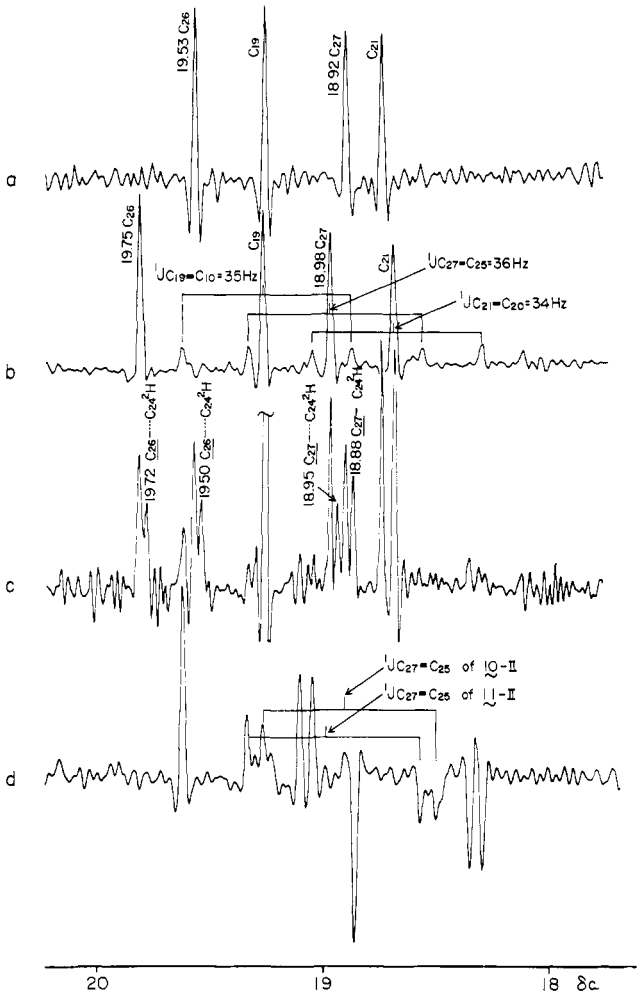
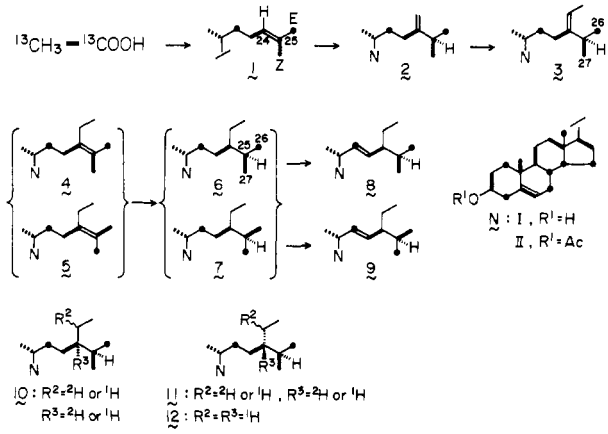


Figure 1. ^{1}H-complete-decoupled ^{13}C NMR spectra, region of C-26 and C-27 of (a) clionasteryl acetate (**12**-II), (b) sitosteryl acetate (**6**-II) from [1,2-^{13}C]acetate in tissue cultures of *P. peruviana*, (c) a mixture of [^{13}C,24,28-^{2}H]sitosteryl acetate (**10**-II) and [^{13}C,24,28-^{2}H]clionasteryl acetate (**11**-II) derived from **3**-II which was biosynthesized from [1,2-^{13}C]acetate in *P. peruviana*, and (d) the same sample determined using Freeman's "INADEQUATE" pulse sequence (ref 8). The following ^{13}C–^{13}C coupled signals are observed in d: C_{19} (δ_C 19.24, J_{CC} = 35), C_{21} (δ_C 18.77, J_{CC} = 34), and C_{27} (δ_C 18.92, J_{CC} = 36) coupled to C_{10} (δ_C 36.46), C_{20} (δ_C 36.15), and C_{25} (δ_C 28.84), respectively, for **11**-II; C_{19} (δ_C 19.24 J_{CC} = 35), C_{21} (δ_C 18.72, J_{CC} = 34), and C_{27} (δ_C 18.98, J_{CC} = 36) coupled to C_{10} (δ_C 36.46), C_{20} (δ_C 36.03), and C_{25} (δ_C 29.06), respectively, for **10**-II. The singly labeled C_{26} signals (δ_C 19.53 for **11**-II, δ_C 19.75 for **10**-II) were suppressed in d.

Scheme I



the signal assignments of C-26 and C-27 of sitosteryl and clionasteryl acetates are shown in Table I.

Table I. ^{13}C NMR Spectral Data for C-26 and C-27 of Phytosterols from [1,2-^{13}C]Acetate in Tissue Cultures of Some Higher Plants[a] [10]

	3-II[7]	6-II	12-II	8-II	8A-II	2-II
C-26 δ_C	20.93, s	19.75, s	19.53[b]	21.01, s	21.02, s	21.79, s
C-27 δ_C	21.01,	18.98,	18.92[b]	18.92,	18.93,	21.93,
($^1J_{CC}$, Hz)	d (36)	d (36)		d (36)	d (36)	d (36)

[a] 3-II and 2-II: Isofucosteryl acetate and 24-methylenecholesteryl acetate from *Physalis peruviana*. 6-II: Sitosteryl acetate from *Physalis peruviana, Dioscorea tokoro,*[4] and *Isodon japonicus.*[5] 8-II: Stigmasteryl acetate from *Physalis peruviana, Bupleurum falcatum,* and *Dioscorea tokoro.* 12-II: Clionasteryl acetate. 8A-II: α-Spinasteryl acetate (Δ^7 isomer of 8-II) from *Bupleurum falcatum.* [b] These assignments were reversed in ref 4, 11, 12, and 13.

We examined the labeling patterns of C-26 and C-27 of several typical sterols, sitosterol (**6**-I), stigmasterol (**8**-I), α-spinasterol (**8A**-I), and 24-methylenecholesterol (**2**-I), biosynthesized from [1,2-^{13}C]acetate in cell cultures of some higher plants (see Table I[10]). In all cases, C-26 (*pro-R* methyl group at C-25) predominantly originated from C-2 of MVA and C-27 (*pro-S* methyl group) from C-6.

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Registry No. 2-I, 474-63-5; **3**-I, 481-14-1; **6**-I, 83-46-5; **8**-I, 83-48-7; **8A**-I, 481-18-5; **12**-I, 83-47-6.

(10) Carbon-13 NMR spectra were recorded on a Varian XL-200 NMR spectrometer in a 10-mm spherical cell at 23 °C at 0.02–0.2 M in $CDCl_3$. Typical FT measurement conditions: spectral width, 9058 Hz; pulse width, 6 μs (45°); acquisition time, 1.766 s; number of transients, 70K. Accuracies of δ_C and J_{CC} are within 0.02 ppm and 1 Hz, respectively.

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(12) Koizumi, N.; Fujimoto, Y.; Takeshita, T.; Ikekawa, N. *Chem. Pharm. Bull.* **1979**, *27*, 38–42.
(13) Wright, J. L. C. *Phytochemistry* **1981**, *20*, 2403–2405.

Novel Silicon-Promoted Cyclialkylation of Alkenylmetal Derivatives

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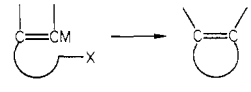
Cyclization of alkenylmetals via cyclialkylation (eq 1) is a



(1)

potentially useful but largely untested methodology.[2] We disclose herein two such reactions in which silicon plays subtle but critical roles. A particularly noteworthy feature of these reactions is that the cis arrangement of the two cyclizing groups, i.e., M and X, that might seem a requisite, either is unimportant or can readily be attained under the cyclization conditions.

In our recent study of the effects of hetero substituents on the Zr-catalyzed carbometalation of alkynes,[3] 1-(trimethylsilyl)-4-bromo-1-butyne (**1b**) was treated with Me_3Al (2 equiv) in the

(1) On leave from Ube Industries, Ltd., Ube, Japan.
(2) For cyclialkylation of aryllithiums, see: Parham, W. E.; Bradsher, C. K. *Acc. Chem. Res.* **1982**, *15*, 300.
(3) (a) For a review of this reaction, see: Negishi, E. *Pure Appl. Chem.* **1981**, *53*, 2333. (b) Rand, C. L.; Van Horn, D. E.; Moore, M. W.; Negishi, E. *J. Org. Chem.* **1981**, *46*, 4093.

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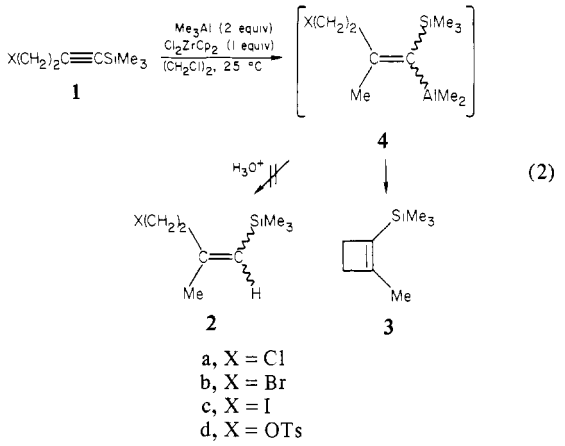
presence of 1 equiv of Cl_2ZrCp_2 (Cp = η^5-C_5H_5) at 25 °C. The reaction did not give the expected carbometalation-protonolysis product **2b**. Instead, it produced within 6 h a cyclic product **3**[4] in 92% yield (eq 2). At no time was there any indication for the

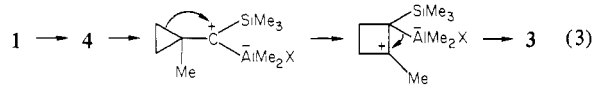


1 4 2 3 (2)

a, X = Cl
b, X = Br
c, X = I
d, X = OTs

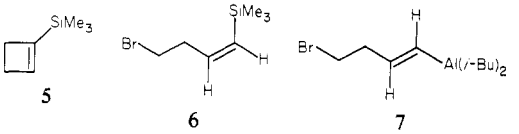
formation of **2b** upon protonolysis of the reaction mixture. The corresponding chloride **1a** and iodide **1c** also produce **3** in 80–100% yields within 24 h, their reactivity being roughly comparable with that of **1b**. The corresponding tosylate reacts more sluggishly, giving **3** in ca. 30% yield after 24 h.

Formation of cyclobutenes via cyclialkylation of alkenylmetals appears to be unprecedented. In addition, the reaction displays a few unexpected features. First, alkylation of alkenylalanes with primary alkyl halides does not occur under comparable conditions.[5] Second, although the Zr-catalyzed carboalumination of alkynylsilanes appears to give *E* and *Z* mixtures,[6] at least 50% of the presumed intermediates **4** must be "wrong" isomers for a σ-type cyclization. On the other hand, the reaction may involve interaction between the π orbital and the C–Br bond, but direct formation of a four-membered ring by a π-type cyclization, i.e., 4-endo-trig, would be an unfavorable process.[7] These considerations and the following observations led us to propose the scheme shown in eq 3 as a likely path.



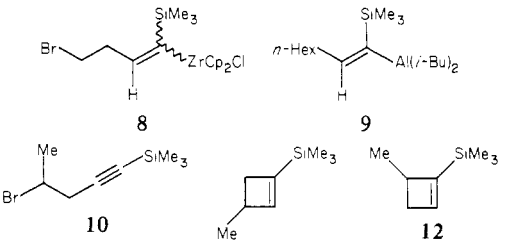
1 → 4 → → 3 (3)

The reaction of **1b** with *i*-Bu_2AlH (DIBAH) in pentane or benzene at 25 °C gives within 1–2 h 1-(trimethylsilyl)cyclobutene[4] (**5**) in 80–100% yield, indicating that neither Cl_2ZrCp_2 nor the β-Me group is essential to the cyclization reaction. The same reaction run in Et_2O does not produce **5** but only the usual hydroalumination product **6**,[4] indicating that donor solvents may prevent the reaction. Both Al and Si appear to be necessary, since neither **6** nor **7** undergoes cyclization under similar conditions.



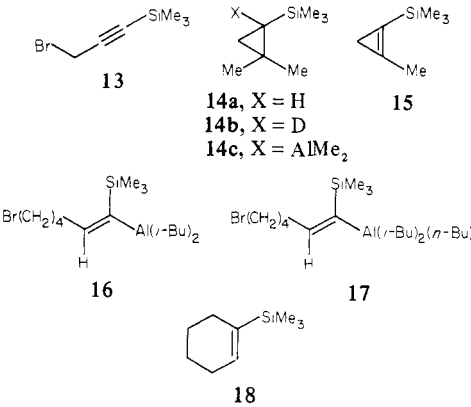
5 6 7

Hydrozirconation[8] of **1b** with Cl(H)$ZrCp_2$ in benzene for 12 h at 25 °C gives **5** only in 10% yield. Examination of the reaction mixture by ^{1}H NMR clearly indicates the formation of **8** as an *E* and *Z* mixture in 80–90% yield. As expected, its treatment with $AlCl_3$ (1.1 equiv) in CH_2Cl_2 at O °C produces **5** in 84% yield, indicating that hydrometalation or carbometalation products can be intermediates for the cyclic products. It is also worth noting that there is no detectable reaction between **9** and homoallyl bromide. Finally, the intermediacy of cyclopropylcarbinyl derivatives is supported by the reaction of **10** with DIBAH in pentane at 25 °C, which produces **11**[4] in 80% yield, the yield of **12**, if any, being <3%. Direct cyclization would have yielded **12** instead of **11**.



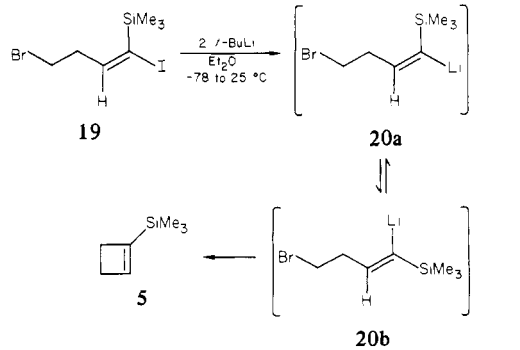
8 9 10 11 12

To explore the scope of the reaction with respect to ring size, 1-(trimethylsilyl)-3-bromo-1-propyne (**13**) was treated with Me_3Al (2 equiv) and Cl_2ZrCp_2 (1 equiv) at 25 °C. On protonolysis, **14a**[4] was obtained in 64% yield rather than the expected product **15**. Even when only 1 equiv of Me_3Al was used, **14a** (50% yield) was essentially the only cyclization product, the balance of the material being the unreacted **13**. Evidently, **15** was formed but reacted further to give **14c** at a faster rate. The formation of **14c** was indicated by its conversion into **14b** (≥95% D) upon deuterolysis. Our attempts to apply the methodology to the preparation of five- and six-membered rings have not been successful. Thus, for example, neither **16** nor its alanate **17** cyclizes to give 1-(trimethylsilyl)cyclohexene (**18**).



13 14a, X = H 14b, X = D 14c, X = $AlMe_2$ 15 16 17 18

In search for an alternate and more general method, **1b** was treated with DIBAH in Et_2O and quenched with I_2 to produce **19**. Attempts to isomerize **19** to its *Z* isomer under the influence of 5 mol % of *t*-BuLi[9] failed, but the reaction did produce a small amount of **5** (eq 4). Instead of catalyzing the desired isomeri-



19 20a 5 20b (4)

(4) All isolated products were adequately characterized by IR, ^{1}H NMR, and high-resolution mass spectrometry. Some of them were further characterized by ^{13}C NMR.

(5) Alkenylalanates are known to react, albeit somewhat sluggishly, with primary alkyl halides [(a) Baba, S.; Van Horn, D. E.; Negishi, E. *Tetrahedron Lett.* **1976**, 1927. (b) Eisch, J. J.; Damasevitz, G. A. *J. Org. Chem.* **1976**, *41*, 2214. (c) Uchide, K.; Utimoto, K.; Nozaki, H. *J. Org. Chem.* **1976**, *41*, 2215].

(6) Snider, B. B.; Karras, M. *J. Organomet. Chem.* **1979**, *179*, C37.

(7) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734, 736, 778.

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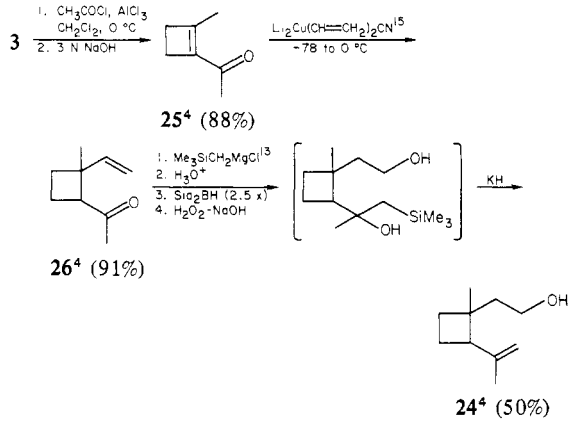
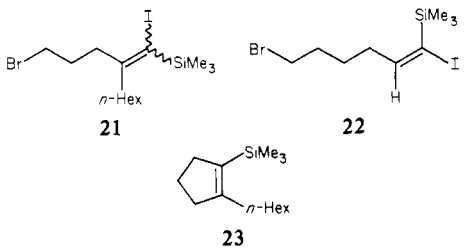
(9) Zweifel, G.; Murray, R. E.; On, H. P. *J. Org. Chem.* **1981**, *46*, 1292.

Scheme I

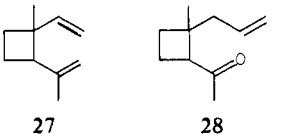


zation, the alkenyllithium **20** must have cyclized. We have indeed found that the treatment of **19** with 2 equiv of *t*-BuLi in Et_2O (−78 to 25 °C) cleanly produces **5** in 81% yield. This reaction, presumably a σ-process, has indeed turned out to be more general with respect to ring size than that described above. Thus, **21**[10] and **22**[4] were converted into **23**[4] (84%) and **18**[4] (64%), respectively,



upon treatment with *t*-BuLi (2 equiv). We then found that **23** could also be obtained cleanly in ca. 80% GLC yield by treating **21** with 1 equiv of *n*-BuLi. Although the applicability of this simplified procedure is yet to be fully explored, the above results indicate that intramolecular displacemenet of a bromide anion is much faster than intermolecular displacement of an iodide anion from *n*-BuI. It should be emphasized that (*E*)-1-iodo-6-bromo-1-hexene does not produce cyclohexene upon treatment with 2 equiv of *t*-BuLi. Nor does it produce any other monomeric product either in Et_2O or in Et_2O–THF. We conclude that polymerization must be the course of the reaction. Clearly, Si plays a critical role in promoting this cyclization as well. The precise nature of the promotion by Si is not clear. However, an increasing number of 1,1-dimetalloalkenes[11] have been shown to exhibit configurational instability presumably through interaction of the C=C bond with low-lying empty metal orbitals.

To demonstrate the synthetic utility of the above-described cyclization reactions, we synthesized grandisol[12] (**24**) from **3**, as shown in Scheme I. Although the formation of a ca. 2:1 mixture of the *Z* and *E* isomers of **26**[4] leaves room for improvement, no other significant byproduct is formed in this four-step conversion of **1** to **24** in overall 37% yield. The use of Me_3SiCH_2MgCl[13] in place of a Wittig-type reagent avoids the intermediacy of **27**, which was used as a key intermediate in one of the reported syntheses but is known to readily undergo the Cope rearrangement.[12b] The reaction of **25** with allyltrimethylsilane in the presence of $TiCl_4$[14] (−30 °C) also gives a ca. 2:1 *Z* and *E* mixture of **28**[4] in essentially quantitative yield.



27 28

Acknowledgments. We thank the National Science Foundation, the National Institutes of Health, and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support. We also thank Professor B. H. Lipshutz for helpful suggestions. Trimethylalane was kindly supplied by Ethyl Corp.

Registry No. 1a, 58435-00-0; **1b**, 69361-41-7; **1c**, 41423-29-4; **1d**, 86994-11-8; **3**, 86994-12-9; **5**, 83094-06-8; **6**, 86994-13-0; (*E*)-**8**, 86994-10-7; (*Z*)-**8**, 87038-35-5; **10**, 86994-14-1; **11**, 86994-15-2; **12**, 86994-16-3; **13**, 38002-45-8; **14a**, 86994-17-4; **14b**, 86994-18-5; **18**, 17874-17-8; **19**, 86994-20-9; **21**, 86994-22-1; **22**, 86994-23-2; **23**, 86994-24-3; **24**, 26532-22-9; **25**, 67223-99-8; (*Z*)-**26**, 30346-11-3; (*E*)-**26**, 30346-12-4; (*Z*)-**28**, 86994-21-0; (*E*)-**28**, 86994-25-4; (*E*)-1-iodo-6-bromo-1-hexene, 86994-19-6.

Supplementary Material Available: Listing of experimental data (2 pages). Ordering information is given on any current masthead page.

(10) The procedure for preparing **21** is due to Dr. J. A. Miller of our laboratory. Its details will shortly be published elsewhere.

(11) See, for example: Yoshida, T.; Negishi, E. *J. Am. Chem. Soc.* **1981**, *103*, 1276.

(12) (a) Tumlinson, J. H.; Hardee, D. D.; Gueldner, R. C.; Thompson, A. C.; Hedin, P. A.; Minyard, J. P. *Science (Washington, D.C.)* **1969**, *166*, 1010. (b) Billups, W. E.; Cross, J. H.; Smith, C. V. *J. Am. Chem. Soc.* **1973**, *95*, 3438. (c) Stork, G.; Cohen, J. F. *Ibid.* **1974**, *96*, 5270.

(13) Chan, T. H.; Chang, E. *J. Org. Chem.* **1974**, *39*, 3264.

(14) Hosomi, A.; Sakurai, H. *J. Am. Chem. Soc.* **1977**, *99*, 1673.

(15) Lipshutz, B. H.; Wilhelm, R. S.; Kozlowski, J. *Tetrahedron Lett.* **1982**, *23*, 3755.

Tungsten Carbene Complexes in Olefin Metathesis: A Cationic and Chiral Active Species

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We have briefly reported[1] the synthesis of the tungsten carbene complexes $W(CHR)(OCH_2R)_2X_2$ (R = *t*-Bu; X = Cl, Br) (**1**) and the conversion to extremely active catalysts for olefin metathesis on addition of 1 mol equiv of AlX_3. Although we formulated the predominant complex in solution under these conditions as the adduct **2a** (Scheme I, A = Al), we could not exclude the possibility that cationic species **2b**, in rapid equilibration with **2a**, was more directly involved in (i.e., within) the catalytic cycle, and we present evidence here that clarifies this important point.

Progressive addition of Ga_2Br_6 to **1** (X = Br) in halobenzene solution was followed by NMR (^1H and ^{13}C) at −35 °C and by conductivity measurements. Two regimes of behavior are observed:

(a) As *n* (the Ga/W ratio) increases from 0 to 1, all resonances[2] (^1H and ^{13}C) are displaced in a *linear* fashion. The formation of a strong 1:1 adduct ($K_1 > 100$ mol^{-1} at −35 °C) is indicated with a structure analogous to that previously proposed involving $AlBr_3$.[1]. Further the conductivity increase is small and at n = 1 a maximum of ca. 15% dissociation into **2b** is possible ($K_2 \sim 0.1$ at 20 °C). Hence the *major* species present under these conditions is indeed **2a** (Scheme I).

(1) Kress, J.; Wesolek, M.; Osborn, J. A. *J. Chem. Soc., Chem. Commun.* **1982**, 514. Note that a square-pyramidal geometry (C_s symmetry) is also consistent with these results but this does not alter the conclusions reached below.

(2) ^1H NMR (C_6D_5Br, −35 °C) for n = 0: δ 11.22 (s, 1 H, C*H*CMe$_3$, J_{W-H} = 11 Hz), 4.44 (s, 4 H, OC*H*$_2$CMe$_3$), 1.18 (s, 9 H, CHC*Me*$_3$), 0.91 (s, 18 H, OCH$_2$C*Me*$_3$). The 4.44 and 0.91 peaks are each resolved into two singlets at room temperature. For n = 1: δ 12.12 (s, 1 H, J_{W-H} = 12 Hz, C*H*CMe$_3$), 4.52, 4.49 (s, 2 H, OC*H*$_2$CMe$_3$), 1.12 (s, 9 H, CHC*Me*$_3$), 0.95, 0.90 (s, 9H, OCH$_2$C*Me*$_3$). ^{13}C NMR (ppm, C_6D_5Br, −35 °C) for n = 0: 297.2 (d, J_{C-H} = 135, J_{C-W} = 159 Hz, *C*HCMe$_3$), 92.2, 90.9 (t, O*C*H$_2$CMe$_3$), 45.3 (s, CH*C*Me$_3$), 34.2, 34.0 (s, OCH$_2$*C*Me$_3$), 31.9 (q, CHC*Me*$_3$), 26.4 (q, OCH$_2$C*Me*$_3$). For n = 1: 315.2 (d, J_{C-H} = 133, J_{C-W} = 158 Hz, *C*HCMe$_3$), 91.5, 91.3 (t, O*C*H$_2$CMe$_3$), 48.2 (s, CH*C*Me$_3$), 35.1, 35.0 (s, OCH$_2$*C*Me$_3$), 31.8 (q, CHC*Me*$_3$), 26.8, 26.4 (q, OCH$_2$C*Me*$_3$).

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