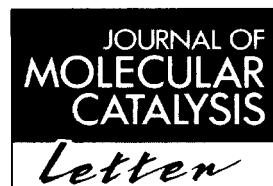


Vapour phase oxidation in the preparation of 3-hydroxypyridine-4-carboxaldehyde: the vitamin B₆ analog*



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(Received June 27, 1990; accepted October 17, 1990)

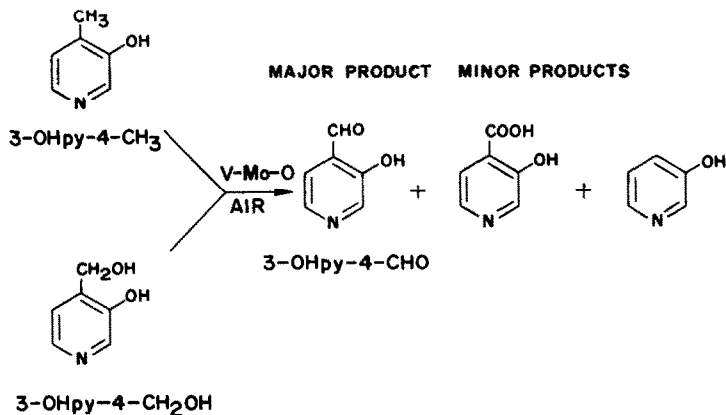
Introduction

Pyridinecarboxaldehydes are highly useful intermediates in the production of pharmaceuticals and pesticides. Recently, the authors reported [1] the preparation of some of the pyridinecarboxaldehydes by the vapour phase oxidation of the corresponding alcohols, for the first time, on a V–Mo–O catalyst system. The 3-hydroxypyridine-4-carboxaldehyde (3-OHpy-4-CHO) is very well known as a model of pyridoxal 5'-phosphate in studies of imine formation and transamination with amino acids [2]. Even though O'Leary and Payne [2] reported an improved synthesis of 3-OHpy-4-CHO starting with 4-picoline-*N*-oxide in four steps, they had adopted the oxidation of 3-hydroxy-4-pyridinemethanol (3-OHpy-4-CH₂OH) by liquid phase oxidation using MnO₂ as an oxidizing agent, resulting in 40% yields of the aldehyde. The 3-OHpy-4-CHO preparation via vapour phase oxidation has not been reported in the open literature. In addition, the availability of this compound so far has been limited, mainly due to the inefficient synthesis steps of its preparation. However, manganese dioxide (MnO₂) has proved a valuable oxidising agent, in particular for converting pyridinemethanols to their corresponding pyridinecarboxaldehydes [3]. The liquid phase catalytic oxidation reactions suffer from certain disadvantages, such as the large volume of catalyst required and its non-regenerability, etc. However, these are minimised in the vapour phase mode of operation.

In view of the above, in the present letter the authors report preliminary results on the vapour phase oxidation of both 3-hydroxy-4-methylpyridine (3-OHpy-4-CH₃) and 3-OHpy-4-CH₂OH to 3-OHpy-4-CHO over V–Mo–O catalyst in the presence of air (Scheme 1).

*IICT Communication No. 2613.

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Scheme 1.

Experimental

The reactants 3-OHpy-4-CH₃ and 3-OHpy-4-CH₂OH were prepared as reported in the literature [4]. The catalyst was prepared by impregnating the α -Al₂O₃ support with solution containing Analar ammonium heptamolybdate, ammonium metavanadate and oxalic acid. For a typical catalyst, the active components V-Mo-O (V/Mo=3.7/1) are 10 wt.% of the reaction mixture. A fixed bed reactor fitted with the usual feed and control facilities and operating under normal atmospheric pressure was used to determine the activities of the catalysts at 375 °C and the products were analysed by gas chromatography. A total of 10–15 g catalyst was used with a molar feed ratio of 3-OHpy-4-CH₂OH/3-OHpy-4-CH₃:air:H₂O = 1:18:80. The surface area of the catalyst was 6 m² g⁻¹.

Results and discussion

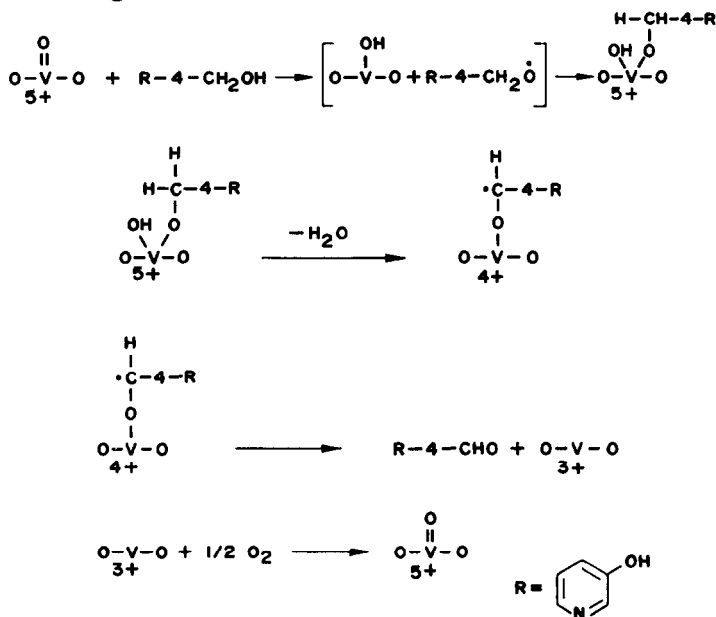
Representative results are shown in Table 1. It is observed that the 3-OHpy-4-CH₂OH conversion and selectivity to the product, *i.e.* 3-OHpy-4-CHO formation, is more than that of 3-OHpy-4-CH₃. This may be due to the higher susceptibility of the alcohol group to oxidations than the methyl group. The present results with the vapour phase oxidation indicate a selectivity which is significantly greater than that obtained in liquid phase [2].

TABLE 1

Vapour phase preparation of 3-hydroxypyridine-4-carboxaldehyde by V-Mo-O catalyst at 400 °C

Feed stock	Conversion of feed stock	Product selectivity		
		aldehyde (%)	acid (%)	others (%)
3-OHpy-4-CH ₃	35	75	5	trace
3-OHpy-4-CH ₂ OH	70	80	10	trace

Knowledge of the compounds formed from 3-OHpy-4-CH₃ has shown that product formation probably occurs via a mechanism similar to that reported for picoline vapour phase oxidations [5, 6]. However, formation of 3-OHpy-4-CHO from 3-OHpy-4-CH₂OH may be explained by assuming the following reaction mechanism:



Probably the abstraction of more acidic hydrogen, *i.e.* the hydrogen bonded with oxygen of the methanolic group, occurs via the vanadium metal-oxygen double bond. The abstraction is followed by adsorption of dehydrogenated alcohol on the vanadium surface, which in turn loses a water molecule and is desorbed while forming the aldehyde. The reduced catalyst is regenerated in the presence of air.

The vapour phase method adopted in this way gives results in conversion and selectivity which are higher than those obtained so far by any other known method of preparation of 3-OHpy-4-CHO.

References

- 1 M. Subrahmanyam and A. R. Prasad, *Appl. Catal.*, **65** (1990) L5.
- 2 M. H. O'Leary and J. R. Payne, *J. Med. Chem.*, **14** (1971) 773 and references therein.
- 3 E. P. Papadopoulos, A. Jarrar and C. H. Issidorides, *J. Org. Chem.*, **31** (1966) 615 and references therein.
- 4 J. D. Crum and C. H. Fuchsman, *J. Med. Chem.*, **30** (1987) 2042.
- 5 A. Anderson, *J. Solid State Chem.*, **42** (1982) 263.
- 6 A. Anderson and S. T. Lundin, *J. Catal.*, **58** (1979) 383.