

# New naphtho[1,8-*ef*]perimidines: synthesis, fluorescence studies and application for detection of nitroanalytes

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## Abstract

A rational approach to the synthesis of substituted naphtho[1,8-*ef*]perimidines based on  $S_N^H$  methodology and cyclization reaction in the series of condensed azines with naphthalene substituents was presented. Photophysical properties of the obtained fluorophores were studied, in particular, green fluorescence in the 485–536 nm range with quantum yield up to 32.4% was detected. HOMO-LUMO energy values and distributions for the new compounds were calculated by the DFT method in comparison with nitroanalytes and perylene. Based on the data obtained, as well as on the results of fluorescence titration, the possibility of using the new diazaperylene as potential chemosensors for the visual detection of nitro-containing explosives was shown.

## Keywords

naphtho[1,8-*ef*]perimidines  
fluorescence  
sensor  
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## 1. Introduction

Polyaromatic compounds are widely used as various types of chemosensors, including ones for the detection of nitro-containing explosives. This is achieved by preferential formation of  $\pi$ -complexes between the sensor and quencher due to high  $\pi$ -deficiency of the latter, as well as hydrogen bonding due to participation in interaction with nitroaromatic analytes of functional groups on the periphery of the chemosensor and formation of inclusion complexes. Triphenylene and its aryl-condensed analogues such as naphthalene, phenanthrene, pyrene, dibenzanthracene, helicenes *etc.* are the typical chemosensors of this group [1]. Perylene and its derivatives deserves special attention in this series due to promising photophysical properties and sensor response to some nitroanalytes [2–5]. It is known that the presence of pyridine nitrogen atom in the structure of polycyclic aromatic hydrocarbons can significantly enhance the susceptibility of such structures to the action of nucleophilic agents, thereby opening the possibility of using the  $S_N^H$  methodology for its functionalization [6, 7]. The aza-heterocycles obtained by this approach can serve as a basis for synthesis of more efficient chemosensors by combining  $\pi$ -conjugated and fluorophore frag-

ments into one molecule for the enhancement of its sensory properties, e.g. towards nitroanalytes, by the creation of  $\pi$ -conjugated donor-acceptor systems [1]. Among currently known poly(hetero)aromatic fluorophores, di-, tri- and tetraazaperylenes possess the most promising photophysical properties. At the same time, they have higher LUMO energies values, which in turn may provide better detection capability, for example, for aliphatic nitro-containing explosives [8, 9]. However, no examples of using azaperylenes as chemosensors for such nitroanalytes have been described in the literature so far. Therefore, in this work we propose a methodology for the synthesis of new fluorophores based on naphtho[1,8-*ef*]perimidine and studying their ability to use for visual detection of nitro-containing analytes.

## 2. Experimental

<sup>1</sup>H NMR spectra were recorded on a Bruker Avance-400 spectrometer (400 MHz), the internal standard was SiMe<sub>4</sub>. Mass-spectra (ionization type – electrospray) were recorded on a MicroTOF-Q II instrument from Bruker Daltonics (Bremen, Germany). Elemental analysis was performed on a Perkin Elmer PE 2400 II CHN analyzer. HOMO-LUMO and optimized molecular structure calculations of com-

pounds were carried out in the Orca 4.0.1 software package using the DFT B3LYP, 6-311G\* method [10]. UV-visible absorption spectra were recorded on a Perkin Elmer Lambda 45. Luminescence spectra were obtained using a HORIBA Scientific FluoroMax-4 spectrofluorometer [11]. The starting quinazoline **2**, 2-naphthol and all reagents were obtained from commercial sources.

### 2.1. 4-(2-Hydroxynaphthalen-1-yl)quinazoline (1)

Trifluoromethanesulfonic acid (1.3 g, 8.77 mmol) was added to the solution of 1.0 g (7.6 mmol) quinazoline **2** in DCM (35 ml). Then 2-naphthol (1.1 g, 7.6 mmol) was added and the resulting mixture was stirring for 1 h at room temperature. Then solvent was removed under reduced pressure. The residue was suspended in THF (35 ml) and solution of  $K_3[Fe(CN)_6]$  (4.6 g, 14.0 mmol) and NaOH (1.1 g, 28.0 mmol) in water (35 ml) was added. A formed suspension was stirred for 8 h at room temperature. After THF was removed under reduced pressure. The product was extracted from the remaining suspension with ethyl acetate (3×90 ml). Organic layer was collected and dried over anhydrous  $Na_2SO_4$ . Then solvent was evaporated under reduced pressure. The residue was purified by column chromatography (hexane:ethyl acetate = 2:1,  $R_f$  = 0.1). White solid. Yield 1.5 g (71%).  $^1H$  NMR spectra is in accordance with published data [12].

### 2.2. 4-(2-methoxynaphthalen-1-yl)quinazoline (3)

4-(2-Hydroxynaphthalen-1-yl)quinazoline **1** (0.2 g, 0.7 mmol) was dissolved in dry DMF (5 ml).  $K_2CO_3$  (0.15 g, 1.1 mmol) was added to the resulting solution. Methyl iodide (1.5 g, 1.1 mmol) was added dropwise and the resulting mixture was stirred in an argon atmosphere for 16 h at room temperature. Then DMF was evaporated under reduced pressure, the residue was suspended in distilled water (10 ml). The reaction product was extracted with ethyl acetate (3×10 ml), the organic layer was dried over anhydrous  $Na_2SO_4$ . The solvent was evaporated under reduced pressure, the residue was purified by column chromatography (ethyl acetate,  $R_f$  = 0.9). Light yellow crystals. Yield 1.4 g (66%).  $^1H$  NMR (400 MHz,  $CDCl_3$ ,  $\delta$ , ppm): 3.79 (s, 3H), 7.08 (d,  $J$  = 8.5 Hz, 1H), 7.28–7.38 (m, 2H), 7.44–7.47 (m, 2H), 7.53 (d,  $J$  = 8.0 Hz, 1H), 7.88–7.92 (m, 2H), 8.06 (d,  $J$  = 9.2 Hz, 1H), 8.16 (d,  $J$  = 8.4 Hz, 1H), 9.52 (s, 1H). ESI-MS,  $m/z$ : 287.11  $[M+H]^+$ . Found, %: C 79.64, H 5.07, N 9.83.  $C_{19}H_{14}N_2O$ . Calculated, %: C 79.70, H 4.93, N 9.78.

### 2.3. General procedure for the synthesis of diazaperylenes (4,5)

The corresponding (naphthalen-1-yl)quinazoline **1,3** (1.05 mmol) was dissolved in dry toluene (25 mL); subsequently, potassium (0.41 g, 10.5 mmol) was added under argon atmosphere. The reaction was stirred at 95 °C for 6 h, quenched with *i*-PrOH, filtered through silica gel. The solvents were removed under reduced pressure. The resi-

due was solved in ethyl acetate (20 ml). The solution was washed with water (3×20 ml). The organic layer was dried over anhydrous  $Na_2SO_4$ . The solvent was removed under reduced pressure. The residue is purified by column chromatography (corresponding eluent). The crystallization ( $CH_2Cl_2$ /hexane) afforded pure product.

### 2.4. 12-Methoxynaphtho[1,8-ef]perimidine (4)

Eluent: DCM:MeOH=20:1,  $R_f$  = 0.8. Yellow-green solids. Yield 38 mg (16%).  $^1H$  NMR (400 MHz,  $CDCl_3$ ,  $\delta$ , ppm): 3.79 (s, 3H), 7.51–7.54 (m, 3H), 7.86–7.90 (m, 2H), 8.24 (d,  $J$  = 8.4 Hz, 1H), 8.33 (d,  $J$  = 8.0 Hz, 1H), 9.02 (d,  $J$  = 8.0 Hz, 1H), 9.57 (s, 1H). ESI-MS,  $m/z$ : 285.09  $[M+H]^+$ . Found, %: C 80.29, H 4.21, N 9.79.  $C_{19}H_{12}N_2O$ . Calculated, %: C 80.27, H 4.25, N 9.85.

### 2.5. Benzo[de]naphtho[1,8-gh]quinolin-12-ol (5)

Eluent: toluene: MeOH = 7:1,  $R_f$  = 0.5. Brown solids. Yield 55 mg (18%).  $^1H$  NMR (400 MHz,  $CDCl_3$ ,  $\delta$ , ppm): 6.95 (d,  $J$  = 8.4 Hz, 1H), 7.43–7.47 (t,  $J$  = 7.6 Hz, 1H), 7.74–7.81 (m, 3H), 8.08–8.13 (m, 2H), 8.38 (d,  $J$  = 7.7 Hz, 1H), 8.48 (d,  $J$  = 8.7 Hz, 1H), 9.36 (s, 1H), 9.42 (s, 1H). ESI-MS,  $m/z$ : 270.08  $[M+H]^+$ . Found, %: C 84.80, H 4.15, N 5.14.  $C_{19}H_{11}NO$ . Calculated, %: C 84.74, H 4.12, N 5.20.

## 3. Results and discussion

Synthesis of diazaperylenes precursor, 4-(2-hydroxynaphthalen-1-yl)quinazoline **1**, was performed according to the described method by direct introduction of 2-hydroxynaphthalene residue into C2 position of quinazoline **2** by  $S_N^H$  method with using trifluoromethanesulfonic acid as an adduct formation activator [12]. Further alkylation of the hydroxyl group of compound **1** with methyl iodide resulted in the formation of 4-(2-methoxynaphthalen-1-yl)quinazoline **3** (Scheme 1).

Further, to realize the cyclization of compound **3** with obtaining the corresponding diazaperylene, an attempt was made to use excess of trifluoromethanesulfonic acid as an activator for the formation of charge transfer complex. However, in this case only the starting compounds were isolated from the reaction mass. The method of intramolecular cyclization [13], according to which the quinazoline **3** was kept in a solution of dry toluene at 95 °C in the presence of potassium for 6 h, was more successful. The yield of 12-methoxynaphtho[1,8-ef]perimidine **4** after purification by column chromatography was 16%, which is acceptable for reactions of this type [8,13]. In addition, 12-oxonaphtho[1,8-ef]pyrimidine **5** was similarly obtained from quinazoline **1** in 18% yield.

Further, the photophysical properties of the obtained fluorophores **4** and **5** were studied. The results obtained are collected in Table 1. Thus, the absorption maxima are located in the visible light region (495 nm) and the emission maxima lie in the green region (485–536 nm). The spectra contain two maxima, which is probably due to the effect of intramolecular charge transfer (ICT). In addition,

compound **4** shows a high value of luminescence quantum yield (32.4%), apparently due to a significant influence of the electron-donating methoxy group on the heteroaromatic chromophore system. This is confirmed by the fact that diazaperylene **5**, containing a hydroxy group, exhibits a value of  $\Phi = 4.5\%$ , which is 7 times lower than that of the methoxy-containing analogue **4**.

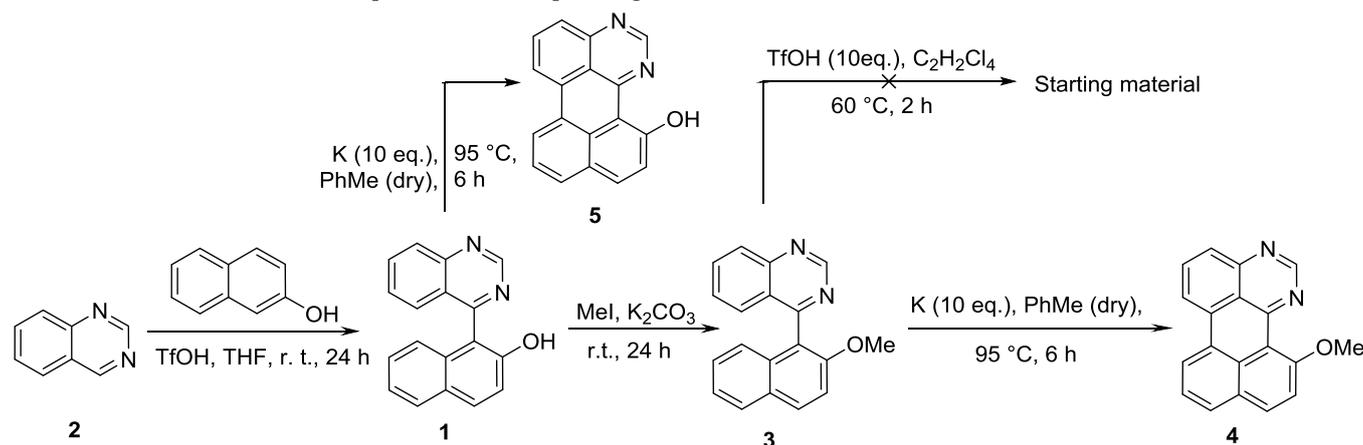
**Table 1** Photophysical characteristics of the obtained fluorophores **4** and **5**

Compound	$\lambda_{\text{abs}}$ , nm	$\lambda_{\text{em}}$ , nm	$\Phi$ [11], %
<b>4</b>	225, 285, 307, 329, 395, 429	485 (sh), 510	32.4
<b>5</b>	226, 433, 464, 495	501, 536	4.5

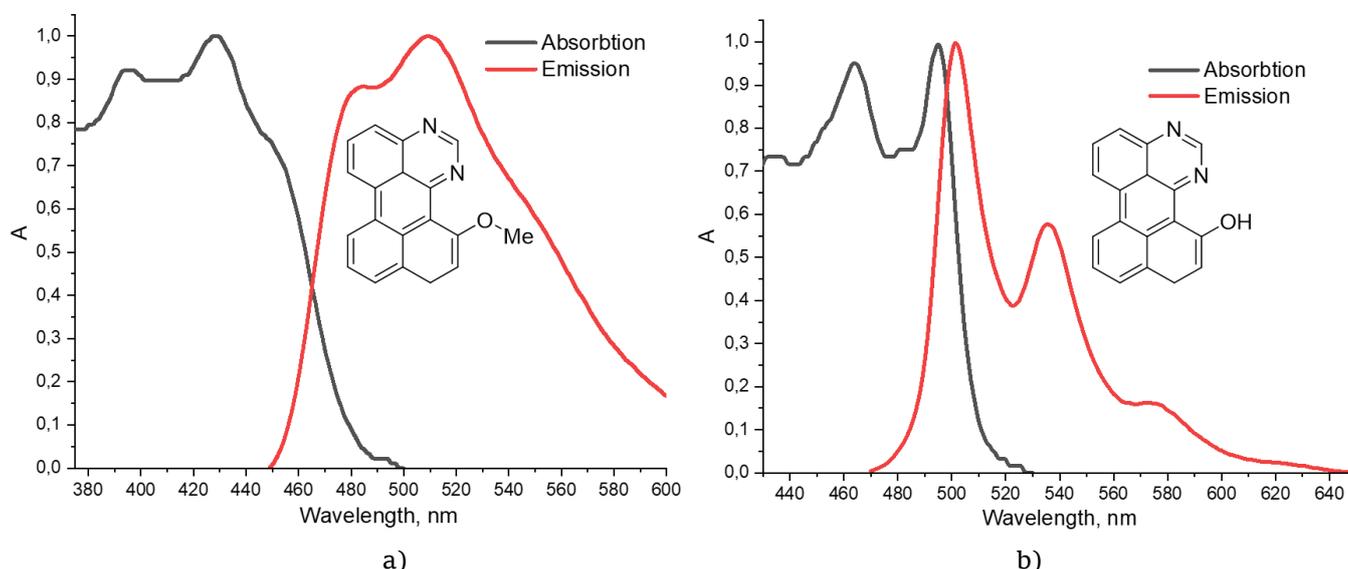
Fig. 1 shows the absorption and emission spectra of diazaperylenes **4,5** in normalised form. For both compounds the absorption/emission spectra profiles are similar and represent distorted mirror images of each other.

The photophysical properties for the naphthopirimidines **4,5** allow predicting their use as potential fluorescent chemosensors for various nitro-containing explosives. For an initial estimation of sensors fluorescence quenching efficiency by nitroanalytes, the LUMO energy difference for the sensor and quencher corresponding to

the thermodynamic driving force of this process was calculated [1, 9]. Using the DFT basis set B3LYP, 6-311G\* values of HOMO-LUMO energies were calculated for the compounds, and their optimized molecular structures were obtained [14–17]. The results are given in Table 2. In comparison with the previously calculated model of the electronic configuration of HOMO/LUMO for unsubstituted perylene [18], the electronic clouds of the obtained fluorophores are shifted in a certain degree relative to the nitrogen atoms of diazaperylene cycle and methoxy groups, which indicates a high probability of intramolecular charge transfer processes. Calculations of the LUMO energy values for the three nitroanalytes, namely RDX, DNT and PETN, show that in the case of methoxy-substituted diazaperylene **4**, the LUMO(sensor)-LUMO(quencher) energy gap values are from 0.1620 to 0.9620 eV, which is comparable with the values for unsubstituted perylene. Whereas for the hydroxysubstituted diazaperylene **5** the energy gap with respect to RDX is  $-0.0277$  eV, which characterises the energy ban on fluorescence quenching. For the other nitro analytes the energy gap values are also significantly inferior to the obtained fluorophore **4** and are 0.6723 eV (DNT) and 0.7723 eV (PETN).



**Scheme 1** Synthesis of diazaperylenes precursor, 4-(2-hydroxynaphthalen-1-yl)quinosaline **1**

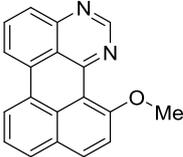
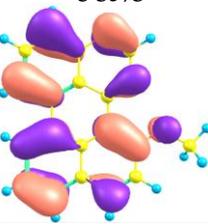
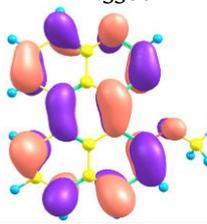
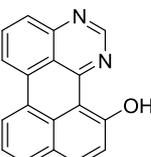
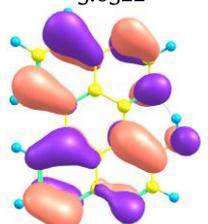
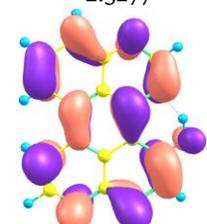
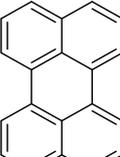
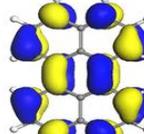
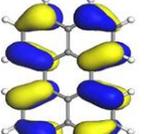


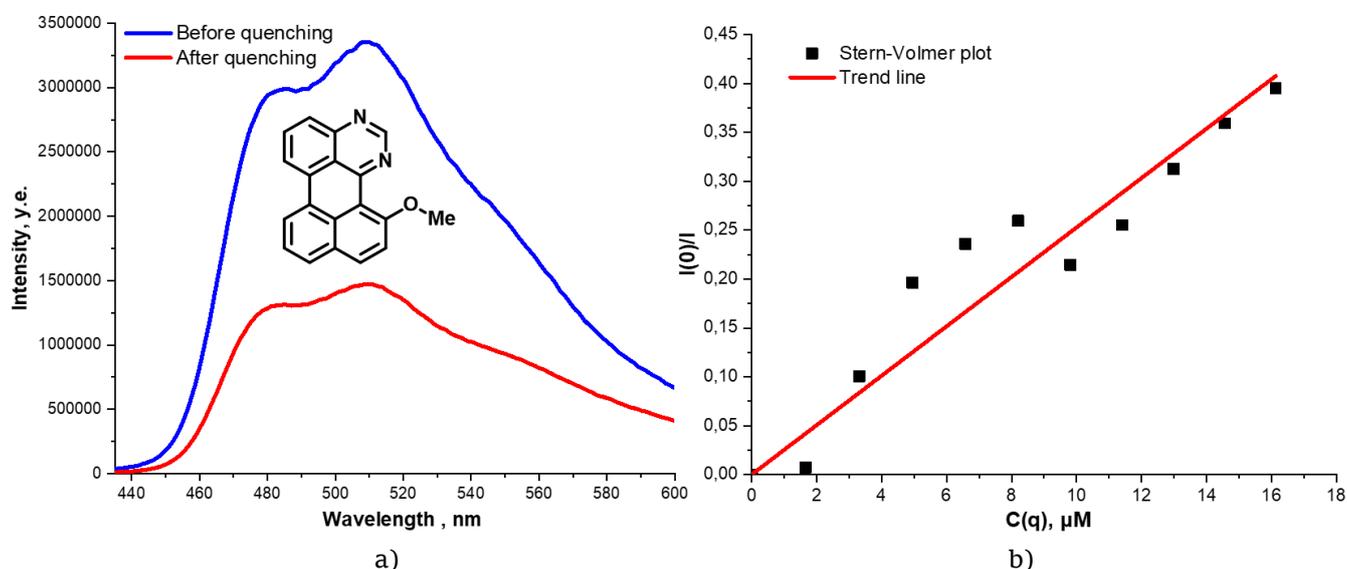
**Fig. 1** Normalised absorption/emission spectra of compounds **4** (a) and **5** (b)

A series of fluorescence quenching experiments were then performed by titrating the chemosensors **4**, **5** and perylene in acetonitrile solutions ( $5 \cdot 10^{-5}$  M) with RDX, DNT and PETN solutions in acetonitrile ( $5 \cdot 10^{-3}$  M) and with 2,4,6-trinitrophenol (picric acid) solution ( $5 \cdot 10^{-4}$  M) to confirm the results. It was found that increasing the PETN concentration does not cause fluorescence quenching for all the sensors considered. In all likelihood this could be due to the low stability of the donor-acceptor complex between these azaheterocycles and PETN. As for the other nitroanalytes, for RDX and DNT in the case of diazaperylene **5** and unsubstituted perylene fluorescence quenching is also practically not observed, and when ti-

trated with picric acid solution these compounds demonstrated Stern-Volmer constants values less than  $4400 \text{ M}^{-1}$ , which is an extremely low values compared to the literature data for other known chemosensors [1]. The opposite results were obtained when titrating naphtho[1,8-*ef*]perimidine **4** with RDX, DNT and picric acid solutions. Here, increasing the concentration of nitroanalytes causes intense quenching of the fluorescence. Thus, as a result of titration of compound **4** solution with picric acid, the resulting Stern-Volmer plot is linear, and the emission spectra of the solutions before and after the addition of the analyte show significant quenching of the fluorescence sensor (Fig. 2).

**Table 2** Results of calculations of HOMO-LUMO energies and driving force quenching of fluorescence of compounds **8,9** in interaction with nitroanalytes

Structure	HOMO, eV	LUMO, eV	LUMO <sub>sensor</sub> - LUMO <sub>quencher</sub> , eV		
			RDX	DNT	PETN
<b>4</b> 	-5.3973 	-2.3380 	0.1620	0.8620	0.9620
<b>5</b> 	-5.6322 	-2.5277 	-0.0277	0.6723	0.7723
[18] 	-4.201 	-2.302 	0.198	0.898	0.998



**Fig. 2** Fluorescence quenching plots of sensor **4** with picric acid solution

The obtained Stern-Volmer constants ( $636 \text{ M}^{-1}$  (RDX),  $1187 \text{ M}^{-1}$  (2,4-DNT),  $25279 \text{ M}^{-1}$  (picric acid)) are in agreement with values described in the literature for most chemosensors for nitro-containing explosives [1].

In addition, based on the fluorescence titration data for naphthoperimidine **4**, the values of the limits of detection (LOD) of the nitroanalytes were calculated according to the described method [19]. The obtained LOD values are 6.6 ppm (RDX), 13.9 ppm (DNT), 1.9 ppm (PA), which also corresponds to the literature data [1].

## 4. Conclusions

In conclusion, we have proposed a synthetic approach to the preparation of new fluorophores of the naphtho[1,8-*ef*]perimidines series based on the  $S_N^H$  methodology and further intramolecular cyclization of (naphthalene-1-yl)substituted quinazolines. The photophysical properties of the obtained diazaperylenes were studied, the HOMO-LUMO energies values and distribution of the obtained fluorophores were calculated by the DFT method and compared to those for nitroanalites and perylene. The possibility of using the obtained compounds as fluorescent chemosensors for the visual detection of nitroaromatic explosives, including RDX, was demonstrated.

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