

## The Effects of Lanthanide Shift Reagents on the NMR Spectra of Diaza- and Dithiacyclophanes

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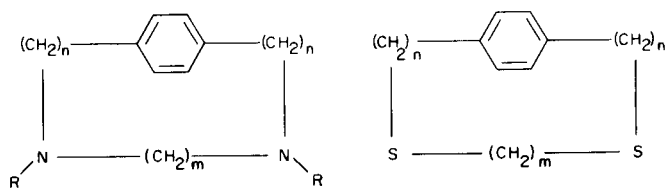
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The effect of a lanthanide shift reagent  $\text{Eu}(\text{dpm})_3$  on the spectra of 3 diazacyclophanes (Ia-c) has been studied together with the effect of a fluorinated shift reagent  $\text{Eu}(\text{fod})_3 \cdot 2.7$  on the nmr spectra of three dithiacyclophanes (IIa-c). The shift reagents remove certain unexpected accidental degeneracies in the original spectra and permit the assignment of the peaks in the expanded spectra to the individual methylene groups. The comparison of the chemical shifts for the methylene groups above the aromatic rings with those of related compounds provides evidence of an upfield shift deriving from the aromatic ring current. The synthesis of two new dithiacyclophanes (IIb-c) is reported.

As a part of another investigation (2) on the electrophilic reactivity of bridged systems containing positive poles, several new diaza (I) and dithia (II) cyclophanes having different ring sizes and with different numbers of methylenic groups between the heteroatoms and the aromatic moiety, have been synthesized.



I<sub>a</sub> n 1, m 8, R H  
I<sub>b</sub> n 2, m 4, R H  
I<sub>c</sub> n 3, m 2, R Me

II<sub>a</sub> n 1, m 6  
II<sub>b</sub> n 2, m 6  
II<sub>c</sub> n 3, m 6

The nmr spectra in deuteriochloroform of the title compounds exhibit some unexpected features which complicate the direct assignment of the resonances.

Fortunately lanthanide shift reagents reduce the complexity of the original spectra to the point that a first-order analysis is possible.

We report here some results concerning the application of paramagnetic shift reagents to compounds (I) and

(II) together with some evidence on the ring currents in the bridged systems investigated.

### Results and Discussion.

The nmr spectra of compounds I and II have been recorded in deuteriochloroform and are shown in Figure 1. The most striking feature of the spectra reported in Figure 1 concerns compounds Ib and IIb in which a well defined sharp singlet corresponding to 8 methylenic protons appears at 7.26 and 7.14  $\tau$  units respectively. This spectral pattern which is not modified by lowering the temperature or by using aromatic solvents, would not have been expected from the structure of the compounds and appears independent on the nature of heteroatom in the methylenic chain. The unequivocal assignment of each resonance for the spectra in Figure 1 is important as a check on the structure of the compounds and to provide evidence on the effect of the aromatic ring currents on the methylenic protons.

Addition of increments of lanthanide shift reagent to a deuteriochloroform solution of the bridge compounds after the manner of Sanders and Williams (3) produces marked modifications in the original spectra of these products. The induced shifts of the various peaks increase with an increase in the Eu resolve/substrate ratio. Figure

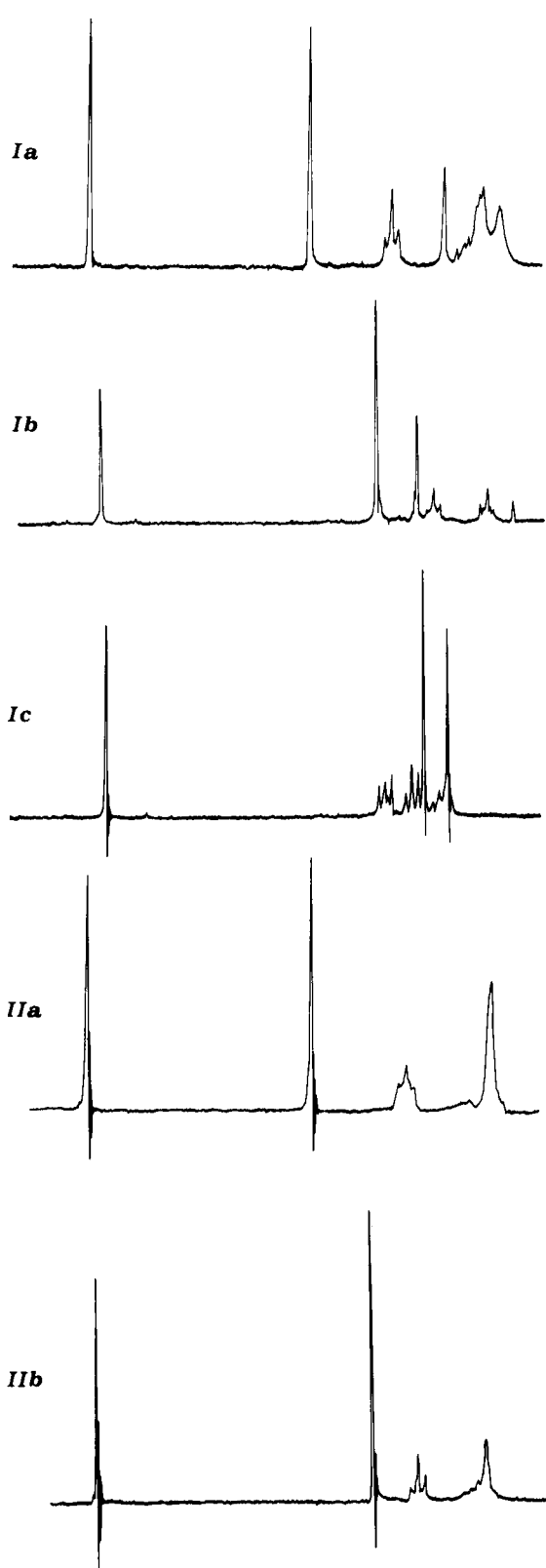


Fig. 1

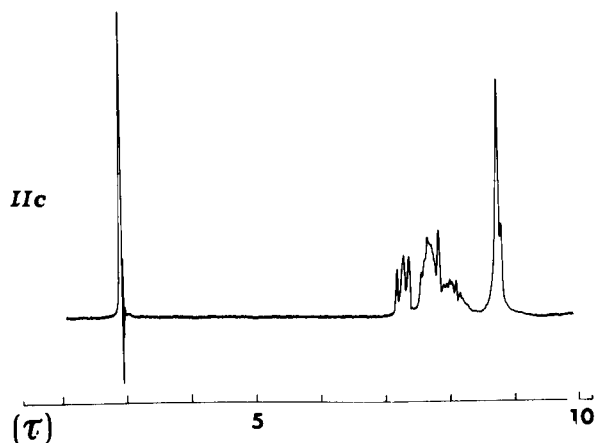


Figure 1. 60 MHz of Ia,-c and IIa,-c compounds in deuteriochloroform solution. TMS used as internal standard.

Figure 2. 60 MHz spectra in deuteriochloroform solution after addition of resolve. Upper trace: Ib with  $\text{Eu}(\text{DPM})_3$  at resolve/substrate ratio of 0.3; lower trace: IIb with  $\text{Eu}(\text{FOD})_3\text{d}_{2,7}$  at resolve/substrate ratio of 1.27.

2 shows the nmr spectra of the two representative compounds Ib and IIb.

The spectra in Figure 2 differ also in the reagent used: whereas, for the cyclic amines,  $\text{Eu}(\text{dpm})_3$  is satisfactory, this reagent requires much larger Eu resolve/substrate ratios to give a significant induced shift with the cyclic sulphides. The use of fluorinated shift reagents such as  $\text{Eu}(\text{fod})_3\text{d}_{2,7}$  overcomes this problem: the introduction of fluorine atoms increases both the solubility and the Lewis acidity of the reagent (4) which can thus be

used with less basic groups.

In the spectra of both Ib and IIb, the addition of the shift reagents gives a significant splitting of the anomalous 8-proton singlets.

Half of the peak, corresponding to 4 protons exhibits a high sensitivity to the shift reagent whereas the induced shift for the remaining part is much less. Such behaviour is typical of the accidental degeneracy of the peaks from two types of methylenic protons at different distances from the coordination site. From the absence of spin-spin coupling in the original singlets, it follows that these peaks (at 7.26 and 7.14  $\tau$  units) can be assigned to the methylenic protons between the heteroatom and the aromatic ring.

The existence of this accidental degeneracy probably depends on the ring size and the strain of the aliphatic chain. Some splitting of the singlet at 7.14  $\tau$  units in IIb, is in fact evident when at constant  $n$ ,  $m$ , is varied to 4 and 8.

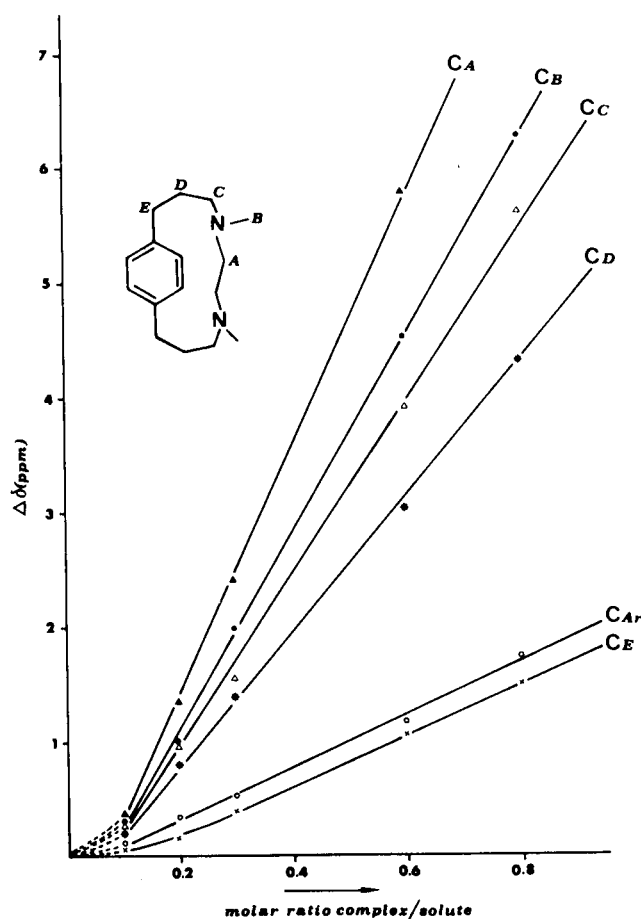


Figure 3. Variation of induced shift with molar ratio  $\text{Eu}(\text{DPM})_3/\text{substrate}$  for Ic in deuteriochloroform solution.

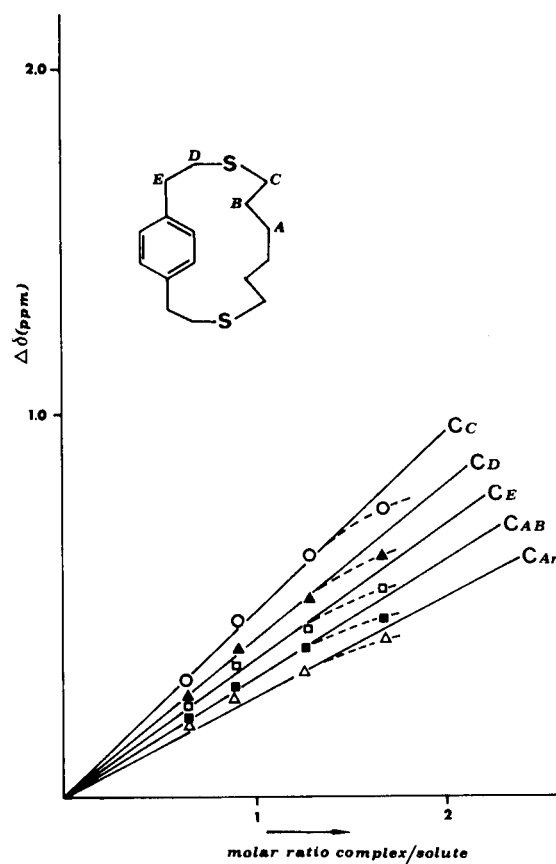


Figure 4. Variation of induced shift with molar ratio  $\text{Eu}(\text{FOD})_3\text{d}_{27}/\text{substrate}$  for IIb in deuteriochloroform solution.

By plotting the induced shifts *vs.* the Eu resolve/substrate ratios, straight lines are obtained with different slopes related to the distance of the protons (3) from the heteroatoms. Since the coordinating power of the shift reagents towards amines is much greater than that to thioethers (5), the gradients of the lines obtained are markedly different in the two groups of substrates (Figures 3 and 4) but for compounds IIa-c the sensitivity is still sufficient for the assignment of the peaks. Figures 3 and 4 demonstrate a linear dependence of the paramagnetic shifts on added Eu resolve at lower concentrations but with compound IIb a certain deviation from linearity is apparent at higher Eu resolve/substrate ratios. Such curves cannot be produced using the dipivalomethanate Eu complex but have been already observed with  $\text{Eu}(\text{fod})_3$  or  $\text{Pr}(\text{fod})_3$  (4) in several cases. Extrapolation of the linear part of the curves in compounds II leads to slopes with a certain extent of uncertainty but for the present purpose of identification of the peaks no more accurate estimates (6) of them are needed.

Our assignment of the peaks for the compounds in

TABLE I

## Assignment of Methylene Peaks in the Expanded Spectra

	Ia		Ib		Ic		IIa		IIb		IIc	
	(ppm)	slope	(ppm)	slope	(ppm)	slope	(ppm)	slope	(ppm)	slope	(ppm)	slope
H <sub>A</sub>	9.25 (t)	5.20	9.02 (m)	8.00	8.43 (s)	10.00	9.05 (bs)	0.38	8.90 (m)	0.27	8.80 (bs)	0.25
H <sub>B</sub>	8.98 (m)	5.20	8.17 (m)	10.62	8.04 (s)	8.70	9.05 (bs)	0.38	8.90 (m)	0.27	8.80 (bs)	0.25
H <sub>C</sub>	8.75 (m)	9.00	7.26 (s)	10.00	7.80 (t)	7.40	7.75 (t)	0.90	7.87 (t)	0.53	8.06 (m)	0.37
H <sub>D</sub>	7.55 (t)	14.50	7.26 (s)	4.69	8.30 (t)	5.80	6.50 (s)	1.25	7.14 (s)	0.40	7.30 (t)	
H <sub>E</sub>	6.25 (s)	16.00			7.40 (t)	2.20			7.14 (s)	0.34	7.70 (m)	
H <sub>Ar</sub>	2.75 (s)	7.00	2.82 (s)	3.62	3.02 (s)	2.20	2.67 (s)	0.46	2.83	0.32	2.90 (s)	0.20

TABLE II

## Melting Points and Analytical Data for Dithiacyclophanes

Compound	Yield %	M.p. (°C)	Formula	Found %				Calculated %				
				C	H	S	M (a)	C	H	S	M	
IIa	(b)											
IIb	52	47-8	C <sub>16</sub> H <sub>24</sub> S <sub>2</sub>	68.4	8.7	22.7	280	68.5	8.6	22.9	280	
IIc	48	64-6	C <sub>18</sub> H <sub>28</sub> S <sub>2</sub>	70.4	9.2	19.9	308	70.1	9.1	20.8	308	

(a) Molecular weights were determined by mass spectrometric analysis using a MAT-111 Varian Instrument. (b) See reference 10 in the text.

Fig. 1 together with the slopes of the shift reagent plots are summarized in Table I. In making this assignment we have assumed that the slopes of the plots decrease along a given methylene chain with the distance of the protons from the coordination site. The results of this assumption are consistent with the original chemical shifts and with the extent of spin-spin coupling. Because of the flexibility of the methylene chain, we have not thought it worthwhile to make explicit allowance for the angular dependence (3) of the induced shifts.

The above assignments provide some evidence for upfield shifts of the methylene peaks deriving from aromatic ring currents (7,8) as observed by Waugh and Fessenden (9) in [10]paracyclophane. However with respect to [10]paracyclophane, a downfield shift of the methylene peaks in compounds I and II would be expected because of the presence of N or S atoms in the methylenic chain.

In the spectrum of 4,7-diaza[10]cyclophane (Ic), the position of resonance of one group of 4 protons (H<sub>C</sub>) $\alpha$  to the nitrogen pole occurs at 7.8  $\tau$  units whereas the other group of 4  $\alpha$ -protons (H<sub>A</sub>) between the two amino groups absorbs at 8.43; this difference of ca. 0.6  $\tau$  units is very similar to that calculated between the corresponding protons in [10]paracyclophane (9). The shielding

effect experienced by the H<sub>A</sub> protons in comparison with the H<sub>C</sub> protons is reasonable in relation to the molecular geometry of this compound for the central methylene groups are close above the  $\pi$ -electron system of the aromatic ring. Another significant feature of the spectrum of Ic comes from the comparison of the chemical shift of the H<sub>A</sub> protons (8.43  $\tau$ ) with that of the methylene protons in *N,N'*-dimethylethylenediamine (7.55  $\tau$ ): an upfield shift of 0.9 units in the bridged compound. Similar observations can be made for the other azacyclophanes: thus the protons of the central methylene groups (H<sub>A</sub>) in Ib absorb at 9.02  $\tau$  whereas the corresponding protons in *N,N'*-dimethylbutanediamine absorb at 8.60  $\tau$ . In the compound Ia the central methylene protons absorb at 9.25  $\tau$ , an unusually high figure for ring methylene groups in spite of the presence of heteroatoms in the ring.

The spectra of the dithiacyclophanes IIa and IIc accord with those of the diazacyclophanes in that the peaks of the central methylene protons are shifted upfield in respect to the other. The magnitude of this shift for the central protons H<sub>A</sub> and H<sub>B</sub> should depend on the proximity with the aromatic  $\pi$ -cloud and therefore on the size of the ring. Resonance in Table I for the H<sub>A</sub>

protons in IIa (8.80  $\tau$ ), IIb (8.90  $\tau$ ) and IIc (9.05  $\tau$ ) provide evidence that when the value of  $m$  is constant, a decrease of  $n$  from 3 to 1 results as expected in a larger upfield shift.

#### EXPERIMENTAL

The diazacyclophanes Ia, Ib and Ic were prepared as previously described (2). The synthesis of the dithiacyclophanes was performed using a method similar to that previously used by Vögtle (10) by reaction between dithioles and the suitable dibromides in the following way: a solution of the dibromide (0.025 mole) and of the dithiole (0.025 mole) in benzene (250 ml.) and a solution of sodium hydroxide (0.050 mole) in 95% ethanol (250 ml.) were added simultaneously and at constant rate by means of two calibrated dropping funnels to a well stirred volume (2 l.) of boiling ethanol, for 5-6 hours. After addition, the reaction mixture was refluxed overnight and the solvent evaporated. The solid residue was taken up in benzene and chromatographed over silica gel, eluting with benzene. Concentration of the eluate gave a white solid which after recrystallization from light petroleum gave the expected products. The physical properties, yields and elemental analyses of the products are reported in Table II. Nmr spectra were measured on Varian HA 100 spectrometer operated at 100 MHz and on Varian T 60 and Jeol C-60 spectrometers operated at 60 MHz. Measurements were made at the ambient probe temperature. Chemical shifts are in  $\tau$  values (parts per million) and are referred to internal tetramethylsilane (TMS). Deuteriochloroform of high purity was obtained from Merck and was dried over preheated (120°C) Molecular Sieves.

The shift reagents Eu(dpm)<sub>3</sub> and Eu(fod)<sub>3</sub>d<sub>27</sub> were obtained from Alfa Inorganic. All solutions were made up in deuteriochloroform containing 0.5 vol% TMS and were between 0.1 and 0.4M in substrate. The amount of shift reagent was continuously varied up to a reagent/substrate molar ratio of ca. 0.8 for diazacyclophanes and of 1.6 ca. for dithiacyclophanes.

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