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The synthesis and spectroscopic properties of novel, functional fluorescent naphthalimide dyes

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Abstract

A series of novel naphthalimide dyes with amino or hydroxyl functional groups were synthesized by the condensation reaction of 4-bromonaphthalic anhydride with primary amines to form the naphthalimide, followed by regio-selective aromatic nucleophilic substitution in basic media. Four of the dyes were selected as representative compounds for analysis by UV absorption and steady state fluorescence spectroscopy in solvents with different polarity. In addition, fluorescence intensity decays of these dyes in dichloromethane were measured. The results suggest that various combinations of the dyes make good donor–acceptor pairs for energy transfer experiments. To anticipate the application of these dyes in the synthesis of dye-labeled polymers by radical polymerizations, the synthesis of a monomer dye containing a methacrylate ester and a dye containing initiator for ATRP polymerization is described.

Keywords: Naphthalimide dyes; Functional fluorescent dyes; Synthesis; Fluorescence lifetimes; Solvent effects

1. Introduction

Fluorescent dyes have broad range of applications in paint, inks, food, cosmetics and in the textile industries. In addition, they have rather specialized applications in biodiagnostic assays [1,2]. Other applications include donor–acceptor pairs for fluorescence resonance energy transfer (FRET) experiments, a powerful technique for measurement of distances on a nanometer scale. This technique is widely used in biology, and in our research group it has been employed for the study of synthetic polymer systems [3–11]. In some applications these energy transfer experiments suffer from competition from background emission from components in the polymer. This emission is particularly problematic for experiments involving dyes that emit at short wavelengths (for example below 400 nm). While donor–acceptor dye pairs that operate in the visible range of wavelengths are commonplace for biological applications involving aqueous systems, the choice of functional dyes is much more limited for synthetic polymers. In this paper, we describe the synthesis, characterization, and spectroscopic properties of a series of functional 1,8-naphthalimide dyes, some of which make potentially useful donor–acceptor pairs.

1,8-Naphthalimide derivatives are a well known class of compounds that have wide range of applications [12–15]. Besides their uses as fluorescent dyes for coloring synthetic polymers and textile materials, they are also used in fluorescent solar energy collectors, as liquid-crystal additives, as electro-optically sensitive materials, in laser technology and as fluorescent markers in medicine and biology [16]. They can also be used as yellow components for daylight fluorescent pigments, as fluorescent dichroic dyes in liquid-crystal displays [17–19], and as fluorescent brighteners in detergents, textiles, paper, plastics and paints [20,21]. Because of their overall high fluorescence quantum yields and photostability, they are considered good candidates for dye lasers. Also the use of 1,8-naphthalimide derivatives as DNA intercalators [22] and in

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quantization of paramagnetic transition metal cations by fluorescent emission enhancement were reported [23].

For many applications, functional dyes are needed. We use the term functional to refer to those dyes that have a functional group that allows them to be covalently attached to a macromolecule. In biological applications, the macromolecule is a biopolymer, whereas our specific interest is in synthetic polymers, particularly latex polymers prepared by free radical polymerization. Useful functional groups for labeling polymers include hydroxyl, carboxyl, and amino groups. For our purposes, these groups can easily be converted to active monomers for introduction into polymers via different polymerization techniques.

There have been previous investigations into the synthesis and properties of 1,8-naphthalimide derivatives, and the possibility of obtaining colored or fluorescent polymers were described in several papers [24–28]. Our contribution is intended to extend the scope of available dyes, and to describe more completely their spectroscopic properties. For example, it is well known that 1,8-naphthalimides with an oxygen substituent at the 4-position have blue-shifted absorption and emission compared to corresponding dyes with a 4-amino substituent. For fluorescent probe applications, one would like a deeper understanding of how the nature of the substituents, as well as the nature of the medium, affects the spectroscopic properties of the dyes.

2. Results and discussion

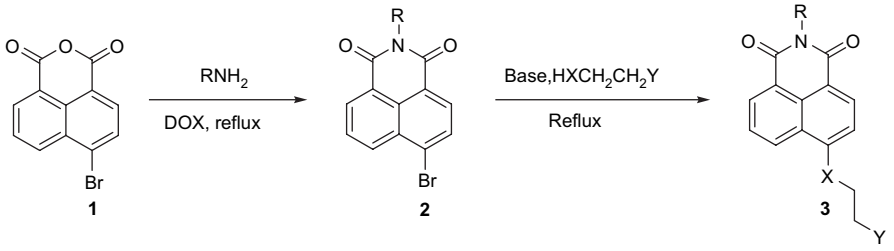
2.1. Synthesis and characterization

The class of dyes of interest to us, with the general structure **3**, are commonly prepared from 4-bromo-1,8-naphthalimides by nucleophilic aromatic substitution by primary or secondary amines, or by alkoxides as shown in Scheme 1. This reaction is facilitated by the presence of two electron withdrawing carbonyl groups on the naphthalimide. We also follow this route for the synthesis of the specific dyes **3a–3l**, whose spectroscopic properties are described below.

The first stage of the reaction, in which 4-Br-1,8-naphthalic anhydride **1** was reacted with the corresponding RNH_2, was performed in boiling 1,4-dioxane (DOX) for an appropriate time interval. Several solvents such as absolute ethanol and dimethyl sulfoxide were examined, with 1,4-dioxane resulting in the highest reaction yield. We were unsuccessful in two attempts to use a diamine in this step to obtain an amine-containing imide substituent. The reactions involving 4-Br-1,8-naphthalic anhydride (**1**) with hexamethylene diamine or dodecamethylenediamine in both 1,4-dioxane and absolute ethanol failed, leading to insoluble compounds and difficulties with further characterization. The structures of the intermediate compounds **2a–2c** are presented in Scheme 2, and the product yields are summarized in Table 1.

In the second step of the synthesis, compounds **2a–c** were reacted with an excess of a bifunctional nucleophile, such as ethylene glycol, ethylene diamine, ethanolamine or 2-methyl aminoethanol in the presence of triethylamine or potassium hydroxide as the base. The reactions were monitored by thin-layer chromatography (TLC) on silica gel eluted with *n*-heptane–acetone. The dyes were characterized by m.p., IR, ^{1}H NMR, ^{13}C NMR and HRMS spectra.

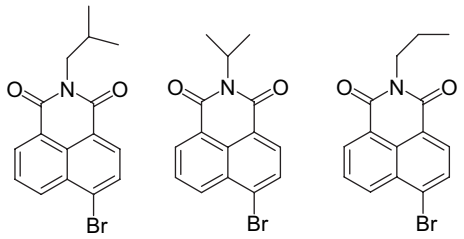
The reaction of **2a** with ethylene diamine took place in high yield with no by-products (entry 1, Table 2). The corresponding reaction of **2a** with aminoethanol was highly regio-selective, yielding only the hydroxyethylamine derivative (entry 2, Table 2). A similar result was obtained with 2-methyl aminoethanol as a nucleophile. The isolated product showed that the *N*-methyl amino moiety was the sole active nucleophile, and there was no evidence for the attack of the hydroxyl group on the aromatic ring (entry 3, Table 2). The reaction of



2a) R = Isobutyl
2b) R = Isopropyl
2c) R = Propyl

3a) R = Isobutyl, X = NH, Y = NH_2
3b) R = Isobutyl, X = NH, Y = OH
3c) R = Isobutyl, X = NMe, Y = OH
3d) R = Isobutyl, X = O, Y = OH
3e) R = Isopropyl, X = NH, Y = NH_2
3f) R = Isopropyl, X = NH, Y = OH
3g) R = Isopropyl, X = NMe, Y = OH
3h) R = Isopropyl, X = O, Y = OH
3i) R = Propyl, X = NH, Y = NH_2
3j) R = Propyl, X = NH, Y = OH
3k) R = Propyl, X = NMe, Y = OH
3l) R = Propyl, X = O, Y = OH

Scheme 1.



Scheme 2.

ethylene glycol with compound **2a** in DOX in the presence of triethylamine formed several by-products, and isolation of the product was extremely difficult. After some optimization experiments, we found that a high yield could be easily obtained by running the reaction in ethylene glycol as the solvent with KOH as the base (entry 4, Table 2). The other compounds listed in Table 2 (**3e–l**) were synthesized using procedures similar to those described above. From the synthesis perspective, if we want to compare the yield of the reactions and nucleophilicity of the reagents under similar conditions, we find ethylene diamine ≅ aminoethanol > 2-methyl aminoethanol > ethylene glycol. The strength of the primary amino group for nucleophilic aromatic substitutions in our system is higher than the secondary amine, and both are stronger than the hydroxyl group.

For a more detailed characterization of 6-((2-hydroxyethyl)(methyl)amino-2-isopropyl-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione) **3g**, we obtained the single-crystal X-ray structure, which is reported elsewhere [29]. This structure establishes that the *N*-methyl amino group is attached to the aromatic ring. This group is twisted out of the plane so that this nitrogen is nearly pyramidal in shape. In the crystal, the free –OH is hydrogen bonded to an imide carbonyl oxygen.

Finally, we prepared derivatives of these dyes to demonstrate that they can be converted into polymerizable functional dyes. We converted **3g** and **3c**, respectively, into its methacrylate ester **4** as shown in Scheme 3, and into the ATRP initiator **5** via reaction with 2-bromoisobutyryl bromide (Scheme 4). In future publications, we will describe polymerization reactions that take advantage of these molecules.

2.2. Spectroscopic properties

Four dyes **3a–d** were selected for spectroscopic investigation. Normalized absorption and emission spectra for each of these dyes in four different solvents – toluene, dichloromethane (DCM), ethyl acetate, and acetone – are presented in Fig. 1. In Table 3 we summarize the measured spectroscopic properties of these dyes. Aromatic dyes containing both electron donating (amine, alkoxy) and electron withdrawing (imide) substituents typically have charge-transfer lowest excited states with absorption and emission spectra that are red shifted in polar solvents. This type of behavior is observed for most of the dyes. For example, in Table 3, one can see that in the absorption spectrum for **3a**, λ_{abs} shifts from 422 to 431 nm as the solvent is changed from toluene to acetone. One of the curious features of the data in Table 3 is that the molar extinction coefficient of the dye **3a** is markedly smaller in toluene than in the other solvents.

Dyes **3a** and **3b** have essentially identical chromophores, with a secondary amine attached to the 4-position of the naphthalene ring. Examination of the spectra in Fig. 1 shows that in each of the solvents examined, the absorption and emission spectra of these two dyes are very similar. Dye **3c** has a tertiary amine substituent at the 4-position of the ring. Here one notices several differences in the spectra compared to **3a** and **3b**. The absorption spectra are blue-shifted for **3c**, leading to a larger Stokes shift, and there appear to be somewhat larger shifts of λ_{max}, both in absorption and in emission, associated with the change in solvent polarity. The blue shift in the absorption spectrum is consistent with the X-ray crystal structure of **3g**, which shows the amino substituent twisted out of the plane of the naphthalene ring. Another curious feature of **3c** is that the emission is very weak for the sample dissolved in acetone. The reader can see this in the high level of noise

Table 1
Synthesis of compounds **2a–c** from compound **1**

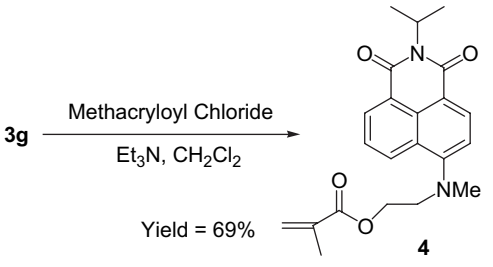
Entry	RNH_2	2	Yield (%)[a]
1	Isobutyl amine	**2a**	75
2	Isopropyl amine	**2b**	70
3	Propyl amine	**2c**	72

[a] Isolated yields. All compounds are characterized by ^{1}H NMR, ^{13}C NMR, HRMS and IR spectroscopy.

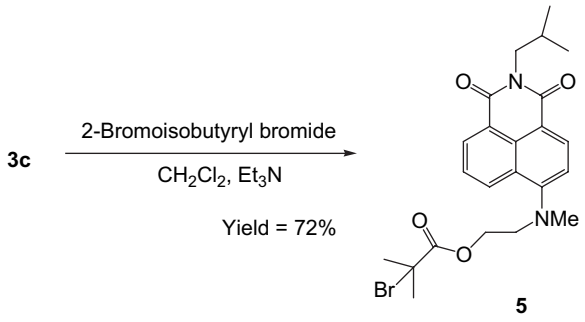
Table 2
Synthesis of compounds **3a–l** by nucleophilic aromatic substitution with different bifunctional reagents

Entry	2	$HXCH_2CH_2Y$	3	Yield (%)[a]
1	**2a**	$H_2NCH_2CH_2NH_2$	**3a**	71
2	**2a**	$H_2NCH_2CH_2OH$	**3b**	76
3	**2a**	$MeNHCH_2CH_2OH$	**3c**	61
4	**2a**	$HOCH_2CH_2OH$	**3d**	77
5	**2b**	$H_2NCH_2CH_2NH_2$	**3e**	70
6	**2b**	$H_2NCH_2CH_2OH$	**3f**	73
7	**2b**	$MeNHCH_2CH_2OH$	**3g**	65
8	**2b**	$HOCH_2CH_2OH$	**3h**	77
9	**2c**	$H_2NCH_2CH_2NH_2$	**3i**	68
10	**2c**	$H_2NCH_2CH_2OH$	**3j**	74
11	**2c**	$MeNHCH_2CH_2OH$	**3k**	60
12	**2c**	$HOCH_2CH_2OH$	**3l**	78

[a] Isolated yields. All compounds are characterized by ^{1}H NMR, ^{13}C NMR, HRMS and IR spectroscopy.



Scheme 3.



Scheme 4.

present in the normalized emission spectrum. We are in the process of investigating this effect, and will report these studies separately.

Dye **3d** has an ether substituent at the 4-position. This leads to a strong blue shift in both the absorption and emission spectra. The absorption spectrum of this dye shows hardly any shift in λ_{max} with a change in solvent polarity. All of the dyes exhibit exponential decay profiles when solutions in aerated dichloromethane were subjected to pulsed excitation. The decay times (Table 3) were approximately 10 ns for **3a**–**3c**, and 7 ns for **3d**.

There is in fact good overlap, in each solvent, of the emission spectrum of **3d** with the absorption spectra of **3a**–**3c**. An example for **3b** and **3d** in dichloromethane is shown in Fig. 2. We conclude that derivatives of **3d** are likely to serve as good donor chromophores for non-radiative energy transfer to derivatives of **3a**–**3c**.

Further information about the solvent sensitivity of the absorption and emission spectra of these dyes can be obtained if

Table 3
Spectroscopic properties of dyes **3a**–**d** in different solvents

Dye	Solvent	$\varepsilon \times 10^{-4}$ (M^{-1} cm^{-1})[a]	λ_{abs} (nm)[b]	λ_{em} (nm)[b]	τ (ns)[c]	Δf
3a	Toluene	0.65	422	482		0.022
	DCM	1.09	428	504	10.2	0.168
	Ethyl acetate	1.09	424	499		0.201
	Acetone	1.14	431	512		0.284
3b	Toluene	1.28	416	481		
	DCM	1.41	423	497	10.3	
	Ethyl acetate	1.40	424	505		
	Acetone	1.45	430	515		
3c	Toluene	0.92	396	491		
	DCM	0.97	402	508	9.9	
	Ethyl acetate	1.04	407	510		
	Acetone	1.06	412	527		
3d	Toluene	1.24	361	421		
	DCM	1.31	363	427	7.3	
	Ethyl acetate	1.28	361	427		
	Acetone	1.41	363	432		

[a] Extinction coefficient.
[b] Wavelengths of maximum absorbance (λ_{abs}) and emission intensity (λ_{em}).
[c] Fluorescence lifetime of the dyes in dichloromethane.

one examines the peak maxima in terms of a Lippert plot. The Lippert equation [30] describes the dependence of the energy difference between the ground state and the excited state (in cm^{-1}) on the refractive index (n) and the dielectric constant (ε) of the solvent:

$$\nu_A - \nu_F = \frac{2}{hc}\left(\frac{\varepsilon - 1}{2\varepsilon + 1} - \frac{n^2 - 1}{2n^2 + 1}\right)\frac{(\mu_E - \mu_G)^2}{a^3} + \text{constant} \qquad (1)$$

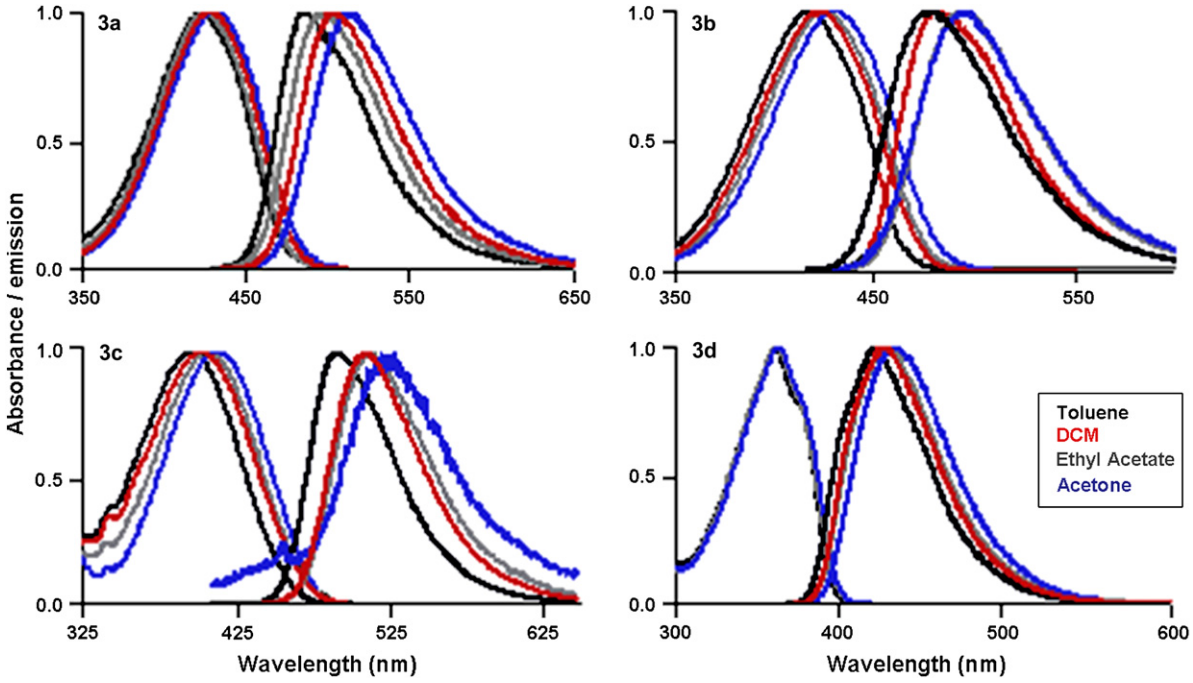


Fig. 1. Absorption and emission spectra of compounds **3a**–**d** in toluene (black), dichloromethane (DCM, red), ethyl acetate (grey), and acetone (blue). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

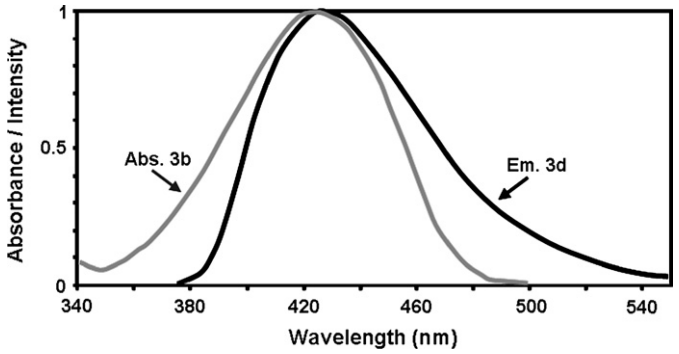


Fig. 2. Normalized spectral overlap of the absorption of **3b** (grey) and the emission of **3d** (black).

Here ν_A and ν_F are the wavenumbers (cm^{-1}) of the absorption and emission maxima, respectively. $h = 6.6256 \times 10^{-27}$ erg s is Planck's constant; $c = 2.9979 \times 10^{10}$ cm/s is the speed of light; and a is the radius of the cavity in which the fluorophore resides. μ_G and μ_E refer to the ground state and excited state dipole moments, respectively. The term inside the brackets in Eq. (1) is called the orientation polarizability (Δf). The slope of the Lippert plot reflects the solvent sensitivity of a fluorophore. This plot of $\Delta\nu$ ($\nu_A - \nu_F$) vs Δf, for the four solvents we examined, is presented in Fig. 3. The calculated values of Δf for each solvent are presented in Table 1.

One can see three features of the dye spectroscopy in Fig. 3. First, the linearity of the plots can be regarded as evidence for the dominant importance of general solvent effects on the spectral shifts (specific solvent effects can lead to nonlinear Lippert plots). Second, one can see from the y-axis that the magnitude of the Stokes shift ($\Delta\nu$) is significantly larger for **3c** than for **3a** or **3b**. Finally, from the fact that the slopes are nearly parallel, we see that all four dyes have similar sensitivities to solvent polarity.

In the future, we plan to investigate the spectroscopic properties of these dyes covalently attached to different polymers.

3. Conclusions

We described the synthesis and characterization of a series of functional naphthalimide dyes. As is known from the work of Grabchev and others [24–28], dyes with a 4-amino substituent have an absorption maximum in the region of 420 nm with $\varepsilon \approx 10^4\ M^{-1}\ cm^{-1}$, and a strong fluorescence centered at ca. 500 nm, whereas the dyes (e.g. **3d**) with a 4-oxo substituent had an absorption maximum at ca. 360 nm and an emission maximum at 420 nm. Based upon the strong spectral overlap between the emission of **3d** and the absorption of 4-amino-dyes, we anticipate that these dye pairs will be useful in FRET experiments, particularly in polymer systems.

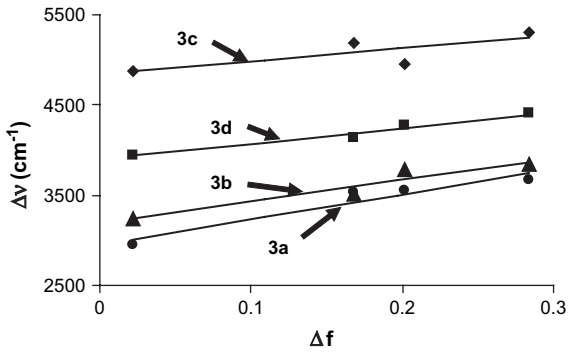


Fig. 3. Lippert plot for dyes **3a–d**.

4. Experimental

4.1. Materials

Commercial grade 4-bromo-1,8-naphthalic anhydride, isobutyl amine, 1,2-diaminoethane (ethylenediamine), 2-aminoethanol (ethanolamine), 2-(methylamino)ethanol, triethylamine, 1,2-ethanediol (ethyleneglycole), potassium hydroxide and magnesium sulfate were purchased from Aldrich. The solvents were of analytical grade. Dichloromethane was distilled under nitrogen from CaH_2 immediately prior to use. 1,4-Dioxane (Sigma–Aldrich) was used as received. Silica gel (Merck, grade 9385, 230–400 mesh, 60 Å) for column chromatography was used as received. All other reagents were purchased from Sigma–Aldrich and used as received unless otherwise noted. Deionized water was collected from a Milli-Q water system. The course of the synthesis and purity of the products were followed by TLC on silica gel plates (Fluka F60254, 20110, 0.2 mm, ready-to-use), using *n*-heptane–acetone as eluent. The eluent for column chromatography was the same as TLC eluent.

4.2. Instrumentation

Melting points were recorded using a Fisher–Johns melting point apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were obtained using either Varian Gemini 300 MHz, Varian Unity 400 MHz or Varian Unity 500 MHz spectrometers. ^1H NMR spectra are referenced to tetramethylsilane (0.00 ppm) and ^{13}C NMR spectra are referenced from the solvent central peak (for example, 77.23 ppm for $CDCl_3$). Chemical shifts are given in ppm. IR spectra were recorded using a Nicolet DX FT IR spectrometer as thin films on NaCl plates. IR is reported as characteristic bands (cm^{-1}) at their maximum intensity. The letters br designate a broad signal. High-resolution mass spectra were obtained using a VG 70-250S (double focusing) mass spectrometer at 70 eV, unless otherwise noted. Optical absorption spectra were collected at room temperature on Perkin–Elmer Lambda 25 spectrometer using 1.00-cm quartz cuvettes. Fluorescence spectra were measured with a SPEX Fluorolog-3 spectrofluorometer (Jobin Yvon/SPEX, Edison, New Jersey). Fluorescence intensity decays were measured using a time correlated single photon counting system equipped with a 456 NanoLED (IBH, Scotland). Solutions were placed in a quartz tube and the instrumental response function was obtained using a silica scattering solution. Fluorescence decays were fit by convoluting a single exponential decay with the

instrumental response function using a quadrature routine, and fitting the convoluted model to the experimental data with the Levenberg–Marquardt algorithm. All of the reported fits were judged to be good, based on the randomness of weighted residual plots and χ^2 values generally less than 1.2.

Extinction coefficients were determined by weighing out on a microbalance one sample for each dye–solvent combination and adding by weight known amounts of solvent for different concentrations. Values of ε were calculated as the slope of the plot of absorbance vs concentration, and have a precision of the order of 5%.

4.3. Synthesis

4.3.1. Synthesis of 6-bromo-2-isobutyl-1H-benzo[de]isoquinoline-1,3(2H)-dione, compound **2a**

In a round-bottomed flask equipped with a magnet and condenser, 4-bromo-1,8-naphthalic anhydride (5 mmol, 1.4 g) was dissolved in 1,4-dioxane (20 mL) and isobutyl amine (2 mL, 20 mmol) was added at room temperature. The solution was refluxed for 5 h, and the course of the reaction was monitored using TLC on silica gel with *n*-heptane–acetone (3:1) as eluent. The solvent was evaporated under vacuum and the product was separated by column chromatography (first fraction) on silca gel and dried under vacuum at 50 °C for 10 h. Yield: 75%, 1.24 g; mp = 126–127 °C; IR (film) ν_{max} cm^{-1}: 2954; 1701; 1654; 1372. ^1H NMR (400 MHz, $CDCl_3$): δ 0.98 (d, $J = 6.8$ Hz, 6H); 2.24 (m, 1H); 4.04 (d, $J = 7.6$ Hz, 2H); 7.85 (dd, $J = 7.2$ Hz, 8.4 Hz, 1H); 8.04 (d, $J = 7.6$ Hz, 1H); 8.41 (d, $J = 7.6$ Hz, 1H); 8.56 (dd, $J = 1.2$ Hz, 8.4 Hz, 1H); 8.65 (dd, $J = 1.2$ Hz, 7.2 Hz, 1H). ^{13}C NMR (100 MHz, dimethyl sulfoxide-d_6): δ 20.6; 27.3; 47.0; 122.4; 123.2; 128.8; 129.3; 129.5; 130.2; 131.5; 131.8; 132.1; 133.0; 163.6; 163.6. HRMS (EI, *m/z*) calcd. for $C_{16}H_{14}BrNO_2$ 331.0207 (M^+), Found 331.0205.

4.3.2. Synthesis of 6-bromo-2-isopropyl-1H-benzo[de]isoquinoline-1,3(2H)-dione, compound **2b**

The procedure is the same as the synthesis of compound **2a**. 4-Bromo-1,8-naphthalic anhydride (5 mmol, 1.4 g), 1,4-dioxane (20 mL) and isopropyl amine (1.72 mL, 20 mmol) were used. Yield: 70%, 1.1 g; mp = 164–165 °C; IR (film) ν_{max} cm^{-1}: 2958; 1699; 1655; 1374. ^1H NMR (400 MHz, $CDCl_3$): δ 1.57 (d, $J = 6.8$ Hz, 6H); 5.38 (heptet, $J = 6.8$ Hz, 1H); 7.81 (t, $J = 8.0$ Hz, 1H); 8.00 (d, $J = 7.4$ Hz, 1H); 8.36 (d, $J = 8$ Hz, 1H); 8.51 (d, $J = 8.0$ Hz, 1H); 8.60 (d, $J = 7.4$ Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.9; 45.7; 123.0; 123.9; 128.3; 129.3; 130.0; 130.7; 131.3; 131.3; 132.1; 133.1; 164.1; 164.1. HRMS (EI, *m/z*) calcd. for $C_{15}H_{12}NO_2Br$ 317.0051 (M^+), Found 317.0048.

4.3.3. Synthesis of 6-bromo-2-propyl-1H-benzo[de]isoquinoline-1,3(2H)-dione, compound **2c**

The procedure is the same as the synthesis of compound **2a**. 4-Bromo-1,8-naphthalic anhydride (5 mmol, 1.4 g), 1,4-dioxane (20 mL) and propyl amine (1.65 mL, 20 mmol) were used. Yield: 72%, 1.14 g; mp = 123–124 °C; IR (film) ν_{max} cm^{-1}: 2955; 1703; 1652; 1370. ^1H NMR (400 MHz, $CDCl_3$): δ 1.01 (t, $J = 7.2$ Hz, 3H); 1.76 (m, 2H); 4.14 (m, 2H); 7.84 (dd, $J = 7.6$ Hz, 8.4 Hz, 1H); 8.04 (d, $J = 8.0$ Hz, 1H); 8.41 (d, $J = 8.0$ Hz, 1H); 8.57 (dd, $J = 1.2$ Hz, 8.4 Hz, 1H); 8.65 (dd, $J = 1.2$ Hz, 7.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.7; 21.6; 42.3; 122.5; 123.4; 128.3; 129.3; 130.4; 130.8; 131.3; 131.4; 132.2; 133.4; 163.8; 163.9. HRMS (EI, *m/z*) calcd. for $C_{15}H_{13}NO_2Br$ 318.0124 ($M^+ + 1$), Found 318.0130.

4.3.4. Synthesis of 6-(2-aminoethylamino)-2-isobutyl-1H-benzo[de]isoquinoline-1,3(2H)-dione, compound **3a**

In a round-bottomed flask equipped with a magnet and condenser, 4-bromo-*N*-isobutylnaphthalimide (**2a**) (1 mmol, 0.331 g) was dissolved in 1,4-dioxane (20 mL) at room temperature and 1,2-diaminoethane (ethylenediamine) (10 mmol, 0.7 mL) and triethylamine (5 mmol, 0.7 mL) were added. The solution was refluxed and the course of the reaction was monitored using TLC on silica gel with *n*-heptane–acetone (1:1) as eluent. After 12 h, the reaction was complete. The solvent was evaporated under vacuum and the product was separated by column chromatography (second fraction) on silca gel. The crystals were dried under vacuum at 40 C for 10 h. Yield: 71%, 0.22 g; mp = 159–160 °C; IR (film) ν_{max} cm^{-1}: 3316; 1683; 1635; 1576; 1373; 1243. ^1H NMR (400 MHz, $CDCl_3$): δ 0.92 (d, $J = 6.8$ Hz, 6H); 2.14 (m, 1H); 2.67 (bs, 2H), 3.11 (t, $J = 6.0$ Hz, 2H); 3.57 (t, $J = 6.0$ Hz, 2H); 3.91 (m, 2H); 6.73 (d, $J = 8.4$ Hz, 1H); 6.98 (bs, 1H); 7.55 (dd, $J = 7.2$ Hz, 8.4 Hz, 1H); 8.21 (d, $J = 8.4$ Hz, 1H); 8.35 (m, 1H); 8.42 (dd, $J = 0.8$ Hz, 8.4 Hz, 1H). ^{13}C NMR (100 MHz, methanol-d_4): δ 20.8; 28.7; 40.6; 45.5; 48.0; 105.2; 110.0; 122.0; 123.4; 125.7; 129.4; 131.2; 132.3; 135.9; 152.4; 166.0; 166.5. HRMS (EI, *m/z*) calcd. for $C_{18}H_{22}N_3O_2$ 312.1706 ($M^+ + 1$), Found 312.1711.

4.3.5. Synthesis of 6-(2-hydroxyethylamino)-2-isobutyl-1H-benzo[de]isoquinoline-1,3(2H)-dione, compound **3b**

In a round-bottomed flask equipped with a magnet and condenser, 4-bromo-*N*-isobutylnaphthalimide (**2a**) (1 mmol, 0.331 g) was dissolved in 1,4-dioxane (20 mL) at room temperature and then 2-aminoethanol (ethanolamine) (10 mmol, 0.6 mL) and triethylamine (5 mmol, 0.7 mL) were added. The solution was refluxed and the course of the reaction was monitored using TLC on silica gel with *n*-heptane–acetone (1:1) as eluent. After 12 h, the reaction was complete. The solvent was evaporated under vacuum and the product was separated by column chromatography (second fraction) on silica gel. The crystals were dried under vacuum at 40 C for 10 h. Yield: 76%, 0.24 g; mp = 178–179 °C; IR (film) ν_{max} cm^{-1}: 3350; 1687; 1630; 1583; 1373; 1241. ^1H NMR (400 MHz, dimethyl sulfoxide-d_6): δ 0.87 (d, $J = 6.8$ Hz, 6H); 2.10 (m, 1H); 3.47 (m, 3H); 3.70 (m, 2H); 3.87 (d, $J = 7.2$ Hz, 2H); 6.81 (d, $J = 8.8$ Hz, 1H); 7.68 (m, 1H); 7.73 (t, $J = 5.6$ Hz, 1H); 8.25 (d, $J = 8.8$ Hz, 1H); 8.43 (d, $J = 7.2$ Hz, 1H); 8.69 (d, $J = 8.8$ Hz, 1H). ^{13}C NMR (100 MHz, methanol-d_4): δ 20.8; 28.7; 46.8; 48.0; 61.0; 105.3; 109.7; 122.0; 123.5; 125.7; 129.4; 131.4; 132.4; 136.1; 152.8; 166.2; 166.7. HRMS (EI, *m/z*) calcd. for $C_{18}H_{21}N_2O_3$ 313.1546 ($M^+ + 1$), Found 313.1551.

*4.3.6. Synthesis of 6-((2-hydroxyethyl)(methyl)amino)-2-isobutyl-1H-benzo[de]isoquinoline-1,3(2H)-dione, compound **3c***

In a round-bottomed flask equipped with a magnet and condenser, 4-bromo-*N*-isobutylnaphthalimide (**2a**) (1 mmol, 0.331 g) was dissolved in 1,4-dioxane (20 mL) at room temperature and then 2-(methylamino)ethanol (*N*-methylethanolamine) (10 mmol, 0.8 mL) and triethylamine (6 mmol, 0.82 mL) were added. The solution was refluxed and the course of the reaction was monitored using TLC on silica gel with *n*-heptane–acetone (1:3) as eluent. After 12 h, the reaction was complete. The solvent was evaporated under vacuum and the product was separated by column chromatography (second fraction) on silica gel. The crystals were dried under vacuum at 40 °C for 10 h. Yield: 61%, 0.2 g; mp = 119–120 °C; IR (film) ν_{max} cm^{-1}: 3387; 1696; 1652; 1576; 1379. ^1H NMR (300 MHz, $CDCl_3$): δ 0.97 (d, $J = 6.6$ Hz, 6H); 2.02 (t, $J = 5.7$ Hz, 1H); 2.23 (m, 1H); 3.08 (s, 3H); 3.50 (t, $J = 5.5$ Hz, 2H); 3.96 (m, 2H); 4.03 (d, $J = 7.2$ Hz, 2H); 7.27 (d, $J = 8.1$ Hz, 1H); 7.69 (dd, $J = 7.4$ Hz, 8.4 Hz, 1H); 8.49 (d, $J = 8.1$ Hz, 1H); 8.57 (dd, $J = 1.2$ Hz, 7.4 Hz, 1H); 8.61 (dd, $J = 1.2$ Hz, 8.4 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.3; 27.4; 41.8; 47.0; 58.6; 59.6; 115.5; 116.5; 123.2; 125.6; 126.2; 130.1; 130.5; 131.2; 132.3; 156.4; 164.3; 164.8. HRMS (EI, *m/z*) calcd. for $C_{19}H_{22}N_2O_3$ 326.1630 (M^+), Found 326.1633.

*4.3.7. Synthesis of 6-(2-hydroxyethoxy)-2-isobutyl-1H-benzo[de]isoquinoline-1,3(2H)-dione, compound **3d***

In a round-bottomed flask equipped with a magnet and condenser, 4-bromo-*N*-isobutylnaphthalimide (**2a**) (1 mmol, 0.331 g) was dissolved in 1,2-ethanediol (ethylene glycol) (20 mL) at room temperature and then potassium hydroxide (2 mmol, 0.112 g) was added. The solution was stirred at 100 °C and the course of the reaction was monitored using TLC on silica gel with *n*-heptane–acetone (1:1) as eluent. After 12 h, the reaction was complete. The reaction mixture was poured in distilled water and the precipitate was filtered and purified by column chromatography (second fraction) on silica gel. The product was dried under vacuum at 50 °C for 10 h. Yield: 77%, 0.24 g; mp = 147–148 °C; IR (film) ν_{max} cm^{-1}: 3465; 2871; 1695; 1654; 1593; 1381; 1350; 1269. ^1H NMR (500 MHz, $CDCl_3$): δ 0.98 (d, $J = 6.5$ Hz, 6H); 2.01 (bs, 1H); 2.22 (m, 1H); 4.03 (d, $J = 7.5$ Hz, 2H); 4.19 (m, 2H); 4.40 (t, $J = 5.0$ Hz, 2H); 7.06 (d, $J = 8.0$ Hz, 1H); 7.71 (dd, $J = 7.0$ Hz, 8.5 Hz, 1H); 8.54 (d, $J = 8.0$ Hz, 1H); 8.60 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.3; 27.4; 47.1; 61.2; 70.3; 106.1; 115.5; 122.5; 123.4; 126.0; 128.3; 129.4; 131.7; 133.4; 159.7; 164.2; 164.8. HRMS (EI, *m/z*) calcd. for $C_{18}H_{19}NO_4$ 313.1314 (M^+), Found 313.1316.

*4.3.8. Synthesis of 6-(2-aminoethylamino)-2-isopropyl-1H-benzo[de]isoquinoline-1,3(2H)-dione, compound **3e***

The procedure is the same as the synthesis of compound **3a**. Compound **2b** (1 mmol, 0.32 g), 1,4-dioxane (20 mL), 1,2-diaminoethane (ethylenediamine) (10 mmol, 0.7 mL) and triethylamine (5 mmol, 0.7 mL) were used. Yield: 70%, 0.2 g; mp = 153–154 °C; IR (film) ν_{max} cm^{-1}: 3380; 1690; 1660. ^1H NMR (300 MHz, $CDCl_3$): δ 1.46 (bs, 2H); 1.59 (d, $J = 6.8$ Hz, 6H); 3.17 (t, $J = 5.1$ Hz, 2H); 3.41 (m, 2H); 5.44 (heptet, $J = 6.8$ Hz, 1H); 6.1 (bs, 1H); 6.70 (d, $J = 8.4$ Hz, 1H); 7.61 (dd, $J = 7.2$ Hz, 8.4 Hz, 1H); 8.14 (dd, $J = 1.2$ Hz, 8.4 Hz, 1H); 8.44 (d, $J = 8.4$ Hz, 1H); 8.55 (dd, $J = 1.2$ Hz, 7.2 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 19.8; 40.2; 44.7; 44.9; 104.5; 114.5; 120.4; 123.7; 124.7; 125.9; 129.8; 130.9; 134.3; 149.4; 164.6; 165.0. HRMS (EI, *m/z*) calcd. for $C_{17}H_{20}N_3O_2$ 298.1550 ($M^+ + 1$), Found 298.1560.

*4.3.9. Synthesis of 6-(2-hydroxyethylamino)-2-isopropyl-1H-benzo[de]isoquinoline-1,3(2H)-dione, compound **3f***

The procedure is the same as the synthesis of compound **3b**. Compound **2b** (1 mmol, 0.32 g), 1,4-dioxane (20 mL), 2-aminoethanol (10 mmol, 0.6 mL) and triethylamine (5 mmol, 0.7 mL) were used. Yield: 73%, 0.22 g; mp = 203–204 °C; IR (film) ν_{max} cm^{-1}: 3380; 1690; 1660. ^1H NMR (400 MHz, acetone-d_6): δ 1.54 (d, $J = 6.8$ Hz, 6H); 2.81 (bs, 1H); 3.60 (m, 2H); 3.91 (t, $J = 5.5$ Hz, 2H); 4.08 (bs, 1H); 5.4 (heptet, $J = 6.8$ Hz, 1H); 6.87 (d, $J = 8.8$ Hz, 1H); 7.65 (dd, $J = 7.2$ Hz, 8.6 Hz, 1H); 8.33 (d, $J = 8.8$ Hz, 1H); 8.46 (dd, $J = 1.2$ Hz, 7.2 Hz, 1H); 8.54 (dd, $J = 1.2$ Hz, 8.6 Hz, 1H). ^{13}C NMR (100 MHz, acetone-d_6): δ 20.1; 44.9; 46.8; 60.6; 104.9; 110.9; 121.5; 124.4; 125.3; 128.0; 130.8; 131.4; 134.9; 151.2; 164.6; 165.2. HRMS (EI, *m/z*) calcd. for $C_{17}H_{18}N_2O_3$ 298.1317 (M^+), Found 298.1315.

*4.3.10. Synthesis of (6-((2-hydroxyethyl)(methyl)amino)-2-isopropyl-1H-benzo[de]isoquinoline-1,3(2H)-dione), compound **3g***

The procedure is the same as the synthesis of compound **3c**. Compound **2b** (1 mmol, 0.32 g), 1,4-dioxane (20 mL), 2-(methylamino)ethanol (10 mmol, 0.8 mL) and triethylamine (6 mmol, 0.82 mL) were used. Yield: 65%, 0.20 g; mp = 147–148 °C; IR (film) ν_{max} cm^{-1}: 3380; 1690; 1660. ^1H NMR (400 MHz, acetone-d_6): δ 1.55 (d, $J = 6.8$ Hz, 6H); 2.68 (bs, 1H); 3.12 (s, 3H); 3.51 (t, $J = 5.6$ Hz, 2H); 3.93 (t, $J = 5.6$ Hz, 2H); 5.39 (heptet, $J = 6.8$ Hz, 1H); 7.34 (d, $J = 8.2$ Hz, 1H); 7.72 (dd, $J = 7.2$ Hz, 8.4 Hz, 1H); 8.39 (d, $J = 8.2$ Hz, 1H); 8.47 (dd, $J = 1.2$ Hz, 7.2 Hz, 1H); 8.77 (dd, $J = 1.2$ Hz, 8.4 Hz, 1H). ^{13}C NMR (100 MHz, acetone-d_6): δ 19.0; 40.3; 44.2; 59.1; 59.4; 114.6; 115.7; 123.6; 124.9; 125.7; 130.0; 130.3; 131.0; 131.8; 156.8; 163.6; 164.1. HRMS (EI, *m/z*) calcd. for $C_{18}H_{20}N_2O_3$ 312.1473 (M^+), Found 312.1469.

*4.3.11. Synthesis of 6-(2-hydroxyethoxy)-2-isopropyl-1H-benzo[de]isoquinoline-1,3(2H)-dione, compound **3h***

The procedure is the same as the synthesis of compound **3d**. Compound **2b** (1 mmol, 0.32 g), 1,2-ethanediol (20 mL) and potassium hydroxide (2 mmol, 0.112 g) were used. Yield: 77%, 0.23 g; mp = 174–175 °C; IR (film) ν_{max} cm^{-1}: 3380; 1690; 1660. ^1H NMR (400 MHz, $CDCl_3$): δ 1.60 (d, $J = 6.8$ Hz, 6H); 2.38 (bs, 1H); 4.20 (t, $J = 4.4$ Hz, 2H); 4.40 (t, $J = 4.4$ Hz, 2H); 5.42 (heptet, $J = 6.8$ Hz, 1H); 7.00 (d, $J = 8.4$ Hz, 1H); 7.65 (dd, $J = 7.6$ Hz, 8.4 Hz, 1H); 8.47 (d,

$J = 8.4$ Hz, 1H); 8.51 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.8; 45.2; 61.2; 70.2; 106.0; 115.8; 122.9; 123.2; 126.0; 128.1; 129.3; 131.5; 133.2; 159.5; 164.4; 164.8. HRMS (EI, *m/z*) calcd. for $C_{17}H_{17}NO_4$ 299.1157 (M^+), Found 299.1163.

4.3.12. Synthesis of 6-(2-aminoethylamino)-2-propyl-1H-benzo[de]isoquinoline-1,3(2H)-dione, compound **3i**

The procedure is the same as the synthesis of compound **3a**. Compound **2c** (1 mmol, 0.32 g), 1,4-dioxane (20 mL), 1,2-diaminoethane (10 mmol, 0.7 mL) and triethylamine (5 mmol, 0.7 mL) were used. Yield: 68%, 0.2 g; mp = 155−156 °C; IR (film) ν_{max} cm^{-1}: 3380; 1690; 1660. ^{1}H NMR (300 MHz, CD_2Cl_2): δ 1.01 (t, $J = 7.4$ Hz, 3H); 1.41 (bs, 2H); 1.76 (m, 2H); 3.18 (m, 2H); 3.41 (m, 2H); 4.13 (m, 2H); 6.12 (bs, 1H); 6.71 (d, $J = 8.4$ Hz, 1H); 7.62 (dd, $J = 7.5$ Hz, 8.4 Hz, 1H); 8.16 (dd, $J = 0.9$ Hz, 8.4 Hz, 1H); 8.47 (d, $J = 8.4$ Hz, 1H); 8.59 (dd, $J = 0.9$ Hz, 7.5 Hz, 1H). ^{13}C NMR (100 MHz, acetone-d_6): δ 11.8; 22.2; 41.9; 45.0; 50.7; 105.1; 110.5; 121.5; 123.9; 125.4; 128.1; 130.1; 131.5; 135.0; 151.3; 164.3; 165.0. HRMS (EI, *m/z*) calcd. for $C_{17}H_{20}N_3O_2$ 298.1550 ($M^+ + 1$), Found 298.1557.

4.3.13. Synthesis of 6-(2-hydroxyethylamino)-2-propyl-1H-benzo[de]isoquinoline-1,3(2H)-dione, compound **3j**

The procedure is the same as the synthesis of compound **3b**. Compound **2c** (1 mmol, 0.32 g), 1,4-dioxane (20 mL), 2-aminoethanol (10 mmol, 0.6 mL) and triethylamine (5 mmol, 0.7 mL) were used. Yield: 74%, 0.22 g; mp = 171−172 °C; IR (film) ν_{max} cm^{-1}: 3380; 1690; 1660. ^{1}H NMR (400 MHz, methanol-d_4): δ 0.91 (t, $J = 7.2$ Hz, 3H); 1.76 (m, 2H); 3.51 (t, $J = 5.6$ Hz, 2H); 3.81 (t, $J = 5.6$ Hz, 2H); 4.00 (m, 2H); 6.73 (d, $J = 8.4$ Hz, 1H); 7.53 (dd, $J = 7.2$ Hz, 8.4 Hz, 1H); 8.24 (d, $J = 8.4$ Hz, 1H); 8.40 (m, 2H). ^{13}C NMR (100 MHz, methanol-d_4): δ 11.9; 22.6; 42.7; 46.8; 61.0; 105.3; 109.8; 122.0; 123.6; 125.6; 129.4; 131.4; 132.3; 136.0; 152.8; 165.9; 166.4. HRMS (EI, *m/z*) calcd. for $C_{17}H_{18}N_2O_3$ 298.1317 (M^+), Found 298.1321.

4.3.14. Synthesis of (6-((2-hydroxyethyl)(methyl)amino)-2-propyl-1H-benzo[de]isoquinoline-1,3(2H)-dione), compound **3k**

The procedure is the same as the synthesis of compound **3c**. Compound **2c** (1 mmol, 0.32 g), 1,4-dioxane (20 mL), 2-(methylamino)ethanol (10 mmol, 0.8 mL) and triethylamine (6 mmol, 0.82 mL) were used. Yield: 60%, 0.19 g; mp = 131−132 °C; IR (film) ν_{max} cm^{-1}: 3380; 1690; 1660. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.01 (t, $J = 7.6$ Hz, 3H); 1.75 (m, 2H); 2.04 (bs, 1H); 3.01 (s, 3H); 3.5 (t, $J = 5.6$ Hz, 2H); 3.95 (m, 2H); 4.12 (m, 2H); 7.26 (d, $J = 8.0$ Hz, 1H); 7.68 (dd, $J = 7.5$ Hz, 8.4 Hz, 1H); 8.48 (d, $J = 8.0$ Hz, 1H); 8.56 (dd, $J = 1.2$ Hz, 7.4 Hz, 1H); 8.60 (dd, $J = 1.2$ Hz, 8.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.7; 21.6; 41.9; 42.0; 58.8; 59.7; 115.7; 116.7; 123.4; 125.8; 126.4; 130.2; 130.7; 131.3; 132.5; 156.6; 164.2; 164.7. HRMS (EI, *m/z*) calcd. for $C_{18}H_{20}N_2O_3$ 312.1473 (M^+), Found 312.1469.

4.3.15. Synthesis of 6-(2-hydroxyethoxy)-2-propyl-1H-benzo[de]isoquinoline-1,3(2H)-dione, compound **3l**

The procedure is the same as the synthesis of compound **3d**. Compound **2c** (1 mmol, 0.32 g), 1,2-ethanediol (20 mL) and potassium hydroxide (2 mmol, 0.112 g) were used. Yield: 78%, 0.23 g; mp = 155−156 °C; IR (film) ν_{max} cm^{-1}: 3380; 1690; 1660. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.02 (t, $J = 7.2$ Hz, 3H); 1.76 (m, 2H); 2.03 (t, $J = 5.6$ HZ, 1H); 4.15 (m, 4H); 4.41 (t, $J = 4.8$ Hz, 2H); 7.05 (d, $J = 8.2$ Hz, 1H); 7.71 (dd, $J = 7.6$ Hz, 8.4 Hz, 1H); 8.54 (d, $J = 8.2$ Hz, 1H); 8.59 (m, 2H). ^{13}C NMR (100 MHz, methanol-d_4): δ 11.5; 21.4; 41.8; 61.3; 70.3; 106.0; 115.6; 122.6; 123.5; 126.0; 128.4; 129.4; 131.6; 133.3; 159.7; 163.9; 164.5. HRMS (EI, *m/z*) calcd. for $C_{17}H_{17}NO_4$ 299.1157 (M^+), Found 299.1156.

4.3.16. Synthesis of (2-((2-isopropyl-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl)(methyl)amino)ethyl methacrylate), compound **4**

Anhydrous dichloromethane (50 mL), compound **3g** (0.312 g, 1 mmol) and triethylamine (0.41 mL, 3 mmol) were added to a three-neck 150 mL round-bottomed flask equipped with a condenser, magnet and a gas inlet. Methacryloyl chloride (0.2 mL, 2 mmol) in dichloromethane (5 mL) was added dropwise into the mixture at 0 °C and stirred for 30 min. It was then warmed to room temperature and stirred for 10 more hours. The completion of the reaction was monitored by TLC with *n*-hexane−acetone (3:1) as eluent. The reaction was quenched with water (5 mL), washed three times with saturated $NaHCO_3$ (10 mL each time) and water (10 mL). The resulting organic layer was dried over anhydrous $MgSO_4$, filtered, and evaporated under vacuum. Purification by column chromatography on silica gel (first fraction) gave the desired product as a green oil. Yield: 69%, 0.26 g; IR (film) ν_{max} cm^{-1}: 3380; 1690; 1660. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.51 (d, $J = 6.8$ Hz, 6H); 1.79 (s, 3H); 3.02 (s, 3H); 3.57 (t, $J = 5.4$ Hz, 2H); 4.38 (t, $J = 5.4$ Hz, 2H); 5.35 (heptet, $J = 6.8$, 1H); 5.45 (bs, 1H); 5.91 (bs, 1H); 7.15 (d, $J = 8.4$ Hz, 1H); 7.57 (dd, $J = 7.4$ Hz, 7.6 Hz, 1H); 8.39 (m, 2H); 8.46 (dd, $J = 0.8$ Hz, 7.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 18.4; 20.0; 41.4; 45.1; 55.9; 61.7; 115.6; 117.0; 123.9; 125.6; 126.1; 126.2; 130.2; 130.4; 131.5; 132.3; 136.1; 156.0; 164.5; 165.0; 167.3. HRMS (EI, *m/z*) calcd. for $C_{22}H_{24}N_2O_4$ 380.1736 (M^+), Found 380.1736.

4.3.17. Synthesis of (2-((2-isobutyl-1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-6-yl)(methyl)amino)ethyl 2-bromo-2-methylpropanoate), compound **5**

Anhydrous dichloromethane (50 mL), compound **3c** (0.326 g, 1 mmol) and triethylamine (0.41 mL, 3 mmol) were added to a three-neck 150 mL round-bottomed flask equipped with a condenser, magnet and a gas inlet. 2-Bromoisobutyryl bromide (0.4 mL, 3 mmol) in dichloromethane (5 mL) was added dropwise into the mixture at 0 °C and stirred for 30 min. It was then warmed to the room temperature and stirred for 7 more hours. The completion of the reaction was monitored by TLC with *n*-hexane−acetone (3:1) as eluent. The reaction was quenched with water (5 mL), washed three times with saturated $NaHCO_3$ (10 mL each time) and

water (10 mL). The resulting organic layer was dried over anhydrous $MgSO_4$, filtered and evaporated in vacuum. Purification by column chromatography on silica gel (first fraction) gave the desired product as a green oil. Yield: 72%, 0.34 g; IR (film) ν_{max} cm^{-1}: 1737; 1695; 1656; 1589; 1380. ^1H NMR (400 MHz, acetone-d_6): δ 0.94 (d, $J = 6.8$ Hz, 6H); 1.79 (s, 6H); 2.21 (m, 1H); 3.18 (s, 3H); 3.80 (t, $J = 5.4$ Hz, 2H); 3.96 (d, $J = 7.5$ Hz, 2H); 4.51 (t, $J = 5.5$ Hz, 2H); 7.42 (d, $J = 8.4$ Hz, 1H); 7.78 (dd, $J = 7.2$ Hz, 8.6 Hz, 1H); 8.43 (d, $J = 8.4$ Hz, 1H); 8.51 (dd, $J = 1.2$ Hz, 7.2 Hz, 1H); 8.64 (dd, $J = 1.2$ Hz, 8.6 Hz, 1H). ^{13}C NMR (100 MHz, acetone-d_6): δ 19.7; 27.2; 40.8; 46.4; 55.1; 56.1; 56.5; 63.0; 115.6; 115.9; 123.2 125.4; 126.0; 130.0; 130.6; 130.9; 132.0; 156.2; 163.5; 164.1; 170.9. HRMS (EI, *m/z*) calcd. for $C_{23}H_{27}N_2O_4Br$ 474.1154 (M^+), Found 474.1158.

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