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OXIDATION-REDUCTION CONVERSIONS OF DERIVATIVES OF 1,4-DIHYDROPYRIDINE AND 4H-PYRAN ON INTERACTION OF ALICYCLIC 1,5-DIKETONES WITH 4-AMINOAZOBENZENE

K. V. Maslov, T. I. Akimova, and V. A. Kaminski

The interaction of 2,2'-methylenedicyclohexanone and 2,2'-methylenedicyclopentanone with 4-aminoazobenzene in acetic acid leads to reduction of the azo group of 1,4-dihydropyridine and 4H-pyran derivatives formed as intermediates. The reduction products were isolated as the corresponding pyridinium salts.

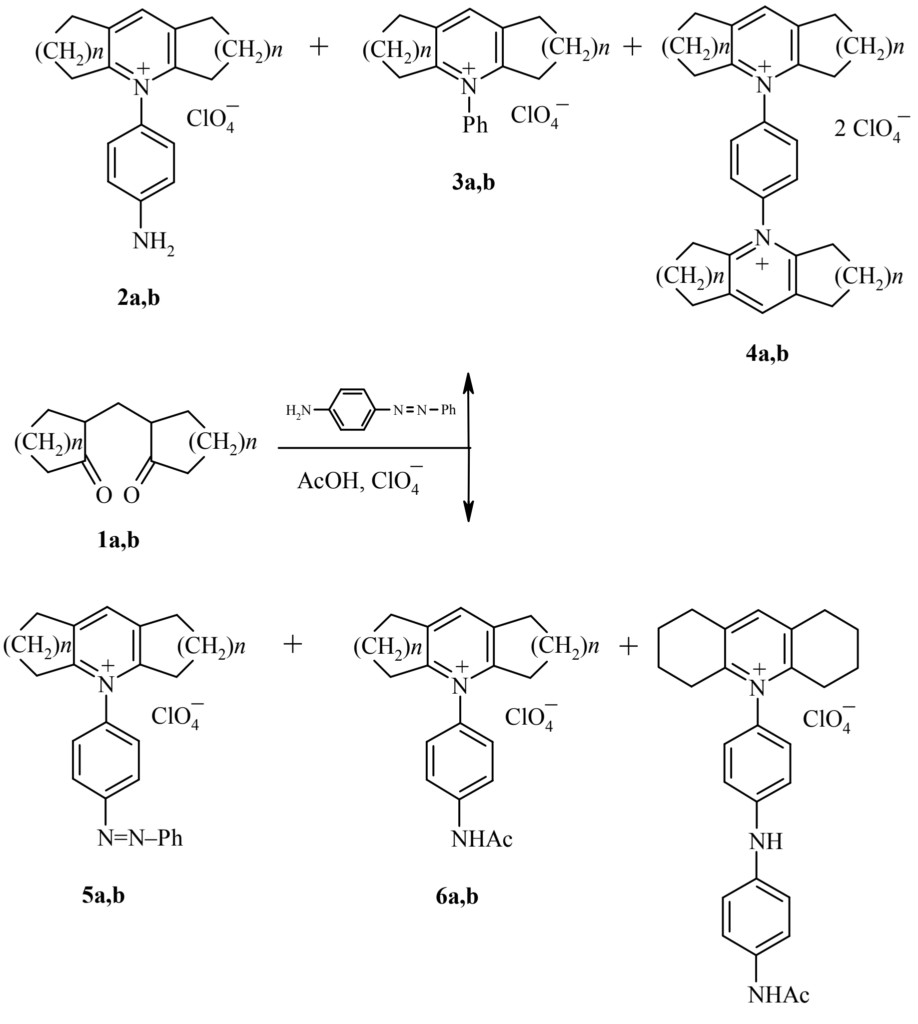
Keywords: 1,4-dihydropyridines, 1,5-diketones, 4H-pyrans, pyridinium salts, reduction.

It is known that the interaction of alicyclic 1,5-diketones with primary amines in acetic acid leads to disproportionation of 1-R-1,4-dihydropyridine derivatives formed as intermediates, the products of which are the corresponding derivatives of 1-R-1,2,3,4-tetrahydropyridine and pyridinium salts [1]. In addition it was shown [2] that in the presence of strong acids the same dihydropyridine derivatives reduce a series of substrates, including nitro and azo compounds. In view of this it seemed of interest to investigate the interactions of 1,5-diketones with primary amines also containing groups capable of being reduced.

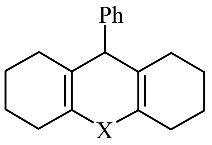
In the present work we have investigated the interaction of alicyclic 1,5-diketones, *viz*. 2,2'-methylenedicyclopentanone (**1a**) and 2,2'-methylenedicyclo-hexanone (**1b**), with aminoazobenzene in acetic acid and have established that, in difference to cases studied previously, the reaction is accompanied not by the reduction of the dihydropyridine nucleus but by the reduction of the azo group. The reaction products are pyridinium salts (all salts were isolated as perchlorates).

If the reaction is carried out at a molar ratio of diketone to 4-aminoazobenzene of 2:1 with slow addition of the latter to a boiling solution of diketone in acetic acid, then a mixture of N-(*p*-aminophenyl)pyridinium salts **2a,b**, N-phenylpyridinium salts **3a,b**, and N,N'-*p*-phenylenebispyridinium salts **4a,b** is formed as a result of the complete reduction of the azo group to amino group. The interaction of equimolar quantities of reactants on heating gives a mixture of N-(*p*-phenylazo)phenylpyridinium salts **5a,b** and N-(p-acetylaminophenyl)pyridinium salts **6a,b**. In the case of diketone **1b** N-[*p*-(*p*-acetylaminophenyl)aminophenyl]-*sym*-octahydroacridinium salt (**7**) – the product of a semidine rearrangement of the hydrazo derivative formed as an intermediate was also isolated.

Far-Eastern State University, Vladivostok, 690600, Russia; e-mail: kamin@chem.dvgu.ru. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 482-486, April, 2002. Original article submitted February 2, 2000.



1–6 a $n = 1$, **b** $n = 2$



8 X = O
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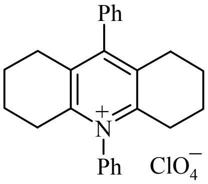

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1,4-Dihydropyridine derivatives formed on interaction of diketones with the amino group of aminoazobenzene may appear to be the reducing agents for the azo group. In this case the reduction may proceed both intramolecularly or intermolecularly. The pure intramolecular variant seems less probable since with equimolar ratio of reactants a significant quantity (of the order of 30%) of salts **5** with unreduced azo group is formed. Dihydropyridine derivatives containing azobenzene reduction products as substituents at the nitrogen atom (such as phenyl or 4-aminophenyl group) may be other reducing agents. In addition 4H-pyran derivatives, which may be formed on heating 1,5-diketones in acetic acid may be the reducing agents [3].

We investigated several reactions to reduce the azo group, using azobenzene as example, with reagents of the types indicated above. Diketones **1a,b** in boiling acetic acid do not reduce azobenzene, 9-phenyl-1,2,3,4,5,6,7,8-octahydro-9H-xanthene (**8**) does not reduce it also. On the other hand 9,10-diphenyl-1,2,3,4,5,6,7,8,9,10-decahydroacridine (**9**) under the same conditions reduces azobenzene to aniline. The reduction of azobenzene occurs even more rapidly on treating it with a mixture of diketone **1b** and benzylamine (i.e. N-benzyldecahydroacridine *in statu nascendi*). Therefore dihydropyridine, but not 4H-pyran, derivatives are reducing agents at least in the first stage of the reduction of the azo group.

We then checked the possibility of reducing hydrazobenzene with the same reagents under the same conditions. Both pyran **8** and dihydropyridine **9** reduce hydrazobenzene with the formation of 9,10-diphenyl-1,2,3,4,5,6,7,8-octahydroacridinium salt (**10**) (isolated as the perchlorate). Formation of aniline was also fixed on reduction with the aid of dihydropyridine **9**. Diketones **1a,b** also reduce hydrazobenzene on boiling in acetic acid (evidently the reducing agents are 4H-pyran derivatives formed as intermediates). Salts **3a,b** are the reaction products. Derivatives of both dihydropyridine and of 4H-pyran may therefore act as reducing agents in the subsequent stages of reduction of the azo group. Compounds **2b, 3a,b, 4b,** and **10** were identified by comparison with known samples. The remaining salts were not known previously.

There were absorption bands in the IR spectrum of salt **2a** at 3360 and 3440 cm^{-1} for the primary amino group. In the spectra of salts **6a,b** and **7** there were absorption bands at 3320-3330 and 1655-1695 cm^{-1} for the CO–NH group. In the spectra of the remaining new salts there was no absorption in the 1620-1800 region nor above 3100 cm^{-1}.

In the NMR spectra of the tricyclic pyridinium salts (Table 1) the aliphatic protons gave three groups of signals. In the 2.95-3.30 and 2.45-3.00 ppm regions there were signals of protons linked respectively with the α- and β-positions of the pyridinium ring, the remaining alicyclic protons gave signals at 1.80-2.35 ppm. The signal

TABLE 1. ^{1}H NMR Spectral Characteristics of Pyridinium Salts

Com-pounds	Chemical shifts, δ, ppm (*J*, Hz)					
	CH$_2$			4-H, s	Ar–H	Other
	*	*^{2}	*^{3}			
2a	3.21, t (*J* = 7.5)	2.91, t (*J* = 7.5)	2.30, q (*J* = 7.5)	8.1	7.57-7.68, m	
4a	3.18, t (*J* = 7)	2.93, t (*J* = 7)	2.22, q (*J* = 7)	8.46	8.08, s	
5a	3.24, t (*J* = 7.5)	2.97, t (*J* = 7.5)	2.32, q (*J* = 7.5)	8.09	7.53-7.59, m, 7.78 d (*J* = 8), 7.95-8.00, m, 8.15 d (*J* = 8)	
5b	3.00, br. d	2.47-2.56, m	1.85, q (*J* = 3)	7.92	7.44-7.56, m, 7.66 d (*J* = 7), 7.90-8.00 m, 8.17 d (*J* = 7)	
6a	3.19, t (*J* = 7.5)	2.89, t (*J* = 7.5)	2.27, m	8.01	7.40, d (*J* = 8), 7.99, d (*J* = 8)	2.26 s (CH$_3$CO), 9.22 s (CONH)
6b	2.97, br. s	2.50 br. s	1.81, br. s	7.86	7.26, d (*J* = 8), 8.02, d (*J* = 8)	2.26 s (CH$_3$CO), 9.09 s (CONH)
7	2.97, br. s	2.50, m	1.82, br. s	7.88	6.86, d (*J* = 8), 7.06, d (*J* = 8), 7.26, d (*J* = 8), 8.02, d (*J* = 8)	2.25 s (CH$_3$CO), 9.09 s (CONH)

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* Protons of CH$_2$ groups linked to positions 2 and 6 of the pyridinium ring.

*^{2} Protons of CH$_2$ groups linked to positions 3 and 5 of the pyridinium ring.

*^{3} Protons of remaining CH$_2$ groups.

TABLE 2. Characteristics of Compounds Synthesized

Compound	Empirical formula	Found, % / Calculated, %			mp, °C	Yield, %
		C	H	N		
2a	$C_{17}H_{19}ClN_2O_4$	58.04 58.20	5.45 5.42	8.12 7.99	243-244	27
4a	$C_{28}H_{30}Cl_2N_2O_8$	57.04 56.66	5.22 5.06	4.60 4.72	300 (dec.)	43
5a	$C_{23}H_{22}ClN_3O_4$	63.11 62.80	4.96 5.00	9.84 9.56	172-176	26
5b	$C_{25}H_{26}ClN_3O_4$	63.95 64.17	5.58 5.56	9.24 8.99	158-164*	31
6a	$C_{19}H_{21}ClN_2O_5$	58.12 58.09	5.61 5.35	7.00 7.13	188-190	12
6b	$C_{21}H_{25}ClN_2O_5$	60.22 59.93	6.13 5.95	6.38 6.66	183-184	4
7	$C_{27}H_{30}ClN_3O_5$	63.51 63.34	6.10 5.87	8.15 8.21	118-120	14

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* Amorphous powder.

of the proton at position 4 of the pyridinium nucleus was displayed as a singlet near 8 ppm. There were signals for the $\underline{CH_3}CO$ and $CO\underline{NH}$ groups in the spectra of salts **6a,b** and **7**. There was also a signal for the NH group in the spectrum of compound **7**. The signals of the aromatic protons of compounds **6a,b** were displayed as two doublets of intensity about 2H, and in compound **7** as four doublets of intensity about 2H.

EXPERIMENTAL

The IR spectra were recorded on a Spectrum BX II (Perkin-Elmer) spectrometer in CH_2Cl_2. The NMR spectra were recorded on a Bruker WM 250 (250 MHz) instrument in $CDCl_3$, internal standard was TMS. Column chromatography was effected on grade II aluminum oxide, eluent was ethyl acetate–acetone. A check on the progress of reactions and the purity of the compounds obtained was carried out by TLC on Silufol UV 254 plates.

The characteristics of compounds synthesized for the first time are given in Table 2.

Interaction of 2,2'-Methylenedicyclanones 1a,b with 4-Aminoazobenzene. A. Solution of 4-aminoazobenzene (1.46 g, 7.5 mmol) in acetic acid (15 ml) was added in portions (1 ml) to a boiling solution of 1,5-diketone **1** (15 mmol) in acetic acid (20 ml). Each new portion was added after decolorization of the solution. Water (120 ml) was added, the solution was neutralized to pH 8-9 with Na_2CO_3, and extracted with ether. Aniline was detected qualitatively in the extract. Saturated aqueous solution of NH_4ClO_4 was added to the aqueous layer, the precipitated solid of mixture of perchlorates was filtered off, washed with water, and dried. The mixture of perchlorates (3 g) was boiled with methylene chloride (15 ml), the insoluble portion was filtered off, recrystallized from mixture of acetonitrile–water, 5:1, and compound **4a** or **4b** was obtained. The filtrate was evaporated to half volume, petroleum ether (30 ml) was added, and the petroleum ether layer was decanted from the precipitated oil. Compound **3a** or **3b** precipitated from the decantate on standing. These salts were recrystallized from 2-propanol. The oil was triturated with tetrahydrofuran (10 ml), compound **2a** or **2b** was filtered off, and was recrystallized from 2-propanol.

B. Mixture of diketone **1** (10 mmol) and 4-aminoazobenzene (10 mmol) in acetic acid (20 ml) was boiled for 3 h, poured into water (100 ml), and extracted with ether. The aqueous layer was neutralized with Na_2CO_3 to pH 8-9, the mixture extracted with ether, and aqueous NH_4ClO_4 solution was added to the aqueous layer. The precipitated solid was filtered off, washed with water, and dried. Compounds **5a** and **5b** were separated by TLC on a binder-free layer with Al_2O_3 of activity grade II, the eluent being ethyl acetate–acetone, 2:1. Compounds **5b**, **6b**, and **7** were separated on a column of Al_2O_3, the eluent was ethyl acetate–acetone from 4:1 to 1:1.

Interaction of 9-Phenyl-1,2,3,4,5,6,7,8-octahydro-9H-xanthene (8) and 9,10-Diphenyl-1,2,3,4,5,6,7,8,9,10-decahydroacridine (9) with Azobenzene and Hydrazobenzene. Mixture of pyran **8** or dihydropyridine (5 mmol) and azobenzene or hydrazobenzene (5 mmol) in acetic acid (10 ml) was treated as in method B. On interaction of dihydropyridine **9** with azobenzene aniline was detected by a qualitative reaction (furfural–acetic acid) and by GLC. No aniline or salt **10** were detected on interacting pyran **7** with azobenzene. Salt **10** was obtained in 86% yield on interacting pyran **8** with hydrazobenzene, and in 82% yield on interacting dihydropyridine **9** with hydrazobenzene.

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