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1-Bromo-1-lithioethene: A Practical Reagent in Organic Synthesis

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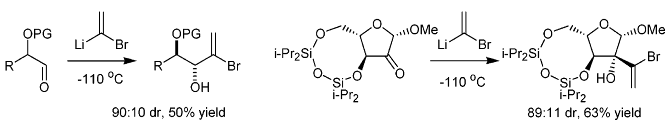

A reliable preparative scale synthesis of 1-bromo-1-lithioethene is reported. This reagent undergoes clean 1,2-addition with a range of aldehydes and ketones at −110 °C to afford the corresponding 2-bromo-1-alken-3-ols in moderate to excellent yield. Trapping with other electrophiles (acylsilanes, chlorosilanes, tributyltin chloride, iodine) cleanly provides practically useful yields of various 1-substituted 1-bromoethene products. Unexpectedly high diastereoselectivities were observed during the addition of 1-bromo-1-lithioethene to α-siloxy aldehydes (typically 10:1, Felkin−Ahn control) and protected ketopyranose and ketofuranose sugars (≥10:1, addition from the less-hindered face). The title organolithium reagent possesses relatively low basicity at low temperature, and is compatible with a variety of common protecting groups. We believe that these unusual properties of 1-bromo-1-lithioethene may originate from the specific crystalline structure of the reagent in which lithium is coordinatively saturated and thus unavailable for chelation.

Introduction

Bromoalkenes are important substrates for the construction of C−C bonds in many modern organic reactions.[1] Recently, our attention was drawn to 1-bromo-1-lithioethene (**1**) as a potential reagent for the convenient one-pot preparation of various bromoalkenes. For example, 2-bromo-1-alken-3-ols **2**, which are formal adducts of **1** with carbonyl compounds, have a considerable potential utility as synthetic building blocks. Some synthetic applications of **2** ($R^1 = H$) in Pd(0)-catalyzed coupling[2−4] as well as in a variety of other reactions[5] have already been demonstrated. The preparation of **2** ($R^1 =$ H) has previously been achieved by 1,2-addition of alkynyllithium,[2a,b] Grignard,[5d,6] or enolate[3,5e,7] nucleophiles to 2-bromoacrolein;[8] Luche reduction of 3-bromo-3-buten-2-one;[5f] ene reaction of 2-bromoacrolein;[9] or HBr addition to terminal alkyn-3-ols.[2,5b,c] However, in a number of cases, the yields of **2** were modest, and in some cases, the separation of regioisomeric products was required.[2b]

Prior to our work in this area, there were no reported approaches to *tertiary* α-bromoallylic alcohols **2** (R_1 and $R_2 \neq$ H). However, a series of closely related acetate ester[10] and ether[11] derivatives have been prepared, in moderate to poor yield and with the derivative typically being a component within a mixture of products, via the Ag^+-mediated opening of the corresponding *gem*-dibromocyclopropane in the presence of acetic acid or an alcohol. We considered that 1-bromo-1-lithioethene (**1**) might offer a convenient synthetic entry to compounds of general structure **2**.

(α-Bromoethenyl)chlorodimethylsilane (**3**) has been used as a building block in the construction of an α-bromoethenyl silyl ether that underwent intramolecular radical cyclization chemistry.[12] However, although

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(1) (a) For examples of Pd(0)-catalyzed cross-coupling, see: *Metal-Catalyzed Cross-Coupling Reactions*; de Meijere, A., Diederich, F., Eds.; Wiley-VCH: Weinheim, Germany, 2004. *Cross-Coupling Reactions – A Practical Guide*; Miyaura, N., Ed.; Topics in Current Chemistry; Springer-Verlag: Berlin, 2002; Vol. 219. *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., de Meijere, A., Eds.; Wiley-Interscience: New York, 2002; Vol. 1 and 2. (b) For examples of organocuprate coupling, see: Lipshutz, B. H.; Sengupta, S. *Org. React.* **1992**, *41*, 135−631. *Modern Organocopper Chemistry*; Krause, N., Ed.; Wiley-VCH: Weinheim, Germany, 2002. Heaney, H.; Christie, S. In *Science of Synthesis*; O'Neil, I. A., Ed.; Thieme Verlag: Stuttgart, Germany, 2004; Vol. 3, pp 305−662. *Organocopper Reagents*; Taylor, R. J. K., Ed.; IRL Press: Oxford, 1994. (c) For examples of Nozaki−Hiyama−Kishi coupling, see: Wessjohann, L. A.; Scheid, G. *Synthesis* **1999**, 1−36. Takai, K.; Nozaki, H. *Proc. Jpn. Acad., Ser. B* **2000**, *76*, 123−131. Furstner, A. *Chem. Rev.* **1999**, *99*, 991−1045. Avalos, M.; Babiano, R.; Cintas, P.; Jiminez, J. L.; Palacios, J. C. *Chem. Soc. Rev.* **1999**, *28*, 169−177.

(2) For examples of Sonogashira coupling, see: (a) Dai, W.-M.; Wu, J.; Fong, K. C.; Lee, M. Y. H.; Lau, C. W. *J. Org. Chem.* **1999**, *64*, 5062−5082. (b) Marshall, J. A.; Sehon, C. A. *Org. Synth.* **1999**, *76*, 263−270. (c) Marshall, J. A.; DuBay, W. J. *J. Org. Chem.* **1994**, *59*, 1703−1708. (d) Marshall, J. A.; DuBay, W. J. *J. Org. Chem.* **1993**, *58*, 3435−3443. (e) Marshall, J. A.; Sehon, C. A. *Org. Synth.* **1999**, *76*, 263−270. (f) McDonald, F. E.; Schultz, C. C. *J. Am. Chem. Soc.* **1994**, *116*, 9363−9364.

(3) For an example of the intramolecular Heck reaction, see: Toyota, M.; Nishikawa, Y.; Fukumoto, K. *Tetrahedron* **1994**, *50*, 11153−11166.

(4) For an example of bromohydroxylation/amination en route to α-methylene-γ-lactams, see: Mori, M.; Chiba, K.; Okita, M.; Kayo, I.; Ban, Y. *Tetrahedron* **1985**, *41*, 375−385.

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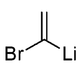

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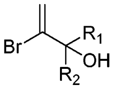

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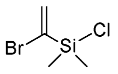

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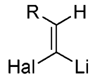

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reasonable yields and selectivities were observed with this reagent, the preparation of **3** required a three-step synthesis, and the utility of the method was limited by the low hydrolytic stability of the intermediate silyl ether required for its application in radical cyclization chemistry. We anticipated that a range of more stable α-bromoethenyl silane derivatives might be conveniently accessed from 1-bromo-1-lithioethene (**1**).

Interestingly, little is known about the use of 1-halo-1-lithioethenes (halo = Cl, Br, I) as synthetic reagents. To our knowledge, only two groups have reported the preparation of 1-chloro-[13] and 1-iodo-1-lithioethene[14] as a separate step. Other groups generated 1-chloro-1-lithioethene[15] and 1-bromo-1-lithioethene[16] in the presence of an electrophile, which severely limited the synthetic utility of the corresponding organometallic reagent. Prior to our work in this area, it appears that only a single example of trapping a 1-halo-1-lithioethene with a carbonyl compound (halo = I, 10% yield with benzophenone) has been published.[14] The apparent reason for the limited usage of 1-halo-1-lithioethenes (and other 1-halo-1-lithio-1-alkenes) in preparative synthesis is their thermal instability, which is especially pronounced for compounds of general structure **4**, in which a hydrogen substituent is positioned trans to the halo substituent.[17,18]

In this paper, we demonstrate that 1-bromo-1-lithioethene (**1**) has sufficient thermal stability to serve as a useful synthetic reagent. We describe the development of a reliable preparative scale synthesis of **1** along with an exploration of its synthetic utility as a 1-bromoethenyl nucleophile for trapping a variety of electrophiles.[19]

Results and Discussion

As was reported in our preliminary communication,[19a] treatment of bromoethene with *n*-BuLi at −110 °C in the Trapp solvent mixture[20] in the presence of 0.2−0.5 equiv of LiBr allowed the clean formation of 1-bromo-1-lithioethene (**1**). Subsequent addition of carbonyl compounds led to the clean formation of the corresponding 1,2-addition adducts **2** in high yield (Table 1). These results offer the first practical entry to *tertiary* α-bromoallylic alcohols **2** (R_1 and $R_2 \neq$ H).

Unexpectedly, no products were observed that originated from possible $H_2C{=}CHLi$ formation by a competing halogen−metal exchange reaction of bromoethene. This result seems to contradict earlier observations[13,16] about the relative rates of bromine−lithium exchange versus deprotonation at an alkene sp^2 carbon using *n*-butyllithium. However, when bromoethene was treated with *tert*-butyllithium under the same conditions, a 7:3 mixture of $H_2C{=}CHLi$ and 1-bromo-1-lithioethene (**1**) was obtained, and was further characterized by electrophilic trapping with chlorotrimethylsilane (Scheme 1).

In an attempt to rationalize these observations, liquid-phase ab initio HF6-31G*/SM5.42R calculations[21] were undertaken. To define the computational task, we assumed that the base used (*n*-BuLi or *t*-BuLi) first underwent partial dissociation induced by THF. This assumption is partially supported by the observation that bromoethene was essentially unreactive toward *n*-BuLi at −110 °C in pentane solution. In addition, it was observed that the presence of more than 0.7 equiv of LiBr in the reaction mixture significantly decreased the rate of the reaction between bromoethene and *n*-BuLi. This was consistent with the participation of a relatively free carbanion in the deprotonation step. This assumption prompted us to examine direct reactions between appropriate alkyl anions and bromoethene (Table 2). To minimize complications resulting from the conforma-

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(5) As a source of functionalized vinyllithium and vinylcuprate reagents, see: Cloninger, M. J.; Overman, L. E. *J. Am. Chem. Soc.* **1999**, *121*, 1092−1093. (b) As a source of vinylstannanes, see: Han, X.; Stoltz, B. M.; Corey, E. J. *J. Am. Chem. Soc.* **1999**, *121*, 7600−7605. (c) For an example of methyldebromination with Me_4CoLi_2, see: Kauffmann, T.; Stach, D. *Chem. Ber.* **1992**, *125*, 913−922. (d) For an example of oxidation to α-bromo enones, see: Della, E. W.; Pigou, P. E. *Aust. J. Chem.* **1983**, *36*, 2261−2268. (e) For examples of dehydration to 2-bromo dienes, see: Kozikowski, A. P.; Tueckmantel, W. *J. Org. Chem.* **1991**, *56*, 2826−2837. Spangler, C. W.; Woods, G. F. *J. Org. Chem.* **1963**, *28*, 2245−2248. (f) For an example of Mitsunobu aminodehydroxylation, see: Murphy, J. A.; Scott, K. A.; Sinclair, R. S.; Martin, C. G.; Kennedy, A. R.; Lewis, N. *J. Chem. Soc., Perkin Trans. 1* **2000**, 2395−2408. (g) For an example of hydrodebromination to the corresponding allyl alcohol using Bu_3SnH/AIBN, see: Chen, C.; Crich, D. *Tetrahedron* **1993**, *49*, 7943−7954. (h) For examples of dehydrobromination to the corresponding propargyl alcohol, see: Lespieau, R. *C.R. Hebd. Seances Acad. Sci.* **1911**, *152*, 879−881. Lespieau, R. *C.R. Hebd. Seances Acad. Sci.* **1910**, *150*, 113−114. Also see ref 5c.

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(7) (a) Spangler, C. W.; Woods, G. F. *J. Org. Chem.* **1963**, *28*, 2245−2248. (b) McDonald, F. E.; Schultz, C. C. *J. Am. Chem. Soc.* **1994**, *116*, 9363−9364.

(8) Smith, A. B.; Levenberg, P. A.; Jerris, P. J.; Scarborough, R. M.; Wovkulich, P. M. *J. Am. Chem. Soc.* **1981**, *103*, 1501−1513.

(9) Barbero, A.; Cuadrado, P.; Fleming, I.; Gonzalez, A. M.; Pulido, F. J.; Rubio, R. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1657−1662.

(10) For an example of an acetate ester derivative ($R_1 = R_2 =$ Me; 50% yield), see: Sandler, S. R. *J. Org. Chem.* **1967**, *32*, 3876−3881.

(11) (a) R_1 = Me, R_2 = Me, Ph, cyclopropyl, $-CH{=}CH_2$ (45−60% yields), see: Molchanov, A. P.; Kostikov, R. R. *Russ. J. Org. Chem.* **1993**, *29*, 429−435. Sydnes, L. K.; Hemmingsen, T. H. *Acta Chem. Scand., Ser. B* **1985**, *39*, 93−102. (b) R_1 = Me, R_2 = COOH (3% yield), see: Svendsen, J. S.; Sydnes, L. K. *Acta Chem. Scand.* **1990**, *44*, 202−204.

(12) Tamao, K.; Maeda, K.; Yamaguchi, T.; Ito, Y. *J. Am. Chem. Soc.* **1989**, *111*, 4984−4985.

(13) Köbrich, G.; Flory, K. *Chem. Ber.* **1966**, *99*, 1773−1781. Köbrich, G. *Angew. Chem., Int. Ed.* **1967**, *6*, 41−52.

(14) Campos, P. J.; Sampedro, D.; Rodriguez, M. A. *Organometallics* **1998**, *17*, 5390−5396.

(15) Kasatkin, A.; Whitby, R. J. *J. Am. Chem. Soc.* **1999**, *121*, 7039−7049.

(16) Shimizu, N.; Shibata, F.; Tsuno, Y. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 777−778.

(17) Stang, P. J. *Chem. Rev.* **1978**, *78*, 383−405.

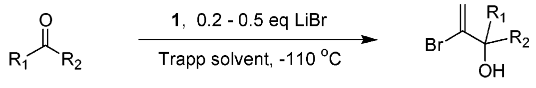
(18) Braun, M. *Angew. Chem., Int. Ed.* **1998**, *37*, 430−451.

(19) A preliminary account of some of these studies has appeared in: Novikov, Y. Y.; Sampson, P. *Org. Lett.* **2003**, *5*, 2263−2266. (b) Novikov, Y. Y.; Sampson, P. Presented at the 228th American Chemical Society National Meeting, Philadelphia, PA, Aug 22−26, 2004; ORGN 595.

(20) The Trapp mixture is THF, ether, and pentane (4:1:1 by volume). This mixture has a sufficiently low viscosity at −110 to −115 °C to provide a useful reaction medium.

(21) Xidos, J. D.; Li, J.; Zhu, T.; Hawkins, G. D.; Thompson, J. D.; Chuang, Y.-Y.; Fast, P. L.; Liotard, D. A.; Rinaldi, D.; Cramer, C. J.; Truhlar, D. G. *GAMESSPLUS*, version 3.9; University of Minnesota: Minneapolis, MN, 2003. Based on the General Atomic and Molecular Electronic Structure System (GAMESS) as described in: Schmidt, M. W.; Baldridge, K. K.; Boatz, J. A.; Elbert, S. T.; Gordon, M. S.; Jensen, J. H.; Koseki, S.; Matsunaga, N.; Nguyen, K. A.; Su, S. J.; Windus, T. L.; Dupuis, M.; Montgomery, J. A. *J. Comput. Chem.* **1993**, *14*, 1347−1363.

TABLE 1. Reaction of 1 with Simple Carbonyl Compounds $R_1C(=O)R_2$



(**2**)

entry	R_1	R_2	product	isolated yield (%)
1	Me	Me	**2a**	77
2	Me	$H_2C{=}CH-$	**2b**	78
3	Me	$H_2C{=}CH-CH_2-CH_2-$	**2c**	84
4	$-CH_2CH_2-CH_2-CH_2-CH_2-$		**2d**	85
5	$-CH{=}CH-C(Me_2)-CH_2-CH_2-$		**2e**[a]	80
6	Ph	H	**2f**	81
7	$H_2C{=}CH-$	H	**2g**[a]	74

[a] No traces of 1,4-addition products were detected.

SCHEME 1. Reaction of Bromoethene with Different Alkyllithium Bases

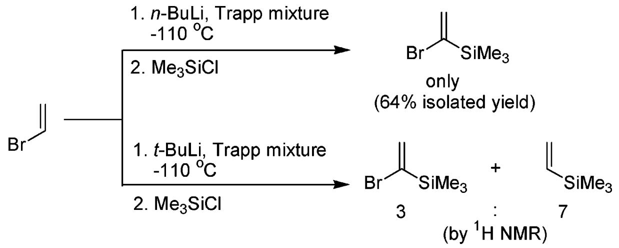
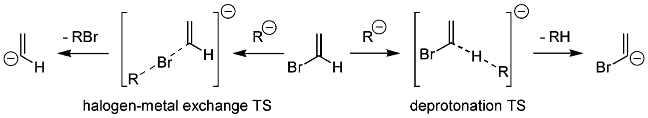


TABLE 2. Calculated Liquid-Phase Transition-State Barriers for Deprotonation and Halogen−Metal Exchange Reactions of Bromoethene in THF



entry	R^-	reaction	TS barrier (kcal/mol)[a]
1	methyl anion	deprotonation	10
2	methyl anion	halogen−metal exchange	16
3	*tert*-butyl anion	deprotonation	5
4	*tert*-butyl anion	halogen−metal exchange	5

[a] Activation energies calculated using liquid-phase ab initio HF6-31G*/SM5.42R methods.[21]

tional freedom of *n*-butyl anion, we used methyl anion as a surrogate nucleophile/base.

Computational results suggest that the formation of 1-bromo-1-lithioethene (**1**) is the kinetically favored process when methyl anion is the nucleophile (Table 2, entries 1 and 2). In contrast, the comparable calculated activation energies for deprotonation (entry 3) and halogen−metal exchange (entry 4) are consistent with the formation of a mixture of products when *tert*-butyllithium was allowed to react with bromoethene.

It is important to note that the bromine atom in **1** seems to originate almost entirely from the starting bromoethene. It is well-known that 1-halo-1-lithioalkenes are quite susceptible to nucleophilic substitution of the halogen.[17,22] However, we were not able to detect any iodine-containing organic compounds when bromoethene was deprotonated in the presence of 0.5 equiv of LiI, and was then trapped by benzaldehyde. 1-Iodo-1-lithioethene should be sufficiently stable to be trapped under these conditions,[14] indicating that no 1-iodo-1-lithioethene is generated during this reaction.

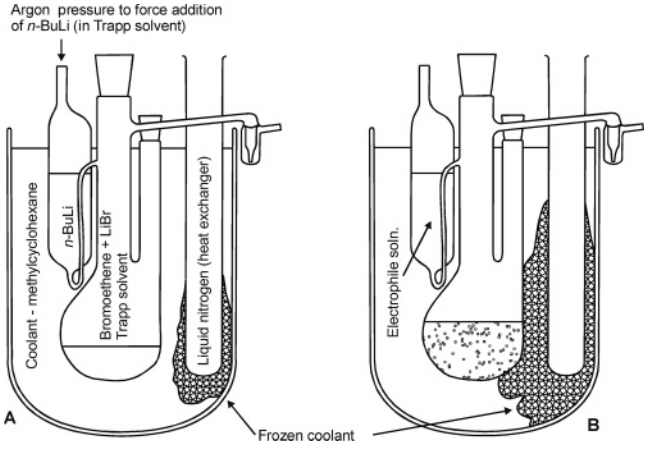


FIGURE 1. Experimental setup used for the preparation (A) and electrophilic trapping (B) of 1-bromo-1-lithioethene (**1**).

During our experimental work, we noticed that the yield of the 2-bromo-1-alken-3-ol products **2** (Table 1) was heavily dependent on the aggregation state of **1**. Only if **1** existed as a solid phase could consistently high yields be obtained in the subsequent trapping with an electrophile. We actually observed that a freshly prepared (at −112 to −115 °C) solution of **1** was metastable; it could spontaneously "crystallize" to produce a solid form of **1** as a white slurry. Fortunately, this phase transition did not dramatically increase the reaction mixture viscosity, so efficient stirring was still possible. Although **1** is not very stable in solution (about 50% decomposition was observed during 1 h at −115 °C), the crystalline form of **1** could be kept for 4 h at −112 to −115 °C without noticeable degradation. When the solution was warmed, a sharp phase transition usually took place over 2−5 min at −105 to −104 °C, after which a clear solution was formed. At this point, no 1-bromo-1-lithioethene (**1**) could be detected in the resulting reaction mixture on the basis of electrophilic trapping experiments.

It is important to note that all experimental results presented above were reliably obtained when our original glass reactor[19] (Figure 1) was used to conduct the deprotonation step. However, when the design of the glass reactor was significantly modified (to allow the option of adding **1** to an electrophile), the desired phase transition did not always reproducibly occur under ap-

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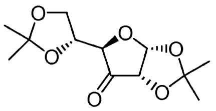
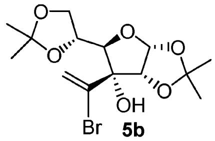
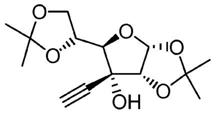
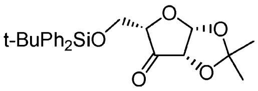
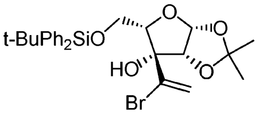
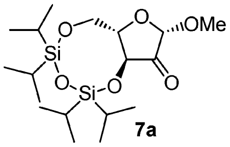
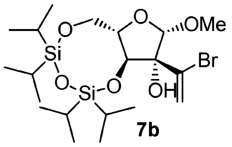
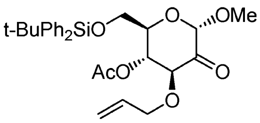
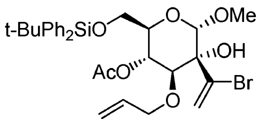
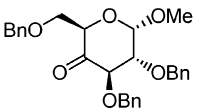
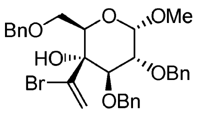
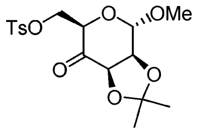
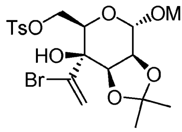
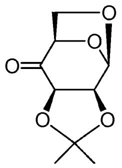
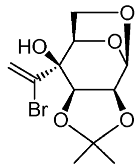
(22) Lucchini, V.; Modena, G.; Pasquato, L. *J. Am. Chem. Soc.* **1995**, *117*, 2297−2300.

TABLE 3. Addition of 1 to Carbohydrate-Derived Ketones

entry	ketone	product(s)	d.r.[a]	isolated yield of the major diastereomer (%)
1	 **5a**	 **5b**  **5c**	100:0[b]	9[c]
2	**5a**	**5b**	100:0[b]	84[d]
3	 **6a**	 **6b**	100:0[b]	67[d]
4	 **7a**	 **7b**	89:11[e]	63[f, g]
5	 **8a**	 **8b**	88:12[e]	50[f]
6	 **9a**	 **9b**	95:5[e]	69[f]
7	 **10a**	 **10b**	100:0[e]	64[f]
8	 **11a**	 **11b**	100:0[b]	70[f]

[a] Determined by ^{1}H NMR analysis of the crude reaction mixture. [b] Attack of **1** from the less-crowded convex face of the ketone is assumed. [c] Yield based on ^{1}H NMR analysis of the crude reaction mixture. The reaction mixture also included 45% of **5c** and 46% of unreacted **5a**. [d] $CeBr_3$ (0.1 equiv) was used as an additive. [e] Major diastereomer structure was assigned using NOE studies. [f] Me_3SiCl (1 equiv) was used as an additive. [g] An inseparable mixture of diastereomers was obtained. In this case, the isolated yield is for this mixture of diastereomeric products.

parently identical conditions. We attempted to reoptimize the solvent system as well as the concentrations of reagents, but still could not achieve complete reproducibility of the crystallization. Attempts to modify the solvent composition by changing from THF (mp −108 °C) to THP (mp −45 °C) and/or from *n*-pentane (mp −130 °C) to *n*-heptane (mp −91 °C) resulted in significantly lower yields of **1**, even at −110 °C, and complete freezing of the reaction mixture was frequently observed in these cases.

To further explore these unexpected observations, we carefully measured the temperature gradients in the apparatus that afforded highly reproducible results (Figure 1). We observed that the viscosity of methylcyclohexane (which was always used in conjunction with liquid nitrogen as the external coolant, mp −127 °C) significantly increased when the temperature dropped below −110 °C. This caused a temperature difference of ca. 15 °C along the height of the reactor, which did not change appreciably with more efficient coolant stirring.

After a short time, the frozen coolant formed a bridge between the bottom of the heat exchanger and the flask wall (Figure 1B). This, in turn, caused the region of the flask wall in contact with the frozen coolant to temporarily cool below −127 °C. This cold spot reproducibly caused the crystallization of **1**. Again, because the average temperature in the reaction flask was usually about −115 °C during this process, the main bulk of the solvent did not freeze. After this crystallization of **1**, the resulting slurry could safely be kept at −112 °C without noticeable decomposition.

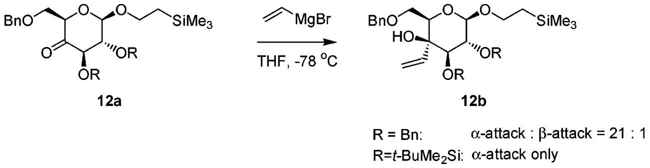
Interestingly, the sequence of temperature changes described above occurs without variation because of the intrinsic properties of the methylcyclohexane coolant. An attempt to use *n*-pentane as the coolant decreased the temperature gradients within the setup to ca. 2 °C (at −120 °C), and instead of crystallization of **1**, freezing of the bulk solution was often observed. The experimental procedure is rather simple, and except for the all-glass reaction vessel itself, no custom-made equipment is necessary. Further technical details are presented in the Experimental Section.

To evaluate the scope and limitations of the synthetic utility of **1**, we next examined more structurally complex carbohydrate-derived ketones as electrophiles. Initial studies were focused on the reaction of **1** with glucose-derived ketone **5a**. To our disappointment, only 9% (by ^{1}H NMR analysis) of the desired bromoethenyl adduct **5b** was formed (albeit as a single diastereomer; Table 3, entry 1), accompanied by 46% of the starting ketone **5a** and 45% of the acetylenic adduct **5c**. It is important to note that **5c** most probably did not originate from the bromoethenyl adduct **5b**. In a separate experiment, the very similar adduct **9b** exhibited no reaction when it was subjected to a solution containing LDA or DBU, even at room temperature. Instead, it seems likely that **5c** was formed via decomposition of **1** to ethynyllithium, followed by nucleophilic addition to **5a**.

After considerable experimentation, we found that addition of $CeBr_3$ (0.1 equiv) dramatically increased the yield of **5b** (from **5a**) as well as **6b** (from **6a**) (Table 3, entries 2 and 3). Further experimentation revealed that Me_3SiCl (0.5−1 equiv) also significantly improved the yields of the desired 1-bromoethenyl adducts (Table 3, entries 4−8). Regardless of the additive used, it was also observed that a 1.5−2-fold excess of 1-bromo-1-lithioethene (**1**) was necessary to obtain reproducible results.

Surprisingly high overall diastereoselectivities were observed, even for ketones that do not possess an obvious intrinsic facial bias. For example, ketone **9a** (entry 6) afforded a 95:5 mixture of diastereomeric products. In contrast, reaction of **9a** with 2-(trimethylsilyl)ethynyllithium (THF, 0 °C) afforded only a 1.5:1 mixture of diastereomeric propargyl alcohol products, with the major diastereomer resulting from the same *β*-axial face attack at the ketone.[23] These authors found that the use of more sterically demanding TBS protecting groups at C-3, C-4, and C-6 allowed for completely diastereoselective axial addition to the *β*-face. Similarly, addition of 1.2 equiv of ethynylmagnesium bromide to ketone **9a** (THF, 0 °C) afforded a 1:1 mixture of diastereomeric adducts.[24] More highly diastereoselective (4:1) *β*-face addition reactions were observed for the addition of 2-(trimethylsilyl)ethynyllithium to the corresponding *β*-anomer of **9a**.[23] Although the highly diastereoselective addition of vinylmagnesium bromide to the closely related *β*-anomeric A-ulose sugar derivatives **12a** has been reported[25] (Scheme 2), these reactions afforded the *epimeric* adducts resulting from an α-face attack at the ketone. The authors attributed the high α-selectivity to Mg^{2+} chelation with the C-4 carbonyl oxygen and oxygen centers within the C-3 protecting group,[26] followed by nucleophilic attack from the less-crowded equatorial direction.[27]

SCHEME 2. Diastereoselectivity of Vinylmagnesium Bromide Addition to 12a



It appears that such chelation effects are not observed with alkynyllithium or alkynyl Grignard reagents, or with 1-bromo-1-lithioethene (**1**). This observation is consistent with reactions of **1** with other sugar-derived ketones (**7a** and **8a**, Table 3, entries 4 and 5), in which the major products formed are consistent with the domination of steric factors over chelation effects.

These studies also demonstrated the remarkable chemoselectivity of **1**. For example, acetate and tosylate moieties proved reasonably stable under the reaction conditions used (Table 3, entries 5 and 7). Ketone **10a** is usually quite susceptible to E_{1cb} elimination; indeed, **10a** could be completely converted to the corresponding α,*β*-unsaturated ketone by treatment with DBU for 15 min at room temperature.[28] However, no traces of such elimination byproducts could be detected in the crude reaction mixture (by ^{1}H NMR analysis) when **10a** was allowed to react with **1**. No evidence for competing enolization was seen in any of the reactions reported in Table 3; the stereochemistry at each epimerizable stereogenic center appeared unchanged after each reaction.

During our preliminary work,[19] we observed that reaction of simple conjugated aldehydes (benzaldehyde, acrolein) with **1** gave good yields of the desired addition products (see Table 1, entries 6 and 7). In contrast, simple aliphatic aldehydes afforded only modest yields of 2-bromo-1-alken-3-ol products on reaction with **1** (Table 4, entry 1). Yields dropped even further when protected α-hydroxy aldehydes were used as electrophiles to trap **1**. Attempts to use various additives invariably led to even lower yields of the desired adducts. In every case, unreacted aldehyde was recovered as the major byproduct. Non-

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[23] Daly, S. M.; Armstrong, R. W. *Tetrahedron Lett.* **1989**, *30*, 5713−5716.

[24] Norris, P. Youngstown State University, Youngstown, OH. Personal communication, 2005.

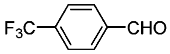
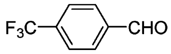
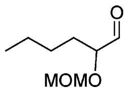
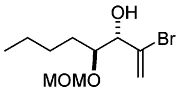
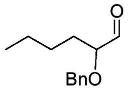
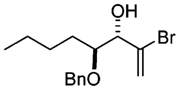
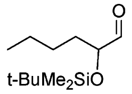
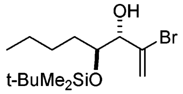
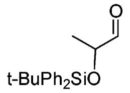
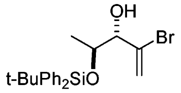
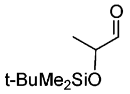
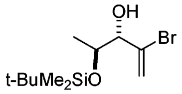
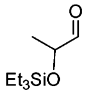
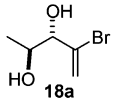
[25] Thoma, G.; Schwarzenbach, F.; Duthalet, R. O. *J. Org. Chem.* **1996**, *61*, 514−524.

[26] Miljkovic, M.; Gligorijevic, M.; Satoh, T.; Miljkovic, D. *J. Org. Chem.* **1974**, *39*, 1379−1384.

[27] Of course, the α-anomer would suffer increased steric crowding on the α-face, which might have eroded this high stereocontrol; unfortunately, no studies along these lines have been published.

[28] Davis, B. G.; Nash, R. J.; Watson, A. A.; Smith, C.; Fleet, G. W. *Tetrahedron* **1999**, *14*, 4501−4520.

TABLE 4. Reaction of 1 with Aldehydes

entry	aldehyde	product (major diastereomer)	dr[a]	isolated yield (%)
1	n-$C_6H_{13}CHO$	**16a**	n/a	50
2	n-$C_6H_{13}CHO$	**16a**	n/a	74[b]
3		**16b**	n/a	40
4		**16b**	n/a	77[b]
5			77 : 23	62[b, c]
6			60 : 40	53[b, c]
7		 **17**	93 : 7	49[b, d]
8			68 : 32	35[b, c]
9		 **18**	89 :11	50[b, d]
10		 **18a**	93 : 7	35[b, d]

[a] Determined by ^{1}H NMR analysis of the crude reaction mixture after hydrolysis of the trimethylsilyl ether group. [b] Two equivalents of Me_3SiCl and three equivalents of **1** were used. [c] Isolated yield for the inseparable diastereomeric mixture. [d] Isolated yield for the major diastereomer.

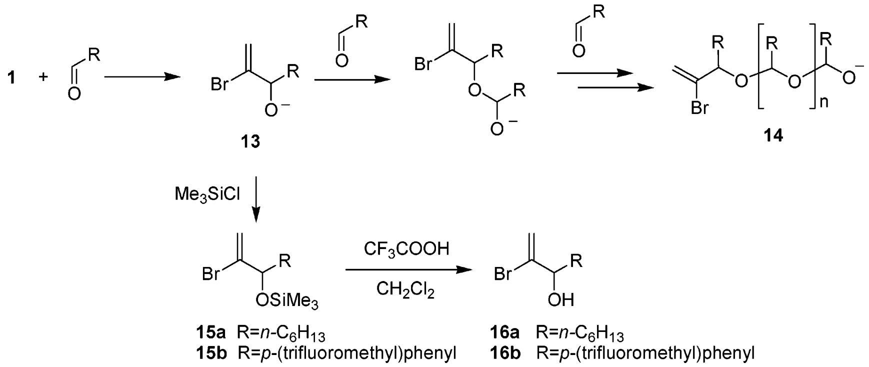
enolizable 4-trifluoromethylbenzaldehyde provided the same low yield of adduct as *n*-heptanal (Table 4, entry 3), indicating that competing aldehyde enolization was not the major problem during these reactions. A separate experiment, in which the products derived from the reaction of **1** with *n*-heptanal were quenched by a slight excess of Me_3SiCl followed by careful removal of the solvent under anhydrous conditions, unexpectedly provided a 1:1 mixture (by ^{1}H NMR analysis) of 1-bromo-1-trimethylsilylethene (trapped unreacted **1**) and 2-bromo-3-trimethylsiloxy-1-nonene (**15a**) (trapped addition product). No traces of silyl enol ethers derived from trapping the *n*-heptanal enolate could be observed.

The above results are consistent with a competitive trapping of the initially formed alkoxide adduct **13** by a second molecule of aldehyde, with the facility of this reaction depending on the electrophilicity of the aldehyde substrate. Less-electrophilic conjugated aldehydes such as benzaldehyde and acrolein presumably react more sluggishly with **13**, allowing efficient trapping of **1** by the aldehyde (Table 1, entries 6 and 7). In contrast, more-electrophilic aldehydes appear to compete effectively for **13**, presumably eventually leading to the formation of an aldehyde oligomerization product **14** (Scheme 3).

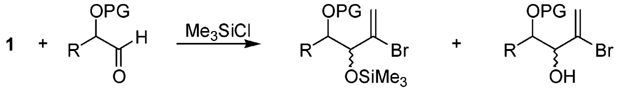
If this mechanism was indeed operating, we considered that the competitive addition of **1** to an aldehyde in the presence of Me_3SiCl might lead to the preferential silylation of the intermediate **13** before it could react with a second molecule of the aldehyde. The success of this approach would depend on the relative rates of silylation for unreacted **1** and for the initially formed adduct **13**. Given the hard nature of the alkoxide anion **13**, we anticipated that Me_3SiCl might react preferentially with **13** over **1**. In practice, addition of a mixture of 2 equiv of Me_3SiCl and 1 equiv of *n*-heptanal to 3 equiv of **1** at −115 °C afforded a complex product mixture that contained trimethylsilyl ether **15a** as the major product, as well as some other byproducts. This reaction mixture promptly hydrolyzed upon contact with silica, precluding purification of the silyl ether **15a**. However, deliberate hydrolysis of the silyl ether (aq CF_3COOH in CH_2Cl_2) followed by vacuum distillation afforded the desired allylic alcohol **16a** in 74% yield (Table 4, entry 2). Similarly, reaction of 4-trifluoromethylbenzaldehyde under these conditions afforded allylic alcohol **16b** in 77% yield (Table 4, entry 4).

To find the most efficient competitive trapping agent, we surveyed several common silylating reagents. Inter-

SCHEME 3. Possible Side Reactions of 1 with Highly Electrophilic Aldehydes



SCHEME 4. Reactions of 1 with Protected α-Hydroxy Aldehydes in the Presence of Me_3SiCl



estingly, the initially chosen Me_3SiCl provided the best overall yields of the desired adducts. Me_3SiI and Me_3SiOTf were excessively reactive toward **1**, resulting in the predominant formation of 1-bromo-1-trimethylsilylethene, whereas Et_3SiCl and *t*-$BuMe_2SiOTf$ were not sufficiently reactive to efficiently intercept **13**.

To further explore the synthetic utility of **1** under these in situ silylation conditions, we examined a series of protected α-hydroxy aldehydes as electrophiles. These reactions were complicated by the formation of bisprotected diols (Scheme 4), which had to be carefully hydrolyzed to afford the desired monoprotected diol product. (Only traces of the corresponding addition products were obtained without the Me_3SiCl additive.)

From a practical standpoint, the *t*-$BuMe_2Si$-protected α-hydroxy aldehydes turned out to be the most useful substrates because it was possible to selectively remove the Me_3Si group while the *t*-$BuMe_2Si$ group remained intact, and then cleanly isolate the products **17** and **18** as single diastereomers by conventional flash chromatography (Table 4, entries 7 and 9).

Again, these results showed that a chelation mechanism did not operate during the addition of **1** to variously protected α-hydroxy aldehydes. In every case, the major diastereomer of the deprotected product was the anti diol, suggesting Felkin–Ahn control during the addition of **1** to the aldehyde.

The anti configuration of the products **17** and **18** (entries 7 and 9) was established after complete deprotection to the corresponding diols **17a** and **18a**, followed by conversion to the cyclic acetonides **17b** and **18b**, respectively. A comparison of the observed $^3J_{H3-H4}$ coupling constants with very closely related literature compounds[29] allowed for determination of the anti stereochemistry (Scheme 5).

High levels of Felkin–Ahn diastereoselectivity were seen with some α-siloxy aldehydes (e.g., Table 4, entries 7, 9, and 10). The much lower levels of stereocontrol observed for the α-benzyloxy aldehyde and α-methoxymethyloxy aldehyde (Table 4, entries 5 and 6) are consistent with the smaller size of the benzyloxy and methoxymethyloxy groups relative to that of the siloxy moieties (entries 7–10). Somewhat surprising is the low level of Felkin–Ahn selectivity seen for the *t*-$BuPh_2SiO$-protected substrate (Table 4, entry 8), whereas the corresponding *t*-$BuMe_2SiO$- and Et_3SiO-protected α-hydroxy aldehydes react with very high Felkin–Ahn control. We currently have no explanation for these observations.

Since acylsilanes are often used as masked aldehydes,[30] we thought it would be of some interest to examine commercially available acetyltrimethylsilane as a trapping reagent for **1**. Somewhat discouragingly, it was reported that reactions of α-substituted vinylmetals with acylsilanes are not clean, and the expected products are susceptible to Brook rearrangement.[31] However, to our surprise, acetyltrimethylsilane reacted cleanly with **1**, providing the α-silyl alcohol **19** in good yield (Scheme 6). No evidence for any rearrangement products was observed. Adduct **19** could be distilled and was stable in THF solution as well as neat in the presence of traces of tertiary amines. However, a solution of **19** in CH_2Cl_2 slowly rearranged at room temperature to produce the unstable α-bromo-α-silyl ketone **20**[32] (Scheme 6). This unusual rearrangement reaction was not appreciably accelerated by the presence of acids (HCl gas, TsOH), and was completely inhibited by weak bases (pyridine, Et_3N) and even THF. We are not aware of a precedent for this rearrangement process.

Overall, the experimental data strongly suggest that the lithium atom in **1** is not available for chelation during the carbonyl addition reactions reported herein. Along with the observation that **1** exists as a solid during the reaction, it seemed likely that the lithium atoms were tightly coordinated to THF molecules in a crystal and/or formed a strong association with a bromo substituent in an adjacent molecule of **1**, thus forming a polymeric structure. The narrow temperature range (2–3 °C) corresponding to the transition of the solid form of **1** into

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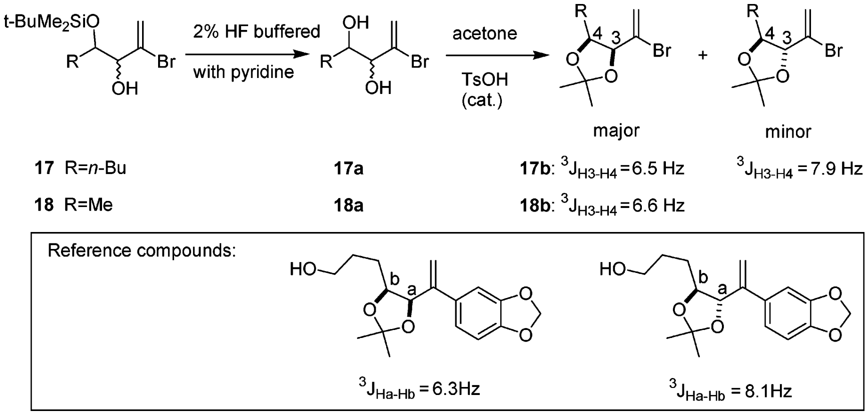
(29) Pearson, W. H.; Lovering, F. E. *J. Org. Chem.* **1998**, *63*, 3607–3617.

(30) For reviews on the use of acylsilanes in organic synthesis, see: (a) Ricci, A.; Deglinnocenti, A. *Synthesis* **1989**, 647–660. (b) Bulman-Page, P. C.; Klair, S. S.; Rosenthal, S. *Chem. Soc. Rev.* **1990**, *19*, 147–195. (c) Bonini, B. F.; Franchini, M. C.; Fochi, M. *Gazz. Chim. Ital.* **1997**, *127*, 619–628. (d) Bonini, B. F.; Comes-Franchini, M.; Fochi, M.; Mazzanti, G.; Ricci, A. *J. Organomet. Chem.* **1998**, *567*, 181–189. (e) Patrocinio, A. F.; Moran, P. J. S. *J. Braz. Chem. Soc.* **2001**, *12*, 7–31.

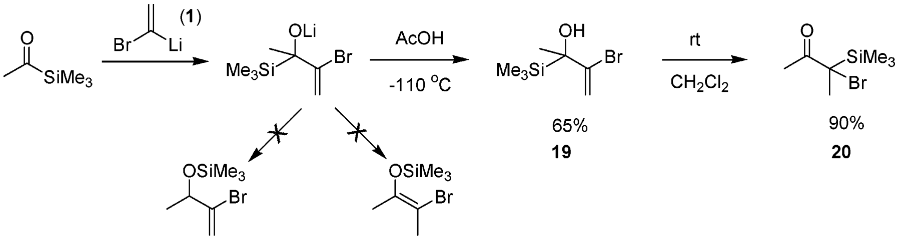
(31) Kato, M.; Mori, A.; Oshino, H.; Enda, J.; Kobayashi, K.; Kuwajima, I. *J. Am. Chem. Soc.* **1984**, *106*, 1773–1778.

(32) A very limited number of α-halo-α-silyl ketones have previously been reported. (a) For an example of Hal = Br, Cl, see: Berti, G.; Canedoli, S.; Crotti, P.; Macchia, F. *J. Chem. Soc., Perkin Trans. 1* **1984**, 1183–1188. (b) For an example of Hal = F, see: Enders, D.; Faure, S.; Potthoff, M.; Runsink, J. *Synthesis* **2001**, 2307–2319.

SCHEME 5. Establishing the Configuration of the Major Diastereomer Resulting from Trapping 1 with Protected α-Hydroxy Aldehydes



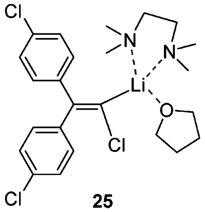
SCHEME 6. Reactions of 1 with Acetyltrimethylsilane



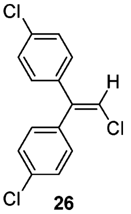
solution, as well as literature data on related organolithium species,[14,18] might suggest that **1** has a crystalline structure rather than a polymeric one. To further test this hypothesis, liquid-phase ab initio HF6-31G*/SM5.42R calculations were undertaken. Because only ground-state structures were being considered, the balance between the level of theory used and maximum complexity of the structure being studied was shifted toward the latter. Given the enormous amount of time[33] required for even a single geometry optimization of structures such as **21** (Figure 2), no attempts were made to locate global minima.

A traditional computational strategy was employed, whereby the starting geometries of solvated dimers **21** and **22** were optimized until local minima were found (no imaginary vibrations after the corresponding Hessian calculations). The same procedures were then applied to their monomeric fragments. Finally, the energetics of the depolymerization reactions were evaluated (Figure 2).

In accordance with reported calculations for the 1-iodo-1-lithioethene dimer,[14] current calculations support the notion that 1-bromo-1-lithioethene dimers might be less energetically favorable than their monomers. In addition, the optimized geometry at C_1 seems significantly more realistic for monomers than for dimers (Table 5). The single related crystal structure[34] determined by low-temperature X-ray crystallography (compound **25**) was included in Table 5 for comparison.



25



26

On the basis of available literature data,[35] our computational results, and the sharp phase transitions observed for **1**, we presume that **1** most probably exists as a regular monomeric crystalline solid rather than a polymer. The low viscosity of the 1-bromo-1-lithioethene (**1**) slurry at −112 °C might also support this conclusion.

Prior to our studies, it was known that 1-bromo-1-lithioethene could be trapped with Me_3SiCl.[16] With a potential one-step synthesis of small 1,1-difunctionalized ethene building blocks in mind,[12] we have examined the use of several non-carbonyl electrophiles to trap 1-bromo-1-lithioethene (**1**).

The low degree of steric crowding in dichlorodimethylsilane resulted in bis-coupling with **1** to afford the bis-ethenylsilane **27** in good yield (Table 6, entry 1). The corresponding chloro-*N*,*N*-diethylaminodimethylsilane did not react with **1** (entry 2), nor did the more crowded dichlorodiphenylsilane (entry 3). It was possible to achieve selective monocoupling with **1** using dichlorodiethylsilane to afford the ethenylchlorosilane **28**, albeit in low yield (entry 4). Much more respectable yields of selective monocoupling products were seen for the more crowded dichlorodiisopropylsilane, leading to the isolation of **29** in 47% yield (entry 5). Compound **29** is a more crowded variant of the bromoethenyl chlorosilane **3** initially proposed by Tamao et al.[12] as a source of a useful silyl tether for efficient radical cyclization chemistry. In our hands, **29** allowed for radical cyclization, to afford **34** in the same yield as that reported by Tamao from the corresponding chlorosilane precursor **3** (Scheme 7). How-

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[33] A typical optimization took about 3 weeks on a desktop 2.4 GHz Pentium 4 computer with 1 GB memory; this precluded the use of an MP2 correlation correction as well as HF/DFT methods available within the GAMESOL package.

[34] Maercher, A. *Angew. Chem., Int. Ed.* **1993**, *32*, 1023−1025.

[35] Braun, M. *Angew. Chem., Int. Ed.* **1989**, *28*, 896−989.

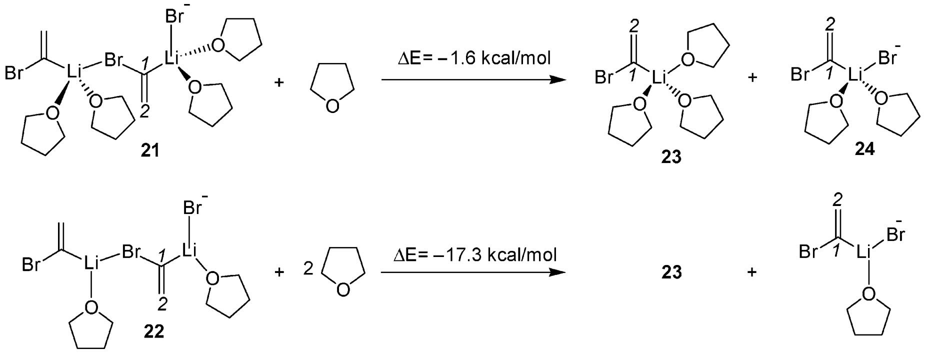


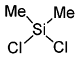
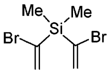
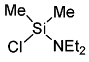
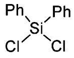
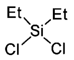
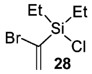
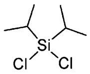
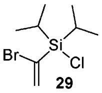
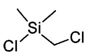
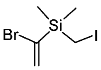
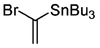
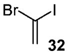
FIGURE 2. Computational attempts to delineate the possible structure of **1**.

TABLE 5. Calculated Geometry Data for 1-Bromo-1-lithioethene (1) Dimers and Monomers

structure	C_1−Hal bond elongation (Å)	C_2−C_1−Hal angle (deg)	C_2−C_1−Li angle (deg)	source of data
25 (reference)	0.12[a]	112.6	137.1	X-ray
24 (monomer)	0.31[b]	107	148	computation
23 (monomer)	0.32[b]	108	170	computation
21 (dimer)	1.00[b]	104	154	computation
22 (dimer)	1.18[b]	98	158	computation

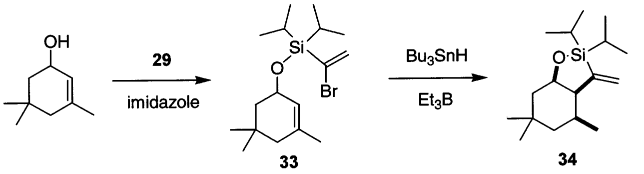
[a] Compared with that of **26**. [b] Compared with the calculated C−Br bond length for bromoethene (same basis set).

TABLE 6. Trapping of 1 with Silicon- and Tin-Based Electrophiles

entry	electrophile	product	isolated yield, % (slow addition)	isolated yield, % (fast addition)
1		 **27**	64	
2		no reaction	0	
3		no reaction	0	
4		 **28**	26	
5		 **29**	47	40
6		 **30**	33[a]	
7	Bu_3SnCl	 **31**	40-60[b]	85
8	I_2	 **32**	0-10[b]	40[c]

[a] Initially formed chloromethylsilane was not isolated but instead converted into iodomethylsilane **30** by reaction with NaI/acetone. [b] Range of yields observed for 5 runs. [c] Losses during distillation limited the preparative yield.

SCHEME 7. Application of 29 in Construction of a Silyl Tether for Radical Cyclization Chemistry



33 (90%)

34 50% isolated yield[a]

[a] Relative stereochemistry is supported by NOE studies.

ever, it should be noted that **29** has two advantages over **3**: its preparation requires only one step (instead of 3 steps for **3**) and all intermediates (e.g., **33** and **34**) are sufficiently stable to be isolated by conventional flash chromatography, whereas the corresponding dimethylsilyl analogues of **33** and **34** are labile on silica.

As expected, chloromethyldimethylsilyl chloride reacts cleanly with **1** at the silicon atom; treatment of the crude product with NaI in anhydrous acetone allowed for the isolation of the bromoethenyl iodomethylsilane **30** (Table 6, entry 6). We envisaged that **30** might serve as a useful building block (analogous to **29**) in the construction of a siloxy tether for radical cyclization chemistry; however, **30** did not react with secondary alcohols under the various conditions examined.

We also were interested in the preparation of bromoethenylstannane **31** as a potential building block. No examples of 1-haloethenylstannanes have previously been reported, although the corresponding 2-haloethenylstannanes have been prepared[36] and, in one case, were shown to be useful substrates for transmetalation and Diels−Alder cycloaddition.[37] Trapping **1** with Bu_3SnCl afforded **31** in moderate yield (Table 6, entry 7) along with unreacted Bu_3SnCl. During this experimental work we noticed that fast addition (over 5−10 s instead of the usual 5−25 min) of a precooled Bu_3SnCl solution to a slurry of **1** uniformly gave better yields of the desired bromoethenylstannane **31** (Table 6, entry 7). Similar improvements in the trapping of **1** by I_2 were also observed (Table 6, entry 8). Surprisingly, 1-bromo-1-iodoethene has not previously been reported.[38] However,

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(36) Barbero, A.; Cuadrado, P.; Fleming, I.; Gonzalez, A. M.; Pulido, F. J.; Rubio, R. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1657−1662.

(37) Singleton, D. A.; Leung, S.-W.; Martinez, J. P.; Lee, Y.-K. *Tetrahedron Lett.* **1997**, *38*, 3163−3166.

(38) The closely related 1-bromo-1-chloroethene was mentioned in the literature (Havel, J. J.; Skell, P. S. *J. Am. Chem. Soc.* **1972**, *94*, 1792−1793. Agre, C. L.; Hilling, W. *J. Am. Chem. Soc.* **1952**, *74*, 3895−3899), but it readily polymerizes and has not found utility as a synthetic reagent. In contrast, 1,1-dichloroethene is an inexpensive article of commerce, and has found some synthetic utility. For an example, see: Qian, M.; Negishi, E. *Org. Process Res. Dev.* **2003**, *7*, 412−417.

given the utility of (*E*)-1-bromo-2-iodoethene as a synthetic building block,[39] we anticipate that 1-bromo-1-iodoethene will be a useful 1,1-difunctionalized ethenyl synthon.

It seems plausible that lithium halides, which were formed along with the desired product in these reactions, were crystallizing on the surface of the solid **1**, thus isolating the organolithium from the electrophile. On the subsequent warm-up step, the rate of diffusion of the electrophile through a crust of solid lithium salts might be lower than the rate of thermal decomposition of residual 1-bromo-1-lithioethene (**1**), resulting in incomplete trapping of the electrophile when it is slowly added to the reaction mixture. Conversely, fast addition of the electrophile caused the internal reaction temperature to rise to −90 °C. At this temperature, **1** became soluble and would be expected to decompose; however, the rate of trapping of dissolved **1** with the added electrophiles was apparently much faster than the rate of its thermal decomposition, allowing for the generation of the adducts **31** and **32** in reasonable to good yields. We intend to explore the synthetic utility of these two new synthetic building blocks; results of these studies will be communicated in due course.

During our experimental work we have encountered some limitations with the synthetic utility of 1-bromo-1-lithioethene (**1**). We found that epoxides were completely unreactive toward **1** even in the presence of $BF_3 \cdot Et_2O$ or $CeBr_3$. In addition, crowded ketones such as 2,6-dimethylcyclohexanone provided only traces of addition product, independent of the conditions used. Finally, attempts to conduct transmetalation reactions by using derivatives of elements that are more electropositive than Si or Sn (e.g., $ZnCl_2$, $ZnBr_2$, $Zn(OTf)_2$, $B(OMe)_3$, $CeCl_3$, $CeBr_3$, $ClTi(O\textit{i}\text{-}Pr)_3$, $Cl_2Ti(O\textit{i}\text{-}Pr)_2$, and $BeCl_2$[40]) under various conditions have failed, to date, to afford any synthetically useful results.

Conclusion

1-Bromo-1-lithioethene (**1**) has proven to be a useful practical reagent for the selective introduction of the 1-bromoethenyl group into various organic and organometallic substrates. At −110 to −115 °C, **1** affords clean 1,2-addition to carbonyl compounds. It possesses low basicity and is compatible with acetate, allyl ether, and tosylate protecting groups. The addition of **1** to chiral aldehydes and ketones proceeded under Felkin−Ahn diastereocontrol, providing unusually high diastereomeric ratios (88:12 to 92:8) of adducts in some cases. Among simple protected α-hydroxy aldehydes, $t\text{-BuMe}_2\text{Si}$-protected compounds provided the highest diastereoselectivities (up to 93:7). For aliphatic aldehydes and protected α-hydroxy aldehydes, Me_3SiCl was necessary as an additive to suppress undesirable side reactions. Epoxides and crowded ketones were not sufficiently electrophilic to react with **1**. However, several dichlorosilanes, acetyltrimethylsilane, tributyltin chloride, and iodine proved to be efficient electrophiles for trapping **1**, providing one-step access to potentially useful small 1,1-difunctionalized ethene building blocks.

Experimental Section

General Procedure A: Reaction of 1-Bromo-1-lithioethene (1) with Acetone To Prepare 3-Bromo-2-methylbut-3-en-2-ol (2a). A solution of bromoethene (3.0 mL, 42.5 mmol), lithium bromide (0.23 g, 3.2 mmol), and the Trapp mixture (THF:ether:pentane, 4:1:1 by volume, 20 mL) was placed into the central flask of the low-temperature reactor described in the Supporting Information. A mixture of anhydrous THF (19 mL) and anhydrous ether (7 mL) was placed into the side tube. The reactor was cooled to −70 °C (methylcyclohexane/liquid N_2), and *n*-butyllithium (8.1 mL, 16.1 mmol, 2 M in pentane) was added to the side tube. The main bubbler was temporarily stopped for ca. 10 s (argon started to bubble through the side tube, mixing the contents of the side tube), and the unit was then further cooled with liquid nitrogen to −110 °C. At this point the auxiliary bubbler was stopped, and the contents of the side tube were slowly transferred to the main flask using argon pressure. (To achieve good yields, this addition should be done over 15−30 min, and the temperature should be in the −110 to −115 °C range.) After the addition, the side tube was washed with the Trapp mixture (2 × 1.5 mL). Liquid nitrogen was added to the heat exchanger tube until the bridge of the frozen coolant between the reactor and the heat exchanger was formed (Figure 1B). This condition was indicated by attempting to slightly move an outer Dewar vessel. When the bridge is formed, the Dewar vessel cannot be moved any more. At this moment, the crystallization of **1** had usually occurred. Addition of liquid nitrogen was ceased until the bridge of the frozen coolant had melted (temperature should not rise above −112 °C). This process was usually completed in 20 to 40 min. The cloudy mixture was stirred for 30−40 min at −112−115 °C to complete the deprotonation of bromoethene.

A solution of acetone (1.0 mL, 14 mmol) in the Trapp mixture (10 mL) was placed into the side tube. After thermal equilibration (usually 5−10 min), the contents of the side tube were transferred as described above to the central flask over 2−15 min. (The time for this addition was not so critical.) The reaction mixture was stirred at −110 to −105 °C for 30 min. A solution of acetic acid (1.05 mL, 1.25 mmol) in the Trapp mixture (15 mL) was placed into the side tube and, 5 min later, it was transferred into the central flask. The cooling bath was removed, and the contents were transferred to a separatory funnel. The organic layer was washed with 4% aq $NaHCO_3$ (10 mL), washed with brine (10 mL), dried ($MgSO_4$), and concentrated at atmospheric pressure. Vacuum distillation gave 3-bromo-2-methylbut-3-en-2-ol (**2a**) (1.79 g, 77%) as a colorless liquid which was 99.5% pure by GC, bp 53 °C at 17 mmHg. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.49 (s, 6H), 2.10 (br s, 1H, OH), 5.49 (d, $^2J = 2.3$ Hz, 1H), 5.89 (d, $^2J = 2.3$ Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.7, 74.1, 115.2, 142.7. Anal. Calcd for C_5H_9BrO: C, 36.39; H, 5.50. Found: C, 36.67; H, 5.85.

2-Bromo-3-methylpenta-1,4-dien-3-ol (2b). 2b was prepared according to General Procedure A from 3-buten-2-one in 78% yield, bp 63 °C at 14 mmHg, and the GC purity was 98%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.55 (s, 3H), 2.25 (s, 1H), 5.23 (dd, $^3J_1 = 10.6$ Hz, $^2J_2 = 0.8$ Hz, 1H), 5.40 (dd, $^3J_1 = 17.2$ Hz, $^2J_2 = 0.8$ Hz, 1H), 5.57 (d, $^2J = 2.3$ Hz, 1H), 5.94 (d, $^2J = 2.3$ Hz, 1H), 6.01 (dd, $^3J_1 = 17.3$ Hz, $^3J_2 = 10.7$ Hz, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 26.7, 76.1, 114.5, 116.6, 140.2, 141.5. Anal. Calcd for C_6H_9BrO: C, 40.71; H, 5.12. Found: C, 40.77; H, 5.25.

2-Bromo-3-methylhepta-1,6-dien-3-ol (2c). **2c** was prepared according to General Procedure A from 5-hexen-2-one in 84% yield, bp 89−91 °C at 14 mmHg, a single peak by GC analysis. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.46 (s, 3H), 1.73 (ddd, $^2J_1 = 13.8$ Hz, $^3J_2 = 9.6$ Hz, $^3J_3 = 7.1$ Hz, 1H), 1.89 (ddd, $^2J_1$

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[39] For examples, see: (a) Qian, M.; Huang, Z.; Negishi, E. *Org. Lett.* **2004**, *6*, 1531−1534. (b) Haleh, G.; Antunes, L. M.; Organ, M. G. *Org. Lett.* **2004**, *6*, 2913−2916.

[40] Krief, A.; Vos, M. J.; Lombart, S.; Bosret, J.; Couty, F. *Tetrahedron Lett.* **1997**, *38*, 6295−6298.

= 13.8 Hz, $^3J_2 = 9.6$ Hz, $^3J_3 = 6.2$ Hz, 1H), 2.03−2.15 (m, 2H), 2.30 (br s, 1H, OH), 4.98 (dm, $^3J = 10.1$ Hz, 1H), 5.05 (ddd, $^3J_1 = 17.2$ Hz, $^2J_1 = 3.2$ Hz, $^4J_1 = 1.6$ Hz, 1H), 5.56 (d, $^2J =$ 2.1 Hz, 1H), 5.83 (ddt, $^3J_1 = 16.9$ Hz, $^3J_2 = 10.3$ Hz, $^3J_3 = 6.7$ Hz, 1H), 5.92 (dd, $^2J_1 = 2.1$ Hz, $^4J_2 = 0.36$ Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 27.2, 28.5, 39.4, 76.8, 115.2, 116.5, 138.5, 140.6. Anal. Calcd for $C_8H_{13}BrO$: C, 46.85; H, 6.39. Found: C, 47.15; H, 6.51.

1-(1-Bromoethenyl)cyclohexanol (2d). 2d was prepared according to General Procedure A from cyclohexanone in 85% yield, bp 62 °C at 1 mmHg, and the GC purity was 98.8%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.20−1.30 (m, 1H), 1.54−1.72 (m, 5H), 1.74−1.82 (m, 5H), 5.57 (d, $^2J = 2.3$ Hz, 1H), 5.91 (d, ^2J = 2.3 Hz, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 21.9, 25.4, 36.0, 74.4, 115.5, 143.6. Anal. Calcd for $C_8H_{13}BrO$: C, 46.85; H, 6.39. Found: C, 47.08; H, 6.43.

1-(1-Bromoethenyl)-4,4-dimethylcyclohex-2-enol (2e). 2e was prepared according to General Procedure A from 4,4-dimethylcyclohex-2-enone in 80% yield, bp 64−65 °C at 1 mmHg, and the GC purity was 96%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.99 (s, 3H), 1.03 (s, 3H), 1.45 (ddd, $J_1 = 13.2$ Hz, $J_2 = 9.7$ Hz, $J_3 = 3.3$ Hz, 1H), 1.59 (ddd, $J_1 = 14.3$ Hz, $J_2 =$ 9.2 Hz, $J_3 = 3.8$ Hz, 1H), 1.74 (ddd, $J_1 = 12.9$ Hz, $J_2 = 9.2$ Hz, $J_3 = 2.8$ Hz, 1H), 2.11 (ddd, $J_1 = 12.6$ Hz, $J_2 = 8.6$ Hz, $J_3 =$ 3.2 Hz, 1H), 2.26 (s, 1H), 5.50 (d, $^2J = 10.0$ Hz, 1H), 5.60 (d, $^2J = 2.0$ Hz, 1H), 5.68 (d, $^2J = 10.0$ Hz, 1H), 5.91 (d, $^2J = 2.0$ Hz, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 28.5, 28.8, 32.2, 33.3, 74.1, 118.0, 126.5, 140.6, 142.2. Anal. Calcd for $C_{10}H_{15}BrO$: C, 51.97; H, 6.54. Found: C, 52.13; H, 6.74.

2-Bromo-1-phenylprop-2-en-1-ol (2f).[41] **2f** was prepared according to General Procedure A from benzaldehyde in 81% yield, bp 87−88 °C at 0.6 mmHg, and the GC purity was 99.5%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.74 (br s, OH, 1H), 5.20 (s, 1H), 5.64 (d, $J = 2.0$ Hz, 1H), 6.00 (ddd, $J = 1.9$, 1.1, 0.2 Hz, 1H), 7.30−7.38 (m, 5H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 78.0, 117.9, 126.9, 128.6, 128.7, 135.8, 139.9.

2-Bromopenta-1,4-dien-3-ol (2g). 2g was prepared according to General Procedure A from acrolein in 74% yield, bp 67 °C at 14 mmHg, and the GC purity was 98.6%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.15 (s, 1H), 4.68 (s, 1H), 5.32 (dt, $^3J_1 =$ 10.4 Hz, $J_2 = 1.2$ Hz, 1H), 5.43 (dt, $^3J_1 = 17.2$ Hz, $J_2 = 1.2$ Hz, 1H), 5.61 (d, $^2J = 2.0$ Hz, 1H), 5.91 (ddd, $^3J_1 = 17.2$ Hz, $^3J_2 =$ 10.4 Hz, $^3J_3 = 5.6$ Hz, 1H), 5.96 (dd, $^2J_1 = 2.1$ Hz, $^4J_2 = 1.0$ Hz, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 76.6, 117.4, 117.6, 135.2, 136.8. Anal. Calcd for C_5H_7BrO: C, 36.84; H, 4.33. Found: C, 36.59; H, 4.48.

General Procedure B: 3-*C*-(1-Bromoethenyl)-1,2:5,6-bis-*O*-(1-methylethylidene)-α-D-allofuranose (5b). Anhydrous $CeBr_3$ (0.588 g, 1.55 mmol) was stirred in the Trapp mixture (14 mL) for 4 h at room temperature. Bromoethene (5.45 mL, 77.4 mmol), lithium bromide (0.35 g, 4.2 mmol), and the Trapp mixture (18 mL) were placed into the central flask of the low-temperature reactor (described above). Anhydrous ether (10 mL) and anhydrous THF (10 mL) were placed into the side tube. The low-temperature reactor was cooled to −60 °C (methylcyclohexane/liquid nitrogen was used as the coolant), and the first aliquot of *n*-butyllithium (9.7 mL, 19.4 mmol, 2.0 M in pentane) was added into the side tube. The reactor was further cooled with liquid nitrogen to −110 °C, and the contents of the side tube were displaced into the central flask over 25 min. Anhydrous ether (10 mL), anhydrous THF (10 mL), and the second aliquot of *n*-butyllithium (9.7 mL, 19.4 mmol, 2.0 M in pentane) were then placed into the side tube. After thermal equilibration (5 min), the contents of the side tube were again displaced into the central flask. The side tube was washed with the Trapp mixture (4 mL). Liquid nitrogen was added into the heat exchanger until a frozen coolant bridge was formed, and then the temperature of the reaction mixture was allowed to rise to −112 °C. The whole process of addition took 90 min. (The addition of *n*-BuLi was done in two steps because of the insufficient volume of the side tube.) The slurry of $CeBr_3$ in the Trapp mixture (prepared as described earlier) was added to the side tube. The main bubbler of the unit was stopped for 3 min, which allowed for gentle bubbling of argon through the contents of the side tube (this was necessary to prevent the precipitation of cerium(III) bromide). The stopper was then removed from the main bubbler, and was placed on the auxiliary bubbler. The argon pressure developed in the side tube (10−20 mmHg) transferred the tube's contents to the central flask in ca. 10 s. This addition should be done quickly to avoid clogging of the capillary tube of the reactor. No rise in reaction temperature was observed. The yellowish mixture was stirred for 5 min, and a solution of the starting ketone **5a**[19] (4.02 g, 15.5 mmol) in the Trapp mixture (20 mL) was placed into the side tube. After thermal equilibration (5 min), the contents of the side tube were slowly added over ca. 5 min to the central flask at −110 °C. The side tube was washed with the Trapp mixture (4 mL). The slurry was stirred for 45 min at −110 to −108 °C, and then the reaction was quenched by addition of a solution of acetic acid (3.5 mL, 62 mmol) in the Trapp mixture (25 mL). The cooling bath was removed, and sat. aq $NaHCO_3$ (25 mL) was added at −20 °C to the flask. The mixture was stirred overnight, and then the organic layer was separated, dried over anhydrous sodium sulfate (5 g), and evaporated. Column chromatography (40 g silica, petroleum ether:ethyl acetate, 6:1) gave the title compound **5b** as a white solid (4.76 g, 84%), mp 113−115 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.35 (s, 3H), 1.41 (s, 3H), 1.45 (s, 3H), 1.63 (s, 3H), 3.28 (s, 1H), 3.96 (d, $J = 7.5$ Hz, 1H), 4.00 (dd, $J_1 = 8.5$ Hz, $J_2 = 5.8$ Hz, 1H), 4.09 (dd, $J_1 = 8.5$ Hz, $J_2 =$ 6.1 Hz, 1H), 4.26 (dt, $J_1 = 7.5$ Hz, $J_2 = 5.9$ Hz, 1H), 4.55 (d, ^3J = 3.9 Hz, 1H), 5.86 (d, $^2J = 1.7$ Hz, 1H), 5.97 (d, $^3J = 4.0$ Hz, 1H), 6.34 (d, $^2J = 1.8$ Hz, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 25.5, 26.56, 26.65, 26.8, 67.1, 73.6, 81.7, 83.0, 83.9, 105.4, 109.5, 112.9, 120.6, 127.9. Anal. Calcd for $C_{14}H_{21}BrO_6$: C, 46.04; H, 5.80. Found: C, 46.25; H, 5.68.

3-*C*-(1-Bromoethenyl)-5-*O*-*tert*-butyldiphenylsilyl-1,2-*O*-(1-methylethylidene)-β-L-lyxofuranose (6b). 6b was obtained from **6a**[19] (1.0 g, 2.34 mmol) using General Procedure B, with the exception that the addition of *n*-butyllithium was done in a single step because of smaller loading. Column chromatography (silica, petroleum ether:diethyl ether, 6:1) gave the title compound **6b** (0.838 g, 67%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.05 (s, 9H), 1.45 (s, 3H), 1.58 (s, 3H), 3.63 (s, 1H), 3.87 (dd, $J_1 = 11.1$ Hz, $J_2 = 6.0$ Hz, 1H), 4.00 (dd, $J_1 = 11.0$ Hz, $J_2 = 5.0$ Hz, 1H), 4.39 (t, $J = 5.5$ Hz, 1H), 4.81 (d, $J = 4.2$ Hz, 1H), 5.63 (d, $^2J = 1.8$ Hz, 1H), 5.81 (d, $J = 4.2$ Hz, 1H), 6.20 (d, $^2J = 1.9$ Hz, 1H), 7.35−7.45 (m, 6H), 7.65−7.70 (m, 4H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 19.1, 26.8, 27.6, 27.7, 62.4, 79.2, 83.3, 85.1, 104.8, 116.1, 118.3, 127.7, 129.7, 133.2, 133.4, 133.6, 135.7, 135.7. Anal. Calcd for $C_{26}H_{33}BrO_5Si$: C, 58.53; H, 6.23. Found: C, 58.58; H, 6.43.

General Procedure C: (2*S*,3*R*,3a*S*,9a*S*)-3-(1-Bromoethenyl)-5,5,7,7-tetraisopropyl-2-methoxy-1,4,6,8-tetraoxa-5,7-disilabicyclo[6.3.0]undecan-3-ol (7b). This procedure used the same approach as described in General Procedure A, except that a solution of ketone **7a**[42] (1.2 g, 3.74 mmol, 1 equiv) and Me_3SiCl (0.47 mL, 3.74 mmol, 1 equiv) in the Trapp mixture was slowly added to the preformed slurry of **1** (2 equiv) over 5−10 min at −112 °C. Column chromatography (silica, petroleum ether:ethyl acetate, 10:1) gave the title compound **7b** (1.01 g, 63%, colorless oil) as an inseparable 89:11 mixture of diastereomers. Data given are for the major diastereomer. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.90−1.00 (m, 2H), 1.02−1.15 (m, 24H), 3.25 (s, 1H), 3.51 (s, 3H), 3.85 (dd, $J_1 = 11.1$ Hz, $J_2 = 7.6$ Hz, 1H), 3.98 (dd, $J_1 = 6.8$ Hz, $J_2 = 3.4$ Hz, 1H), 4.03 (dd, $J_1 = 11.0$ Hz, $J_2 = 3.4$ Hz, 1H), 4.38 (d, $J =$ 6.7 Hz, 1H), 4.90 (s, 1H), 5.84 (d, $^2J = 1.8$ Hz, 1H), 6.29 (d, ^2J

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= 1.8 Hz, 1H). ^{13}C NMR (100.6 MHz, CDCl$_3$): δ 56.1, 65.2, 81.1, 81.7, 104.5, 120.4, 130.2 (resonances due to isopropylsilyl groups are omitted). NOE (400 MHz): irradiation of the vinylic proton (at 6.29 ppm) resulted in enhancement of the H$_1$ proton resonance (at 4.90 ppm). Anal. Calcd for $C_{20}H_{39}BrO_6Si_2$: C, 46.95; H, 7.68. Found: C, 46.73; H, 7.76.

2-*C*-(1-Bromoethenyl)-3-*O*-allyl-4-*O*-acetyl-6-*tert*-butyldiphenylsiloxy-α-D-methylglucopyranoside (8b). 8b was obtained from **8a**[43] (0.90 g, 1.76 mmol) using General Procedure C. Column chromatography (silica, petroleum ether:ethyl acetate, 10:1) gave the title compound **8b** (0.545 g, 50%) as a colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$): δ 1.07 (s, 9H), 1.97 (s, 3H), 3.00 (s, 1H), 3.51 (d, nJ = 6.0 Hz, 3H), 3.65−3.80 (m, 2H), 3.84 (ddd, J_1 = 9.9 Hz, J_2 = 4.8 Hz, J_3 = 2.9 Hz, 1H), 3.90 (d, J = 9.1 Hz, 1H), 4.17 (ddt, J_1 = 13.0 Hz, J_2 = 5.6 Hz, J_3 = 1.53 Hz, 1H), 4.39 (ddt, J_1 = 13.0 Hz, J_2 = 5.3 Hz, J_3 = 1.5 Hz, 1H), 4.96 (s, 1H), 5.15 (dq, J_1 = 10.4 Hz, J_2 = 1.6 Hz, 1H), 5.25 (dq, J_1 = 17.2 Hz, J_2 = 1.7 Hz, 1H), 5.33 (t, nJ = 9.5 Hz, 1H), 5.87 (ddt, J_1 = 17.2 Hz, J_2 = 10.5 Hz, J_3 = 5.3 Hz, 1H), 5.96 (d, ^2J = 2.6 Hz, 1H), 6.53 (d, ^2J = 2.6 Hz, 1H), 7.35−7.45 (m, 6H), 7.65−7.75 (m, 6H). ^{13}C NMR (100.6 MHz, CDCl$_3$): δ 19.2, 20.9, 26.7, 55.5, 62.9, 68.6, 71.5, 74.4, 78.0, 82.1, 101.0, 116.6, 124.0, 127.7, 129.66, 129.70, 131.9, 133.31, 134.7, 135.7, 169.4. NOE (400 MHz): irradiation of the vinylic proton (at 6.53 ppm) resulted in enhancement of the H$_4$ proton resonance (at 5.33 ppm); irradiation of the OH group (at 3.00 ppm) resulted in enhancement of the H$_3$ proton resonance (at 3.90 ppm).

4-*C*-(1-Bromoethenyl)-2,3,6-tri-*O*-benzyl-α-D-methylglucopyranoside (9b). 9b was obtained from **9a**[44] (0.95 g, 2.05 mmol) using General Procedure C. Column chromatography (silica, petroleum ether:ethyl acetate, 3:1) gave the title compound **9b** (0.805 g, 69%) as a colorless oil. ^{1}H NMR (400 MHz, 80% C$_6$D$_6$ + 20% CDCl$_3$): δ 3.18 (s, 3H), 3.60 (dd, J_1 = 9.5 Hz, J_2 = 6.2 Hz, 1H), 3.64 (s, 1H), 3.79 (dd, J_1 = 9.4 Hz, J_2 = 6.8 Hz, 1H), 4.08 (dd, J_1 = 10.1 Hz, J_2 = 3.9 Hz, 1H), 4.20 (d, J = 8.9 Hz, 1H), 4.21 (s, 2H), 4.27 (t, J = 6.5 Hz, 1H), 4.48 (d, J = 11.9 Hz, 1H), 4.60 (d, J = 3.9 Hz, 1H), 4.66 (d, J = 11.9 Hz, 1H), 4.86 (d, J = 11.7 Hz, 1H), 4.97 (d, J = 11.7 Hz, 1H), 5.81 (d, ^2J = 1.8 Hz, 1H), 6.19 (d, ^2J = 1.8 Hz, 1H), 7.15 (m, 11H), 7.27 (d, J = 6.7 Hz, 2H), 7.40 (d, J = 6.7 Hz, 2H). ^{13}C NMR (100.6 MHz, C$_6$D$_6$): δ 54.9, 69.9, 71.0, 73.2, 73.4, 75.7, 78.0, 79.17, 83.6, 98.6, 120.6, 127.44, 127.48, 127.67, 127.70, 128.18, 128.29, 128.31, 128.44. NOE (400 MHz): irradiation of the OH proton (at 3.64 ppm) resulted in enhancement of the H$_6$ (at 3.79 ppm) and H$_5$ (at 4.27 ppm) protons of the carbohydrate backbone; irradiation of the vinylic proton (at 5.81 ppm) resulted in enhancement of the H$_2$ proton resonance (at 4.08 ppm).

4-*C*-(1-bromoethenyl)-2,3-*O*-(1-methylethylidene)-6-*O*-tosyl-α-D-methyltalopyranoside (10b). 10b was obtained from **10a**[28] (1.65 g, 4.27 mmol) using General Procedure C. Column chromatography (silica, petroleum ether:ethyl acetate, 3:1) gave the title compound **10b** (1.35 g, 64%) as a colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$): δ 1.35 (s, 3H), 1.54 (s, 3H), 2.43 (s, 3H), 3.01 (s, 1H), 3.39 (s, 3H), 4.08−4.17 (m, 2H), 4.18 (dd, J_1 = 11.1 Hz, J_2 = 2.6 Hz, 1H), 4.33 (dd, J_1 = 8.33 Hz, J_2 = 2.7 Hz, 1H), 4.62 (d, J = 6.4 Hz, 1H), 4.94 (s, 1H), 5.70 (d, ^2J = 1.8 Hz, 1H), 6.20 (d, ^2J = 1.8 Hz, 1H). ^{13}C NMR (100.6 MHz, CDCl$_3$): δ 21.6, 24.7, 25.9, 55.3, 67.8, 68.3, 72.2, 72.9, 73.5, 97.7, 109.9, 120.9, 128.0, 129.9, 130.9, 132.9, 144.9. NOE (400 MHz): irradiation of the vinylic proton (at 6.20 ppm) resulted in enhancement of the OMe resonance (at 3.39 ppm). Anal. Calcd for $C_{11}H_{15}BrO_5$: C, 43.02; H, 4.92. Found: C, 43.09; H, 4.97.

4-C−(1-Bromoethenyl)-1,6-anhydro-2,3-O-(1-methylethylidene)-*β*-D-talopyranose (11b). 11b was obtained from **11a**[45] (1.15 g, 5.74 mmol) using General Procedure C. Column chromatography (silica, petroleum ether: ethyl acetate, 3:1) gave the title compound **11b** (1.23 g, 70%) as a colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$): δ 1.30 (s, 3H), 1.52 (s, 3H), 3.59 (s, 1H), 3.69 (dd, J_1 = 7.9 Hz, J_2 = 5.8 Hz, 1H), 4.07 (dd, J_1 = 5.8 Hz, J_2 = 3.0 Hz, 1H), 4.27 (d, J = 8.0 Hz, 1H), 4.40 (t, J = 6.3 Hz, 2H), 5.26 (d, J = 3.2 Hz, 1H), 5.79 (d, J = 2.8 Hz, 1H), 6.08 (d, J = 2.9 Hz, 1H). ^{13}C NMR (100.6 MHz, CDCl$_3$): δ 25.9, 26.2, 64.3, 73.1, 74.8, 75.0, 75.7, 99.2, 111.1, 120.4, 136.5. Anal. Calcd for $C_{19}H_{25}BrO_8S$: C, 46.26; H, 5.11. Found: C, 45.64; H, 5.08.

General Procedure D: 2-Bromonon-1-en-3-ol (16a). This procedure used the same approach as described in General Procedure C, except that a solution of *n*-heptanal (1.05 g, 9.19 mmol) and Me$_3$SiCl (2 equiv) in the Trapp mixture was added to the preformed slurry of **1** (3 equiv) at −115 °C. The crude mixture was hydrolyzed by vigorous stirring with a CH$_2$Cl$_2$/water/CF$_3$COOH mixture (1:1:0.1 by volume) overnight at 30−35 °C. Column chromatography (silica, petroleum ether: ethyl acetate, 20:3) gave the title compound **16a** (1.50 g, 74%) as a colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$): δ 0.90 (t, J = 6.8 Hz, 3H), 1.25−1.35 (m, 8H), 1.55−1.75 (m, 2H), 2.14 (s, 1H), 4.09 (t, J = 6.5 Hz, 1H), 5.56 (d, ^2J = 1.9 Hz, 1H), 5.88 (d, ^2J = 1.1 Hz, 1H). ^{13}C NMR (100.6 MHz, CDCl$_3$): δ 14.1, 22.6, 25.1, 29.0, 31.7, 35.3, 76.1, 116.9, 137.7. Anal. Calcd for $C_9H_{17}BrO$: C, 48.88; H, 7.75. Found: C, 49.08; H, 7.80.

1-(4-Trifluoromethylphenyl)-3-propen-1-ol (16b). 16b was prepared according to General Procedure D from *p*-trifluoromethylbenzaldehyde (1.22 g, 7.0 mmol). The crude mixture was hydrolyzed by vigorous stirring with a CH$_2$Cl$_2$/water/CF$_3$COOH mixture (1:1:0.1 by volume) overnight at 30−35 °C. Column chromatography (silica, petroleum ether:ethyl acetate, 5:1) gave the title compound **16b** (1.52 g, 77%) as a colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$): δ 2.81 (s, 1H), 5.32 (s, 1H), 5.72 (d, J = 1.8 Hz, 1H), 6.06 (dd, J_1 = 2.1 Hz, J_2 = 1.0 Hz, 1H), 7.54 (d, J = 8.7 Hz, 2H), 7.64 (d, J = 8.2 Hz, 2H). ^{13}C NMR (100.6 MHz, CDCl$_3$): δ 77.3, 118.5, 122.7, 125.45, 125.49, 127.0, 134.9, 143.6. Anal. Calcd for $C_{10}H_8BrF_3O$: C, 42.73; H, 2.87. Found: C, 43.31; H, 2.94.

***anti*-2-Bromo-4-*tert*-butyldimethylsiloxyoct-1-en-3-ol (17). 17** was prepared according to General Procedure D from 2-*tert*-butyldimethylsiloxyhexanal[46] (1.61 g, 7.0 mmol). The crude mixture was hydrolyzed by vigorous stirring with a CH$_2$Cl$_2$/water/CF$_3$COOH mixture (1:1:0.1 by volume) overnight at 30−35 °C. Column chromatography (silica, petroleum ether: ether, 93:7) gave the title compound **17** (1.18 g, 50%) as a colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$): δ 0.11 (s, 3H), 0.12 (s, 3H), 0.92 (s, 9H), 1.20−1.55 (m, 6H), 2.63 (s, 1H), 4.01 (apparent quintet, J = 3.1 Hz, 1H), 4.19 (br d, J = 4.3 Hz, 1H), 5.62 (t, J = 1.4 Hz, 1H), 6.06 (dd, J_1 = 1.6 Hz, J_2 = 1.2 Hz, 1H). ^{13}C NMR (100.6 MHz, CDCl$_3$): δ −1.83, −1.76, 15.9, 17.0, 24.2, 27.1, 28.6, 30.7, 71.5, 76.5, 114.1, 127.4. Anal. Calcd for $C_{14}H_{29}BrO_2Si$: C, 49.84; H, 8.66. Found: C, 50.38; H, 8.93.

***anti*-2-Bromo-4-*tert*-butyldimethylsiloxypent-1-en-3-ol (18). 18** was prepared according to General Procedure D from 2-*tert*-butyldimethylsiloxypropanal[47] (1.32 g, 7.0 mmol). The crude mixture was hydrolyzed by vigorous stirring with a CH$_2$Cl$_2$/water/CF$_3$COOH mixture (1:1:0.1 by volume) overnight at 30−35 °C. Column chromatography (silica, petroleum ether:ether, 93:7) gave the title compound **18** (1.01 g, 49% yield) as a colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$): δ 0.10 (s, 6H), 0.90 (s, 9H), 1.09 (d, J = 6.1 Hz, 3H), 2.65 (d, J = 2.0 Hz, 1H), 4.05 − 4.16 (m, 2H), 5.61 (dd, J_1 = 1.6 Hz, J_2 = 1.0 Hz, 1H), 6.02 (t, J = 1.5 Hz, 1H). ^{13}C NMR (100.6 MHz, CDCl$_3$): δ −5.0, −4.5, 16.8, 25.8, 68.9, 78.7, 117.6, 132.1. Anal. Calcd for $C_{11}H_{23}BrO_2Si$: C, 44.74; H, 7.85. Found: C, 45.24; H, 7.96.

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(43) The preparation of **8a** is presented in the Supporting Information.

(44) Ketone **9a** was kindly provided by Dr. Peter Norris, Department of Chemistry, Youngstown State University.

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3-Bromo-2-trimethylsilyl-3-buten-2-ol (19). **19** was obtained according to General Procedure A from acetyltrimethylsilane (1.63 g, 14 mmol) as a colorless liquid (2.03 g, 65%), bp 45−46 °C at 0.6 mmHg. (To prevent spontaneous rearrangement to **20**, the distillation glassware was soaked in 40% aq NaOH for 3 min, and then thoroughly rinsed with distilled water prior to use; 1% (v/v) pyridine was added to the product immediately after distillation to stabilize the purified product.) ^{1}H NMR (300 MHz, C_6D_6): δ 0.18 (s, 9H), 1.37 (s, 3H), 5.41 (d, J = 1.8 Hz, 1H), 5.67 (d, J = 1.8 Hz, 1H). ^{13}C NMR (75 MHz, C_6D_6): δ −3.2, 25.1, 72.0, 113.5, 141.3.

3-Bromo-3-trimethylsilylbutan-2-one (20). A solution of **19** in CH_2Cl_2 (ca. 1 M) was kept in a glass vessel under argon for 72 h at room temperature. After the solvent was removed (rt at 20 mmHg), the crude title compound **20** was obtained as a 10:1 mixture with **19**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.17 (s, 9H), 1.81 (s, 3H), 2.38 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ −3.0, 24.9, 61.6, 207.5.

Bis(1-bromoethenyl)dimethylsilane (27). **27** was prepared according to General Procedure A (with the exception that a solution of AcOH was not added) from dichlorodimethylsilane (1.81 g, 14 mmol) as a colorless liquid (1.21 g, 64%), bp 86−88 °C at 16 mmHg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.41 (s, 6H), 6.38 (d, J = 2.0 Hz, 1H), 6.45 (d, J = 2.0 Hz, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ −3.7, 132.9, 133.5. Anal. Calcd for $C_6H_{10}Br_2Si$: C, 26.69; H, 3.73. Found: C, 26.68; H, 3.83.

General Procedure E: Preparation of (1-Bromoethenyl)chlorodiethylsilane (28) from Dichlorodiethylsilane. General procedure A was used but with a different workup procedure: instead of the addition of an AcOH solution, the reaction mixture was warmed and diluted with a 3-fold excess (by volume) of anhydrous pentane. The lithium salts were filtered off, and the solvents were removed from the filtrate by distillation at atmospheric pressure. Vacuum distillation of the residual oil gave title compound **28** as a colorless oil (1.01 g, 26%), bp 72−74 °C at 17 mmHg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.96−1.10 (m, 10H), 6.48 (d, J = 1.9 Hz, 1H), 6.56 (d, J = 1.9 Hz, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 6.5, 7.0, 130.2, 133.9.

(1-Bromoethenyl)chlorodiisopropylsilane (29). **29** was prepared according to General Procedure E from dichlorodiisopropylsilane (2.59 g, 14 mmol) as a colorless liquid (1.68 g, 47%), bp 94−96 °C at 16 mmHg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.08−1.10 (m, 12 H), 1.41 (septet, J = 7.4 Hz, 2H), 6.53 (d, J = 1.9 Hz, 1H), 6.59 (d, J = 1.9 Hz, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 13.2, 16.7, 17.3, 128.5, 134.7.

(1-Bromoethenyl)iodomethyldimethylsilane (30). **30** was prepared according to General Procedure E from chloro(chloromethyl)dimethylsilane (1.74 g, 12.2 mmol). The volatile components were removed from the crude reaction product in vacuo, and the residue was treated with a saturated solution of sodium iodide in anhydrous acetone (10 mL) at reflux for 20 h. Water (20 mL) was added; the mixture was extracted with petroleum ether (2 × 20 mL), and the combined organic extracts were dried ($MgSO_4$). Vacuum distillation gave the title compound **30** as a colorless oil (1.22 g, 33%), bp 105−110 °C at 17 mmHg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.36 (s, 6H), 2.16 (s, 2 H), 6.30 (d, J = 2.1 Hz, 1H), 6.39 (d, J = 2.1 Hz, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ −16.1, −3.5, 131.7, 134.8. Anal. Calcd for $C_5H_{10}BrISi$: C, 19.69; H, 3.30. Found: C, 20.69; H, 3.35.

(1-Bromoethenyl)-tri-*n*-butylstannane (31). **31** was prepared using tributyltin chloride (4.56 g, 14 mmol) according to General Procedure A, except that the addition of tributyltin chloride was completed rapidly over 5−10 s, and a solution of AcOH was not added prior to workup. The title compound was obtained as a colorless liquid (4.71 g, 85%), bp 108−109 °C at 0.1 mmHg. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.92 (t, J = 7.3 Hz, 9H), 1.06 (apparent t, J = 8.1 Hz, 6H), 1.35 (sextet, J = 7.7 Hz, 6H), 1.50−1.70 (m, 6H), 6.13 (d, J = 1.9 Hz, 1H), 6.49 (d, J = 1.9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.0, 13.9, 27.4, 28.9, 131.9, 137.6. Anal. Calcd for $C_{14}H_{29}BrSn$: C, 42.47; H, 7.38. Found: C, 42.83; H, 7.56.

1-Bromo-1-iodoethene (32). **32** was prepared using iodine (3.55 g, 14 mmol) according to General Procedure A, except that the addition of iodine was completed rapidly over 5−10 s, and a solution of AcOH was not added prior to workup. The title compound was obtained as a colorless liquid (1.30 g, 40%), bp 80−81 °C at 160 mmHg. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.72 (d, J = 3.3 Hz, 1H), 6.92 (d, J = 3.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 55.3, 134.9. Anal. Calcd for C_2H_2BrI: C, 10.32; H, 0.87. Found: C, 11.52; H, 1.03.

2,2-Diisopropyl-4,6,6-trimethyl-3-methyleneoctahydro-1,2-benzoxasilole (34). A solution of **33** (119 mg, 0.33 mmol), tributyltin hydride (116 mg, 0.39 mmol), and triethylborane (0.07 mL of a 1 M solution in hexanes) were stirred in benzene (20 mL) at room temperature for 24 h. The mixture was concentrated in vacuo. Purification of the crude product by column chromatography (silica, pentane:ether, 20:1) gave the title compound **34** (46 mg, 50%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.90 (d, J = 3.1 Hz, 6H), 1.00−1.05 (m, 9H), 1.06−1.10 (m, 8H), 1.27 (d, J = 7.3 Hz, 3H), 1.39 (t, J = 13.2 Hz, 1H), 1.51 (dq, J_1 = 13.4 Hz, J_2 = 0.8 Hz, 1H), 2.00−2.10 (m, 1H), 2.78 (sextet, J_1 = 0.8 Hz, 1H), 4.19 (quintet, J = 6.3 Hz, 1H), 5.52 (t, J = 2.7 Hz, 1H), 5.98 (t, J = 2.6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 12.7, 13.2, 17.3, 17.6, 17.7, 17.9, 20.0, 25.1, 30.2, 32.2, 33.2, 41.2, 45.0, 51.5, 76.5, 123.5, 147.4. NOE (400 MHz): irradiation of the vinylic proton (at 5.52 ppm) resulted in enhancement of the Me resonance (at 1.27 ppm). Anal. Calcd for $C_{17}H_{32}OSi$: C, 72.79; H, 11.50. Found: C, 72.58; H, 11.60.

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Supporting Information Available: General experimental procedures, design of the low-temperature glass reactor used in these studies, details of the preparation of the ketone precursor **8a**, experimental details related to Table 4 (entries 5, 6, 8), and copies of ^{1}H and ^{13}C NMR spectra for compounds **2a**−**2g**, **5b**−**11b**, **16a**, **16b**, **17**, **18**, **17a**, **18a**, **17b**, **18b**, **19**, **20**, **28**−**34**, **36**, and **37**. This material is available free of charge via the Internet at http://pubs.acs.org.

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