SYNTHESIS OF 5-VINYLINDOLE BY SIMULTANEOUS DEHYDROGENATION AND DECARBOXYLATION OF 5-ETHYLINDOLE-2-CARBOXYLIC ACID AND ITS ETHYL ESTER

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A new method is proposed for the synthesis of 5-vinylindole by simultaneous catalytic dehydrogenation and decarboxylation of 5-ethylindole-2-carboxylic acid and its ethyl ester, making it possible to more than double the yield of the previously described method.

We have previously developed a method for the synthesis of 5-vinylindole by catalytic dehydrogenation of 5-ethylindole [1]. The latter was obtained by two methods: by thermal decarboxylation of 5-ethylindole-2-carboxylic acid by a known method [2] or by heterogeneous catalytic cyclization of acetaldehyde p-ethylphenyl hydrazone [3].

The classical method for the preparation of 5-ethylindole is a five-step synthesis according to Fischer, including the stages of diazotization of p-ethylaniline, followed by reduction of the diazonium salt, condensation of p-ethylphenylhydrazine with ethyl pyruvate, cyclization of p-ethylphenylhydrazone of ethyl pyruvate, saponificatoin of ethyl 5-ethylindole-2-carboxylate, and thermal decarboxylation of the later into 5-ethylindole. The most time- and labor-consuming is the stage of thermal decarboxylation of 5-ethylindole-2-carboxylic acid.

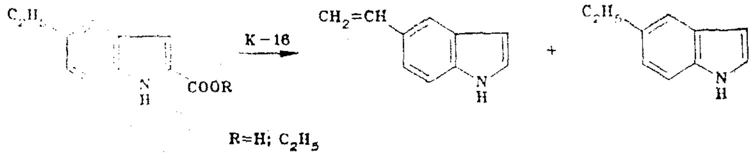
In the preparation of 5-ethylindole the scheme is simplified by cyclizing of acetaldehyde p-ethylphenylhydrazone on aluminum oxide, but the yield of 5-ethylindole based on p-ethyl aniline is 11%, as in the classical Fischer method.

We tried to carry out the synthesis of 5-vinylindole by dehydrodecarboxylation of 5-indole-2-carboxylic acid and its ethyl ester — intermediates in the Fischer synthesis of 5-ethylindole.

There are reports in the literature on the simultaneous dehydrogenation and decarboxylation of acids and esters, but this reaction has not been reported for the indole series.

The catalytic dehydrodecarboxylation was carried out in a vertical flow-type apparatus, at atmospheric pressure, in a nitrogen current in the presence of an industrial dehydrogenation catalyst K-16, which was successfully used previously in the dehydrogenation of 5-ethylindole [1].

From the chromatographic analysis of the catalysts it follows that the main reaction products are 5-vinyl- and 5-ethylindoles — dehydrogenation and decarboxylation products of 5-ethylineole-2-carboxylic acid and its ethyl ester.



Moreover, reaction by-products were detected in the catalyzates formed as a result of cracking — indole, 5-methylindole, and an insignificant amount of unidentifiable compounds, the overall content of which was small, and depending on reaction conditions, varied within 1 to 10%.

To find favorable conditions for the synthesis, we studied the influence of temperature, time of contact, and concentration of the starting compounds on the composition of the reaction products.

We determined the range of constant activity of the catalyst (Fig. 1) within which this investigation was carried out. After 2 h of operation, the content of 5-vinyl- and 5-ethylindoles in the catalyzates was about 60 and 35%, respectively, and remained constant for a long period.

The starting compounds were fed onto the catalyst in the form of a benzene solution, the concentration of which varied from 2 to 10%. Because of the low solubility of the acid, the influence of the concentration on the composition of the reaction products was studied using ethyl 5-ethylindole-2-carboxylate as an example.

Figure 2 shows that in the range studied, the concentration of the starting ester insignificantly influences the content of 5-vinyl- and 5-ethylindoles in the catalyzate, the amount of which varies from 55 to 62 and 35 to 40%, respectively.

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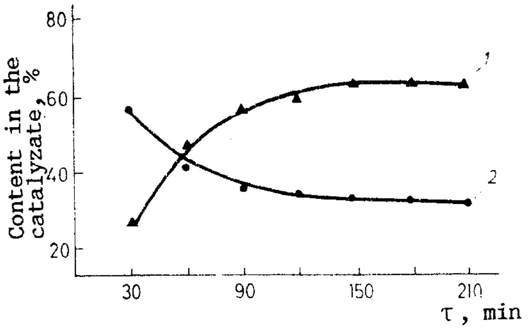

Fig. 1

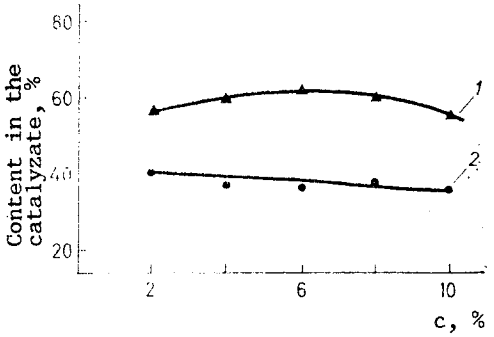

Fig. 2

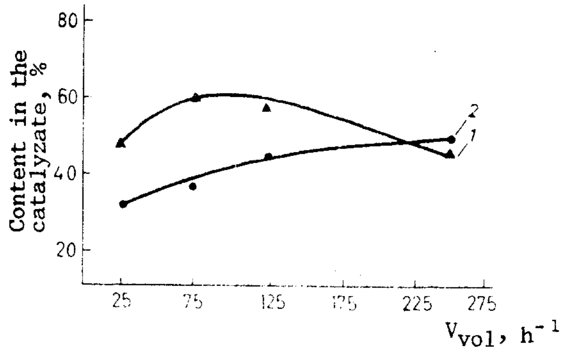

Fig. 3

Fig. 1. Change in the content of reaction products in the catalyzates of the dehydrodecarboxylation of ethyl 5-ethylindole-2-carboxylate as a function of the working time of the catalyst (T 500°C, V_{vol} 1.8 h^{-1}, concentration (c) of ethyl 5-ethylindole-2-carboxylate 4%). Here and in Figs. 2-5: 1) 5-vinylindole; 2) 5-ethylindole.

Fig. 2. Influence of the concentration of ethyl 5-ethylindole-2-carboxylate on the composition of the catalysts (T 500°C, V_{vol} 1.8 h^{-1}).

Fig. 3. Influence of per-volume rate on the composition of the catalyzates from dehydrodecarboxylation of ethyl 5-ethylindole-2-carboxylate (500°C, c 4%).

In the study of the influence of the per-volume feeding rate of ethyl 5-ethylindole-2-carboxylate (Fig. 3), it was found that with decrease in the time of contact, the amount of 5-ethylindole monotonically increases, and that of 5-vinylindole passes through a maximum (60%) at a per-volume feeding rate of 75 h^{-1} (volume of the catalyst 8 ml, feeding rate 0.3 ml/min).

The study of the influence of the temperature on the dehydrodecarboxylation process was carried out over a wide range, from 300 to 600°C.

In the case of ethyl 5-ethylindole-2-carboxylate (Fig. 4), an increase in the content of 5-vinyl- and 5-ethylindoles in the catalyzate is observed with increase in the temperature, amounting to 50 and 46%, respectively, at 400°C. Further increase in temperature leads to a decrease in the yield of 5-ethylindole due to its conversion into 5-vinylindole, the amount of which reaches 62% at 500°C, and then decreases.

During dehydrodecarboxylation of 5-ethylindole-2-carboxylic acid, the same character of the dependence of the content of the reaction products in the catalyzates on the temperature is observed. The highest yield of 5-vinylindole, about 70%, is reached at 500-550°C, while further increase in the temperature leads to a decrease in the yield (Fig. 5).

To verify the possibility of thermal decarboxylation of 5-ethylindole-2-carboxylic acid under conditions of heterogeneous catalysis, we studied the transformation of the acid on quartz under comparable conditions: a 2% benzene solution of the acid was passed at a constant rate over a washed and preliminarily calcined quartz. In the reaction products 5-ethylindole was identified by GLC, the amount of which increased with increase in temperature (Fig. 6). It should be noted that at 350°C only 20% of 5-ethylineole is formed thermally, while in the presence of a catalyst about 60% is obtained. The data obtained show that under the conditions of simultaneous dehydrodecarboxylation a thermal and catalytic decarboxylation of the acid takes place.

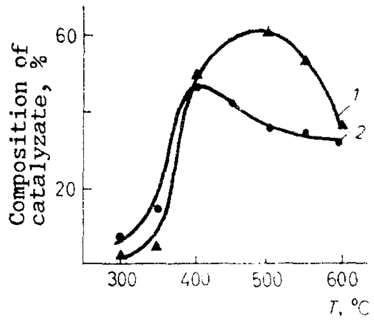

Fig. 4

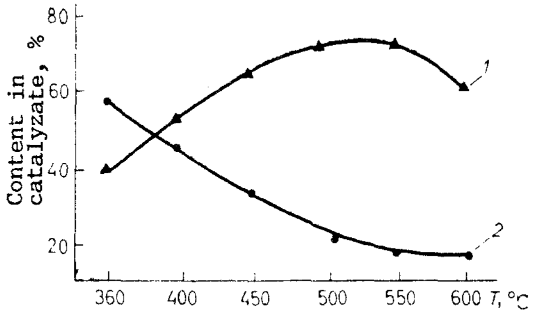

Fig. 5

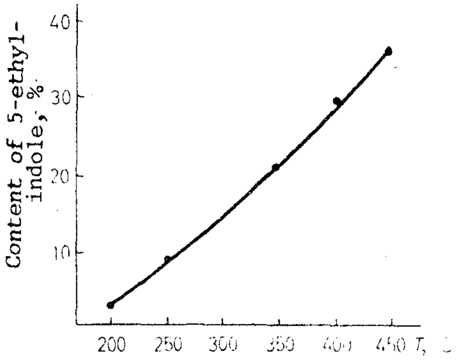

Fig. 6

Fig. 4. Influence of temperature on the composition of catalyzates from dehydrodecarboxylation of ethyl 5-ethylindole-2-carboxylate (V_{vol} 1.8 h^{-1}, c 4%).

Fig. 5. Influence of temperature on the composition of catalyzates from the dehydrodecarboxylation of 5-ethylindole-2-carboxylic acid (V_{vol} 1.8 h^{-1}, c 2%).

Fig. 6. Decarboxylation of 5-ethylindole-2-carboxylic acid on quartz (V_{vol} 1.8 h^{-1}, c 2%).

The investigation revealed the most favorable conditions for the catalytic synthesis of 5-vinylindole by simultaneous dehydrogenation and decarboxylation of 5-ethylindole-2-carboxylic acid and its ethyl ester, at which the yield of 5-vinylindole was 26 and 21%, respectively.

The use of this method made it possible to increase the yield of 5-vinylindole, based on p-ethylalanine by more than twofold, compared with our previously described method of its preparation.

The decarboxylation product (5-ethylindole) isolated from the catalyzate together with 5-vinylindole can be passed over the same catalyst at 550°C, so that an additional amount of 5-vinylindole can be obtained.

The simplicity of the preparation of the starting compounds, the high content of 5-vinylindole in the catalyzate, and also the utilization of the second reaction product — 5-ethylindole — for the synthesis of the desired end product makes this method worthy of consideration for the preparation of 5-vinylindole.

EXPERIMENTAL

The chromatographic analysis of the catalyzates was carried out on a Tsvet-2- chromatograph using a 1 m column, 2.5 mm in diameter, filled with chromaton N-AW-DMC, impregnated with Carbowax 6000 (15%). The column was thermostated at 187°C, carrier gas helium, rate 60 ml/min. The quantitative analysis of the products of dehydrodecarboxylation of ethyl 5-ethylindole-2-carboxylate was carried out by the internal standard method, using carbazole as such. To analyze the catalyzates containing 5-ethyl-indole-2-carboxylic acid, the silylation method was used; a mixture of trimethylchlorosilane and hexamethyldisilalazane in a 1:2 ratio by volume in the presence of pyridine was used as the silylating agent. Study of the dehydrodecarboxylation of 5-ethylineole-2-carboxylic acid and its ethyl ester was carried out on a vertical flow-type apparatus at atmospheric pressure.

The starting compounds were obtained from p-ethylaniline [2].

Dehydrodecarboxylation of 5-Ethylindole-2-carboxylic Acid. A solution of 5-ethylindole-2-carboxylic acid in 180 ml of benzene was passed at a rate of 0.3 ml/min over 8 ml of a K-16 catalyst (particle diameter 1-2 mm) at 550°C in a weak current of nitrogen. The precatalytic treatment of the catalyst was carried out by steam in a nitrogen current for 6 h at 600°C. Directly before the experiment 50 ml of benzene was passed over at 550°C. At the end of the addition of the starting compound, nitrogen was passed for another 30 min, and the catalyzate was withdrawn and collected in a receiver with water cooling. 5-Vinylindole was isolated from the catalyzates on a column 20 mm in diameter and 500 mm long, filled with silica gel L 100/250, suspended in an ethyl acetate—petroleum ether (1:5) mixture, which is used as eluent. After evaporation of the solvent and recrystallization from petroleum ether, white needlelike crystals were obtained, mp 42-43°C, which agrees with our previously obtained data [1]. 5-Ethylindole (0.4 g, 14%) was also obtained from the catalyzate. The yield of vinylindole was 0.7 g (26%).

Dehydrodecarboxylation of ethyl 5-ethylindole-2-carboxylate was carried out in analogy with the above-described procedure. From 4.12 g of ethyl 5-ethylindole-2-carboxylate, 0.56 g of 5-vinylindole (21%) was obtained.

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ACETALS OF LACTAMS AND ACID AMIDES.

67.* POLAROGRAPHIC BEHAVIOR OF ENAMINES OF THE INDOLES SERIES IN ANHYDROUS DMF

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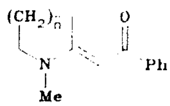
The polarographic behavior of derivatives of 2-aminomethyleneindoxyl and 3-aminomethyleneoxindole in anhydrous DMF has been studied and the results compared with data on the polarographic reduction of substituted aminomethyleneacetophenones and of related enaminoketones and eneaminoamides. It is established that the ease of reduction is determined by the nature of the substituent on the enamine and indole nitrogen atoms and also by the presence or absence of an α-methyl group in the α-position of the eneamines (for noncyclic enaminoketones).

It is known [2] that enaminoketones, I, of the pyrrolidine, piperidine, and hexahydroazepine series, in which the enamine nitrogen atom included in a saturated ring system, are reduced at a mercury drop electrode in anhydrous DMF in two steps, the first of which is reversible and corresponds to a one-electron transfer.

In this paper, we present the results of a polarographic study of enaminoketones of the indoxyl, IIa-d, and 1-acetylindoxyl, IIIa-c, series and also the enaminoamides of the oxindole, IVa-c, series (Table 1).



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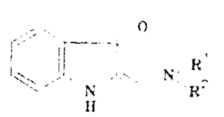
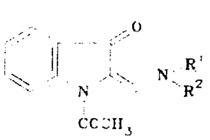
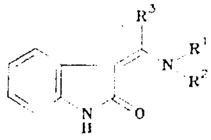


II a-d



III a-c



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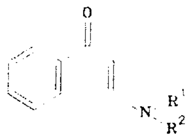

V a-c

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*For Communication 66, see [1].

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