SHORT PAPER

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3-Carboxypyridinium chlorochromate (CPCC): an inexpensive and convenient reagent for efficient oxidation of Hantzsch 1,4-dihydropyridines†

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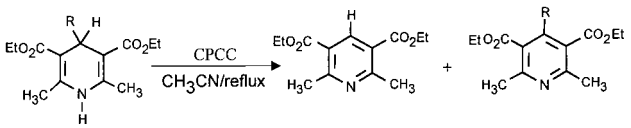
A variety of Hantzsch 1,4-dihydropyridines are oxidized to their corresponding pyridines in excellent yields by 3-carboxypyridinium chlorochromate.

Hantzsch 1,4-dihydropyridines such as amlodepine besylate, nifedepine and niguldepine are calcium channel blockers and are rapidly emerging as one of the most important classes of drugs for the treatment of cardiovascular diseases.[1–3] In the human body, it has been observed that, these compounds are generally oxidized to their corresponding pyridines.[3-8] A number of methods and reagents have been reported recently in the literature for this purpose.[9–27] However, some of these methods suffer from disadvantages such as low yield of the products, the use of strong oxidants, the requirement of severe conditions and the need of excess of the oxidants. Therefore, introduction of a milder, convenient and efficient oxidant for the oxidation of 1,4-dihydropyridines to their pyridines is of practical importance and is still in demand.

Recently, we have introduced 3-carboxypyridinium chlorochromate as a useful oxidant for the cleavage of carbon-nitrogen double bonds and oxidative deprotection of trimethylsilyl and tetrahydropyranyl ethers.[28,29] Now we report the use of 3-carboxypyridinium chlorochromate, an inexpensive, stable and easily prepared oxidant for the effective oxidation of different types of 4-substituted 1,4-dihydropyridines to their corresponding pyridines in refluxing acetonitrile (Scheme 1).



1–15 **16** **17–27**

Scheme 1

As shown in Table 1, oxidation of 1,4-dihydropyridines with secondary alkyl group (**3**) and benzyl groups (**4**, **5**) at the 4-position were performed efficiently and only dealkylated pyridine derivative (**16**) was obtained from the reaction mixture. This is a general trend in the oxidation of 1,4-dihydropyridines.[16,21] Besides **16**, acetone, benzaldehyde and acetophenone were also obtained. However, 4-methyl, 4-aryl and 4-heteroaryl-1,4-dihydropyridines (**2** and **6**-**15**) were oxidized with retention of substitution at 4-position, to afford the corresponding pyridines (**17**-**27**) in excellent yields.

In comparison with acetonitrile, the reaction times were longer and the yields of the products were considerably lower when benzene, dichloromethane and chloroform were employed as solvents.

In summary, 3-carboxypyridinium chlorochromate is an inexpensive and efficient reagent for oxidation of 1,4-dihydropyridines to their corresponding pyridines.

Experimental

1,4-Dihydropyridines were prepared according to described procedures.[30] All products are known compounds; they were identified by comparison of their physical and spectral data with those of authentic samples. 3-Carboxypyridinium chlorochromate was prepared as described previously.[28]

General procedure for the oxidation of 1,4-dihydropyridines.
To a solution of 1,4-dihydropyridine (1 mmol) in MeCN (15 ml) in a 50 ml round-bottomed flask equipped with a condenser and a magnetic stirrer, was added 3-carboxypyridinium chlorochromate (1 mmol) and the mixture was refluxed for the time indicated in Table 1. The progress of the reaction was monitored by GLC or TLC (eluent: CCl_4-EtOAc, 7:1). The mixture was filtered and the solid material

Table 1 Oxidation of 1,4-dihydropyridines with CPCC in refluxing MeCN

Substrate	R	Product	Time (t, h)	Yield (%)[a]	Ref.
1	H	16	0.75	93	24
2	Me	17	3	92	24
3	$(Me)_2CH$	16	0.75	95	24
4	$C_6H_5CH_2$	16	0.7	96	24
5	$C_6H_5(Me)CH$	16	0.3	94	24
6	C_6H_5	18	3	92	24
7	$2\text{-}MeOC_6H_4$	19	0.5	97	25
8	$2,5\text{-}(MeO)_2C_6H_3$	20	1.7	92	27
9	$2\text{-}O_2NC_6H_4$	21	6	95	25
10	$3\text{-}O_2NC_6H_4$	22	4	94	21
11	$4\text{-}O_2NC_6H_4$	23	2.15	96	21
12	2-Furyl	24	4	95	21
13	5-Me-2-furyl	25	8	94	27
14	2-Pyridyl	26	1	97	27
15	2-Thienyl	27	5	99	21

[a] Isolated yield

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† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M)*.

was washed with MeCN (15 ml). The filtrate was evaporated and the resulting crude material was purified on a silica-gel plate. Evaporation of the solvent afforded the pure product; yield 92-99% (Table 1).

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