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Flexible Synthesis of Enantiomerically Pure 2,8-Dialkyl-1,7-dioxaspiro[5.5]undecanes and 2,7-Dialkyl-1,6-dioxaspiro[4.5]decanes from Propargylic and Homopropargylic Alcohols

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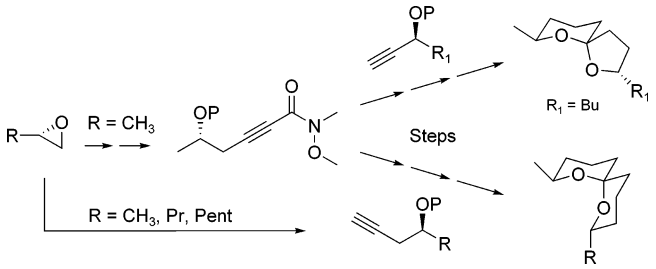

A new approach to enantiomerically pure 2,8-dialkyl-1,7-dioxaspiro[5.5]undecanes and 2,7-dialkyl-1,6-dioxaspiro[4.5]decanes is described and utilizes enantiomerically pure homopropargylic alcohols obtained from lithium acetylide opening of enantiomerically pure epoxides, which are, in turn, acquired by hydrolytic kinetic resolution of the corresponding racemic epoxides. Alkyne carboxylation and conversion to the Weinreb amide may be followed by triple-bond manipulation prior to reaction with a second alkynyllithium derived from a homo- or propargylic alcohol. In this way, the two ring components of the spiroacetal are individually constructed, with deprotection and cyclization affording the spiroacetal. The procedure is illustrated by acquisition of (2*S*,5*R*,7*S*) and (2*R*,5*R*,7*S*)-2-*n*-butyl-7-methyl-1,6-dioxaspiro[4.5]-decanes (**1**), (2*S*,6*R*,8*S*)-2-methyl-8-*n*-pentyl-1,7-dioxaspiro-[5.5]undecane (**2**), and (2*S*,6*R*,8*S*)-2-methyl-8-*n*-propyl-1,7-dioxaspiro[5.5]undecane (**3**). The widely distributed insect component, (2*S*,6*R*,8*S*)-2,8-dimethyl-1,7-dioxaspiro[5.5]undecane (**4**), was acquired by linking two identical alkyne precursors via ethyl formate. In addition, [$^2H_4$]-regioisomers, 10,-10,11,11-[$^2H_4$] and 4,4,5,5-[$^2H_4$] of **3** and 4,4,5,5-[$^2H_4$]-**4,** were acquired by triple-bond deuteration, using deuterium gas and Wilkinson's catalyst. This alkyne-based approach is, in principle, applicable to more complex spiroacetal systems not only by use of more elaborate alkynes but also by triple-bond functionalization during the general sequence.

Introduction

Spiroacetals have emerged as being crucial substructures in a wide variety of natural compounds with diverse origins[1] including plants, fungi, marine organisms,[2] and insects.[3,4] Many of these compounds exhibit important physiological activities, and, consequently, there is sustained interest in the stereocontrolled construction of these moieties. With respect to insects, spiroacetals represent a novel class of semiochemicals with considerable structural and stereochemical diversity, and a group of about 30 constitutionally different spiroacetals have been identified. The absolute stereochemistry of many has been determined by a combination of enantioselective syntheses and chromatography.[3,4] Some examples are shown in Chart 1, and although insect-derived spiroacetals[5] are constitutionally simpler than those from other sources, they often serve as targets for evaluating new synthetic methodologies. A considerable number of strategies have been described and reviewed.[1−4,6] A

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(1) Perron, F.; Albizati, K. F. *Chem. Rev*. **1989**, *89*, 1617.
(2) Jacobs, M. F.; Kitching, W. *Curr. Org. Chem.* **1998**, *2*, 395.
(3) Fletcher, M. T.; Kitching, W. *Chem. Rev.* **1995**, *95*, 789.
(4) Francke, W.; Kitching, W. *Curr. Org. Chem.* **2001**, *5*, 233.

(5) An exhaustive summary of insect-derived spiroacetal structures and their stereochemistry may be found in refs 3 and 4.

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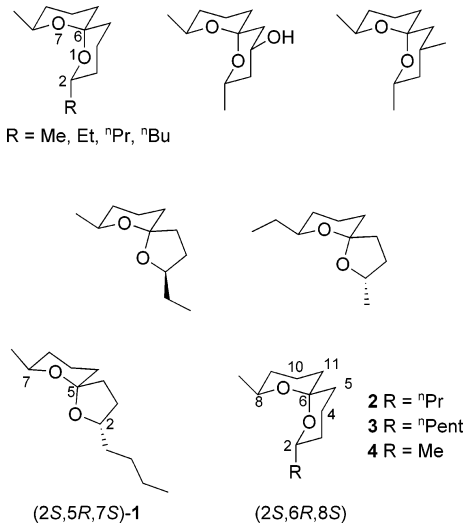
CHART 1. Representative Insect-Derived Spiroacetals

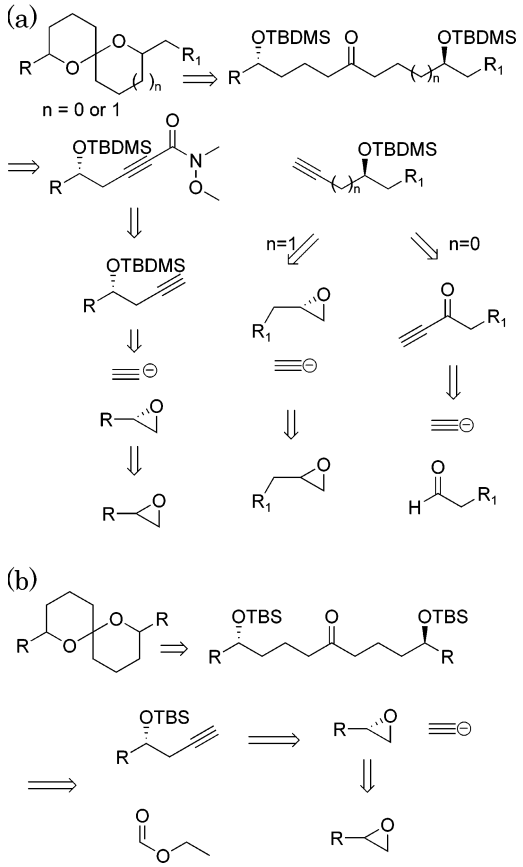


feature of many approaches is arrival at a protected ketodiol intermediate, which spontaneously cyclizes to the spiroacetal unit on release.[7,8] In this report, we utilize an approach that employs readily acquired, enantiomerically pure homopropargylic and propargylic alcohol systems, which are capable of sequential and different functionalization prior to reduction and cyclization. This approach is demonstrated by the synthesis of several enantiopure spiroacetals (**1**−**4**), which were required for comparison with suspected insect components.[9] In addition, the advantage of the presence of two different alkynyl units is demonstrated by the regiospecific synthesis of two isotopomers of **3**, namely, 4,4,5,5-[$^2H_4$]- and 10,10,11,11-[$^2H_4$]-(2*S*,6*R*,8*S*)-2-methyl-8- *n*-propyl-1,7-dioxaspiro[5.5]undecanes. Analysis of the mass spectra of these compounds allowed for the identification of multiple pathways leading to the same fragment ion, which is of significance in biosynthetic studies of the specificity of precursor incorporation into these compounds.

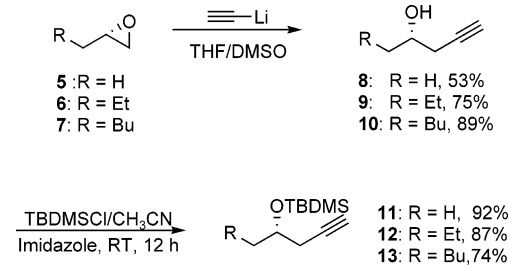
Results and Discussion

The general approach to both unsymmetrical and symmetrical spiroacetals is shown below in Scheme 1. The key stereochemical feature is enantiospecific provision of the secondary ether centers via either homopropargylic alcohols derived from the ring opening of enantiopure epoxides with an acetylene-derived anion or propargylic alcohols obtained through reduction of an acetylenic ketone. The Weinreb amide methodology is utilized to condense differing halves to produce unsymmetrical spiroacetals, whereas ethyl formate provides the central carbon for symmetrical products.

SCHEME 1. (a) General Approach to Unsymmetrical Spiroacetals and (b) General Approach to "Symmetrical" Spiroacetals



SCHEME 2



Synthesis of the Homopropargylic Alcohols. The hydrolytic kinetic resolution of terminal epoxides using Jacobsen's procedure[10] is the pivotal procedure for the introduction of chirality, and after the easy separation of the surviving epoxide enantiomer and (hydrolyzed) 1,2-diol, the latter may be reconstituted to the alternate epoxide enantiomer if desired.[11] These procedures were applied to furnish (*S*)-1,2-epoxypropane (**5**), (*S*)-1,2-epoxypentane (**6**) and (*S*)-1,2-epoxyheptane (**7**), as shown in Scheme 2. The measured optical rotations were in excellent agreement with the reported values and confirm ee's of at least 98% (see the Experimental Section for actual values). Treatment of these epoxides with lithium acetylide, either as the lithium acetylide−ethylenedi-

(6) Doubský, J.; Streinz, L.; Šaman, D.; Zednik, J.; Koutek, B. *Org. Lett.* **2004**, *6*, 4909.
(7) A summary of approaches may be found in Mead, K. T.; Brewer, B. N. *Curr. Org. Chem.* **2003**, *7*, 227 and Tu, Y. Q.; Hubener, A.; Zhang, H.; Moore, C. J.; Fletcher, M. T.; Hayes, P.; Dettner, K.; Francke, W.; McErlean, C. S. P.; Kitching, W. *Synthesis* **2000**, *13*, 1956.
(8) Also see Mori, K. *Tetrahedron* **1989**, *45*, 3233.
(9) Of particular relevance to our studies of the Giant Ichneumon wasp: *Megarhyssa nortoni nortoni* Cresson and the Queensland fruit fly *Bactrocera tryoni*.
(10) Schaus, S. E.; Brandes, B. D.; Larrow, J. F., Tokunaga, M.; Hansen, K. B.; Gould, A. E.; Furrow, M. E.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *124*, 1307.
(11) Paddon-Jones, G. C.; McErlean, C. S. P.; Hayes, P.; Moore, C. J.; König, W. A., Kitching, W. *J. Org. Chem.* **2001**, *66*, 7487.

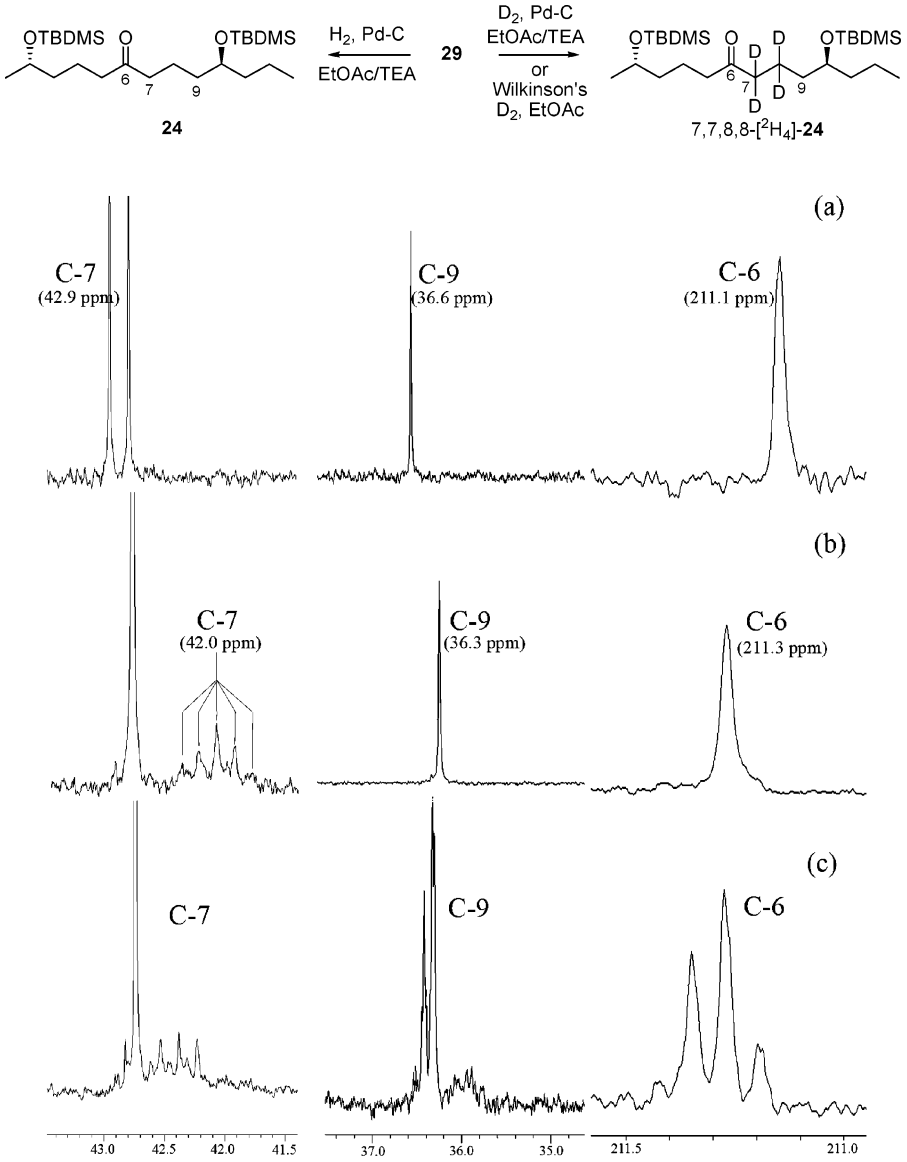


FIGURE 1. Effect of catalyst on regioselectivity of ^2H incorporation upon reduction of ynone **29**. Partial ^{13}C NMR spectrum (125 MHz). Signals of interest are assigned with chemical shifts. (a) Normal reduction with H_2 (1 atm) and 5% Pd−C in EtOAc/TEA. (b) Use of $^2H_2$ and Wilkinson's catalyst in benzene. Note the quintet for C-7 now bearing two ^2H and the singlet for C-6 (C=O). The signal for C-7 in b has experienced an upfield shift associated with both one-bond and two-bond ^2H isotope effects. Similarly, C-9 is upfield in b because of two two-bond ^2H effects. However, C-6 suffers a downfield two-bond isotope effect from $^2H_2$−C-7. (c) Use of $^2H_2$ and 5% Pd−C in EtOAc/TEA. Note the complex signal for C-7, the multiple signals for C-9 suggesting ^2H incorporation here as well as differing arrangements of ^2H on the adjacent carbon atoms, and the three significant signals for C-6 again requiring different arrangements of ^2H on adjacent carbons. Also, other carbons (signals not shown, see the Supporting Information) have ^2H attached.

amine complex or prepared from welding-grade ethyne with lithium in liquid ammonia followed by addition of DMSO provided homopropargylic alcohols **8**−**10** in moderate to good yields. The lowest yield (53%) was acquired for the opening of the volatile epoxypropane (**5**) and resulted from losses during the purification of **8** rather than from problems with the chemical transformation. These alcohols were then converted to *tert*-butyldimethylsilyl ethers **11**−**13**, as summarized in Scheme 2.

Because all of the synthesized spiroacetals incorporated a methyl substituent adjacent to a ring oxygen, protected homopropargylic alcohol **11** was first carboxylated and converted to its Weinreb amide (**15**). Alkynyl addition to Weinreb amides or *N*-methoxy-*N*-methylurea has been described recently for spiroacetal synthesis.[12,13] This amide (**15**) could be reduced with H_2 over Pd−C or for the production of isotopically labeled analogues, with $^2H_2$ and Wilkinson's catalyst. This latter procedure induced no ^2H scrambling on the basis of ^2H effects on the ^{13}C NMR spectra of **16**.

The reduction of propargylic or homopropargylic ketones or alcohols requires some care. In our hands, the reduction of propargylic alcohols with H_2 and 5% Pd−C may lead to, in addition to triple-bond reduction, hydrogenolysis of the secondary alcohol to a methylene or to a

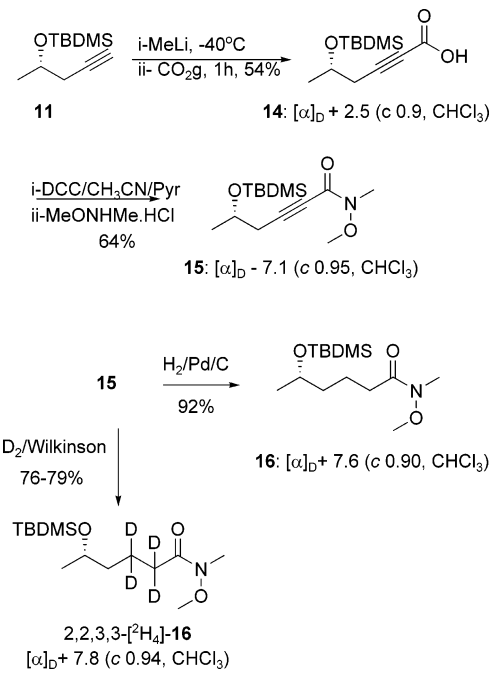
(12) Marshall, J. A.; Yanik, M. M. *J. Org. Chem.* **2001**, *66*, 1373.
(13) Shimizu, T.; Masuda, T.; Hiramoto, K.; Nakata, T. *Org. Lett.* **2000**, *2*, 2153.

ketone by dehydrogenation.[12] These unwanted processes are less noticeable with homopropargylic systems, but the addition of triethylamine (TEA) largely suppresses transformations other than triple-bond reduction, perhaps by prevention of alcohol protonation.[14] The problem of "scrambling" during reduction becomes clear when deuterium gas is employed. The use of Pd−C, TEA, and $^2H_2$ leads to nonregiospecific ^2H incorporation through H/^{2}H exchange reactions and double-bond migration. This is an unsatisfactory outcome when regioselectively ^2H-labeled precursors are required for biosynthetic or spectroscopic investigations (Figure 1). The favored procedure utilizes Wilkinson's catalyst, and with $^2H_2$ it is clear that highly regioselective reduction of propargylic ketones is achieved. These outcomes are made clear in Figure 1, which shows selected parts of the ^{13}C NMR spectrum of the ^2H reduction of **29** with the catalyst systems of Pd−C−TEA and Wilkinson's catalyst. Other recent reports also address the problems of scrambling or racemization during the hydrogenation (or deuteration) of propargylic alcohols.[15−18]

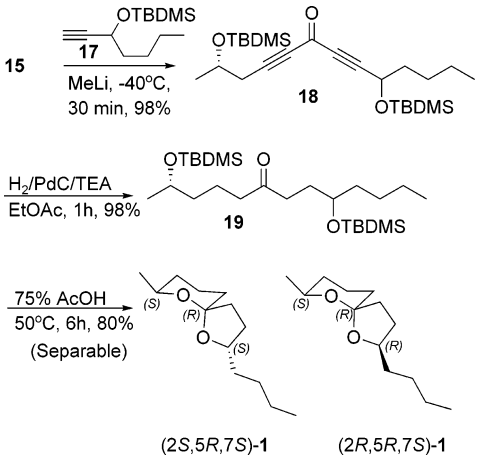
Synthesis of 2-*n*-Butyl-7-methyl-1,6-dioxaspiro-[4.5]decane (1). Our examination of secretions from a Giant Ichneumon wasp suggested that an isomer of the 1,6-dioxaspiro[4.5]decane (**1**) might be present. This compound has been identified previously by mass spectrometry in the mandibular gland secretions of the *Andrena wilkella* bee[19] but has not been prepared, and consequently, its synthesis was undertaken. The Weinreb amide (**15**) on reaction with the alkynyllithium generated from racemic **17** furnished ynone **18**, which on reduction and deprotection afforded the separable (2*S*,5*R*,7*S*)- and (2*R*,5*R*,7*S*)-**1** isomers that are shown below. The anomeric effect, operating more effectively with the axial C_5-O_1 bond, determines the stereochemistry at the C_5 spirocenter. The mass spectra of these isomers are in agreement with those reported for the compound isolated from *Andrena wilkella*.[19]

It was anticipated that NOESY experiments would permit the determination of the relative configuration of these diastereomers,[20] but that was not the case. Consequently, it was necessary to undertake an enantioselective synthesis of one of these, and the procedure outlined below delivered predominantly the (2*S*,5*R*,7*S*) isomer (Scheme 5). The (3*S*) isomer of the protected propargylic alcohol (**17**) was synthesized by MeCBS reduction[21] of the corresponding ketone, with approximately 60% ee by optical rotation comparison. Deprotonation with MeLi afforded the alkynyl anion for addition to the (*S*)-Weinreb amide (**15**), with subsequent elaboration to (2*S*,5*R*,7*S*)-**1** following the route outlined above. There are significant differences in some of the ^{13}C NMR

SCHEME 3



SCHEME 4

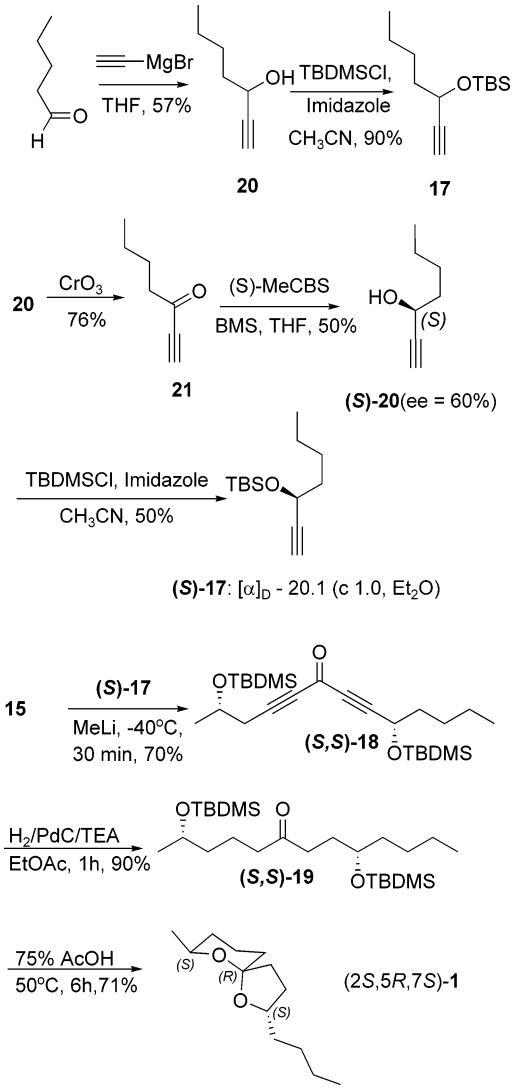


shifts of (2*S*,5*R*,7*S*)-**1** and (2*R*,5*R*,7*S*)-**1** (at C-2, for example), and comparisons with the data for the authentic (2*S*,5*R*,7*S*) isomer provided the stereochemical assignments. Additionally, the ratio of the two diastereomeric forms of **1** that were produced, which arise from the different configurations at C-2 and derive from C-3 of **20**, supports the ee calculated for **20** via optical rotation comparison.

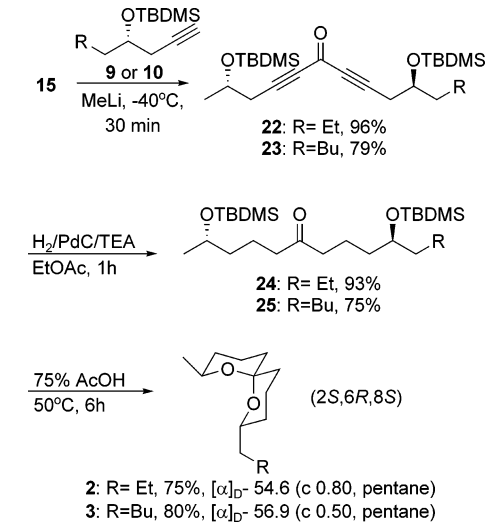
Synthesis of 2-Methyl-8-*n*-propyl and 2-Methyl-8-*n*-pentyl-1,7-dioxaspiro[5.5]undecanes (2 and 3). These dioxaspiro[5.5]undecanes were constructed by the utilization of two homopropargylic systems, with one being the Weinreb amide (**15**) providing the methyl-substituted ring and the other being an appropriate alkynyllithium to furnish the 8-*n*-propyl or 8-*n*-pentyl tetrahydropyran moiety. The procedures are summarized below (Scheme 6). The enantiomeric excesses of (2*S*,6*R*,8*S*)-**2** and **3** are very high as judged by the lack of any detectable *EZ* (2*R*,6*S*,8*S*-**2** and **3**)[22] isomers in the crude reaction mixtures. These diastereomers arise when either C2 or C8 have the *R* configuration, and thus

(14) Tedeschi, R. J. *J. Org. Chem.* **1962**, *27*, 2398.
(15) Abad, J.-L.; Villorbina, G.; Fabriàs, G.; Camps, F. *J. Org. Chem.* **2004**, *69*, 7108.
(16) Mori, K.; Ohtaki, T.; Ohrui, H.; Berkebile, D. R.; Carlson. D. A. *Eur. J. Org. Chem.* **2004**, 1089.
(17) Nelson, D. J.; Li, R.; Brammer, C. *J. Org. Chem.* **2005**, *70*, 761−767.
(18) For a general discussion, see Kieboom, A. R. C.; Rantwitk, E. *Hydrogenation and Hydrogenolysis in Synthetic Organic Chemistry*; Delft University Press: Delft, The Netherlands, 1977.
(19) Bergström, G.; Tengö, J.; Reith, W.; Francke, W. *Z. Naturforsch., C: Biosci.* **1982**, *37*, 1124.
(20) Hayes, P.; Fletcher, M. T.; Moore, C. J.; Kitching, W. *J. Org. Chem.* **2001**, *66*, 2530.
(21) Parker, K. A.; Ladeboer, M. W. *J. Org. Chem.* **1996**, *61*, 3214.

SCHEME 5

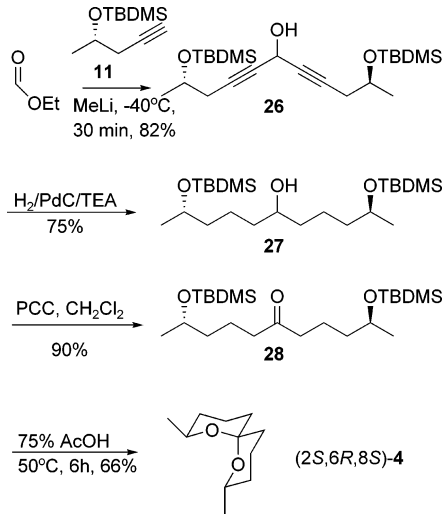


SCHEME 6



the amount of (2*R*,6*S*,8*R*)-**2** and **3** where both centers are *R* configured must be vanishingly small. The optical rotations of −54.6 (*c* 0.8, pentane) for **2** and −56.9 (*c* 0.5, pentane) for **3** support this conclusion, with the most comparable value reported previously for **2** being −40.5 (*c* 1.05, pentane). [23]

SCHEME 7



Synthesis of (2*S*,6*R*,8*S*)-2,8-Dimethyl-1,7-dioxaspiro[5.5]undecane (4). The identical substitution pattern of both pyran rings in (2*S*,6*R*,8*S*)-**4** suggests the linkage of 2 equiv of the (*S*)-homopropargylic alcohol (**11**) with a one-carbon unit that becomes the spirocarbon. Ethylformate functions well for this purpose, and the straightforward synthesis is outlined in Scheme 7. The optical rotation of −56.9 (c 0.5, pentane) agrees well with the literature values (−56.0 (*c* 1.4, pentane)[24] and −57.6 (*c* 1.04, pentane)[25]), and once again the lack of any observable *EZ* diastereomer[22] in the crude reaction mixture suggests an extremely high ee.[24,25] These observations agree with the analysis of product **4** by enantioselective GC (*β*-cyclodextrin) in which the (2*R*,6*S*,8*R*) enantiomer was not observed (detection limit ≪1%).

Selective Deuteration. The presence of α,*β*-ynones in intermediates leading to spiroacetals provides the opportunity for functionalization of these moieties at a convenient stage and thereby the acquisition of more complex spiroacetals. This general idea is illustrated by the regiospecific 1,1,2,2-[$^2H_4$]-tetradeuteration in each of the rings of (2*S*,6*R*,8*S*)-2-methyl-8-*n*-propyl-1,7-dioxaspiro-[5.5]undecane (**2**) and one of the rings of (2*S*,6*R*,8*S*)-2,8-dimethyl-1,7-dioxaspiro[5.5]undecane (**4**), as summarized below.

The mass-spectral fragmentation patterns of such spiroacetals have been reported widely[4] and used extensively to determine the specificity of labeled-precursor incorporation in biosynthetic studies.[26] For example, in **2**, the fragment ion at *m/z* 125 was believed to come mainly from the methyl-substituted ring (Figure 2A). In

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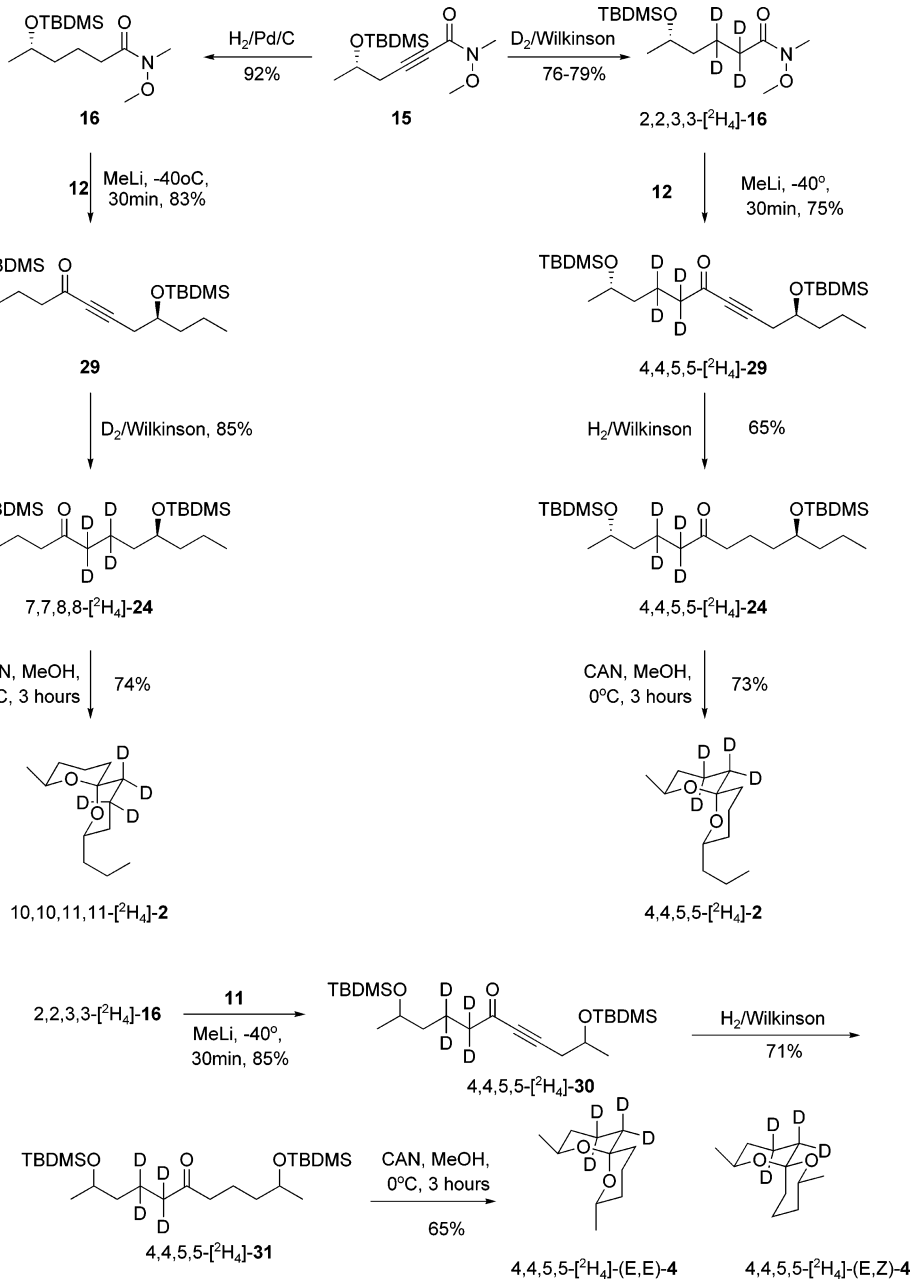
(24) Mori, K.; Watanabe, H. *Tetrahedron* **1986**, *1*, 295−304.

(25) Brown, H. C.; Kulkarni, S. V.; Racherla, U. S.; Dhokte, U. P. *J. Org. Chem.* **1998**, *63*, 7030.

(26) (a)Hungerford, N. L.; Mazomenos, B. E.; Konstantopoulou, M. A.; Krolcos, F. D.; Haniotakis, G. E.; Hübener, A.; Fletcher, M. T.; Moore, C. J.; Kitching, W. *Chem. Commun.* **1998**, 863. (b) Fletcher, M. T.; Wood, B. J.; Brereton, I. M.; Stok, J. E.; De Voss, J. J.; Kitching, W. *J. Am. Chem. Soc.* **2002**, *124*, 7666. (c) Fletcher, M. T.; Mazomenos,

SCHEME 8



the course of work examining the biosynthesis of such spiroacetals, it became important to verify the origin of this fragment. It is clear from the mass spectra of the differentially deuterated **2** (Figure 2B) that the ion at *m/z* 125 arises from two pathways, one of which is derived from the methyl-substituted ring and one that corresponds to the propyl-bearing ring. Although the second pathway has also been postulated previously, its importance relative to the first in this system was unknown and would have been impossible to determine without the specifically labeled compounds that are described here.

Conclusions

A new procedure for the enantio-controlled synthesis of 2,8-dialkyl-1,7-dioxaspiro[5.5]undecanes and 2,7-dialkyl-1,6-dioxaspiro[4.5]decanes is described. The approach utilizes homopropargylic alcohols obtained by lithium acetylide opening of enantiomerically pure epoxides acquired by hydrolytic kinetic resolution of the corresponding racemic epoxides. Carboxylation of the alkynes and Weinreb amide formation set the stage for the addition of the second alkynyl species, with reduction and deprotection affording a spiroacetal of known configuration. Functionalization of the alkynyl intermediates is possible and is demonstrated by regiospecific deuteration using Wilkinson's catalyst and deuterium gas. The general approach has application for relatively simple spiroacetals often generated by insects as well as being

B. E.; Georgakopoulos, J. H.; Konstantopoulou, M. A.; Wood, B. J.; De Voss, J. J.; Kitching, W. *Chem. Commun*. **2002**, 1302. (d) McErlean, C. S. P.; Fletcher M. T.; Wood, B. J.; De Voss, J. J.; Kitching, W. *Org. Lett*. **2002**, *4*, 2775.

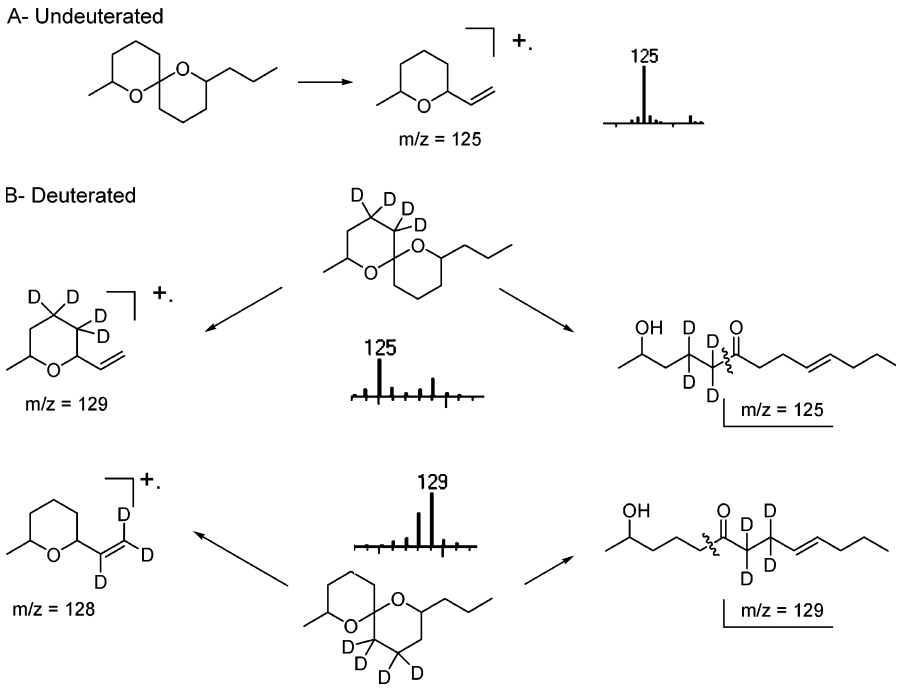


FIGURE 2. Proposed mass spectral fragmentation pathways for (A) undeuterated and (B) deuterated siroacetal **2**. The mass spectral results from the isotopomers clearly indicate that the peak at *m/z* 125 in the unlabeled compound arises from two different fragments.

promising for more complex structures. Other examples exploiting the presence of the α,β-ynone moiety are being developed.

Experimental Section

General Procedure for the Preparation of (*S*)-5, (*S*)-6, and (*S*)-7 by Hydrolytic Kinetic Resolution Using Jacobsen's Catalyst. The procedure described for the hydrolytic kinetic resolution of (±)-propylene oxide **5** is representative.

Acetic acid (0.23 mL) was added to a solution of [(*S*,*S*)-*N*,*N*′-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediaminato(2-)]cobalt(II) (1.21 g, 2.0 mmol, 0.2 mol %) in toluene (10 mL), and the mixture was left stirring open to the air. After 1 h, the toluene and excess acetic acid were removed in vacuo, propylene oxide (70.7 mL, 58.7 g, 1 mole) was added, and the flask was cooled to −10 °C. Water (9.9 mL, 0.055 mol) was added at such a rate that the reaction temperature did not exceed 15 °C (1 h), and the reaction was left to stir for 36 h. The flask was then fitted with a distillation head, a condenser (with 0−5 °C circulating water), and a receiving flask (cooled to −78 °C (CO_2/acetone)) and was gently heated with warm water to isolate (*S*)-propylene oxide (*S*)-**5** (21.2 g, 36%) as a colorless liquid. $[\alpha]^{23}_D$ −11.3 (neat), {lit. $[\alpha]^{23}_D$ −11.6 (neat), 99.7% ee)[10]}. The NMR data of (*S*)-**5** matched those reported in the literature.[27]

(*S*)-1,2-Epoxypentane (**6**). Yield: 39%. $[\alpha]^{23}_D$ −17.4 (*c* 3.90, pentane), {lit. $[\alpha]^{24}_D$ −16.8 (*c* 1.0, pentane), 99.0% ee[28]}. The NMR data of (*S*)-**5** matched those reported in the literature.[29]

(*S*)-1,2-Epoxyheptane (**7**). Yield: 42%. $[\alpha]^{23}_D$ −9.6 (*c* 4.0, $CHCl_3$) {lit. $[\alpha]^{20}_D$ −9.5 (*c* 4.0, $CHCl_3$), ee >99.0%,[30] $[\alpha]^{21}_D$ −10.6 (*c* 0.99, $CHCl_3$)[31]}. The NMR data of (*S*)-**5** matched those reported in the literature.[31]

(*S*)-Pent-4-yn-2-ol (8). Ammonia (600 mL, anhydrous) was drawn into an uncondensed two-necked flask (2 L) fitted with a polyethylene tubing outlet. Acetylene (welding grade) was bubbled steadily via a CO_2/acetone trap into the boiling ammonia by pipet at a rate so as to not cause frothing, while lithium (2.8 g, 0.408 mol) was added cautiously in small portions over 30 min so as to not render the ammonia blue. Once addition was complete, freshly distilled anhydrous DMSO (50 mL) was added cautiously followed by (*S*)-**5** (20 g, 24 mL, 0.34 mol) by pipet. The open polyethylene tubing was then attached to a silicon oil bubbler and monitored for 3 h as the reaction was concentrated from loss of ammonia. After 12 h, the reaction mixture was poured slowly into ice-cold brine (50 mL) in a 2-L conical flask and left stirring slowly until gas evolution had ceased. The H_2O/DMSO mixture was extracted repeatedly with ether (15 × 30 mL), dried ($MgSO_4$), and concentrated by rotary evaporation with the water bath at 10 °C. The crude liquid was distilled carefully to give **8** (15.1 g, 53%) as a colorless oil. bp 126−127 °C {lit.[32] 126 °C}, $[\alpha]^{23}_D$ +14.4 (*c* 1.80 $CHCl_3$) {lit. $[\alpha]^{26}_D$ +17.5 (*c* 0.16, $CHCl_3$)[32]}. ^{1}H NMR (400 MHz, $CDCl_3$, δ): 1.22 (d, *J* = 6.2, 3H), 2.02 (t, *J* = 2.6, 1H), 2.18 (br s, 1H), 2.28 (ddd, *J* = 16.7, 6.4, 2.7, 1H), 2.35 (ddd, *J* = 16.6, 5.3, 2.6, 1H), 3.93 (tq, *J* = 6.2, 5.3, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 22.1, 28.8, 66.1, 70.7, 80.8. GC/MS EI *m/z* (%): 84 (M^+, 0.1), 69 (1), 63 (4), 56 (8), 46 (11), 45 (100), 43 (68) 41 (63), 40 (64).

(*S*)-Hept-1-yn-4-ol (9). Lithium acetylide−EDA complex (0.91 g, 53.4 mmol) was added to a solution of (*S*)-1,2-epoxypentane (**6**, 2 g, 23.2 mmol) in dry DMSO (22 mL), and the mixture was stirred overnight at room temperature. After quenching with ice, 0.5 M H_2SO_4 was used to neutralize the basic solution to pH 7. The solution was extracted with diethyl ether (3 × 50 mL), dried ($MgSO_4$), and concentrated in vacuo to give **9** (2.31 g, 89%) as a colorless oil. $[\alpha]_D$ −0.47 (*c* 2.5, $CHCl_3$), $[\alpha]_D$ −27.2 (*c* 1.1, MeOH). ^{1}H NMR (500 MHz, $CDCl_3$, δ): 0.91 (t, *J* = 7.2, 3H), 1.28−1.62 (m, 4H), 1.88 (brs, 1H, OH), 2.02 (t, *J* = 2.7, 1H), 2.29 (ddd, *J* = 16.7, 6.8 and 2.7, 1H), 2.40 (ddd, *J* = 16.7, 4.7 and 2.7, 1H), 3.72−3.77 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 13.9, 18.8, 27.3, 38.3, 69.6,

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70.7, 80.9. GC/MS EI *m/z* (%): 112 ($M^{+\bullet}$, 0.03), 79 (1), 73 (41), 69 (6), 55 (100), 43 (69).

(*S*)-Non-1-yn-4-ol (10). Lithium acetylide−EDA complex (3.7 g, 40.25 mmol) was added to a solution of (*S*)-1,2-epoxyheptane **7** (2 g, 17.5 mmol) in dry DMSO (18 mL), and the mixture was stirred overnight at room temperature. After quenching with ice, 0.5 M H_2SO_4 was used to neutralize the basic solution to pH 7. The solution was extracted with diethyl ether (3 × 50 mL), dried over $MgSO_4$, and concentrated in vacuo to give **10** (1.84 g, 75%) as a colorless oil. $[\alpha]^{23}_D$ −0.35 (*c* 1.4, $CHCl_3$) {lit. $[\alpha]_D$ +0.39 (*c* 1.2, $CHCl_3$) for the (R) isomer[33]}, $[\alpha]_D$ −25.6 (*c* 1.0, MeOH) {lit. $[\alpha]_D$ +22.2 (*c* 1.0, MeOH) for the (R) isomer[34]}. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 0.86 (t, J = 7.0, 3H), 1.23−1.54 (m, 8H), 1.82 (brs, 1H, OH), 2.03 (t, J = 2.7, 1H), 2.29 (ddd, J = 16.7, 6.8 and 2.7, 1H), 2.40 (ddd, J = 16.7, 4.5 and 2.7, 1H), 3.73 (dddd, J = 6.0, 6.0, 4.7 and 4.5, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 14.0, 22.5, 25.2, 27.3, 31.7, 36.2, 69.9, 70.7, 80.9. GC/MS EI *m/z* (%): 140 (M^+, 0.02), 101 (9), 83 (34), 77 (1), 69 (5), 65 (1), 55 (100), 43 (35), 41 (86).

General Procedure for the Preparation of OTBDMS Ethers (11−13, 17, and (*S*)-17). The procedure described for the preparation of (2*S*)-*tert*-butyl-dimethyl-(1-methyl-but-3-ynyloxy)-silane (**11**) is representative.

(*S*)-Pent-4-yn-2-ol (**8**) (5 g, 59.5 mmol) was dissolved in a solution of DCM (20 mL), CH_3CN (20 mL), and TBDMS chloride (10.5 g, 70 mmol). Imidazole (6 g, 89.5 mmol) was then added portionwise over 2 min and left to stir under nitrogen overnight. The reaction was diluted with DCM (100 mL), washed with brine (20 mL), and dried ($MgSO_4$). The organic layer was concentrated cautiously by rotary evaporation (bath at 10 °C), which afforded an oil that was purified by flash chromatography eluting with pentane to yield **11** (10.8 g, 92%) as a colorless oil, $[\alpha]^{23}_D$ +1.5 (neat), $[\alpha]^{23}_D$ −1.2 (*c* 10.0 $CHCl_3$) {lit. $[\alpha]^{26}_D$ −0.68 (*c* 10.7 $CHCl_3$)[32]}. ^{1}H NMR (400 MHz, $CDCl_3$, δ): 0.052 (s, 3H), 0.059 (s, 3H), 0.87 (s, 9H), 1.21 (d, J = 6.0, 3H), 1.95 (t, J = 2.6, 1H), 2.19−2.25 (ddd, J = 16.4, 7.1, 2.7, 1H), 2.3−2.36 (ddd, 1H, J = 16.5, 5.6, 2.6, 1H), 3.93 (tq, 1H, J = 6.7, 6.0, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): −4.9, −4.8, 18.0, 23.1, 25.7, 29.3, 67.4, 69.6, 81.8. GC/MS EI *m/z* (%): 198 (M^+, 0.03), 197 (0.1), 183 (3), 159 (16), 141 (87), 123 (10), 97 (91), 85 (4), 75 (55), 73 (100), 59 (30), 45 (48).

(4*S*)-*tert*-Butyldimethyl-(1-propyl-but-3-ynyloxy)-silane (12). From (*S*)-pent-1-yn-4-ol (**9**). Yield: 74%. $[\alpha]^{23}_D$ −22.8 (*c* 2.4, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$, δ): 0.04 (s, 3H), 0.06 (s, 3H), 0.87 (s, 9H), 0.89 (t, J = 7.3, 3H), 1.24−1.60 (m, 4H), 1.94 (t, J = 2.7, 1H), 2.28 (dd, J = 3.7 and 2.7, 1H), 2.29 (t, J = 2.7, 1H), 3.77 (dddd, J = 6.8, 5.6, 4.6 and 4.6, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): −4.7, −4.5, 14.1, 18.1, 18.4, 25.8, 27.4, 38.9, 69.7, 70.7, 81.8. GC/MS EI *m/z* (%): 225 (M^+, −1, 0.1), 211 (2), 187 (17), 169 (60), 127 (19), 115 (4), 97 (55), 75 (77), 73 (100), 59 (26.7), 45 (36.4). Anal. Calcd for $C_{13}H_{26}OSi$: C, 68.96; H, 11.57. Found: C, 68.72; H, 12.00.

(4*S*)-*tert*-Butyldimethyl-(1-pentyl-but-3-ynyloxy)-silane (13). From (*S*)-non-1-yn-4-ol (**10**). Yield: 89%. $[\alpha]^{23}_D$ −20.9 (*c* 0.4, $CHCl_3$) {lit. $[\alpha]^{20}_D$ −22.3 (*c* 5.5, $CHCl_3$)[35]}. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 0.066 (s, 3H), 0.081 (s, 3H), 0.88 (s, 9H), 0.089 (t, J = 7.0, 3H), 1.25−1.63 (m, 8H), 1.97 (t, J = 2.7, 1H), 2.31 (t, J = 2.7, 1H), 2.32 (dd, J = 2.7 and 1.8, 1H), 3.79 (dddd, J = 6.7, 5.7, 4.7 and 4.7, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): −4.5, −4.4, 14.1, 18.2, 22.7, 24.9, 25.9, 27.5, 31.9, 36.7, 69.8, 71.0, 82.0. GC/MS EI *m/z* (%): 253 (M^+, −1, 0.1), 239 (1), 215 (20), 197 (43), 183 (3), 159 (6), 141 (4), 127 (20), 115 (7), 97 (55), 75 (100), 73 (99), 69 (15), 59 (25), 47 (18).

***tert*-Butyl(hept-1-yn-3-yloxy)dimethylsilane (17).** From hept-1-yn-3-ol (**20**). Yield: 90%. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 0.90 (t, J = 7.2, 3H), 1.29−1.47 (m, 4H), 1.63−1.76 (m, 2H), 1.86 (brs, 1H, OH), 2.44 (d, J = 2.1, 1H), 4.35 (td, J = 6.6 and 2.1, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): −5.1, −4.6, 14.0, 18.2, 22.3, 25.7, 27.3, 38.3, 62.7, 71.8, 85.7. GC/MS EI *m/z* (%): 225 (M^+, −1, 0.1), 211 (1), 169 (7), 113 (43), 83 (31), 75 (100), 73 (22), 69 (15), 59 (10), 45 (21), 41 (22).

(*S*)-*tert*-Butyl(hept-1-yn-3-yloxy)dimethylsilane ((*S*)-17). (*S*)-**17** was prepared in 50% yield on a 0.8-mmol scale using the same procedure as described for **17**. $[\alpha]^{23}_D$ −20.1 (*c* 1.0, $CHCl_3$); (ee ∼60%); lit. $[\alpha]_D$ −35.0 (*c* 3.3, ether).[36] The spectral data was identical to that of racemic *tert*-butyl(hept-1-yn-3-yloxy)dimethylsilane (**17**).

5*S*-(*tert*-Butyl-dimethyl-silanyloxy)-hex-2-ynoic Acid (14). An excess of methyllithium (0.8 M, 15 mmol, 18.7 mL) was added dropwise to a cooled (−40 °C) solution of **11** (1.98 g, 10 mmol) in dry THF (50 mL), and the temperature was maintained at −40 °C for 30 min. Gaseous CO_2 was then bubbled through the reaction for 1 h as the reaction was warmed to 0 °C. A solution of saturated ammonium chloride (30 mL) was then added, and the THF was removed under vacuum. The aqueous layer was then extracted with ether (3 × 50 mL), and the ethereal solution was washed with brine, dried (Na_2SO_4), and concentrated. The crude residue was purified by flash chromatography (silica, 50% EtOAc in hexane) to give 1.3 g (54%) of the pure acid (**14**) as a colorless oil. $[\alpha]^{23}_D$ +2.5 (*c* 0.9, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$, δ): 0.054 (s, 3H), 0.066 (s, 3H), 0.86 (s, 9H), 1.22 (d, J = 6.0, 3H), 2.32 (dd, J = 16.8 and 7.4, 1H), 2.41 (d, J = 16.8 and 4.5, 1H), 3.95−4.00 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 4.85, 4.76, 18.0, 23.5, 25.8, 29.6, 66.9, 75.8 (very broad), 87.2 (very broad), 158.7. GC/MS EI *m/z* (%) (for the methyl ester prepared via esterification with diazomethane): 255 (M^+, −1, 0.1), 241 (1), 199 (17), 159 (3), 155 (61), 133 (49), 103 (99), 96 (7), 89 (100), 75 (24), 73 (97), 59 (50), 45 (38). HRMS: (M + Na) calcd for $C_{12}H_{22}NaSiO_3$, 265.1236; found, 265.1234.

5*S*-(*tert*-Butyl-dimethyl-silanyloxy)-hex-2-ynoic Acid (Methoxy-methyl-amide 15). Following a procedure described by Mosset,[37] *N*,*O*-dimethylhydroxylamine hydrochloride (582 mg, 5.94 mmol, 1.1 equiv) was added to a solution of 5-(*tert*-butyl-dimethyl-silanyloxy)-hex-2-ynoic acid (1.30 g, 5.4 mmol) in anhydrous acetonitrile (100 mL). The resulting mixture was cooled to 0 °C, and pyridine (0.55 mL, 1.04 equiv) was added dropwise. After 30 min of stirring at 0 °C and then 1 h at room temperature, dicyclohexylcarbodiimide (2.24 g, 10.8 mmol, 2.0 equiv) was added in one portion. After stirring for another 30 min, the reaction was filtered through Celite and concentrated in vacuo. Flash chromatography of the residue (SiO_2, 10% ether in hexane then ether) afforded 950 mg of the pure Weinreb amide (**15**, 64%) as a colorless oil. $[\alpha]^{23}_D$ −7.1 (*c* 0.95, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$, δ): 0.047 (s, 3H), 0.055 (s, 3H), 0.86 (s, 9H), 1.24 (d, J = 6.0, 3H), 2.43 (dd, J = 16.8 and 7.0, 1H), 2.52 (d, J = 16.8 and 4.5, 1H), 3.23 (brs, 3H), 3.74 (s, 3H), 4.02 (tq, J = 6.1 and 6.1, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): −5.2, −5.0, 17.7, 23.1, 25.5, 29.5, 32.0, 61.7 (br), 66.5, 74.3, 90.2 (br), 154.2 (br). GC/MS EI *m/z* (%): 284 (M^+, −1, 0.4), 270 (1), 228 (46), 198 (2), 184 (64), 159 (22), 127 (6), 115 (8), 103 (14), 96 (17), 89 (33), 73 (100), 59 (42), 45 (37). Anal. Calcd for $C_{14}H_{27}NO_3Si$: C, 58.91; H, 9.53; N, 4.91. Found: C, 58.97; H, 9.86; N, 4.82.

5*S*-(*tert*-Butyl-dimethyl-silanyloxy)-hexanoic Acid (Methoxy-methyl-amide 16). Palladium (5 wt %) on activated carbon (10 mg) was added to a solution of Weinreb amide **15** (350 mg, 1.23 mmol) in ethyl acetate (10 mL) in the presence of triethylamine (0.25 mL), and the solution was stirred under a hydrogen atmosphere (balloon, 1 atm). The reduction was followed by GC/MS and was complete after 2 h. The mixture was filtered through Celite and concentrated in vacuo. Purification by flash chromatography (SiO_2, 30% ether in hexane) afforded the corresponding amide (**16**, 325 mg, 92%) as a colorless oil. $[\alpha]^{23}_D$ +7.6 (*c* 0.90, $CHCl_3$). ^{1}H NMR

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(500 MHz, $CDCl_3$, δ): 0.02 (s, 3H), 0.85 (s, 9H), 1.10 (d, J = 6.1, 3H), 1.37−1.47 (m, 2H), 1.54−1.72 (m, 2H), 2.39 (app t, J = 7.2, 2H), 3.15 (s, 3H), 3.65 (s, 3H), 3.78 (sextet, J = 6.1, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): −4.9, −4.6, 17.8, 20.6, 23.5, 25.9, 31.7, 31.9 (br), 39.1, 60.9, 68.2, 174.3. GC/MS EI *m/z* (%): 289 (M^+, 0.3), 288 (1), 274 (4), 258 (1), 232 (88), 229 (17), 213 (4), 202 (4), 186 (4), 171 (26), 158 (17), 145 (11), 129 (25), 115 (11), 100 (37), 89 (19), 75 (92), 73 (100), 69 (51), 61 (35), 59 (34), 55 (53), 45 (42), 43 (42), 41 (79). Anal. Calcd for $C_{14}H_{31}NO_3Si$: C, 58.09; H, 10.79; N, 4.84. Found: C, 58.30; H, 11.02; N, 4.89.

5*S*-(*tert*-Butyl-dimethyl-silanyloxy)-2,2,3,3-[$^2H_4$]-hexanoic Acid (Methoxy-methyl-amide 16). $Cl(PPh_3)_3Rh$[38] (98 mg, 10% mol) was added to a solution of Weinreb amide **15** (300 mg, 1.05 mmol) in benzene (10 mL), and the solution was purged and stirred under an $^2H_2$ atmosphere (1 atm). The reduction was followed by GC/MS and was complete after 4 h. The mixture was diluted with cold hexane, filtered through Celite, and concentrated in vacuo. Purification by flash chromatography (SiO_2, 30% ether in hexane) afforded 2,2,3,3-[$^2H_4$]-**16** (325 mg, 92%) as a colorless oil. $[\alpha]^{23}_D$ +7.8 (*c* 0.94, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$, δ): 0.023 (s, 6H), 0.86 (s, 9H), 1.10 (d, J = 6.1, 3H), 1.39 (dd, J = 13.5, 5.4, 1H), 1.44 (dd, J = 13.5, 6.7, 1H), 3.15 (s, 3H), 3.65 (s, 3H), 3.78 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): −4.8, −4.5, 18.1, 20.1 (quintet, $^1J_{D-C}$ = 19.2 Hz), 23.7, 25.8, 31.1 (br quintet, $^1J_{D-C}$ = 19.6 Hz), 32.0 (br), 39.0, 61.1, 68.4, 174.6 (br). GC/MS EI *m/z* (%): 293 (M^+, 0.1), 292 (1), 278 (3), 262 (1), 236 (67), 233 (13), 217 (2), 206 (2), 190 (2), 175 (25), 162 (14), 147 (11), 133 (13), 115 (6), 103 (29), 101 (17), 89 (18), 75 (51), 73 (100), 58 (26), 45 (36), 43 (44). HRMS: (M + Na) calcd for $C_{14}H_{27}D_4NO_3Si_2Na$, 316.2222; found, 316.2222.

Hept-1-yn-3-ol (20). In a three-necked flask, acetylene (welding grade) was bubbled steadily into anhydrous THF (200 mL) at 0 °C via a CO_2/acetone trap. A solution of freshly prepared ethylmagnesium bromide in THF (1.4 M, 41.9 mmol, 30 mL) was added dropwise over 30 min using an addition funnel and then allowed to stir at room temperature for 90 min, after which time acetylene bubbling was ceased. The solution of ethynylmagnesium bromide was recooled to 0 °C, and a solution of pentanal (3.0 g, 34.9 mmol) in THF (15 mL) was added dropwise over 15 min. The reaction was allowed to warm to room temperature over 2 h, was poured into ice-cold ammonium chloride (40 mL, sat.), and was extracted with ether (3 × 30 mL). The ether layers were combined and washed with brine (20 mL), dried ($MgSO_4$), and concentrated in vacuo to give a residue that was distilled (bp 70−74 °C, 20 mmHg, [lit.[39] 69 °C, 18 mmHg]) to yield **20** (2.22 g, 57%) as a colorless oil. ^1H NMR (500 MHz, $CDCl_3$, δ): 0.09 (s, 3H), 0.11 (s, 3H), 0.88 (t, J = 7.3, 3H), 0.89 (s, 9H), 1.29−1.41 (m, 4H), 1.63−1.68 (m, 2H), 2.34 (d, J = 2.1, 1H), 4.31 (td, J = 6.5 and 2.1, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 13.9, 22.3, 27.1, 37.3, 62.3, 72.8, 85.0. GC/MS EI *m/z* (%): 111 (M^+, −1, 0.4), 97 (2), 83 (14), 79 (18), 70 (20), 55 (100), 41 (75).

General Procedure for the Preparation of α,*β*-Diynones 18, (*S,S*)-18, 22, and 23 from 15. The procedure described for the preparation of 2*S*,9-bis-(*tert*-butyl-dimethyl-silanyloxy)-trideca-4,7-diyn-6-one (**18**) is representative.

A solution of methyllithium (0.8 M, 1.5 mL, 1.2 equiv) was added dropwise to a cooled solution (−40 °C) of OTBDMS-alkyne **17** (274 mg, 1.2 mmol, 1.2 equiv) in THF (30 mL) under an inert atmosphere. The solution was left stirring for 30 min at the same temperature, and then the Weinreb amide (**15**, 285 mg, 1 mmol) in THF (5 mL) was added dropwise. At the end of the addition, the cooling bath was removed, and after stirring for another hour at room temperature, the reaction was quenched by the addition of a saturated NH_4Cl solution (20 mL). After extraction with ether (3 × 30 mL), the organic layer was washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The crude residue was purified by flash chromatography (5% ether in hexane) to afford ynone **18** (440 mg, 98%) as a colorless oil. ^1H NMR (500 MHz, CDCl3, δ): 0.055 (s, 3H), 0.070 (s, 3H), 0.098 (s, 3H), 0.127 (s, 3H), 0.86 (s, 9H), 0.88 (t, J = 7.3, 3H) 0.89 (s, 9H), 1.23 (d, J = 6.0, 3H), 1.29−1.41 (m, 4H), 1.68−1.73 (m, 2H), 2.43 (dd, J = 17.1 and 6.5, 1H), 2.52 (dd, J = 17.1 and 5.9, 1H), 4.01 (sextet, J = 6.1, 1H), 4.47 (t, J = 6.5, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): −5.1, −4.8, −4.7, −4.6, 13.9, 18.0, 18.1, 22.2, 23.6, 25.7, 27.2, 30.0, 37.4, 62.8, 66.8, 83.0, 84.2, 92.9, 93.7, 160.7. GC/MS EI *m/z* (%): 435 (M^+, −15, 0.2), 393 (5). 261 (1), 159 (32), 103 (13), 75 (28), 73 (100). Anal. Calcd for $C_{25}H_{46}O_3Si_2$: C, 66.61; H, 10.29. Found: C, 66.43; H, 10.41.

(2*S*,9*S*)-2,9-Bis(*tert*-butyldimethylsilyloxy)trideca-4,7-diyn-6-one ((*S*)-18). Yield: 70%. $[\alpha]^{23}_D$ −6.2 (*c* 0.64, $CHCl_3$). The spectral data was identical to that of racemic 2,9-bis(*tert*-butyldimethylsilyloxy)trideca-4,7-diyn-6-one (**18**).

(2*S*,10*S*)-Bis-(*tert*-butyl-dimethyl-silanyloxy)-trideca-4,7-diyn-6-one (22). Yield: 96%. $[\alpha]^{23}_D$ −5.6 (*c* 0.86, $CHCl_3$).^1H NMR (500 MHz, $CDCl_3$, δ): 0.037 (s, 3H), 0.045 (s, 3H), 0.053 (s, 3H), 0.069 (s, 3H), 0.86 (s, 9H), 0.87 (s, 9H), 0.89 (t, J = 7.3, 3H), 1.22 (d, J = 6.0, 3H), 1.25−1.41 (m, 2H), 1.47−1.58 (m, 2H), 2.42 (dd, J = 17.2 and 6.4, 1H), 2.48 (d, J = 5.9, 2H), 2.51 (dd, J = 17.2 and 6.0, 1H), 3.85 (dq, J = 6.0 and 6.0, 1H), 4.01 (sextet, J = 6.1, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): −4.8, −4.7, −4.68, −4.6, 14.1, 18.0, 18.3, 23.6, 25.7, 25.8, 28.0, 30.0, 39.3, 66.8, 70.1, 83.2, 83.3, 91.9, 92.1, 161.0. GC/MS EI *m/z* (%): 435 (M^+, −15, 0.25), 393 (3.7). 187 (0.7), 159 (41), 133 (4.6), 103 (15), 75 (26), 73 (100). Anal. Calcd for $C_{25}H_{46}O_3Si_2$: C, 66.61; H, 10.29. Found: C, 66.63; H, 10.59.

(2*S*,10*S*)-Bis-(*tert*-butyl-dimethyl-silanyloxy)-pentadeca-4,7-diyn-6-one (23). Yield: 79%. $[\alpha]^{23}_D$ −4.2 (*c* 0.70, $CHCl_3$).^1H NMR (500 MHz, $CDCl_3$, δ): 0.047 (s, 3H), 0.056 (s, 3H), 0.071 (s, 6H), 0.87 (s, 9H), 0.88 (s, 9H), 0.88 (t, J = 7.3, 3H), 1.22 (d, J = 6.0, 3H), 1.23−1.27 (m, 7H), 1.46−1.61 (m, 3H), 2.42 (dd, J = 17.1 and 6.4, 1H), 2.48 (d, J = 5.9, 2H), 2.51 (dd, J = 17.1 and 6.0, 1H), 3.84 (dq, J = 6.0 and 6.1, 1H), 4.01 (sextet, J = 6.1, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): −4.8, −4.7, −4.6, −4.5, 14.0, 18.0, 22.6, 23.6, 24.7, 25.7, 25.8, 28.0, 30.0, 31.7, 37.1, 66.9, 70.3, 83.2, 83.3, 91.9, 92.2, 161.1. GC/MS EI *m/z* (%): 486 (M^+, 0.1), 421 (3). 215 (34), 159 (29), 133 (4), 103 (11), 75 (24), 73 (100), 59 (12). Anal. Calcd for $C_{27}H_{50}O_3Si_2$: C, 67.72; H, 10.52. Found: C, 67.81; H, 10.88.

General Procedure for the Preparation of Ketones of α,*β*-Diynones (19, (*S,S*)-19, 24, and 25). The procedure described for the preparation of 2*S*,9-bis-(*tert*-butyl-dimethyl-silanyloxy)-tridecan-6-one **19** is representative.

Palladium adsorbed on charcoal (15 mg, 5%) was added to a solution of **18** (440 mg, 0.98 mmol) in ethyl acetate (10 mL) and triethylamine (0.5 mL). The flask was purged with nitrogen, evacuated, and then stirred under hydrogen (1 atm). The reduction was followed by GC. When the reaction was complete, the flask was purged with nitrogen, and the mixture was filtered through a bed of Celite and then concentrated in vacuo. The residue was purified by flash chromatography (5% ether in hexane) to yield the saturated ketone (**19**) as colorless oil (440 mg, 98%).^1H NMR (500 MHz, $CDCl_3$, δ): 0.006 (s, 3H), 0.013 (s, 3H), 0.018 (s, 3H), 0.02 (s, 3H), 0.85 (s, 18H), 0.86 (t, J = 7.3, 3H), 1.09 (d, J = 6.1, 3H), 1.21−1.29 (m, 4H), 1.30−1.42 (m, 4H), 1.52−1.63 (m, 3H), 1.72 (dddd, J = 16.9, 9.5, 6.0 and 4.5, 1H), 2.37 (t, J = 7.4, 2H), 2.43 (dt, J = 9.3 and 6.3, 2H), 3.63 (dq, J = 6.0 and 4.5, 1H), 3.76 (sextet, J = 6.0, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): −4.7, −4.5, −4.42, −4.40, 14.1, 18.0, 18.1, 20.2, 22.8, 23.7, 25.9, 27.4, 30.4, 36.7, 38.2, 39.1, 42.9, 68.3, 71.3, 211.3. GC/MS EI *m/z* (%): 443 (M^+, −15, 0.1), 401 (2), 269 (47), 227 (47), 199 (12), 185 (15), 145 (26), 75 (100), 73 (71), 55 (34), 41 (27). Anal. Calcd for $C_{25}H_{53}O_3Si_2$: C, 65.44; H, 11.86. Found: C, 65.44; H, 11.95.

(2*S*,9*S*)-2,9-Bis(*tert*-butyldimethylsilyloxy)tridecan-6-one ((*S,S*)-19). Yield: 90%. $[\alpha]^{23}_D$ +8.4 (*c* 0.47, $CHCl_3$). The spectral data was identical to that of **19**.

(38) Osborn, J. A.; Jardine, F. H.; Young, J. F.; Wilkinson, G. *J. Chem. Soc. A* **1966**, 1711.

(39) Wotiz, J. H. *J. Am. Chem. Soc.* **1951**, *73*, 693.

2*S*,10*S*-Bis-(*tert*-butyl-dimethyl-silanyloxy)-tridecan-6-one (24). Yield: 93%. $[\alpha]^{23}_D$ +5.8 (*c* 0.50, $CHCl_3$) {lit. $[\alpha]^{23}_D$ +7.3 (*c* 1.1, $CHCl_3$)[25]}. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 0.01 (s, 6H), 0.017 (s, 3H), 0.020 (s, 3H), 0.85 (s, 18H), 0.86 (t, J = 7.3, 3H), 1.09(d, J = 6.1, 3H), 1.17−1.43 (m, 8H), 1.49−1.66 (m, 4H), 2.35 (t, J = 6.9, 2H), 2.35 (t, J = 7.5, 1H), 2.36 (t, J = 7.4, 2H), 3.61 (dq, J = 5.7 and 5.7, 1H), 3.76 (sextet, J = 6.1, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): −4.70, −4.5, −4.4, 14.3, 18.1, 18.5, 19.7, 20.1, 23.7, 25.8, 25.9, 36.5, 39.1, 39.3, 42.7, 42.9, 68.3, 71.8, 211.1. GC/MS EI *m/z* (%:) 57 (M^+, −1, 0.1), 401 (2), 269 (14), 227 (18), 213 (5), 199 (33), 185 (16), 173 (24), 157 (13), 145 (23), 75 (100), 73 (67), 55 (39), 41 (29). Anal. Calcd for $C_{25}H_{54}O_3Si_2$: C, 65.44; H, 11.86. Found: C, 65.14; H, 12.14.

2*S*,10*S*-Bis-(*tert*-butyl-dimethyl-silanyloxy)-pentadecan-6-one (25). Yield: 75%. $[\alpha]^{23}_D$ +7.3 (*c* 0.70, $CHCl_3$).^{1}H NMR (500 MHz, $CDCl_3$, δ): 0.07 (s, 6H), 0.015 (s, 3H), 0.017 (s, 3H), 0.85 (s, 18H), 0.85 (t, J = 7.3, 3H), 1.09 (d, J = 6.1, 3H), 1.20−1.41 (m, 12H), 1.49−1.65 (m, 14H), 2.34 (t, J = 7.3, 1H), 2.35 (t, J = 7.5, 2H), 2.36 (t, J = 7.4, 1H), 3.60 (dq, J = 5.8 and 5.8, 1H), 3.77 (sextet, J = 6.1, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): −4.7, −4.5, −4.44, −4.41, 14.0, 18.1, 19.7, 20.1, 22.6, 23.7, 24.9, 25.8, 25.9, 32.0, 36.5, 37.0, 39.1, 42.7, 42.9, 68.3, 72.1, 211.2. GC/MS EI *m/z* (%): 494 (M^+, 0.3), 429 (3), 337 (2), 297 (12), 255 (12), 241 (4), 215 (6), 199 (33), 185 (17), 171 (5), 157 (12), 145 (22), 75 (100), 73 (65), 55 (34), 41 (31). Anal. Calcd for $C_{27}H_{58}O_3Si_2$: C, 66.60; H, 12.01. Found: C, 66.46; H, 12.19.

Hept-1-yn-3-one (21). Jones's reagent (1.2 equiv, 1.5 mL) was added dropwise to a solution of propargylic alcohol (**20**, 1.12 g, 1.0 mmol) in acetone at −10 °C, which left a persistent yellow tint after 30 min. Excess Jones' reagent was quenched by the addition of 2-propanol (0.2 mL), and stirring continued for another 15 min at the same temperature. The reaction was filtered through Celite and dried ($MgSO_4$), and the solvent was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (10% ether in hexane) to give the title product as a volatile colorless liquid (837 mg, 76%).^{1}H NMR (500 MHz, $CDCl_3$, δ): 0.90 (t, J = 7.4, 3H), 1.29−1.39 (m, 2H), 1.58−1.66 (m, 2H), 2.56 (t, J = 7.4, 2H), 3.17 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 13.7, 22.0, 25.8, 45.1, 78.2, 81.4, 187.5. GC/MS EI *m/z* (%): 109 (M^+, −1, 5), 95 (8), 81 (13), 68 (100), 53 (88), 41 (53).

(*S*)-Hept-1-yn-3-ol ((*S*)-20). A solution of ketone (200 mg, 1.8 mmol) in anhydrous THF (10 mL) was dried over 4-Å molecular sieves for 2 h and subsequently added by syringe to a dry flask charged with (*S*)-2-methyl-CBS-oxazaborolidine solution (3.6 mL, 1 M in toluene) in anhydrous THF (10 mL). The solution was cooled to −30 °C, and then 4.5 mL (9 mmol, 5 equiv) of boron methyl sulfide complex (2 M solution in THF) was added dropwise. After 15 min, the solution was quenched by the addition of MeOH (6 mL). The solution was then diluted with ether (80 mL) and washed with saturated NH_4Cl (2 × 30 mL), 5% $NaHCO_3$ (2 × 30 mL), and brine (2 × 30 mL). The organic layer was dried ($MgSO_4$), filtered trough silica gel, and concentrated. The residue was purified by column chromatography (10% ether in hexane) to afford 100 mg (50%) of the pure alcohol ((S)-**20**). $[\alpha]^{23}_D$ −13.9 (*c* 0.36, ether) (ee ∼60%) {lit. $[\alpha]_D$ −24.6 (*c* 1.2, ether)[40]}. The spectral data was identical to that of racemic hept-1-yn-3-ol (**20**).

General Procedure for the Synthesis of Unlabeled Spiroacetals ((2*S*,5*R*,7*S*)-1, (2*R*,5*R*,7*S*)-1,[19] (2*S*,6*R*,8*S*)-2, and (2*S*,6*R*,8*S*)-3). The procedure described for the preparation of (2*S*,5*R*,7*S*)-**1** and (2*R*,5*R*,7*S*)-**1** is representative.

Ketone **19** (530 mg, 1.15 mmol) was added to an aqueous solution of acetic acid (6 mL, 75%) and heated at 50 °C for 6 h, at which time TLC analysis revealed that the reaction was complete. The solution was allowed to cool to room temperature and was extracted with pentane (4 × 30 mL). The organic phase was added cautiously to ice-cold $NaHCO_3$ (20 mL, sat.) and was allowed to stir for 5 min. The pentane was separated, dried with $MgSO_4$, and concentrated in vacuo. The rotary-evaporator bath was chilled to 5 °C, and the receiving flask was chilled to 0 °C. The crude oil was purified by flash chromatography eluting with pentane and reconcentrated as it was above to give both separated isomers ((2*S*,5*R*,7*S*)-**1** (87 mg) and (2*R*,5*R*,7*S*)-**1** (110 mg)) in 80% combined yield. HRMS: (M + Na) calcd for $C_{13}H_{24}NaO_2$, 235.1674; found, 235.1668. (2*S*,5*R*,7*S*) Isomer: $[\alpha]^{23}_D$ −51.3 (*c* 0.75, pentane).^{1}H NMR (500 MHz, C_6D_6, δ): 0.87 (t, J = 7.3, 3H), 1.12 (dddd, J = 13.1, 13.1, 11.3 and 3.9, 1H), 1.17 (d, J = 6.3, 3H), 1.26−1.30 (m, 4H), 1.38−1.42 (m, 3H), 1.45−1.54 (m, 1H), 1.57−1.65 (m, 4H),1.97−2.06 (m, 3H), 4.05 (dqd, J = 12.6, 6.3 and 2.3, 1H), 4.09−4.15 (m, 1H). ^{13}C NMR (125 MHz, C_6D_6, δ): 14.3, 20.9, 22.4, 23.2, 28.7, 30.2, 33.2, 34.0, 36.0, 38.3, 66.4, 78.1, 106.0. GC/MS EI *m/z* (%): 212 (M^+, 2), 168 (5), 155 (54), 143 (35), 140 (14), 125 (27), 115 (16), 111 (11), 97 (25), 85 (43), 82 (14), 71.0 (15), 69 (20), 67 (16), 57 (30), 55 (90), 43 (87), 41 (100). (2*R*,5*R*,7*S*) Isomer: $[\alpha]^{23}_D$ −42.0 (*c* 0.40, pentane).^{1}H NMR (500 MHz, C_6D_6, δ): 0.89 (t, J = 7.3, 3H), 1.09−1.14 (m, 1H), 1.15 (d, J = 6.3, 3H), 1.30−1.34 (m, 3H), 1.38−1.42 (m, 1H), 1.46−1.60 (m, 6H), 1.68−1.83 (m, 3H), 1.97−2.08 (m, 2H), 3.97−4.03 (m, 1H), 4.09 (dqd, J = 11.3, 6.3 and 2.3, 1H). ^{13}C NMR (125 MHz, C_6D_6, δ): 14.3, 21.0, 22.3, 29.1, 30.4, 33.2, 33.9, 38.1, 39.3, 66.3, 80.7, 105.8. GC/MS EI *m/z* (%): 212 (M^+, 2), 168 (5), 155 (69), 143 (36), 140 (13), 125 (28), 115 (15), 111 (10), 97 (24), 85 (52), 82 (13), 71 (15), 69 (19), 67 (17), 57 (26), 55 (90), 43 (87), 41 (100).

(2*S*,5*R*,7*S*)-2-Butyl-7-methyl-1,6-dioxa-spiro[4.5]-decane ((2*S*,5*R*,7*S*)-1). Yield: 71%. $[\alpha]^{23}_D$ −52.3 (*c* 0.55, pentane). The spectral data was identical to that of the first isomer of (2*S*,5*R*,7*S*)-2-butyl-7-methyl-1,6-dioxa-spiro[4.5]-decane (**1**).

(2*S*,6*R*,8*S*)-2-Methyl-8-propyl-1,7-dioxa-spiro[5.5]-undecane (2). Yield: 75%. $[\alpha]^{23}_D$ −54.6 (*c* 0.80, pentane) {lit. $[\alpha]_D$ −78.1 (*c* 1.71, $CHCl_3$)}[25], $[\alpha]_D$ −40.5 (*c* 1.08, pentane)[23]. ^{1}H NMR (500 MHz, C_6D_6, δ): 0.93 (t, J = 7.3, 3H), 1.06−1.15 (m, 2H), 1.18 (d, J = 6.3, 3H), 1.26−1.42 (m, 8H), 1.50−1.56 (m, 1H), 1.59−1.68 (m, 3H), 1.98−2.11 (m, 2H), 3.61 (dddd, J = 2.3, 4.1, 8.6 and 13.0, 1H), 3.79 (dqd, J = 2.2, 6.3 and 11.3, 1H). ^{13}C NMR (125 MHz, C_6D_6, δ): 14.5, 19.3, 19.5 (2C), 22.2, 31.8, 33.3, 35.8, 36.0, 39.2, 65.2, 68.9, 95.9. GC/MS EI *m/z* (%): 212 (M^+, 2), 169 (7), 143 (11), 140 (11), 125 (14), 115 (35), 112 (28), 97 (28), 83 (14), 82 (11), 71 (18), 69 (22), 67 (13), 55 (75), 43 (84), 41 (100).

(2*S*,6*R*,8*S*)-2-Methyl-8-pentyl-1,7-dioxa-spiro[5.5]-undecane (3). Yield: 80%. $[\alpha]_D$ −56.9 (*c* 0.50, pentane).^{1}H NMR (500 MHz, C_6D_6, δ): 0.90 (t, J = 7.3, 3H), 1.01−1.21 (m, 2H), 1.18 (d, J = 6.3, 3H), 1.24−1.47 (m, 12H), 1.54−1.69 (m, 4H), 2.00−2.12 (m, 2H), 3.63 (dddd, J = 2.2, 4.0, 8.2 and 11.0, 1H), 3.82 (dqd, J = 2.2, 6.3 and 11.4, 1H). ^{13}C NMR (125 MHz, C_6D_6, δ): 14.3, 19.4, 19.5, 22.2, 23.0, 25.9, 31.8, 32.5, 33.3, 35.8, 36.0, 37.0, 65.3, 69.0, 95.9. GC/MS EI *m/z* (%): 240 (M^+, 2), 196 (2), 169 (12), 153 (13), 140 (15), 115 (93), 114 (19), 112 (64), 99 (11), 97 (36), 83 (15), 81 (10), 71 (23), 69 (39), 67 (15), 58 (14), 57 (14), 55 (77), 43 (89), 42 (36), 41 (100). HRMS: calcd for $C_{15}H_{28}O_2$, 240.2089; found, 240.2089.

(2*S*,10*S*)-2,10-Bis-(*tert*-butyl-dimethyl-silanyloxy)-undecan-6-ol (27). Palladium adsorbed on barium sulfate (50 mg, 5%) was added to a solution of **26** (4.25 g, 10 mmol) in 2-propanol (30 mL) and triethylamine (3 mL). The flask was purged with nitrogen, evacuated, and stirred under hydrogen (balloon, 1 atm). The reduction was followed by $AgNO_3$-adsorbed TLC, which revealed that the hydrogenation was complete after 30 min. The flask was purged with nitrogen, and the mixture was filtered through a bed of Celite and then concentrated in vacuo. The residue was purified by flash chromatography (ethyl acetate/hexane 1:20) to yield **27** (3.24 g, 75%) as a colorless oil. $[\alpha]^{23}_D$ +16.9 (*c* 11.8 pentane), $[\alpha]^{23}_D$ +12.5 (*c* 0.2 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 0.026 (s, 12H), 0.86 (s, 18H), 1.10 (d, J = 6.0, 6H), 1.2−1.5 (m, 12H), 3.54−3.59 (m, 1H), 3.74−3.80 (m, J = 6.0, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): −4.7, −4.4, 18.1, 21.7, 21.9, 23.7, 23.8, 25.9, 37.4, 37.5, 39.65, 39.71, 68.50, 68.54, 71.8. GC/MS EI *m/z* (%):

(40) Xiao, L.; Kitazume, T. *Tetrahedron: Asymmetry* **1997**, *8*, 3597.

431 (M^+, −1, 0.03), 357 (0.1), 299 (0.1), 283 (1), 243 (3), 173 (5), 159 (15), 151 (18), 133 (10), 119 (14), 109 (46), 95 (91), 81.1 (45), 75 (100), 73 (66), 67 (39), 55 (21). Anal. Calcd for $C_{23}H_{52}O_3Si_2$: C, 63.82; H, 12.11. Found: C, 64.08; H, 12.32.

(2*S*,10*S*)-2,10-Bis-(*tert*-butyl-dimethyl-silanyloxy)-undeca-4,7-diyn-6-ol (26). 11 (6.62 g, 33.4 mmol) was cooled to −40 °C (EtOH/H_2O/CO_2) in THF (25 mL) under N_2, and *n*-butyllithium (2.2 M in hexane, 15.2 mL, 33.4 mmol) was added dropwise. The solution was allowed to warm to room temperature, stirred for 15 min, and cooled to −40 °C, and then ethyl formate (1.23 g, 16.7 mmol) in THF (20 mL) was added dropwise by syringe for 5 min. The reaction was allowed to warm to room temperature for 3 h and was quenched by pouring the reaction over ice/NH_4Cl. It was then extracted with ether (3 × 50 mL), washed with brine (30 mL), and dried ($MgSO_4$). The organic layer was concentrated in vacuo and purified by flash chromatography (ethyl acetate/hexane 1:30) to yield **26** (5.83 g, 82%) as a colorless oil. $[\alpha]^{23}_D$ +13.7 (*c* 4.2 pentane), $[\alpha]^{23}_D$+ 8.0 (*c* 0.8 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 0.04 (s, 6H), 0.05 (s, 6H), 0.86 (s, 18H), 1.19 (d, J = 6.0, 6H), 2.18 (d, J = 7.1, 1H, OH), 2.22−2.29 (ddd, J = 16.4, 7.0, 2.0, 2H), 2.33−2.39 (ddd, J = 16.48, 5.84, 2.04, 2H), 3.93 (tq, J = 6.9, 6.0, 1H), 5.05 (br dt, J = 6.8, 2.0, 1H). ^{13}C NMR (100 MHz $CDCl_3$, δ): −4.76, −4.71, 18.1, 23.4, 25.8, 29.6, 52.5, 67.5, 79.3, 82.5. GC/MS EI *m/z* (%): 423 (M^+, −1, 0.1), 191 (2), 159 (80) 133 (3), 119 (36), 103 (31), 75 (75), 73 (100), 59 (13), 45 (12). Anal. Calcd for $C_{23}H_{44}O_3Si_2$: C, 65.04; H, 10.44. Found: C, 64.84; H, 10.68.

2,10-Bis-(*tert*-butyl-dimethyl-silanyloxy)-undecan-6-one (28). PCC (2.55 g, 11.83 mmol) was added portionwise to a solution of **27** (3.41 g, 7.90 mmol) in DCM (400 mL) over 10 min. The oxidation was followed by TLC, and after 3.5 h an extra half equivalent of PCC (0.85 g, 3.95 mmol) was added to complete the reaction. The mixture was vacuum filtered through a bed of Celite/silica, washed with diethyl ether, concentrated in vacuo, and purified by flash chromatography (ethyl acetate/hexane 1:30) to yield **28** (3.07 g, 90%) as a colorless oil. $[\alpha]^{23}_D$+ 15.3 (*c* 6.0 pentane), $[\alpha]^{23}_D$+ 14.3 (*c* 0.6 $CHCl_3$) {lit. $[\alpha]_D$ +13.1 (*c* 1.1, $CHCl_3$)},[25] ^{1}H NMR (500 MHz, $CDCl_3$, δ): 0.017 (s, 3H), 0.019 (s, 3H), 0.86 (s, 18H), 1.09 (d, J = 6.1, 6H), 1.30−1.42 (m, 4H), 1.48−1.57 (m, 4H), 1.57−1.66 (m, 4H), 2.36 (t, J = 7.4, 4H), 3.76 (app sextet, J = 6.1, 2H). ^{13}C NMR (125 MHz $CDCl_3$, δ): −4.7, −4.4, 18.1, 20.1, 23.7, 25.9, 39.1, 42.7, 68.3, 211.2. GC/MS EI *m/z* (%): 430 (M^+, 0.04), 373 (2), 283 (1), 241 (13), 199 (42), 185 (18), 167 (5), 159 (12), 145 (49), 119 (7), 107 (9), 75 (100), 73 (60), 55 (26), 43 (20). Anal. Calcd for $C_{23}H_{50}O_3Si_2$: C, 64.12; H, 11.70. Found: C, 64.08; H, 11.98.

(2*S*,6*R*,8*S*)-2,8-Dimethyl-1,7-dioxa-spiro[5.5]undecane (4). (2*S*,6*R*,8*S*)-**4** was prepared in 66% yield on a 6-mmol scale using the same procedure as described for (2*S*,5*R*,7*S*)-**1** and (2*R*,5*R*,7*S*)-**1**. $[\alpha]^{23}_D$ −57.5 (*c* 5.2, pentane) {lit. $[\alpha]_D$ −56.0 (*c* 1.4, pentane)},[24] $[\alpha]_D$ −57.6 (*c* 1.04, pentane).[25] ^{1}H NMR (500 MHz, C_6D_6, δ): 1.10 (tdd, J = 12.8, 11.2, 3.9, 2H), 1.15 (d, J = 6.4, 6H), 1.29 (dt, J = 13.3, 4.5, 2H), 1.37−1.47 (m, 4H), 1.62 (dddd, J = 12.9, 4.0, 2.4 1.5, 2H), 2.02 (qt, J = 13.6, 4.2, 2H), 3.72 (dqd, J = 11.2, 6.3, 2.2, 2H). ^{13}C NMR (125 MHz C_6D_6, δ): 19.4, 22.3, 33.3, 35.7, 65.2, 96.1. GC/MS EI *m/z* (%) 184 (M^+, 3), 169 (1), 140 (7), 125 (58), 114 (27), 112 (61), 97 (38), 83 (20), 69 (39), 58 (25), 55 (66), 43 (100).

2*S*,10*S*-Bis-(*tert*-butyl-dimethyl-silanyloxy)-tridec-7-yn-6-one (29). This ynone **(29)** was prepared in 83% yield on a 1-mmol scale from Weinreb amide **16** using the same general procedure as described for **18**. Yield: 83%. $[\alpha]^{23}_D$ −4.3 (*c* 0.70, $CHCl_3$).^{1}H NMR (500 MHz, $CDCl_3$, δ): 0.025 (s, 3H), 0.027 (s, 3H), 0.044 (s, 3H), 0.059 (s, 3H), 0.86 (s, 9H), 0.87 (s, 9H), 0.90 (t, J = 7.3, 3H), 1.10 (d, J = 6.1, 3H), 1.23−1.75 (m, 8H), 2.46 (d, J = 5.9, 2H), 2.51 (t, J = 7.3, 2H), 3.77 (quintet, J = 5.8, 1H), 3.82 (quintet, J = 6.0, 1H). ^{13}C NMR (125 MHz $CDCl_3$, δ): −4.75, −4.67, −4.57, −4.40, 14.1, 18.0, 18.4, 20.4, 23.7, 25.8, 27.9, 38.8, 39.2, 45.5, 68.2, 70.1, 82.1, 91.4, 188.1. GC/MS EI *m/z* (%): 439 (M^+, −15, 0.2), 397 (1), 325 (2), 265 (11), 223 (7), 209 (3), 187 (84), 151 (12), 131 (23), 115 (10), 75 (52), 73 (100), 59 (14), 41 (14). Anal. Calcd for $C_{25}H_{50}O_3Si_2$: C, 66.02; H, 11.08. Found: C, 66.00; H, 11.38.

General Procedure for the Preparation of α,*β*-ynones (4,4,5,5-[$^2H_4$]-29 and 4,4,5,5-[$^2H_4$]-30). These 4,4,5,5-[$^2H_4$]-ynones (**29** and **30**) were prepared from the Weinreb amide 2,2,3,3-[$^2H_4$]-**16** (racemic or optically active) using the same general procedure described for **18**.

2*S*,10*S*-Bis-(*tert*-butyl-dimethyl-silanyloxy)-4,4,5,5-tetradeutero-tridec-7-yn-6-one (4,4,5,5-[$^2H_4$]-29). Yield: 75%. $[\alpha]^{23}_D$ −5.6 (*c* 0.80, $CHCl_3$).^{1}H NMR (500 MHz, $CDCl_3$, δ): 0.024 (s, 3H), 0.026 (s, 3H), 0.043(s, 3H), 0.058 (s, 3H), 0.86 (s, 9H), 0.87 (s, 9H), 0.89 (t, J = 7.3, 3H), 1.10 (d, J = 6.2, 3H), 1.24−1.43 (m 4H), 1.45−1.56 (m, 2H), 2.46 (d, J = 5.9, 2H), 3.77 (app sextet, J = 6.1, 1H), 3.83 (app quintet, 1J = 5.4, 1H). ^{13}C NMR (125 MHz $CDCl_3$, δ): −4.8, −4.7, −4.6, −4.4, 14.1, 18.0, 18.1, 18.3, 19.6 (quintet, $^1J_{D-C}$ = 19.5), 44.6 (quintet, $^1J_{D-C}$ = 19.5), 23.7, 25.7, 25.8, 27.9, 38.5, 39.2, 68.1, 70.1, 82.1, 91.3, 188.1. GC/MS EI *m/z* (%): 457 (M^+, −1, 0.1), 401 (1), 329 (2), 269 (9), 226 (6), 196 (5), 187 (100), 154 (10), 147 (9), 131 (21), 115 (10), 75 (44), 73 (100), 59 (13), 43 (12). HRMS: (M + Na) calcd for $C_{25}H_{46}D_4O_3Si_2Na$, 481.3447; found, 481.3444.

2,10-Bis-(*tert*-butyl-dimethyl-silanyloxy)-7,7,8,8-tetradeutero-undec-4-yn-6-one (4,4,5,5-[$^2H_4$]-30). Yield: 85%.^{1}H NMR (500 MHz, $CDCl_3$, δ): 0.022 (s, 3H), 0.024 (s, 3H), 0.05 (s, 3H), 0.06 (s, 3H), 0.86 (s, 9H), 0.87 (s, 9H), 1.10 (d, J = 6.1, 3H), 1.22 (d, J = 6.1, 3H), 1.34−1.41 (m, 2H), 2.40 (dd, J = 17.0, 6.6, 1H), 2.48 (dd, J = 17.0, 5.8, 1H), 3.76 (m, 1H), 3.99 (app sextet, J = 6.3, 1H). ^{13}C NMR (125 MHz $CDCl_3$, δ): −4.84, −4.80, −4.7, −4.4, 18.0, 18.1, 19.6 (pentet, $^1J_{D-C}$ = 19.3), 23.5, 23.7, 25.7, 25.8, 29.8, 38.5, 44.6 (pentet, $^1J_{D-C}$ = 19.1), 66.9, 68.2, 82.0, 91.3, 188.2. GC/MS EI *m/z* (%): 430 (M^+, 0.1), 329 (2), 299 (1), 241 (12), 198 (14), 187 (15), 159 (82), 133 (8), 115 (16), 103 (29), 73 (100), 59 (14). HRMS: (M + Na) calcd for $C_{23}H_{42}D_4O_3Si_2Na$, 453.3134; found, 453.3129.

General Procedure for Hydrogenation of Ynones 29, 4,4,5,5-[$^2H_4$]-29, and 4,4,5,5-[$^2H_4$]-30 Using Wilkinson's Catalyst. $Cl(PPh_3)_3Rh$[38] (95 mg, 10% mol) was added to a solution of an acetylenic derivative (1 mmol) in benzene (10 mL), and the solution was purged and stirred under an $^2H_2$ or H_2 atmosphere (balloon, 1 atm). The reduction was followed by GC/MS. When the reaction was complete, the mixture was diluted with cold hexane, filtered through Celite, and concentrated in vacuo. Purification by flash chromatography (SiO_2, hexane) afforded the pure deuterated product as a colorless oil.

2*S*,10*S*-Bis-(*tert*-butyl-dimethyl-silanyloxy)-4,4,5,5-tetradeuterio-tridecan-6-one (4,4,5,5-[$^2H_4$]-24). Yield: 71%. $[\alpha]^{23}_D$ +7.1 (*c* 0.73, $CHCl_3$).^{1}H NMR (500 MHz, $CDCl_3$, δ): 0.008 (s, 6H), 0.014 (s, 3H), 0.017 (s, 3H), 0.85 (s, 18H), 0.86 (t, J = 7.3, 3H), 1.08 (d, J = 6.1, 3H), 1.21−1.42 (m, 8H), 1.50−1.63 (m, 2H), 2.33 (td, J = 7.6 and 2.2, 2H), 3.61 (app quintet, J = 5.7, 1H), 3.76 (app sextet, J = 6.1, 1H). ^{13}C NMR (125 MHz $CDCl_3$, δ): −4.73, −4.45, −4.44, −4.40, 14.3, 18.1, 18.5, 19.3 (quintet, $^1J_{D-C}$ = 19.6), 19.7, 23.7, 25.9, 36.5, 38.9, 39.3, 41.8 (quintet, $^1J_{D-C}$ = 19.6), 42.9, 68.3, 71.8, 211.2. GC/MS EI *m/z* (%): 447 (M^+, −15, 0.1), (10), 230 (14), 213 (5), 203 (27), 187 (20), 173 (27), 160 (9), 147 (34), 133 (7), 115 (7), 75 (100), 73 (91). HRMS: (M + Na) calcd for $C_{25}H_{46}D_4O_3Si_2Na$, 485.3760; found, 485.3753.

2*S*,10*S*-Bis-(*tert*-butyl-dimethyl-silanyloxy)-7,7,8,8-deutero-tridecan-6-one (7,7,8,8-[$^2H_4$]-24). $[\alpha]^{23}_D$ +6.8 (*c* 0.85, $CHCl_3$).^{1}H NMR (500 MHz, $CDCl_3$, δ): 0.002 (s, 6H), 0.011 (s, 3H), 0.013 (s, 3H), 0.84 (s, 18H), 0.85 (t, J = 7.3, 3H), 1.08 (d, J = 6.1, 3H), 1.26−1.39 (m, 8H), 1.50−1.63 (m, 2H), 2.35 (t, J = 7.3, 2H), 3.61 (app quintet, J = 5.7, 1H), 3.76 (app sextet, J = 6.1, 1H). ^{13}C NMR (125 MHz $CDCl_3$, δ): −4.75, −4.7−4.4, 14.3, 18.1, 18.5, 18.9 (quintet, $^1J_{D-C}$ = 19.6), 20.1, 23.7, 25.9, 36.3, 39.1, 39.3, 42.0 (quintet, $^1J_{D-C}$ = 19.6), 42.7, 68.3, 71.8, 211.3. GC/MS EI *m/z* (%): 462 (M^+, 0.05), 273 (12), 231 (19), 215 (6), 202 (34), 185 (18), 175 (34), 159 (11), 145 (33), 133 (7),

115 (7), 101 (7), 75 (100), 73 (73). HRMS: (M + Na) calcd for $C_{25}H_{46}D_4O_3Si_2Na$, 485.3760; found, 485.3754.

2,10-Bis-(*tert*-butyl-dimethyl-silanyloxy)-4,4,5,5-tetradeutero-undecan-6-one (4,4,5,5-[$^2H_4$]-31). Yield: 85%.^{1}H NMR (500 MHz, $CDCl_3$, δ): 0.011 (s, 12H), 0.85 (s, 18H), 1.08 (d, J = 6.1, 6H), 1.29−1.40 (m, 4H), 1.47−1.67 (m 2H), 2.35 (t, J = 7.3, 2H), 3.75 (app sextet, J = 6.3, 2H). ^{13}C NMR (125 MHz $CDCl_3$, δ): −4.8, −4.4, 18.1, 19.3 (quintet, $^1J_{D-C}$ = 19.5), 20.1, 23.7, 25.9, 38.9, 39.1, 41.8 (quintet, $^1J_{D-C}$ = 19.5), 42.7, 68.3, 211.2. GC/MS EI *m/z* (%): 377 (2), 245 (8), 203 (20), 202 (18), 187 (9), 185 (8), 159 (10), 147 (25), 145 (26), 133 (5), 75 (100), 73 (78). HRMS: (M + Na) calcd for $C_{23}H_{46}D_4NaO_3Si_2$, 457.3447; found, 457.3441

General Procedure for the Synthesis of Labeled Spiroacetals (4,4,5,5-[$^2H_4$]-4, 4,4,5,5-[$^2H_4$]-2 and 10,10,11,-11-[$^2H_4$]-2). The procedure described for the preparation of **4,4,5,5-[$^2H_4$]-2** is representative.

A solution of 4,4,5,5-[$^2H_4$]-**24** (180 mg, 0.39 mmol) in anhydrous methanol (3 mL) was cooled to 0 °C, and 2 equiv of CAN (427 mg, 0.78 mmol) was added. The mixture was left in the refrigerator for 3 h, at which point the GC analysis shows total conversion to the corresponding spiroacetal. The solution was extracted with pentane (3 × 30 mL), and then the combined organic layers were dried ($MgSO_4$) and the pentane was cautiously removed in vacuo. The crude oil was purified by flash chromatography, eluting with pentane, and reconcentrated as above to give 4,4,5,5-[$^2H_4$]-**2** (61 mg, 73%) as a colorless oil. ^{1}H NMR (500 MHz, C_6D_6, δ): 0.93 (t, J = 7.3, 3H), 1.06−1.15 (m, 2H), 1.18 (d, J = 6.3, 3H), 1.26−1.42 (m, 6H), 1.50−1.56 (m, 1H), 1.59−1.68 (m, 2H), 1.98−2.11 (m, 1H), 3.61 (dddd, J = 2.3, 4.1, 8.6 and 13.0, 1H), 3.79 (dqd, J = 2.2, 6.3 and 11.3, 1H). ^{13}C NMR (125 MHz, C_6D_6, δ): 14.5, 18.3 (quintet, $^1J_{D-C}$ = 19.5, 1C), 19.3, 19.5, 22.2, 31.8, 33.3, 34.6 (quintet, $^1J_{D-C}$ = 19.5, 1C), 36.0, 39.2, 65.2, 68.9, 95.9. GC/MS EI *m/z* (%): 216 (M^+, 2), 201 (1), 177 (7), 143 (14), 142 (15), 125 (12), 119 (59), 116 (39), 115 (16), 101 (14), 98 (14), 82 (19), 73 (22), 55 (53), 43 (100), 41 (78). HRMS: calcd for $C_{13}H_{20}D_4O_2$, 216.2027; found, 216.2025.

10,10,11,11-Tetradeutero-8-methyl-2-propyl-1,7-dioxa-spiro[5.5]undecane (10,10,11,11-[$^2H_4$]-2). ^{1}H NMR (500 MHz, C_6D_6, δ): 0.93 (t, J = 7.3, 3H), 1.06−1.15 (m, 2H), 1.18 (d, J = 6.3, 3H), 1.26−1.42 (m, 6H), 1.50−1.56 (m, 1H), 1.59−1.68 (m, 2H), 1.98−2.11 (m, 1H), 3.61 (dddd, J = 2.3, 4.1, 8.6 and 13.0, 1H), 3.79 (dqd, J = 2.2, 6.3 and 11.3, 1H). ^{13}C NMR (125 MHz, C_6D_6, δ): 14.5, 18.4 (quintet, $^1J_{D-C}$ = 19.5), 19.5 (2C), 22.2, 31.8, 33.3, 35.8, 35.1 (quintet, $^1J_{D-C}$ = 19.5), 39.2, 65.2, 68.9, 95.9. GC/MS EI *m/z* (%): 216 (M^+, 2), 201 (1), 173 (10), 172 (6), 147 (17), 144 (22), 115 (82), 114 (84), 113 (12), 97 (23), 84 (34), 69 (34), 55 (52), 45 (39), 44 (41), 43 (100), 41 (84). HRMS: calcd for $C_{13}H_{20}D_4O_2$, 216.2027; found, 216.2023.

4,4,5,5-Tetradeutero-2,8-dimethyl-1,7-dioxa-spiro[5.5]-undecane (4,4,5,5-[$^2H_4$]-4). The EE and EZ isomers were easily separated by flash chromatography. Yield: 73% (40% for the EZ and 33% for the EZ). HRMS: calcd for $C_{11}H_{16}D_4O_2$, 188.1714; found, 188.1706. EE-4,4,5,5-[$^2H_4$]-**4**: ^{1}H NMR (500 MHz, C_6D_6, δ): 1.07−1.15 (m, 2H), 1.17 (d, J = 6.3, 6H), 1.29 (dt, J = 13.3, 4.5, 1H), 1.37−1.47 (m, 3H), 1.62 (dddd, J = 12.9, 4.0, 2.4 1.5, 1H), 2.02 (qt, J = 13.6, 4.2, 1H), 3.72 (dqd, J = 11.2, 6.3, 2.2, 2H). ^{13}C NMR (125 MHz C_6D_6, δ): 18.4 (quintet, $^1J_{D-C}$ = 19.5), 19.4, 22.3, 32.9, 33.3, 34.7 (quintet, $^1J_{D-C}$ = 19.2), 35.6, 65.1, 96.0. GC/MS EI *m/z* (%): 188 (M^+, 2), 173 (1), 144 (5), 119 (24), 117 (12), 116 (27), 115 (37), 114 (44), 101 (10), 97 (14), 84 (10), 73 (19), 69 (16), 60 (17), 55 (30), 43 (100), 42 (49), 41 (51). EZ-4,4,5,5-[$^2H_4$]-**4**: ^{1}H NMR (500 MHz, C_6D_6, δ): 1.02−1.18 (m, 5H), 1.15 (d, J = 6.3, 6H), 1.19 (d, J = 6.3, 6H), 1.26−1.33 (m, 3H), 1.36−1.42 (m, 3H), 1.51−1.62 (m, 2H), 1.66−1.80 (m, 2H), 1.88−1.94 (m, 1H), 3.44 (ddq, J = 9.5, 6.3 and 3.3, 1H), 4.27 (dddq, J = 12.6, 6.3, 2.4 and 1.3, 1H). ^{13}C NMR (125 MHz C_6D_6, δ): 17.6−18.5 (m, 2C), 19.1 (2C), 19.2 (2C), 29.7 (quintet, $^1J_{D-C}$ = 19.6, 1C), 30.3 (1C), 32.2 (1C), 32.6 (1C), 33.2 (1C), 33.5 (1C), 36.1 (quintet, $^1J_{D-C}$ = 19.6, 1C), 36.6 (1C), 66.9 (2C), 68.5 (2C), 97.0 (2C). GC/MS EI *m/z* (%): 188 (M^+, 2), 173 (1), 144 (2), 128 (3), 119 (28), 116 (22), 115 (53), 114 (36), 97 (23), 84 (8), 75 (14), 73 (32), 69 (31), 55 (36), 43 (100), 42 (59), 41 (62).

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Supporting Information Available: NMR spectra (^{1}H and ^{13}C) of labeled and unlabeled **1**−**4**, **15**,**16**, **24**, and **29** and mass spectra of labeled and unlabeled **2**, **4**, **15**, **16**, and **24**. This material is available free of charge via the Internet at http://pubs.acs.org

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