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HETERA-p-CARBOPHANES. VI. LONG-RANGE ASYMMETRY EFFECT ON THE PROTON MAGNETIC RESONANCE SPECTRUM IN DIOXATHIA[17]PARACYCLOPHANES¹⁾

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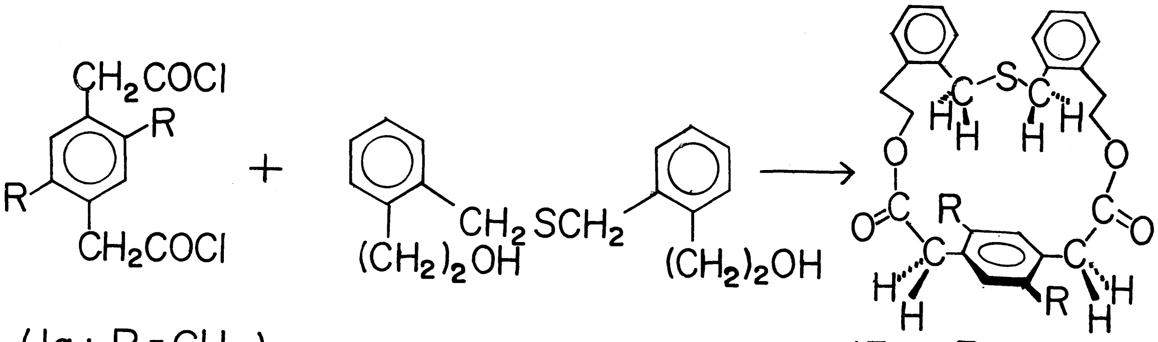
PMR spectrum of a dioxathia[17]paracyclophane derivative showed the nonequivalence of protons of methylene groups which are separated by 8 bonds from an aromatic ring constituting the center of plane asymmetry. The barrier to rotation of the aromatic ring was obtained as 11-12 kcal/mol.

Recently much attention has been focussed on the chemical shift differences of diastereotopic groups.2) If a methylene or a gem-dimethyl group is placed next to a chiral center, it usually exhibits the heterotopic nature. By increasing the intervening groups or atoms between the chiral center and the methylene or the gem-dimethyl group, it is expected that the effect of the chiral center will be lessened. However, things are not so simple and gem-dimethyl protons in the isopropyl group which is remote from a chiral center are known to exhibit the nonequivalence in PMR spectroscopy. For example, Whitesides et al. have observed the nonequivalence in the chemical shifts of methyl protons in the isopropyl group of $C_6H_5CH(CH_3)OCH_2CH_2CH(CH_3)_2$3) and suggested a coiled conformation for exhibiting such nonequivalence.

In this discussion, however, firm experimental support is lacking. Since we have been able to show existence of a pair of nonequivalent methylene protons in ansa chains of some heteraparacyclophanes,4) it is considered interesting to see how far the nonequivalence is observed in a compound possessing a methylene group which is remote from, in a sense of chain length, but is close to the chiral center in a sense of the spatial configuration. The heteraparacyclophanes are considered suited to observe these effects, because the spectrum can be simplified by introducing appropriate heteroatoms.

19,22-Dimethyl-3,15-dioxa-9-thia-2,16-dioxo-6,7,11,12-dibenzo[17]paracyclopha-6,11-diene (3a), mp 128.5-129.0°C, and its desmethyl homolog (3b), mp 125.0-125.5°C, were chosen as model compounds to examine the effect, and was prepared from 1,4-phenylenediacetyl dichlorides (1) and bis(o-2-hydroxyethylbenzyl) sulfide (2) in ca 10% yields under high dilution conditions. Analytical and mass spectral data were satisfactory.



($1a$: $R=CH_3$)
($1b$: $R=H$)

(2)

($3a$: $R=CH_3$)
($3b$: $R=H$)

PMR spectrum of 3a in $CDCl_3$-CS_2(v/v 1:2) at 34°C showed two singlets for isolated methylene groups and two triplets for $ArCH_2CH_2O$ groups (see Fig. 1). At the lower temperatures, however, the two singlets 3a broadened and split into AB quartets, respectively. In contrast to the features of PMR spectra of 3a, 3b exhibited no tendency of splitting of the signals due to methylenes of S-CH_2-C_6H_4 and CO-CH_2-C_6H_4 even at -70°C, although the signals become broad. These results clearly indicate that freezing of the ring flipping of the macrocycle including the three benzene rings is not the cause of the nonequivalence. The chirality of 3a at the lower temperature must be responsible to the appearance of the complex spectra.

Coalescence temperatures, chemical shifts, and coupling constants of 3a were obtained as are shown in Table 1 and free energies of activation at the coalescence temperatures were obtained in a usual manner.[5)] Since compound 3a is a cyclophane derivative with the ansa chain of 17 atoms, the barrier is extraordinarily high, compared with those of other compounds.[1,6)] This appears to indicate that increasing the rigidity of the ansa chain increases the barrier to rotation of the aromatic ring in the cyclophane.

Table 1. PMR Data (60 MHz) and Free Energies of Activation for Internal Rotation of the Dimethylbenzene Ring in 3a.

Proton	$\Delta\delta_{AB}$(Hz)	J_{AB}(Hz)	T_c(°C)	ΔG_c(kcal/mol)
$ArCH_2CO$	10.9	14.8	- 28	$12._1$
$ArCH_2S$	7.1	13.2	- 46	$11._2$

Another interesting feature of the spectrum of 3a at the low temperature is that both the methylene group directly bonded to the pilot atoms and those which

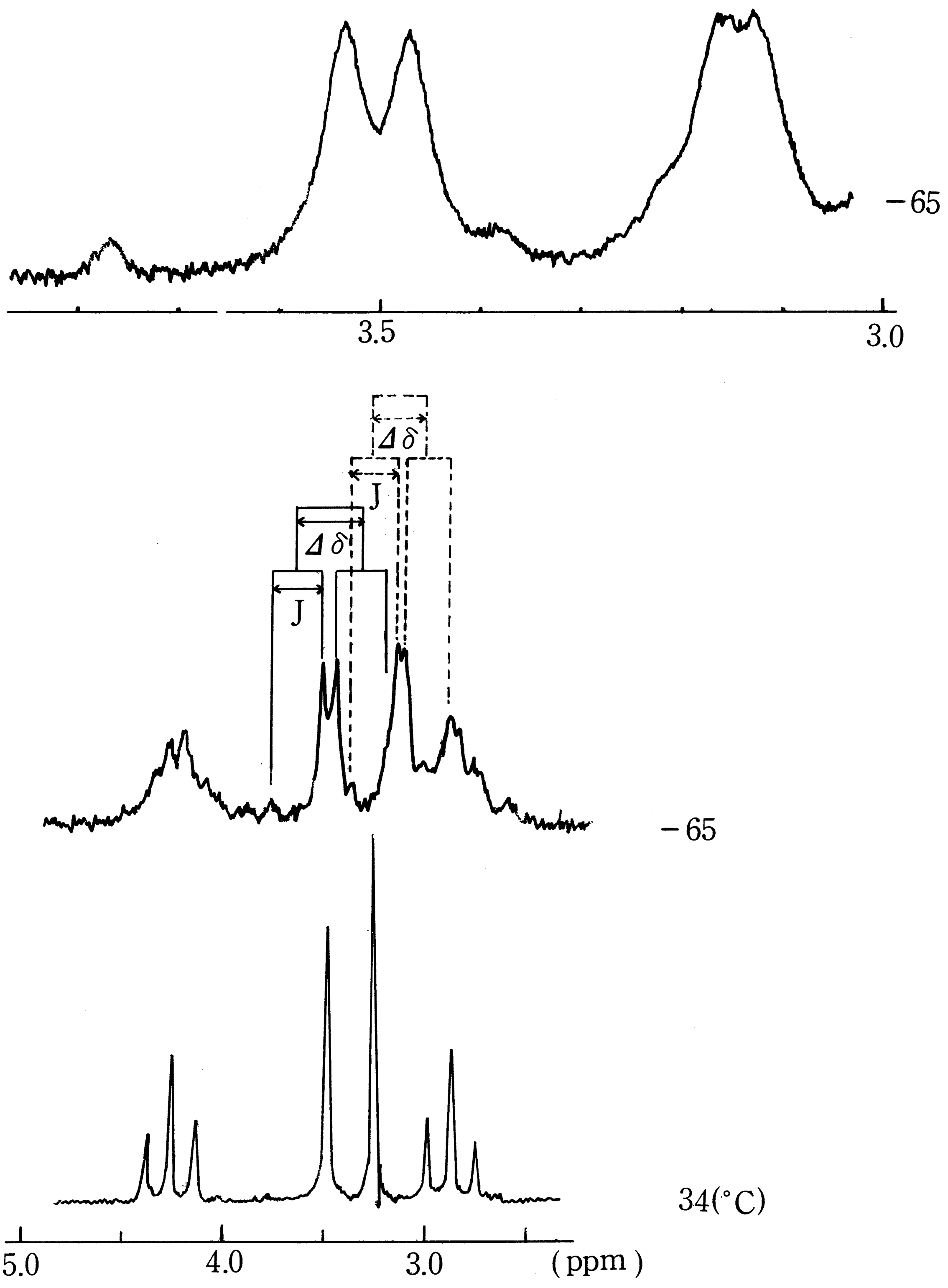


Fig. Temperature dependence of the PMR spectrum of 3a in $CDCl_3$-CS_2.

are separated by at least 6 bonds show nonequivalent protons. Although the methylene protons placed in between the benzene ring and the oxygen atom barely show the tendency of further splitting at -65°C, the degree of nonequivalence of these methylene protons seems to be much smaller than those of S-CH_2-C_6H_4 protons. These results clearly indicate that the effect of nonequivalent environment is conveyed through space to the methylene groups and that the effect is much larger when a group is placed just above the aromatic ring which constitutes the plane in the plane asymmetry. The results further suggest the possibility that methylene protons and gem-dimethyl protons may become nonequivalent when they are located in close proximity of a chiral center because of the steric requirement, irrespective to the chain length.

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