SYNTHESIS OF N-SUBSTITUTED 1-(2-PYRROLYL)-3-ALKANOLS

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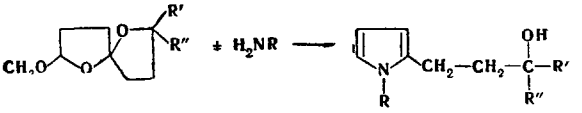
A new method for the synthesis of alcohols of a number of N-substituted pyrroles from 2-methoxy-1,6-dioxaspiro[4,4]nonanes and primary amines is described.

Alcohols of the pyrrole series are of interest in connection with the presence of physiological activity (antimicrobial and anesthetic action) in some of their derivatives, particularly their esters [1-3]. The most widespread methods for the preparation of alcohols of the pyrrole series are based on alkylation of the nitrogen atom of pyrrole and its homologs [1] or on the reaction of 1,4-dicarbonyl compounds with primary amino alcohols [2, 3]. These methods are distinguished by their multistep character [1], by the use of starting compounds that are difficult to obtain [2, 3], and by the possibility of the production of only N-alkanols of the pyrrole series.

We have developed a method for the preparation of N-aryl-, N-alkyl-, and N-hydroxyalkyl-substituted 1-(2-pyrrolyl)-3-alkanols that is based on the reaction of 2-methoxy-1,6-dioxaspiro[4,4]nonane and its homologs with primary aromatic and aliphatic amines or amino alcohols.



The IR spectra of these compounds contain absorption bands characteristic for the pyrrole ring: two bands at 1550-1660 cm^{-1} (C=C) and an intense band at 1274-1295 cm^{-1} for N-alkyl substituted compounds and at 1325-1327 cm^{-1} for N-aryl-substituted compounds, which is in agreement with [4], and vibrations at 3360-3380 cm^{-1} (associated OH).

EXPERIMENTAL

The IR spectra of thin capillary layers of the compounds between potassium bromide plates were recorded with a UR-20 spectrometer.

2-Methoxy-1,6-dioxaspiro[4,4]nonane (XIV), 2-methoxy-7-methyl-1,6-dioxaspiro[4,4]-nonane (XV), and 2-methoxy-7,7-dimethyl-1,6-dioxaspiro[4,4]nonane (XVI) were obtained by known methods [5].

N-Substituted 1-(2-Pyrrolyl)-3-alkanols. 1-(N-Phenyl-2-pyrrolyl)-3-propanol (I). A mixture of 4.74 g (0.03 mole) of XIV, 2.88 g (0.031 mole) of aniline, and 15 ml of propionic acid was heated on a boiling-water bath for 1.5 h, after which it was cooled and poured into 150 ml of water. The aqueous mixture was cooled, and potassium hydroxide was added until it was alkaline. It was then extracted with ether,* and the ether extracts were dried with calcined magnesium sulfate. The ether was removed by distillation, and the residue was vacuum distilled to give 5.25 g (87%) of product.

*When monoethanolamine was used as the starting amine, the extraction was carried out with ethyl acetate, prior to which the aqueous solution was saturated with sodium chloride.

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TABLE 1. N-Substituted 1-(2-Pyrrolyl)-3-alkanols

Compound	R	R′	R″	bp, °C (mm)	n_D^{20}	Empirical formula
I	C_6H_5	H	H	144—145 (2)	1,5760	$C_{13}H_{15}NO$
II	C_6H_5	CH_3	H	158—159 (3)	1,5682	$C_{14}H_{17}NO$
III	C_6H_5	CH_3	CH_3	171,5—173,5 (8)	1,5608	$C_{15}H_{19}NO$
IV	*o*-$CH_3C_6H_4$	H	H	171—172 (9)	1,5610	$C_{14}H_{17}NO$
V	*o*-$CH_3C_6H_4$	CH_3	H	170,5—171,5 (9)	1,5545	$C_{15}H_{19}NO$
VI	*o*-$CH_3C_6H_4$	CH_3	CH_3	140 (1,5)	1,5468	$C_{16}H_{21}NO$
VII	*n*-C_4H_9	H	H	125—126 (1)	1,5015	$C_{11}H_{19}NO$
VIII	*n*-C_4H_9	CH_3	H	116—117 (1)	1,4997	$C_{12}H_{21}NO$
IX	*tret*-C_4H_9	H	H	131 (3)	1,5040	$C_{11}H_{19}NO$
X	*tret*-C_4H_9	CH_3	CH_3	135—136 (5)	1,4968	$C_{13}H_{23}NO$
XI	$HOCH_2CH_2$	H	H	162—163 (3)	1,5187	$C_9H_{15}NO_2$
XII	$HOCH_2CH_2$	CH_3	H	152—153 (2)	1,5180	$C_{10}H_{17}NO_2$
XIII	$HOCH_2CH_2$	CH_3	CH_3	172,5—173 (3)	1,5158	$C_{11}H_{19}NO_2$

Compound	Found, %			Calc., %			IR spectra, ν, cm^{-1}		Yield, %
	C	H	N	C	H	N	O—H	C—N(N—R)	
I	77,6	7,9	6,8	77,6	7,5	7,0	3360	1325	87
II	78,0	8,0	6,7	78,1	8,0	6,5	3380	1325	81
III	78,4	8,4	6,0	78,6	8,4	6,1	3375	1325	73
IV	78,0	8,0	6,4	78,1	8,0	6,5	3380	1327	98
V	78,3	8,8	6,1	78,6	8,4	6,1	3380	1325	81
VI	78,8	8,4	5,6	79,0	8,7	5,8	3370	1327	72
VII	73,0	10,7	7,6	72,9	10,6	7,7	3375	1290	62
VIII	73,7	10,7	7,3	73,8	10,9	7,2	3380	1291	56
IX	72,7	10,6	7,9	72,9	10,6	7,7	3375	1280	44
X	74,3	11,1	6,7	74,6	11,1	6,7	3380	1274	42
XI	63,7	9,2	8,1	63,9	8,9	8,3	3380	1293	56
XII	65,3	9,3	7,7	65,5	9,4	7,6	3375	1295	60
XIII	66,6	9,6	7,1	67,0	9,7	7,1	3380	1295	67

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