and the aqueous phase extracted three times with 50-ml. portions of ether. The ether extracts were dried over "Drierite" and the ether solution then very slowly distilled through a 75-cm. Vigreux column. The fraction boiling at 73–75° (750 mm.) amounted to 13.6–15.2 g. (53–58%) in four different runs based on N-methylformanilide (lit. b.p. 74–75°).

MADISON 6, WISCONSIN

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUQUESNE UNIVERSITY]

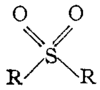
Concerning the Variable Character of the Sulfone Group

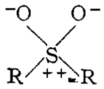
BY H. HARRY SZMANT AND GEORGE SULD

RECEIVED JULY 29, 1955

The apparent acidity constants of a series of benzoic acids and phenols containing sulfur substituents in the *para* positions were determined. By application of the Hammett equation, it is shown that the arylsulfonyl group has a variable effect on the ionization equilibrium depending on the nature of the substituents present in the aryl group and on the particular equilibrium under consideration.

The advent of the octet theory[1] caused a revision of the traditional structure of sulfones (I) and the preferred structure became that showing coordinate covalent sulfur–oxygen bonds (II).


I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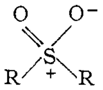
III

With time, however, as it was recognized that the second-row element sulfur may well expand its outer shell of electrons beyond the octet, there began a discussion as to the relative merits of structures I and II, and physical and chemical data were cited[2] in support of either structure I, II or III.[3] The general question of the expansion of the octet involved in the sulfur–oxygen bonds of sulfones (as well as those of sulfoxides, sulfates, etc.) has been closely associated with the question of resonance interactions between the sulfone function and adjacent free electron systems.

In an attempt to explain the results of a cryoscopic study of sulfones in sulfuric acid,[4] the hypothesis was advanced that the presence of electron-withdrawing substituents in phenyl sulfones favors sulfone structure I while electron-donating substituents favor sulfone structure II. The rather unexpected finding that the introduction of a *p*′-nitro group *increases* the basicity of *p*-(phenylsulfonyl)-aniline and the report that a *p*′-amino group has the opposite effect,[5] suggested the study of a series of suitably *p*-substituted benzoic acids and phenols. The assumption that the electronic character of the sulfone group varies with the nature of the substituents (contrary to the conclusions of Koch and Moffitt)[2c] would predict the acidity of these compounds to be directly affected by the relative positive charge at the sulfur atom. It is noteworthy that while one may be uncertain about the exact effect on physical and chemical properties caused by the participation of d-orbitals of sulfur in bond formation, the obvious difference between the structures I, II and III lies in the magnitude of the positive charge localized at the sulfur atom.

Experimental and Results

Materials.—*p*-Nitrobenzoic acid, *p*-nitrophenol and *m*-nitrophenol were Eastman Kodak Co. white label products which were purified before use by crystallization. Benzoic acid, U. S. Bureau of Standards sample 39F, was dried before use, and *p*-thiocyanophenol was supplied generously by Professor F. G. Bordwell. The following compounds were available in this Laboratory: *p*-phenylmercaptobenzoic acid,[6] m.p. 176–177°; *p*-phenylsulfinylbenzoic acid,[7] m.p. 201–202°; *p*-phenylsulfonylbenzoic acid,[8] m.p. 276–278°; *p*-(4-nitrophenylmercapto)-benzoic acid,[7] m.p. 236–238°; *p*-(4-nitrophenylsulfonyl)-benzoic acid,[7] m.p. 298–300°; *p*-(4-carboxyphenylsulfonyl)-benzoic acid,[8] m.p. 370–371°; *p*-(4-aminophenylsulfonyl)-benzoic acid,[7] m.p. 263–264°; these materials were recrystallized and dried before use.

***p*-Methylmercaptobenzoic Acid.**—A mixture of 20 g. of *p*-carboxyphenyl disulfide, 10 g. of sodium sulfide and 300 cc. of water was refluxed with mechanical stirring for 6 hr. To the cooled reaction mixture there was added 9 cc. of dimethyl sulfate and the resulting solution was stirred for 1 hr. The desired acid was precipitated by addition of hydrochloric acid, and after drying it was extracted with carbon disulfide to remove sulfur. The crude acid was extracted in a Soxhlet apparatus with *n*-heptane and further recrystallized from the same solvent to a constant m.p. 192–193° (lit.[9] m.p. 192°).

***p*-Methylsulfonylbenzoic Acid.**—The above acid upon oxidation with chromic acid in glacial acetic acid gave the desired sulfone, m.p. 266–267.5° after two crystallizations from ethanol.

***p*-(4-Nitrophenylsulfinyl)-benzoic Acid.**—A solution of 5 g. of the corresponding sulfide and 7.5 g. of phenyliodosoacetate in 150 cc. of glacial acetic acid was refluxed for 24 hr., cooled and poured on crushed ice. The precipitate, 4.9 g., m.p. 230–235° after several crystallizations from ethanol gave a constant m.p. 239–239.5°.

Anal.[10] Calcd. for $C_{13}H_9NO_5S$: C, 53.60; H, 3.12. Found: C, 53.37; H, 3.15.

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(1) G. N. Lewis, THIS JOURNAL, **38**, 762 (1916).

(2) For references consult the following publications: (a) C. M. Suter, "The Organic Chemistry of Sulfur," John Wiley and Sons, Inc., New York, N. Y., 1944, pp. 658–660; (b) H. P. Koch, *J. Chem. Soc.*, 408 (1949); (c) H. P. Koch and W. E. Moffitt, *Trans. Faraday Soc.*, **47**, 7 (1951); (d) E. A. Fehnel and M. Carmack, THIS JOURNAL, **71**, 231 (1949); (e) C. C. Price and H. Morita, *ibid.*, **75**, 4747 (1953); (f) E. Rothstein, *J. Chem. Soc.*, 815 (1953); (g) W. von E. Doering and L. K. Levy, THIS JOURNAL, **77**, 509 (1955).

(3) E. D. Amstutz, I. M. Hunsberger and J. J. Chessick, *ibid.*, **73**, 1220 (1951).

(4) H. H. Szmant and G. A. Brost, *ibid.*, **73**, 4175 (1951), H. H. Szmant and R. L. Lapinski, *ibid.*, **74**, 4395 (1952).

(5) (a) J. J. McIntosh, M.S. Thesis, Duquesne University, 1951; (b) K. A. Allen, J. Cymerman-Craig and H. H. Diamantis, *J. Chem. Soc.*, 234 (1954).

(6) H. H. Szmant, M. J. Segedi and J. Dudek, *J. Org. Chem.*, **18**, 745 (1953).

(7) H. H. Szmant and G. Levitt, THIS JOURNAL, **76**, 5459 (1954).

(8) H. H. Szmant and F. P. Palopoli, *ibid.*, **72**, 1757 (1950).

(9) J. W. Baker, G. F. C. Barrett and W. T. Tweed, *J. Chem. Soc.*, 2831 (1952).

(10) All microanalyses by Drs. Strauss and Weiler, Oxford, England.

p-**Phenylsulfonylphenol.**—To a mixture of 35.8 g. of benzenesulfonyl chloride and 25 g. of anisole there was added 29.6 g. of anhydrous aluminum chloride over a period of 90 minutes while the reaction mixture was stirred at 75–90°. The mixture was stirred for an additional 4 hr. at 75–100°, treated with dilute hydrochloric acid and ice and finally steam distilled. The residue from the steam distillation was crystallized from dil. alcohol to give 5 g. of *p*-phenylsulfonylanisole, m.p. 89–90.5° (lit.[11] m.p. 90–91°). A mixture of 4 g. of this compound and 25 cc. of 57% hydriodic acid was refluxed for 6 hr., cooled, made slightly basic and extracted with ether. The aqueous solution was treated with hydrochloric acid to give the desired phenol in 91% yield. After repeated crystallizations from benzene, the compound had a constant m.p. 136° (lit.[11] m.p. 136–137°).

p-**(4-Methylphenylsulfonyl)-phenol.**—This compound was prepared starting with 20 g. of *p*-toluenesulfonyl chloride, 20 g. of anisole and 16 g. of aluminum chloride as described for the preceding synthesis. The intermediate *p*-(4-methylphenylsulfonyl)-anisole, m.p. 103–104.5° (lit.[12] m.p. 104–105°), was obtained in 52% yield and was cleaved with hydriodic acid to give a 90% yield of the desired phenol, m.p. 133–137°; after crystallization from benzene, m.p. 140–141° (lit.[13] m.p. 138°).

p-**(4-Fluorophenylsulfonyl)-phenol.**—This material was prepared in two ways: The conventional Friedel–Crafts procedure as described above for the preparation of *p*-phenylsulfonylphenol gave a 43% yield of *p*-(4-fluorophenylsulfonyl)-anisole, m.p. 100–102°. The same product was obtained in 51% yield when a mixture of 3.5 g. of sodium *p*-methoxybenzenesulfonate, 1.55 g. of fluorobenzene and 11 g. of trifluoroacetic anhydride was treated with gaseous boron trifluoride and was hydrolyzed after a 24-hr. period.

The cleavage of the methyl ether from either of the above preparations gave the phenol in 95% yield. Repeated crystallizations from benzene gave a constant m.p. 157–158°. Since a m.p. 111.8–113.1° is reported[14] for this compound, our sample was analyzed.

Anal. Calcd. for $C_{12}H_9O_3SF$: C, 57.18; H, 3.60. Found: C, 57.27; H, 3.75.

p-**(4-Chlorophenylsulfonyl)-phenol.**—Using the above described conventional Friedel–Crafts procedure, there was prepared 14 g. of *p*-(4-chlorophenylsulfonyl)-anisole, m.p. 103–104°, from 13.8 g. of *p*-methoxybenzenesulfonyl chloride, 16.8 g. of chlorobenzene and 10.3 g. of aluminum chloride. The cleavage with hydriodic acid gave an 81% yield of the desired phenol, m.p. 147.5–149°.

Anal. Calcd. for $C_{12}H_9O_3ClS$: C, 53.63; H, 3.38. Found: C, 53.60; H, 3.37.

p-**(4-Bromophenylsulfonyl)-phenol.**—The conventional Friedel–Crafts procedure gave a 65% yield of *p*-(4-bromophenylsulfonyl)-anisole, m.p. 116–119°, starting with 10.2 g. of *p*-bromobenzenesulfonyl chloride, 16.2 g. of anisole and 12 g. of aluminum chloride. The cleavage of the ether with hydriodic acid gave a 90% yield of the desired phenol, m.p. 175–176°, after crystallization from benzene.

Anal. Calcd. for $C_{12}H_9O_3BrS$: C, 45.95; H, 2.89. Found: C, 45.91; H, 2.98.

p-**(4-Iodophenylsulfonyl)-phenol.**—This material was prepared in two ways: A mixture of 10.3 g. of *p*-methoxybenzenesulfonyl chloride, 30.6 g. of iodobenzene and 7.65 g. of aluminum chloride was stirred at room temperature for 3 days. (At higher temperatures a copious evolution of iodine was observed.) The mixture was treated with ice and dilute hydrochloric acid and steam distilled. The residue from the steam distillation was extracted with dilute alkali, and acidification of the alkaline extract gave 0.9 g. of product, m.p. 158–159°. The same material was obtained in 49% yield when a mixture of 2.5 g. of sodium *p*-methoxybenzenesulfonate, 10 g. of trifluoroacetic anhydride and 2.45 g. of iodobenzene was treated with boron trifluoride and, after stirring for 10 hr. at room temperature, was hydrolyzed. Crystallization from a mixture of benzene and heptane gave a constant m.p. 159–160°. The cleavage of the methyl ether from either preparation gave the desired phenol, m.p. 212–213°, after crystallization from benzene.

Anal. Calcd. for $C_{12}H_9O_3IS$: C, 40.01; H, 2.52. Found: C, 40.38; H, 2.52.

p-**(4-Aminophenylsulfonyl)-phenol.**—A mixture of 3.5 g. of sodium *p*-methoxybenzenesulfonate, 11 g. of trifluoroacetic anhydride and 2.21 g. of acetanilide was treated with boron trifluoride, and the reaction mixture was stirred at room temperature for 20 hr. Upon hydrolysis the gummy product was allowed to stand until it solidified, and 5.6 g. of crude material was obtained. Crystallization from aqueous ethanol gave 3.2 g. of product, m.p. 204–205.5°, the analysis of which corresponded to the formula of *p*-(4-trifluoroacetaminophenylsulfonyl)-anisole.

Anal. Calcd. for $C_{15}H_{12}O_4F_3NS$: C, 50.14; H, 3.37. Found: C, 49.75; H, 3.26.

A mixture of 1.70 g. of the above compound and 25 cc. of 56% hydrobromic acid was refluxed for 12 hr., diluted with 40 cc. of water and refluxed for an additional 2 hr. The reaction mixture was cooled, made slightly alkaline and extracted with ether. The aqueous layer was neutralized and 1.1 g. of material separated, which upon crystallization from toluene gave 0.9 g. of the desired compound, m.p. 177–178°. This m.p. agrees with that reported by Owari,[15] but is in disagreement with the m.p. 168°[16] and 193–194°.[17]

Anal. Calcd. for $C_{12}H_{11}O_3NS$: C, 57.81; H, 4.49; N, 5.62; S, 12.9. Found: C, 58.13; H, 4.38; N, 5.85; S, 12.5.

p-**(4-Methoxyphenylsulfonyl)-phenol.**—A mixture of 7 g. of sodium *p*-methoxybenzenesulfonate, 20 g. of trifluoroacetic anhydride and 3.8 g. of anisole was treated with boron trifluoride, and the reaction mixture was stirred at room temperature for 10 hr. Upon hydrolysis there was obtained 7 g. of di-(*p*-methoxyphenyl) sulfone, m.p. 129–131° (lit.[18] m.p. 129–130°). A solution of 3.1 g. of the above compound in 25 cc. of glacial acetic acid and 2.52 g. of 57% hydriodic acid was refluxed for 16 hr., cooled, made slightly alkaline and filtered. The filtrate was extracted with ether and the aqueous solution was made acidic with hydrochloric acid. The crude product, 0.8 g., after crystallization from water and then benzene gave the desired product, m.p. 126–127°.

Anal. Calcd. for $C_{13}H_{12}O_3S$: C, 59.07; H, 4.58. Found: C, 58.87; H, 4.76.

The identical product was obtained by the treatment of di-(*p*-hydroxyphenyl) sulfone with methyl sulfate in the presence of alkali, followed by fractional crystallization.

p-**(4-Nitrophenylsulfonyl)-phenol.**—This material was prepared by two methods: A mixture of 22.5 g. of sodium *p*-nitrobenzenesulfonate, 65 g. of trifluoroacetic anhydride and 10.8 g. of anisole was treated with boron trifluoride and allowed to stir for 14 hr. at room temperature. Following a 5-hr. reflux period the mixture was poured on ice and dilute hydrochloric acid and then neutralized with sodium bicarbonate. The crude product, 14 g., was crystallized from a mixture of benzene and heptane and then from ethanol to give 2.9 g. of pure *p*-(4-nitrophenylsulfonyl)-anisole, m.p. 163–164° (lit.[16] m.p. 162°).

Anal. Calcd. for $C_{13}H_{11}O_5NS$: C, 53.23; H, 3.78; N, 4.8; S, 10.9. Found: C, 53.11; H, 3.71; N, 5.1; S, 10.7.

The cleavage of 2.0 g. of the above compound with 25 cc. of 50% hydrobromic acid gave 1.5 g. of the desired product, m.p. 176–177°, after crystallization from a mixture of chloroform and carbon tetrachloride. The m.p. agrees with that reported in the literature, 172–173°.[15]

Anal. Calcd. for $C_{12}H_9O_5NS$: N, 4.75; S, 11.48. Found: N, 4.75; S, 11.3.

The second synthesis of the desired phenol consisted of the following steps: *p*-(4-nitrophenylmercapto)-acetophenone,[7] 18.7 g., in 150 cc. of glacial acetic acid was treated with 39 g. of 40% peracetic acid, and the mixture after standing at room temperature for 6 days was heated to 70–80° and poured on ice. The product, 16.0 g., on crystallization

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[12] H. Burton and P. F. Hu, *J. Chem. Soc.*, 601 (1948).

[13] German Patent 745,127; *C.A.*, **40**, 1176 (1946).

[14] H. L. Bradlow and C. A. VanderWerf, This Journal, **70**, 654 (1948).

[15] S. Owari, *J. Pharm. Soc. Japan*, **71**, 246 (1951); *C.A.*, **48**, 4498 (1945).

[16] H. Burton and E. Hoggarth, *J. Chem. Soc.*, 468 (1945).

[17] G. W. Raiziss, L. W. Clemence, M. Severna and F. C. Nachod, This Journal, **61**, 2764 (1939).

[18] B. Jones, *J. Chem. Soc.*, 1854 (1936).

from methanol had a constant m.p. 155–156°. Analysis proved it to be the corresponding sulfoxide.

Anal. Calcd. for $C_{14}H_{11}O_4NS$: C, 58.14; H, 3.84; N, 4.8; S, 10.9. Found: C, 57.82; H, 3.81; N, 4.6; S, 10.9.

The treatment of 12 g. of the sulfoxide in 50 cc. of formic acid with an excess of 30% hydrogen peroxide gave after heating to 80° and hydrolysis the previously described *p*-(4-nitrophenylsulfonyl)-acetophenone,[7] m.p. 181–182°, in 97% yield.

The acetophenone, 12 g., in 100 cc. of concd. sulfuric acid was treated with 2.85 g. of sodium azide (dissolved in 50 cc. of cold sulfuric acid). The theoretical volume of nitrogen evolved over a period of 2 hr. Upon hydrolysis there was obtained a 96% yield of product m.p. 215–219°, which after crystallization from tetrahydrofuran had a m.p. 221–225°. The m.p. of *p*-(4-nitrophenylsulfonyl)-acetanilide was reported to be 215–216°[19] and 229–230°.[17]

The above acetanilide, 8 g., was hydrolyzed in 92% yield to the corresponding aniline, m.p. 166–169° (lit.[19] m.p. 167–169°) by heating it with aqueous alcohol in the presence of a small amount of hydrochloric acid. *p*-Amino-*p'*-nitrodiphenyl sulfone, 2.6 g., was then dissolved in 30 cc. of 30% sulfuric acid and to the resulting solution maintained near 0°, there was added a solution of 0.69 g. of sodium nitrite in 10 cc. of water. The solution of the diazonium salt was poured into 60 cc. of a warm solution prepared by mixing 100 cc. of concd. sulfuric acid and 75 cc. of water. The crude product, 2 g., was recrystallized from water in the presence of charcoal and from benzene to a constant m.p. 176–177°. The material was identical with that prepared by the cleavage of *p*-(4-nitrophenylsulfonyl)-anisole.

Determination of Apparent Acidity Constants.—Distilled water was refluxed for at least 12 hr. in a system closed by an Ascarite tube. Stock ethanol (95.6%) was refluxed over potassium hydroxide pellets for 12 hr. and distilled. Equal volumes of water and ethanol were mixed to prepare the 48% solution used as the medium for the titrations. Sodium hydroxide titrant was prepared from the Sørensen solution (saturated aqueous sodium hydroxide centrifuged to remove any carbonate) by taking an aliquot of approximately 1 cc. and mixing it with 48% ethanol contained in the storage vessel of a Machlett automatic buret. Approximately 0.03 *M* sodium hydroxide solutions and approximately 4 × 10^{-3} *M* solutions of the acids or phenols were used for the titrations. Purified nitrogen was bubbled through the titration cell maintained at 25 ± 0.5°, and the Beckman model G *p*H meter was standardized before and after each titration against buffer solutions.

The acidity constants were determined by the graphical method from potentiometric titration plots, and the results could be duplicated to within 0.03 of a *pK* unit.

The apparent acidity constants of the benzoic acids are listed in Table I together with the constants of the four reference compounds (values in parentheses) from which the log K/K° *vs.* σ graph was constructed. The slope of this plot gave ρ 1.460 which agrees well with the value ρ 1.464 reported for the same reaction in 50% ethanol by volume.[20] The σ-constants of the newly studied substituents were read from the log K/K° *vs.* σ plot and the resulting values are listed in Table I.

The apparent acidity constants of the phenols are listed in Table II together with the constants of the reference compounds (values in parentheses), and the σ-constants of the newly studied substituents were read from the log *K vs.* σ plot. The ρ-value determined from the slope of this plot was 2.48 which is in agreement with the ρ-value 2.545 reported[21] for the ionization of phenols in 48.9% ethanol at 20–22°.

TABLE I

APPARENT ACIDITY CONSTANTS OF BENZOIC ACIDS, $p\text{-}RC_6H_4CO_2H$

R	pK_a	pK_a (av.)	$\sigma \pm$ 0.02
H	5.65, 5.65	5.65	(0.00)[a]
NO_2	4.50, 4.53	4.52	(.778)[a]
CH_3S	5.70, 5.74	5.72	(− .047)[a]
CH_3SO_2	4.57, 4.60	4.59	(.72)[b]
C_6H_5S	5.53, 5.54	5.54	.075
C_6H_5SO	4.96, 4.98	4.97	.465
$C_6H_5SO_2$	4.62, 4.63	4.63	.70
$p\text{-}O_2NC_6H_4S$	5.30, 5.30	5.30	.25
$p\text{-}O_2NC_6H_4SO$	4.73, 4.75	4.74	.625
$p\text{-}O_2NC_6H_4SO_2$	4.85, 4.86	4.86	.54
$p\text{-}HO_2CC_6H_4SO_2$	4.73	4.73[c]	.62
$p\text{-}H_2NC_6H_4SO_2$	4.80, 4.80	4.80	.58

[a] H. H. Jaffé, *Chem. Revs.*, **53**, 191 (1953). [b] Reference 20. [c] Only one determination was made due to lack of sufficient material.

TABLE II

APPARENT ACIDITY CONSTANTS OF PHENOLS $p\text{-}RC_6H_4OH$

R	pK_a	pK_a (av.)	$\sigma \pm$ 0.02
Br	10.44	10.44[a]	(0.232)[b]
O_2N	7.81, 7.80	7.81	(1.270)[b]
O_2N[c]	9.27, 9.30	9.29	(0.710)[b,c]
NCS	9.53, 9.54	9.54	.60[d]
$C_6H_5SO_2$	8.63, 8.64	8.64	.95
$p\text{-}CH_3C_6H_4SO_2$	8.69, 8.72	8.71	.925
$p\text{-}CH_3OC_6H_4SO_2$	8.80, 8.80	8.80	.89
$p\text{-}H_2NC_6H_4SO_2$	8.97, 8.97	8.97	.825
$p\text{-}FC_6H_4SO_2$	8.55, 8.57	8.56	.98
$p\text{-}ClC_6H_4SO_2$	8.59, 8.62	8.61	.96
$p\text{-}BrC_6H_4SO_2$	8.50, 8.52	8.51	1.05
$p\text{-}IC_6H_4SO_2$	8.50, 8.52	8.51	1.05
$p\text{-}O_2NC_6H_4SO_2$	8.28, 8.27	8.28	1.09

[a] Determined at half-point. [b] H. H. Jaffé, *Chem. Revs.*, **53**, 191 (1953). [c] *meta*-Substituent. [d] The value of 0.699 given by Jaffé was obtained from a single series of compounds (pK_a measurements of *p'*-substituted *p*-dimethylaminoazobenzenes). The *pK* 8.57 of this phenol in water (Professor Bordwell, private communication) would correspond to a σ-value of 0.60.

Discussion

Considering first the results listed in Table I, it is possible to compare the σ-constants of the $p\text{-}CH_3S$ and the $p\text{-}C_6H_5S$ substituents, and it is apparent that the latter is somewhat more electron-withdrawing. However, since the difference between the corresponding oxygen groups is at least twice as large,[22] it would seem that the contribution of resonance structures $\overset{(-)}{C_6H_5} = \underset{\cdot\cdot}{\overset{(+)}{X}}{}^-$ is greater when X stands for an oxygen atom. The introduction of a 4-nitro group into the *p*-phenylmercapto substituent causes an increase of the σ-constant by 0.18 unit. This difference is of the same magnitude as that reported[23] between the *p*-phenyl and the *p*-(4-nitrophenyl) substituents in benzoic acids.

The σ-value of the *p*-phenylsulfinyl group seems to be slightly smaller than that of the *p*-methylsulfinyl group,[24,25] and while the introduction of a 4-nitro group causes an increase in the electron-withdrawing character of the phenylsulfinyl substituent, this increase is only about 90% of the change observed in the phenylmercapto substituent.

The *p*-phenylsulfonyl substituent is only slightly

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[19] Yu. O. Gabel and F. L. Grinberg, *J. Appl. Chem.* (*U.S.S.R.*), **12**, 1481 (1939); *C.A.*, **34**, 6244 (1940).

[20] F. G. Bordwell and G. D. Cooper, THIS JOURNAL, **74**, 1058 (1952).

[21] G. Schwarzenbach and E. Rudin, *Helv. Chim. Acta*, **22**, 360 (1939).

[22] H. H. Jaffé, *Chem. Revs.*, **53**, 191 (1953).

[23] E. Berliner and L. H. Liu, THIS JOURNAL, **75**, 2417 (1953).

[24] C. C. Price and J. J. Hydock, *ibid.*, **74**, 1043 (1952).

[25] F. G. Bordwell and P. J. Boutan, A.C.S. Meeting, Chicago, Ill., 1953, Abstracts 81-O.

less electron-withdrawing than the *p*-methylsulfonyl group,[20] but the introduction of a 4-nitro group causes a change in the electronic character which is entirely unexpected on the basis of additive inductive effects. Thus, while the 4-nitro group causes an increase in the σ-constants of the *p*-phenylmercapto and *p*-phenylsulfinyl groups, the opposite effect is observed in the *p*-phenylsulfonyl substituent. This phenomenon can be explained by the application of the hypothesis[4] that the presence of the 4-nitro group in the phenylsulfonyl substituent causes a greater double bond character in the sulfur–oxygen bonds; the consequently smaller positive charge at the sulfur atom exerts a smaller electron-withdrawing effect on the benzoic acid moiety. A similar but understandably smaller effect is caused by a 4-carboxy group. The relative acidity of the benzoic acid containing the *p*-(4-aminophenylsulfonyl) substituent indicates that, regardless of which electronic structure of the sulfone is preferred, the large +E effect of the amino group is the governing factor.

The value of the σ-constant of the *p*-methylsulfonyl group was shown by Bordwell and Andersen[26] to increase proportionally with the influence which resonance interactions exert on the species in a given equilibrium. Thus, the value increases sharply when one proceeds from the benzoic acid to the phenol series, and an additional rise is observed in the substituted anilines. The same trend is found in the case of the *p*-phenylsulfonyl group (Table III).

The results listed in Table II show that the variation in the relative acidities of *p*-arylsulfonylphenols is of the same magnitude as that found in the corresponding benzoic acids. The effect of the substituents seems to be in line with the recognized fact that the phenol equilibrium is governed by the resonance stabilization of the phenolate ion. Electron-releasing substituents are believed to favor sulfone structure I but, on the other hand, they compete with the resonance of the phenoxide portion. Contrary to its effect in the benzoic acid series, the *p*-nitro substituent causes an increase in the relative acidity of the phenol. This may be interpreted in terms of increased resonance possibilities in the anion of a phenolic sulfone of structure II. Such an interpretation is supported by the observation that of all the phenolic sulfones listed in Table II only the anion of the *p*-nitro compound is colored.[27]

TABLE III

THE σ-CONSTANTS OF *p*-R-SO_2 SUBSTITUENTS

R	Benzoic Acids	Phenols	Anilines
CH_3	0.72[a]	0.98[a]	1.13[a]
C_6H_5	.70	0.95	1.21[b]
4-$O_2NC_6H_4$	.54	1.09	1.06[b]
4-$H_2NC_6H_4$	.58	0.825	1.33[c]

[a] See reference 26 for a critical tabulation. [b] Tentative values (reference 5a) from potentiometric titrations using perchloric acid in glacial acetic acid. [c] Estimated value from data reported in reference 5b.

The relative basicities of substituted phenylsulfonylanilines will be discussed in a future paper.[28]

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[26] F. G. Bordwell and H. M. Andersen, THIS JOURNAL, **75**, 6019 (1953).

[27] H. H. Szmant and J. Dixon, *ibid.*, in press.

[28] The data for anilines given in Table III can be reconciled with the hypothesis of variable sulfone structure if it is considered that resonance of anilines (unlike that of phenolate ions) causes charge separation.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, LANGSTON UNIVERSITY]

Local Anesthetics. I. β-Diethylaminoethyl Esters of Alkoxybenzoic and Cinnamic Acids

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RECEIVED JANUARY 16, 1956

The β-diethylaminoethyl esters of some dialkoxybenzoic and cinnamic acids were prepared and tested for topical anesthesia. Some of these proved to be highly potent and non-irritating local anesthetics with minimum toxic action. The ethylenic linkage was a factor in the increased anesthetic duration of the compounds. The hydrochloride of β-diethylaminoethyl-3-methoxy-4-ethoxy cinnamate, when tested topically on the rabbit cornea, was shown to be 18.6 times as efficient as procaine.

Synthetic local anesthetics of the benzoic acid ester type have been studied extensively but the short duration of anesthetic action and the toxicity and irritation of most of them leave much to be desired. The majority of the compounds studied have been alkamine esters of the type $XC_6H_4CO_2(CH_2)_yNR_2$ in which X is a primary amino group, *y* is 2, 3 or 4, and R is an alkyl group. Some investigators,[1–5] however, have shown that in the above type formula, X can be an alkoxy group, giving compounds reported to exhibit minimum toxicity and high anesthetic potency. Thus Christiansen and Harris[4] have prepared a series of alkamine esters of both alkoxy benzoic acids and alkyl substituted alkoxybenzoic acids and found them to be effective as local anesthetics. Krayer and co-workers[5] prepared the β-dimethylaminoethyl ester of 3,4-dimethoxybenzoic acid and tested it for its action on the isolated mammalian heart. It was therefore of interest to prepare and evaluate a series of alkamine esters of dialkoxybenzoic acids to test further the effect of alkoxy groups on anesthetic activity.

Corresponding cinnamic acid esters were pre-

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[1] Wildman and Thorp, U. S. Patent 1,193,650 (1916).

[2] C. Rohmann and B. Scheurle, *Arch. Pharm.*, **274**, 110 (1936).

[3] J. S. Pierce, J. M. Salsbury and J. M. Fredericksen, THIS JOURNAL, **64**, 1691 (1942).

[4] W. G. Christiansen and S. E. Harris, U. S. Patent 2,409,663 (1946); U. S. Patent 2,412,966 (1946).

[5] O. Krayer, A. Farah and F. C. Uhle, *J. Pharmacol. Exper. Therap.*, **88**, 277 (1946).