Regiospecific Conversion of Alkenyl Sulphides to α-Sulphenylated Carbonyl Compounds by Oxygenation in the Presence of Thiophenol

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Regiospecific conversion of alkenyl sulphides to α-sulphenylated carbonyl compounds was achieved by oxygenation in the presence of thiophenol; electrolysis was found to be quite effective for initiation of the reaction.

Alkenyl sulphides are versatile synthetic intermediates.[1] One of their most important reactions is hydrolysis[2] to the carbonyl group which can be readily converted to other functionalities. However, in the case of the resulting carbonyl compound being an unsymmetrical ketone where it is necessary to functionalize the α-position, there is the problem of regioselectivity (equation 1). Generally regioselective activation of one of two α-positions of an unsymmetrical ketone is difficult. These positions should be easily distinguished from one another in the original alkenyl sulphide, since one is associated with the olefinic carbon. Various methods exist for the preparation of alkenyl sulphides of a desired structure.[3] For example, deprotonation of the olefinic proton of alkenyl sulphides followed by alkylation is a useful method for the preparation of substituted alkenyl sulphides.[3] The reaction of the anion of phenylthio(trimethylsilyl)methane with carbonyl compounds also affords the alkenyl sulphides *via* Peterson elimination.[4] Therefore a direct method for the regiospecific conversion of alkenyl sulphides to carbonyl compounds with an activating group at the α-position is desirable.

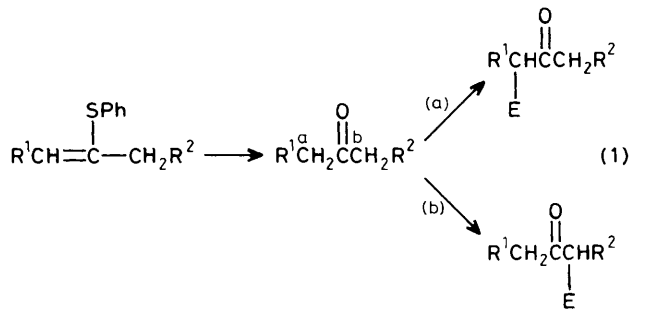
We report here the novel oxygenation of alkenyl sulphides in the presence of thiophenol into α-sulphenylated carbonyl compounds (equation 2). This reaction is also useful for the systems which do not involve the problem of regioselectivity, providing a general and easy access to α-sulphenylated carbonyl compounds. The synthetic versatility of α-sulphenylated carbonyl compounds is well established.[5] Alkylation takes place regioselectively on the carbon bearing sulphur, and oxidation of sulphur followed by elimination affords α,β-unsaturated carbonyl compounds. Thus the present reaction provides a powerful tool in organic synthesis.

The oxygenation reactions were simple to perform. An alkenyl sulphide (1.0 mmol) and thiophenol (2.0—4.0 mmol) were dissolved in acetonitrile or acetic acid and oxygen gas bubbled through the solution at room temperature. Aqueous work-up followed by chromatography afforded the corresponding α-phenylthio carbonyl compound as shown in Table 1. Usually a prolonged reaction time is required for the completion of the reaction, but the reaction could be markedly accelerated by electrochemical means.[6]

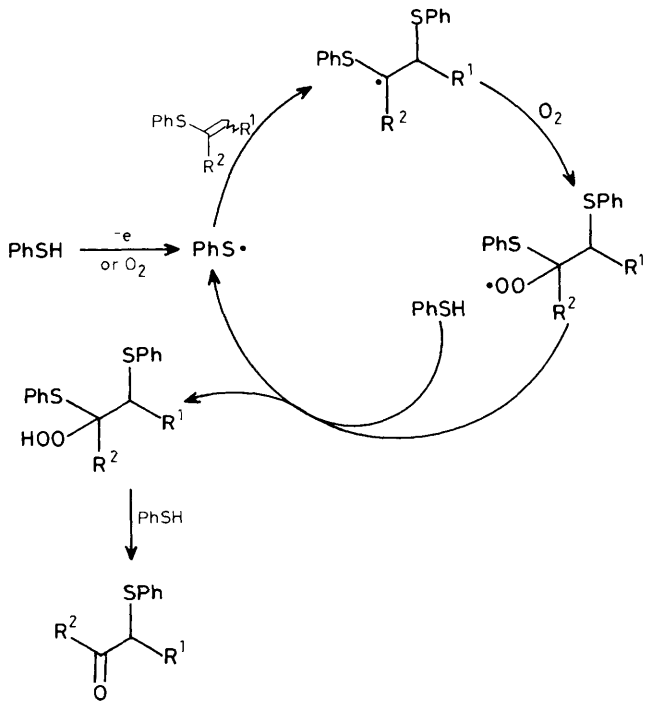
The electro-initiated oxygenation was carried out as follows: an alkenyl sulphide and thiophenol dissolved in Et_4NOTs/MeCN or Et_4NOTs/AcOH were placed in an undivided cell equipped with a carbon rod anode and a platinum plate cathode. An electric current was passed through the cell and oxygen bubbled through (20—50 mA, 1—5 min) at room temperature. After the electric current was turned off the solution was agitated with bubbling oxygen. If the reaction was not complete, the electrolysis was repeated (0.5—1 h interval) until most of the alkenyl sulphide was consumed.

When alkenyl acetate was used in place of the alkenyl sulphide, a similar reaction took place to give the α-sulphenylated carbonyl compound (equation 3), in low yield.

No reaction occurred in the absence of oxygen gas and the addition of a small amount of catechol markedly retarded the reaction. Thus the following radical chain mechanism seems to be reasonable (Scheme 1). Electrochemical oxidation of



Ts = *p*-$MeC_6H_4SO_2$

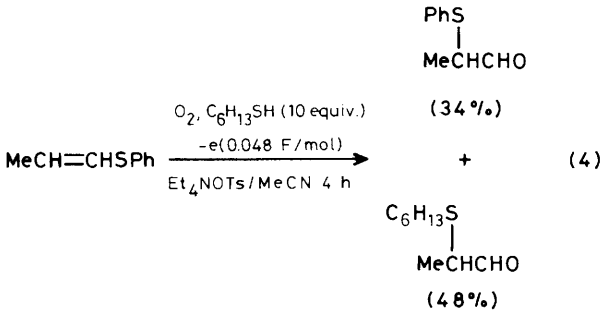


Scheme 1

Table 1. Oxygenation of alkenyl sulphides in the presence of thiophenol.[a]

Alkenyl sulphide		PhSH			Electricity		%
R^1	R^2	(equiv.)[b]	Method[c]	Solvent	(F/mol)[d]	*T*/h	Yield[e]
H	H	2.0	A	MeCN	—	41	52
		2.0	B	MeCN	0.050	2	77
Me	H	2.0	A	MeCN	—	2	70
		2.0	B	MeCN	0.061	1	76
C_7H_{15}	H	2.0	A	MeCN	—	23	71
		2.0	A	AcOH	—	10	74
		2.0	B	MeCN	0.012	2	91
Cyclohexyl	H	3.0	A	MeCN	—	96	74
		3.0	A	AcOH	—	24	83
		3.0	B	MeCN	0.796	8	73
		3.0	B	AcOH	0.125	1.5	81
$PhCH_2CH_2$	H	4.0	A	MeCN	—	31	58
		4.0	B	MeCN	0.250	4	63
H	C_8H_{17}	2.0	A	MeCN	—	96	66
		2.0	B	MeCN	0.021	2	82
C_7H_{15}	Me	2.0	B	AcOH	0.300	3	70
$-(CH_2)_2CH(Me)CH_2-$		4.0	A	AcOH	—	24	74

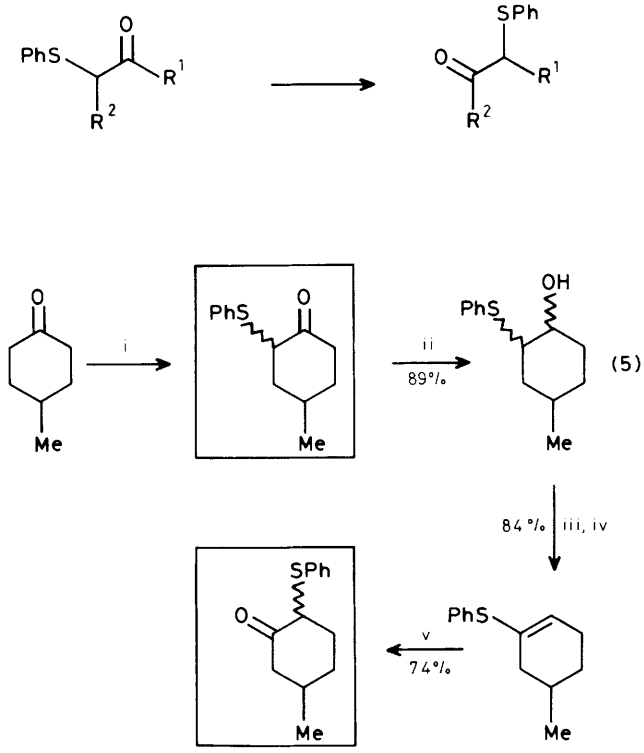
[a] Reactions were normally carried out with 1.0—0.5 mmol of alkenyl sulphides. [b] Based on the alkenyl sulphide. [c] Method A: Oxygenation was carried out in MeCN or AcOH. Method B: Electro-initiated oxygenation was carried out in 0.2 M Et_4NOTs/MeCN or in 0.2 M Et_4NOTs/AcOH using a carbon rod anode and a platinum plate cathode. [d] Based on the alkenyl sulphide. [e] Isolated yields.



thiophenol or reaction of thiophenol with oxygen produces the phenylthio radical which adds to the alkenyl sulphide.[7] The resulting carbon radical reacts with oxygen to give the peroxy radical. Hydrogen abstraction from thiophenol gives the α-hydroperoxysulphide[8] and regenerates the phenylthio radical. The α-hydroperoxysulphide is then decomposed with thiophenol to give the carbonyl compound.

It should be noted that oxygenation of phenyl propenyl sulphide with hexylmercaptan gave a mixture of α-hexylthiopropanal and α-phenylthiopropanal (equation 4). Although the mechanism has not been fully clarified as yet, the present data suggests that phenylthio group liberated from the original alkenyl sulphide was also used for the attack on another molecule of alkenyl sulphide.

The potential utility of the present reaction in organic synthesis is demonstrated by the following net 1,2-transposition of phenylthio group and carbonyl group (Scheme 2). For example, 2-phenylthio-4-methylcyclohexanone is converted to the alkenyl sulphide (equation 5).[9] Oxygenation of the alkenyl sulphide by the present reaction gave the 2-phenylthio-5-methylcyclohexanone in which the phenylthio group is attached to the formal carbonyl carbon and the carbonyl oxygen is attached to the carbon to which the



Scheme 2. *Reagents*: i, LDA, HMPA, THF then PhSSPh; ii, $NaBH_4$, EtOH; iii, MsCl, pyridine; iv, $KOBu^t$, DMSO; v, O_2, PhSH, AcOH.

phenylthio group has been attached. This sequence provides a new method for carbonyl 1,2-transposition[9] in which the position of the carbonyl group and that of the phenylthio group are exchanged.

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