

Carbonylative Ring Opening of Terminal Epoxides at Atmospheric Pressure

Scott E. Denmark* and Moballigh Ahmad

Department of Chemistry, Roger Adams Laboratory, University of Illinois, Urbana, Illinois

61801

SUPPORTING INFORMATION

<i>Table of Contents</i>	<i>page</i>
General Experimental	S1
Dicobalt Octacarbonyl Catalyzed Carbonylation of 1a-p .	S3
References	S23
NMR Spectra	S26
GC/SFC Traces	S43

General Experimental

All carbonylation reactions (except high pressure reactions) were performed in oven (150 °C) and/or flame dried Schlenk flasks. High-pressure reactions (41 bar CO) were performed in a custom built six-cell stainless steel autoclave. THF, CH₂Cl₂ were dried by percolation through a column packed with neutral alumina and a column packed with Q5 reactant, a supported copper catalyst for scavenging oxygen, under a positive pressure of argon. Methanol was freshly distilled from Mg(OMe)₂ prior used. All terminal epoxides were used as received. Propylene oxide and cyclohexene oxide were heated to reflux over calcium hydride for 12 h, then were distilled, and stored in Schlenk flasks.

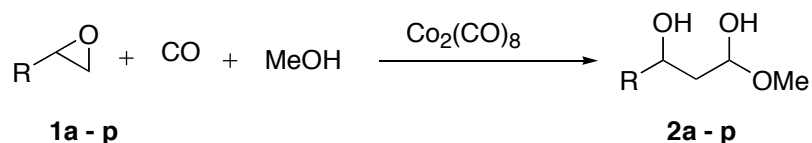
¹H NMR, and ¹³C NMR spectra were recorded at 400 MHz or 500 MHz. Spectra are

referenced to residual chloroform (δ 7.26 ppm, ^1H ; δ 77.0 ppm, ^{13}C). Chemical shifts are reported in ppm. Multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), hept (heptet), and br (broad). Coupling constants J , are reported in Hertz. Low-resolution electron impact (EI) mass spectra were obtained with a typical ionization voltage of 70 eV. Chemical ionization (CI) spectra were obtained using methane as the carrier gas. Data are reported in the form of (m/z). Infrared spectra (IR) are reported in cm^{-1} with indicated relative intensities: s (strong, 67-100%); m (medium, 34-66%); w (weak, 0-33%). Melting point (mp) was determined in sealed tubes and are corrected. Analytical thin-layer chromatography was performed on Merck silica gel 60 with F-254 indicator (pre coated plates). Visualization was accomplished with *p*-anisaldehyde stain. Gas chromatography (GC) was performed using a flame ionization detector and a trifluoroacetyl γ -cyclodextrin (G-TA, 30 x 0.25 mm, manufactured by CHIRALDEXTM). The separations were performed with a H_2 head pressure of 12 psi. Injector temperature was 250 °C; the detector temperature was 300 °C. Analytical supercritical fluid chromatography (SFC) was performed on packed-column SFC built-in photometric detector (λ = 220, 258 nm) using Daicel Chiralpak OD column. Retention times (t_R) and peak areas for SFC and GC were obtained from reporting integrators.

Epoxides **1a**, **1b**, **1c**, **1f**, **1g**, **1h**, **1i**, **1l**, **1p** were obtained from commercial vendors and used as received. Epoxides **1d**,¹ **1e**,² **1j**,³ **1k**,⁴ **1m**⁵ **1n**⁶ and **1o**⁷ were synthesized according to literature procedures. Carbon monoxide was received from Matheson TRI.GAS, C.P grade (CP = Chemically pure), lot number 4005200303. Dicobalt octacarbonyl was purchased from Strem Chemicals and was sublimed in 100 mL glass sublimation chamber at 0.5 mmHg pressure using acetone/dry ice cold finger at room temperature to 35 °C.

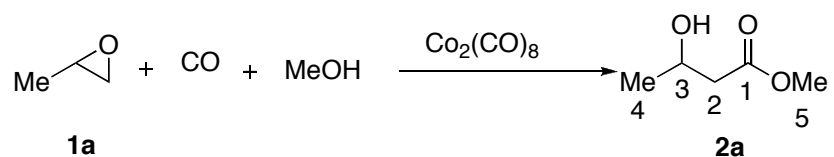
Experimental Procedures

General Procedure I. Dicobalt Octacarbonyl Catalyzed Carbonylation of **1a-p**.



In a glove box, $\text{Co}_2(\text{CO})_8$ (84.5 mg, 0.25 mmol, 0.05 equiv.) was placed in a 100-mL Schlenk flask equipped with a magnetic stir bar. The flask was sealed with a rubber septum and was removed from a dry box. The flask was purged three times for 2 sec. with carbon monoxide (filled in 12.7 cm latex balloon). Freshly distilled methanol (5.0 mL) was added and the mixture was stirred for 2 min. before the epoxides (5 mmol) was added in one portion. The mixture was allowed to stir at room temperature for 24 h. After the given reaction time, the carbon monoxide balloon was removed and carefully vented in the hood. The reaction mixture was diluted with ether (50 mL) and was stirred for 30 – 60 minutes to precipitate the cobalt complex. The mixture was passed through silica gel (20 X 100 mm), using diethyl ether as the eluent and upon careful removal of solvent *in vacuo* provided the products, that can be further purified (if necessary) by flash chromatography on silica gel using hexane/ethyl acetate as the eluent.

Preparation of Methyl 3-Hydroxybutanoate (**2a**) [Table 2, Entry 1]



Following General Procedure I, $\text{Co}_2(\text{CO})_8$ (84.5 mg, 0.25 mmol, 0.05 equiv.), freshly distilled methanol (5.0 mL) and **1a** (350 μL , 5.0 mmol) were stirred under a CO atmosphere (1 atm) at room temperature for 24 h. The reaction mixture was diluted with diethyl ether (50 mL)

and was stirred for 30 min., then passed through silica gel (20 X 100 mm), with diethyl ether (10 mL) as the eluent. Careful removal of solvent under reduced pressure afforded 525 mg (89 %) of **2a** as clear colorless oil. NMR spectral data matched that previously reported in the literature.⁸

Data for **2a**:

¹H NMR (500 MHz, CDCl₃)

4.19 (m, 1 H), 3.70 (s, 3 H), 2.96 (d, 1 H), 2.49 (dd, *J* = 16.3, 3.4, 1 H), 2.42 (dd, *J* = 16.3, 8.7, 1 H), 1.22 (d, 3 H)

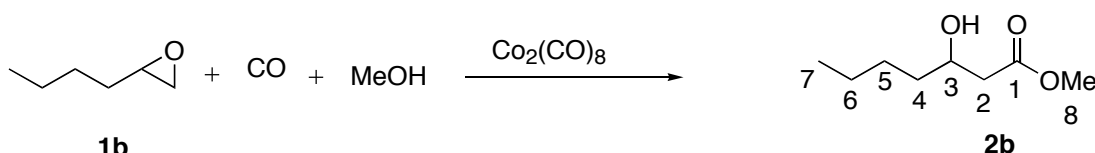
¹³C NMR (125 MHz, CDCl₃)

173.3, 64.2, 51.7, 42.5, 22.4

IR (neat)

3422 (s), 2975 (s), 2930 (s), 2093 (w), 1724 (s), 1439 (m), 1374 (m), 1299 (m), 1261 (m), 1176 (m), 1124 (m), 1088 (m), 1072 (m), 1006 (m), 946 (m), 851 (w)

Preparation of Methyl 3-Hydroxyheptanoate (2b**) [Table 2, Entry 2]**



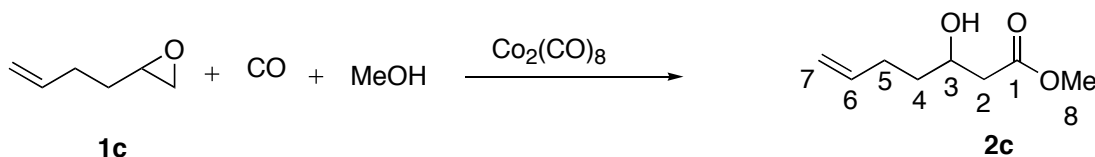
Following General Procedure I, Co₂(CO)₈ (84.5 mg, 0.25 mmol, 0.05 equiv.), freshly distilled methanol (5.0 mL) and **1b** (600 μL, 5.0 mmol) were stirred under a CO atmosphere (1 atm) at room temperature for 24 h. The reaction mixture was diluted with diethyl ether (50 mL) and was stirred for 30 min., then passed through silica gel (20 X 100 mm), with diethyl ether (10 mL) as the eluent. Careful removal of solvent *in vacuo* followed by column chromatography (SiO₂, 20 mm X 20 cm, hexane/EtOAc, hexane, 20/1, 3/1) to afford 710 mg (89 %) of **2b** as clear colorless oil. NMR spectral data matched that previously reported in the literature.⁹

Data for **2b**:¹H NMR (500 MHz, CDCl₃)4.00 (m, 1 H), 3.71 (s, 3 H), 2.86 (d, 1 H), 2.51 (dd, *J* = 16.4, 3.0, 1 H), 2.40 (dd, *J* = 16.4, 9.1, 1 H), 1.29-1.53 (br m, 6 H) 0.90 (t, 3 H)¹³C NMR (125 MHz, CDCl₃)

173.4, 67.9, 51.7, 41.1, 36.2, 27.6, 22.5, 13.9

IR (neat)

3446 (w), 2956 (m), 2932 (m), 2861 (w), 1738 (s), 1438 (m), 1291 (w), 1169 (m), 1125 (w), 1040 (w)

Preparation of Methyl 3-Hydroxy-6-heptenoate (2c) [Table 2, Entry 3]

Following General Procedure I, Co₂(CO)₈ (84.5 mg, 0.25 mmol, 0.05 equiv.), freshly distilled methanol (5.0 mL) and **1c** (564 μL, 5.0 mmol) were stirred under a CO atmosphere (1 atm) at room temperature for 24 h. The reaction mixture was diluted with diethyl ether (50 mL) and was stirred for 30 min., then passed through silica gel (20 X 100 mm), with diethyl ether (10 mL) as the eluent. Careful removal of solvent *in vacuo* followed by column chromatography (SiO₂, 20 mm X 20 cm, hexane/EtOAc, hexane, 20/1, 3/1) to afforded 760 mg (96 %) of **2c** as clear colorless oil. NMR spectral data matched that previously reported in the literature.¹⁰

Data for **2c**:¹H NMR (500 MHz, CDCl₃)

5.82 (m, 1 H), 5.05 (dq, 17.2, 1.7, 1 H), 4.98 (dq, 9.7, 1.4, 1 H), 4.03 (m, 1 H),

3.71 (s, 3 H), 2.90 (d, 1 H), 2.52 (dd, $J = 16.6, 3.1, 1$ H), 2.43 (dd, $J = 16.3, 9.0, 1$ H), 2.18 (m, 2 H), 1.58 (m, 2 H)

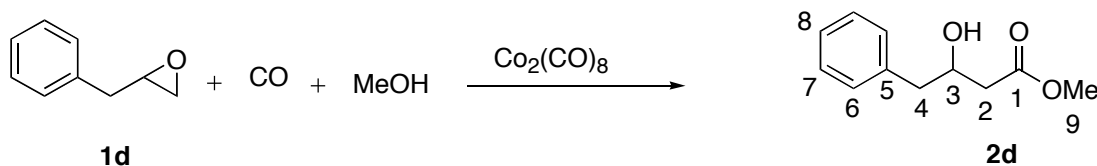
^{13}C NMR (125 MHz, CDCl_3)

173.3, 137.9, 115.0, 67.4, 51.7, 41.1, 35.5, 29.7

IR (neat)

3445 (w), 3077 (w), 2923 (w), 2849 (w), 1737 (m), 1641 (w), 1438 (m), 1359 (w), 1295 (w), 1247 (w), 1200 (w), 1168 (w), 1121 (w), 1082 (w), 1062 (w), 995 (w), 912 (w)

Preparation of Methyl 3-Hydroxy-4-phenylbutanoate (**2d**) [Table 2, Entry 4]



Following General Procedure I, $\text{Co}_2(\text{CO})_8$ (84.5 mg, 0.25 mmol, 0.05 equiv.), freshly distilled methanol (5.0 mL) and **1d** (657 μL , 5.0 mmol) were stirred under a CO atmosphere (1 atm) at room temperature for 24 h. The reaction mixture was diluted with diethyl ether (50 mL) and was stirred for 30 min., then passed through silica gel (20 X 100 mm), with diethyl ether (10 mL) as the eluent. Careful removal of solvent *in vacuo* followed by column chromatography (SiO_2 , 20 mm X 20 cm, hexane/EtOAc, hexane, 20/1, 3/1) to afforded 529 mg (54 %) of **2d** as clear colorless oil. NMR spectral data matched that previously reported in the literature.¹¹

Data for **2d**:

^1H NMR (500 MHz, CDCl_3)

7.31 (br t, 2 H), 7.21-7.25 (br m, 3 H), 4.27 (m, 1 H), 3.70 (s, 3 H), 2.86 (m, 2 H), 2.67 (dd, $J = 13.6, 6.1, 1$ H), 2.53 (dd, $J = 16.3, 3.4, 1$ H), 2.46 (dd, $J = 16.3, 8.8,$

1 H), 1.22 (d, 3 H)

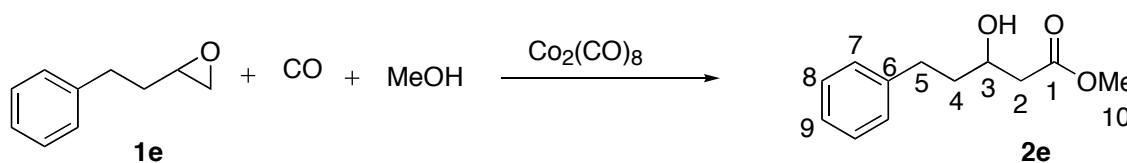
¹³C NMR (125 MHz, CDCl₃)

173.0, 137.5, 129.3, 128.5, 126.6, 69.0, 51.7, 42.9, 40.3

IR (neat)

3433 (m), 3087 (w), 3063 (w), 3029 (w), 3004 (w), 2953 (s), 2852 (w), 1731 (s),
1604 (m), 1495 (m), 1455 (m), 1439 (m) 1269 (s), 1200 (s), 1150 (s), 1083 (s),
1054 (s), 1030 (s), 995 (s), 854 (s), 749 (s), 701 (s)

Preparation of Methyl 3-Hydroxy-5-phenylpentanoate (**2e**) [Table 2, Entry 5]



Following General Procedure I, Co₂(CO)₈ (84.5 mg, 0.25 mmol, 0.05 equiv.), freshly distilled methanol (5.0 mL) and **1e** (657 μ L, 5.0 mmol) were stirred under a CO atmosphere (1 atm) at room temperature for 24 h. The reaction mixture was diluted with diethyl ether (50 mL) and was stirred for 30 min., then passed through silica gel (20 X 100 mm), with diethyl ether (10 mL) as the eluent. Careful removal of solvent *in vacuo* followed by column chromatography (SiO₂, 20 mm X 20 cm, hexane/EtOAc, hexane, 20/1, 3/1) to afforded 625 mg (64 %) of **2e** as clear colorless oil. NMR spectral data matched that previously reported in the literature.¹²

Data for **2e**:

¹H NMR (500 MHz, CDCl₃)

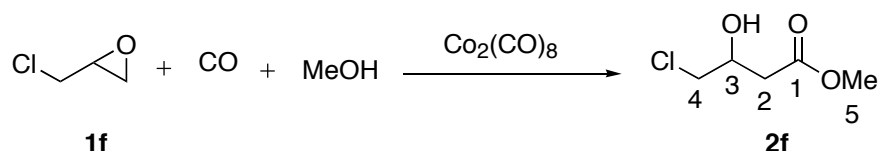
7.32 (m, 2 H), 7.25 (br m, 3 H), 4.06 (m, 1 H), 3.75 (s, 3 H), 3.05 (d, 1 H), 2.87 (m, 1 H), 2.75 (m, 1 H), 2.57 (dd, *J* = 16.6, 3.4, 1 H), 2.50 (dd, *J* = 16.6, 8.7, 1 H), 2.46 (dd, *J* = 16.3, 8.8, 1 H), 1.22 (d, 3 H), 1.88 (m, 1 H), 1.79 (m, 1 H)

¹³C NMR (125 MHz, CDCl₃)

173.3, 141.6, 128.3, 128.5, 125.8, 67.1, 51.7, 41.1, 38.0, 31.7

IR (neat)

3447 (w), 3085 (w), 3062 (w), 3027 (w), 3002 (w), 3027 (w), 2951 (w), 2861 (w),
 1732 (s), 1603 (m), 1496 (m), 1454 (m), 1438 (s), 1302 (s), 1253 (s), 1175 (s),
 1155 (s), 1080 (s), 1025 (s), 1002 (s), 936 (s), 749 (s), 700 (s)

Preparation of Methyl 4-Chloro-3-Hydroxybutanoate (2f) [Table 2, Entry 6]

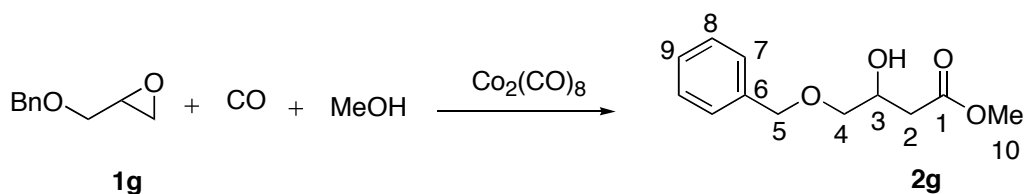
Following General Procedure I, Co₂(CO)₈ (84.5 mg, 0.25 mmol, 0.05 equiv.), freshly distilled methanol (5.0 mL) and **1f** (391 μL, 5.0 mmol) were stirred under a CO atmosphere (1 atm) at room temperature for 24 h. The reaction mixture was diluted with diethyl ether (50 mL) and was stirred for 30 min. in air, then passed through silica gel (20 X 100 mm), with diethyl ether (10 mL) as the eluent. Careful removal of solvent *in vacuo* followed by column chromatography (SiO₂, 20 mm X 20 cm, hexane/EtOAc, hexane, 20/1, 3/1) to afforded 556 mg (73 %) of **2f** as clear colorless oil. NMR spectral data matched that previously reported in the literature.¹³

Data for **2f**:¹H NMR (500 MHz, CDCl₃)

4.26 (m, 1 H), 3.73 (s, 3 H), 3.61 (m, 2 H), 3.05 (d, *J* = 5.1, 1 H), 2.65 (m, 2 H),
 1.22 (d, 3 H)

¹³C NMR (125 MHz, CDCl₃)

172.1, 67.9, 52.0, 48.1, 38.2

IR (neat)3446 (m), 2956 (w), 2359 (w), 1734 (s), 1437 (m), 1370 (w), 1309 (w), 1266 (w),
1199 (w), 1152 (w), 1090 (w), 1057 (w), 961 (w), 926 (w), 853 (w), 759 (w)**Preparation of Methyl 4-Benzyloxy-3-Hydroxybutanoate (2g) [Table 2, Entry 7]**

Following General Procedure I, Co₂(CO)₈ (84.5 mg, 0.25 mmol, 0.05 equiv.), freshly distilled methanol (5.0 mL) and **1g** (762 μL, 5.0 mmol) were stirred under a CO atmosphere (1 atm) at room temperature for 24 h. The reaction mixture was diluted with diethyl ether (50 mL) and was stirred for 30 min in air, then passed through silica gel (20 X 100 mm), with diethyl ether (10 mL) as the eluent. Careful removal of solvent *in vacuo* followed by column chromatography (SiO₂, 20 mm X 20 cm, hexane/EtOAc, hexane, 20/1, 3/1) to afforded 935 mg (83 %) of **2g** as clear colorless oil. NMR spectral data matched that previously reported in the literature.¹⁴

Data for **2g**:¹H NMR (500 MHz, CDCl₃)7.29-7.36 (br m, 5 H), 4.56 (s, 2 H), 4.24 (m, 1 H), 3.69 (s, 3 H), 3.52 (dd, *J* = 9.5, 4.3, 1 H), 3.47 (dd, *J* = 9.6, 6.0, 1 H), 2.93 (d, *J* = 5.3, 1 H), 2.55 (d, *J* = 6.6, 2 H)

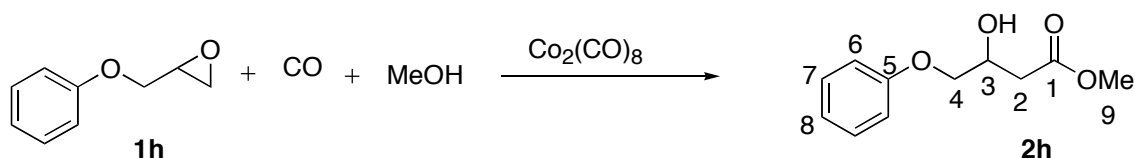
^{13}C NMR (125 MHz, CDCl_3)

172.4, 137.7, 128.3, 127.7, 127.6, 73.3, 73.0, 67.1, 51.7, 38.0

IR (neat)

3453 (m), 3030 (w), 2946 (w), 2931 (w), 2863 (w), 1737 (s), 1496 (w), 1453 (m),
1438 (m), 1361 (m), 1255 (w), 1206 (w), 1170 (m), 1102 (m), 1005 (w), 739 (m),
699 (m)

Preparation of Methyl 4-Phenoxy-3-Hydroxybutanoate (2h) [Table 2, Entry 8]



Following General Procedure I, $\text{Co}_2(\text{CO})_8$ (84.5 mg, 0.25 mmol, 0.05 equiv.), freshly distilled methanol (5.0 mL) and **1h** (678 μL , 5.0 mmol) were stirred under a CO atmosphere (1 atm) at room temperature for 24 h. The reaction mixture was diluted with diethyl ether (50 mL) and was stirred for 30 min in air, then passed through silica gel (20 X 100 mm), with diethyl ether (10 mL) as the eluent. Careful removal of solvent *in vacuo* followed by column chromatography (SiO_2 , 20 mm X 20 cm, hexane/EtOAc, hexane, 20/1, 3/1) to afforded 903 mg (86 %) of **2h** as white solid.

Data for **2h**:

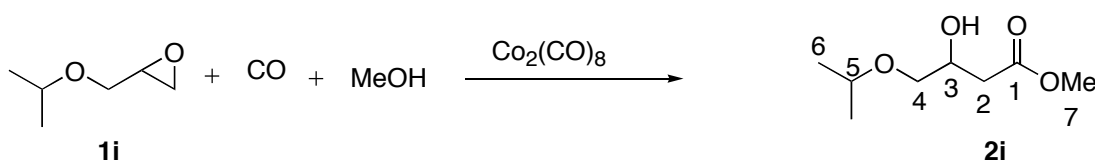
Mp 51-52 $^{\circ}\text{C}$

^1H NMR (500 MHz, CDCl_3)

7.27 (br t, $J = 8.05$, 2 H, HC(7)), 6.96 (br t, $J = 7.3$, 1 H, HC(8)), 6.90 (d, $J = 7.8$, 2 H, HC(6)), 4.42 (m, 1 H, HC(3)), 3.97 (d, $J = 5.1$, 2 H, HC(4)), 3.71 (s, 3 H, HC(9)), 3.40 (d, $J = 4.8$, 1 H, OH) 2.67 (m, 2 H, HC(2))

<u>^{13}C NMR</u>	(125 MHz, CDCl_3)
	172.2 (C(1)), 158.2 (C(5)), 129.3 (C(7)), 120.9 (C(8)), 114.3 (C(6)), 70.5(C(4)), 66.5 (C(3)), 51.7 (C(9)), 37.8 (C(2))
<u>IR</u>	(neat)
	3450 (w), 2952 (w), 2868 (w), 1735 (s), 1599 (m), 1587 (m), 1497 (m), 1454 (w), 1438 (m), 1364 (w), 1292 (m), 1245 (s), 1172 (m), 1078 (w), 1043 (m), 1000 (w), 925 (w), 884 (w), 814 (w), 755 (m), 692 (m)
<u>MS</u>	(CI, 70 eV)
	210 (3), 193 (5), 179 (37), 161 (96), 147 (8), 133 (57), 119 (100), 107 (23), 95 (28), 85 (25), 71 (17), 59 (26)
<u>TLC</u>	R_f 0.20 (hexane/EtOAc, 4/1) [silica gel, p-anisaldehyde stain]
<u>Analysis</u>	$\text{C}_{11}\text{H}_{14}\text{O}_4$ (210.23)
	Calculated: C, 62.85; H, 6.71 %
	Found: C, 63.19; H, 6.68 %

Preparation of Methyl 4-(1-Methylethoxy)-3-Hydroxybutanoate (**2i**) [Table 2, Entry 9]



Following General Procedure I, $\text{Co}_2(\text{CO})_8$ (84.5 mg, 0.25 mmol, 0.05 equiv.), freshly distilled methanol (5.0 mL) and **1i** (632 μL , 5.0 mmol) were stirred under a CO atmosphere (1 atm) at room temperature for 24 h. The reaction mixture was diluted with diethyl ether (50 mL) and was stirred for 30 min in air, then passed through silica gel (20 X 100 mm), with diethyl ether (10 mL) as the eluent. Careful removal of solvent *in vacuo* followed by column chromatography

(SiO₂, 20 mm X 20 cm, hexane/EtOAc, hexane, 20/1, 3/1) to afforded 703 mg (80 %) of **2i** as clear colorless oil.

Data for **2i**:

bp 95 °C at 0.5 mmHg

¹H NMR (500 MHz, CDCl₃)
4.13 (m, 1 H, HC(3)), 3.68 (s, 3 H, HC(7)), 3.57 (hept, *J* = 12.2, 6.1, 1 H, HC(5)),
3.43 (dd, *J* = 9.3, 4.5, 1 H, HC(4)), 3.35 (dd, *J* = 9.5, 6.1, 1 H, HC(4)), 2.97 (d, *J* =
4.6, 1 H, OH), 2.51 (d, *J* = 6.1, 2 H, HC(2)), 1.12 (d, *J* = 6.1, 6 H, HC(6)),

¹³C NMR (125 MHz, CDCl₃)
172.4 (C(1)), 72.1 (C(5)), 71.0 (C(4)), 67.3 (C(3)), 51.7 (C(7)), 38.1 (C(2)), 22.0
(C(6)), 21.9 (C(6))

IR (neat)
3450 (s), 2973 (s), 2930 (s), 2873 (s), 2630 (w), 1736 (s), 1438 (s), 1369 (s), 1336
(s), 1256 (s), 1163 (s), 1129 (s), 1075 (s), 1007 (m), 938 (m), 1599 (m), 884 (w),
824 (w)

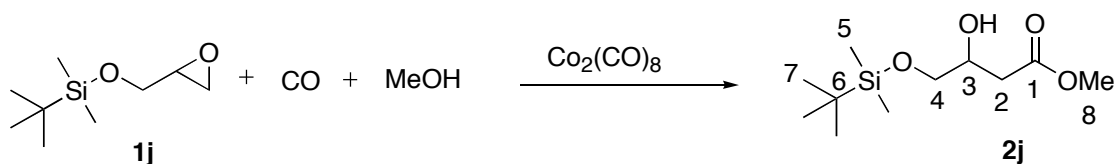
MS (CI, 70 eV)
177 (M⁺, 100), 159 (55), 145 (62), 135 (74), 117 (75), 103 (80), 85 (69), 71 (37),
61 (42)

TLC *R*_f0.22 (hexane/EtOAc, 4/1) [silica gel, p-anisaldehyde stain]

Analysis C₈H₁₆ O₄ (176.21)

Calculated: C, 54.53; H, 9.15 %

Found: C, 54.44; H, 9.52 %

Preparation of Methyl 4-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-3-Hydroxybutanoate (2j)**[Table 2, Entry 10]**

Following General Procedure I, $\text{Co}_2(\text{CO})_8$ (84.5 mg, 0.25 mmol, 0.05 equiv.), freshly distilled methanol (5.0 mL) and **1j** (1000 μL , 5.0 mmol) were stirred under a CO atmosphere (1 atm) at room temperature for 24 h. The reaction mixture was diluted with diethyl ether (50 mL) and was stirred for 30 min in air, then passed through silica gel (20 X 100 mm), with diethyl ether (10 mL) as the eluent. Careful removal of solvent *in vacuo* followed by column chromatography (SiO_2 , 20 mm X 20 cm, hexane/EtOAc, hexane, 20/1, 4/1) to afforded 272 mg (22 %) of **2j** as clear colorless oil.

Data for **2j**:bp 135 °C at 0.5 mmHg ^1H NMR (500 MHz, CDCl_3)

4.08 (m, 1 H, HC(3)), 3.71 (s, 3 H, HC(8)), 3.63 (dd, $J = 10.0, 4.8$, 1 H, HC(4)), 3.56 (dd, $J = 10.0, 5.8$, 1 H, HC(4)), 2.83 (d, $J = 4.8$, 1 H, OH), 2.52 (m, 2 H, HC(2)), 0.89 (s, 9 H, HC(7)), 0.06 (s, 6 H, HC(5))

 ^{13}C NMR (125 MHz, CDCl_3)

172.5 (C(1)), 68.5 (C(3)), 66.1 (C(4)), 51.8 (C(8)), 37.7 (C(2)), 25.8 (C(7)), 18.3 (C(6)), -5.45(C(5)), -5.47(C(5))

IR (neat)

3475 (s), 2950 (s), 2930 (s), 2858 (s), 2733 (w), 2713 (w), 1736 (s), 1463 (s), 1438 (s), 1362 (s), 1253 (s), 1169 (s), 1119 (s), 1072 (s), 1006 (m), 939 (m), 836

(s), 777 (s), 670 (m)

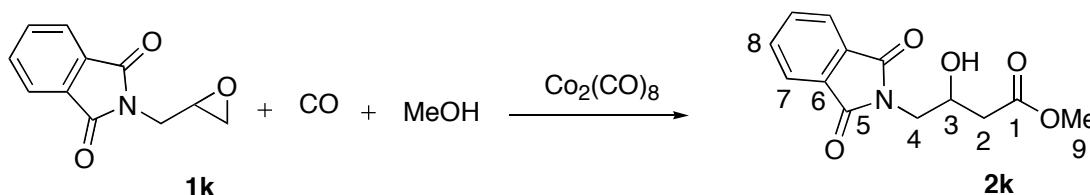
MS (CI, 70 eV)

249 (M^{+1} , 84), 233 (82), 217 (100), 191 (90), 173 (88), 159 (90), 131 (75), 117 (91), 85 (67), 75 (66), 59 (75)

TLC R_f 0.23 (hexane/EtOAc, 4/1) [silica gel, p-anisaldehyde stain]Analysis $C_{11}H_{24}O_4Si$ (176.21)

Calculated: C, 53.19; H, 9.74 %

Found: C, 52.92; H, 9.99 %

Preparation of Methyl 4-(N-Phthalimido)-3-Hydroxybutanoate (2k) [Table 2, Entry 11]

Following General Procedure I, $Co_2(CO)_8$ (84.5 mg, 0.25 mmol, 0.05 equiv.), freshly distilled methanol (5.0 mL) and **1k** (1.01 g, 5.0 mmol) were stirred under a CO atmosphere (1 atm) at room temperature for 24 h. The reaction mixture was diluted with diethyl ether (50 mL) and was stirred for 30 min in air, then passed through silica gel (20 X 100 mm), with diethyl ether (10 mL) as the eluent. Careful removal of solvent *in vacuo* followed by column chromatography (SiO_2 , 20 mm X 20 cm, hexane/EtOAc, hexane, 20/1, 1.5/1) to afford 975 mg (22 %) of **2k** as white solid.

Data for **2k**:mp 124-126 °C

¹H NMR (500 MHz, CDCl₃)

7.86 (dd, $J = 5.3, 2.9$, 2 H, HC(8)), 7.73 (dd, $J = 5.4, 3.0$, 2 H, HC(7)), 4.36 (m, 1 H, HC(3)), 3.89 (dd, $J = 14.0, 7.2$, 1 H, HC(4)), 3.77 (dd, $J = 13.8, 4.6$, 1 H, HC(4)), 3.71 (s, 3 H, HC(9)), 3.2 (d, $J = 4.8$, 1 H, OH), 2.61 (dd, $J = 16.6, 3.9$, 1 H, HC(2)), 2.53 (dd, $J = 16.6, 8.3$, 1 H, HC(2))

¹³C NMR (125 MHz, CDCl₃)

172.0 (C(1)), 168.4 (C(5)), 134.0 (C(6)), 131.7 (C(8)), 123.3 (C(7)), 66.4 (C(3)), 51.8 (C(9)), 42.8 (C(4)), 38.8 (C(2))

IR (neat)

3480 (w), 2952 (w), 1773 (w), 1711 (s), 1467 (w), 1435 (w), 1395 (m), 1301 (w), 1192 (w), 1172 (w), 1058 (w), 1023 (w), 884 (w), 725 (m)

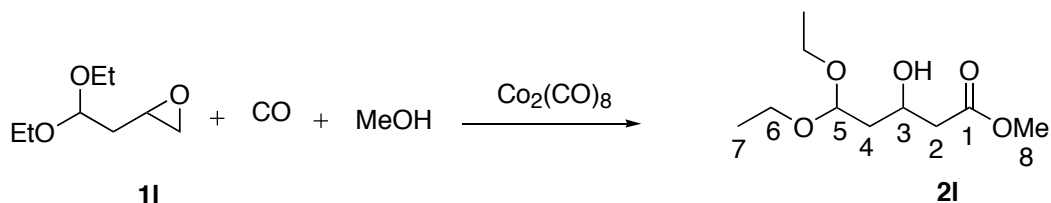
MS (CI, 70 eV)

264 (M^{+1} , 93), 260 (1), 247 (3), 246 (19), 245, (4), 232 (15), 214 (58), 186 (43), 162 (16), 161 (100), 160 (52), 133 (32), 132 (19), 117 (25), 105 (21), 104 (27),

TLC R_f 0.21 (hexane/EtOAc, 1/1) [silica gel, p-anisaldehyde stain]Analysis C₁₃H₁₃NO₅ (263.25)

Calculated: C, 59.31; H, 4.98 N, 5.32 %

Found: C, 59.12; H, 4.92 N, 5.35 %

Preparation of Methyl 5,5-Diethoxy-3-Hydroxybutanoate (2I) [Table 2, Entry 12]

Following General Procedure I, $\text{Co}_2(\text{CO})_8$ (84.5 mg, 0.25 mmol, 0.05 equiv.), freshly distilled methanol (5.0 mL) and **1I** (800 μL , 5.0 mmol) were stirred under a CO atmosphere (1 atm) at room temperature for 24 h. The reaction mixture was diluted with diethyl ether (50 mL) and was stirred for 30 min in air, then passed through silica gel (20 X 100 mm), with diethyl ether (10 mL) as the eluent. Careful removal of solvent *in vacuo* followed by column chromatography (SiO_2 , 20 mm X 20 cm, hexane/EtOAc, hexane, 20/1, 4/1) to afforded 120 mg (11 %) of **2I** as clear colorless oil.

Data for **2I**:

bp 80 °C at 0.5 mmHg

^1H NMR (400 MHz, CDCl_3)

7.86 (t, $J = 5.4, 10.9$, 1 H, HC(5)), 4.23 (m, 1 H, HC(3)), 3.70 (s, 3 H, HC(8)), 3.66 (m, 2 H, HC(6)), 3.52 (m, 2 H, HC(6)), 3.52 (m, 1 H, OH), 2.49 (m, 2 H, HC(2)), 1.21 (t, $J = 14.1, 7.0$, 3 H, HC(7)), 1.21 (t, $J = 13.9, 6.9$, 3 H, HC(7))

^{13}C NMR (125 MHz, CDCl_3)

172.6 (C(1)), 101.5 (C(5)), 65.1 (C(3)), 62.2 (C(6)), 61.9 (C(6)), 51.7 (C(8)), 41.4 (C(4)), 39.9 (C(2)), 15.3 (C(7)), 15.3 (C(7))

IR (neat)

3468 (m), 2976 (m), 2925 (m), 1736 (s), 1438 (w), 1374 (w), 1346 (w), 1266 (w), 1168 (m), 1126 (m), 1060 (m), 1008 (w)

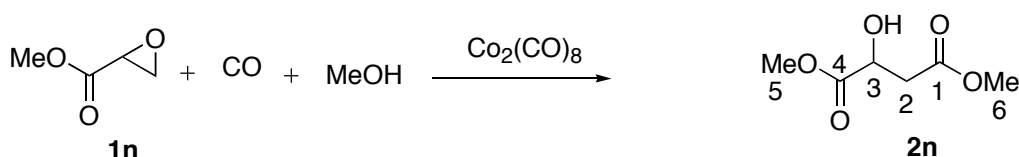
¹³C NMR (125 MHz, CDCl₃)

174.1, 173.0, 67.1, 51.8, 51.7, 41.1, 31.2, 30.2

IR (neat)

3530, 2950, 1740, 1674 (w), 1458 (m), 1375 (w), 1283 (m), 1243 (m), 1169 (m),
1119 (m), 1041 (w), 983 (w), 855 (w), 788 (w)

Preparation of Dimethyl 2-Hydroxybutanedioate (2n) [Table 2, Entry 14]



Following General Procedure I, Co₂(CO)₈ (84.5 mg, 0.25 mmol, 0.05 equiv.), freshly distilled methanol (5.0 mL) and **1n** (440 μ L, 5.0 mmol) were stirred under a CO atmosphere (1 atm) at room temperature for 24 h. The reaction mixture was diluted with diethyl ether (50 mL) and was stirred for 30 min in air, then passed through silica gel (20 X 100 mm), with diethyl ether (10 mL) as the eluent. Careful removal of solvent *in vacuo* followed by column chromatography (SiO₂, 20 mm X 20 cm, hexane/EtOAc, hexane, 20/1, 4/1) to afforded 283 mg (35 %) of **2n** as clear colorless oil. NMR spectral data matched that previously reported in the literature.¹⁶

Data for 2n:

¹H NMR (500 MHz, CDCl₃)

4.49 (m, 1 H), 3.80 (s, 3 H), 3.70 (s, 3 H), 3.27 (d, 1 H), 2.86 (dd, *J* = 16.4, 4.2, 1 H), 2.78 (dd, *J* = 16.6, 6.1, 1 H)

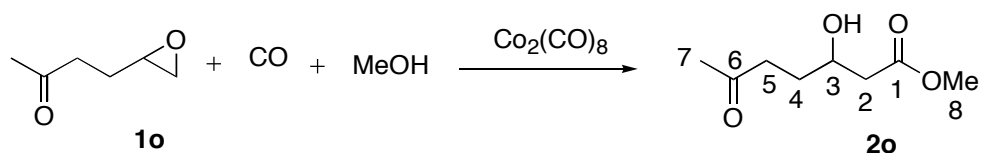
¹³C NMR (125 MHz, CDCl₃)

173.7, 170.9, 67.2, 52.8, 52.0, 38.3

IR (neat)

3458 (m), 3008 (w), 2958 (w), 1731 (s), 1640 (w), 1440 (m), 1370 (w), 1278 (m),
1223 (m), 1173 (m), 1110 (m), 1045 (w), 992 (w), 849 (w), 786 (w)

Preparation of Methyl 3-Hydroxy-6-oxo-heptanoate (2o) [Table 2, Entry 15]



Following General Procedure I, $\text{Co}_2(\text{CO})_8$ (84.5 mg, 0.25 mmol, 0.05 equiv.), freshly distilled methanol (5.0 mL) and **1o** (570 μL , 5.0 mmol) were stirred under a CO atmosphere (1 atm) at room temperature for 24 h. The reaction mixture was diluted with diethyl ether (50 mL) and was stirred for 30 min in air, then passed through silica gel (20 X 100 mm), with diethyl ether (10 mL) as the eluent. Careful removal of solvent *in vacuo* followed by column chromatography (SiO_2 , 20 mm X 20 cm, hexane/EtOAc, hexane, 20/1, 4/1) to afforded 148 mg (17 %) of **2o** as clear colorless oil.

Data for **2o**:

bp 170 °C at 0.5 mmHg

^1H NMR (400 MHz, CDCl_3)

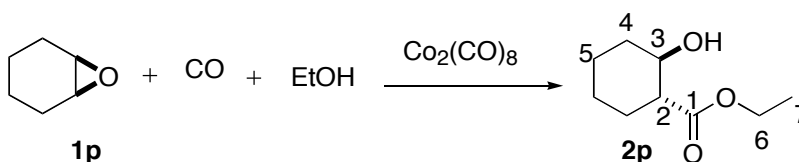
3.98 (m, 1 H, HC(3)), 3.71 (s, 3 H, HC(8)), 3.12 (d, $J = 3.41$, 1 H, OH), 2.64 (m, 2 H, HC(5)), 2.52 (d, $J = 16.6$, 3.4, 1 H, HC(2)), 2.44 (d, $J = 16.6$, 8.5, 1 H, HC(2)), 2.17 (s, 3 H, HC(7)), 1.76 (m, 1 H, HC(4)), 1.70 (m, 1 H, HC(4))

^{13}C NMR (125 MHz, CDCl_3)

208.9 (C(6)), 173.2 (C(1)), 67.2 (C(3)), 51.8 (C(8)), 41.2 (C(2)), 39.6 (C(5)), 30.0 (C(4)), 29.9 (C(7))

<u>IR</u>	(neat)
	3461 (m), 2953 (m), 1736 (s), 1711 (s), 1437 (s), 1363 (s), 1283 (s), 1259 (s), 1197 (s), 1170 (s), 1095 (m), 1012 (m), 934 (w), 885 (w)
<u>MS</u>	(ES, 70 eV)
	197 ($M^+ + Na$, 42), 174 (5), 158 (13), 157 (100), 126 (1), 125 (10), 115 (13)
<u>TLC</u>	<i>R</i> _f 0.25 (hexane/EtOAc, 1/1) [silica gel, p-anisaldehyde stain]
<u>Analysis</u>	$C_8H_{14}O_4$ (174.19)
	Calculated: C, 55.16; H, 8.10 %
	Found: C, 54.93; H, 8.00 %

Preparation of *trans* Ethyl 2-Hydroxycyclohexanoate (2p) [Table 2, Entry 16]



Following General Procedure I, $Co_2(CO)_8$ (84.5 mg, 0.25 mmol, 0.05 equiv.), freshly distilled ethanol (5.0 mL) and **1p** (506 μ L, 5.0 mmol) were stirred under a CO atmosphere (1 atm) at room temperature for 24 h. The reaction mixture was diluted with diethyl ether (50 mL) and was stirred for 30 min., then passed through silica gel (20 X 100 mm), with diethyl ether (10 mL) as the eluent. Careful removal of solvent *in vacuo* followed by column chromatography (SiO_2 , 20 mm X 20 cm, hexane/EtOAc, hexane, 20/1, 4/1) to 175 mg (20 %) of **2p** as clear colorless oil. NMR spectral data matched those previously reported in the literature.¹⁷

Data for **2p**:

<u>1H NMR</u>	(500 MHz, $CDCl_3$)
	4.16 (q, $J = 7.1$, 2 H), 3.75 (m, 1 H), 2.82 (d, $J = 3.4$, 1 OH), 2.23 (ddd, $J = 9.2$,

9.1, 3.2, 1 H), 2.01-2.06 (br m, 2 H), 1.75-1.78 (br m, 1 H), 1.69-1.73 (br m, 1 H),
1.27 (t, $J = 7.0$, 3 H), 1.09-1.38 (br m, 4 H)

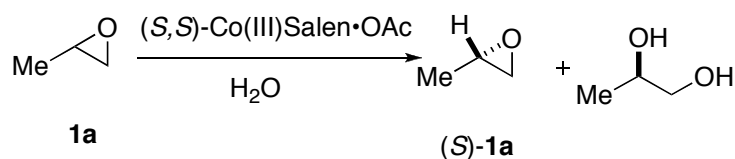
^{13}C NMR (125 MHz, CDCl_3)

175.2, 70.9, 60.6, 51.3, 33.6, 28.0, 25.1, 24.3, 14.2

IR (neat)

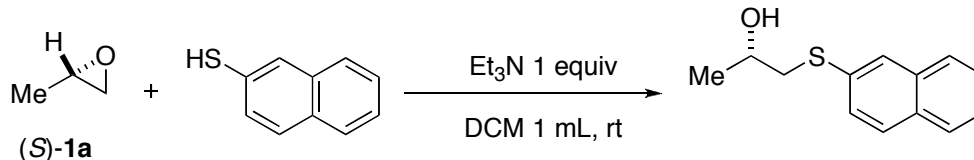
3431 (s), 2980 (w), 2936 (s), 2860 (m), 1718 (s), 1450 (m), 1376 (m), 1323 (m),
1251 (m), 1229 (m), 1180 (s), 1067 (s), 1034 (s), 987 (s), 952 (s), 860 (s)

Preparation of (*S*)-Propylene Oxide ((*S*)-1a) [Scheme 2]



Following Jacobsen Procedure,¹⁸ (*S*)-Cobalt salen complex (242 mg, 400 μmol , 0.002 equiv.), in 5.0 mL toluene (from SDS) was treated with 240 μL AcOH. The crude catalyst obtained after concentration was dissolved in propylene oxide (14.0 mL, 11.6 g, 200 mmol), and H_2O (1.98 mL, 110 mmol, 0.55 equiv) at 0 $^\circ\text{C}$ was added drop wise. After 14 h at rt, propylene oxide (5.14 g, 44 %) was isolated by direct distillation at 34 $^\circ\text{C}$. The ^1H NMR spectrum matched that of the racemic epoxide.

Opt. Rot.: $[\alpha]_{\text{D}}^{23} -11.58$ (neat); lit¹⁹ $[\alpha]_{\text{D}}^{23} -11.6$ (neat)

Determination of Enantiopurity of Propylene Oxide ((*S*)-1a) [Scheme 2]

Oven-dried, 10-mL, round-bottomed flask was charged with 2-naphthalenethiol (160 mg, 1.0 mmol) followed by 1 mL of dichloromethane and triethylamine (134 μL , 1.0 mmol, 1.0 equiv) and was stirred for 30 s whereupon the colorless mixture turned pale yellow. At this point (*S*)-propylene oxide (70 μL , 1.0 mmol) was added drop wise and the mixture was stirred for 6 h (monitored by TLC (silica gel plate, hexane/EtOAc 4/1). The reaction mixture was subjected to column chromatography (SiO_2 , 20 mm X 20 cm, hexane/EtOAc, hexane, 20/1, 4/1) to afford 110 mg (51 %) of 1-(2-naphthalenthio)-2-propanol.²⁰

Data for 1-(2-naphthalenthio)-2-propanol:¹H NMR (500 MHz, CDCl_3)

7.83 (s, 1 H), 7.78 (m, 3 H), 7.47 (m, 3 H), 3.91 (m, 1 H), 3.20 (dd, $J = 13.6, 3.9$, 1 H), 2.95 (dd, $J = 13.7, 8.4$, 1 H), 2.60 (s, 1 H), 6.34 (d, $J = 6.3$, 3 H)

¹³C NMR (125 MHz, CDCl_3)

133.1, 132.5, 131.9, 128.5, 128.1, 127.7, 127.6, 127.0, 126.6, 125.9, 65.6, 43.4, 21.9

IR (neat)

3346 (s), 3043 (m), 2968 (s), 2909 (s), 1586 (m), 1371 (m), 1129 (m), 1074 (w), 1033 (w), 940 (w), 844 (w), 814 (m), 737 (m)

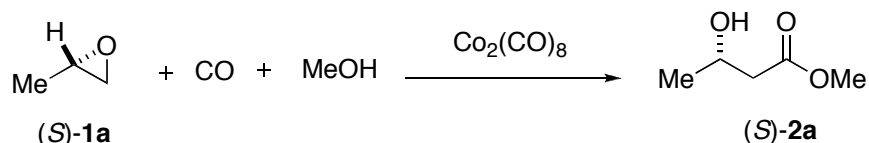
SFC: t_R 6.30 min (98.4%); t_R 6.95 min (1.6%) (Chiralpak OD, 125 psi, 40 $^\circ\text{C}$, 10% MeOH in CO_2 , 3.0 mL/min, 220 nm)

Analysis $C_{13}H_{14}OS$ (218.31)

Calculated: C, 71.52; H, 6.46 %

Found: C, 71.50; H, 6.50 %

Preparation of (*S*) Methyl 3-Hydroxybutanoate (**2a**) [Scheme 2]



Following General Procedure I, $\text{Co}_2(\text{CO})_8$ (84.5 mg, 0.25 mmol, 0.05 equiv.), freshly distilled methanol (5.0 mL) and (*S*)-**1a** (350 μL , 5.0 mmol) were stirred under a CO atmosphere (1 atm) at room temperature for 24 h. The reaction mixture was diluted with diethyl ether (50 mL) and was stirred for 30 min, then passed through silica gel (20 X 100 mm), with diethyl ether (10 mL) as the eluent. Careful removal of solvent under reduced pressure afforded 520 mg (88%) of (*S*)-**2a** as clear, colorless oil. The ^1H NMR spectrum of this product matched that of the racemic material.

Opt. Rot.: $[\alpha]_D^{23} +25.74$ ($c = 0.3$, CHCl_3); lit²¹ $[\alpha]_D^{23} +24.2$ ($c = 0.82$, CHCl_3)

GC: t_R 4.99 min (>99.9%); t_R 5.37 min (<0.1%) (G-TA, 80 $^\circ\text{C}$, isothermal, H_2 head pressure of 15 psi)

References

- (1) (a) Gais, H-J.; Jurgen, M.; Jadhav, V. *J. Org. Chem.* **2001**, 66, 3384-3396. (b) Majetich, G.; Hicks, R. *Synlett*. **1996**, 7, 649-651.
- (2) Mordini, A.; Peruzzi, D.; Russo, F.; Valacchi, M.; Reginato, G.; Brandi, A. *Tetrahedron* **2005**, 61, 3349-3360.
- (3) Yohei, K.; Junji, I.; Kobayashi, Y. *Tetrahedron Lett.* **2002**, 43, 2725-2729.

- (4) Williamson, R. M.; Pietersma, A. L.; Jameson, G. B.; Parker, E. J. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 2339-2342.
- (5) Liu, Z-Y.; Ji, J-X.; Li, B-G. *J. Chem. Soc., Perkin Trans.* **2000**, *1*, 3519-3521.
- (6) Hansen, K. B.; Rabbat, P.; Springfield, S. A.; Devine, P. N.; Grabowski, E. J. J.; Reider, P. J. *Tetrahedron Lett.* **2001**, *42*, 8743-8745.
- (7) Payne, G. B. *Tetrahedron Lett.* **1962**, *18*, 763-765.
- (8) (a) Ema, T.; Sugiyama, Y.; Fukumoto, M.; Moriya, H.; Cui, J.-N.; Sakai, M. *J. Org. Chem.* **1998**, *63*, 4996-5000. (b) Utaka, M.; Watabu, H.; Higashi, H.; Sakai, T.; Tsuboi.; Torii, S. *J. Org. Chem.* **1999**, *55*, 3917-3921. (c) Burk, M. J.; Harper, P. G. T.; Kalberg, C. S. *J. Am. Chem. Soc.* **1995**, *117*, 4423-4424. (d) Hinterding, K.; Jacobsen, E. N. *J. Org. Chem.* **1999**, *64*, 2164-2165.
- (9) Utaka, M.; Watabu, H.; Higashi, H.; Sakai, T.; Tsuboi.; Torii, S. *J. Org. Chem.* **1999**, *55*, 3917-3921.
- (10) (a) Hirama, M.; Uei, M. *J. Am. Chem. Soc.* **1982**, *104*, 4251-4253. (b) Hayakawa, K.; Nagatsugi, F.; Kanematsu, K. *J. Org. Chem.* **1988**, *53*, 860-863.
- (11) Denmark, S. E.; Winter, S. B. D.; Su, X.; Wong, K.-T. *J. Am. Chem. Soc.* **1996**, *118*, 7404-7405.
- (12) Denmark, S. E.; Winter, S. B. D.; Su, X.; Wong, K.-T. *J. Am. Chem. Soc.* **1996**, *118*, 7404-7405.
- (13) (a) Elenkov, M.; Tang, M.; Hauer, L.; Bernhar, J.; Dick, B. *Org. Lett.* **2006**, *8*, 4227-4229. (b) Burk, M. J.; Harper, P. G. T.; Kalberg, C. S. *J. Am. Chem. Soc.* **1995**, *117*, 4423-4424. (c) Bradshaw, C. W.; Fu, H.; Shen, G. J.; Wong, C. H. *J. Org. Chem.* **1992**, *57*, 1526-1532.

(14) (a) Kloetzing, R. J.; Thaler, T.; Knochel, P. *Org. Lett.* **2006**, *6*, 1125-1128. (b) Abood, N. A. *Synth. Commun.* **1993**, *23*, 811-815. (c) Washio, T.; Nakamura, S.; Anada, M.; Hashimoto, S. *Heterocycles*, **2005**, *66*, 567-568. (c) *Syn. Commun.*, 1993, *23*, *6*, 811-815. (d) Hoffmann, T.; Seebach, D. *Liebigs Ann.* **1996**, 1277-1282. (e) Hinterding, K.; Jacobsen, E. N. *J. Org. Chem.* **1999**, *64*, 2164-2165.

(15) Juskiewicz, G.; Asztemborska, M.; Jurczak, J. *Synth. Commun.* **2002**, *32*, 2605-2611.

(16) (a) Larsen, C. H.; Ridgway, B. H.; Shaw, J. T.; Woerpel, K. A. *J. Am. Chem. Soc.* **1999**, *121*, 12208-12209. (b) MacNiel, P. A.; Roberts, N. K.; Bosnich, B. *J. Am. Chem. Soc.* **1981**, *103*, 2273-2280.

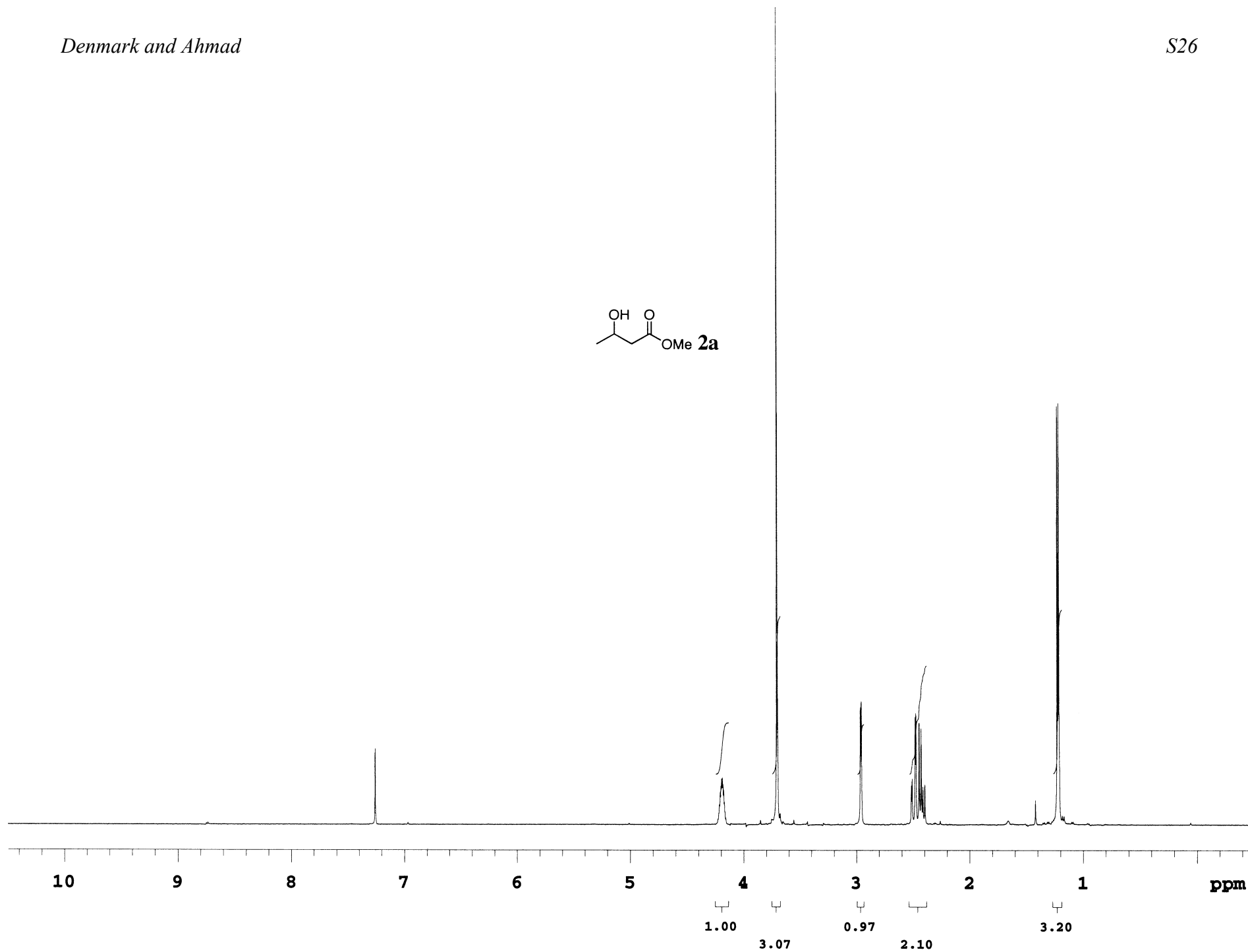
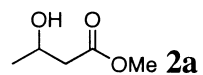
(17) Frater, G. *Helv. Chim. Acta.* **1980**, *63*, 1383-1390.

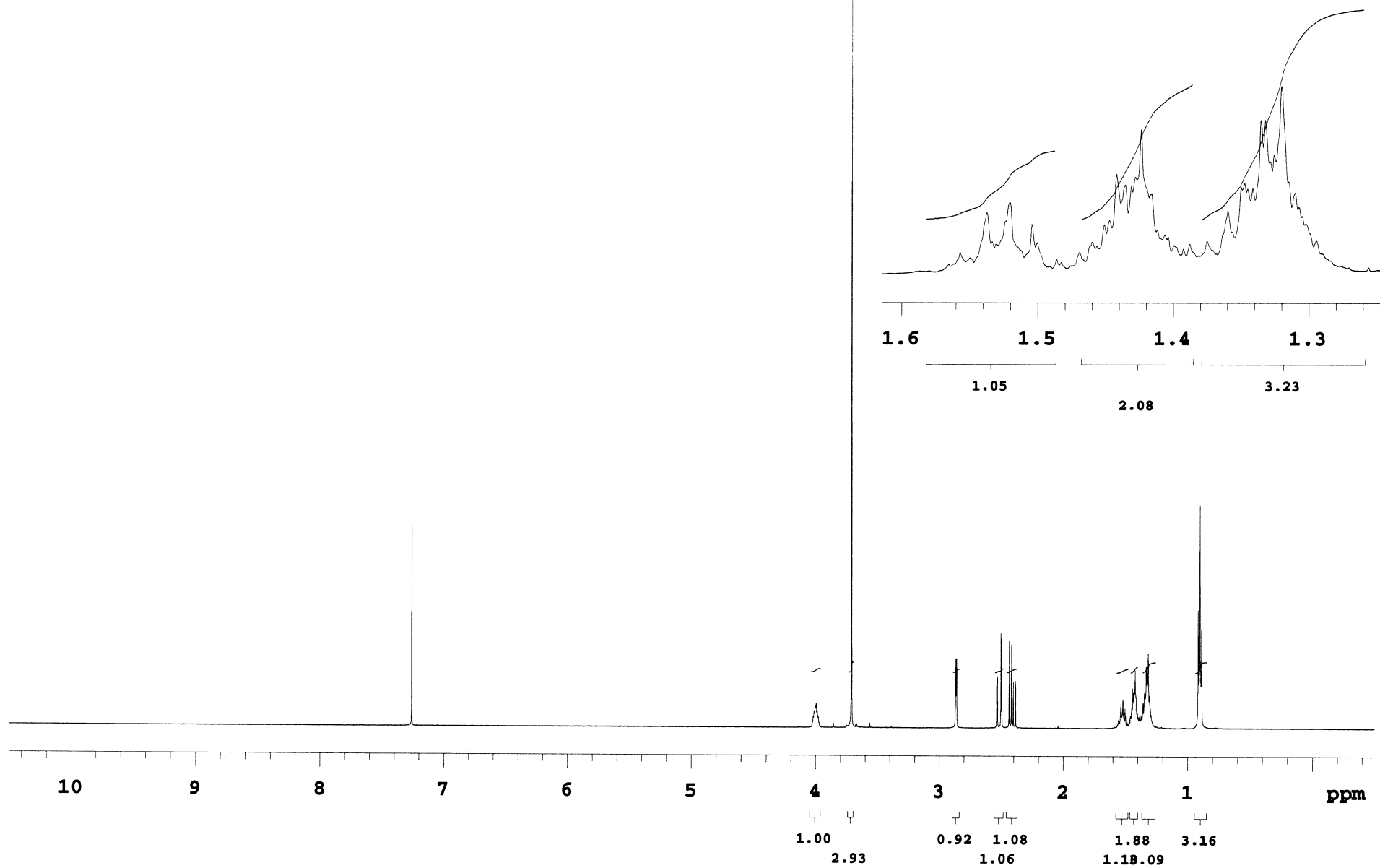
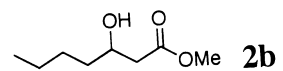
(18) Schaus, S. E.; Brandes, B. D.; Larrow, F. J.; Tokunaga, M.; Hansen, K. B.; Gould, A. E.; Furrow, M. E.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *124*, 1307-1315.

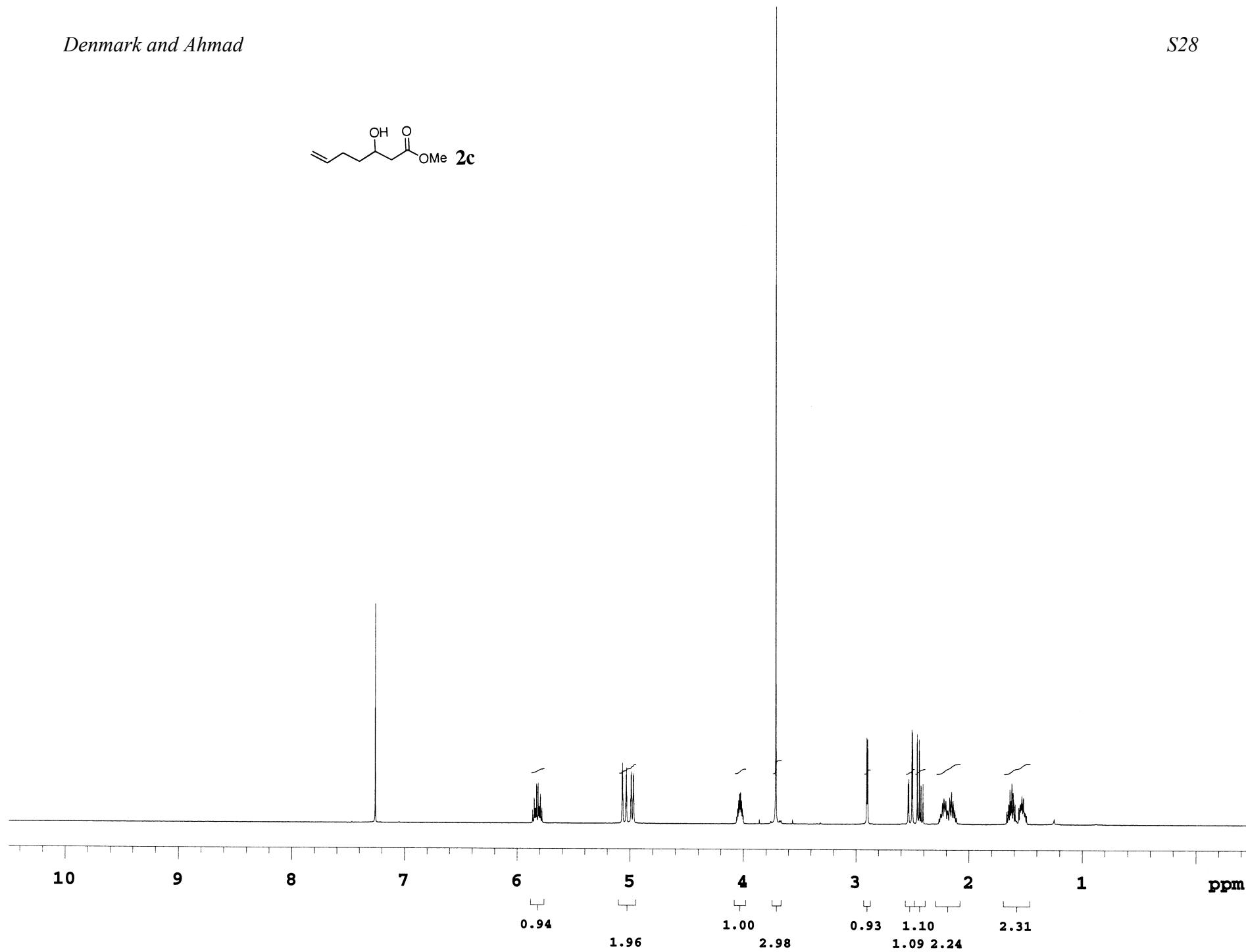
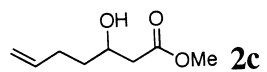
(19) (a) Ellis, M. K.; Golding, B. T. *Org. Synth., Coll. Vol. VII* **1990**, 356-359. (b) Schaus, S. E. Brandes, B. D.; Larrow, J. F.; Tokunga, M.; Hansen, K. B.; Gould, A. E.; Furrow, M. E.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *124*, 1307-1315.

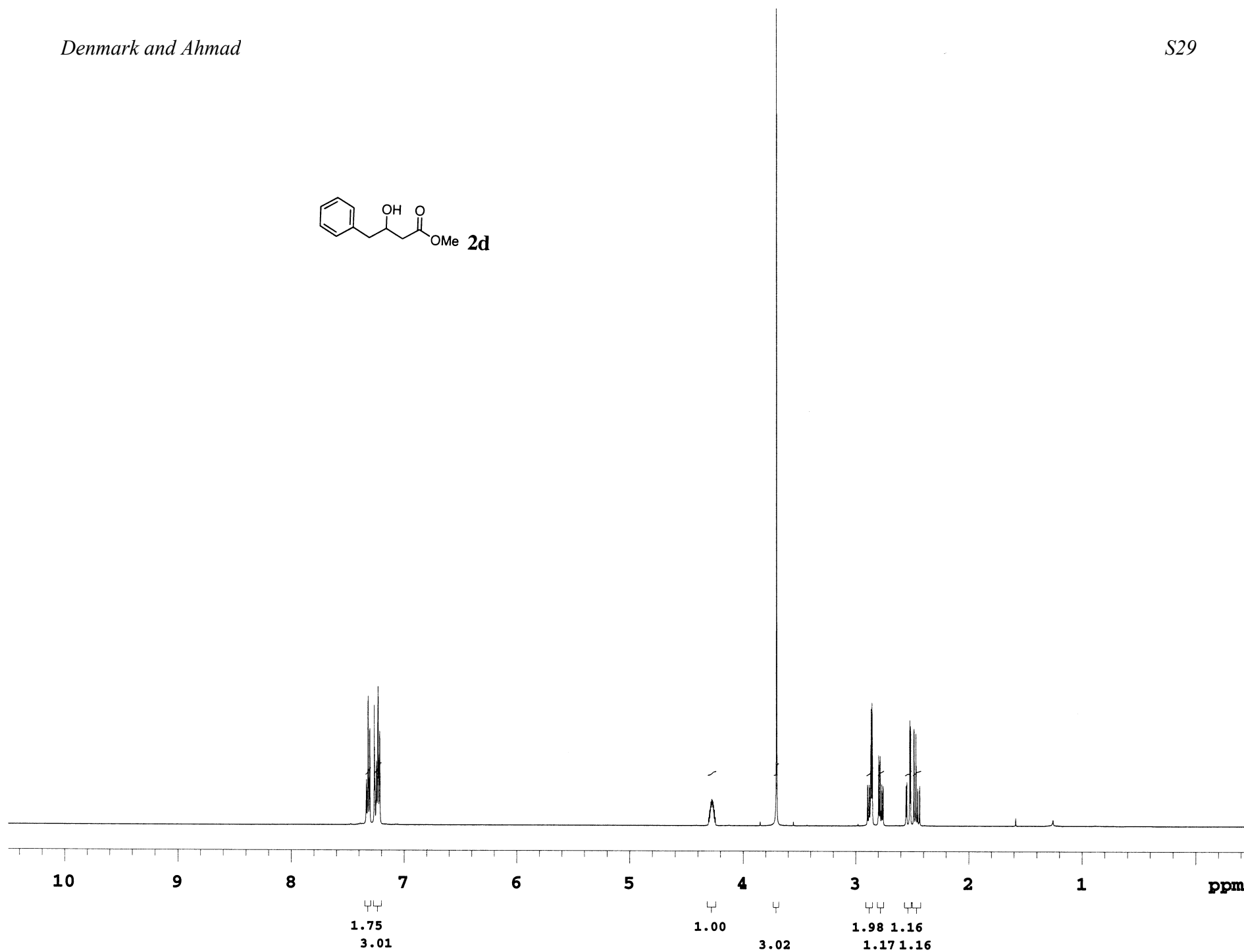
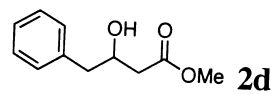
(20) Singh, S.; Kumar, S.; Chimni, S. S. *Tetrahedron: Asymmetry* **2001**, *12*, 2457-2462.

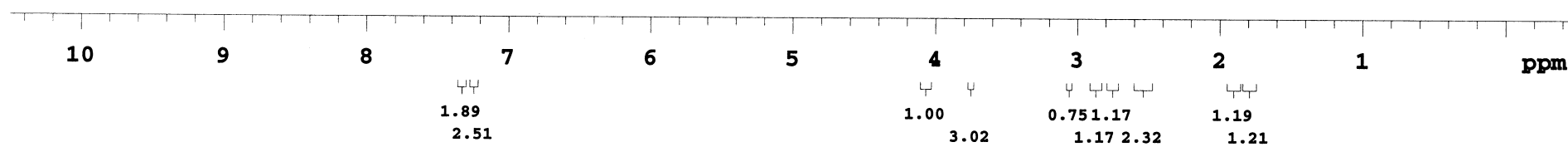
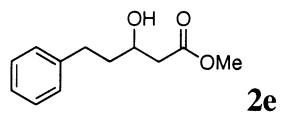
(21) Salvi, N. A.; Chattopadhyay, S. *Tetrahedron: Asymmetry* **2004**, *15*, 3397-3400.

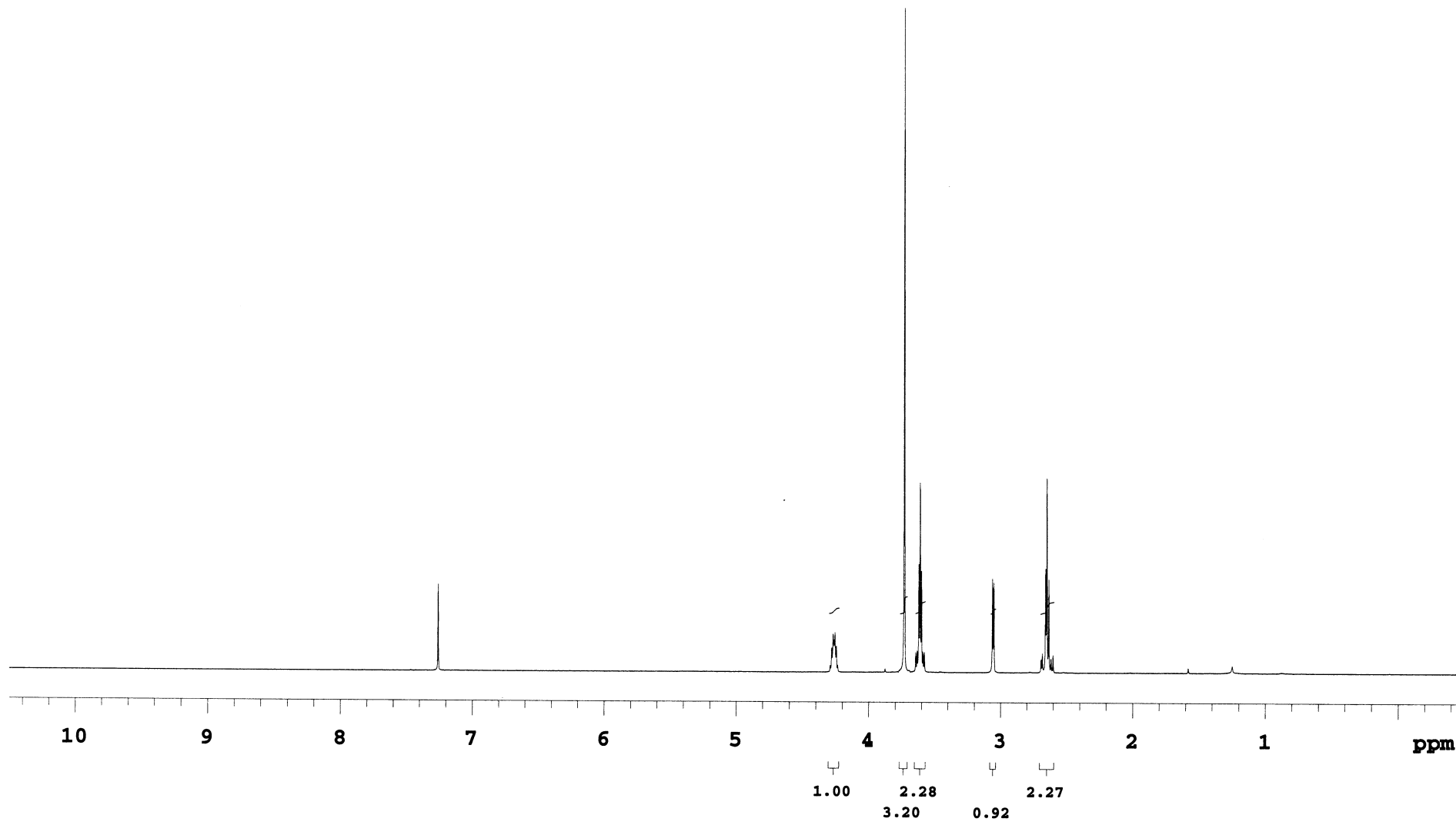
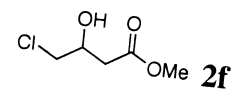


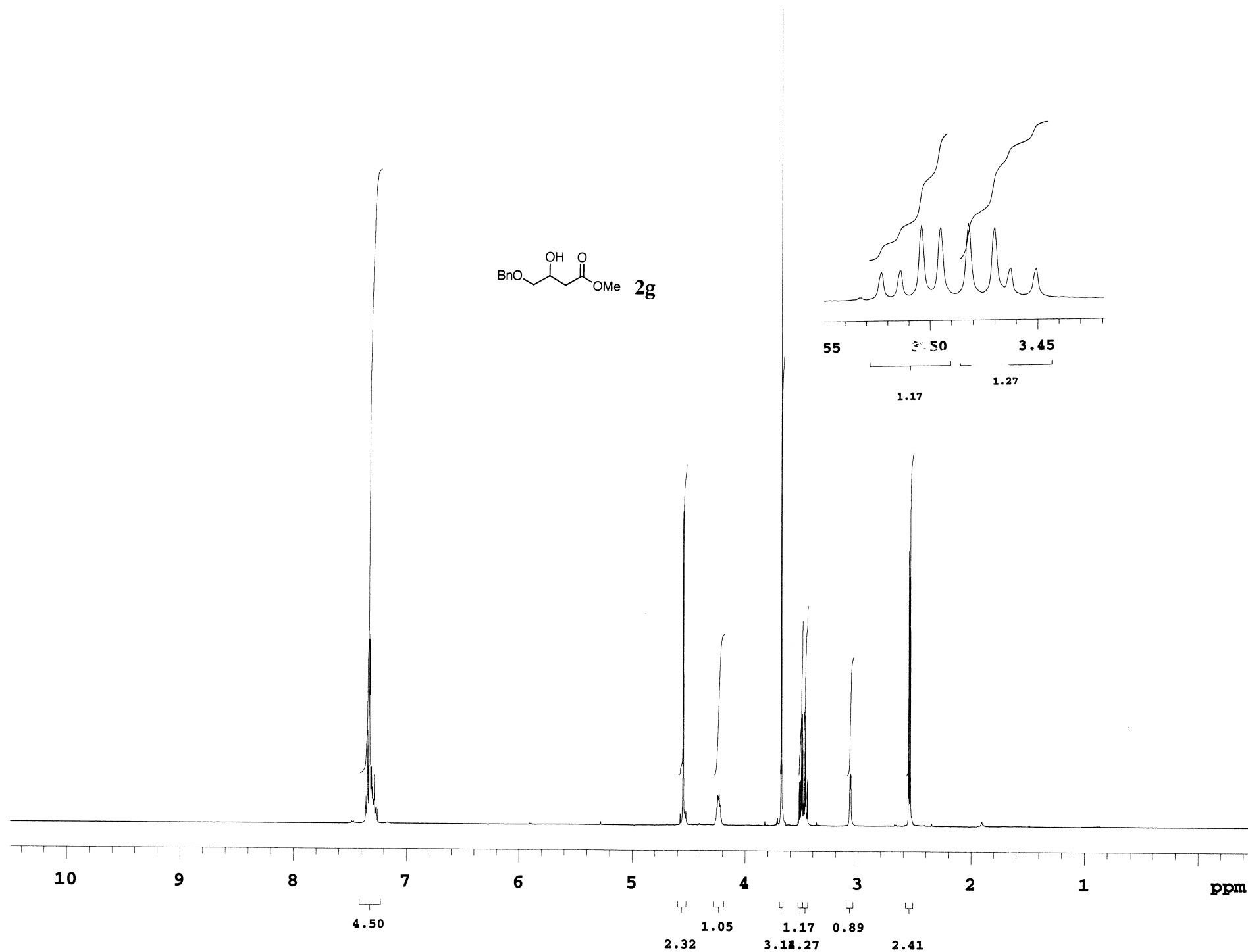


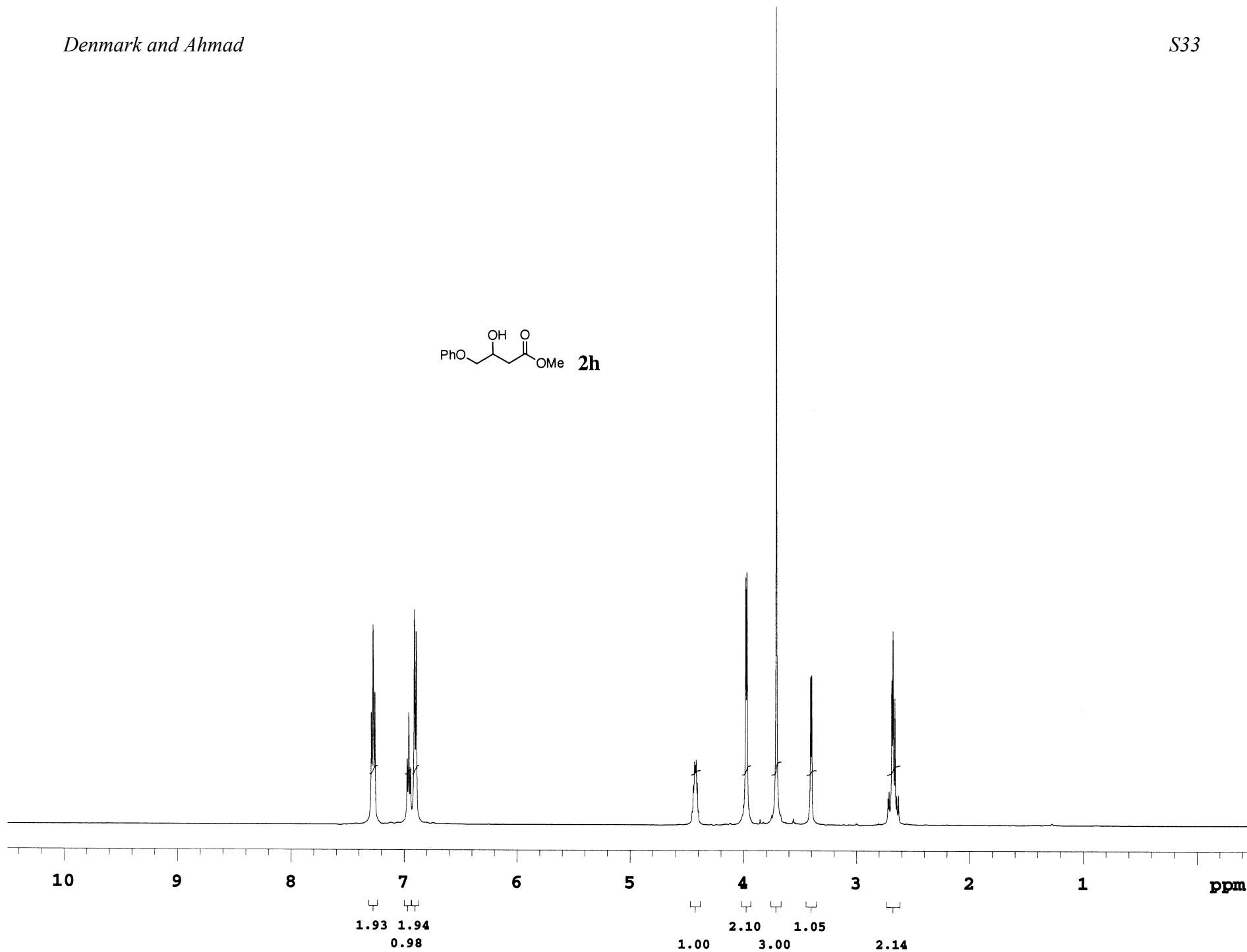
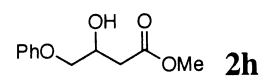


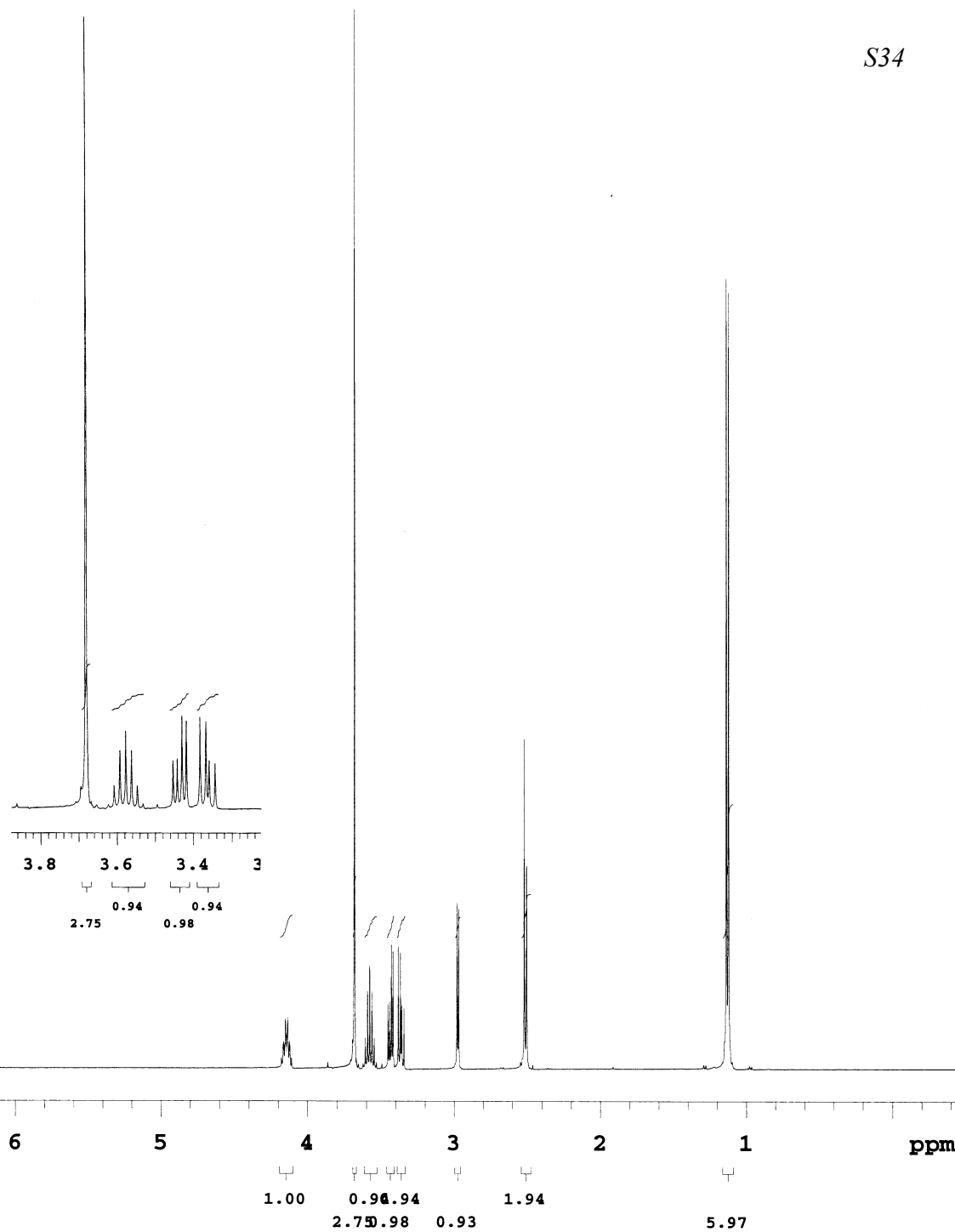
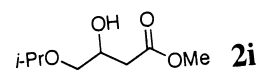


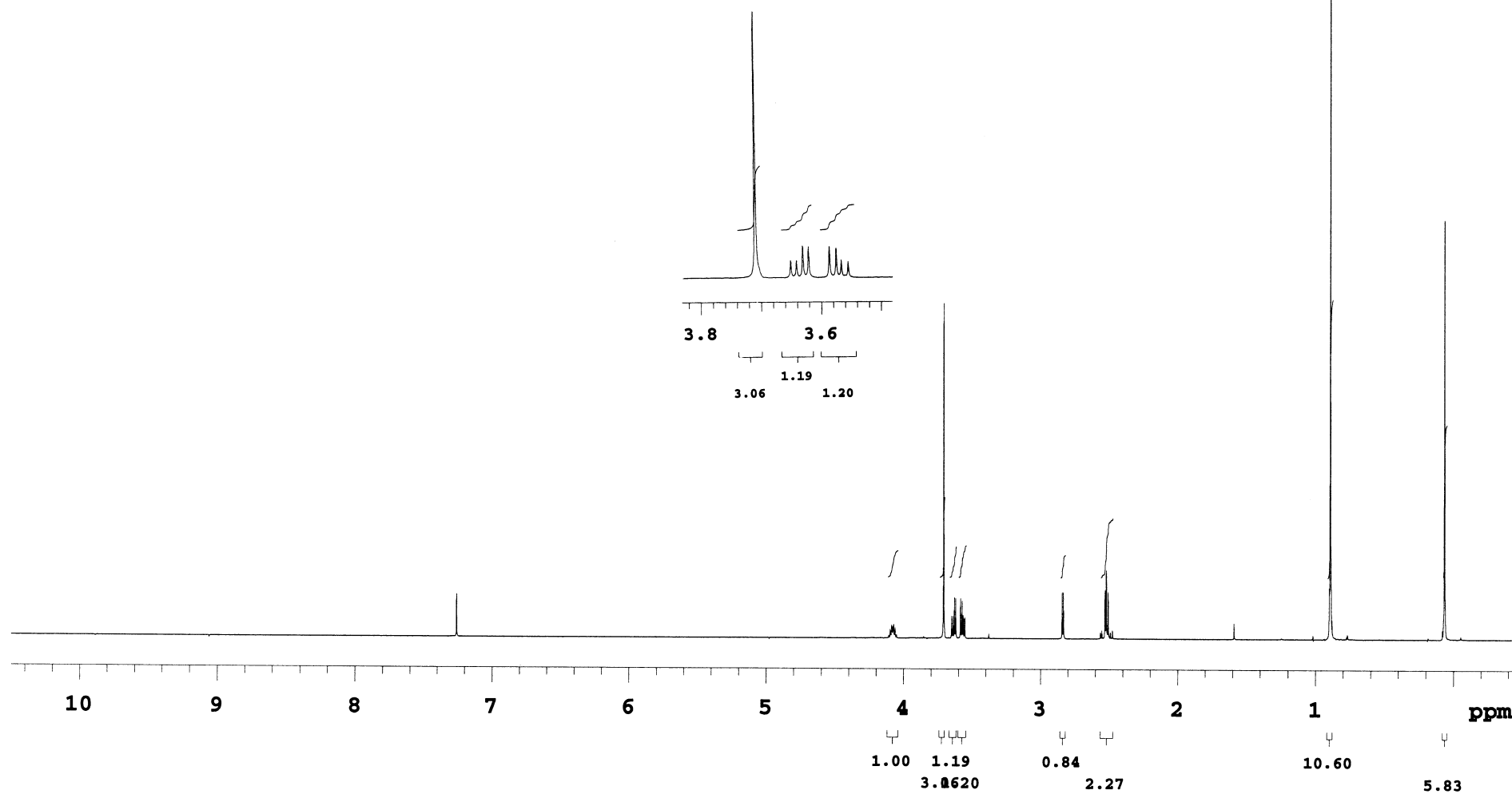
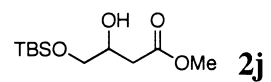


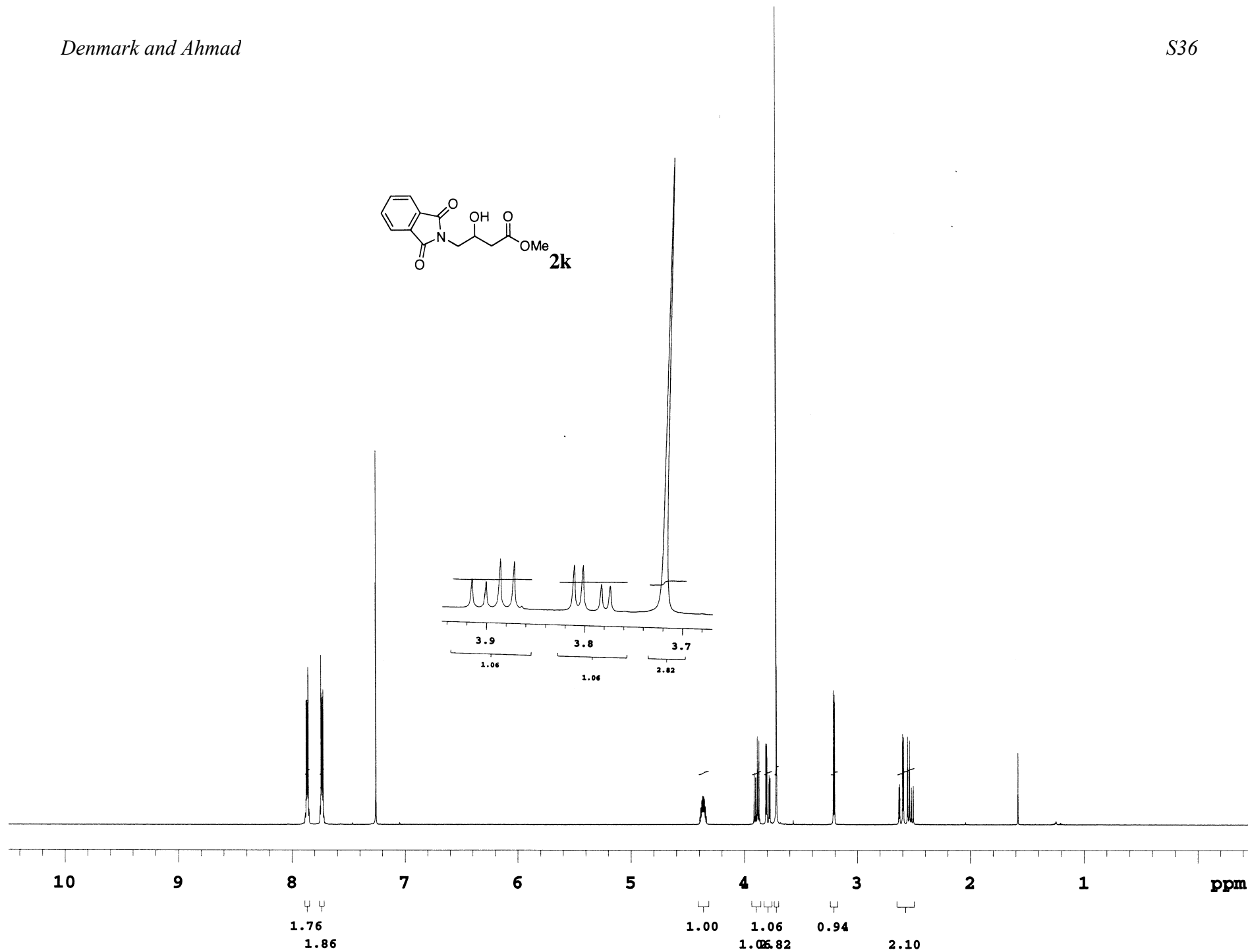
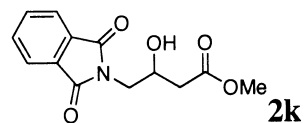


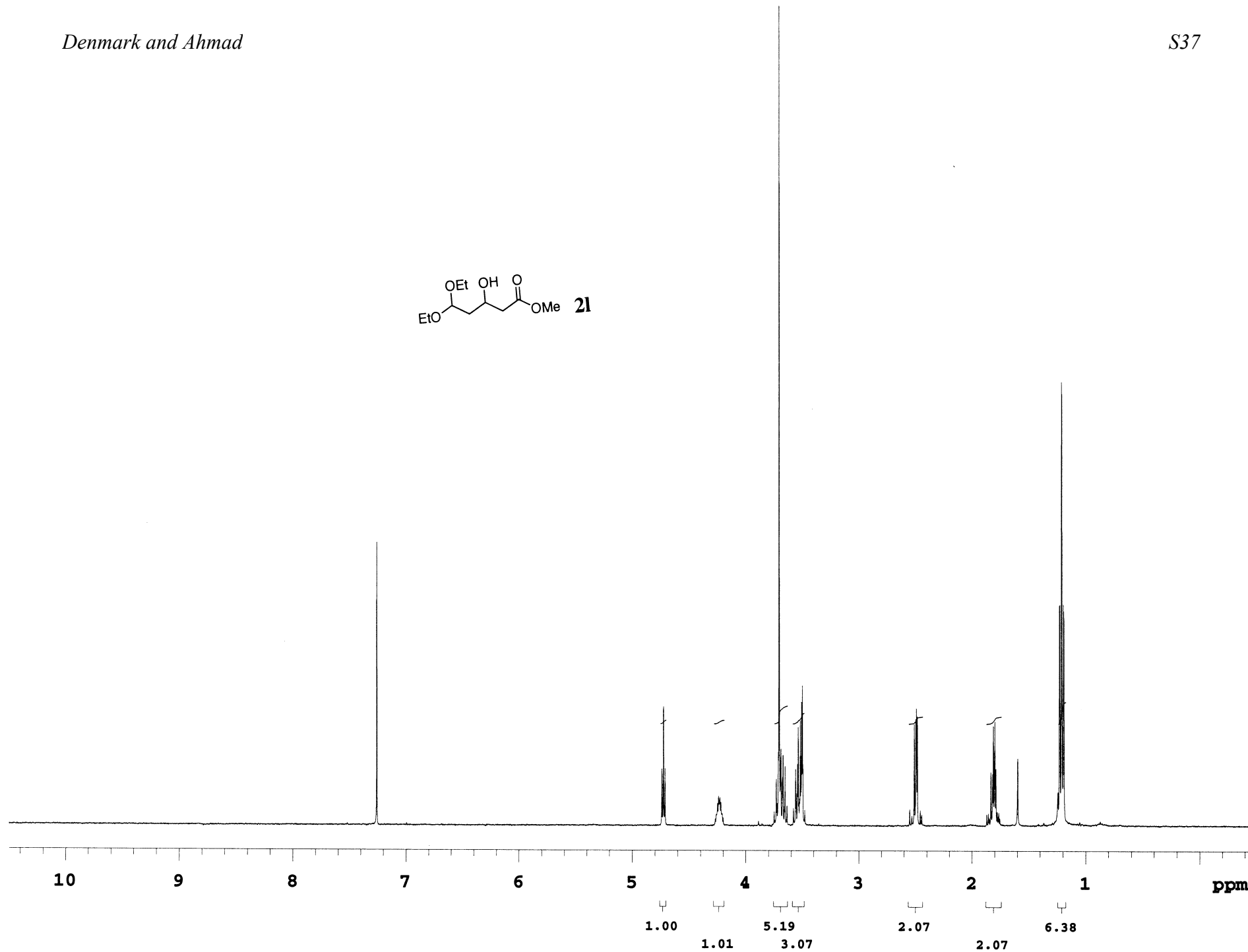
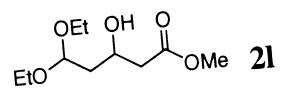


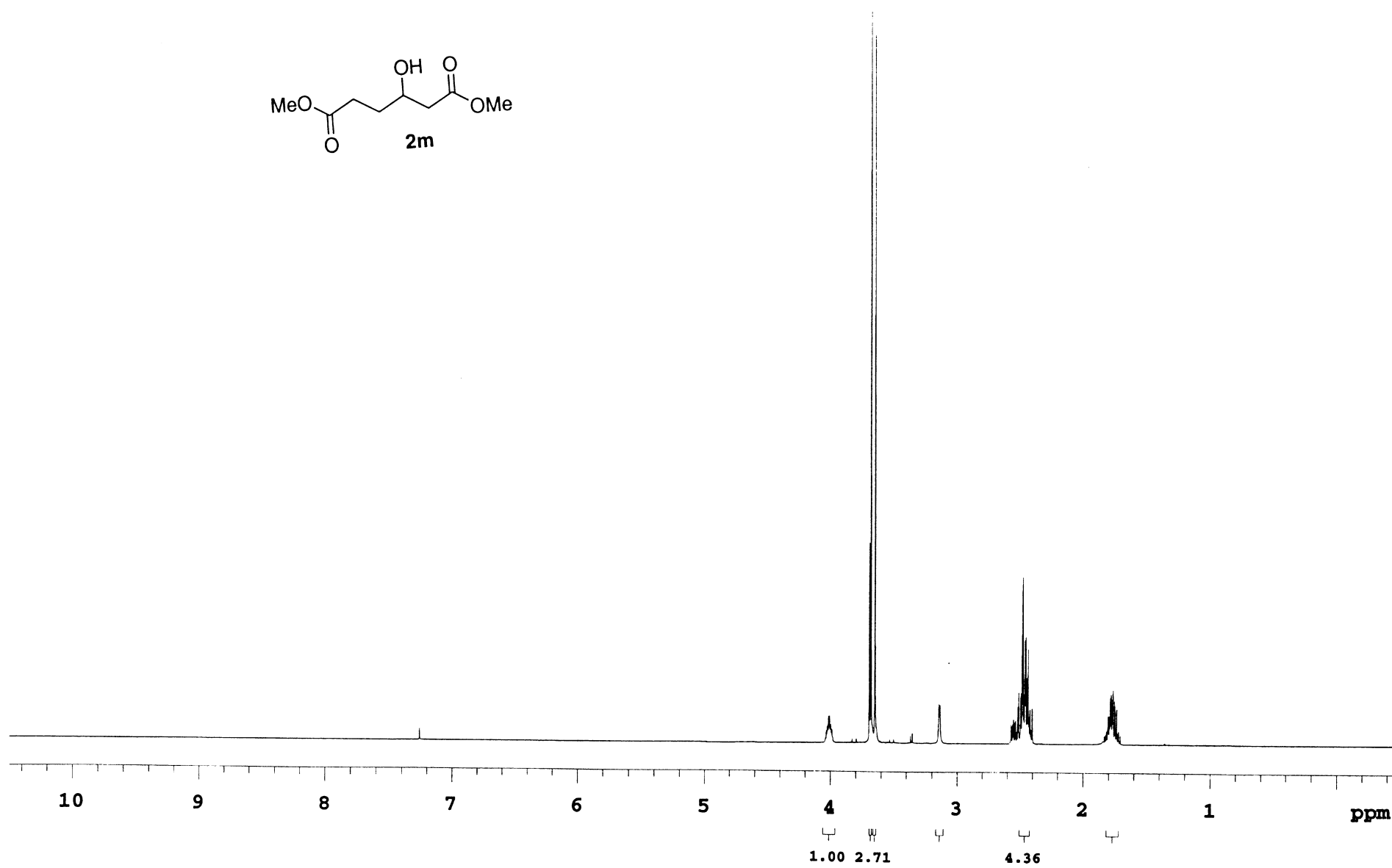
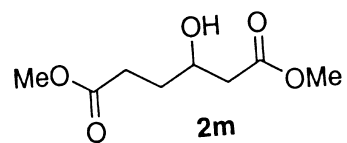


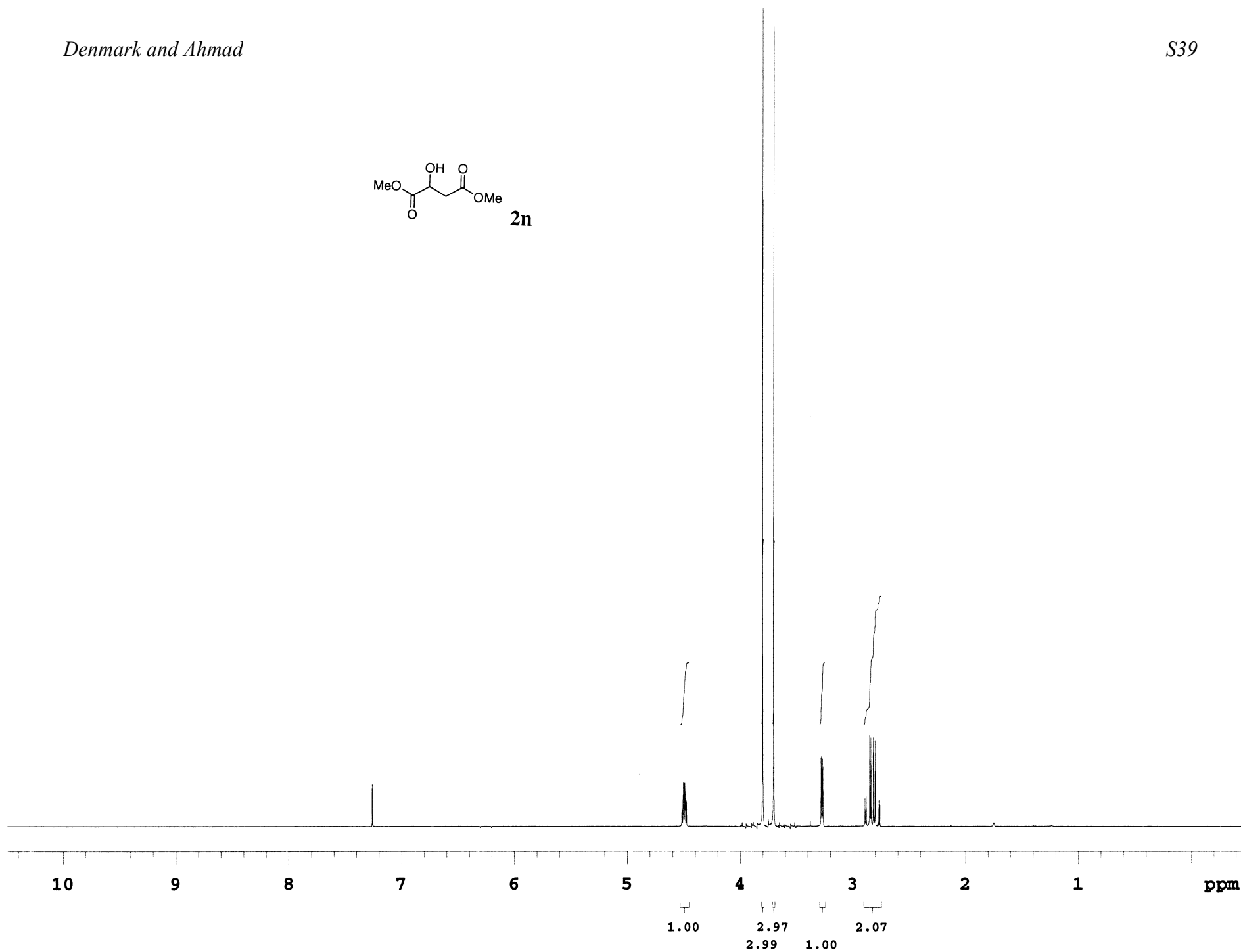
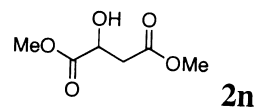


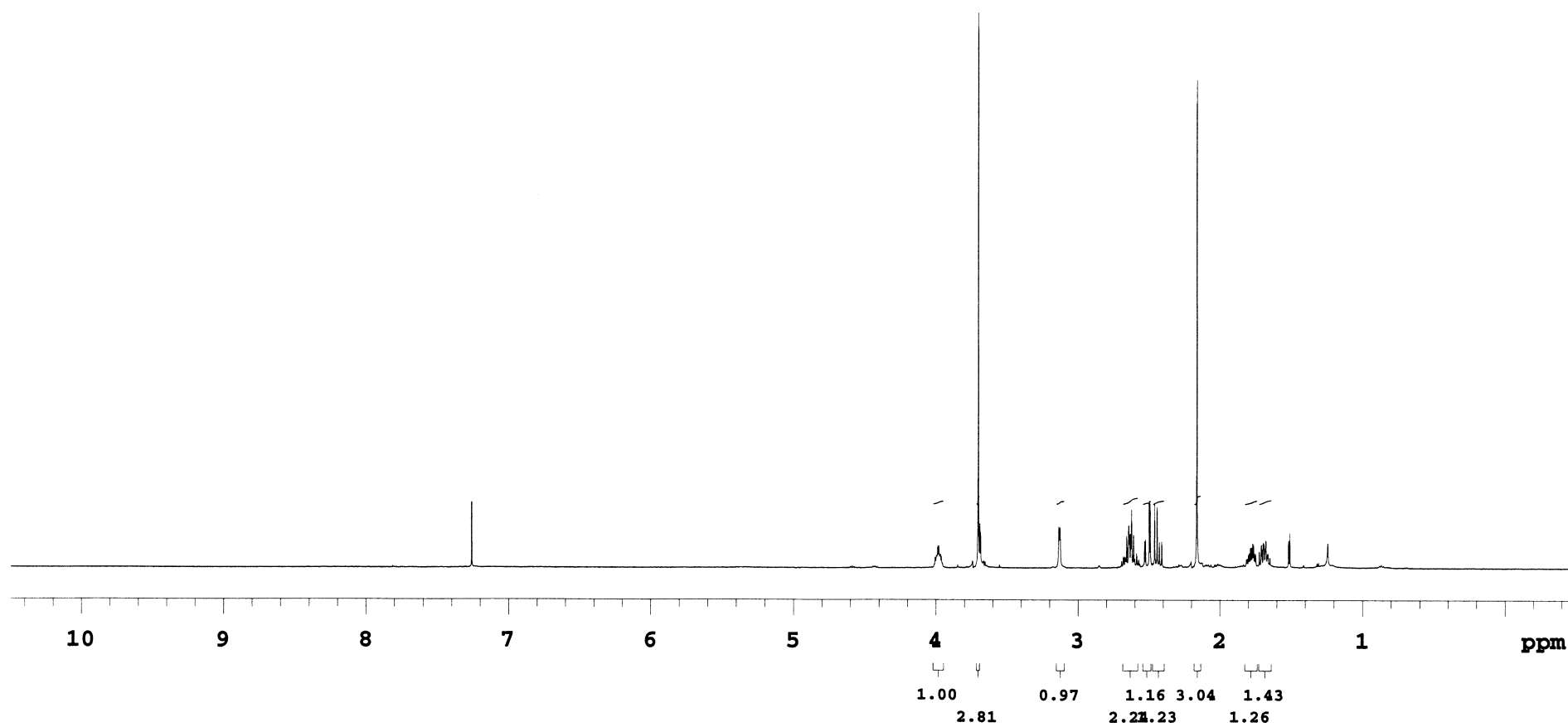
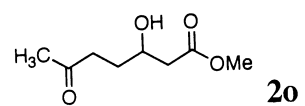


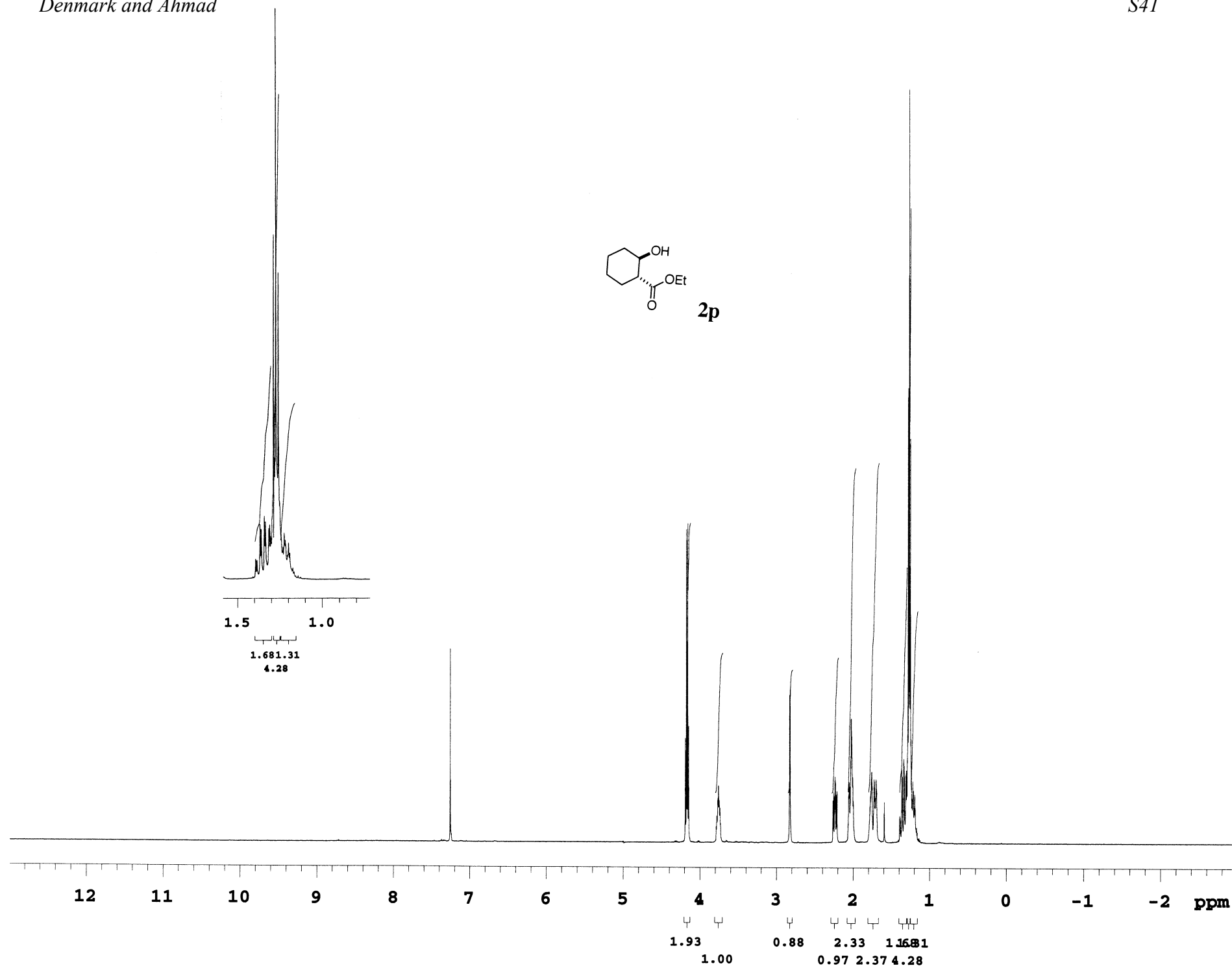


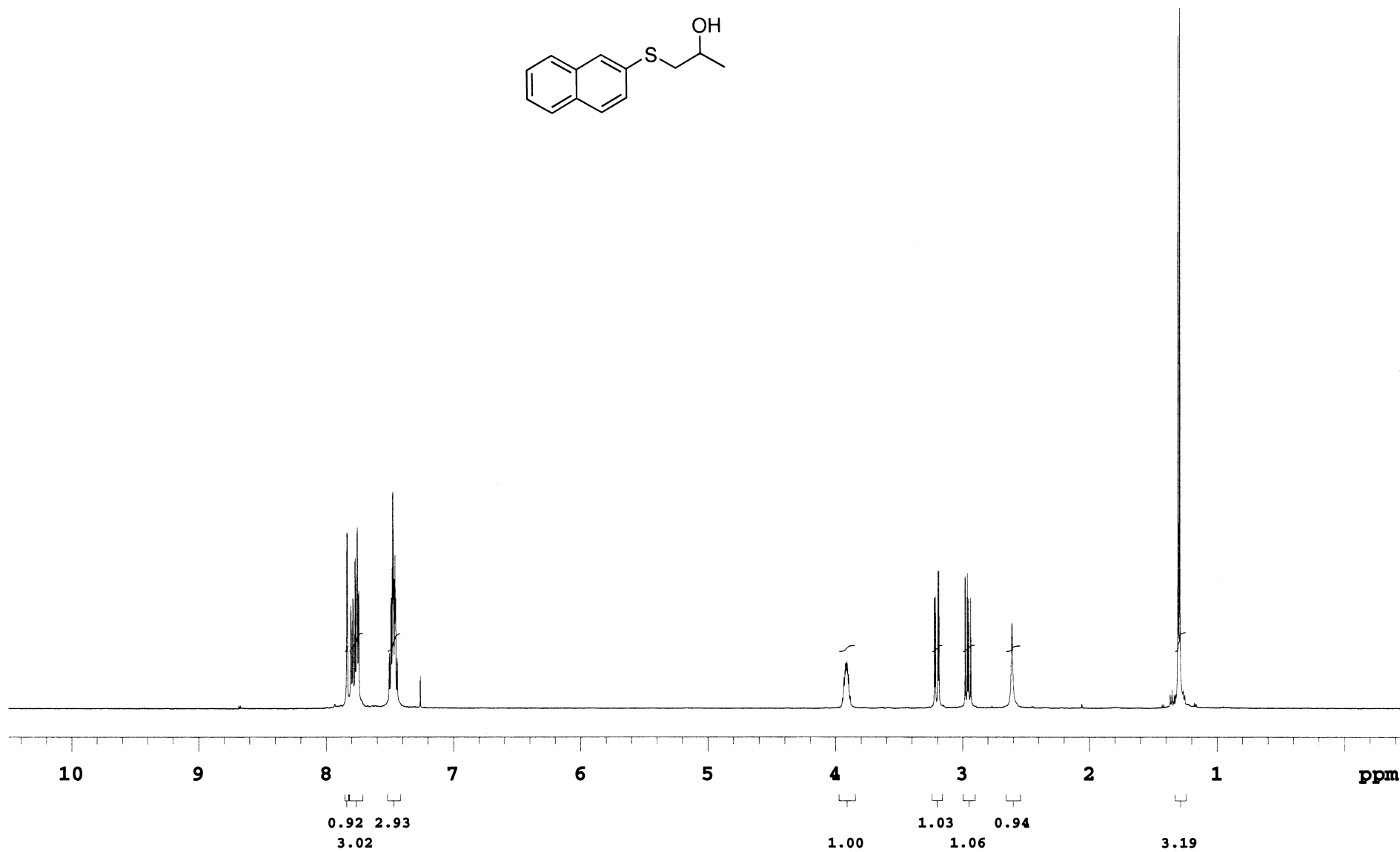
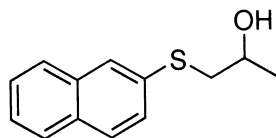








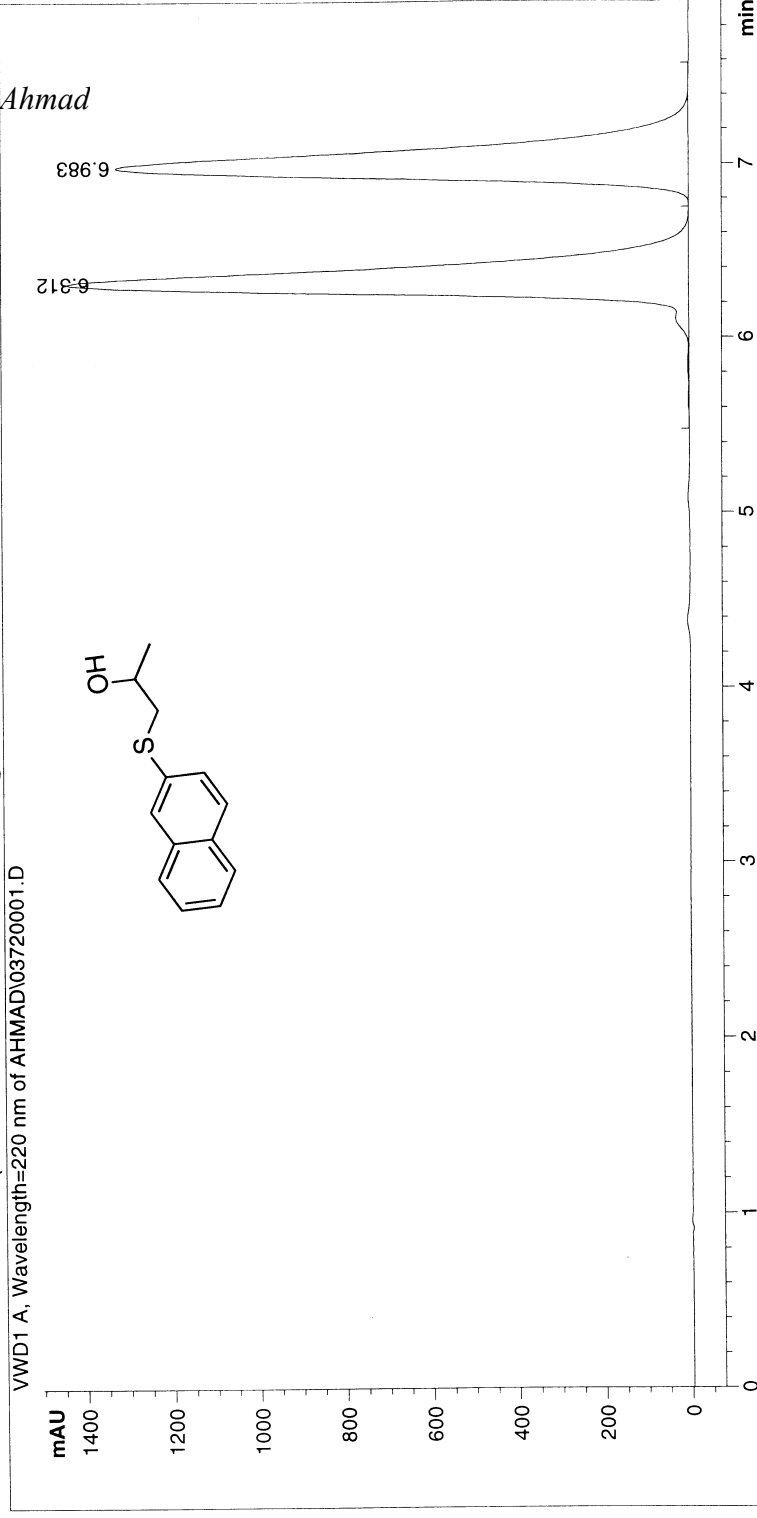




OD, 3ml/min, 125 bar, 10% MeOH

```
=====
Acq. Method   : ODTEST.M                      Seq. Line : -
Acq. Operator : Ahmad                          Vial : 2000
Injection Date: 6/28/2007 8:42:22 PM           Inj : -
Sample Name   : MA-238                        Inj Volume: Unknown
=====
```

Analysis Method : D:\BERGER\1\METHODS\ODTEST.M
(modified after loading)



```
=====
Area Percent Report
=====
```

Sorted by Signal
Multiplier : 1.000000

Signal 1: VWD1 A, Wavelength=220 nm

Peak #	RT [min]	Type	Width [min]	Area [mAU*sec]	Height [mAU]	Area %
1	6.312	BV	0.155	14694.30957	1433.85730	50.0196
2	6.983	VB	0.169	14682.82031	1323.45386	49.9804

Totals : 29377.12891 2757.31104

```
=====
*** End of Report ***
=====
```

S43

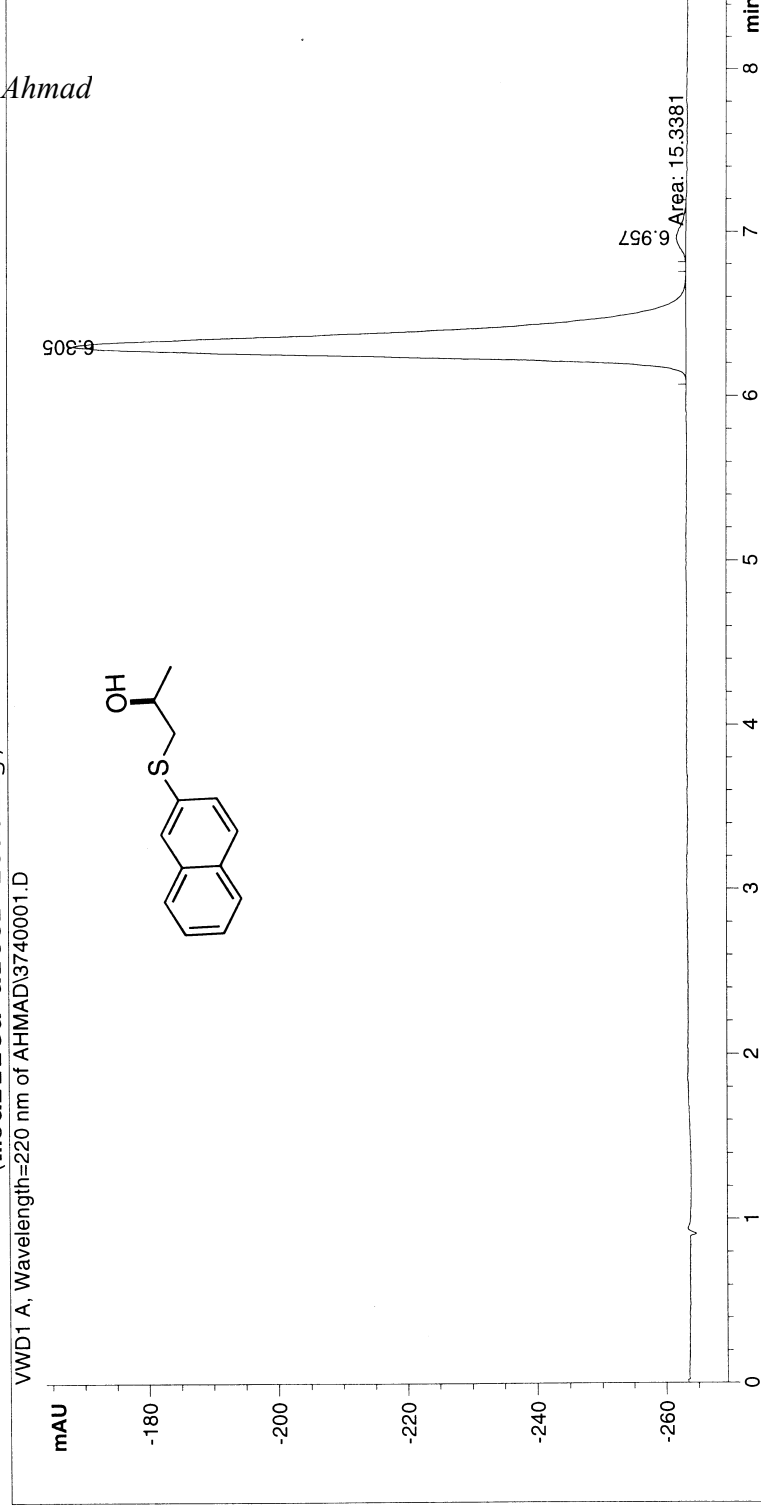
OD, 3.0 ml/min, 10 % MeOH, 125 bar

```
=====
Acq. Method   : ODTEST.M
Acq. Operator : Ahmad
Injection Date : 7/1/2007 4:19:30 PM
Sample Name   : MA-242

Seq. Line : -
Vial : 2000
Inj : -
Inj Volume : Unknown
=====
```

Denmark and Ahmad

Analysis Method : D:\BERGER\1\METHODS\ODTEST.M
(modified after loading)



```
=====
Area Percent Report
=====
```

Sorted by Signal
Multiplier : 1.000000

Signal 1: VWD1 A, Wavelength=220 nm

Peak #	RT [min]	Type	Width [min]	Area [mAU*sec]	Height [mAU]	Area %
1	6.305	BB	0.148	926.21722	94.68026	98.3710
2	6.957	MM	0.166	15.33806	1.53912	1.6290

Totals : 941.55530 96.21938

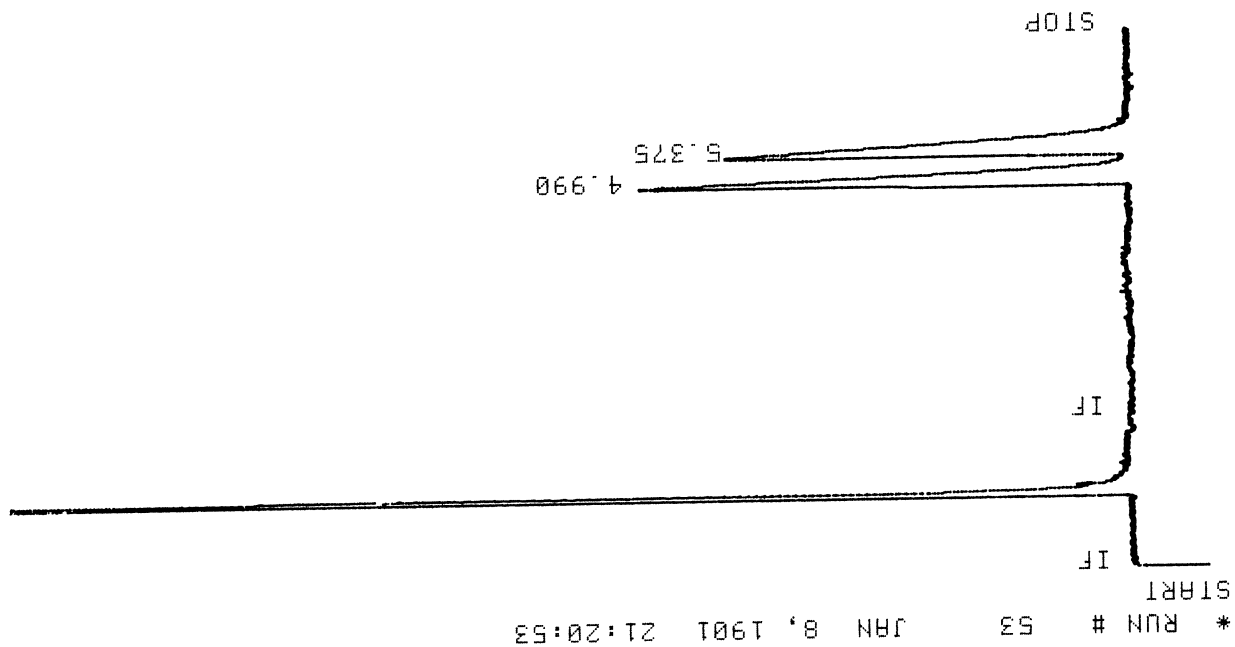
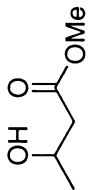
```
=====
*** End of Report ***
=====
```

S44

Agilent Technologies

PART NUMBER 5181-1219 PRINT

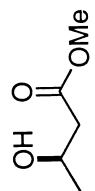
RUN# 53 JAN 8, 1901 21:20:53
AREA%
RT AREA TYPE PU WIDTH AREA%
4.990 3749 PU .142 49.91347
5.375 3762 UP .175 50.08654
TOTAL AREA= 7511
MUL FACTOR=1.0000E+00

G-TA, 80 °C, isothermal, 15 Psi H₂ flow

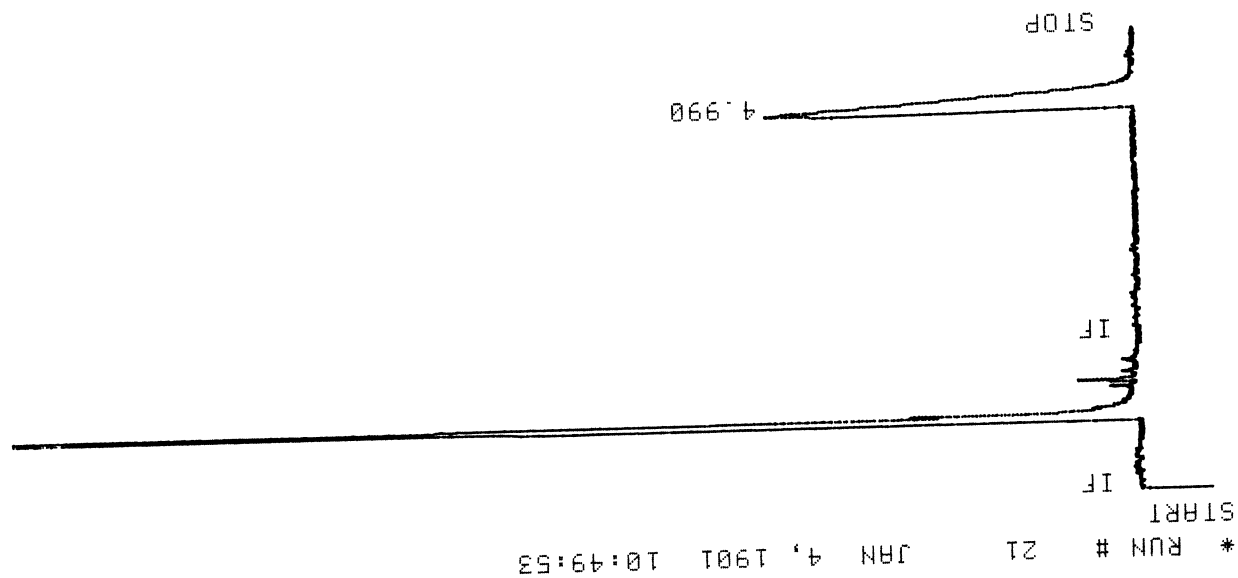
IDE

582117

Agile



G-TA, 80 °C, isothermal, 15 Psi H₂ flow



RUN# 21 JAN 4, 1901 10:49:53

AREA%	RT	AREA TYPE	WIDTH	AREA%
100.00000	4.990	BU	.151	100.00000

TOTAL AREA= 2962
MUL FACTOR=1.0000E+00