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# SYNTHESIS OF NITROGEN CONTAINING HETEROCYCLES OVER COPPER CHROMITE

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*The reactions of 1,2-diaminopropane, 1-amino-2-propanol, 1-amino-2-ethanol and N-(β-aminoethyl)-1,2-diaminoethane in the gas phase over copper chromite have been investigated with the objective of synthesising nitrogen containing heterocycles. At 240-360°C 1,2-diaminopropane gave principally methyl- and 2,5-dimethylpyrazine, whereas the basic reaction for 1-amino-2-propanol was dehydration to give 1-aminoethyl-2-methylaziridine (with a selectivity of up to 78%). The main cyclic product from the dehydration of 1-amino-2-ethanol was pyrazine, while piperazine was formed together with pyrazine from N-(β-aminoethyl)-1-2-diaminoethane.*

Catalytic dehydration of aminoalcohols and deamination of polyamines is a suitable method for the synthesis of nitrogen containing heterocycles, in particular pyrazine bases and other 1,4-diazines [1]. For example, dehydration of 1-amino-2-propanol in a stream of hydrogen over calcium promoted copper chromite led to the selective formation of 2,5-dimethylpyrazine [2]. A considerable amount of 2,5-dimethylpiperazine was also obtained in the initial stages of the process in a reducing atmosphere. The objective of the present work was to study the conversions of 1-amino-2-propanol and, for comparison, some other polyfunctional amines — 1,2-aminopropane, 1-amino-2-ethanol, and diethylenetriamine (N-(β-aminoethyl)-1,2-diaminoethane) — with the same catalyst but not under reducing conditions.

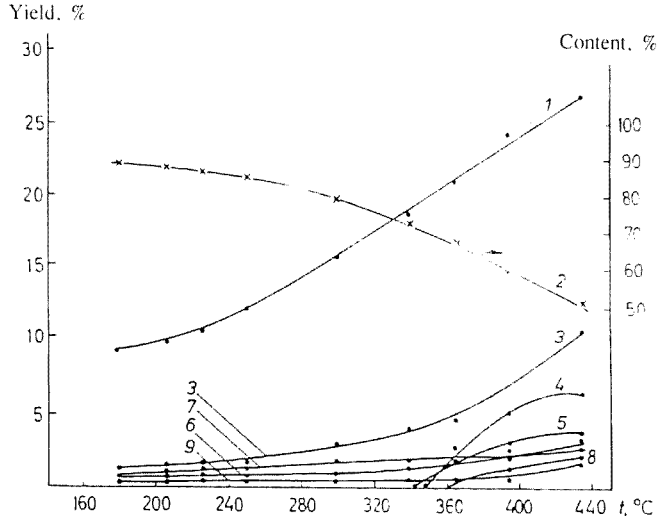


Fig. 1. Dependence of product yields from passing 1-amino-2-propanol over $Cu(CrO_2)_2$ on the reaction temperature: 1) 1-aminoethyl-2-methylaziridine, 2) 1-amino-2-propanol, 3) ethanol, 4) methylamine, 5) 2,3,5-trimethylpyrazine, 6) methanol, 7) 2,5-dimethylpyrazine, 8) 2,5-dimethyl-3-ethylpyrazine, 9) methylpyrazine. Contact time 2 sec.

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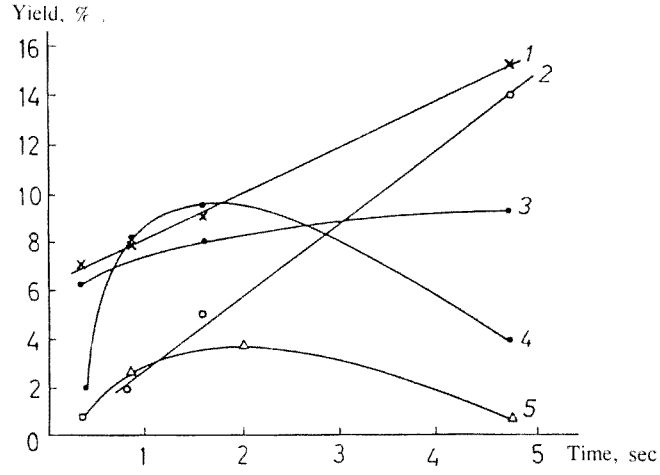
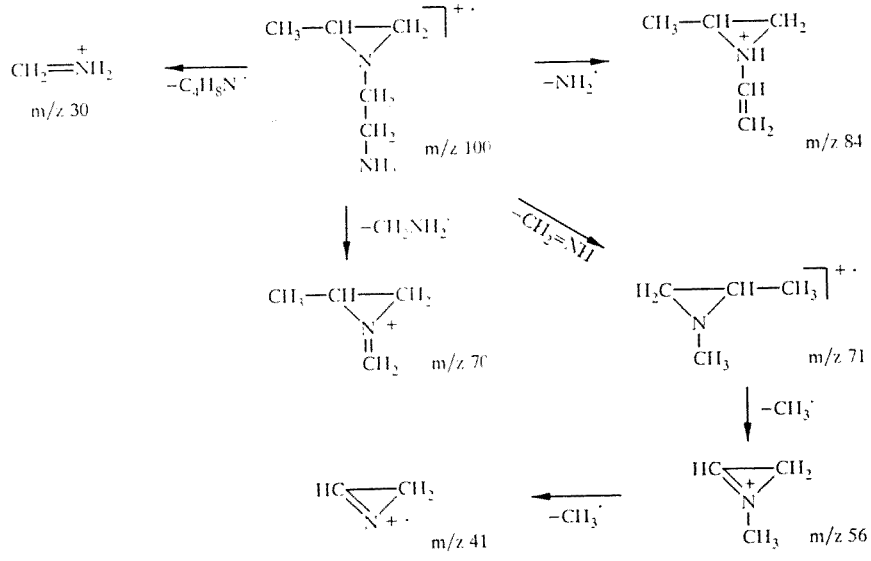



Fig. 2. Dependence on contact time of the yields of products from the reaction of 1-amino-2-propanol over $Cu(CrO_2)_2$ at 420°C: 1) 1-amino-2-methylaziridine, 2) ethanol, 3) 2,5-dimethylpyrazine, 4) 2,5-dimethyl-3-ethylpyrazine, 5) 2,3,5-trimethylpyrazine.

The variation with temperature of the composition of the reaction products from 1-amino-2-propanol passed over a calcium promoted copper chromite catalyst in a stream of air is shown in Fig. 1. The course of the reaction is very different from that carried out in the presence of hydrogen [2]. Unexpectedly pyrazine bases are formed in considerably smaller amounts, piperazine is not formed at all, and the yield of low molecular products is increased (methanol, methylamine, ethanol, isopropanol).

The principal reaction product is the compound $C_5H_{12}N_2$, molecular mass 100, which, according to the mass spectrum, most closely corresponds to 1-aminoethyl-2-methylaziridine. The following possible fragmentation is proposed on the established *m/z* for the fragments:



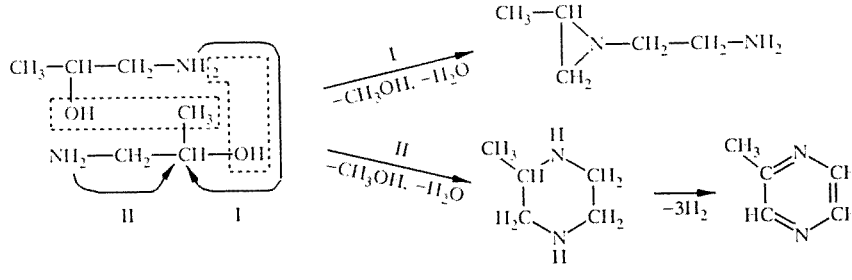

This compound is unstable and underwent further reactions during isolation. Its synthesis has not been described in the literature although the preparation of aziridine and its derivatives by unimolecular cyclodehydration of aminoalcohols is well known (for references on the synthesis of aziridine from 1-amino-2-ethanol over oxide catalysts see [3]).

TABLE 1. Selectivity of the Conversions of Polyfunctional Amines over $Cu(CrO_2)_2$

| Starting materials | T, °C | Conversion, % | Selectivity (%) of the formation of | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1-aminoethyl-2-methylaziridine | piperazine | pyrazine | methylpyrazine | 2,5-dimethylpyrazine | trimethylpyrazine | 2,5,dimethyl-3-ethylpyrazine | 1,2-diaminoethane |
| 1-Amino-2-ethanol | 220 | 11,8 | — | — | 10,2 | — | — | — | — | — |
| | 270 | 12,5 | — | — | 29,4 | — | — | — | — | — |
| | 320 | 16,4 | — | — | 31,4 | — | — | — | — | — |
| | 360 | 24,5 | — | — | 18,5 | — | — | — | — | — |
| 1-Amino-2-propanol | 180 | 11,7 | 78,6 | — | < 1 | 6,0 | 6,0 | — | — | — |
| | 205 | 12,5 | 77,3 | — | < 1 | 3,3 | 16,8 | — | — | — |
| | 225 | 13,6 | 75,8 | — | < 1 | 2,0 | 10,6 | — | — | — |
| | 250 | 15,8 | 74,5 | — | < 1 | 1,5 | 12,1 | — | — | — |
| | 300 | 21,8 | 70,2 | — | < 1 | 1,5 | 6,5 | — | — | — |
| | 340 | 27,8 | 66,3 | — | < 1 | 1,5 | 6,2 | 1,5 | — | — |
| | 365 | 33,7 | 62,1 | — | < 1 | 2,1 | 7,3 | 5,6 | 5,2 | — |
| | 395 | 42,3 | 56,8 | — | < 1 | 5,2 | 6,1 | 5,7 | 4,0 | — |
| | 435 | 49,6 | 52,9 | — | < 1 | 3,4 | 4,0 | 6,3 | 4,6 | — |
| 1-Amino-2-propanol* | 210 | 4,8 | 18,0 | — | — | | 47,0 | 2,5 | 13,0 | — |
| | 230 | 8,7 | 16,0 | — | — | | 40,0 | 2,0 | 14,1 | — |
| | 250 | 21,7 | 15,0 | — | 1,0 | | 20,5 | 18,0 | 24,0 | — |
| | 320 | 29,2 | 17,1 | — | 1,6 | | 18,2 | 17,0 | 28,0 | — |
| 1,2-Diaminopropane | 245 | 15,8 | — | — | — | 48,6 | 5,7 | — | — | — |
| | 320 | 23,0 | — | — | — | 32,7 | 31,8 | — | — | — |
| | 360 | 27,3 | — | — | — | 28,6 | 18,2 | — | — | — |
| | 410 | 46,5 | — | — | — | 13,7 | 14,1 | — | — | — |
| | 465 | 59,8 | — | — | — | 9,6 | 4,4 | — | — | — |
| | 500 | 80,6 | — | — | — | 4,8 | 2,3 | — | — | — |
| Diethylenetriamine | 160 | 37,0 | — | 6,1 | 1,2 | — | — | — | — | 28,3 |
| | 230 | 50,5 | — | 4,1 | 9,3 | — | — | — | — | 27,6 |
| | 270 | 51,2 | — | 8,0 | 17,5 | — | — | — | — | 33,9 |
| | 330 | 72,0 | — | 4,3 | 9,7 | — | — | — | — | 29,1 |
| | 370 | 78,6 | — | 2,4 | 14,0 | — | — | — | — | 22,6 |

*Over freshly prepared catalyst.

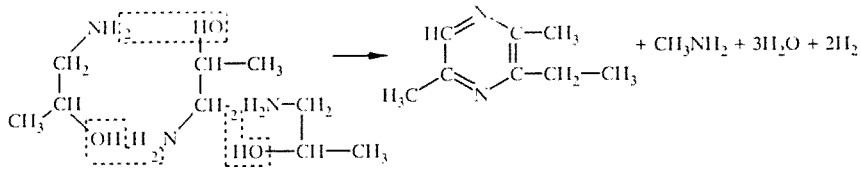
The formation of 1-aminoethyl-2-methylaziridine is a result of a bimolecular reaction, probably occurring as follows:



The second possible reaction mechanism — intramolecular dehydration of 1-amino-2-propanol to 2-methylaziridine with subsequent alkylation by a second aminoalcohol molecule (alkylation of aziridine and its derivatives is well known [4]) appears less likely since the possible intermediate, 2-methylaziridine, was not detected in the reaction mixtures.

Formation of methylpyrazine was observed in parallel with the conversion of the aminoalcohol to 1-amino-2-methylaziridine, but in considerably smaller yield. The increased yields of 1-amino-2-methylaziridine at temperatures above 320°C corresponds to the formation of increasing amounts of methanol (Fig. 1). The formation of more complex alkylated pyrazines, trimethyl- and 2,5-dimethyl-3-ethylpyrazines, began at 340°C and their yields increased with increasing temperature.

The formation of 2,5-dimethyl-3-ethylpyrazine can be represented as a trimolecular condensation with elimination of water and methylamine:



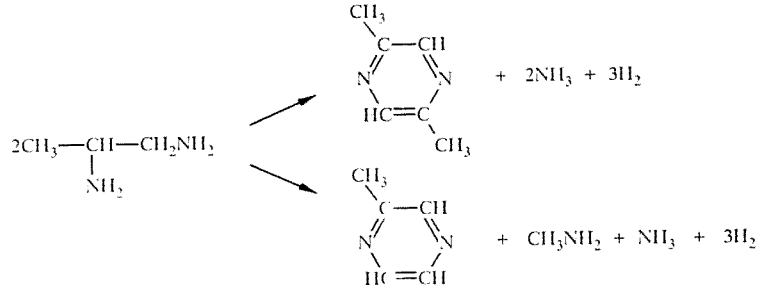
Evolution of methylamine also began at 350-360°C and paralleled the formation 2,5-dimethyl-3-ethylpyrazine. A sequential mechanism (cyclodehydration of 1-amino-2-propanol to 2,5-dimethylpyrazine with subsequent condensation with the methylamine eliminated) is contraindicated by the dependence of product yields on contact time (Fig. 2). The instability of the more complex 2,3,5-trimethyl- and 2,5-dimethyl-5-ethylpyrazines is apparent at increased contact time, whereas the yield of 2,5-dimethylpyrazine changed comparatively little with increasing contact time.

The selectivity of the formation of heterocyclic compounds from 1-amino-2-propanol is reflected in Table 1. The most selective process is the formation of 1-aminoethyl-2-methylaziridine: the selectivity reached 76-79% at 180-220°C. The selectivity curve for 2,5-dimethylpyrazine formation has a maximum at 205°C. The selectivity of this process tended to stabilize above 360°C.

A series of experiments was carried out with freshly prepared catalyst. The course of the reaction differed in comparison with the preformed catalyst (Table 1). In the initial stages of the process (at temperatures from 200 to 230°C) the basic reaction was dehydration of 1-amino-2-propanol to 2,5-dimethylpyrazine with a selectivity three times as great as for the preformed catalyst. The freshly formed catalyst contained more active oxide centres which led to more complex reactions and increased yield of trimethyl- and 2,5-dimethyl-3-ethylpyrazines, while the unstable and reactive 1-aminoethyl-2-methylaziridine was obtained in lesser amounts.

Conversion of 1-amino-2-ethanol over copper chromite under oxidative conditions was not at all selective. The starting material underwent dehydration, deamination, dehydrogenation and hydrogenolysis. Volatile compounds were the principal products: methylamine, ethylamine, methanol, while the only cyclic product was pyrazine in 5% yield (Table 1). Aziridine, the product of monomolecular deaminocyclisation, was not observed in the catalysate.

The reactions of 1,2-diaminopropane and N-(β-aminoethyl)-1,2-diaminoethane on a copper chromite catalyst were also studied. The composition of the catalysate obtained at early stages of the reaction (Fig. 3, Table 1) indicated that reaction of 1,2-diaminopropane occurred in two directions by dehydrodeaminocyclisation to give 2,5-dimethylpyrazine and methylpyrazine:



At 320-400°C the yields from both reactions were about the same, the selectivity curve for 2,5-dimethylpyrazine formation having a maximum at 320°C. Above 400°C destruction of the diamine to give an increased amount of methylamine is the basic reaction. The different kurtosis of the curves for 1,2-diaminopropane conversion at 320-400°C and above 400°C indicates that different mechanisms are involved. In contrast to pyrolysis under reducing conditions, which is characterised by formation of up to 37% yield of 2,5-dimethylpiperazine, reaction in a stream of air gave products of dehydrodeaminocyclisation only. Formation of trimethyl- and dimethylethylpyrazines, characteristic of the reactions of 1-amino-2-propanol at higher temperatures, was also not observed.

Thus more complete conversion of 1-amino-2-propanol and 1,2-diaminopropane occurred in an oxidative system over copper chromite than in the presence of hydrogen. In a reducing medium over a reduced catalyst bimolecular dehydra-(deamino)cyclisation with dehydrogenation to 2,5-dimethylpyrazine was almost the exclusive reaction pathway, while in an oxidising medium with an oxidised catalyst this reaction is accompanied in the early stages (at comparatively low temperatures) by cyclocondensation with the elimination of water (ammonia) and methanol (methylamine) respectively followed by dehydrogenation to methylpyrazine, and in the case of 1-amino-2-propanol without dehydrogenation to give 1-aminoethyl-2-methylpyrazine.

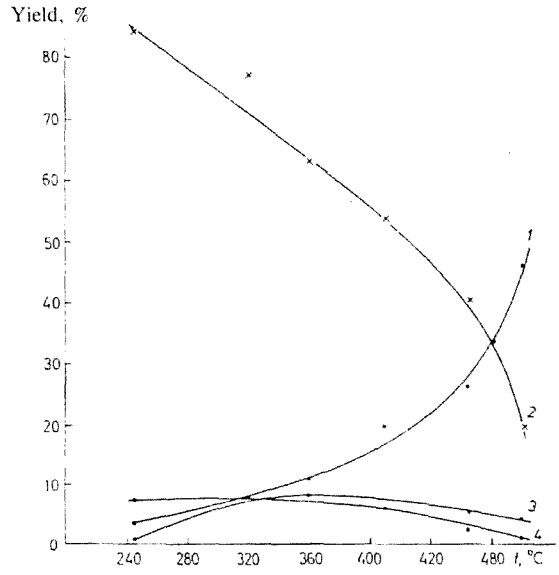



Fig. 3. Dependence on reaction temperature of the product yields from 1,2-diaminopropane on a $Cu(CrO_2)_2$ catalyst. 1) Methylamine, 2) 1,2-diaminopropane, 3) methylpyrazine, 4) 2,5-dimethylpyrazine. Contact time 2 sec.

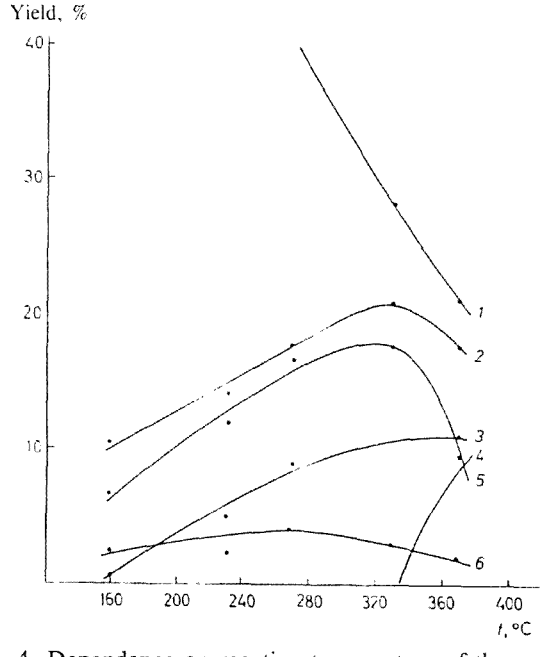



Fig. 4. Dependence on reaction temperature of the product yields from reactions of diethylenetriamine over $Cu(CrO_2)_2$ on reaction temperature.

More complex reactions of 1-amino-2-propanol involving the hydrogen atoms of the methylene groups and leading to the formation of trimethyl and 2,5-dimethyl-3-ethylpyrazines are characteristic of the oxidised from of the copper chromite catalyst. The greater the number of oxide centres on the surface (freshly prepared catalyst) the greater the importance of these reactions while they do not occur at all on the reduced catalyst in a stream of hydrogen.

For comparison, reactions of diethylenetriamine were studied because the structure of this molecule should facilitate the formation of pyrazine and piperazine by a simple unimolecular deamination. The results of Table 1 and Fig. 4 show that

TABLE 2. Mass Spectroscopic Characteristics of Some of the Compounds Synthesized

| Compound | Empirical formula | Values of m/z (relative intensity, %) |
|---|---|---|
| 1-Aminoethyl-2-methylaziridine | $C_5H_{12}N_2$ | 100 (45), 84 (10), 72 (5), 71 (38), 70 (100), 59 (10), 56 (15), 55 (8), 45 (5), 42 (13), 41 (18), 30 (12) |
| 2,5-Dimethylpyrazine | $C_6H_8N_2$ | 108 (100), 81 (10), 42 (45), 40 (17), 28 (5) |
| 2,3,5-Trimethylpyrazine | $C_7H_{10}N_2$ | 122 (100), 81 (10), 66 (5), 54 (10), 42 (60), 39 (10), 28 (5) |
| 2,5-Dimethyl-3-ethylpyrazine | $C_8H_{12}N_2$ | 135 (100), 121 (8), 108 (20), 80 (5), 67 (5), 56 (5), 56 (10) 53 (7), 42 (28), 38 (17), 28 (5) |

cyclisation of diethylenetriamine does take place, but the process occurs by two coupled mechanisms: 1) deamination-ammonolysis and 2) dehydrogenation-hydrogenolysis. 1,2-Diaminoethane is formed together with piperazine as a result of the first pair of reactions, and pyrazine and methylamine as a result of the second pair. The temperature versus product yield curves for the conversion of diethylenetriamine suggest that reactions of the second type predominate: the formation of 1,2-diaminoethane and methylamine almost parallel the formation of pyrazine. At temperatures above 360°C diethylenetriamine underwent hydrogenolysis to give ethylamine. Selectivity for the formation of pyrazine, piperazine and diaminoethane is greatest at the same temperature (270°C).

To achieve a comparatively high selectivity with an oxidised form of a copper chromite catalyst with respect to the formation of compounds such as 1-aminoethyl-2-methylaziridine and 2,5-dimethyl-3-ethylpyrazine, which are difficult to obtain otherwise, is of considerable theoretical and practical interest. However determination of optimal conditions for isolation of these products from the reaction mixture requires further study.

## EXPERIMENTAL

Experiments were carried out using a continuous laboratory catalytic apparatus with a stationary layer of catalyst (thickness 10 mm). Here, 3 $cm^3$ of 0.8-1.0 mm granules of GIPKh-105 copper chromite catalysts, promoted with $CaCrO_4$, were placed in an 18 mm diameter stainless steel tube reactor and activated in a stream of air (100 $cm^3$/min) at 400°C for 4 h. After activation, the reactor temperature was lowered to that required for the beginning of a series of experiments and the starting material was passed into the reactor's evaporator at a rate of 20 $cm^3$/h via a proportionating pump without interrupting the flow of air. In experiments with freshly prepared catalyst, passage of starting material was stopped for 5 min, the next reaction temperature was established and starting material passed through again. In experiments with the aged catalyst, catalysate was collected for analysis beginning after 20 min reaction at the initial temperature. Reaction products were condensed at −70°C.

The reaction products were analyzed by programmed temperature GLC (80-200°C at a rate of 4°C/min) using a Biochrom-1 chromatograph equipped with 3 m × 0.4 cm column filled with 25% Apiezon-L on Chromatone N-AW-DMCS (40-60 mesh) and with a catharometer detector. Quantitative analysis of the catalysate used 2,5-dimethylpyrazine as internal standard, while qualitative analysis used the Kovacs universal indices and chromatography-mass spectrometry (Kratos MS-25 mass spectrometer, ionising current 70 eV).

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