HETEROCYCLIC ANALOGS OF PLEIADIENE.

XL.* REACTION OF 1,8-NAPHTHALENEDIAMINE AND ITS N-PHENYL DERIVATIVE WITH THE SIMPLEST ALIPHATIC ALDEHYDES

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The reaction of 1,8-naphthalenediamine and its N-phenyl derivative with the simplest aldehydes of the aliphatic series under mild conditions was studied. The corresponding 2,3-dihydroperimidines, which were dehydrogenated with sulfur in refluxing xylene to the corresponding perimidines, were obtained.

We have previously reported that 1,8-naphthalenediamine (I) reacts readily with aromatic, heteroaromatic, and aliphatic aldehydes to give 2-substituted 2,3-dihydroperimidines [2, 3]. However, we observed resinification during an attempt to accomplish this reaction with formaldehyde and acetaldehyde [2]. We assumed that resinification is a result of heating, which, as we demonstrated for aromatic aldehydes [3], is unnecessary. The present research was also undertaken to study the reaction between diamine I and its N-phenyl derivative (II) and the simplest aldehydes of the aliphatic series under mild conditions. In addition to formaldehyde and acetaldehyde, we selected chloral and glyoxal as the aldehydes for the study.

An oily product consisting of a mixture of 2,3-dihydroperimidine (IIIa) and 2,3,2',3'tetrahydro-1,1'-diperimidinylmethane (IV) is liberated when equimolecular amounts of a solution of diamine I in alcohol and 10% aqueous formaldehyde solution are mixed. The reaction can be directed completely to favor the formation of bis derivative IV if 1.5 mole of the 10% aqueous formaldehyde solution per mole of diamine I is used. We were able to obtain IIIa in pure form by heating equimolar amounts of diamine I and paraformaldehyde in alcohol. The structures of IIIa and IV are confirmed unambigously by their PMR spectra (see the experimental section). In addition, IV can be obtained by the action of 0.5 equivalent of 10% aqueous formaldehyde solution on 2,3-dihydroperimidine:



The reaction of 1-anilino-8-aminonaphthalene (II) with 10% aqueous formaldehyde solution in alcohol proceeds slowly in the cold and requires brief refluxing for completion. The reaction product in this case is 1-phenyl-2,3-dihydroperimidine (IIIb); a dimer similar to IV is not formed in this case even in the reaction of IIIb with formalin.

The reaction of diamines I and II with acetaldehyde or chloral at room temperature in benzene or alcohol proceeds very readily. The yields of dihydro derivatives IIIc-e are close to quantitative after 2 h. The structures of the compounds obtained are confirmed by the PMR and IR spectroscopic data. The IR spectra of mineral oil suspensions of IIIa, c, e contain the characteristic doublet in the region of stretching vibrations of N-H bonds that is present in the spectra of all 2,3-dihydroperimidines that do not contain N-substituents [4]. In solution this doublet is converted to a vHN single peak at 3410 cm⁻¹.

*See [1] for communication XXXIX.

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After completion of our research we became aware of a paper by Cameron and Sammel [5], who also synthesized 2-methyl-2,3-dihydroperimidine by heating diamine I with acetaldehyde in methanol [5]. However, the compound that they obtained was an oil, whereas according to our data the product is a crystalline substance with mp 72°C. These results confirm our conclusion that it is undesirable to heat diamine I with aliphatic aldehydes, which evidently leads to the formation of impurities.



I R=H; II R=C₆H₅; V a R=R'=H; III, V b R=C₆H₅, R'=H; c R=H, R'=CH₃; III d R=H, R'=CCI₃; e R=C₆H₅, R'=CH₃; V d R=C₆H₅, R'=CH₃

The reaction of diamines I and II with glyoxal also takes place at room temperature, but the product is obtained in a purer state if the bisulfite derivative of glyoxal is used in place of glyoxal. However, in the latter case the process takes place only when the reagents are refluxed in alcohol. Tetrahydro-2,2'-diperimidinyl derivatives (VI) are formed in 70-80% yields as a result of this reaction. This distinguishes 1,8-naphthalenediamines sharply from o-phenylenediamine [6] and 1,2-naphthalenediamine [7], which reacts with glyoxal to give, respectively, quinoxaline and 5,6-benzoquinoxaline. The structure of VIa is confirmed by, in addition to the PMR and IR spectra, its conversion (in 75% yield) to the previously described 2,2'-diperimidiny1 (VII) [8] by heating with sulfur in refluxing xylene. Compound VIb underwent quantitative conversion to 1-phenylperimidine (Vb) during an attempt to aromatize it under the same conditions, i.e., the C-C bond underwent cleavage with subsequent dehydrogenation. We have also noted this sort of lability of C-C bonds for other 2,3-dihydroperimidines containing π -surplus substituents in the 2 position [3]. The conversion of VIb to 1-phenylperimidine is observed when a chloroform solution of this compound is allowed to stand. Compound VIa is similarly converted to perimidine when a solution in chloroform is heated.



VI a R = H; $b R = C_6 H_5$

We were also unable to aromatize dihydro derivatives IIId and IV. Compound IIId is itself unstable, and undergoes resinification when it is heated. Only perimidine was isolated when IV was heated with sulfur. On the other hand, dihydro derivatives IIIa-c, e are readily dehydrogenated by sulfur to give the corresponding perimidines V.

Thus our study showed that 1,8-naphthalenediamines react readily under the proper conditions not only with aromatic aldehydes but also with aliphatic aldehydes. This opens up a pathway to the synthesis of new derivatives of 2,3-dihydroperimidine and perimidine.

EXPERIMENTAL

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

<u>2,3-Dihydroperimidine (IIIa)</u>. A mixture of 15.8 g (0.1 mole) of diamine I and 3 g (0.1 mole) of paraformaldehyde in 300 ml of alcohol was refluxed for 3 h, and the resulting solution was cooled, diluted to twice its original volume with water, and filtered. The filtrate was diluted with water (1:1) and stored in a refrigerator for 10-15 h. The precipitated crystals of dihydroperimidine IIIa were removed by filtration and washed with 10% alcohol to give 13.6 g (80%) of colorless crystals with mp 77°C (from aqueous alcohol). IR spectrum: 3360-3375 (N-H) and 1600 cm⁻¹ (C-Carom). UV spectrum, λ_{max} (log ε): 213 (4.46), 236 (4.32), and 347 nm (3.70). PMR spectrum (in deuteroacetone): 4.15 (2H, s, CH₂), 5.38 (s, NH), 6.25 (2H, q, 4- and 9-H), 6.80 ppm (4H, m, 5-H-8-H). Found: C 77.7; H 5.9; N 16.3%. C₁₁H₁₀N₂. Calculated: C 77.6; H 5.9; N 16.5%.

<u>2-Methyl-2,3-dihydroperimidine (IIIc)</u>. A 0.44-g (0.01 mole) sample of acetaldehyde was added to a solution of 1.6 g (0.01 mole) of diamine I in 20 ml of benzene, and the mixture was stirred at room temperature for 2 h. The benzene was removed by evaporation, and the residue was dissolved in chloroform and passed through a column filled with aluminum oxide (elution with chloroform). The first fraction was collected and worked up to give 1.6 g (90%) of colorless crystals with mp 72°C (from aqueous dioxane). IR spectrum: 3320-3360 (N-H) and 1600 cm⁻¹ (C-Carom). PMR spectrum (in CDCl₃): 1.27 (3H, d, J = 5.9 Hz, CH₃), 4.05 (s, NH), 4.45 (1H, q, 2-H), 6.35 (2H, q, 4- and 9-H), and 7.02 ppm (4H, m, 5-H-8-H). Found: C 78.1; H 6.4; N 15.4%. C₁₂H₁₂N₂. Calculated: C 78.2; H 6.6; N 15.2%.

<u>2-Trichloromethyl-2,3-dihydroperimidine (IIId)</u>. A solution of 15.8 g (0.1 mole) of diamine I and 14.7 g (0.1 mole) of trichloroacetaldehyde in 100 ml of benzene was main-tained at room temperature for 2 h, and the precipitated dihydroperimidine IIId was removed by filtration and washed with benzene to give 28 g (97%) of colorless crystals with mp 86°C (dec., from benzene). IR spectrum: 3290-3360 (N-H) and 1610 cm⁻¹ (C-C_{arom}). Found: C 50.0; H 3.1; Cl 37.0; N 10.0%. $C_{12}H_9Cl_3N_2$. Calculated: C 50.1; H 3.1; Cl 37.0; N 9.7%.

This reaction was also successful in alcohol, but isolation of the resulting dihydroperimidine IIId was difficult, since it is extremely soluble in alcohol and very unstable with respect to heat.

<u>1-Pheny1-2-methy1-2,3-dihydroperimidine (IIIe)</u>. A 0.48-g (0.011 mole) sample of acetaldehyde was added to a solution of 2.3 g (0.01 mole) of diamine II in 30 ml of benzene, and the mixture was maintained at room temperature for 1 h. The benzene was then removed by evaporation, and the residue was dried in vacuo at 50°C to give 2.5 g (95%) of colorless chromatographically pure liquid dihydroperimidine IIIe. IR spectrum (in CHCl₃): 3410 (N-H) and 1595 cm⁻¹ (C-C_{arom}). Found: C 83.2; H 6.2; N 10.8%. C₁₈H₁₆N₂. Calculated: C 83.0; H 6.2; N 10.8%.

<u>1-Pheny1-2, 3-dihydroperimidine (IIIb)</u>. A mixture of 2.3 g (0.01 mole) of diamine II, 3 ml (0.01 mole) of 10% aqueous formaldehyde solution, and 80 ml of alcohol was refluxed for 1 h, and the resulting solution was cooled and diluted to twice its original volume with water. The precipitated crystals of dihydroperimidine IIIb were removed by filtration and washed with 50% alcohol to give 2.3 g (96%) of colorless crystals with mp 101°C (from aqueous alcohol). IR spectrum (in CHCl₃): 3410 (N-H) and 1600 cm⁻¹ (C-Carom). UV spectrum, λ_{max} (log ε): 208 (4.52), 240 (4.55), 365 nm (4.12). Found: C 82.8; H 5.8; N 11.5%. C₁₇H₁₄N₂. Calculated: C 82.9; H 5.7; N 11.5%.

<u>Bis(2, 3-dihydro-1-perimidiny1)methane (IV)</u>. A) A total of 45 ml (0.15 mole) of a 10% aqueous solution of formaldehyde was added to a solution of 15.8 g (0.1 mole) of diamine I in 100 ml of alcohol, and the mixture was maintained at room temperature for 2 h. The precipitated crystals of dihydroperimidine IV were removed by filtration and washed with alcohol. The yield was 21 g (60%).

B) A 1.5-m1 (0.005 mole) sample of a 10% aqueous solution of formaldehyde was added to a solution of 1.7 g (0.01 mole) of dihydroperimidine IIIa in 50 ml of alcohol, and the mixture was maintained at room temperature for 2 h. The precipitated crystals of dihydroperimidine IV were removed by filtration and washed with alcohol to give 3.3 g (95%) of colorless crystals with mp 260-262°C (from propanol). IR spectrum: 3375 (N-H) and 1600 cm⁻¹ (C-C_{arom}). PMR spectrum (in deuteroacetone): 3.88 (2H, s, NCH₂N), 4.15 (4H, s, 2- and 2'-H) 5.40 (2H, s, NH), 6.28 (4H, m, 4-, 9-, and 9'-H), and 6.92 ppm (8H, m, 5-H-8-H, and 5'-H-8'-H). Found: C 78.4; H 5.6; N 16.1%. C_{2.3}H_{2.0}N₄. Calculated: C 78.4; H 5.7; N 15.9%.

<u>2,3,2',3'-Tetrahydro-2,2'-diperimidinyl (VIa)</u>. A mixture of 3.16 g (0.02 mole) of diamine I, 2.66 g (0.01 mole) of the bisulfite derivative of glyoxal, and 100 ml of 75% alcohol was refluxed for 1 h, and the resulting solution was cooled. The precipitated crystals of dihydroperimidine VIa were removed by filtration and washed on the filter with hot water (200 ml) to give 2.4 g (70%) of colorless crystals with mp 190-191°C (from alcohol). IR spectrum: 3350 (N-H) and 1610 cm⁻¹ (C-Carom). PMR spectrum (in deuteroacetone): 4.52 (2H, s, 2- and 2'-H), 5.80 (2H, s, NH; this band vanishes after deuteration), 6.45 (4H, q, 4-, 9-, 4'-, and 9'-H), and 6.95 ppm (8H, m, 5-H-8-H, 5'-H-8'-H). Found: C 78.2; H 5.4; N 16.7%. C₂₂H₁₈N₄. Calculated: C 78.1; H 5.4; N 16.5%.

<u>1,1-Diphenyl-2,3,2',3'-tetrahydro-2,2'-diperimidinyl (VIb)</u>. This compound was similarly obtained from diamine II and the bisulfite derivative of glyoxal. The colorless crystals had mp 199-201°C (from benzene). IR spectrum: 3390 (N-H) and 1600 cm⁻¹ (C-C_{arom}). Found: C 83.1; H 5.4; N 11.6%. C₃₄H₂₆N₄. Calculated: C 83.2; H 5.4; N 11.4%.

<u>1-Pheny1-2-methylperimidine (Vd)</u>. A mixture of 2.6 g (0.01 mole) of dihydroperimidine IIIe, 0.35 g (0.011 mole) 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 with chloroform) to give 2.1 g (85%) of light-yellow crystals with mp 164-165°C. IR spectrum (in CC14): 1635 (C=N) and 1590 cm⁻¹ (C-C_{arom}). UV spectrum, λ_{max} (log ε): 207 (4.62), 238 (4.45), 340 (4.17), 400 nm (2.98). Found: C 83.6; H 5.4; N 11.0%. C₁₈H₁₄N₂. Calculated: C 83.7; H 5.5; N 10.8%. Compounds Va-c were similarly obtained.

2,2'-Diperimidinyl (VII). A mixture of 3.4 g (0.01 mole) of dihydroperimidine VIa, 0.32 g (0.01 mole) of sulfur, and 100 ml of xylene was refluxed for 10 h, and the resulting solution was cooled. The precipitated crystals of perimidine were removed by filtration and washed with hot acetone to give 2.5 g (75%) of dark-red crystals with mp 330°C (dec., from pyridine) [8].

<u>Perimidine (Va)</u>. A solution of 3.4 g (0.01 mole) of dihydroperimidine VIa in 100 ml of chloroform was refluxed for 30 min, after which the chloroform was removed by evaporation, and the residue was crystallized from alcohol. The yield was 3.3 g (100%). The melting point and IR spectrum were identical to those of a genuine sample.

<u>1-Phenylperimidine (Vb)</u>. A 2.45-g (0.005 mole) sample of dihydroperimidine VIb was dissolved in 30 ml of chloroform, and the solution was allowed to stand for 30 min. It was then passed through a column filled with aluminum oxide (elution with chloroform) to give 2.1 g (85%) of light-yellow crystals with mp 110°C (from alcohol) [9].

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