

Supporting Information

Asymmetric Cyclization of ω -Formyl-1,3-dienes Catalyzed by a Zerovalent Nickel Complex in the Presence of Silanes

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Preparation of Substrates

8,8-Dimethoxy-6,6-bismethoxycarbonyl-1,3-octadiene (5).

To a suspension of NaH (60% dispersion in mineral oil, 311 mg, 7.8 mmol) in THF (2.0 mL) was added a solution of 4⁵ (1.37 g, 6.2 mmol) in THF (8.0 mL) at 0 °C, and the mixture was stirred at room temperature for 30 min. To the mixture was added a solution of 5-bromo-1,3-diene⁶ (1.20 g, 8.1 mmol) in THF (3 mL) at 0 °C, and the mixture was stirred at room temperature for 1.5 h. To the reaction mixture was added sat. NH₄Cl aq. solution, and the aqueous layer was extracted with Et₂O. The organic layer was washed with brine, and dried over Na₂SO₄. After removal of the solvent, the residue was purified by column chromatography on silica gel (hexane/AcOEt=4/1) to give 5 as a colorless oil (1.76 g, 99%). IR (neat) 1738, 1652, 1602, 1200, 1124 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 2.20 (d, *J* = 5.6 Hz, 2 H), 2.72 (d, *J* = 7.6 Hz, 2 H), 3.30 (s, 6 H), 3.71 (s, 6 H), 4.45 (t, *J* = 5.6 Hz, 1 H), 5.02 (d, *J* = 10.4 Hz, 1 H), 5.13 (d, *J* = 16.8 Hz, 1 H), 5.49 (dt, *J* = 15.1, 7.6 Hz, 1 H), 6.09 (dd, *J* = 15.1, 10.4 Hz, 1 H), 6.27 (ddd, *J* = 16.8, 10.4, 10.4 Hz, 1 H); EI-LRMS *m/z* 286 (M⁺), 270, 254, 222, 195, 164, 156, 137, 75, 59; EI-HRMS calcd for C₁₄H₂₂O₆ 286.1417, found 286.1397.

3,3-Bismethoxycarbonyl-5,7-octadienal (6).

To a solution of 5 (110 mg, 0.38 mmol) in acetone (26 mL) was added 10% FeCl₃•SiO₂ (175 mg, 0.11 mmol) at room temperature, and the mixture was stirred for 1 h. The mixture was filtered through Florisil[®], and the filtrate was concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane/acetone=20/1) to give 6 as a colorless oil (87 mg, 95%). IR (neat) 2738, 1736, 1721, 1652, 1602, 1208 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 2.79 (d, *J* = 7.7 Hz, 2 H), 2.98 (d, *J* = 1.2 Hz, 2 H), 3.75 (s, 6 H), 5.05 (d, *J* = 10.3 Hz, 1 H), 5.15 (d, *J* = 16.9 Hz, 1 H), 5.49 (dt, *J* = 15.1, 7.7 Hz, 1 H), 6.07 (dd, *J* = 15.1, 10.3 Hz, 1 H), 6.27 (ddd, *J* = 16.9, 10.3, 10.3 Hz, 1 H), 9.60 (t, *J* = 1.2 Hz, 1 H); EI-LRMS *m/z* 240 (M⁺), 208, 197, 180, 164, 148, 137, 120, 113, 91, 67, 59; EI-HRMS calcd for C₁₂H₁₆O₅ 240.0998, found 240.1012.

8-*tert*-Butyldiphenylsilyloxy-6,6-bismethoxycarbonyl-1,3-octadiene (16).

To a suspension of NaH (60% dispersion in mineral oil, 536 mg, 13.4 mmol) in DMF (13.0 mL) was added dimethyl malonate (1.5 mL, 13 mmol) by portions at 0 °C, and the mixture was stirred at room temperature for 30 min. To the mixture was added a solution of 2-bromo-1-*tert*-butyldiphenylsilyloxyethane (2.35 g, 6.5 mmol) in THF (13 mL) at 0 °C, and the mixture was stirred at 50 °C for 66 h. To the mixture was added sat. NH₄Cl aq. solution, and the aqueous layer was extracted with Et₂O. The organic layer was washed with H₂O and brine, and dried over Na₂SO₄. After removal of the solvent, the residue was purified by flash column chromatography on silica gel

(hexane/AcOEt=20/1) to give the malonate derivative as a colorless oil (2.28 g, 85%). To a suspension of NaH (60% dispersion in mineral oil, 181 mg, 4.5 mmol) in THF (1.0 mL) was added a solution of the malonate (1.57 g, 3.8 mmol) in THF (7.0 mL) at 0 °C, and the mixture was stirred at room temperature for 20 min. To the mixture was added a solution of 5-bromo-1,3-pentadiene (675 mg, 4.5 mmol) in THF (2.0 mL) at 0 °C, and the mixture was stirred at room temperature for 45 min. To the mixture was added sat. NH₄Cl aq. solution, and the aqueous layer was extracted with Et₂O. The organic layer was washed with brine, and dried over Na₂SO₄. After removal of the solvent, the residue was purified by flash column chromatography on silica gel (hexane/Et₂O=20/1) to give **16** as a colorless oil (1.78 g, 98%). IR (neat) 1738, 1654, 1602, 1212, 1164 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) δ 1.03 (s, 9 H), 2.34 (t, *J* = 6.7 Hz, 2 H), 2.71 (d, *J* = 7.5 Hz, 2H), 3.63 (s, 6 H), 3.65 (t, *J* = 6.7 Hz, 2 H), 4.99 (d, *J* = 10.1 Hz, 1 H), 5.08 (d, *J* = 16.8 Hz, 1 H), 5.47 (dt, *J* = 15.2, 7.5 Hz, 1 H), 6.00 (dd, *J* = 15.2, 10.1 Hz, 1 H), 6.23 (ddd, *J* = 16.8, 10.1, 10.1 Hz, 1 H), 7.46-7.30 (m, 6 H), 7.85-7.70 (m, 4 H); EI-LRMS *m/z* 480 (M⁺), 449, 423 (M⁺-Bu), 213, 197, 165, 105, 67; EI-HRMS calcd for C₂₄H₂₇O₅Si 423.1628 (M⁺-Bu), found 423.1631.

9-*tert*-Butyldimethylsilyoxy-5,5-bismethoxycarbonyl-1,3-nonadiene (17).

According to the procedure similar to that for synthesis of **16**, the malonate derivative was prepared in 83% yield (1.93 g, 6.32 mmol) from dimethyl malonate (1.2 mL, 10.5 mmol), 3-bromo-1-*tert*-butyldimethylsilyloxypropane (1.93 g, 7.6 mmol), and NaH (60% dispersion in mineral oil, 420 mg, 10.5 mmol) in THF (16 mL)-DMF (8 mL). The malonate derivative (1.56 g, 5.1 mmol) was coupled with 5-bromo-1,3-pentadiene (1.14 g, 7.8 mmol) in the presence of NaH (60% dispersion in mineral oil, 249 mg, 6.2 mmol) in THF at room temperature for 30 min. After usual work-up, the residue was purified by column chromatography on silica gel (hexane/Et₂O=30/1) to give **17** as a colorless oil (1.85 g, 97%). IR (neat) 1736, 1654, 1602, 1260 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) δ 0.04 (s, 6 H), 0.88 (s, 9 H), 1.50-1.48 (m, 2 H), 1.89 (t, *J* = 4.9 Hz, 1 H), 1.92 (t, *J* = 4.9 Hz, 1 H), 2.67 (d, *J* = 7.7 Hz, 2 H), 3.58 (t, *J* = 6.3 Hz, 2 H), 3.71 (s, 6 H), 5.00 (d, *J* = 10.5 Hz, 1 H), 5.10 (d, *J* = 16.8 Hz, 1 H), 5.50 (dt, *J* = 15.0, 7.7 Hz, 1 H), 6.07 (dd, *J* = 15.0, 10.5 Hz, 1 H), 6.27 (ddd, *J* = 16.8, 10.5, 10.5 Hz, 1 H); EI-LRMS *m/z* 313 (M⁺-Bu), 283, 255, 223, 195, 163, 121, 89, 59; EI-HRMS calcd for C₁₅H₂₅O₅Si 313.1471 (M⁺-Bu), found 313.1481.

2,2-Dimethyl-5-(2-hydroxyethyl)-5-(2,4-pentadienyl)-1,3-dioxane (18).

To a solution of **16** (1.77 g, 3.7 mmol) in toluene (6.0 mL) was added DIBAL-H (1.1 M in toluene, 36 mL, 36 mmol) at -78 °C. The mixture was warmed slowly to 0 °C, and stirred at 0 °C for 2 h. To the mixture were added MeOH (3.3 mL, 36 mmol) and sat. potassium sodium tartrate aqueous solution, and the solution was extracted with AcOEt. The organic layer was washed with brine, and dried over Na₂SO₄.

After removal of the solvent, the residue was purified by column chromatography on silica gel (hexane/Et₂O=1/1) to give 8-*tert*-butyldiphenylsilyloxy-6,6-dihydroxymethyl-1,3-octadiene as a colorless oil (918 mg, 59%). IR (neat) 3382, 1652, 1590, 1084 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) δ 1.06 (s, 9 H), 1.67 (t, *J* = 5.1 Hz, 2 H), 2.05 (d, *J* = 7.5 Hz, 2 H), 2.91 (t, *J* = 6.4 Hz, 2 H), 3.66-3.50 (m, 4 H), 3.78 (t, *J* = 5.1 Hz, 2 H), 4.98 (d, *J* = 10.3 Hz, 1 H), 5.08 (d, *J* = 17.6 Hz, 1 H), 5.61 (dt, *J* = 15.4, 7.5 Hz, 1 H), 6.02 (dd, *J* = 15.4, 10.3 Hz, 1 H), 6.26 (ddd, *J* = 17.6, 10.3, 10.3 Hz, 1 H), 7.51-7.35 (m, 6 H), 7.70-7.63 (m, 4 H); EI-LRMS *m/z* 425 (M⁺+H), 289, 239, 213, 183, 169, 151, 135, 91, 67; EI-HRMS calcd for C₂₆H₃₇O₃Si 425.2512 (M⁺+H), found 425.2483.

To a solution of the diol (906 mg, 2.1 mmol) in CH₂Cl₂ (10 mL) were added 2,2-dimethoxypropane (1.3 mL, 11 mmol) and PPTS (54 mg, 0.21 mmol) at room temperature, and the mixture was stirred at the same temperature for 2 h. To the mixture was added sat. NaHCO₃ aq. solution, and the aqueous layer was extracted with Et₂O. The organic layer was washed with brine, and dried over Na₂SO₄. After removal of the solvent, the crude product (966 mg) was dissolved in THF (5.2 mL). To the mixture was added TBAF (1 M in THF, 2.7 mL, 2.7 mmol) at 0 °C, and the mixture was stirred at room temperature for 1.5 h. After usual work-up, the residue was purified by column chromatography on silica gel (hexane/AcOEt=1/1) to give **18** as a colorless oil (454 mg, 94% in 2 steps). IR (neat) 3420, 1648, 1602, 1112, 1086 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) δ 1.42 (s, 3 H), 1.43 (s, 3 H), 1.66 (t, *J* = 6.3 Hz, 2 H), 2.10 (d, *J* = 7.7 Hz, 2 H), 2.56 (br t, *J* = 5.7 Hz, 1 H), 3.64 (d, *J* = 11.4 Hz, 2 H), 3.71 (d, *J* = 11.4 Hz, 2 H), 3.84 (dt, *J* = 5.7, 6.3 Hz, 2 H), 5.02 (d, *J* = 10.3 Hz, 1 H), 5.14 (d, *J* = 16.8 Hz, 1 H), 5.62 (dt, *J* = 15.0, 7.7 Hz, 1 H), 6.10 (dd, *J* = 15.0, 10.3 Hz, 1 H), 6.31 (ddd, *J* = 16.8, 10.3, 10.3 Hz, 1 H); EI-LRMS *m/z* 226 (M⁺), 153, 124, 107, 67; EI-HRMS calcd for C₁₃H₂₂O₃ 226.1569, found 226.1558.

2,2-Dimethyl-5-(formylmethyl)-5-(2,4-pentadienyl)-1,3-dioxane (**19**).

To a solution of **18** (148 mg, 0.66 mmol) in CH₂Cl₂ were added MS 4A (2.2 g) and PCC (426 mg, 2.0 mmol) at 0 °C, and the mixture was stirred at the same temperature for 30 min. The reaction mixture was diluted with Et₂O, and the solution was filtered through Florisil[®]. The filtrate was concentrated in vacuo, and the residue was purified by column chromatography on silica gel (hexane/Et₂O=2/1) to give **19** as a colorless oil (119 mg, 81%). IR (neat) 2728, 1720, 1652, 1602, 1198 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) δ 1.40 (s, 3 H), 1.42 (s, 3 H), 2.23 (d, *J* = 7.9 Hz, 2 H), 2.56 (d, *J* = 2.2 Hz, 2 H), 3.71 (br s, 4 H), 5.04 (d, *J* = 10.3 Hz, 1 H), 5.14 (d, *J* = 17.0 Hz, 1 H), 5.57 (dt, *J* = 15.2, 7.9 Hz, 1 H), 6.08 (dd, *J* = 15.2, 10.3 Hz, 1 H), 6.30 (ddd, *J* = 17.0, 10.3, 10.3 Hz, 1 H), 9.90 (t, *J* = 2.2 Hz, 1 H); EI-LRMS *m/z* 224 (M⁺), 209, 180, 166, 137, 122, 91, 80, 67; EI-HRMS calcd for C₁₃H₂₀O₃ 224.1412, found 224.1399.

4,4-Bismethoxycarbonyl-6,8-nonadien-1-ol (**20**).

To a solution of **17** (1.78 g, 4.8 mmol) in CH₃CN (6.0 mL) was added HF-CH₃CN solution (prepared by mixing conc. HF aq. with CH₃CN (ratio of 1:9), 6.0 mL) at 0 °C, and the mixture was stirred at the same temperature for 30 min. To the mixture was added sat. NaHCO₃ aq. solution, and the aqueous layer was extracted with Et₂O. The organic layer was washed with brine, and dried over Na₂SO₄. After removal of the solvent, the residue was purified by column chromatography on silica gel (hexane/AcOEt=1/1) to give **20** as a colorless oil (650 mg, 53%). IR (neat) 3640, 1738, 1654, 1605, 1263, 1051 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) δ 1.34 (t, *J* = 5.5 Hz, 1 H), 1.55-1.43 (m, 2 H), 1.94 (t, *J* = 7.7 Hz, 2 H), 2.69 (d, *J* = 7.7 Hz, 2 H), 3.63 (dt, *J* = 5.5, 6.5 Hz, 2 H), 3.72 (s, 6 H), 5.02 (d, *J* = 10.5 Hz, 1 H), 5.13 (d, *J* = 16.8 Hz, 1 H), 5.51 (dt, *J* = 15.2, 7.7 Hz, 1 H), 6.10 (dd, *J* = 15.2, 10.5 Hz, 1 H), 6.28 (ddd, *J* = 16.8, 10.5, 10.5 Hz, 1 H); EI-LRMS *m/z* 257 (M⁺+H), 224, 165, 136, 105, 91, 67, 59; EI-HRMS calcd for C₁₃H₂₁O₃ 257.1389 (M⁺+H), found 257.1374.

4,4-Bismethoxycarbonyl-6,8-nonadienal (**21**).

To a suspension of Dess-Martin periodinane (225 mg, 0.53 mmol) in CH₂Cl₂ (0.5 mL) was added a solution of **20** (90 mg, 0.35 mmol) in CH₂Cl₂ (3 mL) at 0 °C, and the mixture was stirred at room temperature for 45 min. To the solution were added 10% Na₂S₂O₃ aq. solution and sat. NaHCO₃ aq. solution, and the aqueous layer was extracted with Et₂O. The organic layer was washed with brine, dried over Na₂SO₄. After removal of the solvent, the residue was purified by column chromatography on silica gel (hexane/Et₂O=3/2) to give **21** as a colorless oil (87 mg, 97%). IR (neat) 2728, 1740, 1732, 1654, 1602, 1204 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) δ 2.19 (t, *J* = 7.9 Hz, 2 H), 2.49 (dt, *J* = 1.2, 7.9 Hz, 2 H), 2.68 (d, *J* = 7.0 Hz, 2 H), 3.72 (s, 6 H), 5.04 (d, *J* = 10.3 Hz, 1 H), 5.14 (d, *J* = 16.8 Hz, 1 H), 5.50 (dt, *J* = 15.1, 7.0 Hz, 1 H), 6.10 (dd, *J* = 15.1, 10.3 Hz, 1 H), 6.27 (ddd, *J* = 16.8, 10.3, 10.3 Hz, 1 H), 9.73 (t, *J* = 1.2 Hz, 1 H); EI-LRMS *m/z* 254 (M⁺), 236 (M⁺-H₂O), 223, 197, 176, 117, 67; EI-HRMS calcd for C₁₃H₁₆O₄ (M⁺-H₂O) 236.1048, found 236.1053.

Experimental Procedures and Spectral Data for Cyclization of **6** and **19**.

Cyclization of **6** Using Ni(cod)₂-PPh₃ catalyst in the Presence of Et₃SiH (Scheme 3).

According to the General Procedure for Cyclization, the crude product, which was prepared from Ni(cod)₂ (16 mg, 0.06 mmol), PPh₃ (30 mg, 0.12 mmol), **6** (69 mg, 0.29 mmol), and Et₃SiH (0.23 mL, 1.4 mmol) in THF (5.8 mL) at room temperature for 12 h, was purified by column chromatography on silica gel (hexane/Et₂O=10/1) to give **7a-I** as a sole product (87 mg, 84%). IR (neat) 1738, 1654, 1264, 1114, cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 0.53 (q, *J* = 7.9 Hz, 6 H), 0.92 (t, *J* = 7.9 Hz, 9 H), 1.72 (d, *J* = 4.5 Hz, 3 H), 2.05 (m, 1 H), 2.37-2.41 (m, 2 H), 2.41-2.54 (m, 2 H), 3.70 (s, 3 H), 3.71 (s, 3 H), 4.11 (m, 1 H), 5.40-5.53 (m, 2 H); EI-LRMS *m/z* 356 (M⁺), 327, 295, 227, 165, 59; EI-HRMS calcd for

$C_{18}H_{32}O_3Si$ 356.2019 found 356.2009.

(1*S,2*R**)-4,4-Bismethoxycarbonyl-2-propylcyclopentan-1-ol (11)** (Scheme 6). To a solution of **7a-I** (61 mg, 0.17 mmol), which was obtained as a sole product in a cyclization using PPh_3 as a ligand, in CH_3CN (1 mL) was added HF- CH_3CN solution (1 mL) at 0 °C, and the mixture was stirred at room temperature for 20 min. After usual work-up, the crude alcohol (64 mg) was dissolved in AcOEt (10 mL). To the solution was added 10% Pd-C (18 mg, 0.017 mmol), and the mixture was stirred at room temperature for 13 h under an atmosphere of hydrogen. The mixture was filtered, and the filtrate was concentrated. The residue was purified by column chromatography on silica gel (hexane/AcOEt=2/1) to give **11** as a colorless oil (38 mg, 93% in 2 steps). IR (neat) 3536, 1732, 1200, 1142 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 0.92 (t, $J = 7.1$ Hz, 3 H), 1.29-1.44 (m, 3 H), 1.51 (m, 1 H), 1.82-1.97 (m, 2 H), 2.01 (dd, $J = 12.5, 12.5$ Hz, 1 H), 2.33 (dd, $J = 14.7, 4.4$ Hz, 1 H), 2.48 (d, $J = 14.7$ Hz, 1 H), 2.51 (dd, $J = 12.5, 7.4$ Hz, 1 H), 3.73 (s, 3 H), 3.75 (s, 3 H), 4.18 (m, 1 H); EI-LRMS m/z 245 ($M^+ + H$), 244 (M^+), 226, 213, 202, 174, 167, 145, 113, 107, 59; EI-HRMS calcd for $C_{12}H_{21}O_3$ ($M^+ + H$) 245.1389, found 245.1377.

According to the same procedure, **11** was obtained in 95% yield as a single isomer from a mixture of **7a-I** and **7a-T**.

(1*S*,2*S*)-4,4-Bismethoxycarbonyl-1-*tert*-butyldimethylsilyloxy-2-[(1*E*)-propenyl]-cyclopentane (7b-I) (Table 2, run 2). According to the General Procedure for Cyclization, the crude product, which was prepared from $Ni(cod)_2$ (7.7 mg, 0.03 mmol), **10** (10.8 mg, 0.056 mmol), **6** (67 mg, 0.28 mmol), and $tBuMe_2SiH$ (0.23 mL, 1.4 mmol) in THF (5.6 mL) at room temperature for 8 h, was purified by column chromatography on silica gel (hexane/ Et_2O =10/1) to give **7b-I** as a colorless oil (83 mg, 83%). IR (neat) 1738, 1654, 1198, 1114 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ -0.01 (s, 3 H), 0.001 (s, 3 H), 0.85 (s, 9 H), 1.65 (d, $J = 6.0$ Hz, 3 H), 2.17 (m, 1 H), 2.34-2.57 (m, 4 H), 3.70 (s, 3 H), 3.71 (s, 3 H), 4.10 (m, 1 H), 5.39-5.53 (m, 2 H); EI-LRMS m/z 341 ($M^+ - Me$), 299 ($M^+ - Bu^t$) 165, 105, 59; EI-HRMS calcd $C_{14}H_{23}O_3Si$ ($M^+ - Bu^t$) 299.1315, found 299.1320; $[\alpha]_D^{24} +2.61$ (c 1.57, $CHCl_3$, 16% ee)

(1*S*,2*S*)-4,4-Bismethoxycarbonyl-2-[(1*E*)-propenyl]-1-triethoxysilyloxy-cyclopentane (7c-I) (Table 3, run 5): According to the General Procedure for Cyclization, the crude product, which was prepared from $Ni(cod)_2$ (7.8 mg, 0.03 mmol), **10** (11.0 mg, 0.056 mmol), **6** (67 mg, 0.28 mmol), and $(EtO)_3SiH$ (0.26 mL, 1.4 mmol) in CH_3CN (5.6 mL) at -30 °C for 8 h, was purified by column chromatography on silica gel (hexane/ Et_2O =10/1) to give **7c-I** as a colorless oil (94 mg, 83%). IR (neat) 1738, 1654, 1170, 1106 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 1.01 (t, $J = 7.0$ Hz, 9 H), 1.65 (d,

$J = 4.7$ Hz, 3 H), 2.23 (dd, $J = 12.4, 6.5$ Hz, 1 H), 2.47 (dd, $J = 14.6, 4.3$ Hz, 1 H), 2.49 (m, 1 H), 2.53 (dd, $J = 14.6, 1.7$ Hz, 1 H), 2.55 (m, 1 H), 3.70 (s, 3 H), 3.71 (s, 3 H), 3.80 (q, $J = 7.0$ Hz, 6 H), 4.31 (m, 1 H), 5.45-5.60 (m, 2 H); EI-LRMS m/z 404 (M^+), 359, 304, 292, 224, 164, 163, 105, 59; EI-HRMS calcd for $C_{18}H_{32}O_8Si$ 404.1866, found 404.1861; $[\alpha]_D^{23} +8.85$ (c 1.78, $CHCl_3$, 73% ee).

(2S, 3S)-7,7-Dimethyl-3-[(1E)-propenyl]-2-triethoxysilyloxy-6,8-dioxaspiro-

[4.5]decane (22c-I). According to the General Procedure for Cyclization, the crude product, which was prepared from of $Ni(cod)_2$ (7.7 mg, 0.03 mmol), **10** (10.9 mg, 0.057 mmol), **19** (63 mg, 0.28 mmol), and $(EtO)_3SiH$ (0.26 mL, 1.4 mmol) in CH_3CN (5.6 mL) at -30 °C for 10 h, was purified by column chromatography on silica gel (hexane/ $Et_2O=10/1$) to give **22c-I** as a colorless oil (87 mg, 80%). IR (neat) 1654, 1200, 1104 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) δ 1.22 (t, $J = 6.9$ Hz, 9 H), 1.40 (s, 3 H), 1.41 (s, 3 H), 1.54 (dd, $J = 14.4, 4.2$ Hz, 1 H), 1.65 (d, $J = 6.3$ Hz, 3 H), 1.66 (m, 1 H), 1.76 (br d, $J = 14.4$ Hz, 1 H), 1.81 (dd, $J = 13.1, 7.5$ Hz, 1 H), 2.42 (m, 1 H), 3.53 (d, $J = 11.2$ Hz, 1 H), 3.57 (d, $J = 11.2$ Hz, 1 H), 3.72 (d, $J = 11.1$ Hz, 1 H), 3.76 (d, $J = 11.1$ Hz, 1 H), 3.82 (q, $J = 6.9$ Hz, 6 H), 4.32 (m, 1 H), 5.47 (dq, $J = 15.4, 6.3$ Hz, 1 H), 5.58 (dd, $J = 15.4, 7.4$ Hz, 1 H); EI-LRMS m/z 388 (M^+), 373, 330, 320, 315, 285, 221, 209, 181, 163, 150, 119, 107, 68; EI-HRMS calcd for $C_{19}H_{36}O_6Si$ 388.2281, found 388.2253; $[\alpha]_D^{23} +9.49$ (c 3.04, $CHCl_3$, 64% ee).

(2S, 3S)-2-Benzoyloxy-7,7-Dimethyl-3-[(1E)-propenyl]-6,8-dioxaspiro[4.5]decane (23-I).

According to the procedure similar to that of the above-mentioned conversion of **7a-I** to **9-I**, the crude product, which was obtained by the reaction of **22c-I** (85 mg, 0.22 mmol) with TBAF (1 M in THF, 1.3 mL, 1.3 mmol) in THF (1.5 mL) followed by treatment of the corresponding alcohols with $BzCl$ (0.26 mL, 2.2 mmol) and DMAP (8.1 mg, 0.07 mmol) in pyridine (1.5 mL) at 50 °C for 11 h, was purified by column chromatography on silica gel (hexane/ $Et_2O=4/1$) to give **23-I** as a colorless oil (73 mg, 100% in 2 steps). IR (neat) 1718, 1654, 1602, 1276, 1112 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) δ 1.40 (s, 3 H), 1.42 (s, 3 H), 1.60 (d, $J = 5.9$ Hz, 3 H), 1.77 (m, 1 H), 1.80 (dd, $J = 15.2, 4.7$ Hz, 1 H), 1.89 (br d, $J = 15.2$ Hz, 1 H), 2.07 (dd, $J = 13.5, 7.7$ Hz, 1 H), 2.73 (m, 1 H), 3.62 (d, $J = 11.3$ Hz, 1 H), 3.65 (d, $J = 11.3$ Hz, 1 H), 3.73 (s, 2 H), 5.41 (m, 1 H), 5.47 (dd, $J = 15.8, 6.9$ Hz, 1 H), 5.55 (dq, $J = 15.8, 5.9$ Hz, 1 H), 7.43 (dd, $J = 7.7, 7.7$ Hz, 2 H), 7.55 (dd, $J = 7.7, 7.7$ Hz, 1 H), 7.99 (d, $J = 7.7$ Hz, 2 H); EI-LRMS m/z 330 (M^+), 315, 252, 208, 150, 133, 119, 105, 77; EI-HRMS calcd for $C_{20}H_{26}O_4$ 330.1831, found 330.1835; $[\alpha]_D^{23} +26.3$ (c 2.55, $CHCl_3$, 64% ee).

Experimental Procedures and Spectral Data for Cyclization of 21.

Typical Procedure for Asymmetric Cyclization of 21 Using Chiral Phosphorane 10 in the

Presence of (EtO)₃SiH (Table 5, run 1). According to the General Procedure for Cyclization, the crude product, which was prepared from Ni(cod)₂ (8.0 mg, 0.03 mmol), **10** (11.0 mg, 0.057 mmol), **21** (71 mg, 0.28 mmol), and (EtO)₃SiH (0.26 mL, 1.4 mmol) in DMF (5.6 mL) at -30 °C for 24 h, was purified by column chromatography on silica gel (hexane/Et₂O=20/1) to give an inseparable mixture of **24c-I** and **24c-T** (60 mg, total yield 51%, ratio of 1:2.6).

Typical Procedure for Separation of 24c-I and 24c-T into 25-I and 26 via Chemo-Selective Wacker Oxidation (Scheme 12). According to the procedure similar to that described above, a mixture of **25-I** and **25-T** was obtained in a total yield of 92% (29 mg) at a ratio of 1 to 2.6 by the reaction of a mixture of **24c-I** and **24c-T** (37 mg, 0.09 mmol) with HF-CH₃CN (1.0 mL) followed by treatment of the corresponding alcohols (21 mg) with BzCl (0.26 mL, 2.2 mmol) and a catalytic amount of DMAP in pyridine (1.5 mL) at 50 °C for 11 h. According to the procedure similar to that described above, a solution of the mixture of benzoate **25-I** and **25-T** (29 mg, 0.11 mmol, ratio of 1:2.6) in 1,4-dioxane-H₂O (10:1, 1.5 mL) was treated with PdCl₂ (2.8 mg, 0.02 mmol) and CuCl (2.1 mg, 0.02 mmol) at room temperature for 1.5 h under an atmosphere of oxygen to give **26** (22 mg, 73%), and unchanged **25-I** (7 mg, 25%) was recovered.

Spectral data of (1R,2S)-25-I: IR (neat) 1732, 1715, 1654, 1602, 1274, 1110 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 1.55 (d, *J* = 6.4 Hz, 3 H), 1.58 (m, 1 H), 1.74 (dd, *J* = 13.0, 13.0 Hz, 1 H), 1.89 (dd, *J* = 14.0, 14.0, 3.7 Hz, 1 H), 2.14 (m, 1 H), 2.39-2.51 (m, 3 H), 3.72 (s, 3 H), 3.80 (s, 3 H), 4.80 (ddd, *J* = 10.8, 10.8, 4.5 Hz, 1 H), 5.37 (dd, *J* = 15.3, 8.0 Hz, 1 H), 5.34 (dq, *J* = 15.3, 6.4 Hz, 1 H), 7.42 (dd, *J* = 8.0, 8.0 Hz, 2 H), 7.53 (dd, *J* = 8.0, 8.0 Hz, 1 H), 7.99 (d, *J* = 8.0 Hz, 2 H); EI-LRMS *m/z* 329 (M⁺-OMe), 292, 252, 238, 179, 119, 105, 77; EI-HRMS calcd for C₁₉H₂₁O₅ (M⁺-OMe) 329.1389, found 329.1413; [α]_D²² -45.5 (*c* 1.51, CHCl₃, 61% ee).

Spectral data of (1R,2S)-26: IR (neat) 1732, 1721, 1715, 1654, 1602, 1160 (neat) cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 1.60-1.70 (m, 2 H), 1.86 (ddd, *J* = 14.0, 14.0, 3.9 Hz, 1 H), 2.08 (s, 3 H), 2.16 (m, 1 H), 2.26 (dd, *J* = 16.6, 8.0 Hz, 1 H), 2.39-2.55 (m, 3 H), 2.64 (dd, *J* = 16.6, 4.6 Hz, 1 H), 3.72 (s, 3 H), 3.84 (s, 3 H), 4.76 (ddd, *J* = 10.8, 10.8, 4.5 Hz, 1 H), 7.43 (dd, *J* = 7.3, 7.3 Hz, 2 H), 7.56 (d, *J* = 7.3 Hz, 1 H), 8.00 (d, *J* = 7.3 Hz, 2 H); EI-LRMS *m/z* 345 (M⁺-OMe), 319, 254, 222, 197, 145, 137, 122, 105, 77; EI-HRMS calcd for C₁₉H₂₁O₆ (M⁺-OMe) 345.1338, found 345.1352; [α]_D²³ -39.5 (*c* 1.24, CHCl₃, 66% ee).

The enantiomeric excess of **25-I** or **26** was determined by HPLC analysis [DAICEL CHIRALCEL OJ-R (CH₃CN/H₂O=99/1) or DAICEL CHIRALCEL OJ (hexane/2-propanol=99/1)], respectively. The enantiomeric excesses of **24e-I** and **24e-T** (Table 5, run 2) were also determined by HPLC analysis after transformation of those to **25-I** and **26** in a similar manner.

Determination of Absolute Configurations of the Cyclized Products 24-I and 24-T (Scheme 13 & 14).

Conversion of 25-I into MTPA Ester 27-I. According to the procedure described above, the crude alcohol, which was prepared from the reaction of **25-I** (10 mg, 0.028 mmol, 48% ee) with K_2CO_3 (39 mg, 0.28 mmol) in CH_3OH (1.5 mL) at room temperature for 11 h followed by treatment with CH_2N_2 , was treated with DCC (23 mg, 0.11 mmol), (*S*)-(-)- α -methoxy- α -(trifluoromethyl)phenylacetic acid (27 mg, 0.11 mmol), and DMAP (14 mg, 0.12 mmol) in CH_2Cl_2 (1.5 mL) at room temperature for 15.5 h. After usual work-up, the residue was purified by column chromatography on silica gel (hexane/ Et_2O =3/1) to give two diastereomers as an inseparable mixture (10 mg, 78% from **25-I**, 48% de). The NMR spectral data of the mixture were fully considered by application of the improved Mosher's method, and it indicates that (*1R,2S*)-**27-I** was a major diastereomer. (*1R,2S*)-**27-I**: 1H NMR (500 MHz, $CDCl_3$) δ 1.52 (d, J = 6.4 Hz, 3 H), 1.61 (m, 1 H), 1.69 (dd, J = 13.2, 13.2 Hz, 1 H), 1.84 (ddd, J = 13.8, 13.8, 3.6 Hz, 1 H), 2.10 (m, 1 H), 2.29 (m, 1 H), 2.40-2.53 (m, 2 H), 3.51 (s, 3 H), 3.71 (s, 3 H), 3.77 (s, 3 H), 4.83 (ddd, J = 10.9, 10.9, 4.5 Hz, 1 H), 5.13 (dd, J = 15.3, 7.9 Hz, 1 H), 5.40 (dq, J = 15.3, 6.4 Hz, 1 H), 7.35-7.41 (m, 3 H), 7.48-7.52 (m, 2 H). (*1S,2R*)-**27-I**: 1H NMR (500 MHz, $CDCl_3$) δ 1.42 (m, 1 H), 1.63 (d, J = 6.7 Hz, 3 H), 1.69 (dd, J = 13.2, 13.2 Hz, 1 H), 1.84 (ddd, J = 13.8, 13.8, 3.6 Hz, 1 H), 2.02 (m, 1 H), 2.34 (m, 1 H), 2.40-2.53 (m, 2 H), 3.51 (s, 3 H), 3.71 (s, 3 H), 3.77 (s, 3 H), 4.83 (ddd, J = 10.9, 10.9, 4.5 Hz, 1 H), 5.26 (dd, J = 15.1, 8.1 Hz, 1 H), 5.55 (dq, J = 15.1, 6.7 Hz, 1 H), 7.35-7.41 (m, 3 H), 7.48-7.52 (m, 2 H).

Other spectral data of a mixture of (*1R,2S*)-**27-I** and (*1S,2R*)-**27-I**: IR (neat) 1738, 1733, 1252 cm^{-1} ; EI-LRMS m/z 441 (M^+ -OMe), 409, 238, 207, 189, 179, 119; EI-HRMS calcd for $C_{22}H_{24}F_3O_6$ 441.1525 (M^+ -OMe), found 441.1547.

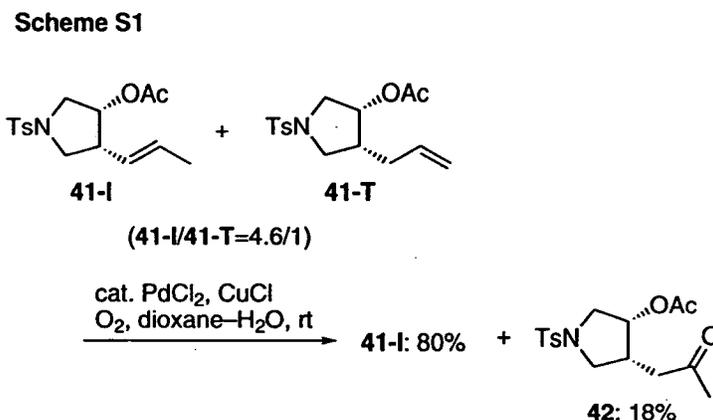
Conversion of (*1R,2S*)-25-I into (*1R,2S*)-26. According to the procedure described above, the crude product, which was prepared from of (*1R,2S*)-**25-I** (35 mg, 0.097 mmol, 61% ee), $PdCl_2$ (5.2 mg, 0.029 mmol), and $CuCl$ (3.4 mg, 0.034 mmol) in $DMF-H_2O$ (10:1, 1.5 mL) at 50 $^{\circ}C$ for 4 days under an atmosphere of oxygen, was purified by column chromatography on silica gel (hexane/ $AcOEt$ =1/1) to give (*1R,2S*)-**26** as a colorless oil (11 mg, 31%, 61% ee), whose spectral data were identical with those described above.

Experimental Procedures and Spectral Data for Cyclization of 28.

Typical Procedure for Asymmetric Cyclization of 28 Using Chiral Phosphorane 10 in the Presence of $(EtO)_3SiH$ (Table 6, run 1). According to the General Procedure for Cyclization, the

crude product, which was prepared from of $\text{Ni}(\text{cod})_2$ (8.0 mg, 0.03 mmol), **10** (11.0 mg, 0.057 mmol), **28** (78 mg, 0.28 mmol), and $(\text{EtO})_3\text{SiH}$ (0.26 mL, 1.4 mmol) in CH_3CN (5.6 mL) at 0 °C for 6 h, was purified by column chromatography on silica gel (hexane/ Et_2O =20/1) to give an inseparable mixture of **29c-I** and **29c-T** (75 mg, total yield 60%, ratio of 4.6:1).

Typical Procedure for Separation of 29c-I and 29c-T into 41-I and 42 via Chemo-Selective Wacker Oxidation.



According to the procedure similar to that described above, a mixture of **41-I** and **41-T** was obtained in a total yield of 100% (45 mg) at a ratio of 4.6 to 1 by the reaction of a mixture of **29c-I** and **29c-T** (65 mg, 0.15 mmol) with $\text{HF-CH}_3\text{CN}$ (1.0 mL) followed by treatment of the corresponding alcohols (38 mg) with Ac_2O (1 mL) and pyridine (2 mL) at room temperature for 11 h. According to the procedure similar to that described above, a solution of the mixture of benzoate **41-I** and **41-T** (43 mg, 0.11 mmol, ratio of 4.6:1) in 1,4-dioxane- H_2O (10:1, 0.3 mL) was treated with PdCl_2 (2.3 mg, 0.01 mmol) and CuCl (1.7 mg, 0.02 mmol) at room temperature for 45 min under an atmosphere of oxygen to give **42** (34 mg, 80%), and unchanged **41-I** (8 mg, 18%) was recovered.

Spectral data of (3R,4R)-41-I: IR (neat) 1740, 1654, 1598, 1374, 1164 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 1.63 (dd, $J = 6.5, 1.1$ Hz, 3 H), 1.76 (s, 3 H), 2.44 (s, 3 H), 2.76 (m, 1 H), 3.13 (dd, $J = 9.6, 9.6$, Hz, 1 H), 3.38 (br d, $J = 12.3$ Hz, 1 H), 3.54 (dd, $J = 9.6, 8.1$ Hz, 1 H), 3.55 (dd, $J = 12.3, 4.1$ Hz, 1 H), 5.03 (m, 1 H), 5.21 (ddq, $J = 15.4, 7.9, 1.1$ Hz, 1 H), 5.54 (dq, $J = 15.3, 6.5$ Hz, 1 H), 7.34 (d, $J = 8.2$ Hz, 2 H), 7.72 (d, $J = 8.2$ Hz, 2 H); EI-LRMS m/z 323 (M^+H), 263, 222, 184, 168, 155, 126, 108, 91, 81; EI-HRMS calcd for $\text{C}_{16}\text{H}_{22}\text{NO}_4\text{S}$ (M^+H) 324.1269, found 324.1266; $[\alpha]_D^{23}$ -1.98 (c 1.95, CHCl_3 , 48% ee).

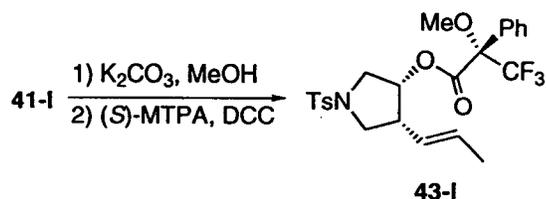
Spectral data of (3R,4R)-42: IR (neat) 1740, 1716, 1596, 1374, 1156 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 1.82 (s, 3 H), 2.11 (s, 3 H), 2.43 (s, 3 H), 2.40-2.49 (m, 1 H), 2.51-2.65 (m, 2 H), 2.96 (dd, $J = 9.7, 9.7$ Hz, 1 H), 3.42 (br d, $J = 12.3$ Hz, 1 H), 3.48 (dd, $J = 12.3, 3.9$ Hz, 1 H), 3.65 (dd, $J = 9.7, 7.4$ Hz, 1 H), 5.11 (m, 1 H), 7.33 (d, $J = 8.3$ Hz, 2 H), 7.70 (d, $J = 8.3$ Hz, 2 H); EI-LRMS m/z 340

(M^+H), 279, 222, 184, 155, 124, 91, 82; EI-HRMS calcd for $C_{16}H_{22}NO_3S$ (M^+H) 340.1218, found 340.1246; $[\alpha]_D^{22} +13.7$ (c 1.18, $CHCl_3$, 67% ee).

The enantiomeric excess of **41-I** or **42** was determined by HPLC analysis [DAICEL CHIRALPAK AD (hexane/2-propanol=9/1) or (hexane/ethanol=9/1)], respectively. The enantiomeric excesses of **29e-I** and **29e-T** (Table 6, run 2) were also determined by HPLC analysis after transformation of those to **41-I** and **42** in a similar manner.

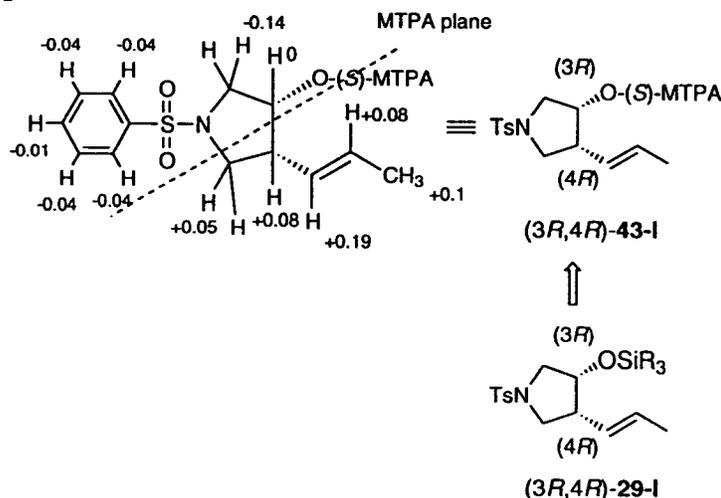
Determination of Absolute Configurations of the Cyclized Products **29-I** and **29-T**.

Scheme S2



Conversion of 41-I into MTPA Ester 43-I. According to the procedure described above, the crude alcohol, which was prepared from the reaction of **41-I** (5 mg, 0.016 mmol, 48% ee) with K_2CO_3 (21 mg, 0.15 mmol) in CH_3OH (1 mL) at room temperature for 2h, was treated with DCC (15 mg, 0.07 mmol), (*S*)-(-)- α -methoxy- α -(trifluoromethyl)phenylacetic acid (17 mg, 0.07 mmol), and DMAP (9 mg, 0.07 mmol) in CH_2Cl_2 (1 mL) at room temperature for 30 min. After usual work-up, the residue was purified by column chromatography on silica gel (hexane/AcOEt=3/1) to give two diastereomers as an inseparable mixture (7 mg, 78% from **41-I**, 48% de). The NMR spectral data of the mixture were fully considered by application of the improved Mosher's method, and it indicates that (*3R,4R*)-**43-I** was a major diastereomer (See, Figure S1).

Figure S1

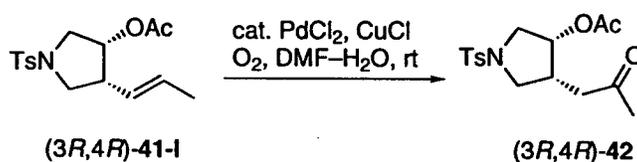


(3*R*,4*R*)-43-I: ¹H NMR (500 MHz, CDCl₃) δ 1.60 (d, *J* = 6.3 Hz, 3 H), 2.41 (s, 3 H), 2.86 (m, 1 H), 3.04 (dd, *J* = 9.7, 9.7 Hz, 1 H), 3.31 (br d, *J* = 12.3 Hz, 1 H), 3.40 (s, 3 H), 3.60 (dd, *J* = 9.7, 7.8 Hz, 1 H), 3.72 (dd, *J* = 12.3, 4.6 Hz, 1 H), 5.17 (dd, *J* = 15.5, 7.7 Hz, 1 H), 5.36 (m, 1 H), 5.56 (dq, *J* = 15.5, 6.3 Hz, 1 H), 7.26 (d, *J* = 8.3 Hz, 2 H), 7.35-7.45 (m, 5 H), 7.65 (d, *J* = 8.3 Hz, 2 H).
 (3*S*,4*S*)-43-I: ¹H NMR (500 MHz, CDCl₃) δ 1.50 (d, *J* = 6.4 Hz, 3 H), 2.42 (s, 3 H), 2.78 (m, 1 H), 3.10 (dd, *J* = 9.8, 9.8 Hz, 1 H), 3.45 (br d, *J* = 12.1 Hz, 1 H), 3.40 (s, 3 H), 3.55 (dd, *J* = 9.8, 8.1 Hz, 1 H), 3.64 (dd, *J* = 12.1, 4.4 Hz, 1 H), 4.98 (dd, *J* = 15.4, 7.7 Hz, 1 H), 5.36 (m, 1 H), 5.48 (dq, *J* = 15.4, 6.4 Hz, 1 H), 7.30 (d, *J* = 8.3 Hz, 2 H), 7.35-7.45 (m, 5 H), 7.69 (d, *J* = 8.3 Hz, 2 H).

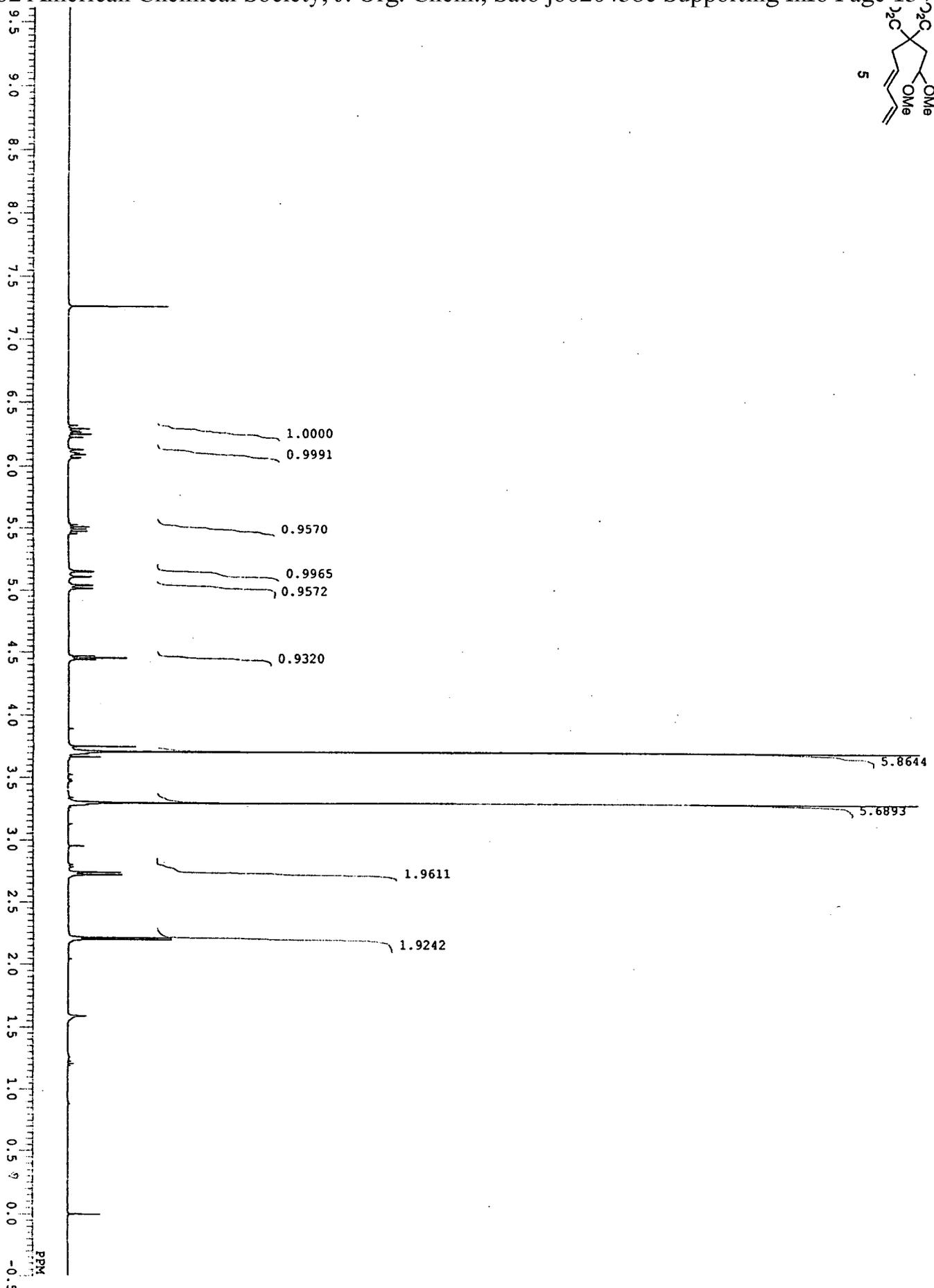
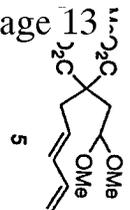
Other spectral data of a mixture of (3*R*,4*R*)-43-I and (3*S*,4*S*)-43-I: IR (neat) 1750, 1654, 1598, 1348, 1164 cm⁻¹; EI-LRMS *m/z* 478 (M⁺-F), 467, 342, 263, 189, 155, 108, 91; EI-HRMS calcd for C₂₄H₂₆F₂O₅NS (M⁺-F) 478.1505, found 478.1499.

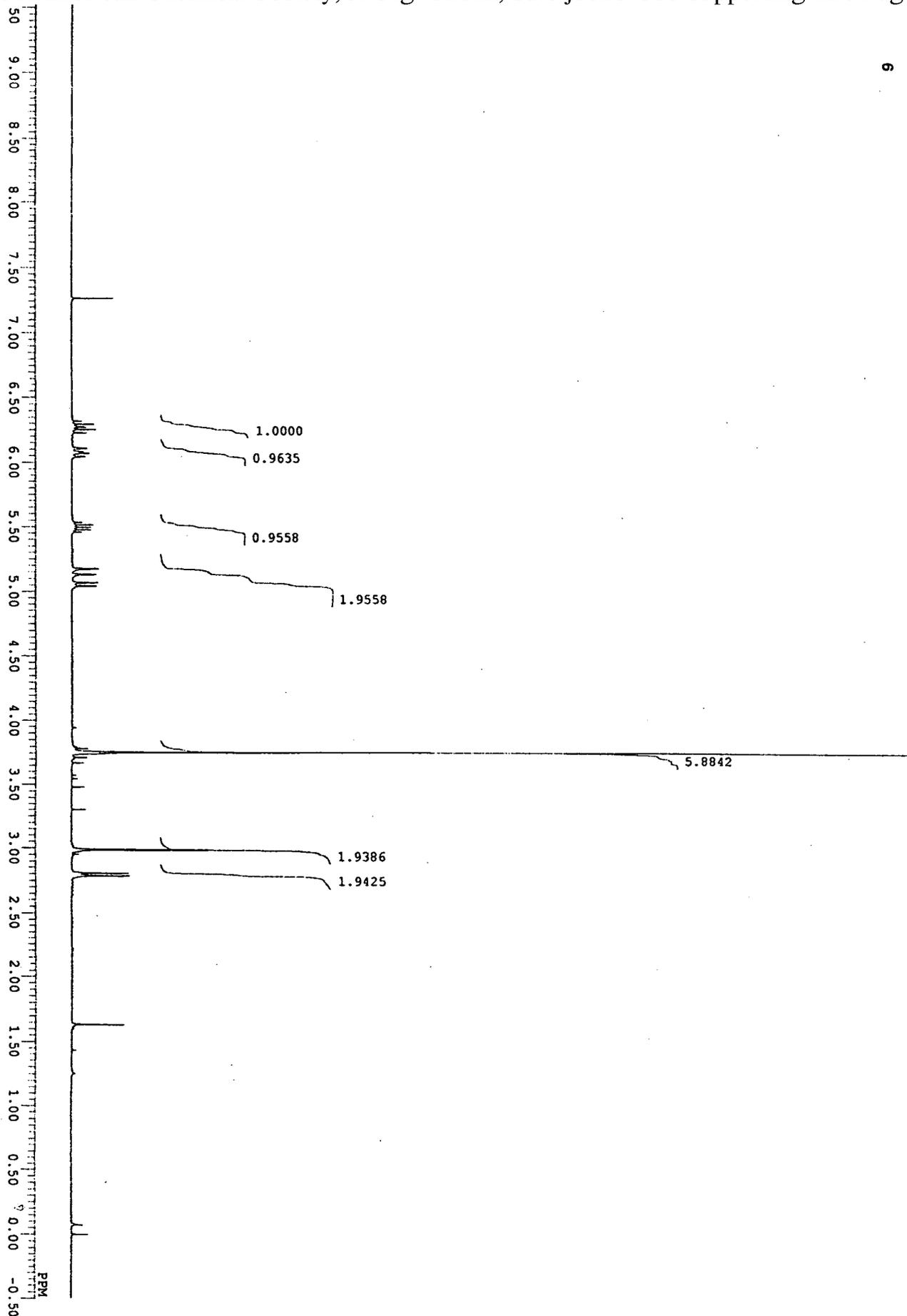
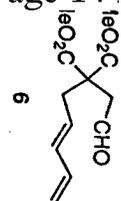
Conversion of (3*R*,4*R*)-41-I into (3*R*,4*R*)-42.

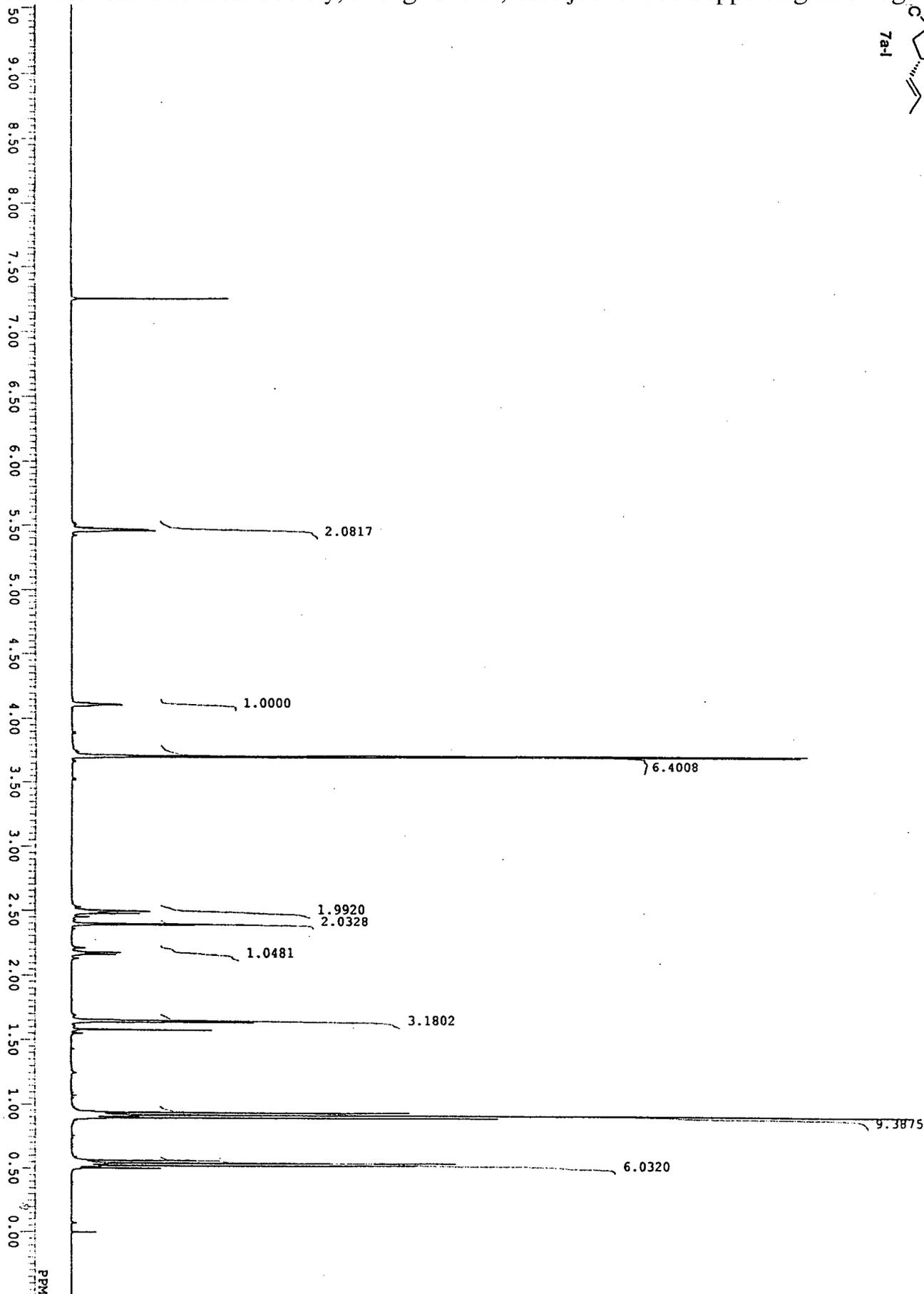
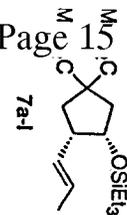
Scheme S3

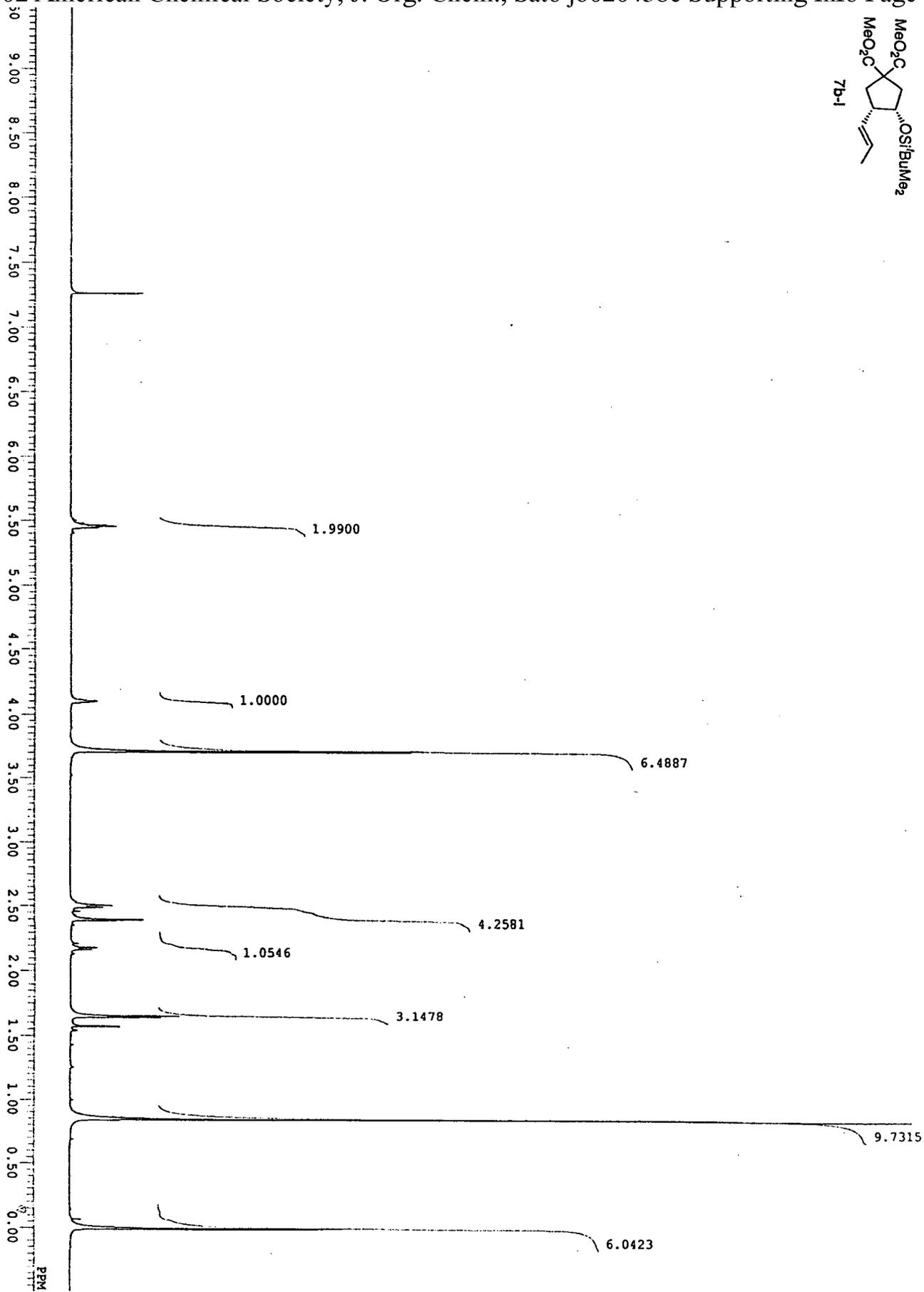
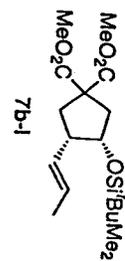


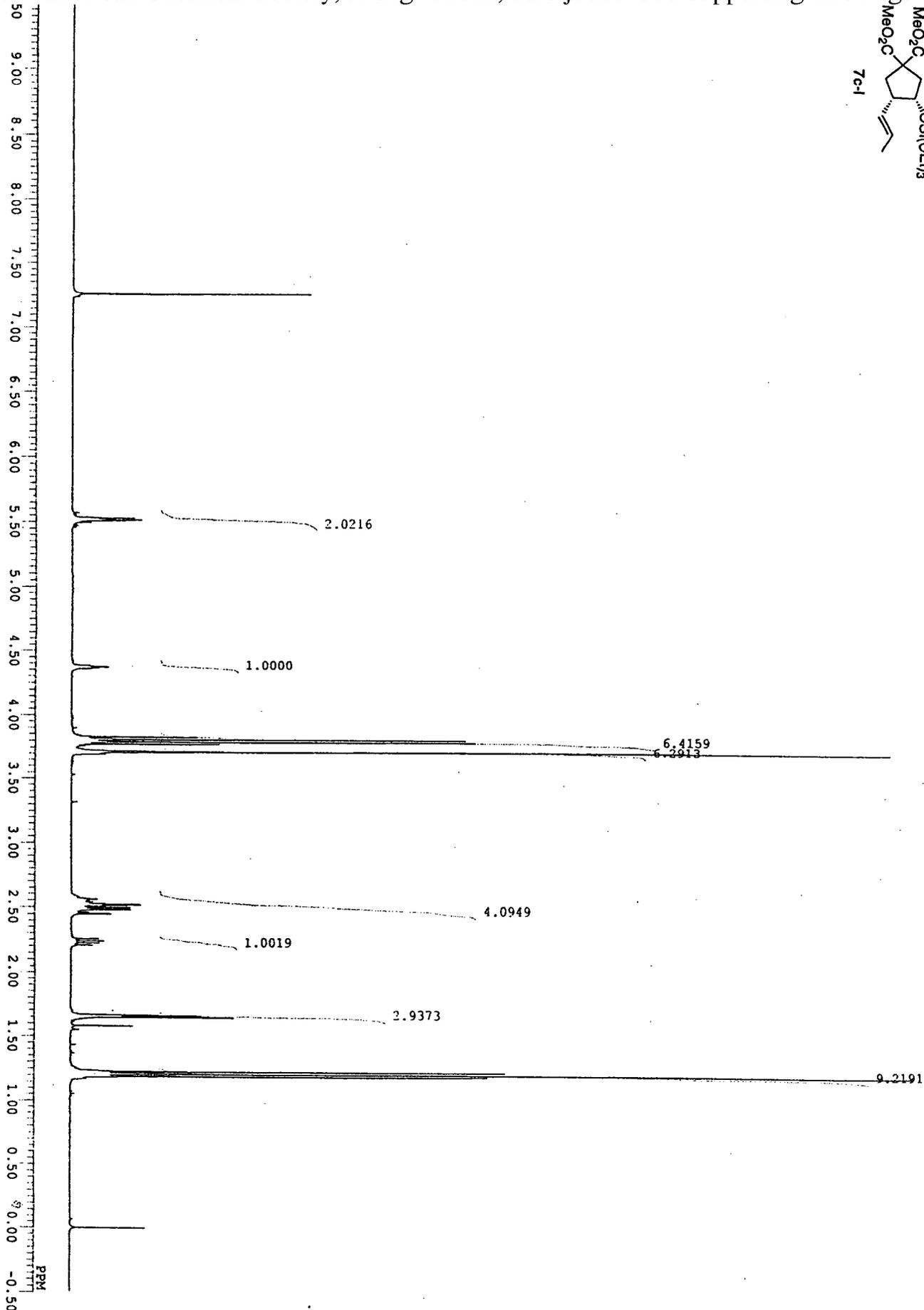
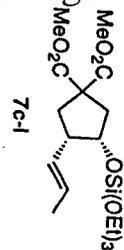
According to the procedure described above, the crude product, which was prepared from of (3*R*,4*R*)-41-I (20 mg, 0.06 mmol, 48% ee), PdCl₂ (1.6 mg, 0.009 mmol), and CuCl (1.2 mg, 0.012 mmol) in DMF-H₂O (10:1, 1.5 mL) at room temperature for 18 h under an atmosphere of oxygen, was purified by column chromatography on silica gel (hexane/AcOEt=1/1) to give (3*R*,4*R*)-42 as a colorless oil (21 mg, 100%, 48% ee), whose spectral data were identical with those described above.

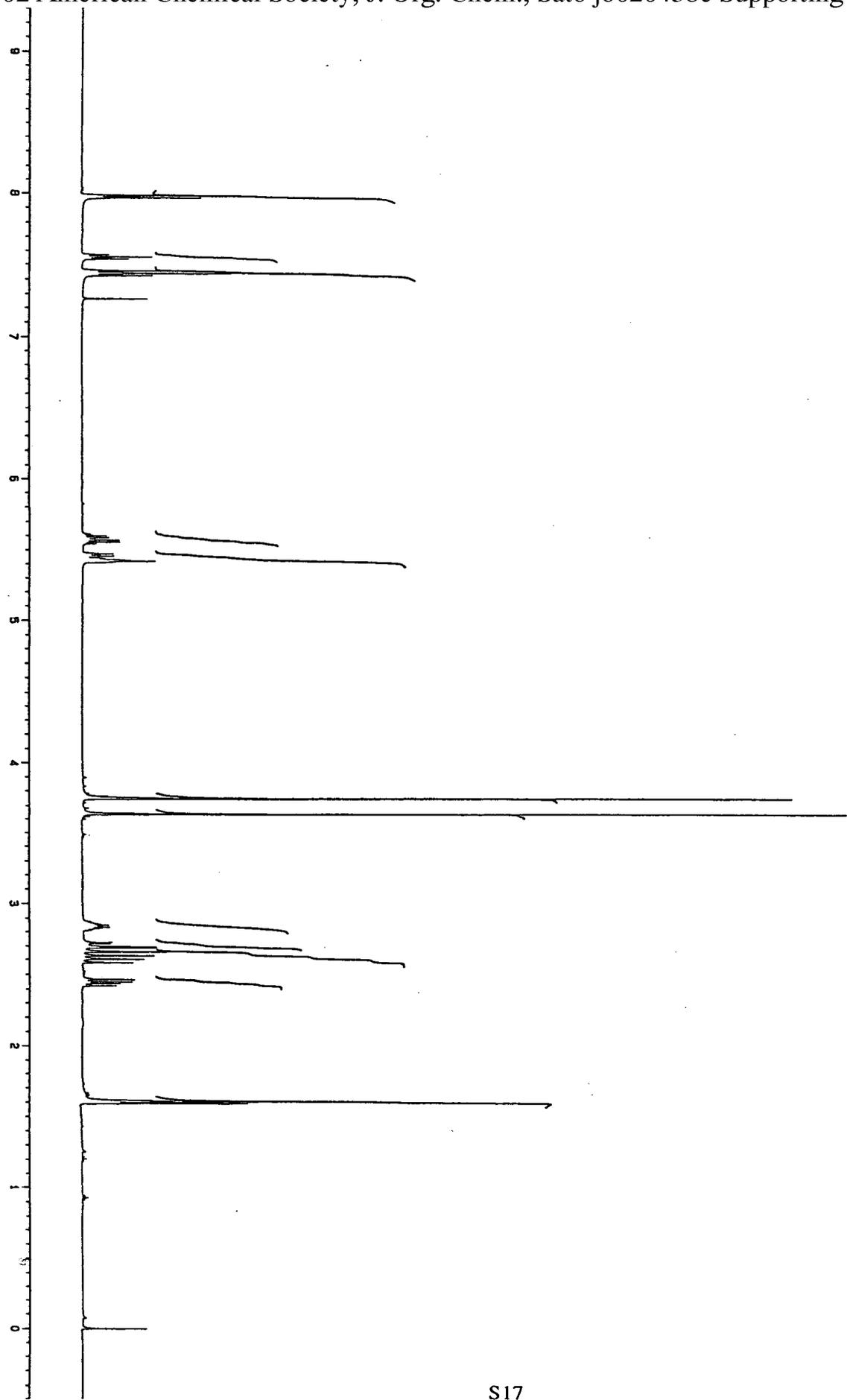
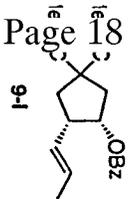


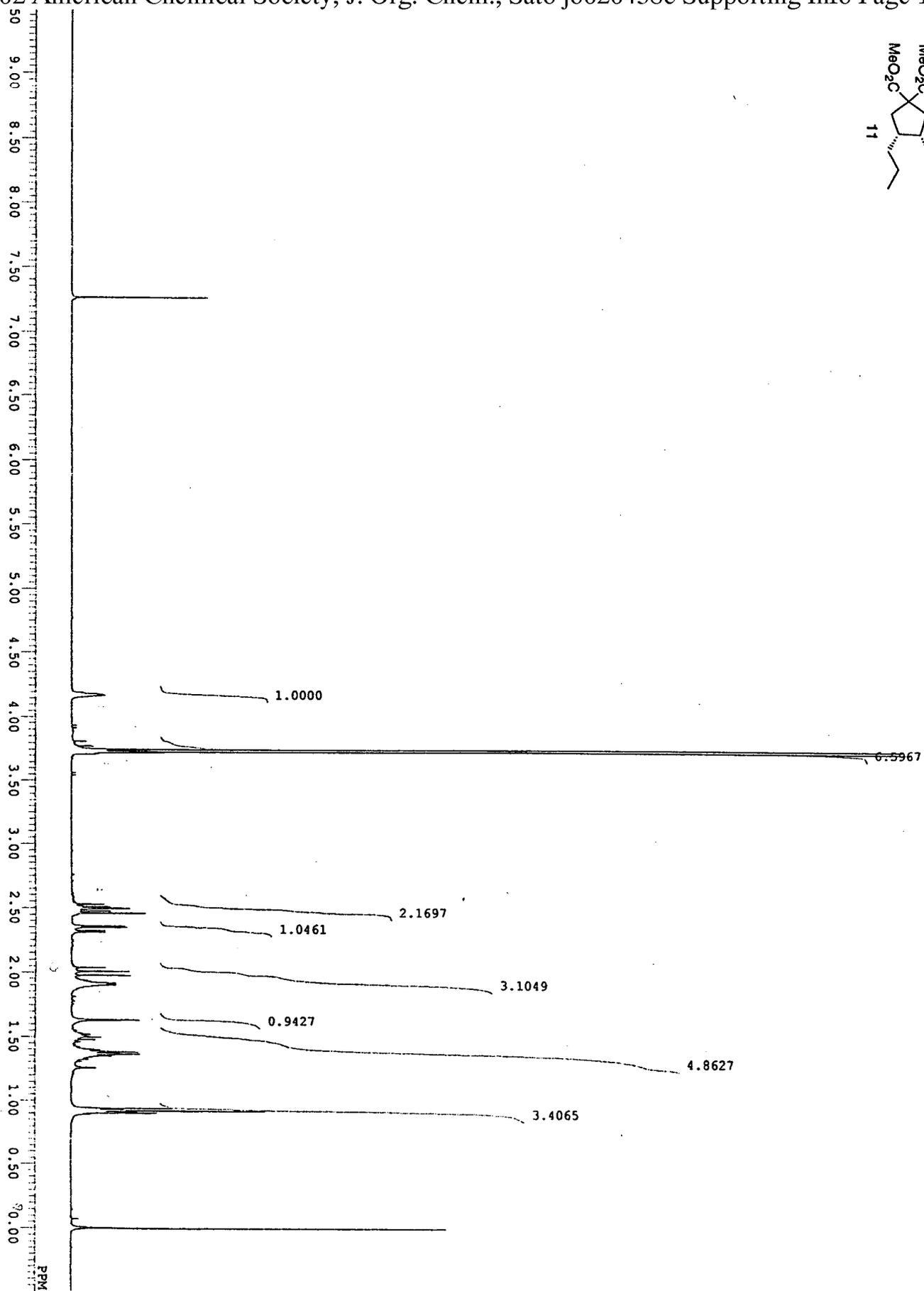
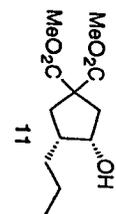


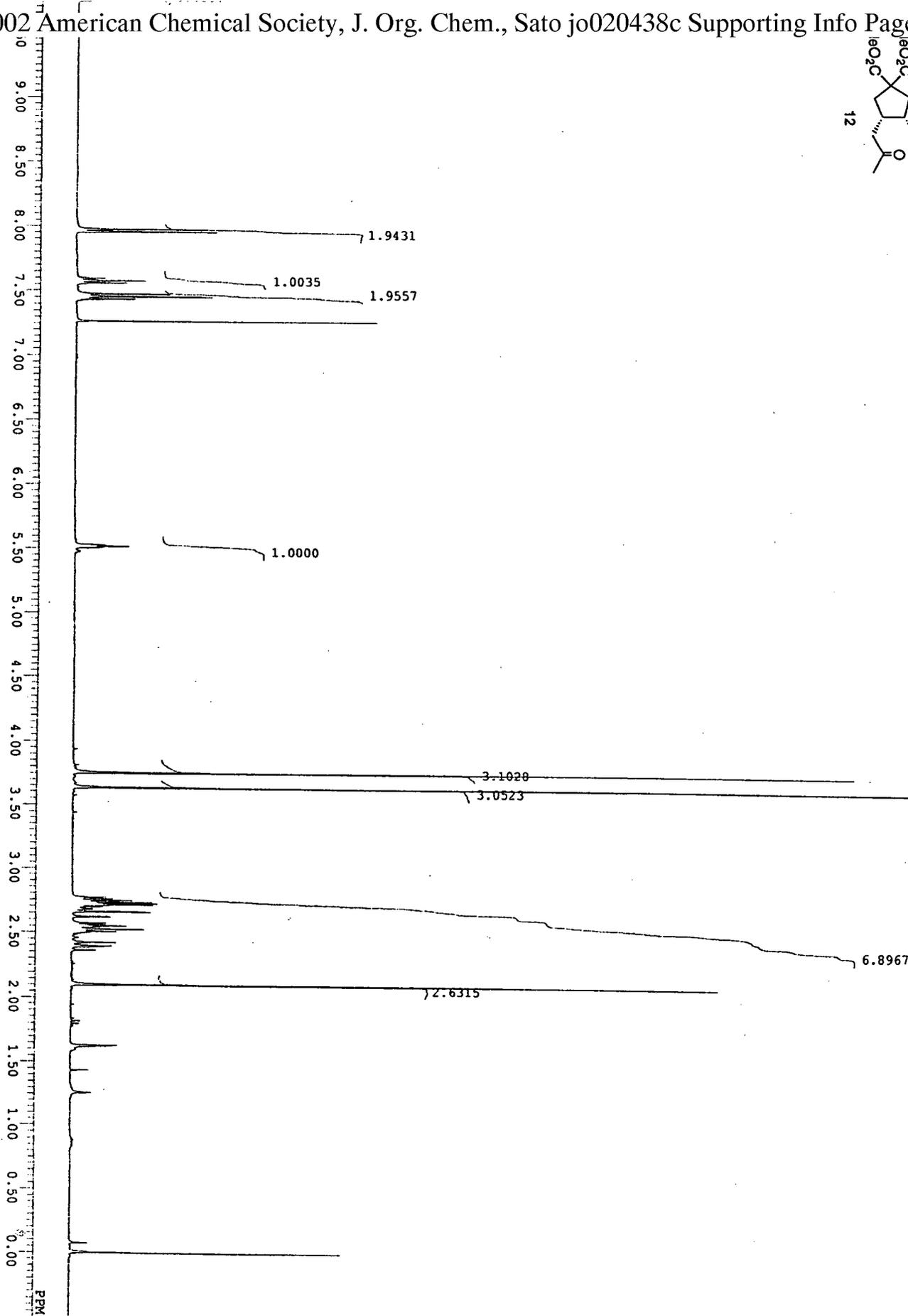
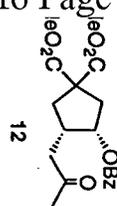


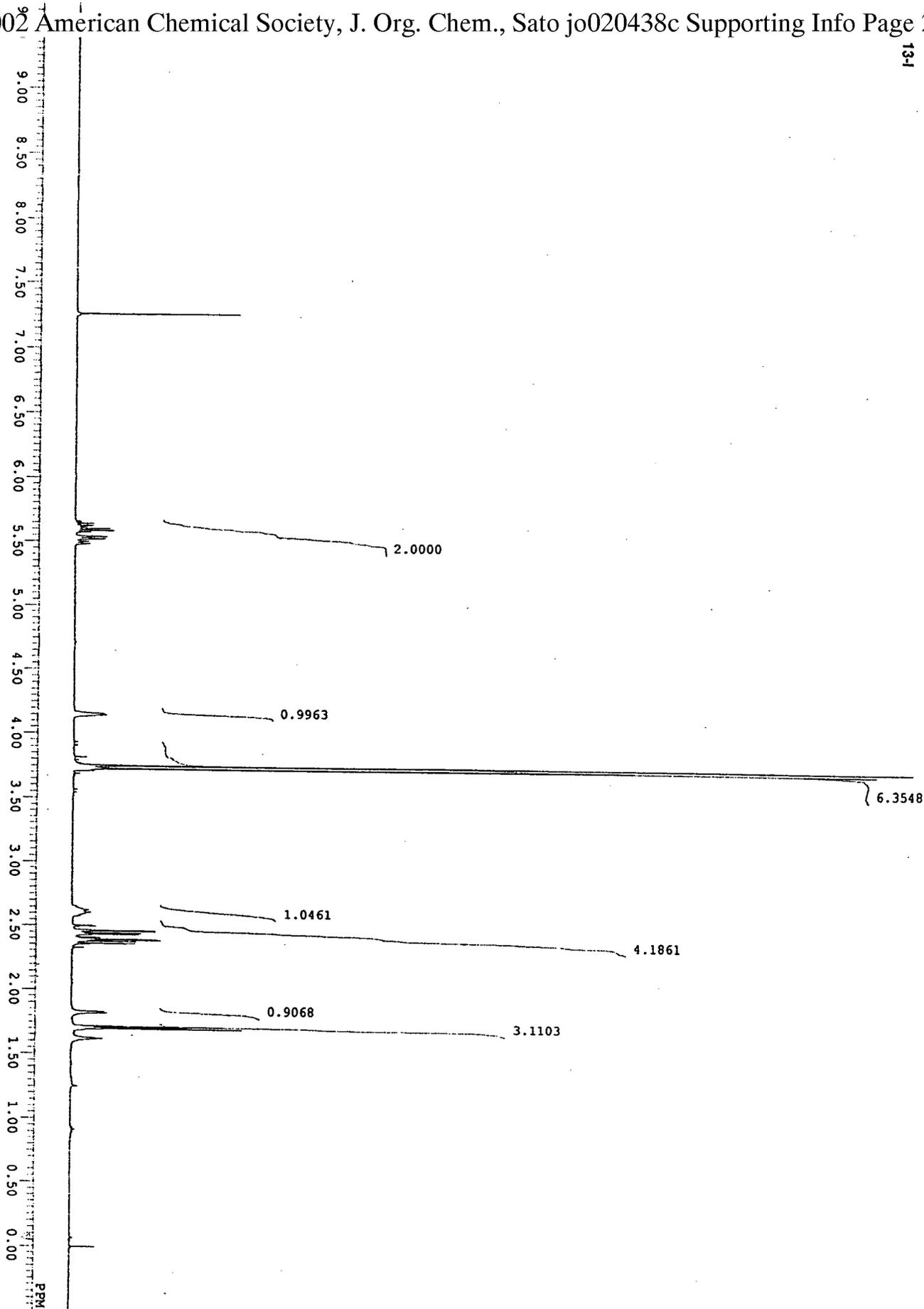
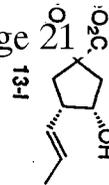


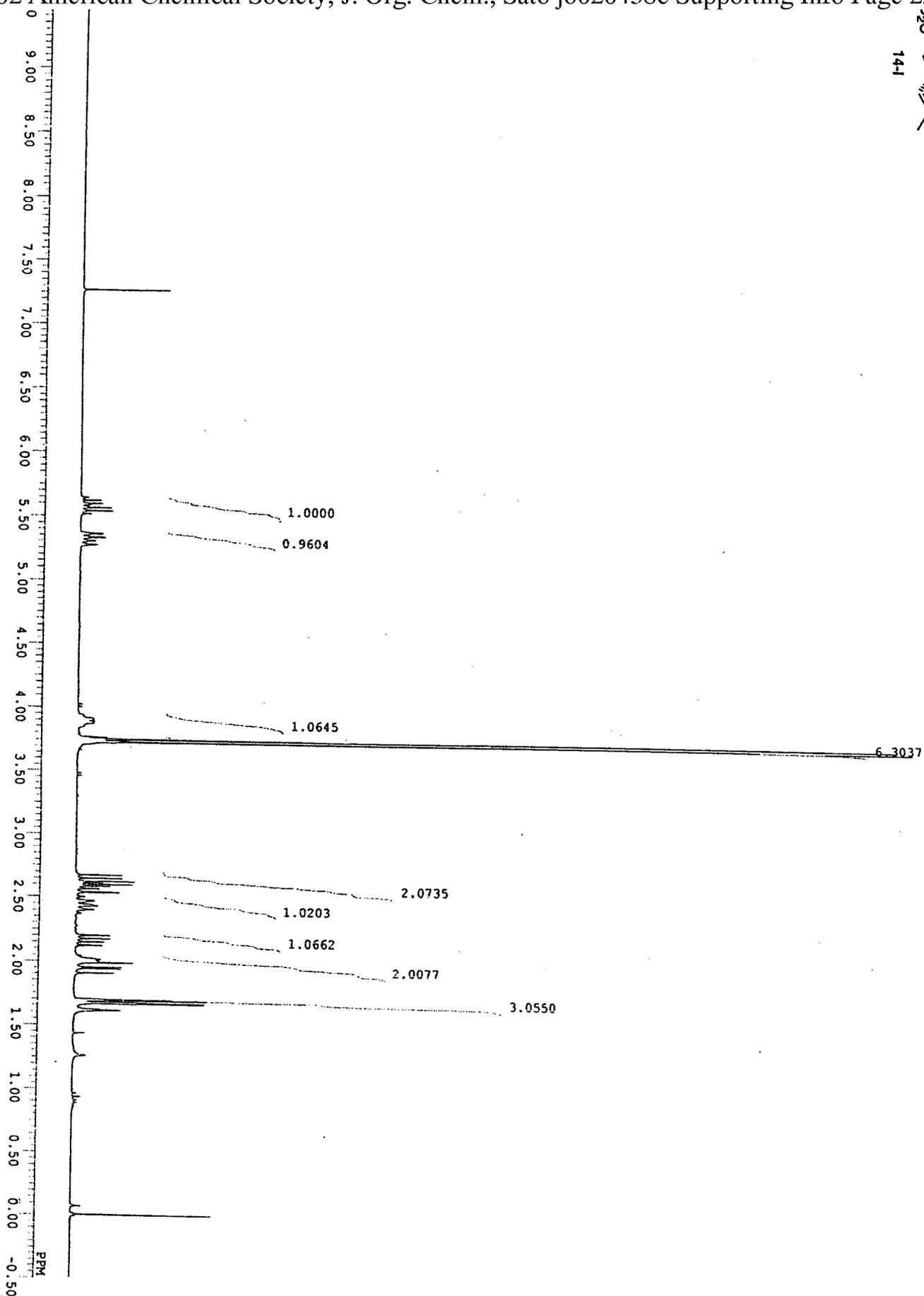
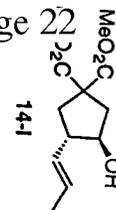


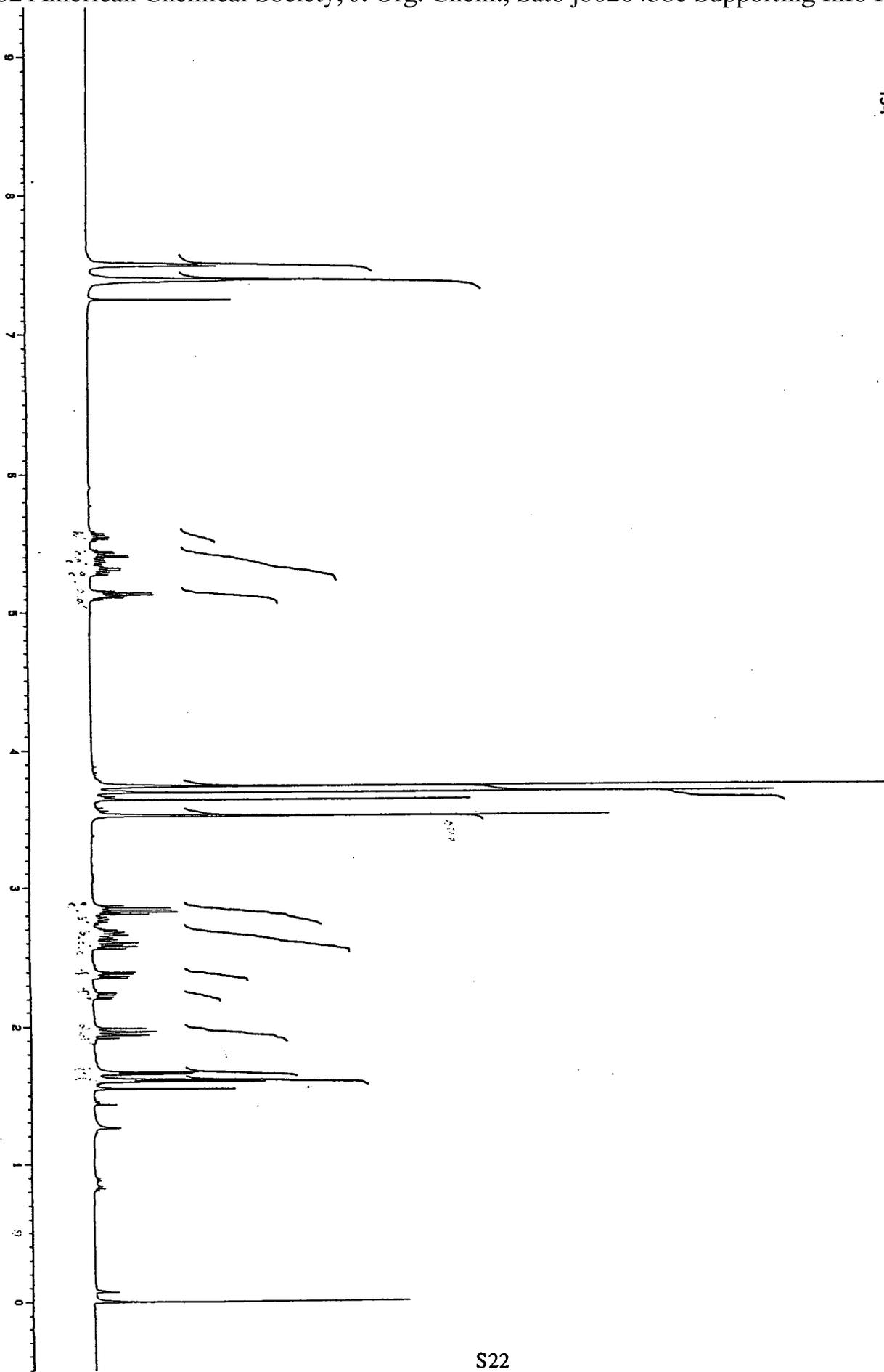
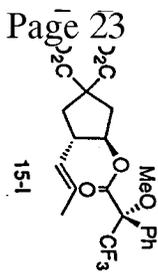


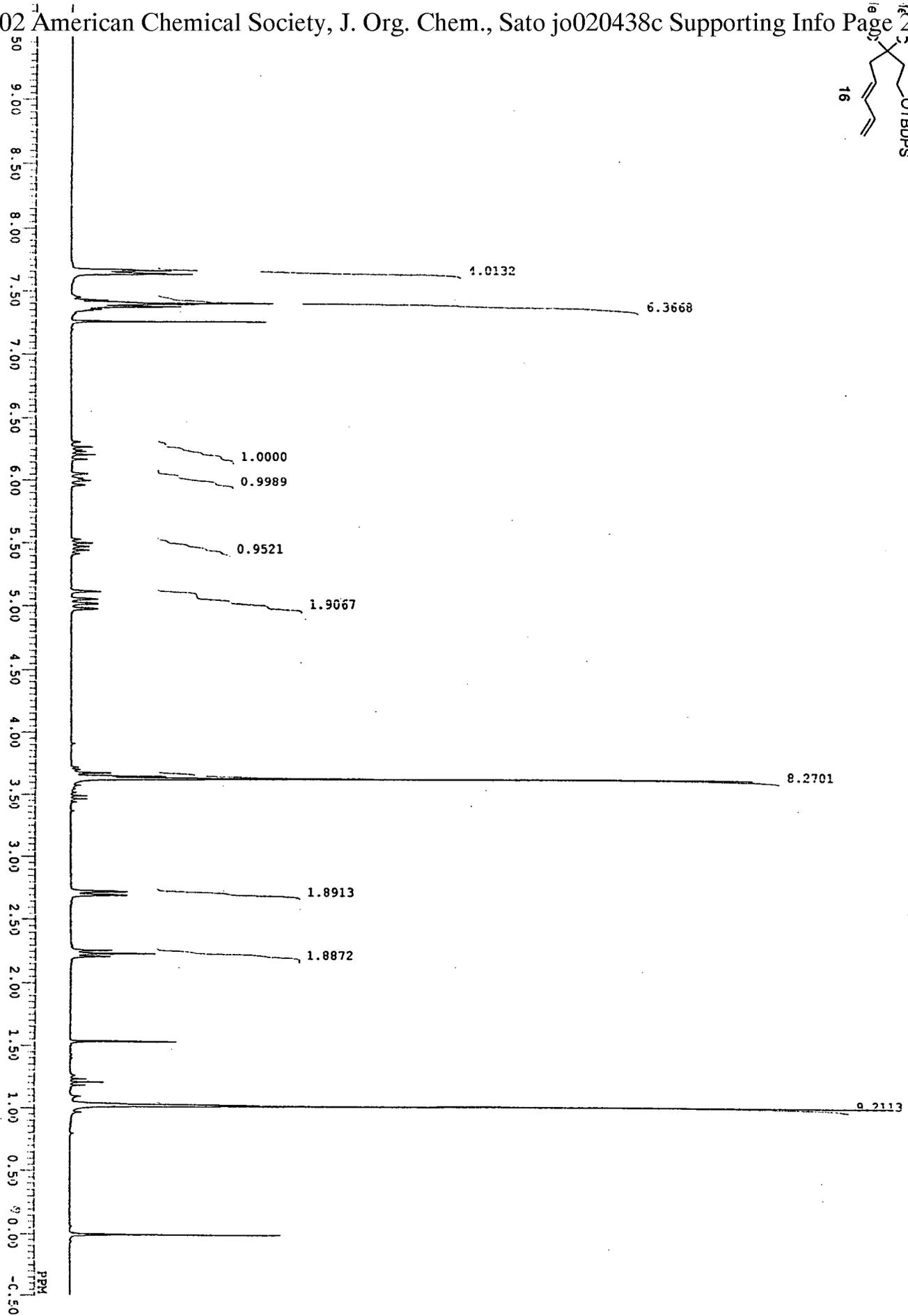
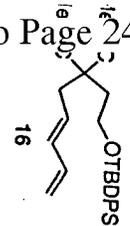


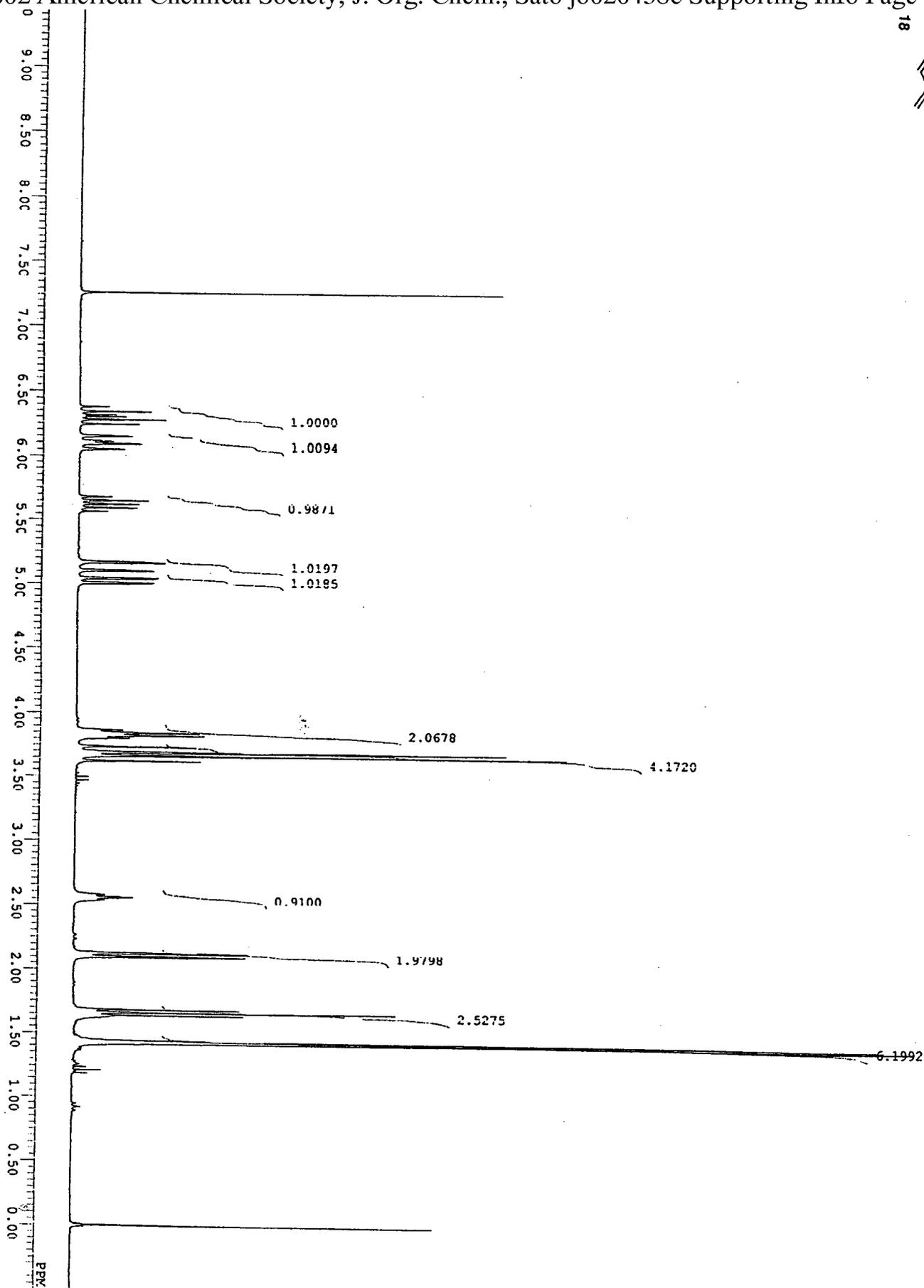
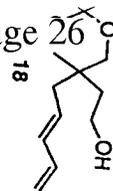


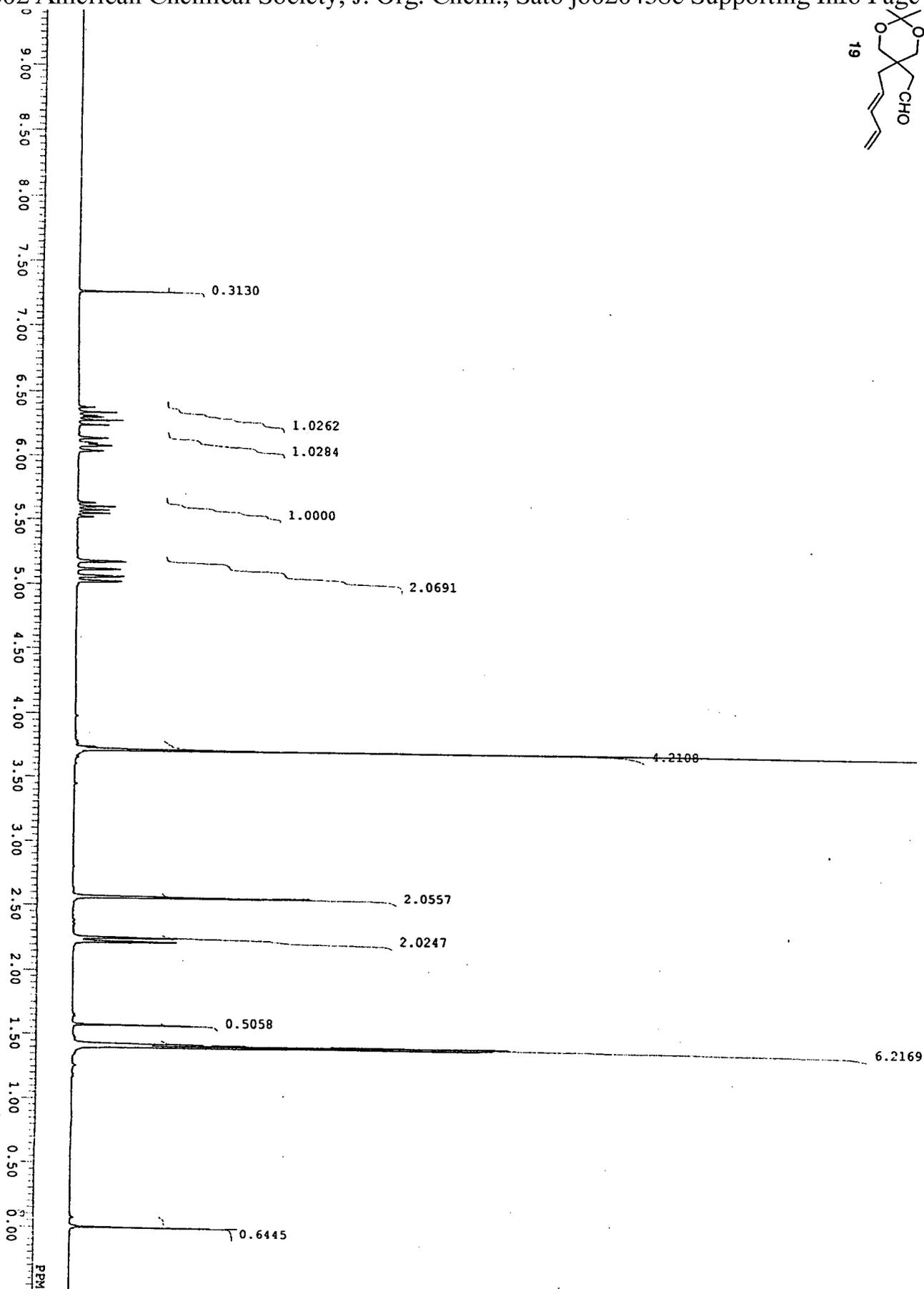
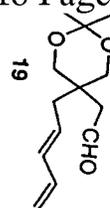




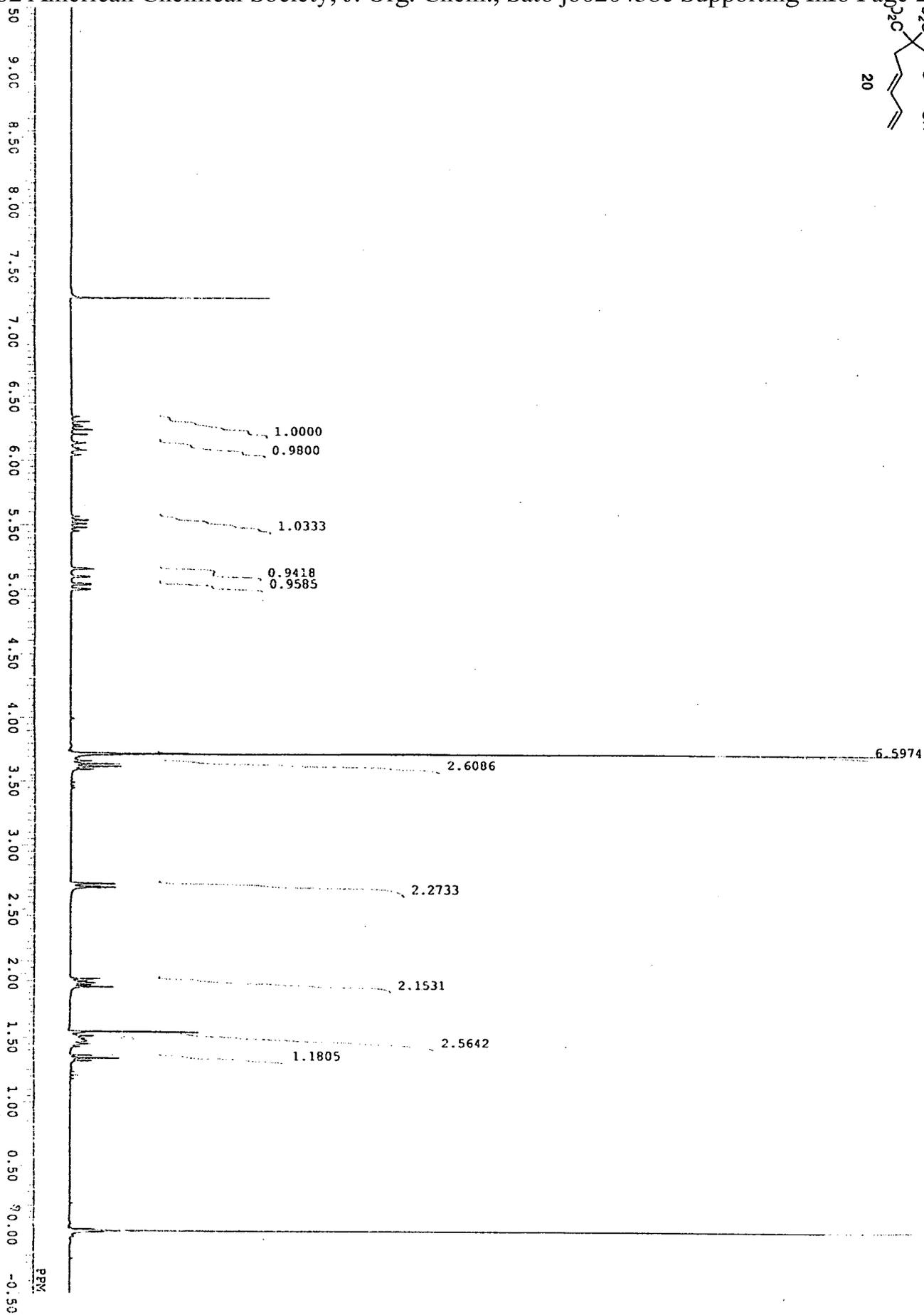
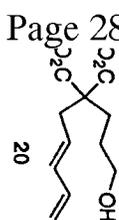




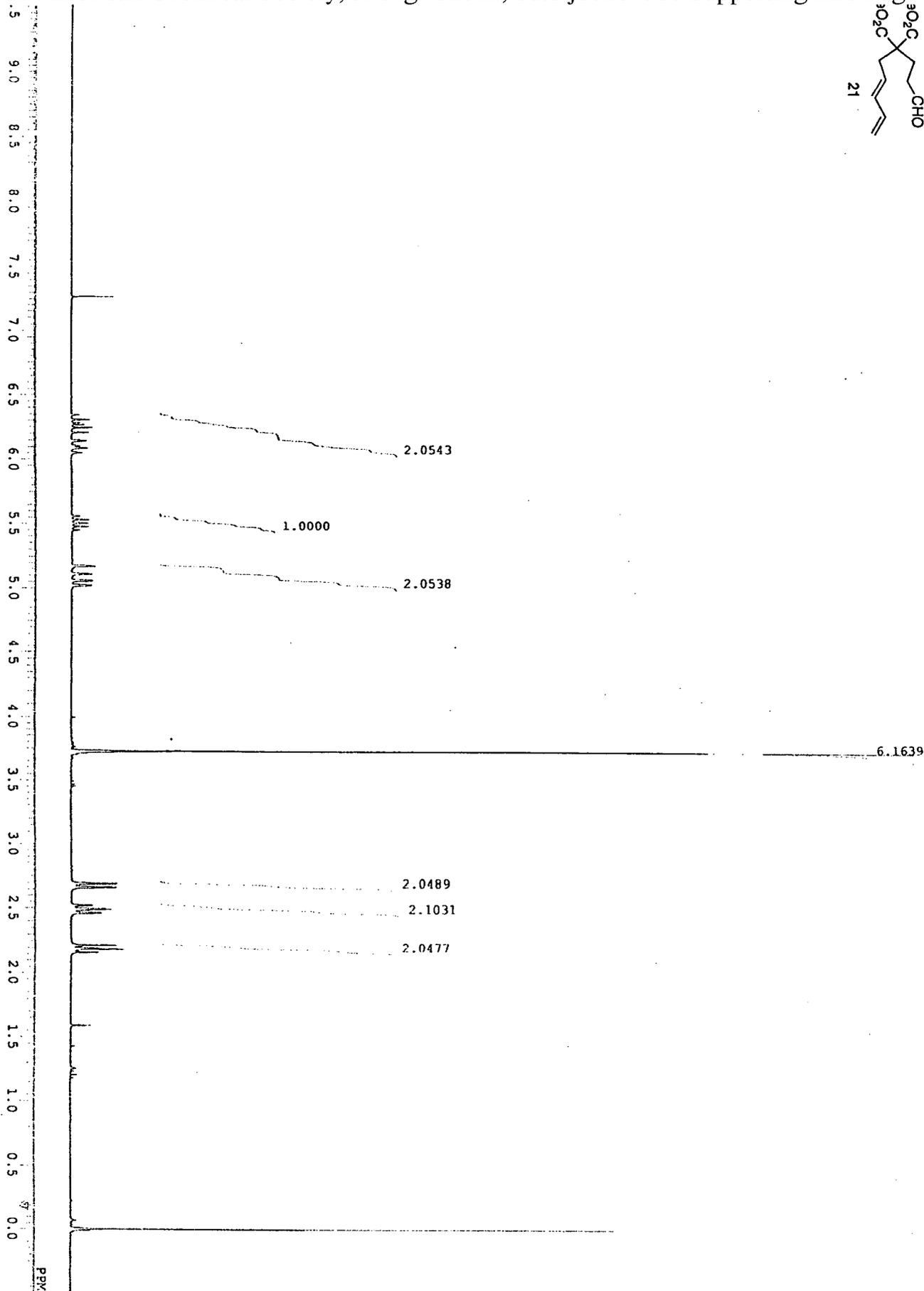
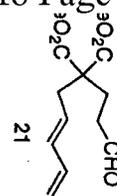


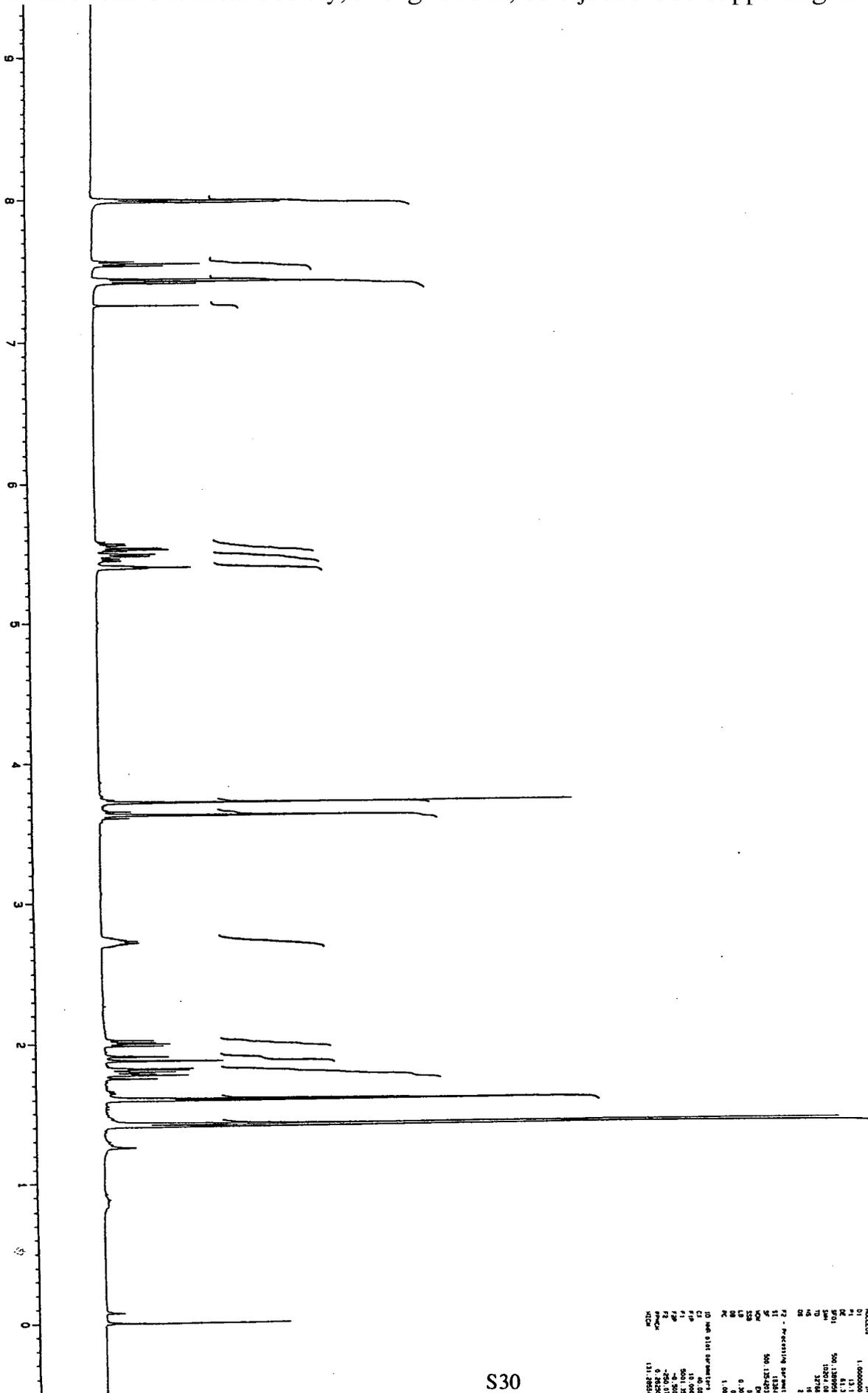
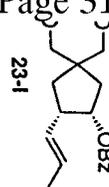


1S186A (EX270, CDCl3)



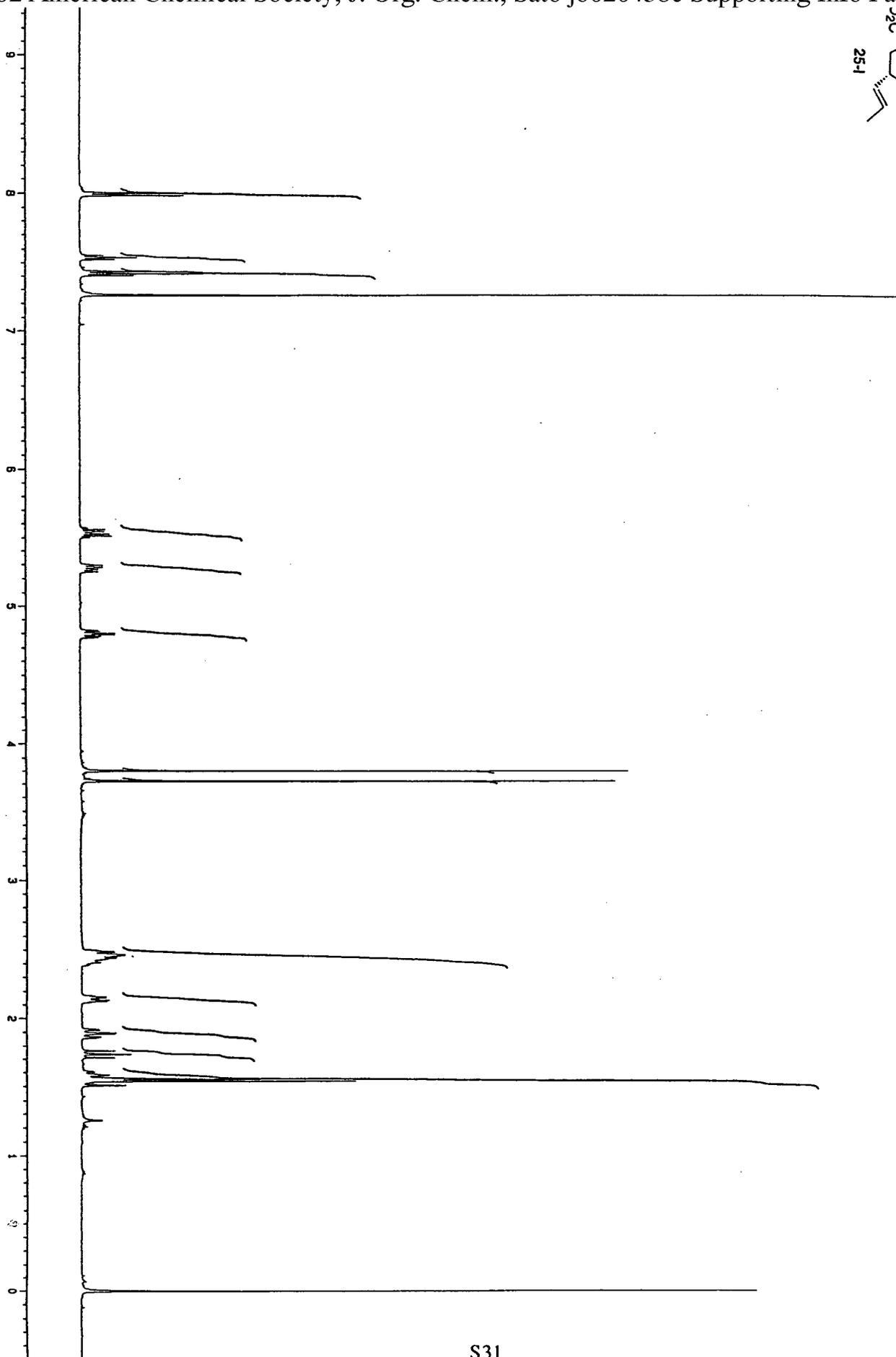
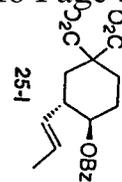
IS187A1EX270.C (CDCl3)





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 PROCNO 1
 F2 - Acquisition Parameters
 Date_ 06/07/01
 Time 13:50
 Name 23-1
 Solvent CDCl3
 NS 1024
 DS 4
 SWH 6553.844 Hz
 FWH 48.8 MHz
 AQ 0.163638 sec
 RG 327.68
 DEC 1824
 NUC1 13C
 NUC2 1H
 P1 13.1 usec
 DE 1.90 usec
 SFO1 500.136090 MHz
 SFO2 125.761370 MHz
 TD 32768
 GB 0
 PC 1
 F2 - Processing parameters
 SI 32768
 SF 500.136090 MHz
 NS 1024
 DS 4
 SWH 6553.844 Hz
 FWH 48.8 MHz
 AQ 0.163638 sec
 RG 327.68
 DEC 1824
 NUC1 13C
 NUC2 1H
 P1 13.1 usec
 DE 1.90 usec
 SFO1 500.136090 MHz
 SFO2 125.761370 MHz

S30



S31

