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Methylation of pyridin-2-one with methanol over γ-alumina in vapor phase

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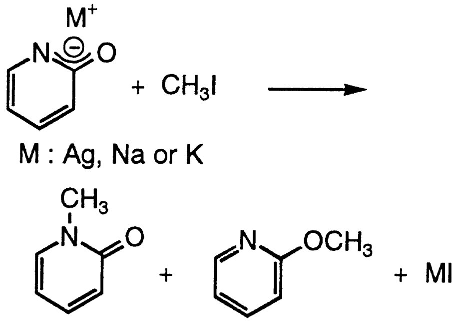
Pyridin-2-one reacts with methanol over γ-alumina in the vapor phase to afford exclusively 1-methylpyridin-2-one. Thus, 1-methylpyridin-2-one was obtained in a 99% selectivity at a 100% conversion at 573 K.

Keywords: pyridin-2-one, methylation, alumina, alkylation

1. Introduction

The alkylation of pyridin-2-ones has been extensively studied for 2-alkoxypyridine and 1-alkylpyridin-2-one, which are valuable synthetic intermediates [1]. The alkylation is generally performed by reacting a metal salt of pyridin-2-one with an alkyl halide [1–3]. The regioselectivity depends on the nature of the metal. Heterogeneous alkylation of the silver salt of pyridin-2-one with methyl iodide usually gives exclusive O-alkylation, whereas alkylation of the sodium or potassium salt predominantly gives N-alkylation:

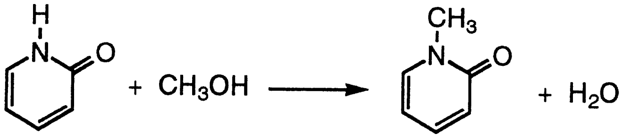


Pyridin-2-one can also be methylated with dimethyl phosphite [4]. This reaction exclusively gives 1-methylpyridin-2-one (81% yield) at 444 K, while the products at 373 K were 1-methylpyridin-2-one (52% yield) and 2-methoxypyridine (5% yield). It has also been shown that pyridin-2-one is easily alkylated with alcohols under Mitsunobu conditions [5].

However, the reaction with methyl halides has some important drawbacks: methyl halides are corrosive and toxic, and a stoichiometric amount of by-product, silver or sodium halide, is formed. Therefore, the method is not environmentally preferable. Moreover, liquid-phase methylation has the difficulty of the work-up procedures such as separation of the products from the reaction mixture. Vapor-phase methylation with methanol, which is non-corrosive and much less toxic than methyl halides, might provide a useful synthetic way to avoid these difficulties.

Ono et al. have reported that nitrogen-containing heterocyclic compounds such as imidazoles can be easily N-alkylated with alcohols over acidic zeolites in the vapor-phase [6–8]. Thus, the reaction of imidazole with methanol gave a 100% yield of 1-methylimidazole over H-Y zeolites.

This is to report that the vapor-phase methylation of pyridin-2-one gives almost exclusively 1-methylpyridin-2-one in a high yield:



2. Experimental

γ-alumina was obtained from Mizusawa Chemical Corp. Ltd. The Si / Al ratios of zeolites H-Y (and Na-Y), H-ZSM-5, H-beta were 2.8, 43.5, and 30, respectively. The reaction was carried out in a fixed-bed reactor at atmospheric pressure at 553 or 573 K. The catalyst (5 g) was packed in a reactor of quartz-tubing (10 mm i.d.) and pretreated in an air stream at 773 K for 1 h. The mixture of pyridin-2-one and methanol was fed to the reactor at a motor-driven syringe. The molar ratio of methanol to pyridin-2-one was 4 or 6, where the partial pressure of methanol was 45 kPa. The flow rate of methanol was 15 or 16 mmol h^{-1}. The products were trapped in ethanol and analyzed by gas-chromatography every 1 h.

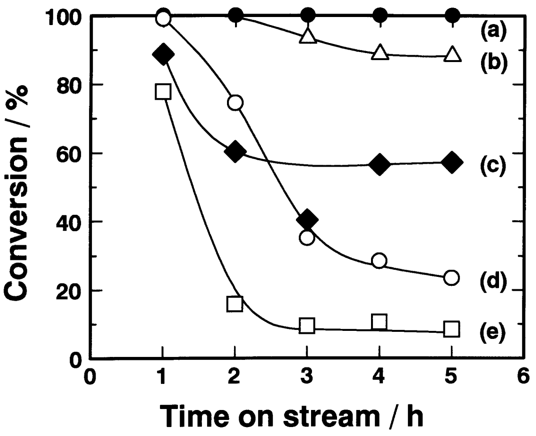


Figure 1. Change in the conversion of pyridin-2-one with time on stream using various catalysts. The amount of catalyst: 0.5 g. Reaction temperature: 573 K. CH_3OH pressure: 45 kPa. (CH_3OH/pyridin-2-one) = 6. Methanol feed rate: 16 mmol h^{-1}. The catalysts are (a) γ-alumina, (b) H-Y, (c) H-ZSM-5, (d) H-β and (e) Na-Y.

Table 1
The conversion of pyridin-2-one and the selectivities for the products over various solid catalysts [a]

Catalyst	Conversion (%)	Selectivity (%)	
		1-methylpyridin-2-one	2-methoxypyridine
γ-alumina	100	99	1
alumina [a]	97	98	0
H-Y	99	79	5
H-ZSM-5	60	89	9
H-β	75	55	3
Na-Y	16	72	20

[a] The amount of catalyst: 0.5 g. Reaction temperature: 573 K. CH_3OH pressure: 45 kPa, (CH_3OH/pyridin-2-one) = 6. Methanol feed rate: 16 mmol h^{-1}. The results were obtained between 1.5 and 2.5 h.

[b] Obtained from Nishio Industry Co. Ltd.

3. Results and discussion

Figure 1 shows the change in the conversion of pyridin-2-one over various solid acids. In the reaction over γ-alumina, a 100% conversion was kept at least for 5 h. Over the other catalysts, especially H-beta and Na-Y, the conversion decreased with time on stream. In table 1, the conversion of pyridin-2-one and the yields of 1-methylpyridin-2-one and 2-methoxypyridine at time on stream of 2 h over these catalysts are listed. γ-alumina gave a 100% conversion and a very high selectivity for N-methylation (99%). This value of the selectivity is higher than that in the liquid-phase reaction of the sodium salt of pyridin-2-one with methyl iodide [1–3]. Alumina from Nishio Industry Co. Ltd. also showed about 100% conversion and a very high selectivity for N-methylation. Over H-Y, a high conversion of pyridin-2-one was also attained, but the selectivity for 1-methylpyridin-2-one was lower. H-ZSM-5 and H-beta were much less active. Na-Y gave a lower conversion, but showed the highest selectivity for O-methylation (20%). The effects of the reaction variables on the methylation of pyridin-2-one are summarized in table 2. The conversion of pyridin-2-one was 80% and 100% at 553 K and 573 K, respectively. When the contact time was varied at 573 K, the conversion increased with increasing contact time. The selectivity for N-methylation was always high (99%).

The plausible mechanism for the methylation is given in scheme 1.

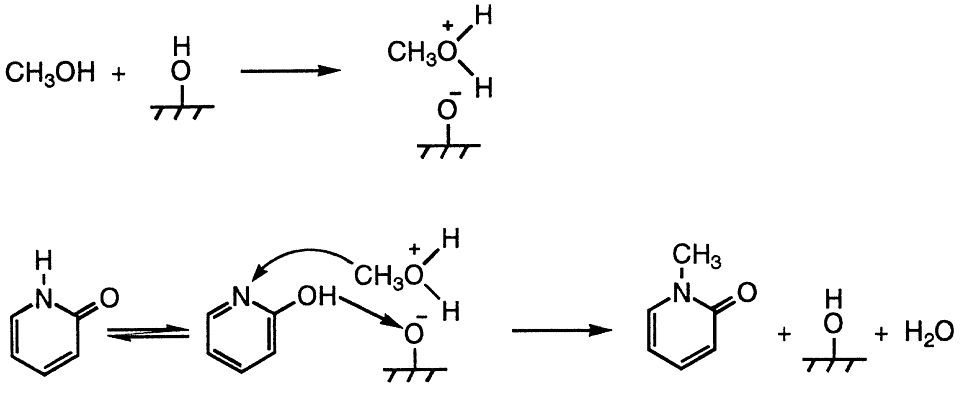
It is presumed that alumina behaves as a Brønsted acid in the presence of water (a reaction product) under the reaction conditions. Methanol molecules interact with the surface acidic OH groups to form protonated methanol. Pyridin-2-one and 2-hydroxypyridine are in tautomeric equilibrium. The protonated methanol attacks at the nitrogen atom of 2-hydroxypyridine rather than the oxygen atom of pyridin-2-one, because the former is more basic than the latter, leading to the formation of 1-methylpyridin-2-one and water. A smaller part of the protonated methanol reacts with pyridin-2-one or 2-hydroxypyridine at their oxygen atoms to form 2-methoxypyridine.

In conclusion, the vapor-phase methylation of pyridin-2-one with methanol over γ-alumina offers a very convenient and selective way to produce 1-methylpyridin-2-one.

Table 2
The conversion of pyridin-2-one and the selectivities for the products over γ-alumina [a]

Temperature (K)	W/F (g h mol^{-1})	Conversion (%)	Selectivity (%)	
			1-methylpyridin-2-one	2-methoxypyridine
573	14.6	100	99	1
573	10.9	98	99	1
573	7.3	83	99	1
553	14.6	80	99	1

[a] The amount of catalyst: 0.5 g. CH_3OH pressure: 45 kPa. (CH_3OH/pyridin-2-one) = 4. Methanol feed rate: 15 mmol h^{-1}.



Scheme 1.

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