Short communication

Rapid and Efficient Oxidation of Hantzsch 1,4-Dihydropyridines with Potassium Ferrate Under Microwave Irradiation

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Abstract

1,4-dihydropyridines were efficiently and rapidly converted to their corresponding pyridine derivatives with potassium ferrate(VI) supported on montmorillonite K-10 under microwave irradiation.

Keywords: 1,4-Dihydropyridines, potassium ferrate, microwave, oxidation

1. Introduction

Hantzsch 1,4-dihydropyridines (1,4-DHPs) have been extensively utilized as the analogs of NAD(P)H coenzymes to study the mechanism and synthetic potential of various redox processes.[1] They play a vital role in many bioreductions by transferring a hydride ion or an electron to the surrounding substrate[2] and possess a high biological activity as a class of useful drugs, particularly as antioxidants. The oxidation of Hantzsch 1,4-dihydropyridines has attracted considerable attention and even in recent years, numerous reagents and procedures have been recommended for this purpose, such as NO,[3] ferric or cupric nitrates on a solid support (clayfen or claycop),[4] ceric ammonium nitrate,[5] clay-supported cupric nitrate accompanied by ultrasound promotion,[6] manganese dioxide or 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ),[7] nitric oxide,[8] bismuth nitrate pentahydrate,[9] pyridinium chlorochromate (PCC),[10] tetrakis-(pyridine) cobalt(II) dichromate (TPCD),[11] $RuCl_3$,[12] S-nitrosoglutathione,[13] $Mn(OAc)_3$,[14] $Fe(ClO_4)_3/HOAc$,[15] $KMnO_4$,[16] CrO_3,[17] HNO_3,[18–19] HNO_2,[20–21] tert-butylhydroperoxide,[22] silica gel supported ferric nitrate (silfen),[23] N_2O_3.[24] Although, some of these reactions are carried out under mild conditions, most of these reactions require an extended period of time for completion, utilize strong oxidants, need of freshly prepared reagents, tedious work-up, and afford only modest yields of the products. Therefore there is still demand to obtain a convenient, rapid and efficient method for oxidation of 1,4-DHPs.

The use of microwave irradiation to simplify and improve classic organic reactions has become a very popular technique because it often results in shorter reaction times, higher yields and cleaner reaction.[25,26] On the other hand, solvent-free chemical synthesis has received much attention recently.[27–29] Solvent-free processes are not only environmentally benign but also economical. Since solvent is not required, toxic wastes can be minimized or eliminated and the cost of solvent and waste treatment is reduced. Furthermore, operational simplicity is an attractive feature. Potassium ferrate has been identified as an effective mild oxidant and this unusual species shows great promise as a potential alternative to more toxic, less selective, oxidizing agents. It has a wide application in wastewater treatment.[30–32] Recent studies have shown that potassium ferrate on mineral support is an effective oxidizing agent for a variety of reductants.[33–35]

We have previously reported a convenient method for the oxidation of 1,4-dihydropyridines.[36,37] Herein, we wish to report that potassium ferrate(VI) supported on montmorillonite K-10 can oxidize 1,4-DHPs under microwave irradiation in high to excellent yields.

2. Results and Discussion

The most practical route for preparation of potassium ferrate was reported by Laszlo et al and it has been claimed to be a low polluting oxidizer.[38] Prompted by stringent environmental protection laws in recent years, there has been increasing emphasis on the use and design of ecofriendly supported reagents to reduce the amount of toxic waste and byproducts arising from chemical processes.[39] We observed that the reaction remained incomplete when the solid support was not used even for an extended period of time and more seriously, the molten reagent is adhered to the walls of vessel.

However, when potassium ferrate(VI) was supported onto montmorillonite K-10, oxidation of 4-alkyl or aryl substituted dihydropyridines to the corresponding pyridine derivatives were occurred efficiently, in high yields (Scheme 1). The results obtained with various 4-substituted 1,4-dihydropyridines are given in Table 1.

According to earlier studies, oxidation of 4-alkyl dihydropyridines containing methyl, benzyl, propyl and isopropyl substitutes produced exclusively 4-alkyl pyridine (entries 2–4, 6). Contrary to this, we observed during our studies that 4-alkyl substituted dihydropyridines (entries 3,4,6) resulted in a mixture of 4-substituted and unsubstituted pyridines (Scheme 1). This is in agreement with observation of Delgado et al.,[40] except for 4-methyl dihydropyridine which gave 4-methyl pyridine (14).

3. Experimental

1,4-Dihydropyridines were synthesized according to Arthur Hantzsch procedure.[24] All products were known and their physical and spectroscopic data were compared with those of authentic samples. Melting points were measured using Barnstead Electrothermal 9100. IR spectra were recorded on a FT-IR Bruker Vector 22 infrared spectrophotometer. All ^{1}H NMR spectra were performed on Bruker AC 80 MHz spectrometer as $CDCl_3$ solutions with TMS as internal reference.

Potassium ferrate (VI) was prepared according to the literature data[38] and impregnated on montmorillonite K-10. A Sears Kenmore microwave oven equipped with a turntable at full power (900 Watts) was used.

Oxidation of dihydropyridines: In a typical experimental procedure, a mixture of K_2FeO_4 (0.12 g, 3 mmol), montmorillonite K-10 (2 g) and 1,4-dihydropyridine (1 mmol) was added to diethyl ether (5 ml). The reaction mixture was thoroughly mixed at room temperature. The air-dried adsorbed material (in a small beaker) was placed inside the microwave oven and irradiated for the

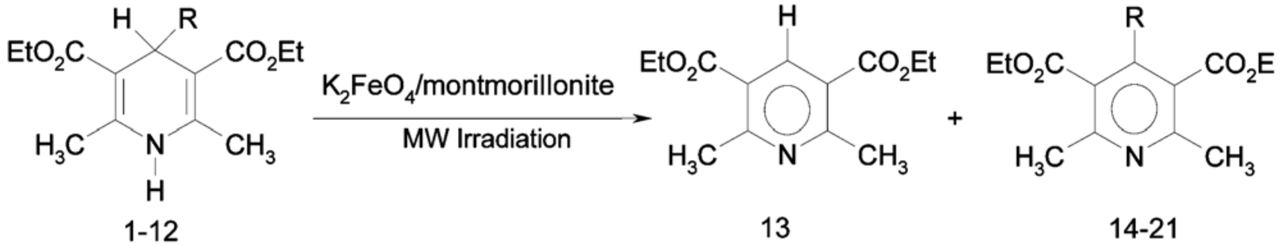

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Table 1. Oxidation of 1,4-dihydropyridines to pyridine derivatives by potassium ferrate under microwave irradiation[a]

Entry	R	Product	Time MW/Min	Yield[b] Normal product 14–21	Dealkylated product 13	mp[c] °C	Lit. mp °C
1	H	13	2	98		70	69–70$^{(7)}$
2	CH_3	14	3	95		liq	liq$^{(9)}$
3	$CH_3CH_2CH_2$	15	3	20	75	68–69	69–70$^{(7)}$
4	$(CH_3)_2CH$	16	3	15	78	68–69	69–70$^{(7)}$
5	C_6H_5	17	3	97		61–62	63–64$^{(20)}$
6	$C_6H_5CH_2$	18	3	<20	>80	68–69	69–70$^{(7)}$
7	4–ClC_6H_4	19	4	94		66–67	65–67$^{(7)}$
8	3–$NO_2C_6H_4$	20	4	94		62–63	61–63$^{(7)}$
9	4–$CH_3OC_6H_4$	21	3	95		51–52	51–53$^{(14)}$
10	4–$CH_3C_6H_4$	22	3	96		72–73	72–73$^{(14)}$
11	2–Furyl	23	3	92		liq	liq$^{(14)}$
12	2–Thienyl	24	3	94		liq	liq$^{(14)}$

[a] All products are known compounds and were characterized by their mps and NMR spectra.
[b] Refers to isolated percent yield.
[c] Melting points are related to major products

time indicated in the Table 1. The progress of reaction was monitored by TLC. After completion of the reaction, the mixture was cooled to room temperature and the reaction mixture was extracted with chloroform, the filtrate evaporated and the residue crystallized from aq. EtOH to afford the corresponding pyridine, (see Table1).

4. Conclusions

In summary we have described a general and practical route for the oxidation of 1,4-dihydropyridines in excellent yields using a nontoxic reagent. Eco-friendly, mild reaction conditions, easy workup procedure, short reaction time and high to excellent yields, are the advantages of this reagent without the use of expensive and hazardous organic solvents.

5. References

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Povzetek

Prispevek obravnava hitro in učinkovito pretvorbo 1,4-dihidropiridinov do odgovarjajočih derivatov piridina s kalijevim feratom(VI), nanešenim na montmorilonit K-10 in obsevanjem z mikrovalovi.