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Short Note

10a,11,11-Trimethyl-10a,11-dihydro-8*H*-benzo[*e*]imidazo[1,2-*a*]indol-9(10*H*)-one

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Abstract: The alkylation of 1,1,2-trimethyl-1*H*-benzo[*e*]indole with 2-chloroacetamide, followed by work-up of the reaction mixture with a base and the subsequent treatment of a crude product with acetic acid gives 10a,11,11-trimethyl-10a,11-dihydro-8*H*-benzo[*e*]imidazo[1,2-*a*]indol-9(10*H*)-one. The structure assignments were based on data from ^{1}H, ^{13}C and ^{15}N NMR spectroscopy. The optical properties of the obtained compound were studied by UV-vis and fluorescence spectroscopy.

Keywords: benzo[*e*]indole; benzo[*e*]imidazo[1,2-*a*]indole; fluorescence

1. Introduction

1,1,2-Trimethyl-1*H*-benzo[*e*]indole is an important precursor for the synthesis of building blocks that have wide application in the preparation of a number of near-infrared fluorescence emitting dyes. Alkylation of 1,1,2-trimethyl-1*H*-benzo[*e*]indole with various alkylating agents, such as iodomethane [1], iodoethane [2], 4-iodobutane [3], 1-iodo-3-phenylpropane [4], benzyl bromides [5, 6] or 3-iodopropanoic acid [7] affords the corresponding *N*-quaternary 1,1,2-trimethyl-1*H*-benzo[*e*]indolium salts. The reactions are usually performed in aprotic solvents such as acetonitrile or toluene with conventional or microwave heating [8]. Upon treatment with various electrophilic counterparts, these salts are converted into dyes, which have found wide application for the development of the near-infrared fluorescent probes [1–7]. Furthermore, organic squaraine dyes based on the *N*-quaternized 1,1,2-trimethyl-1*H*-benzo[*e*]indolium salts have been used for the preparation of dye-sensitized solar cells [9]. It was recently shown by us that the microwave-assisted reaction of 1,1,2-trimethyl-1*H*-benzo[*e*]indole with acrylamide or acrylic acid gave functionalized benzo[*e*]indoline derivatives possessing intense fluorescence and significant Stokes shifts [10]. The aim of the present work is the synthesis of 10a,11,11-trimethyl-10a,11-dihydro-8*H*-benzo[*e*]imidazo[1,2-*a*]indol-9(10*H*)-one as a novel fluorescent building block, through the reaction of 1,1,2-trimethyl-1*H*-benzo[*e*]indole with 2-chloroacetamide. The structurally similar 9,9a-dihydro-1*H*-imidazo[1,2-*a*]indol-2(3*H*)-one derivatives have found application in the preparation of optical molecular switches [11].

2. Results and Discussion

The reaction of 1,1,2-trimethyl-1*H*-benzo[*e*]indole **1** with 2-chloroacetamide was carried out in *o*-xylene at 140 °C and gave a solid, which was separated by filtration. The obtained solid product was dissolved in water, the solution was basified with sodium carbonate and the separated material was extracted with ether. After the solvent removal from the organic phase, the residue was dissolved in ethanol, acetic acid was added and the mixture was refluxed for several minutes. The neutralisation of the solution, followed by the extraction and purification of the crude product by column chromatography on silica gel gave the target compound **2** in 30% isolated yield.

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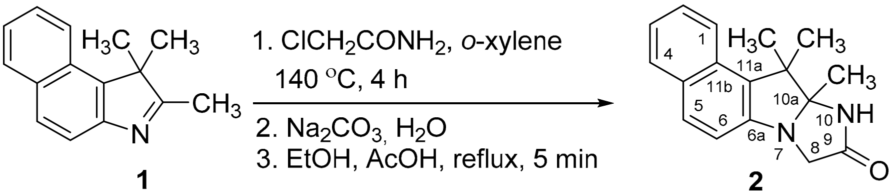
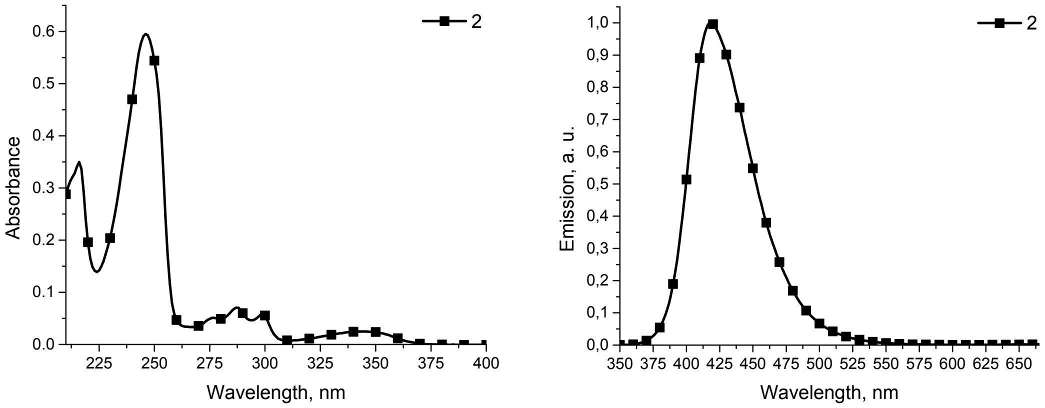
The structure assignment of **2** was based on spectral data. The IR spectrum shows a broad band at 3157 cm^{-1} for NH and a sharp band at 1698 cm^{-1} for the C=O group. The broad-band decoupled ^{13}C NMR spectrum of compound **2**, showed resonances for all 17 carbon atoms. The DEPT-90 and 135 spectra indicated the presence of 3 methyl, 1 methylene and 6 methine carbon atoms. Comparison of the DEPT spectrum with the broad-band decoupled ^{13}C NMR spectrum, revealed the presence of 7 quaternary carbons. The multiplicity edited ^{1}H-^{13}C HSQC spectrum indicated that the methylene protons H-8, which are diastereotopic due to chirality of the molecule and seen as an AB-system with $\delta = 3.92$ and 3.96 ppm in the ^{1}H NMR spectrum, have one bond connectivities with the carbon C-8 at 55.3 ppm. The data from ^{1}H-^{13}C HMBC spectrum revealed long range correlations of those methylene protons with the quaternary carbons C-6a (at 148.0 ppm), C-10a (at 92.1 ppm) and C-9 (174.1 ppm), respectively. The aforementioned protonated carbon C-8 showed correlation with carbonyl carbon C-9 in the 1.1-ADEQUATE spectrum, which revealed also correlations of C-6 with C-6a, and of 10a-CH_3 with C-10a, respectively. The ^{1}H-^{15}N HSQC experiment (optimized for $^{1}J_{NH} = 90$ Hz) indicated that the amide N–H proton at 7.83 ppm has one-bond connectivity with the N-10, which resonates at -243.3 ppm. The resonance for N-10 was also confirmed *via* the ^{1}H-^{15}N HMBC experiment, which additionally revealed the data for N-7 (-288.7 ppm). Both nitrogen atoms showed appropriate strong couplings to the H-8 and 10a-CH_3 protons, and in the case of N-7 it had a weak coupling with the aromatic proton 6-H.



Scheme 1. Synthesis of 10a,11,11-trimethyl-10a,11-dihydro-8*H*-benzo[*e*]imidazo[1.2-*a*]indol-9(10*H*)-one.

The optical properties of compound **2** were investigated by UV–vis spectroscopy and fluorimetric measurement. The electronic absorption spectra of compound in THF did not have absorption bands in the visible part of the electronic spectra (Figure 1, a). The fluorescence spectra of **2**, measured in THF, displayed emission maximum at 418 nm with a Stokes shift of 74 nm (Figure 1, b). The fluorescence quantum yield (Φ_f) of the solution was estimated by the integrating sphere method and gave the Φ_f value of 37.6%.



a) **b)**

Figure 1. (**a**) Absorption spectrum of **2** in THF (0.1 mM, 298 K); (**b**) Fluorescence emission spectrum of **2** in THF ($\lambda_{ex} = 310$ nm).

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3. Materials and Methods

3.1. Materials

The reagents and solvents were purchased from commercial suppliers and used without further purification.

3.2. Instrumentation

For thin layer chromatography (TLC), Merck pre-coated TLC plates (Silica gel 60 F_{254}) were employed. The purification of the products was performed using flash chromatography on a glass column with silica gel (high purity grade 9385, pore size 60 A, 230-400 mesh particle size). The melting points were determined on a Melt-Temp (Capillary Melting point Apparatus) and are uncorrected. The ^{1}H, ^{13}C and ^{15}N NMR spectra were recorded in $CDCl_3$ solutions at 25 °C on a Bruker Avance III 700 (700 Mhz for ^{1}H, 176 MHz for ^{13}C, 71 MHz for ^{15}N) spectrometer equipped with a 5 mm TCI ^{1}H-$^{13}C/^{15}N/D$ z-gradient cryoprobe. The chemical shifts, expressed in ppm, were relative to tetramethylsilane (TMS). The ^{15}N NMR spectra were referenced to neat, external nitromethane (coaxial capillary). The full and unambiguous assignments of the ^{1}H, ^{13}C and ^{15}N NMR resonances were achieved using standard Bruker software and a combination of standard NMR spectroscopic techniques, such as DEPT, COSY, TOCSY, NOESY, gs-HSQC, gs-HMBC, H2BC and 1,1-ADEQUATE. The infrared spectra were recorded on a Bruker TENSOR 27 spectrometer, using potassium bromide pellets. The UV-vis spectra were recorded using 0.1 mM solutions of the compounds in THF on a Shimadzu 2600 UV/Vis spectrometer. The fluorescence spectra were recorded on a FL920 fluorescence spectrometer from Edinburgh Instruments. The PL quantum yields were measured from dilute solutions by an absolute method using Edinburgh Instruments integrating sphere excited with a Xe lamp. Optical densities of the sample solutions were ensured to be below 0.1 to avoid reabsorption effects. All optical measurements were performed at rt under ambient conditions. HRMS spectra were recorded with a Bruker maXis spectrometer.

3.3. Synthesis

To a solution of 1,1,2-trimethyl-1*H*-benzo[*e*]indole (**1**) (1.0 g, 4.8 mmol) in *o*-xylene (5 mL), 2-chloroacetamide (0.51 g, 5.5.mmol) was added and the reaction mixture was heated at 140 °C for 4 h. Then the solvent was removed under reduced pressure and the residue was dissolved in ethanol (5 mL). The obtained solution was diluted with water (15 mL) and treated with sodium carbonate till alkaline pH. The substance separated was extracted with diethyl ether (3 x 15 mL), and the solvent was removed under reduced pressure. The residue was dissolved in ethanol (5 mL), glacial acetic acid (2 mL) was added to the solution and the mixture was refluxed for 10 min. Upon cooling to rt the reaction mixture was diluted with water (30 mL), neutralized with sodium carbonate and extracted with diethyl ether (3 x 15 mL). The residue was purified by flash chromatography on silica gel (dichloromethane/methanol, 20:1→ dichloromethane/methanol, 9:1, v/v) to yield the title compound **2**.

Yield: 380 mg, (30%), brownish crystals, m. p. 225–226 °C.

IR (KBr) ν (cm^{-1}): 3157 (NH), 3054 (CH_{arom}), 2966 (CH_{aliph}), 1698 (C=O), 1351, 1307, 811, 745.

UV/Vis (THF) λ_{max}, nm ($\varepsilon\times10^{3}$, $dm^{3}\,mol^{-1}\,cm^{-1}$): 216 (34.98), 246 (59.49), 287 (7.08); 299 (5.89), 344 (2.49).

^{1}H NMR (700 MHz, $CDCl_3$): δ_H ppm 1.40 (s, 3H, 11-CH_3), 1.58 (s, 3H, 10a-CH_3), 1.75 (s, 3H, 11-CH_3), 3.92 (d, *J* = 16.7 Hz, 1H, $CH_{a}H_{b}$), 3.96 (d, *J* = 16.5 Hz, 1H, $CH_{a}CH_{b}$), 7.02 (d, *J* = 8.7 Hz, 1H, 6-H),

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7.30 (t, *J* = 7.4 Hz, 1H, 3-H), 7.44 (t, *J* = 7.6 Hz, 1H, 2-H), 7.71 (d, *J* = 8.7 Hz, 1H, 5-H), 7.80 (d, *J* = 8.2 Hz, 1H, 4-H), 7.83 (s, 1H, NH), 7.97 (d, *J* = 8.5 Hz, 1H, 1-H).

^{13}C NMR (176 MHz, CDCl$_3$): δ_C ppm 20.7 (10a-CH$_3$), 23.5 (11-CH$_3$), 25.3 (11-CH$_3$), 48.4 (C-11), 55.3 (CH$_2$), 92.1 (C-10a), 114.3 (C-6), 122.0 (C-1), 123.2 (C-3), 126.7 (C-2), 129.0 (C-11a), 129.62 (C-4), 129.64 (C-5), 130.2 (C-11b), 131.2 (C-4a), 148.0 (C-6a), 174.1 (C=O).

^{15}NMR (71 MHz, CDCl$_3$): δ_N ppm –288.7 (N-7), –243.3 (N-10).

HRMS (ESI TOF): [M+Na$^+$]$^+$ found 289.1312. [$C_{17}H_{18}N_2O$+Na$^+$]$^+$ requires 289.1311.

Supplementary Materials: The following are available online at www.mdpi.com/link, Figure S1: ^{1}H NMR spectrum of **2**, Figure S2: ^{13}C NMR spectrum of **2**, Figure S3: ^{13}C and DEPT ^{13}C NMR spectra of compound **2**.

Author Contributions: E.Š.: Experimental synthetic work, NMR interpretation; R.T.: Experimental synthetic work, synthesis planning, NMR interpretation; A.B.: Experimental performance of the NMR, UV-vis, HRMS spectra and fluorimetric measurements, NMR interpretation, and writing of the manuscript; A.Š.: Synthesis planning, literature research, supervision and writing of the manuscript.

Conflicts of Interest: The authors declare no conflict interest.

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