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(*R*)- and (*S*)-4-TIPS-3-butyn-2-ol. Useful Precursors of Chiral Allenylzinc and Indium Reagents

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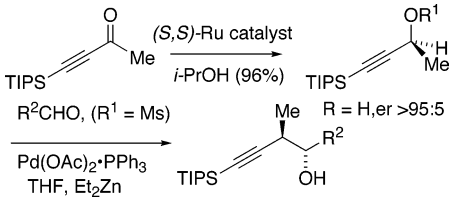


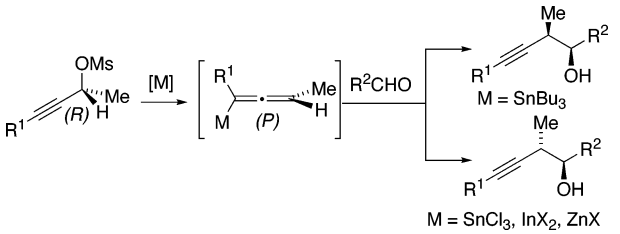
A convenient route to the enantiomers of 4-TIPS-3-butyn-2-ol of >95% enantiomeric purity by reduction of the ynone precursor **4** with the Noyori *N*-tosyl-1,2-diphenylethylenediamineruthenium cymene catalyst is described. The mesylate derivative of the (*S*) enantiomer (**1c**) is converted in situ to an allenylzinc or indium reagent in the presence of a catalyst derived from $Pd(OAc)_2$ and Ph_3P and either Et_2Zn or InI. A second in situ addition of these reagents to aldehydes leads to anti homopropargylic alcohol adducts. The additions proceed in generally high (60−90%) yield with modest to excellent diastereoselectivity and high enantioselectivity. Only slight mismatching (<5%) is observed with chiral α-methyl and α-silyloxy aldehydes. Additions to α-substituted enals are highly diastereoselective, while *β*,*β*-disubstituted enals afford ca. 2:1 mixtures of anti and syn adducts.

Introduction

In recent years, we have developed methodology for the conversion of enantioenriched propargylic mesylates to allenyl tin, zinc, and indium reagents, which undergo enantio- and diastereoselective additions to aldehydes affording syn or anti homopropargylic alcohol adducts (Scheme 1).[1] The methyl-substituted allenyl reagents have proven especially useful for the elaboration of various polyketide natural products by us[2a−j] and by others.[2k−o]

For our earliest preparation of the enantioenriched propargylic alcohol precursors of these reagents, we employed the Darvon alcohol complex of $LiAlH_4$ (Chirald) for the conversion of methyl alkynyl ketones to (*R*)-propargylic alcohols of ca. 90% enantiomeric purity (Scheme 2).[3]

SCHEME 1. Additions of Chiral Allenylmetal Reagents to Aldehydes



However, this methodology is limited to the preparation of the (*R*) enantiomers owing to the unavailability of *ent*-Darvon alcohol. Both (*R*)- and (*S*)-3-butyn-2-ol are commercially

(1) Marshall, J. A. *Chem. Rev.* **1996**, *96*, 31. (b) Marshall, J. A. *Chem. Rev.* **2000**, *100*, 3163.

(2) (a) Zincophorin: Marshall, J. A.; Palovich, M. R. *J. Org. Chem.* **1998**, *63*, 3701. (b) Discodermolide: Marshall, J. A.; Johns. B. A. *J. Org. Chem.* **1998**, *63*, 7885. (c) Callystatin A: Marshall, J. A.; Fitzgerald, R. A. *J. Org. Chem.* **1999**, *64*, 4477. (d) Aplyronine A: Marshall, J. A.; Johns, B. A. *J. Org. Chem.* **2000**, *65*, 1501. (e) Balifomycin: Marshall, J. A.; Adams, N. D. *Organic Lett.* **2000**, *2*, 2897. (f) Tautomycin: Marshall, J. A.; Yanik, M. *J. Org. Chem.* **2001**, *66*, 1373. (g) (−)-Callystatin A: Marshall, J. A.; Bourbeau, M. P. *J. Org. Chem.* **2002**, *67*, 2751. Marshall, J. A.; Bourbeau, M. P. *Org. Lett.* 2002, 4, 3931. (h) Membrenone C: Marshall, J. A.; Ellis, K. C. *Org. Lett.* **2003**, *5*, 1729. (i) Leptofuranin D: Marshall, J. A.; Schaaf, G. M. *J. Org. Chem.* **2003**, *68*, 7428. (j) Cytostatin: Marshall, J. A.; Ellis, K. *Tetrahedron Lett.* **2004**, *45*, 1351. (k) Vancosamine: Parker, K. A.; Chang, W. *Org. Lett.* **2003**, *6*, 2229. (l) Zincophorin: Defosseux, M.; Blanchard, N.; Meyer, C.; Cossy, J. *Org. Lett.* **2003**, *6*, 4037. (m) 1-Deoxy-D-galoctomomonojirimycin: Achnatowicz, M.; Hegedus, L. S. *J. Org. Chem.* **2004**, *69*, 2229. (n) Amphidinolide X: Lepage, O.; Kattnig, E.; Fürstner, A. *J. Am. Chem. Soc.* **2004**, *126*, 15970. (o) Dictyostatin: Prusov, E.; Röhm, H.; Maier, M. E. *Org. Lett.* **2006**, *9*, 1025.

(3) Marshall, J. A.; Wang, X.-J. *J. Org. Chem.* **1991**, *56*, 3211.

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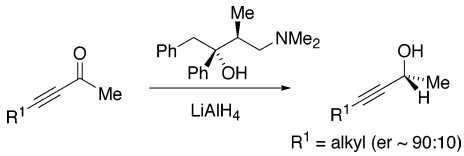
SCHEME 2. Reduction of Methyl Alkynyl Ketones with Chirald



SCHEME 3. Kinetic Resolution of Racemic Alkynyl Methyl Carbinols with Amano AK Lipase

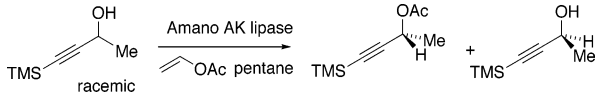
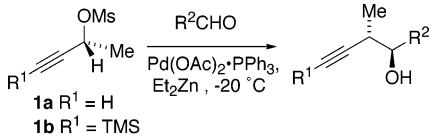


TABLE 1. Comparison of in Situ Additions of Silylated and Unsilylated Allenylzinc Reagents to Achiral Aldehydes



	$R^1 = H^a$		$R^1 = TMS^b$	
R^2	yield (%)	dr	yield (%)	dr
C_6H_{11}	84	96:4[c]	84	96:4[d]
C_6H_{13}	70	88:12	72	85:15
$TBSOCH_2CH_2$	56	88:12	76	85:15

[a] Reaction at 0 °C. [b] Reaction at −20 °C. [c] er = 96:4. [d] er = 97:3.

available, but their high cost limits widespread or large-scale applications.[4]

A solution to this problem was found in our modification of the reported resolution of 4-TMS-3-butyn-2-ol with Amano AK lipase (Scheme 3).[5,6] By performing the resolution in pentane and derivatizing the resolved butynol as the half-succinate, we were able to circumvent the reported chromatographic separation of the enantioenriched acetate and alcohol products and thereby avoid the substantial material losses resulting from their volatility. The diastereoselectivity of additions employing the TMS substituted allenylzinc reagents derived from the TMS butynyl mesylate[6] were comparable to those of the parent allenylzinc reagent (Table 1).[7]

Results and Discussion

The present report is concerned with a further improvement in the methodology through use of the 4-TIPS derivatives of (*R*)- and (*S*)-3-butyn-2-ol as precursors of chiral allenylzinc and indium reagents. Both enantiomers of these alcohols can be prepared in high enantiomeric purity and excellent yield, and the derived allenylmetal reagents show comparable selectivities to the TMS analogues in additions to a variety of aldehydes.

SCHEME 4. Synthesis of 4-TIPS-3-butyn-2-one and Subsequent Reduction with Noyori's (*S,S*)-Ru Catalyst

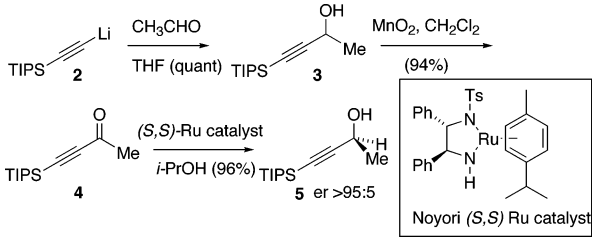
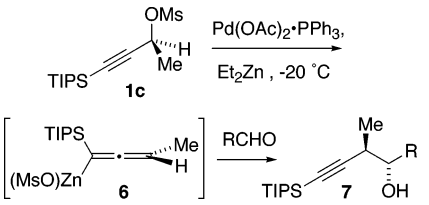


TABLE 2. In Situ Additions of (*P*)-1-TIPS-1,2-butadienylzinc Mesylate to Achiral Aldehydes



R	yield (%)	dr
C_6H_{11} (**7a**)	85	>95:5[a]
C_6H_{13} (**7b**)	96	88:12
$TBSOCH_2CH_2$ (**7c**)	87	88:12

[a] er = 98:2 based on GC analysis on a β-Dex column.

The reduction of 4-TIPS-3-butyn-2-one with ca. 1 mol % of the Noyori chiral Ru catalyst in isopropyl alcohol proceeds rapidly to afford (*S*)- or (*R*)-4-TIPS-3-butyn-2-ol (**5**) in >95% yield and >95% enantiomeric purity (Scheme 4).[8,9] The alcohols are conveniently isolated by conventional extraction without loss from volatility or water solubility. The corresponding mesylates are converted in situ to chiral allenylzinc reagents, which react with aldehydes to form homopropargylic alcohols with high diastereo- and enantioselectivity, comparable to that of the TMS analogues.[9] Additions to representative achiral aldehydes are shown in Table 2.

Removal of the TIPS group from these adducts was easily effected with TBAF in THF. Interestingly, even with as little as 25 mol % of TBAF cleavage was complete in minutes. Evidently, protonolysis of the liberated acetylide by small amounts of water in the TBAF reagent leads to $Bu_4N^+OH^-$, which can effect desilylation of the unreacted alkynylsilane. In accord with this surmise, we were able to effect TIPS cleavage through a somewhat more prolonged exposure to $Bu_4N^+OH^-$ in THF. The TIPS mesylate **1c** could also be desilylated by brief treatment with TBAF in THF to afford the terminal alkynyl mesylate **1a**.

The TIPS allenylzinc reagent exhibited excellent reagent-controlled addition to the chiral α-methyl-β-silyloxypropanals (Scheme 6). Both enantiomeric aldehydes afforded a ca. 90:10 mixture of diastereomeric adducts.

Additions to the enantiomeric OTBS lactic aldehyde derivatives also exhibited a high degree of reagent control but with a slightly greater match/mismatch discrimination. The use of the racemic allenylzinc reagent resulted in a nearly 1:1 ratio of the diastereomeric anti adducts along with a small amount the two

(4) Typical recent price listings: $155.50/g for (*S*)-3-butyn-2-ol and $114.00/g for (*R*)-3-butyn-2-ol.

(5) Burgess, K.; Jennings, L. D. *J. Am. Chem. Soc.* **1991**, *113*, 6129.

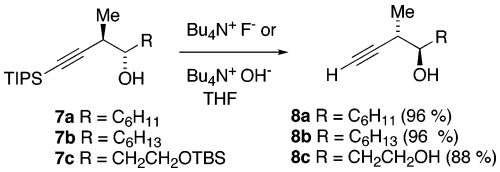
(6) Marshall, J. A.; Yanik, M. M.; Adams, N. D.; Ellis, K. C.; Chobanian, H. R. *Org Synth.* **2004**, *81*, 157. Marshall, J. A.; Chobanian, H. R.; Yanik, M. M. *Org. Lett.* **2001**, *3*, 3369. For an application of the lipase resolution methodology to (*E*)-4-(dimethylphenylsilyl)-3-buten-2-ol and 4-(dimethylphenylsilyl)-3-butyn-2-ol, see: Beresis, R. T.; Solomon, J. S.; Yang, M. G.; Jain, N. F.; Panek, J. S. *Org. Synth.* **1997**, *75*, 78.

(7) (a) Marshall, J. A.; Adams, N. D. *J. Org. Chem.* **1999**, *64*, 5201. (b) Marshall, J. A.; Adams, N. D. *J.* Org. Chem. **1998**, *63*, 3812. Bahadoor, A. B.; Flyer, A.; Micalizio, G. C. *J. Am. Chem. Soc.* **2005**, *127*, 3694.

(8) Matsumura, K.; Hashiguchi, S.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1997**, *119*, 8738.

(9) Preparation of the (*R*) enantiomer is described in the Supporting Information.

SCHEME 5. Desilylation of TIPS Alkynes



SCHEME 6. Reagent-Controlled in Situ Additions of Chiral TIPS Allenylzinc Reagents to Chiral α-Methylpropanals (DPS = Diphenyl-*tert*-butylsilyl)

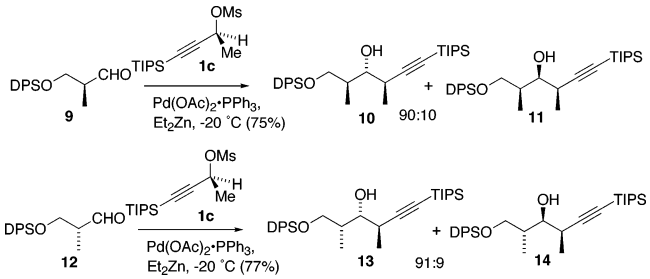
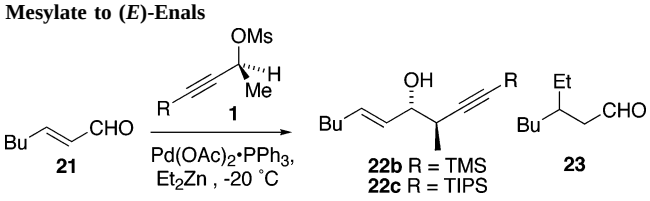


TABLE 3. In Situ Additions of (*P*)-1-TIPS-1,2-Butadienylzinc Mesylate to (*E*)-Enals



R	yield (%)	dr[a]	**22**/**23**
TMS (**1b**)	70	75:25	45:55
TIPS (**1c**)	89	80:20	14:86

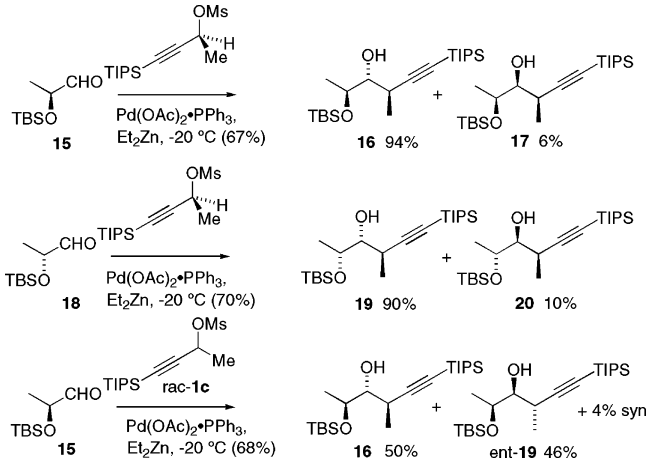
[a] Anti/syn ratio of the alcohol adducts. [b] The enantiomer was used.

syn isomers indicating that both the allenylzinc reagent and its allenylpalladium precursor are configurationally stable under the reaction conditions.[10]

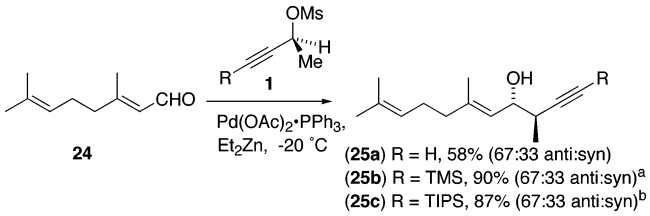
Our next series of experiments was conducted with the simple conjugated aldehyde (*E*)-2-heptenal (Table 3). We had not previously employed enals as substrates for additions of chiral allenylzinc reagents, and therefore, both the TMS and TIPS reagents were examined for comparison of efficiency. Surprisingly, in each case, the major product was the 1,4-adduct derived from diethylzinc.[11] The minor amounts of allenylzinc adduct formed were predominantly anti, but the additions were not highly disastereoselective.

Expecting β-substitution to disfavor 1,4-addition, we examined additions of the parent and the two silylated allenylzinc reagents to geranial (Scheme 8). As expected, all three reagents gave the 1,2 adducts, albeit as 2:1 mixtures of anti and syn

SCHEME 7. Reagent-Controlled in Situ Additions of Chiral TIPS Allenylzinc Reagents to Chiral α-OTBS Propanals (Hoffmann Test)

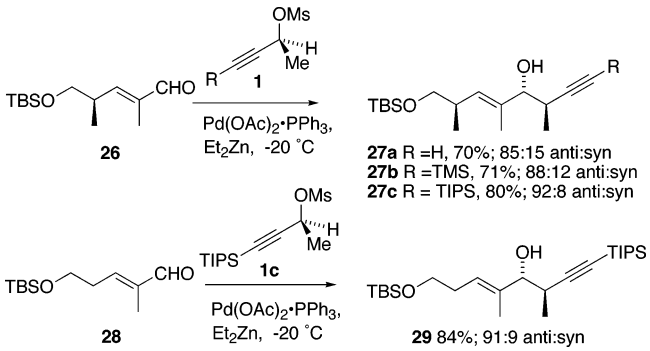


SCHEME 8. In Situ Additions of (*P*)-1-TIPS-1,2-butadienylzinc Mesylate to Geranial



[a] The enantiomeric mesylate was employed. [b] A trace amount of the 1,4-ethyl adduct was detected.

SCHEME 9. In Situ Additions of (*P*)-1-TIPS-1,2-butadienylzinc Mesylate to α-Methylated (*E*)-Enals



isomers, indicative of significant substrate control. A small amount of the 1,4-ethyl adduct was detected from the reaction with the TIPS reagent.

A pair of conjugated aldehydes with an α-methyl substituent was also examined (Scheme 9). These additions proved more diastereoselective than the previous additions to β-methylated enals, and the TIPS analogue proved superior to the TMS or parent allenylzinc reagents.

The poor diastereoselectivity observed in the additions to geranial by all three allenylzinc reagents is suggestive of a high degree of substrate control. Recent ab initio calculations of transition-state parameters for allenylzinc addition to aldehydes support an arrangement in which the substituents on the allenyl terminus of the reagent are eclipsed with the aldehyde alkyl and hydrogen substituents.[12] The presence of a conjugated

(10) Hoffmann, R. W.; Lanz, J.; Hoppe, D.; Metternich, R.; Tarrana, G. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 1145.

(11) Conjugate additions of organozinc compounds to conjugated ketones in the presence of Cu, Ni, and Co catalysts have been reported, but we are unaware of any such additions to enals or of any Pd-catalyzed additions of alkylzinc reagents in the absence of other metal catalysts. We have found that the 1,4-additions of Et_2Zn to heptenal and geranial take place in the absence of the propargylic mesylate but not in the absence of the palladium catalyst. We are currently examining this interesting addition reaction in detail to determine the scope and mechanism. For recent accounts of alkylzinc conjugate additions, see: Lipschutz, B. H.; Wood, M. R.; Tirando, R. *J. Am. Chem. Soc.* **1995**, *117*, 6126. Takahashi, Y. Yamamoto, Y.; Katagiri, K.; Danjo, H.; Yamaguchi, K.; Imamato, T. *J. Org. Chem.* **2005**, *70*, 9009 and references cited.

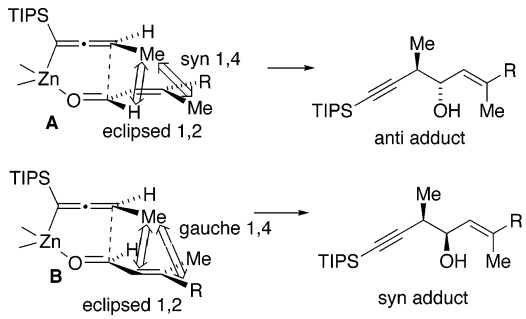
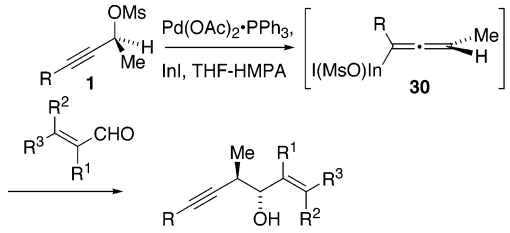


FIGURE 1. Steric interactions in allenylzinc additions to β-methyl enals.

TABLE 4. In Situ Additions of (*P*)-1-TIPS-1,2-butadienylindium Reagent to Enals



31; R = TIPS, $R^1 = R^2 = H$, $R^3 = (CH_2)_3CH_3$
32; R = TIPS, $R^1 = H$, $R^2 = Me$, $R^3 = (CH_2)_2CH{=}C(CH_3)_2$
33; R = TIPS, $R^1 = Me$, $R^2 = H$, $R^3 = CH_2CH_2OTBS$
34; R = TMS, $R^1 = Me$, $R^2 = H$, $R^3 = CH_2CH_2OTBS$

R	R^1	R^2	R^3	yield (%)	dr
TIPS (**1c**)	H	H	$CH_3(CH_2)_3$	75	80:20[a]
TIPS (**1c**)	H	Me	$(CH_3)_2C{=}CH(CH_2)_2$	76	67:33[a]
TIPS (**1c**)	Me	H	$TBSOCH_2CH_2$	87	91:9[a]
TMS (**1b**)	Me	H	$TBSOCH_2CH_2$	81	89:11[a]

[a] er of the anti isomer >95:5 based on ^{1}H NMR analysis of the Mosher ester.

double bond in the aldehyde substrate imposes a restriction for coplanarity with the carbonyl oxygen as illustrated in Figure 1. This restriction causes the enal β-substituents to interact with the methyl substituent of the allenylzinc reagent in the normally favored eclipsed arrangement of the two transition states. The interactions of these β-substituents differ in the transition states for the anti and syn isomer as illustrated. In the former, a type of syn 1,4-interaction between the allenic methyl of the zinc reagent and the β-methyl substituent of the enal is present whereas the equivalent interaction in the process leading to the syn isomer places the allenic methyl in more of a gauche arrangement with the two β-substituents of the enal. The syn 1,4-interaction raises the energy of the normally favored anti relative to the syn transition state resulting in a lower ratio of the two products.

In view of the significant 1,4-additions of diethylzinc observed in the foregoing allenylzinc additions to unsubstituted enals, we briefly explored the use of the TIPS allenylindium reagent for these additions (Table 4).[13] These reactions proceeded readily but with somewhat lower diastereoselectivity than that reported for the comparable allenylzinc additions.[6] As noted for the allenylzinc reactions, geranial proved the least selective substrate of the three enals examined. Interestingly, addition of the TMS and TIPS allenylindium reagents to the α-methyl enal proved highly diastereoselective.

In summary, Noyori reduction of 4-TIPS-3-butyn-2-one offers a convenient and efficient route to enantiomeric propargylic alcohol precursors of chiral allenylzinc and indium reagents generated in situ from the propargylic mesylates and Et_2Zn or InI in the presence of a palladium catalyst.[14] These reagents react with various aldehydes to afford homopropargylic alcohols of high enantiomeric purity. Additions of the allenylzinc reagent to achiral aliphatic aldehydes and chiral α-methyl and α-silyloxy aldehydes are highly diastereoselective favoring the anti isomer with negligible mismatching. However, additions to unsubstituted conjugated enals lead to significant quantities of 1,4-adduct arising from the diethylzinc component of the reaction. This side reaction can be avoided through use of the related allenylindium reagent. Allenylzinc additions to α-methylated enals are more diastereoselective and proceed without competing 1,4-ethyl addition. β-Methylated enals, on the other hand, afford roughly 2:1 mixtures of anti and syn adducts with both allenylzinc and indium reagents.

Experimental Section

4-Triisopropylsilyl-3-butyn-2-ol (3). A flame-dried 250 mL round-bottom flask equipped with a magnetic stir bar was charged with triisopropylsilylacetylene (95%, 6.1 mL, 26.0 mmol) and THF (54 mL). The reaction mixture was cooled to −40 °C (dry ice−acetonitrile bath), and *t*-BuLi (1.7 M in pentane, 18 mL, 32.3 mmol) was added dropwise. The resulting bright yellow mixture was stirred at −40 °C for 30 min, and then acetaldehyde (2.3 mL, 39.2 mmol) was added in one portion. The reaction mixture was stirred for 20 min at −40 °C and then was poured over a rapidly stirring solution of saturated aqueous NH_4Cl (75 mL). After 15 min, the phases were separated, and the aqueous layer was extracted with diethyl ether. The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by bulb-to-bulb distillation (5 mmHg; 104 °C) to yield the racemic alcohol **3** as a clear oil (5.9 g, 100% yield) contaminated with ∼3 mol % of triisopropylsilylacetylene: IR (film) ν 3334, 2961, 2868, 2176, 1438 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.51 (q, J = 6.6 Hz, 1H), 1.43 (d, J = 6.6 Hz, 3H), 1.03 (s, 21H); ^{13}C NMR ($CDCl_3$) δ 109.9, 84.1, 58.6, 24.5, 18.4, 11.0. Anal. Calcd for $C_{13}H_{26}OSi$: C, 68.96; H, 11.57. Found: C, 69.09; H, 11.64.

4-Triisopropylsilyl-3-butyn-2-one (4). A flame-dried 250 mL round-bottom flask equipped with a magnetic stir bar was charged with CH_2Cl_2 (54 mL) and alcohol **3** (5.90 g, 26.0 mmol). MnO_2 (85%, 34.4 g, 337 mmol) was then added in one portion. The reaction mixture was stirred for 30 min and then filtered through a short pad of Celite and concentrated under reduced pressure. The resulting yellow oil was purified by bulb-to-bulb distillation (5 mmHg; 86 °C) to yield the ketone **2** as a clear oil (5.50 g, 94% yield): IR (film) ν 2955, 2875, 2150, 1690, 1471, 1198 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.32 (s, 3H), 1.07 (s, 21H); ^{13}C NMR ($CDCl_3$) δ 184.1, 104.6, 94.9, 32.7, 18.4, 10.9. Anal. Calcd. for $C_{13}H_{24}OSi$: C, 69.58; H, 10.78. Found: C, 69.32; H, 10.89.

RuCl[(*S*,*S*)-NTsCH(C_6H_5)CH(C_6H_5)NH_2](η^6-cymene). A flame-dried 25 mL round-bottom flask equipped with a magnetic stir bar was charged with CH_2Cl_2 (6 mL), (1*S*,2*S*)-(+)-*N*-*p*-tosyl-1,2-diphenylethylenediamine (126 mg, 0.34 mmol), dichloro(*p*-cymene)ruthenium(II) dimer (107 mg, 0.17 mmol), and powdered KOH (141 mg, 2.5 mmol). The resulting orange mixture was stirred for 5 min, and then H_2O (6 mL) was added in one portion. The resulting biphasic mixture was stirred for 10 min, during which time the organic phase turned dark purple. The mixture was

(12) Gung, B. W.; Xue, X.; Knatz, N.; Marshall. J. A. *Organometallics* **2003**, *22*, 3158.

(13) Marshall, J. A.; Grant, C. M. *J. Org. Chem.* **1999**, *64*, 8214.

(14) A more detailed procedure for preparation of (*R* and *S*)-4-TIPS-butyn-2-ols has been submitted to *Org. Synth.*

transferred to a separatory funnel and diluted with H_2O, and the layers were separated. The aqueous phase was then extracted with CH_2Cl_2. The combined organic extracts were dried over CaH, filtered, and concentrated to furnish catalyst (186 mg, 90% yield) as a dark purple solid which was used immediately in the subsequent reduction.

(*S*)-4-Triisopropylsilyl-3-butyn-2-ol (5). A flame-dried 500 mL round-bottom flask equipped with a magnetic stir bar was charged with *i*-PrOH (300 mL) and ketone **4** (5.50 g, 24.6 mmol). The (*S*,*S*)-*c*atalyst (183 mg, 0.30 mmol) was taken up in a minimal amount of CH_2Cl_2 (5 mL) and added to the reaction mixture in one portion. The reaction mixture was stirred for 1.5 h and then concentrated under reduced pressure. The brown oil was purified by bulb-to-bulb distillation (5 mmHg; 104 °C) to yield the (*S*) alcohol **5** as a clear oil (5.30 g, 96% yield): $[\alpha]^{20}_D$ −19.5 (*c* 1.55, $CHCl_3$); IR (film) ν 3334, 2961, 2868, 2176, 1438 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.51 (q, J = 6.6 Hz, 1H), 2.51 (s, 1H), 1.43 (d, J = 6.6 Hz, 3H), 1.03 (s, 21H); ^{13}C NMR ($CDCl_3$) δ 109.9, 84.1, 58.6, 24.5, 18.4, 11.0. Anal. Calcd for $C_{13}H_{26}OSi$: C, 68.96; H, 11.57. Found: C, 68.58; H, 11.59.

(*S*)-4-Triisopropylsilyl-3-butyn-2-yl Mesylate (1c). A flame-dried 500 mL round-bottom flask equipped with a magnetic stir bar was charged with CH_2Cl_2 (250 mL) and alcohol **5** (5.3 g, 23.5 mmol), and the mixture was cooled to −78 °C. Triethylamine (6.6 mL, 47.3 mmol) and MsCl (2.8 mL, 36.1 mmol) were added successively. The reaction mixture was stirred at −78 °C for 45 min and then quenched by the addition of satd aq $NaHCO_3$ (25 mL). The mixture was warmed to room temperature and then transferred to a separatory funnel. The aqueous layer was extracted with ether, and the combined organic extracts were washed with H_2O and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The clear residual oil (6.85 g, 96%) was used without further purification: $[\alpha]^{20}_D$ −80.1 (*c* 1.83, $CHCl_3$); IR (film) ν 2948, 2862, 1469, 1371, 1185 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.30 (q, J = 6.6 Hz, 1H), 3.13 (s, 1H), 1.66 (d, J = 6.6 Hz, 3H), 1.03 (s, 21H); ^{13}C NMR ($CDCl_3$) δ 109.9, 84.1, 58.6, 24.5, 18.4, 11.0.

(1*S*,2*R*)-(+)-1-Cyclohexyl-2-methyl-4-triisopropylsilyl-3-butyn-1-ol (7a). Standard Procedure for Allenylzinc Additions. A flame-dried 50 mL flask was charged with THF (13 mL) and $Pd(OAc)_2$ (15.2 mg, 0.07 mmol, 5 mol %). Upon complete dissolution of the $Pd(OAc)_2$, the mixture was cooled to −78 °C, and PPh_3 (17.7 mg, 0.07 mmol, 5 mol %) was added. When the mixture became homogeneous, TIPS mesylate (*S*)-**1c** (490 mg, 1.61 mmol, 1.2 equiv) and cyclohexanecarboxaldehyde (160 μmL, 1.32 mmol, 1.0 equiv) were added, and then Et_2Zn (1 M in hexanes, 4.0 mL, 4.0 mmol, 3 equiv) was added dropwise over 5 min. The resulting yellow solution was warmed to −20 °C and stirred for 14 h. The reaction was quenched by pouring over a rapidly stirring solution of saturated aqueous NH_4Cl (25 mL), and after 15 min, the phases were separated and the aqueous phase was extracted with Et_2O. The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash chromatography (hexanes to 10% EtOAc/hexanes) to yield alcohol **7a** (363 mg, 85% yield of the anti diastereomer and 17 mg, 4% yield of the syn diastereomer) as a clear oil: $[\alpha]^{20}_D$ +5.5 (*c* 1.28, $CHCl_3$); IR (film) ν 3562, 2925, 2864, 2165, 1462 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.03−3.07 (m, 1H), 2.74−2.79 (m, 1H), 1.96 (d, J = 13.1 Hz, 1H), 1.79−1.42 (m, 5H), 1.23 (d, J = 7.0 Hz, 3H), 1.22−0.98 (m, 27H); ^{13}C NMR ($CDCl_3$) δ 109.3, 83.3, 78.6, 42.3, 31.2, 29.6, 28.3, 26.4, 26.3, 26.1, 18.6, 18.3, 11.2. Anal. Calcd for $C_{20}H_{38}OSi$; C, 74.46; H, 11.87. Found: C, 74.24; H, 12.03.

(3*R*,4*S*)-(+)-3-Methyl-1-trimethylsilyl-1-decyn-5-en-4-ol (31). Standard Procedure for Allenylindium Additions. A flame-dried flask was charged with THF (3 mL) and HMPA (1 mL). *trans*-2-Heptenal (74 mg, 0.66 mmol, 1 equiv) was then added followed by $Pd(OAc)_2$ (9.8 mg, 0.05 mmol, 0.06 equiv) and PPh_3 (12.2 mg, 0.05 mmol, 0.06 equiv). Upon complete dissolution of the PPh_3, the solution was cooled to 0 °C. TIPS mesylate (*S*)-**1c** (247 mg, 0.81 mmol, 1.2 equiv) was added to the solution followed by InI powder (258 mg, 1.1 mmol, 1.6 equiv). The mixture was then stirred at 0 °C for 15 min before being warmed to rt. After 1 h, the reaction mixture was quenched with saturated aqueous NH_4Cl solution (20 mL) and extracted with Et_2O. The Et_2O solution was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography to yield alcohol **31** (159 mg, 75% yield, 80:20 mixture of anti and syn diastereomer separable by flash chromatography with 20% Et_2O−hexanes elutant) as a clear oil: $[\alpha]^{20}_D$ +13.7 (*c* 0.85, $CHCl_3$); IR (film) ν 3408, 2942, 2865, 2162, 1464 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.69−5.78 (m, 1H), 5.44−5.52 (m, 1H), 3.86−3.91 (m, 1H), 2.55−2.64 (m, 1H), 2.09 (s, 1H), 2.05 (q, J = 2.05 Hz, 2H), 1.26−1.40 (m, 4H), 1.19 (d, J = 6.9 Hz, 3H), 1.06 (s, 21H), 0.89 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 134.2, 130.1, 109.7, 83.6, 75.9, 35.1, 32.2, 31.4, 22.4, 18.8, 17.5, 14.1, 11.4. Anal. Calcd for $C_{20}H_{38}OSi$; C, 74.46; H, 11.87. Found: C, 74.37; H, 11.72.

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Supporting Information Available: Experimental procedures and ^1H NMR spectra for key intermediates. This material is available free of charge via the Internet at http://pubs.acs.org.

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