REACTIONS OF 1,5-DIKETONES.

XV.* SYNTHESIS AND AMINOMETHYLATION OF 2,2-DIMETHYL-5-(2-OXOCYCLOHEXYLMETHYL)-TETRAHYDRO-4-PYRONE

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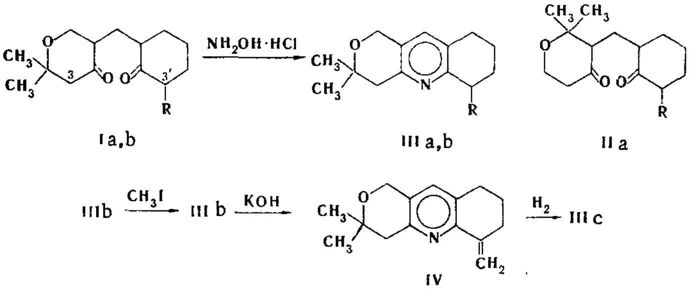
The previously unknown 2,2-dimethyl-5-(2-oxocyclohexylmethyl)tetrahydro-4-pyrone was obtained by condensation of 2,2-dimethyltetrahydro-4-pyrone with 2-dimethylaminomethylcyclohexane. The Mannich reaction of the product leads only to monoaminomethylation to give 2,2-dimethyl-5-(3-dimethylaminomethyl-2-oxocyclohexylmethyl)tetrahydro-4-pyrone. On reaction with hydroxylamine hydrochloride both 1,5-diketones are converted to the corresponding 2-oxahydroacridines.

It has been reported [2] that two aminomethyl groups are readily introduced into the diketone molecule in the 3,3' position in the aminomethylation of 2,2'-methylenebiscyclohexanone. It seemed of interest to study this reaction for diketone Ia — its heteroanalog in which the 3,3' positions are nonequivalent.



Ia,b IIIa,b IIa

IIIb IIIb IV

Ia-IIIa R=H; Ib, IIIb R=CH$_2$N(CH$_3$)$_2$; IIIb R=CH$_2$N(CH$_3$)$_3$I; d R=CH$_3$

We obtained it by **condensation** of 2-dimethylaminomethylcyclohexanone with 2,2'-dimethyltetrahydro-4-pyrone. Alternative structure IIa is refuted by the PMR spectrum of oxaacridine IIIa obtained from the diketone by reaction with hydroxylamine, in which two singlets at 2.5 and 4.5 ppm of the protons attached to C_4 and C_1 are found in place of triplet signals of the hydrogen atoms attached to C_3 and C_4 for possible isomeric structure IIa.

The aminomethylation of diketone Ia in excess amine and aldehyde proceeds only in the 3 position to give aminodiketone Ib; the 3'-CH_2 group does not participate in the reaction, apparently because of the shielding effect of the gem-dimethyl groups, as in other well-known cases [3, 4].

The IR spectrum of aminodiketone Ib differs from the spectrum of starting Ia only with respect to presence of additional absorption bands at 2830 and 2780 cm^{-1}, which are affiliated with the dimethylamino group [5]. Base IIIb is obtained when the hydrochloride of aminodiketone Ib is heated in alcohol with hydroxylamine hydrochloride. Carbonyl absorption is absent in the IR spectrum of IIIb, but the absorption bands of a dimethylamino group are retained at 2830 and 2780 cm^{-1}. 2-Oxahydroacridine methiodide IIIc is con-

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*See [1] for communication XIV.

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TABLE 1. Diketones Ia-b and 2-Oxaoctahydroacridines III-IV Synthesized from Them

Compound	bp, °C (mm)	d_4^{20}	n_D^{20}	MR_D		Empirical formula	Found, %			Calculated, %			Yield, %
				found	calculated		C	H	N	C	H	N	
Ia	152 (1) *	—	—	—	—	$C_{14}H_{22}O_3$	70,6	8,8	—	70,6	8,4	—	82
Ib	—	—	1,4580	—	—	$C_{17}H_{29}NO_3$	69,3	10,2	4,9	69,2	9,9	4,7	65
Picrate of Ia	163—165†	—	—	—	—	$C_{17}H_{29}NO_3 \cdot C_6H_3N_3O_7$	—	—	11,0	—	—	10,7	—
IIIa	48—50†	—	—	—	—	$C_{14}H_{19}NO$	77,5	9,0	7,0	77,4	8,8	6,5	100
Picrate of IIIa	183—185†	—	—	—	—	$C_{14}H_{19}NO \cdot C_6H_3N_3O_7$	—	—	12,5	—	—	12,5	—
IIIb	160—161 (1)	1,0544	1,5342	80,79	80,49	$C_{17}H_{26}N_2O$	74,1	9,9	10,6	74,1	9,5	10,2	95
Dipicrate of IIIb	189—190†	—	—	—	—	$C_{17}H_{26}N_2O \cdot 2C_6H_3N_3O_7$	—	—	15,1	—	—	15,3	—
IIIc	208—210†	—	—	—	—	$C_{18}H_{29}IN_2O$‡	—	—		—	—		81
IIId	133—134 (1)	1,0496	1,5367	68,74	68,79	$C_{15}H_{21}NO$	78,0	9,3	6,4	77,9	9,1	6,1	100
Picrate of IIId	180—182†	—	—	—	—	$C_{15}H_{21}NO \cdot C_6H_3N_3O_7$	—	—	12,1	—	—	12,2	—
IVd	141—143 (1)	1,0699	1,5662	—	—	$C_{15}H_{19}NO$	78,3	9,0	6,5	78,6	8,3	6,1	79
Picrate of IVd	164—166†	—	—	—	—	$C_{15}H_{19}NO \cdot C_6H_3N_3O_7$	—	—	12,6	—	—	12,2	—

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*This compound had mp 65-67° (from hexane).

†This is the melting point.

‡Found: I 30.8%. Calculated: I 30.5%.

verted by Hofmann elimination to methyleneoxahydroacridine IV. The bands at 2830 and 2780 cm^{-1} vanish in its IR spectrum, and adsorption appears at 1630 and 3110 cm^{-1} ($>C=CH_2$). The PMR spectrum of IV contains two singlets at 4.96 and 6.08 ppm of methylene group protons in the trans and cis position relative to the nitrogen atom [6].

Hydrogenation of IV converts it to methyloxahydroacridine IIId, the IR spectrum of which differs from the spectrum of 2-oxahydroacridine IV with respect to the absence of absorption of a $>C=CH_2$ grouping.

EXPERIMENTAL

The IR spectra of $CHCl_3$ solutions of the compounds were recorded with a UR-20 spectrometer. The PMR of $CDCl_3$ solutions were recorded with a ZKR-60 spectrometer. The picrates were obtained by mixing hot alcohol solutions of the appropriate substance and picric acid and were recrystallized from alcohol. The homogeneity of these substances was determined in a thin layer of aluminum oxide; the spots were developed with iodine vapors.

2,2-Dimethyl-5-(2-oxocyclohexylmethyl)tetrahydro-4-pyrone (Ia). A mixture of 48.3 g (0.31 mole) of 2-dimethylaminomethylcyclohexanone [7] and 121 g (0.94 mole) of freshly distilled 2,2-dimethyltetrahydro-4-pyrone [8] was refluxed for 20 min, after which the unchanged pyrone was removed by distillation, and the residue was vacuum distilled. IR spectrum: 1710 cm^{-1} (C=O).

2,2-Dimethyl-5-3-dimethylaminomethyl-2-oxocyclohexylmethyl)tetrahydro-4-pyrone (Ib). The aminomethylation of diketone Ia was carried out similarly [9] with 15.7 g (0.063 mole) of diketone Ia, 6 g (0.2 mole) of paraformaldehyde, and 13 g (0.181 mole) of dimethylamine hydrochloride in 60 ml of alcohol. For purification, the aminodiketone was dissolved in dry ether, and a stream of dry hydrogen chloride was bubbled through the solution until it was saturated. The yield of hydrochloride with mp 187-188° (from propanol) was 14 g (97%). Found: Cl 10.3%. $C_{17}H_{29}NO_3 \times HCl$. Calculated: Cl 10.7%. Free base IV was obtained in quantitative yield by alkalization of the aqueous solution of the pure hydrochloride. The colorless liquid, which was chromatographically homogeneous, decomposed on distillation. IR spectrum, cm^{-1}: 2830, 2780, and 1710.

2-Oxa-sym-octahydroacridines (IIIa, b). A mixture of 0.05 mole of diketone Ia and 0.115 mole of hydroxylamine hydrochloride in 50 ml of alcohol was heated for 2 h on a boiling-water bath, after which the alcohol was removed by distillation, and the residue was dissolved in water. The aqueous solution was made alkaline with concentrated KOH, and base III was extracted with ether.

Methiodide IIIc. A 2.3-ml (0.04 mole) sample of methyl iodide was added to a solution of 9.8 g (0.035 mole) of base IIIb in 100 ml of ether, and the resulting precipitate was removed by filtration and recrystallized from alcohol.

3,3-Dimethyl-2-oxa-5-methylene-sym-octahydroacridine (IV). A suspension of 23 g (55 mmole) of methiodide IIIc in 150 ml of benzene and 80 ml of 10% KOH was heated with stirring at 60-70° for 7 h. It was then cooled, the benzene layer was separated and washed with water, and the benzene was removed by distillation.

3,3-Dimethyl-2-oxa-5-methyl-sym-octahydroacridine (IIId). An 8.36-g (37 mmole) sample of the base in 50 ml of alcohol absorbed 795 ml of hydrogen (1 mole per C=C bond) in the presence of 1 g of Pd/Al_2O_3. The catalyst was removed by filtration, and the alcohol was removed from the filtrate by distillation.

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