REACTIONS OF 1,5-DIKETONES

VII.* REACTION OF 2,3-TETRAMETHYLENE-4-R-BICYCLO[3.3.1]NONAN-9-ON-2-OLS WITH ANILINE

A. N. Saverchenko, V. A. Kaminskii,
and M. N. Tilichenko

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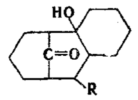
2,3-Tetramethylene-4-R-bicyclo[3.3.1]nonan-9-on-2-ols react with aniline and, depending on the conditions, give 9-R-10-phenyldecahydroacridines, 9-R-10-phenyl-$\Delta^{11(12)}$-dodecahydroacridines, and 9-R-10-phenyl-sym-octahydroacridinium salts.

10-R-Hydroacridines are formed in the reaction of 2,2'-methylenedicyclohexanone with primary amines under various conditions [2]. The reaction of the products of aldol self-condensation of 1,5-diketones – 2,3-tetramethylene-4-R-bicyclo[3.3.1]nonan-9-on-2-ols (I) – with primary amines would be a convenient preparative method for the production of 9,10-disubstituted hydroacridines, since compounds of the I type are considerably more accessible than the corresponding alkylidene(arylidene)bis-2,2'-cyclohexanones. It is known that in a number of cases compounds I react like the corresponding 1,5-diketones, apparently undergoing prior retroaldol cleavage [3].

In the present paper we have studied the reaction of ketols Ia-d with aniline (II).



I a-d

I a R=H; b R=CH$_3$;
c R=C$_6$H$_5$; d R=α-furyl

TABLE 1. 9-R-10-Phenylhydroacridines

Compound	R	mp, °C	Empirical formula	Found, %			Calc., %			Yield, %
				C	H	N	C	H	N	
IIIc	C$_6$H$_5$	96–97	$C_{25}H_{27}N$	88,3	8,0	4,5	88,0	7,9	4,1	88
IIId	α-Furyl	71–73	$C_{23}H_{25}NO$	83,5	7,9	4,4	83,4	7,6	4,2	54
IVc	C$_6$H$_5$	230–231 (dec.)	$C_{27}H_{25}N_3$	81,6	7,9	10,6	82,0	7,8	10,6	36
IVd	α-Furyl	232–233 (dec.)	$C_{25}H_{27}N_3O$	77,8	7,4	11,1	77,9	7,0	10,9	70
Vb	CH$_3$	72–74	$C_{20}H_{27}N$	85,0	10,0	5,1	85,4	9,6	5,0	27
Vc	C$_6$H$_5$	109–111	$C_{25}H_{29}N$	87,9	8,7	3,7	87,5	8,5	4,1	30
VIb	CH$_3$	185–187	$C_{20}H_{24}NClO_4$	63,4	6,6	3,7	63,5	6,4	3,8	40
VIc	C$_6$H$_5$	260–263 (dec.)	$C_{25}H_{26}NClO_4$	68,0	6,3	3,4	68,2	6,0	3,2	40
VId	α-Furyl	240(dec.)	$C_{23}H_{24}NClO_5$	64,0	5,9	3,7	64,3	5,5	3,3	45
VIIb	CH$_3$	169–171	$C_{21}H_{28}N_2$	80,8	9,0	9,8	81,8	9,1	9,1	35
VIIc	C$_6$H$_5$	156–157	$C_{26}H_{30}N_2$	83,9	8,5	7,3	84,3	8,1	7,6	20
VIId	α-Furyl	165–166	$C_{24}H_{28}N_2O$	79,4	7,7	8,4	80,0	7,8	7,8	25
VIIIc	C$_6$H$_5$	270(dec.)	$C_{25}H_{26}IN$	64,1	5,8	3,2	64,2	5,6	3,0	32
VIIId	α-Furyl	216(dec.)	$C_{23}H_{24}INO$	59,9	5,5	3,7	60,4	5,3	3,1	35

* The yields of V-VIII are presented for the reaction of ketols Ib-d with aniline in acetic acid.

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* See [1] for communication VI.

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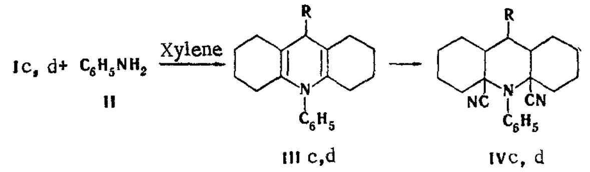
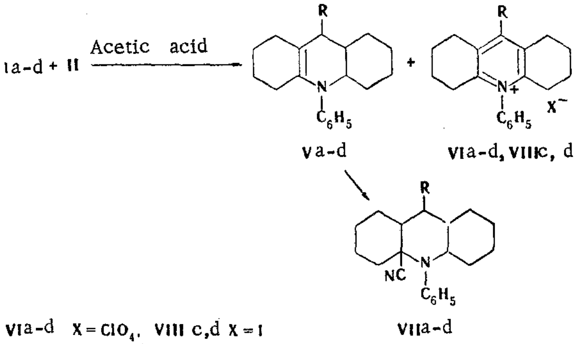
When the reaction was carried out in xylene, 9-R-10-phenyldecahydroacridines (IIIc, d) were isolated in the case of Ic,d. The reaction also proceeds in the case of Ia,b, but the corresponding decahydroacridines could not be isolated because of their low stabilities. The reaction for the formation of III proceeds in the presence of catalytic amounts of p-toluenesulfonic acid.



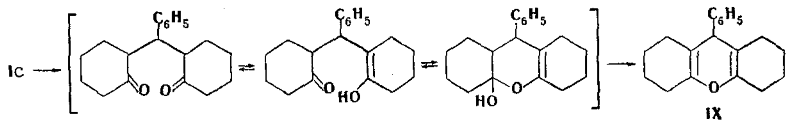
Two peaks, which are characteristic for decahydroacridines [1], are observed at 1670 cm^{-1} and 1700 cm^{-1} in the IR spectra of IIIc,d. There is a one-proton singlet at δ 3.35 (H in the 9 position) in the PMR spectrum of IIIc. Compounds IIc,d add two molecules of HCN to give dinitriles IVc,d. The IR spectra of the latter do not contain the peaks mentioned above, but a band appears at 2240 cm^{-1} (C ≡ N).

The reaction of ketols Ia-d with aniline in acetic acid proceeds only on heating; this is probably necessary for the decyclization of the ketones.



Compounds V were isolated in the form of products of the addition of HCN to them – VIIIa-d; Vb,c themselves were also isolated. The octahydroacridinium salts were isolated in the form of the perchlorates (VIa-d) and iodides (VIIIc,d). Compounds VIa and VIIa were identical to the products of the reaction of 2,2'-methylenedicyclohexanone with aniline in acetic acid [2]. The structures of the products of the reaction of ketols Ib-d were confirmed by the IR spectra: the spectra of Vb,c contain the absorption characteristic for dodecahydroacridines at 1700 cm^{-1} in the form of a single peak [2]. This peak vanishes for nitriles VII, and a peak appears at 2240 cm^{-1} (C ≡ N). When nitrile VIIb is refluxed with 60% sulfuric acid, HCN is split out and Vb is formed. Perchlorates VI have intense absorption at 1100 cm^{-1} (ClO_4). Products Vc and VIc are also formed during disproportionation of IIIc in acetic acid.

9-Phenyldecahydroxanthene (IX) was also isolated along with Vc and VIc in the reaction of ketol Ic with aniline in acetic acid [4]. The formation of decahydroxanthenes was also observed in the case of several other alicyclic 1,5-diketones [5]. Compound IX was also obtained by heating ketol Ic in acetic acid in the absence of aniline. The formation of IX can be represented by the following scheme:



In the case of IIIc, it was shown that the ketols can react with aniline in benzene or alcohol in the presence of CCl_4 to give a 9,10-diphenyloctahydroacridinium salt (VIc). A necessary condition for the successful occurrence of the reaction is the presence of a catalytic amount of p-toluenesulfonic acid and refluxing of the reaction mixture. Decahydroacridine IIIc is oxidized by CCl_4 to give salt VIc both at room temperature and on heating.

EXPERIMENTAL

9-R-10-Phenyldecahydroacridines (IIIc,d). A mixture of 0.02 mole of Ic,d and 0.02 mole of II in 80 ml of xylene was refluxed in the presence of 15-20 mg of p-toluenesulfonic acid with a Dean–Stark trap under argon for 4-6 h until the water had separated completely (0.7 ml). The solvent was removed by vacuum distillation in a stream of argon. Alcohol (25 ml) was added to the residue, and the precipitated IIIc,d were removed by filtration, washed with alcohol, and crystallized from alcohol. Compounds IIIc,d were white crystalline substances that were readily soluble in chloroform, acetone, and dioxane and only slightly soluble in alcohol (Table 1).

9-R-10-Phenyl-11,14-dicyanoperhydroacridines (IVc,d). A 1-g sample of IIIb or IIIc was added with stirring to a solution of 1 g of NaCN in 20 ml of acetic acid, and the mixture was allowed to stand overnight. The precipitate was removed by filtration, washed with water, and crystallized from alcohol.

Reaction of Ketols Ia-d with Aniline in Acetic Acid. A solution of 0.02 mole of Ia-d and 0.02 mole of II in 40 ml of acetic acid was refluxed for 2 h, after which it was allowed to stand overnight. In the case of Ic, IX precipitated and was removed by filtration. The reaction mixture was worked up by one of the following methods: A) The mixture was cooled with water, and 0.02 mole of NaCN in 5 ml of water was added with stirring. The precipitated nitriles (VIIa-d) were removed by filtration, washed with water, and crystallized from alcohol. The filtrate was made alkaline to pH 9 with sodium carbonate solution, and the slightly turbid mixture was extracted with ether. A solution of NH_4ClO_4 or NaI was added to the aqueous layer, and the precipitated VIa-d or VIIIc,d were removed by filtration, washed with water, and crystallized from water. B) (in the case of Ib,c) The reaction mixture was diluted with water and extracted with petroleum ether, and the aqueous layer was made alkaline to pH 9 with sodium carbonate solution. The resulting oil was extracted with ether, and VIc,d were isolated from the aqueous layer as indicated in method A. The ether extract was dried with magnesium sulfate, the ether was removed by distillation, and the residue was crystallized from alcohol to give Vb,c (Table 1). Compound IX was purified by crystallization from alcohol to give a product with mp 97-98° (mp 96-98° [4]) in 26% yield. IR spectrum (in $CHCl_3$): 1670, 1700 cm^{-1} (dihydropyran ring). Found: C 85.3; H 8.2%. $C_{19}H_{22}O$. Calculated: C 85.7; H 8.3%.

Disproportionation of IIIc. A solution of 0.01 mole of IIIc in 20 ml of acetic acid was refluxed for 2 h and then worked up via method A (see above). Compounds VIc and VIIc were identical to the products obtained in the preceding experiment.

Dehydrocyanation of VIIb. A 0.5-g sample of nitrile VIIb was refluxed for 2 h with 15 ml of 60% sulfuric acid, after which the mixture was diluted with water and made alkaline with ammonia. The precipitated Vb, which was identical to a genuine sample, was removed by filtration.

Reaction of Ic with Aniline in the Presence of CCl_4. A mixture of 0.005 mole of Ic, 0.005 mole of II, 0.05 mole of CCl_4, and a few milligrams of p-toluenesulfonic acid in 30 ml of alcohol or benzene was refluxed for 2 h, after which it was diluted with water and extracted with ether. A solution of NH_4ClO_4 was added to the aqueous layer, and the precipitated VIc (50%) was removed by filtration.

LITERATURE CITED

1. A. N. Saverchenko, V. A. Kaminskii, and M. N. Tilichenko, Khim. Geterotsikl. Soedin., 1232 (1972).
2. V. A. Kaminskii, A. N. Saverchenko, and M. N. Tilichenko, Khim. Geterotsikl. Soedin., 1538 (1970).
3. V. I. Vysotskii and M. N. Tilichenko, Khim. Geterotsikl. Soedin., 751 (1969).
4. I. W. Lewis, P. L. Myers, and M. I. Readhead, J. Chem. Soc., C, 771 (1970).
5. V. I. Vysotskii and M. N. Tilichenko, Khim. Geterotsikl. Soedin., 299 (1971).