Journal of Organic and Pharmaceutical Chemistry

Original Research

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UDC 547.658.2

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The Synthesis of N-Substituted 4-Fluoro-1,8-naphthalimides

Abstract

Aim. To synthesize 4-fluoro-1,8-naphthalic acid imide and its derivatives substituted in the imide ring.

Results and discussion. 4-Fluoro-1,8-naphthalimide was obtained using acenaphthene as the starting material. N-alkyl-4-fluoro-1,8-naphthalimides were synthesized *via* the phase transfer catalytic alkylation of 4-fluoro-1,8-naphthalimide with haloalkanes. Imidation of 4-fluoro-1,8-naphthalic anhydride with aminoacids resulted in the formation of N-carboxyalkyl-1,8-naphthalimides. These substances can be considered as potential fluorescent labels capable of binding to amino groups of various biological molecules as they contain carboxylic functionality in their structure.

Experimental part. The structure of the compounds synthesized was confirmed by FT-IR, ^{1}H NMR and ^{13}C NMR spectroscopy, and mass-spectrometry.

Conclusions. It has been shown that 4-fluoro-1,8-naphthalinedicarboxylic acid imide can be obtained following the synthetic route "acenaphthene – 5-fluoroacenaphthene – 4-fluoro-1,8-naphthalic anhydride – 4-fluoro-1,8-naphthalimide". 4-Fluoro-1,8-naphthalimide can be alkylated by butyl iodide and octyl bromide using tetraalkylammonium salts as a phase transfer catalyst resulted in N-butyl-4-fluoro-1,8-naphthalimide and N-octyl-4-fluoro-1,8-naphthalimide. As a result, N-carboxyalkyl-4-fluoro-1,8-naphthalimides have been obtained for the first time by aminolysis of 4-fluoro-1,8-naphthalic anhydride with glycine, β-alanine and 6-aminocaproic acid.

Keywords: acenaphthene; 1,8-naphthalimide; 1,8-naphthalic anhydride; alkylation; imidation

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Синтез N-заміщених 4-флуоро-1,8-нафталімідів

Анотація

Мета. Синтезувати імід 4-флуоро-1,8-нафталевої кислоти та його заміщені в імідному кільці похідні.

Результати та їх обговорення. Синтезовано 4-флуоронафталімід з використанням аценафтену як вихідної речовини. N-алкіл-4-флуоронафталіміди одержано міжфазно-каталітичним алкілуванням 4-флуоронафталіміду. Імідуванням 4-флуоронафталевого ангідриду амінокислотами отримано N-карбоксиалкіл-4-флуоронафталіміди, які є потенційними флуоресцентними мітками завдяки наявності в їхніх молекулах карбоксильної групи.

Експериментальна частина. Будову синтезованих сполук доведено методами ІЧ-, ^{1}Н ЯМР-, ^{13}С ЯМР-спектроскопії та мас-спектрометрії.

Висновки. З'ясовано, що 4-фторонафталімід може бути отриманий у результаті реалізації синтетичної схеми «аценафтен – 5-флуороаценафтен – 4-флуоронафталевий ангідрид – 4-флуоронафталімід». Доведено, що імід 4-флуоро-1,8-нафталендикарбонової кислоти може бути алкілований в умовах міжфазного каталізу солями тетраалкіламонію, у результаті чого вперше було отримано N-бутил-4-флуоронафталімід і N-октил-4-флуоронафталімід. Уперше синтезовано амінолізом 4-флуоронафталевого ангідриду гліцином, β-аланіном і 6-амінокапроновою кислотою та схарактеризовано N-карбоксиалкілзаміщені іміди 4-флуоро-1,8-нафталендикарбонової кислоти.

Ключові слова: аценафтен; нафталімід; нафталевий ангідрид; алкілування; імідування

Citation: Fedko, N. F.; Anikin, V. F.; Veduta, V. V. Synthesis of N-substituted 4-fluoro-1,8-naphthalimides. *Journal of Organic and Pharmaceutical Chemistry* **2022**, *20* (3), 25–30.
https://doi.org/10.24959/ophcj.22.263203
Received: *19 August 2022*; **Revised:** *19 September 2022*; **Accepted:** *21 September 2022*

Funding: The work is a part of the departmental research at the Odesa I. I. Mechnikov National University on the topic "Synthesis and properties of condensation products of substituted naphthalic anhydrides with aromatic and aliphatic amines" (the State Registration No 0120U102722; the research period: 2020–2024).
Conflict of interests: The authors have no conflict of interests to declare.

■ Introduction

Derivatives of 1,8-naphthalene dicarboxylic acid imide have attracted much attention in various fields of industry as dyes [1–3], fluorescent brightening agents [4], organic light emitting diode materials [5], fluorescent probes and labels [6, 7]. Moreover, a number of 1,8-naphthalimide derivatives have a high cytotoxic activity against cells of various tumors and viruses and are applied as anti-cancer and antiviral substances [8–10].

Among 4-halo-1,8-naphthalimides, which can be used to obtain fluorophores and are potential biologically active compounds, 4-fluoro-1,8-naphthalimide and its derivatives substituted in the imide ring are not described in the literature. Therefore, the synthesis of these compounds has become the aim of the present work.

■ Results and Discussion

The most common synthetic routes reported for the preparation of 4-chloro- and 4-bromosubstituted 1,8-naphthalimides involve electrophilic halogenation of acenaphthene followed by oxidation of the corresponding 5-haloacenaphthene and the subsequent imidation of 4-halosubstituted 1,8-naphthalic anhydride. The synthesis of 5-fluoroacenaphthene *via* the Balz-Schiemann reaction is described by authors of the manuscript [11] and is applied by us with some changes.

Nitration of acenaphthene (**1**) was carried out by the concentrated nitric acid in acetic acid at 10–15 °C giving 5-nitroacenaphthene (**2**) with the yield of 87%. Further, compound **2** was reduced with sodium dithionite using ethanol and water as the mixed solvent afforded 5-aminoacenaphthene (**3**) with the yield of 78%. The use of the above reducing system allowed us to increase the yield of amine **3** compared to the procedure given in the manuscript [11] where $SnCl_2$ with HCl were used as a reducing agent. Diazotization of amine **3** and the subsequent thermal decomposition of the derived tetrafluoroborate **4** gave desired 5-fluoroacenaphthene (**5**) with the yield of 37% (Scheme 1).

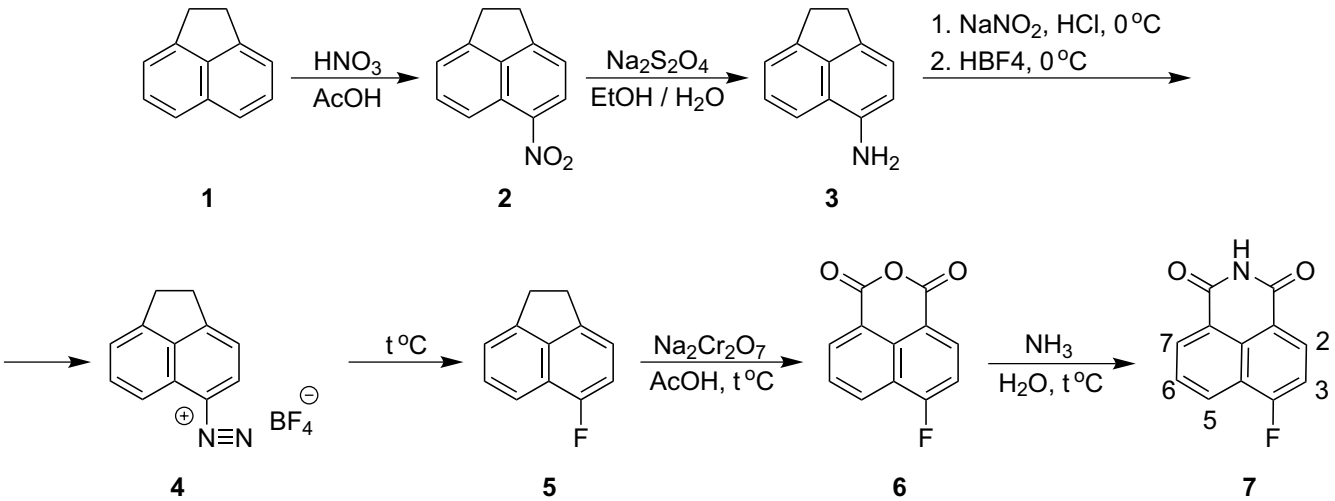
4-Fluoro-1,8-naphthalic anhydride (**6**) was obtained by oxidation of compound **5** with sodium dichromate in acetic acid with the yield of 47%. Initially formed during oxidation 4-fluoro-1,8-naphthalic acid was completely converted to the anhydride by heating at 100–110 °C. Finally, the reaction of anhydride **6** with aqueous ammonia gave the target 4-fluoro-1,8-naphthalimide (**7**) with the yield of 91%.

4-Fluoro-1,8-naphthalimide is a crystalline substance of a light-yellow color with m. p. > 350 °C, which has blue fluorescence.

N-Butyl-4-fluoro-1,8-naphthalimide (**8a**) and N-octyl-4-fluoro-1,8-naphthalimide (**8b**) were synthesized by alkylation of sodium salt of 4-fluoronaphthalimide **7** generated *in situ* with butyl iodide and octyl bromide using tetrabutylammonium bromide (TBAB) as a phase transfer catalyst. The synthesis was carried out in a two-phase system "benzene – 10% aqueous NaOH" resulted in 66% and 62% yields of compounds **8a** and **8b**, respectively (Scheme 2).

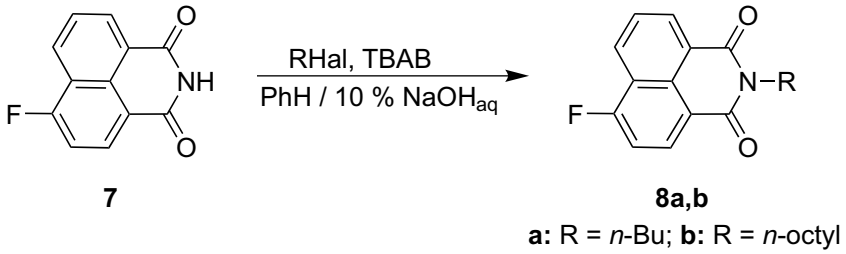
The N-alkyl-4-fluoro-1,8-naphthalimides **8a,b** obtained are light yellow crystalline substances with m. p. 102–103 °C for compound **8a** and 82–84 °C for compound **8b**, which have strong blue fluorescence. These compounds have much higher solubility in organic solvents compared to N-unsubstituted imide **7**.

Additionally, the novel N-carboxyalkyl-4-fluoro-1,8-naphthalimides **9a–c** were obtained by



Scheme 1. The synthesis of 4-fluoro-1,8-naphthalimide

ISSN 2308-8303 (Print) / 2518-1548 (Online)



7 **8a,b**

a: R = *n*-Bu; **b:** R = *n*-octyl

Scheme 2. The synthesis of N-alkyl-4-fluoro-1,8-naphthalimides

acylation of glycine, ß-alanine and 6-aminocaproic acid with 4-fluoro-1,8-naphthalic anhydride (**6**). The reactions were carried out using acetic acid as a solvent in order to avoid the possible nucleophilic substitution of the fluorine atom with the amino group (Scheme 3).

Compounds **9a–c** obtained are light yellow crystalline substances with m. p. 247–249 °C (**9a**), 236–238 °C (**9b**) and 176–178 °C (**9c**), which have strong blue fluorescence. These substances can be considered as potential fluorescent labels capable of binding to amino groups of various biological molecules as they contain carboxylic functionality in their structure.

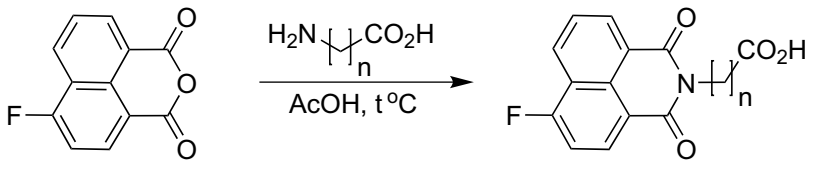
^{1}H and ^{13}C NMR, FT-IR, mass-spectra and data of the elemental analysis fully confirm the structure of compounds **7**, **8a,b**, **9a–c** synthesized.

The FT-IR spectra of compounds **7–9** have two intense absorption bands at 1667–1679 cm^{-1} and 1628–1635 cm^{-1}, corresponding to the characteristic stretching vibrations of the imide carbonyl groups. The absorption band at 1097–1105 cm^{-1} corresponds to the stretching vibrations of the C-F bond. The presence of N-H bond in 4-fluoro-1,8-naphthalimide **7** is confirmed by the absorption at 3170 cm^{-1}. The absorption bands of stretching vibrations of carbonyl and hydroxyl moieties in COOH groups of compounds **9a–c** are observed at 1702–1703 cm^{-1} and 3058–3060 cm^{-1}, respectively.

In the ^{1}H NMR spectra of compounds **7–9** the signals of aromatic protons are observed in the range of 7.6–8.7 ppm (the numeration of aromatic protons is presented in Scheme 1 for imide **7**). Proton H^{3}, interacting with the fluorine nuclei in position 4 and with proton H^{2}, gives the signal in the form of a doublet of doublets with the coupling constant J_{HF} = 10 Hz, while proton H^{2} has the signal in the form of a doublet. The signal of proton H^{6} is observed as a doublet of doublets, interacting with the magnetically inequivalent H^{5} and H^{7}. Protons H^{5} and H^{7} appear in the form of doublets. Signal of the imide proton in compound **7** appears as a singlet at 11.62 ppm. The coupling constants of aromatic protons have the values of 7.6–8.4 Hz, which are common for 1,8-naphthalimide derivatives. The signals of protons of alkyl groups attached to the nitrogen of the imide ring in compounds **8a,b** and **9a–c** are observed in the range of 0.8–4 ppm. The presence of carboxylic proton in the structures of acids **9a–c** is confirmed by the broad singlet in the range of 12.2–12.4 ppm.

Conclusions

It has been shown that 4-fluoro-1,8-naphthalinedicarboxylic acid imide can be obtained following the synthetic route "acenaphthene – 5-fluoroacenaphthene – 4-fluoro-1,8-naphthalic anhydride – 4-fluoro-1,8-naphthalimide". 4-Fluoro-1,8-naphthalimide can be alkylated by butyl iodide and octyl bromide using tetraalkylammonium salts as a phase transfer catalyst resulted in N-butyl-4-fluoro-1,8-naphthalimide and N-octyl-4-fluoro-1,8-naphthalimide. As a result, N-carboxyalkyl-4-fluoro-1,8-naphthalimides have been obtained for the first time by aminolysis of 4-fluoro-1,8-naphthalic anhydride with glycine, ß-alanine and 6-aminocaproic acid.



6 **9a-c**

a: n = 1; **b:** n = 2; **c:** n = 5

Scheme 3. The synthesis of N-carboxyalkyl-4-fluoro-1,8-naphthalimides

Experimental part

All reagents were purchased from commercial suppliers without further purification. ^{1}H NMR and ^{13}C NMR spectra were recorded at ambient temperature on a BRUKER WM 400 instrument using DMSO-d_6 as a solvent and TMS as an internal standard at 400 MHz and 100 MHz, respectively. IR spectra were obtained on a Perkin Elmer Frontier FT-IR spectrometer using KBr pellets. FAB mass spectra were obtained on a VG 70-70EQ mass spectrometer equipped with a Xe ion gun (8kV). The samples were mixed with a *m*-nitrobenzyl alcohol matrix. Elemental analyses were conducted using an elemental analyzer Vario MICRO cube (determination of C, H, N), and a 9000F Fluoride Analyzer (determination of F), their results were found to be in good agreement (not more than ±0.4%) with the calculated values. The control of the reaction progress and purity of the compounds synthesized were monitored by thin layer chromatography on Silicagel 60 F254 plates (Merck), followed by visualization in UV light, using chloroform as an eluent. Melting points were determined with an electrothermal capillary melting point apparatus.

The synthesis of 5-nitroacenaphthene (2)

Acenapthene (25 g, 0.16 mol) and acetic acid (100 mL) were placed in a 500 mL two-necked round-bottomed flask equipped with a magnetic stirrer, a reflux condenser, a thermometer, and a dropping funnel. The mixture was cooled to 10 °C, and nitric acid (20 mL, d = 1.36 g mL^{-1}) was added dropwise over 20 min while maintaining the temperature at 10–15 °C. The reaction mixture was vigorously stirred for 1 h. The resulting precipitate was filtered off, the filter cake was washed with distilled water and dried at 50 °C to give 28.7 g (87%) of the target product **2** as a yellow solid with m. p. 101.5–102.5 °C (Ref. [1] 101–102 °C).

The synthesis of 5-aminoacenaphthene (3)

5-Nitroacenaphthene (12 g, 0.06 mol) was dissolved in ethanol (120 mL), and hot water (60 mL) was poured into the solution. A solution of sodium dithionite (36 g, 0.21 mol) in water (60 mL) was added portionwise, and the reaction mixture was refluxed for 2 h. The solvents were evaporated, and the concentrated hydrochloric acid (45 mL) was added to the residue. The reaction mixture was heated on a water bath for 15 min, water (500 mL) was added; then the mixture was refluxed for 30 min and filtered hot. The filtrate was neutralized with aqueous ammonia to precipitate a crude product. The procedure of precipitation was repeated to give 8.9 g (78%) of the target product **3** as an off-white solid with m. p. 107–108 °C (Ref. [11] 107.5–108 °C).

The synthesis of 5-fluoroacenaphthene (5)

A mixture of 5-aminoacenaphthene (11.3 g, 0.07 mol), hydrochloric acid (21 mL) and water (100 mL) was refluxed for 30 min, then it was cooled to 0 °C and a solution of sodium nitrite (4.75 g, 0.07 mol) in water (12 mL) was added dropwise with vigorous stirring. The color of the solution changed to dark green. The reaction mixture was stirred for 30 min and filtered. The filtrate was cooled to -5 °C, and tetrafluoroboric acid (12 mL) was added, then the mixture was stirred for 30 min at -5 °C, the green precipitate was filtered and washed with cold methanol. The resulting acenaphthene-5-diazonium tetrafluroborate (**4**) was air-dried, followed by drying in a desiccator over the concentrated sulfuric acid. After that compound **4** was thermally decomposed, and the residue was crystallized from acetic acid to give 4.3 g (37%) of 5-fluoroacenaphthene (**5**) as a white solid with m. p. 94–95 °C (Ref. [12] 93–94 °C).

The synthesis of 4-fluoro-1,8-naphthalic anhydride (6)

Anhydrous sodium dichromate (16 g, 0.06 mol) was added portionwise by stirring to the solution of 5-fluoroacenaphthene (2.6 g, 0.015 mol) heated to 60 °C in acetic acid (50 mL), and the reaction mixture was refluxed by stirring for 6 h. After completion of the reaction the mixture was poured into cold water (100 mL), the precipitate was filtered off, washed with water and air-dried. The crude product was dissolved in 10% aqueous sodium hydroxide (100 mL). The solution was filtered hot, and the pH of the filtrate was adjusted to 2 with the concentrated hydrochloric acid. The resulting precipitate was filtered off, washed with water, and dried at 110 °C to give 1.52 g (47%) of the target product **6** as a light-brown solid with m. p. 220.5–221 °C (Ref. [12] 220–221 °C).

Preparation of 4-fluoro-1,8-naphthalimide (7)

A mixture of 4-fluoro-1,8-naphthalic anhydride (1.1 g, 0.005 mol) and 16% aqueous ammonia was heated on a water bath for 3 h. The reaction mixture was diluted with 10 mL of water. The resulting precipitate was filtered, washed with water, and dried at 110 °C. The crude product was purified by crystallization from acetic acid to obtain 4-fluoro-1,8-naphthalimide (**7**) as a light-yellow solid.

Yield – 1 g (93%). M. p. >350 °C (AcOH). Anal. Calcd for $C_{12}H_6FNO_2$, %: C 66.98; H 2.81; F 8.83;

ISSN 2308-8303 (Print) / 2518-1548 (Online)

N 6.51. Found, %: C 66.95; H 2.82; F 8.80; N 6.49. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm: 7.64 (1H, dd, J = 8.5, 10.0 Hz, H^3); 7.91 (1H, dd, J = 7.8, 7.6 Hz, H^6); 8.39 (1H, d, J = 7.8 Hz, H^5); 8.43 (1H, d, J = 8.5 Hz, H^2); 8.47 (1H, d, J = 7.6 Hz, H^7); 10.97 (1H, s, NH). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm: 112.1; 120.9; 125.4; 125.9; 129.8; 130.2; 130.7; 137.6; 138.9; 158.4; 159.1; 168.8 (d, $^1J_{CF}$ = 248 Hz, C^4). FT-IR (KBr), ν, cm^{-1}: 3170 (N-H); 3053; 1698 (C=O); 1672 (C=O); 1583; 1505; 1435; 1356; 1241; 1158; 1105 (C-F); 760. MS (FAB), m/z: 216 [M+H]$^+$.

Preparation of N-butyl-4-fluoro-1,8-naphthalimide (8a)

A mixture of finely ground 4-fluoro-1,8-naphthalimide (0.11 g, 0.5 mmol) and 10% aqueous sodium hydroxide (20 mL) was added to a solution of 1-iodobutane (0.19 g, 1 mmol) and 0.02 g of TBAB in benzene. The reaction mixture was vigorously stirred at 80 °C for 9 h, then it was cooled to the room temperature; the organic layer was separated, dried over calcium chloride and filtered through aluminium oxide to remove the phase transfer catalyst. The solvent was evaporated to give the target product **8a** as a light-yellow solid.

Yield – 0.08 g (66%). M. p. 102–103 °C. Anal. Calcd for $C_{16}H_{14}FNO_2$, %: C 70.84; H 5.20; F 7.00; N 5.16. Found, %: C 70.81; H 5.19; F 7.02; N 5.15. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm: 0.88 (3H, t, J = 6.4 Hz, CH_3); 1.22–1.24 (2H, m, CH_2); 1.62–1.64 (2H, m, CH_2); 4.04 (2H, t, J = 7.2 Hz, CH_2N); 7.60 (1H, dd, J = 8.8, 9.8 Hz, H^3); 8.40 (1H, d, J = 8.0 Hz, H^5); 8.50 (1H, d, J = 7.0 Hz, H^7); 7.88 (1H, dd, J = 8.0, 7.4 Hz, H^6); 8.42 (1H, d, J = 8.8 Hz, H^2). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm: 13.8; 19.8; 29.4; 40.1; 111.6; 120.9; 121.8; 125.7; 125.9; 130.2; 130.7; 137.5; 138.9; 158.5; 159.3; 168.7 (d, $^1J_{CF}$ = 250 Hz, C^4). FT-IR (KBr), ν, cm^{-1}: 2926; 2852; 1673 (C=O); 1631 (C=O); 1598; 1450; 1341; 1234; 1104 (C-F); 752. MS (FAB), m/z: 272 [M+H]$^+$.

Preparation of N-octyl-4-fluoro-1,8-naphthalimide (8b)

Compound **8b** was prepared similarly to compound **8a** using 4-fluoro-1,8-naphthalimide (0.11 g, 0.5 mmol), 10% aqueous sodium hydroxide (20 mL), 1-bromooctane (0.2 g, 1 mmol), benzene (20 mL) and TBAB as a phase transfer catalyst. The title compound was obtained as a light-yellow solid.

Yield – 0.1 g (62%). M. p. 82–84 °C. Anal. Calcd for $C_{20}H_{22}FNO_2$, %: C 73.37; H 6.77; F 5.80; N 4.28. Found, %: C 73.35; H 6.78; F 5.78; N 4.29. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm: 0.83 (3H, t, J = 6.4 Hz, CH_3); 1.22–1.29 (10H, m, $(CH_2)_5$); 1.61–1.63 (2H, m, CH_2); 3.98 (2H, t, J = 6.8 Hz, CH_2N); 7.65 (1H, dd, J = 8.9, 9.4 Hz, H^3); 7.91 (1H, dd, J = 7.8, 7.1 Hz, H^6); 8.45 (1H, d, J = 8.9 Hz, H^2); 8.49 (1H, d, J = 7.8 Hz, H^5); 8.51 (1H, d, J = 7.1 Hz, H^7). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm: 14.2; 22.7; 26.7; 29.1; 29.5; 30.3; 31.9; 40.4; 111.7; 120.8; 121.9; 125.7; 125.9; 130.1; 130.7; 137.6; 138.9; 158.7; 159.5; 168.8 (d, $^1J_{CF}$ = 250 Hz, C^4). FT-IR (KBr), ν, cm^{-1}: 2924; 2851; 1679 (C=O); 1635 (C=O); 1586; 1438; 1373; 1354; 1232; 1097 (C-F); 781. MS (FAB), m/z: 328 [M+H]$^+$.

The procedure for the synthesis of N-carboxymethyl-4-fluoro-1,8-naphthalimide (9a)

A mixture of 4-fluoro-1,8-naphthalic anhydride (0.1 g, 0.46 mmol) and glycine (0.17 g, 2.3 mmol) in acetic acid (20 mL) was refluxed for 36 h, cooled to room temperature, and poured in cold water (100 mL). The resulting precipitate was filtered, air-dried, and crystallized from ethanol to give the target product **9a** as a white solid.

Yield – 0.08 g (64%). M. p. 247–249 °C. Anal. Calcd for $C_{14}H_8FNO_4$, %: C 61.54; H 2.95; F 6.95; N 5.13. Found, %: C 61.58; H 2.94; F 6.97; N 5.14. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm: 4.20 (2H, s, CH_2); 8.00 (1H, dd, J = 7.8, 8.4 Hz, H^6); 8.04 (1H, dd, J = 8.0, 10 Hz, H^3); 8.45 (1H, d, J = 7.8 Hz, H^5); 8.61 (1H, d, J = 8.4 Hz, H^7); 8.63 (1H, d, J = 8.0 Hz, H^2); 12.22 (1H, s, COOH). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm: 42.2; 112.1; 120.9; 125.4; 125.7; 129.7; 130.1; 130.5; 137.8; 138.8; 158.6; 159.2; 168.7 (d, $^1J_{CF}$ = 252 Hz, C^4); 169.5. FT-IR (KBr), ν, cm^{-1}: 3061 (O-H); 1702 (C=O); 1667 (C=O); 1630 (C=O); 1573; 1590; 1506; 1335; 1299; 1226; 1096 (C-F); 852; 775. MS (FAB), m/z: 274 [M+H]$^+$.

The procedure for the synthesis of N-(2-carboxyethyl)-4-fluoro-1,8-naphthalimide (9b)

Compound **9b** was prepared similarly to compound **9a** using 4-fluoro-1,8-naphthalic anhydride (0.1 g, 0.46 mmol) and β-alanine (0.2 g, 2.3 mmol) in acetic acid (20 mL), the mixture was refluxed for 32 h. The title compound was obtained as a white solid.

Yield – 0.11 g (83%). M. p. 236–238 °C. Anal. Calcd for $C_{15}H_{10}FNO_4$, %: C 62.72; H 3.51; F 6.61; N 4.88. Found, %: C 62.70; H 3.52; F 6.59; N 4.89. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm: 2.61 (2H, t, J = 6.8, CH_2); 4.26 (2H, t, J = 6.8, CH_2); 8.00 (1H, dd, J = 7.8, 9.8 Hz, H^3); 8.04 (1H, dd, J = 7.8, 8.2 Hz, H^6); 8.43 (1H, d, J = 7.8 Hz, H^5); 8.59 (1H, d, J = 7.8 Hz, H^2); 8.61 (1H, d, J = 8.2, H^7); 12.34 (1H, s). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm: 31.2; 36.5; 112.1; 120.8; 125.4; 125.7; 129.8; 130.1; 130.4; 137.9; 138.9; 158.7; 159.2; 168.8 (d,

$^1J_{CF}$ = 254 Hz, C^4); 171.5. FT-IR (KBr), ν, cm^{-1}: 3058 (O-H); 2922; 1703 (C=O); 1668 (C=O); 1630 (C=O); 1590; 1440; 1348; 1233; 1221; 1102 (C-F); 853; 781. MS (FAB), m/z: 288 $[M+H]^+$.

The procedure for the synthesis of N-(5-carboxypentyl)-4-fluoro-1,8-naphthalimide (9c)

Compound **9c** was prepared similarly to compound **9a** using 4-fluoro-1,8-naphthalic anhydride (0.1 g, 0.46 mmol) and 6-aminocaproic acid (0.3 g, 2.3 mmol) in acetic acid (20 mL), the mixture was refluxed for 30 h. The title compound was obtained as a white solid.

Yield – 0.08 g, 57%. M. p. 176–178 °C. Anal. Calcd for $C_{18}H_{16}FNO_4$, %: C 65.65; H 4.90; F 5.77; N 4.25. Found, %: C 65.63; H 4.91; F 5.79; N 4.24. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm: 2.52–2.54 (6H, m, $(CH_2)_3$); 2.60 (2H, t, CH_2, J = 6.4 Hz); 4.26 (2H, t, CH_2, J = 6.8 Hz); 8.04 (1H, dd, J = 7.6, 8.4 Hz, H^6); 8.14 (1H, dd, J = 7.7, 9.8 Hz, H^3); 8.42 (1H, d, J = 7.6 Hz, H^5); 8.58 (1H, d, J = 7.7 Hz, H^2); 8.61 (1H, d, J = 8.4 Hz, H^7); 12.4 (1H, s). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm: 24.5; 26.4; 30.5; 34.4; 40.4; 112.5; 120.9; 125.5; 125.8; 129.9; 130.2; 130.5; 137.8; 139.1; 158.9; 159.1; 168.7 (d, $^1J_{CF}$ = 254 Hz, C^4); 177.5. FT-IR (KBr), ν, cm^{-1}: 3060 (O-H); 2940; 1702 (C=O); 1667 (C=O); 1628 (C=O); 1573; 1506; 1437; 1335; 1226; 1103 (C-F); 861; 777. MS (FAB), m/z: 330 $[M+H]^+$.

Acknowledgements

The authors sincerely appreciate the support of the Faculty of Chemistry of Taras Shevchenko National University of Kyiv for performing the spectral analysis of the compounds synthesized. We also gratefully thank all brave defenders of Ukraine that made finalizing this publication possible.

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ISSN 2308-8303 (Print) / 2518-1548 (Online)