Determination of Equilibrium Constants.—Equilibrium constants and molar extinction coefficients were determined in the manner described by Benesi and Hildebrand.[3,8] Measurements were made at 3 points in methylene dichloride solution, at 25°, for the three compounds investigated (4-ethyl- 4-acetyl- and 4-

cyano[2.2]paracyclophane). The mole fractions of the donors were varied from 0.0044 to 0.033 while the TCNE concentrations were maintained nearly constant, around 0.007 M. A good straight line was obtained through the three measured points for the compounds investigated.

[Contribution from the Department of Chemistry of the University of California at Los Angeles, Los Angeles 24, Calif.]

Macro Rings. XXVIII. Structure–Reactivity–N.m.r. Spectra Relationships in the [1.n]Paracyclophanes[1]

By Donald J. Cram and Lawrence A. Singer

The [1.8]-, [1.9]- [1.10]- [1.11]- and [1.12] paracyclophanes and 4,4'-diethyldiphenylmethane were subjected to potassium tert-butoxide-catalyzed hydrogen–deuterium exchange in tert-butyl alcohol-OD at 192–208°. Exchange occurred exclusively at the diarylmethylene position. Crude rate constants for exchange were calculated. The two largest cycles exchanged with rate constants comparable to the open-chain model, but the rate constants dropped off rapidly as the cycles decreased further in size, the maximum spread being about 3 powers of 10. Similar exchange experiments demonstrated that 4-ethyl[2.2]paracyclophane underwent exchange exclusively at the non-bridging methylene position nine times faster than 2,5-dimethylethylbenzene exchanged at the comparable position. Oxidation with chromic acid of [1.8]-, [1.10]- and [1.12]paracyclophanes occurred with increasing ease in the order listed. Monoketones were isolated from the last two cycles, but the smallest cycle produced no ketone. Use of nuclear magnetic resonance (n.m.r.) spectral techniques demonstrated the carbonyl group to be attached to phenyl in the longer of the two bridges. Similar oxidation of 4,4'-diethyldiphenylmethane gave exclusively 4,4'-diethyldiphenylketone. The n.m.r. spectra of the 5 [1.n]paracyclophanes were taken and found to exhibit peculiarities not found in 4,4'-diethyldiphenylmethane. These reactivity and spectral characteristics of the cycles are interpreted in terms of their unusual structures.

Variation of the number of methylene groups (n) in the longer bridge of the [1.n]paracyclophanes provides a series of compounds which allow a systematic study to be made of the effect of structure on reactivity at carbon bound to two aryl groups. Of interest are changes in ease of formation of carbonium ions, carbanions, carbenes and radicals as n is varied.
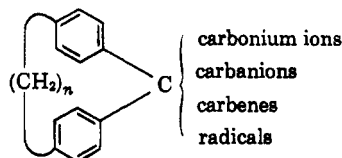

In previous work the [1.n]paracyclophanes with n = 7, 8, 9, 10, 11, and 12 were prepared in satisfactory yields with exception of the smallest cycle, whose synthesis, although achieved, was impractical.[2] The present study deals with the rates of carbanion formation of the [1.8]- to [1.12]paracyclophanes, as well as with the behavior of the compounds when oxidized with chromic acid. The effect of variation of n on the n.m.r. spectra of the hydrocarbons has also been investigated.

Results

Base-catalyzed Hydrogen–Deuterium Exchange Reactions.—The [1.8]-, [1.9]-, [1.10]-, [1.11]- and [1.12]-paracyclophanes and 4,4'-diethyldiphenylmethane (I) were subjected to hydrogen–deuterium exchange reactions in tert-butyl alcohol-OD with potassium tert-butoxide as catalyst at 192 to 208° in sealed ampoules. The amount of deuterium incorporated into the molecule and the position of exchange were determined through n.m.r. analysis. The aromatic, diarylmethylene, benzyl and remaining methylene hydrogens are well separated from one another in the spectra (see later section). Calculations of the extent of exchange for the paracyclophanes were based on the integrated absorptions, with the methylene hydrogens non-adjacent to aryl as standards. For the open-chain model, the hydrogens of the methyl group were

(1) The authors wish to thank the National Science Foundation for a grant used in support of this research.

(2) (a) D. J. Cram and M. F. Antar, J. Am. Chem. Soc., **80**, 3103 (1958); (b) D. J. Cram, Rec. Chem. Progr., **20**, 71 (1959).

similarly employed. All integrations were systematically rechecked at least twice on different days. The results appear in Table I.

For purposes of comparison, 4-ethyl[2.2]paracyclophane[3a] (II) and 2-ethyl-1,4-dimethylbenzene (III) were also subjected to exchange conditions. In the former compound, the benzene rings are known to be non-planar, and the latter compound serves as a planar model. The amounts of exchange that occurred in the bridging methylenes, in the aromatic nucleus and at
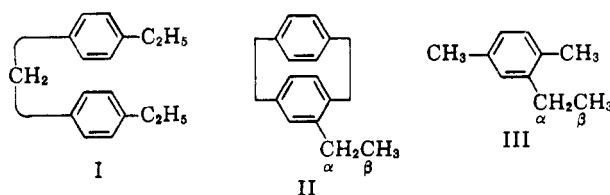
C_α of II could all be measured by n.m.r. techniques with the hydrogens of the β-methyl group as standard. For III, the absorptions of the β-methyl hydrogens were used as standards, and the amounts of exchange at C_α, at the methyl groups of the benzene ring and at the aromatic carbons were measured. Table II records the results.

The rate constants and therefore the rate factors of Tables I and II are very crude (see footnotes of tables), but the factors are large enough compared to experimental error to serve the purposes of this investigation.

Oxidation of the [1.n]Paracyclophanes.—To determine the relative ease of oxidation of the [1.8]-, [1.10]- and [1.12]paracyclophanes and of their open-chain model (I), the substances were treated with 1.7 equivalents of chromic acid in 97% acetic acid–3% water at 25°. The reactions were interrupted before completion and starting material and ketonic products were isolated through chromatographic procedures. The structures of the ketonic products of the reactions were determined through their n.m.r. spectra (see next section). Table III records the results. The ketone produced by oxidation of [1.11]paracyclophane was

(3) (a) L. A. Singer and D. J. Cram, J. Am. Chem. Soc., **85**, 1080 (1963); (b) D. J. Cram and L. A. Singer, ibid., **85**, 1075 (1963).

TABLE I

POTASSIUM *tert*-BUTOXIDE-CATALYZED HYDROGEN–DEUTERIUM EXCHANGE IN *tert*-BUTYL ALCOHOL-OD OF [1.n]PARACYCLOPHANES AND MODEL I[a]

Run	Cmpd.	Concn., M Subst.	Concn., M Base	T, °C.	Time, hr.	Benzhydryl % H exch.[b]	$k_2 \times 10^6$, l. m.$^{-1}$ sec.$^{-1c}$	Rel. rate
1	I[d]	0.27	0.37	194	24	93	79	1
2	[1.12]	.19	.37	195	10	89	162	2
3	[1.11]	.25	.34	192	51	100	..	..
4	[1.11]	.26	.37	192	6	78	178	2.3
5	[1.10]	.26	.37	192	11	22	17	} 0.2
6	[1.10]	.23	.38	193	19	26	11	
7	[1.9]	.27	.38	205	44	64	17	0.06
8	[1.8]	.29	.37	205	70	0	..	..
9	[1.8]	.26	.38	208	382	30	0.7	0.0024

[a] Analysis made on Varian Associates model A-60 n.m.r. spectrometer. [b] For the paracyclophanes, deuterium incorporation into the aromatic rings and the benzyl positions was <5%, or within experimental error of 0; for the open-chain model, exchange at the benzyl position was 14%, but was <5% for the aromatic ring. [c] Single point rate constants corrected to 195° with $\Delta H \neq$ of 25 kcal./mole as assumed activation energy. [d] 4,4′-Diethyldiphenylmethane.

TABLE II

POTASSIUM *tert*-BUTOXIDE-CATALYZED HYDROGEN–DEUTERIUM EXCHANGE IN *tert*-BUTYL ALCOHOL-OD OF 4-ETHYL[2.2]-PARACYCLOPHANE (II) AND MODEL III[a]

Run	Cmpd.	Concn., M Subst.	Base	T, °C.	Time, hr.	% H exch. at C_α	$k_2 \times 10^6$, l. m.$^{-1}$ sec.$^{-1}$	Rel. rate
10	III	0.30	0.40	208	68	78[b]	15	1
11	II	.27	.38	208	108	100[c]	..	..
12	II	.28	.40	208	8	67[c]	97	} 9
13	II	.27	.40	208	5.5	72[c]	162	
1	I	.27	.37	194	24	14	22[d]	1.5

[a] Analysis made on Varian Associates model A-60 n.m.r. spectrometer. [b] Aromatic methyl groups, 75% exchange of hydrogen, <5% in aromatic nucleus. [c] <5% exchange in methylenes of bridges, or aromatic nucleus. [d] Corrected to 208° with $\Delta H \neq$ of 25 kcal./mole as assumed activation energy.

TABLE III

OXIDATION OF [1.n]PARACYCLOPHANES AND THEIR OPEN-CHAIN MODEL I[a]

Start. mat.	% start. mat. recovd.	% –ArCOAr–	% –CH₃COAr–	Total, %
I	45	20	0	65
[1.8]	65	0	0	65
[1.10]	61	0	8	69
[1.12]	34	0	25	59

[a] Excess chromic anhydride (1.7 equivalents) in 97% glacial acetic acid–3% water at 25° for 24 hr.

Nuclear Magnetic Resonance Spectra.

—The n.m.r. spectra of [1.8]-, [1.9]-, [1.10]-, [1.11]- and [1.12]-paracyclophanes and of their model I were taken, and the chemical shifts, multiplicity and peak assignments are shown in Table IV. The coupling constants for the observed splitting of the aromatic hydrogens of the paracyclophanes are recorded in Table V.

Table VI records the peak assignments, numbers of hydrogens and multiplicity associated with the n.m.r. spectra of the four ketones produced by oxidation of [1.10]-, [1.11]- and [1.12]paracyclophanes and of 1,4′-diethyldiphenylmethane (I).

The n.m.r. spectrum of 2,5-dimethylethylbenzene (III) exhibited a multiplet centered at $\tau = 3.2$ (aromatic hydrogens), a quadruplet centered at 7.38 (methylene hydrogens), an unsymmetrical doublet at 7.76 (hydrogens attached to aromatic methyl) and a triplet at 8.83 (hydrogens attached to aliphatic methyl). Non-deuterated 4-ethyl[2.2]paracyclophane gave an n.m.r. spectrum as: a multiplet centered at 3.72 τ (aromatic hydrogens), a multiplet at 7.05 τ (bridge methylene hydrogens), a multiplet at 7.58 τ (methylene hydrogens) and a triplet at 8.93 τ (methyl hydrogens). Both spectra were taken in 1 M carbon disulfide solution on a Varian Associates model A-60 n.m.r. spectrometer.

Attempted Syntheses of [1.n]Paracyclophanes with Functional Groups at the Benzhydryl Position.

—The

TABLE IV

NUCLEAR MAGNETIC RESONANCE SPECTRAL DATA OF [1.n]PARACYCLOPHANES AND THEIR OPEN-CHAIN MODEL I[a]

Cmpd.	Ar–H τ	Mult.	ArCH₂Ar τ	Mult.	ArCH₂C τ	Mult.	C(CH₂)ₓC τ	Mult.	τ	Mult.	τ	Mult.
I[b]	3.02	S.[c]	6.16	S.[c]	7.40	Quad.[d]	..	....	..	..	..	..
[1.8]	3.21	Quad.[d]	6.19	S.[c]	7.50	Trip.[e]	8.70	Mult.[f]	9.10	Mult.[f]	9.70	Mult.[f]
[1.9]	3.01	Quad.[d]	6.26	S.[c]	7.48	Quad.[d]	8.50	Mult.[f]	9.42	Mult.[f]	..	....
[1.10]	3.07	Quad.[d]	6.25	S.[c]	7.50	Quad.[d]	8.58	P.r.[g]	9.22	P.r.[g]	..	....
[1.11]	3.11	Quad.[d]	6.28	S.[c]	7.47	Quad.[d]	8.52	P.r.[g]	9.10	P.r.[g]	..	....
[1.12]	2.97	S.[c]	6.21	S.[c]	7.42	Quad.[d]	8.43	P.r.[g]	9.02	P.r.[g]	..	....

[a] Varian Associates model A-60 n.m.r. spectrometer, 1 M in carbon disulfide; tetramethylsilane as an internal standard. [b] Absorption due to CH₃ observed at $\tau = 8.78$; triplet. [c] Singlet. [d] Quadruplet. [e] Triplet. [f] Multiplet. [g] Poor resolution.

TABLE V

COUPLING CONSTANTS OF AROMATIC PROTONS OF [1.n]-PARACYCLOPHANES AT 60 M.C.[a]

Paracyclophane	J-Values, c.p.s.
[1.8]	6.5
[1.9]	4.0
[1.10]	4.0
[1.11]	2.5
[1.12]	0

[a] Varian Associates model A-60 nuclear magnetic resonance spectrometer.

also prepared under non-standard conditions for spectral comparisons.

monobromides of the [1.n]paracyclophanes substituted at the benzhydryl position were designed for study of carbonium ions and carbenes. Treatment of [1.8]-paracyclophane with an equivalent of N-bromosuccinimide gave a complex mixture of mono- and dibromides. These results are similar to those obtained in bromination of [2.2]paracyclophane.[4] The substance showed little inclination to give one discrete product.

Attempts to ring close compounds V and VI through use of the acyloin reaction gave back starting material,

(4) K. C. Dewhirst and D. J. Cram, *J. Am. Chem. Soc.*, **80**, 3115 (1958).

TABLE VI

NUCLEAR MAGNETIC RESONANCE SPECTRAL DATA OF KETONIC PRODUCTS OF OXIDATION OF [1.n]PARACYCLOPHANES AND THEIR OPEN-CHAIN MODEL I[a]

Starting material	Ar–H			ArCH₂Ar			ArCH₂C + ArCOCH₂C[b]			C(CH₂)₂C[c]	
	τ	No. H	Mult.	τ	No. H.	Mult.	τ	No. H	Mult.	τ	No. H
I[d]	2.63	..	Quad.[e]	6.16	0	..	7.28	..	Quad.	..	..
[1.10]	2.62 ⎰ 7.12	Quad.[e]	6.13	1.89	S.[f]	7.37	3.94	Quad.	8.58 ⎱ 15.1
	3.05 ⎰	Quad.[e]	..	..	..	..	..	...	9.13 ⎰
[1.11]	2.66 ⎰ 7.72	Quad.[e]	6.17	1.63	S.[f]	7.38	4.40	Quad.	8.56 ⎱ 16.3
	3.06 ⎰	Quad.[e]	..	..	..	..	..	...	9.14 ⎰
[1.12]	2.78 ⎰ 7.78	Quad.[e]	6.22	1.89	S.[f]	7.40	4.10	Quad.	8.37 ⎱ 18.1
	3.05 ⎰	S.[f]	..	..	..	..	..	...	9.18 ⎰

[a] Varian Associates model A-60 n.m.r. spectrometer, 1 M in carbon disulfide, tetramethylsilane as an internal standard; numbers of hydrogens counted by allowing total integral to equal theoretical number of hydrogens in molecule. [b] The two types of hydrogen appear in the same place in the spectrum. [c] Unresolved. [d] Methyl group appeared as a triplet at 8.72, spectrum was not integrated. [e] Quadruplet. [f] Singlet.

IV, X = H
V, X = OH
VI, X = (lactone)
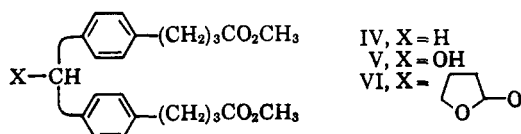
although the parent substance (IV) ring closed in 28% yield.[2a]

Discussion

The data of the last section indicate striking differences in bridgehead reactivity both within the homologous series of the [1.n]paracyclophanes, as well as between the paracyclophanes as a class and their open-chain models. The differences in geometry are also reflected in the n.m.r. spectra of the cycles and their models.

Bridgehead Acidity of the [1.n]Paracyclophanes.— The data of Table I indicate that the kinetic acidity of the diarylmethylene hydrogens of the [1.n]paracyclophanes are comparable to or slightly greater than those of their open-chain model when n is 12 or 11. A rate drop for the exchange reaction by a factor of 10 occurs in passing from n = 11 to n = 10. When n = 9, a further drop by a factor of 3 is observed. With n = 8, the rate declines by an additional factor of 25. The over-all factor by which [1.12]paracyclophane exceeds [1.8]paracyclophane in exchange rate is about 3 powers of 10.

Carbanions undoubtedly intervene as intermediates in the base-catalyzed hydrogen-deuterium exchange reaction. This reaction has low steric requirements, and the homologous cycles and their open-chain models offer little steric differences to the approach of base to their diarylmethylene hydrogens. The inductive effect of the two phenyl groups should differ little in the cycles and their open-chain model. Exchange of the non-bridging methylene hydrogens of 4-ethyl[2.2]para-cyclophane (II) occurs 9 times as fast as III, its open-chain model (see Table II). Since the benzene rings of II are bent[6] more than those of [1.8]paracyclophane, such an effect does not explain the large rate difference between the latter compound and its larger homologs.[6]

n	θ
7	71°
8	84°
9	98°
10	109–113°

[1.n]Paracyclophanes
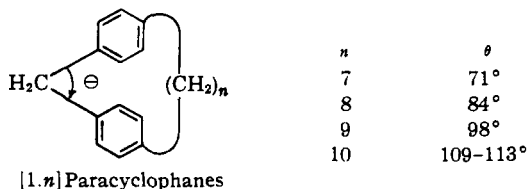
(5) C. J. Brown, J. Chem. Soc., 3265 (1953).

(6) The rate factor of 9 by which 4-ethyl[2.2]paracyclophane exceeds its open-chain model in the exchange reaction is best accounted for by transannular charge distribution in the anion produced. A similar rate factor for carbonium ion formation was observed in the hydrolysis rates of 4-bromomethylene[2.2]paracyclophane and 2,5-dimethylbenzyl bromide, the cycle being the faster by a factor of 7 at 52° [3b]

If all of the strain of the [1.n]paracyclophanes is presumed to concentrate in compression of θ, then the values of θ for various values of n are tabulated.[2a] These values are minimal because strain always distributes itself among as many bond angles as possible. However, θ undoubtedly decreases slightly with decreasing n. As θ decreases, the p-character of the aryl methylene bonds increases to accommodate the strain, and the s-character of the carbon–hydrogen bonds increases, making the protons more acidic. The enhanced acidity of cyclopropane[7d] compared to its larger homologs has been attributed[7a,7b,7c] to similar causes. The effect in the [1.n]paracyclophanes is probably small, and if anything would operate in a direction opposite to the observed result.

The loss of conjugation of the carbanion with the aromatic nuclei as n is decreased is probably mainly responsible for the decreased rates for the lower homologs. Molecular models suggest less flexibility in benzene ring orientation in the [1.12] system than in the open-chain model, particularly with an sp² carbon at the benzhydryl position. This flexibility decreases with decreasing n, until when n = 8, coplanarity of the bonds to the benzhydryl anion and one of the benzene rings is out of the question. This loss in flexibility applies both to the benzhydryl and benzyl positions of the paracyclophanes, but less at the latter. The exclusive attack on the benzhydryl position by base is attributed to the inductive effect (two phenyls vs. one).

An extreme example of the importance of the conjugative effect in carbon acids is found in the remarkable difference in acidity of triphenylmethane and triptycene.[8]

Bridgehead Radicals of the [1.n]Paracyclophanes.— If the initial step in chromic acid oxidation of hydrocarbons involves hydrogen atom abstraction as has been postulated,[9] then bridgehead carbon radicals are intermediates in the oxidations of the paracyclophanes. The rates of oxidation of I and of [1.8]-, [1.10]- and [1.12]paracyclophanes differ very little, as judged by the amount of starting material recovered after a standard length of time (see Table III). The model I oxidized exclusively at the benzhydryl and the [1.10]- and [1.12]paracyclophanes at the benzyl positions (see next section). The ring system of [1.8]paracyclophane probably was disrupted in the oxidation, since no ketonic material was isolated, yet hydrocarbon was consumed.

(7) (a) C. A. Coulson and W. F. Moffitt, J. Chem. Phys., 15, 151 (1947); (b) L. L. Ingraham in Newman's "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., p. 518; (c) N. Muller and D. E. Pritchard, J. Chem. Phys., 31, 768 (1959); (d) E. J. Lanpher, L. M. Redman and A. A. Morton, J. Org. Chem., 23, 1370 (1958).

(8) (a) P. D. Bartlett, M. J. Ryan and S. G. Cohen, J. Am. Chem. Soc., 64, 2649 (1942); (b) P. D. Bartlett and E. S. Lewis, ibid., 72, 1005 (1950).

(9) K. B. Wiberg and R. J. Evans, Tetrahedron, 8, 313 (1960).

These results suggest that conjugation in the transition state is more important in the oxidation than in the exchange reaction. Coplanarity of a trigonal carbon and the benzene ring can be more closely approached at the benzyl than at the benzhydryl position in the cycles, whereas much less difference in constraint exists in the two positions of the open-chain compound. The difference in inductive effect at the two positions probably plays only a minor role in directing the oxidation reaction.

The ease of formation of radicals in the cycloalkane series has been shown to generally decrease with decrease in ring size.[10] Decrease in the values of θ in [1.8]paracyclophane may also contribute to its lack of reactivity in the benzhydryl position. The result of the action of N-bromosuccinimide on [1.8]paracyclophane resembles that of chromic acid in the sense that a bad mixture of products was obtained in each case.

Nuclear Magnetic Resonance Spectra.

—The n.m.r. spectra of the [1.n]paracyclophanes exhibit unusual features not found in that of the open-chain model I. The most striking of these is in the spectral region characteristic of the aromatic hydrogens. The aromatic hydrogens of I and of [1.12]paracyclophane both produce a well defined singlet, the former at 3.02 τ and the latter at 2.97 τ (see Table IV). As n decreases in value, the singlet splits into a near symmetrical quadruplet, whose center moves irregularly upfield with decreasing n. The coupling constant associated with this splitting increases in value from 2.5 c.p.s. with $n = 11$ to 6.5 c.p.s. where $n = 8$ (Table V). This splitting and movement to higher fields is probably due to shielding of the aromatic hydrogens ortho to the benzhydryl position by the induced magnetic field in the transannular benzene ring. The value of θ undoubtedly decreases with decreasing values of n, and the benzene rings with their hydrogens are brought closer together. To the extent that the benzene rings are bent into shallow tubs, their carbon atoms rehybride slightly toward sp^3, which pushes each ortho-hydrogen even closer to the transannular ring.[11]

The [1.n]paracyclophanes differ also in their absorption in the non-benzyl, methylene hydrogen region (Table IV). As expected, the more rigid structures of the smaller cycles make for more discrete conformations, and the absorption bands are better resolved. Thus [1.8]paracyclophane exhibits three groups of absorptions centered at 8.70, 9.10 and 9.70 τ, whereas the other cycles have only two groups of absorptions at fields which are in general lower the greater the value of n. This shift to higher field with decreasing value of n is attributed to increased shielding of the methylene hydrogens by the induced magnetic fields of the two rings.

The n.m.r. spectra of the four ketones obtained by oxidation of I and of [1.12]-, [1.11]- and [1.10]paracyclophanes allow unequivocal structural assignments to be made. The ketone from I has no absorption in the diarylmethylene region (6.16 τ), but possesses absorption centered at 7.28 τ in the benzyl region (Table VI). Hence I produced the expected ketone VII when oxidized. The ketones from the paracyclophanes possessed these characteristics: two sets of

absorptions in the aromatic region (unlike VII); well defined singlets in the benzhydryl region which in intensity accounted for approximately 2 hydrogens; close to the proper number of methylene hydrogens not adjacent to either an aryl or ketone group (Table VI). Clearly the cyclic ketones possess structures VIII, IX and X.

VII

VIII, $n = 9$
IX, $n = 10$
X, $n = 11$
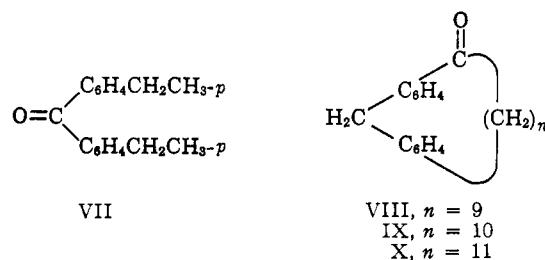
Experimental

Starting Materials for Exchange and Oxidation Studies.—The five [1.n]paracyclophanes were available from a previous study,[2a] and were purified as before until their melting points corresponded to those of the analytical samples.[2a] The substance 4-ethyl[2.2]paracyclophane was also available from other work,[3a] and the same sample was used here. The model compound, 4,4'-diethyldiphenylmethane (I) was prepared by a standard Wolff–Kishner reduction of 4,4'-diacetyldiphenylmethane of m.p. 93–94°, ref. 12. The product I was purified through chromatography on alumina, and gave b.p. 142° (2 mm.), n^{23}D 1.5510, literature[13] b.p. 139–141° (2 mm.). The substance I exhibited only a single peak in a vapor phase chromatogram on a column of 20% silicon rubber on firebrick at 204°, with helium as carrier gas, retention time 3 minutes. Application of a standard Wolff–Kishner reduction to 2,5-dimethylacetophenone[3b] gave 2,5-dimethylethylbenzene (III), b.p. 185° at 1 atm., n^{23}D 1.4988; literature[14] b.p. 185°, n^{17}D 1.5026.

p,p'-**Bis-(γ-carbomethoxypropyl)-benzophenone.**—By an ordinary esterification procedure, γ-phenylbutyric acid of m.p. 45–46° (lit.[15] m.p. 51–52°) was converted to its methyl ester in 92% yield, b.p. 87–89° (1.3 mm.), n^{26}D 1.4960. To 100 ml. of carbon disulfide was added 50 g. of this ester, followed by 17.4 g. of oxalyl chloride. The solution was cooled to 0° and 74 g. of anhydrous aluminum chloride was added slowly. The mixture was then stirred at 25° for 3.5 hr. The solvent was decanted from the heavy brown sirup that separated, and the sirup was stirred with 2 kg. of ice. The mixture was extracted with ether, the ether layer was washed with water, dried, and the solvent was evaporated to a thick orange liquid which was distilled to give 38.8 g. (73%) of faintly yellow liquid, b.p. 280–285° (2 mm.), n^{25}D 1.5510.

Anal. Calcd. for $C_{23}H_{26}O_5$: C, 72.23; H, 6.85. Found: C, 72.10; H, 7.01.

p,p'-**Bis-(γ-carbomethoxypropyl)-benzhydrol (V).**—To 25 ml. of absolute methanol was added 15 g. of the above keto ester. The solution was cooled to 0°, and a solution of 2.0 g. of sodium borohydride in 25 ml. of 90% methanol–10% water was added slowly. The mixture was stirred at 0° for 1 hr. and then at 25° for 9 hr. During this time 0.5 g. of additional sodium borohydride was added. The solution was then poured into 400 ml. of water held at a temperature of 50°, and 6 N hydrochloric acid was added until the pH of the solution was just below 7. The product was extracted with 500 ml. of ether, the ether layer was washed twice with salted water, dried and evaporated to give 13.4 g. of an oil (V) which exhibited no ketonic carbonyl in its infrared spectrum.

Anal. Calcd. for $C_{23}H_{28}O_5$: C, 71.85; H, 7.34. Found: C, 72.05; H, 7.29.

The tetrahydropyran ether VI of V was prepared as follows. To a mixture of 36.2 g. of V and 9.2 g. of dihydropyran was added 1 ml. of concd. hydrochloric acid. The heat liberated in the first 5 min. of reaction was dissipated by cooling the reaction mixture. After standing at 25° for 24 hr., the solution was shaken with water and ether. The ether layer was washed with dilute sodium bicarbonate solution, then with water, and was dried and evaporated. The product was chromatographed on a 28 by 5.5 cm. column of activated alumina slurry packed in pentane. The column was washed with 800 ml. of 10% ether in pentane, and the desired ether was eluted with 1300 ml. of

(10) (a) A. F. Trotman-Dickinson and E. W. R. Steacie, *J. Chem. Phys.*, **19**, 329 (1951); (b) C. G. Overberger, H. Biletch, A. B. Finestone, J. Lilker and J. Herbert, *J. Am. Chem. Soc.*, **75**, 2078 (1953).

(11) Experimental confirmation of this idea is found in the X-ray crystal structure work of C. L. Coulter and K. N. Trueblood (*Acta Cryst.*, in press), who observed that in the structure of tetradehydro[2.2]paracyclophane, the benzene rings are bent into tubs, and the transannularly located aromatic hydrogens are closer to one another than predicted if their carbons were purely sp² hybridized.

(12) M. H. Duval, *Compt. rend.*, **146**, 342 (1908).

(13) I. G. Matveev, D. A. Drapkina and R. L. Globus, *Trudy Vsesoyuz. Nauch.-Issledovatel., Inst. Khim. Reactivov*, **21**, 83 (1956).

(14) O. Jacobsen, *Ber.*, **19**, 2516 (1886).

(15) J. von Braun, *ibid.*, **43**, 2844 (1910).

15% ether in pentane; wt. 10.0 g. of colorless oil (VI), whose infrared spectrum exhibited no absorption in the O–H stretching region.

Anal. Calcd. for $C_{27}H_{34}O_6$: C, 71.77; H, 7.74. Found: C, 71.86; H, 7.99.

Attempted Acyloin Reactions of V and VI.—Application of the usual acyloin ring closure conditions[16] to V with sodium in refluxing xylene gave back about 23% of starting material, the rest being polymer. In a second attempt, a 7% recovery of starting material was obtained along with considerable polymer. A similar attempt with ether VI gave a 62% recovery of starting material in one run, and a 48% recovery in a second, the rest being polymer.

Chromic Acid Oxidations of [1.n]Paracyclophanes and Model I.—The procedure is illustrated as applied to [1.12]paracyclophane. The substance (2.98 g., 8.90 mmoles) was dissolved in 40 ml. of 97% glacial acetic acid–3% water. A solution of 1.0 g. of chromic acid (10 mmoles) in 45 ml. of 97% acetic acid–3% water was added over a 3-hr. period with stirring at 25°. The mixture was stirred for 24 hr. at 25°, poured into salt water, and the resulting mixture was extracted with ether. The ether layer was washed with saturated sodium bicarbonate solution, once with salt water, and was dried. Evaporation of the solvent deposited a waxy solid which was chromatographed on 25 by 2.5 cm. of activated alumina slurry packed in pentane. Starting material (1.0 g.) was washed from the column with 600 ml. of pentane. When treated with 300 ml. of 20% ether in pentane, the column yielded 0.75 g. (24%) of ketonic material, m.p. 78–85°. Recrystallization of this material from carbon tetrachloride gave 0.42 g. of ketone X, m.p. 89.8–90.5°. The substance in carbon tetrachloride solution exhibited bands at the wave lengths (μ): 3.44, 3.52, 5.96, 6.24, 6.62, 6.84, 6.93, 7.08, 7.90 and 8.46.

Anal. Calcd. for $C_{25}H_{32}O$; C, 86.15; H, 9.26. Found: C, 86.06; H, 9.25.

The same procedure applied to [1.10]paracyclophane gave 61% starting material and 8% of ketonic material, recrystallization of which gave VIII, m.p. 76.8–78.2°. The infrared spectrum of the substance in carbon tetrachloride gave bands at the wave lengths (μ): 3.44, 3.53, 5.98, 6.26, 6.64, 6.95 and 7.09.

Anal. Calcd. for $C_{23}H_{28}O$: C, 86.20; H, 8.81. Found: C, 85.94; H, 8.85.

The same procedure applied to [1.8]paracyclophane gave a 65% recovery of starting material and no ketonic material as shown by the absence of a ketonic carbonyl group in the total product before chromatography. Nothing but starting material was recovered from the chromatograph column.

(16) D. J. Cram and H. Steinberg, *J. Am. Chem. Soc.*, **73**, 5691 (1951).

The same procedure applied to 4,4′-diethyldiphenylmethane (I) gave 45% recovery of starting material, and 0.20 g. of ketonic product (VII), m.p. 43–44°, which when recrystallized from carbon tetrachloride gave m.p. 43–44°.

Anal. Calcd. for $C_{17}H_{18}O$: C, 85.67; H, 7.61. Found: C, 85.47; H, 7.87.

A somewhat different procedure was employed for oxidation of [1.11]paracyclophane to its corresponding ketone IX.[17] A mixture of 3.2 g. of [1.11]paracyclophane, 0.8 g. of chromium trioxide, 150 ml. of dry acetic acid and 7.5 ml. of concd. sulfuric acid was stirred for 20 hr. at room temperature. The reaction mixture was worked up by elution chromatography. The hydrocarbon fraction amounted to 2.10 g. (65%) while the ketonic material weighed 0.71 g. (25%), m.p. 82–84.5°. A small sample of this material was recrystallized from hexane to give white plates, m.p. 85–86°.

Anal. Calcd. for $C_{24}H_{30}O$: C, 86.10; H, 9.04. Found: C, 86.09; H, 9.05.

Ultraviolet Spectral Data on [1.10]-, [1.11]- and [1.12]Paracyclophanyl Ketones.[17]—Spectra were recorded on a Cary recording spectrophotometer model 11 PMS in 95% ethanol: 1-keto[1.10]paracyclophane, λ_{max} 258 mμ, log ϵ 4.08; 1-keto-[1.11]paracyclophane, λ_{max} 259 mμ, log ϵ 4.11; 1-keto[1.12]-paracyclophane, λ_{max} 259.5 mμ, log ϵ 4.16 mμ; acetophenone,[18] λ_{max} 242.5 mμ (ϵ 12,700), λ_{max} 279.5 mμ (ϵ 1050).

Hydrogen–Deuterium Exchange Reactions.—In a typical run (2), a carefully weighed portion of hydrocarbon (0.254 g.) was added to a clean, dry, heavy-walled Pyrex tube sealed at one end and constricted at the top. From a stock solution of 0.37 N potassium *tert*-butoxide in *tert*-butyl alcohol-OD[19] (99% of one gram atom of deuterium by combustion and falling drop method) was added by means of a fast draining automatic pipet 4.0 ml. of reaction medium. The resulting solution and tube were flushed with pure dry nitrogen, cooled to 0° and sealed. The tubes were never more than 50% full, since room for expansion of solvent is required. The tube was heated in a Woods metal-bath maintained at 195° for 10 hr., with the tube immersed only to the level of the liquid. The tube was cooled to 0° and opened. No pressure had developed. The solution was shaken with a mixture of 150 ml. of salted water and 100 ml. of pentane. The aqueous phase was extracted with two 50-ml. portions of pentane, and the combined pentane extracts were washed with three 150-ml. portions of salt water, dried and evaporated to give 0.218 g. of product. This material was dried at 25° under 2 mm. pressure and was submitted directly to n.m.r. analysis.

(17) The authors are indebted to Dr. M. F. Antar for this experiment and the ultraviolet spectral data.

(18) G. H. Beaven and E. R. Johnson, *J. Chem. Soc.*, 655 (1957).

(19) D. J. Cram and B. Rickborn, *J. Am. Chem. Soc.*, **83**, 2178 (1961).

Macro Rings. XXIX. Stereochemistry of a 1,6-Cycloaddition Reaction[1]

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RECEIVED NOVEMBER 2, 1962

The naphthalene analog of [2.2]paracyclophane ([2.2]paracyclonaphthane) has been synthesized in 3% yield by an elimination–cycloaddition reaction with 4-methyl-1-naphthyltrimethylammonium hydroxide as starting material. The same isomer was prepared by a 9-step sequence from [2.2]paracyclophane in 0.07% yield. By its nature, the latter synthesis led to the *anti* isomer of [2.2]paracyclonaphthane, a conclusion confirmed by nuclear magnetic resonance (n.m.r.) spectral comparisons. Production of the *anti* isomer in the 1,6-to-1,6-cycloaddition reaction indicates that unlike the Diels–Alder reaction, π–π interactions were minimized in the transition state. In the multistep preparation of [2.2]paracyclonaphthane, n.m.r. spectral evidence was obtained that the homoannular dibenzo derivative of [2.2]paracyclophane was produced as a by-product, although the substance was not obtained in a pure state due to its instability. Benzo[2.2]paracyclophane was also synthesized, and served as a model for n.m.r. and ultraviolet spectral comparisons.

One of the more important stereochemical generalizations of organic chemistry is that in the Diels–Alder reaction the predominant isomer is that whose transition state of formation maximizes π–π-interactions of the two components (Alder's *endo* rule).[3] Although

of a different character, the Cope rearrangement assumes a steric course which minimized π–π interactions in the transition state which leads to the predominant product.[4] The present investigation is addressed to the problem of which isomer is formed (*syn*- or *anti*-II) when intermediate A dimerizes. The formally analogous question of whether *syn*- or *anti*-[2.2]metacyclophane (IV) is formed when dibromide III is treated with sodium has been answered in favor of the *anti* isomer.[5] On the other hand, synthesis of

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W. A. Mueller, *J. Am. Chem. Soc.*, **84**, 297 (1962), and references cited therein.

(4) W. E. Doering and W. R. Roth, *Tetrahedron*, **18**, 67 (1962).