A Highly Efficient and Practical Synthesis of Chromene Derivatives Using Ring-Closing Olefin Metathesis

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Chromenes (2*H*-1-benzopyran derivatives) have been widely employed as important intermediates in the synthesis of many natural products and medicinal agents. There has been recent interest in the use of these common structural elements for a new family of potassium-channel activating drugs.[1] They also serve as the framework of a range of tannins,[2] which are becoming increasingly important because of their health-promoting effects found in teas, vegetables, fruits, fruit juices, and red wines. Despite the several existing methods for the synthesis of chromene derivatives,[3] there still is demand for general strategies which can efficiently provide variously substituted chromene systems.

In this note, we report a practical and highly efficient procedure for preparing diverse chromene derivatives using ring-closing metathesis (RCM),[4] a methodology emerging as a new tool in synthetic organic chemistry.[5,6]

Results and Discussion

A series of 2-styrenyl allyl ethers (**2a**−**j**) was easily prepared in high yields from the readily available compounds; substituted salicylaldehydes or 2-hydroxy aryl ketones (Scheme 1, method A).

O-Allylation with allyl bromide was conveniently performed in the presence of K_2CO_3 and acetone under reflux conditions. Subsequent filtration of the reaction mixture followed by removal of the solvent afforded the intermediates quantitatively. The R^3 group was introduced using a substituted allyl halide under the same aforementioned reaction conditions. The *O*-allylated intermediates were analytically pure and used in the next olefination reactions without further purification. The Wittig reaction of the corresponding carbonyl compounds with methyltriphenylphosphonium bromide provided the dienes **2a**−**j**.

In contrast, dienes with substituents on the R^2 position (**2k**−**l**) were efficiently prepared by the Mitsunobu reaction[7] of 2-vinylphenol with secondary allyl alcohols (Scheme 1, method B). Especially noteworthy is that a chiral center in the R^2 position could be introduced using chiral secondary allyl alcohols, which can be readily obtained by a Sharpless resolution.[8] Nonracemic chromene derivatives could be therefore prepared.

Ring-closing metathesis of the dienes prepared above was next attempted using ruthenium carbene catalyst **1** [$Cl_2(PCy_3)_2Ru{=}CHPh$].[9] Table 1 summarizes the results.

With dienes containing only R^1 substituents, cyclizations were nearly quantitative using only 2 mol % of the complex **1** (CH_2Cl_2, room temperature, 2 h). All functional groups tested in the R^1 position were tolerated under these reaction conditions. In addition, the electronic properties of the substituents have little effect on the efficiency of the ring closure, and chromenes having substituents such as NO_2, Et_2N, Br, or MeO could be prepared with the same efficiency. RCM of naphthyl vinyl allyl ether diene **2j** afforded 2*H*-naphtho[1,2-*b*]-pyran in 89% yield (entry 10).

Cyclization of a diene having another substituent at the R^4 position (**2f**, entry 6) was equally quantitative under the same reaction conditions. In contrast, reaction of dienes with an R^3 substituent was slow. For example, only 45% conversion to the cyclized product was observed for diene **2g** after 24 h using 8 mol % of catalyst **1** (CH_2Cl_2, room temperature). The reaction rate was greatly increased at higher temperatures in benzene, however, and the cyclized product was obtained in excellent yield to give **3g** (6 mol % of **1**, 60 °C, 2 h). This strongly implies that the initial metathesis between complex **1** and dienes **2a**−**l** is on the *O*-allylic olefin rather than the styrenyl double bond. It is noteworthy that excellent yield of cyclization was observed for compound **2i**, where there is a second allyl ether in the molecule. The R^1 allyl ether undergoes nonproductive

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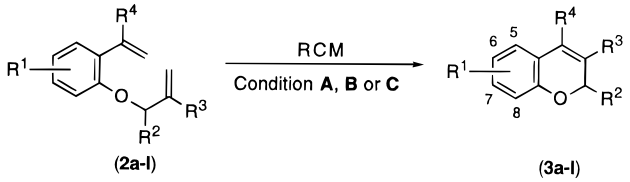
Table 1. Ring-Closing Olefin Metathesis (RCM) of Various Styrenyl Allyl Ether Dienes

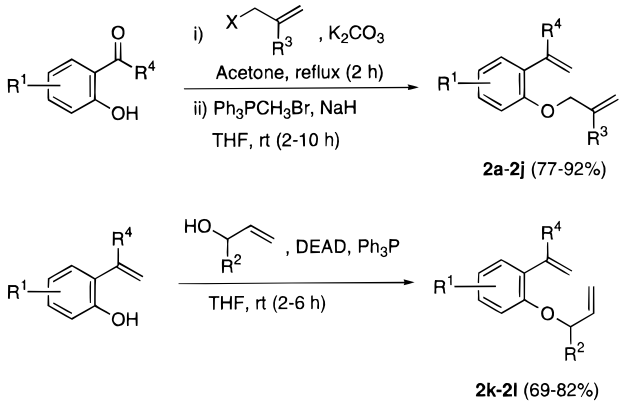


(2a-l) (3a-l)

entry	dienes	cond.[a]	yield (%)[b]
1	**2a** (R^1 = H, R^2 = H, R^3 = H, R^4 = H)	A	95
2	**2b** (R^1 = 6-Br, R^2 = H, R^3 = H, R^4 = H)	A	99
3	**2c** (R^1 = 7-Et_2N, R^2 = H, R^3 = H, R^4 = H)	A	99[c]
4	**2d** (R^1 = 6-NO_2, R^2 = H, R^3 = H, R^4 = H)	A	97
5	**2e** (R^1 = 7-CH_3O, R^2 = H, R^3 = H, R^4 = H)	A	91
6	**2f** (R^1 = 6-Cl, R^2 = H, R^3 = H, R^4 = CH3)	A	94
7	**2g** (R^1 = 7-CH_3O, R^2 = H, R^3 = CH_3, R^4 = H)	B	93
8	**2h** (R^1 = 8-CH_3O, R^2 = H, R^3 = H, R^4 = H)	A	94
9	**2i** (R^1 = 7-$OCH_2CH{=}CH_2$, R^2 = H, R^3 = H, R^4 = H)	A	95
10	**2j** (R^1 = 7-$(CH)_4$-8, R^2 = H, R^3 = H, R^4 = H)	A	89
11	**2k** (R^1 = H, R^2 = CH_3, R^3 = H, R^4 = H)	C	82
12	**2l** (R^1 = H, R^2 = 4-$(CH_3O)C_6H_4$, R^3 = H, R^4 = H)	C	79

[a] Condition **A**: **1** (2 mol %), CH_2Cl_2 (0.2 M), rt (2 h); condition **B**: **1** (6 mol %), C_6H_6 (0.2 M), 60 °C (2 h); condition **C**: **1** (5 mol %), CH_2Cl_2 (0.2 M), rt (10 h). [b] Isolated yields after column chromatography on silica gel except entry 3. [c] NMR yield due to unstability of the product on silica gel.

Scheme 1. Preparation of Styrenyl Allyl Ether Dienes



metathesis on the time scale of the RCM reaction. Dienes having R^2 substituents such as **2k,l** were also readily cyclized (entries 11 and 12) under longer reaction times (5 mol % of **1**, CH_2Cl_2, room temperature, 10 h).

The efficiency of catalytic ring-closing metathesis combined with ease of preparation of the dienes makes this strategy an attractive alternative for the formation of variously substituted chromene systems.

Experimental Section

NMR spectra were recorded on a General Electric QE−300 spectrometer. Chemical shifts are reported in ppm downfield from TMS with reference to internal solvent. High-resolution mass spectra were provided by the Southern California Mass Spectrometry Facility (University of California, Riverside). Analytical thin-layer chromatography (TLC) was performed using silica gel 60 F254 precoated plates (0.25 mm thickness) with a fluorescent indicator. Flash column chromatography was performed using silica gel 60 (230−400 mesh) from EM Science. Alkylidenes **1** was prepared according to the published procedures.[9b]

General Procedure for Preparation of Dienes (Method A). To a solution of salicylaldehyde (1.2 g, 10.0 mmol) and allyl bromide (2.4 g, 19.8 mmol) in acetone (30 mL) was added potassium carbonate (2.7 g, 19.5 mmol), and the reaction mixture was stirred at 60 °C for 2 h. After cooling to room temperature, it was filtered and washed with acetone (50 mL × 2) and then evaporated under reduced pressure to give quantitatively *O*-allylated benzaldehyde intermediate. In a separate flask containing NaH (prewashed with hexane three times, 360 mg, 15.0 mmol) and THF (30 mL) was added methyltriphenylphosphonium bromide (4.6 g, 12.9 mmol) at 0 °C, and it was stirred for 30 min at rt. To the above solution was added a solution of the *O*-allylated benzaldehyde prepared above in THF (10 mL), and the reaction mixture was stirred for 2 h at room temperature. The crude mixture was extracted with EtOAc (100 mL × 2), washed with brine (100 mL), and then dried over $MgSO_4$. Silica gel column chromatography (EtOAc/hexanes = 1:20) afforded the diene **2a** (1.33 g, 83%)[10] as a colorless liquid.

2b (92%, R^1 = 6-Br, R^2 = R^3 = R^4 = H) was prepared by the same procedure from 5-bromosalicylaldehyde: ^{1}H NMR (300 MHz, CD_2Cl_2) δ 7.61 (d, J = 2.4 Hz, 1H), 7.31 (dd, J = 9.0, 2.4 Hz, 1H), 7.02 (dd, J = 17.7, 11.1 Hz, 1H), 6.75 (d, J = 8.7 Hz, 1H), 6.07 (m, 1H), 5.75 (dd, J = 17.7, 0.9 Hz, 1H), 5.43 (dd, J = 17.1, 1.8 Hz, 1H), 5.30 (dd, J = 11.1, 4.2 Hz, 2H), 4.54 (d, J = 5.1 Hz, 2H); ^{13}C NMR (75 MHz, CD_2Cl_2) δ 153.5, 145.2, 132.7, 130.9, 130.2, 128.8, 117.0, 115.2, 113.9, 112.9, 69.1; IR (film) 2866, 1624, 1476, 1409, 1241, 1122, 1016, 916 cm^{-1}; HRMS (EI) calcd for $C_{11}H_{11}BrO$ $[M]^+$ 237.9993, found 237.9991.

2c (77%, R^1 = 7-Et_2N, R^2 = R^3 = R^4 = H) was prepared by the same procedure from 4-(diethylamino)salicylaldehyde: ^{1}H NMR (300 MHz, CD_2Cl_2) δ 7.32 (d, J = 8.7 Hz, 1H), 6.94 (dd, J = 17.7, 11.1 Hz, 1H), 6.27 (dd, J = 8.7, 2.4 Hz, 1H), 6.15 (s, 1H), 6.08 (m, 1H), 5.51 (dd, J = 17.7, 1.8 Hz, 1H), 5.45 (dd, J = 17.4, 1.8 Hz, 1H), 5.30 (m, 1H), 4.96 (dd, J = 11.1, 1.8 Hz, 1H), 4.56 (d, J = 3.6 Hz, 2H), 3.36 (q, J = 7.2 Hz, 4H), 1.16 (t, J = 7.2 Hz, 6H); ^{13}C NMR (75 MHz, CD_2Cl_2) δ 157.1, 148.8, 134.0, 131.4, 127.1, 116.8, 114.3, 108.7, 104.6, 102.6, 96.2, 69.2, 12.5; IR (film) 2964, 1607, 1559, 1506, 1370, 1269, 1215, 1119, 916 cm^{-1}.

2d (81%, R^1 = 6-NO_2, R^2 = R^3 = R^4 = H) was prepared by the same procedure from 2-hydroxy-5-nitrobenzaldehyde: ^{1}H NMR (300 MHz, CD_2Cl_2) δ 8.36 (d, J = 3.0 Hz, 1H), 8.10 (dd, J = 9.9, 3.0 Hz, 1H), 7.05 (dd, J = 17.7, 11.1 Hz, 1H), 6.95 (d, J = 9.0 Hz, 1H), 6.10 (m, 1H), 5.90 (d, J = 18.0, 1H), 5.43 (d, J = 11.1, 1H), 5.38 (m, 2H), 4.69 (d, J = 5.4 Hz, 2H); ^{13}C NMR (75 MHz, CD_2Cl_2) δ 160.4, 141.5, 132.2, 129.8, 127.6, 124.6, 122.0, 118.2, 117.1, 111.7, 69.7; IR (film) 3080, 2925, 1583, 1515, 1336, 1264, 1085, 993, 916 cm^{-1}; HRMS (CI) calcd for $C_{11}H_{15}N_2O_3$ $[M + NH_4]^+$ 223.1082, found 223.1088.

2e (91%, R^1 = 7-CH_3O, R^2 = R^3 = R^4 = H) was prepared by the same procedure from 2-hydroxy-5-methoxybenzaldehyde: ^{1}H NMR (300 MHz, CD_2Cl_2) δ 7.43 (d, J = 8.4 Hz, 1H), 7.01 (dd, J = 17.7, 11.1 Hz, 1H), 6.51 (dd, J = 8.4, 2.1 Hz, 1H), 6.46 (d, J =

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2.4 Hz, 1H), 6.10 (m, 1H), 5.65 (d, J = 18.6 Hz, 1H), 5.46 (dd, J = 17.1, 1.8 Hz, 1H), 5.33 (dt, J = 10.8, 1.5 Hz, 1H), 5.16 (dd, J = 12.0, 1.5 Hz, 1H), 4.55 (dd, J = 4.8, 0.9 Hz, 1H), 3.81 (s, 3H); ^{13}C NMR (75 MHz, CD_2Cl_2) δ 160.6, 156.8, 133.4, 131.2, 127.1, 119.8, 117.1, 111.8, 105.1, 99.4, 69.1, 55.3; IR (film) 3080, 2935, 1607, 1501, 1414, 1264, 1196, 1167, 1114, 1027, 925, 901 cm^{-1}; HRMS (CI) calcd for $C_{12}H_{15}O_2$ $[M + H]^+$ 191.1072, found 191.1073.

2f (94%, R^1 = 8-CH_3O, $R^2 = R^3 = R^4$ = H) was prepared by the same procedure from *o*-vanilline: ^{1}H NMR (300 MHz, CD_2Cl_2) δ 7.13 (d, J = 7.8 Hz, 1H), 7.04 (dd, J = 16.5, 8.1 Hz, 1H), 6.84 (d, J = 8.1, 1H), 6.11 (m, 1H), 5.78 (d, J = 17.7, 1H), 5.36 (dd, J = 17.1, 1.5 Hz, 1H), 5.24 (m, 2H), 4.46 (d, J = 5.7 Hz, 2H), 3.84 (s, 3H); ^{13}C NMR (75 MHz, CD_2Cl_2) δ 152.7, 144.9, 134.1, 130.9, 123.5, 116.9, 116.5, 114.3, 111.1, 102.6, 73.5, 55.2; IR (film) 3080, 2935, 1573, 1472, 1264, 1066, 988, 916 cm^{-1}; HRMS (CI) calcd for $C_{12}H_{15}O_2$ $[M + H]^+$ 191.1072, found 191.1081.

2 g (84%, R^1 = 6-Cl, $R^2 = R^3$ = H, R^4 = CH_3) was prepared by the same procedure from 5′-chloro-2′-hydroxyacetophenone: ^{1}H NMR (300 MHz, CD_2Cl_2) δ 7.20 (m, 2H), 6.80 (d, J = 9.0 Hz, 1H), 6.06 (m, 1H), 5.40 (dt, J = 17.4, 1.8 Hz, 1H), 5.29 (dd, J = 10.8, 1.5 Hz, 1H), 5.18 (t, J = 1.8 Hz, 1H), 5.10 (d, J = 5.1 Hz, 1H), 2.13 (s, 3H); ^{13}C NMR (75 MHz, CD_2Cl_2) δ 143.3, 131.1, 129.2, 127.7, 125.3, 117.3, 115.8, 113.5, 109.8, 102.6, 69.3, 22.8; IR (film) 3080, 2916, 1631, 1588, 1486, 1230, 1109, 1017, 930, 896 cm^{-1}; HRMS (CI) calcd for $C_{12}H_{14}ClO$ $[M + H]^+$ 209.0733, found 209.0739.

2h (85%, R^1 = 7-CH_3O, R^2 = H, R^3 = CH_3, R^4 = H) was prepared by the same procedure from 2-hydroxy-5-methoxybenzaldehyde and 3-chloro-2-methylpropene: ^{1}H NMR (300 MHz, CD_2Cl_2) δ 7.44 (d, J = 8.4 Hz, 1H), 7.02 (dd, J = 17.7, 11.1 Hz, 1H), 6.50 (dd, J = 8.7, 2.4 Hz, 1H), 6.46 (t, J = 2.4 Hz, 1H), 5.67 (dd, J = 17.7, 1.5 Hz, 1H), 5.16 (dd, J = 11.1, 1.8 Hz, 1H), 5.15 (s, 1H), 5.03 (s, 1H), 4.47 (s, 1H), 3.80 (s, 3H), 1.87 (s, 3H); ^{13}C NMR (75 MHz, CD_2Cl_2) δ 147.8, 129.8, 118.1, 116.0, 108.7, 108.4, 105.1, 102.2, 88.5, 80.2, 62.2, 19.3; IR (film) 2925, 1607, 1501, 1443, 1259, 1196, 1119, 1046, 901, 824 cm^{-1}; HRMS (EI) calcd for $C_{13}H_{16}O_2$ $[M]^+$ 204.1150, found 204.1152.

2i (90%, R^1 = 7-$OCH_2CH{=}CH_2$, $R^2 = R^3 = R^4$ = H) was prepared by the same procedure from 2,5-dihydroxybenzaldehyde using 4 equiv of allyl bromide and potassium carbonate: ^{1}H NMR (300 MHz, CD_2Cl_2) δ 7.43 (d, J = 8.1 Hz, 1H), 7.05 (dd, J = 18.0, 11.4 Hz, 1H), 6.50 (dd, J = 11.7, 2.4 Hz, 1H), 6.51 (d, J = 2.4 Hz, 1H), 6.09 (m, 2H), 5.68 (dd, J = 17.7, 1.5 Hz, 1H), 5.50 (m, 1H), 5.43 (m, 1H), 5.35 (m, 1H), 5.31 (m, 1H), 5.20 (dd, J = 11.1, 1.5 Hz, 1H), 4.55 (m, 4H); ^{13}C NMR (75 MHz, CD_2Cl_2) δ 159.2, 156.6, 132.9, 131.0, 126.9, 120.1, 117.5, 117.1, 112.0, 105.8, 100.2, 68.9, 68.7; IR (film) 3070, 2858, 1607, 1501, 1419, 1259, 1182, 993, 925 cm^{-1}; HRMS (CI) calcd for $C_{14}H_{17}O_2$ $[M + H]^+$ 217.1229, found 217.1225.

2j (83%, R^1 = 7-$(CH)_4$-8, $R^2 = R^3 = R^4$ = H) was prepared from 2-hydroxy-1-naphthylaldehyde: ^{1}H NMR (300 MHz, CD_2Cl_2) δ 8.19 (dd, J = 7.8, 0.9 Hz, 1H), 7.87 (dd, J = 7.2, 1.8 Hz, 1H), 7.69 (dd, J = 26.4, 8.7 Hz, 2H), 7.54 (m, 2H), 7.32 (dd, J = 18.0, 11.1 Hz, 1H), 6.29 (m, 1H), 5.95 (d, J = 17.7, 1H), 5.60 (dt, J = 17.1, 1.5 Hz, 1H), 5.47 (d, J = 11.4 Hz, 1H), 5.38 (dt, J = 10.5, 1.2 Hz, 1H), 4.57 (dt, J = 5.4, 1.5 Hz, 2H); ^{13}C NMR (75 MHz, CD_2Cl_2) δ 152.2, 134.7, 134.0, 131.3, 128.6, 127.9, 126.4, 124.3, 123.2, 117.3, 114.9, 109.8, 102.6, 75.8; IR (film) 3051, 2858, 1626, 1564, 419, 1380, 1240, 1182, 1080. 983, 916 cm^{-1}; HRMS (CI) calcd for $C_{15}H_{15}O$ $[M + H]^+$ 211.1123, found 211.1111.

General Procedure for Preparation of Dienes (Method B). To a solution of 2-vinylphenol[11] (300 mg, 2.5 mmol), triphenylphosphine (787 mg, 3.0 mmol), and 3-buten-2-ol (216 mg, 3.0 mmol) in THF (15 mL) was added dropwise a solution of diethyl azodicarboxylate (523 mg, 3.0 mmol) in THF (5 mL) at 0 °C. After stirring for 5 h at room temperature, the reaction mixture was extracted with EtOAc (50 mL × 2), washed with brine solution (100 mL), and dried over $MgSO_4$. After removal of the solvent, the residue was purified by flash column chromatography on silica gel (EtOAc/hexanes = 1:15) to afford **2k** (357 mg, 82%) as a colorless liquid: ^{1}H NMR (300 MHz, CD_2Cl_2) δ 7.51 (dd, J = 7.5, 1.5 Hz, 1H), 7.20 (td, J = 7.8, 1.5 Hz, 1H), 7.12 (dd, J = 17.1, 11.1 Hz, 1H), 6.93 (t, J = 8.7 Hz, 1H), 6.91 (d, J = 6.6 Hz, 1H), 5.97 (m, 1H), 5.76 (dd, J = 18.0, 1.2 Hz, 1H), 5.29 (dt, J = 7.5, 0.9 Hz, 1H), 5.26 (t, J = 1.5 Hz, 1H), 5.18 (dt, J = 10.5, 0.9 Hz, 1H), 4.85 (qd, J = 6.3, 6.2 Hz, 1H), 1.47 (d, J = 6.3 Hz, 3H); ^{13}C NMR (75 MHz, CD_2Cl_2) δ 154.9, 139.1, 131.6, 128.3, 126.1, 120.5, 116.4, 115.0, 114.3, 113.5, 75.1, 20.8; IR (film) 3074, 2973, 1623, 1592, 1481, 1451, 1410, 1289, 1234, 1102, 996, 915, 747 cm^{-1}; HRMS (CI) calcd for $C_{12}H_{15}O$ $[M + H]^+$ 175.1123, found 175.1119.

2l (69%, R^1 = H, R^2 = 4-$(CH_3O)C_6H_4$, $R^3 = R^4$ = H) was prepared by the same procedure from 2-vinylphenol and 1-(4-methoxyphenyl)-2-propen-1-ol: ^{1}H NMR (300 MHz, CD_2Cl_2) δ 7.54 (dd, J = 7.5, 1.8 Hz, 1H), 7.38 (d, J = 6.6 Hz, 2H), 7.21 (dd, J = 12.0, 6.6 Hz, 1H), 7.17 (dd, J = 9.0, 1.8 Hz, 1H), 6.95 (m, 4H), 6.16 (m, 1H), 5.83 (dt, J = 16.5, 1.2 Hz, 1H), 5.70 (d, J = 6.0 Hz, 1H), 5.39 (dt, J = 17.1, 5.4 Hz, 1H), 5.30 (m, 3H), 3.82 (s, 3H); ^{13}C NMR (75 MHz, CD_2Cl_2) δ 159.4, 154.3, 138.3, 131.8, 128.6, 127.8, 126.4, 121.0, 115.9, 114.0, 107.4, 102.6, 80.8, 55.3; HRMS (CI) calcd for $C_{18}H_{19}O_2$ $[M + H]^+$ 267.1385, found 267.1383.

General Procedure of Ring-Closing Metathesis of Dienes 2a−2l. To a solution of diene **2a** (160 mg, 1.0 mmol) in CH_2Cl_2 (5 mL) was added Ru−benzylidene complex **1** (16.5 mg, 0.02 mmol, 2 mol %), and the reaction mixture was stirred at room temperature for 2 h. After removal of the solvent, the residue was purified by silica gel column chromatography (EtOAc/hexanes = 1:25) to give the cyclized product 2*H*-1-benzopyran **3a** (126 mg, 95% yield) as a colorless liquid.

3c (R^1 = 7-Et_2N, $R^2 = R^3 = R^4$ = H) was prepared by the same procedure from the diene **2c**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.87 (d, J = 8.4 Hz, 1H), 6.40 (d, J = 9.6 Hz, 1H), 6.24 (dd, J = 8.4, 2.4 Hz, 1H), 6.19 (s, 1H), 5.54 (dt, J = 9.6, 3.6 Hz, 1H), 4.80 (dd, J = 3.3, 1.5 Hz, 2H), 3.36 (q, J = 7.2 Hz, 4H), 1.19 (t, J = 7.2 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.6, 148.9, 127.5, 124.7, 116.3, 104.6, 102.6, 98.8, 65.8, 44.6, 12.8; IR (film) 2965, 2872, 1617, 1561, 1463, 1350, 1267, 1206, 1123, 825, 788 cm^{-1}; HRMS (CI) calcd for $C_{13}H_{18}NO$ $[M + H]^+$ 204.1388, found 204.1395.

3g (R^1 = 7-CH_3O, R^2 = H, R^3 = CH_3, R^4 = H): ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.85 (d, J = 7.8 Hz, 1H), 6.41 (m, 1H), 6.40 (dd, J = 9.0, 2.7 Hz, 1H), 6.13 (d, J = 1.2 Hz, 1H), 4.68 (s, 2H), 3.78 (s, 3H), 1.79 (d, J = 1.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.9, 153.8, 128.0, 126.3, 118.9, 116.2, 106.7, 101.5, 69.3, 55.4, 18.9; IR (film) 2923, 2830, 1617, 1576, 1504, 1442, 1272, 1190, 1159, 1030, 845 cm^{-1}; HRMS (EI) calcd for $C_{11}H_{12}O_2$ $[M]^+$ 176.0837, found 176.0839.

3i (R^1 = 7-$OCH_2CH{=}CH_2$, $R^2 = R^3 = R^4$ = H): ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.89 (d, J = 8.1 Hz, 1H), 6.46 (dd, J = 8.1, 2.4 Hz, 1H), 6.41 (s, 1H), 6.39 (d, J = 8.1 Hz, 1H), 6.07 (m, 1H), 5.64 (dd, J = 9.9, 3.3 Hz, 1H), 5.50 (dd, J = 17.4, 1.8 Hz, 1H), 5.31 (dd, J = 5.4, 1.5 Hz, 1H), 4.81 (dd, J = 3.3, 1.5 Hz, 1H), 4.52 (dt, J = 5.4, 1.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.6, 155.3, 133.2, 127.3, 124.3, 119.1, 117.8, 107.7, 102.6, 68.9, 65.7; IR (film) 2923, 2851, 1612, 1499, 1458, 1308, 1267, 1144, 1020, 932, 835 cm^{-1}; HRMS (EI) calcd for $C_{12}H_{12}O_2$ $[M]^+$ 188.0837, found 188.0837.

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Registry No. (registry numbers are provided by the authors). **2a**; 19244-42-9, **3a**; 254-04-6; **3b**; 18385-87-0, **3d**; 16336-26-8, **3e**; 18385-89-2, **3f**; 183907-31-0, **3h**; 16336-25-7, **3j**; 230-62-6, **3k**; 2513-24-8, **3l**; 41786-36-1.

Supporting Information Available: Photocopies of ^{1}H NMR spectra of compounds **2a−l**, **3c, 3g**, and **3i** (15 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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