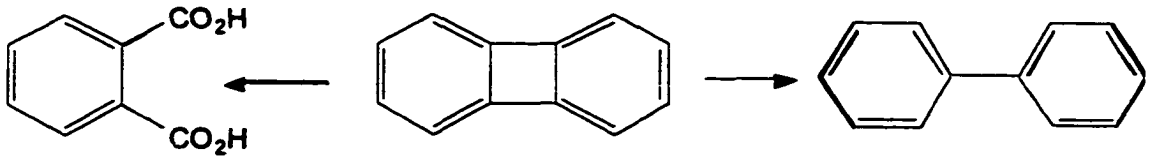
Scheme 23**: Lothrop' s original synthesis of biphenylene **8

Improved yields were recorded with the rapid removal of the product from the reaction mixture (e.g. by sublimation or/and the use of cupric oxalate which decomposes above 350 °C, evolving carbon dioxide which sweeps the product out of the reaction mixture) and the grade of cuprous oxide used. 2,2'-diiodobiaryls give higher yields than 2,2'-dibromobiaryls; the dichlorides were unreactive.

2.2.1.2. Proof of Structure of Biphenylene

Lothrop demonstrated through elemental analysis and a molecular weight determination that the compound which he had obtained had the molecular formula of biphenylene, $C_{12}H_8$; that on oxidation with chromic oxide it gave phthalic acid **54**; and that on reduction with hydrogen over a "red hot copper" catalyst, it gave biphenyl **55** (scheme 24).

***Scheme 24**: Derivatization of biphenylene **8** to prove its structure.*



54 **8** **55**

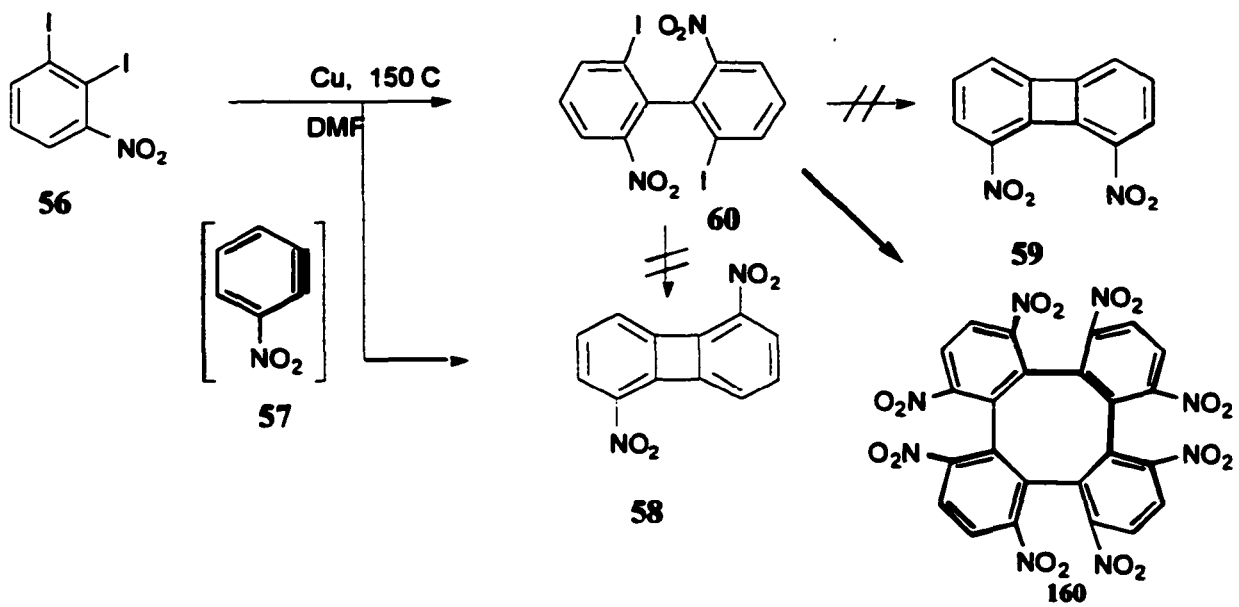
The proposed structure is in agreement with these results since (a) the molecular formula eliminates tetraphenylene from consideration; (b) the formation of phthalic acid **54** indicates that the starting material, 2,2'-dihalobiphenyl underwent carbon-to-carbon bond formation (ring closure) at an ortho position; and (c) the formation of biphenyl **55** by reductive cleavage makes it unlikely that the product resulted from a profound skeletal alteration of the starting material.

2.2.1.3. Using copper: The Ullmann Coupling reaction

Dehalogenations in the absence of solvent proceed by a stepwise Ullman coupling,[123] but those in solution usually involve aryne intermediates.[124] Thus, 3-nitrobenzyne **57** was generated dy deiodination of 1,2-diiodo-3-nitrobenzene **56** in dimethylformamide to afford 1,5-dinitrobiphenylene **58** or the 'complimentary' product. The absence of the 'non-complementary' product, 1,8-dinitrobiphenylene **59** being attributed to

the polarizing effect of the nitro group in the aryne intermediate **57**. Prolonged heating only afforded the octanitrotetraphenylene **160**.

Scheme 25: *Attempt synthesis of dinitrobiphenylenes by Ullman reaction*

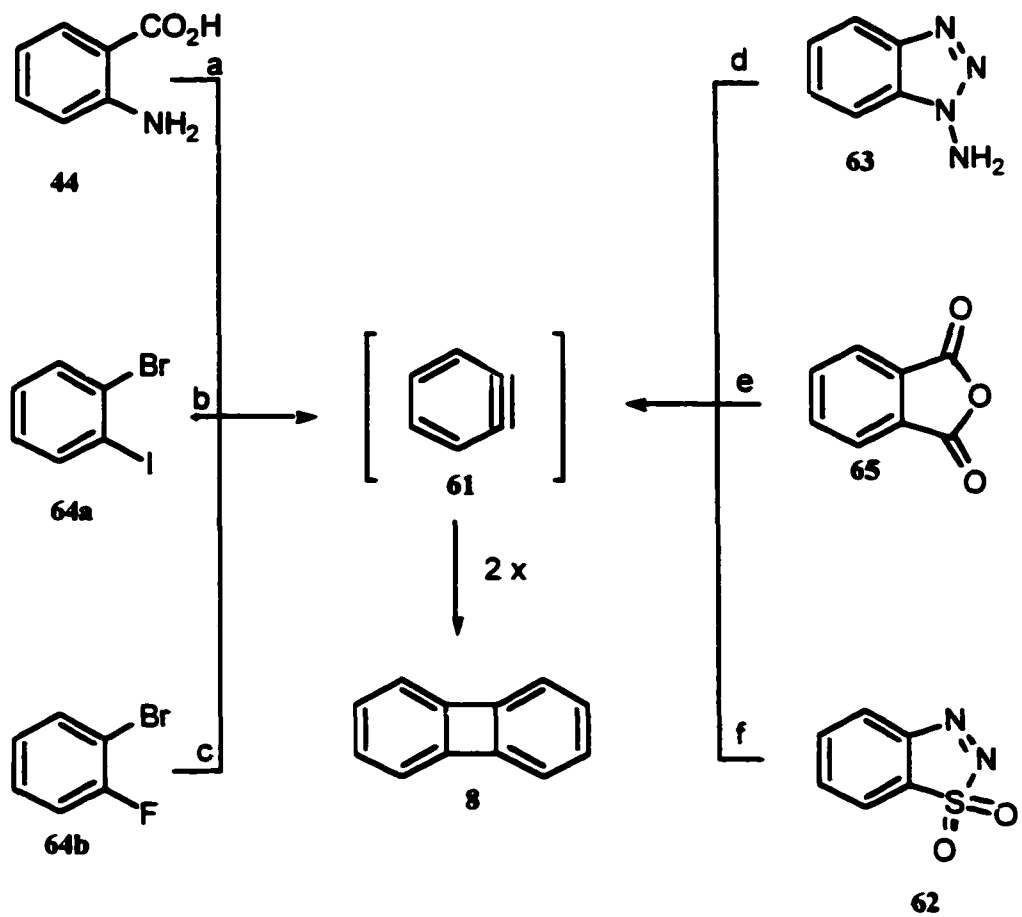


2.2.1.4. Dimerisation of Arynes

Biphenylenes are produced when arynes are generated under conditions in which they can dimerize. Of the methods available[125] for the generation of benzyne itself, it is found that those which avoid the use of strong nucleophiles and polar solvents give the highest yields of the dimer. Benzyne and its analogues can be relatively long-lived at low concentrations. Dimerisation, which is normally unfavorable in comparison

to nucleophilic attack is, however, facilitated by the generation of a high local concentration of any other species which might compete for this intermediate. A prerequisite for dimerisation in solution is a high encounter frequency between the reacting species. Biphenylene formation is facilitated with increasing the aryne stability.

Scheme 26: *Routes to biphenylene* ***8*** *through benzyne* ***61***



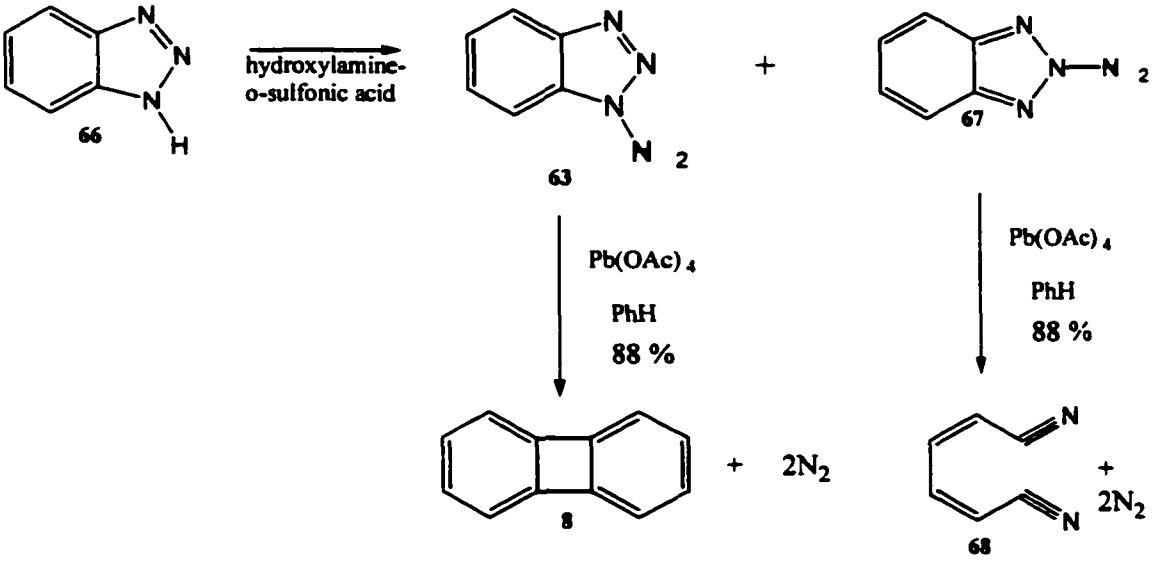
The simplest among these methods (a) involves the aprotic diazotization of anthranilic acid **44**[126] to give benzenediazonium-2-

carboxylate which may then be decomposed into benzyne **61**, carbon dioxide, and nitrogen by heating in an inert solvent.[127] Benzothiadiazole-1,1-dioxide **62** also fragments readily[128], (f) to give benzyne **61** as does the nitrene produced by lead tetraacetate oxidation of 1-aminobenzotriazole **63**[129] (d). Dehalogenation[130] of *o*-dihalobenzene **64** and flash vacuum pyrolysis of phthalic anhydride[131] **65** are, likewise, benzyne-generating methods (scheme 26).

The effects of substituents on the stability of benzyne have shown that arynes behave like typical electron-rich intermediates: that electron-withdrawing substituents increase aryne stability and electron-donating ones have the reverse effect. In some cases unusually high yields of biphenylenes can be obtained if the precursor contains an electron-withdrawing group. Substituents that can reduce the length of the aryne dehydro-bond should also increase stability, by improving orbital overlap, and consequently ring annelation to benzyne has a pronounced effect. The stabilities of the benzannelated arynes parallel the respective bond orders of the parent hydrocarbons, i.e. 9,10-phenanthryne > 1,2-naphthalyne > benzyne > 2,3-naphthalyne with the former being more stable.[132] However the yields of dimers will reflect the increase in cyclobutadienoid character of the products, i.e. in order of decreasing stability.

2.2.1.5. Synthesis of Biphenylene

Amination of benzotriazole **66** in a basic solution with hydroxylamine-*o*-sulfonic acid generated, in 60% yield, 1-aminobenzotriazoles **63** and 2-aminobenzotriazoles **67** in 2 to 1 ratio. Lead tetraacetate oxidation of the former in benzene at room temperature afforded biphenylene **8** in high yield (80-88%). Oxidation of 2-aminobenzotriazole **67** is known to give muconononitrile **68**.[133]



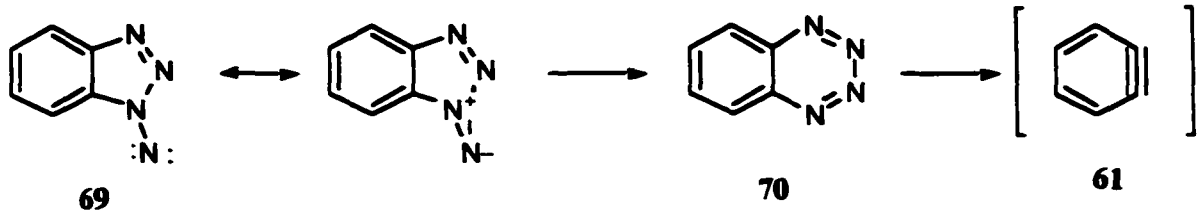
Scheme 27: Biphenylene 8 from oxidation of 1-aminobenzotriazole 63

The yields of biphenylenes obtained by this procedure are remarkably high in comparison with those from other aryne dimerisations. It was speculated[134] that the benzyne could be generated in the triplet state to

favour dimerisation by virtue of its lower reactivity towards nucleophiles. A second consequence of a triplet dimerisation is that polarization of the aryne should have little effect on the product ratio when formation of two isomeric biphenylenes is possible. Thus, addition of 1-aminobenzotriazole to a benzene solution of lead tetraacetate at 55 °C gives biphenylene in 88% yield, this figure being relatively unaffected by variation of the solvent or reaction temperature.

The postulated mechanism of generation of benzyne **61** from 1-aminobenzotriazole **63** is presumed to occur via a sequence of oxidation to the nitrene species **69**, rearrangement to 1,2,3,4-benzotetrazine **70**, and fragmentation to benzyne **61** detected by its subsequent reactions.

Scheme 28: *Postulated*[134] *mechanism of benzyne **61** formation.*



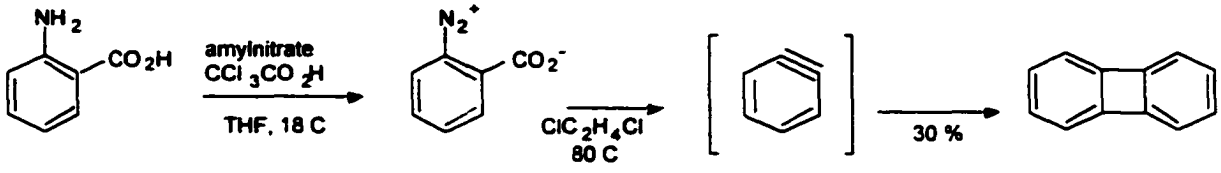
69 **70** **61**

Because the tetrazine **70** has not been detected, and that, the fragmentation of the nitrene from 2-aminobenzotriazole leads to mucononitrile and not biphenylene (nor benzyne evidently), the proposed

intermediacy of the tetrazine **70** is questionable. This remarkable tendency of benzyne **61**, generated by this mild method to dimerize is in contrast to that produced by other methods.

2.2.1.6. Solution Dimerisation of Arynes

The thermal decomposition of benzenediazonium-2-carboxylate **71** in refluxing 1,2-dichloroethane gives biphenylene **8** in 25-30% yield, in addition to traces of triphenylene. It is reported[135] that attempts to extend the reaction to derivatives of biphenylene have had little success.



44 **71** **61** **8**

Scheme 29: *Anthranilic acid route to biphenylene **8***

In our hands, about 30% yield of a 1:1 mixture of 1,5- and 1,8-dimethylbiphenylenes were prepared from 6-methylbenzenediazonium-2-carboxylate.

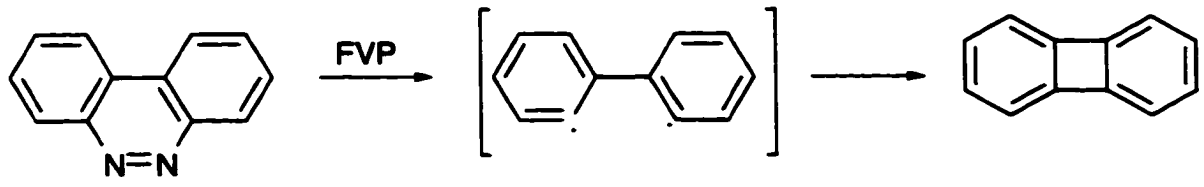
Providing that adequate precautions are taken in handling the violently explosive diazonium carboxylate salt **71** (never to be let dry), this is probably the best method for preparation of **8** and some of its alkyl

derivatives in gram quantity in a one day procedure. The method, unfortunately, fails with nitro- and halogenoanthranilic acids.

2.2.1.7. By Nitrogen Extrusion: Flash Vacuum Pyrolysis (FVP) of Benzo[*c*]cinnolines

Biphenylene and its derivatives can be prepared in gram quantities by Vacuum pyrolysis of the parent benzo[*c*]cinnoline **72** and its alkyl and halo derivatives in the temperature range of 800-950 °C, but because a low throughput is necessary for reasonable yields, preparations on larger scale are impractical. Above 950 °C, the yields decrease as a result of decomposition of the product.

Scheme 30: *FVP of benzo[c]cinnoline route to biphenylene* ***8***

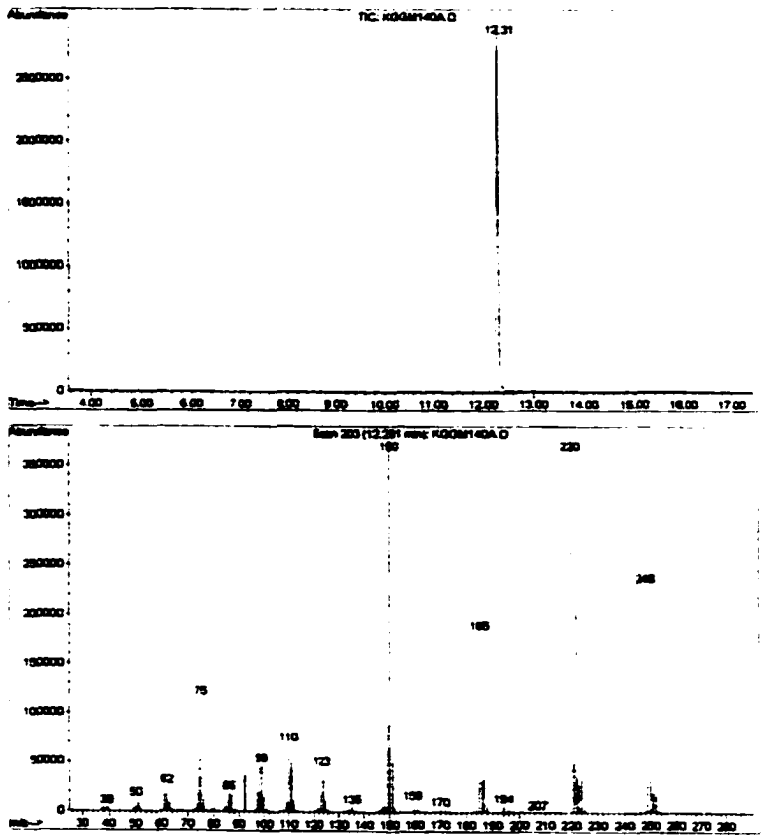


72 **73** **8**

The reaction proceeds via a presumed[136] diradical **73** that cyclizes to biphenylene in the hot zone, precluding fragmentation to benzyne **61** and therefore, of isomeric products. Thus, 1,10-disubstituted benzo[*c*]cinnolines give 1,8-disubstituted biphenylenes.

The mass spectrum of the precursor benzo[*c*]cinnoline often enables a crude prediction as to the outcome of the experiment. Compounds showing an intense (M^+-N_2) fragment ion can be expected to cyclize. Indeed, as depicted in Fig.23, the outcome of the pyrolysis of 1,10-dichlorobenzo[*c*]cinnoline at 800 °C was predicted by the mass spectrum which shows the loss of nitrogen at m/z 220 (-28 from m/z 248) in the fragmentation of the parent 1,10-dichlorobenzo[*c*]cinnoline (m/z 248).

Fig.23: GC (top) and MS (bottom) of 1,10-dichlorobenzo[*c*]cinnoline



The m/z 185 and m/z 150 peaks are due to the consecutive loss of two chlorine atoms (2X35), resulting in biphenylene ion (m/z 150).

Those compounds showing loss of N_2H as the primary fragmentation are prone to rearrangement.

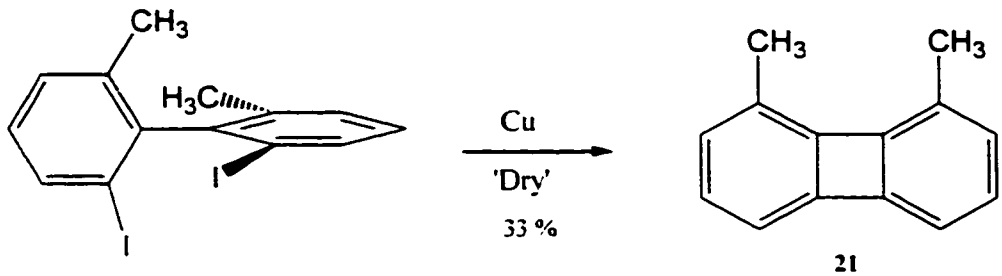
2.3. APPLICATIONS: Syntheses of Disubstituted Biphenylenes

2.3.1. Using Copper: The Modified Lothrop Reaction

Substitution of cuprous oxide by copper bronze in the Lothrop synthesis of biphenylene increased the yields and the reaction, which is really an Ullman reaction, makes the reaction very practical in some cases.[137] However, due to the use of copper as dehalogenating agent, no halo (or dihalo)-biphenylene could be prepared using this method.

2.3.1.1. Synthesis of 1,8-dimethylbiphenylene

We utilized this method to prepare 1,8-dimethylbiphenylene **21** by a 'dry' reaction between 2,2'-diiodo-6,6'-bitolyl **13** and copper at 230 - 240 °C.

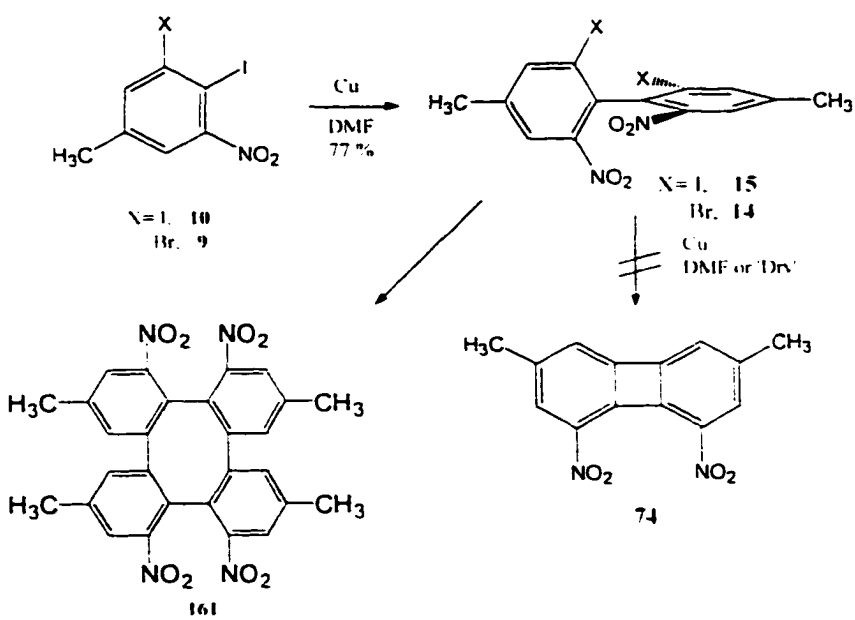


13 21

Scheme 31: *Synthesis of 1,8-dimethylbiphenylene by the Lothrop method*

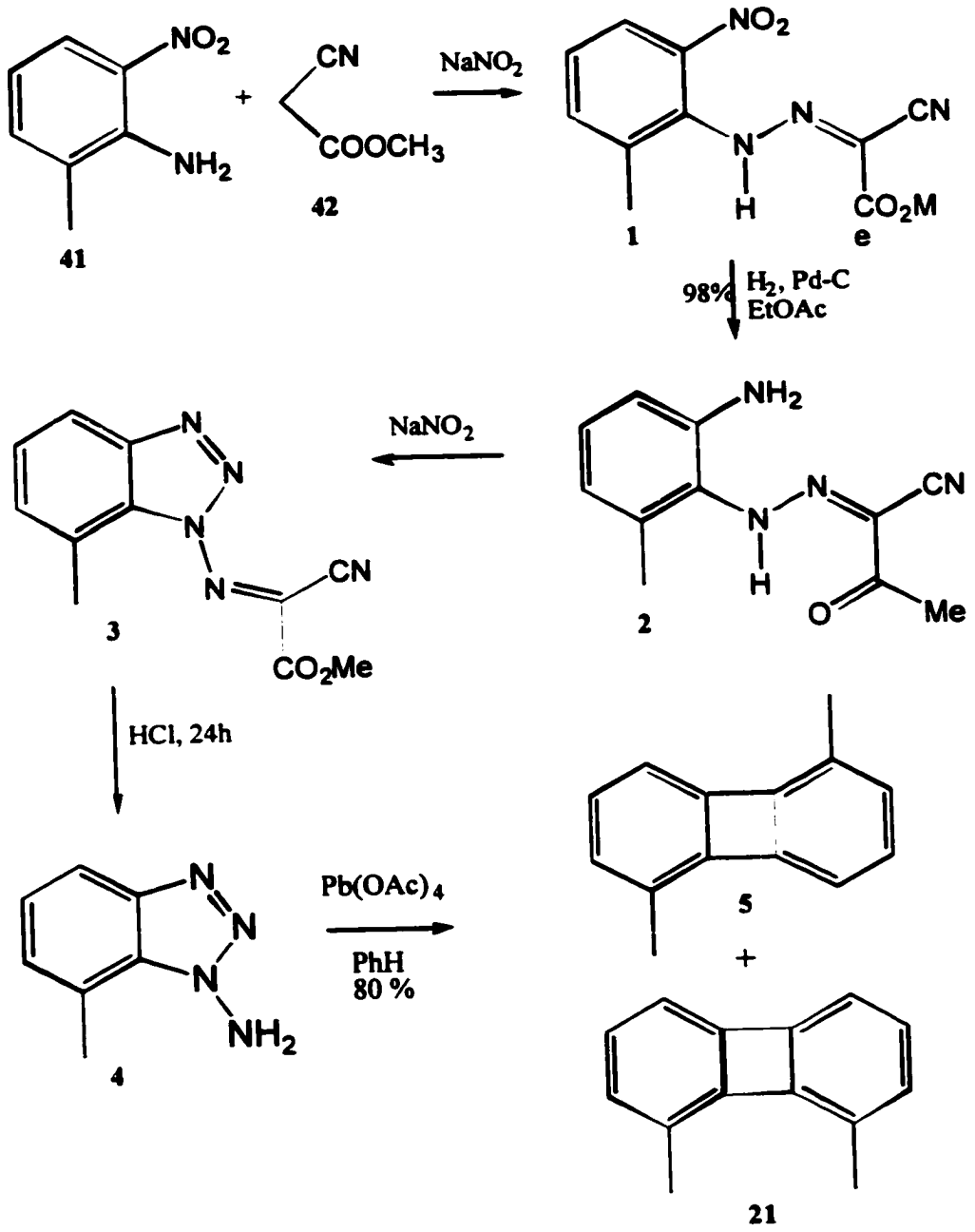
1,8-Dimethylbiphenylene **21** was almost colorless when synthesized by this method, and was identical to the compound obtained through the pyrolytic method (presented in scheme 36), which crystallizes slowly upon standing. In similar preparations, 2,3-diiodo-5-methylnitrobenzene **10** and 3-bromo-2-iodo-5-methylnitrobenzene **9** reacted with copper in dimethylformamide at 155 °C to afford the respective biaryls 2,2'-diiodo-6,6'-dinitro-*p*-bitolyl **15** and 2,2'-dibromo-6,6'-dinitro-*p*-bitolyl **14** in high yields but neither the solution nor the dry reactions of **15** and **14** with copper gave the expected 1,8-dinitro-3,6-dimethylbiphenylene **74** in agreement with findings by others.[138] The only likely product was the tetramethyltetranitrotetraphenylene **161** on prolonged heating.

Scheme 32: *Attempt to synthesize 3,6-dimethyl-1,8-dinitrobiphenylene*



2.3.2.1 By Aryne Generation: Syntheses of 1,5- and 1,8-dimethylbiphenylene by Lead Tetraacetate Oxidation of 4-methyl 1-aminobenzotriazole (The Method of Rees)

Likewise with benzyne, methylbenzynes (toluynes) are generated in high yield by lead tetraacetate oxidation of methyl substituted 1-aminobenzotriazole in mild condition (room temperature, benzene or methylene chloride). However, the method has been limited by the unavailability of ortho methyl substituted 1-aminobenzotriazole for which preparation can be lengthy and tedious. Upon synthesizing 4-methyl-1-aminobenzotriazole (together with the equally useful 4-methyl-3-aminobenzotriazole and the isomeric, but not a benzyne generating, 4-methyl-2-aminobenzotriazole) in five steps (see scheme) and its subsequent oxidation, we obtained, in a 1:1 ratio 1,8-dimethylbiphenylene **21** and 1,5-dimethylbiphenylene **5** (*Scheme 33*). Lead tetraacetate oxidation of 4-methyl-2-aminobenzotriazole afforded 2-methylmuconononitrile as expected.



Scheme 33: *Synthesis of 1,5- and 1,8-dimethylbiphenylene by the method of Rees*

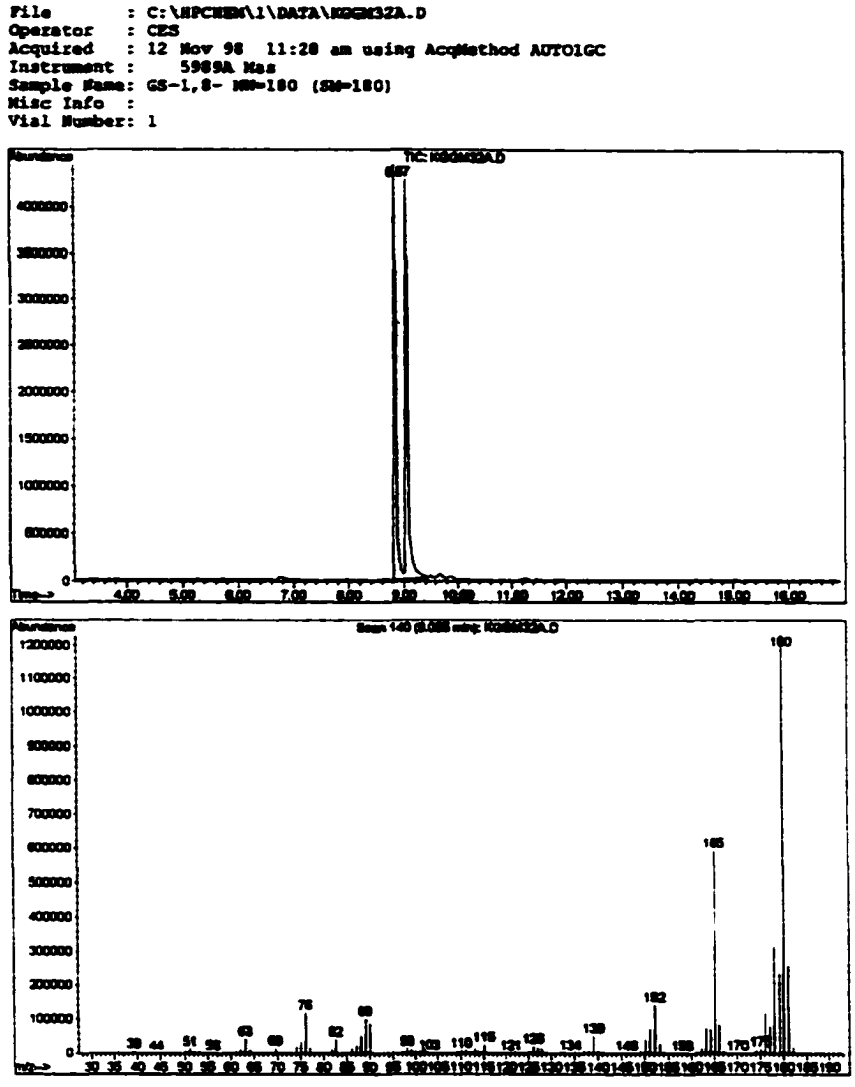


Fig.24: GC (top) and MS (bottom) of the mixture of isomers 1,5 –and 1,8-dimethylbiphenylene (1:1).

The two isomers (m/z 180), as shown by the GC spectrum, have a similar fragmentation pathway. Consecutive loss of methyl groups (m/z 165 and m/z 152, +2Hs) to afford the parent biphenylene.

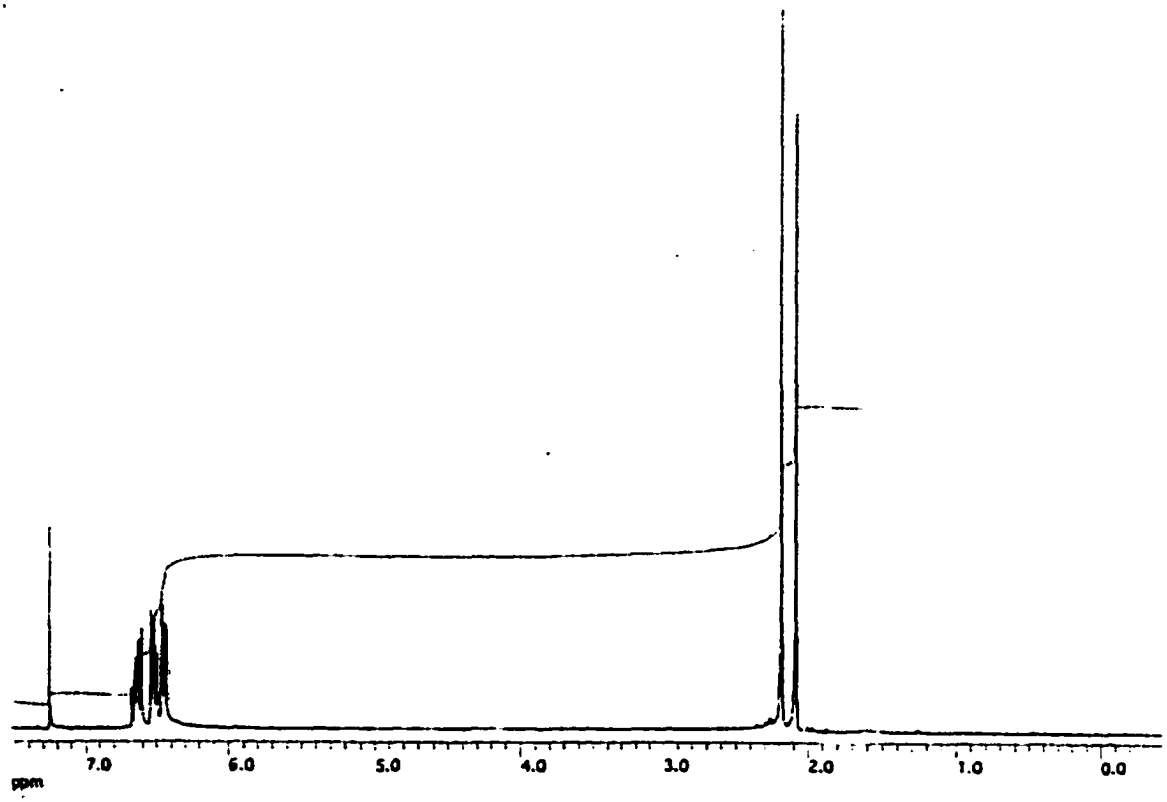
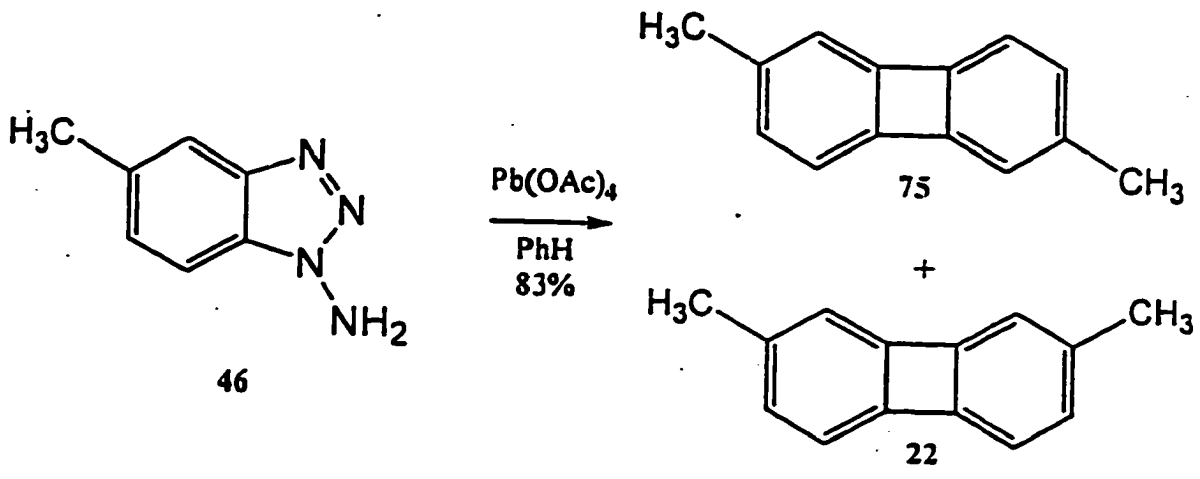


Fig.25: H NMR spectrum of the mixture of isomers 1,5 –and 1,8-dimethylbiphenylene (1:1).

2.3.2.2. Synthesis of 2,6- and 2,7-dimethylbiphenylene by The Rees' s Method

Lothrop reported the first synthesis of 2,7-dimethylbiphenylene[139] shortly after his groundbreaking preparation of the parent biphenylene. This was done, in low yield, by cuprous oxide deiodination of 2,2'-diiodo-4,4'-dimethylbiphenyl and subsequent pyrolysis of 2,7-dimethylbiphenylene-iodonium iodide. The compound described in the literature[140] as 2,6-dimethylbiphenylene, obtained through *m*-methylbenzyne dimerisation is in reality a mixture of both the 2,6- and the 2,7- isomers, as we were able to show. Amination of the commercially available 5-methylbenzotriazole with hydroxylamine-*o*-sulfonic acid in a potassium hydroxide solution afforded all three amino derivatives possible. Lead tetraacetate oxidation of a mixture of 1-amino-5-methylbenzotriazole and 1-amino-6-methylbenzotriazole **46** in methylene chloride (or benzene) at room temperature afforded, in ca. 85% yield, 2,6-dimethylbiphenylene **75** and 2,7 dimethylbiphenylene **22** in 55:45 ratio, in agreement with the observation that these reactions do give approximately 1:1 mixtures of both the 'non-complimentary' (from the methylbenzyne fragment) and the 'complimentary' dimers. While ^{1}H NMR



Scheme 34: Synthesis of 2,6- and 2,7-dimethylbiphenylenes

Fig.26: ^{13}C NMR spectrum of the mixture of isomers 2,6 –and 2,7-dimethylbiphenylene

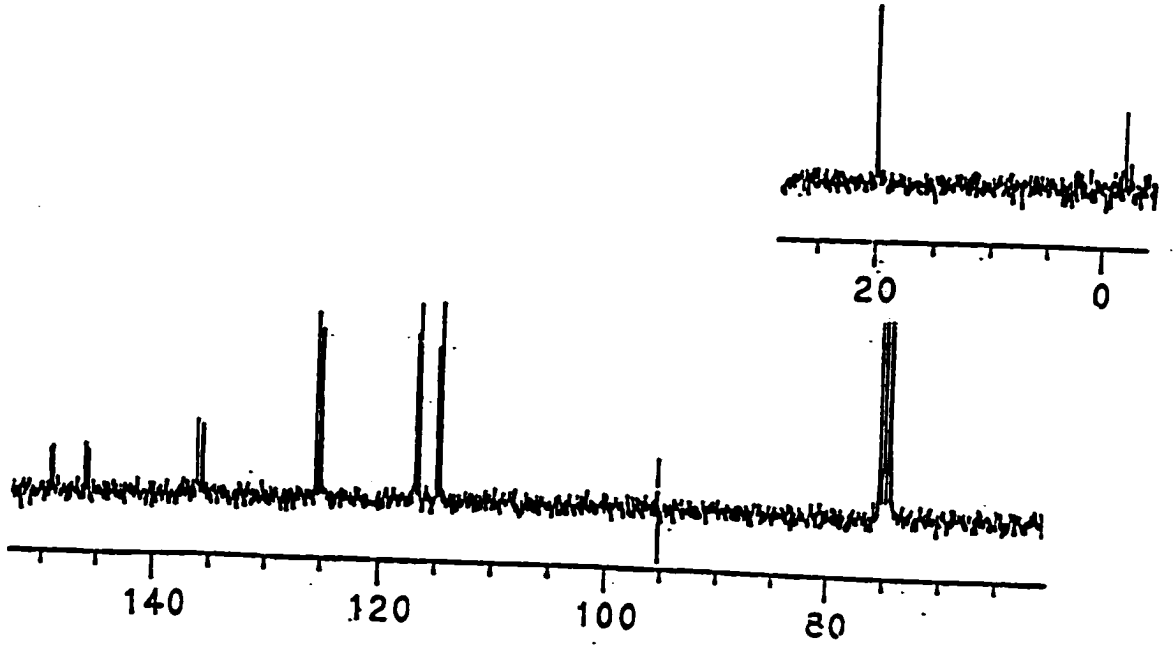
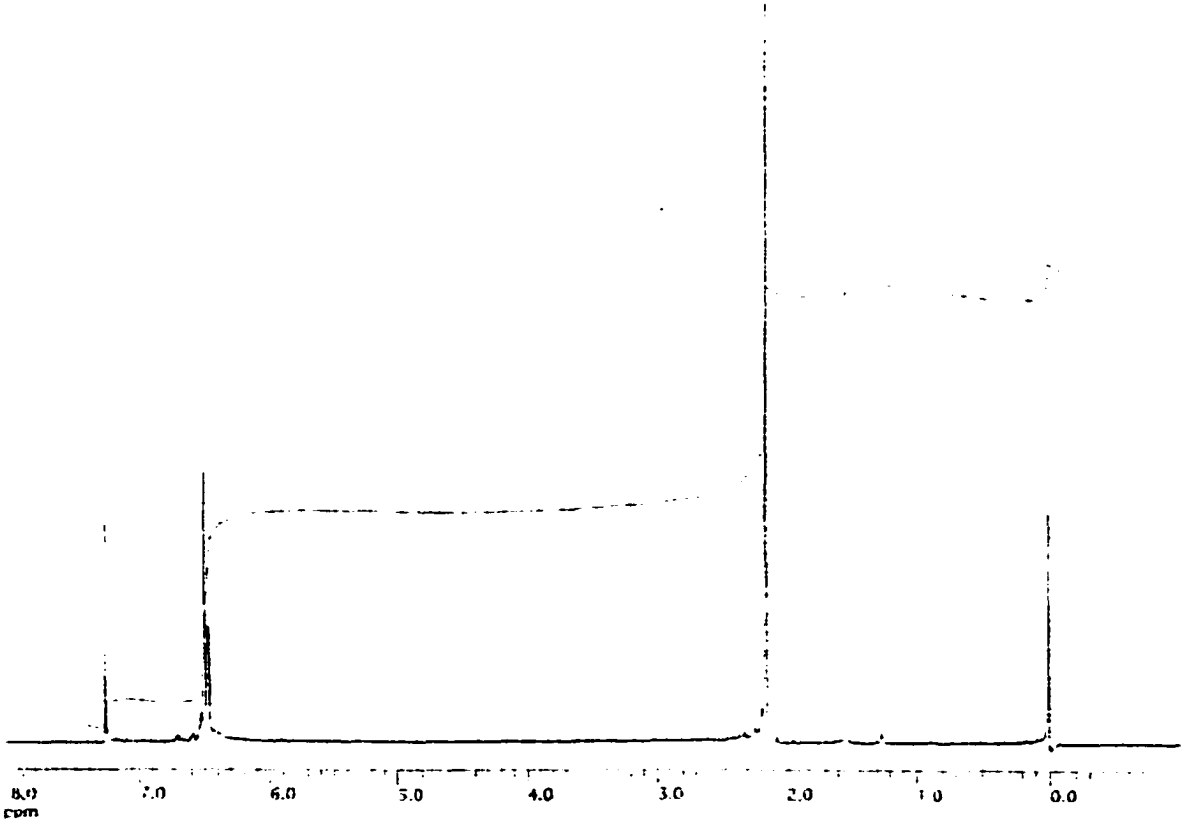
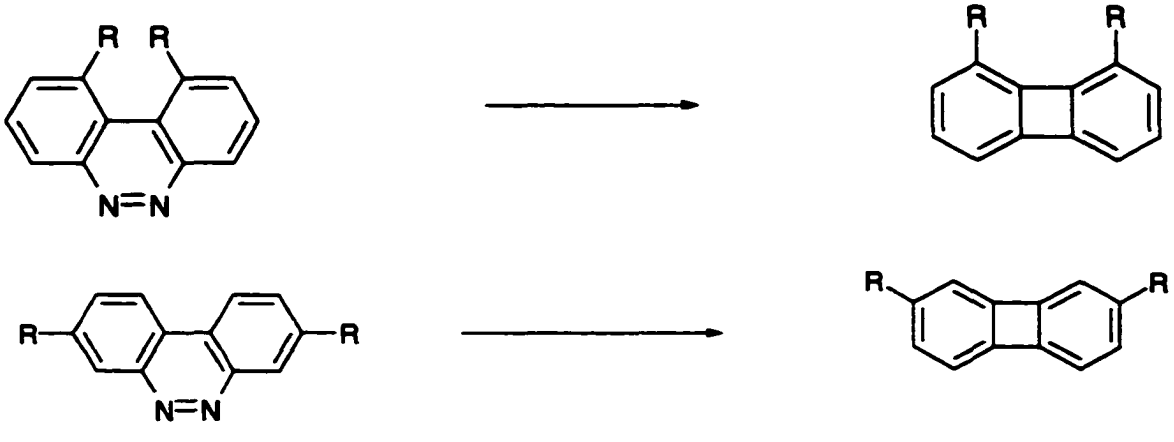


Fig.27: H NMR spectrum of the mixture of isomers 2,6 –and 2,7-dimethylbiphenylene



2.3.2.3. By Extrusion Reactions: Flash Vacuum Pyrolysis of Bridged Biaryls

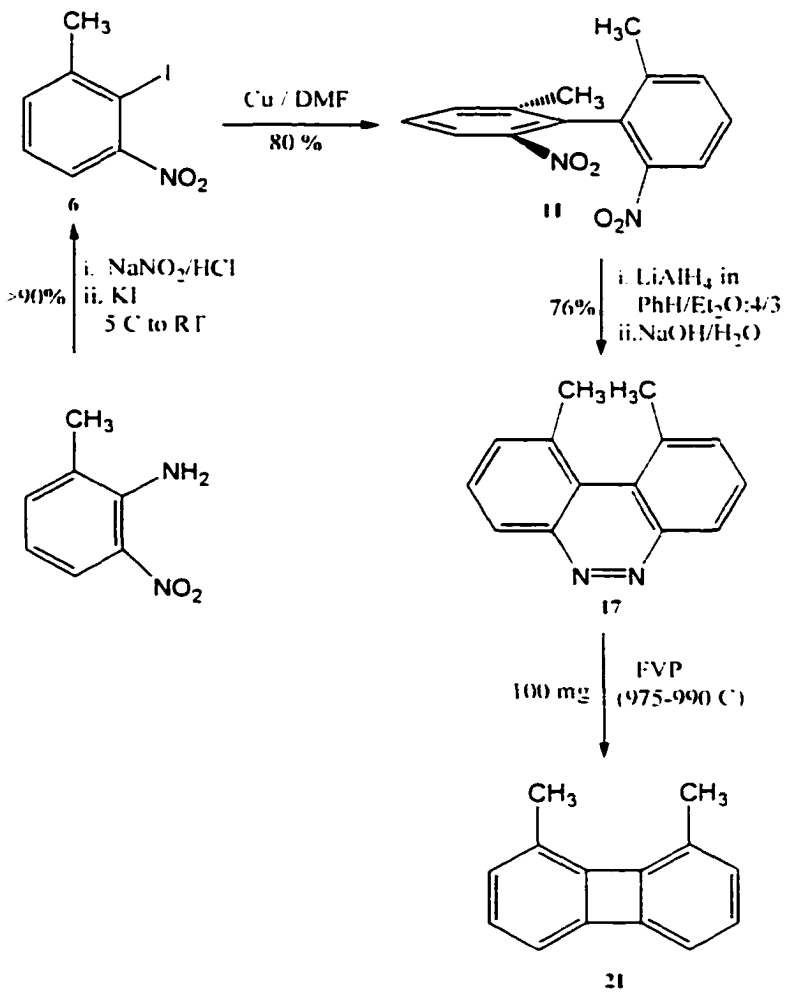
Nitrogen extrusion occurs when benzo[*c*]cinnolines are pyrolysed under vacuum at higher temperatures. Wilcox et al.[141] first and Vogtle et al.[142] prepared substituted dialkylbiphenylene using this method. Guided by the predictions of GCMS analyses of the respective disubstituted benzo[*c*]cinnolines, we prepare 2,7-dimethylbiphenylene **22** from 3,8-dimethylbenzo[*c*]cinnoline **18** (950°C), 1,8-dimethylbiphenylene **21** from 1,10-dimethylbenzo[*c*]cinnoline **17** (970°C), 2,7-dichlorobiphenylene **212** from 3,8-dichlorobenzo[*c*]cinnoline **120** (850°C) and 1,8-dichlorobiphenylene **23** from 1,10-dichlorobenzo[*c*]cinnoline **20** (820-850°C).



***Scheme 35:** General schemes for FVP of disubstituted benzo[c]cinnolines*

2.3.2.4. Synthesis of 1,8-dimethylbiphenylene

Using a slightly modified procedure of Wilcox, we successfully prepare a series of disubstituted biphenylenes in multigram quantities. Starting from the synthesis of 1,8-dimethylbiphenylene that we have accessed previously via a Lothrop-type synthesis, but in low yield.

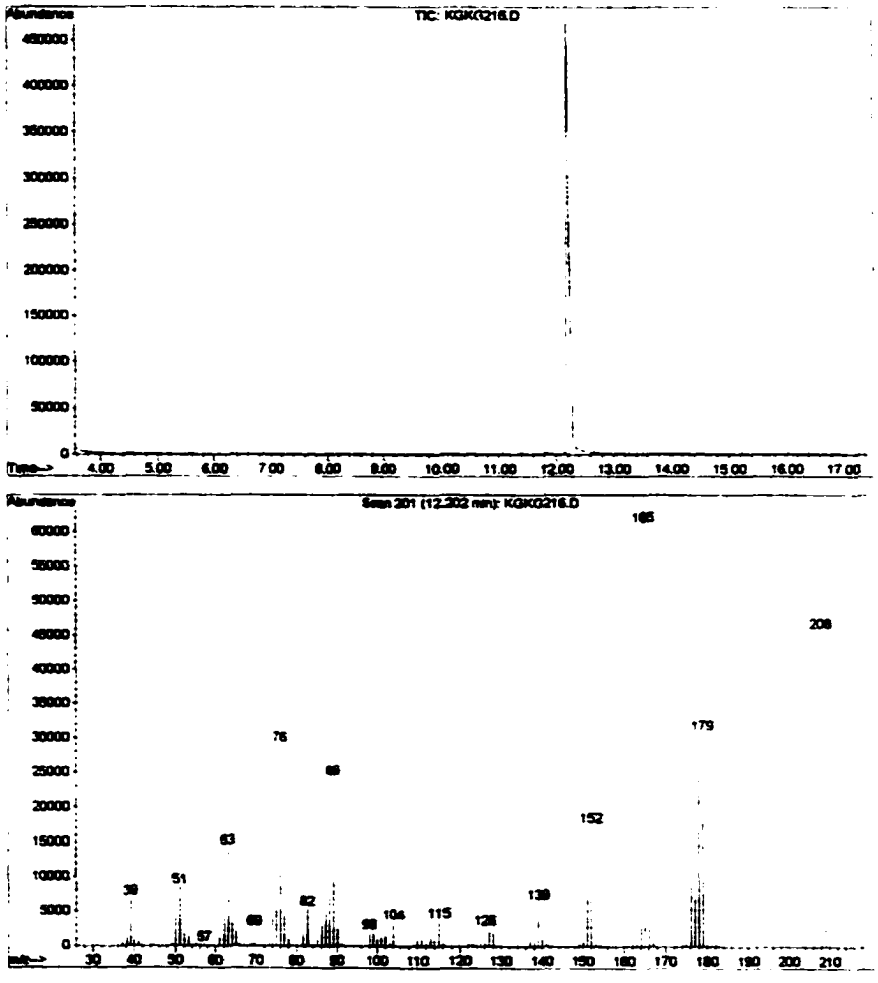


Scheme 36: *Synthesis of 1,8-dimethylbiphenylene 21 by FVP*

Our synthesis of 1,8-dimethylbiphenylene **21** (scheme 36) based upon thermal extrusion of dinitrogen from 1,10-dimethylbenzo[*c*]cinnoline **17** started with the diazotization of an HCl solution of 2-nitro-6-methylaniline by addition of $NaNO_2$. The diazonium chloride that formed was poured into an ice-cold aqueous KI and, after the vigorous evolution of nitrogen and iodine vapor had subsided, excess $NaHSO_3$ was added to reduce the excess iodine formed. The product, 2-nitro-6-methyliodobenzene **6**, was isolated, in high yield, by extraction. Ullman coupling of this product **6** in refluxing dimethylformamide produced 6,6'-dimethyl-2,2'-dinitrobiphenyl **11** in almost quantitative yield. The iodide **6**, Cu powder and dry dimethylformamide were refluxed for 4h before another portion of Cu powder was added to the cooled mixture, which was refluxed for an additional 4h. After the inorganic material was separated by filtration, the solution was poured into water and the precipitated product was collected and recrystallized to afford the deep yellow crystals of the biphenyl **11**. Reduction of the tetrasubstituted biphenyl **11** with $LiAlH_4$ in a mixture of diethylether and benzene provided the benzocinnoline **17** in >90% yield. The optimum ratio of diethylether : benzene was found to be 3 : 4. Chromatography (hexanes) and recry stallization in acetone ensured the purity of the samples for pyrolysis.

GCMS of the precursor benzo[*c*]cinnoline predicted the outcome of this pyrolysis as the parent compound fragmented by, first, losing 1 mole of nitrogen (Fig.28).

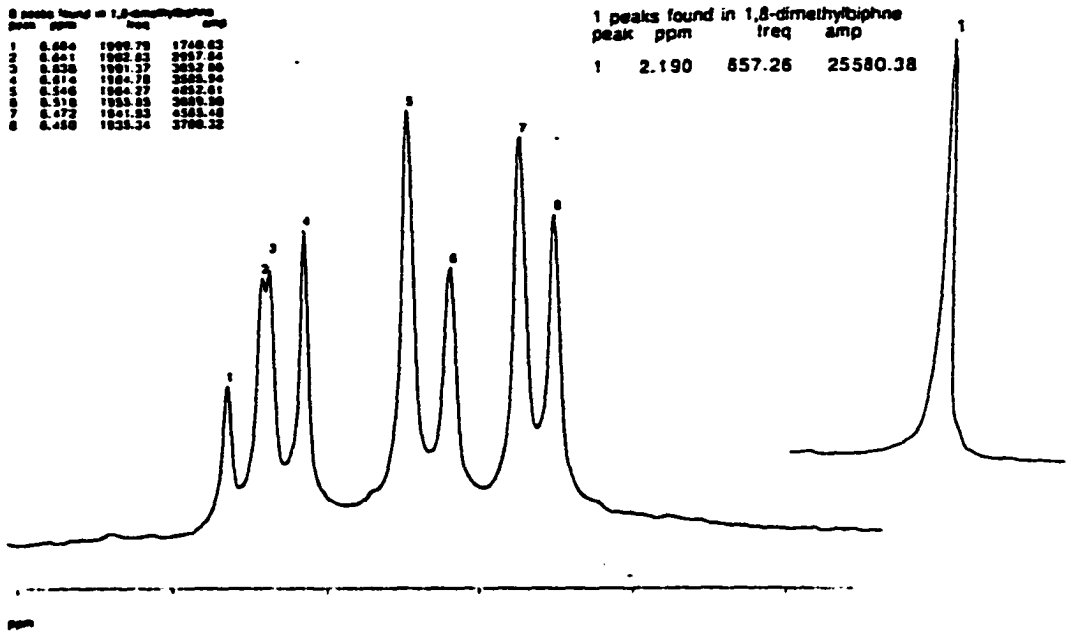
Fig.28: GCMS predicting formation of 1,8-dimethylbiphenylene by extrusion of 1 mole of nitrogen (m/z 179/200) from 1,10-dimethylbenzo[*c*]cinnoline (m/z 208) followed by the losses of the methyl groups (m/z 165 and 152 corresponding to biphenylene).



The best results in preparative runs were obtained when no more than 500mg of starting material was used. The temperature of the pyrolysis was maintained at *ca.*950°C. Attempts to increase the scale of a pyrolysis to 1g resulted in the recovery of much starting material in addition to the product, 1,8-dimethylbiphenylene. The excellent yield coupled with the availability of large quantities of the benzo[*c*]cinnolines made this an attractive method for the preparation of the other dialkyl and dihalo analogues.

^{1}H NMR of 1,8-dimethylbiphenylene (Fig.29) shows two doublets and a triplet at the expected region for a biphenylene derivative bearing electron-donating substituents. The methyl groups are responsible for the shielding effect on the adjacent protons and the cyclobutadienoid ring for a similar effect on the H atom para to the methyl group. The remaining H atom, split by two neighboring H atoms is a doublet of doublet in the region of 6.3-6.7ppm.

Fig.29: H NMR of 1,8-dimethylbiphenylene (6.3 – 6.7 ppm region)



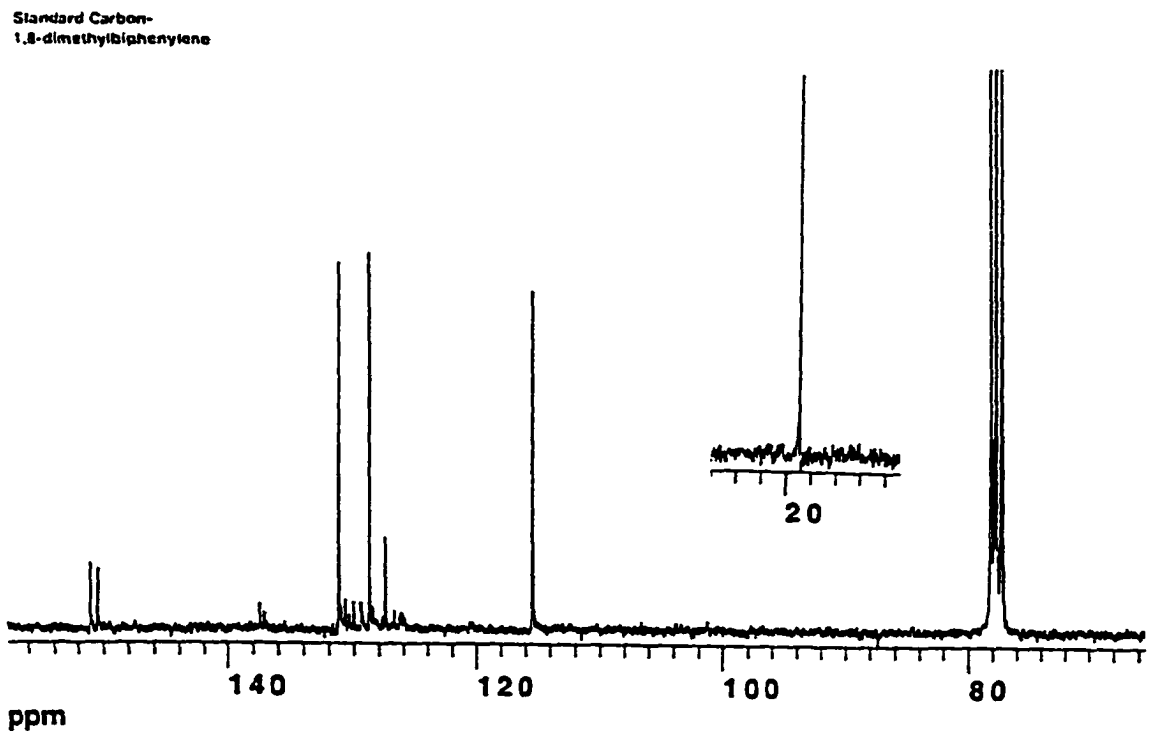
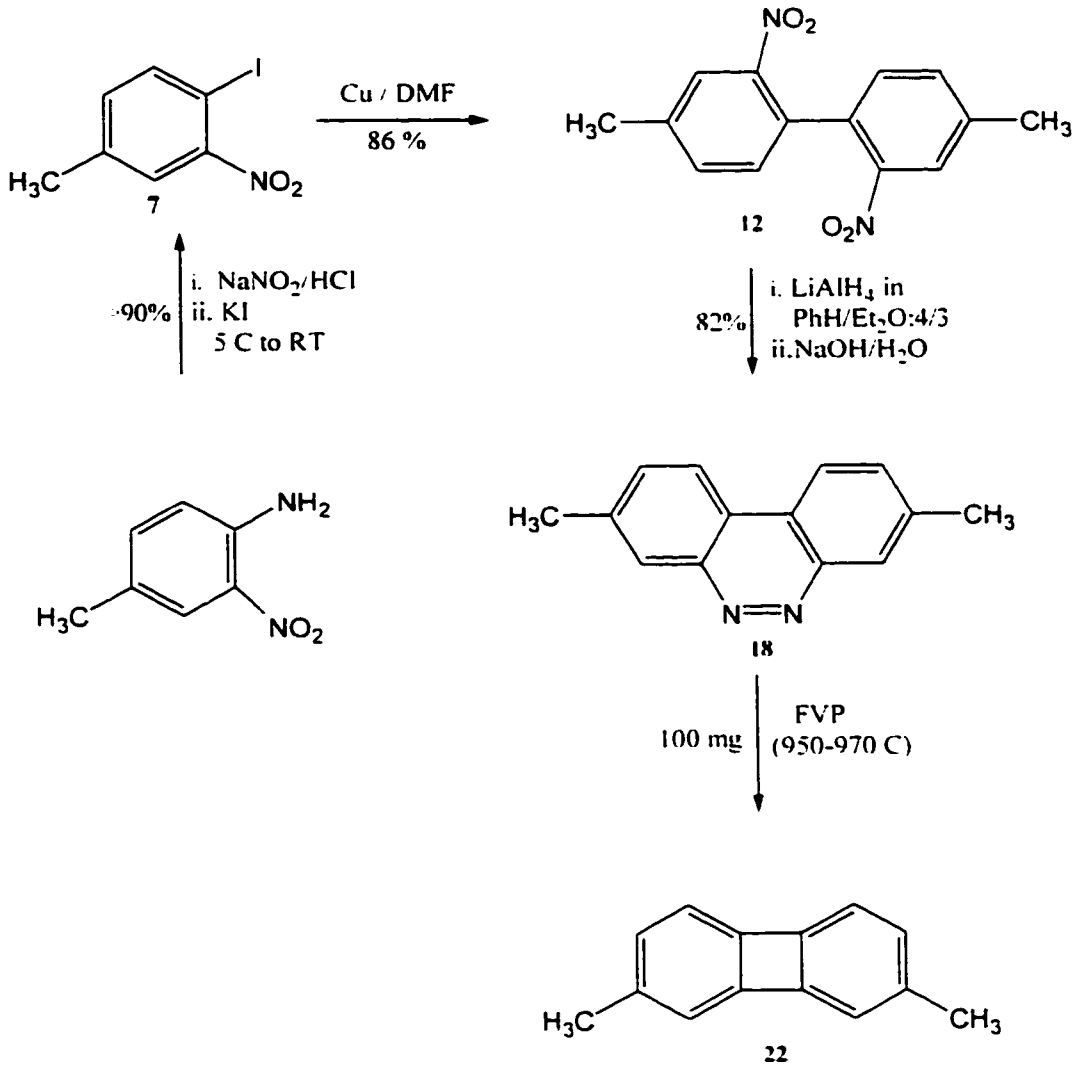


Fig.30: ^{13}C NMR of 1,8-dimethylbiphenylene

2.3.2.5. Synthesis of 2,7-dimethylbiphenylene

Applying the method described above for the preparation of the 1,8-dimethylbiphenylene, we prepared the corresponding 2,7-isomer starting from 2-nitro-4-methylaniline.

Scheme 37: *Synthesis of 2,7-dimethylbiphenylene* ***22*** *by FVP*



pyrolysis could be slightly lowered to *ca.* 950 °C. Fig. shows the ^{1}H NMR aromatic region of 2,7-dimethylbiphenylene. Two overlaps involving the doublet ($H_{4/5}$) and the singlet ($H_{1/8}$) in one hand and that between the doublet ($H_{3/6}$) and the doublet ($H_{4/5}$) in the other give an excentred multiplet.

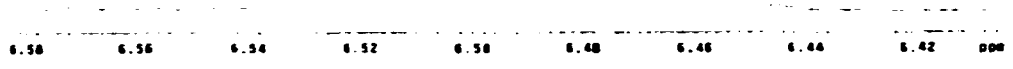


Fig.31: ^{1}H NMR (500 MHz of 2,7-dimethylbiphenylene (aromatic H's only)

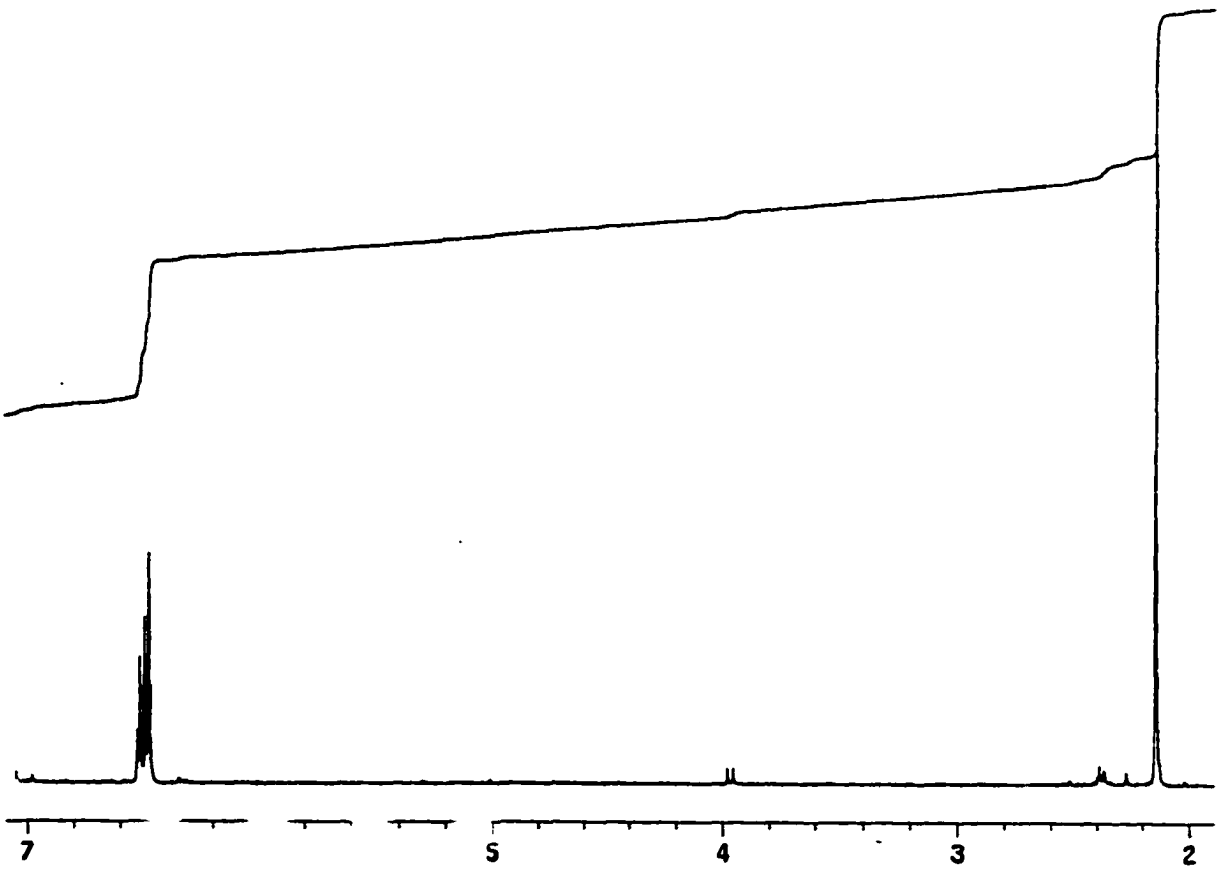


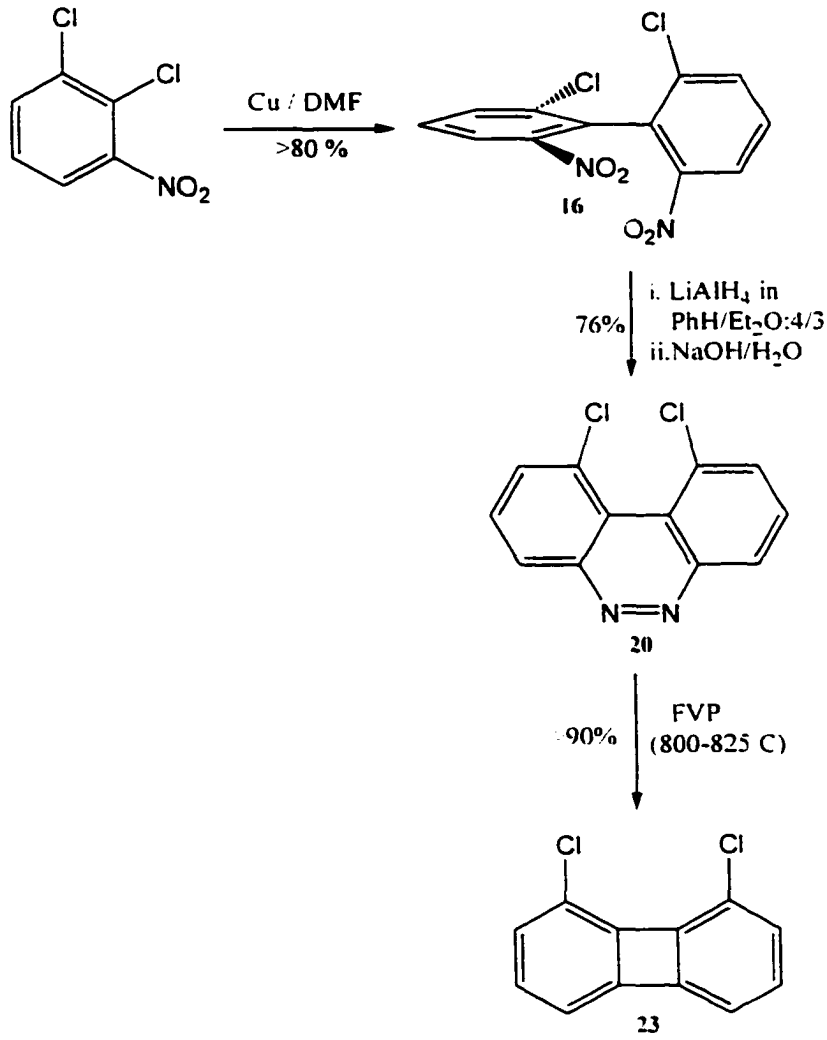
Fig.32: ^{1}H NMR (500 MHz) of 2,7-dimethylbiphenylene **22**

2.3.2.6. Synthesis of 1,8-dichlorobiphenylene

Ullman coupling reaction is known to be accelerated by an electron withdrawing group ortho to the iodine.[143] In the preceding syntheses, we illustrated that by using the nitro moiety. Use of the chlorobenzene instead of the usual iodobenzene as substrate in the Ullman reaction hasn' t been very popular but we found that it works quite well. Given that neither the diiodo- nor the dibromobenzo[*c*]cinnolines are suitable for pyrolysis at elevated temperature without decomposition, we turned to the

dichlorobenzo[c]cinnolines in virtue of their remarkable ease of preparation (fewer steps than the dimethyl analogues).

Scheme 38: *Synthesis of 1,8-dichlorobiphenylene 23 by FVP*



Ullman coupling of commercial 2,3-dichloronitrobenzene in refluxing dimethylformamide proceeded smoothly to afford the tetrasubstituted biaryl

in very good yield. The 2,2'-dichloro-6,6'-dinitrobiphenyl **16** was reduced with lithium aluminum hydride in the mixture of diethylether / benzene :3/4 as previously described to produce 1,10-dichlorobenzo[*c*]cinnoline **20** which was the precuror for 1,8-dichlorobiphenylene **23**.

The mass spectrum of 1,10-dichlorobenzo[*c*]cinnoline **20** predicted a facile loss of dinitrogen (presented in Fig. 23). Flash vacuum pyrolysis of this benzocinnoline at *ca.* 800 °C, smoothly and completely converted the starting **20** to the faintly greenish 1,8-dichlorobiphenylene **23** after purification by column chromatography. ^{1}H NMR spectrum of 1,8-dichlorobiphenylene is characteristic of biphenylene derivatives (Fig.33) in that the chemical shifts are in the region around 6.7 – 7.0 ppm.

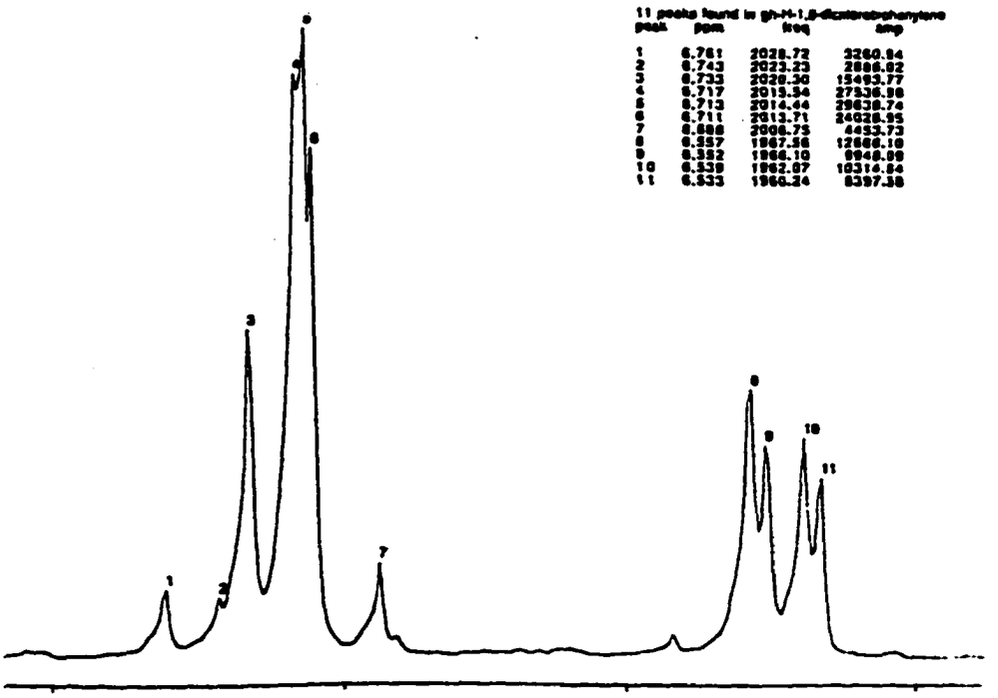
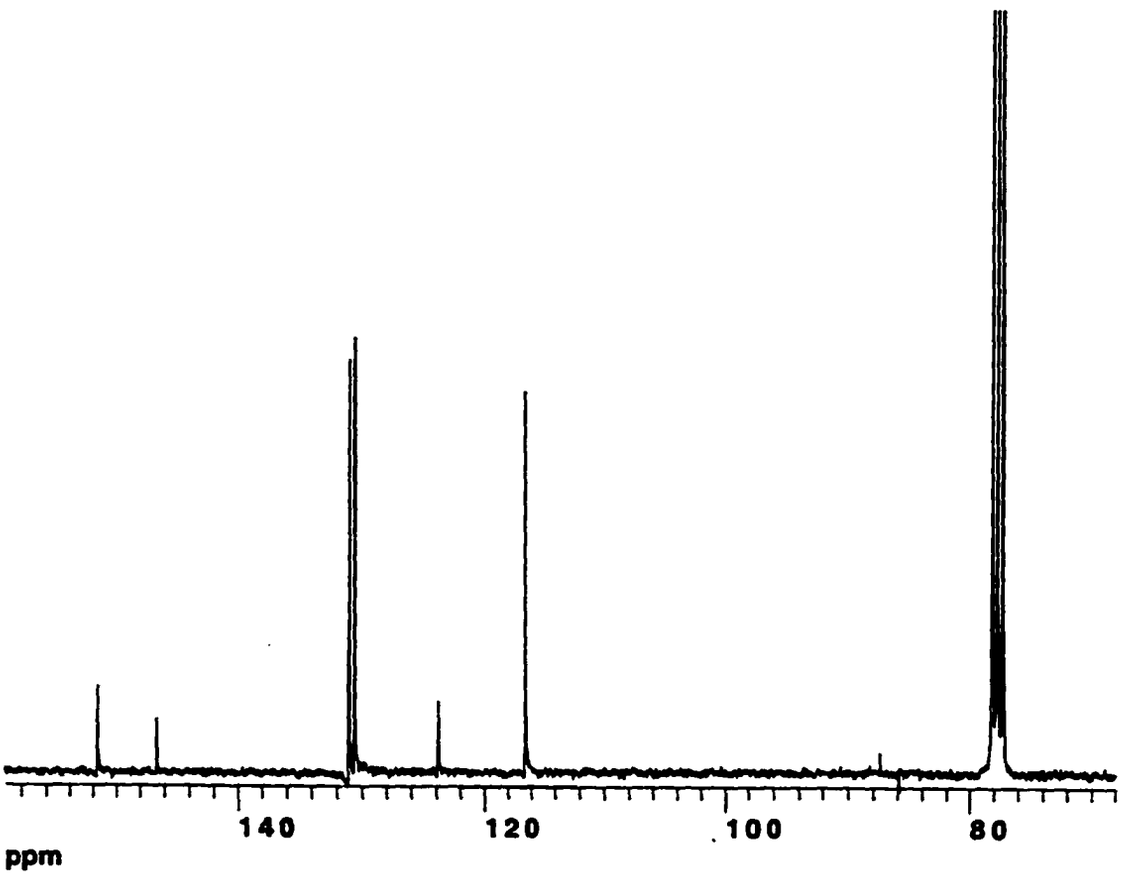


Fig.33: ^{1}H NMR of 1,8-dichlorobiphenylene

Fig.34: ^{13}C NMR of 1,8-dichlorobiphenylene



2.3.2.7. Synthesis of 2,7-dichlorobiphenylene

The procedure could therefore be generalized, at least in the chloro series, to prepare the para substituted 2,7-dichlorobiphenylene **212** according to the scheme below.

***Scheme 39**: Synthesis of 2,7-dichlorobiphenylene **212** by FVP*

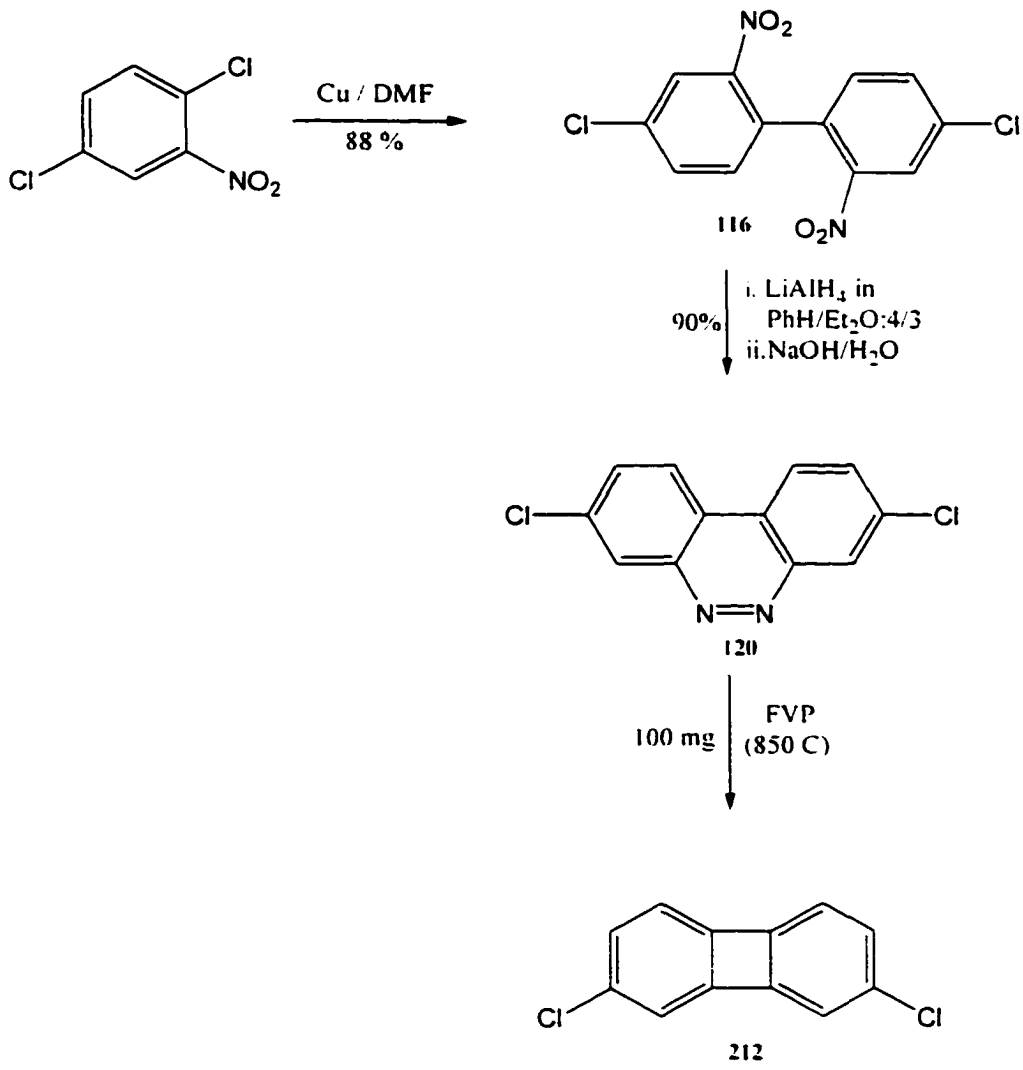


Fig.35: ^{1}H NMR of 2,7-dichlorobiphenylene

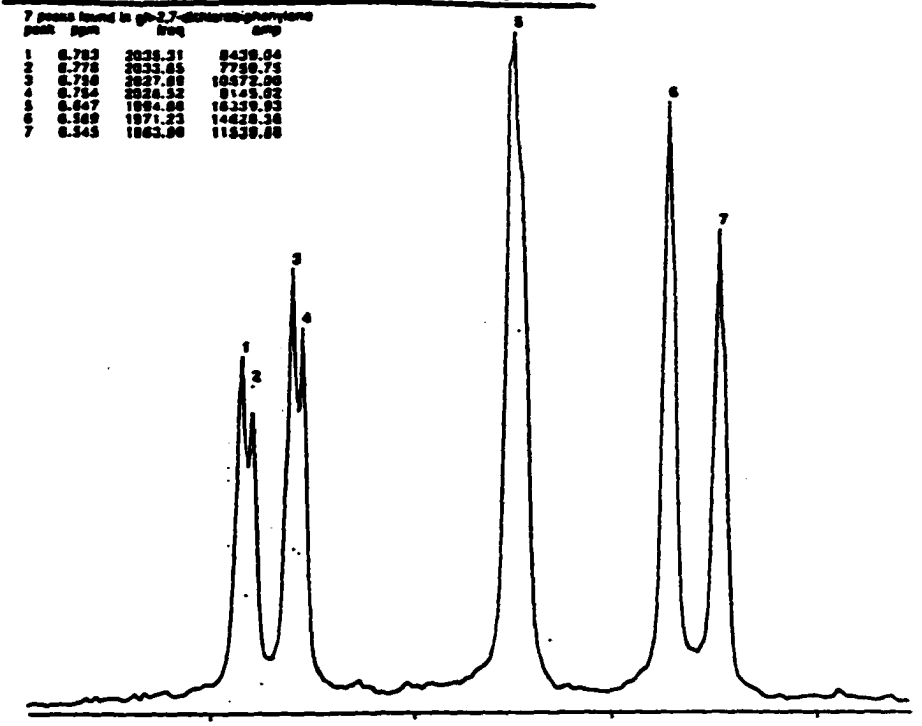
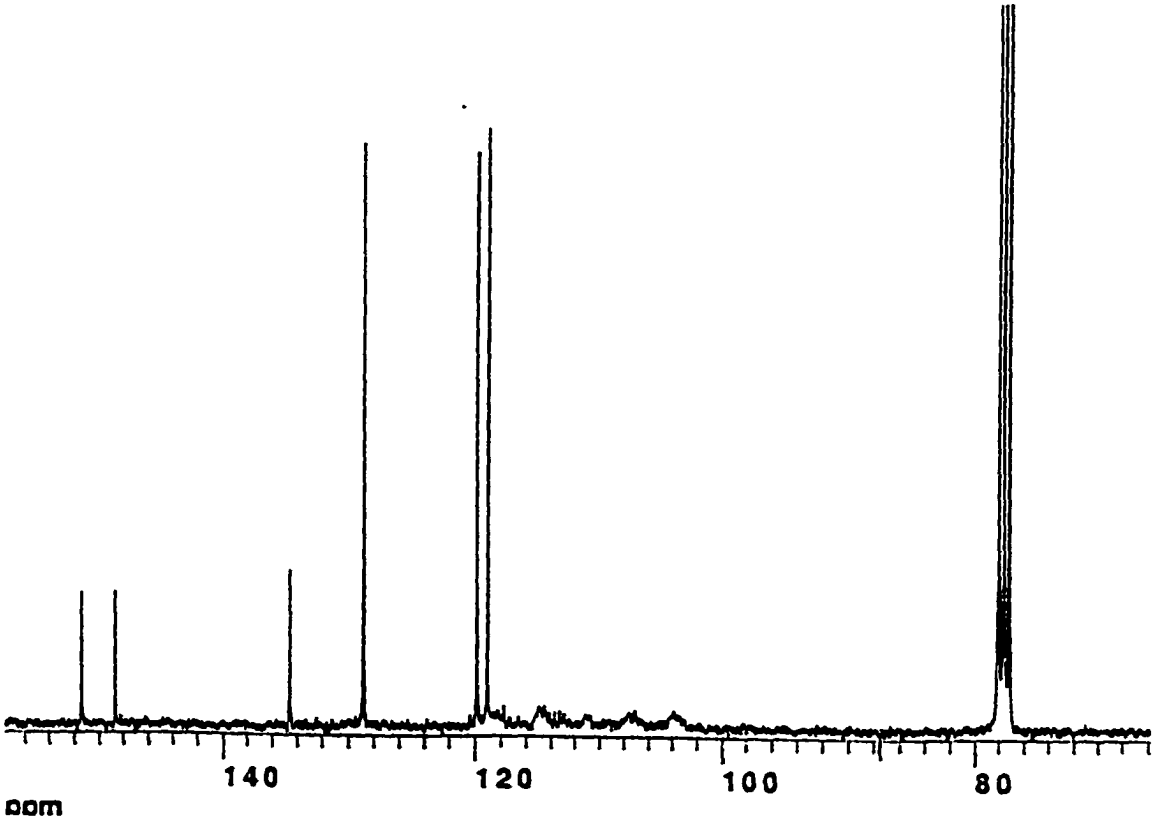


Fig.36: ^{13}C NMR of 2,7-dichlorobiphenylene

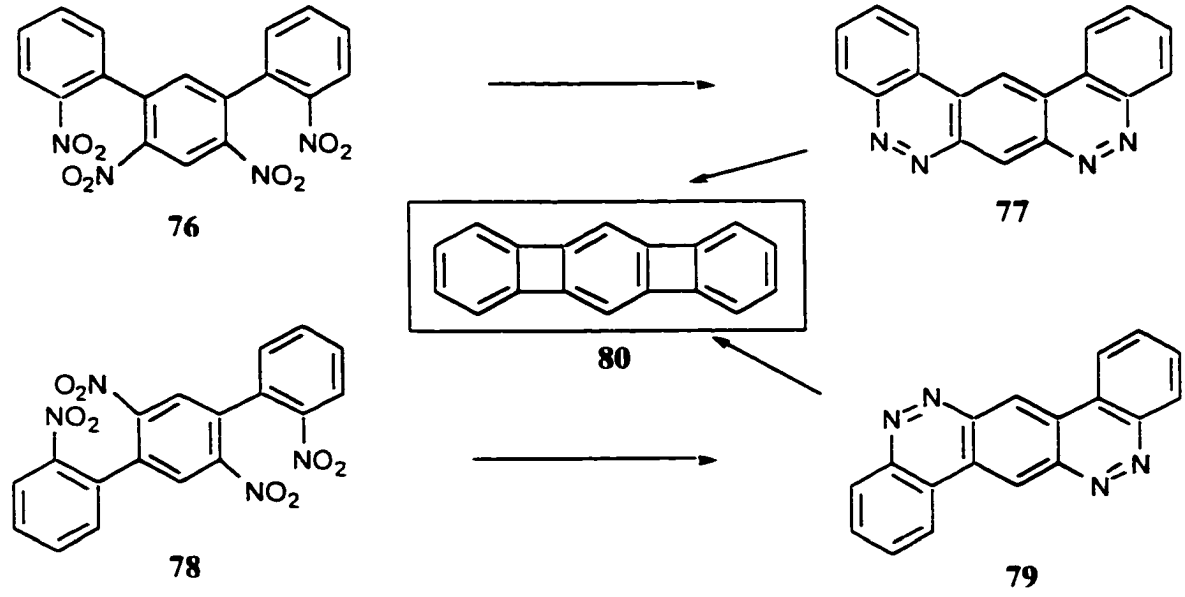


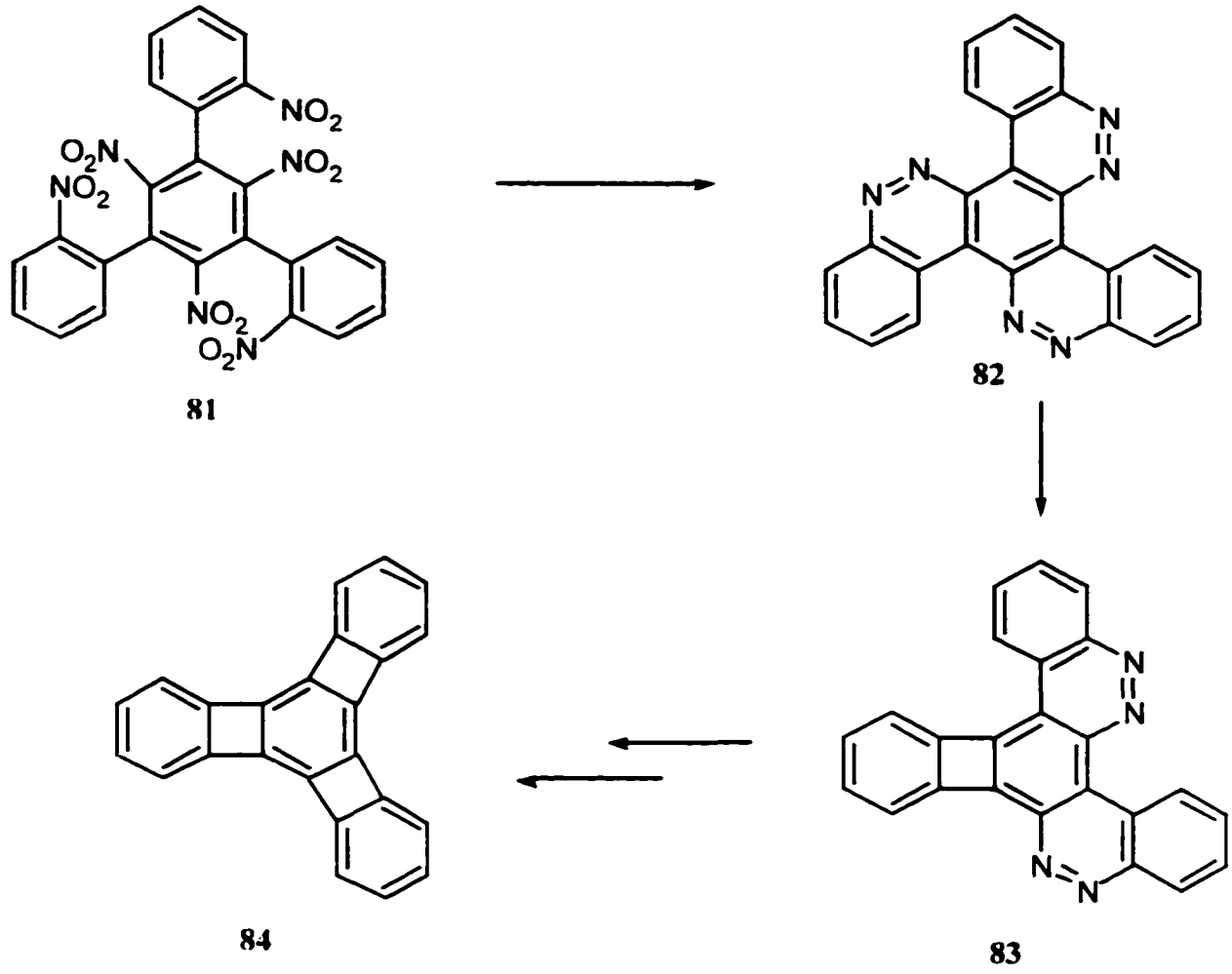
2.3.2.8. Other Applications of FVP Method

The FVP method was successfully[145,146] applied to benzo[*c*]-di and tri-cinnoline to synthesize angular (e.g. **84**) and linear [N]phenylenes (such as **80**) and biphenyleno[2,1-a]biphenylene prior to the Vollhardt cyclization[147] which gives much better yields for the syntheses of [N]phenylenes.

Barton et al.[148] was able to synthesize a number of benzocyclobutabiphenylenes from benzodicinnolines (linear sesquibiphenylene) and benzotricinnolines (angular sesquibiphenylene).

Scheme 40: *Synthesis of linear [3]phenylene* ***80*** *by FVP*



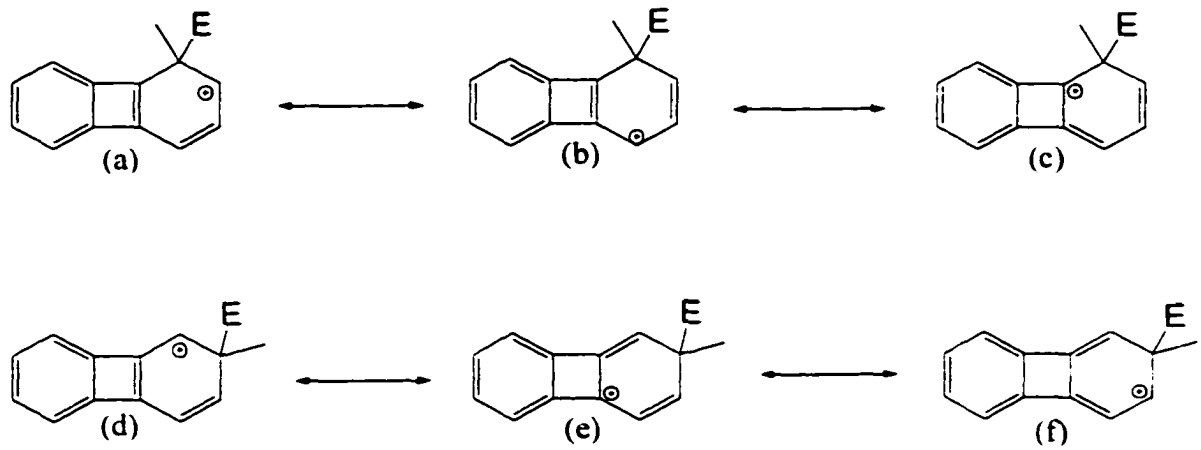


Scheme 41: *FVP route to the synthesis of angular [4]phenylene* ***84***

2.3.3. Electrophilic Substitution of Biphenylene–Syntheses of 2,6 and 2,7- dibromobiphenylenes

Electrophilic substitution of biphenylene occurs exclusively at the β- (or 2-) position of biphenylene **8**. The direct introduction of substituents to an α- (or 1-) position in **8** is difficult even when all the β–sites are blocked. The relative rate of tritiation of biphenylene at the 2- to the 1-position, k_2/k_1, has been determined, by Streitweiser and Schwager, as 64 in a mixture of trifluoroacetic acid and perchloric acid.[149] The reluctance of the α–protons to exchange under acidic conditions has been utilised in the preparation 2,3,6,7-D_4-biphenylene; complete deuteratation is not competitive with decomposition (the synthesis of the 1,4,5,8-D_4-isomer can be accomplished using calcium deuteroxide, by virtue of the higher acidity of the α–hydrogens). According to Finnegan[150] and Streitweiser,[151] the strain inherent in biphenylene leads to a rehybridization of the bridgehead carbons, such that orbitals of high 'p' character are utilized in the bonding to the small ring. The α–carbons are thus bound by an orbital of higher 's' character and are subjected to a deactivating inductive effect. This would be less marked at the more distant β-position, and so in biphenylene the 1-position shows lower reactivity towards electrophiles than the 2-position. The argument advanced by Vaughan[152] and Taylor[153] to explain the reduced

electrophilic reagents towards aryl positions adjacent to a strained fused ring relies on comparison of the relative strain in the wheland intermediates for α– and β-substitution. The principal canonical forms for each are illustrated below. (a) and (b) should be less favorable energetically than that for β-substitution, which has only one (d).



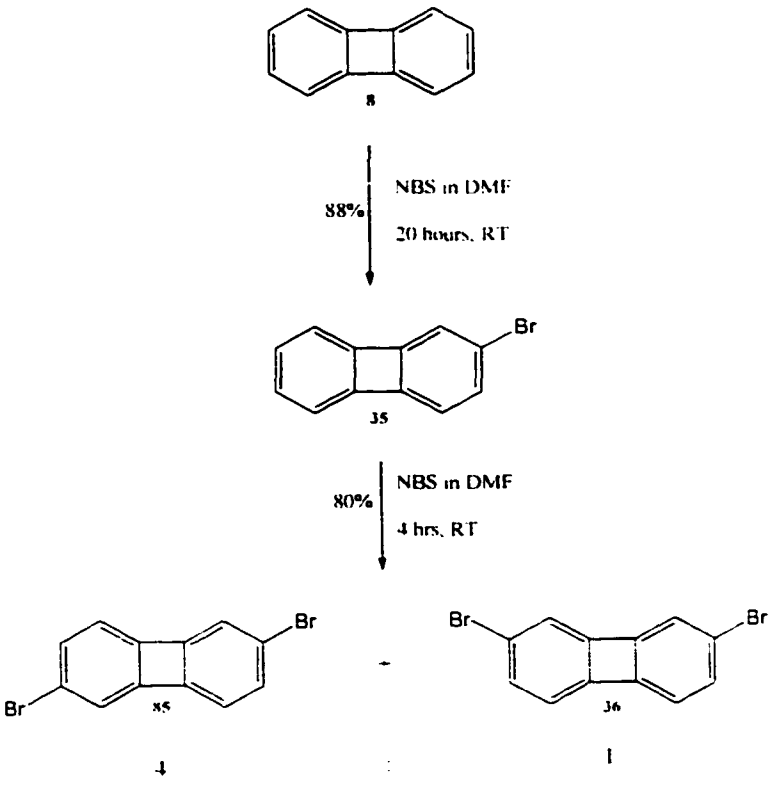
***Scheme 42**: Wheland intermediates for α– (top) and β– (bottom) substitution*

Cava and Mitchell[154] have drawn attention to the fact that – substitution should also be preferred on the grounds that these contributors are cyclobutadienoid species and would therefore be of higher energy than the resonance forms containing double bonds exocyclic to the four-membered ring.

2.3.3.1. Substitution of Substituted Biphenylene

Deactivated monosubstituted biphenylenes undergo substitution in the unsubstituted ring provided that substitution occurs at the β–carbon of highest electron density. Therefore the 2-halobiphenylenes should favor attack at the 7-position over the 6-position. In practice, *N*-bromosuccinimide bromination of 2-bromobiphenylene in dimethylformamide was less specific and gave a mixture of the 2,6- and 2,7-dibromides in a 4 to 1 ratio respectively (*scheme 43*, see below).

Scheme43:*Synthesis of 2,6+ 2,7-biphenylenes by substitution of biphenylene*



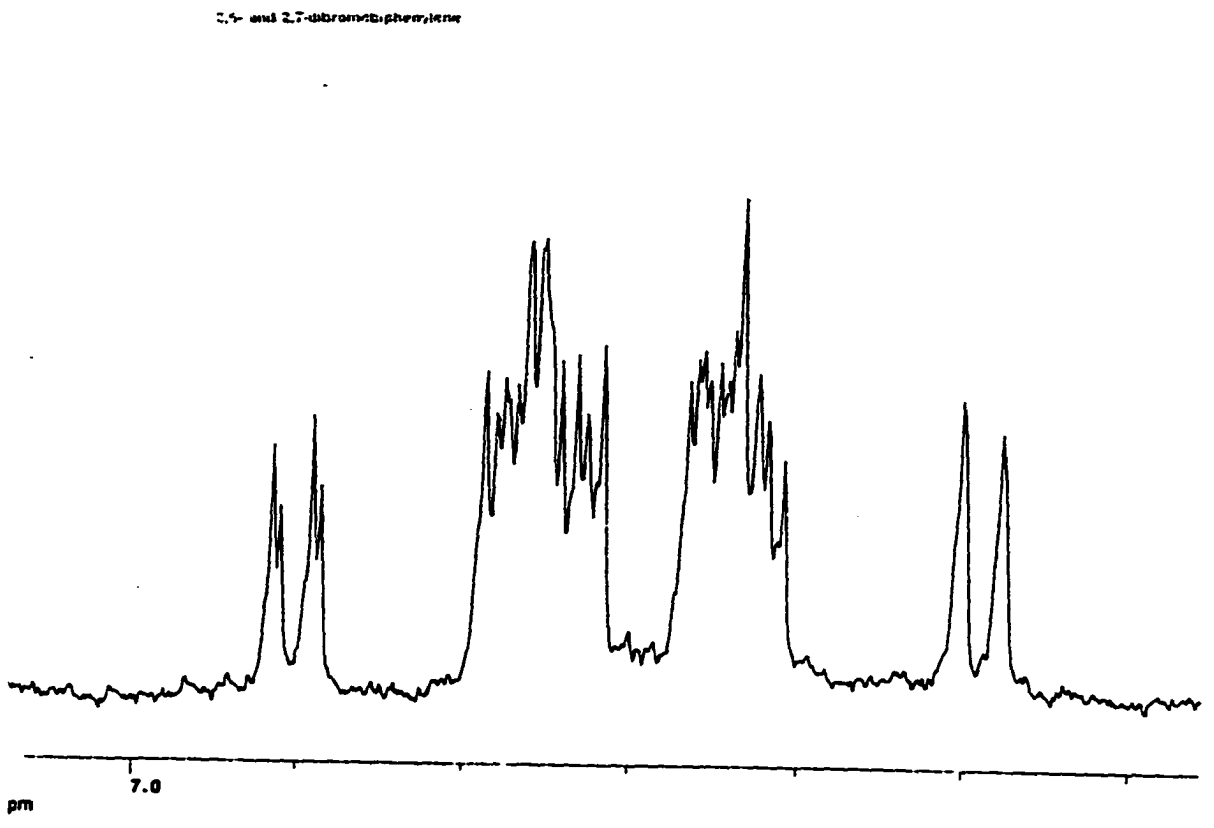
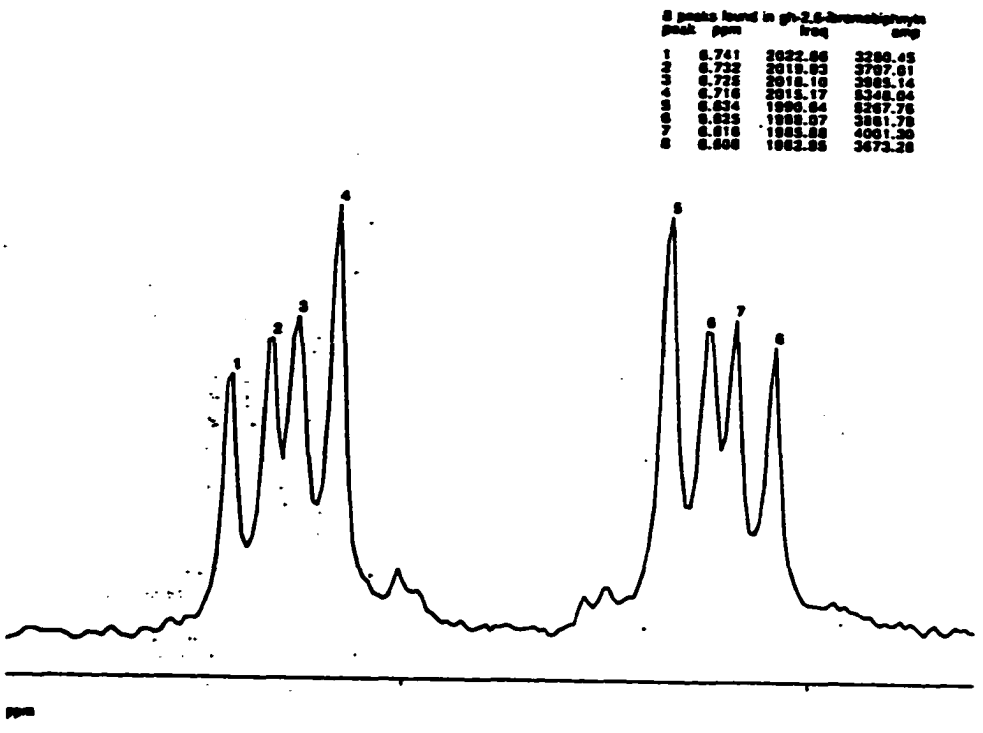


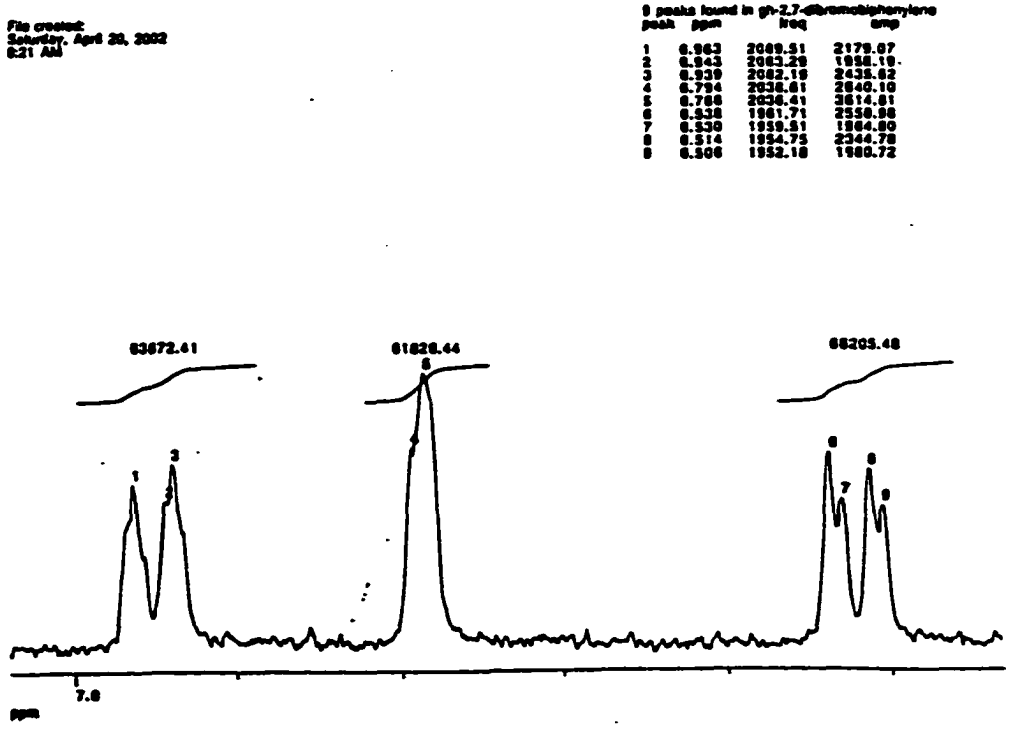
Fig.37: ^{1}H NMR of 2,6- and 2,7-dibromobiphenylene

2-Bromobiphenylene **35** can be obtained in high yield (ca. 90 %) from the reaction of biphenylene **8** with (a) bromine in the presence of thallium triacetate or (b) N-bromosuccinimide in dimethylformamide. Further bromination under the second set of conditions gave a mixture of 2,6-dibromobiphenylene **85** and 2,7-dibromobiphenylenes **36** (Fig.37) from which the 2,7-isomer was purified by fractional crystallisation (Fig.38).

Fig.38: H NMR (zoom) of



2,6-dibromobiphenylene (above) and 2,7-dibromobiphenylene (below)



2.3.4. Synthesis of 1,8-dihalobiphenylenes

Substitution at α-position being difficult, 1,8-dibromobiphenylene could not be accessed by the direct substitution method described above. It has been known for half a century that biphenylene can be generated in moderate yield by the oxidative coupling of biphenylyl-2,2'-dimagnesium dibromide with cupric chloride (the Krizewsky-Turner reaction). When the biaryl is tetrasubstituted at ortho positions, the biphenylene obtained will bear substituents in position 1 and 8. In 1996, Rajca used cuprate oxidation[155] to prepare 1,8-dibromobiphenylene and 1,8-dibromo-3,6-di-*tert*-butylbiphenylene by oxidizing the respective cuprate salts from 2,2',6,6'-tetrabromobiphenyl and 2,2',6,6'-tetrabromo-4,4'-di-*tert*-butylbiphenyl with oxygen at low temperature.

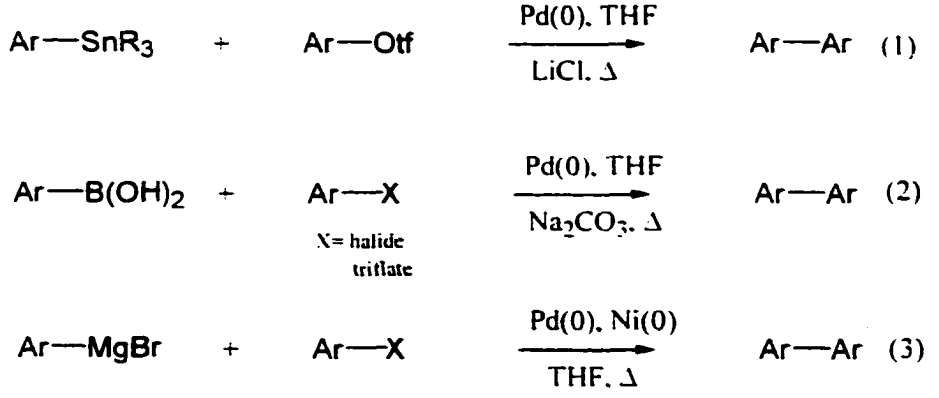
2.3.4.1. Synthesis of Disubstituted Biphenylene by Intramolecular Coupling of Biaryls with Higher Order (H.O.) Cyanocuprates

The biaryl nucleus is one of the more interesting substructures of many naturally occurring compounds.[156] Its formation as part of a sequence of steps oftentimes represents the key transformation in the series and can ultimately determine the levels of success associated with much synthetic effort. Biaryls also play an important role in many other areas of endeavor,

including their uses as nonracemic catalysts (e.g., Noyori's, 2,2'-binaphthols and BINAP), as bidentate ligands (e.g. bipyridils) and as precursors to conducting polymers (e.g. polythiophenes). Therefore methodologies leading to controlled bond formation in biaryls are highly valued.[157]

Literature routes commonly in use, which effectively address in a general way the more challenging goal of unsymmetrical biaryl C-C bond construction tend to rely on organometallic chemistry. Notable among these are (1) Stille couplings[158] based on reactions between aryl halides and aryl stannanes, which proceed via an arylpalladium intermediate; (2) Suzuki couplings[159] which involve the same aryl halides but utilize arylboronic acids in the presence of catalytic Pd(0), and the routes[160] based on aromatic nucleophilic substitution by an aryl Grignard often leading to sterically congested systems (atropisomerism as observed in the tetrasubstituted biphenyls).

Scheme 44: *Some modern organometallic based coupling reactions*



The feature shared by all of these contributions is that in order to arrive at cross-coupled products from intermolecular reactions it is essential that the two aromatic compounds used are functionally or electronically very different. Electron-rich compounds must be allowed to react with electron-poor partners in order to shift the normally statistical product distribution towards the crossed products.

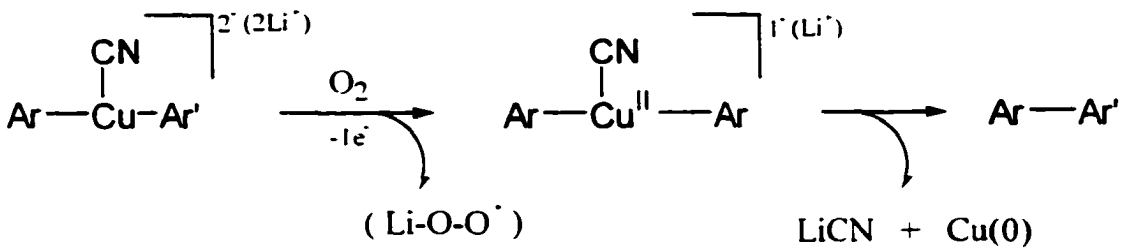
The unique aspect of biaryl synthesis with higher order (H.O.) cyanocuprates is that, both ligands participating in these cuprate-mediated oxidative couplings are introduced as anions, and hence, from two aryllithium species comes one C-C bond.

Cuprate oxidations have been utilized in the past for various reasons and many reviews have appeared on the subjects.[161-164] It was almost always in connection to intermolecular reactions leading to biaryls. Few examples of an intramolecular application of this coupling reaction were recorded in the literature before the synthesis of disubstituted biphenylene nucleus by a sequence of two symmetrical aryl-aryl coupling steps. Lithium/halogen exchange in the first step allows for the resultant aryllithium to be oxidized with Cu(II). The arylcuprate thus formed collapses to the biaryl. Further lithium/halogen exchange followed by conversion to a higher order cuprate

with CuCN set the stage for an intramolecular C-C bond formation by treating the mixture with an oxidizing reagent.

Mechanistically, the reaction is likely to proceed via a Cu(II) species following electron transfer to oxygen. Reductive coupling of the ligands would afford the biarylene together with LiCN and Cu(0), which is likely to be oxidized as the black CuO which probably, considerably darkens those reaction mixtures.

Scheme 45: *Mechanism of aryl-aryl coupling by H.O. cuprate reagent*

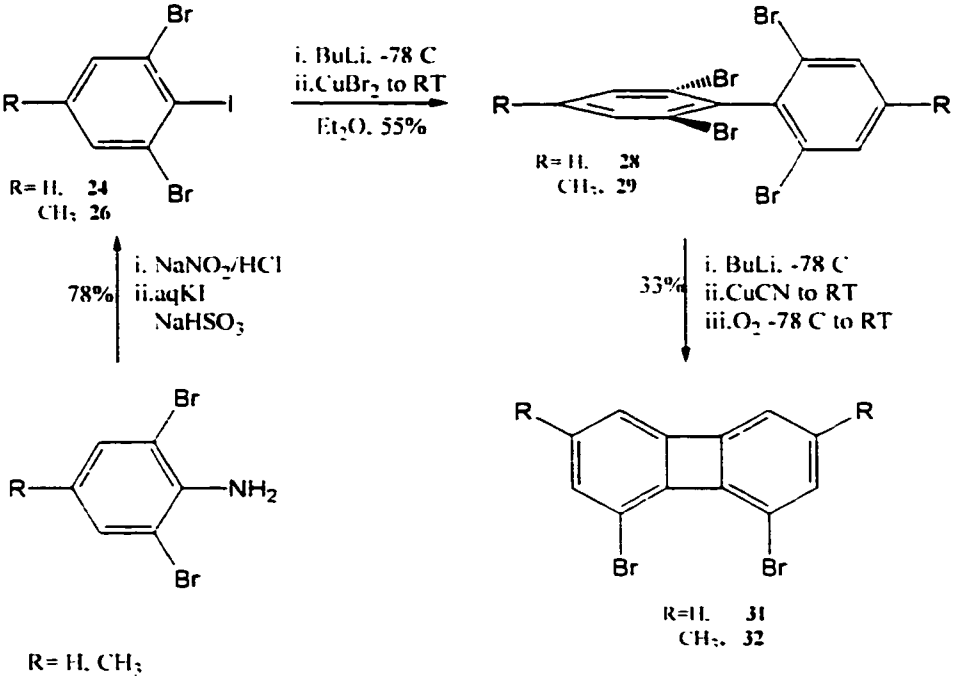


2.3.4.2. Synthesis of 1,8-dibromobiphenylene 31 and 1,8-dibromo-3,6-dimethylbiphenylene 32

Starting from 2,6-dibromoaniline, diazotization in cold hydrochloric acid using sodium nitrite gave the diazonium salt, which was converted to the iodide 24 when it was poured into a cold aqueous solution of potassium iodide. Aryl coupling occurred when the copper salt obtained by lithiation of 2,6-dibromoiodobenzene 24 and treatment with cupric bromide at low

temperature was allowed to warm to room temperature over 12h period. The tetrasubstituted biaryl obtained, namely 2,2',6,6'-tetrabromobiphenyl 28 obtained in 50% yield, was then treated with butyllithium and copper cyanide to generate the higher order cuprate salt which, in contact with oxidizing agents promoted, likely via free radicals, 1,8-dibromobiphenylene 31 and the byproducts inorganic salts. The same procedure was used to prepare 1,8-dibromo-3,6-dimethylbiphenylene with the exception that, here, the starting material was p-toluidine. Bromination of p-toluidine in acetic acid provided the 2,6-dibromo-p-toluidine 26.

Scheme 46: *Syntheses of 1,8-dibromobiphenylene* ***31*** *and its analog* ***32***



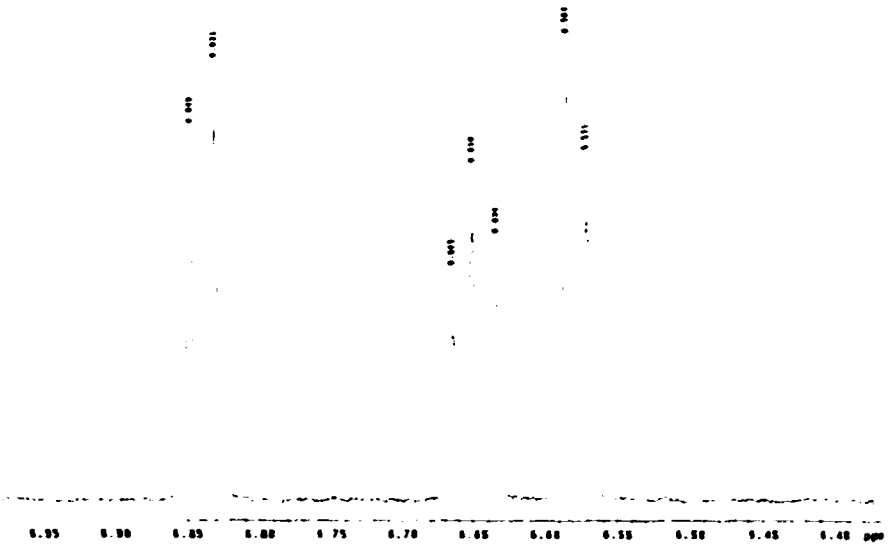


Fig.39: ^{1}H NMR of 1,8-dibromobiphenylene (top: aromatic H's only)

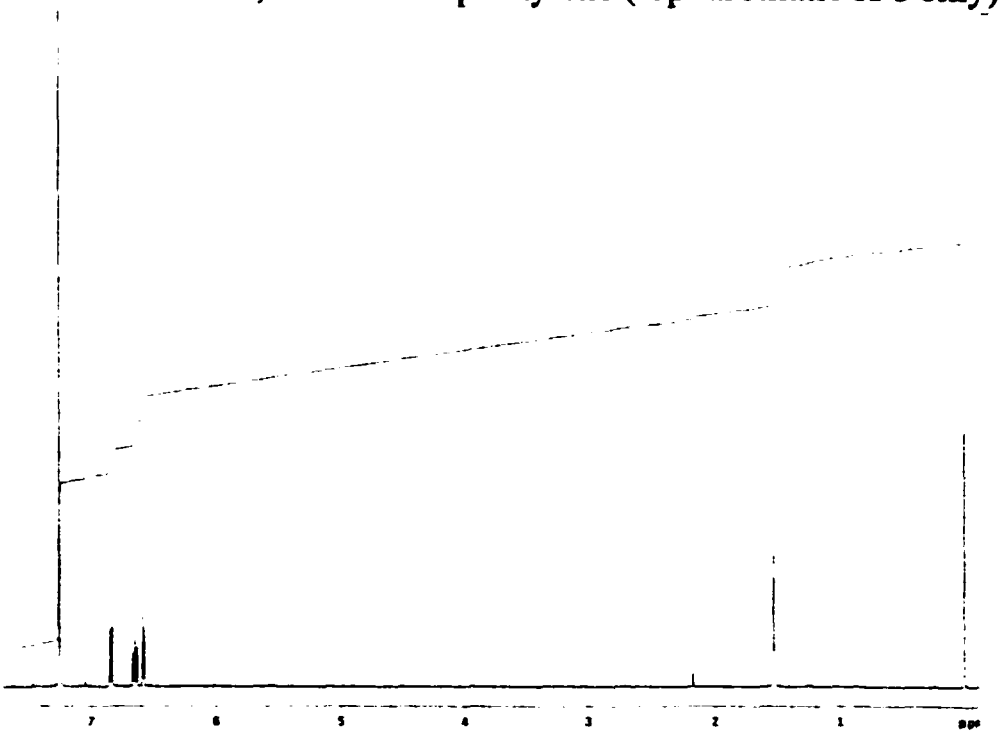
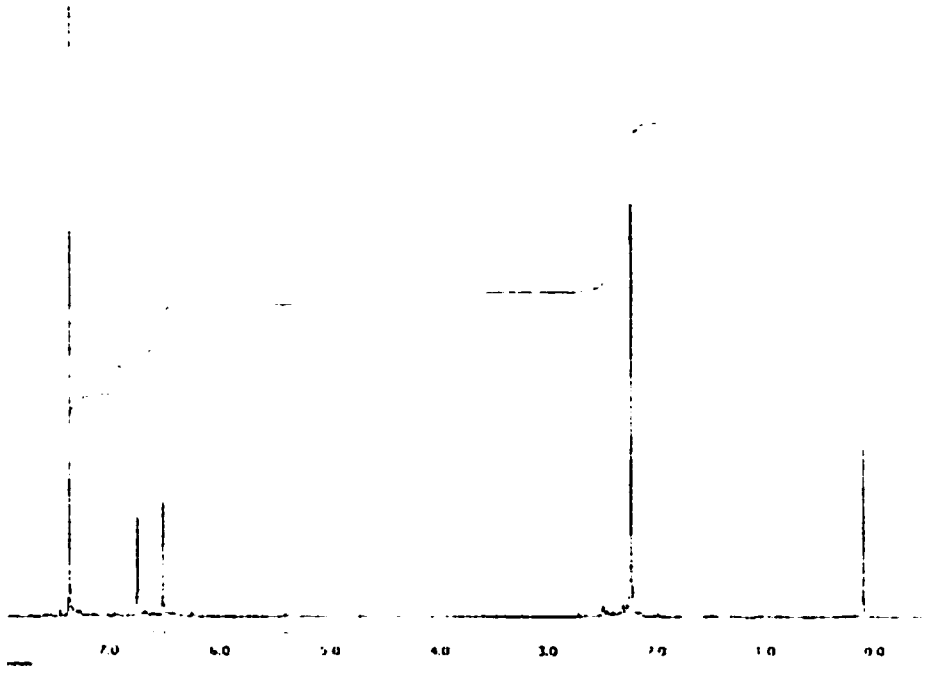


Fig.40: ^{1}H NMR of 1,8-dibromo-3,6-dimethylbiphenylene



2.3.5. Miscellaneous Approaches:

2.3.5.1. Extrusion of Carbon Monoxide: Vacuum Thermolysis and Plasmolysis

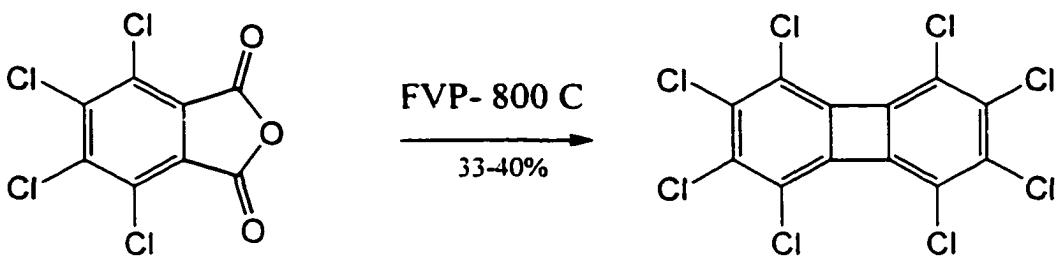
While only traces of biphenylene are formed on flash vacuum thermolysis of fluorenone, the yield becomes essentially quantitative on decomposition of fluorenone in a low energy glow discharge, as suggested by the mass spectrum of the compound showing a strong peak for the (M+ - CO) fragment corresponding to biphenylene.

Likewise, the mass spectra of 9,10 anthraquinone and 9,10-phenanthroquinone gave indication of sequential loss of two molecules of carbon monoxide and therefore of biphenylene formation, as confirmed by plasmolysis of both compounds. Similarly, biphenylene is obtained from plasma decomposition of anthrone and benzophenone with a probable intermediate formation of fluorenone, isolated as a biproduct.

2.3.5.2. Gas-Phase Thermolytic Generation of arynes

Under vacuum or an inert atmosphere the only decomposition pathways available to benzyne should be via dimerisation to biphenylene and by trimerisation to triphenylene should the aryne encounter frequency be

high enough. Biphenylene was isolated in 54% yied by the flash detonation of 1,2,3-benzothiadiazole-1,1-dioxide and in lower yield by flash photolysis of benzenediazonium-2-carboxylate or phthalic anhydride. For example,[165] pyrolysis at 800 °C of tetrachlorophthalic anhydride **99**, gives the expected octachlorobiphenylene (32%) **100**. This route has been widely used for co-pyrolysis of mixture to prepare crossed aryne dimers and heterocyclic biphenylenes.



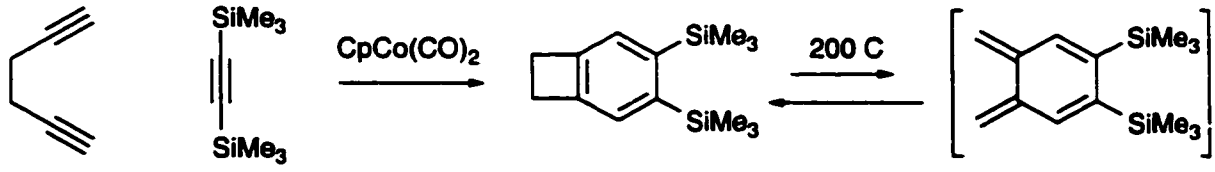
99 **100**

Scheme 47: *Synthesis of substituted biphenylene by FVP of phthalic anhydride*

2.3.5.3. Alkyne Cyclotrimerization: The Vollhardt Cyclisation and Related Reactions

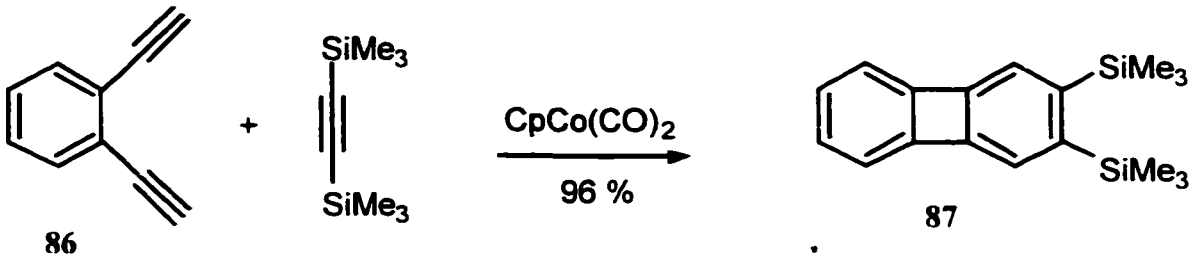
In 1866, Berthelot[166] reported that benzene can be formed by the cyclotrimerization of acetylene at ca. 400 °C. In 1975, Vollhardt[167] reported the important observation that a catalytic amount of

η^5 cyclopentadienylcobalt dicarbonyl, $CpCo(CO)_2$ can effect a cyclotrimerization reaction between 1,5-hexadiyne and bis(trimethylsilyl)acetylene (BTMSA) to give 4,5-bis(trimethylsilyl)benzocyclobutene (> 60% yield) , the benzocyclobutene being interesting in that upon heating it converts onto ortho-quinodimethane. The latter species is highly reactive and participates in facile [4+2] cycloaddition reactions with a wide variety of dienophiles.



Scheme 48: *Cyclotrimerisation of 1,5-hexadiyne and protected acetylene*

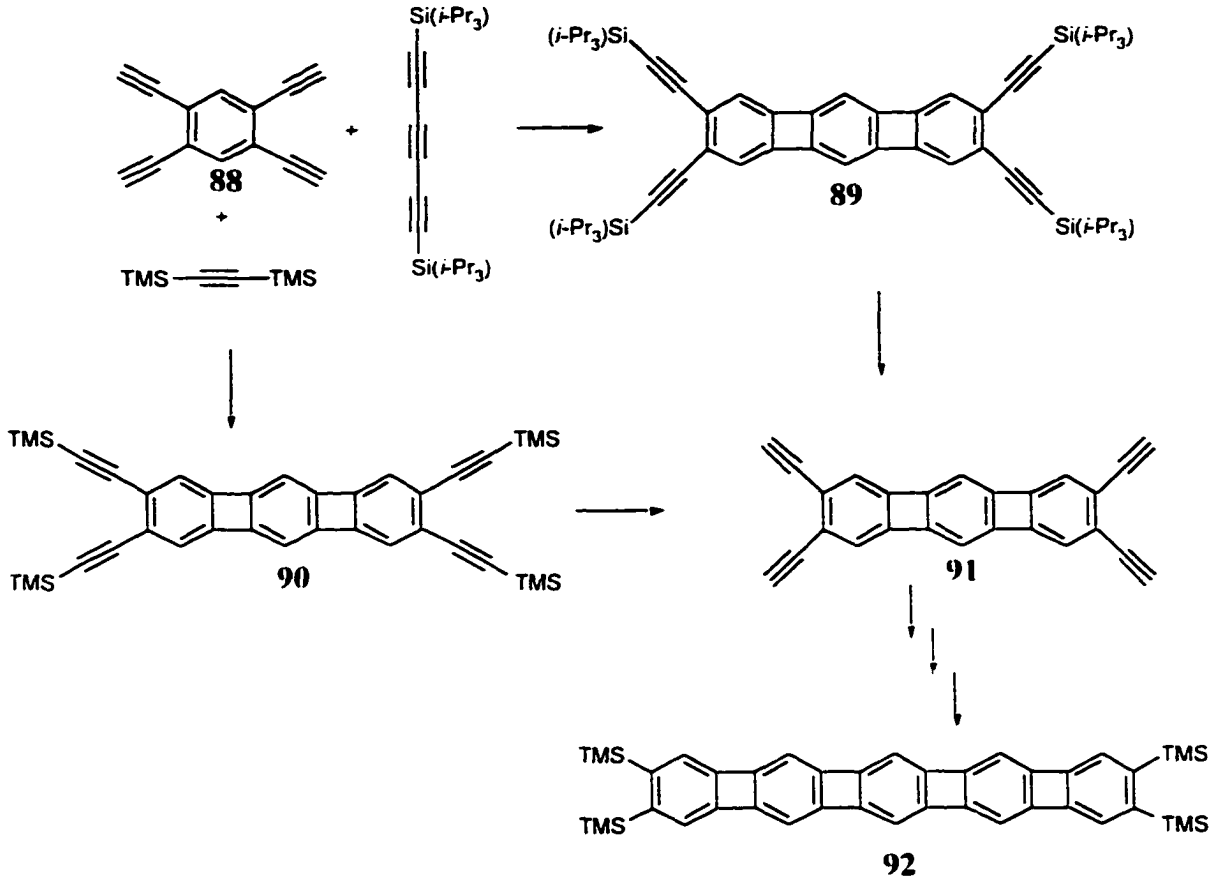
This method was quickly extended to different substrates, including 1,2-diethynylbenzene, resulting in the near quantitative formation of 2,3-bis(trimethylsilylethynyl)-biphenylenes.



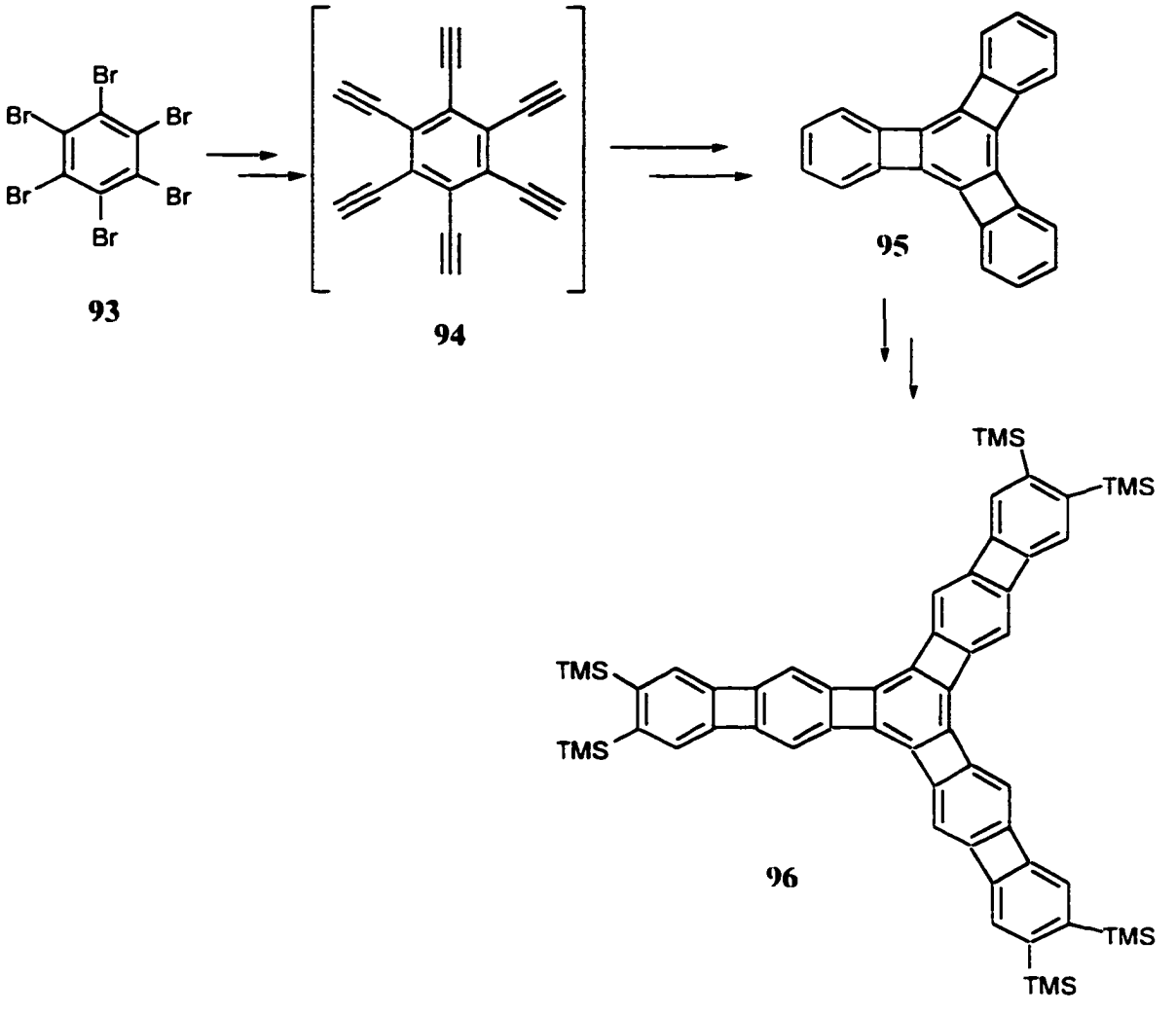
86 87

Scheme 49: *Synthesis of biphenylene derivative* ***87*** *by cyclotrimerisation of o-diethynylbenzene* ***86*** *and bistrimethylsilylacetylene*

The 'crossed' [2+2+2] cyclotrimerisation between 1,2-diethynylbenzene **86** and substituted acetylenes, gives 2,3-disustituted biphenylenes **87** in moderate to high yield. Application of the method to the syntheses of extended phenylenes, both linear and angular has led to the preparations of compounds **89-92** and **95-96** respectively.



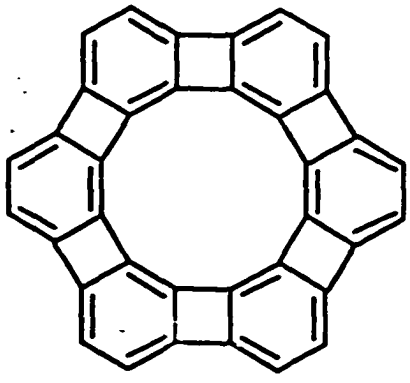
Scheme 50: *Syntheses of linear [N]phenylenes by cyclotrimerisation reactions*



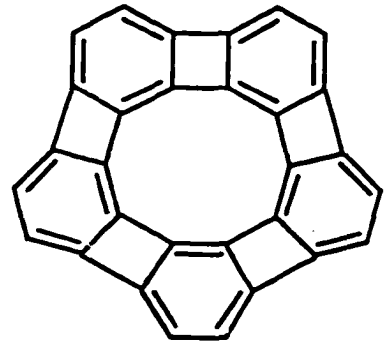
Scheme 51: *Route to angular [7]phenylenes by cyclotrimerisation reactions*

This reaction has not yet reached its limits with the preparation of the angular [5]phenylene among others and [6]phenylene (antikekulene) **97** being the next on line and the putative cyc[5]phenylene **98** which is bowl-shaped and constitutes the cap of a novel carbon cluster, C_{120} dubbed

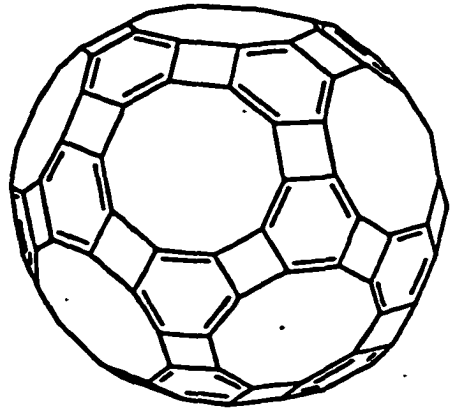
archimedene (see Fig.41), made of 30 four-membered rings, 20 six-membered rings and 12 ten-membered rings.



97



98



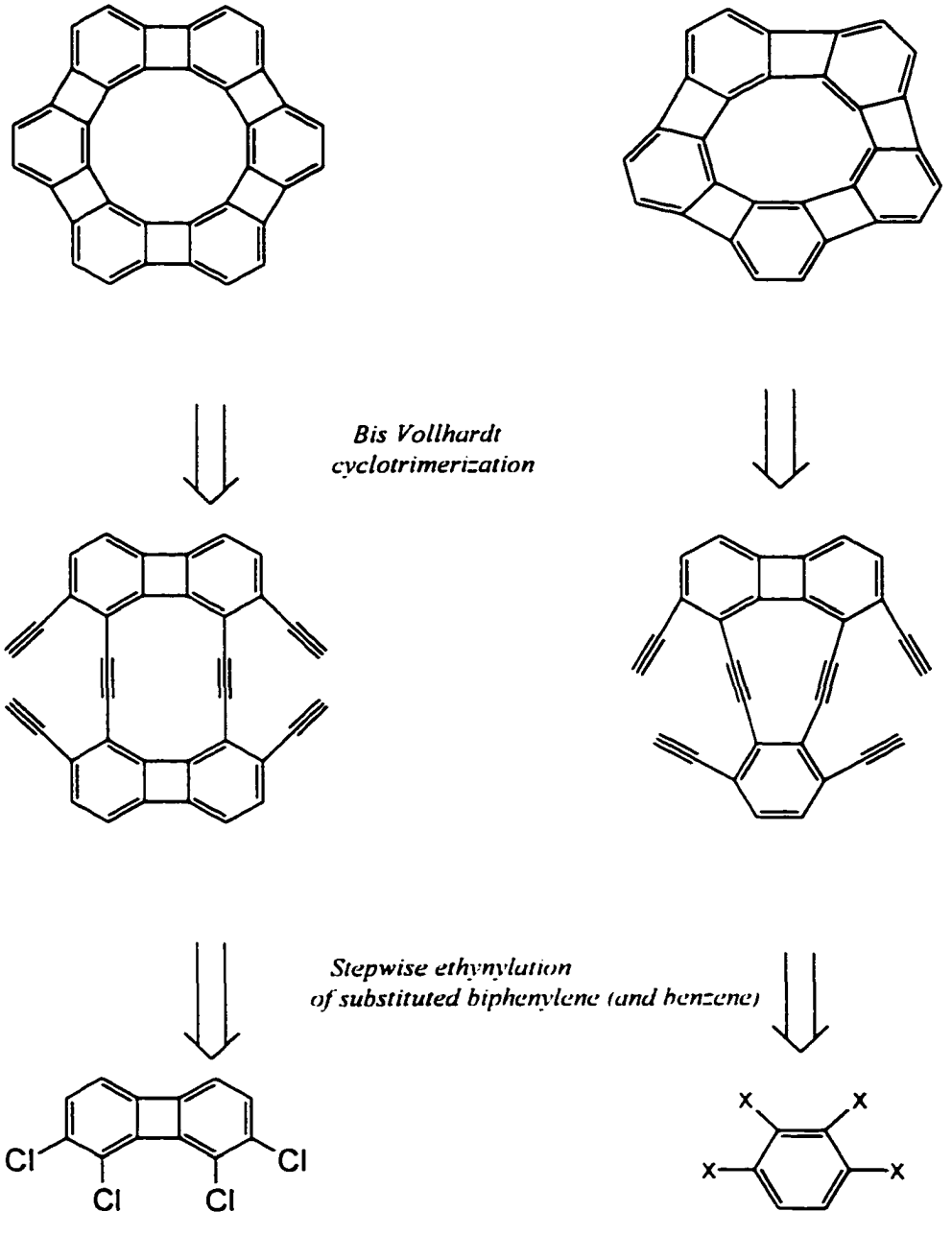
Scheme 52: Cyclic [5] 98 and [6]phenylenes 97 (top) and (bottom) archimedene (bottom)

2.3.5.4. Looking Ahead

Accessibility to the cyclic [N]phenylenes is looming in the near horizon. A possible entry to these exciting molecules can be provided by the chemistry that we have developed (chapter three) coupled with Vollhardt cyclotrimerization reaction. In the following schemes, we propose a retrosynthetic plan for the syntheses of [N]phenylenes with N= 5 and 6.

Tetrasubstituted biphenylene have been synthesized by flash vacuum thermolysis of substituted phthalic anhydride and tetrasubstituted benzene are commercially available. With, either the Sonogashira or the Grignard acetylide coupling reaction, ethynyl moeities are anchored to the arenes. The rigidity of the biphenylenic system would promote, as would be demonstrated in the next chapter, alkyne-alkyne oxidative coupling. The resulting cyclic 'biphenyleneyne' unit would have the exo-acetylenes just in place for a double Vollhardt-type cyclotrimerization to afford antikekulene. The intermediate compound leading to cyc[5]phenylene might be more difficult to access because of the angle strain imposed in coupling biphenylene and benzene. Wilcox obtained an analogous compound by a double Wittig reaction and bromination-dehydrobromination of the divinyl cyclic intermediate. Provided this could be repeated with adequately

functionalized biphenylene and benzene, cyc[5]phenylene could be prepared as outlined in scheme 53 below.



Scheme 53: *Proposed retrosynthetic routes to [5] -and [6]phenylenes*

Summary:

Syntheses of biphenylene and its alkyl and halo-derivatives can be achieved by several methods as reviewed in this chapter. Among these, nitrogen extrusion procedure by the Flash Vacuum Pyrolysis (FVP) of benzo[*c*]cinnoline and its derivatives is preferred for synthesis of desired isomers of methyl and chloro-disubstituted biphenylenes. In the next chapter, we will describe the synthesis and characterization of 1,8-diethynyl biphenylene and investigate some reactions of annulation of this novel diacetylene. The synthesis and characterization of "biphenylenediyne" will be described.

CHAPTER THREE

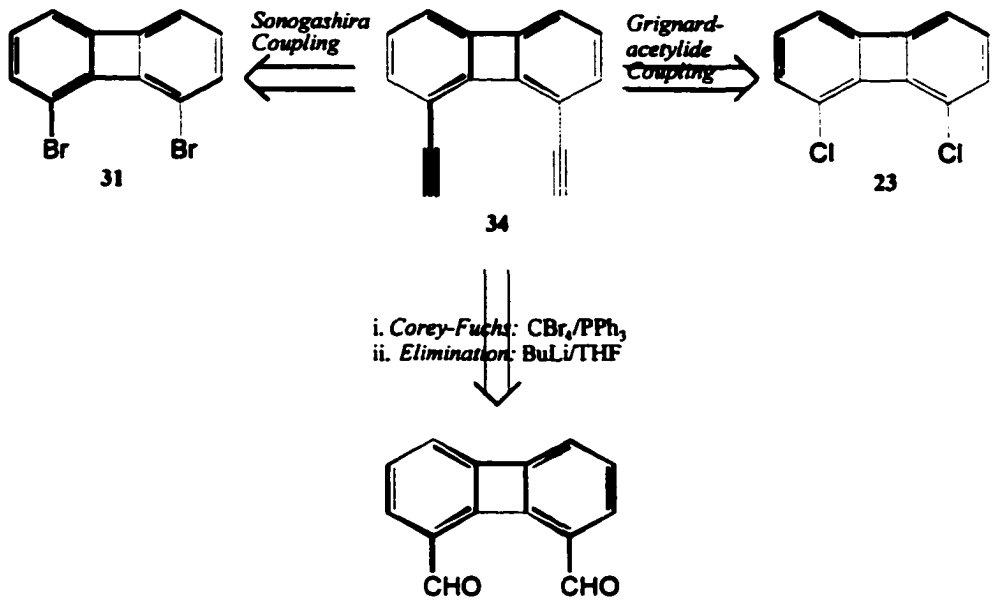
3.0. SYNTHESES AND INVESTIGATION OF BIPHENYLENE ANNELATED STRUCTURES

3.1. The Acetylene Building Block

Rigid acetylenic frameworks are being used with increasing frequency for the fabrication of molecular nanostructures exhibiting interesting non-linear optical properties and can also function as molecular wires.[169] A common feature in the efforts directed towards the preparation of carbon-rich systems is the use of the C-C triple bond as a functional group and linking unit.

The alkyne group, through one of its most important reactions, *the oxidative dimerization of terminal alkynes*, can be elongated to polyacetylenes which can polymerize to conjugated polyenepolyynes which are interesting in connection with organic conducting materials as well as possible precursors for C_{60} and other fullerenes.[170] Furthermore, the extensive development of palladium-catalyzed cross-coupling reactions[171] using alkynes allows easy access to key intermediates.

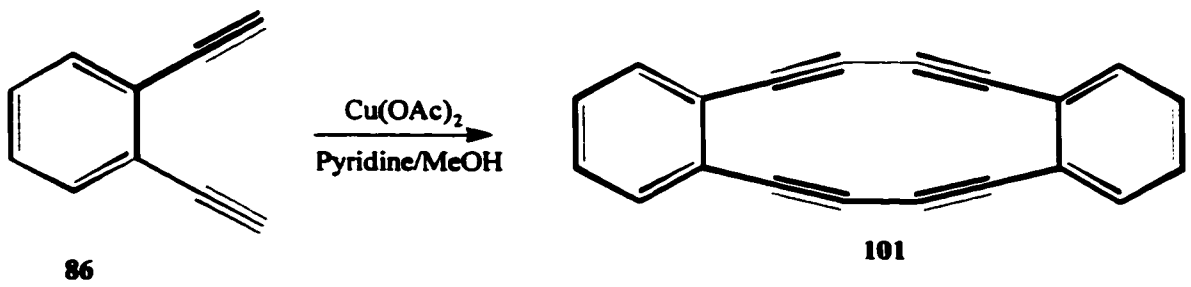
3.1.1. RETROSYNTHETIC APPROACH TO ETHYNYL ANNULATED BIPHENYLENES



Scheme 54: *Retrosynthetic routes to 1,8-diethynylbiphenylene 34*

1,8-Diethynylbiphenylene **34** can be prepared by either the coupling reaction of 1,8-dibromobiphenylene with trimethylsilylacetylene (*the Sonogashira reaction*), the coupling reaction of 1,8-dichlorobiphenylene with trimethylsilylacetylene magnesium bromide or by the reaction between 1,8-biphenylene dicarboxaldehyde and carbon tetrabromide in the presence of triphenylphosphine (*the Corey-Fuchs reaction*[172]) followed by

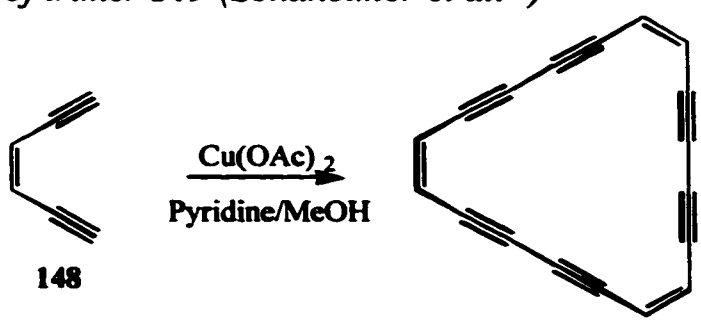
dehydrobromination. The resulting 1,8-diethynylbiphenylene, then, undergoes oxidative coupling under the conditions of Eglinton to afford the cyclic tetrayne dimer **215**. By oxidative coupling of 1,8-diethynylanthracene **213**, Nakagawa and coworkers obtained the corresponding dimeric tetrayne **216** in very high yield (see scheme 69). At about the same time, Eglinton and coworkers, applying the same method, in high dilution, to *o*-diethynylbenzene **86**, were able to synthesize the highly strained dimeric tetrayne **101** as the sole product.



86 **101**

Scheme 55:** Eglinton's coupling of o-diethynylbenzene **86

The product of the reaction is not always a dimer. Sondheimer and Okamura prepared the trimer **149** by the oxidative coupling of the enediyne **148**. ***Scheme 56:** Synthesis of trimer **149** (Sondheimer et al.[48])*



148 **149**

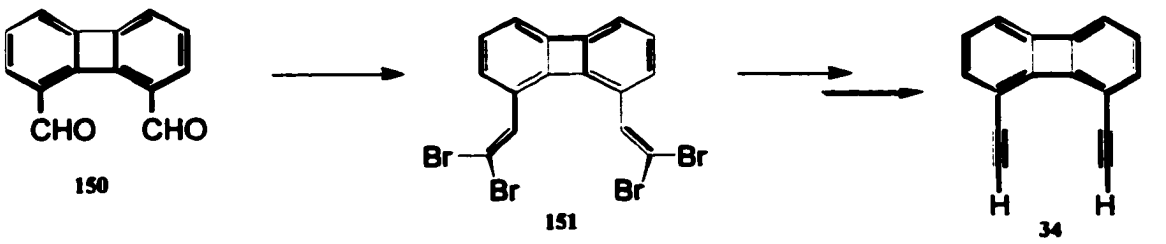
Grohmann and Benshafrut applied the same method in their synthesis of the trimeric compound **102** (see Fig.14).[173] The rigidity of the starting diethynyl substrates has been invoked for the efficiency of the dimerization as opposed to trimerization. We therefore suspected the highly rigid, novel 1,8-diethynylbiphenylene **34** to undergo an Eglinton-type oxidative coupling to afford the dimeric tetrayne **215** which is a precursor to an all-carbon net, a novel carbon allotrope with anticipated optical, material, electronic and magnetic properties.[174]

3.1.2. Methods of Preparation of 1,8-diethynylbiphenylene 34

The diethynylbiphenylenyl unit combines two rigid spacers: biphenylene and acetylene. Incorporation of ethynyl moeity to arenes can be done by the Sonogashira modification[175] of the Heck reaction[176] to acetylenes or, when the halogen in the arene is chlorine, a nickel(0)-catalyzed grignard-acetylide coupling reaction. We used both methods in our synthesis of the title-compound and its anthracene analog **213**.

Besides these coupling methods, the ethynyl moiety can be elaborated by the condensation of 1,8-biphenylene-dicarboxaldehyde **150** and carbon tetrabromide in the presence of triphenylphosphine followed by elimination of two moles of hydrobromic acid from the tetrabromide intermediate **151**

and solvolysis of the lithium diacetylide to give 1,8-diethynylbiphenylene **34** (scheme 57).



***Scheme 57:** Possible route **34** to/from 1,8-biphenylenedicarboxaldehyde*

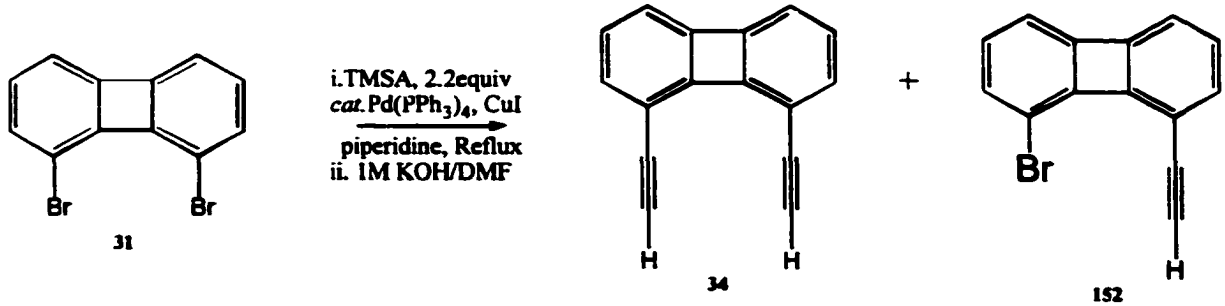
The dialdehyde **150**[177] can be synthesized from 1,8-dimethylbiphenylene by N-bromosuccinimide bromination and further oxidation of the dibromide with sodium acetate affords the diacetate which is reduced to the dihydroxymethyl. Subsequent oxidation of this diol can be effected using PyridiniumChloroChromate (PCC) in CH_2Cl_2 to yield the not so air-stable 1,8-biphenylene-dicarboxaldehyde **150**. In view of the length of this route, we relied on the coupling methods rather to access the diacetylene **34** as described below.

3.1.3. Using The Sonogashira Reaction

1,8-Diethynylbiphenylene can be synthesized by the Sonogashira reaction when the substituents in the biphenylene are strictly either iodine

or/and bromine. The reaction would be milder (room temperature) and faster with 1,8-diiodobiphenylene which has yet to be prepared. We successfully applied the method to 1,8-dibromobiphenylene **31**. Addition of trimethylsilylacetylene to a solution of the dibromide **31**, $Pd(PPh_3)_4$ and CuI in catalytic amounts in piperidine (or triethylamine, isopropylamine failing to effect the coupling) and reflux for 12h yielded the trimethylsilyl-protected diethynylbiphenylene after acidic workup. The yield was good, around 70%, when stoechiometric amount of trimethylsilylacetylene (TMSA) was used and almost quantitative when more equivalents of TMSA were used. In the former case, the partial (30%) incorporation of trimethylsilylacetylene was observed to afford 1-bromo-8-ethynylbiphenylene **152** useful for its well known self coupling reaction under the Castro-Stephens condition. We have been contemplating this as a possible way of accessing the putative biphenyleneyne **103** (see page 129).

Scheme 58: *Coupling of 1,8-dibromobiphenylene **31** with TMSA*



3.1.4. Characterization

1,8-Diethynylbiphenylene **34** was characterized both ^{1}H and ^{13}C NMR, IR and by UV-Vis spectroscopies.

The Infrared spectrum of **34** shows an absorption at 3287.37 cm^{-1} indicating the presence of terminal acetylene as illustrated in Fig. 41

Fig.41: IR of 1,8-diethynylbiphenylene 34

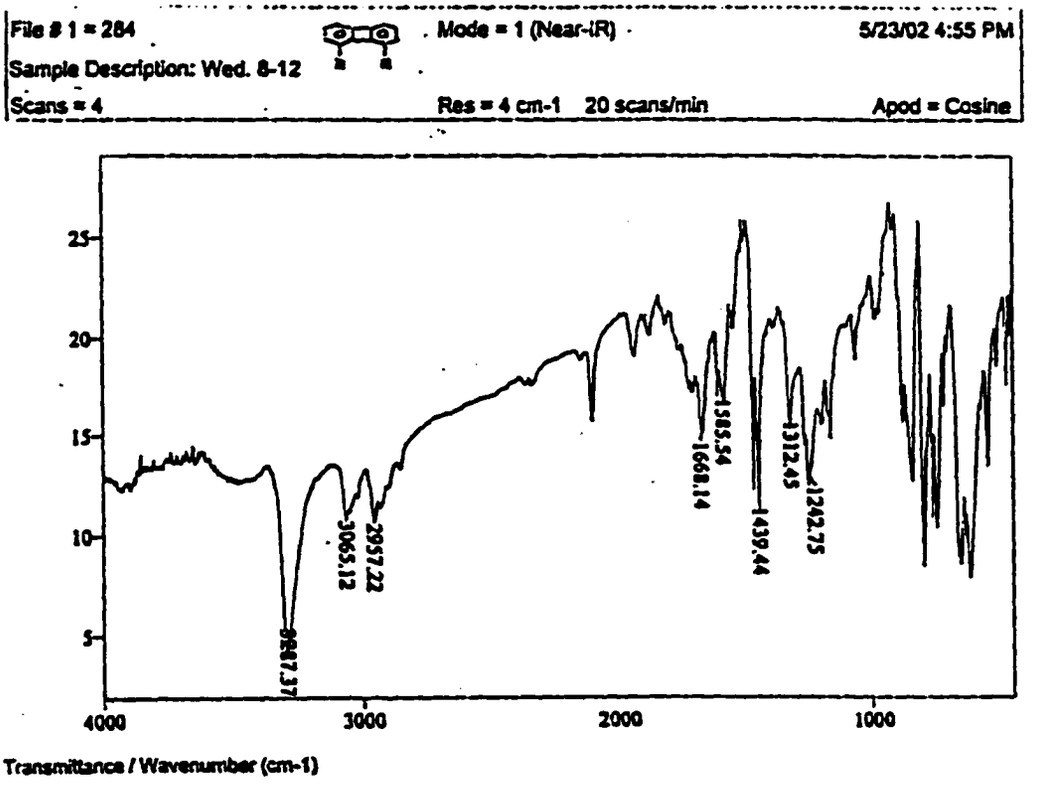


Fig.42: H NMR of 1,8-diethynylbiphenylene

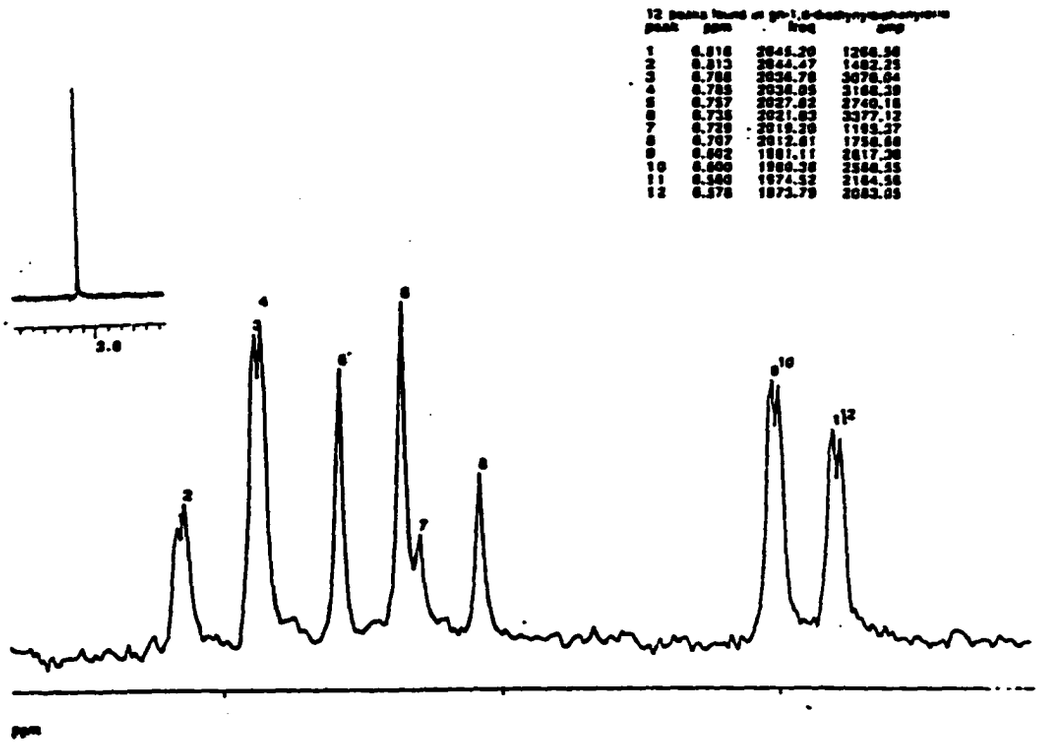
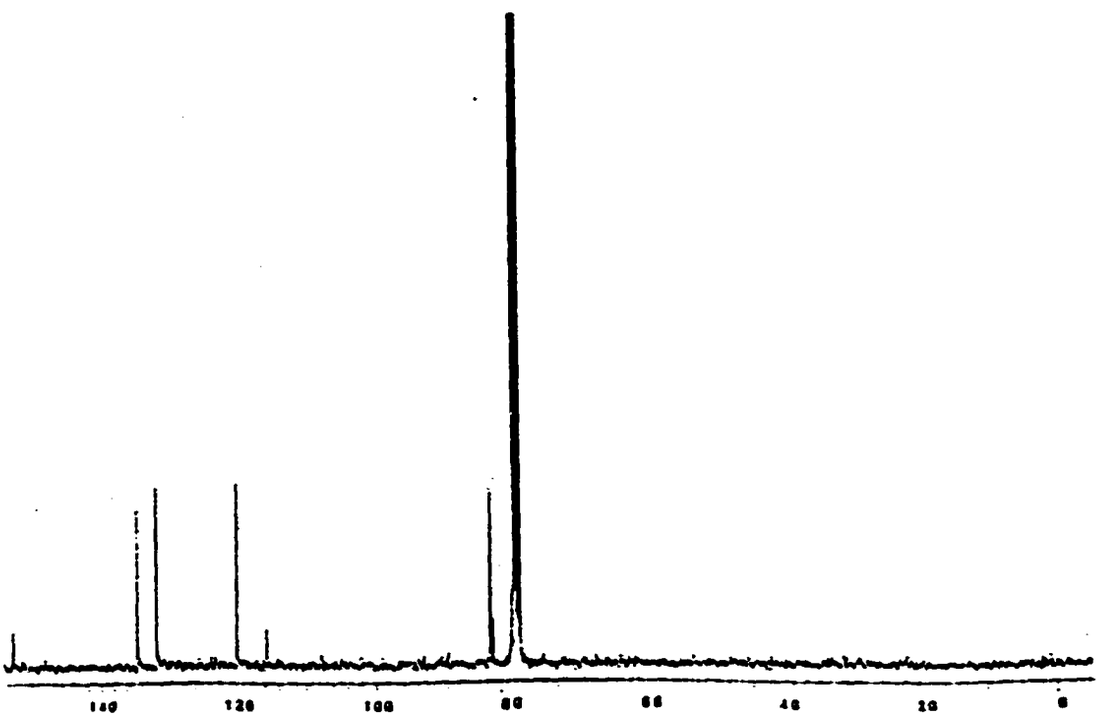


Fig.43: ^{13}C NMR of 1,8-diethynylbiphenylene



3.1.5. Coupling of Grignard Acetylide with organic Halides

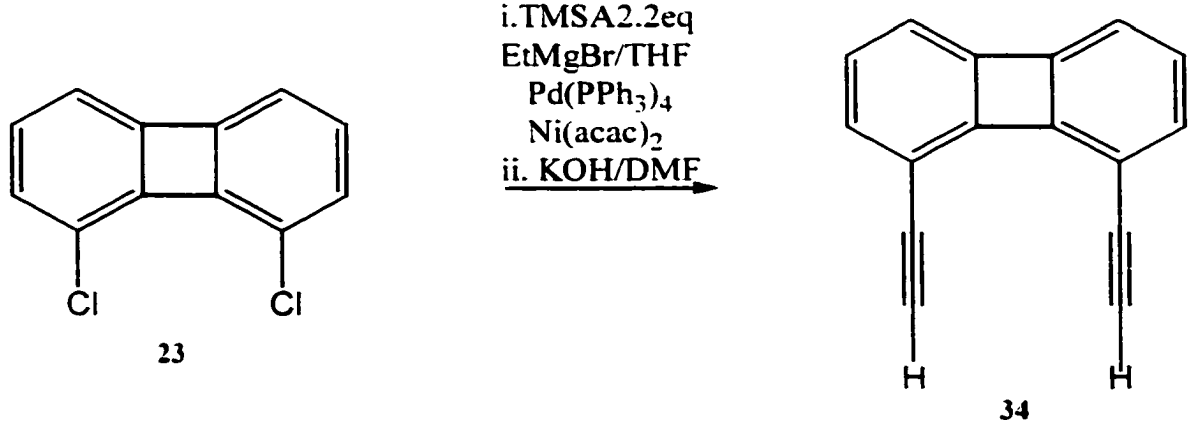
The cross-coupling reaction between an organic halide and an organomagnesium (Grignard) halide has been known for over 40 years. The last decade has witnessed a return to this highly efficient process and hundreds of examples have now been explored.[178]

$$RX + R'MgX \xrightarrow{[Ni]} R{-}R' + MgX_2$$

Because of the scarcity of 1,8-dibromobiphenylene **31** and the rather easy access to 1,8-dichlorobiphenylene **23** (see chapter 2 section) the Ni/Pd coupling of protected Grignard acetylide with either 1,8-dibromo- or 1,8-dichlorobiphenylene became a valuable alternative. The trimethylsilylacetylene magnesium bromide is generated *in situ* by the reaction, in tetrahydrofuran (THF), of the trimethylsilylacetylene (TMSA) and ethylmagnesium bromide or methylmagnesium bromide. Addition of this solution to a solution of 1,8-dichlorobiphenylene, $Ni(acac)_2$ and - $Pd(PPh_3)_4$ followed by gentle refux of the mixture for 48h proceeded smoothly to afford the TMS-protected diethynylbiphenylene **33**. The yields are good (excess of 80% with the deprotection step) when a slight excess of TMSA was used and when additional catalysts were added after 24h. In

practice, the protected product was never isolated, excepted for a small analytical sample, making the reaction an attractive one-pot process. The only side reaction detected was the dimerization product of trimethylsilylacetylene magnesium bromide, the bis(trimethyldisilylacetylene) by the reaction conditions. Protodesilylation was done just prior to oxidative alkyne-alkyne coupling. This was achieved by stirring the TMS-protected 1,8-diethynylbiphenylene **33** in an alkalin solution (1M aqueous KOH in DMF) for two hours. The isolated product **34** was identical to the material described and characterized in the preceding section.

Scheme 59: *Synthesis of 1,8-diethynylbiphenylene **34** from of 1,8-dichlorobiphenylene **23***



23 **34**

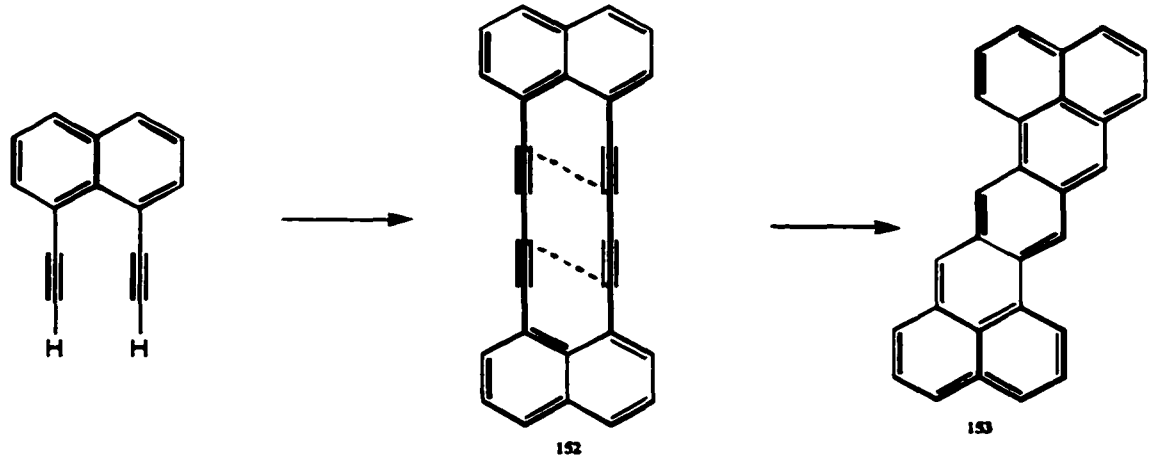
3.2.0. Synthesis of 1,8-diethynylanthracene (213)

In consideration of the simplification brought about by acetylene coupling to dihalobiphenylenes, we proposed to reinvestigate the synthesis of 1,8-diethynylanthracene **213** by this newest route. Compound **213** engages in oxidative coupling to afford the cyclic dianthraceno tetrayne **216** which in addition to being a good reference model to our compound **215**, could in its own right be considered as precursor of a novel carbon allotrope based on this unit.

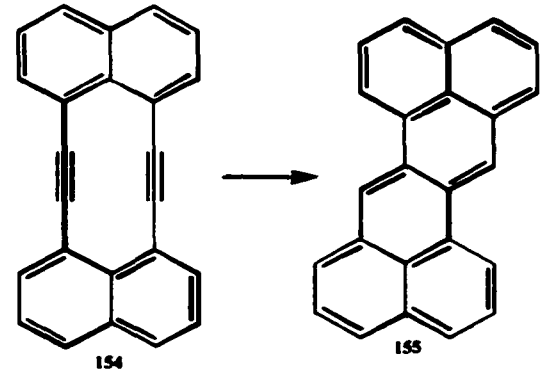
The 1,8-anthracenediethynyl group is a rigid framework offering a ca. 5 Å bridging distance with minimal steric interference from the anthracene ring. This factor is important and useful in the synthesis of complexing agents in 'host-guest' complexes or simply in order to juxtapose other groups without unwanted transannular reactions taking place as observed by Mitchell and Sondheimer in the naphthalene series. These authors aimed at preparing dinaphtho-octadehydro[14]annulene **152** by the Eglinton oxidative coupling of 1,8-diethynylnaphthalene. But the reaction product was found to be the zethrene (tribenzo[de, mn]naphthacene) **153** (scheme 60), presumably by the rapid transannular cycloaromatization (chapter 1) of the highly unstable **152** formed. This unstability has been related to the distance d between the 'yne' groups facing each other in the cyclic dimer.

Cycloaromatization occurred equally during the attempt, by Staab et al.[179] to prepare the corresponding [10]annulene **154**. Instead, the isolated product was the dibenzo[de, mn]naphthacene **155** (scheme 61).

Scheme 60: *Attempts oxidative coupling of 1,8-diethynylnaphthalene*



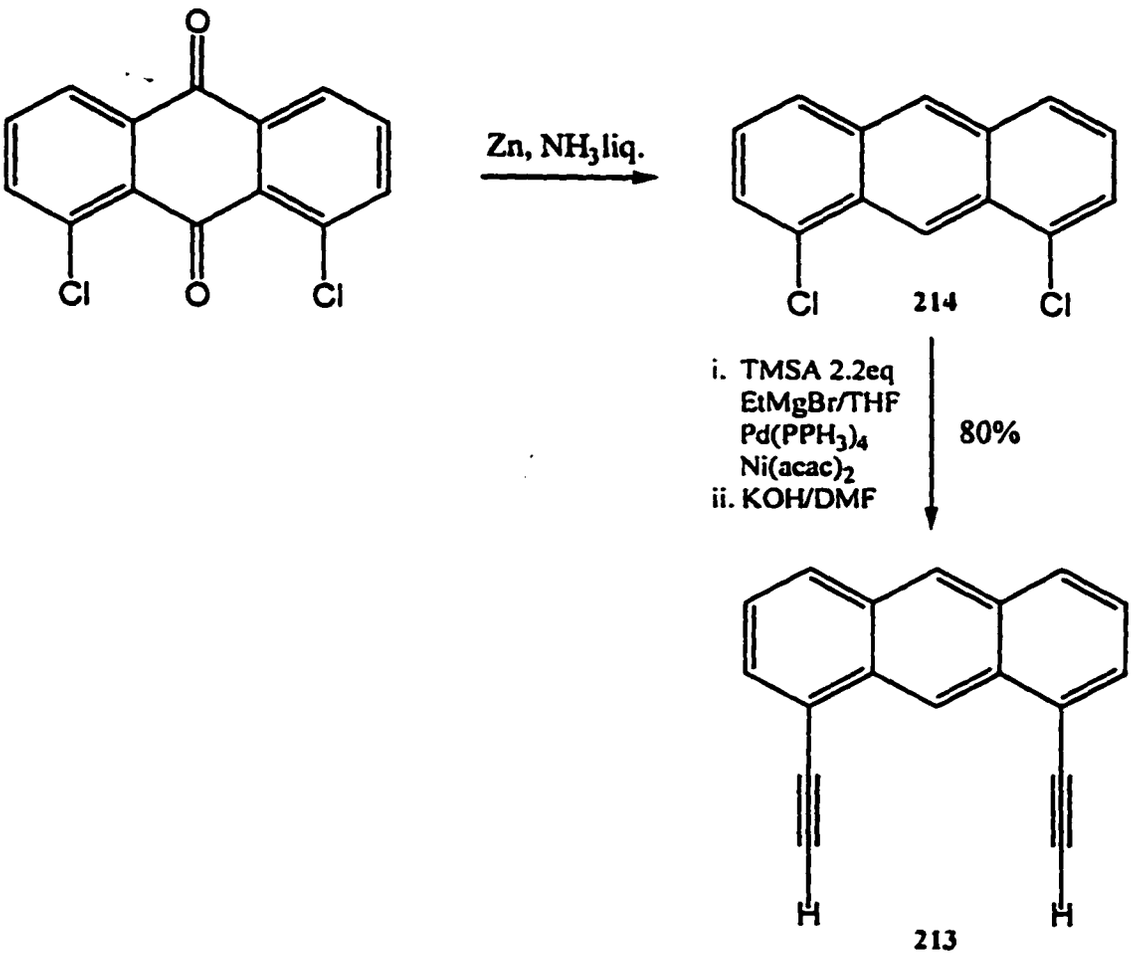
Scheme 61: *transannular reaction of bis naphthalene diacetylene **154***



In order to avoid such an internal interaction, the spacing d separating the 'yne' groups must be greater than 3.2 Å (see chapter 1).[180]

The synthesis of **213** (scheme) using a slight modification of the methodology described above is a great improvement over the one previously reported by Nakagawa and coworkers, in which a mixture of diacetylanthracenes was prepared and separated and the 1,8-isomer was converted to the compound **213** in 5-10% overall yield from anthracene.

Scheme 62: *Synthesis of 1,8-diethynylanthracene 213*



1,8-Dichloroanthracene **214** was prepared from 1,8-dichloroanthraquinone by the method of House[181] except that 1,2-

dichloroethane was used instead of dichloromethane to extract the crude dihydronaphthol intermediate. [(Trimethylsilyl)ethynyl]magnesium bromide, made as previously described, was employed as the nucleophile for the nickel/palladium catalyzed substitution of 1,8-dichloroanthracene. Substitution of the second chlorine is slower than the first, especially at lower temperature. The product, 1,8-diethynylanthracene **213** was characterized by ^{1}H and ^{13}C NMR, IR and UV-Vis spectroscopies.

Fig.44: IR of 1,8-diethynylanthracene 213

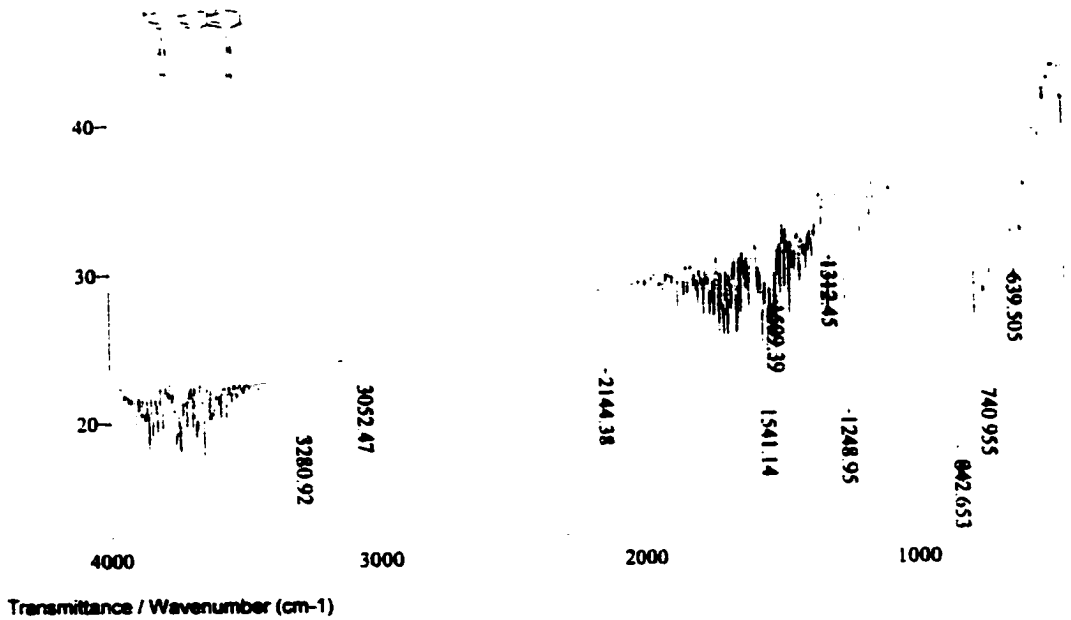


Fig.44 shows the IR of 1,8-diethynylanthracene. It shows an absorption at 3280 cm^{-1} which indicate the presence of terminal acetylene and the typical C-C triple bond absorbing at 2144 cm^{-1}.

Fig.45: ^{13}C NMR of 1,8-diethynylanthracene

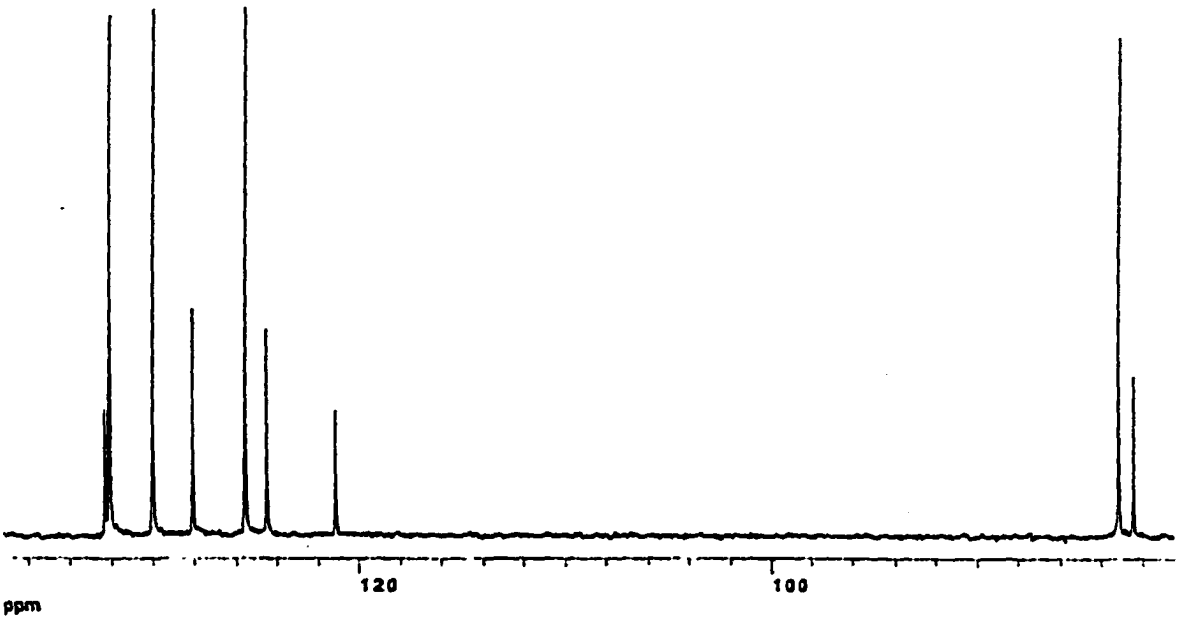
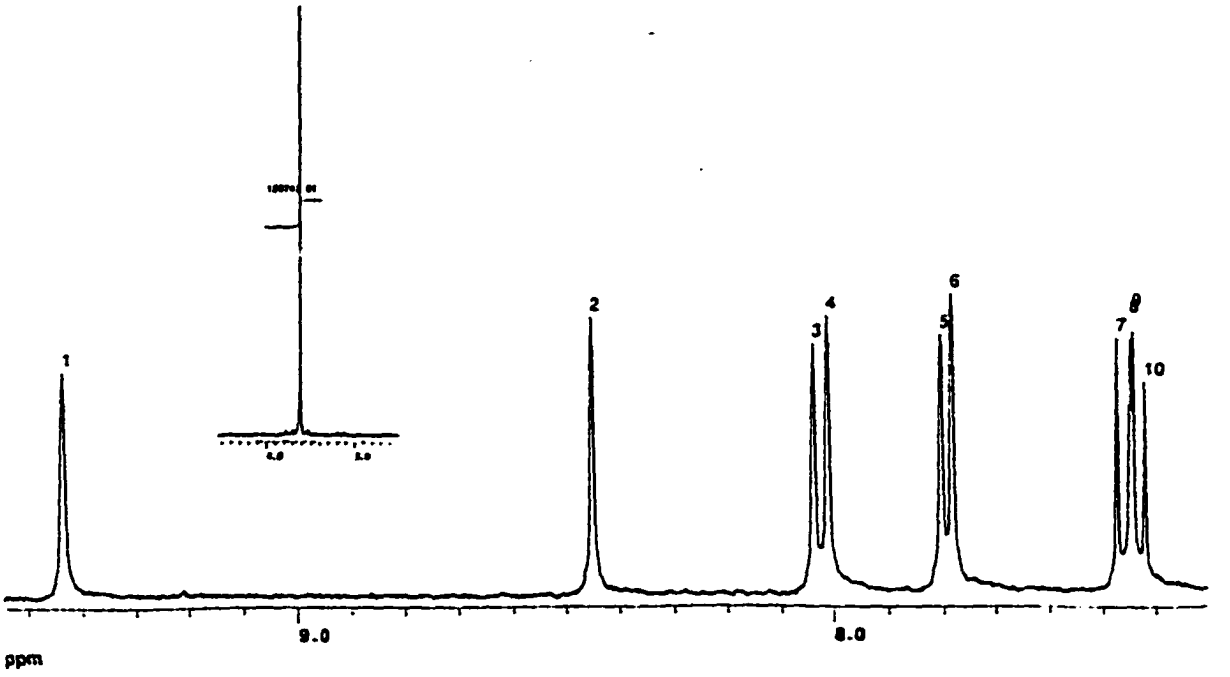
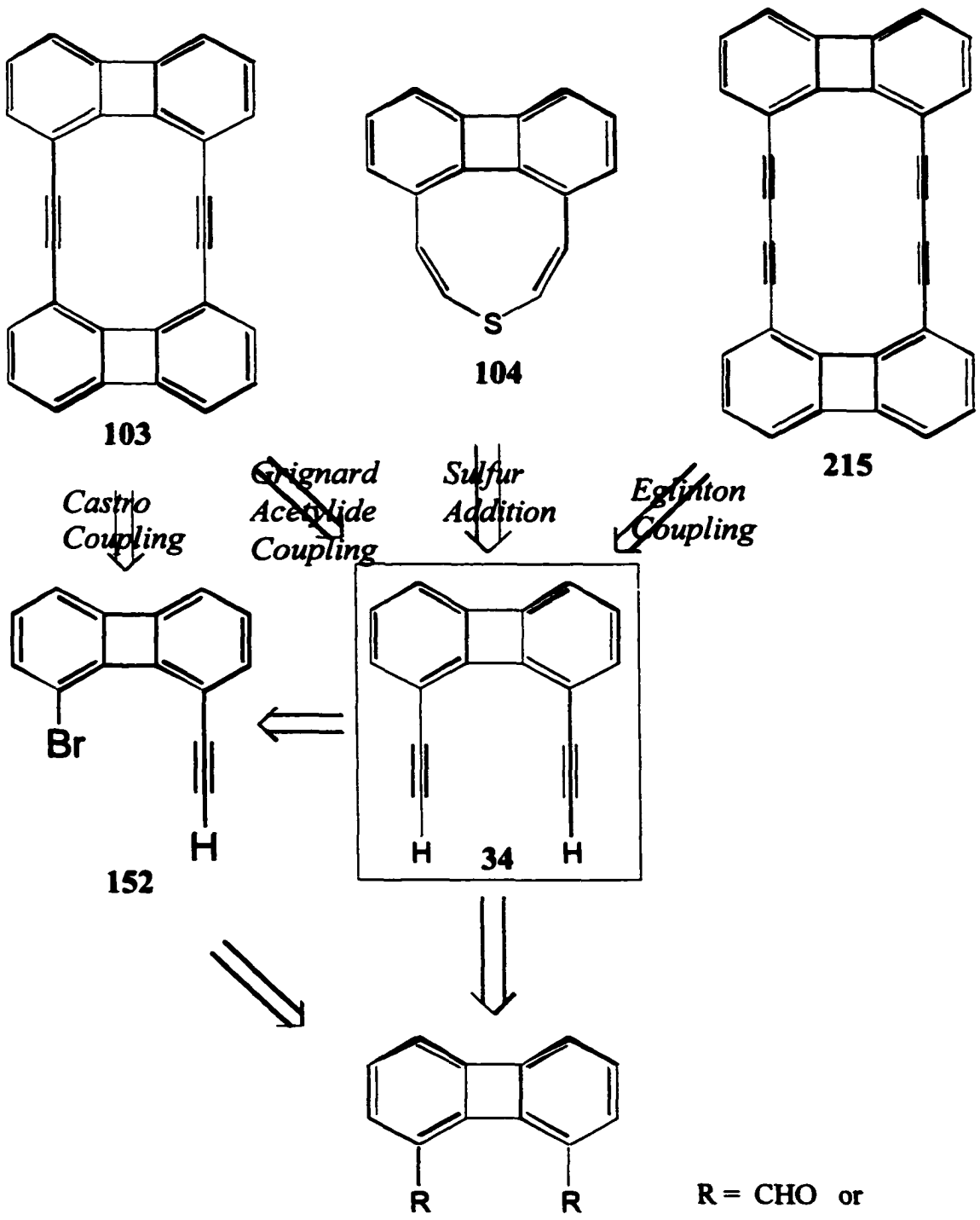


Fig.46: H NMR of 1,8-diethynylanthracene



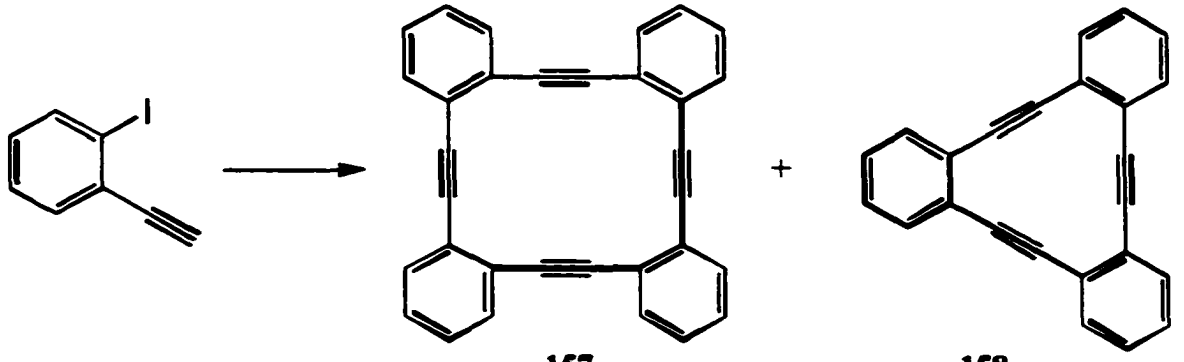
3.3.0. Chemistry of 1,8-diethynylbiphenylene (34)



1,8-Diethynylbiphenylene **34** is a versatile starting material capable to participate in numerous transformations by virtue of its being a stable diacetylene.

3.3.1. Synthesis of "Biphenyleneyne" (103) By the Castro-Stephens or/and the Grignard Acetylide Coupling Reactions:

It is assumed that both the mildly-generated copper and the lithium acetylides (and diacetylides) from 1,8-diethynylbiphenylene **34** would be susceptible to react with a variety of electrophiles. The copper acetylide is known to engage in the so-called Castro-Stephens coupling with iodoarenes and iodoheteroarenes to give cyclic diyne compounds. Eglinton et al.[182] were able to prepare the tetrayne **157** together with the triyne **158** by the Castro coupling of 1–iodo-2-ethynylbenzene.



157 **158**

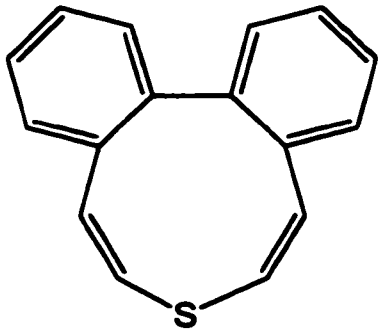
Scheme 63: Synthesis of 157 and 158 by a Castro-Stephens reaction

We therefore propose the synthesis of the first dimer of what could be coined 'biphenyleneyne' **103** (in keeping with the naming method so far encountered in the literature) by the Castro coupling of the copper diacetylide of 1,8-diethynylbiphenylene and 1,8-dibromobiphenylene or, by a modified Castro coupling between 1,8-diethynylbiphenylenyl magnesium bromide and 1,8-dichlorobiphenylene, as shown by Katz, who was able to condense his lithium diacetylide from 1,8-diethynylanthracene **213** with catecholboron chloride in high yield. The same biphenyleneyne **103** is expected from the Castro cross coupling of the copper acetylide generated from 1-bromo-8-ethynylbiphenylene.

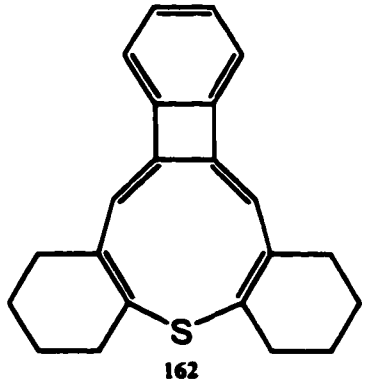
3.3.2. Synthesis of Biphenylenothionin 217

Biphenylenothionin **217** is the first compound which is overall planar and incorporates a planar nine-membered ring having 10 π-electrons, a heteroaromatic system. Thus far, no planar 10 π–electrons structure has been found. The 'cyclodecapentaene problem', could be approached in this way as well, just as Vogel' s aromatic 1,6-methanocyclodecapentaene provided a promising approach to the elusive [10]annulene in the late 1960s. The seven-membered ring, non-planar thiepins have been synthesized[183] and studied in

connection to their ability to extrude the sulfur atom and, hence, aromatize into benzene. We envisioned the thionin **217** (see scheme 64) to be rather planar, precluding sulfur extrusion, due to the fused biphenylene, which is both planar and rigid. Garratt et al.[184] reported the synthesis of a biphenyl-fused dibenzothionin **161**, which failed to assume planarity, existing in buckled, nonplanar conformation. Benzannelation did not lead to the adoption of a planar, aromatic conformation. Neither did planarization of the central thionin occur in the case of **162** in which substitution at C_2 and C_7 is to prevent spontaneous sulfur extrusion.[185]



161



162

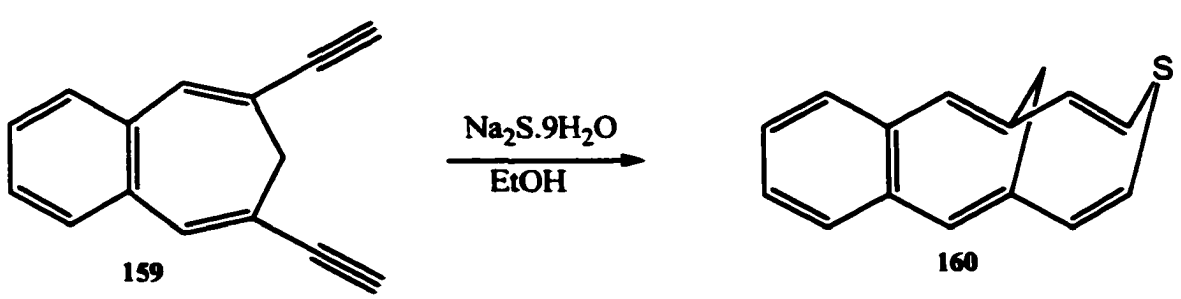
Grohmann and Benshafrut' s naphtho[2,3-d]thiepin **160** (see below) was shown[186] by X-ray to adopt a stable syn conformation (relative to the methano bridge). Access to thio-aromatic compounds has been gained

through either a bis Wittig condensation between a phthaldehyde and a thia bisphosphonium ylide or by sodium sulfide is addition of a sulfur atom to terminal diacetylene. 1,8-diethynylbiphenylene provided just the right substrate for such a reaction.

Our quest to the thionin **217** led us to some unexpected results. Indeed, the Mass Spectrum did not reveal the parent peak for **217** but what appeared to be biphenylenecyclooctatetraene **104**, formed according to the expected sulfur extrusion pathway that has never been found to occur in this type of compounds. These findings, still preliminary, need further investigation.

3.3.3. Attempted Synthesis of to Biphenylene-Thionin 217: (Possible Synthesis of Biphenylenecyclooctatetraene 104)

Grohmann and Benshafrut synthesized the thiepin **160** by addition of sodium sulfide nonahydrate to the terminal diethynyl moieties of 1,6-diethynyl-3,4-benzocycloheptatriene **159** as shown below.



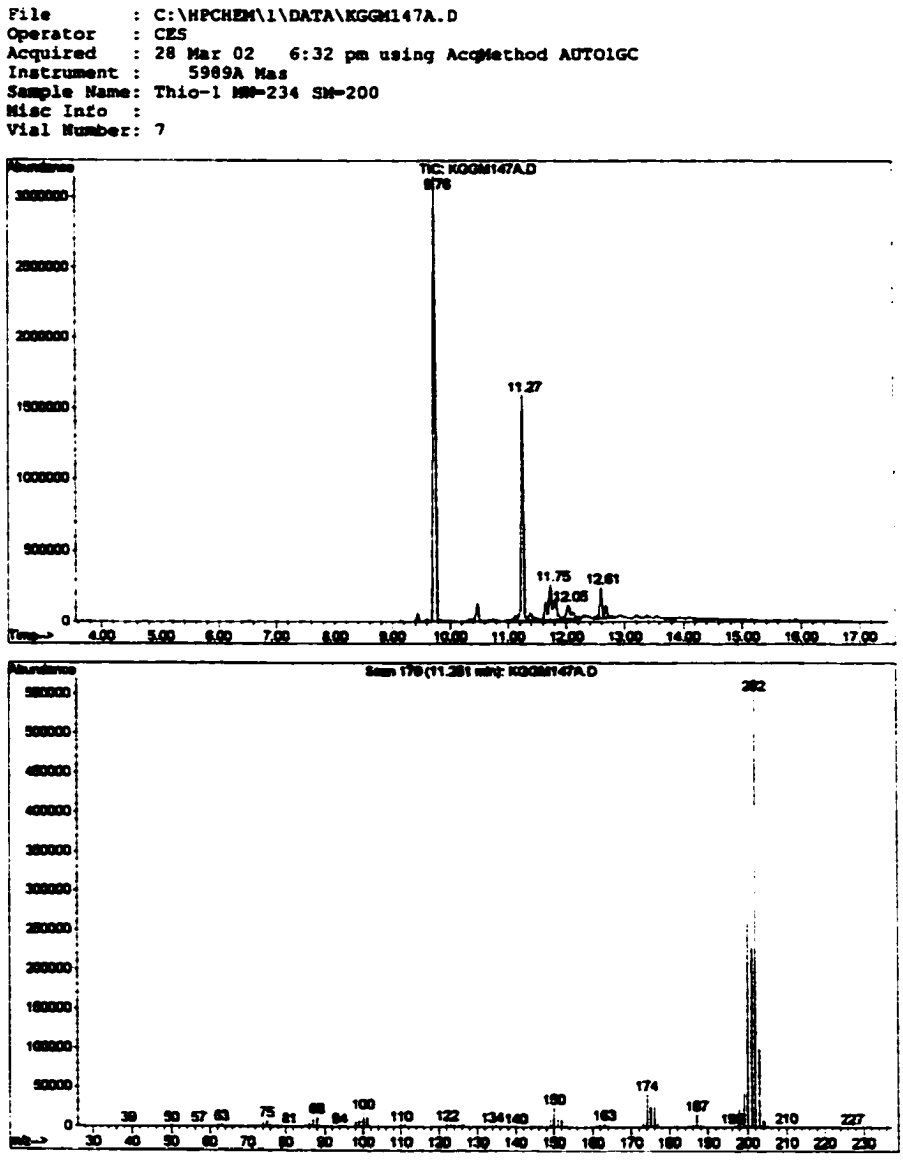
159 **160**

Thiepin **160**, was found to be stable without decomposition at –30 °C and at room temperature in the dark. It was not planar since the inclusion of one sulfur' s lone pair into the conjugation system results in a high energy antiaromatic system. They were able to show that the syn –conformation (as depicted in the scheme) was more stable than the anti-conformation.

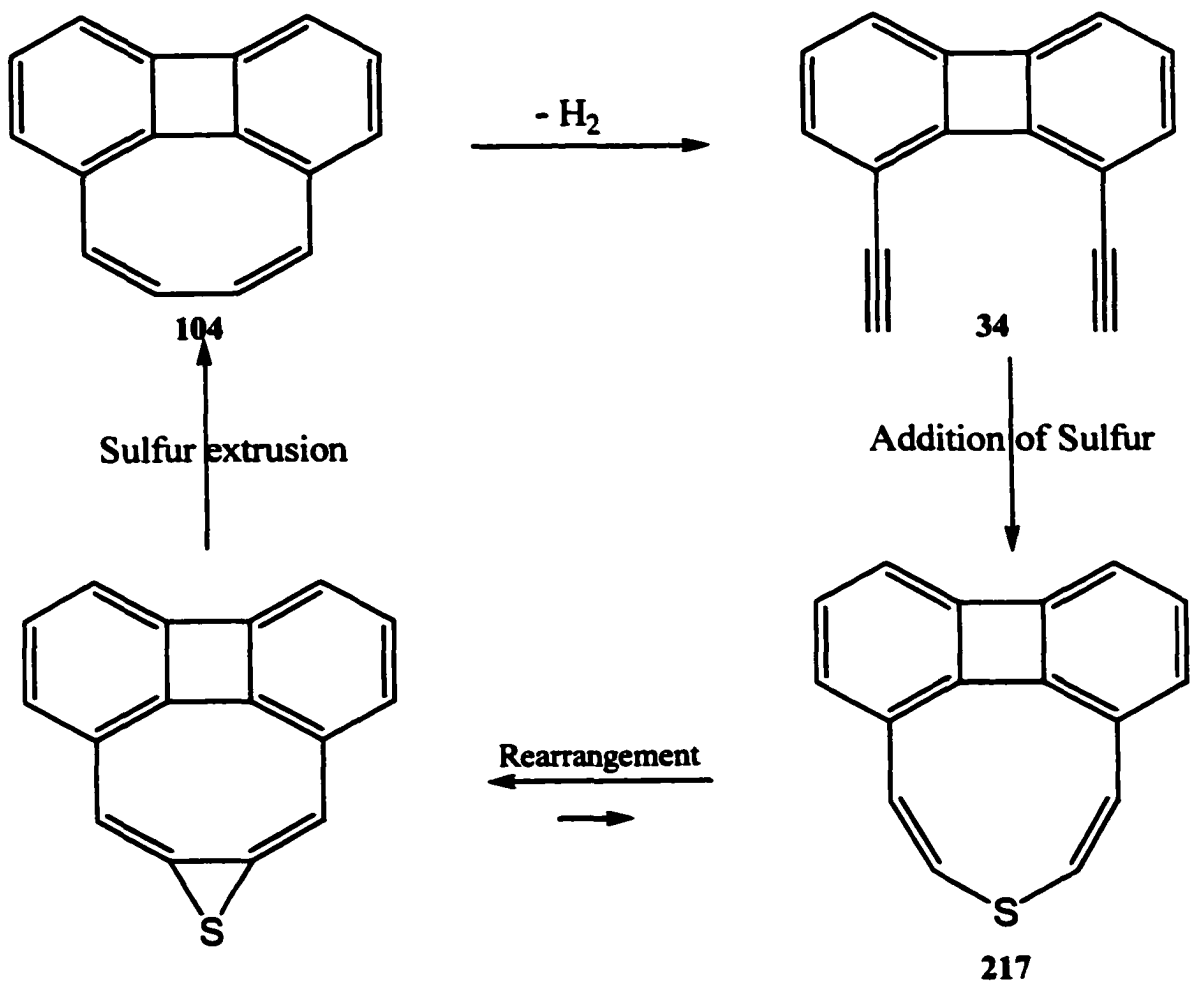
We were therefore intrigued to what might happen in the case of a rigid framework such as 1,8-diethynylbiphenylene incorporating one sulfur atom and, therefore, proposed to study the outcome of sodium sulfide nonahydrate addition to the diethynylbiphenylene system. Using similar conditions, we refluxed the mixture in ethanol for 12h and monitored the reaction by tlc. An additional spot with a greater rf than the starting material in the tlc appeared. GCMS (see Fig.47) of the crude product revealed a peak corresponding to the molecular weight of the starting material and another peak having two additional protons in what would seem to be terminal vinyl and ethynyl groups instead of two terminal ethynyl groups of the starting material. No peak attributable to the thionin was found. The deeply green crude solid was diluted in deuterochloroform for NMR study, which revealed mainly the starting diacetylene. No 1-ethynyl-8-vinylbiphenylene could be detected. We therefore suspected a fragmentation of a transcient cyclooctatetraene to revert back to the starting diacetylene since

biphenylenecyclooctatetraene is known to be deep-colored, unstable and air-sensitive (scheme 64). The GCMS peak, thought to belong to a putative 1-ethynyl-8-vinylbiphenylene would then be the peak belonging to a short-lived biphenylenecyclooctatetraene.

Fig.47: GCMS of biphenylenecyclooctatetraene



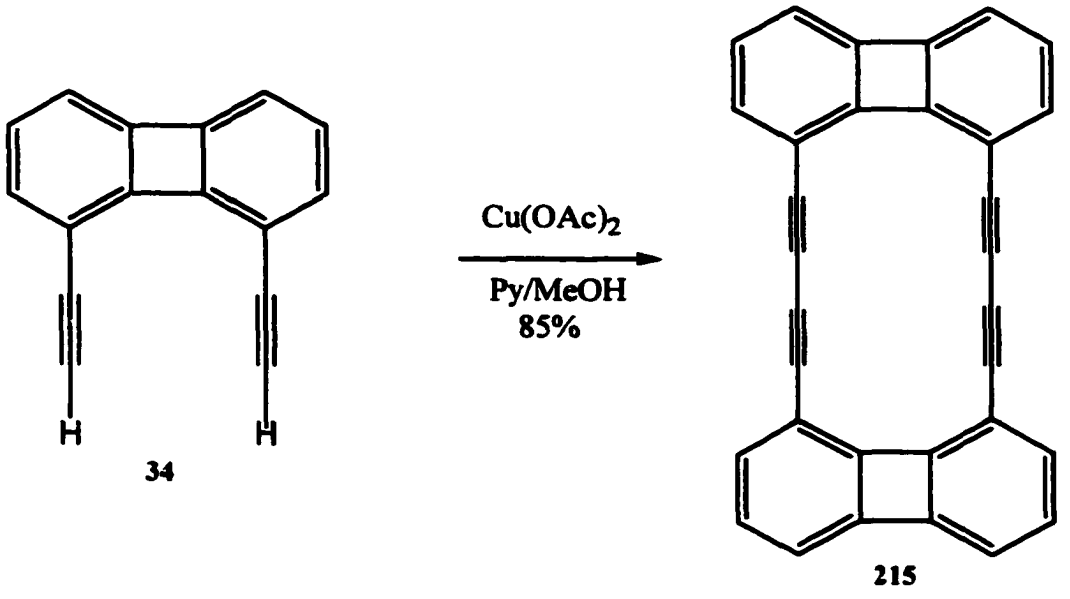
Further studies are underway in order to isolate the biphenyleno-cyclooctatetraene, at least at lower temperature and allow for its characterization and, thus, the confirmation of the mechanism of sulfur extrusion.



***Scheme 64:** Addition (and extrusion of) of sulfur to 1,8-diethynylbiphenylene*

It appeared therefore that sulfur extrusion is as spontaneous in the larger thionin ring just as it is reported to occur in the smaller thiepin ring when not substituted at α-positions to the sulfur atom. That is because it exists in unfavorable equilibrium with the thianorcaradiene system.

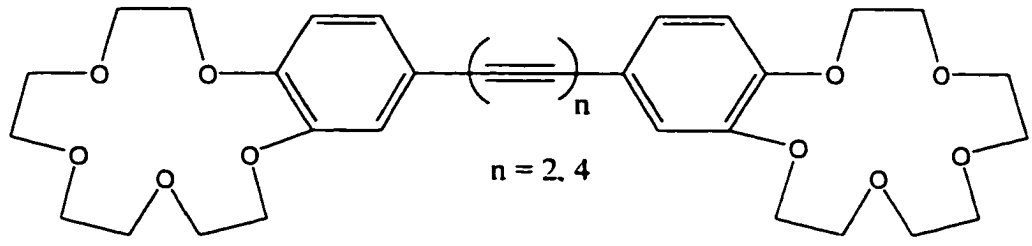
3.3.4. Synthesis and Investigation of Biphenylenediyne (215)



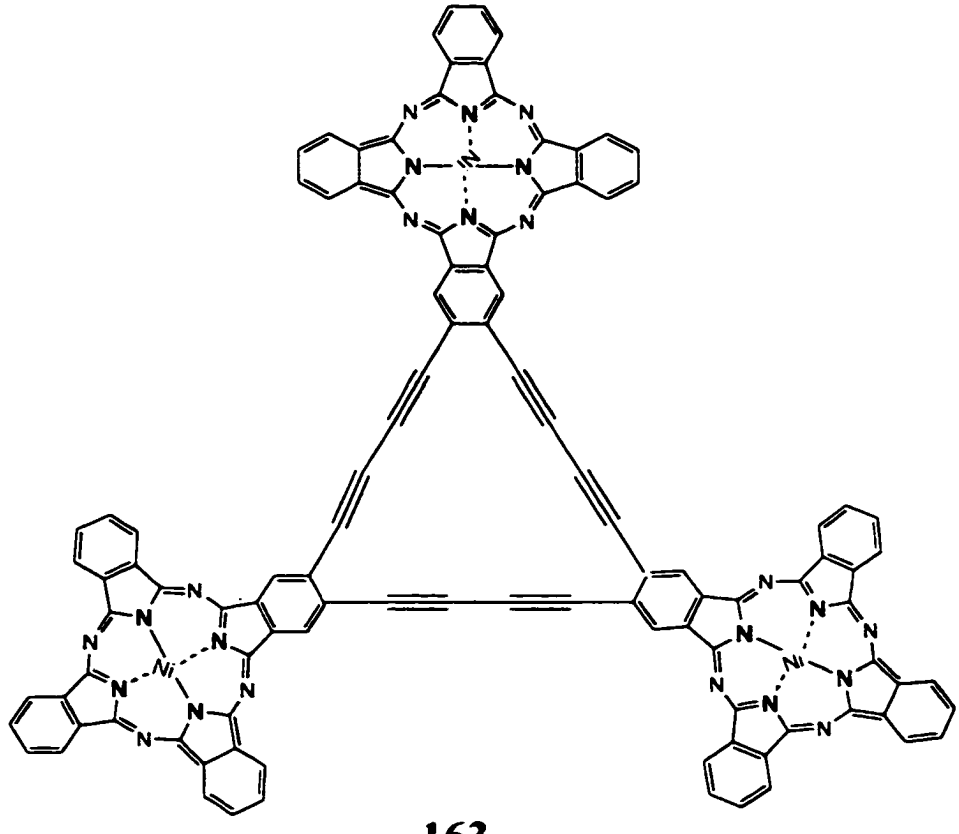
***Scheme 65**: Synthesis of biphenylenediyne **215** by oxidative coupling*

Ever since the synthesis by Sondheimer and Wolovsky of completely conjugated planar eighteen-membered monocyclic hexaene-triyne (see chapter 1 section), it has been of great theoretical interest to synthesize cyclic acetylenes. Recently, the resurgence in the study of both the cyclic and the acyclic polyalkynes carrying a conjugated carbon backbone has been linked to their potentially useful optical and electronic properties.[187] Work by Lagow et al.[188] demonstrated the use of benzo-crown ethers **162** in these

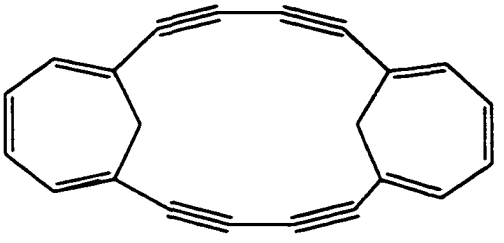
phthalocyaninodehydroannulenes **163**, which polymerized upon heating. Ojima et al.[190]has synthesized the dimethano-bridged dehydroannulenes **164** and **165**.



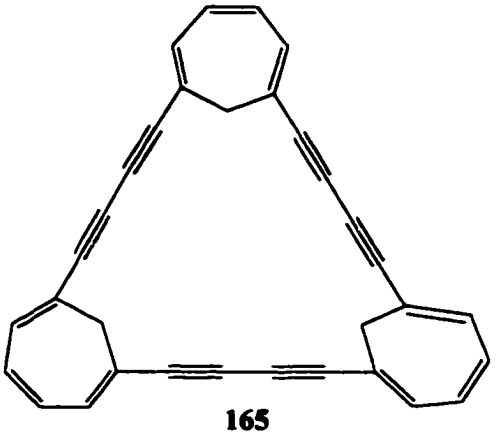
162



163



164



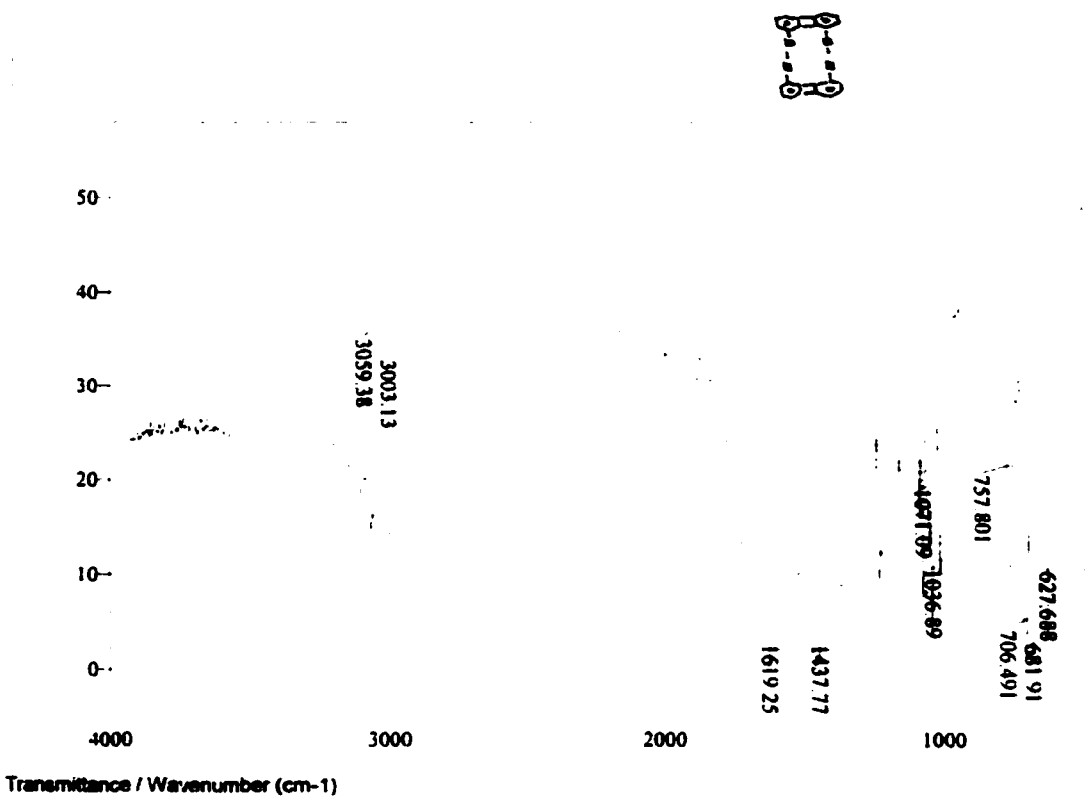
165

We chose to prepare the biphenylene-based cyclic tetraacetylene **215**, dubbed 'biphenylenediyne', using the oxidative coupling reaction of terminal diethynyl, known to favor ring formation.

The oxidative coupling of 1,8-diethynylbiphenylene **34** (scheme 65) was conducted according to the procedure of Eglinton, in a pyridine-methanol solvent system (ratio of 20 to 1). The dimer crystals were orange and of poor solubility in organic solvents, as expected of such macrocycle having a high ratio of Carbon to Hydrogen atoms. The structure of **215** was assigned to the substance from the method of preparation and from the following evidences.

1)The absence in the infrared spectrum (see fig.48) of free ethynyl absorption (3200-3300 cm^{-1} region) suggested a cyclic nature for **215**.

Fig.48: IR of 'biphenylenediyne'

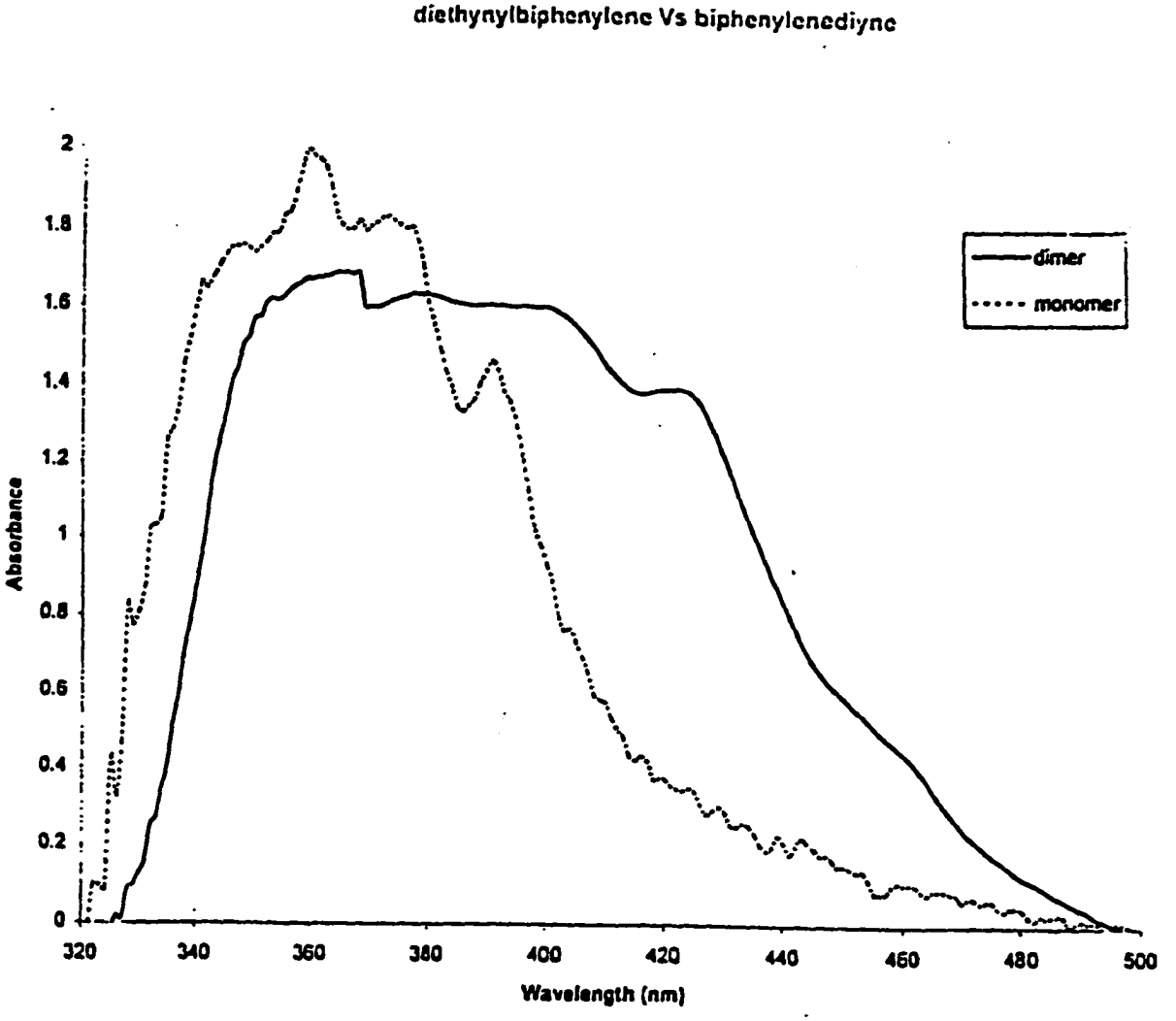


2) UV-Visible spectrum (Fig.49) which is in perfect qualitative agreement with different dimers presenting similar acetylenic linkage such as Nakagawa's 'anthracenediyne' **216** or/and others.[188,189]

3) Although various methods for determining NMR spectra and structural insight into compound **215** were tried unsuccessfully as a result of the poor

well for comparison purpose, 500 MHz H NMR using C_6D_6 (see below) seems to suggest that some polymerization has occurred.

Fig.49: UV-Vis

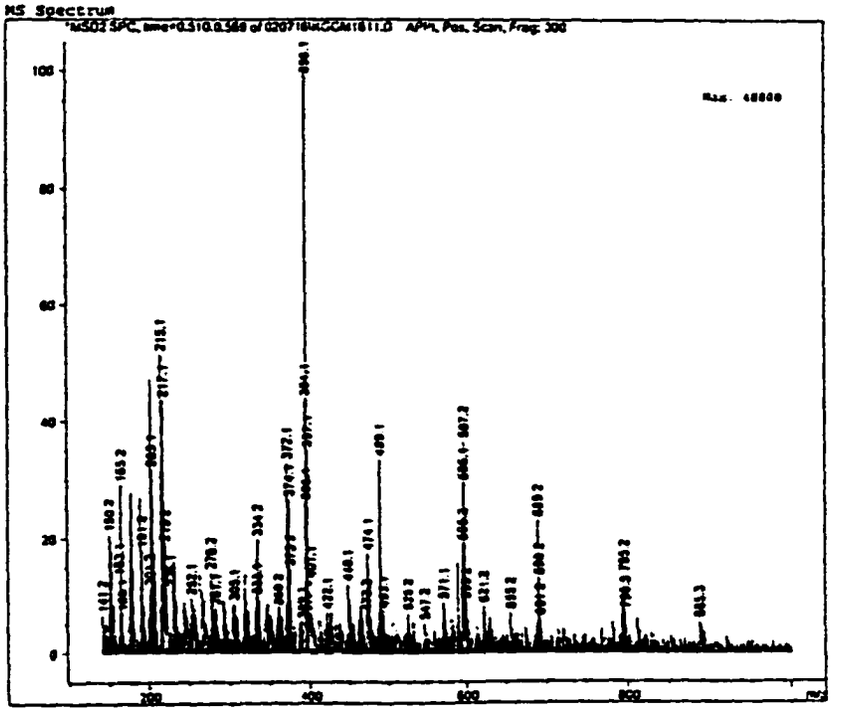


3) Positive APPI Mass Spectrum, although not conclusive, is pointing towards the same direction. Indeed, in addition to the expected peak for biphenylenediyne at m/z 396.1, the peak at m/z 793.2 could well be that of the polymer having double the molecular weight. The other peaks present would be due either to several decomposition pathways (not studied at this preliminary stage) or/and possible reaction products.

Injection Date : 7/16/2002 9:10:.6 PM
Sample Name : 8-Tetrayne Fr.1 Location : -
Acq. Operator :
Inj Volume : External

Method : D:\HPCHEM\1\METHODS\APPI1.M
Last changed : 7/16/2002 8:58:00 PM
(modified after loading)

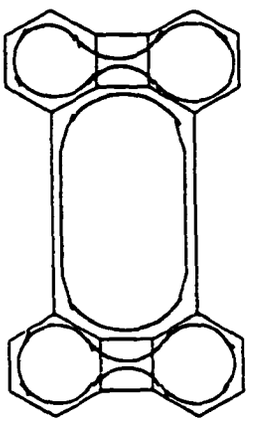
APPI
Low Molecular Weight /
Positive Ion Mode



Instrument 1 7/16/2002 9:16:23 PM Page 1 of 1

The UV-Vis. spectrum (fig.49) shows a contrast between the monomer 1,8-diethynylbiphenylene and the dimer biphenylenediyne, which.

in addition to its unusual stability, seems to display an enhanced interaction of π-electrons (a bathochromic shift in all aspect similar to the one displayed by Nakagawa's compound **216** shown in Fig.51) of the acetylenic bonds with the benzenoids in the biphenylene. It is not possible to predict the extent of π-delocalisation into the cyclobutadienoid (if any) at this time but there lies the interesting question on the versatility of the biphenylene system. It would therefore be of prime importance to acquire unambiguous NMR data correlating the observed stability with, what we predict to be, aromatization of the entire system with no bond-length alternation in the biphenylene such as in the figure below.

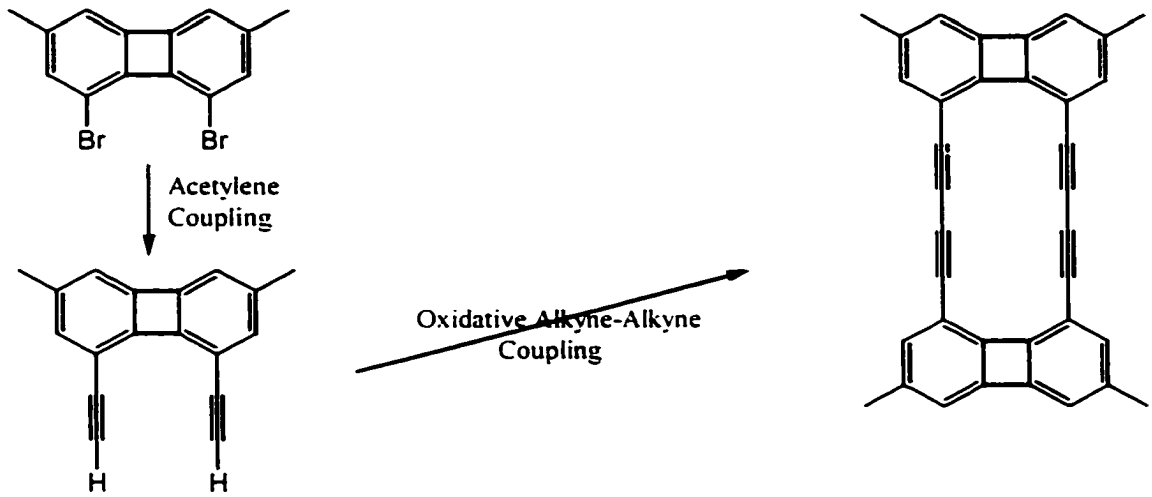


It seems that biphenylene (aromatic) annelation to the [16]annulene (antiaromatic) brings about tremendous stabilization, thus the experimental difficulty associated with solubility (or lack thereof for NMR purpose). Substituting the system with side chains should improve its lipophilicity and solubility in NMR solvents.

Glance to the future:

We are proposing the synthesis of tetramethylbiphenylenediyne (below) from our already prepared 1,8-dibromo-3,6-dimethylbiphenylene **32** by the same methodology applied so successfully for the synthesis of both biphenylenediyne **215** and anthracenediyne **216**. Substituting the methyl groups by the bigger *tert*-butyl could also be envisaged.

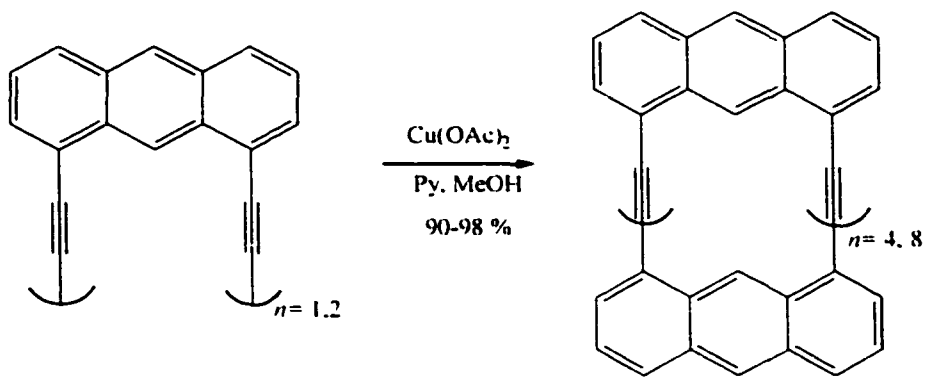
***Scheme 66**: Proposed synthesis of 'tetramethylbiphenylenediyne'*



3.3.5. Synthesis of A Cyclic Tetraacetylene (216) Containing Anthracene Nuclei

As stated earlier, Nakagawa pioneered the syntheses of fully conjugated cyclic tetraacetylene containing anthracene moieties as well as their higher homologue, namely the cyclic octaacetylene, attracted by their exceptional stability and the high yielding copper acetate-mediated oxidative dimerisation of rigid diethynyl and dibutadiynyl substrates (scheme).

Scheme 67: *Synthesis of the cyclic anthracene tetrayne*



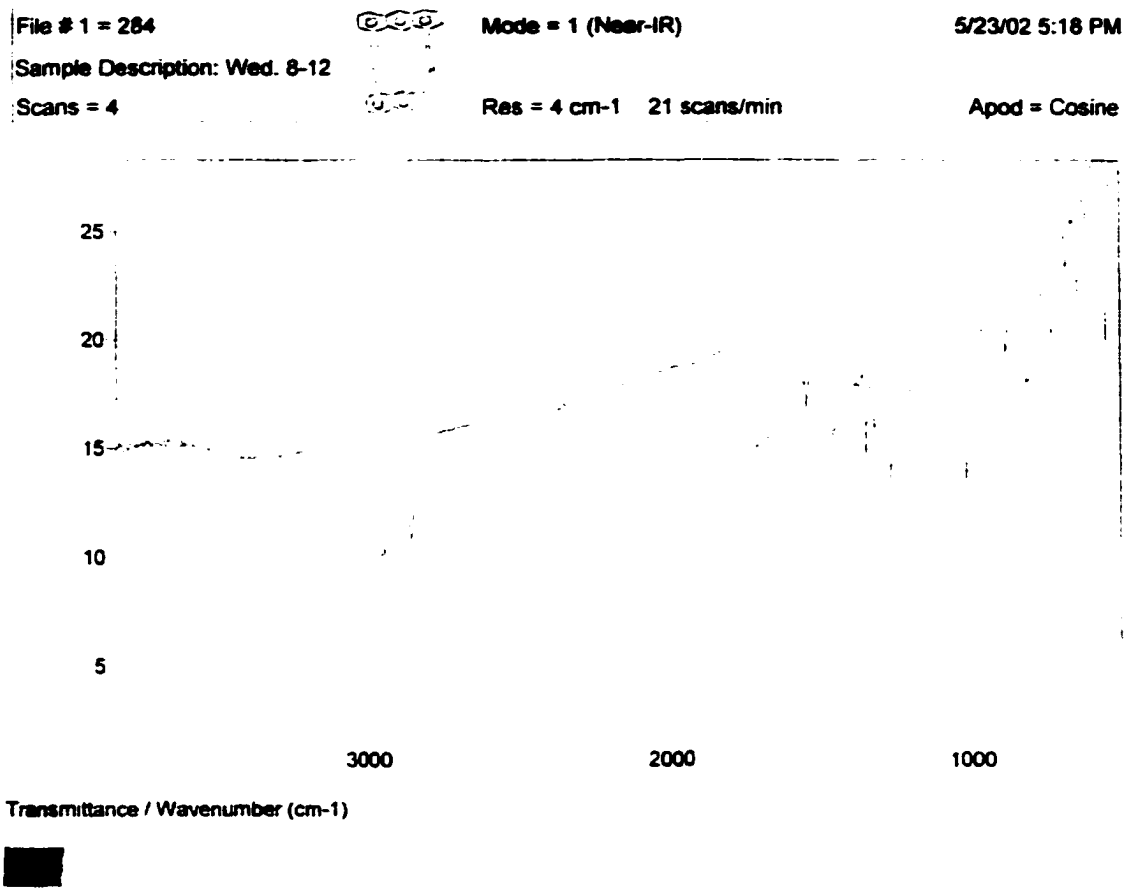
With the introduction of newer and more efficient methodologies of preparing the ethynyl- and butadiynyl-substituted arenes and the current drive for carbon-rich material, cyclic polyacetylene containing stable derivatives are targeted as starting units in subsequent polymerzations towards novel carbon allotropes. The extremely high reactivity of Staab and Sondheimer cyclic tetraacetylene containing naphthalene nuclei, signaled the

need for a spacer between the acetylene moeities in order to preclude transannular interactions. Both biphenylene and anthracene provide such spacer and the opportunity of developping larger carbon nets.

Our synthesis of the cyclic tetraacetylene based on anthracene nuclei aimed at illustrating the advantages of our synthetic strategy to access this type of compounds, which give the possibility of a general approach to novel carbon allotropes.

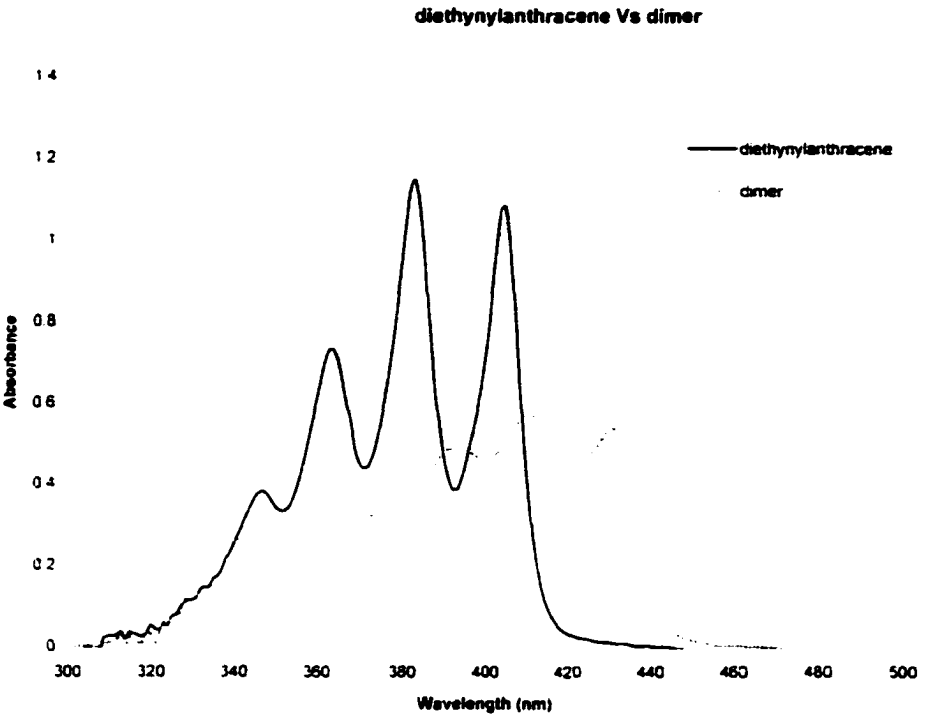
Dimerisation of 1,8-diethynylanthracene **213** to the cyclic tetraacetylene **216** occurred as a mixture of **213** and cupric acetate was refluxed in pyridine-methanol solvent system (The Eglinton conditions). The orange crystals, obtained in high yield, were unsoluble in most organic solvents, just like biphenylenediyne discussed above. When highly diluted, the compound exhibits an intense, beautiful lilac/violet fluorescence, as observed by Nakagawa. The infrared spectrum of **216** also matched the literature one, revealing its cyclic structure by the absence of free ethynyl absorption (fig. 50).

Fig.50 IR of 'anthracenediyne'



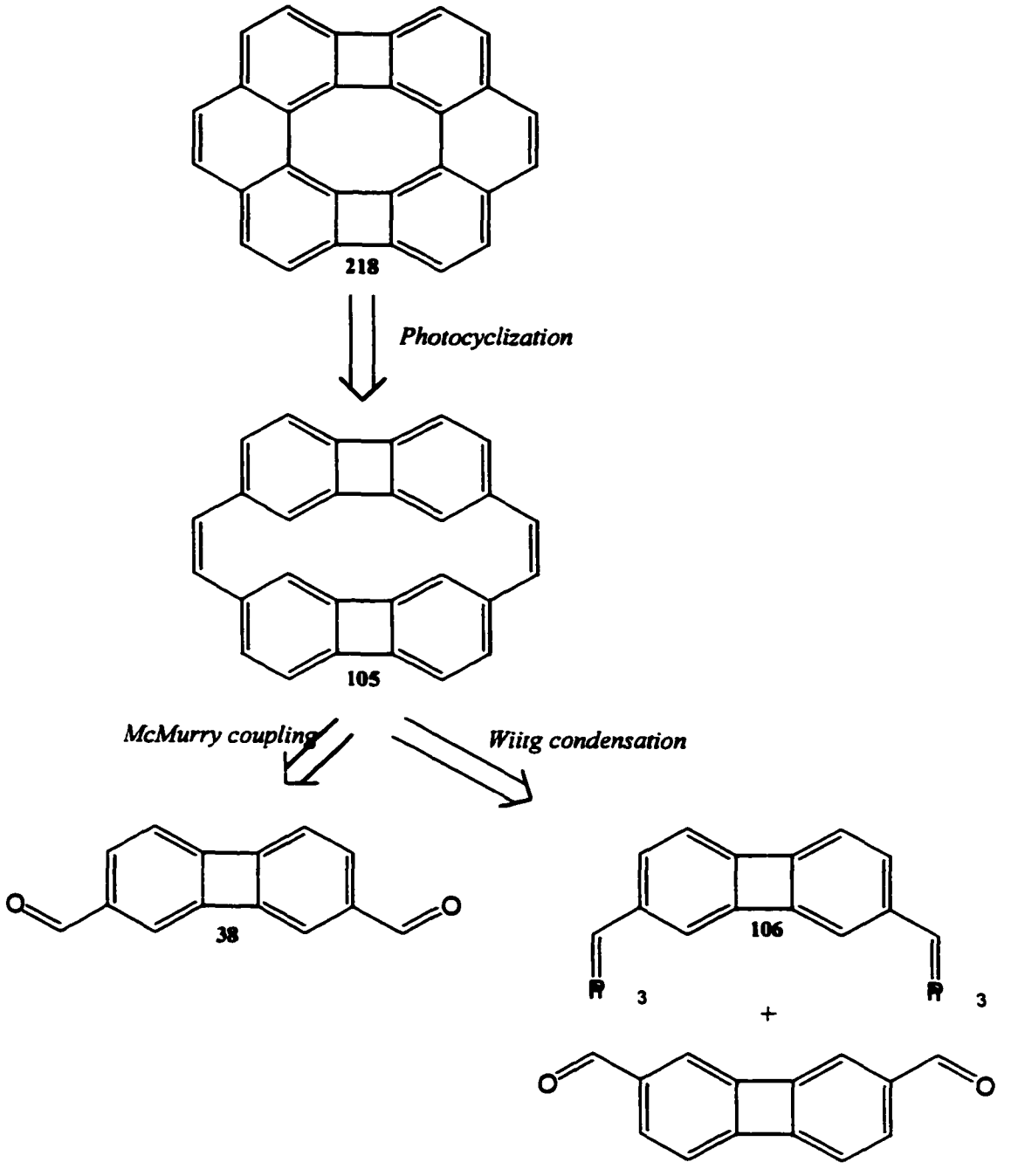
The ultraviolet spectra of 1,8-diethynylanthracene **213** and the cyclic tetraacetylene **216** are illustrated in Fig.(51) The marked increase in the absorption intensities and the remarkable red-shift of the spectrum of **216** indicate that the cyclic tetraacetylene cannot be regarded as a simple derivative of anthracene and, again, seem to point to an enhanced interaction of π-electrons of the acetylenic bonds with those of the aromatic system.

Fig.51: UV-Vis



Such red-shifts were also found by Lagow, Cook and others[191] and were always rationalized in terms of π–conjugation increase relatively to that of the starting monomer. In fact, oxidative couplings leading to the cyclic dimer could be monitored by visible-region spectroscopy as convincingly illustrated by Cook et al. Furthermore, our visible-region spectrum is identical to the UV-vis spectrum of Nakagawa et al. for the same compound.

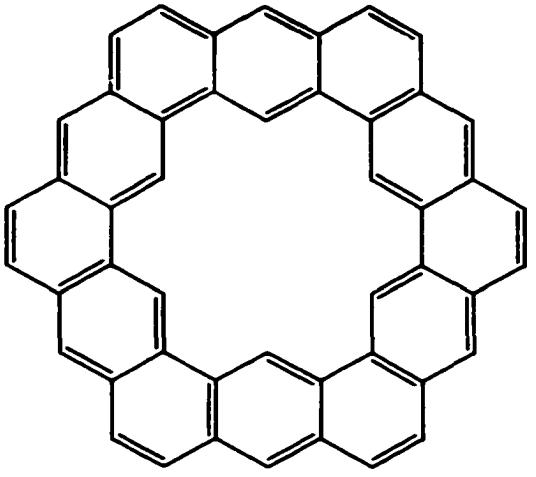
3.4.0. SYNTHESIS OF BIS(CYCLOBUTA)PHENANTHRENE 218



Scheme 68

Aromaticity has played a central role in the development of the theory of chemical bonding.[192] The theory of aromaticity has been developed to the point where the chemical and physical properties of the new π structures can be predicted with fair confidence as aromatic, olefinic and antiaromatic.[193] And much of the current interest in π systems is with molecules that lie on or near the borders of this classification scheme.[194] The title compound is an intriguing example of a compound which falls into all three categories. The polyarene structure was designed in such a way that the rigidity of the biphenylene subunits conbined with the geometry and dimensions of the benzene rings would constrain the hydrocarbon to be planar. Synthesis of **218** thus promised to provide one of the few examples[195] of a hydrocarbon containing a planar cyclooctatetraene ring whose antiaromatic contribution can then be studied by NMR.

Compound **218** can also be viewed as a subtle combination of circulene and [N]phenylene. Circulenes are cycloarenes and they are interesting aromatic systems with regard to the problem of π-bond delocalisation. For instance, Kekulene below, which has no less than 200 different "kekule" resonance forms, was considered as a test model for the 'sextet' concept of Clar.[196]

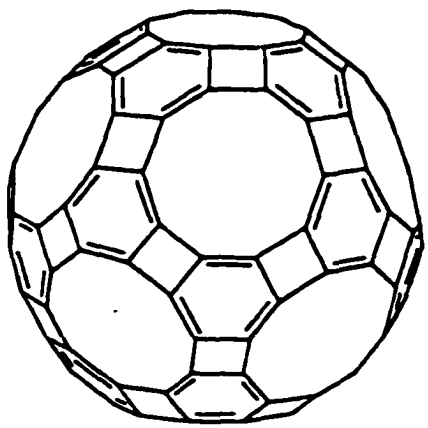


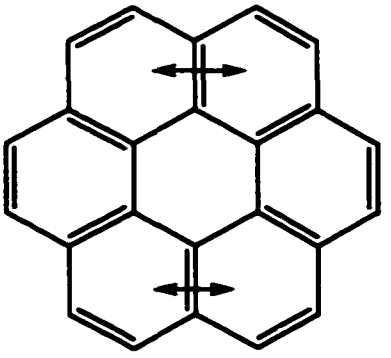
Kekulene' s unique feature is that the protons in the inner cavity should make it possible to decide, by ^{1}H NMR spectroscopy, to what extent the diatropicity in the macrocyclic system can compete with the ring current induction within the benzenoid subunits.

The [N]phenylenes constitute a relatively new class of polyarenes,[197] biphenylene being the parent compound. They comprise the linear, angular and cyclic phenylenes. In a recent paper,[198] calculations were made that tied nicely the circulenes to the phenylenes. The cyclic [N]phenylenes are still in the development stage although the ultimate member of the series, dubbed "antikekulene" has been invoked as the prototype for 'superdelocalisation'.[199] In Schulman and Disch' s view,[198] the relationship between circulenes such as coronene (6-circulene) and the [N]phenylenes such as antikekulene (cyc[6]phenylene) is one of '*phenylation*'. These

authors suggested that the [N]phenylenes be "obtained" from the condensed benzenoids by changing fused benzene bonds into biphenylene moieties or a formal interpolation of C_2 fragments. And so, coronene or 6-circulene is phenylated into antikekulene or cyc[6]phenylene by an 'explosion' of the C-C bond between benzene rings in circulenes to become cyclobutadiene rings between benzene rings in cyclic [N]phenylenes. The power of their calculations is such that they have predicted the 'phenylation' of virtually all known circulenes into their corresponding [N]phenylenes, even the phenylation of buckminsterfullerene C_{60} to the putative 'archimedene' C_{120}.[200]

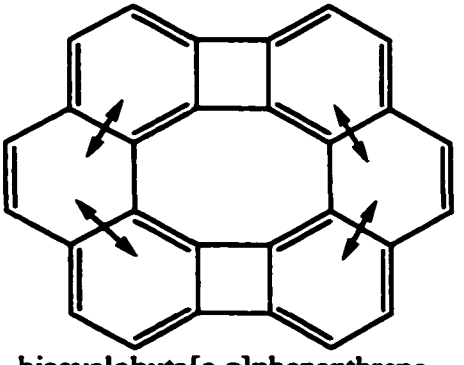
Fig. 52: archimedene C_{120} (only the front of the sphere is represented)





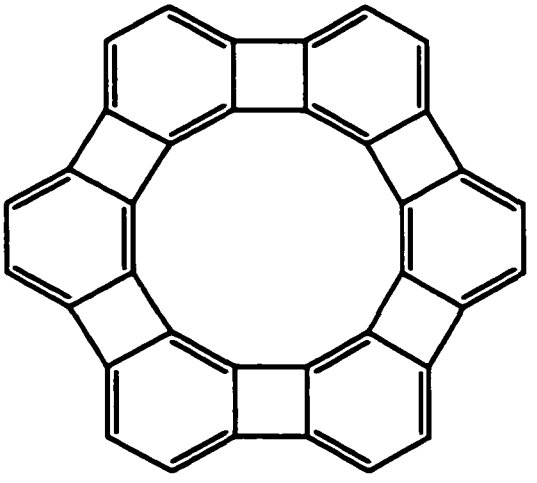
CIRCULENE

coronene - 6-circulene



partially *'PHENYLATED'*
CIRCULENE

biscyclobuta[c,g]phenanthrene



'PHENYLATED'
CIRCULENE

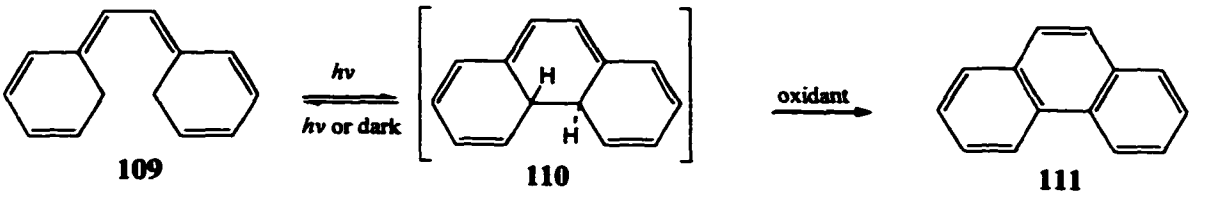
antikekulene - [6]phenylene

While synthetic routes to antikekulene have been pursued, the intermediate compound between 6-circulene and [6]phenylene (see preceding scheme), obtained by partial phenylation of 6-circulene and which is really a kind of both, has attracted our attention because of its unique structural features and the availability of synthetic methods leading to its preparation (see retrosynthetic scheme). The most obvious route is based on photochemical cyclodehydrogenation ring closing reaction.

3.4.1. Photochemical Cyclodehydrogenation of Stilbenes

Photochemical cyclodehydrogenation of stilbenes **109** to form phenanthrenes **111** and related systems has been recently improved by Katz *et al.*[201] with the addition of propylene oxide to the original protocole of Mallory *et al.*[202] Katz has extended the use of the method to much larger systems such as helicenes and others.[203] Mechanistically, Stegemeyer showed that the initial rate of phenanthrene formation on ultraviolet radiation of *trans*-stilbene was zero, but in the case of *cis*-stilbene, the initial rate was finite.[204] Mallory and his coworkers showed that, in the complete absence of oxygen, ultraviolet irradiation of *cis*- or *trans*-stilbene gave only a *cis-trans* isomerisation. They proposed[205] that the dihydrophenanthrene **110** was an intermediate in the reaction and that the function of the oxygen

was to remove the tertiary allylic hydrogen atoms. Without oxygen, the dihydrophenanthrene would undergo ring-opening and revert to *cis*-stilbene **109**.



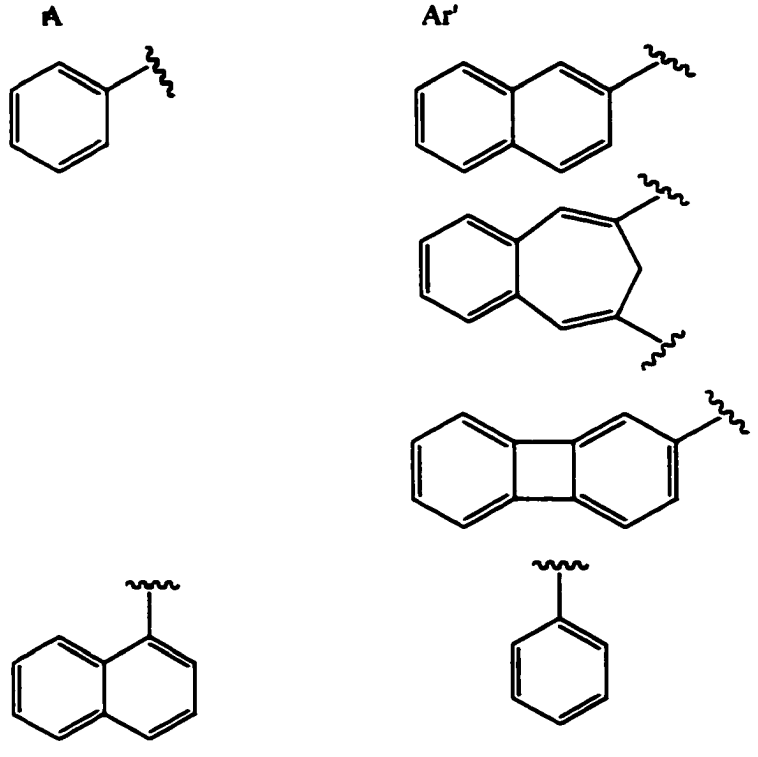
109 **110** **111**

Scheme 69:** Synthesis of pyrene **111

The oxidative photocyclisation reaction has been used for a large number of arene analogs of stilbenes including 1- and 2-styrylnaphthalene[206] (to form chrysene and benzo[a]phenanthrene repectively), *o*-terphenyls to form triphenylene, dibenzo[c,g]phenanthrene to synthesize benzo[ghi]perylene and many others[207]. We therefore synthesized a series of compounds susceptible to undergo oxidative photocyclisation. Among these, 1- and 2-styrylnaphthalenes **114** and **113**, useful as references, followed by 1,6-bis(styryl)benzocycloheptatriene **112** and, in the biphenylene series, 2-styrylbiphenylene **110** and its chlorosubstituted analog **111**. Indeed, Wittig reactions between aldehydes and corresponding phosphonium ylides proceed to give the various styryl systems as described later. While the product of the oxidative photocyclisation of 1-styrylnaphthalene was known to be

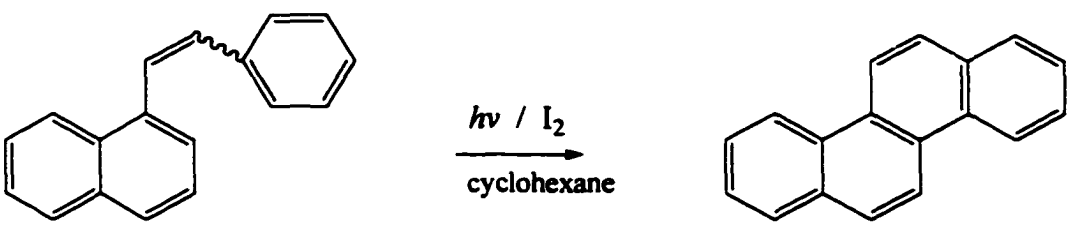
chrysene, 2-styrylnaphthalene gave benzo[c]phenanthrene. Results that we have been able to obtain. The generalization of the reaction to different systems such as 1,6-bis(styryl)benzocycloheptatriene and the styrylbiphenylenes could then pursued. In the case of the former, an interesting novel heptacyclic system, as confirmed by GCMS resulted. The styrylbiphenylenes, accessible by similar Wittig reactions[208] widely used to synthesize stilbene derivatives, starting with the appropriate arylmethyl halide and aryl aldehyde, were synthesized in an attempt to extend the scope of this, already general, reaction to the biphenylene series.

$$\underset{\text{(X=Cl or Br)}}{ArCH_2X} \xrightarrow[\text{ii. Base}\\\text{iii.Ar'CHO}]{\text{i. } PPh_3 \text{ or } (EtO)_3P} ArCH{=}CHAr'$$



3.4.2. Photocyclisation of 1- and 2-styrylnaphthalenes

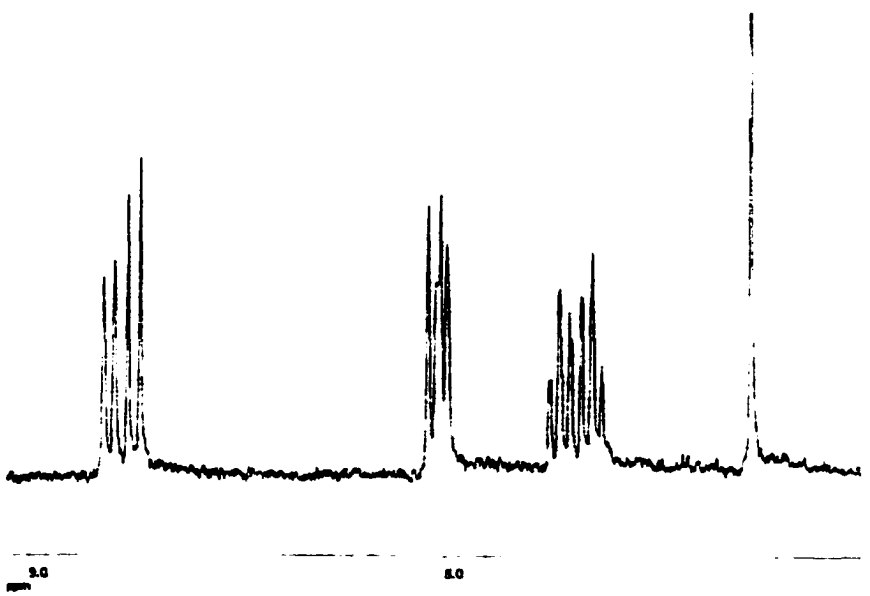
1-Styrylnaphthalene **114** synthesized by Wittig condensation of 1-naphthaldehyde and the phosphonium salt of benzylbromide was oxidatively cyclized to chrysene **115** in >70 % yield. **115** was characterized by both GCMS and NMR (Fig.53) displaying the typical ABB'A' sets of symmetrical proton peaks.



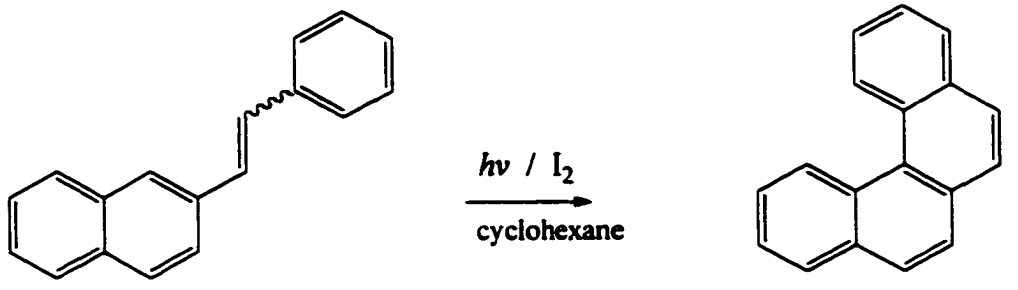
114 **115**

Scheme 70: Synthesis of chrysene 115

Fig. 53: H NMR of chrysene (aromatic H's)



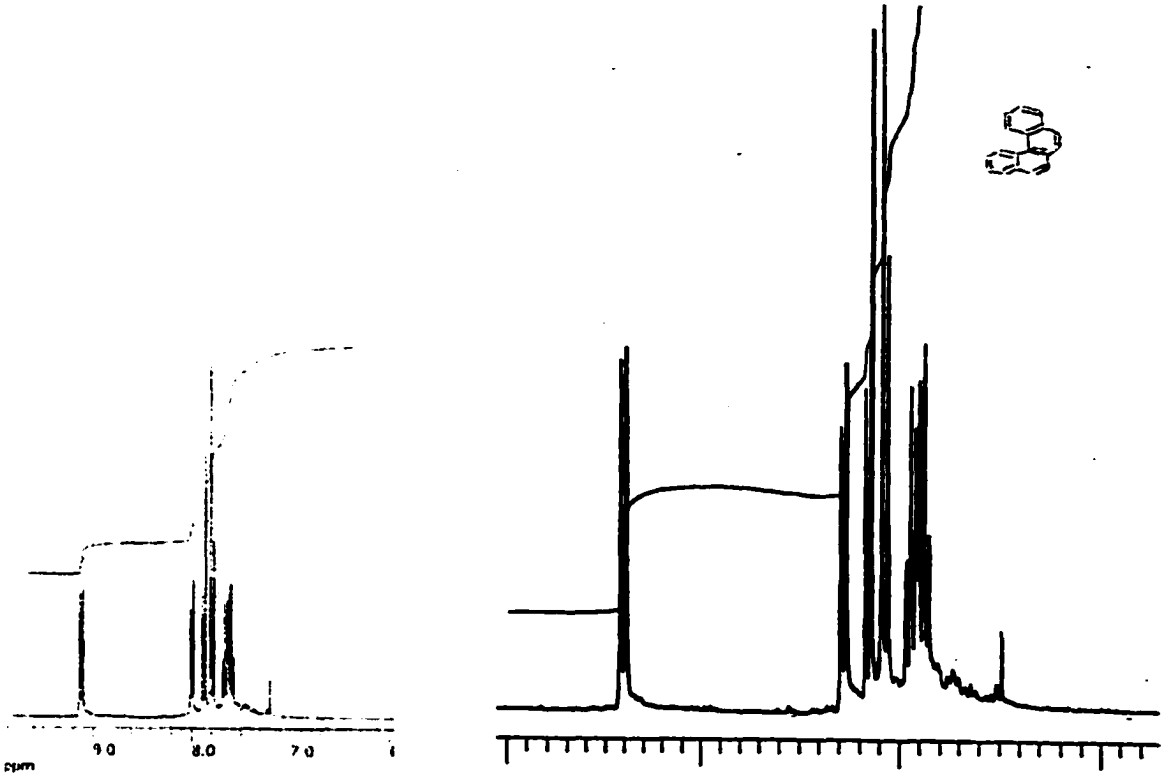
With 2-styrylnaphthalene **113**, the oxidative photocyclisation has been shown[209] to be highly selective, giving almost exclusively the product resulting from cyclisation to the free 1-position of the naphthalene ring rather than that from cyclisation to the 3-position. This preference for the more stable dihydro intermediate –with an aromatic stabilisation- was clearly demonstrated,[210] when lower iodine concentration was used, in that benzo[c]phenanthrene **211** was the sole product obtained. The ^{1}H NMR of **211** below is consistent to what can be considered a symmetrical dibenzonaphthalene rather than benzanthracene (which wouldn't include an ABB'A' system).



113 **211**

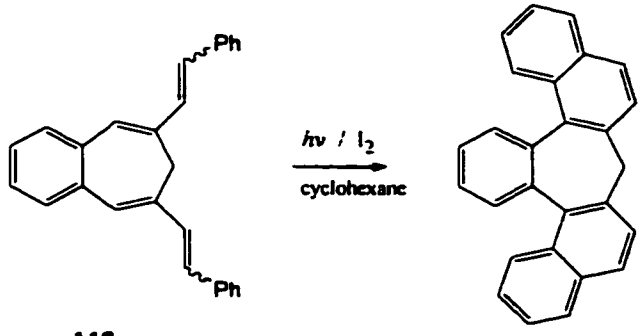
Scheme 71: Synthesis of benzo[c]phenanthrene

Fig. 54: H NMR of benzo[a]phenanthrene



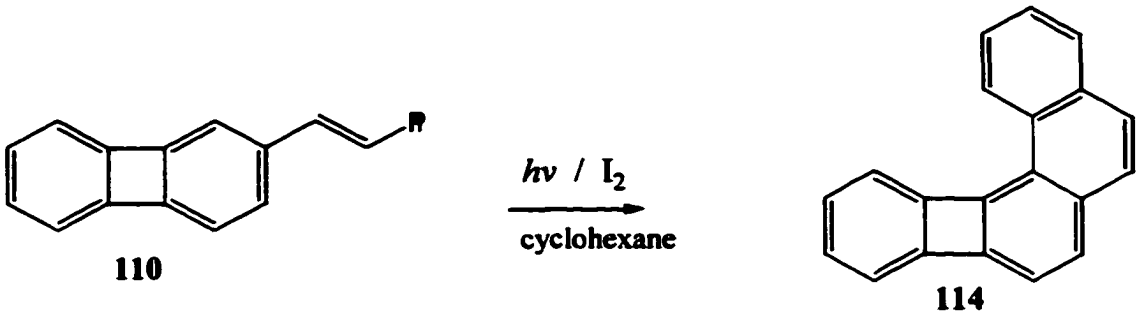
Likewise, the Wittig reaction product **112**, from the condensation of 3,4-benzcycloheptatriene-1,6-dicarboxaldehyde **209** with the phosphonium salt **205** (from benzylbromide) was subjected to oxidative photocyclisation, affording a deep brown-colored compound **113** presumably by the same cyclisation pattern. Compound **113** was established by GCMS and NMR, although the overlaps between similar aromatic protons rendered any attempt to assign individual peak quite difficult.

Scheme 72**: Photocyclisation of 1,6-distyrylbenzocycloheptatriene **112



112 **113**

It remained therefore to apply the methodology to the derivatives of biphenylene starting with the easily accessible 2-styrylbiphenylene **110** which was predicted to cyclise in the pattern of 2-styrylnaphthalene. Thus, 2-biphenylenecarboxaldehyde, synthesized by formylation of biphenylene[211] with chloromethyl methyl ether and stannic chloride, was condensed with the phosphonium salt **205** (obtained from benzylbromide and triphenylphosphine). The resultant 2-styrylbiphenylene **110** was subjected to photochemical cyclodehydrogenation in cyclohexane, first and then in benzene, without yielding the expected result, namely the cyclized product **114**.



110 114

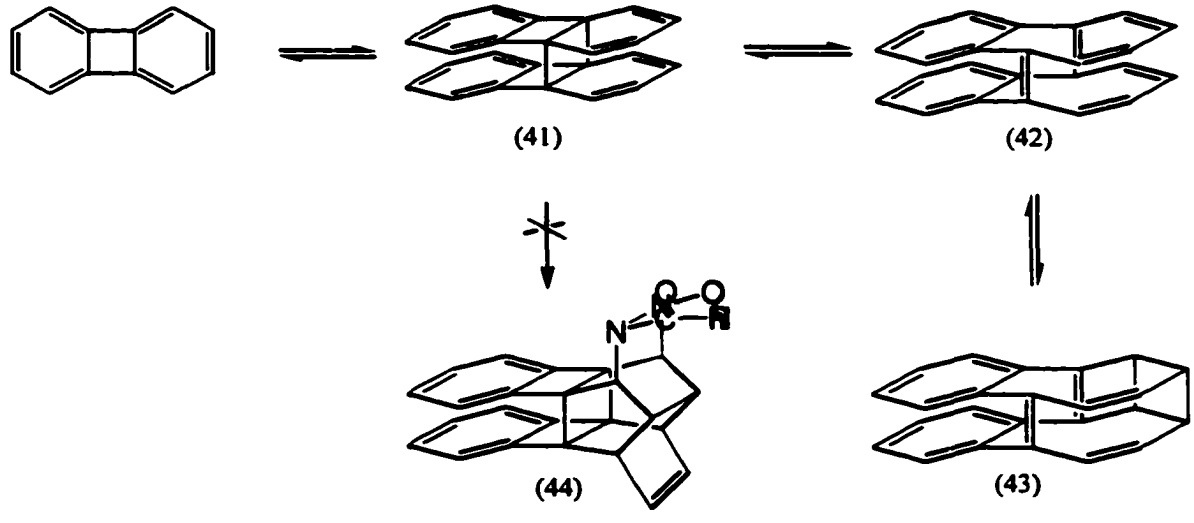
Scheme 73: *Attempted oxidative photocyclization of 2-styrylbiphenylene* ***110***

Instead the starting 2-styrylbiphenylene was recovered despite various modification of the reaction conditions and/or addition of propylene oxide.[212]

Chlorinated styrylbiphenylene **111** was prepared in an attempt to promote cyclisation by elimination of hydrogen chloride. Wittig reaction of 2-formylbiphenylene and the phosphonium salt from *o*-chloro benzylchloride provided **111** in high yield. Oxidative photocyclisation, as above, was attempted on this new system without success, despite changing the solvent system from cyclohexane to benzene and addition of propylene oxide and heating the mixture for longer period of time.

Biphenylene has been reported to dimerise to tetraphenylene in low yield (less than 1%) on photolysis in hexane at 254 nm or 354 nm.[213] Goldman and Ruden found[214] that irradiation of a 1% solution of

biphenylene in hexane deposited a single photodimer (42), the reaction proceeding to near completion in three days but this reaction is further complicated in that biphenylene is allegedly regenerated from (42) by thermal cycloreversion and attempts to trap the presumed intermediate (41)failed.

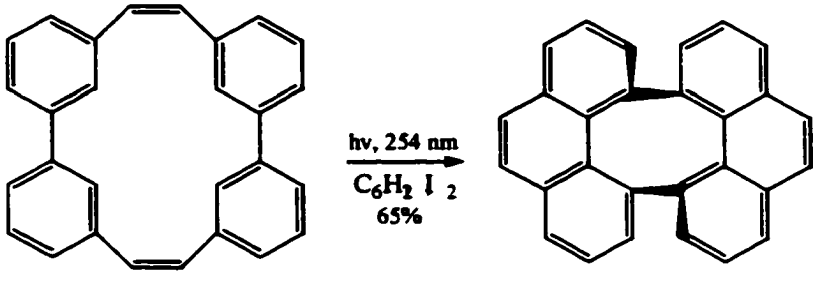


Scheme 74: *Photochemical transformation of biphenylene*

Nevertheless, we reasoned that in the proposed bisvinylbiphenylene **105** intermediate (see scheme 77), which is more rigid, the intramolecular photocyclisation would be favored by virtue of strain release and aromatization.

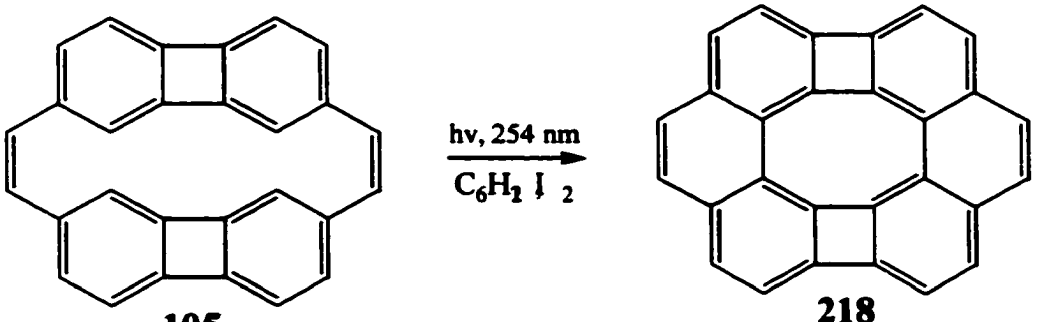
The synthesis by Thulin and Wennerstrom of a closely related compound, bi-4,5-phenanthrylene **116**, by intramolecular photochemical cyclodehydrogenation of [2.0.2.0]metacyclophanediene **115** (fig.) is an encouraging example.[215]

Scheme 75: *Synthesis of bi-4,5-phenanthrylene* ***116***



115 **116**

Since the difference between their system, **115** and ours, **105**, is one of biphenyl (nonplanar) versus biphenylene (planar), cyclisation in our case should readily occur.

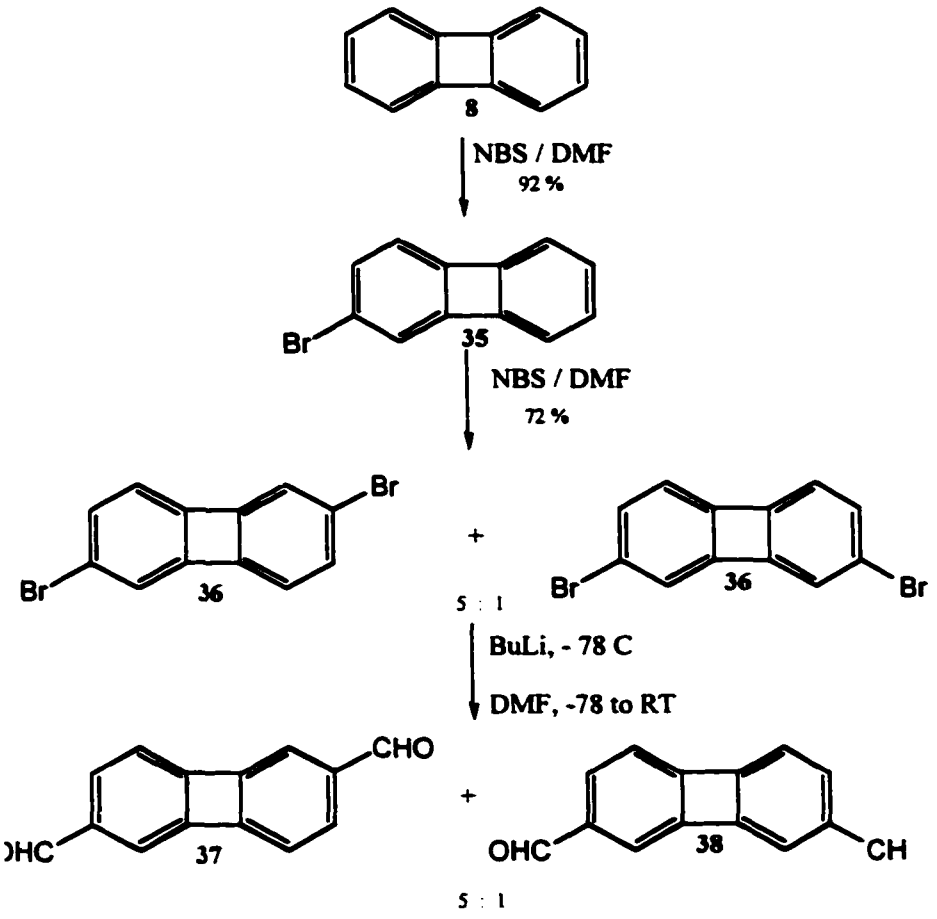


105 **218**

Scheme 76: *Proposed oxidative cyclodehydrogenation of* ***105***

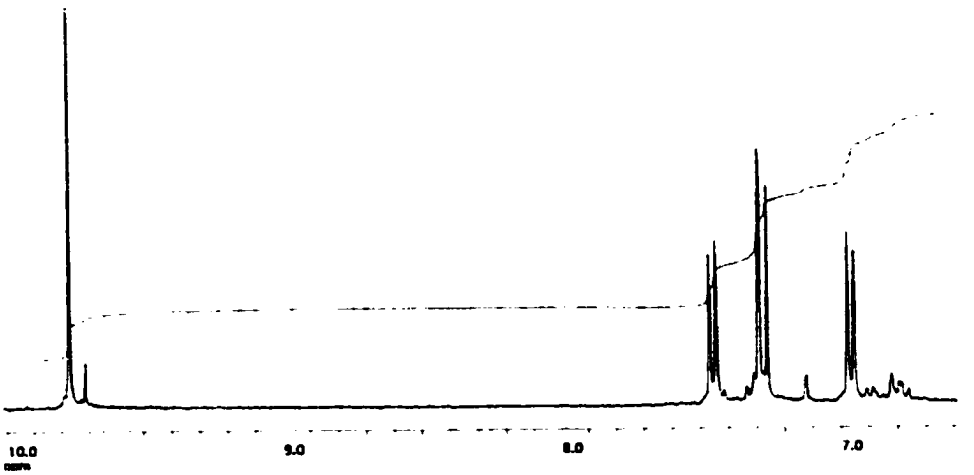
3.4.3. SYNTHETIC APPROACH TO THE 2, 7- AND 2, 6-BIPHENYLENEDICARBOXALDEHYDES

2,7-Biphenylenedicarboxaldehyde **38** was the cornerstone of this synthesis as it constituted the unique starting material in the McMurry dialdehyde coupling or one of them in the double-Wittig dimerisation, along with the bis-ylide salt. Its synthesis, and subsequent separation from its *p*-isomer, 2,6-biphenylenedicarboxaldehyde **37** proceeded in three steps from parent biphenylene **8**.



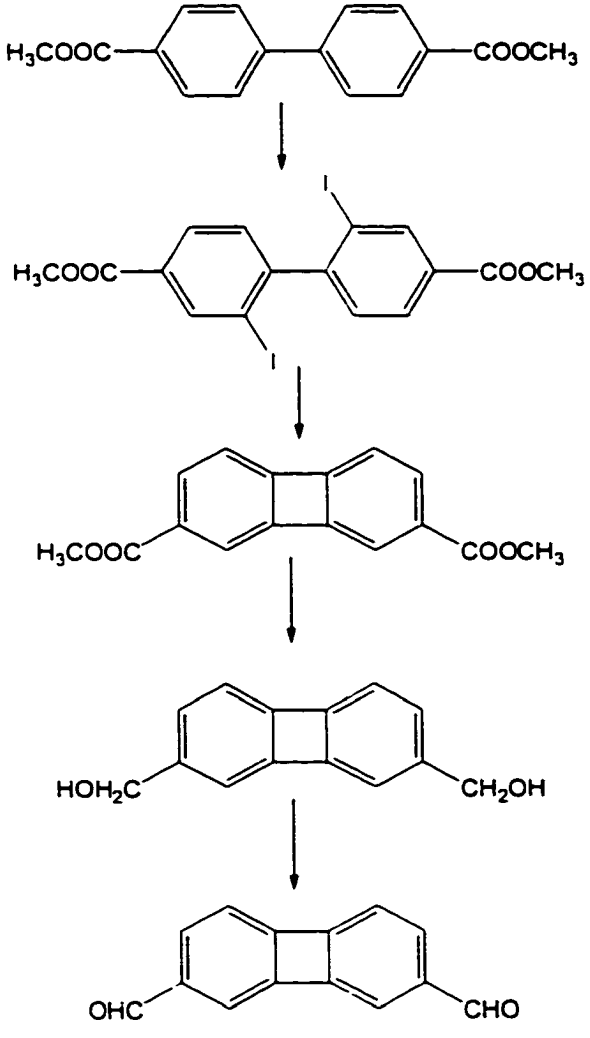
The synthesis started with N- bromosuccinimide bromination of biphenylene in dimethylformamide at room temperature. The resulting 2-bromobiphenylene **35** was subjected to further bromination in the same system (NBS/DMF) to provide a mixture of the 'complimentary' 2,6- and the 'non-complimentary' 2,7- dibromobiphenylene **36** in a ratio of 5 to 1 favoring the 'complimentary' isomer. The two isomers could only be separated by lengthy fractional crystallization. In practice, a mixture of isomers in THF at low temperature (-78 °C) were treated with butyllithium (3 equivalents) and the resulting milky suspension was quenched with excess dimethylformamide. The deep red oil obtained after aqueous workup was then chromatographed in a column of silica gel and eluted with benzene/petroleum ether (1/4), collecting first unreacted 2, 6-dibromobiphenylene as light yellow crystals with a ^{1}H NMR spectrum reminiscent of parent biphenylene, then 2,6-biphenylenedicarboxaldehyde as an orange solid. The desired, deep red 2,7-biphenylenedicarboxaldehyde was collected. The NMR of the 2,7- isomer shows a set of doublets for symmetrical protons (3,4 and 5,6 positions) in addition to the singlets of the remaining positions (1,8) and the aldehyde hydrogen atoms further downfield.

Fig. 55: H NMR of 2,7-biphenylenedicarboxaldehyde



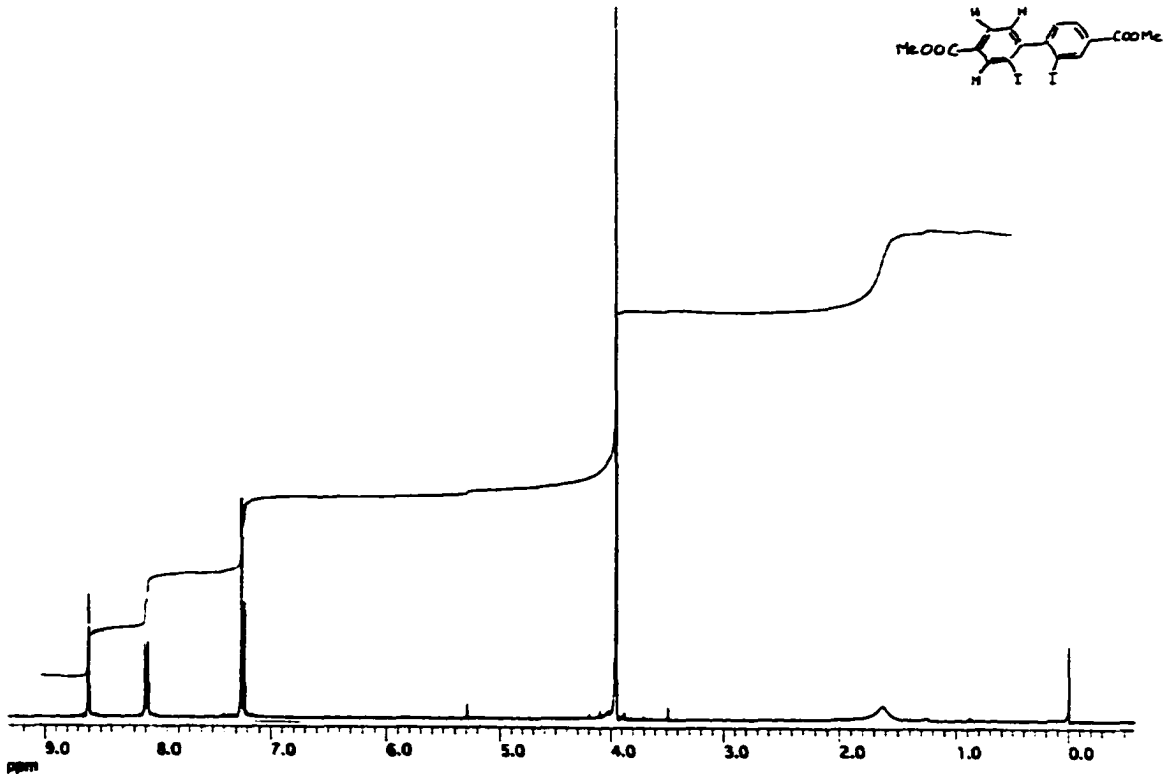
A different approach for the synthesis of 2,7-biphenylene dicarboxaldehyde based on reduction of 2,7-dimethylbiphenylene dicarboxylate was pursued as an alternative. The retrosynthetic scheme is presented below. Key to the implementation of this procedure was the Ullman coupling step to form the biphenylene nucleus.

Scheme 77:



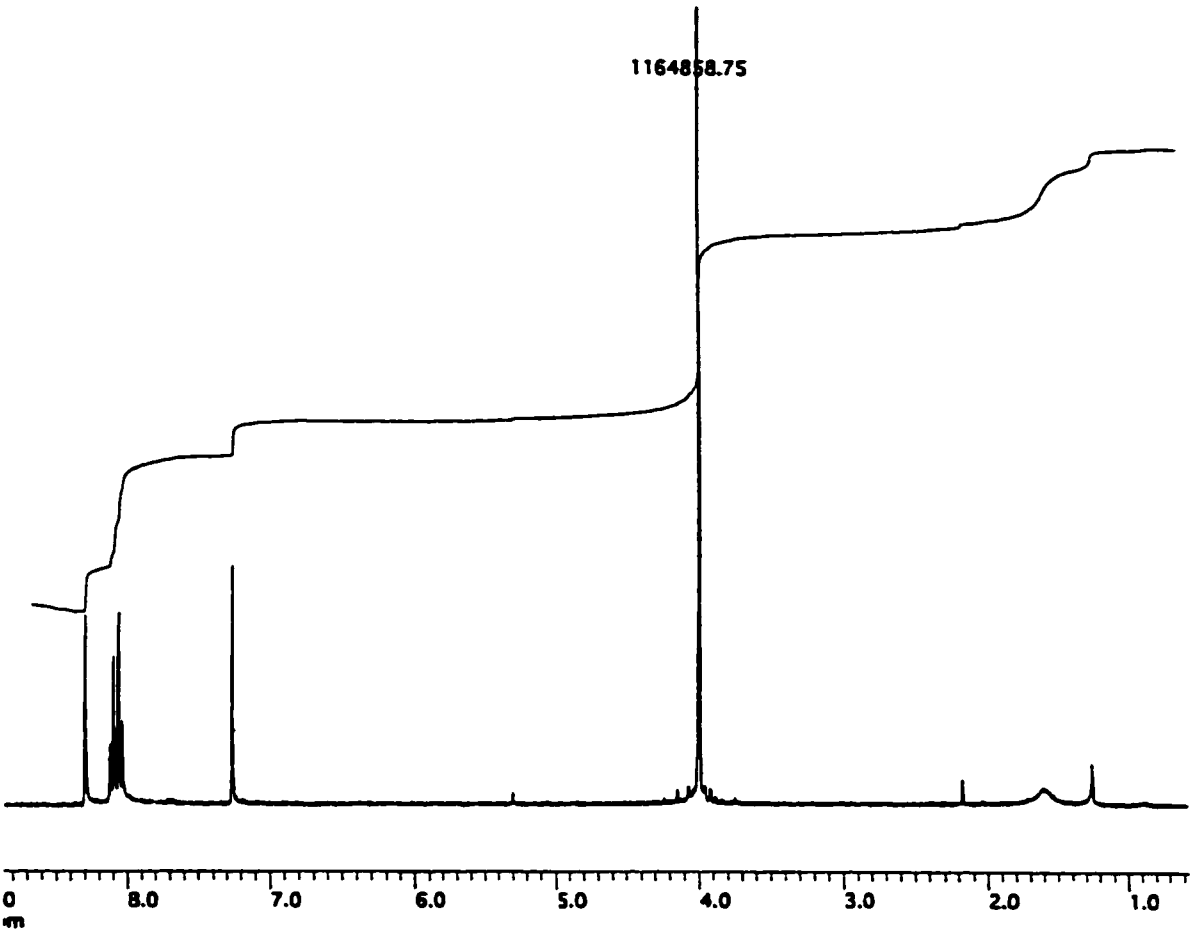
3.4.4. Synthesis of Dimethyl-2,2'-Diiodobihenyl-4,4'-Dicarboxylate

Dimethyl biphenyl-4,4'-dicarboxylate (25g) and 85g silver sulfate were charged into a 500-mL three-necked flask equipped with a mechanical stirrer and dissolved in 300 mL of concentrated sulfuric acid. Iodine (55g) was added to the reaction mixture in several portions. After the addition of iodine the reaction mixture was stirred for 1hr at room temperature. The reaction temperature was then raised to 80 °C and the reaction was continued for 18 hr. After, the reaction mixture was poured over ice and the yellow solid was filtered. The moisture and excess iodine were removed from the precipitate under vacuum at a temperature of 80 °C. The dried solid was extracted in a soxhlet extractor with methanol as solvent for 24hr and the product was crystallized from methanol solution during extraction. Crystals were collected and recrystallized from methanol. The final colorless crystals were obtained in 85% yield and had a melting point of 150-151 °C.



Synthesis of 2,7-dimethylbiphenylene dicarboxylate

This compound was prepared by an Ullman-type aryl coupling of the diiodo-biphenyl derivative (above) in a pyridine solvent. The reaction is dependent on the type of the copper-bronze employed and results were not always reproducible. The highest yield obtained was about 30 % and the diester was separated from the diiodobiphenyl by tedious chromatography. Because of this and the availability of a slightly easier way to access the biphenylenedicarboxaldehyde (above), we did not pursue this route further.



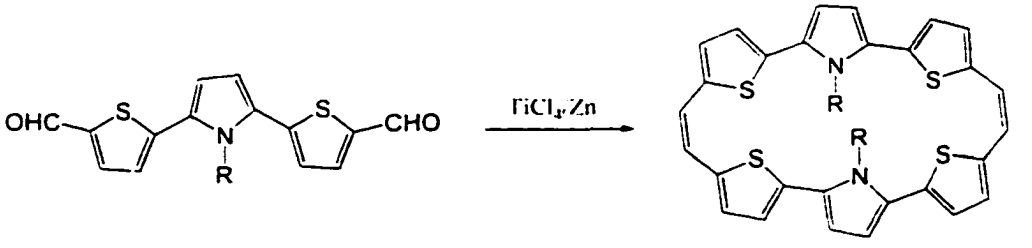
3.4.5. The McMurry coupling of dialdehyde

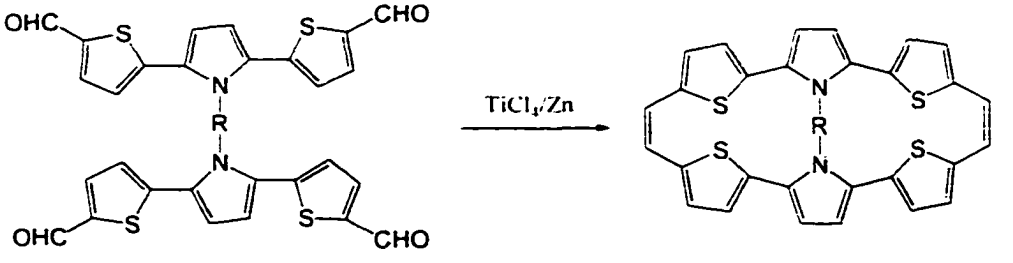
The titanium(IV)chloride mediated coupling of dialdehyde is a powerful metathesis method which has been used to synthesized macrocycles. Recently, Grohmann and Hsu were able to couple the dialdehyde **209** via the McMurry process and, thus, generate the compound **107** and its trans isomer.

Scheme 78: *Grohmann' s synthesis of* ***107*** *via McMurry reaction*

209 **107**

The McMurry reaction was also utilized by Cava et al. in his synthesis of a series of new thiophene--pyrrole-derived annulenes containing 6 and 10

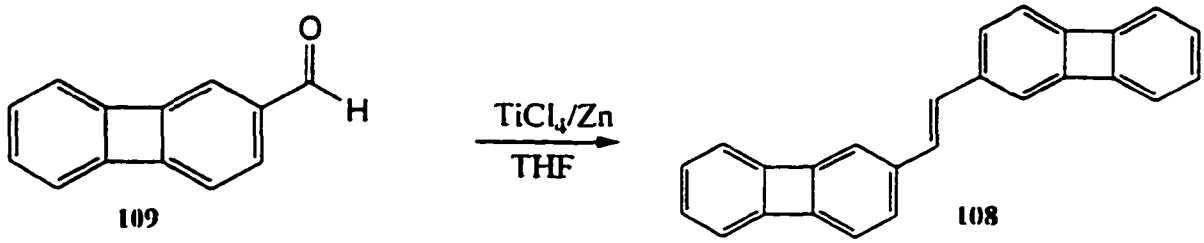




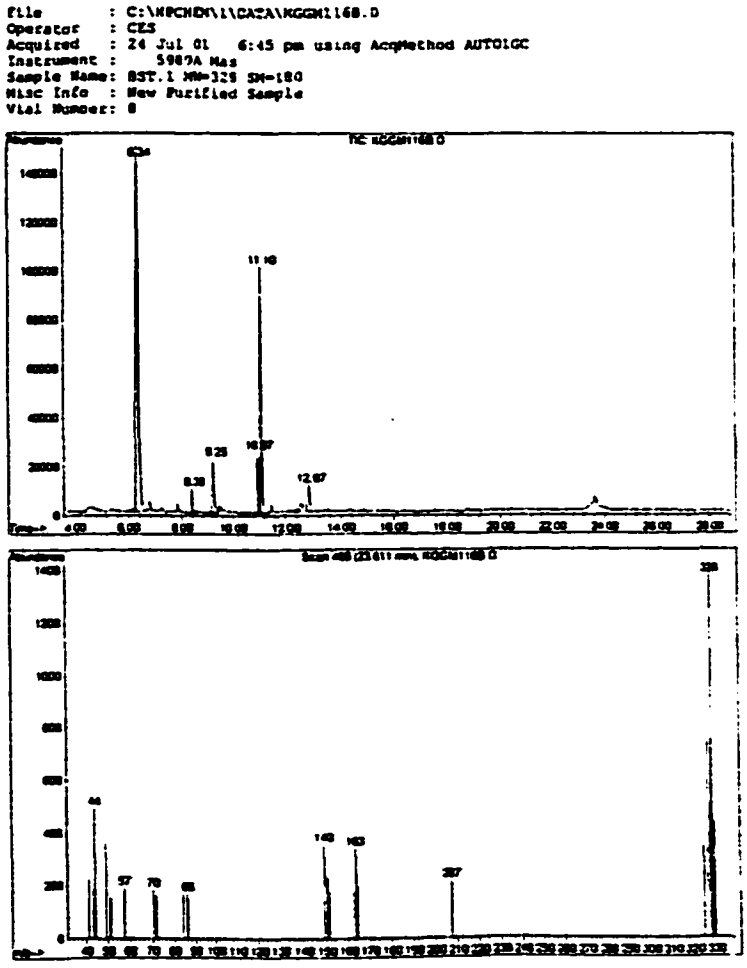
heterocyclic units.

In a preliminary study of the McMurry reaction, 2-formylbiphenylene **109** was subjected to the same conditions as above. GCMS revealed a 13% yield of the coupled compound **108** (below).

***Scheme* 80:**

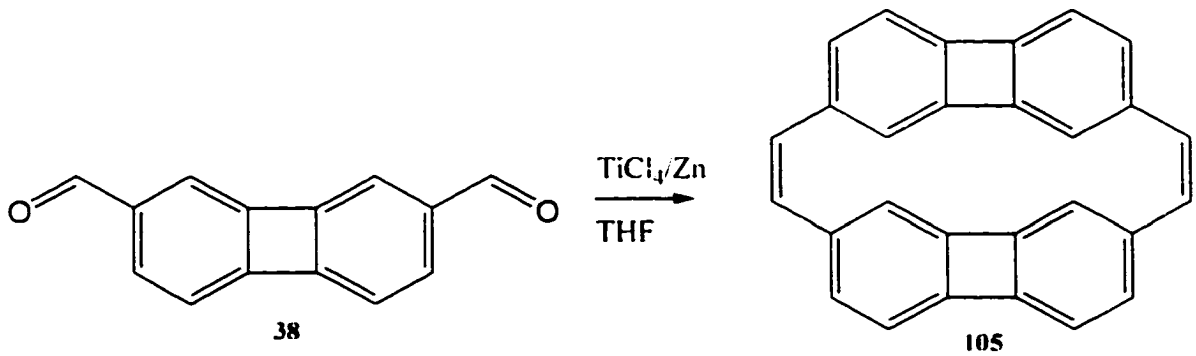


109 **108**



These results suggested that the McMurry reaction on the dialdehyde would be favorable. With an improved synthesis of 2,7-biphenylenedicarboxaldehyde in hand, this synthesis is our next target.

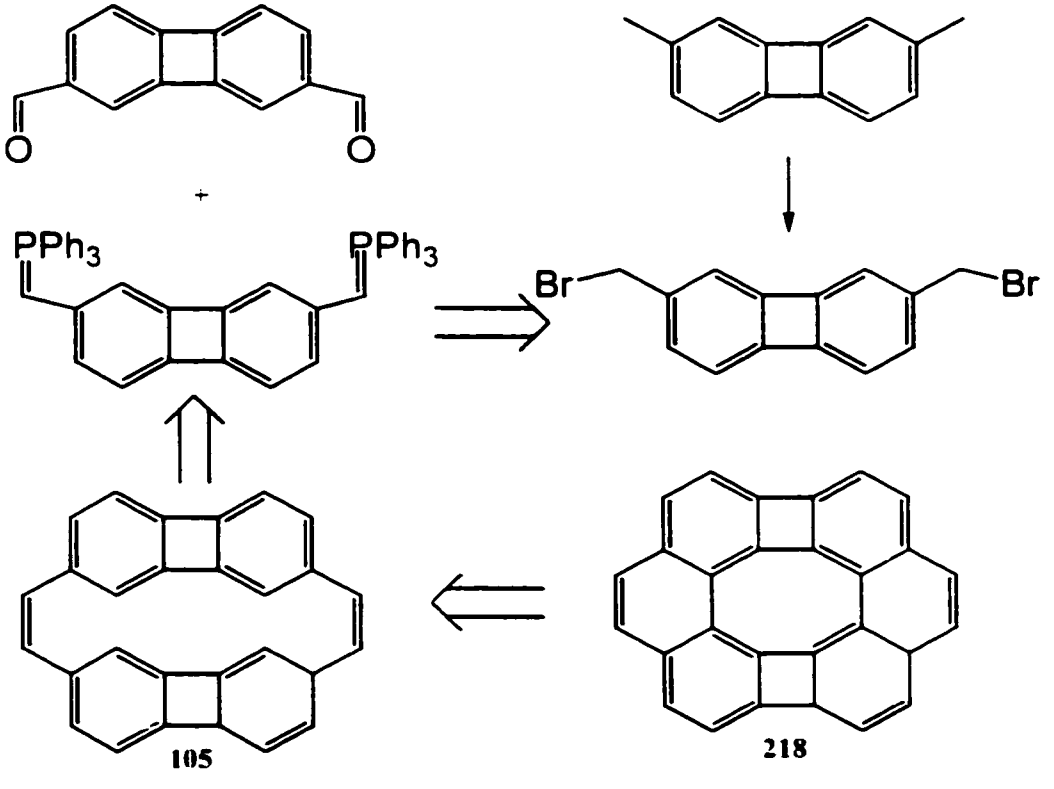
Scheme 80: *McMurry coupling of 2,7-biphenylenedicarboxaldehyde* ***38***



38 **105**

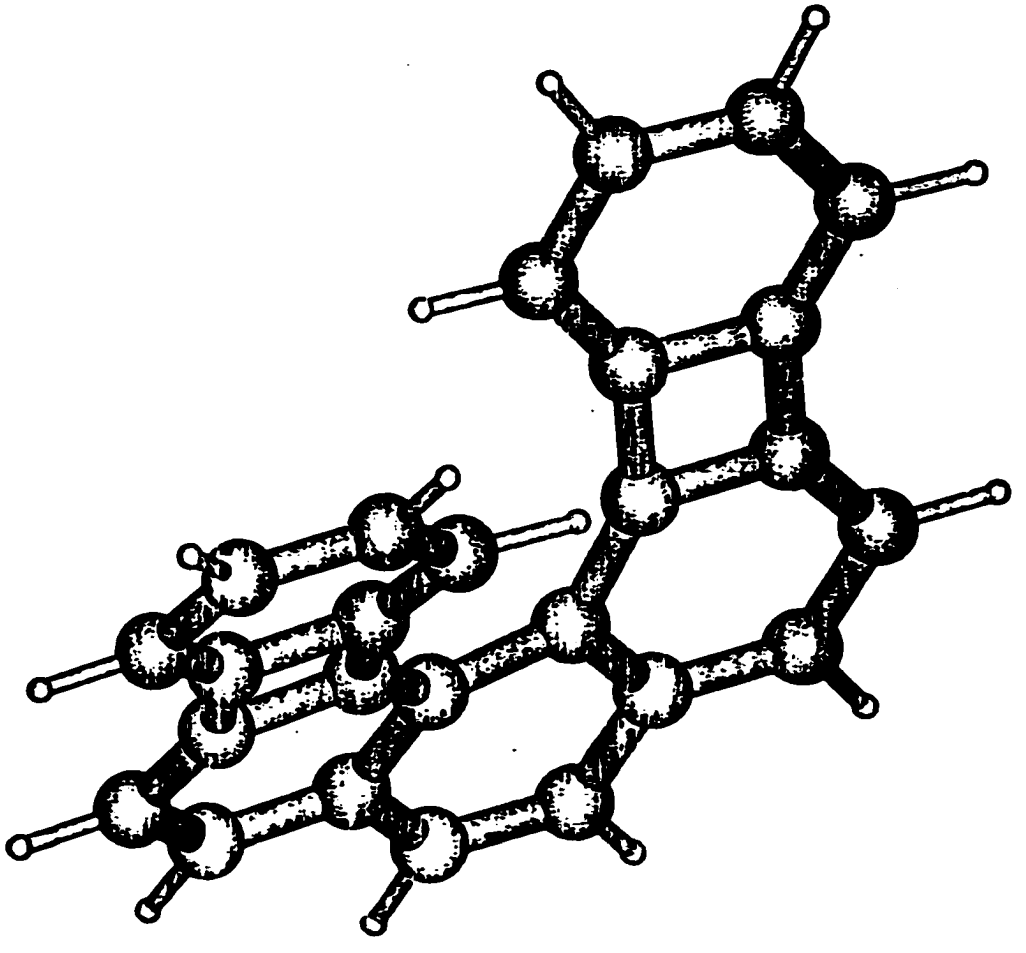
Future direction:

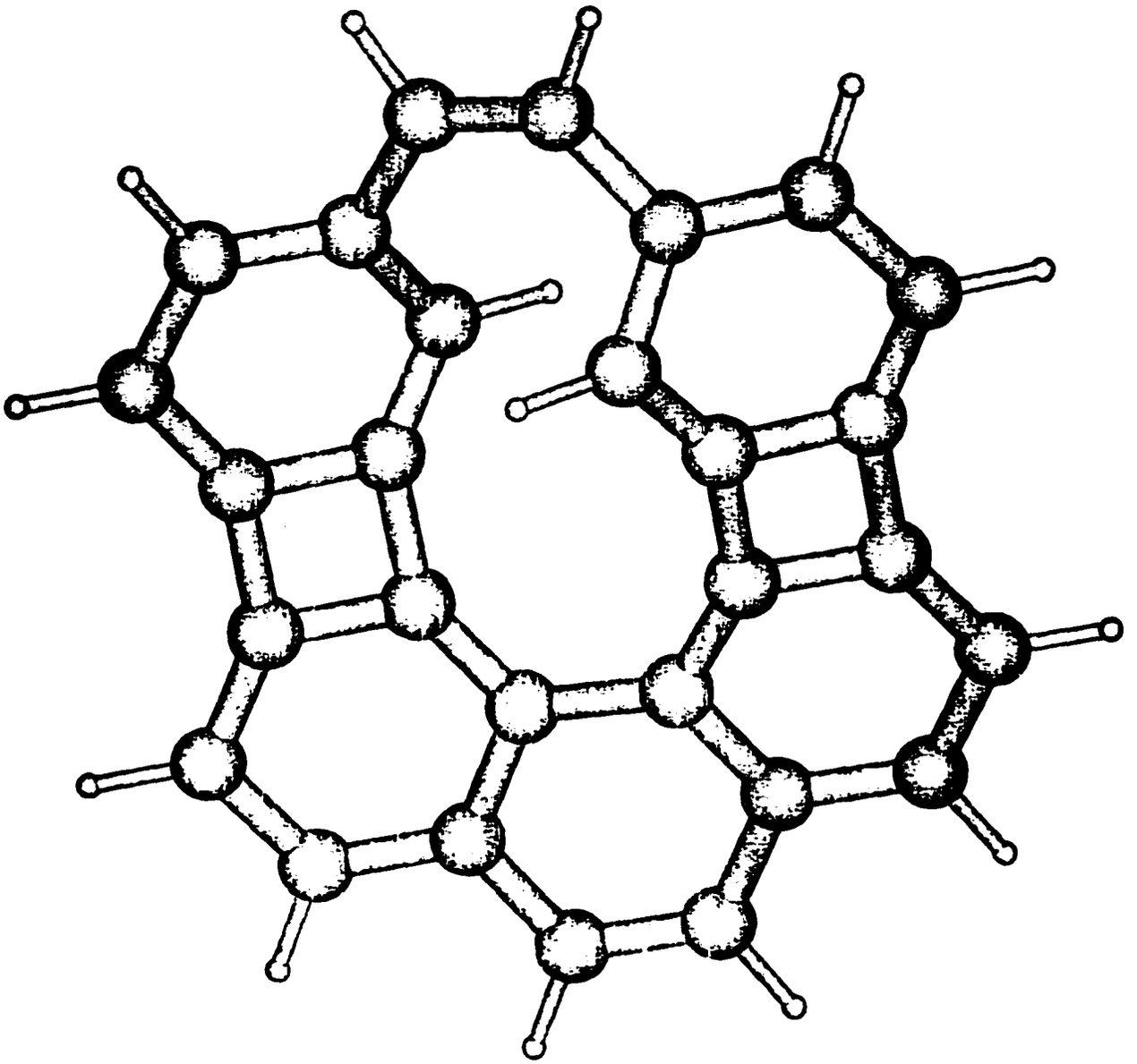
Implementing the protocol described above in order to establish, first, the McMurry metathesis and then, what is foreseen to be a facile oxidative photocyclisation. The McMurry step is bolstered by the possibility of utilizing the bis-Wittig protocol (scheme) which has been the key to the syntheses of numerous otherwise unaccessible intermediates.



Scheme 81: *Proposed Wittig route to* ***218***

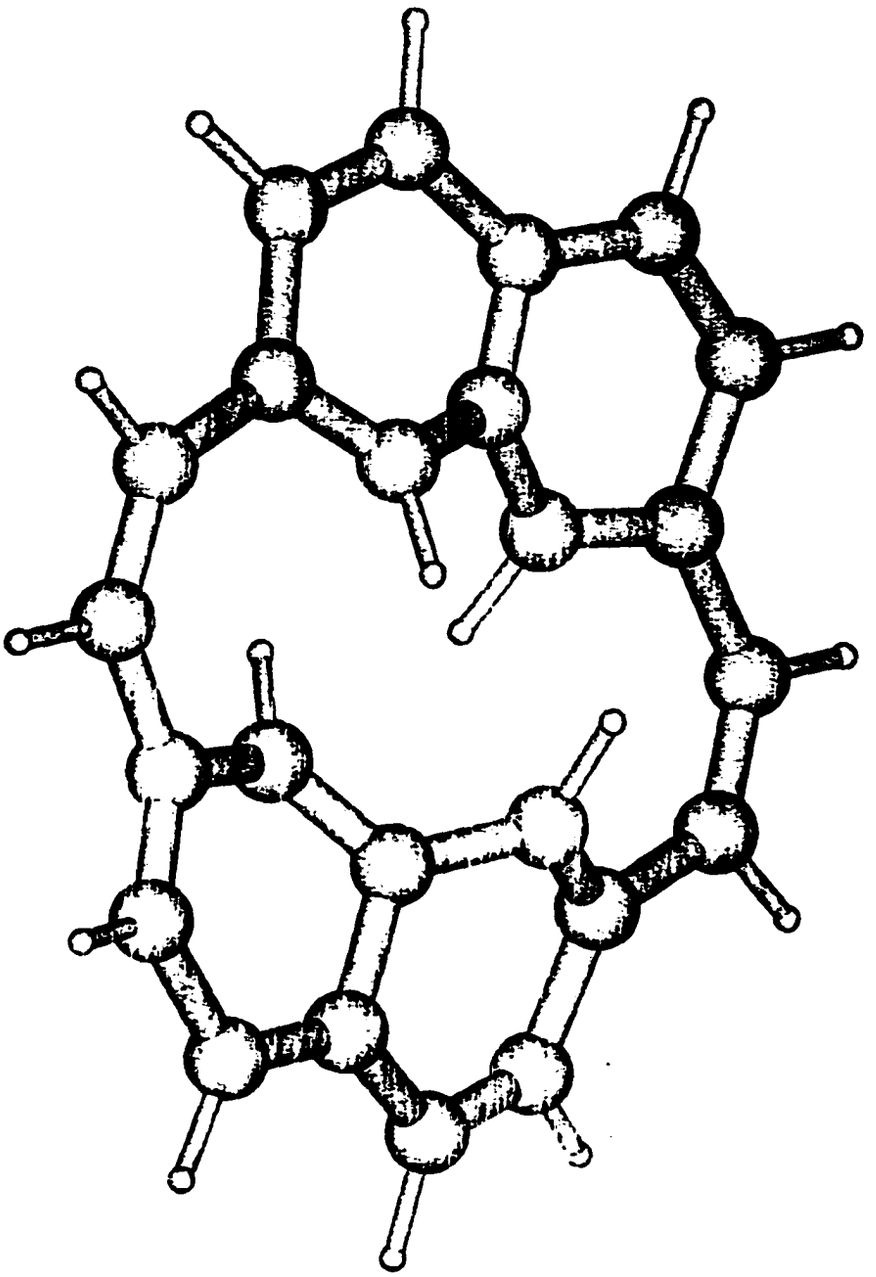
*Molden Drawing of Interesting Intermediate Structures Towards **218** and Theoretically Comparable Structures:*



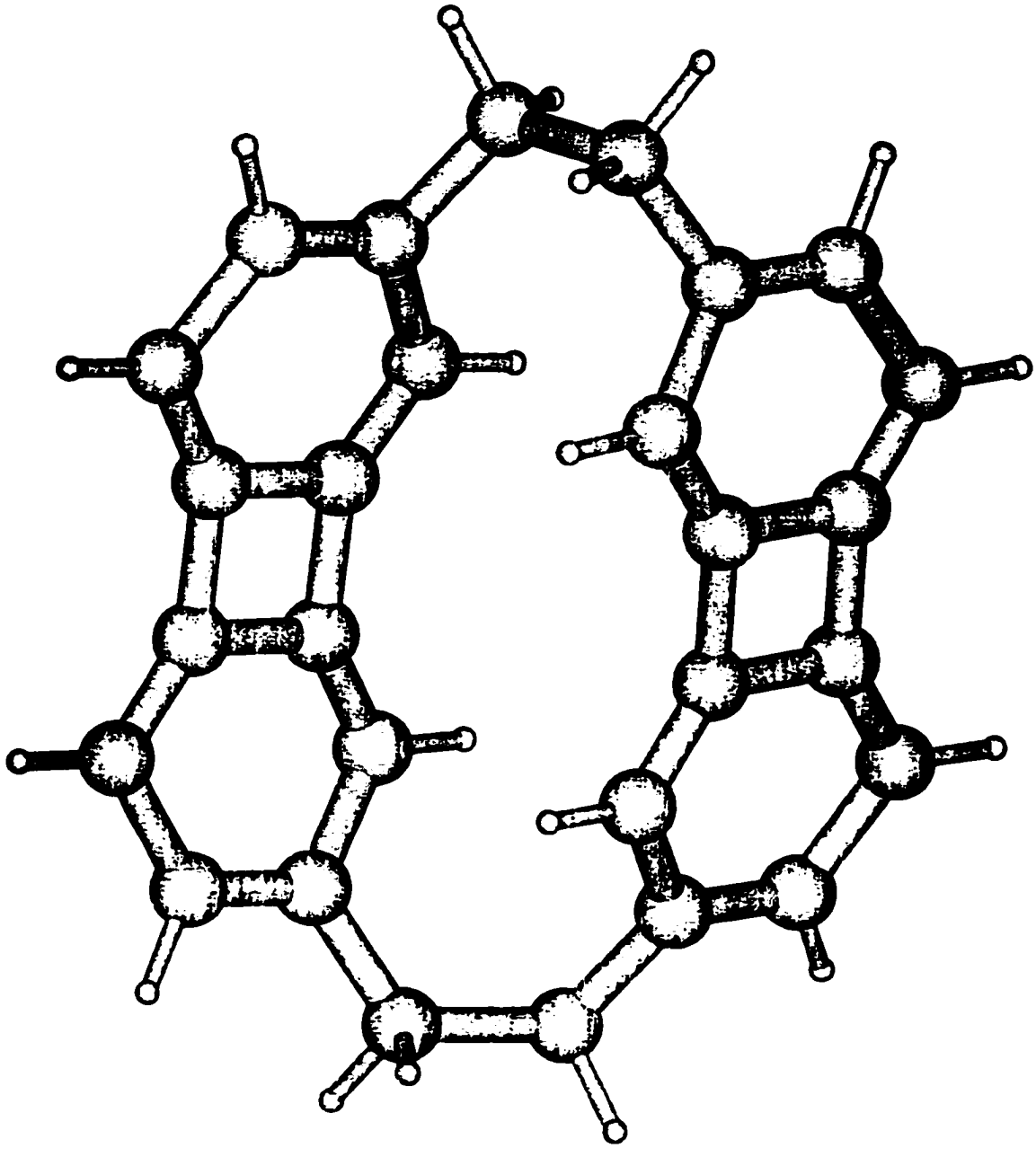


default used

single point



single point
default used



MOLDEN

defaults used

single point

EXPERIMENTAL

General methods- Infrared spectra were recorded on a Perkin-Elmer model spectrometer. ^{1}H and ^{13}C NMR spectra were recorded at 300 MHz unless otherwise noted. All chemical shifts are reported relative to TMS. Mass spectra on a Hewlet Packard 5989 GC-MS seriesII spectrophotometer at the Mass Spectrometry facility of Hunter College. UV-Vis spectra were determined on a Varian spectrophotometer and refer to dichloromethane solutions. Infrared spectra were determined on a BOMEM spectrophotometer with a prism-grating double monochromator. Irradiations were carried out using a Hanovia 400W medium-pressure mercury lamp, surrounded by a water-cooled jacket constructed either in quartz or in pyrex. All reactions were stirred and monitored by Thin Layer Chromatography using UV light. Solvents were removed under reduced pressure on a rotatory evaporator. The flash vacuum pyrolysis experiments were performed with use of a beads-packed quartz tube (40cmX2.0cm i.d.) heated over the central 30cm by an horizontal tube oven. Pressures were measured with a mercury manometer located between the trap on the receiver and the pump, prior to the experiments. Temperatures were measured with a thermocouple placed inside the tube

and near the center and hot zone. Compounds to be pyrolyzed were placed in a quartz/pyrex boat and stoppered before the crystals were sublimed into the tube by heating with a burner. The receiving end of the tube was fitted with a cold-finger quartz flask filled (after the desired temperature of the oven has stabilized) with dry ice and 2-propanol for cooling/trapping the pyrolysate. The apparatus was evacuated, and the oven was heated to the desired temperature. Merck silica gel was used for flash column chromatography. Dichloromethane, hexanes, dimethylformamide (DMF) and ethyl acetate were distilled over calcium hydride. Tetrahydrofuran (THF) was distilled over potassium and the other reagents and solvents used were standard commercial grades.

Me 2-nitro-6-methylphenylazocyanoacetate (1)

2-methyl-6-nitroaniline **41** (7.6g, 50mmol) was dissolved in methanol (75mL) and concentrated hydrochloric acid (16mL) was added, at 0°C the mixture was treated with an excess of sodium nitrite (4.2g) in water (10mL). Me cyanoacetate **42** (5g, 50mmol) in methanol (25mL) was added at 5°C and the mixture was shaken for 1 hour. An excess of sodium acetate (30g) in water (125mL) was slowly added and the mixture was shaken for two additional hours. The precipitate was collected and

recrystallized (from methanol) to give 9.3g (yield: 71%) of an orange solid (m.p.139-140°C).

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ2.52 (s, 3H), 3.95 (s, 3H), 7.25 (t, 1H), 7.52 (d, 1H), 7.95 (d, 1H), 14.1(s broad, 1H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ20, 52.5, 106, 117, 123, 125, 132, 133, 137, 160.5.

IR: vmax 3141 (NH), 2224 (CN), 1710 (C=O), 1501, 1329 (NO_2).

Me 2-amino-6-methylphenylazocyanoacetate (2)

Me 2-nitro-6-methylphenylazocyanoacetate **1** (2.62g, 10mmol) was dissolved in ethyl acetate (250mL) and stirred at 0-5°C in a 300mL hydrogenation flask which was connected to the hydrogenation apparatus after the catalyst Pd-C- has been added. After approximately 6h, the catalyst was filtered off and the resulting mixture was concentrated under reduced pressure to afford reddish crystals which, recrystallized with ethanol gave 2g (90%) of a red solid (m.p.137-138°).

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ2.32 (s, 3H), 3.9 (s, 3H), 5.1 (s broad, 1H), 6.55 (dd, 2H), 6.95 (t, 1H), 13.6 (s broad, 1H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ16, 51, 114, 118, 122, 125, 126, 137, 162.

IR: vmax: 3464, 3365 (NH_2), 3180 (NH), 2214 (CN), 1674 (C=O), 1546, 1384.

Me (7-methylbenzotriazole-1-ylimino)cyanoacetate (3)

To Me 2-amino-6-methylphenylazocyanoacetate **2** (4.68g, 20.2mmol) in methanol (100mL) was added a mixture of sodium nitrite (1.53g, 22.2mmol) in water (25mL). This mixture was added dropwise to a cold-0-5°C- solution of hydrochloric acid (50mL) in water (200mL). The precipitate was collected at the büchner filter and washed with cold water and recrystallized from dilute AcOH to give 3.60g (yield: 75%) of brown needles (m.p. 104-105°C).

^1H NMR (300 MHz, $CDCl_3$): δ2.32 (s, 3H), 4.25 (s, 3H), 7.45 (t, 1H), 7.49 (d, 1H), 8.0 (d, 1H).

IR: vmax: 2222 (CN), 1754 (C=O), 1565, 874.

1-Amino-7-methylbenzotriazole (4)

Me (7-methylbenzotriazole-1-yl-imino)cyanoacetate **3** (3.60g, 15mmol) was refluxed in concentrated hydrochloric acid (80mL) until the solution

was completely homogenous (12 hours). Water (100mL) was added, the solution extracted with ether (3 X 50mL portions) and the ethereal solutions were discarded. The aqueous acid layer was neutralized with solid sodium carbonate, and ether extraction gave a solid which crystallized from benzene-petroleum (b.p. 60-80°C) to give 1.5g (yield: 71%) of 1-amino-7-methylbenzotriazole (m.p.116-118°C).

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ2.8 (s, 3H), 5.8 (s broad, 2H), 7.3(t, 1H and d, 1H), 7.8 (d, 1H).

IR: vmax: 3310, 3194 (NH2), 1654, 1253, 992, 701.

MS (EI): M+ 148, 133, 104, 77, 51, 39 (100%) m/z

2-Methyl-6-nitroiodobenzene (6)

In a 500 mL three-necked round-bottomed flask bearing a low temperature thermometer and an addition funnel, 2-Methyl-6-nitroaniline **41** (15.2-100mmol) were suspended in methanol (75mL) and concentrated HCl (60mL). The mixture was cooled to ca 5°C. Then sodium nitrite (7.5g-110mmol) dissolved in water (30mL) were added dropwise, while maintaining the temperature at 5°C. The diazonium chloride formed were poured into an ice cold aqueous solution of sodium iodide (34g-200mmol). Then, acid workup using $Na_2S_2O_5$ and brine. The ether layer

was dried with magnesium sulfate and evaporated in vacuo to afford (23.72g-95%) of yellowish crystals. Mp. 115-117°C.

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ2.6 (s, 3H), 7.35 (t, 1H), 7.42 (dd, 2H).

4-Methyl-2-nitroiodobenzene (7)

In a 500 mL three-necked round-bottomed flask bearing a low temperature thermometer and a addition funnel, 4-Methyl-2-nitroaniline **43** (30.4g-200mmol) were suspended in methanol (200mL) and concentrated HCl was added (120ml). The mixture was cooled to ca. 5°C. Then sodium nitrite (15.2g-220mmol) dissolved in water (60mL) were added dropwise, while maintaining the temperature at 5°C. The diazonium chloride formed were poured into an ice cold aqueous solution of sodium iodide (60,0g-400mmol). Then acid workup using $Na_2S_2O_5$ and brine. The ether layers were dried in magnesium sulfate and evaporate in vacuo to afford (40.25g) of yellowish crystals. Mp. 117-119°C.

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ2.4 (s, 3H), 7.05 (d, 1H), 7.7 (s, 1H), 7.85 (d, 1H).

MS (EI): M+ 226, 210, 196, 152, 115, 77 (100%) m/z:

Biphenylene (8)

A solution of anthranilic acid **44** (34.2-0.25mol), trichloroacetic acid (0.3g) in THF (250mL) was prepared in a (600mL) beaker equipped with a thermometer and cooled in an ice-water bath. The solution was stirred and isoamyl nitrite (55mL-48g-0.41mol) was added over a period of 1-2 min. The reaction mixture was maintained at 18-25 °C (deep red color) and stirred for about 1-1.5h (orange precipitate had formed and was gradually being converted into a bright tan precipitate). The precipitate was cooled to ca. 10 °C and collected via suction filtration with a plastic (caution) büchner funnel because of the danger of detonation, a three-way adapter providing the means of controlling the rate of filtration such as the cake is maintained wet . The wet cake was washed with ice-cold THF and an ice-cold 1,2-dichloroethane until the washings were colorless. The slurry was carefully poured (through a plastic funnel) into a 2000mL beaker containing boiling 1,2-dichloroethane and the plastic büchner was thoroughly washed with 1,2-dichloroethane. The solution was covered with a watch glass and gently boiled over 1h. After the frothing has receded, the red-brown mixture is cooled and transferred into a round-bottomed flask equipped with a Claisen distillation column and a water-

cooled condenser. 1,2-Dichloroethane (bp. 83-84 °C) was distilled (oil bath) first with stirring in order to maintain even ebullition, and when about 75mL of a dark residue was left in the flask, about 300mL of ethylene glycol was added into the flask, a fractional column replaced the Claisen column and the mixture was distilled using a water-pump, collecting the fraction up to 95°C.

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ6.62(AA'BB", 4H), 6.72(AA'BB', 4H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ118, 129, 152.

MS (EI): M+ 152, 76 (100%) m/z;

1,5 + 1,8-Dimethylbiphenylene (5) (method of Friedman and Logullo)

A solution of 6-methylanthranilic acid **45** (45.0g-0.25mol), trichloroacetic acid (0.3g) in THF (250mL) was prepared in a 600mL beaker equiped with a thermometer and cooled in an ice-water bath. The solution was stirred and isoamyl nitrite (55mL) was added over a period of 1-2 min. The reaction mixture was maintained at 18-25 °C (deep red color) and stirred for about 1-1.5h (orange precipitate had formed and was gradually being converted into a bright tan precipitate). The precipitate was cooled to ca. 10 °C and collected via suction filtration with a plastic (caution)

büchner funnel because of the danger of detonation, a three-way adapter providing the means of controlling the rate of filtration such as the cake is maintained wet . The wet cake was washed with ice-cold THF and an ice-cold 1,2-dichloroethane until the washings were colorless. The slurry was carefully poured (through a plastic funnel) into a 2000mL beaker containing boiling 1,2-dichloroethane and the plastified büchner funnel was thoroughly washed with 1,2-dichloroethane. The solution was covered with a watch glass and gently boiled over 1h. After the frothing has receded, the red-brown mixture is cooled and transferred into a round-bottomed flask equipped with a Claisen distillation column and a water-cooled condenser. 1,2-Dichloroethane (bp.83-84°C) was distilled (oil bath) first with stirring in order to maintain even ebullition, and when about 75mL of a dark residue was left in the flask, about 300mL of ethylene glycol was added into the flask, a fractional column replaced the Claisen column and the mixture was codistilled using a water-pump, collecting the fraction up to 95 °C. The yield, 4.4-5.6g-21-30%- is based on methylanthranilic acid.Mp. 109-112°C.

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ2.1(s, 6H), 2.2(s, 6H), 6.45(d, 4H), 6.57(ABB'A', 8H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ18, 19, 126.5, 127, 127.8, 128, 129.5, 130, 148, 150, 151, 152.

MS (EI): M+ 180, 165, 152 (100%) m/z;

1,5-and 1,8-Dimethylbiphenylene (5) (method of Rees)

To a suspension of lead tetraacetate (2.3g-5.2mmol) in dichloromethane (45mL) at 20°C was added, dropwise, a solution of 7-methyl-1-aminobenzotriazole **4** (1g-4.4mmol) in methylene chloride (30mL). Immediate vigorous reaction followed with increase of temperature to ca. 30°C and formation of a white precipitate. After 60 min, the reaction mixture was filtered and the filtrate was washed with water and brine (2x100mL) and extracted with dichloromethane (2x200mL), dried over $MgSO_4$ and evaporated to yield a pale yellow solid, identical to the product above. Yield 2.00g (80 %), mp.109-112°C.

2,6-and 2,7-Dimethylbiphenylene (5) (method of Rees)

To a suspension of lead tetraacetate (2.3g-5.2mmol) in dichloromethane (45mL) at 20°C was added, dropwise, a solution of 5-methyl-1-aminobenzotriazole **46** (1.13g-4.8mmol) in methylene chloride (50mL). Immediate vigorous reaction followed with increase of temperature to ca. 30°C and formation of a white precipitate. After 60 min, the reaction mixture was filtered and the filtrate was

washed with water and brine (2x100mL) and extracted with dichloromethane (2x200mL), dried over $MgSO_4$ and evaporated to yield a pale yellow solid, identical to the product above. Yield 1.00g (89 %), mp.149-155°C.

^1H NMR (300 MHz, $CDCl_3$, TMS): δ2.4(s, 12H), 6.5(ABB'A', 8H), 6.6(s, 4H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ20, 114.8, 114.9, 116.9, 117, 125, 125.1, 135.9, 136, 147.9, 148.

MS (EI): M+ 182, 167, 152, 89, 76 (100%) m/z;

MS (EI): M+ 180, 165, 152, 89, 76 (100%) m/z;

2-Bromo-4-methyl-6-nitroiodobenzene (9)

In a 500 mL three-necked round-bottomed flask bearing a low temperature thermometer and a addition funnel, 2-bromo-4-Methyl-6-nitroaniline **48** (2.31g-0.01mol) were suspended in concentrated HCl (20mL). The mixture was cooled to ca 5°C. Then sodium nitrite (0.83g-12mmol) dissolved in water (10mL) were added dropwise, while maintaining the temperature at 5°C. The diazonium chloride formed were poured into an ice cold aqueous solution of sodium iodide (3g-20mmol). Then acid workup using $Na_2S_2O_5$ and brine. The ether layers were dried in

magnesium sulfate and evaporate in vacuo to afford (2.65g-80%) of yellowish crystals.

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ2.4(s, 3H), 7.34(s, 1H), 7.7(s, 1H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ21, 91.5, 124, 133, 136.2, 142, 157.

2-Iodo-4-methyl-6-nitroiodobenzene (10)

In a 50mL three-necked round-bottomed flask bearing a low temperature thermometer and an addition funnel, 2-Iodo-4-Methyl-6-nitroaniline **49** (2.78g-0.01mol) were suspended in methanol (10mL) and concentrated HCl (10mL). The mixture was cooled to ca. 5°C. Then sodium nitrite (0.69g-0.01mol) dissolved in water (10mL) were added dropwise, while maintaining the temperature at 5°C. The diazonium chloride formed were poured into an ice cold aqueous solution of sodium iodide (3g-0.02mol). Then acid workup using $Na_2S_2O_5$ and brine. The ether layers were dried in magnesium sulfate and evaporate in vacuo to afford (3.3g-92%) of yellowish crystals.

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ2.5(s, 3H), 8.0(s, 1H), 8.1(s, 1H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ22, 102, 126, 138, 142, 145, 147.5.

2,2'-Dimethyl-6,6'-dinitrobiphenyl (11)

The iodide **6** (5.3g-) was dissolved in dry DMF in a 100-mL round-bottomed flask fitted with a stirrer. Cu dust (6.0g) were added and the mixture was refluxed for 4h. The mixture was cooled before additional Cu dust (6.0g) were added and the mixture refluxed for an additional 4h. The cooled mixture were poured upon an ice water beaker and extracted with ether, washing the combined ether layer with brine and drying with $MgSO_4$. Evaporating the solvent in vacuo afforded 4.56g (85%) yellow crystals.

^1H NMR (300 MHz, $CDCl_3$, TMS): δ2.05 (s, 6H), 7.49 (t, 2H), 7.59 (d, 2H), 8.0 (d, 2H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ20, 123, 129, 132, 136, 138.5, 148.5.

4.4'-Dimethyl-2,2'-dinitrobiphenyl (12)

The iodide **7** (3.50g) was dissolved in dry DMF (50mL) in a 100-mL round-bottomed flask fitted with a stirrer. Cu dust (5.0g) were added and the mixture was refluxed for 4h. The mixture was cooled before additional Cu dust (2.5g) were added and the mixture refluxed for an additional 4h. The cooled mixture were poured upon an ice water beaker and extracted

with ether, washing the combined ether layer with brine and drying with $MgSO_4$. Evaporating the solvent in vacuo afforded yellow crystals, 2.06g, 80% yield, mp. 138-40°C (recrystallized from ethanol).

^1H NMR (300 MHz, $CDCl_3$, TMS): δ2.5 (s, 6H), 7.1 (d, 2H), 7.45 (d, 2H), 7.92 (s, 2H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ22, 126, 132, 132.2, 135, 140.2.

2,2'-Dimethyl-6,6'-diiodobiphenyl (13)

^1H NMR (300 MHz, $CDCl_3$, TMS): δ2.01 (s, 6H), 7.0 (t, 2H), 7.28 (d, 2H), 7.80 (d, 2H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ22.0, 101.5, 130, 131, 137.3, 138, 148.

2,2'-Dibromo-4,4'-dimethyl-6,6'-dinitrobiphenyl (14)

The iodide **9** (2.0g-5.85mmol) was dissolved in dry DMF in a 100-mL round-bottomed flask fitted with a stirrer. Cu dust (3.0g) were added and the mixture was refluxed for 4h. Then the mixture were cooled before additional Cu dust (3.0g) were added and the mixture refluxed for an additional 4h. The cooled mixture were poured upon an ice water beaker and extracted with ether, washing the combined ether layer with brine and

drying with $MgSO_4$. Evaporating the solvent in vacuo afforded 1.0g of almost pure yellow crystals.

^1H NMR (300 MHz, $CDCl_3$, TMS): δ2,5(s, 6H), 7.8(s, 2H), 8.05(s, 2H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ21, 91.5, 124, 133, 136.2, 142, 157.

2,2'-Diiodo-4,4'-dimethyl-6,6'-dinitrobiphenyl (15)

The iodide **10** (0.78g-2mmol) was dissolved in dry DMF in a 100 mL round-bottomed flask fitted with a stirrer. Cu dust (1g) were added and the mixture was refluxed for 4h. The mixture was cooled before additional Cu dust (1g) were added and the mixture refluxed for an additional 4h. The cooled mixture were poured upon an ice water beaker and extracted with ether, washing the combined ether layer with brine and drying with $MgSO_4$. Evaporating the solvent in vacuo afforded 300mg of yellow crystals.

^1H NMR (300 MHz, $CDCl_3$, TMS): δ2.55(S, 6H), 8.1(s, 2H), 8.15(s, 2H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ21.5, 102, 126, 138.5, 142, 145.8, 146.5.

MS (EI): M+ 524, 397, 351, 224, 167, 97 (100%) m/z:

2,2'-Dichloro-6,6'-dinitrobiphenyl (16)

1,2-dichloro-3-nitrobenzene **50** (10.0g), Cu dust (5.0g) was suspended over DMF (80mL) into an oven-dried 50-mL round-bottomed flask equipped with a stiirrer. The mixture was refluxed overnight before additional Cu dust (5.0g) were added and reflux resumed for an additional 4h. Usual workup followed filtration of the inorganic material and the organic layer was dried and evaporated to yield 6,7g- 90% of the desired product. Mp. 105-107 °C.

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ7.6 (t, 2H), 7.8 (d, 2H), 8.2 (d, 2H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ124.0, 130.6, 131.1, 135.2, 135.8.

MS (EI): M+ 312, 266, 203, 175, 140, 75 (100%) m/z:

4,4'-Dichloro-2,2'-dinitrobiphenyl (116)

1,4-dichloro-3-nitrobenzene **51** (10.0g), Cu dust (5.0g) was suspended over DMF (80mL) into an oven-dried 50-mL round-bottomed flask equipped with a stiirrer. The mixture was refluxed overnight before additional Cu dust (5.0g) were added and reflux resumed for an additional 4h. Usual workup followed filtration of the inorganic material and the

organic layer was dried and evaporated to yield 7g- 93% of the desired product. Mp. 119-120 °C.

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ7.26 (d, 2H), 7.68 (dd, 2H), 8.4 (s, 2H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ126.0, 132, 132.6, 134.1, 136.2, 146.5.

1,10-Dimethylbenzocinnoline (17)

An oven-dried 200-mL three-necked round-bottomed flask equipped with a magnetic stirrer, an addition funnel, a condenser and nitrogen inlet, was charged with $LiAlH_4$ (1.9g) in suspension in dry diethyl ether (30mL). A solution of 2,2"-dimethyl-6,6'-dinitrobiphenyl **11** (2.72g-10mmol) in dry benzene (40mL) was added dropwise over a 40 min period. The mixture was stirred an additional 30min and water was carefully added to the mixture and the mixture was extracted with ether. The combined ether layers were dried over anhydrous $MgSO_4$. Removal of the solvent in vacuo afforded 1.7g-83% of yellow crystals that were further purified by column chromatography using Hexanes/EtOAc:3/1. Mp. 74-76 °C.

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ2.65 (s, 6H), 7.7 (d, 2H), 7.8 (t, 2H), 8.5 (d, 2H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS) δ22.1, 121, 128, 128.5, 133, 134, 146.2.

3,8-Dimethylbenzo[*c*]cinnoline (18)

An oven-dried 200-mL three-necked round-bottomed flask equipped with a magnetic stirrer, an addition funnel, a condenser and nitrogen inlet, was charged with $LiAlH_4$ (2.0g-50mmol) in suspension in dry diethyl ether (30mL). A solution of 2,2'-dinitro-4,4'-dimethylbiphenyl **12** (2.72g-10mmol) in dry benzene (40mL) was added dropwise over a 40 min period. The mixture was stirred an additional 30min and water was carefully added to the mixture and the mixture was extracted with ether. The combined ether layers were dried over anhydrous $MgSO_4$. Removal of the solvent in vacuo afforded yellow crystals (1.72g, 88 %) that were further purified by column chromatography using Hexanes/EtOAc:3/1.

^1H NMR (300 MHz, $CDCl_3$, TMS): δ2.7 (s, 6H), 7.7 (d, 2H), 8.4 (d, 2H), 8.5 (s, 2H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS):δ22, 118.5, 121, 130, 133.5, 139, 145.5.

MS (EI): M+ 208, 179, 165, 152, 76 (100%) m/z:

1,10-Dibromo-3,8-dimethylbenzo[*c*]cinnoline (19)

An oven-dried 200-mL three-necked round-bottomed flask equipped with a magnetic stirrer, an addition funnel, a condenser and nitrogen inlet, was charged with $LiAlH_4$ (1.06g) in suspension in 30mL of dry diethyl ether. A solution of 2,2'-dibromo-4,4'-dimethyl -6,6'-dinitrobiphenyl **14** (0.98g) in dry benzene (40mL) was added dropwise over a 40 min period. The mixture was stirred an additional 30min and water was carefully added to the mixture and the mixture was extracted with ether. The combined ether layers were dried over anhydrous $MgSO_4$. Removal of the solvent in vacuo afforded 420mg-81% of yellow crystals that were further purified by column chromatography using Hexanes/EtOAc:3/1.

^1H NMR (300 MHz, $CDCl_3$, TMS): δ2.65(s, 6H), 7.94(s, 2H), 8.41(s, 2H).

1,10-Dichlorobenzo[*c*]cinnoline (20)

An oven-dried 200 mL-three-necked round-bottomed flask equipped with a magnetic stirrer, an addition funnel, a condenser and nitrogen inlet, was charged with LiAlH4 (1g) in suspension in 30mL of dry diethyl ether. A solution of 2,2'-dichloro-6,6'-dinitrobiphenyl **16** (1.62g) in dry benzene (40mL) was added dropwise over a 40 min period. The mixture was

stirred an additional 30min and water was carefully added to the mixture and the mixture was extracted with ether. The combined ether layers were dried over anhydrous $MgSO_4$. Removal of the solvent in vacuo afforded 1.2g-84% of yellow crystals that were further purified by column chromatography using Hexanes/EtOAc:3/1. Mp. 74-76 °C.

^1H NMR (300 MHz, $CDCl_3$, TMS): δ7.86 (t, 2H), 7.94 (d, 2H), 8.63 (d, 2H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ118.9, 129.3, 130.1, 131.9, 133.9, 147.6.

MS (EI): M+ 248, 220, 185, 150, 75 (100%) m/z:

3,8-Dichlorobenzo[*c*]cinnoline (120)

An oven-dried 200-mL three-necked round-bottomed flask equipped with a magnetic stirrer, an addition funnel, a condenser and nitrogen inlet, was charged with LiAlH4 (1g) in suspension in 30mL of dry diethyl ether. A solution of 4,4'-dichloro-2,2'-dinitrobiphenyl **116** (1.62g) in dry benzene (40mL) was added dropwise over a 40 min period. The mixture was stirred an additional 30min and water was carefully added to the mixture and the mixture was extracted with ether. The combined ether layers were dried over anhydrous $MgSO_4$. Removal of the solvent in vacuo afforded

1.36g-88% of yellow crystals that were further purified by column chromatography using Hexanes/EtOAc:3/1.

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ7.92 (d, 2H), 8.52 (d, 2H), 8.8 (s, 2H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ119.9, 123.9, 131.5, 133.6, 135.9, 146.

MS (EI): M+ 220, 185, 151, 101, 85 (100%) m/z;

1,8-Dimethylbiphenylene (21) By The Lothrop Synthesis

100 Mg of compound **13** was heated into dissolution in oil bath at 160°C and Cu powder was added in portion (5x20mg). The temperature was raised to ca. 240°C and the mixture was left to reflux during 4h. Upon cooling and treatment with ice-cold water, the precipitate was extracted with dichloramethane (2x100mL). The organic extracts were washed with water and brine and dried over magnesium sulfate and evaporated. The oily, colorless product crystallized slowly upon standing (22mg, 44%). Mp. 78°C

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ2.2 (s, 6H), 6.46 (d, 2H), 6.53 (d, 2H), 6.64 (t, 2H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ18.9, 115.4, 127.5, 128.7, 131.2, 150.4, 151.03.

MS (EI): M+ 180, 165, 152, 76 (100%) m/z;

1,8-Dimethylbiphenylene (21) By Flash Vacuum Pyrolysis

1,10-Dimethylbenzo[*c*]cinnoline **17** (0.62g) was pyrolyzed at 800°C and 0.1 Torr. The crude product was purified by column chromatography with hexane and recrystallization from methanol yielded 0.25g (47%) of faintly yellow needles identical to the foregoing material.

2,7-Dimethylbiphenylene (22)

3,8-Dimethylbenzo[*c*]cinnoline **18** (1.0g-0.48mmol) was pyrolyzed at 800°C and 0.1 Torr. The crude product was purified by column chromatography with hexane and recrystallization from methanol yielded 0.63g (77%) of faintly yellow needles. Mp.112°C.

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ2.18(s, 6H), 6.6(m, 6H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ23, 117.5, 119.8, 128, 138, 149, 152.

1,8-Dichlorobiphenylene (23)

1,10-Dichlorobenzo[*c*]cinnoline **20** (1.20g-) was pyrolyzed at 800°C and 0.1 Torr. The crude product was purified by column chromatography with hexane and recrystallization from methanol yielded 1.0g (97%) of faintly green needles. Mp. 125-127°C.

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ6.54 (dd, 2H), 6.72 (dd, 4H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ116.5, 123.7, 130.6, 131.0, 146.6, 151.5.

MS (EI): M+ 220, 185, 150, 110, 73 (100%) m/z;

2,7-Dichlorobiphenylene (212)

3,8-Dichlorobenzo[*c*]cinnoline **120** (1.0g-0.48mmol) was pyrolyzed at 800 °C and 0.

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ6.56(d, 2H), 6.66(s, 2H), 6.78(d, 2H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ119, 120, 129, 134.8, 148.5, 151.9.

1-Iodo-2,6-Dibromobenzene (24)

2,6-dibromoaniline (10.04g-40mmol) were suspended in concentrated HCl (50mL) in a 200mL three-necked round-bottomed flask equipped with a low temperature thermometer and an addition funnel. The mixture

was cooled to ca. 5°C while stirring and a solution of sodium nitrite (45mmol-3.1g) in water (20mL) was slowly added at ca. 10°C. After 0.5h, the diazonium chloride formed were poured into an ice-cold aqueous (60mL) solution of potassium iodide (45mmol-7.47g) contained in a 1000mL beaker. Excess of solid sodium bisulfite was added to neutralize the excess of iodine while stirring and the mixture was extracted with ether (3x200mL). The combined organic layers were washed with 4N HCl, 10% aqueous sodium bisulfite, water and brine. Drying upon magnesium sulfate and removal of solvent on a rotary evaporator yielded pinkish crystals. Recrystallization in ethanol afforded 12.6g (89%) of colorless crystals, mp. 99-100°C.

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ7.08 (t, 1H), 7.54 (d, 2H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ131, 132, 132.05.

MS (EI): M+ 362, 235, 156, 75 (100%) m/z;

2,6-Dibromo-*p*-toluidine (25)

Aniline (18.6g-0.2mol) was dissolved in glacial acetic acid (60mL) and while stirring, bromine (80g-0.48mol) in glacial acetic acid was added dropwise. The reaction was instantaneous. The reaction mixture was poured into a beaker containing ice and water. After stirring, the

precipitate was collected in a büchner funnel and washed with cold water. Recrystallization in methanol yielded 37g (quantitative) colorless crystals. Mp.68-70°C.

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ2.2(s. 3H), 3.8(s broad, 2H), 7.2(s, 2H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ21, 109, 130, 136, 140.

MS (EI): M+ 265, 184, 104 (100%) m/z

1-Iodo2,6-Dibromo-4-methylbenzene (26)

2,6-dibromo-*p*-toluidine **25** (7.5g-28mmol) were suspended in concentrated HCl (50mL) in a 200mL three-necked round-bottomed flask equipped with a low temperature thermometer and an addition funnel. The mixture was cooled to ca.5°C while stirring and a solution of sodium nitrite (28mmol-2.0g) in water (20mL) was slowly added while maintaining the temperature below 10°C. After 0.5h, the diazonium chloride formed were poured into an ice-cold aqueous (60mL) solution of potassium iodide (28mmol-4.6g) contained in a 1000mL beaker. Excess of solid sodium bisulfite was added to neutralize the excess of iodine while stirring and the mixture was extracted with ether (3x200mL). The combined organic layers were washed with 4N HCl, 10% aqueous sodium

bisulfite, water and brine. Drying upon magnesium sulfate and removal of solvent on a rotary evaporator yielded pinkish crystals. Recrystallization in ethanol afforded ca. 10.g (85%) of colorless crystals, mp. 78°C.

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ2.3(s, 3H), 7.40(s, 2H).

MS (EI): M+ 376, 295, 168, 89 (100%) m/z

1-Iodo-2,6-Dichlorobenzene (27)

2,6-dichloroaniline (32.4g-0.2mol) were suspended in concentrated HCl (200mL) in a 200mL three-necked round-bottomed flask equipped with a low temperature thermometer and an addition funnel. The mixture was cooled to ca. 5 °C while stirring and a solution of sodium nitrite (0.2mol-14g) in water (50mL) was slowly added while maintaining the temperature below 10 °C. After 0.5h, the diazonium chloride formed were poured into an ice-cold aqueous (100mL) solution of potassium iodide (0.2mol-33.2g) contained in a 1000mL beaker. Excess of solid sodium bisulfite was added to neutralize the excess of iodine while stirring and the mixture was extracted with ether (3x200mL). The combined organic layers were washed with 4N HCl, 10% aqueous sodium bisulfite, water and brine. Drying upon magnesium sulfate and removal of solvent on a

rotary evaporator yielded pinkish crystals. Recrystallization in ethanol afforded 12.6g (89%) of colorless crystals.

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ7.3(t, 1H), 7.48(d, 2H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ128, 130.5, 136.

MS (EI): M+ 274, 145, 109, 74 (100%) m/z;

2,2',6,6'-Tetrabromobiphenyl (28)

n-BuLi (14.4mmol-5.74mL of a 2.5M solution in hexane) was added to a solution of 1-iodo-2,6-dibromobenzene **24** (12.0mmol-4.35g) in ether (180mL) at -78°C. After the solution was stirred for 2h at -78°C, $CuBr_2$ (72.0mmol-16.2g) was added, and then the reaction mixture was allowed to attain ambient temperature over a 12h period. Cold water was added to the reaction mixture, and usual aqueous workup gave a brown oil. Treatment of the crude product with cold hexane (10mL) afforded 2.16g-55% of a white solid. Mp. 214-216°C.

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ7.16 (dd, 2H), 7.66 (d, 4H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ124.2, 131, 132.2, 142.

MS (EI): M+ 470, 391, 310, 231, 150, 75 (100%) m/z;

2,2',6,6'-Tetrabromo-4,4'-dimethylbiphenyl (29)

n-BuLi (14.4mmol-6mL of a 2.5M solution in hexane) was added to a solution of 2,6-dibromo-4-methyliodobenzene **26** (12mmol-4.51g) in ether (180mL) at -78°C. After the solution was stirred for 2h at -78°C, $CuBr_2$ (72mmol-17g) was added, and then the reaction mixture was allowed to attain ambient temperature over a 12 h period. Cold water was added to the reaction mixture, and usual aqueous workup gave a brown oil. Treatment of the crude product with cold hexane (10mL) afforded (2.06g-50%) of a white solid.

^1H NMR (300 MHz, $CDCl_3$, TMS): δ2.38 (s, 6H), 7.47 (s, 4H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ21.0, 124.8, 133.2, 139.5, 142.5.

MS (EI): M+ 498, 417, 338, 257, 176, 88 (100%) m/z;

2,2',6,6'-Tetrachlorobiphenyl (30)

n-BuLi (14.0mmol-5.7mL of a 2.5M solution in hexane) was added to a solution of 1-iodo-2,6-dichlorobenzene **27** (12.0mmol-3.28g) in ether (180mL) at -78°C. After the solution was stirred for 2h at -78°C, $CuBr_2$ (72mmol-17.0g) was added, and then the reaction mixture was allowed to attain ambient temperature over a 12h period. Cold water was added to the reaction mixture, and usual aqueous workup gave a brown oil. Treatment

of the crude product with cold hexane (10mL) afforded 7.82g-60% of a white solid.

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ7.31 (dd, 2H), 7.45 (d, 4H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ128, 130.05, 135.8.

MS (EI): M+ 292, 257, 220, 185, 150 (100%) m/z

1,8-Dibromobiphenylene (31)

n-BuLi (2.5equiv.-2.5mmol-1mL of a 2.5M solution in hexane) was added to a solution of 2,2',6,6'-tetrabromobiphenyl **28** (1mmol-0.47g) in dry THF (50mL) at - 78°C. After the mixture was stirred for 2h at -78°C, CuCN (2.5equiv.-2.5mmol-0.23g) was added and the mixture was allowed to attain ambient temperature . After the CuCN has completely dissolved (red color solution), the reaction was recooled to -78 °C and dry O_2 was bubbled through the reaction mixture for 1h. Subsequently, the dark colored reaction mixture was allowed to warm to ambient temperature. The usual aqueous workup was followed with flash chromatography (silica gel) using hexane. The product, 120mg-33%, was obtained as powder. Mp. 145-146°C.

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ6.56(d, 2H), 6.62(dd, 2H), 6.85(d, 2H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ111, 116, 130.05, 133, 150, 152.05.

MS (EI): M+ 310, 231, 150, 75 (100%) m/z;

1,8-Dibromo-3,6-dimethylbiphenylene (32)

n-BuLi (2.5equiv.-2.5mmol-1mL of a 2.5M solution in hexane) was added to a solution of 2,2',6,6'-tetrabromo-4,4'-dimethylbiphenyl **29** (0.498g-1mmol) in THF (50mL) at - 78°C After the mixture was stirred for 2h at -78°C CuCN (0.23g) was added and the mixture was allowed to attain ambient temperature . After the CuCN has completely dissolved (red color solution), the reaction was recooled to -78°C and dry O_2 was bubbled through the reaction mixture for 1 h. Subsequently, the dark colored reaction mixture was allowed to warm to ambient temperature. The usual aqueous workup was followed with flash chromatography (silica gel) using hexane. The product. 180mg-48%, was obtained as powder.

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ2.15 (s, 6H), 6.47 (s, 2H), 6.71 (s, 2H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ22, 110.1, 118.8, 132, 141.2, 146.5, 151.9.

(1.8-biphenylenediyldiethynylene)bis(trimethylsilane) (33) by the Sonogashira Reaction

1, 8-dibromobiphenylene **31** (0.35mmol-0.11g) were placed in a schlenck flask equipped with a condenser and flushed with argon. Piperidine (50mL) was added and the mixture was stirred under argon. CuI (0.009mmol-1.74mg) and $Pd(PPh_3)_4$ (0.009mmol-2.52mg) were added and the mixture turned light brown. After 10 min of stirring, trimethylsilylacetylene-TMSA- (0.77mmol-0.1mol) was slowly (30min) added to the mixture via a seringe. The, now green, solution was refluxed 48 hours at 110°C under a flow of nitrogen. Then, the reaction mixture was cooled and poured into an ice-cold solution of concentrated HCl (50mL) in ice-water (200mL) and extracted using methylene chloride (2x200mL). The combined organic extracts were dried and concentrated in vacuo to yield a brown oil which was chromatographed (Hexanes/CH_2Cl_2: 10/1). The product, 80mg-66%, was obtained as white crystals. Mp. 172-174°C.

^1H NMR (300 MHz, $CDCl_3$, TMS): δ0.234 (s, 18H), 6.58 (d, 2H), 6.65 (dd, 2H), 6.84 (d, 2H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ0.03, 99.8, 102.4, 114, 117, 128.5, 134, 150, 151.

MS (EI): M+ 344, 329, 241, 75 (100%) m/z;

(1.8-biphenylenediyldiethynylene)bis(trimethylsilane) (33)

by Katz Method

To a suspension of 1, 8-dichlorobiphenylene **23** (100mg-0.5mmol), $Ni(acac)_2$ (0.25mg) and $Pd(PPh_3)_4$ (0.55mg) in THF (20mL) was added a solution of [(trimethylsilyl)ethynyl]magnesium bromide prepared from trimethylsilylacetylene (1.0g-12mmol, excess) and ethylmagnesium bromide (12mL, excess) in THF (25mL) at 0°C (and let to warm to room temperature during 45 min) with vigorous gas evolution. Then, the mixture was heated at reflux for 48h. Usual aqueous workup with ether gave an oil that was chromatographed with hexanes to give 80mg-80% of white crystals identical to the crystals described above.

1, 8-diethynylbiphenylene (34)

(1.8-biphenylenediyldiethynylene)bis(trimethylsilane) **33** (150mg) was dissolved in freshly distilled dimethylformamide (30mL) and 5mL of a 1N solution of KOH was added and the mixture was let to stir at room temperature for 2h before being poured into a beaker of ice-water and

extracted with ether. The combined ether extracts were dried and evaporated on the rotary evaporator to afford >100mg of white crystals.

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ3.12 (s, 2H), 6.59 (d, 2H), 6.74 (dd, 2H), 6.8 (d, 2H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ81.7, 82, 114, 117.9, 129.8, 132.2.

MS (EI): M+ 200, 174, 150, 100, 74 (100%) m/z;

2-Formylbiphenylene (35)

To a stirred solution of biphenylene **8** (3.04g, 0.02 mol) and dichloromethyl methyl ether (12.7g, 0.11mol) in 200mL of ethylene dichloride chilled in an ice-water bath was added tin (IV) chloride (8.6g) under argon over a period of 2 min. When the addition was complete, the reaction mixture was allowed to warm to room temperature and was stirred for 24h. The reaction mixture was cooled and slowly poured with stirring into 300mL of 3M HCl cooled in an ice-water bath. The mixture was extracted with dichloromethane (3 x100mL). The organic layers were combined and washed with 5% sodium bicarbonate solution (2 x 50mL) and were dried over magnesium sulfate. The solvent was removed on a rotary evaporator and the residue was dissolved in benzene. Removal of the benzene gave 2-formylbiphenylene (**35**): mp 78-79°C.

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ6.8-6.9(m, 3H), 7.1(s, 1H), 7.3(d, 1H), 7.38(s, 2H), 9.7(s, 1H)

^{13}C NMR (300 MHz, $CDCl_3$, TMS) δ115, 118, 119.5, 120, 129, 130, 131, 137.5, 138, 150.3, 152.5, 192.

MS (EI): M+ 180, 151, 76 (100%) m/z;

Benzyl triphenylphosphonium bromide (205)

(39.30g-0.15mol) of PPh_3 and (24.15g-0.15mol) of benzylbromide were heated at 110 °C in DMF (80mL) for 10h. After cooling the mixture, the precipitate was collected in a büchner funnel and recrystallized in the least amount of hot chloroform and ethyl acetate. The phosphonium salt thus formed (60.0g-) was used in the following reaction.

2- styrylBiphenylene (36)

Benzyl triphenylphosphonium bromide **205** (1.4mmol-0.61g) and 2-formylbiphenylene **35** (1.4mmol-0.25g) were mixed together in methylene chloride (10mL) in a 100 mL-round-bottomed flask equipped with a magnetic bar. And 50% aqueous potassium hydroxide (10mL) was added and the mixture was vigorously stirred, while being monitored by tlc. After 2h, tlc showed no more trace of the starting materials. The

mixture was extracted with dichloromethane to afford both the cis (Rf= 0.2) and the trans (Rf= 0.15) isomers of 2-styrylbiphenylene in high (0.91g-87%) yield, which overtime converted to the thermodynamically more stable trans-2-styrylbiphenylene.

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ6.65(m, 3H), 6.8(m, 3H), 6.95(s+d, 2H), 7.27(s, 2H), 7.35(t, 2H), 7.48(d, 2H).

Irradiation of 2-styrylbiphenylene

2-Styrylbiphenylene (0.5mmol-0.127g) was dissolved in cyclohexane 1000mL) and irradiated (100W lamp) for 12h after iodine (0.32mg) has been added. After 12h, the mixture remained pinkish. Heating for an additional 12h did not seem to change the color of the mixture. Work up involved neutralizing the iodine with aqueous sodium bisulfite and extracting with methylene chloride. The sum of organic layers were dried and evaporated to afford the starting 2-styrylbiphenylene, 0.127g.

2-Chlorobenzyl triphenylphosphonium chloride (206)

(39.30g-0.15mol) of PPh_3 and (24.15g-0.15mol) of 2-chlorobenzylchloride were heated at 110 °C in DMF (80mL) for 10h. After cooling the mixture, the precipitate was collected in a buchner

funnel and recrystallized in the least amount of hot chloroform and ethyl acetate. The phosphonium salt thus formed (60.0g-) was used in the following reaction.

2-*o*-chlorostyryl Biphenylene (37)

2-*o*-Chlorobenzyl triphenylphosphonium chloride **206** (1.5mmol-0.64g) and 2-formylbiphenylene **35** (1.5mmol-0.27g) were mixed together in methylene chloride (20mL) in a 100mL-round-bottomed flask equipped with a magnetic bar. And 50% aqueous potassium hydroxide (12mL) was added and the mixture was vigorously stirred, while being monitored by tlc. After 2h, tlc showed no more trace of the starting materials. The mixture was extracted with dichloromethane to afford both the cis (Rf= 0.25) and the trans (Rf= 0.15) isomers of 2-styrylbiphenylene in high (1.1g-85%) yield, which overtime converted to the thermodynamically more stable trans-2-*o*-chlorostyrylbiphenylene.

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ6.65(m, 3H), 6.8(m, 3H), 6.95(s+d, 2H), 7.27(s, 2H), 7.35(t, 2H), 7.48(d, 2H).

MS (EI): M+ 288, 252, 126, 113 (100%) m/z;

Irradiation of 2-*o*-chlorostyrylbiphenylene

2-*o*-chlorostyrylbiphenylene **37** (0.5mmol-0.127g) was dissolved in cyclohexane (1000mL) and irradiated (100W lamp) for 12h after iodine (0.32mg) has been added. After 12h, the mixture remained pinkish. GC-MS of an analytical sample did not reveal the peak (m/z 252) of the cyclized product. Heating for an additional 12h did not seem to change the color of the mixture. Work up involved neutralizing the iodine with aqueous sodium bisulfite and extracting with methylene chloride. The sum of organic layers were dried and evaporated to afford the starting 2-styrylbiphenylene, 0.127g, identical to **37**.

1,6-benzocycloheptatetraenedicarboxaldehyde (209)

1,6-distyryl-3,4-Benzocycloheptatetraene (38)

(2.0g-0.01mol) of 1,6-benzocycloheptatetraenedicarboxaldehyde **209** reacted with the ylid from (8.8g-0.02mol) benzyltriphenylphosphonium bromide **205** in a Wittig (as above) reaction to give the products, a mixture of trans and cis isomers of 1,6-distyryl-3,4-benzocycloheptatetraene, as confirmed by mass spectroscopy, which

could be separated from the phosphine oxide by flash chromatography using pure hexanes.

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ2.5(s, 2H), 6.2(d, 2H), 6.4(d, 2H), 6.7(s, 2H), 7.15(m, 10H), 7.20(m, 4H).

MS (EI): M+ 346, 255, 215, 129, 91, 77 (100%) m/z;

Irradiation of 1,6-distyryl-3,4-benzocycloheptatetraene

1mmol-346mg of 1.6-distyryl-3,4-Benzocycloheptatetraene **38** and a catalytic amount of iodine were dissolved in cyclohexane (1000mL) and the mixture was irradiated with a 100W mercury lamp.. After 1-1.5h, beige crystals started to precipitate as the characteristic color of iodine receded. The reaction vessel was cooled and the mixture was poured in a separatory funnel and extracted with methylene chloride, washing with aqueous sodium bisulfite. The sum of organic layers were dried over magnesium sulfate anhydrous and evaporated to afford a brown oil which was further purified by flash chromatography using hexanes as the eluent. Mass spectrometry showed the peak corresponding to the bicyclization product.

2-naphthyl triphenylphosphonium chloride (207)

(6.026g-23mmol) of PPh_3 and (5g-22.6mmol) of 2-(bromomethyl)-naphthalene were heated at 110 °C in DMF (20mL) for 10h. After cooling the mixture, the precipitate was collected in a büchner funnel and recrystallized in the least amount of hot chloroform and ethyl acetate. The phosphonium salt thus formed (10.0g-) was used in the following reaction.

2-naphthaldehyde (210)

2-styrylnaphthalene (39)

Benzyl triphenylphosphonium bromide **205** (10mmol-4.34g) and 2-naphthaldehyde **210** (10mmol-1.56g) were mixed together in methylene chloride (50mL) in a 100mL round-bottomed flask equipped with a magnetic bar. And 50% aqueous potassium hydroxide (50mL) was added and the mixture was vigorously stirred, while being monitored by tlc. After 2h, tlc showed no more trace of the starting materials. The mixture was extracted with dichloromethane to afford both the cis (Rf= 0.33) and the trans (Rf= 0.2) isomers of 2-styrylnaphthalene in high (0.91g-87%)

yield, which overtime converted to the thermodynamically more stable trans-2-styrylbiphenylene.

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ6.65(m, 3H), 6.8(m, 3H), 6.95(s+d, 2H), 7.27(s, 2H), 7.35(t, 2H), 7.48(d, 2H).

MS (EI): M+ 230, 215, 114 (100%) m/z;

Irradiation of 2-styrylnaphthalene: Synthesis of benzo[*a*]phenanthrene (211)

2-Styrylnaphthalene **39** (0.230g-1mmol) was dissolved in cyclohexane 1000mL) and irradiated (100W lamp) for 12h after iodine (0.32mg) has been added. The cyclization occurred after 1-2h as monitored by tlc, all starting material was converted into benzophenanthrene (0.16g-90%) after usual work up as described above. Mp. 67-68 °C.

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ7.6(AA'BB', 4H), 7.75(d, 2H), 7.85(d, 2H), 8.0(d, 2H), 9.12(d, 2H).

MS (EI): M+ 228, 113 (100%) m/z;

1-naphthyl triphenylphosphonium chloride (208)

1-styrylnaphthalene (40)

1-naphthyl triphenylphosphonium chloride **208** (0.01mol-4.4g) and benzaldehyde (0.01mol-1.1g) were mixed together in methylene chloride (100mL) in a 100 mL-round-bottomed flask equipped with a magnetic bar. And 50% aqueous potassium hydroxide (50mL) was added and the mixture was vigorously stirred, while being monitored by tlc. After 2h, tlc showed no more trace of the starting materials. The mixture was extracted with dichloromethane to afford both the cis (Rf= 0.5) and the trans (Rf= 0.25) isomers of 1-styrylnaphthalene in high (5.4g-97%) yield, which overtime converted to the thermodynamically more stable trans-1-styrylnaphthalene.

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ6.65(m, 3H), 6.8(m, 3H), 6.95(s+d, 2H), 7.27(s, 2H), 7.35(t, 2H), 7.48(d, 2H).

MS (EI): M+ 230, 215, 152, 114 (100%) m/z:

Irradiation of 1-styrylnaphthalene: Synthesis of chrysene (41)

-Styrylnaphthalene **40** (1mmol-0.23g) was dissolved in cyclohexane 1000mL) and irradiated (100W lamp) for 12h after iodine (0.32mg) has been added. The cyclization occurred after 1-2h as monitored by tlc, all

starting material was converted into chrysene (0.20g-97%) after usual work up as described above.

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ7.65(t, 2H), 7.7(t, 2H), 8.0(d+d, 4H), 8.7(d, 2H), 8.8(d, 2H).

2-bromobiphenylene (35)

Biphenylene **8** (4.56g-30mmol) was dissolved in 50mL dimethylformamide in a round-bottomed flask equipped with a stirring bar and *N*-bromosuccinimide (NBS) (4.5g) was added. The mixture was stirred at room temperature for 4h before being poured into ice-water (400mL) with stirring. After the ice had melted, the mixture was extracted using ether (3x100mL) and all the combined ether layers were washed with water (2 X 100 mL) and dried (magnesium sulfate anhydrous). Removal of the solvent in vacuo afforded dark yellow crystals. Sublimation of these crystals then afforded 2-bromobiphenylene as pale yellow crystals that were used in the following reaction.

2,6 + 2,7-dibromobiphenylene (36)

To a stirred solution of 2-bromobiphenylene **35** (0.77g-) in 50mL dimethylformamide in a round bottomed flask was added N-bromo

succinimide (1.00g-) and the mixture was stirred at room temperature for 4 hours and then slowly poured into ice-water (400mL) with stirring. After 1 hr, the solution was extracted with ether (3x100mL) and the combined ether layers were washed with water (2 x 100mL) and dried and evaporated in vacuo to afford yellowish crystals of the two isomers. The two isomers could be separated by fractional crystallization.

MS (EI): M+ 308/310/312, 229, 150, 75 (100%) m/z;

MS (EI): M+ 310/312, 263, 184, 128, 76 (100%) m/z;

2,6-biphenylenedicarboxaldehyde (37) and 2,7-biphenylenedicarboxaldehyde (38)

To a mixture of 2,6- and 2,7-dibromobiphenylene (1.0g-3.3mmol) in 50mL dry THF at -78°C (dry ice-acetone/dewar bath) was slowly injected a 2.5M hexane solution of n-butyllithium (8.25mmol-6.3mL) and the resulting white suspension was stirred for 1h at –78°C before being quenched with dry dimethylformamide (9.9mmol-73mg). The resulting reddish solution was slowly warmed to room temperature, stirring for 12h and extracted with ether (3x100mL). The combined ether layers were washed with water (2 x 100mL) and dried and evaporated in vacuo to afford reddish oil. The two isomers of 2,6- and 2,7-

biphenylenedicarboxaldehyde could be separated by flash chromatography using a solution of hexane and ethyl acetate in 4 to 1 ratio at the beginning and increasing to pure ethyl acetate as the deep orange crystals of 2,6-biphenylenedicarboxaldehyde are collected upfront. The red 2,7- isomer is somewhat reactive in the column and part thereof undergoes reduction to the corresponding diol. It is also slowly decomposed in solution.

2,6-biphenylenedicarboxaldehyde (37)

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ6.96(d, 2H), 7.28(d, 2H), 7.43(dd, 2H), 9.77(s, 2H).

2,7-biphenylenedicarboxaldehyde (38)

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ7.0(d, 2H), 7.27(s, 2H), 7.40(d, 2H), 9.8(s, 2H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ117, 119, 138, 138.4, 151, 157, 191.

MS (EI): M+ 208, 179, 150, 75 (100%) m/z;

Dimethyl-2,2'-diiododiphenyl-4,4'-dicarboxylate (211)

Commercially available dimethyl diphenyl-4,4'-dicarboxylate (25g-20mmol) and silver sulfate (85g) were charged into a 500-mL three-necked flask equipped with a stirrer and the mixture was dissolved in 300mL of concentrated sulfuric acid. Iodine (55g-0.2mol) was added to the reaction mixture in several portions and the reaction mixture was stirred for 1h at room temperature and then at 80 °C for 18h. After cooling, the reaction mixture was poured over ice and the yellow solid was filtered. The moisture and excess iodine were removed from the precipitate under vacuum at 80 °C. The dried solid was extracted in a Soxhlet extractor with methanol as solvent for 24h and the product was crystallized from methanol solution during extraction. Crystals were collected and recrystallized from methanol in 85.2% (36.4g) yield, mp.150-151 °C.

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ4.0(s, 6H), 7.26(d, 2H), 8.1(d, 2H), 8.6(s, 2H)

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ54, 99.9, 130, 130.2, 132, 140.8, 153, 166.

MS (EI): M+ 522, 395, 268, 150 (100%) m/z

2,7-dimethyl biphenylenedicarboxylate (39)

Compound **211** (10g-19.1mmol) and Cu powder (20g) were mixed in dry pyridine in a 300mL round-bottomed flask that was previously swept with nitrogen and the reaction mixture was refluxed with stirring under nitrogen atmosphere for 40h. After 48h, the reaction mixture was cooled, filtered under vacuum and washed with fresh pyridine. The filtrate was slowly poured into a beaker containing 1Kg of ice and 200mL of hydrochloric acid. A precipitate was obtained and filtered under vacuum yielding a paste that was extracted (Soxhlet) with diethyl ether and the crude product diester was recrystallized from acetone yielding 0.5g (14%) of bright yellow-green crystals, mp.190-193 °C.

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ4.0(s, 6H), 8.05(ABB'A', 4H), 8.3(s, 2H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ54, 114, 121.9, 125, 128, 130.5, 158, 167.

2,7-Bis-hydroxymethylbiphenylene (40)

Sodium borohydride (80mg) in ethanol (30mL) was added to 2,7-biphenylenedicarboxaldehyde (210mg-1mmol) in THF (20mL). After 0.5h the mixture was evaporated to dryness and the residue boiled with

water () for 1h. The diol (212mg-100% yield) was collected as pale green plates.

^1H NMR (300 MHz, $CDCl_3$, TMS): δ1.6(s broad, 2H), 4.48(s, 4H), 6.61(d, 2H), 6.7(s, 2H), 6.74(d, 2H)

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ66, 117-118, 127

MS (EI): M+ 212, 141, 111, 71 (100%) m/z;

McMurry reaction of 2-formylbiphenylene

A 500mL three-necked flask fitted with a reflux condenser, dropping funnel and an argon inlet was charged with dry THF (100mL) and cooled to −78°C (all adapters were greased). $TiCl_4$ (3.0mL) was then added slowly, followed by Zn powder (1g) and dry pyridine (2mL). The resultant black mixture was refluxed under argon for 1h and a solution of 2-formylbiphenylene (40mg) in dry THF (100mL) was then added dropwise (over 24h) to the stirred mixture. After refluxing for a further 12h the reaction mixture was ice-cooled and quenched by 10% aqueous K_2CO_3. The grey precipitate was filtered off and both filter-cake and filtrate thoroughly extracted with dichloromethane. The combined organic layers were washed with water, dried ($MgSO_4$) and the solvent evaporated

to give an orange solid residue. GC/MS revealed a minor peak corresponding to the cyclized product.

McMurry reaction of 2,7-biphenylenedicarboxaldehyde

A 500mL three-necked flask fitted with a reflux condenser, dropping funnel and an argon inlet was charged with dry THF (100mL) and cooled to −78°C (all adapter greased). $TiCl_4$ (1.52g-8mmol) was then added slowly, followed by Zn powder (1.04g) and dry pyridine (2mL). The resultant black mixture was refluxed under argon for 1h and a solution of 2,7-biphenylenedicarboxaldehyde (50mg-0.24mmol) in dry THF (100mL) was then added dropwise (over 24h) to the stirred mixture. After refluxing for a further 12h the reaction mixture was ice-cooled and quenched by 10% aqueous K_2CO_3. The dark precipitate was filtered off and both filter-cake and filtrate thoroughly extracted with dichloromethane. The combined organic layers were washed with water, dried ($MgSO_4$) and the solvent evaporated to give an orange solid residue. GC/MS revealed no peak corresponding to the cyclized product.

Synthesis of 1,8-dichloroanthracene (214)

A mixture of 1,8-dichloroanthraquinone **219** (2.515g-9.1mmol), Zinc dust (12.5g) and 50mL aqueous 20% NH_3 was heated on a steam bath with stirring for 30 min and then cooled and filtered. The residue and the filtrate were each extracted with dichloromethane and the combined dichloromethane extracts were concentrated. A solution of the residual white solid in 250mL of isopropyl alcohol containing 2mL of aqueous 12M HCl was refluxed for 3h and then concentrated and partitioned between CH_2Cl_2 and $NaHCO_3$. The organic layer was concentrated and the residue was recrystallized from isopropyl alcohol to separate 1.655g (74%) of 1,8-dichloroanthracene, mp.149-157°C. Recrystallization afforded the pure dichloride as pale yellow needles: mp.156.5-158°C.

^1H NMR (300 MHz, $CDCl_3$, TMS): δ7.4(t, 2H), 7.62(d, 2H), 7.93(d, 2H), 8.48(s, 1H), 9.25(s, 1H).

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ122, 126, 126.5, 128, 128.5, 130, 133

MS (EI): M+ 246, 211, 176, 149, 88, 75 (100%) m/z:

1.8-Diethynylanthracene (213) by Katz Method

To a suspension of 1, 8-dichloroanthracene **214** (8.0g-0.033mol), $Ni(acac)_2$ (16mg) and $Pd(PPh_3)_4$ (33mg) in THF (60mL) was added a solution of [(trimethylsilyl)ethynyl]magnesium bromide prepared from trimethylsilylacetylene (16g-0.17mol, excess) and ethylmagnesium bromide (80mL, 2M in THF, 0.16mol) in THF (125mL) at 0°C (and let to warm to room temperature during 45 min) with vigorous gas evolution. Then, the mixture was heated at reflux for 3 days. The crude mixture was then treated with 6.0g of potassium fluoride in 500mL of ethanol for 2h at reflux. The solvent was removed and the residue taken up in 300mL of water and 200mL of toluene. The aqueous layer was extracted with 100mL of additional toluene. The combined toluene layers were concentrated to 6.2g (85% overall yield from dichloroanthracene). Mp. 150°C

^1H NMR (300 MHz, $CDCl_3$, TMS): δ3.65(s, 2H), 7.4(t, 1H), 7.45(t, 1H), 7.6(d, 1H), 7.8(d, 1H), 7.95(d, 1H), 8.05(d, 1H), 8.45(s, 1H), 9.33(s, 1H)

^{13}C NMR (300 MHz, $CDCl_3$, TMS): δ82, 82.9, 121, 124.5, 126, 128, 130, 132

MS (EI): M+ 226, 112, 74 (100%) m/z;

Oxidative coupling of 1,8-diethynylbiphenylene: biphenylenediyne (215)

To a solution of 1,8-diethynylbiphenylene **34** (60mg-2.7mmol) in pyridine (30mL) and methanol (5mL) was added cupric acetate monohydrate (100mg), and the mixture was vigorously stirred for 4h at 55°C. stirring was continued for a further 3h period at room temperature. The reaction mixture was filtered and the solid obtained was washed thoroughly with water, a small amount of benzene and ethanol, successively. The cyclic tetrayne was obtained as orange crystals, 50mg (92%). This substance, which decomposed (becomes black) above 310°C, was very insoluble and only showed peaks belonging to the deuterated solvents in all attempts to acquire NMR data.

Oxidative coupling of 1,8-diethynylanthracene: anthracenediyne (216)

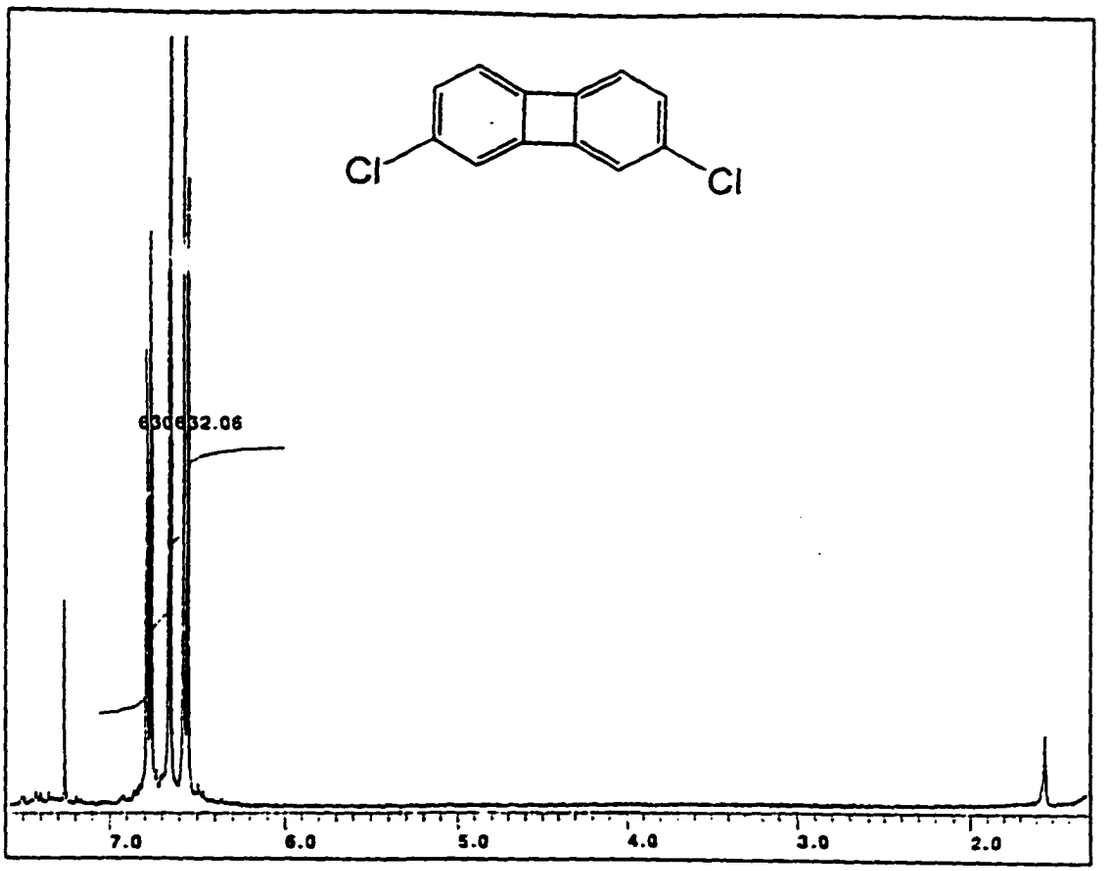
To a solution of **213** (600mg-27mmol) in pyridine (100mL) and methanol (8mL) was added cupric acetate monohydrate (12g), and the mixture was vigorously stirred for 4h at 55°C. stirring was continued for a further 3h

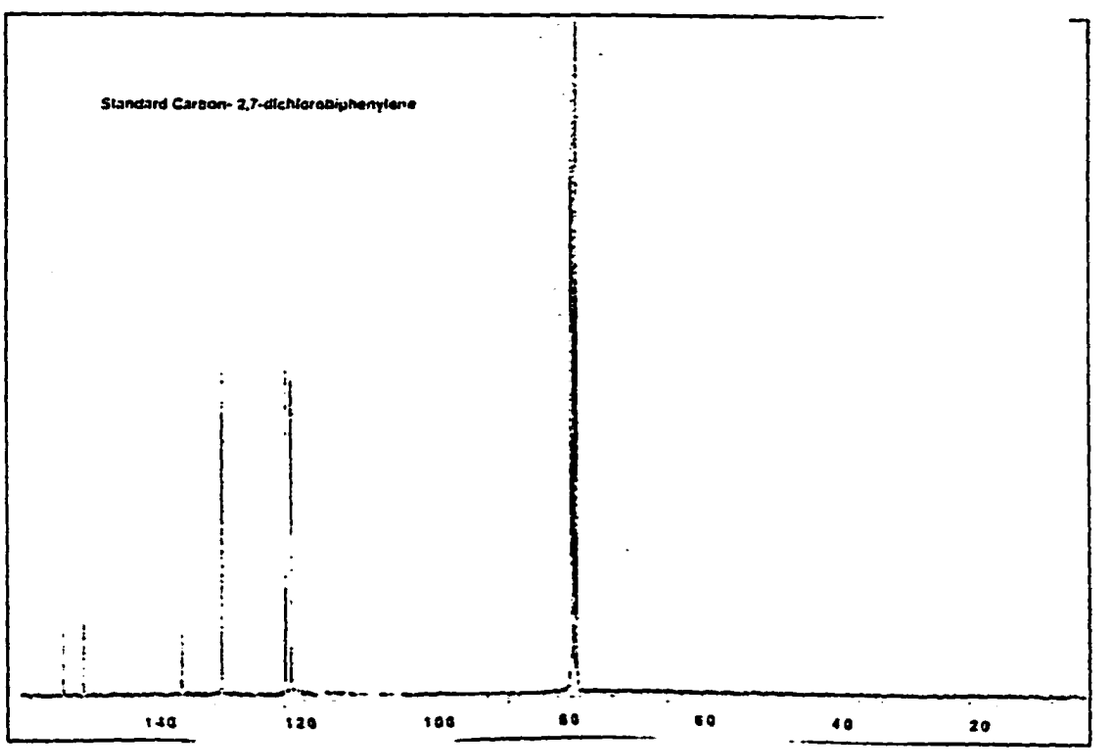
period at room temperature. The reaction mixture was filtered and the solid obtained was washed thoroughly with water, a small amount of benzene and ethanol, successively. The cyclic tetrayne was obtained as orange crystals, 550mg (94%). This substance, which blackens over 370°C, was insoluble in most organic solvents and when it did dissolve, no NMR signal was present even after lengthy acquisition period.

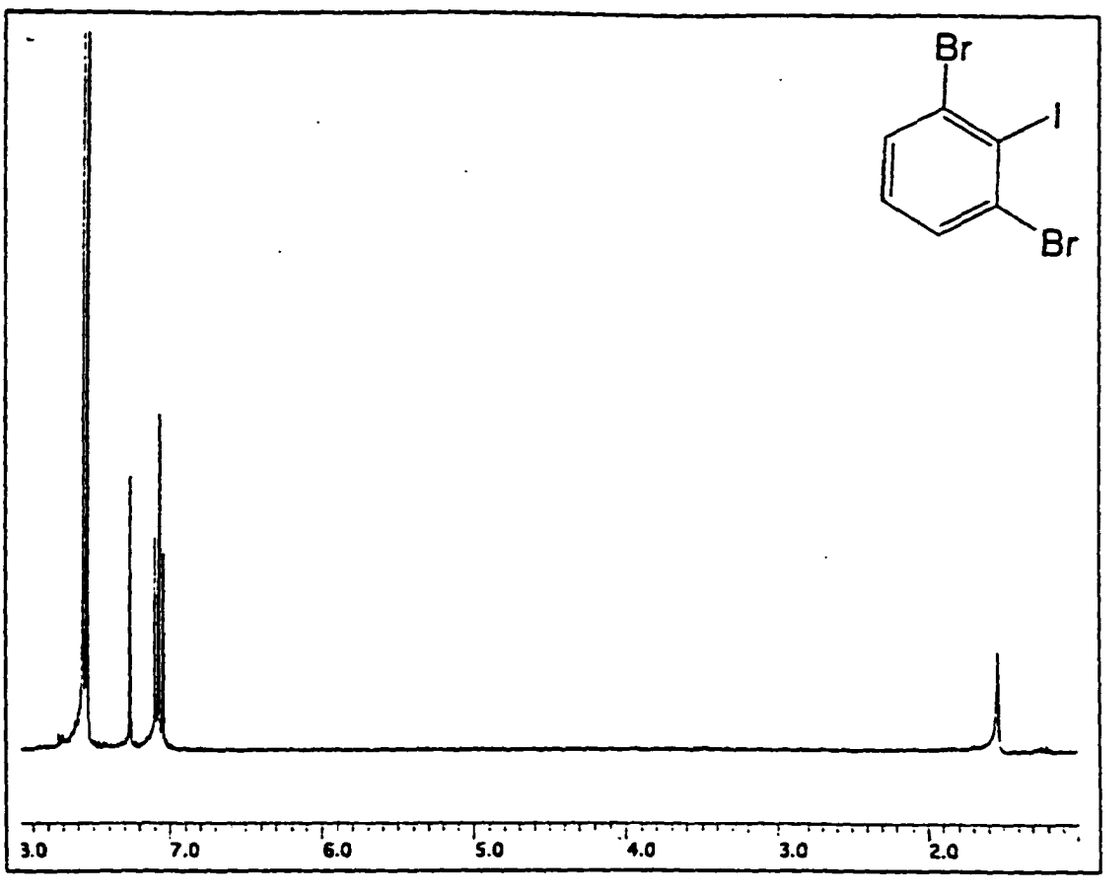
Attempt to synthesize biphenylene-thionin (217)

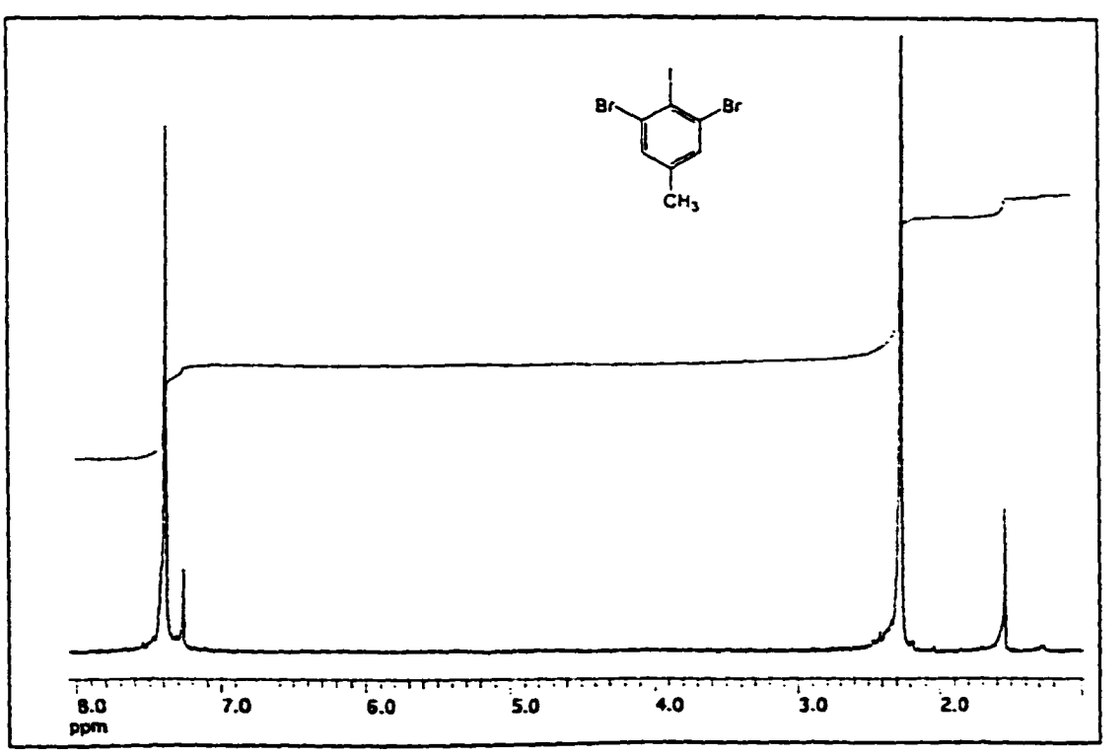
Sodium sulfide nonahydrate (96mg-0.38mmol) was charged in a 100mL round-bottomed flask containing a stirred solution of 1,8-diethynylbiphenylene (40mg-0.2mmol) in absolute ethanol. The mixture was heated to reflux for 12h and the yellow suspension visible from the flask was cooled before being poured in a beaker of ice and water. Extraction of the mixture using ether, drying of the ether layers (magnesium sulfate) and concentration of the ether layers yielded a light brown oil which was passed into a short column of silica with hexane. The product was mainly the starting material, 1,8-diethynylbiphenylene and an unidentified solid that corresponded to a GCMS peak at 220.

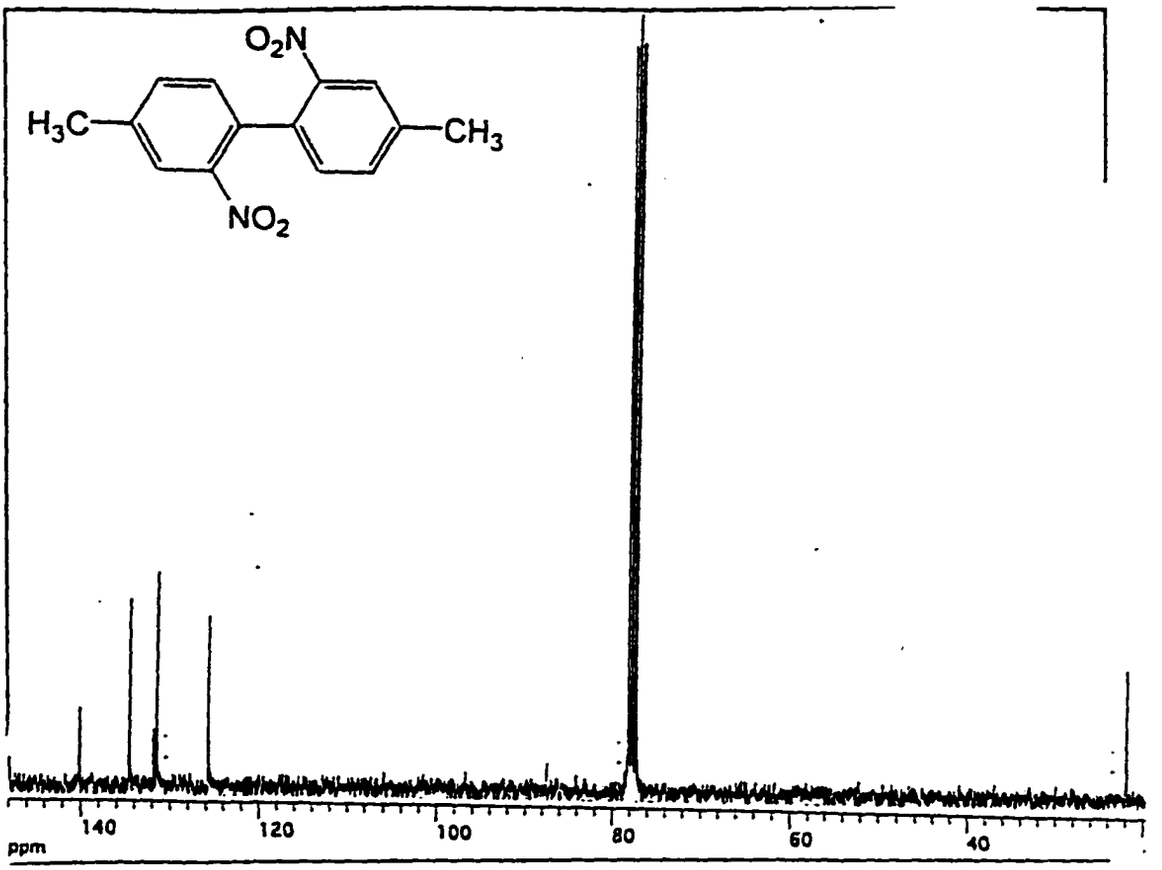
^{1}H and ^{13}C NMR Of Some Selected Compounds

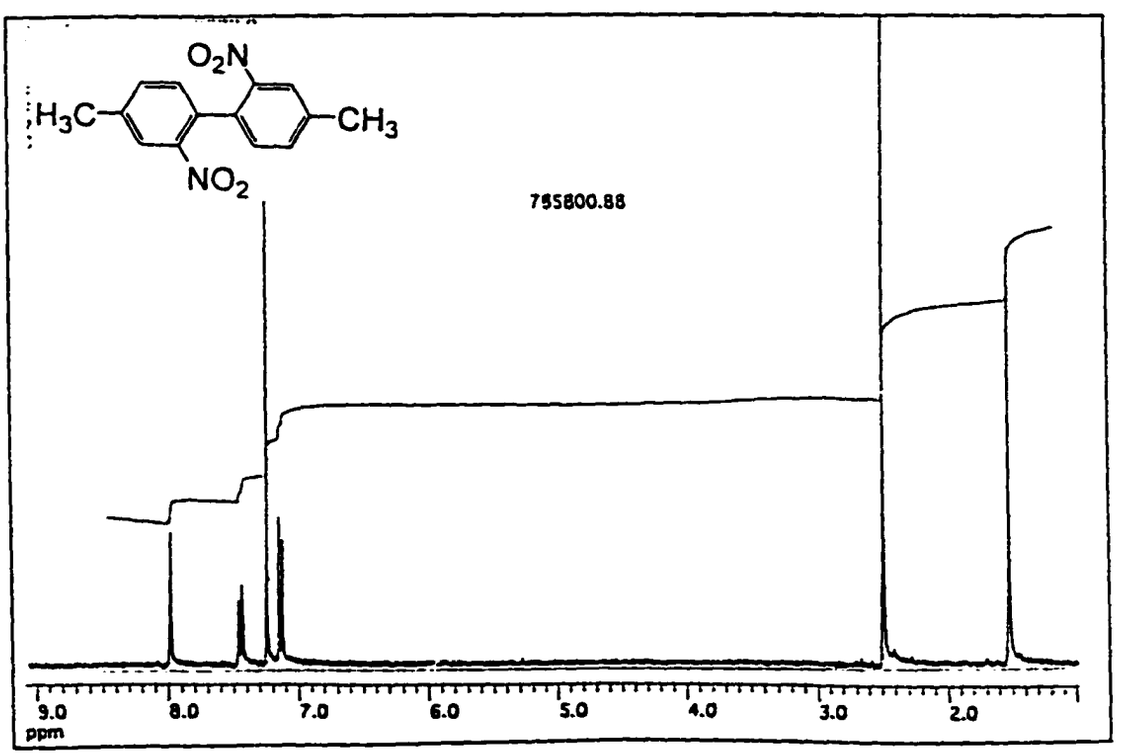


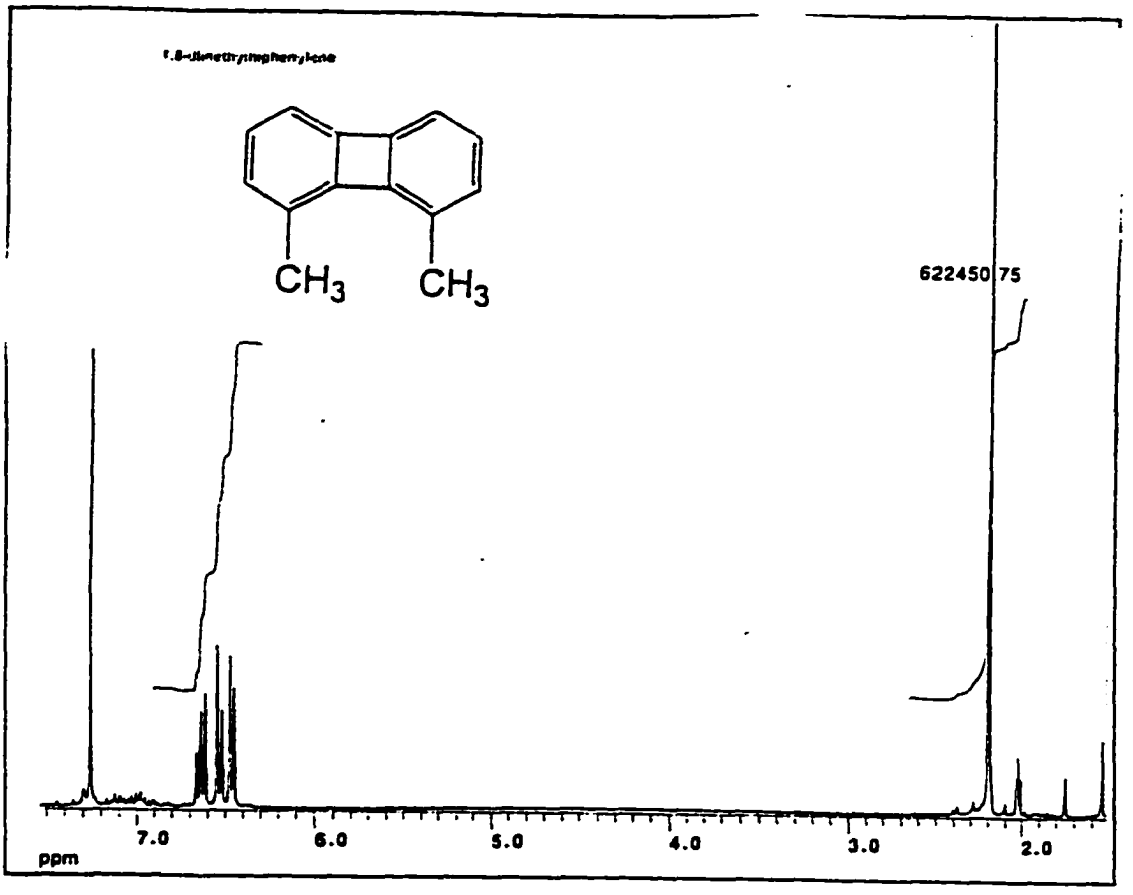


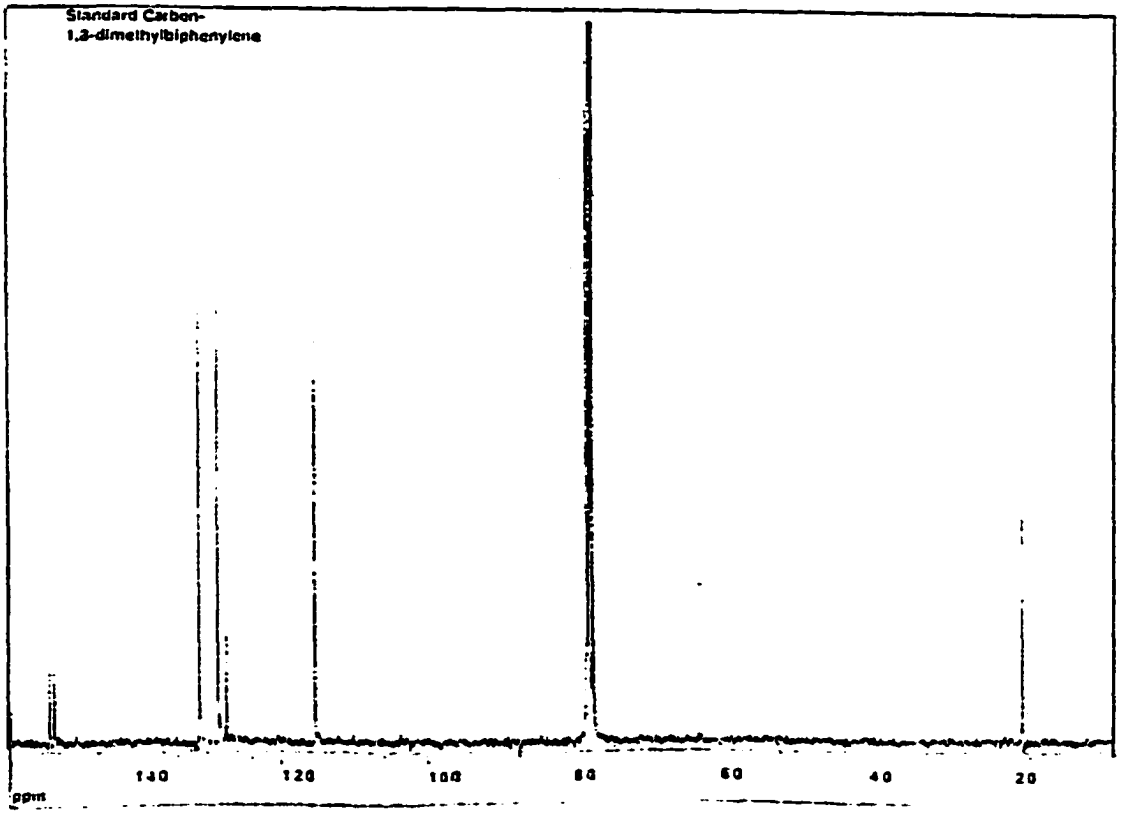


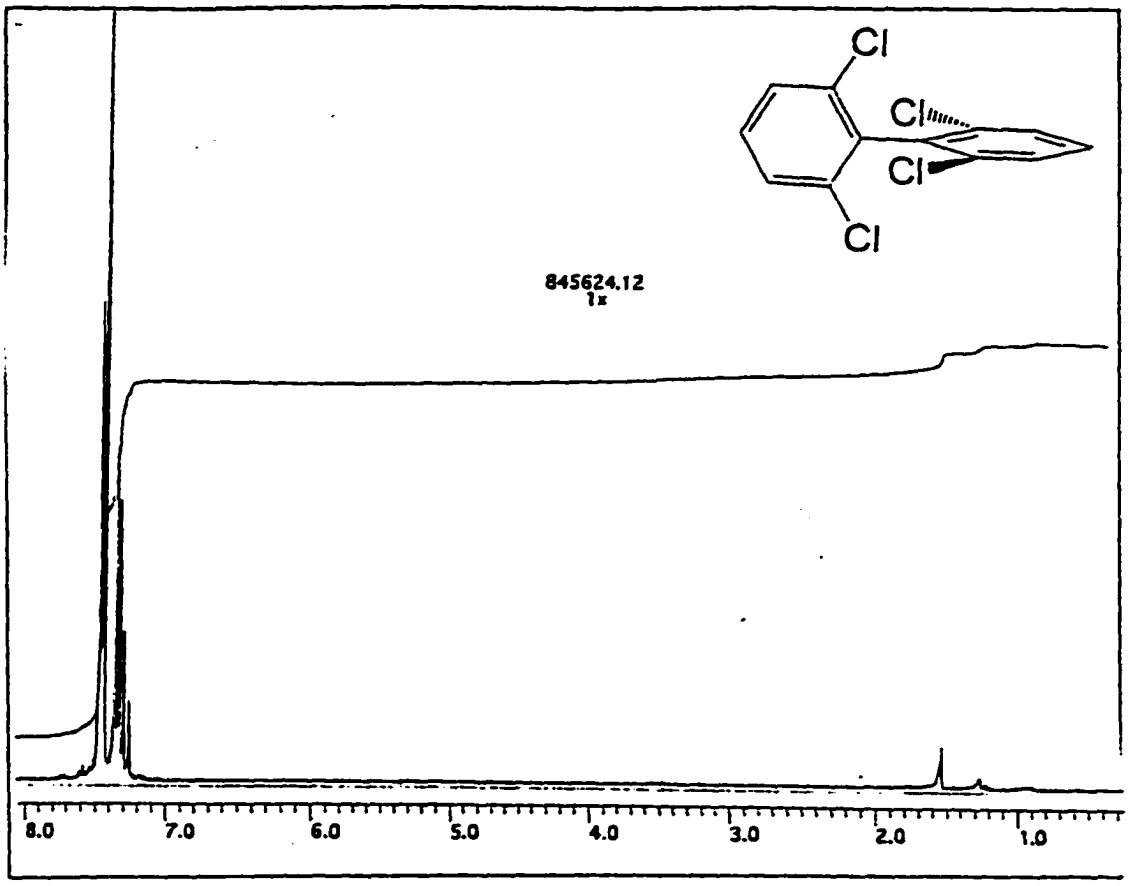


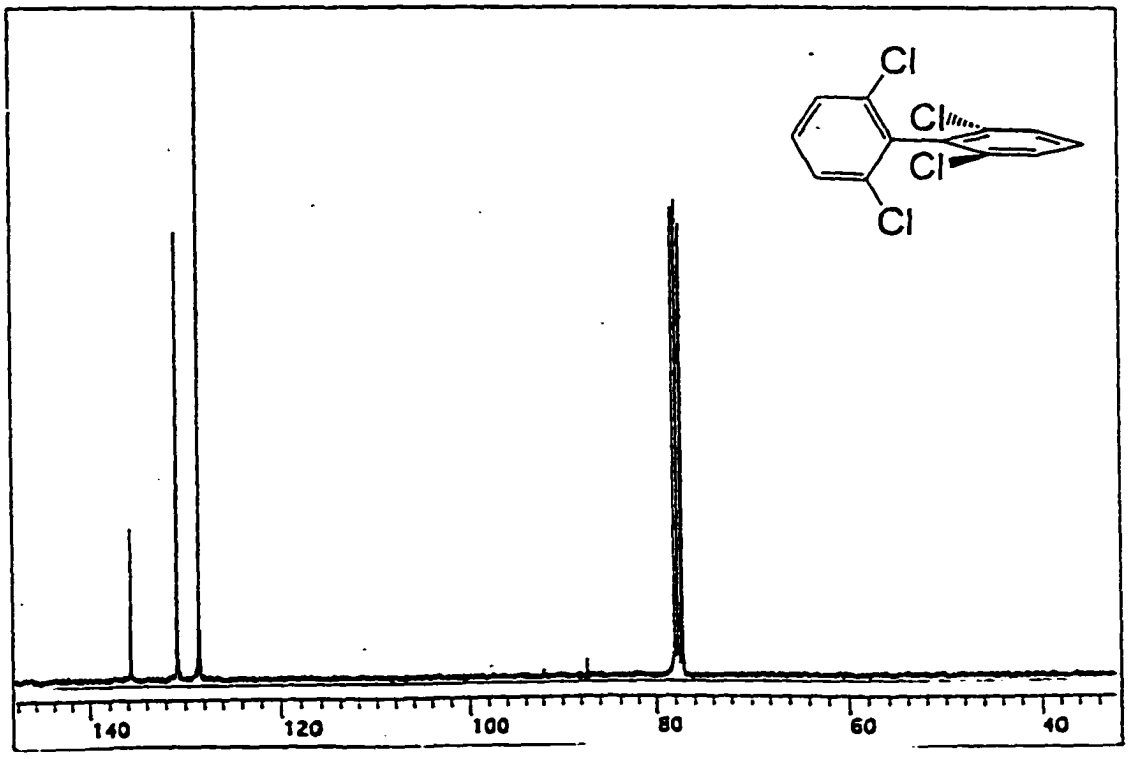


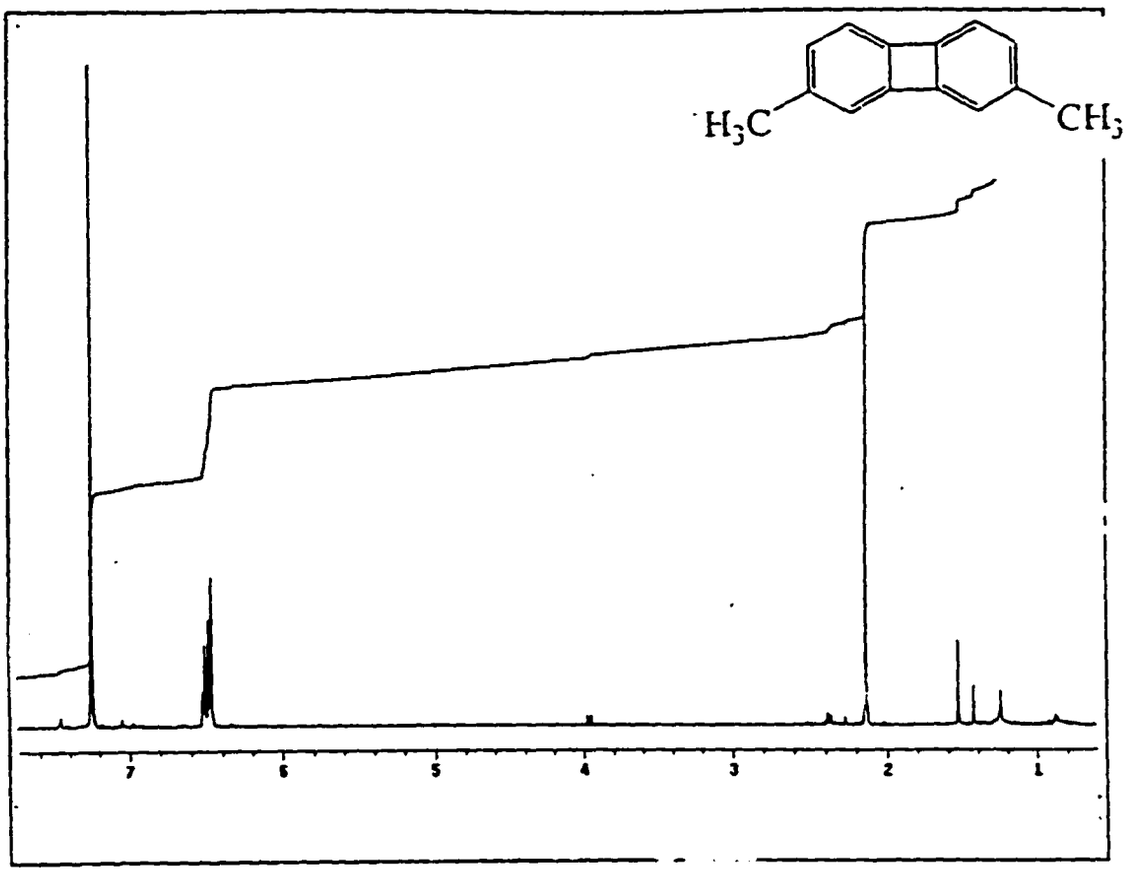


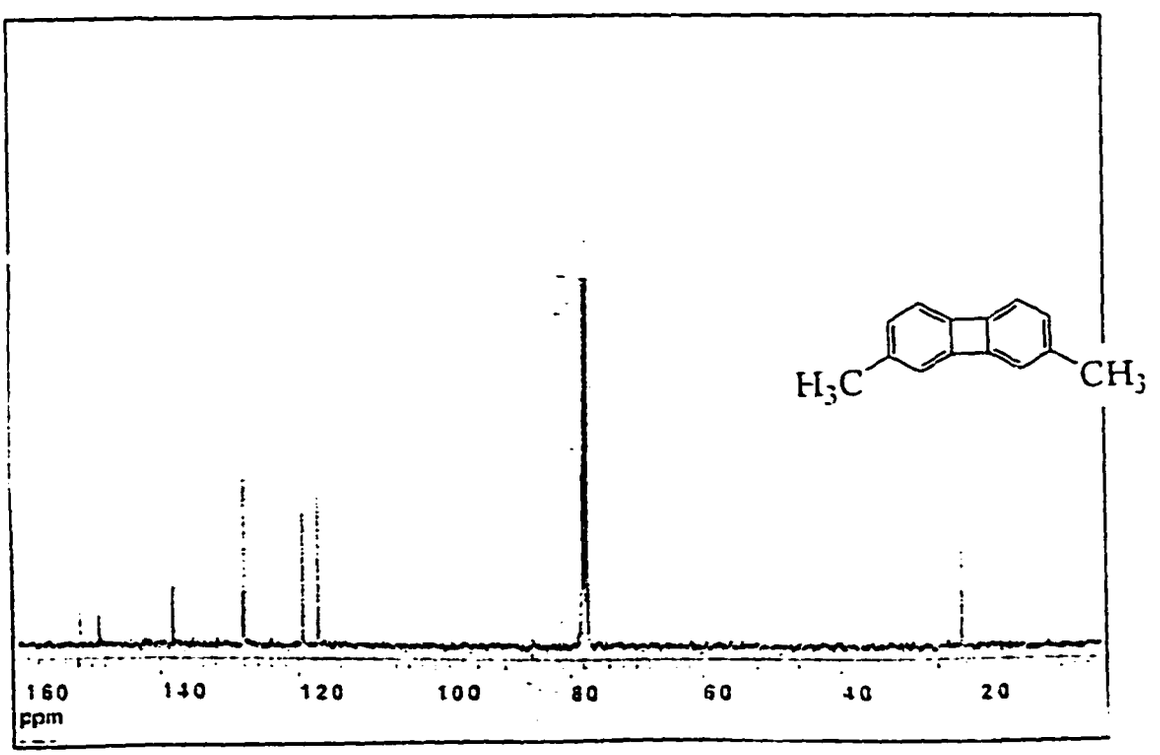


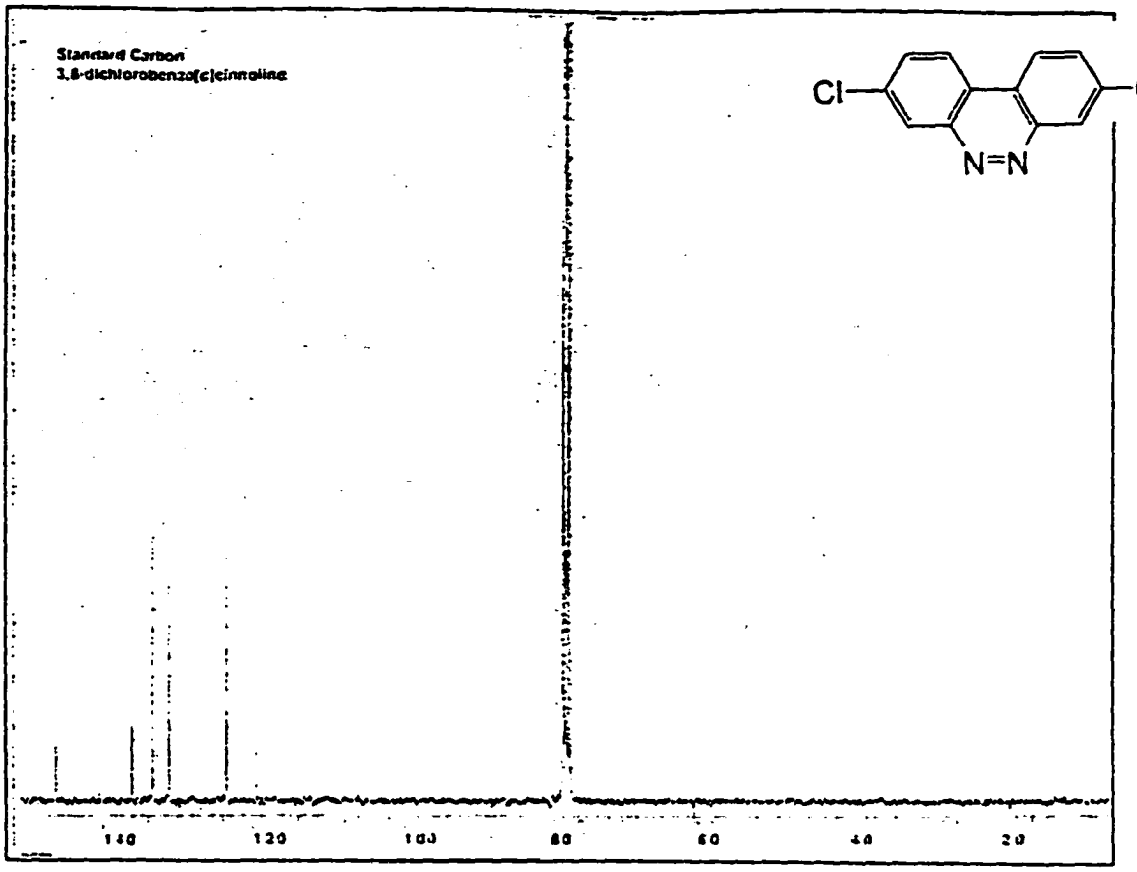


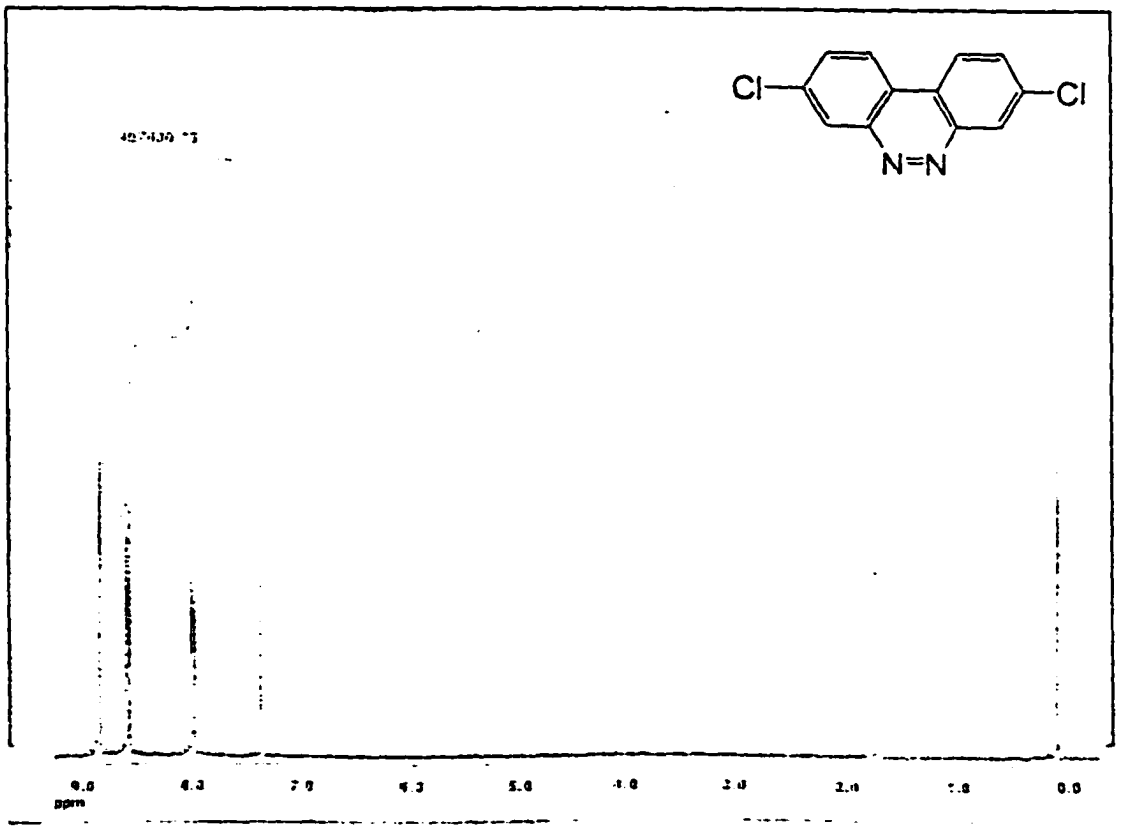


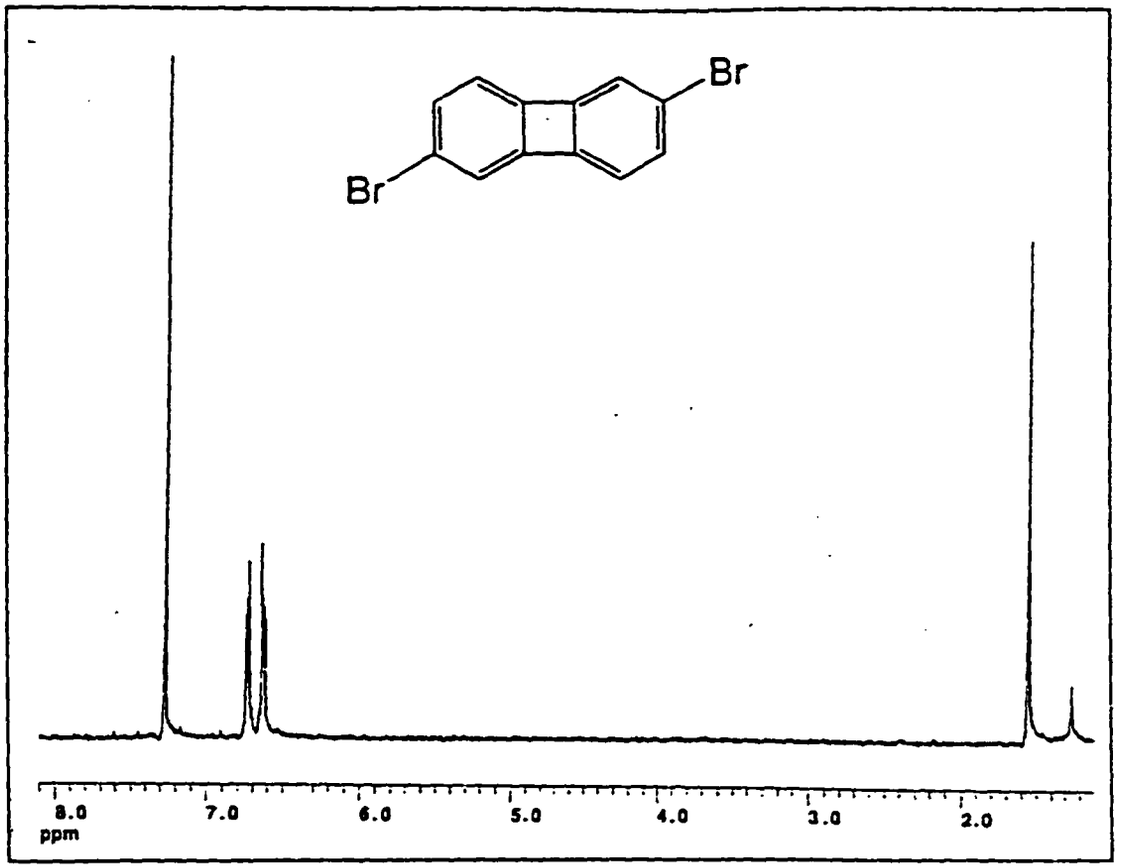


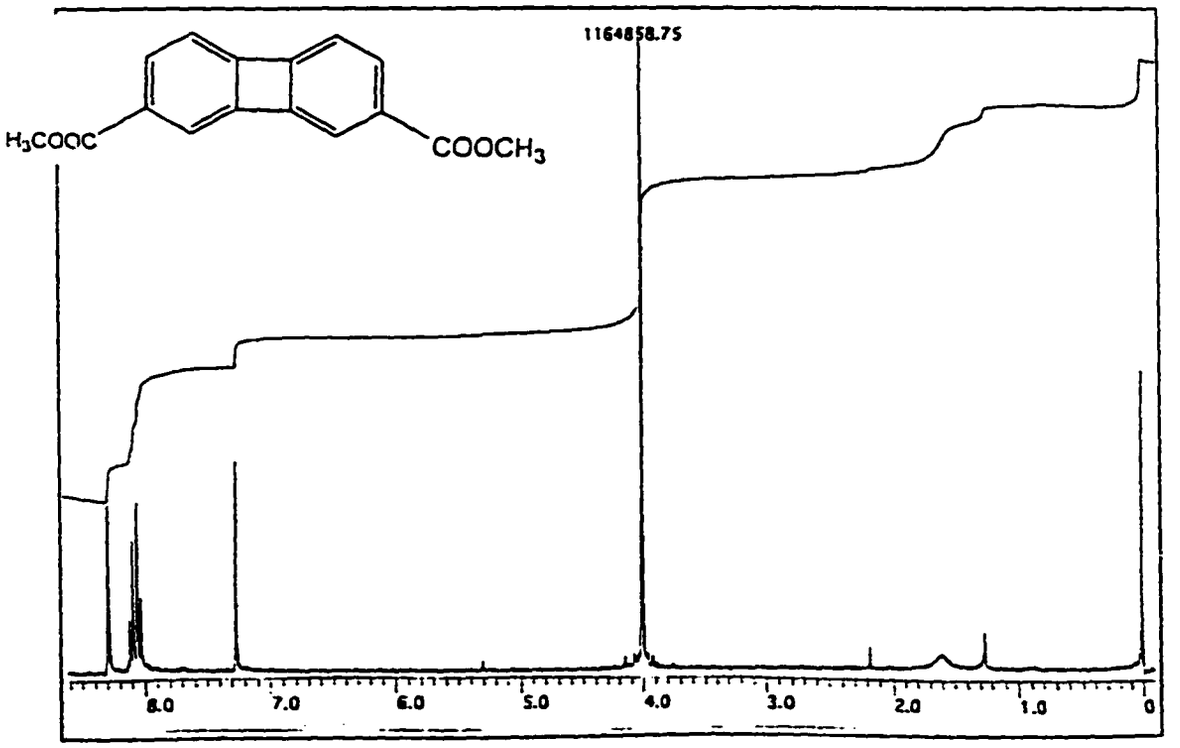


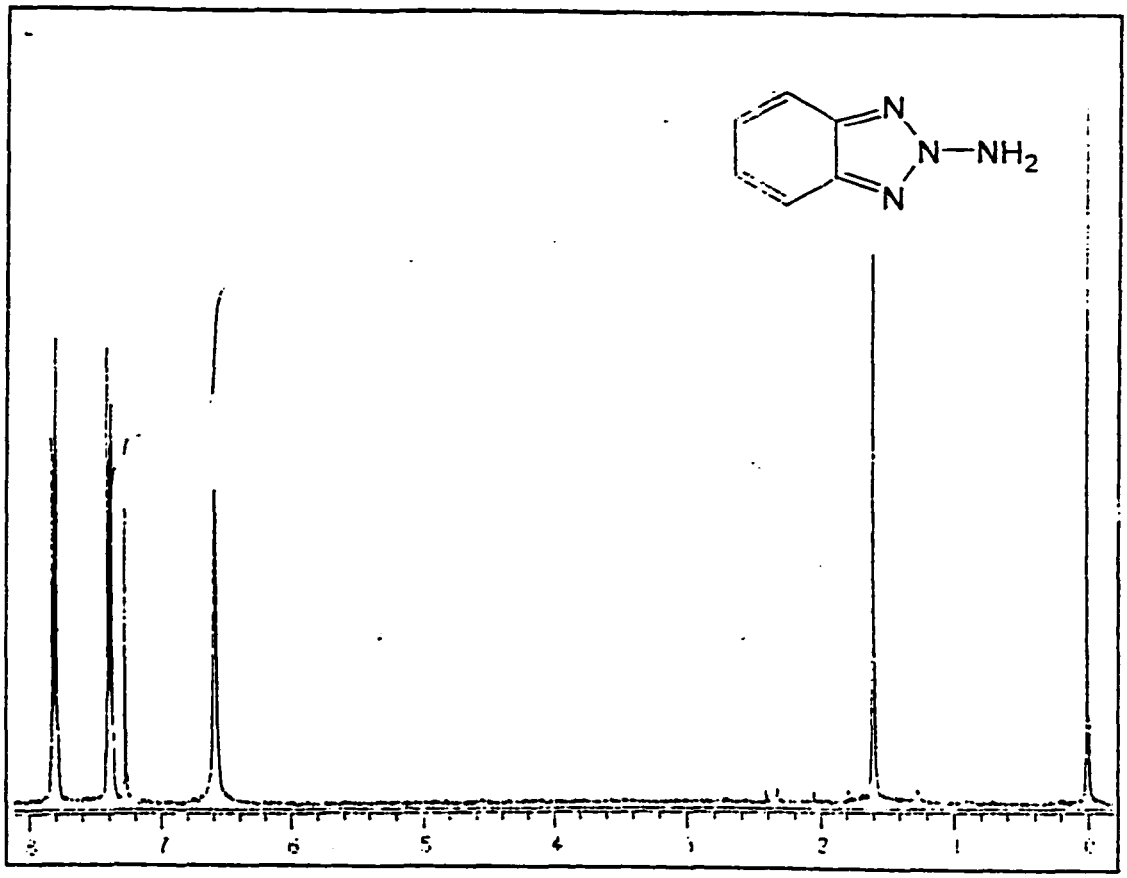


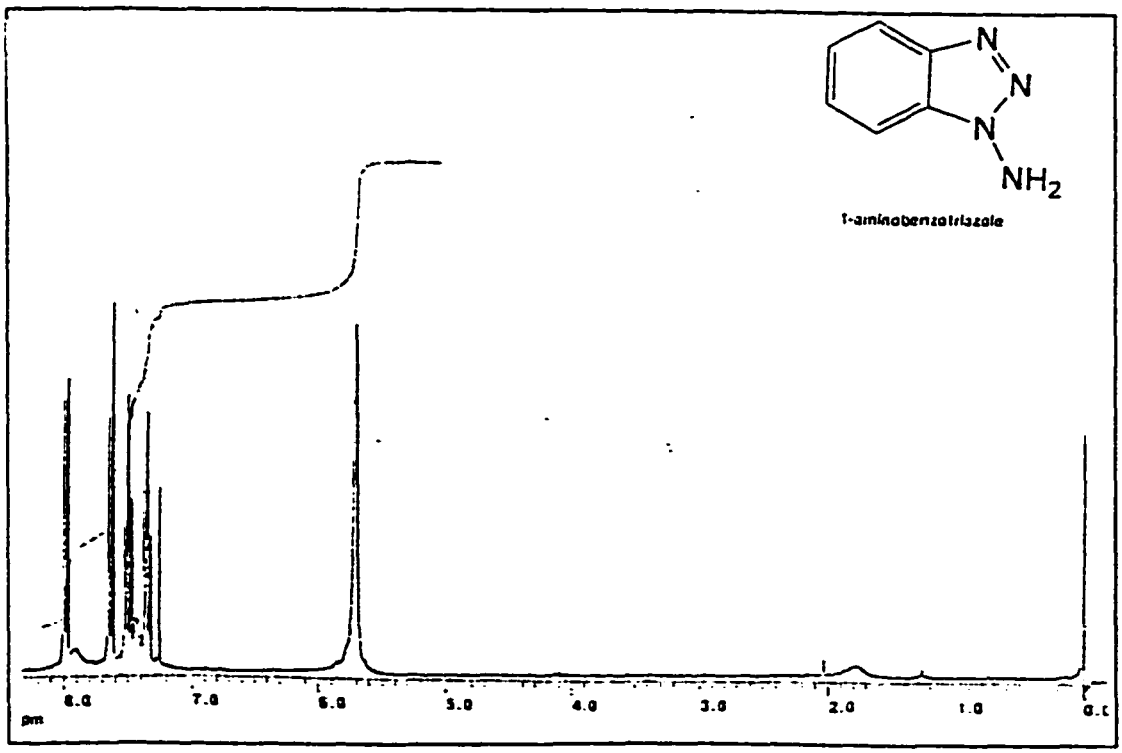


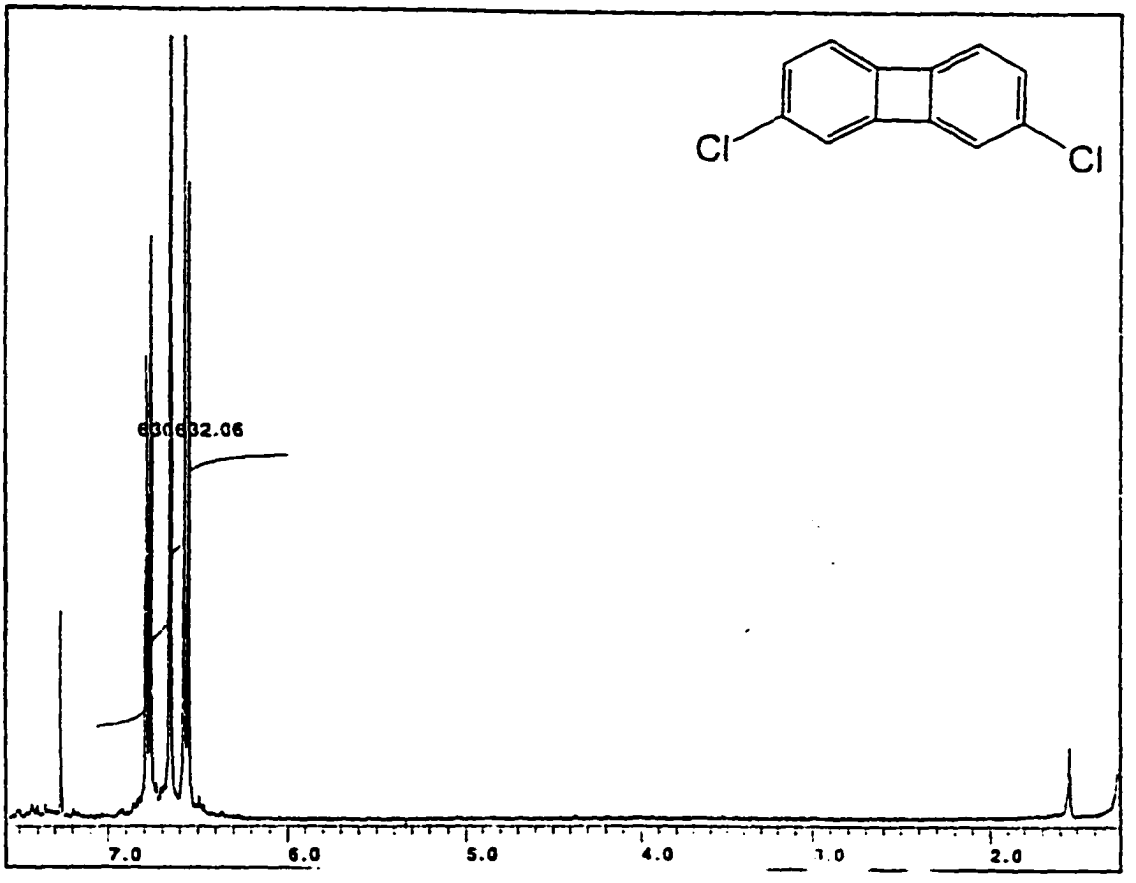


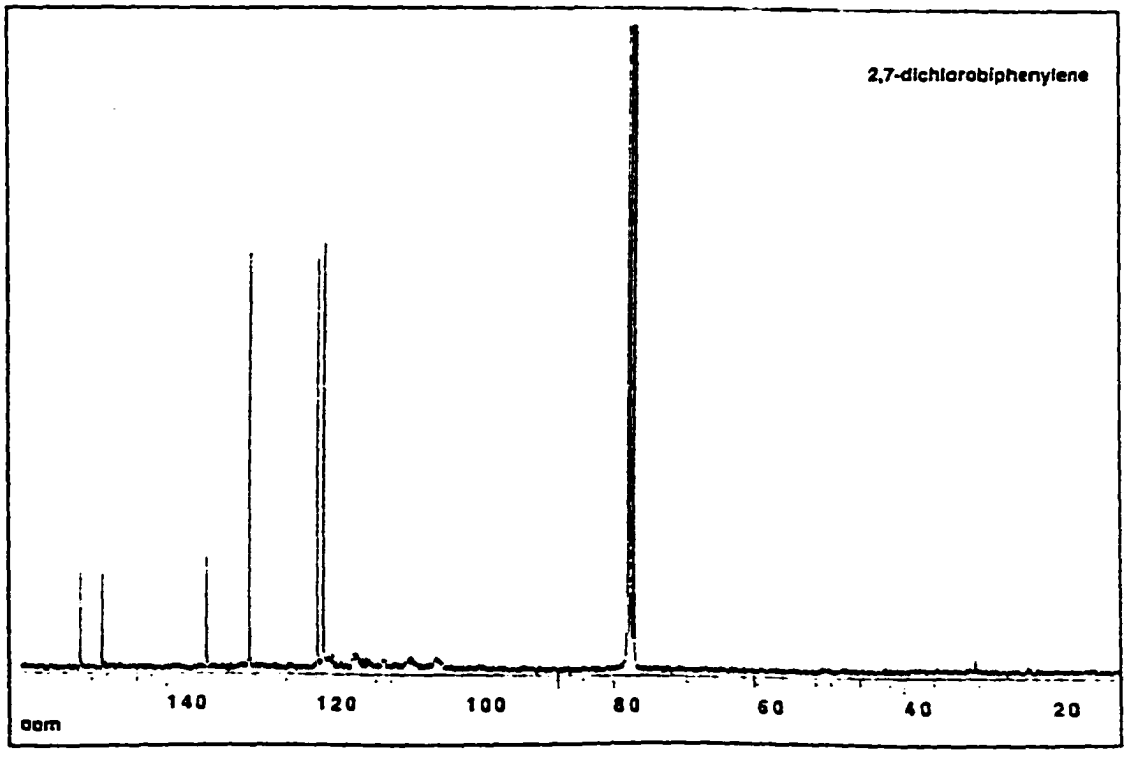


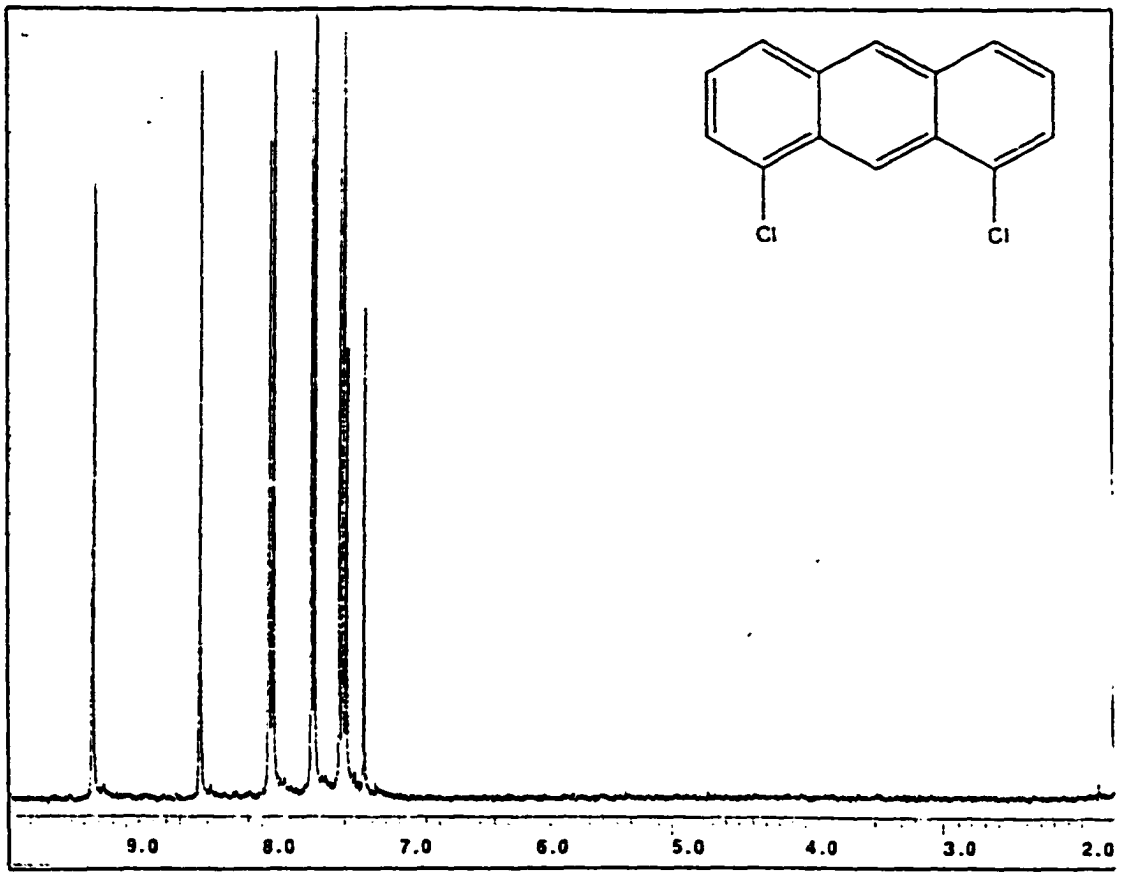


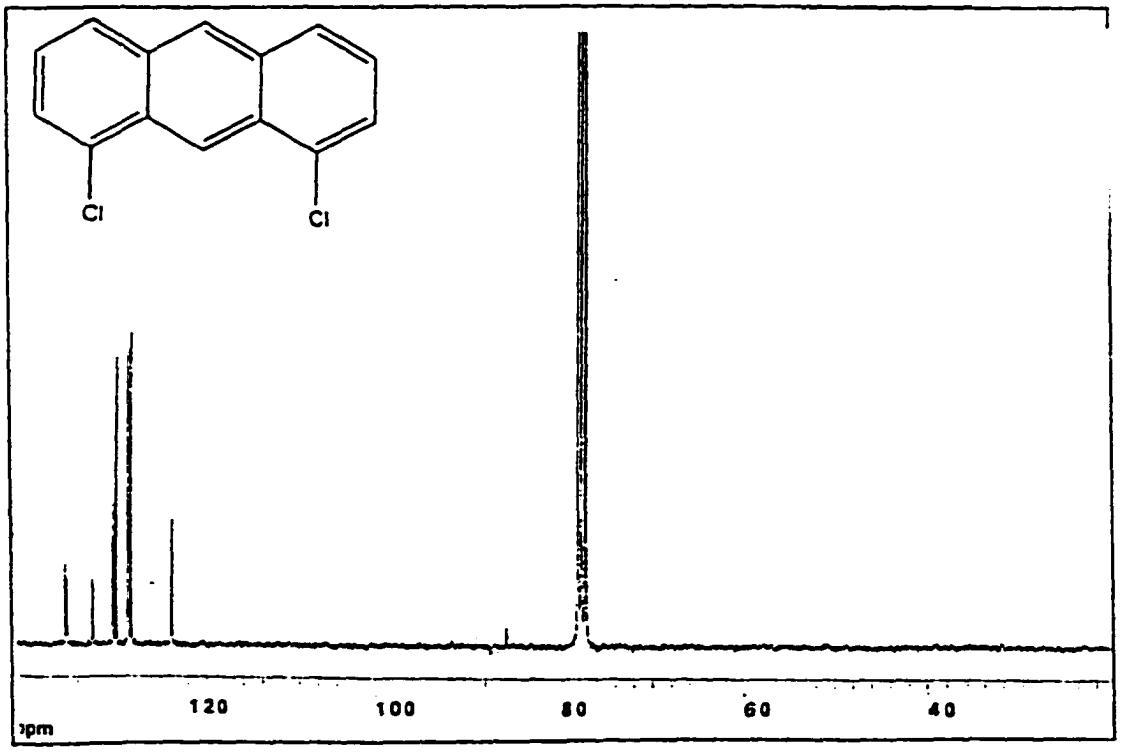


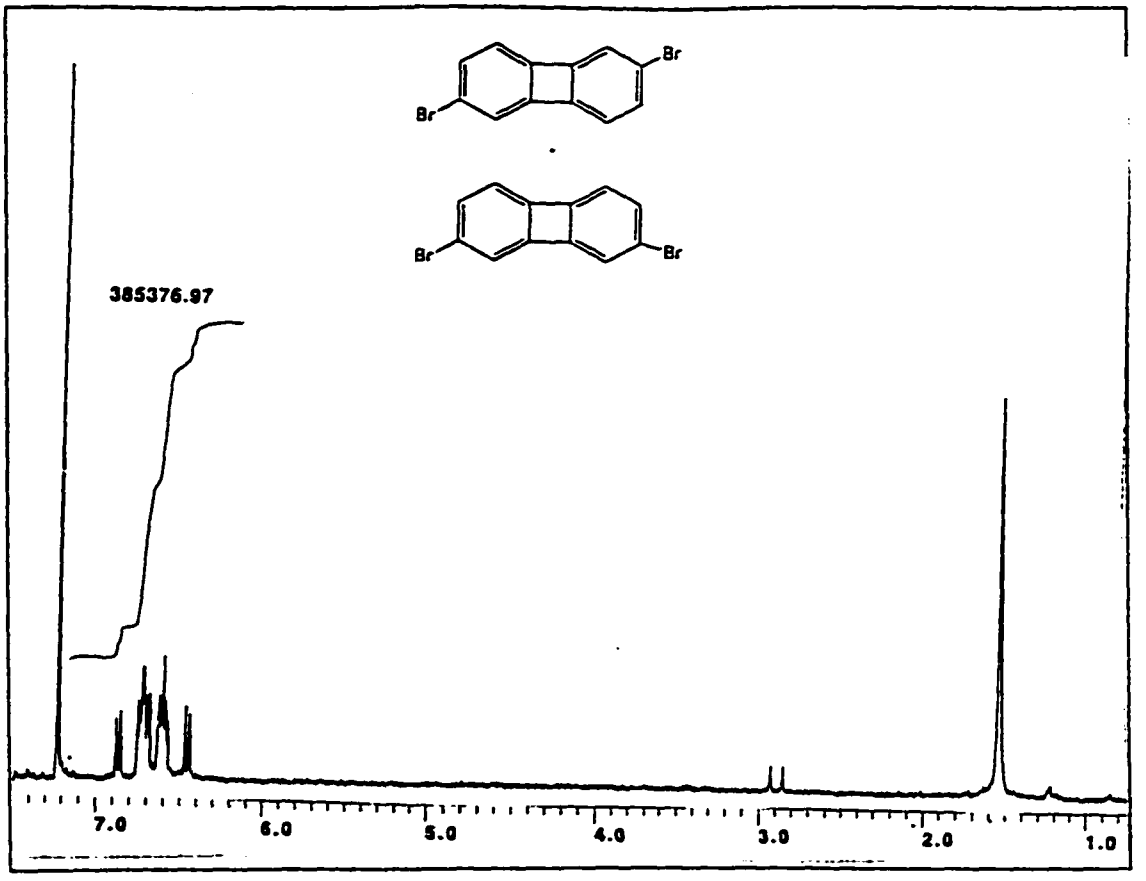


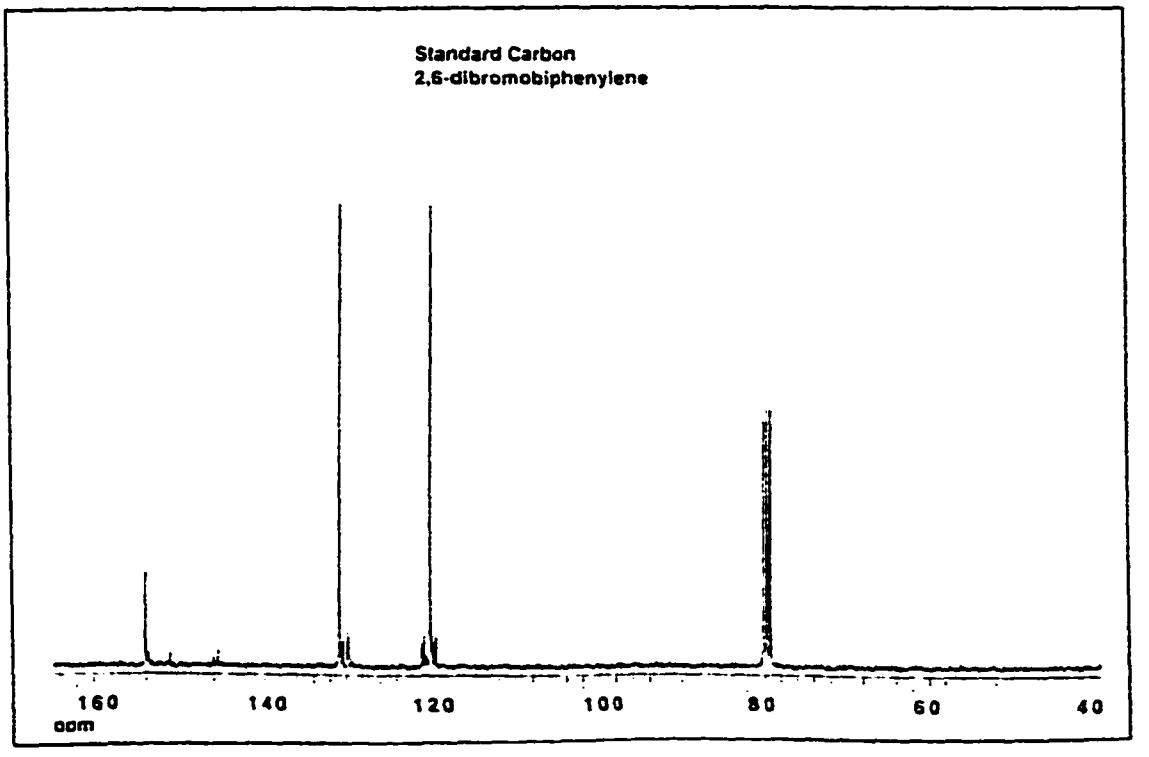


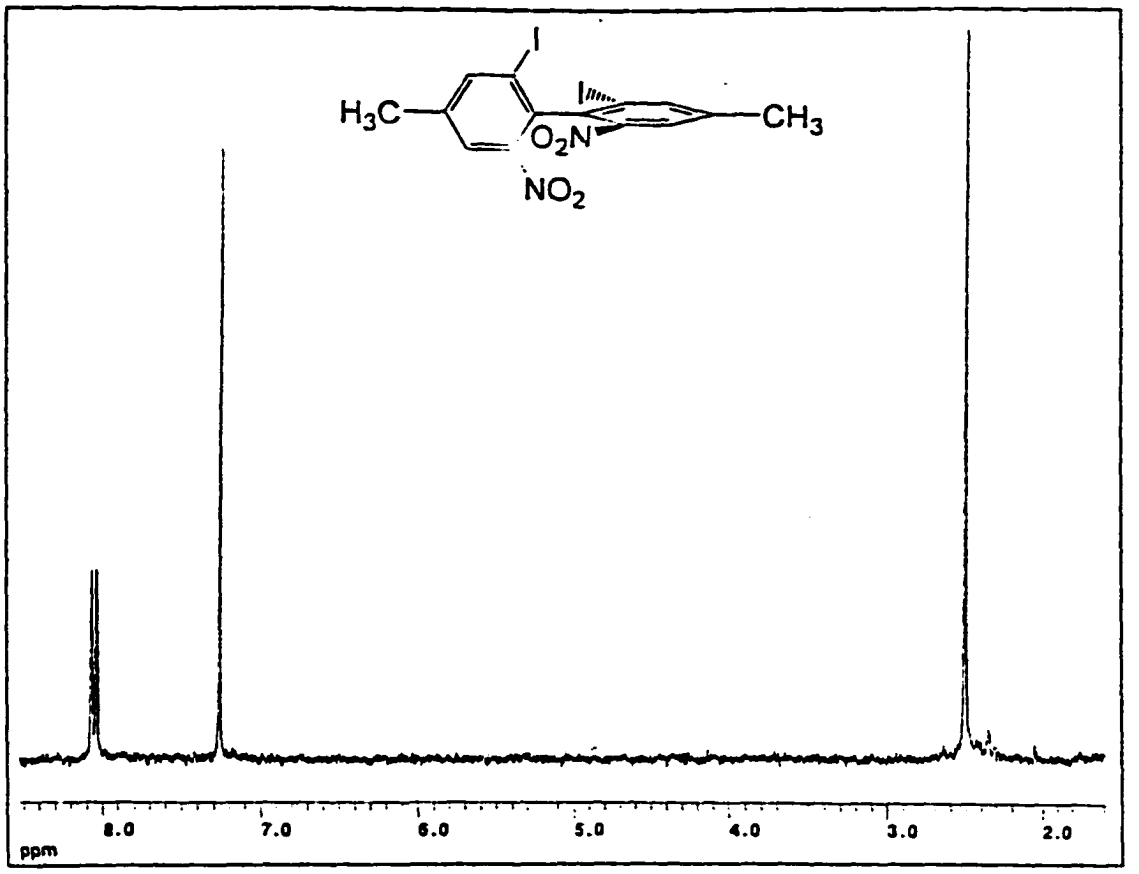


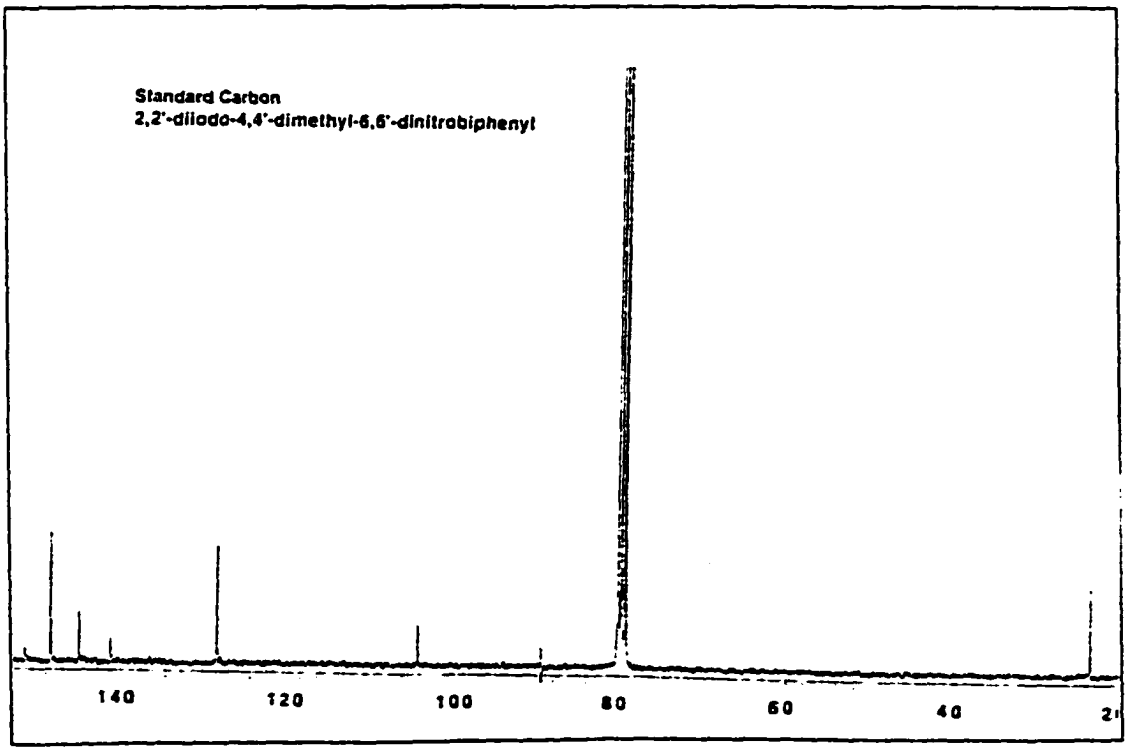


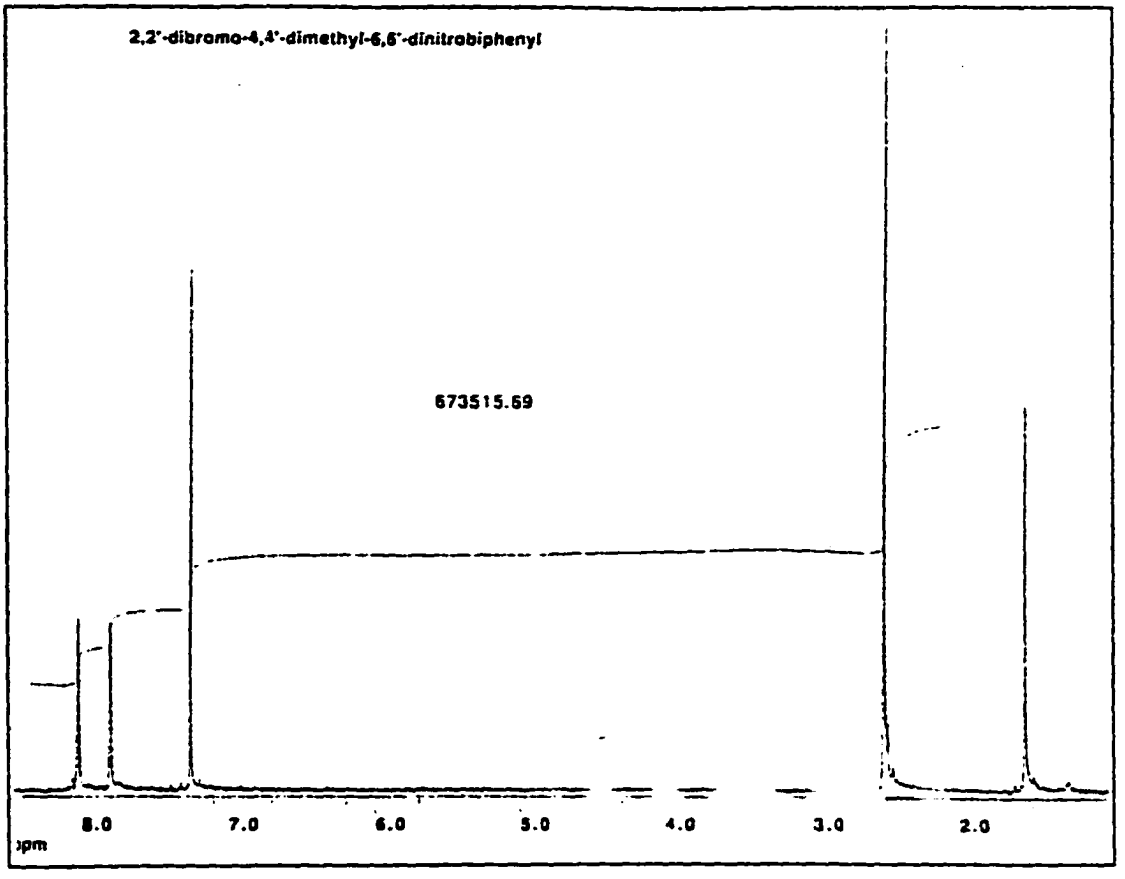


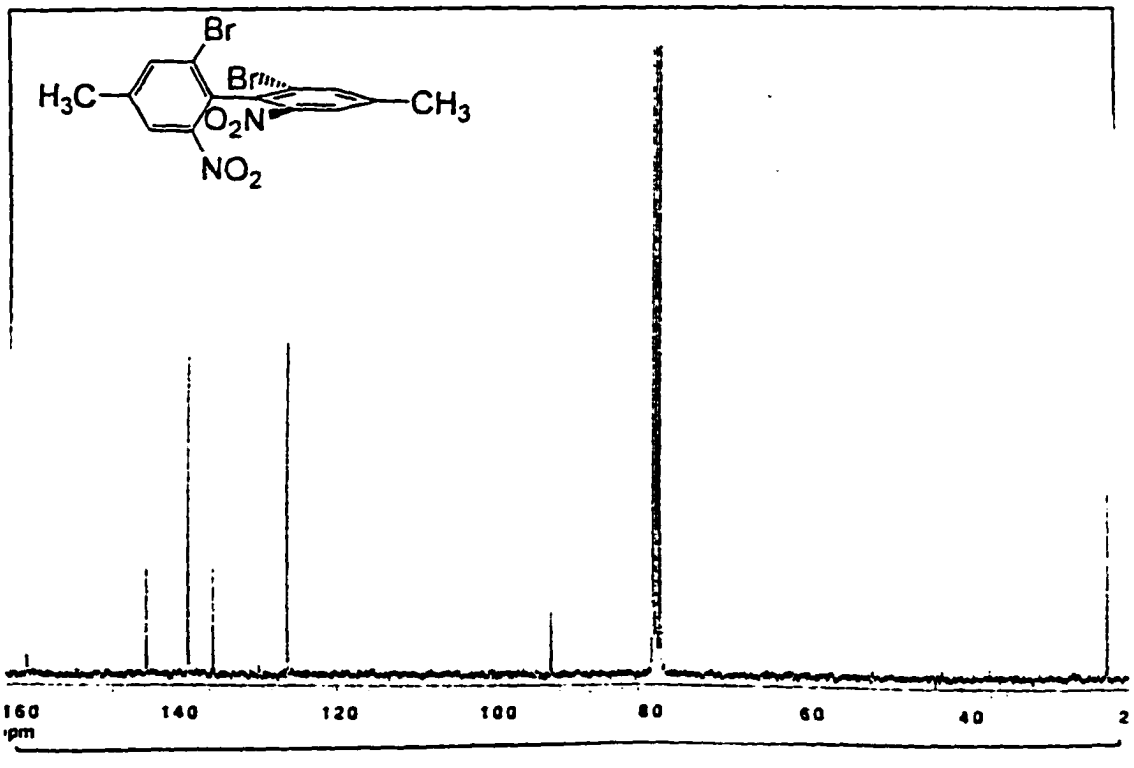


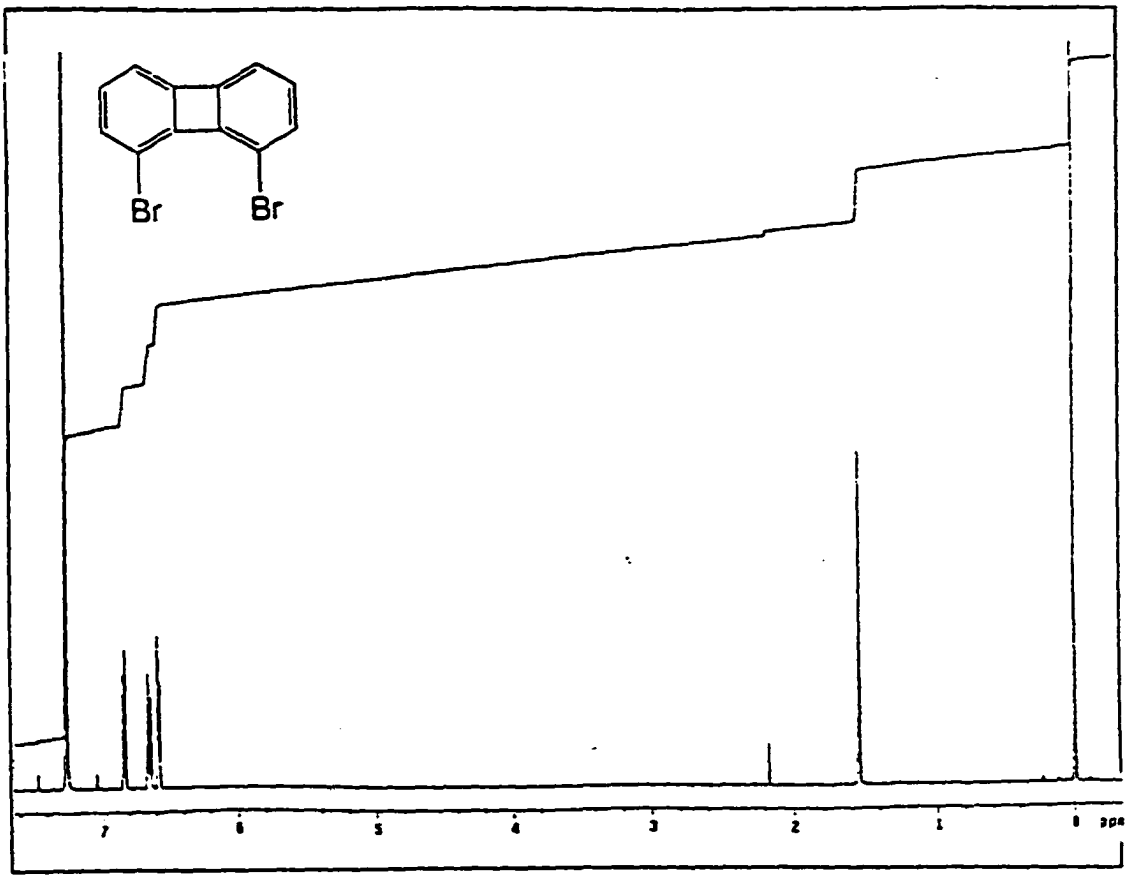


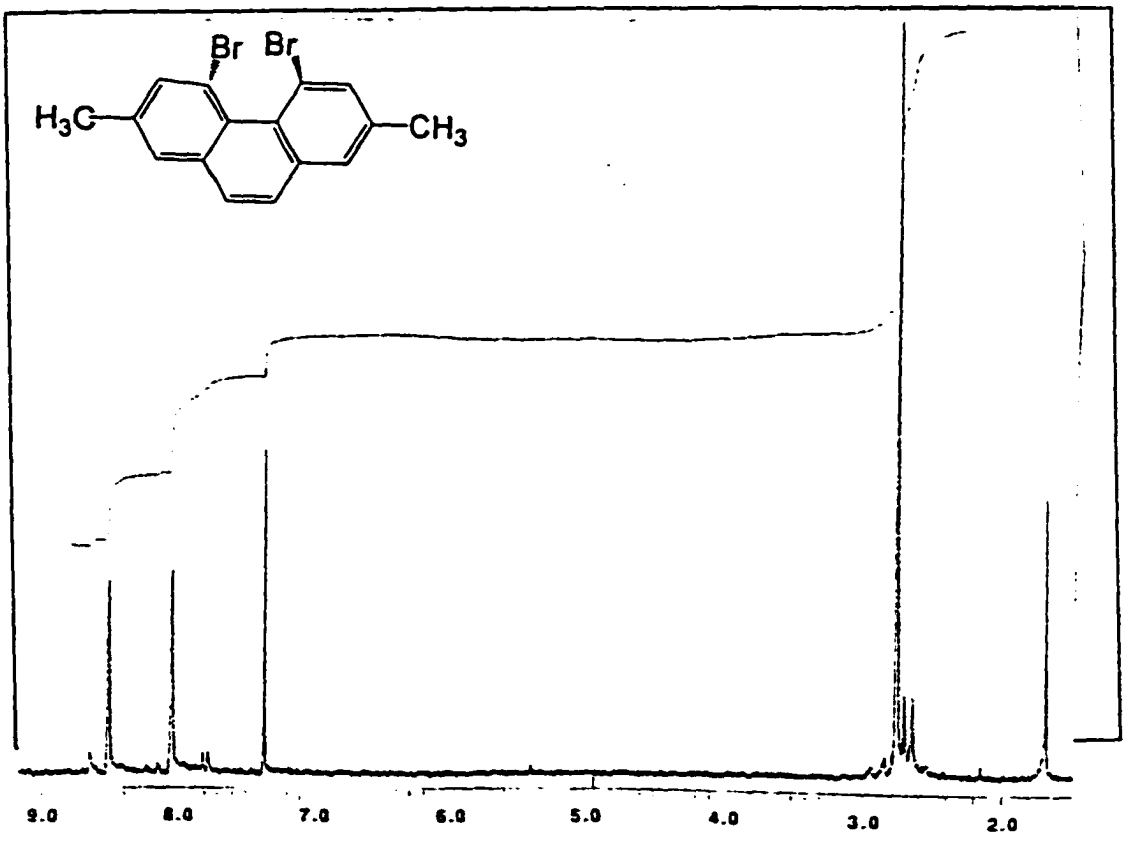


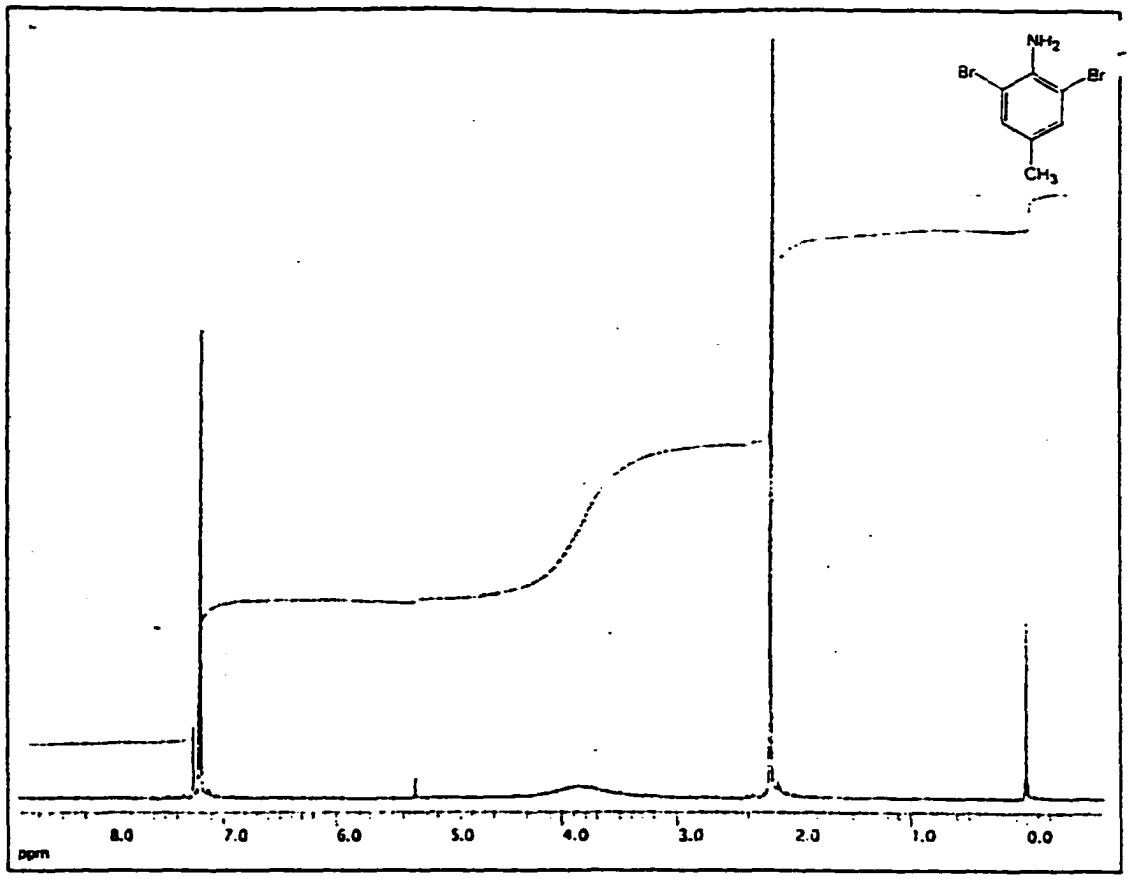


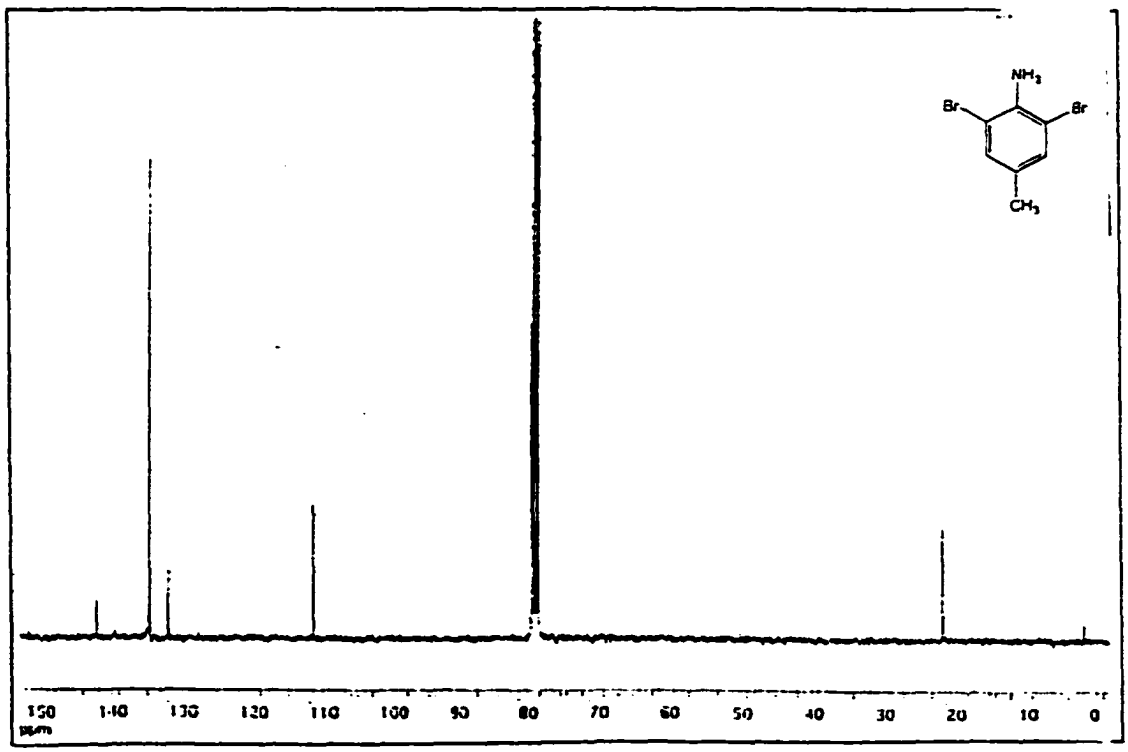


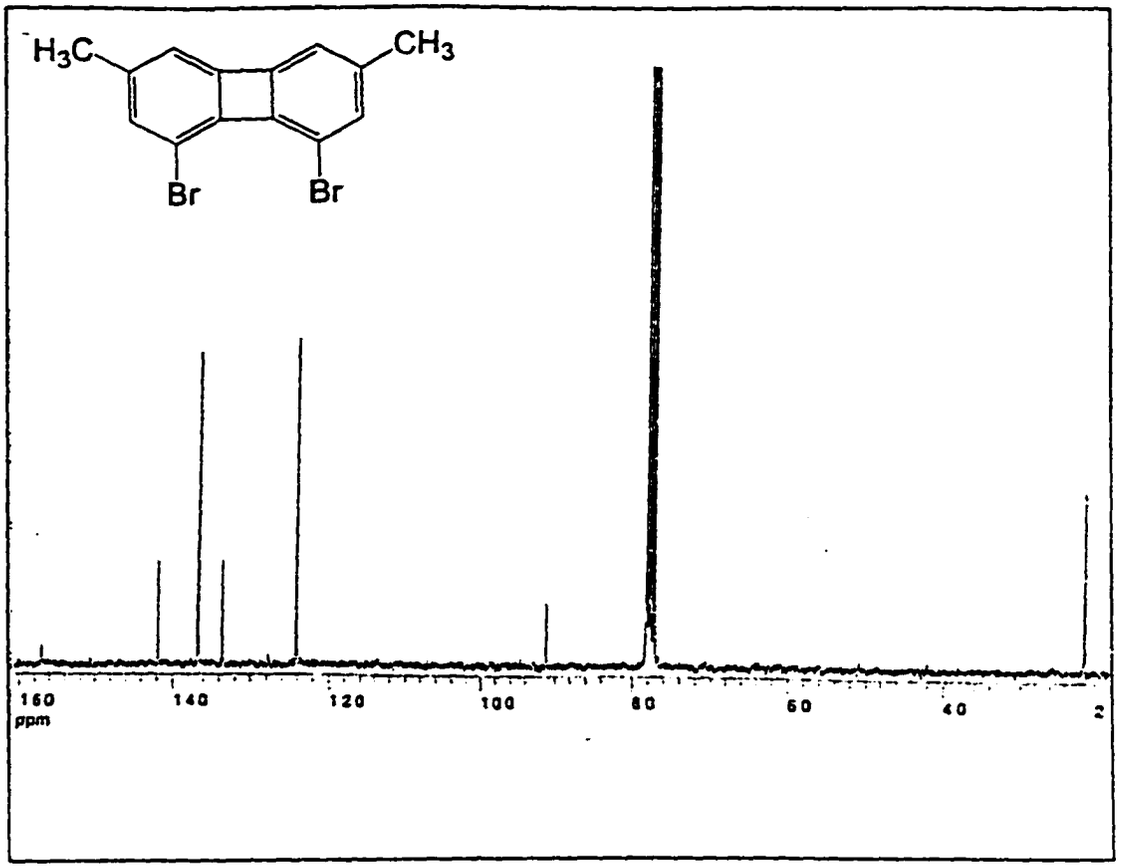


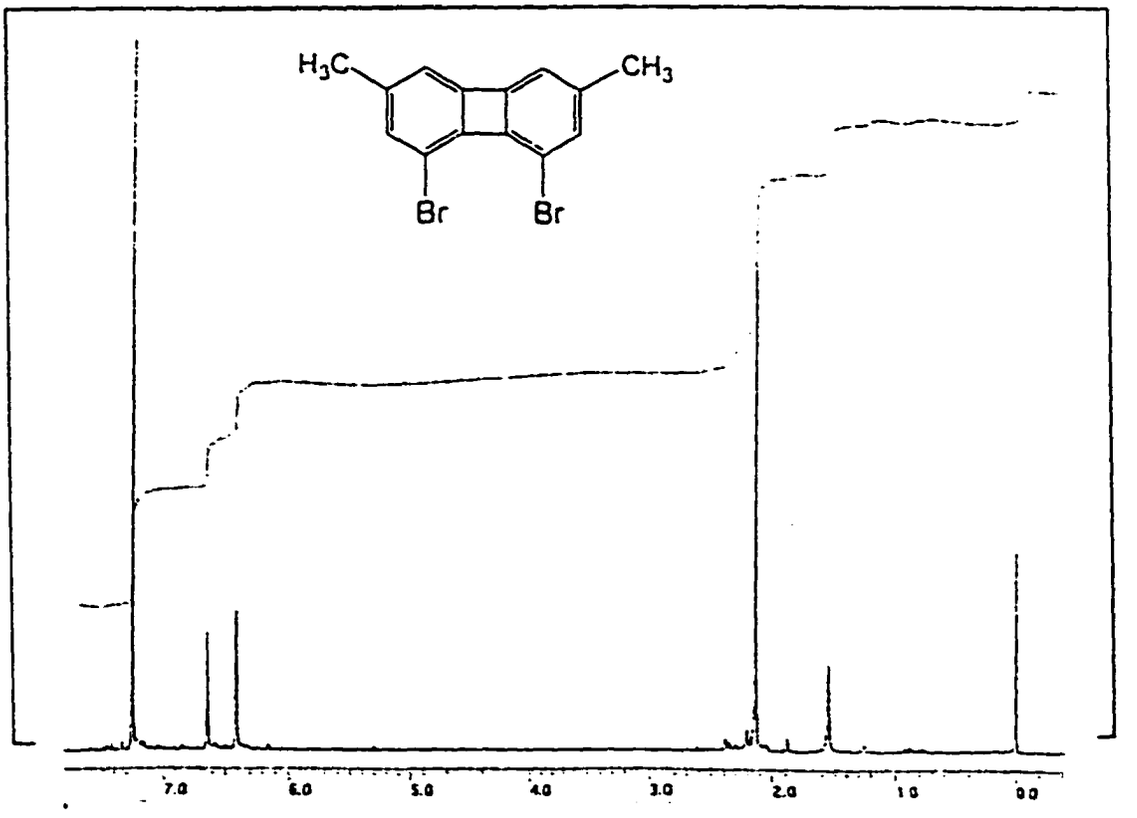


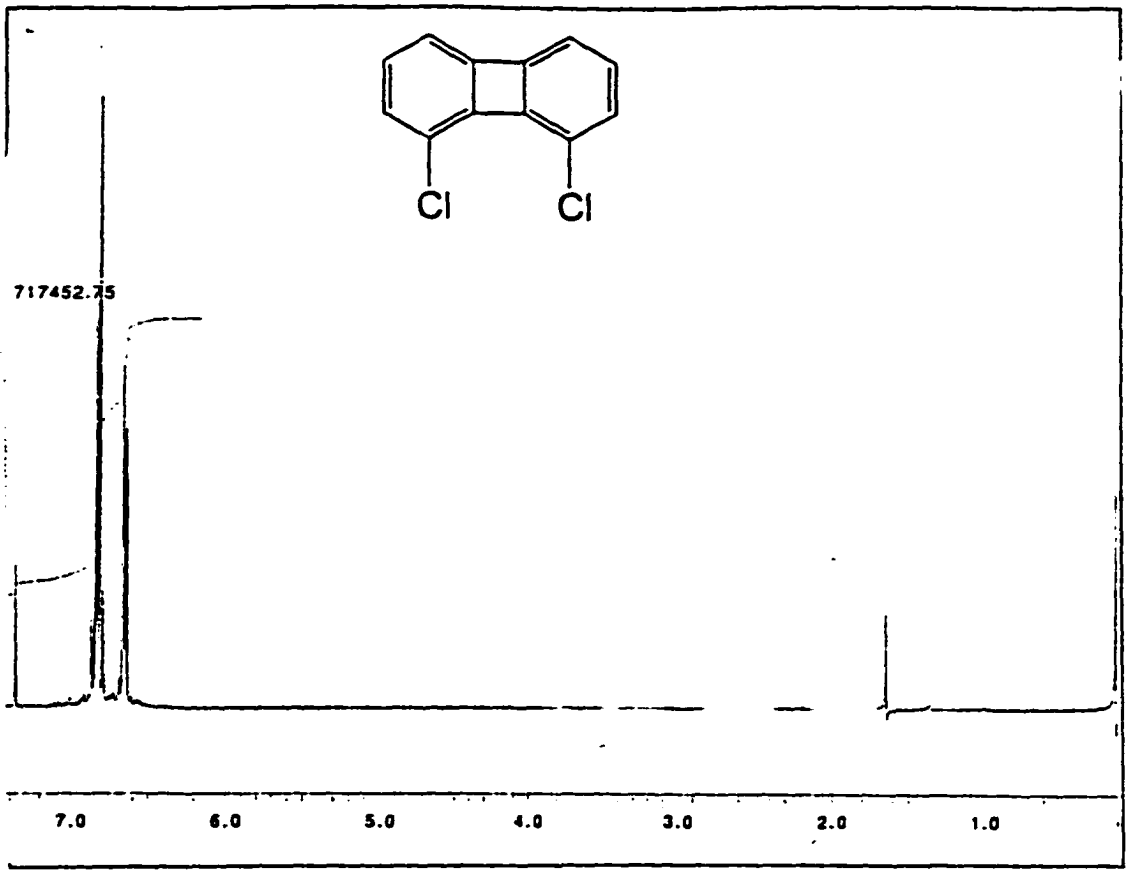


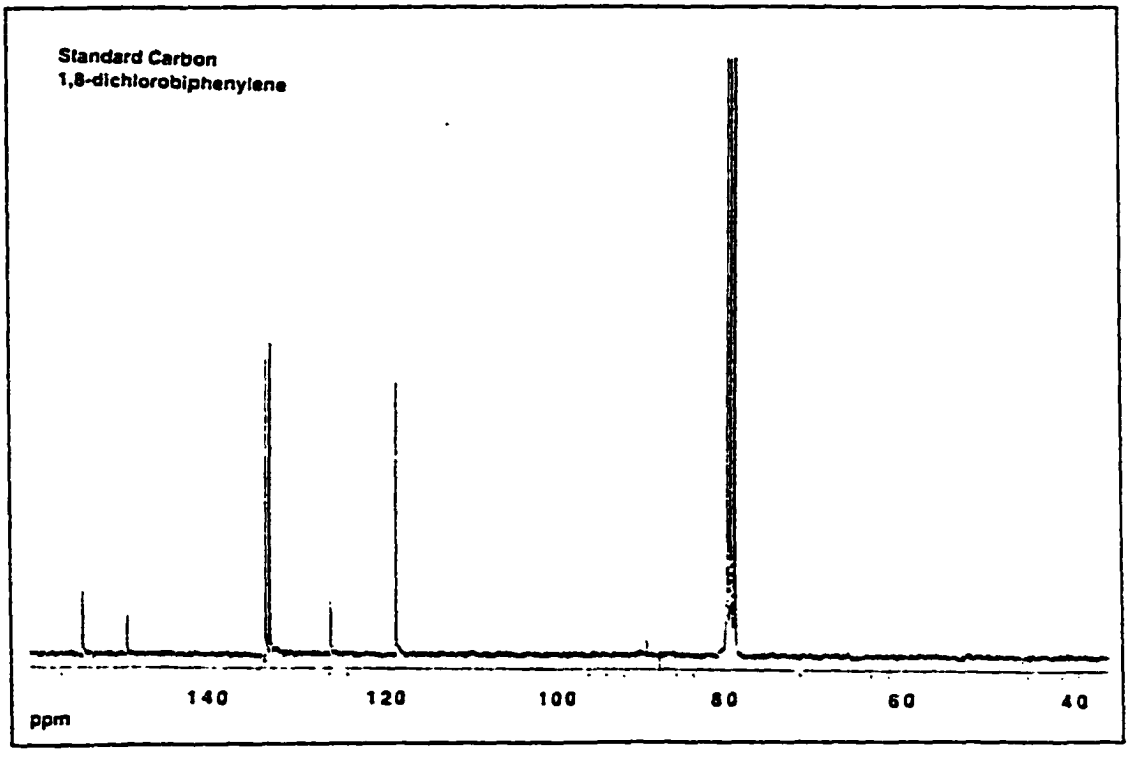


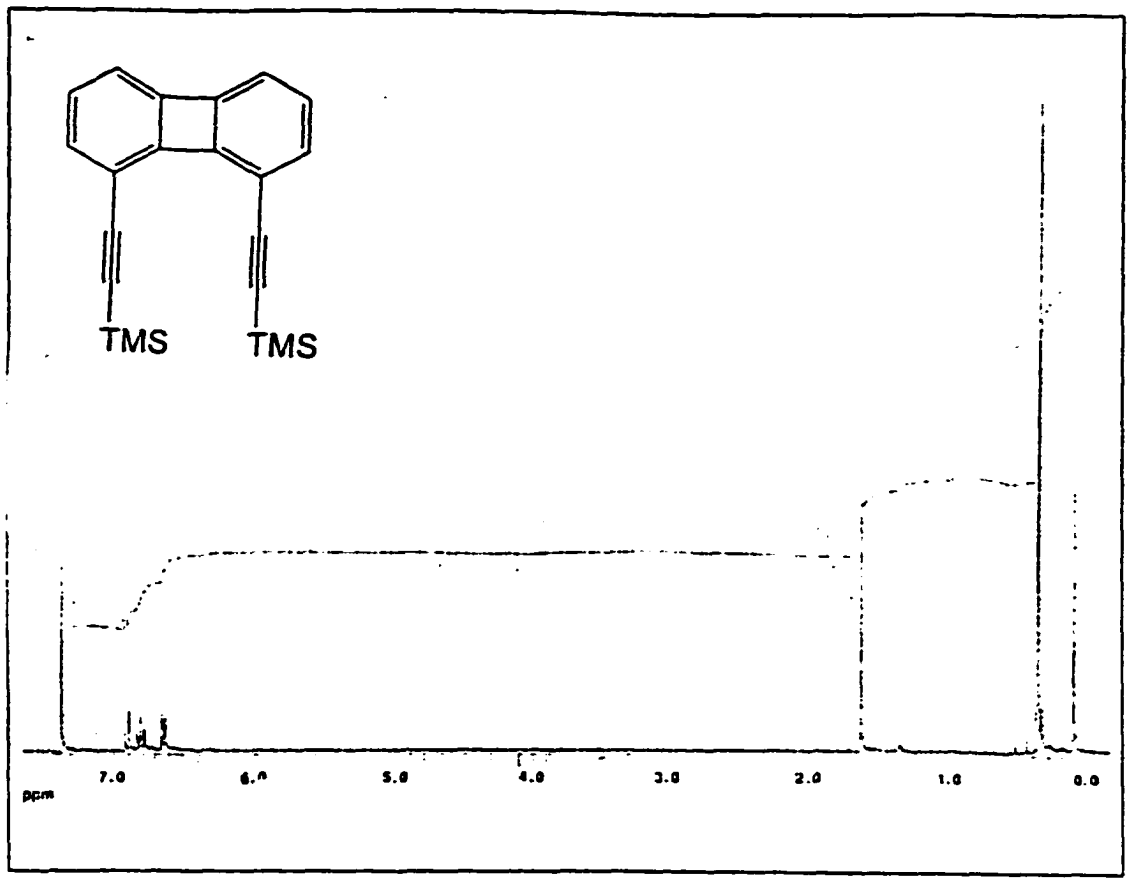


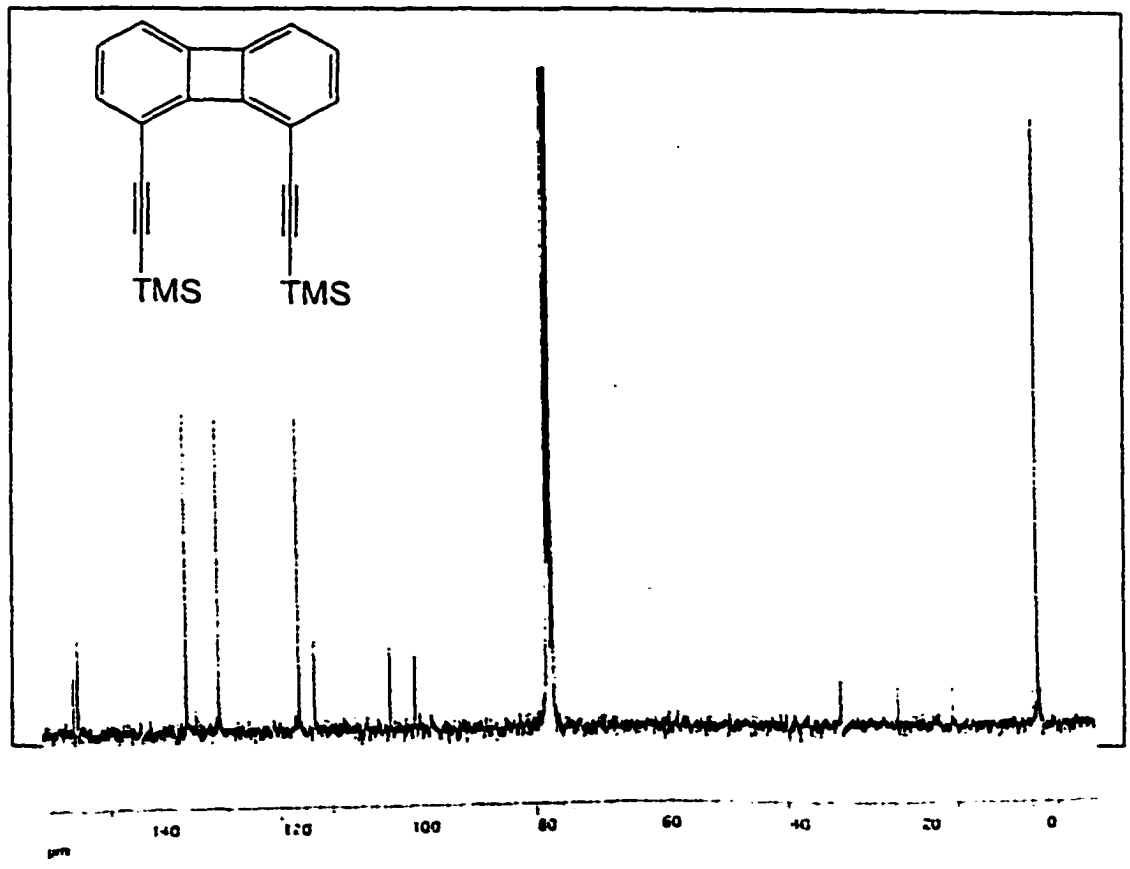


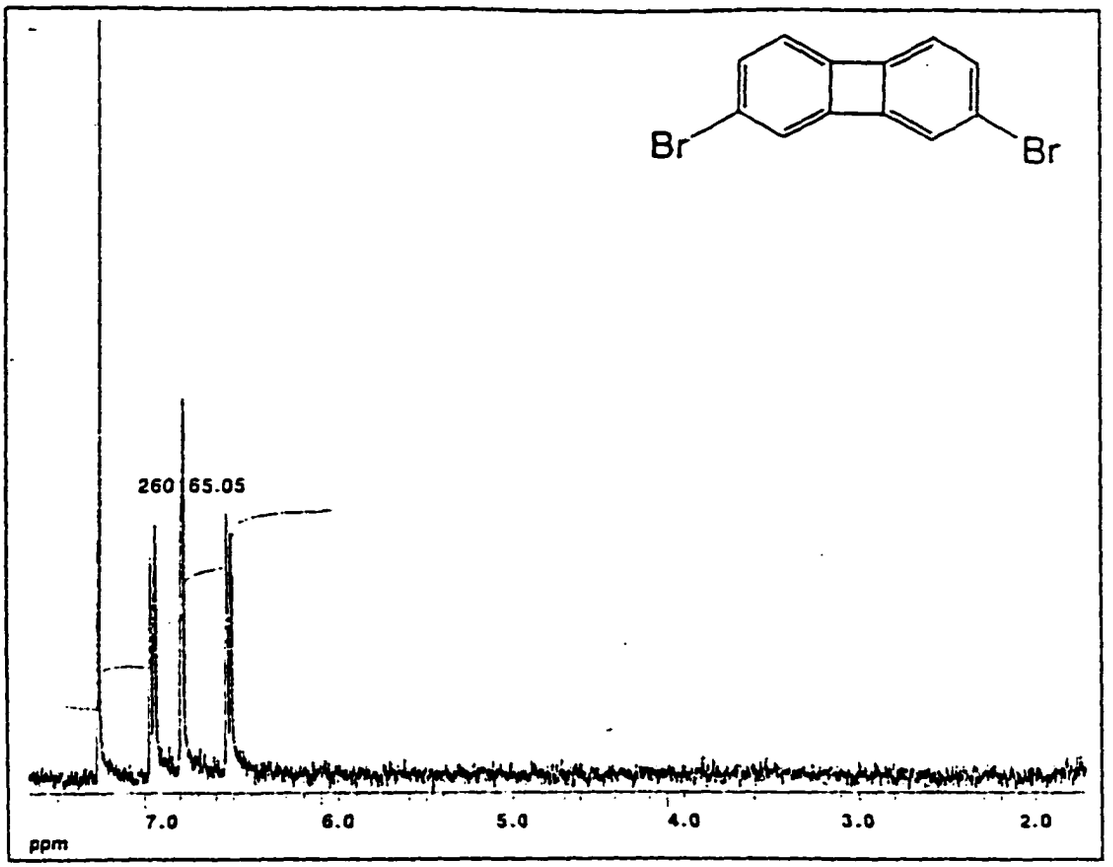


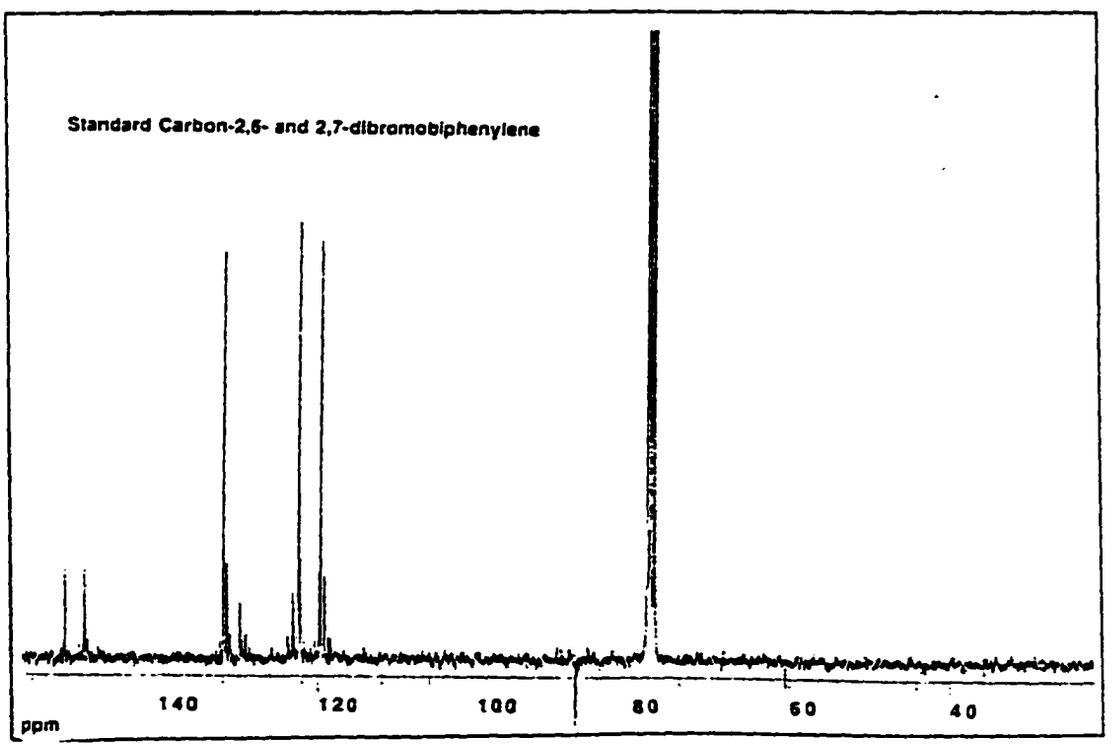


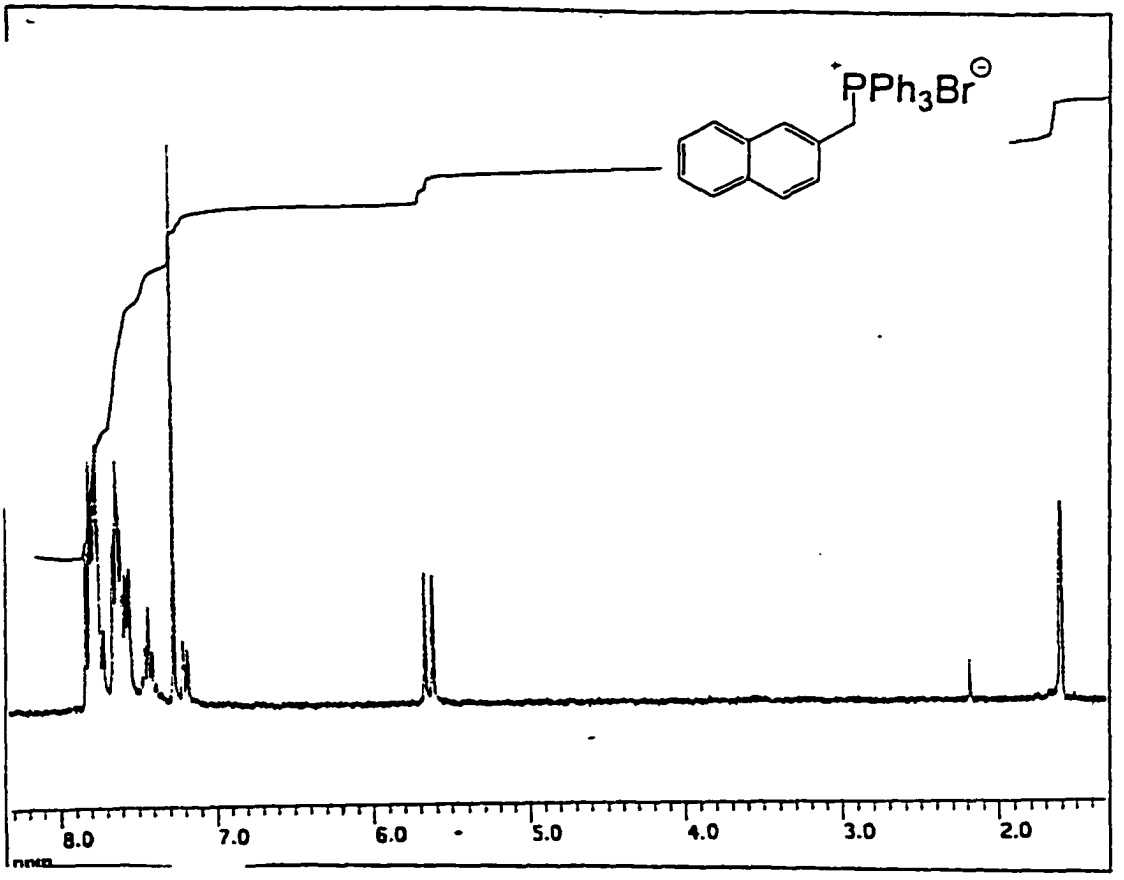


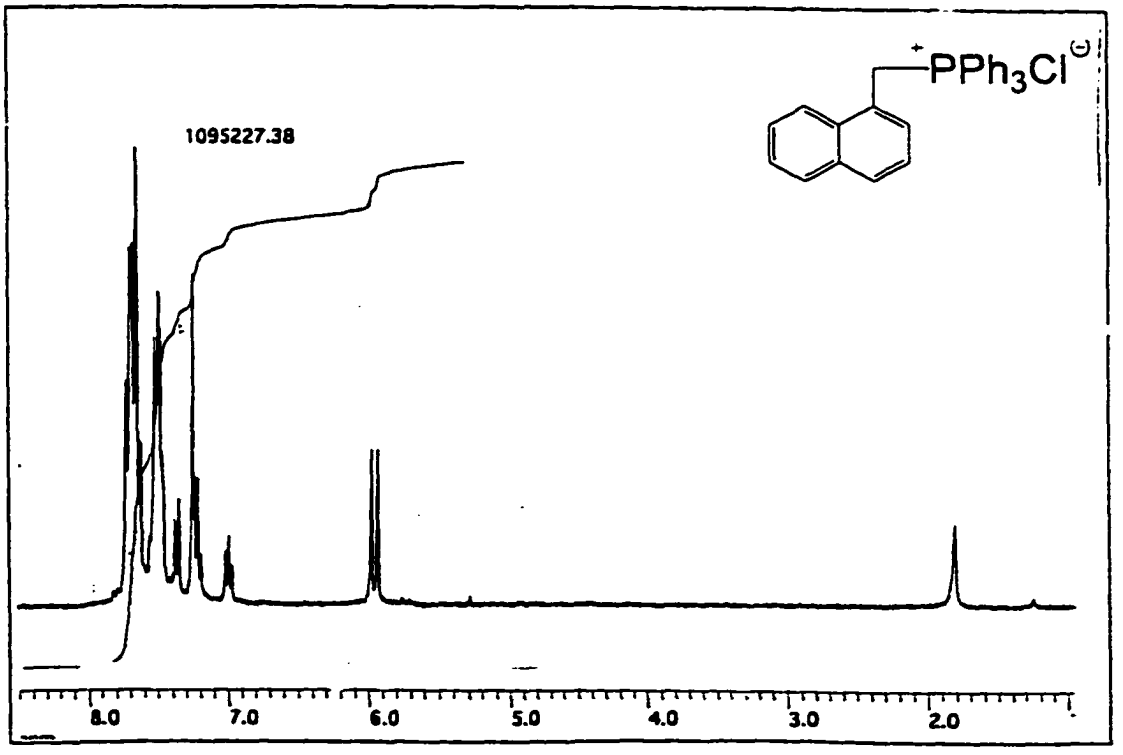


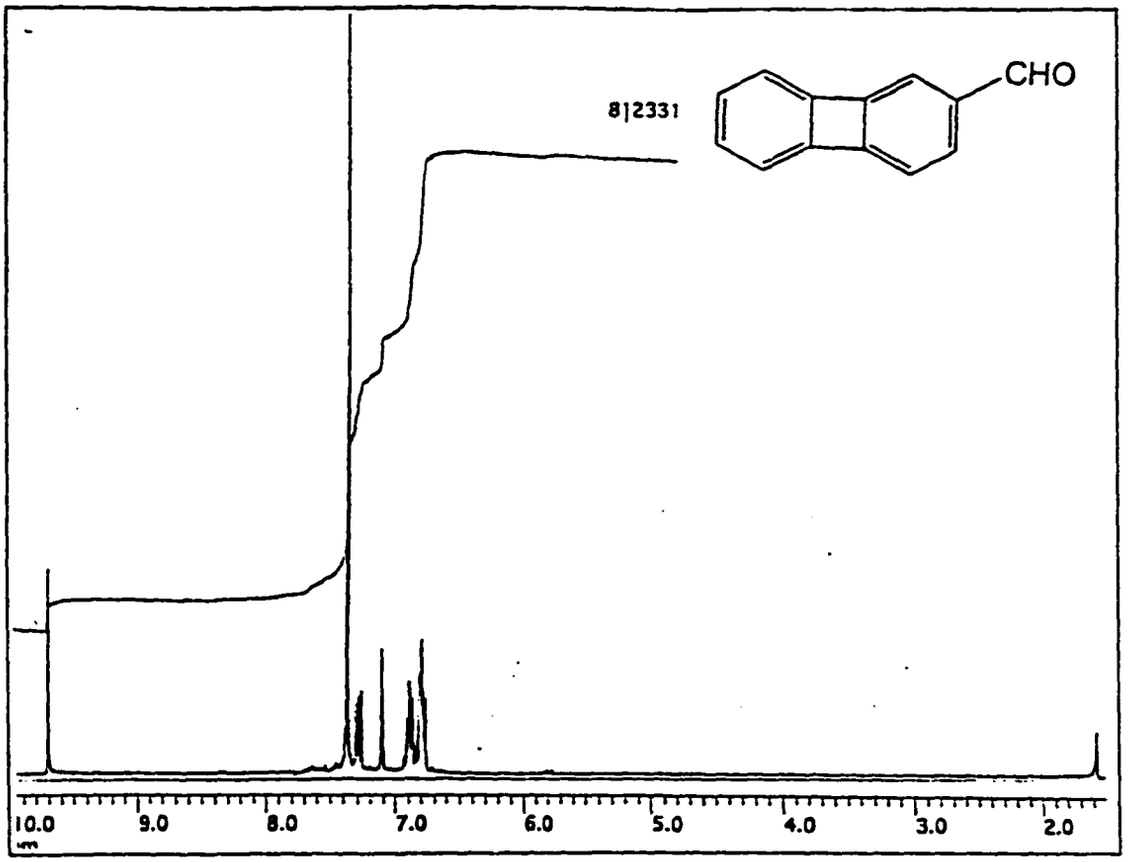


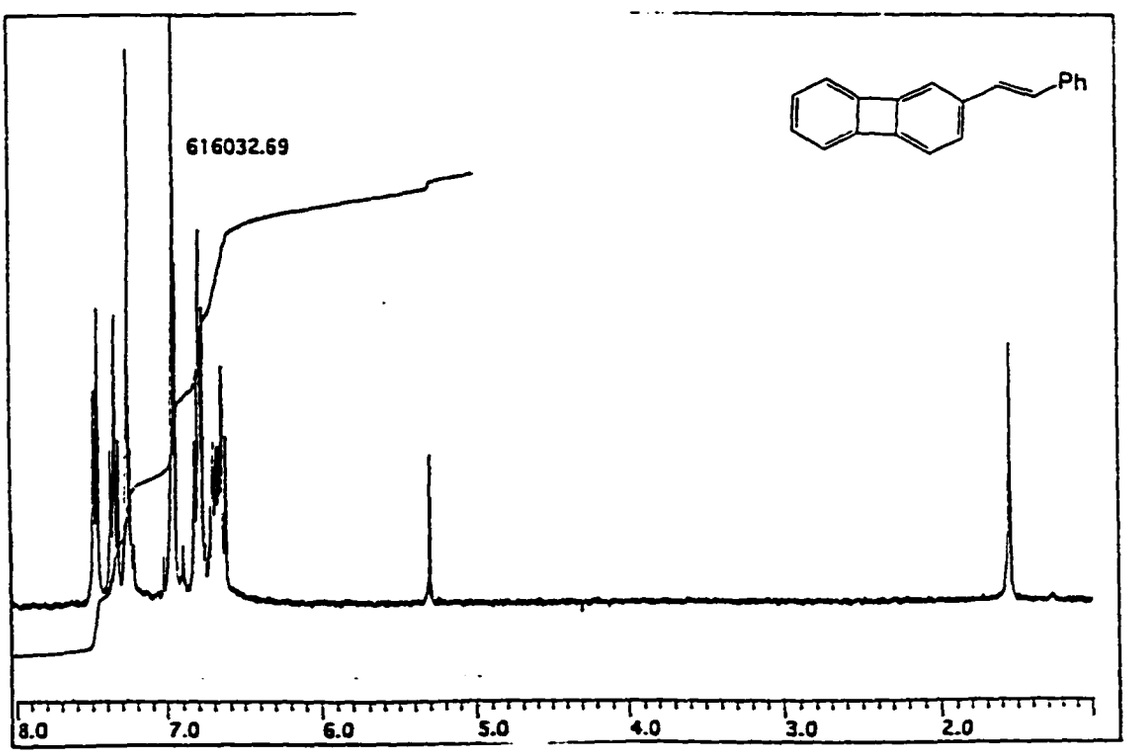


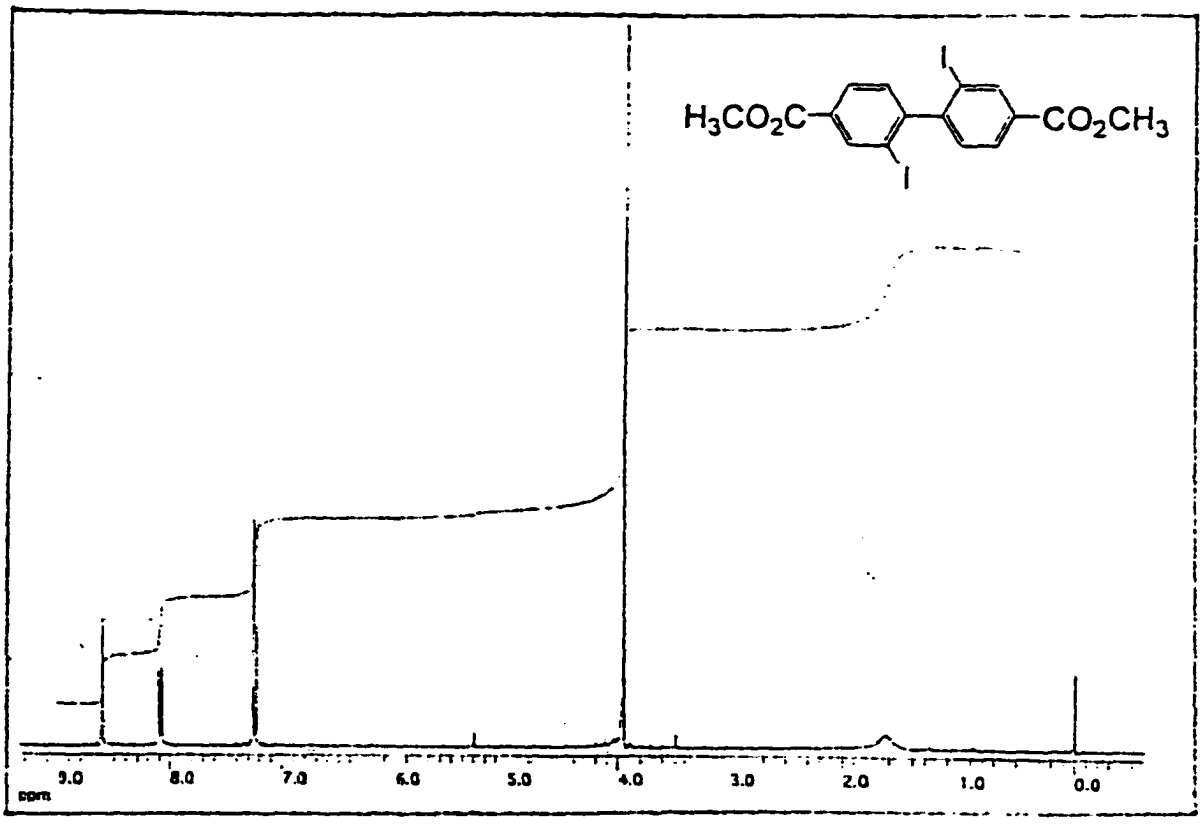


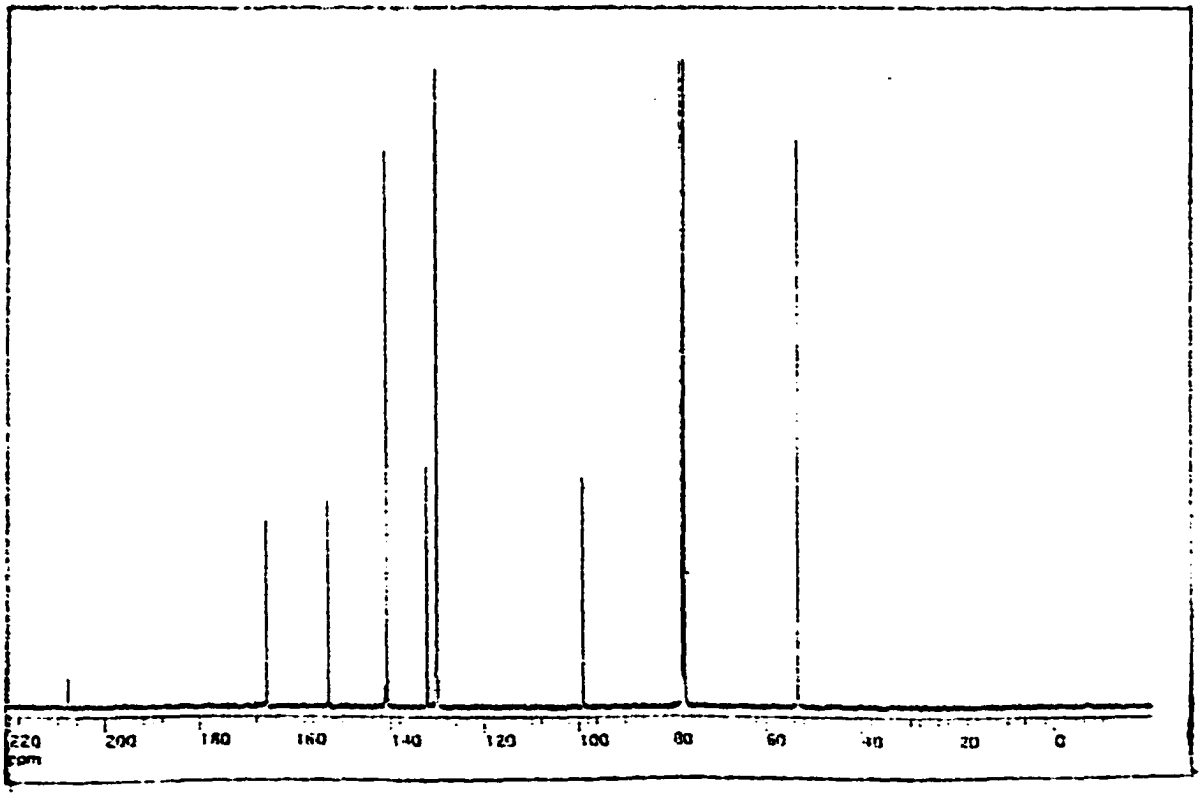


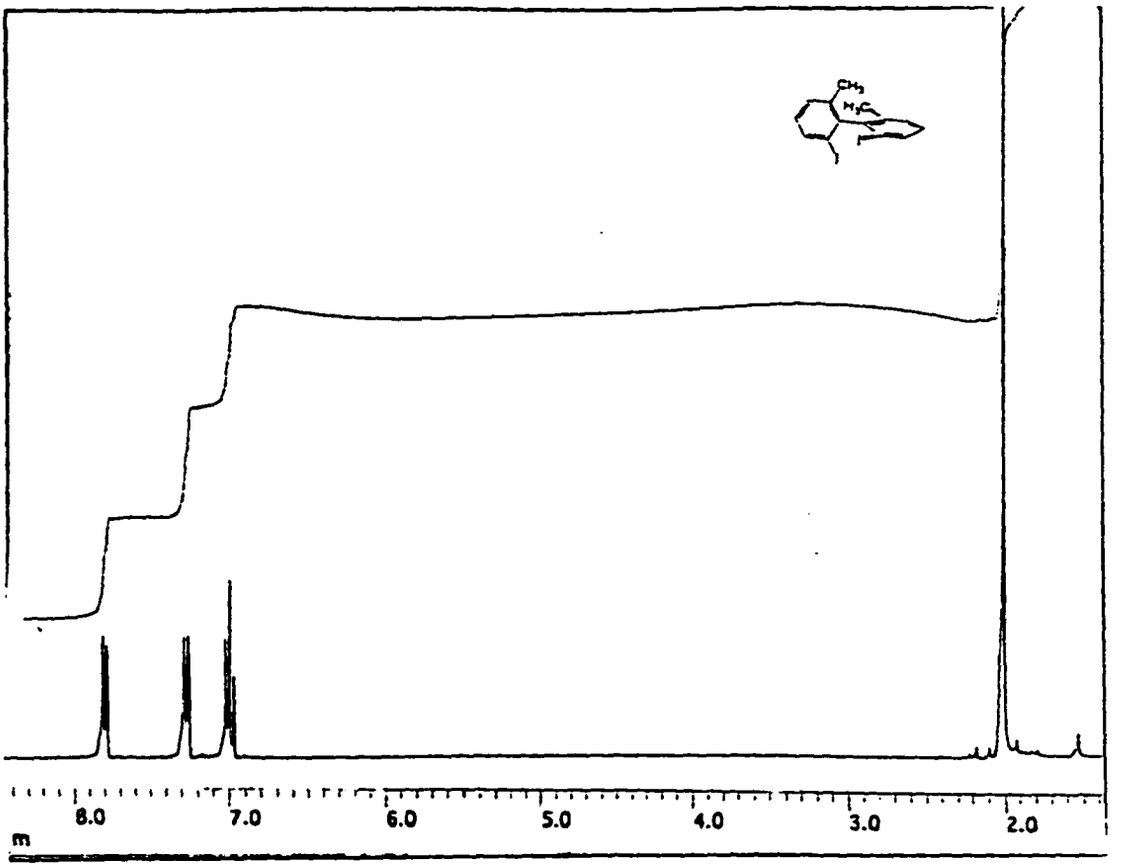


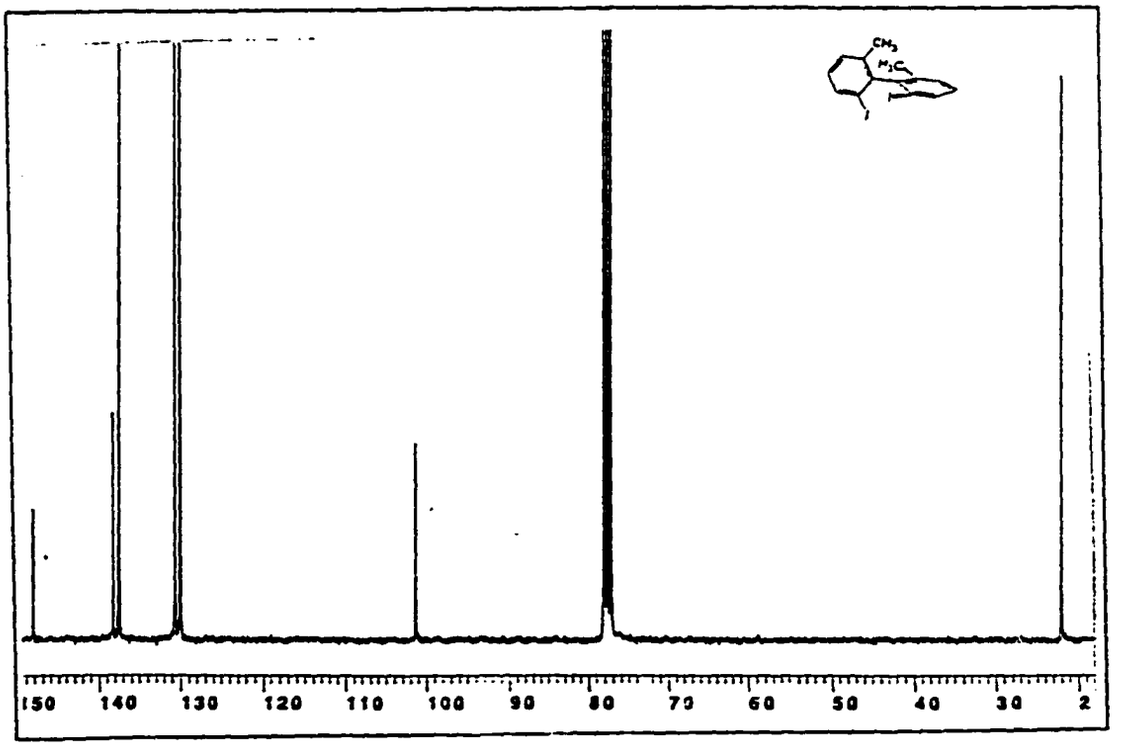


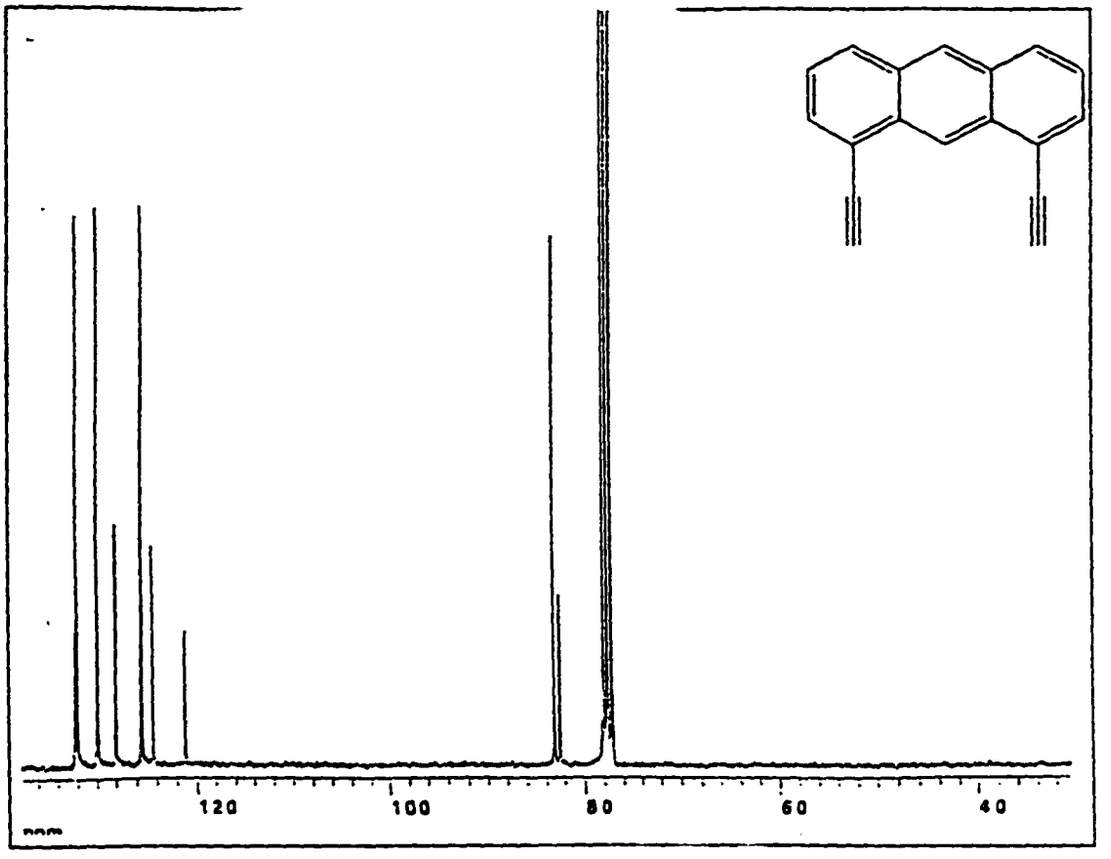


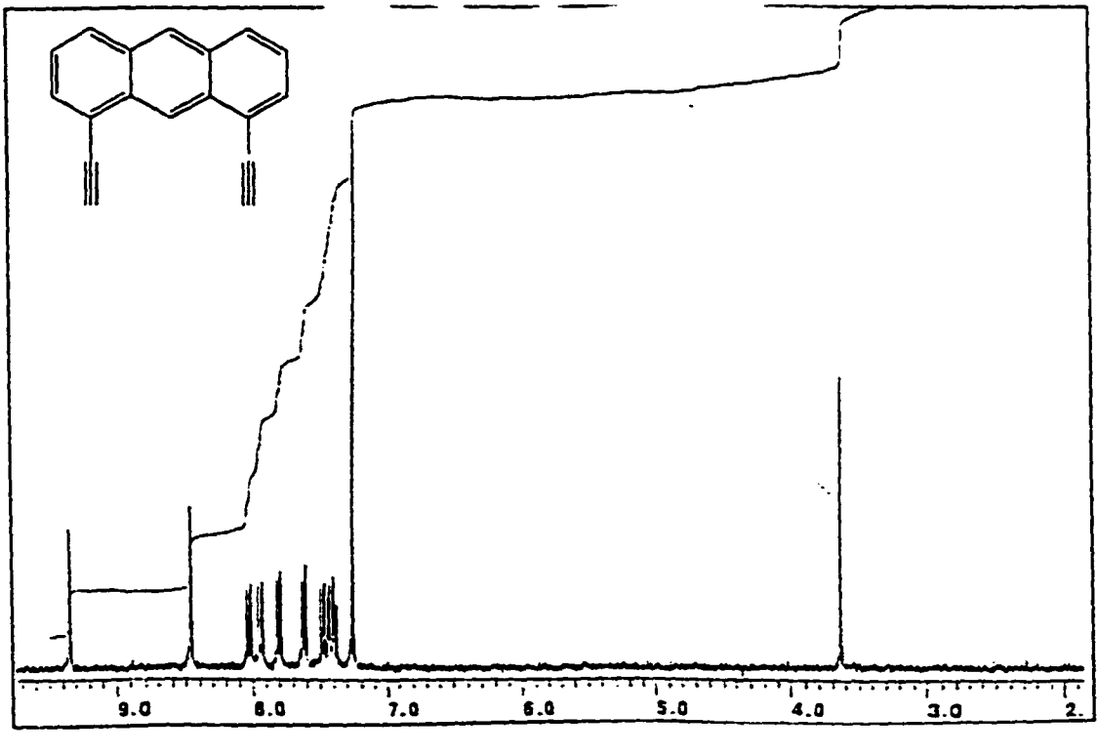


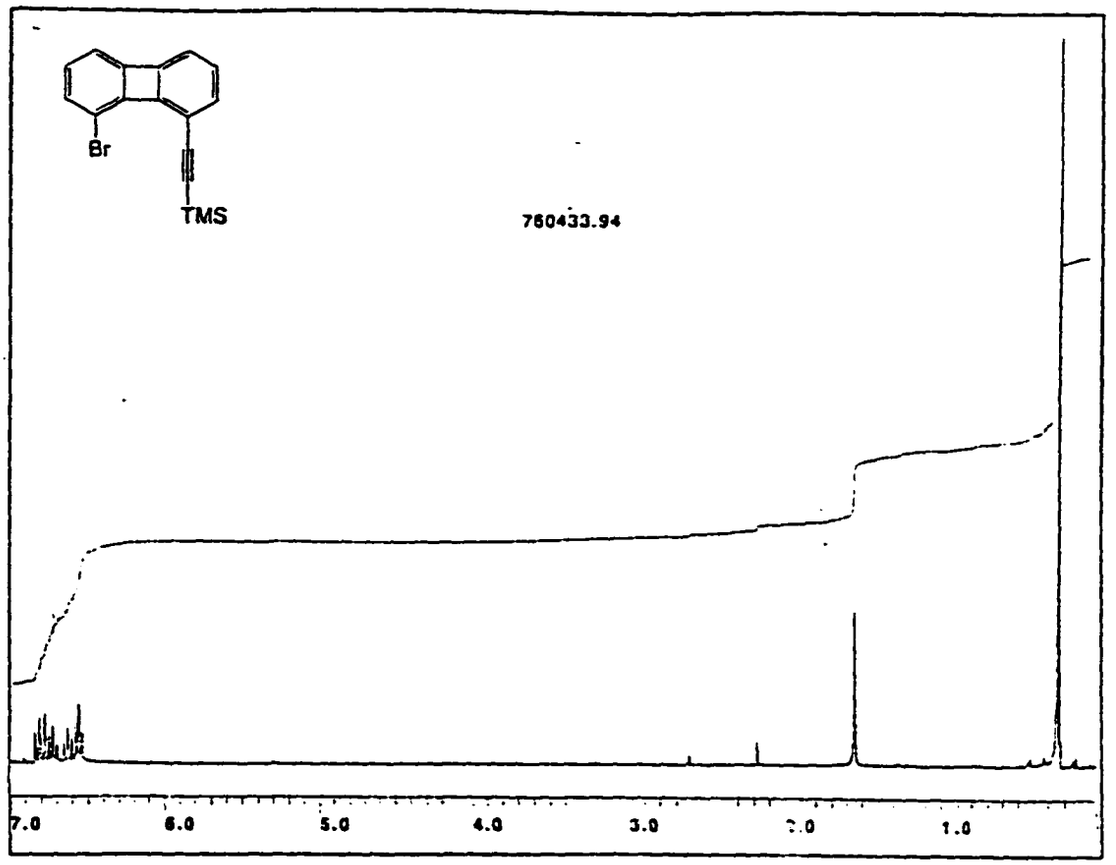


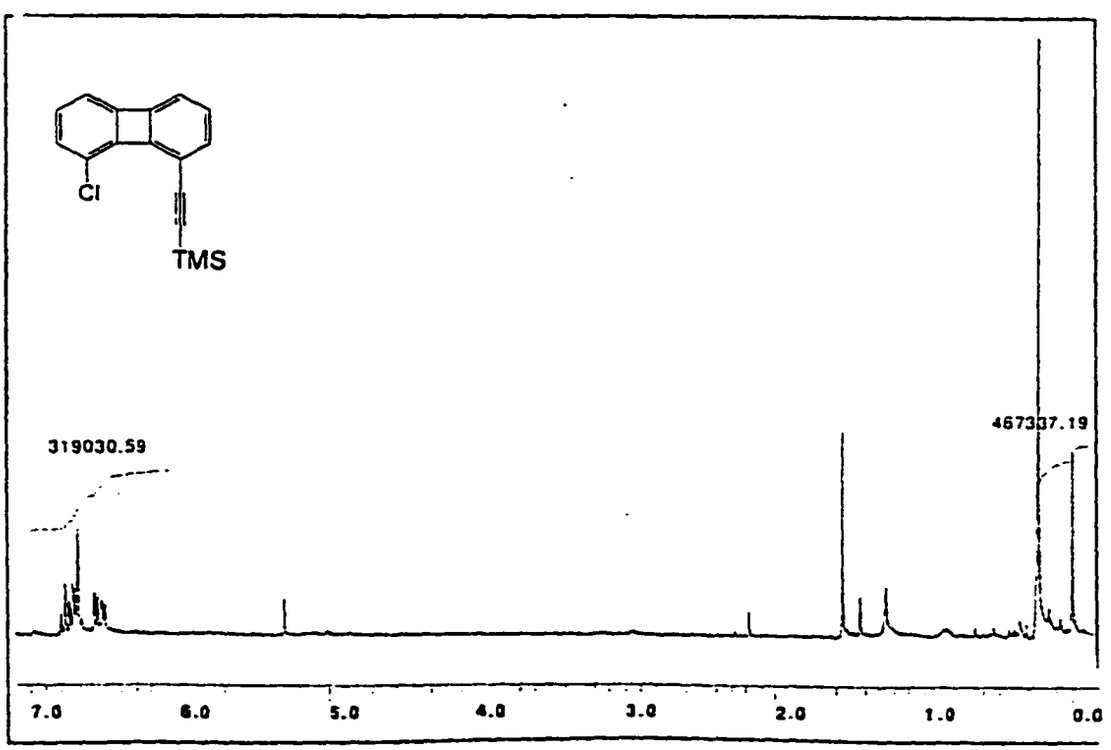


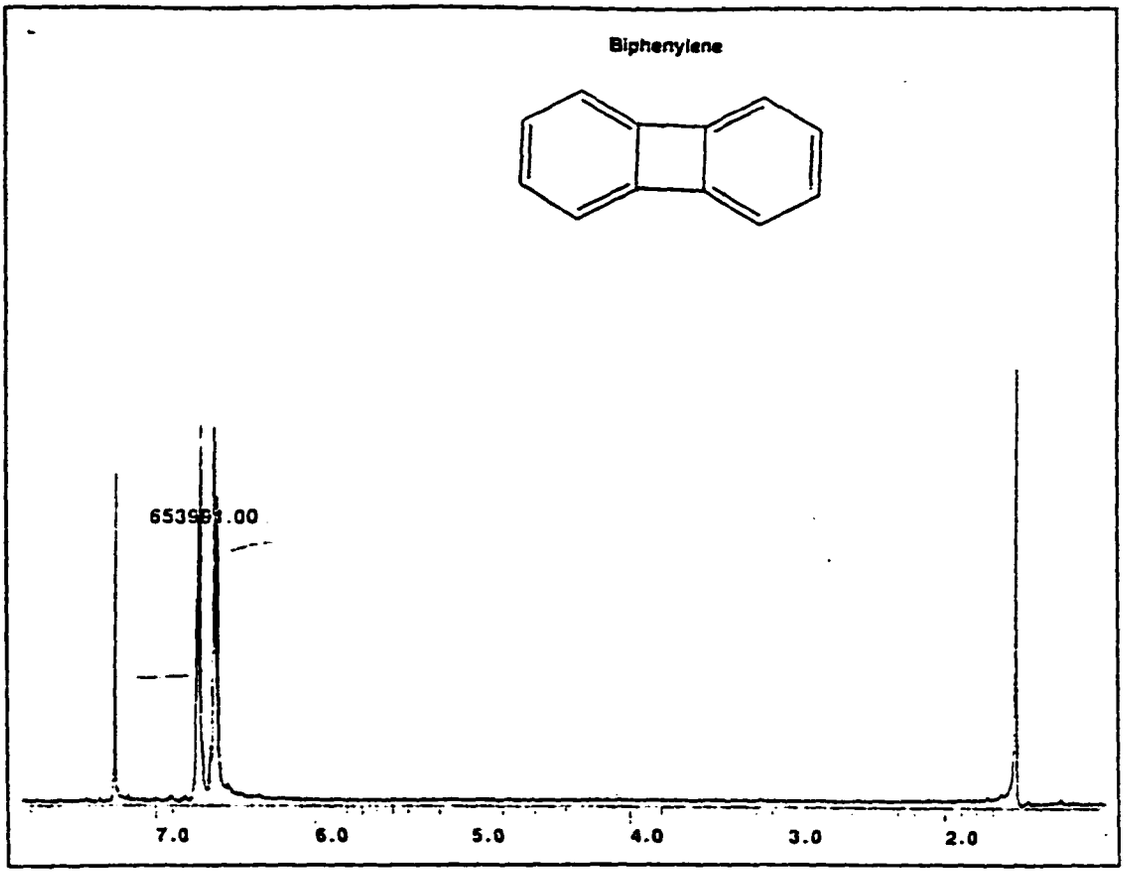


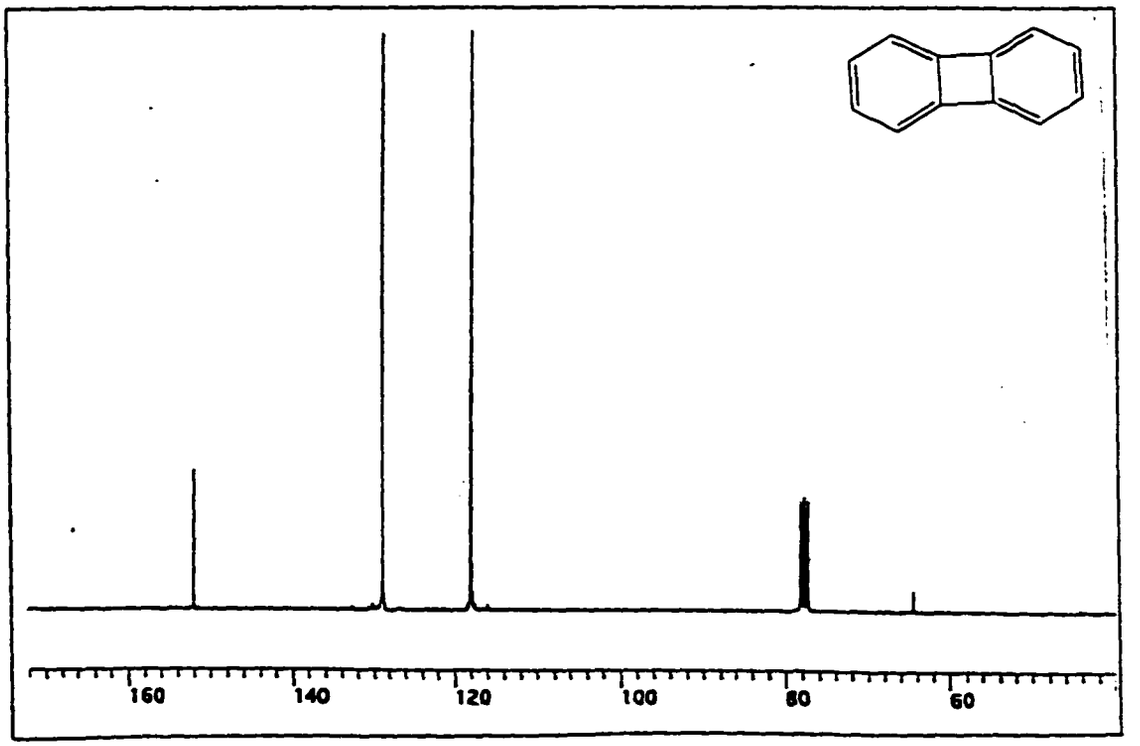


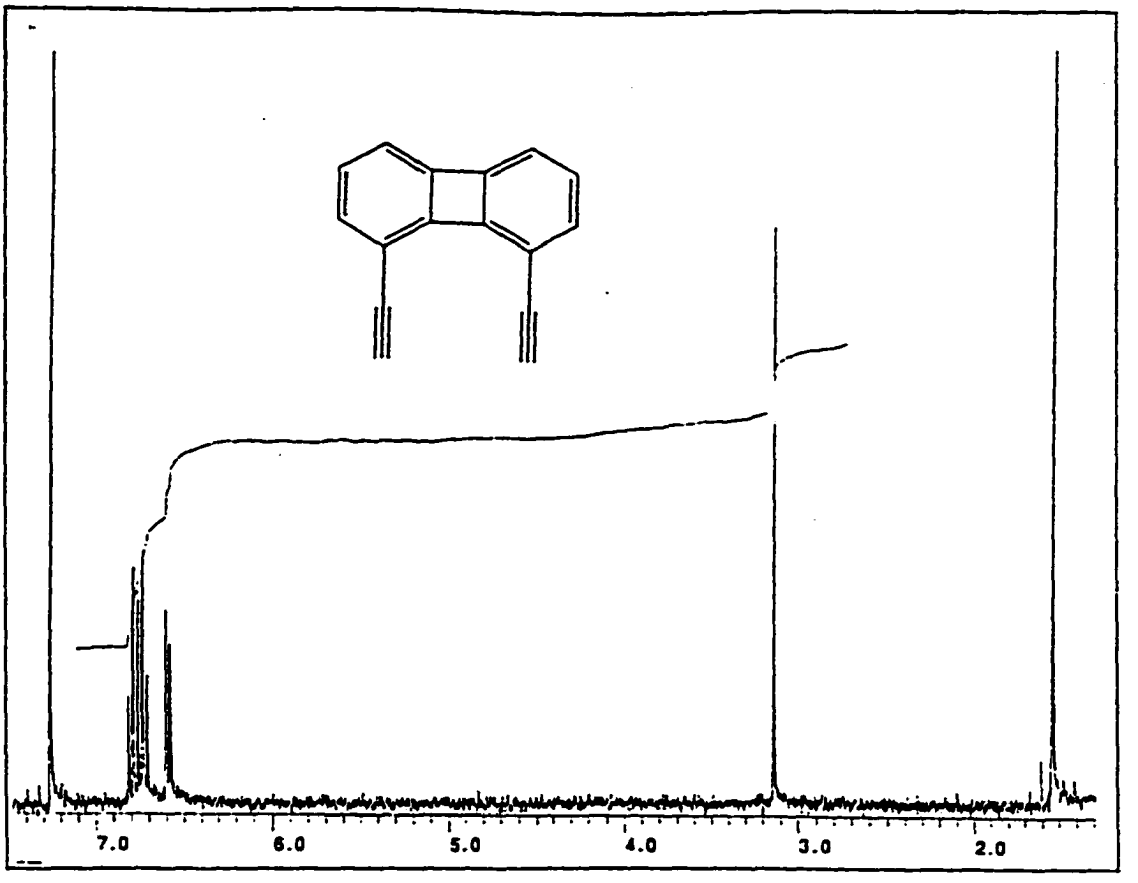


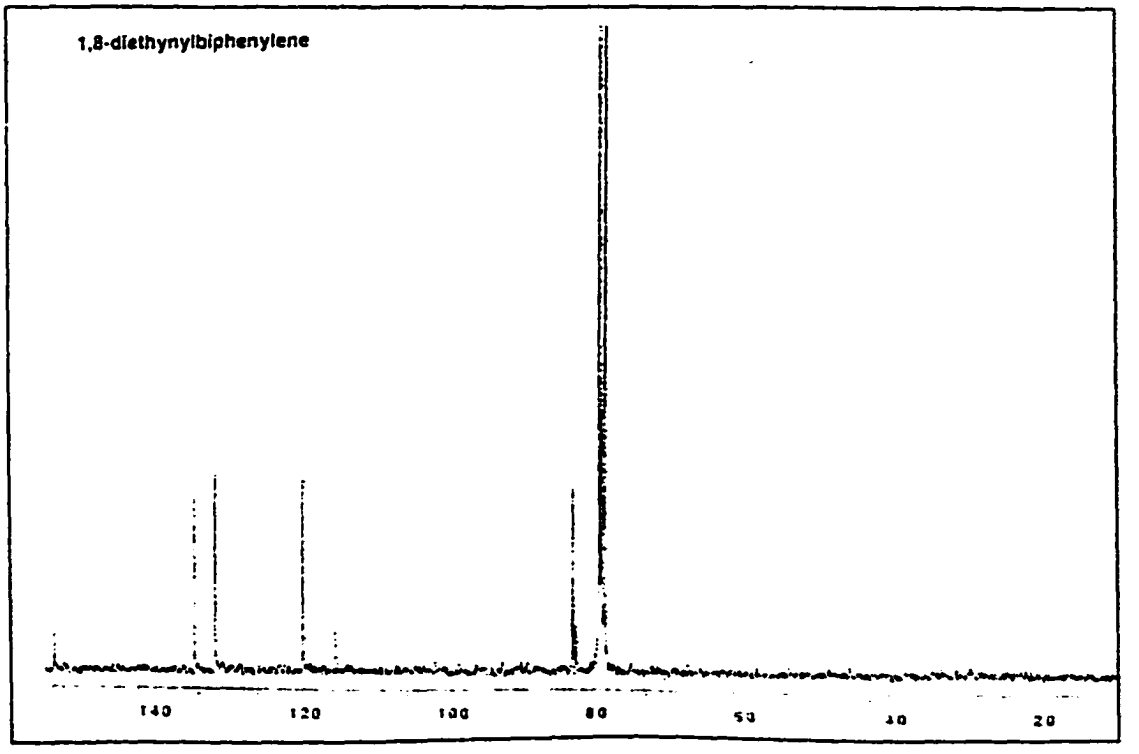


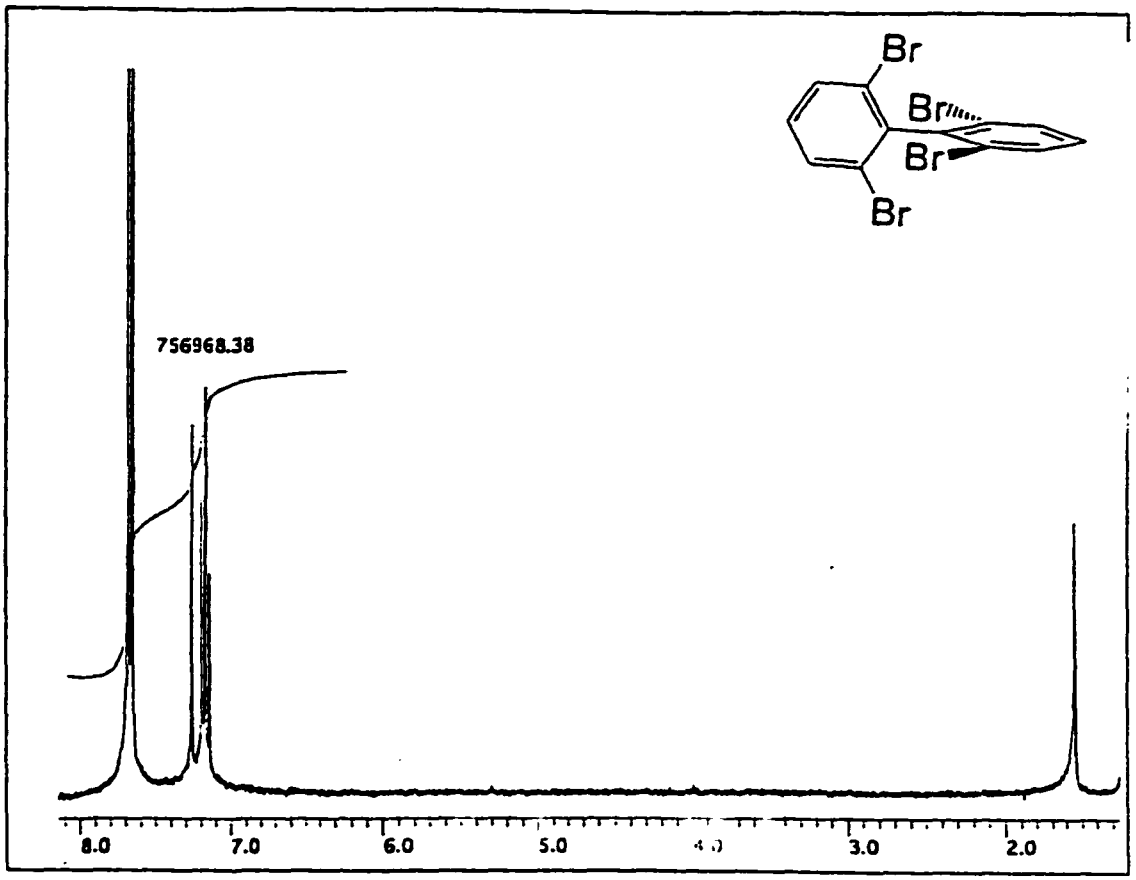


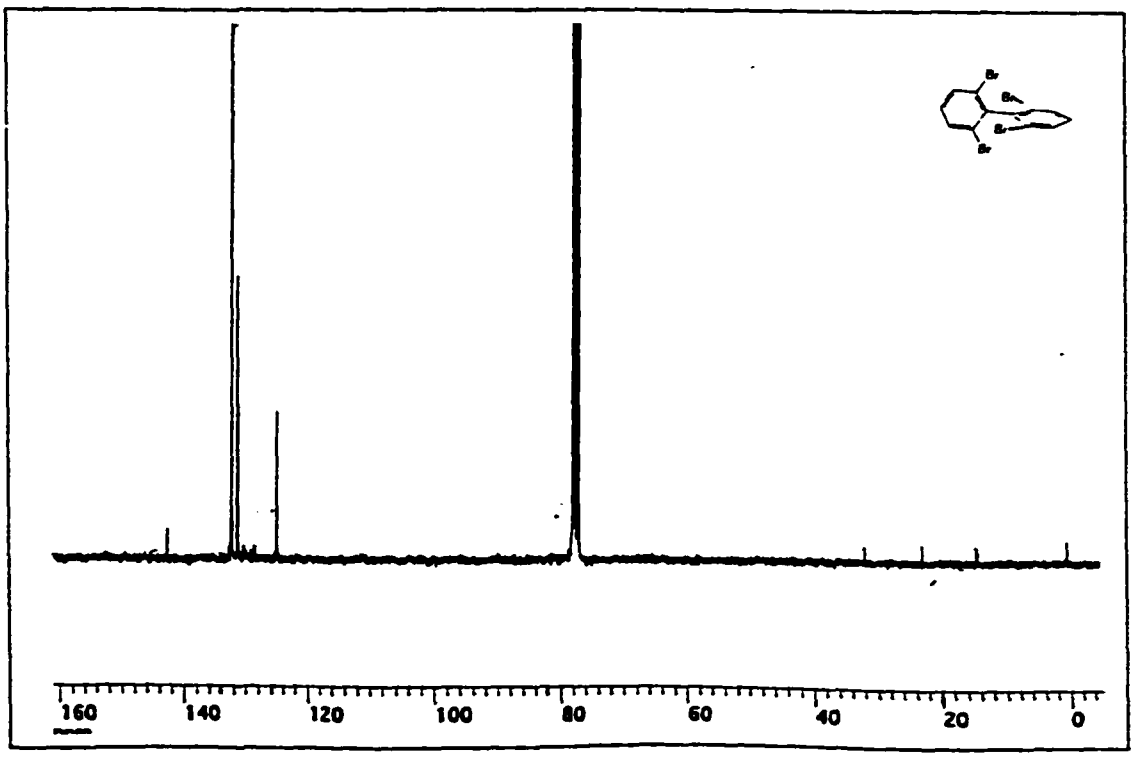


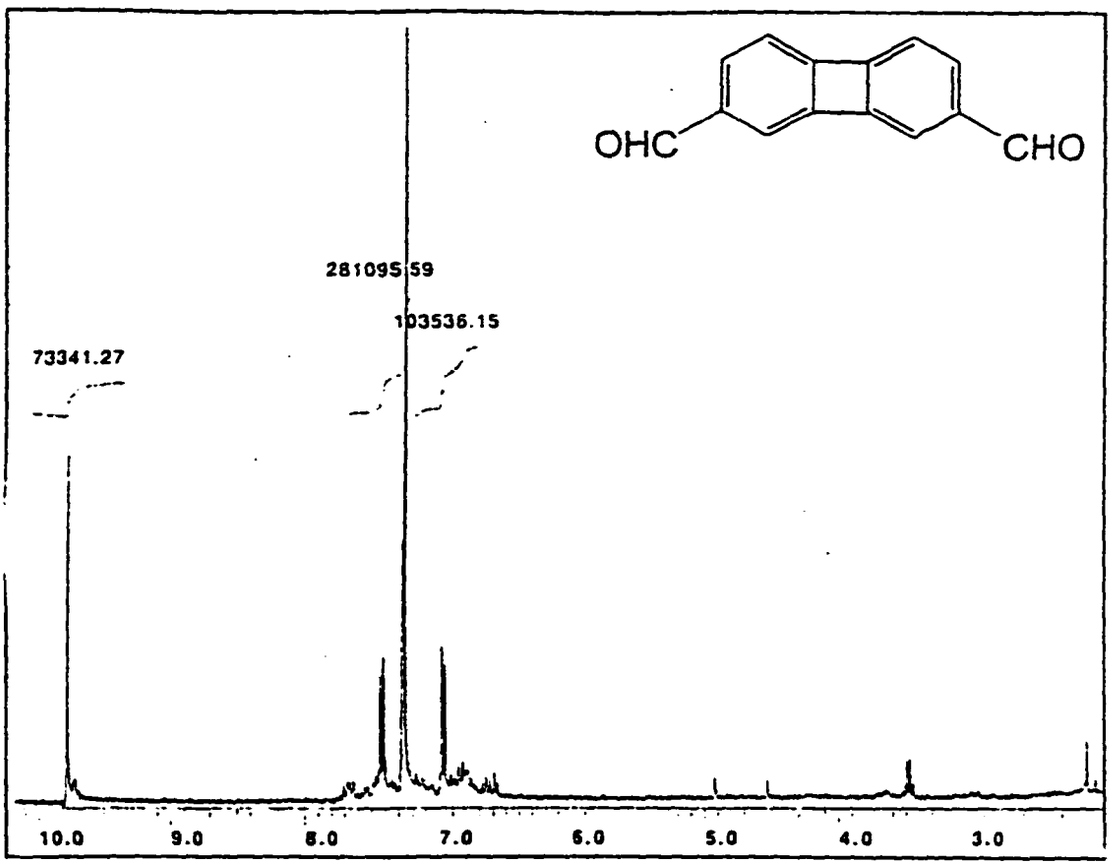


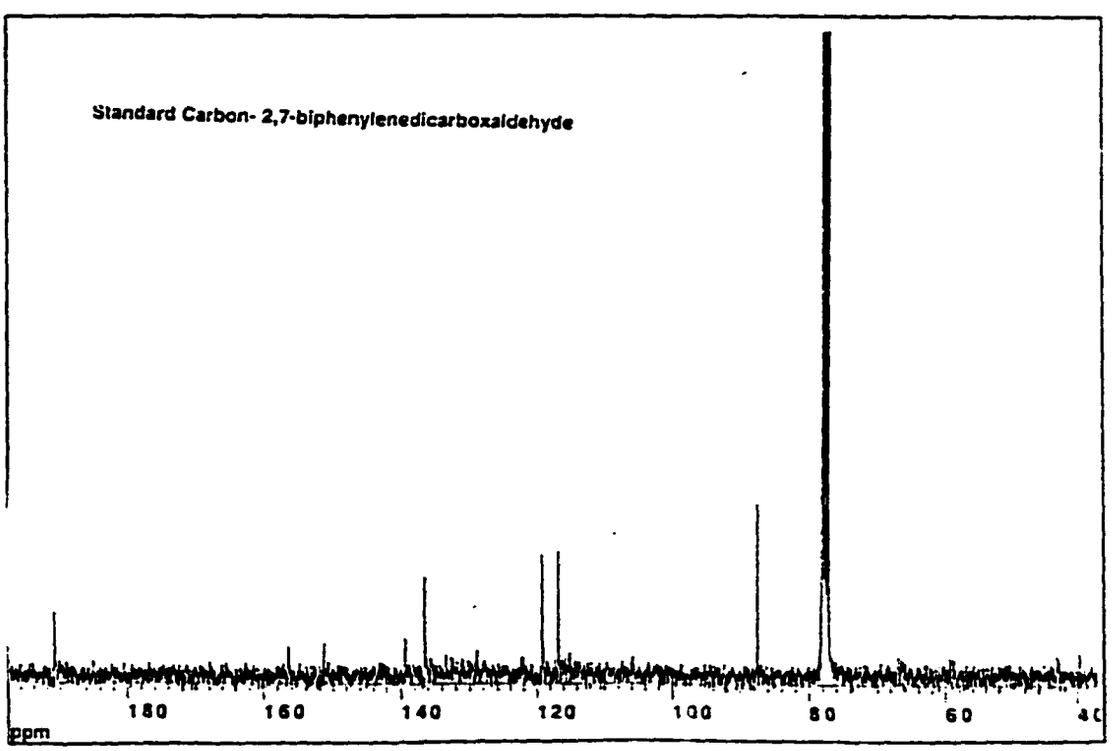


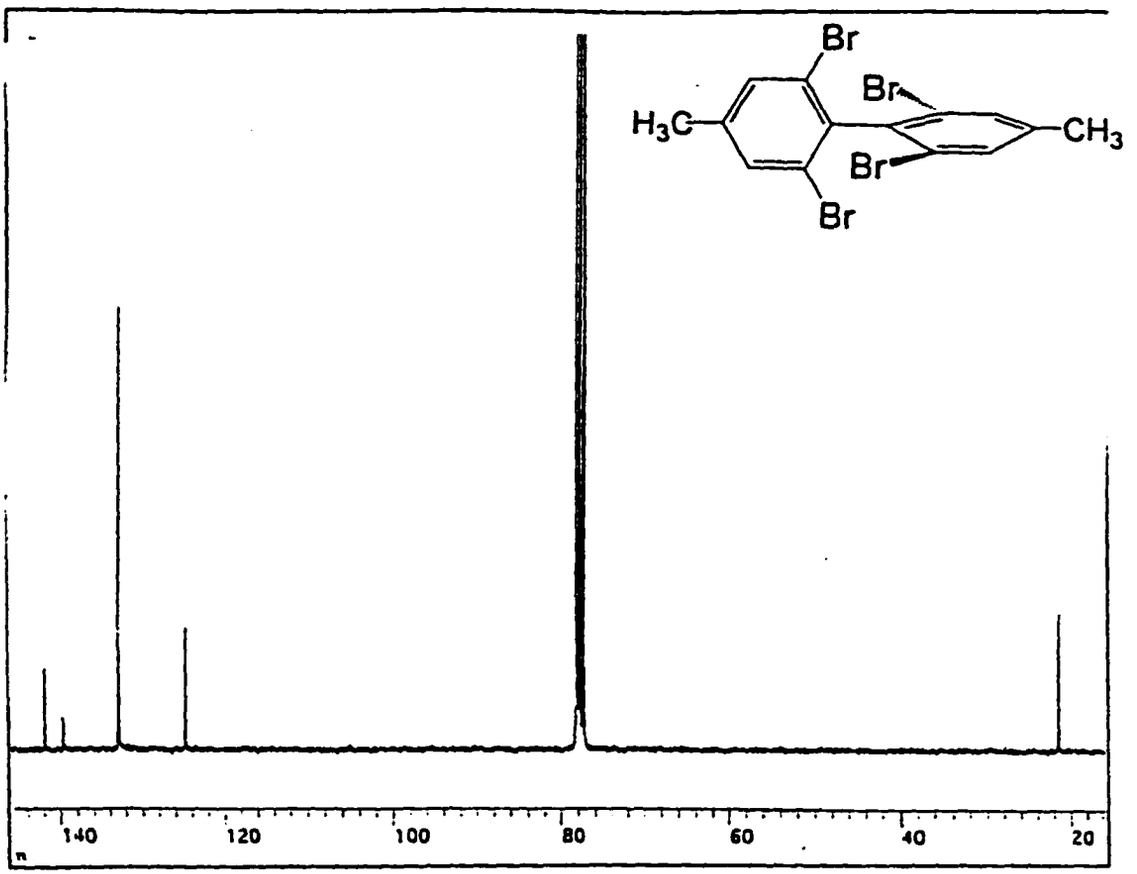


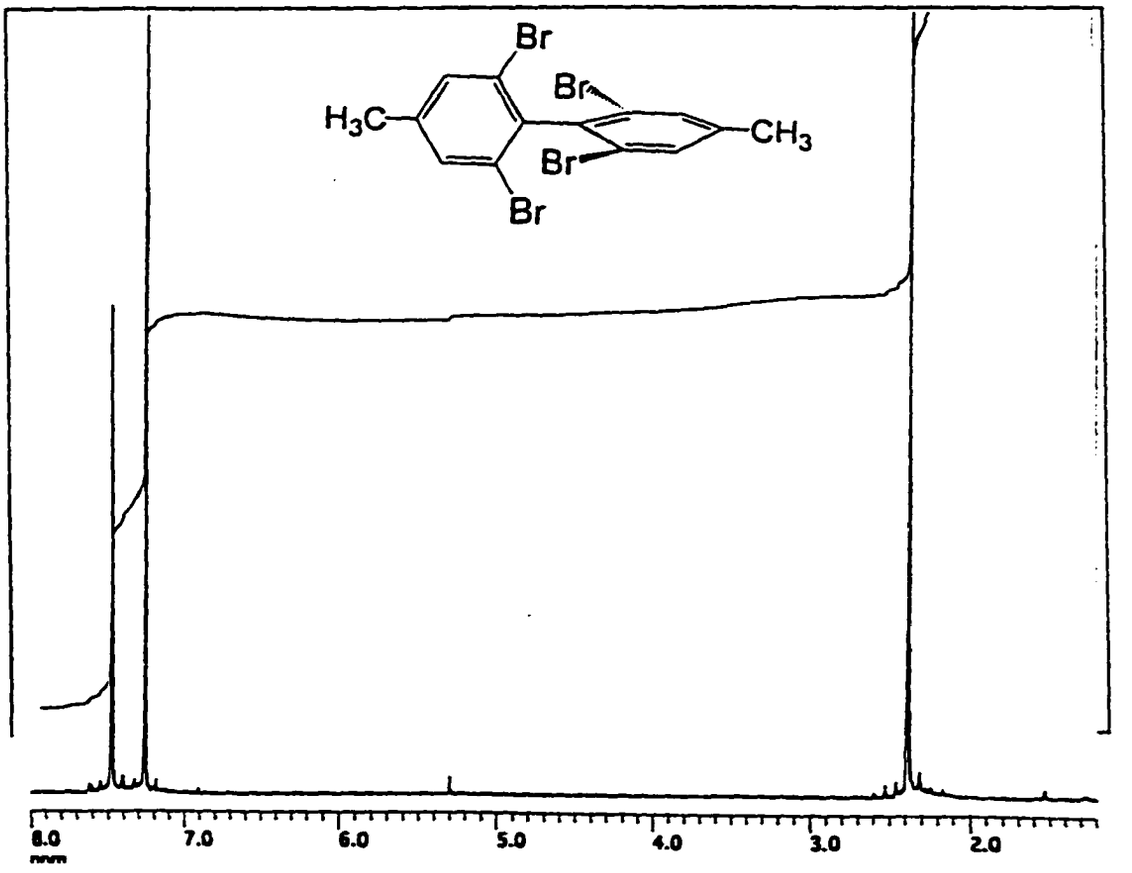


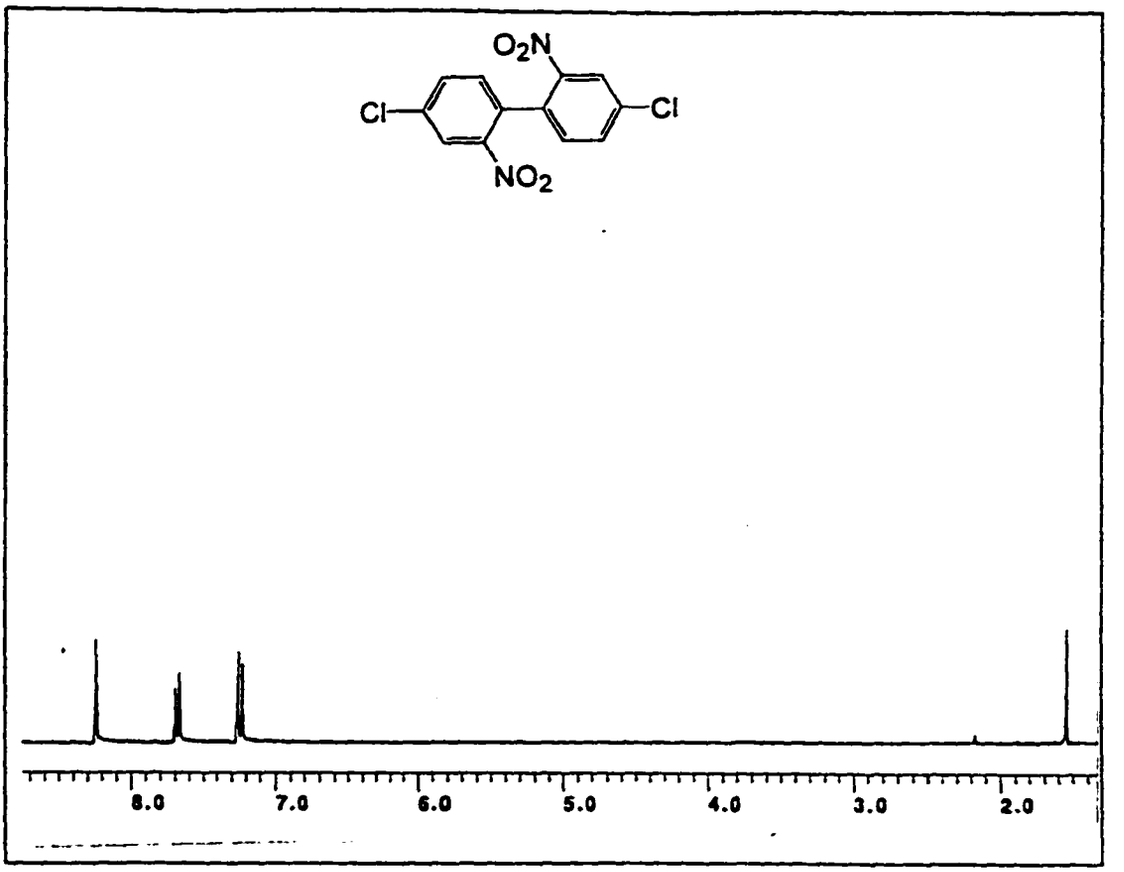


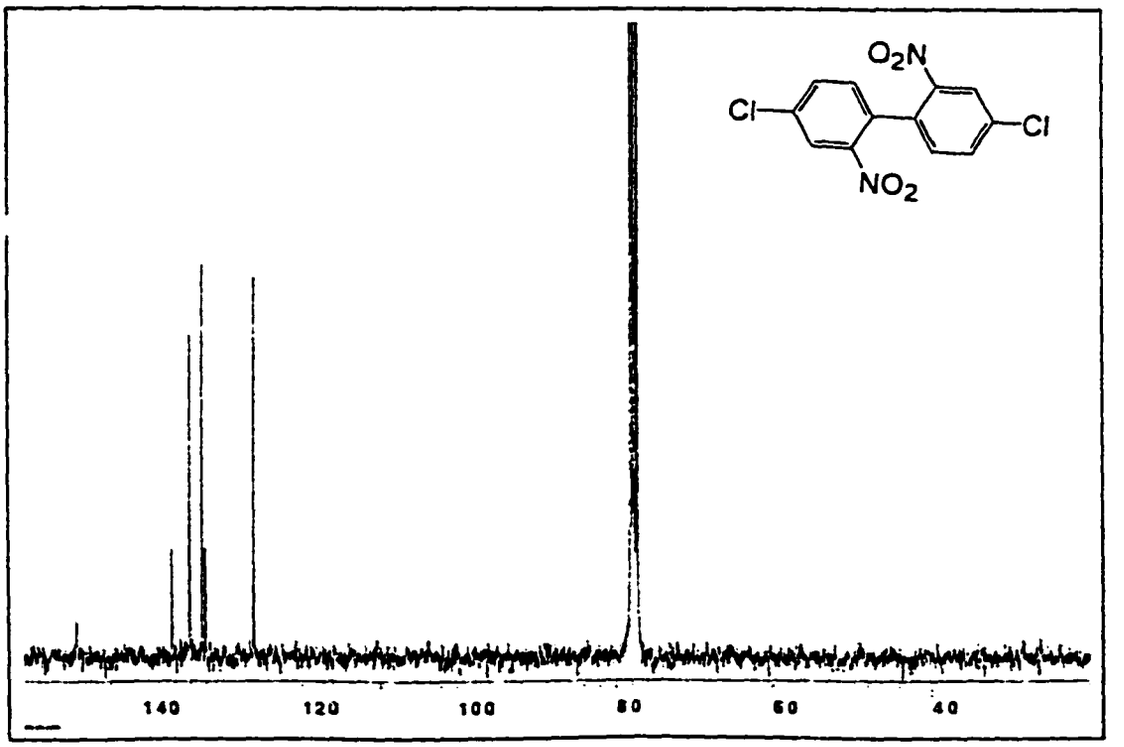


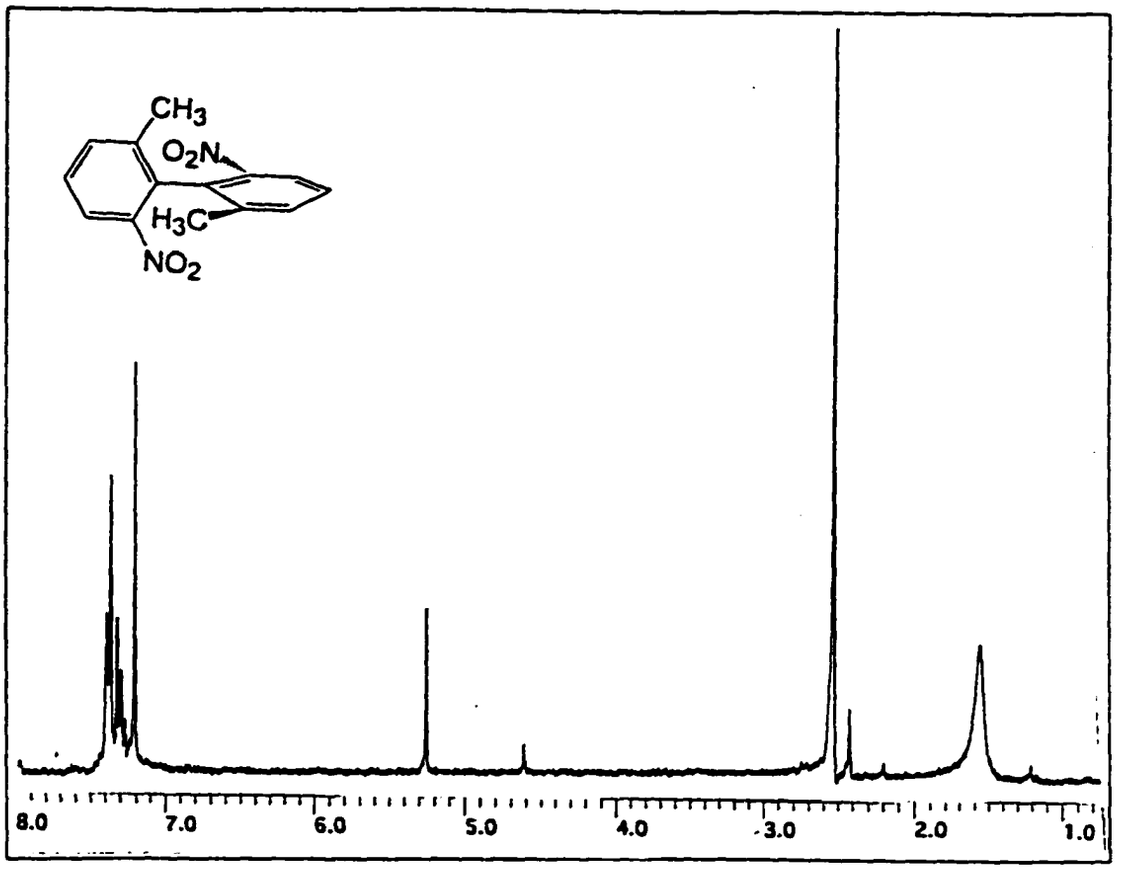


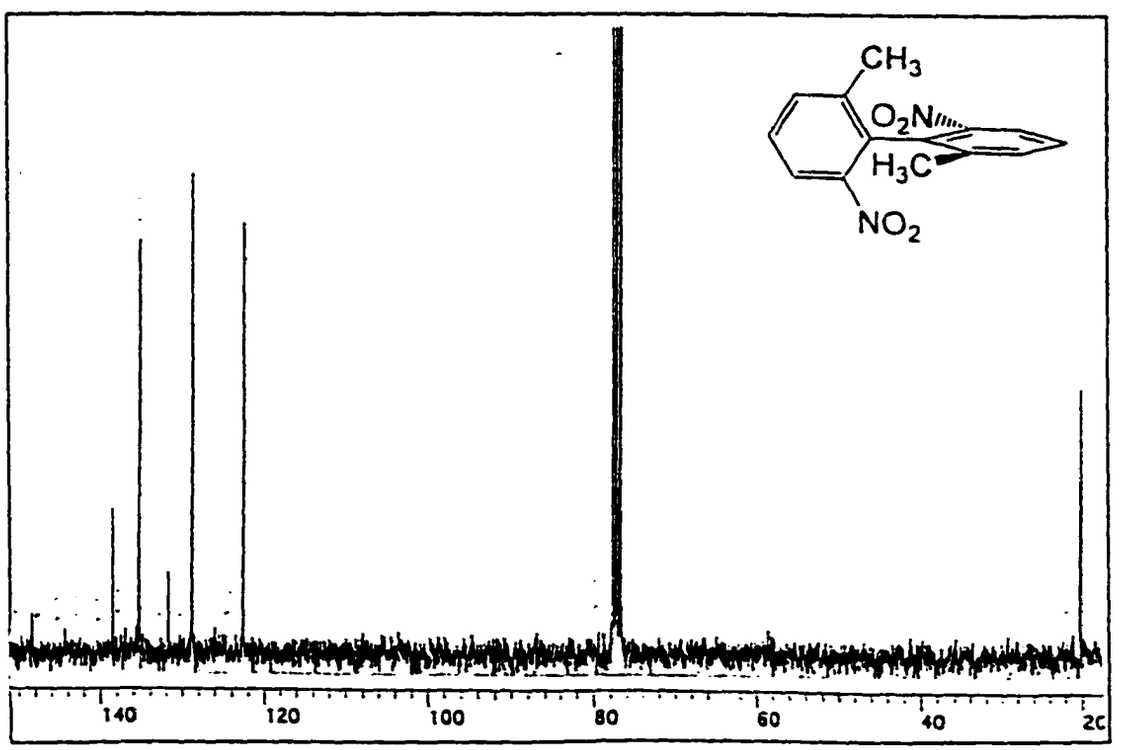


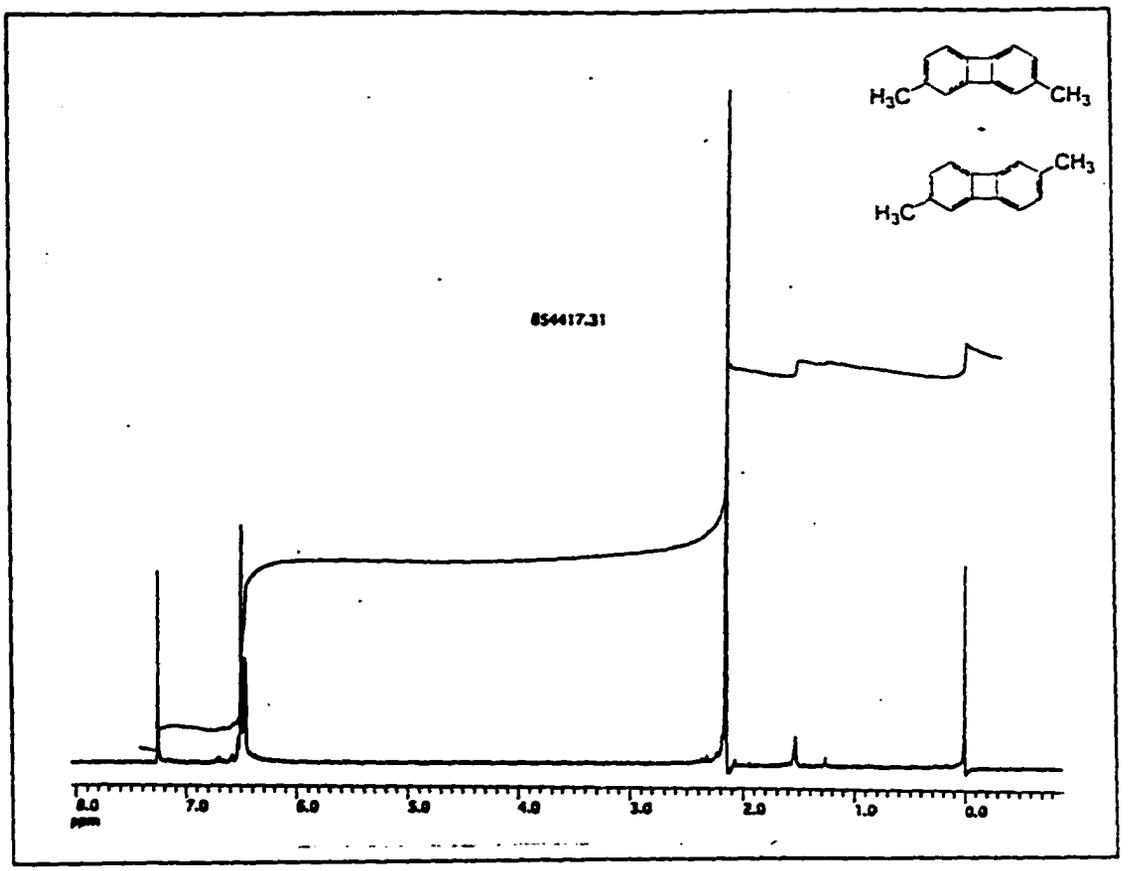


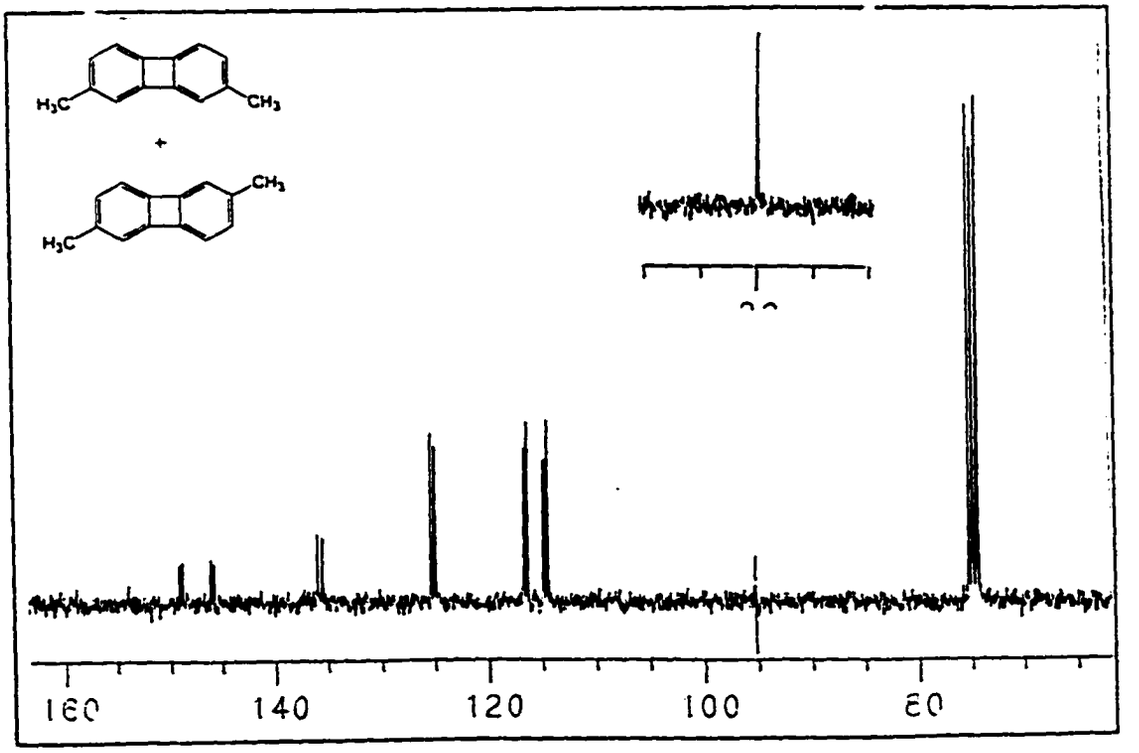


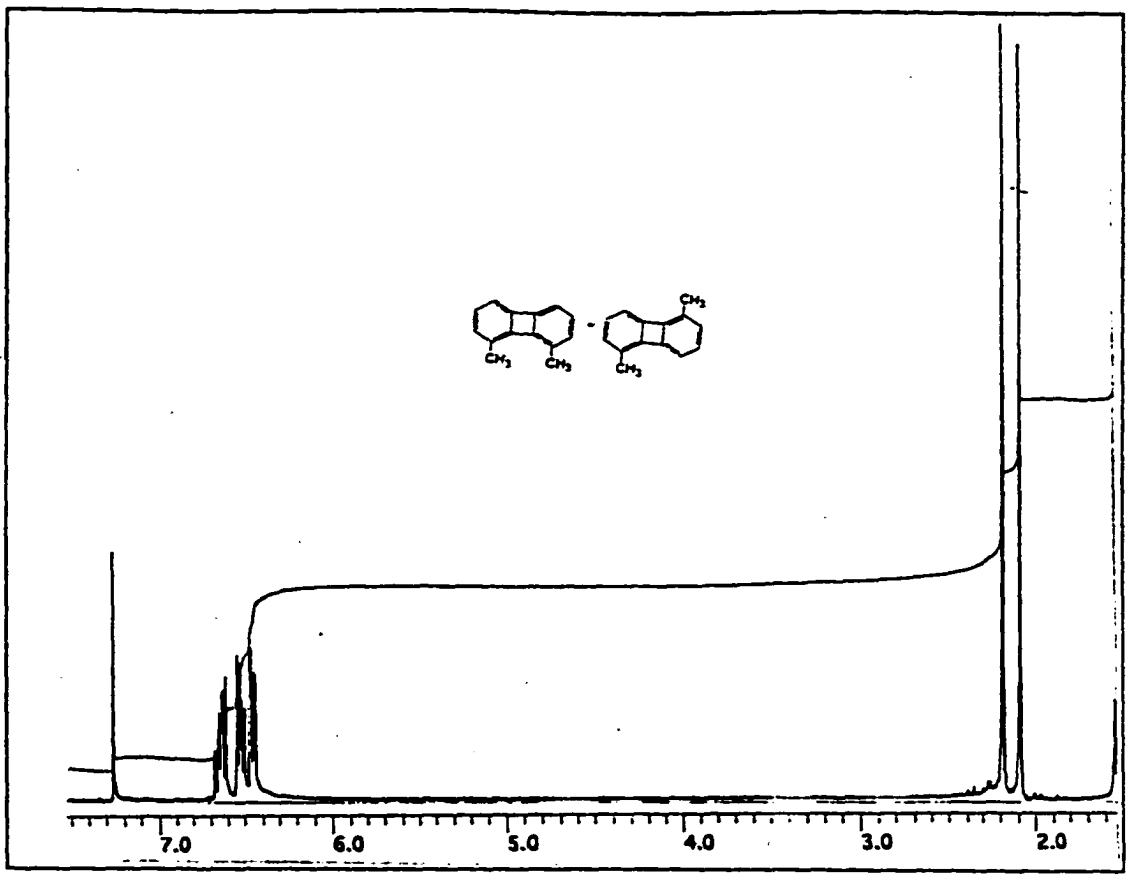


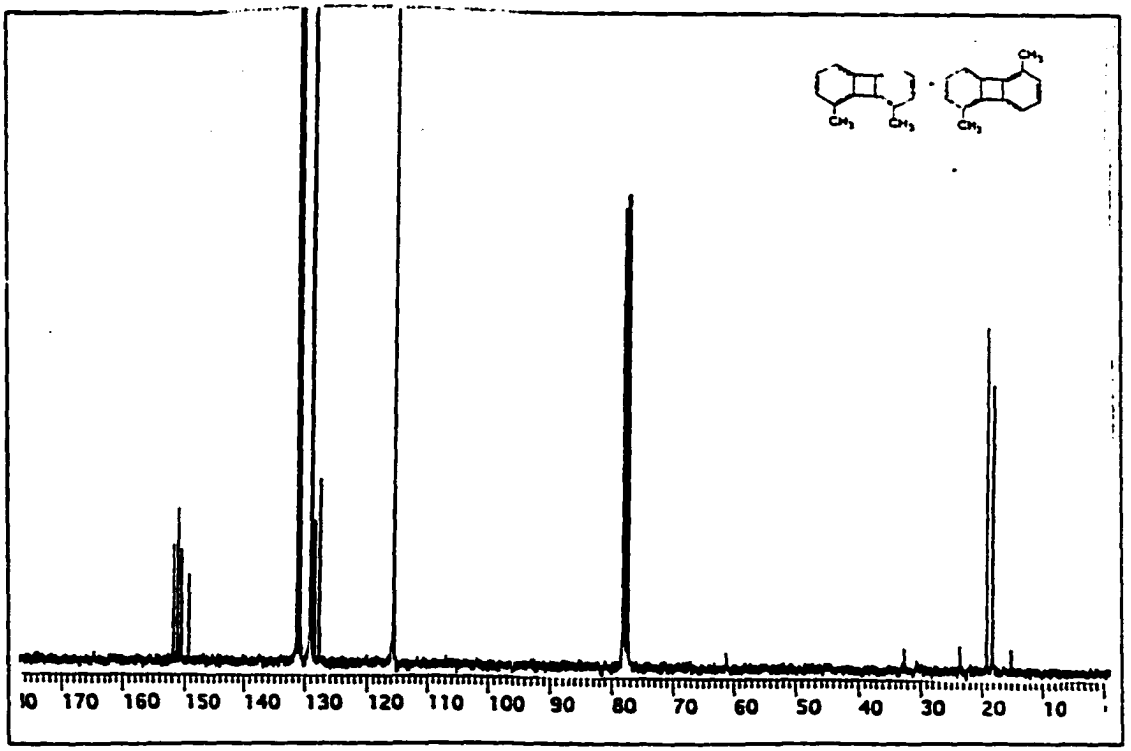


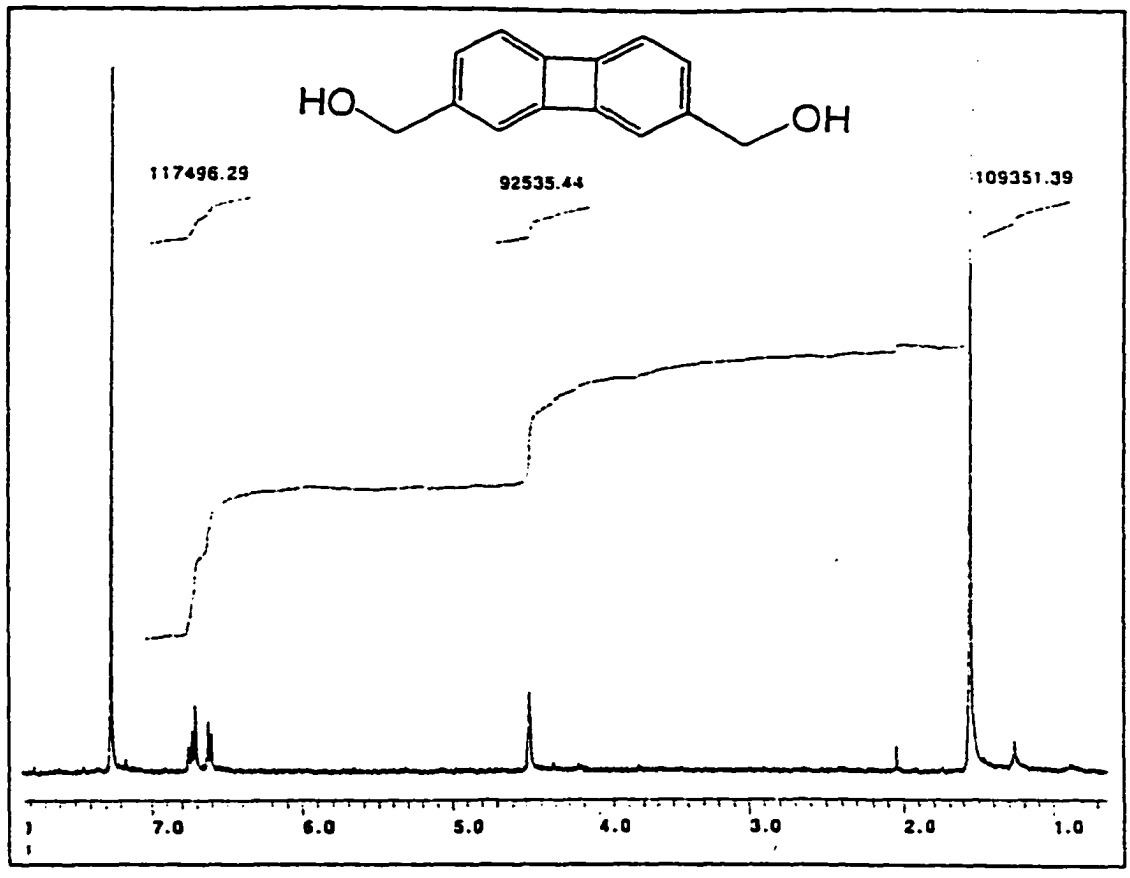


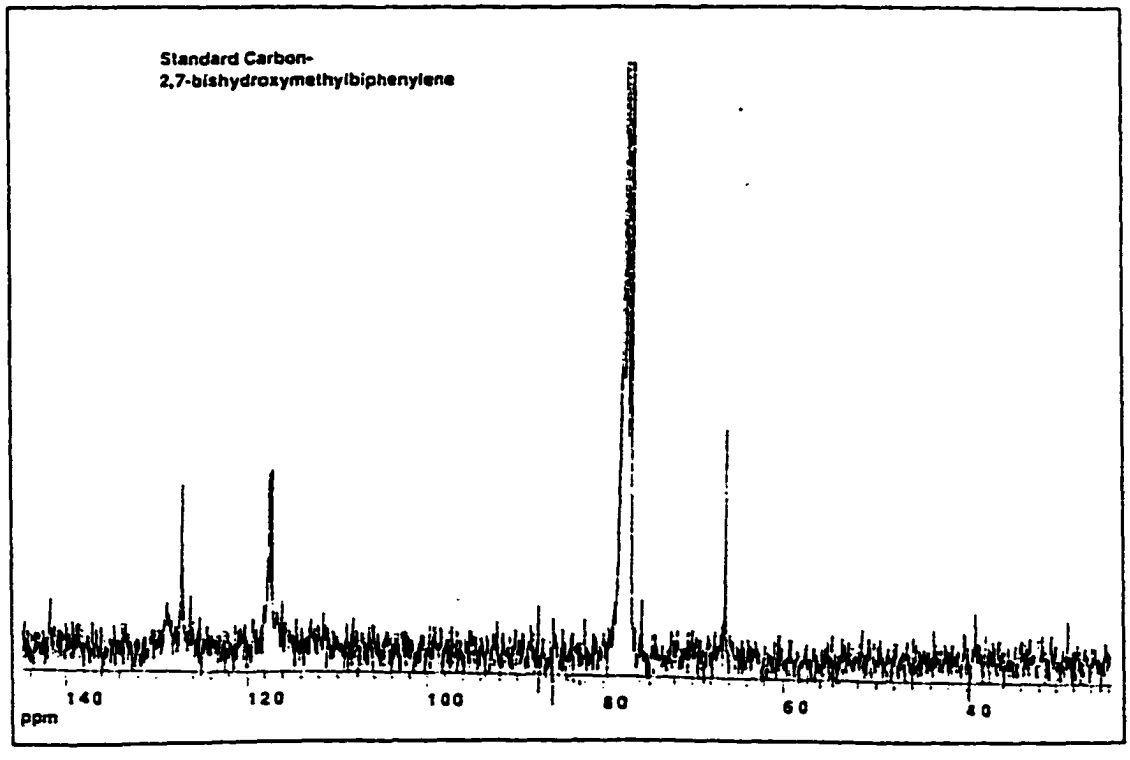












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