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ORIGINAL PAPER

Synthesis and fluorescence study of Naphthalimide-Coumarin, Naphthalimide-Luminol conjugates

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Abstract Fluorescent naphthalimide-coumarin and naphthalimide-luminol conjugates were prepared by nucleophilic substitution reaction. The synthesized conjugates were characterized by ^{1}H-NMR, ^{13}C-NMR, mass and IR spectra. The absorption and fluorescence of these conjugates revealed that naphthalimide-luminol conjugates are more fluorescent than the naphthalimide-coumarin conjugates. In proton accepting DMSO solvent the fluorescence of the conjugates was quenched, while in proton donating ethanol solvent enhanced fluorescence was noticed. Based on the excitation maxima and fluorescence maxima it was found that in naphthalimide-coumarin conjugates coumarin acting as donor and naphthalimide acting as acceptor where as in naphthalimide-luminol conjugates naphthalimide acts as donor and luminol acts as acceptor.

Keywords Naphthalimide · Fluorescence · 1,8-Naphthalic anhydride · Luminol and 7-Hydroxy-4-methylcoumarin

Introduction

Naphthalimides, one type of cyclic imides with strong hydrophobicity and desirable large π-conjugated backbone, could easily interact with various active targets in biological system via non-covalent forces such as π–π stacking. They exhibit diverse biological activities including anticancer [1], antibacterial [2], anti trypanosomal [3], analgesic [4], photobiological [5], antinociceptive [6] potency. Some naphthalimide derivatives such as amonafide and elinafide have been on the clinical trials stage for the treatment of cancer [7]. 1,8-Naphthalimide derivatives are a special class of environmentally sensitive fluorophore and luminophore compounds that are widely used in various fields of science and technology [8]. Because of their strong fluorescence and good photostability, 1,8-naphthalimide derivatives used in different areas including the coloration of polymers [9], laser active media [10], potential photosensitive biological units [11], fluorescent markers in biology [12], light emitting diodes [13], photo induced electron transfer sensors [14], fluorescence switchers [15], electroluminescent materials [16], liquid crystal displays [17] and ion probes [18]. Cho et al. [19] synthesized 1,8-naphthalimide-linker-phenothiazine dyads and investigated their intramolecular exciplex and intermolecular excimer formation. Jisha et al. [20] synthesized dyads based on dansyl and naphthalimide units linked through polymethylene group and studied their photophysical and interactions with various metal ions. In these dyads naphthalimide part acts as donor and dansyl part acts as acceptor. These dyads act as visual fluorescence ratiometric probe for the selective recognition of Cu^{2+} ions based on FERT mechanism. Naphthalimide is known candidate in the energy transfer systems, hence we intended to prepare a few energy donor-acceptor conjugates keeping naphthalimide as the focused molecule. Therefore in this paper we report the synthesis of naphthalimide-coumarin and naphthalimide-luminol conjugates and present their photophysical properties in five different solvents of varying polarity.

Results and Discussion

Synthesis of Naphthalimide-Coumarin and Naphthalimide-Luminol Conjugates

Synthesis of naphthalimide-coumarin and naphthalimide-luminol conjugates was carried out starting from naphthalene monoanhydride in good yields as shown in Scheme 1.

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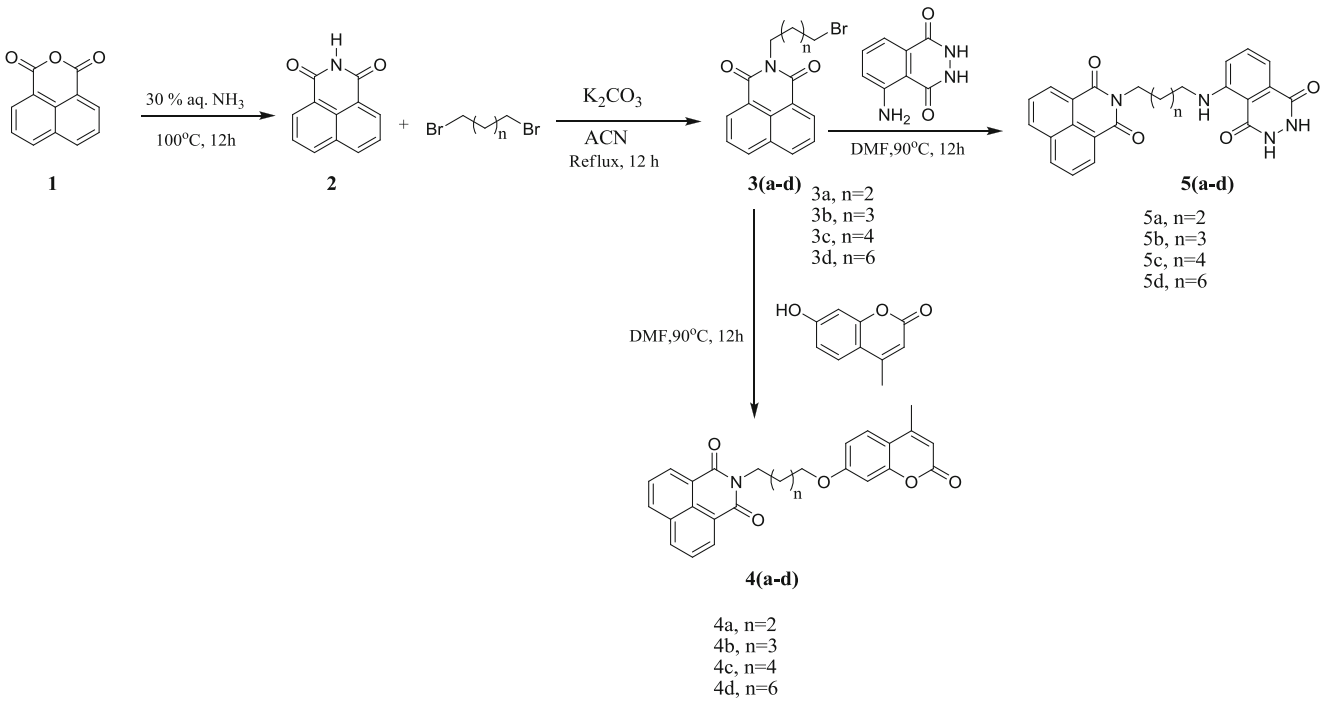

Scheme 1 Synthesis of naphthalimide-coumarin and naphthalimide-luminol conjugates

One Gram of 1,8-naphthalic anhydride (1) was taken in 60 mL NH_3 solution and stirred at 100 °C for 8 h to obtain a pale yellow solid (2). The structure of this compound was characterized by the signal at 11.69 ppm corresponding to imide proton. It was exchanged with D_2 in D_2O solvent. The naphthalimide was further reacted with corresponding α,ω-diboromo alkanes to produce the respective N-boromoalkylnaphthalimides 3(a-d). Appearance of signals of aliphatic protons indicated the formation of N-boromoalkylatednaphthalimides. These N-boromoalkylnaphthalimides when treated with 7-hydroxy-4-methylcoumarin (6) in presence of potassium carbonate in DMF at 90 °C yielded naphthalimide-coumarin conjugates 4(a-d). The proton and ^{13}C-NMR spectra of 4d were given in Figs. 1 and 2. In the proton nmr spectrum appearance of signals of aromatic protons at 6.83 ppm (dd, 1H, ArH), 6.77 ppm (1H, ArH), 6.11 ppm (s, 1H) and methyl protons at 2.37 ppm (s, 3H) indicated the formation of naphthalimide-coumarin conjugates 4(a-d). Similarly, luminol (7) also reacted with 3(a-d) to yield coumarin-luminol conjugates 5(a-d) which are characterized by the signals in proton NMR at 7.35, 6.97 and 6.81 ppm.

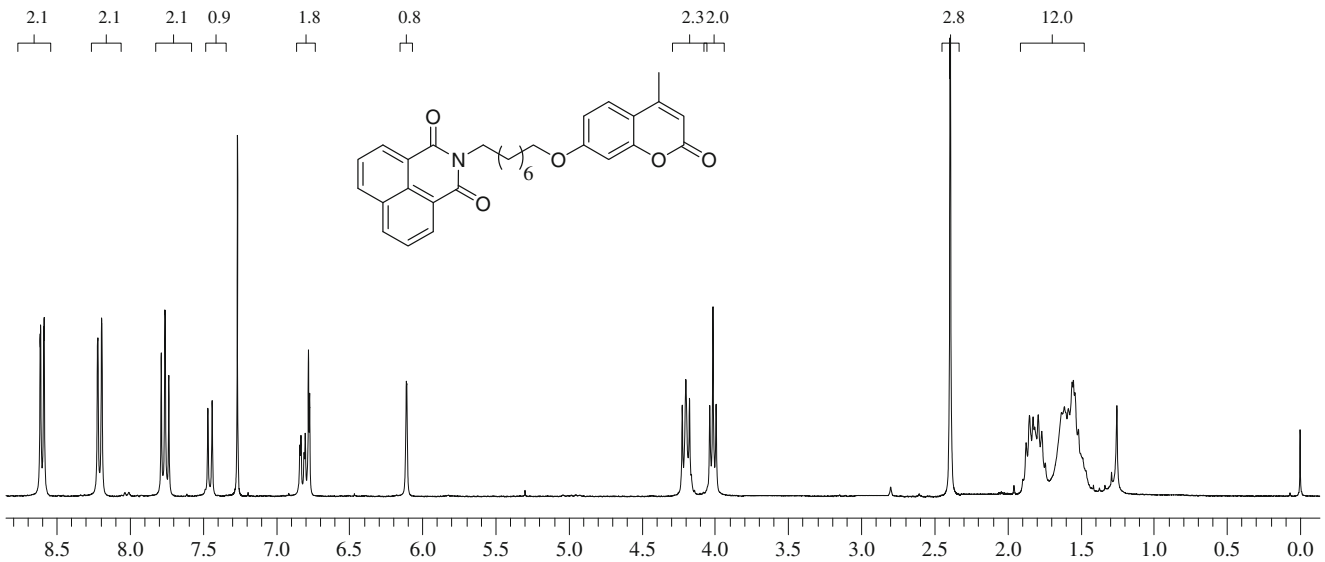

Fig. 1 ^{1}H-NMR spectrum of 2-[8-(4-Methyl-2-oxo-2*H*-chromen-7-yloxy)octyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (4d)

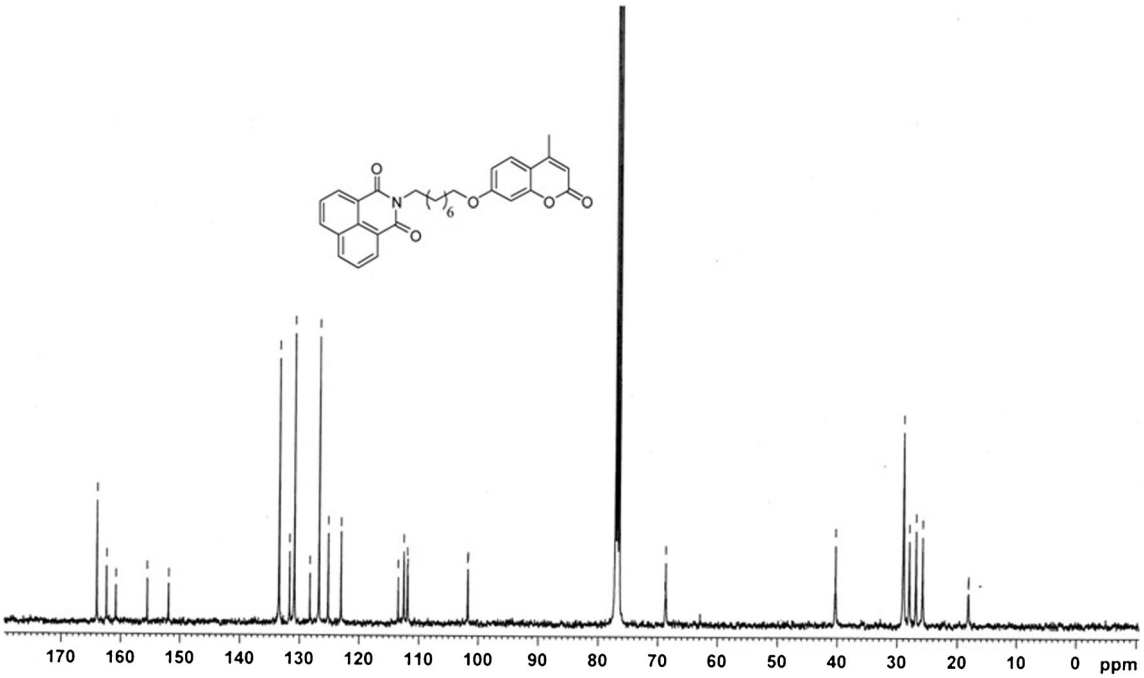

Fig. 2 ^{13}C-NMR spectrum of 2-[8-(4-Methyl-2-oxo-2*H*-chromen-7-yloxy)octyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (4d)

Steady State Fluorescence

Investigation of naphthalimide conjugates fluorescent properties would enable their utility as fluoroprobes. Naphthalimide is converted to N-boromoalkylnaphthalimides 3(a-d), there is no change in the excitation and emission wavelengths. But when the 3(a-d) are converted to naphthalimide-coumarin conjugates 4(a-d), the excitation wavelength shifted towards blue region (λ_{ex} 324 nm). The steady state fluorescence of coumarin conjugates were studied in five different solvents.

Table 1 Photophysical properties of **2, 3a, 3b** and **3c** in different solvents

Compound number	Solvent	λ_{ex} (nm)	λ_{em} (nm)	Stokes shift $\Delta\nu$ (cm^{-1})	Φ
2	Chloroform	333	362, 380	2,406,3,715	0.103
	Acetone	341	359, 377, 398	1,470, 2,800, 4,200	0.010
	Acetonitrile	331	360, 377	2,434, 3,686	0.028
	Ethanol	335	383	3,741	0.056
	DMSO	333	373,413,437	3,221, 5,817, 7,147	0.002
3a	Chloroform	335	363,381	2,302, 3,604	0.086
	Acetone	344	361,379	1,368, 2,684	0.022
	Acetonitrile	332	362,380	2,496, 3,805	0.054
	Ethanol	335	385	3,876	0.104
	DMSO	337	375,395,414,438	3,007, 4,356, 5,519, 6,842	0.004
3b	Chloroform	335	363,381	2,302,3,604	0.081
	Acetone	344	361,379	1,369, 2,684	0.022
	Acetonitrile	332	362,379	2,496, 3,735	0.053
	Ethanol	336	385	3,786	0.1
	DMSO	338	376,395,415,440	2,990, 4,269, 5,489, 6,858	0.004
3c	Chloroform	335	363,381	2,302,3,604	0.083
	Acetone	343	361,380,400	1,454, 2,839, 4,154	0.023
	Acetonitrile	332	362,379	2,496, 3,735	0.053
	Ethanol	335	385	3,876	0.099
	DMSO	337	375,395,414,438	3,007, 4,357, 5,519, 6,842	0.004

Table 2 Photophysical properties of **3d, 4a, 4b** and **4c** in different solvents

Compound number	Solvent	λ_{ex} (nm)	λ_{em} (nm)	Stokes shift $\Delta\nu$ (cm^{-1})	Φ
3d	Chloroform	335	364,381	2,378, 3,604	0.081
	Acetone	345	361,378	1,285, 2,530	0.022
	Acetonitrile	331	362,379	2,587, 3,826	0.052
	Ethanol	334	385	3,966	0.098
	DMSO	337	375,395,414,438	3,007, 4,357, 5,519, 6,842	0.004
4a	Chloroform	324	363,381	3,316, 4,618	0.045
	Acetone	337	361,378	1,973, 3,218	0.009
	Acetonitrile	327	362,379	2,957, 4,196	0.022
	Ethanol	327	386	4,675	0.056
	DMSO	332	372,410	3,240, 5,730	0.005
4b	Chloroform	324	363,381	3,316, 4,618	0.052
	Acetone	337	361,378	1,973, 3,218	0.011
	Acetonitrile	327	362,379	2,957, 4,196	0.024
	Ethanol	327	386	4,675	0.057
	DMSO	332	372,410	3,240, 5,730	0.005
4c	Chloroform	325	364,381	3,297, 4,523	0.045
	Acetone	328	361,377	2,787, 3,962	0.012
	Acetonitrile	321	363,379	3,604, 4,767	0.023
	Ethanol	324	386	4,958	0.058
	DMSO	324	374,411	4,127, 6,534	0.006

Table 3 Photophysical properties of **4d, 5a, 5b** and **5c** in different solvents

Compound number	Solvent	λ_{ex} (nm)	λ_{em} (nm)	Stokes shift $\Delta\nu$ (cm^{-1})	Φ
4d	Chloroform	327	363,381	3,033, 4,335	0.057
	Acetone	337	361,377,401,426,461	1,973, 3,148, 4,736, 6,199, 7,982	0.001
	Acetonitrile	326	362,379,468	3,050, 4,289, 9,307	0.024
	Ethanol	326	385	4,700	0.057
	DMSO	331	369,412,437,471	3,111, 5,940, 7,328, 8,980	0.006
5a	Chloroform	352	408	3,900	0.037
	Acetone	347	403	4,005	0.032
	Acetonitrile	348	401	3,798	0.033
	Ethanol	348	409	4,286	0.048
	DMSO	350	414	4,591	0.015
5b	Chloroform	349	408	4,144	0.036
	Acetone	347	403	4,005	0.032
	Acetonitrile	346	401	3,963	0.033
	Ethanol	348	409	4,286	0.047
	DMSO	349	413,435	4,440, 5,665	0.015
5c	Chloroform	352	409	3,960	0.035
	Acetone	347	400	3,818	0.034
	Acetonitrile	346	399	3,839	0.035
	Ethanol	346	408	4,392	0.046
	DMSO	354	411	3,918	0.016

Table 4 Photophysical properties of **5d** in different solvents

Compound number	Solvent	λ_{ex} (nm)	λ_{em} (nm)	Stokes shift $\Delta\nu$ (cm^{-1})	Φ
5d	Chloroform	352	409	3,960	0.038
	Acetone	347	400	3,818	0.035
	Acetonitrile	346	399	3,839	0.036
	Ethanol	346	408	4,392	0.048
	DMSO	354	411	3,918	0.018

The fluorescence spectral data including Stokes shift is given Tables 1, 2, 3 and 4. The solvents employed are chloroform, ethanol, acetonitrile, acetone and dimethylsulfoxide (DMSO). Coumarin conjugates were more fluorescent in ethanol and is less fluorescent in DMSO. The order of its fluorescence intensity in the solvents investigated is ethanol>chloroform>acetonitrile>acetone>DMSO. The relative fluorescence quantum efficiency, (Φ), is evaluated by employing 9,10-diphenyl anthracene as standard (Φ=0.9) following the Eq. 1 and the results obtained are given in Tables 1, 2, 3 and 4: Investigation of naphthalimide conjugates fluorescent properties would enable their utility as fluoroprobes. Naphthalimide is converted to N-boromoalkylnaphthalimides 3(a-d), there is no change in the excitation and emission wavelengths. But when the 3(a-d) are converted to naphthalimide-coumarin conjugates 4(a-d), the excitation wavelength shifted towards blue region (λ_{ex} 324 nm). The steady state fluorescence of coumarin conjugates were studied in five different solvents. The fluorescence spectral data including Stokes shift is given Tables 1, 2, 3 and 4. The solvents employed are chloroform, ethanol, acetonitrile, acetone and dimethylsulfoxide (DMSO). Coumarin conjugates were more fluorescent in ethanol and is less fluorescent in DMSO. The order of its fluorescence intensity in the solvents investigated is ethanol>chloroform>acetonitrile>acetone>DMSO. The relative fluorescence quantum efficiency, (Φ), is evaluated by employing 9,10-diphenyl anthracene as standard (Φ=0.9) following the Eq. 1 and the results obtained are given in Tables 1, 2, 3 and 4.

$$\Phi=\Phi_{std}\left(\frac{I_{unk}}{I_{std}}\right)\left(\frac{A_{std}}{A_{unk}}\right)\left(\frac{\eta_{unk}}{\eta_{std}}\right)^2 \quad (1)$$

Where Φ_{unk}, Φ_{std}, I_{unk}, I_{std}, A_{std}, A_{unk}, η_{unk} and η_{std} are the fluorescence quantum efficiency, the integral of the emission intensities, the absorbance at the excitation wavelength and the refractive indexes of the corresponding solvents of the unknown samples and the standard respectively. The relative fluorescence quantum efficiency, Φ_F, of these compounds varies between 1.04×10^{-1} and 1×10^{-3}.

The fluorescence spectrum of octylcoumarin derivative of naphthalimide, 4d conjugate in different solvents is given in Fig. 3. From the above figure it can be noticed that 4d conjugate, is more fluorescent in ethanol than in the remaining solvents. From the Fig. 3 it can be observed that in chloroform 4d has given an emission doublet maxima at 363 and 381 nm

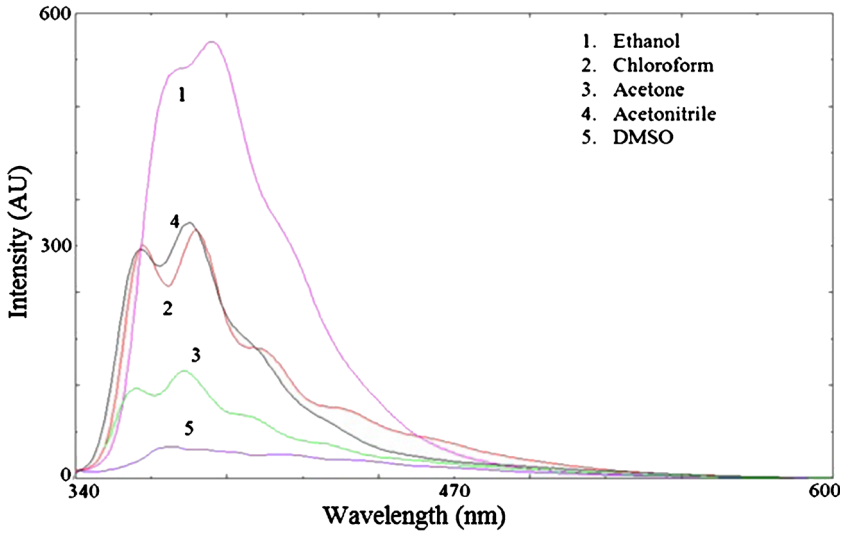

Fig. 3 Emission spectra of 2-[8-(4-Methyl-2-oxo-2*H*-chromen-7-yloxy)octyl]-1*H*-benzo[*de*] isoquinoline-1,3(2*H*)-dione (4d) conjugate [2.11×10^{-6} M] in different solvents

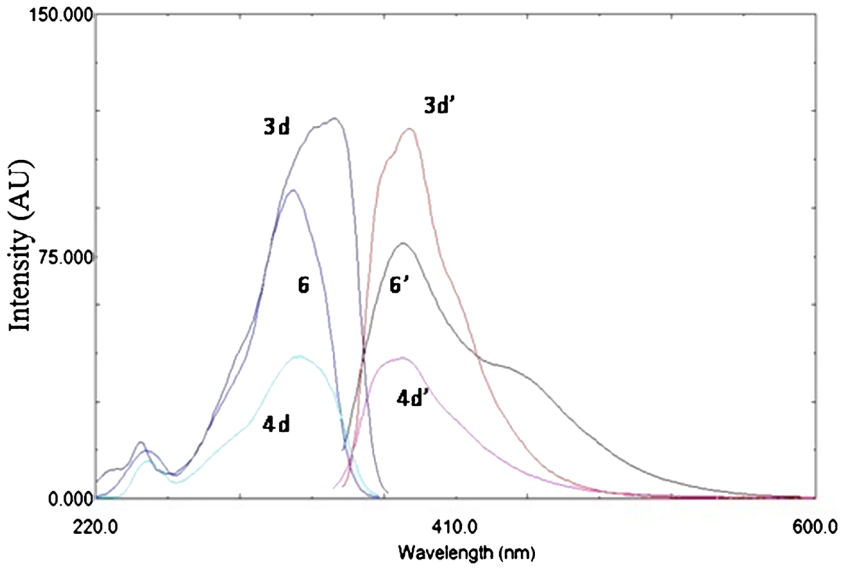

Fig. 4 Excitation and emission spectra of 2-(8-Bromooctyl)-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (3d), 2-[8-(4-Methyl-2-oxo-2*H*-chromen-7-yloxy)octyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (4d) and 7-hydroxy-4-methylcoumarin (6) in ethanol solvent. (3d, 4d, and 6 are excitation spectra of 3d, 4d and 7 respectively. 3d′, 4d′, and 7′ are emission spectra of 3d, 4d and 6 respectively)

with a well developed shoulder at 403 nm and a subdued shoulder at 432 nm. In acetone compound 4d has given an emission doublet maxima at 361 and 378 nm with a well developed shoulder at 399 nm and a subdued shoulder at 426 nm. In acetonitrile 4d exhibited emission doublet maxima at 362 and 379 nm while the shoulders at 407 and 430 nm disappeared. When the fluorescence spectrum of 4d was taken in ethanol, the distinct doublet emission maxima at 367 and 386 nm were merged into a diffused broad maxima centering at 386 nm while the shoulders at 407 and 430 nm disappeared. In DSMO solvent 4d has given an emission maximum at 372 nm and with a well developed shoulder at 410 nm and a subdued shoulder at 435 nm. The difference in the fluorescence spectra of these compounds in the protic solvent ethanol compared to other solvent media may be associated with the aggregation of these molecules. The shoulders at longer wavelengths in the emission spectrum of 4d in chloroform, acetone, DMSO may be due to the excimers. These excimers are not found in more polar solvents like acetonitrile or proton donating solvents like ethanol. The fluorescence of 4(a-d) is quenched in DMSO and acetone. The absorption and fluorescence spectra of naphthalimide, coumarin and naphthalimide-coumarin conjugate 4d in ethanol solvent is given in Fig. 4 and spectral data obtained is given in Table 5. From the Fig. 4 it can be observed that in naphthalimide-coumarin conjugate 4d, system coumarin acting as donor and naphthalimide acting as acceptor.

When the 3(a-d) is converted to naphthalimide-luminol conjugates 5(a-d), emission wavelength maxima of the later shifted towards red region compound to former. The steady state fluorescence of luminol conjugates were studied in five different solvents. The solvents employed are chloroform, ethanol, acetonitrile, acetone and DMSO. The fluorescence spectral data including Stokes shift is given in Tables 3 and 4. Luminol conjugates were more fluorescent in ethanol and are less fluorescent in DMSO. The order of its fluorescence intensity in the solvents investigated is ethanol>chloroform>acetonitrile>acetone>DMSO. The fluorescence spectrum of octylluminol derivative, 5d in different solvents is shown in Fig. 5. From the above figure it can be noticed that 5d is more fluorescent in ethanol than in the remaining solvents. From the Fig. 5 it can be observed that in chloroform 5d has given emission maxima at 386 nm with a shoulder at 405 nm and a subdued shoulder at 437 nm. In DMSO compound 5d has exhibited an emission maximum at 413 nm with a shoulder at 399 nm and a subdued shoulder at 436 nm. When the fluorescence spectrum of 5d was taken in ethanol, the shoulders at 399, 405 and 430 nm have merged into a diffused broad maxima centering at 413 nm. Similarly in acetonitrile and acetone it showed the emission maximum at 400 nm and 399 nm respectively. The difference in the fluorescence spectra of these compounds in the protic solvent ethanol compared to chloroform and DMSO solvents may be associated with the aggregation of these molecules in the later solvents. The shoulders at longer wavelengths

Table 5 Photophysical properties of 3d, 4d, 5d, 7-hydroxy-4-methy-coumarin and luminol in ethanol

Compound number	λ_{ex} (nm)	λ_{em} (nm)
3d	334	385
4d	326	385
5d	346	408
6	325	382
7	354	413

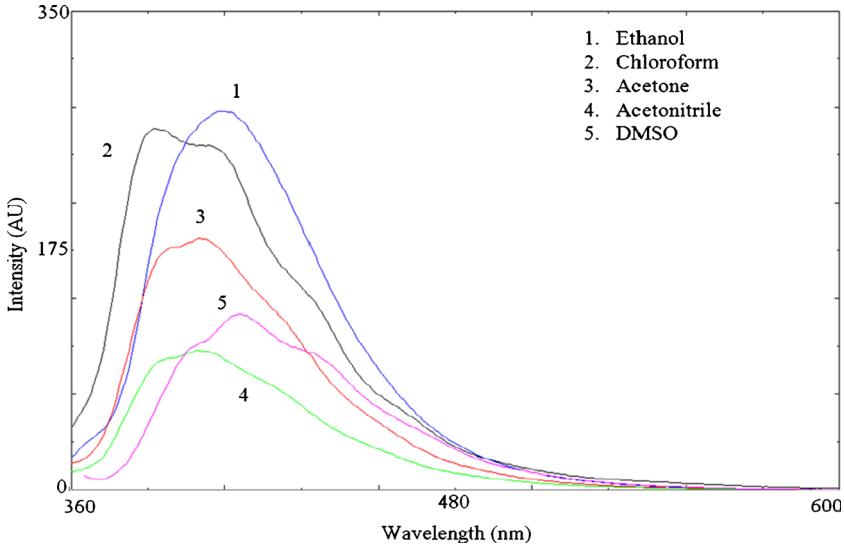

Fig. 5 Emission spectra of 2-[8-(1,4-Dioxo-1,2,3,4-tetrahydrophthalazin-5-ylamino) octyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (5d) conjugate [1.1×10^{-6} M] in different solvents

in the emission spectrum of 5d in chloroform, DMSO may be due to the excimers. These excimers are not found in more polar solvents like acetonitrile, acetone or proton donating solvent like ethanol. The reason for fluorescence quenching in these aprotic polar solvents is unknown and probably due to structural changes, i.e., change from a more rigid puckered form to a planar system as was observed in NMR spectral investigation [21]. The rigid cyclic systems have a decreased non radiative deactivation of excited states over a planar system leading to higher emission efficiency. The fluorescence of 4(a-d) is quenched in DMSO and acetone. The absorption and fluorescence spectra of naphthalimide, luminol and naphthalimide-luminol conjugate 5d in ethanol solvent is given in Fig. 6. From the Fig. 6 it can be observed that in naphthalimide-luminol conjugate, 5d system naphthalimide acting as donor and luminol acting as acceptor.

Conclusion

We have reported the synthesis of new fluorescent naphthalimide-coumarin and naphthalimide-luminol conjugates. The fluorescence spectrum of naphthalimide-luminol conjugates is similar to the fluorescence spectrum of luminol while the fluorescence spectra of naphthalimide-coumarin conjugates resemble the fluorescence spectra of naphthalimide. The formation of excimer is solvent and

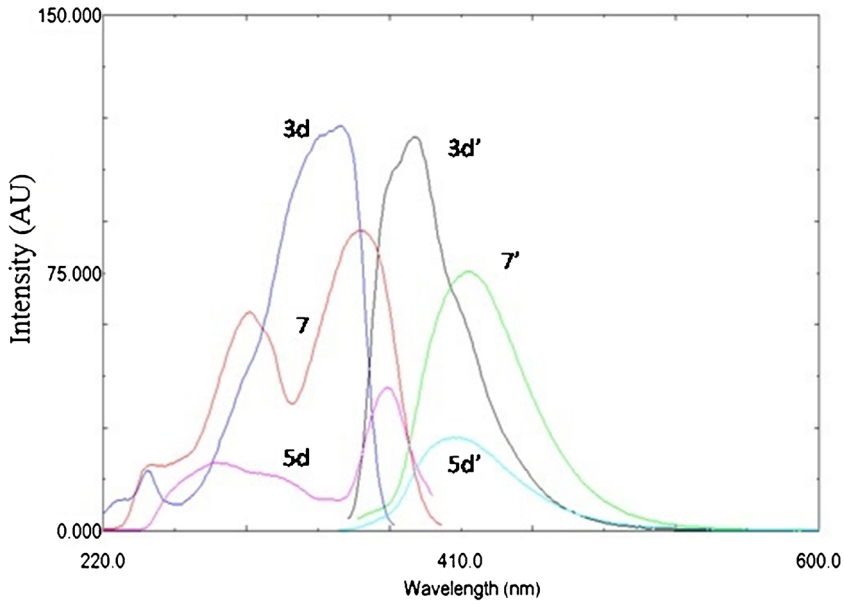

Fig. 6 Excitation and emission spectra of 2-(8-Bromooctyl)-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (3d), 2-[8-(1,4-Dioxo-1,2,3,4-tetrahydrophthalazin-5-ylamino)octyl]-1*H*-benzo[*de*] isoquinoline-1,3(2*H*)-dione (5d) and luminol (7) in ethanol solvent. (3d, 5d, and 7 are excitation spectra of 3d, 4d and 7 respectively. 3d′, 4d′, and 7′ are emission spectra of 3d, 5d and 7 respectively)

conjugate specific. Naphthalimide-coumarin conjugates exhibits excimers in chloroform, DMSO, acetone and acetonitrile; where as in naphthalimide-luminol conjugate excimers were observed only in chloroform and DMSO solvents.

Experimental

Materials 1,8-Naphthalic anhydride, luminol and other starting compounds were purchased from Aldrich chemicals and were used without further purification. All the chemicals and solvents were of spectroscopic grade purchased from Sigma-Aldrich Chemicals.

Instrumentation ^{1}H NMR and ^{13}C NMR spectra were performed on 400 MHz and 100 MHz Bruker Ultra shield (Avance-III) Nano Bay spectrometer. All the spectra were recorded at 298 K.^{1}H NMR data are reported as follows: s: singlet, d: doublet, t: triplet, bs: broad singlet. TLC analysis was carried out using silica gel 60 F_{254} plates. Infrared spectra were obtained employing on Bruker FT-Infrared model Tensor-27using KBr pellets. The melting points reported were uncorrected and determined in Polmon instrument (model No. MP-96). Mass spectroscopy was performed on VG Micro mass 7070 H (ESI-MS). Steady state fluorescence was investigated on RF-5301PC spectrofluorophotometer, Shimadzu with 5 nm excitation and emission slit widths at 18 °C employing 1 cm^3 quartz cell.

Synthesis of 1H-benzo[*de*]isoquinoline-1,3(2*H*)-dione (2) 1,8-Naphthalic anhydride (**1**) (1 g, 5.07 mmol) was taken in ammonia solution (60 mL) and stirred at 100 °C for 8 h. After cooling, a yellow solid obtained, to this, 200 mL of ice cold water was added and filtered at pump. The solid product was dried in oven at 100 °C. The compound is characterized by IR and ^{1}HNMR and mass spectra. Yield (91.7 %), m.p. 262-264 °C. light yellow color, ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): (δ)=8.58 (d, 2H, naphthalene, J=7.36 Hz), 8.27 (d, 2H, naphthalene, J=8.12 Hz), 7.79 (t, 2H, naphthalene, J= 7.55 Hz), 11.5 (s, 1H, NH, D_2O exchanged). IR (KBr): 3,440, 3,059, 1,701, 1,676, 1,622, 1,586 cm^{-1}. MS (ESI): m/z 198[M+1].

Synthesis of 2-(4-bromobutyl)-1H-benzo[*de*]isoquinoline-1,3(2*H*)-dione **(3a):** To a solution of compound **2** (0.5 g, 1 mmol) in acetonitrile (30 mL), anhydrous potassium carbonate (553 mg, 4 mmol) and 1,4-dibromobutane (561 mg, 3 mmol) were added and the mixture was refluxed for 12 h. After completion of the reaction, potassium carbonate was removed by filtration and the solvent was evaporated under reduced pressure to get the crude product. This was further purified by column chromatography (10 % EtOAc–hexane) to afford the compound **3a**. Yield (88.4 %), m.p. 100-103 °C. white color, ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.60 (d, 2H, naphthalene, J= 7.2 Hz), 8.21 (d, 2H, naphthalene, J=8.4 Hz), 7.75 (t, 2H, naphthalene, J=8 Hz), 4.23 (t, 2H, NCH_2), 3.47 (t, 2H, CH_2Br) 1.87-2.03 (m, 4H, 2-CH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 164.15, 133.96, 131.54, 131.25, 128.10, 126.93, 122.53, 39.34, 33.18, 30.25, 26.89. IR (KBr): 3,095, 1,697, 1,664, 1,588 cm^{-1} MS (ESI): m/z 332[M+1].

Following the above procedure compounds 3b, 3c and 3d were synthesized and characterized as follows.

2-(5-Bromopentyl)-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (3b): Yield (87.2 %), m.p. 118–120 °C. white color, ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.62 (d, 2H, naphthalene, J=7.4 Hz), 8.23 (d, 2H, naphthalene, J= 8.0 Hz), 7.78 (t, 2H, naphthalene, J=7.6 Hz), 4.21 (t, 2H, J=7.6 Hz, NCH_2) 3.45 (t, 2H, J=6.8 Hz, CH_2Br), 2.00-1.93 (m, 2H, CH_2), 1.83-1.75 (m, 2H, CH_2), 1.63-1.58 (m, 2H, CH_2). IR (KBr): 3,060, 2,954, 1,695, 1,660, 1,589, 1,512 cm^{-1}. MS (ESI): m/z 346[M+1].

2-(6-Bromohexyl)-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (3c): Yield (85.8 %), m.p. 90-94 °C. white color, ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.55 (d, 2H, naphthalene, J=7.36 Hz), 8.16 (d, 2H, naphthalene, J=8.03 Hz), 7.73 (t, 2H, naphthalene, J=7.93 Hz), 4.14 (t, 2H, J= 7.6 Hz, NCH_2) 3.37 (t, 2H, J=6.79 Hz, CH_2Br), 1.93-1.84 (m, 2H, CH_2), 1.79-1.69 (m, 2H, CH_2), 1.59-1.41 (m, 4H, 2CH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 164.14(CO), 133.65, 131.10, 128.44, 126.92, 123.19, 40.33, 33.28, 32.87, 28.01, 26.39. IR (KBr): 3,061, 2,954, 2,932, 1,694, 1,662, 1,587, 1,512 cm^{-1}. MS (ESI): m/z 360[M+1].

2-(8-Bromooctyl)-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (3d): Yield (80.6 %), m.p. 70-75 °C. white color, ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.59 (d, 2H, naphthalene, J=7.2 Hz), 8.20 (d, 2H, naphthalene, J=8.0 Hz), 7.75 (t, 2H, naphthalene, J=7.2 Hz), 4.17 (t, 2H, J= 7.6 Hz, NCH_2) 3.39 (t, 2H, J=6.8 Hz, CH_2Br), 1.80–1.87 (m, 2H, CH_2), 1.69–1.77 (m, 2H, CH_2), 1.30–1.44 (m, 8H, 4CH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 164.06(CO), 133.61, 131.63, 131.02, 128.20, 126.82, 122.91, 40.34, 33.58, 32.77,29.02, 28.55, 28.06, 28.01, 26.93. IR (KBr): 3,061, 2,934, 1,697, 1,661, 1,588, 1,510 cm^{-1}. MS (ESI): m/z 374[M+1].

Synthesis of 2-[4-(4-methyl-2-oxo-2*H*-chromen-7-yloxy)butyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (4a): 2-(4-Bromobutyl)-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**3a**) (0.2 g, 0.602 mmol) was taken in of N, N-dimethylformamide (15 mL) and to this, 124 mg (1.807 mmoles) of potassium carbonate and 7-hydroxy-4-methylcoumarin (0.105 mg, 0.602 mmol) was added and stirred at 90 °C temperature overnight (12 h). The reaction was monitored by TLC. After the completion of reaction

potassium carbonate was removed by filtration and the N,N-dimethylformamide was removed under the vacuum rotavapour and washed with water and hexane to obtain solid product. The compound is characterized by NMR and mass spectral data. Yield (88.2 %), m.p. 230-234 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.61 (d, 2H, naphthalene, J=7.2 Hz), 8.21 (d, 2H, naphthalene, J=8.1 Hz), 7.76 (t, 2H, naphthalene, J=7.55 Hz), 7.43 (d, 1H, J=8.68 Hz, ArH), 6.83 (dd, 1H, J_1=2.45, J_2=8.68, ArH), 6.77 (d, 1H, J=2.45, ArH), 6.11 (s, 1H), 4.28 (t, 2H, J=6.79), 4.08 (t, 2H, J=5.85), 2.37 (s, 3H), 1.92–2.01 (m, 4H, 2-CH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 163.96, 162.17, 160.41, 155.23, 153.45, 134.57, 131.81, 131.07, 127.92, 127.51, 126.63, 113.61, 112.81, 111.63, 101.95, 68.58, 26.64, 24.70, 18.36. MS(ESI): M+1 m/z 428.

Employing above procedure compounds **4b, 4c, 4d, 5a, 5b, 5c** and **5d** were synthesized and characterized as follows.

2-[5-(4-Methyl-2-oxo-2*H*-chromen-7-yloxy)pentyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (4b): Yield (86.7 %), ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.63 (d, 2H, naphthalene, J=7.2 Hz), 8.24 (d, 2H, naphthalene, J=8.4 Hz), 7.78 (t, 2H, naphthalene, J=7.6 Hz),7.48 (d, 1H, J=8.8 Hz, ArH), 6.85 (dd, 1H, J_1=2.46, J_2=8.69, ArH), 6.80 (d, 1H, J=2.34**,** ArH), 6.14 (d, 1H, J=0.8 Hz), 4.25 (t, 2H, J=7.6), 4.05 (t, 2H, J=6.4), 2.37 (d, 3H, J=1.2 Hz), 1.62–1.95 (m, 6H, 2-CH2). MS(ESI) : M+1 m/z 442

2-[6-(4-Methyl-2-oxo-2*H*-chromen-7-yloxy)hexyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (4c): Yield (84.8 %), ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.59 (d, 2H, naphthalene, J=7.36 Hz), 8.20 (d, 2H, naphthalene, J=8.12 Hz), 7.75 (t, 2H, naphthalene, J=7.8 Hz),7.45 (d, 1H, J=8.8 Hz, ArH), 6.81 (dd, 1H, J_1=2.46, J_2=8.69, ArH), 6.77 (d, 1H, J=2.46, ArH), 6.10 (d, 1H, J=0.8 Hz), 4.19 (t, 2H, J=7.3), 4.01 (t, 2H, J=6.42), 2.39 (d, 3H, J=1.1 Hz), 1.51–1.89 (m, 8H, 4-CH2). ^{13} C NMR (100 MHz, $CDCl_3$): δ 164.01, 162.33, 160.76, 155.51, 151.88, 133.50, 131.71, 130.94, 128.27, 126.76, 125.20, 123.01, 113.50, 112.52, 111.97, 111.89, 101.82, 101.76, 68.64, 40.14, 28.82, 27.92, 26.64, 25.59, 18.16. MS(ESI) : M+1 m/z 456

2-[8-(4-Methyl-2-oxo-2*H*-chromen-7-yloxy)octyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (4d): Yield (82.8 %), ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.59 (d, 2H, naphthalene, J=7.17 Hz), 8.20 (d, 2H, naphthalene, J=7.74 Hz), 7.75 (t, 2H, naphthalene, J=7.93 Hz),7.46 (d, 1H, J=8.87 Hz, ArH), 6.84 (dd, 1H, J_1=2.44, J_2=8.68, ArH), 6.79 (d, 1H, J=2.45, ArH), 6.11 (s, 1H), 4.17 (t, 2H, J=7.5), 3.99 (t, 2H, J=6.42), 2.38 (s, 3H), 1.826-1.64 (m, 6H, 3-CH_2),1.15-1.30 (m, 6H, 3-CH2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 163.99, 162.38, 160.77, 155.52, 151.89, 133.45, 131.70, 130.91, 128.28, 126.75, 125.20, 123.06, 113.49, 112.56, 111.96, 101.80, 68.71, 40.30, 28.95(3 C), 27.96, 26.85, 25.76, 18.16. MS(ESI) : M+1 m/z 484

2-[4-(1,4-Dioxo-1,2,3,4-tetrahydrophthalazin-5-ylamino)butyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (5a): Yield (76.8 %), ^{1}H NMR (400 MHz, $CDCl_3$+DMSO-d_6): δ=8.53 (d, 2H, naphthalene, J=7.3 Hz), 8.27 (d, 2H, naphthalene, J=8.1 Hz), 7.84 (t, 2H, naphthalene, J=7.6 Hz), 7.35 (t, 1H, aromatic, J=7.9 Hz), 6.97 (d, 1H, aromatic, J=6.9 Hz), 6.81 (d, 1H, aromatic, J=8.3 Hz), 4.24 - 4.14 (m, 4H), 1.97 -1.85 (m, 4H), 11.02 (s, 1H, NH, D_2O exchange), 5.95 (s, 2H, NH, D_2O exchange). MS(ESI) **:** M+1 m/z 429

2-[5-(1,4-Dioxo-1,2,3,4-tetrahydrophthalazin-5-ylamino)pentyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (5b): Yield (75.2 %), ^{1}H NMR (400 MHz, $CDCl_3$ +DMSO-d_6): δ=8.58 (d, 2H, naphthalene, J=7.17 Hz), 8.27 (d, 2H, naphthalene, J=8.1 Hz), 7.78 (t, 2H, naphthalene, J=7.5 Hz), 7.37 (t, 1H, aromatic, J=7.7 Hz), 7.05 (d, 1H, aromatic, J=7.6 Hz), 6.84 (d, 1H, aromatic, J=8.3 Hz), 4.26 - 4.19 (m, 4H), 1.97-1.58 (m, 6H), 10.62 (s, 1H, NH, D_2O exchange), 6.75 (s, 2H, NH, D_2O exchange). MS(ESI): M+1 m/z 443

2-[6-(1,4-Dioxo-1,2,3,4-tetrahydrophthalazin-5-ylamino)hexyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (5c): Yield (74.6 %), ^{1}H NMR (300 MHz, $CDCl_3$ +DMSO-d_6): δ=8.59 (d, 2H, naphthalene, J=7.2 Hz), 8.20 (d, 2H, naphthalene, J=8 Hz), 7.74 (t, 2H, naphthalene, J=7.2 Hz), 7.45 (t, 1H, aromatic, J=8 Hz), 7.14 (d, 1H, aromatic, J=7.6 Hz), 6.79 (d, 1H, aromatic, J=8 Hz), 4.23 - 4.16 (m, 4H), 1.85 -1.58 (m, 8H), 9.11 (s, 1H, NH, D_2O exchange), 6.35 (s, 2H, NH, D_2O exchange). MS : M+1 m/z 457

2-[8-(1,4-Dioxo-1,2,3,4-tetrahydrophthalazin-5-ylamino)octyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (5d): Yield (72.7**%**), ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.62 (d, 2H, naphthalene, J=6.8 Hz), 8.22 (d, 2H, naphthalene, J=8.4 Hz), 7.77 (t, 2H, naphthalene, J=7.6 Hz), 7.491 (t, 2H, aromatic, J=8 Hz), 7.17 (d, 2H, aromatic, J=7.6 Hz), 6.82 (d, 2H, aromatic, J=8 Hz), 4.24 - 4.18 (m, 4H), 1.84 -1.75 (m, 4H), 1.35-1.58 (m, 8H), 8.99 (s, 1H, NH, D_2O exchange), 6.37 (s, 2H, NH, D_2O exchange). MS : M+1 m/z 485.

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References

1. Ingrassia L, Lefranc F, Kiss R, Mijatovic T (2009) Naphthalimides and azonafides as promising anti-cancer agents. Curr Med Chem 16: 1192–1213

2. Fuente RDL, Sonawane ND, Arumainayagam D, Verkman AS (2006) Small molecules with antimicrobial activity against *E.coli* and *P.aeruginosa* identified by high throughput screening. Br J Pharmacol 149:551–559
3. Muth M, Hoerr V, Glaser M, Ponte-Sucre A, Moll H, Stich A, Holzgrabe U (2007) Antitrypanosomal activity of quaternary naphthalimide derivatives. Bioorg Med Chem Lett 17:1590–1593
4. Andricopulo AD, Muller LA, Cechinel V, Cani GS, Roos JF, Correa R, Santos ARS, Nunes RJ, Yunes RA (2000) Analgesic activity of cyclic imides: 1,8-naphthalimide and 1,4,5,8-naphthalenedimide derivatives. IL Farmaco 55:319–321
5. Xu YF, Qian XH, Yao W, Mao P, Cui JN (2003) Novel naphthalimide hydroperoxide photonucleases: The role of thiocyclic-Fused area and the difference in spectra, photochemistry and photobiological activity. Bioorg Med Chem 11:5427–5433
6. De Souza MM, Correa R, Cechinel V, Grabchev I, Bojinov V (2002) 4-Nitro-1,8-naphthalimides exhibit antinociceptive properties. Pharmazie 57:430
7. Costanza ME, Berry D, Henderson IC, Ratain MJ, Wu K, Shapiro C, Duggan D, Kalra J, Berkowitz I, Lyss AP (1995) Amonafide: an active agent in the treatment of previously untreated advanced breast cancer-a cancer and leukemia group B study (CALGB 8642). Clin Cancer Res 1:699–704
8. Bojinov VB, Georgiev NI, Nikolov PS (2008) Synthetic and photophysical properties of fluorescence sensing ester-and amido-amine-functionalized 1,8-naphthalimides J. Photochem Photobiol A 193:129–138
9. Patrick LGF, Whiting A (2002) Synthesis and application of some ploycondensable fluorescent dyes. Dyes Pigments 52:137–143
10. Martin E, Weigand R, Pardo A (1996) Solvent dependence of the inhibition of intramolecular charge-transfer in N-substituted 1,8-naphthalimide derivatives as dye lasers. J Lumin 68:157–164
11. Tao ZF, Qian X (1999) Naphthalimide hydroperoxides as photonucleases:substituent effects and structural basis. Dyes Pigments 43:139–145
12. Stewart WW (1981) Synthesis of 3,6-disulfonated 4-aminonaphthalimides. J Am Chem Soc 103:7615–7620
13. Facoetti H, Robin P, Le Barny P, Schott M, Bouche CM, Berdague P (1996) Side-chain electroluminescent polymers. Synth Met 81:191–195
14. Tian H, Gan J, Chen K, He J, Song Q, Hou XY (2002) Positive and negative fluorescent imaging induced by naphthalimide polymers. J Mater Chem 12:1262–1267
15. Poteau X, Brown A, Brown R, Holmes C (2000) Fluorescence switching in 4-amino-1,8-naphthalimides:"on-off-on" operation controlled by solvent and cations. Dyes Pigments 47:91–105
16. Zhu W, Hu M, Yao R, Tian H (2003) A novel family of twisted molecular luminescent materials containing carbazole unit for single-layer organic electroluminescent devices. J Photochem Photobiol A 154:169–177
17. Grabchev I, Chovelon JM (2003) Synthesis and functional properties of green fluorescent ploy(methylmethacrylate) for use in liquid crystal systems. Polym Adv Technol 14:601–608
18. Cosnard F, Wintgens V (1998) A new fluoroionophore derived from 4-amino-N-methyl-1,8-naphthalimide. Tetrahedron Lett 39:2751–2754
19. Cho DW, Fujitsuka M, Choi KH, Park MJ, Yoon UC, Majima T (2006) Intramolecular exciplex and intermolecular excimer formation of 1,8-naphthalimide-linker-phenothiazine dyads. J Phys Chem B 110:4576
20. Jisha VS, Anu JT, Ramaiah D (2009) Fluorescence ratiometric selective recognition of Cu^{2+} ions by dansyl-naphthalimide dyads. J Org Chem 74:6667–6673
21. Sheshashena Reddy T, Ram Reddy A (2012) Synthesis and fluorescence study of 3-aminoalkylamidonapthalimide. J Photochem Photobiol A Chem 227:51–58