

and suggest that substituents bearing  $n$  electrons can exert a leveling effect on electrophilic reactivity.

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further study. However, in circumstances where a nucleophilic solvent or counterion is available to effect alkyl transfer, it seems possible that even the "intramolecular" rearrangements<sup>6,12</sup> might involve double displacements and intimate ion pairs.

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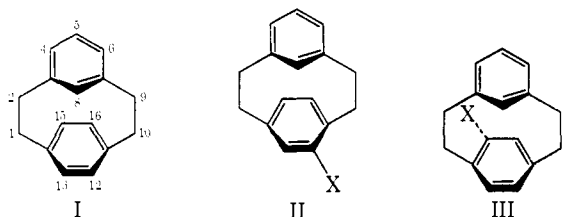
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## Barriers to Ring Rotation in [2.2]Metaparacyclophane and Derivatives<sup>1</sup>

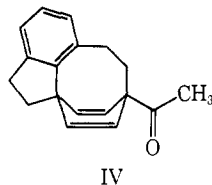
Sir:

With both nmr and stereochemical techniques we have studied the ring rotation and condensation potentialities of [2.2]metaparacyclophane<sup>2</sup> (I) and its derivatives in connection with our electrophilic substitution studies.<sup>3</sup> Others<sup>4</sup> have reported recently that I undergoes ring inversion at rates observable on the nmr time scale. Our work differentiates between one-ring and two-ring inversion possibilities.

Acetylation of I<sup>2</sup> at  $-25^\circ$  in dichloromethane with acetyl chloride and aluminum chloride gave a mixture of IIa,<sup>5</sup> mp  $67-68^\circ$  (20%), and IV, mp  $87-88.6^\circ$  (37%). The structural assignment of IIa was based on its nmr (see below) and mass spectrum, and the reactions IIa  $\rightarrow$  IIb<sup>5</sup>  $\rightarrow$  I, which involved oxidation of IIa with sodium hypobromite to give acid IIb (80%), followed by decarboxylation by heating IIb to  $237^\circ$  with copper carbonate-quinoline (40%). The structural assign-



IIa, X = COCH<sub>3</sub>  
IIb, X = CO<sub>2</sub>H  
IIc, X = CO<sub>2</sub>CH<sub>3</sub>  
IId, X = CH<sub>2</sub>OH  
IIe, X = CHO  
IIIf, X = CH<sub>3</sub>



(1) The authors wish to thank the National Science Foundation for a grant used in support of this research. D. T. H. also wishes to thank the National Science Foundation for a Traineeship, 1965-1969.

(2) D. J. Cram, R. C. Helgeson, D. Lock, and L. A. Singer, *J. Amer. Chem. Soc.*, **88**, 1324 (1966).

(3) A full paper is being prepared.

(4) (a) F. Vögtle, *Chem. Ber.*, **102**, 3077 (1969); (b) S. Akabori, S. Hayashi, M. Nawa, and K. Shiomi, *Tetrahedron Lett.*, 3727 (1969).

(5) Combustion analysis gave carbon and hydrogen values less than 0.2% from theory.

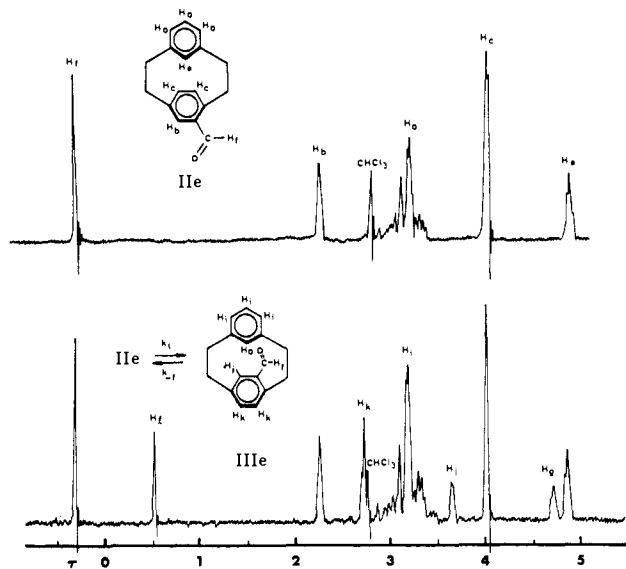


Figure 1. Nmr spectrum of 12-aldehyde[2.2]metaparacyclophane (IIe); top spectrum, at  $-50^\circ$ , pure IIe; bottom spectrum, at  $37^\circ$ , equilibrium mixture of IIe and IIIe (CDCl<sub>3</sub>, 60 MHz, spectrum amplitude not equal for both spectra).

ment of IV was based on its uv, ir, and nmr (both <sup>1</sup>H and <sup>13</sup>C) spectra, and on the production of 1,2,3-benzenetricarboxylic acid when oxidized with alkaline potassium permanganate in water at reflux for 8 hr (50%). Compounds IIc-IIf,<sup>5</sup> prepared from IIb by conventional reactions, gave the following melting points: IIb,  $163-163.5^\circ$ ; IIc,  $75-76.2^\circ$ ; IId,  $88-90^\circ$ ; IIe,  $73-79^\circ$ ; IIIf,  $42-44^\circ$ .

Although IIa-IIf crystallized as single compounds, when dissolved they equilibrated with their corresponding III isomers, a process detected by nmr spectroscopy. For example, Figure 1 shows a spectrum of aldehyde IIe obtained by adding crystalline material to frozen deuteriochloroform, warming the mixture to  $-50^\circ$  in an nmr tube, and recording the spectrum. The observed spectrum is that expected for IIe. The solution, when warmed to  $37^\circ$ , gave a nontime dependent curve consistent with that expected for IIe  $\rightleftharpoons$  IIIe. Peak integrations of the nmr spectra of (II  $\rightleftharpoons$  III)<sub>equil</sub> at  $37^\circ$  provided the equilibrium constants ( $K_{37^\circ}$ ) listed in Table I. The rate constants  $k_1$  and  $k_{-1}$  were deter-

Table I

X	II:III	$K_{37^\circ}$
CO <sub>2</sub> CH <sub>3</sub>	7:1	0.14
COCH <sub>3</sub>	3.9:1	0.26
CH <sub>3</sub>	3.3:1	0.31
CH <sub>2</sub> OH	2.2:1	0.45
CHO	2.1:1	0.48
H	1:1	1.00

mined for IIe  $\rightleftharpoons$  IIIe at  $-13.5^\circ$  making use of the two aldehyde proton peaks in the nmr ( $\tau -0.32$  for IIa and  $0.52$  for IIIa) and  $k_1 = 1.72 \times 10^{-4} \text{ sec}^{-1}$  and  $k_{-1} = 3.83 \times 10^{-4} \text{ sec}^{-1}$  ( $K_{-13.5^\circ} = 0.45$ ).<sup>6</sup> The rate constants were also determined at the coalescence tempera-

(6) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," 2nd ed, John Wiley & Sons, Inc., New York, N. Y., 1961, p 186.

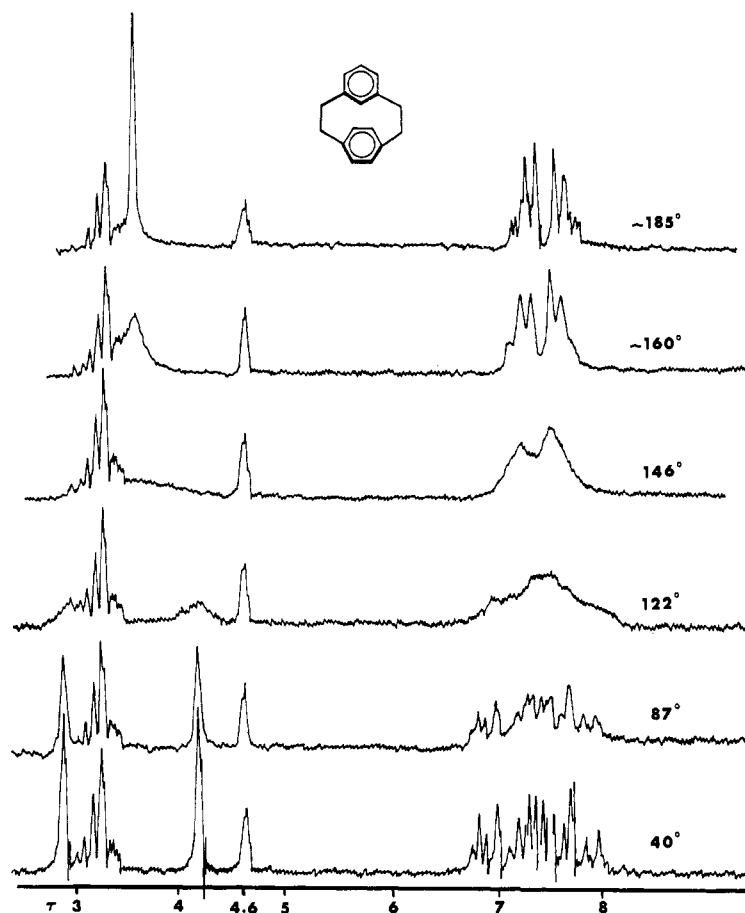


Figure 2. Nmr spectra of [2.2]metaparacyclophane (I) in hexachlorobutadiene (60 MHz).

ture ( $T_c = 140^\circ$ ) of the protons:  $k_1 = 85 \text{ sec}^{-1}$ ,  $k_{-1} = 175 \text{ sec}^{-1}$  ( $K_{140^\circ} = 0.48$ ). The activation parameters are listed. From these the half-life at  $25^\circ$  of IIe, with regard to reaching equilibrium with IIIe, was 14 sec.

Rate constant	$\Delta H^\ddagger$ , kcal mol $^{-1}$ , at $-14$ – $140^\circ$	$\Delta G_{140^\circ}^\ddagger$ , kcal mol $^{-1}$	$\Delta S_{140^\circ}^\ddagger$ , eu
$k_1$	$17.7 \pm 0.3$	$20.8 \pm 0.4$	$-7.8 \pm 2.2$
$k_{-1}$	$17.6 \pm 0.3$	$20.2 \pm 0.4$	$-6.1 \pm 2.4$

Hydrocarbon I also exhibited ring rotation<sup>4</sup> in its nmr spectrum in hexachlorobutadiene (Figure 2). Protons  $H_{12}$  and  $H_{13}$  ( $\tau$  2.87) and  $H_{15}$  and  $H_{16}$  ( $\tau$  4.12,  $J \approx 1.5 \text{ Hz}$ ) were observed to coalesce at  $146^\circ$ .<sup>7</sup> By ca.  $185^\circ$  these protons formed a sharp singlet and the methylene protons a symmetrical multiplet (AA'BB'). With  $\Delta\nu = 75 \text{ Hz}$  and the equation,  $k = \pi\Delta\nu/\sqrt{2}$ ,<sup>8</sup>  $k = 167 \text{ sec}^{-1}$  at  $146^\circ$ , and  $\Delta G_{146^\circ}^\ddagger = 20.6 \pm 0.3 \text{ kcal mol}^{-1}$ . This energy barrier indicates a half-life for ring inversion at  $25^\circ$  also on the order of seconds.

Carboxylic acid IIb was resolved through its brucine salt (recrystallized to constant rotation five times from methanol) to give material (23%), mp  $168$ – $169^\circ$  (unchanged by recrystallization),  $[\alpha]_{546}^{25} 34.2^\circ$  ( $c$  1.07,  $\text{CHCl}_3$ ). At  $25^\circ$  the rotation was time independent, a fact that demonstrates that only one of the two rings is flipping. Should both turn over with respect to one another, (+)-IIb would racemize as well as

(7) Our chemical shifts and coalescence temperatures are more in agreement with those of ref 4a than those of ref 4b.

(8) J. W. Emsley, J. Feeney, and L. H. Sutcliffe, "High Resolution Nuclear Magnetic Resonance," Vol. 1, Pergamon Press, Oxford, 1965, p 481.

pseudoepimerize (go to optically active IIIb). A sample of (+)-IIc when heated at  $200^\circ$  for 25 hr neat gave back (+)-IIc of unchanged rotation. Examination of molecular models of IIe indicates that the steric barrier to passing  $H_a$  of the *meta* past the *para* ring should be vastly less than that to passing the  $H_c$ 's of the *para* past the *meta* ring.<sup>9</sup>

(9) The authors wish to thank Professor F. A. L. Anet and his co-workers for their assistance and fruitful discussions, and Dr. H. J. Reich for carrying out and interpreting the C-13 nmr on IV.

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### Biosynthesis of Lycopodine. The Incorporation of Pelletierine<sup>1</sup>

Sir:

Based on our observation<sup>2</sup> of nonrandom incorporation of radioactivity from  $[2\text{-}^{14}\text{C}]$ - and  $[6\text{-}^{14}\text{C}]$ lysine into lycopodine (III), we made the suggestion that the Lycopodium alkaloids originate from two pelletierine (I) units, whose piperidine nucleus is derived from lysine. The structural correspondence of pelletierine (I) to the obscurine skeleton (II), and hence to lycopodine (III),

(1) This investigation was supported by a grant from the National Research Council of Canada.

(2) R. N. Gupta, M. Castillo, D. B. MacLean, I. D. Spenser, and J. T. Wrobel, *J. Am. Chem. Soc.*, **90**, 1360 (1968).