Electrophilic Substitution at Saturated Carbon. XXV. Structural Requirements for Functional Groups Centered around Second-Row Elements to Preserve Asymmetry of Carbanions[1,2]

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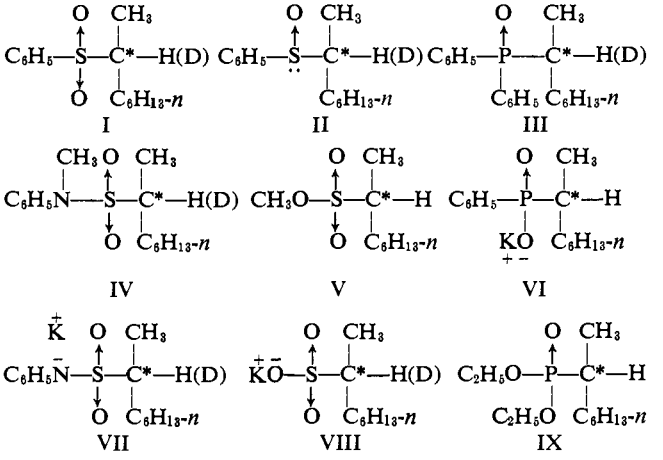
Abstract: The stereochemical course of base-catalyzed hydrogen–deuterium exchange at asymmetric carbon has been examined in six new systems in which the intermediate carbanion is stabilized by different functional groups centered about second-row elements. The first three systems, *n*-$C_6H_{13}(CH_3)C^*HSO_2N(CH_3)C_6H_5$, *n*-$C_6H_{13}(CH_3)C^*HSO_2OCH_3$, and *n*-$C_6H_{13}(CH_3)C^*HP\bar{O}_2(C_6H_5)$, gave values of k_e/k_α (rate constant for isotopic exchange over rate constant for racemization) that ranged from 37 to 17 in *t*-butyl alcohol-O-*d*–potassium *t*-butoxide. The first system (deuterated) gave k_e/k_α values of 34 and 17 in dimethyl sulfoxide–methanol and in ethylene glycol–potassium ethylene glycoxide. In contrast, the second three systems, *n*-$C_6H_{13}(CH_3)C^*HSO_2\bar{N}C_6H_5$, *n*-$C_6H_{13}(CH_3)C^*HS\bar{O}_3$, and *n*-$C_6H_{13}(CH_3)C^*HPO(OC_2H_5)_2$, gave k_e/k_α values close to unity (1.1 to 2.9). These results coupled with those obtained previously with 2-octyl phenyl sulfone, 2-octyl phenyl sulfoxide, and 2-octyldiphenylphosphine oxide provide the following generalizations. Functional groups centered around second-row elements that bear two charge-carrying negative elements induce asymmetry in attached carbanions. Functional groups centered around second-row elements that bear one or three charge-carrying negative elements do not induce asymmetry in attached carbanions. The triethylamine-catalyzed reaction of 2-octylsulfonyl chloride with methanol-O-*d* gave methyl 2-octylsulfonate whose 2 position was 87% deuterated. This reaction as well as others of the sulfonyl chloride and the corresponding azide appeared to involve sulfene intermediates.

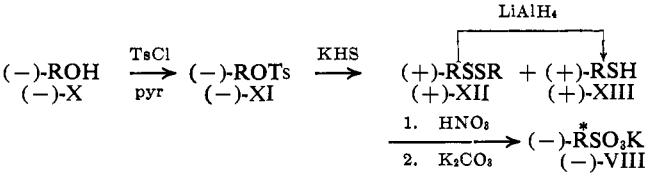
In previous investigations three functional groups centered about second-row elements were examined to determine their effects on the symmetry properties of attached carbanions. The benzenesulfonyl group has been demonstrated to preserve the asymmetry of attached carbanions[3] whereas the benzenesulfinyl and diphenylphosphinoxy groups did not exhibit this property.[4] Thus, k_e/k_α (ratio of rate constants of base-catalyzed hydrogen isotope exchange to that of racemization) for I was $\geqq 10$ in a variety of solvents,[1b] whereas the values of the ratio for II and III were not far from unity in a variety of solvents.[4]

The present investigation was undertaken to determine the structural features associated with functional groups that induce carbanion asymmetry and those that do not. Six new optically active systems were prepared (IV–IX), each of which contains a 2-octyl attached to a carbanion stabilizing group centered around a second row element. These systems all underwent base-catalyzed isotopic exchange with solvent under appropriate conditions, and k_e/k_α values (one-point rate constants) were determined.



Results

Starting Materials. Potassium sulfonate VIII was prepared from both optically pure (−)-2-octanol[5] and from optically pure 2-octanol-2-*d* by the method formulated.[6] The rotation of 2-octyl-mercaptan checked the highest literature value,[6a] but the rotation of the



R = 2-octyl

(1) The authors wish to thank the U. S. Public Health Service for a grant which partially supported this investigation. Part of this research was sponsored by the U. S. Army Research Office (Durham).

(2) Some of these results appeared in communication form: D. J. Cram, R. D. Trepka, and P. St. Janiak, *J. Am. Chem. Soc.*, **86**, 2731 (1964).

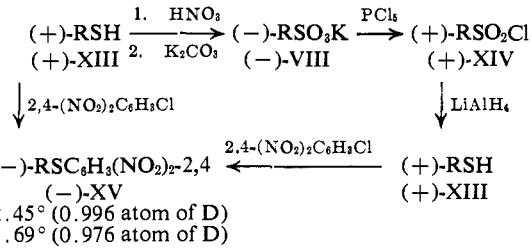
(3) (a) D. J. Cram, W. D. Nielsen, and B. Rickborn, *ibid.*, **82**, 6415 (1960); (b) D. J. Cram, D. A. Scott, and W. D. Nielsen, *ibid.*, **83**, 3696 (1961); (c) D. J. Cram and A. S. Wingrove, *ibid.*, **85**, 1100 (1963); (d) E. J. Corey and E. T. Kaiser, *ibid.*, **83**, 490 (1961); (e) E. J. Corey, H. Konig, and T. H. Lowry, *Tetrahedron Letters*, **12**, 515 (1962); (f) E. J. Corey and T. H. Lowry, *ibid.*, **13**, 793 (1965); (g) E. J. Corey and T. H. Lowry, *ibid.*, **13**, 803 (1965); (h) H. L. Goering, D. L. Towns, and B. Dittmar, *J. Org. Chem.*, **27**, 736 (1962).

(4) (a) D. J. Cram, R. D. Partos, S. H. Pine, and H. Jager, *J. Am. Chem. Soc.*, **84**, 1742 (1962); (b) D. J. Cram and S. H. Pine, *ibid.*, **85**, 1096 (1963); (c) D. J. Cram and R. D. Partos, *ibid.*, **85**, 1093 (1965).

(5) (a) J. Kenyon in "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, New York, N. Y., 1946, p 418; (b) W. E. Doering and R. W. Young, *J. Am. Chem. Soc.*, 74, 3891 (1952).

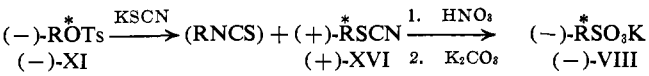
(6) (a) J. Kenyon, H. Phillips, and V. P. Pittman, *J. Chem. Soc.*, 1072 (1935); (b) R. C. Arnold, A. P. Lien, and R. M. Alm, *J. Am. Chem. Soc.*, **72**, 721 (1950); (c) P. A. Levene and L. A. Mikeska, *J. Biol. Chem.*, **75**, 337 (1927).

potassium sulfonate, $[\alpha]^{31.5}_{546}$ −12.04° (*c* 5.48, water), was a fraction of the reported value,[6a] $[\alpha]^{20}_{589}$ +134.7° (*c* 1.34, water). Therefore, mercaptan and sulfonate were interrelated by a cyclic series of transformations which demonstrated the two substances and all intervening compounds to be of the same optical purity. Thus (+)-2-octyl-2-*d* mercaptan was converted through the sulfonic acid salt to the sulfonyl chloride, which was reduced to the mercaptan.[7] Each sample of mercaptan (initial material and product) was transformed into its 2,4-dinitrophenyl thioether derivative,[8] which was an easily purified crystalline solid. The rotations and deuterium content of the two samples were identical within experimental error. Control experiments demonstrated that no optical fractionation could have accompanied the crystallization of the solid derivative. Thus the high rotations previously reported for 2-octylsulfonic acid and its salts are probably in error, particularly since the same authors[6a] report $[\alpha]^{25}_{589}$ +1.14° (*c* 6, water) for the sodium salt of 2-butylsulfonic acid.



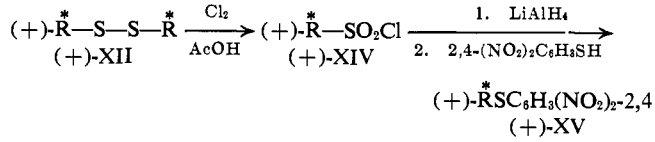
R = 2-octyl-2-*d*

In a second synthesis of the potassium sulfonate salt, optically pure (+)-2-octyl tosylate was treated with potassium thiocyanate in acetone, and the thiocyanate produced was oxidized to the desired salt. This material was only 66% optically pure, and the synthesis also had the additional undesirable feature that isothiocyanate was produced as well as thiocyanate. The partial racemization probably resulted from salt-catalyzed ion pair formation during the preparation of the thiocyanate.[9] The facts reported by earlier investigators who prepared 2-octyl thiocyanate[6a,10] also suggest similar difficulties.



R = 2-octyl

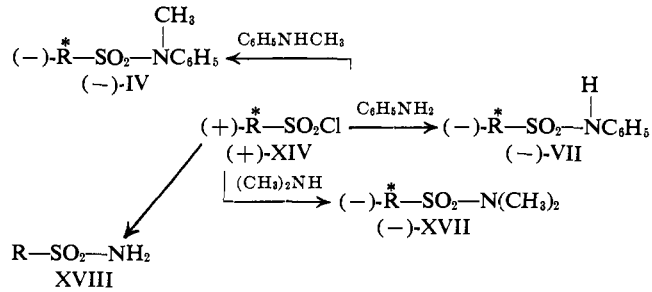
In a synthesis of (+)-2-octyl-2-*d*-sulfonyl chloride,[10b,11] (+)-2-octyl-2-*d* disulfide was submitted to oxidative chlorination in glacial acetic acid.[12] A portion of the sulfonyl chloride was converted to (+)-2,4-dinitrophenyl-2-octyl-2-*d* thioether ((+)-XV), which contained 0.95 atom of deuterium per molecule, and whose rotation was essentially identical with the undeuterated material prepared from sulfonyl chloride made from the sulfonic acid. Thus the sulfonyl chloride prepared by the two routes appears to be of the same optical purity. The fact that little (~2%) or no deuterium was lost in



R = 2-octyl

the reactions leading to thioether XV also indicates that no racemization occurred in the reaction sequences.

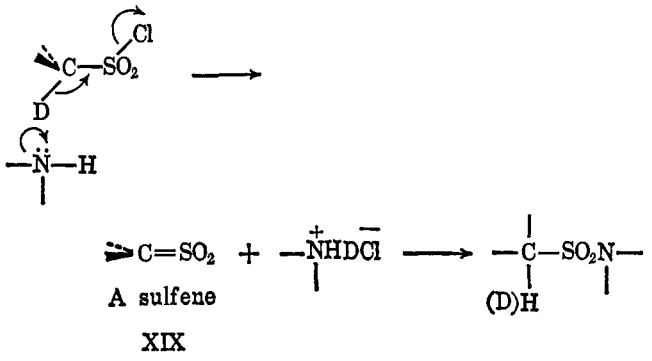
Three sulfonamides were prepared (under minimum conditions of time and temperature) from deuterated optically active sulfonyl chloride, compounds IV, VII, and XVII. Of these, the N-methylsulfonanilide (IV) suffered no deuterium loss, whereas sulfonanilide VII contained 8% less and N,N-dimethylsulfonamide XVII 46% less deuterium than the starting sulfonyl chloride. Thus IV is probably optically pure, VII, 92–100% optically pure, and XVII, 54–100% optically pure. Sulfonamide XVIII was prepared from racemic protio acid chloride XIV.



R = 2-octyl

The deuterium loss in the preparation of (−)-XVII-*d* and (−)-VII-*d* can be attributed to either isotopic exchange of the sulfonyl chloride ((+)-XIV-*d*) with the amine in a reaction competitive with amide formation, or to sulfene (XIX) intervention as an intermediate in formation of the amides.[13] Since sulfenes possess a plane of symmetry, they give only racemic product. Clearly most of the amide was formed by direct substitution at sulfur. The difference in deuterium loss in the reactions of the three amines seems to best correlate with their steric requirements and with the yields of amides. Thus the most hindered amine (N-methylaniline) gave amide IV with no loss of deuterium but in the lowest yield (16%) whereas the less hindered dimethylamine and aniline gave much higher yields (30–65%). Possibly sulfene capture by amine is more subject to steric effects than direct substitution at sulfur, and although sulfene may be produced with N-methylaniline, it could go to side products. The balance in sulfene production *vs.* direct substitution undoubtedly is also a function of basicity *vs.* nucleophilicity of the amines involved. The sulfonamide products required much more drastic conditions for isotopic exchange and racemization than those found in their formation.

(7) C. S. Marvel and P. D. Caesar, *J. Am. Chem. Soc.*, **72**, 1033 (1950).
(8) R. W. Bost, J. O. Turner and R. D. Norton, *ibid.*, **54**, 1985 (1932).
(9) (a) A. Fava and A. Iliceto, *Ric. Sci.*, **25**, 54 (1955); (b) G. Caprioli and A. Iliceto, *ibid.*, **26**, 2714 (1956).
(10) (a) W. G. Rose and H. L. Haller, *J. Am. Chem. Soc.*, **58**, 2648 (1936); (b) H. F. Herbrandson, W. S. Kelly, and J. Versnell, *ibid.*, **80**, 3301 (1958).
(11) C. Ziegler and J. M. Sprague, *J. Org. Chem.*, **16**, 621 (1951).
(12) I. B. Douglass, B. S. Farah, and E. G. Thomas, *ibid.*, **26**, 1996 (1961).
(13) (a) J. F. King and T. Durst, *J. Am. Chem. Soc.*, **86**, 287 (1964); (b) W. E. Truce, R. W. Campbell, and J. R. Norell, *ibid.*, **86**, 288 (1964).



A sulfene

XIX

Reaction of the sulfonic acid (prepared from its potassium salt) (+)-VII-*h* with diazomethane gave (+)-methyl 2-octylsulfonate, (+)-V-*h*.[14] Treatment of the sodium salt of 2,4,6-trimethylphenoxide with racemic sulfonyl chloride XIV gave ester XX. Since optically active or deuterated material was not employed, it is not clear whether sulfene XIX was an intermediate in this reaction.

$$\underset{\text{(+)-VIII-}h}{\overset{*}{\text{R}}\text{—SO}_3\text{H}} \xrightarrow[2.\ \text{CH}_2\text{N}_2]{1.\ \text{H}^+} \underset{\text{(+)-V-}h}{\overset{*}{\text{R}}\text{—SO}_3\text{CH}_3}$$

$$\underset{\text{XX}}{\text{R—SO}_3\text{C}_6\text{H}_2(\text{CH}_3)_3\text{-2,4,6}}$$

R = 2-octyl

Azide (−)-XXI-*d* was prepared from sulfonyl chloride (−)-XIV-*d* with sodium azide[15] in ethanol. About 10% of the atom of deuterium was lost even though minimum conditions for reaction were used. It is not clear whether this small loss occurred before, during, or after azide formation.

$$\underset{\text{(−)-XIV-}d}{\overset{*}{\text{R}}\text{—SO}_2\text{Cl}} + \text{NaN}_3 \longrightarrow \underset{\text{(−)-XXI-}d}{\overset{*}{\text{R}}\text{—SO}_2\text{N}_3}$$

R = 2-octyl

Sulfene formation from sulfonyl chloride (XIV-*h*) was studied by treating the material with triethylamine in benzene–methanol-O-*d*.[14] The ester produced (V-*d*) contained 0.87 atom of deuterium per molecule as compared to 0.99 atom of deuterium per molecule in the methanol-O-*d*. Clearly some ester was formed by direct substitution at sulfur. When sulfonyl chloride (+)-XIV-*d* was treated with triethylamine in benzene–methanol-O-*h*, no ester could be isolated. The rate of ester formation from deuterated XIV was considerably slower than from protonated XIV, and in the last experiment, the ester formed decomposed at a rate faster than the sulfonyl chloride reacted. This substantial isotope effect points to sulfene formation from both sulfonyl chloride and ester.

Formation of the sulfene intermediate XIX from azide XXI-*h* in benzene, triethylamine, and methanol-O-*d* was not observed. However, when XXI-*h* was treated with potassium methoxide in methanol-O-*d*, the resulting ester (V) contained 0.92 atom of deuterium per molecule. Again reaction did not *only* occur by means of the sulfene intermediate.

(14) R. B. Scott, Jr. and R. E. Lutz, *J. Org. Chem.*, **19**, 830 (1954), previously prepared the ethyl ester by this method.
(15) Procedure resembled that of Th. Curtins, *J. Prakt. Chem.*, **125**, 303 (1930).

Treatment of optically pure (−)-2-octyl tosylate with the sodium salt of phenylphosphinic acid *n*-butyl ester[16] gave (+)-phenyl-2-octylphosphinic acid *n*-butyl ester as a mixture of diastereomers. These were separated by chromatography to give (+)-XXIIA and (+)-XXIIB, the latter predominating by about a factor of 2. Ester B was converted to (+)-phenyl-2-octylphosphinic acid, (+)-VI, with lithium chloride at high temperature followed by acidification.[17]

$$\underset{\text{(−)-XI}}{\overset{*}{\text{R}}\text{—OTs}} + \text{NaP}(\text{O})(\text{C}_6\text{H}_5)(\text{OC}_4\text{H}_9\text{-}n) \longrightarrow$$

$$\underset{\text{(+)-XXIIA}}{\overset{*}{\text{R}}\text{—P}(\text{O})(\text{C}_6\text{H}_5)(\text{OC}_4\text{H}_9\text{-}n)} + \underset{\text{(+)-XXIIB}}{\overset{*}{\text{R}}\text{—P}(\text{O})(\text{C}_6\text{H}_5)(\text{OC}_4\text{H}_9\text{-}n)} \xrightarrow[2.\ \text{H}^+]{1.\ \text{LiCl}} \underset{\text{(+)-VI}}{\overset{*}{\text{R}}\text{—P}(\text{O})(\text{C}_6\text{H}_5)(\text{OH})}$$

(conjugated acid)

R = 2-octyl

Optically active (+)-diethyl 2-octylphosphonate ((+)-IX) was prepared from optically pure (−)-2-octyl tosylate and the sodium salt of diethyl phosphite.[18] This ester was hydrolyzed to give (+)-2-octylphosphonic acid (XXIII). Treatment of this acid with thionyl chloride provided (+)-2-octylphosphonic acid dichloridate ((+)-XXIV), which was hydrolyzed back to starting acid of the same rotation. Thus no optical activity was lost in either the chloridate formation or hydrolysis. Likewise, (+)-2-octylphosphonic acid was reesterified to give (+)-diethyl 2-octylphosphonate of the same optical purity as the starting material.

$$\underset{\text{(−)-XI}}{\overset{*}{\text{R}}\text{—OTs}} + \text{NaP}(\text{O})(\text{OC}_2\text{H}_5)_2 \longrightarrow \underset{\text{(+)-IX}}{\overset{*}{\text{R}}\text{—P}(\text{O})(\text{OC}_2\text{H}_5)_2} \underset{\text{NaOH, C}_2\text{H}_5\text{I}}{\overset{1.\ \text{OH};\ 2.\ \text{H}^+}{\rightleftharpoons}}$$

$$\underset{\text{(+)-XXIII}}{\overset{*}{\text{R}}\text{—P}(\text{O})(\text{OH})_2} \underset{1.\ \text{K}_2\text{CO}_3}{\overset{\text{SOCl}_2}{\rightleftharpoons}} \underset{\text{(+)-XXIV}}{\overset{*}{\text{R}}\text{—P}(\text{O})\text{Cl}_2} \xrightarrow{(\text{CH}_2)_5\text{NH}}$$

$$\underset{\text{XXV}}{\overset{*}{\text{R}}\text{—P}(\text{O})(\text{Cl})\text{—N}(\text{CH}_2)_5} \xrightarrow[2.\ \text{H}^+]{1.\ \text{K}_2\text{CO}_3} \underset{\text{XXVI}}{\overset{*}{\text{R}}\text{—P}(\text{O})(\text{OH})\text{—N}(\text{CH}_2)_5}$$

Treatment of the dichloridate, (+)-XXIV, with piperidine provided its piperidine derivative, XXV. Hydrolysis of this derivative in acid provided (+)-XXIII whose rotation was 23% lower than that of starting material. Partial hydrolysis of XXV gave amide acid, XXVI, which when hydrolyzed to (+)-XXIII gave material which was 22% racemized. Racemization possibly occurred during the formation of XXV by hydrogen chloride loss from XXIV to form symmetrical intermediate XXVII, similar to a sulfene.

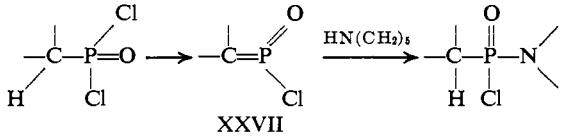
(16) G. N. Kosolapoff, *J. Am. Chem. Soc.*, 72, 4292 (1950).
(17) Method was inspired by work of V. M. Clark and A. R. Todd, *J. Chem. Soc.*, 2030 (1950).
(18) A. Michaelis and T. Becker, *Ber.*, 30, 1003 (1897).

Table I. Stereochemical Course of Base-Catalyzed Hydrogen–Deuterium Exchange Reactions

Run no.	Substrate: Nature	Substrate: Concn, M	Solvent	Base: Nature	Base: Concn, M	Temp, C°	Time, hr	% exchange	% racmn	$k_e \times 10^6$ sec^{-1}	$k_\alpha \times 10^6$ sec^{-1}	k_e/k_α
1	IV-*h*	0.087	*t*-BuOD[a]	*t*-BuOK	0.060	25	3.5	71.7	6.4	100	5.2	19
2	IV-*d*[b]	0.086	*t*-BuOH	*t*-BuOK	0.089	25	1.9	69.1	3.1	173	4.7	37
3	IV-*d*[b]	0.086	$(CH_3)_2SO$[c]	CH_3OK	0.189	25	4.0	84.7	5.3	130	3.8	34
4	IV-*d*[b]	0.085	$(CH_2OH)_2$	$HOCH_2CH_2OK$	0.551	100	14	52.7	4.3	15	0.87	17
5	V-*h*	0.148	*t*-BuOD[a]	*t*-BuOK	0.020	25	0.40	42.5	0–2	380	<14	>28
6	VI-*h*	0.130	*t*-BuOD[a]	*t*-BuOK	0.289	225	51	73[d]	6.5	7.1	0.033	22
7	VI-*h*	0.134	*t*-BuOD[a]	*t*-BuOK	0.366	225	47	57[e]	3.5	5.0	0.024	21
8	VII-*h*	0.228	*t*-BuOD[a]	*t*-BuOK	1.18	150	21.5	85	49	25	8.6	2.9
9	VII-*d*[f]	0.166	*t*-BuOH	*t*-BuOK	1.11	150	24.3	66	41	12	6	2
10	VII-*d*[f]	0.139	$(CH_3)_2SO$[c]	CH_3OK	0.400	150	50.0	38	17	2.6	1	2.5
11	VIII-*h*	0.252	*t*-BuOD[a]	*t*-BuOK	1.19	146	45.0	62.5	46.6	6.1	3.9	1.6
12	VIII-*d*[g]	0.256	*t*-BuOH	*t*-BuOK	1.11	146	69.0	75.4	57.2	5.7	3.4	1.7
13	IX-*h*	1.01	*t*-BuOD[a]	*t*-BuOK	1.03	100	55[h]	13.3	12.9	0.72	0.70	1.0
14	IX-*h*	1.04	*t*-BuOD[a]	*t*-BuOK	0.28	100	76[i]	18.4	16.5	0.74	0.67	1.1
15	IX-*h*	0.95	*t*-BuOD[a]	*t*-BuOK	0.28	100	74[j]	20.2	17.3	0.86	0.72	1.2

[a] 0.97 atom of deuterium per molecule. [b] 0.95 atom of deuterium per molecule. [c] 92% $(CH_3)_2SO$, 8% CH_3OH by weight, or 2.6 *M* in CH_3OH. [d] Combustion analysis showed four atoms of deuterium per molecule. Nmr analysis against an internal standard (diiodomethane) indicated 3.27 atoms of deuterium in the aryl and 0.73 atom in the tertiary position. [e] Combustion analysis. Combustion analysis showed 3.59 atom of deuterium per molecule. Nmr analysis against an internal standard (diiodomethane) indicated 3.02 atoms of deuterium in the benzene ring and 0.57 atoms of deuterum in the tertiary position. [f] 0.883 atom of deuterium per molecule. [g] 0.95 atom of deuterium per molecule. [h] 60% recovered. [i] 76% recovered. [j] 74% recovered.

Similar racemization mechanisms can also be envisioned for XXV → XXVI, or from XXVI → XXIII.



XXVII

Isotopic Exchange and Racemization. Systems IV to IX were submitted to base-catalyzed hydrogen–deuterium exchange and racemization reactions with the solvent as the hydrogen or deuterium pool. In all runs except those that involved sulfonate salt VIII, the reactions were interrupted at the appropriate time, product was isolated (the whole sample and without fractionation), and its deuterium content and rotation were measured. In those runs involving salt VIII, the product was converted (without fractionation) to its 2,4-dinitrophenyl thioether derivative (XV), whose rotation and deuterium content were measured. From the values obtained, one-point, first-order rate constants were calculated for isotopic exchange (k_e) and for racemization (k_α) through use of eq 1. Kinetic isotope effects were disregarded, since their treatment has only a minor effect on the ratio. This ratio serves as a convenient index of the stereochemical course of

$$k_e/k_\alpha = \frac{\log\left(\frac{100}{100 - \%\text{ isotopic exchange}}\right)}{\log\left(\frac{100}{100 - \%\text{ racemization}}\right)} \quad (1)$$

the reactions (see Discussion). Representative runs were titrated when over to see if any base was consumed. Table I records the results. Base loss was observed only in runs 10 and 5 due to decomposition of dimethyl sulfoxide and substrate, respectively. Optically pure materials were used throughout except in runs 9 and 10 (93% optically pure) and run 8 (80% optically pure). Since the ratio, k_e/k_α, should be independent of time, base concentration, and optical purity of the substrate, no adjustments were needed in the calculations. Justification for utilization of one-point rate constants is found in the fact that the qualitative picture obtained for sulfone I from one-point rate constants[3a] was changed only in detail when a complete kinetic examination was made.[3b]

Attempts to exchange sulfonate salt VIII in dimethyl sulfoxide–methanol–potassium methoxide required temperatures high enough so that the dimethyl sulfoxide decomposed, thus destroying base. Attempts at exchange of sulfonate ester V in methanol–potassium methoxide resulted in formation of potassium sulfonate and dimethyl ether. Even in *t*-butyl alcohol–potassium *t*-butoxide, some displacement on carbon occurred. Attempts to exchange azide XXI in *t*-butyl alcohol–potassium *t*-butoxide resulted in formation of the potassium sulfonate. Recovered azide showed no exchange. When methanol–potassium methoxide was used, the methyl sulfonate ester was formed. Even under drastic conditions 2,4-dinitrophenyl-2-octyl thioether (XV) could not be induced to undergo exchange.

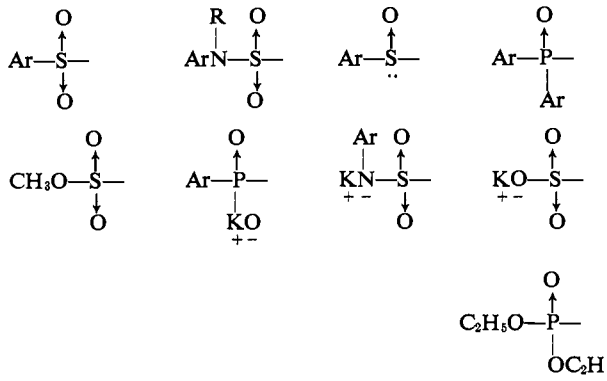
Discussion

Relation between Symmetry Properties of Carbanions and Structure of Attached Functional Groups. The carbon acids whose carbanions are stabilized by second-row-element functional groups fall into two distinct classes: (1) those whose exchange reactions exhibit values of k_e/k_α that are well in excess of unity; (2) those whose values are close to unity. The former systems appear to produce intrinsically asymmetric carbanions, which undergo substitution with high retention of configuration. The latter appear to owe the low stereospecificity of their substitution reactions to asymmetric solvation of an intrinsically symmetrical anion,[19] or of a pair of rapidly equilibrating enantiomeric anions within an asymmetric cavity.

Comparison of the structural features of these two classes of groups indicates that *those which induce asymmetry have two electronegative atoms that carry*

(19) D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press Inc., New York, N. Y., 1965, pp 88.

Functional groups that induce carbanion asymmetry



Functional groups that provide symmetrical carbanions or their equivalent

partial negative charge bound to the second-row element, and those which do not induce asymmetry carry either one or three such atoms. The presence or absence of a *formal* negative charge on the system seems to make no qualitative difference. Although the side reaction of some of the functional groups made it impossible to study the range of solvents needed to unequivocally separate asymmetric solvation effects from asymmetric carbanion effects, enough solvent data are available in Table I and from other studies[3b,4] to strongly support the above generalization. This correlation of carbanion symmetry properties with structure applies only to acyclic systems, since others have shown that incorporation of a sulfone-stabilized carbanion into a five-membered ring system leads to nonstereospecific reactions.[3e] To the extent that data are available (only sulfone systems), the generalization applies to carbanions generated with either hydrogen or carbon leaving groups.[3c,3g] Data on other systems are desirable.

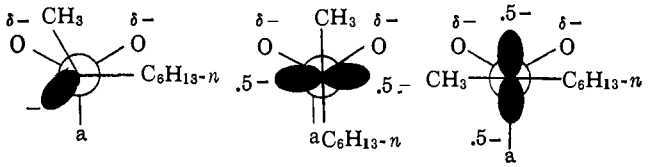
Nature of Asymmetry of Carbanions Stabilized by Functional Groups Centered around Second-Row Elements. Sulfone system I is the prototype of IV, V, and VI, and has been the most studied. Two general explanations have been advanced for the asymmetry induced in the carbanion by the sulfone group. (1) The carbanion is tetrahedral, and the partial charge on the oxygens provides electrostatic inhibition of inversion (and hence racemization) of this asymmetric species.[3b] (2) The carbanion is planar, is formed and captured in an asymmetric conformation for electrostatic and steric reasons, and rotation of the carbanion is slower than proton capture.[3b,e,g] The correlation between structure and symmetry properties of attached carbanions stated above is compatible with either type of these two asymmetric structures. Chart I indicates how a pyramidal carbanion structure conforms to the generalization, and Chart II how a planar might explain the same facts.

Examination of the pK_a's of a large number of cyclic and acyclic sulfones led to the conclusion that overlap between the d orbitals of second-row elements and the orbital occupied by the two electrons of the carbanion did not have configurational or conformational requirements that outweighed electrostatic or solvation requirements.[20] The same might be true of the other functional groups of this study. If carbanions are pyramidal, the electrons are in an orbital richer in s character (sp^3) than if they are planar (p), and the higher the s character, the more nuclear and electronic charge separation is minimized. Furthermore, in those carbon acids that provide asymmetric carbanions, electrostatic repulsion between the carbanion and the two negative oxygens is minimized with a pyramidal configuration and a particular conformation. Carbanion inversion is also electrostatically inhibited, which might make proton capture the faster process. The presence of either one or three negative atoms on the functional group provides less driving force for a pyramidal configuration to start with, and less of an electrostatic barrier to inversion of a pyramidal carbanion.

If the carbanion is presumed to be trigonal, then the asymmetry of systems that contain two negative oxygens must be due to formation and consumption of the carbanion when it is in an asymmetric conformation (see Chart II), possibly the one that minimizes electrostatic repulsions. Furthermore, the leaving and entering groups must be involved only with the same face

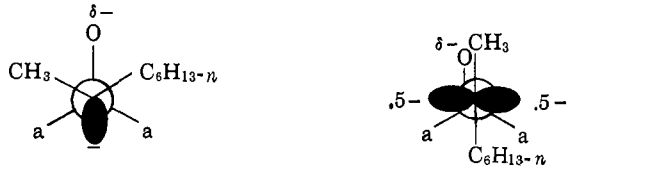
(20) See ref 19, p 80.

Chart I. Pyramidal Carbanions Stabilized by Functional Groups Centered around Second-Row Elements



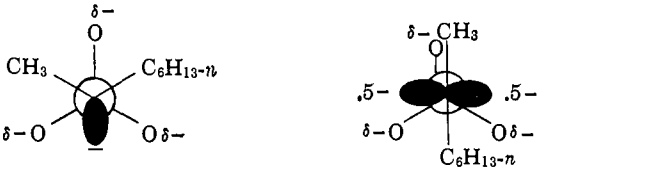
conformation and hybridization that minimize electrostatic repulsion

possible transition states for pyramidal carbanion inversion; charges are concentrated compared to ground state



conformation and hybridization that minimize electrostatic repulsion

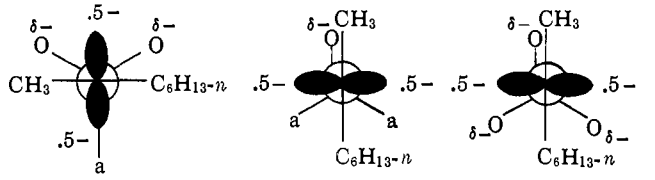
transition state that minimizes electrostatic repulsion; not much different electrostatically from the ground state



one of three conformations and the hybridization that minimize electrostatic repulsion

one of three transition states that minimize electrostatic repulsion; not much different electrostatically from ground state

Chart II. Trigonal Carbanions Stabilized by Functional Groups Centered around Second-Row Elements. Conformations that Minimize Electrostatic Repulsion in Transition State for Carbanion Formation and Consumption



asymmetric

symmetric

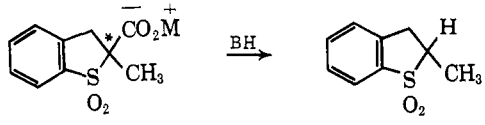
symmetric

of the carbanion to provide the observed substitution with retention of configuration. With systems whose functional groups contain one or three negative atoms, the conformations that minimize electrostatic repulsion are symmetrical.

The results do not allow a differentiation of the two general types of asymmetry. A blend of the two might even apply.

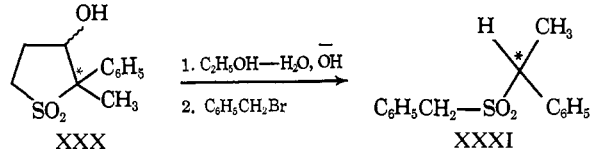
Sulfonanilide VII provided values of k_e/k_α (2–2.9) somewhat higher than the other systems that provided symmetrical carbanions (1.1–1.7). This result may reflect a slightly unequal negative charge distribution between the two oxygens and the nitrogen atom, which between them possess one formal negative charge. Had the charge been very largely concentrated on the two oxygens, much higher stereospecificity would be anticipated.

Corey and co-workers[3e,g] devised three sulfone systems whose stereochemical behavior on electrophilic substitution bears on the question of carbanion geometry. Although the experiments are ingenious and the results interesting, in our view they do not provide a basis for unequivocal choice between the two types of asymmetry. In contrast to open-chain analogs, optically active salt, XXVIII, was reported to decarboxylate to give racemic XXIX. The enforced conformation for the anion of XXIX provides no electrostatic driving force for a pyramidal configuration, nor an electrostatic barrier to rapid inversion if the carbanion was pyramidal. Thus the cyclic system is a poor model for an open-chain system.



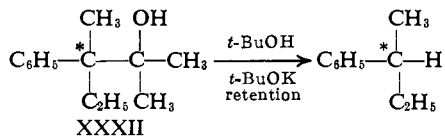
XXVIII, optically active — XXIX, racemic

Cyclic system XXX was found[3f] to cleave to give XXXI with high inversion of configuration. This unusual result with a sulfone can be explained equally well with either a planar or pyramidal carbanion. The essential element that provides inversion may be



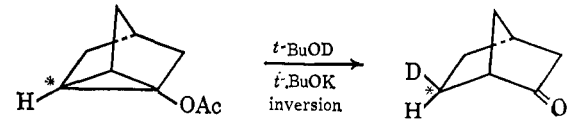
XXX — XXXI

that the leaving carbonyl group is part of a ring system, and as such shields (solvates) the front of the carbanion from proton donors, until eventually proton capture occurs from the rear. Analogy for a switch in stereochemistry in passing from an open-chain to a ring system is found in the facts that in *t*-butyl alcohol–potassium *t*-butoxide, XXXII cleaves to give high retention[21] whereas XXXIII gives high inversion.[22]



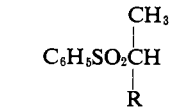
XXXII

(21) D. J. Cram, F. Hauk, K. R. Kopecky, and W. D. Nielsen, *J. Am. Chem. Soc.*, **81**, 5767 (1959).



XXXIII

Compound XXXIV was found to undergo base-catalyzed hydrogen–deuterium exchange at a rate of about four powers of ten faster than I, but the stereochemical courses in the two systems were comparable (k_e/k_α = 41–44).[3e] The rate enhancement



XXXIV, R = C_6H_5
I, R = C_6H_{13}-*n*

for XXXIV compared to I involves at least three factors: the electron-releasing inductive effect of the hexyl groups of I, the electron-withdrawing inductive effect of the phenyl in XXXIV, and the charge delocalizing ability of aryl. At least two of the four powers of ten can be attributed to the two inductive effects,[23] which leaves a maximum of two powers of ten attributable to the delocalization effect The difference in rate of base-catalyzed isotopic exchange of methane and toluene is probably at least five powers of ten,[24] and thus less than half of the full electron-delocalizing effect of the phenyl group of XXXIV is felt in carbanion stabilization. Although electron delocalization is best if the electron pair is in a p orbital, considerable delocalization is possible if the pair occupies an sp^3 orbital. Thus it is far from clear whether the carbanion of XXXIV is planar or pyramidal, or in between.

Experimental Section

Physical Data. All melting points are uncorrected, and all temperatures are in degrees Centigrade. Rotations were taken in a Zeiss circular polarimeter (+0.02° observed). All deuterium combustion analyses were performed by J. Nemeth (Urbana, Ill.) by the combustion and falling-drop method.

Infrared spectra were taken with a Beckman IR-5 or a Perkin-Elmer IR-21 spectrophotometer. Nuclear magnetic resonance spectra were taken with a Varian Associates A-60 spectrometer.

In many of the following sections the detailed procedures for preparation of the racemic materials are described in detail, and then the results for optically active materials summarized.

(±)-2-Octyl Mercaptan (XIII). Application of the S-alkylthiouronium salt reaction with 2-octyl tosylate[25] gave only a 36% yield of 2-dioctyl disulfide, bp 150–160° (1.5 mm). A more satisfactory method was as follows. To absolute ethanol, 370 ml (dried over Linde molecular sieves), was added in small portions under dry pure nitrogen with cooling 50.4 g of potassium metal. After reaction was complete, dry hydrogen gas was introduced underneath the surface with stirring and cooling. After no more precipitate formed, 147 g of 2-octyl tosylate was added dropwise over a period of 1 hr while hydrogen sulfide was also bubbled through the cooled (ice) stirred solution. The solution was then stirred at 25° for 1 hr and at 100° for 1 hr with hydrogen sulfide flowing into the system. The solution was cooled and shaken with 400 ml of water. The organic layer was separated, the water layer extracted with three 125-ml portions of ether, and the organic layers were combined. The solution was washed with water, dried, and evaporated to a colorless oil which was distilled. Three fractions were collected, 2-

(22) A. Nickon, J. H. Hammons, J. L. Lambert, and R. O. Williams, *ibid.*, **85**, 3713 (1963).
(23) See ref 19, p 55.
(24) See ref 19, p 19.
(25) G. G. Urquhart, J. W. Gates, Jr., and R. Connor in "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p 363.

octyl mercaptan (XIII), 44.6 g (59%), bp 81–83 (36 mm); a red oil, 0.5 g, bp 60° (1.5 mm); and 12.4 g (17%) of di-2-octyl disulfide (XII), bp 120–130° (1.5 mm). *Anal.* Calcd for $C_{16}H_{34}S_2$: C, 66.13; H, 11.79. Found: C, 66.09; H, 11.87.

The disulfide (XII) was reduced to the mercaptan (XIII) as follows. Lithium aluminum hydride (0.404 g) was mixed with purified tetrahydrofuran, and 3.3 g of the disulfide was added over a period of 15 min under nitrogen. The mixture was then held at reflux for 20 min and cooled to 0°, and the excess reagent was decomposed cautiously with 10 ml of water. The mixture was acidified, and the product (XIII) was isolated by the usual extraction procedure and distilled under vacuum to give 2.6 g (82%) of mercaptan.

2-Octylsulfonic Acid Potassium Salt (VIII). To concentrated nitric acid (75 ml) was added dropwise 43 g of the mercaptan with stirring over a period of 2 hr. Reaction was initiated with heat (steam bath), but once initiated was very exothermic and self-sustaining. After addition was complete, the reaction mixture was refluxed for 15 hr and evaporated in an air stream to near dryness, and the residue was dissolved in 100 ml of water. The aqueous solution was extracted with 100 ml of ether. The water was evaporated, fresh water was added and evaporated, and the process was repeated until a negative test (ferrous sulfate) for nitrate ion was obtained. The acid was obtained as a dark yellow oil very soluble in water and somewhat less soluble in ether. A water solution of the acid was neutralized with potassium carbonate, evaporated to dryness, and dried at 100° under vacuum. An infrared spectrum (potassium bromide pellet) showed the presence of potassium sulfate. The salt was recrystallized from absolute ethanol in a cold room. The material quickly turned to an oil at 25°, and extensive foaming occurred. The product was placed in a desiccator evacuated in the cold room. Once dry, this salt could be heated to 300° without melting. After two additional recrystallizations, 21.5 g (32%) of pure salt, free of sulfate (infrared spectrum), was obtained. The dry salt was moderately hydroscopic, and was dried at 100° for several days at 100° before analysis. *Anal.* Calcd for $C_8H_{17}KO_3S$: C, 41.34; H, 7.38; K, 16.82. Found: C, 40.09; H, 7.24; K, 16.63. The carbon value is unreliable in the presence of potassium due to potassium carbonate formation during combustion, which results in low values, as was observed.

(+)-2-Octylsulfonic Acid Potassium Salt ((+)-VIII-*h*). The substance (+)-2-octanol (51.0 g, $[\alpha]^{28}_{546}$ +11.55, neat)[5a] was converted to its tosylate[5a,26] which in turn was converted to 35.4 g (62%) of (−)-2-octyl mercaptan ((−)-XIII), $[\alpha]^{28}_{546}$ −36.9° (*c* 4.45, absolute ethanol), $n^{25}D$ 1.4476 (lit. $n^{25}D$ 1.4481[27]). The disulfide formed (7.2 g) was reduced to the mercaptan, which was added to the main sample. The combined sample (34.0 g) was oxidized to the salt which was recrystallized six times from absolute ethanol to give 21.5 g (40%) of pure material ((+)-VIII-*h*), $[\alpha]^{32}_{546}$ +12.04° (*c* 5.48, water). *Anal.* Calcd for $C_8H_{17}KO_3S$: K, 16.82. Found: K, 16.99.

(−)-2-Octyl-2-*d*-sulfonic Acid Potassium Salt ((−)-VIII-*d*). Labeled (−)-2-octanol-2-d[5a,28] (59.5 g, $[\alpha]^{24}_{546}$ −11.56°, neat) was converted to 43.2 g (65%) of mercaptan (+)-XIII-*d*, $[\alpha]^{26}_{546}$ +37.3 (neat),[29] $[\alpha]^{26}_{546}$ +37.6° (*c* 5.05, absolute ethanol), $n^{25}D$ 1.4482. This material exhibited a weak C–D stretching band at 2160 cm^{-1} in its infrared spectrum. Oxidation of 29.5 g of (+)-XIII-*d* gave 22.5 g (0.096 mole or 48%) of (−)-VIII-*d*, $[\alpha]^{27}_{546}$ −12.13° (*c* 5.03, water). Deuterium analysis of this material gave 1.01 atoms of deuterium per molecule. No C–D stretching bands were identifiable in the infrared spectrum of the substance in a potassium bromide pellet.

2-Octylsulfonyl Chloride (XIV). Thoroughly dried sulfonic acid potassium salt (VIII), 7.5 g, and 15 g of phosphorus pentachloride (Baker Analyzed) were warmed and stirred in a dry atmosphere at 110° for 30 min while the liquid that formed gently refluxed. The mixture was cooled and dissolved in 75 ml of benzene, and the potassium chloride that separated was filtered and washed with benzene. The combined filtrates were washed at 0° with two 20-ml portions of ice water, dried, and evaporated. The resulting yellow oil was distilled to give 4.0 g (59%) of sulfonyl chloride XIV, bp 85–92° (1 mm).[11,30]

(−)-2-Octylsulfonyl Chloride ((−)-XIV). Potassium salt, (+)-VIII-*h*, 37.7 g, was converted to its sulfonyl chloride (see above procedure). The crude product, 20 g, was chromatographed on a 225-g silica gel (Baker Analyzed Reagent, 80–200 mesh) column, 200-ml fractions being collected. The product, 8.97 g (26%), was eluted with 1% ether–99% pentane, $[\alpha]^{28}_{546}$ −2.72° (*c* 8.63, absolute ethanol), $[\alpha]^{28}_{546}$ −1.12° (neat, *l* = 1 dm), $n^{25}D$ 1.4608.

Conversion of 2-Octylsulfonyl Chloride (XIV) to 2-Octyl Mercaptan (XIII). To a stirred mixture of 2.4 g of lithium aluminum hydride and 25 ml of purified tetrahydrofuran was added dropwise under pure nitrogen at 0° a solution of 4.5 g of 2-octylsulfonyl chloride in 10 ml of purified tetrahydrofuran. After addition (30 min) the mixture was refluxed for 90 min, after which time hydrogen was no longer evolved. The mixture was cooled to 0°, the excess reagent was cautiously destroyed with water, 15% sulfuric acid was added, and the product was isolated by extraction in the usual way and distilled to give 1.42 g (46%) of 2-octyl mercaptan, bp 90° (35 min). This material was subjected to analytical vpc chromatography on a dual column programmed temperature gas chromatograph with a column of 20% silicone gum on firebrick, a temperature of 90–120°, and a helium pressure of 6 psi. The mercaptan came off at 102° after 12 min. Two impurities came off with shorter and one with a longer retention time.

2,4-Dinitrophenyl 2-Octyl Thioether (XV). To a stirred solution of 0.12 g of sodium hydroxide and 0.44 g of 2-octyl mercaptan in 5 ml of methanol was added 0.6 g of 1-chloro-2,4-dinitrobenzene dissolved in 5 ml of methanol. The resulting yellow solution was held at reflux for 10 min, filtered while hot, cooled, and shaken with water and ether. The water layer was washed with ether and the combined extracts were dried and evaporated. The residual oil was chromatographed on 25 g of silica gel (100-ml fractions). The desired thioether (XV) was eluted with 97% pentane–3% ether, and was crystallized from ethanol water to give 0.5 g (53%), mp 49.5–50.0°. *Anal.* Calcd for $C_{14}H_{20}N_2O_4S$: C, 53.83; H, 6.45. Found: C, 53.78; H, 6.33.

(−)-2,4-Dinitrophenyl 2-Octyl-2-*d* Thioether ((−)-XV-*d*). Application of the above procedure to 0.44 g of (+)-XIII-*d*, $[\alpha]^{26}_{546}$ +37.3° (neat), gave 0.58 g (62%) of thioether, (−)-XV-*d*, $[\alpha]^{27}_{546}$ −52.45° (*c* 5.72, chloroform), mp 54–54.6°. The substance analyzed for 0.996 atom of deuterium per molecule.

Control of Fractionation during Preparation and Chromatography of 2,4-Dinitrophenyl 2-Octyl Thioether. To eliminate the possibility of racemate enantiomer fractionation during chromatography of thioether XV, 0.2204 g of (+)-XIII-*d* of $[\alpha]^{26}_{546}$ +37.3° (neat) and 0.2216 g of racemic XIII-*h* were mixed and converted to 0.601 g (64%) of thioether XV, $[\alpha]^{27}_{546}$ −26.15° (*c* 5.35, chloroform). This rotation differed by 0.35% from that calculated (−26.06°) assuming no fractionation.

Conversion of (−)-2-Octylsulfonic Acid Potassium Salt ((−)-VIII-*d*) to (−)-2,4-Dinitrophenyl 2-Octyl-2-*d* Thioether ((−)-XV-*d*). Dry potassium salt (−)-VII-*d*, 7 g, $[\alpha]^{27}_{546}$ −12.13° (*c* 5.03, water), was converted to its sulfonyl chloride ((+)-XIV) in 70% yield (4.5 g). This material was reduced with lithium aluminum hydride to mercaptan (+)-XIII-*d*, which was distilled to give 1.64 g, $[\alpha]^{27}_{546}$ +22.66° (*c* 5.34, absolute ethanol), of impure material. A sample of this impure material was submitted to analytical vpc as before, the column being programmed at 1° rise per minute. Three components were detected: impurity, 15.5% came off at 100° after 10 min; (+)-XIII-*d*, 73% came off at 104° after 14 min; impurity, 11.5% came off at 110° after 20 min. A small sample, 0.44 g, of impure (+)-XIII-*d* was converted to 0.37 g (39%) of thioether (−)-XV-*d*, $[\alpha]^{27}_{546}$ −51.60° (*c* 4.43, chloroform), mp 53.4–54.0°. This material analyzed for 0.976 atom of deuterium per molecule.

2-Octyl Thiocyanate (XVI). Acetone, 150 ml dried over Linde molecular sieves, and 30 g of potassium thiocyanate (Baker Analyzed Reagent) were stirred at reflux, and 25 g of 2-octyl tosylate was added dropwise (20 min). The solution was refluxed for 6 hr, filtered, and evaporated to give an orange residue. This material was shaken with pentane and water, and the pentane layer was washed, dried, and evaporated to give 12.5 g (83%) of yellow-orange oil. An infrared spectrum of this material indicated it to be a mixture of 2-octyl thiocyanate and isothiocyanate. The thiocyanate exhibited a very sharp peak at 2155 cm^{-1}, while the isocyanate a broad peak at 2080 cm^{-1}.[31] To this material was added 5.5 g of cyclohexylamine and 15 ml of cyclohexane. When cooled to −5° for 12 hr,

(26) A. Streitwieser, Jr., and W. D. Schaeffer, *J. Am. Chem. Soc.*, **78**, 5597 (1956).
(27) L. M. Ellis, Jr., and E. E. Reid, *ibid.*, **54**, 1674 (1932).
(28) A. Streitwieser, Jr., *ibid.*, **75**, 5014 (1953).
(29) d^{24}_4 0.8329 (ref 27).
(30) J. M. Sprague and T. B. Johnson, *J. Am. Chem. Soc.*, **59**, 1837 (1937).
(31) (a) A. Iliceto, A. Fava, V. Mazzicato, and O. Rossetto, *ibid.*, **83**, 2729 (1961); (b) L. S. Luskin, G. E. Gantert, and W. E. Craig, *ibid.*, **78**, 4965 (1956).

crystals separated, which were collected. The filtrate was extracted with 10% hydrochloric acid, washed with water, dried, and evaporated to give 7.6 g (50%) of 2-octyl thiocyanate.

(−)-2-Octyl Thiocyanate ((−)-XVI-*h*). From (+)-2-octanol, 12.2 g, $[\alpha]^{28}_{546}$ +11.55° (neat), was obtained 25.3 g of the corresponding tosylate, which was converted to its corresponding thiocyanate. The product was distilled to give 7.35 g (46%) of (−)-2-octyl thiocyanate, $[\alpha]^{28}_{546}$ −83.3° (*c* 5.04, absolute ethanol) and $[\alpha]^{28}_{546}$ −143.85° (*c* 5.04, absolute ethanol), bp 72–74 (0.8 mm), $n^{25}D$ 1.4604. *Anal.* Calcd for $C_9H_{17}NS$: C, 63.10; H, 10.00. Found: C, 63.27; H, 10.19.

Oxidation of (−)-2-Octyl Thiocyanate ((−)-XVI-*h*) to (+)-2-Octylsulfonic Acid Potassium Salt ((+)-VIII-*h*). A mixture of 13.3 ml of concentrated nitric acid, 1.7 ml of water, and 4.25 g of (−)-2-octyl thiocyanate was held at reflux for 4 hr, and an additional 13.3 ml of concentrated nitric acid and 1.7 ml of water were added. The mixture was held at reflux for 20 more hr. The resulting clear solution was treated as in the previous procedure to give after one recrystallization 4.6 g (80%) of potassium salt, (+)-VIII-*h*. This slightly yellow material gave $[\alpha]^{25.5}_{546}$ +7.96° (*c* 5.15, water). After four additional recrystallizations a constant rotation of $[\alpha]^{27}_{546}$ +8.01° (*c* 5.12, water) was obtained.

2-Octylsulfonyl Chloride (XIV) by Oxidative Chlorination of Di-2-octyl Disulfide (XII). The procedure of Douglass, *et al.*,[12] was applied with some modification. A mixture of di-2-octyl disulfide, 10 g, in 4.15 g of glacial acetic acid was cooled under nitrogen to −10°, and chlorine gas, 7.35 g, was slowly bubbled into the solution with stirring. As the chlorine was added, the solution turned a slight yellow and became less viscous. Near the end of the addition, the solution was cooled to −20°, and after all the chlorine had been added, the solution was allowed to warm to 25°, whereupon gas was evolved. The acetyl chloride was evaporated under reduced pressure, and 20 ml of water was added to give two layers. Chlorine gas was bubbled into the mixture until saturation occurred (temperature was about 40°). The mixture was then extracted twice with ether, and the ether extracts were dried and evaporated, and the residual oil was distilled to give 6.9 g (47%) of the sulfonyl chloride, bp 91–97° (1 mm). *Anal.* Calcd for $C_8H_{17}ClO_2S$: C, 45.16; H, 8.05. Found: C, 45.06; H, 8.16.

Attempts to prepare the same sulfonyl chloride from 2-octyl mercaptan produced a mixture of the desired product and product in which the octyl groups had been chlorinated.

Oxidation of (+)-2-Octyl-2-*d* Mercaptan ((+)XIII-*d*) to (+)-Di-2-octyl-2-*d* Disulfide ((+)-XII-*d*). The method was patterned after that of McAllan, *et al.*[32] To an ice-cold solution of 16.28 g of sodium hydroxide and 0.09 g of potassium iodide in 115 ml of distilled water was added dropwise with stirring 59.8 g of (+)-2-octyl-2-*d* mercaptan. After the addition was about half complete, sodium mercaptide separated, but solution was effected by addition of ethanol. The solution was stirred for 10 min after addition was complete, and 51.78 g of iodine was slowly added in small portions. The mixture was stirred for 30 additional min, and the excess iodine was destroyed with sodium thiosulfate. The organic layer was separated, and the water layer was extracted with pentane. The combined organic layers were washed three times with water, dried, and evaporated. The residual oil was distilled to give 45.76 g (77%) of (+)-XII-*d*, $[\alpha]^{30}_{546}$ +68.95° (*c* 6.86, absolute ethanol), $n^{25}D$ 1.4815. The infrared spectrum of this material exhibited a weak C–D stretching band at 2160 cm^{-1}.

(+)-2-Octyl-2-*d*-sulfonyl Chloride ((+)-XIV-*d*) by Oxidative Chlorination of Di-(+)-2-octyl-2-*d* Disulfide ((+)-XII-*d*). Disulfide (+)-XII-*d*, 48.10 g, $[\alpha]^{30}_{546}$ +68.95° (*c* 6.68, absolute ethanol), was oxidized with chlorine (see above) to give 22.19 g (63%) of sulfonyl chloride, $[\alpha]^{26.5}_{546}$ +2.65° (*c* 8.31, absolute ethanol), $n^{25}D$ 1.4606.

A 1.3-g portion of this material was converted to 0.42 g (21%) of thioether (−)-XV-*d* as before. The product exhibited $[\alpha]^{28}_{546}$ −52.06° (*c* 5.19, chloroform) and had weak C–D bands in its infrared spectrum at 915, 1083, 1117, and 11.39 cm^{-1}. Analysis for deuterium revealed the presence of 0.950 atom of deuterium per molecule.

2-Octylsulfonyl Chloride (XIV) from 2-Octyl Chloride. The Grignard reagent, 2-octylmagnesium chloride, was prepared from 126 g of 2-octyl chloride and 22.43 g of dry magnesium turnings in 1 l. of ether under dry pure nitrogen. Anhydrous sulfur dioxide was bubbled into the solution which was held just below reflux temperature. A thick green precipitate of sulfinic acid salt separated. Over a period of 30 min, 175 g of sulfuryl chloride was added. The mixture was cooled to hold it just below reflux temperature. The resulting mixture (white precipitate) was stirred for 1 hr at 25° and filtered. The filtrate was evaporated, and the resulting mush was triturated with 600 ml of pentane and filtered. The pentane filtrate was dried and evaporated, and the residual oil was distilled to give 110 g (61%) of 2-octylsulfonyl chloride, bp 108–115° (4 mm), $n^{25}D$ 1.4602.

2-Octylsulfonamide (XVIII). To 40 ml of concentrated ammonium hydroxide was added 4.0 g of 2-octylsulfonyl chloride. The mixture was shaken in a closed system for 12 hr, and the solution was extracted with ether. The combined ether extracts were washed with water, dried, and evaporated. The residual oil was chromatographed on 100 g of silica gel, 200-ml fractions being collected. The product (XVIII) was eluted with 50% ether–50% benzene, and was recrystallized twice from ethanol–water to give 1.15 g (32%) of XVIII, mp 44.5–45°. *Anal.* Calcd for $C_8H_{19}NO_2S$: C, 49.70; H, 9.91. Found: C, 49.73; H, 9.76.

2-Octyl-N,N-dimethylsulfonamide (XVII). To 1.0 g of 2-octylsulfonyl chloride in 10 ml of absolute ether cooled to −20° was added 3 ml of dimethylamine in 4 ml of absolute ether. The mixture was allowed to come to 25° and 20 ml of 5% hydrochloric acid was added. The ether layer was separated, and the aqueous layer was washed with ether. The combined organic layers were dried and evaporated. The residual yellow oil was chromatographed on 35 g of silica gel, and 200-ml fractions were collected. The sulfonamide (XVII), 0.66 g (63%), was eluted with 17% ether–83% pentane, $n^{25}D$ 1.4552. *Anal.* Calcd for $C_{10}H_{23}NO_2S$: C, 54.26; H, 10.47. Found: C, 54.14; H, 10.45.

(−)-2-Octyl-2-*d*-N,N-dimethylsulfonamide ((−)-XVII-*d*). An ether solution of 0.90 g of sulfonyl chloride (+)-XIV-*d*, $[\alpha]^{28}_{546}$ +2.65° (*c* 8.31, absolute ethanol), which contained 0.976 atom of deuterium per molecule was treated with dimethylamine as before. The reaction time was 50 min, and the temperature was held below 0°. The sulfonamide, (−)-XVII-*d*, 0.276 g (30%), had $[\alpha]^{28}_{546}$ −5.88° (*c* 4.6, absolute ethanol), $n^{25}D$ 1.4552, and analyzed for only 0.531 atom of deuterium per molecule. Thus 46% of the deuterium originally present in the sulfonamide was lost in the conversion.

2-Octylsulfonanilide (VII). To a stirred mixture of 75 ml of pyridine (Karl Fischer reagent) and 6.70 g of freshly distilled aniline was added under nitrogen at 25° 15.0 g of 2-octylsulfonyl chloride. After the mixture had stirred for 7 min at 25°, it was heated for 20 min at 95°. The dark red-orange solution was cooled, and then poured onto a mixture of 300 ml of ice and 75 ml of concentrated hydrochloric acid. This mixture was extracted with four 100-ml portions of pentane; the combined extracts were washed with water, dried, and evaporated to give 12 g of oil. This material was chromatographed on 453 g of silica gel, and 400-ml fractions were collected. The product was eluted with 15% ether–85% pentane, and was obtained as a yellow oil, 8.50 g (45%). *Anal.* Calcd for $C_{14}H_{23}NO_2S$: C, 62.41; H, 8.61. Found: C, 62.22; H, 8.48.

(+)-2-Octylsulfonanilide ((+)-VII-*h*). The minimum conditions for sulfonanilide formation were determined by following the disappearance of the sulfonyl chloride by use of thin layer chromatography (75° for 30 min). From 8.05 g of (−)-sulfonyl chloride (optically pure) was obtained 6.00 g of sulfonanilide ((+)-VII), $[\alpha]^{26}_{546}$ +21.58° (*c* 5.19, chloroform). *Anal.* Calcd for $C_{14}H_{23}NO_2S$: C, 62.41; H, 8.61. Found: 62.37; H, 8.40.

(−)-2-Octylsulfonanilide ((−)-VII-*d*). Under the above minimum reaction conditions, 5.00 g of (+)-XIV-*d* (optically pure) was converted to (−)-VII-*d*, 4.03 g (65%), $[\alpha]^{28}_{546}$ −25.08° (*c* 6.50, chloroform). This material exhibited a weak band in the infrared spectrum associated with deuterium substitution at 1097 cm^{-1} and shoulders between 1124 and 1163 cm^{-1}. The region near 915 cm^{-1} was obscured by another band. The substance analyzed for 0.88 atom of deuterium per molecule.

2-Octyl-N-methylsulfonanilide (IV). To a mixture stirred under dry nitrogen of 6 ml of dry pure pyridine and 0.70 g of dry pure N-methylaniline was added dropwise at 25°, 1.2 g of 2-octylsulfonyl chloride. The mixture was stirred for 20 min at 25° and for 30 min at reflux (under dry nitrogen). The mixture was cooled and stirred with 20 ml of water, 40 ml of ice, and 10 ml of concentrated hydrochloric acid. The mixture was extracted with pentane, and the combined pentane extracts were washed with water, dried, and evaporated. The residual brown oil was chromatographed on 25 g of silica gel, and 100-ml fractions were collected. The desired product, 0.41 g (27%), was eluted with 5% ether–95% pentane. *Anal.* Calcd for $C_{15}H_{25}NO_2S$: C, 63.56; H, 8.89. Found: C, 63.80; H, 8.88.

(32) D. T. McAllan, T. V. Cullum, R. A. Dean, and F. A. Fidler, *J. Am. Chem. Soc.*, 73, 3627 (1951).

(−)-2-Octyl-N-methylsulfonanilide ((−)-IV-*h*). Optically pure (+)-2-octylsulfonyl chloride, 8.63 g, was converted in 16% yield to its N-methylsulfonanilide, mp 34.5–35°, $[\alpha]^{26}_{545}$ −18.27 (*c* 5.58, absolute ethanol). *Anal.* Calcd for $C_{15}H_{25}SO_2N$: C, 63.56; H, 8.69. Found: C, 63.43; H, 8.90.

(−)-2-Octyl-2-*d*-N-methylsulfonanilide ((−)-IV-*d*). Optically pure (+)-2-octyl-2-*d*-sulfonyl chloride, 1.1 g, was converted to its N-methylanilide in 16% yield, mp 38.2–38.4°, $[\alpha]^{28}_{546}$ −18.35° (*c* 5.34, absolute ethanol). This material showed a weak deuteration band in the infrared spectrum at 1119 and at 1134 cm^{-1}, and shoulders between 1060 and 1090 cm^{-1}. The region near 915 cm^{-1} was obscured by another peak. The substance analyzed for 0.97 atom of deuterium per molecule.

A similar preparation gave (−)-IV-*d* in 23% yield, $[\alpha]^{27}_{546}$ 18.31° (*c* 4.86, absolute ethanol), mp 38°. This material analyzed for 0.95 atom of deuterium per molecule.

(+)-Methyl 2-Octylsulfonate ((+)-V-*h*). An ethereal solution of approximately 6 g of diazomethane in ether was slowly added in portions to 20.0 g of optically pure (+)-2-octylsulfonic acid dissolved in 100 ml of absolute ether at −70°. The addition was stopped when the characteristic color of diazomethane was no longer discharged. The solution was then allowed to warm to 25°, the ether was evaporated, and the residue, 23.32 g, was chromatographed on 200 g of silica gel, and 200-ml fractions were collected. The ester, (+)-V-*h*, 7.82 g (37%), was eluted with 5% ether–95% pentane, and was distilled at 74–76° (0.23 mm), $[\alpha]^{25}_{546}$ +5.62° (neat, *l* = 1 dm), $n^{25}D$ 1.4408. *Anal.* Calcd for $C_9H_{20}O_3S$: C, 51.89; H, 9.68. Found: C, 51.95; H, 9.76.

(+)-Methyl 2-Octyl-2-*d*-sulfonate ((+)-V-*d*). Optically pure (+)-2-octyl-2-*d*-sulfonic acid, 20.0 g, was converted to 16.7 g (78%) of its methyl ester, α^{27}_{546} +5.52 (neat, *l* = 1 dm), $n^{25}D$ 1.4407. This material exhibited weak deuteration bands in its infrared spectrum at 927, 1098, 1126, and 1147 cm^{-1}, and analyzed for 0.93 atom of deuterium per molecule. The 2–3% loss of deuterium probably occurred in an earlier synthetic step when the sulfonic acid was overheated. This ester was not used in this study.

2,4,6-Trimethylphenyl 2-Octylsulfonate (XX). To a stirred slightly cooled solution of 1.0 g of 2,4,6-trimethylphenol in 20 ml of dry tetrahydrofuran under nitrogen was added 0.12 g of clean sodium metal. To the resulting purple solution was slowly added a solution of 1.0 g of 2-octyl-2-sulfonyl chloride in 10 ml of dry tetrahydrofuran. The mixture was filtered, solvent was evaporated, and the residue chromatographed on 150 g of silica gel. The ester (XX), 0.513 g (34%), was eluted with 2% ether–98% pentane, $n^{25}D$ 1.4952. *Anal.* Calcd for $C_{17}H_{28}O_3S$: C, 65.34; H, 9.03. Found: C, 65.52; H, 9.14.

2-Octylsulfonyl Azide (XXI). To sodium azide, 9.75 g, in 60 ml of water and 200 ml of ethanol was added dropwise 25 g of 2 octylsulfonyl chloride in 60 ml of ethanol. The mixture was stirred for 1 hr at 25°, and for 30 min at 65°. The cooled solution was mixed with 400 ml of water and pentane. The pentane extract was washed with water, dried, and evaporated to give 23.5 g of crude material, which was chromatographed on 500 g of silica gel (400-ml fractions were collected). The product was eluted with 1% ether–99% pentane and was rechromatographed to give 17.68 g (69% of azide XXI), $n^{25}D$ 1.4626. *Anal.* Calcd for $C_8H_{17}N_3O_2S$: C, 43.81; H, 7.81. Found: C, 43.78; H, 7.87. Several small-scale reactions were run that demonstrated the above conditions were minimal.

(−)-2-Octyl-2-*d*-sulfonyl Azide ((−)-XXI-*d*). Optically pure sulfonyl chloride (−)-XIV-*d*, 1.0 g, was converted to 0.89 (85%) of azide (−)-XXI-*d*, $[\alpha]^{27}_{546}$ −6.75° (*c* 5.04, chloroform), α^{27}_{546} −7.92 (neat, *l* = 1 dm), $n^{25}D$ 1.4626. This material exhibited weak deuteration bands in the infrared spectrum at 922, 1094, and 1124 cm^{-1} and a shoulder at 1145 cm^{-1}, and analyzed for 0.848 atom of deuterium per molecule. Thus, about 10% of the deuterium was lost during synthesis.

Deuterium–Hydrogen Exchange during Conversion of 2-Octylsulfonyl Azide to Methyl 2-Octylsulfonate (V). A solution of 7 ml of 0.45 *N* potassium methoxide in methanol-O-*d* (0.99 atom of deuterium per molecule) was added to 0.616 g of azide XXI. An immediate precipitate of potassium azide formed. After 5 min, the solution was shaken with water and pentane, and the pentane layer was washed with water, dried, and evaporated. The residue was distilled to give 0.356 g (61%) of ester V, which was pure to thin layer chromatography. This ester was shown to contain 0.916 atom of deuterium per molecule.

Treatment of azide XXI with triethylamine, benzene, and methanol at 25° produced no ester.

Deuterium–Hydrogen Exchange during Conversion of (−)-2-Octylsulfonyl Chloride ((−)-XIV-*h*) to Methyl 2-Octylsulfonate (V-*d*). A solution of 0.7 ml of triethylamine (dry, pure), 4.8 ml of methanol-O-*d* (0.99 atom of deuterium per molecule), and 9 ml of dry benzene was added to 0.897 g of (−)-XIV-*h*, α^{28}_{546} −1.12° (neat, *l* = 1 dm) at 23.5°. The disappearance of the sulfonyl chloride was followed by thin layer chromatography. The reaction was quenched with water at the end of 4 hr and the ester isolated as in the other experiments and distilled to give 0.353 g (40%) of methyl 2-octylsulfonate shown to be pure by thin layer chromatography. This material had no observable rotation (less than 5% of optical purity could have been detected). The material analyzed for 0.87 atom of deuterium per molecule.

(+)-Phenyl-2-octylphosphinic Acid *n*-Butyl Ester ((+)-XXII). To 13.6 g of sodium in 150 ml of dioxane (freshly distilled from lithium aluminum hydride) was added over a period of 1 hr phenylphosphinic acid *n*-butyl ester[16] (bp 89–90° at 0.1 mm), 130 g. The yellow suspension of the corresponding sodium salt was refluxed for 4 hr (stirring) in a nitrogen atmosphere. Optically pure (−)-2-octyl tosylate (prepared from (−)-2-octanol optically pure), 95 g, dissolved in 300 ml of purified dioxane was added. The yellow color faded and a white precipitate formed. The reaction mixture was refluxed for 8 hr under nitrogen. The mixture was cooled and wet ether was added, followed by 75 ml of water. The organic layer was washed with water and saturated sodium chloride solution, and the solvent was evaporated at reduced pressure. The residue, 105 g, was subjected to high-vacuum distillation (0.21 mm) to give two fractions, bp 118–122° (14.7 g) and bp 122–127 (42.0 g), and a 39.3-g residue. The 42-g fraction was chromatographed on silica gel (3 lb), 200-ml fractions being collected. The desired products were eluted with 75% ether–25% pentane. Fractions 43–54 contained 11.90 g of ester A, whose P→O bond exhibited a band at 1250 cm^{-1} in the infrared spectrum, $[\alpha]^{27}_{546}$ +0.306° (*c* 23, chloroform). Fractions 55–75 gave 18.21 g of ester B, whose P→O bond exhibited a band at 1235 cm^{-1} in the infrared spectrum; $[\alpha]^{27}_{546}$ +6.62° (*c* 19, chloroform). *Anal.* Calcd for $C_{18}H_{31}O_2P$: C, 69.64; H, 10.06. Found: C, 69.66; H, 10.07. These two esters are probably diastereomers, with the same configurations at carbon and different configurations at phosphorus. Ester B was used in the subsequent work.

(+)-Phenyl-2-octylphosphinic Acid ((+)-VI). This procedure was patterned after that applied to other esters.[17] Ester B (see above), 14.7 g, was dissolved in Ethyl Cellosolve (150 ml), and lithium chloride (6.05 g) was added. The reaction mixture was held at reflux with stirring for 48 hr, the solvent was evaporated under reduced pressure, and 15 ml of water and 15 ml of 0.5 *M* sodium hydroxide was added. The unhydrolyzed ester (10.8 g) was extracted with ether, and the water layer was acidified and extracted with ether. The ether was evaporated to give 2.38 g of acid, which was chromatographed on 30 g of silica gel, 50-ml fractions being collected. Product was collected with chloroform saturated with 90% formic acid as developer, 2.31 g, mp 34–36°, $[\alpha]^{27}_{546}$ +20.15° (*c* 10, chloroform). *Anal.* Calcd for $C_{14}H_{23}O_2P \cdot H_2O$: C, 61.74; H, 9.25. Found: C, 61.53; H, 9.22.

(+)-Diethyl 2-Octylphosphonate ((+)-IX). This preparation was patterned after that of others.[18] To a mixture of 4.60 g of sodium and 100 ml of pure dioxane (distilled from lithium aluminum hydride) stirred under pure nitrogen was added dropwise 30 g of diethyl phosphite dissolved in 50 ml of dioxane. The mixture was refluxed for 5 hr, and then optically pure (−)-2-octyl tosylate (49.7 g) dissolved in 100 ml of dry dioxane was added over a period of 1 hr. A white precipitate started to form immediately. The reaction mixture was refluxed under nitrogen for 24 hr, and cooled, and 300 ml of wet ether followed by 100 ml of water was added. The resulting layers were separated, and the water layer was washed three times with ether. The combined organic layers were washed with saturated sodium chloride solution, dried and evaporated under vacuum. The residual oil distilled at 89° (0.19 mm) to give 30.0 g (60%) of product. This material was chromatographed on 500 g of silica gel, and the product ((+)-IX) was eluted with 1:1 ether–pentane, 28 g, $[\alpha]^{26}_{546}$ +7.80° (*c* 20, chloroform). *Anal.* Calcd for $C_{12}H_{27}PO_3$: C, 57.57; H, 10.86. Found: C, 57.23; H, 10.89.

(+)-2-Octylphosphonic Acid Dichloridate ((+)-XXIV). Hydrolysis of (+)-diethyl 2-octylphosphonate was accomplished as follows.[33] A solution of 14.6 g of (+)-diester, $[\alpha]^{26}_{546}$ +7.80° (*c*

(33) G. M. Kosolapoff, *J. Am. Chem. Soc.*, 67, 1180 (1945).

21, chloroform), in 150 ml of concentrated hydrochloric acid was held at reflux for 15 hr, concentrated to 100 ml under reduced pressure, and extracted with ether (300 ml). The ether layer was washed three times with water, dried, and evaporated to give 10.8 g of a heavy syrup, $[\alpha]^{25}_{546}$ +11.85 (*c* 20, chloroform). This acid was analyzed as its anilinium salt, precipitated from an ether solution, mp 40° dec. *Anal.* Calcd for $C_{14}H_{26}O_3PN$: C, 58.52; H, 9.24. Found: C, 58.57; H, 9.18. This material, 9.0 g, and 20 g of thionyl chloride were heated at reflux for 15 hr, and then an additional 10 g of thionyl chloride was added and the mixture was refluxed for an additional 15 hr. The excess thionyl chloride was evaporated under reduced pressure, and the residue distilled at 83° (0.3 mm), $[\alpha]^{25}_{546}$ +4.48 (*c* 30, carbon tetrachloride), to give 9.5 g of product. *Anal.* Calcd for $C_8H_{17}POCl_2$: C, 41.57; H, 7.42. Found: C, 41.45; H, 7.51.

A sample of the above material (1.1 g) was hydrolyzed at 25° with 25 ml of saturated aqueous potassium carbonate solution for 48 hr. The resulting solution was acidified with dilute sulfuric acid and extracted with ether, and the ether solution was dried and evaporated to give (+)-2-octylphosphonic acid (0.85 g), $[\alpha]^{25}_{546}$ +11.70 (*c* 28, chloroform).

2-Octylphosphonic Acid Piperidino Chloridate ((+)-XXV). To a solution of 8.0 g of the above dichloride ((+)-XXIV) in 200 ml of dry ether under pure nitrogen was added 5.84 g of dry piperidine in 200 ml of dry ether with stirring at 25°. The solvent was evaporated under reduced pressure and the residual oil was chromatographed on 100 g of silica gel. Product was eluted with 9:1 ether to give 6.0 g (66%) of XXI (no satisfactory rotation was obtained due to insolubility and reactivity). *Anal.* Calcd for $C_{13}H_{27}OPClN$: C, 58.74; H, 10.24. Found: C, 58.87; H, 10.38.

A sample of this material (2.9 g) was stirred for 3 days at 27° in 25 ml of 1 *N* hydrochloric acid. The solution was then extracted with ether, the ether solution was washed with water and dried, and the solvent was evaporated to give 2.1 g of (+)-2-octylphosphonic acid, $[\alpha]^{25}_{546}$ +8.87 (*c* 29, chloroform). This material gave a neutralization equivalent of 1.98, calculated 2.00. The rotation indicates that the acid is 23% racemized.

2-Octylphosphonic Acid Piperidinamide ((+)-XXVI). The above chloro amide ((+)-XXV, 6 g) was dissolved in 50 ml of acetone and added to a solution of 5.1 g of potassium bicarbonate in 50 ml of water. The solution was held at reflux for 24 hr. The basic solution was washed three times with ether, cooled to 0°, and acidified with cold 2 *N* hydrochloric acid to a pH of 3. The resulting aqueous solution was extracted three times with ether and the ether layer was washed twice with water and once with saturated sodium chloride solution. The solvent was evaporated and the residue dried by distilling from it 100 ml of benzene, 4.5 g (81%). The material was dried as a film for 18 hr at 100° (0.1 mm). *Anal.* Calcd for $C_{13}H_{28}PO_2N$: C, 59.74; H, 10.80. Calcd for $C_{13}H_{28}PO_2N \cdot 3H_2O$; C, 49.54; H, 10.86. Found: C, 49.22; H, 10.80.

A sample of this material (3.3 g) was hydrolyzed by the same method applied to chloro amide XXV to give 1.8 g of 2-octylphosphonic acid, $[\alpha]^{26}_{546}$ +8.92 (*c* 21.8, chloroform). This material is 22% racemized.

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. Deuterated *t*-butyl alcohol (0.97 atom of deuterium per molecule) was prepared as before[3b] and stored over molecular sieves. The basic solutions were prepared by adding clean potassium metal to the solvent under dry nitrogen. Ethylene glycol was similarly purified and stored, and its potassium salt was similarly prepared (low temperature). Dimethyl sulfoxide was purified and stored in the same way. The basic solution in dimethyl sulfoxide was prepared by dissolving clean potassium in methanol under dry nitrogen at low temperature and adding the resulting solution to dimethyl sulfoxide. Methanol was refluxed and distilled from calcium hydride and then stored over molecular sieves. Methanol-O-*d* (0.99 atom of deuterium per molecule) was prepared as before.[3b] Final base concentrations were obtained by titrations with standard acid. Nitrogen was purified by passing it through calcium sulfate and ascarite, and then through copper turnings heated to 300°, and finally again over calcium sulfate and ascarite.

Isotopic Exchange of (−)-2-Octyl-2-*d*-sulfonic Acid Potassium Salt ((−)-VIII-*d*) with Potassium *t*-Butoxide in *t*-Butyl Alcohol. A heavy walled glass tube was charged with 0.897 g of (−)-VIII-*d*, $[\alpha]^{28}_{546}$ −12.13° (*c* 5.03, water), and 15 ml of 1.11 *N* potassium *t*-butoxide in *t*-butyl alcohol. The tube was flushed with purified nitrogen, sealed, and heated in an oil bath (only submerged to the meniscus, halfway up the tube) for 60 hr at 146°. The product was cooled, dissolved in 25 ml of water, and titrated with 32.56 ml of 0.5113 *N* sulfuric acid (no base was consumed). The neutral solution was evaporated with an air stream, and the residue was extracted with three 25-ml portions of boiling absolute ethanol. The ethanol was evaporated to give 0.90 g of impure salt. This material was converted to thioether (−)-XV as before, $[\alpha]^{28}_{546}$ −22.12° (*c* 4.52, chloroform). This material analyzed for 0.240 atom of deuterium per molecule, and had undergone 57% racemization and 74% deuterium loss.

Exchange of (+)-2-Octylsulfonic Acid Potassium Salt ((+)-VIII-*h*) with Potassium *t*-Butoxide in *t*-Butyl Alcohol-O-*d*. Potassium salt (+)-VIII-*h*, $[\alpha]^{32}_{546}$ +12.04 (*c* 5.48, water), 1.170 g, was treated with 20 ml of 1.19 *N* potassium *t*-butoxide in *t*-butyl alcohol-O-*d* as before for 45 hr at 146°. The recovered thioether (+)-XV had $[\alpha]^{27}_{546}$ +27.59° (*c* 5.40, chloroform) and was 46.6% racemized. Deuterium analysis indicated 0.606 atom of deuterium per molecule, which corresponded to 62.5% exchange.

Representative Exchange of 2-Octylsulfonanilide (VII) with Potassium *t*-Butoxide in *t*-Butyl Alcohol. A heavy walled glass tube was charged with 0.246 g of (+)-VII-*h*, $[\alpha]^{27}_{546}$ +21.58° (*c* 5.19, chloroform), and 4 ml of 1.18 *N* potassium *t*-butoxide in *t*-butyl alcohol-O-*d* and heated in an oil bath at 150° for 21.5 hr. The tube was cooled, and the contents was neutralized and extracted with pentane (greaseless equipment). The pentane solution was washed with water, dried, and evaporated to an oil. The nmr spectrum of this material showed no detectable deuterium on nitrogen (less than 10%). Complete loss of deuterium from nitrogen was ensured by dissolving the material in a minimum amount of 10% sodium hydroxide solution and 20 ml of water. The solution was stirred for 30 min, neutralized, and extracted as before. This procedure was again repeated to give 0.1230 g of sulfonanilide (+)-VII, $[\alpha]^{25}_{546}$ +11.11° (*c* 5.22, chloroform), or 49% racemized. The substance analyzed for 0.828 atom of deuterium per molecule, or had undergone 85% exchange.

Exchange of (−)-2-Octyl-2-*d*-sulfonanilide ((−)-VII-*d*) with Potassium Methoxide in Dimethyl Sulfoxide–Methanol. A heavy walled tube was charged with 0.750 g of (−)-VII-*d*, $[\alpha]^{28}_{546}$ −25.08° (*c* 5.50, chloroform), and 20 ml of 0.40 *N* potassium methoxide in dimethyl sulfoxide–methanol (6% methanol by weight or 2.04 *M*) and heated at 150° for 50 hr. The contents turned black, and some pressure developed. The tube was opened at −80°, the product was extracted as before, twice redissolved in potassium hydroxide solution, and recovered as before. The resulting dark oil, 0.55 g, was filtered through 50 g of silica gel, the orange residue was dissolved in 200 ml of dichloromethane, the resulting solution was refluxed for 30 min with 5 g of decolorizing charcoal and filtered, and the light brown oil from the filtrate was chromatographed on a 60-g silica gel column, 100-ml fractions being collected. The sulfonanilide IV, 0.2163 g, was eluted as a colorless oil with 25% ether–75% pentane, $[\alpha]^{25}_{546}$ −20.75° (*c* 5.30, chloroform), or was 17% racemized. The material analyzed for 0.552 atom of deuterium per molecule, and thus had undergone 38% exchange.

Representative Exchange of 2-Octyl-N-methylsulfonanilide ((−)-IV-*h*). A dry flask was charged under nitrogen with 0.123 g of (−)-IV-*h*, $[\alpha]^{27}_{546}$ −18.27° (*c* 5.58, absolute ethanol), and 5 ml of 0.60 *N* potassium *t*-butoxide in *t*-butyl alcohol-O-*d*, and thermostated at 25° for 3.5 hr. The product was shaken with 30 ml of water and 30 ml of pentane in greaseless equipment and the pentane layer was washed with water, dried, and evaporated. The residual oil was film dried for 10–15 hr at 1 mm, 0.10 g, $[\alpha]^{27}_{546}$ −17.11 (*c* 5.96, absolute ethanol), or was 6.4% racemized. The material contained 0.695 atom of deuterium per molecule, or was 72% exchanged.

Exchange of (+)-Methyl 2-Octylsulfonate ((+)-V-*h*) with Potassium *t*-Butoxide in *t*-Butyl Alcohol-O-*d*. A dry flask was charged under nitrogen with 0.7605 g of (+)-V-*h*, $[\alpha]^{25}_{546}$ +5.62° (neat, *l* = 1 dm), and 28 ml of 0.148 *N* potassium *t*-butoxide in *t*-butyl alcohol-O-*d*, and was placed in a 25° water bath for 24 min. During this time a white precipitate formed, probably the potassium salt of the sulfonic acid. The mixture was shaken with water and pentane in greaseless equipment and the pentane layer was washed with water, dried, and evaporated to a colorless oil, which was vacuum distilled (0.1 mm) to give 0.558 g of ester, $[\alpha]^{26}_{546}$ +5.57 (neat, *l* = 1 dm), which was 1.0% racemized. This material analyzed for 0.412 atom of deuterium per molecule.

Representative Exchange of (+)-Diethyl 2-Octylphosphonate ((+)-IX-*h*). To 6 ml of an 0.28 *M* solution of potassium *t*-butoxide

in *t*-butyl alcohol-O-*d* (0.99 atom of deuterium per molecule) was added 1.5 g of the ester, $[\alpha]^{27}_{546}$ +7.80° (*c* 20.2, chloroform). The mixture was sealed in a heavy walled tube under pure nitrogen and heated to 100° for 74 hr. The cooled contents was shaken with a mixture of water and pentane, the pentane extract was washed with water, dried, and evaporated, and the residue was chromatographed on 75 g of silica gel. Product was eluted with 1:1 ether–pentane, and was film dried at 1 mm, 1.1 g (74%), $[\alpha]^{27}_{546}$ 6.45° (17% racemized). This material analyzed for 0.20 atom of deuterium per molecule (20% exchanged).

Representative Exchange of (+)-Phenyl-2-octylphosphinic Acid ((+)-VI). Under pure nitrogen, 1.22 g of the acid $[\alpha]^{27}_{546}$ +20.15° (*c* 3, chloroform) was dissolved in 20 ml of 0.366 *M* potassium *t*-butoxide solution in *t*-butyl alcohol-O-*d* (0.99 atom of deuterium per molecule) and sealed in a dry heavy walled tube to less than the halfway mark. The tube was immersed to the meniscus in a bath at 225° for 51 hr, cooled to −78°, opened, and the contents mixed with enough 0.5 *N* hydrochloric acid to give a pH of 1 to 2. The product was extracted with ether, the ether was dried and evaporated, and the residue was chromatographed on 20 g of silica gel. The product was eluted with chloroform saturated with 90% formic acid, and the eluate was shaken with ether, washed with 0.1 *N* hydrochloric acid, dried, evaporated, and film dried, 0.62 g (51%), $[\alpha]^{27}_{546}$ +18.8° (*c* 3, chloroform), 6.5% racemized. Combustion and falling drop method of deuterium analysis indicated 4.00 atoms of deuterium exchanged. Nmr analysis in deuteriochloroform against methylene iodide as internal standard indicated 3.27 protons of the benzene ring had exchanged, and by difference, 0.73 proton must have exchanged in the 2 position of the octyl group, to give 74% exchange.

Electrophilic Substitution at Saturated Carbon. XXVI. Base-Catalyzed Intramolecular 1,3- and 1,5-Proton Transfer[1,2]

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Abstract: The intra- *vs.* intermolecular character of base-catalyzed 1,3- and 1,5-proton transfers in an acetylene–allene and in a triene–benzenoid system have been investigated. In the isomerization of triphenylpropyne-3-*d* (Id) to triphenylallene (II) in the presence of proton donors and bases, the intramolecularity ranged from 88% in dimethyl sulfoxide–methanol–triethylenediamine to 19% in methanol–potassium methoxide. In the isomerization of triene III to aromatic compound IV (1,5 proton shift) in the presence of deuteron donors and bases, the intramolecularity ranged from 98% in triethylcarbinol-O-*d*–potassium triethylcarboxide to 17% in ethylene glycol-O-*d*–potassium ethylene glycoxide. In 50% *t*-butyl alcohol–50% dioxane–triethylenediamine, the conversion of III to IV was found to be first order in substrate over a ninefold change in concentration, and first order in base over a 16-fold change in concentration. The isomerization in this medium in the presence of triethylenediamine–mono hydrogen iodide salt was 95 ± 3% intramolecular. In methanol–potassium methoxide, conversion of III to IV was found to be first order in base over about a tenfold change in concentration in base. The reaction exhibited 57% intramolecularity. The activation parameters were determined in these two solvent–base systems, and the entropy for the isomerization catalyzed by the amine (noncharged) was 14 eu more negative than that catalyzed by methoxide anion (charged base).

Since the first report of a base-catalyzed intramolecular 1,3-proton transfer,[3] enough other examples[4] have appeared in the literature to suggest that the phenomena might be rather general. Support for this view is found in a number of examples of enzyme-catalyzed intramolecular proton transfers that have been observed,[5] as well as thermal isomerizations of carbon acids[6] of pK_a of about 19.[7]

In studies of the stereochemistry of base-catalyzed hydrogen–deuterium exchange of V and VI, examples of intramolecular racemization (isoracemization) were interpreted as occurring by a series of intramolecular proton transfers (conducted tour mechanism).[8] Some of the stages involved 1,6-proton transfers across a nitrofluorene system (V), others 1,3-proton transfers from carbon α to a cyano group to nitrogen and back to carbon (VI).

In the present study two systems have been devised that serve as models for the intramolecular proton migration stages of the conducted tour mechanisms of V and VI (see Scheme I). Triene III[9] when treated with various bases in a variety of solvents undergoes ready isomerization to triarylmethane IV,[2] and this 1,5-proton transfer resembles one of the steps in the isoracemization of V. Similarly, acetylene I[10] undergoes a base-catalyzed isomerization to allene II.[2] This reaction is similar in character to one of the stages in the isoracemization of nitrile VI. This paper re-

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