Tetracyclic Hydrocarbon XXVII. Xylene, 20 ml, was first deaerated by bubbling through nitrogen and then 120 mg (0.5 mmol) of aldehyde XXVI and 486 mg (0.5 mmol) of tristriphenylphosphinerhodium(I) chloride were added. The mixture was refluxed under nitrogen for 29 hr. The xylene was then evaporated under reduced pressure and the mixture was chromatographed on 12 g of silica gel in pentane. After 100 ml of pentane, 62 mg of XXVII, an oil, was eluted. Glc analysis showed the hydrocarbon XXVII to have a shorter retention time than the hydrogenated tetrabromide product XXVIII. The uv and nmr spectra of XXVII were also different but similar to XXVIII. The spectral data of XXVII were nmr τ 2.97 (m, 3, ArH), 7.18 (m, 4, aliphatic), and 8.18 ppm (m, 13, aliphatic); uv λ_{max} 274.5 nm (ϵ 455), sh 270 (390), 266 (490), sh 260 (362), minimum 236 (56), sh 220 (10,200). *Anal.* Calcd for $C_{16}H_{20}$: C, 90.50; H, 9.50. Found: C, 90.64; H, 9.57.

Tetracyclic Hydroxymethylene Compound XVIII. Lithium aluminum hydride, 0.8 g (20 mmol), was added slowly to a solution of 1.5 g (6 mmol) of XVII in 200 ml of ether. The reaction was stirred overnight with a drying tube on the flask. Excess hydride was destroyed with saturated sodium carbonate solution. The solution was filtered and washed successively with dilute potassium hydroxide solution, sodium bicarbonate solution, and saturated sodium chloride solution. The ethereal solution of the alcohol was adsorbed onto silica gel and chromatographed. Elution with 20% ether–pentane produced 1.17 g of a thick oil of XVIII, with the following spectral properties: uv λ_{max} 278 nm (ϵ 496), 270 (563), sh 265 (458), sh 230 (4770); nmr τ 3.07 (m, 3, ArH), 3.88 and 4.13 (AB quartet, 4, J = 9.0 Hz), 6.47 (s, 2, CH_2OH), 7.03 (m, 4, CH_2CH_2), 7.70 (s, 1, OH), 7.87 (m, 2, CH_2), 8.32 ppm (m, 2, CH_2). *Anal.* Calcd for $C_{17}H_{18}O$: C, 85.67; H, 7.61. Found: C, 85.78; H, 7.40.

Formation of the 3,5-dinitrobenzoate ester of XVIII using 3,5-dinitrobenzoyl chloride in pyridine produced an orange solid, mp 157.5–159°. *Anal.* Calcd. for $C_{24}H_{20}N_2O_6$: C, 66.65; H, 4.66. Found: C, 66.69; H, 4.89.

Macro Rings. XLII. Ring Rotation in [2.2]Metaparacyclophane[1,2]

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Received November 12, 1970

Abstract: With nmr and stereochemical techniques the ring rotation of [2.2]metaparacyclophane (I) and its derivatives have been studied. Crystallization of monosubstituted derivatives of I with the substituent in the para ring provides only the 12-isomer (substituent anti to the meta ring). When dissolved at −50° in deuteriochloroform, only the nmr spectra of the 12-isomers were visible. When warmed to 37°, the spectra became those of a mixture of the 12- and 15-isomers (substituent syn to the meta ring) by rotation of either the meta or para ring (or both). At 37°, K_{equil} = (15-isomer)/(12-isomer) were measured for para ring derivatives: CO_2CH_3, K = 0.14; $COCH_3$, K = 0.26; CH_3, K = 0.31; CH_2OH, K = 0.45; CHO, K = 0.48; H, K = 1. For CHO as substituent, k_1 and k_{-1} at −13.5° were determined for 12-isomer $\rightleftarrows$ 15-isomer (τ −0.32 for 12-isomer and 0.52 for 15-isomer), and were $k_1 = 1.72 \times 10^{-4}$ sec^{-1} and $k_{-1} = 3.83 \times 10^{-4}$ sec^{-1}. The same rate constants were also determined at the coalescence temperature (T_c = 140°) of the aldehyde proton: k_1 = 85 sec^{-1}, k_{-1} = 175 sec^{-1} ($K_{140°}$ = 0.48). The activation parameters were calculated from these rate constants: $\Delta H^{\ddagger}$ 17.7 ± 0.3 kcal mol^{-1}, $\Delta G_{140°}^{\ddagger}$ = 20.8 ± 0.4 kcal mol^{-1}, $\Delta S_{140°}^{\ddagger}$ = −7.8 ± 2.2 eu from k_1's; $\Delta H^{\ddagger}$ = 17.6 ± 0.3 kcal mol^{-1}, $\Delta G_{140°}^{\ddagger}$ = 20.2 ± 0.4 kcal mol^{-1}, $\Delta S^{\ddagger}$ = −6.1 ± 2.4 eu from k_{-1}'s. The parent hydrocarbon's nmr spectrum in hexachlorobutadiene also was temperature dependent. Protons at C-12 (C-13) and C-15 (C-16) coalesced at 146°. When heated to *ca.* 185° these protons formed a sharp singlet, and the aliphatic protons went from a complex multiplet to an AA'BB' pattern. With $\Delta\nu$ = 75 Hz, at 146° k = 167 sec^{-1} and $\Delta G_{146°}^{\ddagger}$ = 20.6 ± 0.3 kcal mol^{-1}. To determine whether only one or both rings rotated, 12-carbomethoxy[2.2]metaparacyclophane was prepared optically pure. When heated to 200° and recovered, optically pure material retained its optical purity. Clearly only one ring rotated, undoubtedly the meta ring. *Had both rings rotated racemic* material *would have resulted.*

In the previous paper,[3] it was reported that pure crystalline derivatives of [2.2]metaparacyclophane (I)[4] could be prepared with substituents in the 12 position (II). When dissolved at room temperature, these substances exhibited nmr spectra that indicated isomers II had equilibrated by ring rotation with isomers III. The system offered the unusual advantage for study of ring rotation phenomena in which one of the two components of an equilibrating mixture could be isolated, and its rate of equilibration measured. The system also poses the interesting and answerable questions of whether just one (which one) or both of the benzene rings of the [2.2]metaparacyclophane rotate with respect to one another. We therefore undertook to study the rates and equilibria involving II and III, as well as the ring inversion of the parent hydrocarbon (I). This system possesses the advantages that the chemical shifts of the different protons of I, II, and III show considerable sensitivity to their positions in the molecule, and ring rotation is easily followed. After our work was completed,[2] reports of two other studies of ring rotation of hydrocarbon I appeared.[5]

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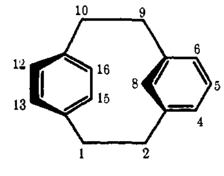
(1) The authors thank the National Science Foundation for a grant used in support of this research. D. T. Hefelfinger also thanks the National Science Foundation for a Traineeship, 1965–1969. The authors warmly acknowledge Professor F. A. L. Anet's suggestions concerning the nmr spectral parts of the work.

(2) A preliminary account of this work has appeared: D. T. Hefelfinger and D. J. Cram, *J. Amer. Chem. Soc.*, **92**, 1073 (1970).

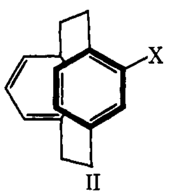
(3) D. T. Hefelfinger and D. J. Cram, *J. Amer. Chem. Soc.*, **93**, 4754 (1971).

(4) D. J. Cram, R. C. Helgeson, D. Lock, and L. A. Singer, *ibid.*, **88**, 1324 (1966).

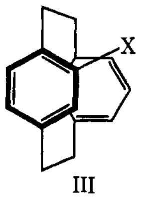
(5) (a) F. Vögtle, *Chem. Ber.*, 102, 3077 (1969); (b) S. Akabori, S. Hayashi, M. Nawa, and K. Shiomi, *Tetrahedron Lett.*, 3727 (1969).



I



II



III

a, X = $COCH_3$
b, X = CO_2H
c, X = CO_2CH_3
d, X = CH_2OH
e, X = CHO
f, X = CH_3

Results

High-Temperature Nmr Spectrum of [2.2]Metaparacyclophane (I). Figure 1 reveals that the nmr spectrum of hydrocarbon I is temperature dependent. At 40°, the four protons on the para ring give an A_2X_2 pattern, $\Delta\nu_{AX} = 75$ Hz, $J_{AX} \sim 1.5$ Hz. One of the signals, attributed to C-12 and C-13 protons, has the normal benzene-like chemical shift and the other, attributed to C-15 and C-16 protons, is diamagnetically shielded by the meta ring.[4] As the temperature was raised, protons on C-12 and C-13 (A portion of A_2X_2 system) exchanged with the protons on C-15 and C-16 (X portion). The para ring protons coalesced at $T_c = 146 \pm 3°$ from their A_2X_2 system (τ 2.87 and 4.12) to a broad singlet, which became a sharp singlet at 185°. The highly coupled aliphatic protons (ABCD system) progressed from a very wide unsymmetrical and finely split multiplet to a multiplet with a center of symmetry at 185°, and approached an AA′BB′ system as the temperature was raised. Application of the equation for an intermediate exchange rate at coalescence[6] gave $k = \pi\Delta\nu/\sqrt{2} = 167\ \text{sec}^{-1}$ at $146 \pm 3°$ ($\Delta\nu = 75$ Hz).[7] This rate corresponds to $\Delta G_{146°}^{\ddagger} = 20.6 \pm 0.3$ kcal mol^{-1}. This energy barrier indicates a half-life for ring inversion at 25° on the order of seconds.

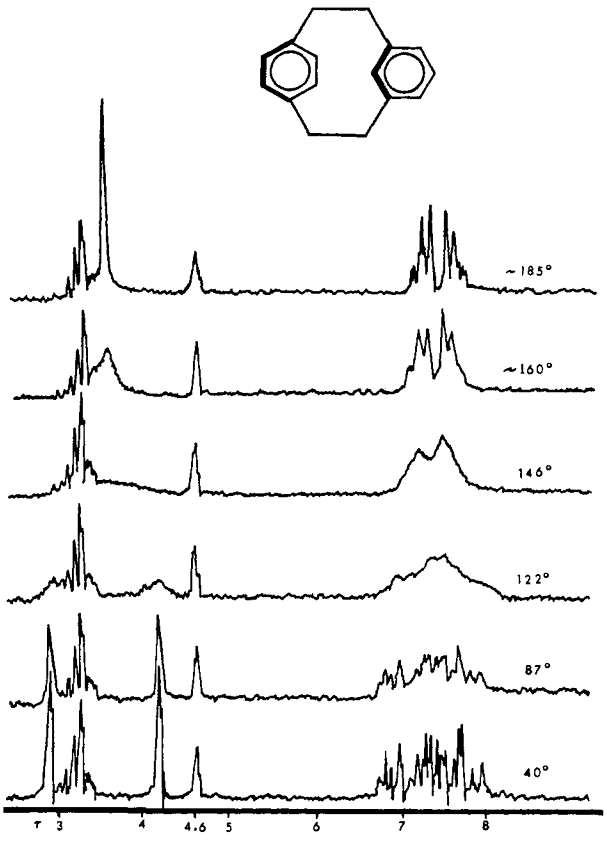


Figure 1. Nmr spectrum of [2.2]metaparacyclophane (I) in hexachlorobutadiene (60 MHz).

Equilibrium Constants for Para Ring Substituted [2.2]Metaparacyclophanes. At 25° the chemical shifts of proton-carrying substituents on the para ring in the 12 position (II) are different from those in the 15 position (III)[3]. Since these isomers are in equilibrium at 37°, integration of each signal provides data from which equilibrium constants can be calculated. Table I lists the constants for $K_{37°}$ [III]/[II]. Aldehyde IIe was prepared by oxidation of alcohol IId for purposes of this study (see below). The other compounds were already available.[3]

Table I. Equilibrium Constants for 12-Substituted $\rightleftarrows$ 15-Substituted [2.2]Metaparacyclophanes (II $\rightleftarrows$ III) at 37° in Deuteriochloroform

Substituent	K	$\Delta G_{37°}$, kcal mol^{-1}
CO_2CH_3	0.14 ± 0.01	1.22
$COCH_3$	0.26 ± 0.02	0.83
CH_3	0.31 ± 0.02	0.72
CH_2OH	0.45 ± 0.02	0.49
CHO	0.48 ± 0.02	0.45
H	1.00	0

Kinetics of Equilibration. When crystalline 12-acetyl-[2.2]metaparacyclophane (IIa) was added to frozen deuteriochloroform in an nmr tube and allowed to warm to −50°, the nmr spectrum was that of only the 12-isomer with only one methyl signal ($COCH_3$, τ 7.40). When warmed to 0° the solution gave a new spectrum superimposed on the old. Most noticeably, a new methyl signal appeared ($COCH_3$, τ 7.92). This upfield position of the methyl protons in the acetyl group of the 15-isomer (IIIa) is due to the diamagnetic shielding of the meta ring. For comparison, the methyl resonance of acetophenone in the same medium occurs at τ 7.41.

All of the derivatives prepared with one substituent in the para ring of I underwent preferential crystallization of the 12-isomer. With substituents $COCH_3$ and CH_3, the methyl signals were superimposed on the aliphatic protons, a fact that made quantitative measurement of the rate of appearance of the 15-isomer difficult. With substituent CO_2CH_3, IIc and IIIc each gave signals isolated from other signals, but the low-valued equilibrium constant of IIc $\rightleftarrows$ IIIc made it difficult to measure the appearance of a peak comprising only one-eighth of the equilibrium composition. The 12-aldehydo[2.2]metaparacyclophane (IIe) was ideal for kinetic purposes. Isomers IIe and IIIe gave sharp bands (τ −0.32 and τ 0.52, respectively) that are widely separated from other signals (Figure 2), and at equilibrium, [IIe]/[IIIe] = 2.1.

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(6) J. W. Emsley, J. Feeney, and L. H. Sutcliffe, "High Resolution Nuclear Magnetic Resonance Spectroscopy," Vol. 1, Pergamon Press, New York, N. Y., 1966, p 481.

(7) Our chemical shifts and coalescence temperatures are more in agreement with those of ref 5a than 5b.

When solid IIe was added to frozen deuteriochloroform and the mixture warmed to −50°, the nmr spectrum of IIe was obtained (Figure 2). When warmed to 37° (probe temperature), the nmr spectrum was that of IIe ⇄ IIIe. A −50° solution of IIe was prepared and rapidly brought to and held at −13.5° in the nmr spectrometer. The rate of attainment of equilibrium

$$\mathrm{IIe} \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} \mathrm{IIe}$$

was measured as IIIe appeared at the expense of IIe. Use was made of the aldehyde proton signal intensities of the two substances. From the expressions $k_{-13.5} = k_1/k_{-1} = 0.45$ and $k_{\text{obsd}} = k_1 + k_{-1}$ were calculated $k_1 = 1.72 \times 10^{-4}$ sec^{-1} and $k_{-1} = 3.83 \times 10^{-4}$ sec^{-1}. The half-life of IIe at −13.5° is *ca.* 20 min.

A solution of IIe ⇄ IIIe in hexachlorobutadiene provided a coalescence temperature for the nmr signals of the two aldehyde protons at T_c 140 ± 5°. Use of Saunders'[8] computer program for exchange between multiple sites for modification of the equation[6] $k = \pi\Delta\nu_{AB}/\sqrt{2}$ allowed calculation of k_1 and k_{-1} at 140°. The rate constants were determined by fitting computer-drawn spectra obtained by selecting trial values for the rate constants to the observed spectra. The summation of the forward and reverse rate constants was 260 sec^{-1}, and $K_{\text{equilibrium}}$ prior to coalescence was 0.48, so $k_1 = 85$ sec^{-1} and $k_{-1} = 175$ sec^{-1}. From the values of k_1 and k_{-1} at the two temperatures were calculated the activation parameters: for IIe → IIIe, $\Delta G_{140°}^{\ddagger} = 20.8 \pm 0.4$ kcal mol^{-1}, $\Delta H^{\ddagger} = 17.7 \pm 0.3$ kcal mol^{-1}, and $\Delta S_{140°}^{\ddagger} = -7.8 \pm 2.2$ eu; for IIIe → IIe, $\Delta G_{140°}{\ddagger} = 20.2 \pm 0.4$ kcal mol^{-1}, $\Delta H^{\ddagger} = 17.6 \pm 0.3$ kcal mol^{-1}, and $\Delta S_{140}°^{\ddagger} = -6.1 \pm 2.4$ eu. At 25° the rate constants were calculated, $k_1 = 1.6 \times 10^{-2}$ sec^{-1} and $k_{-1} = 3.3 \times 10^{-2}$ sec^{-1}. Thus at room temperature, a half-life for IIe going to equilibrium is about 14 sec, and ring rotation is rapid.

Optical Stability of Optically Active 12-Carbomethoxy[2.2]metaparacyclophane ((+)-IIc). A sample of 12-carboxy[2.2]metaparacyclophane (IIb)[3] was resolved through its brucine salt (to constant rotation) to give (+)-IIb of mp 167.7–169.7° ((±)-IIb gave mp 160–161.5°). The rotation, $[\alpha]^{25}_{546}$ +34.5° (*c* 1.04, $CHCl_3$), and melting point did not change on further recrystallization. From the mother liquors of the brucine salt crystallization was recovered (−)-IIb, which was recrystallized to constant melting point and rotation, mp 165–167.5°, $[\alpha]^{25}_{546}$ −33.1° (*c* 1.04, $CHCl_3$). Ester (+)-IIc was prepared from (+)-IIb.

Both ester (+)-IIc and acid (+)-IIb gave rotations at 25° that did not change with time, but no attempt was made to take rotations quickly after solutions were prepared. When heated neat in a sealed, evacuated tube at 200° for 25 hr, ester (+)-IIc was quantitatively recovered and exhibited the same rotation as before this treatment.

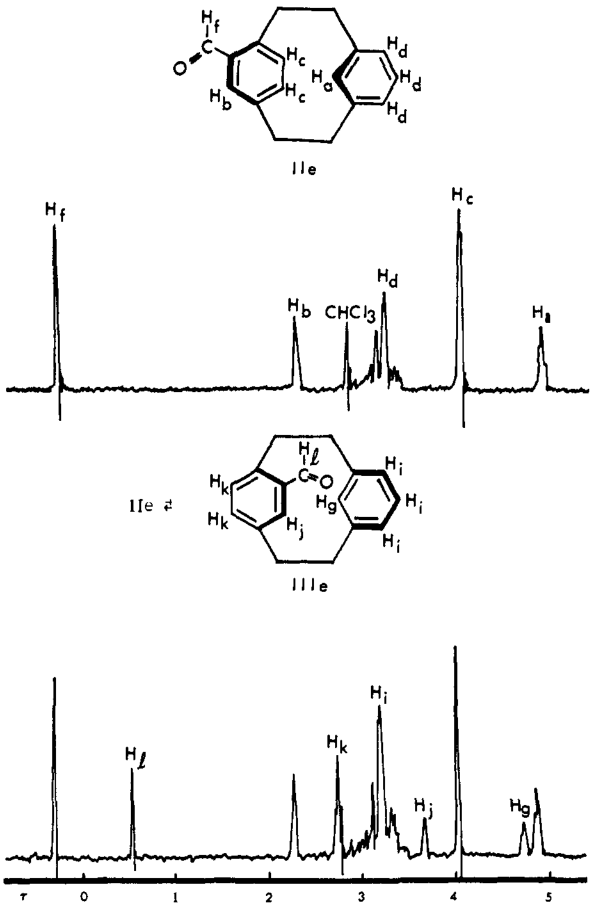

Figure 2. Nmr spectrum of 12-aldehydo[2.2]metaparacyclophane (II_e) at −50°, and of equilibrium mixture of 12- and 15-aldehydo[2.2]metaparacyclophane (III_e) at 37° ($CDCl_3$, 60 MHz, spectrum amplitude not equal for two traces).

Discussion

Origin of Ring Rotation in [2.2]Metaparacyclophane (I) and Its Derivatives. Since the two benzene rings in this system are different, the possibilities exist that either the meta or para rings or both rings rotate with respect to one another. That at least one of these three alternatives applies is demonstrated by the time and temperature dependence of the nmr spectra reported in the Results. The demonstrated equilibrations, IIa–e ⇄ IIIa–e, do not differentiate between these three alternatives. The approach of the aliphatic protons to an AA'BB' pattern in the nmr spectrum of I as the temperature is raised (Figure 1) indicates that at least the meta ring is rotating with respect to the para ring, but provides no information with respect to the para ring. The information that the meta ring rotates, coupled with the optical stability of ester (+)-IIc to 200°, demonstrates conclusively that the para ring up to that temperature does not rotate with respect to the meta ring.

The formulas of Chart I show the stereochemical relationships involved. Formulas IIa–e and II'a–e are enantiomers of one another, as are IIIa–e and III'a–e. Just meta ring rotation interconverts IIa–e and IIIa–e, or II'a–e and III'a–e. Just para ring rotation interconverts IIa–e and III'a–e, or II'a–e and IIIa–e. Thus rotation of both rings 180° with respect to one another is required for interconversion of enantiomers, IIa–e ⇄ II'a–e or IIIa–e ⇄ IIIa'–e. The nmr data indicate the meta ring rotates. The stereochemical data indicate that *both rings* do not rotate. Thus only the meta ring and not the para ring rotates. Clearly the rate constants, k_1 and k_{-1}, obtained in the kinetic measurements,

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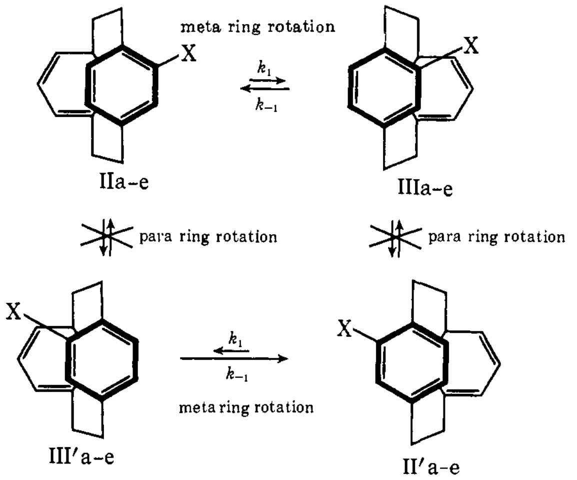
[8] (a) M. Saunders and E. L. Hagen, *J. Amer. Chem. Soc.*, **90**, 6881, 6882 (1968); (b) F. A. L. Anet and A. J. R. Bourn, *ibid.*, **89**, 760 (1967); (c) F. A. L. Anet, private communication.

Chart I

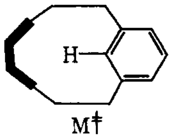


and the derived activation parameters pertained to the process of passing C-8 and its attached hydrogen of the meta ring past the face of the para ring.

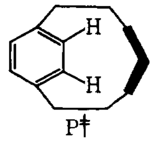
Rates and Equilibria for Meta Ring Rotation. The values of the equilibrium constants for II $\rightleftarrows$ III provide a scale for repulsive interactions between the face of a benzene and substituents. The order reveals that more than steric interactions are involved. Thus the CH_2OH group is certainly larger than CH_3, yet ΔG is 0.49 for the former and 0.72 kcal mol^{-1} for the latter group. Probably the CH_2OH group is hydrogen bonded to the π system of the meta ring. Another interesting comparison involves CO_2CH_3 (ΔG = 1.22 kcal mol^{-1}) and CH_3 (ΔG = 0.72 kcal mol^{-1}). On the free energy scale based on equilibria between axial and equatorial substituents on a cyclohexane ring, for CH_3, ΔG = 1.5–1.9 and for $CO_2C_2H_5$, ΔG = 1.1 kcal mol^{-1}.[9] Thus in III repulsions between a phenyl and carbomethoxy group are greater than between a phenyl and a methyl group, but a methyl group would rather occupy the more spacious equatorial position of a cyclohexyl ring than would a carbomethoxy group.

The free energies of activation for meta ring rotation in [2.2]metaparacyclophane (I) and its para-ring-substituted aldehyde derivative (IIe) were the same within error. Thus for I, $\Delta G_{146^\circ}{}^{\ddagger} = 20.6 \pm 0.3$ kcal mol^{-1}, and for IIe, $\Delta G_{140^\circ}{}^{\ddagger} = 20.2 \pm 0.4$ kcal mol^{-1}. The lack of effect of the aldehyde group on the activation energy is not surprising. Steric inhibition of conjugation between the aldehyde and aryl groups, although of somewhat differing character, is present in both ground and transition states for meta ring rotation, and apparently balance out.

Examination of molecular models of transition states for meta ring ($M^{\ddagger}$) and para ring ($P^{\ddagger}$) rotation in [2.2]-metaparacyclophane indicates why the activation energy for the latter is so much higher than the former. In meta ring rotation, only one hydrogen has to pass over the face of a benzene ring whereas in para ring rotation there are two. Furthermore, overall bond angle deformation in $P^{\ddagger}$ appears concentrated in fewer bond angles than in $M^{\ddagger}$.

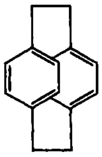


$M^{\ddagger}$

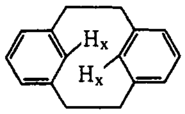


$P^{\ddagger}$

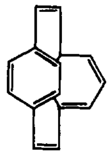
Comparison of Ring Rotation in [2.2]Metaparacyclophane (I) with That of Other Cyclophanes. Comparisons are made here of the activation energies for ring inversion of I with that of other aliphatic–aromatic ring compounds in which an aromatic proton must pass through the center of the largest ring of the system. Compound I contains both a para and meta bridge, and its largest ring is 11-membered. Comparisons will be limited to 10-, 11- and 12-membered rings either para or meta bridged. Ring rotations without ring rupture in the closest relatives of I, namely [2.2]paracyclophane[10] (IV) or [2.2]metacyclophane (V) up to 180°,[11] have not been observed. It has been estimated that $\Delta G^{\ddagger}$ for ring inversion of V would be >27 kcal mol^{-1}.[12] The observation that tetradehydro[2.2]metaparacyclophane (VI)[13] gives a singlet for its four aromatic para ring protons in the nmr at ordinary temperature (presumably) suggests but does not prove that ring inversion occurs faster in VI than in I.[13]



IV

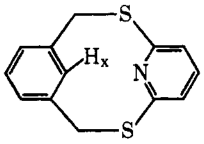


V

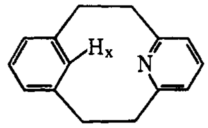


VI

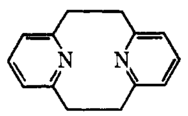
Systems VII and IX undergo ring rotation at attainable temperatures. System VII has $\Delta G_{125^\circ}{}^{\ddagger} \sim 20$ kcal mol^{-1} for H_x passing the pyridine ring,[11] a value not far from what we observe for I. Clearly the H_x to H_x nonbonded interactions in the transition state for ring rotation in V inhibit rotation in that substance, but are absent in VII. Apparently N: to HC interactions offer less of a barrier than CH to HC. The N: to :N interactions of IX provide $\Delta G_{25^\circ}{}^{\ddagger} \sim 15$ kcal mol^{-1} for ring rotation.[14a] However, up to 200°, no ring rotation was observed for VIII,[14b] although the behavior of VII[11] suggests that VIII at high temperatures might have undergone ring rotation.



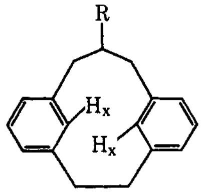
VII



VIII



IX



X

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[9] E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill, New York, N. Y., 1962, p 236.

[10] H. J. Reich and D. J. Cram, *J. Amer. Chem. Soc.*, **91**, 3517 (1969).

[11] F. Vögtle, *Tetrahedron Lett.*, 3623 (1968).

[12] (a) R. W. Griffin, Jr., and R. C. Coburn, *J. Amer. Chem. Soc.*, **89**, 4638 (1967); (b) T. Sato, S. Akabori, M. Kainosho, and K. Hata, *Bull. Chem. Soc. Jap.*, **41**, 218 (1968).

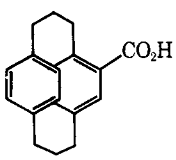
[13] V. Boekelheide and P. H. Anderson, *Tetrahedron Lett.*, 1207 (1970).

[14] (a) I. Gault, B. J. Price, and I. O. Sutherland, *Chem. Commun.*, 540 (1967); (b) J. R. Fletcher and I. O. Sutherland, *ibid.*, 1504 (1969).

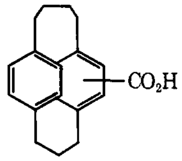
Unlike ring rotation in these [2.2]metacyclophanes, that of the meta ring of [2.2]metaparacyclophane involves mainly C–H to π-electron repulsions in the transition state. Deformation of the π-electron system of the para ring through rehybridization probably is one of the forms of accommodation the system makes in the transition state.

The system closest to [2.2]metaparacyclophane in ring size is [3.2]metacyclophane. The 2-substituted derivatives of X have been studied.[12a] The $\Delta G^{\ddagger}$ for ring inversion for compounds X vary between 15.8 and 19.1 kcal mol^{-1} (at 60–120°) depending on the bulk of R. These values are not far from the 20 kcal mol^{-1} free energy barrier to rotation at 140° for the meta ring of [2.2]metaparacyclophane. Both systems are eleven-membered, and differ by one in the number of aromatic *vs.* aliphatic carbons in their largest rings.

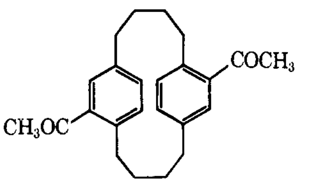
The inability of the para ring in IIe to rotate is not surprising, in view of the optical stability of optically active XI up to 240°,[15] and the fact that optically active XII has $\Delta G_{160°}^{\ddagger}$ ~33.5 kcal mol^{-1} [16] for racemization. Even compound XIII[17] exhibits $\Delta G_{15°}^{\ddagger}$ ~ 15 kcal mol^{-1}.[10,18]



XI



XII



XIII

Experimental Section

General. Melting points are uncorrected and were taken on a Thomas-Hoover Uni-Melt capillary apparatus. Solvents are reagent grade unless otherwise specified. Optical rotations were determined with a Perkin-Elmer 141 polarimeter and a 1-dm thermostated cell in chloroform. Nmr determinations were made with a Varian A-60D in *ca.* 10% solutions. All spectra were run in deuteriochloroform with tetramethylsilane as an internal standard. In descriptions of nmr data, s = singlet, d = doublet, t = triplet, m = multiplet, and the numbers that follow these letters indicate the number of protons the signal represents. For multiplets the chemical shift of the strongest peak is reported.

12-Aldehydo[2.2]metaparacyclophane (IIe). To 16 ml of pyridine cooled to 15°, chromium trioxide (0.800 g, 8 mmol) was added in small amounts over a 15-min period. Then a solution of 390 mg (1.64 mmol) of the alcohol IId[3] and 4 ml of pyridine was added all at once to the above (temperature rose to 30°). The reaction was heated to 65° in 3 min using a heated air gun. After 1 min of rapid stirring at 65° the reaction mixture was poured onto an ice–water slurry. This mixture was extracted three times with 60 ml of ether. The ethereal extracts were combined and washed three times with 30 ml of 6 *M* HCl, water, dilute potassium hydroxide solution, and saturated sodium bicarbonate solution, and dried. After the ether was removed an oil remained which crystallized from cold ether–pentane to give white crystals of aldehyde IIe, mp 76–79° (190 mg, 49%). The nmr spectrum showed the 12- to 15-isomer ratio in solution to be 2.09–1.00, respectively, by integration of aldehydic protons. At 37° two superimposed spectra were visible: 12-isomer, τ −0.32 (s, 1, CHO), 2.27 (broad s, 1, *p*-ArH), 3.17 (m, 3, *m*-ArH), 4.00 (d, 2, $J \sim 1.5$ Hz, *p*-ArH), 4.85 (broad s, 1, *m*-ArH), 5.9–8.0 ppm (m, 8, CH_2CH_2); 15-isomer, τ 0.52 (s, 1, CHO), 2.70 (d, 2, $J \sim 1.5$ Hz, *p*-ArH), 3.17 (m, 3, *m*-ArH), 3.63 (d, 1, $J \sim 1.5$ Hz, *p*-ArH), 4.70 (broad s, 1, *m*-ArH), 5.9–8.0 ppm (m, 8, CH_2CH_2). *Anal.* Calcd for $C_{17}H_{16}O$: C, 86.40; H, 6.83. Found: C, 86.37; H, 6.61.

Resolution of 12-Carboxy[2.2]metaparacyclophane ((+)-IIb and (−)-IIb). Attempts to form a crystalline salt of the acid with quinine using either methanol or acetone were unsuccessful. A mixture of 2.0 g (7.95 mmol) of 12-carboxy[2.2]metaparacyclophane, 3.2 g (8.10 mmol) of brucine (mp 178–182°, recrystallized from acetone), and 200 ml of acetone was stirred to give solution. The solvent was then evaporated to give a glass. Addition of 10 ml of methanol to this glass forced most of the salt out of solution as button-shaped crystals. This salt was fractionally crystallized four times from methanol to give 1.5 g of salt, $[\alpha]^{25}_{546}$ −32.7°, $[\alpha]^{25}_{436}$ −61.7° (*c*, 1.07, $CHCl_3$). Since the rotation of the salt remained constant upon further recrystallization, it was converted to the free acid with 6 *N* hydrochloric acid (weaker acid was later found to give better yield) and ether. The aqueous phase was again extracted with ether. The ether extracts were combined, washed with water, dried ($MgSO_4$), and concentrated, and the acid crystallized from ether–pentane to give 450 mg (23%) of (+)-IIb: mp 167.7–169.7°; $[\alpha]^{25}_{546}$ 34.2°, $[\alpha]^{25}_{436}$ 116° (*c* 1.01, $CHCl_3$, unchanged by further recrystallization). A sample of less optically pure salt, $[\alpha]^{25}_{546}$ −34.8°, gave partially optically pure (+)-IIb, $[\alpha]^{25}_{546}$ 33.3° (*c* 1.02, $CHCl_3$), which had a low and broad melting point, mp 161–167°. *Anal.* Calcd for $C_{17}H_{16}O_2$: C, 80.92; H, 6.39. Found: C, 81.01; H, 6.31.

Crystals (0.78 g) of brucine salt formed in the mother liquor, which had a different shape, gave rotation $[\alpha]^{25}_{546}$ −34.5°, $[\alpha]^{25}_{436}$ −87.2° (*c* 1.09, $CHCl_3$). Recovery of acid with 1 *N* hydrochloric acid and ether as above gave 251 mg of (−)-IIb: $[\alpha]^{25}_{546}$ −31.7°, $[\alpha]^{25}_{436}$ −107° (*c* 0.99, $CHCl_3$); mp 158–168.8°. Crystallation gave fractionation yielding 70 mg of (−)-IIb: $[\alpha]^{25}_{546}$ −33.1°, $[\alpha]^{25}_{436}$ −112°, $[\alpha]^{25}_{365}$ −520° (*c* 1.04, $CHCl_3$); mp 165–167.5°. *Anal.* Calcd for $C_{17}H_{16}O_2$: C, 80.92; H, 6.39. Found: C, 80.70; H, 6.20.

Optically Active 12-Carbomethoxy[2.2]metaparacyclophane ((+)-IIc). A mixture of 200 mg of acid ((+)-IIb, $[\alpha]^{25}_{546}$ 34.2°, mp 167.7–169.7°), 20 ml of methanol, and 0.5 ml of concentrated sulfuric acid was refluxed for 4 days. The solution was then cooled, washed with sodium bicarbonate solution and saturated sodium chloride solution, dried ($MgSO_4$), and evaporated to remove solvent. The product remaining was an oil which later crystallized from pentane in the freezer. The ester was sublimed twice and recrystallized from pentane to give 120 mg of crystalline (+)-IIc: mp 58.7–62°; $[\alpha]^{25}_{546}$ 26.5°, $[\alpha]^{25}_{436}$ 84.0°, $[\alpha]^{25}_{365}$ 340° (*c* 0.995, $CHCl_3$). *Anal.* Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.21; H, 6.68.

Thermal Stability of (+)-12-Carbomethoxy[2.2]metaparacyclophane ((+)-IIc. Exactly 31.5 mg of (+)-IIc ($[\alpha]^{25}_{546}$ 26.5°, $[\alpha]^{25}_{436}$ 84.0°, $[\alpha]^{25}_{365}$ 340° (*c* 0.995, chloroform), mp 58.7–62°) was sealed under vacuum in a glass ampoule and immersed in a 200° Wood's metal bath for 25 hr. The sample had not discolored and a rotation was taken directly. Recovered was 30.5 mg of IIc (oil which crystallized on standing) which gave a rotation of $[\alpha]^{25}_{546}$ 26.6° (*c* 1.53, chloroform). The material was sublimed to give 26 mg of material with mp 58–59.7° and $[\alpha]^{25}_{546}$ 26.0°, $[\alpha]^{25}_{436}$ 82.0°, $[\alpha]^{25}_{365}$ 331° (*c* 1.02, $CHCl_3$). These data are in agreement with a retention of configuration greater than or equal to 97.5%. Similar results of quantitative retention of optical activity were obtained for (+)-IIc for a heating period of 7.5 hr at 155°

Ring Rotation Rates for 12-Aldehydo[2.2]metaparacyclophane (IIe) at −13.5°. The aldehyde was added to frozen deuteriochloroform in an nmr tube and warmed to −50° to attain solution. The spectrometer was then adjusted to −13.5° by calibration with a methanol standard.[19] The aldehyde proton at τ −0.32 (H_f, Figure 2) was then observed to decrease with respect to time as the signal at τ 0.52 (H_l, 15-isomer) increased. Since the heights of the two peaks were proportional to the areas (widths at half height were the same) the peak height was used as the integration

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(15) M. Sheehan, Ph.D. Dissertation, University of California at Los Angeles, 1969.

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(17) D. J. Cram and R. H. Reeves, *ibid.*, **80**, 3094 (1958).

(18) In ref 10, the value of ~7 kcal mol^{-1} reported was miscalculated.

(19) A. L. Van Geet, *Anal. Chem.*, 40, 2227 (1968).

Table II

Time, min	Nmr signal intensities: Relative height H_t	H_l	$H_t/(H_t + H_l)$	$(A_0 - A_e)/(A - A_e)$
0.0	100	0.0	1.00	31/31
2.8	20.1	0.9	0.957	31/26.7
4.8	21.5	1.3	0.943	21/25.3
7.0	21.1	1.6	0.929	1.30
9.3	20.4	1.8	0.919	1.35
12.5	19.0	2.0	0.905	1.44
15.0	18.9	2.6	0.879	1.64
18.8	17.8	3.0	0.856	1.87
25.0	18.3	4.0	0.820	2.38
31.0	19.0	4.7	0.802	2.77
41.5	20.4	5.7	0.782	3.38
48.4	20.4	5.7	0.748	5.35
64.0	19.7	7.4	0.727	8.37
72.0	20.4	8.1	0.716	11.91
82.0	20.3	8.4	0.707	18.25
94.0	19.9	8.8	0.694	77.50

value. The data of Table II were recorded over a period of 94 min. The sum of the forward and reverse rate constants was obtained with eq 1,[20] where A_0 = original moles of the 12-isomer,

$$\ln\left[\frac{A_0 - A_e}{A - A_e}\right] = (k_1 + k_{-1})t \qquad (1)$$

A_e = equilibrium number of moles of the 12-isomer, A = instanteous moles of the 12-isomer, and k_1 and k_{-1} are rate constants for the equilibrium

$$\text{12-isomer} \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} \text{15-isomer}$$

From a plot of ln $[(A_0 - A_e)/(A - A_e)]$ *vs.* t is obtained $(k_1 + k_{-1}) = 5.55 \pm 0.60 \times 10^{-4}\ \text{sec}^{-1}$. Applying $k_1/k_{-1} = 0.45 \pm 0.02$ (which was obtained from the final value of H_t/H_l), $k_1 = 1.72 \pm 0.26 \times 10^{-4}\ \text{sec}^{-1}$ and $k_{-1} = 3.83 \pm 0.57 \times 10^{-4}\ \text{sec}^{-1}$ at $-13.5°$.

Ring Rotation Rates for 12-Aldehydo[2.2]metaparacyclophane (IIe) at 140°. When aldehyde IIe was dissolved in hexachlorobutadiene and the solution degassed, the coalescence of the aldehyde protons in the nmr spectrum appeared at 140°. Since the populations were not equivalent a computer treatment of the data was necessary. By applying the Saunders'[8] computer program for exchange between multiple sites the best fit between the experimental spectrum and computer spectra was obtained for $k_1 = 85\ \text{sec}^{-1}$ and $k_{-1} = 175\ \text{sec}^{-1}$. The following equations were then applied to determine activation parameters: $\Delta H^{\ddagger} = R(T'T/T' - T)\ \ln\ (k'T/kT')$, $k = \kappa(kT/h)\ \exp(-G/RT)$ assuming κ, transmission coefficient, = 1 or $\Delta G^{\ddagger} = 2.303RT(10.319 - \log k + \log T)$, and $\Delta G = \Delta H - T\Delta S$.[20]

Equilibrium Constants between 12-Substituted- and 15-Substituted-[2.2]Metaparacyclophanes (II ⇄ III). These constants were determined by integration of the nmr spectra of their equilibrium mixtures. For IIa, IIc, and IIf the methyl protons were employed. For IId the methylene protons of the CH_2OH group were used. For IIe, the aldehyde proton was integrated. In all cases, the spectra were integrated about 10 min after the solutions were prepared to allow for equilibration ($t_{1/2}^{25°} \sim 14$ sec).

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Carbon-13 Magnetic Resonance. Conformation in Some *tert*-Butyl-1,3-dioxanes[1a]

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Salt Lake City, Utah 84112. *Received December 3, 1970*

Abstract: The natural abundance carbon-13 nuclear magnetic resonance spectra of 12 *tert*-butyl-1,3-dioxanes and pertinent supporting data are described. The chemical shifts of the ring and substituent carbon atoms are affected by the positions and by the conformations of the substituents. It is suggested that substituent shift correlations can in most instances be transferred from cyclohexane derivatives to their heterocyclic analogs provided one takes into consideration the deshielding effects of the ring oxygens on axial 5-substituents.

The potential of carbon-13 magnetic resonance spectroscopy as a tool in conformational analysis has by now become generally recognized. It is clear that the carbon-13 chemical shift is not only capable of providing detailed information concerning charge distribution in a molecular system,[2] but also is a sensitive index of the nature of the conformational environment in which a given carbon atom may be found.[3-9]

Classically cyclohexane and its derivatives have provided the most important test case for any criteria concerning conformational analysis. It is perhaps, therefore, not too surprising that most of the preceding

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(1) (a) Presented at the 161st National Meeting of the American Chemical Society, Los Angeles, Calif., April 1, 1971; (b) University of Alberta; (c) University of Notre Dame; (d) University of Utah.

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