INDOLES

XXV.* CYCLIC ENAMINES IN THE SYNTHESIS OF TRYPTAMINES AND HOMOTRYPTAMINES

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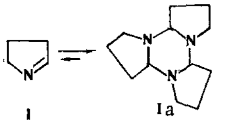
A number of tryptamines and homotryptamines were obtained by the reaction of arylhydrazine salts with cyclic enamine salts.

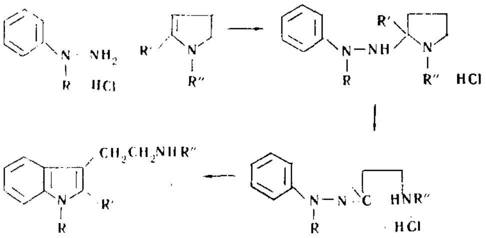
Continuing our investigation of the reaction of arylhydrazine salts with cyclic enamine salts [2], we have obtained a number of tryptamines and homotryptamines. We successfully used isopropyl alcohol in place of the previously used dimethylformamide [2]. The replacement of the solvent was caused by the fact that, in a number of cases, we detected a side reaction involving the formylation of the arylhydrazine by dimethylformamide. In addition, when dimethylformamide is replaced by isopropyl alcohol, there is less resinification, and it is easier to isolate the reaction products.

Since the use of Δ^1-piperidine trimer in the reaction with arylhydrazine salts led to homotryptamines [2], we attempted to use Δ^1-pyrroline (I) for the synthesis of tryptamine.



Like Δ^1-piperideine, Δ^1-pyrroline is also isolated only as the trimer (Ia). A modification of the Schöpf method [3] was chosen for its synthesis.

To obtain tryptamines III, IV, VIII, and IX, we used solutions of trimer Ia or the trimers of substituted pyrrolines in isopropyl alcohol containing an equivalent amount of hydrogen chloride.



Homotryptamines II, V-VII, and X (Tables 1 and 2) were obtained from the appropriate piperideines via a similar scheme.

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*See [1] for communication XXIV.

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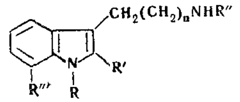
TABLE 1.



Comp.	R	R′	R″	R‴	n	bp, °C (mm)	UV spectra*		R_f†	IR spectra, cm^{-1}‡	Empirical formula	Found, %		Calc., %		Yield, %
							λmax, nm	lg ε				C	H	C	H	
II	i-C_3H_7	H	H	H	2	178—180 (1—2)	226 290	4,46 3,65	0,82	[1375, 1410, 1465, 1620] 3300 (NH_2)	$C_{14}H_{20}N_2$	77,5	9,6	77,7	9,3	48
III	$C_6H_5CH_2$	H	H	H	1	170—175 (1)	222 285 293	4,53 3,71 3,67	0,87	[1360, 1470, 1500, 1600] 3300 (NH_2)	$C_{17}H_{18}N_2$	81,0	7,4	81,6	7,3	21
IV	$C_6H_5CH_2$	CH_3	H	H	1	170—172^4 (1)	243 278 284	4,40 3,79 3,80	0,85	[1370, 1460, 1510, 1600] 3300 (NH_2)	$C_{18}H_{20}N_2$			81,8	7,6	68
V	$C_6H_5CH_2$	CH_3	H	H	2	179—183^5 (1—2)	228 280 285 299	4,60 3,85 3,89 3,90	0,83	[1380, 1460, 1475, 1505] 3300 (NH_2)	$C_{19}H_{22}N_2$			82,0	8,0	51
VI	$C_6H_5CH_2$	CH_3	CH_3	H	2	183—185 (1—2)	230 248 284	4,10 4,16 3,59	0,86	[1455, 1480, 1500, 1600] 3350 (NH)	$C_{20}H_{24}N_2$	81,4	8,5	82,2	8,3	20
VII	C_6H_5	H	$COCH_3$	H	1	168—172 (1—2)	221 280 288	4,15 3,54 3,47	0,95	[1375, 1440, 1490] 3350 (NH) 1640 (C=O)	$C_{19}H_{20}N_2O$	77,7	6,5	78,0	6,9	43
VIII	$C_6H_5CH_2$	C_6H_5	H	H	1	220—230 (1—2)	225 295	4,52 4,11	0,93	[1440, 1455, 1485, 1590] 3300 (NH_2)	$C_{23}H_{22}N_2$	84,0	6,9	84,6	6,8	75
IX	$C_6H_5CH_2$	CH_3	CH_3	H	2	180—185 (1—2)	247 250 285	4,23 4,20 3,50	0,91	[1440, 1490, 1600] 3350 (NH)	$C_{19}H_{22}N_2$	81,2	7,6	82,0	8,0	44
X	H	H	H	CH_3	2	178—180 (1—2)	246 292	4,18 3,65	0,87	[1450, 1500, 1600] 3350 (NH_2)	$C_{12}H_{16}N_2$	76,8	8,9	76,6	8,6	12

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*Recorded with an Hitachi EPS-3T spectrophotometer (ethanol).

†With Leningrad Volodarsk Plant "fast" chromatographic paper, a benzene—methanol system (9 : 1), and development with 5% ninhydrin in alcohol.

‡Recorded from chloroform solutions with a Jasco IR-S spectrophotometer. The stretching vibrations of the indole ring are given in brackets.

TABLE 2. Picrates of the Tryptamines and Homotryptamines

Picrates of	mp, °C	Empirical formula	N, %	
			found	calc.
II	165—167	$C_{14}H_{20}N_2 \cdot C_6H_3N_3O_7$	15,2	15,7
III	146—148	$C_{17}H_{18}N_2 \cdot C_6H_3N_3O_7$	13,9	14,6
IV	188—189[4] *	$C_{18}H_{20}N_2 \cdot C_6H_3N_3O_7$		
V	184—186[5] *	$C_{19}H_{22}N_2 \cdot C_6H_3N_3O_7$		
VI	140—141	$C_{20}H_{24}N_2 \cdot C_6H_3N_3O_7$	13,7	13,4
VIII	230—235 (dec.)	$C_{23}H_{22}N_2 \cdot C_6H_3N_3O_7$	12,6	12,6
X	168—171	$C_{12}H_{16}N_2 \cdot C_6H_3N_3O_7$	17,0	16,8

* The picrate did not depress the melting point of a picrate of known structure.

EXPERIMENTAL

α-Tripiperideine and N-acetyl-Δ^2-piperideine were synthesized according to the method in [6]. α-Isopropyl-α-phenylhydrazine was obtained by the method in [7]. Tripyrroline was obtained by the action of methanolic alkali on N-chloropyrrolidine at room temperature [3]. Because of the great instability, even at 0°, we did not isolate N-chloropyrrolidine but used a concentrated solution of it in ether in the dehydrochlorination. 2-Methyl-Δ^1-pyrroline [8], n_D^{20} 1.4312; UV spectrum: λ_{max} 212 nm, log ε 2.26; IR spectrum*: 1685 cm^{-1} ($\nu_{C=N}$). 1,2-Dimethyl-Δ^2-pyrroline [9], UV spectrum: λ_{max} 232 nm, log ε 2.15; IR spectrum: 1643 cm^{-1} ($\nu_{C=C}$). 2-Methyl-Δ^1-piperideine [10], UV spectrum: λ_{max} 231 nm, log ε 2.38. 1,2-Dimethyl-Δ^2-piperideine [11], n_D^{20} 1.4825; UV spectrum: λ_{max} 238 nm, log ε 3.90. 2-Phenyl-Δ^1-pyrroline [12], UV spectrum: λ_{max} 243 nm, log ε 4.11; IR spectrum: 1612 cm^{-1} ($\nu_{C=N}$).

General Method for the Synthesis of Tryptamines and Homotryptamines.† A solution of 0.05 mole of pyrroline or piperideine in 20 ml of isopropyl alcohol containing 0.05 mole of hydrogen chloride was added to a solution of 0.05 mole of arylhydrazine salt in 60 ml of isopropyl alcohol. The mixture was refluxed for 8 h. The solvent was then removed with a rotary evaporator, and 80 ml of water was added. The neutral impurities were extracted with ether, and the water layer was made alkaline with sodium hydroxide. The tryptamine was extracted with benzene and vacuum distilled in a stream of an inert gas (see Table 1).

PMR spectrum‡ of N-isopropylhomotryptamine: 1-CH_3 1.42 d (J 7 Hz); 1-CH 4.74 q (J 7 Hz); 3β-CH_2 1.8 q (J 7.5 Hz); 3α- and 3γ-CH_2 overlapped triplets 2.75; aromatic protons 6.9-7.5. Spectra of 1-benzyl- and 1-benzyl-2-phenyltryptamines: NH_2 group 2.27 and 1.99 (broadened signals); 3α- and 3β-CH_2 overlapped triplets centered at 2.87 and 2.76; 1-$CH_2C_6H_5$ 5.15 s.

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* The IR spectra were obtained from liquid films.

† A method smilar to that used to synthesize N-acylated homotryptamines was used to synthesize VI.

‡ The proton magnetic resonance spectra were recorded with a JNM-C-60H spectrometer with deuterochloroform as the solvent and tetramethylsilane as the internal solvent. The chemical shifts are given in the δ scale. The following abbreviations were used: d is doublet, q is quintet, t is triplet, and s is singlet.