The First [2.2]Phane Diagonally Hetero-substituted in the Bridges

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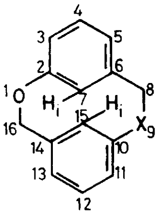
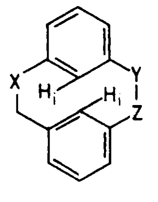
The novel sulphide (**1a**) is much less stable than its isomer (**2a**), and the stable sulphone (**1b**) could be resolved into the helical enantiomers ($t_{\frac{1}{2}}$ 92.5 min at 100 °C; free enthalpy of racemisation 127 kJ/mol; n.m.r. and c.d. data and results of molecular mechanics calculations are compared to those of isomeric helical molecules.

Owing to increasing transannular ring strain it appeared not to be possible to shorten the bridge-lengths in [2.2]phane hydrocarbons. In 1984 we reported on [2.2]metacyclophanes substituted in the 1,10-position by oxygen, nitrogen, and sulphur.[1] Their interesting chiroptical properties should be compared with those of hitherto unknown diagonally substituted isomeric phanes (**1a,b**), which should also be helical-chiral on account of the different C–O/C–S bonds in the two bridges (two-bladed propellers).

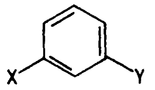
The [2.2]metacyclophanes (**1a,b**)† were obtained after a sequence of eight steps starting with the compounds (**3**) and (**5**). After many unsuccessful runs the decisive intramolecular cyclisation (**11**) → (**1a**) succeeded in yields of less than 1%. Special conditions included application of the 'caesium-effect' and high dilution [the bromide (**11**) (2.0 g, 6.47 mmol) in benzene (250 ml) was slowly added dropwise into refluxing



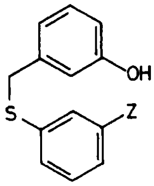
(**1a**) X = S[a]
(**1b**) X = SO_2



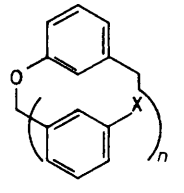
	X	Y	Z
(**2a**)	O	S	CH_2
(**2b**)	O	SO_2	CH_2
(**13**)	CH_2	CH_2	SO_2
(**14**)	CH_2	CH_2	S
(**15**)	CH_2	CH_2	O
(**16**)	S	N-tosyl	CH_2



	X	Y
(**3**)	CH_2OH	OH
(**4**)	CH_2Br	OH
(**5**)	H	CO_2H
(**6**)	SO_2Cl	CO_2H
(**7**)	SH	CO_2H
(**8**)	SH	CO_2Et



	Z
(**9**)	CO_2Et
(**10**)	CH_2OH
(**11**)	CH_2Br



(**12**); X = S, SO_2; n = 2, 3

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[a] Numbers on this formula correspond to *X*-ray analysis, they differ from cyclophane numbering, see ref. 1.

† Satisfactory elemental analyses and spectroscopic data were obtained for all new compounds.

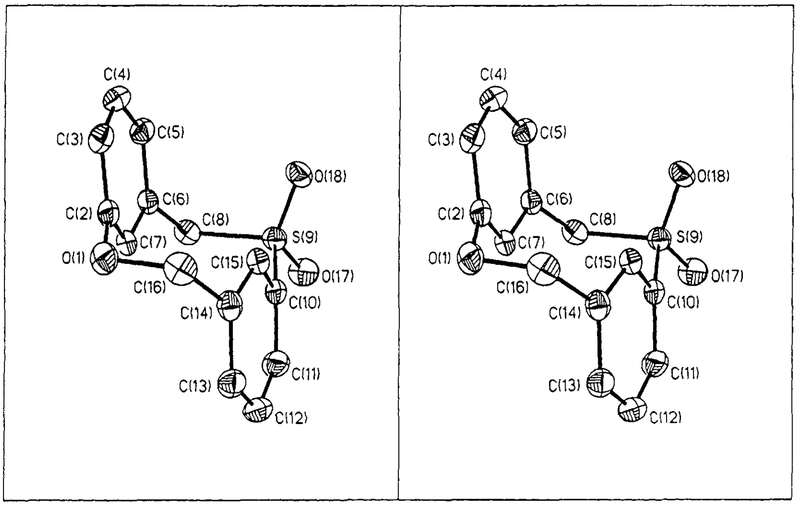

Figure 1. Stereo picture of the crystal structure of (**1b**); $\alpha = 3.9°$, $\beta = 4.1°$, $\gamma = 8.1°$, $\delta = 7.1°$; $C(7) \cdots C(15)$ distance = 2.639 Å

Table 1. Comparison of ^1H n.m.r. data of the H_i-protons in some [2.2]phanes.

	δ		δ
(**1a**)	5.08, 3.93	(**13**)	4.52, 5.19
(**1b**)	5.35, 4.12	(**14**)	4.32, 4.85
(**2a**)	4.52, 4.44	(**15**)	4.46, 3.86

Table 2. Comparison of X-ray and MMPMI[6] calculation results.

	Distance/pm					
	Intra-annular C–C		O–C		C–S	
	MMPMI	X-Ray	MMPMI	X-Ray	MMPMI	X-Ray
(**2a**)	275	262	142	147	183	185
(**1b**)	279	263	142	146	184	182
(**1a**)	275	—	142	—	183	—

ethanol (2 l) during 10 h]. The low yields in the ring formation reaction (**11**) → (**1a**) may be due to the ring strain of the ten-membered monomeric product (**1a**). In addition to high molecular weight products, oligomeric compounds of type (**12**) with $n > 2$ were obtained in high yields.

Surprisingly the strained 1,9-oxathia[2.2]metacyclophane (**1a**) (m.p. 107—109 °C) is not sufficiently stable even at room temperature to be studied conveniently. It was therefore transformed to the sulphone (**1b**) (m.p. 175—178 °C) using hydrogen peroxide/anhydrous acetic acid/benzene at room temperature [the half-life of (**1a**) at room temperature is in the range of days depending on purity and conditions].

The sulphone (**1b**) turned out to be stable. Its reduction to the sulphide (**1a**) failed. As stated in the literature[2—4] the reduction is followed by further reactions. This was confirmed by the irreversible course of the cyclic voltammogram of (**1b**).[‡]

The 200 MHz ^1H n.m.r. spectra of the phanes (**1a,b**) show AB patterns for the geminal H-atoms of the bridges typical of conformationally fixed [2.2]metacyclophanes. The characteristic chemical shifts at high field-strength of the internal hydrogens (H_i) are summarized in Table 1 and compared to data for related [2.2]phanes.

The ^1H n.m.r. absorptions of (**2a**) and (**1a,b**) show significant differences, which hint at characteristic structural dissimilarities. The chemical shifts of the H_i-protons illustrate that there is a correlation between upfield shift and geometry.

Figure 1 gives a stereo drawing of the crystal structure resulting from the X-ray analysis of racemic (**1b**).[5] The X-ray analysis proves the *anti*-conformation of the aromatic rings, which is responsible for the high field shifts of the intra-annular hydrogen atoms H_i. There are strong differences between the X-ray structures of (**2**) and (**1b**) on the one hand and molecular mechanics MMPMI[6] calculations of both compounds on the other. The angles α, β, γ, and δ,[§] typical for helical cyclophanes,[1] as well as the C–S and C–O bond lengths differ clearly. The measured and calculated distances and angles show strong differences; as a consequence it will remain difficult to predict, using the results of structures previously synthesized, the geometries of unknown [2.2]metacyclophanes. Calculations therefore cannot as yet replace the synthesis and structural analysis of such highly strained molecules. Table 2 gives some differences between the X-ray structural and molecular mechanics[6] data. As a result there seems to be no linear correlation between the high-field shift of the intra-annular H_i-hydrogens and the ring strain as can be seen from the internal C–C distance of the corresponding [2.2]phanes (**1a,b**) and (**2a**).

[‡] We are obliged to Professor E. Steckhan and Professor E. Niecke, Bonn University, for assistance in the electrochemical and X-ray structure analyses.

[§] *Crystal data* for (**1b**): $C_{14}H_{12}O_3S$, $M = 236.3$, monoclinic, space group $P2_1/c$, colourless crystals, dimensions $0.5 \times 0.5 \times 0.5$ mm^3, $a = 8.344(2)$, $b = 5.405(1)$, $c = 25.887(4)$ Å, $\beta = 91.96(2)°$, $U = 1.167$ nm^3, $Z = 4$, $D_c = 1.34$ g cm^{-3}, $\mu(\text{Mo-}K_\alpha) = 0.25$ mm^{-1}. 2036 Symmetry independent reflections ($2\theta_{\text{max.}} = 50°$), 1740 reflections with $|F| > 4\sigma(F)$ were used for the structure solution (direct methods) and refinement (163 parameters), non-hydrogen atoms were refined anisotropically, H-atoms localized by difference electron density determination and refined using a 'riding' model. $R = 0.037$ [$R_w = 0.042$, $w^{-1} = \sigma^2(F) + 0.0003 F^2$]. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Cystallographic Data Centre. See Notice to Authors, Issue No. 1.

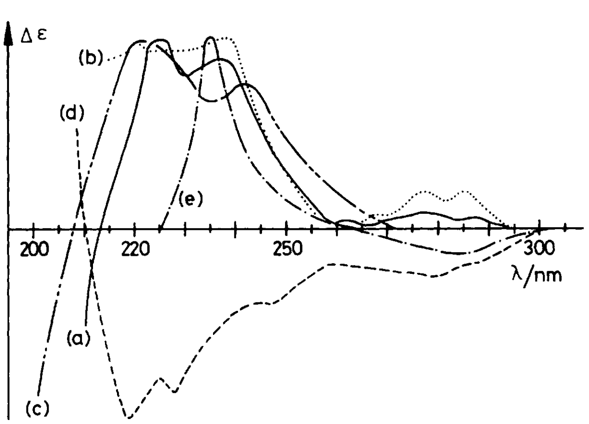

Figure 2. C.d. spectra of (**1b**) compared to related heterocyclic [2.2]metacyclophanes: (a) (**14**); (b) (**15**); (c) (**2a**); (d) (**13**); ¶ (e) (**1b**).

The separation of the enantiomers of the new chiral phane (**1b**) was successfully accomplished using the baseline separation obtained with Okamoto's resin[7] and h.p.l.c.: (+)-enantiomer: $[\alpha]_{365}^{21}$ 123.2°, (−)-enantiomer $[\alpha]_{365}^{21}$ −136.21° (in methanol). The optical rotations of sulphides and sulphones[8] measured before show differences of about 800°. The optical rotation of (−)-(**2a**)[1] is found to be $[\alpha]_{365}^{RT}$ −1545°. For the pure enantiomer of (**1a**) even higher optical rotations may be presumed from this result. The enantiomers of (**1b**) are stable at room temperature; the half-life of racemisation at 100 °C was determined to be 92.5 min from the Eyring equation [$\Delta G^{\ddagger}$ for (**1b**) is determined to 127 kJ/mol; for (**2**) $\Delta G^{\ddagger} = 121$ kJ/mol].

The c.d. spectra of (**1b**), (**2a**), and (**13, 14, 15**) are displayed in Figure 2. All phanes compared show intense Cotton effects in the wavelength range of 220—250 nm. The new sulphone (**1b**) exhibits only one positive Cotton effect between 220 and 250 nm. The theoretical analysis of these c.d. curves, and their correlation to chromophores and transitions seem not to be easy. The interactions of chromophores in these relatively simple and clearly defined structures is more complicated than is figured out in the present exciton-chirality methods[9] or MO-models.[10,11]

Nevertheless it will be important to develop new rigid helical phane geometries [lacking any other chirality elements[12] like (**1a,b**)] to obtain more facts and detailed information for future correlations.[13—15]

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¶ The structure/chiroptic correlations are remarkable with respect to that of the sulphone (**13**) described previously; the relative configuration of this sulphone should be determined again.