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Short Note

N,N-Bis(7-nitrobenz[c][1,2,5]oxadiazol-4-yl)cystamine

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Abstract: Background: New amino derivatives of NBD type are of high interest due to their strong fluorescence, while compounds containing a disulphide moiety are of high interest in nano-chemistry due to their easiness of attaching to noble nanoparticles. Therefore, in this work a new fluorescent derivative of NBD and cystamine was obtained. Methods: The reaction between cystamine and NBD-chloride occurs straightforwardly, and the isolated new compound was characterized by IR, UV-Vis, fluorescence, ^{1}H- and ^{13}C-NMR, MS, etc. Results: Structural analysis confirmed the proposed structure and highlighted the fluorescence behavior. Conclusions: A new fluorescent derivative of cystamine was obtained and characterized by different means.

Keywords: fluorescence; derivatization; NBD; cystamine

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1. Introduction

Amino-derivatives of nitrobenzofurazan are usually highly fluorescent compounds used in a plethora of chemical and analytical processes [1]. These derivatives are simply obtained from an amine in reaction with 4-chloro-7-nitrobenz[*c*][1,2,5]oxadiazole (known as NBD-chloride or NBD-Cl). NBD-Cl is a non-fluorescent reagent that after reaction with primary or secondary amines yields the fluorescent compounds. Therefore, NBD chloride has been extensively used as a derivatizing reagent for easily obtaining fluorescent derivatives employed in the detection and analysis of many amines of interest, including amino acids [2–4].

The possibility of attaching different compounds onto noble metal nanoparticle surfaces occurs through chemical interaction, one of the most-used classes of compounds being thiols or disulphides, and this structural motif is required, considering the strong affinity of sulphur for noble metals such as gold or silver is well-known [5,6].

The literature data has shown that for nano-chemistry processes a lot of NBD-derivatives have been synthesized and studied, including those derived from dendrimers, and so on [7]. In the quest for obtaining new fluorescent disulphides, we present in this communication the synthesis and characterization of a new, unpublished compound that brings together in a simple molecule the disulphide moiety as an anchor for nanoparticle ligand exchange and the NBD-moiety as a fluorescent label.

2. Results and Discussion

The synthesis of the title compound occurs straightforwardly from commercially available materials, such as cystamine and NBD-Cl (Figure 1). The reaction is fast and does not require supplementary heating, taking place at room temperature in the presence of a base (sodium hydrogen carbonate, necessary to retain the hydrochloric acid formed during the reaction). Isolation of the final compound is achieved either by solvent removal or by precipitation from water, and purification is carried out by column chromatography.

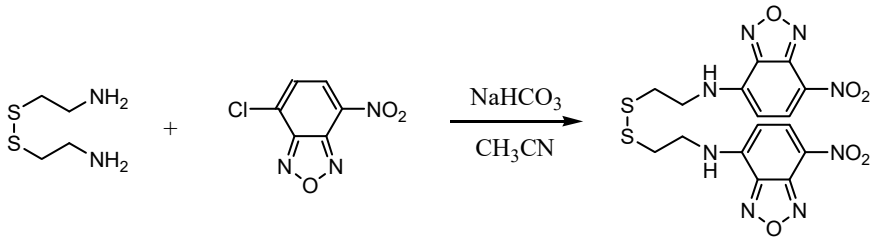

Figure 1. Chemical synthesis of the NBD-derivative of cystamine.

Structural analysis confirmed the structure of the compound. Thus, the IR spectrum (see Figure S1 from Supplementary Material) showed the presence of the amino groups at about 3340 cm^{-1}, aromatic bonds at 3050 cm^{-1}, and aliphatic moieties at 2920 cm^{-1}, while nitro groups could be found at 1580 cm^{-1}.

The UV-Vis spectrum had as its main characteristic the absorption band at 329 nm and 460 nm (Figure S2 from Supplementary Material), and the fluorescence band appeared at 536 nm (Figure S3 from Supplementary Material). These also confirm the well-known characteristics of the NBD moiety as chromophore and fluorophore [8,9]. The ^{1}H-NMR spectrum (Figure S4 from Supplementary Materials) presented the N*H* at 9.49 ppm, and the two hydrogen nuclei from the NBD moiety appeared as doublets at 8.46 and 6.42 ppm, while the aliphatic CH_2 were encountered at 3.75 and 3.08 ppm. The ^{13}C-NMR spectrum (Figure S5 from Supplementary Materials) and ESI-MS spectrum (Figure S6 from Supplementary Materials) also confirmed the structure.

3. Materials and Methods

Chemicals and apparatus. All chemicals, solvents, and materials were obtained from Merck, Sigma-Aldrich, or Chimopar, and were used as received.

For the UV-Vis spectrum, a V-560 Jasco UV-Vis apparatus was employed using 1 cm path length quartz cells and methanol as a solvent, while for fluorescence a FP-6500 Jasco spectrofluorometer was employed (Jasco Int. Co. Ltd., Tokyo, Japan). The fluorescence was recorded using λ_{ex} = 460 nm. The infrared spectrum (4000–400 cm^{-1}) was recorded on a Jasco FTIR 4700 spectrophotometer equipped with an ATR PRO ONE accessory at 4 cm^{-1} resolution. The ^{1}H- and ^{13}C-NMR were recorded in deuterated dimethylsulfoxide (DMSO-d_6) at room temperature using a Bruker Advance spectrometer operating at 500 MHz for ^{1}H and 125 MHz for ^{13}C. The residual solvent peaks were taken as the internal reference and the chemical shifts δ were reported as ppm values. For the MS spectrum a Varian 310—MS LC/MS/MS triple quadrupole mass spectrometer was used.

Synthesis. A total of 200 mg cystamine (1.1 mmol) and 500 mg NBD-chloride (2.5 mmol) dissolved in 50–100 mL acetonitrile was stirred at room temperature for a day in the presence of 2–3 g of solid sodium hydrogen carbonate. After filtration and removal of the solvent, the residue was purified by column chromatography on silica gel using DCM/ethyl acetate 9/1 or hexane/ethyl acetate 1/1 as an eluent, yielding a yellow solid (40%); similar results could be obtained by precipitation with water.

$C_{16}H_{14}N_8O_6S_2$, M.M. 478. R_f: 0.43 (silica gel with DCM/ethyl acetate 9/1 *v*/*v*). Melting point 163 °C. Elemental analysis: calc.: C: 40.16%, H: 2.95%, N: 23.42%, S: 13.40%; found: C: 39.99%, H: 2.94%, N: 23.35%, S: 13.55%. IR (ν, cm^{-1}): 3343; 3188; 3052; 2921; 2852; 1716; 1618; 1578; 1487; 1442; 1402; 1313; 1285; 1254; 1217; 1180; 1117; 1015; 995; 893; 803; 725; 587; 512; 467. ^{1}H-NMR (500 MHz, DMSO-d_6, δ ppm, *J* Hz): 9.49 (s, 2H, N*H*); 8.46 (d, 2H, C*H*-arom, 8.8 Hz); 6.42 (d, 2H, C*H*-arom, 8.9 Hz); 3.75 (s, 4H, CH_2); 3.08 (t, 4H, CH_2, 6.7 Hz). ^{13}C-NMR (125 MHz, DMSO-d_6, δ ppm): 145.1; 144.8; 144.4; 138.2; 121.7; 99.7; 42.9; 36.1. (-)ESI-MS: 477 ($M\text{-}H^+$).

4. Conclusions

Starting from commercially available compounds, a new fluorescent derivative of NBD and cystamine was obtained and characterized by different means. The physical

and chemical properties of the new compound allow us to recommend it for use in nano-chemistry and fluorescent studies.

Supplementary Materials: The following supporting information are available online, Figure S1: IR spectrum (ATR); Figure S2: UV-Vis spectrum recorded in methanol; Figure S3: Fluorescence spectrum recorded in methanol; Figure S4: 1H-NMR spectrum recorded in DMSO-d6; Figure S5: 13C-NMR spectrum recorded in DMSO-d6; Figure S6: ESI-MS spectrum.

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References

1. Elbashir, A.A.; Suliman, F.E.O.; Aboul-Enein, H.Y. The application of 7-chloro-4-nitrobenzoxadiazole (NBD-Cl) for the analysis of pharmaceutical-bearing amine group using spectrophotometry and spectrofluorimetry techniques. *Appl. Spectrosc. Rev.* **2011**, *46*, 222–241. [CrossRef]
2. Ahnoff, M.; Grundevik, I.; Arfwidsson, A.; Fonselius, J.; Persson, B.-A. Derivatization with 4-chloro-7-nitrobenzofurazan for liquid chromatographic determination of hydroxyproline in collagen hydrolysate. *Anal. Chem.* **1981**, *53*, 485–489. [CrossRef]
3. Zhang, J.-Y.; Yang, B.-B.; Yang, Y.-D.; Wang, R.; Li, L. Specific chiroptical sensing of cysteine *via* ultrasound-assisted formation of disulfide bonds in aqueous solution. *Ultrason. Sonochem.* **2022**, *86*, 106007. [CrossRef] [PubMed]
4. Aly, H.; El-Shafie, A.S.; El-Azazy, M. Utilization of 7-chloro-4-nitrobenzo-2-oxa-1,3-diazole (NBD-Cl) for spectrochemical determination of L-ornithine: A multivariate optimization-assisted approach. *RSC Adv.* **2019**, *9*, 22106–22115. [CrossRef]
5. Muniz-Miranda, M.; Del Rosso, T.; Giorgetti, E.; Margheri, G.; Ghini, G.; Cicchi, S. Surface-enhanced fluorescence and surface-enhanced Raman scattering of push–pull molecules: Sulfur-functionalized 4-amino-7-nitrobenzofurazan adsorbed on Ag and Au nanostructured substrates. *Anal. Bioanal. Chem.* **2011**, *400*, 361–367. [CrossRef] [PubMed]
6. Giorgetti, E.; Cicchi, S.; Muniz-Miranda, M.; Margheri, G.; Del Rosso, T.; Giusti, A.; Rindi, A.; Ghini, G.; Sottini, S.; Marcelli, A.; et al. Forster resonance energy transfer (FRET) with a donor–acceptor system adsorbed on silver or gold nano island films. *Phys. Chem. Chem. Phys.* **2009**, *11*, 9798–9803. [CrossRef] [PubMed]
7. Bertorelle, F.; Lavabre, D.; Fery-Forgues, S. Dendrimer-tuned formation of luminescent organic microcrystals. *J. Am. Chem. Soc.* **2003**, *125*, 6244–6253. [CrossRef] [PubMed]
8. Abdellatef, H.E.; Shalaby, A.A.; Elsaid, H.M.; Ayad, M.M. Colorimetric and titrimetric methods for determination of some cephalosporins in their pure and dosage forms. *Sci. Pharm.* **2000**, *68*, 263–273. [CrossRef]
9. Haggag, R.; Belal, S.; Shaalan, R. Derivatization with 4-chloro-7-nitro-2,1,3-benzoxadiazole for the spectrophotometric and differential pulse polarographic determination of acetylcysteine and captopril. *Sci. Pharm.* **2008**, *76*, 33–48. [CrossRef]