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UNUSUAL REACTION OF 1*H*-PERIMIDINES WITH SODIUM AZIDE AND BENZOYL HYDRAZINE IN POLYPHOSPHORIC ACID

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Azapyrenes are used as organic luminophores and dyes, and they include compounds with high cytostatic and analgesic activity [1-3]. None the less there are a limited number of methods for the synthesis of such compounds, particularly those with functional groups. In this work, we propose a one-pot method for preparing the 10-amino-1,2,6,8-tetraazapyrenes **8a-c**, based on our recently discovered method for the amination of perimidines with sodium azide in polyphosphoric acid (PPA) [4, 5].

It was found that a reaction of perimidines **1a-c** with NaN_3 in PPA at 70-80ºC, and further with benzoyl hydrazine in the ratio 1:3:1 at 125-135ºC gave the previously unknown 10-amino-1,2,6,8-tetraazapyrenes **8a-c** in 34-41% yields.

The reaction scheme, as reported in the studies [4, 5], includes the formation of the intermediates **2a-c** which are acylated by benzoyl hydrazine to give compounds **3a-c** (found in equilibrium with **4a-c**). Through an intramolecular nucleophilic substitution the latter are converted to the 1,6-dihydro-1,2,6,8-tetraazapyrenes **5a-c**. These compounds are aminated by a scheme similar to that proposed for the amination of perimidines. After hydrolysis and, likely, oxidation of the dihydro derivatives **7a-c** by atmospheric oxygen, they are converted to the amines **8a-c**.

IR spectra were recorded on a UR-20 instrument using KBr pellets. ^{1}H NMR spectra were recorded on a Bruker WP-200 instrument (200 MHz) using DMSO-d_6 with TMS as internal standard. Elemental analysis was carried out on a KOVO CHN-1 CHN analyzer. Melting points were determined on a PTP-M apparatus (Khimlaborpribor). Monitoring of the reaction course and the purity of the synthesized compounds was carried out on Silufol UV-254 plates with EtOAc–EtOH (1:1) as eluent. PPA with an 86% content of P_2O_5 was prepared by the method [6].

10-Amino-3-phenyl-1,2,6,8-tetraazapyrenes 8a-c (General Method). A mixture of perimidine **1a-c** (1 mmol) and NaN_3 (0.13 g, 2 mmol) in 86% PPA (2-3 g) was heated at 70-80ºC for 2 h with vigorous stirring. An additional portion of sodium azide (0.065 g, 1 mmol) was added and heating was continued for another 2 h. Benzoyl hydrazine (0.136 g, 1 mmol) was then added, the reaction mixture temperature was raised to 125-135ºC,

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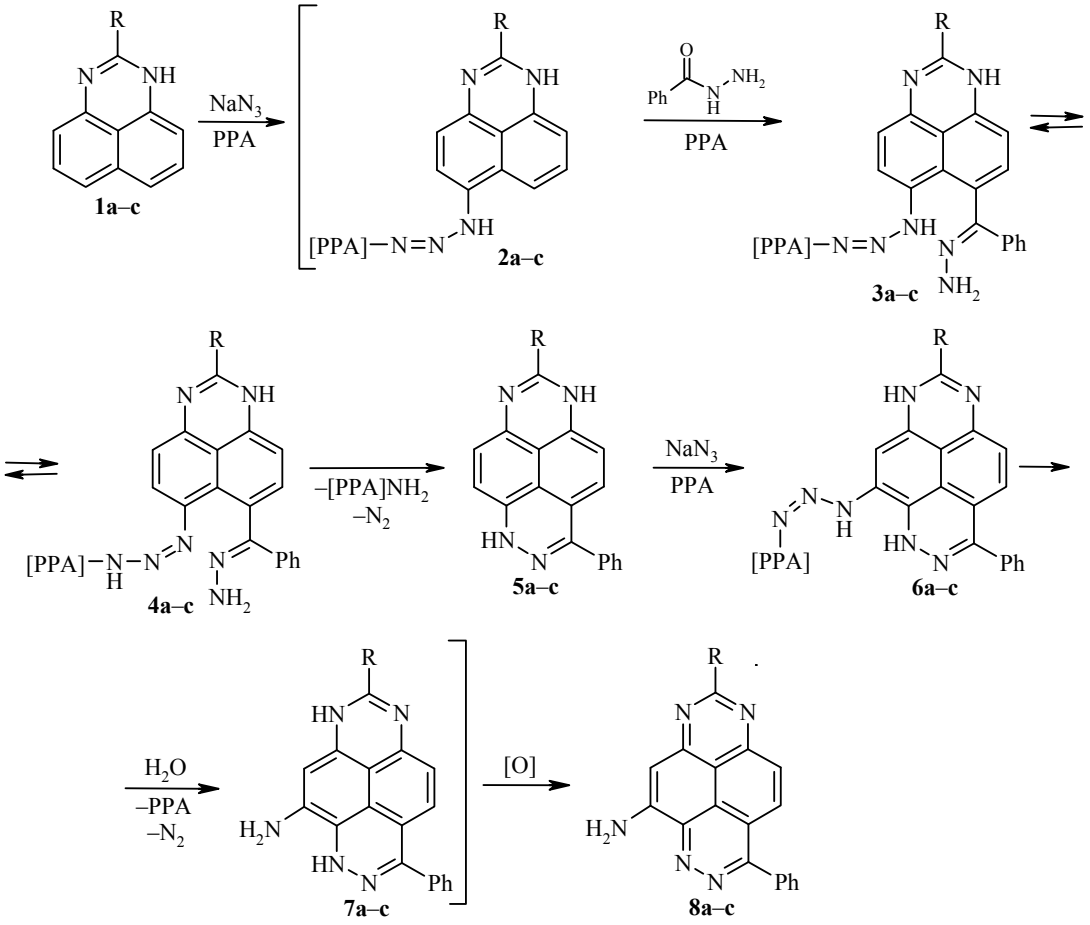
and heating was continued for 5 h. The reaction mixture was cooled, poured into water (50 ml), neutralized with ammonia solution, and extracted with BuOH (5×50 ml). The butanol was evaporated, and the residue was separated by flash chromatography. The obtained compounds **8a-c** were recrystallized from EtOAc.



a R = H, **b** R = Me, **c** R = Ph

10-Amino-3-phenyl-1,2,6,8-tetraazapyrene (8a). Yield 0.119 g (40%); mp 194-195ºC. R_f 0.6 (EtOAc–EtOH, 1:1). IR spectrum, ν, cm^{-1}: 3420 (NH_2). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.30 (2H, br. s, NH_2); 7.51 (1H, s, H-9); 7.65-7.72 (3H, m, H-3,4,5 Ph); 7.91 (2H, d, *J* = 7.5, H-2,6 Ph); 8.39 (1H, d, *J* = 9.4, H-4); 8.83 (1H, d, *J* = 9.4, H-5); 9.93 (1H, s, H-7). Found, %: C 72.88; H 3.68; N 23.44. $C_{18}H_{11}N_5$. Calculated, %: C 72.72; H 3.73; N 23.55.

10-Amino-7-methyl-3-phenyl-1,2,6,8-tetraazapyrene (8b). Yield 0.127 g (41%); mp 182-183ºC. R_f 0.6 (EtOAc–EtOH, 1:1). IR spectrum, ν, cm^{-1}: 3407 (NH_2). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.11 (3H, s, CH_3); 7.36 (2H, br. s, NH_2); 7.51 (1H, s, H-9); 7.65-7.71 (3H, m, H-3,4,5 Ph); 7.93 (2H, d, *J* = 7.6, H-2,6 Ph); 8.42 (1H, d, *J* = 9.4, H-4); 8.83 (1H, d, *J* = 9.4, H-5). Found, %: C 73.42; H 4.19; N 22.41. $C_{19}H_{13}N_5$. Calculated, %: C 73.30; H 4.21; N 22.49.

10-Amino-3,7-diphenyl-1,2,6,8-tetraazapyrene (8c). Yield 0.127 g (34%); mp 215-216ºC. R_f 0.42 (EtOAc). IR spectrum, ν, cm^{-1}: 3436 (NH_2). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.45 (2H, br. s, NH_2); 7.52 (1H, s, H-9); 7.60-7.70 (6H, m, H-3,4,5 (3,7-Ph)); 7.93 (2H, d, *J* = 7.6, H-2,6 (3-Ph)); 8.46 (1H, d, *J* = 9.4, H-4); 8.84 (1H, d, *J* = 9.4, H-5); 8.95 (2H, d, *J* = 8.2, H-2,6 (7-Ph)). Found, %: C 77.32; H 3.98; N 18.70. $C_{24}H_{15}N_5$. Calculated, %: C 77.20; H 4.05; N 18.75.

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