α,β-Epoxy Sulfoxides as Useful Intermediates in Organic Synthesis. IV.[1] A Novel Synthesis of α-Acetoxy Ketones from α,β-Epoxy Sulfoxides

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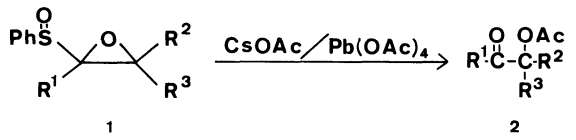
Synopsis. The treatment of α,β-epoxy sulfoxides, prepared from 1-chloroalkyl phenyl sulfoxides with ketones or aldehydes, with cesium acetate in dimethyl sulfoxide in the presence of lead tetraacetate afforded α-acetoxy ketones in moderate to good yields.

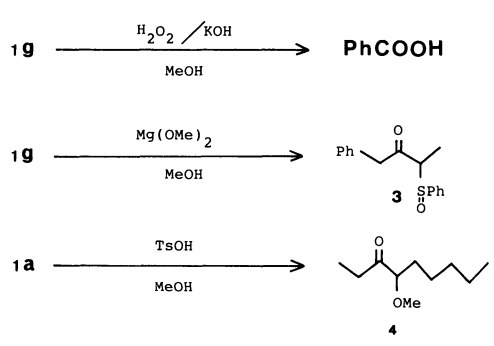
α-Oxygenated ketones are useful intermediates in synthetic organic chemistry. Recent years have seen a dramatic development in the synthetic procedures for α-hydroxy ketones and their derivatives. Among them, the acyloin condensation method[2] is one of the most well-known. The addition of acyl anion equivalents, such as lithium aldimines,[3] α-methoxyvinyllithium,[4] or carbanion of dithioacetal[5] to carbonyl compounds is a convenient procedure for constructing α-hydroxy ketones. The reaction of enol silyl ethers or enol acetates with *m*-chloroperbenzoic acid followed by hydrolysis,[6] acetoxylation of ketones with lead tetraacetate,[7] or direct oxidation of enolates with oxidants[8] are other good methods for the preparation of α-hydroxy ketones and their derivatives.

Recently, we reported[9] a new and versatile procedure for synthesizing α-substituted carbonyl compounds from α,β-epoxy sulfoxides (**1**). In the course of studies on the synthesis of α-substituted carbonyl compounds from α,β-epoxy sulfoxides (**1**), a new and efficient procedure was found which has a very different methodology from those mentioned above for the synthesis of α-acetoxy ketones (**2**). Such a procedure is given in Scheme 1.



1 2

Scheme 1.



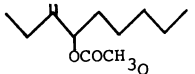
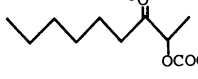
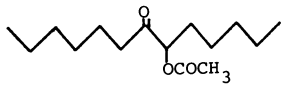
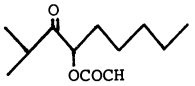
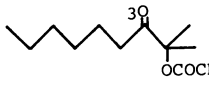
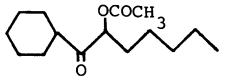
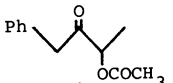
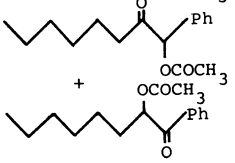
Scheme 2.

It has already been reported[9] that the β-carbon of α,β-epoxy sulfoxides is highly reactive with various kinds of nucleophiles (including selenolates, thiolates, and amines) to afford carbonyl, α-sulfenylated carbonyl, and α-amino carbonyl compounds, respectively, in good yields. On the other hand, oxygen nucleophiles are known to have fewer nucleophilic properties than those of sulfur and nitrogen. In fact, alcoholates and potassium acetate were found to show almost no reactivity toward α,β-epoxy sulfoxides (**1**) in alcohol or in dimethyl sulfoxide (DMSO) at a temperature below 50 °C (within 30 min). On the other hand, a treatment of **1g** with alkaline hydrogen peroxide in methanol gave benzoic acid in 58% yield. A treatment of **1g** with magnesium methoxide in refluxing methanol yielded a rearranged product, 1-phenyl-3-phenylsulfinyl-2-butanone (**3**), in 63% yield. An acidic opening of the epoxy group of **1a** with *p*-toluenesulfonic acid in methanol gave the desired 4-methoxy-3-nonanone (**4**); however the yield was not sufficient. After much work, we at last found that the treatment of **1** with cesium acetate[10] in DMSO (in the presence of lead tetraacetate) afforded the desired α-acetoxy ketones in good yield. The results are summarized in Table 1.

In reactions in the absence of lead tetraacetate, the yields of the α-acetoxy ketones (**2**) were always less than 50% and α-phenylthio ketones[9a,11] were observed. To prevent the formation of this by-product, some oxidants were added to the reaction mixture and it was found that two equivalents of lead tetraacetate[12] worked well. Further, lead tetraacetate was found to show no reactivity toward α,β-epoxy sulfoxides in DMSO, namely the treatment of the sulfoxide (**1g**) with lead tetraacetate (2 equiv) in DMSO at 70 °C for 30 min afforded only the starting material in almost quantitative yield.

In entries 1—4, and 6—8 the α,β-epoxy sulfoxides have two diastereomers, expressed as L and P.[9b] These isomers show almost the same reactivity toward cesium acetate to afford the desired α-acetoxy ketones (**2**). It is worthwhile noting that regeioselectively acetoxylated products without their isomers are afforded in moderate to good yields (entries 1, 2, 4, and 5). Entry 5 shows that the α,β-epoxy sulfoxide having two alkyl groups on β-carbon exhibits much less reactivity than those having one alkyl group. The epoxy sulfoxide having a benzyl group in R^1 gave low yields of α-acetoxy ketones. This may be interpreted that lead tetraacetate oxidized benzyl group of the product **2g** (entry 7).[13] Entry 8 shows that an α-acetoxy ketone having

Table 1. α-Acetoxy Ketones from α,β-Epoxy Sulfoxides with Cesium Acetate

Entry	α,β-Epoxy sulfoxide (1)				Conditions	α-Acetoxy ketone		Yield[a] %
	R^1	R^2	R^3					
1	**1a** C_2H_5	$CH_3(CH_2)_4$	H	L	100 °C, 45 min		**2a**	84
				P	100 °C, 45 min			73
2	**1b** $CH_3(CH_2)_5$	CH_3	H	L	100 °C, 45 min		**2b**	65
				P	100 °C, 45 min			71
3	**1c** $CH_3(CH_2)_5$	$CH_3(CH_2)_4$	H	L	100 °C, 1 h		**2c**	64
				P	100 °C, 1 h			78
4	**1d** $(CH_3)_2CH$	$CH_3(CH_2)_4$	H	L	100 °C, 1 h		**2d**	78
				P	100 °C, 2 h			74
5	**1e** $CH_3(CH_2)_5$	CH_3	CH_3		100 °C, 9 h		**2e**	48
6	**1f** 	$CH_3(CH_2)_4$	H	L	100 °C, 2 h		**2f**	81
				P	100 °C, 5 h			70
7	**1g** $PhCH_2$	CH_3	H	L	70 °C, 1.5 h		**2g**	48
				P	70 °C, 45 min			29
8	**1h** $CH_3(CH_2)_5$	Ph	H	P	70 °C, 1.5 h		**2h** + **2i**	70[b]

a) Isolated yields after silica-gel column chromatography. b) The yield of a mixture of **2h** and **2i**. The ratio of **2h** : **2i** is 5 : 4, which was determined by ^{1}H-NMR.

highly acidic hydrogens (**2h**) afforded **2i** through acyl migration.

Experimental

General. Infrared (IR) spectra were measured directly on a NaCl plate with a Hitachi 215 spectrometer. ^{1}H NMR spectra were measured in a $CDCl_3$ solution with a JEOL-FX-100 pulse Fourier-transform spectrometer using Me_4Si as an internal standard. All α,β-epoxy sulfoxides (**1**) used in this study are given in Refs. 9b and 11.

Treatment of 1g with Alkaline Hydrogen Peroxide. To a solution of **1g** (54 mg) in MeOH (3 ml) was added 10% KOH (1 ml) and 40% H_2O_2 (0.2 ml) and the solution was stirred at room temperature for 4 d. The MeOH was evaporated and the residue was extracted with benzene. The water layer was acidified and extracted with benzene. The usual work-up gave 14.2 mg (58%) of benzoic acid as colorless crystals.

1-Phenyl-3-phenylsulfinyl-2-butanone (3). A solution of $Mg(OMe)_2$ was prepared from dry MeOH (2 ml) and Mg (24.3 mg; 1 mmol) in a dry flask. To this was added a solution of **1g** (54.4 mg; 0.2 mmol) in MeOH; then the reaction mixture was refluxed under N_2 for 2 h. After the usual work-up, the product was purified by silica-gel column chromatography to afford 34 mg (63%) of **3** (diastereomeric mixture) as colorless oil. IR (neat): 1710 (CO), 1045 (SO) cm^{-1}; ^{1}H NMR δ=1.20, 1.34 (each d, J=7 Hz), 3.68—4.20 (m), 7.00—7.74 (m); MS m/z (%): 272 (M^+, trace), 147 (75), 125 (30), 91 (100); Found: m/z 272.0881. Calcd for $C_{16}H_{16}O_2S$: M, 272.0870.

4-Methoxy-3-nonanone (4). A solution of **1a** (53 mg; 0.2 mmol) in MeOH (1 ml) was added to a solution of $TsOH \cdot H_2O$ (190 mg; 1 mmol) in MeOH (1 ml) and the reaction mixture was refluxed under N_2 for 20 h. The MeOH was evaporated and the residue was extracted with benzene. After the usual work-up, the product was purified by silica-gel chromatography to give 9.4 mg (27%) of **4** as colorless oil. IR (neat): 1720 (CO) cm^{-1}; ^{1}H NMR δ=0.88 (3H, t, J=7 Hz), 1.07 (3H, t, J=7 Hz), 1.16—1.78 (8H, m), 2.56 (2H, q, J=7 Hz), 3.38 (3H, s), 3.62 (1H, t, J=6 Hz); MS m/z (%): 172 (M^+, 8), 115 (100).

General Procedure for the Preparation of α-Acetoxy Ketones (2) from α,β-Epoxy Sulfoxides (1). A typical procedure is described for the synthesis of 4-acetoxy-3-nonanone (**2a**). A solution of 3,4-epoxy-3-phenylsulfinylnonane (**1a**; 270 mg; 1 mmol) in DMSO (2.5 ml) was added to a mixture of CeOAc (1.92 g; 10 mmol) and $Pb(OAc)_4$ (985 mg; 2 mmol) in DMSO (2.5 ml). The reaction mixture was stirred at 100 °C under N_2 for 45 min. To the reaction mixture was added 10 ml of 10%-HCl and the whole was extracted with ether. Then the ether layer was washed with sat. aq $NaHCO_3$ followed by brine. The product was purified by silica-gel column chromatography to afford 170.7 mg (84%) of **2a** as a colorless oil. IR (neat): 1745, 1730 (CO) cm^{-1}; ^{1}H NMR δ=0.90 (3H, t, J=7 Hz), 1.08 (3H, t, J=7 Hz), 1.18—1.92 (8H, m), 2.18 (3H, s), 2.50 (2H, m), 5.04

(1H, dd, J=5, 6 Hz); MS m/z (%): 200 (M^+, trace), 157 (3), 130 (5), 83 (6), 43 (100).

2-Acetoxy-3-nonanone (2b). Colorless oil; IR (neat): 1745, 1730 (CO) cm^{-1}; ^1H NMR δ=0.89 (3H, t, J=7 Hz), 1.00—1.72 (8H, m), 1.40 (3H, d, J=7 Hz), 2.15 (3H, s), 2.50 (2H, m), 5.11 (1H, q, J=7 Hz); MS m/z (%): 200 (M^+, trace), 113 (80), 87 (17), 43 (100).

6-Acetoxy-7-tridecanone (2c). Colorless oil; IR (neat): 1745, 1730 (CO) cm^{-1}; ^1H NMR δ=0.89 (6H, t, J=6 Hz), 1.08—1.90 (16H, m), 2.16 (3H, s), 2.46 (2H, m), 5.05 (1H, dd, J=5, 7 Hz); MS m/z (%): 256 (M^+, trace), 113 (78), 85 (10), 43 (100); Found: m/z 256.2033. Calcd for $C_{15}H_{28}O_3$: M, 256.2036.

4-Acetoxy-2-methyl-3-nonanone (2d). Colorless oil; IR (neat): 1745, 1730 (CO) cm^{-1}; ^1H NMR δ=0.90 (3H, t, J=7 Hz), 1.00—1.90 (8H, m), 1.10, 1.16 (each 3H, d, J=8 Hz), 2.15 (3H, s), 2.60—3.00 (1H, m), 5.15 (1H, dd, J=5, 7 Hz); MS m/z (%): 214 (M^+, 1), 171 (4), 71 (45), 43 (100).

2-Acetoxy-2-methyl-3-nonanone (2e). Colorless oil; IR (neat): 1735, 1720 (CO) cm^{-1}; ^1H NMR δ=0.89 (3H t, J=6 Hz), 1.08—1.76 (8H, m), 1.48 (6H, s), 2.09 (3H, s), 2.46 (2H, t, J=7 Hz); MS m/z (%): 214 (M^+, 1), 171 (11), 113 (65), 85 (11), 43 (100).

2-Acetoxy-1-cyclohexyl-1-heptanone (2f). Colorless oil; IR (neat): 1750, 1730 (CO) cm^{-1}; ^1H NMR δ=0.90 (3H, t, J=6 Hz), 1.00—2.08 (18H, m), 2.15 (3H, s), 2.20—2.72 (1H, m), 5.14 (1H, dd, J=5, 7 Hz); MS m/z (%): 254 (M^+, 1), 184 (5), 111 (60), 83 (100), 43 (70); Found: m/z 254.1872. Calcd for $C_{15}H_{26}O_3$: M, 254.1880.

3-Acetoxy-1-phenyl-2-butanone (2g). Colorless oil; IR (neat): 1740, 1725 (CO) cm^{-1}; ^1H NMR δ=1.28 (3H, d, J=7 Hz), 2.14 (3H, s), 3.84 (2H, s), 5.20 (1H, q, J=7 Hz), 7.08—7.52 (5H, m); MS m/z (%): 206 (M^+, 3), 91 (48), 87 (18), 43 (100).

A Mixture of 1-Acetoxy-1-phenyl-2-octanone (2h) and 2-Acetoxy-1-phenyl-1-octanone (2i). Colorless oil; IR (neat): 1745, 1730 (CO) cm^{-1}; ^1H NMR δ=0.84 (t, J=7 Hz), 0.88 (t, J=6 Hz), 1.00—2.00 (m), 2.18, 2.20 (each s), 2.24—2.56 (m), 5.90 (dd, J=6, 7 Hz), 6.00 (s), 7.12—7.72 (m); MS m/z (%): 262 (M^+, 1), 149 (40), 113 (35), 107 (61), 105 (92), 43 (100).

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