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Expeditious Synthesis of a Common Intermediate of L-1-Deoxyallonojirimycin and L-1-Deoxymannojirimycin

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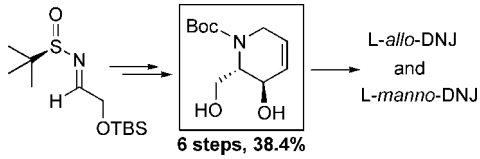
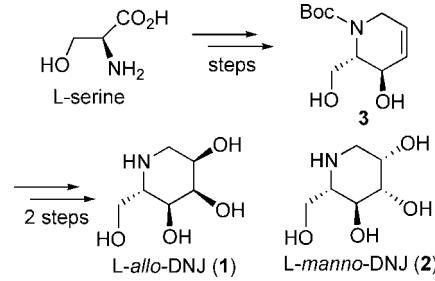


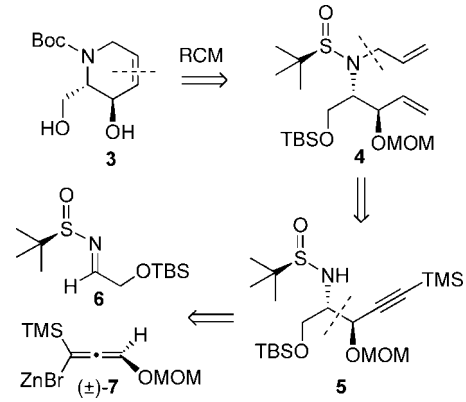
The expeditious synthesis of a common intermediate of L-1-deoxyallonojirimycin (L-*allo*-DNJ) and L-1-deoxymannojirimycin (L-*manno*-DNJ) is reported. This intermediate is obtained in highly diastereo- and enantioselectivity with 38.4% overall yield in six steps involving the unprecedented ring-closing metathesis of a *tert*-butylsulfinyl allylamine as the key step.

Azasugars are known to be widespread in plants and microorganisms and generally exhibit remarkable biological activities by mimicking a glycopyranosyl cation[1] through the protonation of the ring nitrogen at physiological pH. Due to their ability to inhibit glycosidases and glycosyl transferases, they can be regarded as potential leads for the development of new therapeutics for the treatment of diseases associated with carbohydrate-related metabolic disorders (diabetes,[2] cancer,[3] viral infections,[4] and AIDS[5]). In recent years, the structural diversity and remarkable bioactivities of azasugars have meant that methods for their stereoselective preparation, from both carbohydrate and noncarbohydrate sources, have been investigated.[6]

SCHEME 1. Takahata's Synthesis of L-*allo*-DNJ (1) and L-*manno*-DNJ (2)



SCHEME 2. Proposed Retrosynthesis for Compound 3



Recently, Asano and co-workers demonstrated that L-1-deoxyallonojirimycin (L-*allo*-DNJ) (**1**) is a much better inhibitor of human lysosomial α-mannosidases (IC_{50} = 64 μmol) than all its D- and L-1-deoxyazasugar congeners (IC_{50} > 1000 μmol).[7] Aiming to synthetize D- and L-1-deoxyazasugars, Takahata's group showed that L-*allo*-DNJ (**1**) can be obtained in two steps from (2*S*,3*R*)-3-hydroxy-2-(hydroxymethyl)-3,6-dihydro-2*H*-pyridine-1-carboxylic *tert*-butyl ester (**3**) (Scheme 1).[8,9] This group prepared **3**, which is also an intermediate of L-1-deoxymannojirimycin (L-*manno*-DNJ) (**2**), in four steps with 39.4% overall yield from L-serine-derived Garner aldehyde.

As for us, we have envisioned the preparation of **3** from allyl *tert*-butylsulfinylamine **4** via an unprecendented ring-closing metathesis and functionalization of the resulting piperidine (Scheme 2).We reasoned that **4** could be obtained from 1,2-sulfinamidoalkyl ether **5** by desilylation and semihydrogenation of the C−C triple bond followed by *N*-allylation of the sulfinamide moiety. Furthermore, **5** can be obtained using a methodology developed in our group[10] which implies the reaction of enantiopure Ellman (R_S)-*tert*-butylsulfinylimine **6** and racemic 3-(methoxymethoxy) allenylzinc bromide **7**. This methodology has been previously applied to the elaboration of acetylenic 1,2-amino alcohols[11] and to the synthesis of (−)-α-

(1) For a recent review, see: Butters, T. D.; Dwek, R. A.; Platt, F. M. *Chem. Rev.* **2000**, *100*, 4683.
(2) For a selected recent reference, see: Somsak, L.; Nagya, V.; Hadady, Z.; Docsa, T.; Gergely, P. *Curr. Pharm. Des.* **2003**, *9*, 1177.
(3) For selected recent references, see: (a) Nishimura, Y. *Curr. Top. Med. Chem.* **2003**, *3*, 575. (b) Nishimura, Y. In *Studies in Natural Products Chemistry*; Atta-ur-Rahman, Ed.; Elsevier Science, B.V.: Amsterdam, 1995; Vol. 16, pp 75−121.
(4) Asano, N.; Nash, R. J.; Molyneux, R. J.; Fleet, G. W. J. *Tetrahedron: Asymmetry* **2000**, *11*, 1645, and references cited therein.
(5) Greimel, P.; Spreitz, J.; Stütz, A. E.; Wrodnigg, T. M. *Curr. Top. Med. Chem.* **2003**, *3*, 513.
(6) For a recent review, see: Afarinkia, K.; Bahar, A. *Tetrahedron: Asymmetry* **2005**, *16*, 1239.
(7) Kato, A.; Kato, N.; Kano, E.; Adachi, I.; Ikeda, K.; Yu, L.; Okamoto, T.; Banba, Y.; Ouchi, H.; Takahata, H.; Asano, N. *J. Med. Chem.* **2005**, *48*, 2036.
(8) Takahata, H.; Banba, Y.; Sasatani, M.; Nemoto, H.; Kato, A.; Adachi, I. *Tetrahedron* **2004**, *60*, 8199.
(9) For a recent carbohydrate-based synthesis of L-1-deoxyallonojirimycin, see: Ghosh, S.; Shashidhar, J.; Dutta, S. K. *Tetrahedron Lett.* **2006**, *47*, 6041.

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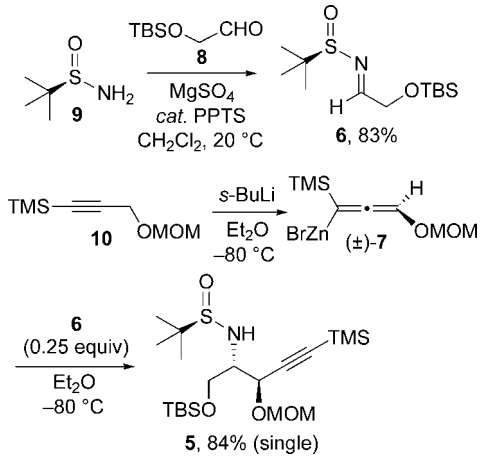
SCHEME 3. Stereoselective Synthesis of 1,2-Sulfinamidoalkyl Ether 5

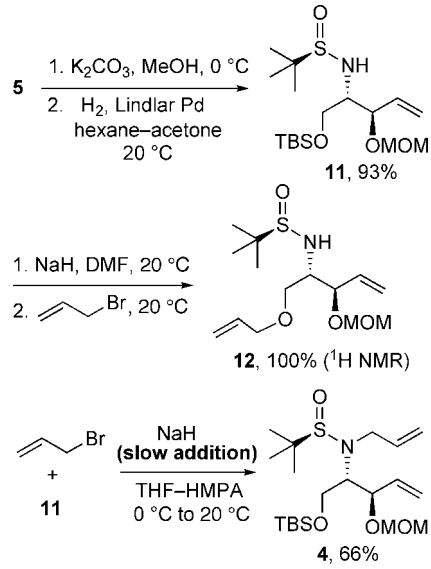


conhydrine[12] and (−)-1-hydroxyquinolizidinone,[13] a common intermediate of (−)-epiquinamide and (−)-homopumiliotoxin 223G.

With these considerations in mind, our synthesis started with the preparation of (R_S)-*tert*-buylsulfinylimine **6** in 83% yield. It was obtained through the condensation of (*tert*-butyldimethylsilyloxy)acetaldehyde (**8**)[14] with enantiopure (>99% ee) Ellman (R_S)-*N*-*tert*-butylsulfinamide (**9**), commercially available or readily prepared from cheap *tert*-butyl disulfide[15] (Scheme 3). Further reaction of enantiopure **6** at −80 °C with racemic allenylzinc **7** (4 equiv), derived from methoxymethyl 3-(trimethylsilyl)prop-2-ynyl ether (**10**),[11] gave the desired acetylenic 1,2-sulfinamidoalkyl ether **5** as a single isomer with 84% yield after flash silica gel chromatography (Scheme 3). Its relative and absolute configuration was assigned according to our previous works indicating that the organometallic species **7** approches from the *si*-face of the C−N double bond.

Treatment of 1,2-sulfinamidoalkyl ether **5** with K_2CO_3 (5 equiv) in MeOH resulted in the clean desilylation of the acetylenic position within 2 h at 0 °C. The resulting crude deprotected acetylenic intermediate was then subjected to hydrogenation in the presence of Lindlar palladium catalyst (20 wt % of Pd) and 3,5-dithia-1,2-octanediol (4 wt %). When performing the semihydrogenation in hexane as the solvent, the desired alkene **11** was obtained with 82% yield from **5** after flash silica gel chromatography (Scheme 4). However, under these conditions, **11** is accompanied by about 10% of an inseparable and unidentified byproduct. Interestingly, running the reaction in the presence of 5% of acetone as the cosolvent resulted in the formation of **11** in high purity with an improved isolated overall yield of 93%.

SCHEME 4. Access to Allyl *tert*-Butylsulfinylamine 4



To obtain the allyl *tert*-butylsulfinylamine **4**, intermediate **11** was first deprotonated with NaH (3 equiv) in DMF at 20 °C for 1 h. This led to the corresponding sodium sulfinamide which was subsequently treated with allyl bromide (6 equiv) for 40 min. Unexpectedly, after usual workup, only *O*-allyl 1,2-sulfinamidoalkyl ether **12** could be identified from the ^{1}H and ^{13}C NMR spectra of the crude (Scheme 4). This strongly suggests that sodium sulfinamide intermediate presumably underwent an aza-Brook rearrangment giving the *N*-silyl sodium alkoxide which, upon reaction with allyl bromide and then hydrolysis, furnished **12**. To prevent this unexpected reactivity, we then envisaged generation of the desired sodium sulfinamide under Barbier conditions. The best results were obtained when NaH (8 equiv) was slowly added in portions at 0 °C (over a period of 1 h) to a solution of **11** and allyl bromide (ca. 20 equiv) in a 10:1 THF−HMPA mixture. To our delight, only the desired allyl *tert*-butylsulfinylamine **4** could be observed by ^{1}H NMR after acidic workup. Further flash silica gel chromatography allowed **4** to be isolated in high purity with 66% yield (Scheme 4).

At this stage, we envisioned constructing the 3,6-dihydro-2*H*-pyridine ring system of the target molecule **3** by subjecting allyl *tert*-butylsulfinylamine **4** to ring-closing metathesis. It is worth noting that when we started our study, ring-closing metathesis as well as cross-metathesis involving sulfinylamines (both *p*-tolyl- and *tert*-butylsulfinylamines) were very rarely documented in the literature.[16−18] In addition, to the best of our knowledge, there was no example to date of ring-closing metathesis implying such sulfinylamines for the synthesis of nitrogen-containing heterocycles. Nevertheless, we were pleased to find that **4** can be converted into 3,6-dihydro-2*H*-pyridine sulfinamide **3** by means of Grubbs II catalyst (Scheme 5). Importantly, the completion of the reaction was reached within 60 h in CH_2Cl_2 at 40 °C provided that 12 mol % of Grubbs II

(10) (a) Roy, B.; Pérez-Luna, A.; Ferreira, F.; Botuha, C.; Chemla, F. *Tetrahedron Lett.* **2008**, *49*, 1534. (b) Botuha, C.; Chemla, F.; Ferreira, F.; Pérez-Luna, A.; Roy, B. *New J. Chem.* **2007**, *31*, 1552. (c) Chemla, F.; Ferreira, F. *Synlett* **2006**, 2613. (d) Palais, L.; Chemla, F.; Ferreira, F. *Synlett* **2006**, 1039. (e) Ferreira, F.; Audouin, M.; Chemla, F. *Chem.—Eur. J.* **2005**, *11*, 5269. (f) Chemla, F.; Ferreira, F. *J. Org. Chem.* **2004**, *69*, 8244. (g) Ferreira, F.; Denichoux, A.; Chemla, F.; Bejjani, J. *Synlett* **2004**, 2051. (h) Chemla, F.; Ferreira, F. *Synlett* **2004**, 983.

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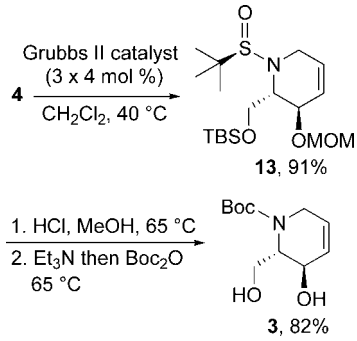
(15) For a review on *tert*-butylsulfinylimines, see: Ferreira, F.; Botuha, C.; Chemla, F.; Pérez-Luna, A. *Chem. Soc. Rev.* **2009**, DOI: 10.1039/B809772K.

(16) For an example of ring-closing metathesis with a *p*-tolylsulfinyl allylamine, see: Davis, F.; Wu, Y. *Org. Lett.* **2004**, *6*, 1269.

(17) For examples of ring-closing metathesis with *tert*-butylsulfinylamines for the construction of amino-substituted heterocycles, see: (a) Dirscherl, G.; Rooshenas, P.; Schreiner, P. R.; Lamatry, F.; König, B. *Tetrahedron* **2008**, *64*, 3005. (b) Grainger, R. S.; Welsh, E. J. *Angew. Chem., Int. Ed.* **2007**, *46*, 5377.

(18) For an example of cross-metathesis with *tert*-butylsulfinylamines, see: González-Gómez, J. C.; Foubelo, F.; Yus, M. *Synlett* **2008**, 2777.

SCHEME 5. Access to the Target Molecule 3



catalyst was used in three subsequent additions (3 × 4 mol %) separated by periods of 20 h. Under these conditions, **13** was obtained in 91% isolated yield without any detectable undesirable isomerizatrion into the corresponding enamine derivative.[19,20] It should be noted that all our attempts to decrease the amount of Grubbs II catalyst failed. More particularly, running the reaction with 5% of catalyst in toluene at 70 °C only resulted in degradation and poor-yielding formation of **13** (<10%). All these results strongly suggest that the ruthenium species is deactivated, probably through coordination to the *tert*-butylsulfinyl moiety, as previously reported similarly for Hoveyda−Blechert catalyst in the cross-metathesis of *tert*-butylsulfinyl homoallylamines with methyl vinyl ketone[18] and for Grubbs I catalyst in the ring-closing metathesis involving an unsaturated *tert*-butylsulfinylamine.[17a]

Finally, the target molecule **3** was obtained by acidic removal of the *tert*-butylsulfinyl auxiliary and concomitent deprotection of the two ether functions with dry HCl at 65 °C in MeOH, followed by the successive additions of Et_3N and Boc_2O. After intensive extraction with EtOAc and flash silica gel chromatography of the crude, (2*S*,3*R*)-3-hydroxy-2-(hydroxymethyl)-3,6-dihydro-2*H*-pyridine-1-carboxylic *tert*-butyl ester (**3**) was isolated in 82% yield as an analytically pure compound. Compound **3** so obtained exhibits physical and spectroscopical data [($[\alpha]^{20}_D = -113.5$ (*c* 2.25, $CHCl_3$)] in good agreement with those reported in the literature for its (2*R*,3*S*)-antipode [($[\alpha]^{24}_D = +86.2$ (*c* 2.25, $CHCl_3$)], although a proton is missing in the described ^1H NMR spectrum.[8]

In summary, we have disclosed an expeditious asymmetric synthesis of (2*S*,3*R*)-3-hydroxy-2-(hydroxymethyl)-3,6-dihydro-2*H*-pyridine-1-carboxylic *tert*-butyl ester (**3**), a common intermediate of L-1-deoxyallonojirimycin (**1**) and L-1-deoxymannojirimycin (**2**), in six steps with 38.4% overall yield from (*R*$_S$,*E*)-*N*-[2-(*tert*-butyldimethylsiloxy)ethylidene]-2-methylpropane-2-sulfinamide (**6**). The two key steps of our approach are (i) the highly stereoselective addition of a racemic allenylzinc bromide onto a *tert*-butylsulfinylimine and (ii) an unprecedented high-yielding ring-closing metathesis involving an allyl *tert*-butylsulfinylamine for the construction of the 3,6-dihydro-2*H*-pyridine ring system. Thus, our methodology represents a competitive alternative to that reported previously for **3** which uses the chiral pool as starting material.

(19) (a) Hong, S. H.; Sanders, D. P.; Lee, C. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **2005**, *127*, 17160. (b) Moïse, J.; Arseniyadis, S.; Cossy, J. *Org. Lett.* **2007**, *9*, 1695.

(20) For a recent example of enamine isomerization, see: Rengasamy, R.; Curtis-Long, M. J.; Seo, W. D.; Jeong, S. H.; Jeong, I.-Y.; Park, K. H. *J. Org. Chem.* **2008**, *73*, 2898.

Experimental Section

(−)-(2*S*,3*R*)-3-Hydroxy-2-(hydroxymethyl)-3,6-dihydro-2*H*-pyridine-1-carboxylic *tert*-Butyl Ester (3). Under an argon atmosphere, HCl (4 M in 1,4-dioxane, 3.25 mL, 13.10 mmol) was added dropwise at room temperature to a solution of **13** (1.025 g, 2.62 mmol) in absolute MeOH (52 mL). After 2 h of stirring at reflux, Et_3N (5.45 mL, 39.30 mmol) and Boc_2O (3.00 mL, 13.10 mmol) were successively added. The resulting mixture was refluxed for an additional 3 h, cooled to room temperature, quenched with aqueous 1 M HCl (50 mL), and then extracted with EtOAc (7 × 50 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ (10 mL) and brine (10 mL), dried over $MgSO_4$, and concentrated in vacuo. The residual brown oil was purified by flash chromatography on silica gel (70%−90% EtOAc/cyclohexane) to give the title compound **3** (491 mg, 82%) as a colorless amorphous solid: ^1H NMR (400 MHz, $CDCl_3$) δ 5.99−5.95 (m, 1H), 5.95−5.91 (m, 1H), 4.49 (t, $J = 7.2$ Hz, 1H), 4.36−4.19 (m, 1H), 4.19−4.08 (m, 1H), 3.67−3.48 (m, 3H), 2.60−2.32 (m, 2H), 1.50 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.2, 127.6 and 127.1 (br, two rotamers), 124.4, 80.2, 62.6, 60.5, 58.8 and 57.7 (two rotamers), 41.0 and 40.2 (two rotamers), 28.3; HRMS (ESI) calcd for $C_{11}H_{19}NNaO_4$ $[M + Na]^+$ 252.1206, found 252.1204; $[\alpha]^{20}_D$ −113.5 (*c* 2.25, $CHCl_3$) [Lit. ($[\alpha]^{24}_D$ +86.2 (*c* 2.25, $CHCl_3$) for the (2*R*,3*S*)-antipode].[8]

(+)-(*R*$_S$)-*N*-Allyl-*N*-[(1*S*,2*R*)-1-[(*tert*-butyldimethylsiloxy)methyl]-2-(methoxymethoxy)but-3-enyl]-2-methylpropane-2-sulfinamide (4). Under an argon atmosphere, to a stirred solution of **11** (2.04 g, 5.38 mmol) and allyl bromide (10 mL, 115.7 mmol) in anhydrous THF (50 mL) and HMPA (5 mL) was added at 0 °C, over a period of 1 h, NaH (60% in mineral oil, 1.72 g, 43.06 mmol). The resulting gray suspension was allowed to warm to room temperature and, after an additional 2 h of stirring at this temperature, was cooled to 0 °C and carefully quenched with aqueous 1 M HCl (50 mL). The solution was warmed to room temperature, the layers were separated, and the aqueous layer was extracted with Et_2O (3 × 50 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ (20 mL), water (20 mL), and brine (20 mL), dried over $MgSO_4$, and concentrated in vacuo. The residual oil was purified by flash chromatography on silica gel (30% EtOAc/cyclohexane) to give the title compound **4** (1.48 g, 66%) as a pale yellow oil: ^1H NMR (400 MHz, $CDCl_3$) δ 5.94 (ddd, $J = 17.1$, 10.3, 7.4 Hz, 1H), 5.88−5.76 (m, 1H), 5.36−5.23 (m, 3H), 5.15 (dd, $J = 10.3$, 1.2 Hz, 1H), 4.69 (d, $J = 6.6$ Hz, 1H), 4.58 (d, $J = 6.6$ Hz, 1H), 4.35 (dd, $J = 6.5$, 6.1 Hz, 1H), 4.14−4.06 (m, 1H), 3.91 (ABX system, $J = 11.0$, 4.6 Hz, 1H), 3.81 (ABX system, $J = 11.0$, 7.9 Hz, 1H), 3.44−3.41 (m, 1H), 3.40 (s, 3H), 3.38−3.31 (m, 1H), 1.21 (s, 9H), 0.90 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.6, 136.2, 119.0, 117.5, 95.4, 78.3, 65.7, 62.3, 58.7, 56.4, 47.5, 26.2, 24.0, 18.5, −5.0, −5.1; HRMS (ESI) calcd for $C_{20}H_{42}NO_4SSi$ $[M + H]^+$ 420.2598, found 420.2598; $[\alpha]^{20}_D$ +10.4 (*c* 0.85, $CHCl_3$).

(−)-(*R*$_S$)-*N*-[(1*S*,2*R*)-1-[(*tert*-Butyldimethylsiloxy)methyl]-2-(methoxymethoxy)-4-(trimethylsilyl)but-3-ynyl]-2-methylpropane-2-sulfinamide (5). Under a nitrogen atmosphere, at −80 °C, to a stirred solution of methoxymethyl 3-(trimethylsilyl)prop-2-ynyl ether (**10**) (5.30 mL, 28.00 mmol) and TMEDA (0.42 mL, 2.80 mmol) in anhydrous Et_2O (240 mL) was added dropwise *s*-BuLi (1.3 M in hexane−cyclohexane, 21.50 mL, 28.00 mmol). The resulting clear pale orange mixture was stirred at −80 °C for 1 h, and then a 1 M etheral solution of $ZnBr_2$ (28.00 mL, 28.00 mmol) was added. After the mixture was stirred at −80 °C for 15 min, a solution of *tert*-butylsulfinylimine **6** (1.94 g, 7.00 mmol) in anhydrous Et_2O (28 mL) was added dropwise. The mixture was stirred at −80 °C for 1 h and then quenched with aqueous 1 M HCl (150 mL) and warmed to room temperature. The layers were separated, and the aqueous layer was extracted with Et_2O (3 × 150 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ (25 mL), water (2 × 50 mL), and brine (50 mL),

dried over $MgSO_4$, and concentrated in vacuo. The residual oil was purified by flash chromatography on silica gel (20% EtOAc/cyclohexane) to give the title compound **5** (2.64 g, 84%) as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.94 (d, J = 6.6 Hz, 1H), 4.62 (d, J = 6.6 Hz, 1H), 4.48 (d, J = 6.6 Hz, 1H), 3.98 (ABX system, J = 10.1, 3.3 Hz, 1H), 3.89 (d, J = 9.1 Hz, 1H), 3.78 (ABX system, J = 10.1, 5.4 Hz, 1H), 3.54−3.47 (m, 1H), 3.40 (s, 3H), 1.26 (s, 9H), 0.92 (s, 9H), 0.17 (s, 9H), 0.12 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 102.0, 94.3, 92.1, 66.2, 62.6, 60.9, 56.3, 55.7, 25.8, 22.7, 18.1, −0.2, −5.4, −5.6; $[\alpha]_D^{20}$ −63.8 (*c* 0.76, $CHCl_3$). Anal. Calcd for $C_{20}H_{43}NO_4SSi_2$: C, 53.41; H, 9.64; N, 3.11. Found: C, 53.38; H, 9.43; N, 3.07.

(−)-(R_S)-*N*-[(1*S*,2*R*)-1-[(*tert*-Butyldimethylsiloxy)methyl]-2-(methoxymethoxy)but-3-enyl]-2-methylpropane-2-sulfinamide (11). At 0 °C, K_2CO_3 (4.06 g, 29.40 mmol) was added in one portion to a stirred solution of **5** (2.64 g, 5.88 mmol) in absolute MeOH (30 mL). After 2 h of stirring at 0 °C, water (15 mL) was added, and the solution was warmed to room temperature. The layers were separated, and the aqueous layer was extracted with Et_2O (3 × 45 mL). The combined organic layers were washed with water (2 × 20 mL) and brine (20 mL), dried over $MgSO_4$, and concentrated in vacuo.

The residual yellow oil (2.23 g) was taken up in a mixture of hexane (200 mL) and acetone (10 mL). To the resulting solution were added 5% Lindlar Pd (8.92 g, i.e., 20 wt % of Pd) and 3,5-dithia-1,2-octanediol (89 mg, 4 wt %). The flask was flushed with H_2 (3×). After 4 h of stirring at room temperature under 1 atm of H_2, the reaction mixture was filtered through a pad of Celite and the catalyst was rinsed with EtOAc. Removal of the solvents in vacuo gave an orange oil which was purified by flash chromatography on silica gel (30% EtOAc/cyclohexane) to yield the title compound **11** (2.07 g, 93%) as a pale yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.72 (ddd, J = 17.1, 9.5, 7.4 Hz, 1H), 5.32−5.29 (m, 1H), 5.29−5.23 (m, 1H), 4.69 (AB system, J = 6.6 Hz, 1H), 4.55 (AB system, J = 6.6 Hz, 1H), 4.11 (t, J = 7.4 Hz, 1H), 3.97 (ABX system, J = 10.0, 3.3 Hz, 1H), 3.81 (d, J = 9.6 Hz, 1H), 3.78 (ABX system, J = 10.0, 4.4 Hz, 1H), 3.37 (s, 3H), 3.36−3.31 (m, 1H), 1.20 (s, 9H), 0.91 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.8, 119.3, 94.1, 76.4, 62.5, 60.7, 56.1, 55.6, 25.8, 22.7, 18.1, −5.4, −5.5; HRMS (ESI) calcd for $C_{17}H_{38}NO_4SSi$ $[M + H]^+$ 380.2285, found 380.2287; $[\alpha]^{20}_D$ −68.2 (*c* 0.93, $CHCl_3$).

(−)-(R_S)-*N*-[(2*S*,3*R*)-2-[(*tert*-Butyldimethylsiloxy)methyl]-3-(methoxymethoxy)-3,6-dihydro-2*H*-pyridinyl]-2-methylpropane-2-sulfinamide (13). Under an argon atmosphere, to a stirred refluxed solution of **4** (1.257 g, 3.00 mmol) in anhydrous CH_2Cl_2 (1 L) was added Grubbs II catalyst (3 × 102 mg, 3 × 0.12 mmol) in three portions separated by periods of 20 h. After the solution was cooled to room temperature, removal of the solvent in vacuo gave a dark oil which was purified by flash chromatography on silica gel (20−30% EtOAc/cyclohexane) to yield the title compound **13** (1.060 g, 91%) as a brown oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.01 (td, J = 10.1, 3.3 Hz, 1H), 5.96−5.89 (m, 1H), 4.71 (AB system, J = 6.8 Hz, 1H), 4.68 (AB system, J = 6.8 Hz, 1H), 4.16 (dd, J = 5.0, 1.3 Hz, 1H), 3.82 (ABX system, J = 10.1, 5.7 Hz, 1H), 3.61 (ABX system, J = 10.1, 8.8 Hz, 1H), 3.58−3.54 (m, 2H), 3.52−3.46 (m, 1H), 3.39 (s, 3H), 1.23 (s, 9H), 0.90 (s, 9H), 0.08 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 128.7, 124.0, 95.1, 68.7, 63.2, 61.0, 59.5, 55.6, 38.7, 26.1, 23.5, 18.4, −5.1, −5.3; HRMS (ESI) calcd for $C_{18}H_{38}NO_4SSi$ $[M + H]^+$ 392.2285, found 392.2287; $[\alpha]^{20}_D$ −11.3 (*c* 0.86, $CHCl_3$).

Supporting Information Available: General information, experimental procedure for compound **6**, and ^{1}H and ^{13}C spectra for compounds **3**−**6**, **11**, and **13**. This material is available free of charge via the Internet at http://pubs.acs.org.

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