CHEMISTRY LETTERS, pp. 1957 - 1960, 1984.

A NOVEL SYNTHESIS OF DIALKYL KETONES AND α-SULFENYLATED CARBONYL COMPOUNDS FROM α,β-EPOXY SULFOXIDES

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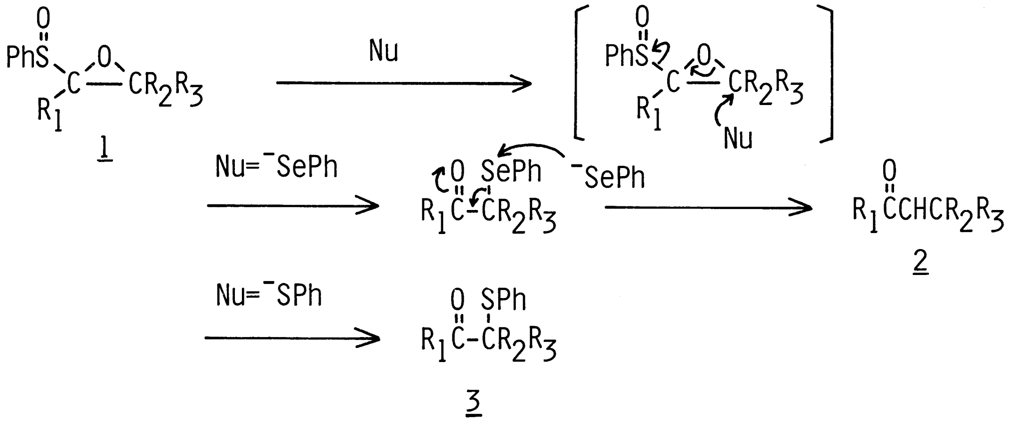
Treatment of α,β-epoxy sulfoxides with excess sodium phenylselenide and various kinds of alkylthiolates gave dialkyl ketones and α-sulfenylated carbonyl compounds, respectively, in good yields under mild conditions.

Ketones play central role in synthetic organic chemistry. A great number of methods for construction of alkyl, alkenyl, or alkynyl ketones have been reported,[1)] in which the "umpolung"[2,3)] reagents involved sulfur compounds acting as masked acyl anions[3)] are one of the most important ones. α,β-Epoxy sulfoxides (1) were initially reported by Durst[4)] in 1969. In spite of the studies on the synthesis of α,β-unsaturated ketones or aldehydes from α,β-epoxy sulfoxides,[5)] this interesting compound has been received a scant attention. On the other hand, the methods for synthesis of α-substituted ketones or aldehydes from α,β-epoxy sulfones were reported by Durst[6)] and Watt.[7)]

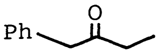
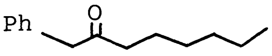
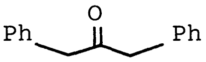
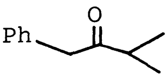
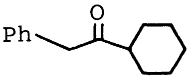
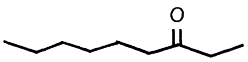
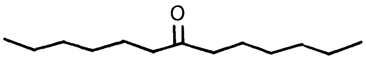
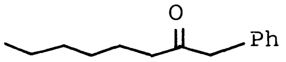
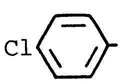
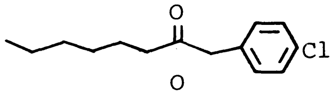
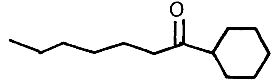
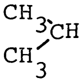
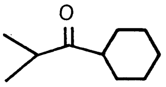
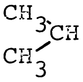
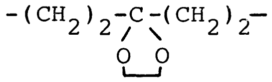
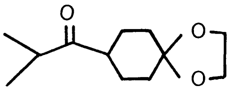
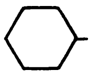
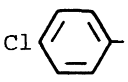
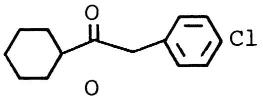
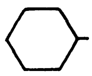
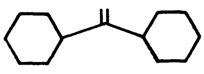
In this communication we report a novel and versatile method for the synthesis of dialkyl ketones (2) and α-sulfenylated carbonyl compounds (3) from α,β-epoxy sulfoxides (1) according to Eq. 1.



(1)

α,β-Epoxy sulfoxides (1)[4)] were easily prepared starting from alkylation of chloromethyl phenyl sulfoxide[8)] or alkylation of sodium phenylthiolate with alkyl halides[9)] in good overall yields. We found that the β-carbon of the α,β-epoxy sulfoxides (1) were very reactive to various kinds of nucleophiles such as

Table 1.
Preparation of dialkyl ketones from α,β-epoxy sulfoxides and sodium phenylselenide

R_1	R_2	R_3	NaSePh equiv.	Conditions	Ketone 2	yield[a] %
$PhCH_2$	CH_3	H	3	r.t. 20 min		92
$PhCH_2$	$CH_3(CH_2)_4$	H	3	r.t. 20 min		92
$PhCH_2$	Ph	H	3	r.t. 3 h		80
$PhCH_2$	CH_3	CH_3	5	r.t. 3 h		86
$PhCH_2$	——$(CH_2)_5$——		6	60 °C, 2 h		90
$CH_3(CH_2)_5$	CH_3	H	3	r.t. 5 min		80
$CH_3(CH_2)_5$	$CH_3(CH_2)_4$	H	3	r.t. 5 min		89
$CH_3(CH_2)_5$	Ph	H	5	r.t. 20 min		94
$CH_3(CH_2)_5$		H	3	r.t. 20 min		85
$CH_3(CH_2)_5$	——$(CH_2)_5$——		7	70 °C, 2 h		83
 $^{CH_3}_{CH_3}\!\!>CH$	——$(CH_2)_5$——		6	reflux 19 h		84
 $^{CH_3}_{CH_3}\!\!>CH$	 $-(CH_2)_2-\underset{O\quad O}{C}-(CH_2)_2-$		6	reflux 16 h		89
		H	6	r.t. 50 min		98
	——$(CH_2)_5$——		6	reflux 16 h		75

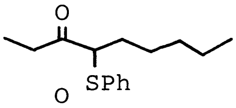
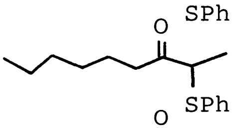
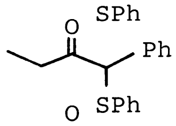
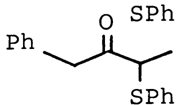
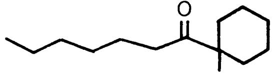
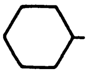
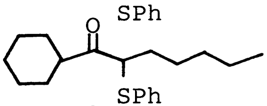
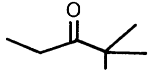
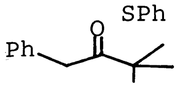
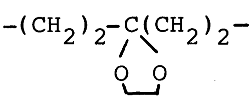
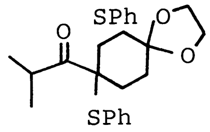
a) Isolated yields after silica gel column chromatography. The reactions were carried out in ethanol.

alkyl selenides, alkyl thiolates etc. to afford α-substituted ketones under very mild conditions in good yields.[10] Especially when sodium phenylselenide was used as a nucleophile, initially formed α-phenylseleno ketones were attacked by second phenylselenide to give dialkyl ketones (2) and diphenyl diselenide.[11] In this particular case, phenylselenide acted as an hydride equivalent to the α,β-epoxy sulfoxides (1).

As shown in Table 1, various kinds of dialkyl ketones were synthesized in good to excellent yields under mild conditions. Di-sec-alkyl ketones were also synthesized with no problem though higher temperature was required.

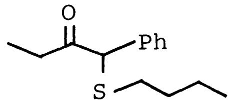
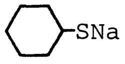
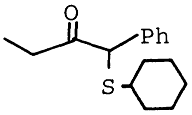
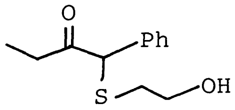
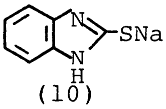
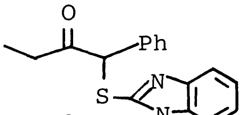
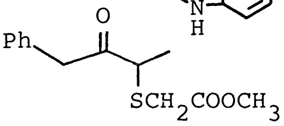
The results of the reaction of α,β-epoxy sulfoxides (1) with sodium phenylthiolate were shown in Table 2. Various kinds of α-sulfenylated carbonyl compounds, which are very fascinating compounds in synthetic organic chemistry,[12)] were synthesized by this method. More noticeable is the regiochemistry of the products. In entries 1, 2 and 3, 4, regioselectively sulfenylated carbonyl compounds are synthesized without any contamination of their regioisomers in very good yields under mild conditions. Also entries 5, 6 show the usefulness of the present method. The other effectiveness of this method is that the thiolates having functional groups are easily introduced to the β-carbon of α,β-epoxy sulfoxides to afford α-sulfenylated carbonyl compounds under very mild conditions, which is shown in Table 3.

Table 2.
Synthesis of α-phenylsulfenylated carbonyl compounds from α,β-epoxy sulfoxides (1) and sodium phenylthiolate

Entry	Epoxy sulfoxides (1) R_1	R_2	R_3	NaSPh equiv.	Conditions	Ketone 3	Yield[a)] %
1	CH_3CH_2	$CH_3(CH_2)_4$	H	2	r.t. 45 min		87
2	$CH_3(CH_2)_5$	CH_3	H	2	0 °C, 30 min		80
3	CH_3CH_2	Ph	H	2	r.t. 1 h		74
4	$PhCH_2$	CH_3	H	3	0 °C, 2.5 h		92
5	$CH_3(CH_2)_5$	$—(CH_2)_5—$		7	reflux 2.5 h		96
6		$CH_3(CH_2)_4$	H	3	0 °C, 6 h		93
7	CH_3CH_2	CH_3	CH_3	7	50 °C, 2.5 h		91
8	$PhCH_2$	CH_3	CH_3	7	r.t. 3 h		91
9	CH_3>CH CH_3	 $-(CH_2)_2-C(CH_2)_2-$ (O O)		10	reflux 24 h		66 (92)[a)]

a) Isolated yields after silica gel column chromatography. The yield in parenthesis is calculated from consumed starting material.

Table 3.
Synthesis of α-sulfenylated carbonyl compounds from α,β-epoxy sulfoxides (1) and thiolates other than phenylthiolate

Entry	Epoxy sulfoxides (1) R_1	R_2	R_3	Thiolate (equiv.)	Conditions	Ketone 3	Yield$^{a)}$ %
1	CH_3CH_2	Ph	H	$CH_3(CH_2)_3SNa$ (10)	0 °C, 2 h		73
2	CH_3CH_2	Ph	H	 (10)	r.t. 30 min		73
3	CH_3CH_2	Ph	H	$HO(CH_2)_2SNa$ (10)	0 °C, 30 min		53
4	CH_3CH_2	Ph	H	 (10)	r.t. 20 min		82
5	$PhCH_2$	CH_3	H	$NaOCOCH_2SNa$ (5)	r.t. 20 min		95$^{b)}$

a) Isolated yields after silica gel column chromatography.

b) Isolated as a methyl ester.

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(Received July 20, 1984)