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DIPYRIDINE-CHROMIUM(VI) OXIDE OXIDATION OF ALCOHOLS IN DICHLOROMETHANE

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The extensive use of acid-labile protecting groups in organic syntheses prompted rapid adoption of dipyridine-chromium(VI) oxide[1] in pyridine as the reagent[2] of choice for numerous conversions of secondary alcohols to ketones.[3] Yields of ketones are usually satisfactory but oxidations of primary alcohols to aldehydes are capricious[3] and isolation of products from the pyridine medium often presents technical difficulties. In order to improve the oxidizing properties of the complex, we initiated a search for a solvent medium for the oxidation in which chromate ester formation and decay[4] might be facilitated and from which the products could be isolated more readily.

The complex, prepared essentially as described,[5] initially precipitates in an intractable, yellow microcrystalline form but, on continued stirring at 15°, was found to revert to a deep red, macrocrystalline form which could be isolated, dried and stored with ease. Sisler[1] noted that the complex varied from yellow to red and attributed this to crystal size, but polymorphs may be involved.

TABLE I

Solubility of Dipyridine-Chromium(VI) Oxide (25.0°)

Solvent	g/100ml	Solvent	g/100ml
Dichloromethane	12.5	1,2-Dichloroethane	3.2
cis-1,2-Dichloroethylene	7.1	1,1-Dichloroethane	1.5
Pyridine	6.1	Tetrachloromethane	1.4
Trichloromethane	4.5	trans-1,2-Dichloroethylene	0.5

Solubility of the complex in chlorocarbons roughly parallels the polarity of the medium. As expected, the complex is extremely hydrophilic, hydrating readily to form chlorocarbon-insoluble dipyridinium dichromate. Anal Calcd. for $C_{10}H_{12}Cr_2N_2O_7$: Cr, 27.64. Found: Cr, 27.62. Because of the extreme ease of hydration, precautions must be taken to limit exposure of the complex to moisture during isolation and use.[6]

Ebulliometric determination of the molecular weight of the complex in dichloromethane (Calcd. for monomer: 258; Found: 275 ± 16) suggests that it is monomeric in this solvent as well as in pyridine.[1]

Oxidations of primary and seconday alcohols with the complex in dichloromethane were accomplished merely by mixing solutions of the alcohol and the complex. Oxidations of the alcohols reported below were conducted using 6:1 mole-ratio of complex-to-alcohol, 5% complex in dichloromethane, at 25°. The reactions proceeded to completion within 5 to 15 minutes with deposition of brownish-black, polymeric chromium reduction products.

TABLE II

Alcohol Oxidations in Dichloromethane

Alcohol	Aldehyde or Ketone Yield	Analysis Method[a]
2-Butanol	98%	vpc
2-Octanol	97%	vpc
Cyclohexanol	98%	vpc
Benzhydrol	96%	Isolated, mp 50-51.5°
Cholesterol[b]	64% (Δ^5)	Isolated, mp 119.5-121°
1-Heptanol	93%	vpc
Benzyl Alcohol	95%	vpc
4-Nitrobenzyl Alcohol	97%	Isolated, mp 105-6°
3-Hydroxybenzyl Alcohol	87%	Isolated, mp 101-3°

[a] Chromatographic analyses were conducted on Theed and 15% Carbowax-on-Chromosorb columns on an Aerograph Model A-90-P instrument using toluene as the internal standard. Products not isolated directly were identified as derivatives.

[b] Cholesterol oxidation was conducted for 30 min. at 10°; the product solution was washed with 3% hydrochloric acid to prevent epimerization by traces of pyridine.

Stoichiometric analysis of the oxidation of 2-butanol at 25° using 2:1, 4:1 and 6:1 mole-ratios of complex-to-alcohol in 6% complex solutions provided 56%, 79% and 98% end-point conversions to 2-butanone, respectively (vpc analysis). This low oxidizing efficiency is undoubtedly due to the fact that reduced chromium products, as well as alcohol, react with the reagent - no active complex remained in solution following the oxidations even when the 6:1 ratio was used. Higher oxidizing efficiencies were obtained at lower temperature and by using a suspension of phosphorous pentoxide in the reagent but, even using the 6:1 ratio, the products were obtained readily by filtration and evaporation of the solvent.

Holm[3], using 3:1 mole-ratio of oxidant to alcohol in pyridine for 15-22 hours at 25°, reported yields of 18% for 2-octanol to 71% for benzhydrol and 10% for 1-heptanol to 75% for 3-hydroxybenzyl alcohol. We repeated the oxidation of 2-octanol with a 6:1 ratio of complex to alcohol in pyridine at 25° and found 65% conversion to the ketone in 1 hour by vpc analysis. It is possible that the 3:1 ratio of complex to alcohol commonly used in pyridine may be insufficient for certain oxidations and that much of the complex is converted to dipyridinium dichromate if precautions are not taken to exclude moisture. Our data, as well as the fact that respectable yields have been reported for numerous steroid alcohols, suggest that the low yields reported by Holm for the simple alcohols may have been due to his analytical techniques.

Although we have conducted no detailed kinetic study of the oxidations in dichloromethane versus pyridine, the above data for 2-octanol indicates that the reaction is appreciably faster in dichloromethane. The selectivity of the reagent in dichloromethane is illustrated by the conversion of cholesterol to cholest-5-en-3-one, $[\alpha]_D^{20}$ -2.7 ($CHCl_3$)[7], without shifting the double bond into conjugation and the reasonable yield of 3-hydroxybenzaldehyde obtained without protecting the phenol. The cholesterol oxidation yielded two other products: cholest-4-en-3,6-dione (10%), and cholest-4-en-3-ol-6-one (8%), which are the major products obtained on direct chromic acid oxidation. No cholest-4-en-3-one could be detected in the reaction product, but the cholest-5-en-3-one obtained readily isomerized on an alumina column to give cholest-4-en-3-one (95% yield), mp 83-4°, $[\alpha]_D^{20}$ +88° ($CHCl_3$), $\lambda_{max}^{234\ m\mu}$ (log (4.1).[7]

W. S. Johnson and C. A. Harbert have informed us that they have obtained trans-5,9-dimethyl-5,9-decadienal, bp 60-70 (0.05 mm) (Anal. Calcd. for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.6; H, 11.1) from the corresponding alcohol in 92% yield (99% pure by vpc analysis) using the complex in dichloromethane.[9]

The high yields of aldehydes realized using this anhydrous oxidizing medium provides further evidence for the thesis that aldehydes are oxidized to acids by chromic acid primarily via the aldehyde hydrate. The exceptional solubility of dipyridine-chromium(VI) oxide in dichloromethane should allow more detailed studies of chromium(VI) complexes and esters.

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REFERENCES

1) H. H. Sisler, J. D. Buch and O. E. Accountius, J. Am. Chem. Soc., 70, 3827 (1948).

2) First reported use of the complex in pyridine to oxidize alcohols was by G. I. Poos, G. E. Arth, R. E. Beyler and L. H. Sarrett, ibid., 75, 425 (1953). See ref. 3 for a review of the use of the reagent in pyridine.

3) J. R. Holum, J. Org. Chem., 26, 4814 (1961).

4) F. Holloway, M. Cohen and F. H. Westheimer, J. Am. Chem. Soc., 73, 65 (1951).

5) Chromium(VI) oxide (80g, dried over phosphorous pentoxide) was added in small portions to 600ml of anhydrous pyridine with stirring at 15-20°. References 1 and 2 should be consulted for precautions to be observed in preparing the complex. The complex was isolated by washing several times by decantation with petroleum ether, filtration and drying at 10mm (higher vacuum causes surface decomposition).

6) A commercial sample of "bis(pyridine)chromium oxide" was found to be insoluble in dichloromethane, probably due to hydration to the salt.

7) L. F. Fieser, "Organic Syntheses", Vol. 35, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 43.

8) L. F. Fieser and M. Fieser, "Natural Products Related to Phenanthrene", Rheinhold Pub. Co., New York, N. Y., 1949, p. 230.

9) Personal communication from William S. Johnson and Charles A. Harbert, Stanford University, Stanford, California. A report of this work will appear elsewhere.