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Synthesis of Bioactive Speciosins G and P from *Hexagonia speciosa*

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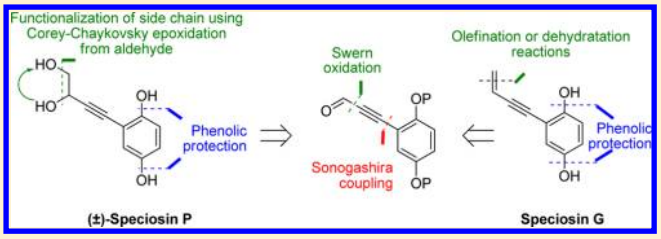
Supporting Information

ABSTRACT: The first total synthesis of speciosins P and G, previously isolated from *Hexagonia speciosa*, is reported. These compounds have been synthesized by Sonogashira coupling from readily available starting materials. Siccayne was also synthesized from the same starting material in two steps along with a number of other derivatives. The compounds were tested in the wheat coleoptile bioassay. The most active compound was the intermediate **18**, followed by **29** and **17**. The structural requirements for activity in these compounds are the presence of methoxy groups in the aromatic ring and a formyl or hydroxy group in the side chain.



In 2009[1] and 2011,[2] Jiang and co-workers isolated a series of substituted hydroquinones, named speciosins A−T, from the Chinese fungus basidiomycete *Hexagonia speciosa*. Speciosins G (**1**) and P (**2**) are structurally similar to the biologically active siccayne (**3**) (Figure 1), which was isolated from the fungus

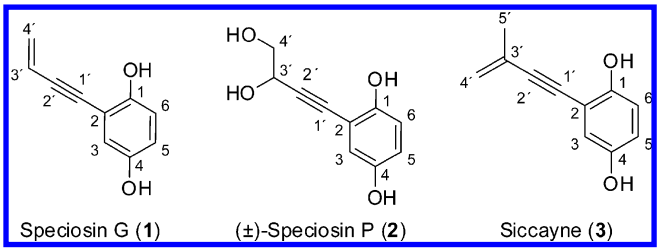


Figure 1. Structures of speciosin G (**1**), (±)-speciosin P (**2**), and siccayne (**3**).

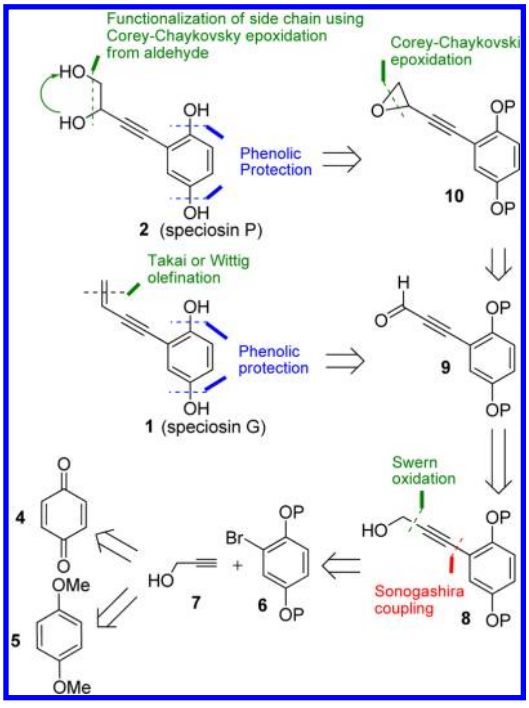
Helminthosporium siccans in 1968 and the marine basidiomycete *Halocyphina villosa* in 1981.[3,4] Related compounds such as siccayne, which are present in bacteria, fungi, higher plants, and mollusks, have a wide range of bioactivities.

Compound **3** showed moderate antibiotic activity, inhibited mitochondrial respiration in *Saccharomyces cerevisiae*,[5] and showed cytotoxic activity against the human cancer cell lines HeLa and HT29,[5,6] making speciosins G and P potential targets in the development of drugs or pesticides.

A retrosynthetic analysis for compounds **1** and **2** is shown in Scheme 1. The key point in this strategy is the attachment of the carbon chain to the aromatic nucleus. The starting materials required to generate the corresponding aryl bromide **6** are readily available and cheap [*p*-benzoquinone (**4**), *p*-dimethoxybenzene (**5**)].

Compound **6** could be linked with propargyl alcohol **7** by Pd-catalyzed Sonogashira coupling to give **8**, which in turn would provide key aldehyde **9** by oxidation. Compound **9** would allow access to **1** and **2** by functionalization reactions.

Scheme 1. Retrosynthetic Analysis for Speciosins G (1) and P (2)



A second aim of this work was the preparation of analogues of these compounds, along with siccayne (**3**), in order to study their structure−activity relationships.

RESULTS AND DISCUSSION

Synthesis. Compound **6a**[7] was obtained from **4**.[8] The key reaction is the Sonogashira cross-coupling with propargyl

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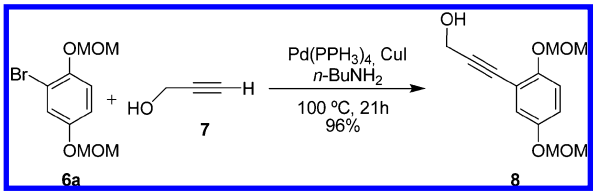
alcohol.[9−11] This reaction was initially carried out under the conditions reported for the preparation of siccayne (**3**). In this process *n*-butylamine was used as the solvent and $Pd(PPh_3)_4$ as the catalyst at 78 °C. The yields obtained using these conditions were about 80%.[8] The introduction of Cu(I) as a cocatalyst led to a decrease in the yield. However, when the reactor was sealed and heated to 100 °C, the yields increased to 96%, i.e., better than previously reported yields (Scheme 2). The reaction conditions

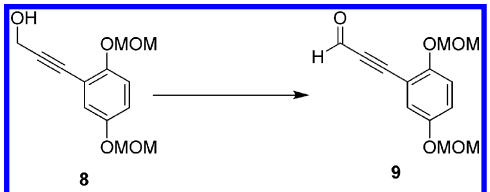
Scheme 2. Conditions for the Pd−Cu-Catalyzed Cross-Coupling of sp^2-C Halides with Terminal Acetylenes



involved the use of equimolecular amounts of aryl bromide **6a** and propargyl alcohol (**7**) in the presence of the commercially available catalyst tetrakis(triphenylphosphine)palladium(0) (3−5 mol %) and *n*-butylamine as solvent.

The feasibility of the oxidation of **8**[12] to aldehyde **9** was assessed using the Corey−Suggs reagent, pyridinium chlorochromate (PCC),[13−15] Dess−Martin periodinane (DMP),[16] and Swern oxidation (Scheme 3).[17] The latter conditions were selected and permitted scale-up to 3.1 mmol with 91% yield.

Scheme 3. Synthesis of the Key Aldehyde 9

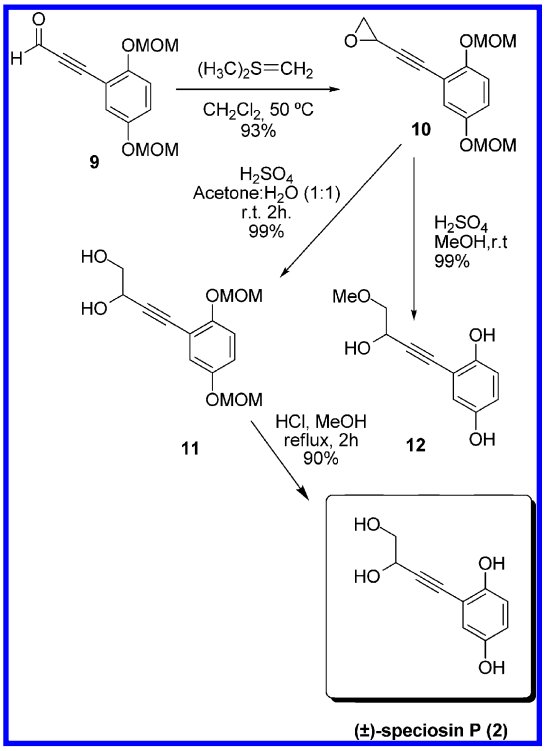


Oxidation conditions	Yield (%)
i) Oxalyl chloride, DMSO, -78 °C ii) Et_3N, -78 °C to r.t.	91
DMP, CH_2Cl_2, r.t.	62
PCC, CH_2Cl_2, r.t. 2 h	57

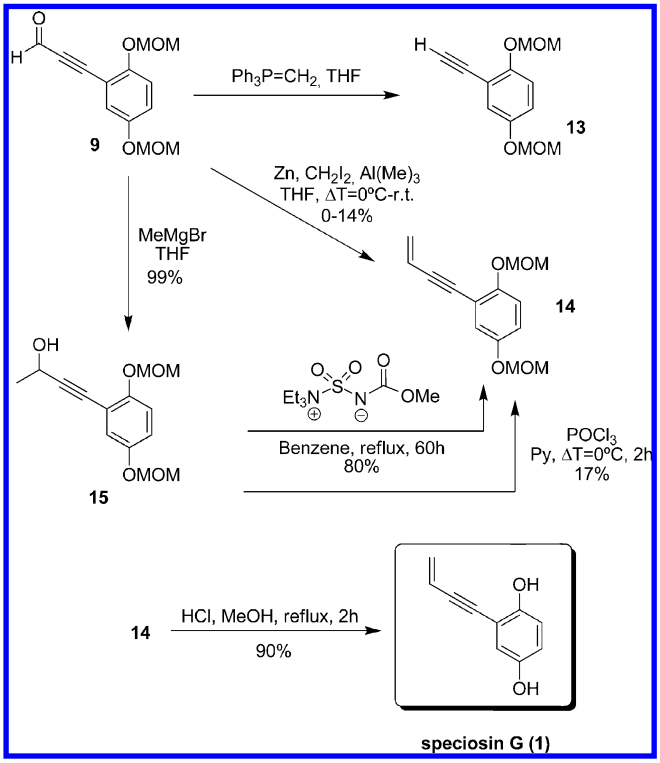
Homologation of the side chain was achieved by the Corey−Chaykovsky reaction (Scheme 4).[18−20] Thus, epoxide **10** was obtained by in situ generation of the dimethylsulfonium methylide[12] and subsequent addition of a dichloromethane solution of the aldehyde **9**. Quantitative acid-mediated hydrolysis of epoxide **10** was performed in acetone/H_2SO_4 to give compound **11**. Deprotection of the OMOM groups was carried out in a solution of HCl in MeOH to give (±)-speciosin P (**2**) in 90% yield (72% overall yield).[2] Simultaneous hydrolysis and deprotection was not possible. When this reaction was carried out in MeOH/H_2SO_4, the methoxy derivative **12** of (±)-speciosin P (**2**) was obtained.

The synthesis of speciosin G requires olefination of aldehyde **9** (Scheme 5). Wittig reaction of **9** with methyltriphenylphosphonium iodide under standard conditions[21] provided compound **13** after decarbonylation, as observed previously for other alkynyl

Scheme 4. Synthesis of (±)-Speciosin P (2) through Corey−Chaykovsky Epoxidation



Scheme 5. Synthesis of Speciosin G (1) through Olefination of the Key Intermediate 9 and Burgess Dehydration of 15



aldehydes.[22] The modification reported by Takai, in which zinc dust, trimethylaluminum, and CH_2I_2 are used, was also employed to synthesize **14**, albeit in a yield less than 15%. Alternatively, Grignard coupling[23] gave a satisfactory yield of **15**, and this was subsequently dehydrated. The commonly used method with

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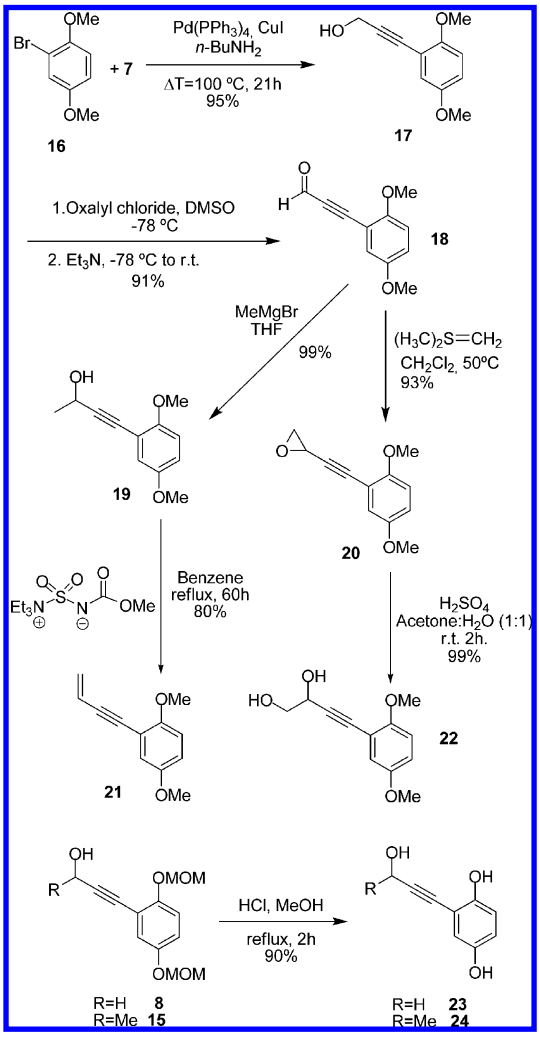
$POCl_3$ led to poor yields (17−20%). The use of Burgess' reagent (6 equiv added in three portions over 60 h) under reflux and dry conditions gave **14** in 80% yield.[24] Deprotection under acidic conditions yielded speciosin G (**1**) in 90% yield (62% overall yield).

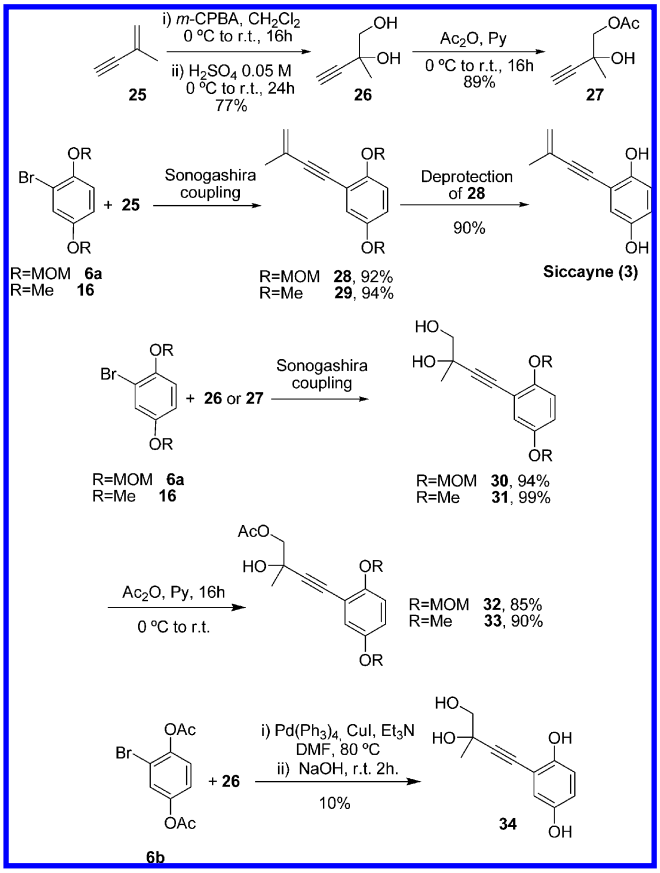
The presence of hydroxy and/or methoxy groups can markedly change the bioactivity of phenolic compounds.[25] Thus, we also prepared all of the intermediates with methoxy groups in the aromatic ring. Several intermediates of speciosins were also deprotected to give the corresponding hydroxy compounds for subsequent assay. The reactions are summarized in Scheme 6.

Scheme 6. Preparation of the Methoxy and Deprotected Derivatives



Siccayne (**3**) and its derivatives were also target compounds. Siccayne (**3**) was synthesized in 94% yield by direct Sonogashira reaction with the MOM-protected bromohydroquinone **6a**. The initial reaction temperature was 0 °C, and this was increased gradually to 100 °C due to the volatility of alkyne **25**. Deprotection also gave siccayne (**3**) in good yield (90%) under the conditions used for speciosins. Modification of the initial chain of **25** to give diol **26**[26] and acetate **27** permitted the synthesis of siccayne derivatives with or without methoxy groups in the aromatic ring (Scheme 7). The acetyl group was removed during the Sonogashira reaction in all cases. It was not possible to obtain

Scheme 7. Preparation of the Racemic Syccaine Derivatives



compound **34** by deprotection of **30**. The acetylated derivative of **6** was prepared by Sonogashira coupling of **6b**.[7]

The preparation of speciosin G (**1**) and (±)-speciosin P (**2**) was optimized by carrying out a number of Sonogashira reactions under different conditions, which included changes in temperature, the use of CuI as a cocatalyst, and altering the number of equivalents of reagents. The results are summarized in Table 1. The presence of primary hydroxy groups in the alkynyl chain at 100 °C was better tolerated when CuI was not used (entries 3, 6, 16, and 17). The presence of tertiary hydroxy groups did not have any influence, and better results were obtained on using a cocatalyst (entries 18 and 24). In general, higher yields were obtained by increasing the reaction temperature. It was not necessary to use a temperature above 100 °C, and this led to low overpressure and allowed the accurate control of the reaction.

Speciosins G (**1**) and P (**2**) have been synthesized for the first time in overall yields of 72% and 62%, respectively, from **6a** in five steps. Siccayne (**3**) was also synthesized from the same starting material in two steps with an overall yield of 83%. This procedure was simpler and more efficient than the reported process.[8,27]

Bioactivity. A total of 16 compounds were evaluated by the wheat coleoptile bioassay. This is a rapid test that is sensitive to a wide range of bioactive substances, including plant growth regulators, herbicides, antimicrobials, mycotoxins, and assorted pharmaceuticals.[28−30] The results are shown in Figure 2, in which negative values signify inhibition, positive values denote activation, and zero represents control.

The most active compound was **18**, followed by **29** and **17**. This trend can be seen more clearly by calculating the IC_{50} values for the assayed compounds (Table 2), which have values of 323, 670, and 952 μM, respectively.

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Table 1. Optimization of the Conditions for the Sonogashira Reaction[a]

entry	substrates	$Pd(PPh_3)_4$ (mol %)	Cu(I) (mol %)	T (°C)	product (yield, %)
1	**6** + **7**[b]	10		78	**8** (82)
2		5	3	100	**8** (59)
3		5		100	**8** (96)
4	**16** + **7**[b]	5	3	100	**17** (62)
5		3	3	100	**17** (52)
6		5		100	**17** (95)
7	**6** + **25**[c]	3	3	0 to 100	**28** (87)
8		5	3	0 to 100	**28** (92)
9	**16** + **25**[c]	3	3	0 to 100	**29** (72)
10		5	3	0 to 100	**29** (94)
11		5	5	25	**29** (75)
12	**6** + **26**[d]	5	3	100	**30** (94)
13		5		100	**30** (94)
14	**16** + **26**[d]	5	3	100	**31** (94)
15		3	3	100	**31** (12)
16		5		100	**31** (99)
17		3		100	**31** (81)
18	**6** + **27**[c]	5	3	100	**30** (80)
19		3	3	100	**30** (31)
20		5		100	**30** (65)
21		3		100	**30** (62)
22		3	3	78	**30** (44)
23		3		78	**30** (41)
24	**16** + **27**[c]	5	3	100	**31** (91)
25		3	3	100	**31** (34)
26		5		100	**31** (72)
27		3		100	**31** (45)
28		3	3	78	**31** (33)
29		3		78	**31** (30)

[a]The reaction time was 21 h in all cases. The solvent was nBuNH$_2$ except for entries 22, 23, 28, and 29, where TEA, DIPEA, and THF were used. [b]1 equiv. [c]1.2 equiv. [d]1.1 equiv.

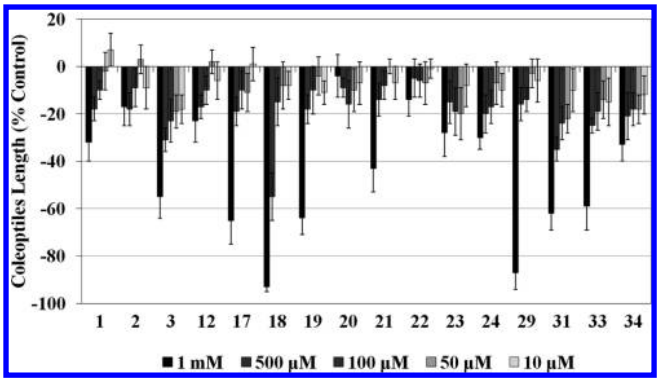

Figure 2. Effect of the compounds tested on etiolated wheat coleoptiles. The bioassays were carried out in triplicate.

Regarding the structural requirements for activity, comparison of pairs (**29**, **3**), (**31**, **34**), and (**21**, **1**) shows that the presence of the methoxy group led to an increase in activity. On the other hand, the compounds with only one hydroxy group in the chain are more active than those that contain two hydroxy groups [cf. (**22**, **19**) and (**2**, **24**)]. Comparison of the siccayne (**3**, **29**, **31**, and **34**) and speciosin (**1**, **2**, **21**, and **22**) derivatives revealed that the siccayne derivatives are more active than the speciosins.

In summary, a number of derivatives were prepared and tested in the wheat coleoptile bioassay. The optimum structural requirements for activity in these compounds are the presence of methoxy groups in the aromatic ring and a formyl or hydroxy group in the chain.

Table 2. IC_{50} Values Obtained in the Wheat Coleoptile Bioassay

compound	IC_{50} (μM)	R^2	compound	IC_{50} (μM)	R^2
1	2568	0.9867	**21**	2010	0.9922
2	14 440	0.9804	**22**	62 260	0.9958
3	1253	0.9682	**23**	7890	0.9638
12	5799	0.9857	**24**	4354	0.9826
17	952.4	0.9753	**29**	670.2	0.9174
18	322.6	0.974	**31**	821	0.9731
19	1055	0.9703	**33**	1160	0.977
20			**34**	4434	0.9724

EXPERIMENTAL SECTION

General Experimental Procedures. Commercially available reagents and solvents were analytical grade or were purified by standard procedures prior to use. Compounds were analyzed by IR, ^{1}H NMR, and ^{13}C NMR spectroscopy and by high-resolution ESI mass spectrometry. The data obtained are consistent with the proposed structures. Infrared spectra were recorded on a PerkinElmer FT-IR Spectrum 1000 Mattson 5020 system. HRMS were obtained on a Waters SYNAPT G2 mass spectrometer (70 eV). ^{1}H NMR, ^{1}H−^{1}H gCOSY, ^{1}H−^{13}C gHSQC, and ^{1}H−^{13}C gHMBC NMR spectra were recorded on Agilent INOVA-400 and INOVA-500 spectrometers using $CDCl_3$ or methanol-d_4. Chemical shifts (δ) are reported in parts per million (ppm) relative to either a TMS internal standard or solvent signals. HRMS data were obtained on a Waters SYNAPT G2 mass spectrometer (70 eV). Column chromatography was performed on silica gel (35−75 mesh), and TLC analysis was carried out using aluminum precoated silica gel plates. Synthetic products were purified by preparative HPLC using a Lichrosorb silica 60 semipreparative column (Lichrospher SiO_2, Merck, 7 and 10 μm, 150 × 10 nm) and Lichrosorb silica 60 analytical columns (Lichrospher SiO_2, Merck, 7 and 10 μm, 250 × 10 mm) in conjunction with a Hitachi Lachrom D-7000 PLC system with a Hitachi L-7490 RI detector and Hitachi L-7420 UV detector.

General Procedure for the Sonogashira Coupling.[8,10,11] Compounds **6a**[31] and **16**[8] were synthesized according to literature procedures. Aryl halide **6a** or **16** (9.21 mmol) in n-butylamine (6.4 mL) was placed in a flame-dried round-bottomed flask under an argon atmosphere. A mixture of terminal alkynes **7**, **25**, **26**, or **27** (9.21 mmol) in n-butylamine (10 mL) and $Pd(Ph_3)_4$ (5% or 3%) was added, with the optional addition of CuI (3%) where appropriate. The mixture was heated for 21 h at 98 °C and poured into H_2O (80 mL). The product was extracted with EtOAc (3 × 80 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. The crude product was purified by silica gel column chromatography (EtOAc/hexanes, 10−50%).

3-[2,5-Bis(methoxymethoxy)phenyl]prop-2-yn-1-ol[12] ***(8)***. Yield 96%; colorless oil; IR (KBr) ν_{max} 3310, 2230 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.46 (3H, s, H-4b), 3.51 (3H, s, H-1b), 4.51 (2H, s, H-1a), 5.09 (2H, s, H-4a), 5.17 (2H, s, H-1a), 6.95 (1H, dd, J = 9 and 3.0 Hz, H-5), 7.03 (1H, d, J = 9.0 Hz, H-6), 7.10 (1H, d, J = 3.0 Hz, H-3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 51.81 (C-9), 56.05 (C-4b), 56.38 (C-1b), 81.74 (C-7), 91.56 (C-8), 95.14 (C-4a), 95.88 (C-4b), 114.19 (C-2), 117.13 (C-5), 118.50 (C-3), 121.20 (C-6), 151.95 (C-4), 153.06 (C-1); HRESIMS m/z 275.0900 [M + Na]$^+$ (calcd for $C_{13}H_{16}O_5$ 275.0896).

3-(2,5-Dimethoxyphenyl)prop-2-yn-1-ol[12] ***(17)***. Yield 95%; yellow microcrystalline solid; mp 67−68 °C; IR (KBr) ν_{max} 2230, 3396 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.73 (3H, s, H-4a), 3.82 (3H, s, H-1a), 4.52 (2H, s, H-9), 6.78 (1H, d, J = 8.3 Hz, H-6), 6.83 (1H, dd, J = 9.0 and 3.0 Hz, H-5), 6.94 (1H, d, J = 3.0 Hz, H-3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 51.76 (C-9), 55.84 (C-4a), 56.43 (C-1a), 81.80 (C-7), 91.62 (C-8), 111.99 (C-3), 112.24 (C-2), 115.92 (C-5), 118.43 (C-6), 153.23

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(C-1), 154.49 (C-4); HRESIMS m/z 215.0694 $[M + Na]^+$ (calcd for $C_{11}H_{12}O_3$ 215.0685).

1,4-Bis(methoxymethoxy)-2-(3-methylbut-3-en-1-yn-1-yl)-benzene[8] ***(28)***. Yield 92%; colorless oil; IR (KBr) ν_{max} 2194, 1493 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.99 (3H, s, 10-H), 3.46 (3H, s, 4b-H)*, 3.51 (3H, s, 1b-H)*, 5.09 (2H, s, 4a-H), 5.17 (2H, s, 1a-H), 6.95 (1H, d, J = 9.0 and 3.0 Hz, 5-H), 7.03 (d, J = 9.0 Hz, 1H, 6-H), 7.10 (1H, d, J = 3.0 Hz, 3-H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 23.40 (C-10), 55.92 (C-4a)*, 56.38 (C-1a)*, 84.44 (C-7), 94.51 (C-8), 95.01 (C-4b)*, 95.81 (C-1b)*, 113.30 (C-2), 116.35 (C-5), 117.48 (C-3), 121.39 (C-6), 121.94 (C-11), 126.85 (C-9), 151.91 (C-4), 152.70 (C-1); HRESIMS m/z 263.1286 $[M + H]^+$ (calcd. for $C_{15}H_{18}O_4$ 263.1284).

1,4-Dimethoxy-2-(3-methylbut-3-en-1-yn-1-yl)benzene[32] ***(29)***. Yield 94%; yellow oil; IR (KBr) ν_{max} 1670, 2192 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.0 (3H, s, H-11), 3.75 (3H, s, H-4a), 3.82 (3H, s, H-1a), 5.29 (1H, d, J = 1.6 Hz, H-10a), 5.41 (1H, d, J = 1.6 Hz, H-10b), 6.78 (1H, d, J = 9.0 Hz, H-6), 6.81 (1H, dd, J = 9.0 and 3.0 Hz, H-5), 7.11 (1H, d, J = 3.0 Hz, H-3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 23.47 (C-11), 55.71 (C-4a), 56.42 (C-1a), 84.56 (C-7), 94.54 (C-8), 112.07 (C-3), 112.87 (C-2), 115.60 (C-5), 118.00 (C-3), 121.93 (C-10), 126.87 (C-9), 153.15 (C-1), 154.32 (C-4); HRESIMS m/z 203.1073 $[M + H]^+$ (calcd for $C_{13}H_{14}O_2$ 203.1073).

4-[2,5-Bis(methoxymethoxy)phenyl]-2-methylbut-3-yne-1,2-diol ***(30)***. Yield 94%; colorless oil; IR (KBr) ν_{max} 3412, 2193 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.53 (3H, s, H-11), 3.45 (3H, s, H-4b), 3.49 (3H, s, H-1b), 3.56, 3.73 (each 1H, d, J = 11.0 Hz, H-10), 5.08 (2H, s, H-4a), 5.15 (2H, s, H-1a), 6.93 (1H, d, J = 9.0 and 2.9 Hz, H-5), 6.98 (1H, d, J = 9.0 Hz, H-6), 7.07 (1H, d, J = 2.9 Hz, H-3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.93 (C-11), 55.88 (C-1a), 56.32 (C-4a), 69.26 (C-9), 70.98 (C-10), 80.62 (C-7), 94.88 (C-8), 94.95 (C-1b), 95.85 (C-4b), 113.76 (C-2), 117.03 (C-6), 118.45 (C-5), 120.50 (C-3), 151.82 (C-1), 152.88 (C-4); HRESIMS m/z 279.1235 $[M - H_2O + H]^+$ (calcd for $C_{15}H_{20}O_6$ 279.1233).

4-(2,5-Dimethoxyphenyl)-2-methylbut-3-yne-1,2-diol ***(31)***. Yield 12%; yellow oil; IR (KBr) ν_{max} 2226, 3394 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.54 (3H, s, H-11), 3.73 (3H, s, H-4a), 3.80 (3H, s, H-1a), 3.55, 3.73 (each 1H, d, J = 11.0 Hz, H-10), 6.76 (1H, d, J = 8.0 Hz, H-6), 6.83 (1H, dd, J = 9.0 and 3.0 Hz, H-5), 6.89 (1H, d, J = 3.0 Hz, H-3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.87 (C-11), 55.70 (C-1a), 56.34 (C-4a), 69.33 (C-9), 71.03 (C-10), 80.87 (C-7), 94.94 (C-8), 111.83 (C-2), 111.89 (C-6), 115.90 (C-5), 117.75 (C-3), 153.12 (C-1), 154.39 (C-4); HRESIMS m/z 219.0973 $[M - H_2O + H]^+$ (calcd for $C_{13}H_{16}O_4$ 235.0971).

Generation of the Key Aldehyde.[17] Oxalyl chloride (272.3 μL, 3.12 mmol) in dry CH_2Cl_2 (9 mL) was added to a stirred solution of DMSO (332 μL, 4.68 mmol) in dry CH_2Cl_2 (1.5 mL) under an argon atmosphere at −78 °C. The mixture was stirred for 15 min, and the alcohol **8** (393.5 mg, 1.56 mmol) or alcohol **17** (300 mg, 1.56 mmol) in dry CH_2Cl_2 (12 mL) was added dropwise (Note: Swern oxidation could be scaled-up to 1.56 mmol of starting material). After the starting material had been consumed (nearly 2 h), Et_3N (1.88 mL, 7.8 mmol) was added. The reaction mixture was stirred at −78 °C for a further 30 min and was allowed to warm to rt and quenched with saturated NH_4Cl and H_2O, and the mixture was stirred for 30 min. The organic phase was decanted off, and the aqueous layer was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure.

3-[2,5-Bis(methoxymethoxy)phenyl]prop-2-ynal ***(9)***. Yield 91%; colorless oil; IR (KBr) ν_{max} 1660, 2194 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 3.46 (3H, s, H-4b), 3.51 (3H, s, H-1b), 5.10 (2H, s, H-4a), 5.21 (2H, s, H-1a), 7.09 (1H, dd, J = 9.2 and 1.2 Hz, H-6), 7.12 (1H, dd, J = 9.1 and 2.2 Hz, H-5), 7.22 (1H, dd, J = 2.2 and 1.3 Hz, H-3), 9.44 (1H, s, H-9); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 56.18 (C-4b), 56.54 (C-1b), 92.05 (C-8), 92.27 (C-7), 95.22 (C-4a), 95.58 (C-1a), 110.70 (C-2), 116.72 (C-6), 122.0 (C-5), 122.09 (C-3), 151.85 (C-4), 154.88 (C-1), 176.92 (C-9); HRESIMS m/z 273.0741 $[M + Na]^+$ (calcd for $C_{13}H_{14}O_5$ 273.0739).

3-(2,5-Dimethoxyphenyl)propiolaldehyde ***(18)***. Yield 91%; colorless oil; IR (KBr) ν_{max} 1656, 2186 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 3.77 (3H, s, H-4a), 3.88 (3H, s, H-1a), 6.86 (1H, d, J = 9.0 Hz, H-6), 7.01 (1H, dd, J = 9.0 and 3.1 Hz, H-5), 7.05 (1H, d, J = 3.0 Hz, H-3), 9.45 (1H, s, H-9); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 56.02 (C-4a), 56.48 (C-1a), 92.37 (C-8), 92.56 (C-7), 108.94 (C-2), 112.36 (C-6), 119.05 (C-5), 119.97 (C-3), 153.29 (C-1), 156.49 (C-4), 176.92 (C-9); HRESIMS m/z 213.0529 $[M + Na]^+$ (calcd. for $C_{11}H_{10}O_3$ 213.0528).

General Procedure for Acetylation. Acetylations were carried out using the standard methodology, which involved dissolving the compound in dry pyridine (5 mL) and adding an excess of Ac_2O at 0 °C. The reaction was complete after 16 h, warmed from 0 °C to room temperature, and quenched by adding distilled H_2O. The product was extracted with EtOAc (3 × 25 mL), and the combined organic layers were washed several times with saturated aqueous $CuSO_4$ until the pyridine had been removed. The organic layer was then dried over anhydrous $NaSO_4$, filtered, and concentrated under vacuum.

2-Hydroxy-2-methylbut-3-yn-1-yl acetate[33] ***(27)***. Yield 89%; colorless oil; IR (KBr) ν_{max} 3278, 2116, 1737 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.48 (3H, s, H-4), 2.11 (3H, s, H-7), 2.45 (1H, s, H-1), 4.10 (2H, dd, J = 7.4 and 11.1 Hz, H-5); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.91 (C-7), 25.98 (C-4), 66.64 (C-1), 70.82 (C-3), 72.53 (C-5), 84.83 (C-2), 171.04 (C-6); HRESIMS m/z 157.0856 $[M + H]^+$ (calcd for $C_8H_{12}O_3$ 157.0865).

4-[2,5-Bis(methoxymethoxy)phenyl]-2-hydroxy-2-methylbut-3-yn-1-yl acetate ***(32)***. Yield 85%; colorless oil; IR (KBr) ν_{max} 3278, 2116, 1737 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.57 (3H, s, H-11), 2.11 (3H, s, H-13), 3.43 (3H, s, H-4b), 3.48 (3H, s, H-1b), 4.10, 4.31 (each 1H, d, J = 11.1 Hz, H-10), 5.07 (3H, s, H-4a), 5.13 (3H, s, H-1a), 6.92 (1H, dd, J = 9.0 and 2.9 Hz, H-5), 6.98 (1H, d, J = 9.0 Hz, H-6), 7.05 (1H, d, J = 2.9 Hz, H-3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.78 (C-13), 25.94 (C-11), 55.85 (C-1a), 56.15 (C-4a), 67.21 (C-9), 70.86 (C-10), 80.34 (C-7), 93.74 (C-8), 94.89 (C-4b), 95.74 (C-4b), 113.81 (C-2), 117.32 (C-5), 118.45 (C-3), 120.84 (C-6), 151.79 (C-4), 152.88 (C-1), 170.77 (C-12); HRESIMS m/z 321.1342 $[M - H_2O + H]^+$ (calcd for $C_{17}H_{22}O_7$ 321.1366).

4-(2,5-Dimethoxyphenyl)-2-hydroxy-2-methylbut-3-yn-1-yl acetate ***(33)***. Yield 90%; yellow oil; IR (KBr) ν_{max} 3445, 2228, 1747 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.60 (3H, s, H-11), 2.14 (3H, s, H-13), 3.74 (3H, s, H-4a), 3.80 (3H, s, H-1a), 4.11, 4.37 (each 1H, d, J = 11.1 Hz, H-10), 6.78 (1H, d, J = 9.0 Hz, H-6), 6.83 (1H, dd, J = 9.0 and 3.1 Hz, H-3), 6.94 (1H, d, J = 3.6 Hz, H-5); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.85 (C-13), 25.94 (C-11), 55.77 (C-4a), 56.38 (C-1a), 67.38 (C-9), 70.95 (C-10), 80.63 (C-7), 93.62 (C-8), 111.9 (C-3), 112.18 (C-2), 116.04 (C-5), 118.24 (C-6), 153.11 (C-1), 154.59 (C-4), 170.83 (C-12); HRESIMS m/z 261.1138 $[M - H_2O + H]^+$ (calcd for $C_{15}H_{18}O_5$ 261.1154).

General Procedure for the Corey−Chaykovsky Epoxidation.[20] Potassium hydride (1.8 mmol) as a 30% mineral oil dispersion was placed in a 25 mL two-necked, round-bottomed flask and washed four times with 10 mL portions of hexanes by swirling, allowing the hydride to settle, and decanting, in order to remove the mineral oil. In a separate 25 mL two-necked round-bottomed flask, dry CH_2Cl_2 (1 mL) was added to trimethylsulfonium methyl sulfate[20] (1.8 mmol) under an argon atmosphere. This solution was added to the first vessel, and the mixture was stirred at rt for 1 h to obtain dimethylsulfonium methylide. A solution of aldehyde **9** (114 mg, 0.6 mmol) or **18** (150 mg, 0.6 mmol) in dry CH_2Cl_2 (3.5 mL) was added, and the reaction mixture was heated under reflux at 60 °C for 6 h under argon to generate the epoxides. Water (10 mL) was added at rt, and the solution was stirred for 30 min. The organic phase was decanted off, and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic phases were washed with brine and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave a residue, which was purified on Sephadex LH-20 eluting with 95% CH_2Cl_2/hexanes.

2-{[2,5-Bis(methoxymethoxy)phenyl]ethynyl}oxirane ***(10)***. Yield 85%; IR (KBr) ν_{max} 2231 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 3.01 (2H, m, H-10), 3.47 (3H, s, H-4b), 3.51 (3H, s, H-1b), 3.57 (1H, t, J = 3.4 Hz, H-9), 5.01 (2H, s, H-4a), 5.13 (2H, s, H-1a), 6.93 (1H, dd, J = 9.0 and 2.9 Hz, H-6), 6.99 (1H, dd, J = 9.0 and 3 Hz, H-5), 7.08 (1H, dd, J = 2.9 and 2.9 Hz, H-3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 40.19 (C-9), 48.97 (C-10), 55.76 (C-4b), 56.07 (C-1b), 79.41 (C-7), 89.55 (C-8),

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94.86 (C-4a), 95.57 (C-1a), 113.30 (C-2), 116.84 (C-6), 118.66 (C-5), 121.00 (C-3), 151.65 (C-1), 153.24 (C-4); HRESIMS *m/z* 287.0905 $[M + Na]^+$ (calcd for $C_{14}H_{16}O_5$ 287.0895).

*2-[(2,5-Dimethoxyphenyl)ethynyl]oxirane (**20**).* Yield 93%; colorless oil; IR (KBr) ν_{max} 2192 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 3.03 (2H, m, H-10), 3.64 (1H, m, H-9), 3.75 (3H, s, H-4a), 3.84 (3H, s, H-1a), 6.80 (1H, d, *J* = 9.1 Hz, H-6), 6.86 (1H, dd, *J* = 9.0 and 3.1 Hz, H-5), 6.95 (1H, d, *J* = 3.1 Hz, H-3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 40.60 (C-9), 49.38 (C-10), 55.96 (C-4a), 56.54 (C-1a), 79.88 (C-7), 89.83 (C-8), 111.67 (C-2), 112.15 (C-6), 116.57 (C-5), 118.54 (C-3), 153.27 (C-4), 155.08 (C-1); HRESIMS *m/z* 205.0865 $[M + H]^+$ (calcd for $C_{12}H_{12}O_3$ 205.0865).

Epoxide Hydrolysis. *4-[2,5-Bis(methoxymethoxy)phenyl]but-3-yne-1,2-diol (**11**).* Compound **10** (42 mg, 0.16 mmol) in H_2O/acetone (1:1) (5 mL) was placed in a flame-dried round-bottomed flask under an argon atmosphere. H_2SO_4 (80 μL) was added dropwise to the solution. The reaction mixture was stirred at rt for 90 min under argon, and the mixture quenched with saturated NH_4Cl (5 mL) and stirred for a further 30 min. The organic layer was separated. The aqueous layer was extracted with EtOAc (4 × 10 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. The crude material was purified by flash silica gel column chromatography, eluting with 40% $CHCl_3$/acetone to give compound **11** (40.4 mg, 90% yield) as a gray, amorphous solid: IR (KBr) ν_{max} 3336, 2197 cm^{-1}; ^1H NMR (CD_3OD, 400 MHz) δ 3.42 (3H, s, H-4b), 3.48 (3H, s, H-1b), 3.64 (1H, dd, *J* = 7.2 and 11.2 Hz, H-10a), 3.70 (1H, dd, *J* = 4.7 and 10.1 Hz, H-10b), 4.55 (1H, d, *J* = 4.7 and 7.2 Hz, H-9), 5.09 (2H, s, H-4a), 5.15 (2H, s, H-4b), 6.80 (1H, dd, *J* = 3.0 and 9.1 Hz, H-5), 6.86 (1H, d, *J* = 9.1 Hz, H-6), 6.94 (1H, d, *J* = 3.0 Hz, H-3); ^{13}C NMR (CD_3OD, 100 MHz) δ 56.12 (C-4a), 56.55 (C-1a), 64.78 (C-9), 67.38 (C-10), 81.98 (C-7), 93.14 (C-8), 96.09 (C-1a), 96.97 (C-4a), 115.62 (C-2), 118.49 (C-6), 119.30 (C-5), 121.93 (C-3), 153.33 (C-1), 156.24 (C-4); HRESIMS *m/z* 282.1053 $[M + Na + H]^+$ (calcd for $C_{12}H_{18}O_6$ 282.1080).

*4-(2,5-Dimethoxyphenyl)but-3-yne-1,2-diol (**22**).* Compound **20** (20 mg, 0.1 mmol) in dry CH_2Cl_2 (2 mL) was placed in a flame-dried round-bottomed flask under an argon atmosphere, and H_2SO_4 (1M, 8 mL) was added to the solution. The reaction mixture was heated under reflux at 50 °C for 24 h under argon. The mixture was cooled to rt and stirred for 16 h, the mixture was cooled to 0 °C, $NaHCO_3$ was added to give pH = 7, and the solution was stirred for 30 min. The organic phase was decanted off, and the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. The crude material was purified by silica gel column chromatography, eluting with 60% EtOAc/hexanes, to give compound **22** (18.9 mg, 87% yield) as a gray, amorphous solid: IR (KBr) ν_{max} 3346, 2187 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 3.75 (3H, s, H-4a), 3.81 (2H, s, H-10), 3.82 (3H, s, H-1a), 4.70 (1H, m, H-9), 6.79 (1H, d, *J* = 9.0 Hz, H-6), 6.85 (1H, dd, *J* = 9.0 and 3.0 Hz, H-5), 6.94 (1H, d, *J* = 3.0 Hz, H-3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 55.80 (C-4a), 56.33 (C-1a), 64.05 (C-9), 66.65 (C-10), 82.77 (C-7), 90.83 (C-8), 111.57 (C-2), 11.87 (C-6), 116.23 (C-5), 118.09 (C-3), 153.16 (C-1), 154.62 (C-4); HRESIMS *m/z* 205.0871 $[M - H_2O]^+$ (calcd for $C_{12}H_{14}O_4$ 205.0892).

General Procedure for the Grignard Reaction.[23] Compound **9** (150 mg, 0.599 mmol) or **18** (50 mg, 0.26 mmol) in dry THF (7.5 mL) was placed in a flame-dried round-bottomed flask under an argon atmosphere at 0 °C. The mixture was stirred for 5 min, and MeMgBr in THF (1M, 1.5 equiv) was added dropwise to the solution over 5 min. The reaction mixture was warmed to rt and stirred for 2.5 h. The mixture was cooled to 0 °C, quenched with saturated NH_4Cl, and stirred for a further 30 min. The aqueous layer was extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave a residue, which was purified on Sephadex LH-20 eluting with 95% CH_2Cl_2/hexanes to give compound **15** (159 mg, 99% yield) or compound **19** (54 mg, 99% yield) as a yellow oil.

4-[2,5-Bis(methoxymethoxy)phenyl]but-3-yn-2-ol[23] *(**15**).* IR (KBr) ν_{max} 3398, 2226 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.51 (3H, d, *J* = 6.6 Hz, H-10), 3.43 (3H, s, H-4b), 3.48 (3H, s, H-1b), 4.74 (1H, q, *J* = 6.6 Hz, H-9), 5.06 (3H, s, H-4a), 5.14 (3H, s, H-1a), 6.90 (1H, dd, *J* = 9.0 and 3.0 Hz, H-5), 6.98 (1H, d, *J* = 9.0 Hz, H-6), 7.06 (1H, d, *J* = 3.0 Hz, H-3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.28 (C-10), 55.91 (C-4b), 56.25 (C-1b), 58.70 (C-9), 79.86 (C-7), 94.96 (C-4a), 95.41 (C-8), 95.83 (C-1a), 114.33 (C-2), 117.25 (C-6), 118.23 (C-5), 120.94 (C-3), 151.87 (C-4), 152.81 (C-1); HRESIMS *m/z* 289.1057 $[M + Na]^+$ (calcd for $C_{14}H_{18}O_5$ 289.1154).

4-(2,5-Dimethoxyphenyl)but-3-yn-2-ol[23] *(**19**).* IR (KBr) ν_{max} 3427, 2193 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.57 (3H, d, *J* = 7.0 Hz, H-10), 3.76 (3H, s, H-4a), 3.83 (3H, s, H-1a), 4.80 (1H, q, *J* = 6.6 Hz, H-9), 6.79 (1H, d, *J* = 9.0 Hz, H-6), 6.84 (1H, dd, *J* = 9.0 and 3.0 Hz, H-5), 6.94 (1H, d, *J* = 3.0 Hz, H-3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.46 (C-10), 55.93 (C-4a), 56.55 (C-1a), 59.14 (C-9), 80.35 (C-7), 95.22 (C-8), 112.16 (C-6), 112.35 (C-2), 116.0 (C-5), 118.46 (C-3), 153.31 (C-1), 154.42 (C-4); HRESIMS *m/z* 189.0918 $[M - H_2O + H]^+$ (calcd for $C_{12}H_{14}O_3$ 189.0943).

Dehydration Methodology.[24] (Carboxysulfamoyl)triethylammonium hydroxide inner salt methyl ester[34,35] (Burgess' reagent) (70 mg, 0.29 mmol, 3.9 equiv) in dry benzene (2 mL) and **15** (20 mg, 0.19 mmol) in dry benzene (1 mL) were placed in a flame-dried round-bottomed flask under an argon atmosphere. The mixture was heated under reflux at 110 °C for 18 h. A further portion of Burgess' reagent (54 mg, 0.23 mmol, 3 equiv) was added to the reaction mixture, and this was heated under reflux for 24 h. Finally, an additional 3 equiv of Burgess' reagent was added to the reaction mixture, and this was heated under reflux for 24 h. The reaction mixture was cooled to rt, quenched with saturated brine (5 mL), and stirred for a further 30 min, and the organic layer was decanted off. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and evaporated under reduced pressure. The crude material was purified by silica gel column chromatography, eluting with 15% EtOAc/hexanes, to give compound **14** (15.1 mg, 81% yield) as a yellow oil.

*2-But-3-en-1-yn-1-yl-1,4-bis(methoxymethoxy)benzene (**14**).* IR (KBr) ν_{max} 2330, 1741 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 3.46 (3H, s, H-4b), 3.52 (3H, s, H-1b), 5.10 (3H, s, H-4a), 5.17 (3H, s, H-1a), 5.53 (1H, dd, *J* = 11.1 and 2.1 Hz, H-10), 5.73 (1H, dd, *J* = 17.5 and 2.1 Hz, H-10), 6.04 (1H, dd, *J* = 17.5 and 11.1 Hz, H-9), 6.93 (1H, dd, *J* = 9.0 and 3.0 Hz, H-5), 7.02 (1H, d, *J* = 9.0 Hz, H-6), 7.11 (1H, d, *J* = 3.0 Hz, H-3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 56.08 (C-4b), 56.39 (C-1b), 86.21 (C-8), 92.17 (C-7), 95.17 (C-4a), 96.03 (C-1a), 114.97 (C-2), 117.40 (C-6), 117.47 (C-9), 118.40 (C-5), 120.96 (C-3), 127.06 (C-10), 152.05 (C-4), 152.95 (C-1); HRESIMS *m/z* 287.0905 $[M + Na]^+$ (calcd for $C_{14}H_{16}O_5$ 287.0896).

*2-But-3-en-1-yn-1-yl-1,4-dimethoxybenzene (**21**).* Yield 80%; colorless oil; IR (KBr) ν_{max} 2194 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 3.75 (1H, s, H-4a), 3.84 (1H, s, H-1a), 5.53 (1H, dd, *J* = 11.2 and 2.1 Hz, H-10), 5.75 (1H, dd, *J* = 17.5 and 2.1 Hz, H-10), 6.06 (1H, dd, *J* = 17.5 and 11.2 Hz, H-9), 6.79 (1H, d, *J* = 9.0 Hz, H-6), 6.83 (1H, dd, *J* = 9.0 and 2.9 Hz, H-5), 6.95 (1H, d, *J* = 2.9 Hz, H-3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 56.43 (C-1a), 55.79 (C-4a), 86.17 (C-7), 92.09 (C-8), 111.97 (C-2), 112.75 (C-9), 115.84 (C-6), 117.33 (C-5), 118.1 (C-3), 126.84 (C-10), 153.18 (C-4), 154.38 (C-1); HRESIMS *m/z* 189.0920 $[M + H]^+$ (calcd for $C_{12}H_{12}O_2$ 189.0916).

Deprotection Study. *4-[2,5-Bis(methoxymethoxy)phenyl]-2-methoxy-2-methylbut-3-yn-1-ol (**12**).* Compound **10** (0.1 mmol) in MeOH (2.8 mL) was placed in a flame-dried round-bottomed flask under an argon atmosphere. H_2SO_4 (95 μL) was added dropwise to the solution, and this was stirred for 30 min. The reaction mixture was quenched with saturated NH_4Cl and stirred for a further 30 min, and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. The crude material was purified by silica gel column chromatography, eluting with 60% EtOAc/hexanes, to give compound **12** (27.9 mg, 90% yield) as a colorless oil, which was highly air-sensitive (the compound needs to be frozen and kept in the dark under argon). IR (KBr) ν_{max} 3336, 2197 cm^{-1}; ^1H NMR (CD_3OD, 400 MHz) δ 3.43 (3H, s, H-11), 3.70 (2H, m, H-10), 4.26 (1H, dd, *J* = 6.3 and 5.1 Hz, H-9), 6.73 (1H, s, H-3), 6.73 (1H, d, *J* = 1.0 Hz, H-5), 6.78 (1H, dd, *J* = 2.4 and

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1.1 Hz, H-6); ^{13}C NMR (CD_3OD, 100 MHz) δ 55.75 (C-11), 64.83 (C-10), 73.28 (C-9), 82.53 (C-7), 90.46 (C-8), 109.74 (C-2), 116.16 (C-6), 117.50 (C-5), 117.97 (C-3), 149.95 (C-4), 151.53 (C-1); HRESIMS m/z 207.0714 $[M - H]^+$ (calcd for $C_{11}H_{12}O_4$ 207.0736).

Speciosin P. Compound **11** (22 mg, 0.078 mmol) in MeOH (1 mL) was placed in a flame-dried round-bottomed flask under an argon atmosphere, and $HCl_{[33\%]}$ (10 μL) was added to the solution. The reaction mixture was heated under reflux at 70 °C for 2 h. The mixture was cooled to rt, and saturated $KHCO_3$ (5 mL) was added to adjust the pH of the solution to 7. The aqueous phase was extracted with EtOAc (4 × 10 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. The crude material was purified by silica gel column chromatography, eluting with 40% $CHCl_3$/acetone, to give the natural product (±)-speciosin P (**2**) (15.1 mg, 90% yield) as a colorless oil. The spectroscopic data corresponded to the literature data.[2]

*2-(3-Hydroxyprop-1-yn-1-yl)benzene-1,4-diol (**23**).* Compound **8** (20 mg, 0.079 mmol) in MeOH (1 mL) was placed in a flame-dried round-bottomed flask under an argon atmosphere, and $HCl_{[33\%]}$ (10 μL) was added to the solution. The reaction mixture was heated under reflux at 70 °C for 2 h under argon. The mixture was cooled to rt, and saturated $KHCO_3$ (5 mL) was added to adjust the pH of the solution to 7. The aqueous phase was extracted with EtOAc (4 × 10 mL), and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. The crude material was purified by silica gel column chromatography, eluting with 40% $CHCl_3$/acetone, to give **23** (12 mg, 94% yield) as a colorless oil: IR (KBr) ν_{max} 3270, 2193 cm^{-1}; ^{1}H NMR (CD_3OD, 400 MHz) δ 4.41 (2H, s, 9-H), 6.63 (1H, dd, J = 8.0 and 2.6 Hz, 3-H), 6.67 (1H, d, J = 8.0 Hz, 5-H), 6.71 (1H, dd, J = 2.6 Hz, 3-H); ^{13}C NMR (CD_3OD, 100 MHz) δ 51.43 (C-9), 81.92 (C-7), 92.58 (C-8), 111.53 (C-2), 117.15 (C-6), 118.22 (C-3), 119.40 (C-5), 151.03 (C-4), 152.47 (C-1); HRESIMS m/z 163.0387 $[M - H]^+$ (calcd for $C_9H_8O_3$ 163.0395).

*2-(3-Hydroxybut-1-yn-1-yl)benzene-1,4-diol (**24**).* Yield 90%; colorless oil; IR (KBr) ν_{max} 3342, 2197 cm^{-1}; ^{1}H NMR (C_2D_6CO, 500 MHz) δ 1.44 (3H, d, J = 6.6 Hz, H-10), 4.69 (1H, q, J = 6.6 Hz, H-9), 6.70 (1H, dd, J = 8.7 and 2.7 Hz, H-5), 6.73 (1H, dd, J = 8.7 and 0.8 Hz, H-5), 6.75 (1H, dd, J = 2.7 and 0.8 Hz, H-3); ^{13}C NMR (C_2D_6CO, 125 MHz) δ 24.94 (C-10), 58.64 (C-9), 79.33 (C-7), 97.73 (C-8), 111.10 (C-2), 116.99 (C-6), 118.05 (C-5), 118.78 (C-3), 150.89 (C-4), 152.06 (C-1); HRESIMS m/z 179.0713 $[M + H]^+$ (calcd for $C_{10}H_{10}O_3$ 179.0709).

Speciosin G. Compound **14** (20 mg, 0.081 mmol) in MeOH (2 mL) was placed in a flame-dried round-bottomed flask under an argon atmosphere, $HCl_{[33\%]}$ (20 μL) was added to the solution, and the reaction mixture was heated under reflux at 70 °C for 90 min. The mixture was cooled to rt, and saturated aqueous $KHCO_3$ (5 mL) was added to adjust the pH of the solution to 7. The aqueous phase was extracted with EtOAc (4 × 10 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. The crude material was purified by HPLC D7000, eluting with 30% EtOAc/hexanes, to give the natural product speciosin G (**1**) (11.6 mg, 90% yield) (retention time 12.3 min) as a colorless oil. The spectroscopic data corresponded to the literature data.[1]

Wheat Coleoptile Bioassays. Wheat seeds (*Triticum aestivum* L. cv. Catervo) were sown in 15 cm diameter Petri dishes moistened with H_2O and grown in the dark at 22 ± 1 °C for 3 days.[36] The roots and caryopses were removed from the shoots and were placed in a Van der Weij guillotine, and the apical 2 mm was cut off and discarded. The next 4 mm of the coleoptiles was removed and used for the bioassay. All manipulations were performed under a green safelight.[37] Test solutions of each compound were prepared in a phosphate-citrate buffer solution containing 2% sucrose adjusted to pH 5.6 at concentrations of 1000, 333, 100, 33, and 10 μM. Parallel controls were also run. Five coleoptiles were placed in each test tube containing test or control solutions (2 mL) (three replicates per dilution). The test tubes were rotated at 0.25 rpm on a roller tube apparatus for 24 h at 22 °C in the dark. The coleoptiles were digitally photographed and measured. Data were statistically analyzed using Welch's test,[38] and results are presented as percentage differences from control. Thus, zero represents the control, positive values represent growth stimulation, and negative values represent growth inhibition.

■ ASSOCIATED CONTENT

Supporting Information

Analytical data including ^{1}H and ^{13}C NMR spectra and selected mass spectra for new compounds are illustrated. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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