ir spectrum of the sample isolated by the preparative gas chromatographic technique. The yield of benzonitrile was estimated to be *ca.* 640 mg. Other products were left unidentified.

Registry No.—Fumaronitrile, 764-42-1; maleonitrile, 928-53-0.

Acknowledgment.—The authors are grateful to Dr. S. Tatsuoka, General Manager of the Division, for encouragement throughout this work. Thanks are also due to Mr. K. Shinozaki for measurement of nmr spectra.

Chemistry of Sulfoacetic Acid Derivatives. II.[1a-c] Reactions of Phenyl Esters and Anilides of Sulfoacetic Acid

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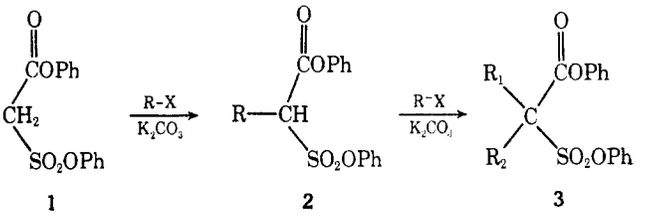
Diphenyl sulfoacetate (1) has been alkylated in an alkaline medium to produce both mono and dialkyl derivatives. 1 was nitrosated in acetic acid–acetic anhydride to form diphenyl acetoximinosulfoacetate (5) and was coupled with benzenediazonium chloride in aqueous alkaline medium to form the phenylhydrazone (6) of diphenyl oxosulfoacetate. Aminolysis of diphenyl sulfoacetate (1) with amines in pyridine medium occurs easily at both the carbonyl and the sulfonyl groups to produce diamides (14, 15, 16, and 17). Phenyl ester and anilide derivatives (1, 14, 18, and 19) of sulfoacetic acid in aqueous acidic medium undergo hydrolysis exclusively at the carbonyl group to form the corresponding carboxylic acids (8 and 23). Under aqueous alkaline conditions, hydrolysis occurs at both the carbonyl and the sulfonyl groups. In constrast, hydrolysis of phenyl ester and anilide derivatives (1, 2, 14, 18, 19, and 21) of sulfoacetic acid in pyridine occurs predominantly at the sulfonyl function, producing the corresponding sulfonic acids, isolated as the pyridinium salts (11, 13, 22, 26, and 28), as the major products. The hydrolysis and aminolysis reactions at the sulfonyl group in pyridine and aqueous alkaline media may occur by the formation of an intermediate sulfene (30), followed by addition of the nucleophilic water or amine to the sulfene.

Derivatives of sulfoacetic acid contain the α-sulfonylacetyl functional grouping, $-SO_2CH_2CO-$. The carbonyl and the sulfonyl groups are both subject to attack by nucleophilic agents, although to distinguishable degrees. The central methylene hydrogen atoms are activated by both the carbonyl group and the sulfonyl group. In summary, derivatives of sulfoacetic acid should show unusual versatility and synthetic utility in the reactions which they undergo and the new products which they form.

The chemistry of sulfoacetic acid and its derivatives has been investigated by Vieillefosse[2] and by Bodendorf and Senger.[3] Derivatives of sulfoacetic acid have been cyclized to form thiadiazines by Hinman[4] and Wawzonek[5] and their coworkers. Loev and coworkers[6] have cyclized N-phenylsulfamylacetic acid to sulfostyril.

Anionic Reactions of Diphenyl Sulfoacetate.—As described earlier,[4c] diphenyl sulfoacetate (1) (Chart I) undergoes reaction with methyl iodide in *t*-butyl alcohol containing *t*-butoxide ion base to form diphenyl α-sulfopropionate (2, R = CH_3) and diphenyl α-sulfoisobutyrate (3, $R_1 = R_2 = CH_3$). Our most recent work has shown that the alkylation of diphenyl sulfoacetate (1) is most conveniently carried out in high yields using refluxing acetone as solvent and anhydrous potassium carbonate as base. Dialkylation of diphenyl sulfoacetate (1) is readily accomplished in high yield by the use of excess alkyl halide and excess potassium carbonate. Monoalkylation, with a minimum of dialkylation, is best achieved by the slow addition of 1 equiv of solid potassium carbonate to an acetone solution of the alkyl halide and diphenyl sulfoacetate (1) (Scheme I).

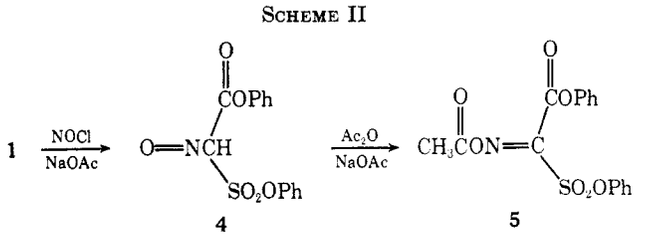
SCHEME I



1 2 3

Diphenyl sulfoacetate (1) undergoes nitrosation at the methylene group on treatment with nitrosyl chloride in an anhydrous mixture of acetic acid, acetic anhydride, and sodium acetate. The nitroso compound (4) initially formed was isolated from the reaction mixture as the oxime acetate (5) (Scheme II).

SCHEME II



4 5

(1) (a) Part I: B. E. Hoogenboom, E. D. Hoganson, and M. S. El-Faghi, *J. Org. Chem.*, **33**, 2113 (1968). (b) Supported by a F. G. Cottrell grant from the Research Corp., Public Health Service Grant GM12153, and National Science Foundation Undergraduate Research Participation, Grant No. GY-3078, GE-1021, GE-2955, and GE-9467. (c) Presented in part before the Organic Division of the American Chemical Society at its 156th National meeting in Atlantic City, N. J., Sept., 1968. (d) To whom all inquiries should be addressed.

(2) R. Vieillefosse, *Compt. Rend.*, **208**, 1406, 1505 (1939); R. Vieillefosse, *Bull. Soc. Chim. Fr.*, 351, 356 (1947).

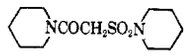
(3) K. Bodendorf and N. Senger, *Ber.*, **72 B**, 571 (1939).

(4) (a) R. L. Hinman and L. Locatell, Jr., *J. Amer. Chem. Soc.*, **81**, 5655 (1959); (b) B. E. Hoogenboom, R. Abbott, L. Locatell, Jr., and R. L. Hinman, *J. Org. Chem.*, **24**, 1983 (1959); (c) R. L. Hinman and B. E. Hoogenboom, *ibid.*, **26**, 3461 (1961).

(5) S. Wawzonek and R. Abbott, *J. Med. Chem.*, **6**, 603 (1963).

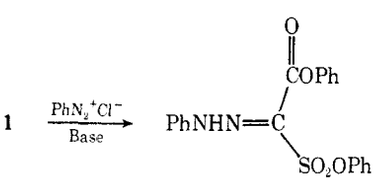
(6) B. Loev, M. Kormendy, and K. Snader, *J. Org. Chem.*, **31**, 3531 (1966).

CHART I

Compd no.	Structure
1	$PhO_2CCH_2SO_2OPh$
2	$RCH(SO_2OPh)(O{=}COPh)$
3	$R_1R_2CSO_2OPh$, $O{=}COPh$
4	$O{=}NCHSO_2OPh$, $O{=}COPh$
5	$CH_3CO_2N{=}CSO_2OPh$, $O{=}COPh$
6	$PhNHN{=}CSO_2OPh$, $O{=}COPh$
7	$CH_3CONHCHSO_2OPh$, $O{=}COPh$
8	$HO_2CCH_2SO_2OPh$
9	CH_3SO_2OPh
10	$HO_2CCH_2SO_2OH$
11	$HO_2CCH_2SO_2OH{:}Pyr$
12	$PhO_2CCH_2SO_2OH$
13	$PhO_2CCH_2SO_2OH{:}Pyr$
14	$PhNHCOCH_2SO_2NHPh$
15	$PhCH_2NHCOCH_2SO_2NHCH_2Ph$
16	$PhNCOCH_2SO_2NPh$, CH_3, CH_3
17	
18	$PhNHCOCH_2SO_2OPh$
19	$PhO_2CCH_2SO_2NHPh$
20	$PhCH_2CH_2SO_2OPh$
21	$PhCH_2CHSO_2NHPh$, $O{=}CNHPh$
22	$PhCH_2CHSO_2OH{:}Pyr$, $O{=}COPh$
23	$HO_2CCH_2SO_2NHPh$
24	CH_3SO_2NHPh
25	$PhNHCOCH_2SO_2OH$
26	$PhNHCOCH_2SO_2OH{:}Pyr$
27	$PhNHCOCH_2SO_2NPh$, CH_3
28	$PhCH_2CHSO_2OH{:}Pyr$, $O{=}CNHPh$
29	$PhNCOCH_2SO_2NHPh$, CH_3
30	$PhNHCOCH{=}SO_2$

In a weakly alkaline solution of either potassium carbonate or sodium acetate in aqueous acetone, diphenyl sulfoacetate (**1**) reacts with benzenediazonium chloride to form the phenylhydrazone (**6**) of diphenyl oxosulfoacetate

SCHEME III

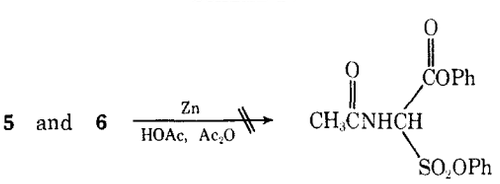


6

Diethyl oximinomalonate[7] and the *p*-bromophenylhydrazone of diethyl mesoxalate[8] are both reduced by zinc dust and acetic acid in acetic anhydride[9] to form diethyl acetamidomalonate. Neither the oxime acetate (**5**) nor the phenylhydrazone (**6**) of diphenyl oxosulfoacetate, however, could be reduced to diphenyl acetamidosulfoacetate (**7**) under any of a variety of conditions.

Reducing agents sufficiently reactive to produce a change in **5** or **6** invariably promoted reduction of the sulfonyl group with the liberation of unidentifiable volatile sulfides.

SCHEME IV



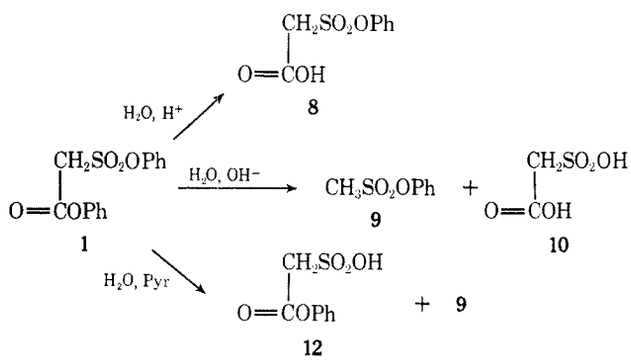
7

Hydrolysis and Aminolysis of Ester Derivatives of Sulfoacetic Acid.—The reactions of the diacid chloride of sulfoacetic acid with the nucleophiles water, phenol, and aniline have already been described.[1a] We now wish to report the behavior of ester derivatives of sulfoacetic acid with water and amines. Phenyl ester derivatives of sulfoacetic acid, rather than simple alkyl esters, were employed to preclude nucleophilic attack by either a solvolytic or an SN2 mechanism at a saturated carbon atom of an alkyl group and to limit nucleophilic attack to the electron deficient carbonyl and sulfonyl groups. Hydrolysis reactions were carried out in pyridine and in both acidic and alkaline aqueous media. Aminolysis reactions were carried out mainly in pyridine. The relative reactivities of the carbonyl and sulfonyl groups toward nucleophiles were estimated on the basis of product composition.

(7) A. J. Zambito and E. E. Howe, *Org. Syn.* **40**, 21 (1960).
(8) A. Hantzsch and K. J. Thompson, *Ber.*, **38**, 2272 (1905).
(9) K. Pfister, III, C. A. Robinson, A. C. Shabica, and M. Tishler, *J. Amer. Chem. Soc.*, **71**, 1101 (1949).

Diphenyl sulfoacetate (**1**) undergoes hydrolysis in aqueous acidic medium only at the carbonyl portion of the molecule to form phenyl carboxymethanesulfonate (**8**, 81%). The product of acidic hydrolysis was identified by its melting point and by decarboxylation in refluxing pyridine containing cupric oxide to phenyl methanesulfonate (**9**). The most easily isolable product of hydrolysis of diphenyl sulfoacetate in alkaline aqueous medium is phenyl methanesulfonate (**9**). The low yield (20%) of phenyl methanesulfonate obtained from alkaline hydrolysis suggests that attack of the hydroxide ion nucleophile at the sulfonyl group to form the sulfonic acid may be quite extensive. The second major product formed was identified as sulfoacetic acid (**10**) and was isolated in pure form as the pyridine salt (**11**) in 49% yield (Scheme V). In

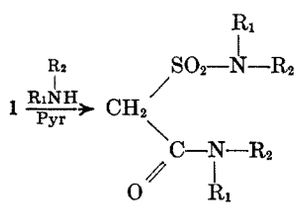
SCHEME V



contrast, the aqueous pyridine hydrolysis of diphenyl sulfoacetate produces phenyl methanesulfonate (**9**) as the major isolable product (57–65%); carbophenoxymethanesulfonic acid (**12**) was isolated from the reaction mixture as the pyridine salt (**13**) in 30–35% yield. Phenyl methanesulfonate (**9**), when subjected to hydrolysis conditions in aqueous acidic, alkaline, or pyridine medium, was recovered unchanged.

When diphenyl sulfoacetate (**1**) is heated in refluxing pyridine with 2 molar equiv of aniline, the dianilide (**14**)[1a,3] of sulfoacetic acid is obtained in good over-all yield (74%) (see Scheme VI). Benzyl-

SCHEME VI

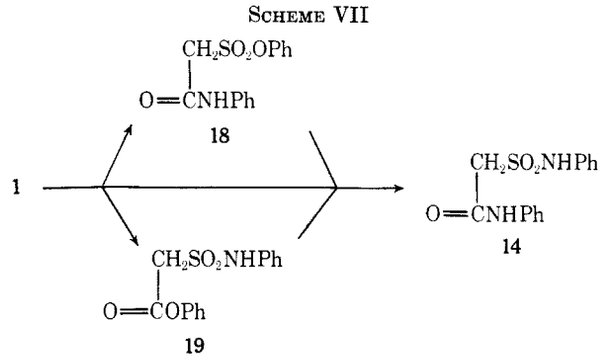


14, R_1 = H; R_2 = Ph
15, R_1 = H; R_2 = CH_2Ph
16, R_1 = CH_3; R_2 = Ph
17, R_1R_2NH = $C_5H_{10}N$

amine, N-methylaniline, and piperidine react with **1** in a similar manner to afford the corresponding diamides (**15**, **16**, and **17**). In an analogous manner, diphenyl malonate and diphenyl methionate[10] both form the corresponding dianilides on treatment with aniline in refluxing pyridine. In contrast, phenyl benzenesulfonate, phenyl *p*-toluenesulfonate, phenyl *m*-nitrobenzenesulfonate, phenyl methanesulfonate (**9**), and phenyl α-toluenesulfonate (phenyl phenylmethanesulfonate) are all completely inert toward aniline in refluxing pyridine.

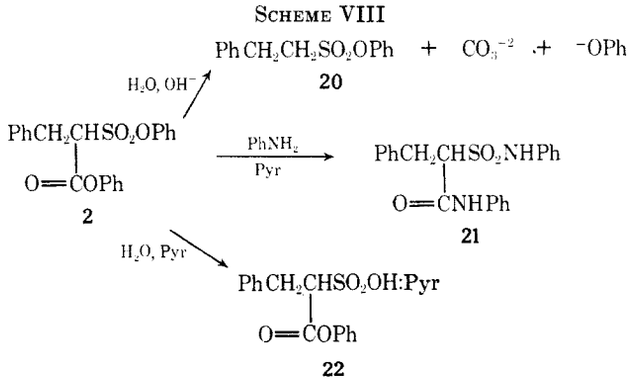
Using 1 equiv of aniline in refluxing pyridine, diphenyl sulfoacetate (**1**) is converted in 65% yield into an anilide phenyl ester derivative of sulfoacetic acid which was identified as phenyl N-phenylcarbamylmethanesulfonate (**18**).[1a,11] Thin layer chromatographic analysis of the aminolysis reaction mixture revealed the presence of both isomeric anilide phenyl esters (**18** and **19**), the dianilide (**14**), unchanged diphenyl sulfoacetate (**1**), and phenol. Both the isomeric anilide phenyl esters (**18** and **19**) undergo further anilinolysis in refluxing pyridine to form the dianilide (**14**) (Scheme VII).

SCHEME VII



The monoalkyl derivatives (**2**) of diphenyl sulfoacetate are not hydrolyzed under refluxing aqueous acidic conditions. The alkaline hydrolysis of the benzyl derivative (**2**, R = $PhCH_2$), like that of diphenyl sulfoacetate (**1**) itself, involves cleavage and the formation of phenyl 2-phenylethanesulfonate (**20**). Diphenyl α-benzylsulfoacetate (**2**, R = $PhCH_2$) readily forms a dianilide (**21**) with aniline in refluxing pyridine. In refluxing pyridine containing at least 1 equiv of water, diphenyl α-benzylsulfoacetate (**2**, R = $PhCH_2$) is converted into the corresponding sulfonic acid, isolated in 51% over-all yield as the pyridinium salt (**22**) (Scheme VIII).

SCHEME VIII



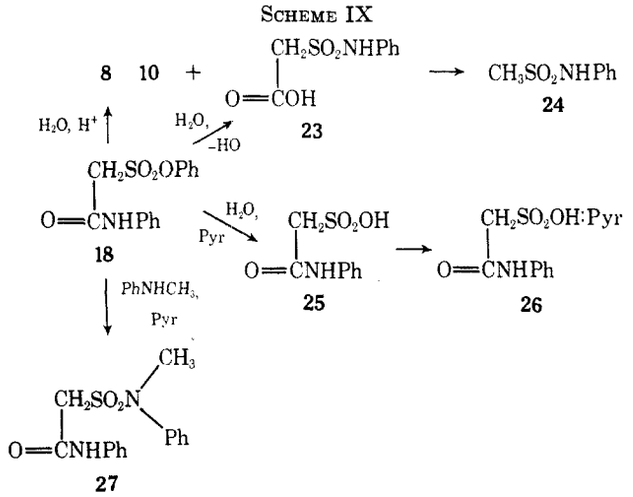
(10) G. Klaver *Rec. Trav. Chim.*, **54**, 208 (1935).

(11) The structure of this product was assigned on the basis of its elementary analysis, its infrared absorption, and its synthesis[1a] from phenyl carboxymethanesulfonate (**8**) by way of the acid chloride. Similarly, when **1** is treated with 1 molar equiv of N-methylaniline in refluxing pyridine, an oily mixture of products is obtained. Subsequent treatment of this mixture with aniline in refluxing pyridine produced a low yield (4.6%) of N-methyl-N-phenylcarbamylmethanesulfonanilide (**29**). This product was identified by its elementary analysis, its infrared absorption spectrum, and thin layer chromatographic comparison with an authentic sample prepared by the aminolysis of **19** with N-methylaniline.

Dialkyl derivatives (**3**) of diphenyl sulfoacetate are resistant, partially for steric reasons, to aminolysis with aniline in refluxing pyridine and to hydrolysis in pyridine and in acidic and alkaline aqueous media.[12]

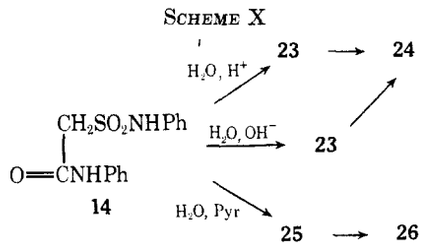
Hydrolysis and Aminolysis of Anilide Derivatives of Sulfoacetic Acid.—Phenyl N-phenylcarbamylmethanesulfonate (**18**) undergoes hydrolysis in aqueous acidic medium primarily at the carboxamide carbonyl group to produce phenyl carboxymethanesulfonate (**8**) in 63% yield. The aqueous alkaline hydrolysis of **18** produces mainly (53%) sulfoacetic acid (**10**). In addition, a smaller (25%) yield of N-phenylsulfamylacetic acid (**23**) is formed. The N-phenylsulfamylacetic acid (**23**) unexpectedly obtained was positively identified by its melting point, its infrared spectrum, and by its decarboxylation in warm pyridine to methanesulfonanilide (**24**). N-Phenylsulfamylacetic acid (**23**) may be formed from phenyl N-phenylcarbamylmethanesulfonate (**18**) by means of saponification of the carboxanilide portion of the molecule to form phenyl carboxymethanesulfonate (**8**), followed by aminolysis with aniline of the phenyl sulfonate ester. Phenyl carboxymethanesulfonate (**8**) may indeed be an intermediate in the transformation of **18** to **23** in alkaline aqueous medium; it is also converted under the same conditions into N-phenylsulfamylacetic acid (**23**). A more plausible mechanism will be offered below. The aqueous pyridine hydrolysis of phenyl N-phenylcarbamymethanesulfonate (**18**) occurs almost exclusively at the sulfonyl group to produce N-phenylcarbamylmethanesulfonic acid (**25**), isolated as the pyridine salt (**26**) in 93% yield. Aminolysis of **18** with N-methylaniline in pyridine also occurs at the sulfonyl group to form N-phenylcarbamylmethane-N-methylsulfonanilide (**27**) in 65% yield (Scheme IX).

SCHEME IX



The hydrolysis of the dianilide (**14**) in either acidic or alkaline aqueous medium produces only the carboxylic acid, N-phenylsulfamylacetic acid (**23**), identified by decarboxylation to methanesulfonanilide (**24**). The high yields (88%) of N-phenylsulfamylacetic acid (**23**) isolated seem to preclude nucleophilic attack at the sulfonyl portion of the dianilide to an appreciable extent in either acidic or alkaline aqueous medium. In striking contrast, however, the hydrolysis of the dianilide in refluxing pyridine containing one or two equivalents of water occurs primarily at the sulfonyl function, producing high yields (68%) of N-phenylcarbamylmethanesulfonic acid (**25**) isolated from pyridine as the pyridinium salt (**26**) (Scheme X). When

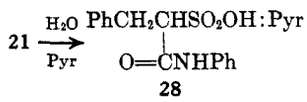
SCHEME X



chromatographically pure dianilide (**14**) is heated with N-methylaniline in refluxing pyridine, both the carboxanilide and the sulfonanilide portions undergo aminolysis producing a mixture of N-phenylcarbamylmethane-N-methylsulfonanilide (**27**) and N-phenyl-N-methylcarbamylmethane-N-methylsulfonanilide (**16**). Both products were produced in low yields. They were identified by thin layer chromatographic comparison with authentic samples of the same compounds prepared by other routes.

The dianilide (**21**) of α-benzylsulfoacetic acid is converted in refluxing aqueous pyridine into the corresponding sulfonic acid, isolated in 53% over-all yield as the pyridinium salt (**28**) (Scheme XI).

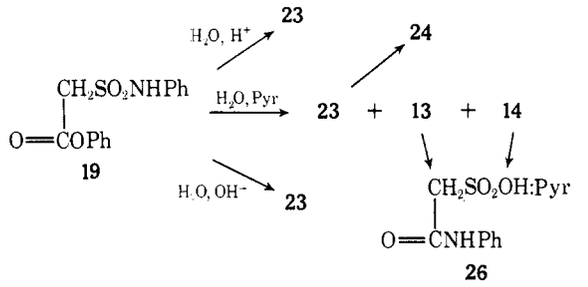
SCHEME XI



Carbophenoxymethanesulfonanilide (**19**) undergoes hydrolysis in aqueous acidic or alkaline medium to produce N-phenylsulfamylacetic acid (**23**) as the only isolable product; the yield of product in either case is low, being 48.5% from acidic medium and 36% from alkaline medium. When carbophenoxymethanesulfonanilide (**19**) was heated for 6 hr in refluxing pyridine containing 2.5 equiv of water, only the dianilide (**14**) was isolated in low (18.4%) yield. When the reaction was repeated and the mixture heated for a period of 147 hr, no dianilide (**14**) was obtained. Instead, pyridinium N-phenylcarbamylmethanesulfonate (**26**, 25%) and methanesulfonanilide (**24**, 37%) were obtained. Although no dianilide (**14**), pyridinium carbophenoxymethanesulfonate (**13**), or N-phenylsulfamylacetic acid (**23**) were isolated from this reaction mixture, it seems reasonable that they might be involved as intermediates in the formation of the observed products (**26** and **24**). In a separate experiment it was found that pyridinium carbophenoxymethanesulfonate (**13**) undergoes aminolysis with aniline in refluxing pyridine to form pyridinium N-phenylcarbamylmethanesulfonate (**26**) slowly but in good yield (80%) (Scheme XII). The treatment of carbophenoxymethanesulfonanilide (**19**) with N-methylaniline produces N-methyl-N-phenylcarbamylmethane-

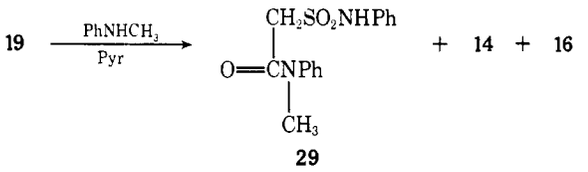
(12) The dibenzyl derivative of diphenyl malonate is saponified by heating with potassium hydroxide in boiling ethylene glycol to form dibenzylacetic acid. Prolonged heating of the dialkyl derivatives (**3**) of diphenyl sulfoacetate under the same conditions produced only neutral products of undetermined structures and unidentifiable acid products resembling sulfonic acids.

SCHEME XII



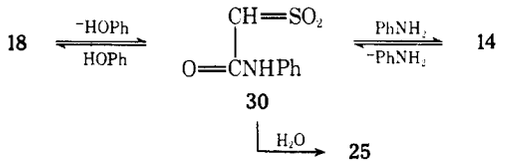
sulfonanilide (**29**) as the major product (84%). Thin layer chromatographic analysis of the crude reaction mixture revealed the presence of **29** and the dianilides **14** and **16** (Scheme XIII).

SCHEME XIII



Mechanism of Reaction of the Sulfonyl Group with Nucleophiles.—In summary, it can be said that in ester and amide derivatives of sulfoacetic acid, the sulfonyl group is much less reactive than the carbonyl group toward nucleophiles under acidic conditions. In aqueous alkaline and in pyridine media, however, the sulfonyl portion of the sulfonylacetyl system is as reactive as the carbonyl group and in some cases is clearly more reactive than the carbonyl group toward nucleophiles. The sulfonyl group in derivatives of sulfoacetic acid is more reactive toward nucleophiles in aqueous alkaline and in pyridine media than would be expected of phenyl ester and anilide derivatives of simple sulfonic acids, such as methanesulfonic acid and benzenesulfonic acid. Under similar conditions, phenyl benzenesulfonate, phenyl methanesulfonate (**9**), and methanesulfonanilide (**24**) are totally inert toward aminolysis and hydrolysis. Moreover, phenyl esters of negatively substituted sulfonic acids, such as phenyl *m*-nitrobenzenesulfonate and phenyl *o*-carbamylbenzenesulfonate,[13] are similarly unreactive under conditions which should readily promote hydrolysis and aminolysis by nucleophilic attack at the sulfonyl group. It seems likely, therefore, that in the hydrolysis and aminolysis of derivatives of sulfoacetic acid a mechanism not involving a simple direct initial attack of a nucleophile at the sulfonyl sulfur atom is operative. An attractive alternative mechanism has been suggested by the work of Truce,[14] King,[15] Opitz,[16] and their coworkers, who have shown the existence of sulfene intermediates generated in the presence of triethylamine from methanesulfonyl chloride, α-toluenesulfonyl chloride, and other alkanesulfonyl chlorides having at least one α-hydrogen atom. Although the base promoted generation of sulfenes from compounds other than alkanesulfonyl chlorides has not yet been reported, it seems quite probable that in the aqueous alkaline or pyridine promoted hydrolysis and aminolysis of ester and anilide derivatives of sulfoacetic acid sulfene intermediates, such as **30** (Scheme XIV), are also involved. A sulfene intermediate would be favorably formed when it can be stabilized by the interaction of its unsaturation with an adjacent electron-withdrawing group, such as a carbonyl group. The effect of other electron-withdrawing groups in the α position on the stabilization and ease of formation of sulfenes has been briefly reported.[14] The rapid hydrolysis of 2-hydroxy-5-nitro-α-toluenesulfonic acid sultone (5-nitro-3H-benzoxathiole 2,2-dioxide) might possibly occur *via* a sulfene intermediate stabilized by a nitroaryl group.[17]

SCHEME XIV



The conversion of phenyl sulfonate esters (**1** and **18**) into dianilides (**14** and **27**), the conversion of sulfonanilide derivatives (**14** and **19**) into N-methylsulfonanilides (**16** and **27**), and the hydrolysis of the dianilide (**14**), phenyl N-phenylcarbamylmethanesulfonate (**18**), and carbophenoxymethanesulfonanilide (**19**) into the same sulfonic acid (**25**) in pyridine may occur by way of a common sulfene intermediate. Several transformations observed (such as **19** into **25**, **18** into **23**, and **18** into **14** into **25**) suggest, moreover, that sulfenes, such as **30**, can be formed reversibly from either sulfonanilide or phenyl sulfonate derivatives of sulfoacetic acid.

In an attempt to trap a sulfene intermediate, it was found that an analytically and chromatographically pure sample of the dianilide (**14**) was converted by heating with excess phenol in refluxing pyridine into phenyl N-phenylcarbamylmethanesulfonate (**18**). This product (**18**) was not produced in isolable quantities but was detected and positively identified by thin layer chromatography. None of the isomeric anilide-phenyl ester (**19**) was detectable in the reaction mixture.

Phenyl ester and anilide derivatives of sulfoacetic acid having at least one α-hydrogen atom, such as diphenyl benzylsulfoacetate (**2**, R = $PhCH_2$), are reactive at the sulfonyl group toward nucleophiles in basic medium. In contrast, phenyl sulfonate esters incapable of forming sulfenes, such as phenyl benzenesulfonate and the dialkyl derivatives (**3**) of diphenyl sulfoacetate, in general, do not react easily with nucleophiles under basic or acidic conditions.[12,18]

(13) B. Loev and M. Kormendy, *J. Org. Chem.*, **27**, 2448 (1962).
(14) W. E. Truce and R. W. Campbell, *J. Amer. Chem. Soc.*, **88**, 3599 (1966).
(15) J. F. King and T. Durst, *ibid.*, **87**, 5684 (1965).
(16) G. Opitz, *Angew. Chem. Intern. Ed. Engl.*, **6**, 107 (1967).
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(18) Hydrolysis of the carbophenoxy group of **3** ($R_1 = R_2 = PhCH_2$) in refluxing ethylene glycol containing potassium hydroxide, followed by decarboxylation, may result in the formation of a dialkyl derivative of phenyl methanesulfonate, which is capable of forming a sulfene and, subsequently, a sulfonic acid.

Experimental Section[19]

Monoalkylation of Diphenyl Sulfoacetate (1).—To a refluxing and stirred solution of 5.0 g (17.1 mmol) of diphenyl sulfoacetate (1),[4b] 2.16 g (17.1 mmol) of benzyl chloride, and 3.0 g of sodium iodide in 5 ml of anhydrous acetone was added in small portions over a period of 15 hr a total of 2.36 g (17.1 mmol) of anhydrous potassium carbonate. Stirring and refluxing of the mixture was continued for another 9 hr. After removal of the acetone under aspirator pressure, the residual solid material was made slightly acidic with dilute hydrochloric acid. The resulting insoluble material was removed by filtration and recrystallized from ethanol to yield 4.66 g (71.2%) of product, mp 81–84°. A second recrystallization from a dilute solution of ethanol provided 3.45 g (52.8%) of pure diphenyl benzylsulfoacetate (2, R = $PhCH_2$), mp 82–83°. The filtrate yielded 1.51 g of an impure form of diphenyl dibenzylsulfoacetate (3, $R_1 = R_2 = PhCH_2$).

Anal. Calcd for $C_{21}H_{18}O_5S$: C, 65.95; H, 4.74. Found: C, 66.09; H, 4.74.

Diphenyl *p*-bromobenzylsulfoacetate (2, R = p-$BrC_6H_4CH_2$), mp 87–87.5°, was prepared by the same procedure in 57% yield.

Anal. Calcd for $C_{21}H_{17}BrO_5S$: C, 54.67; H, 3.72. Found: C, 54.89; H, 3.69.

Dialkylation of Diphenyl Sulfoacetate (1).—A mixture of 0.5 g (1.71 mmol) of diphenyl sulfoacetate (1), 0.432 g (3.42 mmol) of benzyl chloride, 0.5 g (3.62 mmol) of anhydrous potassium carbonate, 0.6 g of sodium iodide, and 25 ml of anhydrous acetone was refluxed and stirred for a period of 2 days. Work-up of the reaction mixture in the manner described above afforded 0.556 g of a white crystalline solid, mp 101–104°. Recrystallization from ethanol yielded 0.443 g (55%) of pure diphenyl dibenzylsulfoacetate (3, $R_1 = R_2 = PhCH_2$), mp 103–104°. Diphenyl dibenzylsulfoacetate (3, $R_1 = R_2 = PhCH_2$) was also prepared by the alkylation of diphenyl benzylsulfoacetate (2, R = $PhCH_2$) by a similar procedure.

Anal. Calcd for $C_{28}H_{24}O_5S$: C, 71.16; H, 5.12. Found: C, 70.99; H, 5.18.

Diphenyl di(p-nitrobenzyl)sulfoacetate (3, $R_1 = R_2 = p$-$O_2NC_6H_4CH_2$), mp 156.5–157°, was also prepared by a similar procedure in 43% yield.

Anal. Calcd for $C_{28}H_{22}N_2O_9S$: C, 59.58; H, 4.28; N, 4.96. Found: C, 59.81; H, 3.99; N, 5.31.

Preparation of Acetoximinosulfoacetate (5).—A solution of 5.0 g (17.1 mmol) of diphenyl sulfoacetate (1), 5.0 g (61.0 mmol) of anhydrous sodium acetate, 50 ml of acetic anhydride, and 10 ml of glacial acetic acid was stirred at room temperature for 1 hr. The clear solution was then cooled to 10° and treated with a slow stream of a mixture of dry nitrogen and nitrosyl chloride generated according to the method of Bachmann and Hoffman.[20] After approximately 5 hr nitrosyl chloride was found to be present in excess and a light yellow precipitate was present. The mixture was then poured into ice and the resulting solid removed by filtration and washed with cold water to yield 5.1 g of a yellow solid, mp 60–66°. Recrystallization from an ethanol–n-heptane mixture afforded 3.7 g (55.6%) of pale yellow platelets: mp 73–74°; ir absorption at 5.5, 5.68 (C=O), 7.96–8.85 (SO_2) μ.

Anal. Calcd for $C_{16}H_{13}NO_7S$: C, 52.89; H, 3.61; N, 3.86. Found: C, 53.04; H, 3.66; N, 3.76.

This material cound not be reduced under any conditions to diphenyl acetamidosulfoacetate (7).

Preparation of the Phenylhydrazone (6) of Diphenyl Oxosulfoacetate.—A solution of 5.0 g (17.1 mmol) of diphenyl sulfoacetate (1) in 50 ml of anhydrous acetone was stirred at room temperature for 30 min wtih 6.0 g (43.5 mmol) of anhydrous potassium carbonate. The mixture was then chilled to 0–5° and treated dropwise with a cold (0–5°) solution of benzenediazonium chloride prepared by diazotizing 2.22 g (17.1 mmol) of aniline hydrochloride dissolved in 12.5 ml of 1.5 N hydrochloric acid with a solution of 1.28 g (18.6 mmol) of sodium nitrite in 10 ml of water. The addition of the diazonium salt was carried out with rapid stirring over a period of 1 hr. The reaction mixture was kept basic by the addition, when necessary, of more solid potassium carbonate. When the addition was complete, the mixture was stirred for another 10 min and then poured into ice. The resulting yellow solid was removed by filtration and washed thoroughly with water. The crude product (6.35 g, 93.6%) was recrystallized from an ethanol–water mixture to yield 5.38 g (79.4%) of yellow powdery solid: mp 101–102°; ir absorption at 3.13 (NH, weak), 5.90 (C=O), 8.1–8.8 (SO_2), 11.51, 13.32, and 14.52 (C_6H_5) μ.

Anal. Calcd for $C_{20}H_{16}N_2O_5S$: C, 60.66; H, 4.07; N, 7.07. Found: C, 60.55; H, 4.08; N, 6.60.

This material could not be reduced under any conditions to diphenyl acetamidosulfoacetate (7).

Aminolysis of Phenyl Ester Derivatives of Sulfoacetic Acid.—The phenyl ester and the amine were heated in refluxing pyridine for a period of about 4 hr. The reaction mixture was then poured into ice and acidified with hydrochloric acid to solubilize the pyridine solvent and excess amine. The crude amide was separated by filtration and recrystallized from either 95% ethanol or benzene. See Tables I and II.

TABLE I

AMINOLYSIS REACTIONS

Phenyl ester	Amine[a]	Product	Yield, %
1	Aniline[b]	18	65
1	Aniline	14	81
1	Benzylamine	15	81
1	N-Methylaniline	16	83
1	Piperidine	17	96
2, R = $PhCH_2$	Aniline	21	57
8	Aniline	23	11.1[c]
13	Aniline	26	80
18	Aniline	14	91
18	N-Methylaniline	27	65
19	Aniline	14	89
19	N-Methylaniline	29	84

[a] Excess amine was used unless otherwise indicated. [b] 1 molar equiv of aniline was used per 1 mol of 1. Thin layer chromatographic analysis of the crude product indicated that carbophenoxymethanesulfonanilide (19) and the dianilide (14) of sulfoacetic acid were also formed. [c] The reaction was carried out in strongly alkaline aqueous medium and large amounts of sulfoacetic acid were undoubtedly formed.

Hydrolysis Reactions of Derivatives of Sulfoacetic Acid. A. Acidic Aqueous Medium.—Approximately 1 g of the compound was covered with 30 ml of concentrated hydrochloric acid and the mixture heated under partial reflux, allowing volatile products to distil. In the case of hydrolysis of carbophenoxy derivatives (1 and 19) of sulfoacetic acid, the heating was continued until phenol no longer distilled. Hydrolysis was usually complete in less than 10 hr. Chilling of the reaction mixture caused the separation of the carboxylic acid. Additional product was obtainable by dilution of the fitrate and continuous extraction of the solution with ether. Purification was usually effected by recrystallization from benzene. See Table III.

B. Alkaline Aqueous Medium.—Approximately 1 g of the compound was covered with 30 ml of 5–10% sodium hydroxide solution containing 10 ml of ethanol to facilitate solution of the compound. The resulting mixture was heated under partial reflux, allowing volatile products to distill. In the case of anilide derivatives (14, 18, and 19), it was found that aniline codistilled with water. The hydrolysis reactions were usually complete in less than 10 hr, the average length of heating being about 4 hr. The cooled reaction mixtures were first extracted continuously with ether to remove neutral components. The remaining alkaline solution was then passed through a column of Dowex-50W-X4 cation exchange resin (J. T. Baker Chemical Co.); the strongly acidic eluent was reduced in volume and then extracted with ether continuously to remove ether soluble acidic components. The remaining aqueous solution was then treated with excess pyridine to form the pyridine salt of strongly acidic sulfonic acid products, isolated by evaporation of the aqueous solution. See Table IV.

C. Aqueous Pyridine Medium.—Approximately 1 g of the compound was dissolved in 5–10 ml of freshly distilled pyridine

(19) Melting points are uncorrected and were taken on a Fisher–Johns apparatus. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn. Infrared spectra were recorded on a Beckman IR-8 instrument using Nujol mulls or potassium bromide pellets. Thin layer chromatograms were developed on Eastman chromatogram sheets (silica gel). Chloroform was most often used as the tlc developing solvent; spots were visualized in an atmosphere containing iodine vapor.

(20) W. E. Bachmann and R. A. Hoffman, *Org. Reactions*, **2**, 251 (1944).

TABLE II

AMIDE DERIVATIVES OF SULFOACETIC ACID

Compound	Formula	mp, °C	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
14	$C_{14}H_{14}N_2O_3S$	150–151[a]						
15	$C_{16}H_{18}N_2O_3S$	143–144	60.35	5.70	8.80	60.46	5.75	8.89
16	$C_{16}H_{18}N_2O_3S$	81–82[b]	60.35	5.70	8.80	60.30	5.73	9.11
17	$C_{12}H_{22}N_2O_3S$	102.5–103	52.55	8.03	10.22	52.52	7.90	10.07
18	$C_{14}H_{18}N_2O_4S$	122–123.5[c]						
19	$C_{14}H_{18}N_2O_4S$	133–135[d]						
21	$C_{21}H_{20}N_2O_3S$	193–194	66.12	5.55	7.34	66.33	5.44	7.34
23	$C_8H_9NO_4S$	112–113[e]	44.64	4.22	6.51	44.80	4.30	6.70
27	$C_{15}H_{16}N_2O_3S$	118–119	59.19	5.30	9.20	59.51	5.36	9.24
29	$C_{15}H_{16}N_2O_3S$	174–175	59.19	5.30	9.20	59.46	5.19	9.12

[a] Lit.[1a,3] mp 151°. [b] Lit.[6] mp 79–81°. [c] Lit.[1a] mp 122–123.5°. [d] Lit.[1a] mp 133–135°. [e] Lit.[6] mp 118–119°.

TABLE III

ACIDIC AQUEOUS HYDROLYSIS REACTIONS

Reactant	Product	Yield, %
1	8[a]	53
14	23[b]	88
18	8[a]	63
19	23[b]	48.5

[a] Product **8**, phenyl carboxymethanesulfonate, mp 86–87° (lit.[4a] mp 86–87°), was decarboxylated to form phenyl methanesulfonate (**9**), mp 59.5–60°, in 70% yield by heating for 6 hr in refluxing pyridine. [b] Product **23**, carboxymethanesulfonanilide, was decarboxylated to form methanesulfonanilide (**24**), mp 99.5–100°, in 31% yield by heating in refluxing pyridine containing a trace of cupric oxide.

TABLE IV

ALKALINE AQUEOUS HYDROLYSIS REACTIONS

Reactant	Product	Yield, %
1	10[a]	49
	9	20
2, R = $PhCH_2$	20[b]	42
14	23	88
18	10[a]	53
	23	25
19	23	36

[a] Isolated and purified as the pyridine salt (**11**) (see Table VI). [b] Mp 69–69.5°. *Anal.* Calcd for $C_{14}H_{14}O_3S$: C, 64.10; H, 5.38. Found: C, 64.21; H, 5.46.

containing 1–10 molar equiv of water.[21] The mixtures in various trials were refluxed for periods varying from 4 to 147 hr. Following the reflux period, the clear and usually colorless reaction mixtures were cooled to room temperature and then diluted with ether to the cloud point. Further chilling in ice caused the crystallization of the sulfonic acid products as the pyridine salts. Following separation of the pyridine salts by filtration, the filtrates were evaporated in a rotary evaporator under aspirator pressure to recover the neutral components of the mixtures. Alternatively, the pyridine filtrates were diluted with water, acidified, and extracted continuously with ether to remove the neutral fractions.

The pyridine salts of sulfonic acid products may be converted to the free sulfonic acids by passing the salts dissolved in water through a column of Dowex-50W-X4 cationic exchange resin (J. T. Baker Chemical Co.). Evaporation of the strongly acidic eluent affords the sulfonic acid in nearly pure form. In this manner, pyridinium N-phenylcarbamylmethanesulfonate (**26**) was converted into the sulfonic acid, N-phenylcarbamylmethanesulfonic acid (**25**), mp 230° in 95% yield. See Tables V and VI.

TABLE V

AQUEOUS PYRIDINE HYDROLYSIS REACTIONS

Reactant	Equiv of water used	Reflux time, hr	Product	Yield, %
1	1–3	2–68	13	30–35
			9	57–65
2, R = $PhCH_2$	6	5	22	51
14	2	22	26	68
14	4	22	26	54
18	1	22–24	26	81–93
19	2	147	26	25
			24	37
19	2–2.5	5–6	14	18.4
19	10	26	24	46
21	2.5	7	28	53

TABLE VI

PYRIDINIUM SALTS OF SULFONIC ACIDS

Compound	Formula	mp, °C	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
11	$C_7H_9NO_5S$	151–152	38.40	4.14		38.44	4.37	
13	$C_{13}H_{13}NO_5S$	124–126	52.85	4.41	4.74	52.83	4.71	4.58
22	$C_{20}H_{19}NO_5S$	131–132	62.32	4.97	3.63	61.49	4.68	3.61
26	$C_{13}H_{14}N_2O_4S$	145–151	53.05	4.79	9.52	53.20	4.83	9.24
28	$C_{20}H_{20}N_2O_4S$	133–135	62.48	5.24	7.29	62.44	5.34	7.30

(21) If no water is used, diphenyl sulfoacetate (**1**) can be recovered unchanged. Under anhydrous conditions, the refluxing pyridine solution of **1** rapidly darkens; as refluxing continues, the amount of recoverable diphenyl sulfoacetate diminishes.

Registry No.—**2** (R = CH_2Ph), 21372-67-8; **2** (R = *p*-$BrC_6H_4CH_2$), 21372-68-9; **3** ($R_1 = R_2 = PhCH_2$), 21372-69-0; **3** ($R_1 = R_2 = p$-$O_2NC_6H_4CH_2$), 21372-70-3; **5**, 21372-71-4; **6**, 21372-72-5; **11**, 21372-73-6; **13**, 21372-74-7; **15**, 21372-75-8; **17**, 21372-76-9; **21**, 21372-77-0; **22**, 21372-78-1; **26**, 21372-79-2; **27**, 21372-80-5; **28**, 21372-81-6; **29**, 21372-82-7.