Synthesis of 1,3-diazapyrenes by the reaction of 1*H*-perimidines with 1,3-dicarbonyl compounds

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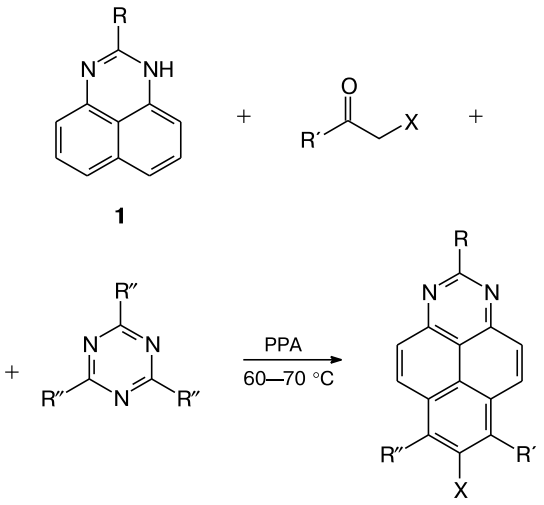
A method for the synthesis of 1,3-diazapyrenes has been developed based on the reaction of 1*H*-perimidines with 1,3-dicarbonyl compounds in polyphosphoric or 70% aq. sulfuric acid.

Key words: perimidines, 1,3-diazapyrene.

Azapyrenes belong to the class of multinuclear heteroaromatic compounds, which are of interest in both theoretical (aromaticity, mechanism of electrophilic and nucleophilic substitution, stability of radical ions, *etc.*), and applied aspects.[1] For example, intercalating properties of 4(9)- (see Refs 2 and 3) and 2,7-diazapyrene[4—6] derivatives are under active study, results on investigation of their biological activity are published[7—10] and their use in supramolecular chemistry is described.[11] No more than 20 azapyrene structures from almost 300 possible have been synthesized so far.[12] A few existing methods for the synthesis of 1,3-diazapyrenes[1,12,13] allow one to obtain them either without substituents at positions 6 and 8 or with an aryl substituent. The most efficient method is based on a three-component reaction of 1*H*-perimidines **1** with carbonyl compounds and 1,3,5-triazines in polyphosphoric acid (PPA) with 86% content of P_2O_5 (Scheme 1).[14] The use of expensive and, hence, poorly available 1,3,5-triazines is a disadvantage of this method.

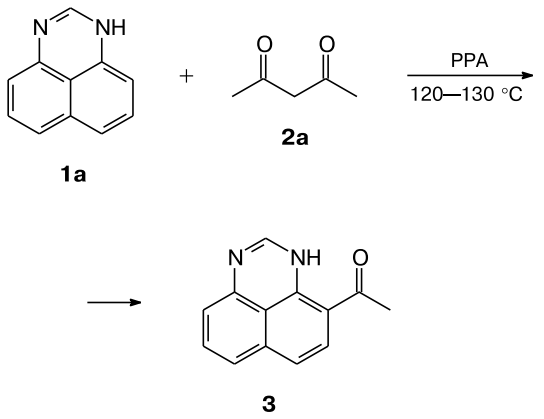
Scheme 1



In the present work, a simple and efficient method for the synthesis of 1,3-diazapyrenes based on the reaction of 1*H*-perimidines **1** with 1,3-dicarbonyl compounds is suggested.

Earlier,[13] it has been reported that the reaction of 1*H*-perimidines **1** with acetylacetone **2a** in PPA with 80% content of P_2O_5 begins only at temperatures higher 100 °C and leads to 4(9)-acetylperimidine (**3**) in 10% yield (Scheme 2). No formation of 1,3-diazapyrenes (**4**) was observed under these conditions.[13]

Scheme 2



Based on the reported results,[14] we suggested that such a result is due to the reaction conditions. In fact, a reduction of the temperature to 70—75 °C (PPA with 80% content of P_2O_5) allows one to obtain diazapyrene **4a** in 71% yield (Scheme 3). The yield of ketone **3** under these conditions was 11%.

Earlier,[15] it has been reported that, depending on the amount of P_2O_5 (80 or 86%) in PPA, the regioselectivity

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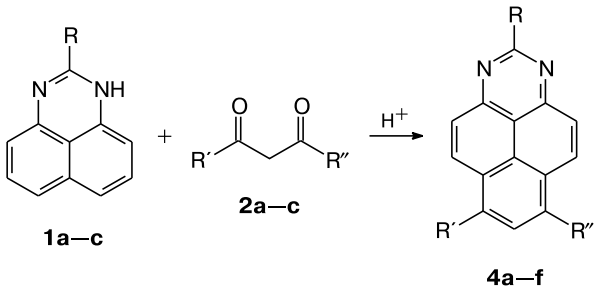
Scheme 3



Compound	R	R′	R″
1a	H	—	—
1b	Me	—	—
1c	Ph	—	—
2a	—	Me	Me
2b	—	Me	Ph
2c	—	Ph	Ph
4a	H	Me	Me
4b	H	Me	Ph
4c	H	Ph	Ph
4d	Me	Me	Me
4e	Me	Ph	Ph
4f	Ph	Ph	Ph

of the reaction of compound **1** with unsaturated carboxylic acids can change. Therefore, a change in regioselectivity of the reaction of compound **1** with 1,3-dicarbonyl compounds could have been also expected. It turned out that an increase in the content of P_2O_5 to 86% at the same temperature leads to a decrease in the content of diazapyrene **4a**. Its yield was 62%, the yield of ketone **3**, 26%.

To sum up, an increase in the concentration of P_2O_5 promotes cleavage of the diketone and side acylation of 1*H*-perimidines **1**. The running the reaction in 100% aq. orthophosphoric acid or more available 70% aqueous sulfuric acid allows one to completely avoid the formation of the acylation products and increase the yield of diazapyrene **4a** to 82%. This reaction can be applied to other 1,3-dicarbonyl compounds.

In conclusion, we developed a method for the synthesis of 1,3-diazapyrenes based on the reaction of 1*H*-perimidines with 1,3-dicarbonyl compounds.

Experimental

^{1}H NMR spectra were recorded on a Bruker WP-200 spectrometer (200 MHz) using Me_4Si as the internal standard and $CDCl_3$ as the solvent. Perimidine,[16] 2-phenylperimidine,[16] 2-methylperimidine,[16] PPA with 80% and 86% content of P_2O_5[17] were obtained according to the specified procedures.

Reaction in polyphosphoric acid (method *A*). A mixture of perimidine **1** (1 mmol), dicarbonyl compound **2** (2.5 mmol), and polyphosphoric acid (3—4 g) (with 80 or 86% content of P_2O_5) was heated for 3—4 h at 70—75 °C, then poured into some cold water, which was made basic with aq. ammonia to pH ~8. A precipitate formed was filtered off. The filtrate was additionally extracted with ethyl acetate, the solvent was evaporated. The product was recrystallized from ethyl acetate.

Reaction in sulfuric acid (method *B*). A mixture of perimidine **1** (1 mmol), dicarbonyl compound **2** (2.5 mmol), and 70% aq. sulfuric acid (10 mL) was heated for 3—4 h at 95—100 °C, then poured into some cold water, which was made basic with aq. ammonia to pH ~8. A precipitate formed was filtered off. The filtrate was additionally extracted with ethyl acetate, the solvent was evaporated. The product was recrystallized from ethyl acetate.

4(9)-Acetylperimidine (3). The yield was 0.023 g (11%) (80% P_2O_5), 0.054 g (26%) (86% P_2O_5) (method *A*, from perimidine and acetylacetone). M.p. 201—202 °C (ethyl acetate) (*cf.* Ref. 13: m.p. 201—202 °C). Found (%): C, 74.41; H, 4.73; N, 13.27. $C_{13}H_{10}N_2O$. Calculated (%): C, 74.27; H, 4.79; N, 13.32. ^{1}H NMR, δ: 2.56 (s, 3 H, CH_3CO); 6.99 (d, 1 H, H(7), J = 9.1 Hz); 7.11 (dd, 1 H, H(4), J = 7.6 Hz, J = 1.1 Hz); 7.26 (dd, 1 H, H(6), J = 8.1 Hz, J = 1.1 Hz); 7.44 (d, 1 H, H(8), J = 9.1 Hz); 7.51 (dd, 1 H, H(5), J = 7.6 Hz, J = 8.1 Hz); 7.68 (d, 1 H, H(2), J = 3.1 Hz); 12.60 (br.s, 1 H, NH...O=).

6,8-Dimethyl-1,3-diazapyrene (4a). The yield was 0.165 g (71%) (80% P_2O_5), 0.144 g (62%) (86% P_2O_5) (method *A*), 0.19 g (82%) (method *B*). M.p. 207—209 °C (ethyl acetate) (*cf.* Ref. 14: m.p. 207—209 °C). Found (%): C, 82.89; H, 5.15; N, 11.96. $C_{16}H_{12}N_2$. Calculated (%): C, 82.73; H, 5.21; N, 12.06. ^{1}H NMR is analogous to that given in Ref. 14.

6-Methyl-8-phenyl-1,3-diazapyrene (4b). The yield was 0.23 g (79%) (method *B*). M.p. 198—199 °C (ethyl acetate) (*cf.* Ref. 13: m.p. 198—199 °C). Found (%): C, 85.79; H, 4.72; N, 9.49. $C_{21}H_{14}N_2$. Calculated (%): C, 85.69; H, 4.79; N, 9.52. ^{1}H NMR is analogous to that given in Ref. 13.

6,8-Diphenyl-1,3-diazapyrene (4c). The yield was 0.21 g (59%) (method *A*, 80% P_2O_5), 0.29 g (82%) (method *B*). M.p. 175—176 °C (ethyl acetate) (*cf.* Ref. 13: m.p. 175—176 °C). Found (%): C, 87.81; H, 4.46; N, 7.73. $C_{26}H_{16}N_2$. Calculated (%): C, 87.62; H, 4.52; N, 7.86. ^{1}H NMR is analogous to that given in Ref. 13.

2,6,8-Trimethyl-1,3-diazapyrene (4d). The yield was 0.11 g (45%) (method *A*, 80% P_2O_5), 0.19 g (77%) (method *B*). M.p. 241—243 °C (ethyl acetate). Found (%): C, 83.07; H, 5.66; N, 11.27. $C_{17}H_{14}N_2$. Calculated (%): C, 82.90; H, 5.73; N, 11.37. ^{1}H NMR, δ: 2.96 (s, 3 H, Me(2)); 3.05 (s, 6 H, Me(6), Me(8)); 7.86 (s, 1 H, H(7)); 8.17 (d, 2 H, H(5), H(9), J = 9.5 Hz); 8.71 (d, 2 H, H(4), H(10), J = 9.5 Hz).

2-Methyl-6,8-diphenyl-1,3-diazapyrene (4e). The yield was 0.19 g (51%) (method *A*, 80% P_2O_5), 0.25 g (67%) (method *B*). M.p. 182—183 °C (ethyl acetate) (*cf.* Ref. 13: m.p. 182—183 °C). Found (%): C, 87.67; H, 5.09; N, 7.64. $C_{27}H_{18}N_2$. Calculated (%): C, 87.54; H, 4.90; N, 7.56. ^{1}H NMR is analogous to that given in Ref. 13.

2,6,8-Triphenyl-1,3-diazapyrene (4f). The yield was 0.23 g (53%) (method *A*, 80% P_2O_5), 0.31 g (72%) (method *B*). M.p. 267—268 °C (ethyl acetate) (*cf.* Ref. 13: m.p. 267—268 °C). Found (%): C, 88.96; H, 4.81; N, 6.35. $C_{32}H_{20}N_2$. Calculated (%): C, 88.86; H, 4.66; N, 6.48. ^{1}H NMR is analogous to that given in Ref. 13.

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