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Novel covalently linked pyrene–aryl azide systems: synthesis of 1-(4-azidobenzoyloxy)pyrene

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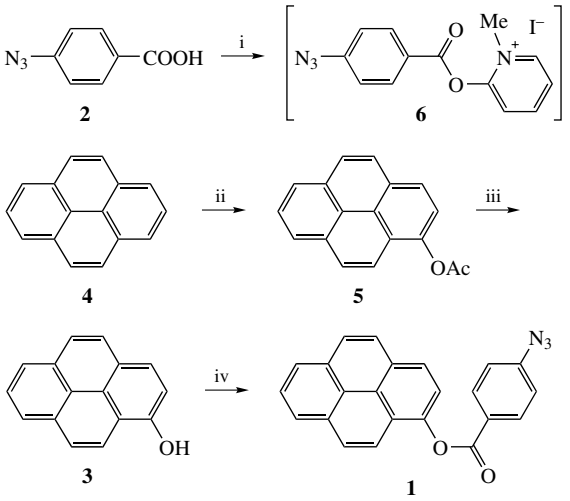
Lead tetraacetate oxidation of pyrene followed by hydrolysis affords 1-hydroxypyrene whose esterification with 4-azidobenzoic acid gives a new bifunctional luminophore characterized by UV and luminescence spectroscopy.

The bridged pyrene–aryl azide systems, a narrow and poorly investigated group of compounds,[1,2] can be interesting for studying photoaffinity labeling of biopolymers by binary reagents.[3–6] Binding of the pyrenyl and azidoaryl groups by bridges (X) of various lengths and structures allows one to vary the rate constants of elementary processes and investigate their dynamics and mechanism. Recently,[1] we have synthesized the first esters of pyren-1-ylalkanols with 4-azido-2,3,5,6-tetrafluorobenzoic acid. Primary physical and chemical processes that occur upon photoexcitation of these molecules have been studied using picosecond and nanosecond absorption and luminescence spectroscopy, and quantum chemistry.[1,7] Quenching of the local pyrene fluorescence by the azidoaryl moiety was revealed to occur by the electron and energy transfer mechanisms. Here, we report the synthesis and spectroscopic properties of previously unknown 1-(4-azidobenzoyloxy)pyrene **1**.

The esterification of 4-azidobenzoic acid **2**[8] with 1-hydroxypyrene **3**[9(a),(b)] was supposed to be the optimal access to compound **1**. Despite a simple structure of the 1-hydroxypyrene **3**, all known ways[9] of its synthesis from pyrene **4** are very complicated and require the use of special reagents and conditions. In this study, we used a direct acetoxylation of condensed polycyclic aromatic hydrocarbons with lead tetraacetate.[10,11] It was reported[12–14] that such an oxidation of pyrene **4** furnished 1-acetoxypyrene **5** and isomeric 1,6- and 1,8-diacetoxypyrenes, however, detailed procedures, product yields and approval of their structure were not given.



Scheme 1 *Reagents and conditions*: i, 2-chloro-1-methylpyridinium iodide, Et_3N; ii, $Pb(OAc)_4$, PhH–AcOH; iii, NaOH, EtOH–H_2O; iv, **2**, 2-chloro-1-methylpyridinium iodide, Et_3N, CH_2Cl_2, room temperature, 4 h.

In our hands, pyrene **4** was fully oxidized with a ~10% molar excess of $Pb(OAc)_4$ in a boiling (3 h) mixture of benzene and acetic acid (9:1 v/v). According to TLC and the chromatomass-spectrometric analysis, the reaction affords 1-acetoxypyrene **5** and diacetoxypyrene (Scheme 1). After a preparative chromatographic separation, compound **5** was obtained in 49% yield.[†] The structure of the target 1-acetoxypyrene **5** was identified by melting point, IR and mass spectra. The IR spectrum of **5** demonstrates a characteristic absorption band of an ester carbonyl group at 1763 cm^{-1}, and the mass spectrum contains the signal of molecular ion at *m*/*z* 260.

In the IR spectrum of diacetoxypyrene (yield 13%), the absorption bands for the carbonyl groups appear at 1763 cm^{-1}. Its mass spectrum exhibits the molecular ion at *m*/*z* 318. However, as compared with acetoxyarene **5**, diacetate looks in the chromatospectrogram as a broadened peak. These data along with ^1H NMR spectrum testify to the presence of isomers. The ^1H NMR spectrum contains double set of neigboring singlets for the protons of the methyl groups at ~2.5 ppm and the well-separated doublet signals from all protons of the pyrene nucleus in the 7.76–8.24 ppm region of close intensity. Most probably, this material is a mixture of 1,6- and 1,8-diacetoxypyrenes in a ~1:1 molar ratio.

1-Acetoxypyrene **5** was hydrolyzed in a boiling aqueous-ethanol NaOH solution. The following evaporation of organic solvent from the reaction mixture and its acidification afforded a white fine-crystalline precipitate of high-purity pyrenol **3**,[†] which was identified by its melting point, IR and mass spectra.

The esterification on using 2-chloro-1-methylpyridinium iodide (the Mukaiyama reagent)[15] was the method of choice to access 1-(4-azidobenzoyloxy)pyrene **1** (see our previous related studies[1]). Although Mukaiyama works[15] present no reactions of aromatic carboxylic acids with phenols, we anticipated that this method may be used for condensation of the chemically labile 4-azidobenzoic acid **2** with pyrenol **3** into ester **1** under similar condi-

[†] The course of reactions and the purity of products were controlled by TLC monitoring on Silufol UV 254 plates under UV light (eluents: benzene, dichloromethane, a mixture of benzene or dichloromethane and hexane).

tions, the salt **6** being an intermediate. In fact, 1-hydroxypyrene **3** readily reacted with acid **2** in the presence of pyridine salt and triethylamine at room temperature to give the expected ester **1** (36% yield after chromatographic separation) and by-products. The structure of ester **1** was fully confirmed by the IR and ^{1}H NMR spectra as well as by the HRMS data.† The mass spectra of **1**, obtained by the methods of electron and laser ionization, display the signals of molecular ion at *m*/*z* 363. The mass spectrum of **1**, recorded using the method of laser ionization, contains a characteristic signal with *m*/*z* 335, whose value corresponds to the molecular mass of 4-(pyren-1-yloxycarbonyl)phenylnitrene.

We also recorded the UV-VIS and luminescence spectra of 1-(4-azidobenzoyloxy)pyrene **1** (Figure 1).‡ The structure and positions of the absorption bands of compound **1** were found to be practically independent of the solvent polarity (hexane and acetonitrile), only small bathochromic shift of the long-wavelength bands (about 5 nm) was observed. The efficiency of compound **1**

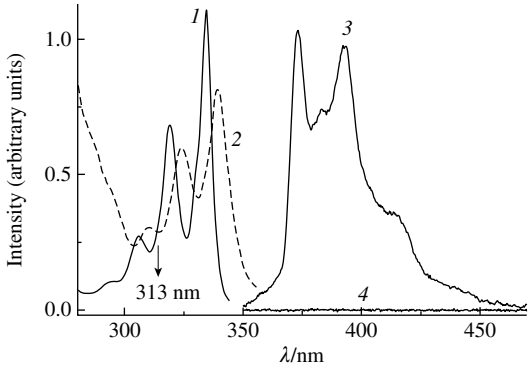


Figure 1 (*1*, *2*) UV-VIS and (*3*, *4*) luminescence spectra of (*1*, *3*) pyrene **4** and (*2*, *4*) (azidoaroyl)pyrene **1** in deoxygenated acetonitrile solution at room temperature; spectra (*3*, *4*) detected upon 313 nm photoexcitation.

fluorescence is negligible compared to that of pyrene **4** (see Figure 1). This is due to very efficient intramolecular quenching of the local pyrene fluorescence by the aryl azide group. The quantum yield of pyrene **4** fluorescence is about 0.3 and its singlet state lifetime is about 300 ns.[16,17] Thus, the quantum yield of compound **1** fluorescence could be estimated to be less than 5×10^{-4} and the singlet state lifetime to be less than 1 ns. A similar situation was observed for hexane solutions of **1**.

Note that UV irradiation of 1-(4-azidobenzoyloxy)pyrene **1** solutions leads to its rapid photodestruction accompanied by an increase of the structureless absorption in the 200–600 nm region.

Thus, we have prepared the new bifunctional compound 1-(4-azidobenzoyloxy)pyrene whose spectral data demonstrate very efficient intramolecular quenching of local pyrene fluorescence. This compound seems promising for further studies of the photoaffinity labeling mechanisms.

1-Acetoxypyrene **5** *and diacetoxypyrenes*. A solution of 0.30 g (1.48 mmol) of pyrene **4** and 0.73 g (1.65 mmol) of $Pb(OAc)_4$ in a mixture of 1.2 ml of glacial AcOH and 10.8 ml of anhydrous benzene was stirred under reflux for 3 h. The mixture was cooled, diluted with 25 ml of benzene and washed with H_2O (3×25 ml). The organic layer was evaporated *in vacuo*. The oily residue was chromatographed on silica gel with benzene to give a fraction, containing monoacetoxypyrene **5**, yield 0.19 g (49%), mp 104–105 °C (benzene–hexane, lit.,[12] 104–105 °C). IR ($CHCl_3$, ν/cm^{-1}): 1763 (C=O). MS, *m*/*z* (%): 260 (12, M$^+$), 218 (100), 189 (61), 163 (4), 95 (5), 43 (8). Then benzene was replaced by chloroform and finally, diacetoxypyrenes were eluted, yield 0.06 g (13%), mp 179–180 °C (benzene–hexane). ^{1}H NMR ($CDCl_3$), δ: 2.54 and 2.55 (2 s, 6 H, Me), 7.80 (d, 2 H, *J* 8.3 Hz), 8.05 and 8.09 (2 d, 4 H, *J* 8.1 Hz), 8.18 and 8.19 (2 d, 2 H, *J* 8.3 Hz). IR ($CHCl_3$, ν/cm^{-1}): 1763 (C=O). MS, *m*/*z* (%): 318 (10, M$^+$), 276 (12), 234 (100), 205 (15), 176 (28), 150 (5), 43 (14).

1-Hydroxypyrene **3**. A solution of 0.19 g (0.73 mmol) of 1-acetoxypyrene **5** and 0.19 g (4.75 mmol) of NaOH in a mixture of 8.1 ml of EtOH and 5.4 ml of H_2O was heated under reflux for 2.5 h. EtOH was distilled off *in vacuo* and the small portions of 2.7 ml of conc. HCl were added dropwise on cooling and stirring. The precipitate of **3** was filtered, washed with an excess of H_2O and dried in a dessicator over NaOH. Yield 0.15 g (94%), mp 180–182 °C (crystals from the reaction mass) (lit.,[9(a),(b)] 179–181 °C). IR ($CHCl_3$, ν/cm^{-1}): 3594 (OH). MS, *m*/*z* (%): 218 (100, M$^+$), 189 (82), 163 (6), 109 (9), 94 (32), 82 (4).

Synthesis of 1-(4-azidobenzoyloxy)pyrene **1**. Triethylamine (0.15 g, 0.21 ml, 1.52 mmol) and 2-chloro-1-methylpyridinium iodide (0.20 g, 0.78 mmol) were added to 4-azidobenzoic acid **2**[8] (0.13 g, 0.79 mmol) in 6.5 ml of dichloromethane at room temperature. The mixture was stirred for 20 min and 1-hydroxypyrene **3** (0.15 g, 0.69 mmol) was added. After that the reaction mixture was stirred for 4 h at the same temperature and then passed through silica gel with dichloromethane eluting. The eluate was concenrated on a rotary vacuum evaporator until complete removal of the solvent at a bath temperature not higher than 35 °C. The residue was triturated with 1 ml of hexane. The crystals of **1** were separated by filtration and washed with hexane (3×0.5 ml), 0.09 g of **1** (36%) was obtained, mp 164–165 °C (dichloromethane–hexane). ^{1}H NMR ($CDCl_3$), δ: 7.22 (d, 2 H, *J* 9.3 Hz), 7.90 (d, 1H, *J* 8.3 Hz), 7.97–8.13 (m, 5 H), 8.14–8.26 (m, 3 H), 8.40 (d, 2 H, *J* 8.7 Hz). IR ($CHCl_3$, ν/cm^{-1}): 1737 (C=O), 2107 and 2124 (N_3). HRMS (EI), *m*/*z* (%): 363.2 (15, M$^+$, calc. for $C_{23}H_{13}N_3O_2$, *m*/*z*: 363.1002282), 337.2 (4), 278.2 (3), 257.3 (3), 218.2 (17), 217.1 (31), 202.1 (4), 190.1 (7), 189.1 (41), 179.2 (23), 177.2 (4), 163.2 (4), 151.2 (6), 149.1 (34), 146.1 (20), 145.2 (10), 139.2 (8), 123.2 (14), 120.1 (73), 118.1 (29), 111.2 (25), 97.1 (37), 86.0 (42), 84.0 (68), 83.1 (38), 81.1 (32), 71.1 (66), 69.0 (53), 67.0 (24), 57 (100). HRMS (MALDI), *m*/*z* (%): 363.096 (15, M$^+$), 354.110 (8), 335.111 (16), 326.120 (4), 307.138 (10), 293.132 (7), 284.349 (4), 265.093 (5), 236.099 (10), 218.100 (100), 208.108 (10), 180.121 (4), 120.081 (25), 39.948 (18).

‡ The visible and UV-VIS absorption spectra were recorded on a Cary 50 (Varian) spectrophotometer. A MPF-4 fluorimeter (Hitachi) in combination with 16-bit analog-to-digital converter was used for luminescence measurements which were carried out in quartz cuvettes with optical layer thickness of 1 cm. Prior to measurements, the solutions of compound **1** were deoxygenated by bubbling argon for 15–20 min. Extra pure acetonitrile and hexane (Cryochrom Company) were used as the solvents.

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