# SYNTHESIS OF 2,7-DIMETHYLPYRENE

by

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## SUMMARY

An improved synthesis of 2,7-dimethylpyrene (1) has been accomplished in four steps starting with mesitylene. Bromination of mesitylene with two molar equivalents of N-bromosuccinimide proceeded readily to give α,α'-dibromomesitylene (5) which was converted into 5,13-dimethyl[2.2]-metacyclophane (4) by a modified Wurtz reaction. Mild oxidation of 4 by the method of Allinger produced 2,7-dimethyl-4,5,9,10-tetrahydropyrene which was dehydrogenated over palladium on charcoal at 270° to give the desired compound 1.

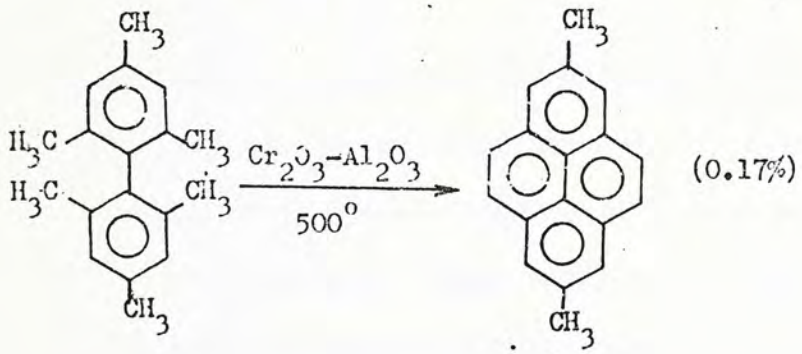
Further attempts have been made to synthesize 5,13-dimethyl[2.2]meta-cyclophane-1,9-diene, a precursor to 1. The Wittig reaction between 5-methylisophthalaldehyde and α,α'-mesitylenebis(triphenylphosphonium bromide) failed to give the desired intermediate. A sequence of reactions modeled after the synthesis of the parent unsubstituted [2.2]-metacyclophane-1,9-diene by Boekelheide and Mitchell was halted at the last stage because unexpected results. Unusual features in this series of reactions are the conversion into 7,17-dimethyl-2,3,12,13-tetrathia[4.4]-metacyclophane (17) from mesitylene-α,α'-dithiol and 5 and the formation of S,S,6,15-tetramethyl-2,11-dithia[3.3]metacyclophane bissulfonium fluoroborate from methylation of 17 with dimethoxycarbonium fluoroborate.

CONTENTS

# INTRODUCTION

2,7-Dimethylpyrene (1) occurs chiefly in petroleum and coal tar[1]. It can be obtained in trace amounts by high-pressure hydrogenation of tar oils[2] and cracking of lignite[3].

Although the parent pyrene was synthesized early at the beginning of this century[4], the title compound was not synthesized until 1952 by Orchin and coworkers[5]. They reported a 0.1% yield of 1 by passing bimesityl through a column of chromia on alumina at 500°.

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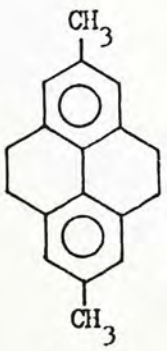
In a study of the effects of methyl substituents on the fluorescene emission of the pyrene nucleus[6], the title compound was desired in gram-quantities. Since neither of the previously reported methods is of any synthetic utility, we have undertaken to seek more practical routes leading to 1.

## SYNTHETIC PLANS

Conventionally, the pyrene ring-system is constructed from biphenyl derivatives[4,7], from naphthalene derivatives[8], and from phenanthrene derivatives[9] using a combination of the Friedel-Crafts acylation, reduction of carbonyl groups and dehydrogenation steps. Since these methods often require lengthy procedures with erratic results, they were not adopted in the present investigation. Instead, the feasibilities of three different synthetic routes possibly leading to the desired dimethylpyrene 1 were examined.

In contemplating a suitable scheme for the synthesis of 1, it appeared that the route of most probable success would involve the obtention of a carbon skeleton possessing conveniently placed functionality which would facilitate the formation of the pyrene nucleus. Accordingly, 2,7-dimethyl-4,5,9,10-tetrahydropyrene (2) and 5,13-dimethyl[2.2]metacyclophane-1,9-diene (3) were

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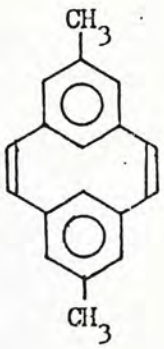


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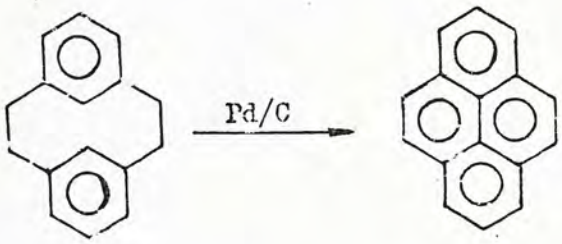
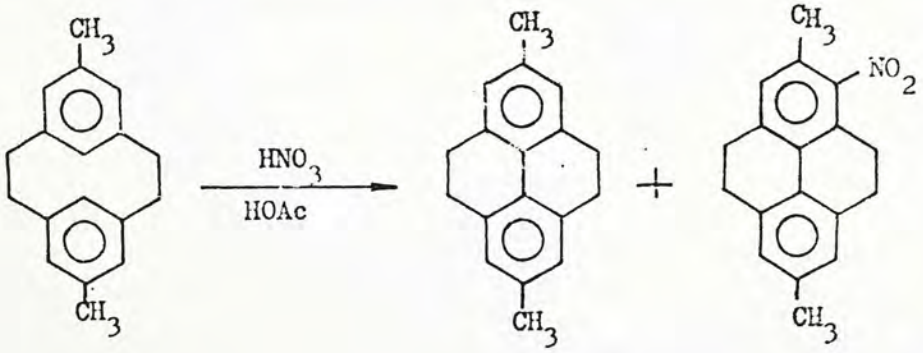
regarded as potential candidates for structure 1. In the projected synthetic route to the tetrahydropyrene 2 and the two routes to the diene 3 outlined below, mesitylene was chosen as the common starting material for two reasons. Firstly, this compound offers exactly one-half portion of the structures 2 and 3 and possesses benzylic methyl groups which would allow manipulation in various manners. Secondly, some degree of flexibility was envisioned by using a common starting material for three different schemes.

Baker and coworkers[10] reported an one-step conversion of [2.2]metacyclophane into pyrene by heating the former over palladized charcoal.




More recently, Allinger and coworkers[11] reported that nitration of 5,13-dimethyl[2.2]metacyclophane (4) under mild conditions gave a mixture of 1-nitro-2,7-dimethyl-4,5,9,10-tetrahydropyrene and 2. A similar transannular

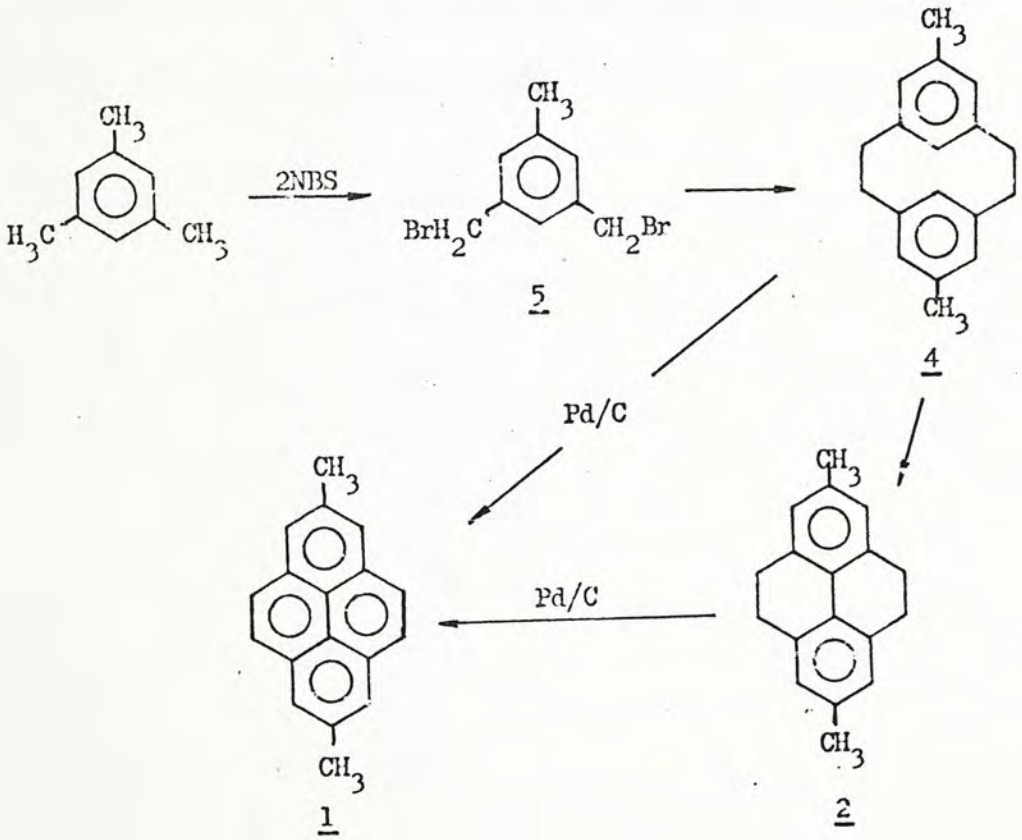



4 2

reaction giving 2 as the sole product was later acheived by Sato and coworkers[12] by treatment of 4 with iodine and silver perchlorate.

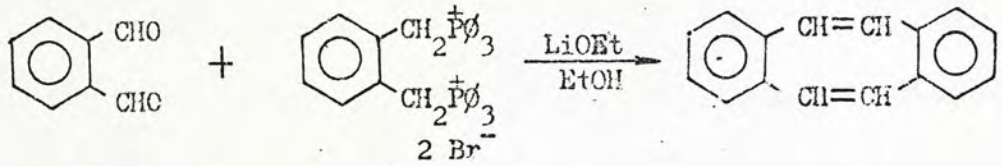
Intrigued by the novel aspects of these reactions, we were led to repeat the synthesis of 4 in the hope that it could be dehydrogenated directly, or indirectly by the way of 2, into the desired dimethylpyrene 1. The proposed route is summarized in Scheme I.

SCHEME I. Projected Synthesis of 1 via 2.



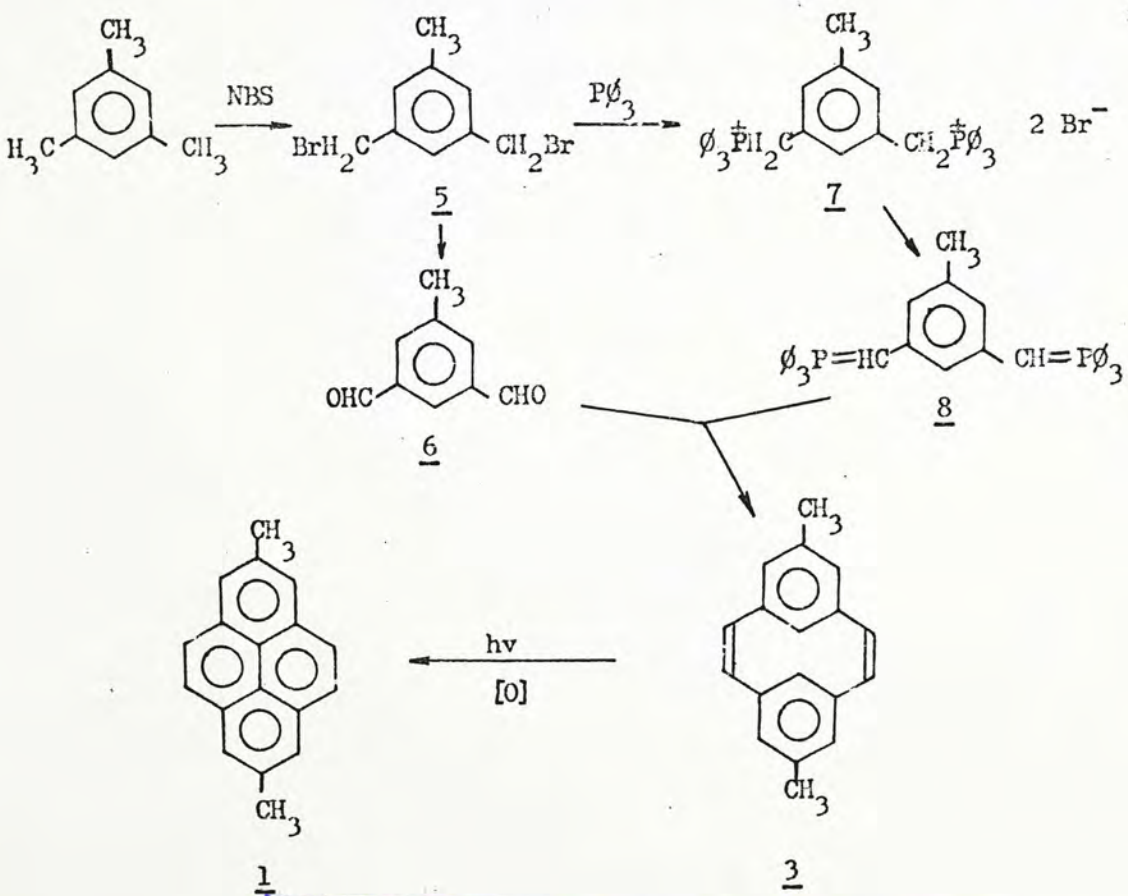

In principle, with the two methyl groups being symmetrically held at fixed positions, structure 3 would lead directly to the desired dimethyl-

pyrene 1 in a one-step photochemical cyclodehydrogenation. The report of Griffin and coworkers[13] on the successful synthesis of 1,2,5,6-dibenzocyclo-octatetraene by application of the Wittig reaction prompted us to devise a




similar series of reaction which would allow the preparation of the required diene 3. The projected synthesis is outlined in Scheme II.

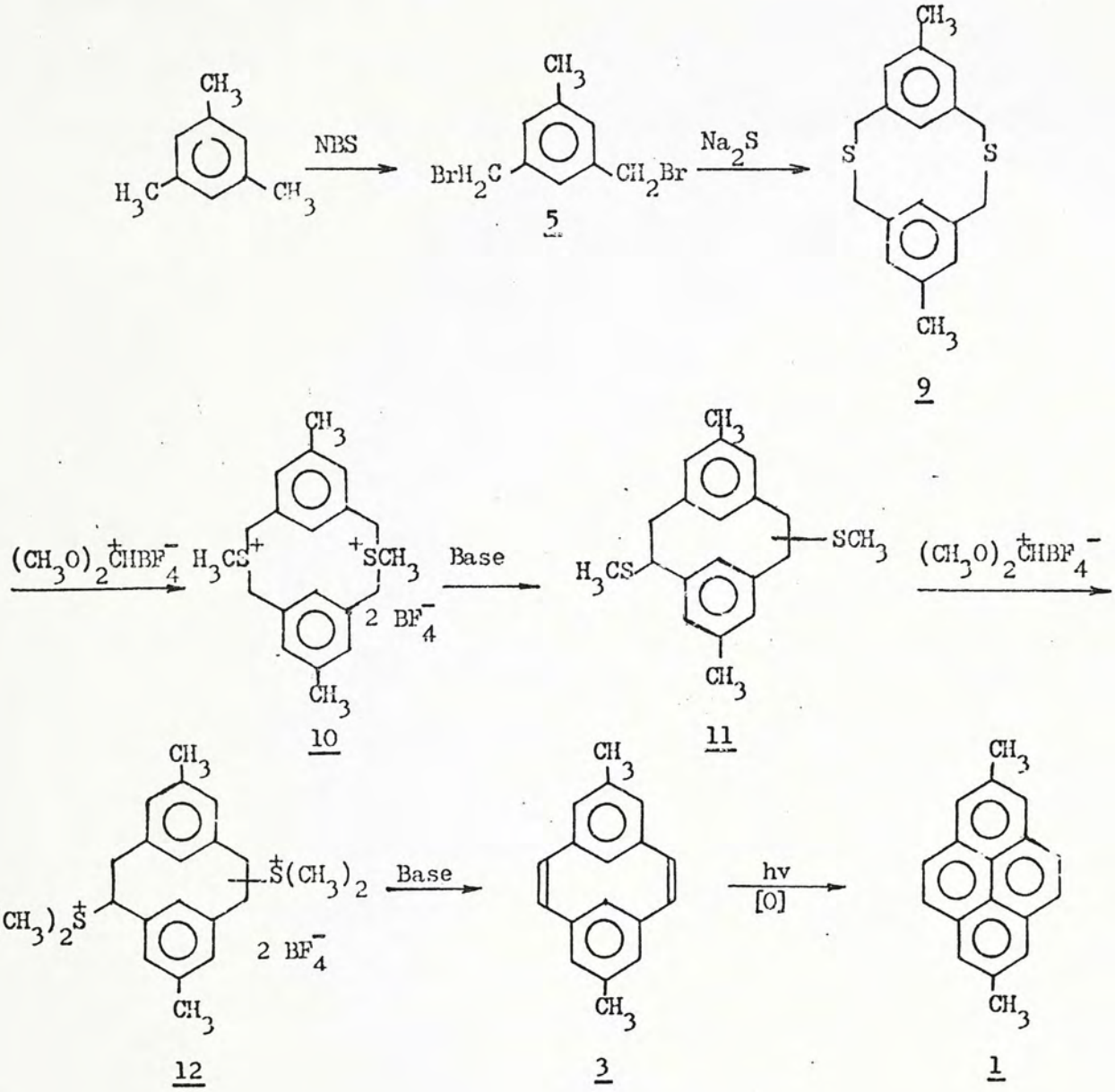
SCHEME II. Projected Synthesis of 1 by Application of the Wittig Reaction.



Bromination of mesitylene with two molar equivalents of N-bromosuccinimide would give α,α'-dibromomesitylene(5) which might be converted into 5-methylisophthalaldehyde (6) by the Sommelet reaction[14]. Cyclization between dialdehyde 6 and bisphosphorane 8 derived from the corresponding bisphosphonium salt 7 would be expected to generate 3. The facile photochemical oxidative cyclization of the parent [2.2]metacyclophane-1,9-diene to pyrene has been amply demonstrated by Boekelheide and coworkers[15]. In view of their structural similarities, compound 3 was anticipated to follow the same course to form 2,7-dimethylpyrene 1.

In the synthesis of trans(15,16)dihydropyrene and related compounds[15,16], Boekelheide has utilized a combination of the Stevens rearrangement and elimination to effect the transformation of a sulfide linkage into an olefinic function. Following this approach, the reaction sequence outlined in Scheme III would provide an alternate route to 3 and, eventually, to the desired compound 1.

SCHEME III. Projected Synthesis of 1 by Application of the Boekelheide Method.



One aspect of the reaction Scheme III deserves comments. This Scheme differs from that reported by Boekelheide for the synthesis of trans(15,16)-dihydropyrene[15] only in respect to the additional methyl substituents present in the starting dibromide 5. Since these methyl groups are remoted from the reaction centres in subsequent transformations, they were not expected to alter the overall reaction course.

## RESULTS AND DISCUSSION

**Synthesis of 2,7-Dimethylpyrene 1 by Dehydrogenation of 2,7-Dimethyl-4,5,9,10-tetrahydropyrene 2.** — As shown in Scheme I, 5,13-dimethyl[2.2]-metacyclophane 4 was prepared in 10 - 12 % yields by coupling $\alpha,\alpha'$-dibromo-mesitylene 5 with phenyllithium according to the method reported by Allinger[11]. However, we found that the isolation procedure could be simplified considerably and that the yields of the product were generally improved ( 33% ) when the organometallic reagent was substituted by the sodium-tetraphenylethylene complex[17]. The product obtained had the same melting point reported previously, and its structure was confirmed by the nmr spectrum ( Fig.1 ) which showed a methyl singlet at δ 2.38 ( 6H ), and an incomplete AA'BB' system for four methylene hydrogens centered at δ 2.58, a singlet for two intra-annular hydrogens at δ 4.20 and an aryl singlet at δ 6.94.

Some features of the nmr spectrum of 4 merit mentioning. As is shown by the temperature-independence of the methylene resonance of the parent [2.2]metacyclophane between -80 and +190° [18], this molecule adopts a rigid conformation in solution with no detectable ring inversion. Thus, the methylene protons of the two bridges in 4 are nonequivalent due to a fixed, staggered arrangement ( Fig.2 ), and they should appear as an AA'BB'

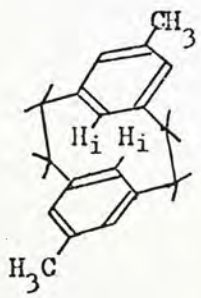



Fig.2. Staggered conformation of 5,13-dimethyl[2.2]metacyclophane.

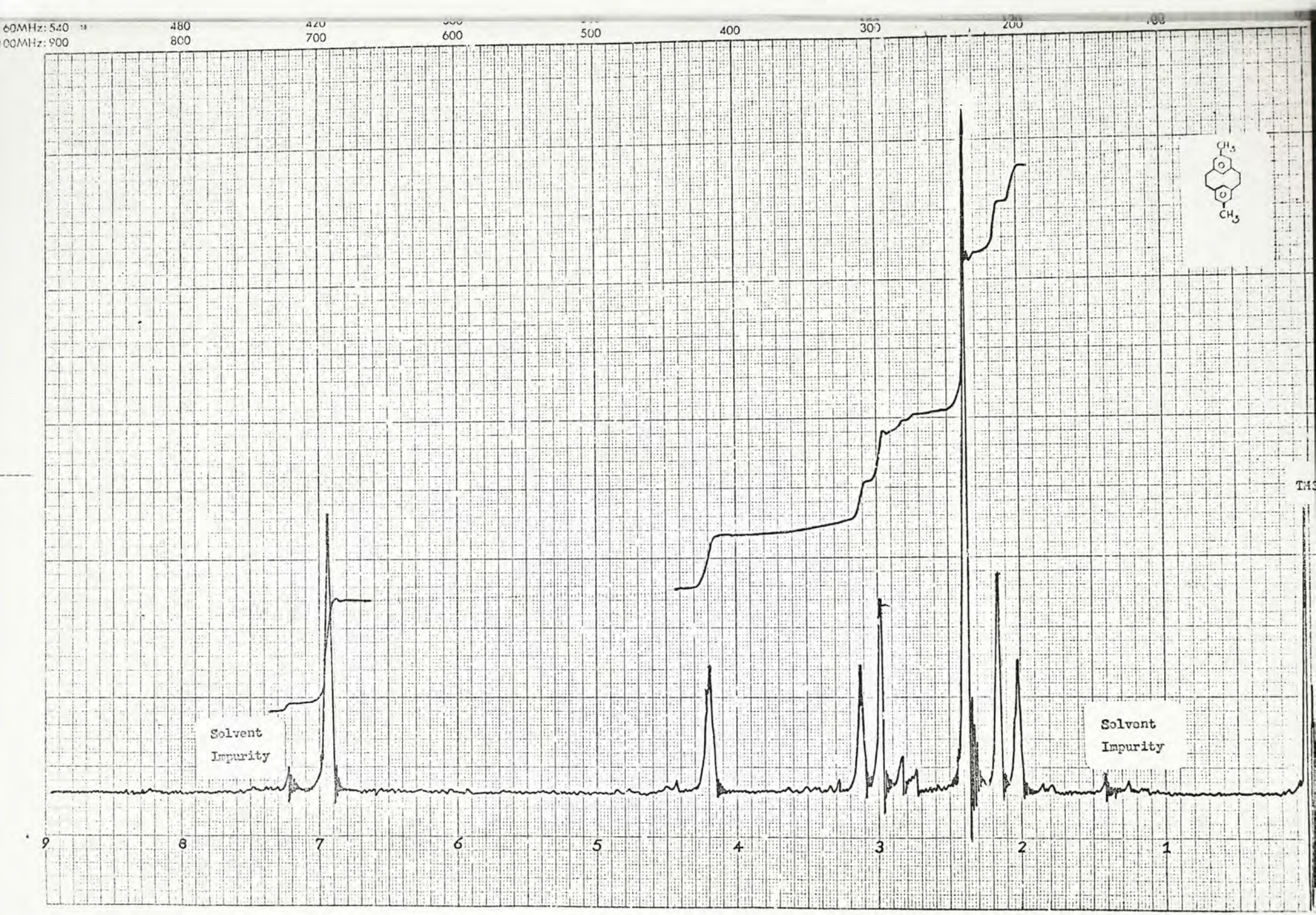



Fig. 1 The nmr spectrum of 5,13-Dimethyl[2.2]metacyclophane (4) ( $CDCl_3$ )

system characterized by two intense outer doublets and two weak inner doublets. However, this expected pattern is not revealed fully owing to considerable overlapping between the high-field inner doublet and the strong methyl signal. Finally, the absorption of the intra-annular protons $H_i$ at high field can be readily explained by the fixation of their steric positions above the aromatic rings.

Direct cyclodehydrogenation of 4 to 1 at 270° in the presence of palladised charcoal did not proceed as readily as [2.2]metacyclophane to pyrene[10]. The reaction was accompanied by the formation of a dark amorphous substance and gave only low yields of the desired product 1.

The yields of the desired product 1 were improved a great deal by employing an indirect route. Thus, 4 was first converted into 2,7-dimethyl-4,5,9,10-tetrahydropyrene 2 by nitrating 4 under mild conditions as described previously[11]. As noted earlier by Allinger, a small amount of 1-nitro-2,7-dimethyl-4,5,9,10-tetrahydropyrene was isolated as a by-product in the nitration procedure. The nmr spectrum of 2 which displayed six methyl protons at δ 2.31, eight methylene protons at δ 2.81 and four aryl protons at δ 6.88 was in complete agreement with the assigned structure ( Fig.3 ).

In an attempt to improve the yield of 1, dehydrogenation of 2 was carried out in refluxing p-cymene in the presence of palladized charcoal. However, under these conditions the reaction took a different course. Analysis by nmr spectrometry indicated that the crude products were consisted of a mixture of 1 and 4 in the ratio 3:4, approximately. Obviously, the outcome was caused by disproportionation of the starting material 2.

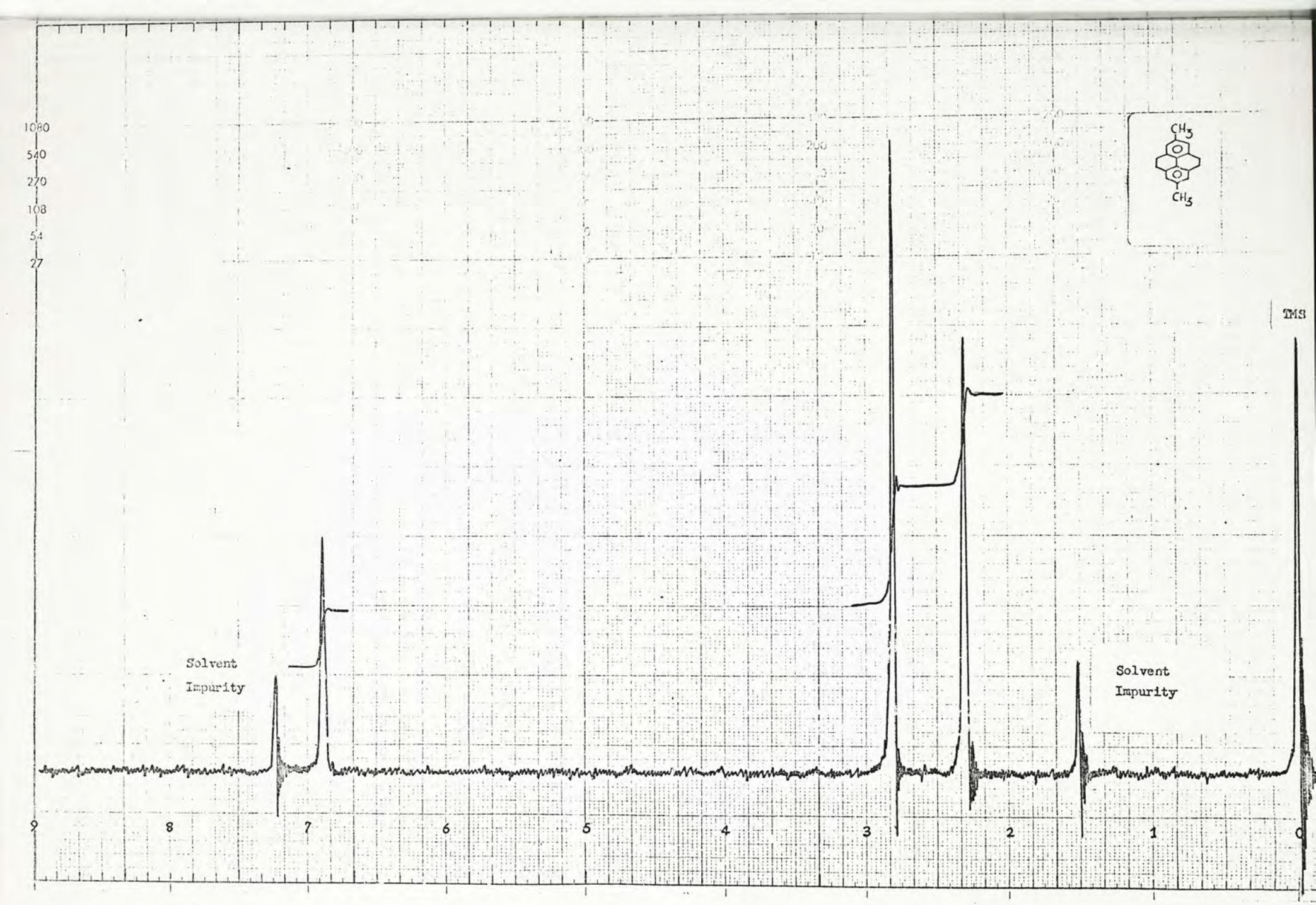
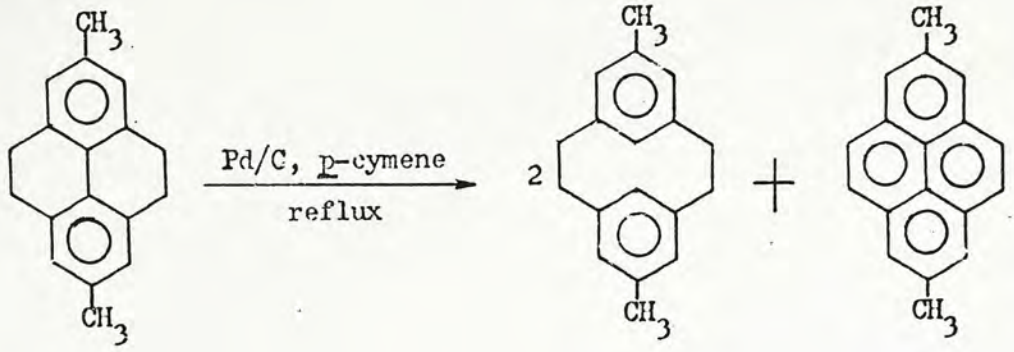



Fig. 3 The nmr spectrum of 2,7-Dimethyl-4,5,9,10-tetrahydropyrene (2) ($CDCl_3$)




2 4 1

Finally, the synthesis of 2,7-dimethylpyrene 1, obtained in 48% overall yield starting from 4, was accomplished by heating an intimate mixture of 2 and palladium on charcoal at 270° for 5hrs. Structural proof of the final product was obtained by comparing its nmr spectrum (Fig.4 ) with that reported by Clar and coworkers[19].

Attempted Synthesis of 5,13-Dimethyl[2.2]metacyclophane-1,9-diene 2 by Application of the Wittig Reaction. — As outlined in Scheme II, α,α'-dibromomesitylene 5 was obtained in 50% yield from mesitylene. The dialdehyde 6 and bisphosphonium salt 7 were readily prepared, respectively, from 5 by the Sommelet reaction and by reacting with two molar equivalents of triphenyl phosphine either in dimethylformamide or in chloroform. The bisphosphonium salt 7 was found to be extremely hygroscopic; it was dried and used without further purification in the Wittig reaction.

Bergelson[20], House[21], and Drefahl[22] have found that the cis/trans ratio of the olefinic product from the reaction of a carbonyl compound with a semi-stabilized or non-stabilized ylid was increased by using protic

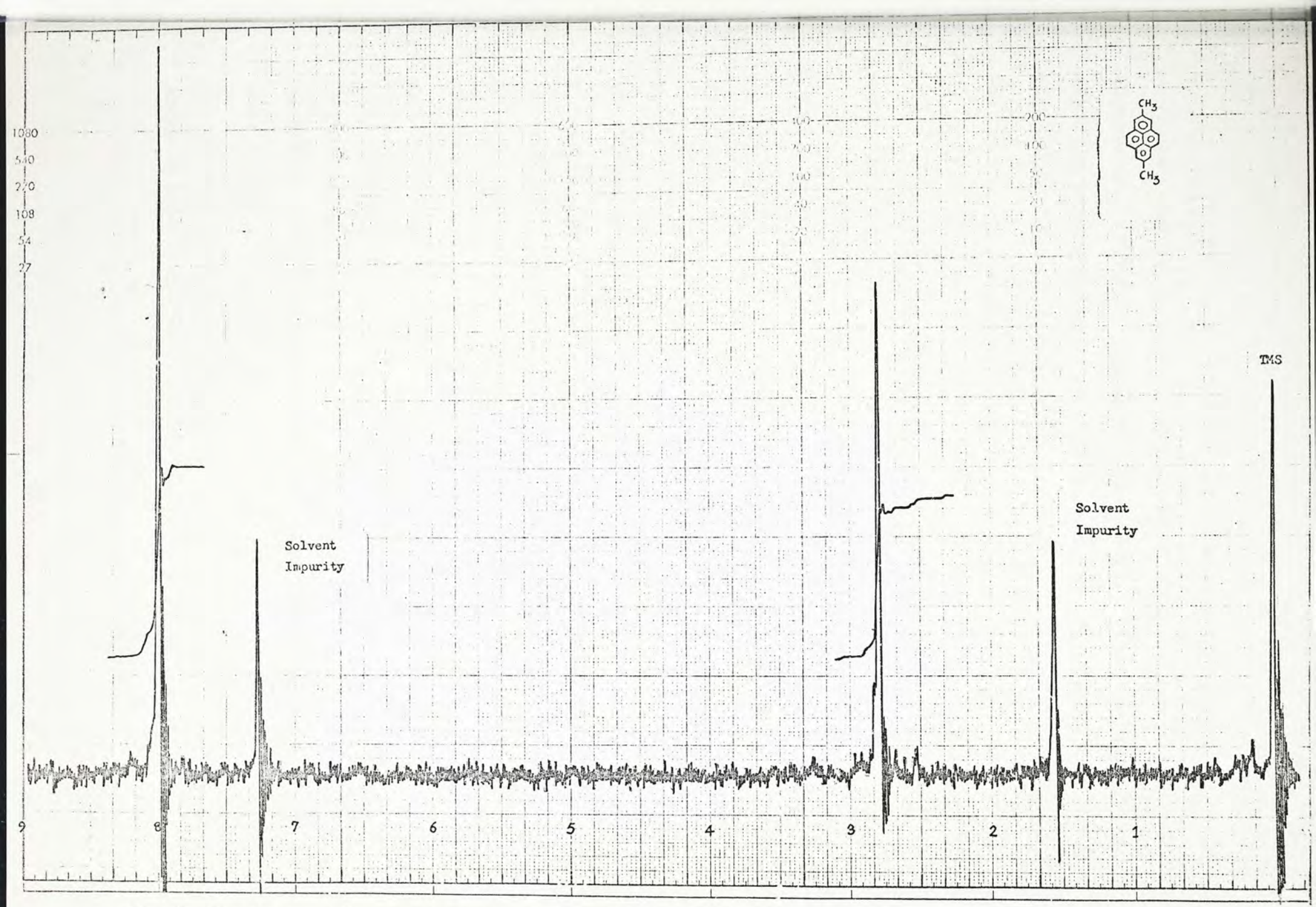
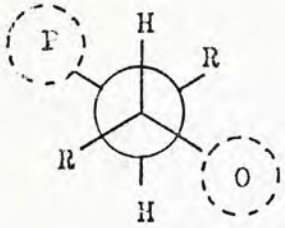



Fig. 4 The nmr spectrum of 2,7-Dimethylpyrene (1) ( $CDCl_3$ )

or dipolar, aprotic solvents. This was believed to be due to the decreased electrostatic interaction between the positively charged phosphorus and the negatively charged oxygen by extensive solvation or complexation[23]. Accordingly, the steric repulsion between the solvated groups would favor the formation of the more stable erythro-betaine 13. As a result, the



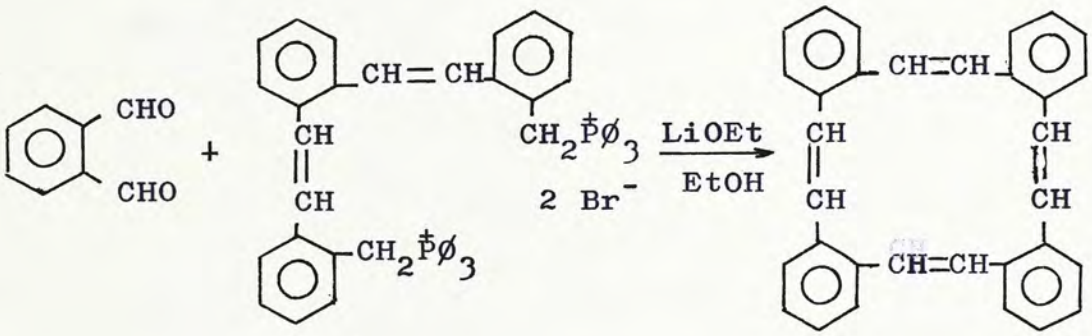

13

cis/trans ratio of the olefinic products is increased.

Structure 3 would require either a stepwise or a simultaneous ring-closure into two cis olefinic bonds. Thus, following the above arguments, attempts were made to cyclize the bisphosphonium salt 7 and the dialdehyde 6 at high dilution in typical polar solvents such as ethanol and dimethyl-formamide in the presence of lithium ethoxide. In the course of the reaction an orange color first appeared and gradually faded in a manner usually observed in the Wittig reaction. After separation from triphenylphosphine oxide, the crude product was purified by combination of column and thick-layer chromatography. In the case where DMF was used as solvent, an intractable gummy substance was obtained in all instances. However, a white solid with ill-defined melting point was isolated in trace amount using ethanol as solvent. The nmr spectrum of this material measured in $CCl_4$ showed a broad singlet at δ 2.20 ( 6H ) and two unresolved signals with maxima at δ 6.47 and δ 6.90 ( totally 10H ). These data seem to fit the

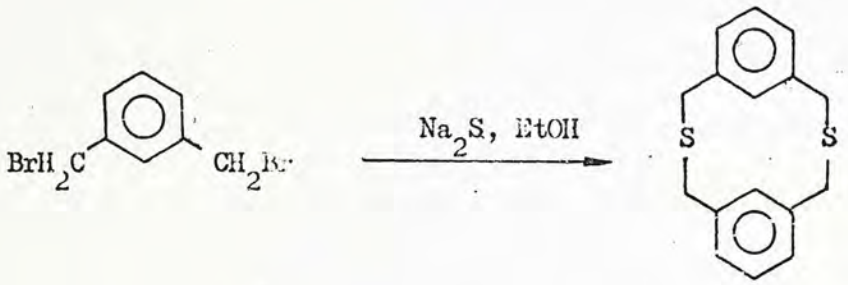
structure of a polymeric substance rather than the expected 5,13-dimethyl-[2.2]metacyclophane-1,9-diene 3. In addition, a chemical change was not observed upon prolonged irradiation of an aerated solution of this product in tetrahydrofuran.

It is unlikely that the failure of cyclization between 6 and 7 is due to ring size, for under similar conditions 1,2-bis(o-triphenyl-phosphonium methylstryl)benzene and o-phthalaldehyde have been known to cyclize with ease into the macrocyclic 1,2,5,6,9,10,13,14-tetrabenzocyclohexadeca-1,3,5,7,9,11,13,15-octaene[24]. The difficulty in our case may be attributed

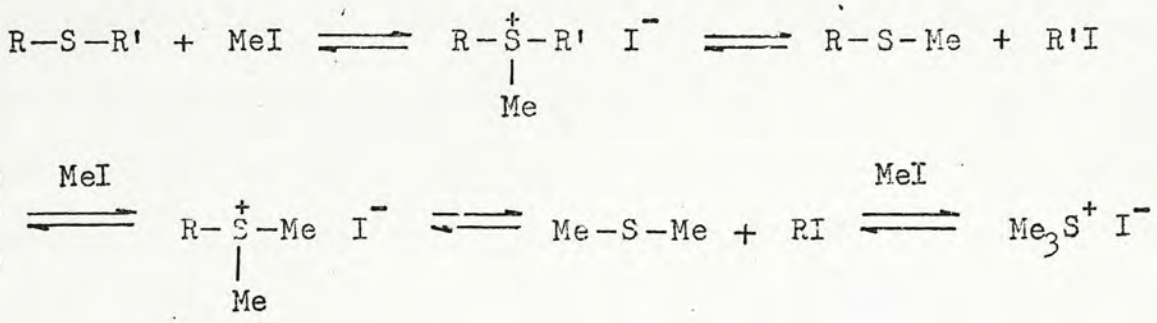



to the low conversion into cis-olefinic bonds due to the large steric repulsion between the aryl groups, and/or the steric repulsion between the two internal hydrogen atoms that would be present in the desired product 3. Conceivably, either one of these factors may cause extensive polymerization even in dilute solutions.

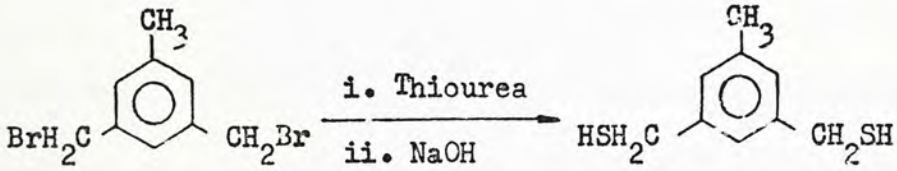
Attempted Synthesis of 2,7-Dimethylpyrene 1 by Application of the Boekelheide Method.-- As outlined in Scheme III, initial attempts were made to prepare 6,15-dimethyl-2,11-dithia[3.3]metacyclophane(9) by reaction of dibromide 5 with molar equivalents of sodium sulfide in boiling ethanol under high dilution conditions. This essentially was the procedure reported by Mitchell and Boekelheide[15] for the synthesis of 2,11-dithia[3.3]metacyclophane from α,α'-dibromo-m-xylene. However, in our case where α,α'-




dibromomesitylene 5 was used as a reactant the reaction failed to give the desired product 9. In almost all instances, a viscous oil of unknown structure was obtained by column chromatography. This substance gave inconsistent nmr and ir spectral data but showed a positive test for sulfur by qualitative elemental analysis. Interestingly, when a dichloromethane solution of this material was allowed to react with excess methyl iodide at room temperature for five to seven days, trimethylsulfonium iodide was obtained. From these results, it appears likely that the product contained the benzyl sulfide linkage. In at least one precedent case, benzyl sulfide was reported to be converted into trimethylsulfonium iodide by excess methyl iodide[25]. A probable reaction pathway is outlined below:



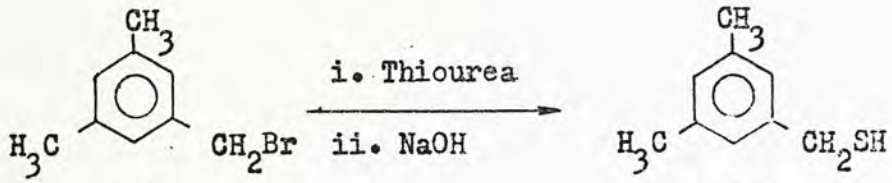
The failure to cyclize the dibromide 5 by sodium sulfide into 9 led us to investigate the reaction between mesitylene-α,α'-dithiol (14) and 5. With prior incorporation of the sulfur atoms into the organic framework, it was expected that cyclization would proceed more readily. The synthesis of the dithiol 14 was accomplished in good yield by reaction of dibromide 5 with thiourea followed by alkaline hydrolysis of the resulting adduct. The



5 14

structure of 14 was confirmed by its nmr spectrum in $CCl_4$ which revealed a methyl singlet at δ 2.27 ( 3H ), a methylene doublet at δ 3.57 ( 4H ), three aryl protons unsplit at δ 6.90 and an exchangeable triplet for two mercapto protons at δ 1.53. In some instances when crude samples of the dibromide 5 were used as starting materials, mesitylene-α-thiol (15) was formed as a by-product. Its structure was identified by nmr spectrometry

which showed a methyl singlet at δ 2.25 ( 6H ), a methylene doublet at δ 3.58 ( 2H ), an unresolved signal for the three aryl protons at δ 6.84 and an exchangeable triplet for one mercapto proton at δ 1.42. Analysis by glp chromatography showed that the proportion of this mono-thiol varied from 5 - 10 %. Presumably, the formation of 15 arised from α-bromomesitylene (16), which in turn was a by-product in the dibromination of mesitylene.




16 15

In an attempt to effect the formation of 6,15-dimethyl-2,11-dithia[3.3]-metacyclophane 9, a solution of 14 in ethanol containing two molar equivalents of sodium ethoxide and a separate ethanolic solution of dibromide 5 were added dropwise and simultaneously into a large volume of boiling ethanol kept under nitrogen. In all instances except one ( see below ), a white solid in needle form, designated Thia-I, m.p. 210°, was isolated by column chromatography. The nmr spectrum of this product measured in $CS_2$ displayed singlets at δ 2.12 ( 6H ), 3.58 ( 8H ), 6.50 ( 2H ) and 6.61 ( 4H ). These data seemed to fit the expected structure 9. However, it was ruled out by quantitative elemental analysis which gave an empirical formula $C_{18}H_{20}S_4$. Consequently, we assign structure 17, 7,17-dimethyl-2,3,12,13-tetrathia[4.4]-metacyclophane for this compound which fits equally well the observed nmr spectrum ( Fig.5 ).

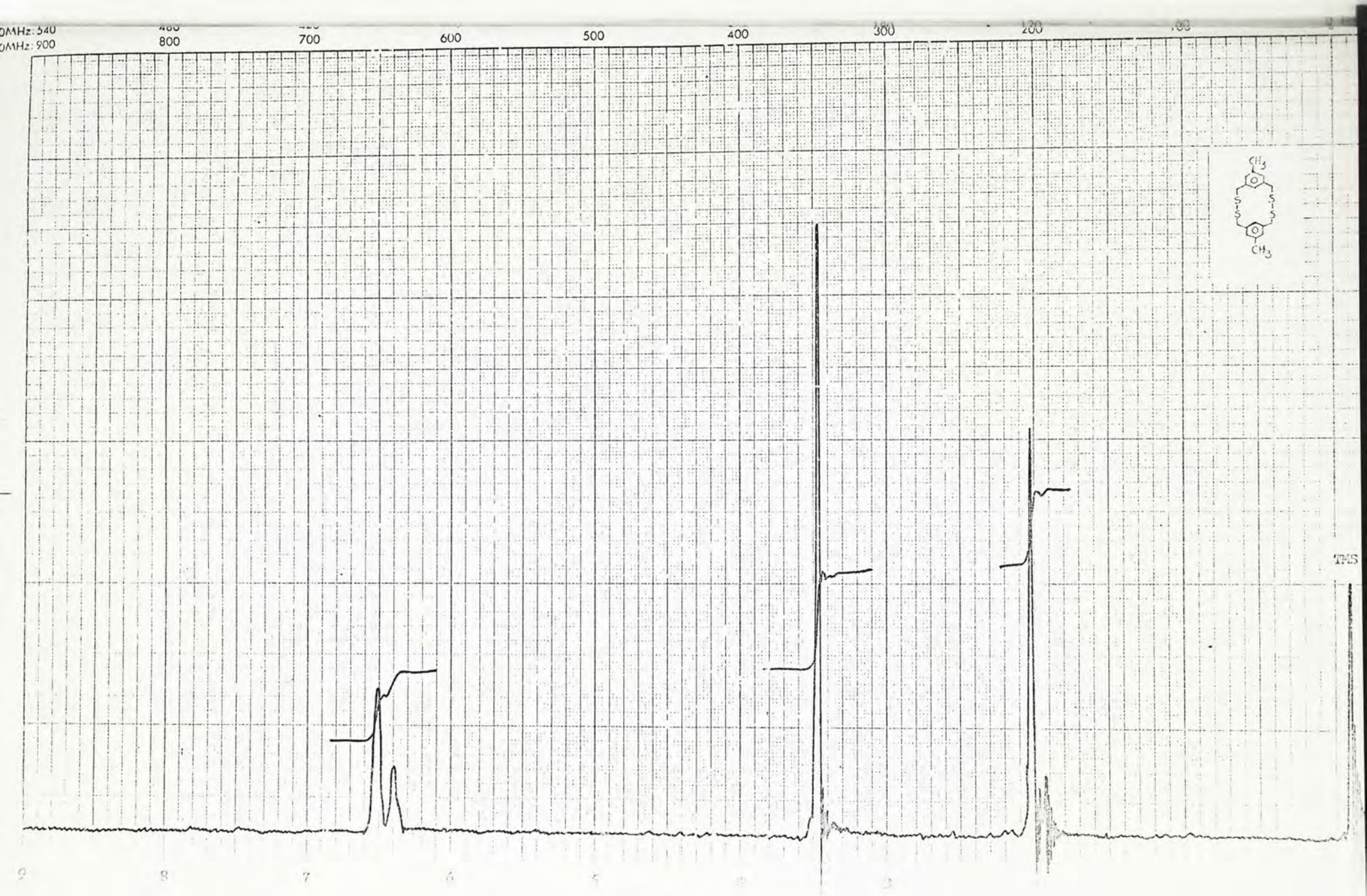
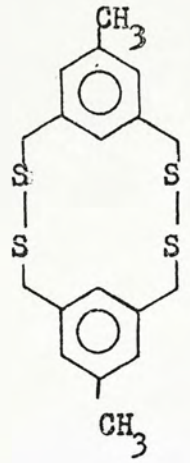
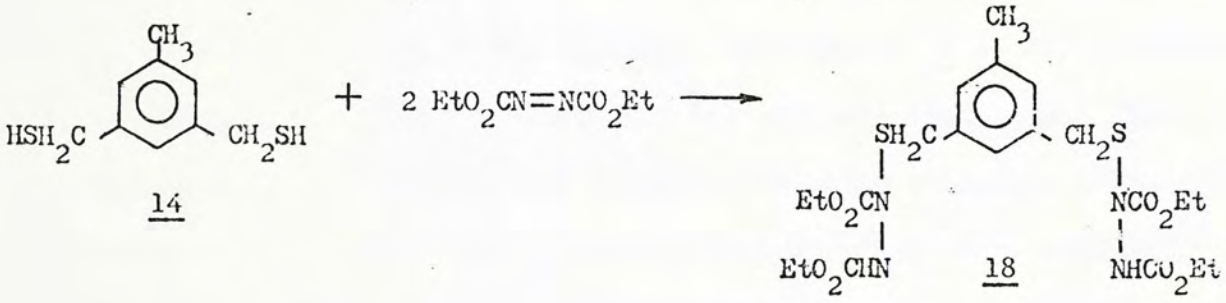



Fig. 5 The nmr spectrum of 7,17-Dimethyl-2,3,12,13-tetrathia[4.4]metacyclophane ( $CS_2$ )



17

Verification of this structure comes from an independent synthesis. Following a similar method originated by Boekelheide[26], an authentic sample, m.p. 210°, was prepared by the cyclization of 14 and the methylene-α,α'-dithiol -- ethyl azodicarboxylate adduct 18.



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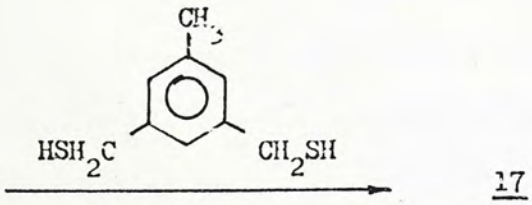


Refluxing benzene

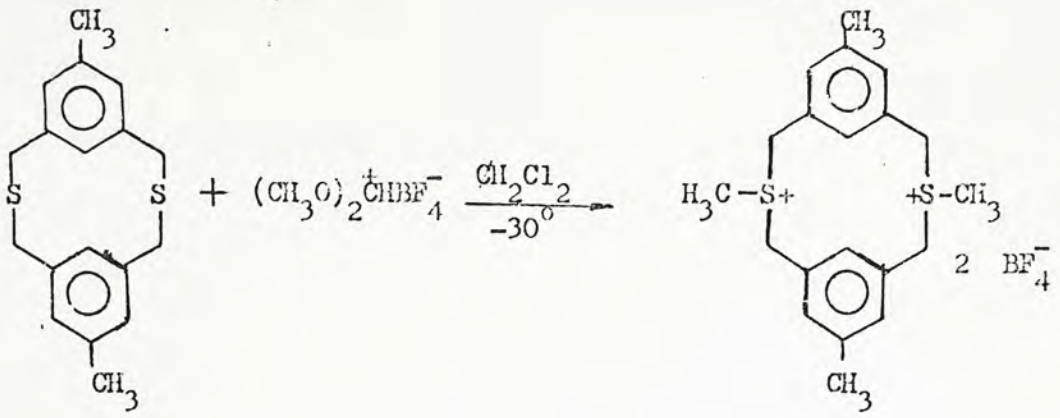
17

The structure for Thia-I was finally established unequivocally by comparing its ir and nmr data with those of the authentic sample.

In only one instance of the dozen runs carried out under the same set of conditions followed by the same work-up procedure were we able to obtain the expected dithia[3.3]metacyclophane 9, m.p. 105°, from the reaction of 5 and 14. Although the nmr spectrum of this product was almost identical to that of 17, its ir spectrum was clearly distinguishable. On the basis of quantitative elemental analysis, structure 9 was assigned.

The non-reproducibility of the above-mentioned reaction cannot be accounted for readily. Furthermore, the formation of 17 cannot be rationalized with the available information. It was first thought that 17 might have arised from oxidative coupling of 14 since this type of reaction is well known for thiols[27]. However, this possibility was ruled out as a result of a stability test. For example, exposure of 14 to air for several days changed neither its nmr spectrum nor its glc retention time. Two additional control experiments were conducted in which ethanolic solutions of 14 and sodium ethoxide, and 14 and sodium hydroxide, were refluxed for two days. Similarly, 14 was recovered unchanged. It seemed therefore the dibromide 5 did play a role in the formation of the tetrathia[4.4]-metacyclophane 17. The mechanism of this reaction remains to be elucidated.

Methylation of the dithia[3.3]metacyclophane 9 was effected readily by using a method popularized by Borch[28]. Reaction of this compound with excess dimethoxycarbonium fluoroborate gave essentially a quantitative yield of the expected bissulfonium salt 10. The structure of the latter was consistent



9 10

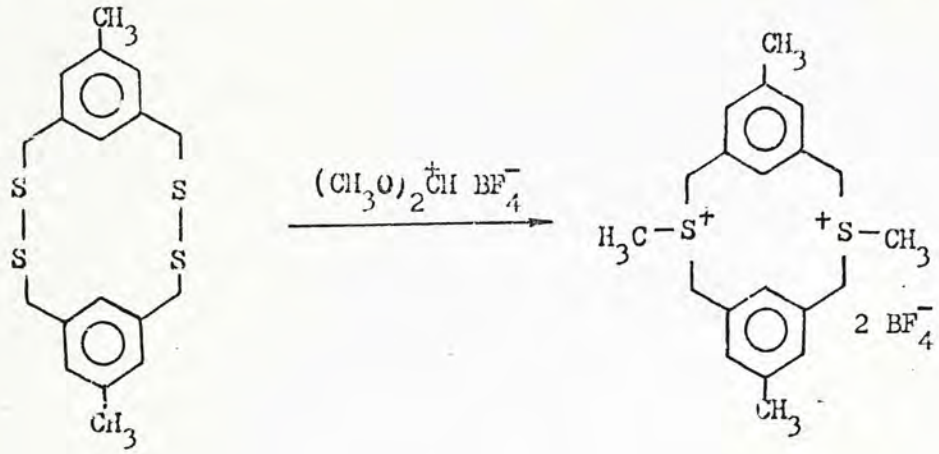
with its nmr spectrum.

The reaction of organic disulfides with alkylating agents such as alkyl halides[29] and trimethyloxonium trinitrobenzenesulfonate[30] has been demonstrated to proceed with extrusion of sulfur resulting in the ultimate formation of sulfonium salts. For example, treatment of diethyl disulfide with ethyl iodide gave triethylsulfonium iodide[31] and reaction of aryl disulfides with trimethyloxonium trinitrobenzenesulfonate gave diaryl methylsulfonium salts[30]. In the cases of n-butyl disulfide and sec-butyl disulfide, treatment with the oxonium salt gave initially n-butylmethylbutylthiosulfonium and sec-butylmethylbutylthiosulfonium trinitrobenzenesulfonate, respectively. These salts subsequently decomposed into the corresponding sulfonium salts during recrystallization[30].

$$R-S-S-R \xrightarrow{Me_3O^+(NO_2)_3C_6H_2SO_3^-} R-S-\overset{+}{S}(Me)-R \longrightarrow R-\overset{+}{S}(Me)-R$$

R = n-Butyl or sec-Butyl.

In view of these findings, methylation of the tetrathia[4.4]metacyclophane 17 was carried out with the hope to generate the bissulfonium salt 10. Indeed, reaction of 17 with dimethoxycarbonium fluoroborate proceeded readily to yield 10 which was identical in all respects with the sample originated from 9.




17 10

It was soon realized that the synthetic utility of the Boekelheide method would not be diminished, for the tetrathia[4.4]metacyclophane 17 served equally well for the preparation of the bissulfonium salt 10. In fact the alternate synthesis of 17 via ethyl azodicarboxylate became more appealing on account of its higher yield. Thus, proceeding toward our final goal, the Stevens rearrangement of bissulfonium salt 10 was attempted. However, this reaction was unexpectedly sluggish under various conditions. The yields ranged from 15 - 26 % with potassium t-butoxide in tetrahydrofuran or with sodium hydride in the same solvent. That the expected product(s) 11, i.e. 1,9-bis(methylthio)-5,13-dimethyl[2.2]metacyclophane and/or 1,10-bis(methylthio)-5,13-dimethyl[2.2]metacyclophane, were formed was verified by nmr spectrometry which revealed a singlet at δ 4.30 ascribable to the presence of intra-annular hydrogens in the products.

All attempts to methylate 11 with dimethoxycarbonium fluoroborate were unfruitful. In dichloromethane at -30° the reaction mixture invariably turned dark without giving a precipitate. Upon standing at room temperature for 5hr, a minute amount ( 5mg ) of a white amorphous solid m.p. 250-80° was isolated. Insoluble in most solvents, this material could not be purified by fractional crystallization. As a result the synthesis of the desired compound 1 was halted at this point.

## EXPERIMENTAL

Melting points were measured using a Kofler micro-heating stage and are reported uncorrected. Nmr spectra were measured with a JOEL 60-HL spectrometer; the chemical shifts are reported in ppm units with respect to internal TMS standard. Elemental analyses were performed by Australian Microanalytical Service, CSIRO, Parkville, Victoria, Australia, with the exception of α,α'-dibromomesitylene (5) and 5-methyl-isophthalaldehyde (6) which were determined by Mr. Y. H. Law at New Asia College.

α,α'-Dibromomesitylene (5).- To a 500ml round-bottom flask equipped with a magnetic stirrer, and a condenser attached with a calcium chloride drying tube, was added 250ml of carbon tetrachloride (previously distilled over $P_2O_5$), 53.4g( 0.3mole ) of N-bromosuccinimide, 18.0g( 0.15mole ) of mesitylene and a trace amount of benzoyl peroxide. The mixture was stirred and heated under reflux for 8hr. After the reaction was completed, the insoluble succinimide was removed by filtration, and the solvent of the filtrate was removed under reduced pressure. The residue, after recrystallization from petroleum ether, afforded 21.5g( 50% ) of white needles, m.p. 62-3° (lit. 60-1°)[32]. The nmr spectrum of this compound ( $CCl_4$ ) showed singlets at 2.30 ( 3H ), 4.33 ( 4H ), 7.10 ( 2H ), and 7.30 ( 1H ).

Anal. Calcd. for $C_9H_{10}Br_2$ : C, 38.88; H, 3.63. Found : C, 38.94; H, 3.47.

5,13-Dimethyl[2.2]metacyclophane (4).- (A) In a 2-l, three-necked, round-bottomed flask, equipped with a reflux condenser, mechanical stirrer,

and addition funnel, phenyllithium was prepared under a nitrogen atmosphere by adding 71.0g( 0.45mole ) of bromobenzene in 150ml of benzene over 1hr to 6.3g( 0.9gram-atom ) of lithium wire in 250ml of absolute ether. External heating was applied to initiate the reaction, but was discontinued after the reaction began. After addition was completed, heating was again applied and the dark brown solution was allowed to reflux gently overnight under nitrogen. A solution of 65.0g( 0.24mole ) of 5 in 250ml of reagent ether was added over 10hr. The resulting solution was stirred and refluxed for a period of four days, after which water was added slowly to decompose excess phenyllithium. The organic layer was separated, washed with water and dried over anhydrous sodium sulfate. After removal of solvent, the yellow residue was extracted repeatedly with boiling ethanol. The combined extracts were concentrated and treated with activated charcoal. The crude yellow product was chromatographed over neutral alumina( E.Merck, Activity I ), using ether as an eluent. Evaporation of solvent left a white solid which was recrystallized from ethanol to afford 2.7g( 9.5% ) of the product, m.p. 148° (lit. 147-9°)[11]. The nmr spectrum of this compound ($CDCl_3$) showed singlets at 2.40 ( 6H ), 4.20 ( 2H ) and 6.95 ( 4H ), a quartet centered at 2.59 ( 8H ).

(B). A solution of 1.0g( 0.003mole ) of tetraphenylethylene in 200ml of dry tetrahydrofuran was added to approximately 10g ( 0.44gram-atom ) of sodium sand prepared in the usual manner by vigorous shaking melted metallic sodium in hot toluene. To the resulting deep-red mixture was added dropwise a solution of 34.0g( 0.12mole ) of 5 in 600ml of dry tetrahydrofuran. Total addition required a period of 30hr during which the reaction mixture

was constantly stirred and kept under nitrogen. After addition was completed, a few drops of ethanol were added to destroy the organometallic complex, and the suspension was decanted from most of the unreacted sodium. The reaction flask was washed with additional tetrahydrofuran, and the clear light yellow filtrate was concentrated and extracted repeatedly with hot ethanol. The ethanolic solution was concentrated, treated with charcoal and evaporated to dryness. The residue was taken up in chloroform and applied to a column of neutral alumina( E.Merck, Activity I ). The fraction eluted with ether-petroleum ether ( 1:2 ) gave a white solid which upon recrystallization from ethanol yielded 4.0g( 28.2% ) of white needles, m.p. 147°.

Anal. Calcd. for $C_{18}H_{20}$ : C, 91.5; H, 8.49. Found : C, 91.45; H, 8.64.

2,7-Dimethyl-4,5,9,10-tetrahydropyrene (2).- To a stirred solution of 450mg( 1.9mmole ) of 4 in 96ml of glacial acetic acid, was added a solution of 3.3ml of concentrated nitric acid in 2.1ml of glacial acetic acid in 3 min. After stirring for 2 min, it was poured into ice water. The white solid was collected, washed with water, and dried. It was then dissolved in petroleum ether( 50-75° ) and subjected to a neutral alumina( E.Merck, Acivity I ) column eluting with n-hexane. The first fractions afforded 250mg( 56% ) of white needles, m.p. 140-1° (lit. 146.5-8°)[11]. The nmr spectrum of this compound ($CDCl_3$) showed singlets at 2.31 ( 6H ), 2.81 ( 8H ) and 6.88 ( 4H ).

2,7-Dimethylpyrene (1).- A mixture of 250mg( 1.08mmole ) of 2 and 0.15g of 10% palladium-on-charcoal was heated in a long tube at 270° for 5hr. The resulting material was extracted with hot chloroform. After removal of

solvent, a yellow solid was obtained which upon recrystallization from ethanol gave 200mg ( 86.0% ) of the product, m.p. 227-8° (lit. 228-32°)[5] The nmr spectrum which showed singlets at 2.80 ( 6H ) and 8.03 ( 8H ) is identical with that reported by Clar and coworkers[19].

5-Methylisophthalaldehyde (6).- To a rapidly stirred solution of 6.3g( 0.05mole ) of hexamethylenetetramine in 25ml of chloroform was added 5.6g( 0.02mole) of 5 in one lot. An exothermic reaction commenced in 3 or 4 min causing the mixture to reflux spontaneously. After the reaction subsided, the mixture was held under reflux for an additional period of 15min. After being cooled, the salt was filtered and washed successively with two 10ml-portions of fresh chloroform and two 10ml-portions of ether. The hexamine salt collected was first air-dried for one hour and then briefly dried under vacuum. Decomposition of the salt was carried out by steam distillation. After one recrystallization from aqueous ethanol, 8.5g( 22% ) of white needles was obtained from 10runs, m.p. 92-3°. The nmr spectrum of this compound ($CDCl_3$) showed singlets at 2.50 ( 3H ), 8.07 ( 2H ), 8.26 ( 1H ) and 10.29 ( 2H ).

Anal. Calcd. for $C_9H_8O_2$ : C, 72.97; H, 5.40. Found : C, 73.15; H, 5.36.

α,α'-Mesitylenebis(triphenylphosphonium bromide) (7).- A solution containing 5.6g( 0.02mole ) of 5 and 10.5g( 0.04mole ) of triphenyl phosphine in 30ml of chloroform was allowed to stand at room temperature overnight. Removal of solvent followed drying under vacuum at 100°, gave a quantitative yield of white solid, m.p. > 340°.

Attempted synthesis of 5,13-dimethyl[2.2]metacyclophane-1,9-diene (3).- (A) About 1.4g( 0.2gram-atom ) of freshly cut lithium metal was added by pieces into 750ml of absolute ethanol. The separate solutions of 3.0g( 0.02 mole ) of 6 in 50ml of absolute ethanol and 16.0g( 0.02mole ) of 7 in 50ml of absolute ethanol were added simultaneously and dropwise into vigorously stirred basic solution. Total addition required 4hr. The reaction mixture was continually stirred at room temperature overnight. The dark brown residue obtained after removal of ethanol, was extracted repeatedly with petroleum ether. The extracts were combined and concentrated to dryness. The yellow oil thus obtained was chromatographed over a column of neutral alumina. A white solid of ill-defined melting point ( 85-125° ) was obtained. The nmr spectrum of this material in $CCl_4$ showed broad singlet at 2.20 ( 6H ), and two unresolved signals with maxima at 6.47 and 6.90 ( totally 10H ). Further purification by thick-layer chromatography did not change its characteristics. Prolonged irradiation of this substance in tetrahydrofuran at 254mμ did not give rise to a chemical change as indicated by nmr.

(B) Two separate solutions of 3.0g( 0.02mole ) of 6 and 16g( 0.02mole ) of 7 in 100ml of dimethylformamide and 5.2g( 0.1mole ) of lithium ethoxide in 100ml of absolute ethanol were added simultaneously and dropwise into 1 litre of dry dimethylformamide under nitrogen at 90°. Total addition required 10hr The product was worked up as in (A), however, only oily material was obtained.

Attempted synthesis of 6,15-dimethyl-2,11-dithia[3.3]metacyclophane (9) using sodium sulfide.- A solution of 7.2g( 0.03mole ) of $Na_2S.9H_2O$ in 400ml of 40% aqueous ethanol and another solution of 8.3g( 0.03mole ) of 5 in 400ml of ethanol were simultaneously added dropwise into 1 litre of rapidly stirred

ethanol held under reflux. Total addition required 11hr. The reaction mixture was refluxed for an additional hour after the addition had been completed. After removal of solvent under reduced pressure, the residue was taken up in dichloromethane. The solution was dried with anhydrous magnesium sulfate and filtered. The yellow oil obtained after removal of solvent was chromatographed over silica gel. Examination of the various fractions revealed that this residue contained a small amount of the starting dibromide and a viscous oil. To the solution of the above-mentioned oily material in 15ml of dichloromethane was added 5ml of methyl iodide. Upon standing at room temperature for one week, a white crystalline solid was obtained. The product was collected by filtration and washed with dichloromethane. Recrystallization from ethanol gave 1.0g of trimethylsulfonium iodide, identical in all respects with an authentic sample.

Mesitylene-α,α'-dithiol (14).- A mixture of 31.2g( 0.11mole ) of 5 and 16.5g( 0.22mole ) of thiourea in 250ml of ethanol was heated under reflux for 4hr. A solution of 12g( 0.3mole ) of sodium hydroxide in 20ml of water was added, and the mixture was refluxed for another 3hr. The resulting yellow solution was acidified by cold dilute hydrochloric acid, and extracted with ether. The organic layers were combined and dried over anhydrous sodium sulfate. After removal of ether, the residue was distilled under vacuum to give 12.5g( 76.2% ) of a colorless liquid, b.p. 110-20°( 0.1mm ). The nmr spectrum of this compound ($CS_2$) showed singlets at 2.35( 3H ) and 6.90 ( 3H ); a doublet at 3.60 ( 4H ) and a triplet at 1.50 ( 2H ).

Anal. Calcd. for $C_9H_{12}S_2$ : C, 58.68; H, 6.52; S, 34.78. Found: C, 58.47; H, 6.71; S, 34.80.

Mesitylene-α-thiol (15).- Whenever a crude sample of 5 was used in the preparation of 14, mesitylene-α-thiol was formed as a by-product. An analytical sample of the mono-thiol was obtained by preparative glc ( Silicone Rubber, 170° ).

Anal. Calcd. for $C_9H_{12}S$ : C, 71.05; H, 7.89; S, 21.05. Found : C, 71.25; H, 8.12; S. 21.10.

Cyclization reaction between mesitylene-α,α'-dithiol (14) and α,α'-dibromomesitylene (5): (A) 7,17-Dimethyl-2,3,12,13-tetrathia[4.4]meta-cyclophane (17).- A solution of 5.52g( 0.03mole ) of 14 and 2.72g( 0.04mole ) of sodium ethoxide in 400ml of absolute ethanol and a solution of 8.34g ( 0.03mole ) of 5 in 400ml of absolute ethanol were added dropwise and simultaneously into 1 litre of boiling ethanol in a three-necked, round-bottom flask. Total addition required 24hrs during which a nitrogen atmosphere was maintained. The resulting solution was evaporated to dryness under reduced pressure. The residue was extracted with dichloromethane, washed with water, and dried . Concentration in vacuo of the dried organic layer gave a yellowish oil which was taken up in benzene and chromatographed over silica gel. Elution with benzene-petroleum ether( 50-75° ) ( 1:2 ), gave a white solid. Recrystallization of the crude product from petroleum ether ( 50-75° ) afforded 1.3g( 16.3% ) of colorless needles, m.p. 210°. The nmr spectrum of this compound ($CS_2$) showed singlets at 2.12 ( 6H ), 3.58 ( 8H ), 6.50 ( 2H ) and 6.61 ( 4H ). This compound was identical in all respects to an authentic sample prepared independently ( see below ).

Anal. Calcd. for $C_{18}H_{20}S_4$ : C, 59.29; H, 5.56; S, 35.19. Found : C, 58.99; H, 5.52; S, 35.5.

(B) 6,15-Dimethyl-2,11-dithia[3.3]metacyclophane (9).- In one of the

the dozen runs carried out under identical conditions, this compound was obtained by following the same work-up procedure described above. Recrystallization from petroleum ether ( 50-75° ) afforded 1.2g( 10.3% ) of white needles, m.p. 105-6°. Its nmr ($CS_2$) spectrum displayed singlets at 2.08 ( 6H ), 3.58 ( 8H ), 6.42 ( 2H ) and 6.58 ( 4H ). Further recrystallizations from petroleum ether furnished an analytical sample.

Anal. Calcd. for $C_{18}H_{20}S_2$ : C, 72.00; H, 6.67; S, 21.33. Found : C, 71.90; H, 6.80; S, 21.50.

Independent synthesis of 7,17-dimethyl-2,3,12,13-tetrathia[4.4]metacyclophane (17).- Two solutions containing 5.52g( 0.03mole ) of mesitylene-α,α'-dithiol 14 in 400ml of dry benzene and an adduct of 5.52g( 0.03mole ) of 14 and 10.44g( 0.06mole ) of ethyl azodicarboxylate in 400ml of dry tetrahydrofuran were added simultaneously and dropwise into 1 litre of boiling dry benzene kept under a nitrogen atmosphere. Total addition required 15hr after which the reaction mixture was allowed to reflux for an additional hour. The residue obtained by removal of solvent in vacuo was extracted with benzene. The combined benzene extracts was concentrated and chromatographed over a column of silica gel. Elution with petroleum ether ( 50-75° ) — benzene ( 2:1 ) gave a white solid which upon recrystallization from petroleum ether ( 50-75° ) gave 3.1g( 28.3% ) of white needles, m.p. 206-8°. The nmr spectrum of this compound ($CS_2$) showed singlets at 2.43 ( 6H ), 3.83 ( 8H ), 6.90 ( 2H ) and 7.10 ( 4H ).

S,S,6,15- Tetramethyl-2,11-dithia[3.3]metacyclophane bissulfonium fluoroborate (10).- To 0.6ml( 5mmole ) of trimethylorthoformate at -30° was added a solution of 0.6( 5mmole ) of boron trifluoride — etherate in 1 ml of dichloromethane dropwise with stirring in 1 min. The mixture was

then decanted, fresh dichloromethane was added. A solution of 0.6g( 2mmole ) of 9 in 2ml of dichloromethane was added to the resulting dimethoxycarbonium fluoroborate with stirring at room temperature under nitrogen. A white solid which melt with decomposition at 240° was obtained. The yield was quantitative. The nmr spectrum of the compound (DMSO-$d_6$) showed singlets at 2.15( 6H ), 3.10( 6H ), 4.85( 8H ) and three peaks at 6.92, 7.10 and 7.30 ( totally 6H ). Repeated recrystallization from aqueous ethanol furnished an analytical sample. The nmr spectrum (DMSO-$d_6$) of this material ( previously dried for 40hr at 90° under 5mm ) showed an additional singlet at 3.33 which was exchangeable with added $D_2O$ . The appearance of the new peak was ascribable to the incorporation of strongly bonded water of crystallization. Its exact content could not be determined by nmr integration owing to residual water impurity in the solvent. Results from elemental analysis, however, indicated that this material was a monohydrate salt.

Anal. Calcd. for $C_{20}H_{26}S_2B_2F_8 \cdot H_2O$ : C, 46.00; F, 29.13; H, 5.37; S, 12.27. Found : C, 46.28; F, 29.40; H, 5.14; S, 13.05.

An identical product was obtained in 90% by methylating 17 under similar conditions.

Stevens rearrangement of (10).- To a refluxing solution of 0.9g( 8.0 mmole ) of potassium t-butoxide in 25ml of dry tetrahydrofuran was added 1.8g( 3.6mmole ) of 10 in portions under a nitrogen atmosphere. The reaction was completed in 30 min. The filtrate was evaporated to dryness and triturated with methanol. A white solid, m.p. 160-200°, was obtained. The yield was 0.3g( 25.7% ). The formation of 1,9-bis(methylthio)-5,13-dimethyl[2.2]metacyclophane and/or 1,10-bis(methylthio)-5,13-dimethyl[2.2]-metacyclophane (11) was confirmed by the nmr spectrum of this product which revealed a singlet for the internal hydrogens at 4.30.

Methylation of (11).- A suspension of 0.63g( 5 mmole ) of dimethoxy-carbonium fluoroborate in 20ml of dichloromethane was added dropwise a solution of 0.3g( 1.8mmole ) of 11 in 10ml of dichloromethane. The reaction mixture was kept at -30° and under a nitrogen atmosphere. The solution changed into a dark brown color and did not give a precipitate upon standing at room temperature. After 5hr, the mixture was treated with water. A trace amount ( 1-5mg ) of white solid, m.p. 250-80° was obtained. Further reaction of this solid with potassium t-butoxide in tetrahydrofuran at 0° under nitrogen gave an intractable viscous oil.

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