

Short Note

N-isobutyl-1,8-bis(isobutylamino)-naphthalimide

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Abstract: Naphthalimides make up a class of organic molecules characterised by excellent spectroscopic properties due to their extended conjugate system. Furthermore, various asymmetric or symmetric compounds can be obtained from naphthalimides by the different functionalization that can be performed on the nitrogen and/or on the aromatic rings. The introduction of a wide range of substituents in different positions allows chemical and spectroscopic properties to be regulated. In this contribution, we report the synthesis and characterization of a new 4,5-amino-1,8-naphthalimide bearing three isobutyl substituents.

Keywords: naphthalimides; isobutyl; fluorescence

1. Introduction

Naphthalimides make up a class of organic molecules characterized by the presence of three fused rings, two of which are aromatics (Figure 1) [1]. The presence in the third ring of two sp^2 carbon atoms and a nitrogen atom leads to an extended conjugated system, thus leading to interesting spectroscopic properties.

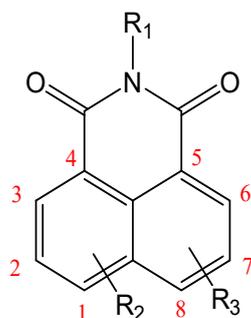


Figure 1. Generic chemical structure of a naphthalimide.

The naphthalimide nitrogen and aromatic rings can be functionalized with different substituents. In particular, although all aromatic carbon atoms can be functionalized, the naphthalimides functionalized in position 1 and 8 are the most diffused. These compounds can be obtained, starting from acenaphthene, which can be functionalized in the aromatic rings by introducing one of two substituents (see Scheme 1), leading to the final compounds of asymmetric [2] or symmetric [3] naphthalimides, respectively. The oxidation of aliphatic carbons in the starting acenaphthene leads to the corresponding anhydride, which can be easily functionalized with an aliphatic amine, introducing R_1 substituents. The nucleophilic substitutions in the aromatic rings, introducing R_2 , requires stronger conditions, particularly higher temperatures.



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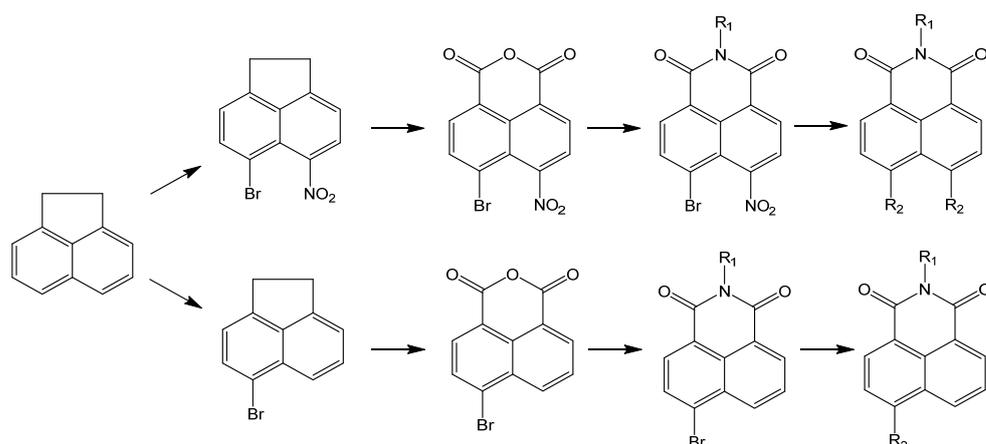
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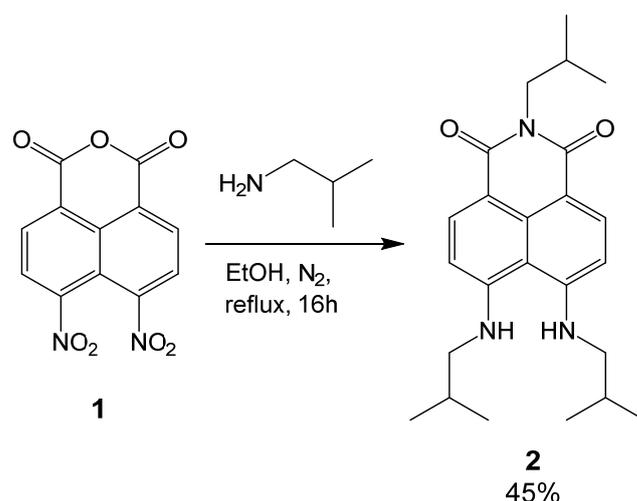


Scheme 1. Generic pathways for the synthesis of naphthalimides.

The introduction of a wide range of substituents in different positions leads to the possibility of tuning both chemical and spectroscopic properties. Naphthalimides show a large emission range (450–800 nm) with a strong Stoke shift; for these reasons, they are used as chromophores in a various fields, such as those relating to anticancer [4], cellular imaging [5–7], therapeutics [8], OLED materials [9], and explosive detection [10].

2. Results

Tri-isobutyl-substituted 4,5-diamino-1,8-naphthalimide **2** was obtained by the reaction of 4,5-dinitro-1,8-naphthalic anhydride **1** [11] with isobuthylamine in absolute ethanol (Scheme 2). In particular, the 4,5-dinitro-1,8-naphthalic anhydride **1** was obtained by the nitration of commercial acenaphthene, followed by the oxidation of aliphatic carbon atoms and the further nitration of the aromatic scaffold (see Scheme S1 in the Supplementary Materials).



Scheme 2. The synthesis of tri-isobutyl-substituted 4,5-diamino-1,8-naphthalimide **2**.

The reaction of **1** with a stoichiometric amount of isobuthylamine, both at room temperature and at reflux, did not lead to an appreciable amount of the desired compound **2**. After the addition of five equivalents of the amine, compound **2** could be obtained with a good yield. The reaction was performed at reflux, under nitrogen atmosphere overnight. The conversion of the starting reagent was monitored by TLC analysis. After the disappearance of the anhydride, the solvent was removed and the crude product was purified by flash chromatography. The desired compound was confirmed by ^1H , ^{13}C NMR,

and ESI-MS analyses. In particular, the ^1H NMR spectrum showed the presence of two signals at 8.43 and 6.77 ppm (doublets) relative to the aromatic protons (Figure 2, blue and green circles, respectively). In addition, two different signal patterns relative to the isobutyl groups could be found in the spectrum. The isobutyl group linked to the imide gave two doublets at 4.00 and 0.96 ppm, respectively, and a multiplet at 2.25 ppm; on the other hand, the two isobutyl groups linked to the aromatic scaffold offered a similar pattern, as well as a higher intensity with respect to the other, at 3.09, 2.05, and 1.11 ppm, respectively. In addition, NH protons appeared at 5.86 ppm as triplet (red circle in Figure 2). It can clearly be noted that the molecule had a plane of symmetry.

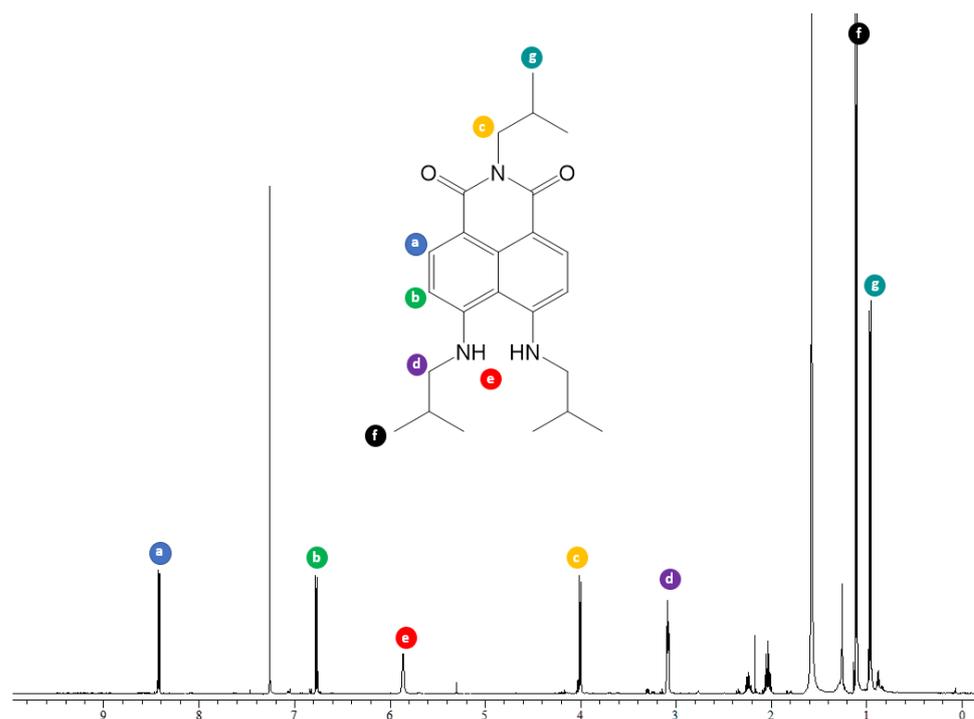


Figure 2. ^1H NMR spectrum of **2** in CDCl_3 and molecular structure, with correlation between signals and protons.

The ^{13}C NMR spectrum confirmed the structure of the molecule by the presence of 13 different signals (see Supplementary Materials). Furthermore, the ESI-MS spectrum of **2** in methanol showed the presence of two signals at m/z 396 and 428, relative to $[\text{M}+\text{H}]^+$ and $[\text{M}+\text{H}+\text{CH}_3\text{OH}]^+$, respectively (see Supplementary Materials).

The UV-vis spectrum of **2** in CHCl_3 showed an intense band, centered at 440 nm with $\epsilon = 43,351$, and a shoulder at 421 nm with $\epsilon = 38,147$ (Figure 3, red curve). Upon excitation at 440 nm, a large emission band with a maximum at 530 nm could be observed (Figure 3, black curve), with a Stoke shift of 90 nm.

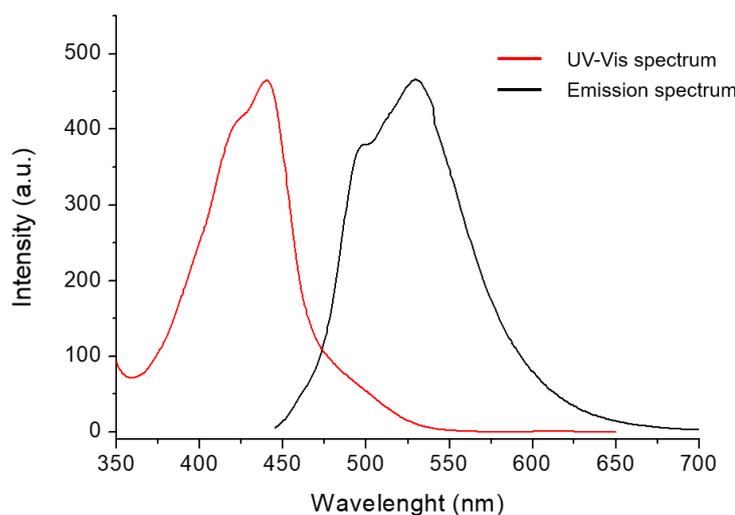


Figure 3. Normalized UV-vis (in red) and emission spectra (in black, λ_{ex} 440 nm) of **2** in CHCl_3 (1×10^{-6} M).

3. Experimental Section

3.1. General

The NMR experiments were carried out at 27 °C on a Varian UNITY Inova 500 MHz spectrometer (^1H at 499.88 MHz and ^{13}C NMR at 125.7 MHz) equipped with a pulse-field gradient module (Z axis) and a tuneable 5 mm Varian inverse detection probe (ID-PFG). The ESI mass spectrum was acquired on a API 2000-ABSciex (positive-ion mode). A JASCO V-560 UV-vis spectrophotometer, equipped with a 1 cm path-length cell, was used for UV-vis measurements (a resolution 0.1 nm). Luminescence measurements were carried out using a Cary Eclipse fluorescence spectrophotometer at room temperature. The emission was recorded at 90° with respect to the exciting line beam, using 5:5 slit widths for all measurements. All chemicals were of reagent grade and were used without further purification.

3.2. Synthesis of **2**

Next, 1.00 g (3.47×10^{-3} mol) of **1** [11] was transferred to a 100 mL two-neck flask and solubilized with 40 mL of absolute ethanol. Then, 1.72 mL of isobutylamine (0.0173 mol) was added to the solution, turning orange. The reaction was stirred at reflux in N_2 atmosphere for 16 h. Conversion was monitored by TLC analysis (silica gel: *n*-hexane/EtOAc 7:3), and the disappearance of the starting reagent and the presence of several spots were observed. Then, 0.62 g (yield 45%) of **2** was isolated by flash chromatography (*n*-hexane/EtOAc from 9:1 to 7:3). ^1H NMR (500 MHz; CDCl_3): δ 0.9 (d, $J = 6.5$ Hz, 6H, CH_3), 1.1 (d, $J = 6.5$ Hz, 12H, CH_3), 2.06 (m, 2H, CH), 2.2 (m, 1H, CH), 3.1 (d, $J = 6.5$ Hz, 4H, N- CH_2), 4.0 (d, $J = 6.5$ Hz, 2H, N- CH_2), 6.7 (d, $J = 8.5$ Hz, 2H, ArH), 8.4 (d, $J = 8.5$ Hz, 2H, ArH) ppm. ^{13}C NMR (125 MHz; CDCl_3): δ 20.3, 20.7, 27.3, 28.0, 46.7, 52.7, 107.0, 111.7, 112.4, 132.1, 133.6, 152.6, 164.8 ppm. Anal. Calcd. For $\text{C}_{24}\text{H}_{33}\text{N}_3\text{O}_2$: C, 72.88; H, 8.41; O, 8.09. Found: C, 72.81; H, 8.35; O, 8.01.

4. Conclusions

The synthesis and spectroscopic characterization of a new naphthalimide with three isobutyl substituents were both reported. This compound in the UV-vis spectrum shows an intense band, centered at 440 nm, and in the emission spectrum a broad band with a maximum at 530 nm and a Stoke shift of 90 nm, ideal for sensing application. In particular, the presence of two NH groups directly bounded to the chromophore helped to establish hydrogen bonds with many guests and monitor this event by fluorescence measurement. For this reason, we are working on the realization of the sensing platform, based on array

technology, containing also naphthalimide derivatives for the supramolecular recognition of different analytes, such as explosives, air pollutants, and human biomarkers.

Supplementary Materials: The following supporting information can be downloaded online. Scheme S1. Synthesis of **1**. Reagents and conditions: (a) HNO₃, CH₃COOH, 15 °C, 10 h; (b) Na₂Cr₂O₇, CH₃COOH, 120 °C, 12 h; (c) HNO₃, H₂SO₄, 70 °C, 2 h; Figure S1: ¹³C NMR spectrum of **2**. Figure S2: ESI-MS spectrum of **2**.

Author Contributions: Methodology, I.M.C. and R.S.; formal analysis and data curation, R.S.; conceptualization, G.T.S.; writing, review and editing, G.T.S. All authors have read and agreed to the published version of the manuscript.

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Data Availability Statement: Data are contained within the article. Compounds **1** and **2** can be provided by the authors.

Conflicts of Interest: The authors declare no conflict of interest.

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