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HETEROCYCLIC ANALOGS OF PLEIADENE.

71*. SYNTHESIS OF 1,3-DIAZAPYRENE

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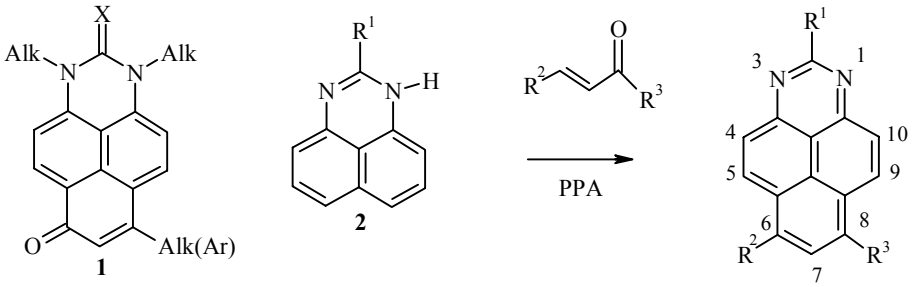
The reaction of perimidine and 2-R-perimidines with α,β-unsaturated carbonyl compounds in polyphosphoric acid has yielded the previously unknown 1,3-diazapyrene and its 6,8-di- and also 2,6,8-trisubstituted derivatives. Their spectroscopic parameters are discussed.

Keywords: 1,3-diazapyrene, perimidine, polyphosphoric acid, C-alkylation.

We have previously synthesized partially hydrogenated 1,3-diazapyrene derivatives **1** which have proved to be, in particular, good luminophores [2, 3]. However the parent heterocyclic system has remained unknown until recent times. Meanwhile, the investigation of its aromaticity, physicochemical parameters, and reactivity are of considerable interest*[2]. In this article we describe the preparation of 1,3-diazapyrene and a series of its simple derivatives (for preliminary report see [1]).

We have shown that the reaction of perimidine and 2-R-perimidines **2** with α,β-unsaturated ketones in polyphosphoric acid (PPA) gives, respectively, 6,8-di and 2,6,8-trisubstituted 1,3-diazapyrenes **3a-f** in 25-40% yield.



1 X = O, H_2, S; **2 a** R^1 = H; **b** R^1 = Me; **c** R^1 = Ph; **3 a–d**, **g** R^1 = H, **e** R^1 = Me, **f** R^1 = Ph, R^1 = Ph; **a**, **c–f** R^2 = Me, **g** R^2 = H; **a**, **b**, **e**, **f** R^3 = Ph, **c** R^3 = *p*-BrC_6H_4, **d** R^3 = *p*-$MeOC_6H_4$, **g** R^3 = H

* For Communication 70 see [1].

*[2] Evidence of other aromatic heterocycles of this type is restricted to the 4,9- and 4,10-diazapyrenes, e.g. [4-10].

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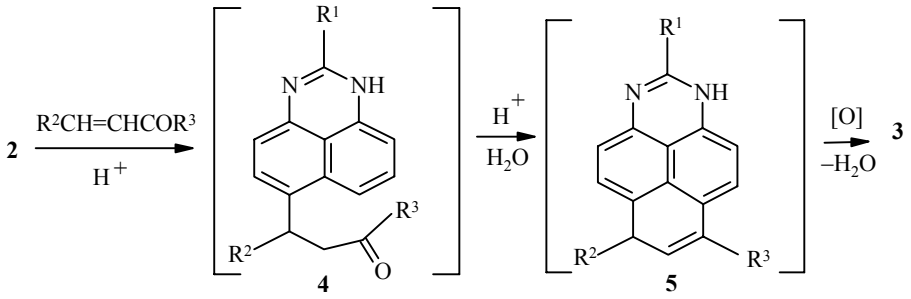
Compound **3d** was prepared from perimidine both by the action of *p*-methoxybenzalacetophenone and of benzal-*p*-methoxyacetophenone under the same conditions. During the course of the reaction of the α,β-unsaturated ketones, and possibly also the intermediate materials, they are partially polymerized to give oily products. Attempts to increase the yield of the target substance by an increase in the molar ratio of starting chalcone or by an increase in temperature gave more tarring and did not lead to the desired result. We believe that the initial stage of the reaction is an electrophilic C-alkylation by the chalcone at the 6(7) position of the corresponding perimidine (Scheme 1). Subsequent intramolecular hydroxyalkylation and dehydration of the ketones **4** then gives the dihydrodiazapyrene **5** which spontaneously oxidizes to **3** (compare with the ready autooxidation of dihydro-1,3,6,8-tetraazapyrene derivatives [12, 13]).

Scheme 1



Unfortunately, confirmation of this sequence of stages proved difficult since, even when carrying out the reaction at room temperature (7 days; yield of **3a** 51%) no kind of intermediate product could be detected. None the less, an indirect reason to support Scheme 2 is the fact that *p*-nitrobenzalacetophenone (which is much less basic than the unsubstituted chalcone) does not participate in this reaction. This indicates that the rate limiting stage of the process is the first step. We have further shown that the formation of diazapyrenes is also catalyzed by 60% perchloric acid, but due to more extensive tarring the product yield is significantly less in this case. The ease of oxidative aromatization of the intermediates **5** points to the high thermodynamic stability of the 1,3-diazapyrene system.

We expected to obtain analogs of the intermediate products **5** by the alkylation of perimidine by β,β-disubstituted, unsaturated ketones of the type $R^1R^2C{=}CHCOR^1$ but in this case the aromatization is not possible. However, with dypnone (R^1 = Ph, R^2 = Me) the reaction does not occur, even when heated above 100°C and in the case of mesityl oxide ($R^1 = R^2$ = Me) complete tarring is observed.

The unsubstituted 1,3-diazapyrene **3g** can be prepared similarly to phenalenone [14] by the reaction of perimidine with glycerol at 138°C in 70% H_2SO_4 in the presence of sodium *m*-nitrobenzenesulfonate as oxidant. However, in preparative mode, it is more convenient to use the system glycerol–PPA at 180-190°C without oxidant (the use of the latter has no effect on the 27% yield). Basically, this is the reaction of perimidine with acrolein *in situ*.

β-Diketones prove to be a good synthon for the preparation of 1,3-diazapyrenes from perimidine. In the example of acetylacetone the reaction in PPA is initiated only above 100°C but the sole product (in 10% yield) is the rather unexpected 4(9)-acetylperimidine (**7**). Evidently, this is the result of a retroaldol condensation of intermediate **6** (Scheme 2). Introduction of an electrophile at position 4 can account for the repeated observation of isomerization of the initially formed 6(7)-acylation product to the 4(9) isomer [15].

TABLE 1. Spectroscopic Parameters for Compound **3**

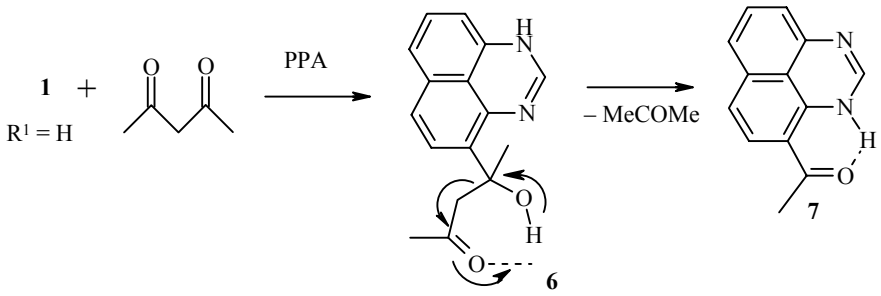
Compound	^{1}H NMR spectrum, δ, ppm, (*J*), Hz*								
	2H, s	4H, d	10H, d	5H, d	9H, d	7H	R_1	R_2	R_3
3a	9.81	8.74 (*J* = 9.14)		8.26 (*J* = 9.14)		8.20, s	—	7.58-7.66, m	
3b	9.76	8.77 (*J* = 9.39)	8.98 (*J* = 9.39)	8.32 (*J* = 9.39)	8.49 (*J* = 9.39)	8.14, s	—	3.19, s	7.62, s
3c	9.79	8.62 (*J* = 9.43)	8.68 (*J* = 9.43)	8.21 (*J* = 9.43)	8.22 (*J* = 9.43)	8.10, s	—	7.40-7.75, m	
3d	9.66	8.53 (*J* = 9.98)	8.57 (*J* = 10.65)	8.08-8.11, m		8.08-8.11, m	—	3.88 (s, CH_3O); 7.17 (*m*-H*^{2}, d, *J* = 7.80, C_6H_4); 7.64 (*o*-H*^{2}, m, C_6H_4 and C_6H_5)	
3e	–	8.64 (*J* = 9.44)		8.12 (*J* = 9.44)		8.10, s	3.12, s	7.50-7.68, m	
3f	–	8.60 (*J* = 9.47)		8.20 (*J* = 9.47)		8.09, s	8.80 (dd, *J* = 8.31 (*o*-*m*), *J* = 1.4 (*o*-*p*) *o*-H)*^{2}; 7.49-7.69 (m, *m*- and *p*-H*^{2})	7.49-7.69, m	
3g*^{3}	9.75	8.70 (*J* = 8.39)		8.24 (*J* = 8.39)		8.27 (t, *J* = 7.69)	—	—	

* Solvent: $CDCl_3$ (**3a-c,e,f**), DMSO-d_6 (**3d**), and CD_3CN (**3g**).

*^{2} *o*-, *m*-, and *p*-H relative to the 1,3-diazapyrene ring.

*^{3} δ, ppm (*J*, Hz): 8.58 (6H, 8H, d, *J* = 7.69).

Scheme 2



The synthesized 1,3-diazapyrenes are slightly yellowish, crystalline materials with a violet or blue fluorescence under UV light. They readily dissolve in conc. HCl but the hydrochloride is hydrolyzed upon dilution with water to yield the base as a precipitate. Quantum-chemical calculations (Fig. 1) point to a significant π-deficiency in the molecule **3g** while the change in effective charge on the hydrogen atoms matches the position of their signals in the ^{1}H NMR spectrum (see Table 1).

Overall, the signals of all of the protons of the diazapyrene ring are shifted to low field and appear at $\delta > 8$ ppm. The lowest field signal is that of the H-2 proton (δ 9.7-9.8 ppm) and the highest are those of the H-5(9) and H-7 protons (δ 8.10-8.27). The increased anisotropy close to the conjugated ring [16] accounts for the fact that the 6-CH_3 group of compound **3b** appears to lower field than the CH_3 group in the electron deficient position 2 in compound **3e** (δ 3.19 and 3.12 ppm respectively).

As expected, the IR spectra of compounds **3** show the presence of the stretching vibrations of the aromatic ring (1620-1500 cm^{-1}) and the absence of any other characteristic absorption bands.

The high intensity of the molecule ion peak (100%) in the mass spectrum of **3b** indicates, in our view, the stability of the cation radical derived from the 1,3-diazapyrene. Besides the [M+1] signal with the correct calculated intensity, the spectrum shows (in particular) peaks for [M-15] and [M-77] corresponding to the loss of methyl or phenyl radicals.

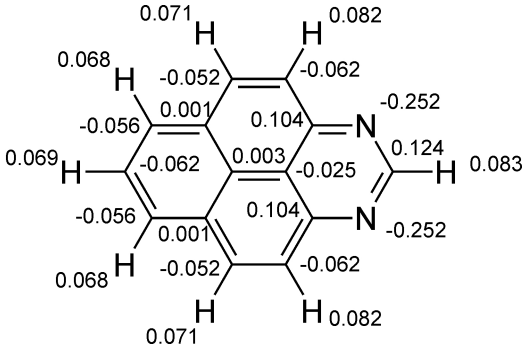


Fig. 1. Effective charges on the atoms in 1,3-diazapyrene (*ab initio* method).

EXPERIMENTAL

^{1}H NMR spectra were recorded on a Bruker WP-200 (200 MHz) instrument using TMS as internal standard and signal assignments were carried out using the double resonance method. IR Spectra were taken on a UR-20 spectrometer and mass spectra on an MX-1321A instrument. Monitoring of the course of the reaction

and the purity of the synthesized compounds was carried out on Silufol UV-254 plates. The column chromatography was performed using L40/100 silica gel from the supplier Chemapol.

General Method for the Synthesis of 1,3-Diazapyrene Derivatives 3. A mixture of perimidine or 2-R-perimidine (0.002 mol), the corresponding chalcone (0.003 mol) and PPA (4 g) was stirred for 3 h at 60-65°C and then poured as a thin stream into water (100 ml) with vigorous stirring. After basification to pH ~ 8 with aqueous ammonia the precipitate was filtered off, washed with water, and dried. It was then extracted with refluxing benzene (3 × 10 ml), cooled, and transferred to a silic gel chromatographic column where it was initially eluted with benzene and then with ethyl acetate. The first fraction contained a small amount of oily material and was not used. Evaporation of solvent from the second fraction gave the corresponding 1,3-diazapyrene.

6,8-Diphenyl-1,3-diazapyrene (3a). Yield 0.26 g (36%) (from benzalacetophenone). Pale yellow crystals with mp 175-176°C (from octane; revision from the data in [11]). Found, %: C 87.49; H 4.64; N 7.92. $C_{26}H_{16}N_2$. Calculated, %: C 87.62; H 4.52; N 7.86.

6-Methyl-8-phenyl-1,3-diazapyrene (3b). Yield 0.17 g (29%) (from benzalacetone). Pale yellow crystals with mp 198-199°C (benzene). IR spectrum (vaseline oil), ν, cm^{-1}: 1620, 1595, 1568 (ring). Mass spectrum, *m/z* (*I*, %): 294 [M^+] (100), 295 (23), 279 (24), 217 (7). Found, %: C 85.65; H 4.89; N 9.79. $C_{21}H_{14}N_2$. Calculated, %: 85.69; H 4.79; N 9.52.

8-*p*-Bromophenyl-6-phenyl-1,3-diazapyrene (3c). Yield 0.28 g (32%) (from *p*-bromobenzal-acetophenone). Pale cream crystals with mp 216-217°C (ethyl acetate). Found, %: C 71.59; H 3.44; N 6.62. $C_{26}H_{15}BrN_2$. Calculated, %: C 71.74; H 3.47; N 6.44.

8-*p*-Methoxyphenyl-6-phenyl-1,3-diazapyrenene (3d). Yield 0.31 g (40%) (*p*-methoxybenzal-acetophenone) and 0.22 g (28%) (from benzal-*p*-methoxyacetophenone). Pale yellow crystals with mp 160-161°C (benzene–petroleum ether). Samples obtained by the two methods did not give a depression of melting point. Found, %: C 83.84; H 4.74; N 7.39. $C_{27}H_{18}N_2O$. Calculated, %: C 83.94; H 4.66; N 7.25.

2-Methyl-6,8-diphenyl-1,3-diazapyrene (3e). Yield 0.20 g (27%) (from 2-methylperimidine and benzalacetophenone). Pale yellow crystals with mp 182-183°C (benzene–hexane). 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.

2,6,8-Triphenyl-1,3-diazapyrene (3f). Yield 0.22 g (25%) (from 2-phenylperimidine and benzal-acetophenone). Yellowish crystals with mp 267-268°C (benzene–hexane). IR Spectrum (vaseline oil), ν, cm^{-1}: 1618, 1593, 1568 (ring). Found, %: C 88.96; H 4.80; N 6.36. $C_{32}H_{20}N_2$. Calculated, %: C 88.86; H 4.66; N 6.48.

1,3-Diazapyrene (3g). A. *Condensation in H_2SO_4.* Perimidine (6.72 g, 0.04 mol), ferrous sulfate (1.74 g), and glycerol (10.4 g, 0.11 mol) were mixed with 70% H_2SO_4 (100 g) and the mixture was heated to 110°C. Over the course of 15 min, sodium *m*-nitrobenzenesulfonate (3 g, 0.013 mol) was added. The mixture was heated to 138°C, held for 40 min, and then cooled to room temperature. The solution was filtered through a glass filter and the filtrate was poured into a mixture of NaOH (40%, 150 ml) and ice (150 g). The precipitate was filtered off, washed with water, and dried. The product was extracted with refluxing octane (5 × 50 ml) which after evaporation gave compound **3g** (3.23 g, 40%) as pale yellow crystals with mp 178-180°C (octane). Found, %: C 82.48; H 4.03; N 13.60. $C_{14}H_8N_2$. Calculated, %: C 82.34; H 3.95; N 13.72.

B. *Condensation in PPA*. Glycerol (2 g, 0.022 mol, previously dried by heating at 170°C) was added dropwise over 15-20 min with stirring into to a mixture of perimidine (0.34 g, 0.002 mol) and PPA (5 g) which had been heated to 190°C. After 1.5 h the mixture was cooled to 70°C and poured into ground ice (75 g). It was then basified with ammonia solution to pH ~ 8 and extracted with ethyl acetate (3 × 50 ml). The solution evaporated to 30 ml was chromatographed through a small amount of silica gel, washing the product with ethyl acetate. Evaporation of solvent gave 1,3-diazapyrene (0.12 g, 29%).

Reaction of Perimidine with Ethyl Acetate in PPA. A mixture of perimidine (0.34 g, 0.002 mol), acetylacetone (0.3 g, 0.003 mol), and PPA (4 g) was stirred for 1.5 h at 120-130°C. After cooling to 80-85°C the mixture was poured with vigorous stirring into cold water (100 ml), basified with aqueous ammonia to pH ~ 8,

extracted with ethyl acetate (3 × 10 ml), the solution dried and purified by refluxing with silica gel and then the solvent was evaporated. After crystallization from benzene, the 4(9)-acetylperimidine **7** (0.04 g, 10%) was obtained with mp 201-202°C, agreeing with the corresponding data [15]. The IR spectrum was identical to that of a known sample of compound **7**.

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