[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY]

The Preparation of β-Keto Sulfones by the Claisen Condensation[1]

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RECEIVED NOVEMBER 5, 1954

The Claisen condensation has been extended to include the condensations of esters with sulfones. Compounds of the type $CH_3SO_2(CH_2)_nCOOEt$, when treated with sodium ethoxide, gave the following products: $n = 2$, an elimination reaction; $n = 3$, tetrahydrothiapyran-3-one-1-dioxide; $n = 4$, 2-methylsulfonylcyclopentanone; $n = 5$, 2-methylsulfonylcyclohexanone. Ethyl methylsulfonylpivalate gave 4,4-dimethyltetrahydrothiophene-3-one-1-dioxide. Intermolecular condensations were observed between ethyl benzoate and both methyl phenyl sulfone and dimethyl sulfone.

A convenient method of synthesis for several β-keto sulfones was desired in connection with an investigation of the acidity of these compounds.[3] Since the Claisen condensation of keto esters has been employed to prepare various acyclic[4] and cyclic[5-7] β-diketones, it was thought that the analogous condensation of sulfone esters might prove useful. Reactions of this type, *i.e.*, between a carbalkoxy group and a carbanion stabilized solely by a sulfone group, never have been reported. Consequently an investigation to determine the scope of this reaction was undertaken.

Most of the studies on the activating influence of a sulfone group on adjacent hydrogen atoms have dealt largely with keto sulfones, alkyl or arylsulfonic acids and their derivatives, disulfones, aryl benzyl sulfones and benzyl sulfones.[8] All of the reported condensations of sulfones with esters have involved other activating groups on the carbon holding the labile hydrogen in addition to the sulfone group.[9-12] A few cases are known in which monosulfones undergo reactions that are considered typical of compounds containing hydrogen activated by unsaturated groups (such as carbonyl). The lateral metalation of sulfones[13-15] is analogous to the reaction of organometallics with ketones in which steric hindrance prevents addition to the carbonyl group. The base-catalyzed condensation of benzaldehyde with methyl *p*-tolyl sulfone to give styryl *p*-tolyl sulfone in low yields is analogous to that of benzaldehyde with acetophenone.[16]

A homologous series of sulfone esters of the type $CH_3SO_2(CH_2)_nCOOEt$ was prepared ($n = 2, 3, 4, 5$) and treated with sodium ethoxide in an attempt to effect condensation. Ethyl β-methylsulfonylpropionate (I) was prepared by oxidation and esterification of β-methylmercaptopropionic acid.[17] *A priori*, one might expect to obtain tetrahydrothiophene-3-one-1-dioxide; however on treating I with sodium ethoxide, decomposition occurred as evidenced by the formation of tar during the reaction and by the evolution of sulfur dioxide on acidification of the reaction mixture. In all probability, the base removes a proton α to the carbethoxy group of I with simultaneous elimination of the methanesulfinate anion. In order to preclude this elimination reaction, the α-hydrogen atoms of I were replaced by methyl groups. This homologous sulfone ester, ethyl methylsulfonylpivalate (XIV), was prepared by treating chloropivalic acid (VIII)[18] with sodium ethoxide followed by sodium methylmercaptide to yield, after acidification, methylmercaptopivalic acid (X). Compound X was oxidized and esterified to XIV. The first step to this reaction probably proceeds *via* the conversion of the initially formed sodium chloropivalate to α,α-dimethylpropiolactone (IX) by a neighboring group nucleophilic displacement[19] involving the carboxylate ion, followed by ring opening of the lactone by methylmercaptide ion to give the sodium salt of X. Direct displacement by methylmercaptide ion on the β-carbon atom of sodium chloropivalate seems improbable in view of the neopentyl-halide character of chloropivalic acid (VIII). By treatment of XIV with sodium ethoxide, 4,4-dimethyltetrahydrothiophene-3-one-1-dioxide (XV) was obtained in 65% yield.

An attempt was made to synthesize XV independently by the following method: chloropivalic acid (VIII) was treated with an equimolar amount of sodium ethoxide followed by an equimolar amount of the sodium salt of ethyl mercaptoacetate to yield carbethoxymethylmercaptopivalic acid (XI) after acidifying. This portion of the synthesis probably proceeds in a manner analogous to the reaction of the sodium salt of chloropivalic acid (VIII) with sodium methylmercaptide. Compound XI was esterified to the corresponding ester XIII which then was cyclized by the conventional Dieckmann procedure to 2-carbethoxy-4,4-dimethyltetrahydrothiophene-3-one (XVI). Compound XVI was hydrolyzed and decarboxylated to

(1) Abstracted from a portion of the Ph.D. thesis of Robert H. Knospe, Purdue University, 1955. Presented at the Cincinnati Meeting of the American Chemical Society, March 30, 1955.

(2) Purdue Research Foundation Fellow, 1953–1954.

(3) W. E. Truce and R. H. Knospe, unpublished results.

(4) E. E. Royals, "Advanced Organic Chemistry," Prentice-Hall, Inc., New York, N. Y., 1954, p. 816.

(5) C. Le Peletier de Rosanbo, *Ann. chim.* (*Paris*), **19**, 327 (1923).

(6) D. Vörlander, *Ann.*, **294**, 270 (1897).

(7) E. E. Blaise and A. Koehler, *Bull. soc. chim.*, [4] **7**, 710 (1910).

(8) C. M. Suter, "The Organic Chemistry of Sulfur," John Wiley and Sons, Inc., New York, N. Y., 1944, p. 687.

(9) C. G. Overberger, S. P. Ligthelm and E. A. Swire, THIS JOURNAL, **72**, 2856 (1950).

(10) C. G. Overberger, R. A. Gadea, J. A. Smith and I. C. Kogon, *ibid.*, **75**, 2075 (1953).

(11) R. H. Eastman and R. M. Wagner, *ibid.*, **71**, 4089 (1949).

(12) A. Cohen and S. Smiles, *J. Chem. Soc.*, 406 (1930).

(13) L. Field, THIS JOURNAL, **74**, 3919 (1952).

(14) H. A. Potter, paper presented at the spring meeting of the Midland Section of the A.C.S. in 1951.

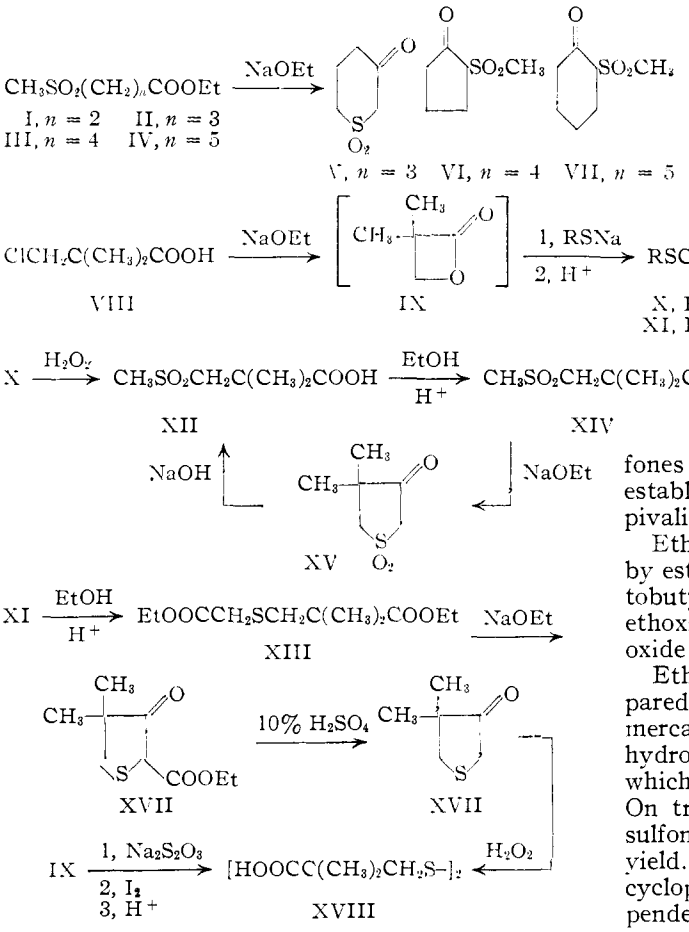
(15) (a) L. Field and J. W. McFarland, THIS JOURNAL, **75**, 5583 (1953); (b) W. E. Truce and K. R. Buser, *ibid.*, **76**, 3577 (1954).

(16) E. P. Kohler and H. A. Potter, *ibid.*, **57**, 217 (1935).

(17) C. D. Hurd and L. L. Gershbein, *ibid.*, **69**, 2328 (1947).

(18) M. S. Kharasch and H. C. Brown, *ibid.*, **62**, 925 (1940).

(19) For other examples *cf.* J. F. Lane and H. W. Heine, *ibid.*, **73**, 1348 (1951); H. W. Heine, A. D. Miller, W. H. Barton and R. W. Greiner, *ibid.*, **76**, 4778 (1953); C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Bell and Sons, Ltd., London, 1953, p. 387.



4,4-dimethyltetrahydrothiophene-3-one (XVII). This sequence of reactions is similar to that used by Ghosh in preparing 4-ethyltetrahydrothiophene-3-one.[20] On oxidation of XVII with 30% hydrogen peroxide, a crystalline material was isolated which was found to consist of a compound other than the desired keto sulfone XV. It was soluble in 5% cold sodium bicarbonate with the evolution of carbon dioxide, had a neutral equivalent of 132 and an empirical formula of $C_{10}H_{18}S_2O_4$. One possible structure which is consistent with these data is bis-(2-carboxy-2-methylpropyl) disulfide (XVIII). Compound XVIII was prepared independently by treating chloropivalic acid (VIII) with sodium thiosulfate. The resulting Bunte salt[21] was treated with iodine[22] to give XVIII which gave no mixed melting point depression with the compound obtained on oxidation of XVII.

TABLE I

Frequency, cm.$^{-1}$	Related group
2725, 2625	-OH (strongly hydrogen bonded)
1710	>C=O of -COOH
1385, 1368	$-CH_3$ of $(CH_3)_2C<$
958	-OH (deformation)
710	C-S (stretching)

The infrared spectra of both disulfides are identical and are consistent with the proposed structure as shown in Table I.

Other attempts to oxidize XVII to XVIII also failed. Difficulty also was experienced during the oxidation of 2-methylmercaptocyclopentanone and 2-methylmercaptocyclohexanone to the corresponding sulfones. In addition it has been found that methylmercaptoacetone and tetrahydrothiophene-3-one did not yield any identifiable product on oxidation with hydrogen peroxide.[3] On the other hand, both the six-[23] and the seven-membered[24] cyclic keto sulfides gave the corresponding sulfones in good yield. The identity of XV was established by base hydrolysis to methylsulfonylpivalic acid (XII).

Ethyl γ-methylsulfonylbutyrate (II), obtained by esterification and oxidation of γ-methylmercaptobutyric acid,[25] underwent cyclization with sodium ethoxide to give tetrahydrothiapyran-3-one-1-dioxide (V) in 51% yield.

Ethyl δ-methylsulfonylvalerate (III) was prepared by treating δ-chlorovaleronitrile with methylmercaptan in the presence of excess aqueous sodium hydroxide to give δ-methylmercaptovaleric acid, which subsequently was esterified and oxidized. On treating III with sodium ethoxide, 2-methylsulfonylcyclopentanone (VI) was obtained in 36% yield. An attempt to prepare 2-methylmercaptocyclopentanone, as an intermediate in the independent synthesis of VI, failed using the procedure reported by Brintzinger for the preparation of 2-methylmercaptocyclohexanone.[26] Compound VI was synthesized successfully by treating 2-chlorocyclopentanone with sodium methylmercaptide followed by oxidation of the resulting keto sulfide.

Ethyl ε-methylsulfonylcaproate (IV) was prepared by treating ethyl ε-bromocaproate[27] with sodium methylmercaptide followed by oxidation of the resulting sulfide. On treating IV with sodium ethoxide, 2-methylsulfonylcyclohexanone (VII) was obtained in 34% yield. Compound VII was synthesized independently by the oxidation of the corresponding sulfide, 2-methylmercaptocyclohexanone. The latter compound was prepared by the method of Brintzinger in low yield[26]; a better method involved treating 2-chlorocyclohexanone with sodium methylmercaptide. It is interesting to note that on treating 2-chlorocyclohexanone with sodium methylmercaptide a simple displacement takes place whereas sodium methoxide produces a Faworski rearrangement.[28] This is probably a consequence of the high nucleophilicity and low basicity of the methylmercaptide ion as compared to the methoxide ion. Similar

(20) R. Ghosh, J. R. McOmie and J. P. Wilson, *J. Chem. Soc.*, 705 (1945).

(21) H. E. Westlake, Jr., and G. Dougherty, THIS JOURNAL, **63**, 658 (1941).

(22) H. E. Westlake, Jr., and G. Dougherty, *ibid.*, **64**, 149 (1942).

(23) E. A. Fehnel, *ibid.*, **74**, 1571 (1952).

(24) S. B. Maerov, Ph.D. Thesis, University of Washington, 1954

(25) H. Plieninger, *Chem. Ber.*, **83**, 265 (1950).

(26) H. Brintzinger and M. Langheck, *ibid.*, **86**, 562 (1953).

(27) G. B. Brown and C. W. H. Partridge, THIS JOURNAL, **66**, 834 (1944).

(28) R. B. Loftfield, *ibid.*, **72**, 633 (1950); **73**, 4707 (1950).

replacement reactions of α-halocyclohexanones with mercaptides also have been reported.[29]

An attempt was made to cyclize methyl *o*-methylsulfonylbenzoate to the corresponding bicyclic keto sulfone. The only material isolated from the reaction was *o*-methylsulfonylbenzoic acid in 25% yield; an appreciable quantity of tar also was formed. Cohen and Smiles also have observed the resistance of this sulfone ester to cyclization.[12] They were able, however, to cyclize methyl *o*-benzylsulfonylbenzoate to the corresponding bicyclic keto sulfone.

Intermolecular condensations of a methyl sulfone and an ester also can be effected. Thus ethyl benzoate has been condensed with both methyl phenyl sulfone and dimethyl sulfone to give ω-phenylsulfonylacetophenone and ω-methylsulfonylacetophenone, respectively.

Experimental[30]

Ethyl β-Methylsulfonylpropionate (I).—Hydrogen peroxide (30%, 300 ml.) was added to a solution of 74.1 g. (0.618 mole) of β-methylmercaptopropionic acid[18] in 600 ml. of a 50:50 mixture of acetic acid and acetic anhydride. After standing overnight, the excess peroxide was destroyed by adding a trace of manganese dioxide and the solvent was removed by distillation. The crude β-methylsulfonylpropionic acid, which solidified on cooling, was esterified by refluxing with 300 ml. of absolute ethanol in the presence of several grams of *p*-toluenesulfonic acid for 14 hours. After being concentrated by distillation the residue was dissolved in ether; the ether solution was washed with 2% sodium carbonate and water, and was dried over anhydrous sodium carbonate. The product (31.0 g., 28%) was isolated by evaporation of the ether solution to dryness; m.p. 68–69° after recrystallization from absolute ethanol.

Anal. Calcd. for $C_6H_{12}O_4S$: C, 39.98; H, 6.71. Found: C, 39.81; H, 6.80.

Ethyl γ-Methylmercaptobutyrate.—γ-Methylmercaptobutyric acid,[19] 119.5 g. (0.89 mole), was esterified by refluxing with 150 ml. of ethanol in the presence of 1 g. of *p*-toluenesulfonic acid for 16 hours. The reaction mixture was concentrated by distillation and the residue was dissolved in ether; the ether solution was washed with 2% aqueous sodium carbonate and water, dried and concentrated by distillation. The residual oil was vacuum distilled to give 97.5 g. (68% yield) of product, b.p. 70° (2 mm.).

Ethyl γ-Methylsulfonylbutyrate (II).—Hydrogen peroxide (30%, 60 ml.) was added to a solution of 30 g. (0.185 mole) of ethyl γ-methylmercaptobutyrate in 120 ml. of a 50:50 mixture of acetic acid and acetic anhydride. After standing for 18 hours, the excess peroxide was destroyed by adding a trace of manganese dioxide. The solution was concentrated by distillation and the oily residue was vacuum distilled to give 30.4 g. (84% yield) of product, b.p. 135–150° (0.6 mm.). The fraction submitted for analysis had b.p. 139–140° (0.4 mm.), m.p. 24–25°, $n^{20}D$ 1.4616.

Anal. Calcd. for $C_7H_{14}O_4S$: C, 43.28; H, 7.26. Found: C, 43.19; H, 7.28.

δ-Methylmercaptovaleric Acid.—The procedure of Mooradian[31] for the next lower homolog was followed. From 57.6 g. (1.2 moles) of methyl mercaptan and 117.5 g. (1.0 mole) of δ-chlorovaleronitrile[32] there was obtained 81.3 g. (55%) of product, b.p. 107° (0.3 mm.), $n^{27}D$ 1.4800–1.4815. The fraction submitted for analysis had b.p. 107° (0.3 mm.), $n^{27}D$ 1.4800.

Anal. Calcd. for $C_6H_{12}O_2S$: C, 48.61; H, 8.16. Found: C, 48.71; H, 8.31.

Ethyl δ-Methylmercaptovalerate.—δ-Methylmercaptovaleric acid, 53.8 g. (0.364 mole), was esterified by refluxing with 300 ml. of absolute ethanol in the presence of 1 g. of *p*-toluenesulfonic acid for 16 hours. The solvent was removed by distillation and an ether solution of the residue was washed with 2% aqueous sodium carbonate and water, dried over anhydrous sodium sulfate and concentrated by distillation. The residue was vacuum distilled to give 51.4 g. (80%) of product; b.p. 65° (10.5 mm.), $n^{25}D$ 1.4587–1.4595; analytical fraction, b.p. 65° (10.5 mm.), $n^{25}D$ 1.4594.

Anal. Calcd. for $C_8H_{16}O_2S$: C, 54.51; H, 9.15. Found: C, 54.74; H, 9.29.

Ethyl δ-Methylsulfonylvalerate (III).—Hydrogen peroxide (30%, 150 ml.) was added to a solution of 51.4 g. (0.292 mole) of ethyl δ-methylmercaptovalerate in 300 ml. of a 50:50 mixture of acetic acid and acetic anhydride. After standing for 16 hours a catalytic amount of manganese dioxide was added to destroy the excess peroxide and the solution was concentrated by distillation. The oily residue was vacuum distilled to give 49.5 g. (82%) of product, b.p. 147–151° (0.4 mm.), $n^{25}D$ 1.4603–1.4608; analytical fraction, b.p. 148° (0.4 mm.), $n^{25}D$ 1.4608.

Anal. Calcd. for $C_8H_{16}O_4S$: C, 46.13; H, 7.74. Found: C, 46.02; H, 7.44.

Ethyl ε-Methylsulfonylcaproate (IV).—To an alcoholic solution of sodium methylmercaptide, prepared from 5.75 g. (0.25 g. atom) of sodium metal, 500 ml. of absolute ethanol and 20 g. (0.322 mole) of methyl mercaptan, was added 48.75 g. (0.25 mole) of ethyl ε-bromocaproate.[27] After being refluxed for 18 hours the reaction mixture was concentrated to dryness and the residue was extracted with acetone. The crude ethyl ε-methylmercaptocaproate, obtained on evaporation of the acetone extracts, was oxidized with 100 ml. of 30% hydrogen peroxide in 400 ml. of a 50:50 mixture of acetic acid and acetic anhydride. After standing for 36 hours, the excess peroxide was destroyed with manganese dioxide and the solution was concentrated by distillation. The oily residue was vacuum distilled to give 19.8 g. (36%) of product, b.p. 181–183° (0.8 mm.), $n^{20}D$ 1.4626–1.4636; analytical fraction, b.p. 181–182° (0.8 mm.), $n^{20}D$ 1.4630.

Anal. Calcd. for $C_9H_{18}O_4S$: C, 48.62; H, 8.16. Found: C, 48.76; H, 8.40.

Methylmercaptopivalic Acid (X).—An alcoholic solution of sodium ethoxide, prepared from 58.2 g. (2.53 g. atoms) of sodium metal and 700 ml. of absolute ethanol, was added to a solution of 345 g. (2.53 moles) of chloropivalic acid[18] in 500 ml. of ethanol. This entire mixture, which had a definite ester-like odor, was added to a solution of sodium methylmercaptide in ethanol, prepared from 61 g. (2.65 moles) of sodium metal, 700 ml. of absolute ethanol and 135 g. (2.80 moles) of methyl mercaptan. After being refluxed for 24 hours, the precipitated sodium chloride was filtered off and the filtrate was concentrated by distillation. The residue was shaken with dilute hydrochloric acid; the organic layer was separated and combined with the ether extracts of the aqueous layer, dried over anhydrous magnesium sulfate and concentrated by distillation. The oily residue was distilled under vacuum to give 271 g. (72%) of product, b.p. 77–81° (0.3 mm.), $n^{25}D$ 1.4719–1.4740. The fraction submitted for analysis had b.p. 77–78° (0.3 mm.), $n^{25}D$ 1.4736.

Anal. Calcd. for $C_6H_{12}O_2S$: C, 48.62; H, 8.16. Found: C, 49.40, 49.46; H, 8.35, 8.39.

Methylsulfonylpivalic Acid (XII).—Hydrogen peroxide (30%, 800 ml.) was added to a solution of 240 g. (1.62 moles) of methylmercaptopivalic acid (X) in 1600 ml. of acetic acid at ice-bath temperature. After being warmed to room temperature and refluxed for three hours, the reaction mixture was allowed to stand overnight. A catalytic amount of manganese dioxide was added to destroy the excess peroxide and the solution was evaporated to dryness. The solid residue was recrystallized from 90–100° b.p. petroleum ether–absolute ethanol to give 228.3 g. (78%) of product, m.p. 133–134° after further recrystallization from the same solvent.

Anal. Calcd. for $C_6H_{12}O_4S$: C, 39.98; H, 6.71. Found: C, 40.10; H, 6.86.

(29) (a) K. Rabindran and B. D. Tilak, *Current Sci. (India)*, **20**, 207 (1951); (b) M. Mousseron and R. Jacquier, *Compt. rend.*, **229**, 374 (1949).

(30) All melting points are uncorrected. The infrared samples were run in KBr discs on a Perkin-Elmer Model 21 spectrophotometer equipped with a NaCl prism.

(31) A. Mooradian, *et al.*, THIS JOURNAL, **71**, 3372 (1949).

(32) A research sample was kindly furnished by E. I. du Pont de Nemours & Co., Inc., Wilmington, Del.

The phenacyl ester was prepared according to the usual procedure[33]; m.p. 112.5–113.5° after recrystallization from 95% ethanol.

Anal. Calcd. for $C_{14}H_{18}O_5S$: C, 56.36; H, 6.08. Found: C, 56.03; H, 6.35.

Ethyl Methylsulfonylpivalate (XIV).—Methylsulfonylpivalic acid (XII), 213 g. (1.18 moles), was esterified by refluxing with 500 ml. of absolute ethanol in the presence of 2 g. of *p*-toluenesulfonic acid for 24 hours. The ether solution of the residual oil obtained on concentration of the reaction mixture was washed with 2% sodium carbonate and water, dried over magnesium sulfate and then concentrated by distillation. The oily residue was vacuum distilled to give 128.7 g. (52%) of product, b.p. 114–120° (0.6 mm.). Analytical fraction, b.p. 109.5° (0.4 mm.), $n^{25}D$ 1.4563.

Anal. Calcd. for $C_6H_{16}O_4S$: C, 46.13; H, 7.74. Found: C, 46.41; H, 7.54.

General Claisen Condensation Procedure.—The sulfone ester (or sulfone and the ester) was added to a suspension of alcohol-free sodium ethoxide[34] in benzene, toluene or xylene with stirring under a nitrogen atmosphere. An alternative condensing agent consisted of two equivalents of sodium (in the form of a dispersion) per equivalent of sulfone ester plus a few drops of absolute ethanol. The reaction mixture was refluxed for 5–72 hours with stirring, cooled and was hydrolyzed with water or dilute aqueous acid. The products were isolated by separating the aqueous layer, acidifying, concentrating to dryness (or to an oil), extracting with acetone and evaporating the acetone extracts to dryness (or an oil). In the case of solid products, the residue was recrystallized; liquid products were distilled under vacuum.

Attempted Cyclization of Ethyl β-Methylsulfonylpropionate (I).—Ethyl β-methylsulfonylpropionate (I), 18.0 g. (0.10 mole), was treated with sodium ethoxide, prepared from 2.76 g. (0.12 g. atom) of sodium, in toluene for 24 hours. The reaction mixture turned dark immediately and sulfur dioxide was evolved on acidification. None of the desired product was obtained in this or subsequent runs in which shorter reaction times and lower temperatures were used.

Tetrahydrothiapyran-3-one-1-dioxide (V).—Ethyl γ-methyl sulfonylbutyrate (II), 19.4 g. (0.10 mole), was treated with sodium ethoxide, prepared from 2.76 g. (0.12 g. atom) of sodium, in toluene for 24 hours. The product, 7.5 g. (51% yield), was recrystallized from absolute ethanol; m.p. 141–142°, lit.[22] 140–140.5°. The product gave no mixed m.p. depression with an authentic sample.[35]

A semicarbazone was prepared by the usual method[33]; m.p. 205–206° after recrystallizing from water; lit.[23] m.p. 206–207°. This material gave no mixed m.p. depression with an authentic sample.[35]

2-Methylsulfonylcyclopentanone (VI).—Ethyl δ-methylsulfonylvalerate (III), 5.2 g. (0.025 mole), was treated with sodium ethoxide, prepared from 0.575 g. (0.025 g. atom) of sodium, in benzene for 17 hours. The ethanol formed during the reaction was removed by azeotropic distillation. The product, 1.46 g. (36% crude), b.p. 117–146° (0.3 mm.), could not be purified sufficiently for analysis. A 2,5-dinitrophenylhydrazone was prepared by the usual method[33]; m.p. 197° dec. after recrystallization from absolute ethanol; no mixed melting point depression with an authentic sample.

Anal. Calcd. for $C_{12}H_{14}N_4O_6S$: C, 42.10; H, 4.12; N, 16.37. Found: C, 42.18; H, 4.24; N, 16.70.

2-Methylmercaptocyclopentanone.—An attempt was made to use the procedure employed by Brintzinger for preparing 2-methylmercaptocyclohexanone.[26] Methanesulfenyl chloride,[36] 12 g. (0.145 mole), was added slowly to 12.2 g. (0.145 mole) of cyclopentanone at 0° with stirring. The reaction mixture was allowed to warm to room temperature and then was heated until the evolution of hydrogen chloride stopped. A black viscous oil resulted from which no product was obtained.

2-Methylmercaptocyclopentanone was prepared successfully by treating 11.85 g. (0.1 mole) of 2-chlorocyclopentanone[37] in 100 ml. of absolute ethanol with an alcohol solution of sodium methylmercaptide at 0°, prepared from 2.3 g. (0.1 g. atom) of sodium, 5.76 g. (0.12 mole) of methyl mercaptan and 100 ml. of absolute ethanol. The cold solution was filtered and concentrated by distillation under reduced pressure. The residue was shaken with dilute acetic acid and the organic layer was separated and combined with the ether extracts of the aqueous layer. After drying the ether solution over sodium sulfate it was concentrated by distillation; the residual oil was vacuum distilled to give 5.8 g. (45%) of product, b.p. 71–72° (6 mm.), $n^{25}D$ 1.5018–1.5054.

2-Methylsulfonylcyclopentanone (VI). Independent Synthesis.—Hydrogen peroxide (30%, 50 ml.) was added to a solution of 12.36 g. (0.095 mole) of 2-methylmercaptocyclopentanone in 50 ml. of a solution (50:50) of acetic acid and acetic anhydride at 0°. After standing overnight at room temperature the excess peroxide was destroyed with manganese dioxide and the solution was concentrated by distillation under reduced pressure. The residual oil was vacuum distilled to give 5.90 g. (38%) of product, b.p. 115–135° (0.6–1.0 mm.).

A 2,4-dinitrophenylhydrazone was prepared by the usual method[33]; m.p. 195–196° dec. after recrystallization from absolute ethanol.

2-Methylsulfonylcyclohexanone (VII).—Ethyl ε-methylsulfonylcaproate (IV), 8.75 g. (0.0349 mole), was treated with sodium ethoxide, prepared from 1.38 g. (0.06 g. atom) of sodium, in toluene for 24 hours to yield 2.33 g. (34%) of product, m.p. 57–58° after recrystallization from 60–70° b.p. petroleum ether, no mixed m.p. depression with an authentic sample.

Anal. Calcd. for $C_7H_{12}O_3S$: C, 47.70; H, 6.86. Found: C, 47.89; H, 7.10.

A 2,4-dinitrophenylhydrazone was prepared by the usual method[33]; m.p. 189–190° dec. after recrystallization from absolute ethanol, no mixed melting point depression with an authentic sample.

Anal. Calcd. for $C_{13}H_{16}N_4O_6S$: C, 43.81; H, 4.53; N, 15.72. Found: C, 43.53; H, 4.75; N, 16.13.

2-Methylmercaptocyclohexanone.—The first procedure used was that described by Brintzinger.[26] From 17 g. (0.206 mole) of methanesulfenyl chloride[36] and 20.2 g. (0.206 mole) of cyclohexanone there was obtained 2.83 g. (10%) of product, b.p. 95–109° (9 mm.), $n^{25}D$ 1.5151–1.5170.

A better method was similar to the procedure used for the synthesis of 2-methylmercaptocyclopentanone as described above. From 26.5 g. (0.20 mole) of 2-chlorocyclohexanone,[38] 4.6 g. (0.20 g. atom) of sodium and 9.6 g. (0.20 mole) of methyl mercaptan there was obtained 19.3 g. (67%) of product, b.p. 90–93° (10 mm.), $n^{25}D$ 1.5068–1.5076. The fraction submitted for analysis had b.p. 91–92° (10 mm.) $n^{25}D$ 1.5073.

Anal. Calcd. for $C_7H_{12}OS$: C, 58.29; H, 8.38. Found: C, 58.56; H, 8.41.

2-Methylsulfonylcyclohexanone (VII). Independent Synthesis.—Hydrogen peroxide (30%, 50 ml.) was added to a solution of 16.86 g. (0.177 mole) of 2-methylmercaptocyclohexanone in 50 ml. of a 50:50 mixture of acetic acid and acetic anhydride at ice-bath temperature. After warming to room temperature and standing overnight the excess peroxide was decomposed by adding a trace of manganese dioxide. The solution was concentrated to dryness and the residue was recrystallized from 60–70° b.p. petroleum ether to give 9.33 g. (45%) of product, m.p. 57–58°.

A 2,4-dinitrophenylhydrazone was prepared by the usual method[33]; m.p. 189–190° dec. after recrystallization from absolute ethanol.

4,4-Dimethyltetrahydrothiophene-3-one-1-dioxide (XV).—Ethyl methylsulfonylpivalate (XIV) was treated with sodium ethoxide, prepared from 1.54 g. (0.0670 g. atom) of sodium, in benzene for 24 hours. Recrystallization of the crude product from 60–70° b.p. petroleum ether–absolute ethanol gave 7.05 g. (65%) of product, m.p. 130–131° after further recrystallization.

(33) R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds," 3rd ed., John Wiley and Sons, Inc., New York, N. Y., 1948.

(34) C. R. Hauser and B. E. Hudson, Jr., "Organic Reactions," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1947, p. 279.

(35) An authentic sample was kindly furnished by Dr. E. A. Fehnel, Swarthmore College, Swarthmore, Pa.; *cf.* ref. 23.

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Anal. Calcd. for $C_6H_{10}O_3S$: C, 44.42; H, 6.21; neut. equiv., 162.2. Found: C, 44.60; H, 6.21; neut. equiv., 162.6.

Base Hydrolysis of 4,4-Dimethyltetrahydrothiophene-3-one-1-dioxide (XV).—One gram of XV was refluxed for 15 hours with 25 ml. of 8% sodium hydroxide solution. After acidification and evaporation to dryness the residue was recrystallized from 90–100° b.p. petroleum ether–absolute ethanol to give 0.95 g. (85%) of methylsulfonylpivalic acid (XII), m.p. 133–134°, no mixed m.p. depression with an authentic sample.

The phenacyl ester was prepared by the usual procedure[33]; m.p. 112.0–113.0° after recrystallization from 95% ethanol. No mixed m.p. depression with an authentic sample.

Ethyl Carbethoxymethylmercaptopivalate (XIII).—The procedure used was similar to that of Ghosh for the preparation of ethyl β-(carbethoxy)-butylmercaptoacetate.[20] A solution of sodium ethoxide, prepared from 2.3 g. (0.1 g. atom) of sodium and 100 ml. of absolute[18] ethanol was added to a solution of 13.6 g. (0.1 mole) of chloropivalic acid in 100 ml. of ethanol. An alcoholic solution of the sodium salt of ethylmercaptoacetate, prepared from 2.53 g. (0.11 g. atom) of sodium, 13.2 g. (0.11 mole) of ethyl mercaptoacetate and 100 ml. of absolute ethanol, then was added. After refluxing for 5 hours the reaction mixture was concentrated and the residue was dissolved in water and acidified. The organic layer was combined with the ether extracts of the aqueous layer. The crude carbethoxymethylmercaptopivalic acid (XI), which resulted on evaporation of the dried ether solution, was esterified by refluxing for 24 hours with 200 ml. of absolute ethanol in the presence of 1 g. of *p*-toluenesulfonic acid. The ether solution of the residue obtained on concentration of the reaction mixture was washed with 2% aqueous sodium carbonate and water, was dried over anhydrous sodium carbonate and concentrated by distillation. The oily residue was distilled to give 12.79 g. (52%) of product, b.p. 100–104° (0.6 mm.), $n^{25}D$ 1.4580–1.4602. Analytical fraction, b.p. 103.2–103.4° (0.6 mm.), $n^{25}D$ 1.4596.

Anal. Calcd. for $C_{11}H_{20}O_4S$: C, 53.20; H, 8.11. Found: C, 53.03; H, 8.29.

2-Carbethoxy-4,4-dimethyltetrahydrothiophene-3-one (XVI).—The procedure of Ghosh for the preparation of 2-carbethoxy-4-ethyltetrahydrothiophene-3-one was used.[20] From 38.54 g. (0.155 mole) of ethyl carbethoxymethylmercaptopivalate (XIII) and sodium ethoxide, prepared from 3.58 g. (0.155 g. atom) of sodium, there was obtained 20.69 g. (66%) of product, b.p. 121–123° (10 mm.), $n^{25}D$ 1.4841–1.4843. The fraction submitted for analysis had b.p. 121.5° (10 mm.), $n^{25}D$ 1.4841.

Anal. Calcd. for $C_9H_{14}O_3S$: C, 53.44; H, 6.98. Found: C, 53.37; H, 6.89.

4,4-Dimethyltetrahydrothiophene-3-one (XVII).—2-Carbethoxy-4,4-dimethyltetrahydrothiophene-3-one (XVI) was decarboxylated by the method of Ghosh[20] for 2-carbethoxy-4-ethyltetrahydrothiophene-3-one. From 19.41 g. (0.0961 mole) of XVI was obtained 9.35 g. (75%) of product, b.p. 78.0–78.5° (20 mm.), $n^{25}D$ 1.4946–1.4950; analytical fraction, b.p. 78.0° (20 mm.), $n^{25}D$ 1.4948.

Anal. Calcd. for $C_6H_{10}OS$: C, 55.34; H, 7.74. Found: C, 55.68; H, 7.80.

Bis-(2-carboxy-2-methylpropyl) Disulfide (XVIII).—Hydrogen peroxide (30%, 10 ml.) was added to a solution of 3.97 g. (0.0305 mole) of 4,4-dimethyltetrahydrothiophene-3-one (XVII) in 20 ml. of a 50:50 mixture of acetic acid and acetic anhydride at ice-bath temperature. After warming to room temperature and allowing to stand for several days, a crystalline material separated from solution. Partial evaporation of the mother liquor yielded a total of 1.09 g. (27%) of product, m.p. 147.5–148.5° after recrystallization from 60–70° b.p. petroleum ether–absolute ethanol; no mixed m.p. depression with an authentic sample.

Anal. Calcd. for $C_{10}H_{18}O_4S_2$: C, 45.09; H, 6.81; S, 24.08; neut. equiv., 133. Found: C, 44.99, 45.13; H, 6.91, 6.81; S, 24.06, 24.09; neut. equiv., 131, 132.

Bis-(2-carboxy-2-methylpropyl) Disulfide (XVIII). Independent Synthesis.—The general procedure of Westlake and Dougherty was used.[21,22] A solution of 2.2 g. (0.0161 mole) of chloropivalic acid was neutralized with sodium carbonate and refluxed with 4.0 g. (0.0161 mole) of sodium thiosulfate in 20 ml. of water for 24 hours. After being cooled, the solution was treated with iodine until the color no longer persisted, and then was acidified and extracted with ether. The solid obtained on evaporation of the dried extracts was recrystallized from 90–100° b.p. petroleum ether to give 0.41 g. (19%) of product, m.p. 148.5–150.5°.

Attempted Cyclization of Methyl *o*-Methylsulfonylbenzoate.—Methyl *o*-methylsulfonylbenzoate,[39] 9.1 g. (0.0425 mole), was treated with sodium ethoxide, prepared from 2.0 g. (0.0870 g. atom) of sodium in the form of a dispersion, in xylene for 72 hours. On working up the reaction mixture, the only product isolated was 4.31 g. (25%) of *o*-methylsulfonylbenzoic acid, m.p. 139–140° after recrystallization from benzene, lit.[39] 138–140°, no mixed m.p. depression with an authentic sample.[39]

Anal. Calcd. for $C_8H_8O_4S$: neut. equiv., 200. Found: neut. equiv., 201.

ω-Phenylsulfonylacetophenone.—Methyl phenyl sulfone,[40] 6.9 g. (0.0437 mole), and ethyl benzoate, 6.55 g. (0.0437 mole), were treated with sodium ethoxide, prepared from 1.72 g. (0.075 mole) of sodium, in toluene for 20 hours. The crude reaction product was dried and was recrystallized from absolute ethanol to give 3.2 g. (28%) of product, m.p. 93–94°, lit.[13] 93–94°.

ω-Methylsulfonylacetophenone.—Dimethyl sulfone,[41] 4.6 g. (0.05 mole), and ethyl benzoate, 7.5 g. (0.05 mole), were treated with 2.3 g. (0.1 mole) of sodium in the form of a dispersion, in benzene for 5 hours. The crude product was recrystallized from absolute ethanol to give 5.6 g. (44%) of product, m.p. 107.5–108°, lit.[15] 109–110°.

Anal. Calcd. for $C_9H_{10}O_3S$: C, 54.53; H, 5.08. Found: C, 54.54; H, 5.34.

Acknowledgments.—The authors are indebted to the Research Corporation of New York for a grant which made this work possible. We also wish to thank Dr. J. A. B. Nolin for determining and interpreting the infrared spectra.

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