Reaction of piperidine with formaldehyde over alumina and spinel aluminates

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Received 20 July 1995; accepted 7 December 1995

The reaction of piperidine with formaldehyde over γ-alumina, Na^+–γ-alumina, $NiAl_2O_4$ and $CuAl_2O_4$ was studied as a model system in order to understand the mechanism and selectivity of alkylpyridine formation from piperidine and carbonyl compounds. Along with the expected 3-picoline, 2-picoline and other products were also formed. The selectivity for 3-picoline was high on γ-alumina whereas on $NiAl_2O_4$, 2-picoline was selectively formed. The formation of the different products has been rationalized and a probable mechanism for the formation of 2-picoline has been presented.

Keywords: piperidine; formaldehyde; 3-alkylpyridine; selective synthesis; mechanism

1. Introduction

Alkylpyridines are important intermediates for various industries. Direct alkylation of pyridine, unlike that of benzene, is largely unsuccessful, though there are recent reports on the methylation of pyridine in the vapor phase using zeolites and other oxide catalysts [1–4]. Commercially the methylpyridines and other simple alkyl derivatives are obtained by direct ring synthesis procedures [5] or from natural sources. In this context, a reported process for the selective catalytic synthesis of 3-alkylpyridines by the reaction between piperidine and carbonyl compounds [6,7] has assumed importance, especially when the alkyl group consists of three carbons or more for which other selective synthetic procedures are not available.

The process under discussion involves passing a mixture of piperidine and an aldehyde or ketone over γ-alumina at about 420°C. An analogous reaction is the earlier reported formation of 3,5-dibenzylpyridines by the reaction between benzaldehyde or substituted benzaldehydes and piperidine in the liquid phase in the presence of acetic acid [8–10]. The mechanism of the formation of 3-alkylpyridine has been shown to be as depicted in scheme 1, adopted from previous reports [6–10].

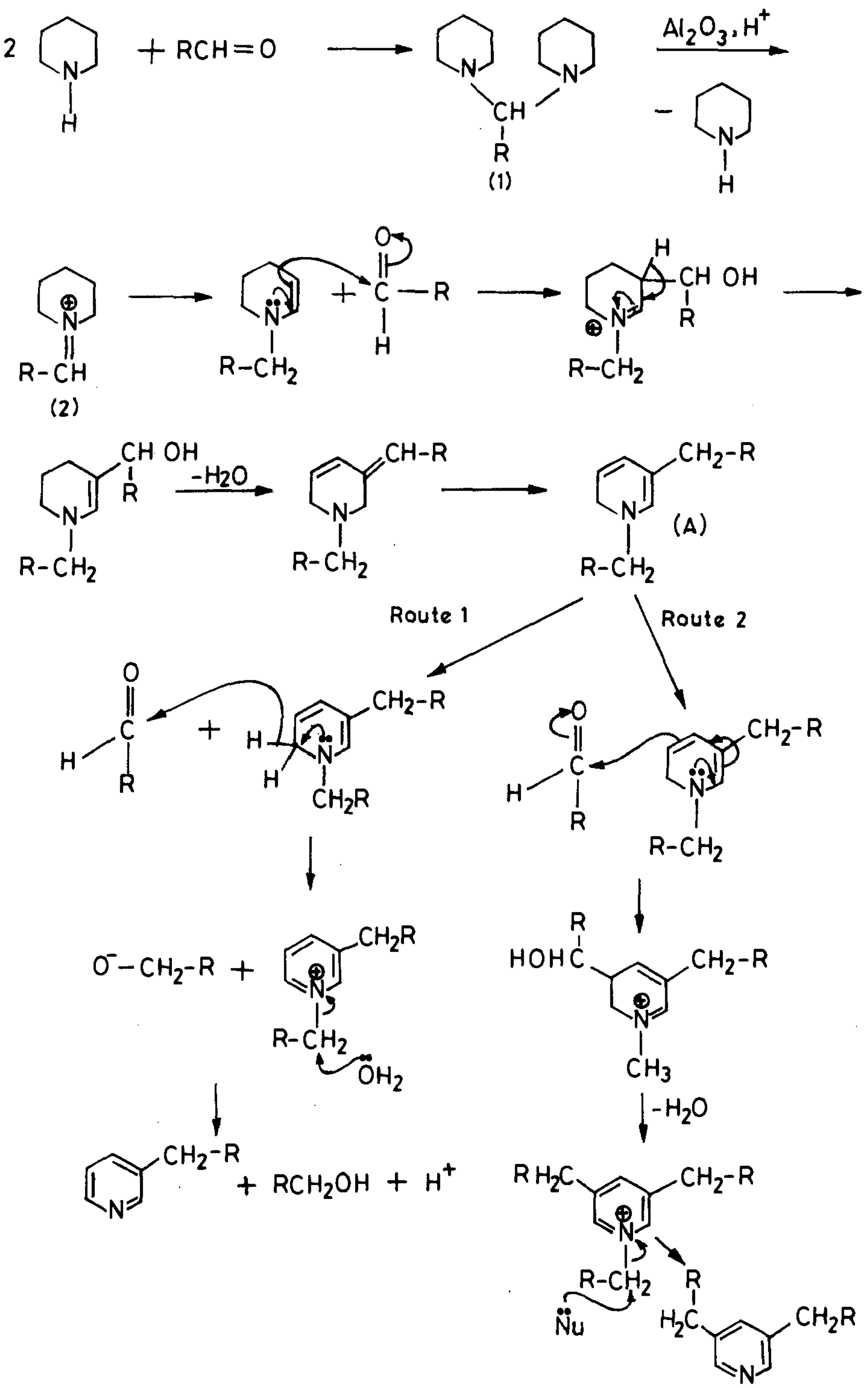
During the course of studies for the development of new catalysts for this reaction for better yields of alkylpyridines, it was found that the high selectivity for 3-alkylpyridines was shown only by γ-alumina and other catalysts such as Na^+–γ-alumina, and mixed oxides such as copper aluminate and nickel aluminate showed less selectivity and on $NiAl_2O_4$, the selectivity was more for 2-alkylpyridines. This suggested that on catalysts other than γ-alumina, the mechanism of the reaction is more complex than that represented in scheme 1. This prompted us to take up a study of the dependence of the selectivity on the nature of the catalysts and alternate mechanisms that might be operating. For this purpose, as a model system, the reaction of piperidine with formaldehyde was taken up even though the reaction is of little commercial value for the production of picolines.

2. Experimental

The γ-Al_2O_3 was a commercial catalyst from Merck-Sarabhai. Na/γ-Al_2O_3 was prepared by impregnating γ-Al_2O_3 with Na_2CO_3 solution (0.01 M) for 12 h under stirring, filtering, washing and drying. The percentage of Na in the sample was estimated by standard volumetric methods.

$NiAl_2O_4$ and $CuAl_2O_4$ were prepared as spinel phases by coprecipitating the nitrate solutions of the respective ions in stoichiometric ratio using 10% ammonia solution at an appropriate pH. After the precipitation was complete, the solutions were aged overnight, filtered and washed thoroughly with hot distilled water (slightly made ammoniacal) and dried at 110°C. Then the precipitates were calcined under slow heating to a final temperature of 980°C and heated with intermittent grindings at this temperature for 24 h. X-ray analysis (Phillips PW 1140) of the samples showed single phase formation of the respective spinels. Surface areas of the samples as measured by Carlo-Erba Strumentazione Microstructure Lab were in the range of 40–120 m^2/g.

Catalytic studies were made using vertical fixed bed flow reactors (i.d. 8 mm) under atmospheric conditions using 1 cm^3 of the catalyst in the temperature range 250–450°C. Piperidine and trioxane were mixed beforehand in the required molar proportions (a small quantity of benzene was used as the solvent when required) and this mixture was injected onto the reactor with the help of a



Scheme 1.

mechanically driven infusion pump at a uniform flow rate of 5 ml/h. The products of the reaction were collected for 1 h from the start of the reaction and were analyzed by GC (Hewlett Packard 5890). Identification of the products was done using authentic samples and comparing the IR and NMR data after fractionation of the product mixture in certain cases.

The catalysts were activated/regenerated by heating at 500°C in air for 4 h and then flushing with N_2 for 2 h at the same temperature. Then the catalysts were cooled

Table 1
Reaction of piperidine with formaldehyde over γ-Al_2O_3 and Na-γ–Al_2O_3 [a]

Catalyst	T (°C)	P/F	% conversion (unit activity per m^2/g)	% selectivity					
				py	2-pic	3-pic	vinpy	dimepy	others
γ-Al_2O_3	250	2.0	25 (0.206)	2.0	2.3	4.5	16.0	69.9	5.3
	300	2.0	27 (0.227)	3.3	8.7	9.3	37.2	37.1	4.4
	350	2.0	33 (0.277)	–	4.4	22.5	55.7	12.9	4.5
	450	2.0	53 (0.438)	–	7.7	56.3	20.0	9.1	6.9
	350	0.5	56 (0.468)	–	4.0	76.0	4.0	9.0	7.0
	375	0.5	67 (0.553)	–	3.0	71.0	6.0	13.0	7.0
	400	0.5	72 (0.60)	–	2.0	68.0	6.0	15.0	9.0
	420	0.5	82 (0.678)	–	1.0	66.0	4.0	19.0	10.0
	450	0.5	76 (0.626)	–	1.1	59.0	5.0	22.0	12.9
	420	5.0	17 (0.142)	–	2.0	98.0	–	–	–
Na/γ-Al_2O_3	360	2.0	19 (0.254)	–	–	24	61	18	4
	400	2.0	32 (0.459)	–	14	50	29	2	6
	450	2.0	27 (0.361)	–	17	50	13	12	–

[a] 10 ml flow rate; P/F: piperidine to formaldehyde molar ratio; py: pyridine; 2-pic: 2-picoline; 3-pic: 3-picoline; vinpy: vinylpyridine; dimepy: dimethylpyridine; others: higher alkylpyridines.

to the required reaction temperatures and the catalytic studies were carried out.

3. Results and discussion

The results of the reaction between piperidine and γ-alumina are presented in table 1. In some of the experiments using formalin instead of trioxane as the source of formaldehyde (not reported in table 1) dipiperidylmethane ([1], scheme 1) was also detected in small quantities. Two piperidine/formaldehyde (P/F) ratios, namely, 2.0 and 0.5 were studied in the temperature range 250–450°C. The liquid flow rate was fixed at 5 ml/h for optimum conversion. In the table the actual %conversion of piperidine as well as conversion per unit surface area of the catalyst are reported, the latter in order to facilitate comparison of activity with other catalysts (table 2) which differ in surface area.

The major monoalkylation product on γ-alumina at all temperatures was 3-picoline, consistent with scheme 1, but 3-picoline was not the only product. Significant quantities of 2-picoline, 3-vinylpyridine, 3,5-dimethylpyridine, higher alkylpyridines and various other minor components were formed. The formation of the first three deserve discussion. At the lower temperature, 250°C, 3,5-dimethylpyridine was the major product.

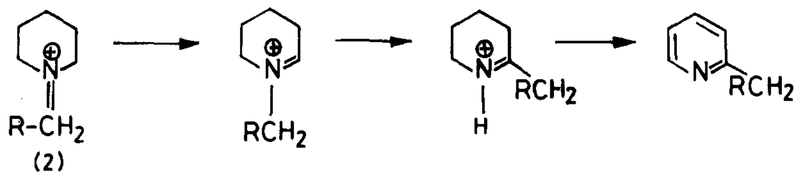
It can be seen from scheme 1 that 3-methyl and 3,5-dimethylpyridine represent the two routes of further reaction of the intermediate (A) (R = H). Route 1, leading to monomethylpyridine involves a hydride transfer step and is likely to have higher activation energy than route 2, which is an enamine reaction. Hence, at the lower temperature 3,5-dimethylpyridine (route 2) predominates. It may be recalled that in the liquid phase reaction between benzaldehyde and piperidine (< 100°C), 3,5-dibenzylpyridine is the only reported product [8–10].

Vinylpyridines are also major products. Base catalyzed condensation of picolines with aldehydes is well known. 2- and 4-methylpyridines are more reactive than

Table 2
Reaction of piperidine with formaldehyde on spinel oxides [a]

Catalyst	T (°C)	P/F	% conversion (unit activity per m^2/g)	% selectivity					
				py	2-pic	3-pic	vinpy	dimepy	others
$NiAl_2O_4$	350	0.5	47 (1.063)	13	28	–	57	2	–
	400	0.5	63 (1.425)	5	55	3	37	10	–
	450	0.5	82 (1.855)	17	61	1	14	7	–
$CuAl_2O_4$	350	0.5	42 (1.129)	–	19	12	26	11	10
	400	0.5	55 (1.478)	–	23	16	20	7	5
	450	0.5	69 (1.855)	13	40	26	11	–	1

[a] P/F: piperidine to formaldehyde molar ratio; py: pyridine; 2-pic: 2-picoline; 3-pic: 3-picoline; vinpy: vinylpyridine; dimepy: dimethylpyridine; others: higher alkylpyridines.



Scheme 2.

3-methylpyridine in this reaction because of the greater acidity of the methyl hydrogen in the former isomers. Vinylpyridines undergo ready polymerization. Yield for vinylpyridine is higher when P/F ratio is 2 than when it is 0.5, and increases to a maximum at 350°C and thereafter decreases. The decrease of yield at higher temperatures may be due to further reactions including polymerization of the vinylpyridine.

Since the formation of vinylpyridine is a function of the basicity of the catalyst, γ-alumina impregnated with Na^+ was prepared. This is expected to increase the basicity of alumina [11]. The Na^+–γ-alumina catalyst showed lower overall activity and a better selectivity for vinylpyridine, as expected.

Contrary to the expectation from previous reports [6,7], 2-picoline was also a minor but significant product over γ-alumina. It is significant because scheme 1 does not allow the formation of 2-picoline. It was also shown by independent experiments that γ-alumina did not catalyze the isomerization of the methylpyridines or the direct alkylation of pyridine by methanol [3,4]. Hence, 2-picoline is formed by a route other than that described in scheme 1. In the earlier studies [6,7] any 2-alkylpyridine formed might have been missed, since they are formed only in small quantities. Slightly more 2-picoline is formed when the P/F ratio is 2 than when it is 0.5. Also, it is substantially more on Na^+–γ-alumina and also on the spinel oxides discussed below.

Table 2 gives the results on two spinel oxides $NiAl_2O_4$ and $CuAl_2O_4$. $NiAl_2O_4$ represents an interesting situation where the selectivity is reversed and the major products are 2-methyl and 2-vinylpyridine with smaller quantity of 2,4-dimethylpyridine and negligible amount of 3-picoline. The selectivity in $CuAl_2O_4$ is intermediate between that on Al_2O_3 and $NiAl_2O_4$. Formation of 2-picoline has analogy in the literature to the isomerization of N-methylpyridinium ion upon heating to 2- and 4-methylpyridines (the Ladenburg rearrangement). The intermediate **2** of scheme 1 can lead to 2-picoline by such a rearrangement (scheme 2). This proposal is speculatory and requires substantiation and a proper explanation for the change in selectivity in going from Al_2O_3 to $NiAl_2O_4$ is yet not available. The two catalysts represent promising routes for the selective synthesis of 3- and 2-alkylpyridines and their application to the synthesis of higher alkylpyridines will be reported at a later date.

Acknowledgement

The authors thank Professor C.S. Swamy for the facilities provided. One of the authors (UK) thanks Department of Science and Technology, New Delhi, India for the funding under the Young Scientist Scheme.

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