SYNTHESIS OF 1,2-DIALKYL-3,6-DIMETHYL-1,2-DIHYDROPYRIDAZINES FROM ACETONYLACETONE

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Condensation of acetonylacetone with symmetrical dimethyl- and diethylhydrazines leads to 1,2-dialkyl-3,6-dimethyl-1,2-dihydropyridazines and 2,3,5,6-tetraalkyl-1,4-dimethyl-2,3,5,6-tetraazabicyclo[2.2.2]octanes.

Although 1,2-dihydropyridazines have found application for the preparation of bicyclic systems, viz., 2,3-diazabicyclo[2.2.0]hexenes [1] and 2,3,5,6-tetraazabicyclo[2.2.2]octenes [2], only a few representatives of this class of compounds are known, and there is no general method for their synthesis. Their formation in the diene synthesis of dialkylazodicarboxylates with α-pyrone has been reported [2]; 1,2-dicarbethoxy-1,2-dihydropyridazine and its 3,6-diphenyl-substituted derivative were synthesized from the corresponding Δ^4-tetrahydropyridazines [3]; the formation of 1,2-dihydropyridazines as side products has been noted [4].

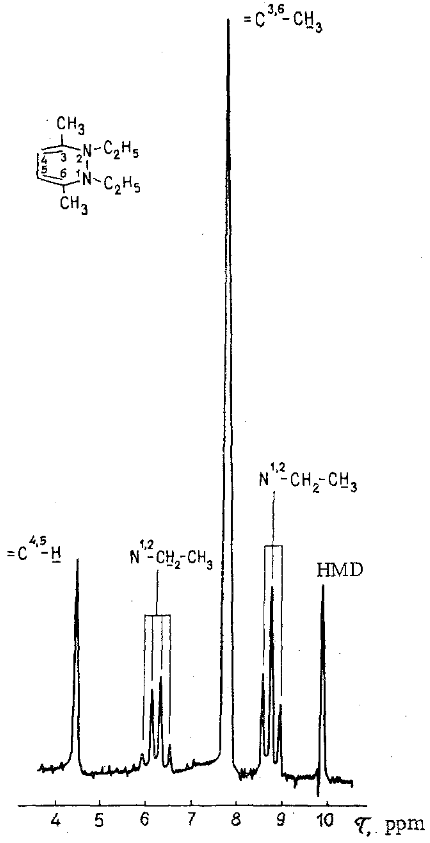
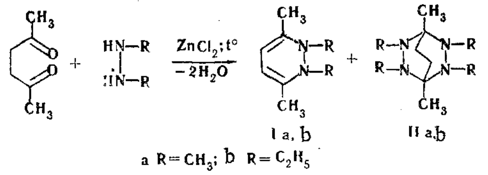


Fig. 1. PMR spectrum of 1,2-diethyl-3,6-dimethyl-1,2-dihydropyridazine.

The possibility of closing into a 1,2-dihydropyridazine ring in the reaction of 1,2-dialkylhydrazines with 1,4-diketo compounds has not been discussed previously. However, considering the ease of formation of 1,4-dihydropyridazines from 1,4-dicarbonyl compounds with monoalkylhydrazines [5, 6], positive results might have been expected from the condensation of their 1,2-disubstituted analogs.

In fact, 1,2-dimethyl- and diethyl-3,6-dimethyl-1,2-dihydropyridazines (Ia-b, respectively; Table 1) were isolated in 30-40% yields after the reaction of acetonylacetone with symmetrical dimethyl- and diethylhydrazines; the reaction is accompanied by spontaneous heating in the presence of $ZnCl_2$ and is completed after refluxing in inert solvents.



These compounds, which are colorless liquids with a specific, sharp odor, whose structures were established by gas-liquid chromatography, in contrast to 1,4-dihydro isomers are less inclined to oxidation.

Their IR spectra contain a set of intense absorption bands which are characteristic for conjugated dienes [7] (two

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frequencies at 1610-1660 cm^{-1} and 3080-3100 cm^{-1}) and a band at 760 cm^{-1} which is accompanied by an overtone of medium intensity at 1520 cm^{-1}. The PMR spectra for Ia-b (at 40 MHz) are distinguished by their simplicity: in addition to signals of the protons in the alkyl substituents attached to the nitrogen atom (τ_{N-CH_3} at 6.70 ppm for Ia, $\tau_{N-CH_2-CH_3}$ at 6.22 ppm, quartet, J ~ 7 Hz, $\tau_{N-CH_2-CH_3}$ at 8.85 ppm, triplet, J ~ 7 Hz in the case of Ib) they also contain two narrow signals: $\tau_{C^{3,6}-CH_3}$ at 7.78-7.85 ppm and $\tau_{C^{4,5}-H}$ at 4.47 ppm (Fig. 1).

An indication of the 1,2-dihydropyridazine structure is the hydrolysis of I in acid media with subsequent isolation of acetonylacetone bis(2,4-dinitrophenylhydrazone).

In addition to I, the reaction mixtures contain considerable amounts of high-boiling condensation products. Their distillation under high vacuum (~0.02 mm) is accompanied by decomposition, but chromatography of the reaction mixture (after distillation of I) on Al_2O_3 made it possible to isolate products IIa-b [2,3,5,6-tetraalkyl-1,4-dimethyl-2,3,5,6-tetraazabicyclo[2.2.2]octanes (Table 1)].

The proposed structure for II is confirmed by elementary analysis and the spectral characteristics. They are transparent at 1600-1900 cm^{-1} and 3000-3600 cm^{-1}, which indicates the absence of multiple bonds and OH and NH groupings. The spectrum of IIa has an intense absorption at 2780 cm^{-1} which corresponds to the $N-CH_3$ group. The PMR spectra of II contain the following signals: $\tau_{C^{1,4}-CH_3}$ at 9.06 ppm, singlet, and $\tau_{C^7H_2-C^8H_2}$ at 8.03-8.25 ppm, multiplet. The signal corresponding to the $N-CH_3$ groups in the spectrum of IIa is broadened (at 7.72 ppm), while two triplets and a quartet with the same splitting (J ~ 7 Hz) at 8.92, 8.99, 7.48, and 7.57 ppm correspond to the ethyl groups for IIb. This apparently serves as an indication of the magnetic nonequivalence of the protons of the N-alkyl groups, as in the cases in [8].*

The isolation of II does not seem surprising since cyclization to symmetrical hexahydrotetrazines is characteristic for the reaction of aldehydes and ketones with symmetrical dialkylhydrazines [9-11].

Although this reaction proceeds ambiguously, the satisfactory yields and the simplicity of isolation make it possible to recommend it as a convenient method for the preparation of I.

EXPERIMENTAL

The IR spectra in a 20- to 40-nm layer were obtained with a UR-10 spectrometer. The PMR spectra of CCl_4 solutions were obtained with a YaMR-5535 spectrometer (40 MHz) using hexamethyldisiloxane (HMD) as the internal standard. Gas-liquid chromatographic analysis was carried out with a "Tsvet-4" chromatograph using a 2-m long column with 5% polyethylene glycol oxide on Celite C-50

TABLE 1. Products of the Condensation of 1,2-Dialkylhydrazines with Acetonylacetone

Compound	Bp, °C (pressure, mm)	d_4^{20}	n_D^{20}	MR_D		M		Empirical formula	Found, %			Calculated, %			Yield, %
				found	calc.	found	calc.		C	H	N	C	H	N	
Ia	51,5 (8)	0,9173	1,4961	44,01	43,96	138,9 137,0	138,21	$C_8H_{14}N_2$	69,72 69,75	10,17 10,18	20,56 20,50	69,52	10,21	20,37	36
Ib	43,0 (0,5)	0,9018	1,4882	53,13	53,26	165,3 164,9	166,26	$C_{10}H_{18}N_2$	72,02 72,20	10,88 10,75	16,72 16,80	72,24	10,91	16,85	39
IIa	32—34*	—	—	—	—	—	198,31	$C_{10}H_{22}N_4$	60,63 60,71	11,11 11,23	28,50 28,45	60,56	11,18	28,26	10
IIb	—	0,9319	1,4890	78,70	78,49	—	254,41	$C_{14}H_{30}N_4$	66,16 66,14	11,81 11,79	22,11 21,97	66,09	11,89	22,02	8

*Melting point.

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*This circumstance, like the problem of the possible nonequivalence of the N-alkyl groups for I, cannot be reliably ascertained at a resolution of 40 MHz and will be examined separately.

with nitrogen as the gas carrier at 100°. Thin-layer chromatography and column chromatography were carried out on activity I Al_2O_3 with hexane–ether (1 : 2) as the eluent.

1,2-Dimethylhydrazine [12], 1,2-diethylhydrazine [13, 14], and acetonylacetone [15] were synthesized with reproducible yields and constants.

Condensation of Acetonylacetone with Symmetrical Dialkylhydrazines. A mixture of 0.2 mole of acetonylacetone and 0.4 mole of the hydrazine in 150 ml of solvent (hexane or ether) in the presence of 20 g of $ZnCl_2$ was refluxed for 4 h under nitrogen with a Dean–Stark adapter. The drying agent was filtered, the solvent was removed in vacuo, and Ia-b were isolated by distillation with a column (10 theoretical plates).

Hydrolysis of Ia-b. A total of 0.005 mole of the compound was refluxed with a 1.5-fold excess of 2,4-dinitrophenylhydrazine sulfate. The precipitate of acetonylacetone bis(2,4-dinitrophenylhydrazone) [2.2 g (95%)] had mp 265° (without depression with an authentic sample prepared from acetonylacetone).

Compounds IIa-b. These were isolated from the still residue by chromatography with a 150-cm long chromatographic column 15 mm in diameter.

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