ORGANIC LETTERS
2007
Vol. 9, No. 21
4183−4186

Synthesis, Photophysical Properties, and Laser Behavior of 3-Amino and 3-Acetamido BODIPY Dyes

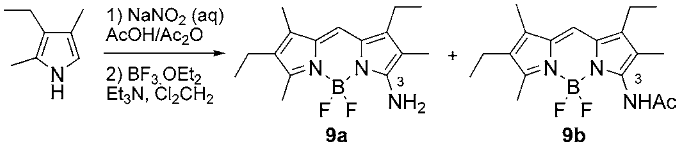
**Marta Liras,[*,†,‡] Jorge Bañuelos Prieto,[§] Mercedes Pintado-Sierra,[‡]
Fernando López Arbeloa,[§] Inmaculada García-Moreno,[⊥] Ángel Costela,[⊥]
Lourdes Infantes,[⊥] Roberto Sastre,[||] and Francisco Amat-Guerri[*,‡]**

Universidad Miguel Hernández (UMH), Ferrocarril s/n, Edificio Torrevaillo, Elche, 03202 Alicante, Spain, Instituto de Química Orgánica (IQO), CSIC, Juan de la Cierva 3, 28006 Madrid, Spain, Departamento de Química-Física, Universidad del País Vasco (UPV-EHU), Apartado 644, 48080 Bilbao, Spain, Instituto de Química-Física "Rocasolano" (IQFR), CSIC, Serrano 119, 28006 Madrid, Spain, and Instituto de Ciencia y Tecnología de Polímeros (ICTP), CSIC, Juan de la Cierva 3, 28006 Madrid, Spain

famat@iqog.csic.es

Received July 16, 2007

ABSTRACT



The asymmetrically substituted BODIPY dyes 9a and 9b have been synthesized through a key redox step involving the α-nitroso derivative of the starting pyrrol. Both dyes emit fluorescence with quantum yields of ca. 0.7, but only 8b behaves as a good laser dye, with an efficiency of 48% in ethanol solution.

Dipyrromethene compounds with the basic structure **1** (Figure 1), first described in regard to the synthesis of the porphyrin core,[1] easily react with boron trifluoride in the presence of amines giving rise to borondifluorodipyrromethene dyes with the chromophore **2**, also known as BODIPY or BDP dyes. BDP dyes were first synthesized in 1968 as the fortuitous result of the tentative α-acetylation of 2,4-dimethylpyrrole with acetic anhydride in the presence of boron trifluoride diethyl etherate.[2] Two decades later, these dyes were rediscovered because of their high fluorescence quantum yields, high photostability,[3] and efficient laser emission in solution.[4] These properties can be modulated by the substituents of **2**, and there is an intense research effort on the design, synthesis, and evaluation of new BDP dyes for different applications.[5]

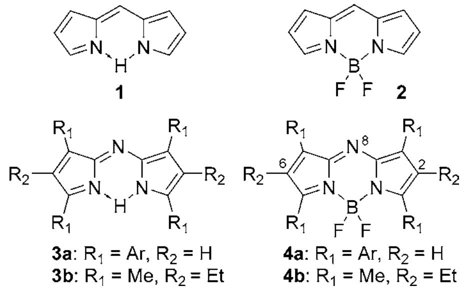


Figure 1. Basic structures of BDP (**2**) and 8-aza-BDP (**4**) dyes and of their corresponding precursors **1** and **3**.

[†] UMH.
[‡] IQO.
[§] UPV-EHU.
[⊥] IQFR.
[||] ICTP.
(1) Fischer, H.; Eismayer, K. *Ber.* **1914**, *47*, 2019.
(2) Treibs, A.; Kreuzer, K. *Liebigs Ann. Chem.* **1968**, *718*, 208.

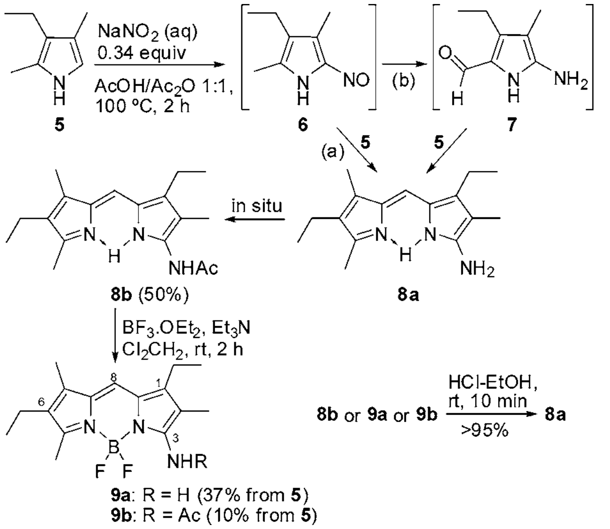
10.1021/ol701674b CCC: $37.00 © 2007 American Chemical Society
Published on Web 09/19/2007

As a part of our interest in developing highly efficient lasing dyes,[6] the 8-aza-BDP (ABDP) chromophore attracted our attention. Tetraaryl-substituted ABDP dyes **4a** show fluorescence emission at 710−815 nm and modest fluorescent quantum yields, Φ_f ca. 0.3.[7] We speculated that these low Φ_f values—if compared with those of many alkyl-substituted BDP dyes—could be due to dissipation of the excitation energy by rotation of the aryl groups in the excited state.[8] Consequently, we decided to synthesize and study the emission of new alkyl-substituted ABDP compounds such as **4b**.

The aryl-substituted dyes **4a** are obtained from the corresponding precursors **3a**,[9,10] which have been synthesized by two methods: the reaction of *β*-nitrodihydrochalcones with ammonium salts[7,9,11,12] and the reaction of 2-nitroso-3,5-diarylpyrroles with 2,4-diarylpyrroles.[7,12] In our case, the tentative synthesis of **4b** via **3b** was assayed in two steps in a one-pot process, following conditions described for the synthesis of dyes **4a**:[7,12] 2,4-dimethyl-3-ethylpyrrole (**5**) was treated with aqueous sodium nitrite in the presence of acetic acid/acetic anhydride, and the crude reaction product was made to react with boron trifluoride diethyl etherate in the presence of triethylamine. Unexpectedly, the BDP dye **9a** and its *N*-acetyl derivative **9b** were identified as the main reaction products (Scheme 1).

Both dyes must come from the corresponding precursors **8**a and **8b**, formed through a redox step with the participation of the nitroso pyrrole **6**.[13] This step may be a bimolecular reaction with **5** (pathway (a), Scheme 1), with N═O reduction to NH_2 and simultaneous oxidative coupling between the α-H of **5** and the 5-methyl group of **6**. An alternative would be a unimolecular redox reaction of **6**, yielding 5-amino-3-ethyl-4-methylpyrrole-2-carbaldehyde (**7**) (pathway (b), Scheme 1). A subsequent condensation of **7**—via the aldehyde group—with **5**—via the α-H—can yield **8a**.

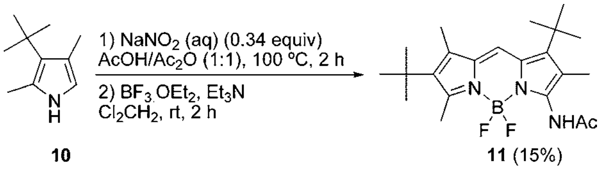
Scheme 1



An elusive intermediate with molecular weight 152, the same as that of **6** and **7**, was detected by GC-MS analysis of the crude mixture from the first stages of the reaction. In the reaction medium, amino groups are acetylated, and **8a** gives rise to **8b**. The possible appearance of **8b** via the reaction between in situ generated *N*-acetyl **7** and pyrrole **5** cannot be discarded. Eventually, the reaction of **8b** with boron trifluoride yields the dye **9b**, as well as its deacetylated derivative **9a**, which must appear through the formation in the medium of the intermediate **8a**, because under the same conditions **9b** is not deacetylated to **9a**. Under HCl-catalyzed deacetylation conditions, **8b** or **9b**, or even **9a**, gave rise to **8a** quantitatively.

A similar two-step process with 3-*tert*-butyl-2,4-dimethylpyrrole (**10**) yielded only the acetylated dye **11**, and the corresponding deacetylated compound was not detected (Scheme 2). Under the same conditions, 2,4-dimethylpyrrole gave rise to 2-acetyl-3,5-dimethylpyrrole (12%), among other minor products, suggesting that the former redox reaction takes place only when the position 3 in the starting pyrrole is substituted. To our knowledge, this redox reaction is new in the chemistry of pyrroles.

Scheme 2



The structures of **9a** and **9b** were deduced from their ^1H and ^{13}C NMR spectra and confirmed by single-crystal X-ray spectroscopy. The crystal of **9a** shows two independent molecules differing mainly in the conformation of the substituents of the indacene core (Figure 2A), while **9b** crystallizes as one independent molecule (Figure 2B).

---

(3) (a) Pavlopoulos, T. G.; Boyer, J. H.; Shah, M.; Thangaraj, K.; Soong, M. L. *Appl. Opt.* **1990**, *29*, 3885. (b) Pavlopoulos, T. G.; Boyer, J. H.; Thangaraj, K.; Sathyamoorthi, G.; Shah, M. P.; Soong, M. L. *Appl. Opt.* **1992**, *31*, 7089. (c) Boyer, J. H.; Haag, A. M.; Sathyamoorthi, G.; Soong, M. L.; Thangaraj, K.; Pavlopoulos, T. G. *Heteroat. Chem.* **1993**, *4*, 39. (d) Guggenheimer, S. C.; Boyer, J. H.; Thangaraj, K.; Shah, M. P.; Soong, M. L. *Appl. Opt.* **1993**, *32*, 3942. (e) O'Neil, M. P. *Opt. Lett.* **1993**, *18*, 37. (f) Vos de Wael, E.; Pardoen, J. A.; van Koeveringe, J. A.; Lugtenburg, J. *J. Royal Neth. Chem. Soc.* **1997**, *96*, 3060. (g) Gorman, A. A.; Hamblett, I.; King, T. A.; Rahn, M. D. *J. Photochem. Photobiol., A* **2000**, *130*, 127. (h) Pavlopoulos, T. G. *Prog. Quant. Electron.* **2002**, *26*, 193.

(4) (a) Pavlopoulos, T. G.; Shah, M.; Boyer, J. H. *Appl. Opt.* **1988**, *27*, 4998. (b) Pavlopoulos, T. G.; Shah, M.; Boyer, J. H. *Opt. Commun.* **1989**, *70*, 425.

(5) Porrès, L.; Mongin, O.; Blanchard-Desce, M. *Tetrahedron* **2006**, *47*, 1913, and references cited therein.

(6) Costela, A.; García-Moreno, I.; Sastre, R. *Phys. Chem. Chem. Phys.* **2003**, *5*, 4745.

(7) Zhao, W.; Carreira, E. K. *Chem.−Eur. J.* **2006**, *12*, 7254−7263.

(8) Chen, J.; Burghart, A.; Derecskei-Kovacs, A.; Burguess, K. *J. Org. Chem.* **2000**, *65*, 2900.

(9) Gorman, A.; Killoran, J.; O'Shea, C.; Kenna, T.; Gallagher, W. M.; O'Shea, D. F. *J. Am. Chem. Soc.* **2004**, *126*, 10619.

(10) Killoran, J.; Allen, L.; Gallagher, J. F.; Gallagher, W. M.; O'Shea, D. F. *Chem. Commun.* **2002**, 1862.

(11) Rogers, M. A. T. *J. Chem. Soc.* **1943**, 590.

(12) (a) Hall, M. J.; McDonnell, S. O.; Killoran, J.; O'Shea, D. F. *J. Org. Chem.* **2005**, *70*, 5571. (b) Zhao, W.; Carreira, E. K. *Angew. Chem., Int. Ed.* **2005**, *44*, 1677. (c) Hall, M. J.; Allen, L. T.; O'Shea, D. F. *Org. Biomol. Chem.* **2006**, *4*, 776.

(13) For a review on the synthesis of nitroso compounds, see: Gowenlock, B. G.; Richter-Addo, G. B. *Chem. Rev.* **2004**, *104*, 3315.

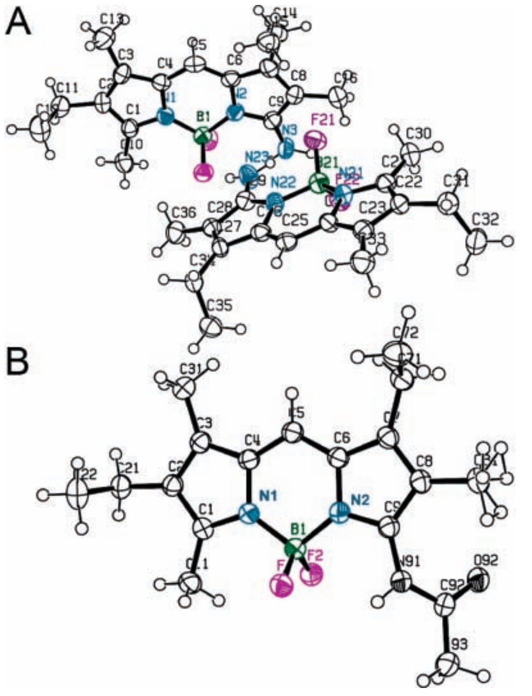


Figure 2. X-ray molecular structures of the dyes **9a** (A) and **9b** (B) showing the atomic numbering scheme. Ellipsoids are drawn at the 50% probability level for non-H atoms, and the H atoms are denoted as spheres of 0.1 Å radius.

Table 1. Photophysical Properties of the Dyes **9a** (2.0 μM) and **9b** (2.4 μM) in Several Solvents: Wavelengths of Maximum Absorption (λ_a) and Fluorescence Emission (λ_f), Molar Absorption Coefficient (ϵ_{max}), Fluorescence Quantum Yield (Φ_f), and Lifetime (τ) and Wavelength of Laser Emission (λ_{laser}) and Laser Efficiency (Eff) of 0.40 mM Solutions of **9b**

dye	solvent	λ_a (nm)[a]	λ_f (nm)[a]	ϵ_{max} (10^4 M^{-1} cm^{-1})	Φ_f[b]	τ (ns)[c]	λ_{laser} (nm)	Eff (%)
9a	EtOH	503	529	2.8	0.72	4.17	–	–
	EtOAc	506	529	3.0	0.69	3.89	–	–
	cyclohexane	526	532	5.6	0.71	4.06	–	–
9b	EtOH	534	547	5.4	0.70	5.89	564	48
	EtOAc	538	549	7.1	0.68	5.63	567	45
	cyclohexane	545	553	8.4	0.68	5.44	571	43

[a] ±0.1 nm. [b] ±0.05. [c] ±0.05 ns.

The wavelength of maximum absorption (Table 1) and the absorption spectral shape of the dyes **9a** and **9b** (Figure 3) strongly depend on the solvent polarity, with sharper bands in apolar solvents. For both dyes, the emission maximum shows a higher Stokes shift value in polar solvents. Acetylation of the amino group of **9a** gives rise to a bathochromic shift of 20−43 nm in the absorption band, with an increase of the molar absorption coefficient and with a parallel shift of 12−21 nm to longer wavelengths in the emission maximum. On the contrary, the fluorescent quantum yields and lifetimes show similar values in both compounds.

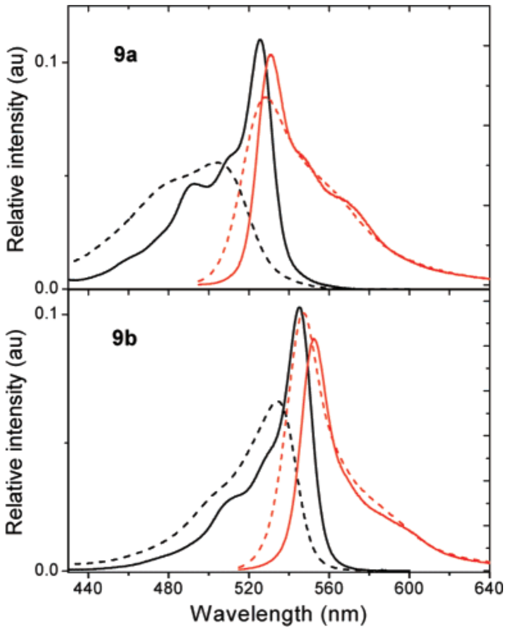


Figure 3. Absorption (black) and fluorescence emission (red) spectra of the dyes **9a** and **9b** in cyclohexane (solid line) and ethanol (dashed line).

The similar emission properties of both dyes do not correspond with the very different laser behavior in solution. **9a** does not show laser emission when excited with 532 nm (pump energy 5.5 mJ/pulse, repetition rate 10 Hz), even at concentrations of ca. 1.5 mM. On the contrary, under the same conditions, the acetylated dye **9b** emits laser light at 564−571 nm (Table 1), with higher solvent dependence than in the case of symmetric BDP dyes,[14] thus allowing a higher laser modulation. The laser efficiencies are in the range 43−48%, values higher than those of the reference laser dye PM567 in the same solvents.[15] Aggregation of **9a** in solution is not the cause of the absence of laser emission, because the shape of the absorption spectrum does not change with the dye concentration, at least until 1.5 mM. The causes of this very different laser behavior are under study.

In ethanol solution, the laser emission wavelength and the efficiency (percentage of the excitation energy converted into laser emission) of **9b** depend on the dye concentration, with a maximum efficiency of 48% at 0.40 mM (Figure 4). From this point on, further increases in the dye concentration result in a slight decrease in the lasing efficiency.

Similar photophysical properties and laser behavior were observed for the dye **11**, with laser emission at 564 nm with 58% efficiency (0.45 mM solution in EtOH).

---

(14) Costela, A.; García-Moreno, I.; Sastre, R.; Amat-Guerri, F.; Liras, M.; López Arbeloa, F.; Bañuelos Prieto, J.; López Arbeloa, I. *J. Phys. Chem. A* **2002**, *106*, 7736.

(15) López Arbeloa, F.; López Arbeloa, T.; López Arbeloa, I.; García-Moreno, I.; Costela, A.; Sastre, R.; Amat-Guerri, F. *Chem. Phys. Lett.* **1999**, *299*, 315.

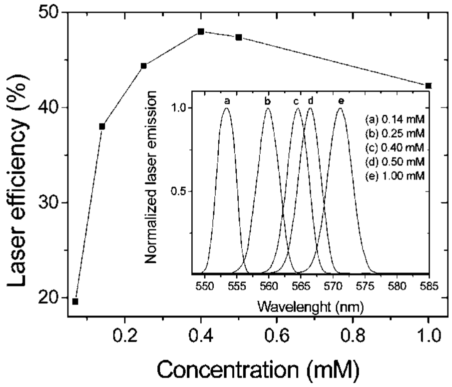


Figure 4. Laser efficiency (main) and normalized laser emission spectra (inset) of the dye **9b** in ethanol, as a function of the dye concentration. Excitation at 532 nm; optical density in the range 7.4−54.

The laser emission wavelength also depends on the dye concentration, shifting to lower energies as the concentration increases. This trend must be related to the effect of reabsorption/reemission phenomena on the emission intensity and could be the origin of the lasing efficiency decrease observed in the more concentrated solutions.[16]

The laser emission was also assayed with a solid solution of **9b** (0.4 mM) in poly(methyl methacrylate) (Figure 5), the concentration that gives rise to the highest lasing efficiency in liquid solution. This material emits laser radiation at 563 nm with 25% efficiency, a value similar within experimental error to that of the reference dye PM567 in the same polymer and comparative conditions (28%). However, the photostability of **9b** is lower than that of other BDP laser dyes[17] because its laser emission disappears after only 20 000 pump pulses.

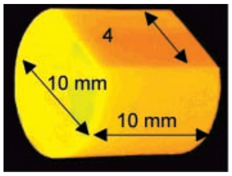


Figure 5. Polymeric solid laser sample with **9b** (0.40 mM).

In short, we have established an easy synthetic method for the synthesis of asymmetric 3-amino- and 3-acetamido-BDP dyes from 2,3,4-trialkyl-substituted pyrroles. The acetylated dye **9b**, and not its precursor **9a**, has demonstrated good laser emission properties. In addition, BDP dyes with the 3-amino group directly bonded to the chromophore core can be used for the labeling of molecules of biological interest with these highly fluorescent groups.

Acknowledgment. This work was supported by Project MAT2004-04643-C03-01 and -02 of the Spanish CICYT. M.L. and M.P.-S. thank Ministerio de Educación y Ciencia for a “Juan de la Cierva” contract and a grant, respectively.

Supporting Information Available: General experimental procedures, synthesis and characterization of compounds, and X-ray crystallographic data. This material is available free of charge via the Internet at http://pubs.acs.org.

OL701674B

---

(16) López Arbeloa, I. *J. Photochem.* **1980**, *14*, 97.

(17) García-Moreno, I.; Amat-Guerri, F.; Liras, M.; Costela, A.; Infantes, L.; Sastre, R.; López Arbeloa, F.; Bañuelos Prieto, J.; López Arbeloa, I. *Adv. Func. Mater.* **2007**, DOI 10.1002/adfm.20061103.