Solvent-Free Oxidations of Alcohols, Oximes, Aldehydes and Cyclic Acetals by Pyridinium Chlorochromate

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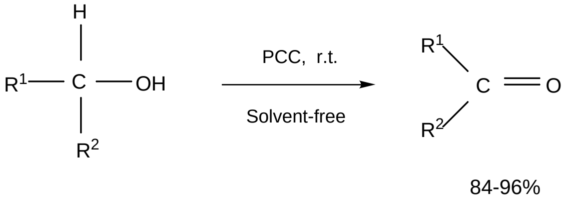
Abstract: Oxidative transformations of alcohols, oximes and cyclic acetals to carbonyl compounds proceed efficiently by pyridinium chlorochromate (PCC) under solvent-free conditions. The oxidation of aromatic and cinnamylic aldehydes to carboxylic acids, which does not occur by PCC in solution, is achieved satisfactorily in the absence of solvent.

Key words: oxidations, alcohols, aldehydes, acetals, pyridinium chlorochromate

Recently considerable attention has been paid to solvent-free reactions.[1,2] These reactions are not only of interest from an ecological point of view, but in many cases also offer considerable synthetic advantages in terms of yield, selectivity and simplicity of the reaction procedure.

After introduction of pyridinium chlorochromate (PCC) as a reagent for oxidation of primary and secondary alcohols,[3] this oxidant has found wide applications in organic synthesis.[4–6] In continuation of our studies on the preparation and application of chlorochromate derivatives in organic synthesis,[7] we wish to report the unexplored potentials of PCC for the oxidative transformations of organic functional groups in the absence of solvent.

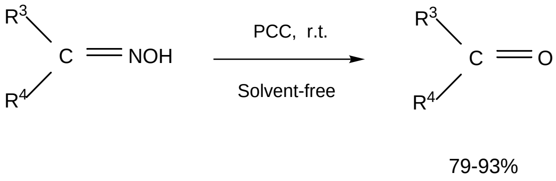
One of the most important reactions of alcohols, which have long been the objective of many research papers, is their oxidation to carbonyl compounds. We have investigated the reaction of different types of primary and secondary alcohols under solvent-free conditions by PCC at room temperature (Scheme1, Table 1).



Scheme 1

Benzylic alcohols with electron-releasing and electron-withdrawing substituents were oxidized in the presence of an equimolar amount of the oxidant and the corresponding carbonyl compounds were isolated in excellent yields after short reaction times (Table 1, entries 1–12). The oxidation of 2-nitrobenzyl alcohol (Table 1, entry 5) in 94% yield is an outstanding point since a similar reaction has not been reported with other oxidants. In the oxidation of furfuryl alcohol and 2-thienyl methanol (Table 1, entries 8,9) the heterocyclic ring remained intact during the course of the reaction. Allylic model compounds as well as saturated linear and cyclic alcohols were also converted to the corresponding aldehydes and ketones in good to excellent yields (Table 1, entries 13–20).

Oximes are useful intermediates in organic chemistry and are utilized for purification and characterization of aldehydes and ketones. An alternative pathway to aldehydes and ketones is the synthesis of oximes from non-carbonyl substrates followed by a deoximation step.[8] Chromium oxidizing agents are not very efficient deoximating compounds.[9,10] Chromium oxidants coupled with hydrogen peroxide or *t*-butyl hydroperoxide seem to improve the yield of deoximation.[11] However, they are still not satisfactory for the regeneration of aldehydes and other sensitive carbonyl compounds. Oxidative deoximation by PCC in dichloromethane has already been reported, however, carbonyl compounds were produced in low yields with long reaction times.[12] By performing similar reactions in the absence of solvent the corresponding carbonyl compounds were produced in good to excellent yields without any overoxidation of aldehydes (Scheme 2). Several examples of oxidative deoximation of different types of substrates including allylic and benzylic aldoximes and ketoximes together with saturated cyclic and linear model compounds are represented in Table 2.



Scheme 2

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Table 1 Oxidation of Alcohols by PCC under Solvent-Free Conditions at Room Temperature.

Entry	R^1	R^2	Time (min)	Oxid./Sub. (mole ratio)	Yield(%)	mp of 2,4-DNP[a] (Lit.)[b]
1	Ph	H	15	1	96[c]	233–235 (237)
2	4-BrC_6H_4	H	15	1.5	96	253–255 (256–258)[18]
3	4-$MeOC_6H_4$	H	5	1	94	251–252 (253–254)[19]
4	4-ClC_6H_4	H	10	1	93	253–254 (254)
5	2-$NO_2C_6H_4$	H	20	1	94	264 (264)
6	2-MeC_6H_4	H	10	1	96	191–193 (193–194)
7	4-$PhCH_2OC_6H_4$	H	20	1.5	92	227–229 (231–232)[20]
8	2-thienyl	H	1	1	96	240–241 (242)[21]
9	2-furyl	H	1	1	94	228–230 (230)
10	1-naphthyl	Me	1	1	95	182–184 (184)[22]
11	Ph	Ph	1	1	96	238–240 (238–239)
12	Ph	Me	10	1	95	248–250 (249–250)
13	PhCH=CH	H	15	1	95	253–255 (255)
14	PhCH=CH	Ph	1	1	95	243–244 (244)
15	CH_2=CH	C_5H_{11}	110	1.5	84	121–123
16	C_6H_{13}	H	150	2.5	85	105–107 (108)
17	C_5H_{11}	Me	120	2	88	73–75 (73–74)[23]
18	-$CH_2(CH_2)_4CH_2$-		100	1.5	95	146–148 (148)
19	-$CH_2(CH_2)_5CH_2$-		80	1.5	91	173–175 (173–177)[24]

[a] Mp of 2,4-dinitrophenylhydrazone derivatives.
[b] Ref. [17] unless otherwise stated.
[c] Based on the weight of 2,4-dinitrophenylhydrazone derivative.

Table 2 Oxidation of Oximes to Carbonyl Compounds by PCC, under Solvent-Free Conditions at Room Temperature.

Entry	R^3	R^4	Time (h)	Oxid./Sub. (mole ratio)	Yield (%)	mp of 2,4-DNP[a] (Lit.)[b]
1	Ph	H	2	2	80[c]	235–236 (237)
2	4-ClC_6H_4	H	4.5	2	79	253–254 (254)
3	4-$NO_2C_6H_4$	H	5.5	3	83	318–319 (320)
4	2-OHC_6H_4	H	1.5	1	93	247–249 (248–252)
5	2,4-$(MeO)_2C_6H_3$	H	4.5	3	90	256–257
6	4-MeC_6H_4	Me	20	4	80	258–260 (260)
7	Ph	Ph	3.5	2	80	239–240 (238–239)
8	-$CH_2(CH_2)_3CH_2$-		5	3	89	161–162 (162)
9	C_9H_{19}	H	5.5	3	83	103 (104)
10	PhCH=CH	H	9	5	80	253–254 (255)

[a] Mp of 2,4-dinitrophenylhydrazone derivatives.
[b] Ref.[17]
[c] Based on the weight of 2,4-dinitrophenylhydrazone derivative.

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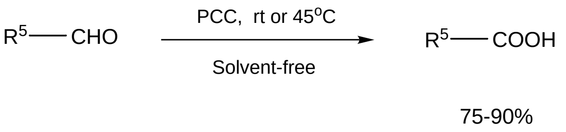
Table 3 Oxidation of Aldehydes to Carboxylic Acids by PCC, under Solvent-Free Conditions.

Entry	R^5	Time (h)	Oxid./Sub. (mole ratio)	Temp.(ºC)	Yield (%)	mp (Lit.)[a]
1	Ph	2	3	r.t.	90	121–122 (122)
2	$4\text{-}NO_2C_6H_4$	4	5	45	75	238–240 (241)
3	$2\text{-}MeC_6H_4$	2.5	3	r.t.	81	106–108 (107–108)
4	$3\text{-}BrC_6H_4$	3.5	4	45	89	154 (155)
5	$4\text{-}ClC_6H_4$	5	4	45	81	240–242 (240–243)
6	2-furyl	6	4	r.t.	82	131–132 (132)
7	PhCH=CH	4	4	r.t.	85	132–133 (133)
8	$4\text{-}Me_2NC_6H_4CH{=}CH$	4	4	r.t.	80	241 (242)
9	C_9H_{19}	24	5	45	no reaction	

[a] Ref.[17]

Oxidation of aldehydes to carboxylic acids does not occur at all by PCC in solution. There are only a few reports on the cyclization of some special kinds of aromatic aldehydes in dichloromethane by PCC.[13] However by the present method the oxidation of aromatic and cinnamylic aldehydes by PCC in the absence of solvent is reported for the first time (Scheme 3, Table 3). The furan ring remained untouched in the oxidation of furfural at room temperature (Table 3, entry 6). Attempted oxidation of linear saturated aldehydes failed and substrates remained intact in the reaction conditions after several hours (Table 3, entry 9).

Selective protection and deprotection of carbonyl groups frequently represent essential steps in synthetic organic chemistry.[14,15] Mild regeneration of parent compounds under non-aqueous conditions is vital for complex compounds with sensitive functional groups. Many reagents have been used for this purpose in solution but solvent-free deprotections are rare.[16]



Scheme 3

Several examples of different substituted 1,3-dioxolanes were converted satisfactorily to their corresponding aldehydes and ketones by PCC under neat conditions without any overoxidation of the aldehydes (Scheme 4, Table 4). Benzaldehyde, 4-chlorobenzaldehyde, and butyraldehyde as aromatic and aliphatic aldehydes were produced safely by the present method (Table 4, entries 1,2,7). Regeneration of other aromatic and aliphatic ketones were also achieved in few hours in good yields.

Table 4 Oxidation of Cyclic Acetals to Carbonyl Compounds by PCC, under Solvent-Free Conditions.

Entry	R^6	R^7	Time (h)	Oxid./Sub. (mole ratio)	Temp. (ºC)	Yield (%)	mp of 2,4-DNP[a](Lit.)[b]
1	Ph	H	1.5	5	45	80[c]	236–237 (237)
2	$4\text{-}ClC_6H_4$	H	2	5	45	80	254 (254)
3	Ph	Me	3	3	45	77	248–250 (249–250)
4	$4\text{-}MeC_6H_4$	Me	3	3	45	75	257–259 (260)
5	$PhCH_2$	Me	2	3	50	85	155–156 (156)[23]
6	$CH_2(CH_2)_3CH_2$		1.5	5	50	83	161–162 (162)
7	Bu	H	1.5	3	45	89[c]	104–106 (106)[23]
8	C_5H_{11}	Me	2.5	4	45	91	85–87 (89)[23]

[a] Mp of 2,4-dinitrophenylhydrazone derivatives.
[b] Ref.[17] unless otherwise stated.
[c] Based on the weight of 2,4-dinitrophenylhydrazone derivative.

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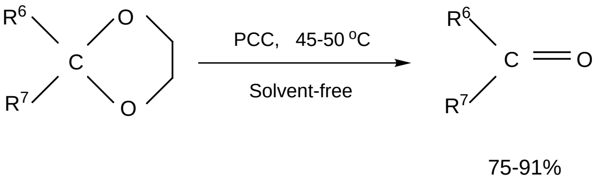

Scheme 4

In conclusion, PCC as a well-known oxidant can be used for the oxidation of organic functional groups in the absence of solvent. These transformations enjoy the chemical and environmental advantages of solvent-free reactions. Also some reactions, which do not proceed satisfactorily in solution occur under solid phase conditions. The results are quite reproducible and the reactions could be carried out on a gram scale.

All of the products are known compounds and were characterized by comparison of their spectral data (^{1}H NMR, IR) and physical properties with those of authentic samples. Progresses of the reactions were followed by TLC using silica gel polygrams SIL G/UV 254 sheets. Yields refer to isolated products or for slightly volatile carbonyl compounds are based on the weight of their 2,4-dinitrophenylhydrazone derivatives. Melting points were determined in open capillaries with a Galen-Kamp melting point apparatus and are corrected.

General Procedure for the Oxidation of Alcohols, Oximes or Cyclic Acetals to Carbonyl Compounds by Pyridinium Chlorochromate under Solvent-Free Conditions

PCC (3–15 mmol) was added to the substrate (3 mmol) in a mortar. Starting materials were instantly mixed and then stored for the appropriate period at room temperature or in an oven without any further agitation (see Tables 1, 2 and 4). The progress of the reaction was monitored by dissolving a sample in acetone and using TLC on silica gel (hexane–Et_2O, 3:1). Upon completion of the reaction HCl (20%, 30 mL) was added and extracted with Et_2O (3 × 25 mL). The organic layer was separated and dried ($MgSO_4$). Evaporation of the solvent gave the corresponding carbonyl compounds in 75–96% yields.

Oxidation of Aldehydes to Carboxylic Acids by PCC under Solvent-Free Conditions; General Procedure

A mixture of aldehyde (3 mmol) and PCC (9–15 mmol) was prepared in a mortar. Starting materials were stored at appropriate temperature (see Table 3) until the presence of aldehyde could not be further detected. The progress of the reaction was followed by dissolving a sample in CH_2Cl_2 and monitoring by TLC sheets (hexane–Et_2O, 2:1). Upon completion of the reaction HCl (20%, 30 mL) was added and extracted with Et_2O (3 × 25 mL). Concentration of the organic layer under reduced pressure afforded the desired carboxylic acids in 75–90% yields.

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