One-Pot Preparation of 1-Acyl-1-methoxycarbonyloxiranes and 1-Acyl-1-cyanooxiranes from Methyl 3-Hydroxy-2-methylenealkanoates or 3-Aryl-3-hydroxy-2-methylenepropanenitriles

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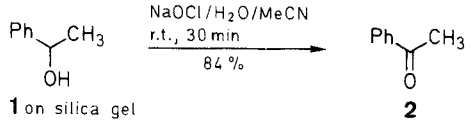
The reaction of sodium hypochlorite with methyl 3-hydroxy-2-methylenealkanoates or 3-aryl-3-hydroxy-2-methylenepropanenitriles, dispersed on silica gel, in acetonitrile leads to oxidation of the alcohol function and epoxidation of the methylene group to give 2,2-disubstituted oxiranes in good yield.

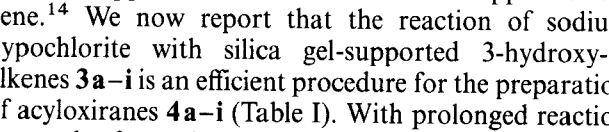
The oxidation of alcohols to carbonyl compounds is still the subject of many investigations. A large number of reagents such as chromium(VI) ion,[1,2,3] manganese(IV) oxide,[4] potassium permanganate adsorbed on a solid support[5] or with triethylamine,[6] sodium hypochlorite in the presence of acetic acid[9,10] using a phase-transfer catalyst[8] or micellar media[12] have been used. Benzyl alcohols are oxidized by inorganic hypochlorites.[7,13] Calcium hypochlorite oxidizes secondary alcohols to ketones in the presence of acetic acid.[11]

We have found that oxidation of 1-phenylethanol (**1**) to acetophenone (**2**) proceeds smoothly when a concentrated aqueous sodium hypochlorite solution is added to the alumina- or silica gel-supported alcohol in acetonitrile.

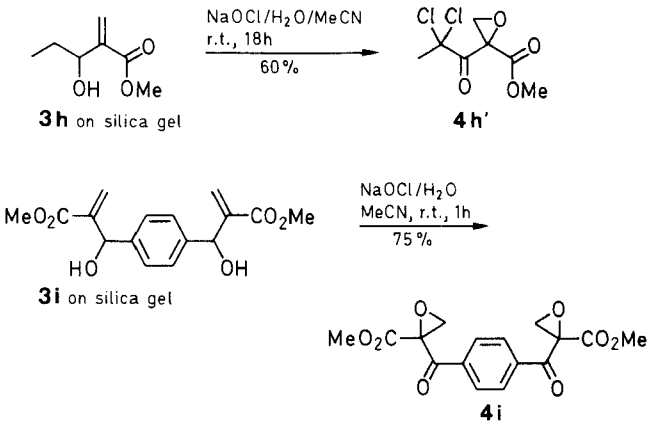


Silica gel or alumina is essential for efficient oxidation (2% yield of **2** after 30 min without silica gel or alumina). The reaction using silica gel (84% yield of **2** after 30 min) is faster than that using alumina (44% yield of **2** after 30 min).

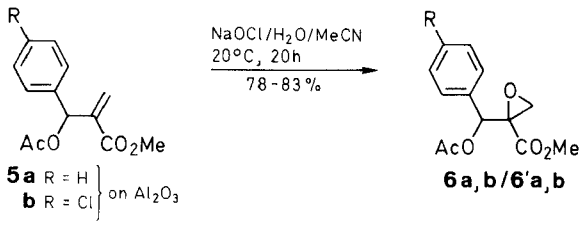
It is known that epoxidation of electrophilic alkenes proceeds well when sodium hypochlorite is added to the alumina-supported or montmorillonite-supported alkene.[14] We now report that the reaction of sodium hypochlorite with silica gel-supported 3-hydroxy-1-alkenes **3a–i** is an efficient procedure for the preparation of acyloxiranes **4a–i** (Table I). With prolonged reaction times, the formation of benzoic acids, (from **3a–g**) is observed. In the case of **3h**, the initial transformation of alcohol to ketone is followed by fast halogenation at C-4 (haloform reaction) and epoxidation to give 2-(2,2-dichloropropanoyl)-2-methoxycarbonyloxirane (**4h'**).



3, 4	R^1	R^2	3, 4	R^1	R^2
a	CO_2Me	H	e	CO_2Me	Me
b	CO_2Me	Cl	f	CN	H
c	CO_2Me	NO_2	g	CN	Cl
d	CO_2Me	OMe			



The procedure is also applicable to the epoxidation of methyl 3-acetoxy-2-methylene-3-phenylpropanoates **5a** and **5b**. However, in these cases the reaction is faster with alumina than with silica gel.



Compounds **5a** and **5b** are converted into mixtures of diastereoisomers **6a/6'a** (83:17) and **6b/6'b** (74:26), respectively.

Although the oxidation of alcohols is promoted by silica gel and epoxidation is easier with alumina, the best support for the preparation of **4** from **3** is silica gel.

The present method is simple, it uses easily available reagents and affords good yields, and it avoids the necessity to prepare the α-methylene-β-oxo esters, which are not easy to obtain.

Compounds **3a**,[18] **3d**,[18] **3f**,[17] **5a**,[18] and the new alkenes **3b,c,e,g–i** and **5b** are prepared according to literature methods[15–18] (Table 1).

Oxidation of 1-Phenylethanol (1) to Acetophenone (2):
To a stirred solution of 1-phenylethanol (0.61 g, 5 mmol) in MeCN (5 mL) is added silica gel (5 g, 230–400 mesh). The mixture is treated with 2 M aq NaOCl (6.5 mL) for 30 min at r.t. and then extracted with Et_2O (2 × 10 mL). The organic layer is dried (Na_2SO_4) and evaporated under reduced pressure. The residue is analyzed by ^{1}H-NMR and shown to be 97% pure acetophenone; yield: 0.50 g (84%).

2-Acyl-2-methoxycarbonyloxiranes 4a–i; General Procedure:
To a stirred solution of hydroxy ester **3a–i** (5 mmol) in MeCN (5 mL) is added silica gel (5 g). The mixture is treated with 2 M aq

Table 1. 2-Alkenoic Esters and 2-Alkenenitriles Prepared

Product	Reaction Time[a] (h)	Yield (%)	Molecular Formula[b]	mp (°C) (solvent) or bp (°C)/mbar	^{1}H-NMR ($CDCl_3$/TMS)[d] δ, J(Hz)
3b	72	95	$C_{11}H_{11}ClO_3$ (226.5)	42 (Et_2O)	3.72 (s, 1H), 3.77 (s, 3H), 5.65 (s, 1H), 5.90 (s, 1H), 6.45 (s, 1H), 7.30 (m, 4H)
3c	18	95	$C_{11}H_{11}NO_5$ (237.1)	74 (Et_2O)	3.60 (s, 1H), 3.71 (s, 3H), 5.62 (s, 1H), 5.85 (s, 1H), 6.37 (s, 1H), 8.1–7.5 (m, 4H)
3e	720	95	$C_{12}H_{14}O_3$ (206.1)	95–100/0.015 34 (hexane)	2.26 (s, 3H), 3.15 (s, 1H), 3.62 (s, 3H), 5.47 (s, 1H), 5.80 (s, 1H), 6.26 (s, 1H), 7.0–7.3 (m, 4H)
3g	100	91	$C_{10}H_8ClNO$ (193.5)	52 (hexane)	3.70 (s, 1H), 5.17 (s, 1H), 5.92 (d, 1H, J = 2), 6.00 (d, 1H, J = 2), 7.25 (m, 4H)
3h	108	50	[c]	oil	0.95 (t, 3H, J = 6), 1.62 (m, 2H), 3.75 (s, 3H), 3.95 (s, 1H), 4.41 (t, 1H, J = 5), 5.86 (d, 1H, J = 1.6), 6.22 (d, 1H, J = 1.6)
3i	360	95	$C_{16}H_{18}O_6$ (306.1)	101 (Et_2O)	3.55 (s, 2H), 3.62 (s, 6H), 5.45 (s, 2H), 5.82 (s, 2H), 6.25 (s, 2H), 7.24 (s, 4H)
5b		96	[c]	oil	2.05 (s, 3H), 3.70 (s, 3H), 5.90 (s, 1H), 6.40 (s, 1H), 6.65 (s, 1H), 7.20 (s, 4H)

[a] Time of the reaction of aldehyde with methyl acrylate[15,16] or acrylonitrile[17] in the presence of diazabicyclooctane to give **3**.
[b] Satisfactory microanalyses: C ±0.21, H ±0.25, N ±0.10, Cl ±0.17.
[c] Used without purification.
[d] Recorded on a Bruker WP 80 Spectrometer.

Table 2. Oxiranes **4** and **6** Prepared

Product	Reaction Time (h)	Yield[a] (%)	mp (°C) (solvent) or bp (°C)/mbar	Molecular Formula[b]	HRMS (70 eV)[c] m/z found (calc.)	^{1}H-NMR ($CDCl_3$/TMS)[d] δ, J(Hz)
4a	1.25	92	100/0.02	$C_{11}H_{10}O_4$ (206.1)		3.20, 3.40 (AB, 2H, J = 8), 3.75 (s, 3H), 7.55 (m, 3H), 7.99 (m, 2H)
4b	2	83	102/0.01	$C_{11}H_9ClO_4$ (240.5)		3.19, 3.39 (AB, 2H, J = 7), 3.75 (s, 3H), 7.4–8.0 (m, 4H)
4c	3	60	160–163/0.015 79 (MeOH)	$C_{11}H_9NO_6$ (251.1)		3.21–3.43 (AB, 2H, J = 8), 3.77 (s, 3H), 8.25 (m, 4H)
4d	1.5	85	170/0.02	$C_{12}H_{12}O_5$ (236.1)	236.0688 (236.0685)	3.16–3.36 (AB, 2H, J = 6.4), 3.75 (s, 3H), 3.85 (s, 3H), 6.87–8.02 (m, 4H)
4e	1.5	85	150/0.02	$C_{12}H_{12}O_4$ (220.1)	220.0743 (220.0735)	2.37 (s, 3H), 3.16, 3.34 (AB, 2H, J = 6.4), 3.72 (s, 3H), 7.20–7.92 (m, 4H)
4f	3	66	95–100/0.25	$C_{10}H_7NO_2$ (173.1)	173.0471 (173.0476)	3.26, 3.55 (AB, 2H, J = 7), 7.60 (m, 3H), 8.04 (m, 2H)
4g	4	98	oil[e]	$C_{10}H_6ClNO_2$ (207.5)		3.16, 3.56 (AB, 2H, J = 5.6), 7.43–8.05 (m, 4H)
4h'	18	60	85–87/0.01	$C_7H_8Cl_2O_4$ (227.0)	225.9802 (225.9800)	2.25 (s, 3H), 3.23, 3.43 (AB, 2H, J = 6), 3.82 (s, 3H)
4i	1	75	131 (CH_2Cl_2)[f]	$C_{16}H_{14}O_8$ (334.1)		3.18, 3.41 (AB, 2H, J = 6), 3.75 (s, 6H), 8.07 (s, 4H)
6a/6'a	20	83[g]	100–102/0.01	$C_{13}H_{14}O_5$ (250.1)	250.0840 (250.0841)	*Isomer* **6a**: 2.02 (s, 3H), 2.40, 2.95 (AB, 2H, J = 6), 3.77 (s, 3H), 6.55 (s, 1H), 7.30 (s, 5H) *Isomer* **6'a**: 2.02 (s, 3H), 3.04, 3.08 (AB, 2H, J = 6), 3.69 (s, 3H), 6.56 (s, 1H), 7.30 (s, 5H)
6b/6'b	20	78	130/0.01	$C_{13}H_{13}ClO_5$ (284.55)	224.0245[h] (224.0240)	*Isomer* **6b**: 2.07 (s, 3H), 2.38, 2.95 (AB, 2H, J = 6), 3.75 (s, 3H), 6.45 (s, 1H), 7.30 (s, 4H) *Isomer* **6'b**: 1.97 (s, 3H), 3.05 (s, 2H), 3.67 (s, 3H), 6.50 (s, 1H), 7.30 (s, 4H)

[a] Yield of isolated product, based on **3** or **5**.
[b] Satisfactory microanalyses: C ±0.49, H ±0.40, N ±0.37.
[c] Measured with a Varian MAT 311 instrument.
[d] Measured using a Bruker WP 80 Spectrometer.
[e] The crude product is purified by chromatography on silica gel eluting with Et_2O/CH_2Cl_2 2:10.
[f] Major diastereoisomer isolated.
[g] 43% Yield with silica gel as support.
[h] $(M - CH_3CO_2H)^+$, calc. for ^{35}Cl.

NaOCl (12.5 mL). After the time indicated in Table 2, the mixture is extracted with Et_2O (2 × 10 mL). The organic layer is dried (Na_2SO_4) and evaporated. The residue is purified by Kugelrohr distillation or recrystallization.

2-Benzoyl-2-methoxycarbonyloxirane **(4a):**

^{13}C-NMR ($CDCl_3$/TMS): δ = 51.3 (s), 53.3 (q, ^1J = 149 Hz), 59.0 (t, ^1J = 185 Hz), 127.2 (s), 129.0 (d, ^1J = 163 Hz), 129.3 (d, ^1J = 163 Hz), 134.4 (d, ^1J = 162 Hz), 167.8 (s), 190.7 (s).

2-(α-Acetoxybenzyl)-2-methoxycarbonyloxirane (6a/6'a) and 2-(α-Acetoxy-4-chlorobenzyl)-2-methoxycarbonyloxirane (6b/6'b):

To a stirred solution of the acetoxy ester **5a** or **5b** (5 mmol) are added alumina (5 g) and 2 M aq NaOCl (12.5 mL). The mixture is stirred at 20 °C for 20 h, then extracted with Et_2O (2 × 10 mL). The solvent is removed and the residue is purified by Kugelrohr distillation to give the product oxirane as a mixture of diastereoisomers **6a/6'a** or **6b/6'b**, respectively.

2-(α-Acetoxybenzyl)-2-methoxycarbonyloxirane **(6a/6'a)**:

^{13}C-NMR ($CDCl_3$/TMS): δ of diastereoisomer **6a**: 20.86 (q, ^1J = 130 Hz), 49.17 (t, ^1J = 180 Hz), 52.81 (q, ^1J = 148 Hz), 57.57 (s), 72.61 (d, J = 150 Hz), 128.07 (d), 128.40 (d), 128.8 (d), 134.4 (s), 168.7 (s), 169.4 (s), δ of diastereoisomer **6'a**: 20.80 (q, ^1J = 130 Hz), 49.70 (t, ^1J = 180 Hz), 52.68 (q, ^1J = 150 Hz), 58.44 (s), 70.78 (d, ^1J = 150 Hz), 128.07 (d), 128.5 (d), 128.8 (d), 135.6 (s), 168.5 (s), 169.3 (s).

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