STUDY OF FURAN COMPOUNDS

LI.* SYNTHESIS AND CATALYTIC HYDROGENATION OF FURYL NITRO ALKANOLS

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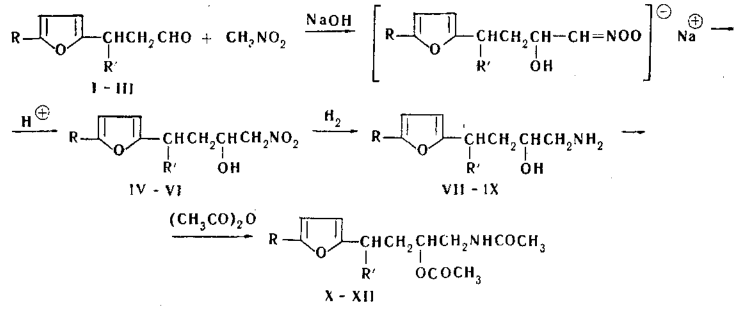
Furyl nitro alkanols were obtained by the condensation of 1-(2'-furyl)-3-propanols with nitromethane. Catalytic hydrogenation of the products gave the corresponding furyl amino alkanols.

A considerable number of studies [3-6] have been devoted to the condensation of furfural with nitromethane, which was first described by Priebs [2]. The product in the presence of alkaline condensing agents is α-(α'-furyl)-β-nitroethylene.

Kanao [7] studied the condensation of furfural with various nitroalkanes using $KHCO_3$ or K_2CO_3 as condensing agent and obtained good yields of the corresponding furyl nitro alcohols.

This communication is devoted to a study of the condensation of 1-(2'-furyl)-3-propanols with nitromethane for the synthesis of furyl nitro alkanols. The starting compounds were 1-(2'-furyl)- (I), 1-(5'-methyl-2'-furyl)- (II), and 1-(2'furyl)-1-methyl-3-propanol (III).



I, IV VII, X $R=R'=H$; II, V VIII, XI $R=CH_3, R'=H$; III, VI, IX, XII $R=H$, $R'=CH_3$

The condensation was carried out in ethanol with cooling in the presence of sodium hydroxide, and the furyl nitro alkanols were obtained in high yields (73-80%).

The structure of compounds IV-VI was confirmed by the IR spectra, which contain absorption bands at 1553 and 1345 cm^{-1} that correspond to the asymmetrical and symmetrical stretching vibrations of the nitro group. The presence of a hydroxyl group was confirmed by the broad absorption band at 3450 cm^{-1} (stretching vibrations of the associated OH groups).

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*See [1] for communication L.
†Deceased.

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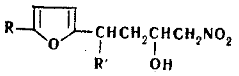
TABLE 1

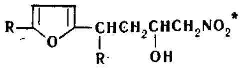


Compound No.	R	R′	bp, °C (pressure, mm)	d_4^{20}	n_D^{20}	IR spectrum, cm^{-1}			
						ν_{NO_2}	ν_{OH}	$\nu_{C=C}$	$\nu_{=CH}$
IV	H	H	133—135 (1)	1,2280	1,5010	1552 1345	3450	1600 1510	3100
V	CH_3	H	135—138 (2)	1,1807	1,4990	1553 1357	3450	1619 1510	3100
VI	H	CH_3	130—132 (2)	1,1750	1,4970	1553 1345	3450	1625 1510	3090

Table 1 (continued)

Compound No.	MR_D		Empirical formula	Found, %			Calc., %			Yield, %
	found	calc.		C	H	N	C	H	N	
IV	44,36	44,79	$C_8H_{11}NO_4$	52,09	6,00	7,34	51,89	5,99	7,56	78
V	49,54	49,41	$C_9H_{13}NO_4$	54,72	6,54	7,04	54,26	6,58	7,03	73
VI	49,61	49,41	$C_9H_{13}NO_4$	54,34	6,79	6,90	54,26	6,58	7,03	80

TABLE 2. Conditions and Results of the Catalytic Hydrogenation of Furyl Nitro Alkanols



Furyl nitro alkanols			Catalyst	Solvent	Temp., °C	Furyl amino alkanols	
compound	R	R′				compound	yield, %
IV	H	H	NiR	Ethanol	50	VII	40
			NiR	Ethanol saturated with ammonia	100	VII	60
			PtO_2	Methanol saturated with ammonia	100	VII	50
			5% Ru/C	Ethanol	25	VII	65
			10% Ru/C	The same	25	VII	65
V	CH_3	H	NiR	" "	50	VIII	22
			5% Ru/C	" "	25	VIII	75
VI	H	CH_3	NiR	" "	50	IX	—
			5% Ru/C	" "	25	IX	—
			10% Ru/C	" "	25	IX	30

*The initial hydrogen pressure was 100-140 atm.

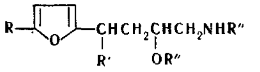
The furyl nitro alkanols (the physical constants, the results of the analyses, and some characteristics of the IR spectra are presented in Table 1) are viscous, yellow, unstable liquids that darken **rapidly** on standing and decompose to the starting compounds.

We also accomplished the catalytic hydrogenation of the nitro alcohols in order to obtain furyl amino alkanols, which are of interest for subsequent transformations, including the preparation of 4-(2′-furyl)-n-butylamines and for the synthesis of aminomethyl-1,6-dioxaspiro[4.4]-3-nonenes. Data on the conditions and the results of the hydrogenation of the nitro alcohols are presented in Table 2. The data in Table 2 are evidence that the yields of the amino alcohols are determined by the structure of the starting nitro alcohol and the type of catalyst. The best yields of the target products are obtained when ruthenium catalysts are used. The physical constants, results of analyses, and several characteristic frequencies of the IR spectra of the furyl amino alkanols, their diacetyl derivatives, and oxalates are presented in Table 3.

Very intense bands at 1736-1740 and 1662 cm^{-1}, which are due to the stretching vibrations of the C=O groups of esters and secondary amides, respectively, are observed in the IR spectra of X-XII. The presence of hydroxyl and primary amino groups in VII-IX is thereby confirmed.

An investigation of the antibacterial activity of furyl nitro alkanols IV-VI with respect to Gram-positive and Gram-negative bacteria demonstrated that the antibacterial properties are expressed most clearly

TABLE 3



Compound	R	R′	R″	bp, °C (pressure, mm)	n_D^{20}	IR spectrum, cm^{-1}			
						$\nu_{C=C}$	$\nu_{=CH}$	$\nu_{C=O}$ ester	$\nu_{C=O}$ amide
VII	H	H	H	125—127 (3)	1,5050	1600 1506	3100	—	—
VIII	CH_3	H	H	152—155 (4)	1,5070	1615 1570	3100	—	—
IX	H	CH_3	H	117—120 (1)	1,5110	1600 1510	3100	—	—
X	H	H	$COCH_3$	166—170 (2)	1,4900	1600 1510	3100	1736	1662
XI	CH_3	H	$COCH_3$	168—169 (1)	1,4920	1600 1570	3100	1740	1662
XII	H	CH_3	$COCH_3$	157—159 (1)	1,4985	1600 1510	3100	1736	1662

TABLE 3 (continued)

Compound	Empirical formula	Found, %			Calc., %			Oxalates		
		C	H	N	C	H	N	mp, °C	N, % found	N, % calc.
VII	$C_8H_{13}NO_2$	61,69	8,51	9,12	61,93	8,40	9,03	213—214	6,67	6,99
VIII	$C_9H_{15}NO_2$	63,65	8,57	8,02	63,88	8,09	8,27	208—209	6,41	6,54
IX	$C_9H_{15}NO_2$	63,86	8,26	7,95	63,88	8,09	8,27	178—180	6,03	6,54
X	$C_{12}H_{17}NO_4$	60,52	7,10	5,83	60,24	7,17	5,85	—	—	—
XI	$C_{13}H_{19}NO_4$	61,25	7,67	5,53	61,64	7,56	5,52	—	—	—
XII	$C_{13}H_{19}NO_4$	62,79	7,13	5,39	61,64	7,56	5,52	—	—	—

with respect to St. aureus.* The bacteriostatic titers of the preparations are 17.5 μg/ml. Compound V displays fungistatic activity, inhibiting the growth of Candida fungi at a concentration of 25 μg/ml.

Amino alchols VII-IX and their diacetyl derivatives (X-XII) do not have antibacterial properties with respect to the tested bacteria.

EXPERIMENTAL†

1-(2′-Furyl)- (I) [8] and 1-(5′-Methyl-2′-furyl)-3-propanol (II) [9]. These compounds were obtained by known methods. Raney nickel, 5% Ru/C [10], 10% Ru/C [11], and Adams PtO_2 [12] were used as catalysts.

1-(2′-Furyl)-4-nitro-3-butanol (IV). A 100 ml three-necked round-bottom flask equipped with a mechanical stirrer, thermometer, and dropping funnel was charged with 13.6 g (0.11 mole) of I, 20.4 g (0.33 mole) of nitromethane, and 30 ml of ethanol. A total of 11 ml of 10 N aqueous sodium hydroxide was added dropwise with constant stirring and cooling in such a way that the temperature of the mixture did not rise above +10°C. At the end of the addition of the alkali, the reaction mass was stirred for 1 h at 20-25°. The resulting abundant crystalline precipitate was dissolved in ice water, and the solution was acidified to pH 6 with 10% acetic acid. The oil that formed was separated, and the aqueous portion was extracted several times with ether. The oil and ether extracts were combined and dried over calcined magnesium sulfate. The ether was removed by distillation, and the residue was vacuum distilled to give 15.8 g (78%) of IV. Compounds V and VI (Table 1) were similarly obtained.

1-(2′-Furyl)-4-amino-3-butanol (VII). A) A rotating 250 ml autoclave was charged with 10 g of IV, 130 ml of ethanol, and 1 g of Raney nickel. The initial hydrogen pressure was 120 atm at 50°. The hydrogenation was carried out until hydrogen absorption ceased. The catalyst was removed by filtration, and the ethanol was removed by distillation at reduced pressure. The resulting amino alcohol was isolated as the hydrochloride in a yield of 3.3 g (40%).

B) When the reaction was carried out in the presence of ethanol saturated with ammonia and a Raney nickel catalyst, a hydrogen pressure of 120 atm at 100° was used. At the end of the hydrogenation, the cat-

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*The antibacterial activity was studied by candidate of biological sciences L. K. Kulikova.

†N. Bashtova participated in the experimental work.

alyst was removed by filtration, the solvent was removed by distillation under reduced pressure, and the residue was vacuum distilled to give 60% of VII.

C) When 5% or 10% Ru/C was used as the catalyst, the initial hydrogen pressure was 100 atm at 25°, and the yield was 65%.

D) When the hydrogenation was carried out in the presence of a PtO_2 catalyst, methanol saturated with ammonia was used as the solvent, and the initial hydrogen pressure was 140 atm at 100°. The yield was 50%. The hydrogenation of V and VI (Table 2) was accomplished similarly.

Diacetyl Derivative of 1-(2'-Furyl)-4-amino-3-butanol (X). A mixture of 3.2 g (0.02 mole) of VII and 10.2 g (0.1 mole) of acetic anhydride was refluxed at 120° for 3 h. At the end of the reaction, the excess acetic anhydride and the acetic acid formed were removed by distillation at reduced pressure, and the residue was vacuum distilled to give 3.2 g (64%) of X. Compounds XI and XII were similarly obtained.

1-(2'-Furyl)-4-amino-3-butanol Oxalate. A 0.56 g (0.0036 mole) sample of VII was dissolved in anhydrous ethanol and mixed with a solution of 0.16 g (0.0018 mole) of oxalic acid in anhydrous alcohol to give 0.6 g (50%) of a white crystalline precipitate. The oxalates of VIII and IX (Table 3) were similarly obtained.

The IR spectra were recorded with an H-800 (Hilger) spectrophotometer at 700-4000 cm^{-1} with a sodium chloride prism. All of the substances were investigated in the liquid state as a capillary-thin layer between sodium chloride plates.

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