Facile Preparation of Disulfides by Peracid Oxidation of β-Thioxoketones[1]

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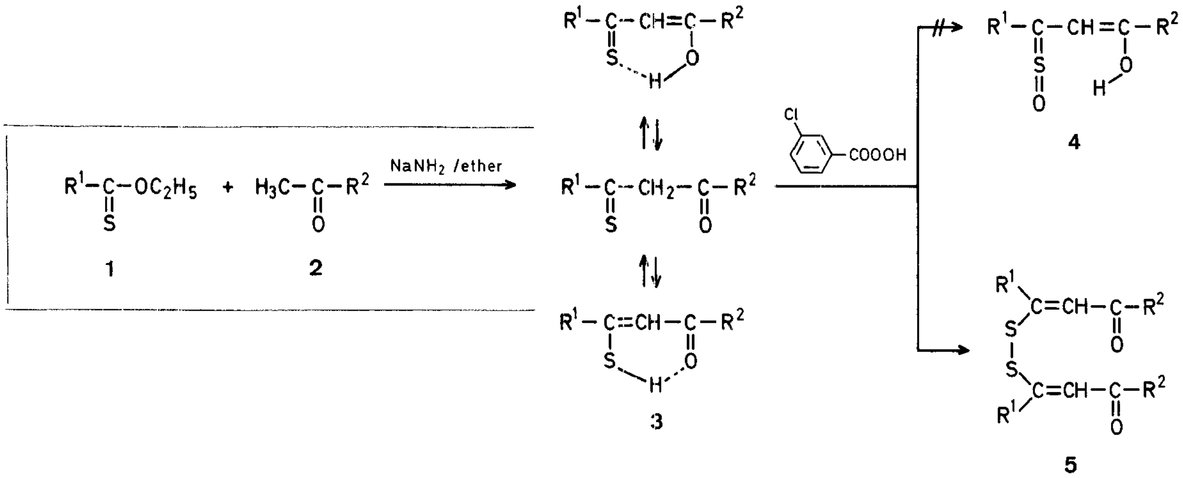
In connection with our current studies on the enol-enethiol tautomerism of β-thioxoketones[1,2] we were interested in derivatives possessing the pure enol or enethiol structure. For this purpose we have investigated the peracid oxidation of a series of β-thioxoketones[3] **3**. In principle two reaction routes are possible, leading to different products: (a) oxidation of the thiocarbonyl group of the enol form to give a thiocarbonyl-*S*-oxide (a sulfine)[4] **4** with preservation of the enol structure and (b) formation of a disulfide **5** containing the enethiol skeleton. The former possibility was considered plausible because of the fact that monothiodibenzoylmethane (**3c**) is known to exist exclusively as the enol form in the crystalline state[5] and predominantly as the enol form in solution[6]. On the other hand, **3c** has been reported to be slowly oxidized in ethanolic solution by air to give the disulfide **5c** in low yield[7].

We have found that β-thioxoketones **3** in concentrated ether solutions (0.4 molar) upon treatment with *m*-chloroperbenzoic acid give exclusively the corresponding disulfides **5**, which precipitate spontaneously in high yields as yellow to orange crystals. The disulfide structures were assigned on the basis of spectral data (Table 2) and microanalyses.



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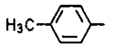
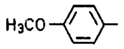
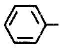
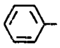
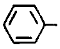
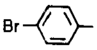
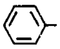
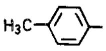
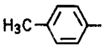
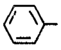
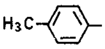
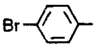
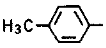
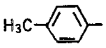
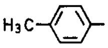
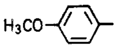
a	CH$_3$	
b	CH$_3$	
c		
d		
e		
f		
g		
h		
i		

Table 1. β-Thioxoketones (**3**) synthesized by Claisen condensation reaction of Acetophenones (**2**) with Thioesters (**1**)[12]

Compound	Yield [%]	m.p.	Molecular formula[a]
3a	79	67°[c]	$C_{11}H_{12}OS$ (192.3)
3b	63	56–57°[c]	$C_{11}H_{12}O_2S$ (208.3)
3c[b]	82	78–79°[d]	$C_{15}H_{12}OS$ (240.3)
3d	38	129°[d]	$C_{15}H_{11}BrOS$ (319.3)
3e	43	124–125°[d]	$C_{16}H_{14}OS$ (254.4)
3f	58	39–40°[c]	$C_{16}H_{14}OS$ (254.4)
3g	60	143°[e]	$C_{16}H_{13}BrOS$ (333.3)
3h	73	121°[d]	$C_{17}H_{16}OS$ (268.4)
3i	75	90–91°[e]	$C_{17}H_{16}O_2S$ (284.4)

[a] All products gave satisfactory microanalyses (C ±0.43%, H ±0.15%, S ±0.29%, Br ±0.08%); analyses were performed by the microanalytical laboratory of this institute.

[b] The product was identical with that obtained by the acid-catalysed reaction of dibenzoylmethane with hydrogen sulphide[13].

[c] Recrystallized from light petroleum (50–70°).

[d] Recrystallized from light petroleum (80–110°).

[e] Recrystallized from cyclohexane.

Table 2. Disulfides **5** obtained by the Peracid Oxidation of β-Thioxoketones **3**

Compound	Yield [%]	m.p.	Molecular formula[a]	^{1}H-N.M.R. ($CDCl_3$)[b] δ [ppm]	I.R. (KBr) ν [cm^{-1}]	U.V. (CH_3Cl_2) λ[nm] (log ε)
5a	77	164–165°	$C_{22}H_{22}O_2S_2$ (382.6)	2.39 (s, 3H), 2.41 (s, 3H), 7.20 (s, 1H)	1635, 1605	275 (4.24), 334 (4.55)
5b	79	148–150°	$C_{22}H_{22}O_4S_2$ (414.6)	2.39 (s, 3H), 3.82 (s, 3H), 7.22 (s, 1H)	1627, 1599	295 (4.33), 339 (4.77)
5c	52 79[c]	149–150°	$C_{30}H_{22}O_2S_2$ (478.6)	7.06 (s, 1H)	1632, 1597	267 (4.12), 336 (4.23)
5d	64	200–202°	$C_{30}H_{20}Br_2O_2S_2$ (636.4)	6.98 (s, 1H)	1638, 1583	280 (4.38), 341 (4.37)
5e	61	177–179°	$C_{32}H_{26}O_2S_2$ (506.8)	2.36 (s, 3H), 6.99 (s, 1H)	1630, 1608	280 (4.37), 338 (4.46)
5f	73	127–128°	$C_{32}H_{26}O_2S_2$ (506.8)	2.10 (s, 3H), 7.00 (s, 1H)	1630, 1590	267 (4.34), 339 (4.43)
5g	64	209–210°	$C_{32}H_{24}Br_2O_2S_2$ (664.6)	2.16 (s, 3H), 6.97 (s, 1H)	1639, 1591	279 (4.32), 343 (4.37)
5h	77	178–180°	$C_{34}H_{30}O_2S_2$ (534.8)	2.10 (s, 3H), 2.40 (s, 3H), 7.00 (s, 1H)	1634, 1605	290 (4.34), 340 (4.42)
5i	75	158–160°	$C_{34}H_{30}O_4S_2$ (566.8)	2.19 (s, 3H), 3.90 (s, 3H), 6.98 (s, 1H)	1638, 1602	297 (4.34), 343 (4.56)

[a] All products gave moderately satisfactory microanalyses (C ±0.75%, H ±0.30%, S ±0.60%, Br ±0.54%); analyses were performed by the microanalytical laboratory of this institute.

[b] Aromatic proton signals in the region δ=7.0–8.0 ppm.

[c] Chloramine-T was used as oxidizing agent.

A characteristic band at around 1635 cm^{-1} was observed in the I.R. spectra and was assigned to the C=O stretching vibration. The structurally related compound 3-methylthio-1,3-diphenyl-1-oxo-prop-2-ene is known[8] to exhibit the C=O band at 1640 cm^{-1}. The ^{1}H-N.M.R. spectra showed the signals expected for the aryl, alkyl, and vinylic protons. No signal corresponding to enolic or enethiolic chelate protons could be detected in the range δ=0 to δ=20 ppm. The U.V. spectra were all characterized by two bands, assigned to the π→π* transitions in the Ar-CO[9] and the S—C=C—C=O[1,2] chromophores, respectively.

The presence of the two double bonds in the disulfides implies the possibility of the existence of three isomers (*cis*/*cis*, *cis*/*trans*, and *trans*/*trans* disulfides). However, the spectral data and T.L.C. analyses clearly showed that only one isomer, most probably the *cis*/*cis* **5**, had actually been formed. In one experiment **3c** was reacted with chloramine-T instead of *m*-chloroperbenzoic acid under otherwise identical reaction conditions, and the disulfide **5c** was obtained in 79% yield; a potential *S*-imide derivative[10] of the enol tautomer of **3c** could not be detected.

The initial β-thioxoketones were synthesized in good yields by Claisen condensation of *O*-ethyl thioacetate or *O*-ethyl thiobenzoate **1** with the appropriate acetophenone **2** employing a modification of the procedure described[11] for the synthesis of monothiodibenzoylmethane. The structure and purity of the β-thioxoketones were checked by spectroscopic measurements[12], m.p.'s, and microanalyses (Table 1).

General Procedure for the Preparation of β-Thioxoketones (3): A solution of the acetophenone (**2**; 0.1 mol) in dry ether (50 ml) was added dropwise over a period of 15 min to a stirred suspension of sodium amide (0.1 mol) in dry ether (100 ml) at 0°. After stirring for 1 h at 0° a solution of the thioester (**1**; 50 mmol) in dry ether (50 ml) was added dropwise during 30 min with stirring. The stirring was continued overnight, during which time the mixture attained room temperature. Ice/water (200 ml) were stirred in, the aqueous layer was isolated, and washed twice with ether. Ether (200 ml) was then again added, followed by 2 normal aqueous hydrogen chloride in small portions with stirring until the aqueous layer had pH 2. The etheral layer was separated, the aqueous layer was extracted with a further portion of ether (200 ml), and the combined ethereal extracts were washed once with water and dried ($CaSO_4$). The ether was removed by evaporation and the residue recrystallized from cyclohexane or light petroleum to give the analytically pure product.

General Procedure for the Peracid Oxidation of β-Thioxoketones to the Corresponding Disulfides (5):
A solution of *m*-chloroperbenzoic acid (400 mg, 2.2 mmol) in ether (5 ml) was added to the solid β-thioxoketone (2.0 mmol) and the mixture was stirred vigorously for 3 min. The precipitated disulfide was isolated by filtration, washed with ether (3 × 2 ml), and dried in vacuo. All products obtained in this way were found to be analytically pure.

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[1] β-Thioxoketones Part III. For part II, see F. Duus, *J. Org. Chem.* submitted for publication.

[2] F. Duus, J. W. Anthonsen, *Acta Chem. Scand.* in press.

[3] For simplicity, the β-thioxoketones are named as such regardless of the individually preferred tautomeric forms, which are in general the intramolecularly chelated enol and/or enethiol forms[1,2].

[4] (a) J. Strating, L. Thijs, B. Zwanenburg, *Tetrahedron Lett.* **1966**, 65.
(b) B. Zwanenburg, L. Thijs, J. Strating, *Recl. Trav. Chim. Pays-Bas* **86**, 577 (1967).

[5] L. F. Power, K. E. Turner, F. H. Moore, *Tetrahedron Lett.* **1974**, 875.

[6] E. Uhlemann, H. Müller, P. Thomas, *Z. Chem.* **11**, 401 (1971).

[7] S. H. H. Chaston, S. E. Livingstone, T. N. Lockyer, V. A. Pickles, J. S. Shannon, *Aust. J. Chem.* **18**, 673 (1965).

[8] S. H. H. Chaston, S. E. Livingstone, *Aust. J. Chem.* **20**, 1065 (1967).

[9] *Absorption Spectra in the Ultraviolet and Visible Region*, L. Lang, Ed., Akademiai Kiudo, Budapest, Vol. VI, p. 88.

[10] S. Tamagaki, S. Oae, *Tetrahedron Lett.* **1972**, 1159.

[11] E. Uhlemann, H. Müller, *Angew. Chem.* **77**, 172 (1965); *Angew. Chem. Int. Ed. Engl.* **4**, 154 (1965).

[12] The spectra of the β-thioxoketones will be presented and discussed in a separate paper: F. Duus, L. Carlsen, manuscript in preparation.

[13] F. Duus, S.-O. Lawesson, *Ark. Kemi* **29**, 127 (1968).