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STUDIES OF 1-AZABICYCLIC COMPOUNDS. III*. THE MANNICH REACTION WITH 1,2-DIHYDROPYRROLIZINES

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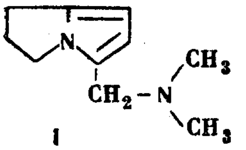
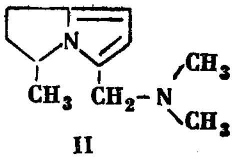
1,2-Dihydropyrrolizines with position 5 unsubstituted react with aliphatic and cyclic secondary amines under mild conditions to give Mannich bases. The picrates are prepared, and some physical properties of the bases synthesized are described.

The present paper deals with aminoalkylation of 1,2-dihydropyrrolizines. It is known that pyrrole and N-substituted pyrroles can undergo the Mannich reaction [1-3] to give mono- and bis-α-dialkylaminomethylpyrroles. It is recorded [3] that β-substitution can occur with a 2,5-dialkylpyrrole.

Since 1,2-dihydropyrrolizine corresponds in structure to N,α-dialkylpyrroles, it might be expected that they would undergo the Mannich reaction with one equivalent of amine, because of the single free α position in the molecule [1-5], and experiments carried out supported this hypothesis. Upon condensation at room temperature with equimolecular amounts of reactants, dimethylamine, morpholine, piperidine, and hexamethyleneimine give the hitherto unknown corresponding Mannich bases, viz., 5-dimethylaminomethyl-1,2-dihydropyrrolizine (I), 3-methyl-5-dimethylaminomethyl-1,2-dihydropyrrolizine (II), 3-methyl-5-(N-morpholinomethyl)-1,2-dihydropyrrolizine (III), 3-methyl-5-(N-piperidinomethyl)-1,2-dihydropyrrolizine (IV), 3-methyl-5-(N-hexamethyleneiminomethyl)-1,2-dihydropyrrolizine (V), and 2,3-tetramethylene-5-dimethylaminomethyl-1,2-dihydropyrrolizine (VI).


I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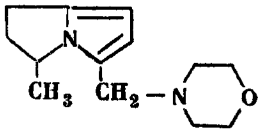
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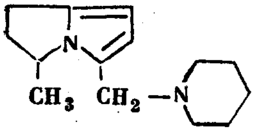
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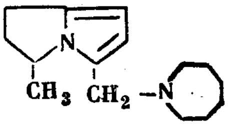
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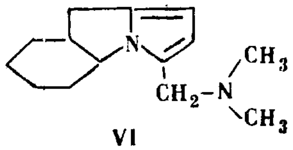
VI

These are liquids with a characteristic odor and give crystalline picrates with one equivalent of picric acid, with the exception of dihydropyrrolizine III which gives an oil. Properties and analyses of the substances are given in Table 1.

The UV spectra of the Mannich bases synthesized are characterized by two absorption maxima, an intense one at 220-222 mμ and a less intense one at 296 mμ, the positions of these absorption bands being uninfluenced by substituents in the 3 and 5 positions in the dihydropyrrolizines (Table 2).

The IR spectra of the Mannich bases prepared are characterized by numerous high-intensity absorption bands in the region 700-1800 cm^{-1}. Among them was observed a series of bands whose positions and intensities were the same for all compounds investigated, at 1029, 1060, 1276, and 1310 cm^{-1}. These are probably connected with vibration of the dihydropyrrolizine ring skeleton. In the region of valence vibrations of the C═C bond there are two bands at 1517 and 1574 cm^{-1}, corresponding to the data for pyrrole [6]. Characteristic of all the compounds is a C—H deformation vibrations band at 764 cm^{-1}, and intense deformation vibration bands due to C—H in —CH_2— and —CH_3 groups in the regions 1370-1390 cm^{-1} and 1450-1480 cm^{-1}. The figure shows the IR spectra for dihydropyrrolizines I and IV; spectra of II, III, V and VI are similar in appearance.

EXPERIMENTAL

The 1,2-dihydropyrrolizine, 3-methyl-1,2-dihydropyrrolizine, and 2,3-tetramethyl-1,2-dihydropyrrolizine used as starting materials are prepared as previously described [7].

The Mannich bases were synthesized by a known method [1].

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*For part II see [5].

TABLE 1

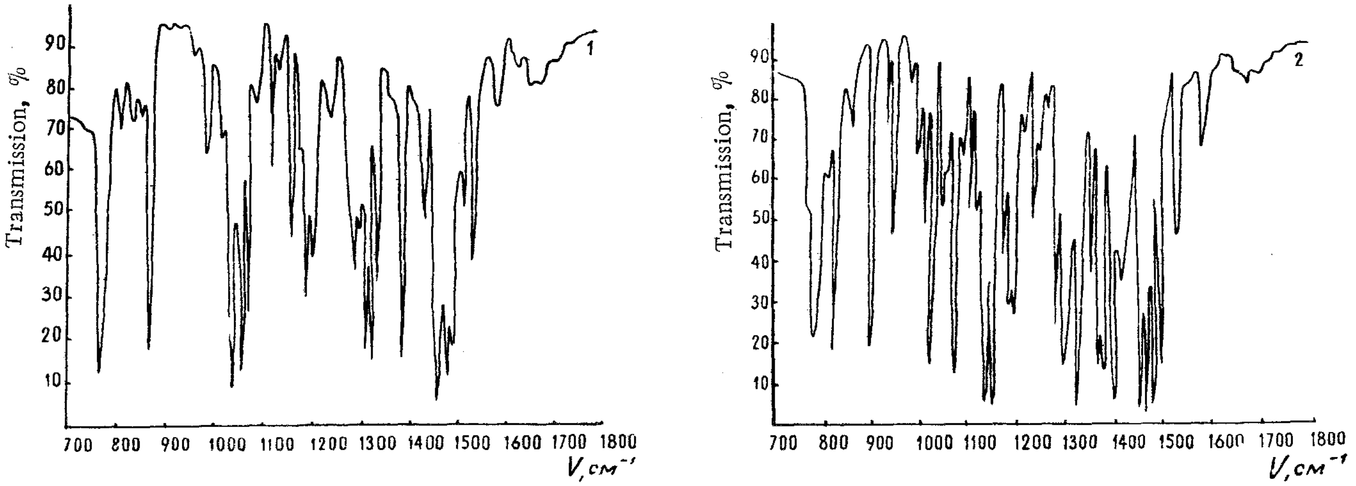
Properties and analyses of Mannich bases synthesized and their picrates

Compound	Yield, %	B.p. (mm)	d_4^{20}	n_D^{20}	MR_D		Found, %			Empirical formula	Calculated, %			Picrates				
					Found	Calculated	C	H	N		C	H	N	Yield, %	M.p., °C	Empirical formula	N, % Found	N, % Calculated
I	68.6	98—99° (8)	0.9712	1.5150	51.00	50.93	73.35 73.19	9.91 9.70	16.96 16.94	$C_{10}H_{16}N_2$	73.12	9.82	17.06	86	111—112 (from methanol)	$C_{16}H_{19}N_5O_7$	17.67 17.23	17.76
II	62.54	104—106 (10)	0.9526	1.5080	55.78	55.54	74.24	10.42	16.23 15.76	$C_{11}H_{18}N_2$	74.10	10.18	15.72	88	102—103 (from methanol)	$C_{17}H_{21}N_5O_7$	17.41 17.33	17.19
III	61.2	156—158 (10)	1.0540	1.5285	64.42	64.22	70.52 70.67	9.06 9.33	12.67 12.39	$C_{13}H_{20}N_2O$	70.87	9.15	12.72	—	—	—	—	—
IV	75.5	112—113 (5)	0.9898	1.5260	67.71	67.20	76.87 76.83	10.15 10.48	12.81 13.08	$C_{14}H_{22}N_2$	77.01	10.16	12.83	83	117—118 (from methanol)	$C_{20}H_{25}N_5O_7$	15.56 15.38	15.65
V	60.0	140—141 (2)	0.9972	1.5288	71.84	71.82	77.65 77.06	10.70 10.45	12.04 11.92	$C_{15}H_{24}N_2$	77.53	10.41	12.06	92	112—113 (from methanol)	$C_{21}H_{27}N_5O_7$	15.01 15.21	15.07
VI	70.16	148—150 (10)	0.9933	1.5272	67.59	67.20	77.26 76.84	10.12 10.24	12.68 12.46	$C_{14}H_{22}N_2$	77.01	10.16	12.83	83	156—157 (from methanol)	$C_{20}H_{25}N_5O_7$	15.32 15.38	15.65

TABLE 2

UV spectra of Mannich bases (in methanol)

Compound	λ_{max}, μμ	lg ε_{max}
I	222 296	3.94 1.55
II	220 296	3.96 1.75
III	223 296	4.02 1.93
IV	221 296	3.87 1.68
V	221 296	3.92 1.70
VI	220 298	3.85 2.12



IR spectra: 1) 5-dimethylaminomethyl-1, 2-dihydropyrrolizine (I);
2) 3-methyl-5-(N-piperidinomethyl)-1, 2-dihydropyrrolizine (IV).

3-Methyl-5-dimethylaminomethyl-1, 2-dihydropyrrolizine (II). 10 g 3-methyl-1, 2-dihydropyrrolizine are placed in a 100 ml 3-necked flask, and 7.1 g dimethylamine hydrochloride in 7.3 g 36% formalin added dropwise with stirring over 30 min. The mixture is warmed (take care that the temperature does not exceed 60°). After addition is complete, stirring is continued for a further 2 hr, and the mixture then left overnight. Next day it is treated with 20 ml 25% sodium hydroxide solution. The reddish oil separating out is extracted with ether, the ether extracts washed with water (2 × × 20 ml), and then dried over sodium sulfate. Yield 9.2 g (62.5%) of a colorless, mobile liquid.

Picrate. Hot alcoholic solutions of 0.65 g picric acid and 0.5 g 3-methyl-5-dimethylaminomethyl-1, 2-dihydropyrrolizine are mixed. The resultant precipitate is recrystallized from methanol, yield 1 g (88%), yellow plates.

I, III, IV, V, VI and their picrates are prepared in the same way. With IV and V the reaction mixture is worked up the same day, after 3 hrs stirring.

UV spectra of the Mannich base were determined with an SF-4 spectrophotometer. The solvent used was anhydrous methanol, with the base concentration 10^{-4}-10^{-2} mole/l, and a layer thickness of 1 cm.

IR spectra were measured with an H-800 Hilger double-beam spectrometer, over the range 700-1800 cm^{-1}, using a rock salt prism and pure liquids (capillary-thin layer between NaCl plates).

The UV and IR spectra were determined by A. D. Peshekhonova.

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