Regioselective *N*-Alkylation of Imidazoles with Alcohols over Zeolites

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Vapour-phase alkylation of 4(5)-methylimidazole with MeOH over Y-zeolites selectively gave 1,5-dimethylimidazole in high yield, while the alkylation over Beta-zeolite gave 1,4-dimethylimidazole predominantly.

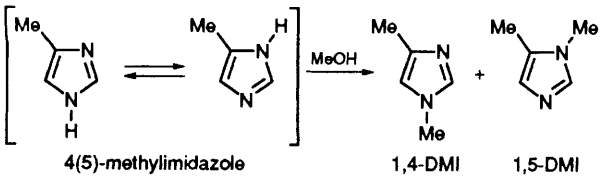
Methyl halides or dimethyl sulfate have been used as methylating agents for imidazoles.[1–5] However, alkyl halides and dialkyl sulfates are highly toxic and corrosive, and more than a stoichiometric amount of strong bases such as $NaNH_2$ and NaOH is required. To avoid these disadvantages, we tried the vapour-phase *N*-alkylation of imidazoles using alcohols as the alkylating agents and zeolites catalysts. Among zeolites, Y-type zeolites were found to be the most active.

4-Methylimidazole exists in a tautomeric equilibrium with 5-methylimidazole,[1,2,6] and so selective *N*-alkylation of 4(5)-methylimidazole to 1,4-dimethylimidazole (1,4-DMI) or 1,5-dimethylimidazole (1,5-DMI) (Scheme 1) is difficult. It has been reported that methylation of 4(5)-methylimidazole with methyl iodide or dimethyl sulfate gives 1,4-DMI and 1,5-DMI in *ca.* 2 : 1 ratio.[2,4,5]

We report here that 4(5)-methylimidazole can be selectively transformed into 1,5-dimethylimidazole with MeOH over Y-zeolites.

The zeolites used are NaX (SiO_2/Al_2O_3 = 2.5), NaY (SiO_2/Al_2O_3 = 5.6), H-ZSM-5 (SiO_2/Al_2O_3 = 43.5), and H-Beta (SiO_2/Al_2O_3 = 60). The Na form of Y-zeolite was ion-exchanged with NH_4Cl to obtain the NH_4 form, which was converted into H-Y by heating in the reactor at 823 K. The reactions were carried out with a fixed-bed reactor (10 mm i.d.) under atmospheric pressure. A solution in MeOH of 4(5)-methylimidazole (3 : 1 molar ratio) was fed into the reactor with a motor driven syringe. The products were collected in an ice trap and analysed by GC.

The catalytic activities of various zeolites for methylation of imidazole were examined at 553 K. Imidazole, MeOH and N_2 were fed to 0.5 g of catalyst with flow rates of 9.6, 28.6 and 40.7 mmol h^{-1}, respectively. Only *N*-methylation occurred in every case. Among zeolites studied, H-Y was far more active than any of the other catalysts. H-Y gave 100% conversion of imidazole into 1-methylimidazole, while H-Beta and H-ZSM-5 gave 1-methylimidazole in yields of 65 and 64%, respectively. Alkaline metal exchanged zeolites showed much lower activity than H-Y, indicating protons are active centres for the methylation. No catalyst deactivation was observed. H-Y was also active for ethylation of imidazole by EtOH into 1-ethylimidazole. Thus, a 100% yield of 1-ethylimidazole was obtained at 573 K. 2-Methylimidazole is also *N*-alkylated by MeOH and EtOH to the corresponding 1-alkyl-2-methylimidazole at 573 K in 92.5 and 93% yields, respectively.



Scheme 1

Table 1 *N*-Alkylation of 4(5)-methylimidazole by alcohols over zeolites[a]

Alcohol	Catalyst	*T*/K	Conversion (%)	Selectivity (%) 1,4	1,5
Methanol	H-Y	503	32	6	94
	H-Y	533	77	11	89
	H-Y	553	100	23	77
	H-Beta	553	12	78	22
	H-Beta[b]	553	45	69	31
	H-ZSM-5	533	14	72.5	27.5
Ethanol	H-Y	533	59	17	83
	H-Y	573	100	23	77
Propan-1-ol[c]	H-Y	573	45	19	81
	H-Y	593	61	22	78

[a] Flow rate of 4(5)-methylimidazole, 8.7 mmol h^{-1} (*b* 4.4 mmol h^{-1}), imidazole : alcohol : N_2 molar ratio, 1 : 3 : 4.5. Catalyst, 0.5 g. [b] 0.80 g catalyst. [c] 0.82 g catalyst.

The results of the alkylation of 4(5)-methylimidazole by alcohols over H-Y, H-Beta, and H-ZSM-5 are listed in Table 1. The most interesting feature is that the selectivity for 1,4-DMI and 1,5-DMI depends on the zeolite used. In the methylation over H-Beta and H-ZSM-5, 1,4-DMI was the predominant product. With methylation over H-Beta, the ratio of 1,4-DMI/1,5-DMI was 3.5, which is greater than the ratios (*ca.* 2) reported for the methylation by MeI[2,5] or dimethyl sulfate.[2,4] As in the methylation of imidazole, H-Y showed much higher activity than H-Beta or H-ZSM-5. In contrast to H-Beta and H-ZSM-5, H-Y gave a very high selectivity for 1,5-DMI. Thus, at 553 K, the yield of DMI was 100%, the ratio of 1,4-DMI : 1,5-DMI being 23 : 77. At 503 K, this ratio was still higher, 6 : 94. The preferential formation of 1,5-isomers in the alkylation of 4(5)-methylimidazole has never been reported. The alkylation of 4(5)-methylimidazole was also carried out over non-zeolite catalysts, namely $H_3PW_{12}O_{40}$ and phosphoric acid supported on silica. These two strongly acidic catalysts gave similar conversion and selectivity values to H-Beta and H-ZSM-5, showing that the selectivity is not determined by the pore structure, but by the acid strength of the catalysts. The weakly acidic catalyst like H-Y favours the formation of 1,5-dimethylimidazole.

Preferential formation of 1,5-isomers was also observed in the alkylation of 4(5)-methylimidazole by EtOH and propan-1-ol over H-Y. As shown in Table 1, the ratio of 1-ethyl-4-methylimidazole and 1-ethyl-5-methylimidazole for the ethylation product was 23 : 77 and 17 : 83 at 573 K and 533 K, respectively. The ratio of 1-propyl-4-methylimidazole and 1-propyl-5-methylimidazole was 19 : 81 for the propylation at 573 K and 22 : 78 at 593 K. 1-Isopropyl-4(or 5)-methylimidazole was not formed, indicating that the dehydration of alcohol molecules and *N*-alkylation proceed in a concerted manner and that no free alkyl cations are formed as intermediates.

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