INDOLES

XIV.* METHOD FOR THE SYNTHESIS OF 2-SUBSTITUTED HOMOTRYPTAMINES

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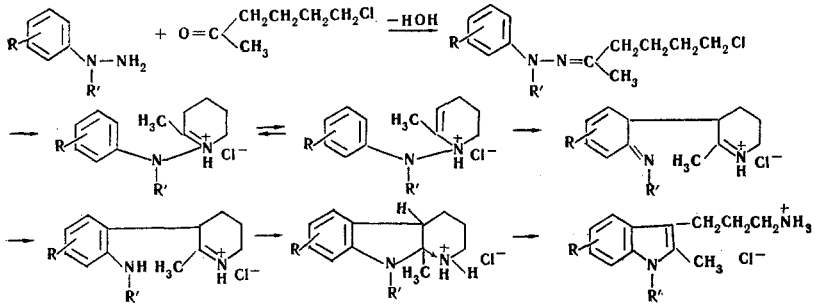
UDC 547.75.07

A new, one-step method is proposed for the synthesis of 2-substituted homotryptamines. The method is based on the reaction of arylhydrazines with δ-halocarbonyl compounds.

In previous communications [2, 3] we described a method for obtaining tryptamines from arylhydrazines and γ-halocarbonyl compounds. While investigating the range of application of this method we observed that refluxing of arylhydrazines with δ-halocarbonyl compounds in neutral water–alcohol solutions gives good yields of 2-substituted homotryptamines. The scheme proposed for the reaction is based on the scheme for the synthesis of tryptamines, which we have partially proved [4, 5].

The homotryptamine salts formed in the reaction are converted, without isolation, to the free bases, which were purified by distillation, recrystallization, or high-vacuum sublimation. All of the compounds obtained were identified by paper chromatography with the help of the UV and PMR spectra. Two maxima at 225 and 280 nm, which are characteristic for absorption by the indole chromophore, are observed in the UV spectra of the homotryptamines. The PMR spectra also indicate the homotryptamine structure (Table 1).



The new method for the synthesis of homotryptamines opens great possibilities in the synthesis of physiologically active substances. We have not encountered virtually any difficulties on changing the structure of the reacting components.

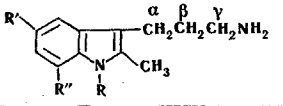
EXPERIMENTAL

General Method for Preparing 2-Substituted Homotryptamines. A solution of 0.1 mole of 6-chloro-2-hexanone [6] in 60 ml of 90% ethanol was added to a refluxing solution of 0.2 mole of substituted phenylhydrazine in 60 ml of 90% ethanol, and the reaction mass was refluxed on a water bath for 8 h. The solvent was removed with a water aspirator, and the residue was treated with 100 ml of 0.1-N hydrochloric acid. The mixture was extracted with ether. The aqueous layer was separated and filtered, and the filtrate was made alkaline with 40% NaOH. The oil that separated was extracted with benzene, and the benzene extract was filtered and distilled in vacuo under nitrogen. The yields and constants of the homotryptamines are presented in Table 2.

*See]1[for Communication XIII.

K. A. Timiryazeva Moscow Agricultural Academy. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 11, pp. 1495-1498, November, 1970. Original article submitted June 24, 1969.

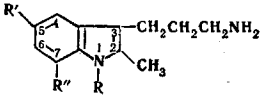
TABLE 1. PMR Spectra of 2-Substituted Homotryptamines*



R	R′	R″	2-CH_3	3α-CH_2 (J, Hz)	3β-CH_2 (J, Hz)	3γ-CH_2 (J, Hz)	NH_2	Substituent protons	Aromatic ring protons				Solvent
									H_4 (J, Hz)	H_5	H_6 (J, Hz)	H_7 (J, Hz)	
H	H	H	2,14 s	2,58 t (7)	1,63 qui (7)	2,58 t (7)	1,40 s	—	6,95—7,17 m			7,33 d ($j_{7,6}$=9)	$CDCl_3$
H	H	CH_3	2,28 s	2,70 t (7)	1,72 qui (7)	2,70 t (7)	1,61 s	2,39 s (R″)	6,87—7,67 m				$CDCl_3$
H	OCH_3	H	2,25 s	2,56 t (7)	1,75 qui (7)	2,62 t (7)	—	3,75 s (R′)	6,91 d ($j_{4,6}$=1,5)		6,64 q ($j_{7,6}$=8, $j_{6,4}$=1,5)	7,08 d ($j_{7,6}$=8)	CD_3OD
H	H	OCH_3	2,27 s	2,70 t (7)	1,75 qui (7)	2,74 t (7)	1,40 s	3,87 s (R″)	6,42—7,43 m				$CDCl_3$
CH_3	H	H	2,30 s	2,68 t (7)	1,70 qui (7)	2,76 t (7)	1,02 s	3,56 s (R)	6,95—7,32 m			7,55 q ($j_{7,6}$=9, $j_{7,5}$=2,5)	CCl_4

*The PMR spectrum of 2-methylhomotryptamine was obtained with a JNM-100 spectrometer with an operating frequency of 100 MHz, while the spectra of the remaining compounds were obtained with a JNM-60 spectrometer with an operating frequency of 60 MHz; s indicates singlet, d doublet, t triplet, q quartet, qui quintet, and m multiplet; the chemical shifts are given in the δ scale (ppm); the internal standard was hexamethyldisiloxane.

TABLE 2



R	R'	R''	Bp, °C (mm)	Mp, °C (after sublim.)	Empirical formula	Found %		Calc. %		R_f*	UV spectra †		Acid tartrate, mp, °C	Picrate				Yield, %
						C	H	C	H		λ_{max}, nm	lg ε		mp, °C	empirical formula	found N, %	calc. N, %	
H	H	H	166—170 (1)[7]	55—56	$C_{12}H_{16}N_2$	76,63 76,58	8,60 8,58	76,54	8,56	0,72	225, 282, 289, 323	4,46, 3,86, 3,83, 3,41	160—162 (decomp)	182—183	$C_{12}H_{16}N_2 \cdot C_6H_3N_3O_7$	16,95 16,90	16,80	62
H	H	CH_3	163—165 (1)	101—102	$C_{13}H_{18}N_2$	77,32 77,30	9,00 8,98	77.17	8,98	0,76	225, 273, 280, 290, 312	4,61, 3,94, 3,96, 3,79, 2,78	—	172—173	$C_{13}H_{18}N_2 \cdot C_6H_3N_3O_7$	16,30 16,26	16,25	38
H	OCH_3	H	194—200 (1)	101—103	$C_{13}H_{18}N_2O$	71,70 71,68	8,35 8,30	71,52	8,32	0,74	226, 284, 294	4,16, 3,73, 3,71	166—168	146—147	$C_{13}H_{18}N_2O \cdot C_6H_3N_3O_7$	15,80 15,72	15,67	65
H	H	OCH_3	180—185 (2)	118—120	$C_{13}H_{18}N_2O$	71,71 71,54	8,35 8,33	71,52	8,32	0,57	228, 270, 275, 286	4,71, 3,87, 3,85, 3,68	—	197—199	$C_{13}H_{18}N_2O \cdot C_6H_3N_3O_7$	15,60 15,57	15,67	23
$CH_2C_6H_5$	H	H	197—198 (2)	—	$C_{19}H_{22}N_2$	82,01 81,96	7,97 7,94	82,07	7,98	0,58	228, 279, 285, 290	4,59, 3,86, 3,90, 3,89	130—135 (decomp)	190—192 (decomp)	$C_{19}H_{22}N_2 \cdot C_6H_3N_3O_7$	13,78 13,56	13,81	80
C_6H_5	H	H	180—185 (1)	—	$C_{18}H_{20}N_2$	81,62 81,44	7,65 7,58	81,76	7,64	0,62	222, 268, 285	4,44, 4,02, 4,02	152—153 (decomp)	170—171	$C_{18}H_{20}N_2 \cdot C_6H_3N_3O_7$	14,57 14,52	14,21	20
CH_3	H	H	160—165 (1)	—	$C_{13}H_{18}N_2$	77,24 77,00	9,17 9,00	77,17	8,98	0,80	227, 277, 284, 290	4,55, 3,75, 3,79, 3,78	167—168 (decomp)	199—201 (decomp)	$C_{13}H_{18}N_2 \cdot C_6H_3N_3O_7$	16,35 16,21	16,23	63

*"Fast" paper from the Volodarskii Plant, pyridine–water–butanol system (1 : 1 : 1), development with the Erlich reagent.
†In all cases the UV spectra were obtained with an EPS-3T spectrometer (Hitachi) in ethanol.

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