THE USE OF THIACYCLOPHANES TO PREPARE NOVEL CONJUGATED AROMATIC COMPOUNDS

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Dithia-[3.3]cyclophanes are easily ring contracted to cyclophanes containing a thio-substituent on the bridge. This substituent can then be eliminated to give a conjugated aromatic system. This article gives a survey of the use of this sequence to prepare novel systems.

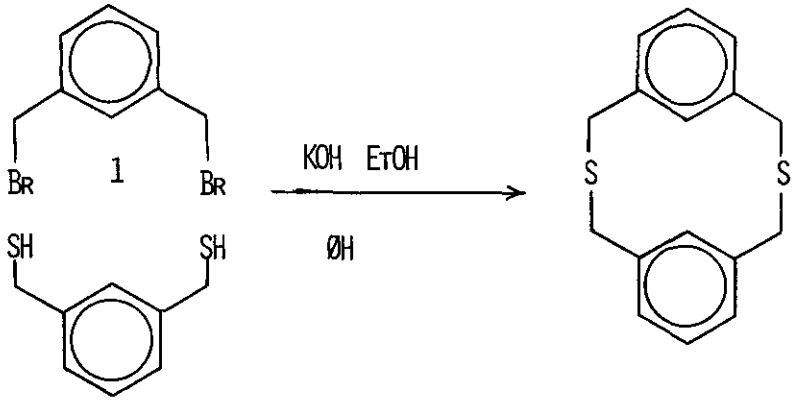
1. Preparation of thiacyclophanes
2. Ring contraction methods
3. Elimination of thio-substituent
4. Examples of conjugated systems

4.1 Hydrocarbons with substituents within the π-cavity

4.2 Cyclophane-enes

4.3 Polycyclic aromatics

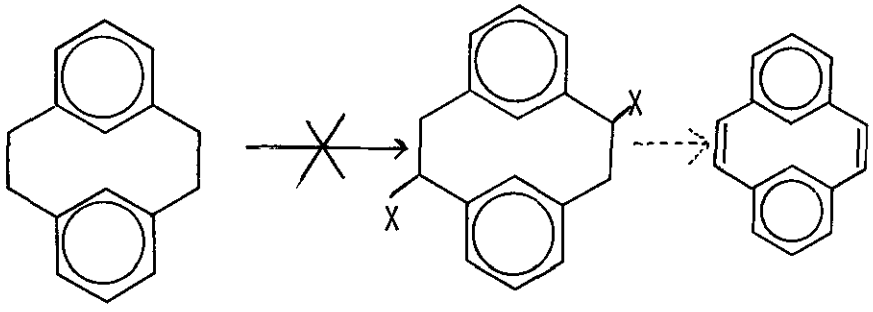
1. Dithia[3.3]cyclophanes are very easily prepared in high yield by reaction of a benzyllic halide with a benzyllic thiol: for example reaction of m-xylylene dibromide (1) with m-xylylene dithiol (2) yields 2,11-dithia[3.3]metacyclophane (3) in 82% yield.[1,2] The reaction is best affected by very



2 3

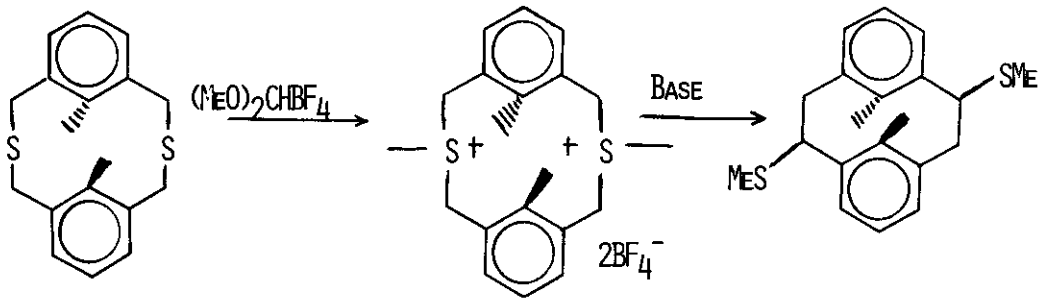
slow addition at room temperature of a solution of the bromide and thiol mixed in benzene to a dilute solution of KOH in 90% ethanol (Method A).[2] In our experience this technique provides the highest yields using simple procedure and makes special apparatus[3,4] unnecessary. Method A is superior to adding separate solutions of thiol (or thiolate) and bromide through two dropping funnels (Method B) or by using bromide in one funnel and a solution of sodium sulphide in the other (Method C). Several examples of each method can be found in the tables below. Other more specialised methods of coupling have also been described.[5]

2. There are a number of methods available[6] to ring contract thiacyclophanes such that the sulphur atom(s) is extruded to give a cyclophane. A



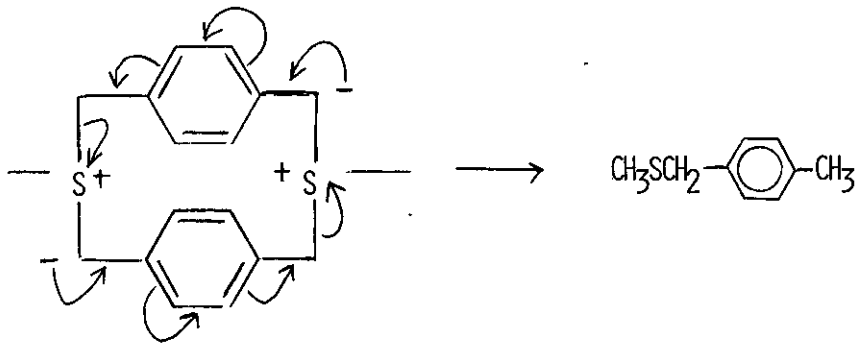
4 5

myriad of these molecules has been prepared.[6,7] Unfortunately it is not possible to functionalise the bridges of [2.2]metacyclophane (4) in order to introduce unsaturation to yield the cyclophanediene (5). Thus, in order to produce molecules such as (5), ring contraction of the thiacyclophane leaving a substituent on the bridge is desired, such that the substituent could be eliminated to introduce the unsaturation in the bridge. This was first achieved by Mitchell and Boekelheide[8] in 1970 using a Stevens rearrangement: the thiacyclophane (6) was quantitatively methylated by dimethoxycarbonium fluoroborate[9] to give the sulphonium salt (7) which readily underwent rearrangement with base to give the thiomethyl substituted cyclophane (8) in almost quantitative yield.

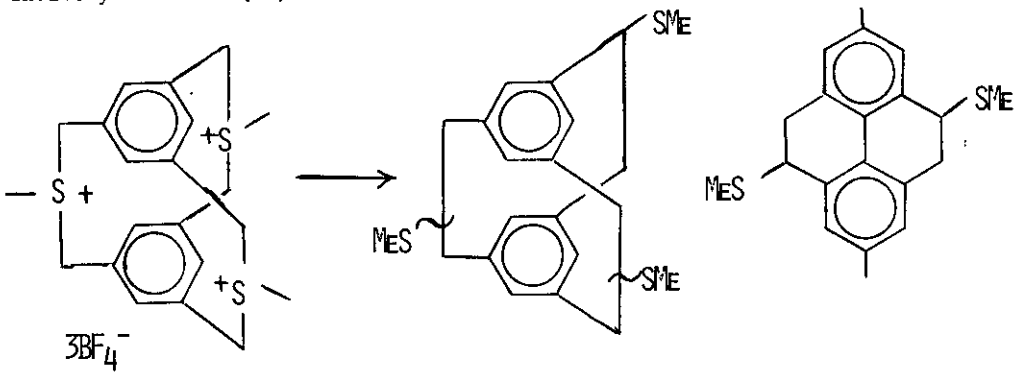


6 7 8

In the case of (7) the choice of base is quite wide, potassium t-butoxide in THF probably being most convenient. In some cases the choice of base is quite critical, since in some cyclophanes other alternatives are possible: e.g. in paracyclophanes scission of the molecule can occur:

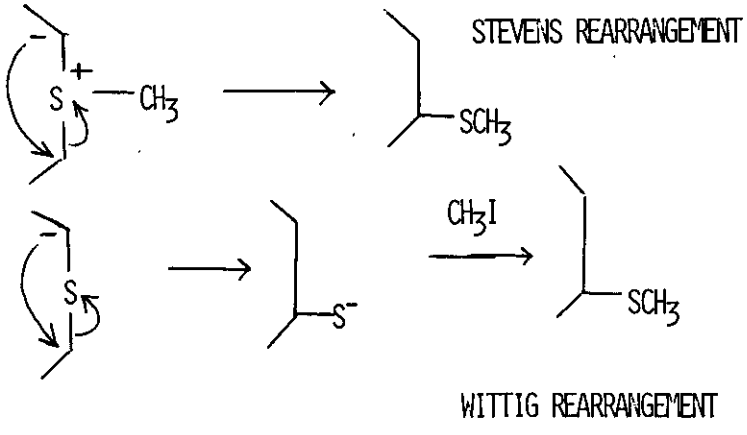


Reiss[4] has also observed similar results. Under these circumstances sodium hydride in THF often gives best results,[4,10] e.g. treatment of (9) with NaH/THF gave 42% yield of the desired (10) whereas use of NaH/DMSO gave entirely unwanted (11).



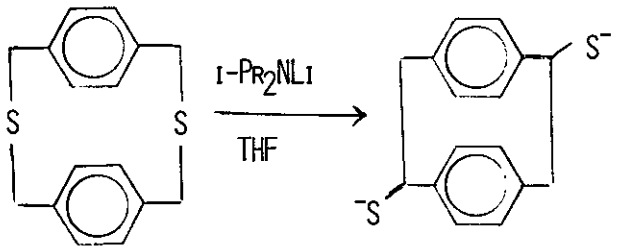
9 10 11

More recently the Wittig rearrangement of thiacyclophanes has been developed.[2]



This often gives higher yields than the Stevens rearrangement and is certainly more convenient since it is not necessary to prepare the intermediate sulphonium salt.

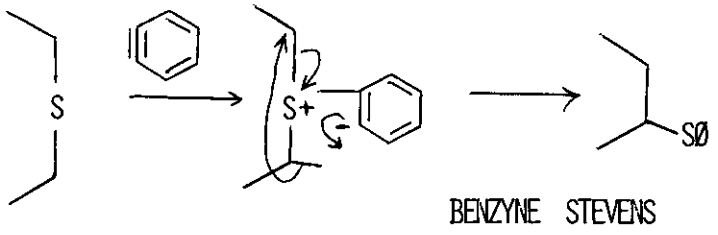
In some cases, e.g. in the paracyclophane (12), Wittig rearrangement works whereas Stevens does not.[2] Lithium diisopropylamide in THF is



12

probably the best base to use. Many examples of both the Stevens and Wittig rearrangements are presented in the tables below.

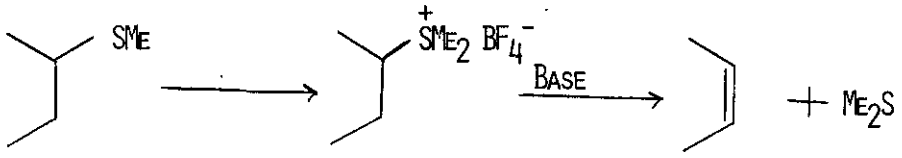
Both the Stevens and Wittig rearrangements mentioned above produce a thioalkyl substituent. Boekelheide and Otsubo[11] introduced a useful variant, the benzyne induced Stevens rearrangement which produces a



BENZYNE STEVENS

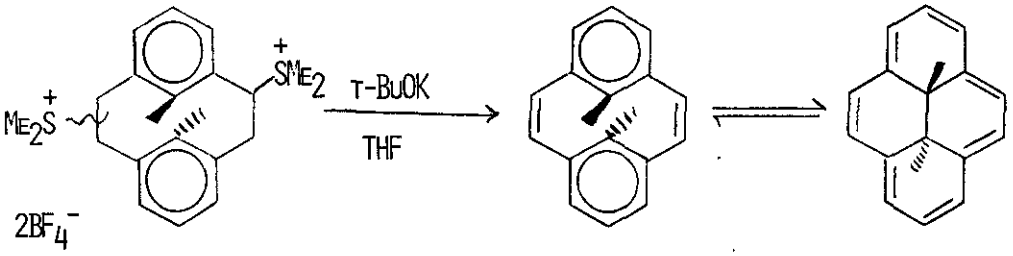
thioaryl substituent, and in some cases, e.g. (12) above works better (45%) than either the Wittig (24%) or Stevens (0%) rearrangements.

3. Elimination of the thiosubstituent has been affected in a number of ways, the most often used being a Hofmann elimination:



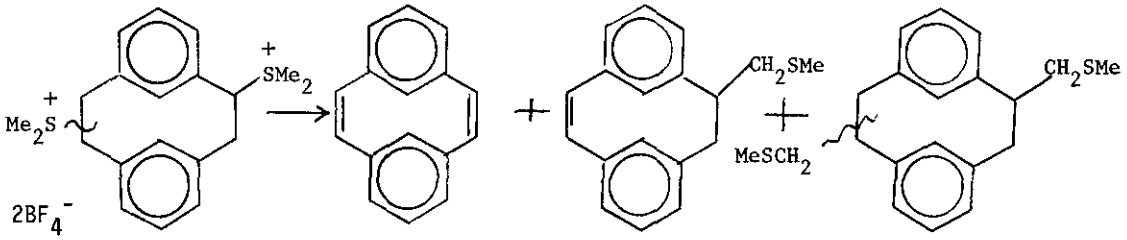
HOFMANN ELIMINATION

This works extremely well in some cases, e.g. (13) with t-BuOK/THF at reflux gives an 85% yield[8] of the bis-eliminated product (14).



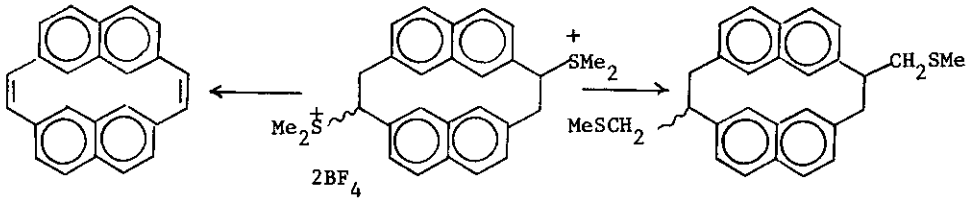
13 14A 14B

However the yield and nature of the product does depend very much on the geometry of the molecule under investigation and on the base-solvent system. For example (15) which is analogous to (13) but has internal H atoms only gives[1] 35% bis-elimination to (16a), 35% mono-elimination-mono Stevens to (17) and 30% bis Stevens to (18).



15 16A 17 18

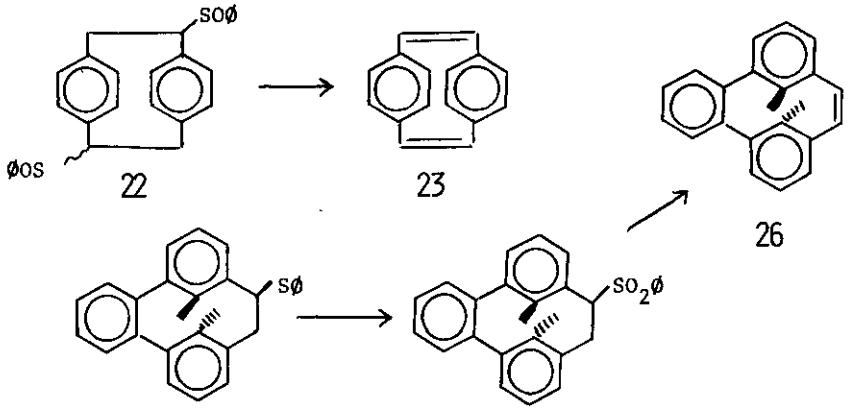
Reiss[12] has obtained similar results in the naphthalene series where (19) in fact only gives (20) with NaH/THF or potassium 2,6-di-t-butyl-



21 19 20

phenoxide in THF, whereas gives[13] the desired (21) with KOH in ethanol in 25% yield. Whereas t-BuOK/THF has been the most widely used base-solvent, sometimes other combinations e.g. NaH-THF, amberlite IRA-400, OH^-/THF work better. The tables below give several examples of such cases.

Unfortunately despite much work by my group there are very few alternatives to the Hofmann elimination. Boekelheide[11] has found one, a thermal sulphoxide elimination which can be performed either at ca. 300°C under vacuum or in refluxing xylene, e.g. (22) gives 54% yield of the paracyclophane-diene (23) in xylene.



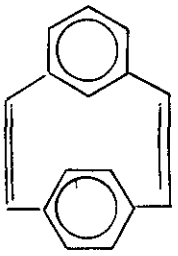
22 23 24 25 26

This method offers some advantage for para-substituted systems where under base conditions the molecule often splits (1,6-elimination).

We have had some success recently in base induced sulphinate eliminations:

The benzocyclophane (24) readily forms the sulphone (25) with H_2O_2/ acetic acid which on treatment with t-BuOK/THF gave an 85% yield[14] of (26). Our preliminary results suggest that this elimination is fairly general, however the yields are rather variable and depend very much on base-solvent used.

4. A wide variety of novel conjugated systems have now been prepared from thiacyclophanes by use of one of the above sequences. These are set out in the tables below under three classes. Table 4.1 gives examples of molecules which have substituents within the π-cavity. The first[8] to be prepared by this method was trans-10b,10c-dimethyl-10b,10c-dihydropyrene (14b). Eleven analogues of (14b) have now been prepared in this way, as well as a further eleven examples of larger systems derived from the hexahydrocoronene skeleton. Table 4.2 gives examples of cyclophane-enes such as metaparacyclophane-diene (27) and the tris-bridged cyclophane-triene (28).



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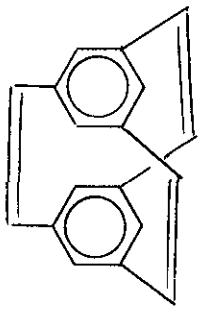

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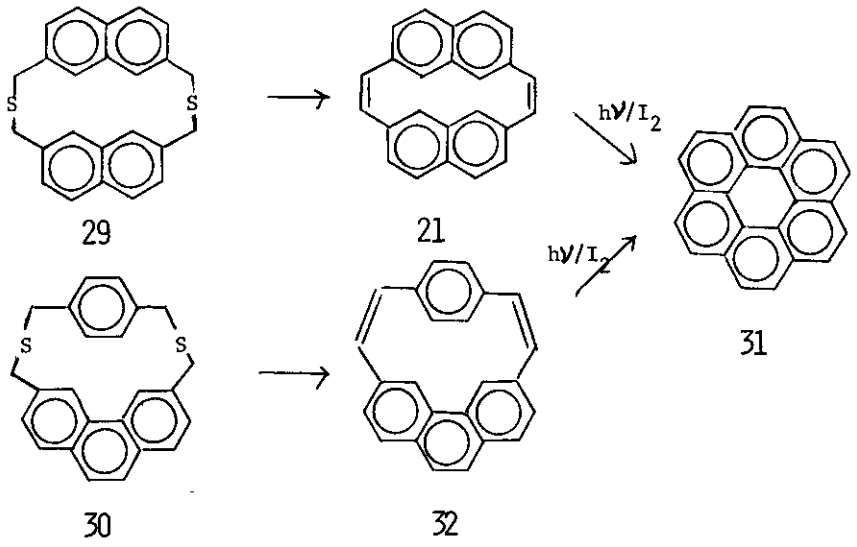
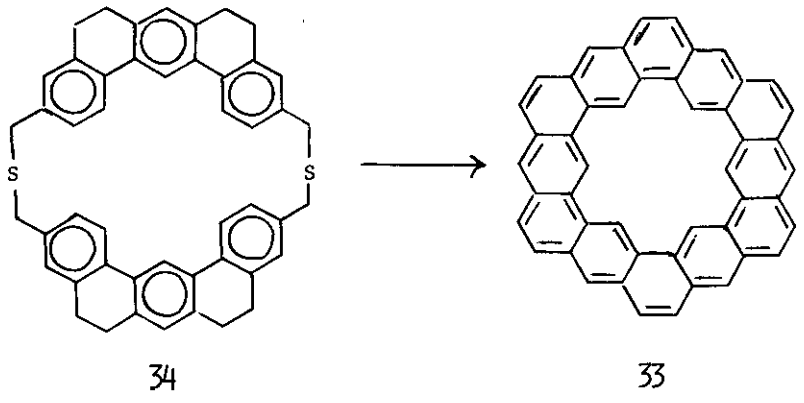
Table 4.3 provides some examples whereby large polycyclic hydrocarbons have been prepared, e.g. the novel coronene syntheses of Reiss[15] where

cyclophanes (29) and (30) both yielded coronene (31) through the dienes (21) and (32) respectively.



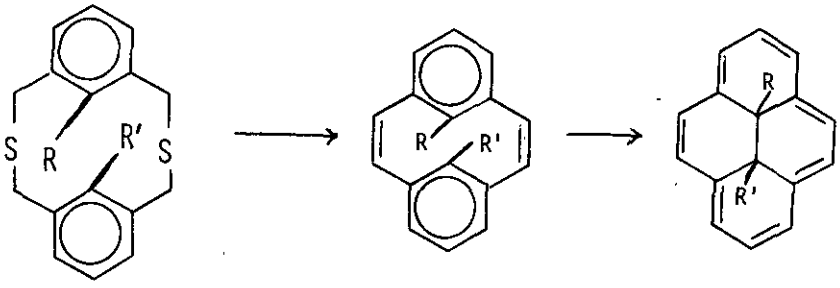
The most recent and perhaps most spectacular demonstration of the power of the thiacyclophane route is Staab's[16] synthesis of Kekulene (33) from thiacyclophane (34).



ABBREVIATIONS USED IN TABLES

Method	A,B,C	See text p.1
Method	S	Stevens rearrangement
	W	Wittig rearrangement
	B	Benzyne induced Stevens
	H	Hofmann elimination
	P	Pyrolysis of sulphoxide

Table 4.1. Preparation of Hydrocarbons with Substituents within the π-cavity.



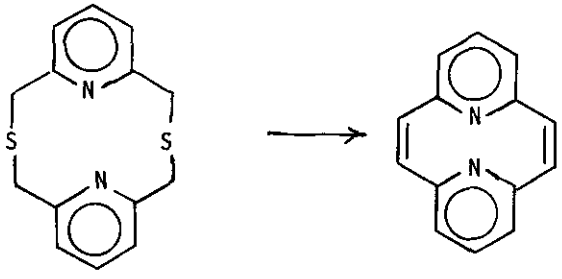
IA IB IC

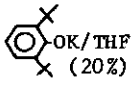
Ia	Method (Yield)	Rearrangement Method(Yield)	Elimination Method(Yield)	Product	Ref.
R=R'=CH_3 ANTI	A(65%) B(16%)	S: t-BuOK/THF(99%) NaH/THF (99%) W: i-Pr_2NLi/THF(99%) B: (76%)	H: t-BuOK/THF (80%) P: vac(34%)	Ic	1,2,8 11
R=R'=CH_3 SYN	A(11%) B(2%)	S: NaH/THF (25% cis) W: i-Pr_2NLi/THF (59% cis)	H: t-BuOK/THF (10% cis)	Ic	1,2,17
R=R'=H ANTI	A(82%) B(80%) C(48%)	S: t-BuOK/THF (93%) W: i-Pr_2NLi/THF(94%) B: (78%)	H: t-BuOK/THF (35%) P: vac(37% pyrene)	Ib	1,2,18 11

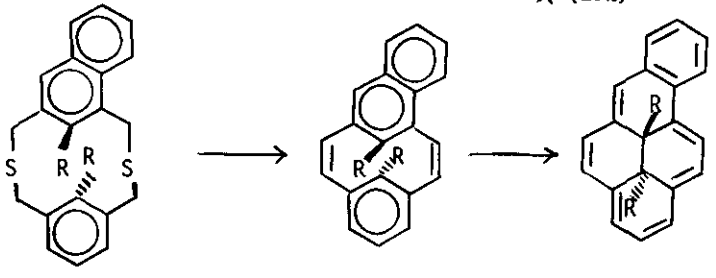
Table 4.1 continued

Ia	Method (Yield)	Rearrangement Method(Yield)	Elimination Method(Yield)	Product	Ref.
R=R'=F SYN	C(37%)	S: t-BuOK/THF (50%)	H: t-BuOK/THF (80%)	Ib	19
R=H,R'=Me ANTI	B(38%)	S: t-BuOK/THF (65%)	H: t-BuOK/THF (40%)	Pyrene	20
R=Me,R'=Bu ANTI	A(80%)	W: BuLi/THF(80%)	H: NaH/THF (68%)	Ic	21

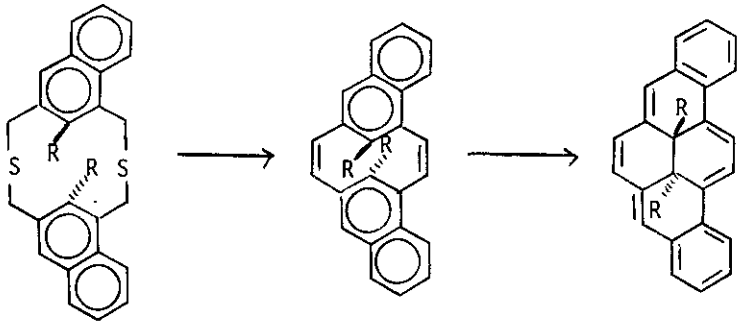
OTHER DERIVATIVES OF I.



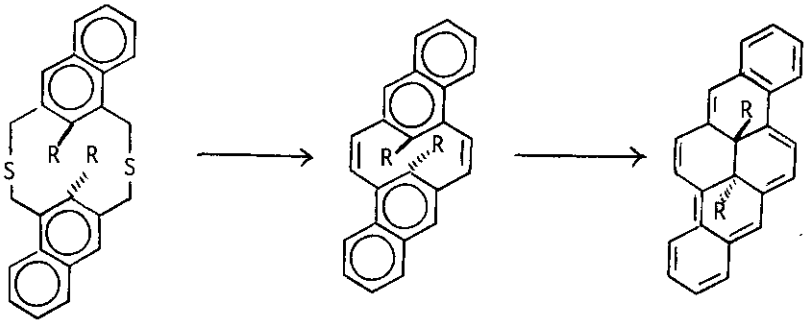
C(25%) S: t-BuOK/THF(42%) H:  OK/THF (20%) 22



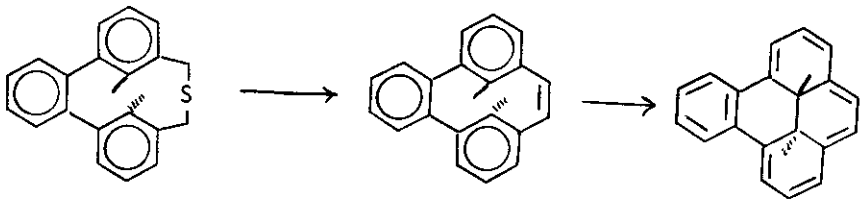
R=H	A(82%)	W: BuLi/THF(92%)	H: t-BuOK/THF (20%)	B	23
$R=CH_3$	A(86%)	W: i-Pr_2NLi/THF(90%)	H: t-BuOK/THF (80%)	B	24



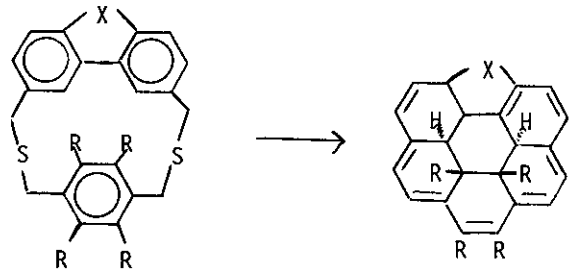
R=H	A(40%) + other isomer	W: i-Pr_2NLi/THF(90%)	H: t-BuOK/THF (20%)	24
R=CH_3	A(40%) + other isomer	W: i-Pr_2NLi/THF(90%)	H: t-BuOK/THF (70%)	24



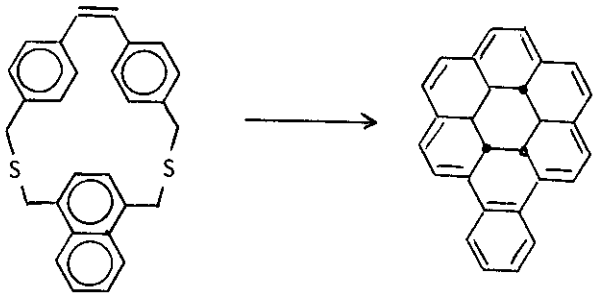
R=H	A(40%) + other isomer	W: i-Pr_2NLi/THF(90%)	H: t-BuOK/THF (∿20%)	A	24
R=CH_3	A(40%) + other isomer	W: i-Pr_2NLi/THF(90%)	H: t-BuOK/THF (∿60%)	B	24



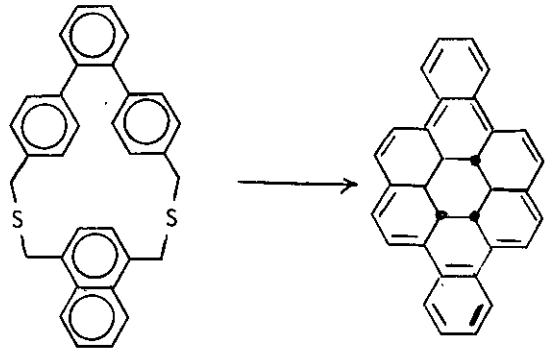
	C(40%)	W: i-Pr_2NLi/THF(95%)	H: t-BuOK/THF (80%)	25



X=H, R=H	A(52%)	S: t-BuOK/THF(22%)	H: t-BuOK/THF (13%)	26,27
X=CH_2CH_2 R=H	A(86%)	S: t-BuOK/THF(21%)	H: t-BuOK/THF(3%)	26,27
X=CH=CH, R=H	A(86%)	S: t-BuOK/THF(51%)	H: t-BuOK/THF(3%)	27
X=S, R=H	A(88%)	S: t-BuOK/THF(22%)	H: t-BuOK/THF (19%)	27,28
X=S, R=Me	A(42%)	S: t-BuOK/THF(23%)	H: t-BuOK/THF (40%)	27



A(62%) S: t-BuOK/THF(26%) P: vac(16%) 29
B: (0%)



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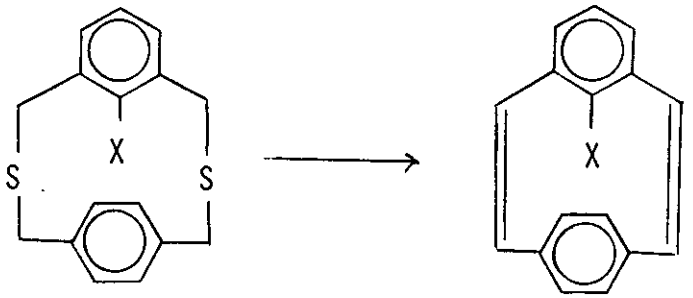
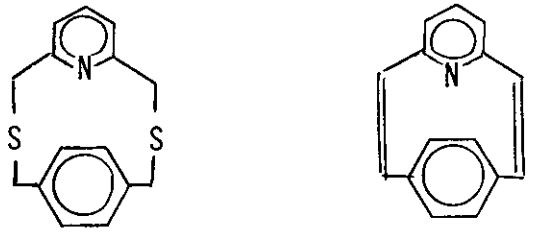
A(85%) S: t-BuOK/THF(69%) P: vac(8%)

Table 4.2. Preparation of Cyclophane-enes



X=H	A(81%)	S: NaH-DMSO(67%)	H: NaH/THF(72%)	
	B(43%)	S: IRA 400-OH^-/THF(45%)	H: BuLi/Et_2O(50%)	
		W: i-Pr_2NLi/THF(65%)		
		B: (70%)	P: xylene(24%)	2,11,30
X=CH_3	B(44%)	S: t-BuOK/THF(31%)	H: t-BuOK/THF(26%)	31
X=F	B(44%)	S: t-BuOK/THF(52%)	H: t-BuOK/THF(92%)	2,30
		W: i-Pr_2NLi/THF(53%)		
X=CN	B(27%)	S: IRA-400,OH^-/THF (77%)	H: IRA-400,OH^-/THF (63%)	30



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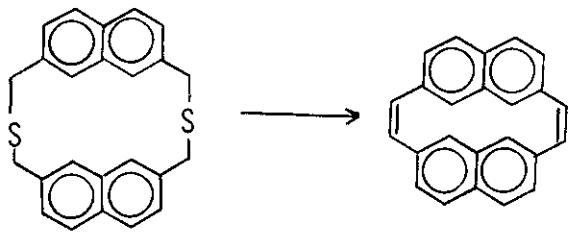
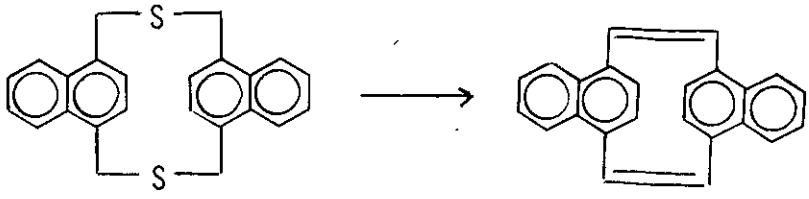
B(48%) S: t-BuOK/THF(33%) H: IRA-400,OH^-/THF (42%)



A(67%)	W: BuLi/THF(100%)	H: KOH/EtOH(6%)	33
A(53%)	H: NaH/THF(88%)	H: KOH/EtOH(25%) P: vac(85%)	15 4



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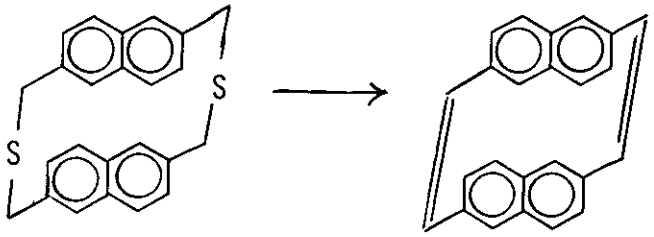
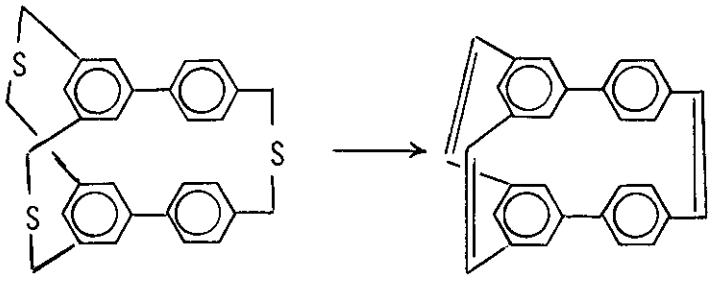
SYN	A(11%)	B: (64%)	P: vac(0.6%)
ANTI	A(53%)	B: (58%)	P: vac(4%)



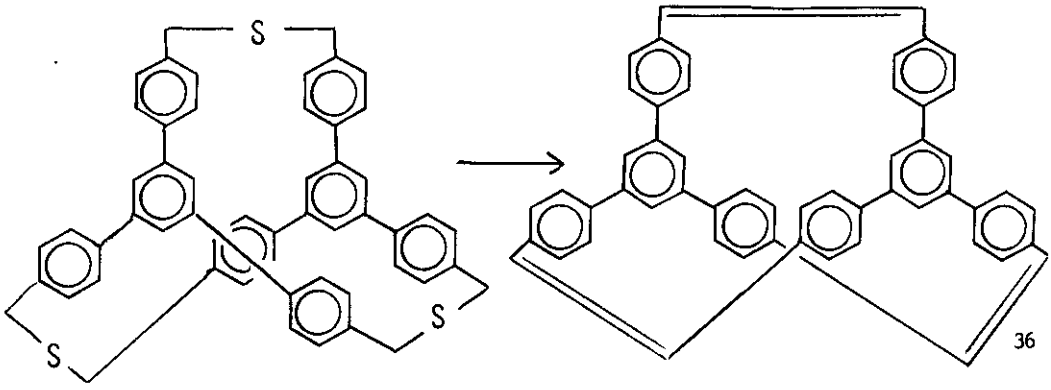
34

B(40%) S: NaH/THF(56%) H: t-BuOK/THF(35%)



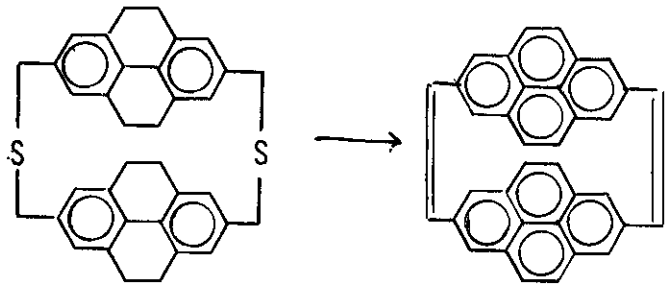
35

B(14%) S: t-BuOK/THF(60%) H: t-BuOK/THF(22%)



36

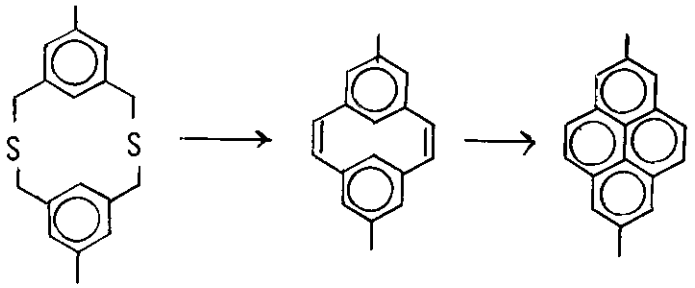
B(35%) S: t-BuOK/HOBu-t(55%) H: t-BuOK/t-BuOH(25%)



37

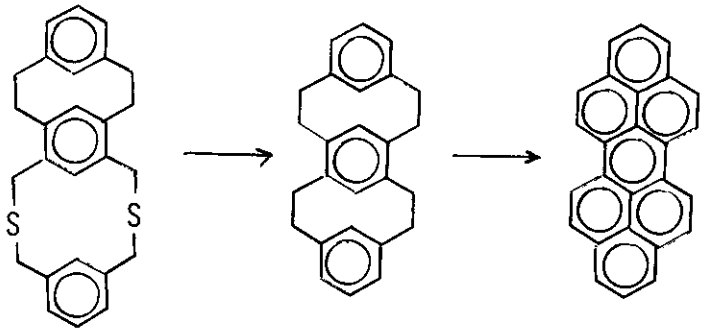
B(40%) S: t-BuOK/THF(58%) H: t-BuOK/THF;DDQ
(28%) (95%)

Table 4.3. Preparation of polycyclic aromatic hydrocarbons.



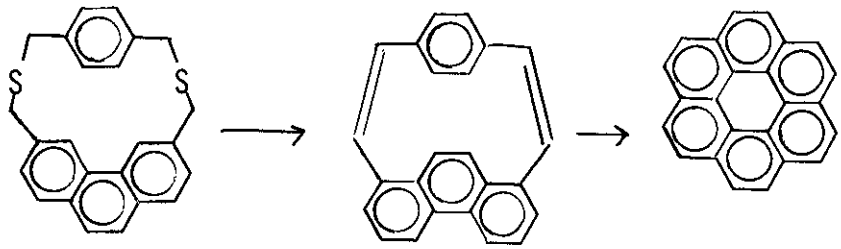
38

A(80%) S: t-BuOK/THF(95%) H: t-BuOK/THF;hν (40%)



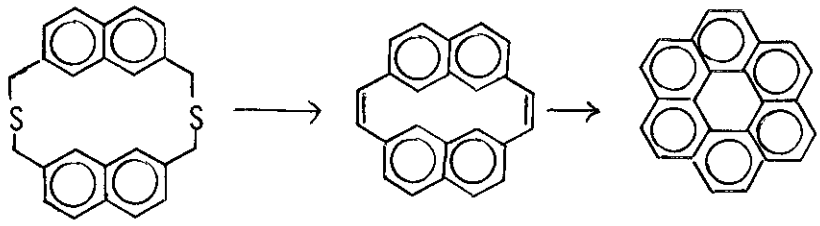
39

A(75%) S: t-BuOK/THF(80%)



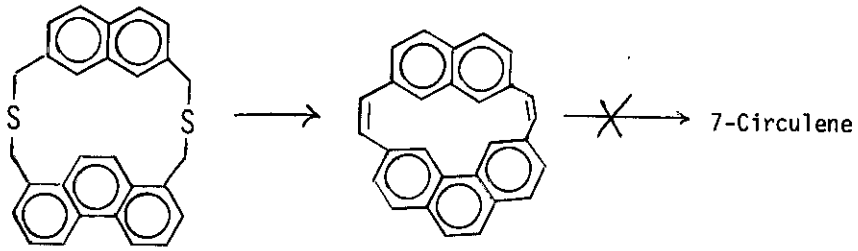
4,15

A(58%) S: NaH/THF(15%) P: vac(40%)
: t-BuOK/THF(0%)



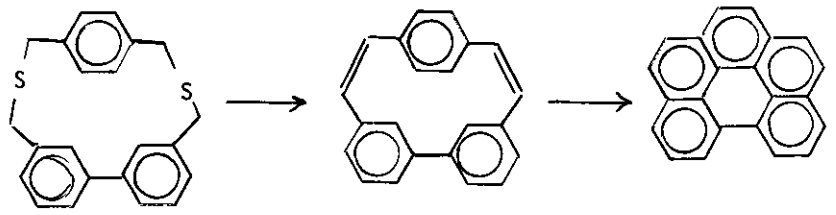
4,15

A(53%) S: NaH/THF(88%) P: vac(85%)



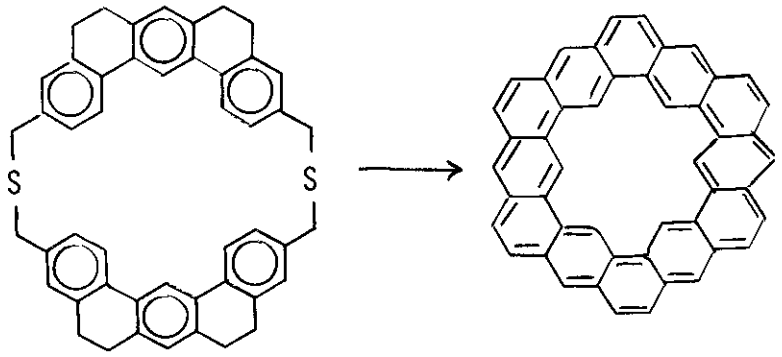
40

A(58%) S: NaH/THF(97%) H: 0%
P: vac(63%)



15

B(49%) S: t-BuOK/THF(low) P: vac(32%)
W: BuLi/THF (72%)



B(55%) S: t-BuOK/THF(90%) H: t-BuOK/THF(9%)

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