

Pyridinium Fluorochromate or Benzyltrimethylammonium Chlorochromate for Selective Oxidation of Alcohols

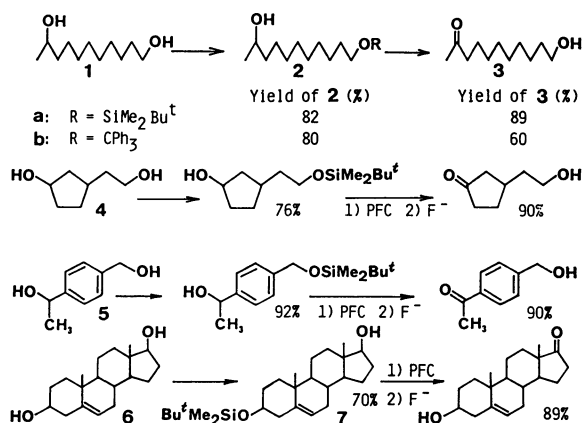
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Synopsis. Selective oxidation of secondary alcohols in the presence of primary ones has been achieved by the following sequences, (1) selective protection of primary alcohols with *t*-BuMe₂SiCl, (2) oxidation of secondary alcohols with title reagents, and (3) deprotection of primary hydroxyls.

The reagents containing the chromium(VI) as a key atom are most commonly used for the oxidation of alcohols to carbonyl compounds because of their ready accessibility and operational simplicity.¹⁾ A large number of them, however, cannot be applied to modern organic synthesis and there still exists a need for new methods for the oxidation of complex or highly sensitive substrates. Here we wish to describe the preparation and reaction of several chromium(VI) reagents which oxidize alcohols under slightly acidic or neutral conditions.

Among many reagents examined, only pyridinium fluorochromate (PFC)²⁾ was as reactive as pyridinium chlorochromate (PCC) and oxidation took place at 25 °C. The reaction with benzyltrimethylammonium chlorochromate (BTMACC) proceeded very sluggishly at 25 °C and the completion of oxidation required heating at 80 °C in 1,2-dichloroethane. Tetrabutylammonium chlorochromate (TBACC) was marginal and tetramethylammonium chlorochromate, tetramethylammonium fluorochromate, and tetrabutylammonium fluorochromate were inert for the oxidation of alcohols. The results of representative experiments by means of PFC together with those by BTMACC and TBACC are summarized in Table 1.

It is worth noting that PFC is less acidic than PCC, thus even such acid-labile compounds as SiMe₂Bu^t ethers or trityl ethers survive without buffering the reaction mixture with bases. Combination of this oxidation procedure with selective protection of primary hydroxyl groups provides us with a simple route to the selective oxidation of primary, secondary diols at the secondary positions.³⁾



Treatment of 1,10-undecanediol with Bu^tMe₂SiCl and Et₃N in the presence of a catalytic amount of 4-dimethylaminopyridine gave monosilyl ether **2a** in 82% yield. Similarly, the diols **4** and **5** could be transformed into their monoethers. Oxidation of monosilyl ether **2a** with PFC or BTMACC followed by desilylation (Bu^tNF) provided 11-hydroxy-2-undecanone (**3**) in 89% or 90%, respectively. In contrast, the reaction of **2a** with PCC gave *t*-butyldimethylsilyl ether of keto alcohol (**3**) (68%) along with 10-oxoundecanal (20%). Trityl ether **2b** was also converted into the ketone **3** with PFC followed by deprotection (*p*-TsOH).⁴⁾ As exemplified below, the selective oxidation of secondary, secondary

TABLE 1. OXIDATION OF ALCOHOLS WITH PFC, BTMACC, OR TBACC

Alcohol	Oxidant	Conditions		Yield/% ^{a)} of carbonyl compound
		Temp °C	Time h	
4- <i>t</i> -Butylcyclohexanol	PFC ^{b)}	25	6	92
Cyclododecanol	PFC	25	6	93
	BTMACC ^{c)}	80	10	97
	TBACC ^{c)}	80	30	68
PhCH(OH)Me	PFC	25	6	88
4-Dodecanol	PFC	25	8	96
1-Dodecanol	PFC	25	6	78
	BTMACC	80	10	92
	TBACC	80	30	58
Carveol	PFC	25	2	96
	BTMACC	80	4	87
	TBACC	80	2	72
Geraniol	PFC	25	2	80 ^{d)}
	BTMACC	80	6	83 ^{e)}
	TBACC	80	3	58 ^{f)}
Nerol	PFC	25	2	82 ^{g)}
Borneol	PFC	25	8	77
3β-Cholesterol	PFC	25	6	96
	BTMACC	80	10	98
<i>p</i> -Bromobenzyl alcohol	PFC	25	2	97
1-Menthol	PFC	25	6	92
2-Cyclododecen-1-ol	PFC	25	4	87
THP ether	PFC	25	4	78 ^{h)}

a) Yields represent isolated purified products. b) 2 mmol of alcohols and 4 mmol of PFC were employed. c) 2 mmol of alcohols and 6 mmol of BTMACC or TBACC were employed. d) A mixture of *cis* and *trans* citral was obtained. The ratio of *cis*:*trans* was 15:85. e) *cis*:*trans* = 29:71. f) *cis*:*trans* = 13:87. g) *cis*:*trans* = 68:32. h) THP ether remained untouched.

diol, 5-androstene-3 β ,17 β -diol to the 17-keto steroid, has been also achieved.

Experimental

Distillation was carried out in Kugelrohr (Büchi) and boiling points were determined by measuring the bath temperature. All mp and bp are not corrected. All ^1H -NMR spectra (tetramethylsilane as an internal standard) were obtained in ppm units. The IR spectra of neat liquid film samples were measured on a Shimadzu IR-27 or Hitachi IR-215 spectrometer. Microanalysis was performed at the Elemental Analyses Center of Kyoto University. Preparative TLC plates were prepared with Merck Kiesel-gel PF₂₅₄. Column chromatography was carried out with silica gel (Wakogel C-200) at atmospheric pressure.

Preparation of Benzyltrimethylammonium Chlorochromate (BTMACC). Anhydrous chromium trioxide (5.0 g, 50 mmol) was dissolved in 6 M[†] HCl (9.0 ml, 55 mmol) at 0 °C. After stirring for 5 min, a solution of benzyltrimethylammonium hydroxide (40% in H₂O, 23 g, 55 mmol) was carefully added over 10 min to give an orange solid which was collected, washed, and dried for 5 h *in vacuo* (yield 13.1 g, 96%, mp 85 °C (decomp)). Found: C, 41.69; H, 5.43; N, 4.80%. Calcd for C₁₀H₁₆ClNO₃Cr: C, 42.11; H, 5.61; N, 4.91%. Other chromium(VI) reagents were prepared in a similar fashion.

Oxidation of 4-*t*-Butylcyclohexanol to 4-*t*-Butylcyclohexanone. A Typical Procedure for the Oxidation of Alcohols with PFC, BTMACC, or TBACC: A solution of 4-*t*-butylcyclohexanol (0.31 g, 2.0 mmol) in CH₂Cl₂ (2.0 ml) was added in one portion to the CH₂Cl₂ (8.0 ml) suspension of PFC (0.80 g, 4.0 mmol). After stirring for 6 h at 25 °C, the resulting mixture was diluted with ether (20 ml) and the supernatant was decanted. The residue was washed twice with 10 ml portions of ether. The combined organic solution was washed with NaHSO₃ and brine. Purification by silica gel column chromatography gave 4-*t*-butylcyclohexanone (0.28 g) in 92% yield.

General Procedure for the Preparation of Mono Ethers. According to the reported method,⁵ diols **1**, **4**, and **5** were transformed into their monosilyl ethers on treatment with Bu[†]Me₂SiCl and Et₃N in the presence of 4-dimethylaminopyridine. Similarly, trityl ether **2b** was prepared from diol **1** and Ph₃CCl instead of Bu[†]Me₂SiCl.⁶

11-(*t*-Butyldimethylsiloxy)-2-undecanone. A dichloromethane solution of 11-(*t*-butyldimethylsiloxy)-2-undecanol (0.6 g, 2.0 mmol) was combined with PFC (0.8 g, 4.0 mmol) and the whole was stirred for 3 h at 25 °C. Workup (Et₂O, NaHSO₃) and purification by preparative TLC gave the title compound (0.53 g, 89% yield) as an oil: Bp 116–118 °C (bath temp, 1 Torr^{††}); IR (neat) 2890, 2820, 1705, 1250, 1090, 830 cm⁻¹; NMR (CDCl₃) δ 0.03 (s, 6H), 0.91 (s, 9H), 1.2–1.4 (m, 10H), 1.4–1.6 (m, 4H), 2.13 (s, 3H), 2.40 (t, $J=7.4$ Hz, 2H), 3.57 (t, $J=6.5$ Hz, 2H). Found: C, 67.78; H, 12.32%. Calcd for C₁₇H₃₆O₂Si: C, 67.94; H, 12.07%.

11-Hydroxy-2-undecanone (3). A THF solution of siloxyl ketone (0.30 g, 1.0 mmol) was treated with Bu[†]NF

(1.0 M THF solution, 1.1 ml) for 30 min at 25 °C to give the hydroxy ketone (0.30 g) quantitatively: Mp 42–43 °C; IR (neat) 3424, 1709, 1358, 1042 cm⁻¹; NMR (CCl₄) δ 1.1–1.8 (m, 14H), 2.09 (s, 3H), 2.36 (t, $J=6.6$ Hz, 2H), 3.58 (t, $J=6.8$ Hz, 2H), 3.78 (b, 1H). Found: C, 70.65; H, 11.90%. Calcd for C₁₁H₂₂O₂: C, 70.92; H, 11.90%.

3-[2-(*t*-Butyldimethylsiloxy)ethyl]cyclopentanone: Bp 137 °C (bath temp, 1 Torr); IR (neat) 1730, 1250, 1100, 830, 770 cm⁻¹; NMR (CDCl₃) δ 0.03 (s, 6H), 0.85 (s, 9H), 1.2–2.5 (m, 11H), 3.62 (t, $J=5.8$ Hz, 2H). Found: C, 64.51; H, 10.96%. Calcd for C₁₃H₂₆O₂Si: C, 64.46; H, 10.74%.

p-[(*t*-Butyldimethylsiloxy)methyl]phenyl Methyl Ketone: Bp 103 °C (bath temp, 1 Torr); IR (neat) 2900, 1670, 1600, 1266, 1092 cm⁻¹; NMR (CDCl₃) δ 0.05 (s, 6H), 0.85 (s, 9H), 2.44 (s, 3H), 4.64 (s, 2H), 7.2–7.9 (m, 4H). Found: C, 68.10; H, 9.35%. Calcd for C₁₅H₂₄O₂Si: C, 68.18; H, 9.09%.

Conversion of 5-Androstene-3 β ,17 β -diol (6) to 3 β -Hydroxy-5-androsten-17-one. Following the Hosoda's procedure,⁷ diol **6** was converted into monosilyl ether **7** in 70% yield. This compound (0.20 g, 0.5 mmol) was treated successively with PFC (0.20 g, 1.0 mmol) and Bu[†]NF (5.5 mmol) to give 17-keto steroid (0.13 g, 89% yield) which was identical with an authentic sample.

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[†] 1 M=1 mol dm⁻³.

^{††} 1 Torr=133.322 Pa.