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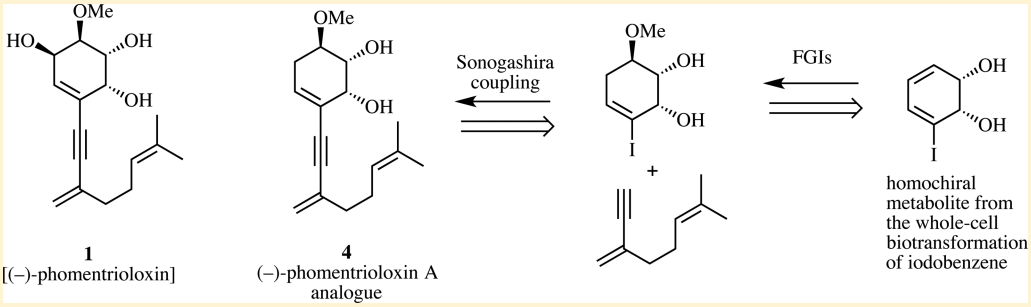
The Synthesis of Certain Phomentrioloxin A Analogues and Their Evaluation as Herbicidal Agents

Ehab S. Taher,[†] Prue Guest,[†] Amanda Benton,[†] Xinghua Ma,[†] Martin G. Banwell,*[,†] Anthony C. Willis,[†] Tobias Seiser,[‡] Trevor W. Newton,[‡] and Johannes Hutzler[‡]

[†]Research School of Chemistry, Institute of Advanced Studies, The Australian National University, Canberra, Australian Capital Territory 2601, Australia

[‡]BASF SE, Carl-Boschstrasse 38, Ludwigshafen 67056, Germany

Supporting Information



ABSTRACT: A series of 28 analogues of the phytotoxic geranylcyclohexentriol (−)-phomentrioloxin A (**1**) has been synthesized through cross-couplings of various enantiomerically pure haloconduritols or certain deoxygenated derivatives with either terminal alkynes or borylated alkenes. Some of these analogues display modest herbicidal activities, and physiological profiling studies suggest that analogue **4** inhibits photosystem II in isolated thylakoids in vitro.

INTRODUCTION

Among agricultural pests, weeds have the most significant adverse effects on crop productivity,[1] and the absence of good means for controlling them is a primary source of concern for farmers.[2] As a consequence, herbicidal applications outstrip the combined use of fungicides and insecticides in the U.S.A. and probably in many other countries as well.[3] The ongoing development of resistance to current herbicides has prompted an intense search for new ones with novel modes of action, but there has been little recent success in this regard.[4]

Natural products have attracted attention as potential sources of new agrochemicals or at least inspirations for them.[5] However, in contrast to the impressive contributions natural products have made to the development of new therapeutic agents,[6] they have not, thus far, been particularly useful sources of herbicides.[4,5] In an effort to redress this situation, certain studies have focused on phytotoxic metabolites produced by fungi associated with economically significant weeds. For example, while seeking new agents to control the saffron thistle (*Carthamus lantus* L. ssp. *lanatus*), a widespread winter-growing annual weed of both pastures and crops that has been declared noxious throughout Australia, Evidente and co-workers[7] identified pathogenic strains of *Phomopsis* sp. and the teleomorph *Diaporthe gulyae* associated, respectively, with diseased strains of the saffron thistle and with the sunflower (*Helianthus annuus* L.). Three of the various phytotoxic metabolites produced by these fungi were identified as phomentrioloxins A−C (structures **1**−**3**, respectively, in Figure 1) that embody a polyoxygenated cyclohexene "core" and a geranyl-type "side-chain". The illustrated structure of the first of

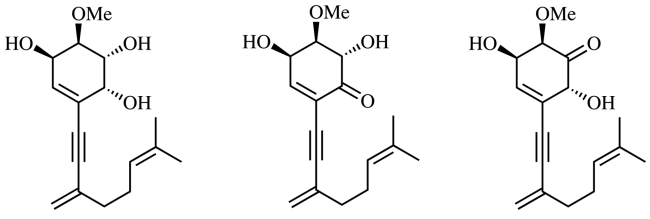


Figure 1. Structures of phomentrioloxins A−C (**1**−**3**, respectively).

these metabolites, *viz.* compound **1**, was confirmed by our synthesis[8] of it from a homochiral *cis*-1,2-dihydrocatechol of defined absolute stereochemistry that is readily produced through the whole-cell biotransformation of iodobenzene. A key feature of our synthesis was the linking of an iodinated mono-*O*-methylated conduritol with the relevant terminal alkyne using a Sonogashira cross-coupling reaction.

Evidente and co-workers carried out a small structure−activity relationship study on derivatives of phomentrioloxin A. This

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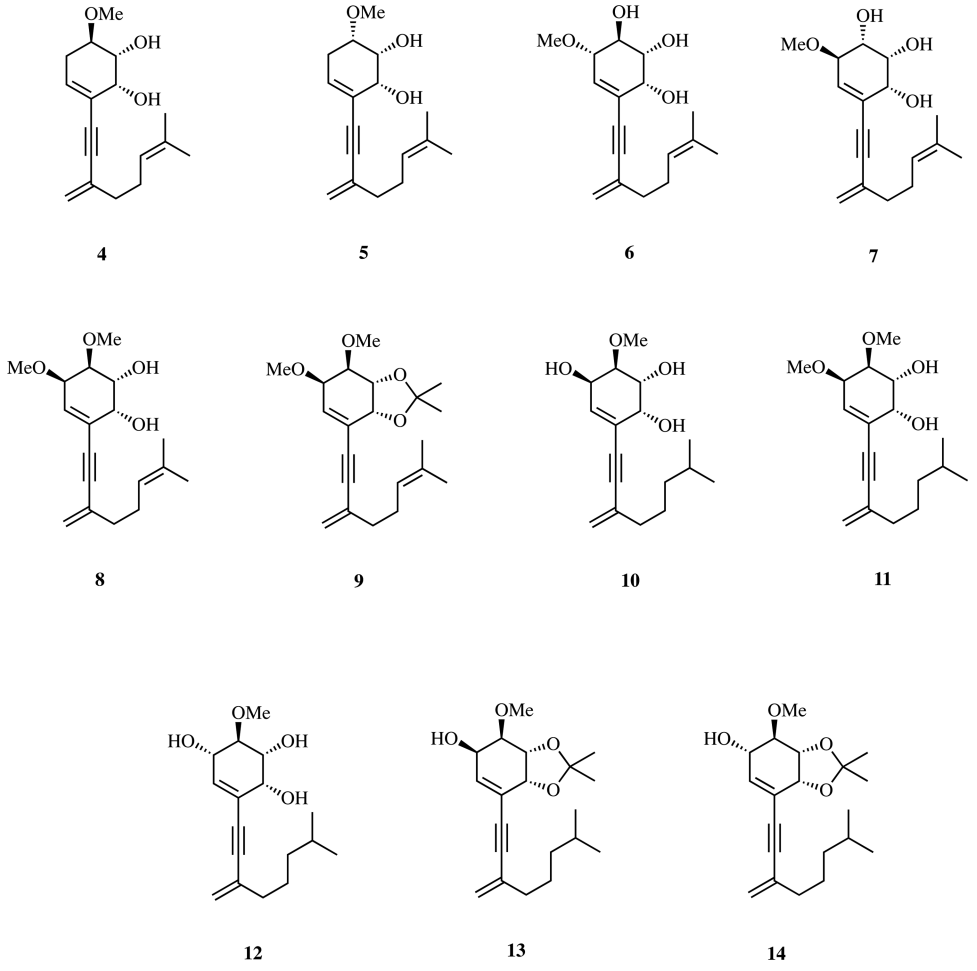

Figure 2. Phomentrioloxin analogues **4**–**14** prepared for the present study that retain the geranyl-type side-chain.

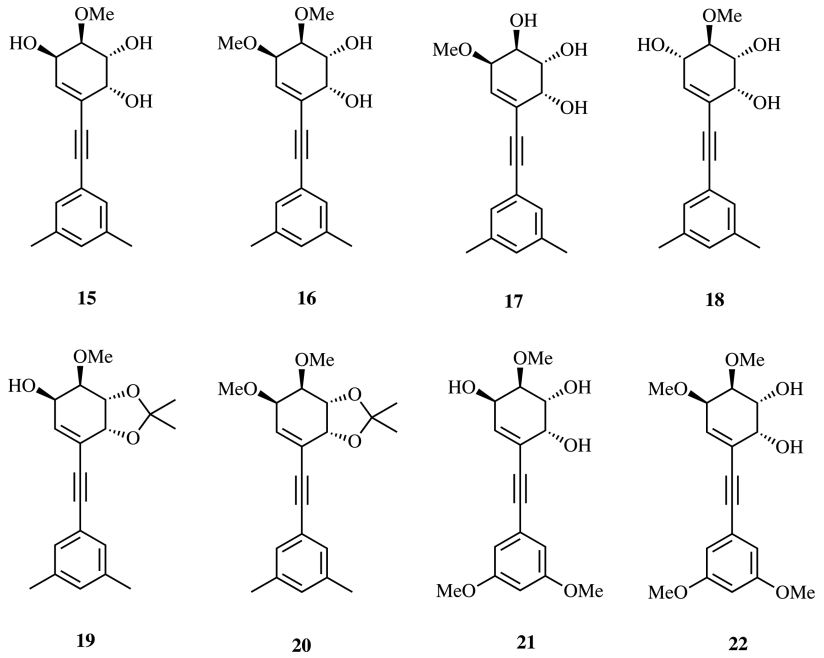

Figure 3. Phomentrioloxin analogues **15**–**22** prepared for the present study and incorporating a phenylacetylene-type side-chain.

revealed that various structural modifications of it led to changes in phytotoxic properties[7a,9] and, as a result, it was suggested that such natural products could form the basis for developing mycoherbicides for the biocontrol of noxious weeds including saffron thistle. Given the potential flexibility of our synthetic route to natural product **1**, we sought to prepare a collection of

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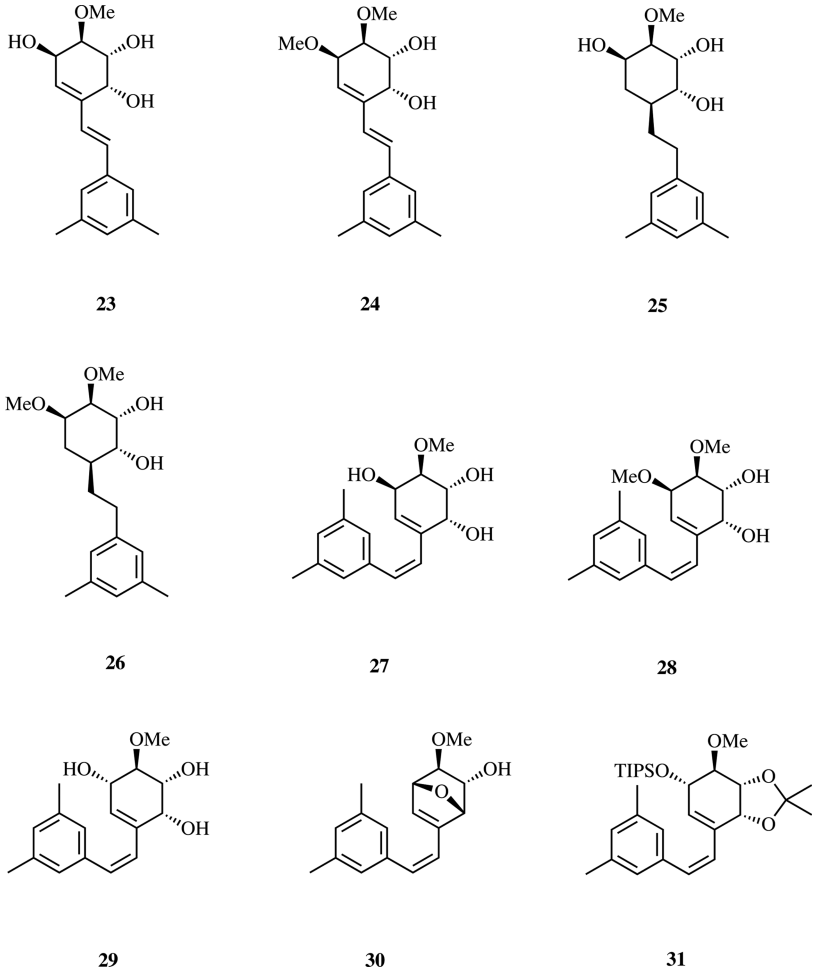

Figure 4. Phomentrioloxin analogues **23**–**31** prepared for the present study and incorporating a styrenyl or phenylethane-type side-chain.

otherwise difficult-to-access analogues and subject these to commercially relevant screening regimes, including ones that could provide insights into their modes of action. The outcomes of such studies are reported here.

RESULTS AND DISCUSSION

Chemical Synthesis Studies. The first tranche of phomentrioloxin analogues to be prepared were compounds **4**–**14** (Figure 2), wherein variations were made to the nature of the oxygenation pattern in the cyclohexene core and, in parallel, to the degree of unsaturation in the geranyl-type tail (see structures **10**–**14**).

The second tranche of analogues, namely compounds **15**–**22** (Figure 3), also involved variations in the nature of the oxygenation pattern within the core and, more significantly, variations to the side-chain. Specifically, the geranyl-type tail associated with the natural product **1** was replaced with a C_{10}-containing arylacetylene unit that it was thought would represent a similarly lipophilic but potentially more stable motif. Several 3,5-dimethoxy-substituted arylacetylene side-chains were introduced in an effort to explore the impact of modifications to electron density within this part of the molecular framework.

The final tranche of analogues, namely compounds **23**–**31** (Figure 4), involved, *inter alia*, systems incorporating *E*- or *Z*-configured styrenyl or *β*-arylethyl-type side-chains as well as variations within the core. Throughout the collection of analogues, certain acetonide-containing precursors were also tested as another means of investigating the impact of increased lipophilicity of the cyclohexene core on activity. The exhaustively protected precursor, **31**, to triol **29** was also subject to biological evaluation for the same reasons.

The reaction sequence shown in Scheme 1 is indicative of the protocols employed in the synthesis of the above-mentioned phomentrioloxin A analogues. It follows that employed in our synthesis of the "parent" system **1**.[8] Thus, the *cis*-1,2-dihydrocatechol **32**, which is readily obtained in enantiomerically pure form through the whole-cell biotransformation of iodobenzene,[10,11] was converted into the corresponding acetonide under previously defined conditions and thus affording the known[12] and rather unstable compound **33**. Regio- and diastereo-selective *cis*-dihydroxylation of the nonhalogenated double bond within diene **33** proceeded readily under the UpJohn conditions[13] to give diol **34**[12] (62% from **32**) that was subject to 2-fold *O*-methylation using methyl iodide and thus providing the bis-ether **35** in 47% yield. Sonogashira cross-coupling of this last compound with the known[14] and readily accessible terminal alkyne **36** under standard conditions using cuprous iodide and $PdCl_2(PPh_3)_2$ in the presence of diethylamine then gave the targeted phomentrioloxin analogue **9** in 48% yield.

Hydrolytic cleavage of the acetonide residue within the last compound could be achieved by heating it in an acetic acid/water mixture at 70 °C for 5 h and thus affording an *O*-methyl ether derivative, **8**, of phomentrioloxin in 81% yield. All the spectral

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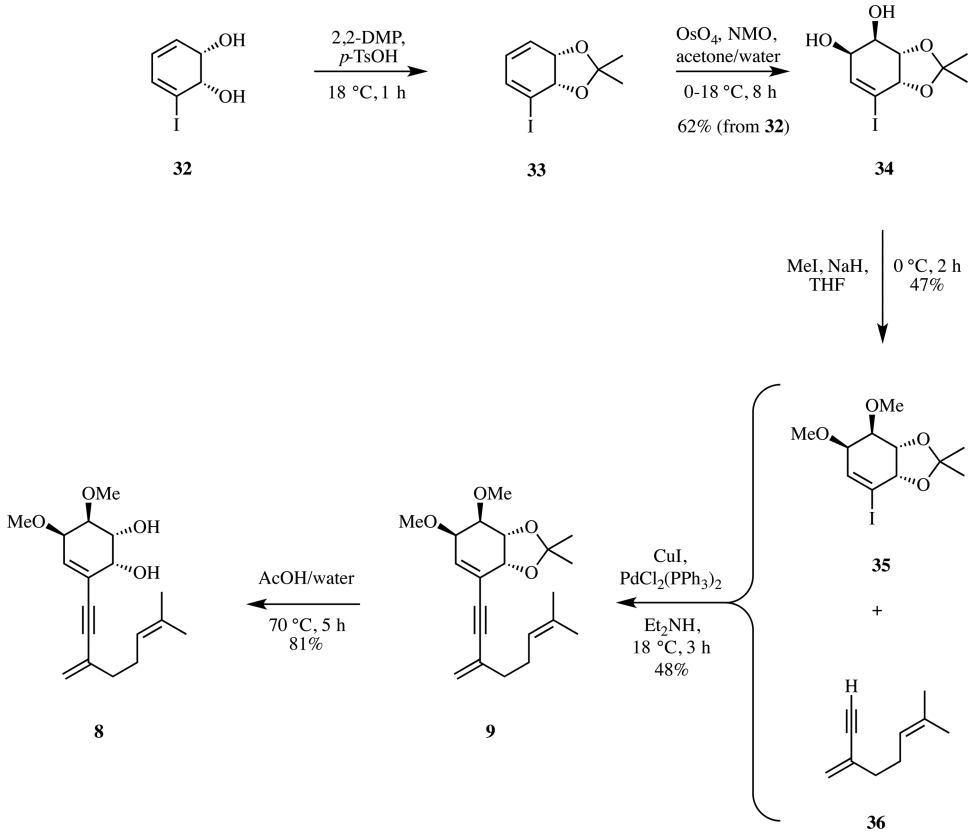
Scheme 1. Synthetic Sequence Used To Prepare Phomentrioloxin Analogues 8 and 9



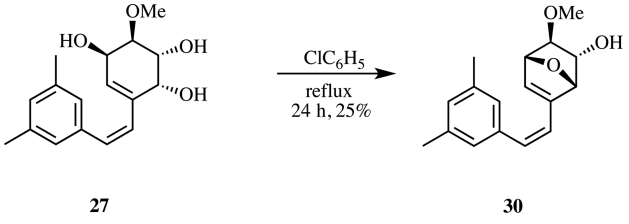
data acquired on compounds **8** and **9** were in complete accord with the assigned structures.

The syntheses of remaining analogues used in this study are detailed below. In broad terms, these involved straightforward modifications of the protocols defined above with the head and tail "sections"/side-chains of these analogues being linked through either Sonogashira or Suzuki–Miyaura cross-coupling protocols. Post-coupling chemical modifications included acetonide group cleavages, thermally induced *Z*- to *E*-olefin isomerizations, and/or exhaustive catalytic hydrogenation of the olefinic residues within compounds **23** and **24** (and thus affording, as single diastereoisomers, **25** and **26**, respectively).

The formation of the 7-oxabicyclo[2.2.1]heptene-containing analogue **30** from precursor **27** on thermolysis in refluxing chlorobenzene (Scheme 2) clearly involves a cyclodehydration reaction. Interestingly, under the conditions used there was no accompanying *Z*- to *E*-isomerization of the styrenyl double bond.

Single-crystal X-ray analyses were secured on compounds **15**, **23**, and **27** as well as certain precursors to congeners **7**–**9** and **17**.

Scheme 2. Thermally Induced Cyclodehydration of Triol 27 Leading to Compound 30



Details of these are provided in the Experimental Section and the SI.

The reaction sequence used to prepare compound **4**, one of the more active of the phomentrioloxin analogues, is shown in Scheme 3. Thus, the previously reported epoxide **38**,[15] which is readily obtained over two steps from diol **34**, was subjected to reductive cleavage with DIBAl-H and thus providing the homoallylic alcohol **39** (72%). *O*-Methylation of the last compound under Irvine–Purdie conditions then gave ether **40** (47%), the acetonide residue of which was cleaved using acidified AG-50W-X8 resin in THF/methanol to afford *cis*-diol **41** (88%). Finally, Sonogashira coupling of compound **41** with dienyne **36** under essentially the same conditions as described above for the conversion **35** + **36** → **9** gave analogue **4** in 64% yield.

A related sequence of reactions, as shown in Scheme 4, was used to obtain analogue **5**. Thus, compound **32**[10] was treated with *N*-bromosuccinimide (NBS) in wet THF, and the resulting bromohydrin **42**[16] immediately treated with 2,2-dimethoxypropane (2,2-DMP) and *p*-toluenesulfonic acid monohydrate (*p*-TsOH·H_2O) and so producing acetonide **43** (71% from **32**). Reaction of this last compound with sodium hydroxide in a water/glyme mixture then gave epoxide **44** (44%) that was reductively cleaved with DIBAl-H and produced alcohol **45** (66%) that was *O*-methylated under standard conditions and thus providing ether **46** (71%). An acetonide hydrolysis/Sonogashira coupling sequence then gave, via intermediate diol **47** (64%), the target analogue **5** in 60% yield over the last step.

Phomentrioloxin analogue **6** was readily produced from epoxide **38** (Scheme 5) by reacting this with methanol in the presence of (+)-camphorsulfonic acid [(+)-CSA]. The protected conduritol **48** (45%) thus obtained was subjected to acetonide hydrolysis under standard conditions, affording triol **49** (75%).

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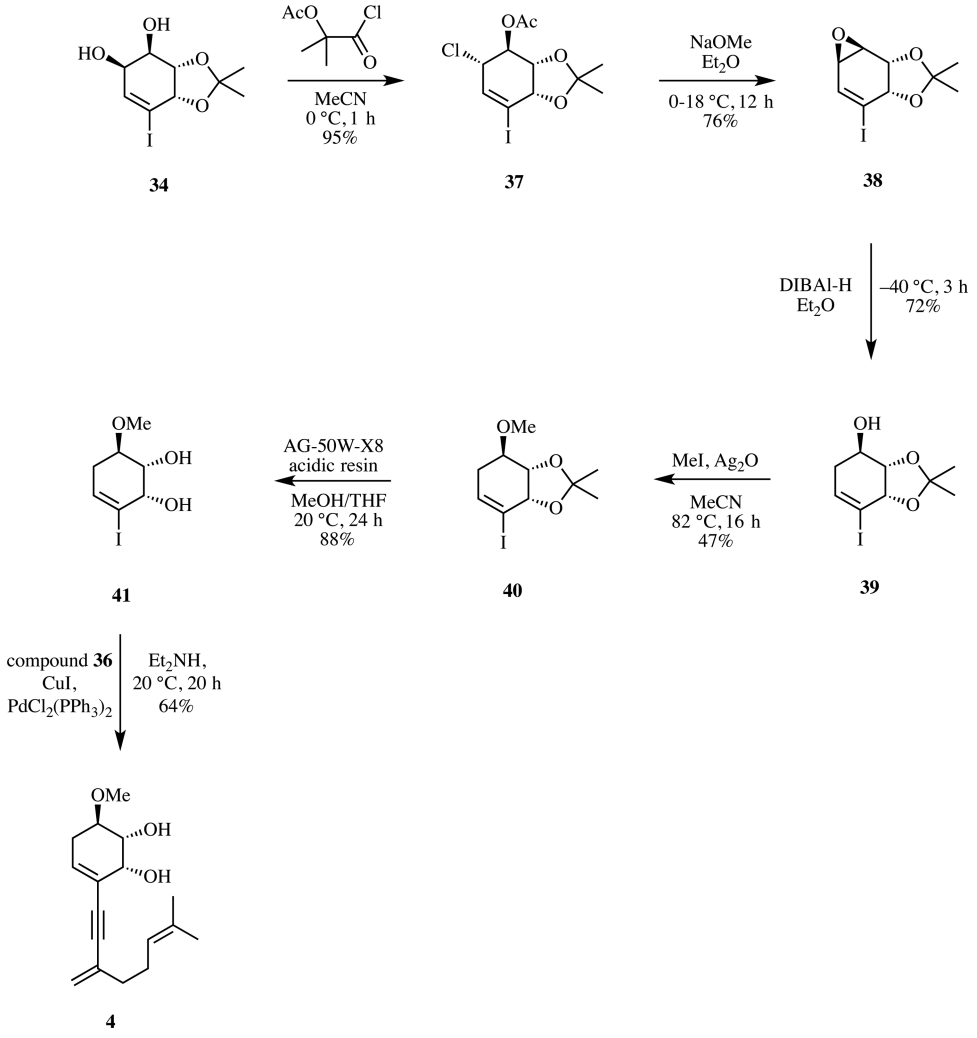
Scheme 3. Reaction Sequence Leading to Phomentrioloxin A Analogue 4



Sonogashira cross-coupling of this last compound with terminal alkyne **36** then gave compound **6** (40%).

The preparation of analogue **7** followed the same sort of synthetic pathway (Scheme 6). Thus, the acetonide unit within the product, **50** (93%), of acid-catalyzed methanolysis of epoxide **44** was cleaved in the usual way to give triol **51** (36%) that was itself cross-coupled with alkyne **36**, affording compound **7** (34%).

The reaction sequence used to prepare the enyne side-chain synthon required for the preparation of analogues **10**–**14** is shown in Scheme 7. This started with the commercially available and unsaturated ketone **52** that was hydrogenated under conventional conditions to afford its saturated counterpart **53**[17] (81%). This was converted, via a kinetically controlled deprotonation process, into the enol triflate **54** (68%) that was itself subjected to a Sonogashira cross-coupling reaction with trimethylsilylacetylene, affording the silyl-capped alkyne **55** (85%). Treatment of this last compound with potassium carbonate in methanol resulted in removal of the silyl group and the formation of the required terminal alkyne **56** (73%).

The side-chain synthon **56** was first exploited in the synthesis of the phomentrioloxin analogue **10** by using the reaction sequence shown in Scheme 8. Thus, alcohol **57**,[8] the previously reported product of the regio-controlled *O*-silylation of diol **34**, was subject to reaction with methyl iodide in the presence sodium hydride, and a chromatographically separable mixture of the regio-isomeric *O*-methyl ethers **58** (8%) and **59**[8] (90%) thereby was obtained. Heating a solution of the latter product with wet acetic acid resulted in hydrolysis of the acetonide group and formation of triol **60**[8] (68%) that was coupled with compound **56** under the now standard Sonogashira conditions and thus producing analogue **10** in 80% yield.

In a slightly different timing of the side-chain installation process, bis-ether **35** (Scheme 9) was cross-coupled with enyne **56** to give compound **61** (96%) that was itself subject to acetonide hydrolysis using acetic acid/water. By such means, analogue **11** was obtained in 60% yield.

As was the case with analogue **6**, epoxide **38** served as the starting material for the synthesis of the cyclohexene-containing headgroup associated with target compounds **12** and **14** (Scheme 10). In the present case, however, the three-membered ring within compound **38** was cleaved with potassium hydroxide, and the *trans*-diol **62**[15] (72%) so-formed was selectively silylated at the oxygen of the allylic alcohol moiety (rather than the homoallylic one) using triisopropylsilyl triflate (TIPSOTf) in the presence of 2,6-lutidine and produced compound **63** (49%). *O*-Methylation of this last compound proceeded uneventfully, and product **64** (65%) was then treated with tetra-*n*-butylammonium fluoride (TBAF) to give the protected conduritol **65** (90%) that could be cross-coupled with terminal alkyne **56** to give analogue

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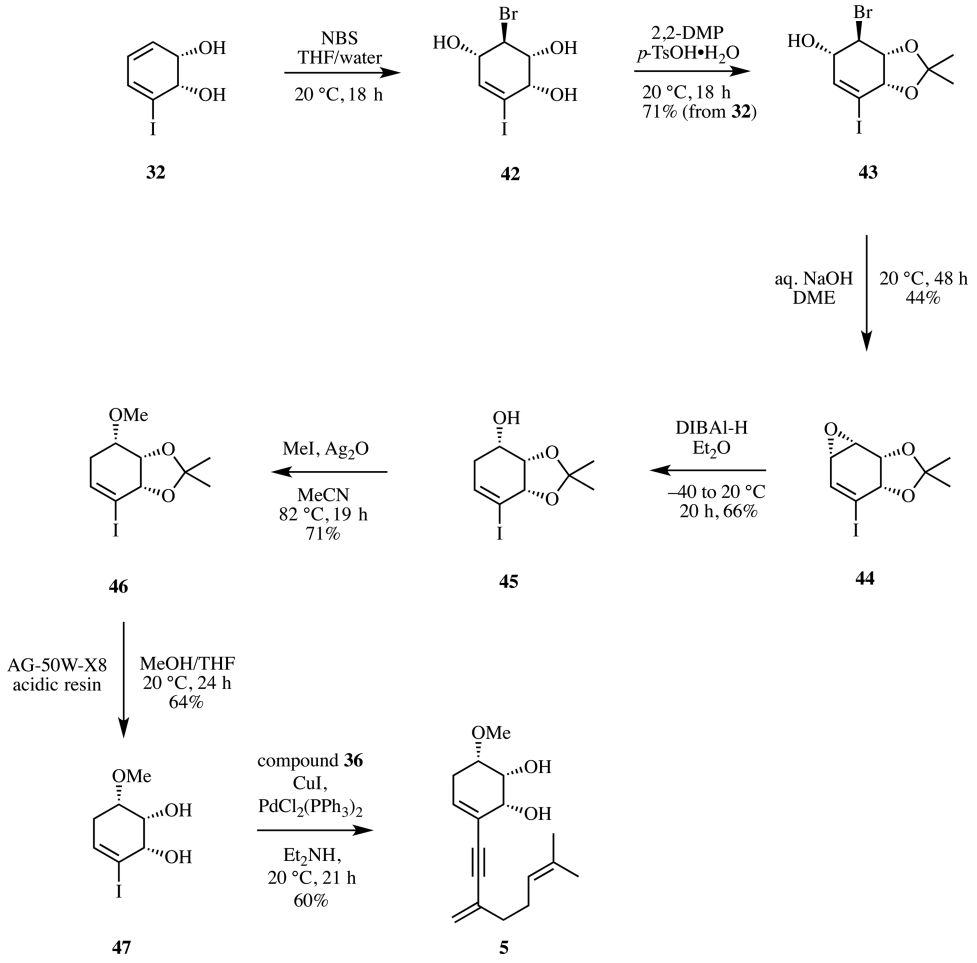
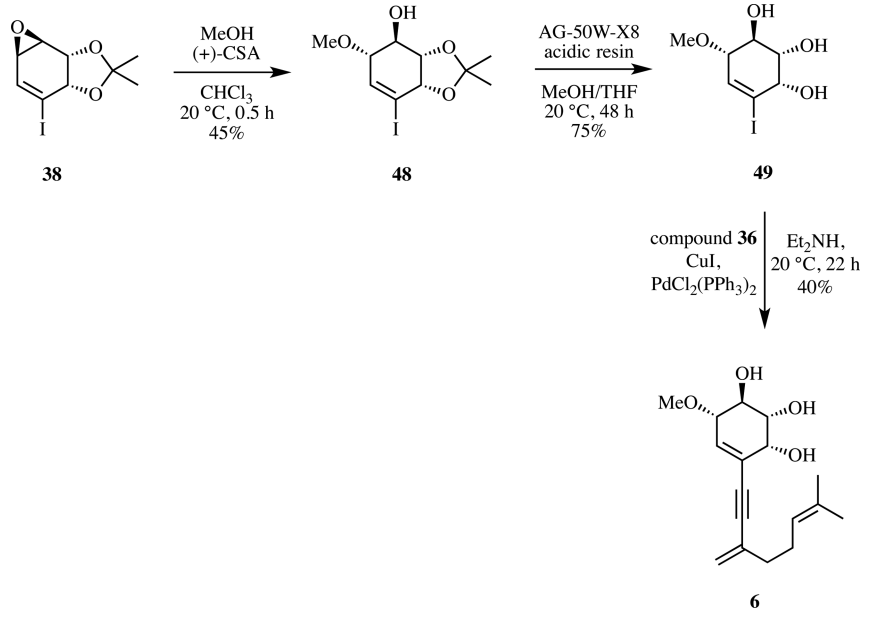
Scheme 4. Reaction Sequence Leading to Phomentrioloxin A Analogue 5



Scheme 5. Reaction Sequence Leading to Phomentrioloxin A Analogue 6



14 (68%). Cleavage of the acetonide residue within this last compound was a straightforward matter, and analogue **12** (72%) was thereby obtained.

The synthesis of analogue **13** is shown in Scheme 11 and exploited an intermediate associated with the preparation of congener **10** (see Scheme 8). Thus, silyl ether **59** was treated with TBAF, and the resulting alcohol **66**[8] (88%) was then cross-

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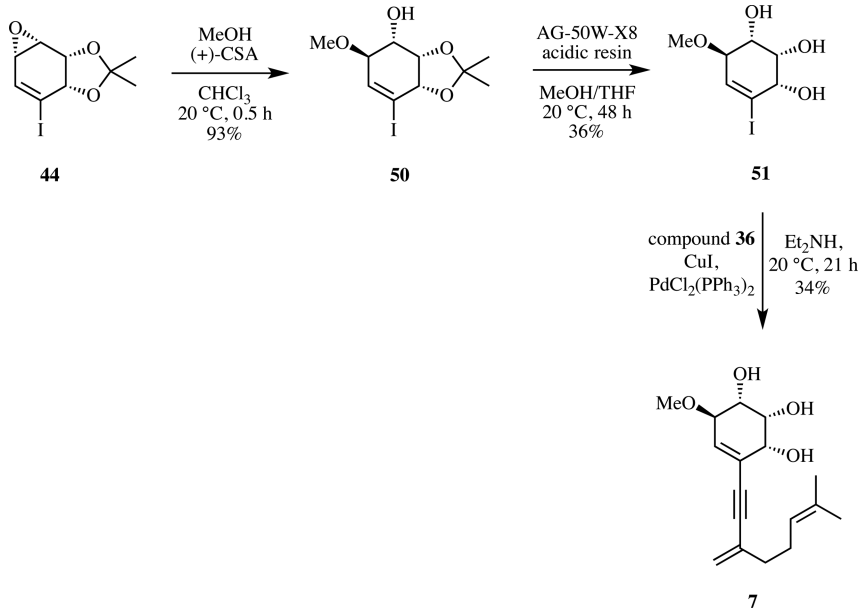
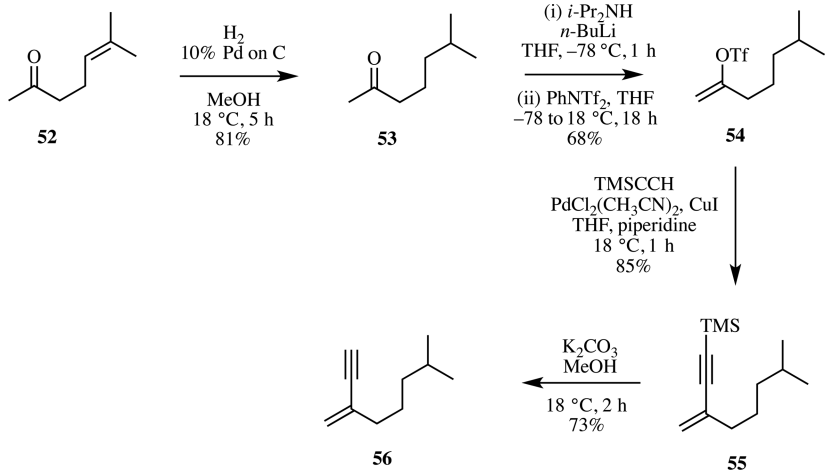
Scheme 6. Reaction Sequence Leading to Phomentrioloxin A Analogue 7



Scheme 7. Reaction Sequence Leading to the Side-Chain Synthon 56 for the Preparation of Analogues 10−14



coupled with enyne **56** in the usual manner, affording target compound **13** (70%).

The aromatic side-chain synthon required for the assembly of the phomentrioloxin analogues **15**−**20** was prepared by the very straightforward reaction sequences shown in Scheme 12. Thus, the commercially available iodide **67** was cross-coupled with trimethylsilylacetylene, and the product alkyne **68** (68%) was treated with potassium carbonate in methanol and thus delivering the required and previously reported synthon **69**[18] in 72% yield. The corresponding dimethoxylated synthon **70** was a commercially available material.

Synthon **69** was first exploited in the synthesis of analogues **15** and **19** by cross-coupling the former compound with the iodinated cyclohexene **66** (Scheme 13). This process delivered compound **19** (76%), and the associated acetonide residue was cleaved using aqueous acid and thus affording the triol **15**, albeit in just trace amounts.

A closely related reaction sequence, as shown in Scheme 14, lead from conduritol **35**, via analogue **20** (72%), to diol **16**, although, once again, this last compound was only obtained in trace amounts.

The synthesis of analogue **17** was a little more involved and started (Scheme 15) by treating silyl ether **58** with TBAF. The acetonide residue associated the product alcohol **71** (80%) was hydrolyzed using aqueous acetic acid, and the resulting triol **72** (72%) cross-coupled with alkyne **69** to give the target compound **17** (73%).

Closely related reactions sequences were used to prepare analogues **18** (Scheme 16), **21** (Scheme 17), and **22** (Scheme 18).

The synthesis of the final side-chain synthon required for the present study is shown in Scheme 19 and simply involved the rhodium-catalyzed and selective addition of pinacol borane (**75**) to terminal alkyne **69**, affording the *Z*-configured and *β*-substituted styrene **76** in 52% yield.

Side-chain synthon **76** was first exploited in the preparation of the phomentrioloxin analogues **23**, **25**, and **27** as shown in Scheme 20. Thus, Suzuki−Miyaura cross-coupling of compound **76** with the conduritol **60** gave analogue **27** (80%), which upon hydrogenation using 5% rhodium on carbon as catalyst delivered the cyclohexane **25** in 47% yield and as a single diastereoisomer. The illustrated configuration at the newly created stereogenic

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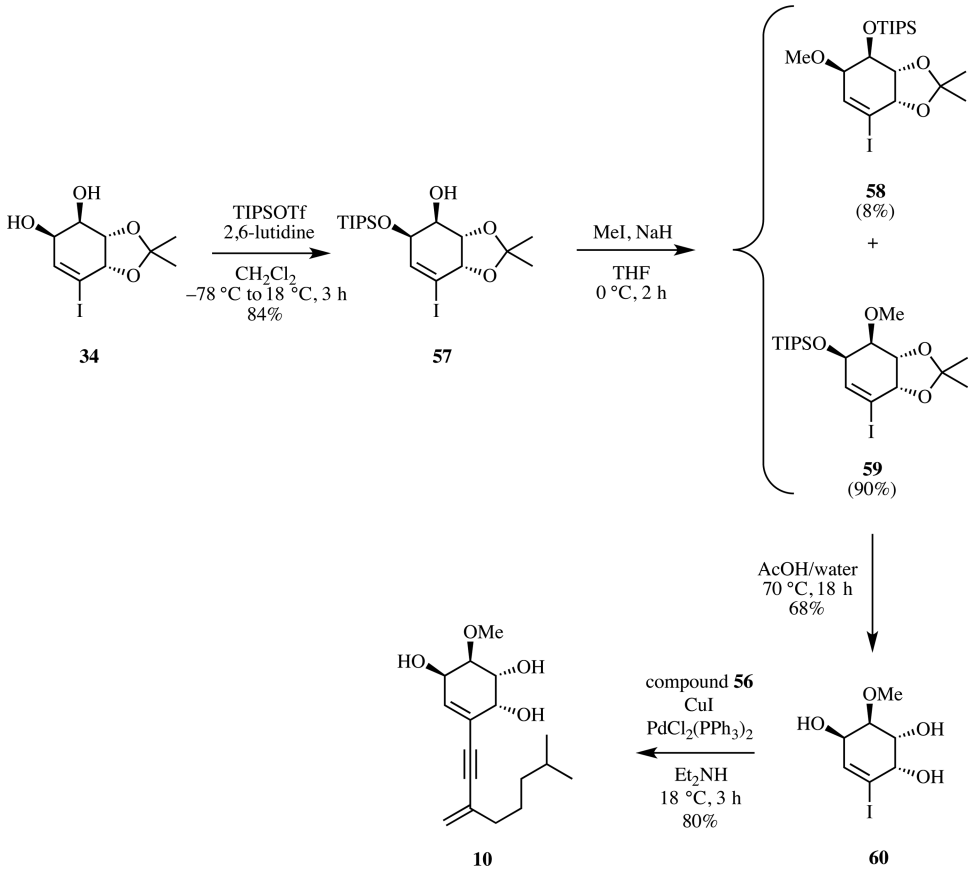
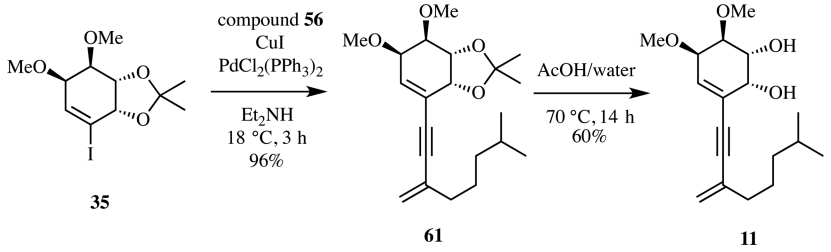
Scheme 8. Reaction Sequence Leading to Phomentrioloxin A Analogue 10



Scheme 9. Reaction Sequence Leading to Phomentrioloxin A Analogue 11



center within compound **25** is assigned on the basis that the hydroxyl groups within substrate **27** will direct the delivery of hydrogen from the α-face and establish a β-oriented side-chain. Extended thermolysis of the *Z*-configured alkene **27** in refluxing chlorobenzene afforded the corresponding *E*-isomer **23** in 85% yield based on recovered starting material (brsm).

An analogous series of reactions (Scheme 21) starting with diol **74** led, via *Z*-alkene **28** (78%), to the *E*-alkene **24** (80% brsm) and to cyclohexane **26** (40%).

A more involved reaction sequence was required to secure analogues **29** and **31**. Thus, as shown in Scheme 22, the homochiral *cis*-1,2-dihydrocatechol **77** was first converted into the corresponding and well-known acetonide **78** (85%) under relatively standard conditions, and the latter then was subject to a regio- and diastereo-selective epoxidation reaction using *m*-chloroperbenzoic acid (*m*-CPBA). The product oxirane **79** (85%) was then cleaved using potassium hydroxide in aqueous THF, and the resulting *trans*-diol **80**[19] (70%) was selectively mono-*O*-silylated using TIPSOTf in the presence of 2,6-lutidine. The homoallylic alcohol **81** (51%) so-formed was *O*-methylated using methyl iodide in the presence of sodium hydride, and the methyl ether **82** (41%) thus obtained engaged in a Suzuki–Miyaura cross-coupling reaction with the borylated alkene **76** to afford analogue **31** (78%). Interestingly, when the last compound was heated in aqueous acetic acid, the associated acetonide and silyl ether residues were cleaved, but the *Z*-configured alkene moiety remained intact and such that analogue **29** was obtained in 70% yield.

Biological Evaluation Studies. The biological evaluations of compounds **1** and **4**–**31** were carried out at BASF's facilities at Limburgerhof in Germany. Preliminary evaluations of herbicidal activity were conducted in a green house. The plant species used for this purpose were *Setaria viridis* (SETVI, green foxtail) and *Amaranthus retroflexus* (AMARE, pigweed). The outcomes of conducting such tests are presented in Table 1 and represent the average rating for each of the two plant species involved. In broad terms, the active compounds caused a generalized necrosis of the aerial moieties of the plant species against which they were tested, suggesting they are eliciting their effects via a nonspecific pathway. In structure–activity terms, variations in the locations,

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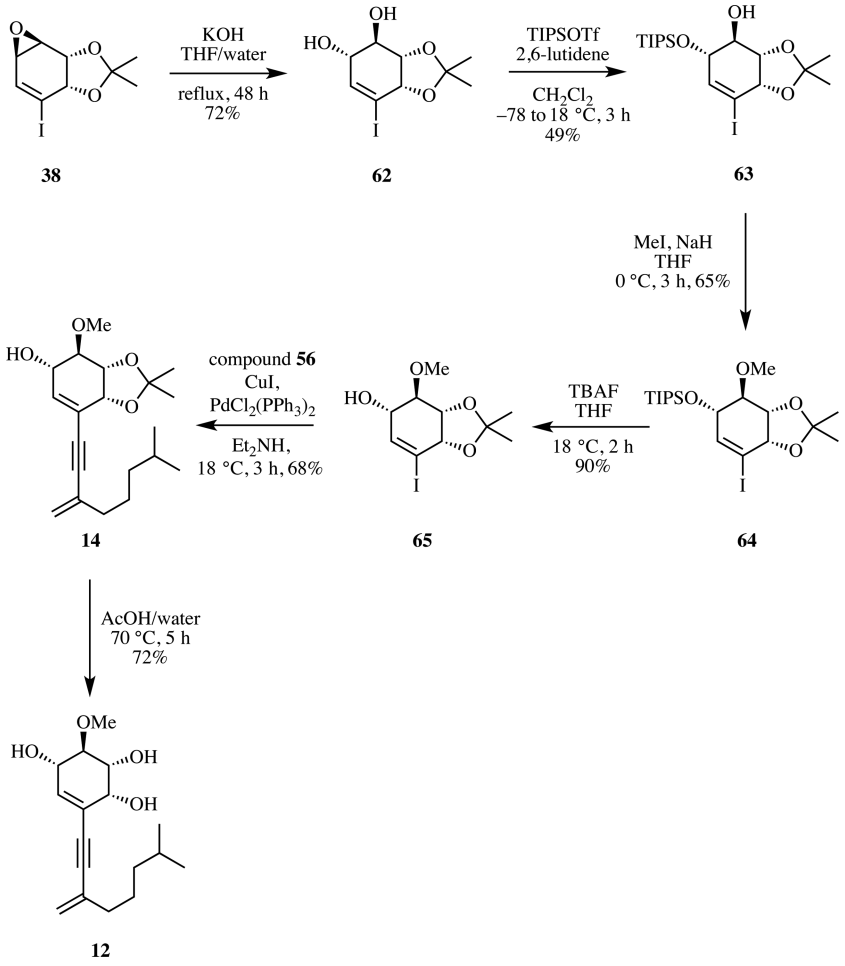
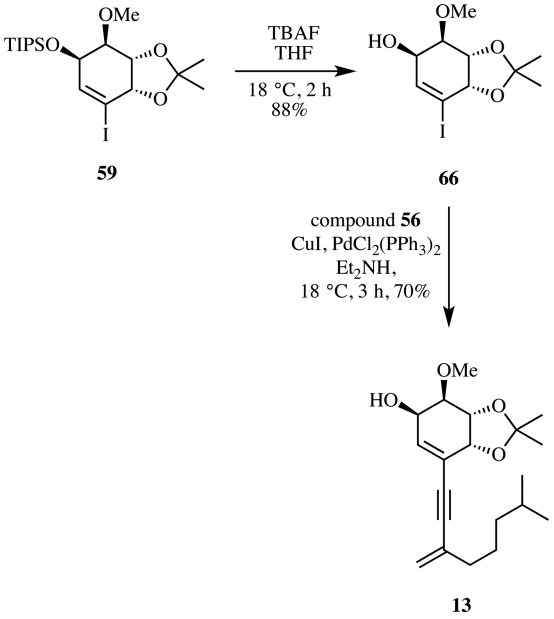
Scheme 10. Reaction Sequence Leading to Phomentrioloxin A Analogues 12 and 14



Scheme 11. Reaction Sequence Leading to Phomentrioloxin A Analogue 13



configurations, degrees of *O*-methylation, and/or deletions of oxygen-containing groups could have deleterious impacts on activity (see entries 4 and 6) and certainly no obviously beneficial ones (relative to the parent system **1**). Increasing the degree of saturation in the geranyl-type side-chain also had generally negative effects, but replacement of such a moiety with an arylacetylene equivalent led to series of analogues with more pronounced herbicidal effects (see entries 14, 16, 18, and 20). In contrast, introduction of a styrenyl or β-arylethyl side-chain had a generally negative effect on activity; there were certainly no beneficial ones. A simple interpretation of these results is that those compounds containing the more stable/durable arylacetylenic side-chains probably had the longest half-lives under the extended testing conditions involved and were thus able to exert more sustained herbicidal effects.

Physiological profiling (PP) protocols were used for the purposes of trying to draw conclusions regarding the mode of action of the phomentrioloxin analogues as herbicides as well as for ranking their selectivities and potencies. PP[20] involves an array of physiological and bioassays that allow for differentiation between the distinct responses of different structures (whole plant, tissue, meristem cells, organelles), developmental stages (seed germination, vegetative growth), types of metabolism (phototrophic, heterotrophic), and physiological processes. The assays are designed to be sensitive, allow facilitated uptake and translocation of the applied compounds, and include all potential herbicidal target sites. The bioassays included those involving heterotrophic cleaver (*Galium mollugo*) and photoautotrophic green alga (*Scenedesmus obliquus*) cell suspensions, isolated white mustard (*Sinapis alba*) shoots, and germinating cress (*Lepidum*

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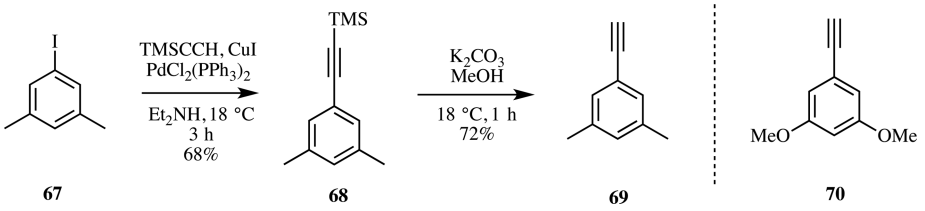
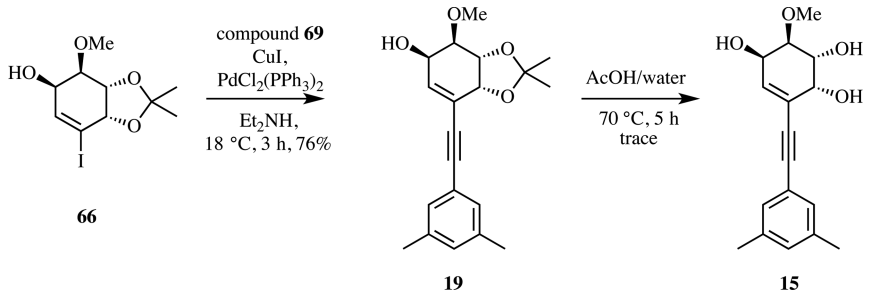
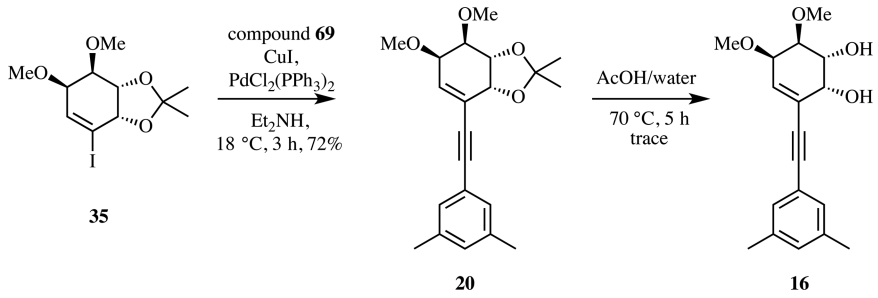
Scheme 12. Reaction Sequence Leading to the Side-Chain Synthon 69 for the Preparation of Analogues 15−20



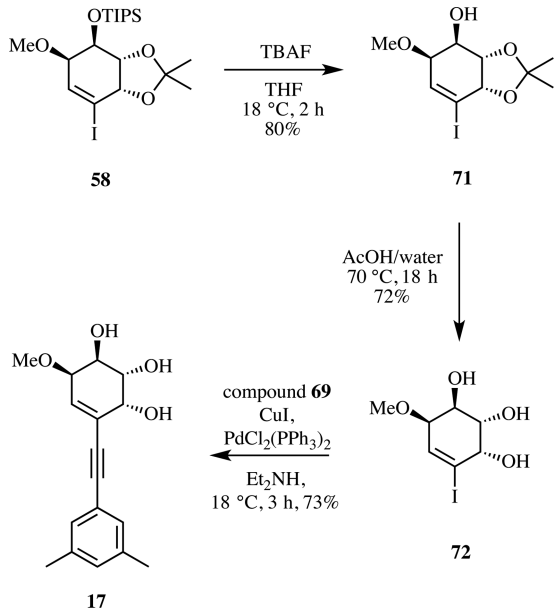
Scheme 13. Reaction Sequence Leading to Phomentrioloxin A Analogues 15 and 19



Scheme 14. Reaction Sequence Leading to Phomentrioloxin A Analogues 16 and 20



Scheme 15. Reaction Sequence Leading to Phomentrioloxin A Analogue 17



sativum) seeds. The physiological assays included studies of the Hill reaction of isolated wheat thylakoids, respiration measurements in cleaver cell suspensions, the formation of reactive oxygen species, chlorophyll fluorescence and ATP measurements in *Lemna* plants, carbon dioxide assimilation measurements in cleaver (*Galium aparine*) plants, and toluidine blue staining of cress hypocotyls for detecting any inhibition of very long-chain fatty acid (VLCFA) biosynthesis.

In broad terms, phomentrioloxin A (**1**) as well as analogues **9** and **20** generated weak/inconclusive PPs. Analogues **5**−**7** and **11** had minor effects on the growth of heterotrophic *Galium* suspension cells, unicellular algae, and *Lemna* plants, indicating uptake limitations or rapid metabolic detoxification. In addition, analogue **7** caused moderate inhibition of cress germination in a light-dependent manner. The most consistent effect among these compounds was a moderate inhibition of carbon dioxide assimilation, indicating a not-further-characterized inhibitory effect on photosynthesis. Analogues **15**, **16**, **19**, and **22** caused moderate inhibition of cell division in heterotrophic suspension cells together with intensified green leaf pigmentation in *Lemna* plants. The origins of these effects remain unknown. The PP of compound **4** differed somewhat from the others, as this analogue caused moderate inhibition of the Hill reaction and must thus have an effect on photosynthetic electron-flow. In addition, light-dependent inhibition of cress germination was observed. Inhibition of the Hill reaction is a typical finding for photosystem II (PS II) inhibitors. However, such inhibitors are also usually strong inhibitors of algae and *Lemna* growth, a feature not observed for analogue **4**. This might indicate that the compound is able to inhibit PSII in isolated thylakoids *in vitro* but is rapidly detoxified in a cellular environment.

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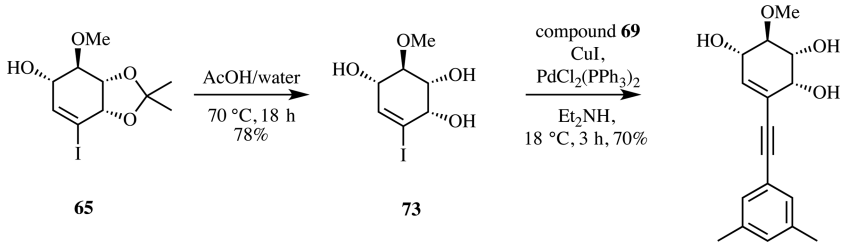
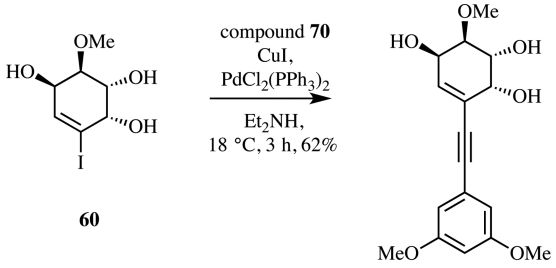
Scheme 16. Reaction Sequence Leading to Phomentrioloxin A Analogue 18



65 73 18

Scheme 17. Reaction Sequence Leading to Phomentrioloxin A Analogue 21



60 21

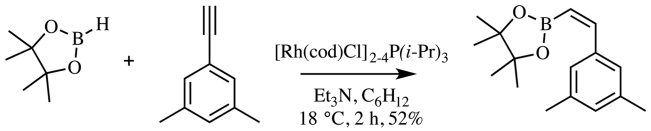
CONCLUSIONS

The present study serves to highlight the utility of our previously reported[8] synthesis of phomentrioloxin A in generating a diverse range of analogues. However, the biological evaluation of these analogues has revealed that, as a class and despite some earlier indications to the contrary,[7a,9] the phomentrioloxins are unlikely to be useful leads for the development of new herbicidal agents.

EXPERIMENTAL SECTION

General Protocols. Unless otherwise specified, proton (^{1}H) and carbon (^{13}C) NMR spectra were recorded at room temperature in base-filtered $CDCl_3$ on a spectrometer operating at 400 MHz for proton and 100 MHz for carbon nuclei. The signal due to residual $CHCl_3$ appearing at δ_H 7.26 and the central resonance of the $CDCl_3$ "triplet" appearing at δ_C 77.0 were used to reference ^{1}H and ^{13}C NMR spectra, respectively. ^{1}H NMR data are recorded as follows: chemical shift (δ) [multiplicity, coupling constant(s) J (Hz), relative integral] where multiplicity is defined as s = singlet; d = doublet; t = triplet; q = quartet; and m = multiplet or combinations of the above. Infrared spectra (ν_{max}) were recorded on a FTIR spectrometer. Samples were analyzed as thin films on KBr plates. Low-resolution ESI mass spectra were recorded on a single-quadrupole liquid chromatograph−mass spectrometer, while high-resolution measurements were conducted on a time-of-flight instrument. Low- and high-resolution EI mass spectra were recorded on a magnetic-sector machine. Melting points were measured on an automated melting point system and are uncorrected. Analytical thin-layer chromatography (TLC) was performed on aluminum-backed 0.2 mm thick silica gel 60 F_{254} plates. Eluted plates were visualized using a 254 nm UV lamp and/or by treatment with a suitable dip followed by heating. These dips included phosphomolybdic acid:ceric sulfate:sulfuric acid (conc.):water (37.5 g:7.5 g:37.5 g:720 mL), potassium permanganate:potassium carbonate:5% sodium hydroxide aqueous solution:water (3 g:20 g:5 mL:300 mL)), *p*-anisaldehyde or vanillin:sulfuric acid (conc.):ethanol (15 g:2.5 mL:250 mL). Flash chromatographic separations were carried out following protocols defined by Still et al.[21] with silica gel 60 (40−63 μm) as the stationary phase and using the AR- or HPLC-grade solvents indicated. Starting materials, reagents, drying agents, and other inorganic salts were generally commercially available and were used as supplied. Tetrahydrofuran (THF), methanol, and dichloromethane were dried using a solvent purification system that is based upon a technology originally described by Grubbs et al.[22] Where necessary, reactions were performed under an nitrogen atmosphere.

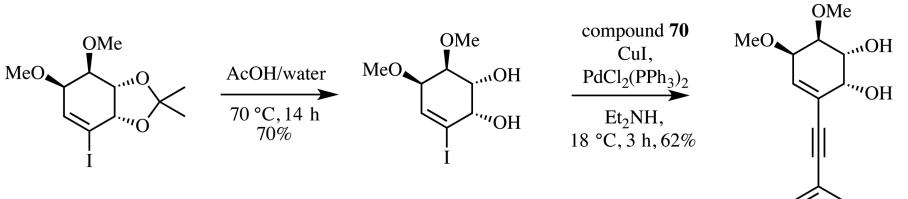
Scheme 19. Reaction Sequence Leading to the Side-Chain Synthon 76 for the Preparation of Analogues 27−31



75 69 76

*The Synthesis of Analogues **8** and **9** as Representative Chemical Transformations: (3aS,4R,5R,7aS)-7-Iodo-4,5-dimethoxy-2,2-dimethyl-3a,4,5,7a-tetrahydrobenzo[d]-[1,3]dioxole (**35**).* Sodium hydride (115 mg of a 60% dispersion in mineral oil, 2.88 mmol) was added to a magnetically stirred solution of compound **34**[12] (150 mg, 0.48 mmol) and iodomethane (300 μL, 4.80 mmol) in dry THF (25 mL) maintained at 0 °C under a nitrogen atmosphere. Stirring was continued for 2 h at 0−18 °C, then the reaction mixture was treated with ice/water (60 mL; *Caution: potential for evolution of hydrogen gas*). The separated aqueous phase was extracted with ethyl acetate (1 × 25 mL), and the combined organic phases were then dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The ensuing light-yellow oil was

Scheme 18. Reaction Sequence Leading to Phomentrioloxin A Analogue 22



35 74 22

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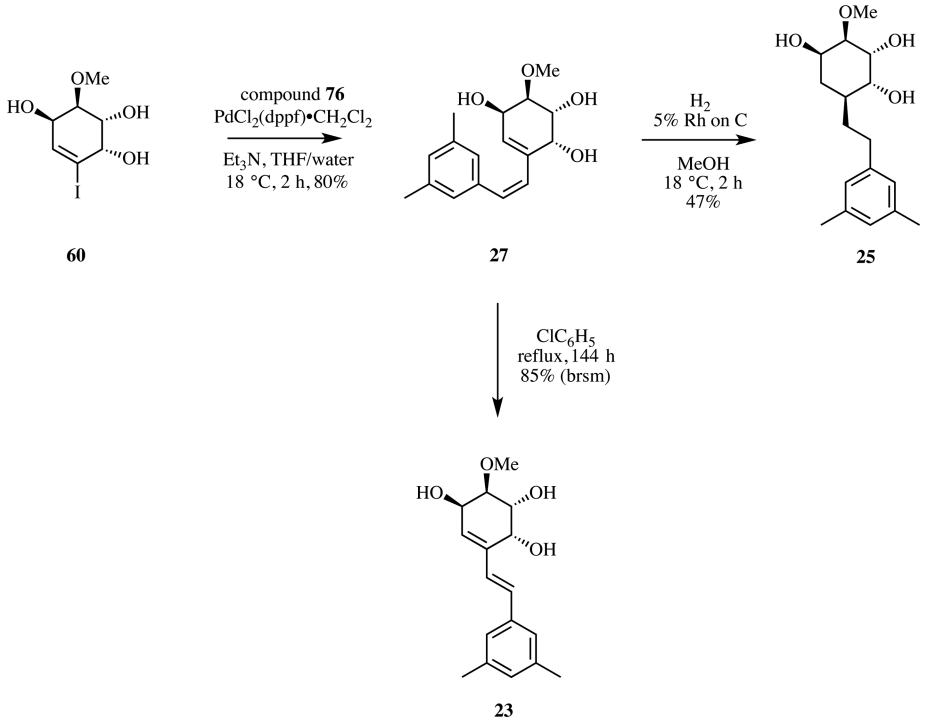
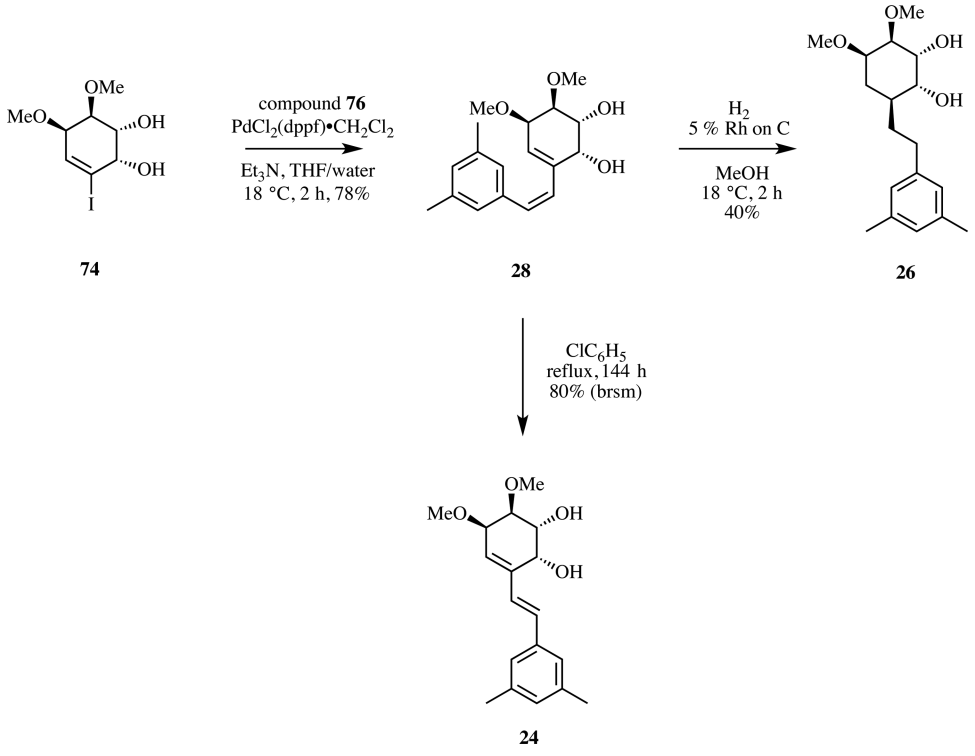
Scheme 20. Reaction Sequence Leading to Phomentrioloxin A Analogues 23, 25, and 27



Scheme 21. Reaction Sequence Leading to Phomentrioloxin A Analogues 24, 26, and 28



subjected to flash chromatography (silica, 1:1 v/v ethyl acetate/hexane gradient elution) to give, after concentration of the appropriate fractions (R_f = 0.4 in 1:4 v/v ethyl acetate/hexane), compound **35** (77 mg, 47%) as a white, crystalline solid, mp =46−49 °C; $[\alpha]_D^{20}$ = −33.8 (c = 3.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.50 (d, J = 3.2 Hz, 1H), 4.60 (d, J = 5.7 Hz, 1H), 4.38 (m, 1H), 3.88 (t, J = 3.4 Hz, 1H), 3.76 (m, 1H), 3.48 (s, 3H), 3.40 (s, 3H), 1.39 (s, 3H), 1.35 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.5, 109.4, 100.2, 78.8, 77.7, 76.1, 74.5, 59.2, 57.3, 27.4, 25.9; IR ν_{max} 2984, 2929, 2826, 1630, 1459, 1381, 1371, 1233, 1101, 1079, 1039, 1005, 868 cm^{-1}; MS (EI, 70 eV) m/z 340 ($M^{+\bullet}$, 11%), 325 [$(M\text{-}CH_3\bullet)^+$, 8%], 115 (100); HRMS $M^{+\bullet}$ calcd for $C_{11}H_{17}{}^{127}IO_4$ 340.0172, found 340.0173.

*(3aR,4R,5R,7aR)-4,5-Dimethoxy-2,2-dimethyl-7-(7-methyl-3-methyleneoct-6-en-1-yn-1-yl)-3a,4,5,7a-tetrahydrobenzo[d][1,3]-dioxole (**9**).* Cuprous iodide (11 mg, 0.05 mmol) and $PdCl_2(PPh_3)_2$ (25 mg, 0.04 mmol) were added to a magnetically stirred solution of compounds **35** (120 mg, 0.35 mmol) and **36**[14] (95 mg, 0.71 mmol) in anhydrous diethylamine (3 mL) maintained at 18 °C under a nitrogen

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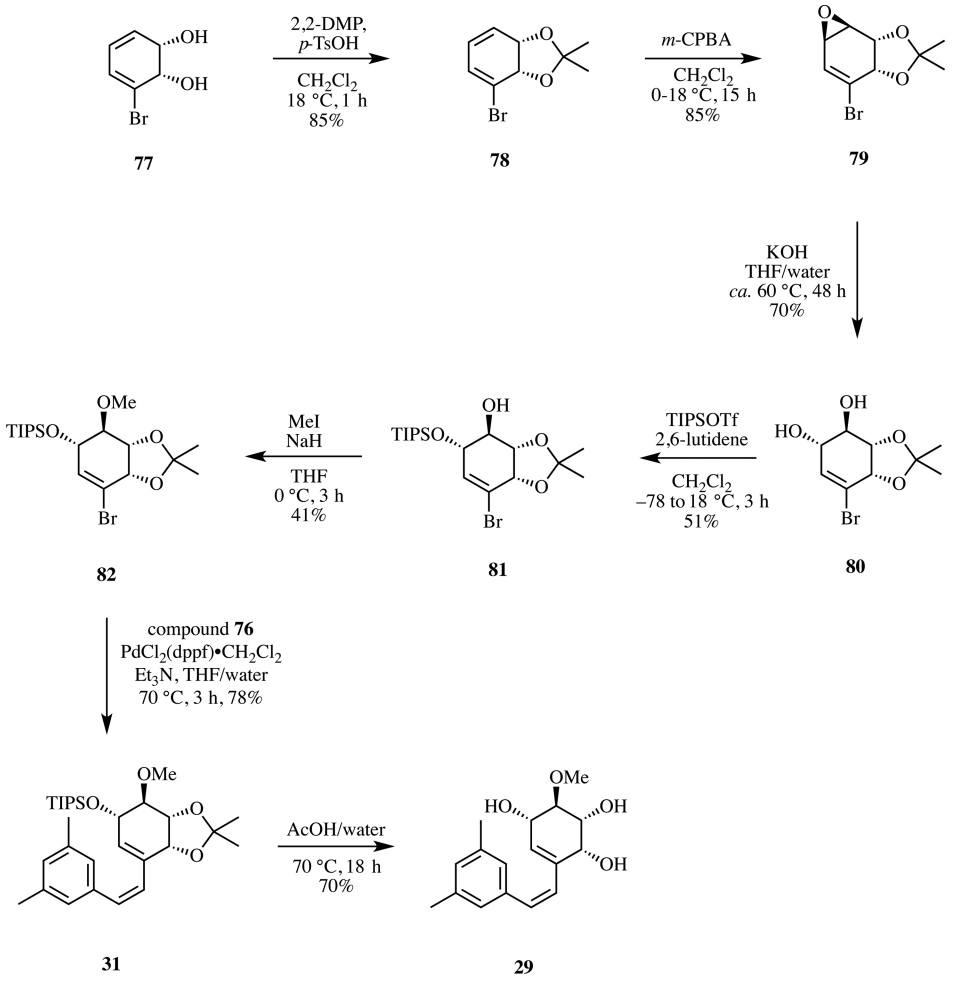
Scheme 22. Reaction Sequence Leading to Phomentrioloxin A Analogues 29 and 31



atmosphere. After 3 h, the reaction mixture was concentrated under reduced pressure, and the residue thus obtained was subjected to flash chromatography (silica, 1:4 v/v ethyl acetate/hexane gradient elution). Concentration of the appropriate fractions (R_f = 0.3 in 1:4 v/v ethyl acetate/hexane) afforded compound **9** (59 mg, 48%) as a clear, light-yellow oil, $[\alpha]_D^{20} = -17.7$ (c = 0.7, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.25 (d, J = 4.0 Hz, 1H), 5.37 (d, J = 2.0 Hz, 1H), 5.26 (d, J = 2.0 Hz, 1H), 5.10 (m, 1H), 4.64 (d, J = 6.2 Hz, 1H), 4.46 (t, J = 6.2 Hz, 1H), 4.04 (t, J = 3.8 Hz, 1H), 3.66 (m, 1H), 3.53 (s, 3H), 3.45 (s, 3H), 2.20 (broadened s, 4H), 1.69 (s, 3H), 1.62 (s, 3H), 1.45 (s, 3H), 1.39 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 133.6, 132.2, 131.2, 123.4, 123.2, 121.7, 109.5, 90.8, 87.4, 79.0, 74.2, 74.0, 73.8, 58.8, 57.4, 37.3, 27.6, 26.8, 25.7, 25.5, 17.7; IR ν_{max} 2983, 2930, 2825, 1631, 1605, 1454, 1379, 1370, 1234, 1113, 1082, 1038, 961, 896, 874 cm^{-1}; MS (EI, 70 eV) m/z 331 [(M-CH_3•)$^+$ 6%], 257 (14), 115 (100); HRMS (M-CH_3•)$^+$ calcd for $C_{20}H_{27}O_4$ 331.1909, found 331.1907.

*(1R,2R,5R,6S)-5,6-Dimethoxy-3-(7-methyl-3-methyleneoct-6-en-1-yn-1-yl)cyclohex-3-ene-1,2-diol (**8**).* Compound **9** (33 mg, 0.09 mmol) was treated with acetic acid/water (3 mL of a 4:1 v/v mixture), and the solution thus obtained was heated at 70 °C for 5 h, then cooled, and concentrated under reduced pressure. Subjection of the ensuing light-yellow residue to flash chromatography (silica, 3:2 v/v ethyl acetate/hexane gradient elution) delivered, after concentration of the appropriate fractions (R_f = 0.4 in 4:2 v/v ethyl acetate/hexane), compound **8** (24 mg, 81%) as a clear, light-yellow syrup, $[\alpha]_D^{20} = -14$ (c = 0.5, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.27 (d, J = 4.5 Hz, 1H), 5.38 (d, J = 1.9 Hz, 1H), 5.28 (d, J = 1.9 Hz, 1H), 5.11 (m, 1H), 4.36 (d, J = 4.2 Hz, 1H), 4.17 (m, 1H), 4.10 (t, J = 4.2 Hz, 1H), 3.70 (dd, J = 8.8 and 3.9 Hz, 1H), 3.51 (s, 3H), 3.48 (s, 3H), 2.79 (d, J = 2.0 Hz, 1H), 2.69 (d, J = 2.0 Hz, 1H), 2.20 (s, 4H), 1.69 (s, 3H), 1.62 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 132.4, 132.3, 130.9, 124.6, 123.2, 122.2, 91.4, 87.1, 77.4, 72.6, 68.6, 67.5, 58.1, 57.6, 37.2, 26.8, 25.7, 17.8; IR ν_{max} 3400, 3301, 2953, 2922, 2852, 1633, 1603, 1462, 1377, 1261, 1099, 995, 897 cm^{-1}; MS (EI, 70 eV) m/z 306 (M$^{+\bullet}$, <1%), 275 (7), 259 (22), 217 (76), 189 (100), 185 (78), 69 (79); HRMS (M+Na)$^+$ calcd for $C_{18}H_{26}NaO_4$ 329.1729, found 329.1729.

*(3aS,4R,7aS)-7-Iodo-2,2-dimethyl-3a,4,5,7a-tetrahydrobenzo[d]-[1,3]dioxol-4-ol (**39**).* A magnetically stirred solution of epoxide **38**[15] (2.91 g, 9.88 mmol) in anhydrous diethyl ether (60 mL) was cooled to −40 °C and then treated with DIBAL-H (11.9 mL of a 1 M solution in hexanes, 11.9 mmol) over 0.08 h. The ensuing mixture was maintained at this temperature for 3 h, then treated with tartaric acid (50 mL of a saturated aqueous solution), and stirred for a further 0.5 h while being allowed to warm to 20 °C. The organic phase was separated, and the aqueous layer was extracted with diethyl ether (2 × 50 mL). The combined organic layers were then washed with water (1 × 100 mL) before being dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (silica, 1:1 v/v ethyl acetate/hexane gradient elution) to furnish, after concentration of the appropriate fractions (R_f = 0.4 in 1:1 v/v ethyl acetate/hexane), the title compound **39** (2.10 g, 72%) as a white, crystalline solid, mp = 101−103 °C, $[\alpha]_D^{20} = -9.3$ (c = 1.5, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.43 (m, 1H), 4.65 (d, J = 5.9 Hz, 1H), 4.09 (dd, J = 7.1 and 5.9 Hz, 1H), 3.96 (m, 1H), 2.48 (dt, J = 17.4 and 4.9 Hz, 1H), 2.12 (m, 1H), 1.96 (broad s, 1H), 1.49 (s, 3H), 1.42 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.7, 109.4, 94.6, 79.4, 78.6, 67.4, 33.5, 28.1, 26.2; IR ν_{max} 3435, 2985, 2932, 1701, 1633, 1380, 1222, 1161, 1071, 1050, 867 cm^{-1}; MS (EI, 70 eV) m/z 296 (M$^{+\bullet}$, 12%), 281 (100); HRMS M$^{+\bullet}$ calcd for $C_9H_{13}{}^{127}IO_3$, 295.9909, found 295.9913.

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Table 1. Evaluation of Phomentrioloxin Derivatives as Nonspecific Herbicides Against *A. retroflexus* and *S. viridis*

entry	compd[a]	averaged result[b]	entry	compd[a]	averaged result[b]
1	**1**[c]	+	16	**18**	++
2	**4**[c]	+	17	**19**	+
3	**5**[c]	+	18	**20**	++
4	**6**[c]	0	19	**21**	+
5	**7**[c]	+	20	**22**	++
6	**8**	0	21	**23**	0
7	**9**	+	22	**24**	0
8	**10**	0	23	**25**[d]	0
9	**11**[c]	+	24	**26**[d]	+
10	**12**	0	25	**27**	+
11	**13**	+	26	**28**	0
12	**14**	0	27	**29**[d]	+
13	**15**	+	28	**30**	+
14	**16**	++	29	**31**	+
15	**17**	+	–	–	–

[a]Compounds applied at 2 kg a.i./ha unless otherwise specified. [b]Qualitative result over the two plant species used. [c]Compounds **1**, **4**–**7**, and **11** were applied at 1 kg a.i./ha. [d]Compounds **25**, **26**, and **29** were applied at 1.145, 1. 333 and 1.625 kg a.i./ha, respectively. Evaluation was carried out using a scale from 0–100, where 100 means complete destruction of at least the aerial moieties, and 0 means no damage, or normal course of growth; 0–25: 0 (no or very low activity); >25–50: + (moderate activity); >50–75: ++ (good activity); >75: +++ (very good activity).

*(3aS,4R,7aS)-7-Iodo-4-methoxy-2,2-dimethyl-3a,4,5,7a-tetrahydrobenzo[d][1,3]-dioxole (**40**).* Silver(I) oxide (1.81 g, 7.81 mmol) and methyl iodide (970 μL, 15.6 mmol) were added to a magnetically stirred solution of compound **39** (2.10 g, 7.10 mmol) in acetonitrile (40 mL) maintained under a nitrogen atmosphere. The ensuing mixture was heated at 82 °C for 16 h, then cooled to 20 °C, and filtered through a pad of diatomaceous earth that was washed with ethyl acetate (2 × 20 mL). The combined filtrates were concentrated under reduced pressure, and the material so obtained subjected to flash chromatography (silica, 1:1 v/v ethyl acetate/hexane gradient elution). Concentration of the appropriate fractions (R_f = 0.5 in 1.5:1 v/v ethyl acetate/hexane) gave the title compound **40** (1.04 g, 47%) as a light-yellow oil, $[\alpha]_D^{20}$ = −14 (*c* = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.37 (t, *J* = 4.3 Hz, 1H), 4.59 (d, *J* = 5.6 Hz, 1H), 4.21 (t, *J* = 5.6 Hz, 1H), 3.61 (m, 1H), 3.43 (s, 3H), 2.43 (dm, *J* = 17.6 Hz, 1H), 2.15 (m, 1H), 1.47 (s, 3H), 1.40 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 136.6, 109.2, 96.7, 78.8, 76.3, 75.7, 57.7, 29.9, 27.9, 26.3; IR ν_{max} 2985, 2932, 2896, 2824, 1749, 1728, 1636, 1455, 1379, 1370, 1339, 1213, 1163, 1104, 1071, 1032, 968 cm^{-1}; MS (EI, 70 eV) *m*/*z* 310 ($M^{+\bullet}$, 11%), 295 (100); HRMS $M^{+\bullet}$ calcd for $C_{10}H_{15}{}^{127}IO_3$, 310.0066, found 310.0064.

*(1R,2S,6R)-3-Iodo-6-methoxycyclohex-3-ene-1,2-diol (**41**).* A solution of compound **40** (1.04 g, 3.36 mmol) in methanol/THF (20 mL of a 1:1 v/v mixture) was treated with acidified AG-50W-X8 acidic resin (2.09 g, 200 wt %). The resulting mixture was stirred vigorously at 20 °C for 24 h and then filtered through a pad of diatomaceous earth that was washed with ethyl acetate (2 × 10 mL). The combined filtrates were concentrated under reduced pressure, and subjection of the residue to flash chromatography (silica, 1:1 v/v ethyl acetate/hexane gradient elution) gave, after concentration of the appropriate fractions (R_f = 0.2 in 1:1.5 v/v ethyl acetate/hexane), the title compound **41** (797 mg, 88%) as a light-cream colored solid, mp = 87 °C, $[\alpha]_D^{20}$ = −140 (*c* = 0.2, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.37 (m, 1H), 4.40 (d, *J* = 4.2 Hz, 1H), 3.84 (m, 1H), 3.59 (m, 1H), 3.42 (s, 3H), 2.79 (broad s, 2H), 2.63 (dt, *J* = 17.5 and 5.3 Hz, 1H), 2.01 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.7, 96.3, 74.7, 74.6, 72.2, 57.2, 33.1; IR ν_{max} 3391, 2971, 2926, 2821, 1633, 1432, 1395, 1196, 1097, 988, 961, 823, 684 cm^{-1}; MS (EI, 70 eV) *m*/*z* 270 ($M^{+\bullet}$, 8%), 252 (13), 74 (100); HRMS $M^{+\bullet}$ calcd for $C_7H_{11}{}^{127}IO_3$ 269.9753, found 269.9757.

*(1R,2R,6R)-6-Methoxy-3-(7-methyl-3-methyleneoct-6-en-1-yn-1-yl)cyclohex-3-ene-1,2-diol (**4**).* Alkyne **36** (594 mg, 4.43 mmol) was added to a magnetically stirred solution of compound **41** (519 mg, 2.95 mmol) in anhydrous diethylamine (25 mL), and the ensuing solution was sparged with nitrogen for 0.5 h. $PdCl_2(PPh_3)_2$ (207 mg, 0.30 mmol) and cuprous iodide (84 mg, 0.44 mmol) were then added, and the resulting mixture was stirred at 20 °C for 20 h before being concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (silica, 1:4 → 1:1 e v/v ethyl acetate/hexane gradient elution) to give, after concentration of the appropriate fractions (R_f = 0.3 in 1:1 v/v ethyl acetate/hexane), the title compound **4** (519 mg, 64%) as a clear, light-yellow oil, $[\alpha]_D^{20}$ = + 86 (*c* = 1.7, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 100 MHz) δ 6.10 (m, 1H), 5.33 (d, *J* = 2.0 Hz, 1H), 5.24 (d, *J* = 2.0 Hz, 1H), 5.10 (m, 1H), 4.34 (d, *J* = 4.0 Hz, 1H), 3.74 (dd, *J* = 9.2 and 4.0 Hz, 1H), 3.61 (m, 1H), 3.43 (s, 3H), 2.72 (dt, *J* = 18.8 and 5.3 Hz, 2H), 2.19 (m, 4H), 2.08 (m, 2H), 1.68 (s, 3H), 1.61 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 134.0, 132.2, 131.2, 123.3, 121.6, 121.4, 89.4, 87.9, 75.2, 71.5, 69.1, 57.1, 37.4, 30.1, 26.8, 25.7, 17.8; IR ν_{max} 3401, 2918, 2191, 1671, 1605, 1443, 1376, 1196, 1101, 988, 903 cm^{-1}; MS (ESI, + ve) *m*/*z* 299 [$(M + Na)^+$, 100%]; HRMS $(M + Na)^+$ calcd for $C_{17}H_{24}NaO_3$ 299.1623, found 299.1623.

*(3aR,4R,5S,7aS)-4-Bromo-7-iodo-2,2-dimethyl-3a,4,5,7a-tetrahydrobenzo[d][1,3]dioxol-5-ol (**43**).* A solution of compound **32**[10] (3 g, 12.6 mmol) in THF/water (38 mL of a 4:1 v/v mixture) was treated with *N*-bromosuccinimide (3.37 g, 18.9 mmol), and the ensuing mixture was protected from light and stirred magnetically at 20 °C for 18 h, then quenched with $Na_2S_2O_3$ (70 mL of a saturated aqueous solution), and extracted with diethyl ether (2 × 70 mL). The combined organic phases were washed with brine (1 × 70 mL), then dried ($MgSO_4$), filtered, and concentrated under reduced pressure to afford an orange solid **42**.[18] This material was dissolved in anhydrous 2,2-dimethoxypropane (30 mL), and the resulting solution maintained under a nitrogen atmosphere and, while being protected from light, was treated with *p*-TsOH·H_2O (434 mg, 2.28 mmol). The resulting mixture was stirred at 20 °C for 18 h, then treated with $NaHCO_3$ (30 mL of a saturated aqueous solution), and extracted with ethyl acetate (2 × 40 mL). The combined organic layers were then dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The resulting light-yellow oil was subjected to flash chromatography (silica, hexane →1:4 v/v ethyl acetate/hexane gradient elution) and gave, after concentration of the appropriate fractions (R_f = 0.2 in 1:4 v/v ethyl acetate/hexane), the title compound **43** (3.38 g, 71%) as a voluminous, white solid, mp = 80–82 °C, $[\alpha]_D^{20}$ = +14 (*c* = 2.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.65 (dd, *J* = 4.4 and 0.7 Hz, 1H), 4.67 (d, *J* = 5.1 Hz, 1H), 4.57 (t, *J* = 5.1 Hz, 1H), 4.30 (t, *J* = 5.0 Hz, 1H), 4.25 (m, 1H), 2.92 (dd, *J* = 9.3 and 0.7 Hz, 1H), 1.53 (s, 3H), 1.42 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.7, 111.8, 100.5, 78.3, 77.6, 71.1, 48.1, 27.9, 26.4; IR ν_{max} 3422, 3339, 2990, 2940, 2873, 1630, 1374, 1260, 1211, 1068, 1047, 1011, 857, 727 cm^{-1}; MS (EI, 70 eV) *m*/*z* 376 and 374 ($M^{+\bullet}$, both 6%) 361 and 359 (100 and 98), 174 and 172 (33 and 34); HRMS $M^{+\bullet}$ calcd for $C_9H_{12}{}^{79}Br^{127}IO_3$, 373.9015, found 373.9018.

*(3aS,5aS,6aS,6bS)-4-Iodo-2,2-dimethyl-3a,5a,6a,6b-tetrahydrooxireno-[2′,3′:3,4]ben -zo[1,2-d][1,3]dioxole (**44**).* NaOH (4.5 mL of a 2.0 M aqueous solution, 9.00 mmol) was added, dropwise, to a magnetically stirred solution of compound **43** (3.38 g, 9.00 mmol) in 1,2-dimethoxyethane (50 mL). The resulting mixture was protected from light, stirred at 20 °C for 48 h, and then concentrated under reduced pressure. The residue thus obtained was partitioned between dichloromethane (50 mL) and water (50 mL), and the separated organic layer was washed with brine (1 × 50 mL), then dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Subjection of the material so obtained to flash chromatography (silica, 1:7 v/v ethyl acetate/hexane gradient elution) provided, after concentration of the appropriate fractions (R_f = 0.1 in 1:9 v/v ethyl acetate/hexane), the title compound **44** (1.18 g, 44%) as a white, crystalline solid, mp = 46–47 °C, $[\alpha]_D^{20}$ = −82 (*c* = 1.3, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.00 (d, *J* = 4.2 Hz, 1H), 4.78 (dd, *J* = 6.7 and 1.8 Hz, 1H), 4.46 (dd, *J* = 6.7 and 2.7 Hz, 1H), 3.66 (m, 1H), 3.32 (t, *J* = 4.2 Hz, 1H), 1.55 (s, 3H), 1.41 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.2, 108.1, 100.0, 79.5, 73.7, 54.5, 50.9, 27.2, 25.3; IR ν_{max} 2987, 2937, 2881, 1626, 1371, 1208, 1159, 1056,

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864 cm^{-1}; MS (EI, 70 eV) m/z 294 ($M^{+\bullet}$, 18%), 279 (100), 237 (26), 207 (22), 110 (55), 109 (42); HRMS $M^{+\bullet}$ calcd for $C_9H_{11}{}^{127}IO_3$ 293.9753, found 293.9750.

*(3aS,4S,7aS)-7-Iodo-2,2-dimethyl-3a,4,5,7a-tetrahydrobenzo[d]-[1,3]dioxol-4-ol (**45**).* A magnetically stirred solution of epoxide **44** (2.36 g, 8.06 mmol) in anhydrous diethyl ether (40 mL) was cooled to −40 °C and then treated with a DIBAL-H (9.67 mL of a 1.0 M solution in hexanes, 9.67 mmol) over 0.08 h. The resulting solution was allowed to warm to 20 °C over 20 h before being treated with tartaric acid (50 mL of a saturated aqueous solution). After a further 1 h, the aqueous layer was separated and then extracted with diethyl ether (2 × 50 mL), and the combined organic layers were then dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (silica, 1:1 v/v ethyl acetate/hexane gradient elution), and concentration of the appropriate fractions (R_f = 0.4 in 1:1 v/v ethyl acetate/hexane) afforded the title compound **45** (1.57 g, 66%) as a colorless, microcrystalline solid, mp =101 °C, $[\alpha]_D^{20}$ = + 41 (c = 1.2, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.35 (dd, J = 6.0 and 2.8 Hz, 1H), 4.62 (m, 1H), 4.39 (m, 1H), 3.99 (m, 1H), 2.39 (m, 1H), 2.30 (m, 1H), 1.45 (s, 3H), 1.43 (s, 3H), (signal due to hydroxyl group proton not observed); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 136.4, 110.2, 98.9, 80.6, 77.3, 66.6, 32.4, 27.3, 26.6; IR ν_{max} 3413, 2985, 2932, 2870, 1629, 1379, 1371, 1230, 1083, 1046, 864 cm^{-1}; MS (EI, 70 eV) m/z 296 ($M^{+\bullet}$, 6%), 281 (100), 94 (75); HRMS $M^{+\bullet}$ calcd for $C_9H_{13}{}^{127}IO_3$ 295.9909, found 295.9909.

*(3aS,4S,7aS)-7-Iodo-4-methoxy-2,2-dimethyl-3a,4,5,7a-tetrahydrobenzo[d][1,3]dioxole (**46**).* Silver(I) oxide (1.35 g, 5.84 mmol) and iodomethane (730 μL, 11.7 mmol) were added to a magnetically stirred solution of alcohol **45** (1.57 g, 5.31 mmol) in anhydrous acetonitrile (40 mL). The ensuing mixture was stirred at 82 °C for 19 h, then cooled to 20 °C, and filtered through a pad of diatomaceous earth that was washed with ethyl acetate (2 × 50 mL). The combined filtrates were concentrated under reduced pressure, and the residue thus obtained was subjected to flash chromatography (silica, 1:1 v/v ethyl acetate/hexane gradient elution). Concentration of the appropriate fractions (R_f = 0.6 in 1.5:1 v/v ethyl acetate/hexane) provided the title compound **46** (1.17 g, 71%) as a light-yellow oil, $[\alpha]_D^{20}$ = −32 (c = 1.2, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.35 (m, 1H), 4.59 (m, 1H), 4.49 (m, 1H), 3.59 (m, 1H), 3.44 (s, 3H), 2.41−2.35 (complex m, 2H), 1.44 (s, 3H), 1.43 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 136.1, 110.6, 99.8, 80.8, 75.1, 75.0, 56.7, 28.8, 27.4, 26.8; IR ν_{max} 2984, 2932, 2822, 1626, 1454, 1380, 1370, 1233, 1168, 1111, 1066, 1035, 865 cm^{-1}; MS (EI, 70 eV) m/z 310 ($M^{+\bullet}$, 3%), 295 (100), 115 (37), 108 (79); HRMS $M^{+\bullet}$ calcd for $C_{10}H_{15}{}^{127}IO_3$ 310.0066, found 310.0069.

*(1R,2S,6S)-3-Iodo-6-methoxycyclohex-3-ene-1,2-diol (**47**).* A solution of acetonide **46** (1.17 g, 3.78 mmol) in methanol/THF (30 mL of a 1:1 v/v mixture) was treated with acidified AG-50W-X8 acidic resin (2.35 g, 200 wt %), and the ensuing mixture was stirred vigorously at 20 °C for 24 h. The reaction mixture was then filtered through a pad of diatomaceous earth that was washed with ethyl acetate (2 × 10 mL). The combined filtrates were concentrated under reduced pressure, and the residue thus obtained was subjected to flash chromatography (silica, 1:1 v/v ethyl acetate/hexane elution) to give, after concentration of the appropriate fractions (R_f = 0.2 in 1:2 v/v ethyl acetate/hexane), the title compound **47** (650 mg, 64%) as a light-yellow oil, $[\alpha]_D^{20}$ = + 1.5 (c = 0.8, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.33 (t, J = 4.0 Hz, 1H), 4.09 (m, 1H), 3.94 (m, 1H), 3.71 (broad s, 1H), 3.37 (s, 3H), 2.92 (broad s, 2H), 2.50 (dt, J = 18.1 and 4.4 Hz, 1H), 2.19 (d, J = 18.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 135.4, 100.0, 78.1, 75.0, 69.4, 57.5, 31.1; IR ν_{max} 3400, 2928, 2830, 1627, 1395, 1151, 1101, 1078, 980, 844 cm^{-1}; MS (EI, 70 eV) m/z 270 ($M^{+\bullet}$, 9%), 252 (3), 196 (14), 74 (100); HRMS $M^{+\bullet}$ calcd for $C_7H_{11}{}^{127}IO_3$ 269.9753, found 269.9750.

*(1R,2R,6S)-6-Methoxy-3-(7-methyl-3-methyleneoct-6-en-1-yn-1-yl)cyclohex-3-ene-1,2-diol (**5**).* Alkyne **36** (485 mg, 3.62 mmol) was added to a magnetically stirred solution of compound **47** (650 mg, 2.41 mmol) in anhydrous diethylamine (20 mL). The resulting solution was sparged with nitrogen for 0.5 h, and then $PdCl_2(PPh_3)_2$ (169 mg, 0.24 mmol) and cuprous iodide (68.8 mg, 0.36 mmol) were added. The ensuing mixture was stirred at 20 °C for 21 h and then concentrated under reduced pressure, and the residue thus obtained was subjected to flash chromatography (silica, 1:4 →1:1 v/v ethyl acetate/hexane gradient elution). Concentration of the appropriate fractions (R_f = 0.3 in 1:1 v/v ethyl acetate/hexane) gave the title compound **5** (400 mg, 60%) as a clear, light-yellow oil, $[\alpha]_D^{20}$ = +11 (c = 1.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.05 (t, J = 4.1 Hz, 1H), 5.35 (d, J = 1.6 Hz, 1H), 5.25 (d, J = 1.6 Hz, 1H), 5.11 (m, 1H), 4.09 (m, 1H), 3.88 (m, 1H), 3.66 (m, 1H), 3.38 (s, 3H), 2.95 (broad s, 1H), 2.89 (d, J = 10.0 Hz, 1H), 2.59 (dm, J = 19.2 Hz, 1H), 2.31 (complex m, 1H), 2.25−2.17 (complex m, 4H), 1.68 (s, 3H), 1.61 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 132.2, 132.0, 131.2, 123.3, 121.4, 89.6, 87.8, 78.4, 69.6, 68.7, 57.3, 37.4, 28.5, 26.8, 25.7, 17.8; IR ν_{max} 3427, 2931, 2190, 1717, 1667, 1446, 1376, 1217, 1084, 755 cm^{-1}; MS (ESI, + ve) m/z 575 [$(2\ M + Na)^+$, 15%], 299 [$(M + Na)^+$, 100]; HRMS $(M + Na)^+$ calcd for $C_{17}H_{24}NaO_3$ 299.1623, found 299.1622.

*(3aS,4R,5S,7aS)-7-Iodo-5-methoxy-2,2-dimethyl-3a,4,5,7a-tetrahydrobenzo[d][1,3] diox-ol-4-ol (**48**).* A magnetically stirred solution of epoxide **38**[15] (326 mg, 1.11 mmol) in methanol/$CHCl_3$ (7.5 mL of a 1:1 v/v mixture) maintained at 20 °C was treated with (1*S*)-(+)-10-camphorsulfonic acid (52 mg, 0.22 mmol), and the ensuing mixture maintained in the dark for 0.5 h. After this time, the reaction mixture was concentrated under reduced pressure, and the residue was subjected to flash chromatography (silica, 1:1 v/v ethyl acetate/hexane gradient elution). Concentration of the appropriate fractions (R_f = 0.4 in 1.5:1 v/v ethyl acetate/hexane) then gave the title compound **48** (166 mg, 45%) as a clear, colorless oil, $[\alpha]_D^{20}$ = +34 (c = 4.4, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.53 (s, 1H), 4.68 (d, J = 6.5 Hz, 1H), 4.13 (m, 1H), 3.64 (s, 1H), 3.63 (m, 1H), 3.47 (s, 3H), 2.67 (broad s, 1H), 1.54 (s, 3H), 1.41 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 140.3, 110.3, 93.1, 81.3, 79.5, 77.1, 72.4, 57.5, 28.0, 25.8; IR ν_{max} 3442, 2986, 2933, 2828, 1632, 1455, 1376, 1249, 1217, 1163, 1072, 972, 948, 912, 868, 790, 744 cm^{-1}; MS (EI, 70 eV) m/z 326 (1%), 311 [$(M - CH_3\bullet)^+$, 100], 251 (10), 239 (28), 226 (32), 124 (50), 101 (75); HRMS $(M - CH_3\bullet)^+$ calcd for $C_9H_{12}{}^{127}IO_4$ 310.9780, found 310.9781.

*(1S,2S,3S,6S)-4-Iodo-6-methoxycyclohex-4-ene-1,2,3-triol (**49**).* A magnetically stirred solution of acetonide **48** (489 mg, 1.50 mmol) in a mixture of methanol/THF (10 mL of a 1:1 v/v mixture) was treated with acidified AG-50W-X8 acidic resin (979 mg, 200 wt %), and the ensuing mixture was stirred vigorously at 20 °C for 48 h while being protected from light. The ensuing mixture was filtered through a pad of diatomaceous earth that was washed with ethyl acetate (2 × 20 mL). The combined filtrates were concentrated under reduced pressure, and the residue so obtained was subjected to flash chromatography (silica, ethyl acetate gradient elution) to give, after concentration of the appropriate fractions (R_f = 0.3 in ethyl acetate), the title compound **49** (323 mg, 75%) as a white, crystalline solid, mp =123−124 °C, $[\alpha]_D^{20}$ = − 2.4 (c = 0.5, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.50 (d, J = 2.3 Hz, 1H), 4.41 (t, J = 4.3 Hz, 1H), 3.81 (m, 1H), 3.70−3.64 (complex m, 2H), 3.48 (s, 3H), 3.03 (d, J = 6.4 Hz, 1H), 2.87 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.2, 98.4, 82.7, 75.3, 70.7, 70.2, 57.3; IR ν_{max} 3306, 2989, 2927, 2909, 2848, 1620, 1455, 1362, 1270, 1224, 1186, 1147, 1074, 993, 950, 877 cm^{-1}; MS (ESI, + ve) m/z 309 [$(M + Na)^+$, 100%]. HRMS $(M + Na)^+$ calcd for $C_7H_{11}{}^{127}INaO_4$ 308.9600, found 308.9600.

*(1S,2R,3R,6S)-6-Methoxy-4-(7-methyl-3-methyleneoct-6-en-1-yn-1-yl)cyclohex-4-ene-1,2,3-triol (**6**).* Alkyne **36** (1.11 g, 8.28 mmol) was added to a magnetically stirred solution of iodide **49** (1.18 g, 4.14 mmol) in anhydrous diethylamine (40 mL). The resulting solution was sparged with nitrogen for 0.5 h, and then $PdCl_2(PPh_3)_2$ (291 mg, 0.41 mmol) and cuprous iodide (118 mg, 0.62 mmol) were added. The ensuing mixture was stirred at 20 °C for 22 h and then concentrated under reduced pressure, and the dark brown residue so obtained was subjected to flash chromatography (silica, hexane →1:7:2 v/v/v methanol/ethyl acetate/hexane gradient elution). Concentration of the appropriate fractions (R_f = 0.5 in 1:7:2 v/v/v methanol/ethyl acetate/hexane) gave the product **6** (484 mg, 40%) as a clear, light-yellow oil, $[\alpha]_D^{20}$ = +34 (c = 2.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.11 (d, J = 2.4 Hz, 1H), 5.36 (s, 1H), 5.26 (d, J = 1.1 Hz, 1H), 5.10 (m, 1H), 4.28 (d, J = 4.1 Hz, 1H), 4.05 (broad s, 2H), 3.89 (m, 1H), 3.80 (m, 1H), 3.63 (m, 1H), 3.56 (m, 1H), 3.48 (s, 3H), 2.19 (m, 4H), 1.68 (s, 3H), 1.61 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 134.2, 132.3, 131.0, 123.2, 123.1, 122.0,

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90.6, 87.5, 81.1, 71.1, 70.2, 69.8, 57.1, 37.2, 26.7, 25.7, 17.8; IR ν_{max} 3400, 2925, 1631, 1605, 1438, 1376, 1083, 943, 894 cm^{-1}; MS (ESI, + ve) m/z 315 [$(M + Na)^+$, 100%]; HRMS $(M + Na)^+$ calcd for $C_{17}H_{24}NaO_4$ 315.1572, found 315.1571.

*(3aS,4S,5R,7aS)-7-Iodo-5-methoxy-2,2-dimethyl-3a,4,5,7a-tetrahydrobenzo[d][1,3]-diox-ol-4-ol (**50**).* A magnetically stirred solution of epoxide **44** (1.18 g, 3.99 mmol) in methanol/$CHCl_3$ (45 mL of a 2:1 v/v mixture) was treated with (1*S*)-(+)-10-camphorsulfonic acid (186 mg, 0.80 mmol), and the resulting mixture was stirred in the dark for 0.5 h. The solvent was then removed under reduced pressure, and the residue thus obtained was subjected to flash chromatography (silica, 1:1 v/v ethyl acetate/hexane gradient elution). Concentration of the appropriate fractions (R_f = 0.2 in 1:3 v/v ethyl acetate/hexane) gave the title compound **50** (1.21 g, 93%) as a clear, colorless solid, mp = 72−78 °C, $[\alpha]_D^{20}$ = −29 (*c* = 7.5, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 6.47 (d, *J* = 1.8 Hz, 1H), 4.63 (m, 1H), 4.47 (m, 1H), 3.94 (d, *J* = 8.3 Hz, 1H), 3.81 (dd, *J* = 8.3 and 2.6 Hz, 1H), 3.50 (s, 3H), 2.61 (broad s, 1H), 1.43 (s, 3H), 1.41 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.1, 110.6, 100.6, 80.6, 79.7, 76.3, 71.2, 57.6, 27.4, 26.4; IR ν_{max} 3390, 2984, 2918, 2843, 1697, 1618, 1381, 1217, 1073 cm^{-1}; MS (EI, 70 eV) m/z 311 [$(M - CH_3\bullet)^+$, 14%], 239 (23), 226 (100); HRMS $(M - CH_3\bullet)^+$ calcd for $C_9H_{12}{}^{127}IO_4$ 310.9780, found 310.9773.

*(1R,2S,3S,6R)-4-Iodo-6-methoxycyclohex-4-ene-1,2,3-triol (**51**).* A magnetically stirred solution of acetonide **50** (1.21 g, 3.70 mmol) in methanol/THF (20 mL of a 1:1 v/v mixture) was treated with acidified AG-50W-X8 ion-exchange resin (2.40 g, 200 wt %), and the ensuing mixture was stirred vigorously at 20 °C for 48 h while being protected from light. The solvent was then removed under reduced pressure, and the residue thus obtained was subjected to flash chromatography (silica, ethyl acetate gradient elution). Concentration of the appropriate fractions (R_f = 0.2 in 0.5:9.5 v/v ethyl acetate/hexane) gave the title compound **51** (379 mg, 36%) as a white, crystalline solid, mp = 73−77 °C, $[\alpha]_D^{20}$ = −61 (*c* = 0.8, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 6.56 (s, 1H), 4.20 (s, 2H), 3.90 (m, 2H), 3.46 (s, 3H), 3.26 (broad s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 136.5, 104.7, 80.1, 73.6, 72.1, 70.1, 57.4; IR ν_{max} 3217, 2918, 2861, 2821, 1660, 1620, 1415, 1336, 1099, 1081, 1045, 1028, 847 cm^{-1}; MS (EI, 70 eV) m/z 309 [$(M + Na)^+$, 100%]; HRMS $(M + Na)^+$ calcd for $C_7H_{11}{}^{127}INaO_4$, 308.9600, found, 308.9600.

*(1R,2R,3R,6R)-6-Methoxy-4-(7-methyl-3-methyleneoct-6-en-1-yn-1-yl)cyclohex-4-ene-1,2,3-triol (**7**).* Alkyne **36** (684 mg, 5.10 mmol) was added to a magnetically stirred solution of triol **51** (951 mg, 3.33 mmol) in diethylamine (30 mL) maintained at 20 °C. The ensuing mixture was sparged with nitrogen for 0.5 h, and then $PdCl_2(PPh_3)_2$ (234 mg, 0.33 mmol) and cuprous iodide (95.1 mg, 0.55 mmol) were added. After 21 h, the reaction mixture was concentrated under reduced pressure, and the brown residue thus obtained was subjected to flash chromatography (silica, hexane →9:1 ethyl acetate/hexane gradient elution). Concentration of the appropriate fractions (R_f = 0.4 in 1:7:2 v/v/v methanol/ethyl acetate/hexane) gave the title compound **7** (331 mg, 34%) as a clear, light-yellow oil, $[\alpha]_D^{20}$ = − 15 (*c* = 0.8, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 6.17 (m, 1H), 5.38 (s, 1H), 5.29 (s, 1H), 5.10 (m, 1H), 4.21 (m, 2H), 4.05 (m, 1H), 3.81 (d, *J* = 6.8 Hz, 1H), 3.47 (s, 3H), 2.98 (broad s, 1H), 2.87 (broad s, 1H), 2.83 (broad s, 1H), 2.21 (m, 4H), 1.69 (s, 3H), 1.62 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 132.3, 131.7, 131.0, 124.4, 123.2, 122.0, 91.3, 86.8, 78.6, 72.0, 70.5, 69.2, 57.1, 37.2, 26.7, 25.2, 17.7; IR ν_{max} 3390, 2958, 2923, 2857, 2193, 1634, 1438, 1377, 1261, 1084 cm^{-1}; MS (ESI, + ve) m/z 315 [$(M + Na)^+$, 100%]; HRMS $(M + Na)^+$ calcd for $C_{17}H_{24}NaO_4$ 315.1572, found 315.1570.

*6-Methylheptan-2-one (**53**).* A magnetically stirred mixture of the commercially available ketone **52** (2.00 g, 15.85 mmol) and Pd on carbon (100 mg of 10% material) in MeOH (5 mL) was placed under a balloon of hydrogen at 20 °C. After 5 h, the reaction mixture was filtered through a short pad of diatomaceous earth, and the filtrate was concentrated under reduced pressure to give compound **53**[19] (1.64 g, 81%) as a clear, pale-yellow oil. ^1H NMR (500 MHz, $CDCl_3$) δ 2.36 (t, *J* = 7.5 Hz, 2H), 2.1 (s, 3H), 1.57−1.45 (complex m, 3H), 1.11 (m, 2H), 0.83 (d, *J* = 6.4 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.2, 43.9, 38.3, 29.7, 27.7, 22.4, 21.6; IR (KBr) ν_{max} 2955, 2872, 1717, 1468, 1365, 1168, 1107, 861 cm^{-1}.

*6-Methylhept-1-en-2-yl trifluoromethanesulfonate (**54**).* A magnetically stirred solution of diisopropylamine (2.9 mL, 20.69 mmol) in THF (30 mL) maintained between −15 and −20 °C under a nitrogen atmosphere was treated, dropwise, with *n*-BuLi (12 mL of a 1.6 M solution in hexanes, 19.2 mmol). After 0.25 h, the cooling bath was removed, and stirring was continued for 0.5 h. The reaction mixture thus obtained was cooled to −78 °C and then treated with compound **53** (1.66 g, 12.97 mmol). After stirring at −78 °C for 1 h, $PhNTf_2$ (5.6 g, 15.68 mmol) was added, and the ensuing mixture was stirred for a further 18 h while being allowed to warm to 20 °C and then poured into NH_4Cl (80 mL of a saturated aqueous solution). The separated aqueous phase was extracted with diethyl ether (1 × 60 mL), and the combined organic phases were washed with brine (1 × 80 mL), then dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Subjection of residue thus obtained to flash chromatography (silica, 1:50 v/v diethyl ether/pentane gradient elution) delivered, after concentration of the appropriate fractions (R_f = 0.5 in 1:80 v/v ethyl acetate/hexane), compound **54** (2.31 g, 68%) as a clear, pale-yellow oil. ^1H NMR (500 MHz, $CDCl_3$) δ 5.09 (d, *J* = 3.5 Hz, 1H), 4.93 (m, 1H), 2.31 (t, *J* = 7.6 Hz, 2H), 1.59−1.51 (complex m, 3H), 1.30−1.21 (complex m, 2H), 0.88 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.1, 118.6 (q, J_{C-F} = 320 Hz), 103.9, 37.8, 34.0, 27.7, 23.8, 22.3; IRν_{max} 2959, 2874, 1670, 1419, 1246, 1211, 1141, 937, 897, 612 cm^{-1}; MS (EI 70 eV) m/z 111 [$(M\text{-}TfO\bullet)^+$, 36%], 109 (32), 95 (67), 69 (100); HRMS $(M\text{-}TfO\bullet)^+$ calcd for C_8H_{15} 111.1174, found 111.1173.

*Trimethyl(7-methyl-3-methyleneoct-1-yn-1-yl)silane (**55**).* Trimethylsilylacetylene (1.9 mL, 13.45 mmol) was added to a magnetically stirred mixture of compound **54** (2.33 g, 8.94 mmol), cuprous iodide (255 mg, 1.34 mmol), and $PdCl_2(CH_3CN)_2$ (232 mg, 0.90 mmol) in piperidine/THF (30 mL of a 2:1 v/v mixture) maintained under a nitrogen atmosphere. After stirring at 20 °C for 1 h, the reaction mixture was treated with diethyl ether (40 mL) and then NH_4Cl (100 mL of a saturated aqueous solution). The separated aqueous phase was extracted with diethyl ether (40 mL), and the combined organic phases were washed with NH_4Cl (1 × 100 mL of a saturated aqueous solution) before being dried ($MgSO_4$), filtered, then concentrated under reduced pressure. Subjection of the residue thus obtained to flash chromatography (silica, pentane elution) delivered, after concentration of the appropriate fractions (R_f = 0.6 in hexane), compound **55** (1.58 g, 85%) as a clear, pale-yellow oil. ^1H NMR (500 MHz, $CDCl_3$) δ 5.35 (d, *J* = 2.0 Hz, 1H), 5.22 (m, 1H), 2.12 (m, 2H), 1.58−1.49 (complex m, 3H), 1.21−1.16 (complex m, 2H), 0.88 (d, *J* = 6.3 Hz, 6H), 0.19 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 132.0, 121.7, 105.8, 93.7, 38.1, 37.2, 27.8, 25.7, 22,6, − 0.0(3); IR ν_{max} 2957, 2870, 2147, 1605, 1468, 1250, 879, 842, 759 cm^{-1}; MS (EI 70 eV) m/z 208 ($M^{+\bullet}$, 33%), 193 (45), 123 (82), 73 (100); HRMS $M^{+\bullet}$ calcd for $C_{13}H_{24}Si$ 208.1647, found 208.1642.

*7-Methyl-3-methyleneoct-1-yne (**56**).* Compound **55** (1.25 g, 5.99 mmol) in methanol (5 mL) was treated with K_2CO_3 (2.48 g, 17.95 mmol). After stirring at 18 °C for 2 h, the reaction mixture was filtered through a short pad of diatomaceous earth, and the filtrate then was concentrated under reduced pressure. Subjection of the residue thus obtained to flash chromatography (silica, pentane elution) delivered, after concentration of the appropriate fractions (R_f = 0.7 in hexane), compound **56** (594 mg, 73%) as a clear, pale-yellow oil. ^1H NMR (500 MHz, $CDCl_3$) δ 5.41 (d, *J* = 1.9 Hz, 1H), 5.29 (m, 1H), 2.88 (s, 1H), 2.14 (m, 2H), 1.54−1.49 (complex m, 3H), 1.21−1.15 (complex m, 2H), 0.88 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 131.0, 122.6, 84.2, 76.7, 38.1, 37.2, 27.8, 25.7, 22.6; IR ν_{max} 3310, 2955, 2870, 1611, 1468, 1384, 1367, 1249, 902, 637, 612 cm^{-1}; MS (EI, 70 eV) m/z 136 ($M^{+\bullet}$, 13%), 135 (47), 121 (25), 73 (100); HRMS $M^{+\bullet}$ calcd for $C_{10}H_{16}$ 136.1252, found 136.1249.

*(((3aR,4R,5R,7aS)-7-Iodo-5-methoxy-2,2-dimethyl-3a,4,5,7a-tetrahydrobenzo[d]-[1,3]dioxol-4-yl)oxy)triisopropylsilane (**58**) and (((3aS,4S,5R,7aS)-7-Iodo-4-methoxy-2,2-dimethyl-3a,4,5,7a-tetrahydrobenzo[d][1,3]dioxol-5-yl)oxy)triisopropylsilane (**59**).* Sodium hydride (300 mg of a 60% dispersion in mineral oil, 7.50 mmol) was added to a magnetically stirred solution of compound **57**[8] (1.16 g, 2.48 mmol) and iodomethane (460 μL, 7.39 mmol) in dry THF (25 mL) maintained at 0 °C under a nitrogen atmosphere. Stirring was continued at 0 to 18 °C for 2 h, then the reaction mixture was treated

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with ice/water (60 mL). The separated aqueous phase was extracted with ethyl acetate (1 × 25 mL), and the combined organic phases were then dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The ensuing light-yellow oil was subjected to flash chromatography (silica, 1:50 v/v ethyl acetate/hexane gradient elution) to give two fractions, A and B.

Concentration of fraction A (R_f = 0.4 in 0.5:2.5:5.5 v/v/v ethyl acetate/dichloromethane/hexane) gave compound **58** (100 mg, 8%) as a white, crystalline solid, mp = 66−67 °C, $[\alpha]_D^{20}$ = −27.5 (c = 0.2, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.44 (d, J = 1.9 Hz, 1H), 4.62 (dd, J = 5.3 and 1.6 Hz, 1H), 4.50 (m, 1H), 4.29 (t, J = 5.0 Hz, 1H), 3.84 (m, 1H), 3.41 (s, 3H), 1.41 (s, 3H), 1.39 (s, 3H), 1.07 (m, 21H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.7, 109.8, 98.9, 79.5, 77.9, 77.2, 69.7, 57.3, 27.5, 26.3, 18.0(4), 17.9(7), 12.6; IR ν_{max} 2940, 2888, 2865, 1636, 1462, 1383, 1335, 1241, 1221, 1198, 1139, 1122, 1081, 1040, 996, 881, 858, 681 cm^{-1}; MS (EI, 70 eV) m/z 467 [(M-CH_3•)$^+$, 6%], 439 (35), 381 (42), 349 (37), 257 (40), 254 (100), 222 (55), 145 (88); HRMS (M-CH_3•)$^+$ calcd for $C_{18}H_{32}{}^{127}IO_4Si$ 467.1115, found 467.1112.

Concentration of fraction B (R_f = 0.3 in 0.5:2.5:5.5 v/v/v ethyl acetate/dichloromethane/hexane) gave compound **59**[8] (1.07 g, 90%) as a white, crystalline solid. The physical and spectroscopic data recorded on this material were essentially identical with those reported[8] previously.

*(1S,2R,3R,4R)-6-Iodo-3-methoxycyclohex-5-ene-1,2,4-triol (**60**).* Compound **59** (200 mg, 0.42 mmol) was treated with acetic/water (10 mL of a 7:1 v/v mixture), and the resulting solution was heated at 70 °C for 18 h, then cooled, and concentrated under reduced pressure. Subjection of the residue thus obtained to flash chromatography (silica, 1:6:3 v/v/v methanol/ethyl acetate/hexane gradient elution) gave, after concentration of the appropriate fractions (R_f = 0.4 in 1:7:2 v/v/v methanol/ethyl acetate/hexane), compound **60**[8] (81 mg, 68%) as a white, crystalline solid. The physical and spectroscopic data recorded on this material were essentially identical with those reported[8] previously.

*(1R,2R,3R,4R)-3-Methoxy-6-(7-methyl-3-methyleneoct-1-yn-1-yl)-cyclohex-5-ene-1,2,4-triol (**10**).* Cuprous iodide (5 mg, 0.03 mmol) and $PdCl_2(PPh_3)_2$ (14 mg, 0.03 mmol) were added to a magnetically stirred solution of compounds **60** (120 mg, 0.42 mmol) and **56** (57 mg, 0.42 mmol) in anhydrous diethylamine (10 mL) maintained at 20 °C under a nitrogen atmosphere. After 3 h, the reaction mixture was concentrated under reduced pressure, and the residue thus obtained was subjected to flash chromatography (silica, 1:6:3 v/v/v methanol/ethyl acetate/hexane gradient elution). Concentration of the appropriate fractions (R_f = 0.5 in 1:7:2 v/v/v methanol/ethyl acetate/hexane) gave compound **10** (99 mg, 80%) as a clear, light-yellow oil, $[\alpha]_D^{20}$ = −49.1 (c = 2.6, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.15 (d, J = 4.2 Hz, 1H), 5.36 (s, 1H), 5.28 (s, 1H), 4.49 (s, 1H), 4.33 (m, 1H), 4.19 (m, 1H), 3.68 (m, 1H), 3.53 (s, 3H), 2.73 (broad s, 2H), 2.15 (t, J = 7.5 Hz, 2H), 2.09 (s, 1H) 1.56−1.46 (complex m, 3H), 1.25−1.14 (complex m, 2H), 0.88 (s, 3H), 0.86 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 134.6, 131.3, 123.9, 122.0, 91.6, 86.6, 78.6, 68.4, 67.4, 64.0, 58.5, 38.1, 37.2, 27.8, 25.9, 22.6; IR ν_{max} 3400, 2953, 2869, 1630, 1604, 1466, 1384, 1239, 1105, 1094, 1040, 989 cm^{-1}; MS (EI, 70 eV) m/z 294 (M$^{+\bullet}$, 5%), 276 (15), 247 (37), 220 (100), 150 (53); HRMS M$^{+\bullet}$ calcd for $C_{17}H_{26}O_4$ 294.1831, found 294.1832.

*(3aR,4R,5R,7aR)-4,5-Dimethoxy-2,2-dimethyl-7-(7-methyl-3-methyleneoct-1-yn-1-yl)- 3a,4,5,7a-tetrahydrobenzo[d][1,3]dioxole (**61**).* Cuprous iodide (26 mg, 0.14 mmol) and $PdCl_2(PPh_3)_2$ (63 mg, 0.09 mmol) were added to a magnetically stirred solution of compounds **35** (306 mg, 0.90 mmol) and **56** (184 mg, 1.35 mmol) in diethylamine (10 mL) maintained under under a nitrogen atmosphere. After stirring at 20 °C for 3 h, the reaction mixture was concentrated under reduced pressure, and the residue thus obtained was subjected to flash chromatography (silica, 1:5 v/v ethyl acetate/hexane gradient elution). Concentration of the appropriate fractions (R_f = 0.5 in 2:2.5:5.5 v/v/v ethyl acetate/dichloromethane/hexane) then gave compound **61** (179 mg, 96%) as a pale-yellow oil, $[\alpha]_D^{20}$ = −54 (c = 0.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.23 (d, J = 3.9 Hz, 1H), 5.34 (d, J = 2.0 Hz, 1H), 5.24 (m, 1H), 4.63 (d, J = 6.1 Hz, 1H), 4.44 (t, J = 6.1 Hz, 1H), 4.02 (m, 1H), 3.65 (m, 1H), 3.51 (s, 3H), 3.43 (s, 3H), 2.14 (m, 2H), 1.56−1.49 (complex m, 3H), 1.44 (s, 3H), 1.38 (s, 3H), 1.19−1.15 (complex m, 2H), 0.87 (d, J = 6.6 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.5, 131.6, 123.2, 121.5, 109.4, 90.9, 87.2, 79.0, 74.2, 74.0, 73.8, 58.8, 57.4, 38.1, 37.3, 27.8, 27.5, 25.8, 25.5, 22.6; IR ν_{max} 2984, 2953, 2934, 1605, 1463, 1381, 1369, 1234, 1200, 1115, 1081, 874 cm^{-1}; MS (EI, 70 eV) m/z 348 (M$^{+\bullet}$, 3%), 333 (6), 234 (17), 115 (100), 75 (15); HRMS M$^{+\bullet}$ calcd for $C_{21}H_{32}O_4$ 348.2316, found 348.2301.

*(1R,2R,5R,6S)-5,6-Dimethoxy-3-(7-methyl-3-methyleneoct-1-yn-1-yl)cyclohex-3-ene-1,2-diol (**11**).* Compound **61** (121 mg, 0.35 mmol) was treated with acetic/water (10 mL of a 7:3 v/v mixture). The ensuing mixture was heated at 70 °C for 14 h, then cooled, and concentrated under reduced pressure. Subjection of the residue thus obtained to flash chromatography (silica, 1:6:3 v/v/v methanol/ethyl acetate/hexane elution) delivered, after concentration of the appropriate fractions (R_f = 0.5 in 1:4:5 v/v/v methanol/ethyl acetate/hexane), compound **11** (64 mg, 60%) as a light-yellow semisolid, $[\alpha]_D^{20}$ = −135 (c = 0.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.24 (dd, J = 4.5 and 0.6 Hz, 1H), 5.35 (d, J = 2.3 Hz, 1H), 5.26 (dd, J = 2.3 and 1.0 Hz, 1H), 4.34 (d, J = 4.1 Hz, 1H), 4.16 (m, 1H), 4.10 (m, 1H), 3.69 (m, 1H), 3.50 (s, 3H), 3.46 (s, 3H), 2.94 (broad s, 2H), 2.14 (m, 2H), 1.57−1.49 (complex m, 3H), 1.19−1.15 (complex m, 2H), 0.87 (d, J = 6.6 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 132.3, 131.4, 124.7, 121.9, 91.4, 87.0, 77.4, 72.6, 68.7, 67.5, 58.0, 57.6, 38.1, 37.2, 27.7, 25.8, 22.6; IR ν_{max} 3307, 2952, 2899, 2871, 1603, 1465, 1316, 1124, 1103, 885 cm^{-1}; MS (ESI, + ve) m/z 331 [(M+Na)$^+$, 100%]; HRMS (M+Na)$^+$ calcd for $C_{18}H_{28}NaO_4$, 331.1885, found 331.1888.

*(3aS,4S,5S,7aS)-7-Iodo-2,2-dimethyl-5-((triisopropylsilyl)oxy)-3a,4,5,7a-tetrahydro-benzo[d][1,3]dioxol-4-ol (**63**).* Triisopropylsilyl trifluoromethanesulfonate (1.02 mL, 3.78 mmol) was added, dropwise, to a magnetically stirred solution of compound **62**[15] (982 mg, 3.15 mmol) and 2,6-lutidine (1.5 mL, 12.90 mmol) in dichloromethane (25 mL) maintained at −78 °C under a nitrogen atmosphere. The ensuing mixture was allowed to warm to 20 °C over 3 h and then treated with NH_4Cl (60 mL of a saturated aqueous solution). The separated aqueous phase was extracted with dichloromethane (1 × 40 mL), and the combined organic phases were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The resulting light-yellow oil was subjected to flash chromatography (silica, 3:100 v/v ethyl acetate/hexane gradient elution) to give, after concentration of the appropriate fractions (R_f = 0.3 in 0.5:2.5:5.5 v/v/v ethyl acetate/dichloromethane/hexane), compound **63** (722 mg, 49%) as a clear, colorless oil, $[\alpha]_D^{20}$ = +12.6 (c = 0.3, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.42 (d, J = 1.2 Hz, 1H), 4.67 (d, J = 6.6 Hz, 1H), 4.17 (d, J = 8.2 Hz, 1H), 4.11 (m, 1H), 3.56 (m, 1H), 2.41 (broad s, 1H), 1.55 (s, 3H), 1.41 (s, 3H), 1.10 (m, 21H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 136.4, 117.7, 110.9, 77.4, 77.0, 74.6, 72.6, 28.0, 25.8, 18.0(0), 17.9(8), 12.4; IR ν_{max} 3416, 2943, 2892, 2867, 1644, 1463, 1383, 1248, 1218, 1070, 1015, 997, 882, 829, 682 cm^{-1}; MS (EI, 70 eV) m/z 453 [(M-CH_3•)$^+$, 5%], 367 (41), 240 (100); HRMS (M-CH_3•)$^+$ calcd for $C_{17}H_{30}{}^{127}IO_4Si$ 453.0958, found 453.0957.

*(((3aS,4S,5S,7aS)-7-Iodo-4-methoxy-2,2-dimethyl-3a,4,5,7a-tetrahydrobenzo[d]- [1,3]-dioxol-5-yl)oxy)triisopropylsilane (**64**).* Sodium hydride (300 mg of a 60% dispersion in mineral oil, 7.50 mmol) was added to a magnetically stirred solution of compound **63** (1.16 g, 2.48 mmol) and iodomethane (460 μL, 7.39 mmol) in dry THF (25 mL) maintained at 0 °C under a nitrogen atmosphere. Stirring was continued at 0 to 18 °C for 3 h, and then the reaction mixture was treated with ice/water (60 mL) (*Caution: possibility of hydrogen generation*). The separated aqueous phase was extracted with ethyl acetate (1 × 25 mL), and the combined organic phases were then dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The ensuing light-yellow oil was subjected to flash chromatography (silica, 1:50 v/v ethyl acetate/hexane elution) to give, after concentration of the appropriate fractions (R_f = 0.4 in 0.5:2.5:5.5 v/v/v ethyl acetate/dichloromethane/hexane), compound **64** (780 mg, 65%) as a clear, light-yellow oil, $[\alpha]_D^{20}$ = +33.1 (c = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.55 (d, J = 3.2 Hz, 1H), 4.60 (d, J = 6.0 Hz, 1H), 4.18 (t, J = 6.0 Hz, 1H), 4.04 (t, J = 6.0 Hz, 1H), 3.58−3.48 (complex m, 1H), 3.40 (s, 3H), 1.48 (s, 3H), 1.38 (s, 3H), 1.11 (m, 21H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.9, 110.1, 99.5, 81.2, 78.4, 77.9, 71.1, 57.5, 27.6, 26.1, 18.1, 18.0, 12.5; IR ν_{max} 2941, 2866, 1635, 1463, 1381, 1251, 1214, 1166, 1125, 1075, 975, 882, 768m 679 cm^{-1}; MS (EI, 70 eV) m/z 467 [(M-CH_3•)$^+$, 12%], 439 (46), 381 (82),

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349 (46), 254 (100), 222 (64), 145 (73); HRMS (M-CH_3•)$^+$ calcd for $C_{18}H_{32}{}^{127}IO_4Si$ 467.1115, found 467.1110.

*(3aS,4R,5S,7aS)-7-Iodo-4-methoxy-2,2-dimethyl-3a,4,5,7a-tetrahydrobenzo[d][1,3]-diox-l-5-ol (**65**).* A magnetically stirred solution of compound **64** (972 mg, 2.02 mmol) in THF (10 mL) maintained at 18 °C under a nitrogen atmosphere was treated with tetra-*n*-butylammonium fluoride (3 mL of 1.0 M solution in THF, 3.00 mmol). After 2 h, the reaction mixture was concentrated under pressure, and the residue so-formed subjected to flash chromatography (silica, 1:2 v/v ethyl acetate/hexane gradient elution). Concentration of the appropriate fractions (R_f = 0.4 in 4:2.5:5.5 v/v/v ethyl acetate/dichloromethane/hexane) then gave compound **65** (592 mg, 90%) as a clear, light-yellow oil, $[\alpha]_D^{20}$ = +42.5 (*c* = 0.4, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.51 (s, 1H), 4.67 (d, *J* = 6.7 Hz, 1H), 4.12 (t, *J* = 6.7 Hz, 1H), 3.61 (m, 2H), 3.46 (s, 3H), 2.85 (broad s, 1H), 1.52 (s, 3H), 1.39 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 140.3, 110.3, 93.2, 81.3, 79.5, 77.2, 72.4, 57.5, 28.0, 25.8; IR ν_{max} 3399, 2987, 2932, 2830, 1642, 1457, 1380, 1252, 1218, 1074, 945, 869 cm^{-1}; MS (EI, 70 eV) *m*/*z* 326 (8%), 311 [(M-CH_3•)$^+$, 73], 225 (32), 124 (58), 101 (100), 55 (51); HRMS (M-CH_3•)$^+$ calcd for $C_9H_{12}{}^{127}IO_4$ 310.9780, found 310.9778.

*(3aR,4R,5S,7aR)-4-Methoxy-2,2-dimethyl-7-(7-methyl-3-methyleneoct-1-yn-1-yl)-3a,4,5,7a-tetrahydrobenzo[d][1,3]dioxol-5-ol (**14**).* Cuprous iodide (25 mg, 0.13 mmol) and $PdCl_2(PPh_3)_2$ (59 mg, 0.09 mmol) were added to a magnetically stirred solution of compounds **65** (275 mg, 0.85 mmol) and **56** (230 mg, 1.69 mmol) in anhydrous diethylamine (3 mL) maintained at 18 °C under a nitrogen atmosphere. After 3 h, the reaction mixture was concentrated under reduced pressure, and the residue obtained was subjected to flash chromatography (silica, 2:5 v/v ethyl acetate/hexane gradient elution). Concentration of the appropriate fractions (R_f = 0.5 in 4:2.5:5.5 v/v/v ethyl acetate/dichloromethane/hexane) then gave compound **14** (192 mg, 68%) as a clear, light-yellow oil, $[\alpha]_D^{20}$ = +11.5 (*c* = 0.2, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.19 (d, *J* = 1.8 Hz, 1H), 5.36 (s, 1H), 5.27 (s, 1H), 4.58 (d, *J* = 6.4 Hz, 1H), 4.10 (dd, *J* = 9.0 and 6.4 Hz, 1H), 3.73 (d, *J* = 8.9 Hz, 1H), 3.64 (t, *J* = 8.9 Hz, 1H), 3.47 (s, 3H), 2.75 (s, 1H), 2.16 (t, *J* = 7.6 Hz, 2H), 1.55 (m, 3H), 1.53 (s, 3H), 1.40 (s, 3H), 1.21−1.15 (complex m, 2H), 0.88 (s, 3H), 0.87 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 135.6, 131.4, 121.9, 119.5, 110.8, 91.0, 86.4, 79.7, 77.3, 74.5, 72.5, 57.3, 38.1, 37.2, 28.2, 27.8, 25.9, 25.8, 22.6; IR ν_{max} 3345, 2922, 2883, 2861, 1649, 1465, 1382, 1259, 1207, 1123, 1060, 1022, 872 cm^{-1}; MS (EI, 70 eV) *m*/*z* 334 (M$^{+\bullet}$, 5%), 319 (23), 259 (42), 247 (63), 115 (18), 101 (100); HRMS M$^{+\bullet}$ calcd for $C_{20}H_{30}O_4$ 334.2144, found 334.2140.

*(1R,2R,3R,4S)-3-Methoxy-6-(7-methyl-3-methyleneoct-1-yn-1-yl)-cyclohex-5-ene-1,2,4-triol (**12**).* Compound **14** (360 mg, 1.08 mmol) was treated with acetic/water (10 mL of a 4:1 v/v mixture), and the solution thus obtained was heated at 70 °C for 5 h, then cooled, and concentrated under reduced pressure. Subjection of the ensuing light-yellow residue to flash chromatography (silica, 1:6:3 v/v/v methanol/ethyl acetate/hexane gradient elution) delivered, after concentration of the appropriate fractions (R_f = 0.5 in 1:7:2 v/v/v methanol/ethyl acetate/hexane), compound **12** (228 mg, 72%) as a clear, light-yellow oil, $[\alpha]_D^{20}$ = −31.7 (*c* = 0.7, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.15 (d, *J* = 2.2 Hz, 1H), 5.37 (s, 1H), 5.28 (s, 1H), 4.32 (d, *J* = 4.1 Hz, 1H), 3.89−3.78 (complex m, 2H), 3.60 (m, 1H), 3.49 (s, 3H), 3.03 (broad s, 1H), 2.92 (broad s, 1H), 2.67 (broad s, 1H), 2.16 (t, *J* = 7.7 Hz, 2H), 1.57−1.50 (complex m, 3H), 1.25−1.16 (complex m, 2H), 0.86 (d, *J* = 7.0 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 134.1, 131.4, 123.2, 121.8, 90.6, 87.4, 81.2, 71.1, 70.0, 69.9, 57.1, 38.1, 37.2, 27.7, 25.8, 22.6; IR ν_{max} 3399, 2954, 2928, 1672, 1462, 1384, 1367, 1234, 1185, 1096, 1081, 952 cm^{-1}; MS (EI, 70 eV) *m*/*z* 294 (M$^{+\bullet}$, 2%), 247 (47), 234 (92), 164 (100); HRMS M$^{+\bullet}$ calcd for $C_{17}H_{26}O_4$ 294.1831 found 294.1833.

*(3aS,4R,5R,7aS)-7-Iodo-4-methoxy-2,2-dimethyl-3a,4,5,7a-tetrahydrobenzo[d][1,3]-dioxol-5-ol (**66**).* A magnetically stirred solution of compound **59** (972 mg, 2.02 mmol) in THF (10 mL) maintained at 18 °C under a nitrogen atmosphere was treated with tetra-*n*-butylammonium fluoride (3 mL of 1.0 M solution in THF, 3.00 mmol). After 2 h, the reaction mixture was concentrated under pressure, and the residue so-formed was subjected to flash chromatography (silica, 1:2 v/v ethyl acetate/hexane gradient elution). Concentration of the appropriate fractions (R_f = 0.4 in 4:2.5:5.5 v/v/v ethyl acetate/dichloromethane/hexane) then gave compound **66**[8] (578 mg, 88%) as a white, crystalline solid. The physical and spectroscopic data recorded on this material were essentially identical with those reported[8] previously.

*(3aR,4R,5R,7aR)-4-Methoxy-2,2-dimethyl-7-(7-methyl-3-methyleneoct-1-yn-1-yl)-3a,4,5,7a-tetrahydrobenzo[d][1,3]dioxol-5-ol (**13**).* Cuprous iodide (50 mg, 0.25 mmol) and $PdCl_2(PPh_3)_2$ (118 mg, 0.17 mmol) were added to a magnetically stirred solution of compounds **66** (550 mg, 1.68 mmol) and **56** (460 mg, 3.38 mmol) in anhydrous diethylamine (3 mL) maintained at 20 °C under a nitrogen atmosphere. After 3 h, the reaction mixture was concentrated under reduced pressure, and the residue thus obtained was subjected to flash chromatography (silica, 2:5 v/v ethyl acetate/hexane gradient elution). Concentration of the appropriate fractions (R_f = 0.5 in 4:2.5:5.5 v/v/v ethyl acetate/dichloromethane/hexane) then gave compound **13** (397 mg, 70%) as a clear, light-yellow oil, $[\alpha]_D^{20}$ = −9.0 (*c* = 1.4, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.11 (d, *J* = 3.5 Hz, 1H), 5.35 (d, *J* = 2.0 Hz, 1H), 5.25 (d, *J* = 2.0 Hz, 1H), 4.57 (d, *J* = 5.7 Hz, 1H), 4.48 (t, *J* = 5.7 Hz, 1H), 4.39 (m, 1H), 3.67 (m, 1H), 3.53 (s, 3H), 2.54 (d, *J* = 8.3 Hz, 1H), 2.15 (t, *J* = 7.5 Hz, 2H), 1.61−1.47 (complex m, 3H), 1.43 (s, 3H), 1.39 (s, 3H), 1.21−1.13 (complex m, 2H), 0.87 (d, *J* = 7.0 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 135.5, 131.6, 122.5, 121.5, 109.7, 90.7, 87.2, 79.6, 73.7, 73.1, 64.7, 58.9, 38.2, 37.3, 27.8, 27.6, 26.0, 25.8, 22.6; IR ν_{max} 3454, 2980, 2949, 2935, 2896, 2865, 1631, 1604, 1461, 1379, 1369, 1231, 1109, 1076, 1037, 985 cm^{-1}; MS (EI, 70 eV) *m*/*z* 334 (M$^{+\bullet}$, 3%), 319 (7), 259 (5), 247 (12), 115 (100); HRMS M$^{+\bullet}$ calcd for $C_{20}H_{30}O_4$ 334.2144, found 334.2142.

*((3,5-Dimethylphenyl)ethynyl)trimethylsilane (**68**).* Commercially available 1-iodo-3,5-dimethylbenzene **67** (300 mg, 1.29 mmol), $PdCl_2(PPh_3)_2$ (45 mg, 0.07 mmol), and cuprous iodide (12 mg, 0.07 mmol) were placed in an oven-dried flask under a nitrogen atmosphere. Dry diethylamine was added, and the resulting suspension was stirred magnetically while being cooled at 0 °C. Trimethylsilylacetylene (0.28 mL, 1.94 mmol) was then added dropwise to the reaction mixture that was then allowed to warm to 20 °C and stirred at this temperature for 3 h. The ensuing reaction mixture was concentrated under reduced pressure, and diethyl ether (20 mL) then was added to the residue thus obtained. The ensuing mixture was filtered through a short pad of diatomaceous earth, and the filtrate was washed with brine (1 × 20 mL) before being dried (Na_2SO_4), filtered, and then concentrated under reduced pressure. Subjection of the residue thus obtained to flash chromatography (silica, pentane elution) delivered, after concentration of the appropriate fractions (R_f = 0.5 in hexane), compound **68**[18] (177 mg, 68%) as a clear, light-yellow syrup. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.11 (s, 2H), 6.95 (s, 1H), 2.28 (s, 6H), 0.24 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.7, 130.4, 129.6, 122.7, 105.5, 93.2, 21.1, 0.0(1); IR ν_{max} 2962, 2923, 2247, 2150, 2107, 1599, 1251 cm^{-1}; MS (EI, 70 eV) *m*/*z* 202 (M$^{+\bullet}$, 28%) 187 (100); HRMS M$^{+\bullet}$ calcd for $C_{13}H_{18}Si$ 202.1178, found 202.1184.

*1-Ethynyl-3,5-dimethylbenzene (**69**).* A magnetically stirred solution of compound **68** (850 mg, 4.21 mmol) in MeOH (5 mL) maintained at 20 °C was treated with K_2CO_3 (1.63 g, 8.41 mmol), and after 1 h, the reaction mixture was filtered through a pad of diatomaceous earth, and the filtrate was concentrated under reduced pressure. Subjection of the residue thus obtained to flash chromatography (silica, pentane elution) delivered, after concentration of the appropriate fractions (R_f = 0.5 in hexane), compound **69**[18] (396 mg, 72%) as a clear, light-yellow syrup. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.13 (s, 2H), 6.99 (s, 1H), 3.01 (s, 1H), 2.29 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.9, 130.7, 129.8, 121.7, 84.0, 76.3, 21.1; IR ν_{max} 3307, 3039, 2952, 2922, 2249, 2108, 1601, 1475 cm^{-1}; MS (EI, 70 eV) *m*/*z* 130 (M$^{+\bullet}$, 6%), 102 (100); HRMS M$^{+\bullet}$ calcd for $C_{10}H_{10}$ 130.0783, found 130.0782.

*(3aR,4R,5R,7aR)-7-((3,5-Dimethylphenyl)ethynyl)-4-methoxy-2,2-dimethyl-3a,4,5,7a -tetrahydrobenzo[d][1,3]dioxol-5-ol (**19**).* Compound **66** (250 mg, 0.77 mmol), $PdCl_2(PPh_3)_2$ (27 mg, 0.04 mmol), and cuprous iodide (7 mg, 0.04 mmol) were placed in an oven-dried flask under a nitrogen atmosphere. Dry diethylamine (10 mL) was then added, and the resulting suspension cooled and stirred magnetically at 0 °C. After the dropwise addition of 1-ethynyl-3,5-dimethylbenzene (**69**)

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(166 μL, 1.15 mmol) was complete, the reaction mixture was stirred at 20 °C for 3 h and then concentrated under reduced pressure, and diethyl ether (20 mL) was added to the residue thus obtained. The ensuing mixture was filtered through a pad of diatomaceous earth, and the filtrate was washed with brine (1 × 30 mL) before being dried (Na_2SO_4), filtered, and then concentrated under reduced pressure. Subjection of the ensuing residue to flash chromatography (silica, 1:4 v/v ethyl acetate/hexane elution) delivered, after concentration of the appropriate fractions (R_f = 0.4 in 1:6 v/v ethyl acetate/hexane), compound **19** (191 mg, 76%) as a clear, yellow syrup, $[\alpha]_D^{20}$ = +54.5 (*c* = 0.2, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.11 (s, 2H), 6.94 (s, 1H), 6.19 (d, *J* = 3.5 Hz, 1H), 4.65 (d, *J* = 5.7 Hz, 1H), 4.52 (t, *J* = 5.7 Hz, 1H), 4.44 (complex m, 1H), 3.71 (t, *J* = 4.7 Hz, 1H), 3.55 (s, 3H), 2.58 (d, *J* = 8.6 Hz, 1H), 2.28 (s, 6H), 1.45 (s, 3H), 1.42 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.7, 135.6, 130.3, 129.5, 122.5(0), 122.4(8), 109.8, 90.4, 86.8, 79.6, 73.7, 73.1, 64.8, 59.0, 27.7, 26.0, 21.1; IR ν_{max} 3455, 2986, 2934, 2831, 2204, 1597, 1456, 1371, 1233, 1164, 1076, 955, 872, 850, 689 cm^{-1}; MS (EI, 70 eV) *m*/*z* 328 ($M^{+\bullet}$, 15%), 115 (100); HRMS $M^{+\bullet}$ calcd for $C_{20}H_{24}O_4$ 328.1675, found 328.1675.

*(1R,2R,3R,4R)-6-((3,5-Dimethylphenyl)ethynyl)-3-methoxycyclohex-5-ene-1,2,4-triol (**15**).* Compound **19** (50 mg, 0.15 mmol) was treated with acetic/water (10 mL of a 7:3 v/v mixture), and the resulting solution was heated at 70 °C for 5 h, then cooled, and concentrated under reduced pressure. Subjection of the residue thus obtained to flash chromatography (silica, 1:6:3 v/v/v methanol/ethyl acetate/hexane gradient elution) gave, after concentration of the appropriate fractions (R_f = 0.4 in 9:1 v/v ethyl acetate/hexane), compound **15** (trace) as a white, crystalline solid, mp =157−159 °C, $[\alpha]_D^{20}$ = −33.3 (*c* = 0.4, $CHCl_3$). ^{1}H NMR [$(CD_3)_2CO$, 400 MHz] δ 6.84 (s, 2H), 6.77 (s, 1H), 5.85 (d, *J* = 3.8 Hz, 1H), 4.24 (m, 1H), 4.00 (m, 1H), 3.92 (m, 1H), 3.79 (m, 1H), 3.50 (d, *J* = 7.2 Hz, 1H), 3.39 (m, 1H), 3.26 (s, 3H), 2.68 (broadened s, 6H) (signal due to one hydroxyl group proton not observed); ^{13}C NMR [$(CD_3)_2CO$, 100 MHz] δ 139.5, 137.7, 131.6, 130.7, 125.8, 124.7, 90.8, 89.8, 81.5, 69.9, 69.8, 66.3, 59.6, 21.8; IR ν_{max} 3389, 3303, 2915, 2848, 1958, 1597, 1432, 1381, 1291, 1093, 1060, 1034, 849, 686 cm^{-1}; MS (EI, 70 eV) *m*/*z* 288 ($M^{+\bullet}$, 12%), 214 (100); HRMS $M^{+\bullet}$ calcd for $C_{17}H_{20}O_4$ 288.1362, found 288.1360.

*(3aR,4R,5R,7aR)-7-((3,5-Dimethylphenyl)ethynyl)-4,5-dimethoxy-2,2-dimethyl-3a,4,5,7a-tetrahydrobenzo[d][1,3]dioxole (**20**).* Compound **35** (100 mg, 0.30 mmol), $PdCl_2(PPh_3)_2$ (11 mg, 0.02 mmol), and cuprous iodide (3 mg, 0.02 mmol) were placed in an oven-dried flask under a nitrogen atmosphere. Dry diethylamine (10 mL) was added, and the resulting suspension was cooled and magnetically stirred at 0 °C. After the dropwise addition of 1-ethynyl-3,5-dimethylbenzene (**69**) (65 μL, 0.44 mmol), the reaction mixture was stirred at 20 °C for 3 h and then concentrated under reduced pressure. The residue thus obtained was treated with diethyl ether (10 mL), the resulting mixture filtered through a pad of diatomaceous earth, and the filtrate was washed with brine (1 × 20 mL) before being dried (Na_2SO_4), filtered, and then concentrated under reduced pressure. Subjection of the residue thus obtained to flash chromatography (silica, 1:4 v/v ethyl acetate/hexane gradient elution) gave, after concentration of the appropriate fractions (R_f = 0.5 in 1:5 v/v ethyl acetate/hexane), compound **20** (72 mg, 72%) as a clear, yellow syrup, $[\alpha]_D^{20}$ = −7.3 (*c* = 0.3, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.11 (s, 2H), 6.94 (s, 1H), 6.32 (d, *J* = 3.9 Hz, 1H), 4.71 (d, *J* = 6.1 Hz, 1H), 4.48 (m, 1H), 4.07 (m, 1H), 3.69 (m, 1H), 3.54 (s, 3H), 3.46 (s, 3H), 2.28 (s, 6H), 1.48 (s, 3H), 1.42 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.7, 133.6, 130.3, 129.5, 123.2, 122.5, 109.5, 90.7, 86.9, 79.1, 74.3, 74.1, 74.0, 58.9, 57.4, 27.6, 25.6, 21.1; IR ν_{max} 2985, 2933, 2827, 2201, 1598, 1457, 1380, 1370, 1212, 1164, 1107, 1081, 1037, 873, 851, 689 cm^{-1}; MS (EI, 70 eV) *m*/*z* 342 ($M^{+\bullet}$, 20%), 327 (13), 228 (37), 115 (100); HRMS $M^{+\bullet}$ calcd for $C_{21}H_{26}O_4$ 342.1831, found 342.1830.

*(1R,2R,5R,6S)-3-((3,5-Dimethylphenyl)ethynyl)-5,6-dimethoxycyclohex-3-ene-1,2-diol (**16**).* Compound **20** (50 mg, 0.15 mmol) was treated with acetic/water (10 mL of a 7:3 v/v mixture) and the resulting solution was heated at 70 °C for 5 h then cooled and concentrated under reduced pressure. Subjection of the residue thus obtained to flash chromatography (silica, 9:1 v/v ethyl acetate/hexane gradient elution) gave, after concentration of the appropriate fractions (R_f = 0.4 in 9:1 v/v ethyl acetate/hexane), compound **16** (trace) as light-yellow oil, $[\alpha]_D^{20}$ = −79.4 (*c* = 0.82, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.10 (s, 2H), 6.96 (s, 1H), 6.35 (d, *J* = 4.5 Hz, 1H), 4.43 (d, *J* = 4.5 Hz, 1H), 4.21 (m, 1H), 4.13 (t, *J* = 4.2 Hz, 1H), 3.72 (dd, *J* = 8.9 and 3.8 Hz, 1H), 3.53 (s, 3H), 3.50 (s, 3H), 2.80 (s, 1H), 2.74 (s, 1H), 2.29 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.8, 132.3, 130.4, 129.3, 124.8, 122.1, 91.1, 86.7, 77.4, 72.7, 68.7, 67.6, 58.0, 57.5, 21.0; IR ν_{max} 3412, 2920, 2825, 1629, 1597, 1464, 1194, 1098, 990, 850, 689 cm^{-1}; MS (EI, 70 eV) *m*/*z* 302 ($M^{+\bullet}$, 4%), 253 (15), 228 (100), 213 (50), 199 (35), 185 (46), 157 (30); HRMS $M^{+\bullet}$ calcd for $C_{18}H_{22}O_4$ 302.1518, found 302.1519.

*(3aS,4R,5R,7aS)-7-Iodo-5-methoxy-2,2-dimethyl-3a,4,5,7a-tetrahydrobenzo[d][1,3]-dioxol-4-ol (**71**).* A magnetically stirred solution of compound **58** (100 mg, 0.21 mmol) in THF (10 mL) maintained at 18 °C under a nitrogen atmosphere was treated with tetra-*n*-butylammonium fluoride (0.3 mL of 1.0 M solution in THF, 0.30 mmol). After 2 h the reaction mixture was concentrated under pressure. The residue so-formed was subjected to flash chromatography (silica, 1:2 v/v ethyl acetate/hexane gradient elution) to provide, after concentration of the appropriate fractions (R_f = 0.4 in 4:2.5:5.5 v/v/v ethyl acetate/dichloromethane/hexane), compound **71** (54 mg, 80%) as a white, crystalline solid, mp = 79.5 °C, $[\alpha]_D^{20}$ = −29.4 (*c* = 0.4, $CHCl_3$).[1] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.42 (d, *J* = 2.6 Hz, 1H), 4.64 (m, 1H), 4.45−4.36 (complex m, 1H), 3.87 (m, 1H), 3.46 (s, 3H), 2.42 (d, *J* = 2.4 Hz, 1H), 1.42 (s, 3H), 1.40 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 136.2, 109.8, 101.2, 78.3, 76.6, 75.8, 66.9, 57.1, 27.6, 26.2; IR ν_{max} 3520, 2998, 2934, 2872, 2828, 1627, 1458, 1379, 1148, 1082, 1051, 1025, 996, 930, 897, 871, 860 cm^{-1}; MS (EI, 70 eV) *m*/*z* 326 ($M^{+\bullet}$, 14%), 310 (21), 268 (20), 226 (18), 101 (100); HRMS $M^{+\bullet}$ calcd for $C_{10}H_{15}{}^{127}IO_4$ 326.0015, found 326.0016.

*(1S,2S,3S,6R)-4-Iodo-6-methoxycyclohex-4-ene-1,2,3-triol (**72**).* Compound **71** (50 mg, 0.10 mmol) was dissolved in acetic/water (10 mL of a 7:1 v/v mixture) and the resulting solution was heated at 70 °C for 18 h then cooled and concentrated under reduced pressure. Subjection of the residue thus obtained to flash chromatography (silica, 1:6:3 v/v/v methanol/ethyl acetate/hexane gradient elution) gave, after concentration of the appropriate fractions (R_f = 0.4 in 1:7:2 v/v/v methanol/ethyl acetate/hexane), compound **72** (32 mg, 72%) as a white, crystalline solid, mp =117 °C, $[\alpha]_D^{20}$ = −111.3 (*c* = 0.3, $CHCl_3$). ^{1}H NMR [$(CD_3)_2SO$, 400 MHz] δ 6.29 (d, *J* = 1.4 Hz, 1H), 5.17 (m, 1H), 4.99 (s, 1H), 4.82 (m, 1H), 3.99 (broad s, 2H), 3.83−3.77 (complex m, 2H), 3.36 (s, 3H); ^{13}C NMR [$(CD_3)_2SO$, 400 MHz] δ 136.4, 106.9, 76.9, 70.5, 70.1, 67.6, 55.8; IR ν_{max} 3354, 2923, 2857, 2821, 1628, 1461, 1384, 1186, 1098, 1069, 967, 917, 878 cm^{-1}; MS (EI, 70 eV) *m*/*z* 286 ($M^{+\bullet}$, > 1%), 267 (13), 226 (100), 99 (75); HRMS $M^{+\bullet}$ calcd for $C_7H_{11}{}^{127}IO_4$ 285.9702, found 285.9696.

*(1S,2R,3R,6R)-4-((3,5-Dimethylphenyl)ethynyl)-6-methoxycyclohex-4-ene-1,2,3-triol (**17**).* Compound **72** (100 mg, 0.35 mmol), $PdCl_2(PPh_3)_2$ (13 mg, 0.02 mmol) and cuprous iodide (4 mg, 0.02 mmol) were placed in an oven-dried flask under a nitrogen atmosphere. Dry diethylamine (5 mL) was added and the resulting suspension was cooled and magnetically stirred at 0 °C. After the dropwise addition of 1-ethynyl-3,5-dimethylbenzene (**69**) (101 μL, 0.70 mmol) was complete the reaction mixture was stirred at 18 °C for 3 h then concentrated under reduced pressure and diethyl ether (10 mL) was added to the ensuing residue. The mixture thus obtained was filtered through a pad of diatomaceous earth and the filtrate was washed with brine (1 × 25 mL) then dried (Na_2SO_4), filtered and concentrated under reduced pressure. Subjection of the residue so-formed to flash chromatography (silica, 1:6:3 v/v/v methanol/ethyl acetate/hexane gradient elution) delivered, after concentration of the appropriate fractions (R_f = 0.4 in 9:1 v/v ethyl acetate/hexane), compound **17** (73 mg, 73%) as a clear, light-yellow oil, $[\alpha]_D^{20}$ = −101.9 (*c* = 0.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.10 (s, 2H), 6.96 (s, 1H), 6.29 (m, 1H), 4.44 (s, 1H), 4.12−4.08 (complex m, 2H), 4.00 (m, 1H), 3.49 (s, 3H), 2.85 (s, 1H), 2.76 (s, 1H), 2.56 (m, 1H), 2.29 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.9, 131.7, 130.6, 129.4, 125.1, 122.0, 91.6, 86.4, 74.8, 69.4, 68.4, 67.9, 57.4, 21.1; IR ν_{max} 3400, 2917, 2821, 1597, 1318, 1097, 1070, 1035, 941, 912, 849, 688 cm^{-1}; MS (EI, 70 eV) *m*/*z* 288 ($M^{+\bullet}$, 17%), 228 9100), 213 (54), 199 (60), 185 (59); HRMS $M^{+\bullet}$ calcd for $C_{17}H_{20}O_4$ 288.1362, found 288.1361.

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*(1S,2R,3R,4S)-6-Iodo-3-methoxycyclohex-5-ene-1,2,4-triol (**73**).* Compound **65** (208 mg, 0.43 mmol) was dissolved in acetic/water (10 mL of a 7:1 v/v mixture) and the resulting solution heated at 70 °C for 18 h then cooled and concentrated under reduced pressure. Subjection of the residue thus obtained to flash chromatography (silica, 1:6:3 v/v/v methanol/ethyl acetate/hexane gradient elution) gave, after concentration of the appropriate fractions (R_f = 0.4 in 1:7:2 v/v/v methanol/ethyl acetate/hexane), compound **73** (142 mg, 78%) as a clear, light-yellow oil, $[\alpha]_D^{20}$ = +2.0 (c = 0.3, $CHCl_3$). ^{1}H NMR [$(CD_3)_2CO$, 400 MHz] δ 6.14 (d, J = 2.5 Hz, 1H), 4.54 (s, 1H), 4.25 (m, 1H), 4.14 (s, 1H), 4.02 (s, 1H), 3.73 (m, 1H), 3.63 (m, 1H) 3.54 (m, 1H), 3.43 (s, 3H); ^{13}C NMR [$(CD_3)_2CO$, 100 MHz] δ 133.0, 125.6, 83.7, 74.8, 73.0, 72.0, 58.4; IR ν_{max} 3355, 2929, 2826, 1643, 1454, 1262, 1105, 1076, 1002, 942, 882, 820, 697 cm^{-1}; MS (ESI, + ve) m/z 309 [(M +Na)$^+$, 58%], 263 (95), 261 (100), 120 (5); HRMS (M+Na)$^+$ calcd for $C_7H_{11}{}^{127}INaO_4$ 308.9600, found 308.9600.

*(1R,2R,3R,4S)-6-((3,5-Dimethylphenyl)ethynyl)-3-methoxycyclohex-5-ene-1,2,4-triol (**18**).* Compound **73** (50 mg, 0.18 mmol), $PdCl_2(PPh_3)_2$ (7 mg, 0.01 mmol) and cuprous iodide (2 mg, 0.01 mmol) were placed in an oven-dried flask under a nitrogen atmosphere. Dry diethylamine (3 mL) was added and the resulting suspension was cooled to 0 °C while being stirred magnetically. After the dropwise addition of 1-ethynyl-3,5-dimethylbenzene (**69**) (51 μL, 0.35 mmol) was complete the reaction mixture was stirred at 20 °C for 3 h then concentrated under reduced pressure and diethyl ether (10 mL) then added to the residue thus obtained. The resulting mixture was filtered through a pad of diatomaceous earth and the filtrate washed with brine (1 × 10 mL) before being dried (Na_2SO_4) filtered and then concentrated under reduced pressure. Subjection of the residue thus obtained to flash chromatography (silica, 1:6:3 v/v/v methanol/ethyl acetate/hexane gradient elution) afforded, after concentration of the appropriate fractions (R_f = 0.4 in 9:1 v/v ethyl acetate/hexane), compound **18** (35 mg, 70%) as a clear, light-yellow oil, $[\alpha]_D^{20}$ = +15.0 (c = 0.1, $CHCl_3$). ^{1}H NMR [$(CD_3)_2CO$, 400 MHz] δ 7.07 (s, 2H), 7.01 (s, 1H), 6.11 (d, J = 2.6 Hz, 1H), 4.35 (d, J = 4.7 Hz, 1H), 4.24 (t, J = 4.7 Hz, 1H), 4.06 (m, 1H), 3.86 (d, J = 6.3 Hz, 1H), 3.90−3.70 (complex m, 2H), 3.47 (s, 3H), 2.77 (s, 1H), 2.28 (s, 6H); ^{13}C NMR [$(CD_3)_2CO$, 100 MHz] δ 139.6, 136.7, 131.8, 130.7, 125.2, 124.5, 90.7, 89.9, 83.1, 73.0, 72.3, 71.4, 58.4, 21.8; IR ν_{max} 3368, 2916, 2857, 2826, 1597, 1455, 1373, 1263, 1099, 1083, 952, 941, 848, 688 cm^{-1}; MS (EI, 70 eV) m/z 288 ($M^{+\bullet}$, 17%), 277 (40), 228 (100), 185 (57); HRMS $M^{+\bullet}$ calcd for $C_{17}H_{20}O_4$ 288.1362, found 288.1373.

*(1R,2R,3R,4R)-6-((3,5-Dimethoxyphenyl)ethynyl)-3-methoxycyclohex-5-ene-1,2,4-triol (**21**).* Compound **60** (200 mg, 0.70 mmol), $PdCl_2(PPh_3)_2$ (25 mg, 0.04 mmol) and cuprous iodide (7 mg, 0.04 mmol) were placed in an oven-dried flask under a nitrogen atmosphere. Dry diethylamine (10 mL) was added and the resulting suspension was cooled and stirred magnetically at 0 °C. After the dropwise addition of commercially available 1-ethynyl-3,5-dimethoxybenzene (**70**) (252 μL, 1.40 mmol) was complete the reaction mixture was stirred at 20 °C for 3 h then concentrated reduced pressure and diethyl ether (25 mL) was added. The mixture thus obtained was filtered through a pad of diatomaceous earth and the filtrate washed with brine (1 × 25 mL) before being dried (Na_2SO_4) filtered and concentrated under reduced pressure. Subjection of the residue thus obtained to flash chromatography (silica, 1:6:3 v/v/v methanol/ethyl acetate/hexane gradient elution) delivered, after concentration of the appropriate fractions (R_f = 0.4 in 9:1 v/v ethyl acetate/hexane), compound **21** (139 mg, 62%) as a clear, light-yellow oil, $[\alpha]_D^{20}$ = −38.3 (c = 1.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.62 (d, J = 2.4 Hz, 2H), 6.46 (t, J = 2.4 Hz, 1H), 6.26 (d, J = 4.2 Hz, 1H), 4.52 (m, 1H), 4.41 (s, 1H), 4.23 (m, 1H), 3.78 (s, 6H), 3.71 (dd, J = 7.9 and 4.1 Hz, 1H), 3.55 (s, 3H), 2.68 (m, 2H), 2.51 (d, J = 6.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.5, 135.3, 123.8, 123.7, 109.5, 102.1, 91.0, 86.5, 78.6, 68.3, 67.4, 64.0, 58.5, 55.4; IR ν_{max} 3400, 2936, 2839, 1589, 1455, 1420, 1205, 1156, 1095, 1063, 989, 837, 681 cm^{-1}; MS (EI, 70 eV) m/z 320 ($M^{+\bullet}$, 23%), 273 (18), 270 (21), 246 (100), 217 (33), 189 (39); HRMS $M^{+\bullet}$ calcd for $C_{17}H_{20}O_6$ 320.1260, found 320.1260.

*(1R,2S,5R,6S)-3-Iodo-5,6-dimethoxycyclohex-3-ene-1,2-diol (**74**).* Compound **35** (120 mg, 0.35 mmol) was treated with acetic/water (5 mL of a 7:1 v/v mixture) and the resulting solution heated at 70 °C for 14 h then cooled and concentrated under reduced pressure. Subjection of the residue thus obtained to flash chromatography (silica, 4:1 v/v ethyl acetate/hexane gradient elution) gave, after concentration of the appropriate fractions (R_f = 0.4 in 4:1 v/v ethyl acetate/hexane), compound **74** (75 mg, 70%) as a white, crystalline solid, mp =78.3−83.3 °C, $[\alpha]_D^{20}$ = −162.5 (c = 0.2, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.62 (d, J = 4.5 Hz, 1H), 4.40 (s, 1H), 4.22 (m, 1H), 3.95 (t, J = 4.1 Hz, 1H), 3.66 (m, 1H), 3.49 (s, 3H), 3.46 (s, 3H), 3.12 (broad s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.5, 103.5, 77.2, 74.9, 74.0, 68.0, 58.2, 57.8; IR ν_{max} 3401, 2980, 2929, 2826, 1629, 1455, 1369, 1344, 1195, 1097, 1051, 997, 928, 916, 865, 805 cm^{-1}; MS (EI, 70 eV) m/z 300 ($M^{+\bullet}$, 2%), 282 (5), 226 (100), 99 (63); HRMS $M^{+\bullet}$ calcd for $C_8H_{13}{}^{127}IO_4$ 299.9859, found 299.9859.

*(1R,2R,5R,6S)-3-((3,5-Dimethoxyphenyl)ethynyl)-5,6-dimethoxycyclohex-3-ene-1,2-diol (**22**).* Compound **74** (165 mg, 0.55 mmol), $PdCl_2(PPh_3)_2$ (20 mg, 0.03 mmol) and cuprous iodide (5 mg, 0.03 mmol) were placed in an oven-dried flask under a nitrogen atmosphere. Dry diethylamine (10 mL) was added and the resulting suspension was cooled and magnetically stirred at 0 °C. After the dropwise addition of 1-ethynyl-3,5-dimethoxybenzene (**70**) (198 μL, 1.10 mmol) to the reaction mixture was complete it was stirred at 20 °C for 3 h then concentrated under reduced pressure and diethyl ether (25 mL) added to the residue thus obtained. The resulting mixture was filtered through a pad of diatomaceous earth and the filtrate washed with brine (1 × 25 mL) then dried (Na_2SO_4,), filtered and concentrated under reduced pressure. Subjection of the residue so-formed to flash chromatography (silica, 4:1 v/v ethyl acetate/hexane gradient elution) delivered, after concentration of the appropriate fractions (R_f = 0.4 in 5:1 v/v ethyl acetate/hexane), compound **22** (114 mg, 62%) as a clear, light-yellow oil, $[\alpha]_D^{20}$ = −90.2 (c = 0.5, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.62 (d, J = 2.3 Hz, 2H), 6.45 (t, J = 2.3 Hz, 1H), 6.37 (d, J = 4.5 Hz, 1H), 4.44 (m, 1H), 4.20 (m, 1H), 4.13 (t, J = 4.2 Hz, 1H), 3.77 (s, 6H), 3.71 (dd, J = 8.9 and 3.9 Hz, 1H), 3.52 (s, 3H), 3.49 (s, 3H), 2.87 (d, J = 1.9 Hz, 1H), 2.85 (d, J = 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.5, 133.0, 124.6, 123.9, 109.5, 102.2, 90.8, 86.9, 77.5, 72.6, 68.7, 67.6, 58.1, 57.7, 55.4; IR ν_{max} 3429, 2934, 2909, 2837, 1589, 1455, 1420, 1205, 1156, 1096, 1064, 990, 867, 838, 681 cm^{-1}; MS (EI, 70 eV) m/z 334 ($M^{+\bullet}$, 20%), 285 (20< 261 (30), 260 (100), 245 (65), 231 (45), 217 (48); HRMS $M^{+\bullet}$ calcd for $C_{18}H_{22}O_6$ 334.1416, found 334.1415.

*(Z)-2-(3,5-Dimethylstyryl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**76**).* A 50 mL Schlenk tube equipped with a magnetic stirring bar was charged with 1,5-cyclooctadienerhodium(I) chloride dimer {[RhCl(cod)]$_2$} (6 mg, 0.01 mmol) and the flushed with argon. Cyclohexanone (3 mL), triisopropylphosphine [P(i-Pr)$_3$] (10 μL, 0.05 mmol), triethylamine (1 mL) and pinacolborane (HB_{pin}) (**75**) (110 μL, 0.77 mmol) were then added in that order. After the reaction mixture had been stirred at 20 °C for 2 h 3,5-dimethylphenylacetylene (**69**) (200 mg, 1.54 mmol) was added in one portion and the mixture thus formed stirred at 20 °C for 2 h then quenched with methanol (5 mL). The ensuing mixture was filtered through a pad of diatomaceous earth and the filtrate concentrated under reduced pressure to give a light-brown oil. Subjection of this material to flash chromatography (silica, 5:95 v/v ethyl acetate/hexane gradient elution) delivered, after concentration of the appropriate fractions (R_f = 0.3 in 1:9 v/v ethyl acetate/hexane), compound **76** (205 mg, 52%) as a clear, light-yellow oil, $[\alpha]_D^{20}$ = +4.7 (c = 0.9, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.15 (m, 3H), 6.91 (s, 1H), 5.54 (d, J = 14.9 Hz, 1H), 2.30 (s, 6H), 1.30 (s, 12H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.2, 138.4, 137.3, 129.7, 126.4, 83.4, 24.8, 21.2 (signal due to one carbon obscured or overlapping); IR ν_{max} 2978, 2918, 1627, 1601, 1458, 1436, 1379, 1349, 1324, 1262, 1144, 995, 970, 849 cm^{-1}; MS (EI, 70 eV) m/z 258 ($M^{+\bullet}$, 100%), 158 (90), 157 (77), 142 (76); HRMS $M^{+\bullet}$ calcd for $C_{16}H_{23}BO_2$ 258.1791, found 258.1791.

*(1R,2R,3R,4R)-6-((Z)-3,5-Dimethylstyryl)-3-methoxycyclohex-5-ene-1,2,4-triol (**27**).* A magnetically stirred solution of alcohol **60** (300 mg, 1.05 mmol), (Z)-2-(3,5-dimethylstyryl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**76**) (271 mg, 1.05 mmol), $PdCl_2$dppf•CH_2Cl_2 (60 mg, 0.08 mmol) and triethylamine (2 mL) in THF/water (6 mL of a 9:1 v/v mixture) was purged with nitrogen for 0.5 h and then stirred at 20 °C for 2 h before being poured into water (10 mL) and extracted with ethyl

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acetate (3 × 10 mL). The combined organic phases were washed with brine (1 × 20 mL) then dried (Na_2SO_4), filtered and concentrated under reduced pressure. The ensuing light-yellow oil was subjected to flash chromatography (silica, 1:6:3 v/v/v methanol/ethyl acetate/hexane gradient elution) and after concentration of the relevant fractions (R_f = 0.3 in 9:1 v/v ethyl acetate/hexane) gave compound **27** (242 mg, 80%) as a white, crystalline solid, mp =123−127 °C, $[\alpha]_D^{20}$ = −301.6 (c = 0.2, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.00 (s, 2H), 6.86 (s, 1H), 6.53 (d, J = 12.2 Hz, 1H), 6.11 (d, J = 12.2 Hz, 1H), 5.85 (dd, J = 4.6 and 1.5 Hz, 1H), 4.41 (t, J = 4.6 Hz, 1H), 4.33 (m, 1H), 4.07 (m, 1H), 3.62 (dd, J = 8.9 and 4.2 Hz, 1H), 3.52 (s, 3H), 2.44 (broad s, 3H), 2.27 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.7, 137.5, 136.8, 132.4, 129.1, 128.4, 126.5, 78.7, 68.0, 67.9, 63.8, 58.2, 21.2 (signal due to one carbon obscured or overlapping); IR ν_{max} 3401, 2914, 2830, 1598, 1456, 1398, 1246, 1093, 1052, 988, 918, 852 cm^{-1}; MS (EI, 70 eV) m/z 290 ($M^{+\bullet}$, 53%), 212 (58), 198 (100), 119 (53); HRMS $M^{+\bullet}$ calcd for $C_{17}H_{22}O_4$ 290.1518, found 290.1518.

*(1R,2R,3R,4R)-6-((E)-3,5-Dimethylstyryl)-3-methoxycyclohex-5-ene-1,2,4-triol (**23**).* A magnetically stirred solution of compound **27** (100 mg, 0.35 mmol) in chlorobenzene (5 mL) maintained under nitrogen was heated under reflux for 144 h then cooled and concentrated under reduced pressure. Subjection of the residue thus obtained to flash chromatography (silica, ethyl acetate gradient elution) gave, after concentration of the appropriate fractions (R_f = 0.4 in 9:1 v/v ethyl acetate/hexane), compound **23** (33 mg, 85% brsm) as a white, crystalline solid, mp =85 °C, $[\alpha]_D^{20}$ = −128.5 (c = 0.2, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.06 (s, 2H), 6.90 (s, 1H), 6.86 (d, J = 16.3 Hz, 1H), 6.73 (d, J = 16.3 Hz, 1H), 6.01 (d, J = 5.5 Hz, 1H), 4.74 (d, J = 4.0 Hz, 1H), 4.57 (t, J = 4.8 Hz, 1H), 4.04 (m, 1H), 3.65 (dd, J = 10.3 and 4.1 Hz, 1H), 3.56 (s, 3H), 2.74 (broad s, 1H), 2.31 (s, 6H) (signals due to two hydroxyl group protons not observed); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.7, 138.0, 136.8, 131.4, 129.8, 127.6(2), 127.5(6), 124.6, 78.3, 67.8, 66.4, 63.3, 57.8, 21.3; IR ν_{max} 3395, 2916, 2827, 1597, 1446, 1384, 1242, 1104, 1094, 1066, 989, 963, 851 cm^{-1}; MS (EI, 70 eV) m/z 290 (<1%), 289 [(M-H•)$^+$, 2], 272 (8), 211 (15), 183 (17), 133 (100); HRMS (M-H•)$^+$ calcd for $C_{17}H_{21}O_4$ 289.1441, found 289.1440.

*(1R,2R,3R,4R,6S)-6-(3,5-Dimethylphenethyl)-3-methoxycyclohexane-1,2,4-triol (**25**).* A magnetically stirred solution of compound **27** (30 mg, 0.10 mmol) in methanol (1 mL) was treated with rhodium on carbon (9 mg of 5% material). The reaction flask was connected to a balloon of hydrogen and after stirring the reaction mixture for 2 h at 20 °C the catalyst was removed by filtration through a pad of diatomaceous earth and the filtrate concentrated under reduced pressure. Subjection of the residue thus obtained to flash chromatography (silica, 1:6:3 v/v/v methanol/ethyl acetate/hexane gradient elution) gave, after concentration of the appropriate fractions (R_f = 0.4 in 9.5:0.5 v/v ethyl acetate/hexane), compound **25** (14 mg, 47%) as a light-yellow oil, $[\alpha]_D^{20}$ = +21.9 (c = 0.6, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.81 (s, 3H), 4.09 (m, 1H), 4.04 (m, 1H), 3.65 (m, 1H), 3.53 (t, J = 4.3 Hz, 1H), 3.48 (s, 3H), 2.68 (m, 1H), 2.49 (m, 1H), 2.28 (s, 6H), 2.00 (broad s, 3H), 1.97−1.88 (complex m, 2H), 1.79 (m, 1H), 1.61−1.47 (complex m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 142.3, 137.8, 127.4, 126.2, 82.1, 72.5, 69.5, 67.0, 58.4, 36.1, 34.2, 33.0, 31.5, 21.3; IR ν_{max} 3396, 2919, 2861, 2830, 1605, 1458, 1403, 1103, 1087, 1050, 972, 844 cm^{-1}; MS (EI, 70 eV) m/z 294 ($M^{+\bullet}$, 10%), 244 (20), 133 (40), 132 (100), 120 (55), 119 (72); HRMS $M^{+\bullet}$ calcd for $C_{17}H_{26}O_4$ 294.1831, found 294.1828.

*(1R,2R,5R,6S)-3-((Z)-3,5-Dimethylstyryl)-5,6-dimethoxycyclohex-3-ene-1,2-diol (**28**).* A magnetically stirred solution of alcohol **74** (100 mg, 0.33 mmol), compound **76** (86 mg, 0.33 mmol), $PdCl_2$dppf•CH_2Cl_2 (19 mg, 0.03 mmol), and triethylamine (1 mL) in THF/water (2 mL of a 9:1 v/v mixture) was purged with nitrogen for 0.5 h, stirred at 18 °C for 2 h then poured into water (6 mL) and extracted with ethyl acetate (3 × 10 mL). The combined organic phases were washed with brine (1 × 10 mL) then dried (Na_2SO_4), filtered and concentrated under reduced pressure. The ensuing light-yellow oil was subjected to flash chromatography (silica, 3:2 v/v ethyl acetate/hexane gradient elution) and concentration of the relevant fractions (R_f = 0.4 in 2:1 v/v ethyl acetate/hexane) gave compound **28** (79 mg, 78%) as a clear, light-yellow oil, $[\alpha]_D^{20}$ = −178.6 (c = 0.7, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.00 (s, 2H), 6.85 (s, 1H), 6.51 (d, J = 12.2 Hz, 1H), 6.16 (d, J = 12.2 Hz, 1H), 5.96 (dd, J = 5.0 and 1.5 Hz, 1H), 4.36 (dd, J = 4.5 and 1.6 Hz, 1H), 4.13 (m, 1H), 3.99 (t, J = 4.5 Hz, 1H), 3.62 (m, 1H), 3.49 (s, 3H), 3.35 (s, 3H), 2.82 (d, J = 1.7 Hz, 1H), 2.63 (d, J = 2.1 Hz, 1H), 2.27 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.5, 137.7, 136.7, 132.1, 129.0, 128.6, 126.6, 125.9, 77.5, 71.9, 68.4, 67.8, 57.4, 57.2, 21.2; IR ν_{max} 3411, 2971, 2916 2823, 1598, 1454, 1381, 1196, 1107, 1095, 1044, 989, 852 cm^{-1}; MS (EI, 70 eV) m/z 304 ($M^{+\bullet}$, 2%), 272 (12), 230 (78), 212 (85), 198 (100), 183 (55); HRMS $M^{+\bullet}$ calcd for $C_{18}H_{24}O_4$ 304.1675, found 304.1673.

*(1R,2R,5R,6S)-3-((E)-3,5-Dimethylstyryl)-5,6-dimethoxycyclohex-3-ene-1,2-diol (**24**).* A magnetically stirred solution of compound **28** (100 mg, 0.33 mmol) in chlorobenzene (5 mL) maintained under nitrogen was heated under reflux for 144 h then cooled and concentrated under reduced pressure. Subjection of the residue thus obtained to flash chromatography (silica, 1:1 v/v ethyl acetate/hexane gradient elution) delivered, after concentration of the appropriate fractions (R_f = 0.4 in 1:3 v/v ethyl acetate/hexane), compound **24** (36 mg, 80% brsm) as clear, light-yellow oil, $[\alpha]_D^{20}$ = +14.2 (c = 1.4, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.07 (s, 2H), 6.88 (s, 1H), 6.90 (d, J = 16.3 Hz, 1H), 6.73 (d, J = 16.3 Hz, 1H), 6.09 (d, J = 5.4 Hz, 1H), 4.74 (d, J = 4.2 Hz, 1H), 4.15−4.11 (complex m, 2H), 3.66 (m, 1H), 3.53 (s, 3H), 3.51 (s, 3H), 2.31 (s, 6H) (signals due to hydroxyl group protons not observed); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.2, 138.0, 136.8, 131.6, 129.7, 127.7, 125.9, 124.6, 77.7, 71.8, 67.8, 66.1, 57.8, 57.3, 21.3; IR ν_{max} 3400, 2917, 2831, 1599, 1463, 1383, 1257, 1196, 1114, 1093, 1046, 963, 851 cm^{-1}; MS (EI, 70 eV) m/z 304 ($M^{+\bullet}$, 100%), 286 (42), 254 (56); HRMS $M^{+\bullet}$ calcd for $C_{18}H_{24}O_4$ 304.1675, found 304.1674.

*(1R,2R,3S,4R,6S)-6-(3,5-Dimethylphenethyl)-3,4-dimethoxycyclohexane-1,2-diol (**26**).* A magnetically stirred solution of compound **28** (30 mg, 0.10 mmol) in methanol (1 mL) was treated with rhodium on carbon (9 mg of 5% material). The flask was then connected to a balloon of hydrogen and after stirring for 2 h at 20 °C the catalyst was removed by filtration through a pad of diatomaceous earth and the filtrate concentrated under reduced pressure. Subjection of the residue thus obtained to flash chromatography (silica, 9:1 v/v ethyl acetate/hexane gradient elution) gave, after concentration of the appropriate fractions (R_f = 0.4 in 4:1 v/v ethyl acetate/hexane), compound **26** (12 mg, 40%) as a clear, light-yellow oil, $[\alpha]_D^{20}$ = +16.6 (c = 0.8, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.82 (s, 1H), 6.81 (s, 2H), 4.07 (t, J = 4.2 Hz, 1H), 3.66 (m, 3H), 3.48 (s, 3H), 3.41 (s, 3H), 2.68 (m, 1H), 2.50 (m, 1H), 2.28 (s, 6H), 1.98−1.86 (complex m, 3H), 1.76 (m, 1H), 1.63−1.55 (complex m, 2H) (signal due to a hydroxyl group proton not observed); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 142.3, 137.8, 127.4, 126.1, 79.4, 76.6, 72.4, 70.2, 58.4, 56.8, 36.4, 34.2, 33.1, 27.4, 21.3; IR ν_{max} 3401, 2924, 2826, 1606, 1455, 1383, 1195, 1108, 1095, 1055, 974, 844 cm^{-1}; MS (ESI, + ve) m/z 331 [(M+Na)$^+$, 100%]; HRMS (M+Na)$^+$ calcd for $C_{18}H_{28}NaO_4$ 331.1885, found 331.1885.

*(3aS,4S,5S,7aS)-7-Bromo-2,2-dimethyl-5-((triisopropylsilyl)oxy)-3a,4,5,7a-tetrahyd-robenzo[d][1,3]dioxol-4-ol (**81**).* Triisopropylsilyl trifluoromethanesulfonate (1.95 mL, 7.25 mmol) was added, dropwise, to a magnetically stirred solution of compound **80**[19] (1.4 g, 5.30 mmol) and 2,6-lutidine (2.50 mL, 21.5 mmol) in dichloromethane (30 mL) maintained at −78 °C under a nitrogen atmosphere. The ensuing mixture was allowed to warm to 20 °C over 3 h then treated with NH_4Cl (60 mL of a saturated aqueous solution). The separated aqueous phase was extracted with dichloromethane (1 × 50 mL) and the combined organic phases were dried ($MgSO_4$), filtered then concentrated under reduced pressure. The resulting light-yellow oil was subjected to flash chromatography (silica, 3:100 v/v ethyl acetate/hexane gradient elution) to give, after concentration of the appropriate fractions (R_f = 0.3 in 0.5:2.5:5.5 v/v/v ethyl acetate/dichloromethane/hexane), compound **81** (1.15 g, 51%) as a light-yellow oil, $[\alpha]_D^{20}$ = +23.2 (c = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.42 (d, J = 1.6 Hz, 1H), 4.66 (d, J = 6.6 Hz, 1H), 4.17 (m, 1H), 4.11 (m, 1H), 3.55 (t, J = 8.7 Hz, 1H), 2.45 (s, 1H), 1.54 (s, 3H), 1.40 (s, 3H), 1.15−1.04 (complex m, 21H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 144.5, 110.2, 92.2, 79.3, 77.0, 74.5, 73.6, 28.0, 25.7, 18.0(1), 17.9(9), 12.4; IR ν_{max} 3469, 2943, 2892, 2866, 1635, 1463, 1382, 1248, 1218, 1162, 1142, 1070, 1019, 997, 882, 866, 828 cm^{-1}; MS (ESI, + ve) m/z 445 and 443 [(M+Na)$^+$, 100 and

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97%]; HRMS $(M+Na)^+$ calcd for $C_{18}H_{33}{}^{79}BrONaO_4Si$ 443.1229, found 443.1232.

*(((3aS,4S,5S,7aS)-7-Bromo-4-methoxy-2,2-dimethyl-3a,4,5,7a-tetrahydrobenzo[d]- [1,3]dioxol-5-yl)oxy)triisopropylsilane (**82**).* Sodium hydride (257 mg of a 60% dispersion in mineral oil, 6.43 mmol) was added to a magnetically stirred solution of compound **81** (900 mg, 2.14 mmol) and iodomethane (294 μL, 4.73 mmol) in dry THF (20 mL) maintained at 0 °C under a nitrogen atmosphere. Stirring was continued at 0 to 18 °C for 3 h then the reaction mixture was treated with ice/water (60 mL) (*Caution: possible evolution of hydrogen*). The separated aqueous phase was extracted with ethyl acetate (1 × 25 mL) and the combined organic phases were then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The ensuing light-yellow oil was subjected to flash chromatography (silica, 1:50 v/v ethyl acetate/hexane gradient elution) to give, after concentration of the appropriate fractions (R_f = 0.4 in 0.5:2.5:5.5 v/v/v ethyl acetate/dichloromethane/hexane), compound **82** (385 mg, 41%) as a light-yellow oil, $[\alpha]_D^{20}$ = +70.8 (c = 0.5, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.54 (d, J = 3.2 Hz, 1H), 4.60 (d, J = 6.0 Hz, 1H), 4.18 (t, J = 6.0 Hz, 1H), 4.03 (t, J = 5.6 Hz, 1H), 3.56 (m, 1H), 3.40 (s, 3H), 1.48 (s, 3H), 1.38 (s, 3H), 1.14−1.04 (complex m, 21H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.9, 110.1, 99.4, 81.2, 78.4, 77.9, 71.1, 57.5, 27.6, 26.1, 18.1, 18.0, 12.5; IR ν_{max} 2941, 2879, 2865, 1636, 1463, 1380, 1273, 1251, 1214, 1167, 1126, 1076, 952, 882, 865, 768, 679 cm^{-1}; MS (ESI, + ve) m/z 459 and 457 [$(M+Na)^+$, 98 and 96%], 355 (100); HRMS $(M+Na)^+$ calcd for $C_{19}H_{35}{}^{79}BrNaO_4Si$ 457.1386, found 457.1389.

*(((3aR,4S,5S,7aR)-7-((Z)-3,5-Dimethylstyryl)-4-methoxy-2,2-dimethyl-3a,4,5,7a-tetrahydrobenzo[d][1,3]dioxol-5-yl)oxy)-triisopropylsilane (**31**).* A magnetically stirred solution of compound **82** (70 mg, 0.16 mmol), compound **76** (41 mg, 0.16 mmol), $PdCl_2dppf{\cdot}CH_2Cl_2$ (9 mg, 0.01 mmol), and triethylamine (0.5 mL) in THF/water (3 mL of a 9:1 v/v mixture) was purged with nitrogen for 0.5 h, heated at 70 °C for 3 h, then cooled, poured into water (6 mL), and extracted with ethyl acetate (3 × 10 mL). The combined organic phases were washed with brine (1 × 10 mL) before being dried (Na_2SO_4), filtered, and then concentrated under reduced pressure. The ensuing light-yellow oil was subjected to flash chromatography (silica, 3:97 v/v ethyl acetate/hexane gradient elution), and concentration of the relevant fractions (R_f = 0.3 in 1:9 v/v ethyl acetate/hexane) afforded compound **31** (61 mg, 78%) as a clear, light-yellow oil, $[\alpha]_D^{20}$ = −73.0 (c = 0.2, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.02 (s, 2H), 6.83 (s, 1H), 6.51 (d, J = 12.3 Hz, 1H), 6.05 (d, J = 12.3 Hz, 1H), 5.81 (s, 1H), 4.61 (d, J = 6.5 Hz, 1H), 4.07 (t, J = 7.0 Hz, 1H), 3.85 (t, J = 7.3 Hz, 1H), 3.56 (m, 1H), 3.24 (s, 3H), 2.26 (s, 6H), 1.47 (s, 3H), 1.20 (s, 3H), 1.13−1.05 (complex m, 21H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.4, 137.1, 132.7, 132.0, 128.7, 128.1, 127.8, 126.5, 109.5, 80.2, 78.5, 73.9, 73.3, 56.7, 27.9, 25.5, 21.2, 18.2, 18.1, 12.7; IR ν_{max} 2941, 2865, 1600, 1463, 1379, 1250, 1213, 1137, 1098, 1063, 947, 883, 850, 680 cm^{-1}; MS (EI, 70 eV) m/z 486 ($M^{+\bullet}$, < 1%), 443 (12), 385 (86), 353 (100), 257 (98), 223 (73); HRMS $M^{+\bullet}$ calcd for $C_{29}H_{46}O_4Si$ 486.3165, found 486.3166.

*(1R,2R,3R,4S)-6-((Z)-3,5-Dimethylstyryl)-3-methoxycyclohex-5-ene-1,2,4-triol (**29**).* Compound **31** (50 mg, 0.10 mmol) was treated with acetic/water (10 mL of a 7:3 v/v mixture), and the resulting solution was heated at 70 °C for 18 h, then cooled, and concentrated under reduced pressure. Subjection of the residue thus obtained from flash chromatography (silica, 1:6:3 v/v/v methanol/ethyl acetate/hexane gradient elution) gave, after concentration of the appropriate fractions (R_f = 0.4 in 9:1 v/v ethyl acetate/hexane), compound **29** (21 mg, 70%) as a clear, light-yellow oil, $[\alpha]_D^{20}$ = −93.0 (c = 0.3, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.96 (s, 2H), 6.88 (s, 1H), 6.53 (d, J = 12.2 Hz, 1H), 6.10 (d, J = 12.2 Hz, 1H), 5.83 (s, 1H), 4.25 (d, J = 4.3 Hz, 1H), 3.87 (m, 1H), 3.75 (m, 1H), 3.52 (m, 1H), 3.36 (s, 3H), 2.27 (s, 6H), 1.62 (broad s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.9, 136.9, 136.2, 132.1, 129.1, 128.3, 126.3, 80.8, 71.4, 70.6, 68.3, 56.3, 21.3 (signal due to one carbon obscured or overlapping); IR ν_{max} 3369, 2917, 2826, 1599, 1452, 1376, 1261, 1079, 945, 853 cm^{-1}; MS (EI, 70 eV) m/z 290 ($M^{+\bullet}$, 7%), 224 (44), 198 (100), 183 (47), 119 (45); HRMS $M^{+\bullet}$ calcd for $C_{17}H_{22}O_4$ 290.1518, found 290.1523.

*(1S,2R,3S,4R)-6-((Z)-3,5-Dimethylstyryl)-3-methoxy-7-oxabicyclo-[2.2.1]hept-5-en-2-ol (**30**).* A magnetically stirred solution of compound **27** (50 mg, 0.17 mmol) in chlorobenzene (5 mL) was heated under reflux for 24 h, then cooled, and concentrated under reduced pressure. Subjection of the residue thus obtained to flash chromatography (silica, 3:2 v/v ethyl acetate/hexane elution) gave, after concentration of the appropriate fractions (R_f = 0.4 in 3:2 v/v ethyl acetate/hexane), compound **30** (14 mg, 30%) as light-yellow oil, $[\alpha]_D^{20}$ = −333.2 (c = 0.9, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.98 (s, 3H), 6.54 (d, J = 9.7 Hz, 1H), 6.01 (dd, J = 9.7 and 4.9 Hz, 1H), 5.89 (s, 1H), 5.79 (d, J = 4.8 Hz, 1H), 4.96 (m, 1H), 4.23 (s, 1H), 3.87 (m, 1H), 3.49 (s, 3H), 2.31 (s, 6H), 2.20 (d, J = 1.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 140.5, 138.5, 135.1, 130.3, 127.5, 126.3, 125.2, 123.4, 87.5, 82.5, 77.5, 67.2, 57.6, 21.3; IR ν_{max} 3421, 2920, 1693, 1607, 1462, 1382, 1243, 1156, 1123, 1089, 957, 851 cm^{-1}; MS (ESI, + ve) m/z 295 [$(M+Na)^+$, 100%], 273 (10), 195 (12); HRMS $(M+Na)^+$ calcd for $C_{17}H_{20}NaO_3$ 295.1310, found 295.1311.

Crystallographic Studies. *Crystallographic Data. Compound **15**.* $C_{17}H_{20}O_4$, M = 288.34, T = 200 K, monoclinic, space group $P2_1$, Z = 2, a = 4.6659(3) Å, b = 11.9898(9) Å, c = 13.673(1) Å; β = 90.470(4)°; V = 764.89(9) Å^3, D_x = 1.252 g cm^{-3}, 1423 unique data ($2\theta_{max}$ = 50°), R = 0.036 [for 1295 reflections with $I > 2.0\sigma(I)$]; Rw = 0.083 (all data), S = 1.03.

*Compound **23**.* $C_{17}H_{22}O_4$, M = 290.36, T = 150 K, monoclinic, space group $P2_1$, Z = 2, a = 4.7176(2) Å, b = 11.7310(4) Å, c = 13.7171(6) Å; β = 90.035(4)°; V = 759.13(5) Å^3, D_x = 1.270 g cm^{-3}, 1556 unique data ($2\theta_{max}$ = 143°), R = 0.080 [for 1536 reflections with $I > 2.0\sigma(I)$]; Rw = 0.220 (all data), S = 1.01.

*Compound **27**.* $C_{17}H_{22}O_4$, M = 290.36, T = 150 K, orthorhombic, space group $P2_12_12_1$, Z = 4, a = 4.5847(2) Å, b = 11.7037(5) Å, c = 29.754(3) Å; V = 1596.54(19) Å^3, D_x = 1.208 g cm^{-3}, 1901 unique data ($2\theta_{max}$ = 146.8°), R = 0.065 [for 1563 reflections with $I > 2.0\sigma(I)$]; Rw = 0.151 (all data), S = 1.00.

*Compound **35**.* $C_{11}H_{17}IO_4$, M = 340.16, T = 200 K, orthorhombic, space group $P2_12_12_1$, Z = 4, a = 7.8130(1) Å, b = 11.5034(2) Å, c = 14.4925(2) Å; V = 1302.53(3) Å^3, D_x = 1.735 g cm^{-3}, 3799 unique data ($2\theta_{max}$ = 60°), R = 0.021 [for 3669 reflections with $I > 2.0\sigma(I)$]; Rw = 0.051 (all data), S = 1.00.

*Compound **51**.* $C_7H_{11}IO_4{\cdot}H_2O$, M = 304.08, T = 150 K, monoclinic, space group $C2$, Z = 4, a = 17.5832(15) Å, b = 4.7115(1) Å, c = 13.4131(8) Å; β = 111.360(12)°; V = 1034.86(14) Å^3, D_x = 1.952 g cm^{-3}, 1906 unique data ($2\theta_{max}$ = 143.8°), R = 0.022 [for 1871 reflections with $I > 2.0\sigma(I)$]; Rw = 0.059 (all data), S = 1.00.

*Compound **72**.* $C_7H_{11}IO_4{\cdot}H_2O$, M = 304.08, T = 200 K, monoclinic, space group $C2$, Z = 4, a = 16.8154(8) Å, b = 4.5652(2) Å, c = 15.7010(8) Å; β = 120.5922°; V = 1037.53(9) Å^3, D_x = 1.947 g cm^{-3}, 3024 unique data ($2\theta_{max}$ = 60.2°), R = 0.031 [for 2812 reflections with $I > 2.0\sigma(I)$]; Rw = 0.073 (all data), S = 0.99.

Structure Determination. Images for compound **15**, **35**, and **72** were measured on a diffractometer (Mo Kα, graphite monochromator, λ = 0.71073 Å) fitted with an area detector, and the data were extracted using the DENZO/Scalepack package.[23] Images for compounds **23**, **27**, and **51** were measured on a diffractometer (Cu Kα, mirror monochromator, λ = 1.54184 Å) fitted with an area detector, and the data were extracted using the CrysAlis package.[24] The structure solutions for all six compounds were solved by direct methods (SIR92)[25] and then refined using the CRYSTALS program package.[26] Atomic coordinates, bond lengths, and angles, and displacement parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC nos. 1504203, 1504204, 1504205, 1504206, 1504207, and 1504208). These data can be obtained free-of-charge via www.ccdc.cam.ac.uk/data_request/cif, by emailing data_request@ccdc.cam.ac.uk or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, United Kingdom; fax: +44 1223 336033.

Biological Testing. The test results shown in Table 1 were derived from green house studies. The culture vessels used were plastic flowerpots containing loamy sand with approximately 3% of humus as the substrate. For the postemergence treatment, the test plants were first grown separately as seedlings, and several of these were transplanted into the culture vessels a few days prior to treatment. After they reached a height of 3−10 cm, depending on the plant habit, they were treated

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with the active ingredients which had been emulsified through the addition of 3.6 mL of a mixture of cyclohexanone/DMSO/Wettol EM31 (2:2:1 v/v/v mixture) and 2% Dash diluted with deionized water to the corresponding spray volume and sprayed on the plants via an ultrasonic spray nozzle. Unless otherwise specified, the application rate corresponded to 2 kg/ha with an application volume of 750 L/ha. The plants were kept and tended at 15−22 °C over a test period of 21 days. The responses of the plants to the individual treatments were visually evaluated after 21 days. The outcomes of these evaluations are presented in Table 1.

The physiological profiling (PP) studies were conducted using previously published protocols.[20a,27]

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02372.

Crystallographic data for **15** (CIF)
Crystallographic data for **23** (CIF)
Crystallographic data for **27** (CIF)
Crystallographic data for **35** (CIF)
Crystallographic data for **51** (CIF)
Crystallographic data for **72** (CIF)
Crystallographic data and anisotropic displacement ellipsoid plots derived from the single-crystal X-ray analyses of compounds **15**, **23**, **27**, **35**, **51** and **72**. ^{1}H and ^{13}C NMR spectra of phomentrioloxin analogues **4**-**7** and **10**-**31** as well as their precursors (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: Martin.Banwell@anu.edu.au.

ORCID

Martin G. Banwell: 0000-0002-0582-475X

Notes

The authors declare no competing financial interest.

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