Procedure.—A 1-ml. aliquot of the reaction mixture was pipeted into a 50-ml. volumetric flask containing a 5-ml. aliquot of aqueous sodium hydroxide (20 g. per 100 ml. of water) and the flask was heated for 10 min. on a steam bath. The flask was cooled and 2.3 ml. of concentrated hydrochloric acid was added in portions with intermittent cooling. A 25-ml. aliquot of aqueous ferric chloride solution ($\geq$0.5 g. per 300 ml. of water plus several drops of concentrated hydrochloric acid) was added and the flask diluted to the mark with distilled water. The absorption of the solution was then immediately measured with a Klett-Summerson photoelectric colorimeter; the blank solution consisted of a 25-ml. aliquot of the ferric chloride solution diluted to 50 ml. The same ferric chloride solution was used throughout a kinetic run. The recorded time of the aliquot is that of complete drainage of the 1-ml. pipet.

The absorbancy (A) reading of the colorimeter is directly proportional to the concentration of the original sodium benzoyl aliphatic hydroxamate. The first-order rate equation then is[20]

$$\log (A - A_\infty) = \frac{-kt}{2.303} + \log (A_0 - A_\infty) \qquad (3)$$

The rate constants were determined from the slope of the graph of log A *vs.* t, $A_\infty = 0$. Good straight lines were obtained; see Fig. 1 for typical examples. All rates were followed to *ca.* 75% complete reaction except for those at 20° (to *ca.* 67% complete reaction) and the determinations of sodium benzoyl acetohydroxamate (to 40–50% complete reaction). The enthalpies and entropies of activation were calculated from rate constants determined at two different temperatures by use of the usual equation.[21]

(20) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," John Wiley and Sons, Inc., New York, N. Y., 1953, p. 28.

(21) Ref. 20, p. 96.

Organic Disulfides and Related Substances. X. Synthesis of 2-Acetamidoethyl Arene- and Alkanethiolsulfonates[1a,b]

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Synthesis of 2-acetamidoethyl thiolsulfonates was studied as typifying alkyl arenethiolsulfonates and alkyl alkanethiolsulfonates, and also because of the possibility that the products would protect against ionizing radiation. Of numerous approaches examined, the most general was by reaction of a sulfonyl iodide and a silver thiolate; preparations were developed for requisite alkanesulfonyl iodides, a class hitherto unknown, and for a representative sodium alkanesulfinate needed as precursor to an iodide. A smooth but less general synthesis involved thioalkylation of sulfinate salts by a thiolsulfonate.

The previous paper of this series reported good protective activity against lethal effects of ionizing radiation for certain thiolsulfonates of structure RSO_2SR' (**1**) in which R and R′ were identical and were aminoethyl or derivatives thereof.[1b] This paper reports syntheses in which R′ is 2-acetamidoethyl. As group R, *p*-tolyl, methyl, and 2-ethylhexyl were chosen to typify the general classes of unsymmetrical alkyl arenethiolsulfonates and alkanethiolsulfonates.

Early syntheses of unsymmetrical thiolsulfonates have been reviewed.[2] Subsequent ones include reaction of a thiol with a sulfonic anhydride[3a] or with a sulfinic acid and ethyl nitrite,[3b] oxidation of an unsymmetrical disulfide[3c,d] or chlorinolysis of two symmetrical disulfides,[3e] and interaction of a disulfide with a sulfinic acid.[3f] All of these methods presently are handicapped, either intrinsically or for want of demonstration of their generality.

The syntheses found best by us thus far are illustrated in Chart I. The reaction of sulfonyl iodides and silver thiolates was our first choice for exploration because it had no obvious limitations except the unavailability of alkanesulfonyl iodides; methanesulfonyl chloride and silver 2-acetamidoethanethiolate (**2**) failed to give an isolable thiolsulfonate.

The reaction of iodides and silver thiolates has been used only with aromatic compounds.[4,5] For synthesis of an alkyl thiolsulfonate, *p*-toluenesulfonyl iodide first was used because it was readily obtainable by reaction of arenesulfinate salts in water with iodine in methanol.[4] With the silver thiolate (**2**) it gave the alkyl arenethiolsulfonate (**3**) in 47% yield. Ether, acetonitrile, benzene, and diglyme gave similar results as solvents; dimethyl sulfoxide reacted. The identity of **3**, and also of **4** and **5** described below, was established by analysis, infrared spectrum, and an acidic reaction on pH test paper upon treatment with *p*-thiocresol.[6]

The alkanesulfonyl iodides needed for synthesis of alkyl alkanethiolsulfonates **4** and **5** apparently represented an unknown class. They could not be obtained by the method used for *p*-toluenesulfonyl iodide; methanesulfonyl iodide was soluble in methanol–water and 2-ethylhexanesulfonyl iodide was hydrolyzed. Attempted conversion of methanesulfonyl chloride by means of sodium iodide failed, perhaps because of reduction.[7] Methanesulfonyl iodide was obtained in good

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(1) (a) Reported in part at the Southeastern Regional Meeting of the American Chemical Society, Gatlinburg, Tenn., Nov. 1-3, 1962. This investigation was supported by the U. S. Army Medical Research and Development Command, Department of the Army, under Research Contract No. DA-49-193-MD-2030. Results are abstracted from portions of the Ph.D. dissertation of R. R. C., Vanderbilt University, 1963, and the forthcoming dissertation of T. F. P. (b) Paper IX: L. Field, A. Ferretti, R. R. Crenshaw, and T. C. Owen, *J. Med. Chem.*, **7**, 39 (1964). (c) Du Pont Postgraduate Teaching Assistant, 1962-1963. (d) Texaco Fellow in Chemistry, 1961-1962.

(2) R. Connor, "Organic Chemistry, An Advanced Treatise," Vol. I, H. Gilman, Ed., 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1943, pp. 906-908.

(3) (a) L. Field, *J. Am. Chem. Soc.*, **74**, 394 (1952). This method was used only for symmetrical thiolsulfonates, but should be adaptable to unsymmetrical ones. (b) G. Kresze and W. Kort, *Ber.*, **94**, 2624 (1961). (c) G. Leandri and A. Tundo, *Ann. chim.* (Rome), **44**, 74 (1954); *Chem. Abstr.*, **49**, 4563 (1955). (d) L. Field, H. Härle, T. C. Owen, and A. Ferretti, *J. Org. Chem.*, **29**, in press; (e) I. B. Douglas and B. S. Farah, *ibid.*, **24**, 973 (1959). (f) J. L. Kice and K. W. Bowers, *J. Am. Chem. Soc.*, **84**, 2384 (1962).

(4) D. T. Gibson, C. J. Miller, and S. Smiles, *J. Chem. Soc.*, **127**, 1821 (1925).

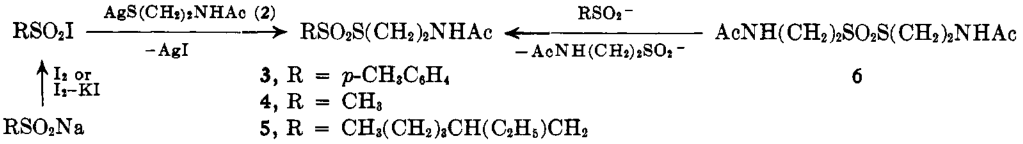
(5) R. Child and S. Smiles, *ibid.*, 2696 (1926).

(6) A consequence of the reaction $RSO_2SR' + R''SH \rightarrow RSO_2H + R'SSR''$ (*cf.* D. Barnard and E. R. Cole, *Anal. Chim. Acta*, **20**, 540 (1959), and ref. 1b and 3d).

(7) *Cf.* A. Perret and R. Perrot, *Bull. soc. chim. France*, [5]**1**, 1531 (1934).

Chart I

PREPARATION OF THIOLSULFONATES



$$\begin{tikzcd} \mathrm{RSO_2I} \arrow[r, "\mathrm{AgS(CH_2)_2NHAc}\ (2)", "-\mathrm{AgI}"'] & \mathrm{RSO_2S(CH_2)_2NHAc} & \mathrm{AcNH(CH_2)_2SO_2S(CH_2)_2NHAc} \arrow[l, "\mathrm{RSO_2^-}"', "-\mathrm{AcNH(CH_2)_2SO_2^-}"] \\ \mathrm{RSO_2Na} \arrow[u, "\mathrm{I_2\ or\ I_2{-}KI}"'] & & \end{tikzcd}$$

3, R = p-$\mathrm{CH_3C_6H_4}$

4, R = $\mathrm{CH_3}$

5, R = $\mathrm{CH_3(CH_2)_3CH(C_2H_5)CH_2}$

6

yield, however, by reaction of aqueous solutions of iodine–potassium iodide and sodium methanesulfinate. Since the green-black product evolved iodine under vacuum it could not be dried for analysis, but its characterization seems assured by its conversion using the silver thiolate (**2**) to 2-acetamidoethyl methanethiolsulfonate (**4**) in 58% yield, as well as by the similarity of its infrared spectrum to that of methanesulfonyl chloride.

2-Ethylhexanesulfonyl iodide decomposed extensively when prepared in the manner used for methanesulfonyl iodide, probably because of hydrolysis. It was prepared by adding sodium 2-ethylhexanesulfinate to iodine in benzene–ether. The iodide, treated *in situ* with the silver thiolate (**2**) gave 2-acetamidoethyl 2-ethylhexanethiolsulfonate (**5**) in 79% yield.

Comment should be added on the preparation of sodium 2-ethylhexanesulfinate. It was obtained quantitatively by chlorinolysis of 2-ethylhexyl disulfide and alkaline hydrolysis, probably according to the following sequence.[3e,8]

$$\mathrm{(RS)_2} \xrightarrow{\mathrm{Cl_2}} \mathrm{2RSCl_3} \xrightarrow{\mathrm{AcOH}} \mathrm{2RS(O)Cl} \xrightarrow{\mathrm{NaHCO_3}} \mathrm{2RSO_2Na}$$

This procedure was based on the useful methods developed by Douglass and co-workers.[3e,8,9] Douglass, Brower, and Martin obtained sodium ethanesulfinate by hydrolysis of ethylsulfur trichloride, itself derived by chlorine oxidation of ethanethiol.[8] Douglass pointed out the ready availability of sulfinic acids from disulfide oxidation, but used them without isolation.[9] The present direct synthesis of an alkanesulfinate salt was quantitative and, if general, should be superior to methods now available.

The second approach to synthesis (Chart I) involved thioalkylation of a sulfinate salt by a thiolsulfonate. It proved to be the best method of those tried. The interchange equilibrium on which it is based has been studied in some detail,[10,11] but without report of yields of products, perhaps because of the difficulty of separating the desired thiolsulfonate. The method should be valuable for synthesis, however, in situations where the desired thiolsulfonate separates well from a solvent, while the other thiolsulfonate and sulfinate salts remain dissolved. This situation prevailed in the reaction of 2-acetamidoethyl 2-acetamidoethanethiolsulfonate (**6**, water-soluble) with the appropriate sodium sulfinates (water-soluble), and thiolsulfonates **3**, **4**, and **5** (extractable into organic solvents) were obtained at room temperature in yields of 65–100%.

Other approaches to unsymmetrical thiolsulfonates proved unattractive. Ultraviolet irradiation of a sulfonyl iodide–disulfide mixture gave very low yields of impure thiolsulfonates (*cf.* Experimental). Reaction of thiols and sulfonic anhydrides under acidic conditions (presence of aluminum chloride or of a sulfonic acid), instead of with pyridine,[3a] resulted in no isolable amounts of thiolsulfonates; indeed, 2-acetamidoethanethiol and p-toluenesulfonic anhydride gave no significant amount of thiolsulfonate **3** even in the presence of pyridine.

Under a variety of conditions, di-p-tolyl- and dicyclohexylcarbodiimide failed to effect conversion of p-toluenesulfonic acid to p-tolyl p-toluenethiolsulfonate with p-thiocresol or to **3** with 2-acetamidoethanethiol. The adduct (**7**) of p-thiocresol and di-p-tolylcarbodiimide would not yield a thiolsulfonate with a sulfonic acid. The adduct (**7**), nevertheless, is not

$$\mathrm{C_7H_7SH} + \mathrm{C_7H_7N{=}C{=}NC_7H_7} \longrightarrow \underset{\mathbf{7}}{\mathrm{C_7H_7NHC(SC_7H_7){=}NC_7H_7}}$$

without interest, since it exhibits some protection against ionizing radiation.[12] It may be added that thiolsulfonate **3** was poor in protective activity and toxic and that silver thiolate **2** was not protective; evaluations of **4** and **5** are pending.[12]

Efforts were unavailing to apply the chlorinolysis procedure of Douglass and Farah[3e] to synthesis of **3** from p-tolyl disulfide and 2-acetamidoethyl disulfide, p-tolyl p-toluenethiolsulfonate being the only isolable product. Since 2-acetamidoethyl disulfide alone in this procedure gave none of thiolsulfonate **6**, the amide function evidently interferes.

Also ineffective were efforts to develop a synthesis for thiolsulfonates which would be a counterpart of the preparation of alkylthiosulfates ($\mathrm{RSSO_3^-}$) from an alkyl disulfide and a sulfite in the presence of cupric ammonium complex.[13] Thus attempted reaction of sodium p-toluenesulfinate and 2-acetamidoethyl disulfide in the presence of cupric ammonium sulfate gave no isolable amount of **3**.

We conclude that the sulfinate–thiolsulfonate interchange is the least burdensome route of those explored and the method of choice when availability and relative solubility of materials is satisfactory. The reaction of sulfonyl iodides with silver thiolates should be general; owing to the development of routes to alkanesulfonyl iodides, it should be practical as well.

Experimental[14]

Preparation of Thiolsulfonates from Sulfonyl Iodides and Silver 2-Acetamidoethanethiolate (2). A. 2-Acetamidoethyl p-Tol-

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[8] I. B. Douglass, K. R. Brower, and F. T. Martin, *J. Am. Chem. Soc.*, **74**, 5770 (1952).

[9] I. B. Douglass, "Organic Sulfur Compounds," Vol. 1, N. Kharasch, Ed., Pergamon Press, New York, N. Y., 1961, p. 350.

[10] J. D. Loudon and A. Livingston, *J. Chem. Soc.*, 896 (1935).

[11] D. T. Gibson and J. D. Loudon, *ibid.*, 487 (1937).

[12] Protective activities against ionizing radiation were determined through the courtesy of Dr. T. R. Sweeney and Dr. D. P. Jacobus of the Walter Reed Army Institute of Research, Washington, D. C.

[13] J. M. Swan, *Nature*, **180**, 643 (1957).

[14] Melting points are corrected. Analyses were by Galbraith Microanalytical Laboratories, Knoxville, Tenn. Infrared spectra were obtained using a Perkin-Elmer Model 137B Infracord spectrophotometer with films of liquids or Nujol mulls of solids. Moist extracts usually were dried using anhydrous magnesium sulfate or calcium sulfate and, after removal of drying agent by filtration, were evaporated in a rotating evaporator under reduced pressure for recovery of products.

uenethiolsulfonate (**3**).—2-Acetamidoethanethiol[15] was converted to silver 2-acetamidoethanethiolate (**2**), essentially according to the undetailed general procedure,[4] by adding silver nitrate (20 g.) in water (80 ml.) to the thiol (14 g.) in water (60 ml.); anhydrous sodium acetate (9.67 g.) in water (60 ml.) then was added, the mixture was cooled, and the white thiolate (**2**) was separated and dried under vacuum to a constant weight of 24.1 g. (90%).

The thiolate **2** (25.3 g.) was added during 0.5 hr. to 31.6 g. of *p*-toluenesulfonyl iodide[16] in 300 ml. of dry benzene. The solution was stirred for an additional 0.5 hr. Silver iodide and unchanged **2** were removed by filtration, and the benzene solution was washed with 10% aqueous solutions of sodium bicarbonate and sodium bisulfite (10 ml. of each). Drying and evaporation (40°) of the benzene solution gave 17 g. of dark tar. Chromatography on a 2.25 × 50 cm. column of acid-washed alumina, with ether–chloroform elution, gave 14.3 g. (47%) of thiolsulfonate **3** as white crystals, m.p. 58–61.5°. Recrystallization from ether gave 9.3 g. (30%) of pure **3**, m.p. 62.5–64°. The infrared spectrum of the **3** was consistent with expectation, bands being found at 3300, 1650, 1560, 1340, 1140, and 825 cm.$^{-1}$.

Anal. Calcd. for $C_{11}H_{15}NO_3S_2$: C, 48.40; H, 5.54; N, 5.14; S, 23.45. Found: C, 48.38; H, 5.47; N, 5.06; S, 23.42.

B. **2-Acetamidoethyl Methanethiolsulfonate** (**4**).—Methanesulfonyl iodide was prepared: Iodine (6.85 g.) was dissolved in a solution of potassium iodide (13 g.) in water (20 ml.). The mixture then was poured with stirring into a solution of 5.0 g. of sodium methanesulfinate[18] in 20 ml. of water. Green-black needles which formed were removed by filtration, pressed dry under a rubber diaphragm, and amounted to 4.2 g. (82%) of presumed methanesulfonyl iodide, m.p. 85–90° dec. (Kofler). The infrared spectrum of the iodide was much like that of methanesulfonyl chloride, but with absorptions at slightly lower wave number; strong bands occurred at 1300, 1150, 960, and 730 cm.$^{-1}$. The iodide has fair stability, except under reduced pressure where iodine is evolved readily; after *ca.* 2 months of storage at atmospheric pressure, methanesulfonic acid and an unidentified white solid were left. Drying for analysis seemed impracticable and the presumed methanesulfonyl iodide was used directly.

For conversion to thiolsulfonate **4**, freshly prepared moist methanesulfonyl iodide was dried in a desiccator over calcium chloride at atmospheric pressure for 0.5 hr.; then 15.00 g. was dissolved in 400 ml. of dry benzene. The silver thiolate (**2**, 16.4 g.) was added during 20 min., and the mixture was stirred for 1 hr. more. The benzene solution was decanted and evaporated to yield 2.2 g. (16% of **4**) of yellow oil which solidified when chilled. Recrystallization from 1-butanol–pentane and ether–pentane gave 0.94 g. (7%) of **4**, m.p. 48–50°; the infrared spectrum of this material was identical with that of pure **4** described below.

The yellow precipitate left after decantation was washed with methanol. Evaporation of the methanol left 11.7 g. of oil. The oil upon standing for 2 days deposited 3.0 g. of 2-acetamidoethyl disulfide, which was removed by filtration. The residual oil was chromatographed on a 2.25 × 50 cm. column of acid-washed alumina. Elution with ether–chloroform yielded 7.3 g. (51%) of white **4**, m.p. 45–50° (a trace of disulfide remained up to 70°). Recrystallization of the second and third fractions (5.6 g.) from chloroform–carbon tetrachloride gave 2.75 g. (19%) of **4**, m.p. 45–49°. Several recrystallizations of the first fraction (1.7 g., 12%) gave **4** that had constant m.p. 52–53°; the infrared spectrum was consistent with expectation for **4**, bands being found at 3400, 1660, 1570, 1325 and 1140 cm.$^{-1}$.

Anal. Calcd. for $C_5H_{11}NO_3S_2$: C, 30.40; H, 5.62; N, 7.11; S, 32.55. Found: C, 30.18; H, 5.58; N, 7.09; S, 32.50.

In another experiment, purification was attempted of crude product by sublimation, zone melting, and paper chromatography, but none of these methods showed promise.

C. **2-Acetamidoethyl 2-Ethylhexanethiolsulfonate** (**5**).—Sodium 2-ethylhexanesulfinate was prepared: A stirred solution of 31.5 g. of 2-ethylhexyl disulfide and 13 g. of glacial acetic acid in 15 ml. of methylene chloride was cooled to −5°, and *ca.* 32 g. of chlorine was slowly introduced during *ca.* 1 hr. (by allowing a chilled container to warm). Water (10 ml.) then was added and the mixture was allowed to warm to room temperature. The solution was extracted with 10% aqueous sodium bicarbonate until the organic layer was neutral, and the aqueous extract then was evaporated. The solid left was extracted with several portions of hot absolute ethanol (total volume, 1 l.) which removed the sodium sulfinate. Evaporation of the ethanol left 44.0 g. (102%) of waxy sodium 2-ethylhexanesulfinate, which reduced aqueous permanganate and had infrared bands at 1015 and 1060 cm.$^{-1}$.

For preparation of 2-ethylhexanesulfonyl iodide, *in situ*, sodium 2-ethylhexanesulfinate (23.5 g.) was added to a stirred solution of 13.7 g. of iodine in 200 ml. of 3:1 benzene–ether.

After 10 min., 15.8 g. of silver thiolate **2** was added slowly during 40 min. with stirring. The mixture was stirred 1 hr. more, and the benzene–ether solution was decanted from the slimy precipitate. The precipitate was washed with benzene, ether, and chloroform. The organic solutions were washed with 10% aqueous sodium sulfite until colorless. Drying and evaporation of the organic solution gave 12.6 g. (79%) of oily **5**, n^{26}_{D} 1.4951, the infrared spectrum of which was essentially identical with that of the analytical sample described below. The oil could not be induced to crystallize, and 10.7 g. was chromatographed on a 2.25 × 50 cm. column of Merck acid-washed alumina with ether–chloroform elution. The yield was 8.0 g. (59%) of **5**, n^{27}_{D} 1.5048, the infrared spectrum of which was identical with that of analytically pure **5**. Short-path distillation at 90° (0.03 mm.) gave only a small amount of distillate (n^{26}_{D} 1.5008) after 10 hr. and much decomposition occurred.

Preparation of Thiolsulfonates by Thioalkylation of Sulfinate Salts with 2-Acetamidoethyl 2-Acetamidoethanethiolsulfonate (**6**). A. **2-Acetamidoethyl** ***p*****-Toluenethiolsulfonate** (**3**).—A solution of **6** (1.34 g.)[19] in water (15 ml.) was added to a stirred solution of sodium *p*-toluenesulfinate (4.46 g.) in water (35 ml.). Benzene (*ca.* 50 ml.) was added, and the mixture was shaken mechanically for 3 hr. After an overnight period, the benzene layer was separated, dried, and evaporated to an oil, which solidified on standing. The yield of **3** was 0.90 g. (66%), m.p. 58–61°, undepressed by authentic **3**; the infrared spectrum was identical with that of pure **3** described above.

B. **2-Acetamidoethyl Methanethiolsulfonate** (**4**).—As in A, thiolsulfonate **6** (1.34 g.)[19] in water (15 ml.) was added to sodium methanesulfinate (2.55 g.)[18] in water (35 ml.). After the mixture had been shaken with benzene (100 ml., 5 hr.) and let stand, evaporation of the benzene layer gave only a small amount of thiolsulfonate **4**. The water layer, therefore, was extracted with ten 25-ml. portions of chloroform. The chloroform extract was separated, dried, and evaporated. The yield of **4** was 0.64 g. (65%), m.p. 50–51.5°, infrared spectrum identical with that of authentic **4**.

C. **2-Acetamidoethyl 2-Ethylhexanethiolsulfonate** (**5**).—As in A, thiolsulfonate **6** (1.34 g.)[19] in water (15 ml.) was added to sodium 2-ethylhexanesulfinate (5.00 g.) in water (35 ml.). The mixture was shaken with 100 ml. of benzene (5 hr.) and then let stand overnight. Evaporation of the benzene gave 1.53 g. (103%) of **5** as clear oil, n^{27}_{D} 1.5050. The infrared spectrum had strong $-SO_2-$ bands at 1140 and 1340 cm.$^{-1}$ and strong amide bands at 1550, 1670, and 3375 cm.$^{-1}$. In the light of earlier experience, the oily **5** was analyzed without further attempts to purify it.

Anal. Calcd. for $C_{12}H_{25}NO_3S_2$: C, 48.80; H, 8.54; N, 4.75; S, 21.75. Found: C, 48.88; H, 8.69; N, 4.95; S, 21.99.

Preparation of Thiolsulfonates by Irradiation of Sulfonyl Iodides in the Presence of Disulfides.—2-Ethylhexanesulfonyl iodide was prepared *in situ* by treating 6.7 g. of sodium 2-ethylhexanesulfinate with 4.06 g. of iodine in 150 ml. of benzene in a quartz flask. 2-Acetamidoethyl disulfide (1.70 g.) and 50 ml. more of benzene were added, and the mixture was strongly irradi-

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[15] R. Kuhn and G. Quadbeck, *Ber.*, **84**, 844 (1951).

[16] Prepared by the general method of Gibson, Miller, and Smiles[4]; m.p. 82–84°, lit.[17] m.p. 84–85°.

[17] R. Otto and J. Tröger, *Ber.*, **24**, 479 (1891).

[18] From reduction of methanesulfonyl chloride with sodium sulfite according to L. Field and J. W. McFarland, *J. Am. Chem. Soc.*, **75**, 5582 (1953).

[19] L. Field, T. C. Owen, R. R. Crenshaw, and A. W. Bryan, *ibid.*, **83**, 4414 (1961).

ated with ultraviolet light for 16 hr. The mixture then was washed with a solution of sodium sulfite and dried. Evaporation left 0.56 g. (13%) of dark oil, the infrared spectrum of which showed it to be largely 2-acetamido 2-ethylhexanethiolsulfonate (**5**), $n^{25}D$ 1.5103.

Reaction of *p*-toluenesulfonyl iodide (16 mmoles) and 2-acetamidoethyl disulfide (7.2 mmoles) in similar fashion gave a dark oil, which had an infrared spectrum indicating it to be largely **3**, but the yield was only 2%.

Irradiation of *p*-toluenesulfonyl iodide and *p*-tolyl disulfide, much as before, resulted in *p*-tolyl *p*-toluenethiolsulfonate in 7% yield; characterization was effected by melting point and the infrared spectrum. However, a control experiment in which the disulfide was omitted also resulted in about the same yield of the thiolsulfonate.

N,N,S-Tri-*p*-tolylisothiourea (7).—A solution of 8.37 g. of *p*-thiocresol in 50 ml. of benzene was added rapidly to a stirred refluxing solution of 15.00 g. of di-*p*-tolylcarbodiimide in 100 ml. of benzene; heating was continued for 4 hr. After 5 days at *ca.* 25°, the solution was evaporated and the solid was rubbed with boiling ethanol (175 ml.). Chilling of the entire mixture at 4° and filtration resulted in 19.85 g. (85%) of white solid, m.p. 85–90°. Recrystallization from hexane gave the adduct (**7**) as needles with constant m.p. 89.5–90.5°.

Anal. Calcd. for $C_{22}H_{22}N_2S$: C, 76.26; H, 6.40; S, 9.25. Found: C, 76.00; H, 6.45; S, 9.31.

Further Studies on the Anomalous Hunsdiecker Reaction of Triaryl-Substituted Aliphatic Acids

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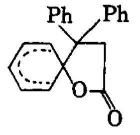
The phenyl shift previously observed in the Hunsdiecker reaction with β,β,β-triarylpropionic acids (such as I) failed to occur significantly with γ,γ,γ-triphenylbutyric acid (IV). Two sets of conditions were employed with IV. The normal Hunsdiecker reaction on the silver salt yielded primarily brominated parent acid, together with a small yield of the normal Hunsdiecker product, γ,γ,γ-triphenylpropyl bromide (VI). The recently described Cristol–Firth modification of the Hunsdiecker reaction using the free acid gave essentially the same results, though the yield of VI was increased. In addition, γ,γ,γ-triphenylbutyryl peroxide (X) was prepared and decomposed in refluxing carbon tetrachloride. No significant rearrangement of the γ,γ,γ-triphenylbutyryloxy radical (XII) was found. As a conclusion from these data, arguments are presented that the anomalous Hunsdiecker reaction of such triarylaliphatic acids proceeds in a radical fashion from the acyloxy radical and that it involves phenyl migration in this radical. The migration is, however, sensitive to the ring size created during the migration, proceeding *via* a five-, but not a six-membered ring.

Previous work[2,3] has shown that β,β,β-triarylpropionic acids such as the parent acid I undergo rearrangement to aryl β,β-diarylacrylates upon attempted degradation by the Hunsdiecker reaction,[4] with little bromodecarboxylation being observed. An Ar_1-5 type intermediate (II),[5] rather than an Ar_2-6 type intermediate (III), appeared to explain the course of the rearrangement, but the radical or ionic nature of the process has remained a difficult point to settle.[6]

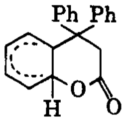
As a natural extension of this work, the question arose as to whether rearrangement *via* an Ar_1-6 intermediate (V) might occur. A study of γ,γ,γ-triphenylbutyric acid (IV) in the Hunsdiecker reaction was made, therefore, and the results of this study are reported here. In addition, the recent report of Cristol and Firth[7] on the bromodecarboxylation of acids using the free acid, bromine, and excess mercuric oxide in the dark led us to examine both the above triphenylbutyric acid (IV) and the previously studied acid I in their process as well.

Ph_3CCH_2COOH

I



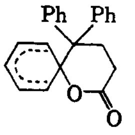
II



III

$Ph_3CCH_2CH_2COOH$

IV



V

II, III, and V apply either as ionic or radical species

The preparation of acid I was as before,[2] while the synthesis of acid IV was straightforward and followed the sequence shown (eq. 1). The displacement reaction

$$\mathrm{I} \xrightarrow[(2)\ \mathrm{LiAlH_4}]{(1)\ \mathrm{SOCl_2}} \underset{(92\%)}{Ph_3CCH_2CH_2OH} \xrightarrow{\mathrm{P + I_2}} \underset{(77\%)}{Ph_3CCH_2CH_2I} \xrightarrow[\mathrm{DMSO}]{\mathrm{NaCN}}$$

$$\underset{(71\%)}{Ph_3CCH_2CH_2CN} \xrightarrow[\Delta]{\mathrm{H_2SO_4}} \underset{(\mathrm{IV},\ 94\%)}{Ph_3CCH_2CH_2COOH} \quad (1)$$

using sodium cyanide failed under the other conditions tried, *viz.*, refluxing the reactants in aqueous alcohols or ethylene glycol. The beneficial use of dimethyl sulfoxide solvent in such reactions previously has been

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(1) Taken in part from the M. S. thesis of J. A. L., Loyola University, May, 1963.

(2) J. W. Wilt and D. D. Oathoudt, *J. Org. Chem.*, **21**, 1550 (1956); **23**, 218 (1958).

(3) J. W. Wilt and J. L. Finnerty, *ibid.*, **26**, 2173 (1961).

(4) R. G. Johnson and R. K. Ingham, *Chem. Rev.*, **56**, 219 (1956).

(5) Throughout this paper, our designation of these as Ar_m-n type rearrangements carries no implication that anchimeric assistance is involved. Our use of the term is meant simply to convey the site of the eventual substitution on the aromatic ring and the size of the ring in the intermediate.

(6) The absence of rearrangement with β,β,β-tris(*p*-nitrophenyl)propionic acid led us to suggest an *ionic* pathway earlier,[2] but the small substituent effects observed later[3] confused the issue and no compelling evidence either way had been found prior to the present study. It is interesting to note that the Ar_2-6 pathway is equally effective as the Ar_1-5 in certain solvolyses [R. Heck and S. Winstein, *J. Am. Chem. Soc.*, **79**, 3114 (1957)] and, therefore, it might be expected to be an equally likely route for the present rearrangement. Though the Ar_2-6 route (see III) does not occur in the anomalous Hunsdiecker reactions of β,β,β-triarylpropionic acids,[3] it seemingly has been observed with β-phenylisovaleric acid (dissertation, C. E. Berr, University of California at Los Angeles, 1952) and quite recently with β,β-diphenylpropionic acid [U. K. Pandit and I. P. Dirk, *Tetrahedron Letters*, **14**, 891 (1963)]. In both cases dihydrocoumarin derivatives were the products. Steric effects probably occasion the switch from Ar_2-6 to Ar_1-5 as the acid studied changes from the two mentioned above to I and its derivatives.

(7) S. J. Cristol and W. C. Firth, Jr., *J. Org. Chem.*, **26**, 280 (1961).