Syntheses of Quaternary Carbon-Containing Oxazatricycle and Spiropyran Libraries via Multicomponent Reactions and Their Molecular Switching Properties

Chi-Hui Lin, Jhih-Rong Chen, and Ding-Yah Yang*

Department of Chemistry, Tunghai University, Taichung 407, Taiwan

Received August 20, 2009

A practical protocol for the preparation of parallel solution-phase libraries of the quaternary carbon-containing oxazatricycles and spiropyrans is reported. Target compounds were obtained in moderate to excellent yields by an Et_3N-mediated multicomponent reaction from various *N*-methylisoquinolium or flavylium salts and 4-hydroxycoumarins or dimedone in acetone. Purification of the final products by recrystallization in ethyl acetate/methylene chloride or by column chromatography allowed easy isolation of nine compounds of each array. Preliminary studies indicated that some of the prepared compounds exhibit redox switching, photochromic, and thermochromic properties.

Introduction

Multicomponent reactions (MCRs)[1] are convergent reactions, in which three or more starting materials react to form a product, where all or most of the atoms contribute to the newly generated product. The MCRs represent an attractive synthetic strategy for a rapid and efficient library generation due to the fact that the products are formed in a single step, and the diversity can be achieved simply by varying the reacting components. After intensive research for the past decade, many different backbone libraries have become accessible. While majority of the available libraries were prepared mainly for their potential biological activities and therapeutic applications, few were aimed at developing of novel organic molecular switches. Molecular switches are molecules that can be transformed into two or more stable states by an external stimulus such as pH, light, temperature, or redox potential. Compounds with molecular switching properties may have wide applications in a number of fields including nanotechnology[2] and biology.[3] Recently, we reported a one-pot tandem four-component reaction for preparation of an oxazabicycle library.[4] After screening approximately 20 compounds, the oxazabicycles **1**[5] and **2**[6] were found to possess photochromic and fluorescence redox switching properties, respectively (Figure 1). This successful experience prompted us to believe that novel molecular switches may potentially be screened from heterocycle libraries generated by new MCRs. To test this speculation, along with our continuing efforts to develop new molecular scaffolds to function as backbones for organic functional materials, we describe here two parallel solution-phase syntheses of the *gem*-dimethyl-substituted quaternary carbon-containing oxazatricycles and spiropyrans by an Et_3N-mediated three-component reaction using acetone as a quaternary carbon source. Their molecular switching properties are also investigated.

* To whom correspondence should be addressed. Phone: 886-4-2359-7613. Fax: 886-4-2359-0426. E-mail: yang@thu.edu.tw.

Results and Discussion

The target oxazatricycles and spiropyrans were obtained, as indicated in Scheme 1, in a one-pot reaction by mixing *N*-methylisoquinolium or flavylium salts and 4-hydroxycoumarins or dimedone in the presence of triethylamine in acetone under reflux conditions for 8 and 0.5 h, respectively. After the reaction was quenched with water, the products were extracted with methylene chloride, dried in $MgSO_4$, concentrated in vacuo, and subsequently purified by recrys-

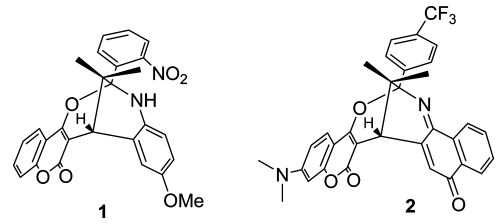
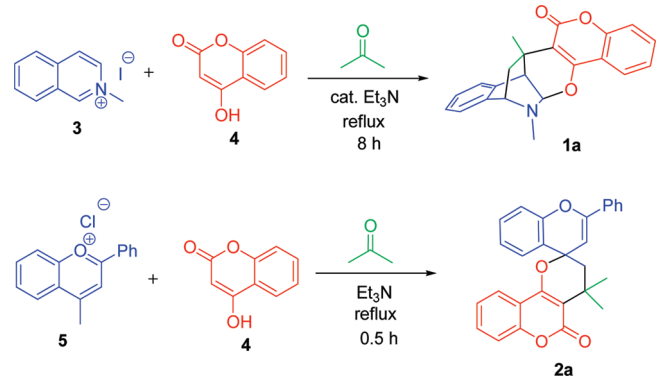


Figure 1. Structures of two oxazabicycles that possess molecular switching properties screened from MCRs.

Scheme 1. Preparation of the Oxazatricycle **1a** and Spiropyran **2a** Using a Three-Component Reaction



10.1021/cc900127g CCC: $40.75
Published on Web 10/27/2009

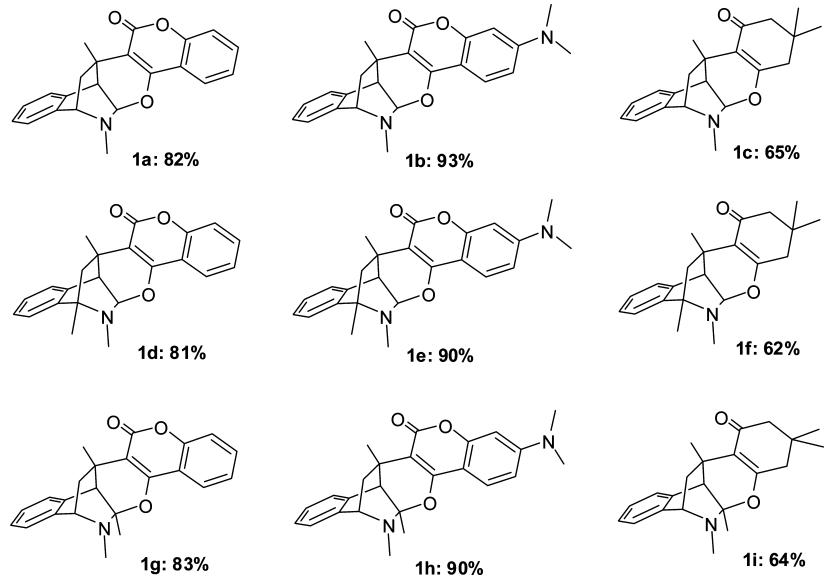


Figure 2. Oxazatricycle library products **1a**−**1i** obtained by a parallel three-component reaction.

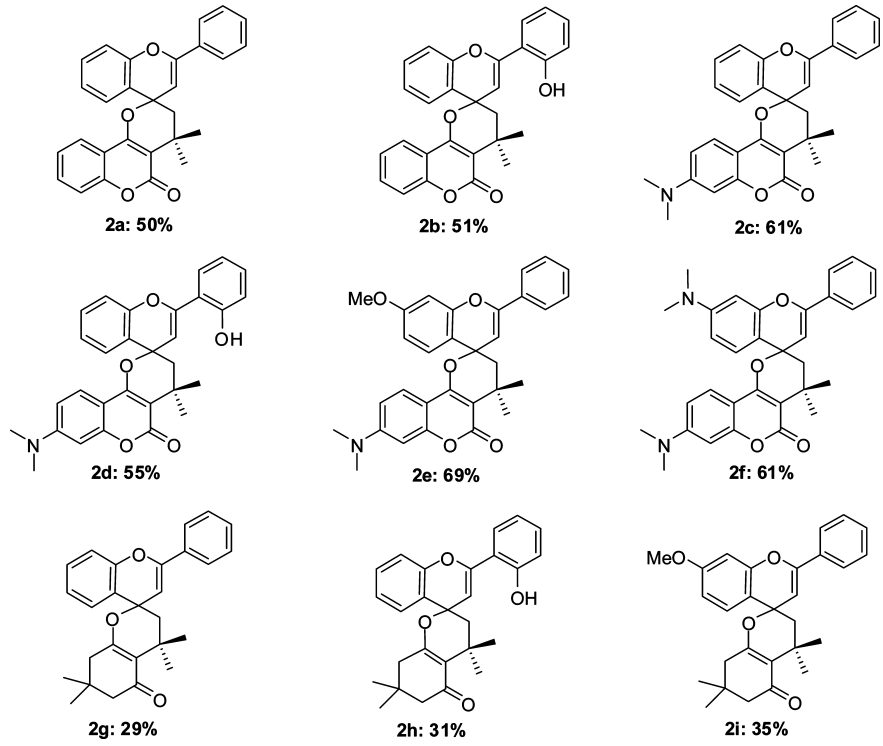


Figure 3. Spiropyran library products **2a**−**2i** obtained by a parallel three-component reaction.

tallization in ethyl acetate/methylene chloride or flash column chromatography. Figures 2 and 3 list the structures of nine compounds of each generated array with the yield given underneath, which demonstrated the versatility of this one-pot reaction through the three-component preparation of libraries of oxazatricycles and spiropyrans. The *N*-methylisoquinolium iodides were synthesized by refluxing corresponding substituted isoquinolines with the methyl iodide in benzene, whereas the flavylium salts were prepared by acid-mediated condensation[7] of substituted phenol and benzoylacetone in ethyl acetate under room temperature. 7-Dimethylamino-4-hydroxycoumarin used for the synthesis of compounds **1b**, **1e**, **1h**, and **2c**−**2f** was prepared according to the literature procedure.[8] It can be observed that both MCRs gave lower yields for dimedone, moderate yields for 4-hydroxycoumarin, and better yields for 7-dimethylamino-4-hydroxycoumarin. The higher yields for the latter is presumably due to the presence of an electron-donating dimethylamino group at the 7-position of the coumarin moiety.

The structural assignment of the prepared oxazatricycles and spiropyrans was based on spectroscopic data (^{1}H, ^{13}C NMR, HRMS). In the ^{1}H NMR spectra, two distinctive bridgehead hydrogen absorption peaks for the oxazatricyclic ring were observed at the chemical shifts of 3.43−3.86 and 2.65−3.01 ppm for all prepared compounds **1a**−**1i**, whereas characteristic AB quartet absorption peaks for methylene hydrogens on the spiropyran ring were detected around 2.47−2.41 and 2.25−1.96 ppm with a coupling constant of 14.4 Hz for compounds **2a**−**2i**. Some of the heterocyclic

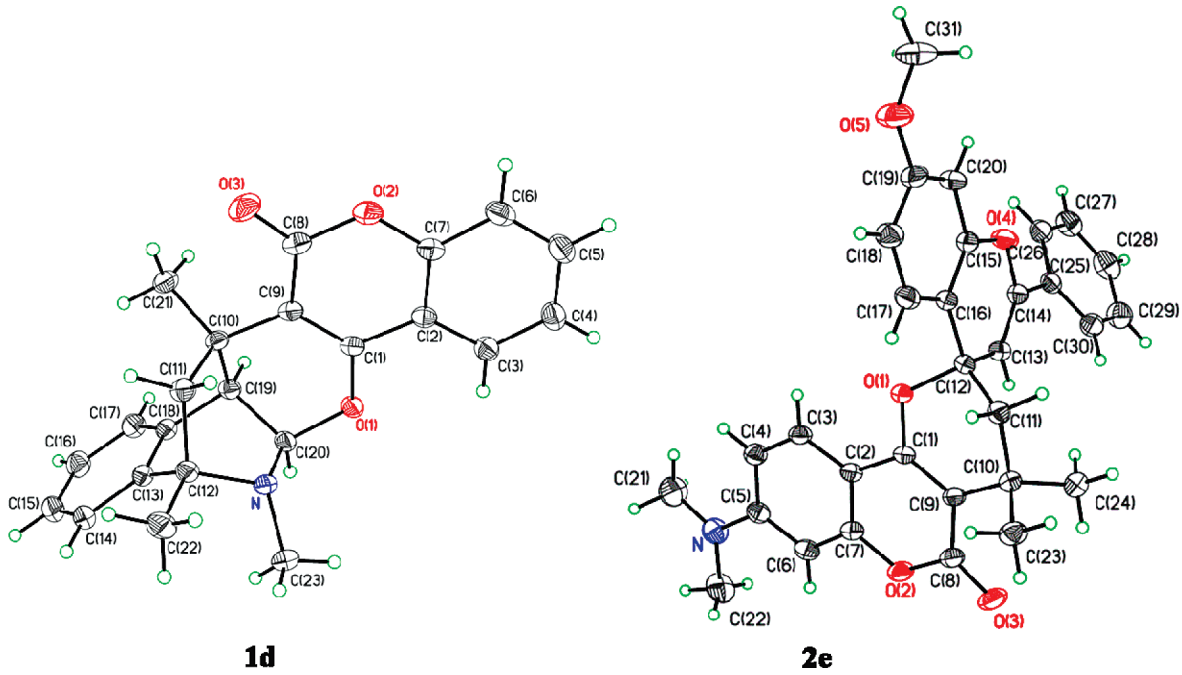
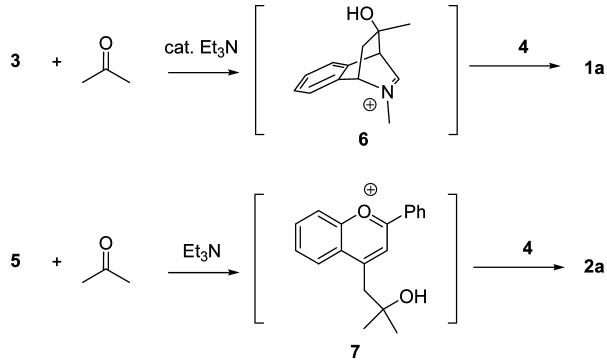


Figure 4. X-ray crystal structures of the oxazatricycle **1d** and spiropyran **2e**.

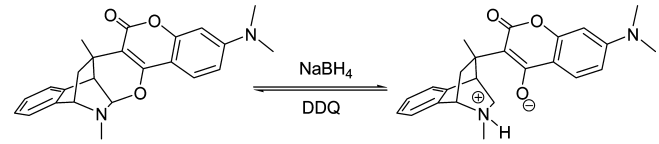
Scheme 2. Proposed Mechanisms for the Formation of the Oxazatricycle **1a** and Spiropyran **2a**



structures were further elucidated by single-crystal X-ray diffraction analysis. Figure 4 shows the ORTEP diagrams of the oxazatricycle **1d** and spiropyran **2e**, which clearly revealed a rigid oxazatricyclic skeleton and a spiropyran moiety, respectively.[9]

The proposed mechanisms for the two MCRs are depicted in Scheme 2. Albeit both MCRs utilize acetone as a *gem*-dimethyl-substituted quaternary carbon source to construct the heterocyclic scaffolds, their reaction mechanisms are considerably different. For the oxazatricycle **1a**, it began with an equilibrium-driven, inverse-electron demand aza-Diels−Alder reaction of acetone enolate and isoquinolium salt to give the iminium-containing cycloadduct **6**.[10] The second step involved a nonequilibrium trapping of **6** with 4-hydroxycoumarin to afford the oxazatricycle **1a**. It is worth mentioning that the bond formation for the construction of the tricyclic skeleton is not only highly efficient with the formation of three C−C bonds and one C−O bond but also regioselective and stereospecific, creating a tricyclic system containing four chiral centers. For the spiropyran **2a**, it involved first deprotonation of flavylium salt **5** by triethylamine and followed by reacting with acetone to afford

Scheme 3. Fluorescence Redox Switches between the Oxazatricycle **1b** and Zwitterion **8**



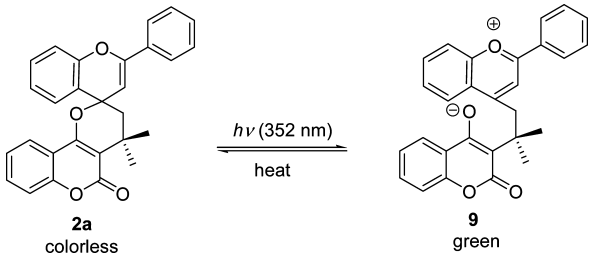
1b
strongly fluorescent

8
weakly fluorescent

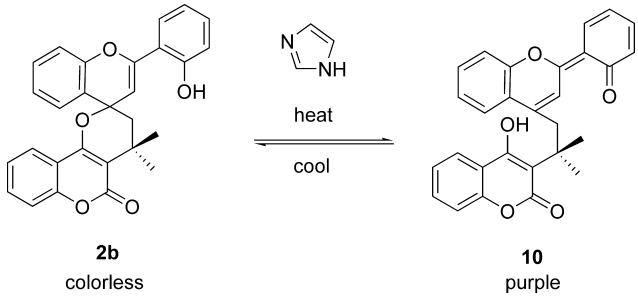
the tertiary alcohol **7**. The subsequent coupling of **7** with 4-hydroxycoumarin yielded the spiropyran **2a**.[11] Similar to the oxazatricycle **1a**, the bond formation during the construction of the spiropyran skeleton is also efficient and atom-economical, with overall formation of two C−C bonds and one C−O bond.

With the availability of these two libraries, their molecular switching properties were then investigated. Some of the oxazatricycles were found to exhibit fluorescence redox switching properties. For instance, the oxazatricycle **1b** emitted strong fluorescence in methanol. Addition of sodium borohydride to **1b** induced the ring-opening of the oxazatricyclic moiety to generate the weakly fluorescent zwitterionic species **8**, which can be swiftly reverted to **1b** by 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) oxidation in methylene chloride (Scheme 3). For the spiropyran library, some exhibit photochromic properties, others show thermochromic properties. As depicted in Schemes 4 and 5, while the colorless spiropyran **2a** is sensitive to light and converts to the green zwitterion **9** upon UV irradiation, the colorless spiropyran **2b**, in the presence of an external proton donor such as imidazole, is sensitive to heat and changes to the purple ring-opened form **10** when temperature is increased. Although the molecular switching properties of these compounds merit further investigations,[12] the present studies have

Scheme 4. Photochromic Switches between the Spiropyran **2a** and Zwitterions **9**



Scheme 5. Thermochromic Switches between the Spiropyran **2b** and Ring-Opened Form **10**



clearly demonstrated the feasibility of discovering of novel molecular switches from new MCRs-generated libraries.

Conclusions

In summary, two practical parallel solution-phase syntheses of the oxazatricycles and spiropyrans using an Et_3N-mediated, one-pot reaction are developed. Purification of the final products can be accomplished by either recrystallization in ethyl acetate/methylene chloride or column chromatography with moderate to excellent yields. Our protocol for these three-component reactions provides a quick access to the *gem*-dimethyl-substituted quaternary carbon-containing oxazatricycles and spiropyrans with diverse substitution patterns using acetone as a quaternary carbon source. Moreover, some of the prepared compounds were found to possess molecular switching properties such as fluorescence redox switch, photochromism, and thermochromism. We have demonstrated that novel molecular switches can be discovered by screening of new heterocycle libraries generated by MCRs.

Experimental Section

Melting points were determined on a Mel-Temp melting point apparatus in open capillaries and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded at 300 and 75 MHz on a Varian VXR300 spectrometer. Chemical shifts were reported in parts per million on the δ scale relative to an internal standard (tetramethylsilane, or appropriate solvent peaks) with coupling constants given in hertz. ^{1}H NMR multiplicity data are denoted by s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). MS were performed on JEOL JMS-SX/SX 102A spectrometer. IR spectra were obtained using a 1725XFT-IR spectrophotometer. Single-crystal structures were determined by a Bruker AXS SMART-1000 X-ray single-crystal diffractometer. Analytical thin-layer chromatography (TLC) was carried out on Merck silica gel 60G-254 plates (25 mm) and developed with the solvents mentioned. Flash chromatography was performed in columns of various diameters with Merck silica gel (230−400 mesh ASTM 9385 kieselgel 60H) by elution with the solvent systems. Solvents, unless otherwise specified, were reagent grade and distilled once prior to use.

General Procedure for 1a−1i. To a solution of *N*-methylisoquinolium iodide (0.50 mmol) in acetone (10 mL) was added 4-hydroxycoumarin (0.50 mmol) and a catalytic amount of triethylamine. The resulting solution was refluxed for 8 h. After completion of the reaction, the mixture was cooled to room temperature and then the solvent was concentrated in vacuo. The residue was poured into water, and the product was extracted twice with methylene chloride. The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated. The resulting crude product was recrystallized in ethyl acetate/methylene chloride to give the product.

Preparation of 1a: white solid; yield 82%; R_f = 0.55 (15% EtOAc/hexanes); mp 184−186 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.85 (dd, J = 6.6, 1.5 Hz, 1H), 7.48−7.54 (m, 1H), 7.31−7.19 (m, 6H), 4.61 (d, J = 3.0 Hz, 1H), 3.63 (d, J = 3.6 Hz, 1H), 2.98 (d, J = 3.0 Hz, 1H), 2.46 (s, 3H), 2.48−2.42 (m, 1H), 1.51 (dd, J = 12.9, 1.2 Hz, 1H), 1.37 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.0, 156.0, 152.7, 140.0, 134.5, 131.1, 127.22, 127.21, 127.0, 123.4, 123.1, 122.9, 116.1, 115.9, 110.0, 93.6, 56.5, 45.5, 43.9, 42.5, 27.3, 24.5; IR ν (KBr) 2903, 1699, 1620, 1572, 1397 cm^{-1}; HRMS (FAB) calcd for $C_{22}H_{20}NO_3$ [M + H] 346.1443, found 346.1446.

Preparation of 1b: white solid; yield 93%; R_f = 0.58 (25% EtOAc/hexanes); mp 198−199 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.64 (d, J = 9.0 Hz, 1H), 7.29−7.19 (m, 4H), 6.59 (dd, J = 9.0, 2.1 Hz, 1H), 6.45 (d, J = 2.1 Hz, 1H), 4.53 (d, J = 3.0 Hz, 1H), 3.63 (d, J = 3.9 Hz, 1H), 3.01 (s, 6H), 2.95 (d, J = 3.0 Hz, 1H), 2.48 (s, 3H), 2.48−2.42 (m, 1H) 1.47 (d, J = 12.6 Hz, 1H), 1.35 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.9, 157.0, 154.7, 152.6, 139.7, 135.0, 127.1, 127.0, 127.0, 123.5, 123.0, 108.3, 105.4, 104.9, 97.2, 93.2, 56.8, 45.7, 44.0, 42.6, 40.0, 26.9, 24.9; IR ν (KBr) 2910, 1702, 1602, 1407, 1102 cm^{-1}; HRMS (FAB) calcd for $C_{24}H_{25}N_2O_3$ [M + H] 389.1865, found 389.1862.

Preparation of 1c: white solid; yield 65%; R_f = 0.51 (15% EtOAc/hexanes); mp 137−138 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.28−7.24 (m, 3H), 7.23−7.14 (m, 1H), 4.29 (d, J = 3.0 Hz, 1H), 3.55 (dd, J = 4.8, 1.5 Hz, 1H), 2.78 (d, J = 3.0 Hz, 1H), 2.39−2.38 (m, 4H), 2.28−2.19 (m, 4H), 1.35 (dd, J = 13.2, 1.5 Hz, 1H), 1.19 (s, 3H), 1.11 (s, 3H) 1.08 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 196.5, 164.7, 139.8, 135.1, 126.825, 126.824, 123.0, 119.4, 92.8, 56.9, 51.6, 45.9, 43.6, 42.7, 42.627, 42.625, 31.0, 29.7, 26.6, 26.2, 25.3; IR ν (KBr) 2948, 1639, 1459, 1353, 1147 cm^{-1}; HRMS (FAB) calcd for $C_{21}H_{26}NO_2$ [M + H] 324.1964, found 324.1966.

Preparation of 1d: white solid; yield 81%; R_f = 0.58 (15% EtOAc/hexanes); mp 184−186 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.85 (dd, J = 8.1, 1.8 Hz, 1H), 7.48−7.45 (m, 1H), 7.33−7.21 (m, 6H), 4.63 (d, J = 3.0 Hz, 1H), 3.0 (d, J = 3.0 Hz, 1H), 2.34 (s, 3H), 2.24, 1.44 (ABq, J = 13.2 Hz, 1H each), 1.51 (s, 3H), 1.35 (s, 3H); ^{13}C NMR ($CDCl_3$,

75 MHz) δ 161.1, 156.2, 152.7, 141.6, 135.0, 131.2, 127.2, 127.1, 126.9, 123.4, 123.0, 121.1, 116.3, 116.0, 110.3, 94.7, 54.4, 52.1, 45.6, 38.8, 29.2, 24.6, 19.2; IR ν (KBr) 2964, 1697, 1616, 1568, 1350 cm^{-1}; HRMS (FAB) calcd for $C_{23}H_{22}NO_3$ [M + H] 360.1600, found 360.1596.

Preparation of 1e: white solid; yield 90%; R_f = 0.53 (25% EtOAc/hexanes); mp 199−201 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.63 (d, J = 8.7 Hz, 1H), 7.32−7.29 (m, 3H), 7.22−7.19 (m, 1H), 6.58 (dd, J = 9.0, 1.5 Hz, 1H), 6.47 (s, 1H), 4.55 (d, J = 2.7 Hz, 1H), 3.01 (s, 6H), 2.96 (d, J = 2.4 Hz, 1H), 2.33 (s, 3H), 2.42, 1.41 (ABq, J = 12.9 Hz, 1H each), 1.50 (s, 3H), 1.35 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 162.0, 157.2, 154.7, 152.6, 141.6, 135.4, 127.0, 126.9, 126.8, 123.7, 121.1, 108.4, 105.7, 105.1, 96.3, 94.3, 54.5, 52.2, 45.8, 40.1, 38.8, 28.9, 24.9, 19.2; IR ν (KBr) 2868, 1602, 1570, 1460, 1377 cm^{-1}; HRMS (FAB) calcd for $C_{25}H_{27}N_2O_3$ [M + H] 403.2022, found 403.2019.

Preparation of 1f: white solid; yield 62%; R_f = 0.58 (25% EtOAc/hexanes); mp 135−136 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.28−7.21 (m, 3H), 7.18−7.15 (m, 1H), 4.30 (d, J = 3.0 Hz, 1H), 2.80 (d, J = 3.0 Hz, 1H), 2.39 (d, J = 17.4 Hz, 1H), 2.28−2.22 (m, 6H), 2.02, 1.30 (ABq, J = 12.9 Hz, 1H each), 1.45 (s, 3H), 1.18 (s, 3H), 1.11 (s, 3H), 1.07 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 196.5, 164.9, 141.5, 135.4, 126.6, 127.0, 120.9, 119.6, 93.8, 54.3, 51.9, 51.5, 45.9, 42.428, 42.425, 38.8, 31.0, 29.6, 28.1, 26.6, 25.2, 19.1; IR ν (KBr) 2937, 1642, 1468, 1353, 1028 cm^{-1}; HRMS (FAB) calcd for $C_{22}H_{28}NO_2$ [M + H] 338.2120, found 338.2122.

Preparation of 1g: white solid; yield 83%; R_f = 0.55 (15% EtOAc/hexanes); mp 190−191 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.84 (dd, J = 7.8, 1.2 Hz, 1H), 7.48−7.43 (m, 1H), 7.29−7.16 (m, 6H), 3.57 (d, J = 3.9 Hz, 1H), 2.80 (s, 1H), 2.40 (dd, J = 12.9, 4.8 Hz, 1H), 2.39 (s, 3H), 1.41 (dd, J = 12.9, 1.2 Hz, 1H), 1.37 (s, 3H), 1.14 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.2, 155.9, 152.6, 139.7, 135.6, 130.9, 127.4, 127.0, 123.2, 122.8, 122.6, 116.2, 115.8, 109.5, 94.6, 57.8, 52.3, 44.0, 36.2, 29.5, 28.9, 24.8, 22.1; IR ν (KBr) 2953, 1697, 1625, 1397, 1066 cm^{-1}; HRMS (FAB) calcd for $C_{23}H_{22}NO_3$ [M + H] 360.1600, found 360.1596.

Preparation of 1h: white solid; yield 90%; R_f = 0.53 (25% EtOAc/hexanes); mp 177−178 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.63 (d, J = 8.7 Hz, 1H), 7.23−7.28 (m, 3H), 7.16−7.18 (m, 1H), 6.58 (dd, J = 8.7, 2.4 Hz, 1H), 6.47 (d, J = 2.4 Hz, 1H), 3.57 (d, J = 4.2 Hz, 1H), 3.01 (s, 6H), 2.77 (s, 1H), 2.45 (dd, J = 12.6, 4.2 Hz, 1H), 2.38 (s, 3H), 1.41 (dd, J = 12.6, 1.2 Hz, 1H), 1.35 (s, 3H), 1.11 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 162.2, 157.0, 154.7, 152.5, 139.9, 136.1, 127.5, 126.9, 126.8, 123.5, 122.6, 108.3, 105.2, 105.2, 97.3, 94.0, 58.2, 52.6, 44.1, 40.1, 36.2, 28.6, 25.2, 22.3; IR ν (KBr) 2852, 1805, 1566, 1403, 1325 cm^{-1}; HRMS (FAB) calcd for $C_{25}H_{27}N_2O_3$ [M + H] 403.2022, found 403.2026.

Preparation of 1i: white solid; yield 64%; R_f = 0.50 (15% EtOAc/hexanes); mp 142−143 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.23−7.17 (m, 3H), 7.13−7.11 (m, 1H), 3.48 (d, J = 3.9 Hz, 1H), 2.60 (s, 1H), 2.32 (s, 3H), 2.29−2.25 (m, 3H), 2.20, 1.27 (ABdq, J = 12.9, 4.8 Hz, 1H each), 1.19 (s, 3H), 1.08−1.05 (m, 7H), 0.96 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 192.4 160.4, 140.5, 136.3, 126.7, 122.9, 119.6, 119.1, 93.2, 58.4, 52.9, 52.8, 43.8, 41.3, 36.3, 31.4, 31.2, 28.0, 27.9, 25.8, 25.7, 22.5; IR ν (KBr) 2809, 1648, 1434, 1323, 1213 cm^{-1}; HRMS (FAB) calcd for $C_{22}H_{28}NO_2$ [M + H] 338.2120, found 338.2117.

General Procedure for 2a−2i. To a solution of flavylium salt **5** (0.5 mmol) in acetone (15 mL) was added triethylamine (0.5 mmol) and 4-hydroxycoumarin (0.6 mmol). The resulting solution was refluxed for 0.5 h. After completion of the reaction, the mixture was cooled to room temperature and then the solvent was concentrated in vacuo. The residue was poured into water and the product was extracted twice with methylene chloride. The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by column chromatography to give the product.

Preparation of 2a: white solid; yield 50%; R_f = 0.50 (10% EtOAc/hexanes); mp 123−124 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.77 (dd, J = 7.8, 1.5 Hz, 1H), 7.71−7.67 (m, 2H), 7.60 (dd, J = 8.1, 1.8 Hz, 1H), 7.51−7.15 (m, 9H), 5.91 (s, 1H), 2.46, 2.22 (ABq, J = 14.4 Hz, 1H each), 1.74 (s, 3H), 1.50 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.1, 158.0, 152.4, 150.4, 148.9, 133.0, 131.5, 129.5, 129.4, 128.5, 126.9, 125.1, 124.2, 123.5, 123.4, 123.1, 116.7, 116.1, 116.0, 108.6, 97.8, 74.4, 53.6, 31.5, 29.7, 27.8; IR ν (KBr) 2968, 1695, 1592, 1524, 1394 cm^{-1}; HRMS (FAB) calcd for $C_{28}H_{23}O_4$ [M + H] 423.1581, found 423.1583.

Preparation of 2b: white solid; yield 51%; R_f = 0.30 (15% EtOAc/hexanes); mp 158−159 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.77 (dd, J = 7.8, 1.5 Hz, 1H), 7.62 (dd, J = 8.1, 1.8 Hz, 1H), 7.51−7.41 (m, 3H), 7.33−7.16 (m, 5H), 7.10 (s, 1H), 7.00−6.90 (m, 2H), 6.02 (s, 1H), 2.46, 2.25 (ABq, J = 14.4 Hz, 1H each), 1.75 (s, 3H), 1.50 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 158.8, 154.5, 152.3, 149.9, 147.7, 132.4, 131.7, 130.8, 129.7, 127.8, 127.1, 124.6, 123.9, 123.6, 122.9, 120.3, 118.9, 117.2, 116.5, 116.1, 108.6, 101.1, 91.2, 74.3, 53.5, 31.6, 29.8, 27.8; IR ν (KBr) 3233, 2981, 1669, 1612, 1564 cm^{-1}; HRMS (FAB) calcd for $C_{28}H_{23}O_5$ [M + H] 439.1545, found 439.1548.

Preparation of 2c: white solid; yield 61%; R_f = 0.25 (10% EtOAc/hexanes); mp 128−129 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.77 (dd, J = 7.8, 1.5 Hz, 1H), 7.71−7.67 (m, 2H), 7.60 (dd, J = 8.1, 1.8 Hz, 1H), 7.51−7.15 (m, 9H), 5.91 (s, 1H), 2.46, 2.22 (ABq, J = 14.4 Hz, 1H each), 1.74 (s, 3H), 1.50 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 162.1, 159.1, 154.4, 152.8, 150.4, 148.6, 133.1, 129.5, 129.3, 128.4, 126.9, 125.1, 124.1, 123.6, 116.6, 108.4, 108.3, 105.0, 103.9, 98.4, 97.3, 73.9, 53.8, 40.1, 40.0, 31.2, 29.9, 28.0; IR ν (KBr) 2916, 1695, 1617, 1597, 1503 cm^{-1}; HRMS (FAB) calcd for $C_{30}H_{28}NO_4$ [M + H] 466.2018, found 466.2014.

Preparation of 2d: white solid; yield 52%; R_f = 0.18 (15% EtOAc/hexanes); mp 141−142 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.63 (dd, J = 7.8, 1.5 Hz, 1H), 7.55 (d, J = 9.0 Hz, 1H), 7.45−7.20 (m, 5H), 7.13 (s, 1H), 6.99−6.88 (m, 2H), 6.51 (dd, J = 9.0, 2.4 Hz, 1H), 6.47 (d, J = 2.4 Hz, 1H), 6.00 (s, 1H), 3.01 (s, 6H), 2.41, 2.20 (ABq, J = 14.4 Hz, 1H each), 1.71 (s, 3H), 1.47 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 162.6, 159.4, 154.6, 154.4, 152.8, 149.9, 147.3, 130.7, 129.4, 127.8, 127.1, 124.4, 124.1, 123.6, 120.1, 119.1, 117.2, 116.3, 108.6, 105.0, 103.9, 102.0, 97.3, 73.6,

53.8, 40.1, 31.1, 29.9, 27.8; IR ν (KBr) 3280, 2939, 1666, 1620, 1594 cm^{-1}; HRMS (FAB) calcd for $C_{30}H_{28}NO_5$ [M + H] 482.1967, found 482.1966.

Preparation of 2e: white solid; yield 69%; $R_f = 0.30$ (12% EtOAc/hexanes); mp 135−136 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.70−7.66 (m, 2H), 7.53 (d, $J = 7.2$ Hz, 1H), 7.47 (d, $J = 8.7$ Hz, 1H), 7.42−7.32 (m, 3H), 6.83 (dd, $J = 8.7$, 2.4 Hz, 1H), 6.67 (d, $J = 2.4$ Hz, 1H), 6.50 (d, $J = 7.2$ Hz, 1H), 6.48 (s, 1H), 5.93 (s, 1H), 3.88 (s, 3H), 3.00 (s, 6H) 2.42, 2.14 (ABq, $J = 14.4$ Hz, 1H each), 1.70 (s, 3H), 1.47 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 162.1, 160.3, 159.2, 154.4, 152.7, 151.4, 148.6, 133.1, 129.2, 128.4, 127.9, 125.0, 124.1, 115.8, 111.6, 108.4, 105.1, 103.7, 100.6, 98.5, 97.2, 73.9, 55.5, 53.6, 40.0, 31.2, 29.9, 28.0; IR ν (KBr) 2926, 1695, 1618, 1597, 1384 cm^{-1}; HRMS (FAB) calcd for $C_{31}H_{30}NO_5$ [M + H] 496.2046, found 496.2044.

Preparation of 2f: white solid; Yield 62%; $R_f = 0.25$ (12% EtOAc/hexanes); mp 136−137 °C;^{1}H NMR ($CDCl_3$, 300 MHz...) δ 7.70−7.67 (m, 2H), 7.54 (d, $J = 9.6$ Hz, 1H), 7.44 (s, 1H), 7.41−7.34 (m, 3H), 6.66 (dd, $J = 8.7$, 2.4 Hz, 1H), 6.52−6.47 (m, 3H), 5.91 (s, 1H), 3.03 (s, 6H), 3.00 (s, 6H), 2.44, 2.13 (ABq, $J = 14.4$ Hz, 1H each), 1.70 (s, 3H), 1.48 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 162.3, 159.2, 154.5, 152.7, 151.4, 148.7, 133.6, 129.0, 128.4, 127.5, 125.1, 124.4, 123.7, 111.3, 109.2, 108.4, 105.3, 103.4, 98.6, 97.3, 91.6, 74.2, 49.1, 40.4, 40.1, 35.6, 31.3, 24.7; IR ν (KBr) 2958, 1705, 1607, 1487, 1368 cm^{-1}; HRMS (FAB) calcd for $C_{32}H_{33}N_2O_4$ [M + H] 509.2440, found 509.2443.

Preparation of 2g: white solid; yield 29%; $R_f = 0.60$ (10% EtOAc/hexanes); mp 134−135 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.70−7.67 (m, 2H), 7.35−7.38 (m, 4H), 7.35 (dd, $J = 7.2$, 2.1 Hz, 1H), 7.24−7.19 (m, 2H), 5.80 (s, 1H), 2.37−2.22 (m, 5H), 1.99 (d, $J = 14.4$ Hz, 1H), 1.56 (s, 3H), 1.34 (s, 3H), 1.09 (s, 3H), 1.08 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 197.6, 167.3, 150.3, 148.5, 133.4, 129.2, 129.1, 128.5, 126.9, 125.2, 124.0, 123.5, 117.4, 116.6, 98.4, 73.3, 54.3, 52.4, 43.5, 31.2, 30.8, 30.6, 29.5, 28.4, 26.7; IR ν (KBr) 2947, 1643, 1627, 1592, 1503 cm^{-1}; HRMS (FAB) calcd for $C_{27}H_{29}O_3$ [M + H] 401.2117, found 401.2114.

Preparation of 2h: white solid; yield 31%; $R_f = 0.55$ (15% EtOAc/hexanes); mp 160−161 °C;^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.54−7.25 (m, 5H), 7.16 (dd, $J = 8.1$, 1.5 Hz, 1H), 7.02−6.92 (m, 2H), 6.00 (s, 1H), 2.31−2.24 (m, 5H), 2.02 (d, $J = 14.4$ Hz, 1H), 1.57 (s, 3H), 1.35 (s, 3H), 1.09 (s, 3H), 1.06 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 198.6, 168.3, 154.8, 150.0, 146.9, 130.5, 129.3, 127.9, 127.0, 124.2, 123.4, 120.0, 119.4, 117.5, 117.0, 116.4, 102.0, 73.3, 54.1, 52.2, 43.6, 31.3, 30.7, 30.6, 29.2, 28.1, 26.9; IR ν (KBr) 3149, 2965, 1620, 1580, 1449 cm^{-1}; HRMS (FAB) calcd for $C_{27}H_{29}O_4$ [M + H] 417.2066, found 417.2068.

Preparation of 2i: white solid; yield 35%; $R_f = 0.65$ (12% EtOAc/hexanes); mp 136−137 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.70−7.67 (m, 2H), 7.45−7.35 (m, 4H), 6.80 (dd, $J = 8.7$, 2.4 Hz, 1H), 6.71 (d, $J = 2.4$ Hz, 1H), 5.85 (s, 1H), 3.85 (s, 3H), 2.36−2.22 (m, 5H), 1.96 (d, $J = 14.4$ Hz, 1H), 1.56 (s, 3H), 1.34 (s, 3H), 1.08 (s, 3H), 1.07 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 197.5, 167.3, 160.2, 151.3, 148.5, 133.4, 129.2, 128.4, 127.7, 125.1, 117.1, 115.7, 111.6, 100.5, 98.5, 73.3, 55.4, 52.3, 43.5, 31.1, 30.7, 30.6, 29.4, 28.4, 26.6; IR ν (KBr) 2957, 1643, 1591, 1358, 1280 cm^{-1}. HRMS (FAB) calcd for $C_{28}H_{31}O_4$ [M + H] 431.2222, found 431.2225.

Acknowledgment. We thank the National Science Council of the Republic of China, Taiwan, for financially supporting this research under Contract No. NSC 98-2113-M-029-003-MY2.

Supporting Information Available. Spectral data for **1a**−**i**, **2a**−**i**, and the x-ray crystallographic data for **1d** and **2e**. This information is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) (a) Ganem, B. *Acc. Chem. Res.* **2009**, *42*, 463–472. (b) Dömling, A. *Chem. Rev.* **2006**, *106*, 17–89. (c) Dömling, A.; Ugi, I. *Angew. Chem., Intl. Ed.* **2000**, *39*, 3168–3210. (d) Dömling, A. *Curr. Opin. Chem. Biol.* **2000**, *4*, 318–323.

(2) (a) Feringa, B. L. *Acc. Chem. Res.* **2001**, *34*, 504–513. (b) Irie, M. *Chem. Rev.* **2000**, *100*, 1685–1716. (c) Feringa, B. L.; van Delden, R. A.; Koumura, N.; Geertsema, E. M. *Chem. Rev.* **2000**, *100*, 1789–1816.

(3) (a) Privman, M.; Tam, T. K.; Pita, M.; Katz, E. *J. Am. Chem. Soc.* **2009**, *131*, 1314–1321. (b) Shin, S. R.; Lee, C. K.; Lee, S. H.; Kim, S. I.; Spinks, G. M.; Wallace, G. G.; So, I.; Jeong, J. H.; Kang, T. M.; Kim, S. *Chem. Commun.* **2009**, 1240–1242. (c) Bitan, G.; Tarus, B.; Vollers, S. S.; Lashuel, H. A.; Condron, M. M.; Straub, J. E.; Teplow, D. B. *J. Am. Chem. Soc.* **2003**, *125*, 15359–15365.

(4) Lai, J. T.; Shieh, P. S.; Huang, W. H.; Yang, D. Y. *J. Comb. Chem.* **2008**, *10*, 381–386.

(5) Yang, D. Y.; Chen, Y. S.; Kuo, P. Y.; Lai, J. T.; Jiang, C. M.; Lai, C. H.; Liao, Y. H.; Chou, P. T. *Org. Lett.* **2007**, *9*, 5287–5290.

(6) Lai, J. T.; Lin, C. H.; Yang, Y. J.; Yang, D. Y. *Chem. Lett.* **2009**, *38*, 590–591.

(7) Fernandes, A. C.; Romao, C. C.; Rosa, C. P.; Vieira, V. P.; Lopes, A.; Silva, P. F.; Macanita, A. L. *Eur. J. Org. Chem.* **2004**, *23*, 4877–4883.

(8) Chen, Y. S.; Kuo, P. Y.; Shie, T. L.; Yang, D. Y. *Tetrahedron* **2006**, *62*, 9410–9416.

(9) Crystallographic data (excluding structure factors) for compounds **1d** and **2e** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC-742565 and -665158, respectively. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, by emailing data_request@ccdc.cam.ac.uk, or by contacting the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K.; fax: +44 1223 336033.

(10) Gupta, R. B.; Franck, R. W. *J. Am. Chem. Soc.* **1987**, *109*, 5393–5403.

(11) Chen, J. R.; Wong, J. B.; Kuo, P. Y.; Yang, D. Y. *Org. Lett.* **2008**, *10*, 4823–4826.

(12) The detailed fluorescence redox switching properties of **1a**−**1i** and the photochromic and thermochromic properties of **2a**−**2i** will be reported elsewhere.

CC900127G