Journal of Molecular Structure 1125 (2016) 705–713

Contents lists available at ScienceDirect

Journal of Molecular Structure

journal homepage: http://www.elsevier.com/locate/molstruc

3,4-Diamino naphthalimides and their respective imidazoles – Synthesis, spectroscopic and theoretical investigation

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ARTICLE INFO

Article history:
Received 19 April 2016
Received in revised form
3 July 2016
Accepted 8 July 2016
Available online 10 July 2016

Keywords:
1,8-Naphthalimides
Imidazo-naphthalimide
N-heterocyclic carbene precursors
Charge transfer states
Fluorescence
Substituent effects

ABSTRACT

A series of compounds containing 1,8-naphthalimide photoactive core were synthesized and studied with respect to their optical properties and applications. Combined spectral measurements and quantum chemical calculations allowed better understanding of the electronic effects in any particular substitution pattern starting from 3,4-diamino naphthalimides, through their respective imidazoles and quaternary N-heterocyclic carbene precursors, to corresponding carbene dimer (tetraaminoethylene). The absorption and fluorescence energies have been calculated with the PCM TDDFT formalism. PBE0 and M06 functionals were found to accurately model the distinctly different photophysical characteristics of the newly synthesized compounds.

1. Introduction

The naphthalimide core continues to prove itself as versatile photoactive structure upon which many fluorescent compounds can be built. Introducing donors to this electron acceptor forms push-pull system with good photostability and high fluorescence quantum yields. Many of these compounds are excellent chemosensors for cations [1] and anions [2], fluorescent cellular imaging agents and DNA intercalators [3], switches and logical gates [4], and used for coating of nanoparticles [5]. While 4- and 4,5 -substituted naphthalimides are the predominant class of investigated naphthalimides, 3,4-disubstituted representatives are surprisingly not studied extensively, although they possess potential for introduction of interesting combinations of electronic factors to provide new and unusual photophysical properties.

4-amino-3-nitro-1,8-naphthalimides were reported in the literature [6] and their spectroscopic properties were studied by us in relation to their sensitivity to bases [7].

Naphthalimides which have five-membered, fused at positions 3 and 4 heterocycles, such as thiazoles and oxazoles were reported as DNA binders and anticancer agents [8–10]. To the best of our knowledge, only few examples of bioactive N-unsubstituted imidazoles [11] and one of a triazole [12] which is *in vivo* fluorescent NO sensor can be found in the literature.

Our goal was to obtain and study photoactive N-heterocyclic carbene precursors **3** (Scheme 1) in which the imidazole ring is substituted at both nitrogen atoms. Chosen strategy was to synthesize 3,4-diamino representatives **1**, by nitro group conversion, followed by inclusion of the two amino groups of **1** in fused imidazoles **2** and subsequent alkylation of the latter to imidazolium salts **3**. Spectral measurements and quantum chemical calculations were chosen to investigate on comparative basis the influence of the substitution pattern on the photophysical properties.

Herein we present the synthesis of 3,4-diamino substituted 1,8-naphthalimides **1**, five-membered fused heterocycles **2** and **3**, and tetraaminoethylene **4**. The photophysical properties of every synthesized compound were studied to track the naphthalimide response to the substitution patterns and gain understanding of the electronic interactions in 3,4-disubstituted naphthalimides. DFT and TDDFT formalism were applied to calculate the structural and electronic properties of ground and excited states. The electrostatic

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http://dx.doi.org/10.1016/j.molstruc.2016.07.018
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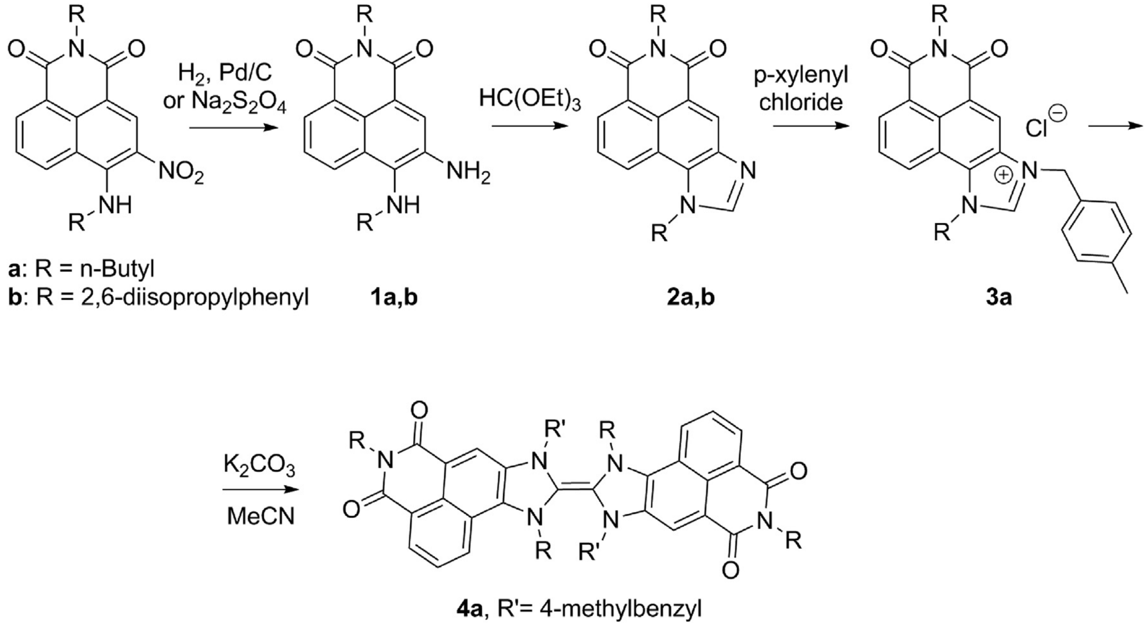

Scheme 1. Synthesis of 1–4.

potential at nuclei was used to rationalize the electron density distribution change between optimized ground and excited states.

2. Material and methods

2.1. Synthesis

Reactions involving air-sensitive compounds were performed under a positive pressure of purified argon using standard Schlenk techniques. Solvents were dried over appropriate materials and distilled prior to use. ^{1}H and ^{13}C NMR spectra were recorded at 298 K (unless stated otherwise) on a Bruker DRX 250 MHz or Bruker Avance II 600 MHz spectrometer. All NMR chemical shifts are in ppm referenced to residual solvent signals or TMS, the coupling constants (J) are in Hertz. Microanalyses were performed on Vario ELIII instrument in CHNS mode. IUPAC numbering scheme is used in the NMR spectra interpretation. The starting materials were prepared according to literature procedures [6,7]. All newly synthesized compounds were purified by recrystallization and/or column chromatography, which was performed on Silica Gel 60 (0.040–0.063 nm).

2.2. Spectroscopic measurements

Electronic absorption (UV/Vis) spectra were measured on a “Thermo Spectronic Unicam UV 500” double-beam spectrophotometer. The fluorescence spectra were taken on a “Cary Eclipse” spectrophotometer. All spectra were recorded using 1 cm path length synthetic quartz glass cells. The absorption and fluorescence measurements were in dimethyl sulfoxide and chloroform. All solvents were of spectroscopic grade (Merck) and used without further purification. Fluorescence quantum yields were determined on the basis of the absorption and fluorescence spectra, using the equation $QY_x = QY_{st}*(GRAD_x/GRAD_{st})*(n_x^2/n_{st}^2)$, where the subscripts x and st denote sample and standard respectively, QY is the fluorescence quantum yield, GRAD the gradient from the plot of integrated fluorescence intensity vs absorbance, and n the refractive index of the solvent. Fluorescein in borate buffer (QY 0.92) and Quinine Sulfate in 0.05 M H_2SO_4 (QY 0.51) were used as a standards [13]. All spectral experiments were carried out at 20 °C.

2.3. Computations

All calculations were performed with the Gaussian 09 program [14]. The minimum energy conformers for the compounds have been optimised and investigated in the ground and excited state. The optimizations have been carried out with DFT [15] and TDDFT [16–19] formalism. The PBE0 [20] and M06 [21] functionals with 6-31 + G(d) basis set [22] have been used. It was reported in several studies that these functionals provide accurate computations for the absorption spectra of compounds with charge transfer [23–26]. The geometry optimization of the ground state structure was performed for each molecule at DFT level and vibrational frequencies were evaluated at the same method/basis set to verify the structure as a minimum. The lowest energy absorption transitions were determined by TDDFT calculations of vertical excitations. Up to twenty excited singlet states were considered. The effect of the media has been taken into account at each step by means of IEFPCM formalism [27,28]. All the computations were performed in chloroform and DMSO solvents to reproduce the experimental conditions.

To simulate the fluorescence, the optimization of the excited state, corresponding to HOMO-LUMO transition was performed at TDDFT. The vibrational frequencies of the excited state were calculated in order to determine the nature of the located stationary point.

2.4. General procedure for synthesis of 3,4-diamino substituted naphthalimides

The 4-amino-3-nitro-naphthalimides (1 g) were suspended in hot ethanol (60 ml) and treated gradually with a solution of sodium dithionite (4 equivalents.) in water (16 ml). The mixture was refluxed for 3 h. After evaporation of the volatiles in vacuo, the precipitate which appeared was redissolved in dichloromethane and filtered to remove inorganic impurities. After the dichloromethane was evaporated, the residues were purified by flash chromatography eluting with cyclohexane:dichloromethane:ethyl