

Conformational Changes in the Sulfur Analogs
of 11- and 12-Membered Metacyclophanes¹

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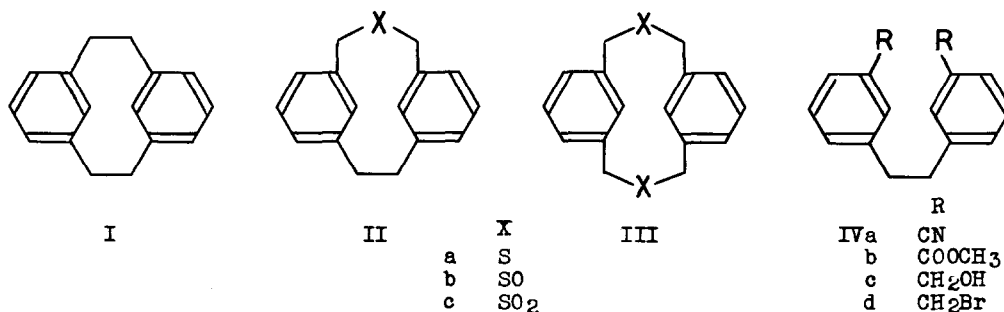
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Recently we have examined the high-temperature NMR spectra of (2.2)metacyclophane (I) and interpreted the results as the indication of rigid nature of the 10-membered ring system.^{2,3} Activation energy required for interconversion between two chair forms was estimated to be more than 26-28 kcal/mole,^{4,5} which was large enough for each of the conformers to exist as a stable species. This was proved to be the case by carrying out the optical resolution of its certain derivatives.^{2,3,6}

Obviously the inversion rate would be dependent on the structural modifications, such as ring size or substitution on the bridge. The syntheses of sulfur analogs of 11- and 12-membered metacyclophanes (II and III) were designed to determine the ring size limitation in the restricted inversion and to obtain a deeper insight into the conformational mobility in the lower members of metacyclophanes.

The treatment of 3,3'-bis(bromomethyl)biphenyl (IVd), obtained through a sequence of reactions starting from 3,3'-dicyanobiphenyl (IVa) via IVb and IVc, with sodium sulfide in methanol under the high-dilution conditions produced 2-thia(3.2)metacyclophane (IIa), mp 90-92°, in a 29.6% yield. The structure was supported by analytical and spectral data.

The molecular weight was deduced from the mass spectrum which showed a



parent peak at m/e 240. The NMR spectrum determined at -54.0° was also indicative of the structure by showing a two-proton signal at δ 5.13 (inner aryl), a four-proton AB system at δ 3.45 and 3.84 (S-methylene, $J=13.4$ cps) and a four-proton A_2B_2 system at δ 2.22 and 3.08 (ethylene, analyzed by an AB approximation). A part of the spectrum is shown at the bottom of Fig. I. The appearance of the high-field aryl proton signal is typical to the lower members of the $[m,n]$ metacyclophane structure.

Oxidation of IIa with hydrogen peroxide afforded, depending on the reaction conditions, either 2-thia[3.2]metacyclophane 2-oxide (IIb), mp $132-133^\circ$, or 2,2-dioxide (IIc), mp $169-170^\circ$. The structures were confirmed by analytical and spectral data. Sulfoxide IIb showed an infrared maximum at 1030 cm^{-1} (SO) and an NMR signal for inner aryl protons at δ 4.94 (at room temperature) together with other typical signals. Likewise sulfone IIc showed sulfone bands at 1120, 1300 and 1315 cm^{-1} and a high-field aryl proton signal at δ 5.18.

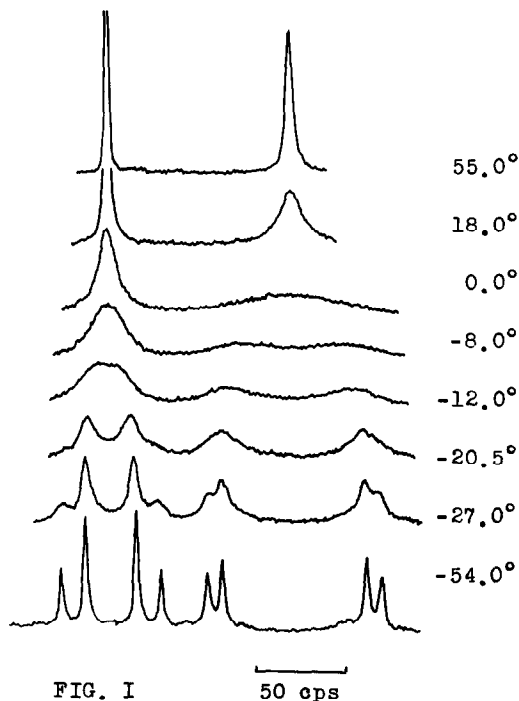
Compared with carbocyclic analogs,^{5,7} these heterophanes offered certain advantages for NMR spectral studies. Incorporation of a sulfur atom not only simplified the methylene signals to an AB system by eliminating complex spin-spin coupling associated with the three-membered carbon bridge but also shifted them to a sufficiently lower field to be observable separately from the ethylene bridge absorption.

Examination of the spectra as a function of temperature using a Varian HA-100 spectrometer revealed that both the ethylene as well as S-methylene groups of IIa and IIc displayed a transition from A_2B_2 and AB patterns respec-

tively at low temperatures to two sharp singlets at higher temperatures as is illustrated by the case of IIa in Fig. I. Activation energy for the inversion was calculated by using the Gutowsky-Holm's equation,⁸ $k/\pi = \sqrt{(\nu^2 - \Delta^2)}/2$, which correlates the inversion frequency k with the chemical shift ν and the frequency separation Δ between the peak maxima at a given temperature. Arrhenius plots of $\ln k/\pi$ vs. $1/T$ using an A_2B_2 part of the spectra showed a good linear relationship.

While the energy barrier for sulfide IIa was calculated to be 8.32 kcal/mole, that for sulfone IIc was found to be as large as 13.7 kcal/mole. The difference could mainly be attributable to the bulkiness of sulfone group compared with bivalent sulfur group. It is then to be expected that sulfoxide IIb requires the activation energy that is intermediate between those of IIa IIc. That this was really the case was confirmed by the calculation of ΔG^\ddagger from coalescence temperature (T_c) and ν . Since the activation energy could principally be estimated by using the AB part of the spectra though less accurately due to smaller ν , it would be possible to deduce the mode of inversion by comparing the spectral changes of both bridges.

Sulfoxide IIb possessed added features and exhibited remarkable temperature-dependent spectra in that not only ethylene and S-methylene proton signals but also inner aryl proton signal experienced a series of transition. Even at the lowest temperature of



-35°, all of the absorptions were clearly recognized as separate patterns. Due to inherent nonequivalence, α -methylene proton signal appeared as a quartet even in an averaged spectrum determined at 99° (in CDBr₃). As the temperature was lowered it further splitted into two sets of AB systems indicating that both of the α -methylene groups became nonequivalent in a frozen conformation. Ethylene bridge protons displayed an ABCD pattern at low temperatures, but, on fast averaging, they gave a sharp singlet. Likewise the inner aryl proton signal experienced coalescence of two peaks observed at low temperatures into one peak at higher temperatures. Pertinent spectral data are summarized in Table I.

Finally, as the check to the ring size limitation, 12-membered bis-sulfide, 2,11-dithis(3.3)metacyclophane (IIIa), mp 155.5-156.5°, m/e 272, was prepared in a 10.0% yield by the treatment of 1,3-bis(bromomethyl)benzene with sodium sulfide under the high-dilution conditions. That the rigidity of the medium-sized ring

TABLE I. Spectral Data^a and Rate Parameters

Compd.	Temp. range, °C (Solvent)	Proton type	δ , ppm	ν , cps	Tc, °C	ΔE^\ddagger kcal/mole
IIa	-54.0 ~ 55.0 (CDCl ₃)	A ₂ B ₂ (CH ₂ CH ₂)	2.22 3.08	86.5	0.5	8.32
		AB (SCH ₂)	3.45 3.84	38.9	-8.0	
IIb	-35.0 ~ 64.5 ^b (CDCl ₃)	ABCD (CH ₂ CH ₂)	2.30 ^c 3.09 ^c	79.7	45.5	ca. 40
		2AB (CH ₂ SOCH ₂)	3.30 4.65	135.4		
			3.69 4.06	37.3		
		inner ArH	4.91 4.99	7.8	11.5	
IIc	6.5 ~ 117.5 (CDBr ₃)	A ₂ B ₂ (CH ₂ CH ₂)	2.32 3.13	81.8	57.5	13.7
		AB (SO ₂ CH ₂)	3.98 4.35	36.9	41.5	

^aOnly temperature-dependent signals are shown. Spectra were recorded with Varian HA-100. Chemical shifts, expressed downfield from TMS as an internal reference, are those determined at the lowest temperatures. ^bSpectra were measured up to 99.0° in CDBr₃. ^cCenter of a pair of doublets determined by decoupling experiments.

system was no longer persisted in this 12-membered homolog was supported by the appearance of methylene proton signal as a sharp singlet at δ 3.62 at room temperature, which remained unsplit even at -80° (in CS_2). The inner aryl protons showed a triplet at almost normal position of δ 6.63. Thus it was clearly demonstrated that the 12-membered metacyclophane existed as a mobile molecule and the energy barrier required for the conformational changes was quite low compared with the lower homologs. Bis-sulfone IIIc, mp $> 260^\circ$, showed a sharp singlet at δ 4.67 (in CF_3COOH) but it was quite insoluble in common solvents and no satisfactory low temperature NMR spectra were recorded.

LITERATURES

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