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Communication

One Pot Synthesis of New Powerful Building Blocks in 1,8-Naphthalimide Chemistry

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Abstract: This communication reports a reliable one-pot synthetic protocol for preparation on a multigram scale of 3-bromo- and 3,4-dibromo-6-nitro-1,8-naphthalic anhydride from commercially available and economical 1,8-naphthalic anhydride. The synthetic steps used were nitration and selective bromination in sulfuric acid at room temperature. The reaction takes place under mild conditions and is completely controllable depending on the equivalents of the brominating reagent used. Both anhydrides are powerful building blocks in naphthalimide chemistry. In addition, their imides and esters were also synthesized.

Keywords: 1,8-naphthalic anhydride; 1,8-naphthalimide; nitration; selective bromination; building blocks

Citation: Mutovska, M.; Anastasova, D.; Simeonova, N.; Zagranyarska, I.; Vlahova, Z.; Ugrinova, I.; Stoyanov, S.; Zagranyarski, Y. One Pot Synthesis of New Powerful Building Blocks in 1,8-Naphthalimide Chemistry. *Molbank* **2024**, *2024*, M1914. https://doi.org/10.3390/M1914

Academic Editor: Nicholas Leadbeater

Received: 14 October 2024
Revised: 4 November 2024
Accepted: 6 November 2024
Published: 11 November 2024

1. Introduction

1,8-Naphthalimides (NI) belong to one of the most studied systems in the field of functional dyes and pigments [1]. They have found numerous applications as industrial colorants [2], dyes for fluorescent solar collectors, chemosensors [3–5], and also in photonics, electrophotographic devices, laser technology, biomarking and bioimaging [6–8], organic solar cells (OSCs) [9], organic semiconductors (OFET) [10,11], host or electron transport materials [12,13], and OLED technologies [14–16].

The introduction of different types of substituents (electron acceptors or electron donors), as well as varying their positions in the naphthalene core, allows a smooth change in the optoelectronic properties of these compounds. The halogen derivatives of NI are the main precursors for such functionalization of the naphthalene core (Figure 1). They can be synthesized by direct halogenation of 1,8-naphthalic anhydride or its imide derivatives, but several positions or combinations of positions can be substituted, so finding the most suitable conditions for achieving the desired substitution pattern is of utmost importance.

Bromination of 1,8-naphthalic anhydride is more selective than chlorination and can proceed in a controlled manner to the tribromo or tetrabromo derivative, depending on the solvent, temperature, and reaction time. Recently, we have synthesized tetrahalogeno-1,8-naphthalic anhydrides, as well as their respective imides and esters [17,18]. A more selective method for the synthesis of 3,4,6-tribromo naphthalic anhydride was also developed to allow new substitution patterns to be exploited [16].

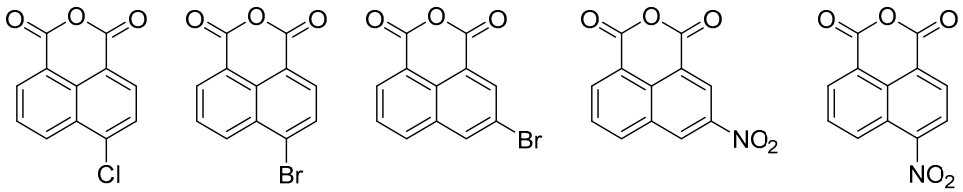


Figure 1. Commercially available 1,8-naphthalic anhydrides.

Other main precursors for NI functionalization are the mononitro derivatives, two of which are commercially available—3-nitro- and 4-nitro-1,8-naphthalic anhydride. The former is easily synthesized in one step from commercial 1,8-naphthalene anhydride [19,20], while the latter requires two steps of nitration and oxidation from acenaphthene [21–23], and its production on a large scale is considerably more difficult.

While combining a nitro and halogen substituent in the same building-block molecule has great potential for further transformations, only one type of such mixed precursor is reported in the literature—4-bromo-3-nitro-1,8-naphthalic anhydride [24–26] and 4-chloro-3-nitro-1,8-naphthalic anhydride [27]. The original procedure for their preparation used nitration of a starting 4-halogen naphthalic anhydride and was followed in numerous examples by other authors. Unfortunately, the anhydride is never obtained pure but as a mixture with a large amount (usually over 20%) of the isomeric 4-bromo-6-nitro-1,8-naphthalic anhydride. Another major drawback of this interesting building-block molecule is that subsequent imidization is accompanied by byproducts of nucleophilic substitution of the halogen at position 4 due to the high activation by the adjacent nitro group.

The lack of commercially available and inexpensive polysubstituted 1,8-naphthalic anhydrides or easily accessible synthetic protocols for their preparation greatly limits the possibility of synthesizing diverse polyfunctional derivatives of 1,8-naphthalimides.

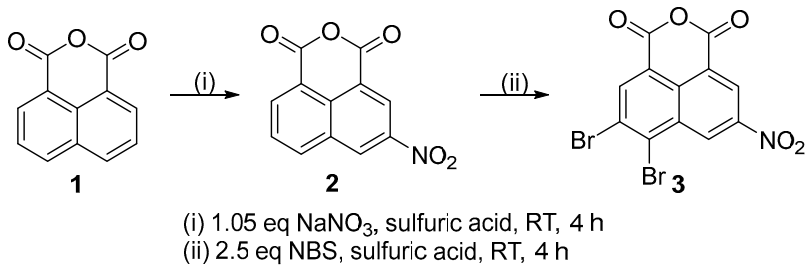
The presence of more than one substituent in the naphthalimide core offers new opportunities for the synthesis of new and interesting functional dyes and pigments based on 1,8-naphthalimide. The main goal was to create a successful protocol for the synthesis of mixed precursors containing bromo- and nitro-substituents simultaneously. The presence of halogen substituents offers a variety of possible reactions—nucleophilic aromatic substitution or metal-catalyzed cross-coupling reactions. On the other hand, the presence of a nitro group allows easy transformation into an amino group or an additional halogen substituent.

2. Results and Discussion

We chose an alternative synthetic strategy with an inverted order of substitutions, i.e., bromination of already nitrated naphthalic anhydride. Despite the strongly deactivated aromatic system due to the combined electron-withdrawing influence of the nitro and the anhydride groups, we envisaged that the use of a powerful brominating reagent such as *N*-Bromosuccinimide (NBS) in concentrated sulfuric acid would lead to a positive result.

Nitration of naphthalic anhydride was carried out in concentrated sulfuric acid and sodium nitrate as a nitrating reagent at room temperature. The reaction proceeded smoothly on a large scale (100 mmol), with complete conversion of the starting anhydride to the target nitro-product observed in 3 h (Scheme 1). After workup and recrystallization from chlorobenzene, we isolated 3-nitro-1,8-naphthalic anhydride **2** in a very high yield (84%).

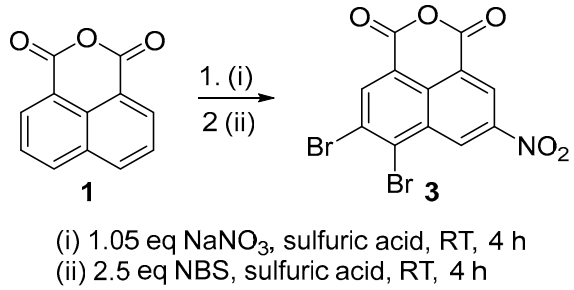
For the subsequent bromination step, we decided to try NBS in concentrated sulfuric acid at room temperature (Scheme 1). It is well known from the literature that this system is a potent brominating agent even for highly deactivated aromatic substrates [17]. The bromination reaction under these conditions proceeded successfully, and in 4 h a complete conversion of the starting 3-nitro-1,8-naphthalic anhydride into a dibrominated product was observed by TLC. After workup and recrystallization of the crude product from toluene, we isolated **3** in a high yield (92% calculated for the dibromo derivative).



Scheme 1. Synthesis of 3,4-dibromo-6-nitro-1,8-naphthalic anhydride.

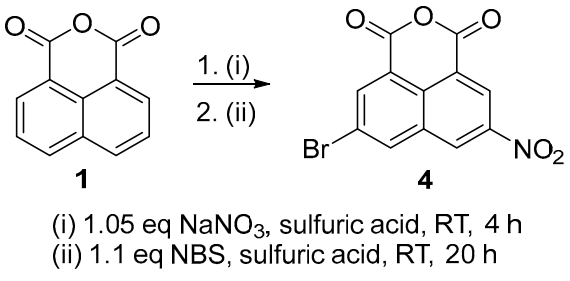
^{1}H- and ^{13}C-NMR spectra (shown in Supplementary Materials) unequivocally proved that the desired structure was obtained.

Since both nitration and bromination reactions take place in concentrated sulfuric acid, we decided to optimize the reaction to obtain 3,4-dibromo-6-nitro-1,8-naphthalic anhydride by conducting it in one pot. The starting 1,8-naphthalic anhydride was successively subjected to nitration and subsequent bromination in concentrated sulfuric acid at room temperature (Scheme 2). The result was impressive, isolating the target product in 90% yield after recrystallization (compared to the total yield of 77% when carried out in two steps).



Scheme 2. One pot synthesis of 3,4-dibromo-6-nitro-1,8-naphthalic anhydride.

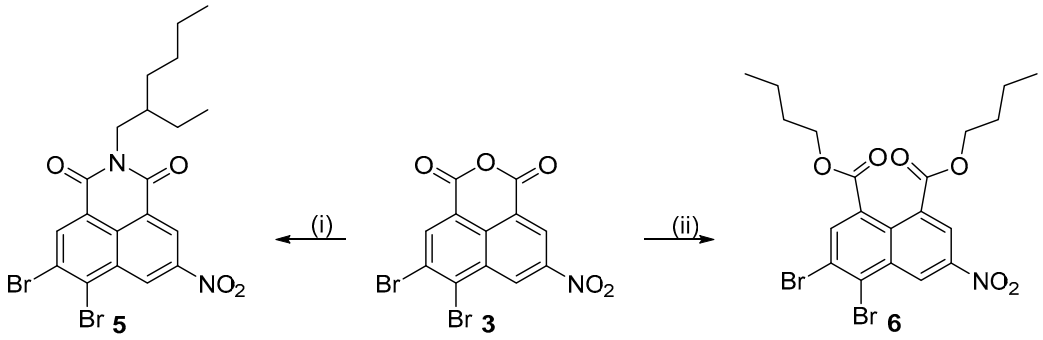
As a relatively more selective process, bromination can often be controlled depending on the amount of brominating agent or reaction conditions [16]. In our case, the use of 1.1 eq. of NBS under the same dibromination reaction conditions resulted in almost quantitative conversion of the starting anhydride to 3-bromo-6-nitro-1,8-naphthalic anhydride (Scheme 3). The slower conversion to the monobrominated product (20 vs. 4 h reaction time) can probably be explained by the lower concentration of brominating reagent.



Scheme 3. One-pot synthesis of 3-bromo-6-nitro-1,8-naphthalic anhydride.

The crude product was purified by recrystallization from toluene, although the higher solubility of the product led to significant losses (65% yield). This shortcoming can be avoided by using the crude product directly for further transformations, as we successfully proved for the imidization and alkylation reactions (*vide infra*). Even if anhydride **4** must be obtained in sufficient purity, the proposed recrystallization remains a good choice considering the reagents' low price and simplified synthetic procedure.

Imide and ester derivatives of functionalized 1,8-naphthalic anhydrides are important intermediates for further functionalization. In order to demonstrate how facile the options for transformation of 3,4-dibromo-6-nitro-1,8-naphthalic anhydride **3** are, it was converted to the corresponding imide and diester (Scheme 4). The imidization of anhydride **3** was carried out in a mixture of *N*-Methyl-2-pyrrolidone (NMP) and acetic acid (AcOH) at 110 °C for 30 min. After column chromatography purification, imide **5** was isolated in a very high yield (94%) on a gram scale.

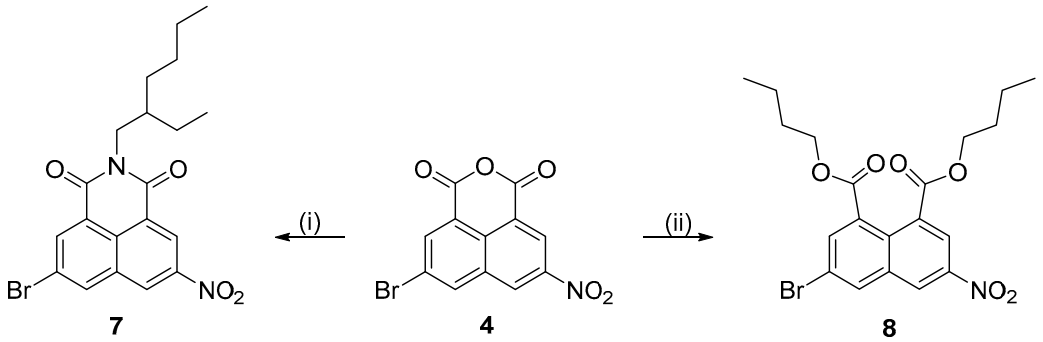


(i) 2-ethylhexylamine, NMP, AcOH, 110°C, 45 min
(ii) 1) KOH, aliquat 336, water 90°C, 15 min; 2) 1-bromobutane, reflux, 2 h

Scheme 4. Functionalization of 3,4-dibromo-6-nitro-1,8-naphthalic anhydride.

The alkylation of anhydride **3** to the corresponding dibutyl ester **6** was carried out under classical conditions. Initially, anhydride **3** was transformed into the dipotassium salt, which was alkylated with 1-bromobutane under phase-transfer catalysis in the presence of an aliquat 336. After workup and purification by column chromatography, ester **6** was isolated in a quantitative yield.

Analogous transformations were used for anhydride **4** to the corresponding imide and ester (Scheme 5). Under the same reaction conditions as for anhydride **3**, the reactions proceed in a very high yield on a gram scale.



(i) 2-ethylhexylamine, NMP, AcOH, 110°C, 45 min
(ii) 1) KOH, aliquat 336, water 90°C, 15 min; 2) 1-bromobutane, reflux, 2 h

Scheme 5. Functionalization of 3,4-dibromo-6-nitro-1,8-naphthalic anhydride.

Since the imidization and alkylation reactions proceed in an almost quantitative fashion, and to avoid recrystallization losses of anhydride **4**, we tried to use the crude anhydride directly in these very common transformations. The results were more than good, with yields just slightly lower compared to when a recrystallized anhydride **4** was used.

3. Materials and Methods

3.1. Materials

All starting materials and solvents were purchased from Fluorochem (Glossop, UK) and Fisher Scientific (Hampton, NH, USA) and used without additional purification.

NMR spectra were recorded on a Bruker Avance 500 MHz instrument (Bruker, Karlsruhe, Germany) operating at 500 and 126 MHz for ^{1}H and ^{13}C, respectively. $CDCl_3$ was used as a solvent. Chemical shifts are reported in δ units (ppm) and referenced to the residual solvent signals (^{1}H at 7.26 ppm and ^{13}C at 77.160 ppm). HRMS were recorded on a ThermoFisher Scientific—Orbitrap Exploris 120 (Source—HESI APCI, Comby Nozzle, Bremen, Germany). Elemental analyses were carried out on a Leco CHNS-932 (Leco Europe, Geleen, The Netherlands). IR spectra were recorded on a Spectrum Two FT-IR spectrometer (PerkinElmer, Waltham, MA, USA) equipped with an ATR accessory. Thin-layer chromatographic (TLC) analysis was performed on silica gel plates (Macherey-Nagel F60 254 40 × 80; 0.2 mm, Macherey-Nagel, Duren, Germany) using the solvent system dichloromethane/methanol as an eluent unless otherwise stated.

3.2. Synthesis of 5-Nitro-1H,3H-benzo[de]isochromene-1,3-dione(3-nitro-1,8-naphthalic Anhydride **2***)*

To a solution of 1,8-naphthalic anhydride (100.0 mmol, 19.82 g) in 150 mL conc. sulfuric acid, sodium nitrate (105.0 mmol, 7.24 g) was added in small portions (~500 mg) for a period of 1 h at room temperature. The reaction mixture was stirred additionally for 3 h at the same temperature. The mixture was poured into ice, and the precipitate was filtered, washed with water, and dried. The crude product was purified by recrystallization from chlorobenzene. Yield: 20.43 g (84%). The ^{1}H and ^{13}C NMR spectra were in agreement with those reported earlier [28].

3.3. Synthesis of 5,6-Dibromo-8-nitro-1H,3H-benzo[de]isochromene-1,3-dione(3,4-dibromo-6-nitro-1,8-naphthalic Anhydride **3***)*

From 3-nitro-1,8-naphthalic anhydride: To a solution of 3-nitro-1,8-naphthalic anhydride (50.0 mmol, 12.16 g) in 100 mL conc. sulfuric acid, N-bromosuccinimide (125.0 mmol, 22.25 g) was added. The reaction mixture was stirred for 4 h at room temperature. The mixture was poured into ice, and the precipitate was filtered, washed with water, and dried. The crude product was purified by recrystallization from toluene. Yield: 18.45 g (92%) as a pale yellow crystals.

From 1,8-naphthalic anhydride: To a solution of 1,8-naphthalic anhydride (100.0 mmol, 19.82 g) in 200 mL conc. sulfuric acid, sodium nitrate (105.0 mmol, 7.24 g) was added in small portions (~500 mg) for a period of 1 h at room temperature. The reaction mixture was stirred for an additional 3 h at the same temperature. *N*-bromosuccinimide (250.0 mmol, 44.50 g) was added at room temperature. The reaction mixture was stirred for an additional 4 h at the same temperature. The mixture was poured into ice, and the precipitate was filtered, washed with water, and dried. The crude product was purified by recrystallization from toluene. Yield 36.01 g (90%) as a pale yellow crystals, mp: 224.2–226.1 °C. ^{1}H NMR ($CDCl_3$, 500 MHz,) δ ppm: 9.62 (1H, d, ^{4}J = 2.1 Hz); 9.37 (1H, d, ^{4}J = 2.1 Hz); 8.92 (1H, s). ^{13}C NMR ($CDCl_3$, 126 MHz), δ ppm: 157.83, 157.80, 148.06, 139.96, 135.78, 132.77, 131.25, 130.98, 128.56, 127.00, 121.92, 119.14. FT-IR ν_{max} 1757, 1593, 1329, 1158, 1075, 1036, 802, 719 cm^{-1}. Anal. calcd. $C_{12}H_3Br_2NO_5$: C, 35.95; H, 0.75; N, 3.49; found: C, 35.78; H, 0.57; N, 3.27. HRMS (ESI) m/z 399.8441 (calcd for $C_{12}H_3Br_2NO_5$ $[M + H]^+$ 399.8451).

3.4. Synthesis of 5-Bromo-8-nitro-1H,3H-benzo[de]isochromene-1,3-dione(3-bromo-6-nitro-1,8-naphthalic Anhydride **4***)*

To a solution of 1,8-naphthalic anhydride (100.0 mmol, 19.82 g) in 200 mL conc. sulfuric acid, sodium nitrate (105.0 mmol, 7.24 g) was added in small portions (~500 mg) for a period of 1 h at room temperature. The reaction mixture was stirred for an additional 3 h at the same temperature. N-bromosuccinimide (110.0 mmol, 19.58 g) was added at

room temperature. The reaction mixture was stirred for an additional 20 h at the same temperature. The mixture was poured into ice, and the precipitate was filtered, washed with water, and dried. The crude product was purified by recrystallization from toluene. Yield: 20.93 g (65%) as an off-white solid, mp: 184.6–187.2 °C. ^{1}H NMR ($CDCl_3$, 500 MHz) δ ppm: 9.33 (1H, d, ^{4}J = 2.1 Hz); 9.15 (1H, d, ^{4}J = 2.1 Hz); 8.87 (d, 1H, ^{4}J = 1.8 Hz); 8.70 (1H, d, ^{4}J = 1.8 Hz). ^{13}C NMR (126 MHz, $CDCl_3$), δ ppm: 158.14, 158.08, 147.31, 139.48, 138.63, 132.57, 130.62, 129.23, 126.56, 124.21, 121.35, 120.92. FT-IR ν_{max} 1713, 1663, 1590, 1330, 1230, 1094, 806 cm^{-1}. Anal. calcd. $C_{12}H_4BrNO_5$: C, 44.75; H, 1.25; N, 4.35; found: C, 44.58; H, 1.33; N, 4.49. HRMS (ESI) *m*/*z* 321.9336 (calcd for $C_{12}H_4BrNO_5$ [M + H]$^+$ 321.9346).

3.5. Synthesis of 5,6-Dibromo-2-(2-ethylhexyl)-8-nitro-1H-benzo[de]isoquinoline-1,3(2H)-dione(N-(2-ethylhexyl)-3,4-dibromo-6-nitro-1,8-naphthalimide **5***)*

To a solution of 3,4-dibromo-6-nitro-1,8-naphthalic anhydride (50.0 mmol, 20.05 g) in 120 mL mixture of NMP and acetic acid (ratio 1:1), 2-ethylhexylamine (1.5 eq, 75.0 mmol, 12.40 mL) was added. The mixture was stirred for 45 min at 110 °C and then poured into a mixture of ice/water (200 g) and 10 mL hydrochloric acid. The precipitate was filtered, washed with water, and dried. The crude product was purified by column chromatography on silica using hexane/dichloromethane as an eluent. Yield: 24.07 g (94%) as an off-white solid mp: 132.7–133.7 °C. ^{1}H NMR ($CDCl_3$, 500 MHz,) δ ppm: 9.51 (1H, d, ^{4}J = 2.1 Hz); 9.33 (1H, d, ^{4}J = 2.1 Hz); 8.87 (1H, s); 4.12 (2H, qd, ^{2}J = 12.9 Hz, ^{3}J = 7.3 Hz); 1.91 (1H, dq, ^{2}J = 12.9 Hz, ^{3}J = 6.3 Hz); 1.28–1.42 (8H, m); 0.93 (3H, t, ^{3}J = 7.4 Hz); 0.88 (3H, t, ^{3}J = 7.0 Hz). ^{13}C NMR ($CDCl_3$,126 MHz) δ ppm: 162.17, 162.12, 147.99, 138.16, 133.61, 132.45, 129.59, 129.43, 127.98, 125.71, 125.03, 123.04, 44.92, 38.01, 30.80, 28.75, 24.14, 23.16, 14.22, 10.70. FT-IR ν_{max} 1713, 1663, 1590, 1329, 1288, 1231, 1094, 808 cm^{-1}. Anal. calcd. $C_{20}H_{20}Br_2N_2O_4$: C, 46.90; H, 3.94; N, 5.47; found: C, 47.01; H, 3.90; N, 5.29.

3.6. Synthesis of Dibutyl 3,4-Dibromo-6-nitronaphthalene-1,8-dicarboxylate **6**

A mixture of 3,4-dibromo-6-nitro-1,8-naphthalic anhydride (50.0 mmol, 20.05 g), KOH (120.0 mmol, 7.92 g) in 200 mL of water was stirred at 90 °C for 15 min. Aliquat 336 (2.0 mL) and 1-bromobutane (200 mmol, 21.58 mL) were added, and the resulting mixture was refluxed for 2 h. The reaction mixture was cooled down to room temperature and extracted with dichloromethane. The organic solvent was evaporated under reduced pressure, and the crude product was purified by column chromatography using hexane/dichloromethane as eluent on silica. Yield: 26.29 g (99%) as pale brownish crystallized oil mp: 48–51 °C. ^{1}H NMR ($CDCl_3$, 500 MHz,) δ ppm: 9.47 (1H, d, ^{4}J = 2.2 Hz); 8.74 (1H, d, ^{4}J = 2.2 Hz); 8.30 (1H s); 4.33 (4H, dt, ^{2}J = 13.4 Hz, ^{3}J = 6.8 Hz); 1.73–1.81 (4H, m); 1.42–1.52 (4H, m); 0.99 (3H, t, ^{3}J = 7.3 Hz); 0.98 (3H, t, ^{3}J = 7.3 Hz). ^{13}C NMR ($CDCl_3$,126 MHz) δ ppm: 166.60, 166.42, 146.22, 136.73, 134.41, 133.67, 131.23, 130.90, 130.12, 128.15, 126.18, 123.56, 66.48, 66.36, 30.61, 19.31, 19.29, 13.87. FT-IR ν_{max} 1714, 1334, 1304, 1242, 1183, 1150, 740 cm^{-1}. Anal. calcd. $C_{20}H_{21}Br_2NO_6$: C, 45.22; H, 3.98; N, 2.64; found: C, 45.42; H, 3.95; N, 2.37.

3.7. Synthesis of 5-Bromo-2-(2-ethylhexyl)-8-nitro-1H-benzo[de]isoquinoline-1,3(2H)-dione(N-(2-ethylhexyl)-3-bromo-6-nitro-1,8-naphthalimide **7***)*

To a solution of 3-bromo-6-nitro-1,8-naphthalic anhydride (50.0 mmol, 16.10 g) in 120 mL mixture of NMP and acetic acid (ratio 1:1), 2-ethylhexylamine (1.5 eq, 75.0 mmol, 12.40 mL) was added. The mixture was stirred for 45 min at 110 °C and then poured into a mixture of ice/water (200 g) and 10 mL hydrochloric acid. The precipitate was filtered, washed with water, and dried. The crude product was purified by column chromatography on silica using hexane/dichloromethane as an eluent. Yield: 19.93 g (92%) as an off-white solid, mp: 121.6–123.3 °C. Yield from crude 3-bromo-6-nitro-1,8-naphthalic anhydride 17.54 g (81%). ^{1}H NMR ($CDCl_3$, 500 MHz) δ ppm: 9.28 (1H, d, ^{4}J = 2.2 Hz); 9.03 (1H, d, ^{4}J = 2.2 Hz); 8.81 (1H, d, ^{4}J = 1.9 Hz); 8.57 (1H, d, ^{4}J = 1.8 Hz); 4.12 (2H, qd, ^{2}J = 12.9 Hz, ^{3}J = 7.3 Hz); 1.91 (1H, dq, ^{2}J = 12.9 Hz, ^{3}J = 6.3 Hz); 1.25–1.42 (8H, m); 0.93 (3H, t, ^{3}J = 7.4 Hz); 0.88 (3H, t, ^{3}J = 7.1 Hz). ^{13}C NMR ($CDCl_3$, 126 MHz) δ ppm: 162.50, 162.48, 147.23, 137.50, 136.97, 132.37, 128.77, 127.74, 125.10, 124.69, 124.53, 123.73, 44.84, 38.02, 30.80,

28.75, 24.13, 23.17, 14.22, 10.70. FT-IR ν_{max} 1708, 1660, 1531, 1337, 1234, 810 cm^{-1}. Anal. calcd. $C_{20}H_{21}BrN_2O_4$: C, 55.44; H, 4.89; N, 6.47; found: C, 55.20; H, 4.99; N, 6.70.

3.8. Synthesis of Dibutyl 3-Bromo-6-nitronaphthalene-1,8-dicarboxylate **8**

A mixture of 3-bromo-6-nitro-1,8-naphthalic anhydride (50.0 mmol, 16.10 g), KOH (120.0 mmol, 7.92 g) in 200 mL of water was stirred at 90 °C for 15 min. Aliquat 336 (2.0 mL) and 1-bromobutane (200 mmol, 21.58 mL) were added, and the resulting mixture was refluxed for 2 h. The reaction mixture was cooled down to room temperature and extracted with dichloromethane. The organic solvent was evaporated under reduced pressure, and the crude product was purified by column chromatography using hexane/dichloromethane as eluent on silica. Yield: 21.15 g (95%) as white crystals. Yield from crude 3-bromo-6-nitro-1,8-naphthalic anhydride 19.00 g (84%) as white crystals mp: 112.3–113.1 °C. ^{1}H NMR ($CDCl_3$, 500 MHz) δ ppm: 8.81 (1H, d, ^{4}J = 2.2 Hz); 8.70 (1H, d, ^{4}J = 2.4 Hz); 8.33 (1H, d, ^{4}J = 2.1 Hz); 8.22 (1H, d, ^{4}J = 2.0 Hz); 4.35 (2H, t, ^{3}J = 6.8 Hz); 4.33 (2H, t, ^{3}J = 6.8 Hz); 1.74–1.82 (4H, m); 1.43–1.52 (4H, m); 0.99 (3H, t, ^{3}J = 7.4 Hz); 0.98 (3H, t, ^{3}J = 7.4 Hz). ^{13}C NMR ($CDCl_3$, 126 MHz) δ ppm: 166.91, 166.79, 145.28, 136.26, 135.42, 134.79, 133.01, 132.67, 128.80, 126.71, 123.14, 121.70, 66.34, 66.26, 30.65, 19.32, 13.88. FT-IR ν_{max} 1714, 1531, 1333, 1260, 1180, 1020, 800 cm^{-1}. Anal. calcd. $C_{20}H_{22}BrNO_6$: C, 53.11; H, 4.90; N, 3.10; found: C, 52.97; H, 5.09; N, 3.27.

4. Conclusions

A reliable one-pot protocol for the multigram-scale synthesis of 3,4-dibromo-6-nitro-1,8-naphthalic anhydride and 3-bromo-6-nitro-1,8-naphthalic anhydride is proposed. Both anhydrides are obtained easily from commercially available and economical 1,8-naphthalic anhydride. Due to their high functionalization, we believe that the proposed anhydrides are powerful building block molecules in naphthalimide chemistry. Facile and effective procedures for conversion to the corresponding imides and esters are demonstrated. Both reactions proceed on a gram scale and in very high yields, giving access to new starting molecules for a variety of further functionalization.

Supplementary Materials: ^{1}H-, ^{13}C-NMR, HRMS, and FT-IR spectra copies of synthesized compounds can be found in the Supplementary Materials.

Author Contributions: Conceptualization, M.M. and Y.Z.; investigation, M.M., D.A., N.S., I.Z. and Z.V.; writing—original draft preparation, Y.Z., S.S. and I.U.; writing—review and editing, S.S., I.U. and Y.Z.; visualization, M.M. and I.Z.; supervision, Y.Z., S.S. and I.U.; project administration, Y.Z. and I.U.; funding acquisition, Y.Z. and I.U. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by the Bulgarian National Science Fund, grant number KP-06-H61/1.

Data Availability Statement: The original contributions presented in this study are included in the article/Supplementary Materials. Further inquiries can be directed to the corresponding author.

Acknowledgments: Y.Z., S.S., and M.M. gratefully acknowledge the funding by the European Union—NextGenerationEU, through the National Recovery and Resilience Plan of the Republic of Bulgaria, project No. BG-RRP-2.004-0008.

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

References

1. Zhang, T.; Zagranyarski, Y.; Skabeev, A.; Müllen, K.; Li, C. Perylene Pigments as Alternatives to Phthalocyanine and Indanthrone Blue. *Dye. Pigment.* **2021**, *196*, 109780. [CrossRef]
2. Dodangeh, M.; Grabchev, I.; Staneva, D.; Gharanjig, K. 1,8-Naphthalimide Derivatives as Dyes for Textile and Polymeric Materials: A Review. *Fibers Polym.* **2021**, *22*, 2368–2379. [CrossRef]

3. Anand, T.; Ashok Kumar, S.K.; Sahoo, S.K. A New Al3+ Selective Fluorescent Turn-on Sensor Based on Hydrazide-Naphthalic Anhydride Conjugate and Its Application in Live Cells Imaging. *Spectrochim. Acta A Mol. Biomol. Spectrosc.* **2018**, *204*, 105–112. [CrossRef]
4. Dey, N.; Bhattacharya, S. Switchable Optical Probes for Simultaneous Targeting of Multiple Anions. *Chem. Asian J.* **2020**, *15*, 1759–1779. [CrossRef] [PubMed]
5. Sun, X.; Dahlhauser, S.D.; Anslyn, E.V. New Autoinductive Cascade for the Optical Sensing of Fluoride: Application in the Detection of Phosphoryl Fluoride Nerve Agents. *J. Am. Chem. Soc.* **2017**, *139*, 4635–4638. [CrossRef]
6. Kaloyanova, S.; Zagranyarski, Y.; Ritz, S.; Hanulová, M.; Koynov, K.; Vonderheit, A.; Müllen, K.; Peneva, K. Water-Soluble NIR-Absorbing Rylene Chromophores for Selective Staining of Cellular Organelles. *J. Am. Chem. Soc.* **2016**, *138*, 2881–2884. [CrossRef] [PubMed]
7. Shang, Z.; Tian, S.; Wang, Y.; Zhang, C.; Meng, Q.; Zhang, R.; Zhang, Z. 1,8-Naphthalimide-Triphenylamine-Based Red-Emitting Fluorescence Probes for the Detection of Hydrazine in Real Water Samples and Applications in Bioimaging in Vivo. *Sens. Actuators B Chem.* **2024**, *398*, 134725. [CrossRef]
8. Day, A.H.; Domarkas, J.; Nigam, S.; Renard, I.; Cawthorne, C.; Burke, B.P.; Bahra, G.S.; Oyston, P.C.F.; Fallis, I.A.; Archibald, S.J.; et al. Towards Dual SPECT/Optical Bioimaging with a Mitochondrial Targeting, 99m Tc(i) Radiolabelled 1,8-Naphthalimide Conjugate. *Dalton Trans.* **2020**, *49*, 511–523. [CrossRef]
9. Liao, Q.; Kang, Q.; Xu, B.; Hou, J. Design and Application of an Asymmetric Naphthalimide-Based Molecule with Improved Hydrophobicity for Highly Stable Organic Solar Cells. *JACS Au* **2022**, *2*, 1918–1928. [CrossRef]
10. Kagatikar, S.; Salunkhe, P.; Sunil, D.; Kekuda, D. Organic and Hybrid Diode Features of an N-Type 1,8-Naphthalimide Derivative. *J. Electron. Mater.* **2023**, *52*, 5401–5411. [CrossRef]
11. Zhu, W.; Song, L.; Yang, Y.; Tian, H. Novel Bisthienylethene Containing Ferrocenyl-Substituted Naphthalimide: A Photo- and Redox Multi-Addressable Molecular Switch. *Chem. A Eur. J.* **2012**, *18*, 13388–13394. [CrossRef] [PubMed]
12. Kolosov, D.; Adamovich, V.; Djurovich, P.; Thompson, M.E.; Adachi, C. 1,8-Naphthalimides in Phosphorescent Organic LEDs: The Interplay between Dopant, Exciplex, and Host Emission. *J. Am. Chem. Soc.* **2002**, *124*, 9945–9954. [CrossRef]
13. Ulla, H.; Kiran, M.R.; Garudachari, B.; Ahipa, T.N.; Tarafder, K.; Adhikari, A.V.; Umesh, G.; Satyanarayan, M.N. Blue Emitting 1,8-Naphthalimides with Electron Transport Properties for Organic Light Emitting Diode Applications. *J. Mol. Struct.* **2017**, *1143*, 344–354. [CrossRef]
14. Ulla, H.; Raveendra Kiran, M.; Garudachari, B.; Satyanarayan, M.N.; Umesh, G.; Isloor, A.M. Blue Emitting Halogen–Phenoxy Substituted 1,8-Naphthalimides for Potential Organic Light Emitting Diode Applications. *Opt. Mater.* **2014**, *37*, 311–321. [CrossRef]
15. Arunchai, R.; Sudyoadsuk, T.; Prachumrak, N.; Namuangruk, S.; Promarak, V.; Sukwattanasinitt, M.; Rashatasakhon, P. Synthesis and Characterization of New Triphenylamino-1,8-Naphthalimides for Organic Light-Emitting Diode Applications. *New J. Chem.* **2015**, *39*, 2807–2814. [CrossRef]
16. Zagranyarski, Y.; Mutovska, M.; Petrova, P.; Tomova, R.; Ivanov, P.; Stoyanov, S. Dioxin-Annulated 1,8-Naphthalimides—Synthesis, Spectral and Electrochemical Properties, and Application in OLED. *Dye. Pigment.* **2021**, *184*, 108585. [CrossRef]
17. Abul-Futouh, H.; Zagranyarski, Y.; Müller, C.; Schulz, M.; Kupfer, S.; Görls, H.; El-khateeb, M.; Gräfe, S.; Dietzek, B.; Peneva, K.; et al. [FeFe]-Hydrogenase H-Cluster Mimics Mediated by Naphthalene Monoimide Derivatives of Peri-Substituted Dichalcogenides. *Dalton Trans.* **2017**, *46*, 11180–11191. [CrossRef]
18. Mutovska, M.; Skabeev, A.; Konstantinov, K.; Cabanetos, C.; Stoyanov, S.; Zagranyarski, Y. One-Pot Synthesis of Fused-Rings Heterocyclic Systems Based on Symmetrically Benzofuran Annulated 1,8-Naphthalimides. *Dye. Pigment.* **2023**, *220*, 4–10. [CrossRef]
19. Grayshan, P.H.; Peters, A.T. New Intermediates and Dyestuffs for Synthetic Fibres. Part IV. 2-Nitronaphthalene-1,8-Dicarboxylic Anhydride. *J. Chem. Soc. C Org.* **1971**, 3599. [CrossRef]
20. Khalaf, H.; Rimpler, M. 5-Isothiocyanato-1, 8-Naphthalindicarbonsäure-4-Methylphenylimid, Ein Neues Fluoreszenzreagenz Für Aminogruppen-Haltige Stoffe. *Hoppe Seylers Z Physiol. Chem.* **1977**, *358*, 505–512. [CrossRef]
21. Vasilev, A.A.; Baluschev, S.; Cheshmedzhieva, D.; Ilieva, S.; Castaño, O.D.; Vaquero, J.J.; Angelova, S.E.; Landfester, K. Assembly of New Merocyanine Chromophores with a 1,8-Naphthalimide Core by a New Method for the Synthesis of the Methine Function. *Aust. J. Chem.* **2015**, *68*, 1399. [CrossRef]
22. Dong, M.; Wang, Y.-W.; Peng, Y. Highly Selective Ratiometric Fluorescent Sensing for Hg^{2+} and Au^{3+}, Respectively, in Aqueous Media. *Org. Lett.* **2010**, *12*, 5310–5313. [CrossRef] [PubMed]
23. Khosravi, A.; Moradian, S.; Gharanjig, K.; Taromi, F.A. Synthesis and Characterization of Some Monoazo Disperse Dyestuffs Based on Naphthalimide Derivatives for Dyeing of Polyester Fabrics. *J. Chin. Chem. Soc.* **2005**, *52*, 495–502. [CrossRef]
24. Li, F.; Cui, J.; Guo, L.; Qian, X.; Ren, W.; Wang, K.; Liu, F. Molecular Design, Chemical Synthesis, and Biological Evaluation of '4-1' Pentacyclic Aryl/Heteroaryl-Imidazonaphthalimides. *Bioorg Med. Chem.* **2007**, *15*, 5114–5121. [CrossRef] [PubMed]
25. Tan, S.; Yin, H.; Chen, Z.; Qian, X.; Xu, Y. Oxo-Heterocyclic Fused Naphthalimides as Antitumor Agents: Synthesis and Biological Evaluation. *Eur. J. Med. Chem.* **2013**, *62*, 130–138. [CrossRef]
26. Suda, A.; Kawasaki, K.; Komiyama, S.; Isshiki, Y.; Yoon, D.-O.; Kim, S.-J.; Na, Y.-J.; Hasegawa, K.; Fukami, T.A.; Sato, S.; et al. Design and Synthesis of 2-Amino-6-(1H,3H-Benzo[de]Isochromen-6-Yl)-1,3,5-Triazines as Novel Hsp90 Inhibitors. *Bioorg. Med. Chem.* **2014**, *22*, 892–905. [CrossRef]

27. Braña, M.F.; Morán, M.; de Vega, M.J.P.; Pita-Romero, I.; Walker, N. Synthesis and Cytostatic Activity of Enynes, Enediynes and Dienediynes Linked to Intercalators. *Tetrahedron* **1995**, *51*, 9127–9138. [CrossRef]
28. Lovrinčević, V.; Zheng, D.; Baudin-Marie, M.; Marić, M.; Uzelac, L.; Škorić, I.; Ma, J.; Vuk, D. Aminonaphthalene and Aminoquinoline Photocages: Meta-Effect and Photo-Release of Carboxylic Acids and Alcohols. *J. Photochem. Photobiol. A Chem.* **2024**, *454*, 115715. [CrossRef]