A. A. PONOMAREV, M. V. NORITSYNA, A. P. KRIVENKO

1964

SovietRxiv

Abstract

Full Text

A. A. PONOMAREV, M. V. NORITSYNA, A. P. KRIVENKO

CATALYTIC SYNTHESIS OF α-PYRROLIDYL- AND α-OCTAHYDROINDOLYLALKANOLS-3

(Presented by Academician A. A. Balandin, 9 XII 1963)

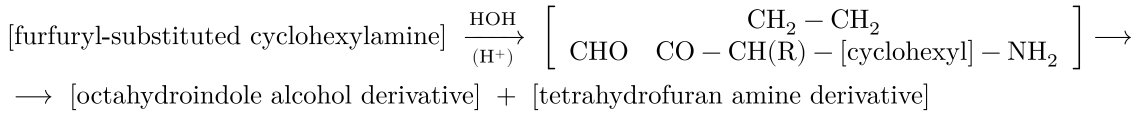
At one time we published the results of a study of the hydrogenation reaction of furan amines under various conditions (^{5,6}). Subsequent investigations concerned carrying out this reaction in acidic aqueous solution (pH 4—5) under pressure at 100—130° in the presence of Raney nickel. Under these conditions, furan amines containing an amino group in the side chain at the carbon atom third from the ring are converted into two products: the corresponding tetrahydrofuran amine (^{6}) and α-pyrrolidylalkanol-3. The formation of the second compound can be explained by the fact that, under the conditions adopted by us, hydrolytic cleavage of the furan ring takes place with formation of an intermediate aminodicarbonyl compound:

$$[\text{furan derivative}] - CHR - CH_2 - CH(NH_2) - R' \xrightarrow[(H^+)]{HOH} \left[\begin{array}{cc} & CH_2 - CH_2 \\ CHO & CO - CHR - CH_2 - CH(NH_2) - R' \end{array} \right]$$

$$\longrightarrow [\text{pyrrolidine derivative}] - CH_2 - CH_2 - CH_2OH$$

Further possibilities are: 1) condensation leading to a cyclic azomethine, followed by its hydrogenation to pyrrolidine; at the same time the aldehyde group is reduced to a hydroxyl group, or 2) hydrogenation of the aminocarbonyl compound to an aminodiol, which then, with elimination of water, is converted into a pyrrolidylpropyl alcohol. In both cases the cyclization process is facilitated by the sterically very favorable mutual arrangement of the amino group and the corresponding oxygen-containing function. If it is assumed that the reaction competing with hydrolysis is direct hydrogenation of the double bonds of the furan ring, then the yields of the final products will be determined by the relative rates of the two processes, which in the final analysis is connected with the structural features of the initial furan amine. At the same time, of course, one cannot completely exclude the possibility of formation of the tetrahydrofuran ring also from the 1,4-aminodiol.

The reaction discovered by us apparently has a rather broad field of application. Thus, it also proceeds with furfuryl-substituted alicyclic amines, which leads to the formation of the corresponding alcohols of the octahydroindole series.



$$\text{[furfuryl-substituted cyclohexylamine]} \xrightarrow[(H^+)]{HOH} \left[\begin{array}{c} CH_2 - CH_2 \\ CHO \quad CO - CH(R) - \text{[cyclohexyl]} - NH_2 \end{array} \right] \longrightarrow$$

$$\longrightarrow \text{[octahydroindole alcohol derivative]} + \text{[tetrahydrofuran amine derivative]}$$

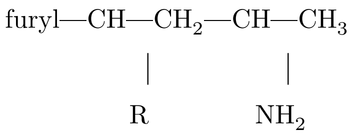
It is very interesting that the yields of pyrrolidine or octahydroindole alcohols depend substantially on the structure of the starting furan amine, namely on the presence and nature of the substituent at the α-carbon atom of the side chain. This is evident from the data given in Table 1.

The same regularity is also observed in the hydrogenation of furfuryl-substituted cyclohexylamines.

This curious fact of the influence of substituents on the cyclization processes of aliphatic systems has already been noted earlier by a number of authors (for example, (7)); we found it in the formation of alkyl-substituted 1,6-dioxaspiro-(4,4)-nonanes upon hydrogenation of 1-(α-furyl)alkanols-3 (8). In this case the aliphatic radicals, according to the degree of their influence on the cyclization process, were arranged in the same order as in the reaction considered by us in the present communication.

Table 1

Hydrogenation products of furan amines of the type



$$\text{furyl}-\underset{R}{CH}-CH_2-\underset{NH_2}{CH}-CH_3$$

Value of R	Yields, % of theoretical: pyrrolidine alcohol	Yields, % of theoretical: tetrahydrofuran amine
H	20	60
C_2H_5	36	42
$CH(CH_3)_2$	49	27

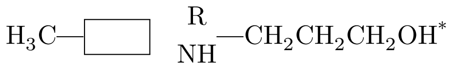
The pyrrolidyl- and octahydroindolylpropanols obtained by us contain asymmetric carbon atoms in the molecule and, consequently, should exist in several stereoisomeric forms. This apparently explains the somewhat broadened boiling-temperature ranges of some of the substances obtained; the latter are viscous, fairly high-boiling liquids.

We did not undertake the separation of isomers. This, as well as the study of the reaction mechanism, will be the subject of further investigations.

The most important properties and analyses of the synthesized substances are given in Tables 2 and 3.

Table 2

Alcohols of the formula



$$H_3C—\boxed{}\overset{R}{\underset{NH}{}}—CH_2CH_2CH_2OH^*$$

No.	Value of R	Obtained from	B.p. temp. (pressure mm)	M.p. temp., °C	Formula	C, % found	C, % calc.	H, % found	H, % calc.	N, % found	N, % calc.	Yield, %
X	H	I	113–114 (5)	20–21	$C_8H_{17}NO$	66.75; 67.20	67.19	12.34; 12.39	11.96	9.54; 9.65	9.78	20.0
XI	C_2H_5	II	136–137 (12)	46–48	$C_{10}H_{21}NO$	70.76; 70.72	70.17	12.00; 12.27	10.28	8.23; 8.31	8.18	36.0
XII	$CH(CH_3)_2$	III	132–134 (18)	23–25	$C_{11}H_{23}NO$	71.73; 71.33	71.35	12.45; 12.37	12.45	7.33; 7.34	7.57	49.0

* N,O-diacetyl derivatives: from X, b.p. 201–203 (5), n_D^{20} 1.4716; from XI, b.p. 170–171° (4), n_D^{20} 1.4730; from XII, b.p. 178–180 (5), n_D^{20} 1.4750.

The structure of the heterocyclic alcohols obtained, in addition to the usual analytical data, is confirmed by the formation of diacetyl derivatives. The IR spectra of pyrrolidine and octahydroindole alcohols contain the frequency of the stretching vibration of the N–H bond at 3260–3267 cm^{-1}, corresponding to the frequency of the stretching vibration of N–H in the pyrrolidine ring (10), whereas tetrahydrofuran amines are characterized by bands at 3355 and 3291 cm^{-1}, which corresponds to the stretching vibration of N–H in primary amines (11). The diacetyl derivatives have bands of the stretching vibration of the carbonyl group of amides at 1645–1667 cm^{-1} and of the ester group at 1752–1757 cm^{-1}.

Table 3

Alcohols of the formula
[[unclear: structural formula with indole ring, substituent R, and $-CH_2-CH_2-CH_2OH$]]*

No.	Value of R	Obtained from	b.p., °C (pressure mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calc.	Formula	C, % found	C, % calc.	H, % found	H, % calc.	N, % found	N, % calc.	Yield, %
XIII	H	V	151–154 (6)	1.0135	1.5022	53.38	53.72	$C_{11}H_{21}NO$	71.65; 71.64	72.08	11.51; 11.68	11.55	7.26; 7.37	7.64	18.0
XIV	C_2H_5	VI	171–174 (9)	0.9995	1.5006	62.22	62.96	$C_{13}H_{25}NO$	73.38; 73.50	73.93	12.29; 12.07	11.85	6.62; 6.82	6.63	42.5
XV	$CH(CH_3)_2$	VII	161–164 (5)	0.9867	1.4990	67.08	67.58	$C_{14}H_{27}NO$	75.02; 75.19	74.73	12.12; 12.42	12.10	6.03; 6.37	6.23	70.0

* N,O-diacetyl derivatives: from XIII b.p. 181–182° (2), n_D^{20} 1.4870; from XIV b.p. 179–180° (2), n_D^{20} 1.4951; from XV b.p. 212–214° (5), n_D^{20} 1.4970.

Experimental Part

The starting furan amines 1-(α-furyl)-3-aminobutane (I), 1-(α-furyl)-1-ethyl-3-aminobutane (II), 1-(α-furyl)-1-isopropyl-3-aminobutane (III), 1-(α-furyl)-5-aminohexane (IV), and 1-(α-furfuryl)-2-aminocyclohexane (V) were obtained by the previously described procedure (5, 9); 1-(α-furyl)-1-(1′-aminocyclohexyl-2′)-propane (VI) and 1-(α-furyl)-1-(1′-aminocyclohexyl-2′)-2-methylpropane (VII) were synthesized from the corresponding ketones, 1-(α-furyl)-1-(cyclohexanone-1′-yl-2′)-propane (VIII) and 1-(α-furyl)-1-(cyclohexanone-1′-yl-2′)-2-methylpropane (IX).

Ketone (VIII) was obtained from ethylmagnesium bromide and monofurfurylidenecyclohexanone by the method (12): liquid with b.p. 100–101.5° (2 mm), d_4^{20} 1.0296, n_D^{20} 1.5105, MR_D 58.92; calculated 58.55.

$C_{13}H_{18}O_2$. Found, %: C 75.56, 75.84; H 8.89, 8.70
Calculated, %: C 75.72; H 8.73

Similarly, from isopropylmagnesium bromide and monofurfurylidenecyclohexanone, ketone (IX) was obtained: b.p. 131° (7 mm), d_4^{20} 1.045, n_D^{20} 1.4986,

MR_D 63.31, calculated 63.17.

$C_{14}H_{20}O_2$. Found, %: C 76.89, 76.55; H 9.26, 9.27
Calculated, %: C 76.36; H 9.09

As a result of reductive amination of ketones (VIII) and (IX) by the method (6), the furan amines (VI) and (VII), respectively, were obtained.

Amine VI –liquid with b.p. 126–127° (8 mm); d_4^{20} 0.9975, n_D^{20} 1.5028, MR_D 61.45, calculated 61.96.

$C_{13}H_{21}NO$. Found, %: C 75.39, 75.49; H 10.39, 10.35; N 6.71, 6.62
Calculated, %: C 75.36; H 10.14; N 6.72

Amine VII –liquid with b.p. 123–124° (6 mm); d_4^{20} 0.9862, n_D^{20} 1.5015; MR_D 61.18, calculated 61.58.

$C_{14}H_{23}NO$. Found, %: C 75.81, 76.10; H 10.56, 10.50; N 6.33, 6.38
Calculated, %: C 76.01; H 10.40; N 6.21

Acetyl derivatives of the amines were obtained by the method (5). N-Acetyl (VI), b.p. 171–172° (3 mm).

$C_{15}H_{23}NO_2$. Found, %: C 72.51, 72.35; H 9.23, 9.00; N 5.34, 5.48
Calculated, %: C 72.29; H 9.29; N 5.62

N-Acetyl (VII), b.p. 175° (3 mm).

$C_{16}H_{25}NO_2$. Found, %: C 73.87, 73.90; H 9.79, 9.87; N 4.92, 4.94
Calculated, %: C 73.01; H 9.50; N 5.30

Pyrrolidyl- and octahydroindolylpropanols were obtained by the following typical procedure.

3-(5′-Methyl-3′-isopropylpyrrolidyl-2′)-propanol-1 (XII) and 1-isopropyl-1-(α-tetrahydrofuryl)-3-aminobutane (XVI). A solution of 36 g of 1-isopropyl-1-(α-furyl)-3-aminobutane in 60 ml of ~10% hydrochloric acid (pH of the solution 4–5) and 5 g of Raney nickel is placed in a rotating autoclave of 250-ml capacity. The initial hydrogen pressure is 100 atm. The temperature is 100°. The reaction is completed after 8 hr, after absorption of the calculated amount of hydrogen (10 liters). The hydrogenate is freed from the catalyst by filtration and neutralized with an excess of solid KOH. The separated oil is removed, and the aqueous layer is extracted with ether. The ether extracts are combined with the oil and dried with solid KOH. The ether is distilled off, and the residue is distilled in vacuo. Within the range 117-118° (14 mm), 1-isopropyl-1-(α-tetrahydrofuryl)-3-aminobutane (XVI) is collected. Yield 9.7 g (28%). At 132-134° (8 mm), 3-(5-methyl-3-isopropylpyrrolidyl-2′)-propanol-1 (XII) distills. Yield 17.8 g (49% of theory).

Compounds X–XII and XIII–XV were obtained analogously. Their diacetyl derivatives were obtained by method (^{5}).

The properties of the tetrahydrofuran amines obtained from I, II, IV, V have been described previously (^{5}, ^{8}). Their yields are, respectively: 60, 42, 60, and 62%.

Below are data on the tetrahydrofuran amines synthesized by us previously but not yet known.

1-Isopropyl-1-(α-tetrahydrofuryl)-3-aminobutane (XVI) was obtained from III as described above. Liquid with b.p. 117–118° (14 mm), d_4^{20} 0.9204, n_D^{20} 1.4635, MR_D 55.51, calculated 55.86.

Found, %: C 70.80, 71.32; H 12.60, 12.81; N 7.46, 7.25
$C_{11}H_{23}NO$. Calculated, %: C 71.31; H 12.53; N 7.57

1-(α-Tetrahydrofuryl)-1-(1′-aminocyclohexyl-2′)-propane (XVII) was obtained from VI in 30% yield. Liquid with b.p. 127–129° (5 mm) (after twofold distillation), d_4^{20} 0.9705; n_D^{20} 1.4892, MR_D 62.87; calculated 62.90.

Found, %: C 74.15, 74.64; H 11.99, 11.92; N 7.06, 6.93
$C_{13}H_{25}NO$. Calculated, %: C 74.00; H 11.94; N 6.64

Their acetyl derivatives were obtained by method (^{5}). **N-Acetyl (XVI)**—a viscous liquid with b.p. 174° (8 mm), n_D^{20} 1.4748.

Found, %: C 68.71, 68.44; H 11.57, 11.26; N 6.52, 6.59
$C_{13}H_{25}NO_2$. Calculated, %: C 68.78; H 11.10; N 6.17

N-Acetyl (XVII)—a viscous liquid with b.p. 184° (6 mm), n_D^{20} 1.4989.

Found, %: C 71.27, 71.64; H 11.16, 10.84; N 5.75, 5.74
$C_{15}H_{27}NO_2$. Calculated, %: C 71.21; H 10.76; N 5.54

The IR absorption spectra of all the substances obtained were recorded by A. D. Peshchonova on a double-beam H-800 spectrometer (Hilger), as a paste with Vaseline oil.

Compounds VI through XVII, as well as the acetyl derivatives of VI, VII, XXII, and XXIII, were obtained for the first time.

Saratov State University
named after N. G. Chernyshevsky

Received
9 XII 1963

REFERENCES

1. F. P. Doyle, M. Mehta, *J. Chem. Soc.*, 1958, 4458.
2. U.S. Patent 3006925; RZhKhim., 22L135 (1962).

3. B. R. Baker, R. E. Schaub, H. Williams, *J. Org. Chem.*, 17, 116 (1952).
4. U.S. Patent 2826588; RZhKhim., 87649 (1959).
5. A. A. Ponomarev, N. P. Maslennikova, A. P. Krivenko, *ZhOKh*, 31, 958 (1961).
6. A. A. Ponomarev, A. P. Krivenko, M. V. Noritsyna, *ZhOKh*, 33, 1778 (1963).
7. C. K. Ingold, *J. Chem. Soc.*, 119, 305, 951 (1921).
8. A. A. Ponomarev, V. A. Sedavkina, Z. V. Til, *ZhOKh*, 33, 1303 (1963).
9. A. A. Ponomarev, *Syntheses and Reactions of Furan Compounds*, 1960.
10. H. Tschamler, H. Voetter, *Monatsh. Chem.*, 83, 302, 321 (1952).
11. L. Bellamy, *The Infra-red Spectra of Complex Molecules*, IL, 1957, p. 297.
12. A. A. Ponomarev, V. A. Sedavkina, *Scientific Notes of Saratov State University*, 71, 143 (1959).

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

Source: Math-Net.Ru and CyberLeninka. Machine translation. Verify with the original.