tubes were also examined by infrared spectroscopy to confirm the identities of the materials present.[25]

COLLEGE OF PHYSICIANS AND SURGEONS
DEPARTMENTS OF BIOCHEMISTRY AND OF OBSTETRICS AND GYNECOLOGY
COLUMBIA UNIVERSITY[26,27]
NEW YORK 32, N. Y.
MEDICAL LABORATORIES OF THE COLLIS P. HUNTINGTON MEMORIAL HOSPITAL OF HARVARD UNIVERSITY AT THE MASSACHUSETTS GENERAL HOSPITAL AND THE DEPARTMENT OF BIOLOGICAL CHEMISTRY OF HARVARD MEDICAL SCHOOL[26,28]
BOSTON 14, MASS.

---

[25] The Perkin-Elmer Model 21 double beam infrared spectrophotometer was used.

[26] This work undertaken independently and simultaneously in the Columbia and Harvard laboratories is published here jointly.

[27] This work was supported in part by gifts from the Squibb Institute for Medical Research and the Damon Runyon Memorial Fund.

[28] This is publication 782 of the Cancer Commission of Harvard University. This work was supported in part by an Institutional Grant from the American Cancer Society, Inc., to the Massachusetts General Hospital and in part by a grant from the National Cancer Institute (U. S. Public Health Service).

The Preparation of β-Ketosulfonyl Chlorides[1]

BY WILLIAM E. TRUCE AND CALVIN W. VRIESEN[2]

RECEIVED JANUARY 7, 1953

The conversion of a β-ketosulfonic acid or its salt to the corresponding sulfonyl chloride does not appear to have been reported previously. The action of chlorosulfonic acid on acetophenone produced the 2,ω-disulfonyl chloride, while acetophenone-4-sulfonic acid with chlorosulfonic acid probably formed the 4,ω-disulfonyl chloride.[3] Treatment of sodium ω-acetophenonesulfonate with the same reagent resulted in the 2,ω-disulfonyl chloride.[3] The preparation of γ- and δ-ketosulfonyl chlorides has been accomplished by conventional methods.[4,5]

When sodium ω-acetophenonesulfonate[6] was treated with phosphorus pentachloride or phosphorus oxychloride, charring occurred. The free sulfonic acid was then prepared by a modification of the procedure of Truce and Alfieri.[6] Separate portions were immediately treated with phosphorus pentachloride, thionyl chloride, or phosphorus oxychloride, but charring occurred in all cases. However, treatment of the acid with phosphorus trichloride,[7] resulted in the formation of ω-acetophenonesulfonyl chloride. The sulfonyl chloride was found to be too unstable to be submitted for analysis; it was necessary to prepare the sulfonamide for that purpose. The instability of the free acid and the sulfonyl chloride is probably due in part to the activity of the methylene group.[8] The activity of the methylene group is further demonstrated by the fact that the ester, ethyl ω-acetophenonesulfonate, can be dissolved in dilute aqueous sodium hydroxide and can be recovered by the addition of acid.

Attempts to reduce the sulfonyl chloride to ω-acetophenonesulfinic acid by conventional methods failed. Friedel–Crafts reactions with the sulfonyl chloride were unsuccessful due to the decomposition of that substance with the evolution of sulfur dioxide.

In an attempt to obtain a more stable β-ketosulfonyl chloride, isobutyrophenone-α-sulfonyl chloride was synthesized. Isobutyrophenone-α-sulfonic acid was prepared by the dioxane-sulfotrioxide method, and the sulfonyl chloride was prepared by means of phosphorus trichloride. These two substances were found to be much more stable than the analogous derivatives of acetophenone, *e.g.*, isobutyrophenone-α-sulfonic acid has been stored in a paraffin sealed bottle for a year with little apparent change. Despite its greater stability, attempts to reduce the sulfonyl chloride to the sulfinic acid and to carry out Friedel–Crafts reactions with it met with failure.

Experimental[9]

ω-Acetophenonesulfonyl Chloride.—Acetophenone (159 g., 1.34 moles) was added to 1.34 moles of the dioxane sulfotrioxide reagent[6] in 400 ml. of ethylene chloride. The reaction mixture was cooled with an ice-bath, whereupon the sulfonic acid separated out. The product was removed by filtration and placed in a vacuum desiccator for three hours. A portion of the acid was recrystallized twice from ethyl acetate; m.p. 75–78°, lit.[8,10] 73–75°, 77–78°. The crude acid and 361 g. (2.62 moles) of phosphorus trichloride were heated on the steam table under gentle reflux for 14 hours. The excess phosphorus trichloride was removed at a water aspirator and the product was recrystallized from chloroform; conversion 122 g. (42% of theory), m.p. 87.5–88.2°.

Dry ammonia was passed into an ether solution of ω-acetophenonesulfonyl chloride until the ammonia odor persisted. The resulting product was recrystallized from ethanol; m.p. 158–159°.

Anal. Calcd. for $C_8H_9O_3NS$: N, 7.04. Found: N, 7.02.

Thirteen grams (0.060 mole) of ω-acetophenonesulfonyl chloride was dissolved in 46 g. (1.0 mole) of absolute ethanol. Heat was liberated and after an hour the solution was cooled with an ice-bath, whereupon crystals of the product separated out; conversion 9.0 g. (64% of theory), m.p. 44.5–45.5° after recrystallization from petroleum ether. The neutral equivalent was obtained by titrating an alcoholic solution of the ester with standard aqueous sodium hydroxide solution to a phenolphthalein end-point; calcd. 228; found, 229 and 227.

Anal. Calcd. for $C_{10}H_{12}O_4S$: C, 52.62; H, 5.29. Found: C, 52.88; H, 5.29.

Isobutyrophenone-α-sulfonyl Chloride.—Using the same procedure as previously described, 84 g. (0.57 mole) of isobutyrophenone (b.p. 217–220° (746 mm.)) was converted to 81 g. (63% of theory) of isobutyrophenone-α-sulfonic acid. A portion of the acid was recrystallized from ethyl acetate and melted at 69.5–72.0°.

Isobutyrophenone-α-sulfonic acid (51 g., 0.22 mole) and 21 g. (0.15 mole) of phosphorus trichloride were heated on a steam-bath overnight. The reaction mixture was decomposed with ice water and extracted with chloroform. After drying over sodium sulfate, chloroform was removed by distillation and the resultant yellow oil was taken up in boiling petroleum ether. White needles separated out; weight 25 g. (44% of theory), m.p. 40.0–41.5°.

Anal. Calcd. for $C_{10}H_{11}ClO_3S$: C, 48.64; H, 4.49. Found: C, 48.75; H, 4.42.

DEPARTMENT OF CHEMISTRY
PURDUE UNIVERSITY
LAFAYETTE, INDIANA

---

[1] An abstract of a portion of a thesis submitted by Calvin W. Vriesen to the Faculty of Purdue University in partial fulfillment of the requirements for the degree of Doctor of Philosophy, August, 1952.

[2] Purdue Research Foundation Fellow.

[3] A. W. Weston and C. M. Suter, THIS JOURNAL, **61**, 389 (1939).

[4] S. Smiles and T. P. Hilditch, *J. Chem. Soc.*, **91**, 522 (1907).

[5] F. S. Kipping and W. J. Pope, *ibid.*, **63**, 548 (1895).

[6] W. E. Truce and C. C. Alfieri, THIS JOURNAL, **72**, 2740 (1950).

[7] W. A. Proell, C. F. Adams and B. H. Shoemaker, *Ind. Eng. Chem.*, **40**, 1129 (1938).

[8] G. D. Parkes and S. G. Tinsley, *J. Chem. Soc.*, 1861 (1934).

[9] All melting points are corrected.

[10] W. von E. Doering and F. M. Beringer, THIS JOURNAL, **71**, 2221 (1949).