Diastereoselective Reactions of δ-Oxy-Substituted Allylic Acetates with Organocopper Reagents

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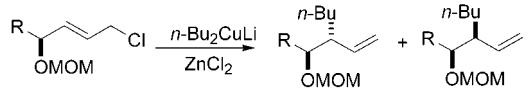
S_N2' (γ) substitutions of δ-substituted allylic acetates with Grignard reagents and copper catalysts proceed with high diastereoselectivities. With benzyloxy, methoxymethoxy, and *tert*-butyldimethylsiloxy groups, reactions favor the anti-isomer with selectivities up to anti:syn = >99:1. With a hydroxyl group, selectivities are reversed and the syn-isomer is favored with selectivities up to anti:syn = <1:99.

Introduction

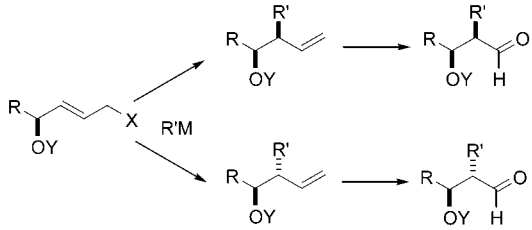
The S_N2' substitution of various allylic substrates with organometallic, particularly organocopper, reagents is a well-established method for C−C bond formation.[1] There is a large body of knowledge on factors influencing regioselectivity[2] in these reactions, but there is a surprising paucity of information regarding diastereoselectivity.[3] With α-substituted carbonyl compounds, it is now possible to reliably predict (usually) the stereochemistry of nucleophilic addition using rational models.[4] With Michael additions of organocopper reagents, there are many examples demonstrating that the stereoselectivity of conjugate additions to α,β-unsaturated carbonyl compounds is influenced by adjacent[5] or remote[6] stereocenters. In S_N2' substitution reactions, many researchers have examined how the stereochemistry of the incoming nucleophile is influenced by the stereochemistry of/around the leaving group.[7] In contrast, only Nakamura has addressed the issue of how the diastereoselectivity of an S_N2' displacement might be influenced by an adjacent stereocenter.[8]

Scheme 1



R = *n*-Bu	3	1
i-Pr	100	0

Scheme 2



Nakamura worked principally with allylic chlorides and found that reactions with organocopper and organozinc reagents could proceed with very high diastereoselectivities, but only if R is a branched alkyl group (Scheme 1). Primary alkyl groups gave modest selectivities, and anti-isomers predominated regardless of the oxygen protecting group.

It is clear that further development of such diastereoselective S_N2' reactions is needed. Since the products should be easily transformed (e.g., by ozonolysis) to aldol-type products (Scheme 2), control of the stereochemistry of these reactions would provide stereoselective routes to syn- or anti-aldol products, compounds of considerable interest as synthetic intermediates.[9] We now report that both syn- and anti-adducts may be prepared with good to excellent selectivities using suitable δ-oxy-substituted allylic acetates.

Results and Discussion

Initial reactions were carried out using allylic acetate **1** (Scheme 3). Unfortunately, this substrate tended to give

(1) For reviews, see: (a) Lipshutz, B. H.; Sengupta, S. *Org. React.* **1992**, *41*, 135−631. (b) Lipshutz, B. H. In *Organometallics in Synthesis*; Schlosser, M., Ed.; Wiley: Chichester, 1994; pp 283−382.

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(3) For a review of enantioselective transition-metal-catalyzed allylic alkylations, see: Trost, B. M.; Van Vranken, D. L. *Chem. Rev.* **1996**, *96*, 395−422.

(4) For an excellent discussion of the evolution of current working models, see: Gawley, R. E.; Aubé, J. *Principles of Asymmetric Synthesis*; Pergamon: New York, 1996; Chapter 4.

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(8) (a) Nakamura, E.; Sekiya, K.; Arai, M.; Aoki, S. *J. Am. Chem. Soc.* **1989**, *111*, 3091−3093. (b) Arai, M.; Kawasujji, T.; Nakamura, E. *J. Org. Chem.* **1993**, *58*, 5121−5129.

(9) Recent reviews: Cowden, C. I.; Paterson, I. *Org. React.* **1997**, *51*, 1−200. (b) Denmark, S. E.; Stavenger, R. A. *Acc. Chem. Res.* **2000**, *33*, 432−440.

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Scheme 3

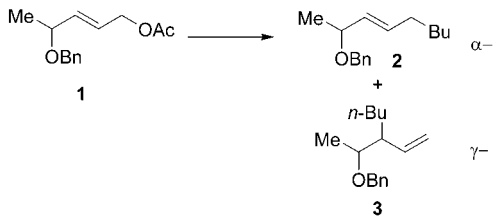
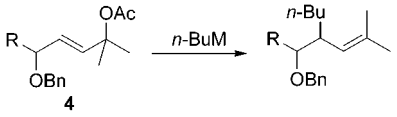


Table 1. Reactions of *n*-Butylcopper Reagents with Acetates 4[a]



a: R = Me, **c**: R = *i*-Pr

entry	substrate	reagent	yield[b]	dr[c]
1	**4a**	*n*-Bu_2CuLi	40	76:24
2	**4a**	*n*-BuMgBr/CuCN	72	86:14
3	**4c**	*n*-BuMgBr/CuI	37	79:21
4	**4c**	*n*-BuMgBr/CuBr	12	84:16
5	**4c**	*n*-BuMgBr/CuCN	80	98.5:1.5

[a] Entry 1 was carried out with 2.0 equiv of reagent in ether; entries 2−5 employed 2.0 equiv of *n*-BuMgBr with 10 mol % CuX. [b] Percentage isolated yields of chromatographed products. [c] Determined by GC/MS of crude products.

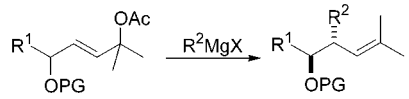
considerable amounts of α- (S_N2) substitution. Thus, reaction of **1** with *n*-Bu_2CuLi afforded exclusively **2**, while *n*-BuMgBr/cat. CuI gave a mixture of regioisomers (**2**:**3** = 60:40). With *n*-BuMgBr/cat. CuCN, **3** was the major product (**2**:**3** = 4:96, dr = 75:25), but it was clear that primary acetates would have problems with regioselectivity.

To circumvent the problem of regioselectivity, we designed a series of substrates **4** containing tertiary acetates that, for steric reasons, would be unlikely to undergo S_N2 substitutions. A survey of *n*-butylcopper reagents (Table 1) showed that these substrates do not give competing α-substitution, but other side reactions, including elimination, occurred in many cases so that low yields of γ-substitution products were obtained. Fortunately, one of the reagents surveyed, *n*-BuMgBr/cat. CuCN, gave reasonably clean reactions with good diastereoselectivities (entries 2, 5).

We therefore reacted a series of reagents RMgX/CuCN with substrates **4**−**6** to examine the scope of this reaction (Table 2). For the benzyloxy-substituted substrates, the following generalizations may be made: (1) Reactions are generally clean and good isolated yields of substitution products were obtained. (2) The stereoselectivity depends on the structure of **4** such that larger R^1 groups show higher selectivities. (3) For most of the Grignard reagents examined, reasonable levels of selectivity could be obtained when R^1 is a methyl group or an *n*-alkyl group. (4) When R^1 is branched (e.g., *i*-Pr in **4c**), stereoselectivities of >98:2 were consistently obtained. (5) Addition of an *i*-Pr group tends to give the lowest selectivities.

A comparison of other protecting groups (MOM and TBS) showed that there is only a small dependence of selectivity on the protecting group (compare Table 2, entries 5, 15, and 17; entries 9, 16, 18). In reactions of α-alkoxy carbonyl compounds with organometallic nucleophiles, reversal of stereoselectivity is often observed with coordinating (e.g., OBn, OMOM) versus noncoordinating

Table 2. Copper Cyanide Mediated Reactions of Grignard Reagents with δ-Alkoxy-Substituted Allylic Acetates[a]



4-6

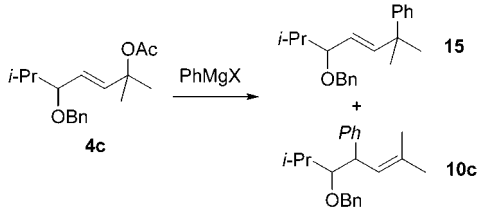
4: PG = Bn, **5**: PG = TBS, **6**: PG = MOM

a: R^1 = Me, **b**: R^1 = *n*-Bu, **c**: R^1 = *i*-Pr

entry	acetate	R_2	product	yield[b]	dr[c]
1	**4a**	*n*-Bu	**7a**	72	86:14
2	**4a**	*i*-Pr	**8a**	70	74:26
3	**4a**	*t*-Bu	**9a**	73	83:17
4[d]	**4a**	Ph	**10a**	64	79:21
5	**4b**	*n*-Bu	**7b**	89	90:10
6	**4b**	*i*-Pr	**8b**	85	79:21
7	**4b**	*t*-Bu	**9b**	89	87:13
8[d]	**4b**	Ph	**10b**	68	88:12
9	**4c**	*n*-Bu	**7c**	80	98.5:1.5
10	**4c**	*i*-Pr	**8c**	76	98.5:1.5
11	**4c**	*t*-Bu	**9c**	94	>99:1
12[d]	**4c**	Ph	**10c**	75	>99:1
13[d]	**4c**	Me	**11c**	77	98:2
14[d]	**4c**	Et	**12c**	84	99:1
15	**5b**	*n*-Bu	**13b**	89	80:20
16	**5c**	*n*-Bu	**13c**	81	95:5
17	**6b**	*n*-Bu	**14b**	85	83:17
18	**6c**	*n*-Bu	**14c**	88	98:2

[a] Reactions were carried out using 2.0 equiv of RMgX with 10 mol % CuCN in ether. [b] Percentage isolated yields of chromatographed products. The diastereomers were not chromatographically separable except for compound **9a**. [c] Determined by GC/MS of crude products. [d] 50 mol % CuCN was used.

Scheme 4



(e.g., OTBS) alkoxy groups.[4] The relatively minor variations in selectivity observed here suggest that coordination is not a major factor in determining stereoselectivity in these S_N2' reactions.

Introduction of a phenyl group proved to be somewhat problematic. With acetate **4c** and PhMgCl under the usual reaction conditions (10 mol % CuCN), the major product isolated was alkene **15** with <10% **10c** isolated (Scheme 4). After considerable experimentation, it was found that the formation of **15** could be suppressed almost completely by using PhMgBr with 50 mol % CuCN. Under these conditions, **10c** could be isolated in good yields with very high diastereoselectivity. Application to acetates **4a** and **4b** gave **10a** and **10b**, respectively, in good yields, although with only moderate selectivities. In experiments with PhMgBr, increasing the amount of CuCN used increased the yield of substitution products but did not affect the diastereoselectivities. With other Grignard reagents, varying the amount of CuCN from 10 to 50 mol % had little effect on either yields or selectivities.

In all cases the major diastereomer produced had the anti-configuration. This relationship was established by conversion of some of the products **7**−**12** to 1,3-diols

Scheme 5

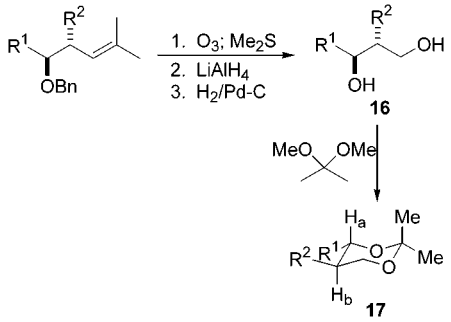
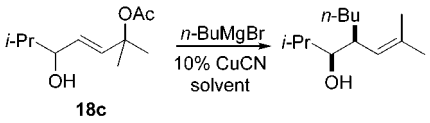


Table 3. Effect of Solvent on the Reaction of 18c with *n*-BuMgBr[a]



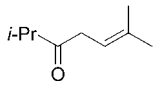
18c

entry	solvent	yield[b]	dr[c]
1	Et_2O	57	75:25
2	THF	45	59:41
3	CH_2Cl_2	46	92:8
4	toluene	48	70:30
5	TBME	44	72:28

[a] Reactions were carried out using 2.0 equiv of RMgX with 10 mol % CuCN. [b] Percentage isolated yields of chromatographed products. [c] Determined by GC/MS of crude products.

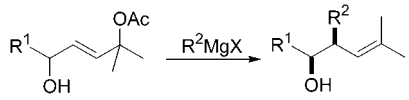
(Scheme 5), cyclization of these diols to 1,3-dioxanes, and examination of their ^{1}H NMR spectra.[10] For all of the dioxanes so prepared, the major isomer showed a large ax−ax coupling ($J_{ab} \approx 10-11$ Hz), consistent with an anti-configuration for the diols. As well, an X-ray crystal structure of the bis(3,5-dinitrobenzoate) of the diol derived from **9c** clearly showed anti-stereochemistry. Other products are tentatively assigned anti-stereochemistry based on trends in ^{1}H NMR spectra (the anti-diastereomers show vinyl proton doublets 0.10−0.35 ppm downfield of the corresponding signals from the syn-isomer) and GC elution profiles (anti elutes before syn on a DB5 column).

Having established that alkoxy groups could effectively participate in 1,2-asymmetric induction such that anti-isomers are preferentially formed, we searched for substrates that might provide the syn-isomer selectively. The only group examined that gave syn selectivity was a hydroxyl group (Table 3). Using acetate **18c** as a probe substrate, it was found that the stereoselectivity was strongly solvent dependent. For example, with *n*-BuMgBr, selectivities varied from 17 to 84% de depending on the solvent used. The best selectivity was observed with CH_2Cl_2 as solvent.[11] Unfortunately, while reactions in CH_2Cl_2 using 10 mol % CuCN gave high selectivities, other side reactions occurred, resulting in modest yields. Similar side reactions occurred under the same conditions in other solvents. With substrate **18c**, the major side-product isolated was **19c**, which probably arises from competing E_2 elimination of the acetoxy group.



19c

Table 4. Copper Cyanide Mediated Reactions of Grignard Reagents with δ-Hydroxy-Substituted Allylic Acetates[a]



18

a: R^1 = Me, **b**: R^1 = *n*-Bu, **c**: R^1 = *i*-Pr

entry	acetate	R_2	product	yield[b]	dr[c]
1	**18a**	*n*-Bu	**20a**	69	89:11
2[d]	**18a**	*n*-Bu	**20a**	76	80:20
3	**18a**	*i*-Pr	**21a**	71	79:21
4	**18a**	*t*-Bu	**22a**	79	97:3
5	**18b**	*n*-Bu	**20b**	84	93:7
6[d]	**18b**	*n*-Bu	**20b**	68	86:14
7	**18b**	*i*-Pr	**21b**	68	86:14
8	**18b**	*t*-Bu	**22b**	83	>99:1
9	**18c**	*n*-Bu	**20c**	79	88:12
10	**18c**	*i*-Pr	**21c**	68	56:44
11	**18c**	*t*-Bu	**22c**	83	94:6

[a] Reactions were carried out using 2.5 equiv of RMgX with 50 mol % CuCN in CH_2Cl_2 unless otherwise noted. [b] Percentage isolated yields of chromatographed products. [c] Determined by GC/MS of crude product. [d] Reaction in Et_2O using 10 mol % CuCN.

On the basis of our previous experience with acetate **4c** and reactions with PhMgX, the quantity of CuCN was increased to 50 mol %. This change effectively eliminated the formation of other side products, and the desired substitution product could be isolated in good yield. Other substrates and Grignard reagents were allowed to react under these new conditions (Table 4). In general, good yields of products were isolated and good to excellent selectivities were observed for transfer of *n*-butyl or *tert*-butyl groups. Variable selectivities were obtained for transfer of an *i*-Pr group. Lower than expected selectivities were also sometimes observed for the transfer of an *i*-Pr group to benzyloxy-substituted substrates (Table 1, entries 2, 6). It is not obvious why this anomalous behavior is observed. For the transfer of an *n*-Bu group, reactions were also run in ether (Table 2, entries 1 vs 2, 5 vs 6) and, as expected on the basis of previous results, higher selectivities were consistently obtained in CH_2Cl_2.

The anti-selectivity observed with δ-alkoxy substituents (e.g., MOMO, BnO, TBSO) may be rationalized using Felkin-Anh/Cram arguments as previously noted by Nakamura.[8] The syn-selectivity observed with a hydroxyl group (which is likely to exist as a Mg alkoxide under the reaction conditions) suggests that coordination to the reagent is taking place so that the alkyl group is delivered from the same face. A similar reversal of stereoselectivity has been previously observed in zirconium-catalyzed ethylmagnesiation of alkenes.[12] The ability of hydroxyl groups to control stereoselectivity in a multitude of reactions (e.g., epoxidations, Simmons−Smith, hydrogenations) is well-documented.[13]

(10) Isaac, M. B.; Chan, T. H. *Tetrahedron Lett.* **1995**, 36, 8957−8960.

(11) Recently, enantioselective S_N2' reactions of Grignard reagents in CH_2Cl_2 have been reported: Alexakis, A.; Malan, C.; Lea, L.; Benhaim, C.; Fournioux, X. *Synlett* **2001**, 927−930.

(12) Hoveyda, A. H.; Xu, Z. *J. Am. Chem. Soc.* **1991**, *113*, 5079−5080.

(13) For a review of substrate-directed reactions, see: Hoveyda, A. M.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307−1370.

Overall, our results suggest that this approach is a viable means of controlling stereochemistry and accessing a wide variety of stereochemically defined homoallylic alcohols that are useful synthetic intermediates (e.g., as precursors to aldol-type products). Since compounds such as **4** are readily accessible in enantiomerically enriched form,[14] this chemistry could be used for the synthesis of enantiomerically enriched compounds.

Experimental Section

General. All reactions were performed using flame-dried glassware under an argon atmosphere. Diethyl ether and THF were freshly distilled from Na/benzophenone. Dichloromethane was freshly distilled from CaH_2. Grignard reagents (EtMgBr, *n*-BuMgBr, *i*-PrMgCl, *t*-BuMgCl) were prepared in ether under standard conditions and stored in sealed bottles under argon. The titer of the reagents was determined by titration with salicylaldehyde phenylhydrazone.[15] MeMgBr and PhMgBr were used as purchased from Aldrich Chemical Co. after titration. CuBr·SMe_2 was prepared as described by Wuts[16] and purified by recrystallization from Me_2S−hexanes. Elemental analyses were performed by MHW Laboratories, Phoenix, AZ. In the ^{13}C NMR peak listings, peaks due to the major diastereomer are denoted with an asterisk (*) if signals due to both diastereomers are distinguishable.

General Procedure A: Copper Cyanide Catalyzed Grignard Reactions of Acetates 4−6. The Grignard reagents (2.0 equiv) were added slowly dropwise to a slurry of the acetate (1.0 equiv) and CuCN (0.10 equiv, unless otherwise noted) in Et_2O (1 mL/10 mg substrate) at −78 °C. The reactions were allowed to warm slowly to room temperature, after which they were quenched with 10% NH_4OH in NH_4Cl. The aqueous layers were extracted with Et_2O (3×) and the combined organic layers were dried over Na_2SO_4. An aliquot was removed for analysis by GC/MS. After the solvent was removed in vacuo, the crude alkenes were typically purified via column chromatography.

5-Benzyloxy-4-butyl-2-methyl-2-hexene (7a). General procedure A was followed using acetate **4a** (125 mg, 0.48 mmol), *n*-BuMgBr (0.35 mL, 2.71 M, 0.95 mmol), and CuCN (22 mg, 0.25 mmol). The crude oil (anti:syn = 86:14 by GC/MS analysis) was purified via column chromatography (4:1 hexane:CH_2Cl_2) to give 90 mg (72%) of a clear, colorless oil: IR (neat) 1672, 696 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.38−7.24 (5H, m), 4.99 (0.86H, d, J = 9.9 Hz), 4.88 (0.14H, d, J = 8.3 Hz), 4.60 (1H, A of AB, d, J_{obs} = 12.1 Hz), 4.48 (0.86H, B of AB, d, J_{obs} = 12.1 Hz), 4.47 (0.14H, B of AB, d, J_{obs} = 11.7 Hz), 3.45 (0.86H, qd, J = 6.9, 3.9 Hz), 3.30 (0.14H, dq, J = 6.7, 6.7 Hz), 2.43−2.34 (1H, m), 1.72 (3H, s), 1.63 (0.42H, s), 1.59 (2.58H, s), 1.32−1.21 (6H, m), 1.15 (0.42H, d, J = 6.7 Hz), 1.11 (2.58H, d, J = 6.9 Hz), 0.87 (3H, t, J = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.3; 132.5; 128.2 (2C); 127.6, 127.5* (2C); 127.3, 127.2*; 126.2; 78.7, 77.8*; 70.8, 70.6*; 44.0, 43.0*; 31.6, 30.4*; 29.9*, 29.5; 26.0; 23.0; 18.2; 17.1, 16.6*; 14.2; MS (EI) m/z (%) 260 (M^+, 0.3), 91 (100). Anal. Calcd for $C_{18}H_{28}O$: C, 83.02; H, 10.84. Found: C, 82.89; H, 10.68.

5-Benzyloxy-4-butyl-2-methyl-2-nonene (7b). General Procedure A was followed using acetate **4b** (203 mg, 0.67 mmol), *n*-BuMgBr (0.48 mL, 2.71 M, 1.3 mmol) and CuCN (8 mg, 0.09 mmol). The crude oil (anti:syn = 90:10 by GC/MS analysis) was purified via column chromatography (6:1 hexane: CH_2Cl_2) to give 178 mg (89%) of a clear, colorless oil. IR (neat) 1672, 697 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.35−7.26 (5H, m), 5.02 (0.90H, d, J = 9.5 Hz), 4.92 (0.10H, d, J = 9.6 Hz), 4.57−4.51 (2H, m), 3.29−3.16 (1H, m), 2.55−2.39 (1H, m), 1.72 (3H, s), 1.60 (3H, s), 1.62−1.12 (12H, m), 0.96−0.79 (6H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.3*, 139.0; 132.3*, 132.2; 128.2* (2C), 127.9; 127.7 (2C); 127.3; 126.5, 126.2*; 83.0, 82.7*; 71.9*, 71.8; 41.7, 41.1*; 31.5, 31.0*; 30.7; 30.0*, 29.7; 28.6*, 27.7; 26.0; 22.9 (2C); 18.4, 18.2*; 14.1 (2C); MS (EI) m/z (%) 245 (M^+ − *n*-Bu, 0.1), 95 (100). Anal. Calcd for $C_{21}H_{34}O$: C, 83.38; H, 11.33. Found: C, 83.12; H, 11.15.

5-Benzyloxy-4-butyl-2,6-dimethyl-2-heptene (7c). General procedure A was followed using acetate **4c** (198 mg, 0.68 mmol), *n*-BuMgBr (0.51 mL, 2.71 M, 1.4 mmol), and CuCN (7 mg, 0.08 mmol). The crude oil (anti:syn = 98.5:1.5 by GC/MS analysis) was purified via column chromatography (10:1 hexane:CH_2Cl_2) to give 158 mg (80%) of a clear, colorless oil: IR (neat) 1672, 696 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.37−7.24 (5H, m), 5.17 (1H, d, J = 10.2 Hz), 4.61−4.53 (2H, m), 3.00 (1H, dd, J = 7.3, 3.6 Hz), 2.53−2.43 (1H, m), 1.79 (1H, dqq, J = 7.3, 6.7, 6.7 Hz), 1.71 (3H, s), 1.60 (3H, s), 1.50−1.08 (6H, m), 0.99 (3H, d, J = 6.7 Hz), 0.89 (3H, d, J = 6.7 Hz), 0.87 (3H, t, J = 6.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.4, 131.6, 128.2 (2C), 127.6 (2C), 127.2, 126.0, 88.8, 75.0, 41.2, 33.1, 31.5, 29.8, 26.0, 23.0, 20.0, 18.9, 18.4, 14.2; MS (EI) m/z (%) 245 (M^+ − *i*-Pr, 0.6), 91 (100). Anal. Calcd for $C_{20}H_{32}O$: C, 83.27; H, 11.18. Found: C, 83.51; H, 10.91.

5-Benzyloxy-4-isopropyl-2-methyl-2-hexene (8a). General procedure A was followed using acetate **4a** (202 mg, 0.77 mmol), *i*-PrMgCl (0.66 mL, 2.30 M, 1.5 mmol), and CuCN (7 mg, 0.08 mmol). The crude oil (anti:syn = 74:26 by GC/MS analysis) was purified via column chromatography (3:1 hexane: CH_2Cl_2) to give 132 mg (70%) of a clear, colorless oil: IR (neat) 1674, 697 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.60−7.24 (5H, m), 5.13 (0.74H, d, J = 10.3 Hz), 4.90 (0.26H, d, J = 10.7 Hz), 4.62 (1H, A of AB, d, J_{obs} = 11.9 Hz), 4.44 (0.26H, B of AB, d, J_{obs} = 11.6 Hz), 4.40 (0.74H, B of AB, J_{obs} = 11.9 Hz), 3.68 (0.74H, qd, J = 6.2, 3.8 Hz), 3.45 (0.26H, dq, J = 8.6, 6.1 Hz), 2.31 (0.26H, ddd, J = 10.7, 8.6, 4.4 Hz), 2.22−2.05 (0.26H, m), 1.98−1.90 (0.74H, m), 1.84−1.75 (0.74H, m), 1.75 (2.22H, s), 1.74 (0.78H, s), 1.63 (0.78H, s), 1.59 (2.22H, s), 1.12 (3H, d, J = 6.2 Hz), 0.88 (2.22H, d, J = 6.6 Hz), 0.82 (3H, d, J = 6.7 Hz), 0.77 (0.78H, d, J = 6.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.5*, 139.2; 133.9, 132.8*; 128.4, 128.3* (2C); 127.9, 127.6*; 127.5*, 127.3 (2C); 124.4; 76.1, 75.9*; 70.8, 70.7*; 51.1*, 49.8; 29.3, 27.8; 26.3*, 26.2; 21.5, 21.4*; 20.5*, 18.7; 18.5*, 17.5; 17.8*, 17.2; MS (EI) m/z (%) 231 (M^+ − Me, 0.2), 91 (100). Anal. Calcd for $C_{17}H_{26}O$: C, 82.87; H, 10.64. Found: C, 82.68; H, 10.50.

5-Benzyloxy-4-isopropyl-2-methyl-2-nonene (8b). General procedure A was followed using acetate **4b** (205 mg, 0.67 mmol), *i*-PrMgCl (0.80 mL, 1.65 M, 1.3 mmol), and CuCN (7 mg, 0.08 mmol). The crude oil (anti:syn = 79:21 by GC/MS analysis) was purified via column chromatography (6:1 hexane: CH_2Cl_2) to give 166 mg (85%) of a clear, colorless oil: IR (neat) 1674, 696 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.34−7.26 (5H, m), 5.16 (0.79H, d, J = 10.8 Hz), 4.90 (0.21H, d, J = 10.9 Hz), 4.57 (0.79H, A of AB, d, J_{obs} = 11.6 Hz), 4.55 (0.21H, A of AB, d, J_{obs} = 11.2 Hz), 4.49 (0.21H, B of AB, d, J_{obs} = 11.2 Hz), 4.47 (0.79H, B of AB, d, J_{obs} = 11.6 Hz), 3.51−3.45 (0.79H, m), 2.45−2.35 (0.21H, m), 2.10−2.00 (1H, m), 1.80 (1H, dqq, J = 6.8, 6.8, 6.8 Hz), 1.74 (3H, s), 1.62 (0.63H, s), 1.59 (2.37H, s), 1.43−1.20 (6H, m), 0.91−0.77 (9H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.4*, 139.0; 133.3, 132.5*; 128.1*, 128.0 (2C); 127.5*, 127.4 (2C); 127.2; 124.2*, 122.7; 80.6*, 79.8; 71.7*, 71.3; 48.4*, 47.0; 31.7*, 30.7; 29.2; 28.2*, 27.0; 26.2, 26.0*; 23.0; 21.5*, 21.4; 20.5; 18.5; 14.1; MS (EI) m/z (%) 197 (M^+ − Bn, 0.2), 91 (100). Anal. Calcd for $C_{20}H_{32}O$: C, 83.27; H, 11.18. Found: C, 83.51; H, 10.99.

5-Benzyloxy-4-isopropyl-2,6-dimethyl-2-heptene (8c). General procedure A was followed using acetate **4c** (206 mg, 0.71 mmol), *i*-PrMgCl (0.83 mL, 1.65 M, 1.4 mmol), and CuCN (8 mg, 0.09 mmol). The crude oil (anti:syn = 98.5:1.5 by GC/MS analysis) was purified via column chromatography (6:1 hexane:CH_2Cl_2) to give 148 mg (76%) of a clear, colorless oil: IR (neat) 1673, 696 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.36−7.24 (5H, m), 5.24 (1H, d, J = 10.8 Hz), 4.58 (2H, m), 3.22 (1H, dd, J = 6.8, 3.8 Hz), 2.17 (1H, ddd, J = 10.8, 7.2, 3.8 Hz), 1.88−1.76 (2H, m), 1.73 (3H, s), 1.59 (3H, s), 0.98 (3H, d, J = 6.7 Hz), 0.95 (3H, d, J = 6.6 Hz), 0.90 (3H, d, J = 6.7 Hz), 0.83 (3H, d, J = 6.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.5, 132.2, 128.1 (2C), 127.4 (2C), 127.1, 124.2, 86.2, 74.7, 47.5, 31.4,

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29.3, 26.1, 21.7, 19.9 (2C), 18.6 (2C); MS (EI) *m*/z (%) 231 (M^+ − *i*-Pr, 0.6), 91 (100). Anal. Calcd for $C_{19}H_{30}O$: C, 83.15; H, 11.02. Found: C, 83.40; H, 10.81.

5-Benzyloxy-4-*tert*-butyl-2-methyl-2-hexene (9a). General procedure A was followed using acetate **4a** (200 mg, 0.76 mmol), *t*-BuMgCl (1.5 mL, 1.03 M, 1.6 mmol), and CuCN (7 mg, 0.08 mmol). The crude oil (anti:syn = 83:17 by GC/MS analysis) was purified via column chromatography (6:1 hexane:CH_2Cl_2) to give 144 mg of ***anti*-9a** and 32 mg of ***syn*-9a** (total 176 mg, 89%) as clear, colorless oils: IR (neat) 1672, 696 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) ***anti*-9a**, δ 7.34−7.26 (5H, m), 5.41 (1H, d, J = 11.0 Hz), 4.60 (1H, A of AB, d, J_{obs} = 11.7 Hz), 4.38 (1H, B of AB, J_{obs} = 11.7 Hz), 3.90 (1H, qd, J = 6.2, 1.6 Hz), 1.92 (1H, dd, J = 11.0, 1.6 Hz), 1.78 (3H, s), 1.59 (3H, s), 1.08 (3H, d, J = 6.2 Hz), 0.91 (9H, s); ***syn*-9a**, δ 7.36−7.24 (5H, m), 5.06 (1H, d, J = 11.0 Hz), 4.51 (2H, m), 3.62 (1H, qd, J = 6.1, 5.0 Hz), 2.40 (1H, dd, J = 11.0, 5.0 Hz), 1.75 (3H, s), 1.65 (3H, s), 1.13 (3H, d, J = 6.1 Hz), 0.90 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) ***anti*-9a**, δ 139.3, 133.0, 128.1 (2C), 127.4, 127.1 (2C), 122.3, 75.0, 70.2, 53.5, 34.2, 28.8 (3C), 26.3, 18.6, 18.3; ***syn*-9a**, δ 139.1, 132.8, 128.2 (2C), 127.7 (2C), 127.3, 123.2, 76.0, 70.1, 51.7, 33.4, 28.7 (3C), 26.2, 18.5, 18.1; MS (EI) *m*/z (%) both diastereomers: 91 (100). Anal. Calcd for $C_{18}H_{28}O$: C, 83.02; H, 10.84. Found: C, 83.29; H, 10.61.

5-Benzyloxy-4-*tert*-butyl-2-methyl-2-nonene (9b). General procedure A was followed using acetate **4b** (202 mg, 0.66 mmol), *t*-BuMgCl (1.3 mL, 1.03 M, 1.3 mmol), and CuCN (6 mg, 0.07 mmol). The crude oil (anti:syn = 87:13 by GC/MS analysis) was purified via column chromatography (10:1 hexane:CH_2Cl_2) to give 180 mg (89%) of a clear, colorless oil: IR (neat) 1671, 696 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.34−7.26 (5H, m), 5.41 (0.87H, d, J = 11.0 Hz), 5.10 (0.13H, d, J = 9.2 Hz), 4.58 (0.87H, A of AB, d, J_{obs} = 11.6 Hz), 4.55 (0.13H, A of AB, d, J_{obs} = 10.2 Hz), 4.43 (0.87H, B of AB, d, J_{obs} = 11.6 Hz), 4.39 (0.13H, B of AB, d, J_{obs} = 10.2 Hz), 3.62−3.58 (0.87H, m), 3.51−3.45 (0.13H, m), 2.48−2.44 (0.13H, m), 2.06 (0.87H, d, J = 11.0 Hz), 1.77 (2.61H, s), 1.74 (0.39H, s), 1.64 (0.39H, s), 1.59 (2.61H, s), 1.42−1.15 (6H, m) 0.91 (9H, s), 0.91 (3H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.3*, 138.9; 132.9*, 132.7; 128.2, 128.1* (2C); 127.4*, 127.3 (2C); 127.1; 123.0, 122.5*; 80.1, 79.9*; 70.6; 50.3*, 49.5; 34.1*, 33.2; 32.1*, 32.0; 28.9*, 28.8 (3C); 28.7*, 28.1; 26.3; 23.0*, 22.8; 18.5*, 18.4; 14.2, 14.1*; MS (EI) *m*/z (%) 245 (M^+ − *t*-Bu, 0.1), 91 (100). Anal. Calcd for $C_{21}H_{34}O$: C, 83.38; H, 11.33. Found: C, 83.52; H, 11.42.

5-Benzyloxy-4-*tert*-butyl-2,6-dimethyl-2-heptene (9c). General procedure A was followed using acetate **4c** (499 mg, 1.7 mmol), *t*-BuMgCl (3.3 mL, 1.03 M, 3.4 mmol), and CuCN (17 mg, 0.19 mmol) to give 464 mg (94%) of a clear, colorless oil. The resulting product was sufficiently clean and did not require purification: IR (neat) 1671, 696 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.38−7.22 (5H, m), 5.49 (1H, d, J = 10.8 Hz), 4.61 (1H, A of AB, d, J_{obs} = 11.5 Hz), 4.57 (1H, B of AB, d, J_{obs} = 11.5 Hz), 3.39 (1H, d, J = 6.9 Hz), 2.17 (1H, d, J = 10.8 Hz), 1.87 (1H, dqq, J = 6.9, 6.9, 6.8 Hz), 1.74 (3H, s), 1.59 (3H, s), 0.98 (3H, d, J = 6.9 Hz), 0.91 (9H, s), 0.87 (3H, d, J = 6.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.5, 131.7, 128.1 (2C), 127.0 (3C), 123.6, 84.3, 72.3, 48.7, 34.4, 32.2, 28.7 (3C), 26.3, 19.4, 19.0, 18.8; MS (EI) *m*/z (%) 245 (M^+ − *i*-Pr, 0.3), 91 (100). Anal. Calcd for $C_{20}H_{32}O$: C, 83.27; H, 11.18. Found: C, 83.09; H, 11.15.

5-Benzyloxy-2-methyl-4-phenyl-2-hexene (10a). General procedure A was followed using acetate **4a** (202 mg, 0.77 mmol), PhMgBr (0.54 mL, 2.82 M, 1.5 mmol), and CuCN (37 mg, 0.41 mmol). The crude oil (anti:syn = 79:21 by ^1H NMR analysis) was purified via column chromatography (3:2 hexane:CH_2Cl_2) to give 139 mg (64%) of a clear, colorless oil: IR (neat) 1672, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.31−7.18 (10H, m), 5.58 (0.79H, d, J = 9.4 Hz), 5.42 (0.21H, d, J = 9.3 Hz), 4.57 (0.79H, A of AB, d, J_{obs} = 12.0 Hz), 4.48 (0.21H, A of AB, d, J_{obs} = 11.6 Hz), 4.43 (0.79H, B of AB, d, J_{obs} = 12.0 Hz), 4.27 (0.21H, B of AB, d, J_{obs} = 11.6 Hz), 3.75−3.65 (1H, m), 3.62−3.55 (1H, m), 1.75 (2.37H, s), 1.72 (0.63H, s), 1.65 (0.63H, s), 1.61 (2.37H, s), 1.20 (0.63H, d, J = 5.9 Hz), 1.09 (2.37H, d, J = 6.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.4; 138.9*, 138.6; 133.1*, 132.9; 128.8*, 128.7 (2C); 128.2 (2C); 128.1*, 128.0 (2C); 127.5 (2C); 127.2; 125.9*, 125.8; 124.8; 80.0, 79.9*; 71.0; 50.9, 50.5*; 26.0; 18.2; 17.9*, 17.5; MS (EI) *m*/z (%) 173 (M^+ − OBn, 4), 91 (100). Anal. Calcd for $C_{20}H_{24}O$: C, 85.67; H, 8.63. Found: C, 85.50; H, 8.48.

5-Benzyloxy-2-methyl-4-phenyl-2-nonene (10b). General procedure A was followed using acetate **4b** (201 mg, 0.66 mmol), PhMgBr (0.47 mL, 2.82 M, 1.3 mmol), and CuCN (31 mg, 0.34 mmol). The crude oil (anti:syn = 88:12 by ^1H NMR analysis) was purified via column chromatography (4:1 hexane:CH_2Cl_2) to give 145 mg (68%) of a clear, colorless oil: IR (neat) 1671, 1093, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.33−7.18 (10H, m), 5.63 (0.88H, d, J = 9.4 Hz), 5.47 (0.12H, J = 9.5 Hz), 4.44 (1H, A of AB, d, J_{obs} = 11.3 Hz), 4.38 (1H, B of AB, d, J_{obs} = 11.3 Hz), 3.71 (1H, dd, J = 9.5, 5.1 Hz), 3.60−3.54 (1H, m), 1.76 (2.64H, s), 1.72 (0.36H, s), 1.64 (0.36H, s), 1.61 (2.64H, s), 1.47−1.35 (2H, m), 1.35−1.20 (4H, m), 0.88−0.82 (3H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.7*, 143.5; 138.9*, 138.6; 133.2*, 132.7; 128.5, 128.3* (2C); 128.2 (2C); 128.1 (2C); 128.0, 127.9* (2C); 127.7, 127.3*; 125.9; 124.8, 124.4*; 83.6; 72.5, 72.4*; 49.0, 48.3*; 32.3*, 31.8; 28.0*, 27.7; 26.1, 26.0*; 22.8; 18.2; 14.1; MS (EI) *m*/z (%) 265 (M^+ − *n*-Bu, 0.1), 91 (100). Anal. Calcd for $C_{23}H_{30}O$: C, 85.66; H, 9.38. Found: C, 85.72; H, 9.48.

5-Benzyloxy-2,6-dimethyl-4-phenyl-2-heptene (10c). General procedure A was followed using acetate **4c** (201 mg, 0.69 mmol), PhMgBr (0.49 mL, 2.82 M, 1.4 mmol), and CuCN (32 mg, 0.36 mmol). The crude oil (only one isomer by GC/MS analysis) was purified via column chromatography (6:1 hexane:CH_2Cl_2) to give 160 mg (75%) of a clear, colorless oil: IR (neat) 1671, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32−7.16 (10H, m), 5.67 (1H, d, J = 9.6 Hz), 4.32 (1H, A of AB, d, J_{obs} = 10.7 Hz), 4.13 (1H, B of AB, d, J_{obs} = 10.7 Hz), 3.78 (1H, dd, J = 9.6, 5.6 Hz), 3.31 (1H, dd, J = 5.6, 5.6 Hz), 1.73 (3H, s), 1.72−1.66 (1H, m), 1.59 (3H, s), 0.97 (3H, d, J = 7.5 Hz), 0.92 (3H, d, J = 7.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.0, 139.0, 132.9, 128.4 (2C), 128.3 (2C), 128.1 (2C), 127.9 (2C), 127.3, 125.9, 124.2, 89.6, 75.2, 47.1, 31.4, 26.0, 20.1, 18.2, 18.0; MS (EI) *m*/z (%) 265 (M^+ − *i*-Pr, 0.3), 91 (100). Anal. Calcd for $C_{22}H_{28}O$: C, 85.66; H, 9.15. Found: C, 85.80; H, 9.12.

5-Benzyloxy-2,4,6-trimethyl-2-heptene (11c). General procedure A was followed using acetate **4c** (152 mg, 0.52 mmol), MeMgBr (0.35 mL, 2.94 M, 1.0 mmol), and CuCN (26 mg, 0.29 mmol). The crude oil (anti:syn = 98:2 by GC/MS analysis) was purified via column chromatography (6:1 hexane:CH_2Cl_2) to give 99 mg (77%) of a clear, colorless oil: IR (neat) 1672, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.36−7.24 (5H, m), 5.21 (1H, d, J = 9.6 Hz), 4.61 (1H, A of AB quartet, d, J_{obs} = 11.2 Hz), 4.56 (1H, B of AB quartet, d, J_{obs} = 11.2 Hz), 2.93 (1H, dd, J = 6.5, 4.6 Hz), 2.69−2.63 (1H, m), 1.80 (1H, qqd, J = 6.9, 6.7, 6.5 Hz), 1.69 (3H, s), 1.61 (3H, s), 0.99 (3H, d, J = 6.9 Hz), 0.98 (3H, d, J = 6.7 Hz), 0.90 (3H, d, J = 6.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.4, 130.5, 128.2 (2C), 127.5 (2C), 127.3, 127.2, 89.6, 75.1, 35.6, 31.3, 25.9, 20.0, 19.0, 18.3, 17.9; MS (EI) *m*/z (%) 246 (M^+, 0.03), 91 (100). Anal. Calcd for $C_{17}H_{26}O$: C, 82.89; H, 10.64. Found: C, 82.55; H, 10.60.

5-Benzyloxy-4-ethyl-2,6-dimethyl-2-heptene (12c). General procedure A was followed using acetate **4c** (151 mg, 0.52 mmol), EtMgBr (0.55 mL, 1.89 M, 1.0 mmol), and CuCN (24 mg, 0.26 mmol). The crude oil (anti:syn = 99:1 by GC/MS analysis) was purified via column chromatography (6:1 hexane:CH_2Cl_2) to give 114 mg (84%) of a clear, colorless oil: IR (neat) 1672, 1097, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.37−7.24 (5H, m), 5.16 (1H, d, J = 10.3 Hz), 4.60−4.55 (2H, m), 3.02 (1H, dd, J = 7.4, 3.6 Hz), 2.42−2.37 (1H, m), 1.79 (1H, dqq, J = 7.4, 6.8, 6.7 Hz), 1.72 (3H, s), 1.61 (3H, s), 1.55−1.48 (1H, A of AB, m), 1.41−1.35 (1H, B of AB, m), 0.98 (3H, d, J = 6.7 Hz), 0.88 (3H, d, J = 6.8 Hz), 0.84 (3H, t, J = 7.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.4, 131.9, 128.2 (2C), 127.5 (2C), 127.2, 125.5, 88.8, 75.0, 43.1, 31.6, 26.3, 26.0, 19.9, 19.0, 18.4, 12.2; MS (EI) *m*/z (%) 217 (M^+ − *i*-Pr, 0.7), 91 (100). Anal. Calcd for $C_{18}H_{28}O$: C, 83.02; H, 10.84. Found: C, 83.21; H, 10.76.

4-Butyl-5-*tert*-butyldimethylsilyloxy-2-methyl-2-nonene (13b). General procedure A was followed using acetate **5b** (149 mg, 0.45 mmol), *n*-BuMgBr (0.51 mL, 2.77 M, 1.4 mmol), and CuCN (6 mg, 0.07 mmol). The crude oil (anti:syn

= 81:19 by ^{1}H NMR analysis) was purified via column chromatography (hexane) to give 130 mg (89%) of a clear, colorless oil: IR (neat) 1672 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.94 (0.81H, d, J = 10.0 Hz), 4.90 (0.19H, d, J = 10.0 Hz), 3.51−3.45 (0.81H, m), 3.46 (0.19H, dt, J = 5.5, 5.5 Hz), 2.28−2.21 (1H, m), 1.69 (0.57H, s), 1.68 (2.43H, s), 1.58 (3H, s), 1.46−0.96 (12H, m), 0.88−0.83 (6H, m), 0.87 (9H, s), 0.02 (2.43, s), 0.01 (3.57, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.9*, 131.2; 127.6, 126.5*; 76.0, 75.4*; 43.6, 43.2*; 34.4, 33.6*; 30.7, 30.6*; 30.1*, 29.7; 28.3*, 27.0; 26.1; 26.0 (3C); 23.0 (2C); 18.4*, 18.3; 18.2, 18.1*; 14.2 (2C); −4.2, −4.3*; −4.4*, −4.5; MS (EI) m/z (%) 312 (M^+ − 15, 1), 73 (100). Anal. Calcd for $C_{20}H_{42}OSi$: C, 73.54; H, 12.96. Found: C, 73.35; H, 12.78. The major isomer was identified as the anti-isomer by desilylation and comparison of GC retention times with **20b**.

4-Butyl-5-*tert*-butyldimethylsilyloxy-2,6-dimethyl-2-heptene (13c). General procedure A was followed using acetate **5c** (200 mg, 0.63 mmol), *n*-BuMgBr (0.47 mL, 2.71 M, 1.3 mmol), and CuCN (8 mg, 0.09 mmol). The crude oil (anti:syn = 95:5 by GC/MS analysis) was purified via column chromatography (hexane) to give 160 mg (81%) of a clear, colorless oil: IR (neat) 1672 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.06 (1H, d, J = 10.0 Hz), 3.29 (1H, dd, J = 5.1, 3.8 Hz), 2.35−2.26 (1H, m), 1.74−1.64 (1H, m), 1.68 (3H, s), 1.56 (3H, s), 1.39−1.05 (6H, m), 0.88 (9H, s), 0.87−0.79 (9H, m), 0.00 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 130.6, 127.2, 80.4, 42.2, 33.1, 32.3, 30.0, 26.2 (3C), 26.1, 23.1, 20.2, 18.6, 18.5, 18.4, 14.2, −3.7 (2C); MS (EI) m/z (%) 312 (M^+, 0.1), 187 (100). Anal. Calcd for $C_{19}H_{40}OSi$: C, 73.00; H, 12.90. Found: C, 72.84; H, 12.83. The major isomer was identified as the anti-isomer by desilylation followed by benzylation and comparison of GC retention times with **7c**.

4-Butyl-5-methoxymethyl-2-methyl-2-nonene (14b). General procedure A was followed using acetate **6b** (150 mg, 0.58 mmol), *n*-BuMgBr (0.43 mL, 2.71 M, 1.17 mmol), and CuCN (7 mg, 0.08 mmol). The crude oil (anti:syn = 83:17 by GC/MS analysis) was purified via column chromatography (1:1 hexane:CH_2Cl_2) to afford 126 mg (85%) of a clear, colorless oil: IR (neat) 1675 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.98 (0.83H, d, J = 8.9 Hz), 4.95 (0.17H, d, J = 8.9 Hz), 4.70−4.62 (2H, m), 3.47−3.32 (1H, m), 3.39 (3H, s), 2.50−2.33 (1H, m), 1.72 (3H, s), 1.62 (3H, s), 1.58−1.03 (12H, m), 0.90−0.86 (6H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 132.8*, 132.5; 126.1, 125.9*; 96.2*, 95.9; 81.5; 55.8, 55.6*; 41.7*, 41.6; 31.5*, 31.4; 31.2, 31.0*; 30.1*, 29.8; 28.4*, 27.7; 26.1; 23.1; 23.0; 18.4, 18.3; 14.2 (2C); MS (EI) m/z (%) 167 (49), 81 (100). Anal. Calcd for $C_{16}H_{32}O_2$: C, 74.94; H, 12.58. Found: C, 75.12; H, 12.70. The major isomer was identified as the anti-isomer by comparison with the MOM ether prepared from **20b**.

4-Butyl-5-methoxymethyl-2,6-dimethyl-2-heptene (14c). General procedure A was followed using acetate **6c** (150 mg, 0.61 mmol), *n*-BuMgBr (0.45 mL, 2.71 M, 1.22 mmol), and CuCN (6 mg, 0.07 mmol). The crude oil (anti:syn = 97.5:2.5 by GC/MS analysis) was purified via column chromatography (1:1 hexane:CH_2Cl_2) to afford 130 mg (88%) of a clear, colorless oil: IR (neat) 1663, 1149, 1096, 1042 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.08 (1H, d, J = 9.4 Hz), 4.69 (1H, A of AB, d, J_{obs} = 6.8 Hz), 4.64 (1H, B of AB, d, J_{obs} = 6.8 Hz), 3.40 (3H, s), 3.13 (1H, dd, J = 6.7, 3.8 Hz), 2.51−2.36 (1H, m), 1.83 (1H, qqd, J = 6.8, 6.7, 6.7 Hz), 1.72 (3H, s), 1.61 (3H, s), 1.48−1.10 (6H, m), 0.94 (3H, d, J = 6.8 Hz), 0.91 (3H, t, J = 6.8 Hz), 0.90 (3H, d, J = 6.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.8, 126.0, 98.2, 88.0, 56.0, 40.8, 32.9, 31.1, 29.7, 26.0, 23.0, 19.9, 18.7, 18.4, 14.2; MS (EI) m/z (%) 167 (78), 69 (100). Anal. Calcd for $C_{15}H_{30}O_2$: C, 74.33; H, 12.47. Found: C, 74.50; H, 12.58. The major isomer was identified as the anti-isomer by comparison with the MOM ether prepared from **20c**.

(*E*)-5-Benzyloxy-2,6-dimethyl-2-phenyl-3-heptene (15). General procedure A was followed using acetate **4c** (199 mg, 0.68 mmol), PhMgBr (0.49 mL, 2.82 M, 1.4 mmol), and CuCN (7 mg, 0.07 mmol) in THF. The crude oil was purified via column chromatography (6:1 hexane:CH_2Cl_2) to give 182 mg (86%) of **15** as a clear, colorless oil: IR (neat) 1663, 698 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37−7.17 (10H, m), 5.82 (1H, d, J = 15.8 Hz), 5.40 (1H, dd, J = 15.8, 8.5 Hz), 4.62 (1H, A of AB, d, J_{obs} = 12.1 Hz), 4.37 (1H, B of AB, d, J_{obs} = 12.1 Hz), 3.44 (1H, dd, J = 8.5, 7.4 Hz), 1.84 (1H, dqq, J = 7.4, 6.8, 6.7 Hz), 1.45 (3H, s), 1.43 (3H, s), 0.98 (3H, d, J = 6.7 Hz), 0.90 (3H, d, J = 6.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.7, 144.6, 139.1, 128.2 (2C), 128.1 (2C), 127.6 (2C), 127.2, 126.1 (2C), 125.8, 125.4, 85.6, 69.9, 40.6, 33.0, 28.8 (2C), 19.0, 18.6; MS (EI) m/z (%) 265 (M^+ − *i*-Pr, 3), 91 (100). Anal. Calcd for $C_{22}H_{28}O$: C, 85.66; H, 9.15. Found: C, 85.80; H, 8.96.

General Procedure B: Grignard Additions to Hydroxy Acetates 18. The desired Grignard reagent (2.5 equiv) was added to a slurry of the acetate (1.0 equiv) and CuCN (0.5 equiv) in CH_2Cl_2 (1 mL/10 mg substrate) at −78 °C. The reaction was allowed to warm to −25 °C, where it was kept until completion (monitored by TLC, 2−12 h). Quench and workup of the reaction mixture was performed as outlined previously.

2,6-Dimethyl-5-hepten-3-one (19c).[17] This was the main side product from reactions of **18c** with Grignard reagents using 10 mol % CuCN: IR (neat) 1714, 1677 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.30 (1H, t, J = 7.0 Hz), 3.17 (2H, d, J = 7.0 Hz), 2.66 (1H, septet, J = 6.9 Hz), 1.75 (3H, s), 1.63 (3H, s), 1.11 (6H, d, J = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.2, 135.2, 116.1, 40.2 (2C), 25.7, 18.2 (2C), 18.0; MS (EI) m/z (%) 140 (M^+, 13), 71 (100).

3-Butyl-5-methyl-4-hexen-2-ol (20a). General procedure B was followed using hydroxy acetate **18a** (76 mg, 0.44 mmol), *n*-BuMgBr (0.39 mL, 2.77 M, 1.1 mmol), and CuCN (20 mg, 0.23 mmol). The crude oil (anti:syn = 11:89 by GC/MS analysis) was purified via column chromatography (30% Et_2O in hexane) to afford 52 mg (69%) of a clear, colorless oil: IR (neat) 3369 (br), 1675 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.90 (1H, d, J = 10.2 Hz), 3.66 (0.89H, dq, J = 6.3, 6.3 Hz), 3.53 (0.11H, dq, J = 6.3, 6.3 Hz), 2.40−2.30 (0.89H, m), 2.22−2.09 (0.11H, m), 1.77 (0.33H, s), 1.75 (2.67H, s), 1.65 (3H, s), 1.60−1.21 (7H, m), 1.18 (0.33H, d, J = 6.3 Hz), 1.11 (2.67H, d, J = 6.3 Hz), 0.90 (3H, t, J = 7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.5; 125.9, 124.9*; 71.2*, 70.7; 46.4, 45.4*; 31.5*, 31.2; 29.6; 26.1*, 26.0; 22.9*, 22.8; 20.3, 19.9*; 18.5; 14.1; MS (EI) m/z (%) 170 (M^+, 0.1), 69 (100). Anal. Calcd for $C_{11}H_{22}O$: C, 77.58; H, 13.02. Found: C, 77.46; H, 12.98.

4-Butyl-2-methyl-2-nonen-5-ol (20b). General procedure B was followed using hydroxy acetate **18b** (100 mg, 0.47 mmol), *n*-BuMgBr (0.42 mL, 2.77 M, 1.2 mmol), and CuCN (22 mg, 0.25 mmol). The crude oil (anti:syn = 7:93 by GC/MS analysis) was purified via column chromatography (15% Et_2O in hexane) to afford 83 mg (84%) of a clear, colorless oil: IR (neat) 3368 (br), 1675 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.94 (0.07H, d, J = 11.2 Hz), 4.90 (0.93H, d, J = 10.2 Hz), 3.48−3.34 (1H, m), 2.42−2.30 (1H, m), 1.77 (0.21H, s), 1.74 (2.79H, s), 1.64 (3H, s), 1.56 (1H, br s), 1.51−1.08 (12H, m), 0.90 (3H, t, J = 6.8 Hz), 0.88 (3H, t, J = 7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.1, 133.8*; 125.6*, 125.4; 75.3*, 74.6; 44.5*, 44.4; 34.2, 33.6*; 31.5, 31.1*; 29.6; 28.3*; 28.0; 26.0; 22.9; 22.7; 18.5, 18.4*; 14.1 (2C); MS (EI) m/z (%) 194 (M^+ − H_2O, 7), 95 (100).

4-Butyl-2,6-dimethyl-5-hepten-3-ol (20c). General procedure B was followed using hydroxy acetate **18c** (101 mg, 0.50 mmol), *n*-BuMgBr (0.45 mL, 2.77 M, 1.3 mmol), and CuCN (24 mg, 0.27 mmol). The crude oil (anti:syn = 12:88 by GC/MS analysis) was purified via column chromatography (7.5% Et_2O in hexane) to afford 73 mg (73%) of a clear, colorless oil: IR (neat) 3401 (br), 1676 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.98 (0.12H, d, J = 10.2 Hz), 4.86 (0.88H, d, J = 10.1 Hz), 3.18 (1H, dd, J = 7.5, 4.0 Hz), 2.36−2.26 (1H, m), 1.80−1.69 (1H, m), 1.76 (0.36H, s), 1.72 (2.64H, s), 1.65 (0.36H, s), 1.62 (2.64H, s), 1.44 (1H, br s), 1.34−1.04 (6H, m), 0.95 (3H, d, J = 6.9 Hz), 0.90 (3H, t, J = 7.1 Hz), 0.85 (3H, d, J = 6.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.8, 132.1*; 126.6*, 125.4; 80.0*, 79.0; 42.0*, 41.6; 31.8, 30.8*; 30.4*, 30.2; 29.4; 25.9; 23.0; 20.3*, 20.1; 18.4; 16.4, 15.6*; 14.2; MS (EI) m/z (%) 198 (M^+, 0.1), 69 (100). Anal. Calcd for $C_{13}H_{26}O$: C, 78.72; H, 13.21. Found: C, 78.58; H, 13.24.

(17) Kosugi, M.; Hagiwara, I.; Sumiya, T.; Migita, T. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 242−246.

3-Isopropyl-5-methyl-4-hexen-2-ol (21a). General procedure B was followed using hydroxy acetate **18a** (101 mg, 0.58 mmol), *i*-PrMgCl (0.89 mL, 1.64 M, 1.5 mmol), and CuCN (26 mg, 0.29 mmol). The crude oil (anti:syn = 21:79 by GC/MS analysis) was purified via column chromatography (25% Et_2O in hexane) to afford 64 mg (71%) of a clear, colorless oil: IR (neat) 3368 (br), 1674 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.05 (0.21H, d, J = 10.7 Hz), 4.93 (0.79H, J = 10.7 Hz), 3.86 (0.79H, qd, J = 6.9, 6.3 Hz), 3.77 (0.21H, dq, J = 6.4, 6.2 Hz), 2.22 (0.79H, ddd, J = 10.7, 6.8, 6.3 Hz), 2.05−1.95 (0.21H, m), 1.87−1.70 (1H, m), 1.80 (0.63H, s), 1.77 (2.37H, s), 1.65 (3H, s), 1.51 (1H, br s), 1.18 (0.63H, d, J = 6.2 Hz), 1.10 (2.37H, d, J = 6.9 Hz), 0.89 (3H, d, J = 6.9 Hz), 0.84 (2.37H, d, J = 6.9 Hz), 0.82 (0.63H, d, J = 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.8, 135.6*; 122.1*, 122.0; 68.5; 51.9*, 51.5; 28.8, 28.7*; 26.2; 21.7, 20.9*; 20.8, 19.9*; 19.0; 18.5*, 17.8; MS (EI) m/z (%) 156 (M^+, 0.2), 69 (100). Anal. Calcd for $C_{10}H_{20}O$: C, 76.86; H, 12.90. Found: C, 76.75; H, 12.78.

4-Isopropyl-2-methyl-2-nonen-5-ol (21b). General procedure B was followed using hydroxy acetate **18b** (101 mg, 0.47 mmol), *i*-PrMgCl (0.71 mL, 1.64 M, 1.2 mmol), and CuCN (22 mg, 0.24 mmol). The crude oil (anti:syn = 14:86 by GC/MS analysis) was purified via column chromatography (20% Et_2O in hexane) to afford 63 mg (68%) of a clear, colorless oil: IR (neat) 3368 (br), 1673 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.07 (0.14H, d, J = 10.7 Hz), 4.91 (0.86H, d, J = 10.7 Hz), 3.58 (1H, ddd, J = 6.8, 6.8, 2.1 Hz), 2.19 (0.86H, ddd, J = 10.7, 6.8, 6.8 Hz), 2.06 (0.14H, ddd, J = 10.7, 6.8, 6.0 Hz), 1.87 (1H, dqq, J = 6.8, 6.7, 6.7 Hz), 1.79 (0.42H, s), 1.76 (2.58H, s), 1.64 (3H, s), 1.58−1.05 (7H, m), 0.92 (3H, t, J = 7.0 Hz), 0.91 (0.42H, d, J = 6.7 Hz), 0.88 (2.58H, d, J = 6.7 Hz), 0.83 (2.58H, J = 6.7 Hz), 0.82 (0.42H, d, J = 6.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.8, 135.1*; 122.5*, 122.3; 72.5*, 72.1; 50.7*, 50.0; 34.7, 33.4*; 28.8, 28.5*; 28.3*, 27.9; 26.2; 22.8, 22.7*; 21.5, 21.0*; 18.6; 18.5; 14.1; MS (EI) m/z (%) 180 ($M^+ - H_2O$, 4), 69 (100). Anal. Calcd for $C_{13}H_{26}O$: C, 78.72; H, 13.21. Found: C, 78.36; H, 13.01.

4-Isopropyl-6-methyl-5-hepten-2-ol (21c). General procedure B was followed using hydroxy acetate **18c** (100 mg, 0.50 mmol), *i*-PrMgCl (0.76 mL, 1.64 M, 1.3 mmol), and CuCN (23 mg, 0.25 mmol). The crude oil (anti:syn = 44:56 by GC/MS analysis) was purified via column chromatography (15% Et_2O in hexane) to afford 63 mg (68%) of a clear, colorless oil: IR (neat) 3401 (br), 1673 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.09 (0.50H, d, J = 9.3 Hz), 4.84 (0.50H, d, J = 10.7 Hz), 3.41 (0.50H, dd, J = 9.8, 2.8 Hz), 3.35 (0.50H, dd, J = 5.9, 5.9 Hz), 2.30 (0.50H, ddd, J = 10.7, 9.8, 2.8 Hz), 2.21−2.09 (1H, m), 1.82−1.68 (1.50H, m), 1.77 (1.50H, s), 1.72 (1.50 H, s), 1.64 (1.50H, s), 1.63 (1.50H, s), 1.44 (0.50H, br s), 1.43 (0.50H, br s), 1.00−0.74 (12H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.3, 133.4, 122.3, 121.8, 76.8, 76.4, 47.2, 47.1, 30.4, 30.2, 28.7, 27.9, 26.2, 26.1, 21.6, 21.4, 20.8, 19.9, 18.7, 18.6, 18.5, 16.8, 16.0, 13.9; MS (EI) m/z (%) 184 (M^+, 0.1), 69 (100). Anal. Calcd for $C_{12}H_{24}O$: C, 78.20; H, 13.12. Found: C, 78.28; H, 12.93.

3-*tert*-Butyl-5-methyl-4-hexen-2-ol (22a). General procedure B was followed using hydroxy acetate **18a** (101 mg, 0.59 mmol), *t*-BuMgBr (1.5 mL, 0.99 M, 1.5 mmol), and CuCN (27 mg, 0.30 mmol). The crude oil (anti:syn = 3:97 by GC/MS analysis) was purified via column chromatography (25% Et_2O in hexane) to afford 79 mg (79%) of a clear, colorless oil: IR (neat) 3392 (br), 1672 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.12 (1H, d, J = 11.2 Hz), 4.03−3.87 (1H, m), 2.34 (1H, dd, J = 11.2, 4.8 Hz), 1.79 (3H, s), 1.66 (3H, s), 1.34 (1H, d, J = 8.4 Hz), 1.14 (3H, d, J = 6.4 Hz), 0.92 (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.5, 121.6, 68.4, 54.3, 33.3, 28.6 (3C), 26.3, 21.2, 18.4; MS (EI) m/z (%) 170 (M^+, 0.1), 57 (100). Anal. Calcd for $C_{11}H_{22}O$: C, 77.58; H, 13.02. Found: C, 77.60; H, 13.25.

4-*tert*-Butyl-2-methyl-2-nonen-5-ol (22b). General procedure B was followed using hydroxy acetate **18b** (99 mg, 0.46 mmol), *t*-BuMgBr (1.2 mL, 0.99 M, 1.2 mmol), and CuCN (21 mg, 0.24 mmol). The crude oil was purified via column chromatography (12.5% Et_2O in hexane) to afford 83 mg (83%) of a clear, colorless oil that was homogeneous by GC/MS and ^1H NMR analysis: IR (neat) 3436 (br), 1671 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.08 (1H, d, J = 11.2 Hz), 3.79−3.63 (1H, m), 2.31 (1H, dd, J = 11.2, 5.0 Hz), 1.77 (3H, s), 1.65 (3H, s), 1.55−1.13 (6H, m), 1.20 (1H, d, J = 8.2 Hz), 0.92 (9H, s), 0.90 (3H, t, J = 6.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.7, 122.5, 72.8, 54.2, 34.7, 33.5, 28.9 (3C), 28.5, 26.4, 22.8, 18.4, 14.2; MS (EI) m/z (%) 194 ($M^+ - H_2O$, 5), 57 (100). Anal. Calcd for $C_{14}H_{28}O$: C, 79.18; H, 13.29. Found: C, 79.32; H, 13.31.

4-*tert*-Butyl-6-methyl-5-hepten-3-ol (22c). General procedure B was followed using hydroxy acetate **18c** (100 mg, 0.50 mmol), *t*-BuMgBr (1.3 mL, 0.99 M, 1.3 mmol), and CuCN (22 mg, 0.25 mmol). The crude white solid (anti:syn = 6:94 by GC/MS analysis of the derived acetates) was purified via column chromatography (10% Et_2O in hexane) to afford 82 mg (83%) of a white, crystalline solid (mp = 45−47 °C): IR (KBr) 3415 (br), 1385 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.26 (0.06H, d, J = 10.9 Hz), 4.88 (0.94H, d, J = 11.0 Hz), 3.49 (0.94H, dd, J = 9.0, 7.0 Hz), 3.41 (0.06H, dd, J = 8.6, 7.6 Hz), 2.17 (0.06H, dd, J = 10.9, 8.6 Hz), 2.08 (0.94H, dd, J = 11.0, 9.0 Hz), 1.79−1.72 (1H, m), 1.60 (3H, s), 1.55 (3H, s), 1.09 (1H, d, J = 7.0 Hz), 0.93 (9H, s), 0.93−0.89 (3H, m), 0.72 (3H, d, J = 6.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.4, 131.5*; 124.5*, 121.0; 77.3, 76.9*; 51.6*, 48.9; 34.2*, 34.0; 33.3, 30.8*; 29.0*, 28.5 (3C); 26.4, 26.0*; 20.9*, 19.8; 19.0, 18.6*; 13.6; MS (EI) m/z (%) 198 (M^+, 0.03), 57 (100). Anal. Calcd for $C_{13}H_{26}O$: C, 78.72; H, 13.21. Found: C, 79.02; H, 13.07.

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Supporting Information Available: Experimental procedures for the preparation of compounds **1**−**6** and **18**, spectral data for compounds **1**−**6** and **18**, details for GC analysis of diastereomer ratios, and determination of relative configurations. This material is available free of charge via the Internet at http://pubs.acs.org.

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