REACTIONS OF 1,5-DIKETONES

X.* REACTION OF ALICYCLIC 1,5-DIKETONES WITH PRIMARY ALIPHATIC AMINES

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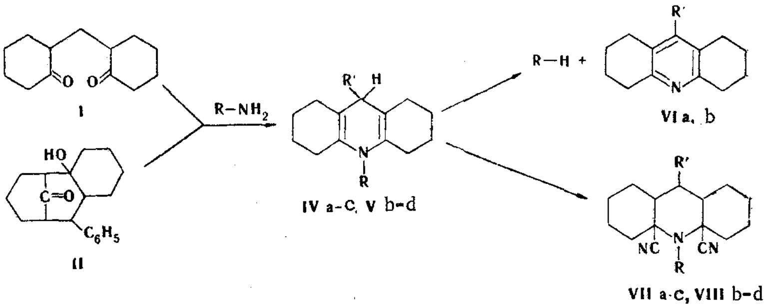
N-R-9-R'-Decahydroacridines, which are formed as a result of the reaction of alicyclic 1,5-diketones with primary aliphatic amines, split out a substituent from the nitrogen atom and a hydrogen atom from the 9 position to give 9-R'-sym-octahydroacridines. On the basis of the IR spectra, it was concluded that the N-(β-hydroxyethyl)-9-R'-decahydroacridines cyclize.

The literature data on the reaction of 1,5-diketones with primary aliphatic amines are meager [2, 3]. In particular, it is indicated that 2,2'-methylenedicyclohexanone (I) forms the corresponding N-alkyldecahydroacridines with methylamine and its homologs [3].

We selected I and the product of intramolecular aldolization of 2,2'-benzylidenedicyclohexanone – 4-phenyl-2,3-tetramethylenebicyclo[3.3.1]nonan-2-ol-9-one (II) – as the diketones for our study. The primary amines used were methylamine (IIIa), ethanolamine (IIIb), benzylamine (IIIc), and glycine ethyl ester (IIId).

A tendency for splitting out of substituents from the nitrogen atom and a hydrogen atom from the 9 position of the resulting N-R-9-R'-decahydroacridines (IV, V) was observed when the reaction was carried out in a nonpolar solvent (benzene, m-xylene); this leads to the corresponding sym-octahydroacridine derivatives (VIa, b).



IV, V, VII, VIII a $R=CH_3$; b $R=CH_2CH_2OH$; c $R=CH_2C_6H_5$; d $R=CH_2COOC_2H_5$, IV, VII $R'=H$; V, VIII $R'=C_6H_5$; VI a $R'=H$; b $R'=C_6H_5$

The ease of aromatization depends on the reaction temperature (the reaction proceeds to a greater extent in xylene than in benzene) and on the nature of group R, and the ease of cleavage decreases in the order $CH_2COOC_2H_5 > CH_2C_6H_5 > CH_3 > CH_2CH_2OH$. Thus only octahydroacridine VIa is obtained in the reaction of ketone I with amine IIId even in benzene. Compounds IVc, Vc, and Vd are formed in a mixture with aromatized VIa or, respectively, VIb. Compound IVa contains only a small amount of VIa; IVb and Vb are formed without contamination by VIa or VIb. Ketol II and IIIa do not form products of the hydroacridine series; in this case, 9-phenyloctahydroxanthene was isolated [4]. All IV and V are smoothly converted to

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*See [1] for communication IX.

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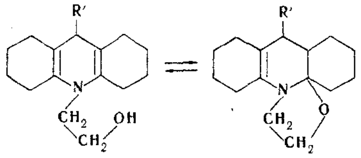
VIa or, respectively, VIb on heating to 240-280°. The same result is observed in the thermolysis of N-R-9-R'-11,14-dicyanoperhydroacridines VII and VIII.

There are no data on aromatization proceeding with splitting out of an alkyl group from the nitrogen atom of dihydropyridine in the review literature [5]. Only a single case of this sort of reaction is described [2]; an assumption regarding the possibility of aromatization of N-methyldecahydroacridine is stated in [6]. A comparison of the data that we obtained with the previously detected exceptionally facile aromatization of N-aminodecahydroacridine derivatives [1] makes it possible to conclude that aromatization is quite general in the decahydroacridine series.

The decahydroacridines that we isolated in the individual state (IVb, Vb, and Vc) add two molecules of HCN to give dicyanides VIIb, VIIIb, and VIIIc. Dicyanides VIIa, VIIc, and VIIId, respectively, were isolated by treatment with HCN of mixtures of IVa and IVc with VIa and of a mixture of Vd with VIb. The absorption of an OH group at 3050-3700 cm^{-1} is absent in the IR spectra of N-(β-hydroxyethyl)decahydroacridines IVb and Vb. In place of the two bands at 1670-1700 cm^{-1} that are characteristic for decahydroacridines [7] (this sort of doublet is observed in the spectrum of Vc), there is only one peak at 1670 cm^{-1}; this is characteristic for dodecahydroacridines [8]. At the same time, the IR spectra of dicyanides VIIb and VIIIb contain the absorption band of an OH group at 3600 cm^{-1}. This makes it possible to assume reversible cyclization of IVb and Vb of the type involving nucleophilic addition to 1,4-dihydropyridines:



As previously established [9], carrying out of the reaction of diketone I with primary aliphatic amines in the presence of CCl_4 leads to a sym-octahydroacridinium salt only in the case of amine IIIc. However, when a more active oxidizing agent – bromoform – was used, we were able to obtain N-R-sym-octahydroacridinium salts with amines IIIb and IIId (but not with IIIa). The reaction of diketone I with amine IIIb is accompanied by replacement of the OH group by bromine under the influence of the HBr formed during the decomposition of bromoform; the reaction product is an N-(β-bromoethyl)-sym-octahydroacridinium salt (IX). An N-methyl-sym-octahydroacridinium salt (X) is formed in the reaction of diketone I with amine IIId in the presence of bromoform. This is apparently the result of hydrolysis of the ester group by the water liberated in the condensation of I and IIId with subsequent decarboxylation of the N-carboxymethyl-sym-octahydroacridinium salt.

EXPERIMENTAL

The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-20 spectrometer. In all cases, VIa and VIb were identical to genuine samples [10, 11] according to the results of thin-layer chromatography (TLC) [activity II Al_2O_3, in ether–ethyl acetate (7:1); R_f 0.7 for VIa and 0.4 for VIb]. The picrate of VIa and base VIb did not depress the melting points of genuine samples.

Reaction of Diketones I and II with Primary Aliphatic Amines. A mixture of 0.02 mole of I or II and 0.02 mole of amine in 30-40 ml of benzene or m-xylene was refluxed with a Dean–Stark trap until water liberation ceased (4-6 h); in the reaction with II, the catalytic addition of p-toluenesulfonic acid was necessary. The solvent was then vacuum evaporated.

Reaction of Diketone I with Amine IIId (I + IIId). The residue consisted almost entirely of octahydroacridine VIa.

I + IIIc. When the reaction was carried out in xylene, the residue was a mixture of decahydroacridine IVc and octahydroacridine VIa with predominance of the latter (according to TLC). When the reaction was carried out in benzene, when IVc > VIa, the mixture was treated with a solution of KCN in acetic acid, and N-benzyl-11,14-dicyanoperhydroacridine (VIIc) (52% yield) was removed by filtration after 2 h; it was identical to a genuine sample [8] according to the IR spectrum. Aromatization of IVc occurred during vacuum distillation of the mixture of IVc and VIa, and pure VIa, with bp 125-127° (2 mm), was obtained in the distillate.

I + IIIa and I + IIIb. The residue was vacuum distilled to give, respectively, decahydroacridine IVa [with a small amount of octahydroacridine VIa (according to TLC)], with bp 140-154° (2 mm), in 73% yield

TABLE 1. N-R-9-R'-Decahydroacridines (IV, V) and N-R-9-Phenyl-11,14-dicyanoperhydroacridines (VIII)

Compound	mp, deg C	Empirical formula	Found, %			Calc., %			Yield, %
			C	H	N	C	H	N	
IVb	152—154 (2)*	$C_{15}H_{23}NO$	77,0	9,9	6,6	77,2	9,9	6,0	70
Vb	93—94	$C_{21}H_{27}NO$	81,1	9,3	5,0	81,6	8,7	4,5	74
Vc	101—102	$C_{26}H_{29}N$	87,6	8,6	3,8	87,9	8,2	3,9	60
VIIIb	168—169	$C_{23}H_{29}N_3O$	76,8	8,5	11,2	76,0	7,9	11,5	70
VIIIc	233—234	$C_{28}H_{31}N_3$	81,6	8,1	10,3	82,1	7,6	10,3	70
IIId	172—174	$C_{25}H_{31}N_3O_2$	74,0	8,5	9,8	74,1	7,6	10,4	70

* This is the boiling point (nm, mercury standard).

(the product could not be freed from VIa on repeated distillation) and pure IVb (see Table 1). N-Methyl-11, 14-dicyanoperhydroacridine (VIIa), which was identical to a genuine sample [12] according to the IR spectrum, was similarly obtained from the mixture of IVa and VIa obtained by distillation.

II + IIIa and II + IIIb. The residue was treated with alcohol and removed by filtration: in the case of IIIa, 9-phenyloctahydroxanthene (in 34% yield), which was identical to a genuine sample [4] according to the IR spectrum, was obtained, while Vb (see Table 1) was isolated in the case of IIIb. Treatment of Vb with KCN in acetic acid gave dicyanide VIIIb.

II + IIIb. The residue was treated with acetone, the mixture was cooled to −50°, and Vb (Table 1) was removed by filtration. Dicyanide VIIIb was obtained from Vb.

II + IIId. When the reaction was carried out in xylene, the residue consisted primarily of VIb; in benzene the residue contained primarily Vd, which could not be isolated. The residue was treated with KCN in acetic acid, and dicyanide VIIId was removed by filtration. IR spectrum: 2230 (CN) and 1760 (ester carbonyl) cm^{-1}.

Aromatization of N-R-9-R'-Decahydroacridines and N-R-9-R'-11,14-Dicyanoperhydroacridines. A 0.2 g sample of decahydroacridine Vb or Vc was heated at 240-250° for 1 h to give pure octahydroacridine VIb. Similarly, VIa containing starting IVb (according to TLC) was obtained from 1 g of IVb after 3 h at 260-280°. Destructive distillation of 2.3 g of VIIc gave 0.6 g of VIa. The volatile thermolysis products were collected in a trap cooled with dry ice; toluene was detected in the products by gas–liquid chromatography. A 0.2 g sample of VIIId was heated at 240° for 1 h to give pure VIb.

Reaction of IVb with Bromoform. A solution of 1 g of IVb in 2 ml of bromoform was refluxed for 3 h, after which it was diluted with 15 ml of water, shaken, and extracted with ether. The aqueous layer was treated with NH_4ClO_4 solution, and the mixture was filtered to give 0.8 g (47%) of IX with mp 234°. Found, %: C 45.9; H 5.7; Br 20.1; Cl 8.9; N 4.0. $C_{15}H_{21}BrClNO_4$. Calculated, %: C 45.5; H 5.3; Br 20.3; Cl 9.0; N 3.5. IR spectrum: 1100 cm^{-1} (ClO_4); no absorption at 3000-3700 cm^{-1}.

Reaction of I with IIIb and IIId in Bromoform. A mixture of 0.02 mole of I, 0.02 mole of IIIb or IIId, and 0.04 mole of bromoform in 20 ml of benzene was refluxed for 4 h, after which it was worked up as in the preceding method. In the case of IIIb, IX was isolated in 47% yield, while X, which was identical to a genuine sample [8] according to the IR spectrum, was isolated in 33% yield in the case of IIId.

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