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Novel three-component *peri*-annelation reactions of carbocyclic and pyridine rings with perimidines—synthesis of 1,3-diazapyrenes and 1,3,7-triazapyrenes

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Abstract

A new effective synthetic method for 1,3-diazapyrenes and 1,3,7-triazapyrenes is developed based on the three-component reaction of perimidines or 1,8-diaminonaphthalene with 1,3,5-triazines and carbonyl compounds or benzonitrile in polyphosphoric acid (PPA).

Keywords: Perimidines; 1,3,5-Triazines; Polyphosphoric acid; 1,3-Diazapyrenes; 1,3,7-Triazapyrenes

Polyazapyrenes belong to a potentially abundant but still poorly understood class of polynuclear heteroaromatic compounds. During recent years, synthetic methods, theoretical, and applied aspects of various azapyrenes have been actively studied.[1]

Earlier, a series of methods for carbocyclic ring annelation of naphthalenes and phenalenones was developed,[2] which enabled the synthesis of phenalenones and pyrenes including 1,3-diazapyrenes.[3] These methods included the reactions of naphthalene or phenalenone with unsaturated carbonyl compounds and the condensation of two carbonyl compounds followed by ring closure. In the present Letter, we report a new three-component carbocyclic ring annelation of perimidines **1** using 1,3,5-triazines **2a**–**c** and carbonyl compounds **4** in polyphosphoric acid.

Earlier, we have shown that 1,3,5-triazines in PPA are effective reagents for the acylation of perimidines **1**[4] (Scheme 1). At higher temperatures, ring opening occurs in intermediate **3** resulting in the annelation of the triazine and formation of 1,3,7-triazapyrenes.[5]

We propose that the addition of a carbonyl compound to the reaction mixture may change the course of the reaction in the direction of carbocyclic ring formation (Scheme 2).

Indeed, reaction of 1 mmol of perimidine **1a**–**c** with 2 mmol of 1,3,5-triazines **2a**–**c** and 3 mmol of carbonyl compound **4a**–**d** in 3–4 g of PPA[6] leads to the formation of 1,3-diazapyrenes **6** in moderate yields, Table 1.

In a similar way, the reaction also proceeds with 1,8-diaminonaphthalene (**7**) with the yields indicated in Table 1 (Scheme 3). In this case 3 mmol of the triazine was used.

Using this idea, we further hypothesized that the reaction should be applicable for 1,3,7-triazapyrene synthesis. Addition of benzonitrile instead of a carbonyl compound to the reaction mixture may change the course of the reaction in the direction of pyridine ring formation (Scheme 4).

Indeed, the reaction of 1 mmol of perimidine **1a**–**c** with 3 mmol of 1,3,5-triazine **2a** and 5 mmol of benzonitrile in 3–4 g of PPA led to the formation of 1,3,7-triazapyrenes **8a**–**c** in the yields indicated in Table 2. Diaminonaphthalene **7** could also be used instead of perimidines **1**, but in this case, 3 mmol of triazine was required (Scheme 4).

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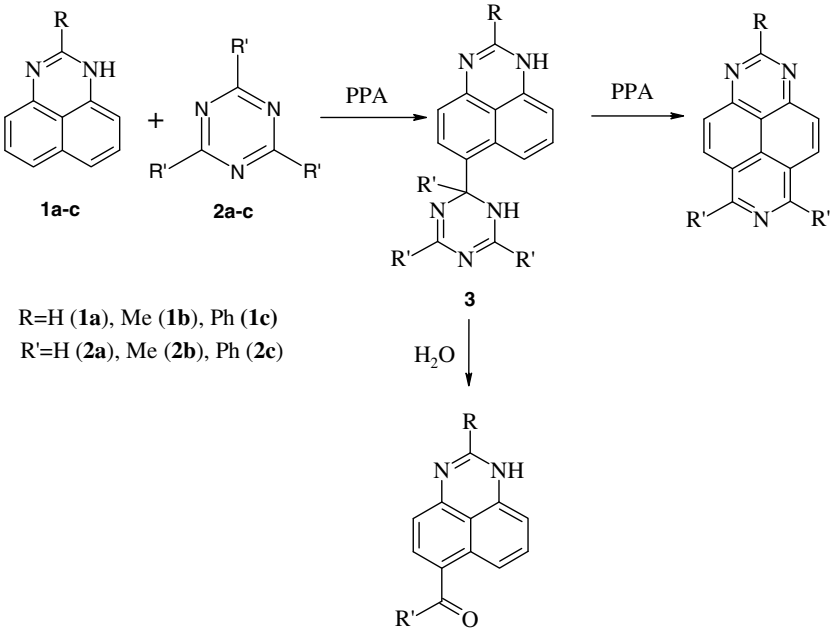
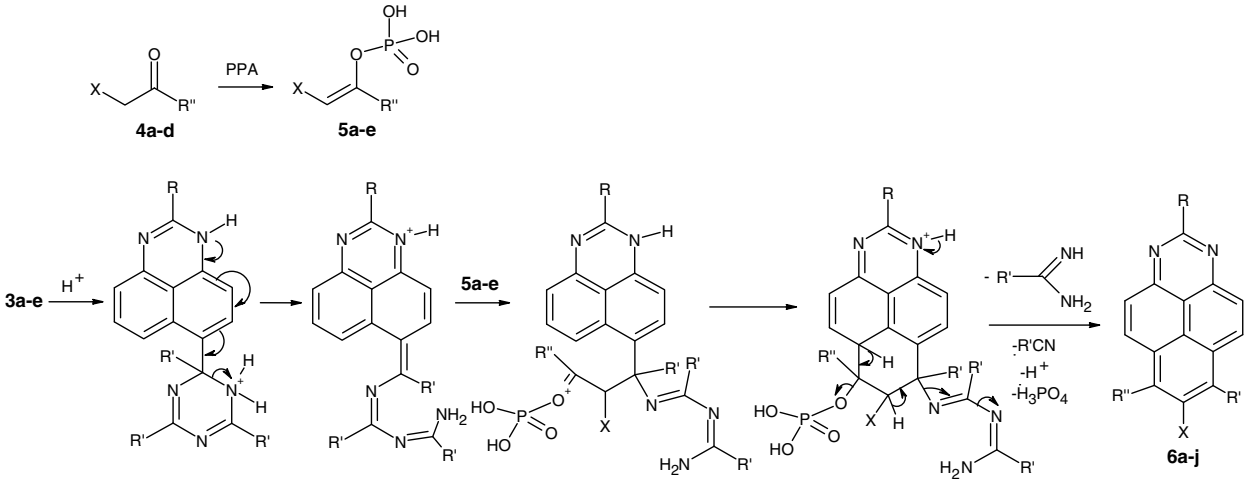


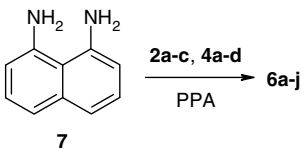
Scheme 1. Perimidine acylation and 1,3,7-triazapyrene syntheses.



Scheme 2. 1,3-Diazapyrene **6a**–**j** synthesis from perimidines **3a**–**e**.

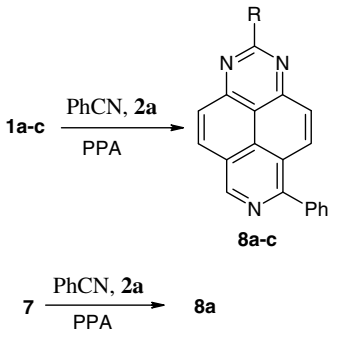
Table 1
Synthesis of 1,3-diazapyrenes

Entry	R	R′	R″	X	Product	Yield (%), from	
						1	**7**
1	H	H	Me	H	**6a**	47	34
2	H	Me	Me	H	**6b**	45	—
3	H	H	Ph	H	**6c**	75	63
4	H	H	Me	COMe	**6d**	57	58
5	H	H	Me	CO_2Et	**6e**	43	41
6	H	Me	Ph	H	**6f**	73	—
7	H	Ph	Ph	H	**6g**	43	—
8	Me	H	Me	CO_2Et	**6h**	57	—
9	Ph	Ph	Ph	H	**6i**	51	42
10	H	Me	Me	COMe	**6j**	37	—



Scheme 3. 1,3-Diazapyrene synthesis from 1,8-diaminonaphthalene **7**.

In conclusion, the advantages of the method described for carbocyclic and pyridine cycle *peri*-annelation include reagent availability, experimental simplicity, and applicability to the synthesis of a broad range of substituted diaza- and triazapyrenes.[7]



Scheme 4. 1,3,7-Triazapyrene **8a–c** synthesis.

Table 2
Synthesis of 1,3,7-triazapyrene **8**

Entry	R	Product	Yield (%), from	
			1	**7**
1	H	**8a**	75	72
2	Me	**8b**	71	—
3	Ph	**8c**	74	—

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6. PPA containing 86% P_2O_5 was used; preparation according to: Uhlig, F. *Angew. Chem.* **1954**, *66*, 435.
7. *General procedure*: A mixture of compound **1** or **7** (1 mmol), 1,3,5-triazine (**2a–c**) (2 mmol for **1** or 3 mmol for **7**), carbonyl compound (**4a–d**) (3 mmol) or benzonitrile (5 mmol) and PPA (3–4 g) was stirred at 60–70 °C, for 9 h. The reaction mixture was poured into cold water (25 ml) with vigorous stirring and ammonia was added to pH ~ 8. The resulting precipitate was filtered off, washed with water, and dried. To increase the yield, the filtrate was extracted with ethyl acetate (3 × 50 ml) and the combined organics evaporated. Compounds **6** and **8** were purified by flash chromatography on silica gel, eluting with ethyl acetate.
Data for 6-methyl-1,3-diazapyrene (**6a**): Mp 178–180 °C (ethyl acetate). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.11 (3H, s, Me); 8.04 (1H, d, $J = 7.67$ Hz, 7-H); 8.20 (1H, d, $J = 9.50$ Hz, 9-H); 8.30 (1H, d, $J = 9.50$ Hz, 5-H); 8.37 (1H, d, $J = 7.67$ Hz, 8-H); 8.55 (1H, d, $J = 9.50$ Hz, 10-H); 8.82 (1H, d, $J = 9.50$ Hz, 4-H); 9.80 (1H, s, 2-H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 19.23, 125.97, 126.54, 127.61, 128.90, 129.16, 129.49, 131.00, 132.60, 134.41, 136.35, 138.62, 152.76, 153.28, 155.91. Anal. Calcd for $C_{15}H_{10}N_2$: C, 82.55; H, 4.62; N, 12.83. Found: C, 82.67; H, 4.56; N, 12.77.
Data for 6,8-dimethyl-1,3,7-triazapyrene (**6b**): Mp 207–209 °C (ethyl acetate). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.04 (6H, s, Me); 7.88 (1H, s, 7-H); 8.19 (2H, d, $J = 9.46$ Hz, 5/9-H); 8.74 (2H, d, $J = 9.50$ Hz, 4/10-H); 9.73 (1H, s, 2-H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 19.56, 123.39, 125.29, 126.51, 132.36, 135.55, 137.93, 145.51, 153.45, 155.59. Anal. Calcd for $C_{16}H_{12}N_2$: C, 82.73; H, 5.21; N, 12.06. Found: C, 82.89; H, 5.15; N, 11.96.
Data for 6-phenyl-1,3-diazapyrene (**6c**): Mp 193–195 °C (ethyl acetate). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.59–7.64 (5H, m, Ph); 8.15 (1H, d, $J = 7.72$ Hz, 7-H); 8.32 (1H, d, $J = 9.42$ Hz, 5-H); 8.41 (1H, d, $J = 7.72$ Hz, 8-H); 8.48 (1H, d, $J = 9.42$ Hz, 9-H); 8.76 (1H, d, $J = 9.42$ Hz, 4-H); 8.98 (1H, d, $J = 9.42$ Hz, 10-H); 9.76 (1H, s, 2-H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 126.32, 126.98, 128.22, 128.72, 128.95, 129.17, 129.24, 129.32, 129.41, 130.76, 132.54, 134.23, 134.64, 136.28, 138.65, 152.41, 153.29, 156.75. Anal. Calcd for $C_{20}H_{12}N_2$: C, 85.69; H, 4.32; N, 9.99. Found: C, 85.82; H, 4.25; N, 8.93.
Data for 6-methyl-7-acetyl-1,3-diazapyrene (**6d**): Mp 161–163 °C (ethyl acetate). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.86 (3H, s, COMe); 3.14 (3H, s, Me); 8.23 (1H, d, $J = 9.13$ Hz, 9-H); 8.31 (1H, d, $J = 9.51$ Hz, 5-H); 8.54 (1H, d, $J = 9.13$ Hz, 10-H), 8.55 (1H, s, 8-H); 8.90 (1H, d, $J = 9.51$ Hz, 4-H); 9.83 (1H, s, 2-H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 16.31, 31.08, 123.82, 127.12, 127.34, 127.57, 127.63, 128.99, 132.75, 135.65, 136.07, 139.58, 153.43, 154.25, 156.62, 172.79, 203.28. ν_{max}(KBr)/cm^{-1} 1645 (C=O); Anal. Calcd for $C_{17}H_{12}N_2O$: C, 78.44; H, 4.65; N, 10.76. Found: C, 78.59; H, 4.58; N, 10.71.
Data for 6-methyl-1,3-diazapyrene-7-carboxylic acid ethyl ester (**6e**): Mp 153–154 °C (ethyl acetate). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.52 (3H, t, $J = 6.87$ Hz, CH_3CH_2); 3.26 (3H, s, Me); 4.55 (2H, q, $J = 6.87$ Hz, CH_3CH_2); 8.22 (1H, d, $J = 9.51$ Hz, 9-H); 8.31 (1H, d, $J = 9.51$ Hz, 5-H); 8.55 (1H, d, $J = 9.51$ Hz, 10-H), 8.85 (1H, s, 8-H); 8.93 (1H, d, $J = 9.51$ Hz, 4-H); 9.80 (1H, s, 2-H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 14.51, 29.77, 61.89, 127.08, 127.17, 127.48, 128.56, 130.21, 132.85, 136.16, 136.36, 138.11, 153.51, 154.49, 156.81, 168.21, 177.22. ν_{max}(KBr)/cm^{-1} 1720 (C=O); Anal. Calcd for $C_{18}H_{14}N_2O_2$: C, 74.47; H, 4.86; N, 9.65. Found: C, 74.58; H, 4.81; N, 9.58.
Data for 6-methyl-8-phenyl-1,3-diazapyrene (**6f**): Mp 198–199 °C (ethyl acetate). Lit.[3f] mp 198–199 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.19 (3H, s, Me); 7.62 (5H, m, Ph); 8.14 (1H, s, 7-H); 8.32 (1H, d, $J = 9.39$ Hz, 5-H); 8.49 (1H, d, $J = 9.39$ Hz, 9-H); 8.77 (1H, d,

$J = 9.39$ Hz, 4-H); 8.98 (1H, d, $J = 9.39$ Hz, 10-H); 9.76 (1H, s, 2-H). Anal. Calcd for $C_{21}H_{14}N_2$: C, 85.69; H, 4.79; N, 9.52. Found: C, 85.79; H, 4.72; N, 9.49.

Data for 6,8-diphenyl-1,3-diazapyrene (**6g**): Mp 175–176 °C (octane). Lit.[3f] mp 175–176 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.58–7.65 (10H, m, Ph); 8.20 (1H, s, 7-H); 8.26(2H, d, $J = 9.14$ Hz, 5/9-H); 8.74 (2H, d, $J = 9.14$ Hz, 4/10-H); 9.81 (1H, s, 2-H). Anal. Calcd for $C_{26}H_{16}N_2$: C, 87.62; H, 4.52; N, 7.86. Found: C, 87.81; H, 4.46; N, 7.73.

Data for 2,6-dimethyl-1,3-diazapyrene-7-carboxylic acid ethyl ester (**6h**): Mp 129–130 °C (ethyl acetate). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.51 (3H, t, $J = 6.89$ Hz, CH_3CH_2); 3.12 (3H, s, 6-Me); 3.21 (3H, s, 2-Me); 4.54 (2H, q, $J = 6.89$ Hz, CH_3CH_2); 8.21 (1H, d, $J = 9.49$ Hz, 9-H); 8.32 (1H, d, $J = 9.49$ Hz, 5-H); 8.55 (1H, d, $J = 9.49$ Hz, 10-H), 8.84 (1H, s, 8-H); 8.89 (1H, d, $J = 9.49$ Hz, 4-H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 14.52, 24.12, 29.78, 61.77, 127.09, 127.17, 127.46, 128.51, 130.21, 132.81, 136.12, 136.39, 138.15, 153.48, 154.41, 156.78, 168.22, 177.22. ν_{max}(KBr)/cm^{-1} 1722 (C=O); Anal. Calcd for $C_{19}H_{16}N_2O_2$: C, 74.98; H, 5.30; N, 9.20. Found: C, 75.14; H, 5.21; N, 9.11.

Data for 2,6,8-triphenyl-1,3-diazapyrene (**6i**): Mp 267–268 °C (octane). Lit.[3f] mp 267–268 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.49–7.69 (13H, m, 6,8-Ph, *m*- and *p*-H 2-Ph); 8.09 (1H, s, 7-H); 8.21 (2H, d, $J = 9.47$ Hz, 5/9-H); 8.59 (2H, d, $J = 9.47$ Hz, 4/10-H); 8.78 (2H, d, $J = 9.31$ Hz, *o*-H 2-Ph). Anal. Calcd for $C_{32}H_{20}N_2$: C, 88.86; H, 4.66; N, 6.48. Found: C, 88.96; H, 4.81; N, 6.35.

Data for 6,8-dimethyl-7-acetyl-1,3-diazapyrene (**6j**): Mp 165–167 °C (ethyl acetate). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.84 (3H, s, COMe); 3.18 (6H, s, 6/8-Me); 8.23 (2H, d, $J = 9.14$ Hz, 5/9-H); 8.54 (2H, d, $J = 9.13$ Hz, 4/10-H); 9.81 (1H, s, 2-H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 16.31, 31.08, 127.24, 127.61, 128.99, 132.75, 135.81, 139.58, 153.43, 156.62, 172.33, 203.11. ν_{max}(KBr)/cm^{-1} 1638 (C=O); Anal. Calcd for $C_{18}H_{14}N_2O$: C, 78.81; H, 5.14; N, 10.21. Found: C, 78.97; H, 5.06; N, 10.13.

Data for 6-phenyl-1,3,7-triazapyrene (**8a**): Mp 174–176 °C (octane). ^{1}H NMR (300 MHz, $CDCl_3$):δ 7.68 (3H, m, 3/4/5-Ph); 7.91 (2H, d, $J = 8.04$ Hz, 2/6-Ph); 8.29 (1H, d, $J = 9.5$ Hz, 10-H); 8.33 (1H, d, $J = 9.13$ Hz, 4-H); 8.75 (1H, d, $J = 9.5$ Hz, 9-H); 8.91 (1H, d, $J = 9.13$ Hz, 5-H); 9.86 (1H, s, 8-H); 9.89 (1H, s, 2-H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 118.48, 124.63, 127.42, 127.95, 128.41, 128.69, 130.02, 132.10, 133.12, 133.38, 147.29, 152.94, 153.67, 153.89, 167.23. Anal. Calcd for $C_{19}H_{11}N_3$: C, 81.12; H, 3.94; N, 14.94. Found: C, 81.27; H, 3.87; N, 14.86.

Data for 2-methyl-6-phenyl-1,3,7-triazapyrene (**8b**): Mp 246–248 °C (octane). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.19 (3H, s, Me); 7.63 (3H, m, 3/4/5-Ph); 7.88 (2H, d, $J = 8.06$ Hz, 2/6-Ph); 8.18 (1H, d, $J = 9.5$ Hz, 10-H); 8.24 (1H, d, $J = 9.24$ Hz, 4-H); 8.60 (1H, d, $J = 9.24$ Hz, 5-H), 8.76 (1H, d, $J = 9.5$ Hz, 9-H); 9.69 (1H, s, 8-H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 26.57, 111.95, 118.48, 124.63, 127.42, 127.95, 128.41, 128.69, 130.02, 132.10, 133.12, 133.38, 147.29, 152.94, 153.67, 153.89, 167.17. Anal. Calcd for $C_{20}H_{13}N_3$: C, 81.34; H, 4.44; N, 14.22. Found: C, 81.44; H, 4.38; N, 14.18.

Data for 2,6-diphenyl-1,3,7-triazapyrene (**8c**): Mp 197–199 °C (octane). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.63 (6H, m, 3/4/5-(2)Ph, 3/4/5-(6)Ph); 7.90 (2H, d, $J = 8.06$ Hz, 2/6-(6)Ph); 8.30 (1H, d, $J = 9.5$ Hz, 10-H); 8.35 (1H, d, $J = 9.18$ Hz, 4-H); 8.63 (1H, d, $J = 9.18$ Hz, 5-H); 8.76 (1H, d, $J = 9.5$ Hz, 9-H); 8.84 (2H, d, $J = 8.06$ Hz, 2/6-(2)Ph); 9.68 (1H, s, 8-H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 117.25, 123.48, 124.63, 127.42, 127.95, 128.41, 128.69, 130.02, 132.10, 133.12, 133.38, 147.29, 152.94, 153.67, 153.89, 167.53. Anal. Calcd for $C_{25}H_{15}N_3$: C, 84.01; H, 4.23; N, 11.76. Found: C, 84.14; H, 4.19; N, 11.67.