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OXIDATION–REDUCTION CONVERSIONS OF 1,4-DIHYDROPYRIDINE DERIVATIVES ON INTERACTION OF ALICYCLIC 1,5-DIKETONES WITH NITROANILINES

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On interaction of alicyclic 1,5-diketones and the products of their intramolecular aldol condensation with 2- and 4-nitroanilines and 2,4-dinitroaniline reduction occurs of the nitro group by the intermediately formed 1,4-dihydropyridine derivatives. The reaction products are N-nitrophenyl- and N-aminophenylpyridinium salts and also N,N-phenylenebispyridinium salts.

Keywords: alicyclic 1,5-diketones, 2,4-dinitroaniline, 2-nitroaniline, 4-nitroaniline, pyridinium salts, reduction.

The reductive properties of 1,4-dihydropyridine derivatives are widely known [1,2]. The majority of the derivatives investigated contain electron-accepting substituents in positions 3 and 5. The special features of the reductive properties of dihydropyridines without electron-withdrawing groups has been investigated using derivatives of 1,2,3,4,5,6,7,8,9,10-decahydroacridine as examples. They reduce various substrates fairly readily [3], and are also able to disproportionate with the formation of pyridinium salts and derivatives of 1,2,3,4-tetrahydropyridine [4]. A specific variant of oxidation–reduction conversions with the participation of dihydropyridines is the interaction of 1,5-diketones with primary amines, containing fragments capable of being reduced. In this case both disproportionation of the intermediate dihydropyridines and reduction of the fragments mentioned above is possible. It was shown by us that on interaction of alicyclic diketones **1a,b** with 4-aminoazobenzene reduction of the azo group occurs [5]. Dehydration products of 1,5-diketones, 4H-pyran derivatives, also participate in oxidation–reduction conversions together with the dihydropyridine derivatives.

Continuing investigations in this direction we studied the interaction of diketones **1a,b** with 2- and 4-nitroaniline and 2,4-dinitroaniline, and also the bridge ketols **2a,b** with 4-nitroaniline. The reaction was carried out in acetic acid. Under the conditions used by us ketols **2a,b** are first subject to a retroaldol decomposition to the corresponding 1,5-diketones (Scheme 1).

Reduction of the nitro group of the reactant to an amino group occurred in all cases. On interacting equimolar quantities of diketones **1a,b** with 2-nitroaniline in acetic acid a mixture was formed of N-(2-nitrophenyl)pyridinium salts **3a,b** and N-(2-aminophenyl)pyridinium salts **4a,b** at a molar ratio of 2:1 (according to data of NMR spectra). Reaction of the diketones and of ketols **2a,b** with 4-nitroaniline at a molar ratio of diketone (ketol) to amine of 3:2 leads to a mixture of N-(4-nitrophenyl)pyridinium salts **5a,b**-**7a,b** and N,N-phenylenebispyridinium salts **8a,b**-**10a,b**. The latters are evidently formed by the interaction of the excess

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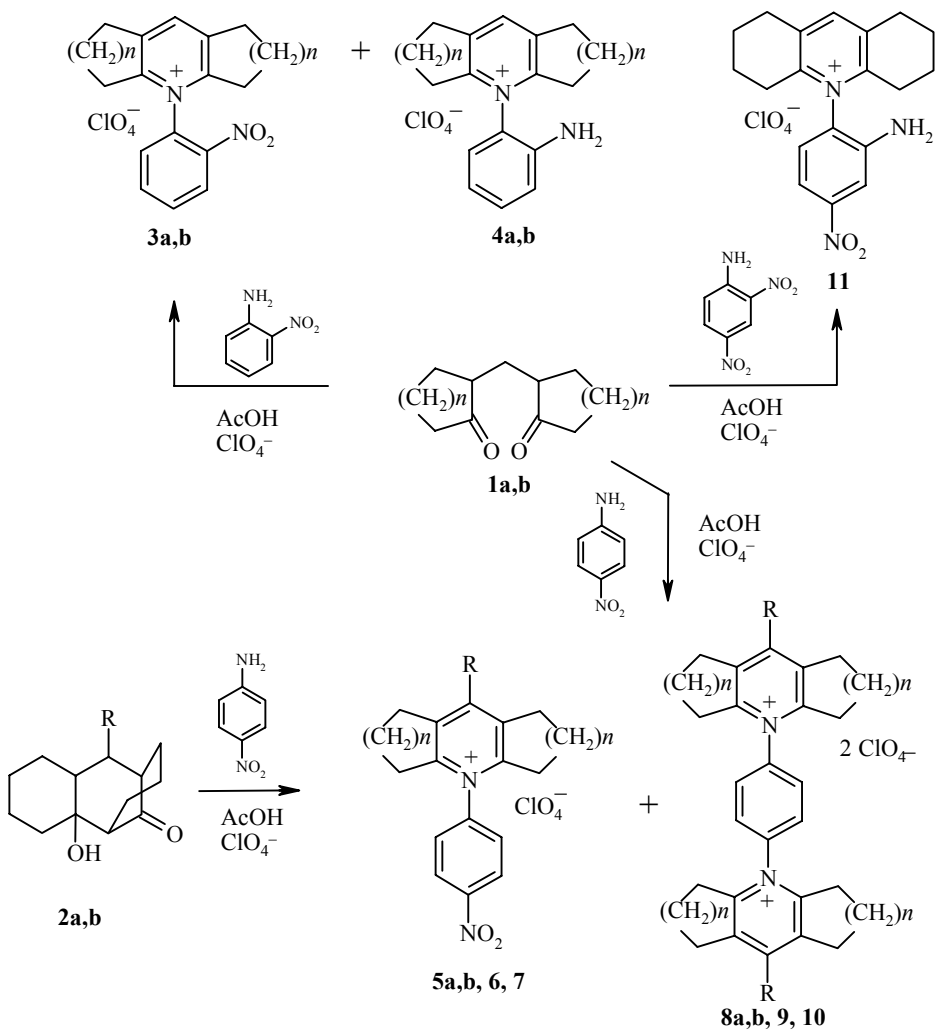
Scheme 1



1, 3-5, 8 a *n* = 1; **b** *n* = 2; **6, 7, 9, 10** *n* = 2; **5, 8** R = H; **6, 9** R = Me; **7, 10** R = Ph

of 1,5-diketones with the intermediate 4-aminophenylpyridinium salts. On interaction of diketone **1b** with 2,4-dinitroaniline only the nitro group in position 2 is reduced, i.e. the N-(2-amino-4-nitrophenyl)pyridinium salt **11** is formed. Diketone **1a** does not react with the very low nucleophilic 2,4-dinitroaniline due to the low reactivity of the carbonyl groups compared to **1b**. Compounds **8a,b** were identical with samples obtained previously [5], the remaining pyridinium salts were obtained for the first time. Salts **4a** and **4b** were failed to obtain in the pure state. According to NMR spectra they contain admixture of salts **3a** and **3b** respectively.

Reduction of the nitro group, as in the case studied previously, may in principle be effected by derivatives of 1,4-dihydropyridine or 4H-pyran formed as intermediates. Our experiments showed that 9-phenyl-1,2,3,4,5,6,7,8-octahydro-9H-xanthene in acetic acid does not reduce nitrobenzene or salt **3a** to the corresponding amino compound. It is probable that 1,4-dihydropyridine derivatives are the reducing agents for the nitro group.

There were pyridinium absorption bands near 1500 and 1600 cm^{-1} in the IR spectra of all the salts obtained and there was no absorption in the carbonyl region 1650-1720 cm^{-1}. Bands at 1340-1360 and 1530-1539 cm^{-1} correspond to absorption of the nitro group, and bands at 3350-3365 and 3400-3450 cm^{-1} to the amino group (in salts **4a,b** and **11**).

TABLE 1. The NMR Spectra of the Pyridinium Salts

Com-pound	Chemical shifts, δ, ppm, *J* (Hz)					
	CH_2*	CH_2*[2]	CH_2*[3]	4-H	Ar-H	Other
3a	2.83 (4H, br. t)	3.16 (4H, br. t)	2.17 (4H, m)	8.47 (1H, s)	8.57 (1H, dd), 8.17 (1H, td), 8.06 (1H, td), 7.99 (1H, dd)	
3b	2.63 (2H, dt), 2.18 (2H, dt)	3.10 (2H, dt), 2.90 (2H, dt)	1.95 (4H, m), 1.77 (4H, m)	7.95 (1H, s)	8.37 (1H, dd), 8.28 (1H, dd), 8.09 (1H, td), 7.90 (1H, td)	
4a*[4]	2.80 (4H, m)	3.12 (4H, br. t)	2.18 (4H, m)	8.31 (1H, s)	7.31 (1H, td), 7.21 (1H, dd), 6.95 (1H, dd), 6.75 (1H, td)	5.53 (2H, br. s, NH_2)
4b*[5]	2.63 (2H, dt), 2.50 (2H, dt)	3.12 (2H, dt), 2.88 (2H, dt)	1.95 (4H, m), 1.78 (4H, m)	7.92 (1H, s)	7.36 (1H, t), 6.78-6.94 (3H, m)	4.50 (2H, s, NH_2)
5a	2.91 (4H, t)	3.23 (4H, t)	2.33 (8H, quintet)	8.11 (1H, s)	8.51 (2H, d), 7.95 (2H, d)	
5b	2.45 (4H, br. s)	2.98 (4H, br. s)	1.86 (8H, m)	7.95 (1H, s)	8.53 (2H, d), 7.84 (2H, d)	
6	2.42 (4H, t)	2.88 (4H, t)	1.85 (8H, m)		8.52 (2H, d), 7.78 (2H, d)	2.44 (3H, s, CH_3)
7	2.50 (8H, m)		1.68-1.85 (8H, m)			
9	2.46 (8H, m)	2.87 (8H, m)	1.75 (16H, m)		7.88 (4H, s)	2.45 (6H, s, CH_3)
10	2.48 (8H, m)	2.61 (8H, m)	1.72 (16H, m)		8.02 (4H, s), 7.65 (6H, m), 7.28 (4H, dd)	
11	2.55 (4H, m)	3.08 (2H, m), 2.92 (2H, m)	1.70-1.95 (8H, m)	7.97 (1H, s)	7.74 (1H, d), 7.64 (1H, dd), 7.06 (1H, d)	5.05 (2H, br. s, NH_2)

* Protons of the CH_2 groups linked with positions 2 and 6 of the pyridinium ring.
*[2] Protons of the CH_2 groups linked with positions 3 and 5 of the pyridinium ring.
*[3] Protons of the remaining CH_2 groups.
*[4] Also contains signals of salt **3a** (**4a**:**3a**, 70:30).
*[5] Also contains signals of salt **3b** (**4b**:**4a**, 90:10).

In the NMR spectra of the pyridinium salts (Table 1) the signals of the CH_2 group protons were found in the same regions as for the salts of the same series obtained previously [5]. However for salts containing a 2-substituted phenyl at the nitrogen atom (**3,4,11**) the picture was generally more complex than for those containing a 4-substituted phenyl at this position. This indicates the nonequivalence of the tri- or tetramethylene fragments condensed with the pyridinium nucleus. This is probably the result of the existence of fairly stable conformations in which the substituent at position 2 of the N-aryl substituent is closer to one of the condensed polymethylene fragments.

TABLE 2. Characteristics of the Synthesized Compounds

Compound	Empirical formula	Found, % / Calculated, %			mp, °C	Yield, %
		C	H	N		
3a	$C_{17}H_{17}ClN_2O_6$	53.28 / 53.61	4.62 / 4.47	7.22 / 7.36	196-198	51
3b	$C_{19}H_{21}ClN_2O_6$	55.90 / 55.81	5.26 / 5.14	6.64 / 6.85	217-218	52
5a	$C_{17}H_{17}ClN_2O_6$	53.66 / 53.61	4.60 / 4.47	7.44 / 7.36	236-238	42
5b	$C_{19}H_{21}ClN_2O_6$	55.72 / 55.81	5.32 / 5.14	6.93 / 6.85	255-256	44
6	$C_{20}H_{23}ClN_2O_6$	56.60 / 56.80	5.48 / 5.44	6.77 / 6.63	239-240	38
7	$C_{25}H_{25}ClN_2O_6$	62.05 / 61.92	5.20 / 5.16	5.68 / 5.78	246-248	31
9	$C_{34}H_{42}Cl_2N_2O_8$	60.50 / 60.27	6.33 / 6.20	4.11 / 4.14	300 (dec.)	55
10	$C_{44}H_{46}Cl_2N_2O_8$	65.78 / 65.92	5.70 / 5.74	3.46 / 3.50	310 (dec.)	50
11	$C_{19}H_{22}ClN_3O_6$	53.72 / 53.84	5.30 / 5.19	9.77 / 9.92	230 (dec.)	36

EXPERIMENTAL

The IR spectra were recorded on a Spectrum BX-II (Perkin-Elmer) spectrometer in CH_2Cl_2, and the NMR spectra on a Bruker WM 250 (250 MHz) instrument in $CDCl_3$, internal standard was TMS. A check on the progress of reactions and the purity of the products obtained was effected by TLC on Silufol UV 254 plates.

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

Interaction of 1,5-Diketones 1a,b and Ketols 2a,b with Nitroanilines. A solution of 1,5-diketone **1** or ketol **2** (5 mmol) and nitroaniline (5 mmol) in acetic acid (15 ml) was boiled for 2-4 h (diketone) or 3-6 h (ketol). Water (80-100 ml) was added, the mixture was neutralized to pH 8-9 with Na_2CO_3, and extracted three times with ether. A saturated aqueous solution of NH_4ClO_4 was added to the aqueous layer, the precipitated mixture of perchlorates was filtered off, washed with water, and dried. To separate the mixture of perchlorates **3a** and **4a** or **3b** and **4b** the mixture of salts (1 g) was dissolved by boiling in methanol (10 ml), cooled, perchlorate **3a** or **3b** was filtered off, and recrystallized twice from methanol. The filtrate was evaporated, the residue recrystallized from methanol, salt **4a** (contaminated with salt **3a**) or **4b** (contaminated with salt **3b**) was obtained. To separate the mixtures of perchlorates **5** and **8**, **6** and **9**, and **7** and **10**, the mixture (2 g) in acetone (10 ml) was heated to boiling, the insoluble solid containing bisperchlorates **8**, **9**, or **10** was filtered off, washed with acetone, and recrystallized from an acetonitrile–water mixture. The filtrate was evaporated, the residue was recrystallized from methanol, and salt **5**, **6**, or **7** was obtained.

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