

The Halogen-Dimethyl Sulphoxide System as an Oxidizing Reagent; a Convenient Method for Preparation of Diaryl Di- and Tri-ketones

By Naomichi Furukawa,* Takeshi Akasaka, Tetsuo Aida, and Shigeru Oae, Department of Chemistry, University of Tsukuba, Sakura-mura, Niihari-gun, Ibaraki, Japan 300-31

Some active methylene compounds are oxidized readily by dimethyl sulphoxide to afford the corresponding ketones in the presence of a catalytic amount of iodine and a strong acid. It is suggested that the reaction proceeds *via* an oxidation-reduction cycle.

RECENTLY, we have shown that dimethyl sulphoxide (DMSO) is reduced to dimethyl sulphide (DMS) in high yield in the presence of a catalytic amount of bromine or iodine (X_2).¹ The process forms a kind of 'oxidation-reduction cycle,'^{2,3} induced by DMSO and a catalytic amount of halogen or hydrogen halide (Scheme 1). If this reaction system were to contain a third component

† Thiols are readily oxidized to the corresponding disulphides quantitatively by use of the reaction cycle.⁴

‡ Under the same conditions, acetylacetone and methyl ethyl ketone gave only polymeric products.

¹ T. Aida, N. Furukawa, and S. Oae, *Tetrahedron Letters*, **1973**, 3853; T. Aida, T. Akasaka, N. Furukawa, and S. Oae, *Bull. Chem. Soc. Japan*, **1976**, **49**, 1117.

² N. Kornblum, J. W. Powers, G. J. Anderson, W. J. Jones, H. O. Larson, O. Levand, and W. M. Weaver, *J. Amer. Chem. Soc.*, **1957**, **79**, 6562; N. Kornblum, W. J. Jones, and G. J. Anderson, *ibid.*, **1959**, **81**, 4113.

which could also react initially with either halogen or hydrogen halide, a new synthetic application of this reaction cycle might be expected.†

We have studied the behaviour of a few active compounds (as third components) on heating with a catalytic amount of iodine and a strong acid (concentrated sulphuric acid) in DMSO, in the hope of synthesizing aldehydes or ketones in one step.

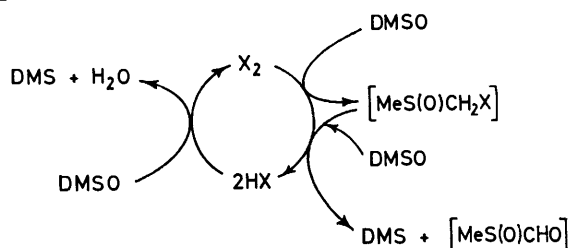
RESULTS AND DISCUSSION

The results are summarized in Table I.‡ Both benzyl phenyl ketone and dibenzoylmethane afford the corresponding (di- or tri-)ketone in substantial yield,

³ L. D. Small, J. H. Bailey, and C. J. Cavellito, *J. Amer. Chem. Soc.*, **1947**, **69**, 1711.

⁴ T. Aida, T. Akasaka, N. Furukawa, and S. Oae, *Bull. Chem. Soc. Japan*, **1976**, **49**, 1441.

but in the case of alkyl aryl ketones, diketones were not obtained; instead the reactions gave complex mixtures of products.



SCHEME 1 Oxidation-reduction cycle

Diphenyl triketone is usually prepared by oxidation of dibenzoylmethane with bromine in three steps (total yield 59%).⁵ However, the present reaction gave diphenyl triketone hydrate in 89% yield, distillation of which afforded diphenyl triketone (total yield 76%).

TABLE I

Reactions of active methylene compounds with the halogen-dimethyl sulphoxide system

Products and yields (%) ^a	
PhCO-CH ₂ Ph	PhCO-COPh 40 (69), PhCO-CH(SMe)Ph 8 (1)
PhCO-CH ₂ Me	PhCO-CH(SMe)Me 25 (29), PhCO-CH(OH)Me 30 (29), recovered ketone 26 (26)
Cyclohexanone	1,2-Dione 15, 2-methylthio-1-one 19, 2-en-1-one 1
PhCH-CH ₂ -COPh	PhCO-C(OH) ₂ -COPh ^b 89
Indane-1,3-dione	Ninhydrin ^c 21 (33)
PhCO-CH ₂ -S(O)Me	PhCO-CO-SMe 13
PhCO-CH ₂ -SMe	PhCO-CO-SMe 5

^a 'Open system' yields in parentheses. ^b Diphenyl triketone was obtained in 76% yield from distillation of the hydrate. ^c Also obtained by E. Schipper (*Tetrahedron Letters*, 1968, 6201).

S-Methyl phenyl(thioglyoxylate), which is readily hydrolysed under acidic conditions,⁶ was the product, obtained in low yield, from the corresponding β -oxo-sulphoxide or -sulphide.

The initial step in the oxidation of benzyl phenyl ketone is iodination to give the α -iodo-derivative,⁷ which is oxidized further to diphenyl diketone by Kornblum oxidation with DMSO.³ α -Iodobenzyl phenyl ketone has also been found to react with DMS, to afford dimethyl-(α -phenylphenacyl)sulphonium iodide, which then yields α -methylthiobenzyl phenyl ketone.

All these oxidation reactions took place only in the presence of a catalytic amount of iodine, the acid, and DMSO: in the absence of any one of these components no reaction was observed.

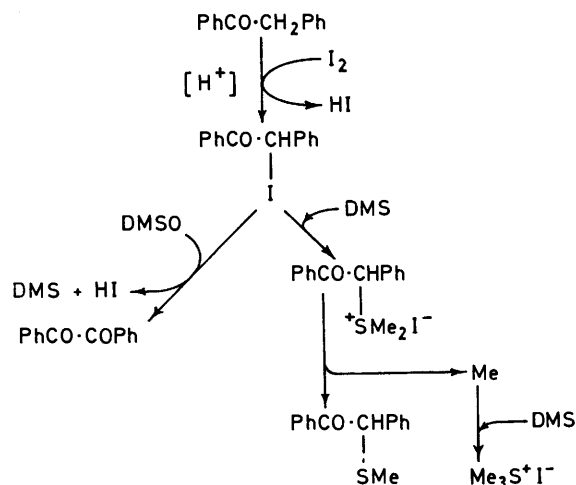
On the basis of these observations, a reasonable mechanism for the reaction is that shown in Scheme 2.

The reaction of acetophenone with the oxidation system unexpectedly afforded (*Z*)- and (*E*)-2-methylthio-1,4-diphenylbutane-1,4-dione (Ia and b).^{*} The olefin

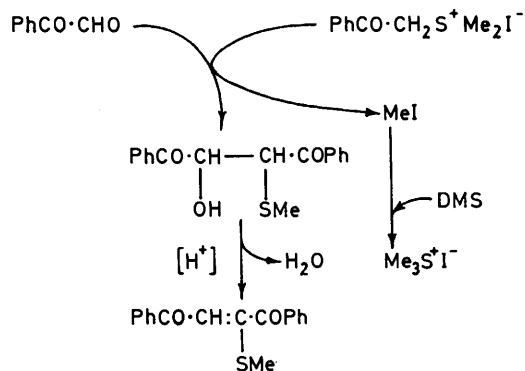
* The isomers were identified by spectroscopic comparison with authentic samples. These results will be published in a later paper.

⁵ L. A. Bigelow and R. S. Hanslick, *Org. Synth.*, Coll. Vol. II, 1943, p. 244.

is presumably obtained *via* condensation of the dimethyl(phenacyl)sulphonium salt and phenylglyoxal formed by the initial Kornblum reaction (Scheme 3). In fact, phenacyl iodide, obtained by iodination of acetophenone with iodine in the presence of a strong acid, is readily oxidized by DMSO to phenylglyoxal.³ Furthermore, phenacyl iodide is known to react with DMS to afford dimethyl(phenacyl)sulphonium iodide. Probably, this sulphonium salt reacts with phenylglyoxal in an aldol-type condensation to afford a β -hydroxy-sulphide, which then is dehydrated in the presence of the strong acid. In order to confirm this



SCHEME 2



(Ia and b)

SCHEME 3

mechanism a control experiment was carried out with phenylglyoxal and dimethyl(phenacyl)sulphonium bromide in the presence of a strong acid in dimethylformamide; the olefins (Ia and b) were obtained in 7 and 10% yields, respectively.

EXPERIMENTAL

I.r. spectra were recorded with a Hitachi 215 spectrometer, n.m.r. spectra with a Hitachi-Perkin-Elmer R-20

⁶ G. A. Russell and G. J. Mikol, *J. Amer. Chem. Soc.*, 1966, **88**, 5498.

⁷ W. D. Langley, *Org. Synth.*, Coll. Vol. I, 1941, p. 127; H. Rheinboldt and M. Perrier, *J. Amer. Chem. Soc.*, 1947, **69**, 3148.

spectrometer (solvent deuteriochloroform; tetramethylsilane as internal standard), and mass spectra, with a Hitachi RMU-6MG spectrometer (at 60 eV). Preparative column chromatography was performed with Wako-gel C-200.

Commercial dimethyl sulphoxide was purified by drying over calcium hydride and distillation. Commercial iodine was used without further purification. Commercial ketones were purified by distillation or recrystallization.

Methyl phenacyl sulphide was prepared in 80% yield from phenacyl bromide and sodium methanethiolate by the reported method;⁸ b.p. 105–106 °C at 3 mmHg (lit.,⁸ 104 °C at 2 mmHg).

Methyl phenacyl sulphoxide was obtained⁹ from sodium methylsulphinylmethanide and methyl benzoate; m.p. 85–87° (lit.,⁹ 86–86.5°).

Reactions of Active Methylene Compounds with the Halogen-Dimethyl Sulphoxide System.—A typical run was performed as follows. Benzyl phenyl ketone (3.92 g, 20 mmol), iodine (0.5 g, 2 mmol), and concentrated sulphuric acid (0.2 g, 2 mmol) dissolved in DMSO (20 ml) were heated in a sealed tube at 100 °C for 5 h. The mixture was then poured into ice-water and the aqueous layer was extracted with methylene chloride; the extract was washed with aqueous sodium sulphite, dried (MgSO₄), and evaporated. The residual oil was separated by column chromatography on silica gel with benzene-n-hexane (1:1) as eluant. Diphenyl diketone, m.p. 94.5–95.5 °C (lit.,¹⁰ 95 °C) and α -methylthiobenzyl phenyl ketone were obtained in 40 and 8% yields, respectively, and identified by comparison (m.p.s and spectra) with authentic samples.

Reactions in an 'open system,' *i.e.* with dimethyl sulphide allowed to evaporate, were carried out in a flask with a condenser.

Reaction of Dibenzoylmethane with the Iodine-Dimethyl Sulphoxide System.—The solution of dibenzoylmethane (0.45 g, 2 mmol), iodine (0.05 g, 0.2 mmol), and concentrated sulphuric acid (0.02 g, 0.2 mmol) in DMSO (3 ml) was heated in a sealed tube at 100 °C for 5 h. The mixture was then quenched with ice-water and extracted with methylene chloride. The organic layer was washed with aqueous sodium sulphite, dried (MgSO₄), and evaporated to

⁸ V. Prelog, V. Hahn, H. Brauchli, and H. C. Beyermen, *Helv. Chim. Acta*, 1944, **27**, 1209; L. M. Long, *J. Amer. Chem. Soc.*, 1946, **68**, 2159.

afford a yellow precipitate of diphenyl triketone hydrate (0.46 g, 89%). Distillation of the hydrate gave diphenyl triketone (0.36 g, 76%), m.p. 69.5–71 °C (lit.,⁵ 68–70 °C).

Reaction of Acetophenone with Iodine-Dimethyl Sulphoxide System.—A mixture of acetophenone (1.2 g, 10 mmol), iodine (0.25 g, 1 mmol) and concentrated sulphuric acid (0.19 g, 1 mmol) in a large excess of DMSO was heated in a sealed tube at 100 °C for 10 h. The usual work up gave products which were separated by column chromatography and identified by spectroscopic and elemental analyses (see Table 2). (*Z*)-2-Methylthio-1,4-diphenylbutane-1,4-dione

TABLE 2

Reaction of acetophenone with the halogen-dimethyl sulphoxide system

Products	Yields (%)
<i>Z</i> -Olefin (Ia)	24
<i>E</i> -Olefin (Ib)	12
PhCO·CH(OH)·CH(SMe)·COPh	4
PhCO·CH ₂ ·SMe	11
PhCO·CHO	(Identified)
Trimethylsulphonium salt	Not determined

(Ia) had m.p. 64–65 °C (from ethanol-n-hexane); ν_{\max} (KBr) 3 075, 2 940, 1 680, 1 640, 1 590, 1 260–1 240, 1 096, and 700 cm⁻¹; δ (CDCl₃) 2.14 (3 H, s), 7.08 (1 H, s), and 7.26–8.15 (10 H, m) (Found: C, 72.3; H, 5.2. C₁₇H₁₄O₂S requires C, 72.3; H, 5.0%). The *E*-isomer (Ib) had m.p. 97–98 °C (from ethanol-n-hexane); ν_{\max} (KBr) 3 075, 2 940, 1 680, 1 640, 1 605, 1 590, 1 540, 1 260–1 240, 1 050, 1 030, and 700 cm⁻¹; δ (CDCl₃) 2.39 (3 H, s), 6.99 (1 H, s), and 7.30–8.04 (10 H, m) (Found: C, 72.2; H, 5.2%).

Reaction of Dimethyl(phenacyl)sulphonium Bromide with Phenylglyoxal.—Dimethyl(phenacyl)sulphonium bromide (prepared from phenacyl bromide and dimethyl sulphide) (0.91 g, 3.5 mmol), phenylglyoxal (0.53 g, 3.5 mmol), and concentrated sulphuric acid (0.03 g, 0.35 mmol), dissolved in dimethylformamide (5 ml) were heated in a sealed tube at 100 °C for 5 h. The usual work up gave the *Z*- and *E*-olefins (Ia and b) in 7 and 10% yields, respectively.

[6/100 Received, 15th January, 1976]

⁹ E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, 1965, **87**, 1345.

¹⁰ M. Weiss and M. Appel, *J. Amer. Chem. Soc.*, 1948, **70**, 3666; B. Klein, *ibid.*, 1941, **63**, 1474.