N-oxidation of pyridines by hydrogen peroxide in the presence of TS-1

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In the production of aromatic N-oxides using the oxidation of N-containing heterocyclic aromatic substrates with H_2O_2 as oxidant, the non-catalysed homogeneous oxidation is found to play an important part in the overall reaction. In addition, when TS-1 is used as a catalyst, there are many potential competitive interactions between the catalyst, the reactants and the products, which limit the effectiveness of the catalyst. It is concluded that the use of TS-1 and other microporous catalysts for the heterogeneous N-oxidation of pyridine and substituted pyridines needs to be interpreted with caution.

KEY WORDS: N-oxidation of pyridine; hydrogen peroxide; TS-1; heterogeneous catalysis; uncatalysed oxygen transfer

1. Introduction

A recent publication [1] describes the use of micro- and mesoporous titanium-containing materials as catalysts for the efficient conversion of substituted pyridines and related heterocyclic compounds into their N-oxides by hydrogen peroxide. No control experiments, carried out in the absence of the catalysts, were reported and the possible contribution of uncatalysed oxidation was ignored. In our investigation of the oxidation of sulfides by hydrogen peroxide in the presence of one of these catalysts, titanium silicalite (TS-1), to form first the corresponding sulfoxide which was then converted into the sulfone [2] we showed that uncatalysed oxygen transfer dominated sulfoxide formation, but that TS-1 catalysis was essential for production of the sulfone. This paper reports that, in the presence of TS-1, uncatalysed oxygen transfer from hydrogen peroxide to pyridine and the picolines does indeed contribute substantially to the yield of the N-oxides, and, from preliminary studies, we show that the efficiency of the catalytic reaction can best be understood in terms of competitive binding effects involving the reactants and the N-oxide produced.

2. Experimental

TS-1 was prepared according to the method of Taramasso et al. [3] and calcined at 550 °C immediately prior to use. Reactions were carried out using the heterocyclic substrate (0.05 mol), aqueous hydrogen peroxide (30 vol%; 0.05 mol) and TS-1 (200 mg). Two procedures were investigated; in method A, the reaction was initiated by adding the premixed reactants to the catalyst, while in method B the catalyst and heterocycle were stirred together for 5 min after which addition of the oxidant started the reaction. The reaction mixtures, consisting of the catalyst suspended in a single aqueous organic liquid phase, were stirred at 60 °C for a period of 24 h, samples of the liquid being removed at intervals, quenched, and then analysed by GC. Product identification was by NMR spectroscopy, GC/MS (Fisons Trio 1000) and by comparison of GC retention times with those of authentic specimens. We have demonstrated [2] that, under these reaction conditions, decomposition of hydrogen peroxide corresponds with the extent of oxygen transfer to the organic substrate; other decomposition pathways of H_2O_2 are negligible.

3. Results and discussion

Control experiments were carried out on N-oxidation of pyridine, 2-, 3- and 4-picolines in the absence of TS-1. The yields of N-oxide after 24 h are in table 1 and indicate that substantial oxidation occurs, the proportion being greater for

Table 1
Oxidation of pyridine and picolines using H_2O_2 as oxidant.[a]

Catalyst/method	N-oxide product yield (%)			
	Pyridine	2-picoline	3-picoline	4-picoline
Non-catalysed	35.5	28.4	15.9	9.6
TS-1 method A	95.3	84.7	42.4	34.7
TS-1 method B	96.0	88.0	51.9	53.2

[a] Substrate (0.05 mol), H_2O_2 (30 vol%, 0.05 mol) reacted at 60 °C for 24 h.

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Table 2
Oxidation of substrate mixtures.[a]

Substrates	N-oxide product yield (%)		
	Pyridine	2-picoline	4-picoline
Pyridine and 2-picoline	80.2	30.3	–
2-picoline and 4-picoline	–	42.6	17.0

[a] Each substrate (0.025 mol) reacted with H_2O_2 (30 vol%, 0.05 mol) at 60 °C with TS-1 (0.2 g) using method A for 24 h.

pyridine (pK_a 5.27 at 20 °C) [4] than for the more basic picolines (pK_a-values: 2- 6.05, 3- 5.75 and 4- 6.10). Since the pH of 30 vol% aqueous H_2O_2 is ca. 5.5, the results suggest that N-protonation is an inhibiting factor in these reactions.

The presence of TS-1 enhances the extent of N-oxidation which was essentially complete in the case of pyridine after 24 h (table 1). Again the picolines were apparently less reactive, and reactions conducted using method B gave higher conversions than by method A. This difference was particularly noticeable for 3- and 4-picoline and may point to partial control of the early stages of reaction by mass transport in these cases. The initial rates of formation of the N-oxides reflected the 24 h conversions, but the increasing production of pyridine N-oxide with time did not fit a simple second-order kinetic law. We suggest that this is a consequence of equilibria, rapidly established in this case, in which pyridine, H_2O_2 and the product pyridine N-oxide compete for occupancy of the intracrystalline volume of the TS-1, reaction occurring only when H_2O_2, activated by interaction with framework titanium, is in the vicinity of a molecule of free pyridine. This situation declines in probability as the amount of N-oxide in the reaction system builds up. An analogous situation has already been described in the acetylation of anisole by acetic anhydride in the presence of zeolite H-β [5].

Further light on this situation is shed by the results of reactions in which 1 : 1 mixtures of pyridine (0.025 mol) and 2-picoline (0.025 mol) and of 2- and 4-picolines (0.025 mol of each) were allowed to compete for H_2O_2 (0.05 mol) using method A. The yields of the two N-oxides produced are given in table 2 and again these reflect the initial reaction rates. Clearly, 2-picoline reduces the conversion of pyridine to the N-oxide somewhat, but the presence of pyridine inhibits the formation of 2-picoline N-oxide almost completely, i.e., to the background level. In the case of the mixture of 2- and 4-picolines, which have closely similar pK_a-values, formation of both products is reduced by about two thirds. Again the pattern of results is consistent with competitive binding of the heterocycles within the pores of TS-1.

We conclude that heterogeneous N-oxidation of pyridine and substituted pyridines using H_2O_2 in the presence of TS-1 and other microporous catalysts needs to be interpreted with caution. The uncatalysed process can make control of the reaction difficult. In addition, reactivity cannot be simply predicted on the basis of the electronic characteristics of the heterocycle, but results from a complex interplay of competitive interactions between the catalyst, the reactants and the products.

References

[1] M.R. Prasad, G. Kamalakar, G. Madhavi, S.J. Kulkarni and K.V. Ragharan, J. Chem. Soc. Chem. Commun. (2000) 1577.

[2] D.J. Robinson, P. McMorn, D. Bethell, P.C. Bulman-Page, C. Sly, F. King, F.E. Hancock and G.J. Hutchings, Phys. Chem. Chem. Phys. (2000) 1523.

[3] M. Taramasso and B. Notari, US Patent 4410501 (1983).

[4] H.H. Perkampus and G. Prescher, Ber. Bunsenges. Physik. Chem. 72 (1968) 429.

[5] E.G. Derouane, C.J. Dillon, D. Bethell and S.B. Derouane-Abd Hamid, J. Catal. 187 (1999) 209.