Synthetic Methods

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Intermolecular Double Prins-Type Cyclization: A Facile and Efficient Synthesis of 1,6-Dioxecanes**

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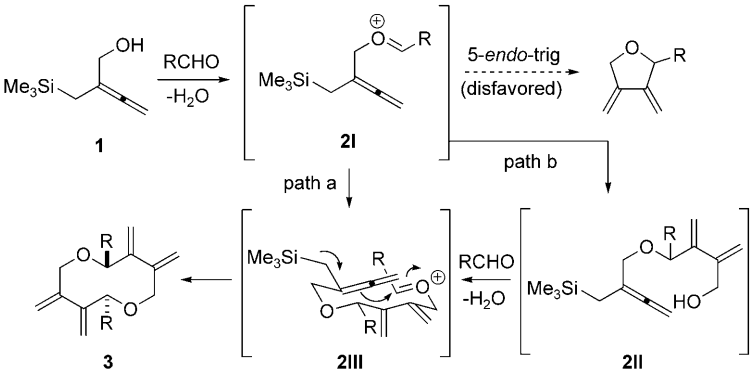
Medium-sized oxygen heterocyclic ring systems, particularly those with ten members, are a common structural feature of numerous natural products as well as functionalized organic molecules.[1] Owing to unfavorable entropic and enthalpic factors,[2] synthetic routes towards such compounds have been difficult to study and as a result, the development of a practical and convenient process to create rings of this size still remains a major synthetic challenge.

The Prins-type cyclization is among the most important ring-forming reactions. It involves an electrophilic addition of an unsaturated carbon–carbon bond to an aldehyde and ketone.[3] When the electrophile is an oxonium ion that is generated in situ from the condensation of an allylic alcohol with an aldehyde or acetal, the cyclization proceeds to form oxacyclic compounds such as tetrahydropyran or tetrahydrofuran derivatives. Recently, we have shown that the use of (allenylmethyl)silane in the Prins-type cyclization can facilitate the terminating step to afford 3,4-dimethylidene tetrahydropyran compounds.[4] On the basis of this study, we have devised a new plan to synthesize medium-sized oxacycles through a Prins-type cyclization. As shown in Scheme 1, the intramolecular 5-*endo*-trig cyclization of the oxonium intermediate **2I**, which is derived from (allenylmethyl)silane **1** and an aldehyde, would be kinetically disfavored according to Baldwin's rule.[5] Thereby, a second oxonium ion **2III** would be generated by either dimerization of **2I** (path a) or intermolecular addition of **1** to **2I** followed by a second condensation of **2II** with an aldehyde (path b). At this point, we envisage that subsequent ring closure of **2III** would occur to afford 1,6-dioxecane derivatives **3** if the rate of Prins cyclization is faster than that of polymerization. To our knowledge, formation of such a medium-size ring system by using consecutive Prins reactions has never been reported.[6]

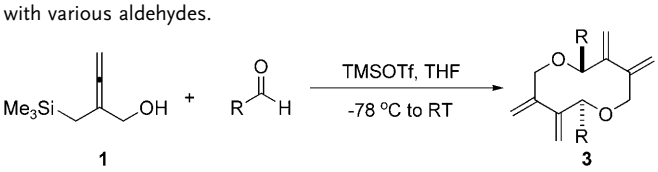


Scheme 1. Concept for the intermolecular double Prins-type cyclization for the synthesis of 1,6-dioxecane derivatives.

Herein, we present the stereoselective synthesis of 1,6-dioxecanes[7] from hydroxy(allenylmethyl)silane/allylsilane and electron-rich aromatic aldehydes through an intermolecular double Prins-type cyclization.

To test our idea, we first screened various Lewis acids including $InCl_3$ and $TiCl_4$, which are conventional Lewis acids for Prins-type cyclizations[8] (see the Supporting Information). Among them, we found that TMSOTf proved to be the best Lewis acid for this type of cyclization (Table 1, entry 1). Indeed, when we applied one equivalent of TMSOTf to the mixture of **1**[9] and benzaldehyde in THF at −78 °C, and then

Table 1: Scope of the intermolecular double Prins-type cyclization of **1** with various aldehydes.



Entry	R	*t* [h]	Product	Yield [%][a]
1	Ph	7	**3a**	73
2	4-$MeOC_6H_4$	7	**3b**	55
3	3-$MeOC_6H_4$	6	**3c**	83
4	2-$MeOC_6H_4$	9	**3d**	50
5	4-MeC_6H_4	6	**3e**	75
6	3-MeC_6H_4	9	**3f**	66
7	4-FC_6H_4	6	**3g**	85
8	4-ClC_6H_4	10	**3h**	76
9	4-$NO_2C_6H_4$	6	**3i**	n.r.[b]
10	2-$NO_2C_6H_4$	6	**3j**	n.r.[b]
11	2-thienyl	10	**3k**	50

[a] Yield of isolated product. [b] No reaction. Tf = trifluoromethanesulfonyl, THF = tetrahydrofuran, TMS = trimethylsilyl.

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allowed the reaction mixture to warm to room temperature over 7 h, we obtained **3a** exclusively in 73% yield.[10] The structure of **3a** was determined by single-crystal X-ray diffraction analysis (Figure 1).[11] Therefore, we selected these reaction conditions for our study.

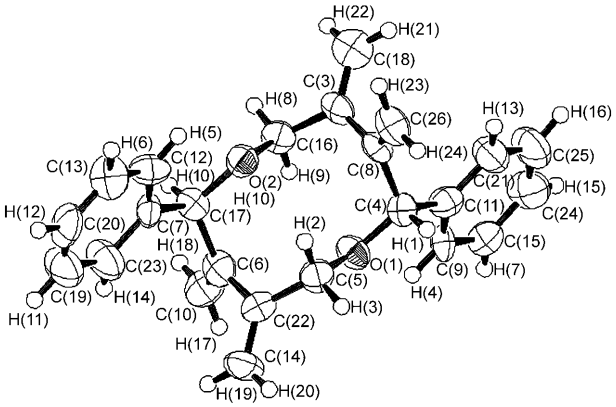
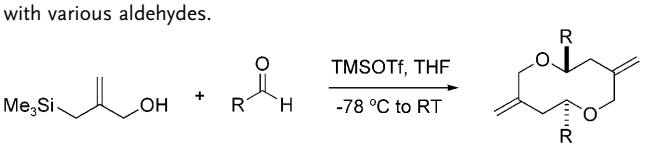


Figure 1. ORTEP plot of 1,6-dioxecane **3a**. The thermal ellipsoids are drawn at the 50% probability level.

Next, we examined the scope of the aldehyde component as shown in Table 1. At first, we found that a wide range of aldehydes were tolerated under the optimized reaction conditions. In general, the intermolecular double Prins-type cyclization reactions of **1** with electron-rich benzaldehydes, such as methoxybenzaldehyde and methylbenzaldehyde, regardless of the substituent position, provided the corresponding 1,6-dioxecane derivatives in good to excellent yield (Table 1, entries 2–6). However, variation in the electronic character of the aldehyde had a large influence on this reaction. Indeed, halobenzaldehydes were still good substrates for this cyclization process (Table 1, entries 7 and 8), but no desired products were isolated from electron-poor substrates such as nitrobenzaldehydes (Table 1, entries 9 and 10). We believe that the electron-withdrawing nature of the nitro group destabilizes the oxonium intermediate and as a result further cyclization by allenylmethylsilane cannot take place. The reaction has also been validated with a heteroaromatic aldehyde such as thiophene-2-carbaldehyde (Table 1, entry 11).

Encouraged by these results, we extended our protocol to synthesize dimethylene-1,6-dioxecanes **5** using hydroxy allylsilane **4**[12] as a precursor (Table 2). Again, various aromatic aldehydes were tolerated (Table 2, entries 1–8) except for ones with electron-deficient substituents (Table 2, entries 9 and 10). In comparison with the results obtained for **1**, the reaction efficiency slightly decreased. Additionally, heteroaromatic aldehydes proved to be effective electrophiles; however, we could obtain only 26% of the desired 1,6-dioxecane derivative from furan-3-carbaldehyde (Table 2, entries 11 and 12). Notably, only single isomers of products **5** were generated in all cases. Structural assignment of **5a** was established based on the single-crystal X-ray diffraction study (see the Supporting Information).[13]

Table 2: Scope of the intermolecular double Prins-type cyclization of **5** with various aldehydes.



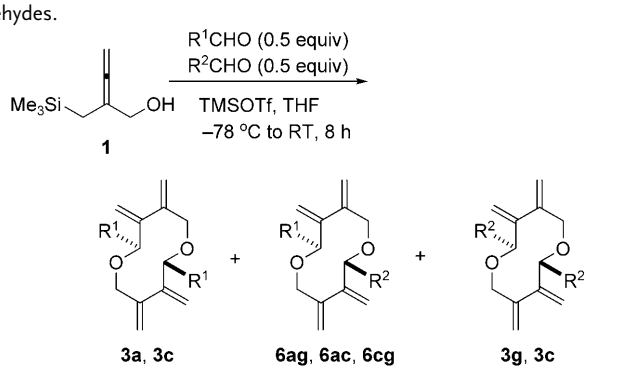
4 **5**

Entry	R	*t* [h]	Product	Yield [%][a]
1	Ph	7	**5a**	72
2	4-MeOC$_6$H$_4$	10	**5b**	40
3	3-MeOC$_6$H$_4$	10	**5c**	70
4	2-MeOC$_6$H$_4$	6	**5d**	74
5	4-MeC$_6$H$_4$	10	**5e**	52
6	3-MeC$_6$H$_4$	10	**5f**	59
7	4-FC$_6$H$_4$	6	**5g**	71
8	4-ClC$_6$H$_4$	10	**5h**	51
9	4-NO$_2$C$_6$H$_4$	6	**5i**	n.r.[b]
10	2-NO$_2$C$_6$H$_4$	6	**5j**	n.r.[b]
11	2-thienyl	9	**5k**	45
12	3-furanyl	9	**5l**	26

[a] Yield of isolated product. [b] No reaction.

To explore the effect that the aldehyde substituent had upon the intermolecular double Prins-type cyclization, we set up cross-over experiments, that is, the reactions of **1** with two different aldehydes as illustrated in Table 3. As anticipated, we observed three different cyclized products, which were separated by HPLC.[14] We found that the ratios of the products varied greatly according to the combination of mixed aldehydes.[15] In particular, the significant quantities of **6**, resulting from two different aldehydes, were generated in good yield. Interestingly, the compounds derived from cyclization of 3-methoxybenzaldehyde (**3c**, **6ac**, **6cg**) were produced predominantly. These results prompted us to carry out NMR experiments to investigate how our cyclization reaction proceeds. Thus, we performed the reaction of **1** with benzaldehyde and 4-fluorobenzaldehyde, and recorded

Table 3: Intermolecular double Prins-type cyclization of mixed benzaldehydes.



3a, **3c** **6ag**, **6ac**, **6cg** **3g**, **3c**

R^1	R^2	Yield [%]	Products (ratio)[a]
Ph	4-FC$_6$H$_4$	81	**3a**/**6ag**/**3g** (2.1:3.4:1.0)
Ph	3-MeOC$_6$H$_4$	70	**3a**/**6ac**/**3c** (1.0:3.5:5.0)
4-MeOC$_6$H$_4$	4-FC$_6$H$_4$	52	**3c**/**6cg**/**3g** (1.6:2.7:1.0)

[a] The product ratios were determined by ^{1}H NMR analysis.

^{1}H NMR spectra at different temperatures ranging from −78 °C to 20 °C (Figure 2). A few new signals (δ = 7.1, 5.6, and 4.1 ppm) that appeared after the addition of TMSOTf continued to exist until the temperature reached −30 °C. We

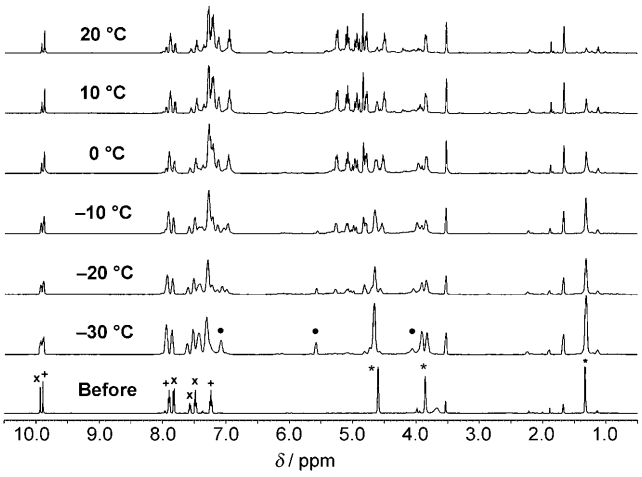


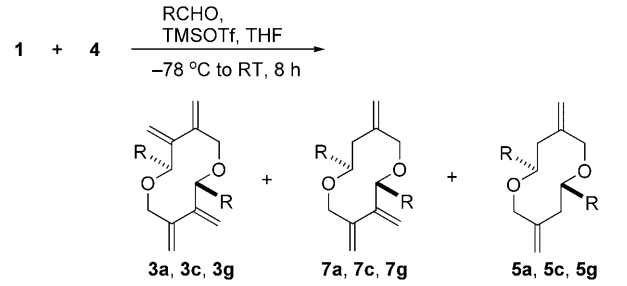
Figure 2. A series of ^{1}H NMR spectra at different temperatures in the reaction of **1** with benzaldehyde and 4-fluorobenzaldehyde. The NMR spectrum at the bottom was measured at 23 °C before the injection of TMSOTf. (*: **1**, ×: benzaldehyde, +: 4-fluorobenzaldehyde, ●: plausible intermediate).

believe that these signals belong to the oxonium intermediate which is in equilibrium with the mixed aldehydes. As these signals disappeared with increasing temperature, we observed other new signals corresponding to those of the cyclized products. These findings implied that the carbon–carbon bond formation rapidly proceeded independent of whether the intermediate came from the benzaldehyde or the 4-fluorobenzaldehyde.[16] In addition, the higher consumption of benzaldehyde compared to that of 4-fluorobenzaldehyde (as indicated by the NMR experiment) indicates that the product ratios outlined in Table 3 may reflect the electronic stabilization effect of each substituent.[17]

Finally, we have designed another interesting cross-over experiment to gain some insight into the effect of (allenylmethyl)silane and allylsilane on our cyclization process (Table 4). The reaction of a mixture of **1** (0.5 equiv) and **4** (0.5 equiv) with substituted benzaldehydes (1.0 equiv) in the presence of TMSOTf afforded three desired cyclized products in reasonable yields. Gratifyingly, the trimethylene dioxecanes **7** were separated by HPLC[14] and their structures were determined by NMR analysis. In all cases, we could obtain the dimethylene dioxecanes **5** as major isomers, which is not in agreement with our postulation from each independent experiment (Tables 1 and 2), that is, the reaction of the more reactive (allenylmethyl)silane would proceed faster to favor **3** or **7**.[18] Although we cannot clearly explain this incongruity, it is probably due to the rapid formation of the first oxonium intermediate (see **2I**, Scheme 1) regardless of using an (allenylmethyl)silane or allylsilane substrate.

To find a use for the cyclized product **3**, our final efforts focused on the Diels–Alder (DA) reaction of the bisdiene of **3**

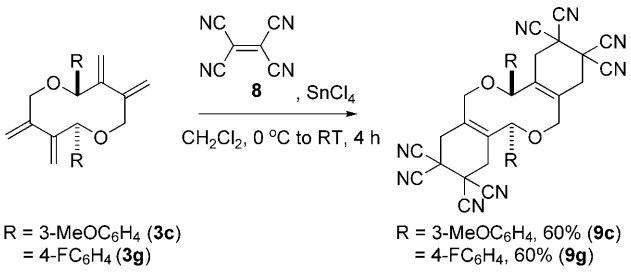
Table 4: Intermolecular double Prins-type cyclization of mixed silanes **1** and **4**.



R	Yield [%]	Products (ratio)[a]
Ph	76	**3a**/**7a**/**5a** (1.1:1.0:2.6)
3-MeOC$_6$H$_4$	71	**3c**/**7c**/**5c** (1.4:1.0:3.5)
4-FC$_6$H$_4$	72	**3g**/**7g**/**5g** (1.5:1.0:1.6)

[a] The product ratios were determined by ^{1}H NMR analysis.

with tetracyanoethylene **8**. On the basis of the X-ray structure of **3a** (see Figure 1), we thought that this transformation might be difficult because the geometry of the diene in **3** (with a 60° dihedral angle) is not suitable for the transition state of a DA reaction. As expected, the initial attempt to explore a thermal DA reaction to generate the cycloadduct **9** failed. However, the cycloaddition of **3** with **8** in the presence of tin(IV) chloride led to the desired tricyclic compounds **9** in 60% yield, respectively (Scheme 2).[19] Thus, this reaction could provide access to a number of synthetically useful tricyclic compounds that contain the 1,6-dioxecane core structure.



Scheme 2. Diels–Alder reactions of **3** and tetracyanoethylene **8**.

In conclusion, we here described the synthesis of 1,6-dioxecanes by an intermolecular double Prins-type cyclization of (allenylmethyl)silane or allylsilane with aromatic aldehydes. This is the first method to show that inter- and intramolecular Prins reactions in a single process can be employed to construct entropically unfavorable medium-sized oxacycles. In addition, we have shown that the Diels–Alder cycloaddition of **3** with **8** can provide a tricyclic ring system such as **9**. We are continuing to probe the scope of our protocol to synthesize ring systems of other sizes. The results of these studies will be reported in due course.

Experimental Section

Typical procedure for the preparation of 3,4,8,9-tetramethylene-2,7-diphenyl-1,6-dioxecane (**3a**): TMSOTf (100 mg, 0.45 mmol) was added dropwise to a stirred solution of the **1** (70 mg, 0.45 mmol) and benzaldehyde (47.5 mg, 0.45) in dry THF (6.0 mL) at −78 °C under nitrogen. The reaction mixture was slowly warmed to room temperature over 4 hours and stirred at room temperature for a further 3 hours. The resulting mixture was quenched with saturated aqueous solution of $NaHCO_3$ and diluted with CH_2Cl_2 (20 mL). The organic layer was separated and dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of the residue by column chromatography on silica gel (*n*-hexane/ethyl acetate 20:1→1:1) afforded the 1,6-dioxecane **3a** (56 mg, 73 %) as a white solid. M.p.: 170–171 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.40$–7.29 (m, 10H), 5.38 (s, 2H), 5.28 (s, 2H), 5.13 (s, 2H), 4.91 (s, 2H), 4.71 (s, 2H), 4.35 (d, 2H, $J = 11.2$ Hz), 4.13 ppm (d, 2H, $J = 10.8$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 150.85$, 146.02, 139.78, 128.18, 127.41, 127.30, 118.08, 117.80, 81.68, 71.84 ppm; IR (thin film): $\tilde{\nu} = 3058$, 2928, 1629, 1209, 1110 cm^{-1}; HRMS (EI): *m*/*z* calcd for $C_{24}H_{24}O_2$ [M^+]: 344.1776; found: 344.1777.

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[1] a) J. Breitenbach, J. Boosfeld, F. Vögtle in *Comprehensive Supramolecular Chemistry, Vol. 2* (Ed.: J. M. Lehn), Pergamon, New York, **1996**, pp. 29–67; b) B. Dietrich, P. Viout, J. M. Lehn, *Macrocyclic Chemistry: Aspects of Organic and Inorganic Supramolecular Chemistry*, Wiley-VCH, Weinheim, **1993**; for selected references for representative compounds containing medium-sized oxacycles and their syntheses, see: c) M. Nur-e-Alam, M. Yousaf, S. Qureshi, I. Baig, S. Nasim, Atta-ur-Rahman, M. I. Choudhary, *Helv. Chim. Acta* **2003**, *86*, 607–614; d) T. Kamikawa, K. Inoue, T. Kubota, M. C. Woods, *Tetrahedron* **1970**, *26*, 4561–4587; e) N. Kise, A. Fujimoto, N. Moriyama, N. Ueda, *Tetrahedron: Asymmetry* **2003**, *14*, 2495–2497; f) H. M. C. Ferraz, F. I. Bombonato, M. K. Sano, L. S. Longo, Jr., *Quim. Nova* **2008**, *31*, 885–900; g) I. Shiina, *Chem. Rev.* **2007**, *107*, 239–273; h) K. C. Nicolaou, G. E. A. Carenzi, V. Jeso, *Angew. Chem.* **2005**, *117*, 3963–3967; *Angew. Chem. Int. Ed.* **2005**, *44*, 3895–3899; i) J. H. Rigby, K. R. Fales, *Tetrahedron Lett.* **1998**, *39*, 1525–1528; j) M. Cinquini, F. Cozzi, F. Sannicolò, A. Sironi, *J. Am. Chem. Soc.* **1988**, *110*, 4363–4364; k) P. Davoli, A. Spaggiari, L. Castagnetti, F. Prati, *Org. Biomol. Chem.* **2004**, *2*, 38–47; l) D. R. Spring, S. Krishman, S. L. Schreiber, *J. Am. Chem. Soc.* **2000**, *122*, 5656–5657.

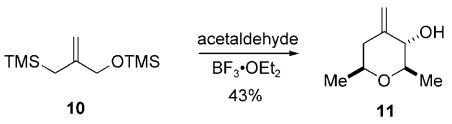
[2] a) G. Illuminati, L. Mandolini, *Acc. Chem. Res.* **1981**, *14*, 95–102; b) L. Mandolini, *Adv. Phys. Org. Chem.* **1986**, *22*, 1–111; c) C. G. Kreiter, K. Lehr, M. Leyendecker, W. S. Sheldrik, R. Exner, *Chem. Ber.* **1991**, *124*, 3–12.

[3] For reviews, see: a) T. L. B. Boivin, *Tetrahedron* **1987**, *43*, 3309–3362; b) I. M. Pastor, M. Yus, *Curr. Org. Chem.* **2007**, *11*, 925–957; for representative Prin cyclization reactions, see: c) T. A. Blumenkopf, G. C. Look, L. E. Overman, *J. Am. Chem. Soc.* **1990**, *112*, 4399–4403; d) R. C. Winstead, T. H. Simpson, G. A. Lock, M. D. Schiavelli, D. W. Thompson, *J. Org. Chem.* **1986**, *51*, 277–279; e) T. A. Blumenkopt, M. Bratz, A. Castaneda, G. C. Look, L. E. Overman, D. Rodriguez, A. S. Thompson, *J. Am. Chem. Soc.* **1990**, *112*, 4386–4399; f) P. C. Ting, P. A. Bartlett, *J. Am. Chem. Soc.* **1984**, *106*, 2668–2671; g) M. Labelle, Y. Guindon, *J. Am. Chem. Soc.* **1989**, *111*, 2204–2210; h) A. Ajamian, J. L. Gleason, *Org. Lett.* **2001**, *3*, 4161–4164; i) K. N. Cossey, R. L. Funk, *J. Am. Chem. Soc.* **2004**, *126*, 12216–12217; j) J. E. Dalgard, S. D. Rychnovsky, *Org. Lett.* **2005**, *7*, 1589–1591; k) J. P. Vitale, S. A. Wolckenhauer, N. A. Do, S. D. Rychnovsky, *Org. Lett.* **2005**, *7*, 3255–3258; l) L. S. Miranda, B. A. Meireles, J. S. Costa, V. L. P. Pereira, *Synlett* **2005**, 869–871; m) D. L. Aubele, S. Wan, P. E. Floreancig, *Angew. Chem.* **2005**, *117*, 3551–3554; *Angew. Chem. Int. Ed.* **2005**, *44*, 3485–3488; n) X. Tian, J. J. Jaber, S. D. Rychnovsky, *J. Org. Chem.* **2006**, *71*, 3176–3183; o) J. S. Yadav, N. N. Kumar, M. S. Reddy, A. R. Prasad, *Tetrahedron* **2007**, *63*, 2689–2694; p) J. S. Yadav, P. P. Rao, M. S. Reddy, N. V. Rao, A. R. Prasad, *Tetrahedron Lett.* **2007**, *48*, 1469–1471.

[4] Y. S. Cho, K. Karupaiyan, H. J. Kang, A. N. Pae, J. H. Cha, H. Y. Koh, M. H. Chang, *Chem. Commun.* **2003**, 2346–2347.

[5] a) J. E. Baldwin, *J. Chem. Soc. Chem. Commun.* **1976**, 734–736; b) J. E. Baldwin, R. C. Thomas, L. I. Kruse, L. Silberman, *J. Org. Chem.* **1977**, *42*, 3846–3852.

[6] It has been reported that the intramolecular silyl-modified Sakurai reaction of **10** and acetaldehyde in the presence of $BF_3{\cdot}OEt_2$ afforded trisubstituted tetrahydropyran **11** by an ene reaction and subsequent Prins-type cyclization; a) I. E. Markó, D. J. Bayston, *Tetrahedron Lett.* **1993**, *34*, 6595–6598; b) I. E. Markó, J.-M. Plancher, *Tetrahedron Lett.* **1999**, *40*, 5259–5262; c) I. E. Markó, R. Dumeunier, C. Leclercq, B. Leroy, J.-M. Plancher, A. Mekhalfia, D. J. Bayson, *Synthesis* **2002**, 958–972.



10 **11**

[7] Selected syntheses of dioxecane derivatives; a) R. W. Alder, A. J. Miller, D. I. Ruchbrook, *J. Chem. Soc. Chem. Commun.* **1989**, 277–279; b) F. Sondheimer, Y. Gaoni, J. Bergman, *Tetrahedron Lett.* **1960**, *1*, 25–29; c) H. A. J. Carless, J. Beanland, S. Mwesigye-Kibende, *Tetrahedron Lett.* **1987**, *28*, 5933–5936; d) K. Nagai, M. Kakayama, S. Hayashi, *Chem. Lett.* **1973**, 665–666.

[8] For Prins cyclizations promoted by titanium or indium catalysts, see: a) C.-M. Yu, S.-K. Yoon, Y.-T. Hong, J. Kim, *Chem. Commun.* **2004**, 1840–1841; b) W. H. Bunnelle, D. W. Seamon, D. L. Mohler, T. F. Ball, D. W. Thompson, *Tetrahedron Lett.* **1984**, *25*, 2653–2654; c) M. L. Melany, G. A. Lock, D. W. Thompson, *J. Org. Chem.* **1985**, *50*, 3925–3927; d) Y. S. Cho, H. Y. Kim, J. H. Cha, A. N. Pae, H. Y. Koh, J. H. Choi, M. H. Chang, *Org. Lett.* **2002**, *4*, 2025–2028; e) C. Shin, S. N. Chavre, J. H. Cha, A. N. Pae, H. Y. Koh, J. H. Choi, M. H. Chang, Y. S. Cho, *Org. Lett.* **2005**, *7*, 1589–1591; f) S. N. Chavre, H. Choo, J. K. Lee, A. N. Pae, Y. Kim, Y. S. Cho, *J. Org. Chem.* **2008**, *73*, 7467–7471; g) X.-F. Yang, M. Wang, Y. Zhang, C.-J. Li, *Synlett* **2005**, 1912–1916; h) K.-P. Chan, T.-P. Loh, *Tetrahedron Lett.* **2004**, *45*, 8387–8397; i) K.-P. Chan, T.-P. Loh, *Org. Lett.* **2005**, *7*, 4491–4494; j) L. E. Overman, A. Castañeda, T. A. Blumenkopf, *J. Am. Chem. Soc.* **1986**, *108*, 1303–1304; k) A. P. Dobbs, S. Martinovic, *Tetrahedron Lett.* **2002**, *43*, 7055–7057; l) C. E. Davis, R. M. Coates, *Angew. Chem.* **2002**, *114*, 509–511; *Angew. Chem. Int. Ed.* **2002**, *41*, 491–493.

[9] 2-[(Trimethylsilyl)methyl]buta-2,3-dien-1-ol (**1**) should be prepared just prior to use because it easily decomposes, even when stored at −20 °C. For the preparation of **1**, see: a) B. M. Trost, H. Urabe, *J. Am. Chem. Soc.* **1990**, *112*, 4983–4984; b) P. H. Lee, K. Bang, H. Ahn, K. Lee, *Bull. Korean Chem. Soc.* **2001**, *22*, 1385–1389.

[10] We have also tested a catalytic amount of TMSOTf (0.3 equiv) for the reaction, but observed only a small quantity of product. Instead, the use of a protic catalyst such as triflic acid (1.0 equiv) gave the cyclized product in 70% yield. It seems that the proton generated upon hydrolysis of TMSOTf during the reaction plays a crucial role in this protocol.

[11] CCDC 699781 (**3a**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[12] 2-[(Trimethylsilyl)methyl]prop-2-en-1-ol (**5**) was prepared by the deacetylation of commercially available 2-[(trimethylsilyl)-methyl]allyl acetate. The spectroscopic data of **5** is identical to that of the reported (T. V. Lee, R. J. Boucher, J. R. Porter, D. A. Taylor, *Tetrahedron* **1988**, *44*, 4233 – 4242).

[13] CCDC 699782 (**5a**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif..

[14] Two conditions were used for HPLC separation; a) for Table 3 and 4-FC_6H_4CHO in Table 4, reverse-phase HPLC was performed by using binary gradients of solvents A and B, where A was 0.1% TFA in water and B was 0.09% TFA in acetonitrile. Analytical reverse-phase HPLC was performed by using a YMC-Pack Pro C18 column at a flow rate of 1 mL min^{-1}, with detection at 254 nm during a isocratic mode of 70% B over 45 min. t_R min = 23.4 (**3a**), 25.1 (**6ag**), 25.6 (**3g**), 20.2 (**6ac**), 21.3 (**6cg**), 22.7 (**7g**), 17.0 (**5g**); b) for PhCHO and 3-$MeOC_6H_4CHO$ in Table 4, analytical RP-HPLC was performed by using a YMC-Pack Pro C18 column at a flow rate of 1 mL min^{-1}, with detection at 254 nm during a isocratic mode of 65% B over 45 min. t_R min = 35.8 (**3a**), 32.2 (**7a**), 22.8 (**5a**), 26.6 (**3c**), 24.3 (**7c**), 18.1 (**5c**).

[15] To avoid variation of the ratios owing to the incomplete reaction, the reactions proceeded until all the aldehydes were consumed (as evident by TLC).

[16] We have tried to isolate a reaction intermediate by quenching the reaction at low temperature or by using an acyl protected form of hydroxy(allenylmethyl)silane as a competitive substrate. However, we were not able to identify any intermediate in both cases.

[17] It is possible to assume that the product ratios outlined in Table 3 may be affected by the relative stability of the final products if ring opening is promoted by acid. However, the product stability is unlikely to effect the ratios because treatment of **3a** and **3c** with TMSOTf or triflic acid under the same reaction condition led to none of the mixed product **6ag**.

[18] The heat of hydrogenation for one carbon–carbon bond of an allene (−41 kcal mol^{-1}) is lower than that of a simple alkene (−29 kcal mol^{-1}). This extra energy makes the allene a more reactive component compared to the alkene. In addition, it was reported that the energy of the $\pi_{1,2}$ molecular orbital of 1-substitued allenes is increased by electron-donating groups such as alkyl, OH, or F. For the reactivity of allenes, see: a) N. Krause, A. S. K. Hashmi, *Modern Allene Chemistry*, *Vol. 2*, Wiley-VCH, Weinheim, **2004**; b) D. J. Pasto, *J. Am. Chem. Soc.* **1979**, *101*, 37 – 46; c) D. J. Pasto, *Tetrahedron* **1984**, *40*, 2805 – 2827.

[19] E. Wada, N. Nagasaki, S. Kanemasa, O. Tsuge, *Chem. Lett.* **1986**, 1491 – 1494.

