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REACTION OF 6(7)-ACYL- AND 6(7)-FORMYLPERIMIDINES WITH 1,3,5-TRIAZINES IN POLY-PHOSPHORIC ACID

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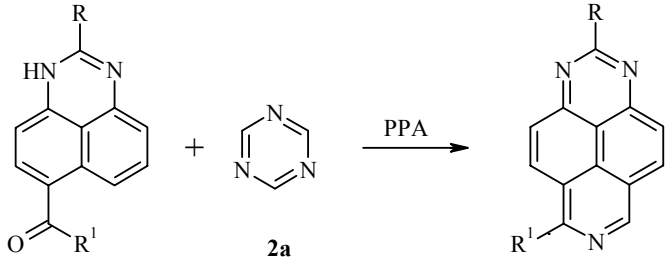
A method has been developed for the synthesis of 1,3,7-triazapyrenes using the reaction of 6(7)-formyl- and 6(7)-benzoylperimidines with 1,3,5-triazines in PPA. Under these conditions, 6(7)-formylperimidine reacts with 2,4,6-trimethyl-1,3,5-triazine to give 6-hydroxy-1,3-diazapyrene.

Keywords: 6(7)-acylperimidines, 6-hydroxy-1,3-diazapyrene, perimidine, PPA, 1,3,7-triazapyrenes, 1,3,5-triazines, 6(7)-formylperimidine, cyclization.

We have already shown that the 1,3,5-triazine–PPA* system is useful for the acylation and formylation of perimidines [2] and the synthesis of 1,2,3,7-tetraazapyrenes from 1H-naphtho[1,8-*de*][1,2,3]triazine (1,2,3-triazaphenalene) [3]. The present study is a continuation of our investigation of the synthetic scope of this system. The reaction of this system with 6(7)-acylperimidines **1a-c** and **1e** and 6(7)-formylperimidine (**1d**) was studied in present work.

Since perimidines [2] and 1,2,3-triazaphenalene [3] undergo, in effect, double electrophilic attack by the system of 1,3,5-triazines **2** in PPA, we might have assumed that perimidines **1** would react analogously. Indeed, 1,3,7-triazapyrenes **3a-d** were obtained in 50-65% yield upon heating **1a-d** with 1,3,5-triazine (**2a**) in PPA.



1, 3 a R = H, R^1 = Ph, **b** R = Me, R^1 = Ph, **c** R = R^1 = Ph,
d R = R^1 = H, **e** R = H, R^1 = Me

* PPA with 86% P_2O_5 prepared according to Uhlig [1] was used.

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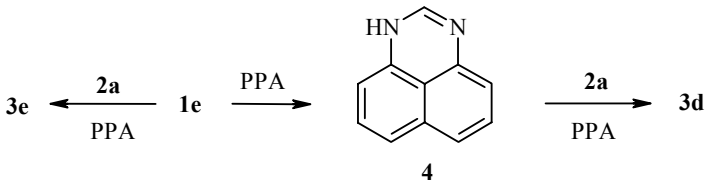
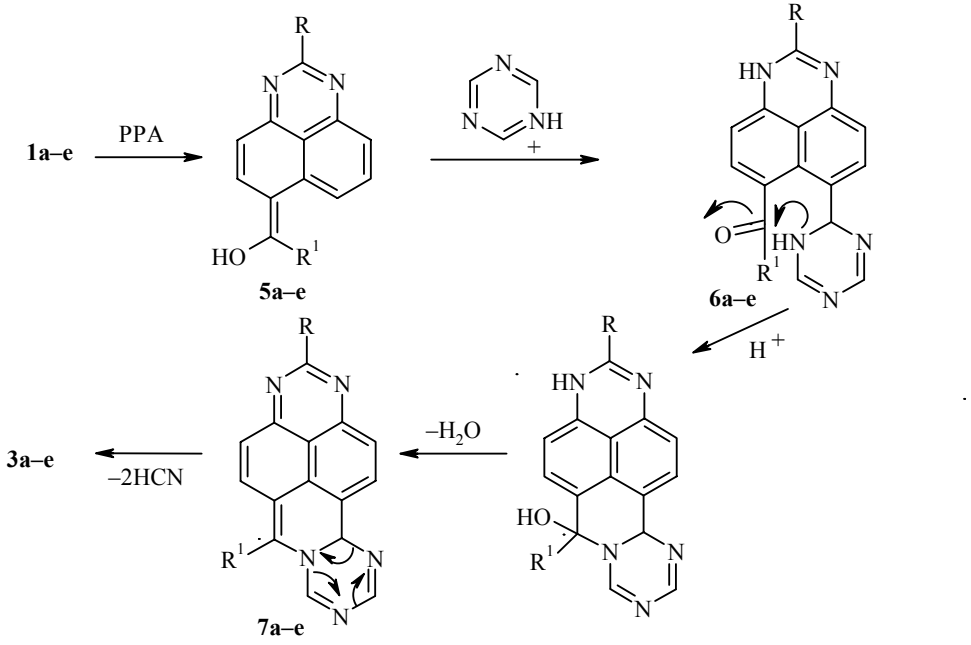
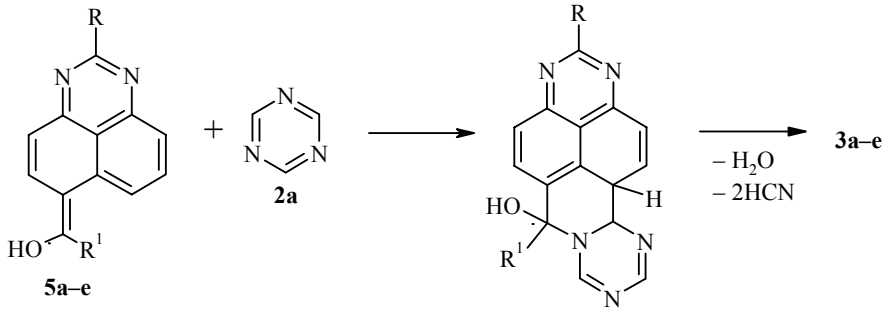
The reaction with **1e** gave a 1:1 mixture of triazapyrenes **3e**,**d** in 61% total yield as indicated by ^{1}H NMR spectroscopy. We were unable to separate the products in light of their similar chromatographic mobility. The formation of compound **3d** may be attributed to the competing deacetylation of acylperimidine **1e** [4] and subsequent reaction of perimidine **4** with triazine **2a**.



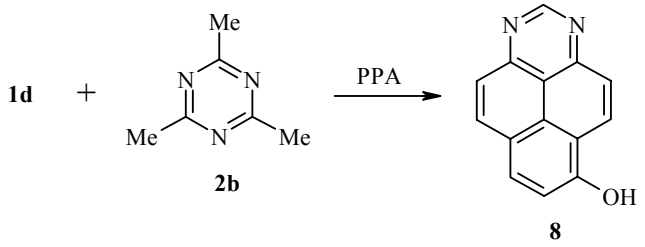
The proposed mechanism for the formation of 1,3,7-triazapyrenes **3** is given in the scheme below. Initial protonation (or phosphorylation) of the carbonyl group oxygen atom in compound **1** gives quinoid structure **5** containing a dienol fragment. This facilitates electrophilic attack of the 1,3,5-triazinium cation at the free *peri* position to give **6**. Subsequent nucleophilic addition at the carbonyl group and dehydration lead to intermediate **7**, which undergoes the cycloelimination of HCN to give triazapyrenes **3**.



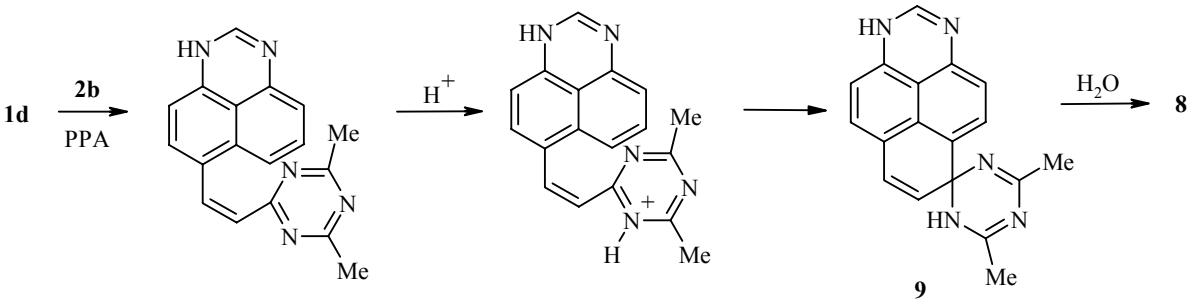
We cannot completely exclude an alternative Diels-Alder reaction mechanism, in which the 1,3,5-triazine acts as a dienophile relative to the diene fragment in the structure **5** and during which the loss of aromaticity in one ring is compensated by the restoration of aromaticity in another ring.



The reaction of the aldehyde **1d** with 2,4,6-trimethyl-1,3,5-triazine (**2b**) unexpectedly led to 6-hydroxy-1,3-diazapyrene (**8**) instead of the corresponding triazapyrene. Diazapyrene **8** was previously obtained by another route [5].



This reaction likely involves the crotonic condensation of trimethyltriazine **2b** with aldehyde **1d** and subsequent intramolecular acylation. The spiro compound **9** formed after hydrolysis and proton transfer converts to hydroxydiazapyrene **8**.



EXPERIMENTAL

The ^{1}H NMR spectra were taken on a Bruker WP-200 spectrometer at 200 MHz with TMS as the internal standard. The mass spectra were taken on a MAT-311A spectrometer. The course of the reactions and purity of the products were monitored by thin-layer chromatography on Silufol UV-254 plates with ethyl acetate as the eluent.

1,3,7-Triazapyrenes 3a-e (General Method). A mixture of corresponding acylperimidine **1** (1 mmol), 1,3,5-triazine (0.12 g, 1.5 mmol), and PPA (4 g) was stirred for 3 h at 100°C (in the preparation of compound **3e**, the reaction was carried out for 2 h at 125°C). The reaction mixture was poured into 30 ml water and brought to pH ~7-8 by adding ammonium hydroxide. The precipitate was filtered off. In the case of compound **3e**, the reaction mixture after being made alkaline was extracted with three 30-ml ethyl acetate portions. The solvent was almost entirely evaporated and the crystals precipitated were filtered off.

6-Phenyl-1,3,7-triazapyrene (3a) was obtained in 60% yield (0.168 mg) as light-yellow crystals; mp 174-176°C (nonane). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 7.68 (3H, m, 3,4,5-C_6H_5); 7.91 (2H, br. d, J = 8.0, 2,6-C_6H_5); 8.29 (1H, d, $J_{9,10}$ = 9.5, H-10); 8.33 (1H, d, $J_{4,5}$ = 9.1, H-4); 8.75 (1H, d, $J_{9,10}$ = 9.5, H-9); 8.91 (1H, d, $J_{4,5}$ = 9.1, H-5); 9.86 (1H, s, H-8); 9.89 (1H, s, H-2). Mass spectrum (EI, 70 eV), *m/z* (I_{rel}, %): 281 $[M]^+$ (100). Found, %: C 81.27; H 3.87; N 14.86. $C_{19}H_{11}N_3$. Calculated, %: C 81.12; H 3.94; N 14.94.

2-Methyl-6-phenyl-1,3,7-triazapyrene (3b) was obtained in 47% yield (0.14 g) as light-orange crystals; mp 246-248°C (nonane). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 3.19 (3H, s, CH_3); 7.63 (3H,

m, 3,4,5-C_6H_5); 7.88 (2H, dd, J = 8.1, J = 1.3, 2,6-C_6H_5); 8.18 (1H, d, $J_{9,10}$ = 9.5, H-10); 8.24 (1H, d, $J_{4,5}$ = 9.2, H-4); 8.60 (1H, d, $J_{4,5}$ = 9.2, H-5); 8.76 (1H, d, $J_{9,10}$ = 9.5, H-9); 9.69 (1H, s, H-8). Found, %: C 81.44; H 4.38; N 14.18. $C_{20}H_{13}N_3$. Calculated, %: C 81.34; H 4.44; N 14.23.

2,6-Diphenyl-1,3,7-diazapyrene (3c) was obtained in 53% yield (0.189 mg) as yellow crystals; mp 197-199°C (nonane). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (J, Hz): 7.63 (6H, m, 3,4,5-(2)C_6H_5, 3,4,5-(6)C_6H_5); 7.90 (2H, dd, J = 8.1, J = 1.6, 2,6-(6)C_6H_5); 8.30 (1H, d, $J_{9,10}$ = 9.5, H-10); 8.35 (1H, d, $J_{4,5}$ = 9.2, H-4); 8.63 (1H, d, $J_{5,4}$ = 9.2, H-5); 8.76 (1H, d, $J_{9,10}$ = 9.5, H-9); 8.84 (2H, dd, J = 8.1, J = 1.6, 2,6-(2)C_6H_5); 9.68 (1H, s, H-8). Found, %: C 84.14; H 4.19; N 11.67. $C_{25}H_{15}N_3$. Calculated, %: C 84.01; H 4.23; N 11.76.

1,3,7-Triazapyrene (3d). The reaction starting with 6(7)-carbaldehyde (**1d**) gave 0.129 g (63%) **3d**. The reaction starting with 6(7)-acetylperimidine (**1e**) gave 30% **3d** as indicated by ^{1}H NMR spectroscopy. The product was obtained as yellow crystals, mp 240-242°C (octane, subl.) (mp 240-242°C [3]). The ^{1}H NMR spectrum for **3d** obtained was the same as the spectrum reported in our previous work [3].

6-Methyl-1,3,7-triazapyrene (3e) was obtained from a mixture with 1,3,7-triazapyrene (**3d**) in 30% yield as indicated by ^{1}H NMR spectroscopy. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (J, Hz): 3.25 (3H, s, CH_3); 8.16 (1H, d, $J_{4,5}$ = 9.1, H-5); 8.22 (1H, d, $J_{9,10}$ = 9.9, H-9); 8.75 (1H, d, $J_{4,5}$ = 9.1, H-4); 8.89 (1H, d, $J_{9,10}$ = 9.9, H-10); 9.61 (1H, s, H-8); 9.78 (1H, s, H-2).

6-Hydroxy-1,3-diazapyrene (8). A mixture of perimidine-6(7)-carbaldehyde (0.182 g, 1 mmol), 2,4,6-trimethyl-1,3,5-triazine (0.184 g, 1.5 mmol), and PPA (4 g) was stirred rapidly for 2 h at 130°C. The reaction mixture was poured into water (30 ml) and brought to pH ~7-8 by adding ammonium hydroxide. The precipitate was filtered off. The mother liquor was heated at reflux until ammonia had been completely evaporated. The crystals formed upon cooling were filtered off to give 0.105 g (47%) **8** as red-brown crystals, mp 303-305°C (ethanol) (mp 303-305°C [5]). A mixture with an authentic sample did not give a depressed melting point. The ^{1}H NMR spectrum was identical to the spectrum reported in previous work [5].

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