Pyridinium Chlorochromate: a Mild and Efficient Oxidant for 2-Nitroalkanols

Goffredo ROSINI*, Roberto BALLINI

Dipartimento di Scienze Chimiche dell'Università, Via S. Agostino n. 1, I-62032 Camerino (MC), Italy

In connection with studies[1,2] on nitro group replacement by hydrogen or deuterium, we attempted to prepare several α-nitro ketones **2** by oxidation of the corresponding 2-nitroalkanols **1** which are readily available by nitro-aldol or Henry reaction[3,4], an important process for the formation of C—C bonds using nitroalkanes[5] and aldehydes. These oxidations are normally carried out by treating the alcohols **1** with chromium trioxide[6,7] or sodium dichromate[7,8,9] in strong acidic media. In our experience, however, yields obtained using these severe reaction conditions were frequently low, perhaps because the derivatives of **1** suffer fragmentation via a retro-aldol process and/or undergo β-elimination to give nitroalkenes.

We now report a mild method for the transformation of 2-nitroalkanols **1** to α-nitro ketones **2** which should broaden the scope and use of this process. Pyridinium chlorochro-

Table. Preparation of α-Nitro Ketones **2a–g** by Oxidation of 2-Nitroalkanols **1** with Pyridinium Chlorochromate

Compound **2**	Yield[a] [%]	b.p. [torr] or m.p.[b] [°C]	Molecular formula[c]	I.R. [cm^{-1}][d] $\nu_{C=O}$	ν_{NO_2}	^{1}H-N.M.R. ($CDCl_3$/TMS)[e] δ [ppm]
a	78	50-55°/1.5	$C_5H_9NO_3$ (131.1)	1725	1549	1.03 (t, *J*=7.5 Hz, 3H); 2.0-2.4 (m, 5H); 5.09-5.29 (dd, *J*=6.0 Hz, 1H)
b	87	55-58°/0.4	$C_7H_{13}NO_3$ (159.2)	1730	1560	1.0-1.4 (m, 9H); 2.0-2.4 (m, 2H); 2.9 (m, 1H); 5.38 (m, 1H)
c	83	48-49°	$C_9H_{15}NO_3$ (185.2)	1723	1552	0.95-2.1 (m, 13H); 2.6 (m, 1H); 5.43 (q, *J*=7.3 Hz, 1H)
d	86	98-100°/0.4	$C_{12}H_{15}NO_3$ (221.3)	1728	1550	0.93 (t, *J*=7.5 Hz, 3H); 1.8-2.3 (m, 2H); 2.8-2.95 (m, 4H); 4.93-5.15 (dd, *J*=6.0 Hz); 7.05-7.4 (m, 5H)
e	78	59-60°	$C_8H_{13}NO_5$ (203.2)	1730	1558	1.33 (s, 3H); 2.30 (s, 3H); 2.5-2.8 (m, 2H); 3.96 (s, 4H); 5.35 (*m*, 1H)
f	61	64-68°/3.8	$C_{10}H_{17}NO_5$ (231.2)	1770	1553	1.0-1.1 (m, 6H); 1.65-2.05 (m, 4H); 2.15-2.5 (m, 1H); 3.6-4.2 (m, 4H); 4.32 (t, *J*=6.75 Hz, 1H); 5.05-5.2 (m, 1H)
g	65	96-99°/1.5	$C_7H_{11}NO_5$ (189.2)	1730	1558	2.33 (s, 3H); 2.4-2.6 (m, 4H); 3.68 (s, 3H); 5.39 (t, *J*=6.4 Hz, 1H)

[a] Yield of isolated pure product. The final liquid products are at least 97% pure, by G.L.C. analysis with a Carlo Erba Fractovap 4160 (column: OV1 duran glass, 25 m × 0.3 mm; film thickness 0.4–0.45 μm; injector temperature: 300 °C; detector: flame ionization: 300 °C; carrier: nitrogen at 3 ml/min; column temperature: 60 °C; programme: 3 min at 60 °C, then from 60 °C to 250 °C at 15 °C/min and held).

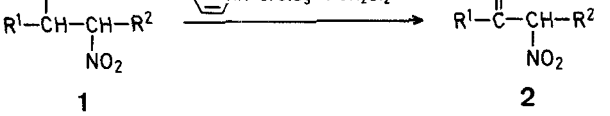
[b] Uncorrected.

[c] Microanalyses were performed using a C,H,N-Analyzer Model 185, Hewlett-Packard Co. Satisfactory results were obtained: C ±0.07, H ±0.04, N ±0.05.

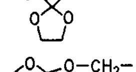
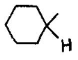
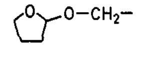
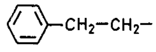
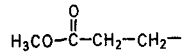
[d] Recorded on a Perkin-Elmer 297 spectrometer.

[e] Recorded at 90 MHz using a Varian EM 390 spectrometer.

mate[10,11,12] allows the efficient oxidation of a wide range of 2-nitroalkanols **1** to α-nitro ketones **2** in dichloromethane at room temperature with a modest excess of oxidant (Table).



1 **2**

1,2	R^1	R^2	1,2	R^1	R^2
a	H_3C	C_2H_5	e	H_3C	
b	*i*-C_3H_7	C_2H_5			
c		CH_3	f	*i*-C_3H_7	
d		C_2H_5	g	H_3C	 $H_3CO-\overset{\overset{O}{\|}}{C}-CH_2-CH_2-$

Although long reaction times are necessary (34-36 h), the oxidation proceeds smoothly even with the substrates in which additional acid-labile protecting groups are present. In fact, groups as tetrahydrofuranyl ethers or cyclic acetals survive chlorochromate oxidation in dichloromethane (Table). The yields of α-nitroketones are high and the oxidation process described should be useful for complex or polyfunctional 2-nitro alcohols, the reaction conditions being so mild as to minimize the possibility of involvement of most functional or protecting groups.

Oxidation of Nitroalkanols 1 to α-Nitro Ketones 2 using Pyridinium Chlorochromate; General Procedure:

In a 100 ml two-neck round-bottom flask equipped with a mechanical stirrer, pyridinium chlorochromate (3.23 g, 15 mmol, from Fluka AG) is suspended in anhydrous dichloromethane (25 ml) in the presence of molecular sieves (2.5 g; 3 Å). The alcohol **1** (10 mmol) is added all at once. The mixture is stirred at room temperature for 24 h and then another portion of PCC (1.62 g, 7.5 mmol) is added. The mixture is stirred at room temperature for additional 12 h. The progress of the reaction is followed by T.L.C. on silica gel using cyclohexane/ethyl acetate (9 : 1) as eluent. The mixture is diluted with ether (40 ml) and the supernatant liquid is decanted from the rest. The organic solution is passed through a short pad of Florisil to give a clear solution. This solution is evaporated and the residual product purified by distillation under reduced pressure or by recrystallization.

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