Macro Rings. XXXVI. Ring Expansion, Racemization, and Isomer Interconversions in the [2.2]Paracyclophane System through a Diradical Intermediate[1,2]

Hans J. Reich and Donald J. Cram

Contribution No. 2280 from The Department of Chemistry of The University of California at Los Angeles, Los Angeles, California 90024.
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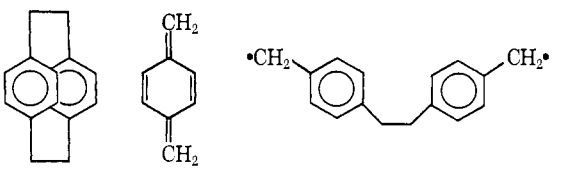
Abstract: When heated to approximately 200°, [2.2]paracyclophane and its derivatives cleave at the benzyl-to-benzyl bond to give the *p,p'*-dimethylenebibenzyl diradical (or derivatives of this diradical), whose fate depends on the medium. For example, optically pure (−)-4-carbomethoxy[2.2]paracyclophane underwent racemization at 200° at a rate little dependent on medium polarity. Without solvent, pseudo-*gem*-bromoacetyl[2.2]paracyclophane[3] (pseudo-*gem*-XIII) and pseudo-*m*-bromoacetyl[2.2]paracyclophane (pseudo-*meta*-XIII) when heated at 200° provide the same equilibrium mixture of pseudo-*gem* and pseudo-*meta* isomers in which the latter dominates by a factor of 5.8. At the same temperature, pseudo-*p*- and pseudo-*o*-bromoacetyl[2.2]paracyclophane (XIII isomers) equilibrate to give a mixture in which the latter dominates by a factor of 1.2. Similar equilibrations have been applied to a large number of disubstituted [2.2]paracyclophanes. When heated at 250° in *p*-diisopropylbenzene, [2.2]paracyclophane (I) gave a 21% yield of *p,p'*-dimethylbibenzyl. When heated in either dimethyl maleate or dimethyl fumarate at 200°, [2.2]paracyclophane gave diester products in which the diradical intermediate had added across the double bond. The resulting *cis*- and *trans*-2,3-dicarbomethoxy[2.4]paracyclophanes (*cis*- and *trans*-XVII) were formed in almost equal amounts (30% each) from either starting ester. The two esters were identified by their interconversion, degradation to the known [2.4]paracyclophane (XXII), and by partial asymmetric hydrolysis of the derived *trans* anhydride (racemate) with brucine and water to give optically active *trans* acid (XX) and *trans* anhydride (XXIII). Of the two diesters, *trans*-XVII was demonstrated to dominate in an equilibrated (base) mixture by a factor of greater than 200. Racemization or isomerization in the [2.2]paracyclophane system was found to occur about three powers of ten faster than hydrogen abstraction from *p*-diisopropylbenzene. The ring expansion process by addition to olefin was one to two powers of ten faster than the same hydrogen atom abstraction process.

The smallest of the [*m.n*]paracyclophanes has $m = n = 2$ (I), and exhibits a strain energy of 31.3 kcal/mol.[4] The highly deformed crystal structure of the molecule[5] reflects the compression of the system, as does the thermal ring opening of the substance at 400° to give *p,p'*-dimethylbibenzyl and *p,p'*-dimethylstilbene,[6] and at 600° to give *p*-xylylene (II).[7] The photochemical ring opening of [2.2]paracyclophane by both homolytic and heterolytic cleavage of the benzyl–benzyl bond also results in the release of this compression energy.[8] Octamethyl[2.2]paracyclophane is much more thermally labile than the parent system, a property attributed to diradical formation followed by polymerization.[9]

We wish to report the results of three types of experiments, all of which point to thermal cleavage of I to the *p,p'*-dimethylenebibenzyl diradical (III) whose fate depends on the medium. In this paper, compounds will be employed as starting materials whose preparation[10a,b] and structure determinations[10] are reported in adjacent papers. On occasion, systematic names for the [*m.n*]paracyclophanes will be used.[11] However, for visualization a colloquial nomenclature for heteroannularly disubstituted [2.2]paracyclophanes has been developed that will be used in most places. The term "pseudo" prefixed to the substituent names indicates the positions of the substituents relative to one another, one in each ring.[3]



I II III

Results and Discussion

Aromatic Ring Rotation in the Paracyclophanes. In aromatic ring-substituted [*m*]- and [*m.n*]paracyclophanes that have sufficiently small bridges, the substituted ring cannot rotate with respect to the rest of the molecule. As a consequence, these substances possess molecular asymmetry and can be resolved into optical antipodes.[12] Attempts to resolve 6-carboxy-[4.4]paracyclophane[12b] and 6-carboxy-9-ethyl[4.4]para-

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(2) Some of this material appeared in preliminary form: H. J. Reich and D. J. Cram, *J. Am. Chem. Soc.*, **89**, 3078 (1967).

(3) The colloquial nomenclature is self-evident: pseudo-*gem* denotes two transannularly adjacent positions on the benzene rings; pseudo-*ortho*, pseudo-*meta*, and pseudo-*para* specify *ortho*, *meta*, and *para* relationships displaced from the usual homoannular into a transannular context.

(4) R. H. Boyd, *Tetrahedron*, **22**, 119 (1966).

(5) P. K. Gantzel and K. N. Trueblood, *Acta Cryst.*, **18**, 958 (1965).

(6) J. R. Schaefgen, *J. Polymer Sci.*, **15**, 203 (1955).

(7) W. F. Gorham, *ibid.*, *A-1*, **4**, 3027 (1966).

(8) R. C. Helgeson and D. J. Cram, *J. Am. Chem. Soc.*, **88**, 509 (1966).

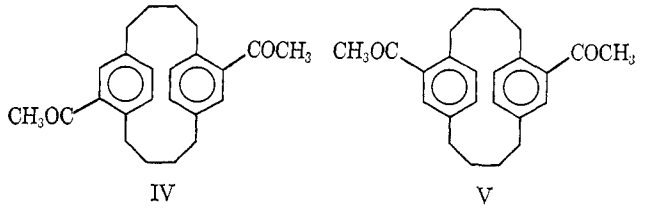
(9) D. T. Longone and L. H. Simanyi, *J. Org. Chem.*, **29**, 3245 (1964).

(10) (a) H. J. Reich and D. J. Cram, *J. Am. Chem. Soc.*, **91**, 3505 (1969); (b) H. J. Reich and D. J. Cram, *ibid.*, **91**, 3527 (1969); (c) H. J. Reich and D. J. Cram, *ibid.*, **91**, 3534 (1969).

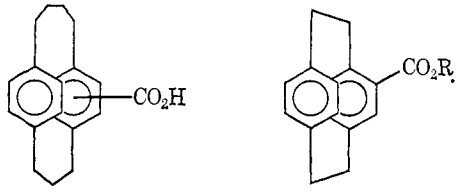
(11) D. J. Cram, *Rec. Chem. Progr.*, **20**, 71 (1959).

(12) (a) D. J. Cram and N. L. Allinger, *J. Am. Chem. Soc.*, 77, 6289 (1955); (b) D. J. Cram, W. J. Wechter, and R. W. Kierstead, *ibid.*, **80**, 3126 (1958); (c) D. J. Cram and R. H. Reeves, *ibid.*, **80**, 3094 (1958).

cyclophane[12c] failed, which indicates that ring rotation at room temperature is fast enough to prevent isolation of optical isomers. The barrier to rotation in these compounds must be less than about 20 kcal/mol. Direct evidence on this point has been obtained through variable temperature nmr studies of the two heteroannular diacetyl[4.4]paracyclophanes.[12c] Above about 45° in deuteriochloroform, isomers IV and V each show sharp methyl singlets at τ 7.56 and 7.50, respectively. When the spectral solution of IV was cooled to −40°, the singlet at τ 7.56 became two sharp singlets at τ 7.37 and 7.50 with an intensity ratio of 2:3, respectively. When the spectral solution of V was cooled to −40°, the singlet at τ 7.50 became two sharp singlets at τ 7.38 and τ 7.50 with an intensity ratio 3:1, respectively. The coalescence temperature for each solution was about 15°, which suggests an activation energy for ring rotation in the neighborhood of 7 kcal/mol.[13] The structures of isomers IV and V are assigned on the basis of these intensity ratios. The ratio pseudo-*meta*/pseudo-*gem* should be higher than pseudo-*ortho*/pseudo-*para* for steric reasons.



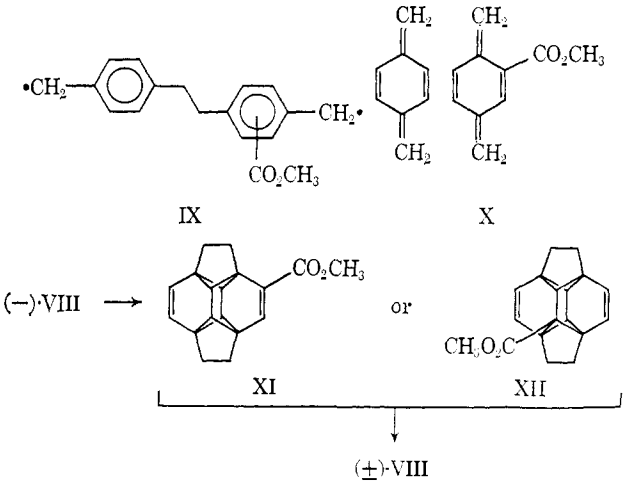
IV V



VI VII, R = H
VIII, R = CH_3

Carboxy[3.4]paracyclophane (VI, ring position unknown) was resolved.[12b] Racemization of the salt of this acid proceeds at 160° with a rate constant of about 1.4×10^{-4} sec^{-1}, and an activation energy for ring rotation of $\Delta F^{\ddagger} \sim 33.5$ kcal/mol.[13b] The resolution of 4-carboxy[2.2]paracyclophane (VII) was also achieved.[12a]

Racemization of (−)-4-Carbomethoxy[2.2]paracyclophane ((−)-VIII). The substantially greater steric barrier to rotation of the aromatic nuclei in [3.4]paracyclophane as compared to [4.4]paracyclophane indicates that in the lower homologs, this type of rotation should be absent. However, (−)-4-carbomethoxy-[2.2]paracyclophane ((−)-VIII) undergoes rapid thermal racemization (without decomposition) at 200° with $\Delta F^{\ddagger} \sim 38$ kcal/mol. This activation energy for racemization is only slightly higher than that for racemization of the [3.4]paracyclophane derivative. The racemization rates showed very little dependence on solvent polarity; the values are nearly the same in dimethyl sulfone and tridecane. Thus, mechanisms that involve ion-pair intermediates are improbable. Ring rotation without bond breakage is impossible in [2.2]paracyclophane, and an alternate mechanism was sought. Three possibilities were visualized. (1) The side chain cleaves to form the substituted *p,p'*-dimethylenebibenzyl diradical IX, the aromatic rings rotate, and cyclization occurs to give racemic ester. (2) Both methylene bridges cleave to form xylylenes X which recombine to racemic starting material. Formation of xylylenes at high temperatures has been reported.[7] (3) Intramolecular double Diels–Alder reactions of ester (−)-VIII would give polycyclic isomers XI and XII, each of which has a plane of symmetry. Double cycloeliminations of either XI or XII would give racemic ester, (±)-VIII. This possible reaction was



sought without success in the [2.2]paracyclophane system,[8] but was demonstrated[14a] in the [2.2]paracyclonaphthane system.[10b,14b]

Thermal Isomerization of Disubstituted [2.2]Paracyclophanes. Thermal isomerization of disubstituted [2.2]paracyclophanes with one substituent in each ring provided a ready means of differentiating between the three mechanisms. The diradical mechanism involves equilibration of pseudo-*gem*[3] and pseudo-*meta*[3], and of pseudo-*ortho*[3] and pseudo-*para*[3] isomers, with no leakage between the two sets of isomers. This mechanism could involve enantiomer interconversion. The *p*-xylylene mechanism involves equilibration of all four isomers, coupled with disproportionation reactions that could, in principle, produce 12 separate compounds from any one starting material, exclusive of enantiomers. The polycyclic mechanism requires isomerization of the pseudo-*gem* to *meta* isomer, and of pseudo-*ortho* to *para* isomer. These processes in effect involve transfer of a substituent from one to the other ring, and could not be accompanied by enantiomer interconversion. Furthermore, the *ortho*, pseudo-*meta*, and pseudo-*para* isomers should not undergo any isomerization besides enantiomer interconversion.

Only the diradical mechanism is consistent with the results, which are summarized in Table I. The four isomers with a bromine substituted in one ring and an acetyl group in the other (XIII)[10a,c] were heated at 200° without solvent (runs 1–4). With the use of nmr chemical-shift differences of the methyl groups to monitor the appearance and disappearance of the four isomers,[10c] the reactions were brought to equilibrium and the equilibrium constants determined. The

(13) (a) H. J. Reich and D. J. Cram, unpublished results. (b) The value of 50 kcal/mol reported before[12b] is in error.

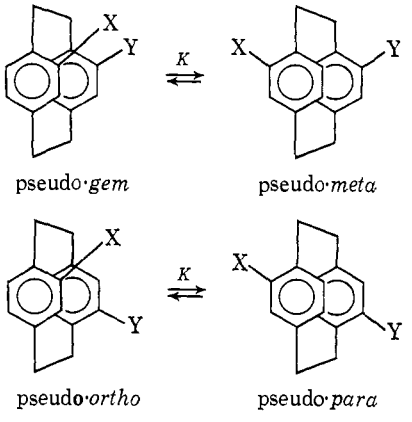
(14) (a) H. H. Wasserman and P. M. Keehn, *J. Am. Chem. Soc.*, **89**, 2770 (1967); (b) D. J. Cram, C. K. Dalton, and G. R. Knox, *ibid.*, **85**, 1088 (1963).

Table I. Thermal Isomerizations of Disubstituted [2.2]Paracyclophanes at 200°, Equilibrium and Rate Constants Estimated

Run no.	Starting materials	Products	Solvent		k, 10^5 sec^{-1}	K
1	Pseudo-*gem*-XIII[a]	Pseudo-*gem* ⇄ pseudo-*meta*				5.7
2	Pseudo-*m*-XIII[a]	Pseudo-*gem* ⇄ pseudo-*meta*				5.8
3	Pseudo-*o*-XIII[a]	Pseudo-*ortho* ⇄ pseudo-*para*				0.77
4	Pseudo-*p*-XIII[a]	Pseudo-*ortho* ⇄ pseudo-*para*				0.83
5	Pseudo-*gem*-XIV[b]	Pseudo-*gem* ⇄ pseudo-*meta*	Dimethyl sulfone		3	9
6	Pseudo-*o*-XIV[b]	Pseudo-*ortho* ⇄ pseudo-*para*	Triglyme		2	1
7	Pseudo-*p*-XIV[b]	Pseudo-*ortho* ⇄ pseudo-*para*	Triglyme		2	1.1
8	Pseudo-*p*-XV[c]	Pseudo-*ortho* ⇄ pseudo-*para*	Triglyme		2	1
9	Pseudo-*gem*-XVI[d]	Pseudo-*gem* ⇄ pseudo-*meta*				>4.6
10	Pseudo-*p*-XVI[d]	Pseudo-*ortho* ⇄ pseudo-*para*				~1

[a] Bromoacetyl derivative. [b] Bromocarbomethoxy derivative. [c] Dibromo derivative. [d] Bromonitro derivative.

pseudo-*gem* and pseudo-*meta* isomers interconverted, and the pseudo-*meta* dominated over the pseudo-*gem* by a factor of 5.75 in the equilibrium mixture. Similarly, the pseudo-*ortho* and pseudo-*para* isomers interconverted, and the pseudo-*ortho* dominated over the pseudo-*para* in the equilibrium mixture by only a factor of 1.25. In each of the two equilibrating systems, the same mixture was obtained from either starting material. No leakage from one system to the other was observed, although as little as 5% could have been observed.

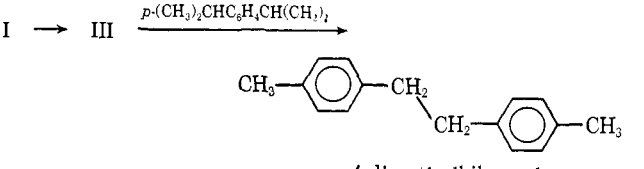


One-point rate constants for approach to equilibrium of a number of other compounds were estimated, as were the resulting equilibrium constants (runs 4–8, Table I). Thus, three of the isomers of bromocarbomethoxy[2.2]paracyclophane[10a] with one substituent in each ring (XIV) were equilibrated, as was pseudo-*p*-dibromo[2.2]paracyclophane (XV).[10b] The estimated reaction rates for equilibration were all about equal to one another, and again the pseudo-*meta* was found to be much more stable than the pseudo-*gem* derivative, and the pseudo-*ortho* and pseudo-*para* derivatives about equally stable. These equilibrium constants probably reflect differences in steric effects and dipole–dipole interactions between the isomers. The instability of the pseudo-*gem* compared to the pseudo-*meta* (1.6 kcal/mol for isomers of XIII) is expected both on steric grounds and on a dipole–dipole interactions basis. Probably the result reflects a blend of the two effects.

These isomerization reactions have been extremely useful for preparative and structure proof purposes. For example, pseudo-*gem*-bromonitro[2.2]paracyclophane (pseudo-*gem*-XVI) is the major product of bromination of 4-nitro[2.2]paracyclophane, and the pseudo-*para* isomer is the easiest to crystallize from the mixture produced by nitration of 4-bromo[2.2]paracyclophane. The isomerization reactions of runs 9 and 10 readily make available all four of the isomers. Again, pseudo-*m*-XVI is more stable than pseudo-*gem*-XVI.

The patterns of interconversions of Table I are inconsistent with either the *p*-xylylene or the polycyclic mechanisms of isomerization.

Reaction of [2.2]Paracyclophane (I) with *p*-Diisopropylbenzene. When [2.2]paracyclophane (I) was heated at 250° as a solution in *p*-diisopropylbenzene, the only nonpolymeric (chromatographable) product aside from the solvent that was observed was *p,p'*-dimethylbibenzyl, which was isolated in 21% yield.



p,p'-dimethylbibenzyl

Although this reaction is considerably slower than the above racemizations and isomerizations, it provides additional support for the intermediacy of diradicals in all three reactions.

1,2- to 1,12-Cycloaddition Reaction of [2.2]Paracyclophane (I) with Olefins. Radical copolymerization reactions are known between olefins and carbon monoxide,[15a] sulfur dioxide,[15b,c] dienes, and other olefins[15d] to form alternating copolymers. Copolymerization studies of styrene and a large variety of olefins to form ABAB type polymers have revealed that the highest alternating tendency observed with styrene is with α,β-unsaturated esters, nitriles, maleic anhydride,[15e] maleate, and fumarate esters.[15d] It seemed likely that if [2.2]paracyclophane were heated to temperatures at which diradical III were formed in the presence of such olefins, a cyclization reaction might occur in which the [2.2]- was expanded to the [2.4]paracyclophane system. Since a temperature of 200–250° might be required, the olefin chosen had to be stable at that temperature toward homopolymerization. Reaction with maleic anhydride was first attempted, but a solution of I in the anhydride at 225° produced only polymeric materials, which appeared to have involved acylation reactions in their formation.

(15) (a) R. E. Foster, A. W. Larchar, R. D. Lipscomb, and B. C. McKusick, *J. Am. Chem. Soc.*, 78, 5606 (1956); (b) L. S. Schroeter, "Sulfur Dioxide," Pergamon Press, New York, N. Y., 1966, p 122; (c) C. Walling, "Free Radicals in Solution," John Wiley & Sons, Inc., New York, N. Y., 1957, pp 118, 129, 212; (d) F. R. Mayo and C. Walling, *Chem. Rev.*, 46, 191 (1950); (e) T. Alfrey, Jr., E. Merz, and H. Mark, *J. Polymer Sci.*, 1, 37 (1946).

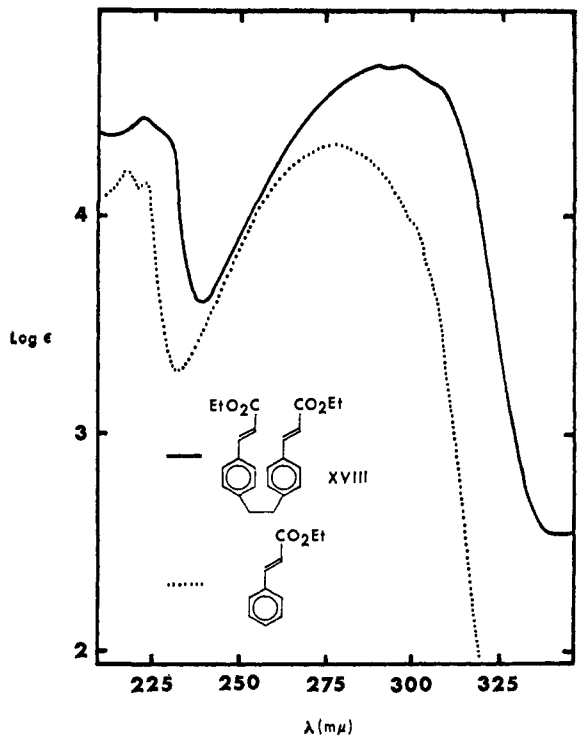
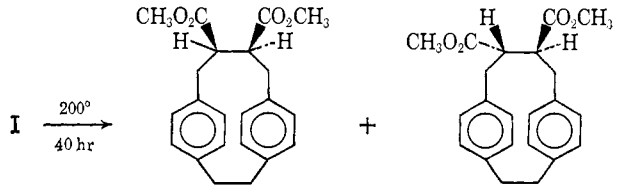


Figure 1. The ultraviolet spectra of XVIII [λ_{max}^{EtOH} mμ (ε): 221 (30,600), 288 (52,400), 294 (52,300)] and ethyl *trans*-cinnamate [λ_{max}^{EtOH} mμ (ε): 216 (16,000), 222 (13,600), 276 (22,400)].

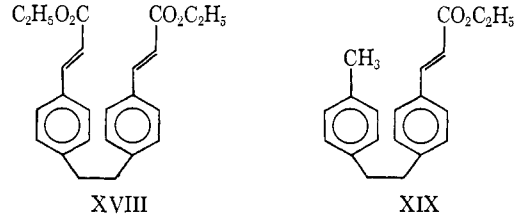
When I was heated with either dimethyl maleate or fumarate esters, the anticipated ring-expanded diester products, *cis*- and *trans*-2,3-dicarbomethoxy[2.4]paracyclophanes (*cis*- and *trans*-XVII), were formed in about equal amounts to give about 60% combined yields. Suitable controls demonstrated that both products and the starting esters did not isomerize appreciably under the reaction conditions. Considerably faster reaction of I with fumarate than with maleate ester was observed. Thus, only 30% of I was recovered from the fumarate



	cis-XVII	*trans*-XVII
Yield in maleate	30%	29%
fumarate	34%	30%

run, as compared to 76% of I recovered from the maleate run.

In a larger preparative reaction, diethyl maleate was employed because of its higher boiling point. Isolated from the reaction mixture was 16% *cis*-cyclic ester,



22% *trans*-cyclic ester, and 5% a mixture of the two. Two minor products, VIII and XIX, were also isolated in 0.4 and 0.2% yields, respectively.

Cycloadditions of [2.2]paracyclophane with furan, diethyl chloromaleate, diethyl chlorofumarate, tetrachloroethylene, diethyl acetylenedicarboxylate, sulfur dioxide, and carbon monoxide were attempted, but did not lead to identifiable products.

Structure Proof of Cycloaddition Products of [2.2]-Paracyclophane. The structures of compounds XVIII and XIX will be discussed first followed by the more complex problem of ring expansion products, *cis*- and *trans*-XVII. The elemental analysis coupled with the ultraviolet, infrared, and nmr spectra of XVIII and XIX provided the structures formulated. The infrared spectrum of XVIII showed carbonyl absorption at 1704 cm^{-1}, conjugated double bond absorption at 1639 cm^{-1}, and a characteristic *trans* double bond absorption at 996 cm^{-1}. Figure 1 records the ultraviolet spectra of XVIII and ethyl *trans*-cinnamate, which serves as a model. The similarity of these curves points to similar chromophores for the two compounds. The nmr spectrum of XVIII gave proton absorptions (in τ values) as follows: AB quartet at 2.35 and 3.62 (J = 16 Hz, 4 H, vinyl protons), A_2B_2 centered at 2.70 (8 H, aromatics), quartet at 5.75 (4 H) and triplet at 8.68 (6 H, ethyl), and singlet at 7.08 (methylene).

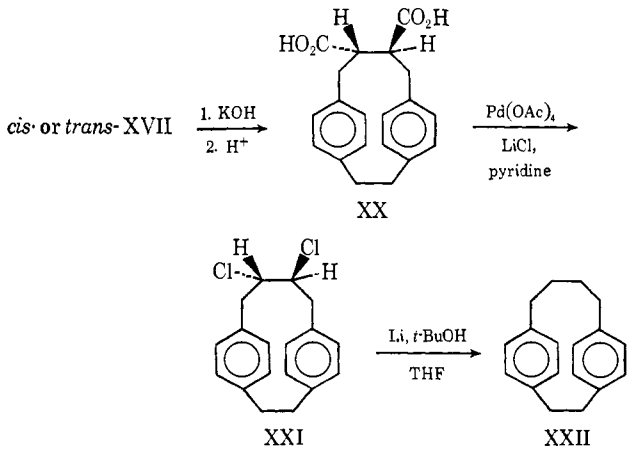
The nmr spectrum of ethyl cinnamate was used as a model, and exhibited the following proton absorptions (in τ values): AB quartet at 2.29 and 3.55 (2 H, J = 16 Hz, vinyl), multiplet, 2.3–2.8 (5 H, aromatics), and quartet at 5.72 (2 H) and triplet at 8.67 (3 H, ethyl). The infrared spectrum of XIX gave bands at 1709 (carbonyl), 1639 (conjugated double bond), and 996 cm^{-1} (*trans*-double bond). The nmr spectrum of XIX contained the following proton absorption bands (in τ values): AB quartet at 2.37 and 3.61 (2 H, J = 16 Hz, vinyl), A_2B_2 at 2.69 and singlet at 2.93 (8 H, aromatic), quartet at 5.73 (2 H) and triplet at 8.67 (3 H, ethyl), singlet at 7.11 (4 H, methylene), and singlet at 7.68 (3 H, methyl).

The gross structures of the cycloaddition products (XVII) were indicated from their molecular weight (Signer), elemental analysis, and nmr spectra integrations to be 1:1 adducts of [2.2]paracyclophane and the olefins employed. The infrared spectrum of both isomers showed an ester carbonyl absorption at 1727 cm^{-1}. The ultraviolet spectra of both isomers are recorded in Figure 2, and are similar to that of [2.4]paracyclophane,[16a] but distinctly different from those of other [*m.n*]paracyclophanes or open-chain materials.[11,16a] The nmr spectrum of *cis*-XVII gave proton absorptions (in τ values) as follows: multiplet at 3.45 (8 H, aromatic), singlet at 6.18 (6H, methyl), and complex multiplet at 6.6–7.5 (10 H, side-chain protons). The nmr spectrum of *trans*-XVII gave proton absorptions (in τ values) as follows: closely spaced multiplets at 3.25 and 3.56 (8 H, aromatic), singlet at 6.28 (6 H, methyl), and complex multiplet at 6.6–7.9 (10 H, side chain). These spectra have characteristic high-field paracyclophane aromatic absorption above τ 3.2 (the aromatic protons of [2.4]paracyclophane absorb at τ 3.48).[16b]

(16) (a) D. J. Cram, N. L. Allinger, and H. Steinberg, *J. Am. Chem. Soc.*, 76, 6132 (1954); (b) D. J. Cram and R. C. Helgeson, *ibid.*, **88**, 3515 (1966).

Isomerization of *cis*-XVII to *trans*-XVII was readily accomplished with sodium methoxide in dimethoxyethane and methanol. Analysis of the product (nmr) indicated that less than 0.5% of the less stable *cis* isomer remained at equilibrium.

Degradation of *cis*- and *trans*-XVII to [2.4]paracyclophane (XXII) provided unambiguous proof that the substances possessed the ring structure indicated. Alkaline hydrolysis of either isomer gave a single dicarboxylic acid (XX), decarboxylation[17] of which with lead tetraacetate in the presence of lithium chloride in pyridine gave *trans*-2,3-dichloro[2.4]paracyclophane (XXI). The nmr spectrum of XXI in the aromatic region, coupled with the difference in spectra between *cis*- and *trans*-XVII, indicates a *trans* structure for XXI. This difference is discussed and placed in context elsewhere.[13a] Dichloro compound XXI when reduced[18] gave [2.4]paracyclophane (XXII) in 57% yield, identical in all respects with authentic material.[16b,19]



Proof that diacid XX possessed a *trans* structure was obtained as follows. This material was obtained from either *cis*- or *trans*-XVII by either base- or acid-catalyzed hydrolysis, and is clearly the more thermodynamically stable isomer by a large factor. Examination of molecular models of both isomers indicates less compression in the *trans* isomer. Diacid XX readily gave anhydride XXIII, whose carbonyl absorptions in the infrared spectra at 1866 and 1779 cm^{-1} are close to those of succinic anhydride (1865 and 1772 cm^{-1}). Partial asymmetric hydrolysis of XXIII with brucine and water in refluxing benzene gave a mixture of unreacted anhydride [73%, $[\alpha]^{25}_{365}$ +0.67° (*c* 8, dichloromethane)] and diacid. Dehydration of this diacid gave anhydride [20%, $[\alpha]^{25}_{365}$ −2.68° (*c* 8, dichloromethane)]. The rotations of recovered anhydride and anhydride obtained from diacid are in opposite directions, and have the correct relative magnitudes. This experiment demonstrates that diacid XX and anhydride XXIII possess *trans* (*dl*) structures, since the *cis* isomers possess a *meso* configuration incapable of optical activity. Comparisons of nmr spectra,[13a] coupled with conversions of *cis* to the more stable *trans* structures, demonstrate the configurations of the isomeric esters (XVII and the two diethyl esters as well).

(17) J. K. Kochi, *J. Am. Chem. Soc.*, 87, 2500 (1965).
(18) P. Bruck, D. Thompson, and S. Winstein, *Chem. Ind.* (London), 405 (1960).
(19) D. J. Cram and H. Steinberg, *J. Am. Chem. Soc.*, 73, 5691 (1951).

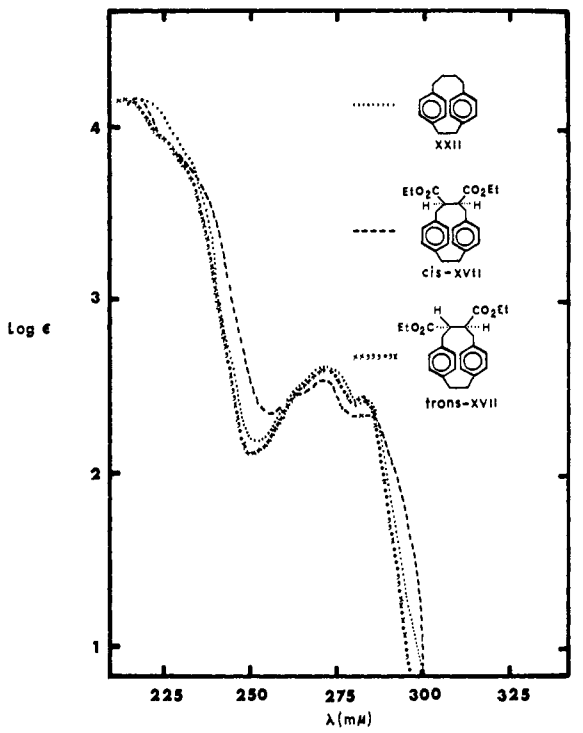
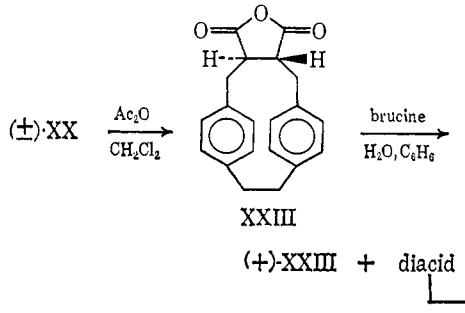


Figure 2. The ultraviolet spectra of [2.4]paracyclophane (XXII) [$\lambda^{c\text{-hexane}}_{max}$ mμ (ε): 216 (14,800), 271 (427), 282 (269)], (*cis*-XVII) [λ^{EtOH}_{max} mμ (ε): 215 (14,550), 271 (341), 283 (213)], and (*trans*-XVII) [λ^{EtOH}_{max} mμ (ε): 214 (14,200), 271 (399), 283 (263)].

Mechanisms of the Thermal Reactions of [2.2]Paracyclophane (I) and Its Derivatives. Crude one-point rate constants for the three thermal reactions, racemization, cycloaddition, and reduction, were determined for 4-carbomethoxy[2.2]paracyclophane (VIII). These



constants, derived comparisons, and the data on which they rest are found in Table II. These comparisons, together with the cycloaddition product studies carried out on [2.2]paracyclophane itself, will be used in the following discussion of mechanism. Ring expansion products of ester VIII were not examined because of the number of isomers that could be produced. The cycloaddition products were detected by vpc, and the course of the cycloaddition reaction was assumed to be similar to that of the parent hydrocarbon. Thus, cycloadditions of I and VIII are not distinguished from one another in parts of the following discussion.

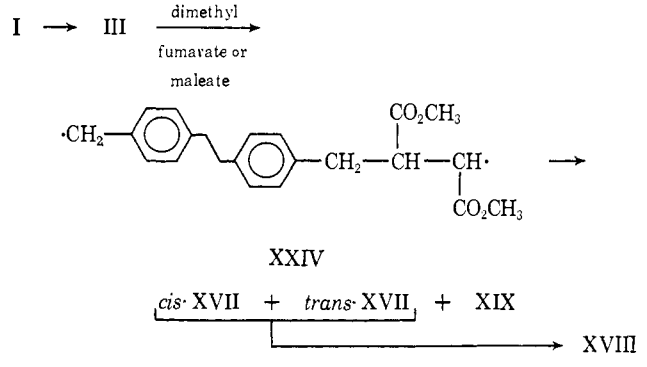
In the cycloaddition reaction, essentially the same ratio of *cis*- and *trans*-XVII was produced from either *cis* or *trans* olefin under conditions that the configurations of these olefins and the addition products maintained their integrity. This result indicates a common intermediate for production of *cis*- and *trans*-XVII, which is incapable of storing information as to its geometric origin. From the lack of dependence of

Table II. Thermal Reactions of 4-Carbomethoxy[2.2]paracyclophane (VIII) at 200°

Solvent	Time, min	Reaction		k,[b] 10^8 sec^{-1}	Rel rate	$\Delta F^{\pm}$, kcal/mol
		Nature	%[a]			
Dimethyl sulfone	780	Racem	93	4230	1100	37.8
Tridecane	193	Racem	51.4	6020	1600	37.4
Tridecane	780	Racem	94.4	6350		
Dimethyl fumarate	666	Cycloadd	17.3	438	110	39.9
Dimethyl fumarate	1980	Cycloadd	39	416		
Dimethyl maleate	1980	Cycloadd	12.6	113	29	41.2
p-Diisopropylbenzene	9594	Reduction	2.6	3.8	1	44.4

[a] Followed by vpc (disappearance of I and appearance of products). [b] One-point rate constants.

rate on medium polarity, the nature of the cycloaddition and side products, the nature of the racemization reactions and of the reduction product, diradical III (or IX) is clearly the initial intermediate, which adds to one or the other olefins to give a new diradical, XXIV. This material lasts long enough to become conformationally equilibrated, both with respect to the groups originally in the paracyclophane and in the olefin molecules. Intramolecular coupling in XXIV leads to *cis*- and *trans*-XVII. This coupling reaction and that observed for diradical IX are favored over intermolecular coupling because of the very low concentration of these diradicals, a consequence of their high reactivities. Side product XVIII from its structure would appear to have arisen from cycloaddition products *cis*- and *trans*-XVII by a process in which hydrogen atoms were transferred to other radicals or diradicals. Side product XIX more likely arose from XXIV by a combined disproportionation–elimination reaction in which a carbethoxycarbene (formally) served as leaving group. The unusually high temperature of these reactions probably makes possible unusual reactions.



The loss of stereochemical memory in conversion of I to the cycloaddition products (XVII) indicates that the activation energies for conformational equilibrations of diradicals such as III, IX, or XXIV are lower than the corresponding activation energies for either adding to olefin or for ring closure.

The attack of diradical III on dimethyl fumarate is very similar to one of the steps during radical copolymerization of styrene and fumarate. Although activation parameters for these reactions are not available, homopolymerization data provide calibration. The relative reactivities of styryl radicals toward styrene, methyl methacrylate, methyl acrylate, and dimethyl fumarate are 1, 1.9, 1.3, and 3.3, respectively.[15c] These small values suggest that the activation energies for homopolymerization propagation provide a reasonable model for those of copolymerization. The activation energies ($\Delta F_p^{\pm}$) for homopolymerization propagation at 60° for styrene, methyl acrylate, and methyl methacrylate range from 14.4 to 16.3 kcal/mol.[20] If $\Delta F^{\pm}$ for III → XXIV is assumed to be about 16 kcal/mol at 200°, then since $\Delta F^{\pm}$ for I → XXIV is about 40 kcal/mol (Table II), diradical III is about 24 kcal/mol higher in energy than I. Since $\Delta F^{\pm}$ for racemization of VIII is about 38 kcal/mol (Table II), then $\Delta F^{\pm}$ for III → I is 14 kcal/mol. This value is considerably higher than the activation energy expected for conformational equilibration of VIII at 200°.

An estimation of the activation energy for cyclization of diradical, XXIV → XVII ($\Delta F_c^{\pm}$), can be made from calculations of others[21] of the self-termination rate of diradicals formed by self-addition of styrene. Without correcting for strain energy in the transition state for cyclization, the expression developed by these authors for the rate of self-termination allows calculation of $\Delta F_c^{\pm}$ values of about 13–14 kcal/mol, depending on the number of styrene units in the ring. The strain energy of [2.4]paracyclophane has not been measured but should be similar to that for [3.3]paracyclophane. Boyd[22] has measured the value by combustion analysis and has found it to be 12 kcal/mol, whereas Gantzel and Trueblood[5] have estimated the strain to be 7 kcal/mol. From these model calculations, it seems probable that the $\Delta F_c^{\pm}$ for diradical adduct XXIV going to XVII is in the neighborhood of 13–20 kcal/mol. This probable value is much greater than the activation energies expected for conformational equilibration of diradical adduct XXIV, and it is not surprising that the cycloaddition reaction is nonstereospecific.

Diradical III added to dimethyl fumarate with a rate constant almost four times that for addition to maleate ($k_f/k_m \sim 4$). In copolymerization studies, values from 6 to 40 for k_f/k_m at much lower temperatures have been observed.[23] Similarly, methyl radicals react nine times faster with diethyl fumarate than with maleate.[24] The lower reactivity of maleate has been explained on the basis of steric inhibition of resonance in the transition state for addition.[23]

Diradical XXIV must cyclize to give products considerably faster than it reverts to olefin and diradical III, since little isomerization of starting olefin occurred. Decomposition of XXIV should give the same mixture of dimethyl fumarate and maleate no matter which was used in its formation.

(20) Calculated from data recorded in ref 15c (p 212) and P. J. Flory, "Principles of Polymer Chemistry," Cornell University Press, Ithaca, N. Y., 1953, pp 158, 254.
(21) B. H. Zimm and J. K. Bragg, *J. Polymer Sci.*, **9**, 476 (1952).
(22) R. H. Boyd, private communication, 1968.
(23) Reference 15c, p 129.
(24) A. R. Bader, R. P. Buckley, F. Leavitt, and M. Szwarc, *J. Am. Chem. Soc.*, **79**, 5621 (1957).

The fact that K_{eq} is greater than 200 for the base-catalyzed isomerization of *cis*-XVII to *trans*-XVII indicates that for the process, $\Delta F < -3.5$ kcal/mol. This value is not far from the value of $\Delta F = -4.2$ kcal/mol for conversion of diethyl maleate to diethyl fumarate.[25]

Diradicals have been postulated frequently as intermediates in thermal decompositions and isomerizations of strained systems. Cyclopropane undergoes ring opening to the trimethylene diradical.[26] Diradicals have been postulated as intermediates in the isomerization of tropilidines[27] and norbornadienes[28] to alkylbenzenes. Cyclopropanone derivatives have been found to add to furan, possibly through a diradical intermediate.[29] Biphenylene as a highly strained system undergoes reactions consistent with an initial homolytic cleavage to form a biphenyl diradical.[30] Pyrolysis of *cis*-1,2-diphenylcyclobutane yielded 10% of the *trans* isomer, possibly through a diradical intermediate.[31]

Experimental Section

General Comments. Melting points are uncorrected, and all solvents are reagent grade unless otherwise specified. Nmr measurements were made with a Varian A-60 spectrometer on dilute solutions (5–20%) in deuteriochloroform using tetramethylsilane as internal standard. Infrared spectra were run in chloroform solution on a Beckman IR-5 spectrophotometer. Ultraviolet spectra were recorded on a Cary 14 spectrometer in absolute ethanol solution. Optical rotations were measured at 25° with a Perkin-Elmer 141 polarimeter and a 1-dm thermostated cell. Thin-layer chromatograms employed Brinkmann silica gel G on glass or Pyrex plates with appropriate cyclohexane–ethyl acetate mixtures as developer. Iodine vapor was used to spot the plates. Silica gel for column chromatography was Baker chromatographic grade. Vapor phase chromatography (vpc) was carried out on an F & M Model 720 instrument using 3 ft × 0.25 in. columns packed with 20% SE 30 on 60–80 Firebrick at a flow rate of 60 cc/min (unless specified otherwise).

(−)-4-Carbomethoxy[2.2]paracyclophane ((−)-VIII). A sample of (−)-4-carboxy[2.2]paracyclophane[12a] [500 mg, $[\alpha]^{25}D$ −158° (*c* 0.94, chloroform)] was esterified by refluxing with 25 ml of 1,2-dichloroethane, 3 ml of methanol, and 0.25 ml of concentrated sulfuric acid for 2 days. Ether (70 ml) was added, and the organic layer was washed with 10% sodium hydroxide, saturated sodium bicarbonate, and saturated sodium chloride solutions. The solution was dried and evaporated to give crude ester with $[\alpha]^{25}D$ −140° (*c* 1.0, chloroform). This material was crystallized from dichloromethane–ether to give 415 mg of (−)-VIII, mp 172.5–173.5°, $[\alpha]^{25}D$ −140° (*c* 1.0, chloroform). This material was crystallized from dichloromethane–ether to give 415 mg of (−)-VIII, mp 172.5–173.5°, $[\alpha]^{25}D$ −148°. A second crystallization gave 281 mg, $[\alpha]^{25}D$ −151°, mp 174–175°. Further crystallization did not alter the melting point or the rotation. *Anal.* Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.36; H, 6.97. The rotations of optically pure (−)-4-carbomethoxy[2.2]paracyclophane are (*c* 1.0, chloroform): $[\alpha]^{25}D$ −151.3°, $[\alpha]^{25}_{546}$ −201°, $[\alpha]^{25}_{436}$ −583°, $[\alpha]^{25}_{365}$ −2150°.

Thermal Racemization of (−)-4-Carbomethoxy[2.2]paracyclophane ((−)-VIII). A. In Tridecane. In a glass tube was placed 40 mg of optically pure (−)-VIII and 0.96 g of tridecane. The tube was cooled, evacuated to 0.03 mm, warmed, cooled, again evacuated, sealed, and heated at 200 ± 1.5° for 13.28 hr. After cooling, the tube was opened and the contents were chromatographed on 15 g of silica gel. Pentane eluted tridecane and 10% ether–pentane gave 37 mg of ester. Sublimation of this material at 70° (0.015 mm) afforded 33 mg of ester, rotation (*c* 1.0, chloroform): $[\alpha]^{25}D$ −8.6° (5.7% optically pure), $[\alpha]^{25}_{365}$ −121.5° (5.7% optically pure). A second sample of optically active ester, heated for 193 min, had (*c* 1.0, chloroform) $[\alpha]^{25}_{546}$ −201° (48.8% optically pure) and $[\alpha]^{25}_{436}$ −282° (48.4% optically pure).

B. In Dimethyl Sulfone. A mixture of 40 mg of (−)-VIII and 0.96 g of dimethyl sulfone was placed in a glass tube which was evacuated to 0.03 mm, sealed, and heated at 200° for 13.28 hr. Chromatography on silica gel and sublimation at 70° (0.015 mm) of the product afforded 33 mg of ester with (*c* 1.0, chloroform) $[\alpha]^{25}D$ −19.8° (13.1% optically pure); $[\alpha]^{25}_{365}$ −288° (13.4% optically pure).

C. Control in Dimethyl Sulfone. A mixture of 30 mg of (−)-VIII and 0.72 mg of dimethyl sulfone was heated for approximately 1 min and worked up as for run B to yield 26 mg of ester with (*c* 1.0, chloroform) $[\alpha]^{25}D$ −148° (98% optically pure); $[\alpha]^{25}_{365}$ −2109° (98% optically pure).

Equilibrations of the Bromoacetyl[2.2]paracyclophanes (XIII) (Runs 1–4). Exactly 100 mg of each bromoacetyl[2.2]paracyclophane was placed in a glass tube. The tube was flushed with nitrogen and evacuated to 0.01 mm, sealed, and heated at 200 ± 2° for 44 hr. After cooling, the product was dissolved in 0.4 ml of deuteriochloroform, and the nmr was taken. For the pseudo-*gem*-XIII and pseudo-*m*-XIII isomers, the methyl resonances at τ 7.37 and 7.57, respectively, were integrated.[10c] For the pseudo-*p*-XIII and pseudo-*o*-XIII isomer mixture, the methyl peaks at τ 7.56 and 7.48, and the aromatic resonances at τ 2.69 and 3.13 (protons pseudo-*gem* to the bromine and *ortho* to the acetyl groups, respectively, in pseudo-*p*-XIII), and τ 2.39 (protons *ortho* to the acetyl group in pseudo-*o*-XIII) were respectively integrated.[10c] All of the spectra indicated the presence of only two of the isomers in the product. Table III contains the results for runs 1–4 of Table I.

Table III. Equilibrium Data at 200° for the Bromoacetyl[2.2]paracyclophanes (XIII)

Starting material	%[a] products (pseudo) *gem*	*meta*	*ortho*	*para*
Pseudo-*gem*	15.0	85.0	0	0
Pseudo-*meta*	14.7	85.3	0	0
Pseudo-*ortho*	0	0	58.6 (54.3)	41.4 (45.7)
Pseudo-*para*	0	0	55.7 (54.2)	44.3 (45.8)

[a] Numbers in parentheses based on integration of aromatic protons, the others on the methyl protons.

Thermal Isomerizations of Bromocarbomethoxy[2.2]paracyclophanes (XIV) (Runs 5–7) and of Pseudo-*gem*-dibromo[2.2]paracyclophane (Pseudo-*gem*-XV) (Run 8). A mixture of 100 mg of paracyclophane and 0.3 ml of technical triglyme in runs 6–8 and 0.5 g of dimethyl sulfone in run 5 were placed in an nmr tube. An initial nmr spectrum was taken (usually at elevated temperatures to obtain a homogeneous solution) and then the tube was placed in a Wood's metal bath thermostated at 200 ± 2°. At appropriate intervals the tube was withdrawn, and integration of the aromatic region was carried out. Infinity points were taken after ten half-lives. The reactions were followed making use of the following absorptions. For run 5, the integrations of the signal at τ 2.66 (proton *ortho* to the acetyl group of pseudo-*gem* XIV) and τ 2.80 and 2.79 (protons *ortho* to acetyl and pseudo-*gem* to bromo, respectively, of pseudo-*m*-XIV) compared to the integration of the remainder of the aromatic protons were used. For runs 6 and 7, the signals at τ 2.31 (protons *ortho* to acetyl in pseudo-*o*-XIV) and τ 2.91 and 2.69 (protons *ortho* to acetyl and pseudo-*gem* to bromo, respectively, in pseudo-*p*-XIV) were used. For run 8, the signal at τ 2.78 (proton pseudo-*gem* to bromo in pseudo-*o*-XV) and the doublet of doublets at τ 2.83 (protons pseudo-*gem* to bromo in pseudo-*p*-XV) were used.

Preparative Thermal Isomerization of Pseudo-*gem*-bromocarbomethoxy[2.2]paracyclophane. Exactly 1.0 g of pseudo-*gem*-bromocarbomethoxy[2.2]paracyclophane was heated under vacuum at 265° for 25 min. The product was chromatographed on 180 g of silica gel. Elution with 8% ether–pentane gave 0.66 of pseudo-*m*-bromocarbomethoxy[2.2]paracyclophane. Crystallization from ether–pentane gave 0.37 g, mp 92–93.5°. A second crystallization

(25) S. Patai, "The Chemistry of Alkenes," Interscience Publishers, New York, N. Y., 1964, p 396.
(26) S. W. Benson, "The Foundations of Chemical Kinetics," McGraw-Hill Book Co., Inc., New York, N. Y., 1960, p 253.
(27) J. A. Berson and M. R. Willcott, III, *J. Am. Chem. Soc.*, **88**, 2494 (1966).
(28) W. G. Woods, *J. Org. Chem.*, **23**, 110 (1958).
(29) N. J. Turro, W. B. Hammond, and P. A. Leermakers, *J. Am. Chem. Soc.*, **87**, 2774 (1965).
(30) (a) D. F. Lindow and L. Friedman, *ibid.*, **89**, 1271 (1967); (b) L. Friedman and P. W. Rabideau, *J. Org. Chem.*, **33**, 451 (1968).
(31) R. M. Dodson and A. G. Zielske, *ibid.*, **32**, 28 (1967).

did not improve the melting point. *Anal.* Calcd for $C_{18}H_{17}BrO_2$: C, 62.62; H, 4.96. Found: C, 62.63; H, 4.94.

Elution with 10% ether–pentane gave starting material mixed with small amounts of the pseudo-*meta* isomer.

Preparative Thermal Isomerization of Pseudo-*p*-bromoacetyl[2.2]paracyclophane. Exactly 4.0 g of pseudo-*p*-bromoacetyl[2.2]paracyclophane was placed in a glass tube and degassed by evacuating to 0.03 mm, melting, and again evacuating. The tube was sealed, heated at 200° for 31.5 hr, and opened. The product was chromatographed on 600 g of silica gel. Elution with 9% ether–pentane (5 l.) gave 2.16 g (54%) of pseudo-*o*-bromoacetyl[2.2]paracyclophane, having an nmr spectrum identical with authentic material.[10c] Elution with 4 l. of 12% ether–pentane gave 1.41 g of starting material.

Preparative Thermal Isomerization of Pseudo-*gem*-bromoacetyl[2.2]paracyclophane. Exactly 370 mg of pseudo-*gem*-bromoacetyl[2.2]paracyclophane was placed in a glass tube, and the tube was flushed with nitrogen, evacuated to 0.01 mm, sealed, and heated at 200° for 24 hr. The product was chromatographed on 40 g of silica gel. Elution with 8% ether–pentane gave 273 mg of pseudo-*m*-bromoacetyl[2.2]paracyclophane which was crystallized from ether–pentane to yield 180 mg of plates, mp 85–86°. A portion was recrystallized to give an analytical sample, mp 85–86°. *Anal.* Calcd for $C_{18}H_{17}BrO$: C, 65.66; H, 5.21. Found: C, 65.79; H, 5.27.

Later fractions of the chromatograph yielded 63 mg of starting material.

Thermal Isomerization of Pseudo-*gem*-bromonitro[2.2]paracyclophane (Pseudo-*gem*-XVI) (Run 9). Exactly 200 mg of pseudo-*gem*-XVI was heated at 200° for 24 hr in a sealed tube under vacuum. The charred product was chromatographed on 20 g of silica gel. Elution with 2% ether–pentane gave 129 mg (65%) of pseudo-*m*-bromonitro[2.2]paracyclophane. Recrystallization from ether and sublimation gave 69 mg, mp 117.5–120°. A second recrystallization did not change the melting point. An analytical sample was prepared by sublimation at 110° (0.02 mm). *Anal.* Calcd for $C_{16}H_{14}BrNO_2$: C, 57.84; H, 4.25. Found: C, 57.52; H, 4.38.

Elution with 6–10% ether–pentane gave 28 mg (14%) of recovered starting material. The crude yields give a minimum value for the equilibrium constant (K = pseudo-*meta*/pseudo-*gem*) of 4.6.

Thermal Isomerization of Pseudo-*p*-bromonitro[2.2]paracyclophane (Pseudo-*p*-XVI) (Run 10). A mixture of 90 mg of pseudo-*p*-XVI and 0.5 ml of benzene was degassed and heated at 200° for 24 hr. The benzene was evaporated and the crude product was sublimed to give 75 mg of product. Examination of the nmr spectrum showed the presence of pseudo-*o*- and pseudo-*p*-bromonitro-[2.2]paracyclophanes[10c] only, in approximately equal amounts. The following proton resonances[10c] were used for analysis: the signals at τ 2.81 and 2.56 (protons *ortho* to nitro and pseudo-*gem* to bromo, respectively, for pseudo-*p*-XVI), and τ 2.16 (proton *ortho* to nitro in pseudo-*o*-XVI).

Reaction of [2.2]Paracyclophane (I) with *p*-Diisopropylbenzene. A mixture of 1.0 g (4.8 mmol) of I and 30 ml of *p*-diisopropylbenzene in a thick-walled glass tube was degassed to 0.05 mm, sealed, and placed in a Wood's metal bath at 250° for 24 hr. The contents of the tube were chromatographed on 200 g of Harshaw alumina (activated by heating at 120° for 20 hr). The size of the fractions was 125 ml; solvent for fraction 1–15 was pentane; 16–25, 1% ether–pentane; 26–32, 2% ether–pentane; 33–45, 3% ether–pentane. Fractions 2–5 contained *p*-diisopropylbenzene. Fractions 24–30 contained 211 mg (21%) of virtually pure (less than 1% of any other peaks on the vpc, only small peaks at τ 9 in the nmr spectrum) *p,p'*-dimethylbibenzyl. This product was recrystallized from pentane to give 96 mg of open-chain material, mp 81–82°, mmp with authentic material,[8,19] 81.0–82.5°. No other significant products were isolated.

Preparative Cycloaddition of [2.2]Paracyclophane (I) and Diethyl Maleate. A mixture of 100 ml of diethyl maleate (Eastman Reagent), 50 g (0.24 mol) of I (purified by crystallization from chloroform), and a small amount of hydroquinone was heated at reflux (235°) for 5 hr. Volatile materials were distilled to give 30 ml, bp 106–107° (12 mm), consisting of 17% diethyl fumarate and 83% diethyl maleate as determined by nmr integration of the vinyl peaks at τ 3.17 and 3.72, respectively. The residue was chromatographed on 3000 g of silica gel, and 300-ml fractions were taken. Eluent for fractions 1–38 was pentane; for fractions 39–78, 5% ether–pentane; 79–100, 8%; 101–128, 10%; 129–200, 12%; 201–210, 15%; 211–222, 20%; and for 223–250, 30%. Fractions 95–110 contained a small amount of a waxy solid. Two crystallizations from pentane yielded 143 mg (0.2%) of XIX, essentially pure by nmr. Two more recrystallizations gave an analytical sample, mp 46–47°. *Anal.* Calcd for $C_{20}H_{22}O_2$: C, 81.59; H, 7.53. Found: C, 81.76; H, 7.74.

Fractions 121–141 yielded, after two recrystallizations from ether–pentane, 14.48 g (16%) of *cis*-2,3-dicarbethoxy[2.4]paracyclophane, mp 71.5–72.5°. *Anal.* Calcd for $C_{24}H_{28}O_4$: C, 75.76; H, 7.42. Found: C, 75.80; H, 7.47.

Initially, the *cis* isomer had been obtained with a melting point of 50.5–52.5° by crystallization of the chromatographic product from pentane. Later it was found that the melting point of this sample depended on the heating procedure. If the sample was inserted at 49°, it melted at 51–52.5°; if heated slowly from room temperature, it gave a melting point of 71–72°. Recrystallization from ether–pentane gave material of mp 71.5–72.5°. The low-melting material could not be obtained subsequently. Apparently, two crystal forms are involved.

Fractions 150–158 contained a mixture of *cis*- and *trans*-cyclic diesters (analysis by tlc on silica gel). Crystallization from ether–pentane yielded 6.0 g of *trans*-2,3-dicarbethoxy[2.4]paracyclophane, essentially free of the *cis* isomer. Fractions 159–196 contained only *trans* isomer, crystallization of which gave 13.5 g. This material was combined with the 6.0 g isolated above and recrystallized from ether–pentane to yield 17.08 g of *trans*-2,3-dicarbethoxy[2.4]-paracyclophane, mp 107.5–108.5°. Recrystallization of this material afforded an analytical sample, mp 108–109°. *Anal.* Calcd for $C_{24}H_{28}O_4$: C, 75.76; H, 7.42. Found: C, 75.98; H, 7.53.

From the combined mother liquors were obtained a further 2.81 g of *trans* diester (total yield 19.89 g, 22%) and 4.5 g of a mixture of *cis* and *trans* diesters (5%).

Fractions 237–248 showed a blue fluorescence and contained solid material. They were combined and crystallized from dichloromethane–ether to yield 0.35 g (0.4%) of open-chain diester, XVIII (mp 145.5–147.0°). *Anal.* Calcd for $C_{24}H_{26}O_4$: C, 76.16; H, 6.93. Found: C, 76.18; H, 6.81.

Reaction of [2.2]Paracyclophane (I) with Dimethyl Fumarate. A glass tube containing 8.0 g (55.6 mmol) of dimethyl fumarate, 3.0 g (14.4 mmol) of I, and 50 mg of hydroquinone was degassed by thrice cooling, evacuating to 0.07 mm, and warming. The tube was then sealed, placed in a bath maintained at 200 ± 1.5° for 39 hr and 14 min, cooled, and opened. The contents were sublimed at 60° (0.07 mm) to give 4.64 g of dimethyl fumarate (less than 5% dimethyl maleate by nmr). The sublimation residue was chromatographed on 300 g of silica gel, and 100-ml fractions were taken. Elution solvent for fractions 1–14 was pentane; for 15–18, 2% ether–pentane; 29–50, 5%; 51–109, 10%; 110–124, 15%; 125–144, 20%. Fractions 35–53 contained 0.902 g of I; fractions 63–73 contained 0.38 g of dimethyl fumarate. Fractions 80–105 were pure *cis*-2,3-dicarbomethoxy[2.4]paracyclophane (*cis*-XVII) by tlc and nmr (0.960 g). This material was crystallized from ether–pentane to give 0.800 g, mp 88–89°; with material prepared by transesterification of *cis*-2,3-dicarbethoxy[2.4]paracyclophane (see below) mmp 86–88°. *Anal.* Calcd for $C_{22}H_{24}O_4$: C, 74.98; H, 6.86. Found: C, 75.10; H, 6.68.

Fractions 106–130 contained mixtures of *cis*- and *trans*-XVII. The composition, determined by nmr integration of the methyl peaks of the two isomers, was 24.2% *cis*-XVII (0.283 g) and 75.8% *trans*-XVII (0.885 g). Fractions 131–141 contained 0.196 g of pure *trans*-XVII. Fractions 106–141 were combined and recrystallized from dichloromethane–ether to give 0.867 g of *trans*-XVII, mp 201–203.5°. Mixture melting point with authentic *trans*-XVII, prepared from diacid XX, was 200–202° (see below). One further crystallization of this material gave an analytical sample, mp 202.5–203.5°. *Anal.* Calcd for $C_{22}H_{24}O_4$: C, 74.98; H, 6.86. Found: C, 75.05; H, 6.67. Nuclear magnetic resonance integration of standard mixtures of *cis*-XVII and *trans*-XVII gave values within 2% of the correct ones. Table IV summarizes the product data.

Table IV

	Initial		Final	
	g	mmole	g	mmole
Dimethyl fumarate	8.0	55.6	5.02	34.9
I	3.0	14.4	0.902	4.33
cis-XVII			1.24	3.53 (× 2)
trans-XVII			1.08	3.05 (× 2)
Total	11.0	70.0	8.24	52.4

Reaction of [2.2]Paracyclophane (I) with Dimethyl Maleate. A mixture of 8.0 g of dimethyl maleate,[32] 3.0 g of [2.2]paracyclophane, and 50 mg of hydroquinone was degassed and heated as in the fumarate reaction. The crude product was placed in 30 ml of dichloromethane and filtered to give 1.49 g of I. The mother liquor was distilled at 150° (20 mm) to give 6.16 g of dimethyl maleate (containing less than 1.2% of fumarate by nmr integration of the vinyl protons). The distillation residue was chromatographed as above to yield: 0.795 g of I; 0.094 g of pure *cis*-XVII; 0.637 g containing 0.024 g of dimethyl maleate (removed by heating at 56° (0.07 mm) for 1 hr) and 0.613 g of a mixture of *cis*-XVII (42.6%, 0.261 g) and *trans*-XVII (57.4%, 0.352 g). Nuclear magnetic resonance integration of standard mixtures of *cis*- and *trans*-XVII gave values within 2% of correct ones. Table V summarizes the product data.

Table V

	Initial		Final	
	g	mmole	g	mmole
Dimethyl maleate	8.0	55.6	6.18	42.8
I	3.0	14.4	2.29	11.0
cis-XVII			0.355	1.01 (× 2)
trans-XVII			0.352	1.00 (× 2)
Total	11.0	70.0	9.18	55.8

Control on Stability of *cis*-2,3-Dicarbomethoxy[2.4]paracyclophane (*cis*-XVIII). In a glass tube were placed 3.5 g of dimethyl maleate, 0.1777 g of *cis*-XVII, and 20 mg of hydroquinone. The mixture was degassed as before and heated at 200° for 48 hr. The tube was opened and the contents were distilled at 140° (20 mm). The residue was chromatographed on 85 g of silica gel using 5–20% ether–pentane as eluent. The fractions containing compound were combined and heated at 56° (0.03 mm) for 1 hr (to remove dimethyl maleate) to yield 170 mg of material containing 3–4% of *trans*-XVII and the remainder *cis*-XVII by nmr integration.

***cis*-2,3-Dicarbomethoxy[2.4]paracyclophane (*cis*-XVII) by Transesterification.** A mixture of 200 mg of *cis*-2,3-dicarbethoxy[2.4]paracyclophane, 25 ml of methanol, and 0.25 ml of sulfuric acid was refluxed 3 days. Ether and water were added, and the organic portion was washed with water, 5% sodium carbonate solution, saturated sodium chloride solution and was dried. After removal of solvent, the product was recrystallized from ether–pentane to give needles of *cis*-XVII, mp 84.5–85.5°. A further recrystallization raised the melting point to 86–87°.

***trans*-2,3-Dicarbomethoxy[2.4]paracyclophane (*trans*-XVII) by Esterification.** Transesterification of *trans*-2,3-dicarbethoxy[2.4]paracyclophane was extremely slow, so *trans*-XVII compound was prepared from diacid XX. Exactly 200 mg of XX was esterified by the same procedure as used for preparation of (−)-4-carbomethoxy-[2.2]paracyclophane (see above). The crude product was crystallized from dichloromethane–ether to give 130 mg of *trans*-XVII, mp 202.5–203.5°. A second crystallization did not change the melting point.

Isomerization of *cis*-2,3-Dicarbomethoxy[2.4]paracyclophane (*cis*-XVII) to the *trans* Isomer (*trans*-XVII). To a solution of 0.14 g of sodium in 5 ml of anhydrous methanol was added 20 ml of purified dimethoxyethane and 100 mg of *cis*-XVII. The solution was refluxed for 30 min and cooled, ether and water were added, and the organic layer was washed with saturated sodium bicarbonate solution and saturated sodium chloride solution. After drying the solution, the solvent was removed to give 67 mg of product. An nmr spectrum showed that no detectable amount of *cis*-XVII remained. The nmr spectrum of a standard containing 1% *cis*-XVII in 99% *trans*-XVII indicated that 0.5% *cis*-XVII would have been readily detectable.

***trans*-2,3-Dicarboxy[2.4]paracyclophane (XX).** A mixture of 15.00 g (0.0395 mol) of *trans*-2,3-dicarbethoxy[2.4]paracyclophane, 20 g of potassium hydroxide, and 300 ml of methanol was refluxed for 3 hr. Water was added and the solution was washed with ether. The aqueous portion was acidified with 400 ml of ice-cold 1 *N* hydrochloric acid. The precipitated acid was extracted with 1000 ml of ethyl acetate, and the solution was washed with water and three portions of saturated sodium chloride solution. After drying, solvent was removed under vacuum below 30° to give 12.9 g of crude XX. A portion of this material was crystallized from ethyl acetate to give a white, microcrystalline solid, mp 234–234.5° (anhydride XXIII mp 234.5–235.5°; see below). Apparently, diacid XX dehydrates to the anhydride at some temperature below the melting point. *Anal.* Calcd $C_{20}H_{20}O_4$: C, 74.05; H, 6.22. Found: C, 73.97; H, 5.98. Calcd for anhydride XXIII, $C_{20}H_{18}O_3$: C, 78.41; H, 5.92.

Decarboxylative Chlorination of 2,3-Dicarboxy[2.4]paracyclophane (XX). Crude acid, XX (12.9 g), was dissolved in 500 ml of pyridine, the reaction vessel was flushed with nitrogen, and 52.5 g (0.118 mol) of lead tetraacetate and 4.6 g (0.109 mol) of dry lithium chloride were added. The mixture was heated under nitrogen at 75–80° for 10 hr and cooled, and 1 l. each of ether and water was added. The organic portion was washed three times with 1 *N* hydrochloric acid, once with water, 5% sodium carbonate solution, and saturated sodium chloride solution, and dried. Removal of solvent gave a crude product which was chromatographed on 900 g of silica gel taking 100-ml fractions. Eluent for fractions 1–40 was pentane; 40–62, 2% ether–pentane; 63–79, 5%; 80–98, 8%; 99–118, 15%; 119–138, 20%; 139–154, 25%.

Fractions 85–95 contained 2.34 g of crude 2,3-dichloro[2.4]-paracyclophane (XXI). Recrystallization of this material from ether–pentane afforded two crops, 1.50 g (mp 145.5–147.5°) and 0.34 g (mp 144–147.5°), a 15% yield. Two further crystallizations from ether–pentane gave an analytical sample of XXI, mp 147–148°. *Anal.* Calcd for $C_{18}H_{18}Cl_2$: C, 70.83; H, 5.94; Cl, 23.23. Found: C, 71.00; H, 6.09; Cl, 23.39.

[2.4]Paracyclophane (XXII). To 8 ml of tetrahydrofuran (freshly distilled over lithium aluminum hydride) were added 0.80 g (2.6 mmol) of 2,3-dichloro[2.4]paracyclophane (XXI) and 0.5 ml of *t*-butyl alcohol (6.8 mmol) under nitrogen. Freshly cut pieces of lithium wire (0.96 g, or 14.3 mmol) were added, and the solution was brought to reflux. The vigorous reaction began immediately with considerable foaming. After 2 hr at reflux the reaction mixture was cooled, water and ether were added, and the layers were separated. The organic portion was washed with water, saturated sodium bicarbonate solution, saturated sodium chloride solution and was dried. Solvent was removed and the residue was chromatographed on 50 g of silica gel, taking 20-ml fractions. Eluent for fractions 1–13 was pentane; 14–21, 2% ether–pentane; and 22–30, 5% ether–pentane. Fractions 15–22 contained [2.4]paracyclophane with several minor contaminants (by nmr). After standing in contact with air for several weeks an insoluble polymer formed. Extraction of this material with ether and filtration chromatography on alumina of the solubles gave 68 mg of [2.4]paracyclophane, essentially pure by nmr. Fractions 23–28 contained 0.501 g of [2.4]paracyclophane (pure by nmr). The combined product was recrystallized from ethanol at −78° to give 307 mg (50%) of XXII with mp 68–71° (lit.[16] 74.4–75°). Two further recrystallizations from ethanol at −20° gave 80 mg, mp 71–73°. A fourth recrystallization gave material of mp 72.5–73°, mixture melting point with [2.4]paracyclophane prepared from 2-keto[2.4]paracyclophane,[16] having mp 73.5–75.5°, was 72.5–73.5°.

Anhydride (XXIII) of 2,3-Dicarboxy[2.4]paracyclophane. A solution of 150 mg of *trans*-2,3-dicarbomethoxy[2.4]paracyclophane (0.4 mmol) and 0.5 g of potassium hydroxide in 25 ml of methanol was refluxed for 2 hr. Most of the methanol was distilled, and 20 ml of redistilled acetic anhydride was added slowly. The reaction mixture was heated on the steam bath overnight. All of the volatile materials were distilled under vacuum, and the residue was refluxed with ether for 0.5 hr, and then filtered. Removal of the solvent from the filtrate and recrystallization of the residue from ether gave 41 mg of white needles of anhydride XXIII, mp 233–235°. The precipitate from the filtration was dissolved in water and ether, the ether layer was washed twice with water and dried, and the solvent was removed. Recrystallization of the residue from ether gave 46 mg of additional XXIII, mp 233–235°. The mother liquors from the two crystallizations gave a further 18 mg for a total yield of 105 mg (87%) of XXIII. One further crystallization of this product from methylene chloride–ether gave an analytical sample, mp 234.5–235.5°. *Anal.* Calcd for $C_{20}H_{18}O_3$: C, 78.41; H, 5.92. Found: C, 78.32; H, 5.87.

In a similar reaction 200 mg of *cis*-2,3-dicarbethoxy[2.4]paracyclophane gave 100 mg of anhydride XXIII, mp 234.5–235.5, mmp with authentic material, 234–235°.

Asymmetric Hydrolysis of Anhydride XXIII. A solution of 400 mg of XXIII, 0.8 g of dry brucine, and 0.015 ml of water in 15 ml of benzene was refluxed for 20 min. Ether was added, and the organic portion was washed three times with ice-cold 1 *N* hydrochloric acid, two times with cold 5% sodium carbonate, once with cold water, and two times with saturated sodium chloride solution.

(32) G. R. Clemo and S. B. Graham, *J. Chem. Soc.*, 215 (1930).

After drying the solution, the solvent was removed and the residue was sublimed at 145° (0.015 mm) to give 291 mg (73%) of sublimate (infrared spectrum identical with that of XXIII). The rotations (*c* 8.0, dichloromethane) were as follows: at 365 mμ, α^{25}_{obsd} +0.054°, or $[\alpha]^{25}_{365}$ +0.67°; at 546 mμ, α^{25}_{obsd} +0.008°, or $[\alpha]^{25}_{546}$ +0.1°.

The sodium carbonate extract from the above solution was acidified with 5 *N* hydrochloric acid and extracted twice with ether. The combined ether washings were washed with water and saturated sodium chloride solution, and the solvent was removed. The residue was refluxed for 4 hr with 2 ml of acetic anhydride in 20 ml of dichloromethane. The reaction mixture was then distilled at 120° (15 mm) to remove acetic anhydride, and the residue was sublimed to give 80 mg (20%) of white solid (infrared spectrum again same as spectrum of XXIII). The rotations (*c* 7.9, dichloromethane) were as follows: at 365 mμ, α^{25}_{obsd} −0.212°, or $[\alpha]^{25}_{365}$ −2.68°; at 546 mμ, α^{25}_{obsd} −0.034°, or $[\alpha]^{25}_{546}$ −0.43°.

As a control, this material was again sublimed to give 75 mg of XXIII, whose rotation (*c* 7.4, dichloromethane) was as follows: at 365 mμ, α^{25}_{obsd} −0.199°, or $[\alpha]^{25}_{365}$ −2.67°; at 546 mμ, α^{25}_{obsd} −0.031°, or $[\alpha]^{25}_{546}$ −0.42°.

Rates of Cycloaddition of 4-Carbomethoxy[2.2]paracyclophane with Dimethyl Maleate and Fumarate. A mixture of 20 mg of 4-carbomethoxy[2.2]paracyclophane, 10–20 mg of *n*-nonadecane (standard), 0.48 g of olefin, and 4.5 mg of hydroquinone was placed in a tube, degassed, and put in a bath at 200 ± 2° for the specified time. After cooling, the contents of the tube were diluted to 2 ml and analyzed by vpc. Detector response was calibrated with standard mixtures. The retention times at 235° were 8.3 and 16.9 min for *n*-nonadecane and 4-carbomethoxy[2.2]paracyclophane, respectively. Results are reported in Table II.

Rate of Ring Opening of 4-Carbomethoxy[2.2]paracyclophane. Reaction conditions were essentially the same as above, except that the hydroquinone was omitted and *p*-diisopropylbenzene was used as solvent. The rate of reaction was too low to observe starting material disappearance. On a 6 ft × 0.25 in. column packed with 30% fluorosilicone oil (Wilkins QF 1) on 30–60 Chromosorb W a large difference in retention time between *p,p'*-dimethylbibenzyl and [2.2]paracyclophane had been observed (the two come very close together on silicone gum). The product of a reaction of 4-carbomethoxy[2.2]paracyclophane with *p*-diisopropylbenzene for 9594 min was analyzed on this column. A peak, amounting to 2.6% of the starting material, appeared, with a retention time of 10.3 min (starting material has a retention time of 26.8 min under the same conditions). Assuming that open chain and paracyclophane material had identical thermal conductivity responses, this would give a value of $k = 3.8 \times 10^{-8}$ sec^{-1} for the rate constant for formation of open-chain reduction product.