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18-Crown-6 Complexes of *n*-Butylammonium and Pyridinium Chlorochromates. Mild and Selective Oxidizing Agents for Alcohols

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Introduction

Among the oxochromium(VI) reagents for the oxidation of organic compounds, chlorochromate−amine oxidants are the most versatile reagents.[2] Significant changes in the oxidation property of the chlorochromate ion has been brought about by varying the nature of the corresponding amine ligand. Thus, complexes of chlorochromate with various ligands such as pyridine,[3] 2,2′-bipyridine,[4] poly(vinylpyridine),[5] 4-(dimethylamino)pyridine,[6] 2-cyanopyridine,[7] pyrazine,[8] phthalazine,[8] 3,5-dimethylpyrazole,[9] trimethylamine,[10] triethylamine,[11] and tributylamine,[12] show various degrees of reactivity and selectivity toward the oxidation of organic compounds. Although no comparative studies have been carried out, it has been suggested that amine−chlorochromate complexes show a trend where the oxidizing strength of the chlorochromate ion is inversely related to the donor strength of the associated amine ligand.[13] For example, in the heterocycle chlorochromate series, 4-(dimethylamino)pyridinium chlorochromate is a milder oxidizing agent than pyridinium chlorochromate.[6] Here we report (a) the preparation and oxidation properties of a chlorochromate salt which incorporates a primary alkylamine (*n*-butylamine) as a ligand for the first time; (b) the effect of complexation of this new ligand with 18-crown-6 on the oxidation properties of the associated chlorochromate ion; and (c) the effect of complexation of pyridinium ion in pyridinium chlorochromate (PCC) with 18-crown-6 on the solubility and oxidation properties of this common oxidizing agent.[14]

Results and Discussion

n-Butylammonium chlorochromate (BACC), n-BuNH$_3^+$-ClCrO$_3^-$, **1**, was conveniently prepared from *n*-butylamine and CrO$_3$ in the presence of HCl. It is an air-stable, moderately light sensitive crystalline compound[15a] (orange plates, mp = 117−120 °C) which oxidizes primary and secondary alcohols selectively to the corresponding carbonyl compounds. The reaction times and yields for some typical alcohols listed in Table 1 indicate that **1** is an efficient oxidant for alcohols.[16] The corresponding data for oxidations with PCC are also listed in Table 1 for comparison purposes.

Like PCC, **1** does not dissolve appreciably in organic solvents such as CH$_2$Cl$_2$ and CHCl$_3$. However, in the presence of 18-crown-6 up to 3:1 molar ratio of **1**:crown ether, respectively, can be solubilized in CH$_2$Cl$_2$ or CHCl$_3$. We have isolated and characterized two stable complexes of BACC incorporating 18-crown-6 from such homogeneous solutions. A 1:1 complex, **2**, n-BuNH$_3^+$·C$_{12}$H$_{24}$O$_6$ ClCrO$_3^-$, an air-stable nonhygroscopic solid with a moderate light sensitivity,[15b] mp = 132.5−134 °C, was isolated in a quantitative yield from homogeneous CH$_2$Cl$_2$ solutions containing equimolar ratios of **1** and 18-crown-6. The NMR (^{1}H and ^{13}C) data as well as the elemental analysis were consistent with a 1:1 BACC: crown ether complex.

A 2:1 complex, **3**, [n-BuNH$_3^+$]$_2$·C$_{12}$H$_{24}$O$_6$ 2ClCrO$_3^-$ was isolated in a 90% yield from homogeneous CH$_2$Cl$_2$ solutions of **1** and 18-crown-6 in a 2:1 molar ratio, respectively. This complex was a darker orange air-stable and nonhygroscopic crystalline solid,[15b] mp = 56−58 °C, also with a moderate light sensitivity. The NMR (^{1}H and ^{13}C) data along with the elemental analysis confirmed the 2:1 stoichiometry. The same 2:1 complex could also be isolated from a homogeneous methylene chloride solution containing **1** and the crown ether in a 3:1 molar ratio, respectively.[17]

On the basis of previous works on complexation of alkyl ammonium ions with 18-crown-6,[18] we suggest the structures **2** and **3** for these complexes (Figure 1).

Compared to the oxidizing properties of **1**, the homogeneous solution of complex **2** in purified CHCl$_3$ is a more selective oxidant for alcohols. Benzylic and allylic alcohols are oxidized at a faster rate than other types of primary and secondary alcohols (Table 2 and Schemes 1 and 2).

The 2:1 complex **3**, while retaining the high selectivity of **2** toward oxidation of benzylic (allylic) alcohols, is also a more reactive oxidizing agent than **2**, as judged by the reaction times required for completion of oxidation (Table

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[1] Undergraduate Research Associates.

[2] (a) Cainelli, G.; Cardillo, G. *Chromium Oxidations in Organic Chemistry*; Springer-Verlag: Berlin, 1984. (b) Luzzio, F. A.; Guziec, F. S., Jr. *Org. Prep. Proc. Int.* **1988**, *20*, 533−584. (c) Hudlicky, M. *Oxidations in Organic Chemistry*; ACS Monograph 186, American Chemical Society: Washington, D.C., 1990.

[3] Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647.

[4] Guziec, F. S., Jr.; Luzzio, F. A. *Synthesis* **1980**, 691.

[5] Fréchet, J. M. J.; Warnock, J.; Farrall, M. J. *J. Org. Chem.* **1978**, *43*, 2618.

[6] Guziec, F. S., Jr.; Luzzio, F. A. *J. Org. Chem.* **1982**, *47*, 1787.

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[8] Bae, S. K.; Lee, S. B.; Park, D. C.; Lee, K. *Taehan Hwahakhoe Chi* **1989**, *33*, 106; *Chem. Abstr.* **1989**, *111*, 77606v.

[9] Parish, E. J.; Scott, A. D. *J. Org. Chem.* **1983**, *48*, 4766.

[10] Acharya, S. P.; Rane, R. A. *Synthesis* **1990**, 127.

[11] Rao, C. G.; Radhakrishna, A. S.; Singh, B. B.; Bhatnagar, S. P. *Synthesis* **1980**, 808.

[12] Santaniello, E.; Milani, F.; Casati, R. *Synthesis* **1983**, 749.

[13] (a) Reference 12. (b) Guerrero, A. F.; Kim, H.-J.; Schlecht, M. F. *Tetrahedron Lett.* **1988**, *29*, 6707.

[14] For a review see: Piancatelli, G.; Scettri, A.; D'auria, M. *Synthesis* **1982**, 245.

[15] (a) Crystals of **1** darken under a direct light within a few hours. Samples of **1** kept in brown jars in desiccators protected from direct light darkened only slightly over a period of six months and did not show any significant changes in their mp or the oxidizing properties. (b) Samples of **2**, **3**, and **6** kept in brown jars in desiccators protected from direct light showed only slight darkening of the color but no change in oxidizing properties over a one year period. Complex **3** appears to have a shorter shelf-life than those of **2** and **6**.

[16] We have also prepared, in 98% yield, the stable benzylammonium chlorochromate (BzACC) from benzylamine and CrO$_3$ in 6 M HCl as an orange crystalline solid, mp = 107−111 °C dec. Our initial studies indicate that benzyl alcohol is oxidized to benzaldehyde in good yield by BzACC. However, we have not pursued its oxidation or complexation properties.

[17] Homogeneous solutions prepared from BACC and 18-crown-6 in 1:1 and 2:1 molar ratios, respectively, exhibit ^{1}H- and ^{13}C-NMR characteristics identical to those prepared from the isolated complexes **2** and **3**, respectively. The homogeneous NMR solution prepared from a 3:1 molar ratio of BACC and 18-crown-6, respectively, exhibits ^{1}H- and ^{13}C-NMR chemical shifts identical to those of complex **3** except that there is a slight deshielding (δ 0.11) of α-methylene hydrogens of butyl group in the ^{1}H-NMR of 3:1 solution.

[18] deJong, F.; Reinhoudt, D. N. *Stability and Reactivity of Crown-Ether Complexes*; Academic Press: New York, **1981**; p 84.

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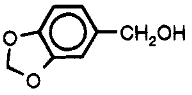
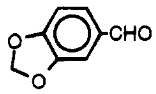
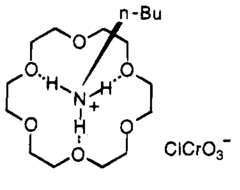
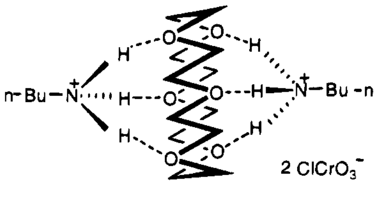
Table 1. Oxidation of Alcohols with BACC (1) and PCC in $CHCl_3$[a]

Alcohol	Product[b]	Oxidation with 1		Oxidation with PCC	
		Time[c] (h)	Yield[d] (%)	Time[c] (h)	Yield[d] (%)
$CH_3(CH_2)CH_2OH$	$CH_3(CH_2)_6CHO$	1.0	63	1.0	69
$CH_3(CH_2)_5CH(OH)CH_3$	$CH_3(CH_2)_5C(=O)CH_3$	1.17	89	1.0	95
$C_6H_5CH_2OH$	C_6H_5CHO	0.83	78	0.5	85
$C_6H_5CHOHCH_3$	$C_6H_5C(=O)CH_3$	0.5	93	0.5	86
$C_6H_5CHOHC_6H_5$	$C_6H_5C(=O)C_6H_5$	0.75	90	1.0	95
		0.75	91	0.5	91

[a] A 4:1 molar ratio of oxidant:alcohol was used. [b] Isolated and identified by NMR. [c] Determined from TLC analysis of the reaction mixture. [d] Isolated crude yields.



2



3

Figure 1.

2). The oxidation of model compounds **4** and **5** shown in Schemes 1 and 2 are especially illustrative of the selectivity of complexes **2** and **3**.

These observations led us to the question of whether or not the versatile oxidant PCC can be solubilized in CH_2Cl_2 or $CHCl_3$ in the presence of 18-crown-6 and if so can its oxidizing properties be affected as a result of possible complexation of pyridinium ligand.[19] In fact, the addition of an equimolar amount of 18-crown-6 to a slurry of PCC in purified $CHCl_3$ resulted in complete dissolution of PCC. Upon the addition of anhydrous ether to the resulting dark orange solution a stable yellow-orange solid[15b] (mp = 143.4–145 °C) was isolated which was identified as a 1:1 complex **6**, $C_6H_5NH^+{\cdot}C_{12}H_{24}O_6\ ClCrO_3^-$, on the basis of its elemental analysis and spectral data.

The results of oxidation of a series of alcohols tabulated in Table 3 indicated that the complex **6** is in fact a milder oxidizing agent than PCC. The reaction times required for complete oxidation as obtained by careful TLC studies were found to be 2–4 times longer for complex **6** than those required for PCC under similar conditions. For example, the complete oxidation of the benzylic hydroxyl group in the model compound **5** at 0 °C required 4.25 h for PCC but 6.75 h for its crown ether complex **6**. The oxidation of both hydroxyl groups in **5** at room temperature required 2.2 h for PCC but 14 h for **6**.

Finally, we have completed several representative oxidations where complexes **2**, **3** and **6** were prepared *in situ* by the addition of an appropriate molar amount of 18-crown-6 to the slurries of **1** and PCC in $CHCl_3$ and have obtained results similar to the corresponding oxidations which employed isolated complexes **2**, **3** and **6**.

In conclusion, we have prepared new chlorochromate reagents **1–3** and **6** and have shown that they selectively oxidize alcohols to their respective carbonyl compounds. Reagent **1** shows oxidation properties similar to those of PCC. Homogeneous solutions of reagents **2**, **3**, and **6** in $CHCl_3$, on the other hand, exhibit significantly milder oxidizing properties, **2** being the weakest oxidant among them. The complex **3** is an efficient oxidizing agent like PCC; however, benzylic alcohols are conveniently oxidizable with this complex selectively in the presence of other primary alcohols, a selectivity which is not observed with PCC (Scheme 2). The potential uses of these reagents in oxidation of other functional groups as well as in oxidative cationic cyclization reactions[20] remains to be explored.

Experimental Section

Liquid alcohols were either simply or fractionally distilled prior to use. 18-Crown-6, from Aldrich Chemical Co., was recrystallized from absolute ethanol. Ethanol free chloroform was prepared according to the literature procedure.[21] *n*-Butylamine was distilled from KOH pellets. Melting points were determined on a Thomas-Hoover Uni-Melt apparatus and are uncorrected. Proton and carbon NMR spectra were recorded on a JEOL FX-90Q spectrometer at 90 and 22.5 MHz, respectively. IR spectra were obtained on a Mattson Polaris FT-IR spectrometer. The preparation of the light sensitive compounds **1–3** and **6** as well as their oxidation reactions were carried out in a hood with lights turned off and in reaction flasks which were protected from direct light by a cardboard box.

***n*-Butylammonium Chlorochromate (BACC) (1).** Chromium trioxide (10.0 g, 0.100 mol) was dissolved in 6 M HCl (18.4 mL, 0.110 mol) in a 125 mL Erlenmeyer flask equipped with a magnetic stirrer. The resulting orange-red solution was cooled to ~0 °C for about 20 min. The ice bath was removed, and *n*-butylamine (7.30 g, 0.100 mol) was added dropwise to the magnetically stirred solution upon which heat was produced. The stirring was stopped, and the resulting dark red solution

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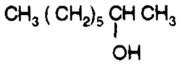
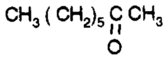
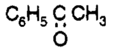
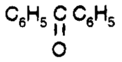
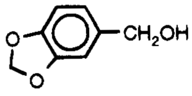
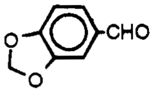
(19) The complexations of trialkylammonium and *N*-methylpyridinium salts with crown ethers have been documented: (a) Izatt, R. M.; Lamb, J. D.; Izatt, N. E.; Rossiter, B. E., Jr.; Christensen, J. J.; Haymore, B. L. *J. Am. Chem. Soc.* **1979**, *101*, 6273. (b) Delasi, G.; Masci, B. *Tetrahedron Lett.* **1993**, *34*, 6635.

(20) Corey, E. J.; Boger, D. L. *Tetrahedron Lett.* **1978**, 2461.

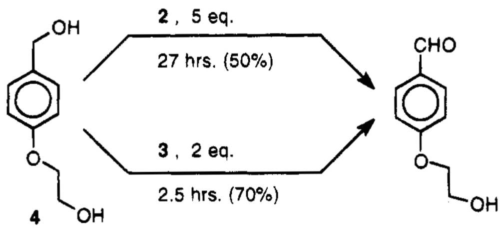
(21) Morgan, S. O.; Lowry, H. H. *J. Phys. Chem.* **1930**, *34*, 2385.

Table 2. Oxidation of Alcohols with Complexes 2 and 3 in $CHCl_3$[a]

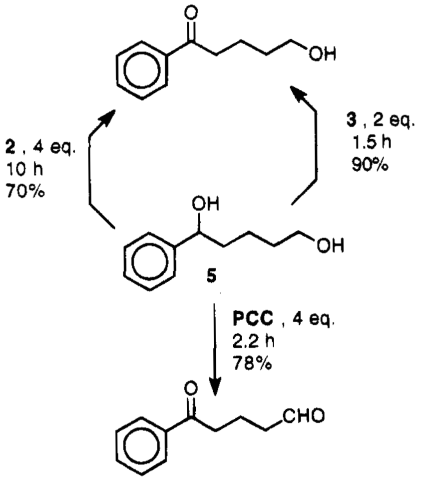
Alcohol	Product[b]	Oxidation with 2		Oxidation with 3	
		Time[c] (h)	Yield[d] (%)	Time[c] (h)	Yield[d] (%)
$CH_3(CH_2)CH_2OH$	$CH_3(CH_2)_6CHO$	94	51	4	54
 $CH_3(CH_2)_5\underset{\large OH}{\underset{\vert}{C}}H\,CH_3$	 $CH_3(CH_2)_5\underset{\large O}{\underset{\Vert}{C}}\,CH_3$	96	93	7	84
$C_6H_5CH_2OH$	C_6H_5CHO	30	67	0.75	73
$C_6H_5CHOHCH_3$	 $C_6H_5\underset{\large O}{\underset{\Vert}{C}}\,CH_3$	19	86	0.5	87
$C_6H_5CHOHC_6H_5$	 $C_6H_5\underset{\large O}{\underset{\Vert}{C}}\,C_6H_5$	19	93	0.75	85
		24	90	0.5	77
$C_6H_5CH{=}CHCH_2OH$	$C_6H_5CH{=}CHCHO$	26	81	2.5	66
$C_6H_5CH_2CH_2CH_2OH$	$C_6H_5CH_2CH_2CHO$	84	70	28	56

[a] A 4:1 ratio of 2:alcohol and a 2:1 molar ratio of 3:alcohol were employed respectively. [b] Isolated and identified by NMR. [c] Determined from TLC analysis of the reaction mixture. [d] Isolated crude yields.

Scheme 1



Scheme 2



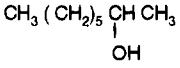
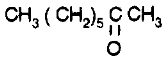
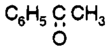
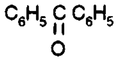
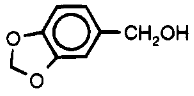
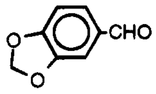
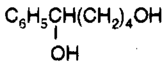
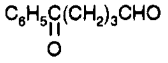
was cooled in an ice–salt bath (~−12 °C) for 1 h. The resulting bright orange plates were collected on a coarse sintered glass funnel (precooled in a freezer) by an aspirator vacuum filtration and were pressed dry with a glass stopper. Further drying in a desiccator stored away from direct light gave 1 as bright orange crystals[15a] (13.10 g, 62.5%): mp = 117–120 °C; ^{1}H-NMR (CD_3CN, 90 MHz) δ 0.89 (t, 3H), 1.45 (m, 4H), 2.99 (m, 2H), 5.85 (s, br, 1H), 6.38 (s, br, 1H), 6.96 (s, br, 1H); ^{13}C-NMR (CD_3CN, 22.5 MHz) δ 12.79 (8), 19.18 (t), 28.82 (t), 40.47 (t); IR (KBr, cm^{-1}) 3154, 2967, 2934, 1592, 1497, 946, 901, 446. Anal. Found (calcd): C, 22.91 (22.93); H, 5.77 (5.97); Cl, 16.06 (16.92); Cr, 24.92 (24.82); N, 6.49 (6.68).

***n*-Butylammonium:18-crown-6Chlorochromate,1:1Complex (2).** *n*-Butylammonium chlorochromate (2.09 g, 10 mmol) and 18-crown-6 (2.64 g, 10 mmol) were dissolved in 5 mL of dry methylene chloride in a 50 mL round-bottom flask with a magnetic stirring bar. To the resulting homogeneous red solution was added with vigorous stirring anhydrous ether (30 mL). The resulting orange precipitate was collected on a sintered glass funnel (medium porosity) and was washed with 2 × 5 mL portions of anhydrous ether to afford the 1:1 complex 2 as orange needle-like crystals[15b] (4.60 g, 97.3% yield): mp 132.5–134 °C; ^{1}H-NMR (CD_3CN, 90 MHz) δ 0.92 (t, 3H), 1.53 (m, 4H), 2.80 (m, 2H), 3.62 (s, 24H), 7.04 (br, 3H); ^{13}C-NMR (CD_3CN, 22.5 MHz) δ 12.95 (8), 19.51 (t), 29.69 (t), 39.39 (t), 69.94 (t); IR (KBr, cm^{-1}) 3115, 2913, 1350, 1101, 947, 434. Anal. Found (calcd): C, 40.38 (40.55); H, 7.69 (7.66); Cl, 7.52 (7.48); Cr, 11.37 (10.97); N, 2.97 (2.96).

***n*-Butylammonium:18-crown-6Chlorochromate,2:1Complex (3).** A 50 mL round-bottom flask with a magnetic stirrer was charged with 20 mL of freshly distilled petroleum ether. The flask was stoppered and its contents was cooled in an ice–water bath with magnetic stirring. A homogeneous solution prepared by dissolving *n*-butylammonium chlorochromate (418 mg, 2 mmol) and 18-crown-6 (264 mg, 1 mmol) in 1 mL anhydrous methylene chloride was added to the stirred petroleum ether. After stirring for a few minutes an orange precipitate was formed. Stirring was continued for 30 min, and the resulting orange solid was collected on a coarse sintered glass funnel under aspirator suction. After washing with a 5 mL portion of ice-cold petroleum ether containing several drops of methylene chloride the funnel was covered with aluminum foil and placed in a desiccator. After drying for 1.5 h, complex 3 was obtained as an orange solid[15b] (612 mg, 89.7% yield): mp 56–58 °C; ^{1}H-NMR (CD_3CN, 90 MHz) δ 0.91 (t, 6H), 1.47 (m, 8H), 2.90 (br, 4H), 3.61 (s, 24H), 6.83 (br, 6H); ^{13}C-NMR (CD_3CN, 22.5 MHz) δ 12.90, 19.34, 29.31, 39.98, 69.94; IR (KBr, cm^{-1}) 3046, 2906, 1604, 1471, 1106, 948, 430. Anal. Found (calcd): C, 35.20 (35.15); H, 7.03 (7.08); Cl, 10.26 (10.37); Cr, 15.55 (15.22); N, 4.18 (4.10).

Pyridinium:18-crown-6 Chlorochromate, 1:1 Complex (6). A solution of 18-crown-6 (2.64 g, 10 mmol) in ethanol free $CHCl_3$ (6 mL) was added dropwise and under nitrogen to a stirred slurry of PCC (2.16 g, 10 mmol) in $CHCl_3$ (8 mL). A gradual dissolution of solid occurred which was complete in ~5 min. After an additional 10 min stirring, the dark red solution

Table 3. Oxidation of Alcohols with PCC and Complex 6 in $CHCl_3$[a]

Alcohol	Product[b]	Oxidation with PCC		Oxidation with 6	
		Time[c] (h)	Yield[d] (%)	Time[c] (h)	Yield[d] (%)
$CH_3(CH_2)CH_2OH$	$CH_3(CH_2)_6CHO$	1.0	69	3.0	87
 $CH_3(CH_2)_5\underset{OH}{\underset{\mid}{C}}HCH_3$	 $CH_3(CH_2)_5\underset{O}{\underset{\|}{C}}CH_3$	1.0	95	3.0	95
$C_6H_5CH_2OH$	C_6H_5CHO	0.5	85	1.0	67
$C_6H_5CHOHCH_3$	 $C_6H_5\underset{O}{\underset{\|}{C}}CH_3$	0.5	86	2.0	89
$C_6H_5CHOHC_6H_5$	 $C_6H_5\underset{O}{\underset{\|}{C}}C_6H_5$	1.0	95	2.25	95
		0.5	91	1.0	84
$C_6H_5CH{=}CHCH_2OH$	$C_6H_5CH{=}CHCHO$	1.25	80	2.0	89
$C_6H_5CH_2CH_2CH_2OH$	$C_6H_5CH_2CH_2CHO$	1.25	94	2.5	85
 $C_6H_5\underset{OH}{\underset{\mid}{C}}H(CH_2)_4OH$	 $C_6H_5\underset{O}{\underset{\|}{C}}(CH_2)_3CHO$	2.20	78	14	76

[a] A 4:1 molar ratio of oxidant:alcohol was used. [b] Isolated and identified by NMR. [c] Determined from TLC analysis of the reaction mixture. [d] Isolated crude yields.

was filtered through a glass wool plug. Anhydrous ether (30 mL) was added dropwise to the stirred filtrate upon which an orange solid formed immediately. After stirring for 10 min, the orange solid was filtered off under an aspirator pressure and was washed with anhydrous ether (15 mL). After drying in a desiccator, complex **6** was obtained as an air stable orange solid[15b] (4.60 g, 96% yield): mp = 143–144 °C; ^1H-NMR (DMSO-d_6, 90 MHz) δ 3.51 (s, 24H), 8.13 (t, 2H), 8.60 (t, 1H), 9.01 (d, 2H), 11.40 (br, 1H); ^{13}C-NMR (DMSO-d_6, 22.5 MHz) δ 69.67, 126.99, 142.37, 145.95; IR (KBr, cm^{-1}) 3061, 2901, 1635, 1610, 1485, 1349, 1106, 949, 430. Anal. Found (calcd): C, 42.77 (42.55); H, 6.23 (6.30); Cl, 7.89 (7.39); Cr, 10.93 (10.84); N, 3.06 (2.92).

Typical Procedure for Oxidation of Alcohols. A slurry of oxidant **1** (2 mmol) or a solution of **2** (2 mmol) or **3** (1 mmol) in ethanol free chloroform (0.5 mL) was prepared in a 20 mL round-bottom flask equipped with a magnetic stirrer. The solution of alcohol (0.5 mmol) in chloroform (0.5 mL) was added by a disposable pipet. The flask was stoppered, and the solution was stirred at room temperature while protected from direct light. The extent of oxidation was followed by TLC using silica gel plates (petroleum ether/ethyl acetate solvent systems). After the completion of oxidation, anhydrous ether (10 mL) was added to the stirred dark reaction mixture. After an additional 10 min stirring, a powdery brown solid was produced. The stirring was stopped and the supernatant was filtered through a short column of silica gel[22] (200–400 mesh) in a coarse sintered glass funnel. The solid and silica gel were washed with 2 × 10 mL portions of anhydrous ether, and the combined ether layer was evaporated at reduced pressure to afford the product. In most cases the NMR analysis of the crude product indicated the presence of only the expected compound and no further purification was necessary. In some instances the crude product was purified by column chromatography on silica gel. Oxidations with complexes **2**, **3**, and **6** prepared *in situ* followed the above procedure except that the oxidants **2**, **3**, and **6** were prepared *in situ* by the addition of an appropriate molar amount of 18-crown-6 to the slurries of **1** and PCC in chloroform.

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Supplementary Material Available: Copies of ^1H and ^{13}C NMR spectra of **1**–**3** and **6** (11 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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[22] The quantities of silica gel and anhydrous ether used for washing are critical for an efficient seperation of the unreacted complexes **2**, **3**, or **6** from the product.