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# $BiBr_3$-Initiated Tandem Addition/Silyl-Prins Reactions to 2,6-Disubstituted Dihydropyrans

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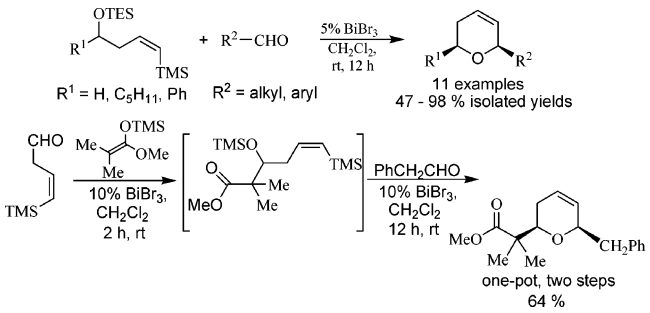


A tandem addition/silyl-Prins reaction efficiently affords *cis*-2,6-disubstituted dihydropyrans (DHPs) using 5 mol % of $BiBr_3$ in $CH_2Cl_2$. The reaction occurs between $\delta$-triethylsilyloxyvinyltrimethylsilanes and a variety of aldehydes to give good to excellent isolated yields of DHPs. The diastereoselectivities in the crude products are significantly affected by aldehyde substitution with electron-rich aldehydes, providing 2−3:1 (*cis:trans*) and neutral (or electron-poor) aldehydes affording dr ≥ 19:1 (*cis:trans*).

Recently, bismuth compounds have gained popularity as convenient, inexpensive, and environmentally benign[1] Lewis acids[2,3] and have become intensively studied catalysts in organic synthesis.[4] Many of the reactions that bismuth compounds initiate are simple silyl protection and deprotection sequences, but bismuth can also be used in the synthesis of tetrahydropyran derivatives by using a silyl-protected alcohol tethered to an aldehyde and/or ketone electrophile.[5] On the basis of the chemistry involving vinyltrimethylsilane as a nucleophile to attack an incipient oxocarbenium ion (i.e., the silyl-Prins reaction), we now report a mild, convenient, and efficient synthesis of 2,6-disubstituted dihydropyrans (DHPs) using 5 mol % of $BiBr_3$ as an initiator for tandem addition/silyl-Prins cyclization reactions. We also present a three-component, one-pot variation of this reaction to provide a functionalized DHP.

Cyclic ethers are widespread in nature, and a variety of substitution patterns are present in tetrahydropyran subunits. The related 2,6-disubstituted dihydropyran ring system is also prevalent. Not only are these latter ethers present in many natural products, such as scytophycin C,[6] but they are also synthetically useful intermediates in the production of polysubstituted tetrahydropyran ring systems, such as those found in the pseudomonic acids.[7] Many common approaches[8,9] have been reported toward dihydropyrans, and some of the more varied methodologies include addition of organozinc reagents to 1,2-dihydropyrans,[10] base-promoted cyclizations of disulfinyl dienols,[11] olefin metathesis,[12] Prins cyclizations of cyclopropyl carbinols,[13] or homoallylic alcohols,[14] and an intramolecular silyl-modified Sakurai reaction (ISMS).[15] Many of these reactions have limitations, such as the need for strictly anhydrous conditions, stoichiometric quantities of Lewis acid initiator, or delivery of a strong Lewis acid at low temperature.

A recent silyl-Prins alternative was described by Dobbs and co-workers[16] and utilized 4-trimethylsilyl-3-butenols to react with aldehydes under $InCl_3$-initiated conditions to obtain dihydropyran units in good yields with high diastereoselectivities for the *cis*-isomers. These authors typically used 0.5−1.0 equiv of $InCl_3$ for reactions of homoallylic silanes and aldehydes, and none of their examples included reactions with aryl-substituted homoallylic silanes. Although the toxicity data for $InCl_3$ have not been established, it is under investigation as a mutagen and is significantly more expensive per mole than $BiBr_3$.[17,18]

(1) The $LD_{50}$ of $BiCl_3$ is listed as 3334 mg/kg (oral, rat) in the MSDS provided by Sigma-Aldrich Chemical Corporation, St. Louis, MO.

(2) Compelling spectroscopic evidence for the role of $Bi(OTf)_3$ as a Lewis acid catalyst in a hydroamination reaction was recently described: Quin, H.; Yamagiwa, N.; Matsunaga, S.; Shibasaki, M. *J. Am. Chem. Soc.* **2006**, *128*, 1611−1614.

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(7) Class, Y. J.; DeShong, P. *Chem. Rev.* **1995**, *95*, 1843−1857.

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(9) For a variety of methods for the synthesis of dihydropyran ring systems, see: (a) Morris, W. J.; Custar, D. W.; Scheidt, K. A. *Org. Lett.* **2005**, *7*, 1113−1116. (b) Lowe, J. T.; Panek, J. S. *Org. Lett.* **2005**, *7*, 1529−1532. (c) Evans, P. A.; Lawler, M. J. *Am. Chem. Soc.* **2004**, *126*, 8642−8643. (d) Viswanathan, G. S.; Yang, J.; Li, C. *Org. Lett.* **1999**, *1*, 993−995. (e) Vares, L.; Rein, T. *J. Org. Chem.* **2002**, *67*, 7226−7237. (f) Brimble, M. A.; Pavia, G. S.; Stevenson, R. J. *Tetrahedron Lett.* **2002**, *43*, 1735−1738. (g) Semeyn, C.; Blaauw, R. H.; Hiemstra, H.; Speckamp, W. N. *J. Org. Chem.* **1997**, *62*, 3426−3427.

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(16) (a) Dobbs, A. P.; Martinović, S. *Tetrahedron Lett.* **2002**, *43*, 7055−7057. (b) Dobbs, A. P.; Guesné, S. J.; Martinović, S.; Coles, S.; Hursthouse, M. B. *J. Org. Chem.* **2003**, *68*, 7880−7883.

(17) According to the 2005−2006 general Aldrich catalog, $InCl_3$ costs $2,092 per mole, whereas $BiBr_3$ costs $393 per mole; Aldrich Chemical Corporation, Milwaukee, WI.

(18) MSDS number I1680, Mallinckrodt Baker, Inc., Phillipsburg, NJ 08865.

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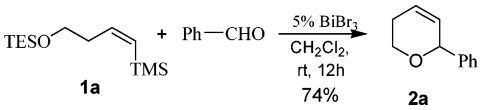
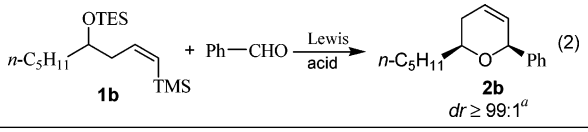
We initially investigated the reaction of simple (*Z*)-1-trimethylsilyl-4-triethylsilyloxybutene, **1a**, with benzaldehyde to establish the feasibility of our approach to dihydropyran systems (eq 1).




(1)

We were gratified to observe that 5 mol % of $BiBr_3$ efficiently catalyzed this reaction and afforded 74% isolated yield of the desired product. Lower quantities of $BiBr_3$ led to significantly slower conversions. Furthermore, the synthesis was conveniently conducted at room temperature in distilled $CH_2Cl_2$. In contrast to our result, the corresponding $InCl_3$ reaction (1.0 equiv)[16a] resulted in a significantly lower yield (39%) using benzaldehyde as the electrophile. The poor reactivity of benzaldehyde has also been documented by others in their syntheses of DHP ring systems.[9d,19]

**TABLE 1. Optimization for the Synthesis of 2-Pentyl-6-phenyl-3,6-dihydro-2*H*-pyran**




(2)

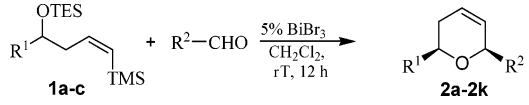
| entry[b] | acid | conditions | yield (%)[c] |
|---|---|---|---|
| 1 | 5% of $BiBr_3$ | rt | 70 |
| 2 | 5% of $BiBr_3$[d] | rt | 55 |
| 3 | 10% of HCl[e] | rt | 45 |
| 4 | 5% of $TiCl_4$ | −78 °C to rt | 18 |
| 5 | 10% of $BF_3{\cdot}OEt_2$ | −78 °C to rt | 60 |
| 6 | 10% of TMSOTf | −78 °C to rt | 54 |

[a] Diastereomeric ratios were verified by capillary GC analysis of crude reaction mixtures. [b] All reactions were carried on 0.5 mmol scale in 5.0 mL of distilled $CH_2Cl_2$ at room temperature using 2.0 equiv of benzaldehyde. [c] Isolated yield of pure *cis*-isomers only, after flash column chromatography. [d] The reaction was carried in 5.0 mL of $CH_3CN$ instead of $CH_2Cl_2$. [e] Reactions with $BiCl_3$ were comparable to those with $BiBr_3$. See ref 20.

We then extended this reaction to homoallylic silanol **1b** (eq 2 and Table 1) to determine the stereoselectivity of the tandem addition/silyl-Prins reaction. Under conditions optimized for **1a**, we observed only a single diastereomer for the product as indicated by GC and $^1H$ NMR spectroscopy. Qualitative NOE measurements[21] established the *cis*-stereochemistry, and only a very minor amount (<1%) of the presumed *trans*-diastereomer was detected by capillary GC analysis of crude reaction mixtures. We then compared this result to the same reaction mediated by other common catalysts (Table 1).

Considering that 1 mol of $BiBr_3$ might generate 2 mol of HBr by hydrolysis with adventitious water, we doubled the relative quantities of commercially available Lewis acids as well as the quantity of anhydrous Brønsted acid, HCl (10%).[20] It is significant to note that conducting the reaction in $CH_2Cl_2$ (entry 1) rather than distilled $CH_3CN$ (entry 2) was beneficial, and use of the more common Lewis acids, TMSOTf and $BF_3{\bullet}OEt_2$ (entries 5 and 6, respectively) resulted in lower isolated yields of the desired product. All of the reactions with different acids provided the *cis*-isomers with high selectivity (>99:1 by GC).

**TABLE 2. Synthesis of Disubstituted Dihydropyrans**




(3)

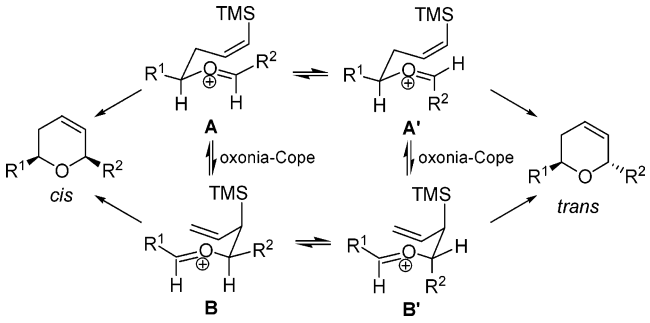
| entry[a] | product | silane **1**, $R^1$ | aldehyde $R^2$ | dr (GC, *cis*/*trans*)[b] | yield (%)[c] |
|---|---|---|---|---|---|
| 1 | **2a** | H | Ph− | | 74 |
| 2 | **2b** | *n*-$C_5H_{11}$− | Ph− | >99:1 | 70 |
| 3 | **2c** | *n*-$C_5H_{11}$− | *p*-$CF_3Ph$− | 73:1 | 74 |
| 4 | **2d** | *n*-$C_5H_{11}$− | *p*-$MeOC_6H_4$− | 2−3:1[d] | 58 |
| 5 | **2e** | *n*-$C_5H_{11}$− | $PhCH_2$− | 45:1 | 97 |
| 6 | **2f** | *n*-$C_5H_{11}$− | *i*-Pr− | >99:1 | 88 |
| 7 | **2g** | *n*-$C_5H_{11}$− | *o*-CHOPh− | >99:1 | 98 |
| 8 | **2h** | Ph | Ph− | 4−5:1 | 55 |
| 9 | **2i** | Ph | *p*-$CF_3Ph$− | >99:1 | 82 |
| 10 | **2j** | Ph | *p*-$MeOC_6H_4$− | 2−3:1[d] | 47 |
| 11 | **2k** | Ph | $PhCH_2$− | 35:1 | 94 |

[a] All the reactions were carried on 0.5 mmol scale in 5.0 mL of $CH_2Cl_2$ at room temperature using 2.0 equiv of the corresponding aldehyde. [b] Diastereomeric ratios were determined by capillary GC analysis of crude reaction mixtures. [c] Isolated yield of pure *cis*-isomers only, after flash column chromatography. [d] Diastereomeric ratios were determined by $^1H$ NMR analysis of crude reaction mixtures.

Of the acids presented in Table 1, the $BiBr_3$ or commercially available HCl in dioxane are the most convenient and operationally simple. TMSOTf and $TiCl_4$ are extremely hygroscopic, and $BF_3{\bullet}OEt_2$ is typically distilled immediately prior to use and dispensed by syringe. Finally, the latter three acids examined are normally used at low temperature in strictly anhydrous $CH_2Cl_2$.

Encouraged by the success with the acid studies and the unsubstituted vinylsilane, we turned our attention to examining different substituents on the homoallylic vinylsilane and aldehyde components (Table 2). Both aliphatic (entries 2−7)- and aromatic (entries 8−11)-substituted vinylsilanes were effective substrates, reacting smoothly to provide the expected *cis*-dihydropyrans in good to excellent isolated yields after column chromatography. The remainder of the *cis*-DHP products were produced in 55−98% isolated yields, and the *cis*-stereochemistry for all products were verified by qualitative NOE enhancements of the methine hydrogens flanking the oxygen atom.[21]

**SCHEME 1. Possible Intermediates in Silyl-Prins Cyclizations**




The general, observed *cis*-stereoselectivity can be explained by the formation of initial (*E*)-oxocarbenium ion, **A** (Scheme 1). In **A**, the two groups adjacent to the oxygen atom occupy the pseudoequatorial positions to eliminate diaxial interactions,

(19) (a) Markó, I. E.; Bayston, D. J. *Tetrahedron Lett.* **1993**, *34*, 6595−6598.

(20) $BiCl_3$ is equally effective for the reactions herein, but HBr was not available as a nonaqueous solution for control experiments. We chose to utilize the quantities of $BiBr_3$ on hand for the remainder of the reactions.

(21) See the Supporting Information.

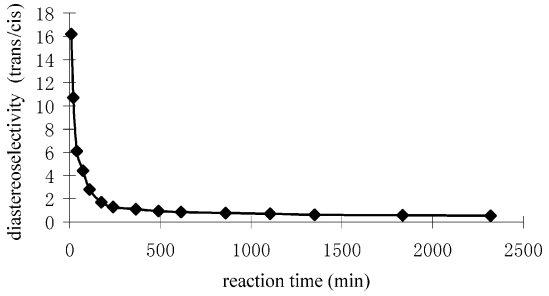



**FIGURE 1.** Correlation between reaction time and diastereoselectivity (*trans*/*cis*) for **2d** (Table 2, entry 4). The reaction was carried in 0.1 mmol scale in 1.0 mL of $CDCl_3$, using 5% $BiBr_3$ as catalyst and 2.0 equiv of anisaldehyde. The $CDCl_3$ was passed through $MgSO_4$ and basic $Al_2O_3$ to eliminate trace water and acid in $CDCl_3$ solvent. The reaction was complete in ca. 110 min, according to the consumption of the vinyltrimethylsilane.

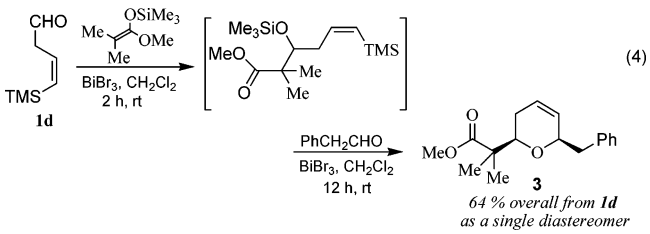
whereas the TMS moiety is oriented axially to allow greater stabilization of the cation that develops $\beta$ to the silane. Stabilization is much more effective than if the TMS were in the equatorial position.[9g,22] A [3,3] sigmatropic oxonia-Cope rearrangement could then occur from **A** to afford oxocarbenium ion, **B**.[23,24] Direct attack on the oxocarbenium carbon by the $\pi$-electrons via either **A** or **B** and subsequent desilylation would then provide the observed *cis*-DHP products. For intermediates that contain electron-donating groups for $R^1$ *and* $R^2$, oxonia-Cope reactions should be facile, both **A** and **B** would be present, and either intermediate would lead to the *cis*-diastereomer through the same secondary $\beta$-silyl cation. Formation of the stereoisomeric (*Z*)-oxocarbenium ion[25] (**A′**) would provide an alternative pathway and lead to the corresponding *trans*-products. In **A′**, $R^2$ is oriented *trans* to both the axial TMS moiety and $R^1$, which relieves steric and/or electronic interactions with the axial TMS.

Compared to aliphatic aldehydes, the use of aromatic analogues sometimes resulted in more complex reaction mixtures and lower isolated yields. Whereas introduction of the electron-withdrawing $-CF_3$ moiety increased yields, the presence of electron-donating groups decreased the yields (entries 2−4 and 5−8). Electron-rich *p*-anisaldehyde generally provides lower yields in such reactions,[9a,26] or the yields are not reported. Under the $BiBr_3$ conditions reported herein, the crude material showed a 2−3:1 diastereoselectivity, and the isolated yield of pure *cis*-**2j** (entry 10) was moderate (47%); the corresponding *trans*-isomer was contaminated with an inseparable, unidentified byproduct.

Intrigued by the low selectivity for **2d**, we followed the progress of the reaction of *p*-anisaldehyde and vinylsilane, **1b** by $^1H$ NMR spectroscopy in $CDCl_3$ at room temperature (Figure 1). The *p*-anisaldehyde electrophile was consumed within 110 min at room temperature, but during the early part of the reaction, the amount of *trans*-**2d** product exceeded that of the *cis*-compound, *cis*-**2d**. During the 40 h of monitoring, the *trans*-diastereomer isomerized to the more thermodynamically stable *cis*-isomer under the reaction conditions. For this particular aldehyde, we propose that the unexpected *trans*-diastereomer is the kinetic product, and this isomerizes to the *cis*-isomer under the reaction conditions. This surely involves a resonance-stabilized benzylic cation.[21] In terms of the mechanistic pathways shown in Scheme 1, *p*-anisaldehyde proceeds through the (*Z*)-oxocarbenium ion, **A′**. Due to the stabilizing effect of the *p*-methoxy group on the ion, intermediate **A′** would not be prone to oxonia-Cope rearrangement to the less stable oxocarbenium ion, **B′**, and direct cyclization from **A′** would rapidly afford the *trans*-product. It should be noted that even for somewhat hindered aliphatic aldehyde electrophiles (e.g., entries 5, 6, and 11) *cis*-diastereoselectivity is significantly higher. Therefore, the origin of the unusual kinetic preference for the *trans*-product likely involves both steric and electronic factors. The low diastereoselectivity for product **2h** (entry 8; $R^1 = R^2 =$ Ph) is anomalous. Efforts to elucidate the origin of the selectivities are underway and will be reported in due course.[27]

Reaction of vinylsilane **1b** with phthaldehyde only provided 2-(6-pentyl-5,6-dihydro-2*H*-pyran-2-yl)benzaldehyde, **2g**, in 98% isolated yield (Table 2, entry 7). Due to the general entropic preference for intramolecular reactions when phthaldehyde reacts with other nucleophiles, such as allyltrimethylsilane, we believed that reaction of both aldehydes might provide an isobenzofuran derivative.[28] Under $BiBr_3$ and vinyltrimethylsilane conditions, however, only one carbonyl group participated in the reaction and no isobenzofuran was detected. This selectivity is powerful because the remaining carbonyl group can be used for further elaboration.

Finally, Le Roux and co-workers reported the $BiCl_3$-catalyzed Mukaiyama aldol reaction between silyl enol ethers and aldehydes in $CH_2Cl_2$.[29] Combining the silyl-Prins cyclization described herein and the Mukaiyama aldol would provide an extremely expedient route toward functionalized *cis*-2,6-disubstituted dihydropyran systems. We chose to investigate the Mukaiyama aldol reaction between $\beta,\gamma$-unsaturated aldehyde, **1d**, and commercially available methyl $\beta,\beta$-dimethylketenetrimethylsilyl acetal (eq 4). The initial aldol was accomplished at room temperature in the presence of 10 mol % of $BiBr_3$ in $CH_2Cl_2$. Once aldehyde **1d** was consumed (ca. 2 h), phenylacetaldehyde (2 equiv) and 10% additional $BiBr_3$ were added to the same flask, and the reaction mixture was stirred until the intermediate aldol adduct was consumed (TLC). Isolation by column chromatography afforded dihydropyran **3** in 64% overall isolated yield. This yield is remarkable given the fact that aldehyde **1d** is unstable and could not be purified before use.




(4)

In summary, we have demonstrated a rapid synthesis of *cis*-2,6-disubstituted dihydropyrans in high yield and good selectivity by using 5 mol % of $BiBr_3$ as a mild and environmentally

(22) (a) Castro, P.; Overman, L. E. *Tetrahedron Lett.* **1993**, *34*, 5243−5246. (b) Daub, G. W.; Heerding, D. A.; Overman, L. E. *Tetrahedron* **1988**, *44*, 3919−3930. (c) Blumenkopf, T. A.; Overman, L. E. *Chem. Rev.* **1986**, *86*, 857−873.

(23) Oxonia-Cope reactions are well documented in Prins cyclizations. For a lead reference, see: Jasti, R.; Anderson, C. D.; Rychnovsky, S. D. *J. Am. Chem. Soc.* **2005**, *127*, 9939−9945.

(24) Castro, A. M. M. *Chem. Rev.* **2004**, *104*, 2939−3002.

(25) The (*Z*)-oxocarbenium ion recently has been suggested as an intermediate for isomerization in the solvolysis of tetrahydropyranyl mesylates. See ref 23.

(26) Crosby, S. R.; Harding, J. R.; King, C. D.; Parker, G. D.; Willis, C. L. *Org. Lett.* **2002**, *4*, 577−580.

benign catalyst or initiator. Aliphatic as well as aromatic aldehydes are effective for this silyl-Prins reaction, although electron-rich aromatic aldehydes resulted in diminished yields. Use of phthaldehyde as an electrophile afforded a functionalized product, 2-(6-pentyl-5,6-dihydro-2*H*-pyran-2-yl)benzaldehyde in nearly quantitative yield. We also present a one-pot, three-component reaction involving an initial $BiBr_3$-mediated Mukaiyama aldol followed by a silyl-Prins cyclization. These Bi(III)-initiated protocols toward disubstituted dihydropyrans represent extremely mild and convenient alternatives to reactions with other Lewis acids such as $BF_3$•$Et_2O$ or TMSOTf. We are currently working toward understanding the kinetic preference for *trans*-**2d** as well the exact role of bismuth in these reactions. The results of these further investigations will be reported in due course.

## Experimental Section

**General Procedure for the Synthesis of Dihydropyrans:** $BiBr_3$ (11.2 mg, 0.025 mmol, 0.050 equiv) was weighed into a 10 mL round-bottom flask, and 5 mL of $CH_2Cl_2$ was added via syringe. Aldehyde (1.00 mmol, 2.00 equiv) and vinylsilane (0.50 mmol, 1.00 equiv) were added by syringe sequentially. The mixture was stirred for 12 h, concentrated in vacuo, filtered through a small $SiO_2$ pipet column with $CH_2Cl_2$ as eluent, and concentrated in vacuo again. The product was then purified by flash column chromatography on silica gel.

**Preparation of *cis*-6-(4-Methoxyphenyl)-2-pentyl-3,6-dihydro-2*H*-pyran, 2d.** According to the general procedure, *p*-anisaldehyde (0.136 g, 1.00 mmol, 2.00 equiv) was treated with (*Z*)-4-(triethylsilyloxy)-1-(trimethylsilyl)non-1-ene, **1b** (0.164 g, 0.500 mmol, 1.00 equiv), to provide 0.076 g (58%) of *cis*-isomer as a colorless liquid, after purification by column chromatography (9:1 pentane:ethyl ether, $R_f = 0.54$): IR (neat) 3036(m), 2932(s), 2861(s), 1614(m), 1513(s), 1458(m), 1247(s), 1177(m), 1072(s), 1040(s), 818(m) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.30 (d, $J = 8.4$ Hz, 2H), 6.88 (d, $J = 8.8$ Hz, 2H), 5.90−5.95 (m, 1H), 5.74 (m, 1H), 5.11 (m, 1H), 3.80 (s, 3H), 3.68−3.75 (m, 1H), 1.99−2.15 (m, 2H), 1.25−1.70 (m, 8H), 0.89 (t, $J = 6.8$ Hz, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 159.2(e), 134.1(e), 130.4(o), 128.7(o), 125.0(o), 114.0(o), 77.4(o), 74.8(o), 55.6(o), 36.4(e), 32.2(e), 31.3(e), 25.5(e), 23.0(e), 14.5(o). Anal. Calcd for $C_{17}H_{24}O$ (260.37): C, 78.42; H, 9.29. Found: C, 78.16; H, 9.49.

**Preparation of *cis*-Methyl-2-(6-benzyl-3,6-dihydro-2*H*-pyran-2-yl)-2-methyl propanoate, 3:** $BiBr_3$ (44.9 mg, 0.010 mmol, 0.10 equiv) was weighed into a 25 mL round-bottom flask, and 10 mL of $CH_2Cl_2$ was added via syringe. (*Z*)-4-(Trimethylsilyl)but-3-enal, **1d** (0.142 g, 1.00 mmol, 1.00 equiv), and methyl trimethylsilyl dimethylketene acetal (0.192 g, 1.10 mmol, 1.10 equiv) were added by syringe simultaneously. The mixture was stirred, and TLC was used to monitor the reaction until (*Z*)-4-(trimethylsilyl)but-3-enal, **1d**, was consumed (3 h). Phenylacetaldehyde (0.240 g, 2.00 mmol, 2.00 equiv) and additional $BiBr_3$ (44.9 mg, 0.010 mmol, 0.10 equiv) were added, and the mixture was stirred for 12 h. The solution was concentrated in vacuo, filtered through a small $SiO_2$ pipet column with $CH_2Cl_2$ as eluent, and concentrated in vacuo again. The product was purified by column chromatography (9:1 petroleum ether:ethyl ether, $R_f = 0.34$) to provide 0.176 g (64%) of *cis*-isomer, **3**, as a colorless oil: IR (neat) 3031(s), 2982(s), 2940(s), 2879(m), 1735(s), 1451(m), 1267(s), 1140(s), 1086(s), 751(m); $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.17−7.28 (m, 5H), 5.77−5.82 (m, 1H), 5.63 (dm, $J = 10.3$ Hz, 1H), 4.27 (br, 1H), 3.77 (dd, $J = 11.0$, 3.3 Hz, 1H), 3.55 (s, 3H), 2.83 (dd, $J = 13.9$, 8.1 Hz, 1H), 2.70 (dd, $J = 13.9$, 8.1 Hz, 1H), 2.06−2.15 (m, 1H), 1.77−1.85 (m, 1H), 1.20 (s, 3H), 1.11(s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 177.2(e), 138.7(e), 129.72(o), 129.70(o), 128.0(o), 126.1(o), 125.0(o), 78.4(o), 76.5(o), 52.0(o), 46.6(e), 42.1(e), 25.4(e), 21.3(o), 20.4(o). Anal. Calcd for $C_{17}H_{22}O_3$ (274.35): C, 74.42; H, 8.08. Found: C, 74.53; H, 8.30.

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**Supporting Information Available:** Detailed experimental procedures, $^1H$ and $^{13}C$ APT NMR spectra, as well as $^1H$ NOE difference spectra for compounds **1a**−**d**, **2a**−**j**, and **3**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(27) Chair conformations in sigmatropic rearrangements are widely accepted (see refs 9g and 22−24). We have not yet ruled out the possibility of a boat topography as reported by Huang and Panek in an allylic system: Huang, H.; Panek, J. S. *J. Am. Chem. Soc.* **2000**, *122*, 9836−9837.

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