Pergamon

SCIENCE DIRECT®

Tetrahedron 59 (2003) 8889–8900

TETRAHEDRON

Tandem silylformylation–allyl(crotyl)silylation: a new approach to polyketide synthesis

Michael J. Zacuto, Steven J. O'Malley and James L. Leighton*

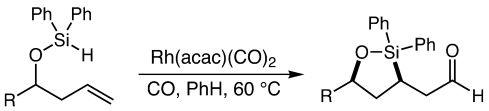
Department of Chemistry, Columbia University, New York, NY 10027, USA

Received 5 April 2003; accepted 14 April 2003

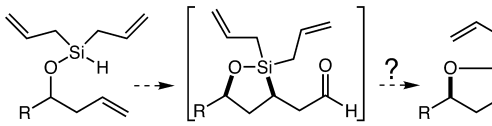
Abstract—Tandem intramolecular silylformylation–allyl(crotyl)silylation reactions have been developed that allow the highly efficient synthesis of polyketide fragments. The substrates are subjected to Rh(I)-catalyzed silylformylation to afford β-(diallyl)silyl aldehydes which undergo spontaneous uncatalyzed allylsilylation. This unusual spontaneous allylsilylation reaction is driven by strain release Lewis acidity, which arises from the ~95° O–Si–C bond angle in the oxasilacyclopentane product of the silylformylation reaction. The methodology has been developed both for alkene and alkyne substrates, may be used to establish as many as three stereocenters, and has been shown to be amenable to use in an iterative fashion.

1. Introduction

Due to the prevalence and clinical relevance of polyketide-derived natural products with the skipped polyol structural motif,[1] we have been engaged in the development of efficient strategies for their synthesis.[2,3] One approach has focused on olefin carbonylation reactions and the general approach is summarized in Scheme 1. Special emphasis has been placed on the direct production of suitably protected polyhydroxy aldehydes, since the next step in the sequence is the addition of an allyl group. In this fashion a highly efficient three step iterative sequence—with no protection steps or oxidation state adjustments—might be realized. Another important advantage to the direct production of aldehydes is that, at least in principle, it is possible to envision the aldehyde allylation step being rendered in tandem with the carbonylation reaction. Given that the previously reported intramolecular alkene silylformylation reaction produces β-silylaldehydes directly (Eq. (1)),[2b] and that allylsilanes are well-known aldehyde allylation agents,[4] it seemed plausible that silylformylation of a diallylsilane might lead to intramolecular aldehyde allylsilylation (Eq. (2)). If successful, this tandem reaction would, upon Tamao oxidation of the product,[5] deliver 1,3,5-triols in a remarkably efficient manner.



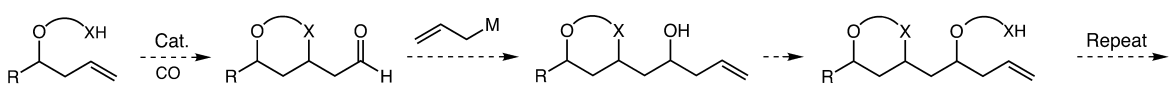
(1)



(2)

2. Alkene substrates

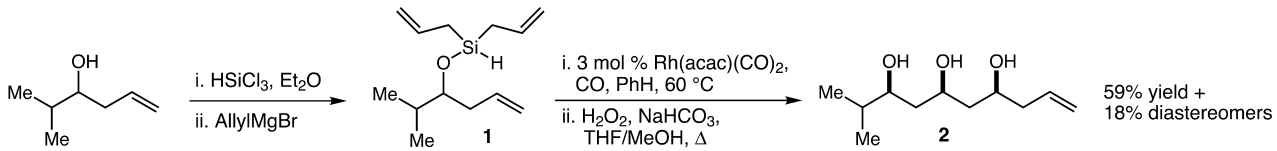
Our studies commenced with diallylsilyl ether **1**, readily prepared from the corresponding homoallylic alcohol in a single step (Scheme 2).[6] Subjection of this silane to the action of 3 mol% $Rh(acac)(CO)_2$ in benzene under 1000 psi CO at 60°C in a stainless steel pressure reactor, followed by evaporation of solvent and subjection of the residue to the conditions of the Tamao oxidation (H_2O_2, $NaHCO_3$, THF/



Scheme 1.

Keywords: polyketides; silylformylation; carbonylation; allylation; strain release Lewis acidity.
* Corresponding author. Tel.: +1-212-854-4262; fax: +1-212-932-1289; e-mail: leighton@chem.columbia.edu

0040–4020/$ - see front matter © 2003 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2003.04.004

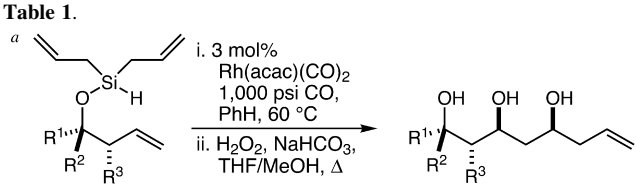


Scheme 2.

MeOH, reflux) led to a mixture of triols in 77% yield. The major product, easily separable from a mixture of minor diastereomers, was isolated in 59% yield and was identified as the *syn*,*syn* triol **2**.[7] ^{1}H NMR analysis of the unpurified product mixture prior to the oxidation revealed a complex spectrum with no peaks in the aldehyde region. Although the spectrum has resonances consistent with the dioxasilabicyclo[3.3.0]octane depicted in Eq. (2), the peaks are quite broad and featureless. Mass spectral analysis indicated high molecular weight material with a repeating fragment pattern suggestive of an oligomeric mixture. Based on these data it is proposed that the initially formed dioxasilabicyclo-[3.3.0]octane undergoes a ring-opening oligomerization through O–Si bonds, a process driven by relief of ring strain. Regardless, it is clear that following the carbonylation an allyl group is transferred, forming a second C–C bond and a second new stereocenter in a single tandem reaction.

With the feasibility of the tandem reaction established, a brief survey of the substrate scope was undertaken (Table 1). As with our previous silylformylation study,[2b] best results were obtained in benzene under 1000 psi CO at 60°C; below ~800 psi CO or ~45°C, the rate of the silylformylation reaction becomes impracticably slow. Entries 1, 2 and 3 establish the tolerance for both silyloxy and alkenyl groups, and reveal the trend of increasing diastereoselectivity with increasing size of the homoallylic substituent. The increased diastereoselectivity of entry 4 relative to entry 1 due to the presence of an *anti* allylic methyl group mirrors a similar increase observed in the diphenylsilane silylformylation reaction.[2b] This suggests that the modest diastereoselectivity observed for entries 1–3 is due mainly to the modest diastereoselectivity of the silylformylation reaction, and that the diastereoselectivity of the allylation reaction is quite high. The use of an achiral substrate corroborates this interpretation and provides a useful benchmark diastereoselectivity (93:7) for the allylation. Finally, we note that in every case we have thus far studied, the major *syn*,*syn* triol is easily separable from a mixture of the other diastereomers.

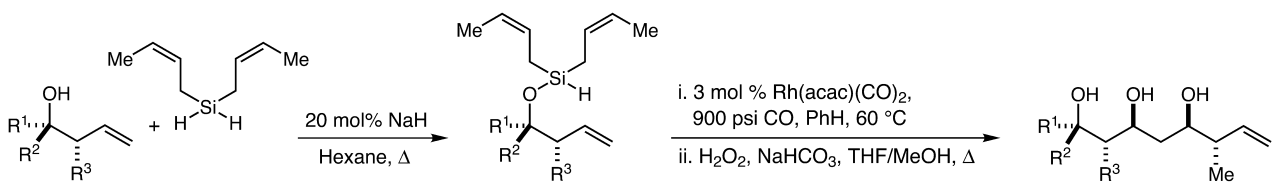
Table 1.



Entry	R^1	R^2	R^3	dr[a]	Yield (%)[b]
1	H	*i*-Pr	H	77:23	59
2	H	$TBSOCH_2CH_2$	H	71:29	45
3	H	$CH_2{=}CHCH_2$	H	69:31	50
4	H	*i*-Pr	Me	92:8	59
5	Me	Me	H	93:7	65

All reactions were conducted in a stainless steel pressure reactor equipped with a pressure guage and a glass liner.
[a] *syn*, *syn* triol:∑ all other diastereomers.
[b] Isolated yield of purified major product.

In principle, this reaction is amenable to the creation of up to as many as four new stereocenters by appropriate substitution of both the alkene substrate and the allyl groups on silicon. Specifically, methyl substitutions could lead to the polypropionate subset of polyketide-derived natural products. While we have found that substitution on the terminal carbon of the substrate alkene has a dramatically deleterious effect on the silylformylation reaction, substitution of the allyl groups on silicon was far more productive. A synthesis of di-*cis*-crotylsilane was developed[2i,8] and we devised a method for its efficient attachment to the substrate alcohols based on hydrosilane alcoholysis.[9,10] Constrained to catalysts that would not also catalyze hydrosilylation of the products,[11] we employed NaH (20 mol%) to catalyze the alcoholysis of di-*cis*-crotylsilane, and the use of hexane as solvent was found to be important to minimize further reaction of the product, which was observed in more polar solvents such as THF. Using this procedure, homoallylic alcohols **3a**, **3b**, and **3c**[12] were transformed into di-*cis*-crotylsilyl ethers **4a**, **4b**, and **4c** in 90, 99 and 85% yields, respectively (Scheme 3). Subjection of silanes **4a**, **4b**, and **4c** to the standard reaction conditions led to the isolation of triols **5a**, **5b** and **5c**, in which three new stereocenters and an *anti* terminal propionate unit have been established in a single tandem reaction. In every case the yield shown is the isolated yield of purified major diastereomer. The diastereoselectivities (major diastereomer: all other diastereomers) parallel closely those observed in the corresponding

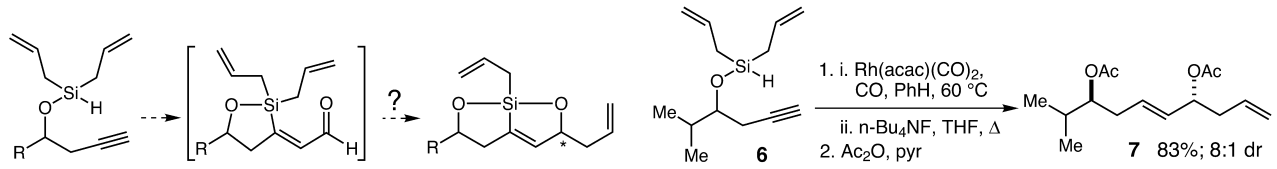


3a R^1, R^3 = H; R^2 = i-Pr
3b R^1 = H; R^2 = i-Pr; R^3 = Me
3c R^1, R^2 = Me; R^3 = H

4a 90%
4b 99%
4c 85%

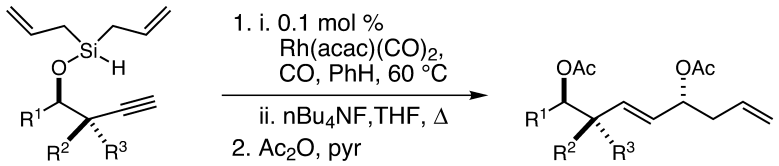
5a 65%; 72:28 dr
5b 67%; 92:8 dr
5c 65%; 93:7 dr

Scheme 3.



Scheme 4.

Table 2.



Entry	R^1	R^2	R^3	dr[a]	Yield (%)[b]
1	*n*-Pr	H	H	4:1	68
2	$HC{\equiv}CCH_2$	H	H	4:1	63
3[c]	$TBSOCH_2CH_2$	H	H	5:1	63
4	*i*-Pr	H	H	8:1	83
5	Ph	H	H	7:1	83
6	*t*-Bu	H	H	10:1	66
7	*i*-Pr	Me	H	23:1	70
8	*i*-Pr	H	Me	7:1	70

[a] 1,5-*anti*:1,5-*syn*; measured by gas chromatography.
[b] Isolated yield of the purified mixture of diastereomers.
[c] The TBS group is cleaved during the protodesilylation step and the triacetate is isolated.

diallylsilane reactions (see Table 1) and we therefore, conclude that the crotylation event is essentially stereospecific.

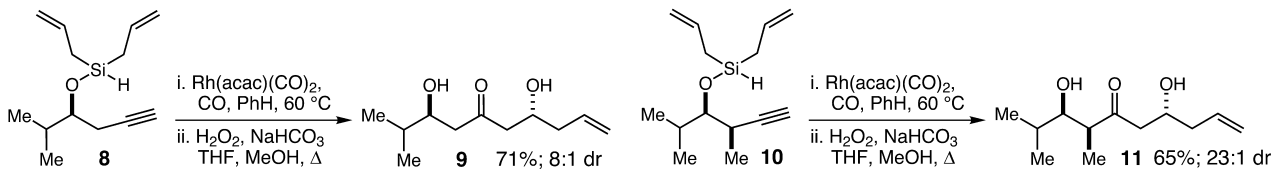
3. Alkyne substrates

Alkynes are well-known substrates for silylformylation, and it seemed plausible that tandem allylsilylation of the resultant unsaturated aldehydes might occur as well (Scheme 4). Interestingly, in this system the carbon bearing silicon is no longer stereogenic. Thus, any diastereoselectivity in the allylsilylation would have to derive from the original homopropargylic stereocenter, and would constitute an example of remote 1,5 stereoinduction. To test the feasibility of this proposal, diallylsilyl ether **6** was prepared and treated to the silylformylation conditions used for alkenes (1.0 mol% of $Rh(acac)(CO)_2$, 1000 psi of CO, benzene, 60°C). The unpurified material was directly subjected to protodesilylation (*n*-Bu_4NF, THF, reflux) and peracetylation (Ac_2O, pyr) to provide an 8:1 mixture of *anti*-diacetate **7**[13] and the *syn* diastereomer in 83% overall yield. Thus, the allylsilylation proceeded with good 1,5 diastereoselectivity, providing the 1,5 *anti* product as the major diastereomer, a result which is opposite to that observed with alkene substrates.

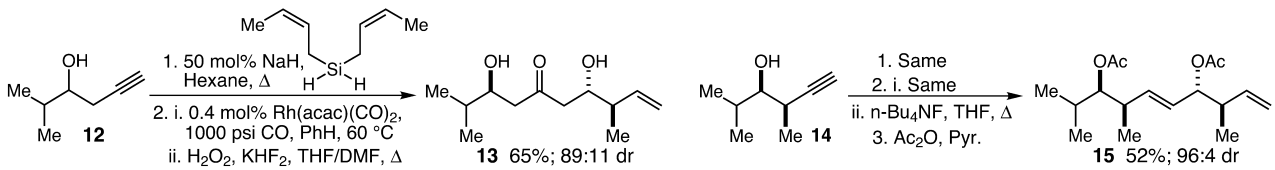
Optimization of the reaction conditions revealed that the catalyst loading could be reduced to 0.1 mol% with no decrease in efficiency. At CO pressures significantly lower than 1000 psi, and/or at temperatures significantly below 60°C there was a small improvement in the diastereoselectivity, accompanied, however, by a significant drop in reaction rate. We therefore, quickly settled on 1000 psi of CO in benzene at 60°C as the standard reaction conditions. With optimal reaction conditions identified, we set out to investigate the scope of the reaction with regard to homopropargylic and propargylic substituents (Table 2). Entries 1–6 clearly establish a direct correlation between the steric size of the homopropargylic substituent and the diastereoselectivity of the reaction, as well as a tolerance for alkyne and silyloxy functional groups. The superior diastereoselectivity of entry 7 indicates the stereochemically reinforcing nature of a *syn* propargylic methyl group, whereas with an *anti* propargylic methyl group (entry 8) useful diastereoselectivity is still observed.

As an alternative to the protodesilylative workup procedure, we have also investigated an oxidative workup of the initially formed vinylsilane products to provide β,β′-dihydroxyketone products. Subjection of silane **8** to the standard tandem silylformylation–allylsilylation conditions followed by evaporation of the solvent and subjection of the residue to the conditions of the Tamao oxidation (H_2O_2, $NaHCO_3$, THF/MeOH, reflux) led to ketodiol **9** in 71% yield with identical diastereoselectivity to entry 4 in Table 1 (Scheme 5). In a similar fashion, diallylsilane **10** was transformed into ketodiol **11** in 65% yield and 23:1 diastereoselectivity. This oxidative workup is noteworthy in the context of polyketide synthesis in that diastereoselective ketone reduction would allow access to stereochemically diverse triol arrays.

In an effort to expand the scope of the alkyne reaction, the crotylsilane chemistry discussed above (Scheme 3) was examined. Thus, alcohol **12** was silylated with di-*cis*-crotylsilane and the resulting silyl ether was subjected to the tandem silylformylation–crotylsilylation conditions using



Scheme 5.



Scheme 6.

the oxidative workup procedure. Ketodiol **13** was isolated in 65% overall yield as an 8:1 mixture of diastereomers (Scheme 6). Using the protodesilylative workup procedure, alcohol **14** was transformed into **15**[13] in 52% overall yield and 96:4 diastereoselectivity. As above, the diastereoselectivities parallel closely those observed in the corresponding diallylsilane reactions (see Table 2 and Scheme 5), leading to the conclusion that the crotylation event is stereospecific.

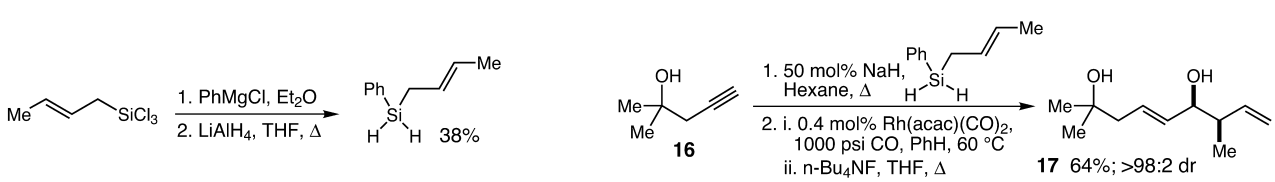
As mentioned above, our attempts to prepare di-*trans*-crotylsilane have been fruitless. The most obvious proposal was to adapt the procedure for the synthesis of *trans*-crotyltrichlorosilane.[14] Even under harsh conditions with many different catalysts however, we could not induce a successful reaction between dichlorosilane and *trans*-crotylchloride. Desiring nevertheless to establish that *trans*-crotyl groups would result in *syn* propionate units in the tandem intramolecular silylformylation–allylsilylation chemistry, we synthesized *trans*-crotyl-phenylsilane as shown in Scheme 7. In order to avoid the creation of a mixture of diasteromers in the silane alcoholysis reaction, we employed achiral alcohol **16**. As shown, the silylation chemistry and the tandem intramolecular silylformylation–allylsilylation chemistry work equally well with a *trans*-crotylsilane to give diol **17** in 64% overall yield. As expected, a *syn*-propionate unit was obtained stereospecifically.

4. Mechanism

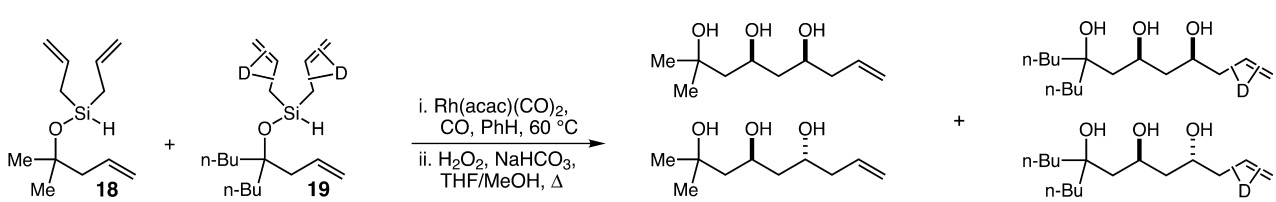
Several intriguing mechanistic issues demanded explication. First, and most importantly, why do the allyl(crotyl)-silylations proceed spontaneously in the absence of an external Lewis acid? Second, what is the origin of the diastereoselectivity, and why do alkene substrates give predominantly 1,5-*syn* products while alkyne substrates favor the 1,5-*anti* products? And third, why do *cis*-crotylsilanes provide the *anti* products, and *trans*-crotylsilanes the *syn* products?

In order to gain mechanistic insight into this unusual allylsilylation reaction, we began by establishing the intramolecular nature of the process with the crossover experiment shown in Scheme 8. Thus, a 1:1 mixture of diallylsilane **18** and deuterium-labeled diallylsilane **19** (each allyl group carried one deuterium) was subjected to the standard conditions and produced the four indicated triol products, each of which was cleanly isolated. No evidence for the incorporation of any deuterium in the products derived from **18** could be detected by ^{1}H, ^{2}H and ^{13}C NMR spectroscopy.

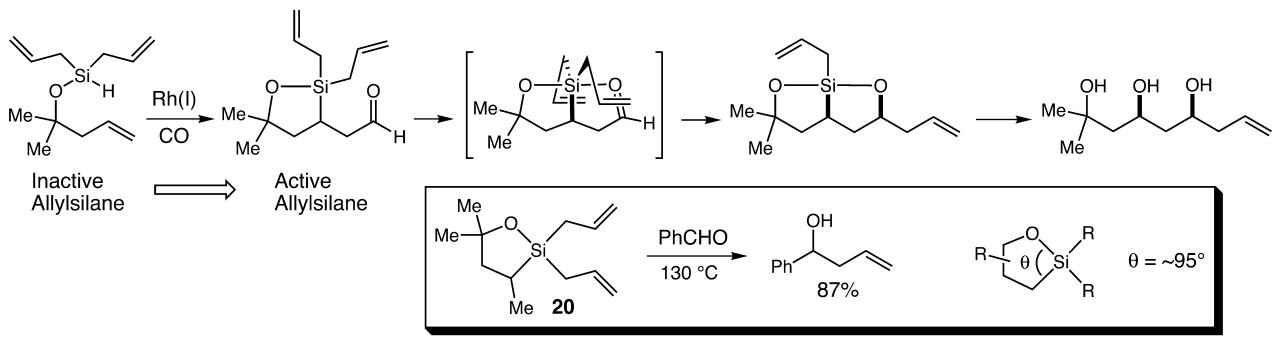
Examples of intramolecular silicon-tethered allylsilane additions to aldehydes,[15] acetoxyazetidinones,[16] and acetals[17] have been reported, but require the use of external



Scheme 7.



Scheme 8.

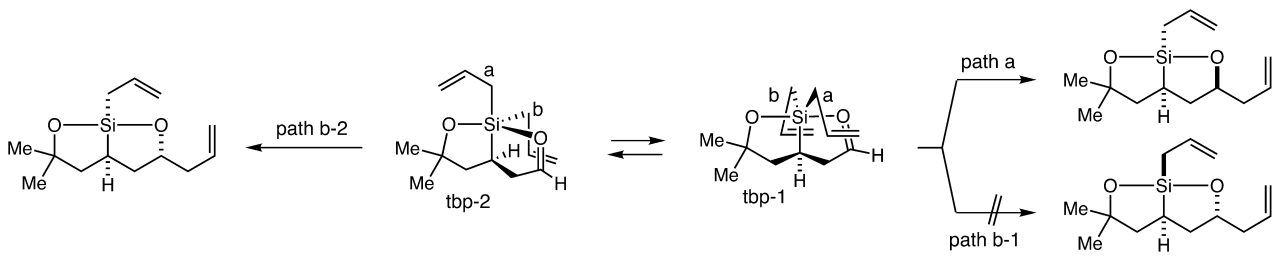


Scheme 9.

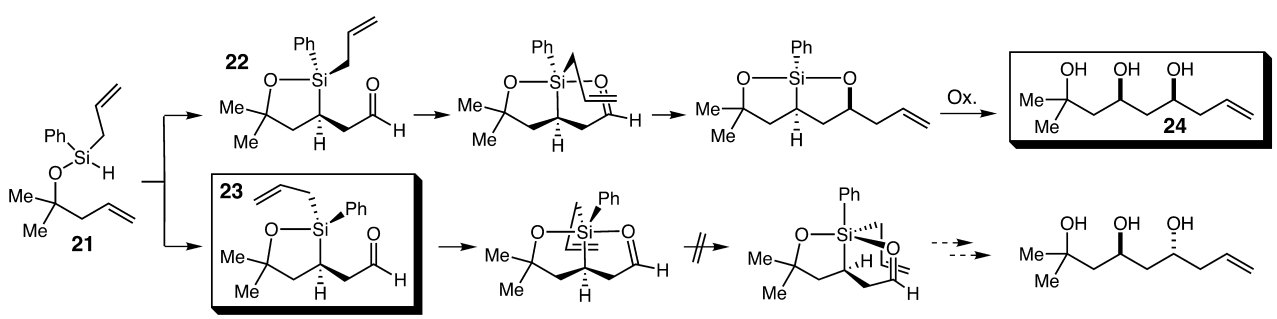
Lewis acids. Utimoto has reported uncatalyzed additions—both inter- and intramolecular—of tetracoordinate allylsilanes to aldehydes and ketones based on the use of strained allylsilacyclobutanes.[18] This report followed the disclosures of Myers[19] and Denmark[20] that enoxysilacyclobutanes engage in uncatalyzed aldol addition reactions. These uncatalyzed reactions proceed through the agency of what Denmark has termed 'strain release Lewis acidity.'[21] In this model the ~80° C–Si–C bond angle imposed by the silacyclobutane favors complexation of an aldehyde with concomitant Si rehybridization to a trigonal-bipyramid with the silacyclobutane spanning apical and equatorial positions (90° ideally). Depsite the fact that the present work involves 5-membered silacycles, we propose that strain release Lewis acidity is operative and responsible for the spontaneous allylation chemistry observed (Scheme 9). Two key observations support this claim. First, the O–Si–C bond angle in oxasilacyclopentanes is typically ~95°,[22] which would be expected to favor a trigonal-bipyramidal geometry at Si in analogy to the silacyclobutane chemistry.[23] And second, pyrolysis of oxasilacyclopentane **20** with benzaldehyde (6.0 equiv.) in a sealed tube at 130°C (Utimoto's conditions) produced homoallylic alcohol **7** in 87% yield.[24]

In an effort to develop a model for the observed stereoselectivities, an analysis was carried out based on the mechanism outlined in Scheme 9 above. To avoid chiral at silicon complexes we have consistently employed diallyl- and dicrotylsilanes, and this mechanism clearly implies that the stereoselectivity of the allylsilylation event is determined by the relative rates at which the two diastereotopic allyl groups react. It was important to secure evidence in support of this hypothesis as it suggested an intriguing possibility: that if chiral at silicon substrates bearing only one allyl group could be diastereoselectively prepared, either diastereomeric product of the allylsilylation event could be accessed. This would greatly increase the scope of this methodology.

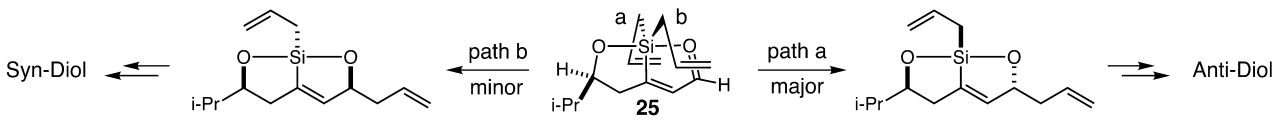
Analysis of the trigonal-bipyramidal (tbp) conformations for the Si–O(aldehyde) complex of the intermediate aldehyde with the constraint that both the oxasilacyclopentane ring and the 5-membered ring formed by Si–O-(aldehyde) complexation must span an apical and an equatorial position, reveals only two reasonable possibilities (tbp-1 and tbp-2, Scheme 10). Transfer of allyl group a in tbp-1 (path a) is expected to be favored, since it is closer to the aldehyde than allyl group b, and leads to the observed major *syn* product. In principle, transfer of allyl group b (path b-1) could be the source of the minor *anti* product, but



Scheme 10.



Scheme 11.



Scheme 12.

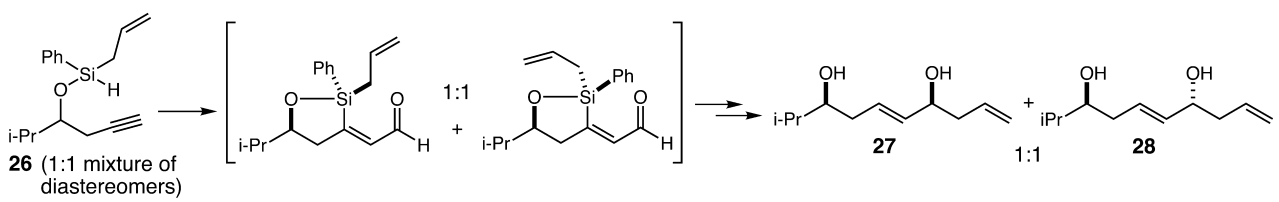
this pathway should be highly disfavored since the initial product would be a highly strained *trans*-fused dioxasilabicyclo[3.3.0]octane. Instead, it is proposed that the minor diastereomer is formed by way of a pseudorotation to tbp-2,[25] followed by transfer of allyl group b (path b-2), leading to production of the illustrated *cis*-fused dioxasilabicyclo[3.3.0]octane.

To shed light on this model, allylphenylsilane **21** was prepared and subjected to the tandem silylformylation–allysilylation reaction (Scheme 11). Presumably proceeding by way of a mixture of diastereomeric aldehydes **22** and **23**, upon oxidative workup the reaction produced *syn*-triol **24** stereospecifically (recall that the diallyl version gave a 93:7 dr, Table 1, entry 5). None of the *anti* diastereomer could be detected. When the unpurified reaction mixture was analyzed by ^{1}H NMR spectroscopy prior to the oxidation step, for the first time we observed an aldehyde intermediate. Unable to achieve a stereochemical proof for this aldehyde due to its instability, we may only tentatively assign it structure **23**. Nevertheless, the apparent reluctance of this aldehyde to undergo allylation to give the *anti*-triol diastereomer may be rationalized within the context of our model by the assertion that the initially formed complex does not undergo pseudorotation to the reactive complex. This pseudorotation places the phenyl group in an apical position, and in his classic studies of pseudorotation of pentacoordinate siliconates, Martin has provided evidence that this would be expected to be disfavored relative to more electronegative substituents.[26]

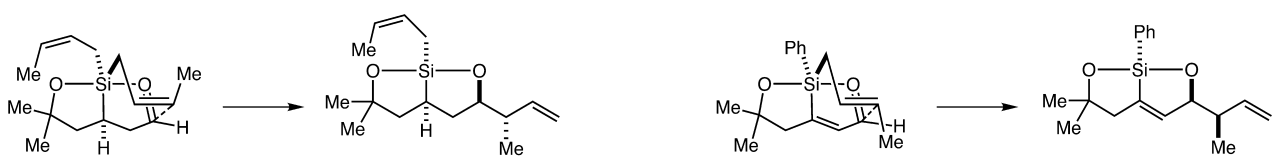
In analogy to this model, a similar scenario may be developed for the reactions of alkyne substrates. A key difference, however, is that the presence of the unsaturation in the aldehyde intermediate obviates consideration of pseudorotation of the type discussed above as this would lead to more highly strained complexes. Thus, binding of the aldehyde by the Lewis acidic silicon is followed by intramolecular allylsilylation as depicted for aldehyde **25** (Scheme 12). In this model, the diastereoselectivity is determined by the relative rates at which the diastereotopic allyl groups transfer (path a vs. path b). A simple working hypothesis for the observed preference for a path would invoke a destabilizing steric interaction between the *i*-Pr group and allyl group b. The correlation between steric size of the homopropargylic substituent and the selectivity observed in entries 1–6 of Table 2 is consistent with this hypothesis as is the high selectivity observed in entry 7. The nearly identical selectivity observed in entries 4 and 8 is less well rationalized by this model and is suggestive of more subtle stereoelectronic effects. Along these lines it is interesting to note that conformational analysis (envelope conformation with the *i*-Pr group pseudoequatorial) suggests that there should be a nearly antiperiplanar relationship between a lone pair on the oxygen and the Si–C bond of the back allyl group, and a nearly orthogonal relationship between the other oxygen lone pair and the Si–C bond of the front allyl group.

Like the model outlined above for the alkene substrate reactions, this model posits that both of the diastereotopic allyl groups can transfer and each leads to a different product diastereomer, but without the need for pseudorotation. It could therefore be surmised that selective replacement of either allyl group with a non-transferable group would lead to a stereospecific reaction. To gain support for this hypothesis we prepared silane **26** as a 1:1 mixture of diastereomers. Subjection of this mixture to the standard reaction conditions led, presumably by way of the illustrated 1:1 mixture of aldehydes, to a 1:1 mixture of diol diastereomers **27** and **28** (Scheme 13). The clear implication of this experiment is that either product diastereomer could be selected for, based only on the availability of the starting chiral silanes in diastereomerically pure form. In fact, we have recently reported a new asymmetric silane synthesis and have employed it to establish conclusively the correctness of this model.[27]

Finally, we note that the unusual observation of *anti*-propionate units from *cis*-crotyl groups and of *syn*-propionate units



Scheme 13.



Scheme 14.

from *trans*-crotyl groups was predicted by, and is fully consistent with the proposed models. Thus, the intramolecular nature of the reaction necessitates that the alkyl chain of the aldehyde occupy a pseudo-axial position on a chair-like arrangement of the 6 reacting atoms (Scheme 14). Thus, the reacting diasteroface of the aldehyde is the reverse of what is normally postulated, leading to the observed reversal from the usual sense of induction.[28]

5. Conclusion

The methodology reported herein allows the highly efficient assemblage of fragments useful for polyketide-derived natural products synthesis. We have reported one such application,[29] and several others are currently in progress. Of further note, the methodology typically requires the use of only inexpensive and readily available reagents (e.g. $HSiCl_3$, AllylMgBr, CO, $NaHCO_3$, H_2O_2, *n*-Bu_4NF).

Conceptually, the focus on methods that directly produce aldehydes (i.e. carbonylation) has indeed led to the development of tandem reactions for polyketide synthesis, and the use of carbonylation in this respect is certainly novel. Perhaps more importantly, this work has led to the discovery that strain release Lewis acidity-induced allylsilylation chemistry may be accessed using 5-membered silacycles and is not restricted to the use of silacyclobutanes. This discovery has profound implications for the development of new asymmetric reaction methodologies as has recently been demonstrated.[30]

6. Experimental

6.1. General procedure for the preparation of diallylsilyl ethers

A three neck flask equipped with an addition funnel is charged with a solution of $HSiCl_3$ (15 mmol) in Et_2O (20 mL) and the solution is cooled to −78°C. A solution of the homoallylic alcohol (10 mmol) in Et_2O (10 mL) is transferred to the addition funnel and added dropwise over 30 min, with venting of HCl to a bubbler charged with 2 M NaOH. Upon completion of the addition, the reaction mixture is allowed to warm to room temperature, and the volatiles ($HSiCl_3$, HCl and Et_2O) are removed by evaporation with a positive flow of N_2. The residue is dissolved in 20 mL of Et_2O and the resulting solution is cooled to −78°C. Allylmagnesium bromide (20 mL, 20 mmol, 1.0 M in Et_2O) is then transferred to the addition funnel and added dropwise with vigorous stirring. Upon completion of the addition, the solution is warmed to room temperature, and then filtered through a pad of Celite, with pentane washes. The filtrate is concentrated in vacuo, and the residue is filtered again through a pad of celite with pentane washes. After concentration, the resulting material generally is >90% pure and can be used without further purification. The major byproduct is triallylsilane, which can be removed in vacuo. If desired, the products could be purified by distillation under reduced pressure. For the substrates reported here, the yields of purified material were 60–90%, with the more sterically hindered alcohols giving better results.

6.1.1. Preparation of di-*cis*-crotylsilane. In an inert atmosphere glove box a 75 mL sealed tube was charged with $Pd(PPh_3)_4$ (290 mg, 0.25 mmol, 0.5 mol%). The tube was fitted with a septum, removed from the glove box, placed under an Ar atmosphere and cooled (−78°C). 1,3-Butadiene (13.0 mL, 150 mmol; condensed in a cooled (−78°C) graduated cylinder fitted with a septum) was added by cannula to the sealed tube. Dichlorosilane (4.2 mL, 50 mmol; condensed in a cooled (−78°C) graduated cylinder fitted with a septum) was added by cannula to the sealed tube. The tube was sealed with a teflon stopper and the solution was stirred at −78°C for 3 h. The solution was then allowed to warm to ambient temperature, and the resulting heterogeneous solution was vigorously stirred for 48 h. The resultant orange–brown heterogeneous mixture was transferred to a 25 mL round bottom flask and distilled under reduced pressure (reduced slowly, to allow for the removal of excess 1,3-butadiene) to afford dichlorodi-*cis*-crotylsilane (bp ≈60°C at 5 Torr) as a clear, colorless liquid.

A solution of the dichlorodi-*cis*-crotylsilane in 10 mL THF was added dropwise by addition funnel to a solution of $LiAlH_4$ (1.05 g, 27. 5 mmol, 0.56 equiv.) in 40 mL THF. The solution was heated at reflux for 22 h. The resultant heterogeneous mixture was cooled, and filtered through a pad of Celite, rinsing with pentane. The filtrate was transferred to a separatory funnel and washed with H_2O (2×10 mL) and brine (10 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated. The residue was distilled under reduced pressure to afford 5.5 g (75%) of di-*cis*-crotylsilane (bp ≈55°C at 15 Torr) as a clear, colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.38–5.49 (m, 4H, $Si(CH_2CH{=}CHCH_3)_2$), 3.67 (quint, 2H, J=3.6 Hz, 2H, SiH_2), 1.65–1.68 (m, 4H, $Si(CH_2CH{=}CHCH_3)_2$), 1.59 (d, 6H, J=5.8 Hz, $Si(CH_2CH{=}CHCH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 125.5, 122.8, 12.5, 10.2; IR (thin film) 3019, 2930, 2136, 1652, 1396, 1362 cm^{-1}.

6.1.2. Preparation of *trans*-crotyl-phenylsilane. To a solution of *trans*-crotyl-trichlorosilane[14] (10.0 g, 52.7 mmol) in 100 mL Et_2O was slowly added phenylmagnesium chloride (29.0 mL, 57.9 mmol, 2.0 M in THF) by cannula at room temperature with vigorous stirring. Upon completion of addition, the reaction mixture was heated at reflux for 3 h, then cooled. The reaction mixture was filtered through a pad of celite and the filtrate was concentrated. The residue was distilled under vacuum (<1.0 Torr; bp 78–80°C) to give a clear liquid (*trans*-crotyl-phenyldichlorosilane). To a solution of $LiAlH_4$ (0.46 g, 12.3 mmol) in 50 mL THF was slowly added a solution of this liquid in 25 mL THF. The mixture was heated at reflux for 48 h, then cooled. The reaction mixture was slowly added to a large flask containing ice water, with vigorous stirring, and the resulting mixture was extracted with pentane (3×50 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated. The residue was distilled under vacuum (<1.0 Torr; bp 56–58°C) to give 3.17 g (38%) of *trans*-crotyl-phenylsilane as a clear colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59–7.56 (m, 2H, two of C_6H_5), 7.43–7.34 (m, 3H, three of C_6H_5), 5.51–5.38 (m, 2H,

C*H*=C*H*), 4.31–4.29 (apparent dt, 2H, *J*=1.7, 3.7 Hz, SiH_2), 1.85–1.82 (m, 2H, SiCH_2), 1.61 (m, 3H, CH=CHCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.2, 132.1, 130.0, 127.9, 125.9, 125.2, 18.0, 15.6; IR (thin film) 3070, 3052, 3015, 2960, 2933, 2917, 2883, 2855, 2138, 1429, 1304, 1163, 1117, 1068, 1048 cm^{-1}; LRMS (EI) calcd for $C_{10}H_{14}Si$ 162.09, found 162.01.

6.2. General procedure for the preparation of di-*cis*-crotylsilyl ethers

A round bottom flask is charged with sodium hydride (8.0 mg, 0.20 mmol, 60% wt. dispersion in mineral oil) and 5 mL hexanes is added. The mixture is stirred vigorously under Ar for 3 min, and then the hexanes/mineral oil solution is removed by cannula. This process is repeated, and 2 mL of hexanes is then added. Di-*cis*-crotylsilane is then added by syringe (154 mg, 0.197 mL, 1.1 mmol), followed by a solution of the homoallylic alcohol (1.0 mmol) in 2 mL hexanes by cannula. The resulting solution is heated at reflux for the required time (typically 45–90 min). The solution is cooled, diluted with hexanes, and filtered through a pad of Celite. The filtrate is concentrated to afford cude material which is generally of sufficient purity for use in the tandem silylformylation–crotylsilylation reaction. Analytical samples of the di-*cis*-crotylsilyl ethers may be obtained by distillation under reduced pressure.

Note. The time of the reaction must be controlled as the monoalkoxy silane will convert to the dialkoxysilane at longer reaction times. The reaction time necessary for full conversion of the alcohol to the monoalkoxysilane varies with the steric hinderance of the alcohol, and should be optimized for each alcohol.

6.3. General procedure for the silylformylation–allylation reaction of alkene substrates

To an oven-dried 45 mL stainless steel Parr bomb equipped with a glass liner, stir bar and septum is added the substrate (1.0 mmol), by cannula, as a solution in benzene (8 mL). The solution is cooled to −78°C until frozen. Rh(acac)-$(CO)_2$ (7.7 mg, 0.03 mmol) is then added, and the bomb is assembled and pressurized to 1000 psi of CO and vented. This purge is repeated twice and then the bomb is pressurized to 1000 psi with CO at −78°C. The apparatus is then immersed in an oil bath and heated at 60°C for 24 h. After cooling to 0°C, the bomb is vented. The solution is concentrated and the residue is used without further purification in the Tamao oxidation reaction.

6.4. General procedure for the Tamao oxidation

The product from the silylformylation–allylation reaction is dissolved in a 1:1 mixture of THF and MeOH (6 mL total). To this solution is added $NaHCO_3$ (120 mg, 1.5 mmol), followed by H_2O_2 (1.6 mL, 15 mmol, 30% solution in H_2O). The flask is then fitted with a reflux condenser and the solution is heated to reflux for 30–60 min. The solution is cooled to room temperature and 2.0 mL of saturated aqueous $Na_2S_2O_3$ is added. The biphasic solution is filtered through a cotton plug into a separatory funnel and extracted with EtOAc (5×10 mL). The combined organic layers are dried over $MgSO_4$, filtered, and concentrated. The residue is purified by flash chromatography on silica gel with EtOAc/hexanes as eluant. In every case reported here, the major *syn*,*syn*-triol eluted first, followed by a mixture of other triol diastereomers.

6.5. General procedure for the silylformylation–allylation reaction of alkyne substrates

A glass liner for a stainless steel 45 mL Parr high pressure reactor equipped with a stir bar and septum is charged with a solution of the diallylsilyl ether substrate (2.0 mmol) in 6.0 mL benzene. The solution is cooled to −78°C and Rh(acac)$(CO)_2$ (0.5 mg, 0.002 mmol) is added. The liner is inserted into the Parr reactor, and the pressure gauge and gas inlet assembly is attached. The reactor is charged to 500 psi with CO, and vented. The reactor is charged to 1000 psi with CO and is then immersed (~2.5 cm) in an oil bath at 60°C. After 2–3 h, the reactor is cooled to 0°C and then vented. The solution is concentrated and the residue is immediately subjected to either workup procedure without further purification.

Protodesilylation workup. To a solution of the residue from the tandem silylformylation–allylsilylation in 10.0 mL THF is added tetra-*n*-butylammonium fluoride (6.0 mL, 6.0 mmol, 1.0 M in THF). The solution is heated at reflux for 2 h, and then cooled. Saturated aqueous NH_4Cl is added, and the mixture is extracted with Et_2O. The combined organic layers are dried ($MgSO_4$), filtered and concentrated. The resulting diols may be purified by chromatography on silica gel.

Tamao oxidation workup. To a solution of the residue from the tandem silylformylation–allylsilylation in 3.0 mL THF and 3.0 mL MeOH is added $NaHCO_3$ (0.15 g, 1.8 mmol) and H_2O_2 (1.5 mL, 35% in H_2O). The solution is heated at reflux for 3 h, and then cooled. Saturated aqueous NaCl is added, followed by saturated aqueous $Na_2S_2O_3$ and the mixture is extracted with Et_2O. The combined organic layers are dried ($MgSO_4$), filtered and concentrated. The resulting ketodiols may be purified by chromatography on silica gel.

6.5.1. Entry 1, Table 1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.77–5.86 (m, 1H, C(9)*H*), 5.12–5.15 (m, 2H, C(7)H_2), 4.32 (s, 1H, O*H*), 4.08–4.13 (m, 1H, C(7)*H*), 3.93–3.94 (m, 1H, C(5)*H*), 3.65–3.68 94 (m, 1H, C(3)*H*), 3.11 (s, 1H, O*H*), 2.26 (s, 1H, O*H*), 2.23–2.26 (m, 2H, C(8)*H*), 1.62–1.69 (m, 1H, C(2)HCH_3), 1.52–1.62 (m, 4H, C(4)H_2 and C(6)H_2), 0.92 (d, *J*=6.8 Hz, 3H, C(1)H_3), 0.91 0.92 (d, *J*=6.8 Hz, 3H, C(2)HCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.3, 118.2, 77.8, 73.9, 71.7, 43.0, 42.5, 39.9, 34.2, 18.2, 17.5; IR (thin film) 3400, 3078, 2958, 1737, 1644, 1440, 1375, 1247 cm^{-1}; HRMS (FAB M+1) calcd for $C_{11}H_{22}O_3$ 202.1569, found 202.1648.

6.5.2. Entry 2, Table 1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.83–5.87 (m, 1H, C(9)*H*), 5.07–5.13 (m, 2H, C(10)H_2), 4.53 (s, 1H, O*H*), 4.2 (s, 1H, O*H*), 4.12–4.16 (m, 2H, C(1)H_2), 3.83–3.96 (m, 3H, C(3)*H* and C(5)*H*) and C(7)*H*), 3.75 (s, 1H, O*H*), 2.21–2.27 (m, 2H, C(8)H_2), 1.47–1.73

(m, 6H, C(2)H_2 and C(4)H_2 and C(6)H_2), 0.89 (s, 9H, Si–C(CH_3)$_3$), 0.08 (s, 6H, Si–(CH_3)$_2$; ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.9, 117.4, 73.4, 73.3, 71.5, 62.6, 43.6, 42.8, 38.5, 25.8, 18.1, −5.6, −5.6; IR (thin film) 3372, 2930, 2852, 2332, 1636, 1464, 1435, 1361, 1322, 1253 cm^{-1}; HRMS (FAB M+1) calcd for $C_{16}H_{34}O_4$ 318.2226, found 318.2308.

6.5.3. Entry 3, Table 1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.75–5.88 (m, 2H, C(2)*H* and C(10)*H*), 5.10–5.16 (m, 4H, C(1)H_2 and C(10)H_2), 4.33 (s, 1H, O*H*), 4.13 (quint., J=6.2 Hz, 1H, C(6)*H*, 3.91–3.95 (m, 2H, C(4)*H* and C(8)*H*), 3.19 (s, 1H, O*H*), 2.22–2.27 (m, 4H, C(3)H_2 and C(9)H_2), 1.55–1.60 (m, 4H, C(5)H_2 and C(7)H_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.3, 118.2, 73.4, 71.6, 42.9, 42.4; IR (thin film) 3356, 3069, 2927, 2355, 1838, 1641, 1440, 1324 cm^{-1}; HRMS (FAB M+1) calcd for $C_{11}H_{20}O_3$ 200.1412, found 200.1496.

6.5.4. Entry 4, Table 1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.77–5.87 (m, 1H, C(9)*H*), 5.11–5.15 (m, 2H, C(10)H_2), 4.77 (s, 1H, O*H*), 3.87–3.95 (m, 2H, C(5)*H* and C(7)*H*), 3.52 (d, J=1.9 Hz, 1H, O*H*), 3.39–3.42 (m, 1H, C(3)*H*), 3.02 (d, J=3.9 Hz, 1H, O*H*), 2.23–2.27 (m, 2H, C(8)H_2), 1.87 (m, 1H, C(4)*H*), 1.74–1.78 (m, 1H, one of C(6)*H*), 1.60–1.66 (m, 1H, C(2)*H*), 1.41–1.50 (m, 1H, one of C(6)*H*), 0.99 (d, J=6.92 Hz, 3H, C(4)HCH_3), 0.85 (d, J=6.79 Hz, 3H, C(1)H_3), 0.78 (d, J=6.89 Hz, 3H, C(2)HCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.5, 118.1, 80.8, 77.7, 72.0, 42.5, 41.8, 39.7, 29.9, 20.1, 13.9, 13.0; IR($CDCl_3$) 3434, 3021, 2969, 2401, 1522, 1469, 1429, 1216 cm^{-1}; HRMS (FAB M+1) calcd for $C_{12}H_{24}O_3$ 216.1725, found 216.1800.

6.5.5. Entry 5, Table 1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.76–5.86 (m, 1H, C(9)*H*), 5.11–5.15 (m, 2H, C(9)H_2), 4.36 (s, 1H, O*H*), 4.24–4.30 (m, 1H, C(6)*H*), 3.95 (m, 1H, C(4)*H*), 3.08 (s, 1H, O*H*), 2.89 (s, 1H, O*H*), 2.23–2.26 (m, 2H, C(7)H_2), 1.72 (dd, J=10.9, 14.4 Hz, 1H, one of C(3)*H*), 1.50–1.61 (m, 2H, C(5)H_2), 1.46 (dd, J=2.1, 14.4 Hz, 1H, one of C(3)*H*), 1.33 (s, 3H, C(1)CH_3), 1.26 (s, 3H, C(2)CH_3: ^{13}C NMR (100 MHz, $CDCl_3$)) δ 134.4, 118.2, 71.7, 71.6, 70.5, 48.3, 43.1, 42.5, 32.0, 27.7; IR (thin film) 3359, 2963, 2928, 1718, 1640, 1430, 1369, 1326, 1145 cm^{-1}; HRMS (FAB M+1) calcd for $C_{10}H_{20}O_3$ 188.1412, found 188.1488.

6.5.6. Triol 5a, Scheme 3. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.69–5.77 (m, 1H, C*H*=CH$_2$), 5.07–5.12 (m, 2H, CH=CH_2), 4.52 (s, 1H, O*H*), 4.05–4.10 (m, 1H, C*H*OH), 3.72–3.67 (m, 1H, C*H*OH), 3.67–3.62 94 (m, 1H, C*H*OH), 3.31 (s, 1H, O*H*), 3.16 (s, 1H, O*H*), 2.18–2.23 (m, 1H, C*H*CH$_3$), 1.47–1.67 (m, 5H, (CH$_3$)$_2$C*H*CHCH_2CHCH_2), 1.02 (d, J=6.9 Hz, 3H, CHCH_3), 0.91 (d, J=6.8 Hz, 3H, one of CH(CH_3)$_2$), 0.89 (d, J=6.8 Hz, 3H, one of CH(CH_3)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.0, 116.3, 77.6, 75.7, 73.9, 44.7, 40.3, 39.9, 34.0, 18.1, 17.5, 15.5; IR (thin film) 3368, 3079, 2961, 1737, 2875, 1640, 1442, 1395, 1370, cm^{-1}; HRMS (FAB, M+H) calcd for $C_{12}H_{24}O_3$ 217.1725, found 217.1809.

6.5.7. Triol 5b, Scheme 3. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.72–5.79 (m, 1H, C*H*=CH$_2$), 5.08–5.13 (m, 2H, CH=CH_2), 3.85–3.89 (m, 1H, C*H*OH), 3.68–3.72 (m, 1H, C*H*OH), 3.42–3.65 (br s, 3H, three O*H*), 3.41 (dd, J=2.6, 8.9 Hz, 1H, C*H*OH), 2.20–2.27 (m, 1H, C*H*CH$_3$), 1.85–1.89 (m, 1H, C*H*(CH$_3$)$_2$), 1.76–1.80 (m, 1H, one of CH_2), 1.60–1.64 (m, 1H, C*H*CH$_3$), 1.41–1.47 (m, 1H, one of CH_2), 1.05 (d, J=6.9 Hz, 3H, CHCH_3), 0.99 (d, J=6.9 Hz, 3H, CHCH_3), 0.85 (d, J=6.8 Hz, 3H, one of CH(CH_3)$_2$), 0.77 (d, J=6.9 Hz, 3H, one of CH(CH_3)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.0, 116.1, 80.5, 77.8, 76.0, 44.6, 41.8, 37.0, 29.9, 20.2, 15.7, 13.9, 13.1; IR (CH_2Cl_2) 3400, 3082, 2967, 2932, 2875, 1638, 1462, 1436, 1387, 1320, 1266, 1143, 1095 cm^{-1}; HRMS (FAB, M+H) calcd for $C_{13}H_{26}O_3$ 231.1882, found 231.1953.

6.5.8. Triol 5c, Scheme 3. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.72–5.81 (m, 1H, C*H*=CH$_2$), 5.10–5.16 (m, 2H, CH=CH_2), 4.25–4.32 (m, 1H, C*H*OH), 3.72–3.76 (m, 1H, C*H*OH), 3.20–3.51 (br s, 3H, three O*H*), 2.19–2.28 (m, 1H, C*H*CH$_3$), 1.71–1.79 (m, 1H, one of CH_2), 1.47–1.56 (m, 3H, one of CH_2 and CH_2), 1.35 (s, 3H, one of C(CH_3)$_2$), 1.27 (s, 3H, one of C(CH_3)$_2$), 1.05 (d, J=6.9 Hz, 3H, CHCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.0, 116.4, 75.8, 71.4, 70.7, 48.2, 44.8, 40.4, 31.9, 27.7, 15.6; IR (thin film) 3369, 3079, 2972, 2940, 1640, 1436, 1380, 1367, 1330 cm^{-1}; HRMS (FAB, M+H) calcd for $C_{12}H_{24}O_3$ 203.1725, found 203.1645.

6.5.9. Entry 1, Table 2. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.70–5.53 (m, 2H, C*H*=CH$_2$ and CH$_2$C*H*=CH), 5.40 (dd, 1H, J=15.4, 6.9 Hz, CH=C*H*CHOAc), 5.18 (apparent q, 1H, J=6.6 Hz, CH=CHC*H*OAc), 5.00 (m, 2H, CH=CH_2), 4.81 (m, 1H, *n*-PrC*H*OAc), 2.30–2.11 (m, 4H, CH_2CH=CH and CH_2CH=CH$_2$), 1.95 (s, 3H, one of CH_3CO$_2$CH), 1.94 (s, 3H, one of CH_3CO$_2$CH), 1.47–1.31 (m, 2H, CH$_3$CH$_2$CH_2), 1.29–1.18 (m, 2H, CH$_3$CH_2CH$_2$), 0.83 (t, 3H, J=7.2 Hz, CH_3CH$_2$CH$_2$); ^{13}C NMR (300 MHz, $CDCl_3$) δ 170.4, 169.9, 133.0, 130.8, 128.9, 117.6, 73.2, 72.6, 38.8, 36.9, 35.5, 21.0, 20.9, 18.3, 13.7; IR (thin film) 3079, 2960, 2875, 1740, 1435, 1373 cm^{-1}; HRMS (FAB+, NaI) calcd for $C_{15}H_{24}O_4Na$ 291.1572, found 291.1582.

6.5.10. Entry 2, Table 2. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.70–5.42 (m, 3H, C*H*=CH$_2$ and C*H*=C*H*), 5.17 (apparent q, 1H, J=6.5 Hz, CH=CHC*H*OAc), 5.00 (m, 2H, CH=CH_2), 4.87 (m, 1H, CH$_2$C*H*OAcCH$_2$), 2.45–2.26 (m, 6H, CH_2CHOAcCH_2 and CH_2CH=CH$_2$), 1.97 (s, 3H, one of CH_3CO$_2$CH), 1.96 (m, 1H, *H*C≡CCH$_2$), 1.95 (s, 3H, one of CH_3CO$_2$CH); ^{13}C NMR (300 MHz, $CDCl_3$) δ 170.0, 169.9, 132.9, 131.6, 127.8, 117.7, 79.2, 73.1, 70.6, 70.4, 38.7, 35.5, 23.1, 21.0, 20.8; IR (thin film) 3293, 3088, 2989, 1732, 1434, 1242 cm^{-1}; HRMS (FAB+, NaI) calcd for $C_{15}H_{20}O_4Na$ 287.1259, found 287.1259.

6.5.11. Entry 3, Table 2. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.75–5.57 (m, 2H, C*H*=CH$_2$ and CH$_2$C*H*=CH), 5.47 (dd, 1H, J=15.4, 6.8 Hz, CH=C*H*CHOAc), 5.23 (apparent q, 1H, J=6.5 Hz, CH=CHC*H*OAc), 5.08–4.94 (m, 3H, CH=CH_2 and CH$_2$C*H*OAcCH$_2$), 4.06 (t, 2H, J=6.4 Hz, AcOCH_2CH$_2$), 2.38–2.12 (m, 4H, CH_2CH=CH and CH_2CH=CH$_2$), 2.02 (s, 3H, one of CH_3CO$_2$CH), 2.01 (s, 3H, one of CH_3CO$_2$CH), 2.00 (s, 3H, one of CH_3CO$_2$CH), 1.87–1.74 (m, 2H, AcOCH$_2$CH_2); ^{13}C NMR (300 MHz, $CDCl_3$) δ 170.9, 170.4, 170.1, 133.0, 131.5, 128.2, 117.8, 73.2, 69.8, 60.6, 38.9, 37.0, 32.4, 21.2, 21.0, 20.8; IR (thin

film) 3079, 2962, 2856, 1732, 1435, 1242 cm^{-1}; HRMS (FAB+, NaI) calcd for $C_{16}H_{24}O_6Na$ 335.1471, found 335.1464.

6.5.12. Entry 4, Table 2. ^1H NMR (300 MHz, $CDCl_3$) δ 5.71–5.53 (m, 2H, C*H*=CH_2 and CH_2CH=CH), 5.41 (dd, 1H, *J*=15.5, 6.9 Hz, CH=C*H*CHOAc), 5.17 (apparent q, 1H, *J*=6.6 Hz, CH=CHC*H*OAc), 5.00 (m, 2H, CH=CH_2), 4.67 (m, 1H, *i*-PrC*H*OAc), 2.30–2.13 (m, 4H, CH_2CH=CH and CH_2CH=CH_2), 1.95 (s, 3H, one of CH_3CO_2CH), 1.95 (s, 3H, one of CH_3CO_2CH), 1.74 (m, 1H, $(CH_3)_2CH$), 0.82 (d, 6H, *J*=6.8 Hz, $(CH_3)_2CH$); ^{13}C NMR (300 MHz, $CDCl_3$) δ 170.4, 169.9, 133.0, 130.6, 129.3, 117.6, 77.0, 73.2, 38.8, 34.2, 30.8, 21.0, 20.8, 18.4, 17.4; IR (thin film) 3080, 2966, 1732, 1644, 1468, 1242 cm^{-1}; HRMS (FAB+, NaI) calcd for $C_{15}H_{24}O_4Na$ 291.1572, found 291.1581.

6.5.13. Entry 5, Table 2. ^1H NMR (300 MHz, $CDCl_3$) δ 7.35–7.23 (m, 5H, C_6H_5), 5.77 (dd, 1H, *J*=7.0, 6.5 Hz, C_6H_5CHOAc), 5.71–5.54 (m, 2H, C*H*=CH_2 and CH_2CH=CH), 5.44 (m, 1H, CH=C*H*CHOAc), 5.21 (apparent q, 1H, *J*=6.6 Hz, CH=CHC*H*OAc), 5.05 (m, 2H, CH=CH_2), 2.65–2.48 (m, 2H, PhCHOAcCH_2), 2.37–2.20 (m, 2H, CH_2CH=CH_2), 2.04 (s, 3H, one of CH_3CO_2CH), 1.99 (s, 3H, one of CH_3CO_2CH); ^{13}C NMR (300 MHz, $CDCl_3$) δ 172.2, 139.7, 133.1, 131.4, 128.3, 127.9, 126.4, 117.7, 74.9, 73.3, 39.1, 38.7; IR (thin film) 3067, 2940, 1732, 1643, 1496, 1234 cm^{-1}; HRMS (FAB+, NaI) calcd for $C_{18}H_{22}O_4Na$ 325.1416, found 325.1406.

6.5.14. Entry 6, Table 2. ^1H NMR (300 MHz, $CDCl_3$) δ 5.71–5.54 (m, 2H, C*H*=CH_2 and CH_2CH=CH), 5.42 (dd, 1H, *J*=15.6, 6.7 Hz, CH=C*H*CHOAc), 5.18 (apparent q, 1H, *J*=6.6 Hz, CH=CHC*H*OAc), 5.03 (m, 2H, CH=CH_2), 4.71 (dd, 1H, *J*=7.7, 2.8 Hz, $(CH_3)_3CCH$OAc), 2.33–2.23 (m, 3H, three of CH_2CH=CH and CH_2CH=CH_2), 2.14–2.03 (m, 1H one of CH_2CH=CH and CH_2CH=CH_2), 1.97 (s, 3H, one of CH_3CO_2CH), 1.96 (s, 3H, one of CH_3CO_2CH), 0.85 (s, 9H, $(CH_3)_3C$); ^{13}C NMR (300 MHz, $CDCl_3$) δ 170.5, 170.0, 133.2, 130.4, 130.3, 117.6, 79.1, 73.1, 38.8, 34.3, 32.9, 25.8, 21.1, 20.8; IR (thin film) 3079, 2965, 1740, 1433, 1372, 1242 cm^{-1}; HRMS (FAB+, NaI) calcd for $C_{16}H_{26}O_4Na$ 305.1729, found 305.1745.

6.5.15. Entry 7, Table 2. ^1H NMR (300 MHz, $CDCl_3$) δ 5.75–5.56 (m, 2H, C*H*=CH_2 and CH_2CH=CH), 5.45 (m, 1H, CH=C*H*CHOAc), 5.25 (apparent q, 1H, *J*=6.3 Hz, CH=CHC*H*OAc), 5.10–5.04 (m, 2H, CH=CH_2), 4.69 (dd, 1H, *J*=7.1, 5.4 Hz, $(CH_3)_2CHCH$OAc), 2.46 (m, 1H, CHOAcC*H*(CH_3)), 2.40–2.33 (m, 2H, CH_2CH=CH_2), 2.05 (s, 3H, one of CH_3CO_2CH), 2.03 (s, 3H, one of CH_3CO_2CH), 1.85 (m, 1H, $(CH_3)_2CH$), 0.95 (d, 3H, *J*=6.8 Hz, CH(CH_3)CH=CH), 0.85 (apparent t, 6H, *J*=6.6 Hz, $(CH_3)_2CH$); ^{13}C NMR (300 MHz, $CDCl_3$) δ 170.9, 170.2, 135.6, 133.2, 129.2, 117.8, 80.3, 73.4, 39.0, 38.2, 29.5, 21.2, 20.9, 19.6, 16.5, 15.2; IR (thin film) 2968, 2936, 2877, 1738, 1462, 1372, 1240 cm^{-1}; HRMS (FAB+, NaI) calcd for $C_{16}H_{26}O_4Na$ 305.1729, found 305.1741.

6.5.16. Entry 8, Table 2. ^1H NMR (300 MHz, $CDCl_3$) δ 5.73–5.54 (m, 2H, C*H*=CH_2 and CH_2CH=CH), 5.41 (dd, 1H, *J*=15.5, 6.8 Hz, CH=C*H*CHOAc), 5.27–5.20 (apparent q, 1H, *J*=6.6 Hz, CH=CHC*H*OAc), 5.08–5.02 (m, 2H, CH=CH_2), 4.61 (apparent t, 1H, *J*=6.2 Hz, $(CH_3)_2CHCH$OAc), 2.42 (m, 1H, CHOAcC*H*(CH_3)), 2.37–2.30 (m, 2H, CH_2CH=CH_2), 2.02 (s, 3H, one of CH_3CO_2CH), 2.01 (s, 3H, one of CH_3CO_2CH), 1.79 (m, 1H, $(CH_3)_2CH$), 0.94 (d, 3H, *J*=6.9 Hz, CH(CH_3)CH=CH), 0.84 (d, 3H, *J*=6.7 Hz, one of $(CH_3)_2CH$), 0.82 (d, 3H, *J*=6.7 Hz, one of $(CH_3)_2CH$); ^{13}C NMR (300 MHz, $CDCl_3$) δ 170.8, 170.1, 134.9, 133.2, 128.7, 117.7, 80.6, 73.3, 39.1, 38.8, 29.4, 21.8, 20.8, 19.1, 17.5, 17.2; IR (thin film) 3080, 2968, 2937, 2877, 1737, 1644, 1462, 1434, 1372 cm^{-1}; HRMS (FAB+, NaI) calcd for $C_{16}H_{26}O_4Na$ 305.1729, found 305.1729.

6.5.17. Ketodiol 9, Scheme 5. ^1H NMR (300 MHz, $CDCl_3$) δ 5.77–5.63 (m, 1H, C*H*=CH_2), 5.03–4.97 (m, 2H, CH=CH_2), 4.05 (m, 1H, $CH_2CH(OH)CH_2$), 3.74 (m, 1H, *i*PrC*H*OH), 2.52–2.35 (m, 4H, CH_2COCH_2), 2.22–2.06 (m, 2H, CH_2CH=CH_2), 1.56 (m, 1H, $(CH_3)_2CH$), 0.80 (apparent t, 6H, *J*=6.6 Hz, $(CH_3)_2CH$); ^{13}C NMR (300 MHz, $CDCl_3$) δ 212.4, 133.9, 117.6, 71.9, 66.7, 49.3, 47.0, 40.0, 33.0, 18.1, 17.5; IR (thin film) 3418, 3075, 2962, 2933, 1708, 1642, 1386 cm^{-1}; HRMS (FAB+, NaI) calcd for $C_{11}H_{20}O_3Na$ 223.1310, found 223.1301.

6.5.18. Ketodiol 11, Scheme 5. ^1H NMR (300 MHz, $CDCl_3$) δ 5.85–5.72 (m, 1H, C*H*=CH_2), 5.12–5.07 (m, 2H, CH=CH_2), 4.12 (m, 1H, $CH_2CH(OH)CH_2$), 3.59 (dd, 1H, *J*=8.5, 3.1 Hz, *i*PrC*H*OH), 2.75–2.53 (m, 3H, $CH(CH_3)COCH_2$), 2.26–2.21 (m, 2H, CH_2CH=CH_2), 1.64 (m, 1H, $(CH_3)_2CH$), 1.07 (d, 3H, *J*=7.1 Hz, CH(OH)CH(CH_3)), 0.99 (d, 3H, *J*=6.6 Hz, $(CH_3)_2CH$), 0.84 (d, 3H, *J*=6.8 Hz, $(CH_3)_2CH$); ^{13}C NMR (300 MHz, $CDCl_3$) δ 215.5, 134.0, 118.0, 75.9, 67.2, 49.1, 46.9, 41.0, 30.7, 19.0, 18.9, 8.6; IR (thin film) 3419, 3078, 2963, 2933, 2876, 1704, 1642, 1460, 1384; HRMS (FAB+, NaI) calcd for $C_{12}H_{23}O_3$ 215.1647, found 215.1655.

6.5.19. Ketodiol 13, Scheme 6. ^1H NMR (300 MHz, $CDCl_3$) δ 5.80–5.68 (m, 1H, C*H*=CH_2), 5.07–5.01 (m, 2H, CH=CH_2), 3.97–3.93 (m, 1H, C*H*OH), 3.84–3.78 (m, 1H, C*H*OH), 3.03 (br s, 2H, two O*H*), 2.62–2.47 (m, 4H, CH_2COCH_2), 2.24–2.17 (m, 1H, C*H*CH_3), 1.67–1.58 (m, 1H, $(CH_3)_2CH$), 1.02–1.00 (d, 3H, *J*=6.8 Hz, CHCH_3), 0.89 (d, 3H, *J*=6.7 Hz, one of $(CH_3)_2CH$), 0.87 (d, 3H, *J*=6.7 Hz, one of $(CH_3)_2CH$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 212.5, 139.5, 115.9, 72.0, 70.5, 47.3, 47.2, 43.3, 33.1, 18.2, 17.6, 15.6; IR (thin film) 3428, 3077, 2964, 2932, 2876, 1706, 1640, 1465, 1385, 1334, 1170, 1170, 1127, 1002 cm^{-1}; HRMS (FAB, M+H) calcd for $C_{12}H_{23}O_3$: 215.1647, found 215.1667.

6.5.20. Ketone 15, Scheme 6. ^1H NMR (300 MHz, $CDCl_3$) δ 5.67–5.42 (m, 2H, C*H*=CH_2 and C*H*=CH), 5.40–5.35 (m, 1H, CH=C*H*), 5.10–4.98 (m, 3H, C*H*OAc and CH=CH_2), 4.69–4.65 (m, 1H, C*H*OAc), 2.44–2.35 (m, 2H, C*H*(CH_3)CH=CH and C*H*(CH_3)CH=CH_2), 2.02 (s, 3H, one of CH_3CO_2CH), 2.00 (s, 3H, one of CH_3CO_2CH), 1.84–1.82 (m, 1H, $(CH_3)_2CH$), 0.95 (d, 3H, *J*=6.3 Hz, CHCH_3), 0.93 (d, 3H, *J*=6.3 Hz, CHCH_3), 0.84 (d, 3H, *J*=6.8 Hz, one of $(CH_3)_2CH$), 0.81 (d, 3H, *J*=6.8 Hz, one of $(CH_3)_2CH$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8, 170.1, 139.5, 136.4, 126.7, 115.4, 80.3, 77.2, 42.0, 38.3, 29.5, 21.1, 20.8, 19.6, 16.4, 15.7, 15.3; IR (thin film) 3080, 2969, 2936,

2877, 1736, 1643, 1460, 1372, 1240, 1184, 1104, 1020 cm^{-1}; HRMS (FAB, NaI) calcd for $C_{17}H_{28}O_4Na$: 319.1885, found 319.1903.

6.5.21. Diol 17, Scheme 7. ^1H NMR (300 MHz, $CDCl_3$) δ 5.81–5.62 (m, 2H, CH═C*H* and C*H*═CH_2), 5.53–5.46 (m, 1H, C*H*═CH), 5.11–5.00 (m, 2H, CH═CH_2), 3.96–3.92 (apparent t, 1H, J=6.2 Hz, C*H*(OH)), 2.51 (s, 1H, one O*H*), 2.38–2.22 (m, 1H, C*H*CH_3), 2.17–2.00 (m, 3H, CH_2 and one O*H*), 1.17 (s, 6H, (CH_3)$_2$C), 1.01–0.99 (d, 3H, J= 6.9 Hz, CHCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.2, 134.7, 127.8, 115.4, 75.8, 70.5, 46.4, 43.7, 29.2, 28.8, 15.1; IR (thin film) 3369, 3080, 2972, 2930, 1666, 1640, 1460, 1415, 1379, 1214, 1153, 1007 cm^{-1}; LRMS (FAB+) calcd for $C_{11}H_{21}O_2$ 185.29, found 185.96.

References

1. Rychnovsky, S. D. *Chem. Rev.* **1995**, *95*, 2012–2040.
2. (a) Leighton, J. L.; O'Neil, D. N. *J. Am. Chem. Soc.* **1997**, *119*, 11118–11119. (b) Leighton, J. L.; Chapman, E. *J. Am. Chem. Soc.* **1997**, *119*, 12416–12417. (c) Sarraf, S. T.; Leighton, J. L. *Tetrahedron Lett.* **1998**, *39*, 6423–6426. (d) Sarraf, S. T.; Leighton, J. L. *Org. Lett.* **2000**, *2*, 403–405. (e) Zacuto, M. J.; Leighton, J. L. *J. Am. Chem. Soc.* **2000**, *122*, 8587–8588. (f) Dreher, S. D.; Hornberger, K. R.; Sarraf, S. T.; Leighton, J. L. *Org. Lett.* **2000**, *2*, 3197–3199. (g) Sarraf, S. T.; Leighton, J. L. *Org. Lett.* **2000**, *2*, 3205–3208. (h) O'Malley, S. J.; Leighton, J. L. *Angew. Chem. Int. Ed.* **2001**, *40*, 2915–2917. (i) Zacuto, M. J.; O'Malley, S. J.; Leighton, J. L. *J. Am. Chem. Soc.* **2002**, *124*, 7890–7891. (j) Wang, X.; Meng, Q.; Nation, A. J.; Leighton, J. L. *J. Am. Chem. Soc.* **2002**, *124*, 10672–10673.
3. For reviews of other approaches, see: Ref. 1, and (a) Oishi, T.; Nakata, T. *Synthesis* **1990**, 635–645. (b) Schneider, C. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 1375–1378.
4. Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207–2293.
5. For a review on the Tamao and Fleming oxidations, see: Jones, G. R.; Landais, Y. *Tetrahedron* **1996**, *52*, 7599–7662.
6. The alcohol is treated with $HSiCl_3$, followed by 2 equiv. of allylMgBr. This reaction provides the desired diallylsilyl ethers in 50–90% yields, with more sterically hindered alcohols giving better results.
7. Stereochemical determinations were made using the method of Rychnovsky: Rychnovsky, S. D.; Rogers, B.; Yang, G. *J. Org. Chem.* **1993**, *58*, 3511–3515.
8. This procedure was adapted from the reported method for the synthesis of (*Z*)-crotyltrichlorosilane: (a) Tsuji, J.; Hara, M.; Ohno, K. *Tetrahedron* **1974**, *30*, 2143–2146. (b) Kira, M.; Hino, T.; Sakurai, H. *Tetrahedron Lett.* **1989**, *30*, 1099–1102. (c) Iseki, K.; Kuroki, Y.; Takahashi, M.; Kishimoto, S.; Kobayashi, Y. *Tetrahedron* **1997**, *53*, 3513–3526.
9. The silane alcoholysis literature prior to 1985 has been reviewed. See: (a) Lukevics, E.; Dzintara, M. *J. Organomet. Chem.* **1985**, *295*, 265–315. See also: (b) Caseri, W.; Pregosin, P. S. *Organometallics* **1988**, *7*, 1373–1380. (c) Yamamoto, K.; Takemae, M. *Bull. Chem. Soc. Jpn* **1989**, *62*, 2111–2113. (d) Luo, X.-L.; Crabtree, R. H. *J. Am. Chem. Soc.* **1989**, *111*, 2527–2535. (e) Doyle, M. P.; High, K. G.; Bagheri, V.; Pieters, R. J.; Lewis, P. J.; Pearson, M. M. *J. Org. Chem.* **1990**, *55*, 6082–6086. (f) Bedard, T. C.; Corey, J. Y. *J. Organomet. Chem.* **1992**, *428*, 315–333. (g) Barton, D. H. R.; Kelly, M. J. *Tetrahedron Lett.* **1992**, *33*, 5041–5044. (h) Burn, M. J.; Bergman, R. G. *J. Organomet. Chem.* **1994**, *472*, 43–54. (i) Gregg, B. T.; Cutler, A. R. *Organometallics* **1994**, *13*, 1039–1043. (j) Lorenz, C.; Schubert, U. *Chem. Ber.* **1995**, *128*, 1267–1269. (k) Chang, S.; Scharrer, E.; Brookhart, M. *J. Mol. Catal. A* **1998**, *130*, 107–119. (l) Ito, H.; Ishizuka, T.; Okumura, T.; Yamanaka, H.; Tateiwa, J.-I.; Sonada, M.; Hosomi, A. *J. Organomet. Chem.* **1999**, *574*, 102–106. (m) Blackwell, J. M.; Foster, K. L.; Beck, V. H.; Piers, W. E. *J. Org. Chem.* **1999**, *64*, 4887–4892. (n) Le Bideau, F.; Coradin, T.; Hénique, J.; Samuel, E. *Chem. Commun.* **2001**, 1408–1409. (o) Chung, M. K.; Ferguson, G.; Robertson, V. *Can. J. Chem.* **2001**, *79*, 949–957.
10. For a seminal report on the monoalcoholysis of a dihydrosilane, see: Corriu, R. J. P.; Moreau, J. J. E. *J. Organomet. Chem.* **1976**, *120*, 337–346.
11. Indeed, tandem alcoholysis–hydrosilylation using dihydrosilanes and allylic and homoallylic alcohols has been described. See: (a) Corriu, R. J. P.; Moreau, J. J. E. *J. Organomet. Chem.* **1976**, *114*, 135–144. (b) Xin, S.; Harrod, J. F. *J. Organomet. Chem.* **1995**, *499*, 181–191. (c) Wang, X.; Ellis, W. W.; Bosnich, B. *Chem. Commun.* **1996**, 2561–2562.
12. All chiral alcohol starting materials used in this study were racemic.
13. The diacetate was prepared to facilitate analysis of the diastereoselectivity by gas chromatography. The diol may be isolated.
14. (a) Furuya, N.; Sukawa, T. *J. Organomet. Chem.* **1975**, *96*, C1–C3. (b) Kira, M.; Hino, T.; Sakurai, H. *Tetrahedron Lett.* **1989**, *30*, 1099–1102. (c) Iseki, K.; Kuroki, Y.; Takahashi, M.; Kishimoto, S.; Kobayashi, Y. *Tetrahedron* **1997**, *53*, 3513–3526.
15. Reetz, M. T.; Jung, A.; Bolm, C. *Tetrahedron* **1988**, *44*, 3889–3898.
16. Uyeo, S.; Itani, H. *Tetrahedron Lett.* **1991**, *32*, 2143–2146.
17. Linderman, R. J.; Chen, K. *J. Org. Chem.* **1996**, *61*, 2441–2453.
18. Matsumoto, K.; Oshima, K.; Utimoto, K. *J. Org. Chem.* **1994**, *59*, 7152–7155.
19. (a) Myers, A. G.; Kephart, S. E.; Chen, H. *J. Am. Chem. Soc.* **1992**, *114*, 7922–7923. For another example of an uncatalyzed silicon-mediated aldol reaction, see: (b) Myers, A. G.; Widdowson, K. L. *J. Am. Chem. Soc.* **1990**, *112*, 9672–9674. (c) Myers, A. G.; Widdowson, K. L.; Kukkola, P. *J. Am. Chem. Soc.* **1992**, *114*, 2765–2767.
20. (a) Denmark, S. E.; Griedel, B. D.; Coe, D. M. *J. Org. Chem.* **1993**, *58*, 988–990. (b) Denmark, S. E.; Griedel, B. D.; Coe, D. M.; Schnute, M. E. *J. Am. Chem. Soc.* **1994**, *116*, 7026–7043.
21. Denmark, S. E.; Jacobs, R. T.; Dai-Ho, G.; Wilson, S. *Organometallics* **1990**, *9*, 3015–3019.
22. Several relevant X-ray structures have been reported. See, for example: Shaw, J. T.; Woerpel, K. A. *J. Org. Chem.* **1997**, *62*, 6706–6707.
23. Hoveyda has reported relevant observations regarding the Lewis acidity of oxasilacyclopentanes of this type. See: Young, D. G. J.; Hale, M. R.; Hoveyda, A. H. *Tetrahedron Lett.* **1996**, *37*, 827–830.
24. These are the conditions employed by Utimoto. See Ref. 18.
25. Myers has elegantly established a mechanism involving

pseudorotation for the uncatalyzed aldol reactions of *O*-silyl ketene *N*,*O*-acetals. See Ref. 19c.

26. (a) Stevenson, W. H., III.; Wilson, S.; Martin, J. C.; Farnham, W. B. *J. Am. Chem. Soc.* **1985**, *107*, 6340–6352. (b) Stevenson, W. H., III; Martin, J. C. *J. Am. Chem. Soc.* **1985**, *107*, 6352–6358.
27. Schmidt, D. R.; O'Malley, S. J.; Leighton, J. L. *J. Am. Chem. Soc.* **2003**, *125*, 1190–1191.
28. Kira and Sakurai, and Roush and Chemler have made similar observations during studies of intramolecular crotylsilylations of β-hydroxy ketones and aldehydes. See: (a) Sato, K.; Kira, M.; Sakurai, H. *J. Am. Chem. Soc.* **1989**, *111*, 6429–6431. (b) Kira, M.; Sato, K.; Kazushi, S.; Gewald, R.; Sakurai, H. *Chem. Lett.* **1995**, 281–282. (c) Chemler, S. R.; Roush, W. R. *J. Org. Chem.* **1998**, *63*, 3800–3801. (d) Chemler, S. R.; Roush, W. R. *Tetrahedron Lett.* **1999**, *40*, 4643–4647. (e) Chemler, S. R.; Roush, W. R. *J. Org. Chem.* **2003**, *68*, 1319–1333.
29. Dreher, S. D.; Leighton, J. L. *J. Am. Chem. Soc.* **2001**, *123*, 341–342.
30. (a) Kinnaird, J. W. A.; Ng, P. Y.; Kubota, K.; Wang, X.; Leighton, J. L. *J. Am. Chem. Soc.* **2002**, *124*, 7920–7921. (b) Wang, X.; Meng, Q.; Nation, A. J.; Leighton, J. L. *J. Am. Chem. Soc.* **2002**, *124*, 10672–10673. (c) Kubota, K.; Leighton, J. L. *Angew. Chem. Int. Ed.* **2003**, *42*, 946–948.