HETEROCYCLIC ANALOGS OF PLEIADIENE.

XXXIX.* REACTION OF N-SUBSTITUTED 1,8-NAPHTHALENEDIAMINES WITH ALDEHYDES. SYNTHESIS AND AROMATIZATION OF N-SUBSTITUTED 2,3-DIHYDROPERIMIDINES

N. M. Starshikov and A. F. Pozharskii

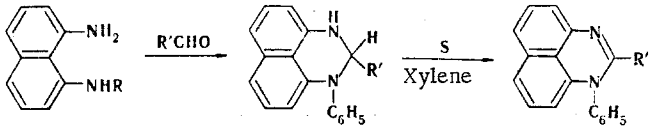
UDC 547.856.7.07:542.941.8'.953.2

The reaction of 1-anilino-8-aminonaphthalene, 1-methylamino-8-aminonaphthalene, and 1-dimethylamino-8-aminonaphthalene with aldehydes and the dehydrogenation of the N-phenyl-2-R-2,3-dihydroperimidines with sulfur in refluxing xylene were studied.

The simplest methods for the preparation of N-substituted 2,3-dihydroperimidines are evidently reduction of 1-R-perimidines with lithium aluminum hydride (LAH) [2, 3] and the addition of organometallic compounds to them [3, 4]. However, considering the ease of the reaction of 1,8-naphthalenediamine (I) with aldehydes [5, 6], which leads to 2,3-dihydroperimidines with free NH groups, the extension of this method to the synthesis of N-substituted 2,3-dihydroperimidines seems promising. The present paper is devoted to a study of this question in the case of N-phenyl- and N-methyl-1,8-naphthalenediamines (II and III).

We have established that the reactivities of 1,8-naphthalenediamines with respect to aldehydes depend substantially on the nature of the N-substituent. Thus 1-anilino-8-aminonaphthalene (II) is appreciably more inert than diamines I with respect to its reactions with aldehydes. Whereas diamine I reacts rapidly with aldehydes in benzene or alcohol at room temperature, the reaction of diamine II under these conditions proceeds very slowly and requires heating for its completion. The behavior of I and II with respect to p-dimethylaminobenzaldehyde may serve as a concrete example of their different activities. This aldehyde was found to be the most inert of all of the aldehydes thus far subjected to reaction with 1,8-naphthalenediamines. Diamine I reacts with it to give 2-(p-dimethylaminophenyl)-2,3-dihydroperimidine (in 95% yield) only when it is refluxed in alcohol, whereas diamine II does not undergo reaction even under these conditions. We were able to accomplish the reaction of diamine II with p-dimethylaminobenzaldehyde only in the presence of acetic acid, which acts as a cyclization catalyst.

1-Phenyl-2,3-dihydroperimidines IV, which we obtained in this research, were aromatized by means of sulfur [7] to 1-phenylperimidines V. It should be noted that the aromatization of dihydro derivatives IV proceeds with considerably greater difficulty than in the case of 2,3-dihydroperimidines that do not contain an N-phenyl group [7]. This can be explained by the electron-acceptor effect of the latter [8], which leads to a decrease in the hydride mobility of IV:



I-III IVa-f Va-d

I R=H; II R=C_6H_5; III R=CH_3; IV, Va R'=n-C_3H_7; b R'=C_6H_5; c R'=p-$C_6H_4N(CH_3)_2$; d R'=α-furyl IVe R'=α-thienyl; f R'=p-$C_6H_4NO_2$

In contrast to diamines I and II, 1-methylamino-8-aminonaphthalene (III) extremely unexpectedly displays complete inertness with respect to aromatic aldehydes (benzaldehyde, p-nitrobenzaldehyde, and furfural were tested) not only at room temperature but even when

---

*See [1] for communication XXXVIII.

Shakhty Technological Institute of Everyday Repairs and Other Serivces, Shakhty 346500. Rostov State University, Rostov-on-Don 344006. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 10, pp. 1413-1417, October, 1978. Original article submitted February 13, 1978.

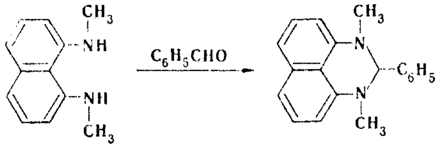
0009-3122/78/1410-1152$07.50

the reagents are refluxed in benzene or alcohol. We were able to carry out the reaction between diamine III and benzaldehyde only in the case of prolonged refluxing of the mixture in butanol in the presence of a small amount of acetic acid. The reaction product was a slightly yellowish crystalline substance (we will call it compound A) with an empirical formula $(C_{18}H_{16}N_2)_n$ corresponding to 1-methyl-2,3-dihydroperimidine or 1-methylamino-8-benzylideneaminonaphthalene, if it is assumed that n = 1. However, this compound is not a Schiff base, since it is not hydrolyzed when it is refluxed with hydrochloric acid and is only slightly soluble in it. The PMR spectrum of A does not contain a signal of an azomethine proton at 8.3 ppm, which, according to our data, is present in the spectra of 1-benzylideneaminonaphthalene and 1-benzylideneamino-8-nitronaphthalene; the spectrum of A does not contain broad signals at 2.42 ($N-CH_3$), 4.05, and 4.8 ppm, as well as a multiplet of aromatic protons centered at 6.40 ppm. It should be noted that the signals at 4.05 and 4.8 ppm could have been assigned to the μ-hydrogen atom of the 2,3-dihydroperimidine structure; however, 1-methyl-2-phenyl-2,3-dihydroperimidine, which could be formed in this reaction, is a known compound and is a liquid [4]. The ratio of the integral intensities of the protons of the $N-CH_3$ group and all the remaining protons is 3:12, which corresponds to the addition of one molecule of benzaldehyde to diamine molecule III with splitting out of water. The diffuse character of all of the signals in the PMR spectrum of A compelled us to assume that it is a mixture or an oligomer. The latter is evidently correct, since measurement of the molecular weight by a cryoscopic method led to a value of 1051, which is close to the value for the $(C_{18}H_{16}N_2)_4$ tetramer (molecular weight 1041).

An extremely similar substance (we will call it compound B) is formed in the reaction under the same conditions of benzaldehyde and 1-dimethylamino-8-naphthalene (VIII). The determination of its molecular weight also indicates tetramer formula $(C_{19}H_{18}N_2)_4$. According to the IR spectroscopic data, both A and B contain an NH group. A characteristic property of these compounds is their high electrifiableness. However, the data obtained are not sufficient to enable one to pronounce even a tentative judgment regarding the structures of A and B.

It is surprising that Schiff bases are not formed in the reactions of III and especially VIII with aldehydes. This can hardly be explained by steric factors, since, as we have established, 1-amino-8-nitronaphthalene reacts extremely readily with benzaldehyde to give an azomethine that is hydrolyzed by acids.

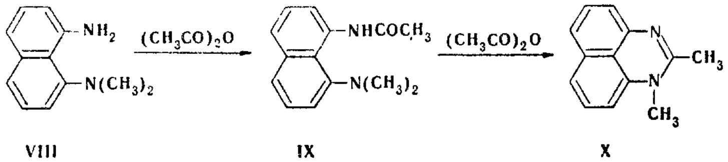
In contrast to III and VIII, 1,8-bis(methylamino)naphthalene (VI) reacts with benzaldehyde to give 1,3-dimethyl-2-phenyl-2,3-dihydroperimidine (VII). This reaction proceeds slowly in the cold, but VII is obtained in almost quantitative yield when the reactants are refluxed in alcohol for 1 h.



VI VII

It is interesting to note that a similar anomaly is not observed in the reaction of N-methyl-o-phenylenediamine with aromatic aldehydes. In this case a Schiff base, which is converted to 1-methyl-2-R-benzimidazoline on heating [9], is formed in the cold. N,N-Dimethyl-o-phenylenediamine also reacts with aldehydes in the cold to give 1,3-dimethyl-2-R-benzimidazolines [9].

The anomalous behavior of III and VIII in reactions with benzaldehyde compelled us to ascertain how other cyclization reactions proceed for them. It was found that diamine III is readily converted to 1-methyl- and 1,2-dimethylperimidines in quantitative yields on brief heating with formic acid or acetic anhydride. Even 1-dimethylamino-8-aminonaphthalene undergoes cyclization when it is heated with acetic anhydride with the loss of one N-methyl group to give 1,2-dimethylperimidine (X). This somewhat curious reaction is also known for N,N-dimethyl-o-phenylenediamine [10].



VIII IX X

TABLE 1. 2,3-Dihydroperimidines IV and Perimidines V

Compound	mp, °C[a]	ν_{N-H}, cm^{-1}	Found, %			Empirical formula	Calc., %			Yield, %
			C	H	N		C	H	N	
IVa	Oil	3412	83,2	6,9	9,8	$C_{20}H_{20}N_2$	83,3	7,0	9,7	95
IVb	151—152	3410	85,6	5,8	8,8	$C_{23}H_{18}N_2$	85,7	5,6	8,7	90
IVc	188—189	3410	82,2	6,4	11,6	$C_{25}H_{23}N_3$	82,2	6,3	11,5	95
IVd	123—124	3400	80,6	5,5	9,1	$C_{21}H_{16}N_2O$	80,7	5,2	9,0	90
IVe	122—123	3380	76,6	5,1	8,6	$C_{21}H_{16}N_2S$[b]	76,8	4,9	8,5	90
IVf	152—153	3410	75,3	4,6	11,6	$C_{23}H_{17}N_3O_2$	75,2	4,7	11,4	95
Va	115—116	—	83,8	6,3	10,0	$C_{20}H_{18}N_2$	83,9	6,3	9,8	90
Vb	232—234	—	86,1	5,0	8,8	$C_{23}H_{16}N_2$	86,2	5,0	8,8	70
Vc	242—243	—	82,7	5,9	11,8	$C_{25}H_{21}N_3$	82,6	5,8	11,6	70
Vd	166—167	—	81,2	4,6	9,1	$C_{21}H_{14}N_2O$	81,3	4,6	9,0	70

[a] The compounds were crystallized: IVb, d, e, f form alcohol, Va from aqueous alcohol, IVc from alcohol—chloroform, IVe from hexane, and Vb-d from ethyl acetate. [b] Found: S 9.8%. Calculated: S 9.8%.

EXPERIMENTAL

The UV spectra of methanol solutions of the compounds were recorded with an SF-16 spectrophotometer. The IR spectra of chloroform solutions were recorded with a UR-20 spectrometer. The PMR spectra were recorded with a Tesla spectrometer (60 MHz) with hexamethyldisiloxane as the internal standard.

1-Phenyl-2-propyl-2,3-dihydroperimidine (IVa, Table 1). A 0.8-g (0.011 mole) sample of butanal was added to a solution of 2.3 g (0.01 mole) of 1-anilino-8-aminonaphthalene (II) in 30 ml of benzene, and the mixture was maintained at room temperature for 1 h. The benzene was removed by distillation, and the residue was dried in vacuo at 50°C to give chromatographically pure dihydroperimidine IVa as a colorless liquid.

1,2-Diphenyl-2,3-dihydroperimidine (IVb, Table 1). A mixture of 2.3 g (0.01 mole) of amine II, 1.1 g (0.01 mole) of benzaldehyde, and 50 ml of alcohol was refluxed for 1 h, after which the resulting solution was cooled, and the precipitated crystals of dihydroperimidine IVb were removed by filtration and washed with alcohol. Compounds IVd-f were similarly obtained (Table 1).

2-(p-Dimethylaminophenyl)-2,3-dihydroperimidine. A mixture of 3.2 g (0.02 mole) of diamine I, 3.0 g (0.02 mole) of p-dimethylaminobenzaldehyde, and 35 ml of alcohol was refluxed for 2 h, after which the resulting solution was cooled, and the precipitated crystals were removed by filtration and washed with alcohol to give 5.5 g (95%) of colorless crystals with mp 114-115°C (from aqueous alcohol). IR spectrum: 3410 (N—H) and 1605 cm^{-1} (C—C$_{arom}$). Found: C 79.0; H 6.7; N 14.6%. $C_{19}H_{19}N_3$. Calculated: C 78.9; H 6.6; N 14.5%.

1-Phenyl-2-(p-dimethylaminophenyl)-2,3-dihydroperimidine (IVc, Table 1). A mixture of 2.3 g (0.01 mole) of amine II, 1.5 g (0.01 mole) of p-dimethylaminobenzaldehyde, 60 ml of alcohol, and two drops of acetic acid was refluxed for 1 h, during which colorless crystals of dihydroperimidine IVc gradually precipitated. The mixture was cooled, and the precipitate was removed by filtration and washed with alcohol.

1,3-Dimethyl-2-phenyl-2,3-dihydroperimidine (VII). A mixture of 1.86 g (0.01 mole) of 1,8-bis(methylamino)naphthalene (VI), 1.06 g (0.01 mole) of benzaldehyde, and 50 ml of alcohol was refluxed for 1 h, and the resulting solution was diluted to twice its original volume with water. The mixture was cooled, and the precipitated crystals were removed by filtration and washed with alcohol to give light-yellow plates with mp 171-172°C (from alcohol) (mp 176-177°C [4]). The UV and IR spectra of the product were identical to the spectrum of an authentic sample.

1-Phenyl-2-propylperimidine (Va, Table 1). A mixture of 2.9 g (0.01 mole) of dihydroperimidine IVa, 0.35 g (0.11 g-atom) of sulfur, and 100 ml of xylene was refluxed for 30 h, after which the xylene was removed by vacuum distillation, and the residue was dissolved in chloroform and passed through a column filled with aluminum oxide. Elution initially with benzene gave a fraction containing sulfur and dihydroperimidine IVa, and product Va was subsequently eluted with chloroform. The chloroform was removed by distillation, and the residue was crystallized from aqueous alcohol. Compounds Vb-d were similarly obtained (Table 1).

1-Dimethylamino-8-acetamidonaphthalene (IX). A mixture of 1.86 g (0.01 mole) of VIII and 5.1 g (0.05 mole) of acetic anhydride was maintained at room temperature for 30 min, 50 ml of water was added to the resulting solution, and the mixture was heated until the acetic anhydride decomposed completely. The solution was cooled, and acetyl derivative IX was extracted with ether. The ether extract was washed twice with water and dried with sodium sulfate. The ether was removed by distillation, and the residue was crystallized from aqueous alcohol to give 1.98 g (95%) of colorless crystals with mp 93-94°C. IR spectrum: 2650-3250 (N—H) and 1680 cm^{-1} (C=O). UV spectrum (in methanol), λ_{max} (log ε): 210 (4.25), 234 (4.63), and 320 nm (4.03). Found: C 73.6; H 7.1; N 12.4%. $C_{14}H_{14}N_2O$. Calculated: C 73.7; H 7.1; N 12.3%.

1,2-Dimethylperimidine (X). A) A mixture of 2.3 g (0.01 mole) of IX and 10.2 g (0.1 mole) of acetic anhydride was refluxed for 10 h, the resulting solution was diluted to twice its original volume with water, and the mixture was heated until the acetic anhydride decomposed completely. The mixture was then neutralized with ammonium hydroxide, and the precipitated crystals of perimidine X were removed by filtration and washed with water. The yield was 1.4 g (70%).

B) A 10.2-g (0.01 mole) sample of acetic anhydride was added to 1.7 g (0.01 mole) of amine III, and the mixture was allowed to stand for 30 min (the mixture began to boil as the reaction commenced). At the end of this period the mixture was diluted to twice its original volume with water, and the aqueous mixture was heated until the acetic anhydride decomposed completely. It was then neutralized with ammonium hydroxide, and the precipitated crystals of 1,2-dimethylperimidine were removed by filtration and washed with water to give 1.9 g (100%) of light-yellow needles with mp 130-131°C (from heptane) [11].

Reaction of 1-Methylamino-8-aminonaphthalene (III) with Benzaldehyde. A mixture of 3.44 g (0.02 mole) of diamine III, 2.1 g (0.02 mole) of benzaldehyde, 50 ml of butanol, and two to three drops of acetic acid was refluxed for 8 h, after which the resulting solution was diluted to twice its volume with 50% alcohol, and the precipitated crystals of compound A were removed by filtration and washed with aqueous alcohol to give 4.4 g (85%) of creamy crystals with mp 230-232°C (from cyclohexane). IR spectrum: 3420 (N—H) and 1603 cm^{-1} ($C—C_{arom}$). UV spectrum (in cyclohexane), λ_{max} (log ε): 240 (5.14) and 360 nm (4.75). PMR spectrum (in CCl_4): 2.42 (3H, s), 4.05 (1H, s), 4.80 (2H, s), and 6.40 ppm (12H, m). Found: C 82.9; H 6.2; N 10.8%; M 1051. $C_{72}H_{64}N_8$. Calculated: C 83.0; H 6.2; N 10.8%; M 1041.

Reaction of 1-Dimethylamino-8-aminonaphthalene (VIII) with Benzaldehyde. The reaction of VIII with benzaldehyde in the presence of catalytic amounts of acetic acid was carried out as in the preceding experiment. The yield of light-yellow crystals of compound B, with mp 225-227°C (from ethyl acetate—alcohol), was 85%. IR spectrum: 3450 and 3250 (N—H); 1595 cm^{-1} ($C—C_{arom}$). UV spectrum (in cyclohexane), λ_{max} (log ε): 250 (5.07) and 360 nm (4.58). PMR spectrum (in $CDCl_3$): 2.55 (6H, s), 6.00 (2H, m), and 7.00 ppm (10H, m). Found: C 83.2; H 6.6; N 10.2%; M 1100. $C_{76}H_{72}N_8$. Calculated: C 83.2; H 6.6; N 10.2%; M 1097.

LITERATURE CITED

1. V. V. Kuz'menko and A. F. Pozharskii, Khim. Geterotsikl. Soedin., No. 10, 1406 (1978).
2. V. Paragamian, M. B. Baker, B. M. Puma, and J. I. Reale, J. Heterocycl. Chem., 5, 591 (1968).
3. V. I. Sokolov, A. F. Pozharskii, I. S. Kashparov, A. G. Ivanov, and B. I. Ardashev, Khim. Geterotsikl. Soedin., No. 4, 558 (1974).
4. A. F. Pozharskii, L. P. Smirnova, B. A. Tertov, I. S. Kashparov, and V. I. Sokolov, Khim. Geterotsikl. Soedin., No. 12, 1682 (1975).
5. H. Vinot, Compt. Rend., 252, 899 (1961).
6. A. F. Pozharskii, N. M. Starshikov, F. T. Pozharskii, and Yu. I. Mandrykin, Khim. Geterotsikl. Soedin., No. 7, 980 (1977).
7. N. M. Starshikov, A. F. Pozharskii, and F. T. Pozharskii, Khim. Geterotsikl. Soedin., No. 7, 986 (1977).
8. A. V. Lizobub and A. F. Pozharskii, Khim. Geterotsikl. Soedin., No. 12 (1978, in press).
9. A. V. El'tsov and Kh. A. Muravich-Aleksandr, Zh. Org. Khim., 1, 1307 (1965).
10. F. Pinnow and G. Pistor, Ber., 27, 602 (1894).
11. V. I. Sokolov, B. I. Ardashev, I. S. Kashparov, and A. F. Pozharskii, Khim. Geterotsikl. Soedin., No. 6, 849 (1973).