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Efficient Synthesis of Bibenzyl Derivatives Bearing Pyranyl Moieties: First Total Synthesis of Bauhinol D

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An efficient and general synthesis of bibenzyl derivatives bearing pyranyl rings was achieved by ethylenediamine diacetate-catalyzed reactions of 3,5-dihydroxybibenzyl with α,β-unsaturated aldehydes in moderate yields. These reactions provided naturally occurring compounds **1** and **2** in single step reaction. As an application of this methodology, biologically interesting natural bauhinol D (**8**) was synthesized by a convergent sequence from readily available benzaldehyde and benzyl phosphonate.

Key Words: Bibenzyls, Pyrans, Bauhinol D

Introduction

Molecules containing the bibenzyl moiety are widely distributed in nature[1] and possess a variety of biological properties, including antioxidant,[2] antimicrobial,[3] anti-HIV-1,[4] antifungal,[5] anti-proliferative,[6] antitumor,[7] cytotoxic,[8] neuroprotective,[9] and antiplatelet aggregation activities.[10] Many of them also find use as versatile intermediates in organic and natural product syntheses.[11] Among these, bibenzyl derivatives bearing pyranyl rings, such as compounds **1** and **2**, have been isolated from *Radula laxiramea*,[12] while **3** and **4** were isolated from *Lethocolea glossophylla* (Fig. 1).[13] Recently, *o*-cannabichromene (**5**) and *o*-cannabicyclol (**6**) were isolated from *Radula appressa* and *Thysananthus spathulistipus*.[14] These compounds inhibit nitric oxide (NO) production in lipopolysaccharide (LPS)-stimulated RAW 264.7 cells.[14] Bauhinols A (**7**) and D (**8**) were isolated from *Bauhinia saccocalyx*.[15] The crude extract of this plant has shown to possess antimalarial and antimycobacterial activities.[15] Bauhinol A (**7**) itself exhibits significant cytotoxicity towards NCI-H187, BC, and KB cell lines with IC_{50} values of 2.7 - 4.5 μg/mL.[15] These biological activities and properties have stimulated research into the synthesis of bibenzyl derivatives bearing pyranyl rings. The structures of natural products **1**-**8** have been established by spectral analysis, but no synthesis of naturally occurring bibenzyls **3**-**8** have been reported yet.

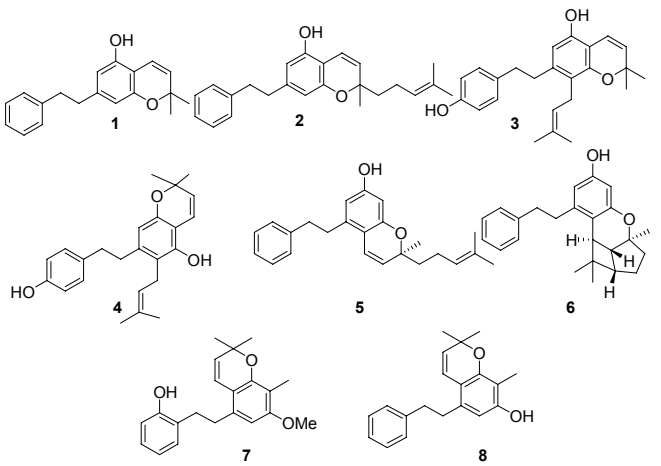


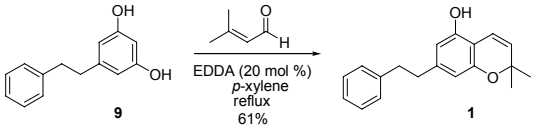
Figure 1. Naturally occurring bibenzyls **1-8** bearing pyranyl rings.

Recently, this lab developed a new and useful methodology for preparing a variety of benzopyrans using ethylenediamine diacetate (EDDA)-catalyzed reactions of resorcinols with α,β-unsaturated aldehydes through a domino aldol-type/6π-electrocyclization reaction.[16] As part of an ongoing study of the synthetic efficacy of this methodology, we describe herein an efficient and general synthesis of a variety of natural and unnatural bibenzyl derivatives fused with pyranyl rings. Also we report the first total synthesis of the naturally occurring bauhinol D (**8**).

Results and Discussion

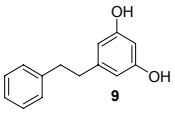
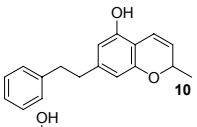
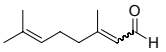
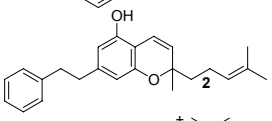
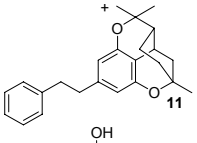
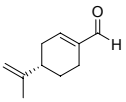
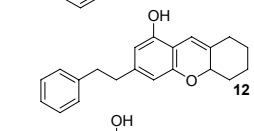
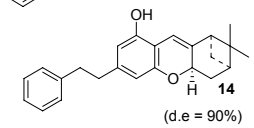
Initial attempts for the synthesis of **1** employed readily available 3,5-dihydroxybibenzyl (**9**) (= dihydropinosylvin) as the starting material (Scheme 1). Reaction of **9** with 3-methyl-2-butenal in the presence of ethylenediamine diacetate (20 mol %) as a catalyst in refluxing *p*-xylene for 10 h afforded **1** in 61% yield. In the ^{1}H-NMR spectrum, two vinyl protons on the pyranyl ring were observed at δ 6.65 (1H, d, J = 10.2 Hz) and 5.59 (1H, d, J = 10.2 Hz) ppm. The spectral data of synthetic material **1** were in agreement with those reported in the literature.[12]

Additional reactions of 3,5-dihydroxybibenzyl (**9**) with several types of α,β-unsaturated aldehydes such as crotonaldehyde, citral, 1-cyclohexene-1-carboxaldehyde, (-)-perillaldehyde, and (-)-myrtenal were carried out in the presence of EDDA (20 mol %) in refluxing *p*-xylene (Table 1). Reaction of **9** with crotonaldehyde for 12 h afforded adduct **10** in 43%

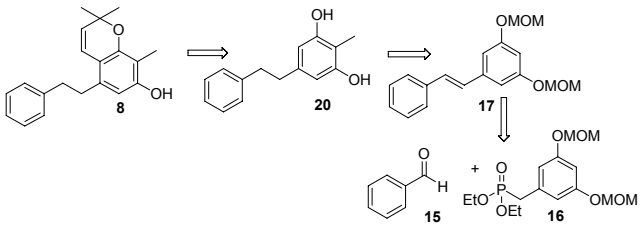


Scheme 1. Reaction of 3,5-dihydroxybibenzyl (**9**) with 3-methyl-2-butenal in the presence of EDDA

Table 1. Reactions of 3,5-dihydroxybibenzyl (**9**) with α,β-unsaturated aldehydes

entry	starting material	α,β-unsaturated aldehyde	condition	product	yield (%)
1			xylene reflux 12 h		43
2			xylene reflux 10 h		32
3			xylene reflux 10 h		48
4			*p*-xylene reflux 10 h		60
5			*p*-xylene reflux 10 h		68
				(d.e = 90%)	65

yield, whereas treatment of **9** with citral for 10 h afforded, interestingly, both naturally occurring compound **2** (32%) and tetracycle **11** (48%). The two compounds were easily separated by column chromatography. The spectroscopic data of **2** were in agreement with those of the natural product.[12] Adduct **11** was confirmed by comparison of its spectral data with those of the known authentic compound.[17] Reactions of **9** with 1-cyclohexene-1-carboxaldehyde and (-)-perillaldehyde in refluxing *p*-xylene provided adducts **12** and **13** in 60 and 68% yields, respectively, as a single compound, whereas treatment with

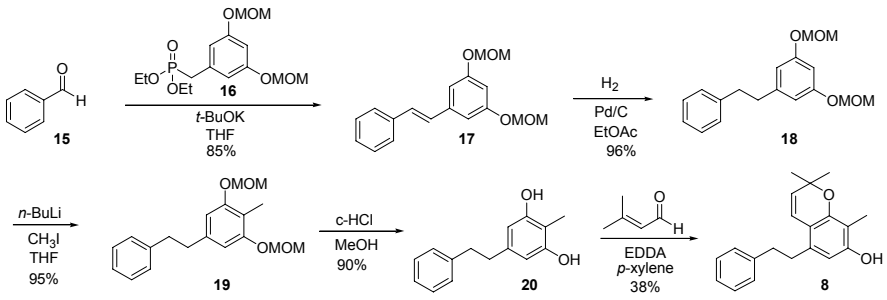


Scheme 2. Retrosynthetic analysis for the synthesis of bauhinol D (**8**)

(-)-myrtenal gave product **14** with 90% diastereoselectivity in 65% yield. The stereochemistry of new compounds **13** and **14** was confirmed by comparison with reported data.[18] These reactions provide a rapid route for the syntheses of bibenzyl derivatives with a variety of substituents on the pyranyl rings.

As an application of this methodology, the total synthesis of bauhinol D (**8**) was next attempted. Scheme 2 shows the retrosynthetic strategy for naturally occurring **8**. Bauhinol D (**8**) could be prepared from **20** by a benzopyran formation reaction. Compound **20** could be generated from **17** by consecutive hydrogenation, alkylation, and deprotection reactions. Compound **17** could be produced *via* a Horner-Wadsworth-Emmons reaction between benzaldehyde (**15**) and benzyl phosphonate **16**.

The synthetic approach for bauhinol D (**8**) is shown in Scheme 3. The Horner-Wadsworth-Emmons reaction of benzaldehyde **15** with benzyl phosphonate **16**[19] provided *trans*-stilbene **17** in 85% yield. Catalytic hydrogenation of **17** over Pd/C (30 psi) in ethyl acetate for 1 h gave **18** in 96% yield. Reaction of **18** with *n*-BuLi, followed by the addition of methyl iodide, provided compound **19** in 95% yield. Deprotection of the two



Scheme 3

MOM ethers with concentrated HCl in methanol afforded compound **20** (90%), known as stilbostemin B. This compound was isolated from *Stemona collinsae*[20] and *S. sessilifolia*,[21] which have long been used in traditional Chinese and Vietnamese medicines for the treatment of inflammatory related diseases. "Baibu", the dried root tuber of *Stemona sessilifolia*, is listed in the Chinese Pharmacopoeia and used to relieve cough and kill insects and worms.[22] In Vietnamese medicine, *S. collinsae* has been used for cough relief and as an antiasthmatic.[23] Naturally occurring stilbostemin B (**20**) showed strong antifungal[24] and antibacterial[25] activities, along with inhibition of leukotriene formation.[27] Treatment of **20** with 3-methyl-2-butenal in the presence of 20 mol% EDDA as a catalyst in refluxing xylene for 12 h gave adduct **8** (38%). The spectroscopic data of synthetic **8** were in agreement with those of the literature.[15]

In conclusion, the formation of a number of natural and unnatural bibenzyl derivatives with a fused pyran moiety has been described starting from 3,5-dihydroxybibenzyl with α,β-unsaturated aldehydes in the presence of ethylenediamine diacetate. As an application of this methodology, the total synthesis of naturally occurring bauhinol D (**8**) was achieved from benzaldehyde and benzyl phosphonate through Horner-Wadsworth-Emmons olefination and benzopyran formation reaction as key steps.

Experimental Section

All experiments were carried out in a nitrogen atmosphere. Merck, pre-coated silica gel plates (Art. 5554) with a fluorescent indicator were used for TLC analysis. Flash column chromatography was performed using silica gel 9385 (Merck). The ^{1}H- and ^{13}C-NMR spectra were recorded using a Bruker Model ARX (300 and 75 MHz, respectively) spectrometer in $CDCl_3$ as the solvent for the chemical shift. The IR spectra were recorded using a Jasco FTIR 5300 spectrophotometer. HRMS spectra were carried out at the Korea Basic Science Institute.

General Procedure for the Synthesis of 1, 2, and 10-14. 3,5-Dihydroxybibenzyl (0.5 mmol) and α,β-unsaturated aldehydes (1 mmol) were dissolved in *p*-xylene (10 mL), and ethylenediamine diacetate (18 mg, 0.1 mmol) was added at room temperature. The mixture was heated to reflux for 10 - 12 h and then cooled to room temperature. Removal of the solvent at reduced pressure left an oily residue, which was then purified by column chromatography on silica gel to give the product.

2,2-Dimethyl-7-phenethyl-2*H*-chromen-5-ol (1): Reaction of **9** (107 mg, 0.5 mmol) with 3-methyl-2-butenal (84 mg, 1.0 mmol) in xylene (10 mL) afforded **1** (86 mg, 61%) as an oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.33 (2H, m), 7.26-.21 (3H, m), 6.65 (1H, d, J = 10.2 Hz), 6.35 (1H, s), 6.21 (1H, s), 5.59 (1H, d, J =10.2), 2.95-2.87 (2H, m), 2.85-2.78 (2H, m), 1.49 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.8, 151.2, 143.5, 141.7, 128.4, 128.3, 125.9, 116.4, 109.1, 107.9, 107.4, 75.9, 37.9, 37.4, 27.8; IR (neat) 3462, 2974, 1622, 1570, 1429, 1424, 1180, 1122, 1064, 746, 700 cm^{-1}; HRMS *m*/*z* (M^+) calcd for $C_{19}H_{20}O_2$: 280.1463. Found: 280.1466.

2-Methyl-7-phenethyl-2*H*-chromen-5-ol (10): Reaction of **9** (107 mg, 0.5 mmol) with crotonaldehyde (70 mg, 1 mmol) in xylene (10 mL) afforded **10** (57 mg, 43%) as an oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29-7.15 (5H, m), 6.63 (1H, d, J = 10.2 Hz), 6.29 (1H,s), 6.11 (1H, s), 5.58 (1H, d, J = 10.2 Hz), 4.90-4.80 (1H, m), 2.88-2.72 (4H, m), 1.42 (3H, d, J = 6.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.0, 151.0, 143.6, 141.8, 128.4, 128.3, 125.9, 124.5, 118.0, 108.8, 108.2, 71.2, 37.8, 37.3, 21.0; IR (KBr) 3431, 2931, 1617, 1594, 1492, 1438, 1366, 1206, 1141, 1065, 918, 846, 737 cm^{-1}; HRMS *m*/*z* (M^+) calcd for $C_{18}H_{18}O_2$: 266.1307. Found: 266.1306.

2-Methyl-2-(4-methyl-pent-3-enyl)-7-phenethyl-2*H*-chromen-5-ol (2) and 2-Methyl-2-(4-methyl-pent-3-enyl)-7-phenethyl-2*H*-chromen-5-ol (11): Reaction of **9** (107 mg, 0.5 mmol) with citral (152 mg, 1 mmol) in xylene (10 mL) afforded **2** (56 mg, 32%) and **11** (84 mg, 48%). Compound **2**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29-7.24 (2H, m), 7.20-7.15 (3H, m), 6.62 (1H, d, J = 10.2 Hz), 6.27 (1H, s), 6.11 (1H, s), 5.49 (1H, d, J = 10.2 Hz), 5.09 (1H, t, J = 7.0 Hz), 4.97 (1H, br s), 2.88-2.82 (2H, m), 2.77-2.71 (2H, m), 2.14-2.04 (2H, m), 1.77-1.67 (2H, m), 1.65 (3H, s), 1.57 (3H, s), 1.37 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.1, 151.2, 143.5, 141.8, 131.7 128.3, 128.3, 127.3, 125.9, 124.1, 116.8, 109.0, 107.7, 107.3, 78.2, 41.0, 38.1, 37.3, 26.1, 25.7, 22.7, 17.6; IR (neat) 3396, 3028, 2926, 1624, 1577, 1496, 1433, 1375, 1253, 1203, 1141, 1084, 1057, 904, 823, 775, 700 cm^{-1}; HRMS *m*/*z* (M^+) calcd for $C_{24}H_{28}O_2$: 348.2089. Found: 348.2089. Compound **11**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26-7.21 (2H, m), 7.16-7.13 (3H, m), 6.34 (1H, s), 6.25 (1H, s), 2.96-2.60 (4H, m), 2.24-2.17 (1H, m), 2.04-1.97 (1H, m), 1.82 (1H, d, J = 13.2 Hz), 1.50 (3H, s), 1.46-1.39 (2H, m), 1.36 (3H, s), 1.25-1.18 (2H, m), 0.98 (3H, s), 0.63-0.58 (1H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.0, 156.7, 141.9, 141.3, 128.4, 128.2, 125.8, 114.4, 109.8, 108.9, 83.6, 74.5, 46.8, 38.1, 37.8, 37.3, 35.3, 29.7, 29.0, 28.1, 23.8, 22.1; IR (neat) 2974, 1620, 1585, 1431, 1367, 1211, 1163, 1128, 1062, 700 cm^{-1}; HRMS *m*/*z* (M^+) calcd for $C_{24}H_{28}O_2$: 348.2089. Found: 348.2087.

3-Phenethyl-5,7,8,10a-tetrahydro-6*H*-xanthen-1-ol (12): Reaction of **9** (107 mg, 0.5 mmol) with 1-cyclohexene-1-carboxaldehyde (110 mg, 1 mmol) in xylene (10 mL) afforded **12** (92 mg, 60%) as an oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29-7.24 (2H, m), 7.20-7.15 (3H, m), 6.28 (1H, s), 6.21 (1H, s), 6.07 (1H, s), 4.91-4.85 (1H, m), 4.68 (1H, br s), 2.87-2.80 (2H, m), 2.75-2.69 (2H, m), 2.48-2.41 (1H, m), 2.24-2.00 (2H, m), 1.91-1.66 (3H, m), 1.52-1.25 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.8, 150.2, 142.2, 141.7, 135.6, 128.4, 128.3, 125.9, 110.0, 108.0, 107.9, 107.2, 77.4, 37.8, 37.4, 35.0, 33.1, 26.7, 24.3; IR (neat) 3402, 3026, 2930, 2856, 1628, 1583, 1496, 1434, 1346, 1161, 1034, 931, 847, 739 cm^{-1}; HRMS *m*/*z* (M^+) calcd for $C_{21}H_{22}O_2$: 306.1620. Found: 306.1616.

6-Isopropenyl-3-phenethyl-5,7,8,10a-tetrahydro-6*H*-xanthen-1-ol (13): Reaction of **9** (107 mg, 0.5 mmol) with (-)-perillaldehyde (150 mg, 1 mmol) in xylene (10 mL) afforded **13** (118 mg, 68%) as an oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28-7.24 (2H, m), 7.19-7.15 (3H, m), 6.32 (1H, s), 6.22 (1H, s), 6.07 (1H, s), 4.99-4.91 (1H, m), 4.79 (1H, br s), 4.73 (2H, s), 2.87-2.82 (2H, m), 2.74-2.69 (2H, m), 2.53-2.48 (1H, m), 2.28-2.23 (1H, m), 2.19-2.10 (2H, m), 1.86-1.76 (2H, m), 1.74 (3H, s), 1.40-1.24 (1H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.8, 150.3, 148.4, 142.4, 141.7, 135.2, 134.6, 128.4, 125.9, 110.3, 109.3, 108.1, 107.9, 107.4, 76.6, 43.2, 39.7, 37.7, 37.4, 32.4, 31.7, 20.7; IR (neat) 3376, 3063, 2934, 2346, 1612, 1580, 1498,

1432, 1352, 1277, 1165, 1045, 963, 890, 738; HRMS *m/z* (M^+) calcd for $C_{24}H_{26}O_2$: 346.1933. Found: 346.1933.

14,14-Dimethyl-7-(2-phenylethyl)-10-oxatetracyclo[11.1.1.0^{2,11}.0^{4,9}]pentadeca-2,4(9),5,7-tetraen-5-ol (14): Reaction of **9** (107 mg, 0.5 mmol) with (-)-myrtenal (150 mg, 1 mmol) in xylene (10 mL) afforded **14** (113 mg, 65%) as a 95:5 mixture of diastereomers. Major: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29-7.24 (2H, m), 7.19-7.16 (3H, m), 6.39 (1 H, s), 6.27 (1H, s), 6.19 (1H, s), 4.98-4.92 (1H, m), 2.88-2.83 (2H, m), 2.80-2.75 (2H, m), 2.64-2.52 (2H, m), 2.41-2.33 (1H, m), 2.15-2.02 (4H, m), 1.29 (3H, s), 0.90 (3H, s); ^{13}C NMR (75 MHz, acetone-d_6) δ 155.4, 150.8, 141.9, 141.7, 139.6, 128.4, 128.3, 125.9, 111.1, 110.0, 108.7, 108.5, 69.9, 49.1, 42.1, 40.3, 37.8, 37.5, 31.9, 25.9, 25.6, 21.8; IR (KBr) 3372, 2932, 1700, 1576, 1502, 1434, 1353, 1206, 1049, 962, 912, 829, 737, 697 cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{24}H_{26}O_2$: 346.1933. Found: 346.1933. Minor: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29-7.24 (2H, m), 7.19-7.16 (3H, m), 6.42(1H, s), 6.27 (1H, s), 6.22 (1H, s), 4.83-4.78 (1H, m), 2.88-2.83 (2H, m), 2.80-2.75 (2H, m), 2.64-2.52 (2H, m), 2.41-2.33 (1H, m), 2.15-2.02 (4H, m), 1.30 (3H, s), 0.83 (3H, s); ^{13}C NMR (75 MHz, acetone-d_6) δ 156.0, 151.4, 142.2, 140.6, 140.0, 128.4, 128.3, 125.9, 111.4, 110.7, 108.7, 108.3, 70.6, 50.5, 41.6, 39.8, 37.8, 37.5, 35.3, 33.4, 26.3, 23.7.

(*E*)-3,5-Bis(methoxymethoxy)stilbene (17): To a solution of **15** (0.318 g, 3.0 mmol) and benzyl phosphonate **16** (1.045 g, 3.0 mmol) in THF (30 mL) was added *t*-BuOK (0.717 g, 6.4 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 30 min. The reaction mixture was quenched by addition of water (30 mL) and extracted with EtOAc (3 × 30 mL). The combined organic layer was washed with NH_4Cl solution (30 mL), water (30 mL), brine (30 mL), dried over $MgSO_4$, and concentrated at reduced pressure. The removal of the solvent under reduced pressure left an oily residue, which was then purified by column chromatography on silica gel using hexane/ethyl acetate (20:1) to give product **17** (0.766 g, 85%) as an oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 (2H, d, *J* = 7.2 Hz), 7.26 (2H, dd, *J* = 7.5, 7.2 Hz), 7.17 (1H, t, *J* = 7.5 Hz), 7.01 (1H, d, *J* = 16.0 Hz), 6.93 (1H, d, *J* = 16.0 Hz), 6.79 (2H, s), 6.57 (1H, s), 5.01 (4H, s), 3.41 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.5, 139.5, 137.0, 129.3, 128.6, 128.3, 127.7, 126.5, 107.8, 104.2, 94.4, 56.0; IR (neat) 2953, 2825, 1591, 1454, 1400, 1282, 1213, 1147, 1084, 1035, 962, 923, 841, 752 cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{18}H_{20}O_4$: 300.1362. Found: 300.1364.

1,3-Bis(methoxymethoxy)-5-styrylbenzene (18): To a solution of **17** (0.451 g, 1.5 mmol) in ethyl acetate (10 mL) was added Pd/C (10 wt %, 0.05 g) and the suspension was hydrogenated over 30 psi for 1 h at room temperature. The reaction mixture was filtered through celite and removal of the solvent at reduced pressure left the residue, which was then purified by column chromatography on silica gel with hexane/EtOAc (20:1) to give **18** (0.435 g, 96%) as an oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28-7.24 (2H, m), 7.20-7.05 (3H, m), 6.58 (1H, d, *J* = 2.1 Hz), 6.60 (2H, d, *J* = 2.1 Hz), 5.18 (4H, s), 3.48 (6H, s), 2.85 (4H, br s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.1, 144.3, 141.6, 128.3, 125.8, 109.8, 102.4, 94.3, 56.0, 38.1, 37.6; IR (neat) 2951, 1597, 1456, 1400, 1282, 1215, 1147, 1084, 1037, 923, 848 cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{18}H_{22}O_4$: 302.1518. Found: 302.1520.

1,3-Bis(methoxymethoxy)-2-methyl-5-styrylbenzene (19): *n*-BuLi (0.44 mL, 2.5 M in hexane, 1.1 mmol) was added at 0 °C to a solution of **18** (0.302 g, 1.0 mmol) in THF (20 mL) and the resulting solution was stirred at 0 °C for 2 h. Methyl iodide (0.156 g, 1.1 mmol) was added dropwise to the reaction mixture at 0 °C, which was stirred at room temperature for 10 h. The reaction mixture was quenched with saturated NH_4Cl solution (20 mL) and extracted with ethyl acetate (3 × 30 mL). The combined extracts were washed water (30 mL), dried ($MgSO_4$), and evaporated under reduced pressure. Flash chromatography on silica gel using hexane/ethyl acetate (10:1) afforded **19** (0.301 g, 95%) as an oil. ^{1}H NMR (300 MHz, $CDCl_3$) 7.28-7.24 (2H, m), 7.19-7.17 (3H, m), 6.58 (2H, s), 5.14 (4H, s), 3.47 (6H, s), 2.87 (4H, br s), 2.12 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.9, 141.7, 140.4, 128.5, 128.2, 125.8, 114.2, 108.3, 94.7, 56.0, 38.1, 37.9, 8.5; IR (neat) 2931, 1593, 1446, 1296, 1208, 1111, 1060, 997, 924, 837, 741cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{19}H_{24}O_4$: 316.1675. Found: 316.1675.

Stibostemin B (20): To a solution of **19** (0.158 g, 0.5 mmol) in methanol (5 mL) was added c-HCl (0.2 mL) and the reaction mixture was stirred at room temperature for 10 h. The reaction mixture was diluted with saturated $NaHCO_3$ solution (30 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 with hexane/EtOAc (5:1) to give **20** (0.103 g, 90%) as a solid. mp 153 - 154 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29-7.24 (2H, m), 7.23-7.15 (3H, m), 6.23 (2H, s), 4.65 (1H, br s), 2.89-2.72 (4H, m), 2.10 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.4, 141.9, 140.0, 128.3, 128.1, 125.6, 108.3, 107.0, 37.5, 37.4, 8.0; (KBr) 3388, 3023, 2926, 1634, 1573, 1500, 1453, 1343, 1289, 1176, 1087, 854, 742; HRMS *m/z* (M^+) calcd for $C_{15}H_{16}O_2$: 228.1150. Found: 228.1149.

Bauhinol D (8): To a solution of **20** (0.068 g, 0.3 mmol) and 3-methyl-2-butenal (0.034 g, 0.4 mmol) in *p*-xylene (10 mL) was added ethylenediamine diacetate (11 mg, 0.06 mmol) at room temperature. The reaction mixture was refluxed for 12 h and then cooled to room temperature. Evaporation of solvent and purification by column chromatography on silica gel using hexane/ethylacetate (4:1) gave **8** (0.034 g, 38%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29-7.24 (2H, m), 7.20-7.15 (3H, m), 6.45 (1H, d, *J* = 10.2 Hz), 6.18 (1H, s), 5.50 (1H, d, *J* = 10.2 Hz), 4.78 (1H, br s), 2.80 (4H, m), 2.06 (3H, s), 1.39 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.0, 152.2, 141.7, 135.5, 128.4, 128.3, 127.6, 126.0, 119.2, 112.6, 109.8, 108.0, 75.3, 37.6, 34.2, 27.7, 7.7; IR (neat) 3406, 2970, 2928, 1598, 1495, 1452, 1420, 1320, 1265, 1103, 743, cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{20}H_{22}O_2$: 294.1620. Found: 294.1621.

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