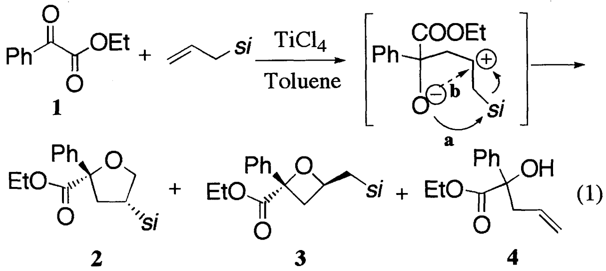
Stereoselective Construction of Oxetane by Titanium(IV) Chloride Promoted [2+2] Cycloaddition of Allylsilane to α-Keto Esters

Takahiko Akiyama* and Mikio Kirino
Department of Chemistry, Gakushuin University, 1-5-1, Mejiro, Toshima-ku, Tokyo 171

(Received May 30, 1995)

Titanium(IV) chloride mediated [2+2] cycloaddition of allylsilanes, which possess bulky substituents at the silicon, to α-keto esters underwent highly stereoselectively in toluene to afford oxetane derivatives in excellent yields.

Allylsilanes have attracted much attention as useful synthetic equivalents of 1,3-dipole:[1] Lewis acid promoted [3+2] cycloaddition of allylsilanes to α,β-unsaturated carbonyl compounds and aldehydes constitute the excellent method for the stereoselective formation of 5-membered carbocycles[2] and heterocycles,[3] respectively. We have previously reported that tin(IV) chloride promoted [3+2] cycloaddition of allylsilanes to an α-keto ester (**1**) afforded silyl-substituted tetrahydrofurans (**2**) with high diastereoselectivity via 1,2-silyl migration (eq. 1, path a).[4] Furthermore, chiral synthesis of **2** was achieved by means of diastereoselective [3+2] cycloaddition[5] of allylsilanes to chiral α-keto esters bearing a chiral cyclitol,[6] which is readily available from L-quebrachitol, as a chiral auxiliary. It should be noted that the Sakurai reaction leading to a homoallyl alcohol (**4**) was suppressed by using bulky substituents at the silicon atom of the allylsilanes, thereby resulting in the preferential formation of the tetrahydrofuran (**2**). If the alkoxide attacked β-silyl carbocation directly in the intermediate (eq. 1, path b), we expected, an oxetane (**3**) should be obtained.[7] We wish to disclose here that the reaction path could be successfully realized by use of *$TiCl_4$ in toluene* to afford **3** in excellent stereoselectivity as well as high yields. This is the first example of the highly stereoselective construction of oxetanes by Lewis acid mediated [2+2] cycloaddition of olefinic compounds and ketones.[8]



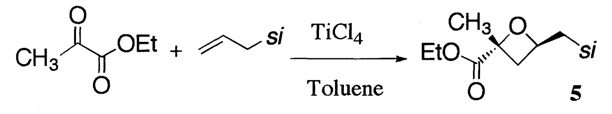
Treatment of **1** with allyl-*t*-butyldiphenylsilane in the presence of tin(IV) chloride in CH_2Cl_2 at room temperature exclusively afforded a [3+2] cycloadduct (**2a**:*si*= Si(*t*-Bu)Ph_2) as a single diastereomer in 96% yield. Use of titanium(IV) chloride as a Lewis acid changed the reaction course and an oxetane (**3a**:*si*=Si(*t*-Bu)Ph_2), which is a [2+2] cycloadduct, was obtained in 57% yield along with 23% of **2a**. Use of *toluene* as a solvent led to the exclusive formation of **3a** in 96% yield as a single diastereomer.[9,10] Other Lewis acids were not effective.[11]

Table 1. $TiCl_4$ catalyzed cycloaddition of **1** to allylsilane[a]

Entry	*si*	Yield of **3**/%	Yield of **4**/%
1	Si(*t*-Bu)Ph_2	96	0
2	Si(*i*-Pr)$_3$	74	19
3	Si(*t*-Bu)Me_2	62	29
4	$SiMe_2Ph$	0	79
5	$SiMe_3$	0	90

[a] The reactions were carried out by using 200 mol% of allylsilane and 100 mol% of titanium(IV) chloride in toluene at 0 °C for 10-30 min.

The effect of the substituent on silicon was next examined and the results are shown in Table 1. *t*-Butyldiphenyl, triisopropyl, and *t*-butyldimethyl group substituted allylsilanes worked efficiently as [2+2] counterpart to afford oxetanes (**3**) in good yields (Entries 1-3). With dimethylphenyl- and trimethyl-substituted allylsilanes, however, Sakurai product (**4**) was the sole compound isolated (Entries 4 and 5). It turned out that the bulky substituent on the silicon was essential for the formation of oxetanes, and this tendency is in good accord with that observed in the formation of the tetrahydrofurans.[12]



5a; *si* = Si(*t*-Bu)Ph_2 95%
5b; *si* = Si(*i*-Pr)$_3$ 95%
5c; *si* = Si(*t*-Bu)Me_2 85%

Titanium(IV) chloride promoted [2+2] cycloaddition with ethyl pyruvate also took place smoothly with allylsilanes to afford oxetanes (**5a-c**) highly stereoselectively as well as high yields as shown in eq. 2.

The present cycloaddition reactions exhibited excellent levels of diastereoselection, producing the oxetanes with de's reaching

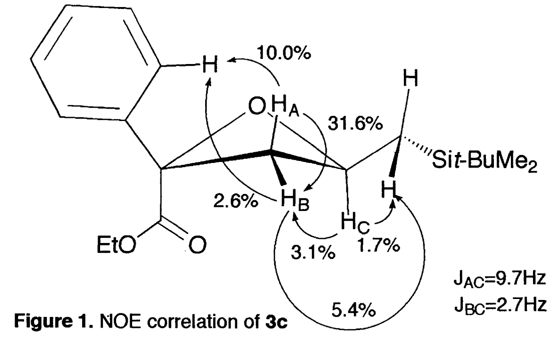


Figure 1. NOE correlation of **3c**

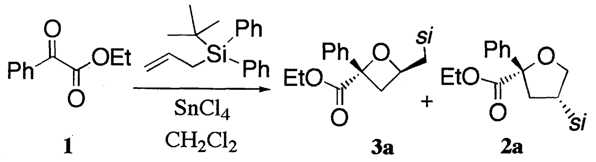


Table 2. Temperature effect of the cycloaddition[a]

Entry	Temp. /°C	Yield of **3a** /%	Yield of **2a** /%
1	0	0	96
2	–45	38	31
3	–78	59	19

[a]The reactions were carried out by using 200 mol% of allylsilane and 100 mol% of tin(IV) chloride in CH_2Cl_2 for 10-30 min.

>96% as determined by ^{1}H (270 MHz) and ^{13}C NMR. The relative stereochemisty of **3c** (*si*=Si(*t*-Bu)Me$_2$) was unambiguously determined by multiple NOE study as shown in Figure 1. The relative stereochemistry of other oxetanes was estimated by the analogy.

Tin(IV) chloride mediated cycloaddition showed intriguing temperature effects and the results are shown in Table 2. Treatment of **1** with allyl-*t*-butyldiphenylsilane in the presence of tin(IV) chloride in CH_2Cl_2 at room temperature led to the exclusive formation of the [3+2] adduct (**2a**) (Entry 1) as described above. As the reaction temperature was lowered, formation of an oxetane (**3a**) increased, and **3a** was preferentially obtained in 59% yield at –78 °C (Entry 3). The experimental observations suggest that the oxetanes are kinetic products whereas the tetrahydrofurans are thermodynamically controlled.

Although oxetanes[13] could been prepared photochemically by the Pateno-Büchi Reaction,[14] present titanium(IV) chloride promoted cycloadditions will be a novel method for the stereoselective synthesis of the oxetanes.

We appreciate the partial financial support for this research by a grant from the Saneyoshi Scholarship Foundation.

References and Notes

1 J. S. Panek, in "Comprehensive Organic Synthesis," ed by B. M. Trost, Pergamon Press, Oxford (1991), Vol. 1, p 579.
2 B. B. Snider and Q. Zhang, *J. Org. Chem.*, **56**, 4908 (1991); R. L. Danheiser, B. R. Dixon, and R. W. Gleason, *J. Org. Chem.*, **57**, 6094 (1992); J. S. Panek and N. F. Jain, *J. Org. Chem.*, **58**, 2345 (1993); R. L. Danheiser, T. Takahashi, B. Bertok, and B. R. Dixon, *Tetrahedron Lett.*, **34**, 3845 (1993); H.-J. Knölker and R. Graf, *Tetrahedron Lett.*, **34**, 4765 (1993); H.-J. Knölker, N. Foitzik, H. Goesmann, and R. Graf, *Angew. Chem., Int. Ed. Engl.*, **32**, 1081 (1993); H.-J. Knölker, N. Foitzik, R. Graf, J.-B. Pannek, and P. G. Jones, *Tetrahedron*, **49**, 9955 (1993); H.-J. Knölker and R. Graf, *Tetrahedron Lett.*, **34**, 4765 (1993); H.-J. Knölker and R. Graf, *Synlett*, **1994**, 131.
3 J. S. Panek and M. Yang, *J. Am. Chem. Soc.*, **113**, 9868 (1991); J. S. Panek and R. Beresis, *J. Org. Chem.*, **58**, 809 (1993); J. S. Panek and R. T. Beresis, *J. Am. Chem. Soc.*, **115**, 7898 (1993); A. Stahl, E. Steckhan, and M. Nieger, *Tetrahedron Lett.*, **35**, 7321 (1994).
4 T. Akiyama, K. Ishikawa, and S. Ozaki, *Chem. Lett.*, **1994**, 627.
5 T. Akiyama, T. Yasusa, K. Ishikawa, and S. Ozaki, *Tetrahedron Lett.*, **35**, 8401 (1994).
6 T. Akiyama, K. Okada, and S. Ozaki, *Tetrahedron Lett.*, **33**, 5763 (1992); T. Akiyama, H. Nishimoto, T. Kuwata, and S. Ozaki, *Bull. Chem. Soc. Jpn.*, **67**, 180 (1994); T. Akiyama, K. Ishikawa, and S. Ozaki, *Synlett*, **1994**, 275.
7 Recently, construction of cyclobutanes by Lewis acid promoted [2+2] cycloaddition of allylsilanes to α,β-unsaturated carbonyl compounds have been reported; G. Audran, H. Monti, G. Léandri, and J.-P. Monti, *Tetrahedron Lett.*, **34**, 3417 (1993); M. Hojo, K. Tomita, Y. Hirohara, and A. Hosomi, *Tetrahedron Lett.*, **34**, 8123 (1993); H. Monti, G. Audran, G. Léandri, and J. -P. Monti, *Tetrahedron Lett.*, **35**, 3073 (1994); H. Monti, G. Audran, J.-P. Monti, and G. Léandri, *Synlett*, **1994**, 403; G. P. Brengel, C. Rithner, and A. I. Meyers, *J. Org. Chem.*, **59**, 5144 (1994); H.-J. Knölker, G. Baum, and R. Graf, *Angew. Chem., Int. Ed. Engl.*, **33**, 1612 (1994).
8 Lewis acid mediated cycloaddition of electron-rich olefins to α-keto esters leading to oxetanes; J. Mattay and K. Buchkremer, *Heterocycles*, **27**, 2153 (1988).
9 ^{1}H-NMR (270 MHz), ^{13}C-NMR (67.5 MHz), and results of the DEPT experiment of **3a**: ^{1}H-NMR($CDCl_3$) δ=7.62-7.52 (4H, m), 7.42-7.15 (11H, m), 4.61-4.48 (1H, m, O-C-$\underline{H}$), 4.14 (2H, q, *J*=7.2 Hz, $C\underline{H_2}CH_3$), 2.65 (1H, dd, *J*=10.4, 15.0 Hz), 2.10-1.95 (2H, m, CH_2Si), 1.84 (1H, dd, *J*=15.0, 9.2 Hz), 1.19 (3H, t, *J*=7.2 Hz, $CH_2C\underline{H_3}$), and 1.01 (9H, s, $C(CH_3)_3$);^{13}C-NMR ($CDCl_3$): δ=174.95 (C=O), 142.39, 136.13, 136.03, 133.80, 133.16, 129.34, 129.29, 127.98, 127.69, 127.67, 127.48, 125.08, 75.78 (quaternary), 62.46 ($O\underline{C}H_2CH_3$), 57.27 (C-H) 49.51 (CH_2), 27.74 23.76 (CH_2Si), 18.18 ($\underline{C}(CH_3)_3$), and 13.78 ($OCH_2\underline{C}H_3$).
10 Other solvents gave inferior results, such as diethyl ether (65%) and hexane (42%).
11 Neither [2+2] nor [3+2] cycloadducts was obtained by other Lewis acids such as BF_3•OEt_2, $AlCl_3$, and Et_2AlCl.
12 The cycloaddition took place only with allylsilane; neither *t*-butylcrotyldiphenylsilane nor *t*-butylmethallyldiphenylsilane afforded cycloaddition products.
13 S. Searles, in "Comprehensive Heterocyclic Chemistry," ed by A. P. Katritzky, Pergamon Press, Oxford (1984), Vol. 7, p 363.
14 J. A. Porco, Jr. and S. L. Shreiber, in "Comprehensive Organic Synthesis," ed by B. M. Trost, Pergamon Press, Oxford (1991), Vol. 5, p 151.