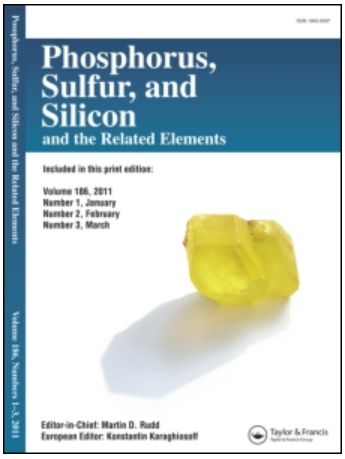


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# ASYMMETRIC ALLYLATION OF ALDEHYDES WITH ETHERIFICATION BY ALLYLTRIMETHYLSILANE PROMOTED BY CHIRAL ALCOHOL MODIFIED ALUMINUM REAGENTS

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# ASYMMETRIC ALLYLATION OF ALDEHYDES WITH ETHERIFICATION BY ALLYLTRIMETHYLSILANE PROMOTED BY CHIRAL ALCOHOL MODIFIED ALUMINUM REAGENTS

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Leiws acid $AlCl_3$ was modified by chiral alcohols, forming chiral aluminum reagents (*ROH/$AlCl_3$). *ROH/$AlCl_3$was used to promote asymmetric allylation of aldehydes with etherification by allyltrimethylsilane, giving the chiral homoallylic ethers in good yields and good to excellent de (51–93%). The monoalkoxy aluminum (*RO)$AlCl_2$ generated *in situ* was determined as an active and stereogenic species in one pot allylation reaction of aldehyde. The turnover of diastereoselectivity with the ratio of menthol to $AlCl_3$ was observed. Two different hemiacetal intermediates were suggested.

*Keywords:* allyltrimethylsilane; asymmetric allylation; homoallylic ether; chiral alcohol; chirally modified aluminum reagent

## INTRODUCTION

Among the Lewis acid promoted C-C bond forming reactions, the allylation of carbonyl compounds with allylsilanes under Lewis acid conditions, first described by Sakurai and Hosomi,[1] is one of the most important reactions in organic synthesis (Scheme 1).[2] It is worthy to note that although high enantioselectivities of the allylation reactions have been achieved *via* the reactions of allylic boranes and stannanes with carbonyl compounds, the research on the enantioselective Sakurai reaction has not had a signifi-

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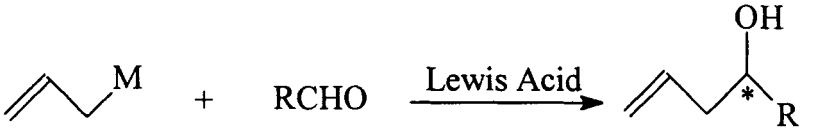
cant breakthrough.[3] Recently, the possibility of using chiral Lewis acid to promote and catalyze asymmetric Sakurai reaction has attracted considerable attention, but only few successful examples of chiral titanium and borane Lewis acid catalyzed asymmetric Sakurai reaction were reported.[4]




M: Sn, Si, B .

SCHEME 1



It is well known that the use of chiral Lewis acid plays an important role in performing enantioselective C-C bond formation reactions.[5] As a first example of chiral aluminum reagent catalyzed asymmetric reaction, Koga[6] described the application of menthoxy-aluminum dichloride in asymmetric Diels-Alder reaction with enantioselective excess (ee) of 72%. The chiral aluminum reagents derived from chiral 1,1-binaphthol were also employed in asymmetric ene reaction[7] and Claisen rearrangement reaction[8] with high enantioselectivity. More recently, Fujisawa[9] reported that the use of a chiral Lewis acid prepared from diethylaluminum chloride and chiral diol, derived from (+)-camphor, in the reaction of ketene silyl acetal with aldehyde gave β-hydroxy ester in high ee.

On the other hand, on the basis of their accessibility and the ease in manipulating functionalities, chirally modified Lewis acids generated *in situ* in the reaction system were widely adopted. Such "one pot" procedure provided a convenient and effective method in asymmetric synthesis.

All this encouraged us to apply the chiral aluminum reagents generated *in situ* by mixing chiral alcohols with $AlCl_3$ in the asymmetric allylation reaction of aldehydes with allyltrimethylsilane in "one pot", in order to improve the stereoselectivity of the reactions of aldehyde with allylsilane.

## EXPERIMENTAL

All the chemicals used were reagent grade. Solvents were dried prior to use. Aluminum trichloride was purified by vacuum sublimation. $^1H$ and

$^{13}C$ NMR spectra were recoded by Varian XL-200 spectrometer. IR spectra were taken with a Perkin-Elmer 782 and Carl Zeiss Specord 75R spectrophotometers. Mass spectra were taken at 60eV with a AEI MS-50/PS-30 instrument. Elemental analyses were performed on a Calro 1102 Element Analysis instrument. Optical rotation was taken with Perkin-Elmer 241 Polameter.

## One pot synthesis of homoallylic ethers

### *Typical procedure*

To a suspension of $AlCl_3$ (133mg, 1mmol) in $CH_2Cl_2$ (3mL) was added by syringe the solution of an alcohol (1mmol) in $CH_2Cl_2$ (3mL) at the given temperature (room temperature for **1c**, while −15°C for other alcohols), followed by stirring for 15min at the same temperature. The mixture was cooled to given temperature (reaction temperature on Table I). Then, a solution of aldehyde (1mmol) in $CH_2Cl_2$ (3mL) and allyltrimethylsilane **2** (1.1mmol) were added stepwise by syringe to the mixture, followed by stirring at the same temperature for 20 h. The reaction was quenched by water (10mL). The mixture was extracted by ethyl ether (3 × 10mL). The combined organic phase was dried over $MgSO_4$ and concentrated by rotary evaporator. The residue was purified by flash chromatography on silica gel using pet. ether/ethyl acetate as eluent to give homoallylic ether. With the same procedure, homoallylic ethers **3**[10]-**13** were synthesized. *4-Benzyloxy-1-nonene* **4.** A colorless liquid. IR (film, $cm^{-1}$): 1635(C=C), 1450, 1350, 1200(C-O). MS *(m/z)*: 191($M^+$-$C_3H_5$, 4). Found: C% 82.27; H% 10.29; Calcd. for $C_{16}H_{24}O$: C% 82.70; H% 10.41; $^1H$-NMR (200MHz, $CDCl_3$, TMS): 0.88(3H, t, *J* 6.6), 1.27–1.52(8H, m), 2.31(2H, m), 3.41(1H, m), 4.46 and 4.56(2H, AA', *J* 11.7), 5.02(2H, m), 5.82(1H, m), 7.31(5H, m); $^{13}C$-NMR (50.31MHz, $CDCl_3$) 14.00, 22.59, 24.96, 31.88, 33.70, 38.25(3-C), 70.79(C-O), 78.45(C-O), 116.69(1-C), 127.31, 127.61, 128.18, 135.01(2-C), 138.90. *4-(1'R, 2'S, 5'R)-(-)-Menthoxy-1-nonene* **5a** and **5b**. The colorless liquid. **5a** and **5b:** IR (film, $cm^{-1}$): 1640(C=C), 1450, 1385, 1080(C-O). MS *(m/z):* 239($M^+$-$C_3H_5$, 2.8). Found: C% 81.27, H% 13.14; Calcd: for $C_{19}H_{36}O$: C% 81.36, H% 12.93. $^1H$-NMR (200MHz; $CDCl_3$) : 0.71–1.38(27H, m), 1.95–2.24(4H, m ), 3.05(1H, dt, *J* 4.2, 10.4), 3.35(1H, m), 4.97–5.05 (2H, m), 5.80(1H, m); **5a** $^{13}C$-NMR (50.31MHz, $CDCl_3$) : 14.11, 15.96, 21.38, 22.44, 22.67,

22.97, 24.67, 25.32, 30.75, 31.60, 32.00, 34.52, 38.57, 41.52, 48.51(3-C), 75.88(C-O), 76.58(C-O), 116.68(1-C), 135.18(2-C); **5b** $^{13}$C-NMR (50.31 MHz, $CDCl_3$): 13.92, 15.87, 21.26, 22.20, 22.53, 22.86, 24.65, 25.84, 29.57, 31.24, 31.95, 34.40, 39.32, 42.02, 48.66(3-C), 76.66(C-O), 76.88(C-O), 116.09(1-C), 135.62(2-C). *4-(1'R, 2'S, 5'R)-(-)-Menthoxy-1-undecene* **6**. A colorless liquid. IR (film, $cm^{-1}$): 1635(C=C), 1450, 1245, 1100(C-O). MS *(m/z):* 267($M^+$-$C_3H_5$, 1.1). Found: C% 81.31, H% 13.04; Calcd. for $C_{21}H_{40}O$ : C% 81.74, H% 13.06%. $^1$H-NMR (200MHz, $CDCl_3$): 0.71–1.42(31H, m), 2.17–2.24(4H, m), 3.04 (1H, dt, *J* 4.2, 10.4), 3.35(1H, m), 4.97–5.05(2H, m), 5.80(1H, m); $^{13}$C-NMR (50.31MHz, $CDCl_3$) 14.04, 15.92, 21.32, 22.38, 22.62, 22.96, 24.65, 25.53, 29.29, 29.71, 31.58, 31.81, 34.52, 38.53, 41.49, 42.69, (48.47, 48.74, 3-C), 76.67(C-O), 77.64(C-O), (116.15, 116.59, 1-C), (135.11, 135.65, 2-C). The $^{13}$C signals in paretheses are from two diastereoisomers (the same below). *4-(1'R, 2'S, 5'R)-(-)-Menthoxy-5-methyl-1-hexene* **7**. A colorless liquid. IR (film, $cm^{-1}$): 1635(C=C), 1380, 1100(C-O). MS *(m/z):* 211($M^+$-$C_3H_5$, 3). Found: C% 80.83, H% 12.47; Calcd. for $C_{17}H_{32}O$ : C% 80.88, H% 12.78; $^1$H-NMR (200MHz $CDCl_3$) : 0.71–1.63(23H, m), 1.95–2.25(4H, m), 3.05 (1H, dt, *J* 3.1, 10.4), 3.13(1H, m), 4.98–5.07(2H, m), 5.79(1H, m), $^{13}$C-NMR (50.31MHz, $CDCl_3$) 18.78, 21.38, 22.46, 23.13, 24.71, 30.53, 31.60, 34.62, 35.18, 41.22, (48.32, 48.70, 3-C), 75.76(C-O), 79.74(C-O), (116.24, 116.82, 1-C), (135.50, 135.91, 2-C). *4-(1'R, 2'S, 5'R)-(-)-Menthoxy-4-phenyl-1-butene* **8**. A colorless liquid. IR (film, $cm^{-1}$): 1640(C=C), 1600, 1450, 1365, 1080(C-O). MS (EI, 70ev) *m/z* 245(M+-$C_3H_5$, 9). Found: C% 83.39, H% 10.53; Calcd. for $C_{20}H_{30}O$: C% 83.86, H% 10.55. $^1$H-NMR (200MHz $CDCl_3$): 0.79–1.57(16H, m), 2.15–2.61(4H, m), 3.13 (1H, dt, *J* 4.2, 10.4), 4.30(1H, m), 4.92–4.96(2H, m), 5.65(1H, m), 7.23–7.29(5H, m); $^{13}$C-NMR (50.31MHz, $CDCl_3$): 16.11, 21.29, 22.23, 22.99, 25.03, 31.56, 34.39, 42.62, (48.33, 49.12, 3-C), 79.00(C-O), 81.57(C-O), (116.76, 116.41, 2-C), 126.61, 127.08, 127.36, 128.00, (134.79, 135.20, 1-C), 142.27. *4-(1R')-(-)-Myrtenoxyl-4-undecene* **9**. A colorless liquid. IR (film, $cm^{-1}$): 1635(C=C), 1460, 1070(C-O). MS *(m/z):* 304($M^+$, 1). Found: C% 82.65, H% 11.90, Calcd. for $C_{21}H_{36}O$ : C% 82.83, H% 11.92. $^1$H-NMR (200MHz $CDCl_3$) : 0.83–1.62(m, 26H), 2.11–2.39(m, 5H), 3.31(m, 1H), 3.81–3.89(m, 2H), 4.98–5.11(m, 2H), 5.45(m, 1H), 5.80(m, 1H), $^{13}$C-NMR (50.31MHz, $CDCl_3$) : 13.90, 20.85, 22.50, 24.80, 26.05, 31.08, 31.33, 31.57, 31.83, 33.61, 37.86, 40.71, 42.54, 43.21, 71.50(C-O), 77.50(C-O), (116.42, 116.31, 2-C), (118.95, 119.11, 3'-C),

(135.12, 135.01, 1-C), 145.78(2'-C). *4-[(2'-Phenyl-2'-methoxy)ethoxy]-1-nonene* **10**. A colorless liquid. IR (film, $cm^{-1}$): 1640(C=C), 1100(C-O). MS *(m/z)*: 235($M^+$-$C_3H_5$, 4), 155(11), 135(60), 121(100), 103(11). Found: C% 78.23, H% 10.19; Calcd. for $C_{18}H_{28}O_2$ : C% 78.21, H% 10.19. $^1$H-NMR (200MHz $CDCl_3$): 0.81–1.43(m, 12H), 2.20–2.23(m, 2H), 3.26(s, 3H), 3.46–3.67(m, 3H), 4.30(m, 1H), 4.98–5.07(m, 2H), 5.71(m, 1H), 7.23–7.30(m, 5H); $^{13}$C-NMR (50.31MHz, $CDCl_3$): 14.03, 22.59, 24.93, 31.89, 33.81, 38.36, 56.93(OMe), 73.87(1'-C), (80.04, 80.10, 4-C), (83.41, 83.60, 2'-C), (116.55, 116.87, 1-C), 126.87, 127.72, 128.24, (135.04, 135.09, 2-C), 139.34. *4-[(2'-Phenyl-2'-methoxy)-ethoxy]-1-undecene* **11**. A colorless liquid. IR (film, $cm^{-1}$): 3060, 2860, 1630(C=C), 1450, 1200, 1090(C-O). MS *(m/z)*: 263($M^+$-$C_3H_5$, 2). Found: C% 78.91; H% 10.73; Calcd, for $C_{20}H_{32}O_2$: C% 78.89, H, 10.91. $^1$H-NMR (200MHz $CDCl_3$): 0.82–1.42(m, 16H), 2.20–2.25(m, 2H), 3.31(s, 3H), 3.46–3.68(m, 3H), 4.30(m, 1H), 4.97–5.07(m, 2H), 5.69(m, 1H), 7.23–7.34(m, 5H); $^{13}$C-NMR (50.31MHz, $CDCl_3$): 14.09, 22.65, 25.39, 29.26, 29.67, 31.81, 33.88, 38.39, 56.99(OMe), 73.87(1'-C), (80.11, 80.16, 4-C), (83.43, 83.61, 2'-C), 116.56(1-C), 126.95, 127.76, 128.28, (135.12, 135.17, 2-C), 139.00. *4-[(2'-Phenyl-2'-methoxy)ethoxy]-5-methyl-1-hexene* **12**. A colorless liquid. IR (film, $cm^{-1}$ ): 2960, 1635(C=C), 1490, 1120(C-O). MS *(m/z)*: 207($M^+$-$C_3H_5$, 5). Found: C% 77.59, H% 9.61; Calcd. for $C_{16}H_{24}O_2$ : C% 77.38, H% 9.74. $^1$H-NMR (200MHz $CDCl_3$): 0.85–0.91(6H, m), 1.72(1H, m), 2.18(2H, m), 3.05(1H, m), 3.27(3H, s), 3.51–3.62(2H, m), 4.25(1H, dd, *J* 4.2 7.3), 4.99–5.07(2H, m), 5.76(1H, m), 7.25–7.30(5H, m); $^{13}$C-NMR (50.31MHz, $CDCl_3$): 18.50, 33.06, 38.66, 56.97(OMe), 74.95(1'-C), 81.54(4-C), 83.64(2'-C), 116.24(1-C), (126.89, 126.94, Ph), 127.70, 128.25, (135.63, 136.00, 2-C), 139.55. *4-[(2'-Phenyl-2'-methoxy)-ethoxy]-4-cyclohexyl-1-butene* **13**. A colorless liquid. IR (film, $cm^{-1}$): 2840, 1635(C=C), 1490, 1120(C-O). MS (*m/z*): 247($M^+$-$C_3H_5$, 8). Found: C, 79.35; H, 9.83; Calc. for $C_{19}H_{28}O_2$: C, 79.12; H, 9.78%. $^1$H-NMR (200MHz $CDCl_3$): 0.85–1.67(16H, m), 2.20–2.23(2H, m), 3.05(1H, m), 3.27(3H, s), 3.51–3.61(3H, m), 4.25(1H, dd, *J* 4.2, 7.3), 4.95–5.04(2H, m), 5.75(1H, m), 7.20–7.32(5H, m); $^{13}$C-NMR (50.31MHz, $CDCl_3$): 24.94, 26.58, 28.79, 35.42, 41.16, 56.94(OMe), 75.04(1'-C), (83.43, 83.65, 4-C), 84.75(2'-C), 116.24(1-C), 126.88, 127.68, 128.24, 135.62(2-C), 139.60.

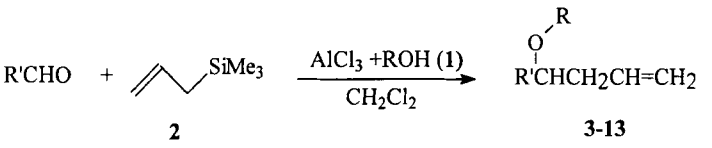
### Formation of 1-nonen-4-ol 21[11]

To a suspension of **10** (138mg, 0.5mmol) and potassium iodide (166mg, 1mmol) in acetonitril (2mL) was added chlorotrimethyl silane (0.12mL, 1mmol) under nitrogen atmosphere, followed by reflexing for 8 h. The cooling mixture was worked up with brine (10mL) and extracted by ethyl ether (3 × 8mL). The combined organic phase was washed by saturated aqueous solution of $Na_2S_2O_3$ and dried over $Na_2SO_4$. The solvent was removed by rotary evaporator and the residue was separated by flash chromatography on silica using pet. ether/ethyl acetal as eluent to give a colorless liquid **21**; $[\alpha]_D$ : +6.4 (c, 0.5, $CHCl_3$); $^1$H-NMR (200MHz, $CDCl_3$): 0.91–1.68(11H, m), 2.05–2.38(2H, m), 3.59–3.71(1H, m), 5.10–5.18(2H, m), 5.85(1H, m).

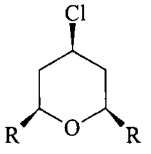


## RESULTS AND DISCUSSION

In general, the allylation of aldehydes with allylsilane in the presence of $AlCl_3$ gave homoallylic alcohols or 2,4,6-trisubstituted-tetrahydropyran, depending on the reaction condition.[12] Meanwhile, if chiral allylsilanes were used in $AlCl_3$ promoted asymmetric allylation of aldehydes, the low to moderate enantioselectivities of the reactions were observed.[12] However, it was found that if the aluminum Lewis acids generated *in situ* by mixing the alcohols (**1a-b**) with $AlCl_3$ were employed in the one pot allylation reaction of aldehyde by allyltrimethylsilane **2**, homoallylic ethers (**3–4**) would be obtained instead of homoallylic alcohol. When $AlCl_3$ was chirally modified by chiral alcohols (**1c-e**), asymmetric allylation of aldehydes with etherification proceeded, giving chiral homoallylic ethers (**5–13**) (Scheme 2). These results are similar to Seebach's observation[13] that dialkoxydichlorotitanium reagents, formed by $TiCl_4$ and alcohols, behave quite differently from $TiCl_4$ in the reaction of aldehydes with **2**, forming the homoallylic ether with high diastereomeric excess (de). Moreover, it was also reported[14] that starting from chiral alcohols, the homoallylic ethers were synthesized through the silyl modified Sakurai (SMS) reaction. All of these demonstrated that in the presence of some alcohol modified Lewis acid, the allylation reactions of aldehyde with allyltrimethylsilane have the different feature from conventional Sakurai reaction.

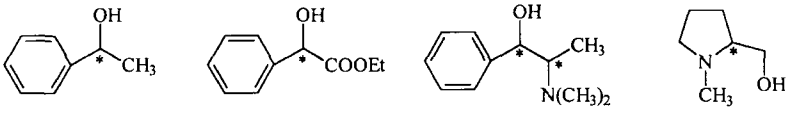



2 3-13




14

ROH: 1a $CH_3CH_2OH$
1b $PhCH_2OH$
1c
1d $CH_2OH$
1e OMe OH Ph




1f 1g 1h 1i

SCHEME 2

The temperature for modification of $AlCl_3$ by alcohols strongly influences the yields and the diastereoselectivities of the subsequent allylation reactions of the aldehydes with **2**. Due to (-)-menthol (**1c**) bearing bulky group, the reaction of **1c** with $AlCl_3$ (**1c** :$AlCl_3$=1:1) must be carried out at room temperature for 15 min to form chirally modified aluminum reagent (**1c**/$AlCl_3$). In comparison with $^1H$ and $^{13}C$ NMR signals of **1c** at $C_1$ ($\delta_H$=3.39 and $\delta_C$=76.6 ppm), the corresponding NMR signals of the **1c**/$AlCl_3$ shifted to $\delta_H$=4.42 and $\delta_C$=84.6 ppm, which verified the formation of the modified aluminum reagent. The **1c**/$AlCl_3$ was used as a promoter in the subsequent one pot allylation reaction of aldehydes with **2** to give chiral homoallylic ethers. However, if modification of $AlCl_3$ performed with primary alcohols, *e.g.* **1a-b** and **1d-e**, at room temperature, a complicated mixture was obtained. Obviously, lower reaction temperature (-15°C) has to be adopted to avoid side reaction.

TABLE I Allylation of aldehydes with **2** promoted by R*OH/$AlCl_3$

| *Entry* | *Alcohol R* | *Aldehyde R'* | *Raction Temp. (°C)* | *Product* | | *R'CHO/$AlCl_3$/ROH* | *Yield (%)* | *De (%)* |
|---|---|---|---|---|---|---|---|---|
| | | | | *R* | *R'* | | | |
| 1 | **1a** | $C_5H_{11}$ | -25 | **3**, $CH_3$ $CH_2$ | $C_5H_{11}$ | 1:0.5:1 | 55 | |
| 2 | **1b** | $C_5H_{11}$ | -25 | **4**, $PhCH_2$ | $C_5H_{11}$ | 1:0.5:1 | 74 | |
| 3 | **1c** | $C_5H_{11}$ | -78 | **5**, Menthyl | $C_5H_{11}$ | 1:1:1 | 70 | 93 |
| 4 | | $C_7H_{15}$ | -25 | **5**, | | 1:0.5:1 | 54 | 51 |
| 5 | | $C_7H_{15}$ | -78 | **6**, | $C_7H_{15}$ | 1:1:1 | 41 | 71 |
| 6 | | $C_7H_{15}$ | -25 | **6**, | | 1:0.5:1 | 74 | 54 |
| 7 | | $(CH_3)_2CH$ | -78 | **7**, | $(CH_3)_2CH$ | 1:1:1 | 68 | 78 |
| 8 | | $(CH_3)_2CH$ | -25 | **7**, | | 1:0.5:1 | 61 | 77 |
| 9 | | $C_6H_5$ | -78 | **8**, | $C_6H_5$ | 1:1:1 | 73 | 20 |
| 10 | **1d** | $C_7H_{15}$ | -78 | **9**, Myrtenyl | $C_7H_{15}$ | 1:1:1 | 66 | 20 |
| 11 | **1e** | $C_5H_{11}$ | -25 | **10**, α:-methoxy phenylethyl | $C_5H_{11}$ | 1:1:1 | 58 | 74 |
| 12 | | $C_7H_{15}$ | -25 | **11**, | $C_7H_{15}$ | 1:1:1 | 54 | 70 |
| 13 | | $(CH_3)_2CH$ | -25 | **12**, | $(CH_3)_2CH$ | 1:1:1 | 59 | 75 |
| 14 | | $C_6H_{11}$ | -25 | **13**, | $C_6H_{11}$ | 1:1:1 | 74 | 65 |

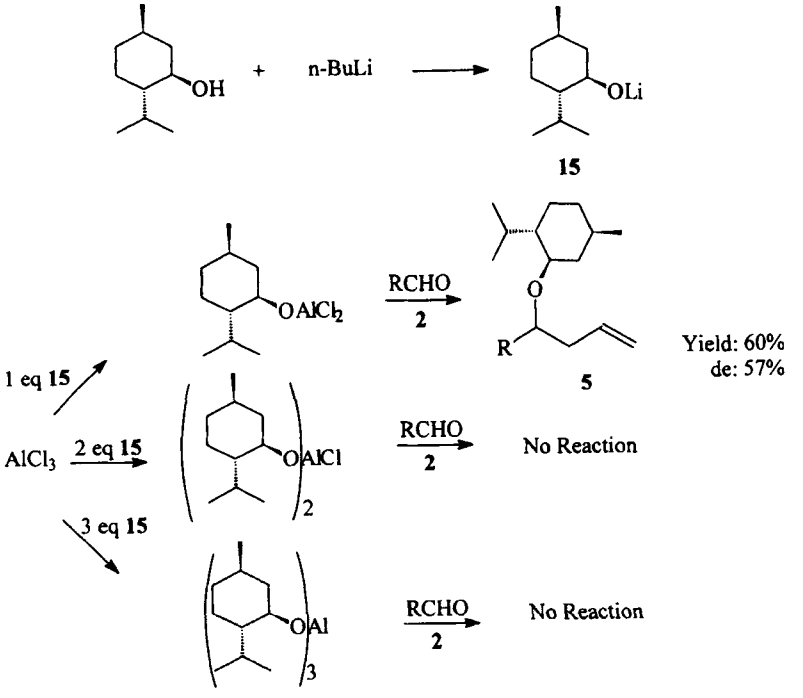
Two diastereoisomers (**5a** and **5b**) were isolated from the product, homoallylic ether **5**, in the allylation reaction of hexanal with **2** promoted by **1c**/$AlCl_3$ (Table I, entry 3). The $^{13}C$ NMR signals of double bond of **5a** and **5b** were found to be at 116.6, 135.2 and 116.1, 135.6 ppm respectively. From the ratio of the two sets of $^{13}C$ NMR signals, diastereomeric excess (de) of the homoallylic ether **5** can be determined. Based on this method, the des of all products were determined by the ratio of the corresponding diastereomeric $^{13}C$ NMR signals. The experimental results are listed on Table I.

It is shown on Table I that in the presence of **1c**/$AlCl_3$, the allylation reactions of aliphatic aldehydes afford the homoallylic ethers in good yields and good to excellent de (51–93%). The yields of the homoallylic ethers slightly depend on the reaction temperature *(cf* entry 3 and 5 *vs* entry 4 and 6), while the des of homoallylic ethers formed at –25°C (51–54%, entry 4 and 6) are lower than that of the homoallylic ethers formed at –78°C (71–93%, entry 3 and 5). However, using isobutyraldehyde bearing bulky group as a substrate, the high de also was obtained, even at higher reaction temperature (-25°C, 77% de, entry 8). (+)-(S)-α-Methoxy-phenylethanol (**1e**) modified aluminum reagent (**1e**/$AlCl_3$) exhibits less reactivity, so higher reaction temperature (-25°C) must be taken. Moreover, the compounds 2,6-dialkyl-4-chloro-tetrahydropyran (**14**) was separated in yields of 10–15%. Although the yields of homoallylic ethers (**10–13**) decreased slightly, the de of the **10–13** still remained relatively higher level (65–75%), even at higher reaction temperature (-25°C). (-)-Myrtenol **1d**/$AlCl_3$ is not good for asymmetric induction. Using aromatic aldehyde as a substrate, the low de was observed (entry 9).

Meanwhile, the molecular structure of chiral alcohol for the modification of $AlCl_3$ is essential to the subsequent allylation reaction. Besides chiral alcohols **1c-e**, (+)-α-phenylethanol (**1f**), methyl (S)-(+)-mandelate (**1g**), N,N-dimethyl-2-amino-phenylpropan-1-ol (**1h**) and (S)-(-)-N-methyl-2-pyrrolidinemethanol (**1i**) were chosen to examine the reactivity of the formed chiral alcohol modified aluminum reagents. Unfortunately, for all of chiral alcohols (**1f-i**) used, after mixing with $AlCl_3$ and subsequent allylation, the starting materials, chiral alcohols and aldehydes, were recovered. It is suggested that the carbonyl and amino groups in **1f-i** would be able to coordinate strongly with aluminum atom and make the empty orbit of the aluminum atom fully occupied by ligands, leading to the lose of the reactivity in allylation reaction of aldehyde. In contrast, the methoxy

group in **1e** possesses relatively weaker ability to coordinate with aluminum atom, therefore, **1e**/$AlCl_3$ still have relatively weaker reactivity and the allylation reaction must be performed at −25°C.

When $AlCl_3$ was added to a solution of the alcohol (ROH) in $CH_2Cl_2$, a mixture of $(RO)AlCl_2$, $(RO)_2AlCl$ and $(RO)_3Al$ was supposed to be formed. It is interesting which is the active species in subsequent allylation reaction. The treatment of $AlCl_3$ with various amounts of lithium menthoxide **15** gave $(RO)AlCl_2$, $(RO)_2AlCl$ and $(RO)_3Al$ respectively (Scheme 3). Among these three species, only $(RO)AlCl_2$ shows the reactivity in promoting the allylation of hexanal with **2** (yield 60%, de 57%), which is consistent with the result of **1c**/$AlCl_3$ promoted allylation of hexanal (entry 4). It indicated that $(RO)AlCl_2$ is solely an active species in the chiral menthol modified aluminum reagent **1c**/$AlCl_3$.




SCHEME 3

By using **1c**/$AlCl_3$, an interesting relationship between the diastereoselectivity and the amounts of $AlCl_3$ used was observed. With reducing the

ratio of $AlCl_3$ to **1c**, the de of homoallylic ether **5** decreased (Table II). In particular, when the percentage of $AlCl_3$ to **1c** was less than 30%, the proportion of **5a** to **5b** was reversed. The turnover of de can be expressed more clearly on Fig 1, which is a plot of percentage of $AlCl_3$ to **1c** (%) *vs* de of homoallylic ether **5** produced. As regards the mechanism of the formation of homoallylic ethers, Seebach[12] suggested that the first step is the addition of an alkoxy group to the aldehyde, and then the resulting hemiacetal undergoes substitution of the former aldehyde oxygen by the allyl group. Although the reason for the turnover of the diastereoselectivity in the allylation of aldehydes with etherification by allyltrimethylsilane, promoted by **1c**/$AlCl_3$, is not very clear, on the basis of Seebach's suggestion and the results on the active species discussed above, the different intermediates involved in the formation of homoallylic ethers can be assumed. When the percentage of $AlCl_3$ to **1c** is more than 30%, the formed active species $MenOAlCl_2$ **16** would coordinate to aldehyde carbonyl group, then forming a intermediate, hemiacetal **17**. However, if the percentage of $AlCl_3$ to menthol is less than 30%, the intermediate with two menthoxy groups, hemiacetal **18**, would be formed dominantly due to the presence of excessive menthol. The attack directions of allyl group of allyltrimethylsilane to monomenthoxy hemiacetal **17** and dimenthoxy hemiacetal **18** would be different, leading to the turnover of the diastereoselectivity.



TABLE II The Change of **5a/5b** with $AlCl_3$ to **1c**

| *Entry*[*] | *$AlCl_3$ to 1c (%)* | *Yield (%)* | *5a:5b* |
|---|---|---|---|
| 1 | 100 | 70 | 96:4 |
| 2 | 50 | 54 | 75:25 |
| 3 | 30 | 49 | 59:41 |
| 4 | 25 | 43 | 32:68 |
| 5 | 20 | 30 | 29:71 |

[*] Reaction temperature; -25°C, execpt entry 1 (at -78°C)

The treatment of **10** with $Me_3SiI$ prepared *in situ* by KI and $Me_3SiCl$ gave a homoallylic alcohol **19** ($[\alpha]_D$:+6.4, c, 0.5, $CHCl_3$) (Scheme 5). In comparison with reported value $[\alpha]_D$ :+8.3[13], the absolute configuration of

newly formed chiral carbon (C-4) in **10** was deduced to be *R* with 77% ee, which is consistent with the magnitude of the de of the **10** (74%, entry 11) determined by diastereomeric $^{13}C$ NMR signals. On the other hand, although the bulky menthoxy group in **1c**/$AlCl_3$ is favorable to get better stereocontrol in the course of the reaction, the bulky menthoxy group also obstructs the cleavage of the ether bond of menthol homoallylic ether **5–7** under the same condition.

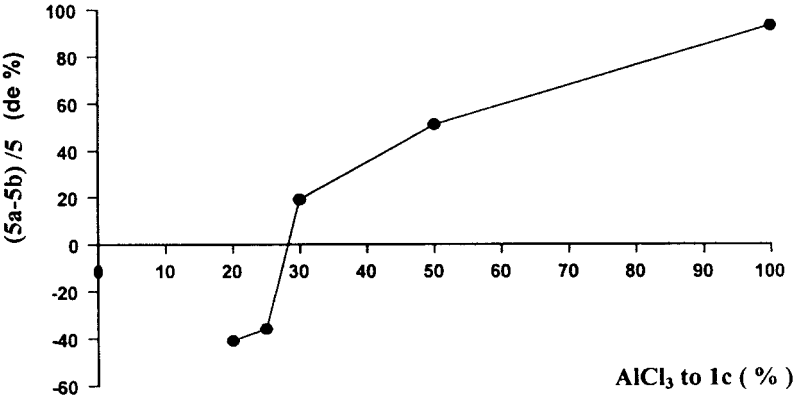
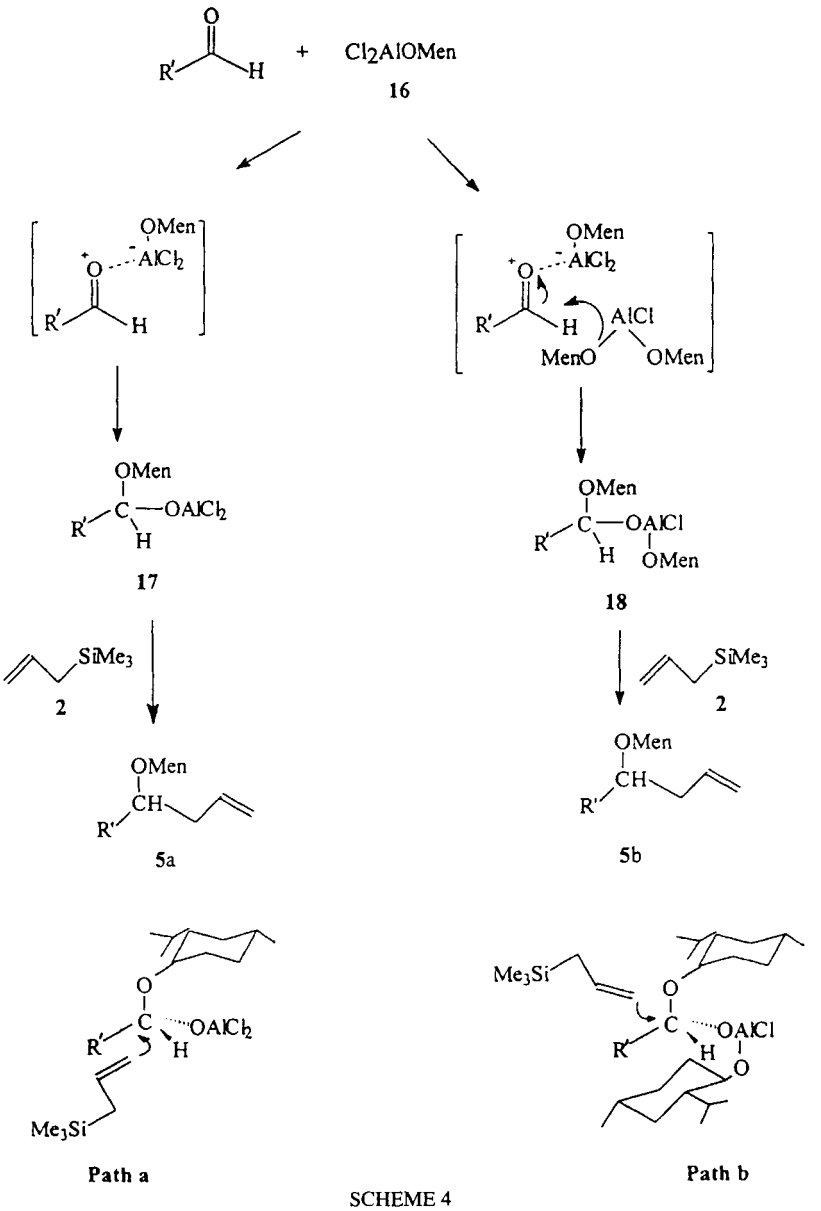



FIGURE 1 Relationship of **5a/5b** with $AlCl_3$ to **1c**

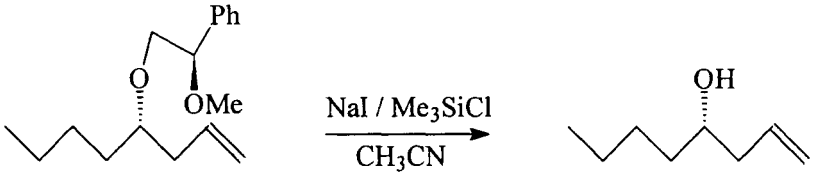
The results on various types of chiral alcohols for modification of $AlCl_3$ and subsequent allylation reactions of aldehydes with allyltrimethylsilane provide a structural basis to look for a novel chiral alcohol: 1) Bearing bulky chiral group is essential for higher asymmetric induction; 2) It should linke with aluminum atom as closely as possible; 3) The coordination of the group in chiral ligand to aluminum atom must be relatively weaker if existed; 4) Chiral alkoxy group in homoallylic ethers produced should be cleaved easily. The investigation of novel chiral alcohol modifier is in progress.

In conclusion, $AlCl_3$ was chirally modified by chiral alcohols, forming chiral aluminum reagents (*ROH/$AlCl_3$). The *ROH/$AlCl_3$ was used in promoting the allylation of aliphatic aldehydes with etherification by allyltrimethylsilane to afford the chiral homoallylic ethers in good yields and good to excellent diastereoselectivities (51–93% de). The monoalkoxy aluminum (*RO)$AlCl_2$ was determined as an active and stereogenic spe-

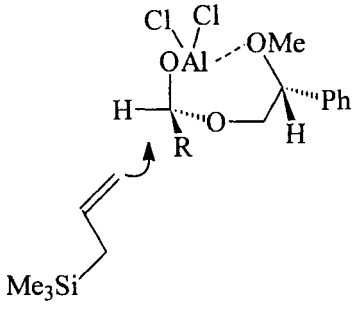



SCHEME 4

cies in one pot allylation of aldehydes. The *ROH/$AlCl_3$ exhibited different behaviors from Leiws acid $AlCl_3$ and higher stereocontrol ability in the allylation of aldehydes with allyltrimethylsilane, which provides a clue to improve the enantioselectivity in asymmetric Sakurai reaction.




**10** **19**




SCHEME 5



***Acknowledgements***

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