Macro Rings. XXXV. Stereochemistry of [2.2]Paracyclophanyl Nucleus as a Neighboring Group in Solvolyses Reactions[1]

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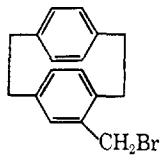
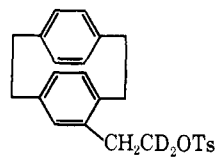
Abstract: The effects of the [2.2]paracyclophanyl nucleus on the kinetics and stereochemistry of carbonium reactions at asymmetric carbon atoms α and β to the system have been examined. Hydrolysis in 9:1 dioxane–water of the trichloroacetate of the α- and β-diastereomers of 4-(1-hydroxyethyl)-[2.2]paracyclophane both gave 1:1 mixtures of the corresponding α and β alcohols, and at rates (first order) that differed by only about 10%. In methanolysis in the presence of potassium acetate, the α and β esters gave ethers whose product composition differed by only 6%. Acetolyses and formolyses of the tosylates of α- and β-4-(2-deuterio-2-hydroxypropyl)-[2.2]paracyclophane were much more stereospecific. Acetolysis at 75° of the α-tosylate gave acetate which was 97% α and 3% β, whereas the β-tosylate gave acetate which was 7% α and 93% β. In formolyses, both diastereomeric tosylates underwent reaction with greater than 99% retention of configuration. The rates of acetolysis of the two diastereomeric tosylates differed by only about 10%. The $\Delta S^{\pm}$ for each diastereomer was about -4 to -5 eu. These facts provide compelling evidence for intervention of a phenonium ion intermediate in the solvolyses of the latter system.

Earlier work[2] demonstrated that the [2.2]paracyclophanyl nucleus was a somewhat better neighboring group than the 2,5-dimethylphenyl group in enhancing the rates of solvolysis in both α-arylmethyl bromide and β-arylethyl tosylate systems. In particular, compounds I and II were found to be more reactive than their open-chain counterparts. In acetolysis of II, although the rates and entropies of activation indicated that aryl participated in ionization, no deuterium scrambling occurred, and therefore the intermediate phenonium ion was opened exclusively at the same position involved when the three-membered ring was closed.

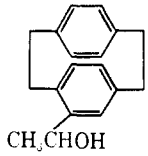


I

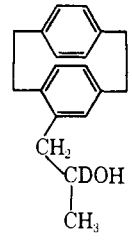


II

In the present work, solvolyses of the trichloroacetates of III and the tosylates of IV were examined. Both systems contain two asymmetric elements, and therefore each is composed of two racemates, III-α and III-β, and IV-α and IV-β. Thus, an examination of the structures of the products of solvolysis of the four racemates allows the stereochemical course of substitution to be determined, which in turn points to the mechanistic details of the transformations.[3]



III-α and III-β



IV-α and IV-β

Syntheses. Racemates III-α and III-β were prepared by lithium aluminum hydride reduction of 4-acetyl[2.2]paracyclophane.[4] The two diastereomers were produced in the ratio $\alpha:\beta$ = 1.32,[5] and are experimentally designated as follows: α, mp 107–107.5°, eluted first from alumina; β, mp 117–118°, eluted second from alumina. Arguments for the relative configurational assignments are found in the Discussion. Attempts to prepare the tosylates of these alcohols failed because of the instability of the expected products. Attempted preparation of the diastereomerically pure chlorides from either alcohol III-α or III-β with anhydrous hydrogen chloride in ether or with thionyl chloride always led to inseparable mixtures of the epimeric chlorides. Consequently, the trichloroacetates of III-α and -β were prepared and employed in the solvolytic studies.[6]

The synthesis of alcohols IV was accomplished through acid V as intermediate,[7] whose synthesis was greatly improved (see Experimental Section). Ketone VI was reduced with lithium aluminum deuteride instead of the common hydride to facilitate nmr analysis of alcohols IV and their derivatives. The diastereomers were separated by silica gel chromatography of their acetates (which lent themselves to nmr analysis), reduction of which with lithium aluminum hydride led to pure IV-α and IV-β. These alcohols were produced in the ratio IV-α:IV-β = 1.26 from the ketone VI. A small amount of 1,3-asymmetric induction is visible in this ratio. These alcohols are given the following experimental designations: IV-α, mp 120–121° (acetate is eluted more rapidly from silica gel); IV-β,

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

(2) D. J. Cram and L. A. Singer, *J. Am. Chem. Soc.*, **85**, 1075 (1963).

(3) D. J. Cram, *ibid.*, **86**, 3767 (1964).

(4) D. J. Cram and N. L. Allinger, *ibid.*, 77, 6289 (1955).

(5) This reaction provides one of the few examples of asymmetric induction caused by molecular asymmetry. For other examples, see J. A. Berson and M. A. Greenbaum, *ibid.*, **80**, 445, 653 (1958), and **81**, 6456 (1959).

(6) E. M. Kosower and S. Winstein, *ibid.*, **78**, 4347 (1956).

(7) D. J. Cram, R. H. Bauer, N. L. Allinger, R. A. Reeves, W. J. Wechter, and E. Heilbronner, *ibid.*, **81**, 5977 (1959).

Table I. First-Order Rate Constants and Activation Parameters for Solvolyses of Trichloroacetates of III-α and III-β and Tosylates of IV-α and IV-β

Run no.	Ester of	Solvent	Temp, °C	$k \times 10^6$, sec^{-1} [a]	$\Delta H^{\pm}$, kcal/mole	$\Delta S^{\pm}$, eu
1	III-α	$O(CH_2CH_2)_2O$–H_2O[c]	24.82	5.27 ± 0.07	20.2 ± 0.2[b]	-14.9 ± 0.7[b]
2	III-α	$O(CH_2CH_2)_2O$–H_2O[c]	49.69	79.0 ± 1.0		
3	III-β	$O(CH_2CH_2)_2O$–H_2O[c]	24.82	5.84 ± 0.06	20.5 ± 0.2[b]	-13.6 ± 0.8[b]
4	III-β	$O(CH_2CH_2)_2O$–H_2O[c]	50.04	94.4 ± 2.1		
5	IV-α	CH_3CO_2H	49.99	9.68 ± 0.04	25.1 ± 0.4[d]	-4.1 ± 1.2[d]
6	IV-α	CH_3CO_2H	74.97	172 ± 1		
7	IV-β	CH_3CO_2H	49.99	8.97 ± 0.05	24.9 ± 0.6[d]	-4.9 ± 1.6[d]
8	IV-β	CH_3CO_2H	74.97	156 ± 1		

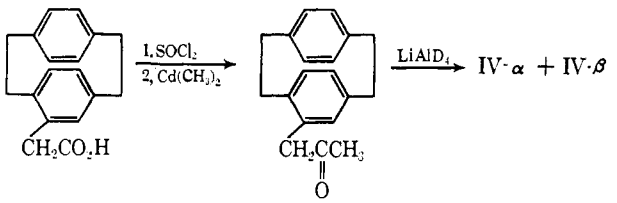
[a] Average of two runs. Standard deviations were used for ± values (see Experimental Section). [b] Calculated at 24.82° (see Experimental Section). [c] Solvent 9:1 dioxane–water by volume. [d] Calculated at 74.97°.

Table II. Solvolysis Products of Trichloroacetates and Methyl Ethers of III-α and III-β and of Tosylate Esters of IV-α and IV-β

Run no.	Compd solvolyzed	Solvent	Temp, °C	Time, hr	% yield sol prodt	% yield olefin	—Prodt compstn— % α	% β
9	III-α-TCA[a]	$O(CH_2CH_2)_2O$–H_2O[b]	50	100	81	12	50	50
10	III-β-TCA[a]	$O(CH_2CH_2)_2O$–H_2O[b]	50	100	75	7	50	50
11	III-α-TCA[a]	CH_3OH	65	11	89	1.4	56	44
12	III-β-TCA[a]	CH_3OH	65	11	81	1.4	57	43
13	III-α-TCA[a]	CH_3OH–KOAc[c]	65	1.75	97	1.3	24	76
14	III-β-TCA[a]	CH_3OH–KOAc[c]	65	1.75	92	0.4	30	70
15	III-α-CH_3[d]	CH_3OH–Cl_3CCO_2H[e]	65	10	90	...	60	40
16	III-β-CH_3[d]	CH_3OH–Cl_3CO_2H[e]	65	10	95	...	53	47
17	IV-α-Ts[f]	AcOH	75	18	92	3.4	97.4	2.6
18	IV-β-Ts[f]	AcOH	75	18	91	4.7	7.2	92.8
19	IV-α-Ts[f]	HCO_2H–NaO_2CH[g]	75	7	76	...	>99	<1
20	IV-β-Ts[f]	HCO_2H–NaO_2CH[g]	75	7	78	...	<1	>99

[a] Trichloroacetate of alcohols III-α or III-β. [b] 9:1 dioxane–water by volume. [c] 1.4 moles based on substrate = 1 mole. [d] Methyl ethers of III-α and III-β. [e] 0.0115 *M*. [f] Tosylates of IV-α and IV-β. [g] 0.025 *M*.

mp 88.7–89.3° (acetate is eluted less rapidly from silica gel). The relative configurations of these alcohols are provisionally assigned in the Discussion. The tosylates of IV-α and IV-β were easily prepared and handled.



V VI

Kinetics. Table I summarizes the kinetic results of hydrolysis in 9:1 dioxane–water (by volume) of the trichloroacetates of III-α and III-β. The reactions exhibited good first-order kinetics (nine points per run) as followed by titration of the liberated trichloroacetic acid with standard base.[6] Activation parameters were calculated from rate constants determined at 25 and 50°.

The kinetics of acetolysis of tosylates of IV-α and IV-β were studied at 50 and 75°. Good first-order rate constants (minimum of ten points) were obtained by titrating the liberated *p*-toluenesulfonic acid with standard sodium acetate in glacial acetic acid. The rate constants and the derived activation parameters are listed in Table I.

Products of Solvolyses. The trichloroacetates of III-α and III-β were hydrolyzed in 9:1 dioxane–water for 100 hr at 50° to produce a mixture of epimeric alcohols (III-α and III-β) and a minor amount of olefin. Control runs demonstrated that these compounds once formed did not epimerize. Table II reports the yields and the relative amounts of the epimeric alcohols produced. The analysis of the alcoholic mixtures made use of the difference in the nmr spectra of α- and β-III.

Each of the epimeric trichloroacetates was also subjected to methanolysis, both with and without added potassium acetate to neutralize the trichloroacetic acid developed. The methyl ethers produced were analyzed by nmr methods, and Table II records the results. The product distribution varied significantly when potassium acetate was added. Control runs indicated that the methyl ethers epimerize under the conditions of the methanolysis in the absence of potassium acetate to neutralize the acid produced. Indeed, in runs 11 and 12, epimeric equilibrium of the methyl ethers was reached in the course of methanolyses run in the absence of potassium acetate, and the α isomer proved to be the more stable of the two (see also runs 15 and 16). Attempts to epimerize to equilibrium alcohols III-α and III-β with aluminum isopropoxide and acetone in 2-propanol[8] were unsuccessful; III-α epimerized only about 10–15%, while III-β gave a mixture of about 52% α, 48% β.

The tosylate esters of IV-α and IV-β were subjected to acetolysis at 75° for 18 hr and the acetate products analyzed (see Table II). Control experiments demon-

(8) (a) W. G. Dauben, G. J. Fonken, and D. S. Noyce, *J. Am. Chem. Soc.*, 78, 2579 (1956); (b) E. L. Eliel and R. S. Ro, *ibid.*, 79, 5992 (1957).

strated that the product acetates did not epimerize under the conditions of the acetolysis. The two tosylate esters also were subjected to formolysis at 75° for 7 hr in the presence of 1.05 equiv of sodium formate. The product formates were then reduced to the alcohols with lithium aluminum hydride and converted to their acetates for analysis. The product distributions are listed in Table II.

Discussion

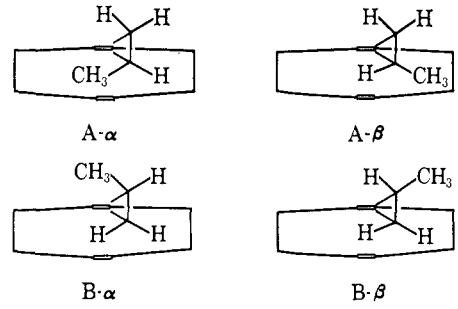
The solvolysis of the tosylate esters of IV-α and IV-β will be discussed first, and an argument presented for the relative configurations for the two epimers. It will be demonstrated that most of the reaction with acetic acid and essentially all of the reaction in formic acid occur *via* the phenonium ion. The solvolysis of the trichloroacetate esters of III-α and III-β will then be discussed, and a provisional assignment of relative configurations of the epimers made.

[2.2]Paracyclophanyl Nucleus as a Neighboring Group. In the acetolysis of the tosylate esters of IV-α and IV-β *retention dominated over inversion of configuration by factors of 37.4 and 12.9, respectively* (runs 17 and 18, Table II). In ordinary simple acetolysis of tosylate esters of secondary alcohols which contain no neighboring groups, *inversion predominates over retention of configuration* by substantial factors.[9] Even more striking are the formolyses results. In formic acid the epimeric tosylates gave formates with retention of configuration by factors of greater than 100. Nothing in open carbonium ion theory provides an explanation for these results, either for the high retention observed, or for the higher stereospecificity observed in formic (less nucleophilic solvent) than in acetic acid. These stereochemical results alone require the intervention of a phenonium ion as a discrete intermediate[10] in these solvolysis reactions.

The interesting question arises as to whether the π electrons between the two benzene rings or on the external faces of the paracyclophane nucleus aid in displacement of the tosylate group. Each of the two possibilities leads to a different type of phenonium ion, the former to A and the latter to B. Of these, B seems the more probable for two reasons. (1) The bending of the benzene rings into a tub[11] represents a slight rehybridization of the π electrons in the direction of sp^3, and thus the external faces of the benzene rings should be more nucleophilic than the internal. (2) Phenonium ion B is much less sterically compressed than phenonium ion A.

Intermediates in which the transannular benzene ring also becomes directly involved in bridged ion formation can also be envisioned, but are considered unlikely for reasons enumerated in earlier studies.[2]

Implicit in the structures of B-α and B-β are the relative configurational assignments of the starting materials and products since each diastereomeric phenonium ion is formed and decomposed with inversion at secondary carbon. Since two inversions are the equivalent of one retention, the stereochemical results and the bridged ion theory are compatible. The small amount of simple inversion observed in the acetolysis



provides a measure of how much open ion was produced compared to the bridged ion.

The relative configurations assigned to B-α and B-β and hence to IV-α and IV-β (and their respective tosylates) are based on two considerations. (1) The tosylate of IV-α solvolyzes $\sim$10% faster than that of IV-β (see Table I, runs 6 and 8). Molecular models suggest that whereas the diastereomeric starting states should be close to one another in energy, B-α and B-β should be somewhat different, with the α bridge being the more stable. Thus, the steric interference between the methyl and methylene groups in B-β is more severe than those in B-α. (2) Compatible with this interpretation is the fact that the faster acetolyzing isomer (α configuration) also gives the higher stereospecificity by a factor of about 3 (37.4:12.9). Thus, the higher energy bridged ion (B-β configuration) should compete with open ion formation less successfully than the more stable bridged ion (B-α configuration).

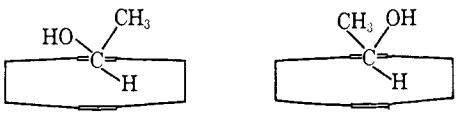
The tosylate of IV-α acetolyzes at 75° 13 times faster than 1-phenyl-2-propyl tosylate,[12] while that of IV-β goes about 12 times faster. In spite of the greater steric compression in forming bridged ions from the paracyclophanyl system than the simple phenyl system, bridged ions have a greater tendency to form from the former system. This conclusion derives from the above rate comparisons as well as from stereochemical comparisons. Thus, acetolysis of 1-phenyl-2-propyl tosylate proceeded with 65% inversion and 35% retention,[12] or retention:inversion = 0.54, as compared to factors of 37.4 and 12.9 for the tosylates of IV-α and IV-β. Again, conformity between conclusions based on kinetic and stereochemical comparisons are evident.

The enhanced ability of the [2.2]paracyclophanyl nucleus to act as a neighboring group probably derives from several factors. Charge delocalization into the transannular ring in the transition state for bridge ion formation and release of some puckering strain are two factors that probably operate. Other work has demonstrated the [2.2]paracyclophane nucleus to be a better π base toward both tetracyanoethylene[13] and strong electrophiles than open-chain model compounds.

Effect of [2.2]Paracyclophane Nucleus on Stereochemistry of Sovolysis at Attached Carbon. An examination of scale molecular models of the epimeric alcohols III indicates that the preferred conformation of the hydroxyl-substituted carbon has the methine hydrogen atom between the two aromatic rings (in the projection formula) and the hydroxyl and methyl groups above the plane of the substituted ring. Furthermore, because the

(9) A. Streitwieser, Jr., "Solvolytic Displacement Reactions," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, pp 59, 73.
(10) D. J. Cram, *J. Am. Chem. Soc.*, **71**, 3863 (1949).
(11) C. L. Coulter and K. N. Trueblood, *Acta Cryst.*, **16**, 667 (1963).
(12) S. Winstein, M. Brown, K. C. Schreiber, and A. H. Schlesinger, *J. Am. Chem. Soc.*, 74, 1140 (1952).
(13) (a) D. J. Cram and R. H. Bauer, *ibid.*, **81**, 5971 (1959); (b) D. J. Cram, W. J. Wechter, and R. W. Kierstead, *ibid.*, **80**, 3126 (1958).

o-methylene is larger than the *o*-hydrogen, the groups above the ring (in profile) are probably rotated somewhat away from the nearest methylene bridge. The configurations indicated in formulas C and D are assigned to the experimentally designated III-α and III-β diastereomeric racemates on the basis of equilibrium data and chromatographic behavior.



C or III-α D or III-β

The methyl ethers of III-α and III-β when treated with trichloroacetic acid in methanol each gave a mixture of epimers in which the α isomer predominated (see runs 15 and 16, Table II). In the methanolysis of the epimeric trichloroacetates in the absence of potassium acetate (runs 11 and 12), the same mixture of ethers was obtained, 57% α and 43% β. Furthermore, III-β when treated with acetone–aluminum isopropoxide gave an epimeric mixture in which III-α dominated. Thus, the α isomers appear to be the more thermodynamically stable by a small amount. Since molecular models suggest that configuration C is more stable than D, the tentative configurational assignment is possible.

The III-α isomer was experimentally designated as being the one that moved faster on a chromatograph column. Examination of scale models of the conformation formulated indicates that the hydroxyl group of C is more exposed to absorbing centers than that of D, and thus the faster moving isomer, III-α, probably possesses the configuration of formula C, and III-β that of D.

These assignments allow the other properties of III-α and III-β to be given a structural interpretation. Thus, the methyl group of III-α absorbs in the nmr at τ 8.76 and the hydroxyl group at τ 8.12, whereas the methyl of III-β absorbs at τ 8.46 and the hydroxyl at τ 8.42. The model compound, 1,4-dimethyl-2-(α-hydroxyethyl)benzene, exhibits a carbinyl methyl signal at τ 8.68 which is between the two diastereomers. In formula C, the methyl group is expected to be more shielded by the ring current than the methyl group in D, and conversely for the hydroxyl group. Thus, assignment of structures C and D to compound III-α and III-β is compatible with the nmr spectra. Similar arguments apply to the methyl ethers and trichloroacetates of the epimeric alcohols.

The nmr spectra of III-α and III-β and their respective ethers and trichloroacetates provide further structural correlations. All α epimers produce a downfield shift of the *ortho* proton, the shift being most noticeable in the trichloroacetate. All β epimers exhibit a downfield shift of a fraction of one proton of the methylene bridges as a multiplet consisting of several small peaks. These two effects suggest an interaction of the protons with the oxygen function, which in each case is a near neighbor of the proton in question. Such effects have been noted in similar systems, and will be reported in a later paper in this series.[14]

The trichloroacetate of III-β underwent hydrolysis at a rate about 12% faster than that of the III-α isomer at 50° (runs 2 and 4 of Table I). Although this rate difference is disappointingly small, it is compatible with the configurational assignments if the trichloroacetate group leaves in a transition state with that group *trans* to the transannular benzene ring. Such a transition state provides for coplanarity of the carbonium ion substituents and the attached benzene ring. The ion from the α configuration should be more compressed than that from the β configuration.

The product data for the hydrolyses of the trichloroacetates of III-α and III-β indicate that III-α and III-β are produced in exactly equal amounts from either diastereomeric ester (runs 9 and 10 of Table II). The fact that both diastereomers produce exactly the same balance of products suggests that the two diastereomeric, coplanar carbonium ions equilibrate. The fact that this balance of products was 1:1 indicates that over-all water capture by the carbonium ion occurred without any asymmetric induction.

In the methanolysis reactions carried out under conditions of kinetic control of products, the ester of III-α gave a product balance in which the ether of III-β predominated over that of III-α by a factor of 3.1. This factor decreased to 2.3 when the ester of III-β was starting material (runs 14 and 15 of Table II). The two carbonium ions appear to have nearly equilibrated in methanol, and some asymmetric induction is apparent in the methanol capture process. The predominance of the β ether in the product is compatible with the predominant capture of the sterically least compressed coplanar carbonium ion from the least hindered side (the side remote from the transannular benzene ring).

Both of the above sets of results are significantly different from those obtained from α-phenylethyl systems, in which inversion is the net steric course under a variety of conditions.[15] For example, α-phenylethyl tosylate undergoes ethanolysis with 20% net inversion. The absence of high degrees of stereospecificity and rate differences in the solvolyses reactions contrast with the results of Richards and Hill,[16] who observed both in solvolyses of the α-acetoxy-1,1′-trimethyleneferrocene diastereomers.

The small predominance of III-α over III-β (factor of 1.3) in the product of lithium aluminum hydride reduction of 4-acetyl[2.2]paracyclophane is compatible with the notion that in the predominant product-determining transition state, the oxygen of the carbonyl group complexed to metal is oriented toward the least hindered position in the molecule, and the hydrogen then approaches the carbonyl group from the side of least hindrance.[17]

Experimental Section

The syntheses described here were usually repeated and the best conditions recorded. Melting points and boiling points are uncorrected. Silica gel G layers, 0.25 mm thick on glass plates, were used in thin layer chromatography (tlc). The plates were developed in an iodine chamber. All infrared spectra were recorded on a Beckman IR-5 spectrophotometer. Solutions were 5–10% in spectrograde chloroform as solvent. Crude [2.2]paracyclophane[18] was

(14) H. Reich, unpublished work.

(15) For a summary, see ref 9.

(16) J. H. Richards and E. A. Hill, *J. Am. Chem. Soc.*, **81**, 3484 (1959); **83**, 3840, 4216 (1961).

(17) D. J. Cram and K. R. Kopecky, *ibid.*, **81**, 2748 (1958), and references cited therein.

(18) D. J. Cram and H. Steinberg, *ibid.*, **73**, 5691 (1951).

crystallized by Soxhlet extraction with chloroform to give octahedra, mp 286–287°. Reagent grade chloroform, dichloromethane, acetone, and methanol were used directly. Diethyl ether was anhydrous Mallinckrodt Analytical Reagent. Pyridine was Karl Fischer reagent grade (Matheson Coleman and Bell), stored over potassium hydroxide pellets. Technical pentane was distilled before use. Dioxane was purified by the method of Fieser[19] and distilled from sodium just prior to use.

Mallinckrodt Analytical Reagent trichloroacetic acid was crystallized from benzene and stored over anhydrous magnesium perchlorate in a vacuum desiccator to give material, mp 59–59.5° (lit.[20] mp 59.5–60.3°). Benzene was distilled from sodium and stored over sodium. Dry acetic acid for acetolysis reactions was prepared by refluxing glacial acetic acid with 3% by weight acetic anhydride for 12 hr and distilling; a center cut was taken, bp 117.1°, and this material was made 1% by weight in freshly distilled acetic anhydride. Formic acid (Baker, 98%) was allowed to stand over boric anhydride for 48 hr, filtered, and distilled from molecular sieves, and a center cut was retained, bp 100.2°.

4-Acetyl[2.2]paracyclophane. A modification of the reported method[4] was employed. A solution of 107.2 g of aluminum chloride (0.96 mole) and 74.8 g of acetyl chloride (0.80 mole) in 800 ml of dichloromethane was cooled to −15°, and 100 g (0.48 mole) of [2.2]paracyclophane was added in one quick addition with efficient mechanical stirring. The temperature was maintained at −20 to −15° for 6 min, and the blood-red reaction mixture was poured into ice–dilute hydrochloric acid. The aqueous layer was separated and extracted with fresh dichloromethane. The organic layers were combined, washed successively with dilute hydrochloric acid, water, saturated aqueous sodium bicarbonate, water, and twice with saturated aqueous sodium chloride, and dried. Solvent was evaporated to leave a yellowish solid which was crystallized from ether to yield 61.0 g (51%) of hard white crystals of the desired ketone, mp 108.5–109.5° (lit.[4] 109.7–110.4°). The mother liquors were concentrated to a viscous yellow oil which was chromatographed over 1.2 kg of silica gel. Elution with 2.5 l. of ether–pentane (25:75) produced a trace of starting material; the next 6.4 l. eluted 22.5 g (18.5%) of additional ketone, mp 108–109°.

4-(1-Hydroxyethyl)-[2.2]paracyclophane (III) and Separation of Diastereoisomers. A 126.6-g portion (0.507 mole) of the above crude ketone, mp 104–108°, was dissolved in a solution of ether and 330 ml of tetrahydrofuran and added dropwise over 2 hr at 25° to a stirred mixture of 20 g (0.53 mole) of lithium aluminum hydride in 150 ml of ether. After addition, the mixture was stirred at 25° for 30 hr and then was carefully hydrolyzed by the addition of saturated aqueous potassium carbonate. The ether layer was washed once with 2% hydrochloric acid and twice with saturated aqueous sodium chloride and dried. Solvent was evaporated to leave 125.9 g of an oil which, except for 2.9 g of residual [2.2]paracyclophane, was dissolved in boiling ether and allowed to stand in the cold until 55 g of white solid (mp 55–110°) separated. The noncrystalline portion (68 g) of the above product was chromatographed on 2540 g of activity 2 alumina. Elution with solvent ranging from ether–pentane 10:90 to ether–pentane 30:70 produced 16.4 g of side products. Elution with solvent ranging from ether–pentane 40:60 to pure ether produced 30.4 g of pure diastereomer α of 4-(1-hydroxyethyl)-[2.2]paracyclophane, III-α, transparent plates, mp 107–107.5° (*vide infra*). Finally, elution with pure ether and then methanol–dichloromethane (5:95) produced 13.0 g of alcohol III enriched in diastereomer β; several crystallizations of this material from ether yielded 4.4 g of pure III-β, mp 117–118° (*vide infra*).

The 55-g portion of white solid mentioned above was chromatographed over 1800 g of Woelm neutral activity 1 alumina. Elution with solvent ranging from ether–pentane 20:80 to pure ether produced 4.0 g of side products. Further elution with ether and then with dichloromethane–ether (3:97) produced 2.5 g of III-α. Elution with dichloromethane–ether (10:90), methanol–dichloromethane (5:95), and finally methanol produced 40.6 g of alcohol III enriched in diastereomer III-β. Several crystallizations of this material from hexane–chloroform yielded 11.8 g of alcohol III-β as fine white needles, mp 117–118°.

Alcohol diastereomer III-α exhibited the usual hydroxyl absorption at 2.8 and 2.9 μ in the infrared. The nmr spectrum was as follows: seven protons as a multiplet at τ 3.25–3.83 (aromatic), one proton as a quartet (J = 6.5 cps) at τ 5.11 (methine), eight protons as a multiplet at τ 6.50–7.44 (bridge), one proton as a singlet at τ 8.12 (hydroxyl), and three protons as a doublet (J = 6.5 cps) at τ 8.76 (methyl). This material had R_f 0.5 on tlc with solvent system pentane–ether–methanol (65:30:5). *Anal.* Calcd for $C_{18}H_{20}O$: C, 85.67; H, 7.99. Found: C, 85.47; H, 8.21.

Alcohol diastereomer III-β exhibited the usual hydroxyl absorption at 2.8 and 2.9 μ in the infrared. The nmr spectrum was as follows: seven protons as a multiplet at τ 3.37–3.91 (aromatic), one proton as a quartet (J = 6.5 cps) at τ 5.23 (methine), eight protons as a multiplet at τ 6.20–7.50 (bridge), one proton as a singlet at τ 8.42 (hydroxyl) overlapped by three protons as a doublet (J = 6.5 cps) at τ 8.46 (methyl). This material had R_f 0.4 on tlc with solvent system pentane–ether–methanol (65:30:5). *Anal.* Calcd for $C_{18}H_{20}O$: C, 85.67; H, 7.99. Found: C, 85.67; H, 8.20.

A solution of 3.00 g of 4-acetyl[2.2]paracyclophane, mp 108.5–109.5°, in 100 ml of ether was added dropwise to a stirred mixture of 0.75 g of lithium aluminum hydride in 250 ml of ether. The reaction mixture was stirred for 2 hr and carefully hydrolyzed by the addition of 100 ml of saturated aqueous magnesium sulfate. The aqueous layer was separated and extracted with another portion of ether, and the ether layers were combined, washed with water, and dried. Evaporation of solvent left 3.08 g of alcohol III as a clear oil which slowly became a white solid, mp 64–76°. A sample of the oil was analyzed by nmr and shown to be 57% alcohol III-α and 43% III-β.

When the same reaction was repeated with "inverse addition" (760 mg of lithium aluminum hydride in ether slurry added to 500 mg of ketone in ether), followed by similar isolation, the product alcohol (white solid, mp 55–75°) was shown by nmr analysis to be 67% alcohol III-α and 33% III-β.

Attempted Thermodynamic Equilibration of Diastereoisomers of 4-(1-Hydroxyethyl)-[2.2]paracyclophane (III). To 50 ml of dry isopropyl alcohol (distilled from calcium oxide) were added 1.00 g (4 mmoles) of alcohol III-β, 0.81 g (4 mmoles) of freshly distilled aluminum isopropoxide, and 1 ml of acetone. The mixture was refluxed for 122 hr, and an aliquot was withdrawn and analyzed by tlc [pentane–ether–methanol (65:30:5) solvent system]. Approach to an equilibrium alcohol mixture seemed to be very slow, even after refluxing for an additional month, so the contents of the reaction flask were sealed in a tube which was then heated at 123° for 6.5 days. The tube was cooled and opened, and the contents were poured into 250 ml of water containing 10 ml of concentrated hydrochloric acid. This mixture was extracted with two 100-ml portions of ether. The ether extracts were combined, washed with water and 5% aqueous sodium bicarbonate, and dried. Solvent was removed to leave a yellow oil which tlc showed to contain alcohols III-α and III-β plus two unidentified components. The mixture was chromatographed over a short column of activated silica gel. Elution with ether–pentane 2:98 produced two unidentified components; elution with ether-pentane 30:70 afforded 500 mg of white solid. Analysis of this material showed it to be approximately 52% alcohol III-α and 48% III-β.

Trichloroacetates of 4-(1-Hydroxyethyl)-[2.2]paracyclophane. To 10 ml of dry pyridine was added 1.50 g (5.96 mmoles) of alcohol III-α, and the solution was cooled to 0°. To 5 ml of dry pyridine, which had been cooled to 0°, was added 1.2 ml of trichloroacetyl chloride (Eastman White Label, *ca.* 11 mmoles) to produce a yellow solution. The trichloroacetyl chloride solution was poured into the alcohol solution, and the reaction mixture was kept at 0° for 15 min with occasional swirling; a precipitate of pyridine hydrochloride formed almost immediately. The reaction mixture was poured into 75 ml of ice water containing 0.75 g of potassium bicarbonate. The yellow solid which separated was extracted with three 125-ml portions of 3:1 ether–pentane, and the combined organic extracts were washed with ice-cold 5% hydrochloric acid (three 75-ml portions), ice-cold 5% aqueous sodium bicarbonate (two 75-ml portions), ice-cold water, and ice-cold saturated aqueous sodium chloride, and dried. Solvent was removed at reduced pressure to leave 2.33 g (99%) of crude yellow, waxy solid which was dissolved in about 15 ml of pentane containing some ether. After 2 days at −20° were deposited hard, transparent prisms. These were collected and recrystallized to give prisms of trichloroacetate of III-α, mp 82–82.5° dec. This compound decomposed at room temperature within a few days but could be stored indefinitely at −20°.

The infrared spectrum of this trichloroacetate showed bands at 5.70 (strong), 7.97 (strong), and 8.2 μ (shoulder). The nmr spectrum was as follows: one proton as a broad singlet at τ 3.33 (*ortho*

(19) L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., Boston, Mass., 1957, p 284.

(20) E. Grunwald and E. Price, *J. Am. Chem. Soc.*, **86**, 4517 (1964).

proton) and six protons as a multiplet at τ 3.40–3.64 (aromatic), one proton as a quartet (J = 6.5 cps) at τ 3.84 (methine), eight protons as a multiplet at τ 6.56–7.34 (bridge), and three protons as a doublet (J = 6.5 cps) at τ 8.62 (methyl). *Anal.* Calcd for $C_{20}H_{19}Cl_3O_2$: C, 60.40; H, 4.81; Cl, 26.74. Found: C, 60.58; H, 4.73; Cl, 26.98.

Exactly as in the procedure described above, 1.50 g of alcohol III-β was converted to its trichloroacetate. This material was isolated as a yellow solid in crude yield of 2.30 g (98%); two crystallizations from ether–chloroform at −20° yielded a voluminous white solid, mp 92.4–92.8° dec (heating rate *ca.* 2°/min; the melting point was dependent on heating rate). This compound decomposed at room temperature within a few days but could be stored indefinitely at −20°.

The infrared spectrum of the trichloroacetate of III-β showed bands at 5.69 (strong), 8.03 (strong), and 8.2 μ (shoulder). The nmr spectrum was as follows: seven protons as a multiplet at τ 3.33–3.77 (aromatic) slightly overlapping one proton as a quartet (J = 6.5 cps) at τ 3.94 (methine), eight protons as a multiplet at τ 6.44–7.30 (bridge), and three protons as a doublet (J = 6.5 cps) at τ 8.28. *Anal.* Calcd for $C_{20}H_{19}Cl_3O_2$: C, 60.40; H, 4.81; Cl, 26.74. Found: C, 60.52; H, 4.74; Cl, 27.01.

β-4-(1-Methoxyethyl)-[2.2]paracyclophane. To a flask were added 0.500 g (2.0 mmoles) of alcohol III-β, 1.22 g (8.0 mmoles) of barium oxide, 1.25 ml (20 mmoles) of methyl iodide, 10 ml of dimethylformamide, and 0.05 ml of water. This mixture was stirred for 27 hr at 25°; after 6.5 hr of this period, an additional 1.25 ml of methyl iodide was added. The yellow reaction mixture was poured into 75 ml of chloroform, washed twice with water, once with dilute aqueous sodium bisulfite, again with water, and once with saturated aqueous sodium chloride, and dried. Solvent was evaporated, and the residue was chromatographed over 40 g of activated silica gel. Elution with ether–pentane 1:99 produced *ca.* 1 mg of a substance which appeared to be α-4-(1-methoxyethyl)-[2.2]paracyclophane; ether–pentane 3:97 eluted 252 mg (48%) of β ether; ether–pentane 50:50 eluted 191 mg of unreacted alcohol III-β.

The ether of III-β was crystallized from ether–pentane to yield a white solid, mp 64.8–65.5°. The infrared spectrum exhibited a band at 9.1 μ (medium, antisymmetric C–O–C stretching).[21] The nmr spectrum was as follows: seven protons as a multiplet at τ 3.40–3.84 (aromatic), one proton as a quartet (J = 6.5 cps) at τ 5.61 (methine), three protons as a sharp singlet at τ 6.92 (methoxy) superimposed on eight protons as a multiplet at τ 6.36–7.43 (bridge), and three protons as a doublet (J = 6.5 cps) at τ 8.47 (methyl). *Anal.* Calcd for $C_{19}H_{22}O$: C, 85.67; H, 8.33. Found: C, 85.61; H, 8.18.

Methanolysis of Trichloroacetates of 4-(1-Hydroxyethyl)-[2.2]-paracyclophane. A. Without Added Potassium Acetate. A solution of 750 mg of trichloroacetate of III-α in 195 ml of methanol was refluxed for 11 hr, cooled, and shaken with a mixture of 100 ml of chloroform and 200 ml of water. The aqueous layer was separated and extracted with another portion of chloroform. The chloroform extracts were combined, washed with water, and dried. Evaporation of solvent left a yellow oil which was chromatographed over a short column of activated alumina. Elution with pentane produced 6 mg of material which was apparently olefinic (infrared analysis) but which was not further characterized; then ether–pentane (7.5:92.5) eluted 447 mg (89%) of a colorless oil which was shown by tlc [ether–pentane (10:90) solvent system] to be two components. Nmr analysis showed this mixture to be 56% ether of III-α (*vide infra*) and 44% ether of III-β

A similar run was made with 500 mg of trichloroacetate of III-β in 130 ml of methanol. Similar work-up and chromatography produced 4 mg of the apparent olefin and 270 mg (81%) of a slightly yellow oil which nmr analysis showed to be 57% ether of III-α (*vide infra*) and 43% ether of III-β.

The above two product oils were combined and a *ca.* 650-mg portion of the mixture was chromatographed over 40 g of activated silica gel. Elution with ether–pentane 1:99 provided 338 mg of ether of III-α and elution with ether–pentane 7.5:92.5 provided 298 mg of ether of III-β, mp 64.5–65.5°.

The ether of III-α was a white solid which was crystallized from pentane–ether, mp 63.5–64.1°. The infrared spectrum showed bands at 8.9 and 9.15 μ (medium, antisymmetric C–O–C stretching).[21] The nmr spectrum was as follows: seven protons as a multiplet at τ 3.33–3.72 (aromatic), one proton as a quartet (J = 6.5 cps) at τ 5.73 (methine), three protons as a sharp singlet at τ 6.45 (methoxy), eight protons as a multiplet at τ 6.51–7.40 (bridge), and three protons as a doublet (J = 6.5 cps) at τ 8.79 (methyl). *Anal.* Calcd for $C_{19}H_{22}O$: C, 85.67; H, 8.33. Found: C, 85.49; H, 8.17.

B. With Added Potassium Acetate. To 125 ml of methanol were added 507 mg (1.28 mmoles) of trichloroacetate of III-α and 177 mg (1.80 mmoles) of freshly fused potassium acetate. The mixture was refluxed for 105 min, cooled, and worked up as described in part A above. Chromatography of the yellow oil, as described above, provided 4 mg of the presumed olefin and 300 mg (97%) of a colorless oil which was a mixture of the diastereomeric ethers by tlc. Nmr analysis showed this mixture to be 24% α ether and 76% β ether.

Similarly, 409 mg (1.03 mmoles) of trichloroacetate of III-β and 142 mg (1.45 mmoles) of freshly fused potassium acetate were refluxed in 100 ml of methanol for 105 min and worked up as above. Chromatography as described provided 1 mg of the presumed olefin and 252 mg (92%) of a slightly yellow oil which was a mixture of the diastereomeric ethers by tlc. Nmr analysis of this mixture showed it to be 30% α ether and 70% β ether.

Trichloroacetic Acid Catalyzed Epimerization of α- and β-4-(1-Methoxyethyl)-[2.2]paracyclophane. To 20 ml of methanol were added 61 mg (0.23 mmole) of α ether and 38 mg (0.23 mmole) of trichloroacetic acid. The solution was refluxed for 10 hr, cooled, and shaken with a mixture of 75 ml of 1:1 ether–pentane and 75 ml of water. The aqueous layer was separated and extracted with another portion of the ether–pentane. The organic layers were combined, washed with water, and dried. Removal of solvent left a yellow oil which was chromatographed on a short column of activated silica gel. Elution with ether–pentane (5:95) produced 55 mg of an oil which tlc showed to be a mixture of the diastereomeric ethers. Nmr analysis of this mixture showed it to be 60% α ether and 40% β ether.

A similar reaction with 125 mg (0.47 mmole) of β ether, 77 mg (0.47 mmole) of trichloroacetic acid, and 40 ml of methanol provided 118 mg of a yellow oil which, after chromatography, proved by nmr analysis to be 53% α ether and 47% β ether.

Kinetics of Hydrolysis of Trichloroacetates of 4-(1-Hydroxyethyl)-[2.2]paracyclophane. Solutions of trichloroacetates of III-α and of III-β were prepared in concentrations of 0.01006 *M* (0.01474 *M* for the β isomer at 50°) by weighing the appropriate amounts of material into volumetric flasks and diluting to the mark with 50:50 dioxane–water (by volume). Aliquots were then withdrawn with an automatic pipet and sealed into clean ampoules. The ampoules were placed in thermostated baths at the indicated temperature and removed at the designated times (from immersion to removal), swirled in ice water, and then stored at −20° until all tubes in a run could be titrated in sequence. The tubes were opened, diluted with 15 ml of water, and titrated to the phenolphthalein end point with 0.02564 *N* sodium hydroxide. End points tended to drift and infinity titrations were always low so that theoretical infinity values were used.

The data were analyzed by a least-squares program on the IBM 7094 computer, and standard deviations are listed with the calculated first-order rate constants. The rate constants for two runs were averaged, along with their standard deviations, and thermodynamic functions (see Table I) were calculated in the usual way. Limits on these functions were determined, using the rate-constant standard deviations, by the method of total differentials.[22] Table III contains a representative sample of the data obtained.

Hydrolysis of Trichloroacetates of 4-(1-Hydroxyethyl)-[2.2]-paracyclophane. A 1.00-g sample of trichloroacetate of III-α was dissolved in 250 ml of 9:1 dioxane–water (by volume) and placed in a constant temperature bath at 50° for 100 hr. The reaction mixture was then poured into 500 ml of water and extracted with four 150-ml portions of 3:1 ether–pentane. The combined extracts were washed three times with saturated aqueous sodium chloride and dried. Solvent was evaporated at reduced pressure to leave a yellow oil which was chromatographed over a short column of activated silica gel. Elution with pentane provided 70 mg (12%) of 4-vinyl[2.2]paracyclophane (*vide infra*), and ether–pentane (30:70) eluted 514 mg (81%) of a white solid, mp 72–89°, which infrared analysis and tlc [pentane–ether–methanol (65:30:5) solvent system, iodine detector] showed to be a mixture of alcohols III-α and III-β. Control experiments showed these alcohols to

(21) K. Nakanishi, "Infrared Absorption Spectroscopy," Holden-Day, Inc., San Francisco, Calif., 1962, p 36.

(22) L. L. Smail, "Analytical Geometry and Calculations," Appleton Century-Crofts, New York, N. Y., 1953, p 544.

Table III. Kinetics of Hydrolysis of Trichloroacetate of III-α at 24.82 ± 0.01°, Concentration 0.01006 *M*, Aliquot Size 4.90 ml, Theoretical Infinity 1.922 ml

Run a NaOH, ml	Time, min	Run b NaOH, ml
0.251	129.68	0.221
0.352	406.0	0.345
0.463	717.0	0.468
0.734	1376.0	0.746
0.980	2165.0	0.960
1.223	3029.0	1.248
1.426	4080.0	1.400
1.553	5088.0	1.572
1.782	7939.0	1.770
$k = 5.31 \pm 0.06 \times 10^{-6}$ sec^{-1}		$k = 5.22 \pm 0.08 \times 10^{-6}$ sec^{-1}
Av $k = 5.27 \pm 0.07 \times 10^{-6}$ sec^{-1}		

be stable to silica gel chromatography. Nmr analysis of this mixture showed it to be 50% III-α and 50% III-β.

A duplicate run also provided 12% of olefin V and 81% of a mixture of alcohols III-α and III-β (mp 72–89°), which nmr analysis showed to be 49% III-α and 51% III-β.

A 1.00-g sample of trichloroacetate of III-β in 250 ml of 9:1 dioxane–water was treated in a manner identical with that described above. The yellow residue was chromatographed over a short column of activated silica gel. Elution with pentane provided 42 mg (7%) of olefin (*vide infra*), followed by 59 mg of an oily mixture which was not identified; elution with ether–pentane (30:70) provided 477 mg (75%) of a mixture of alcohols III-α and III-β as a yellowish solid, mp 71–95°. Nmr analysis of this mixture showed it to be 50% III-α and 50% III-β.

An identical run provided 7% of the olefin, 55 mg of the unidentified mixture, and 76% of the alcohol mixture (mp 71–95°), which nmr analysis showed to be 50% III-α and 50% III-β.

The 4-vinyl[2.2]paracyclophane collected from the above runs was combined, rechromatographed, and crystallized from pentane to yield a white solid, mp 80–81°. The infrared spectrum showed a weak olefinic band at 6.15 μ. The nmr spectrum was as follows: ten protons (aromatic and vinyl) at τ 2.97–4.92 with the aromatic multiplet partially masking the vinyl absorption (similar to that of styrene),[23] and eight protons as a multiplet at τ 6.39–7.51 (bridge). *Anal.* Calcd for $C_{18}H_{18}$: C, 92.26; H, 7.74. Found: C, 92.10; H, 7.74.

Control Experiments for Hydrolysis of Trichloroacetates of 4-(1-Hydroxyethyl)-[2.2]paracyclophane. A solution of 254 mg (1.01 mmoles) of alcohol III-α and 164.5 mg (1.01 mmoles) of trichloroacetic acid in 100 ml of 9:1 dioxane–water (by volume) was held at 50° for 106 hr, then cooled, poured into 400 ml of water, and extracted four times with 175-ml portions of 3:1 ether–pentane. The combined organic layers were washed with 5% aqueous sodium bicarbonate and water and dried. Solvent was removed under reduced pressure. The residue was a solid, mp 102–104°, which tlc [pentane–ether–methanol (65:30:5) solvent system] showed to contain a trace of olefin and a trace of β alcohol III-β in addition to the predominant component, α alcohol III-α. This solid was chromatographed over a short column of activated silica gel, and ether–pentane (30:70) eluted the alcohol, 209 mg (82%). This was shown by nmr analysis to be greater than 99% alcohol III-α and less than 1% III-β. It was determined by the use of known solutions that 1% of either component in the other was the limit of detectability by the nmr technique. This involved scanning the carbinyl methyl doublets at 50-cycle sweep width at high spectrum amplitude to detect the 1% component.

A solution of 260 mg (1.03 mmoles) of alcohol III-β and 168 mg (1.03 mmoles) of trichloroacetic acid in 100 ml of 9:1 dioxane–water was treated as described for III-α above. The crude product, mp 108–111°, was shown by tlc to contain a trace of olefin and a small amount of alcohol III-α in addition to the major component, β alcohol III-β. Chromatography, as above, yielded 241 mg (93%) of the alcohol, shown by nmr analysis to contain about 1% alcohol III-α and 99% III-β.

A solution of 150 mg (0.64 mmole) of 4-vinyl[2.2]paracyclophane and 104 mg (0.64 mmole) of trichloroacetic acid in 20 ml of 9:1 dioxane–water was held at 50° for 66 hr and worked up similarly to the manner just described. Evaporation of solvent left 121 mg (81%) of a yellowish solid, mp 79–80°, which tlc [pentane and pentane–ether–methanol (65:30:5) solvent systems] showed to be unchanged olefin free of any alcoholic products.

1-(2,5-Dimethylphenyl)ethanol. A solution of 5.0 g of 2,5-dimethylacetophenone (Eastman White Label) in 20 ml of anhydrous ether was reduced with 1 g of lithium aluminum hydride in 40 ml of ether, and the product was isolated in the usual way. Removal of solvent left 4.89 g of a colorless oil which was distilled at 123° (pot) (0.1 mm) to yield the desired alcohol,[24] n^{25}D 1.5256. *Anal.* Calcd for $C_{10}H_{14}O$: C, 79.96; H, 9.39. Found: C, 80.20; H, 9.35.

The infrared spectrum of this material showed hydroxyl absorption at 2.8 and 2.9 μ. The nmr spectrum was as follows: one proton as a broad singlet at τ 2.73 (6-proton), two protons as an unsymmetrical doublet (J = 1.5 cps) at τ 3.09 (3- and 4-protons), one proton as a quartet (J = 6.5 cps) at τ 5.08 (methine), one proton as a broad singlet at τ 6.94 (hydroxyl), three protons as a singlet at τ 7.73 (2 methyl), three protons as a singlet at τ 7.82 (5-methyl), and three protons as a doublet (J = 6.5 cps) at τ 8.68 (carbinyl methyl).

4-Thioacetomorpholido[2.2]paracyclophane. To 35 ml of freshly distilled morpholine were added 15.0 g (0.06 mole) of 4-acetyl-[2.2]paracyclophane and 4 g (0.12 mole) of sulfur powder. The mixture was refluxed for 113 hr, during which time yellow crystals formed. The reaction mixture was cooled; the crystals were crushed, and the mixture was poured into 75 ml of absolute ethanol in a vessel which was allowed to stand in the cold, producing 16.3 g (78%) of yellow crystals, mp 205–235°. This material was shown by tlc (1:1 ethyl acetate–cyclohexane solvent system) to be predominantly the desired thioacetomorpholide plus minor amounts of other materials. Crystallization of this substance from ethanol–chloroform gave light tan crystals, mp 244–245° dec. The infrared spectrum showed strong bands for the —C(=S)N< function at 6.72, 6.96, 7.27, and 8.99 μ.[25] *Anal.* Calcd for $C_{22}H_{25}NOS$: C, 75.17; H, 7.17; S, 9.12. Found: C, 75.34; H, 6.98; S, 9.37.

4-Carboxymethylene[2.2]paracyclophane (V). A solution of 2.0 g (5.8 mmoles) of thiomorpholide in 50 ml of glacial acetic acid and 100 ml of concentrated hydrochloric acid was refluxed for 48 hr, during which time white crystals began to appear. The mixture was cooled and poured into 300 ml of water to precipitate a solid which was filtered, washed with water, then dissolved in chloroform, and dried. Evaporation of the chloroform left 1.4 g (93%) of acid V as yellowish crystals. Crystallization of this material from ether or ether–pentane gave white needles, mp 210–212° (lit.[7] mp 210–210.2°). The infrared spectrum showed a carbonyl band at 5.84 μ.

When this reaction was run with significantly larger amounts of material, the product was usually isolated as brownish flakes. Purification was effected by charcoal treatments in hot glacial acetic acid, followed by crystallization. This led to acid of mp 212–214°.

4-Acetonyl[2.2]paracyclophane (VI). A. Reaction of Methyllithium with Acid V. To a dried flask with nitrogen atmosphere were added 60 ml of anhydrous diethyl ether and 0.63 g (2.4 mmoles) of acid V to produce a suspension. Then 6 ml of a 1 *M* solution of methyllithium in ether was slowly added, immediately producing a yellow precipitate. The mixture was refluxed for 25 min and then stirred at 25° for 2.5 days under nitrogen. Dilute hydrochloric acid was added, dissolving the yellow precipitate, and the ether layer was washed with dilute potassium hydroxide (0.11 g of acid V was recovered from this wash) and four times with water and dried. Solvent was removed to leave 0.44 g of a yellow oil which was chromatographed over 44 g of activated silica gel. Elution with ether–pentane (10:90) produced 0.21 g (33%) of the desired ketone VI; elution with ether produced 0.14 g of a yellow waxy solid (*vide infra*).

Ketone VI was sublimed at 80° (0.15 mm) to provide a white solid, mp 97.8–98.8°. The infrared spectrum showed a carbonyl band at 5.86 μ. The nmr spectrum was as follows: six protons (aromatic) as a multiplet at τ 3.17–3.75 and one proton (*ortho*) as a singlet at τ 3.83, ten protons as a multiplet at τ 6.12–

(23) See, for example, J. R. Dryer, "Applications of Absorption Spectroscopy of Organic Compounds," Prentice-Hall, Inc., Englewood Cliffs, N. J., 1965, p 106.

(24) A. Klages and R. Keil, *Ber.*, **36**, 1639 (1903).

(25) K. Nakanishi, "Infrared Absorption Spectroscopy," Holden-Day, Inc., San Francisco, Calif., 1962, p 54.

7.42 (methylene) including the α-keto methylene protons as an apparent AB quartet centered at τ 6.55 and overlapping the bridge-methylene protons, and three protons as a singlet at τ 8.07 (methyl). *Anal.* Calcd for $C_{19}H_{20}O$: C, 86.32; H, 7.63. Found: C, 86.59; H, 7.60.

The yellow solid mentioned above was shown by tlc [ethyl acetate–cyclohexane (30:70)] to be primarily one component, contaminated with some apparently polymeric materials. That this main component was primarily tertiary alcohol was shown by the spectral data. The infrared spectrum showed hydroxyl absorption at 2.8 and 2.9 μ. The nmr spectrum was as follows: aromatic protons as a multiplet at τ 3.25–3.75 with the *ortho* proton as a singlet at τ 3.88, methylene protons as a multiplet at τ 6.32–7.82, hydroxyl proton as a broad singlet at τ 8.38, and methyl protons as a singlet at τ 8.92. This material was not investigated further.

B. Reaction of Acid Chloride or V with Dimethylcadmium. (This is a modification of the method of Cason.)[26] A Grignard reagent was prepared by bubbling gaseous methyl bromide through 500 ml of ether containing 5.39 g (0.22 g-atom) of magnesium turnings until the magnesium had all reacted. The reagent was then cooled to 0°, and 21.56 g (0.118 mole) of anhydrous cadmium chloride (dried overnight at 120°) was added as a solid. The mixture was refluxed for 30 min. Most of the ether was evaporated, and the remaining ether was evaporated in a stream of nitrogen, leaving a brownish sludge. Then 500 ml of dry benzene was added, and the mixture was stirred with a very strong mechanical stirrer.

Acid chloride of V was prepared by stirring 13.8 g (0.052 mole) of acid V overnight with 50 ml of thionyl chloride (taken from a fresh bottle and distilled immediately before use; old thionyl chloride leads to troublesome side reactions). The resulting yellow solution was evaporated at reduced pressure, and 50 ml of dry benzene was added. This solvent was evaporated at reduced pressure, and this procedure was repeated two additional times to remove the last traces of thionyl chloride. The product was a yellow solid which had a carbonyl band at 5.58 μ in the infrared; this solid was not further characterized but was used immediately.

The acid chloride was dissolved in a minimum amount of dry benzene and added rather rapidly at room temperature to the dimethylcadmium reagent with very efficient stirring. A tan sludge formed immediately. The reaction mixture was stirred for 1 hr at 25° (heating leads to side reactions), then cooled in an ice bath and very carefully hydrolyzed with 2 *N* sulfuric acid. The aqueous layer was separated and extracted with ether, which was added to the benzene layer. The resulting solution was washed with water, 5% sodium bicarbonate (this wash yielded 108 mg of acid V), water, and saturated aqueous sodium chloride, and dried; solvent was evaporated to leave 14.8 g of a yellowish solid which tlc (1:1 ethyl acetate–cyclohexane solvent system) indicated to be primarily ketone VI with a small amount of tertiary alcohol and some polymeric materials. The product was chromatographed over 1400 g of activated silica gel which had been slurry packed in ether–pentane (5:95). Elution with this solvent and with ether–pentane 10:90 produced nothing; elution with ether–pentane 15:85 provided 11.5 g (83%) of ketone VI, mp 98–99°. The chromatography was discontinued.

4-(2-Deuterio-2-hydroxypropyl)-[2.2]paracyclophane (IV). A solution of 44.4 g (0.168 mole) of ketone VI in 1300 ml of anhydrous ether was added dropwise to a slurry of 5.86 g (0.14 mole) of lithium aluminum deuteride in 400 ml of ether under nitrogen atmosphere. The mixture was stirred overnight and then hydrolyzed by careful addition of 250 ml of saturated aqueous magnesium sulfate. The aqueous layer was separated and extracted three times with 3:1 ether–pentane. The combined organic layers were washed three times with water and dried. Evaporation of solvent left 44.6 g of alcohol IV as a white solid (mixture of diastereomers), mp 75–88°. The infrared spectrum showed hydroxyl absorption at 2.8 and 2.9 μ. *Anal.* Calcd for $C_{19}H_{21}DO$:[27] C, 85.35; H and D, 8.66. Found: C, 85.56; H and D, 8.54. (See a later part in the Experimental Section for the properties of IV-α and IV-β.)

Acetate of 4-(2-Deuterio-2-hydroxypropyl)-[2.2]paracyclophane and Separation into Diastereomers. To a solution of 10.00 g (0.0377 mole) of alcohol IV in 40 ml of dry pyridine was added a solution of 7.5 ml (*ca.* 0.1 mole) of freshly distilled acetic anhydride in 10 ml of dry pyridine. The resulting solution was refluxed for 2 hr, cooled, and poured into 250 ml of 3:1 ether–pentane. This mixture was washed with 5% hydrochloric acid (three 200-ml portions), water, 5% sodium bicarbonate (two 50-ml portions), and water, and dried. Solvent was removed at reduced pressure to leave 11.4 g (98%) of acetate (mixture of diastereomers) as a white solid, mp 54–59°. *Anal.* Calcd for $C_{21}H_{23}DO_2$: C, 81.52; H and D, 8.58. Found: C, 81.56; H and D, 8.34.

Tlc [ether–pentane (25:75) solvent system] resolved this mixture into two closely spaced spots. The infrared spectrum showed a carbonyl band at 5.80 μ and ether stretching at 7.90 and 8.25 μ (shoulder). Nmr analysis (*vide infra*) showed the mixture to be 56–58% acetate of IV-α and 42–44% acetate IV-β.

A 5.00-g portion of the above mixture was chromatographed over 1100 g of activated silica gel which had been slurry packed in ether–pentane (10:90). Elution with 5.1 l. of this solvent produced only traces of material; the next 1.1 l. brought 2.31 g of pure acetate of IV-α; 0.3 l. brought 0.39 g of material which was a mixture of acetates of IV-α and IV-β; 0.2 l. brought 0.42 g of a mixture of the two acetates which was greatly enriched in β isomer; the next 2.2 l. brought 1.52 g of pure β-acetate.

Several other similar chromatographs were run until 11 g of pure α isomer had been collected; the material which was enriched in β isomer was crystallized from pentane–ether and added to the pure β isomer collected, giving 8.2 g.

The acetate of IV-α was crystallized from pentane–ether to give white flakes, mp 58.7–60.0°. The infrared spectrum showed a carbonyl band at 5.80 μ and ether stretching frequencies at 7.9 and 8.25 μ (shoulder). The nmr spectrum was as follows: seven protons (aromatic) as a multiplet at τ 3.24–4.00, including the *ortho* proton as a broadened singlet at τ 3.95, ten protons as a multiplet at τ 6.25–7.90 (methylene), three protons as a singlet at τ 8.04 (acetoxy methyl), and three protons as a singlet at τ 9.02 (carbinyl methyl).

The acetate of IV-β was crystallized from pentane–ether to give white flakes, mp 89.0–89.8°. The infrared spectrum was identical with that of the α isomer. The nmr spectrum of the β isomer was as follows: seven protons (aromatic) as a multiplet at τ 3.26–3.90, including the *ortho* proton as a broadened singlet at τ 3.85, ten protons as a multiplet at τ 6.53–7.45 (methylene), three protons as a singlet at τ 8.07 (acetoxy methyl), and three protons as a singlet at τ 8.94 (carbinyl methyl).

Diastereomers of 4-(2-Deuterio-2-hydroxypropyl)-[2.2]paracyclophane (IV-α and IV-β). A solution of 8.14 g (0.0263 mole) of α-acetate in 300 ml of ether was reduced in the usual way with 1.5 g of lithium aluminum hydride to give 6.98 g (94%) of IV-α. Crystallization from ether–pentane yielded white flakes, mp 120–121°. The infrared spectrum showed hydroxyl bands at 2.8 and 2.9 μ. The nmr spectrum was as follows: seven protons (aromatic) as a multiplet at τ 3.27–4.00, including the *ortho* proton as a broadened singlet at τ 3.92, ten protons as a multiplet at τ 6.36–7.88 (methylene), one proton as a broad singlet at τ 8.17 (hydroxyl), and three protons as a singlet at τ 8.96 (methyl).

Similar reduction of 5.90 g (0.0191 mole) of acetate of IV-β in 300 ml of ether with 1.1 g of lithium aluminum hydride produced, after work-up, 5.10 g (95%) of alcohol IV-β. Crystallization of this compound from ether–pentane yielded white flakes, mp 88.7–89.3°. The infrared spectrum showed hydroxyl bands at 2.8 and 2.9 μ. The nmr spectrum was as follows: seven protons (aromatic) as a multiplet at τ 3.23–3.97, including the *ortho* proton as a broadened singlet at τ 3.92, ten protons as a multiplet at τ 6.35–7.94 (methylene), one proton as a broad singlet at τ 8.28 (hydroxyl), and three protons as a singlet at τ 8.93 (methyl).

Tosylates of 4-(2-Deuterio-2-hydroxypropyl)-[2.2]paracyclophane (of IV-α and IV-β). A 5.50-g sample (0.020 mole) of alcohol IV-α was dissolved in 33 ml of dry pyridine, and the solution was cooled to 0°. Solid *p*-toluenesulfonyl chloride (4.20 g, 0.022 mole) was added, and the mixture was swirled until all the chloride had dissolved. The solution was kept at 0° for 24 hr, during which time large crystals of pyridine hydrochloride formed. The reaction mixture was poured into water and extracted three times with 3:1 ether–pentane. The combined extracts were washed with water, ice-cold 2 *N* sulfuric acid, 5% sodium bicarbonate, and water and dried. The solvent was concentrated to about 75 ml, diluted with an equal volume of pentane, again concentrated to about 75 ml, and allowed to stand at −18°. A clear oil separated; after several days this oil solidified to produce 6.71 g (78%) of white needles of tosylate of IV-α. This material was recrystallized from pentane–ether to give white needles which decomposed at 100–101°. The

(26) J. Cason, *J. Am. Chem. Soc.*, **68**, 2078 (1946).

(27) The lithium aluminum deuteride used in this reduction was 97–98% fully deuterated. No protio compound could be found in the product by nmr analysis, leading to the conclusion that the alcohols contained 97% or more of one atom of deuterium per molecule at the appropriate carbon atom.

infrared spectrum showed strong bands at 7.34 μ (antisymmetric SO_2)[25] and 8.49 μ (symmetric SO_2).[25] *Anal.* Calcd for $C_{26}H_{27}DO_3S$: C, 74.07; H and D, 6.93. Found: C, 74.29; H and D, 7.05.

By the procedure just described, 4.50 g (0.0164 mole) of alcohol IV-β in 27 ml of dry pyridine was allowed to react at 0° with 3.44 g (0.0180 mole) of *p*-toluenesulfonyl chloride. After similar work-up, the solvent was concentrated to about 50 ml, diluted with an equal volume of pentane, again concentrated to about 50 ml, and allowed to stand at −18°. A clear oil separated; this oil slowly crystallized to form 4.44 g (63%) of tosylate of IV-β as fine white needles. This material was recrystallized from pentane–ether to give white needles, mp 95.8–96.5° (dec *ca.* 120°). The infrared spectrum of this material was identical with that of tosylate of IV-α above. *Anal.* Calcd for $C_{26}H_{27}DO_3S$: C, 74.07; H and D, 6.93. Found: C, 73.94; H and D, 6.98.

Kinetics of Acetolysis of Tosylates of 4-(2-Deuterio-2-hydroxypropyl)-[2.2]paracyclophane (of IV-α and IV-β). Solutions of tosylates of IV-α and IV-β were prepared (0.010 *M*) by weighing the appropriate amounts of material into volumetric flasks and diluting to the mark with dry glacial acetic acid. Aliquots of 5 ml each were withdrawn with automatic pipets and sealed into clean ampoules. The ampoules were then placed in thermostated baths at the indicated temperatures, removed at the designated times, swirled in ice water for 1 min, and then stored at −20° until all tubes in a run could be titrated. The tubes were then opened and titrated to the light yellow end point of brom phenol blue (ten drops, saturated in glacial acetic acid)[28] indicator with 0.0113 *M* sodium acetate in dry glacial acetic acid (prepared by weighing 0.2987 g of dry, pure sodium carbonate into a 500-ml volumetric flask and diluting to the mark with dry glacial acetic acid).

The data were analyzed by a least-squares program on the IBM 7094 computer, and standard deviations are listed with the calculated first-order rate constants. The rate constants for two runs were averaged, along with their standard deviations, and thermodynamic functions (see Table I) were calculated in the usual way.

Table IV. Acetolysis of Tosylate of IV-α at 74.97 ± 0.06°

Series 1 NaOAc, ml	Time, min	Series 2 NaOAc, ml
0.240[a]	6.05	0.240[a]
0.480	12.24	0.480
0.700	18.20	0.700
0.935	25.05	0.950
1.180	32.09	1.180
1.360	38.02	1.340
1.575	45.26	1.565
1.800	54.14	1.805
1.990	63.02	2.010
2.260	75.07	2.270
3.155	135.02	3.150
4.190	(1182)	4.200
$k = 1.73 \pm 0.01 \times 10^{-4}$ sec^{-1}		$k = 1.72 \pm 0.01 \times 10^{-4}$ sec^{-1}
Av $k = 1.72 \pm 0.01 \times 10^{-4}$ sec^{-1}		

[a] Not used in calculation of k.

Limits on these functions were determined, using the rate-constant standard devivations, by the method of total differentials.[22] Table IV records data from a typical run.

Acetolysis of Tosylates of 4-(2-Deuterio-2-hydroxypropyl)-[2.2]-paracyclophane (of IV-α and IV-β). A solution of 1.00 g (2.38 mmoles) of α-tosylate in 100 ml of dry glacial acetic acid was thermostated at 75° for 18 hr. The solution was cooled and shaken with a mixture of 200 ml of water and 100 ml of 1:1 ether–pentane. The aqueous layer was separated and extracted again with ether–pentane. The organic layers were combined, washed with two 100-ml portions of water, and dried. Solvent was evaporated at reduced pressure to leave an oil which was chromatographed over a short column of activated silica gel. Elution of the column with ether–pentane (0.5:99.5) produced 20 mg (3.4%) of a white solid which appeared by melting point (71–75°) and infrared to be a mixture of olefins but was not further characterized; elution with ether–pentane (5:95) produced 674 mg (91.9%) of a mixture of acetates of IV-α and IV-β as an oil which gradually became a white solid. Nmr analysis of this mixture showed it to be 97.4% acetate of IV-α and 2.6% acetate of IV-β. This material was crystallized from pentane–ether to yield acetate of IV-α, mp 57–58.5°. Mixture melting point with an authentic sample gave mp 58–59.5°.

A solution of 1.00 g (2.38 mmoles) of the β-tosylate in 100 ml of dry glacial acetic acid was treated exactly as described above. Chromatography as described yielded 28 mg (4.7%) of the olefin mixture previously mentioned, followed by 663 mg (90.5%) of a mixture of acetates as a white solid. Nmr analysis showed this mixture to be 7.2% α-acetate and 92.8% β-acetate. This material was crystallized from pentane–ether to yield acetate of IV-β, mp 88–89°. Mixture melting point with authentic material gave mp 88–90°.

Control Experiments for Acetolysis Reactions of Tosylates of 4-(2-Deuterio-2-hydroxypropyl)-[2.2]paracyclophane. To 10 ml of dry glacial acetic acid were added 125 mg (0.405 mmole) of α-acetate and 70 mg (0.405 mmole) of anhydrous *p*-toluenesulfonic acid. The solution was kept at 75° for 18 hr and worked up as described for the acetolysis reactions (*vide supra*). Removal of solvent at reduced pressure left 130 mg of a clear, slightly yellow oil in which tlc [ether–pentane (20:80) solvent system] detected only α-acetate. Nmr analysis of this material showed it to be greater than 99% α-acetate and less than 1% β-acetate.

An analogous treatment was carried out with 125 mg of β-acetate. The product was 133 mg of a yellowish solid in which tlc detected only β-acetate. Nmr analysis of this material showed 1% or less of α-acetate and 99% or more of β-acetate.

Formolysis of Tosylates of 4-(2-Deuterio-2-hydroxypropyl)-[2.2]paracyclophane (of IV-α and IV-β). A 0.025 *M* solution of sodium formate in formic acid was prepared by adding 132 mg (1.25 mmoles) of dry, pure sodium carbonate to 100 ml of dry formic acid. Then 1.00 g (2.38 mmoles) of α-tosylate was added, and the mixture was thermostated at 75°. The tosylate dissolved in about 30 min. After 7 hr, the reaction mixture was cooled and shaken with a mixture of 200 ml of water and 100 ml of 3:1 ether–pentane. The aqueous layer was separated and extracted with another portion of 3:1 ether–pentane. The organic layers were combined, washed with two 100-ml portions of water, and dried. The solution was filtered, and 1 g of lithium aluminum hydride was added in small portions. The mixture was stirred overnight and then carefully hydrolyzed with saturated aqueous magnesium sulfate. The ether layer was decanted, and the aqueous layer was extracted with another portion of ether. The ether layers were combined, washed twice with water, and dried. Solvent was evaporated to leave the alcohol as a white solid. This material was dissolved in 5 ml of dry pyridine; 1 ml of freshly distilled acetic anhydride was added, and the solution was refluxed for 3 hr. The reaction mixture was worked up as described for the acetylation of alcohol IV (*vide supra*). The residue was chromatographed over a short column of activated silica gel. Elution with ether–pentane (3:97) afforded 557 mg (76.0%) of acetate as a clear oil which slowly became a white solid. Tlc [ether–pentane (20:80)] detected only acetate of IV-α in this material. Nmr analysis of this acetate showed it to be greater than 99% α-acetate and less than 1% β-acetate. Crystallization from pentane–ether yielded α-acetate as a white solid, mp 57–59°. Mixture melting point with authentic α-acetate gave mp 57–59°.

Tosylate of IV-β was treated in a manner exactly analogous to that described for the α-tosylate. After reduction of the formate to the alcohol and acetylation, the product was chromatographed over a short column of activated silica gel. Elution of the column with ether–pentane (3:97) provided 567 mg (78.3%) of acetate in which tlc detected only β-acetate. Nmr analysis showed this material to be less than 1% α-acetate and greater than 99% β-acetate. This substance was crystallized from pentane–ether to yield a white solid, mp 89–90°. Mixture melting point with authentic β-acetate gave mp 88.5–90°.

Nmr Analysis. All nmr spectral analyses were carried out on a Varian Associates Model A-60 analytical spectrophotometer. Solutions were approximately 2 *M* in deuteriochloroform as solvent (unless otherwise indicated) with tetramethylsilane as internal standard. Peak areas were measured by integration, allowing the total integral to be equal to the theoretical proton content in the molecule. In the spectra of alcohols, the nmr solutions were shaken with deuterium oxide to exchange the hydroxyl protons.

A. Analysis of Products of Hydrolysis and Methanolysis of Trichloroacetates (of III-α, and III-β). The relative amounts of alcohols III-α and III-β or of their ethers in a given mixture were de-

(28) S. Winstein, E. Grunwald, and L. L. Ingraham, *J. Am. Chem. Soc.*, 70, 821 (1948).

termined by integration of their carbinyl methyl doublets. In a given derivative these doublets were completely separated. The integration of each doublet was made ten times and averaged; the amount of each component was then calculated as a percentage of the total. In the case of alcohols III-α and III-β, the nmr solutions were shaken with deuterium oxide to exchange the hydroxyl protons so that the signals from these protons would not interfere with the comparison of the carbinyl methyl signals.

B. Analysis of Products of Acetolysis and Formolysis of Tosylates of IV-α and IV-β. The carbinyl methyl signals in the nmr spectra of the acetate products of the acetolysis reactions and of the derived acetates from the formolysis reactions were used as the indicator in determining the relative amounts of each component (when the percentage of one acetate in a mixture of the two was low, *i.e.*, 10% or less, the acetoxy methyl signals were of no value in this determination). Base line was not reached between the carbinyl methyl signals so that relative integration was impossible. This necessitated the use of the method[29] which is described below.

Four solutions ranging from 1.0% α-acetate and 99.0% β-acetate to 10.0% α-acetate and 90.0% β-acetate and four solutions ranging from 90.0% α-acetate and 10.0% β-acetate to 99.0% α-acetate and 1.0% β-acetate were prepared. The carbinyl methyl signals in a given solution were then scanned ten times at 50-cycle sweep width, and the height of each of the two peaks was measured for each scan. Then the contribution of the lesser component to the total peak height of the two components was calculated (in per cent). This percentage was then plotted as a function of the known percentage of the lesser component in the mixture. The curve thus obtained was used to determine the relative amount of each acetate in the product from a solvolysis reaction. The results are estimated to be accurate to within ±0.5%. This method was useful in determining the presence of as little as 1% of one acetate in a mixture of the two.

(29) The authors are indebted to Professor F. A. L. Anet for suggesting this technique.

Electrophilic Substitution at Saturated Carbon. XXXIII. The Stereochemical Fate of the α-Sulfonylcarbanion in Which Both Anion and Sulfone Groups Are Incorporated in Five-Membered Ring Systems[1]

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Abstract: The stereochemical fate of the α-sulfonylcarbanion in which both anion and sulfone groups are incorporated in five-membered ring systems has been examined. The base-catalyzed decarboxylations of (−)-2-methyl-2,3-dihydrobenzothiophene-2-carboxylic acid 1-dioxide ((−)-I) to give 2-methyl-2,3-dihydrobenzothiophene 1-dioxide (II) and of (+)-2-methyltetrahydrothiophene-2-carboxylic acid 1-dioxide ((+)-III) to give 2-methyltetrahydrothiophene 1-dioxide (IV) were carried out. Optically pure (+)-II was prepared by fractional crystallization of material obtained by decarboxylation of (−)-I (in water buffered with ammonium acetate). Similarly, optically pure (−)-II-*d* was prepared from (+)-I (in buffered deuterium oxide). That optical purity of II was reached was demonstrated by an isotopic dilution–reresolution experiment. Optically pure (+)-IV was prepared by decarboxylation of one of the four optically pure stereoisomers of 5-methyltetrahydrothiophene-2-carboxylic acid 1-dioxide (V). Values of k_e/k_α (one-point rate constant for isotopic exchange over that for racemization) for base-catalyzed reaction of optically active II in various media were determined. Results were as follows: (+)-II-*d* in 91% dimethyl sulfoxide–9% methanol–potassium methoxide at 25° gave k_e/k_α = 0.64; (−)-II-*d* in 70% *t*-butyl alcohol–30% tetrahydrofuran–potassium *t*-butoxide at 25° gave k_e/k_α = 0.66; (−)-II-*d* in methanol–potassium methoxide at 76° gave k_e/k_α = 0.64; (+)-II-*h* in methanol-O-*d*–potassium methoxide at 76° gave k_e/k_α = 0.65. These isotopic exchange reactions occurred with considerable net inversion of configuration. In the run made in *t*-butyl alcohol–tetrahydrofuran, the partially racemized product was reresolved, and the deuterium content of each enantiomer determined. The kinetic isotope effect for racemization of optically active II under the same conditions was shown to be k^H/k^D = 1.3. From these data, the relative rates of three stereochemical processes were extracted: inversion without exchange, 1; net inversion with exchange, 3; racemization with exchange, 9. A conducted tour mechanism for the two inversion processes is formulated. In this mechanism, both carbanion and potassium ion (and ligand) rotations within contact ion pairs are envisioned as occurring without complete breaking of $C^-\cdots HOR$ hydrogen bonds. The stereochemical direction of decarboxylation of salts of (−)-I was studied. The product varied from (−)-II of 3% optical purity in *t*-butyl alcohol to (±)-II in dimethyl sulfoxide to (+)-II of 65% optical purity in water. An assignment of stereochemical course to these reactions is suggested based on the similarity between the pattern of results obtained in this and other systems. Decarboxylations of (+)-III gave IV with stereospecificities and solvent dependence similar to that observed with its benzo analog. In both the decarboxylations and isotopic exchange reactions, the results point to symmetrical (planar) α-sulfonylcarbanions in asymmetric environments as discrete reaction intermediates.

Unlike open-chain α-sulfonylcarbanions whose generation and proton capture proceeded with high retention of configuration,[3] the anion generated in the base-catalyzed decarboxylation of optically active cyclic

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(2) National Science Foundation Predoctoral Fellow, 1962–1966.

(3) (a) D. J. Cram, W. D. Nielsen, and B. Rickborn, *J. Am. Chem*