Corresponding Member of the Academy of Sciences of the USSR A. P. TERENT'EV, M. A. VOLODINA,

N. L. PODLESOVA, and N. E. GOLUBEVA

1957

SovietRxiv

Abstract

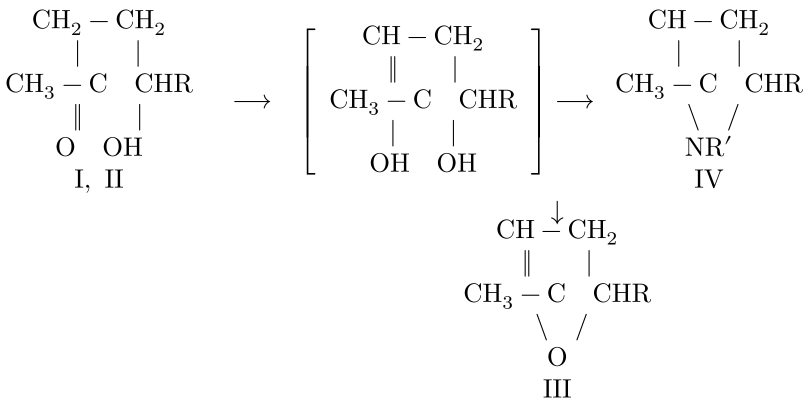
Full Text

CHEMISTRY

Corresponding Member of the Academy of Sciences of the USSR A. P. TERENT'EV, M. A. VOLODINA,
N. L. PODLESOVA, and N. E. GOLUBEVA

SYNTHESIS OF PYRROLES, PYRROLINES, AND PYRROLIDINES FROM -KETO ALCOHOLS

Earlier we showed (^{1}) that the hydroamination reaction of -keto alcohols with formamide or its N-substituted derivatives leads to the formation of a nitrogen-containing heterocycle. The products of the reaction were pyrrolidine bases. The process of formation of a five-membered nitrogen-containing heterocycle from -keto alcohols (I, II) can also be envisaged as proceeding by elimination of water from the molecule of the alcohol and ammonia (or an amine) on a dehydrating catalyst. The product of such a transformation should be the corresponding Δ^2-pyrroline (IV).



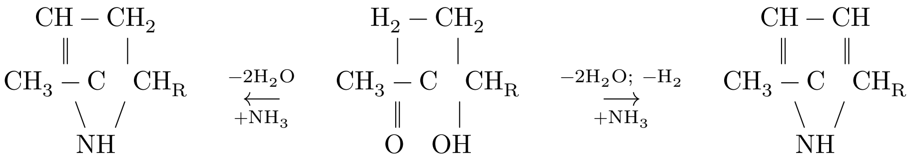
$$R = \text{H (I)},\ \text{CH}_3\ \text{(II)}$$
$$R' = \text{H},\ \text{Alk},\ \text{Ar}.$$

It is quite possible that one of the reaction products is a homolog of 4,5-dihydrofuran (III). The probability of transformations of this kind was supported by data published in the literature for cases of catalytic dehydration of 1,4-diols of the type

$$RR'C(OH)CH_2CH_2C(OH)R''R''' \quad \text{and} \quad RR'C(OH)CH{=}CHC(OH)R''R'''$$

and of their joint catalytic dehydration with ammonia, alkyl- and arylamines ($^{2-4}$). Yu. K. Yur' ev and I. K. Korobitsyna (^{4}) showed that joint catalytic dehydration of cis-butene-2-diol-1,4 leads to the formation of the Δ^3-pyrroline ring only when aniline is used. In the interaction of cis-butene-2-diol-1,4 with ammonia, they detected only traces of pyrrole and did not isolate Δ^3-pyrroline at all.

We set ourselves the task of studying the behavior of -keto alcohols toward dehydrating catalysts, with the aim of finding a route for the synthesis of the comparatively little-studied and difficultly accessible Δ^2-pyrrolines, as well as the products of their dehydrogenation—pyrroles.



VI I, II IV

A similar method for the synthesis of Δ^2-pyrrolines and the behavior of γ-keto alcohols under contact conditions over dehydrating and dehydrogenating catalysts have not hitherto been described in the literature.

The objects of our study were γ-acetopropyl (I) and secondary γ-acetobutyl (II) alcohols.

It turned out that the conversion of γ-acetopropyl alcohol in a stream of ammonia at 450° over alumina and Pd on asbestos (similarly to Ni/Al_2O_3) leads to the formation of α-methylpyrrolidine (V), α-methylpyrrole (VI) in 10-20% yield, and a small amount of α-methyl-Δ^2-pyrroline (IV).

Apparently, the primary product of the reaction is α-methyl-Δ^2-pyrroline; under the contact conditions the latter undergoes disproportionation of the type of Zelinskii irreversible catalysis (^{5}), giving V and VI.

The formation of α-methylpyrrole may be caused by dehydrogenation of α-methyl-Δ^2-pyrroline both under the influence of Pd and under the influence of the alumina itself. The latter cases were observed by Yu. K. Yur' ev and I. K. Korobitsyna in the catalytic conversion of cis-but-2-ene-1,4-diol with aniline (^{4}).

A study of the reaction on alumina without Ni and Pd showed that the main product of the reaction is α-methyl-Δ^2-pyrroline (45%); α-methylpyrrole is obtained under these conditions in very small amounts. Consequently, in our case alumina has practically no effect on the dehydrogenation of IV.

When the reaction of the keto alcohols (I and II) with ammonia is carried out on alumina with metals (Ni, Pd) and without metals at 450°, a large amount of high-boiling resinous substances is formed. To avoid this, we attempted to use a milder catalyst described for processes of dehydrocyclization of anils—chromium oxide/copper on charcoal ([6]).

It was shown that a temperature of 600° and above proved too high for our substrate and caused strong resinification of the substance and cracking. At lower temperatures (480-500°), γ-methyl-Δ^2-pyrroline (25%) (IV) was obtained from γ-acetopropyl alcohol (I) in a stream of ammonia as the main reaction product, and only traces of α-methylpyrrolidine (V) and α-methylpyrrole (VI).

When the copper chromite catalyst is used, the amination process of I is accompanied by the formation of a considerable amount of 2-methyl-4,5-dihydrofuran (III).

Similar transformations under analogous conditions were also observed by us for secondary γ-acetobutyl alcohol.

Thus, the most favorable conditions for the formation of α-methyl-Δ^2-pyrroline from γ-acetopropyl alcohol proved to be the catalyst γ-alumina and a temperature of 310-320°.

Having found satisfactory conditions for the synthesis of α-methyl-Δ^2-pyrroline, we decided to use γ-keto alcohols (I, II) for the synthesis of a series of little-studied and interesting compounds—Δ^2-pyrroline bases.

As is known, some homologs of Δ^2-pyrroline have practical importance as photosensitizers ([7]).

We were able to show that, when keto alcohols (I and II) are passed in a stream of ammonia or an amine, or in a mixture with an aromatic amine, over alumina at 310-320°, Δ^2-pyrroline bases are formed in 25-55% yield. At lower reaction temperatures (280-290°), the pyrroline bases obtained contain a considerable admixture of the corresponding 4,5-dihydrofurans (III).

The study of the reaction mechanism was not the direct subject of our investigation and is subject to further study. In all probability, a more detailed development of the reaction conditions (the use of other dehydrating···

catalysts ([3]), activation of alumina ([2–4])) makes it possible to increase somewhat the yield of pyrroline bases.

Preliminary investigations of the properties of some Δ^2-pyrrolines obtained by this method showed that they readily give haloalkylates,

Table 1

Starting substances	Reagent	Catalyst	Temperature, °C	Obtained, % III	Obtained, % IV	Obtained, % V	Obtained, % VI
γ-Acetopropyl alcohol (I)	Ammonia	$Al_2O_3 + Pd$	450	–	5	10	20
γ-Acetopropyl alcohol (I)	Ammonia	Al_2O_3	330–350	–	35	3	5
γ-Acetopropyl alcohol (I)	Ammonia	$Cr_2O_3\|Cu\|C$	480–500	20	20	4	5
Secondary γ-acetobutyl alcohol (II)	Ammonia	Al_2O_3	330–350	–	30	5	6
Secondary γ-acetobutyl alcohol (II)	Ammonia	$Cr_2O_3\|Cu\|C$	480–500	18	22	3	4

add bromine under the action of dioxane dibromide, react with Grignard reagent; some of them react with phenyl isothiocyanate, etc.

Table 2

Starting substances	Reagent	R and R of the pyrroline base CH_3—pyrroline ring—R′N—R	Picrate m.p., °C	Picrate analysis, % N found	Picrate analysis, % N calc.
$CH_3CO(CH_2)_2CH_2OH$	NH_3	R = H $(^8)$R′ = H	120–120.5	18.01 17.82	17.95

Starting substances	Reagent	R and R of the pyrroline base CH_3—pyrroline ring—R′N—R	Picrate m.p., °C	Picrate analysis, % N found	Picrate analysis, % N calc.
Same	CH_3NH_2	R = CH_3 (10)R′ = H	216-218	17.17 17.01	17.17
» »	$C_6H_5NH_2$	R = C_6H_5 (11)R′ = H	103-105	14.22 14.44	14.45
» »	*n*-$CH_3C_6H_4NH_2$	R = *n*-$CH_3C_6H_4$ (11)*R′ = H	124-126	14.15 13.89	13.93
$CH_3CO(CH_2)_2CHOHCH_3$	NH_3	R = H (12)R′ = CH_3	131-132	17.25 17.38	17.17

Note. Catalyst—alumina. Temperature 308-315°.

* The melting point of the picrate of N-*p*-tolyl-2-methyl-Δ^2-pyrroline differs from the literature data; however, the picrate analysis data and MR_D of the base do not allow one to doubt the purity of the N-*p*-tolyl-2-methyl-Δ^2-pyrroline obtained.

The position of the double bond in the pyrrolines obtained cannot yet be considered fully proved, but most probably they are Δ^2-pyrrolines. This is confirmed by the study of some properties of the pyrrolines obtained and by their identity with substances of definitely known structure.

Preliminary tests of some of the obtained Δ^2-pyrrolines at the Institute of Pharmacology of the USSR Academy of Medical Sciences (laboratory of Prof. S. V. Andreev) showed their considerable physiological activity.

Experimental Part*

Commercial acetopropyl alcohol was used in the study; after distillation in vacuo it had the following properties: b.p. 114-115°/30 mm, n_D^{20} 1.4395; d_4^{20} 1.0068 (8).

Secondary γ-acetobutyl alcohol was obtained by condensation of sodium acetoacetic ester with propylene oxide (9): b.p. 60-61/4 mm; n_D^{20} 1.4328; d_4^{20} 0.9634. The catalysts used in the experiments were: commercial Al_2O_3, Pd on asbestos; Ni/Al_2O_3, Cr_2O_3/Cu on charcoal. The catalysis conditions were as follows: tube diameter 13 mm, catalyst-bed length 40 cm (in the case of Al_2O_3 and Pd—35 cm Al_2O_3 and 20 cm Pd on asbestos), rate of passage of the keto alcohol 0.5 ml/min, ammonia (from a cylinder) or passage of a mixture of keto alcohol with amine in a ratio of 1 : 2.

The experimental results are given in Tables 1 and 2.

Table 1 gives the results of experiments on the joint catalytic dehydration of γ-acetopropyl and secondary γ-acetobutyl alcohols with ammonia over alumina with Pd, alumina without Pd, and a chromocopper catalyst.

The constants of the substances thus obtained are close to the literature data. Pyrrolidines and Δ^2-pyrrolines were characterized by picrates.

Table 2 gives the results of the transformations of keto alcohols (I and II) with ammonia and amines over alumina. The Δ^2-pyrrolines obtained were characterized by picrates. All picrates were analyzed. The constants of the isolated Δ^2-pyrrolines agree with the literature data.

Moscow State University
named after M. V. Lomonosov

Received
12 II 1957

References Cited

1. A. P. Terent' ev, M. A. Volodina, DAN, **88**, 845 (1953).
2. Yu. K. Yur' ev, N. G. Medovshchikov, ZhOKh, **9**, 628 (1939).
3. English patent 505904 (1939); Chem. Abstr., **33**, 9328 (1939); English patent 508548 (1939), Chem. Abstr., **34**, 779 (1940); English patent 510615 (1939), Chem. Abstr., **34**, 5092 (1940); English patent 510949 (1939), Chem. Abstr., **34**, 5466 (1940); American patent 2421650 (1947), Chem. Abstr., **41**, 5552 (1947).
4. Yu. K. Yur' ev, I. K. Korobitsyna et al., Vestn. MGU, **2**, 37 (1951).
5. Yu. K. Yur' ev, T. B. Dubrovina, E. P. Tregubov, ZhOKh, **16**, 843 (1946).
6. C. Hansch, D. G. Crosby, M. Sadoski, J. Am. Chem. Soc., **73**, 704 (1951).
7. P. S. Ugryumov, ZhOKh, **20**, 1848 (1950).
8. I. L. Knunyants, G. V. Chelintsev, E. D. Osetrova, DAN, **1**, 312 (1934).
9. R. Adams, C. A. Vander Werf, J. Am. Chem. Soc., **72**, 1184 (1950).
10. R. Lukes, Chem. Listy, **27**, 97, 121 (1933).
11. J. Markwalder, J. prakt. Chem., (2), **75**, 338 (1907).
12. C. Evans, J. Am. Chem. Soc., **73**, 5230 (1951).

* Some syntheses were carried out with the participation of V. V. Dorokhov and B. S. Kikot'.

Note: Figure translations are in progress. See original paper for figures.