Russian Journal of Applied Chemistry, Vol. 78, No. 7, 2005, pp. 1093–1095. Translated from Zhurnal Prikladnoi Khimii, Vol. 78, No. 7, 2005, pp. 1114–1116.

CATALYSIS

Synthesis of 2-Methylpyrazine on Ternary Oxide Catalysts

A. D. Kagarlitskii, L. A. Krichevskii, and D. S. Balpanov

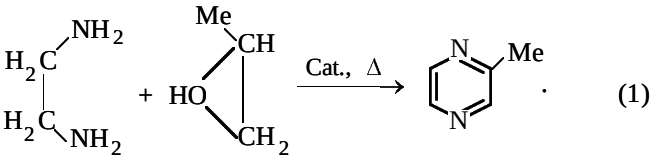
Institute of Phytochemistry, Ministry of Education and Science of the Kazakhstan Republic, Karaganda, Kazakhstan

Received July 20, 2004; in final form, April 2005

Abstract—Synthesis of 2-methylpyrazine by cyclocondensation of ethylenediamine with 1,2-propylene glycol in the presence of zinc–molybdenum–chromium catalysts was studied.

2-Methylpyrazine (MP) is used as an intermediate in synthesis of pyrazine-2-carboxamide (the basis of Pyrazinamide antituberculous drug [1]), but the existing procedures of its preparation are not perfect.

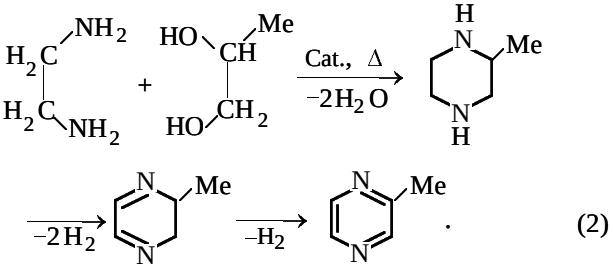
MP can be prepared by the reaction of propylene oxide with ethylenediamine (EDA) in methanol in the presence of zinc–molybdenum–chromium oxide catalyst (yield 63%) [2]:



(1)

The similar process was developed by the Prikladnaya Khimiya Russian Scientific Center [3]. An important draw-back of this process is the use of highly explosive initial products (propylene oxide and hydrogen) and of toxic methanol as a solvent.

From the viewpoint of industrial safety and availability of fairly cheap starting compounds, the catalytic dehydrocyclization of EDA with 1,2-propylene glycol (1,2-PG) is a more promising route to MP:



(2)

The attempts to use Al_2O_3 as a catalyst of this process failed due to its low selectivity [4]. However, the purity of alkylpyrazines was improved and the yield of MP was increased to 64% with zinc oxide catalysts [5–7].

In dehydrocyclization of EDA with 1,2-PG on the Pd/Zn–Cr–O catalyst (Zn : Cr = 1 : 3), the limiting stage of the process is the reaction of 1,2-PG adsorbed on the catalyst surface with EDA supplied with the gas phase to form MP (387°C) [8]. The system EDA–1,2-PG is more complicated than that described by the reaction equation, since synthesis of MP is accompanied by formation of by-products [9].

Initially this process was studied in the presence of granulated binary zinc–molybdenum oxide catalysts. The highest yield (75%) was obtained with the catalyst of the composition ZnO : MoO_3 = 1.0 : 0.3 (granule size 1.0–2.0 mm) [10].

EXPERIMENTAL

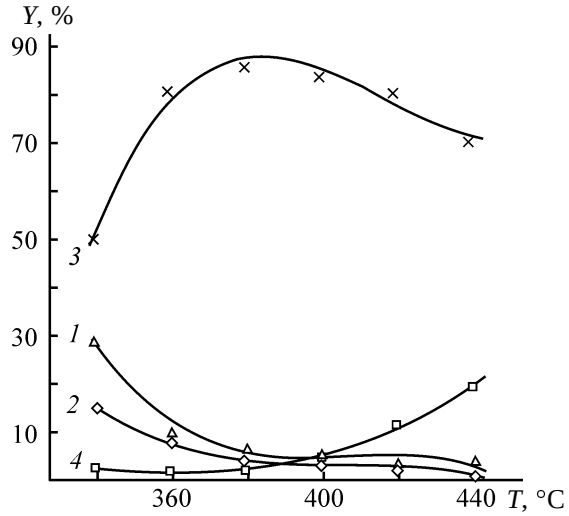
To increase the yield of the target product through decreasing the amount of polymeric deposits at the catalyst surface, it was suggested to add chromium(III) oxide to binary oxide systems, since Cr_2O_3 has high oxidation and dehydrogenation power. In addition, it was assumed that, owing to its characteristics, it will enhance the mechanical strength of the catalyst granules during thermal drying.

Table 1 shows how the ratio of components of

Table 1. Yield of MP at various catalyst compositions. Temperature 460°C, contact time 3.3 s

Molar ratio ZnO : MoO_3 : Cr_2O_3	Catalyst operation time, h	Yield of MP, %
1.00 : 0.30 : 0.05	7	67
1.00 : 0.30 : 0.10	9	78
1.00 : 0.30 : 0.15	10	69
1.00 : 0.40 : 0.10	23	73
1.00 : 0.40 : 0.15	27	82
1.00 : 0.40 : 0.20	21	76
1.00 : 0.50 : 0.15	17	71
1.00 : 0.50 : 0.20	22	76
1.00 : 0.50 : 0.25	24	64

1070-4272/05/7807-1093



Yield in synthesis of MP *Y* as a function of the process temperature *T* at a contact time of 4.2 s. (*1*) EDA, (*2*) 1,2-PG, (*3*) MP, and (*4*) PCPs.

mixed zinc–molybdenum–chromium oxide granulated catalyst affects the MP yield.

The yield of the target product on the catalysts tested was from 65 to 82%. When the content of zinc and molybdenum(III) oxides in these catalysts corresponded to the molar ratio of 1.0 : 0.3, they lost their activity and selectivity in 7–10 h, whereas at the molybdenum(III) oxide content of 0.4 and 0.5 mol per mole of zinc oxide they operated without regeneration for a period from 21 to 27 h depending on the amount of chromium(III) oxide added.

Table 2. Yield of MP at various contact times τ_c. Temperature 390°C

τ_c, s	Unchanged, wt %		Yield, %	
	EDA	1,2-PG	PCPs	MP
1	2	3	4	5
1.5	15	18	2	65
3.0	10	12	1	77
4.4	3	5	4	88
6.0	2	4	10	85
7.5	2	5	21	72
9.0	1	2	32	55

Table 3. Yield of MP at various time τ. Temperature 390°C, contact time 4.4 s

τ_c, s	Unchanged, wt %		Yield, %	
	EDA	1,2-PG	PCPs	MP
10	16	2	5	77
20	8	3	3	86
30	4	5	1	90
40	2	8	2	87
50	1	9	5	85
60	5	11	10	74

The best result were obtained with the catalyst of the composition $ZnO : MoO_3 : Cr_2O_3$ = 1.00 : 0.40 : 0.15.

The yield of MP exceeding 70% is reached on this catalyst in a wide temperature range, from 370 to 430°C, and the highest yield (80–90%), at 380–395°C, which is a relatively low temperature for these reactions (see figure).

As regards contact time, it can be varied in a wide range (from 1.5 to 7.5 s), and in this case the yield of MP can be no less than 65% due to decreasing content of polycondensation products (PCPs) in the catalyzate (Table 2). In the range 4.4–6.0 s, the yield of the target product reaches 80–88%.

Evaluation of the working time of the catalyst showed that the catalyst is able to operate for 55–57 h without noticeable variation of selectivity with respect to the target product, ensuring its yield as high as 85–90% (Table 3).

The $ZnO : MoO_3 : Cr_2O_3$ = 1.0 : 0.4 : 0.15 catalyst was prepared by mixing zinc, molybdenum(III), and chromium oxides to obtain a homogeneous mass. Granules were prepared from this mixture on a pan granulator with adding 5% NaOH and 10% aqueous polyvinyl alcohol for strengthening. The granules were sifted through a sieve, and a 1.0–2.0-mm fraction was collected. Then, the granules were dried for 3 h at 105°C. Dry granules were promoted with 3% aqueous $MnSO_4$ and 1% H_3PO_4. After promotion, the granules were subjected to air calcination for 5 h with a stepwise increase in temperature in the range 100–150, 150–250, 250–350, and 350–600°C. The final catalyst consists of greenish porous granules.

MP was synthesized on an installation equipped with a stainless steel flow-type tubular reactor (tube diameter 20 mm, length 80 cm), in which 150 cm^3 of the catalyst was placed. An equimolar mixture of EDA with 1,2-PG, diluted with water (20 vol %) and preliminarily passed through a vapor heater with a temperature of 280–300°C, was fed to the reactor. The experiments were carried out for 1 h. The reaction products were cooled in a trap system. In a typical synthesis, a mixture containing 67 ml of EDTA (1 mol), 73 ml of 1,2-PG (1 mol), and 28 ml of water

(1.56 mol) was fed into the reaction mixture with a dosing pump at a rate of 0.79 ml min^{-1}. MP was isolated from the reaction mixture by distillation on a column in the form of an azeotropic mixture with water (bp 97°C/737 mm Hg, MP content 45% [11]), from which the target product was extracted with chloroform or diethyl ether. After drying and removal of the solvent, MP was extracted by distillation on a column; a fraction with bp 133–135°C was collected. After the second distillation, MP had the following characteristics: bp 135°C, n_D^{20} 1.5050, d_4^{20} 1.030, which is in good agreement with published data [12].

The quantitative content of the unchanged starting components and the reaction product was determined by gas–liquid chromatography (Chrom-5, flame-ionization detector, glass column 3.5 m long with 0.3 cm inner diameter, packed with Chromaton NAW-HMDS and 5% SE-30 silicone elastomer); column temperature 150°C, vaporizer temperature 180°C, detector temperature 190°C; carrier gas argon, flow rate 20 ml min^{-1}.

Quantitative analysis was performed using benzonitrile as internal reference.

CONCLUSION

The catalyst Zn : MoO_3 : Cr_2O_3 = 1.00 : 0.40 : 0.15 was developed. The use of this catalyst in cyclocondensation of ethylenediamine with 1,2-propyleneglycol allows preparation of 2-methylpyrazine in 85–90% yield. The working life of the new catalyst before regeneration reaches 50–55 h, and the total working life of the catalyst is 400–450 h.

REFERECES

1. Mashkovskii, V.V., Shchekina, E.G., and Chernova, T.M., *Provizor*, 2002, no. 10, pp. 44–46.
2. JPN Patent Appl. no. 55-45610.
3. *TU* (Technical Specifications) *24-44-00480689–94: 2-methylpyrazine*, St. Petersburg: Prikladnaya Khimiya Russia Scientific Center, 1994.
4. Okada, D. and Nakano, K., *Yakugaku Zasshi*, 1971, vol. 91, no. 3, pp. 416–421.
5. US Patent no. 4097478.
6. JPN Patent Appl. no. 54-132588.
7. JPN Patent Appl. no. 53-37675.
8. Forni, L. and Polessel, P., *J. Catal.*, 1999, vol. 130, no. 2, pp. 403–410.
9. Forni, L., *Appl. Catal.*, 1988, vol. 11, no. 1, pp. 199–209.
10. Balpanov, D.S., Kagarlitskii, A.D., and Krichevskii, L.A., *Zh. Prikl. Khim.*, 2001, vol. 74, no. 12, pp. 2065–2067.
11. Ogorodnikov, S.K., Lesteva, T.M., and Kogan, V.B., *Azeotropnye smesi: Spravochnik* (Azeotropic Mixtures: A Handbook), Leningrad: Khimiya, 1971, pp. 1265–1266.
12. Bader, A., Harvey, D., and Nagarkatti, G., *Aldrich Handbook of Fine Chemicals*, Milwaukee, Wisconsin: Aldrich Chem., 1990, p. 1113.