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.

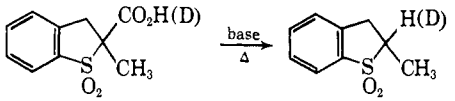
Unlike open-chain α-sulfonylcarbanions whose generation and proton capture proceeded with high retention of configuration,[3] the anion generated in the base-catalyzed decarboxylation of optically active cyclic

(1) This investigation was supported in part by Public Health Service Research Grant No. GM 12640-02 from the Department of Health, Education, and Welfare.

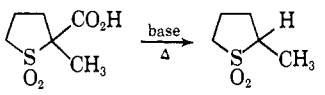
(2) National Science Foundation Predoctoral Fellow, 1962–1966.

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

sulfone I was reported by Corey, *et al.*,[3e] to give "completely racemic sulfone" II. The authors concluded that the lack of stereospecificity of the reaction provided evidence for a planar cyclic α-sulfonylcarbanion as an intermediate in the reaction. In a large number of systems, we had previously shown that in most media planar carbanions were asymmetrically solvated and gave rise to optically active products.[4] Thus, the results of Corey, *et al.*, appeared anomalous and worthy of further scrutiny, particularly since neither the optically active starting materials nor optically active products were demonstrated to be optically stable under the conditions of the reactions.[5] Accordingly, we have reexamined the stereochemical course of the decarboxylation of I under a variety of conditions. Likewise, the decarboxylation of III to give IV has also been studied. However, the most important results of this paper concern the stereochemical course of the base-catalyzed hydrogen–deuterium exchange reaction between I and hydroxylic solvents.



I II

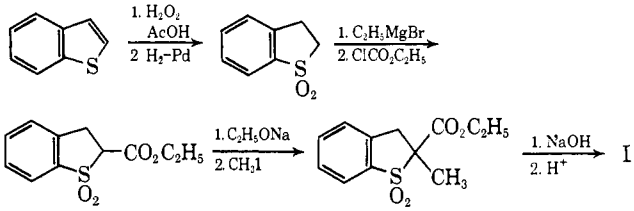


III IV

Results

Syntheses. Sulfone acid I was prepared by the sequence formulated. The substance was initially resolved through its brucine salt and brought to maximum rotation by recrystallization of the acid. Both enantiomers were obtained, (−)-I, $[\alpha]^{29}_{546}$ −83.9° (*c* 3, 95% ethanol), mp 169–171°, and (+)-I, $[\alpha]^{28}_{546}$ +80.5° (*c* 3, 95% ethanol), mp 168–170.5°, in reasonable overall yields.

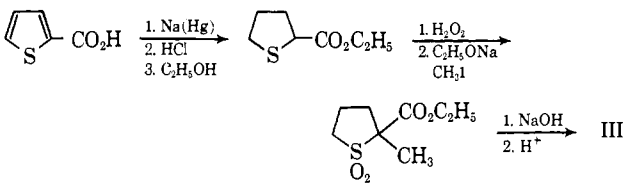
Optically pure (−)-I was converted to its ammonium salt, which was submitted to decarboxylation at 155° in water containing enough acetic acid to provide a well-buffered solution at the end of the reaction. The (+)-II



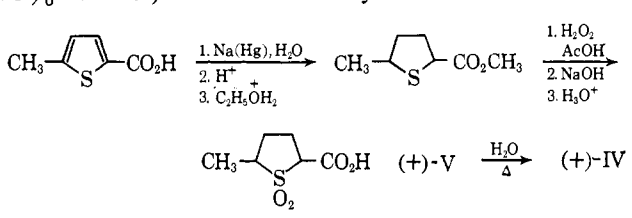
produced (54% optically pure) was crystallized to maximum rotation, $[\alpha]^{25}_{546}$ +24.1° (*c* 4, chloroform), mp 74–75°. Similarly, the ammonium salt N-d_4 of(+)-I was prepared and decarboxylated in deuterium oxide–deuterated acetic acid to give (−)-II-*d* (46% optically pure), which was recrystallized to maximum rotation, $[\alpha]^{25}_{546}$ −24.1° (*c* 4, chloroform), mp 73–74°, 98% of one atom of deuterium per molecule.[6a]

Since the validity of the conclusions of this paper depend on establishment of the rotation of optically pure II, an isotope dilution experiment was conducted.[7] A mixture of racemic II-*d* and active II-*h* was recrystallized until racemate and active II were separated, and each was analyzed for deuterium.[6b] From the rotations, the deuterium analyses, and the amounts of materials used, the maximum rotation of (±)-II was calculated to be $[\alpha]^{25}_{546}$ ±24.04 ± 0.4° (*c* 4, chloroform).

The synthesis of compound III is formulated. The substance was resolved through its brucine salt and brought to maximum rotation by repeated recrystallization of the acid itself, $[\alpha]^{25}_{546}$ +20.4° (*c* 4.7, water), mp 161.5–162.5°. The enantiomer was separated from racemate by fractional crystallization and brought to maximum rotation, $[\alpha]^{28}_{546}$ −20.2° (*c* 4.7, water), mp 159–160°.



In order to establish the maximum rotation of optically active IV, one of the diastereomers of V was prepared (see reaction sequence). This material was resolved to maximum rotation through its brucine salt, followed by crystallization of the acid itself to maximum rotation, $[\alpha]^{26}_{546}$ +35.1° (*c* 4.9, chloroform), mp 78.5–80°. This material was subjected to base-catalyzed decarboxylation in buffered aqueous solution to give optically pure (+)-IV, $[\alpha]^{25}_{546}$ +11.80° (*c* 3.5, 95% ethanol). This decarboxylation was carried out



Soc., 82, 6415 (1960); (b) E. J. Corey and E. T. Kaiser, *ibid.*, 83, 490 (1961); (c) D. J. Cram, D. A. Scott, and W. D. Nielsen, *ibid.*, 83, 3696 (1961); (d) D. J. Cram and A. S. Wingrove, *ibid.*, 84, 1496 (1962); 85, 1100 (1963); (e) E. J. Corey, H. König, and T. H. Lowry, *Tetrahedron Letters*, 515 (1962); (f) E. J. Corey and T. H. Lowry, *ibid.*, 793, 803 (1965).

(4) For a summary, see D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press Inc., New York, N. Y., 1965, pp 85–113 and 137–170.

(5) The following information regarding experimental details of the results reported in ref 3e has been provided by Professor E. J. Corey (private communication). Decarboxylation of optically active I was carried out by heating a homogeneous mixture of I and its pyridinium salt (initial ratio *ca.* 10:1) at 180–185° under vacuum (0.5 mm) so that the sulfone II was distilled from the reaction zone; the specific rotation of II in two runs was zero within experimental error (±0.5°) (work of H. König). In work subsequent to that reported in ref 3e (see T. H. Lowry, Ph.D. Thesis, Harvard University, 1964), the decarboxylation of I admixed with 0.09 equiv of potassium carbonate at 185° and under vacuum was carried out. "The product showed a small rotation ([α]D +3.9° from acid [α]D −77.8°) which could possibly have been due to an impurity but which could not be removed by various purification procedures" (quote from Lowry's thesis, p 43).

In our hands (D. J. C. and T. A. W.), repetition of the König experiment also gave racemic material. However, when the pure pyridinium salt of I was substituted for the 10:1 mixture of I and its pyridinium salt and the experiment repeated, (+)-II of rotation $[\alpha]^{25}_{546}$ +4.1° (*c* 4.6, $CHCl_3$) was produced [starting I was $[\alpha]^{25}_{546}$ −83.9° (*c* 3, C_2H_5OH)]. In our opinion, under the König conditions, most of the pyridine left the reaction zone, and the acid itself (not the salt) was the main species that underwent decarboxylation.

(6) (a) Combustion and falling drop method. (b) Mass spectral method.

(7) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 84.

Table I. Results of Exchange and Racemization of Optically Active 2-Methyl-2,3-dihydrobenzothiophene 1-Dioxide (II)

Run no.	Starting material Type	Concn, M	Solvent	Base Type	Concn, M	Temp, °C	Time, hr	% rac	% exch	k_e/k_α
1	II-*d*[a]	0.33	$(CH_3)_2SO$[b]	CH_3OK	0.16	25.0	72.0	42.0	31.0	0.64[c]
2	II-*d*[a]	0.33	$(CH_3)_3COH$[d]	$(CH_3)_3COK$	0.028	25.0	1.08	56.8	42.7	0.66[c]
3	II-*d*[a]	0.164	CH_3OH	CH_3OK	0.16	76.2	11.5	64.6	48.7	0.64[c]
4	II-*h*[e]	0.164	CH_3OD[f]	CH_3OK	0.16	76.2	9.75	84.5	70.0	0.65
5	II-*d*[a]	0.059	$HOCH_2CH_2OH$	$HOCH_2CH_2OK$	0.059	76.2	143	43.7	34.5	0.73[c]
6	II-*h*[e]	0.10	$DOCH_2CH_2OD$[g]	$DOCH_2CH_2OK$	0.10	76.2	76.0	78.2	65.5	0.70

[a] 97.7% of one atom of deuterium per molecule, $[\alpha]^{25}_{546}$ −24.1° (*c* 3.98, chloroform). [b] Solvent system: $(CH_3)_2SO$–CH_3OH, 93:7 by weight, 2.3 *M* in CH_3OH. [c] Corrected to 100% initial deuterium for substrate. [d] Solvent system: $(CH_3)_3COH$–tetrahydrofuran, 70:30 by volume. [e] $[\alpha]^{25}_{546}$ +24.1° (*c* 4.05, chloroform). [f] 99% of one atom of deuterium per molecule, combustion and falling drop. [g] 1.98 atoms of deuterium per molecule, combustion and falling drop.

under conditions that both starting material and product once formed retained their optical purities.

Base-Catalyzed Hydrogen Isotopic Exchange and Racemization of Sulfone II. Optically pure (+)-II-*h* and (−)-II-*d* were subjected to base-catalyzed hydrogen–deuterium exchange and racemization experiments, and the results are summarized in Table I. One-point, pseudo-first-order rate constants for isotope exchange of II with the medium (k_e) and for racemization of II (k_α) were calculated, and the ratios of k_e/k_α are listed. No base loss was observed in representative runs where the medium was titrated after reaction.

A deeper probe of mechanism was made of the exchange racemization of (−)-II-*d* in *t*-butyl alcohol–potassium *t*-butoxide. Thus, a 1.215-g portion of optically pure (−)-II-*d* was subjected to the same conditions as run 2 until 60% racemization had occurred. The substance was isolated and fractionally crystallized from ether into 99 ± 1% racemic II which contained 0.395 atom of deuterium per molecule,[6b] and optically pure (−)-II which contained 0.700 atom of deuterium per molecule. From these data, the isotopic composition of the (+)-II in the racemate is calculated to be 0.09 atom of deuterium per molecule. This calculation involves the assumption that the (−)-II fraction of the racemate has the same deuterium content as recovered pure (−)-II. The validity of this assumption was demonstrated by the fact that the same rotation for optically pure II was obtained from the isotopic dilution experiment as from crystallization of II to maximum rotation.[8] Furthermore, deuterium in excess of theory was not observed in either recovered racemate or antipode. Over-all racemization was 60% complete. Therefore, under the conditions of run 2, deuterium–hydrogen exchange of (−)-II-*d* in *t*-butyl alcohol proceeded with 2.7% isoinversion (inversion without exchange), 27.3% inversion with exchange, and 21% retention with exchange, while 49% of the starting material did not change. Combination of exchange with inversion and exchange with retention gives exchange with racemization, which amounts to 42 and 6.3% net exchange with inversion. The values for the stereospecific portions of the reaction are minimal since the products of initial exchange underwent further reaction.

The rate constants for racemization of (+)-II-*h* and (−)-II-*d* were carefully measured (13 points taken over the first 75% of the reaction) at 25° under the conditions of run 2, and were as follows: $k_\alpha^H = 2.90 \pm 0.003 \times 10^{-4}$ sec^{-1}; $k_\alpha^D = 2.24 \pm 0.016 \times 10^{-4}$ sec^{-1}; $(k^H/k^D)_\alpha = 1.29 \pm 0.02$. Application of the kinetic equations reported previously[9] to the above data provided the following approximate rate constants ($\times 10^{-4}$ sec^{-1}) at time zero: isoinversion, 0.138; net inversion with exchange, 0.42; racemization with exchange, 1.20.

Steric Course of the Decarboxylation Reactions. Decarboxylation experiments on optically pure (−)-I were carried out in a variety of solvents in the presence of a sufficient amount of base to produce catalysis, but not enough to racemize the product once formed. Table II reports the conditions of each run and the results. In all runs except 8 and 9, either less than 1 equiv of base (ammonium salt of (−)-I or potassium carbonate) was used, or the reaction medium itself was acidic (acetic acid, phenol, or buffered solutions). The decarboxylation media in runs employing less than 1 equiv of base were terminated before all free (−)-I had been consumed. The fact that II was produced with the same rotation in runs 8 and 9, even though the reaction times differed by a factor of 4, points to the optical stability of II once formed under the reaction conditions. Addition of optically active (+)-II to a decarboxylation run identical with run 15 gave results that demonstrated active II to be optically stable to the conditions of run 15. Examination of the rotation of recovered (−)-I from runs 15 and 19 demonstrated this acid to be optically stable under conditions of its decarboxylation. In the absence of base (−)-I was found not to decarboxylate in *t*-butyl alcohol or dimethyl sulfoxide at the temperatures of runs 15 and 19, respectively.

Decarboxylation experiments were also carried out on optically pure (+)-2-methyltetrahydrothiophene-2-carboxylic acid 1-dioxide ((+)-III) in water and *t*-butyl alcohol at 165°. Table III records the results. The ammonium or potassium salts of (+)-III served as the basic catalyst, and the reactions were terminated while free (+)-III was still present. A control run established that (+)-IV was optically stable under the conditions of run 24. Examination of the optical purity of recovered ammonium salt of (+)-III from run 23 established that (+)-III is optically stable under these conditions. Appropriate experiments established the

(8) That deuterium- or hydrogen-labeled compound could be enriched by fractional crystallization of ±II and (−)-II would require that the crystal lattices of either racemate or enantiomer distinguish between deuterated and protonated material. Such discrimination is highly unlikely in view of the frequent inability of lattices to distinguish between much grosser structural features (*e.g.*, a methyl or a bromine).

(9) W. T. Ford, E. W. Graham, and D. J. Cram, *J. Am. Chem. Soc.*, 89, 689, 690 (1967).

Table II. Results of Base-Catalyzed Decarboxylation of (−)-2-Methyl-2,3-dihydrobenzothiophene-2-carboxylic Acid 1-Dioxide[a] ((−)-I)

Run no.	Solvent	Base: Nature	Base: Concn, N	Subst concn, N	Time, hr	Temp, °C	% react.	$[\alpha]^{25}_{546}$ of product,[b] deg	Net steric course,[c] %
7	None	NH_4O_2CR[d]	...	...	0.28	185	79[e]	+5.03	21, inv
8	$HOCH_2CH_2OH$	NH_4O_2CR[d]	0.178	0.178	0.50	165	77[f]	+10.06	41, inv
9	$HOCH_2CH_2OH$	NH_4O_2CR[d]	0.178	0.178	2.0	165	93[f]	+10.07	41, inv
10	H_2O	NH_4O_2CR[d]	0.0275	0.133	16.0	164	57[f]	+14.08	58, inv
11	H_2O	KAPH[g]	0.05	0.067	36.0	164	98[f]	+14.10	58, inv
12	H_2O	KAPH[g,h]	0.05	0.067	36.0	164	92[f]	+13.10	54, inv
13	H_2O	NH_4OAc	0.266	0.133	48.0	155	95[f]	+14.10	58, inv
14	H_2O	KAPH[g]	0.05	0.067	815	103	16[f]	+15.60	64, inv
15	$(CH_3)_3COH$	NH_4O_2CR[d]	0.0133	0.123	14.0	164	35[e]	−0.75	3.1, ret
16	CH_3CO_2H	KO_2CR[i]	0.397	0.133	43.5	200	94[f]	+4.73	20, inv
17	CH_3CO_2H	KO_2CR[i]	0.512	0.133	120	164	92[f]	+5.22	22, inv
18	C_6H_5OH	NH_4O_2CR[d]	0.133	0.133	24.0	200	86[f]	+4.67	19, inv
19	$(CH_3)_2SO$	NH_4O_2CR[d]	0.0133	0.150	1.25	142	55[f]	0.0	100, rac
20	D_2O	ND_4O_2CR[j,k]	5.41	5.41	48.0	155	98[f]	−11.0	45.5, inv
21	H_2O	NH_4O_2CR[d,l]	5.48	5.48	48.0	155	95[f]	+13.23	54.5, inv

[a] $[\alpha]^{25}_{546}$ −83.9° (*c* 3, 95% ethanol). [b] *c* 4, chloroform. [c] Based on +24.2° for (+)-II. [d] Ammonium salt of (−)-I. [e] Based on weight of recovered starting material. [f] Based on product isolated. [g] Potassium acid phthalate. [h] 5.37 *M* in potassium chloride. [i] Potassium salt of (−)-I. [j] Ammonium salt N-d_4 of (+)-I. [k] 6.18 *M* in acetic acid-O-*d*. [l] 5.65 *M* in acetic acid.

Table III. Base-Catalyzed Decarboxylation of (+)-2-Methyltetrahydrothiophene-2-carboxylic Acid 1-Dioxide[a] ((+)-III) at 165 ± 0.2°

Run no.	Solvent	Base: Nature	Base: Concn, N	Starting material concn, N	Time, hr	% react.[b]	$[\alpha]^{25}_{546}$ of product,[c] deg	Net steric course,[d] %
22	H_2O	KO_2CR[e]	0.064	0.192	238	54	+5.31	45, inv
23	H_2O	NH_4O_2CR[e]	0.064	0.192	236	45	+5.60	48, inv
24	$(CH_3)_3COH$	KO_2CR[e]	0.064	0.192	8	68	0.0	100, rac
25	$(CH_3)_3COH$	NH_4O_2CR[e]	0.064	0.192	14	61	+0.35	3, inv

[a] $[\alpha]^{25}_{546}$ +20.4° (*c* 4.71, water). [b] Based on weight of recovered starting material. [c] *c* 10, 95% ethanol. [d] Based on a maximum rotation of $[\alpha]^{25}_{546}$ +11.80° (*c* 4, 95% ethanol) for (+)-2-methyltetrahydrothiophene 1-dioxide. [e] Salts of (+)-III.

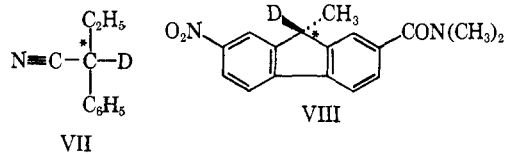
stability of (+)-III in the absence of base under the conditions of the decarboxylations.

Discussion

The following topics are discussed in turn: (1) the configuration of the cyclic α-sulfonylcarbanion; (2) the inversion mechanisms both with and without isotopic exchange (the conducted tour mechanism); and (3) the stereochemical courses for the decarboxylation reaction.

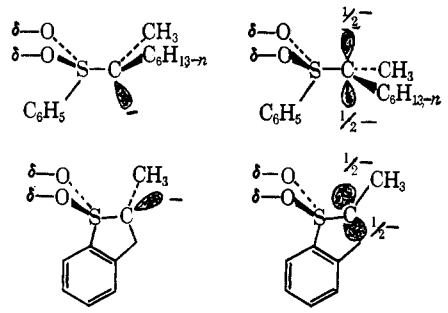
Configuration of the Cyclic α-Sulfonylcarbanion. The over-all stereochemical course of base-catalyzed hydrogen–deuterium exchange reactions can be determined by the values of k_e/k_α: values greater than 1 point to net retention; values equal to 1 indicate racemization; values between 0.5 and 1 indicate net inversion, either with or without isotopic exchange; and values of less than 0.5 point to a net isoinversion mechanism (net inversion without isotopic exchange). In a variety of solvents, optically active 2-phenylsulfonyl-2-octane (VI) underwent base-catalyzed isotopic exchange with values of k_e/k_α that ranged between 10 and ~2000, depending mainly on medium.[3a,c] This result was contrasted with those obtained in systems which generated the 2-phenyl-2-butyl or the 1-methoxy-1-phenylethyl anions, in which nondissociating solvents gave $k_e/k_\alpha > 1$, dimethyl sulfoxide gave $k_e/k_\alpha = 1$, and protic dissociating solvents (such as diethylene glycol) gave $k_e/k_\alpha < 1$.[10] Since the latter systems in which phenyl served as the anion-stabilizing substituent were thought to generate planar or near-planar carbanions, the affinity of the open-chain sulfone system for a retention mechanism in all media was taken as evidence of an asymmetric carbanion. The asymmetry of the anion was attributed to either an electrostatically induced pyramidal anion whose inversion rate was less than that of proton capture, or to a planar carbanion in an asymmetric conformation whose formation and consumption for electrostatic reasons involved predominantly one particular face.[3a,c]

In the anion derived by proton abstraction from cyclic sulfone II, the ring system enforces a conformation which destroys the electrostatic driving force for generation of a pyramidal anion; the ring system also imposes symmetry on the anion if it is planar. Thus, it was anticipated that the pattern of k_e/k_α values obtained in cyclic system II would differ from those in VI, as indeed is observed. In all three types of solvents, k_e/k_α values are 0.64–0.73 (Table I). Thus, system II differs in behavior not only from its open-chain analog (VI), but also from the 2-phenyl-2-butyl anion, which gave $k_e/k_\alpha > 1$ in *t*-butyl alcohol–potassium *t*-butoxide. Indeed, the behavior of II is more similar to systems VII and VIII, which in *t*-butyl alcohol–tripropylamine



VII VIII

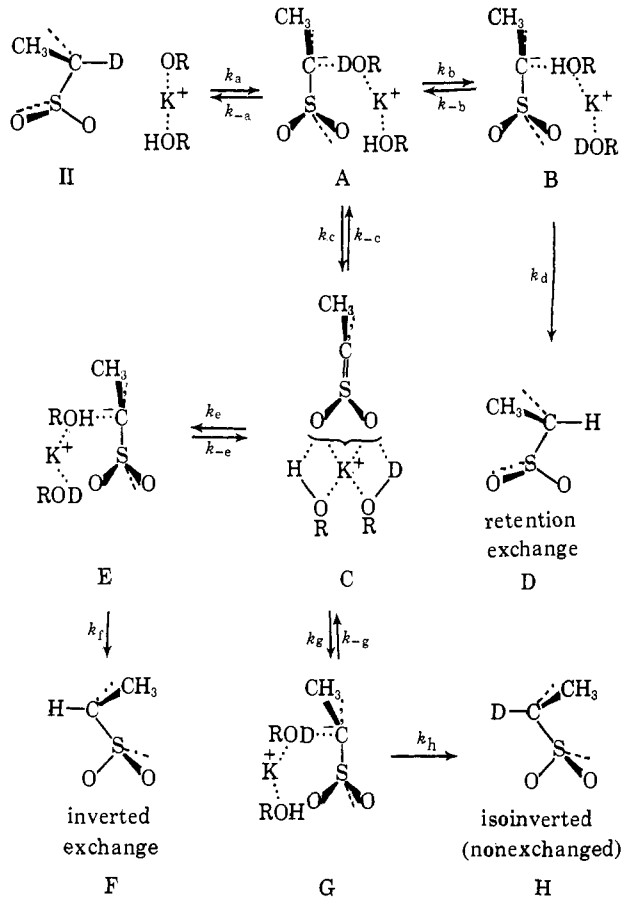
(10) D. J. Cram, C. A. Kingsbury, and B. Rickborn, *J. Am. Chem. Soc.*, 83, 3688 (1961).



produced values of $k_e/k_\alpha < 1$.[11] The anions derived from VII and VIII are clearly close to planar, and on the basis of these comparisons, it seems very probable that the cyclic sulfonyl anion derived from II is also planar.[12]

Isoinversion and the Conducted Tour Mechanism for Intramolecular Proton Transfer. In *t*-butyl alcohol–potassium *t*-butoxide, (−)-II-*d* gave $k_e/k_\alpha = 0.66$, or exchange with net inversion (run 2). However, separate deuterium analysis of the (−)-II and (+)-II produced in the experiment revealed that this ratio reflected a blend of processes, whose relative rates were as follows: inversion without exchange (isoinversion), 1; net inversion with exchange, 3; racemization, 9. The simplest mechanism which provides an explanation of these facts is formulated in Chart I. In this scheme,

Chart I



potassium butoxide ion pair with its ligands of *t*-butyl alcohol detaches deuterium from substrate to form a potassium carbanide ion pair (A) in which the carbanion is hydrogen bonded to the deuterated *t*-butyl alcohol molecule formed by deuterium abstraction, the oxygen of which serves as a ligand to the potassium ion. Rotation of the potassium ion with its ligands provides B, collapse of which leads to exchanged product of retained configuration. Intermediate A can undergo a second reorganization reaction to produce C, in which the oxygens of the sulfone group serve as hydrogen-bonding sites and ligand centers for the potassium ion. Intermediate C can go to A, E, or G. In E, potassium ion with its deuterated and nondeuterated ligands has passed to the back face of the carbanion, and the nondeuterated ligand has become hydrogen bonded to the carbanion. Collapse of E leads to F, the inverted exchanged product. In G, the carbanion is hydrogen bonded at its back face with deuterated ligand. Collapse of G to the covalent state gives isoinverted product, H.

In a sense, the deuterium originally hydrogen bonded at the front face of the carbanion has gone on a *conducted tour* of hydrogen-bonding sites out around the two oxygens of the sulfone group and back to carbon on the opposite face. In the transition states for each stage of A → C → G, a hydrogen bond is made and broken, and the contact ion pair is preserved. Equal amounts of exchange with retention and exchange with inversion blend to give racemization with exchange, and this blend is not differentiatable from stereochemically indiscriminant processes (*e.g.*, those involving ion-pair dissociation). However, the presence of an isoinversion process points also to the inversion and retention with exchange components as distinct stereospecific reactions. Indeed, the data require that exchange with inversion exceeds exchange with retention by a substantial amount. The results of this investigation of the stereochemical capabilities of the anion of II demonstrate the first unequivocable example of the rate of exchange with inversion exceeding the rate of exchange with retention. Clearly, an exchange with retention component must also be present.

The scheme of Chart I provides an explanation for the differences in behavior of sulfone II and 2-phenylbutane (k_e/k_α = 5 to 10 in *t*-butyl alcohol–potassium *t*-butoxide).[10] Although both derived anions are planar, the 2-phenyl-2-butyl anion does not possess the essentially spherical array of hydrogen-bonding sites offered by the sulfone group for conducting protons from the front to the back face of the carbanion.

The net inversion observed in the other media (runs 1 and 3–6 of Table I) also probably reflects blends of isoinversion, inversion, and retention. However, a detailed discussion must await data on the distribution of deuterium between the enantiomeric components of partially racemized product.

The Kinetic Isotope Effect for Racemization of II. The kinetic isotope effect for racemization of optically active II in *t*-butyl alcohol–potassium *t*-butoxide was $(k^H/k^D)_\alpha = 1.29 \pm 0.02$ at 25°. This low isotope effect contrasts with the much higher kinetic isotope effects observed for hydrogen–deuterium exchange of toluene in cyclohexylamine–lithium cyclohexylamide,[13] (k^H/k^D) ~ 10, and of 2-N,N-dimethylcarboxamido-9-methyl-

(11) D. J. Cram and L. Gosser, *J. Am. Chem. Soc.*, 86, 2950, 5457 (1964).

(12) This same conclusion was drawn earlier by Corey, *et al.* (ref 3e), on the basis of equivocal experiments (see introductory section and ref 3).

(13) H. Streitwieser, W. C. Langworthy, and D. E. Van Sickle, *J. Am. Chem. Soc.*, 84, 251 (1962).

fluorene[9] in methanol–potassium methoxide, $(k^H/k^D)_\alpha = 6$. Particularly interesting is the fact that both the latter example[9] and the one of the current paper exhibited an isoinversion component, but rather different isotope effects. The low isotope effect for II in *t*-butyl alcohol–potassium *t*-butoxide points to k_{-a} (Chart I) being higher valued than k_b or k_c or any ion-pair dissociative process.[3c,10,14] Thus, the highest energy transition state for racemization does not involve covalent bond breaking but only a reorganization of hydrogen bonds. If the reaction described by k_{-a} is faster than such reorganization reactions, then the other covalent bond-making processes described by k_d, k_f, and k_h (Chart I) also must be faster. Thus, at the beginning of the reactions when products have not accumulated, the reverse reorganization processes described by k_{-b}, k_{-c}, k_{-e}, and k_{-g} must occur to very little extent.

The Stereochemistry of the Decarboxylation Reactions. The relative configurations of I and II have not been related by any means other than the decarboxylation reaction. Thus, an unequivocal assignment of relative configurations of I and II and of the stereochemical courses for the decarboxylations is not possible. However, several analogies exist which suggest tentative assignments for both. The stereochemical fates of carbanions generated with carbon or hydrogen as leaving groups have been similar to one another. Such has been the case for the 2-phenylsulfonyl-2-octyl,[3] the 2-phenyl-2-butyl, and the 1-methoxy-1-phenyl-1-ethyl carbanions.[15] The first of these anions is thought to be asymmetric and the last two symmetric. Furthermore, the patterns of dependence of the stereochemical results on medium are somewhat similar for the decarboxylations of I and the base-catalyzed cleavages leading to 2-phenylbutane or 1-methoxy-1-phenylethane. Thus, in dimethyl sulfoxide, the decarboxylation goes with total lack of stereospecificity (run 19 of Table II), in ethylene glycol with considerable stereospecificity in one direction (runs 8 and 9), but in *t*-butyl alcohol with low stereospecificity in the other direction (run 15). Cleavages of alcohols to give 2-phenylbutane and 1-methoxy-1-phenylethane go with total racemization in dimethyl sulfoxide, inversion in ethylene glycol, and retention in *t*-butyl alcohol.[16] Likely, the decarboxylations of II to give I follow a similar stereochemical course. Thus, dissociating protic solvents such as water and ethylene glycol give inversion, dissociating nonprotic solvents such as dimethyl sulfoxide produce racemization, and nondissociating solvents such as *t*-butyl alcohol lead to retention. The mechanisms underlying these stereochemical courses have been discussed previously, and need not be detailed here. It is striking that the solvent that provided the highest stereospecificity was water, and that lower temperatures produced the highest values (compare runs 12 and 14 of Table II). Also, water produced a substantially higher stereospecificity than deuterium oxide (compare runs 20 and 21). The same conclusions drawn for the decarboxylation of I to II probably apply equally well for III to IV.

Experimental Section

All melting points were determined by the use of capillary tubes and are uncorrected. All temperatures are in degrees centigrade. Rotations were taken with a Zeiss circular polarimeter (tetrahydrothiophene system) or a Perkin-Elmer Model 141 polarimeter (dihydrobenzothiophene systems). The observed rotations were generally ±0.02° with the Zeiss instrument and ±0.005° with the Perkin-Elmer instrument. Infrared spectra were taken with a Beckman IR-5 spectrophotometer. Nuclear magnetic resonance spectra were taken with a Varian Associates A-60 spectrometer in deuteriochloroform with 2% tetramethylsilane as internal standard unless otherwise specified.

2-Carbethoxy-2,3-dihydrobenzothiophene 1-Dioxide. From 30.0 g of benzothiophene was prepared 24.1 g of benzothiophene 1-dioxide,[17a] mp 141.5–142.5° (lit.[17] mp 142–143°). This sulfone (15 g) was reduced to give 15 g of 2,3-dihydrobenzothiophene 1-dioxide,[17b] mp 90–91° (lit.[17b] mp 88–89°). A Grignard reagent was prepared from 11.2 g of magnesium, 55 g of ethyl bromide, and 480 ml of ether. To the rapidly stirred reagent was added dropwise a solution of 50 g of the sulfone in 350 ml of benzene. A white salt precipitated. When addition was complete, the reaction mixture was refluxed with stirring for 2 hr, and added in small portions to 260 g of freshly distilled ethyl chloroformate cooled in an ice bath and very rapidly stirred. The reaction mixture was refluxed for 18 hr and then filtered. The filter cake was extracted twice with 700-ml portions of chloroform. The extracts were combined with the filtrate and evaporated at reduced pressure, yielding 77 g of a viscous, brown oil. The crude product was not purified, but was used directly in the next step.

2-Methyl-2,3-dihydrobenzothiophene-2-carboxylic Acid 1-Dioxide (I). A sodium ethoxide solution was prepared from 70 g of sodium and 1400 ml of absolute ethyl alcohol. To the basic solution was slowly added a solution of 217 g of crude 2-carbethoxy-2,3-dihydrobenzothiophene 1-dioxide in 950 ml of absolute ethyl alcohol with rapid stirring while the temperature of the reaction mixture was maintained at 70°. The reaction mixture was stirred for 2 hr at 70°, then cooled to 20°; 560 g of methyl iodide was added dropwise, and the reaction mixture was reheated to 60° and stirred for 48 hr. Evaporation of ethanol under reduced pressure yielded a viscous, brown oil which was hydrolyzed in a hot solution of 60 g of sodium hydroxide in 1400 ml of water. Acidification of the hydrolysis reaction mixture with 100 ml of 96% sulfuric acid with ice bath cooling precipitated crude I as a yellow solid. This material was recrystallized from chloroform–methanol, weight 79.8 g (24.8% from 2,3-dihydrobenzothiophene 1-dioxide as colorless needles), mp 181–183°. This material exhibited strong infrared absorptions at 1750 cm^{-1}, characteristic of carboxylic acids, and at 1320 and 1160 cm^{-1}, characteristic of the sulfone group.[18] The nmr spectrum in DMSO-d_6 (tetramethylsilane as standard) showed the following absorptions: aromatic protons (multiplet, 4.0 protons), τ 2.0–2.6; benzyl protons (AB quartet, J_{AB} = 17 cps, ν = 27, 1.97 protons), centered at τ 6.45; methyl protons (singlet, 2.86 protons), τ 8.38. *Anal.* Calcd for $C_{10}H_{10}SO_4$: C, 53.09; H, 4.45; S, 14.17. Found: C, 53.27; H, 4.28; S, 14.44.

(−)-2-Methyl-2,3-dihydrobenzothiophene-2-carboxylic Acid 1-Dioxide ((−)-I). A solution of 169.7 g of I and 295.8 g of brucine in 1793 ml of refluxing 50:50 acetone–water was prepared. The flask containing the salt solution was sealed tightly and allowed to cool slowly to 25° in a large water bath, and the salt (137.7 g) separated as large plates. Recrystallization of the salt from 975 ml of the same solvent yielded 124.3 g (26.6%). A small portion of the salt was converted to the free acid which, after one crystallization from ether, exhibited $[\alpha]^{29}_{546}$ −83.9° (*c* 2.9 ethanol). Additional crystallizations of the salt provided no change in rotation of the derived acid after one crystallization from ether. The optically pure salt (132.3 g) was dissolved in 5000 ml of boiling water, and a solution of 66 g of potassium carbonate in 100 ml of water was added with rapid stirring. The solution was cooled to 0° for 1 hr to complete precipitation of brucine. The slurry was filtered, and the filtrate was reduced in volume to 400 ml under re-

(14) D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press Inc., New York, N. Y., 1965, p 28.
(15) D. J. Cram, K. R. Kopecky, F. Hauck, and A. Langemann, *J. Am. Chem. Soc.*, 81, 5754 (1959), and ref 14, p 137.
(16) D. J. Cram, J. L. Mateos, F. Hauck, A. Langemann, K. R. Kopecky, W. D. Nielsen, and J. Allinger, *ibid.*, 81, 5774 (1959).
(17) (a) F. G. Bordwell, B. B. Lampert, and W. H. McKellin, *ibid.*, 71, 1704 (1949); (b) F. G. Bordwell and W. H. McKellin, *ibid.*, 72, 1986 (1950).
(18) K. Nakanishi, "Infrared Absorption Spectroscopy," Holden-Day, Inc., San Francisco, Calif., 1962, p 54.

duced pressure and filtered. Sulfuric acid, 130 ml, was added slowly to the concentrated filtrate with stirring and cooling, and crude (−)-I separated as an oil which was recovered by extraction with four 400-ml portions of chloroform. The combined extracts were dried and evaporated to dryness, yielding a white solid which was recrystallized from ether (26.8 g, 15.8% as large, colorless crystals), $[\alpha]^{29}_{546}$ −83.9° (*c* 2.9, ethanol), mp 169–171°; lit.[3c] $[\alpha]^{26}_{546}$ +59.0° (not given, ethanol), mp 161–162°; lit.[5] $[\alpha]^{27}_{546}$ −77.8° (*c* 1.8, 95% ethanol), mp 168–170.5°. *Anal.* Calcd for $C_{10}H_{10}SO_4$: C, 53.09; H, 4.45; S, 14.17. Found: C, 53.14; H, 4.50; S, 14.50.

(+)-2-Methyl-2,3-dihydrobenzothiophene-2-carboxylic Acid 1-Dioxide ((+)-I). To the mother liquor from the first crystallization of the brucine salt of I was added a solution of 60 g of potassium carbonate in 1000 ml of water with rapid stirring at 0°. The slurry was filtered, reduced in volume to 450 ml under reduced pressure, and filtered. Chloroform, 700 ml, was added to the basic solution; the solution was cooled in an ice bath and stirred rapidly, and 100 ml of 96% sulfuric acid was added slowly. The layers were separated, and the aqueous phase was extracted with three 430-ml portions of chloroform. The combined chloroform extract was dried and allowed to stand for 18 hr at 25°, whereupon 20.1 g of racemic I separated, mp 182–183°, $[\alpha]^{26}_{546}$ 0.0° (*c* 3.3, ethanol). The chloroform solution was evaporated to dryness under reduced pressure to give 57.0 g of crude (+)-I. This material was refluxed with 1000 ml of ether for 4 hr, and the solution was filtered, reduced in volume to 300 ml, cooled, and filtered again, thereby removing an additional 6.4 g of racemic I. Controlled evaporation of the filtrate yielded 28.1 g of crystalline (+)-I, mp 168–170.5°, $[\alpha]^{28}_{546}$ +80.5° (*c* 2.9, ethanol).

Ammonium Salt of (−)-2-Methyl-2,3-dihydrobenzothiophene-2-carboxylic Acid 1-Dioxide. A 4.0-g portion of optically pure (−)-I was dissolved in 150 ml of ether. Anhydrous ammonia gas was bubbled into the solution for 40 min, and the salt that separated as a white solid (4.2 g, 95%), was dried 4 hr under vacuum, $[\alpha]_{546}$ −61.0° (*c* 2.9, water).

Representative Decarboxylation of (−)-2-Methyl-2,3-dihydrobenzothiophene-2-carboxylic Acid 1-Dioxide ((−)-I) (Run 11). Optically pure (−)-I, $[\alpha]^{25}_{546}$ −83.9° (*c* 3.3, 95% ethanol), 0.300 g, was dissolved in 20 ml of 0.05 *M* potassium biphthalate buffer solution (pH 4.0) contained in a glass ampoule which had been previously purged with nitrogen. The ampoule was sealed and placed in a constant-temperature bath at 164° for 36 hr. The ampoule was opened; 30 ml of benzene was added, and the contents were thoroughly shaken before being transferred to a separatory funnel. The ampoule was rinsed twice with 10-ml portions of benzene which were added to the funnel. The layers were separated, and the aqueous phase was extracted once more with 20 ml of benzene. The combined organic phase was washed with a 30-ml portion of 3% aqueous sodium carbonate solution. The benzene solution of the product was filtered, evaporated to 20 ml on a hot plate, and finally evaporated to dryness on a rotary evaporator. The product, (+)-II (0.235 g, 98%), was chromatographed on a 1 × 30 cm column of silica gel with ether–pentane 40:60 as eluent, weight 0.221 g, $[\alpha]_{546}$ +14.10° (*c* 3.87, chloroform).

General Experimental Procedure for Base-Catalyzed Decarboxylation of (−)-2-Methyl-2,3-dihydrobenzothiophene-2-carboxylic Acid 1-Dioxide ((−)-I). The crude product from run 7 (100% ammonium salt of (−)-I, no solvent) was extracted with 20 ml of hot benzene, and the benzene extract was filtered. The filtrate was evaporated to dryness under vacuum, and the rotation of the product, (+)-II, was determined in chloroform after purification by chromatography on silica gel. Runs 8 and 9 were conducted as follows. Into each of two 1 × 20 cm test tubes was weighed 0.303 g of optically pure ammonium salt of (−)-I, and 7 ml of ethylene glycol was added. In run 8 the tube, open to the atmosphere, was heated in a constant-temperature bath at 165° for 0.5 hr; in run 9 the time of heating was 2.0 hr. The isolation procedure in both runs was the same. The decarboxylation reaction mixture was poured into 25 ml of ice water and extracted with two 25-ml portions of benzene. The combined extracts were washed with two 25-ml portions of water and evaporated to dryness under vacuum. The product was then chromatographed as in run 7.

Run 10 was conducted identically with that of run 11, except that 25 mole % ammonium salt of (−)-I was used as base, and isolation involved addition of ammonium carbonate to convert excess undecarboxylated acid to its ammonium salt (see below). The product, weight 0.165 g (57%), displayed $[\alpha]^{26}_{546}$ +14.08° (*c* 3.2, chloroform).

Run 12 was conducted identically with that of run 11, except that 8.0 g of potassium chloride was added to the decarboxylation reaction mixture before heating.

Run 13 employed 0.300 g of optically pure (−)-I and 0.205 g of ammonium acetate as base in 10 ml of water. Isolation was identical with run 11.

Run 14 was conducted identically with that of run 11, except that the reaction mixture was thermostated at 103°.

Run 15 employed 0.2767 g of (−)-I and 0.0324 g of the ammonium salt of (−)-I (both optically pure) as base (10 mole % base) in 10 ml of *t*-butyl alcohol. After heating, the solvent was removed under reduced pressure, 7 ml of water was added to the residue, and pH of the solution was found to be 3. Sufficient aqueous 10% ammonium carbonate solution was added to make the pH of the solution 8–9, and the product was recovered by benzene extraction and was purified as in run 11. To the aqueous phase was added 1 ml of 96% sulfuric acid and undecarboxylated (−)-I precipitated. The acid was recovered by two extractions with 40 ml of chloroform; the extracts were dried and evaporated, yielding 0.178 g of crude, recovered (−)-I, $[\alpha]^{25}_{546}$ −80.5° (*c* 3.34, 95% ethanol).

Run 16 was conducted as follows. A 0.300-g portion of optically pure (−)-I and 0.390 g of potassium acetate were placed in an ampoule. A 10-ml aliquot of glacial acetic acid was added to the ampoule with the aid of a syringe; the ampoule was purged with nitrogen, sealed, and placed in a constant-temperature bath at 200° for 43.5 hr. After this time, the tube was cooled, and the contents were removed. Evaporation of acetic acid left a viscous oil to which was added 7 ml of water and 7 ml of aqueous 20% potassium carbonate solution. The product was recovered and purified as in run 11, weight 0.223 g (94%), $[\alpha]^{25}_{546}$ +4.73° (*c* 3.9, chloroform).

Run 17 was conducted identically with that of run 16, except that 0.500 g of potassium acetate was used as base.

In run 18, a 300-mg portion of optically pure ammonium salt of (−)-I was placed in an ampoule, 10 ml of warm phenol was added, and the ampoule was purged with nitrogen and sealed. After standing in a constant-temperature bath at 200° for 24 hr, the ampoule was opened, and the contents were poured into 25 ml of water. A 30-ml portion of aqueous 15% sodium hydroxide solution, along with 50 ml of benzene, was added to the water. After thorough shaking, the layers were separated, and the aqueous phase was extracted with an additional 40-ml portion of benzene. The combined benzene extracts were washed with a 30-ml aliquot of aqueous 15% sodium hydroxide solution and twice with 30-ml volumes of water. Isolation and purification of the product were the same as in run 11.

In run 19, a 0.337-g portion of (−)-I and 0.0324 g of the ammonium salt of (−)-I (both optically pure) (8 mole % base) were placed in an ampoule, and 10 ml of dimethyl sulfoxide was added. The ampoule was purged with nitrogen, sealed, and placed in a constant-temperature bath at 142° for 75 min. The tube was opened and the contents removed. Evaporation of the solvent under reduced pressure left a semisolid to which was added 7 ml of water. The pH of the mixture was 2–3. Potassium carbonate solution was added to the acidic mixture until the pH became 8–9 and the product was recovered and purified as in run 11, weight 0.150 g (55%), $[\alpha]^{25}_{546}$ 0.0° (*c* 3.76, chloroform). Undecarboxylated (−)-I recovered from the aqueous phase displayed $[\alpha]^{25}_{546}$ −80.7° (*c* 3.5, 95% ethanol), weight 0.144 g. The optical stability of the product, 2-methyl-2,3-dihydrobenzothiophene 1-dioxide (II), was not tested under the conditions of run 19. Such a control run was made for run 15 (*t*-butyl alcohol as solvent) since the possibility existed that a very small equilibrium concentration of *t*-butoxide anion was formed which rapidly racemized the product. In dimethyl sulfoxide, however, in the presence of excess acid throughout the time of reaction (55% decarboxylation with 8 mole % base), the existence of a strongly basic species seemed remote.

Run 20 was conducted similarly to the experiment described below for the preparation of (−)-II-*d*. Run 21 was conducted similarly to the experiment described below for the preparation of (+)-II-*h*.

In general, if recovery of undecarboxylated (−)-I was desired, the aqueous solution of its ammonium or potassium salt was acidified with excess sulfuric acid after isolation of the product, (+)-II. Recovery of the acid was effected by two or three extractions of the acidic aqueous solution with an equal volume of chloroform per extraction. Evaporation of chloroform after drying yielded crystalline (−)-I. Determination of the optical purity of recovered acid was always done without any purification of the substance because of its marked tendency to fractionate. Thus, the possibility

of error in determining the true optical impurity of recovered (−)-I was reduced.

Two additional decarboxylation experiments (not reported in Table II) were conducted in the absence of solvent. In the first, 250 mg of pyridine salt of optically pure (−)-I was heated at 180° for 44 min to produce 120 mg of II (isolated by above procedures), $[\alpha]^{25}_{546}$ +4.1° (*c* 4.6, chloroform). In a second experiment, 30.5 mg of the same pyridine salt was mixed with 226 mg of optically pure (−)-I, and the melt was heated for 2 hr (~0.5 mm). A white substance sublimed out of the melt. Both starting material [105 mg, $[\alpha]^{25}_{546}$ −78.5° (*c* 2.9, 95% ethanol)] and II (18 mg) were isolated by the above procedures, $[\alpha]^{25}_{546}$ 0.00° (*c* 4.6, chloroform).

Stability of (−)-2-Methyl-2,3-dihydrobenzothiophene-2-carboxylic Acid 1-Dioxide in the Absence of Base. A solution of 0.300 g of (−)-I, $[\alpha]^{25}_{546}$ −83.9° (*c* 3.3, 95% ethanol), in 10 ml of *t*-butyl alcohol was heated for 24 hr at 164°, and the product was put through the same isolation procedure as in run 15. The benzene extracts contained no II. The aqueous phase was acidified with sulfuric acid and extracted with two 30-ml portions of chloroform. The chloroform layer was washed with water, dried, and evaporated under reduced pressure. The recovered acid, 0.277 g (92%), displayed $[\alpha]^{25}_{546}$ −81.5° (*c* 3.4, 95% ethanol). Similar results were obtained in water (48 hr at 164°) and dimethyl sulfoxide (1.3 hr at 142°).

Optical Stability of (+)-2-Methyl-2,3-dihydrobenzothiophene 1-Dioxide ((+)-II) under Conditions of Its Formation (Control for Run 15). A 0.200-g portion of (+)-II, $[\alpha]^{25}_{546}$ +14.0° (*c* 3.9, chloroform), 0.267 g of optically pure (−)-I, and 0.0324 g of ammonium salt of (−)-I, $[\alpha]^{25}_{546}$ −61.0° (*c* 2.9, water) were placed in an ampoule with 10 ml of *t*-butyl alcohol, and the ampoule was sealed under nitrogen. The ampoule was thermostated at 164° for 7 hr, cooled, and opened, and the decarboxylation reaction mixture was worked up identically with that of run 15. The product, (+)-II, 0.238 g, displayed $[\alpha]^{25}_{546}$ +11.2°. Acidification of the aqueous phase followed by extraction with chloroform provided 0.220 g of (−)-I, $[\alpha]^{25}_{546}$ −80.6° (*c* 3.6, 95% ethanol). A calculaton was made of the specific rotation that the product should have had in this experiment if the decarboxylation reaction were zero order in ammonium salt until 90% reaction and if the product of the decarboxylation reaction were optically inactive. In run 15, 35% reaction occurred in 14 hr; therefore, 17% reaction should occur in 7 hr, yielding 0.042 g of product. The total amount of sulfone present should thus have been 0.242 g, $[\alpha]^{25}_{546}$ 0.827 × +14.0° or +11.6°, and 0.241 g of acid should have remained undecarboxylated.

Preparation of (+)-2-Methyl-2,3-dihydrobenzothiophene 1-Dioxide ((+)-II). A solution of 32.3 g of the ammonium salt of (−)-I, $[\alpha]^{25}_{546}$ −61.0° (*c* 3.1, water), was dissolved in 242 ml of distilled water. To this solution was added 8.5 g of glacial acetic acid. The mixture was transferred into a number of 140-ml capacity, heavy-walled glass ampoules, previously purged with nitrogen, in 37.5-ml portions, and the ampoules were sealed. Each was heated to 155° for 48 hr. The ampoules were cooled and opened, and 70 ml of benzene was added to each. After thorough shaking, the layers were separated, and the combined aqueous phase was extracted with an additional 350 ml of benzene. The benzene solution of the product was washed with 150 ml of 10% aqueous sodium carbonate solution and 200 ml of water, dried, and evaporated, yielding 22.85 g of (+)-II, $[\alpha]^{25}_{546}$ +13.23° (*c* 4.0, chloroform) (94.2% as a light yellow solid). The sulfone, 22.8 g, prepared above was fractionally crystallized beginning with 1450 ml of boiling ether as follows: crop 1, 6.15 g, $[\alpha]^{25}_{546}$ +2.3° (*c* 4.1, chloroform); crop 2, 1.1 g (from 1080 ml of ether), +3.18°; crop 3, 2.40 g (from 880 ml of ether), +3.68°; crop 4, 1.65 g (from 525 ml of ether), +6.94°; crop 5, 0.76 g (from 400 ml of ether), +8.68°; crop 6, 0.58 g (from 235 ml of ether), +11.68°; crop 7, 3.47 g (from 130 ml of ether), +23.75°; crop 8, 2.58 g (from 80 ml of ether), +23.93°; crop 9, 1.44 g (from 55 ml of ether), +23.80°; crop 10, 1.12 g (from 30 ml of ether), +24.00°; crop 11, 0.78 g (from 15 ml of ether), +24.20°; crop 12, 0.28 g (from 9 ml of ether), +24.10°; crop 13, 0.28 g (from 3 ml of ether), +24.08°. All rotations were taken in chloroform at 546 mμ in a 1-dm polarimeter tube with *c* 4.0 ± 0.15. The average rotation of the last six fractions was +24.02°. The melting point of racemic 2-methyl-2,3-dihydrobenzothiophene 1-dioxide was 115.5–116.5°, while that of material displaying $[\alpha]^{25}_{546}$ +24.1° was 74–75°. Material with rotation between 0 and +24.1° did not melt sharply. Mixtures of racemic and active II gave material which melted below either single component. *Anal.* Calcd for $C_9H_{10}SO_2$: C, 59.34; H, 5.49; S, 17.60. Found: C, 59.52; H, 5.44; S, 17.75.

Isotopic Exchange of (+)-2-Methyl-2,3-dihydrobenzothiophene-2-carboxylic Acid 1-Dioxide. The acid, 46.7 g, $[\alpha]^{25}_{546}$ +82.0° (*c* 3.3, ethanol), was added to a mixture of 110 g of deuterium oxide (99.77 atom % deuterium) and 100 ml of tetrahydrofuran (freshly distilled from calcium hydride). The mixture was refluxed for 24 hr and cooled, and the tetrahydrofuran was removed under reduced pressure. The exchanged acid was recovered by three extractions of the deuterium oxide with 200-ml portions of chloroform. Evaporation of the chloroform yielded 46.5 g of the deuterated acid.

Ammonium Salt N-d_4 of (+)-2-Methyl-2,3-dihydrobenzothiophene-2-carboxylic Acid-O-*d* 1-Dioxide. The exchanged acid as prepared above, 10.0 g, was dissolved in 625 ml of ethyl ether. Into the rapidly stirred solution was bubbled ammonia-d_3 gas generated by the controlled hydrolysis of 16.0 g of magnesium nitride with 25 ml of deuterium oxide.[19] A slow stream of purified, dry nitrogen gas was kept flowing through the apparatus at all times. A 2 × 60 cm column of potassium hydroxide served to dry the ammonia-d_3 before reaction with the acid. Precipitation of the salt was quantitative after 40 min. The ammonium salt N-d_4, 10.8 g (99%), was obtained as a white solid, $[\alpha]^{25}_{546}$ +59.4° (*c* 3.0, deuterium oxide).

(−)-2-Deuterio-2-methyl-2,3-dihydrobenzothiophene 1-Dioxide ((−)-2-*d*-II). A solution of 2.0 g of the above ammonium salt in 13.5 ml of deuterium oxide prepared. To the solution was added 1.67 ml of 5.80 *M* acetic acid-O-*d* in deuterium oxide (prepared by hydrolysis of freshly distilled acetic anhydride in deuterium oxide under nitrogen at 60° with a trace of sulfuric acid added). The mixture was transferred to a 60-ml, heavy-walled glass ampoule; the ampoule was sealed under nitrogen and placed in a constant-temperature bath at 155° for 48 hr. The ampoule was cooled and opened. A 40-ml aliquot of benzene was added, and the product was isolated as described above, 1.48 g (98% as colorless solid), $[\alpha]^{25}_{546}$ −11.0° (*c* 3.9, chloroform). The deuteriosulfone, 34.33 g, prepared as described above, was fractionally crystallized as in the preparation of nondeuterated material. The rotations of crops 9–13 ranged from $[\alpha]^{25}_{546}$ −24.08 to −24.18° (*c* 4, chloroform). These were combined and crystallized again, 11.2 g, mp 73–74°, $[\alpha]^{25}_{546}$ −24.1° (*c* 4, chloroform).

Combustion and deuterium analysis by the falling drop method gave 97.7% of 1 g atom of deuterium. *Anal.* Calcd for $C_9H_9DSO_2$: C, 58.99; $H_2O + D_2O$, 0.497 mg/mg of sample; S, 17.50. Found: C, 59.09; $H_2O + D_2O$, 0.477 mg/mg of sample; S, 17.50. Racemic II-*d* was obtained by fractional crystallization of the filtrates, 16 g, mp 115–116°.

Maximum Rotation of (+)-2-Methyl-2,3-dihydrobenzothiophene 1-Dioxide ((+)-II) by Isotopic Dilution Analysis. A 0.716-g portion of 99 ± 1% racemic II-*d*, 0.984–0.986 atom of deuterium per molecule,[6b] and 0.478 g of (+)-II, $[\alpha]^{25}_{546}$ +23.8° (*c* 3.9, chloroform) (deuterio racemate–protio antipode 60:40) were dissolved in 85 ml of boiling ether. Upon cooling, a crop of crystals separated, 0.368 g. This material was recrystallized from 32 ml of the same solvent, 0.102 g, $[\alpha]^{25}_{546}$ +0.28° (*c* 4.0, chloroform). The recrystallized, sublimed sulfone was found to contain 0.701 atom of deuterium per molecule.[6b] Continued fractional crystallization of the mother liquor from crop 1 yielded crop 7, 0.183 g, $[\alpha]^{25}_{546}$ +23.8° (*c* 4.5, chloroform). The sublimed recovered (+)-antipode was found to contain 0.427 atom of deuterium per molecule.[6b] Based on the molecular formula $C_9H_{10}SO_2$, the recovered racemate was 70.1% deuterated, while the recovered antipode was 42.7% deuterated. These data were used to calculate the optical purity of (+)-II using material with a specific rotation of +23.8°. The maximum rotation of (±)-II turned out to be $[\alpha]^{25}_{546}$ ±24.04 ± 0.4°.

Solvents, Bases, and Gases. The solvent, *t*-butyl alcohol, was dried over molecular sieves (Linde, Type 4A, pellets) for several days and distilled. The middle fraction was stored over molecular sieves. The basic solutions of *t*-butyl alcohol were prepared by reaction of a weighed amount of clean potassium metal with the solvent in a dry purified nitrogen atmosphere. Ethylene glycol was similarly purified and stored. The basic solution was prepared by adding clean potassium metal to the purified solvent in a dry purified nitrogen atmosphere at ice–salt bath temperature. Ethylene glycol-O-d_2 was available from a previous investigation[3c] (1.97 atoms of deuterium per molecule). Dimethyl sulfoxide was prepared and stored in the same way. The basic solution of dimethyl sulfoxide–methanol was prepared by adding clean potassium metal to pure methanol in a dry purified nitrogen atmosphere and

(19) R. H. Herber, "Inorganic Isotope Synthesis," W. A. Benjamin, Inc., New York, N. Y., 1962, p 36.

adding the resulting solution to dimethyl sulfoxide. Methanol ("Baker Analyzed" reagent) was refluxed over and distilled from calcium hydride and then stored over molecular sieves. Methanol-O-*d* (0.986 atom of deuterium per molecule) was available from another investigation.[20]

Final base concentrations were determined by titration in aqueous solution with standard acid. Nitrogen was purified by first passing through a tube containing calcium sulfate and ascarite, then through two 2 × 20 cm tubes containing copper turnings heated to 300°, and finally through another tube containing calcium sulfate and ascarite.

Typical Exchange and Racemization of (−)-2-Deuterio-2-methyl-2,3-dihydrobenzothiophene 1-Dioxide ((−)-II-*d*) (Run 2). A 0.1809-g portion of (−)-II-*d*, $[\alpha]^{25}_{546}$ −24.1° (*c* 3.95, chloroform), was weighed into a 3-ml volumetric flask, and the flask was filled to the mark with a solution of 0.028 *N* potassium *t*-butoxide in *t*-butyl alcohol–tetrahydrofuran 70:30 (0.331 *M* substrate). The flask was thoroughly shaken and thermostated at 25° within 90 sec from initial contact between the base-solvent and substrate. After 1.05 hr, the contents of the volumetric flask were poured into a 125-ml separatory funnel (Teflon greaseless stopcock) containing 40 ml of water to which 0.50 ml of concentrated hydrochloric acid and 35 ml of benzene had been added. The funnel was vigorously shaken; the layers were separated, and the aqueous phase was extracted with two additional 30-ml portions of benzene. The combined benzene extracts were washed three times with 30-ml portions of water, dried, and evaporated under reduced pressure. The product, 0.179 g, was totally sublimed [80° (0.15 mm)] and examined for optical purity and deuterium content. The substance displayed $[\alpha]^{25}_{546}$ −10.40° (*c* 4.02, chloroform) and was found by the combustion and falling drop method to contain 0.56 atom of deuterium per molecule. This corresponds to 56.8% racemization and 48.3% loss of deuterium (corrected for 0.977 atom of deuterium before exchange).

General Procedure for Racemization and Exchange of (−)-2-Deuterio-2-methyl-2,3-dihydrobenzothiophene 1-Dioxide ((−)-II-*d*). Run 1 was conducted identically with that of run 2, except the solvent was dimethyl sulfoxide–MeOH 91:9 (by volume; 2.3 *M* in CH_3OH), 0.16 *M* in MeOK. Runs 3 and 4 involved ampoule techniques and were conducted as follows. A 0.180-g portion of (−)-II-*d* was weighed into a 6-ml volumetric flask, and the flask was filled to the mark with either 0.16 *N* potassium methoxide (0.96 mmole) in methanol or 0.16 *N* potassium methoxide in methanol-O-*d* (0.164 *M* substrate). The volumetric flask was thoroughly shaken, and its contents were transferred to a nitrogen-purged ampoule with the aid of a syringe. The ampoule was sealed and placed in a constant-temperature bath at 76.0° for 11.5 hr (run 3) or 9.75 hr (run 4). The product was isolated and analyzed as described above, except that the aqueous phase of the run 3 work-up was titrated with standard acid for base. No loss of base occurred during reaction within experimental error (18.7 ml of 0.0513 *M* HCl required for phenolphthalein end point, 0.95 mmole). Run 5 was also conducted in an ampoule. Since the sulfone was insoluble in ethylene glycol, a 0.216-g portion was weighed directly into an ampoule, 20.0 ml of ethylene glycol 0.059 *N* in potassium ethylene glycoside (1.18 mmoles of base) was added from a pipet, and the ampoule was purged and sealed; the sulfone dissolved when heated (0.06 *M* in substrate). Isolation and analysis of the product was conducted similarly to run 3. (Titration of the aqueous phase of the work-up required 22.9 ml of 0.0513 *N* HCl, 1.17 mmoles.) Run 6 was conducted similarly to run 5, except that 0.125 g of sulfone was used. The base-solvent was 0.10 *N* potassium ethylene glycoxide-O-*d* in ethylene glycol-O-d_2.

Large-Scale Racemization and Exchange Experiment on (−)-2-Deuterio-2-methyl-2,3-dihydrobenzothiophene 1-Dioxide ((−)-II-*d*). Into a 20-ml volumetric flask was weighed 1.215 g of (−)-II-*d*, $[\alpha]^{25}_{546}$ −24.08° (*c* 4.0, chloroform). The flask was filled to the mark with the same solvent as used in run 2 (see above), shaken thoroughly, and thermostated at 25.0° for 675 min. The isolated product, 1.194 g of exchanged sulfone, displayed $[\alpha]^{25}_{546}$ −9.68° (*c* 4.0, chloroform), or 59.8% racemized.

This material was fractionally crystallized from ether as follows: crop 1, 0.231 g (from 85 ml), $[\alpha]^{25}_{546}$ −1.49° (*c* 4.0, chloroform). Crop 1 was then recrystallized from 20 ml of ether and crop 1-A separated, 0.127 g, $[\alpha]^{25}_{546}$ −0.2° (*c* 4.0, chloroform). The racemic modification of the exchange product was found to be 60.5% exchanged.[6a] The mother liquor remaining after crop 1 separated was concentrated to 60 ml and crop 2 separated, 0.334 g. Continued fractional crystallization of the exchanged sulfone yielded the following: crop 3, 0.083 g (from 35 ml); crop 4, 0.083 g (from 20 ml); crop 5, 0.042 g (from 10 ml); crop 6, 0.107 g (from 5 ml) (crystal form change); crop 7, 0.117 g (from 2 ml), $[\alpha]^{25}_{546}$ −23.7° (*c* 4.0, chloroform). Evaporation of the mother liquor from crop 7 yielded 0.144 g of exchanged sulfone after chromatography, $[\alpha]^{25}_{546}$ −23.5° (*c* 4.0, chloroform). Crop 7, mp 72.5–73°, was totally sublimed [85° (0.15 mm)] and analyzed for deuterium,[6a] 70.0 atoms % (excess) deuterium, or 28.3% exchanged (corrected for 0.977 atom of deuterium per molecule before exchange). These data were used to determine the relative rates of retention, inversion, and isoinversion, and to reduce k_e/k_α for racemization *vs.* exchange to time zero.

Racemization of (+)-2-Methyl-2,3-dihydrobenzothiophene 1-Dioxide and (−)-2-Deuterio-2-methyl-2,3-dihydrobenzothiophene 1-Dioxide in *t*-Butyl Alcohol. Two racemization runs were conducted at 25.0° with identical concentrations of substrate in the same base-solvent system used in run 2 (see above): 0.1215 g of either (+)-II, $[\alpha]^{25}_{546}$ +24.05° (*c* 4.0, chloroform), or (−)-II-*d*, $[\alpha]^{25}_{546}$ −24.10° (*c* 4.0, chloroform), was weighed into a 2-ml volumetric flask. The flask was filled to the mark with thermostated base-solvent and vigorously shaken. The thermostated polarimeter tube was immediately filled and rotations were taken on a Perkin-Elmer Model 141 polarimeter, the first reading at time 3 min. Thirteen points were taken during the first 75% of the reaction. The logarithm of the rotation was plotted against time, and the slope of the straight line was determined graphically to be 2.90 ± 0.003 × 10^{-4} sec^{-1} (protiosulfone) and 2.24 ± 0.016 × 10^{-4} sec^{-1} (deuteriosulfone) (deviations calculated by least-squares method). These data were used to reduce racemization and exchange kinetics of (−)-II-*d* in *t*-butyl alcohol to time zero. Table IV records the kinetic data for racemization of (−)-II-*d*.

The products from the isotopic dilution experiment, those from the resolution experiment, and a series of standards were analyzed for deuterium on an Associated Electronics Industries MS 9 mass spectrometer by comparison of the relative intensities of the mass 182 and 183 peaks (parent peaks of II-*h* and II-*d*). The deuterium contents found for the standards were within ±0.5% of the theoretical values.

2-Carbethoxytetrahydrothiophene. The substance, tetrahydrothiophene-2-carboxylic acid[21b] (100 g, mp 51°), was esterified with 800 ml of ethyl alcohol and four drops of hydrochloric acid. The reaction mixture was refluxed for 72 hr; excess ethanol was removed by evaporation under reduced pressure leaving a light yellow oil which was distilled. A fraction, bp 102.5–104° (11 mm), 101.2 g (92.5%), was retained. *Anal.* Calcd for $C_7H_{12}SO_2$: C, 52.52; H, 7.50. Found: C, 52.51; H, 7.59.

Table IV. Racemization of a 0.33 *M* Solution of (−)-2-Deuterio-2-methyl-2,3-dihydrobenzothiophene 1-Dioxide ((−)-II-*d*)[a] at 25.0° Followed to >85% Reaction

α_{obsd}, deg	Time, min	α_{obsd}, deg	Time, min
−1.380	3	−0.548	70
−1.253	10	−0.479	80
−1.091	20	−0.419	90
−0.948	30	−0.367	100
−0.825	40	−0.345	105
−0.718	50	−0.209	145
−0.627	60		

$k^D\alpha_{obsd}$ = 2.24 ± 0.016 × 10^{-4} sec^{-1}

[a] 0.98 atom of deuterium per molecule. In *t*-butyl alcohol–tetrahydrofuran (70:30) (0.028 *M* in potassium *t*-butoxide).

2-Carbethoxytetrahydrothiophene 1-Dioxide. To a solution of 25 g of the above ester in 75 ml of glacial acetic acid in a 250-ml flask was added 48 ml of 30% hydrogen peroxide in 2-ml portions with vigorous swirling. Ice-bath cooling, both during and after addition of hydrogen peroxide was complete, was employed *whenever* the temperature of the reaction mixture exceeded 39° until cooling to 35° was achieved. After the exothermic reaction

(20) D. J. Cram and A. S. Wingrove, *J. Am. Chem. Soc.*, 86, 5490 (1964).

(21) (a) E. V. Whitehead, R. A. Dean, and F. A. Fidler, *J. Am. Chem. Soc.*, 73, 3634 (1951); (b) F. Ernst, *Ber.*, 20, 518 (1887).

subsided, the reaction mixture was allowed to stand at 25° for 20 hr. It was then shaken with 200 ml of dichloromethane. The layers were separated, and the aqueous phase was extracted twice more with 200-ml portions of dichloromethane. The combined dichloromethane extracts were cooled to 0° and washed once with 150 ml of ice water, once with 50 ml of cold saturated ferrous sulfate solution, and once with 100 ml of cold saturated sodium bicarbonate solution. Evaporation of dichloromethane after drying yielded an oil which was distilled; the product was collected at bp 117–119° (0.35 mm), 18.2 g (59% as colorless oil). *Anal.* Calcd for $C_7H_{12}SO_4$: C, 43.76; H, 6.25; S, 16.69. Found: C, 43.62; H, 6.44; S, 16.29.

2-Methyl-2-carbethoxytetrahydrothiophene 1,1-Dioxide. A solution of 14.0 g of sodium metal in 300 ml of absolute ethanol was prepared. To the stirred solution, cautiously maintained at 70°, was added dropwise a solution of 73 g of 2-carbethoxytetrahydrothiophene 1-dioxide in 150 ml of absolute ethyl alcohol. The reaction mixture was stirred at 70° for 2 hr and cooled to 40°, and 90 g of methyl iodide was added dropwise. The reaction mixture was then heated very slowly to 70° for an additional 18 hr. The contents of the flask were then shaken with 200 ml of water and 300 ml of ether. The aqueous phase was extracted with two additional 200-ml portions of ether; the ether extracts were combined, cooled once with 100 ml of ice water, and dried. Evaporation of the ether left an oil which was distilled, the product being collected at bp 107–108° (0.35 mm), 69.0 g (88% as light yellow oil). *Anal.* Calcd for $C_8H_{14}SO_4$: C, 46.78; H, 6.72; S, 15.55. Found: C, 46.60; H, 6.84; S, 15.36.

2-Methyltetrahydrothiophene-2-carboxylic Acid 1-Dioxide (III). Into a stirred solution of 15 g of sodium hydroxide in 210 ml of water, 69 g of the above ester was poured in a thin stream. Stirring was continued for 15 min, 40 ml of 96% sulfuric acid was added slowly with ice-bath cooling, and the acidified hydrolysis reaction mixture was saturated with sodium chloride. Continuous extraction with chloroform for 48 hr yielded 59.1 g (92.5%) of III, mp 158–159.5°. *Anal.* Calcd for $C_6H_{10}SO_4$: C, 40.46; H, 5.61; S, 17.96. Found: C, 40.57; H, 5.72; S, 17.80.

(+)-2-Methyltetrahydrothiophene-2-carboxylic Acid 1,1-Dioxide ((+)-III). A solution of 75.3 g of III and 169.3 g of brucine in 1600 ml of hot water was prepared. The solution was allowed to cool very slowly to 7°, and the salt (111.2 g) separated as large plates. Recrystallization of the salt from hot water yielded 93.0 g (38%) of material. A small portion of the salt was converted to the free acid which, after sublimation, exhibited $[\alpha]^{25}_{546}$ +20.4°. Additional crystallizations of the salt provided no change in rotation of the derived acid. The optically pure salt (88 g, 36%) was dissolved in 800 ml of warm water, and a solution of 21 g of potassium carbonate in 50 ml of water was added with rapid stirring. Precipitation of brucine was complete within 15 min. The slurry was filtered; the filtrate was extracted twice with 300-ml portions of chloroform and reduced in volume to 225 ml under vacuum. Sulfuric acid, 45 ml, was added with cooling, and the acidic solution was saturated with sodium chloride. Continuous extraction of the solution with chloroform yielded 22.8 g of crude (+)-III. Recrystallization of the acid from 50 ml of ether gave 16.6 g of (+)-III, mp 161.5–162.5°, $[\alpha]^{28}_{546}$ +20.4° (*c* 4.7, water).

(−)-2-Methyltetrahydrothiophene-2-carboxylic Acid 1,1-Dioxide ((−)-III). To the mother liquors from the first crystallization of the brucine salt of III was added a solution of 25 g of potassium carbonate in 50 ml of water with rapid stirring, and the acid was recovered as before. The crude, partially optically active acid was placed in 55 ml of ether and warmed; the warm solution was filtered. The residue from filtration was found to be racemic, $[\alpha]^{28}_{546}$ 0.0° (*c* 4.7, water). Cooling of the filtrate afforded 14.04 g of (−)-III, mp 159–160°, $[\alpha]^{28}_{546}$ −20.2° (*c* 4.7, water).

Ammonium Salt of (+)-2-Methyltetrahydrothiophene-2-carboxylic Acid 1-Dioxide. Anhydrous ammonia gas was bubbled into a solution of 1 g of (+)-III, $[\alpha]^{29}_{546}$ +20.4°, in 30 ml of ether for 30 min. The salt, 1.058 g (98%), was collected by filtration, washed four times with 25 ml of ethyl ether, and vacuum dried, $[\alpha]^{27}_{546}$ +13.95° (*c* 4.3, water), mp 170° dec.

Representative Decarboxylation of (+)-2-Methyltetrahydrothiophene-2-carboxylic Acid 1-Dioxide ((+)-III) (Run 23). Into a dry ampoule, thoroughly purged with purified nitrogen gas, was introduced a solution of 0.137 g of optically pure ammonium salt of (+)-III, $[\alpha]^{27}_{546}$ +13.95° (*c* 4.3, water), and 0.363 g of optically pure (+)-III, $[\alpha]^{28}_{546}$ +20.4° (*c* 4.7, water), in 10 ml of distilled water. The ampoule was sealed and placed in a constant-temperature bath at 165°. After 236 hr, the ampoule was opened, and the contents were removed. Evaporation of water under reduced pressure left a semisolid which was taken up in 30 ml of ether. Dry ammonia gas was bubbled into the solution for 30 min and ammonium salt of (+)-III separated. The solid ammonium salt was recovered by filtration and dried under vacuum, 0.355 g, $[\alpha]^{26}_{546}$ +13.9° (*c* 4.2, water). The weight of recovered ammonium salt corresponded to 0.199 g of free acid remaining in the decarboxylation reaction mixture after 236 hr. Thus, decarboxylation proceeded to 45% of completion. Evaporation of the filtrate left an oil which was chromatographed on 40 g of silica gel in an 18-mm diameter column with ether–pentane, 75:25, as developer. Optically active IV was obtained analytically pure, 0.075 g, $[\alpha]^{27}_{546}$ +5.60° (*c* 7.0, 95% ethanol). The infrared and nmr spectra of this substance were identical with those of an authentic sample of 2-methyltetrahydrothiophene 1-dioxide (see above).

Run 22 was similarly conducted, except that 0.0435 g of anhydrous potassium carbonate was used as base with 0.450 g of (+)-III in 10 ml of distilled water. Decarboxylation proceeded to 53.6% of completion as determined by recovery of undecarboxylated acid as its ammonium salt. The weight of potassium carbonate used was subtracted from the total weight of recovered solids in determining per cent decarboxylation. Run 24 was conducted identically with that of run 22, and run 25 was conducted identically with that of run 23.

Optical Stability of (+)-2-Methyltetrahydrothiophene 1-Dioxide ((+)-IV) under Conditions of Its Formation (Control for Run 24). Sulfone (+)-IV, 0.155 g, $[\alpha]^{26}_{546}$ +5.41° (*c* 9.7, ethanol), 0.450 g of (+)-III, $[\alpha]^{27}_{546}$ +20.4° (*c* 4.7, water), 0.0435 g of anhydrous potassium carbonate, and 10 ml of *t*-butyl alcohol were placed in an ampoule. The ampoule was purged with dry nitrogen gas, sealed, and placed in a constant-temperature bath at 165° for 3 hr. The product, after isolation in the above manner and purification by chromatography on silica gel, exhibited $[\alpha]^{26}_{546}$ +4.07° (*c* 9.8, ethanol), 0.188 g (theory requires $[\alpha]^{26}_{546}$ +4.0°). The infrared and nmr spectra of (+)-IV recovered in this experiment were identical with those of (+)-IV obtained from other runs and with those taken of IV synthesized by a known procedure.[20a]

Stability of (+)-2-Methyltetrahydrothiophene-2-carboxylic Acid 1-Dioxide *in* the Absence of Base. A solution of 0.450 g of (+)-III in 10 ml of *t*-butyl alcohol was heated to 165° for 24 hr, and the product was put through the same isolation procedure as in run 23. Ammonium salt of (+)-III, 0.470 g (95%), $[\alpha]^{26}_{546}$ +13.8° (*c* 4.2, water) was the only product isolated. Similar results were obtained in water.

5-Methyl-2-carbethoxytetrahydrothiophene. An amalgam was prepared from 69 g of sodium metal and 3500 g of mercury and was added while still molten to a stirred solution of 53 g of 5-methylthiophene-2-carboxylic acid (Marstan Chemical Laboratory) and 16 g of sodium hydroxide in 550 ml of water. After the initial vigorous reaction had subsided, the reaction mixture was heated to 85° and stirred at this temperature for 6 days. The spent amalgam was separated from the aqueous phase, and the latter was acidified with 350 ml of concentrated hydrochloric acid at 0° with rapid stirring. The heavy oil that separated was recovered by extraction with four 250-ml portions of ether. The combined ether extracts were washed twice with 250-ml portions of saturated sodium chloride solution, dried, and evaporated, yielding 48.2 g of crude acid which was esterified directly with 500 ml of absolute ethyl alcohol and four drops of hydrochloric acid. Evaporation of excess ethanol yielded an oil which was distilled, bp 103–105° (12 mm), 44 g (67.5% over-all as colorless oil). *Anal.* Calcd for $C_8H_{14}SO_2$: C, 55.17; H, 8.04; S, 18.41. Found: C, 55.41; H, 8.00; S, 18.18.

5-Methyl-2-carbethoxytetrahydrothiophene 1-Dioxide. To a solution of 30.8 g of 5-methyl-2-carbethoxytetrahydrothiophene in 85 ml of glacial acetic acid in a 250-ml flask was added 54 ml of 30% hydrogen peroxide in 5-ml portions with vigorous swirling. Ice-bath cooling, both during and after addition of hydrogen peroxide was complete, was employed *whenever* the temperature of the reaction mixture exceeded 40°. After the exothermic reaction subsided, the reaction mixture was allowed to stand at 25° for 30 hr and shaken with 200 ml of dichloromethane. The layers were separated, and the aqueous phase was extracted twice more with 200-ml portions of dichloromethane. The combined dichloromethane extracts were cooled to 0° and washed once with 150 ml of ice water, once with 50 ml of cold saturated ferrous sulfate solution, and once with 100 ml of cold saturated sodium bicarbonate solution, in that order. Evaporation of dichloromethane left an oil which was distilled, the product being collected at bp 114–117° (0.25 mm), 20.2 g (55.4% as colorless oil). *Anal.* Calcd for $C_8H_{14}SO_4$: C, 46.61; H, 6.79; S, 15.55. Found: C, 46.78; H, 6.78; S, 15.39.

5-Methyltetrahydrothiophene-2-carboxylic Acid 1-Dioxide (V). Into a stirred solution of 25 g of sodium hydroxide in 210 ml of water was poured 80.7 g of the above ester in a thin stream. Stirring was continued for 45 min; 60 ml of 96% sulfuric acid was added slowly with ice-bath cooling, and the acidic solution was saturated with sodium chloride. Continuous extraction of the solution with chloroform for 48 hr yielded after evaporation of solvent 68 g (99%) of V as a semisolid.

Racemate A of 5-Methyltetrahydrothiophene-2-carboxylic Acid 1-Dioxide (V). The mixture of racemates obtained above was dissolved in 300 ml of boiling chloroform, and hexane was added until the solution was nearly saturated at the boiling point of the mixture. The solution was allowed to cool open to the atmosphere, and a crop of white crystals separated which was recrystallized twice from chloroform, 26 g, mp 121–124°. The nmr spectrum of the recrystallized acid (V-A) contained only one doublet for the methyl group (τ 8.80, J = 6.5 cps), whereas the spectrum of the crude mixture of racemates contained a closely spaced double doublet (τ 8.80, J = 6.5 cps and τ 8.63, J = 6.0 cps). Attempts to resolve this material through its brucine salt were only partially successful.

(+)-5-Methyltetrahydrothiophene-2-carboxylic Acid 1-Dioxide of Racemate B ((+)-V-B). A solution of 42.7 g of V (composition: about 14.9 g of racemate A and 32.3 g of racemate B, nmr analysis) and 104 g of brucine in 236 ml of hot water was prepared. After standing at 25° for 12 days, a crystalline salt began to separate; an additional two weeks was required before separation of the salt ceased, 39.7 g (26.2%). The derived acid recovered after an additional crystallization of the salt from water displayed $[\alpha]^{26}_{546}$ +34.2° (*c* 5.1, chloroform). A third crystallization of the salt gave recovered acid of $[\alpha]^{28}_{546}$ +34.9° (*c* 4.9, chloroform); a fourth crystallization of the salt yielded acid of $[\alpha]^{26}_{546}$ +34.4° (*c* 4.9, chloroform). The salt thrice crystallized as above, 7.35 g, was dissolved in 100 ml of warm water and a solution of 7 g of potassium carbonate in 15 ml of water was added. Precipitation of brucine was complete within 15 min. The slurry was filtered, reduced in volume to 25 ml under vacuum, and filtered. The solution of the potassium salt of (+)-V-B was acidified with sulfuric acid and continuously extracted with chloroform for 48 hr. Recovered (+)-V-B, 1.356 g, $[\alpha]^{28}_{546}$ +34.9° (*c* 4.9, chloroform), mp 79–81°, was recrystallized from ether–pentane, 1.21 g, $[\alpha]^{26}_{546}$ +35.1° (*c* 4.9, chloroform), mp 79.5–81°. An additional crystallization of the substance did not change these properties. *Anal.* Calcd for $C_6H_{10}SO_4$: C, 40.46; H, 5.61; S, 17.96. Found: C, 40.53; H, 5.68; S, 17.67.

Decarboxylation of (+)-5-Methyltetrahydrothiophene-2-carboxylic Acid 1-Dioxide ((+)-V-B). A solution of 0.388 g of optically pure (+)-V-B, $[\alpha]^{25}_{546}$ +35.1° (*c* 4.9, chloroform), and 0.137 g of the ammonium salt of optically pure (+)-V-B, $[\alpha]^{25}_{546}$ +23.61° (*c* 0.66, water), was prepared in 10 ml of water. The solution was placed in an ampoule which had been thoroughly purged with nitrogen. The ampoule was sealed and placed in a constant-temperature bath at 164° for 72 hr. After this time, the ampoule was opened, and its contents were removed. Water was evaporated under reduced pressure, leaving a viscous oil which was taken up in 20 ml of methanol–ether. Ammonia gas was bubbled into the solution for 30 min to convert excess acid to the ammonium salt. The solvent was removed under reduced pressure, and the residue was extracted with two 30-ml portions of boiling ether. The solid ammonium salt remaining after extraction exhibited $[\alpha]^{25}_{546}$ +23.40° (*c* 0.64, water), 0.324 g. Decarboxylation thus proceeded to 43% of completion. Since only 25 mole % ammonium salt was employed as base, the decarboxylation reaction mixture was always acidic. Thus, the product could not have been partially racemized.

The ether extracts were evaporated yielding an oil which was chromatographed on a 1 × 30 cm column of silica gel with ethyl ether–pentane, 70:30, as eluent. The sulfone, optically pure (+)-IV, purified by chromatography, 0.120 g, exhibited $[\alpha]^{25}_{546}$ +11.80° (*c* 3.5, ethanol). The infrared and nmr spectra of this substance were identical with those of (+)-IV obtained by decarboxylation of 2-methyltetrahydrothiophene-2-carboxylic acid 1-dioxide and to those of racemic IV obtained *via* an independent synthesis reported above.[21a]

Electrophilic Substitution at Saturated Carbon. XXXIV. Isoinversion as a Mechanistic Component in Base-Catalyzed Hydrogen–Deuterium Exchange between Carbon Acids and Medium[1]

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Abstract: Analysis of the over-all stereochemical course of base-catalyzed hydrogen–deuterium exchange reactions of carbon acids in terms of mechanistic components is provided by a kinetic model. Rate constants for exchange with retention of configuration, exchange with inversion, and isoinversion (defined as inversion without exchange) have been determined for exchange of I-H_+ in methanol-O-*d* with potassium methoxide at 25° by two experimentally independent methods based on the model. One method used only kinetics, and the other used reresolution of partially racemized material. Exchange of I-D_+ in *t*-butyl alcohol with potassium phenoxide was also investigated by the latter method. Isoinversion is shown to be a contributing mechanistic component in both media. Primary substrate and solvent isotope effects on racemization of I are reported. The results are interpreted by a mechanism in which carbanions are tightly hydrogen bonded to just one solvent molecule at a time.

The stereochemical courses of hydrogen–deuterium exchange reactions of carbon acids have been divided into four categories on the basis of their k_e/k_α (rate constant for exchange over that for racemization) values: exchange with net retention ($k_e/k_\alpha > 1.0$), exchange with total racemization ($k_e/k_\alpha = 1.0$), exchange with net inversion ($0.5 \leq k_e/k_\alpha < 1.0$), and isoracemization (defined as racemization without exchange,

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