Heterocyclic Cyclophanes. Part I. Thiacyclophanes from Thiols

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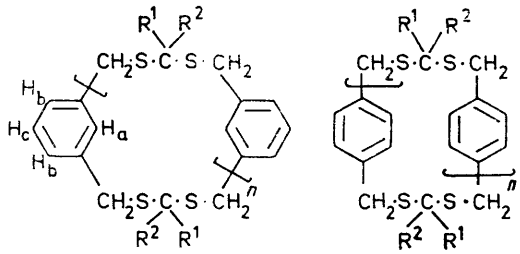
The formation of thia[5,5]cyclophanes from carbonyl compounds and aromatic dithiols has been re-investigated. The synthetic procedure was improved and crystalline thiacyclophane oligomers were also isolated. N.m.r. and u.v. data of the thiacyclophanes were obtained and their usefulness in determining the structures is discussed.

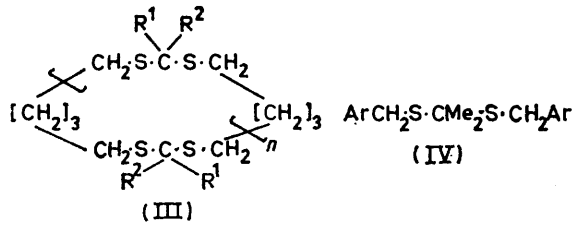
INTEREST has been shown over the last few years in the metacyclophanes and paracyclophanes.[1] Griffin [2] suggested that the thia[5,5]cyclophanes (I; $n = 1$) and (II; $n = 1$),[3,4] warranted re-investigation using modern techniques and this paper reports such an investigation.



(I) (II)

In the original work [3,4] a mixture of the carbonyl compound and the xylene-αα′-dithiol was treated with hydrogen chloride gas in the absence of solvent. Under these conditions yields were not reproducible and a better procedure was to carry out the reaction in ether. Catalysts other than hydrogen chloride found to be effective, were boron trifluoride–ether and methanolic concentrated sulphuric acid.

Autenrieth and Beuttel [3,4] compared their results with similar work on pentane-1,5-dithiol,[5] in which the cyclic thioacetals (III; $R^1 = R^2$ = Me and Et) were obtained. Therefore, thioacetals of pentane-1,5-dithiol were studied and the comparison extended to include 2,2-bisbenzylthiopropane (IV; Ar = Ph) and 2,2-bis-(*m*-methylbenzylthio)propane (IV; Ar = *m*-MeC_6H_4).



(III) (IV)

Some improvements on the original work were achieved in that resinous polymers mentioned in their work but apparently not characterized, were separated from the [5,5]cyclophanes. These polymers were in some cases isolated as crystalline solid oligomers with sharp m.p.s and their physical and spectral properties are summarized in Tables 1—6.

TABLE 1

Dithioacetals (IV)

Ar	Yield (%)	Method
Ph	80	B
m-MeC_6H_4	97	B

TABLE 2

Thia[5,5^n]metacyclophanes (I)

			Yields (%) [a]	
R^1	R^2	n	This work	Autenrieth
H	H	5	33	
H	Me	*n*	90	
H	Ph	1	5	0
		6	31	
H	*o*-MeC_6H_4	*ca.* 34	23	
Me	Me	1	35 [b]	*ca.* 50
		ca. 13	13 [c]	
Me	Et	1	28 [d]	0
		n	3 [d]	
Me	Ph	1	25 [e]	0
		n	5 [e]	
Et	Et	1	69	0
		ca. 11	18	

[a] Yields quoted for this work were obtained by method B. [b] 35%, By method A, 44% by method C, 40% with MeOH–H_2SO_4. [c] 39% By method A, 20% by method C, 20% with MeOH–H_2SO_4. [d] Yield is the same by method C. [e] By method C.

TABLE 3

Thia[5,5^n]paracyclophanes (II)

R^1	R^2	n	Yield (%)	Method
H	Ph	1	65 [a]	B
		ca. 12	18 [a]	B
Me	Me	3	1 [b]	B
		7	60 [b]	B
Me	Et	*n*	75	C
Me	Ph	*n*	75	C

[a] Authenrieth [4] reported a good yield of compound with $n = 1$, and indicated formation of $n = 12$. [b] By method C only, $n = 7$ compound was obtained in 96% yield.

TABLE 4

Thiacycloalkanes (III)

R^1	R^2	n	This work	Autenrieth
H	Ph	*ca.* 20	64 [a]	Not given
Me	Me	1	52 [a]	Good
Me	Et	*n*	58 [b]	
Me	Ph	*n*	75 [b]	
Et	Et	1		Good

[a] Method B. [b] Method C.

Alkylation of *m*-xylene-αα′-dithiol with *gem*-dihalides was investigated as an alternative route to [5,5]metacyclophanes but was only achieved with dibromomethane

[1] B. H. Smith, 'Bridged Aromatic Compounds,' Academic Press, New York, 1964, ch. 1. This system of nomenclature is extended for symmetrical polymeric compounds which are abbreviated to [5,5^n]cyclophanes instead of being written [5,5, . . . 5]cyclophanes. The value of n is readily determined from a formula such as (I) where n is identical to the superscript within the square brackets.

[2] R. W. Griffin, *Chem. Rev.*, 1963, **63**, 45.
[3] W. Autenrieth and F. Beuttel, *Ber.*, 1909, **42**, 4357.
[4] W. Autenrieth and F. Beuttel, *Ber.*, 1909, **42**, 4346.
[5] W. Autenrieth and A. Geyer, *Ber.*, 1908, **41**, 4249.

TABLE 5

N.m.r. spectra of thia[5,5^n]cyclophanes, tetrathiacycloalkanes, and model compounds[a] (τ values, J in Hz)

Compound	ArH	·CH_2·S·	Substituents
m-Xylene-αα′-dithiol	2·78	6·18 (d, *J* 7·5)	8·26 (t, *J* 7·5, SH)
p-Xylene-αα′-dithiol	2·77	6·33 (d, *J* 7·5)	8·27 (t, *J* 7·5, SH)
(VII)	2·13 (H_a), 2·83 ($H_{b/c}$)	6·30	7·4 (m, CH), 8·5 (m, Bu^s), and 8·78 (Me, d)
(IV; Ar = Ph)	2·7 (m)	6·15	8·42 (Me)
(IV; Ar = *m*-MeC_6H_4)	2·88	6·18	8·42 (Me), 7·70 (ArMe)
[5,5]Metacyclophane	3·13 (H_a), 3·15 (J_o 6, J_m 2, H_b), 2·97 (J_o 6, H_c	7·41 (t, *J* 6) [b]	8·5 (br, m, $[CH_2]_3$)
(III; R^1 = H, R^2 = Ph, *n* = *ca.* 20)		7·52 (br, t)	2·65 (Ph), 5·17 (CH), 8·6 (m, $[CH_2]_3$)
(III; R^1 = R^2 = Me, *n* = 1)		7·30 (t, *J* 6·5)	8·4 (m, $[CH_2]_3$ and Me)
(I; R^1 = R^2 = H, *n* = 1) [c]	3·02 (H_a), 2·80 ($H_{b/c}$)	6·28	6·63 (CH_2)
(I; R^1 = R^2 = H, *n* = 5)	2·83	6·23	6·67 (CH_2)
(I; R^1 = H, R^2 = Me, *n* = *n*)	2·82	6·22	6·33 (q, *J* 7, CH), 8·52 (d, *J* 7, Me)
(I; R^1 = H, R^2 = Ph, *n* = 1)	2·5—3·0 (inc. R^2 = Ph)	6·30, 6·52 (dd, *J* 15)	5·83 (CH)
(I; R^1 = H, R^2 = Ph, *n* = 6)	2·80 (inc. R^2 = Ph)	6·26, 6·54 (dd, *J* 13)	5·48 (CH)
(I; R^1 = H, R^2 = *o*-MeC_6H_4, *n* = *ca.* 34)	2·6—3·2 (inc. R^2 = *o*-MeC_6H_4)	6·40 (m) [e]	5·70 (CH), 8·25 (ArMe)
(I; R^1 = R^2 = Me, *n* = 1)	2·22 (H_a), 2·65 ($H_{b/c}$)	5·98	8·30 (Me)
(I; R^1 = R^2 = Me, *n* = *ca.* 13)	2·58 (H_a), 2·70 ($H_{b/c}$)	6·12	8·40 (Me),
(1; R^1 = Me, R^2 = Et, *n* = 1)	2·33 (H_a), 2·83 ($H_{b/c}$)	6·12	8·45 (Me) 8·29(q, *J* 7, CH_2), 8·90 (t, *J* 7, Me)
(I; R^1 = Me, R^2 = Ph, *n* = 1)	*d*	6·27	7·92 (Me)
(I; R^1 = R^2 = Et, *n* = 1)	2·33 (H_a), 2·80 ($H_{b/c}$)	6·13	8·27 (q, *J* 7, CH_2), 8·95 (t, *J* 7, Me)
(I; R^1 = R^2 = Et, *n* = *ca.* 11)	2·68 (H_a), 2·78 ($H_{b/c}$)	6·20	8·29 (q, *J* 7, CH_2), 9·05 (t, *J* 7, Me)
(II; R^1 = H, R^2 = Ph, *n* = 1)	2·87	6·11; 6·56 (dd, *J* 14)	2·67 (Ph), 6·08 (CH)
(II; R^1 = H, R^2 = Ph, *n* = *ca.* 12)	2·94	6·19; 6·46 (dd, *J* 13·5)	2·69 (Ph), 5·50 (CH)
(II; R^1 = R^2 = Me, *n* = 3)	2·70	6·13	8·35 (Me)
(II; R^1 = R^2 = Me, *n* = 7)	2·70	6·13	8·40 (Me)
(II; R^1 = Me, R^2 = Et, *n* = *n*)	2·75	6·4—6·3	8·15—8·5 (q, *J* 6·5 overlapping a singlet, Me/Et)

[a] All peaks as singlets in $CDCl_3$ unless otherwise indicated; dd, AB-type pair of doublets. [b] Benzylic CH_2 group, no S atoms present. [c] Prepared from disodium *m*-xylene-αα′-dithiolate and dibromomethane. [d] No aromatic assignment as spectrum obtained in phenol. [e] τ 6·12, 6·29 (dd, *J* 13·5) in [$^2H_5$]pyridine. [f] Polymer mixture.

TABLE 6

M.p.s and analytical data for compounds (I)—(IV)

Compound	R^1	R^2	*n*	M.p. (°C)	Formula	Found (%) C	H	S	*M* [a]	Required (%) C	H	S	*M*
(I)	H	H	5	Wax	$(C_9H_{10}S_2)_6$				1085				1093
(I)	H	Me	*n*	Resin	$(C_{10}H_{12}S_2)_n$								
(I)	H	Ph	1	209—211	$(C_{15}H_{14}S_2)_2$	69·9	5·4	24·2	470	69·7	5·4	24·9	517
(I)	H	Ph	6	53—57	$(C_{15}H_{14}S_2)_{17}$	69·5	5·5	24·35	1824				1809
(I)	H	*o*-MeC_6H_4	*ca.* 34	93—95	$(C_{16}H_{16}S_2)_{35}$	70·4	5·9	23·9	9180	70·55	5·9	23·55	9248
(I)	Me	Me	1	249—250	$(C_{11}H_{14}S_2)_2$	62·7	6·6	30·05	445 [b]	62·8	6·7	30·4	420
(I)	Me	Me	*ca.* 13	100—102	$(C_{11}H_{14}S_2)_{14}$	62·3	6·7	30·3	3280 [c]				2943
(I)	Me	Et	1	177—180	$(C_{12}H_{16}S_2)_2$	64·3	7·2	29·0	478	64·25	7·2	28·55	449
(I)	Me	Ph	1	218—220	$(C_{16}H_{16}S_2)_2$	70·6	6·2	23·9	532	70·5	5·9	23·6	545
(I)	Me	Ph	*n*	203—205	$(C_{16}H_{16}S_2)_n$								
(I)	Et	Et	1	206—207	$(C_{13}H_{18}S_2)_2$	65·0	7·9	27·5	535	65·5	7·6	26·9	477
(I)	Et	Et	*ca.* 11	103—105	$(C_{13}H_{18}S_2)_{12}$	65·2	7·9	27·2	2665				2622
(II)	H	Ph	1	239—240	$(C_{15}H_{14}S_2)_2$	69·75	5·45	24·55	519	69·75	5·45	24·8	517
(II)	H	Ph	*ca.* 12	118—120	$(C_{15}H_{14}S_2)_{13}$	70·3	5·55	24·2	3425				3359
(II)	Me	Me	3	192·5—193	$(C_{11}H_{14}S_2)_4$	62·3	6·9	30·85	777	62·8	6·7	30·4	841
(II)	Me	Me	7	123—124	$(C_{11}H_{14}S_2)_8$	62·4	6·8	30·2	1670				1682
(II)	Me	Et	*n*	Resin	$(C_{12}H_{16}S_2)_n$								
(III)	H	Ph	*ca.* 20	Resin	$(C_{12}H_{16}S_2)_{21}$				4750				4712
(III)	Me	Me	1	119—120	$(C_8H_{16}S_2)_2$	54·9	9·2	36·55	377·5	54·5	9·2	36·3	353
(III)	Me	Et	*n*	Resin	$(C_9H_{18}S_2)_n$								
(III)	Me	Ph	*n*	Resin	$(C_{14}H_{20}S_2)_n$								
(IV)	Ar = Ph			Oil	$C_{17}H_{20}S_2$	70·55	7·0	21·9		70·8	7·0	22·2	
(IV)	Ar = *m*-MeC_6H_4			Oil	$C_{19}H_{24}S_2$	70·8	7·1	19·5		72·1	7·65	20·25	

[a] Molecular weights were determined ebullioscopically in benzene. [b] 444 by vapour pressure method in benzene. [c] 2720 by vapour pressure method in benzene.

under high dilution conditions to give a low yield of tetrathia[5,5]metacyclophane (I; $R^1 = R^2 = H$, $n = 1$).

The earlier work [3,4] described the successful preparation of crystalline cyclic thioacetals from *m*-xylene-αα′-dithiol and pentane-1,5-dithiol with symmetrical ketones only, and the comparable behaviour of the two dithiols was ascribed to the size of the heterocyclic rings of the products, which in both cases were sixteen membered. The formation of thioacetals from aromatic aldehydes and *p*-xylene-αα′-dithiol was taken to be indicative of the greater ease of formation of paracyclophanes of type (II) compared with that of the metacyclophanes of type (I), since the former included a larger, eighteen-membered ring.

Examination of models suggested that, despite steric crowding in the [5,5]metacyclophanes, the possible 3- and 14-substituents could be any combination of hydrogen, alkyl, or aryl. This was because both these substituents could be orientated away from the crowded centre of the molecule. The results in Table 2, in which [5,5]metacyclophanes were obtained from most of the carbonyl compounds examined, appear to bear out this suggestion.

Formaldehyde and acetaldehyde were notable exceptions. The conformational randomness of the monothiohemiacetal dimer intermediate (see Figure) compared with the dimer transition state when one of the substituents was hydrogen possibly reduced the likelihood of ring closure to form a simple [5,5]metacyclophane. This could also have accounted for the higher yield of the [5,5]metacyclophane (I; R^1 = Me, R^2 = Ph) compared with that of compound (I; $R^1 = H$, R^2 = Ph), despite the smaller steric crowding in the latter.

A further reduction of conformational randomness in the monothiohemiacetal dimer intermediate when $R^1 = R^2$, might account for the good yields of the [5,5]metacyclophanes (I; $R^1 = R^2$ = Me) and (I; $R^1 = R^2$ = Et). This *gem*-dialkyl effect has been observed before.[6]

Reaction with *o*-tolualdehyde, to give (I; $R^1 = H$, $R^2 = o\text{-}MeC_6H_4$), was possibly a unique case in that whilst conformational randomness was probably reduced by the aromatic ring, additional steric hindrance was introduced by the *ortho*-methyl group.

Despite the greater ring size of the [5,5]paracyclophanes, models indicated that the 3- and 14-disubstituted compounds, *viz.* (II; R^1 = Me, R^2 = Me, Ph, and Et) (see Tables 3 and 4), were more sterically hindered than the corresponding [5,5]metacyclophanes. This was because one of the substituents was always orientated towards the crowded centre of the molecule. Such reasoning explained both the absence of [5,5]paracyclophanes in the products obtained from ketones and the good yields reported [4] with aromatic aldehydes and *p*-xylene-αα′-dithiol and obtained in this work with benzaldehyde. Of particular interest was the formation of the oligothia[5,5]paracyclophane (II; $R^1 = R^2$ = Me, $n = 7$) from acetone and *p*-xylene-αα′-dithiol, as any *gem*-dialkyl effect would have favoured [5,5]paracyclophane formation. Clearly this effect was insufficient to overcome the steric inhibition, as demonstrated by the 96% yield of oligomer obtained with boron trifluoride as the catalyst.

Of the carbonyl compounds reacted with pentane-1,5-dithiol only acetone yielded a crystalline product, 2,2,10,10-tetramethyl-1,3,9,11-tetrathiacyclohexadecane (III; $R^1 = R^2$ = Me, $n = 1$) reported by Autenrieth and Geyer,[5] who also reported the analogous tetraethyl compound (III; $R^1 = R^2$ = Et, $n = 1$).

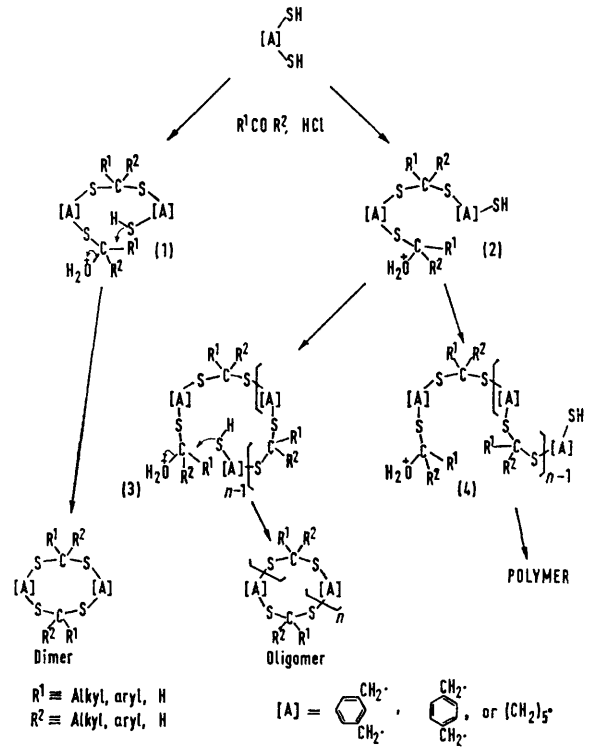


FIGURE (1) Monothiohemiacetal dimer intermediate (in conformations favourable for cyclization to dimer); (2) monothiohemiacetal intermediate (in conformations unfavourable for cyclization to dimer); (3) monothiohemiacetal oligomer intermediate (in conformations favourable for cyclization to oligomer); (4) monothiohemiacetal oligomer intermediate (in conformations unfavourable for cyclization to oligomer)

Examination of models of this ring system indicated little steric crowding because of the mobility of the pentamethylene chains. This lack of rigidity relative to the cyclophanes was possibly the reason for our failure to obtain other substituted tetrathiacyclohexadecanes. The very random nature of the monothiohemiacetal dimer intermediates formed from carbonyl compounds and pentane-1,5-dithiol would make ring closure to obtain small ring compounds very difficult. This correlated with results obtained by Oae and his co-workers [7] on treating acetone and dithiols with an acid catalyst. Propane-1,3-dithiol gave a monomer in 75% yield, and butane-1,4-dithiol gave only a low yield of

[6] A. T. Blomquist, E. S. Wheeler, and Y. Chu, *J. Amer. Chem. Soc.*, 1955, **77**, 6307.

[7] S. Oae, W. Tagaki, and A. Ohno, *Tetrahedron*, 1964, **20**, 427, 437; S. Oae, W. Tagaki, K. Uneyama, and I. Minamida, *ibid.*, 1968, **24**, 5271, 5283.

monomer with a polymeric solid, which may have been the dimer, as the major product. It would appear that as the chain length is increased the greater conformational randomness increasingly reduces the extent of monomer formation. Extending this argument to the pentane chain, the mobility possibly makes even dimer formation difficult, but is sufficiently reduced by the *gem*-dialkyl effect in the cases of acetone and pentan-3-one to allow formation of the dimer transition state. With other carbonyl compounds only polymeric products were obtained.

Absorption Spectra.—Interest in the i.r. spectra was centred on the absorption due to the benzene rings, C–S bonds, and a group of bands attributed to the $\cdot S\cdot C(CH_2R)_2\cdot S\cdot$ group.

The C–S vibration appeared as a strong band near 730 cm^{-1} in the thiacyclophanes prepared, and in many cases another weaker band near 750 cm^{-1} was also observed. In the non-cyclic analogues (IV; Ar = Ph and *m*-MeC_6H_4) the band in the 750 cm^{-1} region was less intense and was weaker still in the tetrathiacycloalkanes (III; R^1 = H, R^2 = Ph and R^1 = Me, R^2 = Me, Ph, and Et). This feature of the spectra in the thiacyclophanes studied was distinguished from that due to aromatic absorption by the absence of any band shift when the spectra of bromoform solutions were observed. The sharpness of the band near 730 cm^{-1} in the thiacyclophanes was possibly associated with restriction of rotation about the C–S bond.

An outstanding feature of the i.r. spectra of all the acetone thioacetals (I, II, and III; $R^1 = R^2$ = Me) and (IV; Ar = *m*-MeC_6H_4) was a group of bands at 1080, 1100, and 1140 cm^{-1}. The 1080 cm^{-1} band was probably partly aromatic absorption, as 1,3-disubstituted benzene rings absorb in this region, but the exceptional intensity of this band could not be attributed to 1,3-disubstituted aromatic absorption alone. This was borne out by the spectrum of tetramethyltetrathiacyclohexadecane (III; $R^1 = R^2$ = Me), which exhibited only a medium intensity band at 1080 cm^{-1}. The spectra of the remaining compounds revealed that this group of bands was only present when the central group had the $\cdot S\cdot C(CH_2R)_2\cdot S\cdot$ structure, *e.g.* some tetrathia[5,5]metacyclophanes exhibited the following absorptions: (I: R^1 = Me, R^2 = Et) 1080, 1090, and 1126 cm^{-1}; (I: $R^1 = R^2$ = Et) 1078, 1090, and 1129 cm^{-1}; (I: R^1 = H, R^2 = Me) 1084 cm^{-1}; (I; R^1 = Me, R^2 = Ph) 1061 and 1077 cm^{-1}.

The modes giving rise to these bands could not be positively assigned, but Scott and McCullogh [8] and Sheppard [9] reported similar less intense bands for aliphatic sulphides of the type $\cdot S\cdot CHMe_2$ and $(MeCH_2\cdot S\cdot)_2$.

The thiacyclophanes exhibited almost no bands at 815 ± 20 cm^{-1} characteristic of aromatic 1,4-disubstitution or at 700 and 800 cm^{-1} for 1,3-disubstitution. Randle and Whiffen [10] attributed absorption in this region to out-of-plane deformation, and the absence of such absorption in these compounds might reflect the presence of steric effects.

The u.v. spectra of the thiacyclophanes, particularly the virtual lack of fine structure, suggested distortion of the benzene ring and/or transannular electronic interaction. The benzene fine structure was distinct in the spectra of the various analogous compounds studied, *e.g.* the acetone thioacetals (IV; Ar = Ph and *m*-MeC_6H_4), [5,5]metacyclophane,[11] and [5,5]paracyclophane,[12] which all closely resembled the corresponding xylene. Thus, the loss of fine structure in the spectra of the thiacyclophanes did not appear to be a consequence of either the nature of the bridge or of cyclization to a [5,5]cyclophane, but a result of the two together. Ingraham [13] stated that lack of fine structure in cyclophanes was the result of a constraint much greater than that found in non-cyclic models. In [2,2]paracyclophane this was probably a consequence of interpenetration of the π-electron clouds of the two benzene rings, *i.e.* transannular electronic interaction, whilst torsional or steric effects brought about a similar loss of fine structure in cyclophanes such as [8]paracyclophane.[14]

Tetrathia[5,5]metacyclophane (I; $R^1 = R^2$ = H, n = 1) exhibited weak fine structure, no torsional band shifts, and an increase in band intensity, possibly indicating increased conjugation compared to *m*-xylene. Since this compound would have little steric hindrance due to to the lack of bridge substituents these observations suggested some transannular interaction.

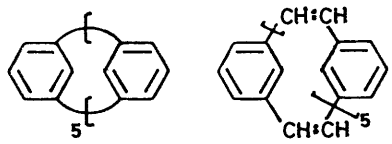
N.m.r. Spectra.—Apart from the n.m.r. spectra of some polymeric products, which exhibited line broadening because of the viscous solutions used, the n.m.r. spectra were readily interpreted in terms of the tetrathia[5,5]-cyclophanes and therefore supported the structural assignments previously made by Autenrieth and his co-workers.

The chemical shift values of the benzylic protons, and of the 3- and 14-substituents were as expected. In compounds (I; R^1 = H, R^2 = Ph, n = 1 and n = 6), (I; R^1 = H, R^2 = *o*-MeC_6H_4, n = *ca.* 34), (II; R^1 = H, R^2 = Ph, n = 1 and n = *ca.* 12) with hydrogen and aryl substituents (R^1 = H, R^2 = Ar), the signals due to the benzylic protons were split to give an AB-type spectrum.

Failure to observed splitting of the signal due to the benzylic protons which exhibited singlets at room temperature when spectra were observed at temperatures down to −50 °C suggested either the possibility of a low energy barrier to conformational interchange or the existence of one strongly favoured conformation in which the benzylic protons were effectively magnetically equivalent.

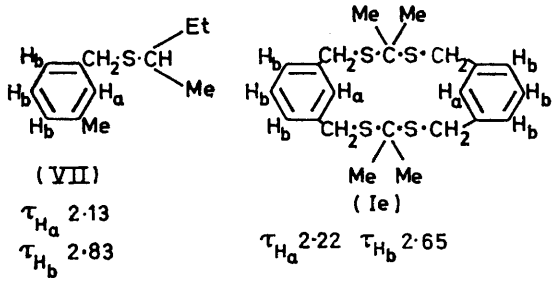
[8] D. W. Scott and J. P. McCullogh, *J. Amer. Chem. Soc.*, 1958, **80**, 3554.
[9] N. Sheppard, *Trans. Faraday Soc.*, 1951, **46**, 533.
[10] R. R. Randle and D. H. Whiffen, ' Conference on Molecular Spectroscopy, 1954,' paper 12.
[11] S. Bien, *J. Chem. Soc.*, 1960, 4015.
[12] D. J. Cram, N. L. Allinger, and H. Steinberg, *J. Amer. Chem. Soc.*, 1954, **76**, 6132.
[13] L. L. Ingraham, *J. Chem. Phys.*, 1957, **27**, 1228.
[14] D. J. Cram and G. R. Knox, *J. Amer. Chem. Soc.*, 1961, **83**, 2204.

The three aromatic protons [H_b, H_c see formula (I)] in the outer ring of the metacyclophanes were distinctly separated, as a somewhat broad peak, from the isolated protons [H_a, see formula (I)], *viz.* 11- and 22-H, *etc.* The shift values for the signals of these three protons were similar to those of the aromatic protons in the paracyclophanes and [5,5]metacyclophane itself, but the remaining proton (H_a) was downfield by *ca.* 0·5 p.p.m. (30 Hz) in the tetrathia[5,5]metacyclophanes (I; R^1 = H, R^2 = Ph; R^1 = Me, R^2 = Me and Et; $R^1 = R^2$ = Et) and *ca.* 0·1 p.p.m. (6 Hz) in the oligomers (I; $R^1 = R^2$ = Me, n = *ca.* 13), (I; $R^1 = R^2$ = Et, n = *ca.* 11). Similar downfield shifts have been found in [0,0^5]metacyclophane [15] (V) and [2,2^5]metacyclophane [16] (VI).



(V) (VI)

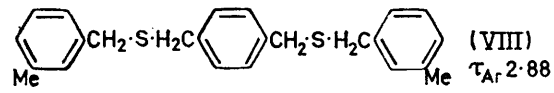
The shift in both these unsaturated compounds was attributed to π-conjugation in the macrocyclic ring, which also involved the unsaturated bridge in (VI). However, the spectrum of α-s-butylthio-*m*-xylene [17] (VII) also exhibited this downfield shift of the flanked proton H_a although π-conjugation was unlikely in this compound.



(VII) (Ie)

τ_{H_a} 2·13 τ_{H_a} 2·22 τ_{H_b} 2·65

τ_{H_b} 2·83

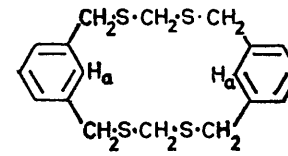


(VIII) τ_{Ar} 2·88

This shift was not observed in the sulphide (VIII),[17] which led to the conclusion that the downfield shift might be accounted for by a steric constraint forcing the proton H_a into the π-field of the aromatic ring. This effect has been observed by several workers,[18,19] and would explain the observed effect for the non-cyclic compound (VII).

An alternative explanation is that the close proximity of the benzene rings in the metacyclophanes might have resulted in a mutual augmentation of the anisotropic effect in the region of the H_a protons.

The spectrum of tetrathia[5,5]metacyclophane (I; $R^1 = R^2$ = H, n = 1), which was less sterically crowded because of the absence of substituents, showed that the signal due to the flanked proton H_a was 0·2 p.p.m. (13 Hz) upfield of the other aromatic protons, typical of a transannular aromatic ring anisotropic shielding effect frequently found in cyclophanes. This result was similar to that found by Burri and Jenny [20] with [2,2^n]metacyclophanes.



(I; $R^1 = R^2$ = H) τ_{H_a} 3·02

In cyclophanes transannular interaction also causes a small downfield shift of the signal due to the benzylic protons but little difference was observed between the signal due to these protons in the unsubstituted tetrathia-[5,5]metacyclophane (I; $R^1 = R^2$ = H, n = 1) and the various substituted analogues. This was possibly because small transannular interactions occurred in all the [5,5]compounds but in the substituted analogues the weak transannular effect was dominated by the steric or π-field effects. The benzylic protons in the [5,5]compounds were about 0·1 p.p.m. (6 Hz) downfield from these protons in the oligomers. Since the latter were not expected to exhibit transannular interaction this observation was understandable.

The n.m.r. spectra of thiacyclophanes with the ·CH_2·S·CHAr·S·CH_2· type bridge provided evidence for the absence of eclipsed sulphur atoms. These compounds exhibited AB-type spectra with large coupling constants (*ca.* 13 Hz) whereas Allingham, Cookson, and Crabb [21] found coupling constants of adjacent methylene groups were considerably reduced by eclipsed sulphur atoms (*ca.* 6 Hz).

EXPERIMENTAL

The thiols were initially prepared by known methods [3-5] from the corresponding bromides. However, better overall yields (and a more agreeable laboratory atmosphere) were obtained by converting the bromide into the thiocyanate and reducing the latter with lithium aluminium hydride in ether at room temperature.[22]

The thioacetals were prepared by the following general methods.

Method A.—The dithiol (0·01 mol) and the carbonyl compound (0·02 mol) were mixed and cooled < −10 °C. Dry hydrogen chloride gas was passed for 10 min into the stirred mixture. The solid mixture was left to stand in the cooling

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[16] K. Burri and W. Jenny, *Helv. Chim. Acta*, 1967, **50**, 2542.
[17] R. E. Busby and D. Huckle, unpublished results.
[18] F. A. L. Anet, A. J. R. Bourn, P. Carter, and S. Winstein, *J. Amer. Chem. Soc.*, 1965, **87**, 5247.
[19] F. Vogtl, *Tetrahedron*, 1969, **25**, 3237.
[20] K. Burri and W. Jenny, *Helv. Chim. Acta*, 1967, **50**, 1978.
[21] Y. Allingham, R. C. Cookson, and T. A. Crabb, *Tetrahedron*, 1968, **24**, 1989.
[22] J. Strating and H. J. Backer, *Rec. Trav. chim.*, 1950, **69**, 638.

bath and the excess of acid vapours were removed by drawing a current of air across the solid which was then purified by trituration and/or recrystallization.

Method B.—Molar proportions of dithiol and carbonyl compound as in (A) were dissolved in anhydrous ether (25 ml) and cooled to < -5 °C. A saturated ethereal solution of hydrogen chloride gas (30 ml) was added and the solution left in a stoppered bottle at *ca.* 0 °C for up to a week. The resulting solid and/or solution were examined.

Method C.—Equimolar proportions of dithiol and carbonyl compound were dissolved in anhydrous ether (0·01 mol in 100 ml ether), boron trifluoride–ether (3 ml) was added, and the solution left at *ca.* 0 °C for up to a week. The resulting solid and/or solution were examined.

Typical Purification Procedure.—**4,4,14,14-***Tetramethyl-***3,5,13,15-***tetrathiatricyclo*[15,3,1,$1^{7,11}$]*docosa*-1(20),7,9,11-(22),17(21),18-*hexaene* (I; $R^1 = R^2 = Me$, $n = 1$) *and oligomer.* Procedure (A) gave a solid which was recrystallized from chloroform–ethanol, as described by Autentrieth and Beuttel,[3] but the product had a much lower m.p. than reported. The product was therefore extracted (Soxhlet) with boiling ethanol for 3 days. The solid in the thimble was recrystallized from benzene–light petroleum (b.p. 60—80 °C) as white prisms of the oligomer (39%), m.p. 100—102 °C. The cooled ethanolic solution gave white needles, m.p. 249—250 °C (lit.,[3] 254 °C), of the metacyclophane (I; $R^1 = R^2 = Me$, $n = 1$) (35%).

Procedure (B) gave a solid, which was extracted with ethanol as before. The solid from the thimble, m.p. 103—105 °C, of identical molecular weight to that obtained by procedure (A), was obtained in 13% yield. The solid from the cooled ethanol of m.p. 250—257 °C was obtained in 35% yield.

Procedure (C) gave a solid which was separated by boiling ethanol, as above, into two fractions of different molecular weight. The low molecular weight compound was obtained in 44% and the oligomer in 20% yield.

For this particular compound an additional procedure was based on that described by Shahak and Bergmann.[23] Equimolar (0·015 mol) proportions of *m*-xylene-αα′-dithiol and acetone in pure, dry dioxan (20 ml) were stirred at room temperature whilst 30% w/w concentrated H_2SO_4–MeOH (25 ml) was added dropwise. No temperature rise was observed, and crystallization rapidly commenced. The mixture was stirred for 1 h, and left overnight, the product was filtered off, washed with dioxan, dried, and separated into two components by ethanol extraction as above. Yields were 40% of low molecular weight compound and 20% of the oligomer.

The sulphone from the metacyclophane (I; $R^1 = R^2 = Me$, $n = 1$) was prepared by treatment with 100 vol. H_2O_2 in glacial acetic at 3 °C for 5 days. The tetrasulphone was obtained as white needles, m.p. 320—324 °C (decomp.) (lit.,[3] 300 °C) (Found: C, 48·7; H, 5·4; S, 3·8. $C_{22}H_{28}O_8S_4$ requires C, 48·2; H, 5·1; S, 23·4%). Analyses and m.p.s of the various products are given in Table 6, and yields in Tables 1—4.

The acetone thioacetals from 2,2-bisbenzylthiopropane (IV; Ar = Ph) and 2,2-bis(*m*-methylbenzylthio)propane (IV; Ar = *m*-MeC_6H_4) were obtained in a pure state by removal of solvent after employing method A.

3,5,13,15-*Tetrathiatricyclo*[15,3,1,$1^{7,11}$]*docosa*-1(20),7,9,11-(22),17(21),18-*hexaene* (I; $R^1 = R^2 = H$, $n = 1$) *and oligomer.* These were prepared as follows. (i) Method A was used, with paraformaldehyde as the source of formaldehyde. No product separated out after 7 days. The solvent was evaporated off, the residual oil was dissolved in chloroform, washed with 2N-NaOH and then water, and dried ($CaSO_4$). Removal of solvent gave a pink, waxy solid, shown to be the required product (I; $R^1 = R^2 = H$, $n = 5$) by the n.m.r. spectrum; the absence of the aromatic resonance at τ 3·02 indicated the absence of the low molecular weight compound.

(ii) Disodium *m*-xylene-αα′-dithiolate was prepared by addition of *m*-xylene-αα′-dithiol (3·4 g, 0·02 mol) to sodium (1·85 g, 0·08 mol) dissolved in absolute ethanol. This solution was added dropwise over 8 h to a vigorously stirred solution of dibromomethane (6·96 g, 0·04 mol) in absolute ethanol (200 ml) under reflux in a nitrogen atmosphere. After completion of addition the mixture was stirred and heated under reflux for 1 h, the ethanol was evaporated off and the residue was dissolved in chloroform and water. The organic layer was separated off, washed with water, 2N-NaOH, water, and dried (Na_2SO_4). Removal of solvent yielded an oil (2·6 g) which was triturated under ethanol–acetone to give a white solid. Recrystallization from ethanol gave white needles of (I; $R^1 = R^2 = H$, $n = 1$) (0·15 g), m.p. 125—126 °C [Found: C, 59·0; H, 5·55; S, 34·8%; *M* (ebullioscopic in benzene), 380. $C_{18}H_{20}S_4$ requires C, 59·3; H, 5·5; S, 35·2%; *M*, 364·4]. The mother liquors from trituration and recrystallization were combined and evaporated to dryness yielding an oil (2·4 g). Spectral analysis indicated some dibromomethane, but the oil was largely the oligomeric compound (I; $R^1 = R^2 = H$, $n = 5$).

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[1/500 *Received*, 7*th April*, 1971]

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