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Abstract

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SYNTHESIS AND SOME CATALYTIC TRANSFORMATIONS OF PRIMARY FURAN AMINES

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Primary amines of the furan series containing an amino group in the side chain are usually obtained by catalytic hydrogenation or reduction of the oximes of the corresponding furan aldehydes or ketones.

Another route to the synthesis of amines consists in the reductive amination of saturated and unsaturated aldehydes and ketones in the presence of ammonia. As applied to carbonyl compounds of the furan series, this method has been little studied. The preparation by this route of furfurylamine from furfural is known (^{1}), as well as of several furan amines from α-β-unsaturated furan ketones (^{2}).

A detailed study of this method has allowed us to establish that, by hydrogenation under pressure in an ammoniacal alcoholic solution in the presence of Raney nickel, not only α-β-monounsaturated furan ketones are readily converted into the corresponding primary furan amines (yields up to 86% of theory), but also dienone ketones (yields up to 84% of theory). Using acetylfuran as an example, it was also shown that saturated furan ketones containing the carbonyl group in position 1 from the furan ring are smoothly converted into primary furan amines. Hydrogenation of the furan ring does not occur under these conditions.

Thus, the general character of this reaction has been established, by means of which various saturated and unsaturated furan ketones can be converted in good yields into primary amines with the amino group in positions 1, 3, and 5 of the side chain:

$$\text{furan} - (\text{CH} = \text{CH})_n - \text{C}(=\text{O}) - \text{R} \xrightarrow[\text{MeOH, NiR}]{\text{H}_2\text{, NH}_3} \text{furan} - (\text{CH}_2 - \text{CH}_2)_n - \text{CH}(\text{NH}_2) - \text{R}$$

$$n = 0,\ 1,\ 2; \qquad \text{R} = \text{H},\ \text{CH}_3,\ \text{CH}_2 - \text{CH}(\text{CH}_3)_2,\ \text{C}_6\text{H}_5 \text{ and others.}$$

The most important properties and analyses of the furan amines obtained in this way are given in Table 1. The same table also lists some physical constants of the *N*-acetyl derivatives of these amines, which are readily formed in yields up to 94% of theory by the action of acetic anhydride on the latter. Hydrogenation over Raney nickel of primary furan amines not substituted at nitrogen proceeds in a complicated manner. However, *N*-acetyl derivatives of amines are readily hydrogenated in dioxane solution to the corresponding derivatives of tetrahydrofuran amines under relatively mild conditions (NiR, 80—120°, H_2 pressure up to 100 atm.). Saponification of the acetyl derivatives of tetrahydrofuran amines is achieved by heating them with an alcoholic solution of sodium hydroxide to 170° in an autoclave.

$$\text{furan}-(\text{CH})_{2n}-\text{CH}(\text{NHCOCH}_3)-\text{R} \xrightarrow{\text{H}_2} \text{tetrahydrofuran}-(\text{CH}_2)_n-\text{CH}(\text{NHCOCH}_3)-\text{R} \xrightarrow{\text{alc. NaOH}} \text{tetrahydr}$$

Table 1

Physical constants and analyses of furan amines

Compound	b.p., °C/mm	n_D^{20}	d_4^{20}	MR_D, found	MR_D, calc.	N, %, found	N, %, calc.	N-acetyl derivatives: b.p., °C/mm	N-acetyl derivatives: m.p., °C
Furyl-CH(NH_2)-CH_3	76-77/60	1.4770	0.9986	31.50	31.83	12.27; 12.43	12.60	136-137/10	48-49
Furyl-$(CH_2)_2$-CH(NH_2)-CH_3	85/18	1.4763	0.9629	40.77	41.07	10.23; 9.90	10.06	163-168/18	54-56
Furyl-$(CH_2)_2$-CH(NH_2)-CH_2-CH$(CH_3)_2$	110-111/10	1.4710	0.9250	54.47	54.92	7.29; 7.44	7.72	178-179/10	42-44
Furyl-CH_2-cyclohexyl-NH_2	119-120/10	1.5086	1.0207	52.35	52.72	7.90; 7.68	7.81	172-174/3	89.5-92
Furyl-$(CH_2)_4$-CH(NH_2)-CH_3	98-100/10	1.4742	0.9140	50.06	50.31	8.39; 8.18	8.37	—	73-74

Compound	b.p., °C/mm	n_D^{20}	d_4^{20}	MR_D, found	MR_D, calc.	N, %, found	N, %, calc.	N-acetyl derivatives: b.p., °C/mm	N-acetyl derivatives: m.p., °C
Furyl-$(CH_2)_4$-$CH(NH_2)$-CH_2-$CH(CH_3)_2$	132–133/10	1.4710	0.9232	63.43	64.16	6.62; 7.04	6.68	197–198/10	17–18
Furyl-$(CH_2)_4$-$CH(NH_2)$-C_6H_5	137/3	1.5370	1.0265	69.76	69.80	6.00; 5.81	6.11	205–208/2.5	80–82

Table 2

Physical constants and analyses of tetrahydrofuran amines and their N-acetyl derivatives

Compound	b.p., °C/mm	n_D^{20}	d_4^{20}	MR_D, found	MR_D, calc.	C, %, found	C, %, calc.	H, %, found	H, %, calc.	N, %, found	N, %, calc.
Tetrahydrofuryl-$(CH_2)_2$-$CH(NHCOCH_3)$-CH_3	139–141/2	1.4741	1.0086	51.62	51.44	65.11; 65.02	64.86	10.49; 10.45	10.27	7.55	7.57
Tetrahydrofuryl-$(CH_2)_4$-$CH(NHCOCH_3)$-CH_3	185–187/4; m.p. 40–42	1.4725	—	—	—	67.75; 67.88	67.57	10.97; 10.00	10.87	6.62	6.56
Tetrahydrofuryl-CH_2-cyclohexyl-$NHCOCH_3$	171–172/3.5	—	—	—	—	69.02; 69.19	69.24	10.41; 10.28	10.21	5.97; 6.04	6.21
Tetrahydrofuryl-$(CH_2)_2$-$CH(NH_2)$-CH_3	93–96/18	1.4570	0.9253	42.15	42.00	66.95; 66.83	67.13	11.43; 11.46	11.88	9.87; 9.40	9.79

Compound	b.p., °C/mm	n_D^{20}	d_4^{20}	MR_D, found	MR_D, calc.	C, %, found	C, %, calc.	H, %, found	H, %, calc.	N, %, found	N, %, calc.
Tetrahydrofuryl-$(CH_2)_4$-$CH(NH_2)$-CH_3	82–84/3	1.4585	0.9134	51.22	51.68	69.81; 70.25	70.06	12.27; 12.43	12.36	7.88; 7.84	8.18

Some properties and analyses of tetrahydrofuran amines and their N-acetyl derivatives are given in Table 2.

All amines of the furan series and their N-acetyl derivatives, irrespective of the position of the amino and amido groups relative to the furan ring, in the ultraviolet region of the spectrum exhibit intense absorption at 215–217 mμ ($\lg\varepsilon_{\max} \sim 3.95$) and less intense absorption at 270–275 mμ ($\lg\varepsilon_{\max} \sim 1.25$). Amines of the tetrahydrofuran series and their N-acetyl derivatives do not show selective absorption in the ultraviolet region. Infrared absorption spectra were taken for the furan and tetrahydrofuran amines; the presence of frequencies in the region 800–1500 cm^{-1} confirms the presence, respectively, of furan and tetrahydrofuran rings; frequencies in the region 3250–3450 cm^{-1} indicate the presence of an amino group.

The furan and tetrahydrofuran amines were then used for the synthesis of pyrrolizidine and dihydrodipyrrole derivatives. The indicated nitrogen-containing heterocycles occur in many alkaloids.

It is known that the synthesis of such substances is usually carried out by a multistage route. Meanwhile, it is not difficult to see that the relative positions of the amino group and the ring oxygen atom in furan and tetrahydrofuran amines with the amino group in position 3 and farther along the side chain are such that they favor the course of an intramolecular cyclization reaction with formation of bicyclic systems having a nitrogen atom common to the two rings. Cyclization of this kind was attempted with 1-(α-furyl)-3-aminopropane [3] over alumina at 400°; however, the product obtained was not characterized, and yields were not indicated.

We carried out experiments on the intramolecular cyclization of 1-(α-furyl)-3-aminopropane, 1-(α-furyl)-3-aminobutane, 2-furfurylaminocyclohexane, and 1-(α-tetrahydrofuryl)-3-aminobutane. Pure alumina and alumina activated with thorium dioxide were used; the formulation for the preparation and use of the latter was kindly provided to us by Yu. K. Yur'ev. It was established that, over the indicated catalysts, furan and tetrahydrofuran amines cyclize to pyrrolizidine or dihydrodipyrrole derivatives according to the scheme:

$$\text{furyl} - (CH_2)_2 - CH(NH_2) - R \xrightarrow{-H_2O} \text{pyrrolizidine derivative,} \qquad R = H,\ CH_3,$$

$$\text{tetrahydrofuryl} - (CH_2)_2 - CH(NH_2) - CH_3 \xrightarrow{-H_2O} \text{methyl-dihydrodipyrrole derivative,}$$

$$\text{furyl} - CH_2 - \text{cyclohexyl-}NH_2 \xrightarrow{-H_2O} \text{fused dihydrodipyrrole derivative.}$$

The yields of dihydrodipyrroles reach 32%, and those of pyrrolizidine derivatives 50% of theory. Table 3 gives data on some physical properties and analyses of the substances obtained by us by the indicated route. Investigations in this area are continuing.

Experimental Part

The experimental conditions are evident from the following examples:

Synthesis of 1-(α-furyl)-3-aminobutane. Into a rotating autoclave of 250 ml capacity are placed 40 g of freshly distilled furfurylideneacetone, 90 ml of methyl alcohol saturated with ammonia at 0°, and 5 g of Raney nickel. The reaction is carried out at 80–100° and a hydrogen pressure of 100–120 atm until absorption of hydrogen ceases (3–4 hours). The hydrogenation mixture is freed from the catalyst by filtration, and the methyl alcohol is distilled off under a nitrogen atmosphere. The residue is diluted with ether and dried over fused caustic potash. The ether is distilled off, and the residue is distilled in vacuum under a nitrogen atmosphere. Yield 35–36 g (85–86% of theory).

Table 3

Physical constants and analyses of several compounds of the dihydropyrrole and pyrrolizidine series

Compound	B.p., °C/mm	n_D^{20}	d_4^{20}	MR_D, found	MR_D, calc.	N, %, found	N, %, calc.
[[structural formula]]	69—70/11	1.5212	0.9870	33.07	33.13	12.5612.38	13.07
[[structural formula, CH_3 substituent]]	63—65/1070—71/15	1.5115	0.9665	37.59	37.75	11.0511.15	11.56

Compound	B.p., °C/mm	n_D^{20}	d_4^{20}	MR_D, found	MR_D, calc.	N, %, found	N, %, calc.
[[structural formula, CH_3 substituent]]	52–53/18	1.4635	0.889	38.74	38.68	11.74 11.76	11.19
[[structural formula, phenyl substituent]]	121–123/10	1.5365	1.1016	49.55	49.40	8.19 8.42	8.7

The acetyl derivative was obtained by treating 28 g of amine with 45 g of acetic anhydride. The reaction product is neutralized with saturated sodium carbonate solution. The separated oil is washed with water, dissolved in ether, dried over ignited $MgSO_4$, and the residue after removal of the ether is distilled in vacuo.

Synthesis of 1-(α-tetrahydrofuryl)-3-acetamidobutane. Into a steel rotating autoclave of 150 ml capacity are charged 22 g of 1-(α-furyl)-3-acetamidobutane, 46 ml of dioxane, and 2 g of Raney nickel. The initial hydrogen pressure is 110 atm, temperature 80°. Hydrogenation is completed after the calculated amount of hydrogen required to saturate two double bonds has been absorbed (5.7 l). The hydrogenation product is filtered from the catalyst and the dioxane is distilled off. The residue is distilled in vacuo. Yield 17.7 g (80% of theory). Saponification of 1-(α-tetrahydrofuryl)-3-acetamidobutane was carried out by heating 29 g of the substance in an autoclave for 10 hr at 170° in the presence of 80 ml of a 2 N solution of NaOH in methyl alcohol. The alcohol is then distilled off; the amine is extracted from the residue with ether and dried over ignited $MgSO_4$. After removal of the ether, the residue is distilled in vacuo.

Cyclization of the amines was carried out in a flow apparatus of the usual type.

Synthesis of 3-methylpyrrolizidine. 16 g of 1-(α-tetrahydrofuryl)-3-aminobutane are passed at a rate of 5–6 drops per minute in a stream of nitrogen at 325° through a glass tube 40 cm long and 1.2 cm in diameter, packed with $Al_2O_3 \cdot ThO_2$ (5% thorium dioxide) as catalyst. In a receiver thoroughly cooled with running water, the liquid catalyzate is collected. The latter is saturated with solid KOH and extracted with ether. The ether extract is dried over ignited $MgSO_4$. After removal of the ether, the residue is distilled in vacuo. Yield 6.9 g (50% of theory).

Absorption spectra in the infrared region were recorded by A. D. Peshekhonova on an H-800 spectrophotometer; absorption spectra in the ultraviolet region were recorded on an SF-4 spectrophotometer.

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REFERENCES

1. J. Robinson, H. Snyder, *Organic Syntheses*, **23**, 70 (1943).
2. Z. Zafiriadis, P. Mastagli, *C. R.*, **236**, 295 (1953).
3. F. Sorm, Z. Arnold, *Collections Czechoslov. Chem. Communs.*, **12**, 467 (1947).

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