lated was composed of XII and a lesser amount of XI. This product on standing for several weeks became enriched in XII and bands due to XI were then barely detectable in the infrared spectrum. Dissolution of this enriched product in refluxing ethanol followed by concentration and cooling of the solution afforded XIII in *ca.* 30% yield.

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE GEORGIA INSTITUTE OF TECHNOLOGY, ATLANTA 13, GA.]

The Carbanion Mechanism for *cis*-Elimination Reactions

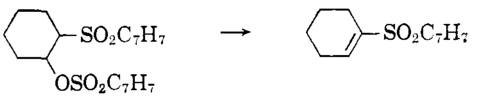
BY JACK HINE[1] AND O. BERTRAND RAMSAY

RECEIVED SEPTEMBER 25, 1961

The kinetics of the sodium hydroxide-catalyzed deuterium exchange of *cis*-2-methoxycyclohexyl *p*-tolyl sulfone and the dehydrofluorination of *cis*-2-fluorocyclohexyl *p*-tolyl sulfone have been studied. The Taft substituent constant (σ^*) for the *p*-toluenesulfonoxymethyl group has been determined by measurements of the acidity of *p*-toluenesulfonoxyacetic acid. By use of a Taft equation correlation it is shown that, contrary to a previous estimate, the reaction of *trans*-2-*p*-toluenesulfonylcyclohexyl *p*-toluenesulfonate with sodium hydroxide (a *cis* elimination) is *not* too fast for carbanion formation to be a plausible intermediate step.

In previous papers from this Laboratory, our knowledge of β-elimination reactions that proceed *via* intermediate carbanions has been reviewed and additional reactions of this type have been described.[2,3] The present paper describes evidence that the *cis*-elimination reactions of certain β-substituted sulfones described in an important series of papers by Bordwell, Pearson and their co-workers[4-7] also proceed *via* intermediate carbanions.

In both the cyclohexane and cyclopentane series the *cis* isomers of the 2-*p*-toluenesulfonyl 1-*p*-toluenesulfonates react with base to yield the α,β-unsaturated sulfone (by *trans* elimination) much faster than the *trans* isomers do (by *cis* elimination).[4,5] The rate of *cis* elimination by the base piperidine was found (in the cyclohexane series) to be unaffected by the addition of piperidine hydrochloride.[5] From these observations it seems clear that the *trans* eliminations are concerted reactions and that even the *cis* eliminations do not involve the *reversible* formation of intermediate carbanions. To rule out the possibility of the formation of an intermediate carbanion that is almost invariably transformed to the final product, a reactivity argument, the strongest type of evidence that could be brought in at this point, was then used. The rate at which hydroxide ions form α,β-unsaturated sulfone from *trans*-2-*p*-toluenesulfonylcyclohexyl *p*-toluenesulfonate is about 84,500 times the rate at which hydroxide ions form carbanions (as measured by the rate of deuterium exchange) from 1-deuteriocyclohexyl *p*-tolyl sulfone.[7] Assuming that the inductive effect of a *p*-toluenesulfonoxy (tosyloxy) group is about the same as that of a chlorine atom, it was argued, from data on the effects of α-chloro substituents on the rates of carbanion formation of acetone and nitroethane, that a β-tosyloxy substituent (and a deuterium kinetic isotope effect) could not increase the rate of carbanion formation by more than 100-fold and certainly not by so much as the 84,500-fold increase that must be postulated if the carbanion mechanism is operative for the *cis* elimination.[7] Therefore the *cis* elimination was held to be a concerted rather than a stepwise process.



We noticed that another method of estimating the effect of a β-tosyloxy group on the rate of carbanion formation gives much different results. From the ionization constants of acetic and chloroacetic acids[8] (for the moment we are approximating the inductive effect of tosyloxy as that of chlorine) the chloro substituent is seen to increase the acidity of a hydrogen three atoms away by $10^{1.9}$. Since inductive substituent effects usually increase by around 2.8-fold (when expressed logarithmically) for every atom the substituent is moved closer to the reaction center,[9] a β-chloro substituent might increase the acidity of a hydrogen atom by $10^{5.3}$. In a rate process in which an unstable reactive intermediate is formed the transition state should resemble the intermediate closely, and therefore the effect of substituents on the rate constant should be almost as large as on the equilibrium constant.[10] According to this argument the formation of unsaturated sulfone from the 2-tosylcyclohexyl tosylate is *not* unreasonably fast for a reaction involving rate-controlling carbanion formation.

In order to resolve this disagreement between two methods of predicting the rate constant to be expected for carbanion formation from 2-tosylcyclohexyl tosylate, we decided to determine the rate of carbanion formation of a *p*-tolyl cyclohexyl sulfone in which the cyclohexyl group contained a β-substituent that was electron-withdrawing but that was not so easily lost as an anion as to make base-catalyzed deuterium exchange at the α-position unobservable. Then by determining the Taft substituent constant for the tosyloxy group

---

[1] Alfred P. Sloan Foundation Fellow, 1956–1960.

[2] J. Hine and L. A. Kaplan, *J. Am. Chem. Soc.*, **82**, 2915 (1960).

[3] J. Hine, R. Wiesboeck and O. B. Ramsay, *ibid.*, **83**, 1222 (1961).

[4] F. G. Bordwell and R. J. Kern, *ibid.*, **77**, 1141 (1955).

[5] J. Weinstock, R. G. Pearson and F. G. Bordwell, *ibid.*, **78**, 3468, 3473 (1956).

[6] F. G. Bordwell and P. S. Landis, *ibid.*, **79**, 1593 (1957).

[7] J. Weinstock, J. L. Bernardi and R. G. Pearson, *ibid.*, **80**, 4961 (1958).

[8] J. F. J. Dippy, *Chem. Revs.*, **25**, 151 (1939).

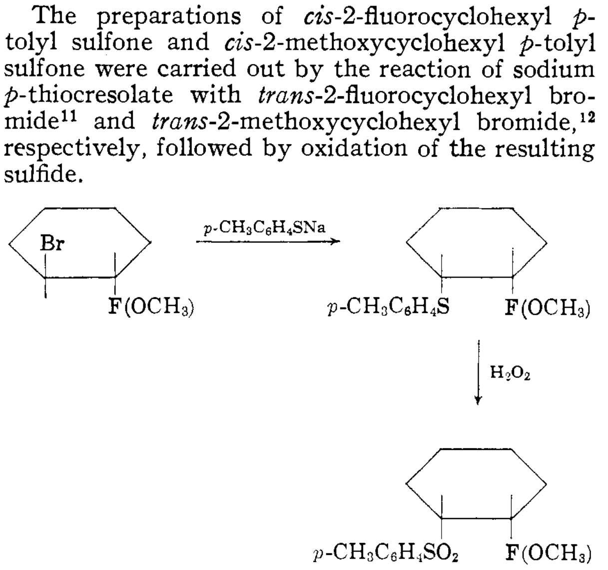
[9] R. W. Taft, Jr., in M. S. Newman's "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1956, p. 592.

[10] *Cf.* J. E. Leffler, *Science*, **117**, 340 (1953); G. S. Hammond, *J. Am. Chem. Soc.*, **77**, 334 (1955).

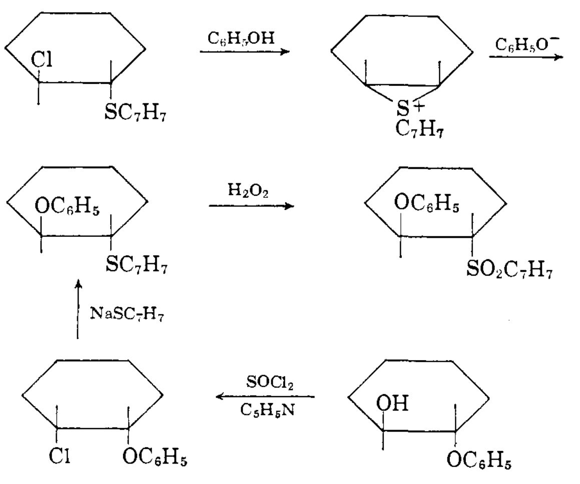
it would be possible to apply the Taft equation to the problem.

Results

The preparations of *cis*-2-fluorocyclohexyl *p*-tolyl sulfone and *cis*-2-methoxycyclohexyl *p*-tolyl sulfone were carried out by the reaction of sodium *p*-thiocresolate with *trans*-2-fluorocyclohexyl bromide[11] and *trans*-2-methoxycyclohexyl bromide,[12] respectively, followed by oxidation of the resulting sulfide.



The preparation of *trans*-2-phenoxycyclohexyl *p*-tolyl sulfone was carried out by two different methods, which yielded identical products. The solvolysis of *trans*-2-chlorocyclohexyl *p*-tolyl sulfide[13] in phenol containing sodium phenoxide yielded an oily sulfide that was oxidized to the solid sulfone. The reaction of *trans*-2-phenoxycyclohexanol[14] with thionyl chloride in pyridine gave *cis*-2-phenoxycyclohexyl chloride, which reacted with sodium *p*-thiocresolate to give the same sulfide and, upon oxidation, the same sulfone.



Winstein and Grunwald[15] have discussed the principles whose consideration assured that the solvolysis of the chlorosulfide in phenol would indeed proceed *via* an intermediate sulfonium ion and would hence lead to retention of configuration. Inversion in the reaction of phenoxycyclohexanol with thionyl chloride in pyridine seems assured in view of the observation of several investigators.[16]

In order to study the deuterium exchange of *cis*-2-methoxycyclohexyl *p*-tolyl sulfone, the 1-deuterio derivative was prepared by refluxing the sulfone with alkaline heavy water. The kinetics of the hydroxide-ion catalyzed exchange of this deuterium compound in 50% dioxane–water were studied by infrared spectral determinations of the deuterium content of the sulfone at various times. To permit an estimate of the deuterium kinetic isotope effect, the kinetics of the deuteroxide-ion catalyzed exchange of the protium compound in 50% dioxane–heavy water were also studied. Rate constants of 2.03×10^{-4} l. mole^{-1} sec.$^{-1}$ and 4.86×10^{-4} l. mole^{-1} sec.$^{-1}$ (both at 25°) were obtained in light and heavy water, respectively.

In an attempt to bring about the deuterium exchange of *trans*-2-phenoxycyclohexyl *p*-tolyl sulfone a sample of the compound was refluxed in D$_2$O–dioxane containing sodium deuteroxide, but under mild conditions undeuteriated starting material was recovered and under more severe conditions the sulfone decomposed. Similar results were obtained when a sodium acetate–deuterioacetic acid buffer was used (at considerably higher temperatures).

The rate constant for dehydrohalogenation of *cis*-2-fluorocyclohexyl *p*-tolyl sulfone by sodium hydroxide was found by acidimetric measurements in 50% aqueous dioxane at 25° to be 1.45 ± 0.08 l. mole^{-1}sec.$^{-1}$.

Tosyloxyacetic acid (glycolic acid *p*-toluenesulfonate) was prepared from glycolic acid and *p*-toluenesulfonyl chloride. Its ionization constant and that of a number of other substituted acetic acids were determined potentiometrically in 50% aqueous ethanol. A plot of the pK values *versus* the Taft σ^*-constants for the various groups (Fig. 1) gave a value of 1.705 for ρ^* and from the pK value for tosyloxyacetic acid (3.24) a value of 1.31 for σ^* for the tosyloxymethyl group.

Discussion

Our results show that a 2-methoxy substituent increases the rate of deuterium exchange of cyclohexyl *p*-tolyl sulfone by 500-fold, a larger factor than the maximum reasonable factor estimated by Weinstock, Bernardi and Pearson[7] for the much more strongly electron-withdrawing tosyloxy substituent. In order to estimate the rate to be expected for carbanion formation by the tosyloxy compound we have plotted (Fig. 2) log k values for the reaction of sodium hydroxide with various 2-X-cyclohexyl *p*-tolyl sulfones *versus* the σ^*-values for the corresponding XCH$_2$ groups. For cyclohexyl *p*-tolyl sulfone and its *cis*-2-methoxy derivative the k's refer to the rate of carbanion formation. To get the desired rate of carbanion formation by the protium compound in a protium oxide solvent it is necessary to estimate either the deuterium kinetic isotope effect, which may be

---

[11] A. Bowers, L. C. Ibáñez, E. Denot and R. Becerra, *J. Am. Chem. Soc.*, **82**, 4001 (1960).

[12] K. Meinel, *Ann.*, **516**, 231 (1935).

[13] H. L. Goering, D. I. Relyea and K. L. Howe, *J. Am. Chem. Soc.*, **79**, 2502 (1957).

[14] M. Mousseron and R. Jacquier, *Compt. rend.*, **229**, 374 (1949).

[15] S. Winstein and E. Grunwald, *J. Am. Chem. Soc.*, **70**, 828 (1948).

[16] W. A. Cowdrey, E. D. Hughes, C. K. Ingold, S. Masterman and A. D. Scott, *J. Chem. Soc.*, 1252 (1937); B. Carroll, D. G. Kubler, H. W. Davis and A. M. Whaley, *J. Am. Chem. Soc.*, **73**, 5382 (1951).

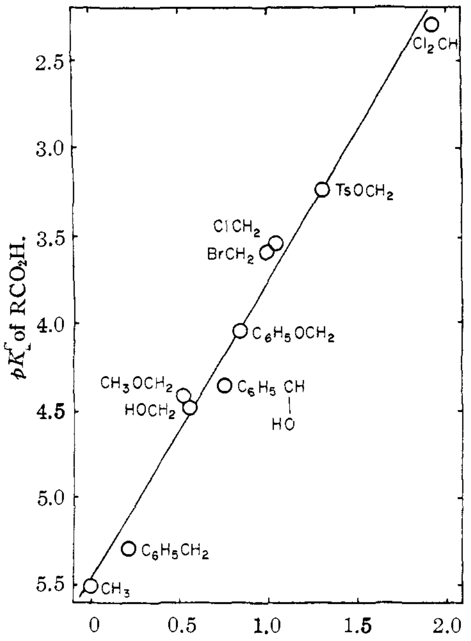


Fig. 1.—Ionization constants of RCO_2H's in 50% aqueous ethanol *vs.* σ*.

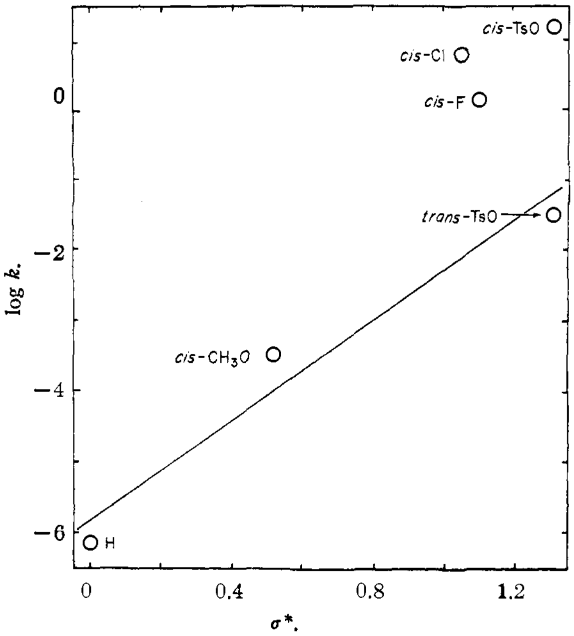


Fig. 2.—Rates of proton removal from 2-X-cyclohexyl *p*-tolyl sulfones *vs.* σ* for XCH_2.

quite small or may be as much as tenfold, or the effect of replacing hydroxide ions in light water by deuteroxide ions in heavy water, which has never been found to be as much as twofold. We have chosen the latter alternative and, as previously,[17] assumed that deuteroxide ions in heavy water remove protons 39% faster than do hydroxide ions in light water (even though in the present case the solvent is only 50% water). This assumption leads to the conclusion that the deuterium kinetic isotope effect (k_H/k_D) is 1.72, a value in the vicinity of that found for haloforms.[17,18] To calculate *k* for the unsubstituted sulfone we assumed the same kinetic isotope effect. For the other sulfones of Fig. 2 the *k* used refers to the rate of elimination. From the best line through the points for the unsubstituted *cis*-2-methoxy and *trans*-2-tosyloxy sulfones, it is seen that the rate of *cis* elimination of the tosyloxy compound is not faster but instead rather *slower* than would be predicted for carbanion formation from the σ*-constants of the groups used.

In view of the evidence for steric effects to be found in the observations of Weinstock, Pearson and Bordwell,[5] we suggest that the reaction of the β-tosyloxy sulfone with base is slowed somewhat by the bulk of the tosyloxy group. In any event, it seems quite possible that the activated *cis* eliminations of cyclic sulfone derivatives[4-7] proceed *via* the intermediate formation of carbanions, although the uncertainties associated with the linear free-energy relationship used are certainly too great for the carbanion mechanism to be regarded as established unequivocally.

Apparently the intermediate carbanions lose as anions such β-substituents as tosyloxy, chlorine[13] and, as we have found, phenoxy, much faster than they recombine with protons. The β-methoxy substituent, however, is so much more difficultly lost that the carbanion usually is protonated instead. The rate of reaction of the *cis*-2-fluoro sulfone, like that of the *cis*-2-chloro and tosyloxy sulfones, seems enough faster than would be expected for carbanion formation to assure that these *trans* eliminations proceed by a concerted mechanism.

Other arguments that *cis* eliminations of the type under consideration proceed by a carbanion mechanism have been presented by Goering, Relyea and Howe.[13]

Experimental

***cis*-2-Fluorocyclohexyl *p*-Tolyl Sulfone.**—To a solution of 3.68 g. (0.16 mole) of sodium in 200 ml. of 2-butanol was added 19.8 g. (0.16 mole) of *p*-thiocresol and 27.4 g. (0.15 mole) of *trans*-2-bromo-1-fluorocyclohexane[11] (d^{23}_4 1.4550). After 4 days of refluxing most of the butanol was removed by distillation and water and ether were added to the residue. The ether solution was dried over magnesium sulfate and distilled. The fraction of b.p. 175–80° at 17 mm. (17.7 g.) was redistilled to give 14.2 g. of *cis*-2-fluorocyclohexyl *p*-tolyl sulfide, b.p. 165–67° (9 mm.), n^{26}D 1.5657, d^{26}_4 1.0758. This was dissolved in a mixture of 40 ml. of glacial acetic acid and 35 ml. of acetic anhydride and allowed to reflux gently while 35 ml. of 30% hydrogen peroxide was added slowly. After an additional hour the solution was cooled and poured into 300 ml. of water. The resultant white precipitate was collected on a filter, washed with water, dried and found to weigh 9.8 g. (0.038 mole). After three recrystallizations from methanol white crystals melting at 163.0–163.5° were obtained.

Anal. Calcd. for $C_{13}H_{17}O_2SF$: C, 60.89; H, 6.69; S, 12.51; F, 7.42. Found: C, 60.59, 60.68; H, 6.81, 6.72; S, 12.66, 12.67; F, 7.33, 7.57.

***cis*-2-Methoxycyclohexyl *p*-Tolyl Sulfone.**—By a method analogous to that used with fluorobromocyclohexane, 31 g. (0.16 mole) of *trans*-2-bromocyclohexyl methyl ether[12] was transformed to 16 g. of *cis*-2-*p*-tolylthiocyclohexyl methyl ether, b.p. 155–157° (3 mm.), n^{25}D 1.5591, d^{25}_4 1.0601, which was then oxidized to 12.4 g. (0.046 mole) of *cis*-2-*p*-toluenesulfonylcyclohexyl methyl ether, m.p. 93–94.5°.

---

(17) J. Hine and N. W. Burske, *J. Am. Chem. Soc.*, **78**, 3337 (1956).

(18) J. Hine, N. W. Burske, M. Hine and P. B. Langford, *ibid.*, **79**, 1406 (1957).

Three recrystallizations from methanol gave a constant m.p. of 96.1–96.8°.

Anal. Calcd. for $C_{14}H_{20}O_3S$: C, 62.65; H, 7.51; S, 11.95. Found: C, 62.48; H, 7.46; S, 12.07.

***trans*-2-Phenoxycyclohexyl *p*-Tolyl Sulfone. a.** ***Via cis*-2-Chlorocyclohexyl Phenyl Ether.**—The method of McKusick[19] was used for the preparation of *trans*-2-phenoxycyclohexanol.[14] The treatment of 30 g. (0.16 mole) of this material with 40.5 g. (0.34 mole) of thionyl chloride in 28.5 g. (0.36 mole) of pyridine at 75° for 2 hours, followed by addition of water and drying and vacuum distillation of the organic layer, gave 11.9 g. (0.056 mole) of *cis*-2-chlorocyclohexyl phenyl ether, n^{29}_D 1.5420, d^{29}_4 1.1324. Application of the method described for fluorobromocyclohexane transformed 11.5 g. (0.055 mole) of this material into 4.65 g. (0.016 mole) of *trans*-2-*p*-tolylthiocyclohexyl phenyl ether, b.p. 150–164° (0.13 mm.), n^{27}_D 1.5971, d^{27}_4 1.1065, of which 1.0 g. was oxidized in unrecorded yield to *trans*-2-*p*-toluenesulfonylcyclohexyl phenyl ether, m.p. 94–96.5°, whose infrared spectrum was identical to that of the sulfone described in the next section.

b. ***Via* Phenolysis of *trans*-2-Chlorocyclohexyl *p*-Tolyl Sulfide.**—A solution of 25 ml. of 15.6 *M* sodium hydroxide in 450 g. of phenol was heated to 125°, driving off some of the water, and 68 g. (0.28 mole) of *trans*-2-chlorocyclohexyl *p*-tolyl sulfide was added slowly over a period of 90 minutes. After an additional 5 hours at 125° the solution was poured into a liter of 5 *M* sodium hydroxide and shaken with ether. The ether extract was washed with alkali, dried over magnesium sulfate and distilled, yielding 35 g. of *trans*-2-*p*-tolylthiocyclohexyl phenyl ether, b.p. 161–165° (0.06 mm.). The oxidation of 29 g. of this material (in 130 ml. of acetic acid) with 70 ml. of 30% hydrogen peroxide, yielded, after recrystallization from aqueous methanol, 6.6 g. of *trans*-2-*p*-toluenesulfonylcyclohexyl phenyl ether, m.p. 94–96.5°. Treatment with a little alkali removed the light tan color of the crystals and two additional recrystallizations gave white crystals, m.p. 96.5–97.5°, whose melting point was not depressed on admixture with the material prepared as described in the previous section.

Anal. Calcd. for $C_{19}H_{22}O_3S$: C, 69.06; H, 6.71; S, 9.70. Found: C, 68.10; H, 6.70; S, 9.55.

Deuterium Exchange of *cis*-2-Methoxycyclohexyl *p*-Tolyl Sulfone.—The treatment of 5 g. of *cis*-2-methoxycyclohexyl *p*-tolyl sulfone with a solution of 0.17 *M* sodium deuteroxide in 55% heavy water–45% dioxane at reflux for 30 minutes followed by cooling to 0° gave a precipitate that on two recrystallizations from methanol yielded 1.95 g. of white solid melting at 96.0–96.8°. This material had virtually lost its former absorption maxima at 8.16, 10.01, 10.58 and 13.15 μ and had gained new ones, the strongest of which were at 9.87, 10.27, 10.74, 12.75 and 13.26 μ. These changes in the infrared spectrum could be completely reversed by treatment with alkaline light water–dioxane.

Kinetic runs on the 1-deuterio-*cis*-2-methoxycyclohexyl *p*-tolyl sulfone prepared as described above were carried out as described for the following typical point. A solution of about 0.5 g. of the deuterio sulfone in 50 ml. of dioxane was mixed with 50 ml. of standard aqueous sodium hydroxide solution in a 25° constant temperature bath. At recorded times 10-ml. samples were removed and added to enough dilute hydrochloric acid solution to neutralize the base present. The water and dioxane were removed under vacuum and the remaining solid extracted twice with isooctane. After evaporating the isooctane from the filtered extracts the remaining solid was dissolved in carbon disulfide and the relative concentrations of the deuterio and protio forms of the sulfone determined by infrared measurements at 8.16, 10.58, 10.74 and 13.26 μ. Rate constants were calculated as described previously,[18] and an average value of $(2.03 \pm 0.12) \times 10^{-4}$ l. mole^{-1} sec.$^{-1}$ was obtained. By an analogous technique the rate constant for the sodium deuteroxide-catalyzed exchange of the protio sulfone in 50% heavy water–dioxane was found to be $(4.86 \pm 0.08) \times 10^{-4}$ l. mole^{-1}sec.$^{-1}$ (also at 25°).

Deuterium Exchange of *trans*-2-Phenoxycyclohexyl *p*-Tolyl Sulfone.—A solution of 0.5 g. of *trans*-2-phenoxycyclohexyl *p*-tolyl sulfone in 4.4 ml. of acetic anhydride, 5.0 ml. of dioxane, 4.0 ml. of heavy water and 3.8 ml. of 9.6 *M* sodium deuteroxide in heavy water was maintained at 200 ± 5° for 43 hours. It was then poured into water and extracted with ether. The ether was removed from the organic layer and the remaining solid, after recrystallization from methanol, was found to have an infrared spectrum identical to that of the starting material. Similar treatment at 237° resulted in the decomposition of the starting material. The reaction product was an oil rather than a solid. It smelled like a mercaptan and decolorized considerable quantities of methanolic iodine solution.

Rate of Reaction of *cis*-2-Fluorocyclohexyl *p*-Tolyl Sulfone with Sodium Hydroxide.—To 15 ml. of 0.001866 *M cis*-2-fluorocyclohexyl *p*-tolyl sulfone was added 12 ml. of water and then, when the solution had reached the temperature of the constant temperature bath (25°), 3 ml. of 0.00979 *M* aqueous sodium hydroxide. At a recorded time 3 ml. of 0.01453 *M* perchloric acid was added to stop the reaction and the excess acid was back-titrated with base to the phenolphthalein end-point. Five such points were taken at times ranging from 123 to 695 seconds.

Glycolic Acid *p*-Toluenesulfonate.—A solution of 10 g. (0.131 mole) of glycolic acid in 41 g. of pyridine was kept below 15° while 25.8 g. (0.134 mole) of *p*-toluenesulfonyl chloride was added slowly. After 15 minutes additional stirring at room temperature, ice-water and then cold concentrated potassium hydroxide were added until the *p*H was 9. After two extractions with ether and acidification with concentrated hydrochloric acid to *p*H 1, the solution was extracted three times with ether and the ether extracts were concentrated to give a white solid, which was recrystallized from water. The 0.75 g. (0.0033 mole) of white crystals obtained melted at 136.5–138° and had a neutralization equivalent of 231 (calcd. 230.2). Lichtenberger and Faure report that glycolic acid *p*-toluenesulfonate obtained by hydrolysis of the nitrile melts at 137°.[20]

Determination of Ionization Constants.—A Beckman Zeromatic *p*H meter that gave a *p*H reading of 2.02 for 0.00967 *M* aqueous hydrochloric acid gave a reading of 2.16 for 0.00967 *M* hydrochloric acid in 50% (vol.) aqueous ethanol. Therefore in order that the reported data should be closer to the true ionization constants a correction factor of 0.14 was added to all readings made in 50% ethanol. For the purposes of this paper, however, only the relative ionization constants are of importance. The *pK*'s were determined from the *p*H at the half-equivalence point, at which the ionic strength was 0.004 *M*.

Acknowledgment.—We should like to acknowledge our indebtedness to the Alfred P. Sloan Foundation for support of this investigation.

---

(19) B. C. McKusick, *J. Am. Chem. Soc.*, **70**, 1976 (1948).

(20) J. Lichtenberger and C. Faure, *Bull. soc. chim. France*, 995 (1948).