

**Practical and Convenient Synthesis of N-Heterocycles:
Stereoselective Cyclization of *N*-Alkenylamide with *t*-BuOI under Neutral Conditions**

Supporting Information

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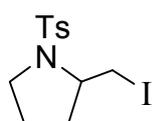
Experimental Procedures

General Methods.

Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. IR spectra were obtained on a Jasco FT/IR-410 infrared spectrophotometer. ¹H and ¹³C-NMR spectra were recorded on a JEOL FT-NMR JNM EX 270 spectrometer (¹H-NMR, 270 MHz; ¹³C-NMR, 68 MHz) using tetramethylsilane as an internal standard. Mass spectra were measured with a Shimadzu Model GCMS-QP5000 spectrometer. High-resolution mass spectral data were obtained on a JEOL DX-303 mass spectrometer. Elemental analyses were performed at the Analytical Center, Faculty of Engineering, Osaka University. Flash column chromatography (FCC) was performed using silica gel FL60D (Fuji Silysia Chemical Co.). Preparative gel permeation liquid chromatography (GPLC) was performed on a JAI (Japan Analytical Industry) LC-908 instrument with JAIGEL 1H-2H columns and chloroform as an eluent. Analytical thin layer chromatography was performed using EM reagent 0.25 mm silica gel 60-F plates. Visualization was accomplished with UV light and spraying with an ethanolic phosphomolybdic acid solution followed by heating.

Synthesis of 2-Iodomethyl-1-(*p*-toluenesulfonyl)pyrrolidine (**2a**).

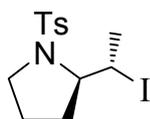
To a mixture of **1a** (111 mg, 0.46 mmol) and NaI (75 mg, 0.50 mmol) in MeCN (3 mL) was added *t*-BuOCl (54 mg, 0.50 mmol). The mixture was allowed to stir in the dark at room temperature for 5 h under an atmosphere of nitrogen. The solvent was evaporated and the residue was purified by flash column chromatography on silica gel (eluent: hexane/ethyl acetate = 9/1) to afford 166 mg (98%) of **2a**.



Spectroscopic data were in agreement with those for previously published material.¹

colorless crystalline solid; TLC R_f 0.24 (hexane/EtOAc, 4:1); ¹H NMR (CDCl₃, 270 MHz) δ 1.50-1.59 (m, 1H, -NCHCHHCH₂-), 1.75-1.92 (m, 3H, -NCHCHHCH₂-), 2.44 (s, 3H, ArCH₃), 3.14-3.25 (m, 2H, -CHHI, -CH₂CHHN-), 3.45-3.53 (m, 1H, -CH₂CHHN-), 3.62 (dd, 1H, $J = 3.0, 9.7$ Hz, -CHHI), 3.70-3.79 (m, 1H, -CHCH₂I), 7.33 (d, 2H, $J = 8.4$ Hz, ArH), 7.73 (d, 2H, $J = 8.4$ Hz, ArH).

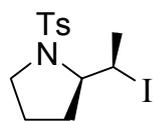
threo-2-(1-Iodoethyl)-1-(*p*-toluenesulfonyl)pyrrolidine (**2b**).



A mixture of **1b** (126 mg, 0.50 mmol), NaI (75 mg, 0.50 mmol), and *t*-BuOCl (55 mg, 0.51 mmol) in MeCN (3 mL) was stirred at room temperature for 5 h to afford 170 mg (90%) of **2b**.

Spectroscopic data were in agreement with those for previously published material.¹ colorless crystalline solid; TLC R_f 0.29 (hexane/EtOAc, 4:1); ¹H NMR (CDCl₃, 270 MHz) δ 1.33-1.43 (m, 1H, -NCHCHHCH₂-), 1.78-1.93 (m, 3H, -NCHCHHCH₂CH₂-), 1.87 (d, 3H, $J = 7.0$ Hz, -CH(CH₃)I), 2.44 (s, 3H, ArCH₃), 3.10-3.17 (m, 1H, -NCHCH(CH₃)I), 3.34-3.39 (m, 2H, -CH₂CH₂N-), 4.71-4.81 (m, 1H, -CH(CH₃)I), 7.32 (d, 2H, $J = 8.3$ Hz, ArH), 7.74 (d, 2H, $J = 8.3$ Hz, ArH).

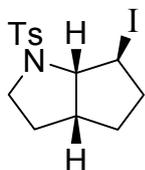
***erythro*-2-(1-Iodoethyl)-1-(*p*-toluenesulfonyl)pyrrolidine (**2c**).**



A mixture of **1c** (127 mg, 0.51 mmol), NaI (78 mg, 0.52 mmol), and *t*-BuOCl (58 mg, 0.54 mmol) in MeCN (3 mL) was stirred at room temperature for 5 h to afford 195 mg (100%) of **2c**.

Spectroscopic data were in agreement with those for previously published material.¹ colorless crystalline solid; TLC R_f 0.29 (hexane/EtOAc, 4:1); ¹H NMR (CDCl₃, 270 MHz) δ 1.35-1.44 (m, 1H, -NCHCHHCH₂-), 1.68-2.07 (m, 3H, -NCHCHHCH₂CH₂-), 1.83 (d, 3H, J = 7.0 Hz, -CH(CH₃)I) 2.45 (s, 3H, ArCH₃), 3.27-3.39 (m, 1H, -CH₂CHHN-), 3.44-3.53 (m, 1H, -CH₂CHHN-), 3.99 (m, 1H, -CHCH(CH₃)I), 4.75 (dq, 1H, J = 3.8, 7.0 Hz, -CHCH(CH₃)I), 7.34 (d, 2H, J = 8.2 Hz, ArH), 7.72 (d, 2H, J = 8.2 Hz, ArH).

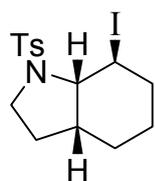
6-Iodo-4-(*p*-toluenesulfonyl)-4-azabicyclo[3.3.0]octane (2d**).**



A mixture of **1d** (133 mg, 0.50 mmol), NaI (78 mg, 0.52 mmol), and *t*-BuOCl (54 mg, 0.50 mmol) in MeCN (3 mL) was stirred at room temperature for 5 h to afford 188 mg (96%) of **2d**.

Spectroscopic data were in agreement with those for previously published material.¹ colorless crystalline solid; TLC R_f 0.27 (hexane/EtOAc, 4:1); ¹H NMR (CDCl₃, 270 MHz) δ 1.47-1.56 (m, 2H, -NCHCH(I)CH₂CHHCHCHHCH₂-), 1.66-1.78 (m, 1H, -NCHCH(I)CH₂CH₂CHCHHCH₂-), 1.95-2.27 (m, 3H, -NCHCH(I)CH₂CHHCH-), 2.44 (s, 3H, ArCH₃), 2.69-2.78 (m, 1H, -CH(I)CH₂CH₂CH-), 3.00 (dt, 1H, J = 7.2, 10.1 Hz, -CHCH₂CHHN-), 3.45 (dt, 1H, J = 5.9, 10.1 Hz, -CHCH₂CHHN-), 4.02 (d, 1H, J = 7.6 Hz, -NCHCHI-), 4.81 (d, 1H, J = 3.8 Hz, -CHI-), 7.35 (d, 2H, J = 8.4 Hz, ArH), 7.72 (d, 2H, J = 8.4 Hz, ArH).

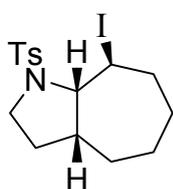
5-Iodo-7-(*p*-toluenesulfonyl)-7-azabicyclo[4.3.0]nonane (2e).



A mixture of **1e** (135 mg, 0.48 mmol), NaI (75 mg, 0.50 mmol), and *t*-BuOCl (55 mg, 0.51 mmol) in MeCN (3 mL) was stirred at room temperature for 5 h to afford 184 mg (94%) of **2e**.

Spectroscopic data were in agreement with those for previously published material.¹ white solid; TLC R_f 0.30 (hexane/EtOAc, 4:1); ¹H NMR (CDCl₃, 270 MHz) δ 1.26-1.78 (m, 6H, -NCHCH(I)CH₂CH₂CH₂CHCH₂CH₂-), 1.90-1.95 (m, 2H, -NCHCH(I)CH₂CH₂-), 2.39-2.45 (m, 1H, -CH(I)CH₂CH₂CH₂CH-), 2.45 (s, 3H, ArCH₃), 3.44-3.60 (m, 2H, -CHCH₂CH₂N-), 3.65 (dd, 1H, $J = 4.3, 4.3$ Hz, -NCHCH(I)-), 5.25 (m, 1H, -NCHCH(I)-), 7.36 (d, 2H, $J = 8.4$ Hz, ArH), 7.71 (d, 2H, $J = 8.4$ Hz, ArH).

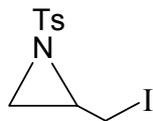
(1*SR*,6*RS*,7*RS*)-6-Iodo-8-(*p*-toluenesulfonyl)-8-azabicyclo[5.3.0]decane (2f).



A mixture of **1f** (147 mg, 0.50 mmol), NaI (75 mg, 0.50 mmol), and *t*-BuOCl (56 mg, 0.52 mmol) in MeCN (3mL) was stirred at room temperature for 5 h to afford 203 mg (97%) of **2f**.

Spectroscopic data were in agreement with those for previously published material.¹ colorless crystalline solid; TLC R_f 0.34 (hexane/EtOAc, 4:1); ¹H NMR (CDCl₃, 270 MHz) δ 1.43-1.80 (m, 7H, -NCHCH(I)CH₂CH₂CH₂CHHCHCH₂CH₂-), 1.90-1.95 (m, 2H, -NCHCH(I)CH₂CH₂-), 2.05-2.17 (m, 1H, -CH(I)CH₂CH₂CH₂CHHCH-), 2.21-2.34 (m, 1H, -CH(I)CH₂CH₂CH₂CH₂CHCH₂-), 2.44 (s, 3H, ArCH₃), 3.14 (dt, 1H, $J = 7.3, 10.4$ Hz, -CHCH₂CHHN-), 3.51 (dt, 1H, $J = 6.3, 10.4$ Hz, -CHCH₂CHHN-), 4.06 (dd, 1H, $J = 4.1, 8.5$ Hz, -NCHCH(I)-), 5.21 (ddd, 1H, $J = 4.1, 4.3, 4.3$ Hz, -NCHCH(I)CH₂-), 7.34 (d, 2H, $J = 8.4$ Hz, ArH), 7.73 (d, 2H, $J = 8.4$ Hz, ArH).

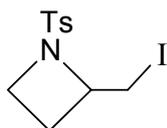
2-Iodomethyl-1-(*p*-toluenesulfonyl)aziridine (**2g**).



A mixture of **1g** (106 mg, 0.50 mmol), NaI (91 mg, 0.60 mmol), and *t*-BuOCl (65 mg, 0.60 mmol) in MeCN (3 mL) was stirred at room temperature for 24 h to afford 164 mg (97%) of **2g**.

Spectroscopic data were in agreement with those for previously published material.² colorless solid; TLC R_f 0.23 (hexane/EtOAc, 4:1); ¹H NMR (CDCl₃, 270 MHz) δ 2.17 (d, 1H, $J = 3.2$ Hz, -NCHCHHN-), 2.46 (s, 3H, ArCH₃), 2.84 (d, 1H, $J = 6.5$ Hz, -NCHCHHN-), 3.02-3.12 (m, 3H, -NCHCH₂I), 7.36 (d, 1H, $J = 8.2$ Hz, ArH), 7.84 (d, 1H, $J = 8.2$ Hz, ArH).

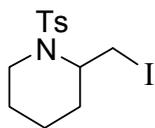
2-Iodomethyl-1-(*p*-toluenesulfonyl)azetizine (**2h**).



A mixture of **1h** (110 mg, 0.49 mmol), NaI (98 mg, 0.65 mmol), and *t*-BuOCl (75 mg, 0.69 mmol) in MeCN (3 mL) was stirred at room temperature for 24 h to afford 47 mg (97%) of **2h**.

colorless crystalline solid; mp. 101 °C; TLC R_f 0.25 (hexane/EtOAc, 4:1); IR (KBr) 2922, 1336, 1159 cm⁻¹; ¹H NMR (CDCl₃, 270 MHz) δ 1.85-1.99 (m, 1H, -NCHCHHCH₂-), 2.03-2.13 (m, 1H, -NCHCHHCH₂-), 2.47 (s, 3H, ArCH₃), 3.28 (dd, 1H, $J = 9.8, 9.9$ Hz, -CHHI), 3.43 (dt, 1H, $J = 8.3, 8.4$ Hz, -CH₂CHHN-), 3.55 (dd, 1H, $J = 3.5, 9.8$ Hz, -CHHI), 3.65 (dt, 1H, $J = 3.8, 8.3$ Hz, -CH₂CHHN-), 3.89-4.00 (m, 1H, -CHCH₂I), 7.38 (d, 2H, $J = 8.2$ Hz, ArH), 7.72 (d, 2H, $J = 8.2$ Hz, ArH); ¹³C NMR (CDCl₃, 68 MHz) δ 9.8, 21.7, 24.1, 45.9, 62.9, 128.2, 129.8, 131.7, 144.2; MS (EI) m/z (relative intensity, %) 351 (M⁺, 1), 210 (M⁺-CH₂I, 38), 155 (43), 91 (100); Anal. Calcd for C₁₁H₁₄INO₂S: C, 37.62; H, 4.02; N, 3.99. Found: C, 37.76; H, 4.00; N, 3.93.

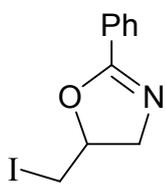
2-Iodomethyl-1-(*p*-toluenesulfonyl)piperidine (**2i**).



A mixture of **1i** (128 mg, 0.51 mmol), NaI (90 mg, 0.60 mmol), and *t*-BuOCl (67 mg, 0.62 mmol) in MeCN (6 mL) was stirred at room temperature for 24 h to afford 153 mg (79%) of **2i**.

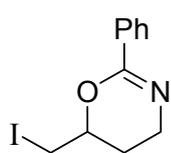
Spectroscopic data were in agreement with those for previously published material.¹ colorless oil; TLC R_f 0.34 (hexane/EtOAc, 4:1); ¹H NMR (CDCl₃, 270 MHz) δ 1.26-1.50 (m, 5H, -NCHCHHCH₂CH₂CH₂-), 2.04-2.11 (m, 1H, -NCHCHHCH₂-), 2.43 (s, 3H, ArCH₃), 2.95 (dt, 1H, $J = 2.1, 14.1$ Hz, -CH₂CH₂CHHN-), 3.23 (dd, 1H, $J = 5.4, 10.1$ Hz, -CHHI), 3.36 (dd, 1H, $J = 10.1, 10.1$ Hz, -CHHI), 3.71 (dd, 1H, $J = 3.5, 14.1$ Hz, -CH₂CH₂CHHN-), 4.24-4.28 (m, 1H, -NCHCH₂I), 7.30 (d, 2H, $J = 8.1$ Hz, ArH), 7.72 (d, 2H, $J = 8.1$ Hz, ArH).

5-Iodomethyl-2-phenyl-2-oxazoline (**7a**).



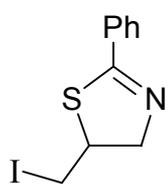
A mixture of **6a** (81 mg, 0.50 mmol), NaI (83 mg, 0.55 mmol), and *t*-BuOCl (60 mg, 0.55 mmol) in MeCN (3 mL) was stirred at room temperature for 5 h to afford 137 mg (95%) of **7a**. colorless oil; TLC R_f 0.16 (hexane/EtOAc, 4:1); IR (neat) 2935, 2870, 1651, 1579, 1495, 1259, 1174, 1061 cm⁻¹; ¹H NMR (CDCl₃, 270 MHz) δ 3.29-3.42 (m, 2H, -CH₂I), 3.81 (dd, 1H, $J = 6.5, 15.1$ Hz, -NCHHCH-), 4.18 (dd, 1H, $J = 9.3, 15.1$ Hz, -NCHHCH-), 4.76-4.87 (m, 1H, -NCH₂CHCH₂I), 7.38-7.52 (m, 3H, ArH), 7.92-7.96 (m, 2H, ArH); ¹³C NMR (CDCl₃, 68 MHz) δ 7.8, 60.7, 78.2, 127.3, 128.0, 128.2, 131.3, 163.2; MS (EI) m/z (relative intensity, %) 287 (M⁺, 32), 160 (M⁺-I, 52), 146 (M⁺-CH₂I, 7); Anal. Calcd for C₁₀H₁₀INO: C, 41.83; H, 3.51; N, 4.88. Found: C, 41.84; H, 3.43; N, 4.87.

5,6-Dihydro-6-iodomethyl-2-phenyl-4*H*-1,3-oxazine(7b).



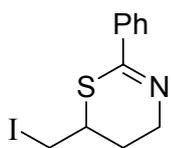
A mixture of **6b** (88 mg, 0.50 mmol), NaI (83 mg, 0.55 mmol), and *t*-BuOCl (61 mg, 0.56 mmol) in MeCN (3 mL) was stirred at room temperature for 24 h to afford 123 mg (82%) of **7b**. colorless oil; TLC R_f 0.13 (hexane/Et₂O, 1:1); IR (neat) 2927, 2856, 1655, 1579, 1493, 1277, 1126, 1068 cm⁻¹; ¹H NMR (CDCl₃, 270 MHz) δ 1.70-1.85 (m, 1H, -NCH₂CHHCH-), 2.13-2.20 (m, 1H, -NCH₂CHHCH-), 3.39 (d, 2H, J = 5.9 Hz, -CH₂I), 3.53-3.76 (m, 2H, -NCH₂CH₂-), 4.22-4.31 (m, 1H, -CHCH₂I), 7.26-7.46 (m, 3H, ArH), 7.93-7.96 (m, 2H, ArH); ¹³C NMR (CDCl₃, 68 MHz) δ 7.6, 27.4, 42.7, 73.7, 126.9, 128.0, 130.4, 133.2, 155.2; MS (EI) m/z (relative intensity, %) 301 (M⁺, 40); HRMS (EI) calcd for C₁₁H₁₂INO (M)⁺ 300.9964, found 300.9976.

5-Iodomethyl-2-phenyl-2-thiazoline (7c).



A mixture of **6c** (87 mg, 0.49 mmol), NaI (76 mg, 0.50 mmol), and *t*-BuOCl (54 mg, 0.50 mmol) in MeCN (3 mL) was stirred at room temperature for 5 h to afford 123 mg (77%) of **7c**. yellow oil; TLC R_f 0.37 (hexane/EtOAc, 4:1); IR (CHCl₃) 3018, 1606, 1578, 1491, 1215 cm⁻¹; ¹H NMR (CDCl₃, 270 MHz) δ 3.23 (dd, 1H, J = 10.0, 10.0 Hz, -CHHI), 3.35-3.41 (dd, 1H, J = 5.0, 10.0 Hz, -CHHI), 4.17-4.26 (m, 1H, -CHCH₂I), 4.27 (dd, 1H, J = 8.0, 18.0 Hz, -NCHHCH-), 4.62 (dd, 1H, J = 1.8, 18.0 Hz, -NCHHCH-), 7.38-7.51 (m, 3H, ArH), 7.79-7.83 (m, 2H, ArH); ¹³C NMR (CDCl₃, 68 MHz) δ 9.9, 51.5, 69.8, 128.4, 128.8, 131.4, 132.8, 166.3; MS (EI) m/z (relative intensity, %) 303 (M⁺, 2), 176 (M⁺-I, 25); Anal. Calcd for C₁₀H₁₀INS: C, 39.62; H, 3.32; N, 4.62. Found: C, 39.80; H, 3.27; N, 4.65.

5,6-Dihydro-6-iodomethyl-2-phenyl-4*H*-1,3-thiazine (7d).



A mixture of **6d** (97 mg, 0.51 mmol), NaI (83 mg, 0.55 mmol), and *t*-BuOCl (60 mg, 0.55 mmol) in MeCN (3 mL) was stirred at room temperature for 24 h to afford 72 mg (47%) of **7d**. yellow oil; TLC R_f 0.23 (hexane/EtOAc, 4:1); IR (CHCl₃) 2924, 1622, 1537 cm⁻¹; ¹H NMR (CDCl₃, 270 MHz) δ 1.66-1.79 (m, 1H, -NCH₂CHHCH-), 2.14-2.24 (m, 1H, -NCH₂CHHCH-), 3.32 (dd, 1H, J = 9.5, 10.0 Hz, -CHHI), 3.45 (dd, 1H, 4.8, 10.0 Hz, -CHHI), 3.61 (dddd, 1H, J = 4.8, 4.8, 9.5, 9.5 Hz, -CHCH₂I), 3.81 (ddd, J = 3.4, 8.4, 16.9 Hz, -NCHHCH₂-), 4.05 (ddd, 1H, J = 3.6, 6.9, 16.9 Hz, -NCHHCH₂-), 7.34-7.45 (m, 3H, ArH), 7.77 (d, 2H, J = 10.1 Hz, ArH); ¹³C NMR (CDCl₃, 68 MHz) δ 9.5, 26.1, 41.1, 47.2, 126.4, 128.3, 130.5, 138.6, 157.7; MS (EI) m/z (relative intensity, %) 317 (M⁺, 3), 190 (M⁺ - I, 27); Anal. Calcd for C₁₁H₁₂INS: C, 41.65; H, 3.81; N, 4.42. Found: C, 41.72; H, 3.63; N, 4.38.

Iodination Reaction: sulfonamide vs. olefin.

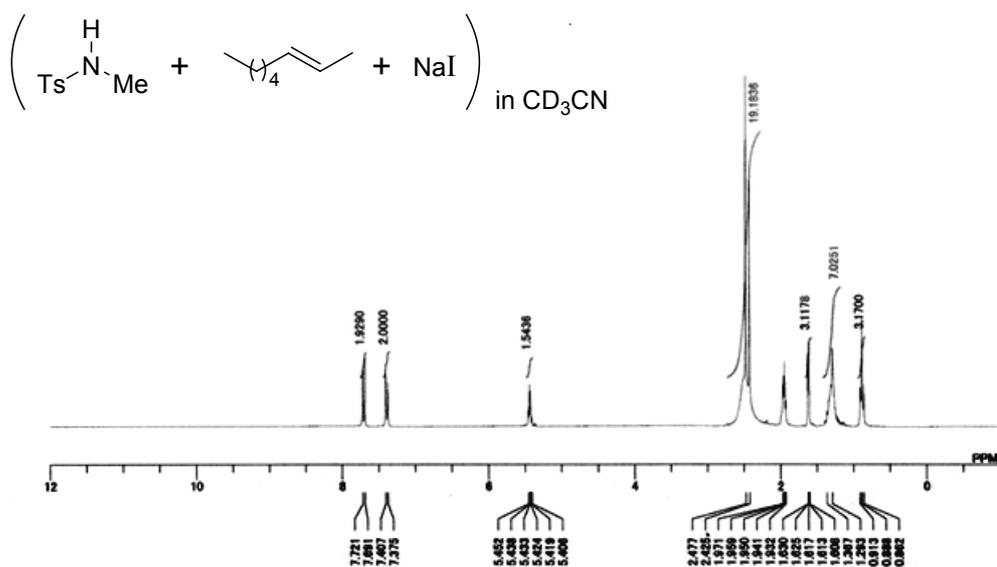


Figure SI-1. $^1\text{H-NMR}$ spectrum of *N*-methyl-*p*-toluenesulfonamide (0.02 mmol), *trans*-2-octene (0.02 mmol) and NaI (0.02 mmol) in CD_3CN (0.5 mL) at room temperature.

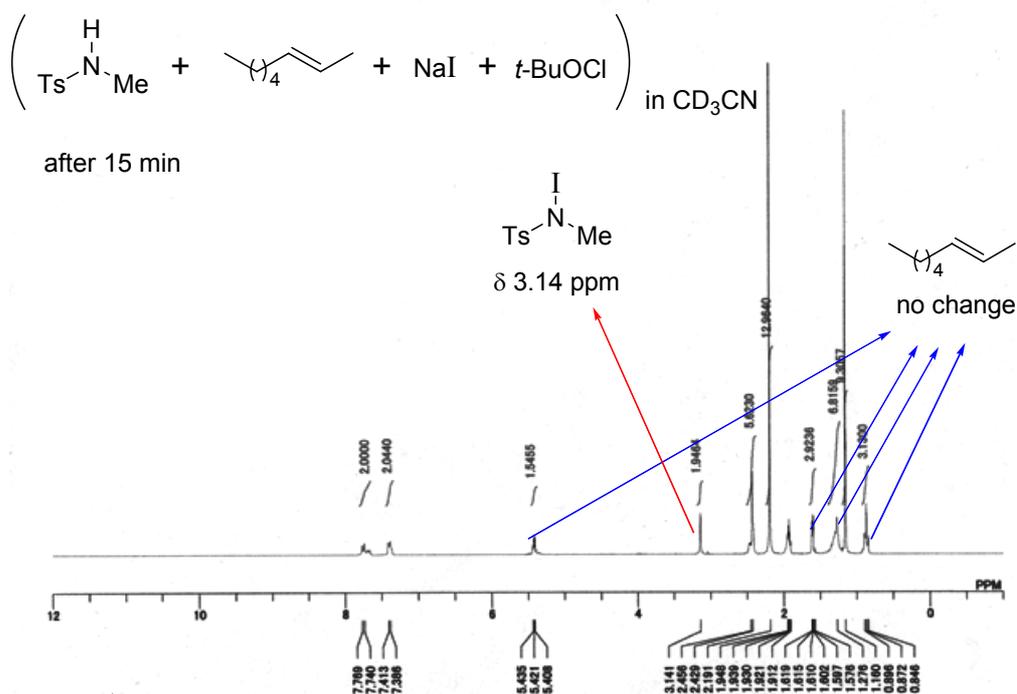
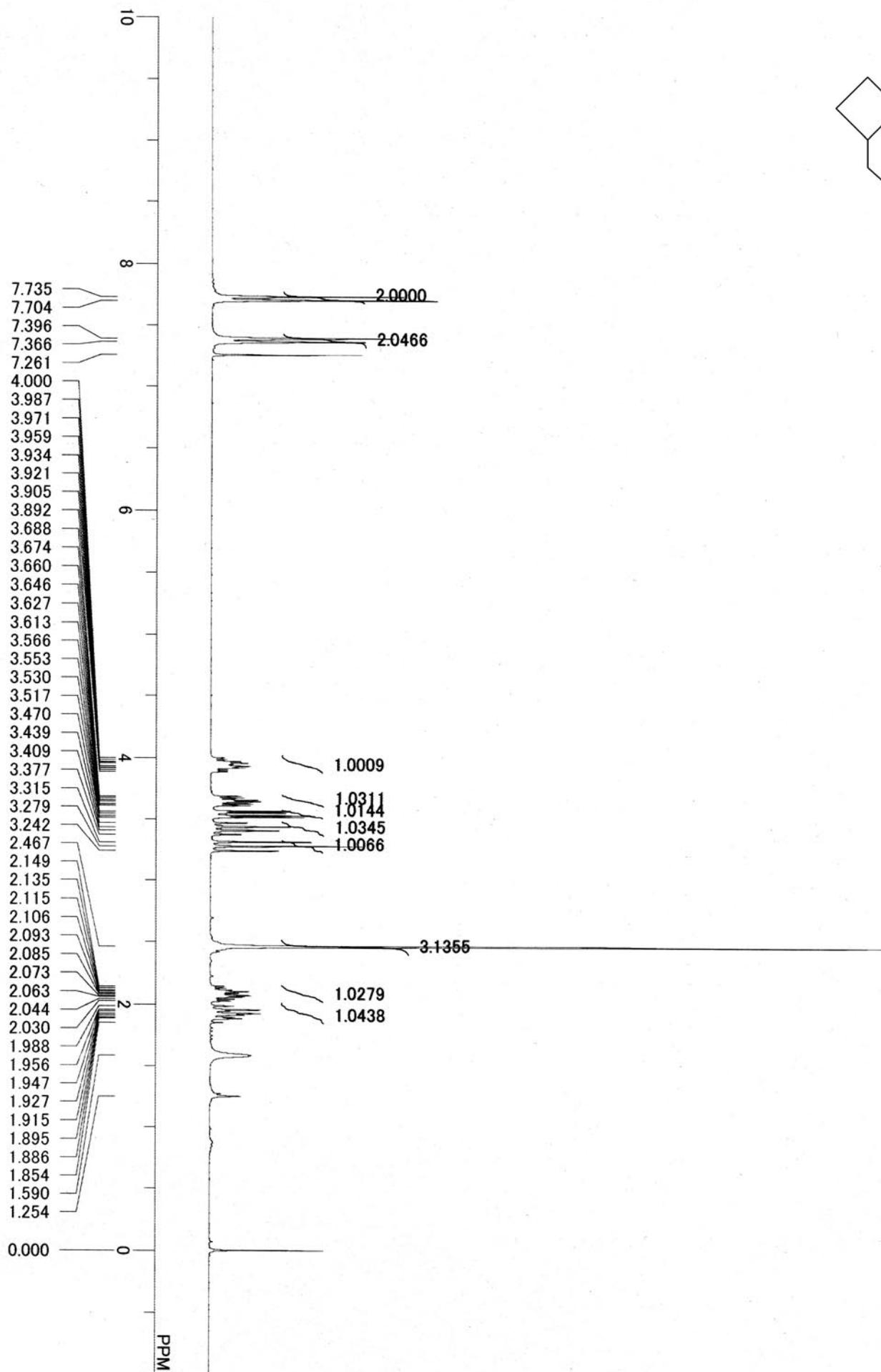
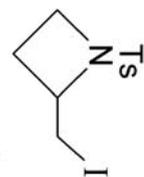


Figure SI-2. $^1\text{H-NMR}$ spectrum after treating the above mixture with *t*-BuOCl (0.02 mmol) in CD_3CN at room temperature.

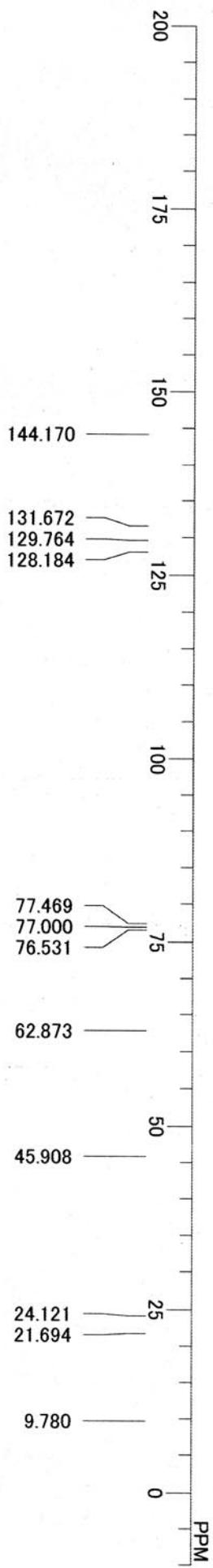
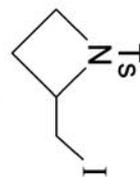
References

- (1) S. Minakata, D. Kano, Y. Oderaotoshi, M. Komatsu, *Org. Lett.* **2002**, *4*, 2097-2099.
- (2) O. Kitagawa, T. Suzuki, T. Taguchi, *J. Org. Chem.* **1998**, *63*, 4842-4845.

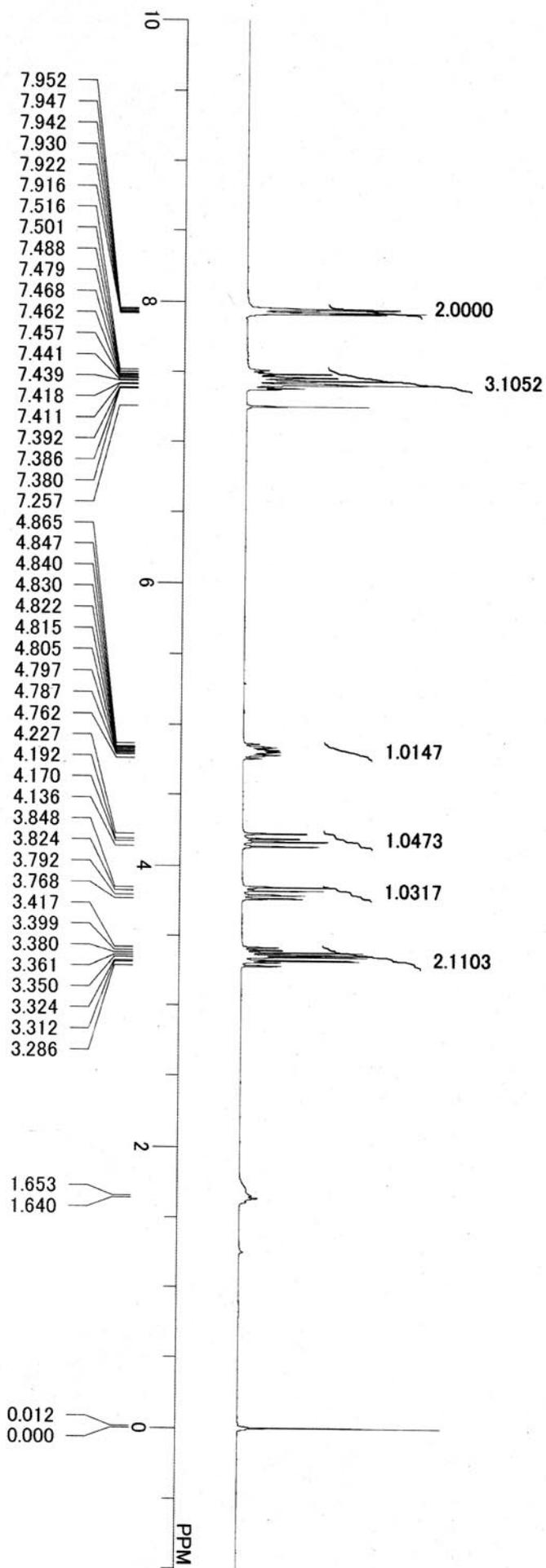
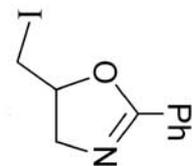
2-Iodomethyl-1-(*p*-toluenesulfonyl)azetizine (**2h**).



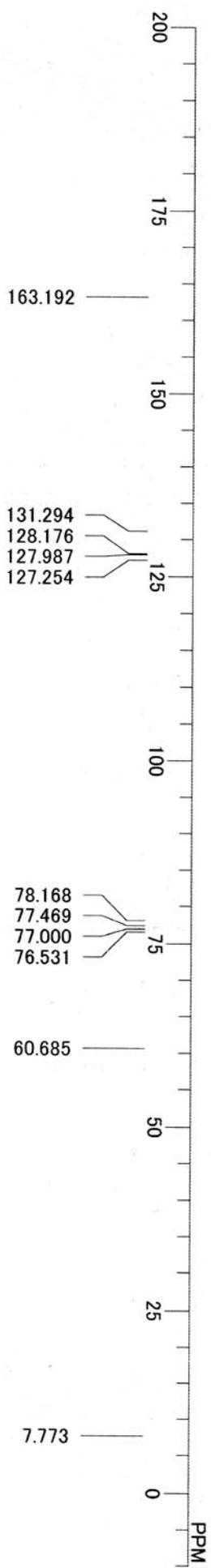
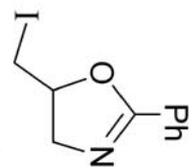
2-Iodomethyl-1-(*p*-toluenesulfonyl)azetizine (**2h**).



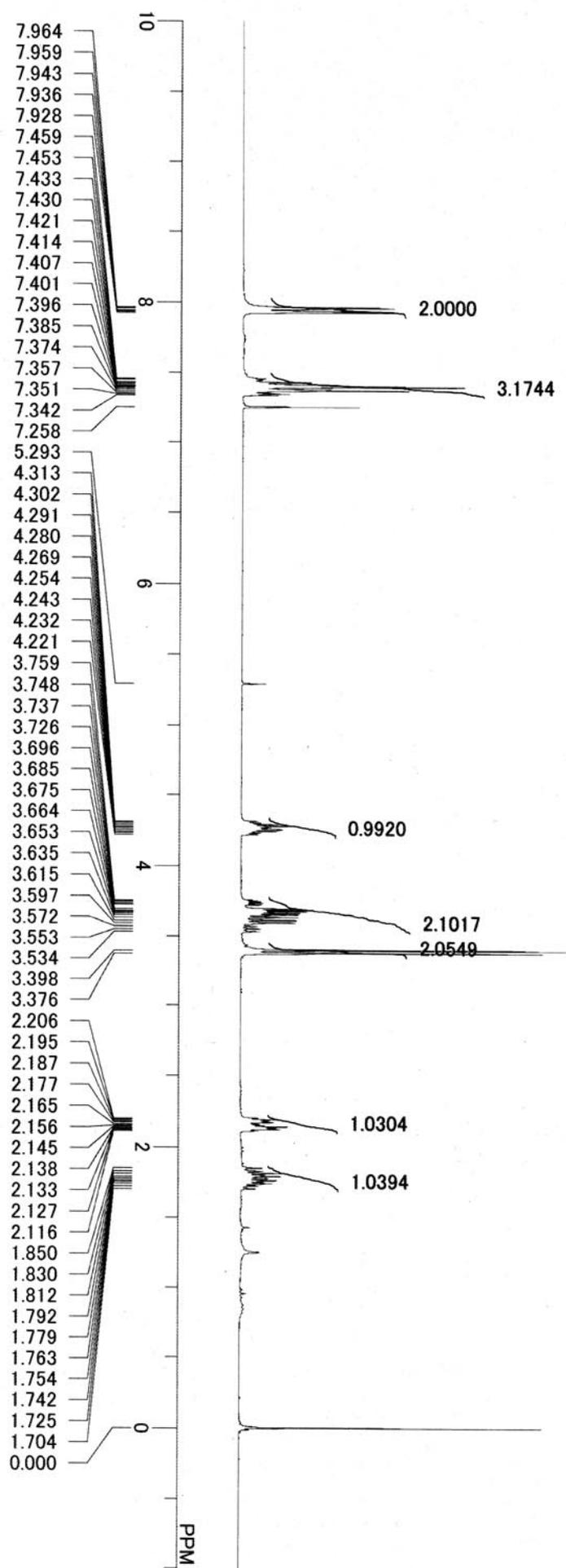
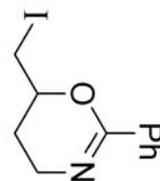
5-Iodomethyl-2-phenyl-2-oxazoline (7a).



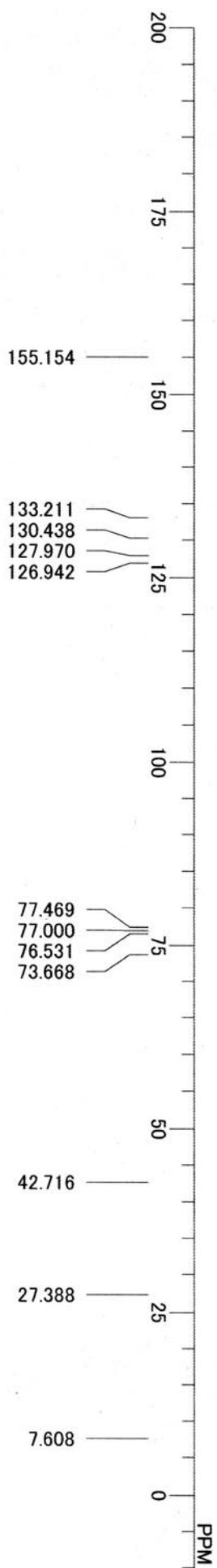
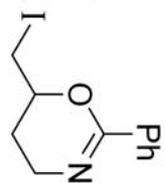
5-Iodomethyl-2-phenyl-2-oxazoline (7a).



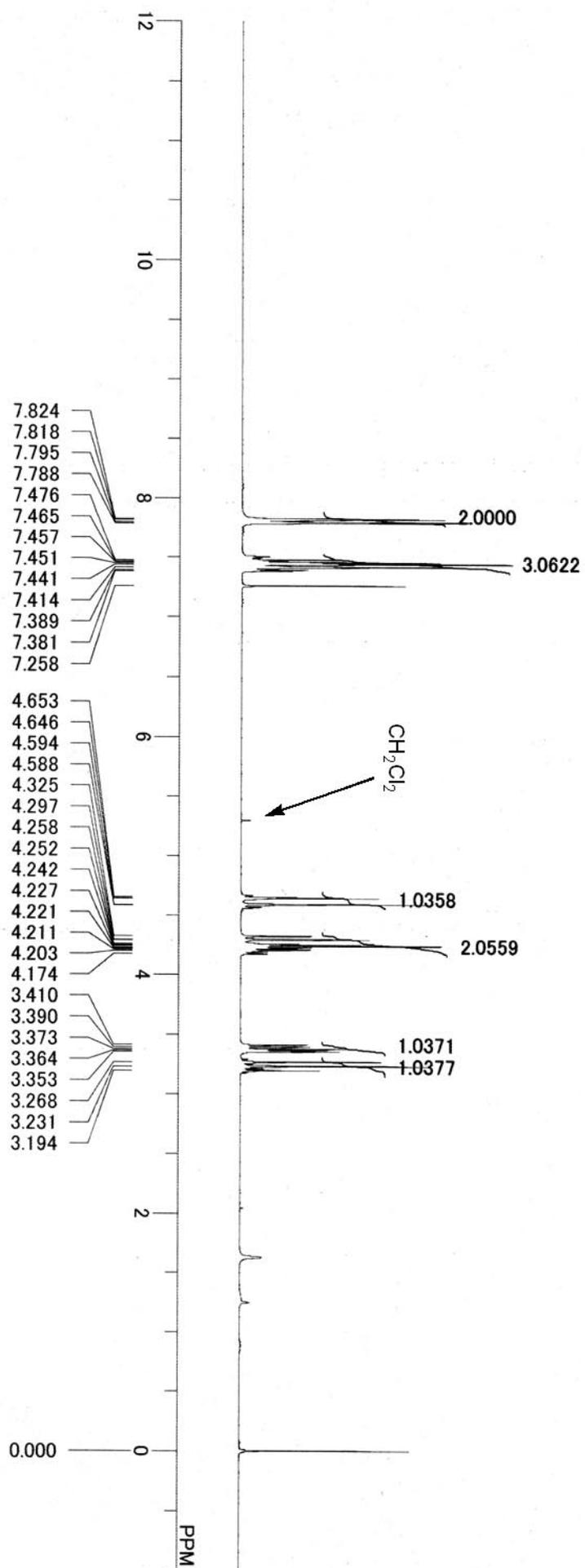
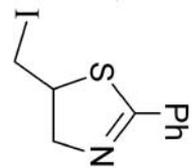
5,6-Dihydro-6-iodomethyl-2-phenyl-4*H*-1,3-oxazine(7b).



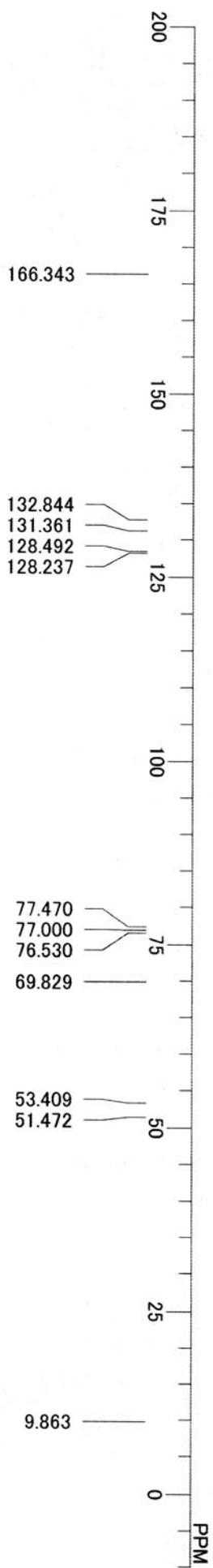
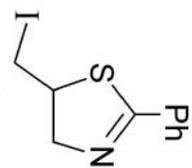
5,6-Dihydro-6-iodomethyl-2-phenyl-4H-1,3-oxazine(7b).



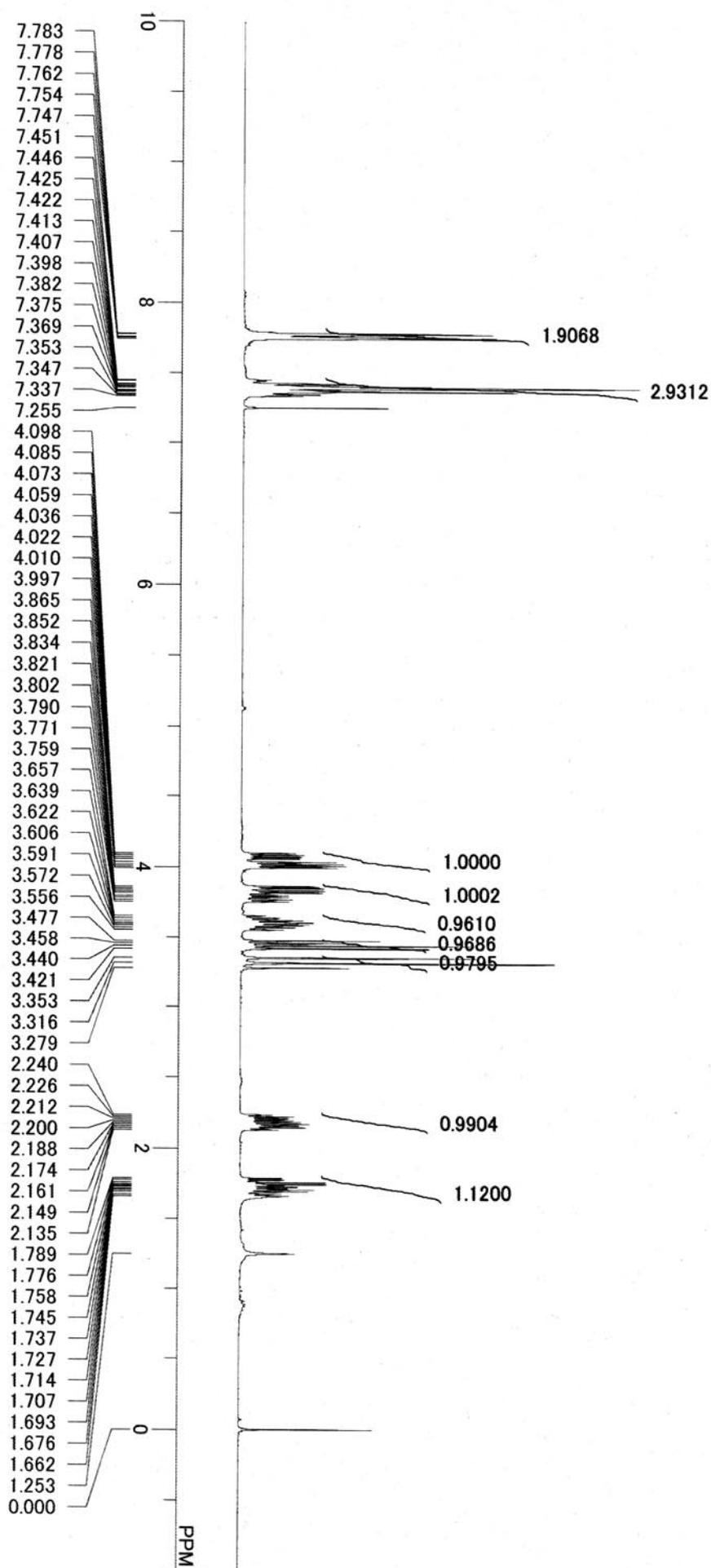
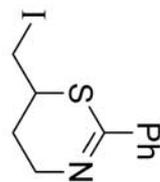
5-Iodomethyl-2-phenyl-2-thiazoline (7c).



5-Iodomethyl-2-phenyl-2-thiazoline (**7c**).



5,6-Dihydro-6-iodomethyl-2-phenyl-4H-1,3-thiazine (7d).



5,6-Dihydro-6-iodomethyl-2-phenyl-4*H*-1,3-thiazine (**7d**).

