JOC Article

Crotylation versus Propargylation: Two Routes for the Synthesis of the C13−C18 Fragment of the Antibiotic Branimycin

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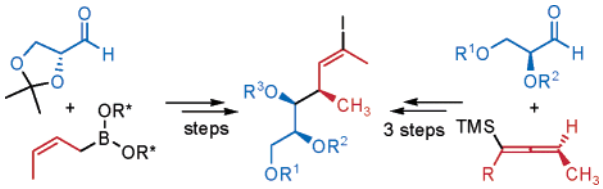

The C13−C18 fragment **3** of the novel antibiotic branimycin was prepared along two highly stereocontrolled routes. The first one uses a standard Roush crotylation protocol, whereas the second one proceeds via an allenyl silane propargylation with unexpected stereochemical consequences, which are discussed in detail.

Introduction

The classical drugs used for treatment of common bacterial diseases are often characterized by serious side effects and high-toxicity profiles.[1] Additionally, in the past decade a rapid development of multidrug-resistant (MDR) strains of bacterial pathogens has been observed. Consequently, there is an urgent need to discover new structural classes of antibacterial compounds and to develop agents that are able to replace (or to be associated with) the drugs that are currently in use.[2]

Several years ago, the Laatsch group in Göttingen isolated and characterized from the streptomyces stem GW 60/1571 a new member of the nargenicin[3] family, branimycin.[4] This new natural compound showed immediately a high activity against *Streptomyces viridochromogenes* combined with a low toxicity and a considerable oral availability.

Although such antibiotics are, in principle, available from fermentation, total synthesis is indispensable for preparing analogs to gain deeper insight into the mode of action and the pharmacologically active moieties of the molecule.

As shown in Scheme 1, our synthetic approach to branimycin is based on a late 1,2-addition of the vinyl lithium derivative **2** to the highly functionalized *cis*-decalin **1**[5] with concomitant epoxide opening and formation of the C7−C12 oxygen bridge. The precursor for **2** is vinyl iodide **3**, which in turn could be easily obtained from alkyne **4**. The protecting groups in **4** were carefully chosen to fit into the overall plan of the synthesis. We describe the stereocontrolled synthesis of **3** along two alternative routes: A and B. Route A features a Roush-type crotylation of isopropylidene glyceraldehyde **5**, whereas route B is based on the addition of a chiral allenyl silane **8** to aldehyde **7**.

Results and Discussion

Route A. The reaction between **5** and **6** is known to produce the *anti*,*syn*-crotylation product **9** in excellent diastereoselec-

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(1) (a) Stein, G. E. *Clin. Infect. Dis.* **2005**, *41*, S293−S302. (b) Mandell, L. A.; Ball, P.; Tillotson, G. *Clin. Infect. Dis.* **2001**, *32*, S72−S79.

(2) *Antibiotic Resistance: Origin, Evolution, Selection and Spread*; Chadwick, D. J., Goode, J., Eds.; Wiley: Chichester, 1997. (b) Levy, S. B. *Sci. Am.* **1998**, *278*, 46−53 and references therein. (c) For reviews on antibiotic resistance, see: Walsh, C. T.; Wright, G. D. *Chem. Rev.* **2005**, *105*, 391−394.

(3) (a) For a review, see: Kallmerten, J. *Studies in Natural Products Chemistry*; Atta-ur-Rahman, Ed.; Elsevier: Amsterdam, 1995; Vol. 17, pp 283−310. (b) Celmer, W. D.; Chmurny, C. N.; Moppett, C. E.; Ware, R. S.; Watts, P. C.; Whipple, E. B. *J. Am. Chem. Soc.* **1980**, *102*, 4203−4209. (c) Whaley, H. A.; Coates, Chidester, C. G.; Mizak, S. A.; Wnuk, R. J. *Tetrahedron Lett.* **1980**, 3659−3662. (d) Celmer, W. D.; Cullen, W. P.; Moppett, C. E.; Jefferson, M. T.; Huang, L. H.; Shibakawa, R.; Tone, J. U.S. Patent 4,418,883, 1979.

(4) Speitling, M.; Grün-Wollny, I.; Hannske, F. G.; Laatsch, H. *12. and 13. IRSEER Naturstofftage der DECHEMA e.V. Irsee* 2000, 2001, poster sessions.

(5) For the synthesis of **1**, see: (a) Enev, V. S.; Drescher, M.; Kählig, H.; Mulzer, J. *Synlett* **2005**, *14*, 2227−2229. (b) Felzmann, W.; Arion, V. B.; Mieusset, J.-L.; Mulzer, J. *Org. Lett.* **2006**, *8*, 3849−3851.

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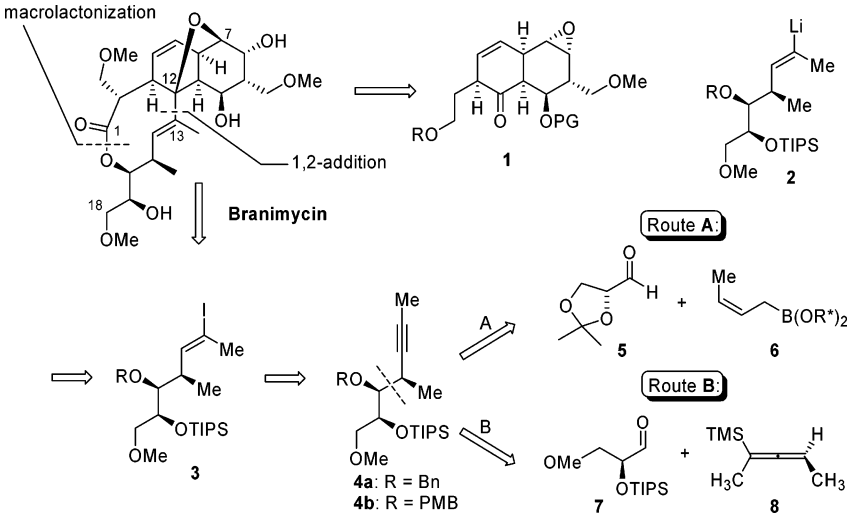
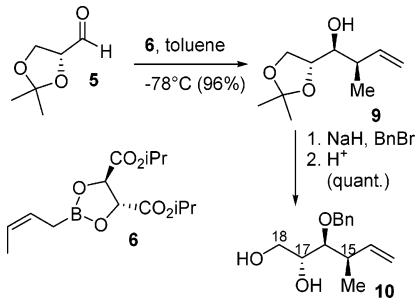
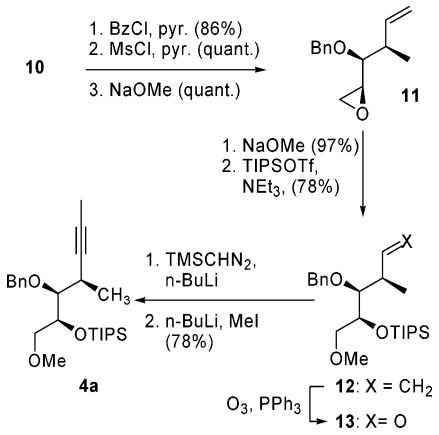
SCHEME 1. Retrosynthesis



SCHEME 2. Synthesis of *anti,syn* Stereotriad 10



SCHEME 3. First-Generation Synthesis of 4a



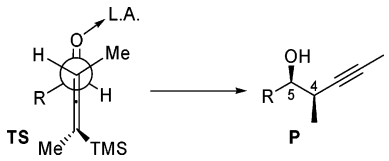
tivity[6] (Scheme 2). The secondary hydroxyl group in **9** was protected as its benzyl ether (the PMB ether turned out to be too unstable in the subsequent reaction sequence), and the acetonide was hydrolyzed to diol **10**. To obtain the desired *syn,syn* stereotriad, the secondary alcohol at C-17 had to be inverted, and the most efficient way to do this was via an epoxide ring formation/ring opening sequence: selective benzoylation of the primary alcohol at C-18, followed by mesylation of the C-17 OH function and subsequent treatment with NaOMe, produced epoxide **11** under clean inversion of configuration (Scheme 3). The epoxide was opened at the primary position with an excess of NaOMe in MeOH, and the C-17 hydroxyl group was silylated with TIPSOTf to give **12** in acceptable yield. Ozonolysis furnished the unstable aldehyde **13**, which was immediately subjected to the Corey−Fuchs alkynylation.[7] This reaction, though successful on a small scale, led to elimination of the benzyloxy group when scaled up. To overcome this problem, conversion of the aldehyde **13** to the alkyne was achieved using trimethylsilyl diazomethane.[8] Methylation of the resulting alkyne finally led to compound **4a** (Scheme 3).

Although this synthetic sequence furnished the desired side chain precursor **4a** in good overall yield (48% over 11 steps), the sequence was linear and involved a significant number of reactions. Thus we devised a more convergent alternative, Route B.

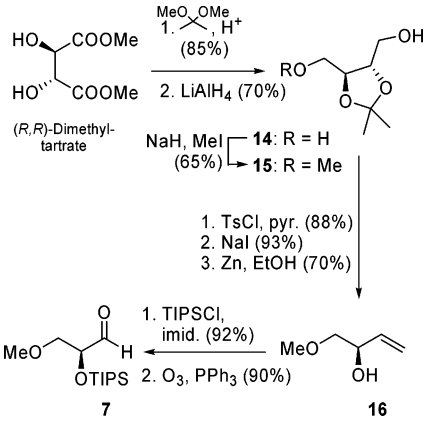
Route B. On the basis of Marshall and Fleming's work on chiral allenylstannanes[9] and allenylsilanes,[10] it was decided to introduce the C13−C15 unit in a single step using an asymmetric propargylation reaction. To avoid too many functional group interconversions at later stages, chiral aldehyde **7** was designated to carry the OMe group at C-18 already in place. Interestingly, in stark contrast to the numerous mechanistic studies on diastereoselective propargylation with chiral allenylstannanes, only limited investigations have been reported for chiral allenylsilanes. On the basis of the experimental data available for allenylstannanes,[9a,b] the propargylation of an achiral aldehyde with allenylsilane **8** should proceed via an antiperiplanar transition state **TS** and lead to adduct **P**, which would have the desired and absolute configurations at C-4 and C-5 (Scheme 4). It had not yet been determined how the two oxygen substituents on the aldehyde would influence the trajectory of the incoming allenyl unit and thus affect the stereochemical outcome of the reaction.

(6) Roush, W. R.; Hoong, L. K.; Palmer, M. A. J.; Straub, J. A.; Palkowitz, A. D. *J. Org. Chem.* **1990**, *55*, 4117−4126.
(7) Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, *36*, 3769−3772.
(8) Colvin, E. W.; Hamill, B. J. *J. Chem. Soc., Chem. Commun.* **1973**, 151−152.
(9) (a) Marshall, J. A. *Chem. Rev.* **1996**, *96*, 31. (b) Marshall, J. A.; Wang, X. *J. Org. Chem.* **1992**, *57*, 1242−1252. (c) Marshall, J. A.; Chobanian, H. *Org. Synth.* **2005**, *82*, 43−50.
(10) (a) Buckle, M. J. C.; Fleming, I. *Tetrahedron Lett.* **1993**, *34*, 2383−2386. (b) Marshall, J. A.; Maxson, K. *J. Org. Chem.* **2000**, *65*, 630−633. (c) Buckle, M. J. C., Fleming, I.; Gil, S.; Pang, K. L. C. *Org. Biomol. Chem.* **2004**, *2*, 749−769.

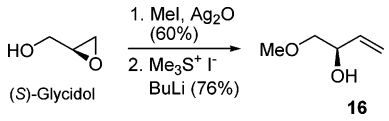
SCHEME 4. *syn*-Preference of the Silyl-allene



SCHEME 5. Synthesis of Aldehyde 7



SCHEME 6. Glycidol-Based Access to 16



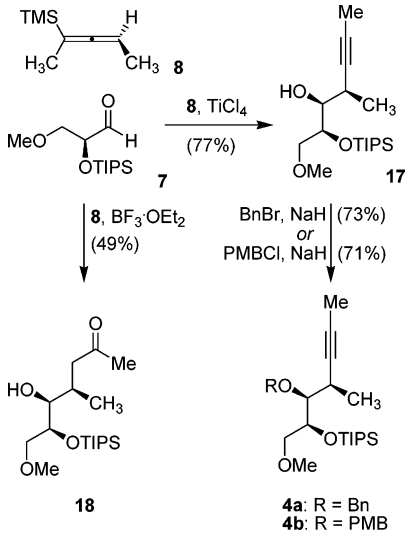
Initially, the enantiomerically pure aldehyde **7** was prepared from (*R*,*R*)-dimethyltartrate.[11] The diol was protected as the acetonide and was then reduced with $LiAlH_4$ to afford diol **14** (Scheme 5). Under standard conditions (NaH, DMF, MeI) the monomethyl ether **15** was formed predominantly and only small amounts of the dimethyl ether were detected. The primary alcohol in compound **15** was tosylated and converted to its corresponding iodide. Reductive elimination of the acetonide with activated Zn, furnished allylic alcohol **16**. TIPS-protection (now possible with TIPSCl), followed by ozonolysis afforded enantiomerically pure (*S*)-aldehyde **7**.

Alternatively, a much shorter route was employed where (*S*)-glycidol was O-methylated and then treated with trimethylsulfonium ylide[12] to give alcohol **16** directly (Scheme 6).

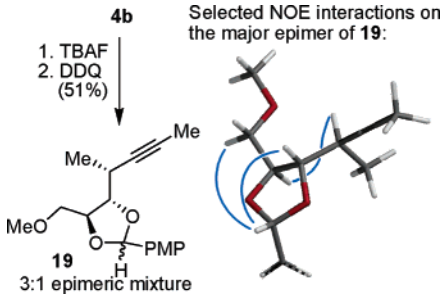
Nonracemic allenylsilane **8** was synthesized as previously described in 41% overall yield.[10c,13] The addition of **8** to aldehyde **7** was mediated with $TiCl_4$, the preferred Lewis acid in these allenyl silane addition reactions. Under these conditions, a homopropargyl adduct was formed as a 20:1 diastereomeric mixture in 77% yield (Scheme 7). To our delight, after O-benzylation, the main diastereomer was found to be identical with **4a** in all respects (^1H and ^{13}C NMR, MS, R_f, and optical rotation).

To corroborate this stereochemical assignment, PMB-ether **4b** was converted to cyclic acetal **19**, and NOESY experiments confirmed the proposed stereochemical assignment (Scheme 8). The propargylation of **7** with allenyl silane **8** was attempted

SCHEME 7. Propargylation-Based Synthesis of 4



SCHEME 8. Structural Confirmation of 4b by PMB-acetal Formation



using $BF_3{\cdot}OEt_2$ as a nonchelating Lewis acid. However, this reaction produced methyl ketone **18**[14] in 49% along with only a minute amount of **17**.

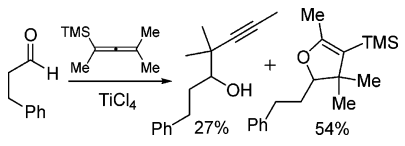
The observed stereochemical outcome of the addition is the result of an allenyl-*re*-aldehyde-*si* face combination (Scheme 9). For such allenylsilane-aldehyde additions, the two transition states **A** and **B** are discussed in the literature.[15] Normally, the antiperiplanar geometry **A** is favored over its synclinal counterpart **B**, and indeed, in our investigations **A** was preferred. It is quite obvious that the C-3 carbon of the allenyl silane will attack the aldehyde from the less hindered (i.e., Me-substituted) *re* face. Much less obvious is the *si* face preference of the aldehyde. The corresponding transition state could be described as **C** or **E**, which are both non-conventional: **C** is an anti-Felkin−Anh geometry, and **E** would imply an even less likely chelate formation to an OTIPS group.[16] It seems more likely that either a chelate transition state **F**, previously postulated for

(11) Rao, A. V. R.; Reddy, E. R.; Joshi, B. V.; Yadav, J. S. *Tetrahedron Lett.* **1987**, *28*, 6497−6500.

(12) Alcaraz, L.; Harnett, J. J.; Mioskowski, C.; Martel, J. P.; Le Gall, T.; Shin, D.-S.; Falck, J. R. *Tetrahedron Lett.* **1994**, *35*, 5449−5452.

(13) Bahadoor, A. B.; Flyer, A.; Micalizio, G. C. *J . Am. Chem. Soc.* **2005**, *127*, 3694−3695.

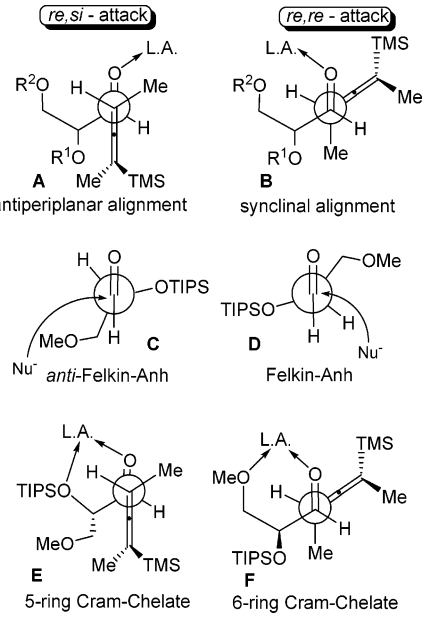
(14) A related transformation has been reported. See ref 15 and Danheiser, R. L.; Kwasigroch, C. A.; Tsai, Y.-M. *J. Am. Chem. Soc.* **1985**, *107*, 7233−7235.



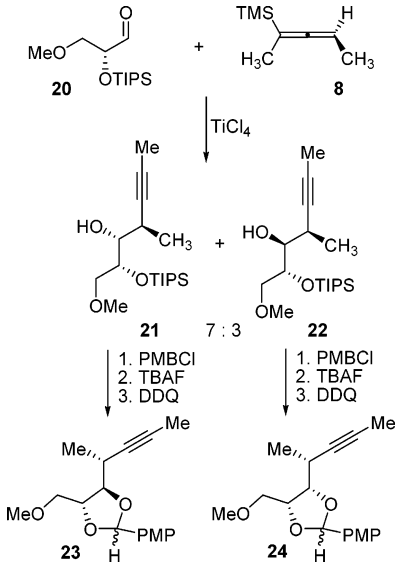
Product **18** might be the product of dihydrofuran hydrolysis followed by proto-desilyation.

(15) Danheiser, R. L.; Carini, D. J.; Kwasigroch, C. A. *J. Org. Chem.* **1986**, *51*, 3870−3878.

SCHEME 9. Rationale for Observed *syn,syn* Selectivity



SCHEME 10. Mismatched Combination



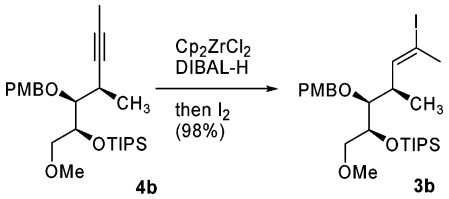
allenylstannane additions to β-benzyloxy α-methyl propanals,[10b] or a "standard" Felkin−Anh geometry **D** with the bulky OTIPS group in the perpendicular position would be expected. Both of these models would, however, lead to a *re* face attack at the aldehyde, which was not observed.

To shed more light on this interesting outcome, allene **8** was treated with the enantiomeric (*R*)-glyceraldehyde derivative **20**[17] (Scheme 10). If the reagent still prefers transition state **A**, then adduct **22** (*anti*-diol configuration) should be formed in excess. In this case, however, the aldehyde could not react via the **C**-type geometry but would have to adopt a Felkin−Anh transition state such as **D**. In reality, the reaction yielded compounds **21** and **22** in a ratio of 7:3; after separation, the relative configuration of each diastereomer was assigned via the cyclic acetals **23** and **24**, respectively.

(16) For a review on influence of the TIPS-protecting group, see: Rücker, C. *Chem. Rev.* **1995**, *95*, 1009−1064.

(17) Prepared analogously from (*R*)-glycidol.

SCHEME 11. Synthesis of (*E*)-Vinyliodide 3b



These results indicate that the aldehyde still prefers transition state geometry **C** and thus the allenyl component must switch to arrangement **B**. Consequently, we postulate that for our system a combination of **7** and **8** represents the matched pair and compounds **20** and **8** represent the mismatched one. In the mismatched combination the aldehyde is the slightly dominating partner.

To return to the overall synthesis of branimycin, alcohol **17** was protected as its PMB ether **4b**. Initial attempts to convert **4b** into the (*E*)-vinyliodide **3b** via a Pd-catalyzed hydrostannylation failed, despite literature precedence.[18] Therefore **4b** was subjected to hydrozirconation,[19] which, upon treatment with iodine, gave the (*E*)-vinyliodide **3b**, which was obtained in seven steps and in an overall yield of 25% (Scheme 11).

Conclusion

In conclusion, we have developed two different routes to the C13−C18 side chain fragment of branimycin. Furthermore, we have shown that allenyl silane additions to glyceraldehyde derivatives can be performed with high stereocontrol; however, the diastereofacial selectivity exhibited by the aldehyde does not fit into the standard transition state models.[20]

We are currently underway to utilize compound **3** to complete the total synthesis of branimycin, which will be reported in due course.

Experimental Section

(2*S*)-3-Methoxy-2-[(1,1,1-triisopropylsilyl)oxy]propanal (7). Compound **16** (255 mg, 2.5 mmol) was dissolved in 5 mL of anhydrous DMF, and imidazole (510 mg, 7.5 mmol) and triisopropylsilyl chloride (1.1 mmol) were added. The mixture was stirred for 14 h. Diethyl ether was then added to the reaction, and the mixture was washed with a 5% solution of $KHSO_4$ (1 × 2 mL), water, and brine, dried over $MgSO_4$, filtered, and concentrated. Purification by column chromatography using hexane/ethyl acetate 50:1 to 20:1 as an eluent yielded the TIPS-protected alcohol as a colorless oil (594 mg, 92%). ^{1}H NMR ($CDCl_3$): δ 5.90 (ddd, J = 17.2, 10.4, 5.8 Hz, 1H), 5.33 (d, J = 17.2 Hz, 1H), 5.17 (d, J = 10.4 Hz, 1H), 4.38 (m, 1H), 3.57−3.30 (m, 2H), 3.38 (s, 3H), 1.08 (m, 21H). ^{13}C NMR ($CDCl_3$): δ 139.7 (CH), 115.5 (CH_2), 78.1 (CH_2), 73.2 (CH), 59.5 (CH_3), 18.1 (CH_3), 12.8 (CH). IR [cm^{-1}]: 2944, 2867, 1700, 1684, 1653, 1647, 1559, 1464, 1420, 1402, 1383, 1366, 1340, 1247, 1197, 1126, 1104, 1035, 1014. $[\alpha]^{20}_D$ +14.0 (*c* 0.2, $CHCl_3$). R_f 0.42 (hexane/ethyl acetate 10:1).

The TIPS-protected alcohol (144 mg, 0.56 mmol) was dissolved in CH_2Cl_2 (15 mL) and cooled to −78 °C, and O_3-enriched air was bubbled through the reaction mixture until a faint blue color persisted. PPh_3 (160 mg, 0.61 mmol) was then added, and the mixture was stored at −18 °C overnight. After addition of 400 mg

(18) Benechie, M.; Skrydstrup, T.; Khuong-Huu, F. *Tetrahedron Lett.* **1991**, *32*, 7535−7538.

(19) Huang, Z.; Negishi, E.-i. *Org. Lett.* **2006**, *8*, 3675−3678.

(20) For examples where these rules are followed, see: (a) Williams, D. R.; Wultz, M. W. *J. Am. Chem. Soc.* **2005**, *127*, 14550−14551. (b) Reymond, S.; Cossy, J. *Eur. J. Org. Chem.* **2006**, 4800−4804.

of SiO_2, the solvent was carefully removed under reduced pressure. Loading the silica-adsorbed material on a column (preconditioned and loaded with 6 g of SiO_2) and fast chromatography using pentane/ethyl ether 20:1 to 7:1 as eluent yielded **7** as a colorless oil (131 mg, 90%). ^{1}H NMR ($CDCl_3$): δ 9.72 (s, 1H), 4.23 (t, J = 4.8 Hz, 1H), 3.65 (dd, J = 4.8, 2.5 Hz, 2H), 3.38 (s, 3H), 1.09 (m, 21H). ^{13}C NMR ($CDCl_3$): δ 203.6 (C), 77.7 (CH), 74.5 (CH_2), 59.9 (CH_3), 18.2 (CH_3), 12.7 (CH). IR [cm^{-1}]: 3056, 2925, 2866, 1740 1701, 1653, 1617, 1465, 1437, 1381, 1306, 1247, 1120, 1028. R_f 0.34 (hexane/ethyl acetate 10:1).

(2*S*,3*S*,4*R*)-1-Methoxy-4-methyl-2-[(1,1,1-triisopropylsilyl)-oxy]-5-heptyn-3-ol (17). A mixture of **7** (150 mg, 0.5 mmol) and allene **8** (105 mg, 0.75 mmol) in CH_2Cl_2 (6 mL) was cooled to −78 °C. $TiCl_4$ (0.5 mL of a 1 M solution in CH_2Cl_2) was then added. After 2 h the solution was warmed to −20 °C and quenched with a solution of NH_4Cl. After warming to room temperature the solvent was removed under vacuum. The residue was redissolved in diethyl ether and then washed with water and brine, dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by flash chromatography, using pentane/ethyl ether 4:1 as eluant, affording **17** as a mixture of diasteroisomers, *syn:anti* = 20:1 (126 mg, 77%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.44 (dd, J = 6.7, 5.7 Hz, 1H), 3.48 (dd, J = 9.3, 6.7 Hz, 1H), 3.41 (dd, J = 9.3, 5.7 Hz, 1H), 3.35 (s, 3H), 2.49 (m, 1H), 2.36 (bd, J = 9.9 Hz, 1H), 1.77 (d, J = 2.6 Hz, 3H), 1.26 (d, J = 6.8 Hz, 3H), 1.21 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 81.4 (C), 78.5 (C), 75.6 (CH), 75.1 (CH_2), 71.4 (CH), 59.3 (CH), 30.8 (CH), 18.5 (CH_3), 18.2 (CH), 13.4 (CH_3), 3.9 (CH_3). $[\alpha]^{20}_D$ +19.8 (*c* 2, $CHCl_3$).

[(1*S*,2*S*,3*R*)-2-(4-Methoxybenzyloxy)-1-(methoxymethyl)-3-methyl-4-hexynyl]oxy(triisopropyl)silane (4b). Compound **17** (186 mg, 0.24 mmol) was dissolved in 5 mL of anhydrous DMF and cooled to 0 °C, and then NaH (34 mg of 60% dispersion in mineral oil, 0.85 mmol) was added. The mixture was stirred for 30 min at 0 °C, then PMBCl (177 mg, 1.13 mmol) and tetrabutyl ammonium iodide (18 mg, 0.06 mmol) were added, and the mixture was warmed to room temperature and stirred for overnight. The reaction was then quenched with ice-cold 1 M NaOH. After stirring for 15 min, the solution was extracted 4 times with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was subjected to flash chromatography, using hexane/ethyl acetate 50:1 to 20:1 as eluant, affording pure **4b** (180 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (d, J = 8.6 Hz, 2H), 6.86 (d, J = 8.6 Hz, 2H), 4.64 (d, J = 11.2 Hz, 1H), 4.54 (d, J = 11.2 Hz, 1H), 4.34 (ddd, J = 6.5, 6.1, 2.7 Hz, 1H), 3.79 (s, 3H), 3.54 (dd, J = 9.1, 6.5 Hz, 1H), 3.43 (m, 2H), 3.31 (s, 3H), 2.89 (m, 1H), 1.75 (d, J = 2.3 Hz, 3H), 1.21 (d, J = 7.1 Hz, 3H), 1.08 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.0 (C), 131.3 (C), 129.0 (CH), 113.6 (CH), 82.7 (CH), 82.1 (C), 77.1 (C), 74.3 (CH_2), 72.8 (CH_2), 72.4 (CH), 58.7 (CH_3), 55.3 (CH_3), 27.1 (CH), 18.2 (CH_3), 18.2 (CH_3), 18.0 (CH_3), 12.9 (CH), 3.6 (CH_3). IR [cm^{-1}]: 2941, 2866, 1613, 1586, 1514, 1464, 1383, 1302, 1248, 1172, 1096, 1062, 1038. MS (EI) *m*/*z* 405 (M^+ − 43, 4), 375 (0.3), 267 (1), 187 (4), 145 (4), 121 (100). HRMS(EI) calcd for $C_{23}H_{37}O_4Si$ 405.2461, found 405.2466. $[\alpha]^{20}_D$ −4.8 (*c* 1.9, $CHCl_3$).

[(1*S*,2*S*,3*R*)-5-Iodo-2-(4-methoxybenzyloxy)-1-(methoxymethyl)-3-methyl-(4*E*)-hexenyl]oxy(triisopropyl)silane (3b). Cp_2ZrCl_2 (59 mg, 0.20 mmol) was dissolved in a Schlenk flask in 1.5 mL of anhydrous THF and cooled to 0 °C. DIBAL-H (0.2 mL, 0.20 mmol, 1 M in hexanes) was added, and the resulting slurry was stirred at room temperature for 1.5 h. The stirring was stopped, and after 5 min the supernatant liquid was removed with a syringe. To the white precipitate was then added a solution of **4b** (30 mg, 0.07 mmol) in 2 mL of freshly destilled benzene. The mixture was then heated to 40 °C; after 5 min the solution became clear, and stirring was continued at this temperature for 3 h. Then, the oil bath was removed, and the reaction mixture cooled to 0 °C. A solution of iodine (51 mg, 0.20 mmol) in 2 mL of benzene was then added slowly. Immediately after completion of the addition, the reaction was quenched by addition of 5 mL of a 1 M $Na_2S_2O_3$ solution. After both layers became colorless, the organic layer was separated, and the aqueous layer was extracted 4 times with diethyl ether. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was subjected to flash chromatography, using hexane/ethyl acetate 50:1 to 20:1 as eluant, affording pure **3b** (38 mg, 98%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26 (d, J = 8.6 Hz, 2H), 6.88 (d, J = 8.6 Hz, 2H), 6.13 (dq, J = 9.7, 1.5 Hz, 1H), 4.61 (d, J = 11.1 Hz, 1H), 4.47 (d, J = 11.1 Hz, 1H), 4.07 (ddd, J = 6.2, 4.1, 4.1 Hz, 1H), 3.80 (s, 3H), 3.56 (dd, J = 9.5, 3.6 Hz, 1H), 3.34 (m, 2H), 3.31 (s, 3H), 2.71 (m, 1H), 2.36 (d, J = 1.5 Hz, 3H), 1.08 (m, 21H), 1.00 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.1 (C), 143.7 (CH), 129.8 (C), 128.3 (CH), 128.2 (CH), 112.7 (CH), 112.6 (CH),91.6 (C), 82.2 (CH), 73.7 (CH_2), 72.3 (CH_2), 71.8 (CH), 57.8 (CH_3), 54.3 (CH_3), 35.6 (CH), 26.7 (CH_3), 17.3 (CH3), 15.5 (CH_3). 11.8 (CH). IR [cm^{-1}]: 2962, 2866, 1612, 1586, 151, 1463, 1382, 1302, 1250, 1196, 1172, 1110. MS (EI) *m*/*z* 533 (M^+ − 43, 3), 407 (1), 285 (2), 187 (6), 121 (100). HRMS(EI) calcd for $C_{23}H_{38}O_4ISi$ 533.1584, found 533.1598. $[\alpha]^{20}_D$ −2.5 (*c* 1.3, $CHCl_3$).

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Supporting Information Available: General experimental methods, detailed procedures, and analytical data for compounds **3**, **4**, **7**−**19** and selected ^{1}H and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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