Applications of Crotonyldiisopinocampheylboranes in Synthesis: Total Synthesis of Restrictinol

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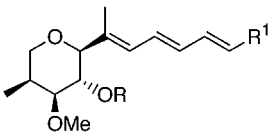
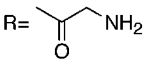
Received July 30, 1998

The total synthesis of restrictinol, the hydrolysis product of the antifungal natural product restricticin, starting from commercially available methyl (*S*)-(+)-3-hydroxy-2-methylpropionate is described. Key stages in the strategy involved (i) the use of Brown's allylboration chemistry to construct an acyclic intermediate bearing three of the four stereogenic centers of the natural product, (ii) formation of a *C*-glycosidic vinyl iodide, and (iii) introduction of the triene side chain via a Suzuki coupling reaction.

Introduction

Restricticin (**1**) and restrictinol (**3**) were first isolated in 1991 by Schwartz and co-workers from the fermentation broth of *Penicillium restrictum*.[1,2] Restricticin (**1**) was found to be unstable due to the lability of the glycine ester side chain toward base-mediated hydrolysis and the tendency of the triene functionality to undergo decomposition. Subsequently, Matsukuma and co-workers reported the isolation of restricticin (**1**) and restrictinol (**3**) from the fermentation broth of *Penicillium sp.* NR6564.[3] In 1992, O' Sullivan et al. reported the isolation of the very closely related compounds lanomycin (**2**) and lanomycinol (**4**) from *Pycnidiophora dispersa*.[4,5] Both restricticin (**1**) and lanomycin (**2**) have been shown to exhibit potent antifungal activity through inhibition of cytochrome P_{450} lanosterol demethylase and therefore are the



R=  R^1=*n*-Pr : restricticin **1**
R^1=CH_3 : lanomycin **2**

R= H R^1=*n*-Pr : restrictinol **3**
R^1=CH_3 : lanomycinol **4**

first natural products to be isolated that share the same mode of action as the commercially successful azole antifungals (e.g. fluconazole).[6] Interestingly the desglycyl restrictinol (**3**) and lanomycinol (**4**) did not exhibit such antifungal activity. This family of compounds have been the subject of considerable interest, and several total syntheses have been published.[7−10] Notably all these syntheses have introduced the triene side-chain via carbonyl olefination chemistry (Wittig, Horner−Emmons, or Julia reactions) and afforded mixtures of geometric isomers which were subsequently separated. Herein we report a synthesis of restrictinol (**3**) in which the introduction of triene side chain is achieved in geometrically pure form using a palladium(0)-catalyzed cross coupling of vinyl iodide **5** and an appropriate "metal" coupling partner **6** (Scheme 1). We considered that vinyl iodide **5** should be available from lactol **8** by formation of acetylenic *C*-glycoside **7** and subsequent zirconocene dichloride-catalyzed methylalumination−iodinolysis according to Negishi.[11] Deprotection and oxidative cleavage of olefin **9**, with concomitant cyclization, was expected to give lactol **8**. We envisaged that intermediate **9** could be prepared from aldehyde **10** and borane **11** using Brown's allylboration chemistry.[12]

Results and Discussion

Methylalumination Approach. Aldehyde **12** was prepared from commercially available methyl (*S*)-(+)-3-hydroxy-2-methylpropionate by protection with triethylsilyl chloride followed by DIBAL-H reduction.[13] Subsequent reaction with borane **18** (prepared and used in situ) according to the procedure of Brown[12] afforded, after

(1) Schwartz, R. E.; Dufresne, C.; Flor, J. E.; Kempf, A. J.; Wilson, K. E.; Lam, T.; Onishi, J.; Milligan, J.; Fromtling, R. A.; Abruzzo, G. K.; Jenkins, R.; Glazomitsky, K.; Bills, G.; Zitano, L.; Mochales del Val, S.; Omstead, M. N. *J. Antibiot.* **1991**, *44*, 463.

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(4) O' Sullivan, J.; Phillipson, D. W.; Kirsch, D. R.; Fisher, S. M.; Lai, M. H.; Trejo, W. H. *J. Antibiot.* **1992**, *45*, 306.

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(7) Jendrzejewski, S.; Ermann, P. *Tetrahedron Lett.* **1993**, *34*, 615.

(8) Tsukuda, T.; Umeda, I.; Masubuchi, K.; Shirai, M.; Shimma, N. *Chem. Pharm. Bull.* **1993**, *41*, 1191.

(9) Kang, S. H.; Kim, C. M. *Synlett* **1996**, 515.

(10) Paterson, I.; Nowak, T. *Tetrahedron Lett.* **1996**, 37, 8243. Honda, T.; Satoh, A.; Yamada, T.; Hayakawa, T.; Kanai, K. *J. Chem. Soc., Perkin Trans. 1* **1998**, 397.

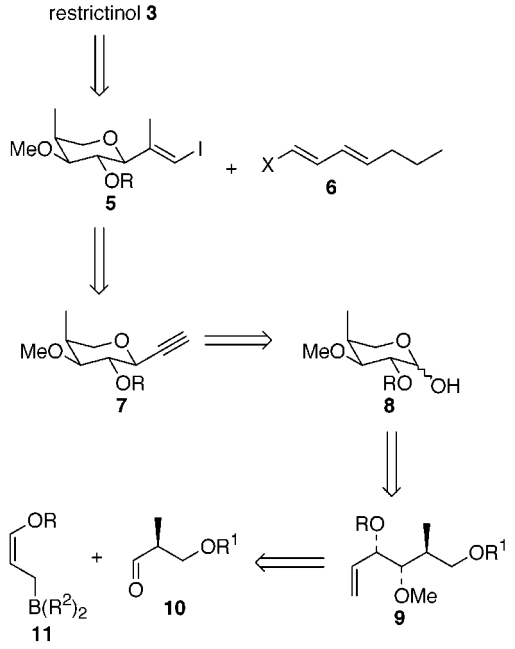
(11) Negishi, E.; Choueiry, D. In *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Ed.; John Wiley and Sons: Chichester, 1995; Vol. 7, p 5192.

(12) Brown, H. C.; Jadhav, P. K.; Bhat, K. S. *J. Am. Chem. Soc.* **1988**, *110*, 1535.

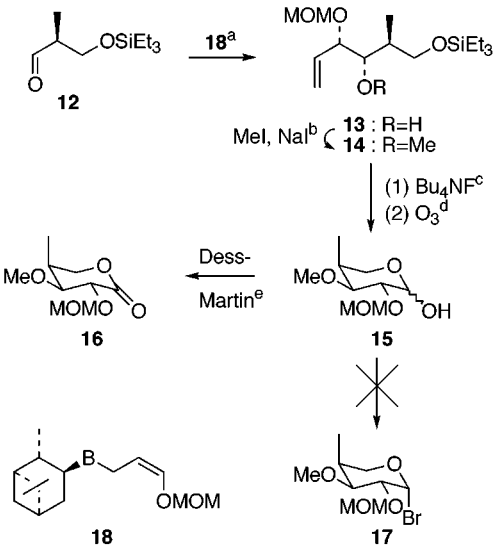
(13) Barrett, A. G. M.; Edmunds, J. J.; Hendrix, J. A.; Horita, K.; Parkinson, C. J. *J. Chem. Soc., Chem. Commun.* **1992**, 1238. Barrett, A. G. M.; Edmunds, J. J.; Hachiya, S. I.; Hendrix, J. A.; Horita, K.; Malecha, J. W.; Parkinson, C. J.; VanSickle, A. Manuscript in preparation.

10.1021/jo9815305 CCC: $18.00
Published on Web 12/11/1998

Scheme 1



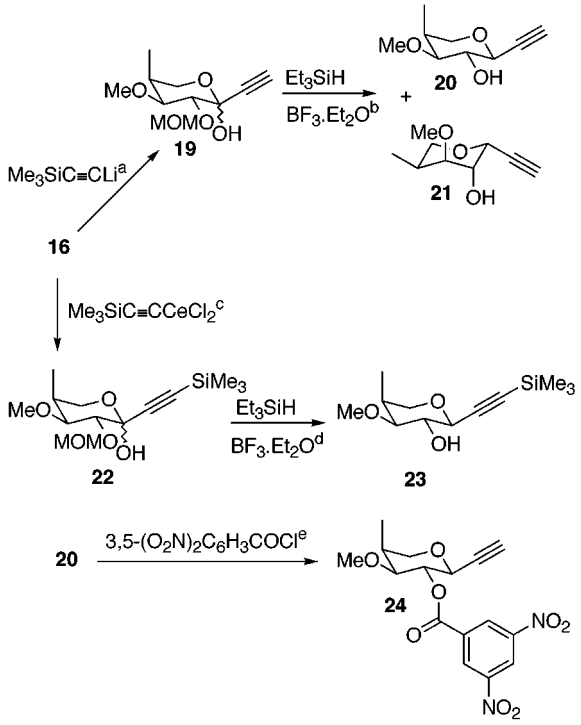
Scheme 2



Reagents and Conditions: (a) **18**, THF, -89 °C, 18 h; MeOH, $NaBO_3.4H_2O$, 36 h, 60 %; (b) NaH, MeI, THF, -10 °C, 2.5 h, 85 %; (c) Bu_4NF, THF, 1h; (d) O_3, CH_2Cl_2, -78 °C; Me_2S, -78 to 20 °C, 86 %; (e) Dess-Martin periodinane, CH_2Cl_2, 0 to 20 °C, 76 %.

oxidative workup, the syn homoallylic alcohol **13** (60%) with greater than 95:5 diastereoselectivity as judged by analysis of key peaks (2-*Me*, 3-*H*, 4-*H*, 5-*H*, and 6-*H*) in the ^{1}H NMR spectrum (Scheme 2). Subsequent methylation of alcohol **13** using sodium hydride and methyl iodide in DMF proceeded smoothly to afford methyl ether **14** (85%). Conversion of the olefin **13** to lactol **15** was accomplished by a two-step procedure involving deprotection with tetrabutylammonium fluoride and then, without purification, ozonolysis with a reductive workup using dimethyl sulfide to afford **15** in 86% overall yield. Initially we sought to convert lactol **15** into the α-anomeric bromide **17** and, subsequently, to convert this into the corresponding acetylenic *C*-glycoside **20** (Scheme 3) by displacement with an appropriate acetylide anion.

Scheme 3



Reagents and Conditions: (a) $Me_3SiC{\equiv}CH$, *n*-BuLi, THF, -78 °C, 2 h; MeOH, -78 to 20 °C 24 h, 81 %; (b) $BF_3.Et_2O$, Et_3SiH, CH_3CN, -20 °C, 2.5 h, 59 % (**20**) + 20 % (**21**); (c) $Me_3SiC{\equiv}CH$, *n*-BuLi, $CeCl_3$, THF, -78 °C, 2 h, 100 %; (d) $BF_3.Et_2O$, Et_3SiH, CH_3CN, -20 °C, 4 h, 68 %; (e) 3, 5-dinitrobenzoyl chloride, DMAP, Et_3N, CH_2Cl_2, 1 h, 80 %.

Unfortunately, under a variety of different conditions none of the desired bromide **17** could be isolated. In an alternative route lactol **15** was oxidized, with Dess–Martin periodinane,[14] to the corresponding lactone **16** so that we might employ Kishi's procedure for the stereoselective synthesis of *C*-glycosides (Scheme 2).[15]

Reaction of lactone **16** with lithium (trimethylsilyl)-acetylide followed by quenching with methanol resulted in the formation of hemiketal **19** (81%), with concomitant (lithium methoxide-mediated) cleavage of the trimethylsilyl group (Scheme 3). Interestingly, when the corresponding cerium reagent was used, derived from lithium (trimethylsilyl)acetylide and cerium(III) chloride, hemiketal **22** was isolated in 100% yield without any cleavage of the trimethylsilyl group. Reduction of hemiketal **19** with a mixture of triethylsilane and boron trifluoride diethyl etherate resulted in the formation of the acetylenic *C*-glycosides **20** and **21** in 59% and 20% yields, respectively. The stereochemistry of these two compounds was initally assigned by analysis of coupling constants in the ^{1}H NMR spectrum. To confirm our stereochemical assignments, we sought an X-ray crystal structure, and to that end *C*-glycoside **20** was converted to its 3,5-dinitrobenzoate derivative **24** under standard conditions in 80% yield. Although we were unable to obtain X-ray quality crystals of 3,5-dinitrobenzoate **24** it proved an ideal substrate for an NOE experiment, and we were able to obtain excellent support for our assignments (Figure 1). Subsequently the structure of *C*-glycoside **21** was

(14) Ireland, R. E.; Liu, L. *J. Org. Chem.* **1993**, *58*, 2899.
(15) Lewis, D. M.; Cha, J. K.; Kishi, Y. *J. Am. Chem. Soc.* **1982**, *104*, 4976.

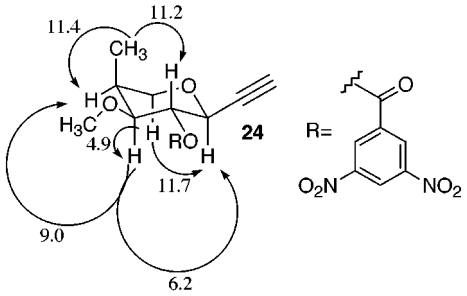
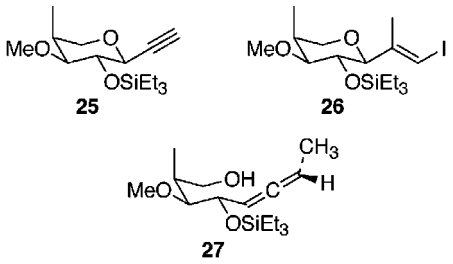


Figure 1.

unambiguously confirmed by a single-crystal X-ray analysis (see Supporting Information). Reduction of hemiketal **23** with a mixture of triethylsilane and boron trifluoride diethyl etherate resulted in formation of the *C*-glycoside **23** (68%) with none of the other epimer being detected.

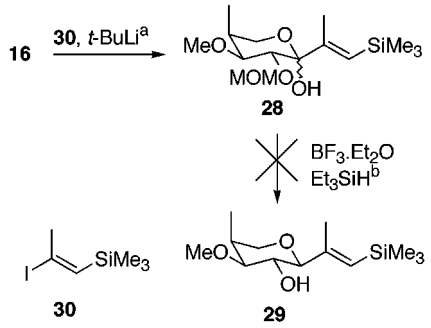
Although zirconocene dichloride-catalyzed methylalumination reactions are often tolerant of free hydroxyl groups, in the first instance, we wished to remove this additional complication from our system and to that *C*-glycoside **20** was converted to the corresponding triethylsilyl ether **25** by treatment with triethylsilyl trifluoromethanesulfonate and triethylamine to afford **25** (85%). Attempts to convert the acetylenic *C*-glycoside **25** to vinyl iodide **26** using a mixture of trimethylaluminum and zirconocene dichloride followed by iodinolysis of the resultant vinylalane according to Negishi's procedure[11] were unsuccessful, our substrate proving inert to the reaction conditions. Wipf has recently reported a dramatic rate acceleration in zirconocene dichloride-catalyzed methylalumination reactions by the addition of water to the preformed organometallic reagent.[16] On a single occasion, using this modification we were able to isolate a trace of our desired vinyl iodide **26**. Unfortunately attempts to repeat this result were completely unsuccessful. All that could be isolated, on occasion, in trace amounts was another compound tentatively assigned as the ring opened hydroxy allene **27**. In consequence this approach was abandoned.



Vinyl Silane-Masked Vinyl Iodide Approach. We envisaged that reaction of lactone **16** with the anion derived from halogen−metal exchange of iodide **30** (as employed by Nicolaou in the synthesis of rapamycin[17]) should provide hemiketal **28** (Scheme 4). Reduction of **28** as before would lead to vinyl silane **29** which in turn could be converted to the corresponding vinyl iodide by treatment with *N*-iodosuccinimide. Indeed, lithiation of **30** followed by addition of lactone **16** afforded the hemiketal **28** (77%). Unfortunately, all attempts to effect

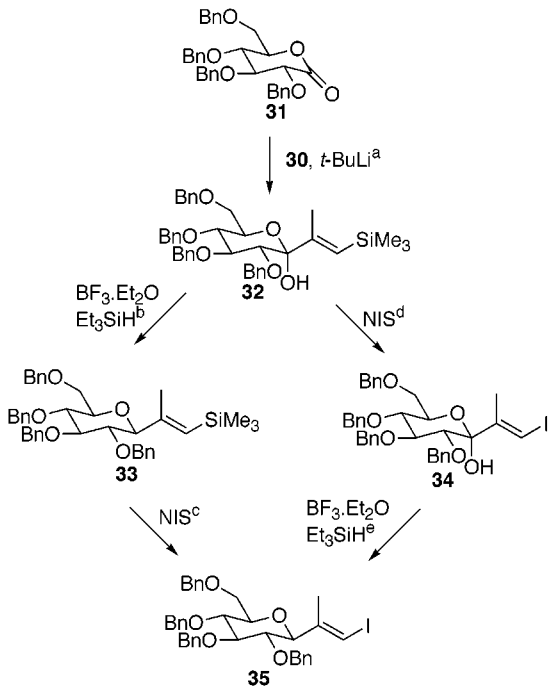
(16) Wipf, P.; Lim, S. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1068.
(17) Pisopio, A. D.; Minowa, N.; Chakraborty, T. K.; Koide, K.; Bertinato, P.; Nicolaou, K. C. *J. Chem. Soc., Chem. Commun.* **1993**, 617.

Scheme 4



Reagents and Conditions: (a) **30**, *t*-BuLi, Et_2O, -78 °C, 1.5 h, 77 %; (b) BF_3. Et_2O, Et_3SiH, CH_3CN, -20 °C.

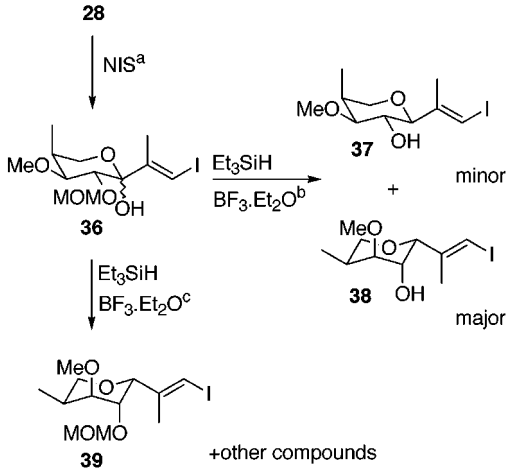
Scheme 5



[a] Reagents and Conditions: (a) **30**, *t*-BuLi, THF, -78 °C, 64 %; (b) $BF_3.Et_2O$, Et_3SiH, CH_3CN/CH_2Cl_2, -40 °C, 15 min, 49 %; (c) NIS, THF, 20 °C, 24 h, 95 % ; (d) NIS, THF, 20 °C, 24 h, 83 %; (e) $BF_3.Et_2O$, Et_3SiH, CH_3CN/CH_2Cl_2, -40 °C, 15 min, 86 % (β:α 85:15).

the reduction of hemiketal **28** as before were unsuccessful giving complex mixtures of products instead. We suspected either the nucleophilic vinyl silane and/or the cleavage of the methoxymethyl ether could be complicating factors in this reaction, and therefore we sought to test the viability of our approach on a model system. For this we chose the known gluconolactone derivative **31**[18] as a starting point (Scheme 5). Lithiation of iodide **30** followed by reaction with lactone **31** afforded hemiketal **32** as a single epimer (64%). Subsequent reduction of **32** with a mixture of boron trifluoride and triethylsilane afforded the *C*-glycoside **33** albeit in a modest 49% yield. Treatment of silane **33** with *N*-iodosuccinimide gave the vinyl iodide **35** (95%). The structure and absolute stereochemistry of this compound were unambiguously confirmed by a single-crystal X-ray analysis (see Supporting Information). Although this established the viability of our approach, the yield of the reduction step was modest

Scheme 6



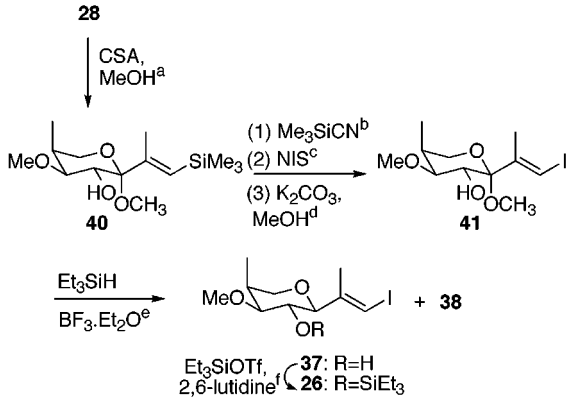
Reagents and Conditions: (a) NIS, THF, 36 h, 81 %; (b) $BF_3.Et_2O$, Et_3SiH, CH_3CN, -20 °C, 2.25 h, 9 % (**37**) + 32 % (**38**); (c) $BF_3.Et_2O$, Et_3SiH, CH_3CN/ CH_2Cl_2 (85:15), -40 °C, 1 h, 42 %.

and, moreover, this transformation had already proved ineffective with lactone **16**. To improve the strategy we chose to reverse the order of the steps in the sequence and to reveal the vinyl iodide prior to the reduction step, thereby carrying out the ionic hydrogenolysis in the absence of a nucleophilic vinyl silane. Thus, in the model system, vinyl silane **32** was converted into vinyl iodide **34** (83%) by treatment with *N*-iodosuccinimide. Much to our delight, subsequent reduction as before afforded vinyl iodide **35** in 86% yield as a 85:15 mixture of epimers in favor of the desired β-C-glycoside.

Following the success of our model studies, hemiketal **28** was allowed to react with *N*-iodosuccinimide to afford the (somewhat unstable) iodide **36** (81%) (Scheme 6). Unfortunately reduction of **36** under standard conditions at −20 °C afforded the desired iodide **37** (9%) and, as the major product, epimeric iodide **38** (32%). Reduction at −40 °C resulted in the formation of iodide **39** as the major product (42%), again with the undesired glycoside stereochemistry but with the methoxymethyl group remaining intact. At this stage, we reasoned that the methoxymethyl ether might be interfering with the reduction step, shielding the α-face and leading to the formation of the undesired epimer. Therefore, hemiketal **28** was allowed to react with camphorsulfonic acid in methanol, affording alcohol **40** (70%) (Scheme 7) which was converted into the iodide **41** using *N*-iodosuccinimide-mediated iododesilylation of the corresponding trimethylsilyl ether (73% overall yield). Reduction of hemiketal **41** using triethylsilane and boron trifluoride diethyl etherate afforded the desired iodide **37** (56%) along with the epimeric iodide **38** (39%). Treatment of iodide **37** with triethylsilyl trifluoromethanesulfonate and 2,6-lutidine gave the corresponding triethylsilyl ether **26** (96%). Gratifyingly, the ^1H NMR of iodide **26** was identical to one previously obtained from our troublesome zirconocene dichloride-catalyzed methylalumination approach.

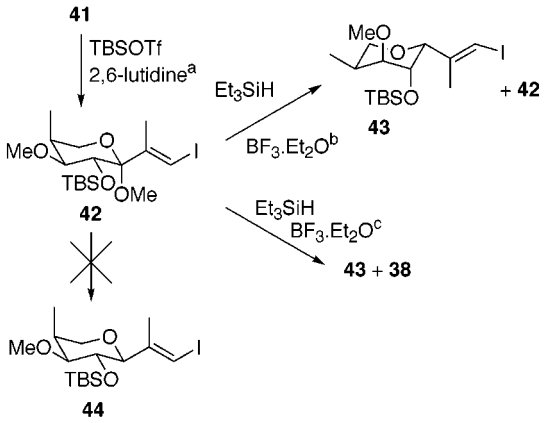
We postulated that the selectivity in our reduction step, leading to the formation of our *C*-glycoside coupling partner, could be improved by the prior protection of the free hydroxyl group of **41** as a *tert*-butyldimethylsilyl

Scheme 7



Reagents and Conditions: (a) CSA, MeOH, 20 °C, 12 h, 70 %; (b) Me_3SiCN, DMF, 1 h; (c) NIS, THF, 36 h; (d) K_2CO_3, MeOH, 1 h, 73 % over 3 steps; (e) $BF_3.Et_2O$, Et_3SiH, CH_3CN/CH_2Cl_2 (85:15), -40 °C, 1.75 h, 56 % (**37**) + 39 % (**38**); (f) Et_3SiOTf, 2,6-lutidine, CH_2Cl_2, -20 °C, 2 h, 96 %

Scheme 8

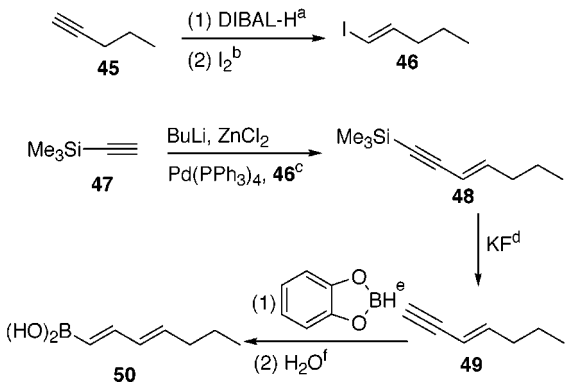


Reagents and Conditions: (a) TBSOTf, 2,6-lutidine, CH_2Cl_2, -20 °C, 97 %; (b) $BF_3.Et_2O$ (1 eq.), Et_3SiH, CH_3CN/CH_2Cl_2 (85:15), -40 °C, 1.5 h, 70 % (**43**) +30 % (**42**); (c) $BF_3.Et_2O$ (1.5 eq.), Et_3SiH, CH_3CN/CH_2Cl_2 (85:15), -40 °C, 1 h, 49 % (**43**) +30 % (**38**)

ether (Scheme 8). We considered that the bulky silyl group would act as a conformational anchor and prevent ring flipping of the intermediate pyran oxonium cation in the reduction step that presumably leads to the undesired stereochemistry in the product. Also were this approach to be successful, then our protection strategy should prove amenable to rationalization with a consumate reduction in the overall number of steps. Protection of **41** under standard conditions afforded the corresponding silyl ether **42** (97%). Much to our chagrin, reduction of **42** with 1 equiv of boron trifluoride diethyl etherate and excess triethylsilane at −40 °C resulted in the formation of the undesired, epimeric *C*-glycoside **43** (70%) along with 30% recovered **42** (30%) and not a trace of the desired epimer **44**. In an attempt to force this reaction to completion, excess boron trifluoride (1.5 equiv) was employed; however in this case, although no starting material remained, we noticed significant cleavage of the *tert*-butyldimethylsilyl ether.

Synthesis of a Dienyl Coupling Partner. 1-Pentyne was converted into vinyl iodide **46** (54%) by treatment with diisobutylaluminum hydride and iodinolysis of the resultant vinylalane to afford **46** (Scheme 9). Subse-

Scheme 9



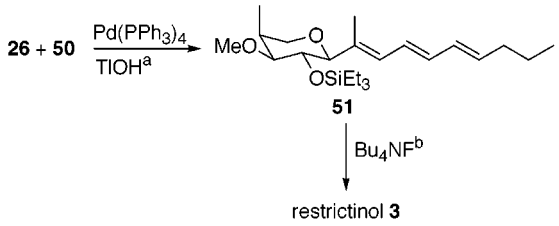
Reagents and Conditions: (a) DIBAL-H, hexane, 55-60 °C, 4 h; (b) I_2, THF, -78 to 0 °C, 54 %; (c) *n*-BuLi, $ZnCl_2$, $Pd(PPh_3)_4$, THF, **46**, -78 to 20 °C, 89 %; (d) KF, DMF, H_2O, 2 h, 61 %; (e) catecholborane, THF, 70 °C, 24 h; (f) H_2O, 67 %.

quently, (trimethylsilyl)acetylene (**47**) was lithiated and treated sequentially with zinc chloride, vinyl iodide **46**, and tetrakis(triphenylphosphine)palladium(0) to afford silyl enyne **48** (89%) which was allowed to react with potassium fluoride in DMF, according to the literature procedure,[19] to afford the volatile enyne **49** which could not be separated from silane residues and was used without further purification. Hydroboration of **49** with catecholborane followed by hydrolysis of the resultant boronic ester afforded boronic acid **50**. Interestingly, when dried under vacuum, boronic acid **50** underwent trimerization to give the corresponding cyclic anhydride (67%). For our purposes we wished to use the free boronic acid **50**, and the anhydride was hydrolyzed with water and dried on a filter paper.

Synthesis of Restrictinol (3). Kishi has reported a dramatic rate acceleration in Suzuki couplings if thallium hydroxide is used as base.[20] This base has subsequently been used in Suzuki couplings in the construction of sensitive polyene functionality, and we therefore chose to utilize it in our synthesis of the sensitive triene of restrictinol (**3**).[21] A mixture of vinyl iodide **26** and boronic acid **50** was allowed to react with 10% aqueous thallium hydroxide and tetrakis(triphenylphosphine)palladium(0) in THF to afford triene **51** (73%) (Scheme 10). Subsequent deprotection with tetrabutylammonium fluoride afforded restrictinol (**3**) which had ^{1}H NMR and ^{13}C NMR identical to that reported for the natural material.[2,22] The optical rotation $[\alpha]^{26}_D$ +64.0 (*c* 0.25 MeOH), was in close agreement to that reported in the literature $[\alpha]^{20}_D$ +51 (*c* 0.20, MeOH).[3]

In conclusion we have developed a concise route to restrictinol (**3**) from commercially available starting materials and for the first time introduced the triene side chain in geometrically pure form via a palladium(0) coupling reaction. The triene coupling methodology is clearly amenable for the elaboration of analogues.

Scheme 10



Reagents and Conditions: (a) TlOH (10% aq. soln.), $Pd(PPh_3)_4$, THF, 12 h, 73 %; (b) Bu_4NF, THF, 2 h, 94 %.

Experimental Section

General Procedures. Unless stated otherwise, solvents and amine bases were dried by distillation under N_2 or Ar, from sodium benzophenone ketyl (THF, Et_2O), CaH_2 (CH_2Cl_2, DMF, MeCN, Et_3N, pentane), KOH (2,6-lutidine), and Mg/I_2 (MeOH). *N*-Iododosuccinimide was recrystallized from CCl_4/1,4-dioxane. All other reagents were used as received from commercial sources. All reactions were performed in oven-dried (150 °C) glassware under N_2 or Ar. Chromatographed and chromatography refer to column chromatography on BDH 40−63 μM grade silica gel. Analytical thin-layer chromatography (TLC) was performed on precoated glass backed plates (Merck Kieslegel 60 F_{254}) and visualized with ceric molybdate or potassium permanganate stains and/or ultraviolet light as appropriate. Bulb to bulb distillation was carried out using a Kugelrohr distillation apparatus with the collection bulb cooled with dry ice. The temperatures quoted are oven temperatures and are approximate.

(2*S*,3*S*,4*S*)-4-(Methoxymethoxy)-2-methyl-1-(triethylsilyloxy)-5-hexen-3-ol (13). To a stirred solution of methoxymethyl allyl ether (2.10 g, ∼90% pure, 18.56 mmol) in THF (40 mL) at ≤−85 °C (solution temperature) was dropwise added *sec*-BuLi in cyclohexane (1.35 M; 13.2 mL, 17.82 mmol). After 3 h, the resultant yellow solution was treated with (+)-*B*-methoxydiisopinocampheylborane (6.11 g, 19.31 mmol) in THF (10 mL), maintaining the internal temperature at ≤−85 °C. The resultant white cloudy solution was stirred at this temperature for 3 h before adding $BF_3{\cdot}Et_2O$ (2.02 mL, 16.40 mmol). After 15 min, aldehyde **12** (3.0 g, 14.8 mmol) in THF (20 mL) at −78 °C was added dropwise via cannula (down the side of the flask), maintaining an internal temperature ≤−85 °C. The reaction mixture was stirred at this temperature for 18 h before being quenched by the dropwise addition of MeOH (5 mL). After 15 min, saturated aqueous sodium perborate (75 mL) was added, and the mixture was allowed to warm to room temperature and stirred for 36 h. The aqueous and organic phases were separated, and the aqueous phase was extracted with Et_2O (5 × 50 mL). The combined organic extracts were washed with water (2 × 100 mL) and brine (100 mL), dried ($MgSO_4$), filtered, and rotary evaporated. The residue was chromatographed (eluant EtOAc:hexanes 1:9) to afford **13** (2.72 g, 60%) as a colorless oil: TLC R_f = 0.25 (Et_2O:hexanes 1:9); $[\alpha]$ = +88.6° (*c* = 1.0, $CHCl_3$); IR (film) 3492, 2955, 2878, 1460 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.90−5.81 (1H, m), 5.30−5.24 (2H, m), 4.70 (1H, d, *J* = 7.0 Hz), 4.55 (1H, d, *J* = 7.0 Hz), 4.50−4.10 (1H, dd, *J* = 4.5, 7.5 Hz), 3.74 (1H, d, *J* = 3.5 Hz), 3.69−3.64 (2H, m), 3.49−3.44 (1H, m), 3.36 (3H, s), 2.02−1.98 (1H, m), 0.95−0.90 (12H, m), 0.62−0.54 (6H, q, *J* = 8.0 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 135.6, 118.6, 94.0, 78.4, 66.7, 55.7, 36.5, 13.6, 6.7, 4.2; MS (CI^+, NH_3) *m*/*z* 305 $(M + H)^+$. Anal. Calcd for $C_{15}H_{32}O_4Si$: C, 59.17; H, 10.59. Found: C, 58.88; H, 10.36.

(2*S*,3*S*,4*S*)-3-Methoxy-4-(methoxymethoxy)-2-methyl-1-(triethylsilyloxy)-5-hexene (14). To a stirred mixture of NaH (987 mg, 60%, 24.68 mmol) and MeI (3.84 mL, 61.70 mmol) in DMF (80 mL) at −10 °C was dropwise added alcohol

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13 (3.75 g, 12.34 mmol) in DMF (20 mL). After 1.5 h, the reaction was quenched with saturated aqueous NH_4Cl (10 mL), diluted with distilled water (150 mL), and extracted with Et_2O (4 × 100 mL). The combined organic extracts were washed with water (2 × 50 mL) and brine (50 mL), dried ($MgSO_4$), filtered, and rotary evaporated. The residue was chromatographed (eluant Et_2O:hexanes 1:19) to afford **14** (3.34 g, 85%) as a colorless oil: TLC R_f = 0.57 (Et_2O:hexanes 1:4); [α] = +51.4° (c = 1.0, $CHCl_3$); IR (film) 3080, 2955, 2878, 2824, 1642 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 5.95−5.82 (1H, m), 5.34−5.25 (2H, m), 4.71 (1H, d, J = 7.0 Hz), 4.56 (1H, d, J = 7.0 Hz), 4.19 (1H, dd, J = 4.0, 7.5 Hz), 3.65 (2H, d, J = 5.0 Hz), 3.48 (3H, s), 3.38 (3H, s), 3.08 (1H, dd, J = 3.5, 7.5 Hz), 2.01−1.96 (1H, m), 1.02−0.93 (12H, m), 0.61 (6H, q, J = 8.0 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 136.1, 118.1, 94.0, 85.6, 77.9, 64.0, 61.2, 55.7, 37.3, 14.2, 6.8, 4.4; MS (CI^+, NH_3) m/z 319 $(M + H)^+$, 287 $(M - OCH_3)^+$, 257 $(M - OCH_2OCH_3)^+$. Anal. Calcd for $C_{16}H_{34}O_4Si$: C, 60.33; H, 10.76. Found: C, 60.05; H, 10.94.

(2*RS*,3*R*,4*S*,5*S*)-2-Hydroxy-4-methoxy-3-(methoxymethoxy)-5-methyltetrahydro-2*H*-pyran (15). To a stirred solution of **14** (3.49 g, 10.97 mmol) in THF (50 mL) was added Bu_4NF in THF (1 M; 12.0 mL 12.0 mmol). After 1 h, the solvent was evaporated in vacuo and the residue filtered through silica gel (eluant Et_2O). After rotary evaporation, the residue was suspended in CH_2Cl_2 (100 mL) and cooled to −78 °C. Ozone-enriched oxygen was passed through the solution until it became blue whereupon Me_2S (15 mL) was added and the mixture allowed to warm to room-temperature overnight. After evaporation in vacuo, the residue was chromatographed (eluant EtOAc:hexanes 2:3) to afford lactol **15** (1.94 g, 86%), a 1:1 mixture of anomers, as a colorless oil: TLC R_f = 0.22 (EtOAc:hexanes 2:3); IR (film) 3411, 1727, 1640 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 4.94−4.76 (1H, m), 4.75−4.72 (2H, m), 4.08−4.04 (1H single anomer, m), 3.77−3.69 (1H, m), 3.65−3.61 (1H, m), 3.53−3.35 (2H, m), 3.47 (3H single anomer, s), 3.42 (3H single anomer, s), 3.40 (3H single anomer, s), 3.39 (3H single anomer, s), 2.27−2.12 (1H, m), 0.92 (3H single anomer, d, J = 7.0 Hz), 0.89 (3H single anomer, d, J = 7.0 Hz); MS (CI^+, NH_3) m/z 224 $(M + NH_4)^+$, 206 $(M - H_2O + NH_4)^+$, 189 $(M - OH)^+$; HRMS (CI^+, NH_3) m/z calcd for $C_9H_{20}N0_4$ $(M - H_2O + NH_4)^+$ 206.1392, found 206.1389.

(3*R*,4*S*,5*S*)-4-Methoxy-3-(methoxymethoxy)-5-methyltetrahydro-2*H*-pyran-2-one (16). To a stirred solution of lactol **15** (300 mg, 1.46 mmol) in CH_2Cl_2 (10 mL) at 0 °C was added Dess−Martin periodinane[14] (929 mg, 2.19 mmol). After 1 h, the mixture was allowed to warm to room temperature and, after a further 3 h, the mixture was dry loaded onto silica and chromatographed (eluant EtOAc:hexanes 1:3) to afford **16** (225 mg, 76%) as a colorless oil: TLC R_f = 0.35 (EtOAc:hexanes 3:7); [α] = +130.3° (c = 1.1, $CHCl_3$); IR (film) 2969, 1744 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 4.99−4.97 (1H, d, J = 6.5 Hz), 4.72−4.70 (1H, d, J = 6.5 Hz), 4.24−4.09 (3H, m), 3.48−3.42 (1H, m), 3.47 (3H, s), 3.43 (3H, s), 2.46−2.38 (1H, m), 1.04−1.01 (3H, d, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.6, 96.3, 80.4, 72.0, 70.4, 58.5, 56.0, 30.6, 10.9; MS (CI^+, NH_3) m/z 222 $(M + NH_4)^+$, 205 $(M + H)^+$. Anal. Calcd for $C_9H_{16}O_5$: C, 52.93; H, 7.90. Found: C, 52.73; H, 7.98.

(2*RS*,3*R*,4*S*,5*S*)-2-Ethynyl-2-hydroxy-4-methoxy-3-(methoxymethoxy)-5-methyltetrahydro-2*H*-pyran (19). To a stirred solution of (trimethylsilyl)acetylene (485 μL, 3.43 mmol) in THF (10 mL) at −78 °C was added *n*-BuLi in hexane (2.44 M; 1.23 mL, 3.00 mmol). After 1 h, the resultant anion was transferred, via cannula, to a stirred solution of lactone **16** (584 mg, 2.86 mmol) in THF (15 mL). MeOH (2 mL) was added after 2 h and the reaction mixture allowed to warm to room-temperature overnight. After 18 h, saturated aqueous NH_4Cl (3 mL) was added and the solvent evaporated in vacuo. The residue was dry loaded onto silica gel and chromatographed (eluant EtOAc:hexanes 1:4) to afford **19** (533 mg, 81%), a 3:1 mixture of anomers, as a colorless oil: TLC R_f = 0.31 (EtOAc:hexanes 2:3); IR (film) 3368, 3257, 2969, 2111 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 5.56 (1H major isomer, s), 4.90 (1H major isomer, d, J = 7.0 Hz), 4.91−4.84 (2H minor isomer, m), 4.77 (1H major isomer, d, J = 7.0 Hz), 3.96 (1H minor isomer, dd, J = 3.0, 11.5 Hz), 3.81−3.32 (4H major isomer and 3H minor isomer, m), 3.48 (3H major isomer, s), 3.46 (3H, s), 3.38 (3H minor isomer, s), 2.59 (1H major isomer, s), 2.57 (1H minor isomer, s), 2.32−2.23 (1H, m), 1.02 (3H minor isomer, d, J = 7.0 Hz), 0.97 (3H major isomer, d, J = 7.0 Hz); MS (CI^+, NH_3) m/z 248 $(M + NH_4)^+$, 230 $(M + NH_4 - H_2O)^+$, 230 $(M - OH)^+$. Anal. Calcd for $C_{11}H_{18}O_5$: C, 57.38; H, 7.88. Found: C, 57.17; H, 7.59.

(2*RS*,3*R*,4*S*,5*S*)-2-Hydroxy-4-methoxy-3-(methoxymethoxy)-5-methyl-2-((trimethylsilyl)ethynyl)tetrahydro-2*H*-pyran (22). $CeCl_3 \cdot 7H_2O$ (123 mg, 0.33 mmol) was heated to 140 °C under vacuum (∼2 mmHg) for 4 h. When cool, THF (1.0 mL) was added and the resultant suspension stirred vigorously overnight before being cooled to −78 °C. To a stirred solution of (trimethylsilyl)acetylene in THF (1.0 mL) at −78 °C was added *n*-BuLi in hexane (2.3 M; 122 μL, 0.28 mmol). After 1 h, the resultant anion was transferred via cannula to the stirred suspension of $CeCl_3$ at −78 °C, and, after a further 2 h, lactone **16** (32 mg, 0.157 mmol) in THF (2 mL) at −78 °C was added via cannula. The mixture was quenched after 2 h with saturated aqueous NH_4Cl (1 mL) and allowed to warm to room temperature. The mixture was decanted from the resultant precipitate (rinsed with Et_2O) and the solvent evaporated in vacuo. The residue was dry loaded onto silica and chromatographed (EtOAc:hexanes 1:4) to afford hemiketal **22** (48 mg, 100%), a 3:2 mixture of anomers, as a colorless oil: TLC R_f = 0.21 (EtOAc:hexanes 1:4); IR (film) 3389, 2963 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 5.71 (1H major isomer, s), 4.92 (1H major isomer, d, J = 7.0 Hz), 4.87 (2H minor isomer, app d, J = 1.0 Hz), 4.74 (1H major isomer, d, J = 7.0 Hz), 3.96 (1H minor isomer, dd, J = 3.0, 11.5 Hz), 3.75−3.38 (4H major isomer and 3H minor isomer, m), 3.49 (3H major isomer, s), 3.46 (3H minor isomer, s), 3.44 (3H major isomer, s), 3.35 (3H minor isomer, s), 2.37−2.18 (1H, m), 1.02 (3H minor isomer, d, J = 7.0 Hz), 0.93 (3H major isomer, d, J = 7.0 Hz), 0.17 (9H major isomer, s), 0.16 (9H minor isomer, s); MS (CI^+, NH_3) m/z 320 $(M + NH_4)^+$, 302 $(M + NH_4 - H_2O)^+$, 285 $(M - OH)^+$. Anal. Calcd for $C_{14}H_{26}O_5Si$: C, 55.60; H, 8.67. Found: C, 55.72; H, 8.64.

(2*S*,3*R*,4*S*,5*S*)-3-Hydroxy-4-methoxy-5-methyl-2-((trimethylsilyl)ethynyl)tetrahydro-2*H*-pyran (23). To a stirred solution of hemiketal **22** (24 mg, 0.079 mmol) and Et_3SiH (64 μL, 0.40 mmol) in MeCN(1.5 mL) at −20 °C was added, $BF_3 \cdot Et_2O$ (20 μL, 0.16 mmol). After 4 h, saturated aqueous $NaHCO_3$ (200 μL) was added and the mixture allowed to warm to room temperature. The solvent was evaporated in vacuo and the residue dry loaded onto silica and chromatographed (eluant EtOAc:hexanes 1:4) to afford acetylenic *C*-glycoside **23** (13 mg, 68%): TLC R_f = 0.18 (EtOAc:hexanes 1:4); [α] = +43.7° (c = 0.27, $CHCl_3$); IR (film) 3450, 2178 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 3.85 (1H, d, J = 9.0 Hz), 3.82 (1H, dd, J = 2.0, 12.0 Hz), 3.66 (1H, app td, J = 2.0, 9.0 Hz), 3.54 (1H, dd, J = 2.5, 12.0 Hz), 3.40 (3H, s), 3.20 (1H, dd, J = 5.0, 9.0 Hz), 2.40 (1H, d, J = 2.5 Hz), 2.22−2.16 (1H, m), 1.03 (1H, d, J = 7.0 Hz), 0.19 (9H, s); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 101.8, 91.1, 83.1, 72.2, 71.1, 70.0, 56.3, 31.8, 10.9, −0.17; MS (CI^+, NH_3) m/z 260 $(M + NH_4)^+$, 243 $(M + H)^+$. Anal. Calcd for $C_{12}H_{22}O_3Si$: C, 59.46; H, 9.15. Found: C, 59.22; H, 8.88.

(2*S*,3*R*,4*S*,5*S*)-2-Ethynyl-3-hydroxy-4-methoxy-5-methyltetrahydro-2*H*-pyran (20) and (2*R*,3*R*,4*S*,5*S*)-2-Ethynyl-3-hydroxy-4-methoxy-5-methyltetrahydro-2*H*-pyran (21). To a stirred solution of hemiketal **19** (504 mg, 2.19 mmol) and Et_3SiH (1.75 mL, 10.95 mmol) in MeCN (30 mL) at −20 °C was dropwise added $BF_3 \cdot Et_2O$ (555 μL, 4.38 mmol). After 2.5 h, the mixture was quenched with saturated aqueous $NaHCO_3$ solution (2 mL), allowed to warm to room temperature, and filtered. The solvent was evaporated in vacuo and the residue dry loaded onto silica and chromatographed (eluant EtOAc:hexanes 7:13) to afford (i) acetylenic *C*-glycoside **21** (74 mg, 20%) as a crystalline white solid and (ii) acetylenic *C*-glycoside **20** (219 mg, 59%) as a colorless oil. **21**: mp 66−68 °C (hexanes); TLC R_f = 0.31 (EtOAc:hexanes 2:3); [α] = +29.3° (c = 1.0, $CHCl_3$); IR (film) 3439, 3281, 2119 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 4.58 (1H, d, J = 2.0 Hz), 3.81−3.72 (2H, m), 3.50−3.46 (1H, m), 3.43 (3H, s), 3.39−3.36 (1H, m), 2.55 (1H, d, J = 2.0 Hz), 2.36 (1H, bs), 2.26−2.18 (1H, m), 0.91 (3H, d, J = 7.0

Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 79.9, 75.4, 68.2, 67.4, 58.0, 30.0, 11.6; MS (CI^+, NH_3) *m/z* 188 $(M + NH_4)^+$. Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.38; H, 7.99. **20**: TLC R_f = 0.20 (EtOAc:hexanes 2:3); [α] = +78.5° (*c* = 1.0, $CHCl_3$); IR (film) 3433, 3280, 2122 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.89 (1H, dd, *J* = 2.0, 9.0 Hz), 3.85 (1H, dd, *J* = 2.0, 12.0 Hz), 3.72 (1H, app td, *J* = 1.5, 9.0 Hz), 3.58 (1H, dd, *J* = 2.5, 12.0 Hz), 3.42 (3H, s), 3.23 (1H, dd, *J* = 5.0, 9.0 Hz), 2.61 (1H, d, *J* = 2.0 Hz), 2.55 (1H, d, *J* = 2.0 Hz), 2.23−2.22 (1H, m), 1.05 (1H, d, *J* = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 83.2, 80.6, 74.0, 71.3, 71.1, 69.9, 56.2, 31.6, 10.8; MS (CI^+, NH_3) *m/z* 188 $(M + NH_4)^+$, 85; HRMS (CI^+, NH_3) *m/z* calcd for $C_9H_{18}NO_3$ $(M + NH_4)^+$ 188.1287, found 188.1284. Crystal data for **21**: $C_9H_{14}O_3$, *M* = 170.2, orthorhombic, $P2_12_12_1$ (no. 19), *a* = 7.408(1), *b* = 7.425(2), *c* = 17.337(2) Å, *V* = 953.6(3) Å^3, *Z* = 4, D_c = 1.186 g cm^{-3}, μ(Cu−Kα) = 7.26 cm^{-1}, *F*(000) = 368, *T* = 293 K; clear blocks, 0.83 × 0.33 × 0.16 mm, Siemens P4/PC diffractometer, ω-scans, 911 independent reflections. The structure was solved by direct methods and the non-hydrogen atoms were refined anisotropically using full matrix least-squares based on F^2 to give R_1 = 0.045, wR_2 = 0.115 for 793 independent observed reflections [$|F_o| > 4\sigma(|F_o|)$, $2\theta \leq 125°$] and 114 parameters. The absolute structure of **21** was determined by internal reference.[23]

(2*S*,3*R*,4*S*,5*S*)-2-Ethynyl-4-methoxy-5-methyltetrahydro-2*H*-pyran-2-yl 3,5-Dinitrobenzoate (24). To a stirred mixture of *C*-glycoside **20** (23 mg, 0.14 mmol), Et_3N (38 μL, 0.27 mmol), and DMAP (5 mg, 0.04 mmol) in CH_2Cl_2 (1 mL) was added 3,5-dinitrobenzoyl chloride (46 mg, 0.20 mmol). After 1 h, distilled water (0.5 mL) was added and the mixture was diluted with Et_2O (20 mL) and washed with distilled water (3 × 10 mL) and brine (10 mL). The organic layer was dried ($MgSO_4$), filtered, and rotary evaporated. The residue was chromatographed (eluant EtOAc:hexanes 1:4) to afford 3,5-dinitrobenzoate **24** (40 mg, 80%) as a pale yellow solid: mp 140−143 °C ($CHCl_3$/hexanes); TLC R_f = 0.22 (EtOAc:hexanes 1:4); [α] = +29.5° (*c* = 1.1, $CHCl_3$); IR (film) 3239, 3103, 1740, 1629, 1547, 1461 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.26 (1H, t, *J* = 2.0 Hz), 9.18 (2H, d, *J* = 2.0 Hz), 5.44 (1H, app t, *J* = 8.0 Hz), 4.33 (1H, dd, *J* = 2.0, 8.0 Hz), 3.94 (1H, dd, *J* = 4.0, 12.0 Hz), 3.65 (1H, dd, *J* = 3.0, 12.0 Hz), 3.54 (1H, dd, *J* = 4.5, 8.0 Hz), 3.38 (3H, s), 2.46 (1H, d, *J* = 2.0 Hz), 2.38−2.35 (1H, m), 1.13 (3H, d, *J* = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 162.0, 149.1, 133.9, 129.9, 123.0, 80.4, 79.1, 75.2, 72.5, 69.8, 68.5, 57.0, 32.3, 11.4; MS (CI^+, NH_3) *m/z* 382 $(M + NH_4)^+$, 365 $(M + H)^+$. Anal. Calcd for $C_{16}H_{16}N_2O_8$: C, 52.75; H, 4.43; N, 7.69. Found: C, 52.89; H, 4.16; N, 7.45.

(2*S*,3*R*,4*S*,5*S*)-2-Ethynyl-4-methoxy-5-methyl-3-(triethylsilyloxy)tetrahydro-2*H*-pyran (25). A stirred mixture of *C*-glycoside **20** (136 mg, 0.80 mmol) and Et_3N (167 μL, 1.20 mmol) in CH_2Cl_2 (5 mL) was cooled in an ice/salt bath. $Et_3SiO_3SCF_3$ (199 μL, 0.88 mmol) was added dropwise, followed, after 1 h, by saturated aqueous $NaHCO_3$ (0.5 mL). The mixture was diluted with Et_2O (25 mL) and washed with distilled water (3 × 10 mL) and brine (5 mL). The organic layer was dried ($MgSO_4$), filtered, and rotary evaporated. The residue was chromatographed (eluant EtOAc:hexane 1:19) to afford **25** (192 mg, 85%) as a colorless oil: TLC R_f = 0.26 (EtOAc:hexanes 1:19); [α] = +42.5° (*c* = 1.1, $CHCl_3$); IR (film) 3312, 3264, 2125 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.89 (1H, dd, *J* = 2.0, 8.0 Hz), 3.79 (1H, dd, *J* = 3.5, 11.5 Hz), 3.69 (1H, app t, *J* = 8.0 Hz), 3.51 (1H, dd, *J* = 2.5, 11.5 Hz), 3.33 (3H, s), 3.09 (1H, dd, *J* = 5.0, 8.0 Hz), 2.43 (1H, d, *J* = 2.0 Hz), 2.22−2.21 (1H, m), 1.01−0.95 (12H, m), 0.66 (6H, m). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 83.7, 81.7, 73.4, 71.8, 70.3, 70.0, 55.9, 31.3, 11.1, 6.9, 5.1; MS (CI^+, NH_3) *m/z* 302 $(M + NH_4)^+$, 285 $(M + H)^+$. Anal. Calcd for $C_{15}H_{28}O_3Si$: C, 63.33; H, 9.92. Found: C, 63.65; H, 9.75.

(2*R*,3*R*,4*S*,5*S*)-2-Hydroxy-4-methoxy-3-(methoxymethoxy)-5-methyl-2-[(*E*)-1-(trimethylsilyl)prop-1-en-2-yl]-tetrahydro-2*H*-pyran (28). To a stirred solution of vinyl iodide **30** (253 mg, 1.06 mmol) in Et_2O (11 mL) at −78 °C was dropwise added *t*-BuLi in pentane (2.0 M; 1.06 mL, 2.11 mmol). After 30 min, lactone **16** (180 mg, 0.88 mmol) in Et_2O (8 mL) at −78 °C was added dropwise via cannula. After a further 1 h, AcOH (80 μL, 1.40 mmol) and then saturated aqueous NH_4Cl (1 mL) were added, and the mixture was allowed to warm to room temperature. The reaction mixture was diluted with EtOAc (100 mL) and washed with distilled water (3 × 30 mL) and brine (30 mL). The organic layer was dried ($MgSO_4$), filtered, and rotary evaporated. The residue was chromatographed (eluant EtOAc:hexanes 1:4) to afford **28** (216 mg, 77%), a 3:1 mixture of anomers (with a trace of ring opened isomer), as a colorless oil: IR (film) 3437, 1671, 1623, cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 5.98 (1H minor isomer, d, *J* = 1.0 Hz), 5.91 (1H major isomer, d *J* = 1.0 Hz), 5.73 (1H minor isomer, s), 4.77 (1H major isomer, d, *J* = 6.5 Hz), 4.58 (2H minor isomer, app d, *J* = 1.0 Hz), 4.52 (1H major isomer, d, *J* = 6.5 Hz), 4.11 (1H major isomer, dd, *J* = 2.5, 11.5 Hz), 3.78−3.38 (4H minor isomer and 3H major isomer, m), 3.56 (3H minor isomer, s), 3.36 (3H major isomer, s), 3.35 (3H minor isomer, s), 3.33 (3H major isomer, s), 2.78 (1H major isomer, s), 2.25−2.20 (1H, m), 1.92 (3H, app s), 1.07 (3H major isomer, d, *J* = 7.0 Hz), 1.03 (3H minor isomer, d, *J* = 7.0 Hz), 0.19 (9H, s); MS (CI^+, NH_3) *m/z* 336 $(M + NH_4)^+$, 301 $(M - OH)^+$, 287 $(M - OMe)^+$. Anal. Calcd for $C_{15}H_{30}O_5Si$: C, 56.57; H, 9.49. Found: C, 56.64; H, 9.36.

(*E*)-2-(1-Hydroxy-2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl)-1-(trimethylsilyl)prop-1-ene (32). To a stirred solution of vinyl iodide **30** (112 mg, 0.47 mmol) in THF (5 mL) at −78 °C was dropwise added *t*-BuLi (1.5 M; 593 μL, 0.89 mmol). After 30 min, lactone **31** (200 mg, 0.37 mmol) in THF (4 mL) at −78 °C was added dropwise via cannula.[18] After 1 h, the mixture was quenched with saturated aqueous NH_4Cl (0.5 mL) and allowed to warm to room temperature. The mixture was filtered and rotary evaporated and the residue azeotroped with MeCN, dry loaded onto silica, and chromatographed (eluant Et_2O:hexanes 1:3) to afford hemiketal **32** (156 mg, 64%) as a crystalline white solid: mp 70−75 °C; TLC R_f = 0.27 (Et_2O:hexanes 3:7); [α] = +47.1° (*c* = 1.0, $CHCl_3$); IR (film) 3531, 3430, 3031, 1620 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.20−7.06 (20H, m), 5.88 (1H, s), 4.72−4.68 (3H, m), 4.54−4.48 (3H, m), 4.42−4.37 (2H, m), 3.91−3.79 (2H, m), 3.68 (1H, dd, *J* = 11.0, 4.0 Hz), 3.61−3.52 (2H, m), 3.44 (1H, d, *J* = 9.0 Hz), 2.70 (1H, s), 1.79 (3H, s), 0.93 (9H, s); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 153.1, 139.0, 138.9, 138.7, 138.1, 128.7, 128.6, 128.3, 128.2, 128.1, 128.0, 128.0, 127.8, 127.7, 127.1, 99.0, 83.9, 80.9, 78.5, 76.9, 76.0, 75.5, 75.3, 73.6, 72.5, 69.3, 17.7, 0.0; MS (CI^+, NH_3) *m/z* 670 $(M + NH_4)^+$, 635 $(M - OH)^+$. Anal. Calcd for $C_{40}H_{48}O_6Si$: C, 73.58; H, 7.41. Found: C, 73.29; H, 7.28.

(*E*)-2-(2,3,4,6-Tetra-*O*-benzyl-β-D-glucopyranosyl)-1-(trimethylsilyl)prop-1-ene (33). To a stirred solution of hemiketal **32** (50 mg, 0.08 mmol) and Et_3SiH (90 mg, 123 μL, 0.77 mmol) in an MeCN/CH_2Cl_2 (85:15) solvent mixture (2.5 mL) at −40 °C was added dropwise $BF_3{\cdot}Et_2O$ (11 μL, 0.08 mmol) in CH_2Cl_2 (100 μL). After 15 min, the mixture was quenched with Et_3N (100 μL) and saturated aqueous $NaHCO_3$ (0.5 mL) and allowed to warm to room temperature. The reaction mixture was filtered and rotary evaporated and the residue azeotroped with MeCN, dry loaded on to silica, and chromatographed (eluant EtOAc:hexanes 1:9) to afford silane **33** (24 mg, 49%) as a crystalline white solid: mp 86−89 °C; TLC R_f = 0.56 (Et_2O:hexanes 3:7); [α] = +29.0° (*c* = 1.0, $CHCl_3$); IR (film) 3064, 3030, 1620 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.37−7.19 (20H, m), 5.74 (1H, s), 4.94−4.83 (3H, m), 4.69−4.56 (5H, m), 3.79−3.63 (5H, m), 3.49−3.45 (2H, m), 1.90 (3H, s), 0.15 (9H, s); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 150.4, 138.7, 138.5, 138.2, 138.1, 132.5, 129.6, 129.1, 128.4, 128.3, 128.0, 127.9, 127.7, 127.6, 127.6, 127.5, 86.8, 86.6, 80.6, 78.7, 78.3, 77.2, 75.6, 75.0, 74.6, 73.4, 69.1, 17.3, −0.2; MS (CI^+, NH_3) *m/z* 654 $(M + NH_4)^+$. Anal. Calcd for $C_{40}H_{48}O_5Si$: C, 75.43; H, 7.60. Found: C, 75.67; H, 7.81.

(*E*)-2-(1-Hydroxy-2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl)-1-iodoprop-1-ene (34). Hemiketal **32** (110 mg, 0.17 mmol) and *N*-iodosuccinimide (191 mg, 0.85 mmol) were mixed together in THF (5 mL). After 60 h, the reaction had not

(23) The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

proceeded to completion, and the volume of solvent was reduced (5 mL to 1 mL) by purging the flask with a stream of nitrogen. After a further 24 h, the mixture was diluted with Et_2O (75 mL), washed with saturated aqueous $Na_2S_2O_3$ (30 mL), distilled water (2 × 30 mL), and brine (30 mL), and rotary evaporated. The residue was chromatographed (Et_2O:hexanes 3:7) to afford **34** (99 mg, 83%) as a colorless oil: TLC R_f = 0.18 (Et_2O:hexanes 3:7); [α] = +6.43° (c = 0.42, $CHCl_3$); IR (film) 3522, 3400, 3087, 3063, 3030 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 7.41−7.19 (20H, m), 6.82 (1H, d, J = 1.0 Hz), 4.91 (2H, s), 4.84 (1H, d, J = 11.0 Hz), 4.70 (1H, d, J = 10.5 Hz), 4.65−4.59 (2H, m), 4.54−4.48 (2H, m), 4.03−3.90 (2H, m), 3.81−3.64 (3H, m), 3.54 (1H, d, J = 9.0 Hz), 3.04 (1H, s), 1.84 (3H, d, J = 1.0 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 147.2, 138.6, 138.5, 138.2, 137.2, 128.8, 128.5, 128.5, 128.4, 128.4, 128.1, 127.9, 127.7, 127.5, 98.7, 83.8, 83.6, 80.1, 78.1, 77.2, 75.8, 75.3, 75.1, 73.4, 72.2, 68.8, 20.7; MS (FAB$^+$) m/z 689 (M + H − H_2O)$^+$. Anal. Calcd for $C_{37}H_{39}O_6I$: C, 62.89; H, 5.56. Found: C, 62.61; H, 5.54.

(*E*)-2-(2,3,4,6-Tetra-*O*-benzyl-β-D-glucopyranosyl)-1-iodoprop-1-ene (35). To a stirred solution of **34** (95 mg, 0.14 mmol) and Et_3SiH (109 μL, 0.68 mmol) in a MeCN/CH_2Cl_2 (85:15) solvent mixture (5 mL) at −40 °C was added dropwise BF_3·Et_2O (52 μL, 0.41 mmol). After 15 min, the mixture was quenched with saturated aqueous $NaHCO_3$ (0.5 mL) and allowed to warm to room temperature. The reaction mixture was filtered and rotary evaporated and the residue azeotroped with MeCN, dry loaded on to silica, and chromatographed (eluant Et_2O:hexanes 1:9) to afford *C*-glycosidic vinyl iodide **35** (83 mg, 86%) as a crystalline white solid (ratio of α:β epimers: 15:85). Data for β epimer: mp 94−95 °C (hexane); TLC R_f = 0.45 (30% Et_2O/hexanes); [α] = −0.59° (c = 1.0, $CHCl_3$); IR (film) 3030, 1496 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 7.39−7.16 (20H, m), 6.47 (1H, d, J = 0.5 Hz), 4.95 (1H, d, J = 11.0 Hz), 4.89 (1H, d, J = 11.0 Hz), 4.83 (1H, d, J = 10.5 Hz), 4.69−4.45 (5H, m), 3.84 (1H, d, J = 9.5 Hz), 3.73−3.59 (4H, m), 3.49−3.42 (2H, m), 1.83 (3H, d, J = 1.0 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 144.7, 138.6, 138.3, 138.1, 137.7, 128.5, 128.5, 128.4, 128.4, 128.0, 127.8, 127.7, 127.6, 127.6, 86.8, 83.4, 82.5, 79.9, 78.9, 78.2, 75.7, 75.1, 74.9, 73.5, 69.0, 19.9; MS (FAB$^+$) m/z 691 (M + H)$^+$. Anal. Calcd for $C_{37}H_{39}O_5I$: C, 64.35; H, 5.69. Found: C, 64.25; H, 5.55. To a stirred solution of vinyl silane **33** (24 mg, 0.04 mmol) in THF (1 mL) was added *N*-iodosuccinimide (55 mg, 0.24 mmol). After 24 h, the mixture was diluted with Et_2O (50 mL), and washed with saturated aqueous $Na_2S_2O_3$ (15 mL), distilled water (2 × 15 mL), and brine (15 mL). The organic layer was dried ($MgSO_4$), filtered, and rotary evaporated. The residue was chromatographed to afford vinyl iodide **35** (25 mg, 95%) as a crystalline white solid. Crystal data for **35**: $C_{37}H_{39}O_5I$, M = 690.6, monoclinic, $P2_1$ (no. 4), a = 13.843(1), b = 8.903(1), c = 14.018(1) Å, β = 101.40(1)°, V = 1693.7(2) Å^3, Z = 2, D_c = 1.354 g cm^{-3}, μ(Cu−Kα) = 77.4 cm^{-1}, F(000) = 708, T = 293 K; clear fine needles, 0.27 × 0.07 × 0.05 mm, Siemens P4/PC diffractometer, ω-scans, 3024 independent reflections. The structure was solved by direct methods, and the non-hydrogen atoms were refined anisotropically using full matrix least-squares based on F^2 to give R_1 = 0.062, wR_2 = 0.138 for 1789 independent observed absorption corrected reflections [$|F_o| > 4\sigma(|F_o|)$, $2\theta \leq 128°$] and 341 parameters. The absolute structure of **35** was determined by a combination of *R*-factor tests [R_1^+ = 0.062, R_1^- = 0.089] and by use of the Flack parameter [x^+ = −0.01(3)].[23]

(2*RS*,3*R*,4*S*,5*S*)-2-Hydroxy-2-((*E*)-1-iodoprop-1-en-2-yl)-4-methoxy-3-(methoxymethoxy)-5-methyltetrahydro-2*H*-pyran (36). To a stirred solution of hemiketal **28** (20 mg, 0.063 mmol) in THF (0.5 mL) was added *N*-iodosuccinimide (17 mg, 0.075 mmol). After 36 h, the mixture was diluted with EtOAc (40 mL), washed with saturated aqueous $Na_2S_2O_3$ (10 mL), distilled water (2 × 10 mL), and brine (10 mL). The organic layer was dried ($MgSO_4$), filtered, and rotary evaporated. The residue was chromatographed (eluant EtOAc:hexanes 1:4) to afford **36** (19 mg, 81%) as a crystalline solid: mp 73−77 °C; IR (film) 3412, 1620 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 6.80 (1H major isomer, q, J = 1.0 Hz), 6.76 (1H minor isomer, J = 1.0 Hz), 5.79 (1H minor isomer, s), 4.86 (1H major isomer, d, J = 7.0 Hz), 4.62 (1H minor isomer, d, J = 7.0 Hz), 4.53 (1H minor isomer, d, J = 7.0 Hz), 4.50 (1H major isomer, d, J = 7.0 Hz), 4.09 (1H major isomer, dd, J = 2.5, 11.5 Hz), 3.80−3.71 (2H minor isomer, m), 3.72 (1H major isomer, d, J = 9.0 Hz), 3.60−3.37 (1H major isomer and 2H minor isomer, m), 3.55 (3H minor isomer, s), 3.52 (1H major isomer, dd, J = 1.5, 11.5 Hz), 3.35 (3H major isomer, s), 3.34 (3H minor isomer, s), 3.31 (3H major isomer, s), 2.94 (1H major isomer, d, J = 0.5 Hz), 2.27−2.22 (1H, m), 1.96 (3H, d, J = 1.0 Hz), 1.06 (3H major isomer, d, J = 7.0 Hz), 0.92 (3H minor isomer, d, J = 7.0 Hz); MS (CI$^+$, NH_3) m/z 390 (M + NH_4)$^+$, 373 (M + H)$^+$, 355 (M − OH)$^+$; HRMS (CI$^+$, NH_3) m/z calcd for $C_{12}H_{25}NO_5I$ (M + NH_4)$^+$ 390.0778, found 390.0773.

(2*R*,3*R*,4*S*,5*S*)-2-((*E*)-1-Iodoprop-1-en-2-yl)-4-methoxy-3-(methoxymethoxy)-5-methyltetrahydro-2*H*-pyran (39). To a stirred mixture of hemiketal **36** (25 mg, 0.07 mmol) and Et_3SiH (55 μL, 0.34 mmol) in a MeCN/CH_2Cl_2 (85:15) solvent mixture (2.5 mL) at −40 °C was dropwise added BF_3·Et_2O (25 μL, 0.20 mmol). After 1 h, the mixture was quenched with saturated aqueous $NaHCO_3$ (100 μL) and allowed to warm to room temperature. The solvent was evaporated in vacuo and the residue dissolved in EtOAc (50 mL) and washed with distilled water (2 × 20 mL) and brine (20 mL). The organic layer was dried ($MgSO_4$), filtered, and rotary evaporated. The residue was chromatographed (eluant EtOAc:hexanes 3:17 then 1:4) to afford *C*-glycoside **39** (10 mg, 42%) as a colorless oil: TLC R_f = 0.41 (EtOAc:hexanes 3:17); [α] = −39.5° (c = 0.55, $CHCl_3$); IR (film) 2929, 1626 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.37−6.36 (1H, m), 4.66 (1H, d, J = 7.0 Hz), 4.52 (1H, d, J = 7.0 Hz), 4.09 (1H, s), 3.76 (1H, dd, J = 1.0, 3.5 Hz), 3.68 (1H, dd, J = 5.0, 11.0 Hz), 3.45 (3H, s), 3.42 (1H, app t, J = 11.5 Hz), 3.34 (3H, s), 3.26 (1H, t, J = 3.0 Hz), 2.24−2.17 (1H, m), 1.84 (3H, d, J = 0.5 Hz), 0.87 (3H, d, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.9, 95.9, 79.0, 78.5, 77.5, 70.5, 68.7, 58.9, 56.0, 30.2, 22.0, 12.1; MS (CI$^+$, NH_3) m/z 374 (M + NH_4)$^+$, 357 (M + H)$^+$; HRMS (CI$^+$, NH_3) m/z calcd for $C_{12}H_{25}NO_4I$ (M + NH_4)$^+$ 374.0828, found 374.0815.

(2*R*,3*R*,4*S*,5*S*)-3-Hydroxy-2,4-dimethoxy-5-methyl-2-((*E*)-1-(trimethylsilyl)prop-1-en-2-yl)-tetrahydro-2*H*-pyran (40). To a stirred solution of **28** (53 mg, 0.17 mmol) in MeOH (3.7 mL) was added (+)-camphorsulfonic acid (38 mg, 0.17 mmol) at 20 °C. After 12 h, Et_3N (50 μL, 0.36 mmol) was added, the solvent was evaporated in vacuo, and the residue was dry loaded onto silica and chromatographed (eluant EtOAc:hexanes 1:4) to afford **40** (34 mg, 71%) as a colorless oil: TLC R_f = 0.21 (EtOAc:hexanes 1:4); [α] = +98.6° (c = 1.04, $CHCl_3$); IR (film) 3480, 1615 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 5.74 (1H, d, J = 1.0 Hz), 3.74 (1H, dd, J = 2.5, 11.5 Hz), 3.55 (1H, dd, J = 1.5, 11.5 Hz), 3.52 (1H, dd, J = 4.5, 9.5 Hz), 3.45 (1H, dd, J = 4.5, 9.5 Hz), 3.40 (3H, s), 3.14 (3H, s), 2.21 (1H, m), 2.09 (1H, d, J = 4.5 Hz), 1.87 (3H, d, J = 1.0 Hz), 1.04 (3H, d, J = 7.0 Hz), 0.14 (9H, s); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 150.1, 127.9, 102.9, 80.7, 71.2, 64.7, 56.8, 49.1, 32.0, 18.3, 10.7, 0.0; MS (CI$^+$, NH_3) m/z 257 (M − OMe)$^+$. Anal. Calcd for $C_{14}H_{28}O_4Si$: C, 58.29; H, 9.78. Found: C, 57.94; H, 9.56.

(2*R*,3*R*,4*S*,5*S*)-3-Hydroxy-2-((*E*)-1-iodoprop-1-en-2-yl)-2,4-dimethoxy-5-methyltetrahydro-2*H*-pyran (41). To a stirred solution of vinyl silane **40** (33 mg, 0.12 mmL) in Me_3SiCN (1 mL) was added DMF (5 drops). After 15 min, the reaction vessel was purged with a stream of nitrogen for 1 h to remove volatiles. The residue was dried in vacuo, suspended in THF (0.5 mL), *N*-iodosuccinimide (155 mg, 0.69 mmol) added, and the mixture stirred for 36 h at 25−30 °C (bath temp). The mixture was diluted with Et_2O (50 mL) and washed with saturated aqueous $NaHCO_3$ (20 mL), saturated aqueous $Na_2S_2O_3$ (20 mL), distilled water (20 mL), and brine (10 mL). The organic layer was dried ($MgSO_4$), filtered, and rotary evaporated. The residue was dissolved in a solution of K_2CO_3 (599 mg, 4.33 mmol) in MeOH (1.5 mL) and stirred. After 2 h, the mixture was diluted with Et_2O (50 mL), filtered, and rotary evaporated. The residue was chromatographed (eluant EtOAc:hexanes 1:3) to afford vinyl iodide **41** (29 mg, 74%) as a crystalline white solid: mp 70−72 °C; TLC R_f = 0.27 (EtOAc:hexanes 3:7); [α] = +77.2° (c = 0.67, $CHCl_3$); IR (film) 3468,

1610 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 6.25 (1H, app q, J = 1.0 Hz), 3.74 (1H, dd, J = 2.5, 11.5 Hz), 3.54 (1H, dd, J = 1.5, 11.5 Hz), 3.50 (1H, dd, J = 4.5, 9.5 Hz), 3.44 (1H, dd, J = 4.5, 9.5 Hz), 3.37 (3H, s), 3.13 (3H, s), 2.36 (1H, d, J = 4.5 Hz), 2.23−2.17 (1H, m), 1.94 (3H, d, J = 1.0 Hz), 1.00 (3H, d, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 145.6, 102.3, 84.0, 80.5, 72.0, 64.6, 56.5, 49.3, 31.5, 21.6, 10.4; MS (CI^+, NH_3) m/z 311 $(M - OMe)^+$; HRMS (CI^+, NH_3) m/z calcd for $C_{10}H_{16}O_3I$ $(M - OMe)^+$ 311.0144, found 311.0133.

(2*S*,3*R*,4*S*,5*S*)-3-Hydroxy-2-((*E*)-1-iodoprop-1-en-2-yl)-4-methoxy-5-methyltetrahydro-2*H*-pyran (37) and (2*R*,3*R*,4*S*,5*S*)-3-hydroxy-2-((*E*)-1-iodoprop-1-en-2-yl)-4-methoxy-5-methyltetrahydro-2*H*-pyran (38). To a stirred solution of **41** (31 mg, 0.091 mmol) and Et_3SiH (74 μL, 0.46 mmol) in a $MeCN/CH_2Cl_2$ (85:15) solvent mixture (2.25 mL) at −40 °C was added dropwise $BF_3{\cdot}Et_2O$ (29 μL, 0.23 mmol). After 1.75 h saturated aqueous $NaHCO_3$ (300 μL) was added and the mixture allowed to warm to room temperature, diluted with Et_2O (50 mL), washed with distilled water (3 × 15 mL) and brine (15 mL), dried ($MgSO_4$), filtered, and rotary evaporated. The residue was chromatographed (eluant EtOAc:hexanes 1:4 then 3:7) to afford (i) iodide **38** (11 mg, 39%) as a colorless oil and (ii) iodide **37** (16 mg, 56%) as colorless oil which slowly crystallized upon standing. **38**: TLC R_f = 0.39 (Et_2O:hexanes 1:3); [α] = −68.1° (c = 1.0, $CHCl_3$); IR (film) 3461, 1622 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 6.37−6.35 (1H, m), 4.14 (1H, s), 3.82−3.78 (1H, m), 3.63 (1H, dd, J = 5.0, 11.0 Hz), 3.45 (3H, s), 3.41 (1H, app t, J = 11.5 Hz), 3.32 (1H, app t, J = 3.0 Hz), 2.21−2.09 (1H, m), 1.83 (3H, dd, J = 0.5, 1.0 Hz), 1.78 (1H, d, J = 6.5 Hz), 0.87 (3H, d, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 67.5 MHz) δ 143.9, 80.2, 78.6, 78.0, 69.0, 65.1, 59.1, 29.7, 22.0, 11.9; MS (CI^+, NH_3) m/z 330 $(M + NH_4)^+$, 313 $(M + H)^+$; HRMS (CI^+, NH_3) m/z calcd for $C_{10}H_{21}NO_3I$ $(M + NH_4)^+$ 330.0566, found 330.0561. **37**: mp 80−86 °C; TLC R_f = 0.13 (EtOAc:hexanes 1:3); [α] = +56.9° (c = 0.8, $CHCl_3$); IR (film) 3437, 1620 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 6.43 (1H, app t, J = 0.5 Hz), 3.81 (1H, dd, J = 1.5, 12.0 Hz), 3.65−3.54 (3H, m), 3.39 (3H, s, OC*H*$_3$), 3.31 (1H, ddd, J = 1.0, 5.0, 7.5 Hz), 2.30 (1H, s), 2.24−2.18 (1H, m), 1.89 (3H, J = 1.0 Hz), 1.03 (3H, d, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 67.5 MHz) δ 145.1, 85.0, 84.1, 81.9, 71.1, 68.0, 55.9, 31.5, 19.9, 10.7; MS (CI^+, NH_3) m/z 330 $(M + NH_4)^+$, 211, 185, 153, 115; HRMS (CI^+, NH_3) m/z calcd for $C_{10}H_{21}NO_3I$ $(M + NH_4)^+$ 330.0566, found 330.0570.

(2*S*,3*R*,4*S*,5*S*)-2-((*E*)-1-Iodoprop-1-en-2-yl)-4-methoxy-5-methyl-3-(triethylsilyloxy)-tetrahydro-2*H*-pyran (26). To a stirred solution of **37** (17 mg, 0.054 mmol) and 2,6-lutidine (34 μL, 0.29 mmol) in CH_2Cl_2 at −20 °C was added dropwise $Et_3SiO_3SCF_3$ (21 μL, 0.096 mmol). After 2 h, saturated aqueous $NaHCO_3$ (0.5 mL) was added and the mixture allowed to warm to room temperature, diluted with Et_2O (50 mL), washed with distilled water (3 × 20 mL) and brine (20 mL), dried ($MgSO_4$), and rotary evaporated. The residue was chromatographed (eluant Et_2O:hexanes 1:24) to afford **26** (22 mg, 96%) as colorless oil: TLC R_f = 0.34 (EtOAc:hexanes 1:19); [α] = +23.1° (c = 1.0, $CHCl_3$); IR (film) 2954, 1621 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 6.31 (1H, d, J = 1.0 Hz), 3.77 (1H, dd, J = 1.5, 11.5 H), 3.61−3.49 (3H, m), 3.29 (3H, s), 3.11 (1H, dd, J = 5.5, 8.5 Hz), 2.21−2.17 (1H, m), 1.84 (3H, d, J = 1.0 Hz), 1.01 (3H, d, J = 7.0 Hz), 0.92 (9H, t, J = 8.0 Hz), 0.63−0.49 (6H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 145.1, 86.5, 84.6, 82.1, 70.9, 69.0, 55.3, 31.6, 19.8, 10.9, 6.9, 5.2; MS (CI^+, NH_3) m/z 444 $(M + NH_4)^+$, 427 $(M + H)^+$; HRMS (CI^+, NH_3) m/z calcd for $C_{16}H_{32}O_3SiI$ $(M + H)^+$ 427.1166, found 427.1168.

(2*R*,3*R*,4*S*,5*S*)-3-(*tert*-Butyldimethylsilyloxy)-2-((*E*)-1-iodoprop-1-en-2-yl)-2,4-dimethoxy-5-methyltetrahydro-2*H*-pyran (42). To a stirred solution of **41** (30 mg, 0.09 mmol) and 2,6-lutidine (92 μL, 0.79 mmol) in CH_2Cl_2 (1.25 mL) at −20 °C was added *tert*-butyldimethylsilyl trifluoromethanesulfonate (61 μL, 0.26 mmol). After 2 h, MeOH (0.2 mL) and saturated aqueous $NaHCO_3$ (0.5 mL) were added. The reaction mixture was allowed to warm to room temperature, diluted with Et_2O (50 mL), washed with distilled water (3 × 20 mL) and brine (20 mL), dried ($MgSO_4$), and filtered. Rotary evaporation and chromatography gave iodide **42** (36 mg, 90%) as a colorless oil: TLC R_f = 0.48 (EtOAc:hexanes 1:19); [α] = +46.9° (c = 1.03, $CHCl_3$); IR (film) 2931, 2896, 2856, 1619 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 6.43 (1H, d, J = 1.0 Hz), 3.69 (1H, dd, J = 2.5, 11.5 Hz), 3.55 (1H, d, J = 9.5 Hz), 3.51−3.43 (2H, m), 3.26 (3H, s), 3.14 (3H, s), 2.27−2.19 (1H, m), 1.85 (3H, d, J = 1.0 Hz), 1.02 (3H, d, J = 7.0 Hz), 0.87 (9H, s), 0.03 (3H, s), −0.01 (3H, s); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 143.5, 104.3, 84.8, 79.9, 71.3, 64.5, 55.5, 49.3, 31.6, 26.2, 21.3, 18.5, 10.6, −3.9, −4.1; MS (CI^+, NH_3) m/z 425 $(M - OMe)^+$; HRMS (CI^+, NH_3) m/z calcd for $C_{16}H_{30}O_3SiI$ $(M - OMe)^+$, 425.1009 found 425.1013.

(2*R*,3*R*,4*S*,5*S*)-3-(*tert*-Butyldimethylsilyloxy)-2-((*E*)-1-iodoprop-1-en-2-yl)-4-methoxy-5-methyltetrahydro-2*H*-pyran (43) and (2*R*,3*R*,4*S*,5*S*)-3-Hydroxy-2-((*E*)-1-iodoprop-1-en-2-yl)-4-methoxy-5-methyltetrahydro-2*H*-pyran (38). To a stirred solution of **42** (35 mg, 0.077 mmol) and Et_3SiH (45 mg, 61 μL, 0.39 mmol) in a $MeCN/CH_2Cl_2$ (85:15) solvent mixture (2 mL) at −40 °C was added dropwise $BF_3{\cdot}Et_2O$ (15 μL, 0.12 mmol). After 45 min, saturated aqueous $NaHCO_3$ (300 μL) was added. The mixture was allowed to warm to room temperature, diluted with Et_2O (50 mL), washed with distilled water (2 × 20 mL) and brine (20 mL), dried ($MgSO_4$), filtered, and rotary evaporated. The residue was chromatographed (eluant EtOAc:hexanes 3:97 then 1:4) to afford (i) iodide **43** (16 mg, 49%) as a colorless oil which slowly crystallized upon standing and (ii) iodide **38** (8 mg, 30%) as a colorless oil. **43**: mp 32−36 °C; TLC R_f = 0.51 (EtOAc:hexanes 1:19); [α] = −27.4° (c = 1.0, $CHCl_3$); IR (film) 2955, 2929, 2857, 1627 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 6.22 (1H, app t, J = 1.0 Hz), 4.10 (1H, s), 3.71 (1H, d, J = 3.0 Hz), 3.61 (1H, dd, J = 5.0, 11.0 Hz), 3.44 (3H, s), 3.38 (1H, app t, J = 11.5 Hz), 3.11 (1H, app t, J = 3.0 Hz), 2.26−2.20 (1H, m), 1.80 (3H, s), 0.88 (9H, s), 0.84 (3H, d, J = 7.0 Hz), 0.04 (3H, s), 0.00 (3H, s); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 144.4, 81.8, 79.0, 78.6, 68.6, 66.4, 58.9, 29.5, 25.7, 22.5, 17.9, 12.3, −4.7, −4.9; MS (CI^+, NH_3) m/z 444 $(M + NH_4)^+$, 427 $(M + H)^+$; HRMS (CI^+, NH_3) m/z calcd for $C_{16}H_{32}O_3SiI$ $(M + H)^+$, 427.1166 found 427.1170.

(*E*)-1-Iodo-1-pentene (46). To 1-pentyne (**45**) (7.88 mL, 80 mmol) in a sealable tube at 0 °C was added DIBAL-H in hexane (1 M; 80 mL, 80 mmol). The tube was sealed and allowed to stand for 30 min at room temperature before being heated to 55−60 °C for 4 h. When cool, the reaction mixture was evaporated in vacuo (using a vacuum manifold) and the residue dissolved in THF (60 mL) at 0 °C. The resultant solution was cooled to −78 °C and I_2 (21.60 g, 85 mmol) in THF (30 mL) added dropwise. The mixture was allowed to warm to 0 °C and transferred via cannula to a stirred mixture of 10% HCl (200 mL) and *n*-pentane (60 mL). The layers were separated, and the aqueous phase was extracted with *n*-pentane (3 × 50 mL). The combined organic extracts were washed with saturated aqueous sodium thiosulfate (50 mL), 1 M NaOH (50 mL), distilled water (50 mL), and brine (50 mL), dried ($MgSO_4$), filtered, and rotary evaporated. The residue was purified by bulb to bulb distillation under reduced pressure (∼50 °C, 20 mmHg) to afford vinyl iodide **46** (8.41 g, 54%) as a colorless oil: IR (film) 3049, 2959, 2929, 2872, 1606 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 6.50 (1H, dt, J = 7.0, 14.5 Hz), 5.97 (1H, dt, J = 1.5, 14.5 Hz), 2.03 (2H, app qd, J = 1.5, 7.5 Hz), 1.42 (2H, app sextet, J = 7.5 Hz), 0.90 (3H, t, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 146.5, 74.4, 38.0, 21.6, 13.4; MS (CI^+, NH_3) m/z 196 $(M)^+$; HRMS (CI^+, NH_3) m/z calcd for C_5H_9I $(M)^+$ 195.9749, found 195.9748 $(M + NH_4)^+$.

(*E*)-1-(Trimethylsilyl)-3-hepten-1-yne (48). To a stirred solution of (trimethylsilyl)acetylene (**47**) (3.70 mL, 26.21 mmol) in THF (12 mL) at −78 °C was dropwise added *n*-BuLi in hexane (2.38 M; 11.01 mL, 26.21 mmol). After 1 h, this solution was added via cannula to a stirred solution of $ZnCl_2$ in THF (0.5 M; 52.42 mL, 26.21 mmol) at −78 °C and the mixture allowed to warm to room temperature. After 1 h, a solution of vinyl iodide **46** (4.67 g, 23.84 mmol) and $Pd(PPh_3)_4$ (1.51 g, 1.31 mmol) in THF (20 mL) was added dropwise via cannula. After approximately 18 h, the mixture was quenched with saturated aqueous NH_4Cl (10 mL), diluted with Et_2O (200 mL), washed with distilled water (2 × 75 mL), saturated aqueous $Na_2S_2O_3$ (75 mL), and brine (75 mL), dried ($MgSO_4$), filtered, and rotary evaporated. The residue was purified by filtration

through silica gel (eluant pentane) to afford **48** (3.50 g, 89%) as a colorless oil: IR (film) 3021, 2961, 2932, 2179, 2142 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 6.22 (1H, dt, J = 16.0, 7.0 Hz), 5.50 (1H, dt, J = 16.0, 1.5 Hz), 2.09 (2H, app dq, J = 7.0, 1.5 Hz), 1.41 (2H, app sextet, J = 7.5 Hz), 0.90 (3H, t, J = 7.5 Hz), 0.18 (9H, s); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 146.1, 109.8, 104.2, 92.4, 35.1, 21.8, 13.6, 0.0; MS (CI^+, NH_3) m/z 184 ($M + NH_4$)$^+$; HRMS (CI^+, NH_3) m/z calcd for $C_{10}H_{22}NSi$ ($M + NH_4$)$^+$ 184.1522, found 184.1520; Anal. Calcd for $C_{10}H_{18}Si$: C, 72.21; H, 10.91. Found: C, 72.03; H, 10.88.

***(E)*-3-Hepten-1-yne (49).** To a stirred solution of **48** (3.47 g, 20.9 mmol) and distilled water (828 μL, 46 mmol) in DMF (16 mL) was added KF (1.34 g, 23 mmol). After 2 h, the mixture was diluted with water (30 mL) and extracted with pentane (3 × 10 mL). The combined organic extracts were washed with water (10 mL) and brine (10 mL) and dried ($MgSO_4$). The solvent was evaporated at atmospheric pressure to afford a mixture of enyne **49** (1.20 g, 61%) and $(Me_3Si)_2O$ (1.34 g, 79%) as determined by ^1H NMR. ^1H NMR ($CDCl_3$, 270 MHz) δ 6.25 (1H, dt, J = 7.0, 16.0 Hz), 5.46 (1H, m), 2.77 (1H, d, J = 2.0 Hz), 2.09 (2H, qd, J = 1.5, 7.0 Hz), 1.43 (2H, app sextet, J = 7.0 Hz), 0.91 (3H, t, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 146.6, 108.7, 75.5, 35.1, 21.8, 13.5, 1.9; MS (EI^+) m/z 94 $(M)^+$; HRMS (EI^+) m/z calcd for C_7H_{10} $(M)^+$ 94.0783, found 94.0782.

***(E,E)*-Hepta-1,3-dienyl-1-boronic Acid (50).** A mixture of enyne **49** (500 mg, 57% by wt, 3.04 mmol) and catecholborane in THF (1 M; 1.26 mL, 1.26 mmol) was heated to 70 °C in a sealed tube. The mixture was allowed to cool and stirred vigorously with distilled water for 4 h. The resultant solid was filtered and washed with distilled water to afford **50** as an off-white solid. For quantification purposes, boronic acid **50** was dried in vacuo to afford the corresponding anhydride (247 mg, 67%) as a pale brown oil. For subsequent chemistry and characterization the anhydride was converted back to the boronic acid **50** by repeating the hydrolysis steps above: IR (DRIFTS) 3275, 3246, 3203, 3174, 3031, 2954, 1622, 1605, 1560, 1540, 1509 cm^{-1}; ^1H NMR (DMSO-d_6, 270 MHz) δ 7.58 (2H, bs), 6.84 (1H, dd, J = 10.5, 17.5 Hz), 6.14−6.05 (1H, m), 5.87−5.79 (1H, m), 5.37 (1H, d, J = 17.5 Hz), 2.53−2.51 (2H, m), 1.47−1.31 (2H, m), 0.89 (3H, t, J = 7.0 Hz); ^{13}C NMR (DMSO-d_6, 68 MHz) δ 147.0, 137.2, 133.1, 125.4, 34.3, 22.0, 13.8; MS (CI^+, NH_3) m/z 158 ($M + NH_4$)$^+$, 140 ($M + H$)$^+$; HRMS (CI^+, NH_3) m/z calcd for $C_7H_{17}BNO_2$ ($M + NH_4$)$^+$ 158.1352, found 158.1353.

(Triethylsilyl)restrictinol (51). To a stirred solution of vinyl iodide **26** (15 mg, 0.035 mmol) and boronic acid **50** in THF (3 mL) were added, dropwise, aqueous ~10% TlOH (465 μL, ~0.21 mmol) and, after 2 min, $Pd(PPh_3)_4$ (10 mg, 8.7 μmol) in THF (200 μL). After 2 and 3 h, further portions of $Pd(PPh_3)_4$ (5 mg, 4.4 μmol) in THF (100 μL) were added. The mixture was stirred overnight, diluted with Et_2O (~15 mL), dried ($MgSO_4$), and filtered through Celite. Rotary evaporation and chromatography (eluant Et_2O:hexanes 3:97) gave triene **51** (10 mg, 73%) as a colorless oil: TLC R_f = 0.56 (EtOAc:hexanes 1:10); IR (film) 3023, 2955, 2933, 2876 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 6.32 (1H, dd, J = 11.0, 14.0 Hz), 6.19−6.09 (2H, m), 6.01 (1H, d, J = 11.0 Hz), 5.70 (1H, dt, J = 7.0, 14.5 Hz), 3.71 (1H, dd, J = 1.5, 11.5 Hz), 3.54−3.50 (2H, m), 3.39 (1H, d, J = 9.0 Hz), 3.27 (3H, s), 3.09 (1H, dd, J = 5.0, 8.5 Hz), 2.20−2.15 (1H, m), 2.19−2.04 (2H, m), 1.74 (3H, d, J = 1.0 Hz), 1.41 (2H, app sextet, J = 7.5 Hz), 0.97 (3H, d, J = 7.0 Hz), 0.90 (3H, t, J = 7.5 Hz), 0.87 (9H, t, J = 8.0 Hz), 0.57−0.43 (6H, m);^{13}C NMR ($CDCl_3$, 125 MHz) δ 135.3, 133.5, 131.2, 129.7, 126.7, 88.1, 85.2, 71.0, 69.4, 55.5, 35.3, 32.1, 30.1, 22.9, 13.9, 12.7, 11.0, 7.0, 5.4; MS (CI^+, NH_3) m/z 412 ($M + NH_4$)$^+$, 395 ($M + H$)$^+$; HRMS (CI^+, NH_3) m/z calcd for $C_{23}H_{43}O_3Si$ ($M + H$)$^+$ 395.2981, found 395.2980.

Restrictinol (3). To a stirred solution of (triethylsilyl)-restrictinol (**51**) (9 mg, 0.023 mmol) in THF (2.5 mL) was added Bu_4NF in THF (1 M; 35 μL, 0.035 mmol). After 2 h, the solvent was evaporated in vacuo and the residue chromatographed (eluant EtOAc:hexanes 3:7) to afford restrictinol (**3**) (6 mg, 94%) as a colorless oil: TLC R_f = 0.35 (EtOAc:hexanes 3:7); [α] = +64.0° (c = 0.25, MeOH); IR (film) 3455, 2960, 2931, 2873, 1683, 1635 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.36 (1H, dd, J = 11.0, 14.5 Hz), 6.22 (1H, dd, J = 10.5, 14.5 Hz), 6.12 (1H, ddt, J = 1.5, 10.5, 14.5 Hz), 6.08 (1H, dd, J = 1.0, 10.5 Hz), 5.73 (1H, dt, J = 7.0, 14.5 Hz), 3.76 (1H, dd, J = 1.5, 11.5 Hz), 3.58 (1H, dd, J = 2.5, 11.5 Hz), 3.56 (1H, app t, J = 9.5 Hz), 3.43 (1H, d, J = 9.5 Hz), 3.36 (3H, s), 3.22 (1H, dd, J = 5.0, 9.0 Hz), 2.22−2.18 (1H, m), 2.11−2.06 (2H, m), 1.78 (3H, d, J = 1.0 Hz), 1.42 (2H, app sextet, J = 7.5 Hz), 1.01 (3H, d, J = 7.0 Hz), 0.90 (3H, t, J = 7.5 Hz);^{13}C NMR ($CDCl_3$, 100 MHz) δ 135.9, 134.6, 134.2, 131.0, 129.5, 126.2, 87.0, 84.6, 71.3, 68.0, 56.1, 35.2, 32.1, 22.8, 13.8, 12.4, 10.9; MS (CI^+, NH_3) m/z 298 ($M + NH_4$)$^+$, 281 ($M + H$)$^+$; HRMS (CI^+, NH_3) m/z calcd for $C_{17}H_{29}O_3$ ($M + H$)$^+$ 281.2117, found 281.2102.

Acknowledgment. We thank Glaxo Wellcome for the most generous endowment (to A.G.M.B), the Wolfson Foundation for establishing the Wolfson Centre for Organic Chemistry in Medical Science at Imperial College, the EPSRC, and Dr. David Gollins for preliminary studies on the addition of acetylides to lactone **16**.

Supporting Information Available: Copies of ^1H and ^{13}C NMR spectra of **15**, **20**, **26**, **36**, **39**, **41**, **37**, **38**, **42**, **43**, **50**, and **51** and X-ray crystallographic data for **21** and **35** (37 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO9815305