b. A solution of 43 mg of the acetate **5** in 2 ml of dry ether was reduced in the same manner as described in a to give 39.2 mg of 6-epimesembranol, oil, ir (CCl_4) 3380 cm^{-1} (OH), identified by the usual chromatographic comparisons with those of an authentic specimen.

CD Spectra of Mesembrine (1) and Dihydrooxocrinine (10). Mesembrine (*c* 0.0196, dioxane at 25°), $[\theta]_{340}$ 0°; $[\theta]^{sh}_{312}$ −1480°; $[\theta]^{sh}_{301}$ −2989°; $[\theta]_{295}$ −3610°; $[\theta]_{260}$ −1243°. Dihydrooxocrinine (*c* 0.0055, dioxane at 25°), $[\theta]_{340}$ 0°; $[\theta]$ −10.610°; $[\theta]_{287}$ 0°.

Kinetics. The saponification rates of the acetates **4** and **5** were carried out at 25 ± 0.1° in aqueous methanol with a large excess of K_2CO_3 to ensure that the reaction would follow pseudo-first-order kinetics. Acetylation reactions of the alcohols **2** and **3** were performed at 0 ± 0.1° in pyridine using a large molar excess of acetic anhydride in order to simplify the kinetic treatment of the results.

Saponification of Acetates 4 and 5. A sample (3.8 mg) of each of the acetates **4** and **5** was weighed accurately and dissolved separately in 1.0 ml of MeOH. After allowing each of these solutions to reach 25°, 0.5 ml of aqueous 0.5 *N* K_2CO_3 solution was added, and the mixtures were stirred. Aliquots were removed periodically and analyzed (in triplicate) by glpc using column B. Each aliquot was first treated with 10% HCl, followed by basification with Na_2CO_3, then extracted with ethyl acetate prior to analysis. Very satisfactory first-order kinetics plots were obtained.

Acetylation of 2 and 3. A solution of mesembranol (35 mg) in 4.5 ml of pyridine was cooled to 0°. The solution was stirred and 0.5 ml of acetic anhydride introduced. Aliquots were removed periodically and transferred to stoppered tubes containing 0.5 ml of saturated Na_2CO_3 solution and *ca.* 0.1 ml of ethyl acetate. The contents of the tubes were shaken vigorously for about 1 min, and a portion of the ethyl acetate layer was removed for analysis (in triplicate) by glpc on column B. Acetylation of 6-epimesembranol (37 mg) was carried out in an identical manner. Excellent first-order kinetic plots were obtained for each of these runs.

Acknowledgment. We are very grateful to Dr. R. J. Highet, National Institutes of Health, for recording the CD spectra and for some preliminary high-resolution ir spectral measurements. We also wish to thank Professor W. C. Wildman, Iowa State University, and Dr. A. Popelak, C. F. Boehringer and Soehne, Manneheim, Germany, for providing generons gifts of mesembrine.

The Conformational Analysis of Saturated Heterocycles. XX.[1] The Stereochemistry of Base-Catalyzed Hydrogen–Deuterium Exchange of Methylene Protons α to a Sulfinyl Group

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Abstract: The base-catalyzed hydrogen–deuterium exchange of the α-sulfinyl protons in the conformationally rigid *cis*- and *trans*-4-phenyltetrahydrothiopyran 1-oxides is stereoselective in water and methanol-1-*d* and nonstereoselective in *t*-butyl alcohol-1-*d* and dimethyl sulfoxide–methanol. The kinetics in methanol-1-*d* are interpreted in terms of two competing pseudo-first-order reactions, one for the α-axial proton and one for the α-equatorial proton. The order of proton acidity adjacent to a sulfinyl group is concluded to be (a) *trans* to S=O and *gauche* to sulfur lone pair, (b) *gauche* to S=O and to sulfur lone pair, (c) *gauche* to S=O and *trans* to sulfur lone pair.

The sulfoxide group activates adjacent C–H atoms toward base-catalyzed hydrogen–deuterium exchange. The methylene hydrogens in benzyl methyl sulfoxide undergo exchange at unequal rates,[4] and Wolfe and Rauk[5] attempted to deduce the stereochemistry of the preferential exchange from nmr considerations. However, it later[6] became clear that the assumptions made regarding the shielding effect of the S=O (↔ S^+—O^-) group might not be valid. Although calculations[7] appear to support the original assignment, it was clearly desirable to obtain direct evidence for the stereochemistry of exchange α to sulfinyl centers. We felt that such evidence could be obtained by the use of conformationally rigid compounds; although such compounds have apparently not been used previously to determine the effect of a functional group on the relative acidities of adjacent methylene protons, this would seem to be a general method. We now describe the results of work on the sulfoxides I and II. 4-Phenyltetrahydrothiopyran was converted into the *cis*-sulfoxide (II) by *t*-butyl hypochlorite oxidation, the method used previously[8] for the 4-*p*-chlorophenyl analog. The conversion of the *cis*- to the *trans*-sulfoxide (I) was accomplished *via* the ethoxysulfonium salt, for which the same analogy exists.[9] The conformation of the *cis*-sulfoxide from 4-*p*-chlorophenyltetrahydrothiopyran has been confirmed by X-ray methods;[10] our conformations were assigned by analogy in preparation and by direct comparison of infrared spectra with the corresponding 4-*p*-chlorophenyl derivatives. Marked similarities were found

(1) Part XIX: R. A. Y. Jones, A. R. Katritzky, and A. C. Richards, *Chem. Commun.*, in press.
(2) National Science Foundation Science Faculty Fellow, 1966–1967, from University of New Hampshire, Durham, N. H.
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(4) A. Rauk, E. Buncel, R. T. Moir, and S. Wolfe, *J. Amer. Chem. Soc.*, **87**, 5498 (1965).
(5) S. Wolfe and A. Rauk, *Chem. Commun.*, 778 (1966).
(6) A. B. Foster, T. D. Inch, M. H. Qadir, and J. M. Webber, *ibid.*, 1086 (1968).
(7) S. Wolfe, A. Rauk, and I. G. Csizmadia, *J. Amer. Chem. Soc.*, **89**, 5710 (1967).
(8) C. R. Johnson and D. McCants, Jr., *ibid.*, **87**, 1109 (1965).
(9) C. R. Johnson, *ibid.*, **85**, 1020 (1963).
(10) R. S. McEwen, G. A. Sim, and C. R. Johnson, *Chem. Commun.*, 885 (1967).

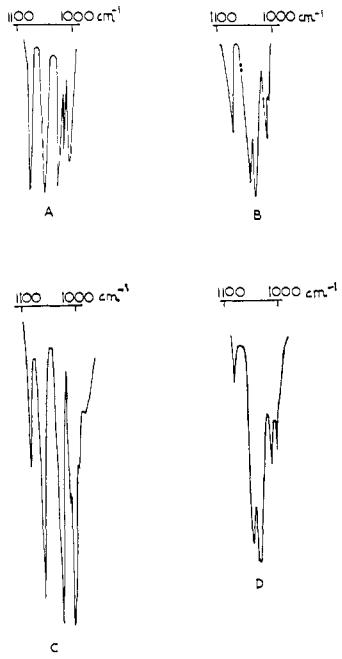
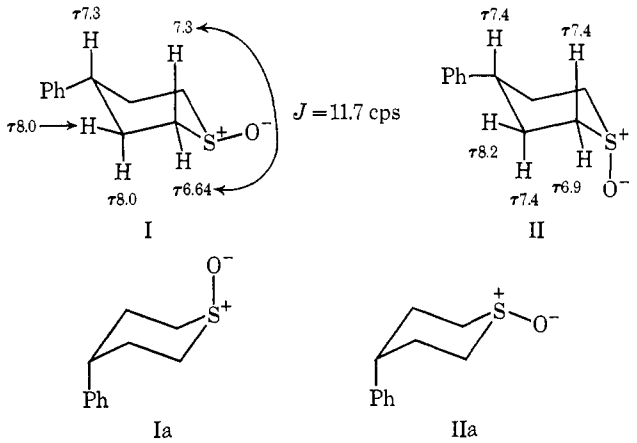


Figure 1. Infrared spectra from 1100 to 1000 cm^{-1}: (a) *cis*-4-*p*-chlorophenyltetrahydrothiopyran 1-oxide, (b) *trans*-4-*p*-chlorophenyltetrahydrothiopyran 1-oxide, (c) compound II, (d) compound I.

pair by pair in the 1100–1000-cm^{-1} region (Figure 1), as have previously been found for sulfoxides of similar configuration.[8]



The conformations are confirmed by the nmr spectra (Figures 2 and 3). The coupling constants derived from the spectra (including decoupling) allow the reasonable assignments shown in structure I for the *trans* isomer; the geminal coupling constant for the α-protons of 11.7 cps (obtained by decoupling) is identical with the 11.7 cps found by Lambert and Keske[11] for the α-geminal coupling for 3,3,5,5-tetradeuteriotetrahydrothiopyran 1-oxide. For the *cis* isomer, assignment II is proposed for the following reasons. A proton 1,3 diaxial to the oxygen of a sulfoxide group should be deshielded by 0.6–1.0 ppm as found in previous work;[6] we therefore believe that this forms part of the five-proton multiplet at *ca.* τ 7.4. The two-proton multiplet at τ 6.9 shows no sign of a large axial–axial splitting and is therefore assigned to the α-equatorial protons. These configurational and nmr assignments are supported by the

(11) J. B. Lambert and R. G. Keske, *J. Org. Chem.*, 31, 3429 (1966).

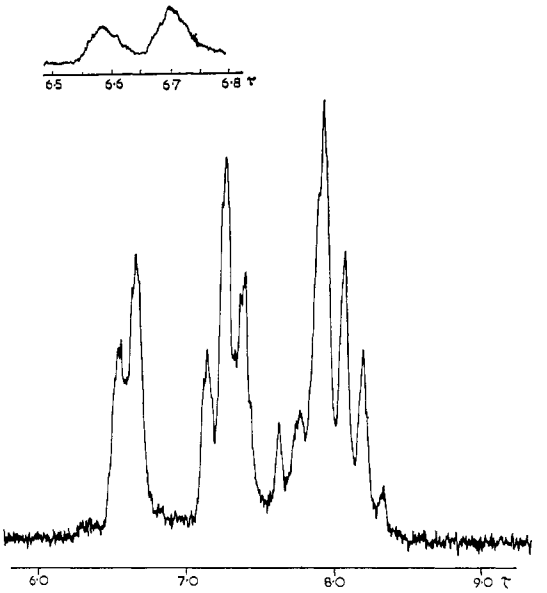


Figure 2. Nmr spectrum of *trans*-4-phenyltetrahydrothiopyran 1-oxide.

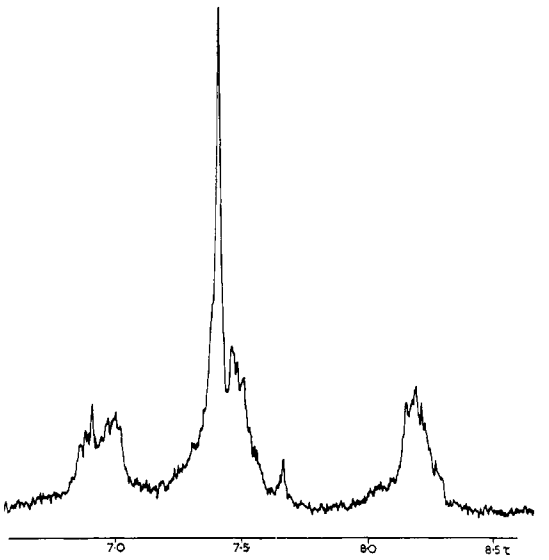


Figure 3. Nmr spectrum of *cis*-4-phenyltetrahydrothiopyran 1-oxide.

chemical-shift difference for the α-protons found by Lambert and Keske[11] for the "frozen" conformers of 3,3,5,5-tetradeuteriotetrahydrothiopyran 1-oxide: equatorial S=O, 0.87 ppm; axial S=O, 0.48 ppm. We find 0.66 and 0.5 ppm, respectively.

Results

To investigate the stereoselectivity of the exchange process, samples of the sulfoxides were heated for known times and temperatures in water, methanol, *t*-butyl alcohol, and dimethyl sulfoxide. The reaction was then quenched, the sulfoxide isolated, and its nmr spectrum used as a criterion for the amount of exchange, with the phenyl group protons functioning as an internal standard. Results are recorded in Tables I–IV. Tables I and IV include results for the back-exchange of deuterated samples of the sulfoxides. The experimental errors are *ca.* ± 0.2 proton. Clearly, the exchange is

Table I. Exchange of *cis*- and *trans*-Sulfoxides *ca.* 0.05 *N* in Water at 90 ± 5°

Run	Isomer	Solvent	Base: Nature	Base: Concn, *N*	Time, hr	No. of aliphatic protons[a]: Before exchange: τ 6.9	τ 7.4	τ 8.2	After exchange: τ 6.9	τ 7.4	τ 8.2	Difference: τ 6.9	τ 7.4	τ 8.2
1	*cis*-H	D_2O	NaOH	0.46	12	2.0	5.0	2.0	1.8	4.0	2.0	0.2	1.0	0
2	*cis*-H	D_2O	NaOD	0.75	66	2.0	5.0	2.0	0.96	2.97	2.0	1.04	2.03	0
3	*cis*-D	H_2O	NaOH	0.54	48	0.55	3.16	2.1	0.70	4.88	2.1	0.15	1.72	0
						τ 6.64	τ 7.3	τ 8.0	τ 6.64	τ 7.3	τ 8.0	τ 6.64	τ 7.3	τ 8.0
4	*trans*-H	D_2O	NaOH	0.69	65	2.0	3.0	4.1	1.54	2.90	4.0	0.46	0.1	−0.1
5	*trans*-H	D_2O	NaOD	0.75	66	2.0	3.0	4.0	1.31	2.92	3.8	0.69	0.08	−0.2
6	*trans*-D	H_2O	NaOH	0.69	63	0.67	2.49	4.0	0.94	2.58	4.0	0.27	0.09	0

[a] From the integral in the nmr.

Table II. Exchange of *cis*- and *trans*-Sulfoxides in Methanol-1-*d*–Sodium Methoxide (1.04 *N* in Base) at 84.5 ± 0.5°

Run	Compound: Isomer	Compound: Concn, *N*	Time, hr	No. of aliphatic protons[a]: Before exchange: τ 6.9	τ 7.4	τ 8.2	After exchange: τ 6.9	τ 7.4	τ 8.2	Difference: τ 6.9	τ 7.4	τ 8.2
1	*cis*-H	0.65	16.4	2.0	5.0	2.0	1.52	3.62	2.12	0.48	1.38	+0.12
2	*cis*-H	0.40	20.5	2.0	5.0	2.0	1.44	3.36	2.05	0.56	1.64	+0.05
3	*cis*-H	0.41	20.5									
				τ 6.64	τ 7.3	τ 8.0	τ 6.64	τ 7.3	τ 8.0	τ 6.64	τ 7.3	τ 8.0
4	*trans*-H	0.6	166	2.0	3.0	4.0	0.72	2.21	3.99	1.28	0.79	−0.01
5	*trans*-H	0.37	240	2.0	3.0	4.0	0.63	2.14	4.02	1.37	0.86	+0.02
6	*trans*-H	0.37	240									

[a] From the integral in the nmr.

Table III. Exchange of *cis*- and *trans*-Sulfoxides in *t*-Butyl Alcohol-1-*d*–Potassium-*t*-Butoxide (0.18 *N* in Base) at 35 ± 1°

Run	Compound: Isomer	Compound: Concn, *N*	Time, hr	No. of aliphatic protons[a]: Before exchange: τ 6.9	τ 7.4	τ 8.2	After exchange: τ 6.9	τ 7.4	τ 8.2	Difference: τ 6.9	τ 7.4	τ 8.2
1	*cis*-H	0.39	5.25	2.0	5.0	2.0	1.47	4.76	2.04	0.53	0.24	+0.04
2	*cis*-H	0.4	12.5	2.0	5.0	2.0	1.13	4.09	2.0	0.87	0.91	0
				τ 6.64	τ 7.3	τ 8.0	τ 6.64	τ 7.3	τ 8.0	τ 6.64	τ 7.3	τ 8.0
3	*trans*-H	0.35	200	2.0	3.0	4.0	1.25	2.10	4.0	0.75	0.9	0

[a] From the integral in the nmr.

Table IV. Exchange of *cis*- and *trans*-Sulfoxides *ca.* 0.5 *N* in DMSO-d_6–Methanol at 35 ± 1°

Run	Isomer	Solvent	Time, hr	No. of aliphatic protons[a]: Before exchange: τ 6.9	τ 7.4	τ 8.2	After exchange: τ 6.9	τ 7.4	τ 8.2	Difference: τ 6.9	τ 7.4	τ 8.2
1	*cis*-H	DMSO-d_6[b]	1	2.0	5.0	2.0	1.31	4.21	1.97	0.69	0.79	−0.03
2	*cis*-H	DMSO-d_6[b]	1.66	2.0	5.0	2.0	1.12	3.98	2.10	0.88	1.02	+0.1
3	*cis*-D	DMSO[c]	2.0	0.12	3.20	1.94	0.49	3.64	2.09	0.37	0.44	+0.15
				τ 6.64	τ 7.3	τ 8.0	τ 6.64	τ 7.3	τ 8.0	τ 6.64	τ 7.3	τ 8.0
4	*trans*-H	DMSO-d_6[b]	15.62	1.93	3.07	3.98	1.70	2.55	4.05	0.23	0.52	+0.07
5	*trans*-H	DMSO-d_6[b]	23.25	2.0	3.0	4.07	1.58	2.54	3.97	0.42	0.46	+0.10
6	*trans*-H	DMSO-d_6[b]	66.5	1.60	2.68	3.72	0.91	1.91	4.27	0.69	0.77	+0.55

[a] From the integral in the nmr. [b] 1 *M* in CH_3OD; *ca.* 0.02 *N* in potassium methoxide. [c] 1 *M* in CH_3OH; *ca.* 0.02 *N* in potassium methoxide.

stereoselective in deuterium oxide and in methanol-1-*d* in which the α-axial proton of the *cis* isomer (II) and the α-equatorial protons of the *trans* isomer (I) are exchanged preferentially in the compounds quoted. Further, the *trans* isomer exchanges over-all more slowly than the *cis* isomer. For *t*-butyl alcohol and dimethyl sulfoxide solutions, the exchange is not stereoselective to within the experimental error.

The over-all exchange rates in methanol-1-*d* and *t*-butyl alcohol-1-*d* were followed kinetically by integrating the increase in OH absorption over time, again using the sulfoxide aromatic protons as internal standard. For the kinetics in methanol-1-*d*, the size of the isotope pool was 15:1 (considering all four replaceable α-sulfinyl protons) and thus reprotonation could be neglected. The integral *vs.* time plots for exchange of the *cis* compound (II) (Figure 4) indicate that the reaction is composed of two competing pseudo-first-order reactions. If the concentrations of the unexchanged, axial-deuterated and equatorial-deuterated species are represented by [A], [X], and [Q], respectively, and if the carbanions are not interconverted and are formed with independent pseudo-first-order rate constants k_{ax} and k_{eq}, then (1) and (2) follow.

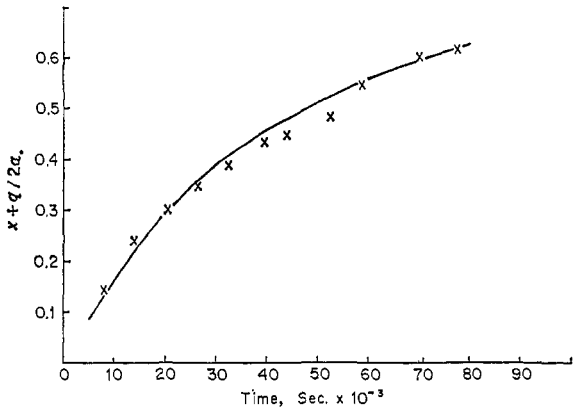


Figure 4. Plot of change in integral *vs.* time for compound II: (×) observed, (———) calculated.

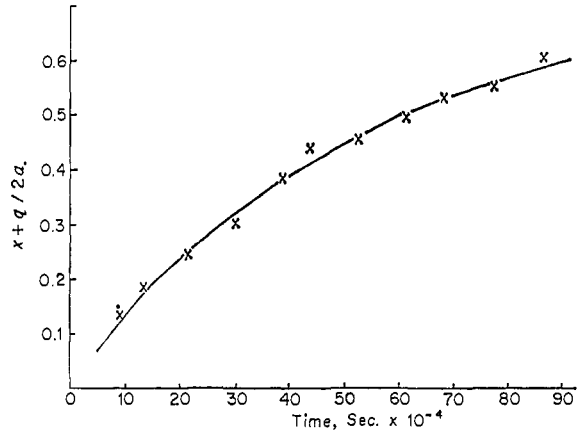


Figure 5. Plot of change in integral *vs.* time for compound I: (×) observed, (———) calculated.

$$\frac{d[X]}{dt} = k_{ax}[A] \quad (1)$$

$$\frac{d[Q]}{dt} = k_{eq}[A] \quad (2)$$

If we put $a = [A]_{initial}$, $x = [X]_t$, and $q = [Q]_t$, then relation 3 follows.[12]

$$\frac{x + q}{2} = 1 - \frac{1}{2}(e^{-k_{ax}t} + e^{-k_{eq}t}) \quad (3)$$

By trial and error, a best value for $k_{ax} = (350 \pm 50)10^{-7}$ sec^{-1} and $k_{eq} = (45 \pm 20)10^{-7}$ sec^{-1} were deduced (Figure 4). Similar reasoning for the *trans*-analog (I) yields a best value of $k_{eq} = (25 \pm 5)10^{-7}$ sec^{-1} and $k_{ax} = (0.40 \pm 0.02)10^{-7}$ sec^{-1}; observed points and calculated lines are compared in Figure 5.

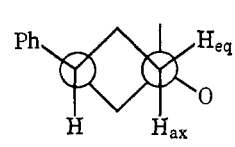
The kinetics of exchange in *t*-butyl alcohol were also investigated. The most probable reason for non-stereospecificity is that under these conditions rapid carbanion inversion occurs. The kinetic model is complicated and could not be adequately tested; at this time no definite conclusion can be drawn.[12]

Determination of initial rates for both isomers in *t*-butyl alcohol and consideration of the heating times (*cf.* Table IV for reaction in dimethyl sulfoxide) indicate that in both the solvents the *cis* isomer exchanges *ca.* 10 times as rapidly as the *trans* analog, just as is found for the other solvents.

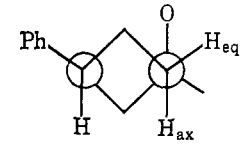
Discussion

We first discuss various complications which could hinder correct interpretation of the results. Evidence from the back-exchange of partially deuterated substrates (Table I, runs 3, 6) indicated that differential isotope effects on the stereochemical course of the reaction were small; similar conclusions regarding isotope effects on stereochemical exchange have been reached by others.[4,13]

The conformational ΔG for the sulfoxide group is 0.2 kcal for the axial position,[11] and that for phenyl groups (in cyclohexane) is 3.1 kcal for the equatorial position.[14] Hence, the proportion of the minor conformers will be: Ia, 0.8%; IIa, 0.4%. An alternative determination by equilibration methods gives 1.3 kcal axial preference for the sulfoxide group;[15] this implies 4 and 0.1% for the minor conformers. Our conclusions below are not invalidated by the presence of 4% of minor conformers, as is shown by the kinetic studies. The steric relation of the α-methylene protons to the sulfoxide group for the major conformer is shown in III and IV.



III



IV

Since the *trans* compound undergoes exchange more slowly than the *cis* analog, it has to be considered whether the 1% (or 4%) of the *trans* derivative with S=O axial contributes substantially to the exchange rate. If this were so, and the axial proton of flipped I (*i.e.*, Ia) underwent exchange, the equatorial proton of I would appear to exchange more rapidly. However, if I exchanged mainly *via* the flipped form, the exchange rate of the equatorial proton of I should be $^1/_{100}$ (or $^1/_{25}$) of that for the axial proton of the *cis* isomer. The experimentally observed value is *ca.* $^1/_{10}$, indicatingth at exchange *via* the flipped form cannot be the major pathway.

Differential steric hindrance to the approach of a base at the equatorial and axial protons is probably of minor importance only, as although the axial protons might be expected to be the more hindered, in the *cis* compound (II), they are in fact exchanged more quickly.

When stereoselective exchange has been observed, it has implicitly been assumed to result from retention of carbanion configuration. Some evidence against the alternative possibility of predominant carbanion *inversion* is provided by the kinetic results: the steric relationship of the equatorial protons to the sulfoxide group is similar for both isomers; the exchange rates of these protons are, as expected, found to be similar.

(12) For full details see B. J. Hutchinson, Ph.D. Thesis, University of East Anglia, 1968.
(13) D. J. Cram, W. T. Ford, and L. Gosser, *J. Amer. Chem. Soc.*, **90**, 2598 (1968).
(14) E. L. Eliel, N. L. Allinger, S. J. Angyal, and R. A. Morrisson, "Conformational Analysis," John Wiley & Sons, Inc., New York, N. Y., 1965.
(15) C. R. Johnson and D. McCants, Jr., *J. Amer. Chem. Soc.*, **86**, 2935 (1964).

However, if inversion were occurring, then the assignment of the rate constants k_{ax} and k_{eq} must be reversed and we now find a discrepancy of a factor of *ca.* 100 between the two rates.

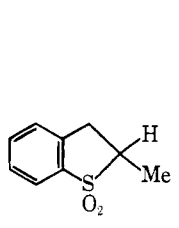
Effect of the Sulfoxide Group on the Kinetic Acidity of Adjacent Protons. Our results indicate that for water and methanol solutions the order of proton acidity adjacent to S=O is: (a) *trans* to S=O and *gauche* to sulfur lone pair, (b) *gauche* to S=O and to sulfur lone pair, and (c) *gauche* to S=O and *trans* to sulfur lone pair.

A possible reason for these differences may involve preferential interactions of the electron pair linking the acidic hydrogen atom with the (d-p)π orbital of the SO double bond.

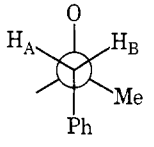
Influence of Solvent on Exchange Rates. The nonstereoselectivity of exchange found in *t*-butyl alcohol or dimethyl sulfoxide indicates the dramatic effect of the solvent. A complicating factor in considering solvent influence is the effect of temperature; thus for $PhCDMeSO_2CDMePh$, the ratio k_{ex}/k_{rac} varies from 196 at 0° to 16 at 100°.[16]

As discussed above, the nonstereoselectivity probably arises from fast inversion of the carbanion in these solvents. It is not clear why *t*-butyl alcohol should favor such inversion: Cram and coworkers[17] found that k_{ex}/k_{rac} for $PhSO_2CHMe$-hexyl was greater in *t*-butyl alcohol than in methanol; unfortunately the corresponding sulfoxide was examined only in *t*-butyl alcohol, so no direct comparison is available.[18] However, the picture may be more complex; detailed study of the optically active compound V showed that inversion without exchange, net inversion with exchange, and racemization all contributed.[19]

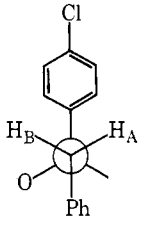
The nonstereoselective exchange in dimethyl sulfoxide as solvent is in line with literature reports which emphasize the inability of this solvent to stabilize carbanions by solvation.[20]



V



VI



VII

Reconciliation of Results with Previous Work. Wolfe and Rauk[5] studied the exchange of benzyl methyl sulfoxide in deuterium oxide solution. They concluded that H_A exchanges by a stereospecific synthesis, and further that exchange occurs on conformation VI, from dipole moment studies which indicate that this is the predominant conformer in nonpolar solvents, and from nmr arguments which indicate that this conformer is also favored in polar solvents. The nmr assignment assumes S=O to have the same anisotropic effect as C=O, which is now known to be unreliable.[6] However, these conclusions are in agreement with our own work, which indicates that, if VI is the conformer on which exchange mainly occurs, H_A should exchange *ca.* 10 times as fast as H_B. Wolfe and Rauk[7] have published MO calculations of the relative stability of rotamers of the hypothetical carbanion CH_2^-SHO. They conclude that the most stable conformation is that with the carbon lone-pair orbital *gauche* to both the S=O and the sulfur lone pair. Another energy minimum occurs for the carbon lone pair *trans* to S=O, but the conformation in which the carbon lone pair is *trans* to the sulfur lone pair is at an energy maximum. Our work indicates that the two energy minima should be interchanged.

Nishio[21] has studied the exchange of benzyl *p*-chlorophenyl sulfoxide in deuterium oxide-dioxane. It is concluded that H_B exchanges in conformation VII. This is directly contrary to our own conclusions, which predict that H_A should exchange *ca.* 100 times as rapidly as H_B in conformation VII. To reconcile this with our results, either the compound does not exchange mainly in conformation VII, which seems unlikely, or the conclusion that H_A exchanges first is incorrect. The proton chemical shifts in VII were assigned on the basis of differential solvent effects by comparison with compounds which may not be reliable models.

Although stereospecific exchange of $PhSOCH_2CO_2H$ has been observed,[22] assignment of the protons was not attempted.

Experimental Section

All melting points were obtained on a Kofler hot-stage melting point apparatus. Nmr spectra at 60 Mcps were recorded on a Perkin-Elmer Model R-10 instrument and those at 100 Mcps on a Varian HA-100 instrument. Infrared spectra were recorded on a Perkin-Elmer Infracord instrument.

1,5-Dibromo-3-phenylpentane. Hydrogen bromide gas was bubbled with stirring into 48 g (0.267 mol) of 3-phenyl-1,5-pentanediol[23] for 12 hr while heating at 130°. The reaction mixture was cooled and diluted with diethyl ether (150 ml). The ethereal solution was washed with 5% aqueous sodium hydrogen carbonate, dried over anhydrous magnesium sulfate, filtered, and concentrated. The residue was fractionated to give 2.46 g of a fore run of 4-phenyltetrahydropyran, bp 88° (0.7 mm), and 55.5 g (68%) of the dibromide, bp 143–145° (0.6 mm).

Anal. Calcd for $C_{11}H_{14}Br_2$: C, 43.17; H, 4.58. Found: C, 43.4; H, 4.78.

4-Phenyltetrahydrothiopyran. To a refluxing solution of sodium sulfide nonahydrate (36 g, 0.15 mol) in 95% ethanol (25 ml) was added dropwise 20 g (0.064 mol) of 1,5-dibromo-3-phenylpentane in ethanol (500 ml). After refluxing for 8 hr solvent was evaporated. Water (100 ml) was added and the whole was extracted with diethyl ether. After drying the solution ($MgSO_4$) and concentrating, an oil was obtained which solidified on standing. Crystallization two times from methanol gave 5.77 g (51%), mp 54–55° (lit.[24] mp 55°).

***cis*-4-Phenyltetrahydrothiopyran 1-Oxide.** To a stirred solution of 2.32 g (0.013 mol) of 4-phenyltetrahydrothiopyran in 125 ml of dry methanol cooled to −70° in an acetone–Dry Ice bath was added dropwise 1.42 g (0.013 mol) of *t*-butyl hypochlorite. When addition was complete, the mixture was warmed to −40° and *ca.* 2 g of sodium carbonate was added. The methanol was removed and the solid was extracted with boiling petroleum ether (bp 80–100°). On cooling, 1 g of solid was obtained. Several recrystallizations from petroleum ether gave 0.6 g (24%) of needles, mp 150–151°.

Anal. Calcd for $C_{11}H_{14}OS$: C, 68.02; H, 7.26. Found: C, 68.29; H 7.42.

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trans-**4-Phenyltetrahydrothiopyran 1-Oxide.** To a solution of 0.292 g (0.00153 mol) of triethyloxonium fluoroborate in *ca.* 5 ml of dry dichloromethane was added 0.29 g (0.0015 mol) of the pure *cis* sulfoxide. The solution was stirred at room temperature for 30 min. Addition of anhydrous diethyl ether at 0° caused precipitation of a crystalline solid. The ethoxysulfonium salt was collected by suction filtration and was then added to 10 ml of 0.1 *N* sodium hydroxide solution. The solution was allowed to stand overnight, then extracted with chloroform. After drying ($MgSO_4$) the chloroform was removed to give crude product (0.195 g). Recrystallization from diisopropyl ether followed by sublimation at 80° (0.1 mm) yielded 0.1 g (38%) of product, mp 137–138.5°.

Anal. Calcd for $C_{11}H_{14}O$: C, 68.02; H, 7.26. Found: C, 67.73; H, 6.90.

Details of Exchange Experiments. Exchanges in D_2O–NaOD. The reactions were carried out in 10-ml volumetric flasks. The sample of sulfoxide was dissolved in the exchange medium and placed in a water bath at 90 ± 5°. After the requisite period of time, the sample was removed, diluted with water, and extracted with chloroform. The chloroform solution was dried over magnesium sulfate and the chloroform was removed. The *cis* isomer was purified by recrystallization from petroleum ether, and the *trans* isomer was purified by sublimation of the sample at 80–90° (0.1 mm).

Exchanges in Methanol-1-*d*–Sodium Methoxide. The solvent was added quickly to the sulfoxide in an nmr tube. The tube was flushed with pure nitrogen for 1 min and was then sealed. The sample was heated in a water bath at 84.5 ± 1°. When the reaction was complete, the sample was opened and the *cis* and *trans* isomers were purified as outlined above.

Exchanges in *t*-Butyl Alcohol–Potassium *t*-Butoxide. The basic solution was prepared immediately prior to use. The sample of sulfoxide was dissolved in *t*-butyl alcohol-1-*d* in an nmr tube and then potassium *t*-butoxide was added to the solution. The tube was capped with a normal cap and the exchange was followed at 35° in the heating block of the spectrometer. The reaction was quenched and worked up as above.

Exchanges in Dimethyl Sulfoxide–Methanol. The basic solution was prepared prior to use by adding a weighed amount of methanol–potassium methoxide to a weighed amount of dimethyl sulfoxide or DMSO-d_6. The sample was made up in an nmr tube, and the reaction was followed in the nmr spectrometer as in the case with *t*-butyl alcohol. The sample was quenched and worked up as outlined above.

Preparation and Purification of Solvents. Methanol-1-*d*–Sodium Methoxide Solution. The deuterated alcohol was prepared from magnesium methoxide (dried under high vacuum at 100°) and the quantitative amount of deuterium oxide by heating at 100° for several hours. The deuterated alcohol was then collected. It was found to contain 1.5% water and was treated further with magnesium methoxide under reflux. The distilled sample contained 0.3% water by a Karl Fischer determination. Integration of the nmr spectrum of CH_3OD showed the presence of 1–2% CH_3OH.

A weighed amount of sodium was added (in a drybox) to a weighed amount of methanol-1-*d* which was cooled in an ice bath. The concentration of the base in the solution was calculated from the weights of sodium and methanol used.

***t*-Butyl Alcohol-1-*d*.** The deuterated alcohol was prepared by treating potassium *t*-butoxide with deuterium oxide. The alcohol was distilled off; it contained less than 0.15% water by a Karl Fischer determination and was about 96% isotopically pure by nmr spectroscopy.

Dimethyl Sulfoxide–Methanol Solutions. Commercial dimethyl sulfoxide was treated twice with sodium hydride and redistilled twice under reduced pressure (0.1 mm). The samples of DMSO-d_6 were dried over molecular sieves and used without further purification.

Potassium metal (weighed out in a drybox) was added to a weighed amount of methanol-1-*d*. The methanol was cooled by the addition of liquid nitrogen (in a drybox) and the potassium metal was added in small portions. The reaction was violent if the temperature was allowed to rise too high.

The base concentration was calculated from the weights of material used. A weighed portion of the methoxide solution was normally added to the sample of DMSO immediately prior to use. The base concentrations shown in Table IV are calculated and are only approximate.

Sodium Deuterioxide–Deuterium Oxide Solution. A sample of commercial NaOD–D_2O was diluted to 25 ml with deuterium oxide. A sample of this solution was titrated and found to be 0.75 *N*.

Examination of the Products of Exchange. The worked-up products were dissolved in deuteriochloroform and the nmr spectrum was taken. The number of protons exchanged was determined from the value of the integral of the α-axial and α-equatorial compared to the phenyl protons. The values of the integrals for the β-protons were checked in all cases and were found not to change. This also served as a check to show that the isomers did not undergo stereomutation under the reaction conditions used.

Kinetics. The kinetics of the exchange in *t*-butyl alcohol-1-*d* and methanol-1-*d* were followed by integrating the appearing alcohol peak using the phenyl peak of the compound as an internal standard.

Acknowledgment. The Karl Fischer determinations were carried out by May and Baker, Norwich, England.