The Use of β-Keto Sulfones as Synthetic Intermediates[1a]

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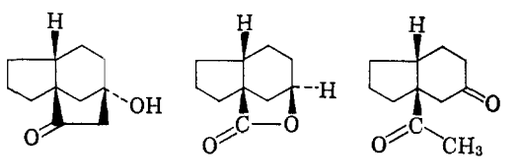
The β-keto sulfone **5** was found to be a more satisfactory intermediate than the corresponding β-keto sulfoxide **4** for the preparation of the tricyclic hydroxy ketone **1**. Examination of several simpler β-keto sulfones **14**, **16**, and **18** indicated that the preparation and C-alkylation of these materials occur as readily as the reactions involving the corresponding β-keto sulfoxides. The β-keto sulfones are more stable to oxidation and reduction procedures than the β-keto sulfoxides. Although the β-keto sulfones can be reductively cleaved to form ketones in good yield, this cleavage process is more rapid with β-keto sulfoxides.

In the course of synthetic studies directed toward the gibberellins, we needed a method to prepare a bicyclo[3.2.1]octane system (*e.g.*, **1**) which contained a hydroxyl substituent at the bridgehead.[2] We elected to



1 **2** **3**

study this problem by use of the previously known[3] lactone **2** as a model starting material. It was our plan to use the related diketone **3**,[3] or a suitably activated derivative, in an intramolecular aldol condensation[2c-f] to form the desired bicyclo[3.2.1]octane derivative **1**. We initially examined the reaction of the lactone **2** with dimethyl sulfoxide anion[4] to form the β-keto sulfoxide **4**. However, this product was not a satisfactory synthetic intermediate; apparently both the reactivity of the sulfoxide function to oxidants and the asymmetry of this group served to complicate the isolation of pure products. The analogous reaction of the lactone with dimethyl sulfone anion[4] to form the β-keto sulfone **5** proved to be a much more satisfactory procedure. Oxidation afforded the diketo sulfone **6** which was reductively cleaved to the known[3] diketone **3**. Since our efforts to convert the diketone **3** to the aldol product **1** in reasonable yield were not successful, we turned our attention to the more acidic β-keto sulfone **6**. Base treatment established an equilibrium between the starting kiketo sulfone and the cyclic condensation product **7**. The tricyclic product **7** was separated from the equilibrium mixture and reductively cleaved to the desired hydroxy ketone **1**. The further transformation of this ketone **1** to the olefin **10** following the general scheme of Nagata and coworkers[2d,e] is illustrated in Scheme I.

The advantages offered by the β-keto sulfone intermediates in terms of stability and lack of asymmetry prompted us to examine several alkylation and reduction reactions with simpler keto sulfones in order to compare their utility with that of the more extensively studied[4] β-keto sulfoxides. The reactions run are summarized in Scheme II. Our general conclusions are (1) the formation of β-keto sulfones from esters is at least as good a preparative procedure as the formation of β-keto sulfoxides; (2) the procedures for C-alkylation seem to be equivalent for the sulfones and the sulfoxides; (3) the β-keto sulfones are definitely superior as synthetic intermediates, if subsequent oxidations or reductions are to be performed; and (4) although both intermediates undergo reductive cleavage of the carbon–sulfur bond to form ketones, this reductive cleavage is more rapid with β-keto sulfoxides. Based on the results obtained in the reduction of the benzoyl sulfone **20**, it would appear that α-aroyl sulfones may be cleaved in better yield with zinc and acetic acid rather than with aluminum amalgam and water. Attempts to reduce the ketone functions of the β-keto sulfoxide **13** and the β-keto sulfone **14** by a modification[5] of the Wolff–Kishner procedure were not successful. Application of the conventional Wolff–Kishner reduction procedure to a β-keto sulfone had been previously reported[6] to yield only cleavage products. In the present case the preparation of the sulfonyl *p*-toluenesulfonylhydrazone **11** was successful. However, reaction of this material with sodium borohydride[5] in methanol yielded a complex mixture from which the one product isolated had properties corresponding to the *p*-toluenesulfonylhydrazone of 1-methoxynonadecan-2-one. We presume that this material arises from the addition of methoxide anion to the intermediate azo compound **15**.

Experimental Section[7]

Preparation of the Lactone 2.—This lactone, bp 90° (0.3 mm), was prepared *via* the corresponding iodolactone following

(1) (a) This research has been supported by a grant from the National Science Foundation (Grant No. GP-5685). (b) Woodrow Wilson Predoctoral Fellow, 1963–1964; National Institutes of Health Predoctoral Fellow, 1964–1967.

(2) For discussion of other possible solutions to this synthetic problem, see (a) G. Stork, S. Malhotra, H. Thompson, and M. Uchibayashi, *J. Am. Chem. Soc.*, **87**, 1148 (1965); (b) L. J. Dolby and R. H. Iwamoto, *J. Org. Chem.*, **30**, 2420 (1965); (c) R. A. Bell, R. E. Ireland, and L. N. Mander, *ibid.*, **31**, 2536 (1966); (d) W. Nagata, T. Sugasawa, M. Narisada, T. Wakabayashi, and Y. Hayase, *J. Am. Chem. Soc.*, **89**, 1483 (1967); (e) W. Nagata, M. Narisada, T. Wakabayashi, and T. Sugasawa, *ibid.*, **89**, 1499 (1967); (f) R. D. Haworth, B. G. Hartley, R. G. Leach, and G. Rodgers, *J. Chem. Soc.*, 2720 (1962).

(3) H. O. House, S. G. Boots, and V. K. Jones, *J. Org. Chem.*, **30**, 2519 (1965).

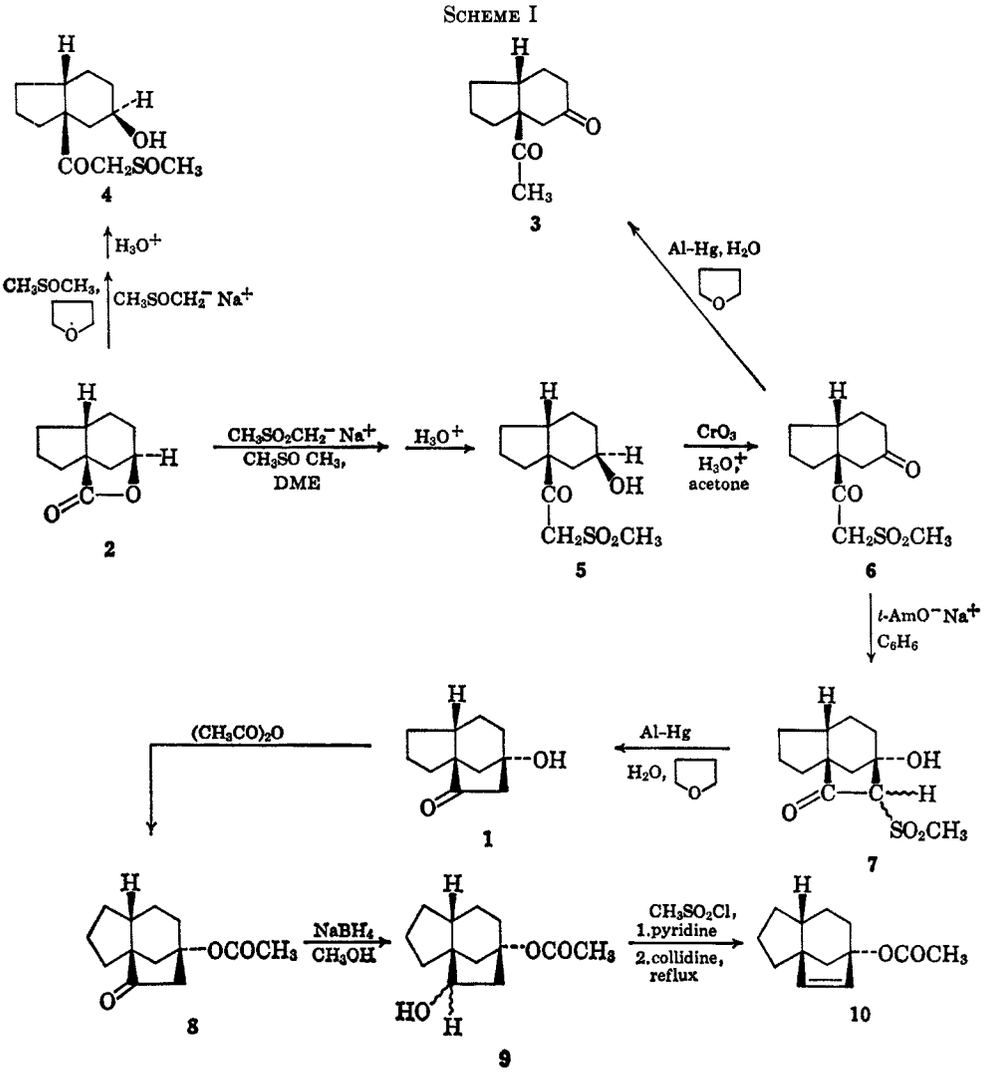
(4) (a) E. J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, **87**, 1345 (1965); (b) H. D. Becker, and G. A. Russell, *J. Org. Chem.*, **28**, 1896 (1963); (c) H. D. Becker, G. J. Mikol, and G. A. Russell, *J. Am. Chem. Soc.*, **85**, 3410 (1963); (d) G. A. Russell and G. J. Mikol, *ibid.*, **88**, 5498 (1966); (e) E. J. Corey and M. Chaykovsky, *ibid.*, **86**, 1639 (1964); (f) P. G. Gassman and G. D. Richmond, *J. Org. Chem.*, **31**, 2355 (1966); (g) J. B. Lee, *Tetrahedron Letters*, No. 46, 5669 (1966).

(5) (a) L. Caglioti and M. Magi, *Tetrahedron*, **19**, 1127 (1963); (b) L. Caglioti, *ibid.*, **22**, 487 (1966).

(6) N. J. Leonard and S. Gelfand, *J. Am. Chem. Soc.*, **77**, 3272 (1955).

(7) All melting points are corrected and all boiling points are uncorrected. Unless otherwise stated magnesium sulfate was employed as a drying agent. The infrared spectra were determined with a Perkin-Elmer Model 237 infrared recording spectrophotometer fitted with a grating. Unless otherwise noted, the ultraviolet spectra were determined in 95% ethanol with a Cary recording spectrophotometer, Model 14. The nmr spectra were determined at 60 Mc with a Varian Model A-60 nmr spectrometer. The chemical-shift values are expressed either in cycles per second or δ values (parts per million) relative to a tetramethylsilane internal standard. The mass spectra were obtained with a CEC Model 21-130 mass spectrometer. The microanalyses were performed by the Scandinavian Microanalytical Laboratory. All reactions involving strongly basic reaction media were run under a nitrogen atmosphere.

SCHEME I



previously described procedures[8] except that the intermediate 1-cyanocyclopentene was hydrolyzed by treatment with aqueous 85% H_3PO_4 at 155°[8] for 6 hr to form crude 1-carboxycyclopentene, mp 116.5–119°, in 72% yield.

Preparation of the β-Keto Sulfoxide 4.—A solution of the sodium salt of dimethyl sulfoxide, prepared from 0.48 g (20 mmoles) of NaH and 6 ml of dimethyl sulfoxide,[4a] was diluted with 5 ml of tetrahydrofuran and then cooled in an ice bath. A solution of 1.04 g (6.25 mmoles) of the lactone **2** in 5 ml of tetrahydrofuran was added, dropwise and with stirring, to the cold solution of the dimethyl sulfoxide anion. The resulting solution was stirred at 25° for 45 min and then poured into aqueous HCl and extracted with chloroform. The organic layer was washed with aqueous NaCl, dried, and concentrated. Crystallization of the residual oil from a cyclohexane–ethyl acetate mixture separated 0.71 g (47%) of the crude β-keto sulfoxide (presumably a mixture of diastereoisomers), mp 89–96°. Recrystallization of a 142-mg portion of this product separated 81 mg of one of the diastereoisomers of the β-keto sulfoxide **4** as fine white prisms: mp 116–117.5°; infrared ($CHCl_3$), 3450 (broad, associated OH) and 1690 cm^{-1} (C=O); ultraviolet maximum, 286 mμ (ε 73); nmr ($CDCl_3$), δ 2.8–4.4 (5 H multiplet, >CHOH, $-COCH_2SO-$, and CH), 2.74 (3 H singlet, $-SOCH_3$), and 1.2–2.4 (12 H, aliphatic CH).

Anal. Calcd for $C_{12}H_{20}O_3S$: C, 58.99; H, 8.25; S, 13.13. Found: C, 58.79; H, 8.09; S, 13.13.

Preparation of the β-Keto Sulfone 5.—A mixture of 3.9 g (0.16 mole) of sodium hydride, 15 g (0.16 mole) of dimethyl sulfone, 20 ml of dimethyl sulfoxide, and 40 ml of 1,2-dimethoxyethane was heated to 60°, with stirring, for 1 hr and then a solution of 12 g (0.075 mole) of the lactone **2** in 15 ml of 1,2-dimethoxyethane was added, dropwise and with stirring. After the resulting mixture had been stirred at 60° for 90 min, it was acidified with acetic acid (2 ml) and then partitioned between aqueous HCl and chloroform. The organic solution was washed successively with aqueous $NaHCO_3$ and aqueous NaCl and then dried and concentrated. The residual oil which crystallized on standing was recrystallized from ethyl acetate to separate 13.6 g (70%) of the β-keto sulfone **5** as white prisms: mp 118–120°; infrared ($CHCl_3$), 3600, 3510 (unassociated and associated OH), and 1710 cm^{-1} (C=O); ultraviolet maximum, 287 mμ (ε 53.5); nmr ($CDCl_3$), δ 1.2–2.0 (12 H multiplet, aliphatic CH), 3.07 (3 H, singlet, CH_3SO_2-), and 2.3–2.7 and 3.5–4.4 (5 H, multiplets, CH, >CHOH, and $-SO_2CH_2CO-$).

Anal. Calcd for $C_{12}H_{20}O_4S$: C, 55.37; H, 7.74; S, 12.32. Found: C, 55.30; H, 7.66; S, 12.50.

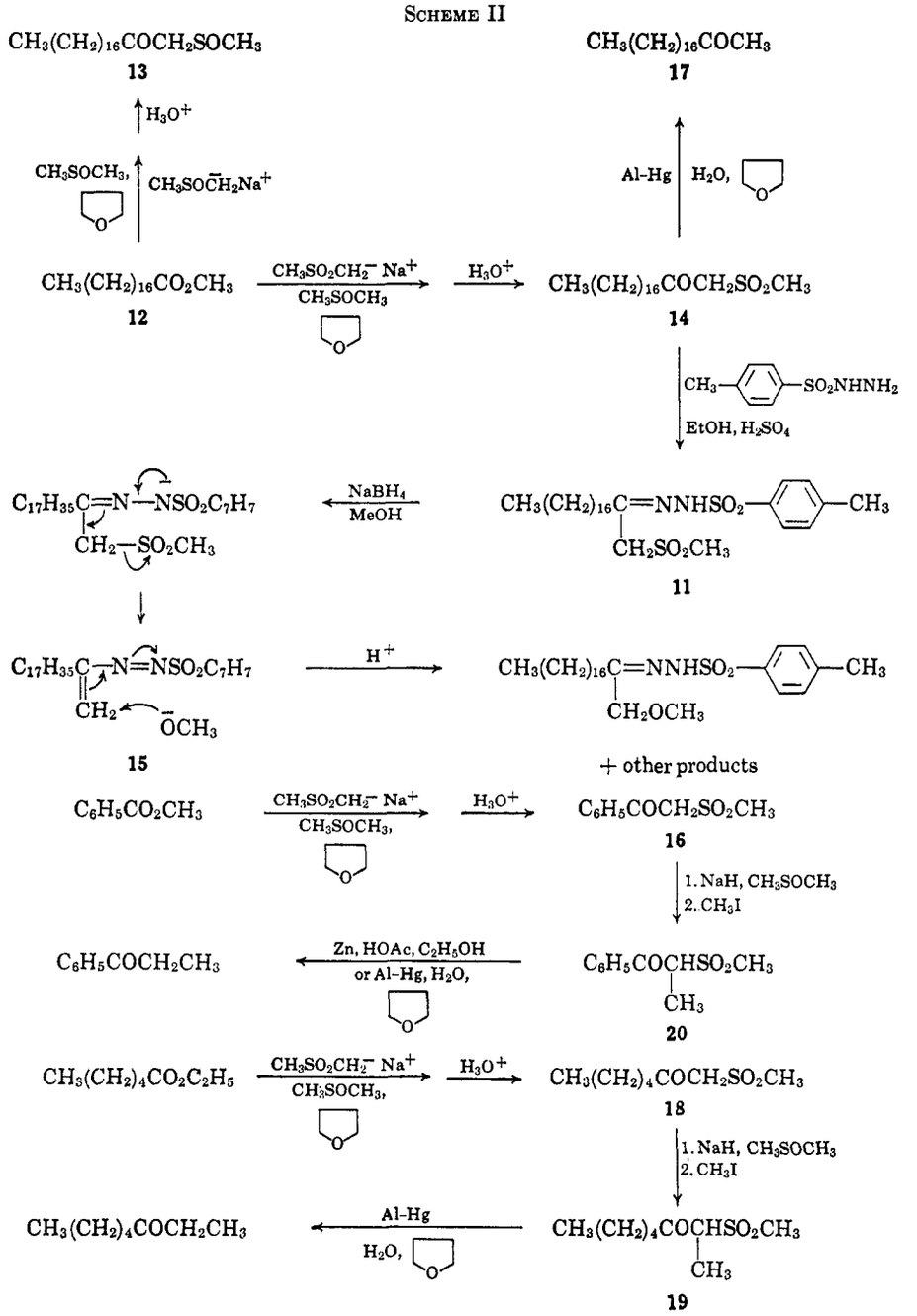
Preparation of the Diketo Sulfone 6.—A cold (0°) solution of 12.8 g (0.049 mole) of the keto sulfone **5** in 200 ml of acetone was treated with 8.0 ml of aqueous 8 *N* chromic acid solution.[9] After the resulting mixture had been stirred at 0° for 45 min, the excess oxidant was consumed with isopropyl alcohol and the chromium salts were separated by filtration and washed with isopropyl alcohol. After the organic solution had been concentrated, a chloroform solution of the residual liquid was washed with aqueous $NaHCO_3$ and with aqueous NaCl and then dried and concentrated. A solution of the residual oil in a cyclohexane–ethyl acetate mixture deposited 11.01 g (87%) of the diketone **6** as white prisms, mp 77–79° (recrystallization raised the melting point to 78.5–80°); infrared ($CHCl_3$), 1715 cm^{-1} (C=O); ultraviolet maximum, 289 mμ (ε 67); nmr ($CDCl_3$), δ 4.24 (2 H singlet, $COCH_2SO_2$), 3.11 (3 H singlet, CH_3SO_2), and 1.2–2.8 (13 H multiplet, aliphatic CH).

Anal. Calcd for $C_{12}H_{18}O_4S$: C, 55.80; H, 7.02. Found: C, 55.70; H, 7.02.

(8) The hydrolysis procedure of O. H. Wheeler and I. Lerner, *J. Am. Chem. Soc.*, **78**, 63 (1956).

(9) D. C. Kleinfelter and P. von R. Schleyer, *Org. Syn.*, **42**, 79 (1962).

SCHEME II



Preparation of the Diketone 3.—A mixture of 5.0 g (19 mmoles) of the diketo sulfone **6**, 300 ml of aqueous tetrahydrofuran (1:9 by volume), and the amalgam[4a] from 5.2 g (190 mg-atoms) of aluminum was stirred at 65° for 3 hr and then cooled, filtered, and concentrated. An ethereal solution of the residue was washed successively with aqueous $NaHCO_3$ and aqueous NaCl and then dried and concentrated. Distillation of the residual oil afforded 1.9 g (56%) of the diketone **3** as a colorless liquid, bp 110° (0.1 mm), which was identified with the previously described[3] sample by comparison of infrared and mass spectra and gas chromatographic retention times.[10]

Preparation of the Tricyclic Keto Sulfone 7.—To a refluxing solution of 6.5 g (0.025 mole) of the keto sulfone **6** in 300 ml of benzene was added, dropwise and with stirring, 15.6 ml of a toluene solution containing 0.025 mole of sodium *t*-amyloxide. The resulting mixture, from which a precipitate separated, was refluxed for an additional 1 hr and then cooled and poured into cold dilute aqueous HCl. After the benzene layer had been separated, the aqueous phase was extracted with chloroform. The combined organic layers were washed with aqueous $NaHCO_3$, dried, and concentrated. Chromatography of the residual oil (8.0 g) on silicic acid separated 0.63 g of the crude tricyclic product **7**, mp 130–160°, eluted in the early fractions with ether–hexane mixtures and 4.5 g of the starting keto sulfone **6** eluted with ethyl acetate in the later fractions. The recovered starting material was subjected to this same base-catalyzed equilibration reaction and separation procedure two additional times to yield a total of 1.23 g (19%) of the crude tricyclic ketone **7** accompanied by 1.7 g (26% recovery) of the starting keto sulfone **6**. Recrystallization of the crude product from ethyl acetate afforded the tricyclic ketone **7** as white needles, which softened at 150° and gave a clear melt at 170°. This melting point was not sharpened by repeated crystallization, suggesting that the product is a mixture of diastereoisomers: infrared ($CHCl_3$), 3550 (associated OH) and 1745 cm^{-1} (C=O in a five-membered ring); ultraviolet maximum, (CH_3CN), 296 mμ (ε 99); nmr ($(CD_3)_2NCDO$), δ 1.2–2.7 (11 H multiplet, aliphatic CH), 3.06 (2 H singlet, $-CH_2-$), 3.47 (3 H singlet, SO_2CH_3), and 4.31 (1 H singlet, $-COCHSO_2-$).

Anal. Calcd for $C_{12}H_{18}O_4S$: C, 55.80; H, 7.02; S, 12.42. Found: C, 55.95; H, 6.90; S, 12.24.

Preparation of the Hydroxy Ketone 1.—Following the previously described reduction procedure, reaction of 2.47 g (9.6 mmoles) of the keto sulfone **7** with the amalgam[4a] from 2.6 g

(10) A gas chromatography column packed with Carbowax 20M suspended on Chromosorb P was employed for this analysis.

(96 mg-atoms) of aluminum foil in a water (15 ml)–tetrahydrofuran (135 ml) mixture for 2.5 hr at 65° yielded 1.53 g (89%) of the crude ketone **1** as an oil which partially crystallized on standing. Recrystallization of a comparable sample from a benzene–petroleum ether (bp 30–60°) mixture afforded the pure hydroxy ketone **1** as white needles: mp 62–64°; infrared (CCl_4), 3610, 3450 (unassociated and associated OH), and 1745 cm^{-1} (C=O in a five-membered ring); ultraviolet maximum, 290 mμ (ε 41); nmr (CCl_4), δ 1.1–2.1 (13 H, aliphatic CH), 2.28 (2 H singlet, CH_2CO), and 3.98 (1 H, broad, OH); mass spectrum, molecular ion peak at *m/e* 180, abundant fragment peaks at *m/e* 137, 96, 95, 79, 67, 55, 43, 41, and 39.

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.28; H, 9.09.

A solution of 1.53 g (8.5 mmoles) of the crude hydroxy ketone **1** in 50 ml of acetic anhydride was refluxed for 3 hr and then the excess anhydride was hydrolyzed with aqueous $NaHCO_3$ and the mixture was partitioned between ether and aqueous $NaHCO_3$. Th crude prouct (a yellow oil) obtained from the organic layer was chromatographed on silicic acid. After separation of 126 mg of an unknown component, eluted first, the acetoxy ketone **8** (1.36 g or 72% as an oil) was eluted with hexane–ether mixtures. Crystallization from a cyclohexane–petroleum ether (bp 30–60°) mixture afforded the pure acetoxy ketone **8** as white prisms: mp 49–51°; infrared (CCl_4), 1745 cm^{-1} (C=O of ester and cyclopentanone); nmr (CCl_4), δ 2.03 singlet ($OCOCH_3$) superimposed on a multiplet in the region 1.1–2.9; mass spectrum, weak molecular ion peak at *m/e* 222, abundant fragment peaks at *m/e* 177, 134, 120, 119, 91, 79, 67, 55, 53, 43, and 41.

Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.20; H, 8.25.

Preparation of the Acetoxy Alcohol 9.—A cold (0°) solution of 1.61 g (7.2 mmoles) of the acetoxy ketone **8**, 278 mg (7.3 mmoles) of $NaBH_4$, and 28 mg of sodium methoxide[11] in 50 ml of methanol was stirred for 2 hr. Then the excess hydride was destroyed by the addition of acetic acid and the solution was concentrated under reduced pressure. After the residue had been partitioned between water and ether, the organic layer was washed with aqueous $NaHCO_3$, dried, and concentrated to leave 1.47 g (91%) of a colorless oil which contained[12] the acetoxy alcohol **9**. A sample of this material was chromatographed on silicic acid and the fractions eluted with hexane–ether mixtures were distilled under reduced pressure in a short-path still (*ca.* 150° at 0.4 mm) to give the pure acetoxy alcohol (presumably a mixture of stereoisomers) as a colorless liquid: infrared (CCl_4), 3620, 3490 (unassociated and associated OH), and 1740 cm^{-1} (ester C=O); nmr (CCl_4), δ 1.1–2.5 (16 H multiplet, OH and aliphatic CH), 1.90 (3 H singlet, $OCOCH_3$), and 4.02 (1 H, pair of doublets with J = 6 and 10 cps, >CHO); mass spectrum, no molecular ion peak, abundant fragment peaks at *m/e* 164, 135, 120, 91, 79, 55, 43, and 41.

Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.53; H, 8.98.

Preparation of the Unsaturated Acetate 10.—To a cold (0°) solution of 1.47 g (6.56 mmoles) of the alcohol **9** in 20 ml of pyridine was added, dropwise and with stirring, 1.5 g (13 mmoles) of methanesulfonyl chloride. The resulting mixture was allowed to stand at 5° for 20 hr and then was partitioned between ether and cold, dilute aqueous HCl. The organic layer was washed successively with aqueous HCl, water, and aqueous $NaHCO_3$ and then dried and concentrated to leave 1.65 g of the crude methanesulfonate ester: mp 72–76°; infrared (CCl_4), 1740 cm^{-1} (ester C=O). A solution of this crude product in 30 ml of collidine was refluxed for 16 hr and then cooled and partitioned between ether and dilute, aqueous HCl. After the organic layer had been washed successively with aqueous HCl, water, and aqueous $NaHCO_3$, it was dried and concentrated. Distillation of the residual oil (1.06 g) in a short-path still (160° at 20 mm) afforded 0.95 g (70%) of the acetoxy olefin **10** as a colorless liquid: infrared (CCl_4), 1740 (ester C=O) and 1630 cm^{-1} (weak, C=C); nmr (CCl_4), δ 1.0–2.6 (13 H multiplet, aliphatic CH), 1.93 (3 H singlet, $OCOCH_3$), and 5.60 (2 H, broad singlet, vinyl CH); mass spectrum, molecular ion peak at *m/e* 206, abundant fragment peaks at *m/e* 164, 146, 135, 96, 91, 43, 41, and 39.

(11) R. E. Davis and J. A. Gottbrath, *J. Am. Chem. Soc.*, **84**, 895 (1962).

(12) A thin layer chromatographic plate coated with silicic acid and eluted with ether–benzene mixtures was employed for this analysis.

Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.66; H, 8.74.

Preparation of the β-Keto Sulfones. A. General Procedure.—After a mixture of 0.48 g (20 mmoles) of sodium hydride, 1.88 g (20 mmoles) of dimethyl sulfone, and 10 ml of dimethyl sulfoxide had been heated to 65° with stirring for 30 min, it was cooled, diluted with 10 ml of tetrahydrofuran and then a solution of 10 mmoles of the ester in 5 ml of tetrahydrofuran was added. The resulting mixture was heated to 65° with stirring for 1 hr and then cooled, poured into a mixture of ice and aqueous HCl, and extracted with six poritons of chloroform. The combined organic extracts were washed successively with water, aqueous $NaHCO_3$, and aqueous NaCl and then dried and concentrated to leave the crude β-keto sulfones which were purified by recrystallization from ethyl acetate–petroleum ether (bp 30–60°) mixtures.

B. Keto Sulfone 14.—From methyl stearate, the crude sulfone (3.1 g, mp 79–83°) was recrystallized to separate 2.99 g (83%) of the sulfone **14** as white needles, mp 82–84° (further recrystallization raised the melting point to 84–86°); infrared ($CHCl_3$), 1720 cm^{-1} (C=O); ultraviolet maximum (CH_3CN), 287 mμ (ε 58); nmr ($CDCl_3$), δ 0.8–1.8 (*ca.* 33 H, aliphatic CH), 2.5–2.8 (2 H multiplet, CH_2CO), 3.02 (3 H singlet, CH_3SO_2–), and 4.02 (2 H singlet, $COCH_2SO_2$).

Anal. Calcd for $C_{20}H_{40}O_3S$: C, 66.61; H, 11.18; S, 8.89. Found: C, 66.46; H, 11.20; S, 8.96.

Application of the comparable, previously described[4a] procedure to the reaction of 20 mmoles of methyl stearate with 40 mmoles of the sodium salt of dimethyl sulfoxide yielded 6.5 g, (95%) of the crude product, mp 90–94°. Recrystallization from ethyl acetate afforded 5.61 g (81%) of the β-keto sulfoxide **13**, mp 93–95° (lit.[4a] mp 98.5–99°).

A solution of 1.01 g (2.80 mmoles) of the keto sulfone and 1.11 g (6 mmoles) of *p*-toluenesulfonylhydrazine in 50 ml of ethanol containing 0.5 ml of sulfuric acid was refluxed for 1 hr and then cooled and diluted with water. The solid which separated was collected and recrystallized from ethanol to separate 1.03 g (70%) of the *p*-toluenesulfonylhydrazone **11** as white needles: mp 114–116° (additional recrystallization raised the melting point to 115–117°); infrared ($CHCl_3$), 3280 and 3190 (associated NH), 1160 and 1320 cm^{-1} (SO_2); ultraviolet maximum, 231 mμ (ε 13,800).

Anal. Calcd for $C_{27}H_{48}N_2O_4S_2$: C, 61.32; H, 9.15; N, 5.30; S, 12.13. Found: C, 61.38; H, 9.12; N, 5.49; S, 12.11.

C. Keto Sulfone 16.—The reaction with methyl benzoate yielded 1.65 g of the crude sulfone (mp 93–97°) which was recrystallized to separate 1.59 g (80%) of the keto sulfone **16** as white needles: mp 104–106° (lit. mp 106–107°,[4b] 107.5–108°[13]); infrared ($CHCl_3$), 1680 cm^{-1} (conjugated C=O); ultraviolet maximum, 250 mμ (ε 13,400) with 283 mμ shoulder (ε 1490); nmr ($CDCl_3$), δ 7.1–8.0 (5 H multiplet, aryl CH), 4.53 (2 H singlet, SO_2CH_2CO), and 3.08 (3 H singlet, SO_2CH_3).

D. Keto Sulfone 18.—The reaction with ethyl hexanoate yielded 1.59 g of crude product. Recrystallization afforded 1.4 g (71%) of the keto sulfone **18** as white needles: mp 37–38°; infrared ($CHCl_3$), 1720 cm^{-1} (C=O); nmr ($CDCl_3$), δ 0.7–2.9 (9 H multiplet, aliphatic CH), 2.4–2.8 (2 H multiplet, CH_2CO–), 2.96 (3 H singlet, CH_3SO_2–), and 3.96 (2 H singlet, SO_2CH_2CO–).

Anal. Calcd for $C_8H_{16}O_3S$: C, 49.96; H, 8.39; S, 16.67. Found: C, 49.94; H, 8.45; S, 16.83.

Reactions of the Keto Sulfone 14. A. Reductive Cleavage.—Reduction of 1.0 g (2.78 mmoles) of the keto sulfone **14** with the amalgam[4a] from 0.75 g (27.8 mg-atoms) of aluminum, 54 ml of tetrahydrofuran, and 6 ml of water at 65° for 80 min following the previously described procedure yielded 0.88 g of the crude ketone **17**, mp 51–52°. Recrystallization from ethanol afforded 0.60 g (81%) of ketone **17**, mp 53–55° (lit.[4a] mp 52–53°).

A solution of 0.50 g (1.8 mmoles) of the ketone and 0.75 g (4 mmoles) of *p*-toluenesulfonyl hydrazine in 15 ml of ethanol containing 0.3 ml of sulfuric acid was refluxed for 1 hr, cooled, and diluted with water. The crude derivative was collected and recrystallized from ethanol to separate 0.367 g (46%) of the *p*-toluenesulfonylhydrazone of ketone **17** as white needles: mp 86.5–88°; infrared ($CHCl_3$), 3210 and 3270 (associated NH), 1160 and 1230 cm^{-1} (SO_2); ultraviolet maximum, 229 mμ (ε 12,500); nmr ($CDCl_3$), δ 7.1–8.0 (4 H, multiplet, aryl CH), 2.42 (3 H singlet, aryl CH_3), 1.75 (3 H singlet, CH_3C=N–), and 0.9–2.2 (*ca.* 35 H multiplet, aliphatic CH).

(13) W. E. Turner and R. H. Knospe, *ibid.*, **77**, 5063 (1955).

Anal. Calcd for $C_{26}H_{46}N_2O_3S$: C, 69.28; H, 10.29; N, 6.22; S, 7.12. Found: C, 69.04; H, 10.06; N, 6.42; S, 7.29.

B. Reduction of the Carbonyl Function.—A mixture of 0.50 g (1.4 mmoles) of the keto sulfone **14**, 10 mg of sodium methoxide, 76 mg (2.0 mmoles) of sodium borohydride, and 50 ml of methanol was stirred at 25° for 3 hr and then concentrated under reduced pressure. After the residue had been partitioned beween water and chloroform, the organic layer was washed successively with dilute aqueous hydrochloric acid, water, aqueous $NaHCO_3$, and aqueous NaCl and then dried and concentrated. Recrystallization of the residual solid from aqueous ethanol separated 0.32 g (64%) of 2-hydroxy-1-methanesulfonylnonadecane as white needles: mp 93–95° (recrystallization from a benzene–cyclohexane mixture raised the melting point to 95–96°); infrared ($CHCl_3$), 3490 (associated OH), 1125 and 1305 cm^{-1} (SO_2); nmr ($CDCl_3$), δ 3.9–4.5 (1 H, br multiplet, >CHO), 2.98 singlet superimposed on a 2.5–3.3 multiplet (5 H, $-CH_2SO_2CH_3$), and 0.9–1.7 (*ca.* 35 H, multiplet, aliphatic CH).

Anal. Calcd for $C_{20}H_{42}O_3S$: C, 66.29; H, 11.60; S, 8.84. Found: C, 66.05; H, 11.60; S, 8.85.

In an effort to reduce the ketone function of the keto sulfone **14** to a methylene group, a mixture of 0.78 g (1.5 mmoles) of the sulfonylhydrazone **11**, 0.38 g (10 mmoles) of sodium borohydride, 30 mg of sodium methoxide, and 50 ml of methanol was refluxed for 12 hr. After the resulting mixture had been concentrated under reduced pressure, the residue was partitioned between water and chloroform. The organic layer was washed successively with dilute aqueous HCl, aqueous $NaHCO_3$, and aqueous NaCl and then dried and concentrated. Recrystallization of the residual solid (0.26 g) from ethanol separated a white solid, mp 65–70°, which was further purified by chromatography on 30 g of silicic acid. The fractions eluted with ether–hexane mixtures afforded 150 mg (11%) of material believed to be a mixture of the geometrical isomers of 1-methoxynonadecan-2-one *p*-toluenesulfonylhydrazone. After an additional recrystallization from ethanol, this product separated as 115 mg of white crystals: mp 75–77°; infrared ($CHCl_3$), 3210 and 3280 (associated NH), 1160 and 1330 cm^{-1} (SO_2); ultraviolet maximum, 230 mμ (ε 12,000); nmr ($CDCl_3$), δ 7.1–7.9 (4 H multiplet, aryl CH), 3.8–4.1 (2 H, multiplet, $N{=}CCH_2O$), 3.24 (more intense) and 3.16 (less intense) (3 H singlets, OCH_3 of the two geometrical isomers), 2.40 (3 H singlet, aryl CH_3), and 0.8–2.2 (multiplet, aliphatic CH).

Anal. Calcd for $C_{27}H_{48}N_2O_3S$: C, 67.47; H, 10.07; N, 5.83; S, 6.66. Found: C, 67.52; H, 10.28; N, 5.47; S, 6.72.

Methylation and Reductive Cleavage of the Keto Sulfone 16.—A mixture of 435 mg (18.1 mmoles) of sodium hydride, 3.6 g (18.1 mmoles) of the keto sulfone **16**, and 20 ml of dimethyl sulfoxide was stirred for 30 min at room temperature at which time hydrogen evolution was complete. The resulting solution was treated with 2.67 g (18.8 mmoles) of methyl iodide and then stirred at room temperature for 1.5 hr. After the reaction mixture had been partitioned between cold, dilute aqueous HCl and chloroform, the organic layer was washed with aqueous NaCl, dried, and concentrated. Crystallization of the residual oil from an ethyl acetate–petroleum ether (bp 30–60°) mixture afforded 2.32 g of the keto sulfone **20** as white needles, mp 56–57.5° (lit.[14] mp 57°), as well as 0.47 g of less pure material, mp 53–56°, total yield 78%. By comparison, methylation of the corresponding sulfoxide was reported[4f] to give the alkylated product in 70% yield. The spectral properties of the keto sulfone **20** were infrared ($CHCl_3$), 1680 cm^{-1} (conjugated C=O); ultraviolet maximum, 252 mμ (ε 13,900) with 285 mμ shoulder (ε 1550); nmr ($CDCl_3$), δ 7.1–8.1 (5 H multiplet, aryl CH), 4.86 (1 H quadruplet, J = 7 cps, $COCHSO_2$), 2.89 (3 H singlet, CH_3SO_2), and 1.68 (3 H doublet, J = 7 cps, CH_3C).

A mixture of 1.63 g (25 mg-atoms) of zinc dust,[4d] 1.06 g (5.0 mmoles) of the keto sulfone **20**, 5 ml of acetic acid, and 7 ml of absolute ethanol was stirred at 28° for 2 hr. After the insoluble material had been separated and washed with ether, the combined organic solutions were washed successively with aqueous $NaHCO_3$ and aqueous NaCl and then dried and concentrated. Distillation of the residual oil separated 525 mg (78%) of propiophenone, bp 100–110° (10 mm), identified with an authentic sample by comparison of gas chromatographic retention times[15] and by comparison of infrared and mass spectra.

Although the same reductive cleavage could be effected with aluminum amalgam in aqueous tetrahydrofuran, the yield was lower. Thus, reduction of 1.0 g (4.3 mmoles) of the keto sulfone **20** with the amalgam[4a] from 1.6 g (4.3 mg-atoms) of aluminum in 54 ml of tetrahydrofuran and 6 ml of water for 40 min at room temperature yielded 0.36 g (57%) of propiophenone, bp 100–110° (10 mm), identified with an authentic sample by comparison of gas chromatographic retention times[15] and mass spectra. The reduction of the corresponding β-keto sulfoxide by this procedure is reported[4f] to be complete in 10 min; the yield of propiophenone (before distillation) was 96%. A series of reductions of the crude keto sulfone **20** with aluminum amalgam in aqueous tetrahydrofuran at room temperature were followed by gas chromatography[15] utilizing tetralin as an internal standard to permit yield calculations. The calculated yields of propiophenone after various reaction times follow: 20 min, 43%; 30 min, 60%; 40 min, 66%; and 60 min, 30%. We presume that the propiophenone is being consumed by further bimolecular reduction to the pinacol as has been noted in other cases.[4d]

Methylation and Reductive Cleavage of the Keto Sulfone 18.—After a mixture of 1.16 g (6.0 mmoles) of the keto sulfone **18**, 145 mg (6.0 mmoles) of sodium hydride, and 7 ml of dimethyl sulfoxide had been stirred at room temperature for 1 hr, 1.0 g (7.1 mmoles) of methyl iodide was added and stirring was continued for 1 hr. The crude product **19**, isolated as previously described, was a pale yellow liquid (1.3 g): infrared ($CHCl_3$), 1715 cm^{-1} (C=O). The nmr spectrum ($CDCl_3$) of the crude product suggested the presence of the monoalkylated keto sulfone accompanied by lesser amount of unalkylated and dialkylated material. Reaction of the crude alkylated product with the amalgam from 1.6 g (60 mg-atom) of aluminum in a water (9 ml)–tetrahydrofuran (81 ml) mixture at 65° for 90 min followed by the usual isolation procedure afforded the crude liquid product. Distillation in a short-path still separated 0.46 g (*ca.* 60%) of the product as a colorless oil which contained (in order of elution)[12] 2-heptanone (10%), 3-octanone (80%), and 2-methyl-3-octanone (2%). Collected samples of each of these materials were identified with an authentic sample by comparison of gas chromatographic retention times and infrared and mass spectra. Attempts to reductively cleave the keto sulfone **19** by reaction with zinc in ethanol–acetic acid mixtures for 2 hr at 25 or at 65° yielded crude products in which no 3-octanone or other products of reductive leavage were detected.[12] Therefore, the reductive procedure using zinc[4d] rather than aluminum amalgam appears to be useful for β-keto sulfones only in cases where the carbonyl group is conjugated with an aromatic ring.

Registry No.—**1**, 14909-87-6; **2**, 14909-88-7; **3**, 14909-89-8; **4**, 14909-90-1; **5**, 14909-91-2; **6**, 15038-78-5; **7**, 15076-98-9; **8**, 14909-92-3; **9**, 14909-93-4; **10**, 14909-94-5; **11**, 15038-79-6; **14**, 14723-70-7; **16**, 3708-04-1; *p*-toluenesulfonylhydrazone of **17**, 14723-72-9; **18**, 14723-73-0; **20**, 14723-74-1; 2-hydroxy-1-methanesulfonylnonadecane, 14723-75-2; 1-methoxynonadecan-2-one *p*-toluenesulfonylhydrazone, 14723-76-3; **19**, 14723-77-4.

(14) H. Böhme and W. Krause, *Chem. Ber.*, **82**, 426 (1949).

(15) A gas chromatography column packed with 1,2,3-tris(β-cyanoethoxy)propane suspended on Chromosorb P was employed for this analysis.