

## First Concise Synthesis of Biologically Interesting Nigrolineabenzopyran A, ( $\pm$ )-Blandachromene II, and ( $\pm$ )-Daurichromene D<sup>†</sup>

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The first efficient synthesis of biologically interesting nigrolineabenzopyran A, blandachromene II, and daurichromene D with the benzopyran moiety has been accomplished using ethylenediamine diacetate-catalyzed reaction as a key step. The key step in these synthetic strategies involves the formation of benzopyran moiety via an electrocyclization reaction.

**Key Words :** Benzopyran, Nigrolineabenzopyran A, Blandachromene II, Daurichromene D

### Introduction

The compounds containing the benzopyran moiety (chromenes) are distributed widely in nature.<sup>1</sup> These compounds have been reported to show biological activity<sup>2</sup> and have been used as versatile intermediates in natural product synthesis.<sup>3</sup> Among these, nigrolineabenzopyran A (**1**) was isolated from *Garcinia nigrolineata*, which is found throughout Malaysia, southern Thailand and Burma (Figure 1).<sup>4</sup> This compound exhibits antibacterial activity against methicillin-resistant *Staphylococcus aureus*. Blandachromene II (**2**) was isolated from *Peperomia blanda* in the Brazilian Atlantic forest.<sup>5</sup> The *Peperomia* genus belongs to the Piperaceae family, comprises of 600 species distributed in southeast Brazil. These species have been studied extensively as natural resources on account of their potential antimicrobial, antitumor, and insecticidal activity.<sup>6</sup> The natural products isolated from the *Peperomia* genus have biological properties such as antiparasitic and analgesic activities. Daurichromene D (**3**) was isolated from *Rhododendron dauricum*, a plant found in areas of northern China, eastern Siberia, inner Mongolia, and Hokkaido.<sup>7</sup> The

dried leaves of this plant are known as “Manshanfong” in China, and are used as expectorants as well as in medications for treating acute-chronic bronchitis.<sup>8</sup> Several natural products isolated from the same plant have shown highly potent anti-HIV activity in acutely infected H9 cells.<sup>9</sup> Daurichromene D (**3**) is also known to have a significant inhibitory effects on the release of histamine from rat mast cells.<sup>7</sup> These wide range of biological activities has stimulated the interest in the synthesis of naturally occurring nigrolineabenzopyran A (**1**), blandachromene II (**2**), and daurichromene D (**3**).

Recently, we developed a new and useful methodology for preparing a variety of benzopyrans using ethylenediamine diacetate-catalyzed reactions of resorcinols to  $\alpha,\beta$ -unsaturated aldehydes. These reactions involve a formal [3+3]-cycloaddition *via* a  $6\pi$ -electrocyclization (Scheme 1).<sup>10</sup> Our efforts in developing these methodologies led to the synthesis of biologically active natural products with the benzopyran skeletons. As an application of our methodology, this paper reports the first total synthesis of biologically interesting natural nigrolineabenzopyran A (**1**), blandachromene II (**2**), and daurichromene D (**3**).

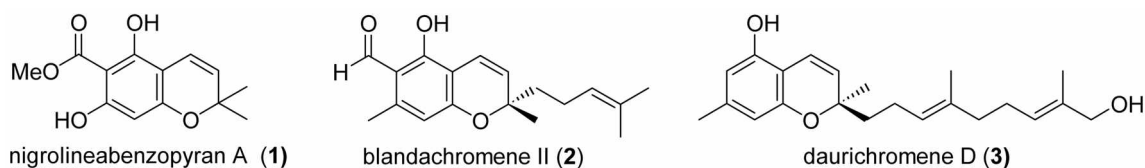
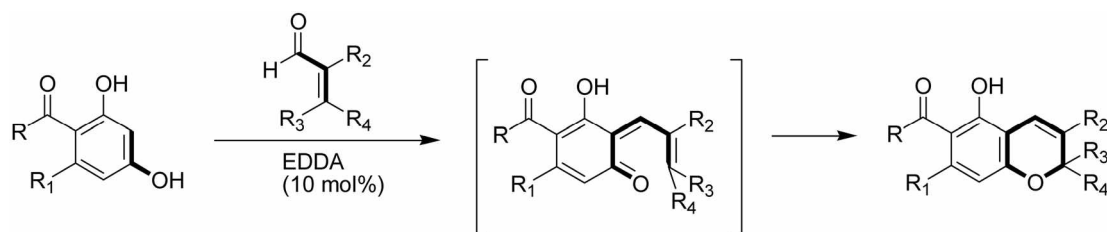


Figure 1



Scheme 1

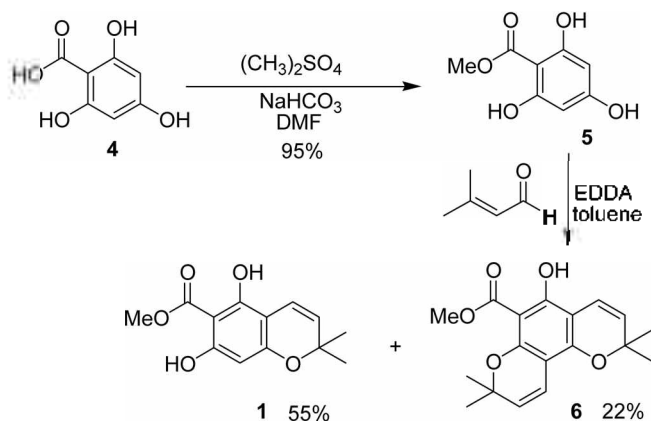
<sup>†</sup>This paper is dedicated to Professor Sang Chul Shim on the occasion of his honorable retirement.

## Results and Discussion

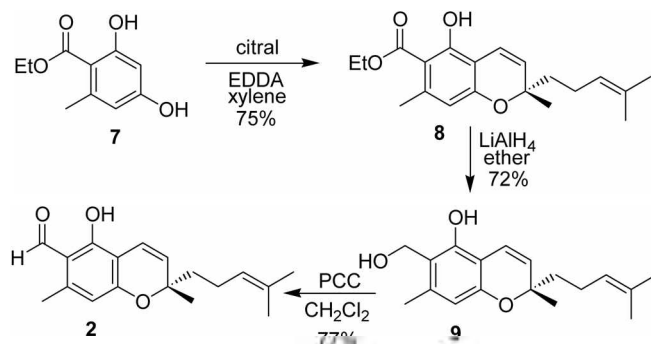
The synthesis of nigrolineabenzopyran A (**1**) was first carried out starting from commercially available 2,4,6-trihydroxybenzoic acid (**4**). Based on the methodology developed by our group,<sup>10</sup> Scheme 2 shows the synthetic strategy. Treatment of compound **4** with dimethylsulfate in DMF at room temperature for 12 h gave the product **5** in 95% yield. The reaction of compound **5** with 3-methyl-2-butenal in the presence of 10 mol % ethylenediamine diacetate (EDDA) in refluxing toluene for 8 h afforded the products **1** and **6** in 55 and 22% yields, respectively. Two compounds were easily separated by column chromatography. The spectroscopic data of **1** synthesized was in agreement with those reported for the natural product.<sup>4</sup>

The synthesis of blandachromene II (**2**) was achieved from commercially available ethyl 2,4-dihydroxy-6-methylbenzoate (**7**) as shown in Scheme 3. A reaction of compound **7** with citral in the presence of 10 mol % of ethylenediamine diacetate in refluxing xylene for 8 h gave the adduct **8** in 75% yield. The reduction of compound **8** with LiAlH<sub>4</sub> in ether at 0 °C for 2 h gave compound **9** in 72% yield. The oxidation of compound **8** with PCC in methylene chloride at room temperature for 10 h afforded the product **2** in 77% yield. The spectral data of **2** synthesized was in good agreement with that of the natural product reported in the literature.<sup>5</sup>

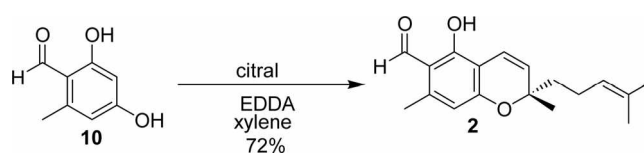
In order to demonstrate a simple synthetic route to blandachromene II (**2**), a one-step reaction was also attempted



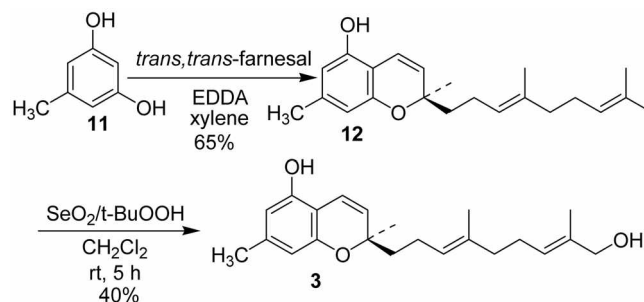
Scheme 2



Scheme 3



Scheme 4



Scheme 5

starting from 2,4-dihydroxy-6-methylbenzaldehyde (**10**) as shown in Scheme 4. A reaction of compound **10** with citral in the presence of 10 mol% of ethylenediamine diacetate in refluxing xylene for 8 h gave the adduct **2** in 72% yield.

Scheme 5 shows the synthetic strategy for daurichromene D (**3**). A reaction of orcinol (**11**) with *trans,trans*-farnesal in the presence of 10 mol % of ethylenediamine diacetate in refluxing xylene for 5 h gave the confluentin **12** in 65% yield, which was recently described.<sup>10a</sup> The conversion of compound **12** to **3** was carried out by allylic oxidation with SeO<sub>2</sub>.<sup>11</sup> A reaction of compound **12** with SeO<sub>2</sub> (1.2 equiv) in refluxing ethanol for 5 h gave the product **3** in low yield (10%). The yield could not be improved with a longer heating time or with the addition of more SeO<sub>2</sub>. However, compound **3** was produced in increased yield (40%) when a 0.5 mol equiv of SeO<sub>2</sub> and 2 equiv of *t*-butyl hydroperoxide were used at room temperature for 5 h in CH<sub>2</sub>Cl<sub>2</sub>.<sup>11</sup> The spectral data of **3** synthesized is in good agreement with those of the natural product reported in the literature.<sup>7</sup>

In conclusion, the first total synthesis of natural nigrolineabenzopyran A (**1**), blandachromene II (**2**), and daurichromene D (**3**) with the benzopyran moiety has been accomplished starting from commercially available compounds **4**, **7**, **10**, and **11**. The key step in these synthetic strategies involves the formation of benzopyrans using a 6 $\pi$ -electrocyclization.

## Experimental

All experiments were carried out under a nitrogen atmosphere. Merck precoated silica gel plates (Art. 5554) with a fluorescent indicator were used for analytical TLC. Flash column chromatography was performed using silica gel 9385 (Merck). The <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were recorded on a Bruker Model ARX (300 and 75 MHz, respectively) spectrometer in CDCl<sub>3</sub> using  $\delta = 77.0$  ppm as the solvent chemical shift. The IR spectra were recorded on a Jasco FTIR 5300 spectrophotometer. The HRMS and MS

spectra were carried out at the Korea Basic Science Institute.

**Methyl 2,4,6-trihydroxybenzoate (5).**  $K_2CO_3$  (1.380 g, 10 mmol) was added to a solution of 2,4,6-trihydroxybenzoic acid (**4**) (340 mg, 2 mmol) in DMF (10 mL) at room temperature. Dimethyl sulfate (252 mg, 2 mmol) was then added dropwise, and the mixture was stirred at room temperature for 12 h. A saturated  $NH_4Cl$  solution (50 mL) was added and the mixture was extracted with ethyl acetate (30 mL  $\times$  3). The organic layer was dried over  $MgSO_4$  and the solvent was removed under reduced pressure to leave an oily residue. The residue was then purified by column chromatography on silica gel using hexane/ethyl acetate (2:1) to give the product **5** (350 mg, 95%) as a solid: mp 98–99 °C;  $^1H$  NMR (300 MHz,  $CDCl_3$  +  $DMSO-d_6$ )  $\delta$  14.05 (1H, s), 5.95 (3H, s), 5.57 (1H, s), 4.02 (3H, s);  $^{13}C$  NMR (75 MHz,  $CDCl_3$  +  $DMSO-d_6$ )  $\delta$  169.3, 164.4, 162.1, 161.9, 95.3, 92.3, 51.8; IR (KBr) 3380, 2925, 1946, 1438, 1281, 1164, 1111, 838  $cm^{-1}$ .

**Nigrolineabenzopyran A (1) and compound 6.** Ethylenediamine diacetate (20 mg, 0.11 mmol) was added to a solution of methyl 2,4,6-trihydroxybenzoate (**5**) (202 mg, 1.1 mmol) and 3-methyl-2-butenal (101 mg, 1.2 mmol) in toluene (20 mL) at room temperature. The mixture was refluxed for 8 h and then cooled to room temperature. The solvent was removed under reduced pressure to leave an oily residue, which was then purified by column chromatography on silica gel using hexane/ethyl acetate (3:1) to give compound **1** (157 mg, 55%) and **6** (76 mg, 22%). Compound **1**: mp 64–65 °C;  $^1H$  NMR (300 MHz,  $CDCl_3$ )  $\delta$  6.54 (1H, d,  $J=10.0$  Hz), 5.39 (1H, d,  $J=10.0$  Hz), 3.96 (3H, s), 1.36 (6H, s);  $^{13}C$  NMR (75 MHz,  $CDCl_3$ )  $\delta$  170.0, 160.6, 160.5, 160.4, 129.8, 115.8, 102.6, 96.7, 93.4, 77.5, 52.4, 28.2; IR (KBr) 3432, 1649, 1588, 1437, 1310, 1246, 1200, 1100, 978, 770  $cm^{-1}$ . Compound **6**: mp 99–100 °C;  $^1H$  NMR (300 MHz,  $CDCl_3$ )  $\delta$  11.96, 6.60 (1H, d,  $J=10.0$  Hz), 6.52 (1H, d,  $J=10.0$  Hz), 5.40 (1H, d,  $J=10.0$  Hz), 5.39 (1H, d,  $J=10.0$  Hz), 3.84 (3H, s), 1.38 (6H, s);  $^{13}C$  NMR (75 MHz,  $CDCl_3$ )  $\delta$  172.3, 159.2, 156.3, 154.3, 125.9, 125.8, 116.8, 116.7, 78.2, 77.9, 52.4, 28.7, 28.1; IR (KBr) 2924, 1732, 1651, 1443, 1366, 1290, 1246, 1211, 1142, 999, 883, 740  $cm^{-1}$ ; HRMS  $m/z$  ( $M^+$ ) calcd for  $C_{13}H_{20}O_3$ : 316.1311. Found: 316.1310.

**5-Hydroxy-2,7-dimethyl-2-(4-methylpent-3-enyl)-2H-chromene-6-carboxylic acid ethyl ester (8).** Ethylenediamine diacetate (36 mg, 0.2 mmol) was added to a solution of ethyl 2,4-dihydroxy-6-methylbenzoate (**7**) (392 mg, 2 mmol) and citral (334 mg, 2.2 mmol) in xylene (20 mL) and at room temperature. The mixture was refluxed for 8 h and then cooled to room temperature. The solvent was removed under reduced pressure to leave an oily residue, which was then purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to give compound **8** (496 mg, 75%) as an oil:  $^1H$  NMR (300 MHz,  $CDCl_3$ )  $\delta$  12.08 (1H, s), 6.72 (1H, d,  $J=10.0$  Hz), 6.16 (1H, s), 5.42 (1H, s,  $d=10.0$  Hz), 5.09–5.04 (1H, m), 4.35 (2H, q,  $J=7.1$  Hz), 2.45 (3H, s), 2.14–2.03 (2H, m), 1.78–1.58 (2H, m), 1.62 (3H, s), 1.55 (3H, s), 1.38 (3H, t,  $J=7.1$  Hz), 1.37 (3H, s);  $^{13}C$  NMR (75 MHz,  $CDCl_3$ )  $\delta$  172.4, 160.2, 143.2, 132.2, 126.6, 124.4, 117.3,

112.0, 110.0, 107.5, 105.4, 80.0, 61.6, 42.0, 27.4, 26.1, 25.0, 23.1, 18.0, 14.7; IR (00000) 2973, 2930, 1651, 1566, 1422, 1379, 1316, 1271, 1175, 1022, 810  $cm^{-1}$ ; MS (EI) 330 ( $M^+$ ), 269, 248, 247, 202, 201, 188, 175, 174, 69; HRMS  $m/z$  ( $M^+$ ) calcd for  $C_{20}H_{26}O_4$ : 330.1831. Found: 330.1833.

**6-Hydroxymethyl-2,7-dimethyl-2-(4-methylpent-3-enyl)-2H-chromen-5-ol (9).** A solution of  $LiAlH_4$  (46 mg, 1.2 mmol) in dry ether (20 mL) was placed in a flask equipped with reflux condenser. Compound **8** (400 mg, 1.2 mmol) in 2 mL of ether was then added very slowly at 0 °C. The reaction mixture was stirred at 0 °C for 2 h and carefully quenched with ice-water and a 1 N-HCl solution. The reaction mixture was extracted with ethyl acetate and washed with brine. The mixture was then dried over  $MgSO_4$  and the solvent was removed under reduced pressure to leave an oily residue, which was then purified by column chromatography on silica gel using hexane/ethyl acetate (5:1) to give compound **9** (249 mg, 72%) as an oil:  $^1H$  NMR (300 MHz,  $CDCl_3$ )  $\delta$  7.97 (1H, s), 6.72 (1H, d,  $J=10.0$  Hz), 6.16 (1H, s), 5.47 (1H, d,  $J=10.0$  Hz), 5.09–5.04 (1H, m), 4.84 (2H, s), 2.14 (3H, s), 2.14–2.03 (2H, m), 1.78–1.60 (2H, m), 1.62 (3H, s), 1.56 (3H, s), 1.34 (3H, s);  $^{13}C$  NMR (75 MHz,  $CDCl_3$ )  $\delta$  153.6, 153.0, 136.2, 132.0, 127.6, 124.6, 117.5, 115.1, 110.2, 108.7, 78.6, 61.2, 41.5, 26.7, 26.1, 23.1, 19.9, 18.0; IR (neat) 3456, 2969, 2924, 1618, 1570, 1453, 1377, 1327, 1263, 1200, 833, 739  $cm^{-1}$ ; MS (EI) 288 ( $M^+$ ), 270, 255, 227, 205, 203, 201, 189, 188, 187, 175, 159, 115, 91, 78, 69, 63, 57, 55; HRMS  $m/z$  ( $M^+$ ) calcd for  $C_{18}H_{24}O_3$ : 288.1725. Found: 288.1723.

**Blandachromene II (2) from 9.** PCC (302 mg, 1.4 mmol) was added to a solution of compound **9** (202 mg, 0.7 mmol) in  $CH_2Cl_2$  (20 mL) at room temperature. The reaction mixture was stirred at room temperature for 10 h and filtered through a silica gel column. After concentrating the filtrate *in vacuo*, the residue was then purified by column chromatography on silica gel using hexane/ethyl acetate (20:1) to give compound **2** (154 mg, 77%) as an oil:  $^1H$  NMR (300 MHz,  $CDCl_3$ )  $\delta$  12.6 (1H, s), 10.0 (1H, s), 6.67 (1H, d,  $J=10.0$  Hz), 6.14 (1H, s), 5.46 (1H, d,  $J=10.0$  Hz), 5.07–5.03 (1H, m), 2.45 (3H, s), 2.09–2.01 (2H, m), 1.79–1.58 (2H, m), 1.63 (3H, s), 1.54 (3H, s), 1.38 (3H, s);  $^{13}C$  NMR (75 MHz,  $CDCl_3$ )  $\delta$  196.0, 160.0, 159.9, 144.9, 131.3, 127.2, 124.0, 114.8, 112.9, 110.9, 106.2, 79.8, 39.8, 26.8, 25.5, 22.3, 18.0, 17.4; IR (neat) 2926, 1634, 1483, 1372, 1294, 1254, 1157, 1074, 989, 806  $cm^{-1}$ .

**Blandachromene II (2) from 10.** Ethylenediamine diacetate (18 mg, 0.1 mmol) was added to a solution of 2,4-Dihydroxy-6-methylbenzaldehyde (**9**) (152 mg, 1 mmol) and citral (182 mg, 1.2 mmol) in xylene (20 mL) at room temperature. The mixture was refluxed for 8 h and then cooled to room temperature. The solvent was removed under reduced pressure to leave an oily residue, which was then purified by column chromatography on silica gel using hexane/ethyl acetate (20:1) to give compound **2** (206 mg, 72%).

**Confluentin (11).** Ethylenediamine diacetate (36 mg, 0.2 mmol) was added to a solution of orcinol (**10**) (248 mg, 2 mmol) and *trans,trans*-famesal (528 mg, 2.4 mmol) in

xylene (20 mL) at room temperature. The mixture was heated under reflux for 5 h and then cooled to room temperature. The solvent was removed under reduced pressure to leave an oily residue, which was then purified by column chromatography on silica gel using hexane/ethyl acetate (20:1) to give the product **11** (424 mg, 65%) as an oil:  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  6.59 (1H, d,  $J = 9.9$  Hz), 6.22 (1H, s), 6.09 (1H, s), 5.48 (1H, d,  $J = 9.9$  Hz), 5.11-5.03 (2H, m), 4.74 (1H, s), 2.16 (3H, s), 2.12-1.87 (6H, m), 1.77-1.65 (2H, m), 1.65 (3H, s), 1.56 (3H, s), 1.55 (3H, s), 1.35 (3H, s);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  154.4, 151.9, 139.9, 135.6, 131.7, 127.3, 124.8, 124.5, 117.5, 109.9, 109.0, 107.4, 78.7, 41.4, 40.1, 27.1, 26.7, 26.2, 23.1, 21.9, 18.1, 16.4; IR (neat) 3429, 2969, 2922, 1626, 1580, 1451, 1377, 1144, 1076, 991  $\text{cm}^{-1}$ ; HRMS  $m/z$  ( $M^+$ ) calcd for  $\text{C}_{22}\text{H}_{30}\text{O}_2$ : 326.2246. Found: 326.2248.

**Daurichromene D(3)**. 0.48 mL (2.4 mmol) of *t*-butyl hydroperoxide (5.0 M in decane) was poured into a stirred suspension of  $\text{SeO}_2$  (68 mg, 0.6 mmol) in 10 mL of  $\text{CH}_2\text{Cl}_2$ . The resulting solution was stirred at room temperature. Compound **11** (400 mg, 1.2 mmol) in 1 mL of  $\text{CH}_2\text{Cl}_2$  was then added over a period of several minutes. The mixture was stirred at room temperature for 5 h. The  $\text{CH}_2\text{Cl}_2$  was removed on a rotary evaporator and ether (50 mL) was added. The organic phase was washed twice with 10 mL of 10% KOH and once with brine. The organic layer was dried over  $\text{MgSO}_4$ . The solvent was removed under reduced pressure to leave an oily residue, which was then purified by column chromatography on silica gel using hexane/ethyl acetate (4:1) to give compound **3** (164 mg, 40%) as an oil:  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  6.59 (1H, d,  $J = 10.0$  Hz), 6.21 (1H, s), 6.10 (1H, s), 6.47 (1H, d,  $J = 10.0$  Hz), 5.35 (1H, t,  $J = 7.0$  Hz), 5.10 (1H, t,  $J = 7.2$  Hz), 3.97 (2H, s), 2.18 (3H, s), 2.13-1.94 (6H, m), 1.79-1.64 (2H, m), 1.63 (3H, s), 1.56 (3H, s), 1.35 (3H, s);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  153.9, 151.6, 139.3, 134.7, 134.3, 126.7, 126.4, 124.4, 117.0, 109.3, 108.4, 106.8, 78.1, 68.9, 40.9, 39.1, 26.2, 26.1, 22.6, 21.5, 15.9, 13.7; IR (neat) 3380, 2924, 1626, 1580, 1453, 1331, 1142, 1063, 993, 826  $\text{cm}^{-1}$ .

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## References

- (a) Nicolaou, K. C.; Pfefferkorn, J. A.; Roecker, A. J.; Cao, G.-Q.; Barluenga, S.; Mitchell, H. J. *J. Am. Chem. Soc.* 2000, 122, 9939. (b) Nicolaou, K. C.; Pfefferkorn, J. A.; Mitchell, H. J.; Roecker, A. J.; Cao, G.-Q.; Affleck, R. L.; Lillig, J. E. *J. Am. Chem. Soc.* 2000, 122, 9954. (c) Nicolaou, K. C.; Pfefferkorn, J. A.; Barluenga, S.; Mitchell, H. J.; Roecker, A. J.; Cao, G.-Q. *J. Am. Chem. Soc.* 2000, 122, 9968. (d) Lee, J. H.; Bang, H. B.; Han, S. Y.; Jun, J.-G. *Bull. Korean Chem. Soc.* 2006, 27, 2104.
- (a) Atwal, K. S.; Grover, G. J.; Ahmed, S. Z.; Ferrara, F. N.; Harper, T. W.; Kim, K. S.; Sleph, P. G.; Dzwonczyk, S.; Russell, A. D.; Moreland, S.; McCullough, J. R.; Normandin, D. E. *J. Med. Chem.* 1993, 36, 3971. (b) Evans, J. M.; Fake, C. S.; Hamilton, T. C.; Poyser, R. H.; Watts, E. A. *J. Med. Chem.* 1983, 26, 1582. (c) Cassidy, F.; Evans, J. M.; Hadley, M. S.; Haladj, A. H.; Leach, P. E.; Stemp, G. *J. Med. Chem.* 1992, 35, 1623. (d) Gericke, R.; Harting, J.; Lues, I.; Schittenhelm, C. *J. Med. Chem.* 1991, 34, 3074. (e) Bergmann, R.; Gericke, R. *J. Med. Chem.* 1990, 33, 492. (f) Atwal, K. S.; Grover, G. J.; Ferrara, F. N.; Ahmed, S. Z.; Sleph, P. G.; Dzwonczyk, S.; Normandin, D. E. *J. Med. Chem.* 1995, 38, 1966. (g) Elomri, A.; Mitaku, S.; Michel, S.; Skaltsounis, A.-L.; Tillequin, F.; Koch, M.; Pierré, A.; Guillaud, N.; Léonce, S.; Kraus-Berthier, L.; Rolland, Y.; Atass, G. *J. Med. Chem.* 1996, 39, 4762. (h) *Chromenes, Chromanones, and Chromones in The Chemistry of Heterocyclic Compounds*; Ellis, G. P., Ed.; John Wiley and Sons: New York, 1977; Chapter 2.
- (a) Hepworth, J. D. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Ed.; Pergamon: New York, 1984; Vol. 3, p 737. (b) Bigi, F.; Chesini, L.; Magi, R.; Sartori, G. *J. Org. Chem.* 1999, 64, 1033. (c) Nielsen, S. F.; Olsen, C. E.; Christensen, S. B. *Tetrahedron* 1997, 53, 5573. (d) Dorta, R. L.; Martin, A.; Suárez, E.; Betancor, C. *J. Org. Chem.* 1997, 62, 2273. (e) Henry, G. E.; Jacobs, H. *Tetrahedron* 2001, 57, 5335. (f) Nguyen, V. T. H.; Langer, P. *Tetrahedron Lett.* 2005, 46, 815. (g) Trost, B. M.; Shen, H. C.; Dong, L.; Surivet, J.-P.; Sylvain, C. *J. Am. Chem. Soc.* 2004, 126, 11966.
- Rukachaisirikul, V.; Tadetch, K.; Watthanaphanit, A.; Saengsanee, N.; Phongpaichit, S. *J. Nat. Prod.* 2005, 68, 1218.
- Veloza, L. S. M.; Ferreira, M. J. P.; Santos, M. I. S.; Moreira, D. L.; Emerenciano, V. P.; Kaplan, M. A. C. *Phytochemistry* 2006, 67, 492.
- (a) Sacchetti, G.; Maietti, S.; Muzzoli, M.; Scaglianti, M.; Manfredini, S.; Radice, M.; Bruni, R. *Food Chem.* 2005, 91, 621. (b) Konishi, T.; Konoshima, T.; Daikonya, A.; Kitanata, S. *Chem. Pharm. Bull.* 2005, 53, 121. (c) Costantini, M. B.; Sartorelli, P.; Limberger, R. P.; Henriques, A. T.; Steppe, M.; Ferreira, M. J. P.; Ohara, M. T.; Emerenciano, V. P.; Kato, M. *J. Planta. Med.* 2001, 67, 771.
- Iwata, N.; Wang, N.; Yao, X.; Kitanaka, S. *J. Nat. Prod.* 2004, 67, 1106.
- Chinese Materia Medica*; Jiangsu New Medical College, Ed.; Shanghai People's Pub. House: Shanghai, 1977; p 2506
- Kashiwada, Y.; Yamazaki, K.; Ikeshiro, Y.; Yamasishi, T.; Fujioka, T.; Milashi, K.; Mizuki, K.; Cosentino, L. M.; Fowke, K.; Morris-Natschke, S. L.; Lee, K.-H. *Tetrahedron* 2001, 57, 1559.
- (a) Lee, Y. R.; Choi, J. H.; Yoon, S. H. *Tetrahedron Lett.* 2005, 46, 7539. (b) Lee, Y. R.; Choi, J. H.; Trinh, D. T. L.; Kim, N. W. *Synthesis* 2005, 3026. (c) Lee, Y. R.; Kim, D. H. *Synthesis* 2006, 603. (d) Lee, Y. R.; Lee, W. K.; Noh, S. K.; Lyoo, W. S. *Synthesis* 2006, 853. (e) Lee, Y. R.; Wang, X. *Bull. Korean Chem. Soc.* 2005, 26, 1933. (f) Lee, Y. R.; Xia, L. *Bull. Korean Chem. Soc.* 2007, 28, 1585. (g) Wang, X.; Lee, Y. R. *Synthesis* 2007, 3044. (h) Lee, Y. R.; Xia, L. *Synthesis* 2007, 3244. (i) Wang, X.; Lee, Y. R. *Tetrahedron Lett.* 2007, 48, 6275. (j) Lee, Y. R.; Kim, J. H. *Synlett* 2007, 2232.
- Umbreit, M. A.; Sharpless, K. B. *J. Am. Chem. Soc.* 1977, 99, 5526.