

- P. J. *J. Phys. Chem.* **1980**, *84*, 2783.
25. Eckert, H.; wachs, I. E. *J. Phys. Chem.* **1989**, *93*, 6796.
26. Reddy, B. M.; Reddy, E. P.; Srinivas, S. T.; Mastikhin, V. M.; Nosov, N. V.; Lapina, O. B. *J. Phys. Chem.* **1992**, *96*, 7076
27. Le Costumer, L. R.; Taouk, B.; Le Meur, M.; Payen, E.; Guelton, M.; Grimblot, J. *J. Phys. Chem.* **1988**, *92*, 1230.
28. Narsimha, K.; Reddy, B. M.; Rao, P. K.; Mastikhin, V. M. *J. Phys. Chem.* **1990**, *94*, 7336.
29. Sobalik, Z.; Lapina, O. B.; Novgorodova, O. N.; Mastikhin, V. M. *Appl. Catal.* **1990**, *63*, 191.
30. Sohn, J. R.; Lee, S. Y. *Appl. Catal. A: General* **1997**, *164*, 127.
31. Olah, F. G. A.; Prakash, G. K. S.; Sommer, J. *Science* **1979**, *206*, 13.
32. Bernhole, J.; Horseley, J. A.; Murrell, L. L.; Sherman, L. G.; Soled, S. *J. Phys. Chem.* **1987**, *97*, 1526.
33. Basila, M. R.; Kantner, T. R. *J. Phys. Chem.* **1967**, *71*, 467.
34. Satsuma, A.; Hattori, A.; Mizutani, K.; Furuta, A.; Miyamoto, A.; Hattori, T.; Murakami, Y. *J. Phys. Chem.* **1988**, *92*, 6052.

Stereocontrolled Preparation of 2,6-Disubstituted 4-Methylenetetrahydropyrans by Lewis Acid Promoted Allylsilane-Acetal Cyclization

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The Lewis acid mediated intramolecular additions of allylsilanes to acetal substrates are described. Excellent regio- and diastereoselectivity are achieved by boron trifluoride promoted cyclization of allylsilane-acetals **5** and **8** derived from hydroxy allylsilanes **3**. Cyclizations occur in moderate to high yields, providing direct routes to *cis*-2,6-disubstituted 4-methylenetetrahydropyrans **6** and **9**.

Introduction

Tetrahydropyrans are important structural units in a variety of biologically active natural products.¹ Consequently, there are many efficient methods for the preparation of the six-membered oxacycles.² However, these methods were not useful for the straightforward synthesis of 4-methylenetetrahydropyrans because of difficult control for the regioselective formation of exomethylene moiety. 4-Methylenetetrahydropyran is a key-subunit present in the novel macrolides such as phorphoxazoles A and B,³ and zampanolide⁴ which exhibit exceedingly potent cytostatic activity against various human solid tumor cell lines.

Intramolecular cyclizations of allylsilanes with an electrophile have become exceedingly useful for highly regio- and stereoselective formation of various ring compounds.⁵ Indeed, Marko *et al.* reported that the intramolecular silyl-modified Sakurai (ISMS) reaction allowed the construction of the 4-methylenetetrahydropyrans, however, 2,6-disubstituted derivatives were not found.⁶

In continuation of our studies on exploring synthetic application of bimetallic reagents containing silicon and tin atoms,⁷ we found that 3-stannyl-2-(silylmethyl)propene **1** reacted smoothly with aldehydes in refluxing toluene even without any catalytic activation to give hydroxy allylsilanes **3** in good yields.⁸

In this paper we present our investigation of the regioselective formation of a variety of 2,6-disubstituted 4-methylenetetrahydropyrans by Lewis acid promoted cyclization of allylsilanes having an acetal group derived from

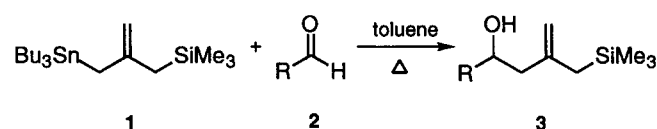




Table 1. Preparation of allylsilane-acetals **5** and their cyclizations to 4-methylenetetrahydropyrans **6**

Entry	Allylsilane-acetal 5		Tetrahydropyran 6 Yield (%) ^d
	R	Yield (%) ^a (Ratio of Diastereomers) ^{b,c}	
a	Ph	92 (70:30)	59 41 (SnCl ₄) ^g <5 (ZnCl ₂) ^f
b	p-NO ₂ C ₆ H ₄	91 (85:15) ^b	80
c	p-EtO ₂ CC ₆ H ₄	95 (75:25)	57
d	<i>trans</i> -PhCH=CH	97 (70:30)	78
e		90 (60:40)	17
f		87 (80:20)	20
g	CH ₃ CH ₂ CH ₂	82 (70:30)	53

^a Isolated yields. ^b The ratio of diastereomers was determined by ¹H NMR analysis. ^c Diastereomers were separated by chromatography (SiO₂, hexane:ether=15:1) unless otherwise noted. The higher R_f diastereomers were major isomers. ^d Reactions were carried out in dichloromethane at -78 °C with 2 equiv of BF₃·OEt₂ unless otherwise noted. ^e SnCl₄, 2 equiv, CH₂Cl₂, -78 °C. ^f ZnCl₂, 2 equiv, CH₂Cl₂, -78 °C-20 °C.

the hydroxy allylsilanes **3**.

Results and Discussion

When hydroxy allylsilanes **3** were allowed to react with ethyl vinyl ether (**4**) in dichloromethane at 0 °C in the presence of a catalytic amount of pyridinium *p*-toluenesulfonate (PPTS), 1-ethoxyethyl ethers **5** were produced in high yields as a mixture of diastereomers. The two isomers could be separated by chromatography on silica gel (hexane : ether =15 : 1). The higher Rf diastereomers were always produced

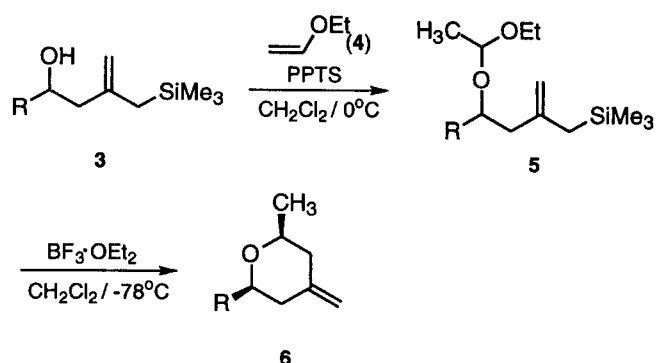


Table 2. ¹H NMR Spectra of Allylsilane-acetals **5**

Compound	Higher Rf diastereomer δ , <i>J</i> (Hz)	Lower Rf diastereomer δ , <i>J</i> (Hz)
5a	0.01 (9H, s), 1.18 (3H, t, <i>J</i> =7.0 Hz), 1.23 (3H, d, <i>J</i> =5.4 Hz), 1.46 (1H, d, <i>J</i> =13.4 Hz), 1.59 (1H, d, <i>J</i> =13.4 Hz), 2.27 (1H, dd, <i>J</i> =14.0, 6.2 Hz), 2.53 (1H, dd, <i>J</i> =14.0, 7.6 Hz), 3.53 (2H, q, <i>J</i> =7.0 Hz), 4.53 (1H, dd, <i>J</i> =7.6, 6.2 Hz), 4.56 (1H, s), 4.61 (1H, s), 4.77 (1H, q, <i>J</i> =5.4 Hz), 7.25-7.35 (5H, m).	0.01 (9H, s), 1.18 (3H, t, <i>J</i> =7.0 Hz), 1.22 (3H, d, <i>J</i> =5.4 Hz), 1.43 (1H, d, <i>J</i> =13.4 Hz), 1.54 (1H, d, <i>J</i> =13.4 Hz), 2.53 (2H, d, <i>J</i> =7.4 Hz), 3.45-3.60 (2H, m), 4.55 (1H, s), 4.60 (1H, s), 4.64 (1H, q, <i>J</i> =5.4 Hz), 4.79 (1H, t, <i>J</i> =7.4 Hz), 6.20-6.26 (1H, m), 6.28-6.32 (1H, m), 7.33-7.39 (1H, m), 0.01 (9H, s), 0.96 (3H, t, <i>J</i> =7.1 Hz), 1.26 (3H, d, <i>J</i> =5.4 Hz), 1.45 (1H, d, <i>J</i> =13.4 Hz), 1.58 (1H, d, <i>J</i> =13.4 Hz), 2.26 (1H, dd, <i>J</i> =13.8, 5.8 Hz), 2.50 (1H, dd, <i>J</i> =13.8, 7.8 Hz), 3.09-3.24 (1H, m), 3.42-3.61 (1H, m), 4.56 (1H, s), 4.60 (1H, s), 4.58 (1H, dd, <i>J</i> =7.8, 5.8 Hz), 4.71 (1H, q, <i>J</i> =5.4 Hz), 7.23-7.37 (5H, m).
5b*	0.00 (9H, s), 0.96, 1.16 (3H, t, <i>J</i> =7.0 Hz), 1.24, 1.26 (3H, d, <i>J</i> =5.4 Hz), 1.44 (1H, d, <i>J</i> =13.5 Hz), 1.55 (1H, d, <i>J</i> =13.5 Hz), 2.16-2.30 (1H, m), 2.40-2.58 (1H, m), 3.14-3.30, 3.42-3.59 (2H, m), 4.46-4.60, 4.72-4.93 (4H, m), 7.41-7.52 (2H, m), 8.11-8.20 (2H, m).	
5c	0.00 (9H, s), 1.16 (3H, t, <i>J</i> =7.0 Hz), 1.23 (3H, d, <i>J</i> =5.4 Hz), 1.39 (3H, t, <i>J</i> =7.2 Hz), 1.45 (1H, d, <i>J</i> =13.4 Hz), 1.57 (1H, d, <i>J</i> =13.4 Hz), 2.25 (1H, dd, <i>J</i> =14.0, 7.0 Hz), 2.52 (1H, dd, <i>J</i> =14.0, 7.0 Hz), 3.51 (2H, q, <i>J</i> =7.0 Hz), 4.37 (2H, q, <i>J</i> =7.2 Hz), 4.51 (1H, q, <i>J</i> =5.4 Hz), 4.55 (1H, s), 4.57 (1H, s), 4.82 (1H, t, <i>J</i> =7.0 Hz), 7.36 (2H, d, <i>J</i> =8.2 Hz), 8.00 (2H, d, <i>J</i> =8.2 Hz).	0.00 (9H, s), 0.95 (3H, t, <i>J</i> =7.0 Hz), 1.25 (3H, d, <i>J</i> =5.4 Hz), 1.41 (3H, t, <i>J</i> =7.2 Hz), 1.44 (1H, d, <i>J</i> =13.4 Hz), 1.56 (1H, d, <i>J</i> =13.4 Hz), 2.24 (1H, dd, <i>J</i> =13.7, 7.0 Hz), 2.51 (1H, dd, <i>J</i> =13.7, 7.0 Hz), 3.12-3.26, 3.43-3.58 (2H, m), 4.37 (2H, q, <i>J</i> =7.2 Hz), 4.54 (1H, q, <i>J</i> =5.4 Hz), 4.51 (1H, s), 4.55 (1H, s), 4.79 (1H, t, <i>J</i> =7.0 Hz), 7.40 (2H, d, <i>J</i> =8.2 Hz), 8.0 (2H, d, <i>J</i> =8.2 Hz).
5d	0.04 (9H, s), 1.21 (3H, t, <i>J</i> =7.0 Hz), 1.31 (3H, d, <i>J</i> =5.4 Hz), 1.59 (2H, s), 2.22 (1H, dd, <i>J</i> =13.8, 7.0 Hz), 2.42 (1H, dd, <i>J</i> =13.8, 7.0 Hz), 3.42-3.66 (2H, m), 4.38 (1H, q, <i>J</i> =7.0 Hz), 4.61 (1H, s), 4.70 (1H, s), 4.80 (1H, q, <i>J</i> =5.4 Hz), 6.05 (1H, dd, <i>J</i> =16.0, 7.0 Hz), 6.53 (1H, d, <i>J</i> =16.0 Hz), 7.21-7.42 (5H, m).	0.03 (9H, s), 1.14 (3H, t, <i>J</i> =7.0 Hz), 1.33 (3H, d, <i>J</i> =5.4 Hz), 1.58 (2H, s), 2.19 (1H, dd, <i>J</i> =13.8, 7.0 Hz), 2.39 (1H, dd, <i>J</i> =13.9, 7.0 Hz), 3.37-3.52 (1H, m), 3.59-3.71 (1H, m), 4.27 (1H, q, <i>J</i> =7.0 Hz), 4.62 (1H, s), 4.69 (1H, s), 4.78 (1H, q, <i>J</i> =5.4 Hz), 6.19 (1H, dd, <i>J</i> =16.0, 7.0 Hz), 6.54 (1H, d, <i>J</i> =16.0 Hz), 7.20-7.41 (5H, m).
5e	0.01 (9H, s), 1.18 (3H, t, <i>J</i> =7.0 Hz), 1.22 (3H, d, <i>J</i> =5.4 Hz), 1.43 (1H, d, <i>J</i> =13.4 Hz), 1.54 (1H, d, <i>J</i> =13.4 Hz), 2.53 (2H, d, <i>J</i> =7.4 Hz), 3.45-3.60 (2H, m), 4.55 (1H, s), 4.60 (1H, s), 4.64 (1H, q, <i>J</i> =5.4 Hz), 4.79 (1H, t, <i>J</i> =7.4 Hz), 6.20-6.26 (1H, m), 6.28-6.32 (1H, m), 7.33-7.39 (1H, m).	0.01 (9H, s), 1.08 (3H, t, <i>J</i> =7.1 Hz), 1.28 (3H, d, <i>J</i> =5.4 Hz), 1.42 (1H, d, <i>J</i> =12.9 Hz), 1.54 (1H, d, <i>J</i> =12.9 Hz), 2.51 (2H, d, <i>J</i> =7.2 Hz), 3.18-3.33 (1H, m), 3.46-3.61 (1H, m), 4.56 (1H, s), 4.60 (1H, s), 4.67 (1H, t, <i>J</i> =7.2 Hz), 4.74 (1H, q, <i>J</i> =5.4 Hz), 6.20-6.24 (1H, m), 6.28-6.31 (1H, m), 7.32-7.48 (1H, m).
5f	0.02 (9H, s), 1.19 (3H, t, <i>J</i> =7.0 Hz), 1.24 (3H, d, <i>J</i> =5.4 Hz), 1.47 (1H, d, <i>J</i> =13.4 Hz), 1.57 (1H, d, <i>J</i> =13.4 Hz), 2.37 (1H, dd, <i>J</i> =13.9, 7.0 Hz), 2.60 (1H, dd, <i>J</i> =13.9, 7.0 Hz), 3.54 (2H, q, <i>J</i> =7.0 Hz), 4.57 (1H, s), 4.64 (1H, s), 4.65 (1H, q, <i>J</i> =5.4 Hz), 5.05 (1H, t, <i>J</i> =7.0 Hz), 6.90-6.94 (2H, m), 7.20-7.26 (1H, m).	0.01 (9H, s), 1.06 (3H, t, <i>J</i> =7.0 Hz), 1.29 (3H, d, <i>J</i> =5.4 Hz), 1.46 (1H, d, <i>J</i> =13.4 Hz), 1.57 (1H, d, <i>J</i> =13.4 Hz), 2.39 (1H, dd, <i>J</i> =13.9, 7.0 Hz), 2.59 (1H, dd, <i>J</i> =13.9, 7.0 Hz), 3.20-3.35 (1H, m), 3.48-3.67 (1H, m), 4.59 (1H, s), 4.63 (1H, s), 4.76 (1H, q, <i>J</i> =5.4 Hz), 4.89 (1H, t, <i>J</i> =7.0 Hz), 6.90-6.96 (2H, m), 7.20-7.27 (1H, m).
5g	0.03 (9H, s), 0.90 (3H, t, <i>J</i> =6.2 Hz), 1.12-1.67 (12H, m), 1.96-2.38 (2H, m), 3.41-3.80 (3H, m), 4.58 (1H, s), 4.64 (1H, s), 4.72 (1H, q, <i>J</i> =5.2 Hz).	0.03 (9H, s), 0.90 (3H, t, <i>J</i> =6.6 Hz), 1.13-1.70 (12H, m), 2.0-2.39 (2H, m), 3.47-3.78 (3H, m), 4.58 (1H, s), 4.64 (1H, s), 4.73 (1H, q, <i>J</i> =5.2 Hz).

*Mixture of diastereomers.

Table 3. Spectral Data of 4-methylenetetrahydropyrans **6**

Compound	¹ H NMR δ , <i>J</i> (Hz)	¹³ C NMR δ	MS m/z (relative intensity, %)
6a	1.34 (3H, d, <i>J</i> =6.0 Hz), 1.98-2.52 (4H, m), 3.53-3.72 (1H, m), 4.36 (1H, dd, <i>J</i> =11.3, 1.5 Hz), 4.82 (2H, s), 7.22-7.48 (5H, m).	22.0, 42.3, 42.6, 74.9, 80.4, 108.5, 125.9, 127.4, 128.3, 142.5, 144.8.	188 (M ⁺ , 30), 144 (99), 129 (100), 107 (90), 105 (25), 104 (32), 91 (12), 77 (45), 67 (85).
6b	1.33 (3H, d, <i>J</i> =6.0 Hz), 1.96-2.53 (4H, m), 3.53-3.71 (1H, m), 4.44 (1H, dd, <i>J</i> =11.4, 1.6 Hz), 4.84 (2H, s), 7.56 (2H, d, <i>J</i> =8.7 Hz), 8.20 (2H, d, <i>J</i> =8.7 Hz).	21.8, 42.0, 42.5, 75.0, 79.0, 109.4, 123.5, 126.5, 143.5, 147.1, 149.9.	233 (M ⁺ , 7), 189 (30), 172 (27), 143 (20), 128 (15), 91 (7), 77 (23), 67 (100).
6c	1.32 (3H, d, <i>J</i> =6.2 Hz), 1.39 (3H, t, <i>J</i> =7.2 Hz), 1.95-2.49 (4H, m), 3.52-3.59 (1H, m), 4.37 (2H, q, <i>J</i> =7.2 Hz), 4.39 (1H, d, <i>J</i> =8.2 Hz), 4.81 (2H, s), 7.45 (2H, d, <i>J</i> =8.2 Hz), 8.02 (2H, d, <i>J</i> =8.2 Hz).	14.3, 21.9, 42.2, 42.6, 60.9, 75.0, 79.8, 108.9, 125.7, 129.5, 129.7, 144.3, 147.6, 166.5.	260 (M ⁺ , 13), 216 (45), 179 (49), 143 (100), 105 (15), 67 (40).
6d	1.30 (3H, d, <i>J</i> =6.0 Hz), 1.90-2.09 (1H, m), 2.12-2.40 (3H, m), 3.43-3.62 (1H, m), 3.92-4.06 (1H, m), 4.78 (2H, s), 6.26 (1H, dd, <i>J</i> =16.1, 6.3 Hz), 6.63 (1H, d, <i>J</i> =16.1 Hz), 7.18-7.43 (5H, m).	21.9, 40.7, 42.3, 74.6, 78.9, 108.7, 126.5, 127.6, 128.5, 130.0, 130.7, 136.8, 144.3.	214 (M ⁺ , 100), 199 (6), 170 (15), 155 (26), 133 (88), 115 (62), 91 (27), 67 (68).
6e	1.29 (3H, d, <i>J</i> =6.2 Hz), 1.96-2.12 (1H, m), 2.20-2.32 (1H, m), 2.35-2.61 (2H, m), 3.46-3.68 (1H, m), 4.39 (1H, dd, <i>J</i> =10.6, 3.6 Hz), 4.79 (2H, s), 6.28-6.37 (2H, m), 7.33-7.40 (1H, m).	21.9, 38.4, 42.2, 73.6, 74.9, 106.6, 109.2, 110.1, 142.2, 143.9, 154.5.	178 (M ⁺ , 10), 134 (60), 119 (14), 97 (100), 67 (53).
6f	1.32 (3H, d, <i>J</i> =6.1 Hz), 1.98-2.15 (1H, m), 2.23-2.64 (3H, m), 3.54-3.72 (1H, m), 4.59 (1H, dd, <i>J</i> =11.1, 2.3 Hz), 4.81 (2H, s), 6.95-7.04 (2H, m), 7.23-7.29 (1H, m).	21.9, 42.2, 42.4, 75.1, 76.1, 109.1, 123.6, 124.6, 126.4, 144.1, 145.7.	196 (M ⁺ , trace), 195 (M+1, 1), 194 (M ⁺ , 12), 179 (trace), 150 (73), 135 (27), 113 (100), 97 (7), 67 (53).
6g	0.91 (3H, t, <i>J</i> =5.7 Hz), 1.22 (3H, d, <i>J</i> =6.12 Hz), 1.30-1.53 (4H, m), 1.80-1.98 (2H, m), 2.12-2.25 (2H, m), 3.18-3.31 (1H, m), 3.31-3.48 (1H, m), 4.69 (2H, s).	14.1, 18.8, 21.9, 38.5, 40.6, 42.6, 74.5, 78.3, 107.8, 145.4.	154 (M ⁺ , 8), 111 (25), 95 (40), 81 (53), 67 (100).

much more than the lower ones (Table 1 and 2).

Allylsilanes bearing an acetal group **5** underwent cyclization at $-78\text{ }^{\circ}\text{C}$ in the presence of 2 equiv of $\text{BF}_3 \cdot \text{OEt}_2$ to give 2-methyl-6-substituted 4-methylenetetrahydropyrans **6** in 17-80% yields (Table 1).

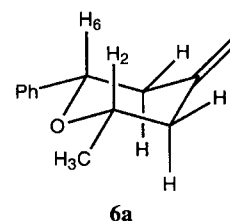
Among the Lewis acids tried boron trifluoride etherate was found to be the optimum Lewis acid. Attempted cyclization with TiCl_4 or AlCl_3 led only to decomposition, while SnCl_4 or ZnCl_2 afforded tetrahydropyran **8a** in low yields (Table 2, entry a). All Lewis acids promoted cyclization were conducted in dichloromethane at substrate concentration of *ca.* 0.1 M.

No trace of other regioisomers was apparent in the 200 MHz ¹H NMR spectrum or capillary GC-MS analysis of the crude products formed from the cyclization reactions of **5**. The exomethylene protons of **6** appear at about δ 4.8 as a singlet in ¹H NMR spectrum (Table 3).

Surprisingly, single *cis* isomers of tetrahydropyrans **6** were observed. The stereochemical assignment for **6a** was made on the basis of ¹H NMR spectrum. For example the H-6 proton of **6a** appears at δ 4.37 as double doublet (*J*=11.4 and 2.2 Hz). This clearly proved the H-6 proton is on the axial position; the larger coupling constant (*J*=11.4 Hz) observed is only consistent with a diaxial arrangement of the two protons involved. Such large coupling constants of H-6 protons are also observed in the tetrahydropyrans **6b**, **6c**, **6e**, and **6f** (Table 3).

The stereochemistry of H-2 proton of **6a** was determined by the decoupling experiment. Irradiation of the methyl protons at δ 1.33 causes the signal at δ 3.53-3.71 (H-2) from

multiplet to doublet of doublet (δ 3.63) whose coupling constants are 11.4 and 2.2 Hz. The large coupling constant (*J*=11.4 Hz) indicates that the proton H-2 of **6a** is also on the axial positions.⁹



In order to examine this procedure could be applied for the synthesis of more diversely substituted tetrahydropyrans, we prepared other mixed allylsilane-acetals **8** from the reaction of hydroxy allylsilanes **3** with α -chloro ethers **7** (prepared¹⁰ in situ from the corresponding acetals) in the presence of ethyl diisopropylamine (Table 4 and 5).

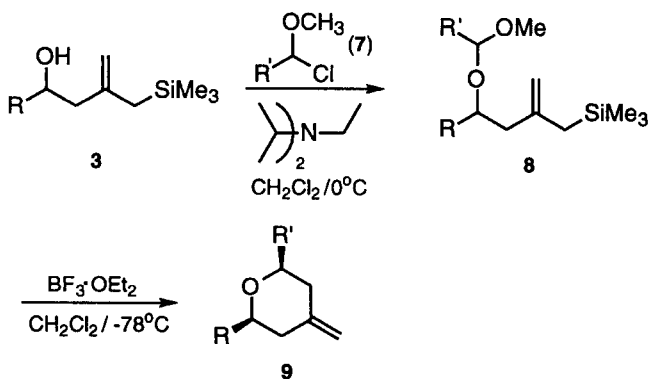
Boron trifluoride promoted cyclization of **8** provided 2,6-disubstituted 4-methylenetetrahydropyrans **9**; other regioisomers were not produced (Table 4). However, all the attempted cyclization of allylsilane-acetal **8k** derived from phenylglyoxal did not give any tetrahydropyran **9k**.

The configuration of the product **9** was deduced from its ¹H NMR spectrum (Table 6). The protons of H-2 and H-6 of **9b** appear at δ 4.59 as doublet (*J*=12.0 Hz), H-3 and H-5 protons appear at δ 2.41 as triplet (*J*=12.0 Hz). This clearly indicates vicinal (*J*₂₃ and *J*₅₆) and geminal (*J*_{33'} and *J*_{55'}) coupling constants are the same (12.0 Hz), and coupling constants of *J*_{23'} and *J*_{56'} are nearly zero. The large coupling con-

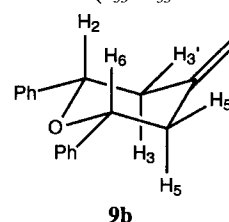
Table 4. Synthesis of variously substituted 4-methylenetetrahydropyrans **9**

Entry	Allylsilane-acetal 8	Yield (%)	Tetrahydropyran 9	Yield (%) ^a
a		96		50 33 (SnCl ₄) ^b
b		71		92
c		66		34
d		61		72
e		86		29
f		15		76
g		95		16
h		82		61
i		90		75
j		93		41
k		63		0

^a Isolated yields. Reactions were performed in CH₂Cl₂ at -78 °C with 2 equiv of BF₃·OEt₂ unless otherwise noted. ^b SnCl₄, 2 equiv, CH₂Cl₂, -78 °C.



stant ($J_{23}=J_{56}=12.0$ Hz) indicates that the protons H-2 and H-6 are on the axial positions. The protons of H-3' and H-5' appear at δ 2.61 as doublet ($J_{33'}=J_{55'}=12.0$ Hz, $J_{23}=J_{56}=0$ Hz).



Since the two stereoisomers of allylsilane-acetals **6** and **9** could be separated by chromatography, we had opportunity to examine cyclizations of each. For example, the yields and structures of **6c** and **9h** were found to be essentially the same in BF₃·OEt₂-promoted cyclizations of either stereoisomers **5c** and **8h**, respectively.

The formation of a single *cis* isomer in their reactions is interesting. Such a stereoselective cyclization would proceed through the chair-like transition state of the oxonium ion **10** which undergoes an intramolecular Sakurai reaction producing the *exo*-methylenetetrahydropyran **9** in which both substituents occupy equatorial positions.^{6b}



In summary, the intramolecular boron trifluoride promoted reactions of allylsilane-acetals provide useful routes to the regio- and diastereoselective preparation of a variety of 2,6-disubstituted 4-methylenetetrahydropyrans.

Experimental

All reactions were performed in oven-dried glassware under a positive pressure of argon. ¹H NMR spectra were recorded on a Varian Gemini-200 (200 MHz) and Varian Unity Plus 300 (300 MHz) spectrometers using chloroform as an internal standard. ¹³C NMR spectra were obtained on a Varian Gemini-200 spectrometer with CDCl₃ as solvent and internal reference. GC-MS spectra were taken on a HP GC/MS 5972 instrument with a 70 eV ionization potential. An HP-1 column (0.2 mm ID, 30 m) was used at 100-270 °C (10 °C/min).

Preparation of 1-Ethoxyethyl Ethers of Hydroxy Allylsilanes **5.** A typical procedure for the synthesis of **5a** is illustrative. To a dichloromethane (3 mL) solution of hydroxy allylsilane **3** (R=Ph) (290 mg, 1.24 mmol) (prepared from the reaction of bismetallic reagent **1** with benzaldehyde following our previous reported procedure⁸) at 0 °C was added freshly distilled ethyl vinyl ether (0.15 mL, 1.6 mmol), and a catalytic amount of pyridinium *p*-toluenesulfonate (22 mg). The reaction mixture was stirred at 0 °C for 4 h and then quenched with anhydrous K₂CO₃ followed by concentration *in vacuo*. The residue was purified by flash chromatography (silica gel, hexane:ether=15:1), which partially separated the allylsilane-acetal diastereomers **5a**: combined yield, 349 mg (92%) of **5a**. The ratio of di-

Table 5. ^1H NMR Spectral of allylsilane-acetals **8**

Compound	Higher Rf diastereomer δ , J (Hz)	Lower Rf diastereomer δ , J (Hz)
8a	0.03 (9H, s), 1.54 (1H, d, $J=13.5$ Hz), 1.63 (1H, d, $J=13.5$ Hz), 2.30 (1H, dd, $J=14.2$, 5.2 Hz), 2.53 (1H, dd, $J=14.2$, 8.4 Hz), 3.36 (3H, s), 4.53 (2H, s), 4.60 (1H, s), 4.68 (1H, s), 4.77 (1H, dd, $J=8.4$, 5.2 Hz), 7.20-7.37 (5H, m).	
8b	0.04 (9H, s), 1.54 (1H, d, $J=13.4$ Hz), 1.66 (1H, d, $J=13.4$ Hz), 2.38 (1H, dd, $J=13.8$, 5.8 Hz), 2.64 (1H, dd, $J=13.8$, 8.0 Hz), 3.13 (3H, s), 4.61 (1H, s), 4.70 (1H, s), 5.00 (1H, dd, $J=8.0$, 5.8 Hz), 5.36 (1H, s), 7.22-7.63 (10H, m).	0.04 (9H, s), 1.34 (1H, d, $J=13.4$ Hz), 1.47 (1H, d, $J=13.4$ Hz), 2.34 (1H, dd, $J=13.8$, 6.2 Hz), 2.61 (1H, dd, $J=13.8$, 7.6 Hz), 3.13 (3H, s), 4.52 (3H, brs), 5.37 (1H, s), 7.22-7.49 (10H, m).
8c*	0.02 (9H, s), 0.85, 0.89 (3H, t, $J=7.6$ Hz), 1.18-1.63 (6H, m), 2.24, 2.25 (1H, dd, $J=13.6$, 6.8 Hz), 2.46-2.61 (1H, m), 3.05, 3.26 (3H, s), 4.27, 4.57 (1H, t, $J=5.4$ Hz), 4.54, 4.57 (2H, s), 4.74, 4.88 (1H, t, $J=6.8$ Hz), 7.42-7.53 (2H, m), 8.13-8.23 (2H, m).	
8d	0.00 (9H, s), 0.82 (3H, t, $J=7.2$ Hz), 1.19-1.63 (6H, m), 1.39 (3H, t, $J=7.2$ Hz), 2.26 (1H, dd, $J=13.6$, 7.0 Hz), 2.53 (1H, dd, $J=13.6$, 7.0 Hz), 3.26 (3H, s), 4.27 (1H, t, $J=5.6$ Hz), 4.37 (2H, q, $J=7.2$ Hz), 4.55 (1H, s), 4.57 (1H, s), 4.82 (1H, t, $J=7.0$ Hz), 7.36 (2H, d, $J=8.2$ Hz), 8.00 (2H, d, $J=8.2$ Hz).	0.01 (9H, s), 0.88 (3H, t, $J=7.2$ Hz), 1.18-1.74 (6H, m), 1.40 (3H, t, $J=7.0$ Hz), 2.26 (1H, dd, $J=13.8$, 7.0 Hz), 2.52 (1H, dd, $J=13.8$, 7.0 Hz), 3.03 (3H, s), 4.37 (2H, q, $J=7.0$ Hz), 4.45-4.58 (1H, m), 4.56 (2H, s), 4.67 (1H, t, $J=7.0$ Hz), 7.41 (2H, d, $J=6.9$ Hz), 8.00 (2H, d, $J=6.9$ Hz).
8e	0.06 (9H, s), 1.63 (2H, s), 2.26 (1H, dd, $J=14.1$, 7.0 Hz), 2.43 (1H, dd, $J=14.1$, 7.0 Hz), 3.40 (3H, s), 4.39 (1H, q, $J=7.0$ Hz), 4.58 (1H, d, $J=6.8$ Hz), 4.65 (1H, s), 4.74 (1H, s), 4.78, 4.79 (1H, d, $J=6.8$ Hz), 6.08, 6.09 (1H, dd, $J=15.8$, 7.0 Hz), 6.58 (1H, d, $J=15.8$ Hz), 7.20-7.43 (5H, m).	
8f	0.04 (9H, s), 0.90 (3H, t, $J=7.2$ Hz), 0.92-1.68 (6H, m), 2.23 (1H, dd, $J=14.0$, 7.0 Hz), 2.43 (1H, dd, $J=14.0$, 7.0 Hz), 3.29 (3H, s), 4.36 (1H, q, $J=7.0$ Hz), 4.59 (1H, t, $J=5.8$ Hz), 4.60 (1H, s), 4.70 (1H, s), 6.02 (1H, dd, $J=16.0$, 7.0 Hz), 6.53 (1H, d, $J=16.0$ Hz), 7.22-7.43 (5H, m).	0.04 (9H, s), 0.93 (3H, t, $J=7.2$ Hz), 1.21-1.68 (6H, m), 2.20 (1H, dd, $J=13.8$, 7.0 Hz), 2.40 (1H, dd, $J=13.8$, 7.0 Hz), 3.28 (3H, s), 4.27 (1H, q, $J=7.0$ Hz), 4.55 (1H, t, $J=5.6$ Hz), 4.61 (1H, s), 4.69 (1H, s), 6.42 (1H, dd, $J=15.8$, 7.0 Hz), 6.55 (1H, d, $J=15.8$ Hz), 7.20-7.42 (5H, m).
8g	0.04 (9H, s), 1.48 (1H, d, $J=13.4$ Hz), 1.64 (6H, brs), 1.69 (1H, d, $J=13.4$ Hz), 2.05 (1H, dd, $J=13.9$, 6.8 Hz), 2.32 (1H, dd, $J=13.9$, 6.6 Hz), 2.89 (2H, d, $J=5.4$ Hz), 3.31 (3H, s), 4.42-4.82 (3H, m), 4.57 (1H, s), 4.65 (1H, s), 7.12-7.35 (5H, m).	0.02 (9H, s), 1.39 (1H, d, $J=13.6$ Hz), 1.47 (1H, d, $J=13.6$ Hz), 1.60 (3H, s), 1.72 (3H, s), 1.97 (1H, dd, $J=13.7$, 7.4 Hz), 2.20 (1H, dd, $J=13.7$, 6.2 Hz), 2.90 (2H, d, $J=5.4$ Hz), 3.28 (3H, s), 4.11-4.25 (1H, m), 4.52 (2H, brs), 4.55-4.65 (1H, m), 5.08-5.20 (1H, m), 7.08-7.48 (5H, m).
8h	0.03 (9H, s), 1.46 (1H, d, $J=13.6$ Hz), 1.57 (1H, d, $J=13.6$ Hz), 2.52 (1H, dd, $J=13.5$, 7.0 Hz), 2.60 (1H, dd, $J=13.5$, 7.0 Hz), 2.79 (1H, dd, $J=14.2$, 5.6 Hz), 2.89 (1H, dd, $J=14.2$, 6.2 Hz), 3.32 (3H, s), 4.58 (1H, s), 4.52-4.61 (1H, m), 4.64 (1H, s), 4.80 (1H, t, $J=7.0$ Hz), 6.07 (1H, d, $J=3.4$ Hz), 6.26 (1H, dd, $J=3.4$, 2.0 Hz), 7.12-7.33 (7H, m).	-0.01 (9H, s), 1.30 (1H, d, 13.4 Hz), 1.39 (1H, d, $J=13.4$ Hz), 2.43 (1H, dd, $J=14.0$, 6.8 Hz), 2.52 (1H, dd, $J=14.0$, 7.8 Hz), 2.92 (2H, d, $J=5.6$ Hz), 3.10 (3H, s), 4.41-4.50 (1H, m), 4.48 (2H, s), 4.66 (1H, t, $J=5.6$ Hz), 6.23 (1H, d, $J=3.2$ Hz), 6.31 (1H, dd, $J=3.2$, 2.0 Hz), 7.10-7.41 (6H, m).
8i	0.03 (9H, s), 1.47 (1H, d, $J=13.6$ Hz), 1.58 (1H, d, $J=13.6$ Hz), 2.58 (1H, dd, $J=13.4$, 7.2 Hz), 2.68 (1H, dd, $J=13.4$, 7.2 Hz), 3.16 (3H, s), 4.59 (1H, s), 4.67 (1H, s), 4.98 (1H, t, $J=7.2$ Hz), 5.45 (1H, s), 6.31 (1H, s), 7.25-7.49 (7H, m).	0.00 (9H, s), 1.36 (1H, d, $J=13.4$ Hz), 1.46 (1H, d, $J=13.4$ Hz), 2.57 (1H, dd, $J=13.4$, 7.0 Hz), 2.66 (1H, dd, $J=13.4$, 7.0 Hz), 3.34 (3H, s), 4.53 (1H, s), 4.57 (1H, s), 4.66 (1H, t, $J=7.0$ Hz), 5.40 (1H, s), 6.22-6.35 (1H, m), 7.22-7.49 (7H, m).
8j*	0.00, 0.04 (9H, s), 0.77, 0.95 (3H, t, $J=7.0$ Hz), 1.04-1.62 (4H, m), 1.84-2.06 (2H, m), 2.11 (1H, dd, $J=13.8$, 7.4 Hz), 2.35 (1H, dd, $J=13.8$, 6.0 Hz), 2.92 (2H, d, $J=5.8$ Hz), 3.33 (3H, s), 3.60-3.80 (1H, m), 4.51-4.61 (2H, m), 4.70 (1H, t, $J=5.8$ Hz), 7.18-7.36 (5H, m).	
8k*	-0.03, -0.02 (9H, s), 1.42 (1H, d, $J=2.8$ Hz), 1.55 (1H, d, $J=2.8$ Hz), 2.40-2.54 (2H, m), 3.18, 3.22 (2H, s), 4.59 (1H, s), 4.67 (1H, s), 4.96 (1H, dd, $J=7.7$, 5.8 Hz), 5.19 (1H, t, $J=6.6$ Hz), 5.55 (1H, s), 7.21-7.68, 7.85-8.12 (10H, m).	

*Mixture of diastereomers.

astereomers was determined by ^1H NMR analysis (Table 1). Separation of diastereomers was achieved by preparative thin layer chromatography (silica gel, hexane : ether=15 : 1).

Preparation of 6-Substituted 2-Methyl-4-methylenetetrahydropyrans **6 by $\text{BF}_3 \cdot \text{OEt}_2$ Promoted Cyclization of Allylsilane-Acetals **5**.** A typical pro-

Table 6. Spectral Data of 4-methylenetetrahydropyrans **9**

Compound	¹ H NMR δ , <i>J</i> (Hz)	¹³ C NMR δ	MS <i>m/z</i> (relative intensity, %)
9a	2.02-2.55 (4H, m), 3.57 (1H, dt, <i>J</i> =2.6, 11.6 Hz), 4.20-4.60 (2H, m), 4.83 (2H, s), 7.22-7.48 (5H, m).	35.0, 43.1, 69.1, 80.9, 108.8, 125.8, 127.5, 128.3, 142.6, 144.5.	174 (M ⁺ , 100), 144 (48), 129 (68), 107 (77), 91 (14), 77 (57), 67 (87).
9b	2.41 (2H, t, <i>J</i> =12.0 Hz), 2.61 (2H, d, <i>J</i> =12.0 Hz), 4.59 (2H, d, <i>J</i> =12.0 Hz), 4.96 (2H, s), 7.26-7.66 (10H, m).	43.0, 80.6, 109.3, 125.8, 127.4, 128.3, 142.5, 144.3.	250 (M ⁺ , 4), 144 (52), 29 (100), 104 (36), 77 (21).
9c	0.95 (3H, t, <i>J</i> =7.2 Hz), 1.17-1.78 (4H, m), 1.95-2.21 (2H, m), 2.26-2.36 (1H, m), 2.46-2.55 (1H, m), 3.40-3.53 (1H, m), 4.43 (1H, dd, <i>J</i> =11.4, 2.4 Hz), 4.84 (2H, s), 7.56 (2H, d, <i>J</i> =8.8 Hz), 8.21 (2H, d, <i>J</i> =8.8 Hz).	14.1, 18.7, 38.4, 40.3, 42.8, 78.7, 78.9, 109.4, 123.6, 126.4, 143.8, 147.1, 150.1.	261 (M ⁺ , 18), 218 (8), 189 (100), 172 (98), 143 (90), 128 (64), 95 (63), 81 (71).
9d	0.94 (3H, t, <i>J</i> =7.0 Hz), 1.26-1.78 (4H, m), 1.39 (3H, t, <i>J</i> =7.0 Hz), 1.97-2.52 (4H, m), 3.39-3.53 (1H, m), 4.30-4.42 (1H, m), 4.37 (3H, q, <i>J</i> =7.0 Hz), 4.82 (1H, s), 7.45 (2H, d, <i>J</i> =8.0 Hz), 8.02 (2H, d, <i>J</i> =8.0 Hz).	14.1, 14.3, 18.7, 38.4, 40.5, 42.8, 60.8, 78.6, 79.5, 108.9, 125.6, 129.4, 129.6, 144.5, 147.8, 166.5.	288 (M ⁺ , 7), 243 (13), 216 (32), 179 (42), 143 (100), 105 (10), 67 (11).
9e	2.15-2.48 (4H, m), 3.57 (1H, dt, <i>J</i> =2.8, 11.0 Hz), 3.90-4.03 (1H, m), 4.11-4.22 (1H, m), 4.80 (2H, s), 6.25 (1H, dd, <i>J</i> =16.0, 6.4 Hz), 6.64 (1H, d, <i>J</i> =16.0 Hz), 7.16-7.48 (5H, m).	35.0, 41.3, 68.6, 79.0, 108.9, 126.5, 127.6, 128.5, 129.8, 130.6, 136.8, 144.0.	200 (M ⁺ , 100), 155 (11), 131 (53), 115 (38), 91 (41), 67 (36).
9f	0.95 (3H, t, <i>J</i> =7.2 Hz), 1.20-1.76 (4H, m), 1.90-2.43 (4H, m), 3.30-3.48 (1H, m), 3.90-4.04 (1H, m), 4.78 (2H, s), 6.27 (1H, dd, <i>J</i> =16.0, 6.0 Hz), 6.63 (1H, d, <i>J</i> =16.0 Hz), 7.20-7.48 (5H, m).	14.1, 18.7, 38.5, 40.6, 41.1, 78.3, 78.8, 108.6, 126.5, 127.5, 128.5, 130.2, 130.3, 136.9, 144.6.	242 (M ⁺ , 57), 199 (7), 170 (25), 155 (23), 133 (100), 115 (48), 91 (22), 67 (13).
9g	1.64 (3H, s), 1.75 (3H, s), 1.87-2.22 (4H, m), 2.70 (1H, dd, <i>J</i> =13.5, 7.2 Hz), 3.06 (1H, dd, <i>J</i> =13.6, 5.8 Hz), 3.48-3.63 (1H, m), 3.94-4.08 (1H, m), 4.65 (1H, s), 4.70 (1H, s), 5.25 (1H, d, <i>J</i> =7.8 Hz), 7.16-7.34 (5H, m).	18.4, 25.7, 39.8, 40.9, 42.9, 75.7, 79.0, 108.6, 125.7, 126.1, 128.2, 129.4, 136.1, 138.4, 144.5.	242 (M ⁺ , 9), 227 (3), 151 (52), 129 (35), 91 (100), 67 (26).
9h	1.98-2.30 (2H, m), 2.43-2.64 (2H, m), 2.76 (1H, dd, <i>J</i> =13.5, 7.5 Hz), 3.14 (1H, dd, <i>J</i> =13.5, 5.5 Hz), 3.60-3.78 (1H, m), 4.43 (1H, dd, <i>J</i> =9.9, 4.0 Hz), 4.75 (1H, s), 4.80 (1H, s), 6.26-6.40 (2H, m), 7.12-7.43 (6H, m).	18.4, 25.7, 39.8, 40.9, 42.9, 75.7, 79.0, 108.6, 125.7, 126.1, 128.2, 129.4, 136.1, 138.4, 144.5.	254 (M ⁺ , 7), 163 (41), 143 (24), 135 (36), 91 (100).
9i	2.30-2.75 (4H, m), 4.47-4.63 (2H, m), 4.92 (2H, s), 6.36 (2H, s), 7.22-7.48 (6H, m).	38.6, 42.6, 74.1, 80.6, 106.7, 109.8, 110.1, 126.0, 127.6, 128.3, 141.9, 142.1, 143.6, 154.4.	256 (M ⁺ , 10), 192 (38), 129 (12), 104 (100), 77 (16).
9j	0.90 (3H, t, <i>J</i> =7.0 Hz), 1.21-1.70 (4H, m), 1.85-2.07 (2H, m), 2.13-2.27 (2H, m), 2.70 (1H, dd, <i>J</i> =13.8, 6.4 Hz), 2.98 (1H, dd, <i>J</i> =13.8, 6.4 Hz), 3.17-3.32 (1H, m), 3.40-3.55 (1H, m), 4.63-4.70 (2H, m), 7.17-7.36 (5H, m).	14.0, 18.7, 38.5, 40.4, 40.8, 42.8, 78.2, 79.1, 108.3, 126.1, 128.1, 129.4, 138.7, 145.0.	229 (M ⁺ -1, trace), 187 (trace), 139 (82), 91 (100).

cedure for the synthesis of 2-methyl-4-methylene-6-phenyl-tetrahydropyran (**6a**) is illustrative. To a solution of the allylsilane-acetal **5a** (343 mg, 1.12 mmol) in dry CH₂Cl₂ (10 mL) at -78 °C was added 0.29 mL (330 mg, 2.4 mmol) of BF₃·OEt₂. The reaction mixture was stirred at -78 °C for 0.5 h and quenched with triethylamine (0.5 mL) followed by saturated aqueous NaHCO₃ at room temperature. The organic phase was separated and aqueous layer was extracted with CH₂Cl₂. The organic layers were combined, dried with Na₂SO₄, concentrated *in vacuo*, and subjected to flash chromatography (silica gel, hexane:ether=10:1) to give 124 mg (59%) of **6a**.

Preparation of 1-Methoxyalkyl Ethers of Hydroxy Allylsilanes 8. A typical procedure for the synthesis of **8b** is illustrative. To a stirring solution of hydroxy allylsilane **3** (R=Ph) (164 mg, 0.7 mmol), dry CH₂Cl₂ (4 mL), and *i*-Pr₂NEt (0.35 mL, 2.0 mmol), at -5 °C was added freshly prepared¹⁰ α -methoxybenzyl chloride (156 mg, 1.0

mmol), and the reaction mixture was maintained at 0 °C for 1 h and at 23 °C for 1 h. The reaction mixture was concentrated and the residue was purified by flash chromatography (silica gel, hexane:ether=15:1), which partially separated the allylsilane-acetal diastereomers **8b**: combined yield, 176 mg (71%).

Preparation of 2,6-Disubstituted 4-Methylenetetrahydropyrans 9 by BF₃·OEt₂ Promoted Cyclization of Allylsilane-Acetals 8. A typical procedure for the synthesis of 2,6-diphenyl-4-methylenetetrahydropyran (**9b**) is illustrative. To a solution of **8b** (288 mg, 0.81 mmol) in dry CH₂Cl₂ (8 mL) at -78 °C was added 0.22 mL (250 mg, 1.80 mmol) of BF₃·OEt₂. The reaction mixture was stirred at -78 °C for 0.5 h and then quenched with triethylamine. The resulting solution was stirred for 10 min, and then saturated aqueous NaHCO₃ was added. The aqueous phase was extracted with CH₂Cl₂. The dichloromethane extracts were dried with K₂CO₃, concentrated *in vacuo*, and

subjected to flash chromatography (silica gel, hexane : ether=15 : 1) to give 184 mg (92%) of **9b**.

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References

- Perron, F.; Albizati, K. M. *Chem. Rev.* **1989**, *89*, 1617.
- Biovin, T. L. B. *Tetrahedron* **1987**, *43*, 3309.
- (a) Searle, P. A.; Molinski, T. F.; Brzezinski, L. J.; Leahy, J. W. *J. Am. Chem. Soc.* **1996**, *118*, 9422. (b) Molinski, T. F. *Tetrahedron Lett.* **1996**, *37*, 7879. (c) Lee, C. S.; Forsyth, C. J. *Tetrahedron Lett.* **1996**, *37*, 6449. (d) Searle, P. A.; Molinski, T. F. *J. Am. Chem. Soc.* **1995**, *117*, 8126.
- Tanaka, J.; Higa, T. *Tetrahedron Lett.* **1996**, *37*, 5535.
- (a) Schinzer, D. *Synthesis* **1988**, 263. (b) Fleming, I.; Dunogues, J.; Smithers, R. *Org. React.* **1989**, *37*, 57.
- (a) Marko, I. E.; Bayston, D. J. *Tetrahedron* **1994**, *50*, 7441, and references there in. (b) 2,6-Dialkyl-3-hydroxy-4-methylenetetrahydropyrans were also prepared from the ISMS reaction of 2-(trimethylsilyloxymethyl)allyltrimethylsilane with aliphatic aldehydes, however, 2,6-diaryl derivatives could not be obtained under the same reaction conditions: Marko, I. E.; Bayston, D. J. *Tetrahedron Lett.* **1993**, *34*, 6595.
- 2-Stannyl-3-silylpropene: (a) Kang, K. -T.; Kim, S. S.; Lee, J. C. *Tetrahedron Lett.* **1991**, *32*, 4341. (b) Kang, K. -T.; Kim, S. S.; Lee, J. C.; U, J. S. *Tetrahedron Lett.* **1992**, *33*, 3495. (c) 3-Stannyl-2-(silylmethyl)propene: Kang, K. -T.; U, J. S.; Park, D. K.; Kim, J. K.; Kim, W. *J. Bull. Korean Chem. Soc.* **1995**, *16*, 464.
- Bismetallic reagent **1** is considerably more reactive than simple allylstannanes due to the extra activation (β -effect) provided by the allylic silyl substituent. Kang, K.-T.; Sung, T. M.; Kim, J. K.; Kwon, Y. M. *Synth. Commun.* **1997**, *27*, 1173.
- Schneider, A.; Sequin, U. *Tetrahedron* **1985**, *41*, 949.
- Goff, D. A.; Harris III, R. N.; Bottaro, J. C.; Bedford, C. D. *J. Org. Chem.* **1986**, *51*, 4711.

Study of Equivalent Retention among Different Polymer-Solvent Systems in Thermal Field-Flow Fractionation

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An equivalent retention has been experimentally observed in thermal field-flow fractionation (ThFFF) for different polymer-solvent systems. It is shown that iso-retention between two sets of polymer-solvent systems can be obtained by adjusting the temperature difference (ΔT) according to the difference in the ratio of ordinary diffusion coefficient to thermal diffusion coefficient. This method uses a compensation of field strength (ΔT) in ThFFF at a fixed condition of cold wall temperature. It is applied for the calculation of molecular weight of polymers based on a calibration run of different standards obtained at an adjusted ΔT . The polymer standards used in this study are polystyrene (PS), polymethylmethacrylate (PMMA), and polytetrahydrofuran (PTHF). Three carrier solvents, tetrahydrofuran (THF), methylethylketone (MEK) and ethylacetate (EtAc) were employed. Though the accuracy in the calculation of molecular weight is dependent on the difference in the slope of $\log \lambda$ vs. $\log M$ which is related to Mark-Houwink constant a , it shows reasonable agreement within about 6% of relative error in molecular weight calculation for the polymer-solvent systems having similar a value.

Introduction

Thermal field-flow fractionation (ThFFF) is useful for the separation and molecular weight characterization of polymers.¹⁻⁶ It utilizes a temperature gradient as an external field to induce thermal diffusion of polymers and this allows polymers to be separated by the differences in their ordinary diffusion coefficients.³ Retention of polymers in ther-

mal FFF is controlled by an applied field strength given by temperature gradient which is also adjustable. Separation in thermal FFF like other FFF techniques is carried out in an open channel which is treated as unique advantage for the study of polymers since the possibility of sample adsorption or degradation can be minimized.⁶

For the calculation of molecular weight and molecular weight distribution (MWD) of polymers in thermal FFF, a calibration is required with narrow standards having an identical chemical composition to analyte to be charac-

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