July, 1984] © *1984 The Chemical Society of Japan* NOTES *Bull. Chem. Soc. Jpn., 57, 2019—2020 (1984)* 2019

Pyridinium Fluorochromate or Benzyltrimethylammonium Chlorochromate for Selective Oxidation of Alcohols

Tsuyoshi Nonaka, Shigekazu Kanemoto, Koichiro Oshima,* and Hitosi Nozaki
Department of Industrial Chemistry, Faculty of Engineering, Kyoto University, Yoshida, Kyoto 606

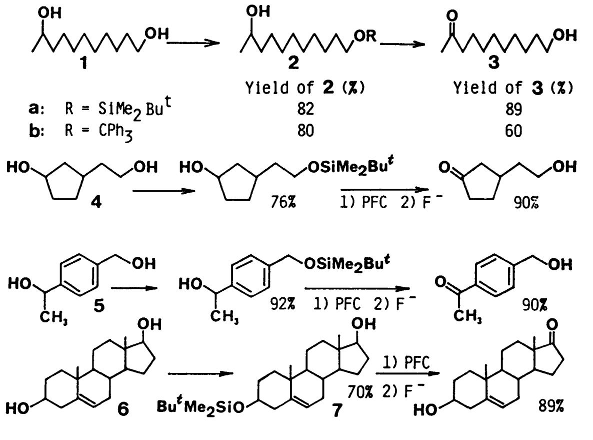
(Received January 20, 1984)

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-BuMe$_2$SiCl, (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.

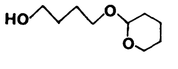
Among many reagents examined, only pyridinium fluorochromate (PFC)[2] was as reactive as pyridinium chlorochromate (PCC) and oxidation took place at 25 °C. The reaction with benzyltrimethylammonium chlorochromate (BTMACC) proceeded very sluggishly at 25 °C and the completion of oxidation required heating 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 SiMe$_2$Bu^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^{t}Me$_2$SiCl and Et$_3$N 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$^n_4$NF) 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 Temp °C	Conditions Time h	Yield/%[a] of carbonyl compound
4-t-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-Cholestanol	PFC	25	6	96
	BTMACC	80	10	98
p-Bromobenzyl alcohol	PFC	25	2	97
1-Menthol	PFC	25	6	92
2-Cyclododecen-1-ol	PFC	25	4	87
	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-3β,17β-diol to the 17-keto steroid, has been also achieved.

Experimental

Distillation was carried out in Kugelrohr (Büchi) and boiling points were determined by mesuring the bath temperature. All mp and bp are not corrected. All ^{1}H-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 PF$_{254}$. 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 H_2O, 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 $C_{10}H_{16}ClNO_3Cr$: 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 CH_2Cl_2 (2.0 ml) was added in one portion to the CH_2Cl_2 (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 $NaHSO_3$ 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^{t}Me$_2$SiCl and Et_3N in the presence of 4-dimethylaminopyridine. Similarly, trityl ether **2b** was prepared from diol **1** and Ph_3CCl instead of Bu^{t}Me$_2$SiCl.[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 (Et_2O, $NaHSO_3$) 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 ($CDCl_3$) 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 $C_{17}H_{36}O_2Si$: 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$^n_4$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 (CCl_4) 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 $C_{11}H_{22}O_2$: 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 ($CDCl_3$) 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 $C_{13}H_{26}O_2Si$: 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 ($CDCl_3$) 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 $C_{15}H_{24}O_2Si$: C, 68.18; H. 9.09%.

Conversion of 5-Androstene-3β,17β-diol (6) to 3β-Hydroxy-5-androsten-17-one. Following the Hosoda's prodcedure,[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$^n_4$NF (5.5 mmol) to give 17-keto steroid (0.13 g, 89% yield) which was identifical with an authentic sample.

Financial supports by the Asahi Glass Foundation for Industrial Technology and a Grant-in-Aid for Scientific Research No. 58550566 from the Ministry of Education, Science and Culture is acknowledged.

References

1) CrO_3·2py: J. C. Collins, W. W. Hess, and F. J. Frank, *Tetrahedron Lett.*, **1968**, 3363; R. Ratcliffe and R. Rodehorst, *J. Org. Chem.*, **35**, 4000, (1970); CrO_2Cl_2: K. B. Sharpless and K. Akashi, *J. Am. Chem. Soc.*, **97**, 5927 (1975); PCC: E. J. Corey and J. W. Suggs, *Tetrahedron Lett.*, **1975**, 2647; PDC: E. J. Corey and G. Schmidt, *ibid.*, **1979**, 399: PDC–$Me_3SiOOSiMe_3$: S. Kanemoto, K. Oshima, S. Matsubara, K. Takai, and H. Nozaki, *ibid.*, **24**, 2185 (1983).

2) PFC has been independently introduced for an efficient oxidant. Reported data have been omitted in this paper. M. N. Bhattacharjee, M. K. Chaudhuri, H. S. Dasgupta, N. Roy, and D. T. Khathing, *Synthesis*, **1982**, 588.

3) Several methods are known for the preferential oxidation of secondary over primary hydroxyls, see Y. Ueno and M. Okawara, *Tetrahedron Lett.*, **1976**, 4597; M. E. Jung and R. W. Brown, *ibid.*, **1978**, 2771; G. H. Posner, R. B. Perfetti, and A. W. Runquist, *ibid.*, **1976**, 3499; M. A. Neirabeyeh, J.-C. Ziegler, and B. Gross, *Synthesis*, **1976**, 811; H. Tomioka, K. Oshima, and H. Nozaki, *Tetrahedron Lett.*, **23**, 539 (1982).

4) Oxidation of trityl ether **2b** with PCC gave a mixture of the desired trityl ether of 11-hydroxy-2-undecanone (39%), 10-oxoundecanal (27%), and Ph_3COH (39%).

5) S. K. Chandhary and O. Hernandez, *Tetrahedron Lett.*, **1979**, 99.

6) S. Hanessian and A. P. A. Staub, *Tetrahedron Lett.*, **1973**, 3555; S. K. Chaudhary and O. Hernandez, *ibid.*, **1979**, 95.

7) H. Hosoda, D. K. Fukushima, and J. Fishman, *J, Org, Chem.*, **38**, 4209 (1973).

---

† 1 M=1 mol dm^{-3}.

†† 1 Torr=133.322 Pa.