Oxidative Desulfenylation of β-Alkylthio- and β-Arylthio-aldehydes and -ketones to α,β-Unsaturated Carbonyl Compounds

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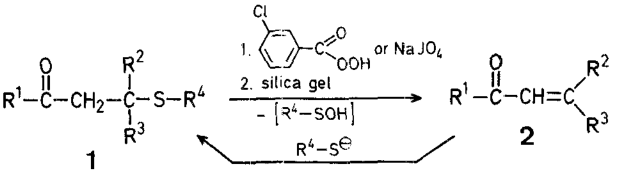
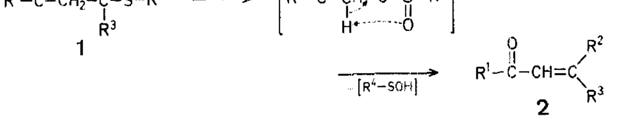
The versatile reactivity of sulfur substituents in organic molecules provides unique opportunities for devising new reactions and reagents in organic synthesis[1]. Particularly useful is the juxtaposition of sulfur substituents and carbonyl groups (2-oxoalkyl sulfides)[1]. We report here a facile synthesis of 2-alkenals (**2**, $R^1 = H$) and 1-alkenyl ketones (**2**, R^1 = alkyl, aryl) by the oxidative desulfenylation of the corresponding β-alkylthio- or β-arylthio-carbonyl compounds (**1**).

Treatment of 2-ethylthiopropyl phenyl ketone (**1a**) with 3-chlorobenzeneperoxoic acid or sodium periodate[2] and chromatographic isolation of the products on a silica gel column affords 1-oxo-1-phenyl-2-butene (**2a**, propenyl phenyl ketone) in 80 and 78% yields, respectively. Similarly other 2-alkylthioalkyl and 2-phenylthioalkyl ketones (**1b-e**), 3-ethylthio-3-phenylpropanal (**1f**), and the 2,2-bis[alkylthio]-alkyl ketones **1g** and **1h** are converted into the corresponding α,β-unsaturated carbonyl compounds (**2b-h**) in good yields by oxidative desulfenylation with 3-chlorobenzenecarboperoxoic acid.



Known compounds were identified by comparison of their boiling points, I.R.-, and ^{1}H-N.M.R. spectra with those of authentic samples. The structures of new compounds **1** were assigned on the basis of microanalyses, I.R.-, and ^{1}H-N.M.R.-spectral data.

The reactions presumably proceeds via *S*-oxidation of **1** to give the corresponding 2-oxoalkyl sulfoxide which is then thermally cleaved to give the 2-alkenal or 1-alkenyl ketone **2**, respectively, and the corresponding (unstable) sulfenic acid. The 2-oxoalkyl sulfoxide could not, however, be isolated as a side product.



In combination with our present cleavage method, the β-alkylthio- and β-arylthio-carbonyl compounds **1**, which are easily prepared from α,β-unsaturated carbonyl compounds (type **2**) and thiolate ion via a Michael-type addition, can be utilized as protected α,β-unsaturated carbonyl compounds.

β-Alkylthio- and β-Arylthio-aldehydes and -ketones (1, Aryl or Alkyl 2-Oxoalkyl Sulfides); General Procedure:

A solution of the 2-alkenal or 1-alkenyl ketone (**2**; 0.01 mol) in ether (20 ml) containing sodium methoxide (from 23 mg sodium and 1 ml methanol) is added dropwise to a stirred solution of an alkylmercaptan or arenethiol (0.015 mol) in ether (10 ml) at 0 °C (ice bath). Stirring is continued for 15 h at room temperature and the mixture then poured into a solution of sodium hydroxide (2 g) in water (50 ml). The mixture is extracted with ether (2 × 50 ml), the extract washed with 0.5 normal hydrochloric acid (50 ml) and water (1 × 50 ml), and dried with magnesium sulfate. The solvent is removed and the residual product purified by distillation or recrystallization.

The 3-oxoaldehyde 1-dithioacetals **1g** and **1h** are prepared according to Ref.[3].

2-Alkenals or 1-Alkenyl Ketones (2) from Compounds 1 by Oxidative Desulfenylation:

Method A, using 3-Chlorobenzenecarboperoxoic Acid; General Procedure: A solution of 3-chlorobenzenecarboperoxoic acid (0.194 g, 1.2 mmol) in chloroform (10 ml) is added slowly to a stirred solution of a sulfenylated aldehyde or ketone (**1**; 1 mmol) in chloroform

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Table 1. Preparation of β-Alkylthio- and β-Arylthio-aldehydes and -ketones (1)

1	R^1	R^2	R^3	R^4	Yield [%]	b.p./torr[a] or m.p. [°C]	Molecular formula[b]
a	C_6H_5	H	CH_3	C_2H_5	72	b.p. 123°/2	$C_{12}H_{16}OS$ (208.3)
b	C_6H_5	H	CH_3	C_6H_5	96	b.p. 155°/2	$C_{16}H_{16}OS$ (256.3)
c	C_6H_5	H	C_6H_5	C_2H_5	81	m.p. 63-64° (ethanol)	$C_{17}H_{18}OS$ (270.3)
d	CH_3	H	C_6H_5	C_2H_5	93	b.p. 125°/2	$C_{12}H_{16}OS$ (208.3)
e	CH_3	CH_3	CH_3	C_2H_5	62	b.p. 60°/2 (b.p. 97-99°/15)[7]	
f	H	H	C_6H_5	C_2H_5	50	b.p. 120°/2	$C_{11}H_{14}OS$ (194.2)
g	C_6H_5	H	$-S-C_2H_5$	C_2H_5	85	m.p. 43-44° (benzene)	$C_{13}H_{18}OS_2$ (254.3)
h	C_6H_5	H	$-S-CH_2-C_6H_5$	$-CH_2-C_6H_5$	90	b.p. 200°/2	$C_{23}H_{22}OS_2$ (378.4)

[a] Kugelrohr temperature.

[b] The microanalyses showed the following maximum deviations from the calculated values: C, ±0.17; H, ±0.35.

Table 2. Spectral Data of Compounds 1

1	I.R. ν [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$/TMS) δ [ppm]
a	3060, 1680, 750, 695	1.26 (t, 3H); 1.36 (d, 2H, $J=6.6$ Hz); 2.60 (q, 2H); 3.18 (m, 2H); 3.35-3.55 (m, 1H); 7.3-7.7 (m, 3H); 7.85-8.0 (m, 2H)
b	3055, 1680, 750, 690	1.37 (d, 3H, $J=6.6$ Hz); 2.6-3.45 (m, 2H); 3.75-3.95 (m, 1H); 7.2-7.6 (m, 8H); 7.85-7.95 (m, 2H)
c	3060, 3030, 1680, 750, 720, 700, 685	1.16 (t, 3H); 2.28 (q, 2H); 3.53 (d, 2H, $J=7.1$ Hz); 4.59 (t, 1H, $J=7.1$ Hz); 7.15-7.55 (m, 8H); 7.85-8.0 (m, 2H)
d	3060, 3030, 1715, 760, 730, 700	1.14 (t, 3H); 2.08 (s, 3H), 2.37 (q, 2H); 2.96 (d, 2H, $J=7.3$ Hz); 4.34 (t, 1H, $J=7.3$ Hz); 7.2-7.4 (m, 5H)
e	1715, 1360	1.24 (t, 3H); 1.42 (s, 6H); 2.19 (s, 3H); 2.58 (q, 2H); 2.70 (s, 2H)
f	3060, 3040, 1725, 750, 700	1.16 (t, 3H); 2.28 (q, 2H); 2.94 (dd, 2H, $J=1.7$, 7.4 Hz); 4.36 (t, 1H, $J=7.4$ Hz); 7.2-7.6 (m, 5H); 9.68 (t, 1H, $J=1.7$ Hz)
g	3060, 1690, 755, 685	1.25 (t, 6H); 2.69 (q, 4H); 3.46 (d, 2H, $J=6.6$ Hz); 4.52 (t, 1H, $J=6.6$ Hz); 7.2-7.6 (m, 3H); 7.7-8.0 (m, 2H)
h	3060, 3030, 1690, 760, 695	3.25 (d, 2H, $J=7.2$ Hz); 3.80 (s, 4H); 4.31 (t, 1H, $J=7.2$ Hz); 7.1-7.5 (m, 13H); 7.6-7.8 (m, 2H)

Table 3. 2-Alkenals (2, $R^1=H$) and 1-Alkenyl Ketones (2, R^1 = alkyl, aryl) obtained from Compounds 1 by Oxidative Desulfenylation

2	R^1	R^2	R^3	Starting Material	Method[a]	Ratio Oxidizing Agent/1	Yield [%]	b.p./torr or m.p. [°C]		Recovery of 1 [%]
								found	reported	
a	C_6H_5	H	CH_3	1a	A	1.2/1	80	85°/2	111-112°/9[4]	16
				1a	A	2.4/1	86			trace
				1a	B	1.2/1	78			trace
				1b	A	1.2/1	85			6.5
c	C_6H_5	H	C_6H_5	1c	A	1.2/1	92	57-58°	58°[4]	trace
d	CH_3	H	C_6H_5	1d	A	1.2/1	89	41-43°	42°[4]	8
e	CH_3	CH_3	CH_3	1e	A	1.2/1	58	125°/760	130-131°/760[4]	39
f	H	H	C_6H_5	1f	A	1.2/1	69	75°/1	130°/20[4]	trace
g	C_6H_5	H	$-S-C_2H_5$	1g	A	1.2/1	70	146-147°/3	125-126°/0.5[5]	6
h	C_6H_5	H	$-S-CH_2-C_6H_5$	1h	A	1.2/1	91	61.5-62.5°	61.5-62.5°[6]	trace

[a] Method A: 3-chlorobenzenecarboperoxoic acid; Method B: sodium periodate.

(20 ml) cooled in an ice bath. Stirring is continued for 15 h at room temperature, the mixture then poured into concentrated aqueous sodium hydrogen sulfite solution (30 ml), and the resultant mixture extracted with chloroform (2 × 50 ml). The extract is washed with sodium hydrogen carbonate solution (50 ml) and then water (1 × 50 ml), and is dried with magnesium sulfate. The solvent is removed and the residual oil chromatographed on a silica gel column using benzene/hexane (9/1) as eluent to give product 2 and the starting material 1.

Method B, using Sodium Periodate; Typical Procedure: A solution of sodium periodate ($NaJO_4$; 0.261 g, 1.2 mmol) in methanol (10 ml) + water (20 ml) is added slowly to a stirred solution 3-ethylthio-1-phenyl-1-butanone (1a; 0.209 g, ~1 mmol) in 2-propanol (10 ml) in an ice bath. Stirring is continued for 15 h at room temperature, the mixture then poured into water (30 ml), and extracted with chloroform (2 × 50 ml). The extract is dried with magnesium sulfate, the solvent removed, and the residual oil chromato-

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graphed on a silica gel column using benzene/hexane (9/1) as eluent to give *1-phenyl-1-butenone* (**2a**) and starting material (**1a**).

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