Arch Pharm Res Vol 26, No 9, 667-678, 2003

Archives of Pharmacal Research
http://apr.psk.or.kr

Mechanism Studies on the CSI Reaction with Allyl Ethers by Varying *p*-Substituent

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(Received August 1, 2003)

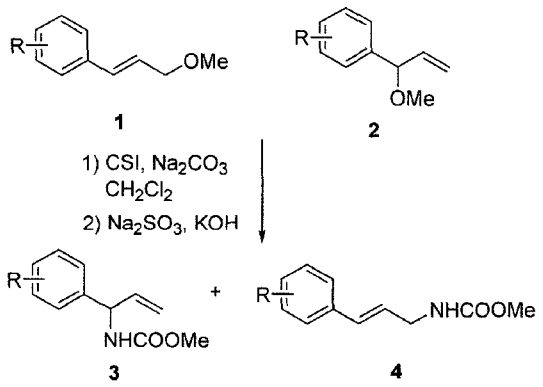
We examined the effect of *p*-substituents in *p*-substituted cinnamyl methyl ethers and 1-(*p*-substituted phenyl)allyl methyl ethers with CSI, and confirmed that the CSI reaction of allyl ethers (*p*-substituted ethers) is a competitive reaction of S_Ni and S_N1 mechanism according to the stability of the carbocation. And, the only terminal allylic amine was obtained through the migration reaction in thermodynamic reaction condition.

Key words: Chlorosulfonyl isocyanate, Allyl ether, Carbamate

INTRODUCTION

Recently we reported a novel synthetic method for *N*-allylcarbamates from allyl ethers using chlorosulfonyl isocyanate (CSI) (Kim *et al.*, 2001; Kim *et al.*, 2000; Jung and Kim, 2001; Jung and Kim, 2000), and we have developed a novel regioselective and diastereoselective synthetic approach to the unsaturated aromatic 1,2-amino alcohols from the epimeric mixture of optically active allylic ethers having a hydroxyl group attached to a allylic chiral center to the π-system using the CSI reaction (Kim *et al.*, 2003). Furthermore, we have found a novel technique for comparing directly the stability of carbocations in the solution phase and have established the stability order of the various carbocations under our reaction conditions (Kim *et al.*, 2002), and we have reported the extension of CSI under new reaction condition to the cleavage of various benzyl and *p*-methoxybenzyl protecting groups of alcohols and phenols in the presence of other functional groups (Kim *et al.*, 2003).

In progress of the examination about the CSI reaction, we found that the CSI reaction of cinnamyl methyl ether produced the mixture of methyl *N*-(1-phenylprop-2-enyl) carbamate and methyl *N*-(3-phenylprop-2-enyl)carbamate as a 1 :2.7 ratio, and 1-phenylallyl methyl ether yielded a similar result (1 : 2.6). But, the treatment of 4-phenylbut-2-enyl methyl ether with CSI furnished methyl *N*-(1-benzylallyl) carbamate and methyl *N*-(4-phenylbut-2-enyl)carbamate as a 1:1.1 mixture of regioisomers, however, the 1-benzylallyl methyl ether gave an inversed product ratio (4.6:1) in favor of the internal allylic amine. It is certain that these reactions were not proceeding through the same allylic carbocation intermediate (Kim *et al.*, 2001).



Scheme 1. Mechanism studies on the CSI reaction by varying *p*-substituent

In order to elucidate the mechanism of our CSI reaction, we tried to examine the effect of *p*-substituents in *p*-substituted cinnamyl methyl ethers and 1-(*p*-substituted phenyl)allyl methyl ethers with CSI (Scheme 1).

MATERIALS AND METHODS

Commercially available reagents were used without additional purification, unless otherwise stated. All anhydrous

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solvents were distilled over CaH_2 or P_2O_5 or Na/ benzophenone prior to reaction. All reactions were performed under an inert atmosphere of nitrogen or argon. Melting points were measured on a Gallenkamp melting point apparatus or Electrothermal IA9300 melting point apparatus and were not corrected. Nuclear magnetic resonance spectra (^{1}H- and ^{13}C-NMR) were recorded on a Varian Unity Inova 500 MHz spectrometer for $CDCl_3$ solutions and chemical shifts are reported as parts per million (ppm) relative to, respectively, residual $CHCl_3$ δ_H (7.26 ppm) and $CDCl_3$ δ_C (77.0 ppm) as internal standards. Resonance patterns are reported with the notations s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). In addition, the notation br is used to indicate a broad signal. Coupling constants (J) are reported in hertz (Hz). IR spectra were recorded on a Nicolet 205 Infrared spectrophotometer or Bruker Vector 22 Infrared spectrophotometer and are reported as cm^{-1}. Thin layer chromatography was carried out using plates coated with Kieselgel $60F_{254}$ (Merck). For flash column chromatography, E. Merck Kieselgel 60 (230-400 mesh) was used. Elemental analyses were performed with an EA 1110 analyzer, and high-resolution mass spectra (HRMS) were recorded on a JEOL, JMS-505 or JMS-600 spectrometer using the chemical ionization (CI) method.

Synthesis of *p*-substituted ethers

General procedure for the preparation of *p*-substituted ether

To a solution of alcohol (4.00 mmol) in THF (16 mL) was added NaH (6.00 mmol, 60% in mineral oil). The reaction mixture was warmed to 45°C under N_2 and MeI (6.00 mmol) was added dropwise. The reaction mixture was stirred at 45°C for 1 h and cooled to room temperature. H_2O (20 mL) was added and the solution was extracted with EtOAc (30 mL). The organic layer was washed with H_2O and brine. The organic was dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (*n*-Hexane/EtOAc).

3-*p*-Bromophenyl-1-methoxyprop-2-ene (1b)

The above general procedure was followed using 3-*p*-bromophenylprop-2-en-1-ol (0.50 g, 2.35 mmol), NaH (0.14 g, 3.52 mmol, 60% in mineral oil) and MeI (0.22 mL, 3.52 mmol) in THF (9 mL). The reaction mixture was purified by column chromatography (*n*-Hexane/EtOAc = 15:1) to afford 0.48 g (90%) of 3-*p*-bromophenyl-1-methoxyprop-2-ene (**1b**) as a white solid. R_f: 0.31 (15:1 *n*-Hexane/EtOAc); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 3.39 (s, 3H), 4.07 (d, 2H, J = 6.0 Hz), 6.28 (dt, 1H, J = 15.5, 6.0 Hz), 6.54 (d, 1H, J = 15.5 Hz), 7.25 (dd, 2H, J = 7.0, 2.0 Hz), 7.43 (dd, 2H, J = 7.0, 2.0 Hz); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 58.41, 73.14, 121.68, 127.06, 128.24, 131.30, 131.92, 135.91; IR (CH_2Cl_2): 2928, 2823, 1588, 1488, 1402, 1378, 1193, 1119, 1072 cm^{-1}; mp: 49~50°C; HRMS (CI) calcd for $C_{10}H_{11}BrO$+H $(M+H)^+$ 227.0072. Found: 227.0081.

3-*p*-Fluorophenyl-1-methoxyprop-2-ene (1d)

The above general procedure was followed using 3-*p*-fluorophenylprop-2-en-1-ol (0.50 g, 3.29 mmol), NaH (0.20 g, 4.93 mmol, 60% in mineral oil) and MeI (0.31 mL, 4.93 mmol) in THF (13 mL). The reaction mixture was purified by column chromatography (*n*-Hexane/EtOAc = 15:1) to give 0.45 g (82%) of 3-*p*-fluorophenyl-1-methoxyprop-2-ene (**1d**) as a colorless oil. R_f: 0.33 (15:1 *n*-Hexane/EtOAc); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 3.39 (s, 3H), 4.07 (d, 2H, J = 6.0 Hz), 6.20 (dt, 1H, J = 15.5, 6.0 Hz), 6.57 (d, 1H, J = 15.5 Hz), 6.99 (d, 1H, J = 9.0 Hz), 7.01 (d, 1H, J = 9.0 Hz), 7.34 (d, 1H, J = 9.0 Hz), 7.35 (d, 1H, J = 9.0 Hz); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 58.76, 73.69, 116.08, 116.25, 126.38, 128.64, 131.93, 133.56, 162.07, 164.03; IR (neat): 2920, 2849, 1505, 1376, 1225, 1108 cm^{-1}; HRMS (CI) calcd for $C_{10}H_{11}FO$-H $(M-H)^+$ 165.0716. Found: 165.0715.

1-Methoxy-3-(2-naphthyl)prop-2-ene (1e)

The above general procedure was followed using 3-(2-naphthyl)prop-2-en-1-ol (Chakraborti *et al.*, 2001) (0.30 g, 1.63 mmol), NaH (98 mg, 2.44 mmol, 60% in mineral oil) and MeI (0.15 mL, 2.44 mmol) in THF (7 mL). The reaction mixture was purified by column chromatography (*n*-Hexane/EtOAc = 30:1) to give 0.28 g (87%) of 1-methoxy-3-(2-naphthyl)prop-2-ene (**1e**) as a white solid. R_f: 0.34 (15:1 *n*-Hexane/EtOAc); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 3.43 (s, 3H), 4.16 (d, 2H, J = 6.0 Hz), 6.43 (dt, 1H, J = 16.0, 6.0 Hz), 6.78 (d, 1H, J = 16.0 Hz), 7.44-7.47 (m, 2H), 7.62 (dd, 1H, J = 8.5, 2.0 Hz), 7.75 (s, 1H), 7.78-7.81 (m, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 58.35, 73.44, 123.83, 126.17, 126.53, 126.59, 126.76, 127.93, 128.26, 128.47, 132.79, 133.29, 133.82, 134.43; IR (CH_2Cl_2): 2987, 2817, 1593, 1468, 1379, 1272, 1226, 1119, 1086 cm^{-1}; mp: 59°C; HRMS (CI) calcd for $C_{14}H_{14}O$+H $(M+H)^+$ 199.1123. Found: 199.1122.

3-Biphenyl-1-methoxyprop-2-ene (1f)

The above general procedure was followed using 3-biphenylprop-2-en-1-ol (0.25 g, 1.19 mmol), NaH (71 mg, 1.78 mmol, 60% in mineral oil) and MeI (0.11 mL, 1.78 mmol) in THF (5 mL). The reaction mixture was purified by column chromatography (*n*-Hexane/EtOAc = 30:1) to give 0.23 g (86%) of 3-biphenyl-1-methoxyprop-2-ene (**1f**) as a white solid. R_f: 0.34 (15:1 *n*-Hexane/EtOAc); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 3.41 (s, 3H), 4.12 (d, 2H, J = 6.0 Hz), 6.35 (dt, 1H, J = 16.0, 6.0 Hz), 6.66 (d, 1H, J = 16.0 Hz), 7.34-7.36 (m, 1H), 7.43-7.48 (m, 4H), 7.56-7.61 (m, 4H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 58.29, 73.39, 126.31,

127.16, 127.19, 127.52, 127.58, 129.05, 132.23, 135.99, 140.38, 140.93; IR (CH_2Cl_2): 3029, 2824, 1487, 1449, 1409, 1265, 1194, 1119, 1007 cm^{-1}; mp: 93~95°C; HRMS (CI) calcd for $C_{16}H_{16}O$+H $(M+H)^+$ 225.1279. Found: 225.1283.

1-Methoxy-3-*p*-methylphenylprop-2-ene (1g)

The above general procedure was followed using 3-*p*-methylphenylprop-2-en-1-ol (0.50 g, 3.57 mmol), NaH (0.20 g, 5.06 mmol, 60% in mineral oil) and MeI (0.31 mL, 5.06 mmol) in THF (13 mL). The reaction mixture was purified by column chromatography (*n*-Hexane/EtOAc = 30:1) to give 0.52 g (95%) of 1-methoxy-3-*p*-methyl phenylprop-2-ene (**1g**) as a colorless oil. R_f: 0.35 (15:1 *n*-Hexane/EtOAc); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 2.34 (s, 3H), 3.39 (s, 3H), 4.08 (d, 2H, *J* = 6.5 Hz), 6.24 (dt, 1H, *J* = 15.5, 6.5 Hz), 6.58 (d, 1H, *J* = 15.5 Hz), 7.13 (dd, 2H, *J* = 8.0, 2.0 Hz), 7.29 (dd, 2H, *J* = 8.0, 2.0 Hz); ^{13}C-NMR (125 MHz, $CDCl_3$): 21.47, 58.19, 73.47, 125.10, 126.65, 129.51, 132.76, 134.16, 137.79; IR (neat): δ 2922, 1513, 1449, 1375, 1319, 1186, 1115 cm^{-1}; HRMS (CI) calcd for $C_{11}H_{14}C$-H $(M-H)^+$ 161.0966. Found: 161.0965.

3-(3,4-Dimethoxyphenyl)-1-methoxyprop-2-ene (1i)

The above general procedure was followed using 3-(3,4-dimethoxyphenyl)prop-2-en-1-ol (Ponpipom *et. al.*, 1986) (1.00 g, 5.15 mmol), NaH (0.31 g, 7.72 mmol, 60% in mineral oil) and MeI (0.49 mL, 7.72 mmol) in THF (21 mL) The reaction mixture was purified by column chromatography (*n*-Hexane/EtOAc = 10:1) to give 0.99 g (92%) of 3-(3,4-dimethoxyphenyl)-1-methoxyprop-2-ene (**1i**) as a colorless oil. R_f: 0.38 (3:1 *n*-Hexane/EtOAc); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 3.39 (s, 3H), 3.88 (s, 3H), 3.39 (s, 3H), 4.07 (d, 2H, *J* = 6.0 Hz), 6.17 (dt, 1H, *J* = 15.5, 6.0 Hz), 6.55 (d, 1H, *J* = 15.5 Hz), 6.81 (d, 1H, *J* = 8.0 Hz), 6.92 d, 1H, *J* = 8.0 Hz), 6.95 (s, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 56.48, 56.59, 58.63, 73.89, 109.51, 111.77, 120.41, 124.66, 130.49, 133.10, 149.59, 149.69; IR (neat): 2932, 2843, 1598, 1499, 1257, 1130, 1029 cm^{-1}; HRMS (CI) calcd for $C_{12}H_{16}O_3$+H $(M+H)^+$ 209.1178. Found: 209.1176.

1-*p*-Bromophenyl-1-methoxyprop-2-ene (2b)

The above general procedure was followed using 1-*p*-bromophenylprop-2-en-1-ol (0.45 g, 2.11 mmol), NaH (0.13 g, 3.17 mmol, 60% in mineral oil) and MeI (0.20 mL, 3.17 mmol) in THF (8 mL). The reaction mixture was purified by column chromatography (*n*-Hexane/EtOAc = 50:1) to give 0.40 g (84%) of 1-*p*-bromophenyl-1-methoxyprop-2-ene (**2b**) as a colorless oil. R_f: 0.40 (15:1 *n*-Hexane/EtOAc); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 3.32 (s, 3H), 4.57 (d, 1H, *J* = 6.5 Hz), 5.22 (dd, 1H, *J* = 10.0, 1.5 Hz), 5.27 (dd, 1H, *J* = 17.0, 1.5 Hz), 5.87 (ddd, 1H, *J* = 17.0, 10.0, 6.5 Hz), 7.21 (dd, 2H, *J* = 8.0, 2.0 Hz), 7.47 (dd, 2H, *J* = 8.0, 2.0 Hz); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 56.70, 84.27, 117.19, 121.76, 128.76, 131.81, 138.49, 140.19; IR (neat): 2936, 2822, 1589, 1485, 1399, 1276, 1189, 1072, 1011 cm^{-1}; HRMS (CI) calcd for $C_{10}H_{11}BrO$-H $(M-H)^+$ 224.9915. Found: 224.9910.

1-*p*-Chlorophenyl-1-methoxyprop-2-ene (2c)

The above general procedure was followed using 1-*p*-chlorophenylprop-2-en-1-ol (Kuroboshi *et. al.*, 1999) (0.40 g, 2.37 mmol), NaH (0.14 g, 3.56 mmol, 60% in mineral oil) and MeI (0.22 mL, 3.56 mmol) in THF (9 mL). The reaction mixture was purified by column chromatography (*n*-Hexane/EtOAc = 50:1) to give 0.41 g (92 %) of 1-*p*-chlorophenyl-1-methoxyprop-2-ene (**2c**) as a colorless oil. R_f: 0.41 (15:1 *n*-Hexane/EtOAc); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 3.32 (s, 3H), 4.59 (d, 1H, *J* = 7.0 Hz), 5.22 (dd, 1H, *J* = 10.5, 1.5 Hz), 5.26 (dd, 1H, *J* = 17.0, 1.5 Hz), 5.87 (ddd, 1H, *J* = 17.0, 10.5, 7.0 Hz), 7.26 (d, 2H, *J* = 8.5 Hz), 7.32 (d, 2H, *J* = 8.5 Hz); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 57.13, 84.66, 117.54, 128.87, 129.30, 134.06, 139.02, 140.13; IR (neat): 2926, 2838, 1479, 1321, 1199, 1092 cm^{-1}; HRMS (CI) calcd for $C_{10}H_{11}ClO$-H $(M-H)^+$ 181.0420. Found: 181.0424.

1-*p*-Fluorophenyl-1-methoxyprop-2-ene (2d)

The above general procedure was followed using 1-*p*-fluorophenylprop-2-en-1-ol (0.40 g, 2.63 mmol), NaH (0.16 g, 3.94 mmol, 60% in mineral oil) and MeI (0.25 mL, 3.94 mmol) in THF (11 mL). The reaction mixture was purifiedby column chromatography (*n*-Hexane/EtOAc = 50:1) to give 0.41 g (92%) of 1-*p*-fluorophenyl-1-methoxyprop-2-ene (**2d**) as a colorless oil. R_f: 0.41 (15:1 *n*-Hexane/EtOAc); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 3.32 (s, 3H), 4.60 (d, 1H, *J* = 6.5 Hz), 5.23 (dd, 1H, *J* = 10.0, 1.5 Hz), 5.26 (dd, 1H, *J* = 17.0, 1.5 Hz), 5.89 (ddd, 1H, *J* = 17.0, 10.0, 6.5 Hz), 7.02 (d, 1H, *J* = 8.0 Hz), 7.04 (d, 1H, *J* = 8.0 Hz), 7.29 (d, 1H, *J* = 8.0 Hz), 7.30 (d, 1H, *J* = 8.0 Hz); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 57.06, 84.66, 115.89, 116.07, 117.29, 129.12, 137.34, 139.25, 162.01, 163.96; IR (neat): 2926, 2838, 1506, 1423, 1372, 1322, 1223, 1093 cm^{-1}; HRMS (CI) calcd for $C_{10}H_{11}FO$-H $(M-H)^+$ 165.0716. Found: 165.0717.

1-Methoxy-1-(2-naphthyl)prop-2-ene (2e)

The above general procedure was followed using 1-(2-naphthyl)phenylprop-2-en-1-ol (Barluenga *et. al.*, 2002) (0.50 g, 2.71 mmol), NaH (0.16 g, 4.07 mmol, 60% in mineral oil) and MeI (0.25 mL, 4.07 mmol) in THF (11 mL). The reaction mixture was purified by column chromatography (*n*-Hexane/EtOAc = 50:1) to give 0.45 g (84%) of 1-methoxy-1-(2-naphthyl)prop-2-ene (**2e**) as a colorless oil. R_f: 0.39 (15:1 *n*-Hexane/EtOAc); ^{1}H-NMR (500 MHz, $CDCl_3$):

δ 3.38 (s, 3H), 4.80 (d, 1H, *J* = 6.5 Hz), 5.25 (dd, 1H, *J* = 10.5, 1.5 Hz), 5.35 (dd, 1H, *J* = 17.0, 1.5 Hz), 6.02 (ddd, 1H, *J* = 17.0, 10.5, 6.5 Hz), 7.45-7.49 (m, 3H), 7.79 (s, 1H), 7.83-7.86 (m, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 56.75, 85.02, 116.82, 125.03, 126.02, 126.16, 126.36, 127.95, 128.20, 128.37, 133.31, 133.35, 138.48, 139.93; IR (neat): 3056, 2932, 2820, 1601, 1508, 1415, 1317, 1273, 1189, 1087 cm^{-1}; HRMS (CI) calcd for $C_{14}H_{14}O$+H $(M+H)^+$ 199.1123. Found: 199.1124.

1-Biphenyl-1-methoxyprop-2-ene (2f)

The above general procedure was followed using 1-biphenylprop-2-en-1-ol (0.30 g, 1.43 mmol), NaH (86 mg, 2.14 mmol, 60% in mineral oil) and MeI (0.13 mL, 2.14 mmol) in THF (6 mL). The reaction mixture was purified by column chromatography (*n*-Hexane/EtOAc = 50:1) to give 0.30 g (94%) of 1-biphenyl-1-methoxyprop-2-ene (**2f**) as a colorless oil. R_f: 0.39 (15:1 *n*-Hexane/EtOAc); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 3.38 (s, 3H), 4.68 (d, 1H, *J* = 7.0 Hz), 5.25 (dd, 1H, *J* = 10.0, 1.5 Hz), 5.35 (dd, 1H, *J* = 17.0, 1.5 Hz), 5.98 (ddd, 1H, *J* = 17.0, 10.0, 7.0 Hz), 7.35-7.38 (m, 1H), 7.41-7.46 (m, 4H), 7.58-7.61 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 56.73, 84.75, 116.80, 127.38, 127.49, 127.53, 129.02, 138.91, 140.18, 140.89, 141.15; IR (neat): 3029, 2932, 1486, 1406, 1339, 1187, 1086 cm^{-1}; HRMS (CI) calcd for $C_{16}H_{16}O$-H $(M-H)^+$ 223.1123. Found: 223.1127.

1-Methoxy-1-*p*-methylphenylprop-2-ene (2g)

The above general procedure was followed using 1-*p*-methylphenylprop-2-en-1-ol (0.50 g, 3.37 mmol), NaH (0.20 g, 5.06 mmol, 60% in mineral oil) and MeI (0.32 mL, 5.06 mmol) in THF (13 mL). The reaction mixture was purified by column chromatography (*n*-Hexane/EtOAc = 50:1) to give 0.52 g (95%) of 1-methoxy-1-*p*-methylphenylprop-2-ene (**2g**) as a colorless oil. R_f: 0.41 (15:1 *n*-Hexane/EtOAc); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 2.35 (s, 3H), 3.32 (s, 3H), 4.59 (d, 1H, *J* = 6.5 Hz), 5.19 (dd, 1H, *J* = 10.0, 1.5 Hz), 5.28 (dd, 1H, *J* = 17.5, 1.5 Hz), 5.93 (ddd, 1H, *J* = 17.5, 10.0, 6.5 Hz), 7.16 (d, 2H, *J* = 8.0 Hz), 7.22 (d, 2H, *J* = 8.0 Hz); ^{13}C-NMR (125 MHz, $CDCl_3$): 21.41, 56.57, 84.80, 116.36, 127.04, 129.41, 137.63, 138.09, 139.15; IR (neat): δ 2925, 2821, 1512, 1449, 1412, 1237, 1181, 1087, 1021 cm^{-1}; HRMS (CI) calcd for $C_{11}H_{14}O$+H $(M+H)^+$ 163.1123. Found: 163.1121.

1-Methoxy-1-*p*-methoxyphenylprop-2-ene (2h)

The above general procedure was followed using 1-*p*-methoxyphenylprop-2-en-1-ol (Kuroboshi *et. al.*, 1999) (1.00 g, 6.09 mmol), NaH (0.37 g, 9.13 mmol, 60% in mineral oil) and MeI (0.58 mL, 9.13 mmol) in THF (25 mL). The reaction mixture was purified by column chromatography (*n*-Hexane/EtOAc = 15:1) to give 0.93 g (85%) of 1-methoxy-1-*p*-methoxyphenylprop-2-ene (**2h**) as a colorless oil. R_f: 0.27 (15:1 *n*-Hexane/EtOAc); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 3.32 (s, 3H), 3.81 (s, 3H), 4.59 (d, 1H, *J* = 6.5 Hz), 5.20 (dd, 1H, *J* = 10.0, 1.5 Hz), 5.26 (dd, 1H, *J* = 17.5, 1.5 Hz), 5.93 (ddd, 1H, *J* = 17.5, 10.0, 6.5 Hz), 6.90 (d, 2H, *J* = 6.5 Hz), 7.26 (d, 2H, *J* = 6.5 Hz); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 55.95, 56.93, 84.91, 114.55, 116.71, 128.82, 133.67, 139.64, 159.87; IR (neat): 2933, 2841, 1501, 1250, 1084 cm^{-1}; HRMS (CI) calcd for $C_{11}H_{14}O_2$+H $(M+H)^+$ 179.1072. Found: 179.1075.

Reaction of *p*-substituted ethers with CSI

General procedure for the reaction of *p*-substituted ether with CSI

A suspension of Na_2CO_3 (6.75 mmol) in anhydrous CH_2Cl_2 (12 mL) was adjusted to 20°C or -78°C, then CSI (4.50 mmol) and *p*-substisuted ether (3.00 mmol) was added under N_2. The reaction mixture was stirred at 20°C or -78°C, quenched with H_2O (10 mL) when the reaction was completed (TLC monitoring), then extracted with EtOAc (10 mL×2). The organic layer was added to an aqueous solution of Na_2SO_3 (25%) and KOH (10%), and the reaction mixture was stirred at room temperature for overnight. The organic layer was washed with H_2O and brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by column chromatography (*n*-Hexane/EtOAc).

Methyl *N*-(1-*p*-bromophenylprop-2-enyl)carbamate (3b) and methyl *N*-(3-*p*-bromophenylprop-2-enyl)carbamate (4b)

The above general procedure was followed using 3-*p*-bromophenyl-1-methoxyprop-2-ene (**1b**) (0.10 g, 0.44 mmol), Na_2CO_3 (0.11 g, 0.99 mmol) and CSI (57 μL, 0.66 mmol) in CH_2Cl_2 (2 mL) at 20°C. The reaction mixture was purified by column chromatography (*n*-Hexane/EtOAc = 6:1) to give 17 mg (14%) of methyl *N*-(1-*p*-bromophenylprop-2-enyl)carbamate (**3b**) as a white solid and 71 mg (61%) of methyl *N*-(3-*p*-bromophenylprop-2-enyl)carbamate (**4b**) as a white solid. **3b**: R_f: 0.40 (3:1 *n*-Hexane/EtOAc); ^{1}H-NMR (500 MHz, $CDCl_3$): 3.68 (s, 3H), 4.95-5.03 (br, 1H), 5.21 (dd, 1H, *J* = 17.5, 1.5 Hz), 5.26 (dd, 1H, *J* = 10.5, 1.5 Hz), 5.27-5.35 (br, 1H), 5.98 (ddd, 1H, *J* = 17.5, 10.5z, 6.5 Hz), 7.17 (dd, 2H, *J* = 8.0, 2.0 Hz), 7.47 (dd, 2H, *J* = 8.0, 2.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 52.60, 56.72, 116.73, 121.83, 129.01, 132.04, 137.29, 140.06, 156.41; IR (CH_2Cl_2): δ 3317, 2952, 1703, 1529, 1488, 1335, 1299, 1244, 1193, 1073 cm^{-1}; mp: 68~69°C; HRMS (CI) calcd for $C_{11}H_{12}BrNO_2$+H $(M+H)^+$ 270.0130. Found: 270.0121. **4b**: R_f: 0.27 (3:1 *n*-Hexane/EtOAc); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 3.71 (s, 3H), 3.96 (dd, 2H, *J* = 5.5, 5.5 Hz), 4.80-4.87 (br, 1H), 6.20 (dt, 1H, *J* = 16.0, 5.5 Hz), 6.46 (d, 1H, *J* = 16.0 Hz), 7.22 (dd, 2H, *J* = 8.5, 1.5 Hz), 7.43 (dd, 2H, *J* = 8.5, 1.5 Hz); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 43.25,

52.54, 121.70, 127.08, 128.16, 130.63, 131.94, 135.72, 157.17 IR (CH_2Cl_2): 3336, 2999, 1694, 1541, 1488, 1446, 1362, 1293, 1189, 1073 cm^{-1}; mp: 101~102°C; HRMS (CI) calcd for $C_{11}H_{12}BrNO_2$+H $(M+H)^+$ 270.0130. Found: 270.0134.

Methyl *N*-(1-*p*-chlorophenylprop-2-enylcarbamate (3c) and methyl *N*-(3-*p*-chlorophenylprop-2-enyl)carbamate (4c)

The above general procedure was followed using 3-*p*-chlorophenyl-1-methoxyprop-2-ene (**1c**) (0.10 g, 0.55 mmol), Na_2CO_3 (0.13 g, 1.23 mmol) and CSI (72 μL, 0.82 mmol) in CH_2Cl_2 (2 mL) at 20°C. The reaction mixture was purified by column chromatography (*n*-Hexane/EtOAc = 6:1) to give 21 mg (17%) of methyl *N*-(1-*p*-chlorophenylprop-2-enyl carbamate (**3c**) as a white solid and 74 mg (60%) of methyl *N*-(3-*p*-chlorophenylprop-2-enyl)carbamate (**4c**) as a white solid. **3c:** R_f: 0.37 (3:1 *n*-Hexane/EtOAc); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 3.66 (s, 3H), 5.17-5.23 (br, 1H), 5.20 (dd, 1H, *J* = 17.0, 1.5 Hz), 5.24 (dd, 1H, *J* = 10.5, 1.5 Hz), 5.27-5.33 (br, 1H), 5.94 (ddd, 1H, *J* = 17.0, 10.5, 6.0 Hz), 7.21 (d, 2H, *J* = 8.5 Hz), 7.30 (d, 2H, *J* = 8.5 Hz); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 53.01, 57.13, 117.07, 129.11, 129.51, 134.11, 137.86, 140.03, 156.90; IR (CH_2Cl_2): 3317, 2955, 1686, 1528, 1263, 1076 cm^{-1}; mp: 59~60°C; HRMS (CI) calcd for $C_{11}H_{12}ClNO_2$+H $(M+H)^+$ 226.0635. Found: 226.0631. **4c**: R_f: 0.20 (3:1 *n*-Hexane/EtOAc); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 3.70 (s, 3H), 3.96 (dd, 2H, *J* = 6.0, 5.0 Hz), 4.80-4.88 (br, 1H), 6.17 (dt, 1H, *J* = 16.0, 6.0 Hz), 6.47 (d, 1H, *J* = 16.0 Hz), 7.26-7.31 (m, 4H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 43.71, 52.80, 127.37, 128.29, 129.44, 131.06, 134.01, 135.73, 157.62; IR (CH_2Cl_2): 3336, 2987, 1696, 1541, 1493, 1447, 1361, 1264, 1231, 1089 cm^{-1}; mp: 93~94°C; HRMS (CI) calcd for $C_{11}H_{12}ClNO_2$+H $(M+H)^+$ 226.0635. Found: 226.0643.

Methyl *N*-(1-*p*-fluorophenylprop-2-enyl)carbamate (3d) and methyl *N*-(3-*p*-fluorophenylprop-2-enyl)carbamate (4d)

The above general procedure was followed using 3-*p*-fluorophenyl-1-methoxyprop-2-ene (**1d**) (0.10 g, 0.60 mmol), Na_2CO_3 (0.14 g, 1.35 mmol) and CSI (78 μL, 0.93 mmol) in CH_2Cl_2 (2 mL) at 20°C. The reaction mixture was purified by column chromatography (*n*-Hexane/EtOAc = 6:1) to give 33 mg (26%) of methyl *N*-(1-*p*-fluorophenylprop-2-enyl)carbamate (**3d**) as a white solid and 74 mg (59%) of methyl *N*-(3-*p*-fluorophenylprop-2-enyl)carbamate (**4d**) as a white solid. **3d**: R_f: 0.30 (3:1 *n*-Hexane/EtOAc); ^{1}H-NMR (500 MHz, $CDCl_3$): 3.69 (s, 3H), 5.00-5.07 (br, 1H), 5.22 (dd, 1H, *J* = 17.5, 1.5 Hz), 5.26 (dd, 1H, *J* = 10.5, 1.5 Hz), 5.30-5.36 (br, 1H), 5.98 (ddd, 1H, *J*=17.5, 10.5, 6.5 Hz), 7.02 (d, 1H, *J* = 9.0 Hz), 7.04 (d, 1H, *J* = 9.0 Hz), 7.26 (d, 1H, *J* = 9.0 Hz), 7.27 (d, 1H, *J* = 9.0 Hz); ^{13}C-NMR (125 MHz, $CDCl_3$): 52.56, 56.57, 115.71, 115.88, 116.34, 128.94, 136.77, 137.64, 156.43, 161.46, 163.42; IR (CH_2Cl_2): 3319, 2954, 1701, 1604, 1509, 1457, 1297, 1225, 1159, 1038 cm^{-1}; mp: 30°C; HRMS (CI) calcd for $C_{11}H_{12}FNO_2$+H $(M+H)^+$ 210.0930. Found: 210.0932. **4d**: R_f: 0.20 (3:1 *n*-Hexane/EtOAc); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 3.71 (s, 3H), 3.96 (dd, 2H, *J* = 6.5, 5.0 Hz), 4.78-4.86 (br, 1H), 6.11 (dt, 1H, *J* = 15.5, 6.5 Hz), 6.49 (d, 1H, *J* = 15.5 Hz), 6.99 (d, 1H, *J* = 8.5 Hz), 7.01 (d, 1H, *J* = 8.5 Hz), 7.32 (d, 1H, *J* = 8.5 Hz), 7.33 (d, 1H, *J* = 8.5 Hz); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 43.76, 52.98, 116.12, 116.28, 126.38, 128.62, 131.21, 133.37, 157.62, 162.06, 164.03; IR (CH_2Cl_2): 3332, 2886, 1693, 1542, 1451, 1363, 1304, 1261, 1224, 1157 cm^{-1}; mp: 84~85°C; Anal. Calcd for $C_{11}H_{12}FNO_2$: C, 63.15; H, 5.77; N, 6.69. Found: C, 63.21; H, 5.77; N, 6.88.

Methyl *N*-[1-(2-naphthyl)prop-2-enyl]carbamate (3e) and methyl *N*-[3-(2-naphthyl)prop-2-enyl]carbamate (4e)

The above general procedure was followed using 1-methoxy-1-(2-naphthyl)prop-2-ene (**2e**) (0.20 g, 1.01 mmol), Na_2CO_3 (0.24 g, 2.27 mmol) and CSI (0.13 mL, 1.51 mmol) in CH_2Cl_2 (4 mL) at -78°C. The reaction mixture was purified by column chromatography (*n*-Hexane/EtOAc = 6:1) to give 35 mg (14%) of methyl *N*-[1-(2-naphthyl)prop-2-enyl]carbamate (**3e**) as a white solid and 0.16 g (66%) of methyl *N*-[3-(2-naphthyl)prop-2-enyl]carbamate (**4e**) as a white solid. **3e**: R_f: 0.33 (3:1 *n*-Hexane/EtOAc); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 3.70 (s, 3H), 5.07-5.12 (br, 1H), 5.27 (dd, 1H, *J* = 17.0, 1.5 Hz), 5.30 (dd, 1H, *J* = 10.0, 1.5 Hz), 5.46-5.53 (br, 1H), 6.08 (ddd, 1H, *J* = 17.0, 10.0, 6.5 Hz), 7.40 (d, 1H, *J* = 8.5 Hz), 7.47-7.49 (m, 2H), 7.75 (s, 1H), 7.81-7.84 (m, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 52.58, 57.33, 116.37, 125.44, 125.98, 126.53, 126.57, 127.91, 128.21, 128.85, 133.09, 133.56, 137.77, 138.27, 156.51; IR (CH_2Cl_2): 3317, 2952, 1700, 1528, 1456, 1321, 1244, 1193, 1085 cm^{-1}; mp: 58~60°C; HRMS (CI) calcd for $C_{15}H_{15}NO_2$+H $(M+H)^+$ 242.1181. Found: 242.1186. **4e**: R_f: 0.27 (3:1 *n*-Hexane/EtOAc); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 3.72 (s, 3H), 4.03 (dd, 2H, *J* = 6.5, 5.5 Hz), 4.82-4.90 (br, 1H), 6.33 (dt, 1H, *J* = 16.0, 6.5 Hz), 6.69 (d, 1H, *J* = 16.0 Hz), 7.43-7.48 (m, 2H), 7.57 (dd, 1H, *J* = 8.5, 2.0 Hz), 7.71 (s, 1H), 7.77-7.81 (m, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 43.49, 52.53, 123.73, 126.19, 126.57, 126.64, 127.93, 128.24, 128.51, 131.99, 133.26, 133.79, 134.24, 157.25; IR (CH_2Cl_2): 3334, 2949, 1688, 1527, 1461, 1247, 1193, 1091 cm^{-1}; mp: 100~101°C; HRMS (CI) calcd for $C_{15}H_{15}NO_2$+H $(M+H)^+$ 242.1181. Found: 242.1172.

Methyl *N*-(1-biphenylprop-2-enyl)carbamate (3f) and methyl *N*-(3-biphenylprop-2-enyl)carbamate (4f)

The above general procedure was followed using 1-

biphenyl-1-methoxyprop-2-ene (**2f**) (0.10 g, 0.45 mmol), Na_2CO_3 (0.11 g, 1.00 mmol) and CSI (58 μL, 0.67 mmol) in CH_2Cl_2 (2 mL) at -78°C. The reaction mixture was purified by column chromatography (*n*-Hexane/EtOAc = 6:1) to give 17 mg (14%) of methyl *N*-(1-biphenylprop-2-enyl) carbamate (**3f**) as a white solid and 81 mg (68%) of methyl *N*-(3-biphenylprop-2-enyl)carbamate (**4f**) as a white solid. **3f**: R_f: 0.33 (3:1 *n*-Hexane/EtOAc); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 3.72 (s, 3H), 5.02-5.09 (br, 1H), 5.25 (dd, 1H, *J* = 17.0, 1.5 Hz), 5.27 (dd, 1H, *J* = 10.5, 1.5 Hz), 5.38-5.42 (br, 1H), 6.06 (ddd, 1H, *J* = 17.0, 10.5, 6.5 Hz), 7.34-7.47 (m, 1H), 7.43-7.47 (m, 4H), 7.57-7.60 (m, 4H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 52.39, 57.23, 116.20, 127.61, 127.71, 127.76, 129.06, 137.76, 139.96, 140.93, 141.83, 156.90; IR (CH_2Cl_2): 3413, 3029, 2924, 1703, 1515, 1486, 1407, 1240, 1077, 1037 cm^{-1}; mp: 96~99°C; HRMS (CI) calcd for $C_{17}H_{17}NO_2$+H $(M+H)^+$ 268.1338. Found: 268.1346. **4f**: R_f: 0.27 (3:1 *n*-Hexane/EtOAc); ^{1}H-NMR (500 MHz, $CDCl_3$): 3.72 (s, 3H), 4.00 (dd, 2H, *J* = 6.0, 5.0 Hz), 4.80-4.86 (br, 1H), 6.25 (dt, 1H, *J* = 16.0, 6.0 Hz), 6.57 (d, 1H, *J* = 16.0 Hz), 7.33 (m, 1H), 7.41-7.46 (m, 4H), 7.55-7.61 (m, 4H); ^{13}C-NMR (125 MHz, $CDCl_3$): 43.45, 52.52, 126.26, 127.08, 127.19, 127.53, 127.61, 129.06, 131.51, 135.81, 140.71, 140.86, 157.21; IR (CH_2Cl_2): 3324, 3055, 1693, 1538, 1487, 1371, 1264, 1195, 1155, 1057 cm^{-1}; mp: 149~150°C; HRMS (CI) calcd for $C_{17}H_{17}NO_2$+H $(M+H)^+$ 268.1338. Found: 268.1329.

Methyl *N*-(3-*p*-methylphenylprop-2-enyl)carbamate (4g)

The above general procedure was followed using 1-methoxy-3-*p*-methylphenylprop-2-ene (**1g**) (0.20 g, 1.23 mmol), Na_2CO_3 (0.29 g, 2.77 mmol) and CSI (0.16 mL, 1.85 mmol) in CH_2Cl_2(5 mL) at -78°C. The reaction mixture was purified by column chromatography (*n*-Hexane/EtOAc = 6:1) to give 0.22 g (87%) of methyl *N*-(3-*p*-methylphenylprop-2-enyl)carbamate (**4g**) as a white solid. R_f: 0.33 (3:1 *n*-Hexane/EtOAc); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 2.34 (s, 3H), 3.70 (s, 3H), 3.96 (dd, 2H, *J* = 6.5, 5.5 Hz), 4.78-4.85 (br, 1H), 6.15 (dt, 1H, *J* = 16.0, 6.5 Hz), 6.49 (d, 1H, *J* = 16.0 Hz), 7.12 (d, 2H, *J* = 8.0 Hz), 7.26 (d, 2H, *J* = 8.0 Hz); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 21.46, 43.46, 52.47, 125.07, 126.54, 129.54, 131.89, 133.99, 137.80, 157.21; IR (CH_2Cl_2): 3318, 2949, 1690, 1544, 1436, 1369, 1298, 1258, 1155, 1056 cm^{-1}; mp: 83~85°C; HRMS (CI) calcd for $C_{12}H_{15}NO_2$+H $(M+H)^+$ 206.1181. Found: 206.1179.

Methyl *N*-(3-*p*-methoxyphenylprop-2-enyl)carbamate (4h)

The above general procedure was followed using 1-methoxy-3-*p*-methoxyphenylprop-2-ene (**1h**) (0.20 g, 1.12 mmol), Na_2CO_3 (0.27 g, 2.52 mmol) and CSI (0.15 mL, 1.68 mmol) in CH_2Cl_2 (4 mL) at -78°C. The reaction mixture was purified by column chromatography (*n*-Hexane/EtOAc = 3:1) to give 0.15 g (62%) of methyl *N*-(3-*p*-methoxyphenylprop-2-enyl)carbamate (**4h**) as a white solid. R_f: 0.24 (3:1 *n*-Hexane/EtOAc); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 3.69 (s, 3H), 3.80 (s, 3H), 3.94 (dd, 2H, *J* = 6.5, 4.5 Hz), 4.82-4.90 (br, 1H), 6.07 (dt, 1H, *J* = 16.0, 6.5 Hz), 6.45 (d, 1H, *J* = 16.0 Hz), 6.84 (d, 2H, *J* = 7.0 Hz), 7.29 (d, 2H, *J* = 7.0 Hz); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 43.95, 52.92, 55.98, 114.68, 124.29, 128.26, 129.99, 131.99, 157.64, 159.97; IR (CH_2Cl_2): 3327, 2960, 2851, 1693, 1537, 1510, 1461, 1377, 1279, 1246 cm^{-1}; mp: 104~106°C; HRMS (CI) calcd for $C_{12}H_{15}NO_3$+H $(M+H)^+$ 222.1130. Found: 222.1132.

Methyl *N*-[3-(3,4-dimethoxyphenyl)prop-2-enyl]carbamate (4i)

The above general procedure was followed using 3-(3, 4-dimethoxyphenyl)-1-methoxyprop-2-ene (**1i**) (0.20 g, 0.96 mmol), Na_2CO_3 (0.23 g, 2.16 mmol) and CSI (0.13 mL, 1.44 mmol) in CH_2Cl_2 (4 mL) at -78°C. The reaction mixture was purified by column chromatography (*n*-Hexane/EtOAc = 2:1) to give 57 mg (24%) of methyl *N*-[3-(3,4-dimethoxyphenyl) prop-2-enyl]carbamate (**4i**) as a white solid. R_f: 0.20 (2:1 *n*-Hexane/EtOAc); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 3.69 (s, 3H), 3.86 (s, 3H), 3.88 (s, 3H), 3.95 (dd, 2H, *J* = 6.0, 5.5 Hz), 4.83-4.90 (br, 1H), 6.06 (dt, 1H, *J* = 16.0, 6.0 Hz), 6.44 (d, 1H, *J* = 16.0 Hz), 6.80 (d, 1H, *J* = 7.5 Hz), 6.88 (d, 1H, *J* = 7.5 Hz), 6.90 (s, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 43.89, 52.90, 56.50, 56.59, 109.42, 111.77, 120.28, 124.64, 130.31, 132.21, 149.58, 149.51, 157.65; IR (CH_2Cl_2): 3360, 2947, 1709, 1517, 1255, 1155, 1022 cm^{-1}; mp: 53~54°C; HRMS (CI) calcd for $C_{13}H_{17}NO_4$+H $(M+H)^+$ 252.1236. Found: 252.1235.

RESULTS AND DISCUSSION

Our previous result showed that the CSI reaction of cinnamyl methyl ether (**1a**, R = H) produced methyl *N*-cinnamylcarbamate (**4a**, R = H) as a major product (1 : 2.7 ratio) at 20°C, and produced **4a** as an only product at 0°C. In the case of 1-phenylallyl methyl ether (**2a**, R = H) at 20°C, the result was similar to the case of **1a** (1 : 2.6 ratio). Accordingly, we examined the CSI reaction of **2a** at 0°C and -78°C. The results are summarized in Table I.

The treatment of 1-phenylallyl methyl ether (**2a**) with CSI at 0°C gave methyl *N*-cinnamylcarbamate (**4a**) as a major product (1 : 2.1 ratio) similar to the case of entry 1, except for the decrease in the ratio (entry 2). However, the CSI reaction at -78°C furnished an inversed product ratio (1.6:1) in favor of methyl *N*-(1-phenylallyl)carbamate (**3a**, R = H) (entry 3). The results of Table I showed that the regioselectivity increases as the temperature decreases.

Table I. Results of the reactions of 1-phenylallyl methyl ether (**2a**) with CSI at different temperature

	Temperature (°C)	Yield (%)	Ratio (**3a** : **4a**)
1	20	87	1 : 2.6
2	0	88	1 : 2.1
3	-78	81	1.6 : 1

Isolated yield of pure material.

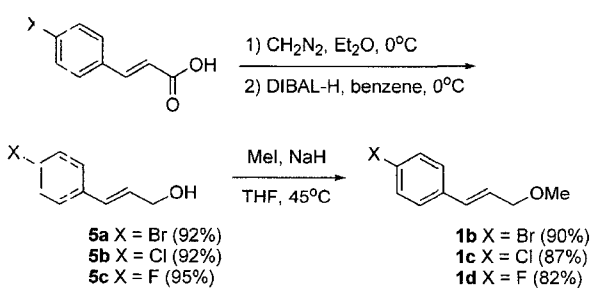
In order to observe the difference according to the resonance and the inductive effect, we examined the CSI reaction of various cinnamyl ethers *p*-substituted by halogens (strong electron-withdrawing (inductive effect) and weak electron-donating (resonance effect) group and nitro group), strong electron-withdrawing group. And, cinnamyl ethers *p*-substituted by alkyl group, weak electron-donating group and methoxy group, strong electron-donating group were tested.

Various *p*-halogencinnamyl methyl ethers were synthesized from the corresponding carboxylic acids. Esterification of acid by CH_2N_2, followed by the reduction with DIBAL-H, led to the corresponding alcohol **5**. The treatment of **5** with MeI gave methyl ether (Scheme 2).

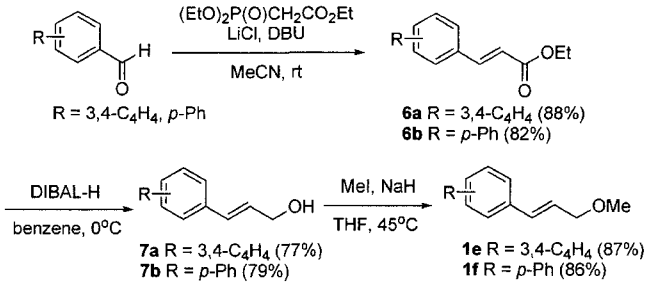
In the cases of 2-naphthyl and *p*-phenyl **1e** and **1f**, the HWE reaction of the corresponding aldehydes produced unsaturated esters. The reduction of ester and methylation afforded methyl ethers (Scheme 3).

The ethers substituted with methyl or methoxy were prepared by the similar method to the synthesis of *p*-halogen cinnamyl ether. For *p*-nitro compound **1j**, commercially available *p*-nitrocinnamyl alcohol was used (Scheme 4).

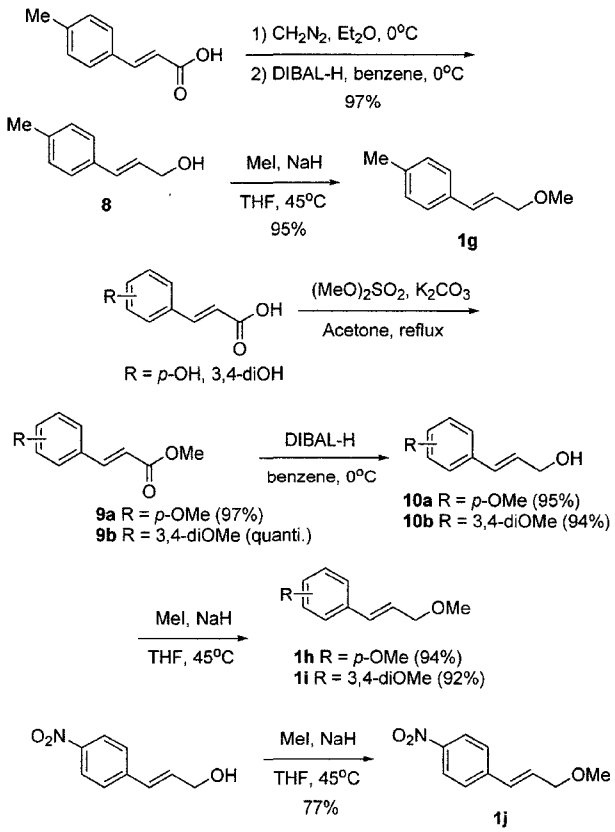
The reaction of *p*-bromocinnamyl methyl ether (**1b**) with CSI gave a 1:4.2 mixture of regioisomers in favor of the terminal allylic amine **4b** (entry 1). Also, in the case of *p*-chloro **1c** (Verlhac and Pereyre, 1990), the terminal allylic amine **4c** was obtained as a major product (entry 2). In the cases of cinnamyl ethers substituted by halogen, the terminal allylic amine increased than cinnamyl methyl ether (**1a**). With *p*-fluoro **1d**, the result was quite similar to that obtained in the cases of entries 1 and 2, except for the decrease in the ratio (entry 3). The results are



Scheme 2. Synthesis of *p*-halogencinnamyl methyl ethers



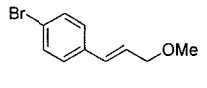
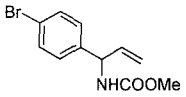
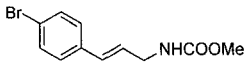
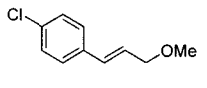
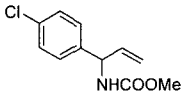
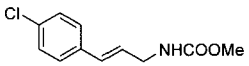
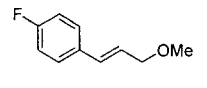
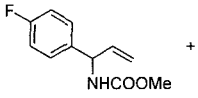
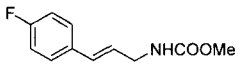
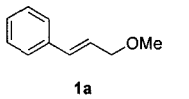
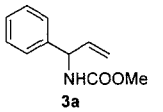
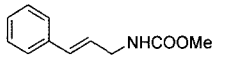
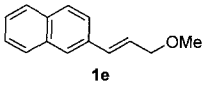
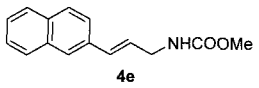
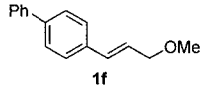
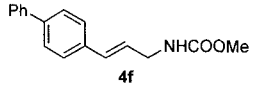
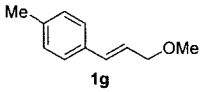
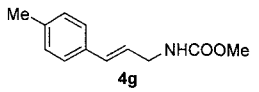
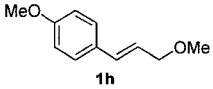
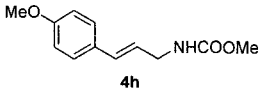
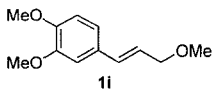
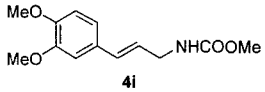
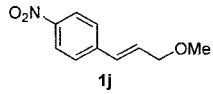
Scheme 3. Synthesis of *p*-substituted cinnamyl methyl ethers



Scheme 4. Synthesis of *p*-substituted cinnamyl methyl ethers

summarized in Table II. Next, we examined the reaction of cinnamyl ether substituted by the electron-donating group and obtained the unexpected results. The treatment of 3-(2-naphthyl)prop-2-enyl methyl ether (**1e**) with CSI gave only one product, methyl *N*-[3-(2-naphthyl)prop-2-enyl] carbamate (**4e**) in 78% chemical yield (entry 5). The similar results were obtained in the cases of *p*-phenyl and *p*-methyl substituted compounds **1f** and **1g** (entries 6 and 7). Also, methoxy substituted compounds **1h** (Verlhac and Pereyre, 1990) and **1i** produced only the terminal allylic amine with a decreased yield (entries 8 and 9). When the strong electron-withdrawing nitro group (Verlhac and Pereyre, 1990) was substituted, the reaction was not processed at all, because the formation of carbocation

Table II. Conversions of *p*-substituted cinnamyl methyl ethers to the corresponding carbamate

	Allyl Ethers	Allylic amines	Yield (%) ratio
1	 **1b**	 **3b** +  **4b**	75 1 : 4.2
2	 **1c**	 **3c** +  **4c**	77 1 : 3.5
3	 **1d**	 **3d** +  **4d**	85 1 : 2.2
4	 **1a**	 **3a** +  **4a**	88 1 : 2.7
5	 **1e**	 **4e**	78
6	 **1f**	 **4f**	77
7	 **1g**	 **4g**	87
8	 **1h**	 **4h**	62
9	 **1i**	 **4i**	24
10	 **1j**	No Reaction	

All the reactions were carried out at 20°C except for entries 5-9 (-78°C).
Isolated yield of pure material.
All yields and ratios were measured when the starting material disappeared (TLC monitoring).

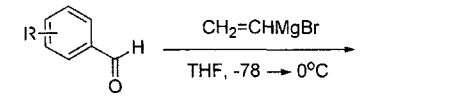
intermediate could not be occurred due to instability (entry 10).

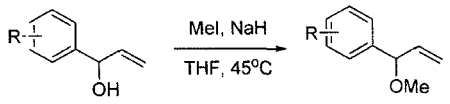
These results showed that the formation of the terminal allylic amine increased as the electron-withdrawing effect or the electron-donating effect of *p*-substituent increased.

We also investigated the regioselectivity in formation of allyl carbocation from 1-(*p*-substituted phenyl)allyl methyl ethers **2** by CSI reaction.

1-(*p*-Substituted phenyl)allyl methyl ethers were obtained from commercial available corresponding aldehyde by the Grignard reaction and methylation (Scheme 5).

As shown in Table III, the results of the reactions of 1-(*p*-substituted phenyl)allyl methyl ethers with CSI were much different to those in Table II. The treatment of 1-(*p*-bromophenyl)allyl ether (**2b**) with CSI furnished methyl *N*-[1-(*p*-bromophenyl)allyl]carbamate (**3b**) and methyl *N*-(*p*-bromocinnamyl)carbamate (**4b**) as a 4.7:1 mixture of regioisomers in 93% chemical yield (entry 1). In the cases of the *p*-chloro and *p*-fluoro substituted compounds **2c** and **2d**, the results were similar to that of *p*-chloro substituted one, except the decrease in the ratio (entries 2 and 3). However, in the cases of **2e** and **2f**, the terminal allylic amines were obtained as a major product (entries 5 and 6). Also, similar to the results in Table II, the CSI





11a R = *p*-Br (82%)
11b R = *p*-Cl (72%)
11c R = *p*-F (77%)
11d R = 3,4-C_4H_4 (81%)
11e R = *p*-Ph (83%)
11f R = *p*-Me (80%)
11g R = *p*-OMe (88%)

2b R = *p*-Br (84%)
2c R = *p*-Cl (92%)
2d R = *p*-F (92%)
2e R = 3,4-C_4H_4 (84%)
2f R = *p*-Ph (94%)
2g R = *p*-Me (95%)
2h R = *p*-OMe (85%)

Scheme 5. Synthesis of 1-(*p*-substituted phenyl)allyl methyl ethers

reaction of **2g** and **2h** afforded only one product, the terminal allylic amines **4g** and **4h** (entries 7 and 8).

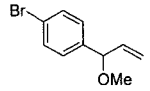
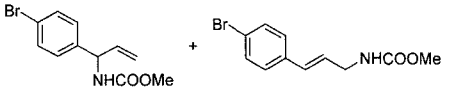
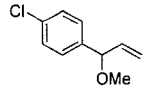
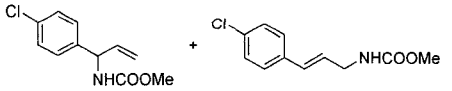
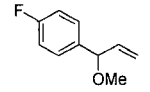
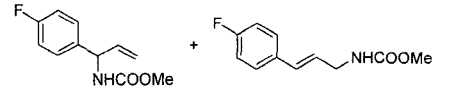
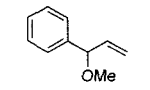
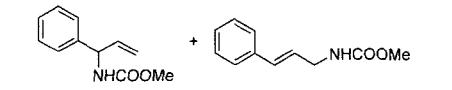
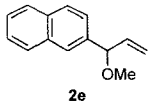
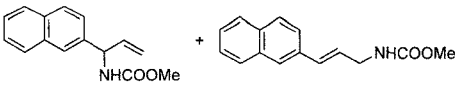
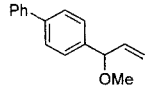
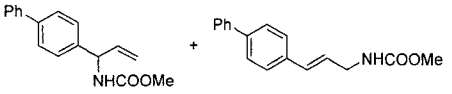
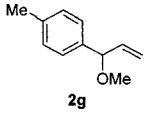
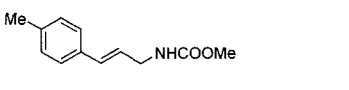
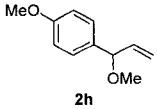
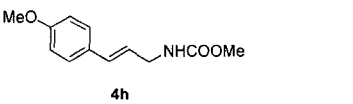
The results of Table III indicated that the internal allylic amine increases as the electron-withdrawing effect of *p*-substituent increases, and the terminal allylic amine increases as the electron-donating effect of *p*-substituent increases.

For additional experiments, we examined the CSI reaction of 1-(*p*-halogen phenyl)allyl ethers at 20°C. The results of the reactions at 20°C were similar to that obtained at -78°C, except for decrease in the ratio. Namely, the internal allylic amine was obtained as a major product. The results are summarized in Table IV.

From the results of Tables I-IV, we concluded that these reactions were not proceeding through the same allylic carbocation intermediate. Also we found that the regioselectivity in CSI reaction depends on the resonance effect and inductive effect of the *p*-substituent of phenyl ring.

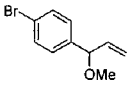
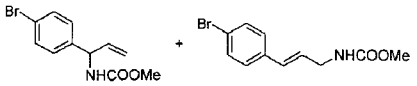
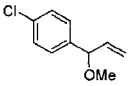
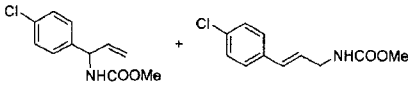
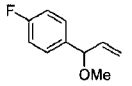
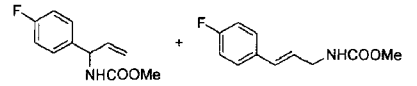
During the study of *p*-substituent on regioselectivity, we found by chance that the formation of the terminal allylic

Table III. Conversions of 1-(*p*-substituted phenyl)allyl methyl ethers to the corresponding carbamates at -78°C

	Allyl Ethers	Allylic amines	Yield (%) ratio
1	 **2b**	 **3b** + **4b**	93 4.7 : 1
2	 **2c**	 **3c** + **4c**	83 3.6 : 1
3	 **2d**	 **3d** + **4d**	89 2.4 : 1
4	 **2a**	 **3a** + **4a**	89 1.6 : 1
5	 **2e**	 **3e** + **4e**	80 1 : 4.6
6	 **2f**	 **3f** + **4f**	82 1 : 4.8
7	 **2g**	 **4g**	83
8	 **2h**	 **4h**	58

Isolated yield of pure material.
All yields and ratios were measured when the starting material disappeared (TLC monitoring).

Table IV. Conversions of 1-(*p*-substituted phenyl)allyl methyl ethers to the corresponding carbamates at 20°C

	Allyl Ethers	Allylic amines	Yield (%) ratio
1	 **2b**	 **3b** + **4b**	88 1.9 : 1
2	 **2c**	 **3c** + **4c**	81 1.3 : 1
3	 **2d**	 **3d** + **4d**	83 1 : 1

Isolated yield of pure material.
All yields and ratios were measured when the starting material disappeared (TLC monitoring).

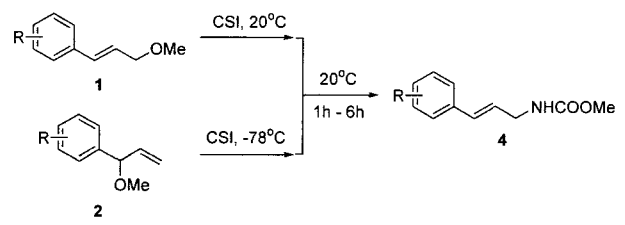
amine increases as the reaction time is prolonged at the same reaction conditions. Therefore, we investigated these reactions more precisely (Scheme 6).

The terminal allyl ethers **1** or internal ones **2** were treated with CSI at 20°C or -78°C respectively. After disappearing of starting materials, the reaction mixtures were continued to react at 20°C until the internal allylic carbamates disappeared.

As shown in Table V, in all the cases of ethers substituted by the electron-withdrawing group or by the electron-donating group, the terminal allylic carbamates were formed as the only product and the reaction time depended on the *p*-substituent of phenyl ring.

As above, we ascertained that the regioselectivity depends on *p*-substituent of phenyl ring. As the electron-withdrawing power of *p*-substituent increases, the ratio of the substitution occurred where the alkoxy moiety was attached increases. Also, as the electron-donating power of *p*-substituent increases, the proportion of the terminal allylic amine increases. These results can be explained by the stability of carbocation intermediate through the S_Ni mechanism (March, 1992; Sykes, 1986) and S_N1 mechanism (Sykes, 1986) (Fig. 1).

In the case of the ethers substituted by the electron-withdrawing group on phenyl ring, the unstable carbocation intermediate is formed and is rapidly attacked by the nucleophile before the formation of the allylic carbocation hybrid. On the other hand, the stable carbocation intermediate formed in the case of the electron-donating substituted compounds is rapidly converted to the stable allylic carbocation hybrid, and then the terminal allylic amine is formed due to the steric hindrance of the phenyl ring and the formation of a stable conjugated product. Namely, the less stable the carbocation intermediate is, the greater is the proportion of S_Ni mechanism. And, the more stable the carbocation intermediate is, the proportion of the S_N1 mechanism increases.



Scheme 6. Migration of the internal amines to the terminal amines

Table V. Migration of the internal amines to the terminal amines

	Allyl Ethers	Reaction Time	Yield (%) (**4**)
1	**1b**	3 h	74
2	**1c**	3 h	73
3	**1e**	3 h	77
4	**1a**	2 h	77
5	**2b**	6 h	79
6	**2c**	6 h	74
7	**2d**	5 h	76
8	**2a**	4 h	73
9	**2e**	1 h	78
10	**2f**	1 h	74

Isolated yield of pure material.

From these results, we found that the reaction of ethers with CSI proceeded through both the S_Ni and S_N1 mechanism, and the ratio depends on the stability of carbocation intermediate.

Next, one plausible mechanism for the migration of the internal allylic amine to the terminal allylic amine is shown

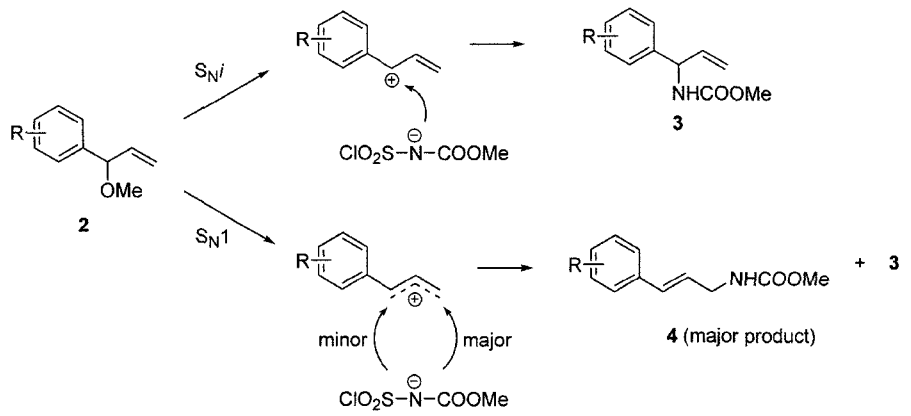


Fig. 1. S_Ni and S_N1 mechanism of the CSI reaction

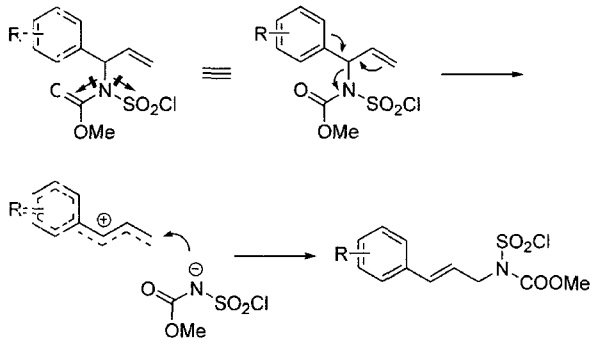


Fig. 2. Possible mechanism for the migration of the internal allylic amine to the terminal allylic amine

in Fig. 2. The carbon and nitrogen bond in the internal allylic carbamate can be easily cleaved to afford the stable carbocation because the *N*-sulfonylcarbamate has a good leaving group, $ClSO_2$-*N*-CO_2Me. And then, the nitrogen anion attacks the terminal carbon to form the terminal allylic carbamate due to the stability of the conjugated product. This migration reaction does not occurred after the desulfonylation.

Therefore, in the case of allyl ether substituted by the electron-donating group, the result that the terminal allylic amine was obtained as a major product can be explained by this migration mechanism.

In conclusion, with the CSI reactions of *p*-substituted ethers, we confirmed that our CSI reaction is a competitive reaction of S_Ni and S_N1 mechanism according to the stability of the carbocation. And, the only terminal allylic amine was obtained through the migration reaction in thermodynamic reaction condition.

ACKNOWLEDGEMENT

This work was supported by grant No. (R01-2002-000-00005-0) from the Basic Research Program of the Korea Science & Engineering Foundation.

REFERENCES

Barluenga, J., Faans, F. J., Sanz, R., Marcos, C., and Trabada, M., On the reactivity of *o*-lithioaryl ethers: tandem anion translocation and wittig rearrangement. *Org. Lett.*, 4, 1587-1590 (2002).

Charetta, A. B., Molinaro, C., and Brochu, C., Catalytic asymmetric cyclopropanation of allylic alcohols with titanium-TADDOLate: Scope of the cyclopropanation reaction. *J. Am. Chem. Soc.*, 123, 12168-12175 (2001).

Jung, Y. H. and Kim, J. D., One-pot synthesis of cinnamylamines with various protecting groups from cinnamyl ethers. *Arch. Pharm. Res.*, 24, 371-376 (2001).

Jung, Y. H. and Kim, J. D., A Novel synthetic methods for α-amino acids from allyl ethers *via* *N*-allylcarbamates. *Arch. Pharm. Res.*, 23, 574-578 (2000).

Kim, J. D., Han, G., Jeong, L. S., Park, H. -J., Zee, O. P., and Jung, Y. H., Study of the stability of carbocations by chlorosulfonyl isocyanate reaction with ethers. *Tetrahedron*, 58, 4395-4402 (2002).

Kim, J. D., Han, G., Zee, O. P., and Jung, Y. H., Deprotection of benzyl and *p*-methoxybenzyl ethers by chlorosulfonyl isocyanate-sodium hydroxide. *Tetrahedron Lett.*, 44, 733-735 (2003).

Kim, J. D., Lee, M. H., Han, G., Park, H., Zee, O. P., and Jung, Y. H., Synthesis of *N*-protected allylic amines from allyl ethers. *Tetrahedron*, 57, 8257-8266 (2001).

Kim, J. D., Lee, M. H., Lee, M. J., and Jung, Y. H., Novel synthetic method for *N*-Allylcarbamates from allyl ethers using chlorosulfonyl isocyanate. *Tetrahedron Lett.*, 41, 5073-5076 (2000).

Kim, J. D., Zee, O. P., and Jung, Y. H., Regioselective and diastereoselective allylic amination using chlorosulfonyl isocyanate. A novel asymmetric synthesis of unsaturated aromatic 1,2-amino alcohols. *J. Org. Chem.*, 68, 3721-3724 (2003).

Kuroboshi, M., Tanaka, M., Kishimoto, S., Goto, K., Takana, H., and Torii, S., Ni/Cr/Al Multi-metal redox-mediated alkeny-

lation of aldehydes. *Tetrahedron Lett.*, 40, 2785-2788 (1999).
March, J., Advanced Organic Chemistry (4th). John Wiley & Sons Inc., New York. pp. 326-327, (1992).
Ponpipom, M. M., Yue, B. Z., Bugianesi, B. L., Brooker, D. R., Chang, M. N., and Shen, T. Y., Total synthesis of kadsurenone and its analogs. *Tetrahedron Lett.*, 27, 309-312 (1986).
Sykes, P., A Guidebook to Mechanism in Organic Chemistry (6th). Longman Scientific & Technical. pp. 90-93, (1986).
Verlhac, J. -B. and Pereyre, M., Organotin homoenolate equivalents-access to β-acyl- and β-aryl-propionaldehydes through heterosubstituted allyltins and vinyltins. *Tetrahedron,* 46, 6399-6412 (1990).