tank, to a pressure of 35 to 38 cm. Hg. The tank was then filled to a total pressure of 74 to 76 cm. Hg with tetrafluoroethylene[16] or chlorotrifluoroethylene. After the pressure had fallen to 35 cm. Hg (in about 4 hr.), 100 ml. of the desired alcohol was placed in a 300-ml. stainless steel high-pressure cylinder,[17] which was attached to the bottom of the tank by means of a suitable valve and coupling in such a manner as to form a removable low-temperature trap. The cylinder was then immersed in a liquid nitrogen bath and evacuated. The valve between the cylinder and the tank was opened, and the contents of the tank were condensed into the cylinder. Noncondensables were pumped off through an outlet valve on the cylinder. The valves to the cylinder were then closed, and the liquid nitrogen bath was replaced with one of ice water. (The alcoholysis is very exothermic, and considerable pressures are built up during this operation. Hence, the apparatus should be suitably barricaded.) The bath was allowed to warm to room temperature over 18 to 20 hr., the cylinder was cautiously detached, and its contents were poured into 500 ml. of water. The lower organic layer was separated, and the aqueous phase was extracted with three 100-ml. portions of methylene chloride. The combined organic phases were washed with 50 ml. of saturated aqueous sodium carbonate, dried over anhydrous magnesium sulfate, filtered, and distilled through a 35-cm. vacuum-jacketed Vigreux column to yield a forerun of methylene chloride and a cut containing mainly the crude ester. This cut was carefully fractionated on a 90-cm. spinning band column at a reflux ratio of 100: 1. The esters prepared and their yields are listed in Table I.

Chromatography. The distilled esters were chromatographed in 1-ml. portions on an 18-mm.-i.d. by 4-m.-long column of di-*n*-decyl phthalate on 42-60 mesh C-22 firebrick (25/100) at temperatures from 115 to 148°. Helium at an inlet pressure of 20 p.s.i.g. was used as the carrier gas. The major impurities in material from the spinning band column were identified as methylene chloride, the parent alcohol, and chlorodinitrotrifluoroethane (when chlorotrifluoroethylene was used as the starting olefin). A dozen or so trace impurities that were also observed were not identified.

Vapor pressures. Vapor pressures were measured over the pressure range of 300 to 800 mm. Hg with an isotenoscope similar to that described by Thomson.[18] The sample was introduced into the evacuated and outgassed isotenoscope by means of liquid nitrogen and was outgassed to constant vapor pressure at 20° through a bypass which was later sealed off. Mercury was used in the U-tube. Pressures were obtained from a Wallace and Tiernan Type FA 145 precision dial manometer.[19] Temperatures were obtained by means of a rapidly stirred silicone oil bath contained in a clear-walled Dewar flask and were observed with an Anschutz melting point thermometer to ±0.1°.

Infrared spectra. Spectra were obtained in the liquid phase in 0.025-mm. fixed-thickness sodium chloride cells on a Perkin-Elmer Infracord spectrometer. Their accuracy is estimated to range from ± 20 cm.$^{-1}$ at the high frequency end of the spectrum to ± 2 cm.$^{-1}$ at the low end.

Acknowledgment. The author is indebted to Mr. Virgil Du Val for assistance in the preparation of the chromatography column.

LIVERMORE, CALIF.

---

(16) Tetrafluoroethylene was prepared by the thermal depolymerization of polytetrafluoroethylene. Chlorotrifluoroethylene and dinitrogen tetroxide were purchased from The Matheson Chemical Co., East Rutherford, N. J.

(17) Hoke, Inc., 1 Tenakill Park, Cresskill, N. J.

(18) G. W. Thomson, Physical Methods of Organic Chemistry, Vol. I, Pt. 1, A. Weissberger, Ed., Interscience Publishers, Inc., New York, 1959, pp. 173–175.

(19) Wallace and Tiernan, Inc., 25 Main St., Belleville 9, N. J.

[CONTRIBUTION FROM THE STAMFORD LABORATORIES, CENTRAL RESEARCH DIVISION, AMERICAN CYANAMID CO.]

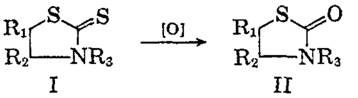
Sulfur Heterocycles. II. 3-Aryl- and 3-Alkyl-2-thiazolidinone 1,1-Dioxides: New Class of Cyclic Sulfone

RICHARD J. GAUL[1] AND WINFRIED J. FREMUTH

Received June 20, 1961

The oxidation of either 3-substituted-2-thiazolidinethiones or 3-substituted-2-thiazolidinones with hydrogen peroxide in hot acetic acid produces a new class of cyclic sulfone. The products have been assigned the structure of 3-substituted-2-thiazolidinone 1,1-dioxides.

The conversion of substituted 2-thiazolidinethiones to the corresponding 2-thiazolidinones (equation 1) generally has been effected either with alkaline hydrogen peroxide[2] or potassium permanganate[3] or mercuric oxide in acetic acid.[4] While these reagents are useful, the presence of certain substituents in the reactant would preclude their use. For example, a nitrile substituent in I would not survive treatment with alkaline hydrogen peroxide and has been shown to undergo hydrolysis in the mercuric oxide-acetic acid procedure.[5]



I II (1)

R_1, R_2, R_3 = H, Alkyl, Aryl

While investigating alternate methods of oxida-

---

[1] Address correspondence to Department of Chemistry, John Carroll University, Cleveland 18, Ohio.

[2] A. H. Cook, J. A. Elvidge, and G. Shaw, *J. Chem. Soc.*, 2367 (1949).

(3) J. Takeda, *J. Pharm. Soc., Japan*, 422, 281 (1917); *Chem. Abstr.*, 11, 2456 (1917).

(4) Y. K. Yur'ev and S. V. Dyatlovitskaya, *Zhur. Obshchei Khim.*, 27, 3152 (1957).

(5) R. J. Gaul, W. J. Fremuth, and M. N. O'Connor, *J. Org. Chem.*, 26, 5106 (1961).

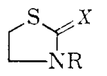
tion, we observed a unique reaction of 3-aryl- and 3-alkyl-2-thiazolidinethiones with hydrogen peroxide in hot acetic acid. This reagent rapidly accomplished the reaction shown in equation 1, did not adversely affect a nitrile substituent and, in addition, converted the heterocyclic sulfur atom to a sulfone. Such a use of hydrogen peroxide in a mildly acidic medium does not appear to have been reported previously.

The procedure consisted in adding gradually five molar equivalents of 30% hydrogen peroxide to a hot (70°) solution of the appropriate 2-thiazolidinethione in acetic acid. After the initial exothermic reaction had subsided and the separation of sulfur was finished, the reaction was completed by maintaining the mixture at 70° for about two hours. Table I summarizes the results of this study.

TABLE I

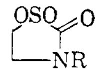
SULFONES DERIVED FROM 3-SUBSTITUTED-2-THIAZOLIDINETHIONES

Reactants



III

Products



IV

III	X	R	IV	Yield, %	M.P.[a]
IIIa	S	CH_2CH_2CN	IVa	78	145.5–6.3
IIIb	S	CH_2CH_2COOH	IVb	81, 90[b]	178.8–9.3
IIIc	S	C_6H_5	IVc	52	171.5–2.3
IIId	S	$CH_2C_6H_5$	IVd	68	156.5–7.2
IIIe	O	$CH_2CH_2CONH_2$	IVe	14.5	172.1–3.6

[a] Melting points are corrected and are for analytical samples. [b] Yield obtained using 0.6 mole of IIIb in the reaction.

On the basis of chemical, spectroscopic and analytical evidence, we have assigned the generic formula IV, that of a 3-substituted-2-thiazolidinone 1,1-dioxide, to the products of the oxidation reaction. Aside from IVb, the products were neutral, fairly high melting solids which were sparingly soluble in cold acetic acid and common organic solvents. The acid IVb and the amide IVe were soluble in hot water, ethanol and acetone and somewhat soluble in cold water.

The oxidation was accompanied by the loss of one gram-atom of sulfur per mole of product and the microanalytical data showed that all the products (except IVe) differed from the reactants only in having lost one sulfur atom and having gained three oxygen atoms.

In one reaction 3-(2-cyanoethyl)-2-thiazolidinethione[6] (IIIa) was treated with three equivalents of hydrogen peroxide. No sulfone (IVa) separated when the solution was chilled; thereupon, two more equivalents of oxidant were added and the solution was warmed to 70° for two hours.[7] The final solution, which contained excess hydrogen peroxide, afforded a very good yield of the sulfone IVa. Thus, complete oxidation apparently required at least three equivalents of oxidant and produced a product which was stable in the presence of excess hydrogen peroxide.

The infrared absorption spectra of the oxidation products were quite similar, particularly with regard to the three strongest and most characteristic bands. These absorption bands are enumerated in Table II.

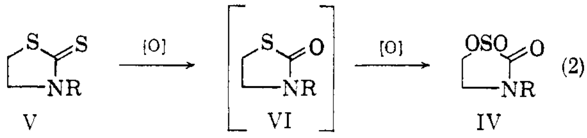
TABLE II

INFRARED BANDS OF 3-SUBSTITUTED-2-THIAZOLIDINONE 1,1-DIOXIDES

Compound	Ring Carbonyl, Cm.$^{-1}$	Sulfone, Cm.$^{-1}$
IVa	1735	1310, 1130
IVb	1740	1315, 1135
IVc	1735	1315, 1135
IVd	1710	1320, 1135
IVe	1730	1310, 1130

While the parent 3-substituted-2-thiazolidinethiones possess no carbonyl absorption ascribable to a ring carbonyl in the 1650–1800-cm.$^{-1}$ region, all the oxidation products possessed an intense absorption band at 1710–1740 cm.$^{-1}$. This band showed such a pronounced shift toward higher frequencies when compared with the carbonyl absorption band in 2-thiazolidinones (1640–1690cm.$^{-1}$)[5,8] that it was interpreted as indicating that the carbonyl group was very probably flanked by a strong electron withdrawing group which counterbalanced the usual amide shift to lower frequencies. The position, reasonable constancy, and degree of separation of the prominent pair of absorption bands at 1310–1320 cm.$^{-1}$ and 1130–1135 cm.$^{-1}$ lead to the conclusion that the oxidation products almost certainly must contain a sulfone grouping.

The rapidity with which sulfur separated in the oxidation of 3-substituted-2-thiazolidinethiones,



V VI IV (2)

coupled with what appeared to be a milder and much slower second reaction, strongly suggested a two-stage process. The two stages probably comprise the conversion of the 2-thiazolidinethione (V) to the corresponding 2-thiazolidinone (VI, Equa-

---

[6] The correct *C.A.* names for the reactants and products are given in the experimental section. The text nomenclature is preferred in order to stress the heterocyclic relationship of the compounds.

[7] Theoretically, three equivalents of oxidant are required to complete the reaction. There was evidence of loss of active oxidant during the course of the reaction. The exact amount thus destroyed was not determined.

(8) M. G. Ettlinger, *J. Am. Chem. Soc.*, **72**, 4699 (1950).

tion 2) followed by a slower oxidation of VI to the sulfone, IV. To determine if a 3-substituted-2-thiazolidinone would form a sulfone, 3-(2-carbamylethyl)-2-thiazolidinone[5] (IIIe) was treated with hydrogen peroxide in acetic acid. 3-(2-Carbamylethyl)-2-thiazolidinone 1,1-dioxide (IVe) was obtained in low yield.

While no attempt has, as yet, been made to isolate the proposed 2-thiazolidinone intermediate (VI), the sequence shown in Equation 2 appears to be quite reasonable. This suggests that proper limitation of the amount of hydrogen peroxide might effect the sulfur-oxygen exchange of equation 1 without further oxidation of the molecule.

EXPERIMENTAL

3-Phenyl-2-thiazolidinethione (IIIc). To a mixture of 16.8 g. (0.3 mole) of potassium hydroxide in 150 ml. of absolute ethanol were added 45.6 g. (0.6 mole) of carbon disulfide and 46 g. (0.3 mole) of 2-anilinoethanethiol.[9] The mixture, which spontaneously heated to gentle reflux, was held at reflux for 8 hr. The crystalline product which separated upon chilling the solution was removed, washed with water, then with ethanol, and dried to give 22.3 g. of IIIc, m.p. 128.6–129.1°. Work-up of the mother liquor and the wash liquors from the above separation afforded an additional 8.0 g. for an over-all yield of 30.3 g. (51.7%). A sample recrystallized from ethanol melted at 128.5–129.3° (lit.[4] m.p. 133–134°).

3-Benzyl-2-thiazolidinethione (IIId). A mixture of 33.5 g. (0.2 mole) of 2-benzylaminoethanethiol,[9] 76.1 g. (0.4 mole) of carbon disulfide, and 1.1 g. (0.02 mole) of potassium hydroxide in 125 ml. of 4:1 dioxane-water was heated under reflux for 6 hr. The product, which separated upon chilling the solution, was removed, washed with dioxane and water, and dried to give 28.4 g. (67.7%) of colorless crystals, m.p. 130.6–131.7°. An analytical sample, m.p. 131.2–131.9°, was obtained by recrystallization from ethanol.

Anal. Calcd. for $C_{10}H_{11}NS_2$: C, 57.38; H, 5.30; N, 6.69; S, 30.63. Found: C, 57.34; H, 5.23; N, 6.53; S, 30.07.

2-Oxo-3-thiazolidinepropionitrile 1,1-dioxide (IVa). Hydrogen peroxide (61.9 g., 1.82 moles, 30% concentration) was added dropwise over a period of 25 min. to a hot (70°), stirred solution of 62.6 g. (0.364 mole) of 2-thioxo-3-thiazolidinepropionitrile[5] (IIIa) in 300 ml. of acetic acid. A strongly exothermic reaction, accompanied by immediate separation of plastic sulfur, required ice bath cooling to hold the temperature at 70–80°. After the exotherm subsided, the resulting colorless solution was held at 70° for an additional two hours. After removal of the plastic sulfur, the solution was allowed to cool slowly. There was obtained 50.9 g. of colorless crystals, m.p. 143.8–145°. Further concentration and chilling of the filtrate gave another 2.7 g. for an over-all yield of 53.6 g. (78.3%). An analytical sample, m.p. 145.5–146.3°, was obtained by recrystallization from glacial acetic acid.

Anal. Calcd. for $C_6H_8N_2O_3S$: C, 38.29; H, 4.28; N, 14.89; S, 17.04. Found: C, 38.54, 38.53; H, 4.35, 4.36; N, 14.05, 14.13; S, 17.51, 17.27.

2-Oxo-3-thiazolidinepropionic acid 1,1-dioxide (IVb). In the same manner as above 19.1 g. (0.1 mole) of 2-thioxo-3-thiazolidinepropionic acid[5] in 100 ml. of acetic acid was oxidized with 17 g. (0.5 mole) of hydrogen peroxide. Vacuum filtration of the hot, colorless solution afforded 2.4 g. (75% of theory for the loss of 1 g.-atom) of amorphous sulfur,[10] m.p. 119–119.6°. From the chilled filtrate there was obtained a total of 16.7 g. (80.7%) of colorless crystals, m.p. 176–176.7° with gas evolution. Analytical material, m.p. 178.8–179.3° with gas evolution, was obtained by recrystallization from glacial acetic acid.

Anal. Calcd. for $C_6H_9NO_5S$: C, 34.78; H, 4.38; N, 6.76; S, 15.47; neut. equiv., 207. Found: C, 35.37, 34.62; H, 4.40, 4.49; N, 6.14, 6.52; S, 15.02; neut. equiv., 200; *p*K, 4.1.

3-Phenyl-2-thiazolidinone 1,1-dioxide (IVc). As described above, a stirred suspension of 19.5 g. (0.1 mole) of 3-phenyl-2-thiazolidinethione (IIIc) in 150 ml. of acetic acid was oxidized with 17 g. (0.5 mole) of hydrogen peroxide. During the course of the reaction the solution changed from orange to red, and finally, to a dark reddish purple. The product was removed from the chilled reaction mixture, washed with water, and dried to give 9.4 g. of deep violet crystals, m.p. 171.7–172.4°. An additional 1.5 g. was obtained from the mother liquor for an over-all yield of 10.9 g. (51.7%). Several recrystallizations from glacial acetic acid, accompanied by treatment with activated charcoal, gave colorless analytical material, m.p. 171.5–172.3°.

Anal. Calcd. for $C_9H_9NO_3S$: C, 51.17; H, 4.29; N, 6.23; S, 15.18. Found: C, 51.27; H, 4.37; N, 6.54; S, 15.13.

3-Benzyl-2-thiazolidinone 1,1-dioxide (IVd). Oxidation of 20.9 g. (0.1 mole) of 3-benzyl-2-thiazolidinethione (IIId) in 150 ml. of acetic acid with 17 g. (0.5 mole) of hydrogen peroxide afforded a total of 15.2 g. (67.6%) of colorless, crystalline product, m.p. 156.5–157.2°. An analytical sample, m.p. 156.5–157.2°, was obtained by recrystallization from glacial acetic acid.

Anal. Calcd. for $C_{10}H_{11}NO_3S$: C, 53.32; H, 4.92; N, 6.22; S, 14.23. Found: C, 53.06; H, 5.06; N, 6.25; S, 14.08.

2-Oxo-3-thiazolidinepropionamide 1,1-dioxide (IVe). Hydrogen peroxide (10 ml. of 30%) was added at once to a warm (40°) solution of 2-oxo-3-thiazolidinepropionamide (IIIe)[5] in 25 ml. of acetic acid. When no exothermic reaction was observed, the solution was warmed to 70° for 2 hr. No product separated when the final solution was chilled whereupon it was concentrated to about 10 ml. and diluted with a little water. Upon chilling this solution 0.65 g. of faintly tan crystals was obtained. Further concentration and chilling produced a second crop of crystals which was combined with the original crop of crystals, dissolved in about 25 ml. of hot water, treated with activated charcoal, filtered, and stored at 5° for several hours. In this manner 0.85 g. (14.4%) of colorless platelets, m.p. 172.1–173.6° dec., was obtained.

Anal. Calcd. for $C_6H_{10}N_2O_4S$: C, 34.94; H, 4.89; S, 15.55. Found: C, 34.74; H, 4.74; S, 15.43.

Acknowledgment. We are indebted to Mr. Norman Colthup for aiding in the interpretation of the infrared spectra and to Dr. Julius Kuck and the members of the Microanalytical Laboratory for the numerous microanalyses.

STAMFORD, CONN.

---

(9) G. I. Braz, *Zhur. Obshchei Khim.*, **21,** 757 (1951) (English Translation).

(10) Only in the oxidation of IIIb was the sulfur obtained in a form amenable to facile separation and weighing. All other oxidations produced plastic sulfur.