β-Keto Sulfoxides. II. Transformations Giving Sulfur-Free Products[1]

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Abstract: The transformations summarized in Chart I have been achieved. The conversions of esters to β-keto sulfoxides and hence to ketones, α-ketols, glyoxals, α-keto acids, glycols, or α-hydroxy acids, all containing one more carbon atom than the starting ester, is an attractive alternate to a number of classical synthetic routes to these compounds. Since β-keto sulfoxides can be alkylated at the α-carbon atom, a variety of other chain extension reactions appear possible.

Preparation of β-keto sulfoxides can be readily accomplished by the condensation of dimethyl sulfoxide with esters in basic solution.[3,4] We have examined the synthetic utility of aromatic β-keto sulfoxides as a means of chain extending a carboxylic ester while at the same time introducing one or two functional groups into the final product. We have particularly examined the transformation of an ester into the seven products listed below and in Chart I.

$$RCO_2R' + CH_3SOCH_3 \xrightarrow{KOC(CH_3)_3} RCOCH_2SOCH_3 + R'OH$$

$$CH_3SOCH_3 + NaH \longrightarrow CH_3SOCH_2^-Na^+ \xrightarrow{RCO_2R'} RCOCH_2SOCH_3 + R'ONa \qquad (a)$$

$$RCO_2Et \longrightarrow \begin{cases} RCOCH_3 & RCH(OH)CH_3 \\ RCOCH_2OH & RCH(OH)CH_2OH \\ RCOCHO & RCH(OH)CO_2H \\ RCOCO_2H \end{cases}$$

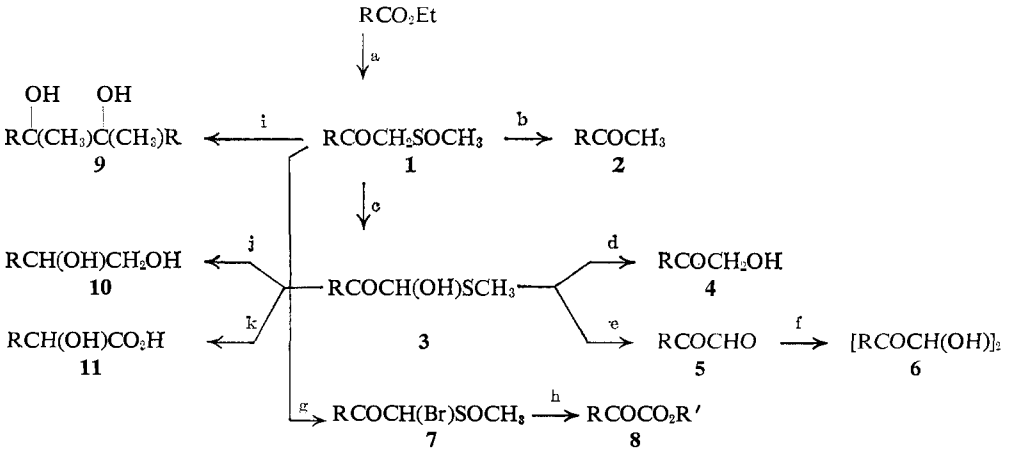
Formation of β-Keto Sulfoxides. Reaction a. Table I summarizes the yield of β-keto sulfoxides formed by condensation of aromatic esters with dimethyl sulfoxide in the presence of potassium *t*-butoxide. It is of interest that under the conditions employed that ethyl *p*-bromobenzoate gives the expected keto sulfoxide without displacement of the aromatic halogen, and ethyl *p*-toluate gives only a small amount of the self-condensation product, $p\text{-}CH_3C_6H_4COCH_2C_6H_4CO_2C_2H_5$.[3]

Table I. Formation of β-Keto Sulfoxides, Reaction a

Compound	R	Yield, %[a]	Mp, °C
1a	C_6H_5	88	85–86
1b	$p\text{-}CH_3C_6H_4$	87	106–107
1c	$p\text{-}CH_3OC_6H_4$	95	101–102
1d	$p\text{-}BrC_6H_4$	79	128–129
1e	$\alpha\text{-}C_{10}H_7$	>95	...
1f	$\beta\text{-}C_{16}H_7$	91	80–81

[a] Condensation conducted on a 50-mmole scale.

Reduction of β-Keto Sulfoxides to Ketones. Reaction b. The facile reduction of α-substituted ketones, such as the α-halo ketones, suggested that β-keto sulfoxides should be readily converted to the methyl ketone. While this work was in progress Corey and Chaykovsky reported an elegant reduction of β-keto sulfoxides, sulfones, and sulfonamides with amalgamated aluminum foil which is a convenient process for small-scale reduction.[4] We have found that β-keto sulfoxides can be conveniently reduced by zinc dust in ethanol–acetic acid mixtures to give yields of the purified ketones **2a**, **2b**, and **2c** in excess of 80%. Attempts to reduce β-hydroxy sulfoxides were unsuccessful. Thus, treatment of 1,1-diphenyl-2-(methylsulfinyl)ethanol for 24 hr with zinc dust in refluxing acetic acid gave 11% of starting material and 60% of 1,1-diphenyl-2-(methylmercapto)ethylene whereas **1a** is reduced to acetophenone in 2 hr at room temperature.



(1) Reactions of Resonance Stabilized Anions. XXIII. This work was supported by a grant from the Army Research Office (Durham).

(2) National Science Foundation Cooperative Fellow, 1964–1966.

(3) H.-D. Becker, G. J. Mikol, and G. A. Russell, *J. Am. Chem. Soc.*, 85, 3410 (1963).

(4) E. J. Corey and M. J. Chaykovsky, *ibid.*, 86, 1639 (1964); 87, 1345 (1965).

$$(C_6H_5)_2C(OH)CH_2SOCH_3 \xrightarrow[\Delta]{Zn,\ HOAC} (C_6H_5)_2C{=}CHSCH_3$$

It seems that the occurrence of reaction b is connected with the fundamental nature of the carbonyl group and not with specific reactions involving the sulfoxide moiety.

$$RCOCH_2X + e \longrightarrow R\dot{C}(O^-)CH_2X \longrightarrow RCOCH_2\cdot + X^-$$
$$X = \text{halogen, } CH_3S, CH_3SO, CH_3SO_2$$

Treatment of **1a** with aluminum–mercuric chloride in a benzene–ethanol mixture led to desulfurization and bimolecular reduction to produce glycol **9a** as a mixture of *meso* and *dl* isomers.

The Pummerer Rearrangement. Reaction c. β-Keto sulfoxides are readily converted to β-keto α-hydroxy sulfides (glyoxal hemimercaptals) by treatment with mild acid.[3] In fact neutralization of the condensation reaction may yield the hemimercaptal directly. Moreover, if the β-keto sulfoxide is not carefully deacidified after isolation it may undergo rearrangement upon storage. Thus, Corey and Chaykovsky report the preparation of **1e** with a pmr spectrum identical with **1e** prepared in the present work. However, we have never been able to crystallize **1e** whereas Corey and Chaykovsky report crystallization upon standing overnight in a cold room to give material melting at 110–113° with softening at 100°. In our hands treatment of **1e** with a trace of acid yields the hemimercaptal, **3e**, mp 110–112°, whose pmr spectrum is completely different from **1e**.

Yields of a variety of glyoxal methyl hemimercaptals are summarized in Table II.

Table II. Yields of Glyoxal Methyl Hemimercaptals ($RCOCH(OH)SCH_3$), Reaction c

Compound	R	Yield, %[a]	Mp, °C
3a	C_6H_5	95	106–107
3b	p-$CH_3C_6H_4$	96	91–92
3c	p-$CH_3OC_6H_4$	87	92–94
3d	p-BrC_6H_4	77[b]	92–93
3e	α-$C_{10}H_7$	63	110–112
3f	β-$C_{10}H_7$	90[b]	86–88

[a] Yield from β-keto sulfoxide, 50-mmole scale. [b] Yield of product before crystallization.

Reduction of β-Keto α-Hydroxy Sulfides. Reactions d and j. Reduction of **3a** with zinc dust in glacial acetic acid produces the α-hydroxy ketone **4a** and 1–4% of 1,4-diphenyl-1,4-butanedione. Above 30°, or in the presence of traces of water, the α-hydroxy ketone is reduced further to yield acetophenone. The preferred conversion of **3a** to **4a** involves reduction with sodium formaldehyde sulfoxylate (SFS = $NaOSOCH_2OH$) at a pH of 7. Yields of ω-hydroxyacetophenone in the range of 60–65% are obtained.

The reaction of **3** with lithium aluminum hydride or sodium borohydride affords the arylethylene glycols in good yield. This reaction is particularly attractive alternative to a Prevost-type reaction,[5] or peracid oxidation of the arylethylene. Over-all yields of **10a** and **10e** of 75 and 58% were obtained from ethyl benzoate and ethyl α-naphthoate, respectively. Yields of **10** are summarized in Table III. The melting point of **10e** (146–147°) did not agree with the literature value (114.5–115°)[6] although the infrared and pmr spectra were consistent with the glycol structure. Conversion of **10e** to the dibenzoate gave material identical with the dibenzoate intermediate in the Prevost reaction[6] and saponification of both benzoates in our hands gave identical materials, **10e**, mp 146–147°.

Table III. Preparation of Arylethylene Glycols ($RCH(OH)CH_2OH$) by Reduction of Glyoxal Hemimercaptals, Reaction j

Compound	R	Yield, % $LiAlH_4$ (Et_2O)	Yield, % $NaBH_4$ (C_2H_5OH)	Mp, °C
10a	C_6H_5	79[a]	95[a]	63–64
10b	p-$CH_3C_6H_4$	95[a]	99,[a] 82[b]	76–77
10c	p-$CH_3OC_6H_4$	...	86,[a] 80[b]	79–81
10e	α-$C_{10}H_7$	73[b]	94[b]	146–147
10f	β-$C_{10}H_7$	...	52[b]	134–135.5

[a] Yield of product before crystallization. [b] Yield of crystallized product.

Arylglyoxals. Reaction e. Compound **5** can be readily prepared from the hemimercaptal or directly from the β-keto sulfoxide by hydrolysis in refluxing aqueous acid solution. However, in practice these conversions work well only on a small scale wherein a large excess of water can be employed.[3] When high solid/liquid ratios were employed the yield of phenylglyoxal from **3a** decreased considerably with the production of the methyl mercaptal of phenylglyoxal and mandelic acid as by-products.[7] The preferred method of effecting the conversion of **3** to **5** is to react the hemimercaptal with cupric acetate in chloroform solution followed by filtration to remove cupric mercaptide, neutralization of the acid, and vacuum distillation to yield the anhydrous arylglyoxals. Table IV summarizes some typical yields. The over-all yield of

Table IV. Formation of Arylglyoxals (RCOCHO), Reaction e

Expt no.	Method[a]	R	% yield for reactions performed on different mole scales: 0.03	0.1–0.25	0.35–0.45
1	A	C_6H_5	69	50	60
2	B	C_6H_5	85	45	40
3	C	C_6H_5		75	64
4	D	C_6H_5	89	87	88
5	E	C_6H_5	70	62	
6	B	p-$CH_3C_6H_4$	73		
7	D	p-$CH_3C_6H_4$	86		
8	B	p-$CH_3OC_6H_4$	78		
9	D	p-$CH_3OC_6H_4$	74		
10	B	p-BrC_6H_4	57		

[a] A, hydrolysis of **1** in aqueous phosphoric acid solution; B, hydrolysis of **3** in hydrochloric acid and aqueous ethanol; C, hydrolysis of **3** in aqueous acetic acid; D, precipitation of methyl mercaptan from **3** with cupric acetate; E, precipitation of methyl mercaptan from **3** by 50:1 mole ratio of HgO and $HgCl_2$. Product isolated as anhydrous phenylglyoxal by distillation except for expt 2, 6, 8 (crystallized as hemihydrate), and expt 10 (crystallized as hydrate); see H.-D. Becker and G. A. Russell, *J. Org. Chem.*, **28**, 1895 (1963).

(5) C. Prevost, *Comp. Rend.*, **196**, 1129 (1933).

(6) E. Balla, *ibid.*, **198**, 947 (1934).

(7) For examples of acid-catalyzed hydride transfer from an aldehydic carbon atom, see V. Prey, H. Berbalk, and E. Steinbauer, *Monatsh.*, **91**, 1196 (1960).

phenylglyoxal from 0.5 mole of ethyl benzoate by procedure D, Table IV, was 64–73% in a number of experiments.

Reductive Dimerization of Phenylglyoxal. Reaction f. The reduction of **5** at pH 7 by SFS or of **3** by hydrogen-deficient Raney nickel in benzene produces a mixture of *meso* and *dl* forms of **6**. This compound has been produced in low yield using magnesium–iodine reduction of phenylglyoxal in benzene[8] and in the *dl* form by oxidation of *trans*-1,4-diphenyl-2-butene-1,4-dione by potassium permanganate.[9] The reaction of **3a** with SFS in the presence of cupric ion proceeds quite readily to give a mixture of **4a** and **6a**. Treatment of phenylglyoxal in aqueous solution with SFS in the presence of a trace of cupric ion yielded the dimeric product **6a** in 60–70% yield and is the preferred route to **6a**. The reaction may well involve the following sequence.

$$Cu^{2+} \xrightarrow{SFS} Cu^{+}$$

$$C_6H_5COCHO + Cu^{+} \longrightarrow [C_6H_5COCHO]\cdot{}^{-}Cu^{2+}$$

$$2[C_6H_5COCHO]\cdot{}^{-} \xrightarrow{2H^{+}} \mathbf{6a}$$

Alternately the aldol condensation of phenylglyoxal and ω-hydroxyacetophenone may be involved.

$$C_6H_5COCH_2OH + C_6H_5COCHO \longrightarrow \mathbf{6a}$$

Reaction of equal molar amounts of ω-hydroxyacetophenone and phenylglyoxal at pH 7 was found to yield the glycol **6a**.

Benzoylformic Esters. Reactions g and h. Oxidation of **1a** and **3a** by a variety of agents invariably led to benzoic acid. It was found that bromination of **1a** in basic solution yielded an α-bromo β-keto sulfoxide (**7a**) in 75% yield as a crystalline mixture of diastereomers, mp 95–100°. After standing 3 days at room temperature the crystalline mixture decomposed to yield 15–30% of benzoylformic acid and an unidentified, unstable oil containing sulfur and halogen. Treatment of **7a** with methanol or ethanol resulted in the formation of methyl and ethyl benzoylformates (**8a**, R′ = CH_3, C_2H_5) with yields in the range of 60–70%. Treatment of **7a** with aqueous, acidic DMSO produced among other products the thio ester, $C_6H_5COCOSCH_3$ (**12**), in 45% yield. The alcoholysis reactions of **7a** also produced an ether, believed to be $C_6H_5COCH(OR')SOCH_3$ or $C_6H_5COC(OR')_2SCH_3$, but not completely identified. The formation of **8** and **12** can be rationalized as Pummerer-type[3] rearrangements (reactions g or g′).

$$RCOCH_2SOCH_3 \xrightarrow{H^{+}} RCOCH_2\overset{\overset{OH}{|}}{\underset{+}{S}}CH_3 \xrightarrow{-H^{+}} RCOCH{=}SCH_3$$

$$RCOCH{=}SCH_3 \longrightarrow RCOCH(OH)SCH_3 + H_2O \qquad (c)$$

$$RCOCH(Br)SOCH_3 \longrightarrow \longrightarrow \xrightarrow{H_2O}$$

$$RCOCSCH_3 \begin{cases} \xrightarrow{H_2O} RCOCO_2H \\ \xrightarrow{CH_3OH} RCOCO_2CH_3 \end{cases} \qquad (g)$$

(Br, OH; RCOCOSCH$_3$, RCOCOBr)

$$RCOCH(Br)SOCH_3 + CH_3OH \longrightarrow$$

$$RCOCH(OCH_3)SOCH_3 \xrightarrow[\text{rearrangement}]{\text{Pummerer}}$$

$$RCOCSCH_3 \begin{cases} \xrightarrow{} RCOCOSCH_3 \\ \xrightarrow{} RCOCO_2CH_3 \end{cases} \xrightarrow{CH_3OH} \qquad (g')$$

(OCH$_3$, OH)

Mandelic Acid. Reaction k. Since the benzilic acid rearrangement of phenylglyoxal yields mandelic acid,[10] it is not surprising that treatment of an alcoholic solution of **3a** with excess aqueous sodium hydroxide at room temperature for 3 days gives yields of mandelic acid in the range of 55–65%. The acid was also obtained in 75% yield by adding cupric acetate to the alcoholic solution and filtration of the precipitated cupric mercaptide followed by treatment with excess aqueous sodium hydroxide at 60–70°.

Alkylation of β-Keto Sulfoxides. Treatment of **1a** with base (sodium hydride) followed by methyl iodide in refluxing tetrahydrofuran gave a high yield of the diastereomeric β-keto sulfoxides **13** (86% over-all yield from ethyl benzoate.)[11] Lower yields of the ethylated and benzylated β-keto sulfoxides were observed (see Experimental Section).

$$\mathbf{1a} + B^{-} + RX \longrightarrow \underset{\mathbf{13}}{C_6H_5COCHRSOCH_3}$$

Reduction of **13** (R = CH_3) with zinc dust in ethanol–acetic acid gave propiophenone in essentially quantitative yields. Recently Gassman and Richmond have reported similar conversions[12] on a small scale by use of aluminum amalgam. Although Gassman and Richmond were unable to effect the alkylation in tetrahydrofuran solution we encountered no difficulty in methylation of the sodium salt of **1a** in refluxing tetrahydrofuran solution.

Compound **13** (R = CH_3) has been converted to 1-phenyl-1,2-propanedione in 55% yield by the Pummerer reaction although the intermediate hemimercaptal has not been isolated (procedure A, Table IV). It is obvious that alkylation of the α-carbon in **1a** greatly reduces the ease with which the Pummerer rearrangement occurs, presumably by decreasing the acidity of the remaining α-hydrogen atom.

Since β-keto sulfones can also be prepared by an ester condensation with dimethyl sulfone,[13a] and can also be readily alkylated[13b] and reduced,[4] the alternative ketone synthesis from the β-keto sulfone deserves consideration.

β-Keto sulfoxides can be readily converted to α-hydroxy aldehydes *via* α-hydroxy mercaptals.[14] This

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(9) G. A. Russell, E. T. Strom, E. R. Talaty, and S. A. Weiner, *ibid.*, 88, 1998 (1966).
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(11) G. A. Russell, E. Sabourin, and G. J. Mikol, *J. Org. Chem.*, 31, 2854 (1966).
(12) P. G. Gassman and G. D. Richmond, *ibid.*, 31, 2355 (1966).
(13) (a) H.-D. Becker and G. A. Russell, *ibid.*, 28, 1896 (1963); (b) N. M. Carroll and W. I. O'Sullivan, *ibid.*, 30, 2830 (1965).
(14) F. Weygand, H. J. Bestmann, H. Ziemann, and E. Klieger, *Ber.*, 91, 1043 (1958).

Table V. Analytical and Proton Magnetic Resonance Data for $RCOCH_2SOCH_3$ (1)[a]

R	Formula	Calcd, % C	Calcd, % H	Calcd, % S	Found, % C	Found, % H	Found, % S	δ_R	δ_{CH_2} (J_{AB}, cps)	δ_{CH_3}
C_6H_5	$C_9H_{10}O_2S$	59.33	5.53	17.56	59.62	5.76	17.45	7.25–8.09	4.45, 4.28 (14)	2.66
p-$CH_3C_6H_4$[b]	$C_{10}H_{12}O_2S$	61.20	6.16	16.34	61.35	6.12	16.50	7.20–7.93	4.50, 4.19 (15.5)	2.75
p-$CH_3OC_6H_4$[c]	$C_{10}H_{12}O_3S$	56.60	5.70	15.08	56.72	5.65	15.31	6.90–8.06	4.43, 4.23 (14)	2.73
p-BrC_6H_4[d]	$C_9H_9BrO_2S$	40.45	3.46	12.28	41.34	3.42	12.41	7.5–7.93	4.35	2.73
α-$C_{10}H_7$	$C_{13}H_{12}O_2S$	67.23	5.21	13.28	67.02	5.16	13.55	7.28–8.10	4.59, 4.29 (14.7)	2.75
β-$C_{10}H_7$	$C_{13}H_{12}O_2S$	67.23	5.21	13.28	66.68	5.00	13.32	7.42–8.47	4.60, 4.30 (14.7)	2.73

[a] All spectra were obtained in deuteriochloroform with TMS as internal standard and gave integrals consistent with structures shown. The methylene appeared as an AB quartet, in all cases except in the p-Br derivative where it appeared as a singlet. [b] p-CH_3, δ 2.42. [c] p-CH_3O, δ 3.88. [d] *Anal.* Calcd: Br, 30.60. Found: 30.58.

conversion and the polymeric structure of the α-hydroxy aldehydes will be discussed in the future.

Experimental Section

Preparation of β-Keto Sulfoxides. General Procedure. A 250-ml, three-necked flask was fitted with a mechanical stirrer, a pressure-equalizing addition funnel containing 50 mmoles of the ester (neat if liquid, dissolved in a small amount of DMSO if solid), and a Claisen distillation apparatus set up for vacuum distillation. The Claisen head was fitted with a pressure-equalizing addition funnel containing 35 ml of dry DMSO. A mineral oil bubble trap served to close the system to the atmosphere.

Clean potassium (2 g, 51.2 g-atoms) and 40 ml of dry *t*-butyl alcohol were placed in the flask in a nitrogen atmosphere and the mixture was stirred with heating at 75–80° until the potassium had dissolved. Following addition of the DMSO and dropwise addition of the ester, the mixture was allowed to react for 2 hr at room temperature. Vacuum distillation of the solvent (oil bath, 60–70°) yielded an extremely viscous residue which was dissolved in 40 ml of cold water. The aqueous solution was extracted with three 25-ml portions of ether, acidified to pH 1–2 by *careful* addition of concentrated hydrochloric acid, quickly extracted with 25 ml of chloroform, and then vigorously extracted with thre e25-ml portions of chloroform. The combined chloroform extracts were extracted with 10 ml of saturated aqueous sodium bicarbonate, dried over magnesium sulfate, and filtered. Removal of the solvent at reduced pressure gave the β-keto sulfoxide as a pale yellow or tan solid, except for **1e**, which was obtained as an amber liquid. The solids were slurried in ether and filtered yielding the β-keto sulfoxides in a high state of purity. The preparation of compounds **1a–c** has been described previously.[3] The method of preparation described above gives 10–15% higher yields than those previously reported. (See Table V for pmr analysis.)

ω-(Methylsulfinyl)-α-acetonaphthone (1e). Ethyl α-naphthoate, 10 g (0.05 mole), with potassium *t*-butoxide (0.051 mole) in DMSO-*t*-butyl alcohol gave 13.8 g (quantitative yield) of **1e** as an amber liquid.

ω-(Methylsulfinyl-β-acetonaphthone (1f). Ethyl β-naphthoate, 6.8 g (0.034 mole), with potassium *t*-butoxide in DMSO-*t*-butyl alcohol gave 6.2 g (91%) of **1f**, mp 77–80°. Recrystallization from chloroform and ether yielded tan needles, mp 80–81°.

ω-(Methylsulfinyl)-p-bromoacetophenone (1d). Ethyl p-bromobenzoate, 22.9 g (0.1 mole), with potassium *t*-butoxide (0.1 mole) in 160 ml of 80% DMSO–20% *t*-BuOH gave **1d** as a white precipitate on acidification of the aqueous basic solution. After filtration, the filtrate was extracted with two 75-ml portions of chloroform, and the solid was dissolved in the chloroform extract and purified as described above, yielding 19.7 g (76%) of **1d** as a white solid, mp 125–126.5°. Recrystallization from chloroform and ether yielded colorless needles, mp 128–128.5°.

Reduction of 1 to Aryl Methyl Ketones. Acetophenone (2a). A solution of 9.1 g (0.05 mole) of ω-(methylsulfinyl)acetophenone, **1a**, in 23 ml of absolute alcohol and 15 ml of glacial acetic acid was added over a 40-min period to a rapidly stirred mixture of 16.3 g (0.25 g-atom) of zinc dust in 23 ml of absolute alcohol and 15 ml of glacial acetic acid, keeping the temperature below 30°. After stirring for 45 min after the addition was completed, the suspended solids were removed by suction filtration and washed three times by slurrying in 50-ml portions of benzene and filtering. Water (100 ml) was added to the solution and the excess acetic acid neutralized by careful addition of 30 g of powdered sodium carbonate. The aqueous solution was extracted with two 100-ml portions of benzene. The combined benzene extracts were extracted with 50 ml of saturated aqueous sodium bicarbonate and 100 ml of 5% aqueous mercuric chloride, dried over magnesium sulfate, and filtered. Removal of the solvent under reduced pressure and distillation of the residue (water aspirator) yielded 5.28 g (88%) of a colorless liquid, bp 105–110°. The infrared spectrum of the product was superimposable with an authentic sample of acetophenone. Vapor phase chromatographic analysis on an SE-30 column at 200° failed to reveal any products other than acetophenone.

Recrystallization of the distillation residue yielded 2–3% of the bimolecular reduction product, 2,3-diphenyl-2,3-butanediol, mp 123–125°.

***p*-Methylacetophenone (2b).** By the above procedure 11.7 g (59 mmoles) of ω-(methylsulfinyl)-p-methylacetophenone, **1b**, was reduced to the ketone. Distillation under reduced pressure yielded 6.6 g (83%) of **2b** as a colorless liquid, the infrared spectrum of which was superimposable with an authentic sample.

***p*-Methoxyacetophenone (2c).** By the above procedure, 21.2 g (0.1 mole) of ω-(methylsulfinyl)-p-methoxyacetophenone was reduced to **2c**. Distillation gave 13 g (87%) of a pale yellow solid, mp 34–35°. The infrared spectrum was superimposable with an authentic sample and a mixture melting point showed no depression.

Reduction of Alkylated Derivatives of 1 to Aryl Alkyl Ketones. Propiophenone. By the above procedure, ω-methyl-ω-(methylsulfinyl)acetophenone, **13** (R = CH_3),[11] 4.05 g (0.021 mole), was reduced to propiophenone. Distillation under reduced pressure yielded 2.71 g (96%) of the ketone as a colorless liquid, whose infrared spectrum was superimposable with that of an authentic sample.

***n*-Butyrophenone.** Following the procedure of Carroll and O'Sullivan[13b] **1a** was ethylated with ethyl iodide, and the product was reduced to *n*-butyrophenone by the procedure described above. After vacuum distillation the ketone was obtained as a colorless to pale yellow liquid whose infrared spectrum was superimposable with an authentic sample. The over-all yield of ketone from **1a** was 35%.

1,3-Diphenyl-1-propanone. Sodium hydride (0.1 mole) suspension in mineral oil was dissolved by heating at 70° with 50 ml of DMSO. A solution of 18.2 g (0.1 mole) of **1a** in 25 ml of DMSO was added and after 0.5 hr heating was stopped, and 12.5 ml (0.11 mole) of benzyl chloride was added over a 10-min period. After cooling and standing at room temperature for 3.5 hr, the solution was pored into 300 ml of ice–water, extracted with two 100-ml portions of Skelly C, acidified to pH 5 with a few drops of hydrochloric acid, and extracted with two 100-ml portions of chloroform.

The chloroform solution was extracted with 100 ml of water and 50 ml of saturated sodium bicarbonate, dried over magnesium sulfate, and evaporated under reduced pressure. Purification of 4.27 g of the crude product by chromatography on silica gel yielded 2.9 g (10.6 mmoles) of ω-benzyl-ω-(methylsulfinyl)acetophenone, **13** (R = $CH_2C_6H_5$), which was reduced by the procedure described above to yield 1.7 g (76.5%) of 1,3-diphenyl-1-propanone, mp 69–71° (recrystallized from methanol), lit.[15] mp 70°.

2,3-Diphenyl-2,3-butanediol (9a). A solution of 9.1 g (0.05 mole) of **1a** in 40 ml of dry benzene and 40 ml of absolute ethanol was mixed with a solution of 1 g (0.0035 mole) of mercuric chloride in 20 ml of absolute ethanol. This solution was added to a 250-ml, two-necked flask equipped with a mechanical stirrer and a reflux condenser and containing 4.9 g (0.182 g-atom) of aluminum foil cut into 1-in. squares. The mixture was vigorously stirred at reflux temperature for 9 hr during which time all the aluminum had dis-

(15) W. H. Perkin and J. Stenhouse, *J. Chem. Soc.*, 1007 (1891).

Table VI. Proton Magnetic Resonance of $RCOCH_A(OH_X)SCH_3$ (3)[a]

R	Formula	Calcd, % C	Calcd, % H	Calcd, % S	Found, % C	Found, % H	Found, % S	δ_R	δ_{HA}	δ_{HX}	δ_{SCH_3}	J_{AB}, cps
C_6H_5	$C_9H_{10}O_2S$	59.33	5.53	17.56	59.48	5.62	17.60	7.40–8.24	6.13	4.38	2.00	8.4
p-$CH_3C_6H_4$[b]	$C_{10}H_{12}O_2S$	56.60	5.70	15.10	56.30	5.78	14.80	7.80–8.02	6.31	4.50	1.95	5.5
p-$CH_3OC_6H_4$[c]	$C_{10}H_{12}O_3S$	61.20	6.16	16.34	61.58	5.95	16.32	6.85–8.17	5.60	4.51	2.00	6.9
p-BrC_6H_4	*d*							7.53–7.98	6.09	4.46	1.98	8.4
α-$C_{10}H_7$	$C_{13}H_{12}O_2S$	67.25	5.21	13.77	68.05	5.29	13.87	7.25–8.20	6.20	4.50	2.06	
β-$C_{10}H_7$	*d*							7.4–8.3	6.24	4.50	2.05	...

[a] Spectra obtained in deuteriochloroform solution with TMS as internal standard and gave integrals consistent with the structures shown. H_A and H_X appeared as a doublet or a broad singlet. [b] p-CH_3, δ 2.40. [c] p-CH_3O, δ 3.86. [d] Samples of adequate purity could not be obtained for analysis for this compound.

solved. The solution was poured into 400 ml of an ice–water slurry containing 50 ml of concentrated hydrochloric acid and the acidic solution was extracted with five 50-ml portions of chloroform. The chloroform extracts were dried over magnesium sulfate and the solvent removed under reduced pressure. The infrared spectrum of the viscous amber liquid residue, 5.9 g (97%), was superimposable with an authentic sample of **9a**, mp 123–124° (lit.[16] mp 122°), prepared by reduction of acetophenone with sodium amalgam. However, only a small amount of the crystalline glycol could be obtained from the stereoisomeric mixture. Reduction of **1a** in absolute ethanol using 20, 10, 5, and 2% sodium amalgam gave 12–15% yields of **9a** in addition to acetophenone, α-phenylethanol, and sulfur-containing products.

Pummerer Rearrangement of β-Keto Sulfoxides. A solution of about 50 g of **1a** or **1b** in 100 ml of DMSO was diluted with 750 ml of water and acidified with 100 ml of concentrated hydrochloric acid. After standing at room temperature for 24 hr, the white precipitate was removed by filtration, washed by slurrying in 400 ml of cold water, filtered, pulverized, and dried for 24–36 hr at room temperature. For the β-keto sulfoxides which were not appreciably soluble in aqueous DMSO (**1c–1f**), the rearrangement was effected by dissolving the β-keto sulfoxide in DMSO (about 5 ml of DMSO per gram of **1**), adding concentrated hydrochloric acid (2 ml per gram of **1**), and allowing the solution to stand at room temperature for 12–24 hr. Water was then added until an oil began to precipitate. Cooling the solution with stirring caused a solid to form. Further dilution with water to four to five times the original volume and cooling in an ice bath for 1 hr followed by filtration yielded the product as a pale yellow solid. (See Table VI for pmr analysis.)

Methyl Hemimercaptal of Phenylglyoxal (3a). By the above method, **1a** was converted to **3a** on a 0.05- to 0.5-mole scale in 93–95% yield. The product was obtained as a white to pale yellow powder, mp 104–106°, and as colorless needles, mp 106–107° on recrystallization from Skelly B.

Methyl Hemimercaptal of p-Methylphenylglyoxal (3b). By the above method 46.1 g (0.237 mole) of **1b** was converted to **3b**, obtained as pale yellow needles, mp 90–91°. Recrystallization from benzene and Skelly B gives colorless needles, mp 91–92°.

Methyl Hemimercaptal of p-Methoxyphenylglyoxal (3c). ω-(Methylsulfinyl)-*p*-methoxyacetophenone, **1c**, 30 g (0.141 mole), gave **3c** in 87% yield, mp 85–87°. Recrystallization from benzene and Skelly B gave colorless crystals, mp 92–94°.

Methyl Hemimercaptal of p-Bromophenylglyoxal (3d). ω-(Methylsulfinyl)-*p*-bromoacetophenone, **1d**, 11 g (0.042 mole), gave **3d** in 77% yield, mp 86–88°. Recrystallization from ethanol–water gave colorless crystals, mp 92–93°.

Methyl Hemimercaptal of α-Naphthylglyoxal (3c). ω-(Methylsulfinyl)-α-acetonaphthone, **1e**, 6 g (0.026 mole), gave a 63% yield of **3c** as pale yellow flakes, mp 98–101°. Recrystallization from benzene and Skelly B gave tan crystals, mp 111–113°.

Methyl Hemimercaptal of β-Naphthylglyoxal (3f). ω-(Methylsulfinyl)-β-acetonaphthone, **1f**, 5.6 g (0.024 mole), gave a 63% yield of **3f** which after two recrystallizations from Skelly B gave tan crystals, mp 86–88°.

Direct Conversion of Ethyl Benzoate to the Methyl Hemimercaptal of Phenylglyoxal (3a). Using a 1-l., three-necked flask calibrated for volumes of 150 and 300 ml, and equipped as described under the preparation of **1a**, 20 g (0.51 g-atom) of clean potassium was dissolved in 425 ml of *t*-butyl alcohol. The system was closed to the atmosphere by a mineral oil bubbler through which the evolved hydrogen escaped and stirred at 80° until the potassium had dissolved. After cooling the unreacted alcohol was removed by vacuum distillation until a thick slurry of potassium *t*-butoxide in *t*-butyl alcohol remained. The potassium *t*-butoxide was dissolved by the addition of 90 ml of dimethyl sulfoxide; the additional *t*-butyl alcohol was removed by heating the solution at 80–90° under vacuum until the volume of the solution was 300 ml. Ethyl benzoate (73 ml, 0.5 mole) was added slowly through the dropping funnel to the warm solution without additional heating and the reaction mixture sitrred at room temperature for 4 hr. Solvent was then removed under vacuum at 80–90° until the volume of reaction mixture has been decreased to 150 ml. The residue was poured into 500 ml of an ice–water slurry and the resulting aqueous solution was extracted with three 100-ml portions of ether. The aqueous solution was acidified with a mixture of 190 ml of concentrated hydrochloric acid and 675 ml of water. The resulting mixture was allowed to stand at room temperature for 30 hr, after which the pale yellow precipitate was removed by suction filtration, washed with 500 ml of cold water, and air dried to yield 69–74 g (76–81%) of phenylglyoxal hemimercaptal, mp 103–105°.

ω-Hydroxyacetophenone (4a). A solution of 9.1 g (0.05 mole) of **3a** in 75 ml of warm ethanol was vigorously stirred for 1 hr with an excess (0.03–0.04 mole) of cupric acetate powder. After filtration the solution was treated with a solution of 7.7 g (0.05 mole) of sodium formaldehyde sulfoxylate dihydrate in 35 ml of water and with 5 ml of 5 *N* sodium hydroxide. After 36 hr at room temperature the reaction mixture was filtered and concentrated under reduced pressure, and the semisolid residue dissolved by shaking with ethyl acetate and water. The organic layer was separated and the aqueous layer was extracted with 25 ml of ethyl acetate. The combined organic extracts were dried over sodium sulfate and evaporated under reduced pressure. The pale yellow solid, 5.4 g (80%), was recrystallized from hot Skelly B yielding colorless crystals, mp 82–84°, lit.[17] mp 86–87°.

Reduction of **3a** by essentially the same procedure except that the precipitation of the mercaptide with cupric ion was omitted resulted in lower yields (40–45%) of the ketol.

Reduction of β-Keto α-Hydroxy Sulfides to Glycols (10). General Procedure. Lithium Aluminum Hydride Reduction. A solution of 0.025 mole of **3** in 15 ml of dry tetrahydrofuran was slowly added to a slurry of an excess (0.035–0.040 mole) of lithium aluminum hydride in 25 ml of ethyl ether. The mixture was refluxed for 28 hr, and hydrolyzed with 10 ml of water and 25 ml of 6 *N* hydrochloric acid. The aqueous layer was extracted with two 25-ml portions of chloroform which were combined with the organic layer, extracted with 20 ml of dilute aqueous sodium bicarbonate solution, dried over magnesium sulfate, and evaporated to dryness. The product was obtained as a white or tan solid or as an oil which solidified on cooling.

Sodium Borohydride Reduction. A solution of 0.025 mole of **3** in 80 ml of absolute ethanol was slowly added to a solution of 0.79 g (0.025 mole) of sodium borohydride in 9 ml of water and 2 ml of 2 *N* aqueous sodium hydroxide. The mixture was refluxed for 3.5 hr, acidified to pH 3 with dilute hydrochloric acid, and concentrated on a steam bath under reduced pressure. The solid was removed by filtration, dissolved in chloroform, and combined with the two 20-ml chloroform extracts of the aqueous filtrate. The chloroform solution was dried over magnesium sulfate and evaporated under reduced pressure.

Recrystallization of **10a–c** was effected by dissolution in carbon tetrachloride or hot Skelly B; **10e** and **10f** were recrystallized from 95% ethanol. Yields and melting points are given in Table III.

(16) K. Sisido and H. Nozaki, *J. Am. Chem. Soc.*, **70**, 776 (1948).

(17) J. Plöchl and F. Blümlein, *Ber.*, **16**, 1292 (1883).

Table VII. Proton Magnetic Resonance of $[ArCOCH_A(OH_X)-]_2$ (6)[a]

Ar	Mp, °C	Solvent	δ_{HA} (area)	δ_{HA} (area)	δ_{HX} (area)	J_{AX}, cps
Ph	119 (*dl*)	$CDCl_3$	M, 7.3–8.1 (5)	D,[b] 5.34 (1)	D,[b] 3.89 (1)	7.5
		$CDCl_3$–D_2O	M, 7.3–8.1 (5)	S, 5.34 (1)	...	...
Ph	128 (*meso*)	$CDCl_3$	M, 7.2–7.9 (5)	S, 5.38 (1)	S, 3.84 (1)	...
		$CDCl_3$–D_2O	M, 7.2–7.9 (5)	S, 5.38 (1)	...	...
p-CH_3Ph[c]	131	$CDCl_3$	Q, 7.74 (4)	D, 5.35 (1)	D, 3.93 (1)	7.46
		$CDCl_3$–D_2O	Q, 7.74 (4)	S, 5.35 (1)	...	...
p-CH_3Ph[c]	165	$CDCl_3$	Q, 7.46 (4)	D,[b] 5.35 (1)	D,[b] 3.99 (1)	6.98
		$CDCl_3$–D_2O	Q, 7.46 (4)	S, 5.35 (1)	...	...

[a] M = multiplet, S = singlet, D = doublet, Q = quartet; symmetrical multiplets are given as the position of the center of the multiplet. [b] Slight further splitting is observed; all splitting is eliminated by minute amounts of acid. [c] The *p*-CH_3 resonance is at δ 2.45 (area 3).

α-Naphthylethylene Glycol (10e). *Anal.* Calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found: C, 77.04; H, 6.72. In addition to the solvent and aromatic resonances, the pmr spectrum of **10e** in DMSO consisted of: a portion of a multiplet, δ 3.37–3.60; triplet (area 1), δ 4.83; multiplet (area 2), δ 5.22–5.44; after OH exchange with deuterium oxide: singlet, δ 3.55; multiplet (area 1), δ 5.22–5.44.

β-Naphthylethylene Glycol (10f). *Anal.* Calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found: C, 76.97; H, 6.34. In addition to the solvent and aromatic resonances, the pmr spectrum of **10f** in DMSO consisted of: multiplet (area 2.2), δ 3.5–3.9; broad singlet (area 1), δ 4.2–4.65; rough triplet (area 1.93), δ 4.65–5.24; after OH exchange with deuterium oxide: multiplet (area 2), δ 3.62–3.85; rough triplet (area 1), δ 4.65–5.1.

1,4-Diphenyl-2,3-dihydroxybutane-1,4-dione (6a). A solution of 6.12 (0.040 mole) of sodium formaldehyde sulfoxylate dihydrate in 40 ml of water was added to a solution of 5.66 g (0.02 mole) of phenylglyoxal hemihydrate and 0.48 g (0.002 mole) of cupric nitrate trihydrate in 60 ml of 95% ethanol. The solution was adjusted to pH 7 by the addition of concentrated aqueous sodium hydroxide and allowed to react at room temperature for 60 hr. The solution was filtered and the residual solid was washed thoroughly with hot ethyl acetate. The filtrate was concentrated under reduced pressure and the aqueous organic mixture was extracted twice with 30-ml portions of ethyl acetate, acidified to pH 3–4, and quickly extracted with 50 ml of ethyl acetate. The combined organic extracts were dried over sodium sulfate and the solvent was removed under reduced pressure. The residual pale yellow oil was mixed with 5 ml of ether and allowed to solidify. After 2 days at room temperature the solid was filtered and washed with carbon tetrachloride yielding 3.17 (60%) of **6a** as a diastereomeric mixture, mp 100–105°. Dilution of the filtrate and freezing for 24 hr gave additional **6a**, total yield 73%.

Partial dissolution of the solid by refluxing slowly with 15 ml of benzene, decanting the liquid, and repeating of the operation left a solid which, on recrystallization from benzene, gave colorless prismatic needles, mp 128–129°. Recrystallization of a portion of the diastereomeric mixture from ethanol gave the *dl* isomer as colorless prisms, mp 118–121°, with some softening around 115°. A mixture melting point with an authentic sample[9] showed no depression. (See Table VII for pmr analysis.)

1,4-Ditolyl-2,3-dihydroxybutane-1,4-dione (6b). A mixture of 4.5 g (0.023 mole) of **3b** in 125 ml of ether and approximately 10 g of Raney nickel was stirred at reflux temperature for 19.5 hr. The mixture was filtered and the residue washed with ether. Evaporation of the solvent from the filtrate gave a solid. Dissolution of the solid in 50 ml of ether gave a small amount of white solid which was removed and recrystallized from 95% ethanol to yield 0.13 g (3.8%) of **6b** as pale yellow needles, mp 165–166.5°. *Anal.* Calcd for $C_{18}H_{18}O_4$: C, 72.24; H, 6.04. Found: C, 71.60; H, 5.81.

Refluxing the ether solution obtained above with 10 g of Raney nickel for 9 hr gave an additional 0.82 g (24%) of **6a** as a colorless diastereomeric mixture, mp 125–130 and 150–155°. The low-melting isomer was obtained from another experiment in which 2 g of Raney nickel in 20 ml of ether was refluxed for 1 hr before a solution of 0.67 g (3.42 mmoles) of **3b** in 15 ml of ether was added. The mixture was stirred at reflux temperature for 8 hr and filtered, and the solvent removed leaving a semisolid residue which on treatment with ether and cooling gave 0.27 g (53%) of a light brown solid. Recrystallization from 95% ethanol gave white crystals with a variable 1° melting range in the temperature range 128–132°. *Anal.* Calcd for $C_{18}H_{18}O_4$: C, 72.24; H, 6.04. Found: C, 72.19; H, 6.08.

ω-Bromo-ω-(methylsulfinyl)acetophenone (7a). Sodium hydride suspension in mineral oil (0.052 mole) was washed by decantation with three 15-ml portions of Skelly B and slurried with 50 ml of dry tetrahydrofuran. A solution of 9.1 g (0.05 mole) of **1a** in 75 ml of tetrahydrofuran was added to the base over a 30–40-min period. When hydrogen evolution ceased, a solution of 8 g (0.05 mole) of bromine in 10 ml of carbon tetrachloride was added over a 1-hr period. The mixture began to turn yellow toward the end of the reaction. The solvent was removed at reduced pressure, and the semisolid mass was shaken with methylene chloride and filtered. The sodium bromide was washed with methylene chloride, and the organic solutions were combined and evaporated to complete dryness at room temperature under reduced pressure to yield a tan solid, 13.3 g, mp 103–105°. Recrystallization by dissolution under reflux in 60 ml of methylene chloride followed by the slow addition of 60 ml of ether and cooling for several hours gave 6.3 g of a white solid, mp 104–105°. Concentration of the filtrate, followed by addition of more ether and cooling, yielded an additional 2.93 g; total yield 9.23 g (71%). In another preparation of this compound, a solid, mp 95–100°, was obtained. The pmr spectrum (deuteriochloroform) indicated that two isomers were present in the approximate ratio of 3:1; $SOCH_3$, δ 2.71 (area 3) and δ 2.83 (area 9); >C(Br)H, δ 6.19 (area 1) and δ 6.26 (area 3); aromatic protons, δ 7.33–8.18 (total area 20). Due to the rapid decomposition of the solid, an analysis was not obtained.

Ethyl Phenylglyoxylate (8a, R′ = C_2H_5). ω-(Methylsulfinyl)-acetophenone, **1a**, was converted to **7a** on a 0.05-mole scale. The solid obtained after evaporation of the methylene chloride solution was washed with ether and dissolved in 100 ml of absolute ethanol and 10 ml of concentrated sulfuric acid and the solution heated at reflux temperature for 6 days, and then concentrated and mixed with 300 ml of water. The mixture was extracted with three 50-ml portions of chloroform. The combined chloroform extracts were extracted with 20 ml of saturated aqueous sodium bicarbonate solution and dried over magnesium sulfate. Evaporation of the solvent and vacuum distillation of the residue gave 5.6 g of a pale yellow liquid, the infrared spectrum of which was superimposable with an authentic sample of ethyl phenylglyoxylate. The over-all yield in the conversion of **1a** to ethyl phenylglyoxylate was 63%.

Methyl Phenylthiolglyoxylate. A solution of 19.3 g (0.074 mole) of **7a** in 75 ml of DMSO, 25 ml of water, and 5 ml of concentrated sulfuric acid was kept at 30–35° for 11.5 days. The solution was poured into 300 ml of water and extracted with four 50-ml portions of chloroform. The chloroform solution was washed with two 15-ml portions of saturated sodium bicarbonate, dried over magnesium sulfate, and evaporated to dryness under reduced pressure. Vacuum distillation gave 6.59 g of a yellow liquid which solidified in a glass vial when scratched with a steel rod. Recrystallization from 95% ethanol gave 5.36 g (40%) of the thiol ester as yellow plates, mp 39.5–41°. *Anal.* Calcd for $C_9H_8O_2S$: C, 60.00; H, 4.48; S, 17.77. Found: C, 59.98; H, 4.44; S, 17.81.

In addition to the aromatic protons, δ 7.72–8.20 (total area 5), the pmr spectrum of crude material (carbon tetrachloride) exhibited a sharp singlet at δ 2.37 (area 3), and two equal intensity singlets at δ 2.60 and 3.25 (total area 0.8). The latter two absorptions have been attributed to methyl methanethiolsulfonate formed from DMSO in the aqueous acidic solution,[18] the presence of which is confirmed by the infrared absorptions at 7.47, 8.78, and 7.51 μ.

The α-keto thiol ester exhibits an intense, slightly broad carbonyl infrared absorption (in carbon tetrachloride) at 5.96 μ and an intense absorption at 9.35 μ which is suggestive of a sulfoxide group.

(18) R. Rätz and O. J. Sweeting, *Tetrahedron Letters*, 529 (1963).

However, this absorption does not show the usual shift to a longer wavelength in chloroform,[19] a characteristic of sulfoxides.

The thiol ester was converted to methyl phenylglyoxylate, **8a** (R′ = CH_3), by refluxing for 24 hr in methanol with a trace of sulfuric acid.

Mandelic Acid (11a). A solution of 9.1 g (0.050 mole) of **3a** in ml of warm ethanol was vigorously stirred for 1 hr with 7.59 g (0.037 mole) of powdered cupric acetate monohydrate. The precipitate was removed by filtration, and the filtrate was mixed with a solution of 8 g (0.2 mole) of sodium hydroxide in 20 ml of water and heated at 65–70° for 7 hr, shaking occasionally to break up the solid mass that formed. The mixture was poured into 200 ml of water, acidified to pH 1 with concentrated hydrochloric acid, filtered, and thoroughly extracted with 450 ml of chloroform in 75-ml portions. Evaporation of the solvent yielded 5.3 g (70%) of **11a**, mp 110–112°. Evaporation of the aqueous solution and extraction of the salts with acetone gave an additional 1.4 g (18%) of the acid. Recrystallization from carbon tetrachloride gave colorless crystals, mp 116–118°, lit.[10] mp 117–118.5°.

1-Phenylpropane-1,2-dione. A mixture of 6.47 g (0.033 mole) of **13** (R = CH_3) in 15 ml of water and 3 ml of 85% phosphoric acid was heated at reflux temperature for 94 hr with rapid stirring. The mixture was cooled, and 25 ml of chloroform was added. The chloroform layer was separated from the aqueous layer and the latter extracted with two 20-ml portions of chloroform. The combined chloroform extracts were dried over magnesium sulfate and concentrated under reduced pressure. Vacuum distillation of the residue gave 2.45 g (50%) of the α-diketone as a clear yellow liquid, bp 55–57° (0.7 mm), lit.[20] bp 55–56° (0.5 mm), the infrared spectrum of which was superimposable with an authentic sample. The pmr spectrum (65% solution in carbon tetrachloride) showed only a 3-proton singlet at δ 2.38 and the expected 5-proton aromatic multiplet at δ 7.15–8.0.

(19) T. Cairns, G. Eglinton, and D. T. Gibson, *Spectrochim. Acta*, **20**, 31 (1964).

(20) W. D. Emmons and J. P. Freeman, *J. Am. Chem. Soc.*, 77, 4415 (1955).

In the preparation of the arylglyoxals, it was noted that the presence of acids causes extensive decomposition of the glyoxal during distillation. In this preparation of the diketone, the chloroform solution was not extracted with dilute aqueous base, perhaps causing some reduction in the yield. The above procedure is a modification of the procedure used to prepare phenylglyoxal directly from the β-keto sulfoxide (procedure A, table IV), described below.

Phenylglyoxal. (Procedure A). A solution of 9.1 g (0.050 mole) of **1a** in 50 ml of water and 10 ml of 85% phosphoric acid was heated at reflux temperature and stirred vigorously for 35 hr, cooled, and extracted with five 50-ml portions of chloroform. The combined chloroform extracts were dried over magnesium sulfate and concentrated under reduced pressure. Vacuum distillation of the residue gave 4.6 g (68.6%) of anhydrous phenylglyoxal as a yellow liquid, bp 60–63° (1 mm).

Repetition of the above procedure using 75.5 g (0.42 mole) of **1a** in 620 ml of water and 62 ml of 85% phosphoric acid yielded 33.3 g (60%) of anhydrous phenylglyoxal.

Phenylglyoxal. (Procedure D). The methyl hemimercaptal of phenylglyoxal (69–74 g, 0.39–0.41 mole), prepared as described for the direct conversion of ethyl benzoate to **3a**, was dissolved in 400 ml of warm chloroform, and 60 g of finely powdered cupric acetate monohydrate (0.3 mole) was added in one portion to the well-stirred solution. The mixture was vigorously stirred at room temperature for 1 hr. The solids were removed by suction filtration and washed twice with 75-ml portions of chloroform. The combined chloroform solution was shaken with 75 ml of water in a separatory funnel. Powdered sodium carbonate (20 g) was added in small portions to the aqueous layer, and the chloroform solution was extracted with the neutralized aqueous solution (caution—carbon dioxide evolution). The aqueous solution was extracted with four 30-ml portions of chloroform. The chloroform extracts were combined and dried with magnesium sulfate, and the chloroform was removed under reduced pressure. Vacuum distillation of the residue, first at a bath temperature of about 70° to remove residual water and methyl disulfide, and then at 90–95°, gave 43–49 g (64–73% based on starting ester) of anhydrous phenylglyoxal as a yellow liquid, bp 63–65° (0.5 mm).

Studies on Sulfate Esters. I. Nucleophilic Reactions of Amines with *p*-Nitrophenyl Sulfate

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Abstract: The nucleophilic reactivity of a series of amines toward *p*-nitrophenyl sulfate exhibits a small sensitivity to the basicity of the amine ($\beta = 0.20$). The reactivity is in the order tertiary > secondary > primary amine; steric hindrance increases rapidly with α substitution. A comparison of the reactions of the same amines with *p*-nitrophenyl phosphate reveals a striking similarity in their nucleophilic reactivity and the mechanism of the displacement. Both appear to involve transition states which feature little bond formation between substrate and amine. The spontaneous hydrolysis of *p*-nitrophenyl sulfate is discussed in terms of a possible elimination of sulfur trioxide in analogy to monomeric metaphosphate formation in the hydrolysis of certain phosphate dianions.

Investigation of the chemistry of sulfate esters was prompted by several considerations: (1) the wide distribution in nature of sulfate esters, *e.g.*, mucopolysaccharides, steroidal and phenolic sulfates;[1] (2) the presence of sulfatase enzymes which catalyze the hydrolysis of such sulfate linkages;[1] (3) the possible relationship between the hydrolytic mechanisms of the sulfatases and other hydrolases (phosphatase, chymotrypsin, etc.); and (4) the hypothesis that mechanistic similarities may occur in the hydrolytic pathways of sulfate and phosphate esters.[2]

(1) J. D. Gregory and P. W. Robbins, *Ann. Rev. Biochem.*, **29**, 347 (1960).

Experimental Section

Reagents. The potassium salt of *p*-nitrophenyl sulfate (Sigma Chemical, lot 124B-5110) assayed spectrophotometrically after complete acidic hydrolysis[3] proved to be of 99+% purity and

(2) E. T. Kaiser, M. Panar, and F. H. Westheimer, *J. Am. Chem. Soc.*, **85**, 602 (1963).

(3) K. S. Dodgson, B. Spencer, and K. Williams, *Biochem. J.*, **64**, 216 (1956).