Caffeinilium Chlorochromate: As a Mild and Efficient Reagent for Oxidation of Alcohols and Chemoselective Oxidative Cleavage of Oximes

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Received October 24, 2002

Key Words : Caffeine, Caffeinilium chlorochromate, Oximes

Oxidation of organic compounds under nonaqueous and aprotic conditions is an important reaction in synthetic organic chemistry. For this purpose different Cr(VI) based oxidants are reported in the literature.[1-9] However, some of the reported reagents suffer from disadvantages such as instability, hygroscopicity, low selectivity, long reaction time, difficulty of preparation and need for a large excess of the reagent. Thus a milder, more selective and inexpensive reagent is still in demand.

In connection with our ongoing research program directed toward the development of new oxidizing agents and systems,[10-14] we wish to report the oxidizing property of a new mild oxidizing agent, caffenilium chlorochromate (CCC). CCC was prepared by the addition of caffeine to a solution of an equimolar amount of CrO_3 in 6 M HCl at 0 °C and obtained in 86% yield as an orange solid. CCC was stable when kept at room temperature for a long period of time. This oxidizing agent is soluble in hot water, acetone and acetonitrile and is insoluble in cold water, benzene and carbon tetrachloride. The structure of CCC was determined by elemental analysis and infrared spectral data.

Primary and secondary benzylic and saturated alcohols are converted to their corresponding carbonyl compounds in good to high yields (Table 1, Entries 1-11). Further oxidation of aldehydes to their carboxylic acids was not observed. Under the same conditions allylic alcohols are selectively oxidized to their corresponding α,β-unsaturated carbonyl compounds without the cleavage of carbon-carbon double bonds (Table 1, Entry 12).

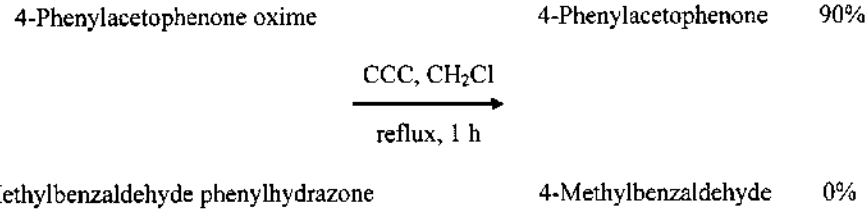
The oxidative cleavage of oximes to their corresponding carbonyl compounds were also performed by this reagent (Table 1, Entries 13-20). Hydrazones do not undergo oxidative cleavage with this method (Table 1, Entries 21, 22). Therefore, this methodology shows selectivity and is suitable for oxidative selection between oximes and hydrazones. This is exemplified by the competitive reaction between 4-phenylacetophenone oxime and 4-methylbenzaldehyde phenylhydrazone (Scheme 1).

In conclusion the mildness, stability, high efficiency, selectivity, reasonable yields of products simple and clean work-up and heterogeneous reaction conditions make this method a useful addition to the present methodologies for the oxidation of alcohols and chemoselective oxidative cleavage of oximes.

Experimental Section

Preparation of caffeinilium chlorochromate: To a solution of CrO_3 (10 g, 0.1 mmol) in 6M HCl (10 mL) was slowly added caffeine (1.92 g, 0.1 mmol) and the mixture was stirred at 0 °C for 2 h. The cold mixture was filtered on a sintered glass funnel and the orange solids were collected. The product was dried in *vacuo* at room temperature for 3 days to give CCC (mp > 240 °C) in 86% yield. ^{1}H NMR ($CDCl_3$) δ 2.70 (s, 6H), 3.63 (s, 3H), 9.5 (s, 1H); IR (KBr pellet) 940, 900, 760 cm^{-1}. Anal. Calcd. for $C_8H_{11}ClCrN_4O_5$: C, 29.06; H, 3.35; N, 16.94. Found: C, 29.08; H, 3.45; N, 17.00.

General procedure for oxidation of alcohols: To a solution of the substrate (1 mmol) in CH_2Cl_2 (5 mL) was added CCC (2 mmol) and the mixture was stirred magnetically under reflux condition for the specified period of time (Table 1). The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was filtered and the solid residue was washed with CH_2Cl_2 (20 mL). Evaporation of the solvent followed by column



Scheme 1

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Table 1. Oxidation of alcohols and oxidative cleavage of oximes with CCC[a]

Entry	Substrate	Product	Time (h)	Yield %[b]
1	Benzyl alcohol	Benzaldehyde	0.75	95
2	2-Bromobenzyl alcohol	2-Bromobenzaldehyde	0.5	90
3	2-Chlorobenzyl alcohol	2-Chlorobenzaldehyde	2.5	87
4	4-Chlorobenzyl alcohol	4-Chlorobenzaldehyde	2	92
5	3-Nitrobenzyl alcohol	3-Nitrobenzaldehyde	4	90
6	1-Phenyl ethanol	Acetophenone	0.75	85
7	Diphenylcarbinol	Benzophenone	3	90
8	Cyclohexanol	Cyclohexanone	0.3	87
9	3-Phenylpropane-2-ol	3-Phenylpropanal	1.2	90
10	1-Phenylpropane-2-ol	Phenylpropane-2-one	1	85
11	Phenylethyleneglycol	Phenylglyoxal	2.7	80
12	Cinnamyl alcohol	Cinnamaldehyde	0.8	80
13	4-Chlorobenzaldehyde oxime	4-Chlorobenzaldehyde	0.75	90
14	2-Methoxybenzaldehyde oxime	2-Methoxybenzaldehyde	0.3	92
15	4-Phenylacetophenone oxime	4-Phenylacetophenone	0.83	87
16	3-Acetylpyridine oxime	3-Acetylpyridine	2	85
17	4-Acetylpyridine oxime	4-Acetylpyridine	5.25	90
18	1-Tetralone oxime	1-Tetralone	1.1	85
19	Champhor oxime	Champhor	3	82
20	Cyclohexanone oxime	Cyclohexanone	1	85
21	4-Phenylylacetophenone phenylhydrazone	4-Phenylylacetophenone	6	0
22	4-Methylacetophenone phenylhydrazone	4-Methylacetophenone	3.5	0

[a]All products were characterized by infrared (IR) and ^{1}H NMR spectroscopy and by comparison with authentic samples. [b]Isolated yield.

chromatography on silica gel gave the corresponding carbonyl compounds in good to high yields.

General procedure for oxidation of oximes: To a solution of the substrate (1 mmol) in CH_2Cl_2 (5 mL), was added CCC (2 mmol) and the mixture refluxed for the specified period of time (Table 1). The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was filtered and the solid material was washed with CH_2Cl_2 (20 mL). The combined filtrates were evaporated on a rotary evaporator and the resulting crude material was purified on silica gel column. Evaporation of the solvent afforded pure carbonyl compounds in good to high yields.

Acknowledgment. We wish to thank Dr. R. Sariri for her help. Also, we are thankful to Guilan University Research Council for the partial support of this work.

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