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Synthesis of New Molecules Containing Head, Spacer, and Label Moieties

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We describe the synthesis and characterization of novel molecules containing head with precise shape, spacer, and label moieties. The protocol is based on a Pd(0)-catalyzed cross-coupling reaction between ethynylphenyl/bromide to obtain a rigid head followed by the attachment of a flexible spacer possessing two reactive functional groups on the termini. The final step consists of forming a covalent bond between spacer and label. In addition, monosubstituted soluble labels were synthesized in good yields.

Introduction

In natural photosynthesis, arrays of antennae collect solar energy and convert it into the chemical potential energy that drives the chemistry of the photosynthetic machinery. The processes involved are very fast and highly efficient.[1,2] Good examples of the scientific progress in light-harvesting systems are the artificial photonic antenna systems, where highly effective energy transport has been reported.[3−7] In these systems, zeolite L crystals are used as a host to organize dye molecules inside monodirectional channels as shown in Figure 1A. Light shining on the cylindrical crystals is first absorbed by donor molecules (D) and then transported to the acceptor molecules (A). These antenna systems work so well that it is a major challenge to modify them to utilize the collected energy. For a number of technological applications, e.g. on a semiconductor surface, it is favorable to trap the excitation energy at the external surface of the crystals. This enables coupling of the antenna function with the environment of the crystals and simultaneously stabilizes the dye-loaded zeolite material.

Our approach involves adding "stopcock" molecules with polar groups at the end of the channels [6,8] as shown schematically in Figure 1B. The stopcock molecule has a part that is too big to penetrate into the channels of zeolite L (head), whereas the label is small enough to be inserted. The head and the label are connected by an inert flexible spacer, which also improves the solubility of the whole molecule. Various types of molecules with a stopcock shape have been explored, including substrates with an affinity for the cytochrome $P450_{cam}$ heme pocket,[9] biomaterials,[10,11] modified amino acids with defined binding sites for transition-metal complexes,[12−14] and selective molecular chemosensors.[15,16] Here, we report the synthesis of products with a combination of structural and functional moieties, which pave the way for their application as dyes or closures for the channels of zeolite L.

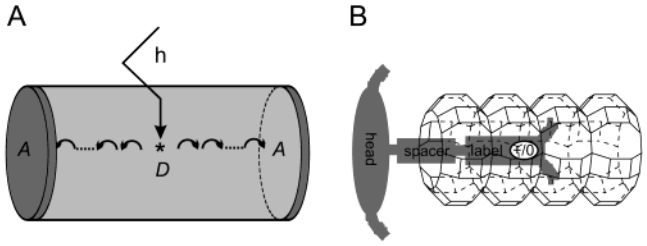

FIGURE 1. (A) Simplified view of a bidirectional photonic antenna. (B) Schematic representation of the typical shape of a stopcock molecule located at the end of a zeolite channel.

Results and Discussion

A synthetic strategy was developed for the preparation of varying stopcock molecules. The adopted procedure

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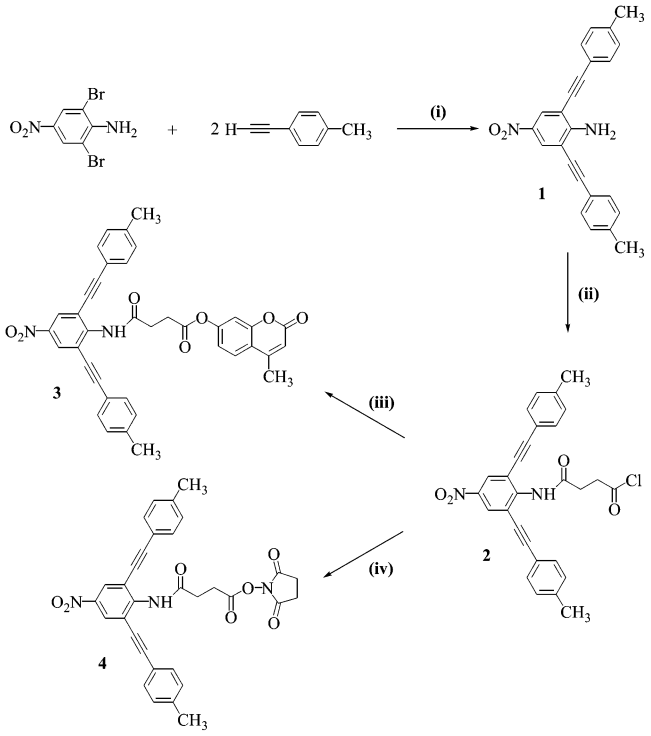
SCHEME 1[a]

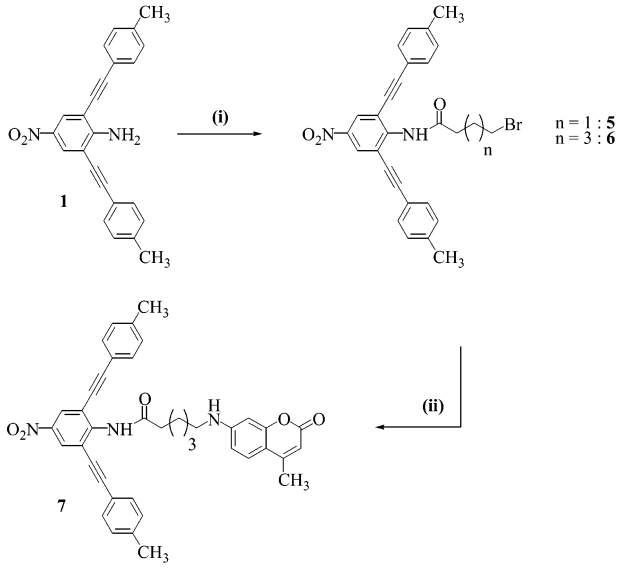


[a] Conditions: (i) $Pd(PPh_3)_4$ (6% mol), $(Et)_3N$ (excess), benzene, 70 °C, 22 h. (ii) succinyl chloride (1 equiv), $(Et)_3N$ (1 equiv), CH_2Cl_2, rt, 16 h. (iii) 7-hydroxy-4-methycoumarin (1 equiv), $(Et)_3N$ (1 equiv), CH_2Cl_2, rt, 30 h. (iv) *N*-hydroxysuccinimid (1 equiv), K_2CO_3 (excess), CH_3CN, 50 °C, 16 h.

utilizes key intermediates **1**, **2**, and **6**. Precursor **1** (Scheme 1) is synthesized by a cross-coupling reaction between 2,6-dibromo-4-nitroaniline and 4-ethynyltoluene in good yield (92%). The use of the catalytic system $Pd(PPh_3)_2Cl_2$/CuI [17,18] in THF overnight at room temperature showed only the monocoupled product. However, this reaction was carried out in the presence of catalytic amounts of $[Pd(PPh_3)_4]$, and an excess of triethylamine in nitrogen-degassed benzene at 70 °C. It is worth knowing that the Sonogashira coupling reaction tolerates the presence of nitro and arylamine functions without significantly perturbing the course of the palladium-promoted catalytic reaction. The emission spectrum of **1** shows a band at 470 nm, after excitation at 300 nm in dichloromethane.

The reaction of the intermediate **1** with succinyl chloride proceeded under nitrogen in dry dichloromethane at room temperature in the presence of 1 equiv of triethylamine.[19,20] After recrystallization from an appropriate solvent, **2** was recovered in 42% yield as a yellow solid. Upon exposure to the atmosphere, after a few days, compound **2** was decomposed and gave a brown solid. Repeating the reaction with an increasing quantity of triethylamine gave a dark mixture. TLC analysis during the course of the reaction showed an increase of

SCHEME 2[a]



[a] Conditions: (i) 4-bromobutyryl chloride (n=1) or 6-bromohexanoyl chloride (n=3) (1 equiv), $(Et)_3N$ (3 equiv), DMAP (10% mol), CH_2Cl_2, rt, 2d. (ii) 7-amino-4-methycoumarin (1.2 equiv), CF_3-CH_3OH, 100 °C, 2 d.

a new low spot R_f (0.27, CH_2Cl_2/hexane, 8/2) due to the unwanted cyclic succinimid product. The ^{13}C NMR spectrum data of **2** show the carbon of acid chloride and amide functions as singlets at 170.6 and 174.2 ppm, respectively.[21] Nonetheless, two singlets at 82.4 and 97.3 ppm being typical for acetylenic signals clearly point to the number of triple bonds in agreement with the expected structure.[22] The absorption spectra of **1** and **2** carried in dichloromethane at room temperature show several bands below 370 nm. Upon excitation of **2** at 300 nm, an emission at 400 nm was observed. The shift with respect to the emission of **1** is ascribed to a perturbation of the conjugated system due to the attached chain.

The preparation of the stopcock molecules **3** and **4** was accomplished by the stoichiometric esterification[23,24] of the acid chloride function from **2**, with 7-hydroxy-4-methylcoumarin and *N*-hydroxysuccinimid in moderate yields of 22 and 34%, respectively. The UV−vis absorption spectra of labeled compounds **3** and **4** measured in dichloromethane exhibited three maxima between 250 and 360 nm. After excitation at 300 nm, an emission maximum was observed around 375 nm with a broad band around 413 nm for **3** and 380 nm for **4**. Because of the low solubility of stopcocks **3** and **4**, other spacers were used, first to improve the solubility and second to vary the distance between head and label.

Further reaction of intermediate **1** with 4-bromobutyryl chloride (Scheme 2) in the presence of 3 equiv of triethylamine and 4-(dimethylamino)pyridine (DMAP) in dry dichloromethane at room temperature[25] afforded intermediate **5**. After purification by flash chromatography

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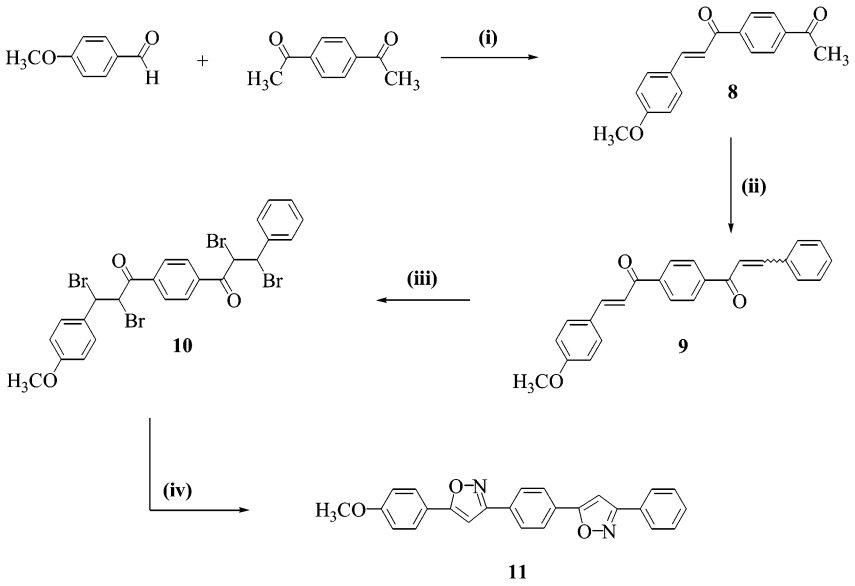
SCHEME 3[a]



[a] Conditions: (i) NaOH, CH_3OH/H_2O, rt, 1 h. (ii) Benzaldehyde (1 equiv), NaOH, CH_3OH/H_2O, rt, 5 h. (iii) Br_2 (2 equiv), $CHCl_3$, rt, 0.5 h. (iv) (a) $NH_2OH{\cdot}HCl$ (2 equiv), EtOH, 80 °C, 2 h; (b) KOH (6 equiv), EtOH, 80 °C, 1.5 h.

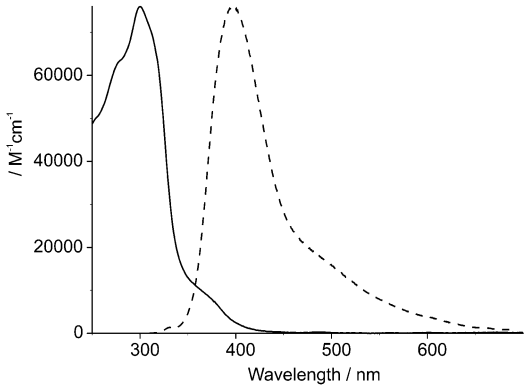


FIGURE 2. Absorption (solid) and luminescence (dotted) spectra recorded for **7**. The luminescence spectrum has been scaled to the absorption maximum.

on alumina and recrystallization in dichloromethane/hexane, **5** was recovered in 68% yield. Under similar conditions, reaction of **1** with 6-bromohexanoyl chloride gave **6**. This compound was obtained by similar workup in 74% yield. The pure intermediates **5** and **6** are soluble in most chlorinated solvents and are isolated as deep-yellow powders.

Stopcock molecule **7** was prepared by *N*-alkylation[26] between compound **6** and 1 equiv of 7-amino-4-methylcoumarin under nitrogen in 2,2,2-trifluoroethanol at 100 °C. After purification, **7** was recovered in 48% yield. The UV−vis absorption spectrum of **7** (Figure 2) measured in dichloromethane at room temperature exhibited a maximum at 300 nm with a shoulder at 275 nm and an additional band at 370 nm. After excitation at 300 nm, the fluorescence maximum was observed at 400 nm together with a long wavelength shoulder. These fluorescence bands can be attributed to the head and label, respectively. This is also confirmed by excitation spectra. The FT-IR spectra recorded for **1** to **7** all show a band between 2208 and 2214 cm^{-1}, associated with the acetylene stretching vibration.

In the second part of this work, we present the synthesis of monofunctionalized dyes with good solubility and linear structural properties. Monocondensation of 1,4-diacetylbenzene with 1 equiv of anisaldehyde (Scheme 3) in methanolic sodium hydroxide solution afforded a mixture of *cis*- and *trans*-1-(3-{4-methoxyaryl}-2-propenoyl)-4-acetylbenzene isomers,[27] where the product resulting from the biscondensation was observed. The monocondensation is profoundly influenced by the concentration, the solvent, and the amount of base. Purification on alumina followed by recrystallization in dichloromethane/hexane gave the trans isomer **8** in 63% yield.

Condensation under similar conditions of **8** with one molar proportion of benzaldehyde gave isomers **9** in 67% yield. Reaction of bromine in chloroform with **9** at room temperature gave compound **10**. Cyclization has been realized by refluxing **10** with 2 equiv of hydroxylammonium chloride in an ethanolic potassium hydroxide solution for about 2 h, affording **11** in 32% yield. The absorption spectrum of **8** shows two bands, one at 265 nm and the other at 349 nm. After reaction with benzaldehyde, **9** was obtained and the absorption maxima shifted to 273 and 341 nm, respectively. Bromation of the double bonds led to compound **10**, which showed only one weak absorption band at 273 nm. The band at 341 nm has disappeared. It can therefore be attributed to the olefins groups. Product **11** has an intense absorption at 280 nm with a long wavelength shoulder.

Esterification of the hydroxy group of 7-hydroxy-4-methylcoumarin (Scheme 4) was carried out by reacting it with 6-bromohexanoyl chloride or 0.5 equiv of succinyl chloride in dichloromethane as a solvent and triethylamine as a base at room temperature to give, after

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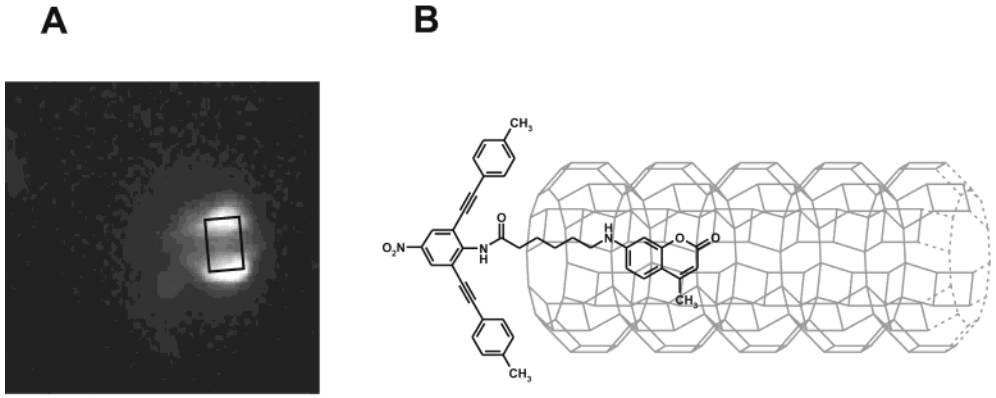
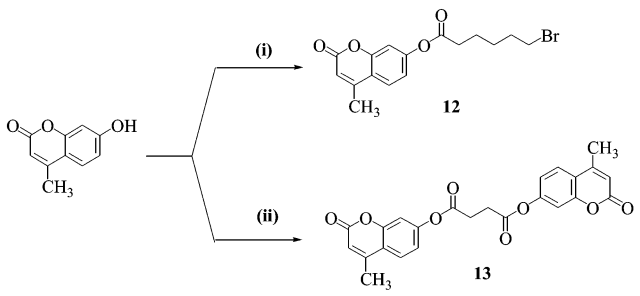


FIGURE 3. (A) Fluorescence microscope image showing a 2000 nm length zeolite L crystal modified with a molecule of **7** on each side of the channels. The sample was excited at 330−385 nm and observed through a cutoff filter at 420 nm. The rectangle indicates a single zeolite L crystal. (B) Schematic picture of **7** plugging a zeolite L channel in a stopcock manner.

SCHEME 4[a]



[a] Conditinos: (i) 6-bromohexanoyl chloride (1 equiv), $(Et)_3N$ (1 equiv), CH_2Cl_2, rt, 6 h (ii) succinyl chloride (0.5 equiv), $(Et)_3N$ (1 equiv), CH_2Cl_2, rt, 2 h.

purification, products **12** and **13** in quantitative yields (84 and 95%). Both absorption spectra of **12** and **13** measured in dichloromethane exhibited two distinct maxima at 272 and 312 nm and they are of almost identical shape. The molar extinction coefficients of **12** and **13** at the 312 nm band are 9800 and 14100 M^{-1} cm^{-1}, respectively. This reflects the number of coumarin units but also the fact that the chain has some influence on the oscillator strength.

Conclusion

We have provided a practical method for the synthesis of new stopcock molecules and soluble dyes with potential value for artificial antenna systems. The ready availability of the reagents, the overall simplicity of the procedure, the use of mild reaction conditions, and the reasonable yields obtained suggest that this methodology is a useful entry for the preparation of hybrid molecules bearing other luminescent fragments.

With product **7** some preliminary experiments with zeolite L crystals were done according to a similar procedure as described earlier.[8] Zeolite L crystals of about 2000 nm length were suspended in dichloromethane and the appropriate amount of **7** for a modification of 2 molecules per crystal channel was added. The suspension was first put in an ultrasonic bath for half an hour and then stirred for 2 h. Some drops were given on a microscope slide and the dichloromethane was evaporated. Then, the crystals were examined under a fluorescence microscope with 100× magnification with use of immersion oil with a refractive index close to that of zeolite L to exclude refraction effects. Figure 3A shows a zeolite L crystal modified with a molecule of **7** on each side of the channels. The image clearly shows that the emission stems from the bases of the cylindrical crystals, which appear as two bright lines. Since the free open diameter of the zeolite L channel is 7.1 Å and **7** is approximately 18 Å wide, the molecules cannot enter the channels, but the label can penetrate into the channel ends and plug them as shown in Figure 3B. This explains why the base surfaces of the crystals strongly emit.

Experimental Section

General Methods. The 300-MHz ^1H and 75-MHz ^{13}C NMR spectra were recorded at room temperature, unless specified, using perdeuterated solvent as an internal standard: δ (H) in ppm relative to residual protiated solvent in $CDCl_3$ (7.26); δ (C) in ppm relative to the solvent in $CDCl_3$ (77.0); all carbon signals were detected as singlets. Melting points were obtained on an open-ended Büchi (type Dr. Tottoli) capillary melting point apparatus and are uncorrected. FT-IR spectra were measured in KBr pellets. UV−vis spectra were measured with a Perkin-Elmer Lambda 900 spectrophotometer in CH_2Cl_2 at room temperature. Fluorescence spectra were recorded on a Perkin-Elmer LS-50B luminescence spectrometer with suitable cutoff filters. El-MS data were provided by analytical research services of the University of Bern. Elemental analyses (C, H, N) were performed with an elemental analyzer. Optical microscopy images of fluorescent samples were recorded under an Olympus BX 60 microscope combined with a Kappa CF 20 DCX Air K2 CCD camera with 100× magnification and an immersion oil.

Materials. 2,6-Dibromo-4-nitroaniline, 4-bromobutyryl chloride, 6-bromohexanoyl chloride, 1,4-diacetylbenzene, 7-amino-4-methylcoumarin and 7-hydroxy-4-methylcoumarin were purchased from Aldrich. $[Pd(PPh_3)_4]$, triethylamine, succinyl chloride, anisaldehyde, and benzaldehyde were purchased from Fluka. 4-Ethynyltoluene was prepared according to a similar procedure in the literature.[17,18] All reactions were carried out under dry nitrogen by using Schlenk-tube techniques.

2,6-Bis(4-ethynyltoluene)-4-nitroaniline (1). A Schlenk flask equipped with a septum, a Teflon-coated magnetic stirring bar, and an nitrogen inlet was charged with 25 mL of nitrogen-degassed benzene, and then 0.500 g (1.689 mmol) of 2,6-dibromo-4-nitroaniline, 0.428 mL (3.378 mmol) of 4-ethynyltoluene, and 0.117 g (0.101 mmol) of $[Pd(PPh_3)_4]$ were added, followed by 3 mL of nitrogen-degassed triethylamine. After heating at 70 °C for 22 h, the solvent was removed under

vacuum, and the purification was performed by flash chromatography on alumina with hexane/CH_2Cl_2 (50 to 80%) as eluant to afford 0.569 g of **1** (92%). Mp 217−8 °C; ^{1}H NMR ($CDCl_3$) δ 2.40 (s, CH_3, 6H), 5.57 (bs, NH_2, 2H), 7.20 (d, J = 7.7 Hz, Ph, 4H), 7.44 (d, J = 8.1 Hz, Ph, 4H), 8.24 (s, Ph, 2H); ^{13}C NMR ($CDCl_3$) δ 21.6, 82.5 (C≡C), 96.8 (C≡C), 119.0, 124.9, 129.4, 131.6, 139.5, 153.1; FT-IR (KBr, cm^{-1}) 3486 (m), 3376 (s), 2208 (w, $\upsilon_{C\equiv C}$), 1606 (s), 1513 (s), 1497 (m), 1341 (s), 1324 (s), 1300 (s), 1287 (s), 895 (m), 812 (s); UV−vis (CH_2Cl_2) λ, nm (ϵ, M^{-1} cm^{-1}) 269 (48 200), 299 (44 500), 368 (34 500); El-MS, *m*/*z* 367 ([M + H]$^+$, 47), 366 ([M]$^+$, 100), 320 ([M − NO_2]$^+$, 45), 305 ([M − NO_2 − NH_2 + H]$^+$, 20). Anal. Calcd for $C_{24}H_{18}N_2O_2$: C, 78.69; H, 4.92; N, 7.65. Found: C, 78.21; H, 5.03; N, 7.46.

2,6-Bis(4-ethynyltoluene)-4-nitro-*N*-(butyryl-4-chloride)-aniline (2). A 0.200 g (0.546 mmol) sample of **1** was dissolved under nitrogen in dry CH_2Cl_2 (20 mL) and 0.061 mL (0.546 mmol) of succinyl chloride was added followed by 0.076 mL (0.546 mmol) of triethylamine. The solution was stirred at room temperature for 16 h and 20 mL of EtOAc was added. After filtration the solid was washed with ether and recrystallized in CH_2Cl_2/hexane to afford 0.111 g of **2** (42%). Mp 205−6 °C dec; ^{1}H NMR ($CDCl_3$) δ 2.39 (s, CH_3, 6H), 2.99 (bs, CH_2, 4H), 7.18 (d, J = 8.1 Hz, Ph, 4H), 7.35 (d, J = 8.1 Hz, Ph, 4H), 8.40 (s, Ph, 2H); ^{13}C NMR ($CDCl_3$) δ 21.6, 28.3, 29.1, 82.4 (C≡C), 97.3 (C≡C), 118.3, 125.6, 126.4, 129.4, 131.7, 140.1, 147.9, 170.6, 174.2; FT-IR (KBr, cm^{-1}) 3082 (w), 2212 (m, $\upsilon_{C\equiv C}$), 1726 (s), 1533 (s), 1456 (m), 1427 (m), 1341 (s), 1363 (s), 1175 (s), 895 (m), 816 (s); UV−vis (CH_2Cl_2) λ, nm (ϵ, M^{-1} cm^{-1}) 254 (30 000), 298 (39 500), 355 (4 700); El-MS, *m*/*z* 448 ([M − Cl]$^+$, 100), 418 ([M − Cl − O_2 + H]$^+$, 29), 366 ([M − $CO(CH_2)_2COCl$ + H]$^+$, 20). Anal. Calcd for $C_{28}H_{21}ClN_2O_4$: C, 69.42; H, 4.34; N, 5.79. Found: C, 69.29; H, 4.32; N, 5.58.

2,6-Bis(4-ylethynyltoluene)-4-nitro-*N*-(butyryl-4-{7-oxy-4-methylcoumarin ester})aniline (3). A 0.100 g (0.207 mmol) sample of **2** was dissolved under nitrogen in dry CH_2Cl_2 (15 mL) and 0.036 g (0.207 mmol) of 7-hydroxy-4-methylcoumarin was added followed by 0.029 mL (0.207 mmol) of triethylamine. The solution was stirred at room temperature for 30 h, 20 mL of water was added, and the product was extracted with CH_2Cl_2. The solvent was evaporated and the residue was washed with ether. The pure compound was obtained by recrystallization from CH_2Cl_2/hexane affording 0.028 g of **3** (22%). Mp 248−9 °C; ^{1}H NMR ($CDCl_3$) δ 2.39 (s, CH_3, 6H), 2.40 (s, CH_3, 3H), 2.99 (bs, CH_2, 4H), 6.14 (s, 1H), 6.80−6.85 (m, 2H), 7.18 (d, J = 7.7 Hz, Ph, 4H), 7.35 (d, J = 8.1 Hz, Ph, 4H), 7.45−7.51 (m, 1H), 8.40 (s, Ph, 2H); FT-IR (KBr, cm^{-1}) 3120 (m), 2216 (m, $\upsilon_{C\equiv C}$), 1790 (w), 1726 (s), 1679 (s), 1597 (s), 1534 (s), 1455 (m), 1366 (s), 1158 (s), 1069 (m), 813 (s); UV−vis (CH_2Cl_2) λ, nm (ϵ, M^{-1} cm^{-1}) 297 (93 800), 353 (11 200); El-MS, *m*/*z* 625 ([M + H]$^+$, 20), 582 (58), 568 (100), 551 (65). Anal. Calcd for $C_{38}H_{28}N_2O_7$: C, 73.08; H, 4.49; N, 4.49. Found: C, 73.22; H, 4.62; N, 4.55.

2,6-Bis(4-ethynyltoluene)-4-nitro-*N*-(butyryl-4-{*N*-oxy-succinimid ester})aniline (4). To a suspension of 0.090 g (0.196 mmol) of **2** in 12 mL of dry CH_3CN was added 0.061 mL (0.546 mmol) of succinyl chloride followed by 0.076 mL (0.546 mmol) of triethylamine. The solution was stirred at 50 °C for 16 h and then 20 mL of water was added. The product was extracted with CH_2Cl_2. The solvent was evaporated and the residue was washed with ether. The pure compound was obtained by recrystallization from CH_2Cl_2/hexane affording 0.111 g of **4** (34%). Mp 235−6 °C; ^{1}H NMR ($CDCl_3$) δ 2.39 (s, CH_3, 6H), 2.74 (bs, CH_2, 4H), 2.99 (bs, CH_2, 4H), 7.18 (d, J = 8.1 Hz, Ph, 4H), 7.35 (d, J = 7.7 Hz, Ph, 4H), 8.40 (s, Ph, 2H); FT-IR (KBr, cm^{-1}) 2212 (m, $\upsilon_{C\equiv C}$), 1782 (s), 1708 (s), 1655 (s), 1531 (s), 1427 (m), 1364 (m), 1219 (s), 1179 (m), 1080 (s), 814 (s); UV−vis (CH_2Cl_2) λ, nm (ϵ, M^{-1} cm^{-1}) 298 (48 500), 356 (5 900); El-MS, *m*/*z* 563 ([M + H]$^+$, 15), 471 ([M − C_7H_7]$^+$, 72), 160 (100). Anal. Calcd for $C_{32}H_{24}N_3O_7$: C, 68.33; H, 4.27; N, 7.47. Found: C, 68.70; H, 4.44; N, 7.62.

2,6-Bis(4-ethynyltoluene)-4-nitro-*N*-(4-bromobutyryl-amide)aniline (5). Compound **1** (0.250 g, 0.683 mmol) was dissolved in dry CH_2Cl_2 (20 mL) and 0.095 mL (0.683 mmol) of triethylamine and 0.008 g (0.068 mmol) of DMAP were added followed by 0.079 mL (0683 mmol) of 4-bromobutyryl chloride. The solution was stirred at room temperature for 2 days. After evaporation, the residue was purified by flash chromatography on alumina with CH_2Cl_2 as eluant to afford 0.239 g of **5** (68%). Mp 230−1 °C; ^{1}H NMR ($CDCl_3$) δ 2.33 (td, J = 13.1 Hz, J = 6.4 Hz, CH_2, 2H), 2.39 (s, CH_3, 6H), 2.72 (t, J = 6.8 Hz, CH_2, 2H), 3.52 (t, J = 6.3 Hz, CH_2, 2H), 7.20 (d, J = 7.7 Hz, Ph, 4H), 7.43 (d, J = 7.7 Hz, Ph, 4H), 7.59 (bs, NH, 1H), 8.35 (s, Ph, 2H); ^{13}C NMR ($CDCl_3$) δ 21.6, 28.0, 33.2, 34.4, 83.4 (C≡C), 97.9 (C≡C), 118.7, 126.8, 129.4, 131.8, 139.9, 143.5, 172.2; FT-IR (KBr, cm^{-1}) 3235 (m), 3184 (m), 2214 (m, $\upsilon_{C\equiv C}$), 1675 (s), 1533 (s), 1511 (s), 1441 (m), 1355 (s), 1333 (s), 1247 (m), 1163 (m), 896 (m), 812 (s); UV−vis (CH_2Cl_2) λ, nm (ϵ, M^{-1} cm^{-1}) 282 (33 800), 298 (48 100); El-MS, *m*/*z* 516 ([M + H]$^+$, 12), 434 ([M − Br + H]$^+$, 100), 366 ([M − $CO(CH_2)_3Br$ + H]$^+$, 29). Anal. Calcd for $C_{28}H_{23}BrN_2O_3$: C, 65.24; H, 4.47; N, 5.44. Found: C, 65.11; H, 4.27; N, 5.12.

2,6-Bis(4-ethynyltoluene)-4-nitro-*N*-(6-bromohexanoyl-amide)aniline (6). Compound **1** (0.300 g, 0.820 mmol) was dissolved in 25 mL of dry CH_2Cl_2 and 0.114 mL (0.820 mmol) of triethylamine and 0.010 g (0.082 mmol) of DMAP were added followed by 0.126 mL (0820 mmol) of 6-bromohexanoyl chloride. The solution was stirred at room temperature for 2 days. After evaporation, the residue was purified by flash chromatography on alumina with CH_2Cl_2 as eluant to afford 0.239 g of **6** (74%). Mp 205−6 °C; ^{1}H NMR ($CDCl_3$) δ 1.50 (quin, J = 7.4 Hz, CH_2, 2H), 1.77 (td, J = 14.7 Hz, J = 7.4 Hz, CH_2, 4H), 2.40 (s, CH_3, 6H), 2.50 (t, J = 7.4 Hz, CH_2, 2H), 3.22 (t, J = 6.8 Hz, CH_2, 2H), 7.19 (d, J = 8.1 Hz, Ph, 4H), 7.40 (d, J = 8.1 Hz, Ph, 4H), 7.60 (bs, NHCO, 1H), 8.31 (s, Ph, 2H); ^{13}C NMR ($CDCl_3$) δ 21.6, 28.0, 33.2, 34.4, 83.4 (C≡C), 97.9 (C≡C), 118.7, 126.8, 129.4, 131.8, 139.9, 143.5, 172.2; FT-IR (KBr, cm^{-1}) 3263 (s), 3186 (m), 2923 (s), 2214 (m, $\upsilon_{C\equiv C}$), 1673 (s), 1533 (s), 1505 (s), 1439 (m), 1355 (s), 1335 (s), 1252 (m), 1178 (m), 893 (m), 815 (s); UV−vis (CH_2Cl_2) λ, nm (ϵ, M^{-1} cm^{-1}) 276 (49 500), 300 (62 000); El-MS,: *m*/*z* 544 ([M + H]$^+$, 11), 462 ([M − Br]$^+$, 40), 366 ([M − $CO(CH_2)_5Br$ + H]$^+$, 31). Anal. Calcd for $C_{30}H_{27}BrN_2O_3$: C, 66.30; H, 4.97; N, 5.16. Found: C, 66.73; H, 5.34; N, 4.77.

2,6-Bis(4-ethynyltoluene)-4-nitro-*N*-(6-*N*-{7-amino-4-methylcoumarin}hexanoylamide)aniline (7). A Schlenk flask was charged under nitrogen with 0.115 g (0.212 mmol) of **6**, 0.045 g (0.254 mmol) of 7-amino-4-methylcoumarin, and 25 mL of 2,2,2-trifluoroethanol. The solution was stirred at 100 °C for 2 days. The solvent was evaporated and the residue was purified by flash chromatography on alumina with CH_2Cl_2/CH_3OH (0 to 15%) as eluant to afford 0.065 g of **7** (48%). Mp 222−3 °C; ^{1}H NMR ($CDCl_3$) δ 1.87 (m, CH_2, 4H), 2.03 (m, CH_2, 2H), 2.39 (bs, CH_3, 9H), 2.77 (t, J = 4.8 Hz, CH_2, 2H), 3.80 (t, J = 4.6 Hz, CH_2, 2H), 6.78−6.81 (m, Ph, 3H), 7.20 (d, J = 8.1 Hz, Ph, 4H), 7.37−7.47 (m, 5H), 8.35 (s, Ph, 2H); FT-IR (KBr, cm^{-1}) 2930 (m), 2213 (w, $\upsilon_{C\equiv C}$), 1679 (s), 1594 (s), 1527 (m), 1448 (m), 1388 (s), 1334 (m), 1240 (s), 1160 (m), 845 (s), 817 (m); UV−vis (CH_2Cl_2) λ, nm (ϵ, M^{-1} cm^{-1}) 300 (76 400); El-MS, *m*/*z* 575 (24), 440 (40), 423 (32), 154 (92), 136(100). Anal. Calcd for $C_{40}H_{35}N_3O_5$: C, 75.35; H, 5.49; N, 6.59. Found: C, 75.26; H, 5.32; N, 6.68.

1-(3-{4-Methoxyaryl}-2-propenoyl)-4-acetylbenzene (8). To a vigorously stirred solution of 0.300 g (1.850 mmol) of 1,4-diacetylbenzene in methanol (40 mL) at room temperature was added an aqueous solution of 0.222 g of NaOH (5.550 mmol) and then 0.252 g (1.850 mmol) of anisaldehyde. After 2 h, the precipitated product was filtered and washed with water/ether. After purification by flash chromatography on alumina with CH_2Cl_2 as eluant, the pure product was obtained by recrystallization in CH_2Cl_2/hexane to afford 0.326 g of **8** (63%). Mp 127−8 °C; ^{1}H NMR ($CDCl_3$) δ 3.86 (s, OCH_3, 3H), 6.95 (d, J = 8.8 Hz, Ph, 2H), 7.38 (d, J = 15.8 Hz, C═C, 1H), 7.61 (d, J = 8.5 Hz, Ph, 2H), 7.80 (d, J = 15.8 Hz, C═C, 1H), 8.06 (s, Ph, 4H);^{13}C NMR ($CDCl_3$) δ 26.9, 55.5, 114.1, 114.5, 119.5, 127.3,

128.3, 128.5, 128.6, 130.5, 139.7. 142.0, 145.8, 162.0, 190.1, 197.6; FT-IR (KBr, cm^{-1}) 2839 (w), 1679 (s), 1655 (s), 1591 (s), 1507 (s), 1510 (s), 1401 (m), 1334 (m), 1306 (s), 1256 (s), 1216 (s), 1171 (m), 1032 (s), 1010 (m), 981 (m), 960 (m); UV−vis (CH_2Cl_2) λ, nm (ϵ, M^{-1} cm^{-1}) 264 (33 500), 349 (23 900); El-MS, *m/z* 280 ($[M]^+$, 100), 265 ($[M - CH_3]^+$, 13), 249 ($[M - OCH_3]^+$, 11), 237 ($[M - COCH_3]^+$, 65), 161 ($[M - C_6H_4\text{-}COCH_3]^+$, 33). Anal. Calcd for $C_{18}H_{16}O_3$: C, 77.14; H, 5.71. Found: C, 76.91; H, 5.52.

1-(3-{4-Methoxyaryl}-2-propenoyl)-4-(3-aryl-2-propenoyl)benzene (9). To a vigorously stirred solution of 0.250 g (0.893 mmol) of **8** in methanol (40 mL) at room temperature was added an aqueous solution of 0.107 g of NaOH (2.679 mmol) and then 0.114 g (1.071 mmol) of benzaldehyde. After 5 h, the precipitated product was filtered and washed with water/ether and recrystallized in CH_2Cl_2/hexane to afford 0.220 g of **9** (67%). Mp 165−6 °C;^{1}H NMR ($CDCl_3$) δ 3.86 (s, OCH_3, 3H), 6.95 (d, J = 8.5 Hz, Ph, 2H), 7.38−7.65 (m, 9H), 7.78−7.86 (m, 2H), 8.10 (s, Ph, 4H); ^{13}C NMR ($CDCl_3$) δ 55.4, 114.5, 119.4, 119.5, 121.8, 127.3, 128.5, 128.7, 129.0, 130.5, 130.9, 134.6, 141.1, 141.4, 141.6, 145.6, 145.7, 145.8, 161.9, 190.0, 190.1; UV−vis (CH_2Cl_2) λ, nm (ϵ, M^{-1} cm^{-1}) 273 (33 400), 341 (34 600); FT-IR (KBr, cm^{-1}) 2834 (w), 1683 (w), 1654 (s), 1590 (s), 1571 (s), 1511 (s), 1423 (m), 1333 (m), 1293 (s), 1255 (s), 1220 (s), 1173 (s), 1036 (s), 1009 (m), 991 (s), 824 (m); El-MS, *m/z* 369 ($[M + H]^+$, 40), 281 ($[M - PhCH]^+$, 20), 155 (80), 119 (100). Anal. Calcd for $C_{25}H_{20}O_3$: C, 81.52; H, 5.43. Found: C, 81.33; H, 5.24.

1-(3-{4-Methoxyaryl}-2,3-dibromopropenoyl)-4-(3-aryl-2,3-dibromopropenoyl)benzene (10). To a solution of 0.150 g (0.407 mmol) of **9** in $CHCl_3$ (10 mL) was added bromine (0.036 mL, 0.815 mmol) in 2 mL of $CHCl_3$ dropwise with vigorous stirring for 15 min and the reaction mixture was allowed to stand for 1 h. The precipitated product was filtered and washed with ether and recrystallized in CH_2Cl_2/hexane to afford 0.207 g of **10** (86%). Mp 178−9 °C;^{1}H NMR ($CDCl_3$) δ 3.86 (s, OCH_3, 3H), 5.65 (dd, J = 11.0 Hz, J = 11.4 Hz, 2H), 5.82 (d, J = 11.0 Hz, 2H), 6.96 (d, J = 8.5 Hz, Ph, 2H), 7.40−7.55 (m, Ph, 7H), 8.25 (s, Ph, 4H); ^{13}C NMR ($CDCl_3$) δ 47.0, 47.3, 49.5, 50.1, 55.4, 114.3, 121.8, 128.4, 128.6, 128.9, 129.1, 129.4, 129.6, 131.0, 134.5, 137.3, 142.5, 146.2, 160.3, 189.9, 190.8; UV−vis (CH_2Cl_2) λ, nm (ϵ, M^{-1} cm^{-1}) 273 (400); FT-IR (KBr, cm^{-1}) 2840 (w), 1690 (s), 1606 (m), 1513 (m), 1406 (m), 1308 (m), 1272 (s), 1225 (s), 1179 (m), 1030 (m), 9761 (m), 834 (m); El-MS, *m/z* 608 ($[M - Br]^+$, 3), 526 ($[M - 2Br]^+$, 37), 448 ($[M - 3Br]^+$, 46), 367 ($[M - 4Br + H]^+$, 100). Anal. Calcd for $C_{25}H_{20}Br_4O_3$: C, 43.60; H, 2.91. Found: C, 43.66; H, 2.87.

1-(5-{4-Methoxyaryl}-3-isoxazolyl)-4-(5-aryl-3-isoxazolyl)benzene (11). To 20 mL of boiling ethanol were added 0.170 g (0.247 mmol) of **10** and 0.034 g (0.494 mmol) of hydroxylamine hydrochloride and the mixture was refluxed for 2 h. Then 0.083 g (1.482 mmol) of KOH in 4 mL of ethanol/water (3/1) was added and the mixture was refluxed for 2 h. The solution was allowed to stand for 1 h and the product thus precipited was filtered and recrystallized in CH_2Cl_2/hexane to afford 0.220 g of **11** (32%). Mp 178−9 °C;^{1}H NMR ($CDCl_3$) δ 3.88 (s, OCH_3, 3H), 5.65 (dd, J = 11.0 Hz, J = 11.4 Hz, 2H), 5.82 (d, J = 11.0 Hz, 2H), 6.96 (d, J = 8.5 Hz, Ph, 2H), 7.40−7.55 (m, Ph, 7H), 8.25 (s, Ph, 4H); UV−vis (CH_2Cl_2) λ, nm (ϵ, M^{-1} cm^{-1}) 280 (47 000); FT-IR (KBr, cm^{-1}) 2840 (w), 1690 (s), 1606 (m), 1513 (m), 1406 (m), 1308 (m), 1272 (s), 1225 (s), 1179 (m), 1030 (m), 9761 (m), 834 (m); El-MS, *m/z* 394 ($[M]^+$, 30), 135 ($[M - C_9H_8O]^+$, 100), 105 ($[M - C_9H_8O - OCH_3]^+$, 65), 77 ($[M - C_9H_8O - Ph]^+$, 60). Anal. Calcd for $C_{25}H_{18}N_2O_3$: C, 75.76; H, 4.55; N, 7.07. Found: C, 75.69; H, 4.43; N, 6.92.

7-(6-Bromohexanoyl)-4-methylcoumarin Ester (12). To a suspension of 0.100 g (0.568 mmol) of 7-hydroxy-4-methylcoumarin in 20 mL of CH_2Cl_2 was added 0.079 mL (0.568 mmol) of triethylamine. After dissolution 0.126 mL (0.568 mmol) of 6-bromohexanoyl chloride was added. The mixture was stirred for 6 h at room temperature. After evaporation, the residue was purified by flash chromatography on alumina with CH_2Cl_2/CH_3OH (0 to 15%) as eluant to afford 0.168 g of **12** (84%). Mp 75−6 °C; ^{1}H NMR ($CDCl_3$) δ 1.58 (quin, J = 7.7 Hz, CH_2, 2H), 1.79 (quin, J = 7.7 Hz, CH_2, 2H), 1.93 (quin, J = 7.4 Hz, CH_2, 2H), 2.43 (s, CH_3, 3H), 2.62 (t, J = 7.4 Hz, $COCH_2$, 2H), 3.44 (t, J = 6.6 Hz, CH_2Br, 2H), 6.26 (s, 1H), 7.05−7.10 (m, 2H), 7.60 (d, J = 8.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 18.7, 23.8, 27.4, 32.2, 33.4, 34.0, 110.3, 114.4, 117.7, 118.0, 125.4, 151.9, 153.0, 154.1, 160.4, 171.2; FT-IR (KBr, cm^{-1}) 3087 (m), 2928 (m), 1757 (s), 1729 (s), 1613 (s), 1566 (m), 1412 (m), 1383 (s), 1327 (m), 1263 (s), 1229 (m), 1154 (s), 1132 (s), 1013 (m), 983 (m), 865 (s); UV−vis (CH_2Cl_2) λ, nm (ϵ, M^{-1} cm^{-1}) 272 (10 600), 312 (9 800); El-MS, *m/z* 354 ($[M + H]^+$, 15), 176 ($[M - CO(CH_2)_5Br + H]^+$, 100), 148 ($[M - CO(CH_2)_5Br - CO]^+$, 30). Anal. Calcd for $C_{16}H_{17}BrO_4$: C, 54.39; H, 4.82. Found: C, 54.35; H, 4.94.

Bis(7-oxy-4-methylcoumarin)succinyl Ester (13). To a suspension of 0.250 g (1.419 mmol) of 7-hydroxy-4-methylcoumarin in 25 mL of dry CH_2Cl_2 was added 0.198 mL (1.419 mmol) of triethylamine. After dissolution, 0.080 mL (0.710 mmol) of succinyl chloride was added. The mixture was stirred at room temperature for 2 h and the precipitated product was filtered and washed successively with water and ether affording 0.585 g of **13** (95%). Mp 238−9 °C; ^{1}H NMR ($CDCl_3$) δ 2.44 (s, CH_3, 3H), 3.05 (m, CH_2, 4H), 6.29 (s, 2H), 7.07−7.14 (m, 4H), 7.62 (d, J = 8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 18.8, 29.2, 111.8, 110.4, 114.6, 118.0, 125.5, 152.8, 162.2, 170.2; FT-IR (KBr, cm^{-1}) 3065 (w), 1732 (s), 1615 (s), 1573 (w), 1391 (m), 1316 (s), 1267 (s), 1154 (s), 1021 (m), 989 (m), 873 (m); UV−vis (CH_2Cl_2) λ, nm (ϵ, M^{-1} cm^{-1}) 272 (15 200), 312 (14 100); El-MS, *m/z* 434 ($[M]^+$, 9), 259 ($[M - C_{10}H_7O_3]^+$, 50), 176 (92), 148 (100). Anal. Calcd for $C_{24}H_{18}O_3$: C, 66.36; H, 4.15. Found: C, 66.21; H, 4.16.

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