

Efficient Synthesis of Biologically Interesting Natural Pyranochalcones from *Mallotus Philippensis* and Their Unnatural Derivatives[†]

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This paper describes efficient synthetic approaches for isolating biologically interesting natural pyranochalcones and their unnatural derivatives from *Mallotus Philippensis*. The key strategies involve ethylenediamine diacetate-catalyzed benzopyran formation reactions and base-catalyzed aldol reactions.

Key Words : Pyranochalcone, Mallotophilippens D and F, Red compound

Introduction

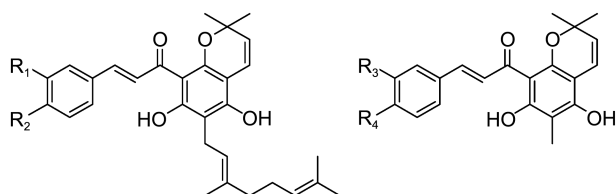
Mallotus philippensis is widely distributed throughout tropical Asia, Australia, and the Philippines.¹ Extracts from the fruits and bark of the plant have been shown to possess antioxidant,² antiulcer,² anti-tumor,³ cytotoxic,⁴ and anti-allergic⁵ activities. Kamara, a red powder consisting of the glandular hairs from this plant, has been used in traditional medicines as an anthelmintic and cathartic.⁶ From this plant, mallotophilippens C (**1**), D (**2**), F (**3**) and 8-cinnamoyl-5,7-dihydroxy-2,2,6-trimethylchromene (**4**), called the red compound, with chalcone moieties were isolated (Figure 1).^{1,7} Mallotophilippens C (**1**) and D (**2**) have been shown to potently inhibit the production of nitric oxide (NO) induced by interferon- γ (IFN- γ) and LPS activated RAW 264.7 cells.¹ They also strongly inhibited inducible nitric oxide synthesis (iNOS), cyclooxygenase-2 (COX-2), interleukin-6 (IL-6), and interleukin-1 β (IL-1 β) mRNA expression.¹ These effects are expected to be used as lead compounds for the development of new drugs to treat rheumatoid arthritis, which involves excessive NO production. Mallotophilippens F (**3**) and red compound (**4**) have shown to possess anti-tuberculosis activity against the H37Rv strain of *Mycobacterium tuber-*

culosis at 16 $\mu\text{g/mL}$ and 64 $\mu\text{g/mL}$, respectively.⁷

Recently, we have reported the concise total synthesis of mallotophilippens C (**1**) starting from commercially available 2,4,6-trihydroxyacetophenone (**12**).⁸ However, the synthesis of mallotophilippens D (**2**) and F (**3**), red compound (**4**), and their unnatural derivatives **5-11** has not been reported. As an expansion and ongoing study of our previous work, we report herein an efficient synthesis of mallotophilippens D (**2**) and F (**3**), red compound (**4**), and their unnatural derivatives **5-11**.

Results and Discussion

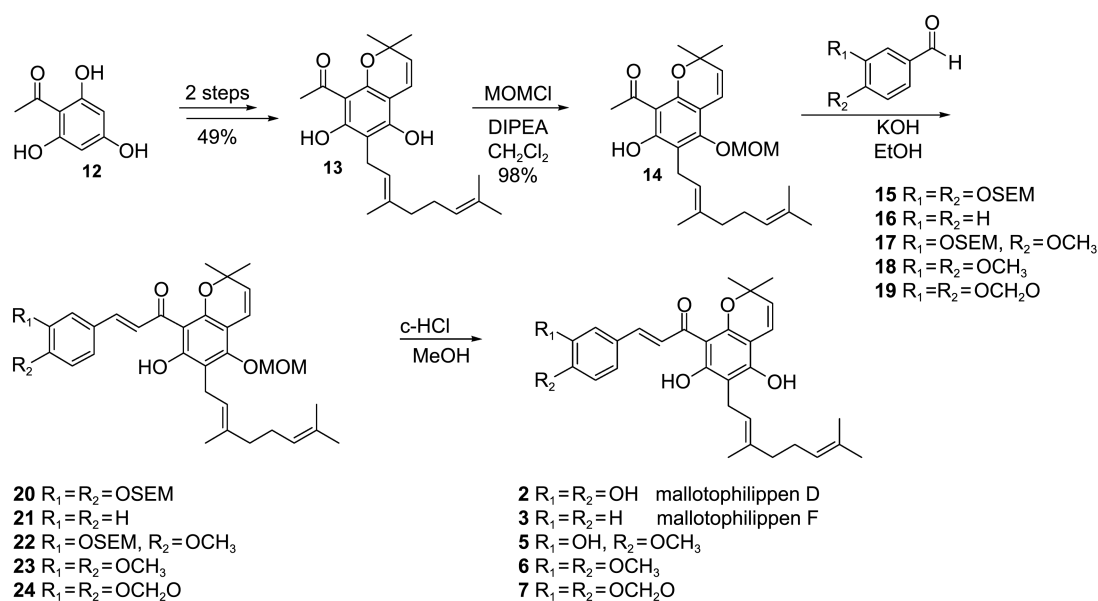
The synthesis of mallotophilippens D (**2**), F (**3**), and their derivatives **5-7** was carried out as shown in Scheme 1. The compound **13** was synthesized starting from 2,4,6-trihydroxyacetophenone (**12**) in 2 steps according to the procedure reported by our group.⁸ Treatment of **13** with 1.1 equiv. of methoxymethyl chloride (MOMCl) in the presence of *N,N*-diisopropylethylamine gave product **14** in 98% yield. The selective methoxymethylation of compound **13** was confirmed by analysis of the ¹H NMR spectrum. The signal for the proton of one hydroxyl group in the benzopyran ring of compound **14** was observed as a singlet associated with a hydrogen bond to a carbonyl group at $\delta = 13.72$ ppm, and a methoxy signal of MOM ether was observed as a singlet at $\delta = 3.51$ ppm. To give chalcone moieties, aldol reactions were attempted. Condensation of compound **14** with aryl aldehyde **15** protected with two SEM groups in an ethanolic KOH solution at room temperature for 48 h afforded **20** in 77% yield, whereas that with benzaldehyde (**16**) at room temperature for 48 h provided **21** in 85% yield. Similarly, reactions with aryl aldehydes **17-19** gave **22-24** in 81, 90, and 79% yield, respectively. Deprotection of **20** and **21** by treatment with concentrated HCl (10 drops) in methanol at room temperature for 5 h gave the expected natural products, mallotophilippens D (**2**) and F (**3**), in 65 and 71% yield, respectively. The spectral data for the synthetic materials **2** and **3** were in agreement with those reported in the literature.^{1,7} Similarly, treatment of **22-24** with concentrated HCl (10 drops) in methanol at room temperature for 5 h gave the unnatural products **5-7** in 61, 76 and 58% yield, respectively.



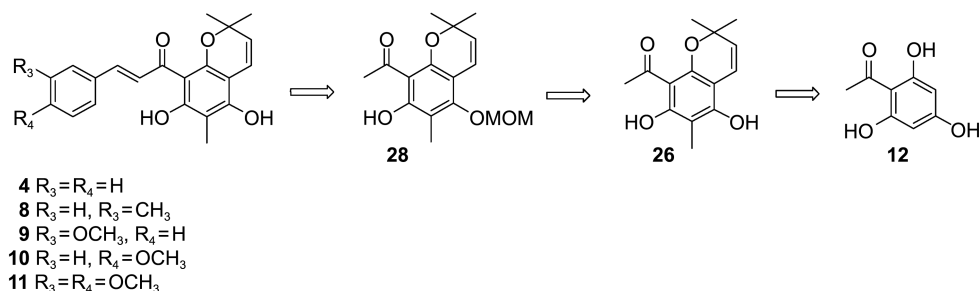
- | | |
|---|--|
| 1 R ₁ =H, R ₂ =OH mallotophilippens C | 4 R ₃ =R ₄ =H red compound |
| 2 R ₁ =R ₂ =OH mallotophilippens D | 8 R ₃ =H, R ₄ =CH ₃ |
| 3 R ₁ =R ₂ =H mallotophilippens F | 9 R ₃ =OCH ₃ , R ₄ =H |
| 5 R ₁ =OH, R ₂ =OCH ₃ | 10 R ₃ =H, R ₄ =OCH ₃ |
| 6 R ₁ =R ₂ =OCH ₃ | 11 R ₃ =R ₄ =OCH ₃ |
| 7 R ₁ +R ₂ =OCH ₂ O | |

Figure 1. Natural pyranochalcones **1-4** isolated from *Mallotus philippensis* and their unnatural derivatives **5-11**.

[†]This paper is dedicated to Professor Eun Lee on the occasion of his honourable retirement.



Scheme 1



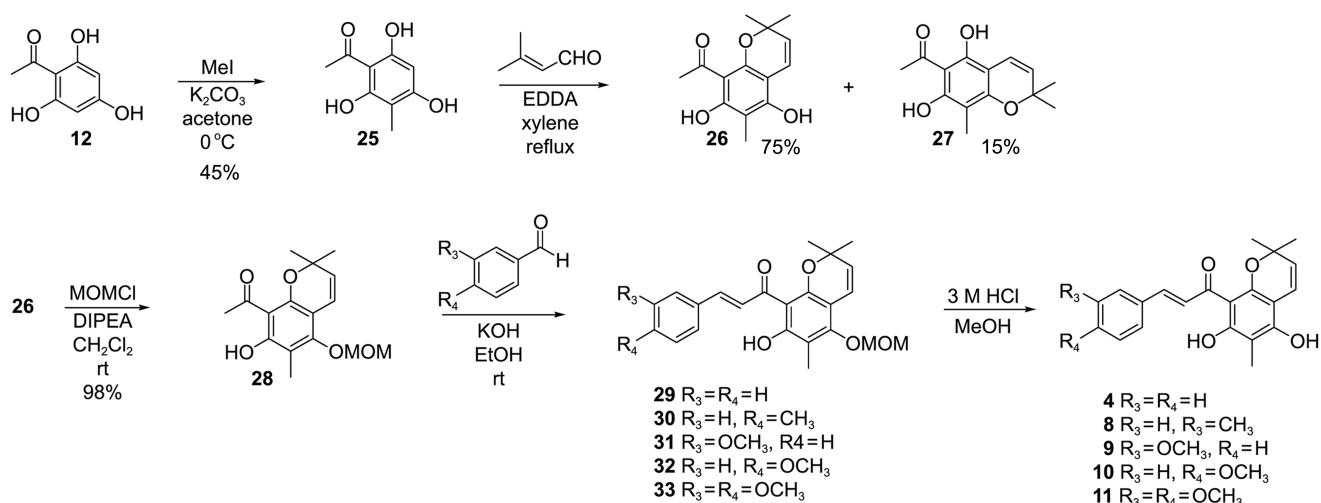
Scheme 2

Scheme 2 shows retrosynthetic approaches for synthesizing the natural red compound (**4**) and its unnatural derivatives **8-11**. Red compound (**4**) and its derivatives **8-11** could be prepared by base-catalyzed aldol reactions of **28** to the corresponding aryl aldehydes. The key intermediate **28** could be also generated from **26** through selective MOM ether protection. The benzopyran **26** could be derived from commercially available 2,4,6-trihydroxyacetophenone (**12**) by *C*-methylation followed by benzopyran formation reaction.

The total synthesis of red compound (**4**) and its derivatives **8-11** were attempted starting from 2,4,6-trihydroxyacetophenone (**12**) as shown in Scheme 3. Previous studies reported that *C*-prenylation can be achieved with prenyl bromide in the presence of either potassium hydroxide⁹ or potassium carbonate.¹⁰ Under these conditions, the desired product **25** was obtained in 45% yield. Treatment of **25** with 3-methyl-2-butenal in the presence of 20 mol % of ethylenediamine diacetate in refluxing xylene for 4 h provided the products **26** and **27** in 75 and 15% yield, respectively. In this reaction, the regioselectivity of the cyclization may result from the presence of a bulky methyl group on the benzene ring of **25**. This similar regioselectivity was observed by Li's group in

the case of cyclization of a polyhydroxychalcone to give flavones.¹¹ These two compounds were readily separated by column chromatography and assigned by spectral analysis. Protection of compound **26** with 1.1 equiv. of MOMCl provided **28** in 98% yield. Condensation of **28** with benzaldehyde in ethanolic KOH solution at room temperature for 48 h gave **29** in 85% yield. Similarly, reaction of **28** with the corresponding aryl aldehydes provided chalcones **30-33** in 95, 87, 90, and 98% yield, respectively. Deprotection of **29** with 3 M HCl in refluxing methanol for 0.5 h afforded **4** in 95% yield. The spectroscopic data for synthetic material **4** were in agreement with that reported in the literature.⁷ Similarly, treatment of **30-33** with 3 M HCl gave chalcones **8-11** in 95, 90, 88, and 97% yield, respectively.

In conclusion, we have described a concise synthetic route for producing biologically interesting natural products, mallotophilippen D and F, and red compound with a pyranochalcone moiety starting from 2,4,6-trihydroxyacetophenone. The key strategies involve benzopyran formation by ethylenediamine diacetate-catalyzed reactions and base-catalyzed aldol reactions.



Scheme 3

Experimental Section

All the experiments were carried out in 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 ¹H NMR and ¹³C NMR spectra were recorded on a Bruker Model ARX (300 and 75 MHz, respectively) spectrometer in CDCl₃ using δ = 77.0 ppm as the solvent. The IR spectra were recorded on a Jasco FTIR 5300 spectrophotometer. The HRMS were carried out at the Korea Basic Science Institute.

Compound 14. Methoxymethyl chloride (0.121 g, 1.50 mmol) was added to a solution of **13** (0.505 g, 1.36 mmol) and diisopropylethylamine (0.879 g, 6.80 mmol) in dry CH₂Cl₂ (10 mL). The reaction mixture was stirred at room temperature for 10 h and then water (20 mL) was added. The reaction mixture was extracted with CH₂Cl₂ (3 × 30 mL). The combined organic extracts were washed with saturated NH₄Cl solution (20 mL) and evaporated in vacuo. Flash chromatography on silica gel using hexane/EtOAc (20:1) afforded **14** (0.552 g, 98%) as an oil; ¹H NMR (300 MHz, CDCl₃) δ 13.72 (s, 1H), 6.48 (d, *J* = 9.9 Hz, 1H), 5.44 (d, *J* = 9.9 Hz, 1H), 5.18 (t, *J* = 7.0 Hz, 1H), 5.02 (t, *J* = 6.8 Hz, 1H), 4.96 (s, 2H), 3.51 (s, 3H), 3.27 (d, *J* = 6.2 Hz, 2H), 2.65 (s, 3H), 2.01-1.95 (m, 4H), 1.73 (s, 3H), 1.69 (s, 3H), 1.53 (s, 3H), 1.45 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 204.6, 163.8, 158.5, 155.2, 135.6, 131.7, 126.2, 124.8, 123.1, 118.3, 115.5, 108.8, 107.1, 100.5, 58.3, 40.1, 34.0, 28.1, 27.0, 26.1, 22.9, 18.1, 16.6; IR (neat) 2930, 1616, 1424, 1364, 1287, 1161, 1134, 1049 cm⁻¹; EIMS *m/z* (%) 414 (M⁺, 66), 399 (22), 370 (17), 369 (58), 367 (11), 313 (10), 291 (17), 285 (25), 271 (26), 259 (12), 247 (54), 246 (15), 245 (12), 232 (15), 231 (100), 217 (14), 213 (13), 69 (14); HRMS *m/z* (M⁺) calcd for C₂₅H₃₄O₅: 414.2406. Found: 414.2408.

Compound 20. To a solution of **14** (0.150 g, 0.36 mmol) in ethanol (4 mL) was added KOH (0.102 g, 1.81 mmol) and aldehyde **15** (0.173 g, 0.43 mmol). The reaction mixture was

stirred at room temperature for 48 h. Evaporation of ethanol, addition of water (10 mL) and 1 N HCl (2 mL), extraction with EtOAc (3 × 15 mL), washing with brine (15 mL), and removal of the solvent followed by flash column chromatography on silica gel using hexane/EtOAc (20:1) gave **20** (0.220 g, 77%) as a yellow oil; ¹H NMR (300 MHz, CDCl₃) δ 7.99 (d, *J* = 15.6 Hz, 1H), 7.78 (d, *J* = 15.6 Hz, 1H), 7.52 (s, 1H), 7.28-7.24 (m, 2H), 6.57 (d, *J* = 9.9 Hz, 1H), 5.52 (d, *J* = 9.9 Hz, 1H), 5.35 (s, 2H), 5.34 (s, 2H), 5.25 (t, *J* = 7.0 Hz, 1H), 5.09 (t, *J* = 6.8 Hz, 1H), 5.03 (s, 2H), 3.85-3.80 (m, 4H), 3.61 (s, 3H), 3.36 (d, *J* = 7.0 Hz, 2H), 2.08-2.02 (m, 4H), 1.79 (s, 3H), 1.66 (s, 3H), 1.60 (s, 3H), 1.58 (s, 6H), 1.02-0.96 (m, 4H), 0.01 (s, 18H); ¹³C NMR (75 MHz, CDCl₃) δ 193.6, 164.1, 158.0, 154.1, 149.4, 147.6, 142.8, 135.1, 131.2, 129.7, 125.8, 125.7, 124.4, 123.7, 122.8, 118.1, 115.9, 115.4, 115.2, 108.9, 106.9, 100.1, 93.7, 93.6, 77.5, 66.6, 66.5, 57.9, 39.7, 27.9, 26.7, 25.7, 22.6, 18.1, 18.0, 17.7, 16.2, -1.4; IR (neat) 2955, 1589, 1507, 1256, 1084, 988, 837, 694 cm⁻¹; HRMS *m/z* (M⁺) calcd for C₄₄H₆₆O₉Si₂: 794.4245. Found: 794.4250.

Compound 21. To a solution of **14** (0.300 g, 0.72 mmol) in ethanol (8 mL) was added KOH (0.203 g, 3.62 mmol) and aldehyde **16** (0.084 g, 0.80 mmol). The reaction mixture was stirred at room temperature for 48 h. Evaporation of ethanol, addition of water (10 mL) and 1N HCl (4 mL), extraction with EtOAc (3 × 50 mL), washing with brine (30 mL), and removal of the solvent followed by flash column chromatography on silica gel using hexane/EtOAc (20:1) gave **21** (0.308 g, 85%) as a yellow oil; ¹H NMR (300 MHz, CDCl₃) δ 13.86 (s, OH), 8.06 (d, *J* = 15.6 Hz, 1H), 7.77 (d, *J* = 15.6 Hz, 1H), 7.61-7.58 (m, 2H), 7.41-7.38 (m, 3H), 6.54 (d, *J* = 9.9 Hz, 1H), 5.51 (d, *J* = 9.9 Hz, 1H), 5.22 (t, *J* = 6.6 Hz, 1H), 5.05 (t, *J* = 6.9 Hz, 1H), 5.00 (s, 2H), 3.57 (s, 3H), 3.32 (d, *J* = 6.6 Hz, 2H), 2.09-2.02 (m, 2H), 2.00-1.97 (m, 2H), 1.76 (s, 3H), 1.63 (s, 3H), 1.56 (s, 3H), 1.53 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 193.8, 164.0, 158.1, 154.2, 142.4, 135.4, 135.2, 131.3, 130.2, 129.0, 128.3, 127.5, 125.8, 124.3, 122.7, 118.0, 115.4, 108.9, 107.0, 100.1, 77.5, 57.9,

39.6, 27.8, 26.6, 25.7, 22.6, 17.7, 16.2; IR (neat) 2970, 2921, 1634, 1589, 1554, 1449, 1339, 1284, 1218, 1146, 1086, 1044, 978, 938, 880, 769, 725, 691 cm^{-1} ; HRMS m/z (M^+) calcd for $C_{32}H_{38}O_5$: 502.2719 Found: 502.2722.

Compound 22. To a solution of **14** (0.150 g, 0.36 mmol) in ethanol (4 mL) was added KOH (0.102 g, 1.81 mmol) and aldehyde **17** (0.123 g, 0.43 mmol). The reaction mixture was stirred at room temperature for 48 h. Evaporation of ethanol, addition of water (10 mL) and 1N HCl (2 mL), extraction with EtOAc (3×15 mL), washing with brine (15 mL), and removal of the solvent followed by flash column chromatography on silica gel using hexane/EtOAc (20:1) gave **22** (0.200 g, 81%) as a yellow oil; ^1H NMR (300 MHz, CDCl_3) δ 7.94 (d, $J = 15.6$ Hz, 1H), 7.74 (d, $J = 15.6$ Hz, 1H), 7.49 (s, 1H), 7.22 (d, $J = 8.4$ Hz, 1H), 6.90 (d, $J = 8.4$ Hz, 1H), 6.54 (d, $J = 9.9$ Hz, 1H), 5.49 (d, $J = 9.9$ Hz, 1H), 5.30 (s, 2H), 5.21 (t, $J = 6.6$ Hz, 1H), 5.04 (t, $J = 6.6$ Hz, 1H), 4.99 (s, 2H), 3.91 (s, 3H), 3.78 (t, $J = 8.1$ Hz, 2H), 3.56 (s, 3H), 3.31 (d, $J = 6.6$ Hz, 2H), 2.08-1.96 (m, 4H), 1.75 (s, 3H), 1.62 (s, 3H), 1.55 (s, 3H), 1.54 (s, 6H), 0.95 (d, $J = 8.1$ Hz, 2H), -0.03 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 193.6, 164.1, 157.9, 154.1, 151.7, 147.2, 142.9, 135.1, 131.2, 128.6, 125.8, 125.4, 124.4, 124.3, 122.8, 118.1, 115.4, 114.5, 111.5, 108.9, 106.9, 100.1, 93.8, 77.5, 66.5, 57.9, 56.0, 39.7, 27.9, 26.7, 25.6, 22.6, 18.1, 17.7, 16.2, -1.5; IR (neat) 2955, 1589, 1507, 1446, 1356, 1256, 1134, 1084, 837, 810 cm^{-1} .

Compound 23. To a solution of **14** (0.150 g, 0.36 mmol) in ethanol (4 mL) was added KOH (0.102 g, 1.81 mmol) and aldehyde **18** (0.072 g, 0.43 mmol). The reaction mixture was stirred at room temperature for 48 h. Evaporation of ethanol, addition of water (10 mL) and 1N HCl (2 mL), extraction with EtOAc (3×15 mL), washing with brine (15 mL), and removal of the solvent followed by flash column chromatography on silica gel using hexane/EtOAc (20:1) gave **23** (0.184 g, 90%) as a yellow oil; ^1H NMR (300 MHz, CDCl_3) δ 7.96 (d, $J = 15.6$ Hz, 1H), 7.75 (d, $J = 15.6$ Hz, 1H), 7.19-7.14 (m, 2H), 6.88 (d, $J = 8.1$ Hz, 1H), 6.55 (d, $J = 9.9$ Hz, 1H), 5.50 (d, $J = 9.9$ Hz, 1H), 5.21 (t, $J = 6.3$ Hz, 1H), 5.05 (t, $J = 6.6$ Hz, 1H), 4.99 (s, 2H), 3.91 (s, 6H), 3.56 (s, 3H), 3.32 (d, $J = 6.3$ Hz, 2H), 2.04-1.97 (m, 4H), 1.75 (s, 3H), 1.62 (s, 3H), 1.55 (s, 3H), 1.53 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 193.4, 164.1, 157.9, 154.0, 151.1, 149.2, 142.8, 135.2, 131.2, 128.4, 125.6, 125.3, 124.3, 123.3, 122.7, 118.2, 115.5, 111.1, 109.4, 108.9, 106.9, 100.1, 77.3, 57.9, 56.0, 55.7, 39.6, 27.8, 26.6, 25.6, 22.6, 17.7, 16.2; IR (neat) 3463, 2967, 1620, 1588, 1537, 1507, 1443, 1419, 1325, 1302, 1262, 1138, 1039, 1020, 954, 844, 801 cm^{-1} ; HRMS m/z (M^+) calcd for $C_{34}H_{42}O_7$: 562.2931. Found: 562.2934.

Compound 24. To a solution of **14** (0.150 g, 0.36 mmol) in ethanol (4 mL) was added KOH (0.102 g, 1.81 mmol) and aldehyde **19** (0.065 g, 0.43 mmol). The reaction mixture was stirred at room temperature for 48 h. Evaporation of ethanol, addition of water (10 mL) and 1N HCl (2 mL), extraction with EtOAc (3×15 mL), washing with brine (15 mL), and removal of the solvent followed by flash column chromatography on silica gel using hexane/EtOAc (20:1) gave **24** (0.156 g, 79%) as a yellow oil; ^1H NMR (300 MHz, CDCl_3)

δ 7.90 (d, $J = 15.6$ Hz, 1H), 7.70 (d, $J = 15.6$ Hz, 1H), 7.12-7.04 (m, 2H), 6.82 (d, $J = 8.1$ Hz, 1H), 6.53 (d, $J = 9.9$ Hz, 1H), 6.00 (s, 2H), 5.50 (d, $J = 9.9$ Hz, 1H), 5.21 (t, $J = 6.9$ Hz, 1H), 5.04 - 4.99 (m, 3H), 3.57 (s, 3H), 3.31 (d, $J = 6.9$ Hz, 2H), 2.10 - 1.92 (m, 4H), 1.75 (s, 3H), 1.62 (s, 3H), 1.55 (s, 3H), 1.52 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 193.5, 164.1, 158.0, 154.1, 149.7, 148.4, 142.6, 135.2, 131.3, 130.0, 125.8, 125.6, 125.1, 124.4, 122.8, 118.1, 115.4, 108.7, 107.0, 106.4, 101.6, 100.2, 77.5, 57.9, 39.7, 27.9, 26.7, 25.7, 22.6, 17.7, 16.3; IR (neat) 2926, 1589, 1549, 1491, 1449, 1331, 1256, 1150, 1042, 932 cm^{-1} ; HRMS m/z (M^+) calcd for $C_{33}H_{38}O_7$: 546.2618. Found: 546.2617.

Mallotophilippen D (2). To a solution of **20** (0.150 g, 0.19 mmol) in ethanol (8 mL) was added concentrated HCl (5 drops) and the reaction mixture was stirred at room temperature for 1 h. The reaction mixture was diluted with saturated NaHCO_3 solution (30 mL) and extracted with EtOAc (3×30 mL). Removal of solvent and purification by column chromatography on silica gel using hexane/EtOAc (10:1) gave **2** (0.060 g, 65%) as a yellow oil; ^1H NMR (300 MHz, CDCl_3) δ 8.20 (d, $J = 15.6$ Hz, 1H), 7.97 (d, $J = 15.6$ Hz, 1H), 7.02 (d, $J = 8.1$ Hz, 1H), 6.98 (s, OH), 6.95 (s, OH), 6.82 (d, $J = 9.9$ Hz, 1H), 6.64 (s, OH), 6.61 (d, $J = 8.1$ Hz, 1H), 6.41 (s, 1H), 5.26 (t, $J = 7.2$ Hz, 1H), 5.16 (d, $J = 9.9$ Hz, 1H), 5.06 (t, $J = 6.8$ Hz, 1H), 3.52 (d, $J = 7.2$ Hz, 2H), 2.04-1.89 (m, 4H), 1.69 (s, 3H), 1.55 (s, 3H), 1.50 (s, 3H), 1.31 (s, 6H); ^{13}C NMR (75 MHz, benzene- d_6) δ 193.7, 164.8, 158.2, 155.3, 146.8, 144.6, 143.0, 139.9, 132.0, 129.4, 126.2, 124.9, 124.2, 122.6, 122.4, 117.3, 115.9, 115.3, 105.0, 106.3, 102.9, 77.8, 39.9, 27.8, 26.5, 25.8, 22.1, 17.7, 15.9; IR (neat) 3410, 2975, 1599, 1537, 1452, 1350, 1282, 1166, 806, 780 cm^{-1} .

Mallotophilippen F (3). To a solution of **21** (0.100 g, 0.20 mmol) in ethanol (8 mL) was added concentrated HCl (5 drops) and the reaction mixture was stirred at room temperature for 1 h. The reaction mixture was diluted with saturated NaHCO_3 solution (30 mL) and extracted with EtOAc (3×30 mL). Removal of solvent and purification by column chromatography on silica gel using hexane/EtOAc (10:1) gave **3** (0.065 g, 71%) as an orange solid: mp 120-122 $^\circ\text{C}$; ^1H NMR (300 MHz, CDCl_3) δ 8.11 (d, $J = 15.6$ Hz, 1H), 7.75 (d, $J = 15.6$ Hz, 1H), 7.61-7.58 (m, 2H), 7.42-7.37 (m, 3H), 6.56 (d, $J = 9.9$ Hz, 1H), 6.45 (s, OH), 5.46 (d, $J = 9.9$ Hz, 1H), 5.29 (t, $J = 7.2$ Hz, 1H), 5.03 (t, $J = 6.6$ Hz, 1H), 3.42 (d, $J = 7.2$ Hz, 2H), 2.14-2.06 (m, 4H), 1.81 (s, 3H), 1.68 (s, 3H), 1.59 (s, 3H), 1.53 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 193.0, 163.8, 157.9, 154.7, 141.9, 140.5, 135.6, 132.4, 130.0, 129.0, 128.2, 127.7, 124.9, 123.5, 121.7, 116.7, 106.1, 105.4, 102.3, 77.8, 39.7, 27.9, 26.1, 25.7, 21.6, 17.7, 16.1; IR (KBr) 3450, 2975, 1605, 1537, 1452, 1350, 1263, 1166 cm^{-1} ; HRMS m/z (M^+) calcd for $C_{30}H_{34}O_4$: 458.2457. Found: 458.2455.

Compound 5. To a solution of **22** (0.150 g, 0.30 mmol) in ethanol (8 mL) was added concentrated HCl (5 drops) and the reaction mixture was stirred at room temperature for 1 h. The reaction mixture was diluted with saturated NaHCO_3 solution (30 mL) and extracted with EtOAc (3×30 mL).

Removal of solvent and purification by column chromatography on silica gel using hexane/EtOAc (10:1) gave **5** (0.068 g, 61%) as a yellow oil; ^1H NMR (300 MHz, benzene- d_6) δ 8.28 (d, $J = 15.6$ Hz, 1H), 8.05 (d, $J = 15.6$ Hz, 1H), 7.44 (d, $J = 2.1$ Hz, 1H), 6.86 (dd, $J = 8.1, 2.1$ Hz, 1H), 6.81 (d, $J = 9.9$ Hz, 1H), 6.38 (brs, OH), 6.26 (d, $J = 8.1$ Hz, 1H), 5.45 (brs, OH), 5.26 (t, $J = 7.2$ Hz, 1H), 5.13 (d, $J = 9.9$ Hz, 1H), 5.06 (t, $J = 6.9$ Hz, 1H), 3.52 (d, $J = 7.2$ Hz, 2H), 3.04 (s, 3H), 2.03-1.91 (m, 4H), 1.68 (s, 3H), 1.54 (s, 3H), 1.49 (s, 3H), 1.33 (s, 6H); ^{13}C NMR (75 MHz, benzene- d_6) δ 193.4, 165.0, 158.0, 155.2, 148.7, 146.7, 142.7, 139.6, 131.9, 130.0, 126.6, 124.8, 124.2, 123.0, 122.5, 117.3, 112.9, 110.7, 106.9, 106.2, 102.7, 77.7, 55.2, 39.8, 27.8, 26.5, 25.8, 22.1, 17.7, 15.9; IR (neat) 3424, 2963, 1611, 1517, 1445, 1358, 1268, 1133, 866, 804 cm^{-1} .

Compound 6. To a solution of **23** (0.150 g, 0.30 mmol) in ethanol (8 mL) was added concentrated HCl (5 drops) and the reaction mixture was stirred at room temperature for 1 h. The reaction mixture was diluted with saturated NaHCO_3 solution (30 mL) and extracted with EtOAc (3 \times 30 mL). Removal of solvent and purification by column chromatography on silica gel using hexane/EtOAc (10:1) gave **6** (0.105 g, 76%) as a yellow oil; ^1H NMR (300 MHz, benzene- d_6) δ 14.49 (s, OH), 8.00 (d, $J = 15.6$ Hz, 1H), 7.73 (d, $J = 15.6$ Hz, 1H), 7.18-7.14 (m, 2H), 6.88 (d, $J = 7.8$ Hz, 1H), 6.58 (d, $J = 9.9$ Hz, 1H), 6.32 (s, OH), 5.43 (d, $J = 9.9$ Hz, 1H), 5.29 (t, $J = 6.9$ Hz, 1H), 5.04 (t, $J = 6.6$ Hz, 1H), 3.90 (s, 6H), 3.41 (d, $J = 6.9$ Hz, 2H), 2.18-2.05 (m, 4H), 1.81 (s, 3H), 1.67 (s, 3H), 1.59 (s, 3H), 1.53 (s, 6H); ^{13}C NMR (75 MHz, benzene- d_6) δ 192.9, 164.0, 157.6, 154.6, 151.3, 149.5, 142.2, 140.1, 132.2, 128.9, 125.8, 124.6, 123.7, 123.0, 121.8, 117.0, 111.5, 110.2, 106.3, 105.7, 102.3, 77.7, 56.0, 55.9, 39.7, 28.0, 26.3, 25.6, 21.7, 17.6, 16.2; IR (neat) 3404, 2962, 1612, 1518, 1447, 1336, 1263, 1143, 1029, 803, 728 cm^{-1} .

Compound 7. To a solution of **24** (0.150 g, 0.27 mmol) in ethanol (8 mL) was added concentrated HCl (5 drops) and the reaction mixture was stirred at room temperature for 1 h. The reaction mixture was diluted with saturated NaHCO_3 solution (30 mL) and extracted with EtOAc (3 \times 30 mL). Removal of solvent and purification by column chromatography on silica gel using hexane/EtOAc (10:1) gave **7** (0.080 g, 58%) as a yellow oil; ^1H NMR (300 MHz, benzene- d_6) δ 8.16 (d, $J = 15.6$ Hz, 1H), 7.95 (d, $J = 15.6$ Hz, 1H), 7.08 (s, H), 6.82 (d, $J = 9.9$ Hz, 1H), 6.75 (d, $J = 8.1$ Hz, 1H), 6.48 (d, $J = 8.1$ Hz, 1H), 6.38 (s, OH), 5.28 (t, $J = 7.2$ Hz, 1H), 5.20 (s, 2H), 5.14 (d, $J = 9.9$ Hz, 1H), 5.08 (t, $J = 6.6$ Hz, 1H), 3.52 (d, $J = 7.2$ Hz, 2H), 2.03-1.90 (m, 4H), 1.68 (s, 3H), 1.54 (s, 3H), 1.49 (s, 3H), 1.28 (s, 6H); ^{13}C NMR (75 MHz, benzene- d_6) δ 193.2, 164.9, 157.8, 154.9, 149.7, 148.8, 142.3, 139.5, 131.8, 130.8, 126.3, 125.2, 124.7, 124.2, 122.4, 117.2, 108.6, 106.7, 106.3, 102.7, 101.3, 77.6, 39.8, 27.7, 26.4, 25.8, 22.0, 17.7, 15.9; IR (neat) 3450, 2975, 1605, 1537, 1487, 1452, 1350, 1263, 1166, 1042, 930 cm^{-1} ; HRMS m/z (M^+) calcd for $\text{C}_{31}\text{H}_{34}\text{O}_6$: 502.2355. Found: 502.2357.

Compound 25. A mixture of **12** (1.862 g, 10.0 mmol), Methyl iodide (5.678 g, 40.0 mmol), and K_2CO_3 (3.455 g,

25.0 mmol) in dry acetone (80 mL) was stirred for 9 h at 0 $^\circ\text{C}$. Evaporation of acetone, addition of 3 N HCl solution (18 mL), and extraction with EtOAc (3 \times 50 mL), washing with brine (50 mL), and removal of the solvent followed by flash column chromatography on silica gel using hexane/isopropanol (50:1) gave **25** (0.820 g, 45%) as a white solid: mp 208-210 $^\circ\text{C}$; ^1H NMR (300 MHz, CDCl_3) δ 9.03 (br s, OH), 8.26 (s, OH), 5.79 (s, 1H), 2.44 (s, 3H), 1.80 (s, 3H); IR (KBr) 3349, 3011, 2934, 1628, 1449, 1372, 1295, 1109, 808, 594 cm^{-1} .

Compound 26 and 27. To a solution of **25** (0.500 g, 2.74 mmol) and 3-methyl-2-butenal (0.277 g, 3.29 mmol) in xylene (10 mL) was added ethylenediamine diacetate (0.099 g, 0.55 mmol). The reaction mixture was refluxed for 4 h. Evaporation of solvent and purification by column chromatography on silica gel using hexane/EtOAc (20:1) gave **26** (0.510 g, 75%) and **27** (0.100 g, 15%). **26**: a yellow solid: mp 130-132 $^\circ\text{C}$; ^1H NMR (300 MHz, CDCl_3) δ 6.54 (d, $J = 9.9$ Hz, 1H), 5.64 (s, OH), 5.43 (d, $J = 9.9$ Hz, 1H), 2.65 (s, 3H), 2.02 (s, 3H), 1.46 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 203.6, 163.3, 155.9, 154.9, 125.1, 116.4, 105.9, 102.1, 101.4, 77.7, 33.2, 27.7, 7.0; IR (KBr) 3280, 2972, 2931, 2727, 2550, 1599, 1430, 1374, 1307, 1235, 1123, 973, 826, 734, 675, 616, 555 cm^{-1} ; HRMS m/z (M^+) calcd for $\text{C}_{14}\text{H}_{16}\text{O}_4$: 248.1049. Found: 248.1051. **27**: a yellow oil; ^1H NMR (300 MHz, CDCl_3) δ 12.03 (brs, OH), 8.58 (s, OH), 6.58 (d, $J = 9.9$ Hz, 1H), 5.46 (d, $J = 9.9$ Hz, 1H), 2.66 (s, 3H), 2.00 (s, 3H), 1.40 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 203.6, 163.3, 158.7, 157.7, 125.7, 115.8, 104.7, 102.1, 101.5, 77.7, 33.0, 28.2, 6.9; IR (neat) 3395, 2972, 2931, 2736, 1611, 1434, 1374, 1286, 1184, 1126, 881, 741, 620 cm^{-1} ; HRMS m/z (M^+) calcd for $\text{C}_{14}\text{H}_{16}\text{O}_4$: 248.1049. Found: 248.1051.

Compound 28. Methoxymethyl chloride (0.130 g, 1.61 mmol) was added to a solution of **26** (0.400 g, 1.61 mmol) and diisopropylethylamine (0.815 g, 8.06 mmol) in dry CH_2Cl_2 (20 mL). The reaction mixture was stirred at room temperature for 10 h and then water (15 mL) was added. The reaction mixture was extracted with CH_2Cl_2 (3 \times 30 mL). The combined organic extracts were washed with saturated NH_4Cl solution (20 mL) and evaporated in vacuo. Flash chromatography on silica gel using hexane/EtOAc (20:1) afforded **28** (0.460 g, 98%) as a yellow oil; ^1H NMR (300 MHz, CDCl_3) δ 13.70 (s, OH), 6.43 (d, $J = 9.9$ Hz, 1H), 5.43 (d, $J = 9.9$ Hz, 1H), 4.94 (s, 2H), 3.52 (s, 3H), 2.62 (s, 3H), 2.02 (s, 3H), 1.42 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 204.0, 163.2, 158.1, 154.4, 125.7, 117.5, 111.0, 108.0, 106.5, 99.6, 77.3, 57.7, 33.4, 27.4, 8.6; IR (neat) 3194, 2971, 1611, 1465, 1424, 1364, 1316, 1286, 1212, 1135, 1062, 1012, 958, 926, 864, 787, 738, 679, 618 cm^{-1} ; HRMS m/z (M^+) calcd for $\text{C}_{16}\text{H}_{20}\text{O}_5$: 292.1311. Found: 292.1309.

Compound 29. To a solution of **28** (0.200 g, 0.68 mmol) in ethanol (8 mL) was added KOH (0.384 g, 6.84 mmol) and aldehyde **16** (0.087 g, 0.82 mmol). The reaction mixture was stirred at room temperature for 48 h. Evaporation of ethanol, addition of 1N HCl (8 mL), extraction with EtOAc (3 \times 20 mL), washing with brine (20 mL), and removal of the solvent followed by flash column chromatography on silica gel

using hexane/EtOAc (10:1) gave **29** (0.292 g, 85%) as a red solid: mp 115-116 °C; ^1H NMR (300 MHz, CDCl_3) δ 13.91 (s, OH), 8.07 (d, $J = 15.6$ Hz, 1H), 7.77 (d, $J = 15.6$ Hz, 1H), 7.61-7.58 (m, 2H), 7.41-7.38 (m, 3H), 6.53 (d, $J = 9.9$ Hz, 1H), 5.51 (d, $J = 9.9$ Hz, 1H), 5.02 (s, 2H), 3.85 (s, 3H), 2.11 (s, 3H), 1.53 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 193.7, 164.0, 158.3, 153.9, 142.5, 135.4, 130.2, 129.0, 128.3, 127.5, 126.0, 117.8, 111.4, 108.7, 107.0, 99.8, 77.5, 57.9, 27.7, 8.9; IR (KBr) 2909, 2940, 1634, 1594, 1552, 1451, 1414, 1388, 1338, 1285, 1214, 1150, 1120, 1095, 1059, 1002, 966, 927, 872, 767, 724, 692 cm^{-1} ; HRMS m/z (M^+) calcd for $\text{C}_{23}\text{H}_{24}\text{O}_5$: 380.1624. Found: 380.1627.

Compound 30. To a solution of **28** (0.100 g, 0.34 mmol) in ethanol (2 mL) was added KOH (0.096 g, 1.71 mmol) and *p*-tolualdehyde (0.049 g, 0.41 mmol). The reaction mixture was stirred at room temperature for 48 h. Evaporation of ethanol, addition of water (10 mL) and 1N HCl (2 mL), extraction with EtOAc (3 \times 20 mL), washing with brine (20 mL), and removal of the solvent followed by flash column chromatography on silica gel using hexane/EtOAc (10:1) gave **30** (0.128 g, 95%) as a red solid: mp 124-126 °C; ^1H NMR (300 MHz, CDCl_3) δ 8.04 (d, $J = 15.3$ Hz, 1H), 7.76 (d, $J = 15.3$ Hz, 1H), 7.49 (d, $J = 7.8$ Hz, 2H), 7.21 (d, $J = 7.8$ Hz, 2H), 6.53 (d, $J = 9.6$ Hz, 1H), 5.51 (d, $J = 9.6$ Hz, 1H), 5.02 (s, 2H), 3.58 (s, 3H), 2.37 (s, 3H), 2.11 (s, 3H), 1.52 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 193.7, 164.0, 158.2, 153.9, 142.7, 140.7, 132.7, 129.7, 128.3, 126.5, 125.9, 117.9, 111.4, 108.7, 99.7, 77.4, 57.9, 27.7, 21.5, 8.9; IR (KBr) 2976, 2930, 1633, 1592, 1550, 1464, 1414, 1391, 1337, 1284, 1150, 1128, 931, 816, 743, 683 cm^{-1} ; HRMS m/z (M^+) calcd for $\text{C}_{24}\text{H}_{26}\text{O}_5$: 394.1780. Found: 394.1778.

Compound 31. To a solution of **28** (0.100 g, 0.34 mmol) in ethanol (2 mL) was added KOH (0.096 g, 1.71 mmol) and *m*-anisaldehyde (0.056 g, 0.41 mmol). The reaction mixture was stirred at room temperature for 48 h. Evaporation of ethanol, addition of water (10 mL) and 1N HCl (2 mL), extraction with EtOAc (3 \times 20 mL), washing with brine (20 mL), and removal of the solvent followed by flash column chromatography on silica gel using hexane/EtOAc (10:1) gave **31** (0.122 g, 87%) as a red oil; ^1H NMR (300 MHz, CDCl_3) δ 13.90 (brs, OH), 8.05 (d, $J = 15.6$ Hz, 1H), 7.73 (d, $J = 15.6$ Hz, 1H), 7.31 (t, $J = 7.5$ Hz, 1H), 7.19 (d, $J = 7.8$ Hz, 1H), 6.94 (d, $J = 7.2$ Hz, 1H), 6.53 (d, $J = 9.9$ Hz, 1H), 5.51 (d, $J = 9.9$ Hz, 1H), 5.02 (s, 2H), 3.82 (s, 3H), 3.58 (s, 3H), 2.11 (s, 3H), 1.53 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 193.7, 164.1, 159.9, 158.4, 153.9, 142.4, 136.8, 129.9, 127.7, 125.9, 121.1, 117.9, 116.3, 112.9, 111.5, 108.7, 106.9, 99.8, 77.5, 57.9, 55.2, 27.7, 8.9; IR (neat) 3047, 2969, 2932, 2837, 1628, 1600, 1549, 1418, 1340, 1285, 1257, 1149, 1129, 973, 932, 827, 734, 555, 507 cm^{-1} ; HRMS m/z (M^+) calcd for $\text{C}_{24}\text{H}_{26}\text{O}_6$: 410.1729. Found: 410.1728.

Compound 32. To a solution of **28** (0.100 g, 0.34 mmol) in ethanol (2 mL) was added KOH (0.096 g, 1.71 mmol) and *p*-anisaldehyde (0.056 g, 0.41 mmol). The reaction mixture was stirred at room temperature for 48 h. Evaporation of ethanol, addition of water (10 mL) and 1N HCl (2 mL), extraction with EtOAc (3 \times 20 mL), washing with brine (20

mL), and removal of the solvent followed by flash column chromatography on silica gel using hexane/EtOAc (10:1) gave **32** (0.126 g, 90%) as a red solid: mp 81-82 °C; ^1H NMR (300 MHz, CDCl_3) δ 7.91 (d, $J = 15.6$ Hz, 1H), 7.74 (d, $J = 15.6$ Hz, 1H), 7.48 (d, $J = 8.7$ Hz, 2H), 6.85 (d, $J = 8.7$ Hz, 2H), 6.47 (d, $J = 9.9$ Hz, 1H), 5.44 (d, $J = 9.9$ Hz, 1H), 4.95 (s, 2H), 3.77 (s, 3H), 3.51 (s, 3H), 2.04 (s, 3H), 1.46 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 193.6, 164.1, 161.4, 158.1, 153.8, 142.6, 130.0, 128.2, 125.8, 125.2, 117.9, 114.4, 111.4, 108.7, 106.9, 99.8, 77.4, 57.9, 55.4, 27.7, 8.9; IR (KBr) 3047, 2969, 2932, 2837, 1628, 1600, 1549, 1418, 1340, 1285, 1257, 1149, 1129, 973, 932, 827, 734, 555, 507 cm^{-1} ; HRMS m/z (M^+) calcd for $\text{C}_{24}\text{H}_{26}\text{O}_6$: 410.1729. Found: 410.1729.

Compound 33. To a solution of **28** (0.100 g, 0.34 mmol) in ethanol (2 mL) was added KOH (0.096 g, 1.71 mmol) and aldehyde **18** (0.068 g, 0.41 mmol). The reaction mixture was stirred at room temperature for 48 h. Evaporation of ethanol, addition of water (10 mL) and 1N HCl (2 mL), extraction with EtOAc (3 \times 20 mL), washing with brine (20 mL), and removal of the solvent followed by flash column chromatography on silica gel using hexane/EtOAc (10:1) gave **33** (0.147 g, 98%) as a red solid: mp 92-94 °C; ^1H NMR (300 MHz, CDCl_3) δ 14.01 (brs OH), 7.88 (d, $J = 15.3$ Hz, 1H), 7.65 (d, $J = 15.3$ Hz, 1H), 7.06 (d, $J = 8.4$ Hz, 1H), 7.03 (s, 1H), 6.78 (d, $J = 8.4$ Hz, 1H), 6.43 (d, $J = 9.6$ Hz, 1H), 5.42 (d, $J = 9.6$ Hz, 1H), 4.91 (s, 2H), 3.83 (s, 3H), 3.81 (s, 3H), 3.80 (s, 3H), 2.01 (s, 3H), 1.44 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 193.1, 163.9, 157.9, 153.5, 151.0, 149.0, 142.8, 128.1, 125.5, 124.9, 123.2, 117.8, 110.9, 109.1, 108.5, 108.4, 106.7, 99.5, 77.1, 57.6, 55.7, 55.5, 27.5, 8.7; IR (KBr) 3115, 3058, 2965, 2935, 2836, 1683, 1628, 1592, 1548, 1513, 1461, 1419, 1332, 1268, 1142, 1025, 930, 872, 842, 810, 732, 566 cm^{-1} ; HRMS m/z (M^+) calcd for $\text{C}_{25}\text{H}_{28}\text{O}_7$: 440.1835. Found: 440.1833.

Red Compound (4). To a solution of **29** (0.100 g, 0.26 mmol) in methanol (8 mL) was added 3M HCl (2 mL) and the reaction mixture was refluxed for 0.5 h. The reaction mixture was diluted with saturated NaHCO_3 solution (12 mL) and extracted with EtOAc (3 \times 30 mL). Removal of solvent at reduced pressure left an oily residue, which was then purified by column chromatography on silica gel using hexane/EtOAc (4:1) to give **4** (0.084 g, 95%) as a red solid: mp 105-107 °C; ^1H NMR (300 MHz, CDCl_3) δ 8.11 (d, $J = 15.6$ Hz, 1H), 7.74 (d, $J = 15.6$ Hz, 1H), 7.60-7.57 (m, 2H), 7.43-7.37 (m, 3H), 6.58 (d, $J = 9.9$ Hz, 1H), 5.73 (s, OH), 5.48 (d, $J = 9.9$ Hz, 1H), 2.06 (s, 3H), 1.52 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 193.1, 164.2, 156.1, 154.3, 142.1, 135.5, 130.0, 128.9, 128.2, 127.6, 125.1, 116.6, 106.3, 102.5, 101.8, 77.7, 27.8, 7.1; IR (KBr) 3418, 2973, 2928, 1625, 1597, 1550, 1463, 1425, 1345, 1291, 1218, 1168, 1131, 977, 924, 884, 863, 804, 763, 742, 702 cm^{-1} ; HRMS m/z (M^+) calcd for $\text{C}_{21}\text{H}_{20}\text{O}_4$: 336.1362. Found: 336.1361.

Compound 8. To a solution of **30** (0.100 g, 0.25 mmol) in ethanol (8 mL) was added 3M HCl (2 mL) and the reaction mixture was refluxed for 0.5 h. The reaction mixture was diluted with saturated NaHCO_3 solution (12 mL) and extracted

with EtOAc (3 × 30 mL). Removal of solvent at reduced pressure left an oily residue, which was then purified by column chromatography on silica gel using hexane/EtOAc (4:1) to give **8** (0.084 g, 95%) as a red solid: mp 134–136 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.32 (d, *J* = 15.6 Hz, 1H), 7.97 (d, *J* = 15.6 Hz, 1H), 7.71 (d, *J* = 6.6 Hz, 2H), 7.43 (d, *J* = 6.6 Hz, 2H), 6.84 (d, *J* = 9.6 Hz, 1H), 6.38 (brs, OH), 5.70 (d, *J* = 9.6 Hz, 1H), 2.60 (s, 3H), 2.31 (s, 3H), 1.76 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 193.1, 164.2, 156.2, 154.3, 142.2, 140.4, 132.8, 129.6, 128.2, 126.6, 125.0, 116.7, 106.1, 102.7, 101.9, 77.4, 27.7, 21.4, 7.1; IR (KBr) 3426, 3050, 3023, 2975, 2922, 2858, 1625, 1593, 1550, 1467, 1423, 1347, 1293, 1167, 1102, 975, 811, 739 cm⁻¹; HRMS *m/z* (M⁺) calcd for C₂₂H₂₂O₄: 350.1518. Found: 350.1519.

Compound 9. To a solution of **31** (0.100 g, 0.25 mmol) in ethanol (8 mL) was added 3M HCl (2 mL) and the reaction mixture was refluxed for 0.5 h. The reaction mixture was diluted with saturated NaHCO₃ solution (12 mL) and extracted with EtOAc (3 × 30 mL). Removal of solvent at reduced pressure left an oily residue, which was then purified by column chromatography on silica gel using hexane/EtOAc (4:1) to give **9** (0.080 g, 90%) as a red solid: mp 135–136 °C; ¹H NMR (300 MHz, CDCl₃) δ 13.94 (brs, OH), 8.09 (d, *J* = 15.6 Hz, 1H), 7.71 (d, *J* = 15.6 Hz, 1H), 7.31 (t, *J* = 7.5 Hz, 1H), 7.18 (d, *J* = 7.8 Hz, 1H), 7.11 (s, 1H), 6.93 (d, *J* = 8.1 Hz, 1H), 6.58 (d, *J* = 9.6 Hz, 1H), 5.56 (brs, OH), 5.48 (d, *J* = 9.6 Hz, 1H), 3.82 (s, 3H), 2.06 (s, 3H), 1.53 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 193.0, 164.2, 159.9, 156.0, 154.3, 142.0, 137.0, 130.0, 127.9, 125.1, 121.0, 116.6, 116.1, 112.8, 106.3, 102.4, 101.8, 77.7, 55.2, 27.8, 7.1; IR (KBr) 3365, 3066, 2967, 2924, 1624, 1602, 1535, 1464, 1427, 1355, 1325, 1259, 1166, 1132, 809 cm⁻¹; HRMS *m/z* (M⁺) calcd for C₂₂H₂₂O₅: 366.1467. Found: 366.1466.

Compound 10. To a solution of **32** (0.100 g, 0.24 mmol) in ethanol (8 mL) was added 3M HCl (2 mL) and the reaction mixture was refluxed for 0.5 h. The reaction mixture was diluted with saturated NaHCO₃ solution (12 mL) and extracted with EtOAc (3 × 30 mL). Removal of solvent at reduced pressure left an oily residue, which was then purified by column chromatography on silica gel using hexane/EtOAc (4:1) to give **10** (0.079 g, 88%) as a red oil; ¹H NMR (300 MHz, CDCl₃) δ 8.00 (d, *J* = 15.6 Hz, 1H), 7.74 (d, *J* = 15.6 Hz, 1H), 7.53 (d, *J* = 7.8 Hz, 2H), 6.91 (d, *J* = 7.8 Hz, 2H), 6.58 (d, *J* = 9.9 Hz, 1H), 5.72 (brs, OH), 5.47 (d, *J* = 9.9 Hz, 1H), 3.83 (s, 3H), 2.06 (s, 3H), 1.52 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 193.0, 164.2, 161.3, 155.8, 154.2, 142.1, 129.9, 128.4, 125.3, 125.0, 116.7, 114.4, 106.3, 102.5, 101.8, 77.5, 55.3, 27.8, 7.1; IR (neat) 3434, 3122, 3054, 2971,

2930, 2841, 1604, 1548, 1463, 1423, 1351, 1296, 1256, 1166, 1130, 1031, 981, 825, 739 cm⁻¹; HRMS *m/z* (M⁺) calcd for C₂₂H₂₂O₅: 366.1467. Found: 366.1469.

Compound 11. To a solution of **33** (0.100 g, 0.23 mmol) in ethanol (8 mL) was added 3M HCl (2 mL) and the reaction mixture was refluxed for 0.5 h. The reaction mixture was diluted with saturated NaHCO₃ solution (12 mL) and extracted with EtOAc (3 × 30 mL). Removal of solvent at reduced pressure left an oily residue, which was then purified by column chromatography on silica gel using hexane/EtOAc (4:1) to give **11** (0.087 g, 97%) as a red solid: mp 122–123 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.99 (d, *J* = 15.6 Hz, 1H), 7.70 (d, *J* = 15.6 Hz, 1H), 7.14 (d, *J* = 8.4 Hz, 1H), 7.11 (s, 1H), 6.85 (d, *J* = 8.4 Hz, 1H), 6.58 (d, *J* = 9.9 Hz, 1H), 6.13 (brs, OH), 5.45 (d, *J* = 9.9 Hz, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 2.04 (s, 3H), 1.50 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 192.8, 164.2, 156.1, 154.1, 150.9, 149.0, 142.4, 128.5, 125.3, 124.8, 123.1, 116.8, 111.0, 109.3, 106.2, 102.7, 101.9, 77.4, 55.9, 55.6, 27.7, 7.1; IR (KBr) 3437, 2969, 2934, 2840, 1704, 1595, 1513, 1463, 1423, 1359, 1336, 1264, 1165, 1100, 1024, 840, 811, 732 cm⁻¹; HRMS *m/z* (M⁺) calcd for C₂₃H₂₄O₆: 396.1573. Found: 396.1573.

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