A GENERAL ROUTE TO LARGE-SIZED CYCLOPHANES

LI Chun Sing (李振聲)

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Thesis Committee :

Dr. T.L. Chan, Chairman

Dr. W.P. Lay

Dr. K.H. Wong

Professor N.C. Yang, External Examiner

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LI Chun Sing

Chemistry Department,

C. U. H. K.

June, 1980

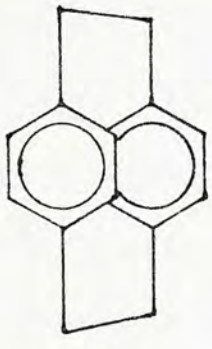
ABSTRACT

A new synthetic route to large-sized [m.m]cyclophanes and [n]cyclophanes is described. This method evokes the use of dithiacyclophane bissulfones as synthetic intermediates, which are readily accessible from simple starting materials. The key steps in the reaction scheme involve extrusion of sulfur dioxide from these bissulfones by a modification of the Ramberg-Bäcklund rearrangement followed by hydrogenation of the resulting cyclophanedienes. Its broad synthetic utility has been demonstrated by the preparation of a series of hitherto unknown [m.m]cyclophanes including [4.4]-, [5.5]-, and [6.6]cyclophanes in which the benzene rings, with or without substituents, are assembled in various manners. The method also provides an option to carry out the preparation of a number of [n]cyclophanes, both new and known, under non-pyrolytic conditions.

CONTENTS

I. INTRODUCTION

The term "phane" refers to any organic molecule containing at least one aromatic nucleus and at least one bridge[1]. Cyclophanes, which feature one or more benzene rings as the aromatic moieties, belong to a subgroup of this class of compounds. [2.2]Paracyclophane (1), [2.2]metacyclophane (2) and [2.2]metaparacyclophane (3) are the most well known examples in which two benzene nuclei are held face to face by two ethano bridges.



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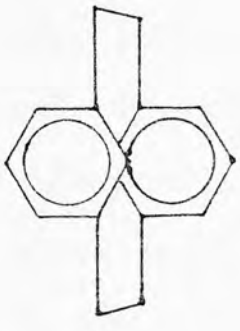

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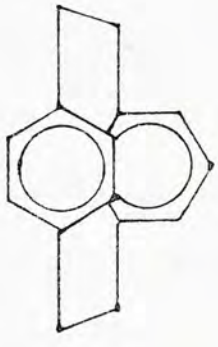

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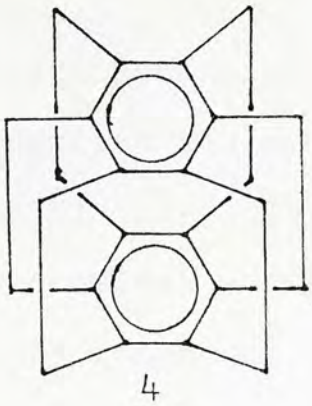
The conformational rigidity of the σ-framework in these systems renders them unique models for testing all manner of questions of strain, bonding and transannular π-π electronic interactions. Thus, the synthesis of strained cyclophanes has been an active area of study with phenomenal growth[2] in the past three decades, culminating in the recent report by Boekolheide on the synthesis of superphane (4)[3], a molecule which is subject to structural torture to an extreme unparralleled in any other system.



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Unlike the small and strained [m.m]cyclophanes, higher homologs with m ≥ 4 have drawn relatively little attention, except for Cram's classical works on the synthesis of [4.4]-, [5.5]- and [6.6]paracyclophanes[4]. The lack of interest in this direction stemmed partly from the predictable absence of unusual physical properties in large-sized cyclophanes and, partly from the difficulties encountered in the construction of macrocyclic molecules. Nevertheless, aside from being a challenge in molecular design and synthesis, [m.m]macrocyclophanes have now emerged as a class of structures which may have the potential for encapsulation and selective affinity[5] toward smaller aromatic species. It was therefore the objective of the present study to explore general synthetic routes to large-sized cyclophanes, which would be amenable to structural variations in respect of both the length of the bridges and the substitution pattern on the aromatic moeities.

II. LITERATURE SURVEY

The chemistry of cyclophanes blossomed into an active area of research when Cram reported the synthesis of 1 by the intramolecular Wurtz coupling of 1,2-bis(4'-bromomethylphenyl)ethane[6]. Prompted by the unusual chemical and physical properties observed in this highly strained hydrocarbon, considerable efforts to discover synthetic routes to related compounds soon ensued. Much of the earlier works independently undertaken by Cram, Baker and Prelog were reviewed in 1963 by Griffin[7]. Interest in this field experienced a second quantum jump in the early 1970s after Vögtle[8] and Boekelheide[9] independently introduced a new methodology involving the use of organosulfides as synthetic intermediates.

In order to provide a framework of reference for the discussions presented in the latter sections of this Thesis, a brief review of the existing methods commonly employed in cyclophane synthesis is given below.

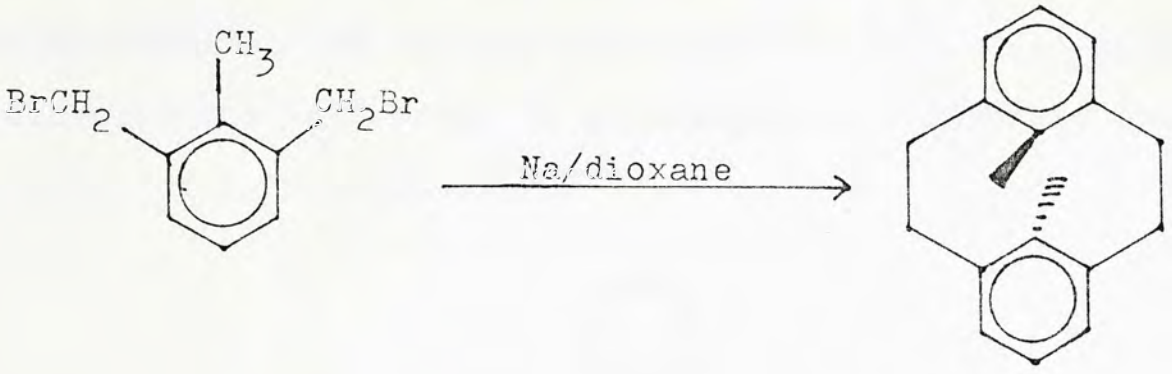
II.1. [2.2]Cyclophanes

a. Wurtz Reaction

The Wurtz reaction was the only available route to [2.2]-metacyclophanes in the early years. This method is typified by the synthesis of 8,16-dimethyl[2.2]metacyclophane (5), in small yield, by the coupling of 2,6-bis(bromomethyl)toluene with sodium in dioxane[10] (Scheme I). Yields were improved considerably on

addition of tetraphenylethylene for complexation with sodium to enhance reaction homogeneity.

Scheme I. Synthesis of 8,16-Dimethyl[2.2]cyclophane (5)



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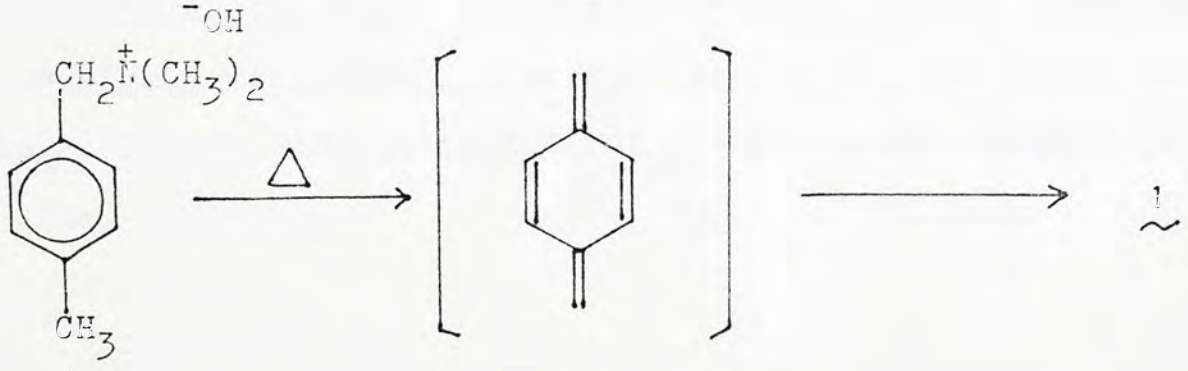
b. Methods Involving p-Xylylene

A standard laboratory synthesis of [2.2]paracyclophane (1)[11] involves a 1,6 elimination followed by a 1,6 to 1,6 cyclo-addition to give 1 (Scheme II). This compound is now a commercial monomer prepared in large-scale by the pyrolysis of p-xylene[12].

Scheme II. Synthesis of [2.2]Paracyclophane (1) by 1,6 Elimination



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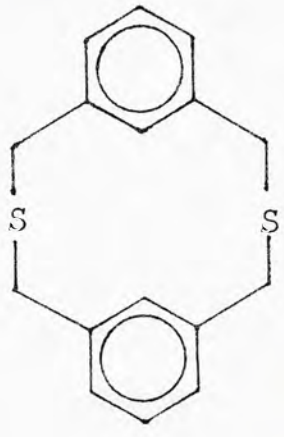
c. Methods Involving the Use of Dithiacyclophane Precursors

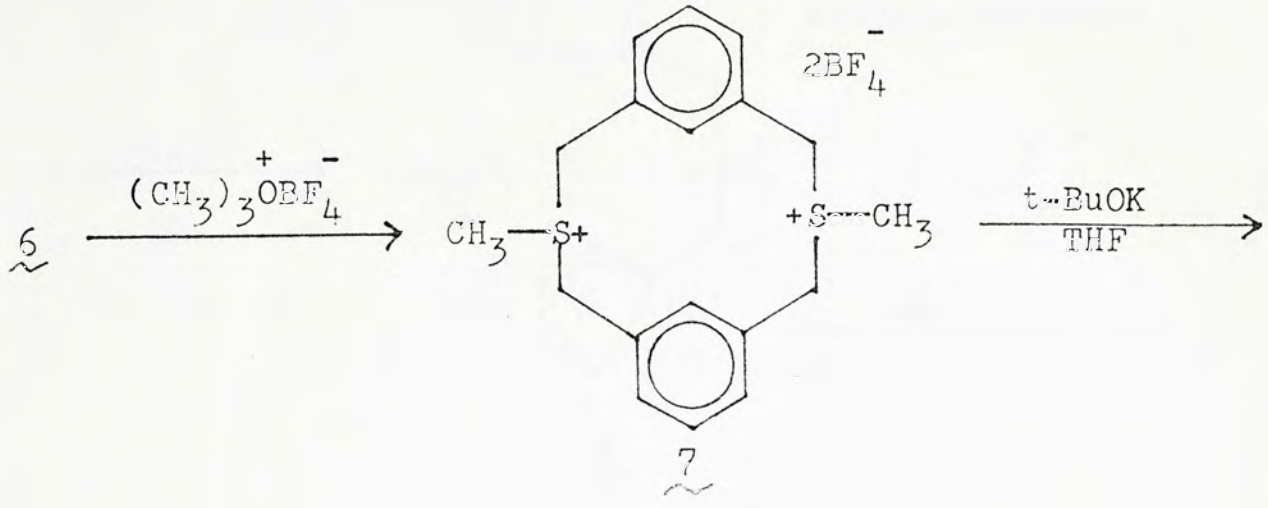
Dithiacyclophanes, readily obtainable by reaction of m- and p-xylylene dibromides and the corresponding bis(mercaptomethyl)benzenes, have been demonstrated to be extremely valuable synthetic intermediates for the preparation of a variety of [2.2]cyclophanes and related compounds[8,9,13,14]. 2,11-Dithia[3.3]-metacyclophane (6) serves as an example to illustrate the versatility of this methodology.

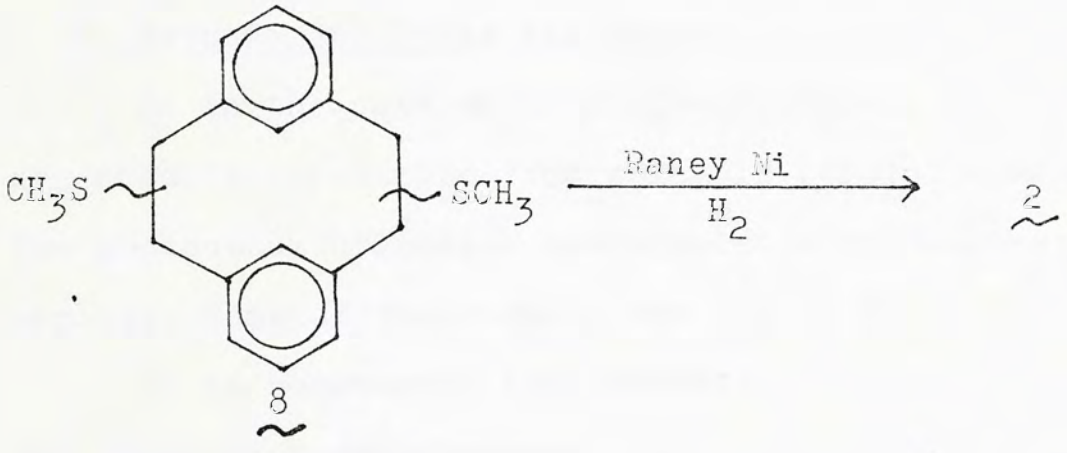


6

A number of routes are now available to effect the desulfurization in 6 leading to 2. In the original procedures (Scheme III) developed by Boekelheide[9], 6 was first converted into a bissulfonium salt 7 which was subjected to a Stevens rearrangement to give bissulfide 8. Desulfurization of 8 over Raney nickel led to 2. Direct desulfurization of 6 can also be accomplished

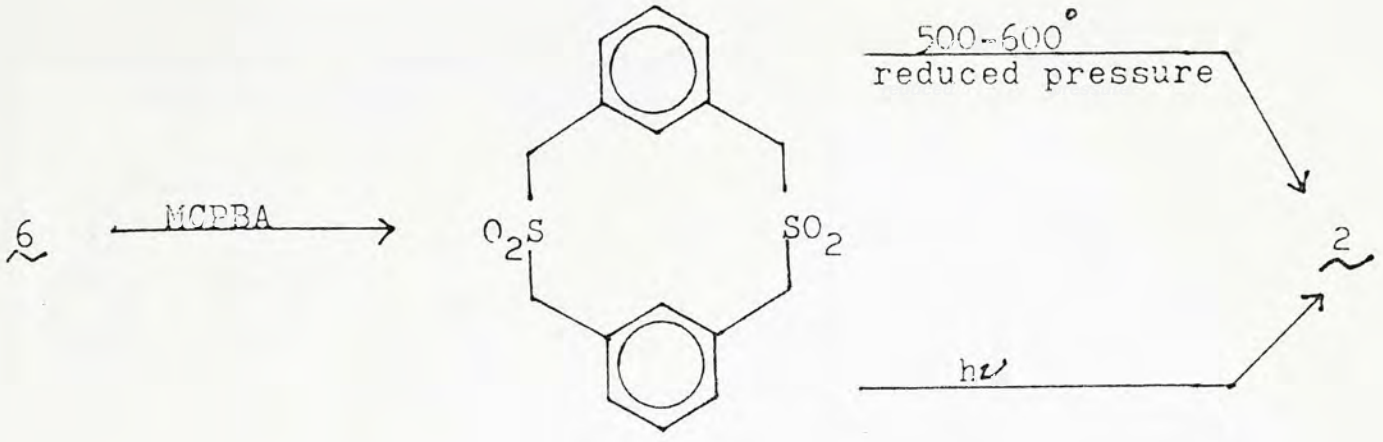
Scheme III. Synthesis of 2 via the Bissulfonium Salt 7





by prolonged ultraviolet irradiation in trivalent phosphorous solvents[15] . Alternatively, 6 may be first oxidized into the corresponding bissulfone 9, which, under pyrolytic[8] or photolytic[16] conditions undergoes sulfur dioxide extrusion to give 2 (Scheme IV).

Scheme IV. Synthesis of 2 via Bissulfone 9



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II.2. [3.3]Cyclophanes

a. Methods Involving the Use of Dithiacyclophane Precursors

As in the case with [2.2]cyclophanes, [3.3]cyclophanes are readily accessible from suitable [4.4]dithiacyclophanes[17]. The photodesulfurization and pyrolytic procedures have both been applied. Some of the results are listed in Table I.

It is noteworthy that whereas [3.3]paracyclophane (10), and [3.3]metaparacyclophane (11) were prepared in satisfactory yields from pyrolysis of the corresponding [4.4]dithiacyclophane bissulfones, the direct photodesulfurization procedure failed in the case for 11[17a]. In addition, [3.3]metacyclophane (12) was obtained only in extremely poor yield by the pyrolytic method and could not be prepared at all from the photodesulfurization procedure[17a].

Table I. [3.3]Cyclophanes from [4.4]Dithiacyclophanes and Their Bissulfones[17a]

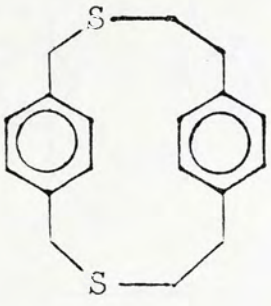
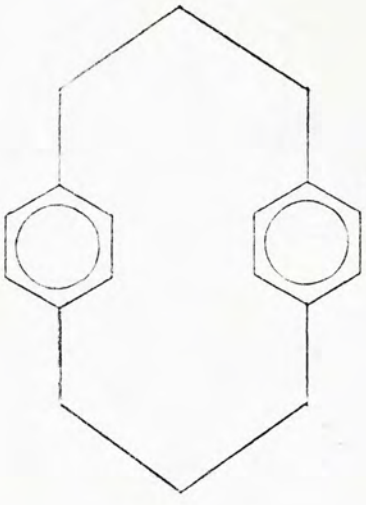
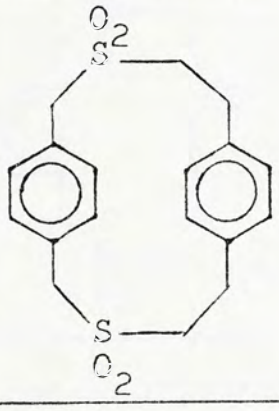
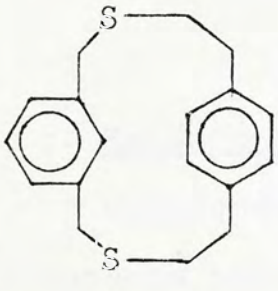
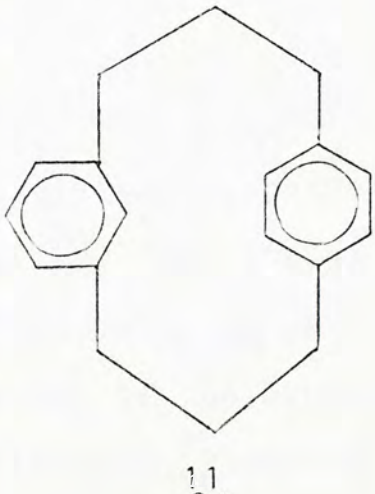
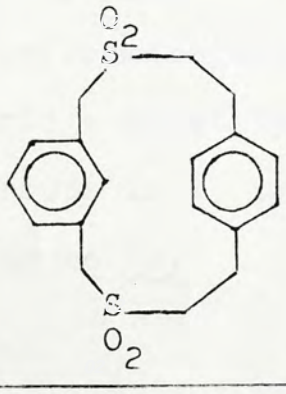
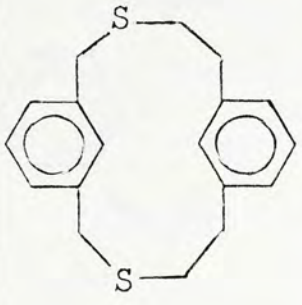
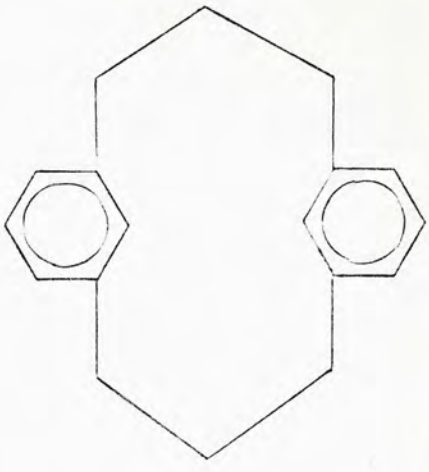
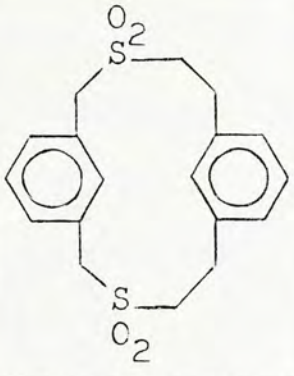
Intermediate	Method*	Yield (%)	Product
	hν	24	 10
	Δ	33	
	hν	0	 11
	Δ	20	

Table I (cont'd)

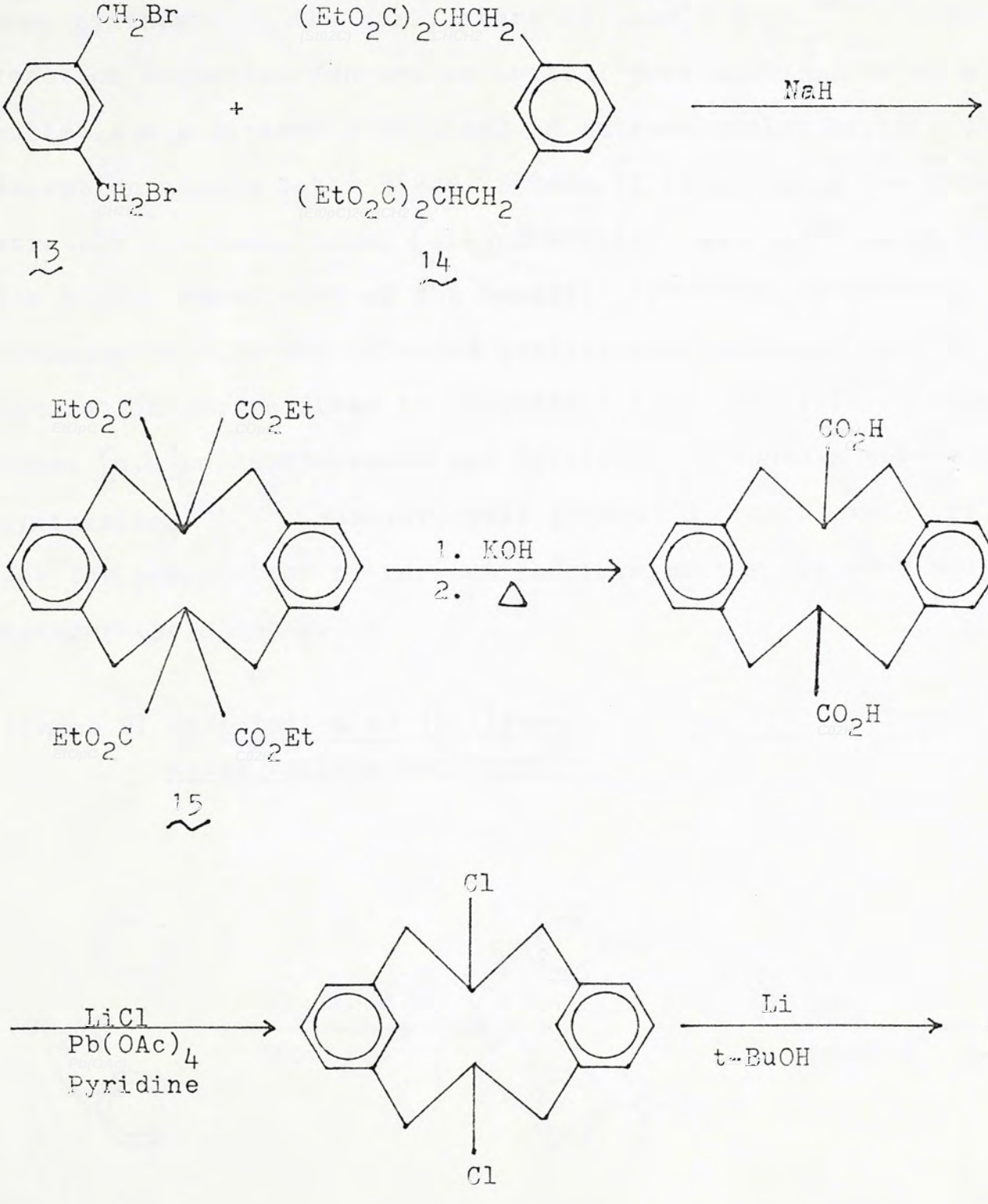
Intermediate	Method	Yield (%)	Product
	hν	0	 12
	Δ	2.7	

* hν = photodesulfurization; Δ = pyrolysis

b. Malonic Ester Synthesis

Complementary to the methods utilizing the [4.4]dithiacyclophane precursors mentioned above, [3.3]metacyclophane (12) was prepared by the malonic ester synthesis[18]. Reaction of 1,3-bis(bromomethyl)benzene (13) with bismalonic ester 14 gave the bridge substituted metacyclophane 15. Removal of the carboethoxy groups in 15 by the reaction sequence outlined in Scheme V finally led to 12.

Scheme V. Preparation of 12 by Malonic Ester Synthesis

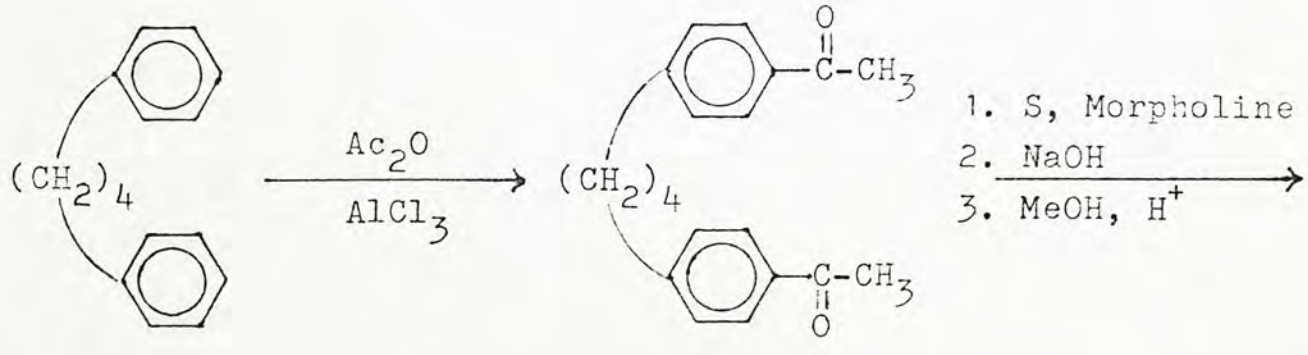


II.3. [m.m]Cyclophanes with m ≥ 4

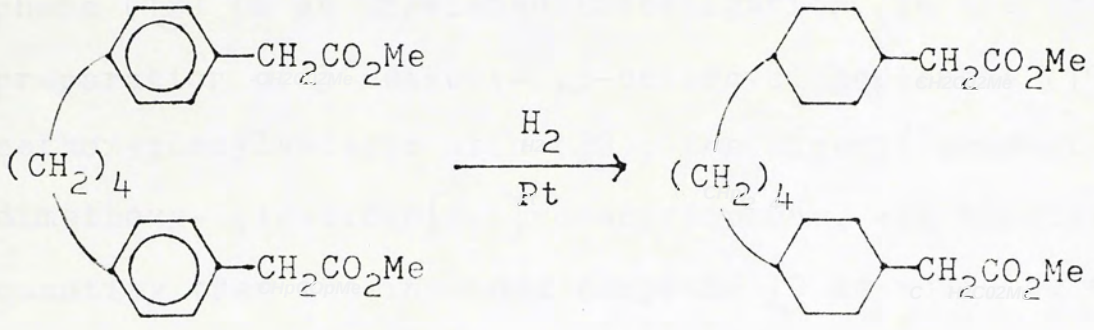
a. Methods by Intramolecular Acyloin Condensation

[m.m]Paracyclophanes with m ≥ 4 were prepared by multi-step synthesis in the early years by Cram's group[4a,b,c]. The reaction sequences feature an initial para acetylation on a suitable α,ω-diphenylalkane and an intramolecular acyloin condensation at the later stage. Scheme VI illustrates the general strategy involved, using [4.4]paracyclophane (16)[4a] as an example. The higher reactivity of the benzylic hydrogens of ester 17 interferred with the intended acyloin condensation, so ring saturation was required to circumvent this difficulty. Other higer [m.m]paracyclophanes and [m.n]paracyclophanes were similarly synthesized[4a,b,c]. However, this general approach cannot be applied for the preparation of large-sized [m.m]metacyclophanes and [m.m]-metaparacyclophanes.

Scheme VI. Preparation of [4.4]Paracyclophane (16) by Intramolecular Acyloin Condensation



Scheme VI. (cont'd)



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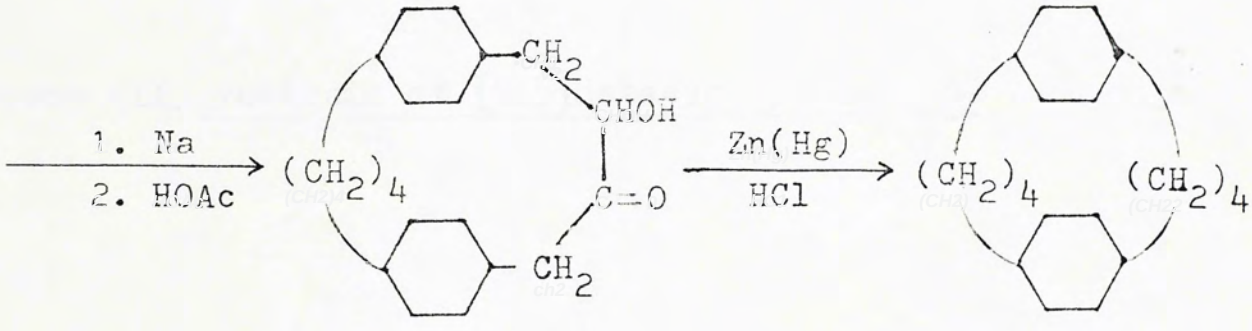

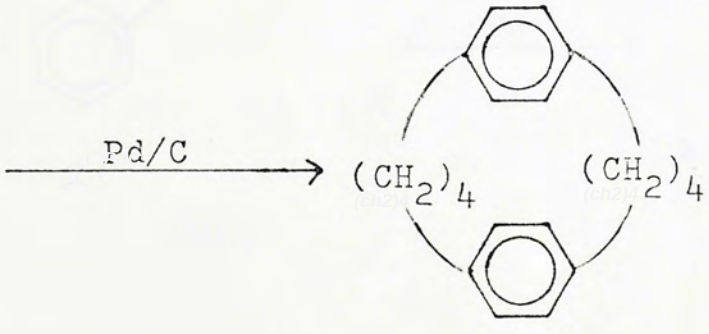

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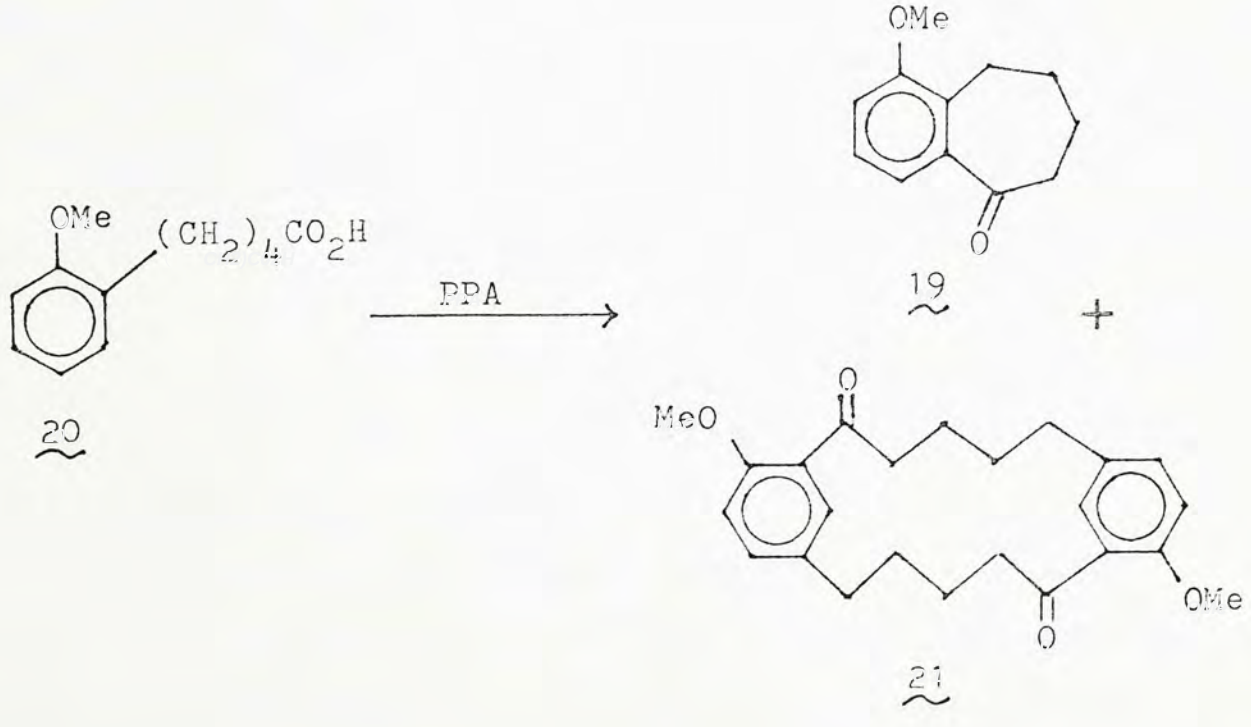
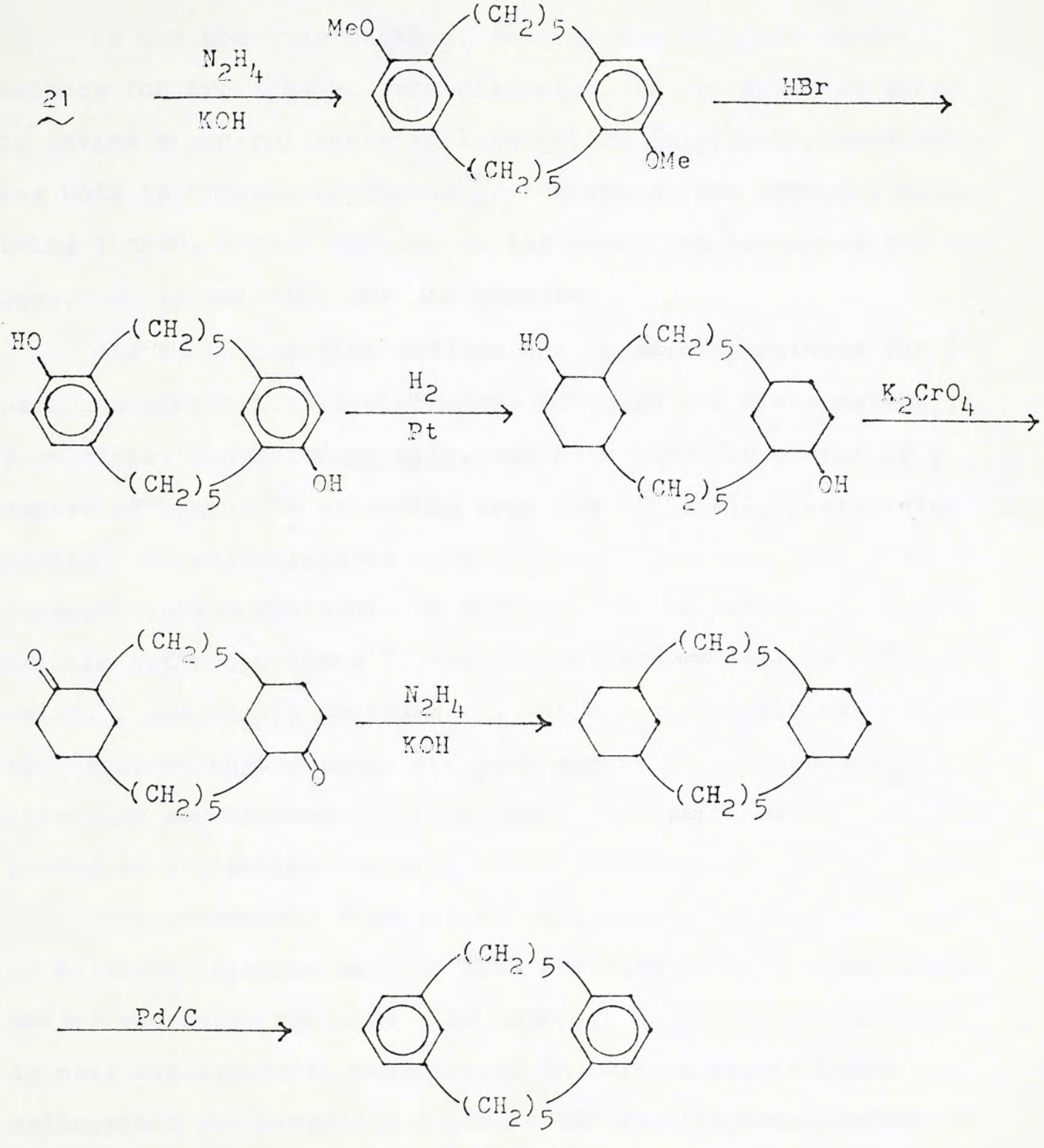
b. The Preparation of [5.5]Metacyclophane (18) by Dimerization Involving Friedel-Crafts Acylation

Bien[19] in 1960 reported the synthesis of [5.5]metacyclophane (18) in an unrelated investigation. In the course of the preparation of 3′methoxy-2,3-benzocycloheptenone (19) from δ-o-methoxyphenylvaleric acid (20), the dimeric product (21), 9,20-dimethoxy-1,12-dioxo[5.5]metacyclophane, was obtained in larger quantity than the intended compound 19 as would be expected from the strong ortho, para directing effect of the methoxy group in 20. Removal of the bridge keto functions and the ring substituents in 21 by the steps outlined in Scheme VII finally gave 18.

Scheme VII. Synthesis of [5.5]Metacyclophane (18)



Scheme VII (cont'd)

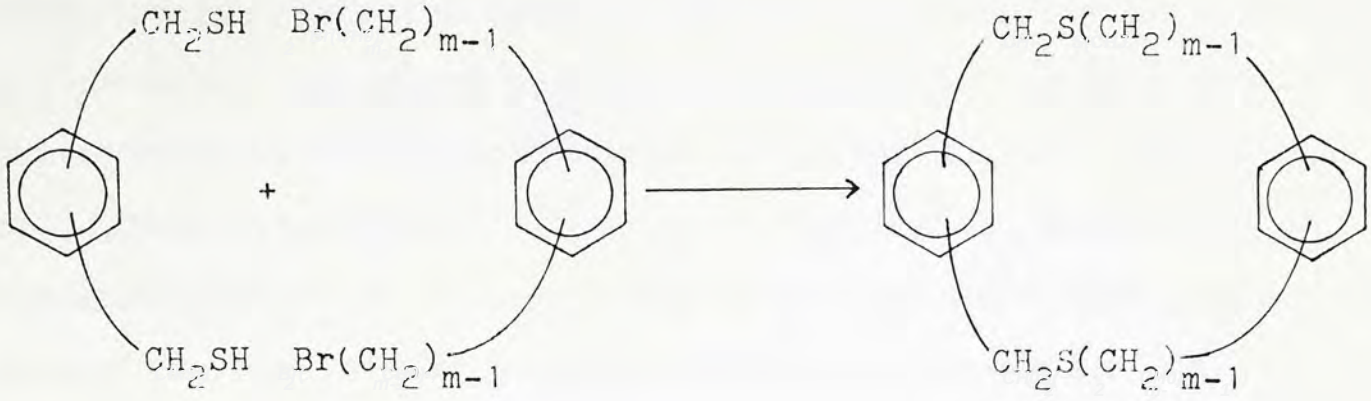


III. SYNTHETIC PLANS

In the previous section, some of the existing synthetic methods for cyclophanes were discussed. As our goal was aimed to devise a general route to large-sized [m.m]cyclophanes varying both in bridge length and in the manner the aromatic rings being linked, a good portion of the reactions mentioned did not appear to be suitable for our purpose.

The Wurtz reaction suffers the apparent ineptness for preparing unsymmetrical cyclophanes. Although the dimerization of p-xylylene, generated *in situ*, has been used for preparing a number of compounds extending from the simple [2.2]paracyclophanes[11] to multi-layered cyclophanes[2e], its application for macrocyclophane synthesis is difficult to be envisaged. The malonic ester synthesis[18], the intramolecular acyloin condensation[4], and Bien's procedure[19], while each has its own merits, all require lengthy steps and lack generality. Consequently, attention was focused onto the ring contraction of dithiacyclophanes as a possible route to macrocyclophanes.

The remarkably high yields encountered in the synthesis of dithiacyclophanes coupled with the flexibility in executing sulfur extrusion rendered this approach an attractive method to meet our synthetic objectives. No serious difficulties were anticipated for preparing suitable dithiacyclophane candidates of the type 22, since the required precusors, i.e., the corresponding bis(mercaptomethyl)benzenes 23 and bis(ω-bromomethyl)-



23 24 22

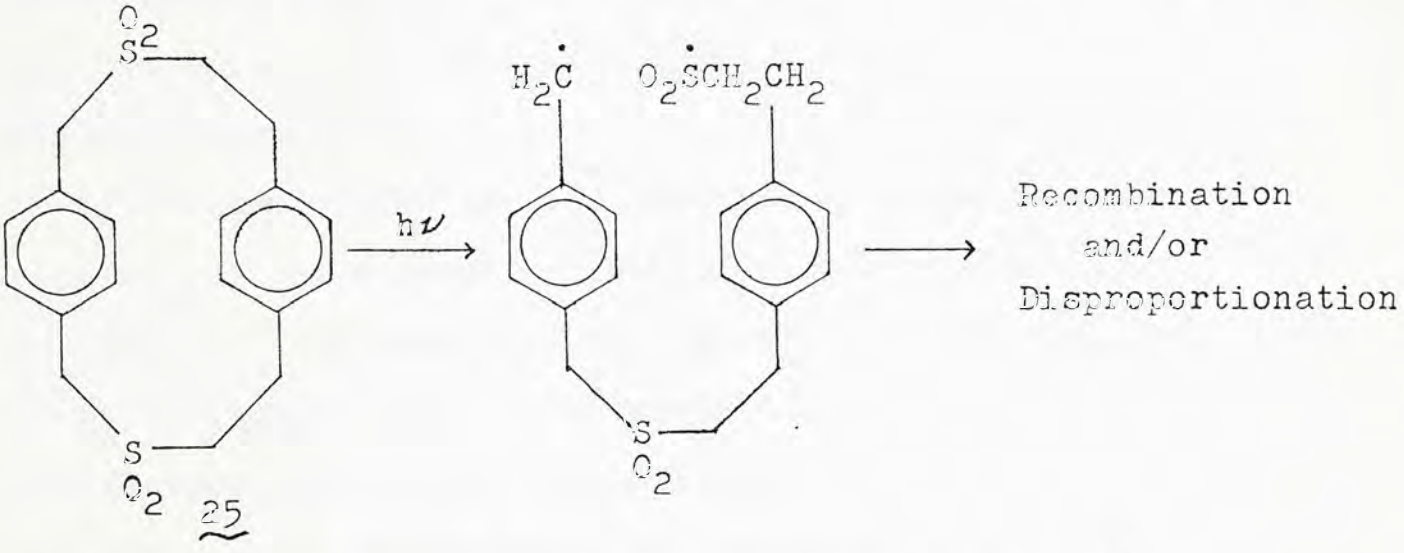
benzenes 24, would be accessible with relative ease (vide infra). What remained to be decided, however, was the method for sulfur removal in 22.

The combination of the Stevens rearrangement on the bis-sulfonium salts of 22 and subsequent desulfurization with Raney nickel, while successful in the cases for [2.2]metacyclophanes, failed in the paracyclophane series where 1,6 elimination became predominant[13c]. Furthermore, as the length of the sulfur-containing bridges is increased, the presence of β-hydrogens would give

rise to concomitant Hofmann elimination, resulting in the disintergration of the pre-constructed aliphatic bridge chains.

The failure observed in the direct photodesulfurization of 3,12-dithia[4.4]metaparacyclophane and 2,13-dithia[4.4]meta-

cyclophane during the preparation of 11 and 12[17a] (Table I), respectively, generated doubt as to its applicability in similar synthesis of higher cyclophane homologs. Other difficulties were experienced in the photoextrusion of sulfur dioxide from dithiacyclophane bissulfones[16,20] owing to the limited solubility of these substances in organic solvents as well as a high activation energy for the initial homolytic benzyl carbon-sulfur bond cleavage. The latter process was thought to be responsible for extensive radical recombination and disproportionation[16]. A case in point is bissulfone 25, which failed to undergo extru-



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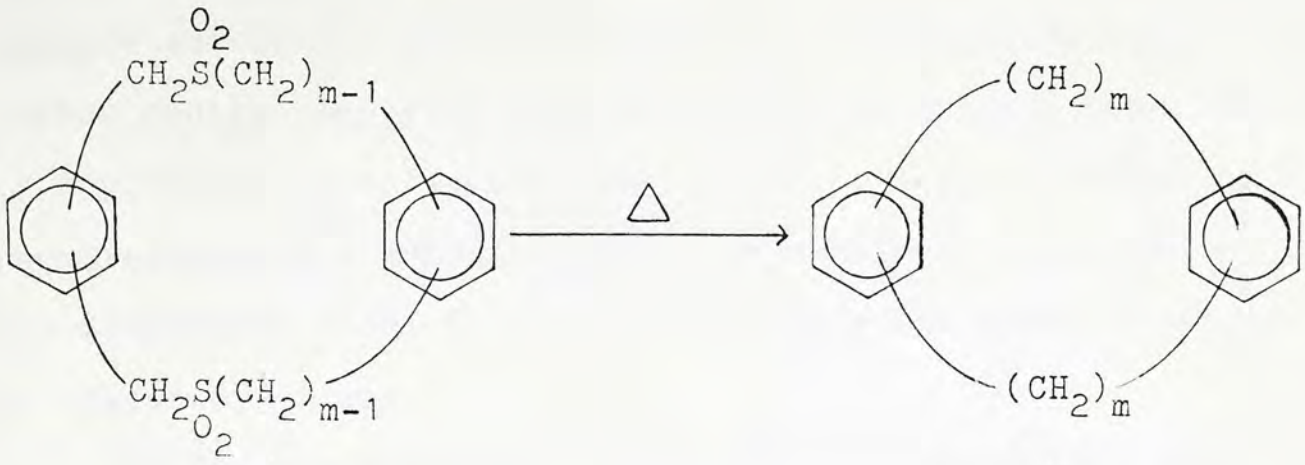
sion of sulfur dioxide even on prolonged photolysis[16].

Extrusion of sulfur dioxide by subjecting bissulfones of the type 26 to pyrolytic conditions is probably the most useful procedure for preparing the corresponding cyclophane 27. However, as with other organic vapor-phase reactions at elevated temperatures under vacuum, the yields fluatuate considerably depending on the extent to which various decompositions take



26 27

place. Without a prior knowledge of the optimal temperature and pressure for individual compounds, the selection of experimental condition by trial and error could sometimes be tedious. Added to this disadvantage is the inconvenience in handling of large-scale preparations.

In veiw of the various undesirable features inherent to each of the above desulfurization procedures, we turned to the exploration of alternative routes to effect the ring contraction of dithiacyclophanes. In contemplating a new experimental design, two factors were worthy of consideration: mild reaction condition and operational simplicity. The Ramberg-Bäcklund rearrangement[21] seemed to meet these requirements.

The Ramberg-Bäcklund rearrangement is a base-induced intramolecular 1,3 elimination of α-halo sulfones, resulting in the

$$RCH_2SO_2\underset{\displaystyle X}{\underset{|}{C}}HR + 3OH^- \longrightarrow RCH{=}CHR + X^- + SO_3^{=} + 2H_2O$$

replacement of the sulfonyl group by a predominantly cis carbon-carbon double bond with loss of halide and sulfite ions. Generally applicable to molecules satisfying the minimal structural requirements of a sulfonyl group, an α-halogen atom, and at least one α-hydrogen atom, this facile reaction has found broad utility in olefin synthesis.

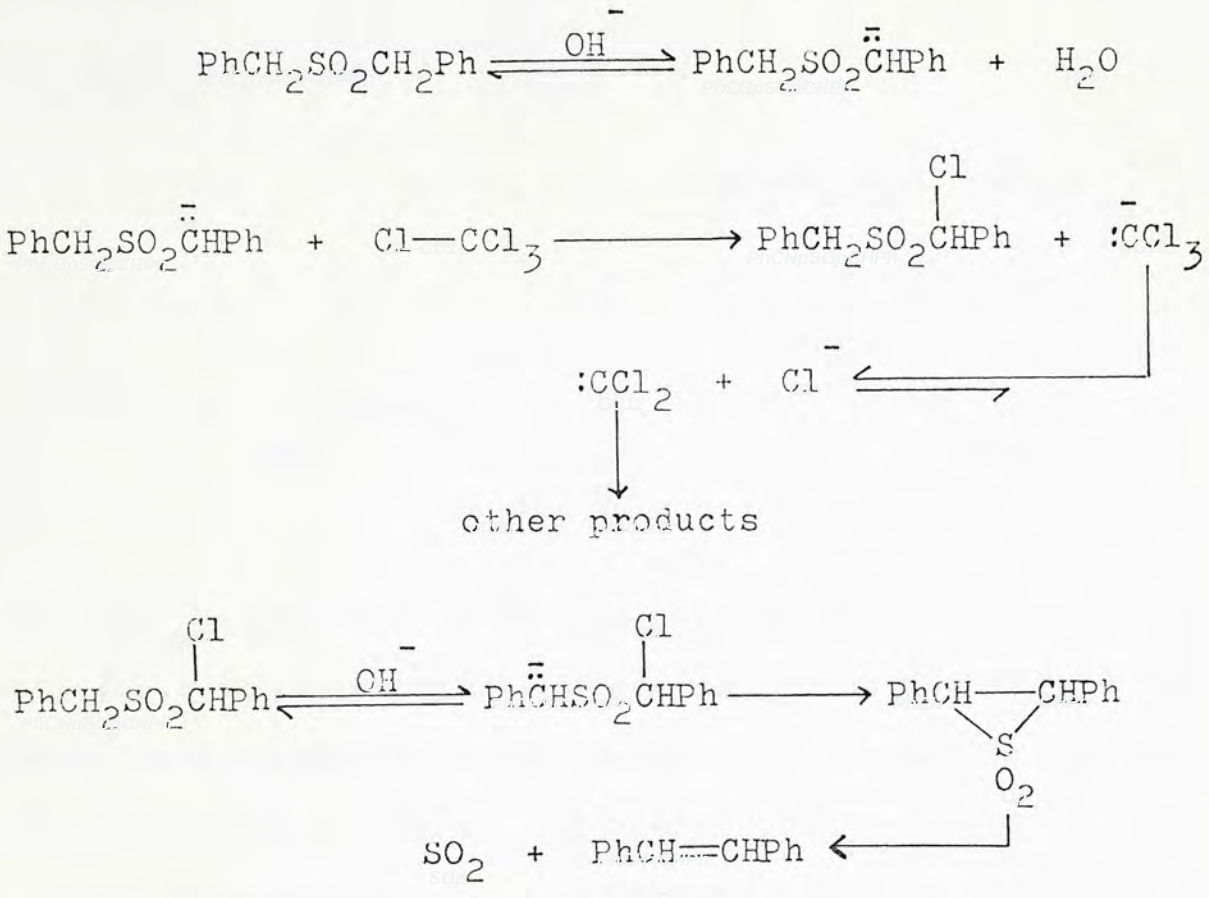
In the conventional Ramberg-Bäcklund procedure, the overall transformation from a sulfide linkage to an olefinic function involves a sequence of three steps: the chlorination of sulfide with chlorine, sulfuryl chloride or N-chlorosuccinimide; oxidation of the α-chloro sulfide with m-chloroperbenzoic acid; and, treatment of the resulting α-chloro sulfone with base. The same transformation can now be accomplished more conveniently by a method known as the Meyers' modification[22]. In this recently developed "one-pot" procedure, a sulfone is treated, usually under mild conditions, with a mixture of potassium hydroxide, carbon tetrachloride and t-butanol. The hydroxide base plays a

$$RCH_2SO_2CH_2R \xrightarrow[t\text{-}BuOH]{KOH,\ CCl_4} RCH_2SO_2\underset{\displaystyle Cl}{\underset{|}{C}}HR \xrightarrow{KOH} RCH{=}CHR$$

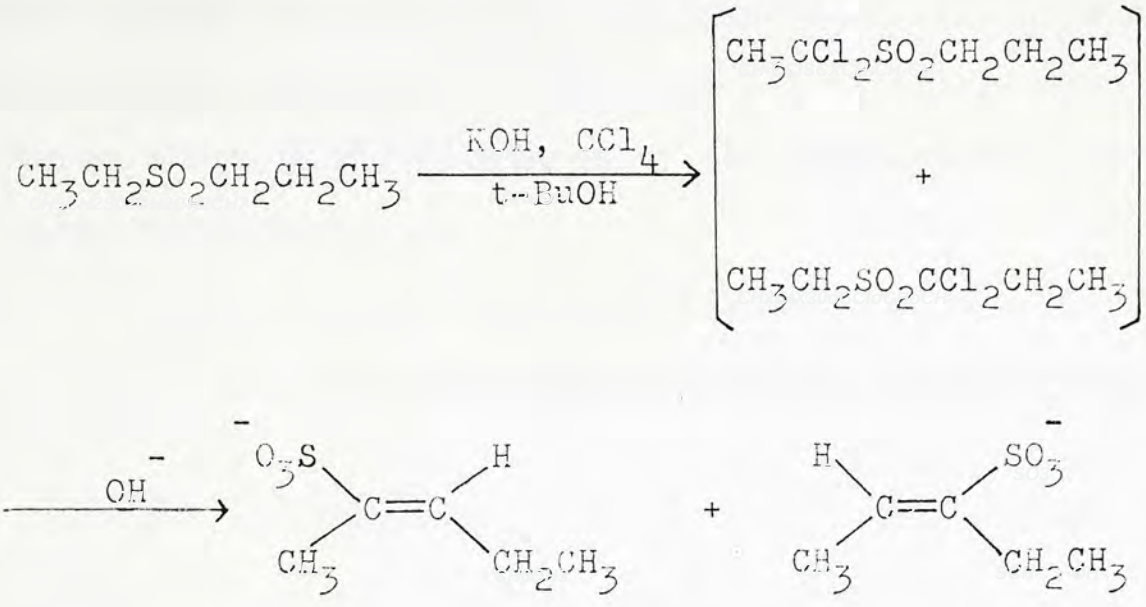
dual role in catalyzing the in situ α-chlorination of the sulfone by carbon tetrachloride via a carbanion mechanism, and in initiating a 1,3 elimination on the resulting α-halo sulfone.

The mechanism for the overall reaction based on the extensive studies by Meyers' group[22] is best represented by the

following steps using dibenzyl sulfone as an example:



An undesirable feature of this reaction is that dichlorocarbene is sometimes generated concomitantly, thus creating a potential hazzard whereby the desired olefin can be diverted into dichlorocyclopropanes. Fortunately, this situation rarely prevails since the decomposition of thiirane-1,1-dioxides almost always proceeds considerably slower than dichlorocarbene consumption by solvent molecules. Benzylic and benzhydryl sulfones are particularly suited to this one-step olefin synthesis[22] but di-primary-alkyl sulfones are converted into cis dialkyl sulfonic acid owing to

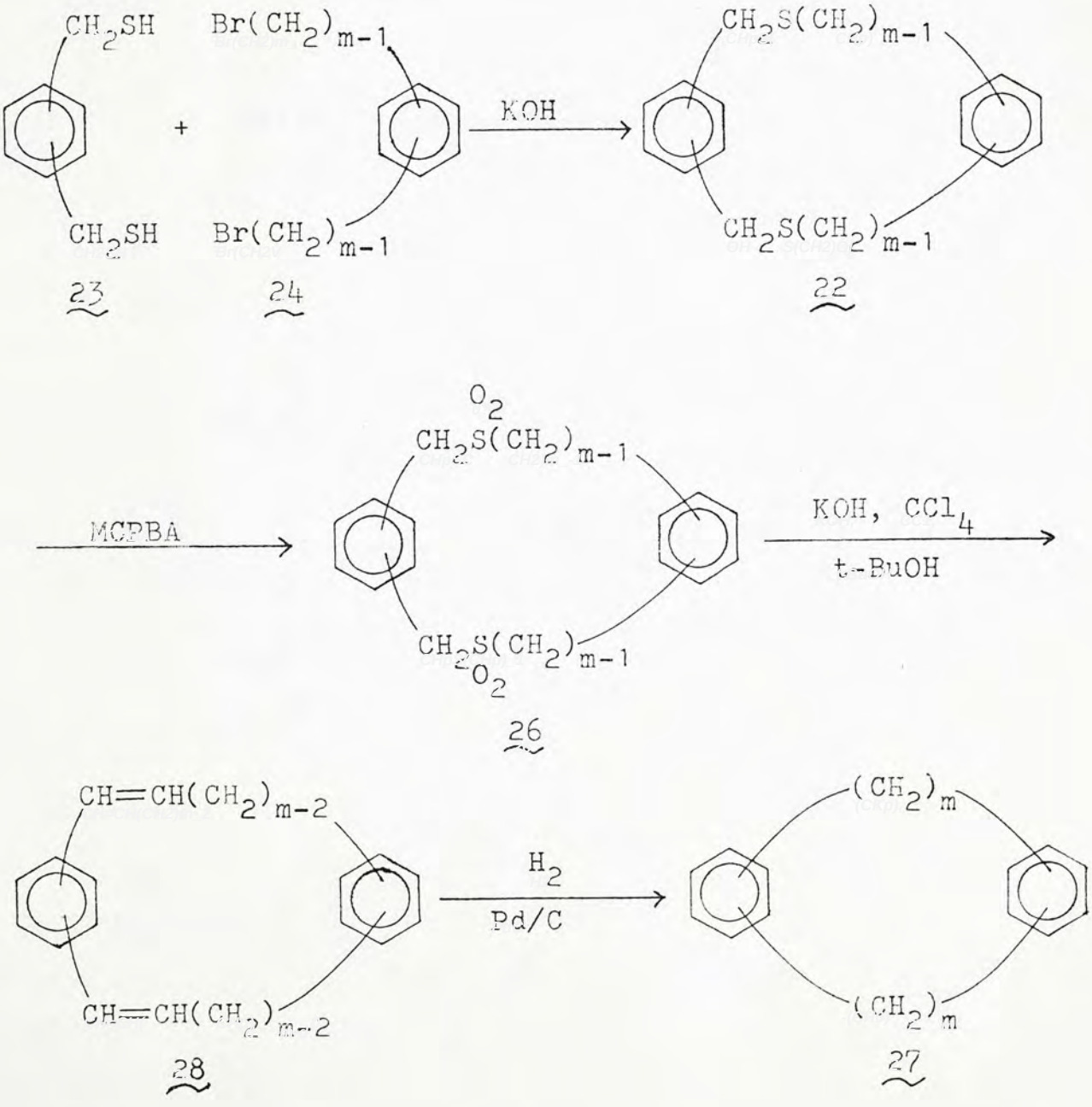


facile gem-dichlorination at the initial stage[23]. The latter limitation notwithstanding, Meyers' modification of the Ramberg-Bäcklund rearrangement offers obvious advantages over conventional procedures in respect of operational simplicity.

The incorporation of the Ramberg-Bäcklund rearrangement to serve as a means for ring contraction in our projected synthetic scheme for macrocyclophanes became more attractive on examination of molecular models. It was revealed that all [m.m]-cyclophanes with m ⩾ 4 could accomodate two cis olefinic functions, one on each bridge, without undue strain. Since Meyers' procedure is amenable to large-scale preparations, hydrogenation of dienes 28 obtainable in this manner would lead to sizable amounts of the desired cyclophanes 27. For proper execution of Meyers' method, benzylic dithiacyclophane bissulfones of the type 26 would be required. With the anticipation that compounds 26 would

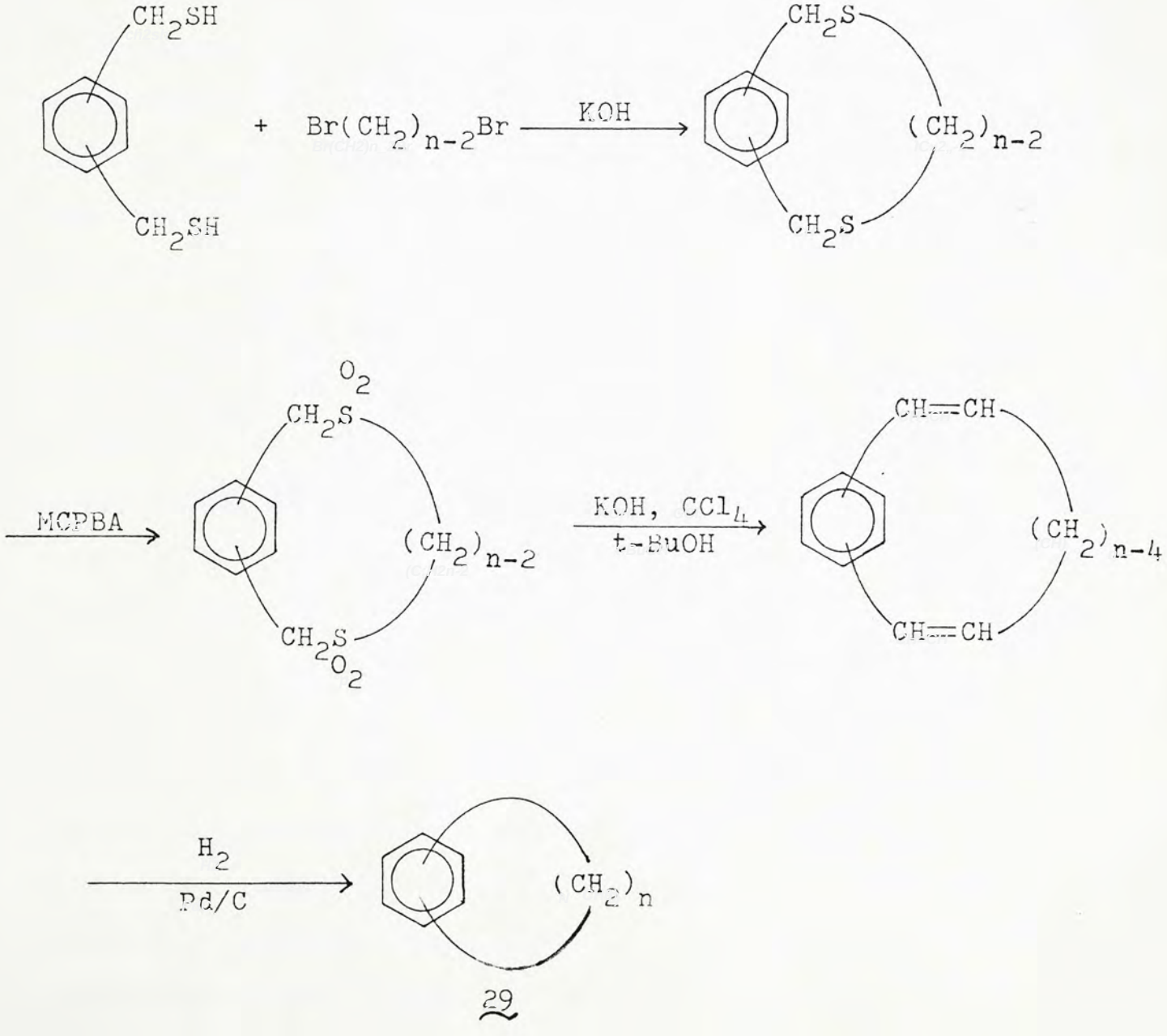
be easily accessible and on further assumption that the proposed sulfur dioxide extrusion step would not meet with unforeseeable complications, we began to undertake the synthesis of a number of large-sized [m.m] cyclophanes by the reaction sequence as outlined in Scheme VIII.

Scheme VIII, Projected Synthesis of Macro [m.m] Cyclophanes



If the above scheme was successful, application of this methodology might be further extended to the synthesis of [n]-cyclophanes 29 according to an analogous reaction sequence starting from α,ω-dibromides as outlined in Scheme IX:

Scheme IX. Projected Synthesis of [n]Cyclophanes



29

Again, the steps in Scheme IX would require only simple operations and would permit large-scale preparations of [n]-cyclophanes 29. It would therefore complement the existing synthetic methods for these compounds[24-26].

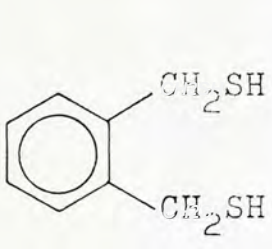
IV. RESULTS AND DISCUSSION

IV.1. Preparation of Starting Materials

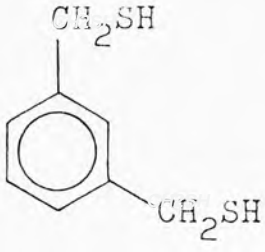
At the outset of the present investigation, the synthesis of large-sized [m.m]cyclophanes was an area largely unexplored Our aim was initially to prepare a series of [m.m]cyclophanes of various gross shapes with m = 4, 5, 6. With relatively little information from the literature, it was desirable to put to test our projected synthetic scheme in a systematic manner. The key intermediates in Scheme VIII were the dithiacyclophanes 22. Previous studies in our laboratory[27] and those of others[17b,18] showed that these systems could be obtained in good yields by the coupling of bis(mercaptomethyl)benzenes 23 with bis(ω-bromoalkyl)benzenes 24. The sulfur atoms in dithiols 23 were accordingly intended to serve as anchor points for constructing the aliphatic bridges of the dithiacyclophanes 22. As the side-chain carbon number in 23 is held constant, the length of both side-chains in dibromides 24 becomes the only variable in determining the size of dithiacyclophanes 22, and eventually, that of cyclophanes 27. The manner in which the two benzene rings are linked in both structures 22 and 27, on the other hand, would depend on the points of attachment of the mercaptomethyl groups and the ω-bromoalkyl groups to the benzene rings in 23 and 24, respectively. With this analysis in mind, it was essential to make available a number of starting materials of various structures so that the generality of our synthetic scheme could be tested.

Dithiols of the type 23 are common compounds. They are best prepared according to a standard procedure[28] by treatment of the corresponding bis(bromomethyl)benzenes with thiourea followed by alkaline hydrolysis of the resulting adducts. The dithiols 30-35 used in the present study are listed in Chart I. The preparations of these compounds were straightforward and uneventful.

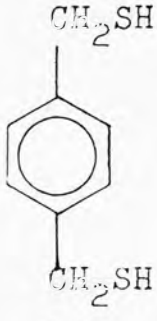
Chart I. Bis(mercaptomethyl)benzenes Used in This Study



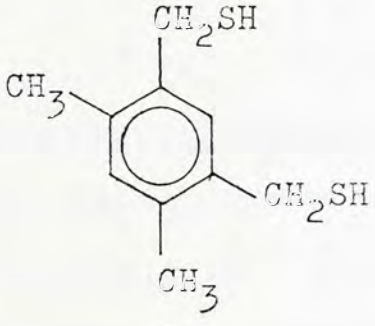
30



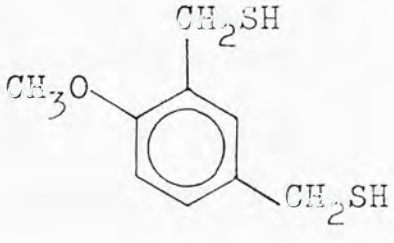
31



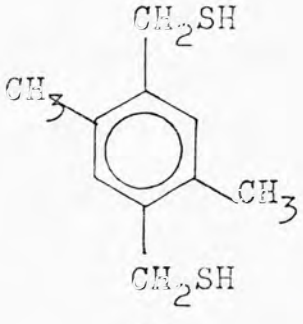
32



33



34

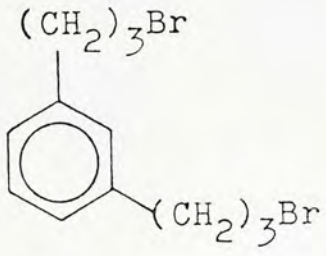


35

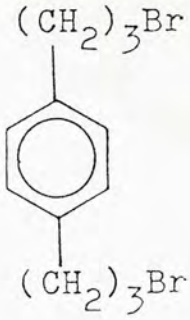
The other co-reactants required for the preparation of dithiacyclophanes 22 were dibromides of the general structures 24. In order for 24 to be suitable for the ultimate construction of [m.m]cyclophanes with $m \geq 4$, the side chains of these dibromides should contain at least three carbon atoms. For this purpose,

bis(ω-bromoalkyl)benzenes 36-39 listed in Chart II were prepared.

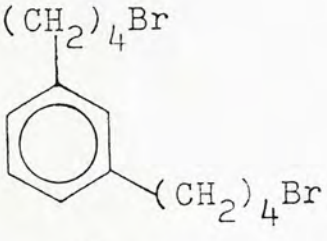
Chart II. Bis(ω-bromoalkyl)benzenes Used in This Study



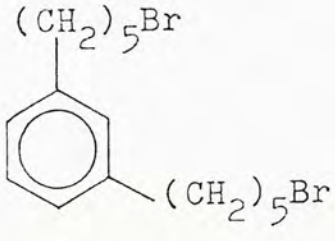
36



37

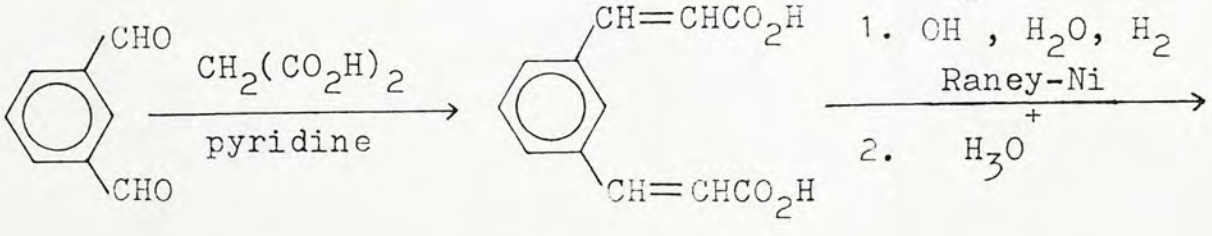


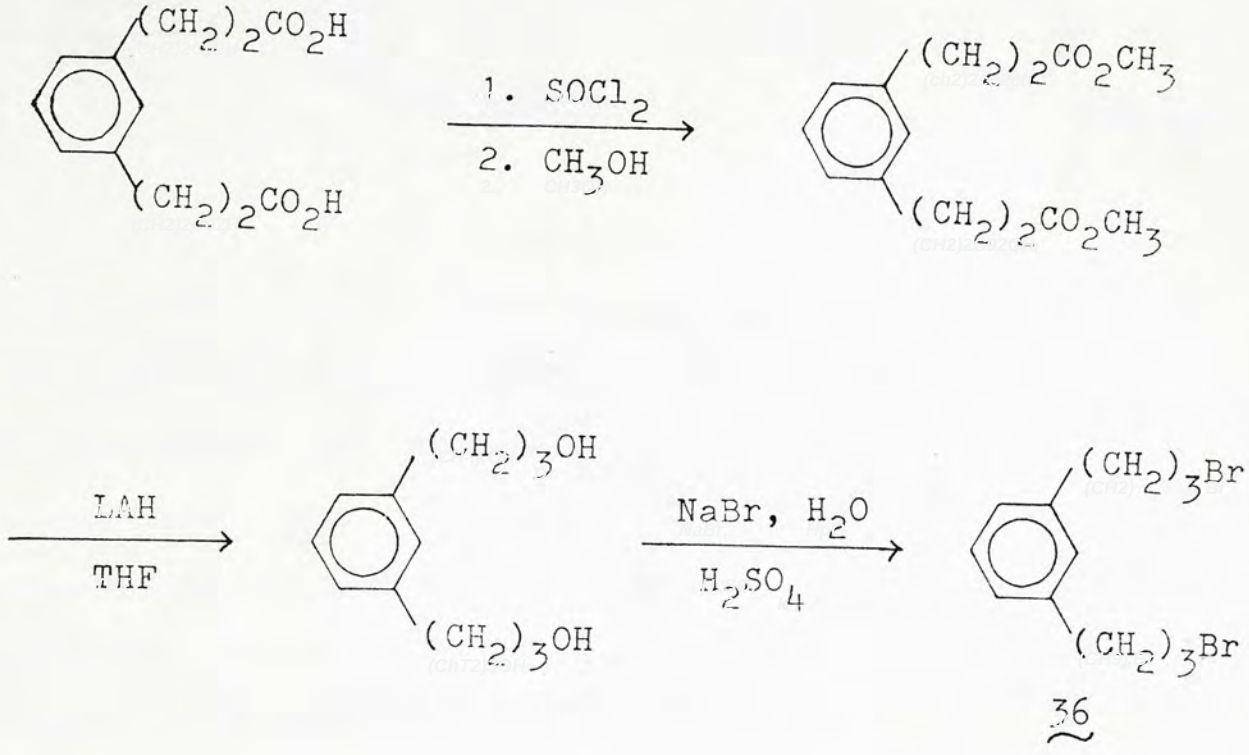
38



39

Of the four dibromides listed in Chart II, both 1,3-bis(3-bromopropyl)benzene (36)[29] and 1,4-bis(3-bromopropyl)benzene (37)[29] were known compounds. Dibromide 36 was previously prepared by Schimelpfenig[30] using a Doebner synthesis on isophthalaldehyde followed by subsequent manipulation of the side chains according to the following steps:

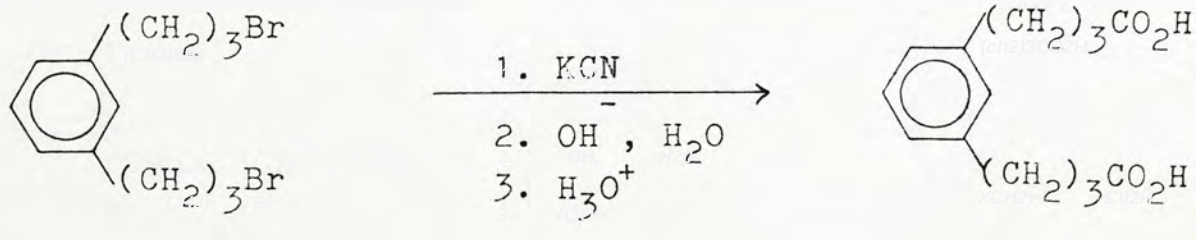




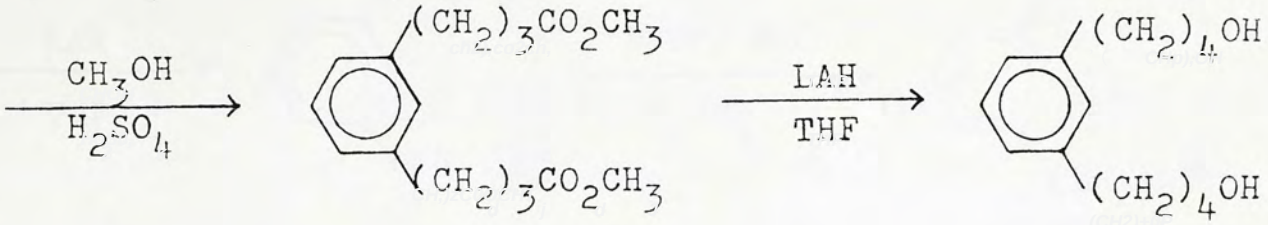
36

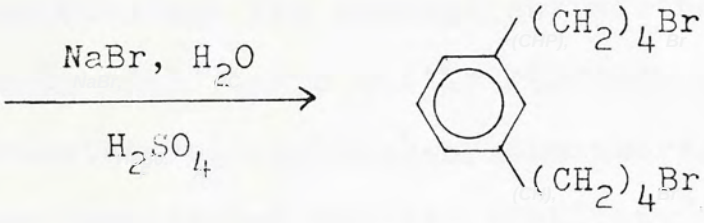
Dibromide 37 was obtained in an analogous manner from terephtalaldehyde.

The remaining two dibromides in Chart II were prepared for the first time. 1,3-Bis(4-bromobutyl)benzene (38) was synthesized in 72 % overall yield by homologation of 36 through a four-step reaction sequence:



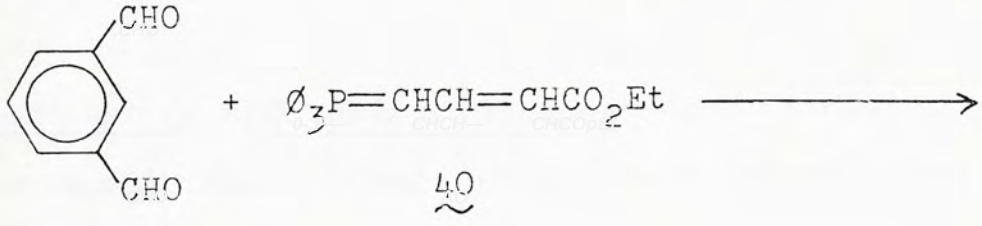
36



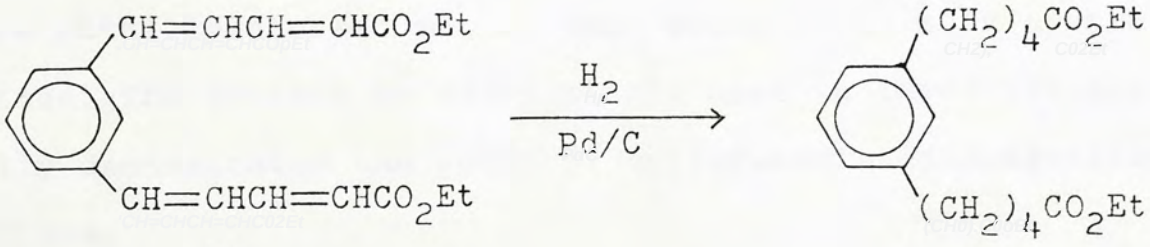


38

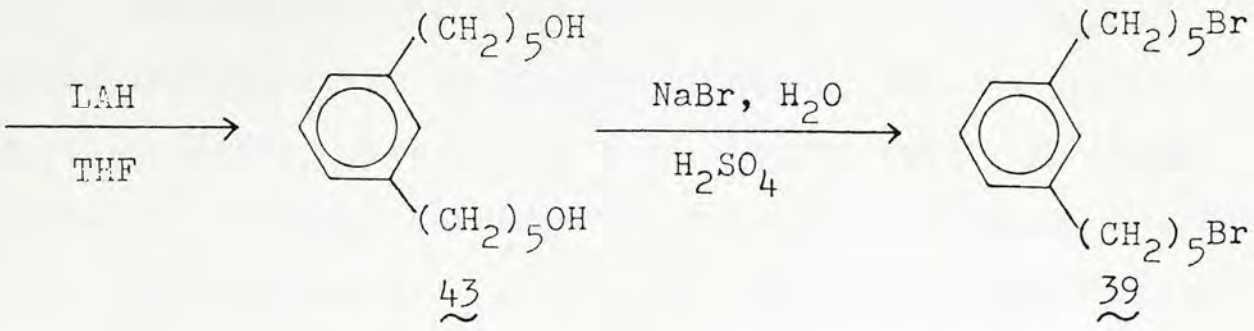
After considerable experimentation, the most reliable preparation of 1,3-bis(5-bromopentyl)benzene (39) was found to be the following sequence of reactions:



40



41 42



43 39

The key step was the procurement of the required five-carbon side-chains by employing a Wittig reaction of isophthalaldehyde with (3-carboethoxyallyl)triphenylphosphorane (40), a ylid well known for its exceptional thermal stability[31]. The resulting diethyl m-benzenedipenta-2,4-dienoate (41), obtained in good yield, was hydrogenated over 5 % palladium on charcoal to afford quantitatively diethyl m-benzenedipentanoate (42). Diester 42 was reduced with lithium aluminium hydride giving m-benzenedipentanol (43) which was treated with sodium bromide in 45 % sulfuric acid to furnish 39.

IV. 2. Synthesis of [m.m]Dithiacyclophanes

With the six dithiols (Chart I) and four dibromides (Chart II) at disposal, it was possible to prepare a maximum of twenty-four [m.m]dithiacyclophanes of the type 22. However, only half were actually carried out in this study in as much as time permitted. The success in every single case in these preparations fully demonstrated the power of sulfur-mediated ring-closure reactions.

The coupling of bis(mercaptomethyl)benzenes 23 and bis(ω-bromoalkyl)benzenes 24 to give dithiacyclophanes 22 is a generally facile reaction with yields that are remarkable considering the sizes of the rings formed. The procedure is simple and requires only the addition of a solution of 23 and 24, under moderately high dilution, to a suitable solvent containing a slight excess of potassium hydroxide. Employing the scale described below, it normally takes two or three days, including isolation, to prepare five to six grams of pure products. The preparation of 2,15-dithia-[5.5]metacyclophane (45) from 1,3-bis(mercaptomethyl)benzene (31) and 1,3-bis(3-bromopropyl)benzene (36) is illustrative. A solution of 20 mmoles each of 31 and 36 in 400 ml of 95 % ethanol was added dropwise under nitrogen over 24 h to a rapidly stirred solution of 70 mmoles of potassium hydroxide in 1 l of the same solvent. Upon further stirring for 12 h the solvent was removed in vacuo. The product, after having been taken up in dichloromethane was isolated by column chromatography to afford pure 45 in 59.4 % yield. Utilization of this simple procedure led to the twelve dithiacyclophanes listed in Chart III. The structure of these compounds were confirmed by nmr, ms and elemental analysis data. As a result, these valuable synthetic intermediates were reliably and routinely prepared.

Chart III. Dithiacyclophanes Prepared in This Study

[5.5]Dithiacyclophanes

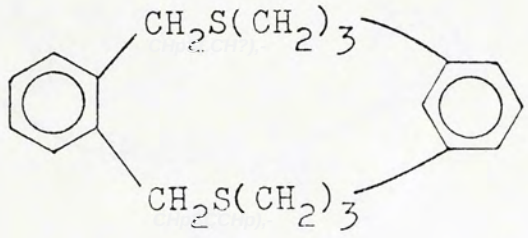
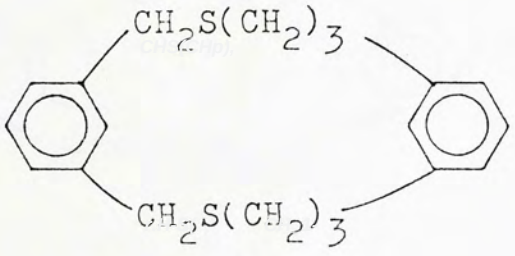
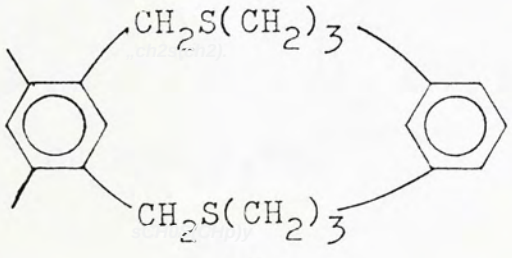
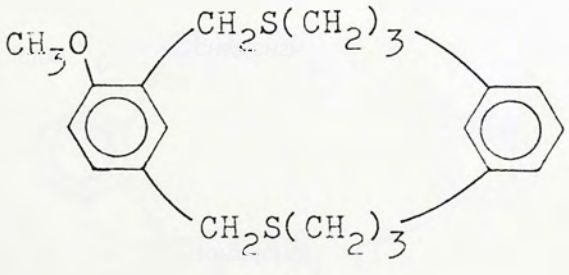
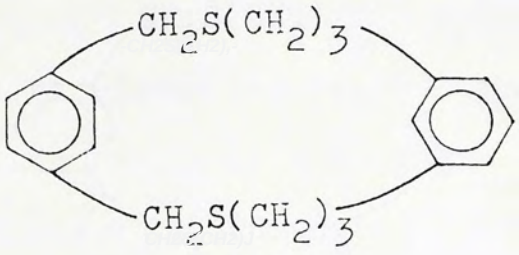
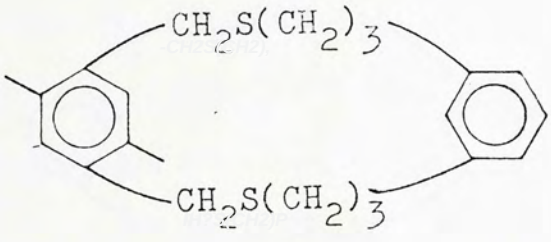
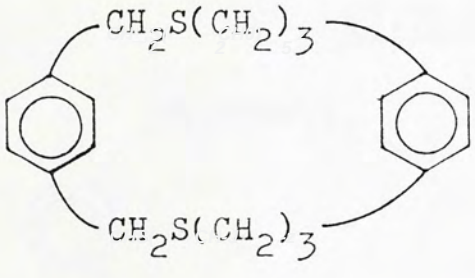
	m.p. (°C)	% Yield
 44	111 - 112	51.8
 45	57 - 59	59.4
 46	124 - 125	63.2
 47	97 - 99	55.9

Chart III.(cont'd)

[5.5]Dithiacyclophanes

	m.p. (°C)	% Yield
 48	72.5 - 73.5	57.9
 49	104 - 105	50.6
 50	151 - 153	51.8

[6.6]Dithiacyclophanes

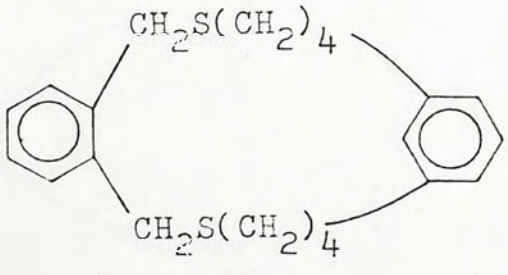
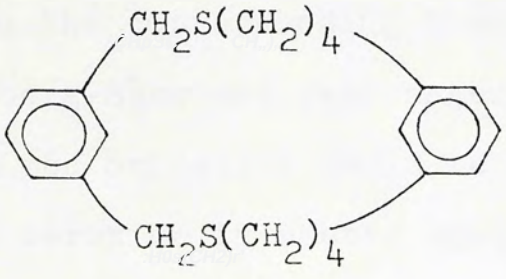
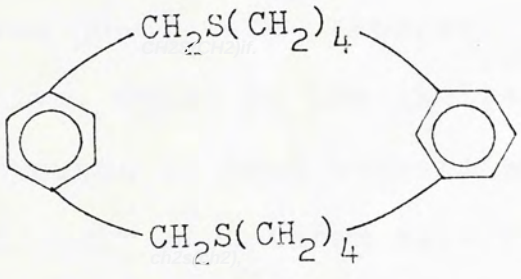
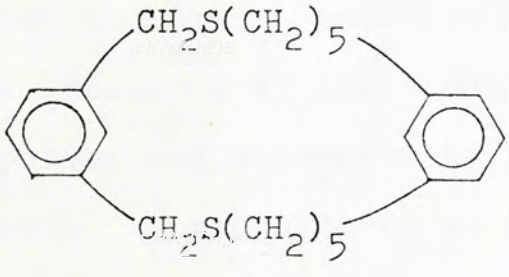
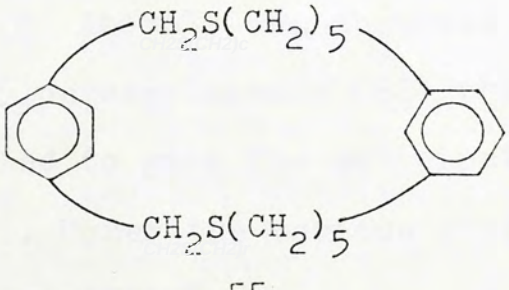
	m.p. (°C)	% Yield
 51	120 - 121	53.4

Chart III. (Cont'd)

[6.6] Dithiacyclophanes

	m.p. (°C)	% Yield
 52	89 - 90	56.2
 53	52 - 53	46.3

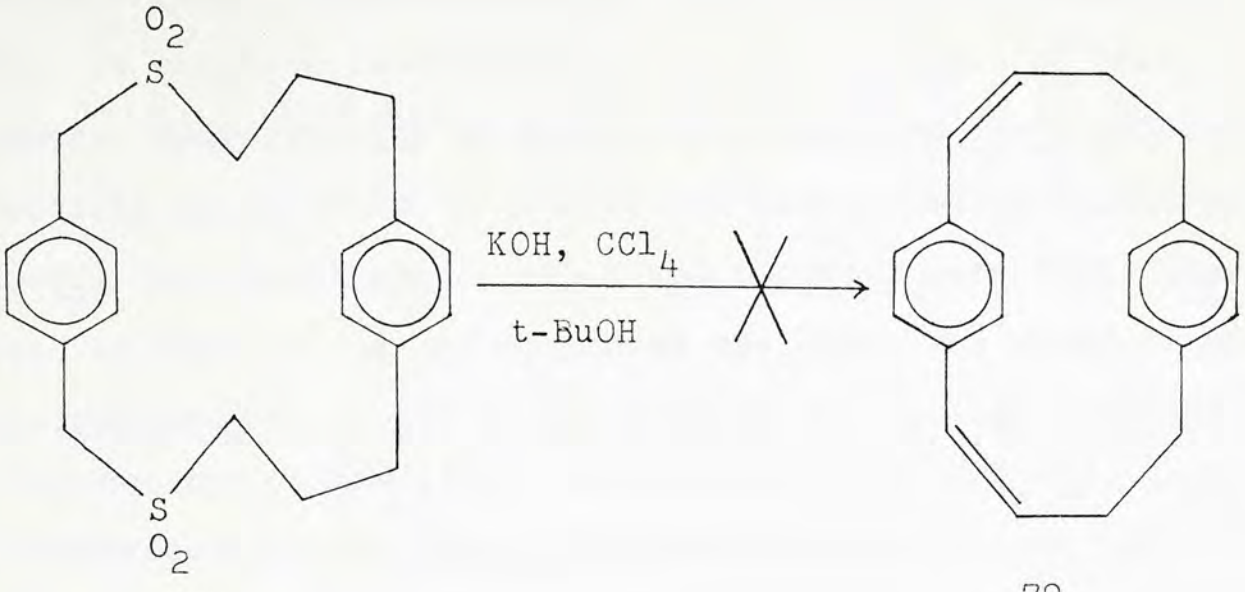
[7.7] Dithiacyclophanes

	m.p. (°C)	% Yield
 54	97 - 98	58.1
 55	100 - 101	44.1

IV.3. Preparation of Large-Sized [m.m]Cyclophanes

According to the steps outlined in Scheme VIII, it was necessary to convert all the dithiacyclophanes listed in Chart III into the corresponding bissulfones prior to the execution of the Ramberg-Bäcklund rearrangement following Meyers' procedure. The desired oxidation could be readily accomplished either with hydrogen peroxide in acetic acid or with m-chloroperbenzoic acid in chloroform. However, the latter reagent was found to give cleaner products. It was thus by this oxidation dithiacyclophane bissulfones 56-67 were prepared. In most cases, the yields were quantitative. Owing to the limited solubility of these high-melting compounds in most organic solvents, they were not further purified but their structures were readily confirmed by the nmr spectra which were usually measured in trifluroacetic acid.

In line with our projected synthetic scheme, each and every member of the series of dithiacyclophane bissulfones 56-67 was subjected to Meyers' modification of the Ramberg-Bäcklund rearrangement. Reaction of individual bissulfones 56-67 with a mixture of pulverized potassium hydroxide, carbon tetrachloride and t-butanol, in proportions as decribed by Meyers, was complete within 3 h under reflux. Extrusion of sulfur dioxide was effected in all but one instance to afford the expected [m.m]cyclophanedienes 68-78. Anomaly was observed for 2,15-dithia-2,2,15,15-tetraoxo-[5.5]paracyclophane (62) which in spite of repeated attempts failed to give the anticipated [4.4]paracyclophane-1,13-diene (79). Under the various conditions employed, 62 underwent extensive decomposition.



62 79

The reason for the above anomalous behavior is not completely clear to us. The possibility of olefinic bond strain was ruled out on inspection of molecular models unless one of the double bonds was trans which was extremely unlikely. Conceivably, in the course of the reaction, cyclophanediene 79 was formed at a rate comparable to the concomitant dichlorocarbene formation as discussed above so that insertion reactions intervened. However, the absence of any identifiable product attributable to dichlorocyclopropanation did not allow confirmation of this conjecture.

Cyclophanedienes 68-78 were obtained as viscous liquids and, being the least polar compenents in the reaction mixtures, were separable with relative ease by column chromatography using light petroleum ether as eluant. The nmr spectra of these com-

pounds were in full accord with their structures. To avoid loss of materials, these dienes were used after preliminary purification, to complete the final step of the synthesis of [m.m]cyclophanes. Hydrogenation of [m.m]cyclophandienes 68-78 proceeded smoothly as expected to furnish the corresponding [m.m]cyclophanes 80-90. The structures of the final products were fully characterized by nmr, ms, uv and elemental analyses. The array of [m.m]-cyclophanes obtainable by the present methodology includes [4.4]-orthometacyclophane (80), [4.4]metacyclophanes 81-83, [4.4]-metaparacyclophanes 84-85, [5.5]orthometacyclophane (86), [5.5]-metacyclophane (87), [5.5]metaparacyclophane (88), [6.6]meta-cyclophane (89) and [6.6]metaparacyclophane (90). The structures of these compounds together with their m.p.s, yields, and corresponding precursors are shown in Chart IV.

The yields, which were not optimized, range from satisfactory to remarkable if due consideration is given to the fact that a double Ramberg-Bäcklund rearrangement is involved in each of the bissulfones. Since these dithiacyclophane bissulfones can be made readily available by scaling-up the amounts of starting materials, there should not be any difficulty in preparing gram quantities of large-sized [m.m]cyclophanes.

It is worthwhile to point out that all the cyclophanes reported here are new compounds except for [5.5]metacyclophane 87 which was prepared in considerably less quantity by Bien[19]. The generality of our present synthetic sequence and its application to the preparation of macro[m.m]cyclophanes are amply demonstrated

Chart IV. [m.m]Cyclophanes Prepared in This Study

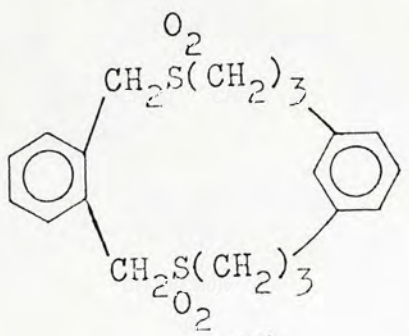
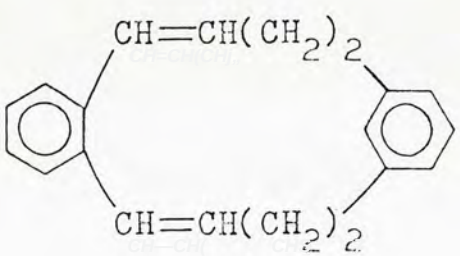
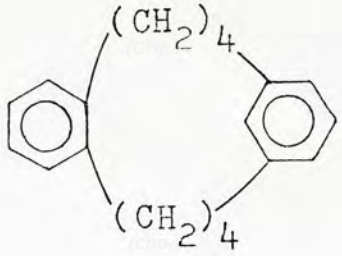
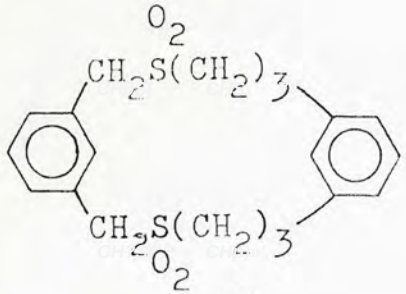
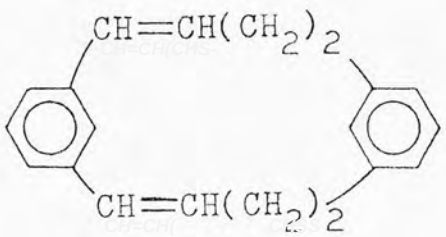
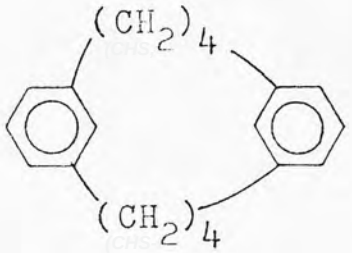
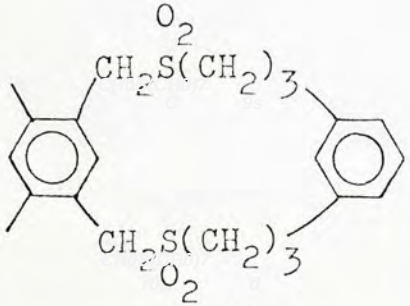
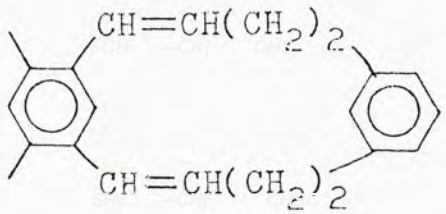
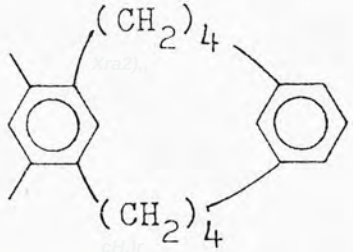
Dithiacyclophane bissulfone	[m.m]Cyclophanediene	[m.m]Cyclophane	m.p. (°C)	% Yield*
 56	 68	 80	84-85	51.1
 57	 69	 81	104-106	19.8
 58	 70	 82	92-93	16.3

Chart IV,(cont'd)

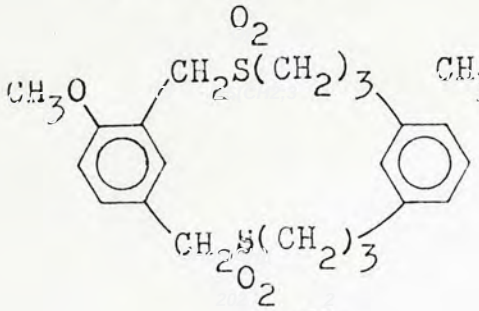
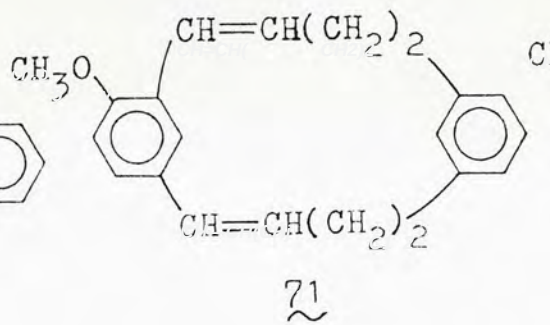
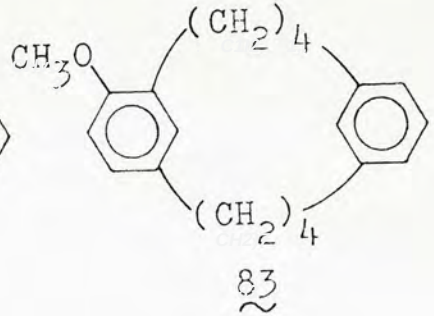
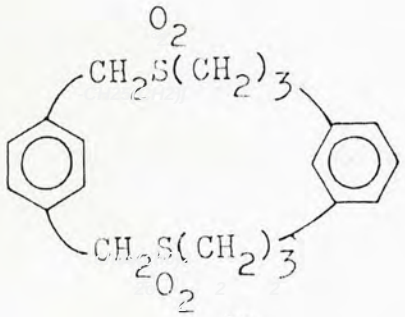
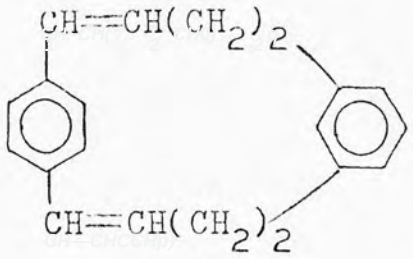
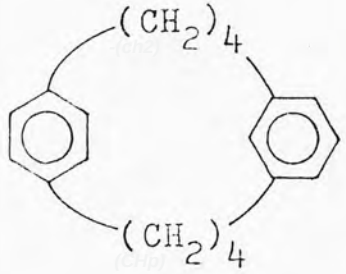
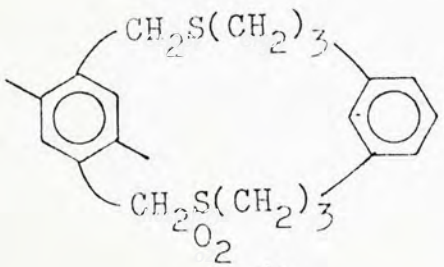
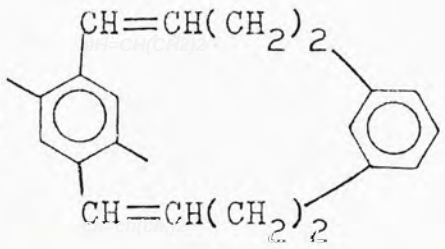
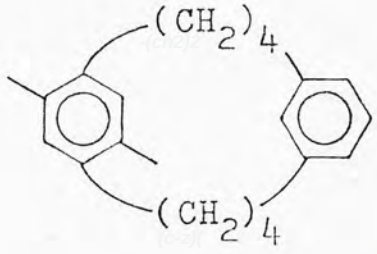
Dithiacyclophane bissulfone	[m.m]Cyclophanediene	[m.m]Cyclophane	m.p. (^{o}C)	% Yield*
 59	 71	 83	75-77	12.3
 60	 72	 84	81-82	24.7
 61	 73	 85	62-64	26.8

Chart IV.(cont'd)

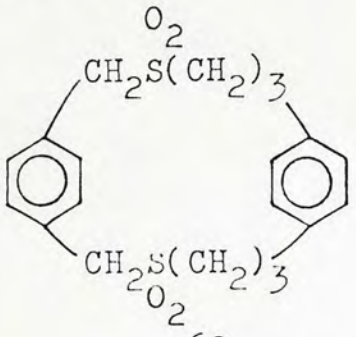
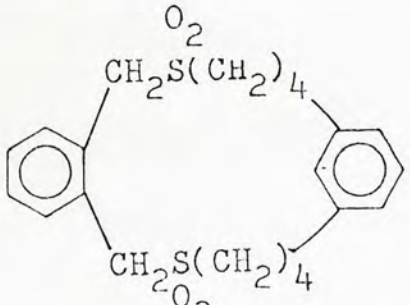
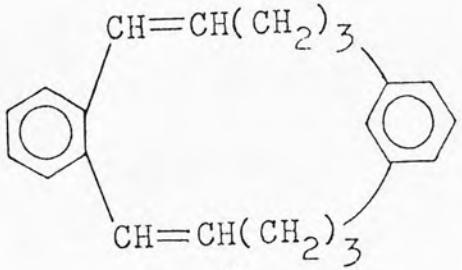
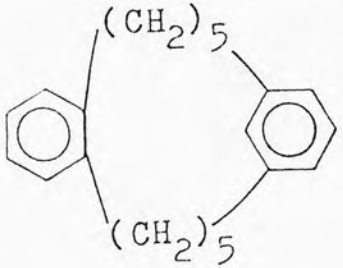
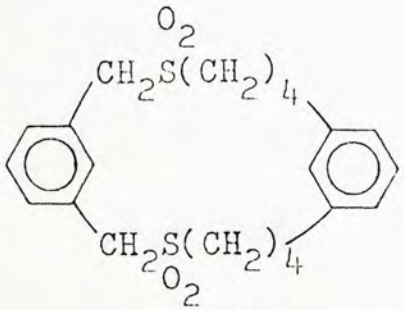
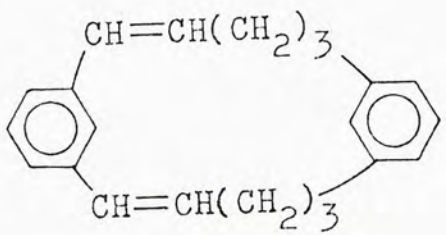
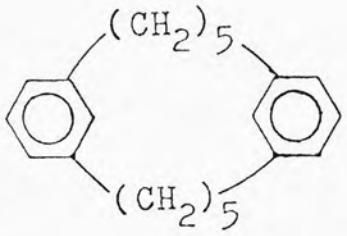
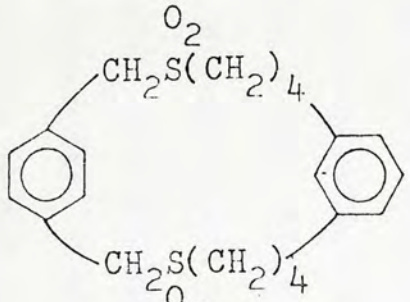
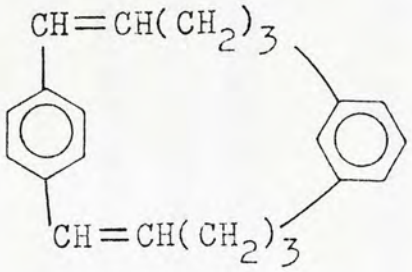
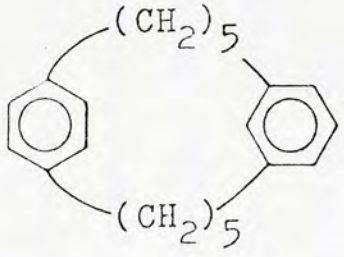
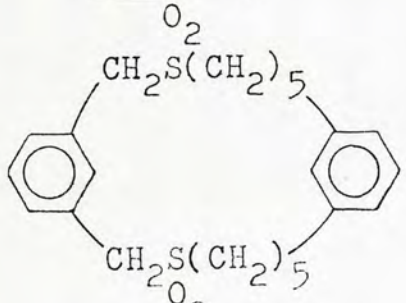
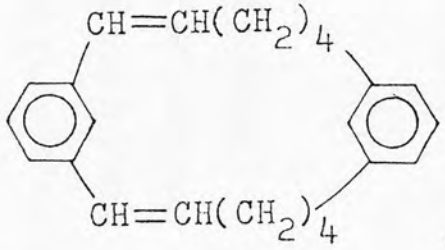
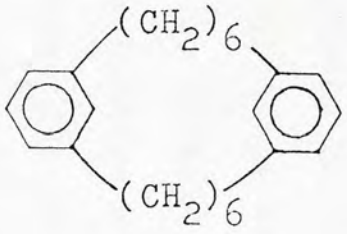
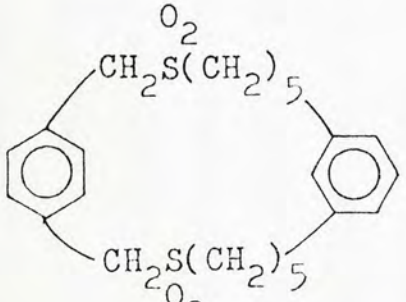
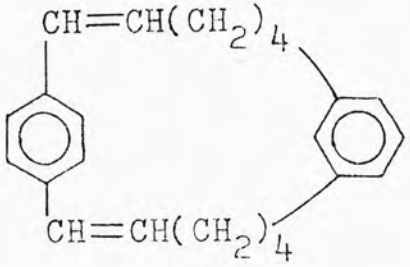
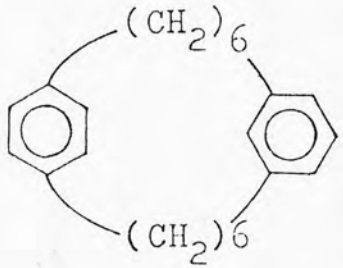
Dithiacyclophane bissulfone	[m.m]Cyclophanediene	[m.m]Cyclophane	m.p. (^{o}C)	% Yield*
 62	—	—	—	—
 63	 74	 86	47-48	19.2
 64	 75	 87	50-51	38.4

Chart IV (cont'd)

Dithiacyclophane bissulfone	[m.m]Cyclophanediene	[m.m]Cyclophane	m.p. (°C)	% Yield*
 65	 76	 88	45-46	21.6
 66	 77	 89	93-94	32.8
 67	 78	 90	62-63	18.0

* Isolated yields based on dithiacyclophane bissulfones

by the structures of the final products listed in Chart IV. Thus, extensive structural variation in respect of bridge-length, the manner in which the aromatic rings are linked, and the substitution pattern in any one or both benzene rings can be attained by proper selection of starting materials.

Examination of both the uv and nmr spectra of the [m.m]-cyclophanes prepared revealed the lack of any detectable transannular effects in these systems. This behaviour was totally expected for [m.m]cyclophanes with the value of m exceeding 3. Since large-sized cyclophanes may be individually regarded as an assembly of two non-interacting alkyl benzene molecules, a possibility is implicated for converting these systems into potential encapsulation hosts[5,32] for smaller hydrophobic aromatic species through structural modification.

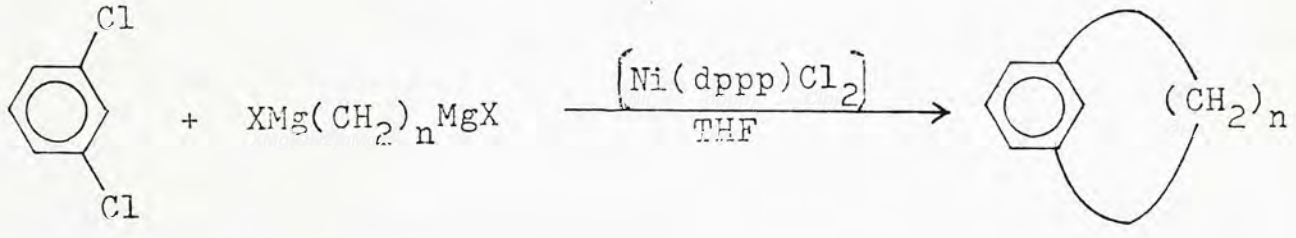
IV.4. Synthesis of [n]Cyclophanes

With a major portion of our synthetic objective having been achieved, attention was turned to the extension of our methodology to include the synthesis of [n]cyclophanes. The abnormalities of small [m.m]- or [m.n]cyclophanes are attributed to one or more of the following effects: (i) π-electron interaction between the two aromatic rings, (ii) distortion of the benzene rings from their normal planar configuration, and, (iii) conformational restraint imposed by the bridges. [n]Cyclophanes are unique in providing the opportunity to separate and identify these effects.

In the early days of the era of cyclophane chemistry,

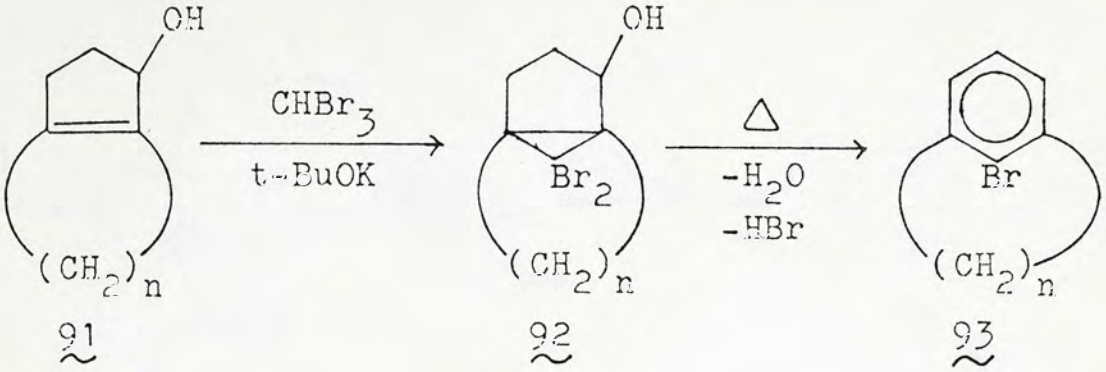
[n]cyclophanes were individually synthesized by various methods which lacked generality. However, as a result of considerable effort in this direction, three methods of general applicability have emerged in recent years.

The first method, developed by Kumada and coworkers[25], involved a one-step cyclocoupling reaction of di-Grignard reagents with aromatic dihalides in the presence of an catalytic amount of dichloro 1,3-bis(di-phenylphosphino)propane nickel II, [Ni(dppp)Cl_2] . A series of [n]metacyclophanes with n = 8,9,10 and 12

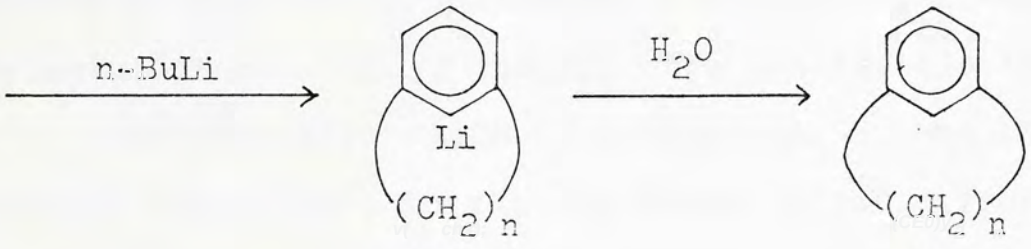


were successfully prepared in yields ranging from 3 to 22 %.

The second of these methods was reported by Hirano in 1975[24]. The reaction sequence involved a dibromocarbene addition to 2,3-polymethylene-2-cyclopentenol (91) and the subsequent thermolysis of the resulting labile tricyclic-2,2-dibromocyclopropylcarbinol derivative 92 to produce bromo-substituted[n]metacyclophane 93. Lithiation of 93 with n-butyllithium and quenching of the lithiocyclophane 94 with water led to unsubstituted [n]cyclophane 95. Three [n]metacyclophanes with n = 6,7, and 10 were successfully prepared.

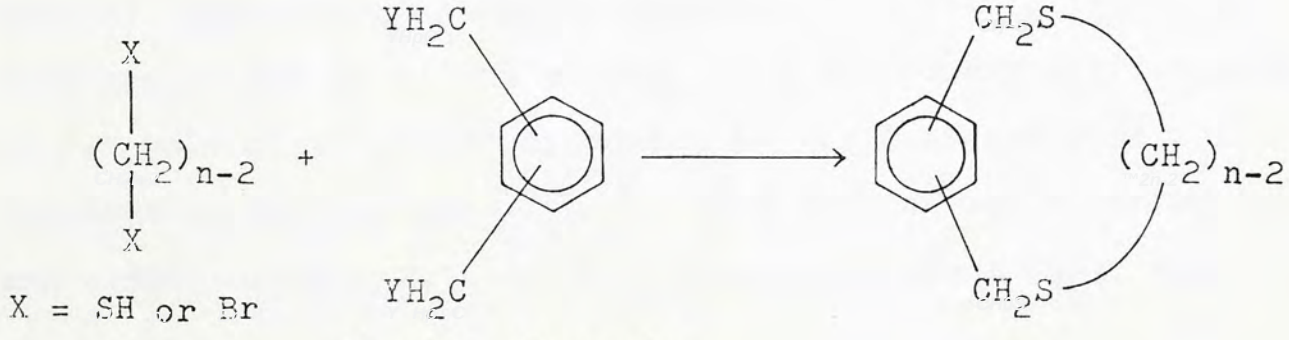


91 92 93



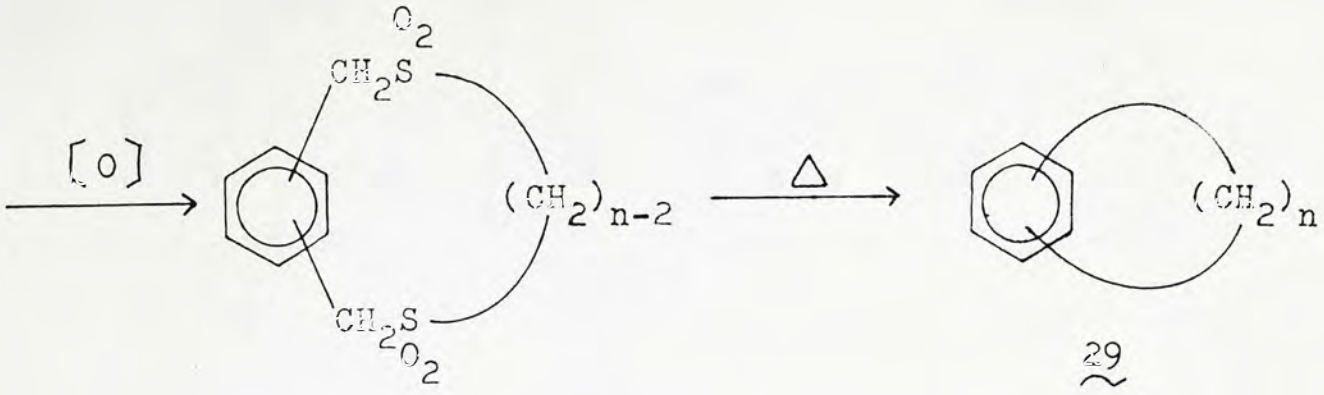
94 95

The third and most versatile of these recent methods was discovered by Misumi and coworkers in 1978[26]. The key step involved pyrolytic extrusion of sulfur dioxide from the [n+2]dithiacyclophane bissulfones which were prepared by the cyclocoupling of suitable dithiols and dihalides followed by oxidation. A



X = SH or Br

Y = SH, Cl or Br

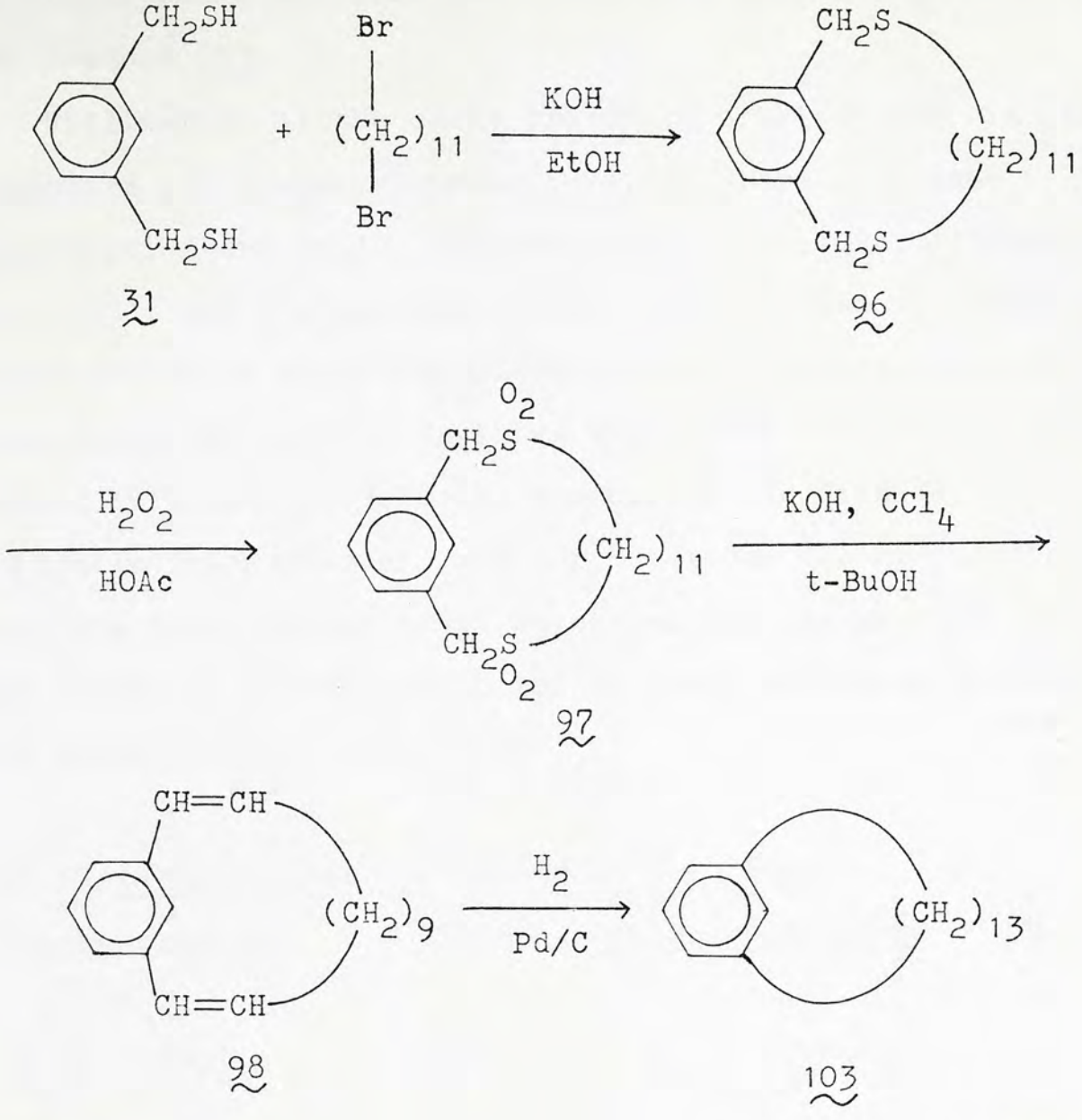


29

series of [n]paracyclophanes (n = 8,9,10,11,12 and 14) and [n]-metacyclophanes (n = 7 and 10) were synthesized in 48-67% yields.

Our synthetic route as outlined in Scheme IX bears a close overall resemblance to that of Misumi's but differs in the manner by which ring contraction of bissulfones is executed. Again, the adoption of the modified Ramberg-Bäcklund rearrangement as a means to achieve ring contraction in our work was intended for facilitating gram-scale preparations.

The application of our method for the synthesis of [n]cyclophanes is illustrated by the preparation of [13]metacyclophane 103, a compound which was not included in Misumi's report. Dropwise addition (24 h at r.t. under N_2) of a solution of 30 mmoles each of 1,3-bis(mercaptomethyl)benzene (31) and 1,11-dibromoundecane in 400 ml of 95% ethanol to a vigorously stirred solution of 0.1 mole of potassium hydroxide in 1.2 l of the same solvent followed by further stirring for 12 h gave, on isolation by column chromatography, 2,14-dithia[15]metacyclophane (96). The latter



31 96 97 98 103

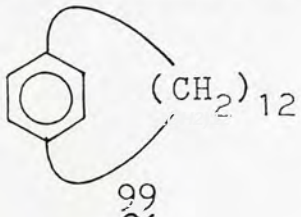
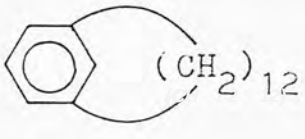
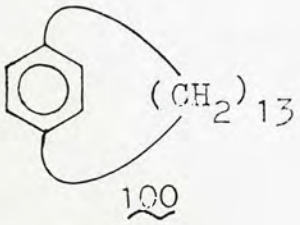
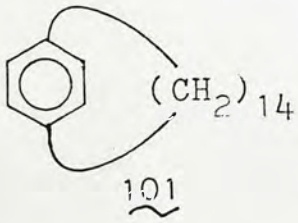
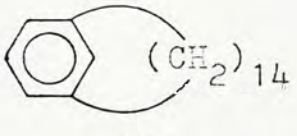
36 % overall yield

was oxidized into 2,14-dithia-2,2,14,14-tetraoxo[15]metacyclophane (97) with hydrogen peroxide in acetic acid. Treatment of 97 with a mixture of pulverized potassium hydroxide, carbon tetrachloride and t-butanol gave [13]metacyclophane-2,12-diene (98) which was separated by column chromatogrpahy. Hydrogenation of 98 over 5% Pd/C provided [13]metacyclophane (103) in an overall yield of 36.4 % based on the starting dithiol and dibromide. There was no difficulty in this particular case to obtain

in a single run a nmr pure sample of more than one gram of the final product 103.

Utilization of the above procedure provided the six [n]-cyclophanes ([12]paracyclophane (99), [13]paracyclophane (100), [14]paracyclophane (101), [12]metacyclophane (102), [13]metacyclophane (103), and [14]metacyclophane (104)) listed in Chart IV. The structures of these compounds were fully established by nmr and ms data. Comparing the yields with those for similar compounds obtained by bissulfone pyrolysis reported by Misumi[26], the yields for [n]metacyclophanes are similar but those for [n]paracyclophanes are lower in our case. Nevertheless, the present synthetic route offers an attractive option to carry out these syntheses under non-pyrolytic conditions.

Chart IV. [n]Cyclophanes Preparaed in This Study

[n]Paracyclophane	% Yield*	[n]Metacyclophane	% Yield*
 99	19.6	 102	41.5
 100	16.6	 103	60.7
 101	21.0	 104	41.6

* Yields based on dithiacyclophane bissulfones

V. CONCLUSION

Extrusion of sulfur dioxide from dithiacyclophane bissulfones by the modified Ramberg-Bäcklund rearrangement, combined with hydrogenation of the resulting cyclophanedienes provides an efficient, convenient route to large-sized cyclophanes. The general utility of this method has been amply demonstrated by the synthesis of a series of hitherto unknown [4.4]-, [5.5]- and [6.6]cyclophanes having the benzene rings, with or without substituents, assembled in various manners. It has further been shown that extension of this procedure offers a useful alternative to the synthesis of [n]cyclophanes under non-pyrolytic conditions. The more important conclusion, however, is that the overall synthetic scheme described here is capable of providing macrocyclophanes in sizeable quantities, allowing adequate studies of their physical and chemical properties to be made in the future.

VI. EXPERIMENTAL

Melting points were measured on a Koefler hot stage and are reported uncorrected. Elemental analyses were performed by Australian Mircoanalytical Service, Parkville, Victoria, Australia. Nuclear magnetic resonance spectra were recorded on a JEOL 60-HL instrument using tetramethylsilane as an internal standard. Ultraviolet absorption spectra were obtained on a Varian SuperScan 3 spectrophotometer. Mass spectra were determined using a VG Micromass 7070F instrument.

Preparation of Dithiols 30-35

Dithiols 30-35 were prepared according to a standard procedure[28] by treatment of the corresponding dibromides with thiourea followed by alkaline hydrolysis of the resulting adducts. The corresponding dibromides were in turn prepared in the following manners: 1,2-bis(bromomethyl)benzene, 1,3-bis(bromomethyl)-benzene and 1,4-bis(bromomethyl)benzene by N-bromosuccimide bromination of o-xylene, m-xylene and p-xylene, respectively; 4,6-bis(bromomethyl)-m-xylene by bis-bromomethylation of m-xylene; 2,4-bis(bromomethyl)anisole by bis-bromomethylation of anisole; 2,5-bis(bromomethyl)-p-xylene by bis-bromomethylation of p-xylene.

m-Benzenedibutanoic Acid

To a stirred and boiling solution of 100 ml of ethanol, 40 ml of water, and 43 g of potassium cyanide was added during a 20 min period 32 g (0.1 mol) of 1,3-bis(3-bromomethyl)benzene

(36)[30]. Upon further stirring and refluxing for 12 h, the reaction mixture was cooled, diluted with 350 ml of water and extracted with benzene. The combined extracts were washed with water and dried over anhydrous magnesium sulfate. Evaporation of solvent gave a brown oil which was hydrolyzed by refluxing in a solution containing 400 ml of ethanol, 100 ml of water and 20 g of sodium hydroxide until evolution of ammonia ceased (ca. 12 h). The ethanol was then removed by distillation, in the course of which was added in small portions 400 ml of hot water. The resulting aqueous solution was chilled and acidified with concentrated hydrochloric acid. The percipitate formed was filtered off, washed with water and dried in vacuo at 80° C to yield 21.5 g (86%) of m-benzenedibutanoic acid as white powder, mp 130-133°C (lit.[30] mp 131-135°C).

Dimethyl m-Benzenedibutanoate

A mixture of 21.5 g (86 mmole) of m-benzenedibutanoic acid, 50 ml of methanol, 200 ml of benzene and 10 ml of concentrated sulfuric acid was refluxed for 16 h. The cooled reaction mixture was washed successively with water, aqueous sodium bicarbonate and water, dried over anhydrous magnesium sulfate and evaporated in vacuo to give a yellow oily residue. Distillation of this material under vacuum afforded 21.8 g (91.2 %) of pure dimethyl m-benzenedibutanoate as a colorless liquid, bp 125°C/0.05 mm (lit.[30] bp 143-146°C/0.2 mm)

m-Benzenedibutanol

To a vigorously stirred suspension of 5.8 g (excess) of lithium aluminum hydroxide in 130 ml of dry tetrahydrofuran was added dropwise over 1 h a solution of 21.7 g (78 mmol) of dimethyl m-benzenedibutanoate[30] in 40 ml of dry tetrahydrofuran. Upon further stirring at room-temperature for 12 h, excess lithium aluminum hydroxide was decomposed by slow addition of 35 ml of ethyl acetate. The resulting mixture was poured to 300 ml of water, acidified with 20 ml of concentrated hydrochloric acid and heated on a steam-bath to remove all tetrahydrofuran. After cooling, the oily suspension was extracted with ether and the combined etheral extracts were washed with water, dried over anhydrous magnesium sulfate and evaporated to furnish 17.0 g (98.1%) of a yellow liquid. This substance was confirmed as m-benzenedibutanol by its nmr ($CDCl_3$) spectrum which showed signals at δ ppm 1.34-1.68 (m, 4H, RCH_2R), 2.32-2.80 (m, 2H, $ArCH_2R$), 3.40-3.78 (m, 3H, RCH_2O and OH) and 6.80-7.35 (m, 2H, ArH). The diol was directly used for the preparation of 1,3-bis(4-bromobutyl)-benzene (38).

1,3-Bis(4-bromobutyl)benzene (38)

To a refluxing mixture of 1.70 g (76 mmol) of m-benzenedibutanol, 27 ml of water and 32 g of sodium bromide was added dropwise 23 ml of concentrated sulfuric acid over a period of 1 h. After further refluxing for 3 h, the mixture was cooled, diluted with 75 ml of water and repeatedly extracted with ether. The combined etheral extracts were washed successively with

aqueous sodium bicarbonate, water, aqueous sodium thiosulfate and water. The organic phase was dried over anhydrous magnesium sulfate and evaporated to give a deep-brown oily residue. Distillation of this substance under vacuum afforded 25.0 g (94.5%) of 38 as a colorless liquid, bp 146°C/0.05 mm; nmr (CCl_4) δppm 1.44-2.15 (m, 2H, RCH_2R), 2.25-2.82 (t, J = 6 Hz, 1H, $ArCH_2R$), 3.10-3.50 (t, J = 6 Hz, 1H, RCH_2Br) and 6.72-7.25 (m, 1H, ArH).

Diethyl m-Benzenedipenta-2,4-dieneoate (41)

A mixture of 74.8 g (0.20 mol) of (3-carboethoxyallyl)triphenylphosphorane (40)[31] and 13.4 g (0.10 mol) of isophthalaldehyde in 650 ml of sodium-dried benzene was refluxed under nitrogen for 6 h. The resulting dark red solution was concentrated *in vacuo* until 400 ml of benzene was removed. To the concentrated solution was added 800 ml of diethyl ether. The precipitate (triphenyl phosphine oxide) formed was filtrated off and the filtrate was evaporated *in vacuo* to yield a dark red oily residue. The crude Wittig reaction product was taken up in *ca* 25 ml of dichloromethane and chromatographed over silica gel. The fraction eluted with petroleum ether (50-75°C)-ethyl acetate (5:1) on evaporation afforded 20.4 g (62.6%) of a colorless oil. Attempted further purification of this product by vacuum distillation caused extensive polymerization. The nmr (CCl_4) spectrum of the oil, which showed signals at δppm, 1.06-1.48 (t, J=7Hz, 3H, CH_3 of OCH_2CH_3), 3.95-4.42 (q, J=7Hz, 2H, CH_2 of OCH_2CH_3) and 5.75-7.60 (m, 6H, ArH and $ArCH{=}{=}CH{-}CH{=}{=}CHCO_2R$), confirmed its structure as diethyl m-benzenedipenta-2,4-dieneoate (41).

Diethyl m-Benzenedipentanoate (42)

A solution of 20.4 g (63 mmol) of diethyl m-benzenedipenta-2,4-dieneoate (41) in 200 ml of ethyl acetate was hydrogenated over 1 g of 5 % Pd/C at room-temperature under 45 psi until hydrogen absorption was completed (ca 6 h). Removal of catalyst and evaporation of solvent afforded 21.0 g (100%) of a colorless oil. The nmr (CCl_4) spectrum of this substance which showed signals at δ ppm 1.02-1.40 (t, J=7Hz, 3H, CH_3 of OCH_2CH_3), 1.24-1.88 (m, 4H, RCH_2R), 1.90-2.78 (m, 4H, RCH_2CO_2R and $ArCH_2R$), 3.84-4.28 (q, J=7Hz, 2H, CH_2 of OCH_2CH_3) and 6.75-7.15 (m, 2H, ArH), was consistent with the structure for diethyl m-benzenedipentanoate (42)[33]. The product was used without further prification for the preparation of 1,3-benzenedipentanol (43) as described in next step.

m-Benzenedipentanol (43)

In the manner described for the preparation of m-benzenedibutanol, 20.0 g (60 mmol) of diethyl m-benzenedipentanoate (42) was reduced with lithium aluminum hydride to give 12.9 g (86.0%) of a yellow oil. The nmr ($CDCl_3$) spectrum of this substance, which showed signals at δ ppm 1.16-1.94 (m, 6H, RCH_2R), 2.36-2.82 (m, 2H, $ArCH_2R$), 3.34-3.80 (m, 3H, RCH_2O and OH) and 6.84-7.38 (m, 2H, ArH), was consistent with the structure for m-benzenedipentanol (43)[33]. The product was used without further purification for the preparation of 1,3-bis(bromopentyl)benzene (39) in the following step.

1,3-Bis(5-bromopentyl)benzene (39)

In the manner described for the preparation of 1,3-bis(4-bromobutyl)benzene (38), 12.9 g (51.6 mmol) of m-benzenedipentanol (43) was treated with sodium bromide and sulfuric acid to give 16.2 g (83.5%) of a colorless liquid, bp 162°C/0.05 mm. The nmr (CCl_4) spectrum of the liquid, which showed signals at δ ppm 1.16-2.20 (m, 3H, RCH_2R), 2.24-2.80 (t, J=6Hz, 1H, $ArCH_2R$), 3.18-3.50 (t, J=6Hz, 1H, RCH_2Br) and 6.74-7.25 (m, 1H, ArH), confirmed its structure as 1,3-bis(5-bromopentyl)benzene (39).

2,15-Dithia[5.5]orthometacyclophane (44)

To a vigorously stirred solution of 4 g of potassium hydroxide in 1 l of 95 % ethanol at room-temperature under nitrogen was added dropwise through a Precision Addition Funnel (Ace Glass) a solution of 6.40 g (20 mmol) of 1,3-bis(3-bromopropyl)benzene (36)[30] and 3.40 g (20 mmol) of 1,2-bis(mercaptomethyl)benzene (30) in 400 ml of 95 % ethanol over a period of 24 h. Upon further stirring for 12 h, the solvent was evaporated *in vacuo*. To the residue was added 400 ml of water and the resulting aqueous suspension was repeatedly extracted with dichloromethane. The combined extracts were washed successively with brine and water, dried over anhydrous magnesium sulfate and evaporated to yield a solid residue. The crude product was taken up in *ca* 20 ml of benzene and chromatographed over silica gel (E. Merck 7733). The fraction eluted with benzene-petroleum ether (50-70°C) (1:2) on evaporation gave a white solid. Recrystallization of this material from n-hexane-acetone (1:1) afforded 3.4 g (51.8%)

of 2,15-dithia[5.5]orthometacyclophane (44) as colorless crystals: mp 111-112°C; nmr ($CDCl_3$) δ ppm 1.66-2.90 (m, 3H, RCH_2R, RCH_2S and $ArCH_2R$), 2.72 (s, 1H, $ArCH_2S$), 6.75-7.45 (m,2H, ArH); ms (70eV) m/e 328 (M^+).

Anal. Calcd for $C_{20}H_{24}S_2$: C, 73.12; H, 7.36; S, 19.52. Found: C, 73.14; H, 7.39; S, 19.4.

2,15-Dithia[5.5]metacyclophane (45)

To a vigorously stirred solution of 4 g of potassium hydroxide in 1 l of 95 % ethanol at room-temperature under nitrogen was added dropwise through a Precision Addition Funnel (Ace Glass) a solution of 6.40 g (20 mmol) of 1,3-bis(3-bromopropyl)benzene (36)[30] and 3.40 g (20 mmol) of 1,3-bis(mercaptomethyl)benzene (31) in 400 ml of 95 % ethanol over a period of 24 h. Upon further stirring for 12 h, the solvent was evaporated in vacuo. To the residue was added 400 ml of water and the resulting aqueous suspension was repeatedly extracted with dichloromethane. The combined extracts were washed successively with brine and water, dried over anhydrous magnesium sulfate and evaporated to give a viscous oil which solidified on refrigeration over-night. The crude product was taken up in ca 20 ml of benzene and chromatographed over silica gel (E. Merck 7733). The fraction eluted with petroleum ether (50-75°C)-benzene (5:2) on evaporation afforded a white solid. Recrystallization of this material from n-hexane gave 3.9 g (59.4%) of 2,15-dithia[5.5]metacyclophane (45) as a white crystalline solid: mp 57-59°C; nmr ($CDCl_3$) δ ppm 1.40-2.80 (m, 3H, RCH_2R, RCH_2S and $ArCH_2R$), 3.56 (s, 1H, $ArCH_2S$),

6.64-7.30 (m, 2H, ArH); ms (70 eV) m/e 328 (M^+).

Anal. Calcd for $C_{20}H_{24}S_2$: C, 73.12; H, 7.36; S, 19.52. Found: C, 73.03; H, 7.22; S, 19.6.

18,20-Dimethyl-2,15-dithia[5.5]metacyclophane (46)

To a vigorously stirred solution of 4 g of potassium hydroxide in 1 l of 95 % ethanol at room-temperature under nitrogen was added dropwise a solution of 6.40 g (20 mmol) of 1,3-bis(3-bromopropyl)benzene (36)[30] and 3.96 g (20 mmol) of 4,6-bis(mercaptomethyl)-m-xylene (33) in 400 ml of 95 % ethanol over a period of 24 h. Upon further stirring for 12 h, the solvent was evaporated in vacuo. To the residue was added 400 ml of water and the resulting aqueous suspension was repeatedly extracted with dichloromethane. The combined extracts were washed successively with brine and water, dried over anhydrous magnesium sulfate and evaporated to give a solid residue. The crude product was taken up in ca 20 ml of benzene and chromatographed over silica gel (E. Merck 7733). The fraction eluted with petroleum ether (50-75°C)-benzene (2:1) on evaporation afforded a white solid. Recrystallization of this material from acetone gave 4.5 g (63.2%) of 18,20-dimethyl-2,15-dithia[5,5]metacyclophane (46) as colorless needles: mp 124-125°C; nmr ($CDCl_3$) δ ppm 1.55-2.45 (m, 7H, $ArCH_3$, RCH_2R and RCH_2S), 2.58-2.78 (t, 4H, J=6Hz, 4H, $ArCH_2R$), 3.50 (s, 2H, $ArCH_2S$), 6.56-7.35 (m, 3H, ArH); ms (70 eV) 356 (M^+).

Anal. calcd for $C_{22}H_{28}S_2$: C, 74.10; H, 7.91; S, 17.98. Found: C, 74.07; H, 7.74; S, 18.0.

18-Methoxy-2,15-dithia[5.5]metacyclophane (47)

To a vigorously stirred solution of 4 g of potassium hydroxide in 1 l of 95 % ethanol at room temperature under nitrogen was added dropwise a solution of 6.40 g (20 mmol) of 1,3-bis(3-bromopropyl)benzene (36)[30] and 4.00 g (20 mmol) of 2,4-bis(mercaptomethyl)anisole (34) in 400 ml of 95 % ethanol over a period of 24 h. Upon further stirring for 12 h, the solvent was evaporated in vacuo. To the residue was added 400 ml of water and the resulting aqueous suspension was repeatedly extracted with dichloromethane. The combined extracts were washed successively with brine and water, dried over anhydrous magnesium sulfate and evaporated to give a solid residue. The crude product was taken up in ca 20 ml of dichloromethane and chromatographed over silica gel (E. Merck 7733). The fraction eluted with petroleum ether (50-75°C)-benzene (2:3) on evaporation gave a white solid. Recrystallization of this substance from acetone-hexane afforded 4.0 g (55.9%) of 18-methoxy-2,15-dithia[5.5]metacyclophane (47) as colorless plates: mp 97-99°C; nmr ($CDCl_3$) δ ppm 1.52-2.46 (m, 8H, RCH_2R and RCH_2S), 2.50-2.70 (t, J=6Hz, 4H, $ArCH_2R$), 3.52 (s, 2H, $ArCH_2S$), 3.58 (s, 2H, $ArCH_2S$), 3.74 (s, 3H, CH_3O), 6.58-7.32 (m, 7H, ArH); ms (70eV) m/e 358 (M^+).

Anal. Calcd for $C_{21}H_{26}S_2O$: C, 70.34; H, 7.31; S, 17.88. Found: C, 70.50; H, 7.69; S, 17.8.

2,15-Dithia[5.5]metaparacyclophane (48)

To a vigorously stirred solution of 4 g of potassium hydroxide in 1 l of 95 % ethanol at room-temperature under nitrogen was added dropwise a solution of 3.4 g (20 mmol) of 1,4-bis(mercaptomethyl)benzene (32) and 6.40 g (20 mmol) Of 1,3-bis(3-bromopropyl)benzene (36)[30] in 400 ml of 95% ethanol over a period of 24 h. Upon further stirring for 12 h, the solvent was evaporated in vacuo and 400 ml of water was added to the residue. The resulting aqueous suspension was repeatedly extracted with dichloromethane. The combined extracts were washed successively with brine and water, dried over anhydrous magnesium sulfate and evaporated to give a viscous oil which solidified on standing overnight at room-temperature. The crude product was taken up in ca 20 ml of benzene and chromatographed over silica gel (E. Merck 7733). The fraction eluted with petroleum ether (50-75°C)-benzene (2.5:1) on evaporation gave a white solid. Recrystalization of this substance from n-hexane yielded 3.8 g (57.9%) of 2,15-dithia[5.5]-metaparacyclophane (48) as white crystalline solid: mp 72.5-73.5°C; nmr ($CDCl_3$) δ ppm 1.32-1.88 (m,1H, RCH_2R), 2.00-2.66 (m, 2H, RCH_2S and $ArCH_2R$), 3.56 (s, 1H, $ArCH_2S$), 6.35-7.30 (m, 2H, ArH); ms (70 eV) m/e 328 (M^+).

Anal. Calcd for $C_{20}H_{24}S_2$: C, 73.12; H, 7.36; S, 19.52. Found: C, 72.87; H, 7.50; S, 19.5.

18,21-Dimethyl-2,15-dithia[5.5]metaparacyclophane (49)

To a vigorously stirred solution of 4 g of potassium hydroxide in 1 l of 95% ethanol at room-temperature under nitrogen

was added dropwise a solution of 6.40 g (20 mmol) of 1,3-bis(3-bromopropyl)benzene (36)[30] and 3.96 g (20 mmol) of 2,5-bis(mercaptomethyl)-p-xylene(35) in 400 ml of 95% ethanol over a period of 24 h. Upon further stirring for 12 h, the solvent was evaporated *in vacuo*. To the residue was added 400 ml of water and the resulting aqueous suspension was repeatedly extracted with dichloromethane. The combined extracts were washed successively with brine and water, dried over anhydrous magnesium sulfate and evaporated to give a solid residue. This material was taken up in *ca* 20 ml of benzene and chromatographed over silica gel (E. Merck 7733). The fraction eluted with petroleum ether (50-75°C)-benzene (2:1) on evaporation afforded a white solid. Recrystallization of this substance from acetone-methanol gave 3.6 g (50.6%) of 18,21-dimethyl-2,15-dithia[5.5]metaparacyclophane (49) as colorless prisms: mp 104-105°C; nmr ($CDCl_3$) δ ppm 1.18-1.76 (m, 2H, RCH_2R), 2.18-2.70 (m, 7H, $ArCH_3$, RCH_2S and $ArCH_2R$), 3.36-3.90 (dd, J_{AB}=15 Hz, 2H, $ArCH_2S$), 6.44-7.28 (m, 3H, ArH); ms (70 eV) *m/e* 356 (M^+).

Anal. Calcd for $C_{22}H_{28}S_2$: C, 74.10; H, 7.91; S, 17.98. Found: C, 74.13; H, 8.06; S, 17.8.

2,15-Dithia[5.5]paracyclophane (50)

To a vigorously stirred solution of 4 g of potassium hydroxide in 1 l of 95% ethanol at room-temperature under nitrogen was added dropwise a solution of 3.4 g (20 mmol) of 1,4-bis(mercaptomethyl)benzene (32) and 6.4 g (20 mmol) of 1,4-bis(3-bromopropyl)benzene (37)[30] in 400 ml of 95% ethanol over a period of

24 h. Upon further stirring for 12 h, the solvent was evaporated in vacuo and 400 ml of water was added to the residue. The resulting aqueous suspension was repeatedly extracted with dichloromethane. The combined extracts were washed successively with brine and water, dried over anhydrous magnesium sulfate and evaporated to give a solid residue. The crude product was taken up in ca 20 ml of benzene and chromatographed over silica gel (E. Merck 7733). The fraction eluted with petroleum ether (50-75°C)-benzene (3:2) on evaporation gave a white solid. Recrystallization of this material from acetone furnished 3.4 g (51.8%) of 2,15-dithia[5.5]paracyclophane (50) as colorless needles: mp 151-153°C; nmr ($CDCl_3$) δ ppm 1.62-2.10 (m, 2H, RCH_2R and RCH_2S) 2.40-2.80 (board, 1H, $ArCH_2R$), 3.60 (s, 1H, $ArCH_2S$), 6.94 (s, 1H, ArH), 7.10 (s, 1H, ArH); ms (70 eV) m/e 328 (M^+).

Anal. Calcd for $C_{20}H_{24}S_2$: C, 73.12; H, 7.36; S, 19.52. Found: C, 73.30; H, 7.39; S, 19.4.

2,17-Dithia[6.6]orthometacyclophane (51)

To a vigorously stirred solution of 4 g of potassium hydroxide in 1 l of 95% ethanol at room-temperature under nitrogen was added dropwise a solution of 6.96 g (20 mmol) of 1,3-bis(4-bromobutyl)benzene (38) and 3.40 g (20 mmol) of 1,2-bis(mercaptomethyl)benzene (30) in 400 ml of 95% ethanol over a period of 24 h. Upon further stirring for 12 h, the solvent was evaporated in vacuo. To the residue was added 400 ml of water and the resulting aqueous supension was repeatedly extracted with dichloromethane. The combined extracts were washed successively with

brine and water, dried over anhydrous magnesium sulfate and evaporated to give a solid residue. The crude product was taken up in ca 20 ml of benzene and chromatographed over silica gel (E. Merck 7733). The fraction eluted with petroleum ether (50-75°C)-benzene (2:1) on evaporation afforded 3.8 g (53.4%) of white crystals. Recrystallization of this substance from acetone gave pure 2,17-dithia[6.6]orthometacyclophane (51) as colorless prisms: mp 120-121°C; nmr ($CDCl_3$) δ ppm 1.24-2.02 (m, 2H, RCH_2R), 2.32-2.84 (m, 2H, RCH_2S and $ArCH_2R$), 3.70 (s, 1H, $ArCH_2S$), 6.86-7.50 (m, 2H, ArH); ms (70 eV) m/e 356 (M^+).

Anal. Calcd for $C_{22}H_{28}S_2$: C, 74.10; H, 7.91; S, 17.98. Found: C, 74.03; H, 7.97; S, 17.6.

2,17-Dithia[6.6]metacyclophane (52)

To a vigorously stirred solution of 4 g of potassium hydroxide in 1 l of 95% ethanol at room-temperature under nitrogen was added dropwise a solution of 6.96 g (20 mmol) of 1,3-bis(4-bromobutyl)benzene (38) and 3.40 g (20 mmol) of 1,3-bis(mercaptomethyl)-benzene (31) in 400 ml of 95% ethanol over a period of 24 h. Upon further stirring for 12 h, the solvent was evaporated in vacuo. To the residue was added 400 ml of water and the resulting aqueous suspension was repeatedly extracted with dichloromethane. The combined extracts were washed successively with brine and water, dried over anhydrous magnesium sulfate and evaporated to give a viscous oil which solidified on standing overnight at room temperature. The crude product was taken up in ca 20 ml of benzene

and chromatographed over silica gel (E. Merck 7733). The fraction eluted with petroleum ether (50-75°C)-benzene (2:1) on evaporation gave 4.0 g (56.2%) of white crystals. Recrystallization of this substance from methanol afforded pure 2,17-dithia[6.6]metacyclophane (52) as colorless needles: mp 89-90°C; nmr ($CDCl_3$) δ ppm 1.15-2.00 (m, 2H, RCH_2R), 2.22-2.75 (m, 2H, RCH_2S and $ArCH_2R$), 3.58 (s, 1H, $ArCH_2S$), 6.82-7.36 (m, 2H, ArH); ms (70 eV) m/e 356 (M^+).

Anal. Calcd for $C_{22}H_{28}S_2$: C, 74.10; H, 7.91; S, 17.98. Found: C, 74.22; H, 7.83; S, 18.0.

2,17-Dithia[6.6]mataparacyclophane (53)

To a vigorously stirred solution of 4 g of potassium hydroxide in 1 l of 95% ethanol at room temperature under nitrogen was added dropwise a solution of 6.96 g (20 mmol) of 1,3-bis(4-bromobutyl)benzene (38) and 3.40 g (20 mmol) of 1,4-bis(mercaptomethyl)-benzene (32) in 400 ml of 95% ethanol over a period of 24 h. Upon further stirring for 12 h, the solvent was evaporated in vacuo. To the residue was added 400 ml of water and the resulting aqueous suspension was repeatedly extracted with dichloromethane. The combined extracts were washed successively with brine and water, dried over anhydrous magnesium sulfate and evaporated to yield a viscous oil which solidified on refrigeration overnight. The crude product was taken up in ca 20 ml of benzene and chromatographed over silica gel (E. Merck 7733). The fraction eluted with petroleum ether (50-75°C)-benzene (5:2) on evaporation afforded 3.3 g (46.3%) of colorless crystals. Recrystallization of this

material from methanol gave pure 2,17-dithia[6.6]metaparacyclophane (53) as colorless needles: mp 52-53°C; nmr ($CDCl_3$) δ ppm 1.15-1.74 (m, 2H, RCH_2R), 2.20-2.65 (m, 2H, RCH_2S and $ArCH_2R$), 3.60 (s, 1H, $ArCH_2S$), 6.50-7.35 (m, 2H, ArH); ms (70 eV) m/e 356 (M^+).

Anal. Calcd for $C_{22}H_{28}S_2$: C, 74.10; H, 7.91; S, 17.89. Found: C, 73.87; H, 8.04; S, 18.1.

2,19-Dithia[7.7]metacyclophane (54)

To a vigorously stirred solution of 2.6 g of potassium hydroxide in 1 l of 95% ethanol at room-temperature under nitrogen was added dropwise a solution of 4.76 g (12.6 mmol) of 1,3-bis(5-bromopentyl)benzene (39) and 2.15 g (12.6 mmol) of 1,3-bis-mercaptomethyl)benzene (31) in 350 ml of 95% ethanol over a period of 24 h. Upon further stirring for 12 h, the solvent was evaporated in vacuo. To the residue was added 400 ml of water and the resulting aqueous suspension was repeatedly extracted with dichloromethane. The combined extracts were washed successively with brine and water, dried over anhydrous magnesium sulfate and evaporated to give a viscous oil which solidified on standing overnight at room-temperature. The crude product was taken up in ca 15 ml of benzene and chromatographed over silica gel (E. Merck 7733). The fraction eluted with petroleum ether (50-75°C)-benzene (3:1) on evaporation yielded 2.9 g (58.1%) of white crystals. Recrystallization of this material from n-hexane afforded pure 2,19-dithia-[7.7]metacyclophane (54) as colorless plates: mp 97-98°C; nmr ($CDCl_3$) δ ppm 0.88-1.84 (m, 3H, RCH_2H), 2.02-2.70 (m, 2H, RCH_2S

and $ArCH_2R$), 3.62 (s, 1H, $ArCH_2S$), 6.78-7.32 (m, 2H, ArH); ms (70 eV) m/e 384 (M^+).

Anal. Calcd for $C_{24}H_{32}S_2$: C, 74.94; H, 8.38; S, 16.67. Found: C, 74.92; H, 7.98; S, 16.8.

2,19-Dithia[7.7]metaparacyclophane (55)

To a vigorously stirred solution of 2.6 g of potassium hydroxide in 1 l of 95% ethanol at room temperature under nitrogen was added dropwise a solution of 4.76 g (12.6 mmol) of 1,3-bis(5-bromopentyl)benzene (39) and 2.15 (12.6 mmol) of 1,4-bis(mercaptomethyl)benzene (32) in 350 ml of 95% ethanol over a period of 24 h. Upon further stirring for 12 h, the solvent was evaporated in vacuo. To the residue was added 400 ml of water and the resulting aqueous suspension was repeatedly extracted with dichloromethane. The combined extracts were washed successively with brine and water, dried over anhydrous magnesium sulfate and evaporated to give a waxy residue. The crude product was taken up in ca 15 ml of benzene and chromatographed over silica gel (E. Merck 7733). The fraction eluted with petroleum ether (50-75°C)-benzene (5:2) on evaporation gave 2.2 g (44.1%) of white crystals. Recrystallization of this substance from methanol afforded pure 2,19-dithia[7.7]metaparacyclophane (55) as colorless needles: mp 100-101°C; nmr ($CDCl_3$) δ ppm 0.95-1.80 (m, 3H, RCH_2R), 2.05-2.70 (m, 2H, RCH_2S and $ArCH_2R$), 3.64 (s, 1H, $ArCH_2S$), 6.80-7.15 (m, 2H, ArH); ms (70 eV) m/e 384 (M^+).

Anal. Calcd for $C_{24}H_{32}S_2$: C, 74.94; H, 8.38; S, 16.67. Found: C, 75.25; H, 8.33; S, 16.8.

2,15-Dithia-2,2,15,15-tetraoxo[5.5]orthometacyclophane (56)

To a stirred solution of 3.0 g (9.15 mmol) of 2,15-dithia-[5.5]orhtometacyclophane (44) in 30 ml of chloroform at 0°C was added dropwise a solution of 10.5 g (excess) of 90% m-chloroperbenzoic acid in 90 ml of chloroform over a period of 1 h. After further stirring at room-temperature for 6 h, the precipitate formed was filtered off, washed successively with 5% aqueous potassium hydroxide and water, and dried at 100°C to afford 2.8 g (78.1%) of bissulfone 56 as white powder: mp 264-266°C; nmr (TFA) δ ppm 2.00-2.70 (m, 1H, RCH_2R), 2.62-3.50 (m, 2H, RCH_2SO_2 and $ArCH_2R$), 4.38 (s, 1H, $ArCH_2SO_2$), 6.92-7.80 (m, 2H, ArH).

2,15-Dithia-2,2,15,15-tetraoxo[5.5]metacyclophane (57)

To a stirred solution of 3.0 g (9.15 mmol) of 2,15-dithia-[5.5]metacyclophane (45) in 30 ml of chloroform at 0°C was added dropwise a solution of 10.5 g (excess) of 90% m-chloroperbenzoic in 90 ml of chloroform over a period of 1 h. Upon further stirring at room-temperature for 6 h, the mixture was diluted with chloroform (ca 150 ml) until a clear solution was obtained. The organic solution was washed successively with 5% aqueous potassium hydroxide and water, dried over anhydrous magnesium sulfate and evaporated in vacuo to give bissulfone 57 in quantitative yield as white powder: mp 220-222°C; nmr (TFA) δ ppm 1.80-2.62 (m, 1H, RCH_2R), 2.44-3.15 (m, 2H, RCH_2SO_2 and $ArCH_2R$), 4.54 (s, 1H, $ArCH_2SO_2$), 6.80-7.72 (m, 2H, ArH).

18,20-Dimethyl-2,15-dithia-2,2,15,15-tetraoxo[5.5]metacyclophane (58)

In the manner described for the preparation of bissulfone 57 3.0 g (8.43 mmol) of 18,20-dimethyl-2,15-dithia[5.5]metacyclophane (46) was oxidized with m-chloroperbenzoic acid to afford bissulfone 58 in quantitative yield as white powder: mp 271-273°C; nmr (TFA) δ ppm 1.82-2.56 (m, 2H of RCH_2R and 3H of $ArCH_3$), 2.56-3.10 (m, 4H, RCH_2SO_2 and $ArCH_2R$), 4.48 (s, 2H, $ArCH_2SO_2$), 6.66-7.44 (m, 3H, ArH).

18-Methoxy-2,25-dithia-2,2,15,15-tetraoxo[5.5]metacyclophane (59)

In the manner described for the preparation of bissulfone 57, 3.5 g (9.78 mmol) of 18-methoxy-2,15-dithia[5.5]metacyclophane (47) was oxidized with m-chloroperbenzoic acid to give bissulfone 59 in quantitative yield as white powder: mp 231-235°C; nmr (TFA) δ ppm 1.82-2.64 (broad, 4H, RCH_2R), 2.44-3.16 (broad, 8H, RCH_2SO_2 and $ArCH_2R$), 3.94 (s, 3H, CH_3O), 4.46 (s, 2H, $ArCH_2SO_2$), 4.62 (s, 2H, $ArCH_2SO_2$), 6.82-7.64 (m, 7H, ArH).

2,15-Dithia-2,2,15,15-tetraoxo[5.5]metaparacyclophane (60)

In the manner described for the preparation of bissulfone 56, 3.0 g (9.15 mmol) of 2,15-dithia[5.5]metaparacyclophane (48) was oxidized with m-chloroperbenzoic acid to give 3.15 g (87.8%) of bissulfone 60 as white powder: mp > 300°C; nmr (TFA) δ ppm 1.72-2.46 (m, 1H, RCH_2R), 2.40-3.08 (m, 2H, RCH_2SO_2 and $ArCH_2R$), 4.42 (s, 1H, $ArCH_2SO_2$), 6.54-7.52 (m, 2H, ArH).

18,21-Dimethyl-2,15-dithia-2,2,15,15-tetraoxo[5.5]metaparacyclophane (61)

In the manner described for the preparation of bissulfone 57, 3.0 g (8.43 mmol) of 18,21-dimethyl-2,15-dithia[5.5]metaparacyclophane (49) was oxidized with m-chloroperbenzoic acid to give bissulfone 61 in quantitative yield as white powder: mp 272-277°C; nmr (TFA) δ ppm 1.62-2.50 (m, 2H of RCH_2R and 3H of $ArCH_3$), 2.50-3.24 (m, 4H, RCH_2SO_2 and $ArCH_2R$), 4.16-4.98 (dd, J_{AB}=15Hz, 2H, $ArCH_2SO_2$), 6.6-7.64 (m, 3H, ArH).

2,15-Dithia-2,2,15,15-tetraoxo[5.5]paracyclophane (62)

In the manner described for the preparation of bissulfone 56, 3.0 g (9.15 mmol) of 2,15-dithia[5.5]paracyclophane (50) was oxidized with m-chloroperbenzoic acid to give 2.6 g (72.5%) of bissulfone 62 as white powder: mp > 300°C; nmr (TFA) δ ppm 1.90-3.40 (m, 3H, RCH_2R, RCH_2SO_2 and $ArCH_2R$), 4.50 (s, 1H, $ArCH_2SO_2$), 7.16 (s, 1H, ArH), 7.50 (s, 1H, ArH).

2,17-Dithia-2,2,17,17-tetraoxo[6.6]orthometacyclophane (63)

In the manner decribed for the preparation of bissulfone 57, 3.5 g (9.8 mmol) of 2,17-dithia[6.6]orthometacyclophane (51) was oxidized with m-chloroperbenzoic acid to give bissulfone 63 in quantitative yield as white powder: mp 234-236°C; nmr (TFA) δ ppm 1.44-2.24 (broad, 2H, RCH_2R), 2.55-3.00 (broad, 1H, $ArCH_2R$), 3.00-3.55 (broad, 1H, RCH_2SO_2), 4.50 (s, 1H, $ArCH_2SO_2$), 6.90-7.65 (m, 2H, ArH).

2,17-Dithia-2,2,17,17-tetraoxo[6.6]metacyclophane (64)

In the manner described for the preparation of bissulfone 57, 4.0 g (11.2 mmol) of 2,17-dithia[6.6]metacyclophane (52) was oxidized with m-chloroperbenzoic acid to give bissulfone 64 in quantitative yield as white powder: mp 230-235°C; nmr (TFA) δ ppm 1.50-2.02 (broad, 2H, RCH_2R), 2.46-3.34 (m, 2H, RCH_2SO_2 and $ArCH_2R$), 4.46 (s, 1H, $ArCH_2SO_2$), 6.70-7.64 (m, 2H, ArH).

2,17-Dithia-2,2,17,17-tetraoxo[6.6]metaparacyclophane (65)

In the manner described for the preparation of bissulfone 57, 3.5 g (9.8 mmol) of 2,17-dithia[6.6]metaparacyclophane (53) was oxidized with m-chloroperbenzoic acid to afford bissulfone 65 in quantitative yield as white powder: mp 240-244°C; nmr (TFA) δ ppm 1.45-2.12 (broad, 2H, RCH_2R), 2.42-3.24 (m, 2H, RCH_2SO_2 and $ArCH_2R$), 4.52 (s, 1H, $ArCH_2SO_2$), 6.76-7.60 (m, 2H, ArH).

2,19-Dithia-2,2,19,19-tetraoxo[7.7]metacyclophane (66)

In the manner described for the preparation of bissulfone 57, 2.60 g (6.77 mmol) of 2,19-dithia[7.7]metacyclophane (54) was oxidized with m-chloroperbenzoic acid to afford bissulfone 66 in quantitative yield as white powder: mp 244-248°C; nmr (TFA) δ ppm 1.04-2.12 (m, 3H, RCH_2R), 2.38-3.20 (m, 2H, RCH_2SO_2 and $ArCH_2R$), 4.44 (s, 1H, $ArCH_2SO_2$), 6.80-7.60 (m, 2H, ArH).

2,19-Dithia-2,2,19,19-tetraoxo[7.7]metaparacyclophane (67)

In the manner described for the preparation of bissulfone

57, 2.0 g (5.2 mmol) of 2,19-dithia[7.7]metaparacyclophane (55) was oxidized with m-chloroperbenzoic acid to give bissulfone 67 in quantitative yield as white powder: mp 222-225°C; nmr (TFA) δ ppm 1.00-2.12 (m, 5H, RCH_2R), 2.40-3.16 (m, 2H, RCH_2SO_2 and $ArCH_2R$), 4.52 (s, 1H, $ArCH_2SO_2$), 6.70-7.70 (m, 2H, ArH).

Preparation of [4.4]Orthometacyclophane (80)

To a vigorously stirred mixture of 2.5 g (6.38 mmol) of bissulfone 56, 50 ml of carbon tetrachloride and 50 ml of t-butanol was added 20 g of powdered potassium hydroxide. After having been refluxed for 3 h, the reaction mixture was cooled, poured to 350 ml of water and extracted with petroleum ether (50-75°C). The combined extracts were washed with water, dried over anhydrous magnesium sulfate and evaporated to afford a yellow oily residue. The nmr (CCl_4) spectrum of this material, which showed signals at δ ppm 2.15-2.85 (m, 2H, $ArCH_2CH_2C{=}C$), 5.35-6.25 (m, 1H, $ArCH{=}CHR$) and 6.76-7.52 (m, 2H, ArH), indicated the presence of [4.4]orthometacyclophane-1,13-diene (68). This diene was used without purification for the preparation of [4.4]-orthometacyclophane (80) in a manner described below.

The diene obtained above was dissolved in 30 ml of ethyl acetate and hydrogenated over 5% palladium on charcoal at room-temperature under 45 psi for 3 h. Removal of catalyst and evaporation of solvent gave a yellow oil which was taken up in ca 3 ml of petroleum ether (50-75°C) and chromatographed over silica gel (E. Merck 7733). The fraction eluted with petroleum ether (50-75°C) on evaporation furnished 0.86 g (51.1%) of white crystals.

Recrystallization from ethanol afforded analytically pure [4.4]-orthometacyclophane (80) as colorless needles: mp 84-85°C; uv (n-hexane) λ_{max} nm 216 (sh, log ϵ 4.21), 257 (2.62), 263 (2.71), 264 (sh, 2.70), 271 (2.62); nmr ($CDCl_3$) δ ppm 1.00-2.06 (m, 1H, RCH_2R), 2.18-2.96 (m, 1H, $ArCH_2R$), 6.94-7.52 (m, 1H, ArH); ms (70 eV) m/e 264 (M^+).

Anal. Calcd for $C_{20}H_{24}$: C, 90.85; H, 9.15. Found: C, 90.64; H, 9.36.

Preparation of [4.4]Metacyclophane (81)

To a vigorously stirred mixture of 3.0 g (7.65 mmol) of bissulfone 57, 60 ml of carbon tetrachloride and 60 ml of t-butanol was added 24 g of powdered potassium hydroxide. After having been refluxed for 3 h, the reaction mixture was cooled, poured into 400 ml of water and extracted with petroleum ether (50-75°C). The combined extracts were washed with water, dried over anhydrous magnesium sulfate and evaporated to give a yellow oily residue. That this substance contained largely [4.4]metacyclophane-1,13-diene (69) was confirmed by its nmr (CCl_4) spectrum which showed signals at δ ppm 2.00-3.05 (m, 2H, $ArCH_2CH_2C{=}C$) and 5.10-7.45 (m, 3H, $ArCH{=}CHR$ and ArH) respectively. Without further purification, the crude diene was used for the preparation of [4.4]metacyclophane (81) in a manner described below.

The Ramberg-Bäcklund product obtained above was dissolved in 30 ml of ethyl acetate and hydrogenated over 5% palladium on charcoal at room temperature under 45 psi for 3 h. Removal of catalyst and evaporation of solvent yielded a yellow oil which

was taken up in ca 3 ml of petroleum ether (50-75°C) and chromatographed over Al_2O_3 (Grade I). The fraction eluted with petroleum ether (50-75°C) on evaporation gave 0.40 g (19.8%) of a colorless oil which solidified on standing overnight. Recrystallization of this material from ethanol afforded analytically pure [4.4]-metacyclophane (81) as colorless needles: mp 104-106°C; uv (n-hexane) λ_{max} nm 214 (logϵ 4.24), 218 (4.16), 259 (2.69), 266 (2.87), 269 (2.64), 273 (2.88); nmr ($CDCl_3$) δ ppm 1.00-1.90 (m, 1H, RCH_2R), 2.02-2.92 (m, 1H, $ArCH_2R$), 6.36-7.32 (m, 1H, ArH); ms (70 eV) m/e 264 (M^+).

Anal. Calcd for $C_{20}H_{24}$: C, 90.85; H, 9.15. Found: C, 90.84; H, 8.92.

Preparation of 6,8-Dimethyl[4.4]Metacyclophane (82)

To a vigorously stirred mixture of 2.2 g (5.24 mmol) of bissulfone 58, 44 ml of carbon tetrachloride and 44 ml of t-butanol was added 18 g of powdered potassium hydroxide. After having been refluxed for 3 h, the mixture was cooled, poured to 350 ml of water and extracted with petroleum ether (50-75°C). The combined extracts were washed with water, dried over anhydrous magnesium sulfate and evaporated to afford a yellow oily residue which was taken up in ca 3 ml of petroleum ether (50-75°C) and chromatographed over silica gel (E. Merck 7733). The fractions eluted with petroleum ether on evaporation gave a colorless oil. Rechromatography of this crude oil on preparative thin-layer plate (silica gel, E. Merck 7747) on elution with n-pentane yielded an colorless oily fractions at R_f 0.6.

This material was dissolved in 10 ml of ethyl acetate and hydrogenated over Raney-Nickel at room-temperature under 45 psi for 12 h. Removal of catalyst and evaporation of solvent afforded 0.25 g (16.3%) of white solid. Recrystallization from ethanol gave analytically pure 6,8-dimethyl[4.4]metacyclophane (82) as colorless plates: mp 92-93°C; uv (n-hexane) λ_{max} nm 266 (log ϵ 2.86), 273 (2.96), 281 (2.85); nmr ($CDCl_3$) δ ppm 1.12-1.88 (m, 4H, RCH_2R), 2.20 (s, 3H, $ArCH_3$), 2.30-2.80 (m, 4H, $ArCH_2R$), 6.48-7.35 (m, 3H, ArH); ms (70 eV) m/e 292 (M^+).

Anal. Calcd for $C_{22}H_{28}$: C, 90.35; H, 9.65. Found: C, 90.13; H, 9.78.

Preparation of 6-Methoxy[4.4]metacyclophane (83)

To a vigorously stirred mixture of 3.5 g (8.29 mmol) of bissulfone 59, 70 ml of carbon tetrachloride and 70 ml of t-butanol was added 28 g of powdered potassium hydroxide. After having been refluxed for 3 h, the reaction mixture was cooled, poured into 400 ml of water and extracted with petroleum ether (50-75°C). The combined extracts were washed with water, dried over anhydrous magnesium sulfate and evaporated to give a yellow oily residue. That this substance contained largely 16-methoxy-[4.4]metacyclophane-1,13-diene (71) was confirmed by nmr (CCl_4) spectrum which showed signals at δ ppm 2.10-3.15 (m, 8H, $ArCH_2R$), 3.66 (s, 3H, OCH_3), 5.05-7.35 (m, 11H, ArCH=CHR and ArH). Without further purification, the crude diene was used for the preparation of 6-methoxy[4.4]metacyclophane (83) in a manner

described below.

The Ramberg-Bäcklund product obtained above was dissolved in 30 ml of ethyl acetate and hydrogenated over 5% palladium on charcoal at room temperature under 45 psi for 3 h. Removal of catalyst and evaporation of solvent yielded a yellow oil which was taken up in ca 3 ml of petroleum ether (50-75°C) and chromatographed over silica gel (E. Merck 7733). The fraction eluted with petroleum ether (50-75°C)-benzene (5:1) on evaporation gave a white solid. Further purification of this solid on preparative thin-layer plate (silica gel, E. Merck 7747, eluted with petroleum ether (50-75°C) afforded 0.30 g (12.3%) of white crystals. Recrystallization from methanol gave analytically pure 6-methoxy-[4.4]metacyclophane (83) as colorless crystalline solid: mp 75-77°C, uv (n-hexane) λ_{max} nm 219 (sh, logϵ 4.18), 230 (sh, 3.88), 273 (3.27), 278 (3.35), 282 (3.33), 288 (3.33); nmr ($CDCl_3$) δ ppm 1.10-1.80 (m,8H, RCH_2R), 2.15-2.80 (m, 8H, $ArCH_2R$), 3.70 (s, 3H, OCH_3), 6.30-7.15 (m, 7H, ArH); ms (70 eV) m/e 294 (M^+).
Anal. Calcd for $C_{21}H_{26}O$: C, 85.66; H, 8.90. Found: C, 85.46; H, 8.94.

Preparation of [4.4]Metaparacyclophane (84)

To a vigorously stirred mixture of 3.0 g (7.65 mmol) of bissulfone 60, 60 ml of carbon tetrachloride and 60 ml of t-butanol was added 24 g of powdered potassium hydroxide. After having been refluxed for 3 h, the reaction mixture was cooled, poured to 400 ml of water and extracted with petroleum ether (50-75°C). The combined extracts were washed with water, dried

over anhydrous magnesium sulfate and evaporated to give a yellow oily residue which was taken up in ca 3 ml of petroleum ether (50-75°C) and chromatographed over silica gel (E. Merck 7733). The fraction eluted with petroleum ether (50-75°C) on evaporation yielded a colorless oil. The nmr (CCl_4) spectrum of this Ramberg-Bäcklund product, which showed signals at δ ppm 2.05-2.80 (m,4H, $ArCH_2CH_2C{=}C$), 5.50-6.15 (m, 1H, $ArC{=}CHR$) and 6.35-7.35 (m, 5H, ArH and $ArCH{=}C$), indicated the presence of [4.4]metaparacyclophane-1,13-diene (72). This diene intermediate was used without further purification for the preparation of [4.4]metaparacyclophane (84) in a manner described below.

The crude diene obtained above was dissolved in 30 ml of ethyl acetate and hydrogenated over 5% palladium on charcoal at room-temperature under 45 psi for 3 h. Removal of catalyst and evaporation of solvent afforded 0.53 g (24.7%) of a colorless oil which solidified on standing at room-temperature overnight. Recrystallization from ethanol gave analytically pure [4.4]metaparacyclophane (84) as colorless needles: mp 81-82°C; uv (n-hexane) λ_{max} 214 (logϵ 4.10), 218 (4.03), 225 (sh, 3.75), 260 (sh, 2.57), 265 (2.70), 268 (2.59), 273 (2.60); nmr ($CDCl_3$) δ ppm 1.14-1.70 (m, 1H, RCH_2R), 2.26-2.54 (m, 1H, $ArCH_2R$), 6.14-7.16 (m, 1H, ArH); ms (70 eV) m/e 264 (M^+).

Anal. Calcd for $C_{20}H_{24}$: C, 90.85; H, 9.15. Found: C, 91.00; H, 9.01.

Preparation of 16,19-Dimethyl[4.4]Metaparacyclophane (85)

To a vigorously stirred mixture of 3.0 g (7.14 mmol) of bissulfone 61, 60 ml of carbon tetrachloride and 60 ml of t-butanol was added 24 g of powdered potassium hydroxide. After having been refluxed for 3 h, the reaction mixture was cooled, poured into 400 ml of water and extracted with petroleum ether (50-75°C). The combined extracts were washed with water, dried over anhydrous magnesium sulfate and evaporated to give a yellow oily residue which was taken up in ca 3 ml of petroleum ether (50-75°C) and chromatographed over silica gel (E. Merck 7733). The fraction eluted with petroleum ether (50-75°C) on evaporation gave a colorless oil. The nmr (CCl_4) spectrum of this Ramberg-Bäcklund product, which showed signals at δ ppm 1.75-2.70 (m, 7H, $ArCH_2CH_2C{=}C$ and $ArCH_3$), 5.55-6.10(m, 1H, $ArC{=}CHR$) and 6.34-6.95 (m, 4H, $ArCH{=}C$ and ArH), indicated the presence of 16,19-dimethyl[4.4]metaparacyclophane-1,13-diene (73). This diene intermediate was used without further purification for the preparation of 16,19-dimethyl[4.4]metaparacyclophane (85) in a manner described below.

The diene obtained above was dissolved in 30 ml of ethyl acetate and hydrogenated over 5% palladium on charcoal at room temperature under 45 psi for 3 h. Removal of catalyst and evaporation of solvent afforded 0.56 g (26.8%) of a colorless oil which solidified on standing at room-temperature overnight. Recrystallization from methanol gave analytically pure 16,19-dimethyl[4.4]-metaparacyclophane (85) as white crystalline solid: mp 62-64°C;

uv (n-hexane) λ_{max} nm 219 (sh, log ϵ 4.11), 266 (2.78), 272 (2.89). 281 (2.77); nmr ($CDCl_3$) δ ppm 1.10-2.18 (m, 4H, RCH_2R), 2.04 (s, 3H, $ArCH_3$), 2.14-2.80 (m, 4H, $ArCH_2R$), 6.18-7.18 (m, 3H, ArH); ms (70 eV) m/e 292 (M^+).

Anal. Calcd for $C_{22}H_{28}$: C, 90.35; H, 9.65. Found: C, 90.14, H, 9.68.

Preparation of [5.5]orthometacyclophane (86)

To a vigorously stirred mixture of 3.0 g (7.14 mmol) of bissulfone 63, 60 ml of carbon tetrachloride and 60 ml of t-butanol was added 24 g of powdered potassium hydroxide. After having been refluxed for 1 h, the mixture was cooled, poured to 400 ml of water and extracted with petroleum ether (50-75°C). The combined extracts were washed with water, dried over anhydrous magnesium sulfate and evaporated to give a yellow oil. That the oil contained largely [5.5]orthometacyclophane-1,15-diene (74) was confirmed by its nmr (CCl_4) spectrum which showed signals at δ ppm 1.62-2.40 (m, 3H, RCH_2R), 2.40-2.82 (t, J=6 Hz, $ArCH_2R$), 5.64-6.62 (m, 1H, ArCH=CHR) and 6.78-7.44 (m, 2H, ArH). The diene was used without purification for the preparation of [5.5]orthometacyclophane (86) in a manner described below.

The Ramberg-Bäcklund product obtained above was dissolved in 30 ml of ethyl acetate and hydrogenated over 5% palladium on charcoal at room-temperature under 45 psi for 3 h. Removal of catalyst and evaporation of solvent yielded a yellow oil which was taken up in ca 3 ml of petroleum ether (50-75°C) and chromatographed over silica gel (E. Merck 7733). The fraction eluted with

petroleum ether (50-75°C) on evaporation afforded 0.4 g (19.2%) of a colorless oil which solidified on refrigeration overnight. Recrystallization of this material from methanol gave analytically pure [5.5]orthometacyclophane (86) as colorless needles: mp 47-48°C; uv (n-hexane) λ_{max} nm 212 (log ϵ 4.27), 259 (3.18), 272 (sh, 2.98), 289 (2.15), 299 (2.01); nmr ($CDCl_3$) δ ppm 0.84-1.96 (m, 3H, RCH_2R), 2.28-2.80 (m, 2H, $ArCH_2R$), 6.86-7.40 (m, 2H, ArH); ms (70 eV) m/e 292 (M^+).

Anal. Calcd for $C_{22}H_{28}$: C, 90.35; H, 9.65. Found: C, 90.57; H, 9.63.

Preparation of [5.5]Metacyclophane (87)

To a vigorously stirred mixture of 3.0 g (7.14 mmol) of bissulfone 64, 60 ml of carbon tetrachloride and 60 ml of t-butanol was added 24 g of powdered potassium hydroxide. After having been refluxed for 3 h, the mixture was cooled, poured to 400 ml of water and extracted with petroleum ether (50-75°C). The combined extracts were washed with water, dried over anhydrous magnesium sulfate and evaporated to give a yellow oily residue. The nmr (CCl_4) spectrum of this oil, which showed signals at δ ppm 1.58-3.02 (m, 1H, $ArCH_2CH_2CH_2C{=}C$) and 5.40-7.38 (m, 1H, ArH and $ArCH{=}CHR$), indicated the presence of [5.5]metacyclophane-1,15-diene (75). This diene was used without purification for the preparation of [5.5]metacyclophane (87) in a manner described below.

The crude diene obtained above was dissolved in 30 ml of ethyl acetate and hydrogenated over 5% palladium on charcoal at

room-temperature under 45 psi for 3 h. Removal of catalyst and evaporation of solvent yielded a yellow oil which was taken up in ca 3 ml of petroleum ether (50-75°C) and chromatographed over silica gel (E. Merck 7733). The fraction eluted with petroleum ether (50-75°C) on evaporation gave 0.8 g (38.4%) of a colorless oil which solidified on standing at 0°C overnight. Recrystallization from methanol afforded analytically pure [5.5]metacyclophane (87) as colorless plates: mp 50-51°C (lit.[19] mp 67°C); uv (n-hexane) λ_{max} nm 213 (log ϵ 4.20), 257 (sh, 2.53), 262 (2.64), 265 (sh, 2.63), 268 (2.56), 272 (2.51); nmr δ ppm 0.60-1.88 (m, 3H, RCH_2R), 2.32-2.78 (t, J=6Hz, 2H, $ArCH_2R$), 6.70-7.26 (m, 2H, ArH); ms (70 eV) m/e 292 (M^+).

Anal. Calcd for $C_{22}H_{28}$: C, 90.35; H, 9.65. Found: C, 90.45; H, 9.49.

Preparation of [5.5]Metaparacyclophane (88)

To a vigorously stirred mixture of 3.0 g (7.14 mmol) of bissulfone 65, 60 ml of carbon tetrachloride and 60 ml of t-butanol was added 24 g of powdered potassium hydroxide. After having been refluxed for 3 h, the mixture was cooled, poured into 400 ml of water and extracted with petroleum ether (50-75°C). The combined extracts were washed with water, dried over anhydrous magnesium sulfate and evaporated to give a yellow oil which was taken up in ca 3 ml of petroleum ether (50-75°C) and chromatographed over silica gel (E. Merck 7733). The fraction eluted with petroleum ether (50-75°C) on evaporation gave a colorless oil. The nmr (CCl_4) spectrum of this material, which showed

signals at δ ppm 1.04-3.62 (m, 1H, $ArCH_2CH_2CH_2C{=}{=}C$) and 5.25-7.20 (m, 1H ArH and $ArCH{=}{=}CHR$), indicated the presence of [5.5]-metaparacyclophane-1,15-diene (76). This product was used without further purification for the preparation of [5.5]metaparacyclophane (88) in a manner described below.

The diene obtained above was dissolved in 30 ml of ethyl acetate and hydrogenated over 5% palladium on charcoal at room-temperature under 45 psi for 3 h. Removal of catalyst and evaporation of solvent yielded 0.45 g (21.6%) of a colorless oil which solidified on refrigeration overnight. Recrystallization from methanol afforded analytically pure [5.5]metaparacyclophane (88) as colorless plates: mp 45-46°C; uv (n-hexane) λ_{max} nm 214 (log ∈ 4.18), 225 (sh, 3.91), 261 (sh, 2.67), 265 (2.75), 268 (2.71), 274 (2.66); nmr ($CDCl_3$) δ ppm 0.80-1.90 (m, 3H, RCH_2R), 2.22-2.76 (m, 2H, $ArCH_2R$), 6.32-7.24 (m, 2H, ArH); ms (70 eV) m/e 292 (M^+).

Anal. Calcd for $C_{22}H_{28}$: C, 90.35; H, 9.65. Found: C, 90.61; H, 9.60.

Preparation of [6.6]Metacyclophane (89)

To a vigorously stirred mixture of 2.5 g (5.71 mmol) of bissulfone 66, 50 ml of carbon tetrachloride and 50 ml of t-butanol was added 20 g of powdered potassium hydroxide. After having been refluxed for 3 h, the reaction mixture was cooled, poured into 350 ml of water and extracted with petroleum ether (50-75°C). The combined extracts were washed with water, dried over anhydrous magnesium sulfate and evaporated to give a yellow

oil. That this material contained largely [6.6]metacyclophane-1,17-diene (77) was confirmed by its nmr (CCl_4) spectrum which showed signals at δ ppm 1.34-2.82 (m, 4H, $ArCH_2CH_2CH_2CH_2C{=}C$) and 5.70-7.56 (m, 3H, ArH and $ArCH{=}CHR$). This Ramberg-Bäcklund product was used without purification for the preparation of [6.6]metacyclophane (89) in a manner described below.

The crude diene above was dissolved in 30 ml of ethyl acetate and hydrogenated over 5% palladium on charcoal at room-temperature under 45 psi for 3 h. Removal of catalyst and evaporation of solvent gave a yellow oil which was taken up in ca 3 ml of petroleum ether (50-75°C) and chromatographed over silica gel (E. Merck 7733). The fraction eluted with petroleum ether (50-75°C) on evaporation afforded 0.6 g (32.8%) of white crystals. Recrystallization from methanol gave analytically pure [6.6]-metacyclophane (89) as colorless needles: mp 93-94°C; uv (n-hexane) λ_{max} nm 213 (logϵ 4.28), 259 (2.66), 265 (2.76), 268 (sh, 2.62), 272 (2.71); nmr ($CDCl_3$) δ ppm 1.06-1.88 (m, 2H, RCH_2R), 2.38-2.74 (t, J=6 Hz, 1H, $ArCH_2R$), 6.70-7.35 (m, 1H, ArH); ms (70 eV) m/e 320 (M^+).

Anal. Calcd for $C_{24}H_{32}$: C, 89.94; H, 10.06. Found: C, 90.21; H, 9.95.

Preparation of [6.6]Metaparacyclophane (90)

To a vigorously stirred mixture of 1.9 g (4.34 mmol) of bissulfone 67, 38 ml of carbon tetrachloride and 38 ml of t-butanol was added 15 g of powdered potassium hydroxide. After having been refluxed for 3 h, the mixture was cooled, poured

into 300 ml of water and extracted with petroleum ether (50-75°C). The combined extracts were washed with water, dried over anhydrous magnesium sulfate and evaporated to give a yellow oil which was taken up in ca 3 ml of petroleum ether (50-75°C) and chromatographed over silica gel (E. Merck 7733). The fraction eluted with petroleum ether (50-75°C) on evaporation gave a colorless oil. The nmr (CCl_4) spectrum of this oil, which showed signals at δ ppm 1.90-2.74 (m, 4H, $ArCH_2R$ and RCH_2R) and 5.38-7.46 (m, 3H, ArH and ArCH=CHR), indicated the presence of [6.6]-metaparacyclophane-1,17-diene (78). This diene was directly used for the preparation of [6.6]metaparacyclophane (90) decribed below

The crude diene obtained above was dissolved in 30 ml of ethyl acetate and hydrogenated over 5% palladium on charcoal at room-temperature under 45 psi for 3 h. Removal of catalyst and evaporation of solvent afforded 0.25 g (18.0%) of white crystals. Recrystallization from methanol furnished analytically pure [6.6]-metaparacyclophane (90) as colorless needles: mp 62-63°C; uv (n-hexane) λ_{max} nm 214 (logϵ 4.22), 218 (sh, 4.18), 224 (4.00), 259 (2.65), 265 (2.76), 268 (2.70), 273 (2.70); nmr ($CDCl_3$) δ ppm 0.84-1.82 (m, 2H, RCH_2R), 2.10-2.70 (m,1H, $ArCH_2R$), 6.14-7.26 (m, 1H, ArH); ms (70 eV) m/e 320 (M^+).

Anal. Calcd for $C_{24}H_{32}$: C, 89.94; H, 10.06. Found: C, 90.24; H, 9.95.

Attempted Preparation of [4.4]Paracyclophane (16)

To a vigorously stirred mixture of 3.0 g (7.65 mmol) of bissulfone 62, 60 ml of carbon tetrachloride and 60 ml of t-butanol was added 24 g of powdered potassium hydroxide. On heating for periods ranging from 1 to 3 h, the mixture underwent extensive decomposition to give an untractable yellowish substance.

Preparation of [n]Cyclophanes 99-104

[n]Cyclophanes 99-104 were synthesized in a similar manner as described for [m.m]cyclophanes. The syntheses were illustrated by the preparation of [13]metacyclophane (103).

a. Preparation of [13]metacyclophane (103)

(i) 2,14-Dithia[15]metacyclophane (96)

To a vigorously stirred solution of 6 g of potassium hydroxide in 1.2 l of 95% ethanol at room-temperature under nitrogen was added dropwise a solution of 9.4 g (30 mmol) of 1,11-dibromoundecane and 5.1 g (30 mmol) of 1,3-bis(mercaptomethyl)benzene (31) in 400 ml of 95% ethanol over a period of 24 h. Upon further stirring for 12 h, the solvent was evaporated *in vacuo*. To the residue was added 400 ml of water and the resulting aqueous suspension was repeatedly extracted with dichloromethane. The combined extracts were washed successively with brine and water, dried over anhydrous magnesium sulfate and evaporated to give a oily residue which was taken up in *ca* 20 ml of benzene and

chromatographed over silica gel (E. Merck 7733). The fraction eluted with petroleum ether (50-75°C)-benzene (3:1) on evaporation afforded 6.9 g (71.4%) of a colorless oil. That this substance was 2,14-dithia[15]metacyclophane (96) was confirmed by nmr (CCl_4) spectrum which showed signals at δ ppm 1.00-1.80 (m, 9H, RCH_2R), 2.14-2.36 (t, J=7Hz, 2H, RCH_2S), 3.62 (s, 2H, $ArCH_2S$) and 7.10-7.30 (m, 2H, ArH).

(ii) 2,14-Dithia-2,2,14,14-tetraoxo[15]metacyclophane (97)

To a refluxing solution of 5.5 g (17 mmol) of 2,14-dithia-[15]metacyclophane (96) in 44 ml of acetic acid was added dropwise 16 ml of 30% aqueous hydrogen peroxide over a period of 1 h. Upon further refluxing for 3 h, the mixture was cooled. The precipitate formed was filtered off, washed thoroughly with water and dried at 100°C to give 5.5 g (83.8%) of bissulfone 97 as white crystals. Recrystallization from acetone furnished an analytically pure sample as colorless plates: mp 235-257°C; nmr (TFA) δ ppm 1.10-2.20 (m, 9H, RCH_2R), 3.04-3.30 (t, J=7Hz, 2H, RCH_2SO_2), 4.55 (s, 2H, $ArCH_2SO_2$), 7.55-7.85 (m, 2H, ArH); ms (70eV) m/e 386 (M^+).

Anal. Calcd for $C_{19}H_{30}S_2O_4$: C, 59.03; H, 7.82; S, 16.59. Found: C, 59.23; H, 7.78; S, 16.6.

(iii) [13]Metacyclophane (103)

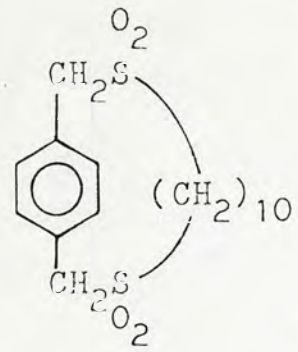
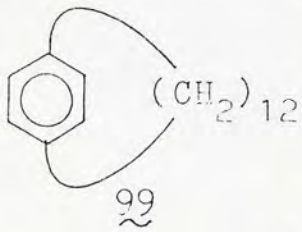
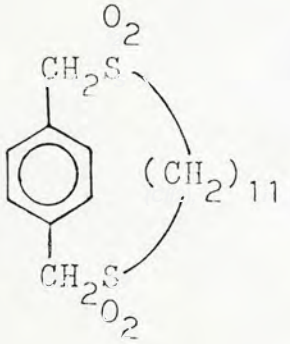
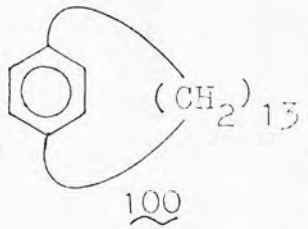
To a vigorously stirred mixture of 3.5 g (9mmol) of bissulfone 97, 70 ml of carbon tetrachloeide and 70 ml of t-butanol was added 28 g of powdered potassium hydroxide. Upon further stirring at room-temperature for 12 h, the reaction mixture was poured into 400 ml of water and extracted with petroleum ether

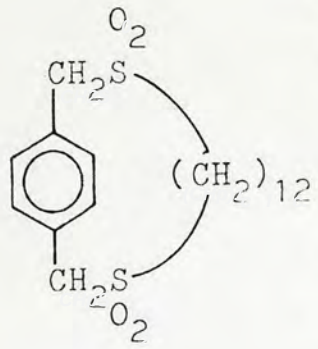
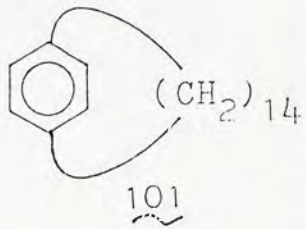
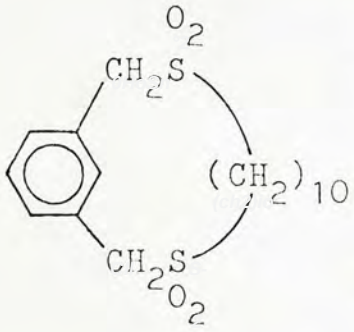
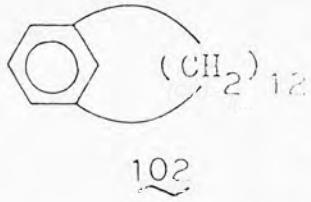
(50-75°C). The combined extracts were washed with water, dried over anhydrous magnesium sulfate and evaporated to give a yellow oily residue which was taken up in ca 3 ml of petroleum ether (50-75°C) and chromatographed over silica gel (E. Merck 7733). The fraction eluted with petroleum ether (50-75°C) on evaporation yielded a colorless oil. The nmr (CCl_4) spectrum of this Ramberg-Backlund product, which showed signals at δ ppm 1.10-1.95 (board, 7H, RCH_2R), 1.95-2.55 (m, 2H, $ArC{=}CCH_2R$), indicated the presence of [13]metacyclophane-1,12-diene (98). This diene intermediate was used without further purification for the preparation of [13]metacyclophane (103) in a manner decribed below.

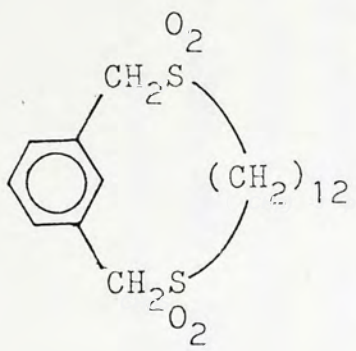
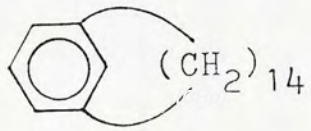
The crude diene obtained above was dissolved in 30 ml of ethyl acetate and hydrogenated over 5% palladium on charcoal at room-temperature under 45 psi for 3 h. Removal of catalyst and evaporation of solvent gave 1.38 g (59.4%) of a colorless oil. That this substance was [13]metacyclophane (103) was confirmed by nmr (CCl_4) spectrum: δ ppm 0.70-1.90 (m, 11H, RCH_2R), 2.48-2.68 (t, J=6Hz, 2H, $ArCH_2R$), 6.72-7.30 (m, 2H, ArH) and by mass spectrum (70 eV): m/e 258 (M^+).

b. Preparation of [n]cyclophanes 99, 100, 101, 102 and 104

These [n]cyclophanes were prepared by similar reaction sequence as for [13]metacyclophane (103). The results are summarized as follows:

Bissulfone Intermediate	[n]Cyclophane Product	% Yield*
		19.6
mp 253-255°C; nmr (TFA) δ ppm 0.94-2.25 (m, 4H, RCH_2R), 2.86-3.30 (m, 1H, RCH_2SO_2), 4.62 (s, 1H, $ArCH_2SO_2$), 7.64 (s, 1H, ArH); ms (70 eV) m/e 372 (M^+). Anal. Calcd for $C_{18}H_{28}S_2O_4$: C, 58.03; H, 7.58; S, 17.21. Found: C, 58.00; H, 7.69; S, 16.9.	nmr (CCl_4) δ ppm 0.50-1.80 (m, 5H, RCH_2R), 2.48-2.66 (t, J=6Hz, 1H, $ArCH_2R$), 7.00 (s, 1H, ArH); ms (70 eV) 244 (M^+).	
		16.6
mp 244-246°C; nmr (TFA) δ ppm 1.00-2.24 (m, 9H, RCH_2R), 2.90-3.36 (m, 2H, RCH_2SO_2), 4.60 (s, 2H, $ArCH_2SO_2$), 7.70 (s, 2H, ArH); ms (70 eV) m/e 386 (M^+). Anal. Calcd for $C_{19}H_{30}S_2O_4$: C, 59.03; H, 7.82; S, 16.59. Found: C, 58.94; H, 8.06; S, 16.3.	nmr (CCl_4) δ ppm 0.50-1.88 (m, 11H, RCH_2R), 2.46-2.64 (t, J=6Hz, 2H, $ArCH_2R$), 6.98 (s, 1H, ArH); ms (70 eV) 258 (M^+).	

Bissulfone Intermediate		[n]Cyclophane Product	% Yield*
	mp 234-237°C; nmr (TFA) δ ppm 1.10-2.24 (m, 5H, RCH_2R), 2.84-3.30 (m, 1H, RCH_2SO_2), 4.62 (s, 1H, $ArCH_2SO_2$), 7.74 (s, 1H, ArH); ms (70 eV) m/e 400 (M^+). Anal. Calcd for $C_{20}H_{32}S_2O_4$: C, 59.97; H, 8.05; S, 16.01. Found: C, 60.01; H, 8.33; S, 16.2.	 101	nmr (CCl_4) δ ppm 0.60-0.86 (m, 6H, RCH_2R), 2.46-2.64 (t, J=6Hz, 1H, $ArCH_2R$), 7.00 (s, 1H, ArH); ms (70 eV) m/e 272 (M^+).	21.0
	mp 204-208°C; nmr (TFA) δ ppm 0.80-2.14 (m, 4H, RCH_2R), 3.05-3.30 (t, J=6Hz, 1H, RCH_2SO_2) 4.62 (s, 1H, $ArCH_2SO_2$), 7.50-7.75 (m, 1H, ArH); ms (70 eV) m/e 372 (M^+). Anal. Calcd for $C_{18}H_{28}S_2O_4$: C, 58.03; H, 7.58; S, 17.21. Found: C, 57.97; H, 7.58; S, 17.1.	 102	nmr (CCl_4) δ ppm 0.50-1.82 (m, 5H, RCH_2R), 2.46-2.64 (t, J=6Hz, 1H, $ArCH_2R$), 6.70-7.22 (m, 1H, ArH); ms (70 eV) 244 (M^+).	41.5

Bissulfone Intermediate	[n]Cyclophane Product	% Yield*
	 104	41.6

mp 246-250°C;
nmr (TFA) δ ppm
1.00-2.26 (m, 5H, RCH_2R),
3.06-3.30 (t, J=6Hz, 1H, RCH_2SO_2),
4.56 (s, 1H, $ArCH_2SO_2$),
7.40-7.80 (m, 1H, ArH);
ms (70 eV) m/e 400 (M^+).
Anal. Calcd for $C_{20}H_{32}S_2O_4$:
C, 59.97; H, 8.05; S, 16.01.
Found: C, 59.84; H, 8.01;
S, 16.0.

nmr (CCl_4) δ ppm
0.60-1.92 (m, 6H, RCH_2R), 2.44-2.62 (t, J=6Hz, 1H, $ArCH_2R$),
6.70-7.56 (m, 1H, ArH);
ms (70 eV) m/e 272 (M^+).

* Yields based on bissulfone intermediates

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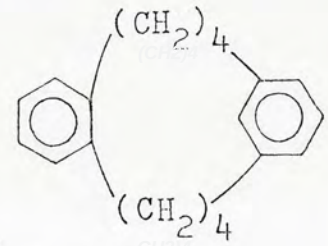
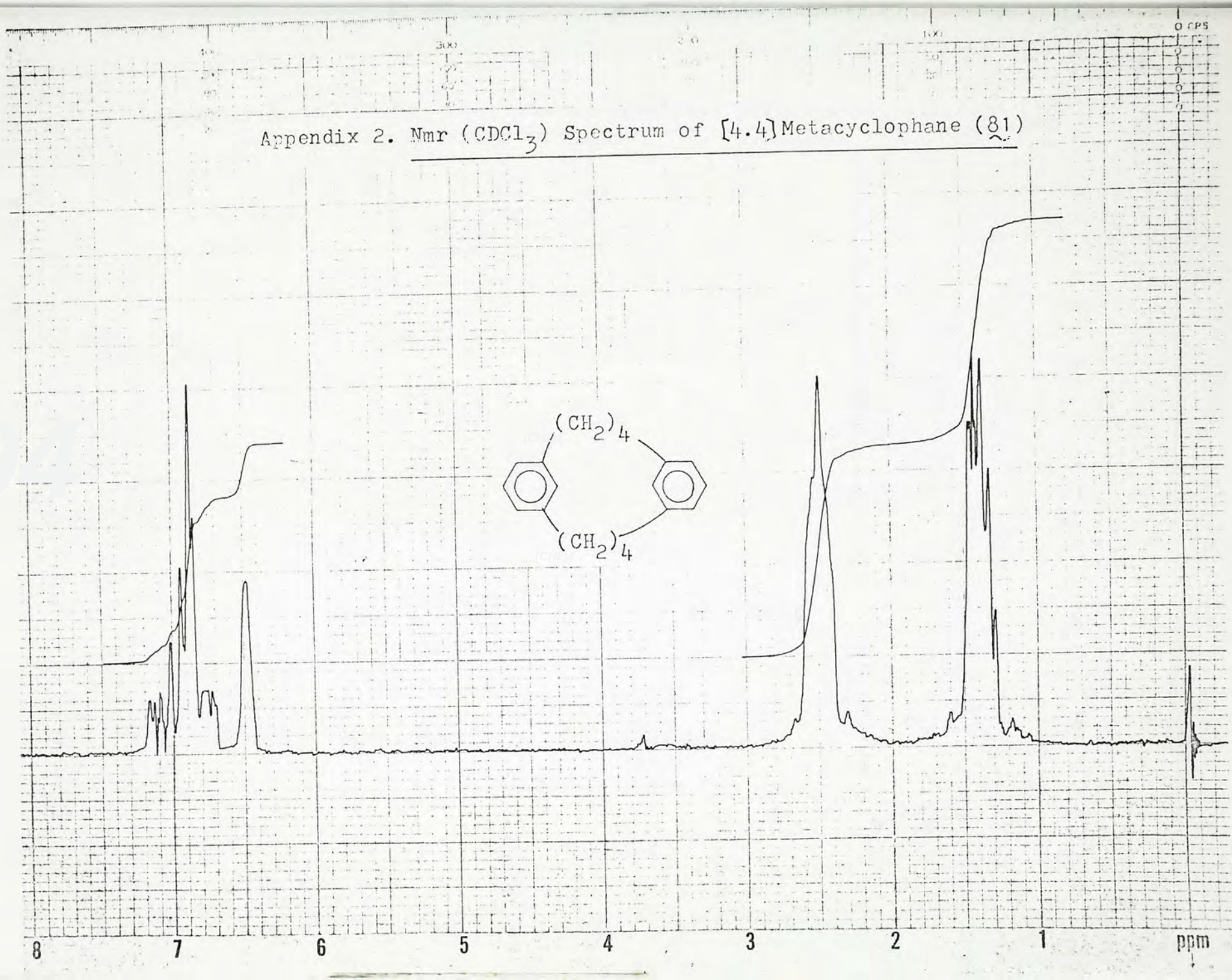
APPENDIX

Nmr Spectra of Cyclophanes

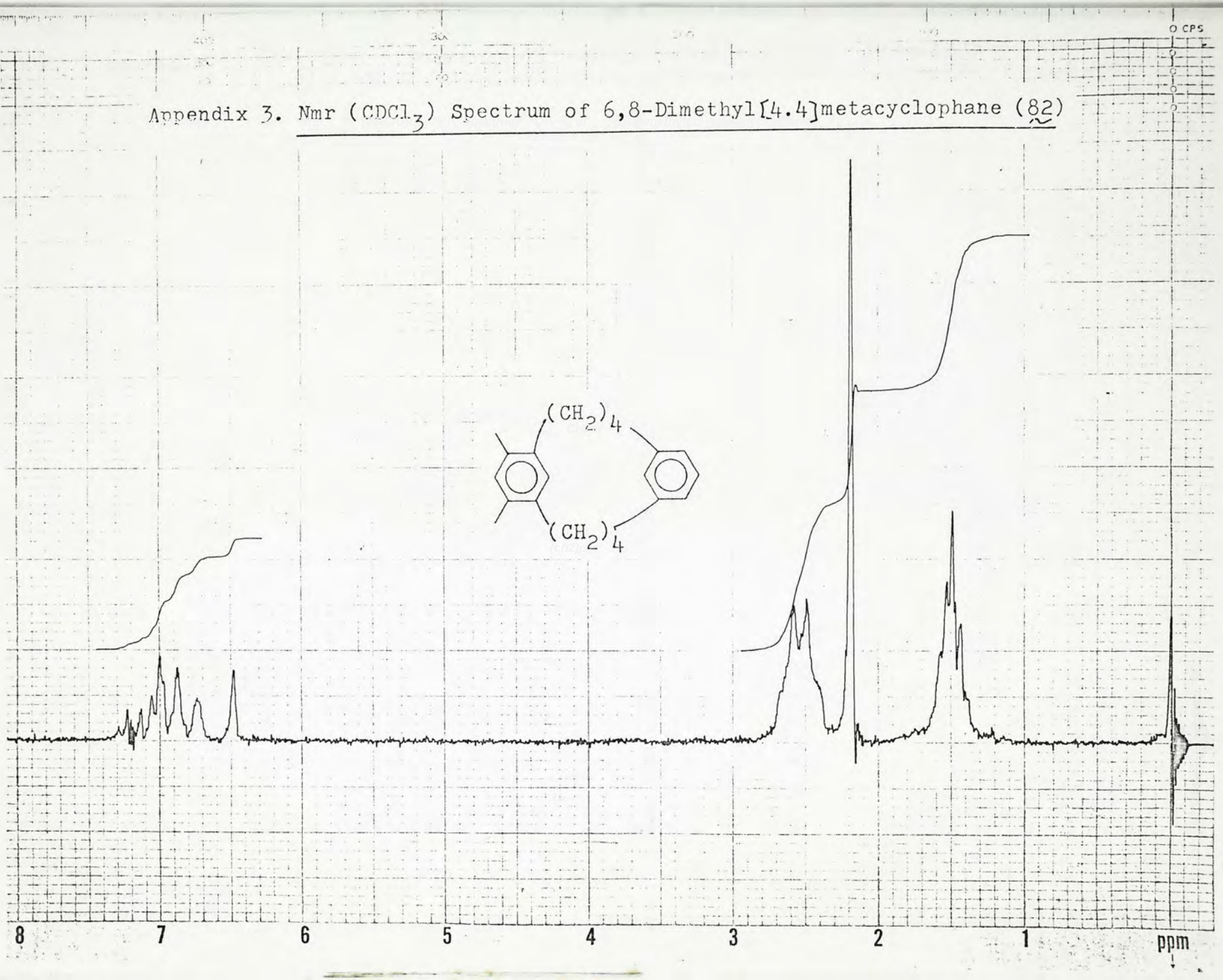
Appendix i. Nmr ($CDCl_3$) Spectrum of [4.4]Orthometacyclophane (80)



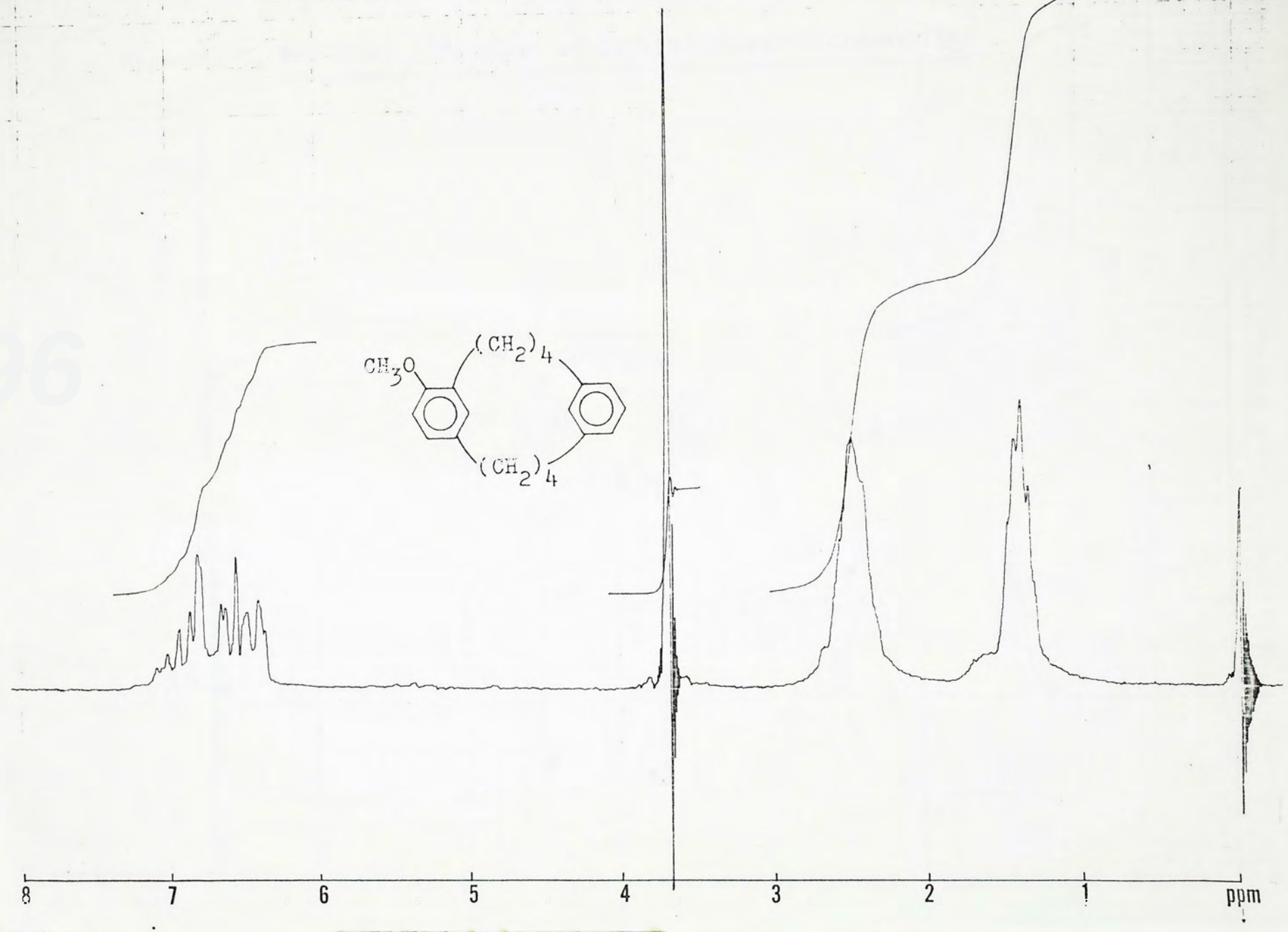
Appendix 2. Nmr ($CDCl_3$) Spectrum of [4.4]Metacyclophane (81)



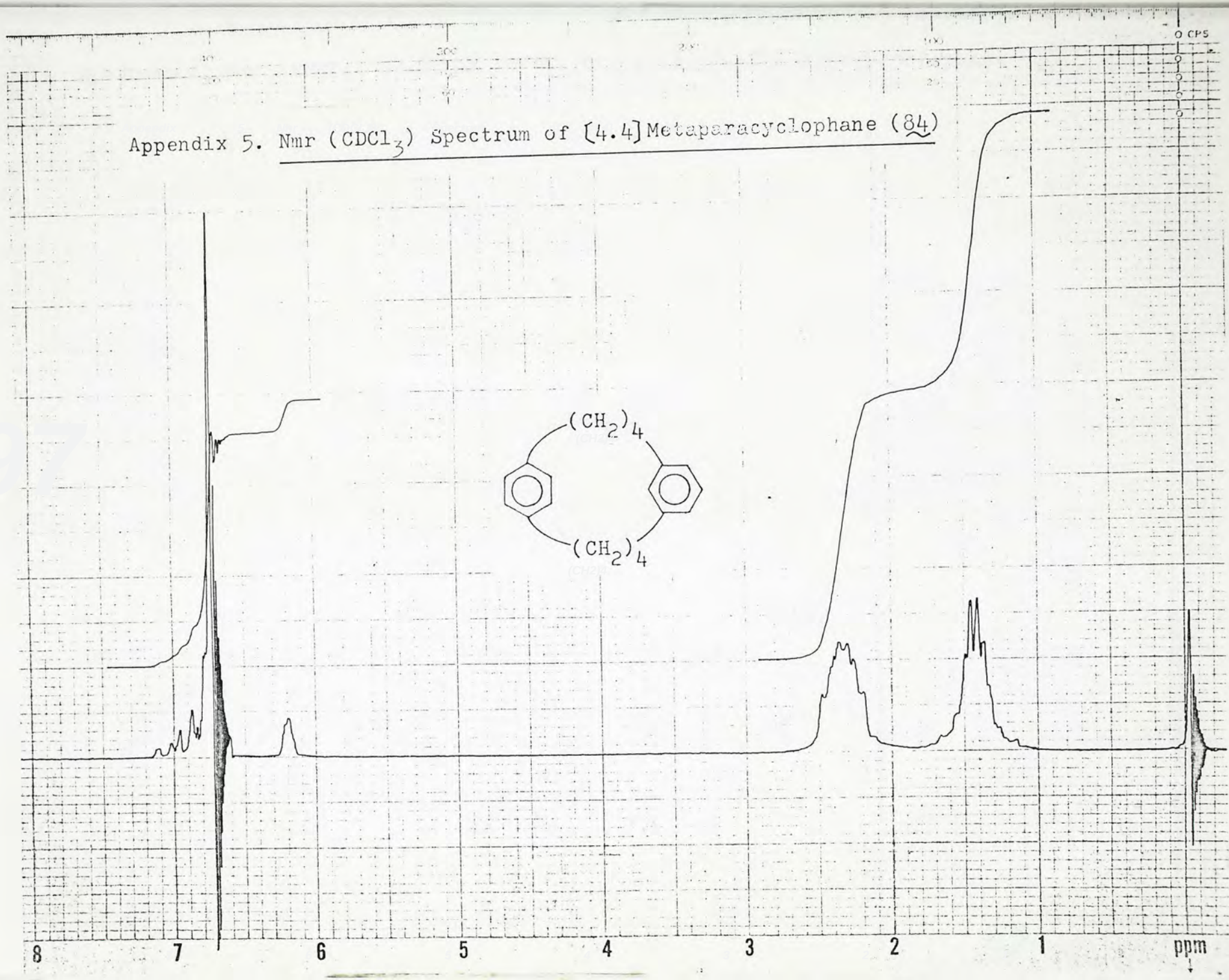
Appendix 3. Nmr ($CDCl_3$) Spectrum of 6,8-Dimethyl[4.4]metacyclophane (82)



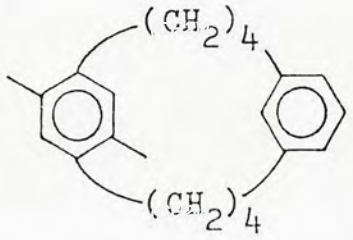
Appendix 4. Nmr ($CDCl_3$) Spectrum of 6-Methoxy[4.4]metacyclophane (83)



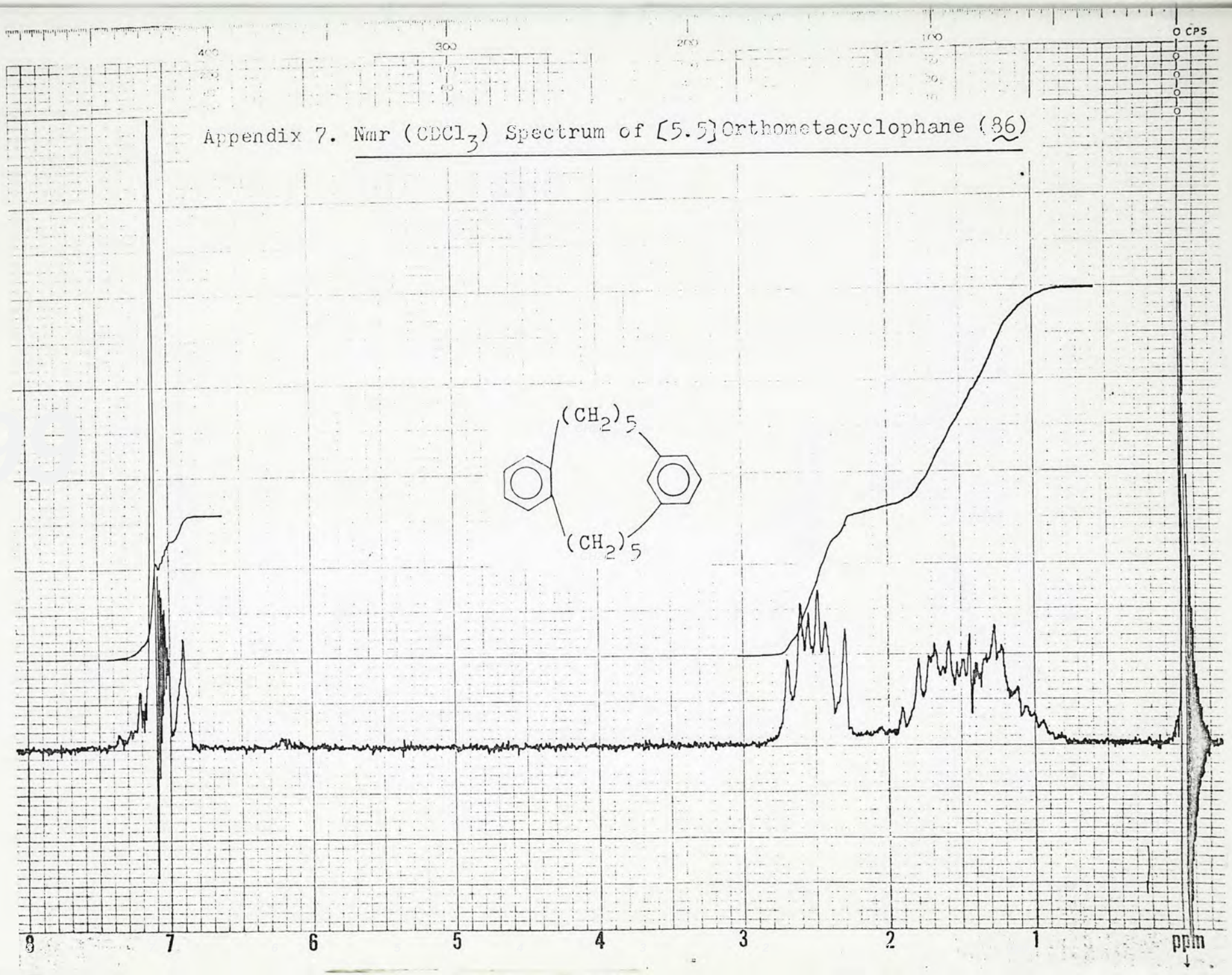
Appendix 5. Nmr ($CDCl_3$) Spectrum of [4.4]Metaparacyclophane (84)



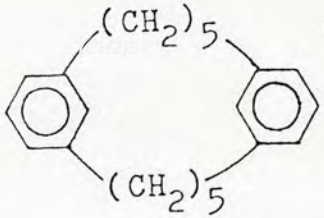
Appendix 6. Nmr ($CDCl_3$) Spectrum of 16,19-Dimethyl[4.4]metaparacyclophane (85)



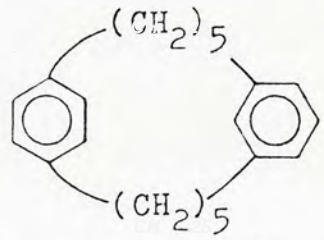
Appendix 7. Nmr ($CDCl_3$) Spectrum of [5.5]Orthometacyclophane (86)



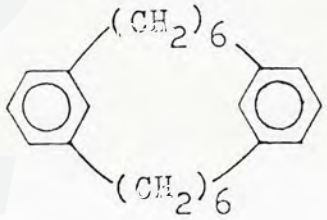
Appendix 8. Nmr ($CDCl_3$) Spectrum of [5.5]Metacyclophane (87)



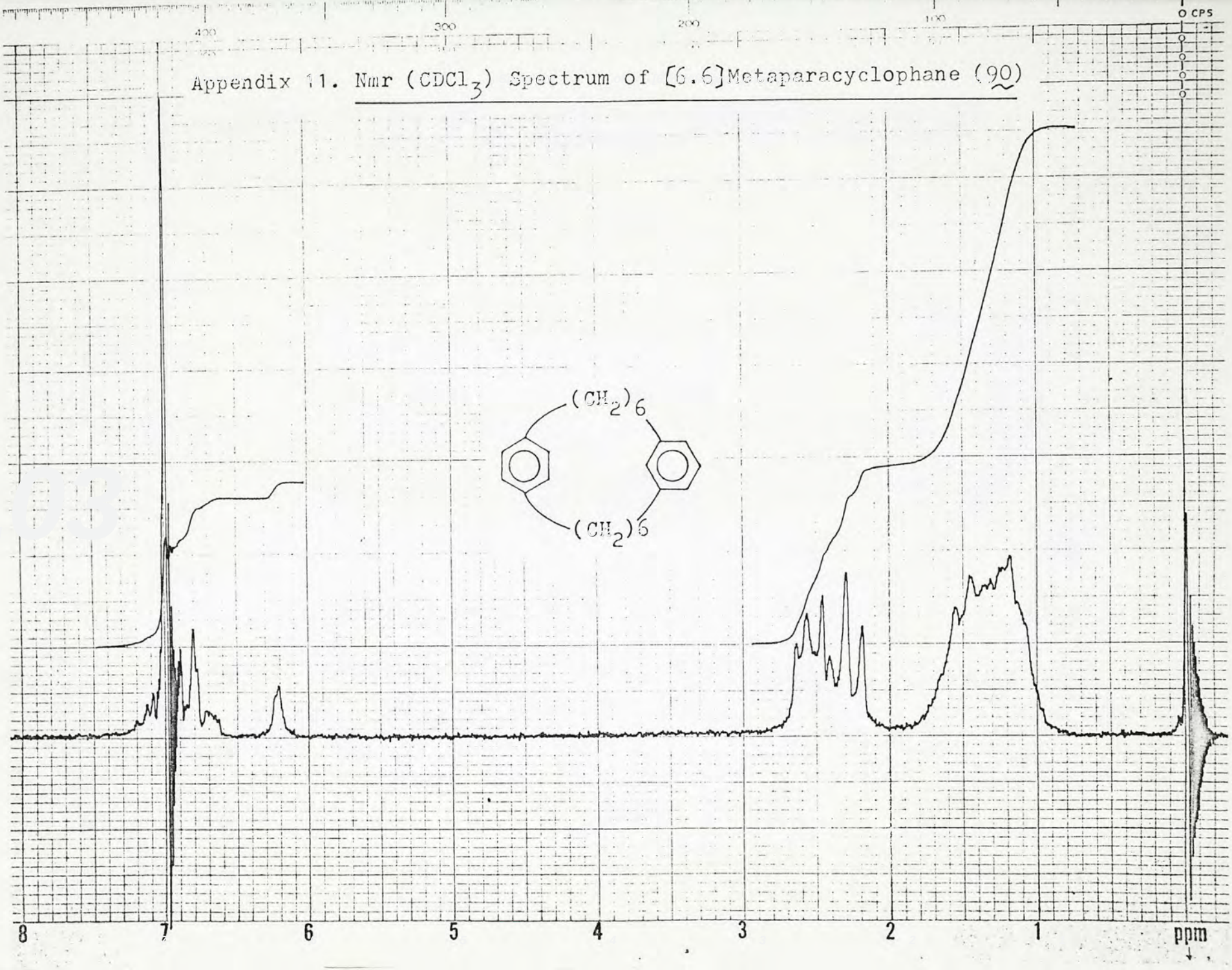
Appendix 9. Nmr ($CDCl_3$) Spectrum of [5.5]Metaparacyclophane (88)



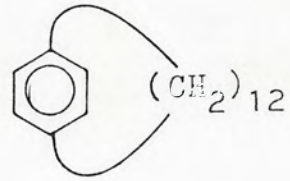
Appendix 10. Nmr ($CDCl_3$) Spectrum of [6.6]Metacyclophane (89)



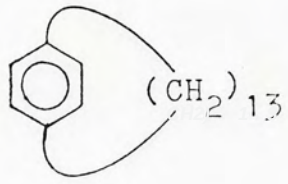
Appendix 11. Nmr ($CDCl_3$) Spectrum of [6.6]Metaparacyclophane (90)



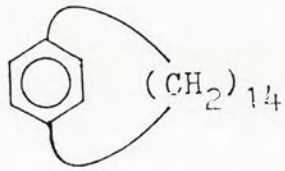
Appendix 12. Nmr (CCl_4) Spectrum of [12]Paracyclophane (99)



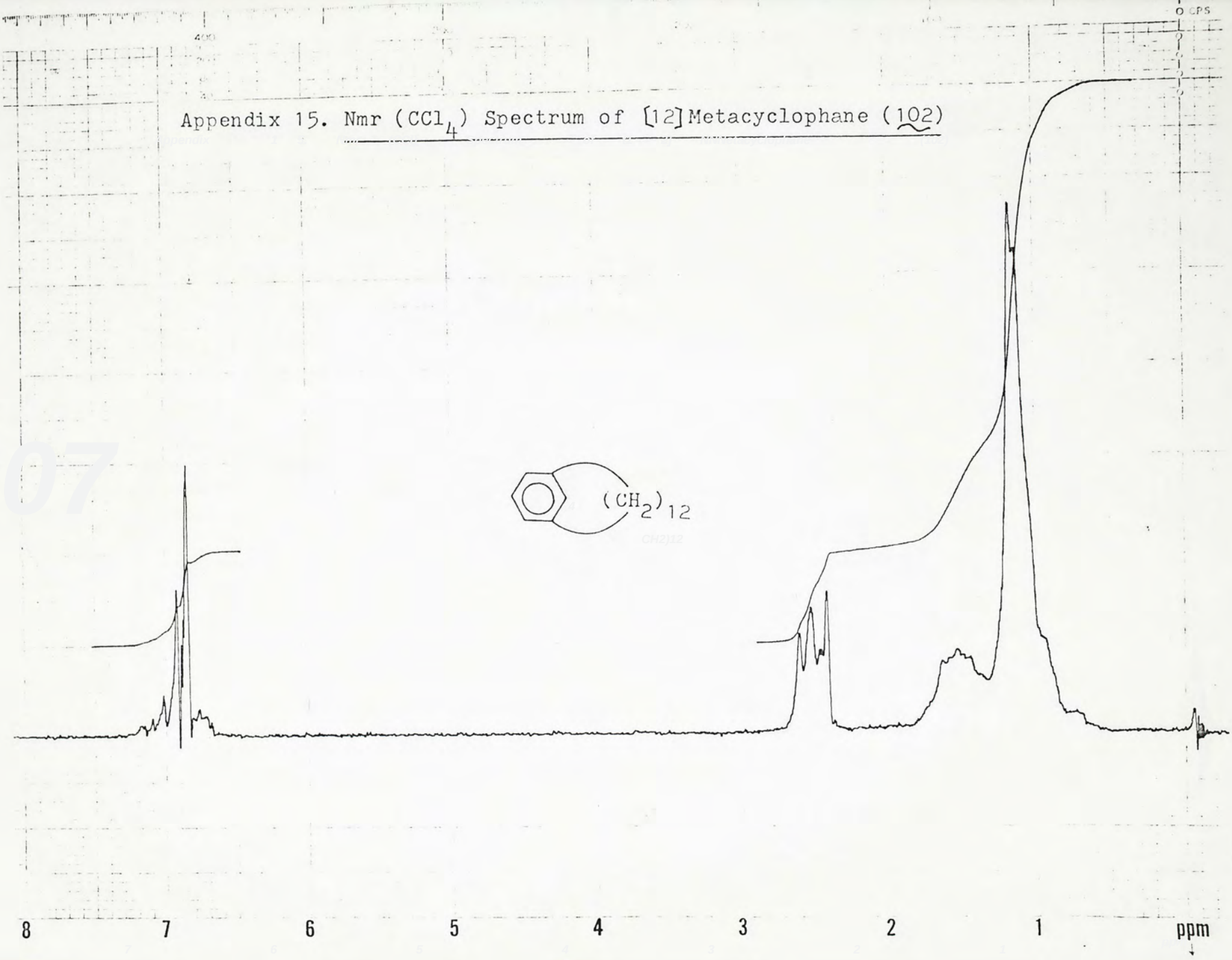
Appendix 13. Nmr (CCl_4) Spectrum of [13]Paracyclophane (100)



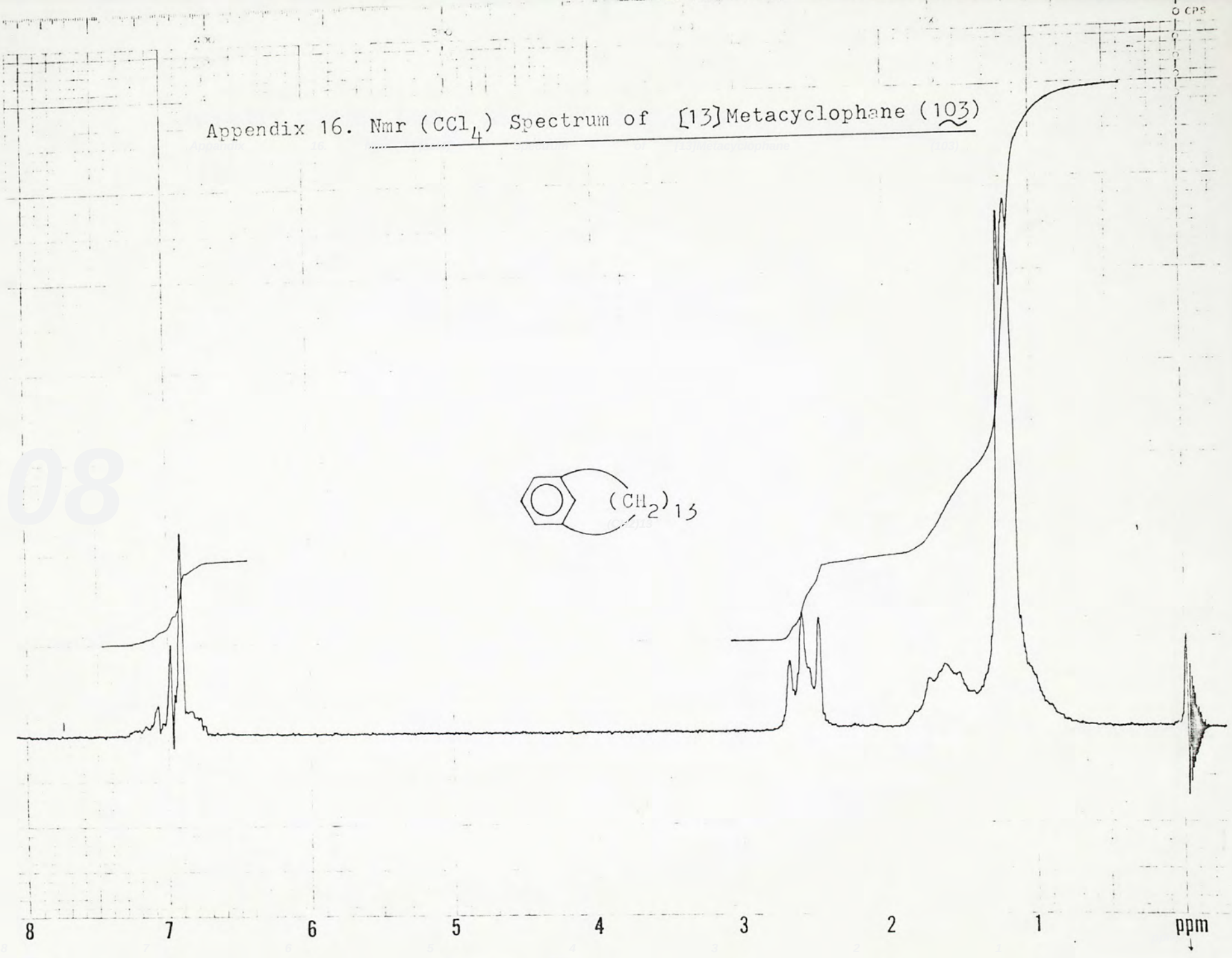
Appendix 14. Nmr (CCl_4) Spectrum of [14]Paracyclophane (101)



Appendix 15. Nmr (CCl_4) Spectrum of [12]Metacyclophane (102)



Appendix 16. Nmr (CCl_4) Spectrum of [13]Metacyclophane (103)



Appendix 17. Nmr (CCl_4) Spectrum of [14]Metacyclophane (104)