The Sulfone Coupling and Double Elimination Strategy for Carotenoid Synthesis

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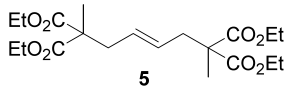
Experimental Procedure

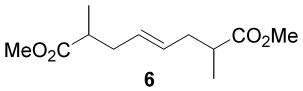
General Experimental. ^{1}H (300.40 MHz) and ^{13}C NMR (75.5 MHz) spectra were recorded in $CDCl_3$ with Me_4Si (δ = 0 ppm) as an internal standard. Solvents for extraction and chromatography were reagent grade and used as received. Column chromatography was performed by the method of Still using silica gel 60, 230–400 mesh ASTM supplied by Merck. Solvents used as reaction media were dried over pre-dried molecular sieve (4 Å) by microwave oven. All reactions were performed under dry argon in oven-dried glassware, except for those reactions with H_2O as a solvent, which were run in air.



5

2,7-Bis(ethoxycarbonyl)-2,7-dimethyl-4-octenedioic acid, diethyl ester (5). To a stirred suspension of NaH (8.0 g, 0.20 mol, 60% dispersion in mineral oil) in THF (200 mL) was added a solution of diethyl methylmalonate (17.60 g, 0.10 mol) in THF (10 mL) at 0 ºC. The mixture was stirred at that temperature for 30 min, and a solution of (*E*)-1,4-dibromo-2-butene (10.70 g, 50.0 mmol) in THF (10 mL) was added. The reaction mixture was slowly warmed to and stirred at room temperature for 14 h, and 1 M HCl solution was added. The mixture was extracted with Et_2O, washed with H_2O and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by SiO_2 flash column chromatography (hexanes:EtOAc = 10:1) to give the tetraester **5** (17.6 g, 44.0 mmol) in 88% yield.

Data for **5**: R_f = 0.58 (hexanes:EtOAc = 4:1); ^{1}H NMR δ 1.24 (t, *J* = 7.2 Hz, 12H), 1.35 (s, 6H), 2.49-2.62 (m, 4H), 4.17 (q, *J* = 7.2 Hz, 8H), 5.33-5.48 (m, 2H) ppm; ^{13}C NMR δ 14.0, 19.6, 38.7, 53.4, 61.1, 128.8, 171.8 ppm; IR (neat) 2984, 1738, 1731, 1464, 1455 cm^{-1}; HRMS (CI, H^+) calcd for $C_{20}H_{33}O_8$ 401.2175, found 401.2170.



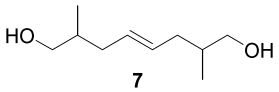
6

2,7-Dimethyl-4-octenedioic acid, dimethyl ester (6). The mixture of **5** (9.4 g, 23.5 mmol) and KOH (26.4 g, 47.0 mmol) in H_2O (200 mL) was heated to reflux for 2 d. The reaction mixture was cooled to

room temperature, and acidified to pH 1 by adding concentrated H_2SO_4. The resulting mixture was heated to reflux for 3 d, and then cooled to room temperature. The mixture was extracted with EtOAc, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product (5.8 g) was dissolved in MeOH (80 mL), and treated with concentrated H_2SO_4 (3.5 mL). The mixture was then stirred at room temperature for 12 h. Most of the solvent was removed under reduced pressure. The concentrate was dissolved in EtOAc, washed with H_2O, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by SiO_2 flash column chromatography (hexanes:EtOAc = 4:1) to give the dimethyl ester **6** (4.75 g, 20.9 mmol) in 89% yield.

Data for **6**: R_f = 0.50 (hexanes:EtOAc = 4:1); ^{1}H NMR δ 1.13 (d, J = 7.0 Hz, 6H), 2.05-2.20 (m, 2H), 2.26-2.40 (m, 2H), 2.48 (tq, J_t = 7.0, J_q = 7.0 Hz, 2H), 3.66 (s, 6H), 5.31-5.48 (m, 2H) ppm; ^{13}C NMR* δ 16.4 (16.3), 36.4 (36.5), 39.4, 51.3, 129.3 (129.3), 176.4 (176.4) ppm; IR (neat) 2953, 1738, 1461, 1436 cm^{-1}; HRMS (CI, H^+) calcd for $C_{12}H_{21}O_4$ 229.1440, found 229.1443.

* The ^{13}C NMR peaks in parenthesis correspond to those of the diastereoisomer.



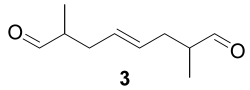
7

2,7-Dimethyl-4-octene-1,8-diol (7). To a stirred suspension of $LiAlH_4$ (1.64 g, 41.0 mmol) in THF (65 mL) was added a solution of **6** (4.67 g, 20.5 mmol) in THF (15 mL) at 0 ºC. The mixture was stirred at that temperature for 30 min, and warmed up and stirred at room temperature for 1 h. The reaction mixture was quenched with 5% NaOH solution, extracted with Et_2O thoroughly, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by SiO_2 flash column chromatography (hexanes:EtOAc = 2:1) to give the diol **7** (3.53 g, 20.5 mmol) in 100% yield.

Data for **7**: R_f = 0.33 (hexanes:EtOAc = 1:1); ^{1}H NMR δ 0.91 (d, J = 6.8 Hz, 6H), 1.69 (ttq, J_t = 6.5, 6.6, J_q = 6.4 Hz, 2H), 1.85-1.97 (m, 2H), 1.93 (s, 2H), 2.05-2.17 (m, 2H), 3.48 (d of A of ABq, J_{AB} = 10.5, J_d = 6.0 Hz, 2H), 3.50 (d of B of ABq, J_{AB} = 10.5, J_d = 6.1 Hz, 2H), 5.37-5.52 (m, 2H) ppm; ^{13}C

NMR* δ 16.4 (16.4), 35.9, 36.6 (36.5), 67.8 (67.8), 129.9 (129.9) ppm; IR (neat) 3343, 2912, 1458, 1035 cm^{-1}; HRMS (CI, H^+) calcd for $C_{10}H_{21}O_2$ 173.1541, found 173.1541.

* The ^{13}C NMR peaks in parenthesis correspond to those of the diastereoisomer.

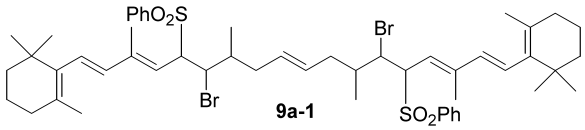


3

2,7-Dimethyl-4-octenedial (3). To a stirred solution of DMSO (0.722 g, 9.24 mmol) in CH_2Cl_2 (10 mL) was added oxalyl chloride (0.40 mL, 4.62 mmol) at –78 ºC. The mixture was stirred for 5 min, and a solution of the diol **7** (0.362 g, 2.1 mmol) in CH_2Cl_2 (3 mL) was added. The resulting mixture was stirred at –78 ºC for 15 min, and Et_3N (2.93 mL, 21 mmol) was added. Stirring for 5 min at that temperature, the mixture was then warmed up to room temperature, and quenched with 1 M HCl solution. The mixture was diluted with CH_2Cl_2, washed with H_2O, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by SiO_2 flash column chromatography (hexanes:EtOAc = 5:1) to give the dial **3** (0.307 g, 1.824 mmol) in 87% yield.

Data for **3**: R_f = 0.86 (hexanes:EtOAc = 1:1); ^1H NMR δ 1.09 (d, *J* = 6.6 Hz, 6H), 2.05-2.20 (m, 2H), 2.34-2.50 (m, 4H), 5.38-5.53 (m, 2H), 9.64 (d, *J* = 1.3 Hz, 2H) ppm; ^{13}C NMR* δ 12.9 (12.9), 33.4 (33.4), 46.0, 129.2, 204.4 ppm; IR (neat) 2971, 2717, 1725, 1457 cm^{-1}; HRMS (CI, H^+) calcd for $C_{10}H_{17}O_2$ 169.1228, found 169.1226.

* The ^{13}C NMR peaks in parenthesis correspond to those of the diastereoisomer.

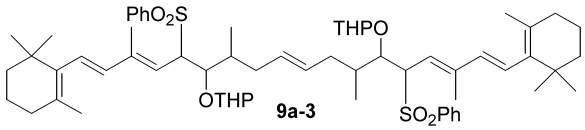


9a-1

5,14-Bis(benzenesulfonyl)-6,13-dibromo-3,7,12,16-tetramethyl-1,18-bis(2,6,6-trimethyl-1-cyclohexenyl)octadeca-1,3,9,15,17-pentaene (9a-1). To a stirred solution of the diol **8a** (1.00 g, 1.17 mmol) in CH_2Cl_2 were added pyridine (0.47 mL, 5.85 mmol) and PBr_3 (0.11 mL, 1.17 mmol) at 0 ºC. The mixture was then stirred at room temperature for 1 h, diluted with CH_2Cl_2, washed with 1 M HCl solution, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give the dibromide

9a-1 (1.10 g, 1.12 mmol) in 96% crude yield as a shiny yellow solid. The peaks of the ^{1}H NMR spectrum of **9a-1** were so broad that those were not able to be assigned.

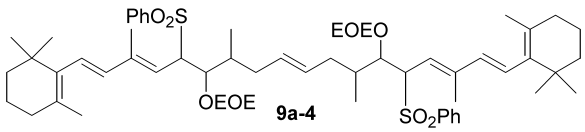
Data for **9a-1**: HRMS (FAB$^+$) Calcd for $C_{46}H_{66}BrO_2S$ ($C_{52}H_{72}Br_2O_4S_2$ – $C_6H_6O_2S$ – Br) 761.3967, found 761.3952.



9a-3

5,14-Bis(benzenesulfonyl)-3,7,12,16-tetramethyl-1,18-bis(2,6,6-trimethyl-1-cyclohexenyl)octadeca-1,3,9,15,17-pentaene-6,13-diol, bis(tetrahydropyranyl) ether (9a-3). To a stirred solution of the diol **8a** (1.59 g, 1.85 mmol) in CH_2Cl_2 (35 mL) were added 3,4-dihydro-2*H*-pyran (1.01 mL, 11.11 mmol) and 10-camphorsulfonic acid (129 mg, 0.56 mmol). The mixture was stirred at room temperature for 14.5 h, diluted with CH_2Cl_2, washed with 10% $NaHCO_3$ solution, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product (2.75 g) was purified by SiO_2 flash column chromatography (hexanes:EtOAc = 9:1 ~ 7:3) to give the THP diether **9a-3** (1.65 g, 1.61 mmol) in 87% yield as a light yellow solid, which contained many stereoisomers due to the presence of eight chiral centers. The major stereoisomer, which was presumed to be all-(*E*)-isomer, was carefully purified again by preparative TLC for spectroscopic analysis.

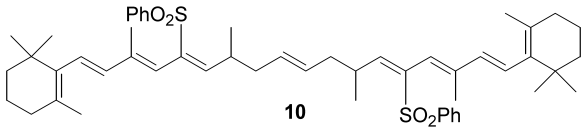
Data for **9a-3** (major): R_f = 0.20~0.25 (hexanes:EtOAc = 4:1); ^{1}H NMR δ 0.96 (s, 12H), 0.99 (s, 6H), 1.23 (s, 6H), 1.40-1.94 (m, 20H), 1.66 (s, 6H), 1.94-2.05 (m, 8H), 2.47 (t, J = 7.2 Hz, 2H), 3.40 (dt, J_d = 9.7, J_t = 6.1 Hz, 2H), 3.76 (dt, J_d = 9.7, J_t = 6.3 Hz, 2H), 4.04 (dd, J = 10.8, 9.4 Hz, 2H), 4.36 (dd, J = 9.1, 1.8 Hz, 2H), 4.57 (dd, J = 4.2, 2.9 Hz, 2H), 4.97 (d, J = 11.2 Hz, 2H), 5.41 (t, J = 4.1 Hz, 2H), 5.96 (s, 4H), 7.35-7.60 (m, 4H), 7.60-7.70 (m, 2H), 7.75-7.85 (m, 4H) ppm; HRMS (FAB$^+$) Calcd for $C_{46}H_{67}O_4S$ ($C_{62}H_{89}O_8S_2$ – 2 x C_5H_8O – $C_6H_6O_2S$) 715.4760, found 715.4767.



9a-4

5,14-Bis(benzenesulfonyl)-3,7,12,16-tetramethyl-1,18-bis(2,6,6-trimethyl-1-cyclohexenyl)octadeca-1,3,9,15,17-pentaene-6,13-diol, bis(1-ethoxyethyl) ether (9a-4). To a stirred solution of the diol **8a** (0.634 g, 0.74 mmol) in CH_2Cl_2 (7 mL) were added pyridinium *p*-toluenesulfonate (0.075 g, 0.30 mmol) and ethyl vinyl ether (0.43 mL, 4.44 mmol) at 0 ºC. After stirring for 2 h at that temperature, it was warmed and stirred at room temperature overnight. The mixture was diluted with CH_2Cl_2 and 10% $NaHCO_3$ solution was added. The organic layer was separated, washed with H_2O, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product (0.75 g) was purified by SiO_2 flash column chromatography (hexanes:EtOAc = 6:1 ~ 4:1) to give the 1-ethoxyethyl diether **9a-4** (0.674 g, 0.673 mmol) in 91% yield as a white solid, which contained many stereoisomers due to the presence of eight chiral centers.

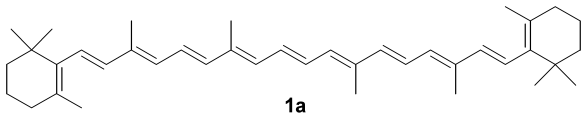
Data for **9a-4**: $\mathbf{R_f}$ = 0.20~0.40 (hexanes:EtOAc = 4:1).



10

5,14-Bis(benzenesulfonyl)-3,7,12,16-tetramethyl-1,18-bis(2,6,6-trimethyl-1-cyclohexenyl)octadeca-1,3,5,9,13,15,17-heptaene (10). The crude dibromide **9a-1** (515 mg, 0.52 mmol) was suspended in cyclohexane (20 mL), and KOMe (184 mg, 2.62 mmol) was added. The mixture was stirred at room temperature for 3 h, diluted with ether, washed with 1 M HCl solution, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product (640 mg) was purified by SiO_2 flash column chromatography (hexanes:EtOAc = 4:1) to give **10** (133 mg, 0.16 mmol) in 31% yield as a white solid.

Data for **10**: R_f = 0.35 (hexanes:EtOAc = 4:1); ^{1}H NMR δ 0.99 (s, 12H), 1.02 (s, 6H), 1.21 (s, 6H), 1.42-1.50 (m, 4H), 1.56-1.67 (m, 4H), 1.68 (s, 6H), 1.97-2.08 (m, 8H), 2.22-2.37 (m, 2H), 5.28 (br s, 2H), 5.71 (s, 2H), 6.06 (s, 4H), 6.75 (d, *J* = 10.3 Hz, 2H), 7.41-7.50 (m, 4H), 7.53-7.62 (m, 2H), 7.73-7.82 (m, 4H) ppm; HRMS (FAB^+) calcd for $C_{52}H_{69}O_4S_2$ 821.4637, found 821.4629.

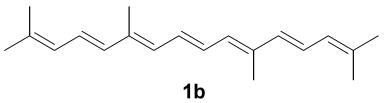


1a

β-Carotene (1a). Condition A. To a stirred suspension of the crude dibromide **9a-1** (1.34 g, 1.36 mmol) in cyclohexane (40 mL) was added KOMe (2.00 g, 28.48 mmol). The mixture was heated to 60 ºC ~ 80 ºC for 8.5 h, and cooled to room temperature. The mixture was then diluted with hexanes/benzene, washed with H_2O and 1 M HCl solution, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a dark-red solid (779 mg). The crude product was purified by dissolving in hexanes (60 mL) and washing with MeCN (30 mL x 3). The MeCN layer was extracted again with hexanes, and the combined hexanes layer was concentrated under reduced pressure to give **1a** (584 mg, 1.09 mmol) in 80% yield as a red solid, which was consisted of a 4:1 mixture of all-(*E*) and 13-(*Z*) stereoisomers. The product was further purified by SiO_2 flash column chromatography to give all-(*E*)-**1a** in 38% yield.

Condition B. To a stirred solution of the THP diether **9a-3** (1.50 g, 1.46 mmol) in cyclohexane (50 mL) was added KOMe (2.05 g, 29.25 mmol). The mixture was heated to 50 ºC ~ 60 ºC for 6 h, and cooled to room temperature. The mixture was then diluted with hexanes/benzene, washed with 1 M HCl solution, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product (1.26 g), which was consisted of a 4:1 mixture of all-(*E*) and 13-(*Z*) stereoisomers, was purified by SiO_2 flash column chromatography (hexanes:EtOAc = 32:1) to give all-(*E*)-**1a** (228 mg, 0.42 mmol) in 29% yield as a red solid.

Condition C. To a stirred solution of 1-ethoxyethyl diether **9a-4** (0.6 g, 0.6 mmol) in cyclohexane (20 mL) was added KOMe (0.842 g, 12.0 mmol). The mixture was heated to 80 ºC for 16 h, and cooled to room temperature. The mixture was then diluted with hexanes, washed 3 times with H_2O, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product (0.317 g), which was consisted of a 4:1 mixture of all-(*E*) and 13-(*Z*) stereoisomers, was purified by recrystallization (THF:MeOH = 1:5) to give all-(*E*)-**1a** (0.226 g, 0.42 mmol) in 70% yield as a red solid.



1b

2,6,11,15-Tetramethyl-hexadeca-2,4,6,8,10,12,14-heptaene (1b). According to the general procedure exemplified for β-carotene (**1a**) starting from **2a** through the diol **8a**, the MOM diether **9a-5** and using the double elimination Method D, the C_{20} carotene **1b** was prepared. The amounts of the reagents and the yields are as follows.

The solution of prenyl sulfone **2b** (0.812 g, 3.86 mmol) in THF (30 mL), which was treated with 1.6 M solution of *n*-BuLi in hexane (2.89 mL, 4.63 mmol), reacted with a solution of **3** (325 mg, 1.95 mmol) in THF (5 mL) at –78 ºC for 2h to give the diol **8b** (1.037 g, 1.76 mmol) in 91% yield as a white solid. The diol **8b** contained many stereoisomers due to the six chiral centers.

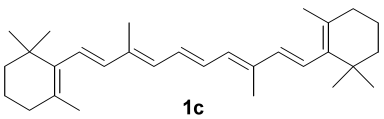
Data for **8b**: $\mathbf{R_f}$ = 0.06~0.13 (hexanes:EtOAc = 4:1).

The diol **8b** (0.447 g, 0.76 mmol) in dimethoxymethane (1.35 mL, 15.2 mmol) was treated twice by 5 h interval, each time with P_2O_5 (0.065 g, 0.456 mmol) at room temperature for 20 h to produce the MOM diether **9b** (0.473 g, 0.70 mmol) in 92% yield as a light yellow solid.

Data for **9b**: $\mathbf{R_f}$ = 0.06~0.13 (hexanes:EtOAc = 4:1).

The reaction of the MOM diether **9b** (0.339 g, 0.5 mmol) and KOMe (0.702 g, 10.0 mmol) in cyclohexane (20 mL) at 80 ºC for 16 h produced the C_{20} carotene **1b** (0.135 g), which was purified by recrystallization (THF:MeOH = 1:5) to give all-(*E*)-**1b** (0.66 g, 0.246 mmol) in 49% yield as a yellow solid.

Data for **1b**: ^{1}H NMR δ 1.81 (s, 12H), 1.93 (s, 6H), 5.93 (d, *J* = 11.0 Hz, 2H), 6.11-6.25 (m, 2H), 6.21 (d, *J* = 15.2 Hz, 2H), 6.46 (dd, *J* = 15.2, 11.0 Hz, 2H), 6.52-6.65 (m, 2H) ppm; ^{13}C NMR δ 12.8, 18.5, 26.3, 124.8, 126.1, 129.4, 131.4, 134.9, 135.7, 136.0 ppm; IR (KBr) 1456, 1361, cm^{-1};HRMS (FAB$^+$) calcd for $C_{20}H_{28}$ 268.2191, found 268.2195.



1c

3,8-Dimethyl-1,10-bis(2,6,6-trimethyl-1-cyclohexenyl)deca-1,3,5,7,9-pentaene (1c). According to the general procedure exemplified for β-carotene (**1a**), the C_{20} carotene **1c** was prepared. The amounts of the reagents and the yields are as follows.

The solution of cyclogeranyl sulfone **2c** (0.93 g, 3.34 mmol) in THF (15 mL), which was treated with 1.6 M solution of *n*-BuLi in hexane (2.28 mL, 3.65 mmol) at 0 ºC for 20 min, reacted with a solution of **3** (0.26 g, 1.52 mmol) in THF (5 mL) at –78 ºC for 1.5 h to give the diol **8c** (0.872 g, 1.2 mmol) in 79% yield as a white solid, which contained many stereoisomers due to the six chiral centers.

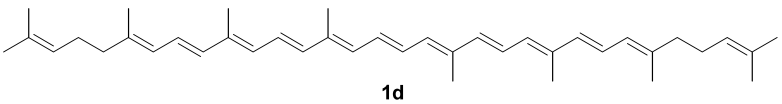
Data for **8c**: $\mathbf{R_f}$ = 0.10~0.18 (hexanes:EtOAc = 4:1).

The diol **8c** (0.58 g, 0.80 mmol) in dimethoxymethane (1.42 mL, 16 mmol) was treated twice by 5 h interval, each time with P_2O_5 (0.07 g, 0.48 mmol) at room temperature for 20 h to produce the MOM diether **9c** (0.584 g, 0.72 mmol) in 90% yield as a light yellow solid.

Data for **9c**: $\mathbf{R_f}$ = 0.12~0.20 (hexanes:EtOAc = 4:1).

The reaction of the MOM diether **9c** (0.553 g, 0.68 mmol) and KOMe (0.954 g, 13.6 mmol) in cyclohexane (25 mL) at 80 ºC for 16 h produced the C_{20} carotene **1c** (0.29 g), which was purified by SiO_2 flash column chromatography by using hexanes as the eluent to give all-(*E*)-**1c** (0.211 g, 0.522 mmol) in 77% yield as a red solid.

Data for **1c**: ^{1}H NMR δ 1.03 (s, 12H), 1.40-168 (m, 8H), 1.72 (s, 6H), 1.94 (s, 6H), 2.02 (t, *J* = 6.1 Hz, 4H), 6.05-6.25 (m, 6H), 6.55-6.70 (m, 2H) ppm; ^{13}C NMR δ 12.6, 18.9, 21.7, 28.9, 28.9, 33.1, 34.2, 39.6, 118.9, 126.6, 129.3, 130.7, 137.7, 155.8, 178.0 ppm; IR (KBr) 2928, 1456, 1361, 966 cm^{-1}; HRMS (FAB$^+$) calcd for $C_{30}H_{44}$ 404.3443, found 404.3454.



1d

Lycopene (1d). According to the general procedure exemplified for β-carotene (**1a**), lycopene (**1d**) was prepared. The amounts of the reagents and the yields are as follows.

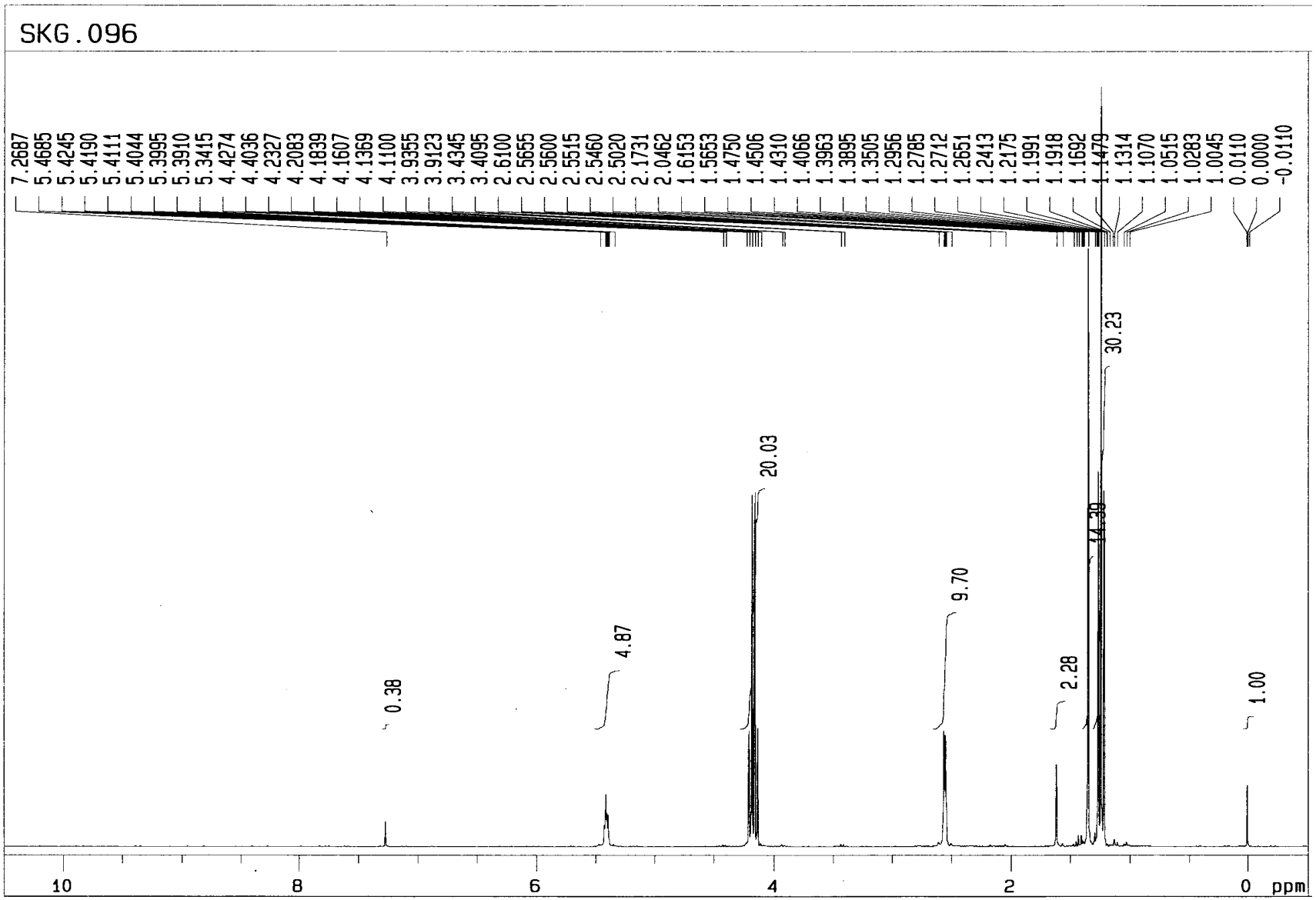
The solution of 1-benzenesulfonyl-2,6,10-trimethyl-dodeca-2,4,6,10-tetraene (**2d**) (0.345 g, 1.0 mmol) in THF (10 mL), which was treated with 1.6 M solution of *n*-BuLi in hexane (0.75 mL, 1.2 mmol) at 0 ºC for 20 min, reacted with a solution of **3** (0.084 g, 0.5 mmol) in THF (3 mL) at –78 ºC for 1.5 h to give the diol **8d** (0.379 g, 0.44 mmol) in 88% yield as a white solid, which contained many stereoisomers due to the six chiral centers.

Data for **8d**: $\mathbf{R_f}$ = 0.05~0.18 (hexanes:EtOAc = 4:1).

The diol **8d** (0.37 g, 0.43 mmol) in dimethoxymethane (0.76 mL, 8.6 mmol) was treated twice by 5 h interval, each time with P_2O_5 (0.037 g, 0.26 mmol) at room temperature for 20 h to produce the MOM diether **9d** (0.272 g, 0.288 mmol) in 67% yield as a light yellow solid.

Data for **9d**: $\mathbf{R_f}$ = 0.08~0.18 (hexanes:EtOAc = 4:1).

The reaction of the MOM diether **9d** (0.27 g, 0.285 mmol) and KOMe (0.4 g, 5.7 mmol) in cyclohexane (20 mL) at 80 ºC for 16 h produced the crude lycopene (0.092 g), which was purified by recrystallization (THF:MeOH = 1:5) to give all-(*E*)-lycopene **1d** (0.043 g, 0.08 mmol) in 28% yield as a red solid. The ^{1}H NMR data of **1d** was identical with those of the authentic sample.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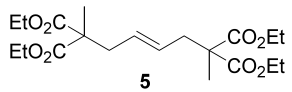
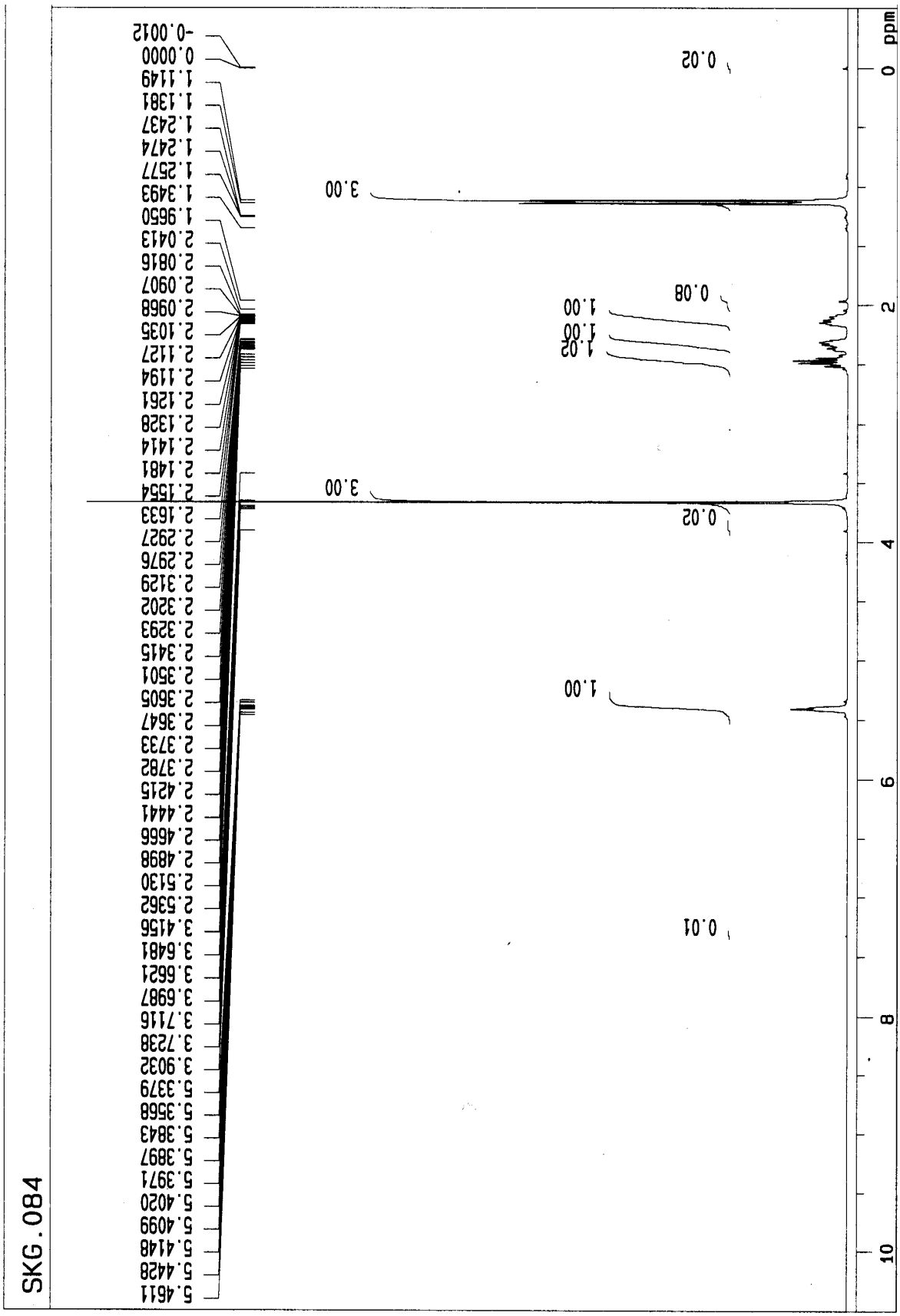
5.4245
5.4190
5.4111
5.4044
5.3995
5.3910
5.3415
4.4274
4.4036
4.2327
4.2083
4.1839
4.1607
4.1369
4.1100
3.9355
3.9123
3.4345
3.4095
2.6100
2.5655
2.5600
2.5515
2.5460
2.5020
2.1731
2.0462
1.6153
1.5653
1.4750
1.4506
1.4310
1.4066
1.3963
1.3895
1.3505
1.2956
1.2785
1.2712
1.2651
1.2413
1.2175
1.1991
1.1918
1.1692
1.1479
1.1314
1.1070
1.0515
1.0283
1.0045
0.0110
0.0000
-0.0110
0.38
4.87
20.03
9.70
14.39
30.23
2.28
1.00
10
8
6
4
2
0
ppm


EtO2C
EtO2C
CO2Et
CO2Et

5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ppm
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2
4
6
8
10
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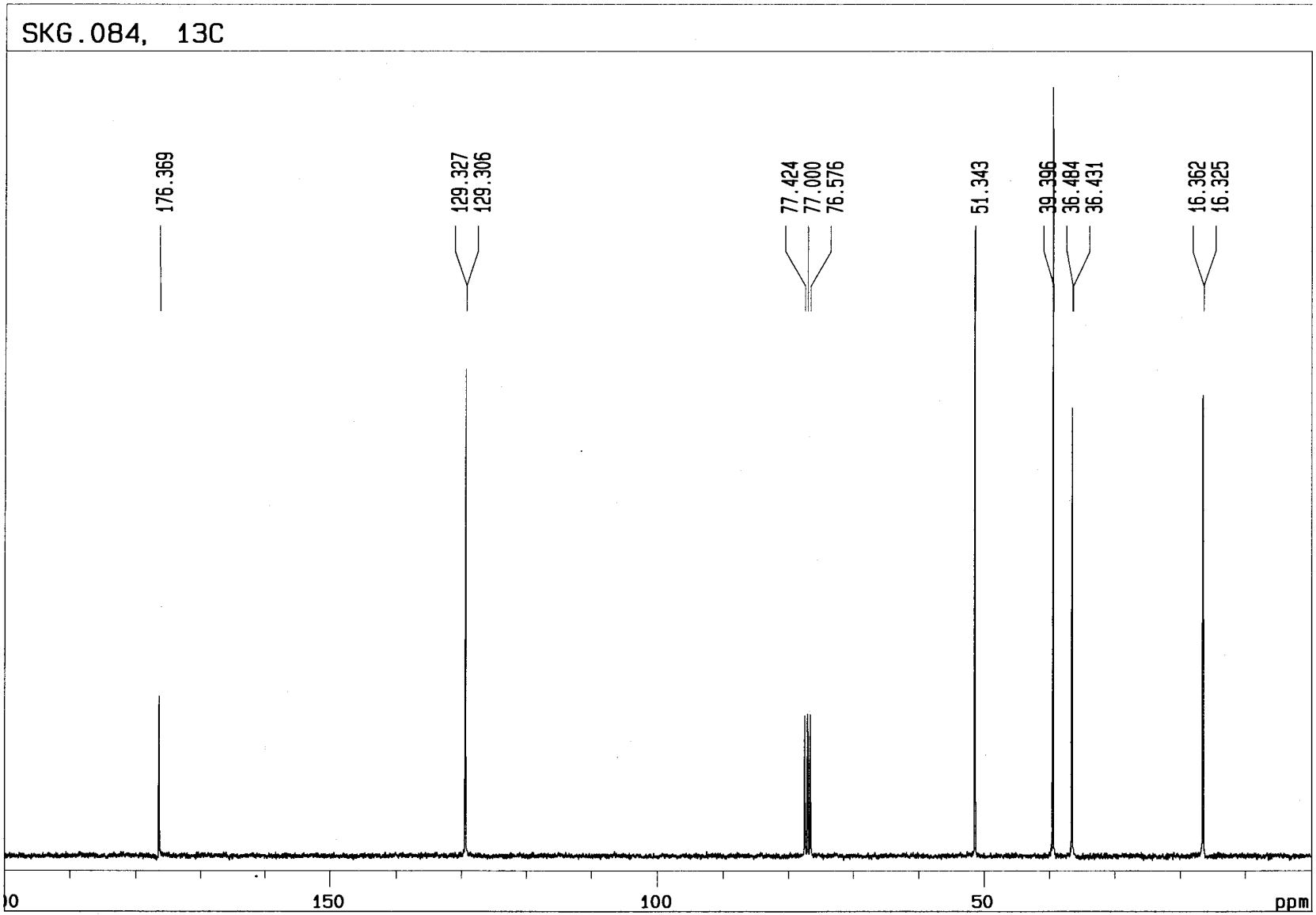
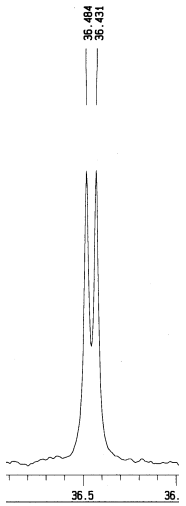
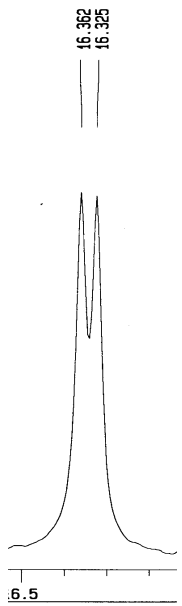
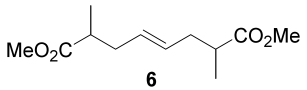
0.08
1.00
1.00
1.02
3.00
0.02
1.00
0.01
CO2Me
MeO2C
6

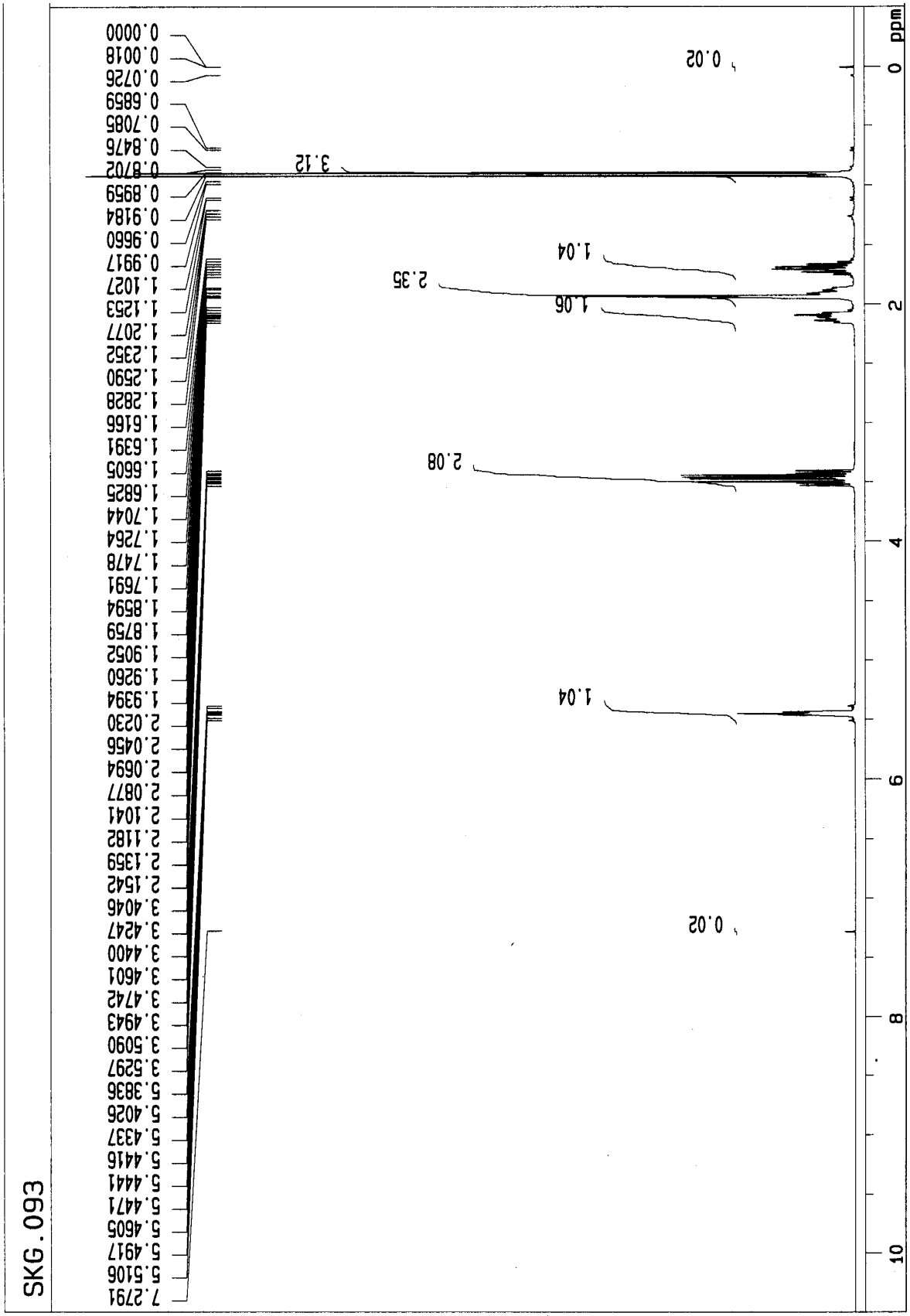

SKG.084, 13C
176.369
129.327
129.306
77.424
77.000
76.576
51.343
39.396
36.484
36.431
16.362
16.325
150
100
50
ppm


36.484
36.431
36.5


16.362
16.325
6.5


MeO2C
CO2Me

6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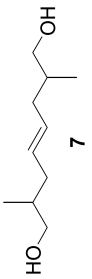
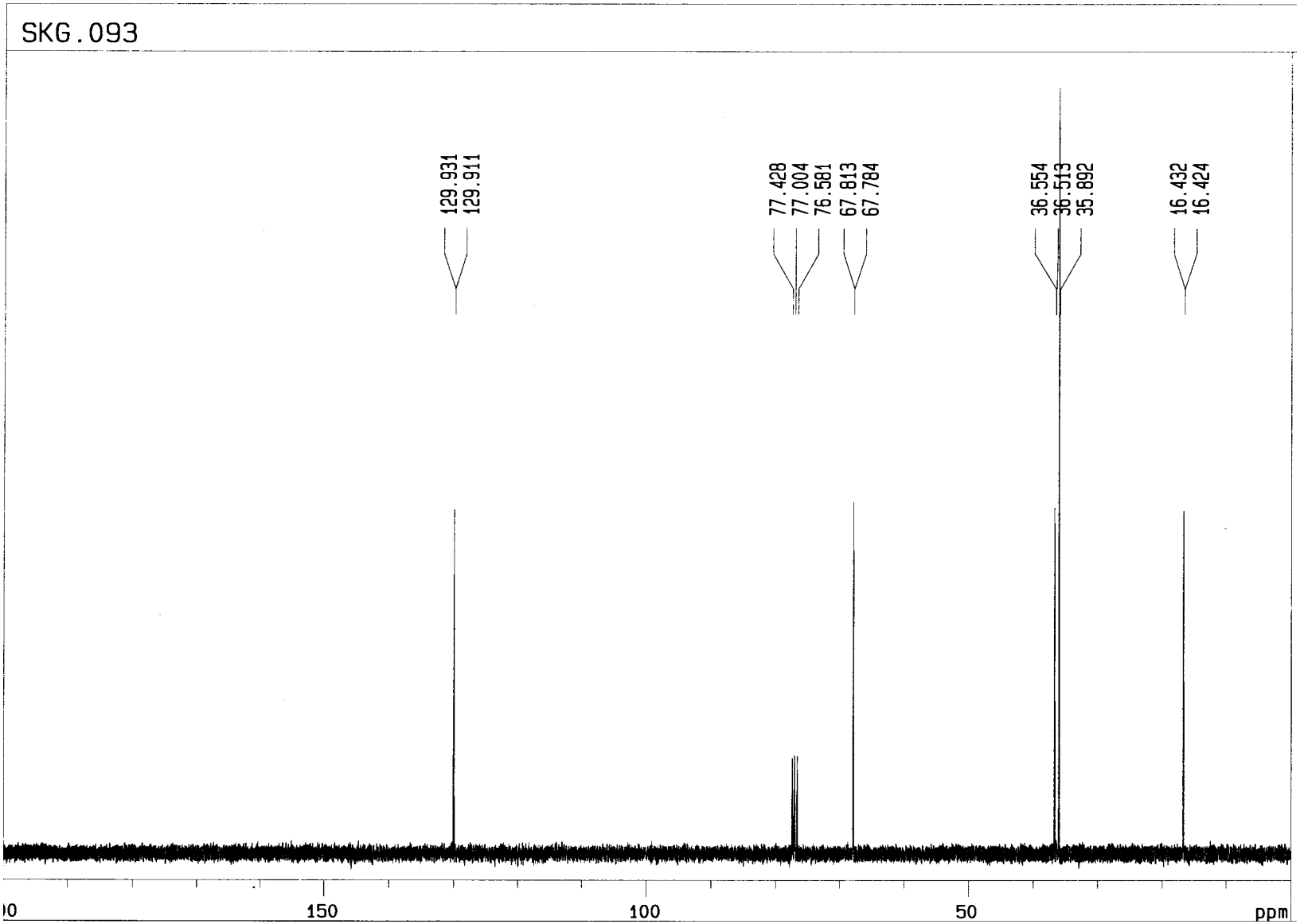
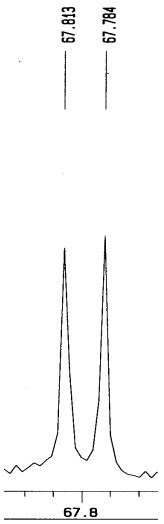
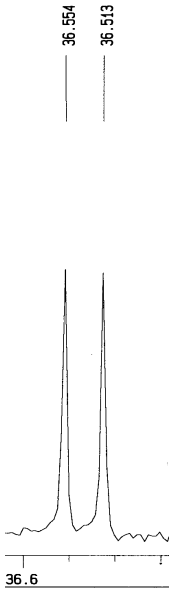
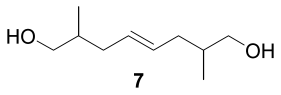
5.4917
5.4605
5.4471
5.4441
5.4416
5.4337
5.4026
5.3836
3.5297
3.5090
3.4943
3.4742
3.4601
3.4400
3.4247
3.4046
2.1542
2.1359
2.1182
2.1041
2.0877
2.0694
2.0456
2.0230
1.9394
1.9260
1.9052
1.8759
1.8594
1.7691
1.7478
1.7264
1.7044
1.6825
1.6605
1.6391
1.6166
1.2828
1.2590
1.2352
1.2077
1.1253
1.1027
0.9917
0.9660
0.9184
0.8959
0.8702
0.8476
0.7085
0.6859
0.0726
0.0018
0.0000
3.12
2.35
2.08
1.04
1.06
1.04
0.02
0.02
ppm
0
2
4
6
8
10


OH
HO
7

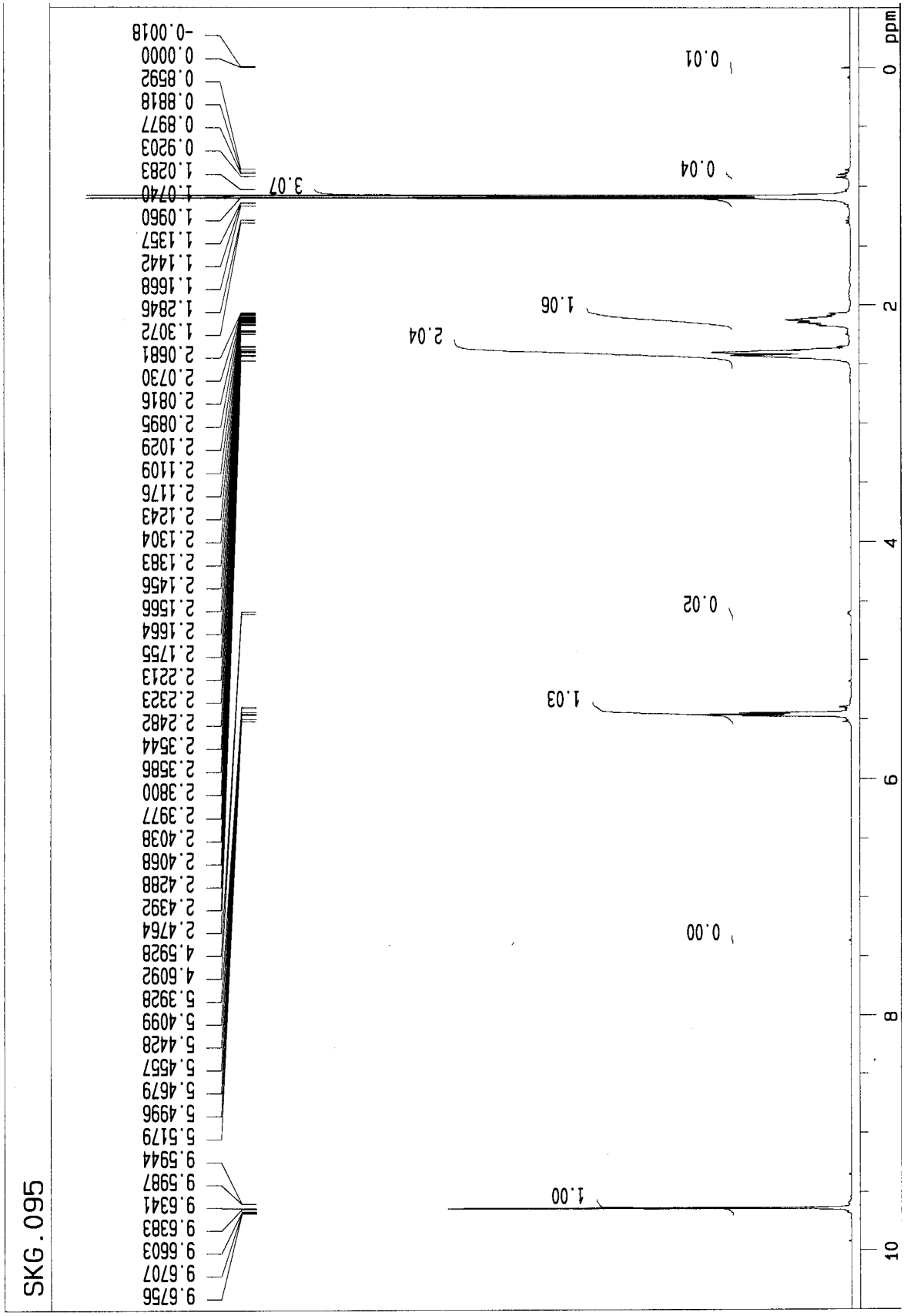

SKG.093
129.931
129.911
77.428
77.004
76.581
67.813
67.784
36.554
36.513
35.892
16.432
16.424
150
100
50
ppm


67.813
67.784
67.8


36.554
36.513
36.6


HO
OH

7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6
8
10
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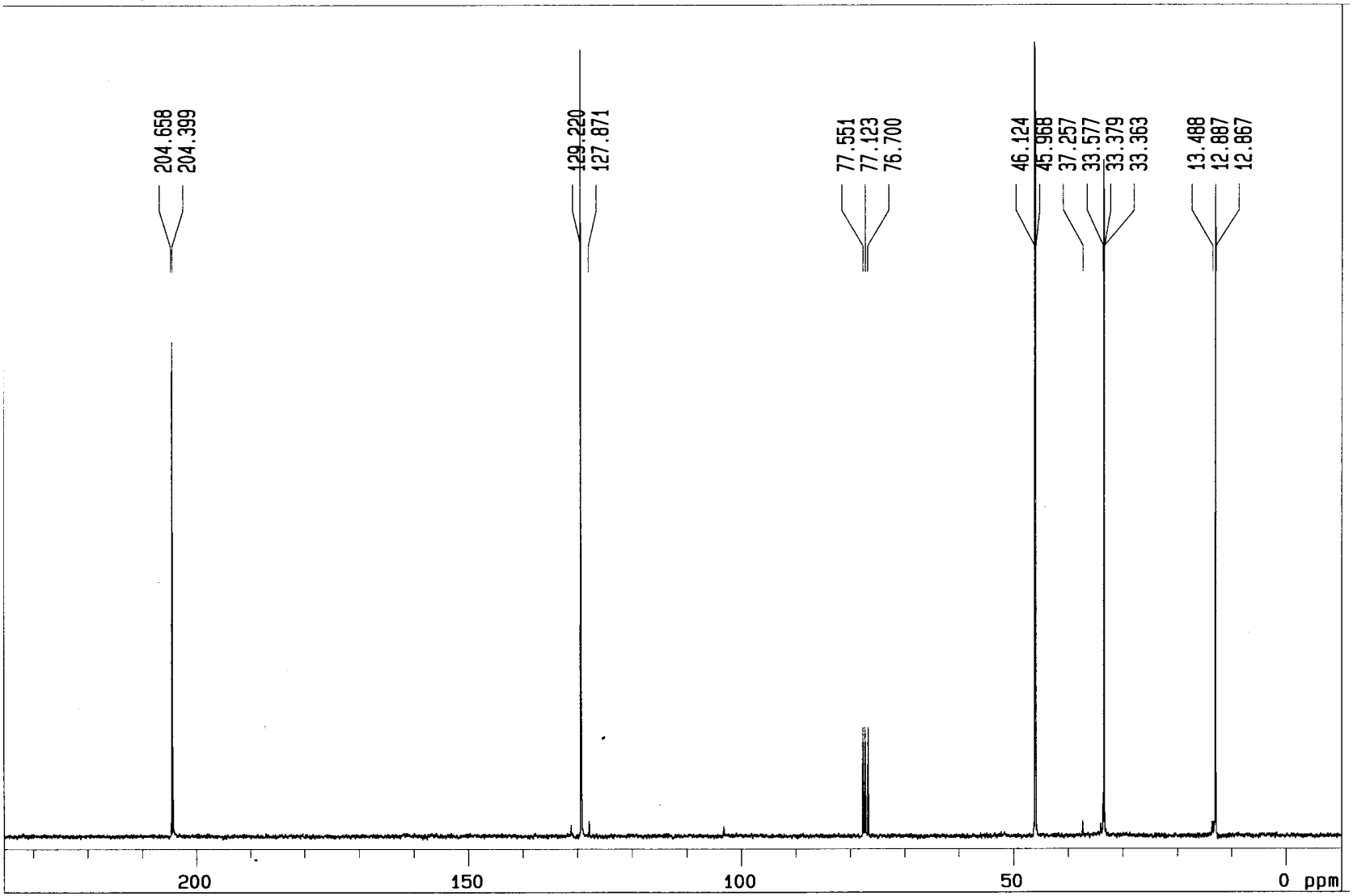
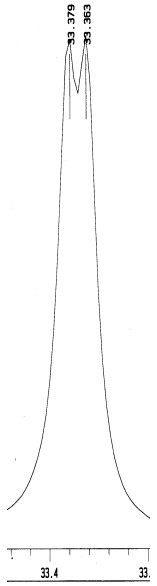
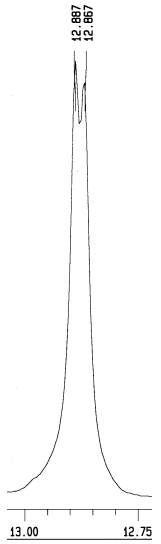
0.00
1.03
0.02
2.04
1.06
3.07
0.04
0.01
-0.0018
0.0000
0.8592
0.8818
0.8977
0.9203
1.0283
1.0740
1.0960
1.1357
1.1442
1.1668
1.2846
1.3072
2.0681
2.0730
2.0816
2.0895
2.1029
2.1109
2.1176
2.1243
2.1304
2.1383
2.1456
2.1566
2.1664
2.1755
2.2213
2.2323
2.2482
2.3544
2.3586
2.3800
2.3977
2.4038
2.4068
2.4288
2.4392
2.4764
4.5928
4.6092
5.3928
5.4099
5.4428
5.4557
5.4679
5.4996
5.5179
9.5944
9.5987
9.6341
9.6383
9.6603
9.6707
9.6756

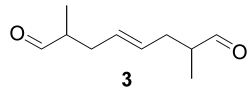

O
3
O

SKG.095, 13C

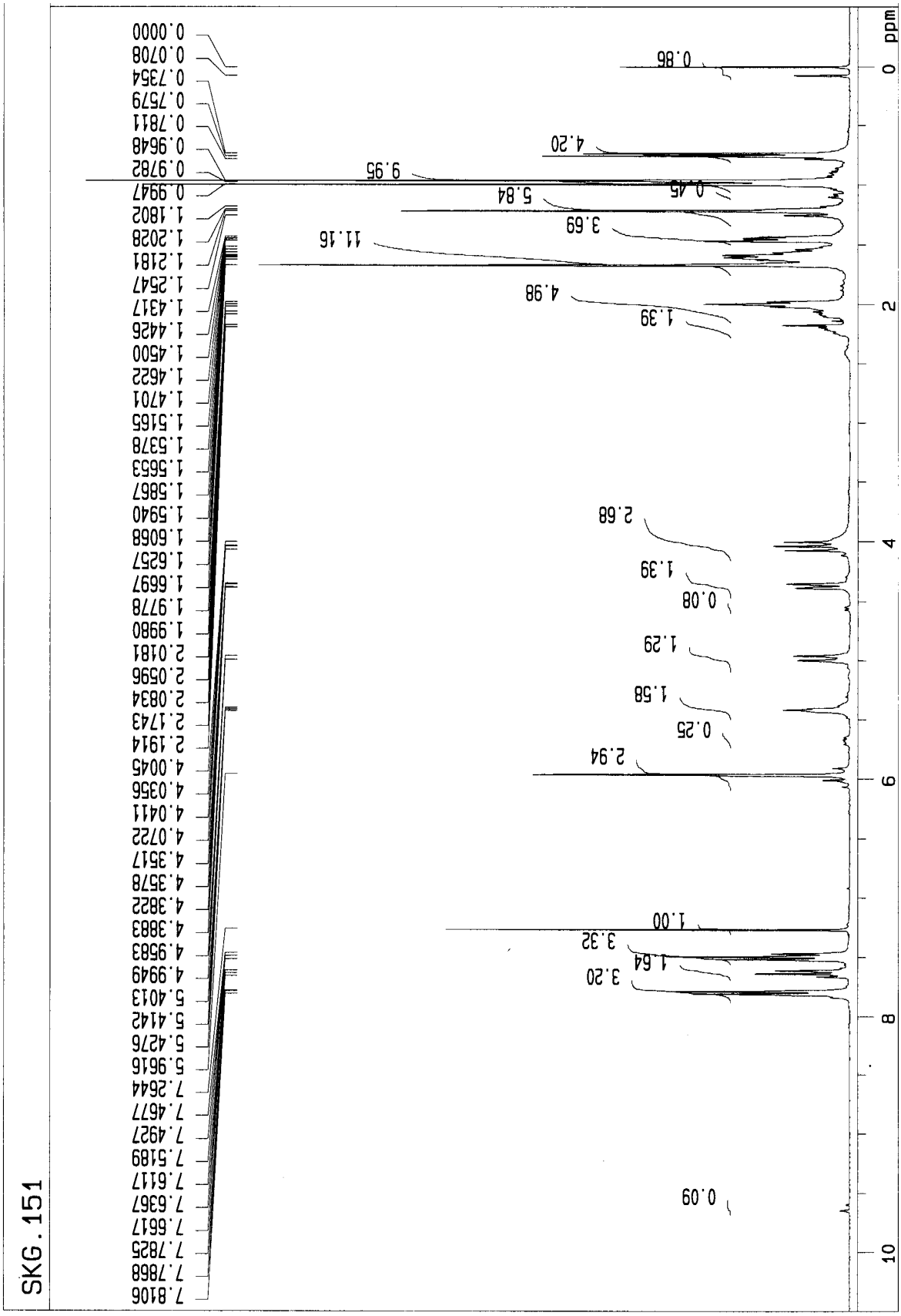

204.658
204.399
129.220
127.871
77.551
77.123
76.700
46.124
45.968
37.257
33.577
33.379
33.363
13.488
12.887
12.867
200
150
100
50
0 ppm


33.379
33.363
33.4
33.


12.887
12.867
13.00
12.75


O
O

3


SKG.151
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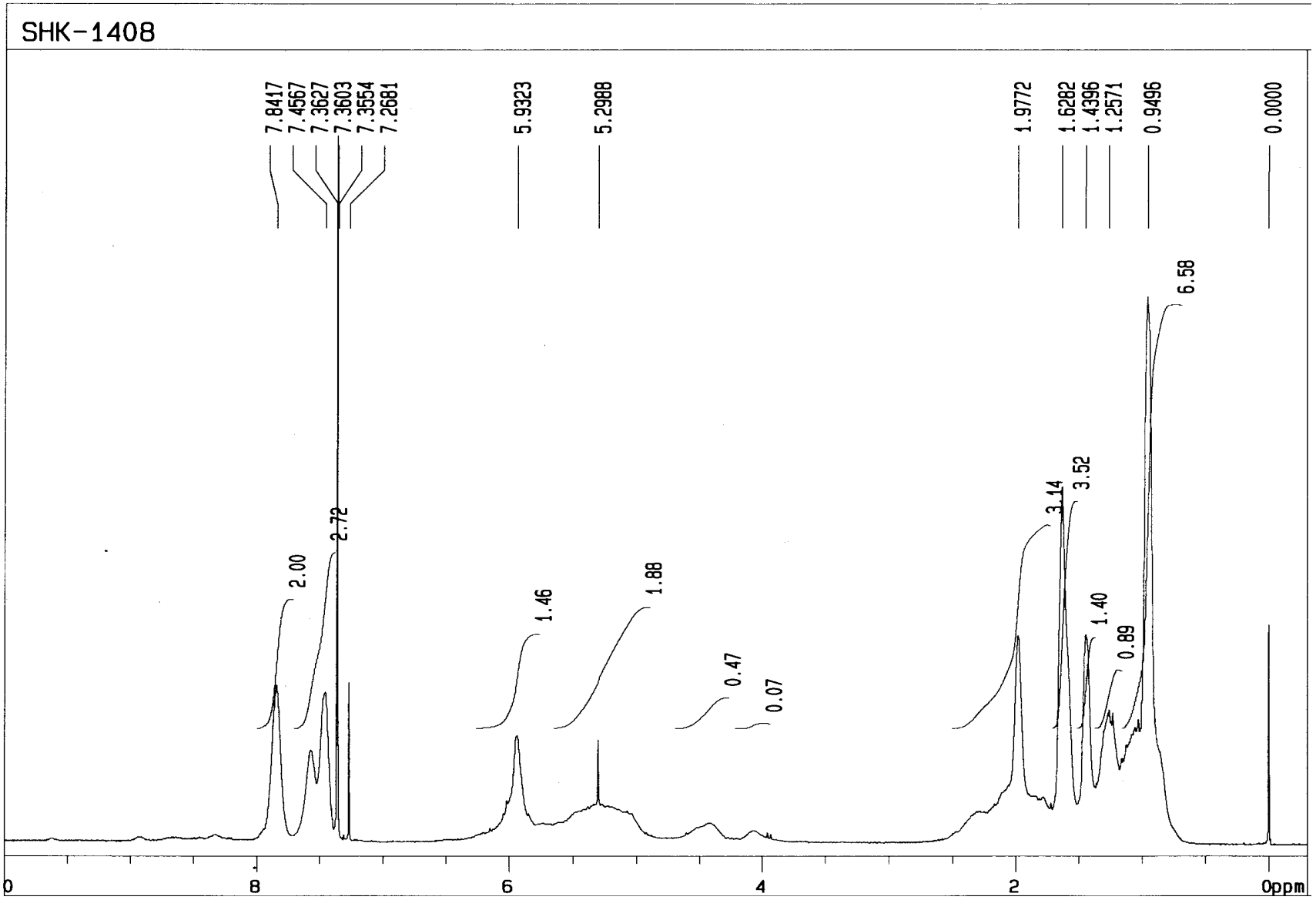
1.64
3.20
2.94
0.25
1.58
1.29
0.08
1.39
2.68
4.98
1.39
11.16
3.69
5.84
0.45
9.95
4.20
0.86
OH
OH
SO_2Ph
PhO_2S
8a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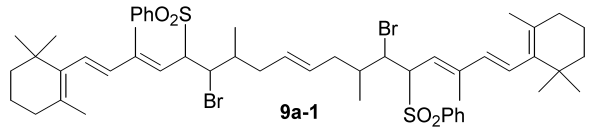
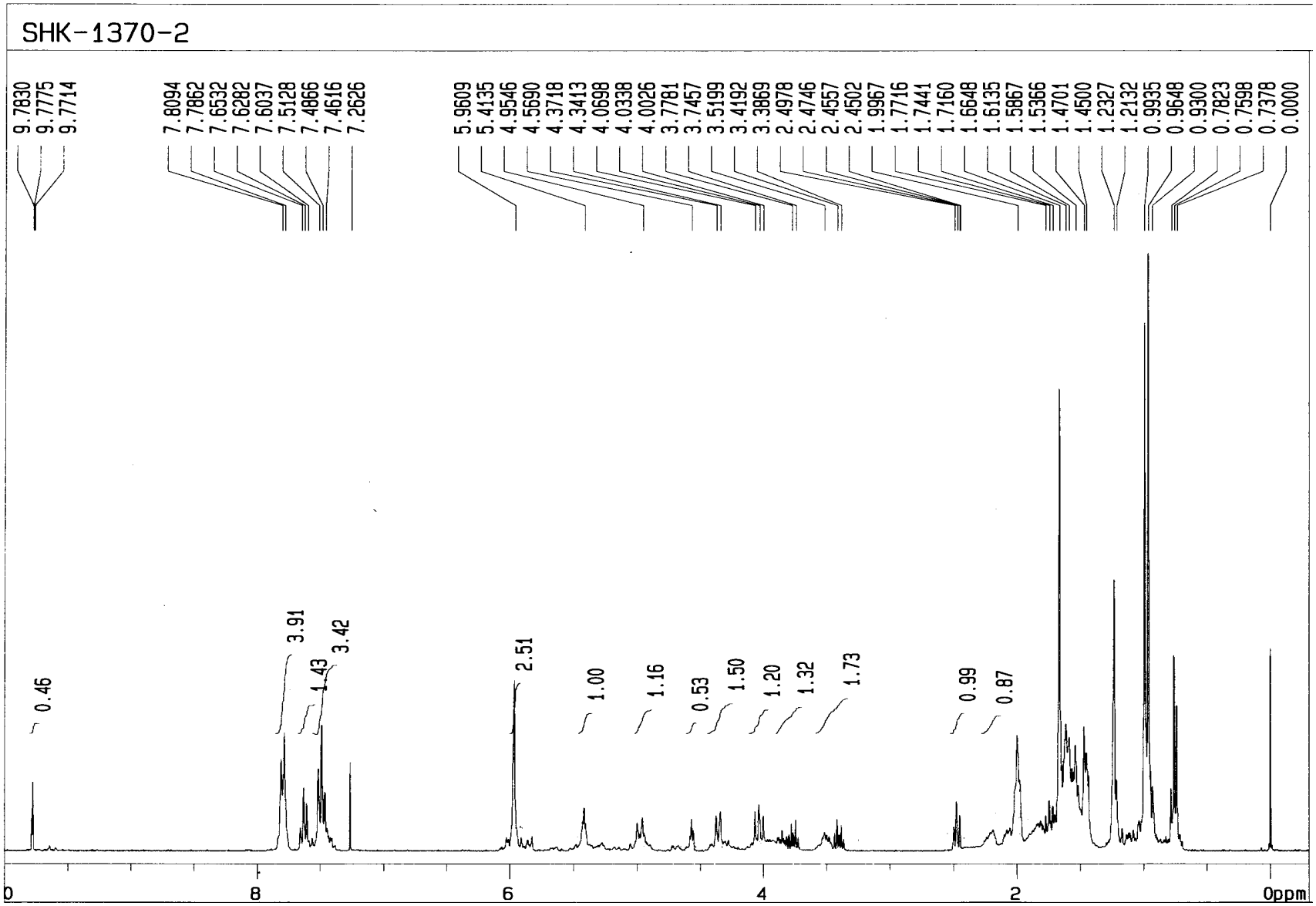
7.3627
7.3603
7.3554
7.2681
5.9323
5.2988
1.9772
1.6282
1.4396
1.2571
0.9496
0.0000
6.58
3.14
3.52
2.72
2.00
1.46
1.88
1.40
0.89
0.47
0.07
0
8
6
4
2
0ppm


PhO2S
Br
Br
SO2Ph

9a-1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9.7714
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7.7862
7.6532
7.6282
7.6037
7.5128
7.4866
7.4616
7.2626
5.9609
5.4135
4.9546
4.5690
4.3718
4.3413
4.0698
4.0338
4.0026
3.7781
3.7457
3.5199
3.4192
3.3869
2.4978
2.4746
2.4557
2.4502
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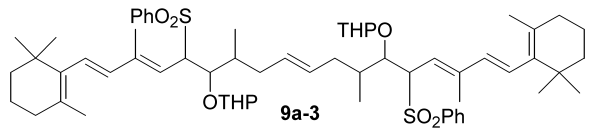
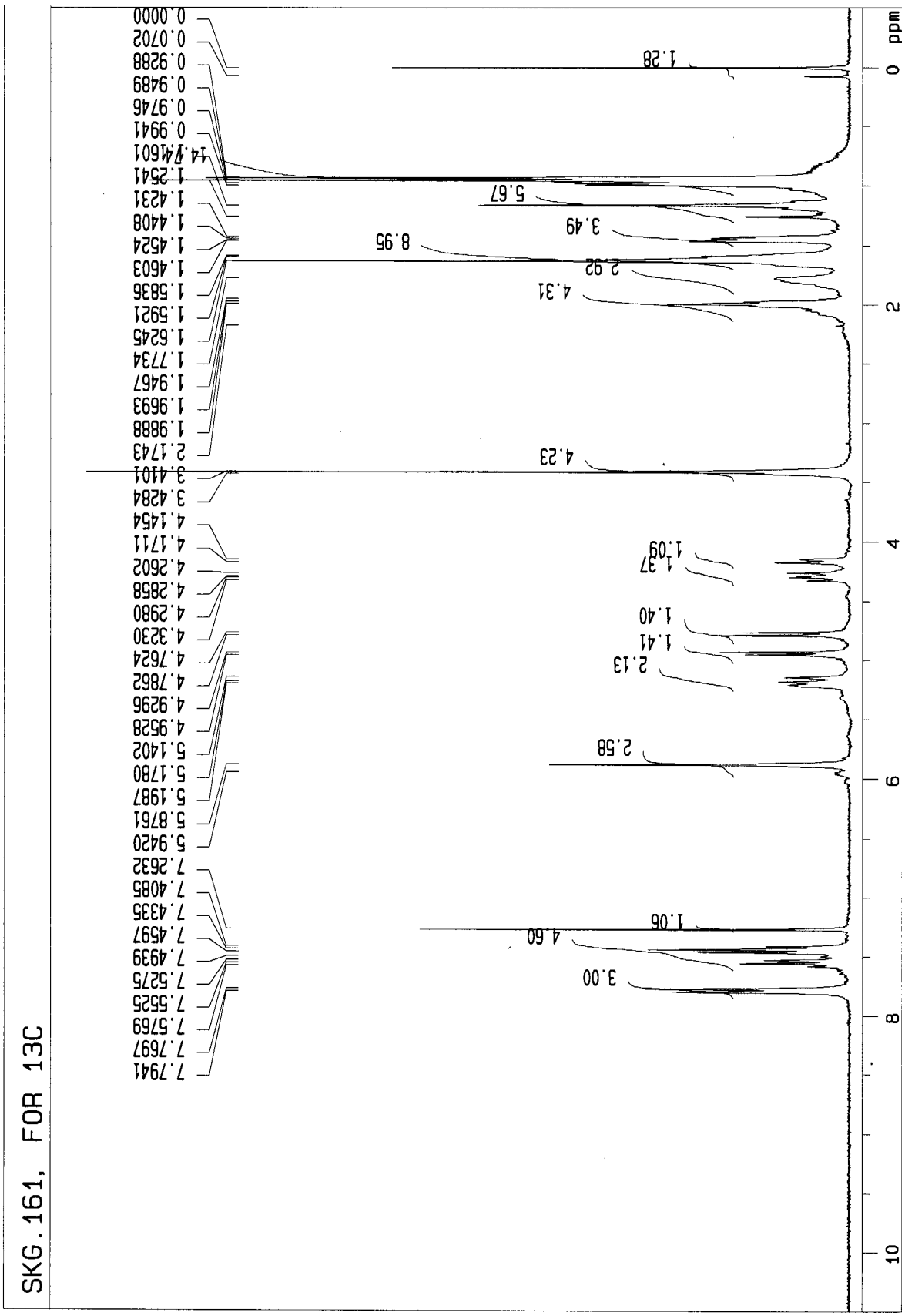
1.7441
1.7160
1.6648
1.6135
1.5867
1.5366
1.4701
1.4500
1.2327
1.2132
0.9935
0.9648
0.9300
0.7823
0.7598
0.7378
0.0000
0.46
3.91
1.43
3.42
2.51
1.00
1.16
0.53
1.50
1.20
1.32
1.73
0.99
0.87
0
8
6
4
2
0ppm


PhO2S
THPO
OTHP
SO2Ph

9a-3


SKG.161, FOR 13C
ppm
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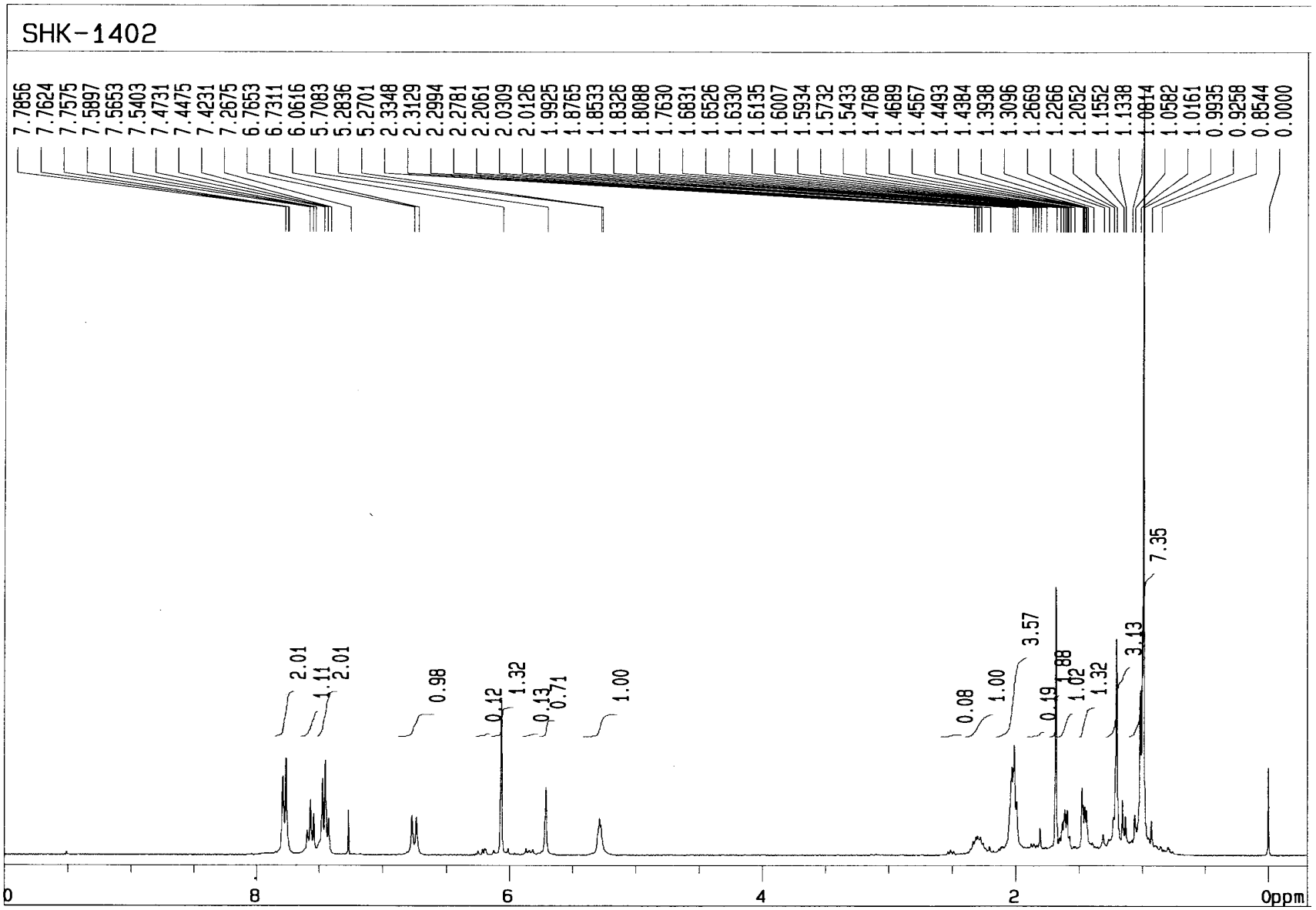
2
4
6
8
10
1.28
5.67
3.49
8.95
2.92
4.31
4.23
1.37
1.09
1.40
1.41
2.13
2.58
1.06
4.60
3.00
MOMO
OMOM
9a-5
PhO2S
SO2Ph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7.5897
7.5653
7.5403
7.4731
7.4475
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6.7653
6.7311
6.0616
5.7083
5.2836
5.2701
2.3348
2.3129
2.2994
2.2781
2.2061
2.0309
2.0126
1.9925
1.8765
1.8533
1.8326
1.8088
1.7630
1.6831
1.6526
1.6330
1.6135
1.6007
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1.5433
1.4768
1.4689
1.4567
1.4493
1.4384
1.3938
1.3096
1.2669
1.2266
1.2052
1.1552
1.1338
1.0814
1.0582
1.0161
0.9935
0.9258
0.8544
0.0000
2.01
1.11
2.01
0.98
0.12
1.32
0.13
0.71
1.00
0.08
1.00
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0.19
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1.32
3.13
7.35
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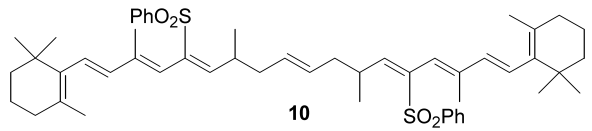
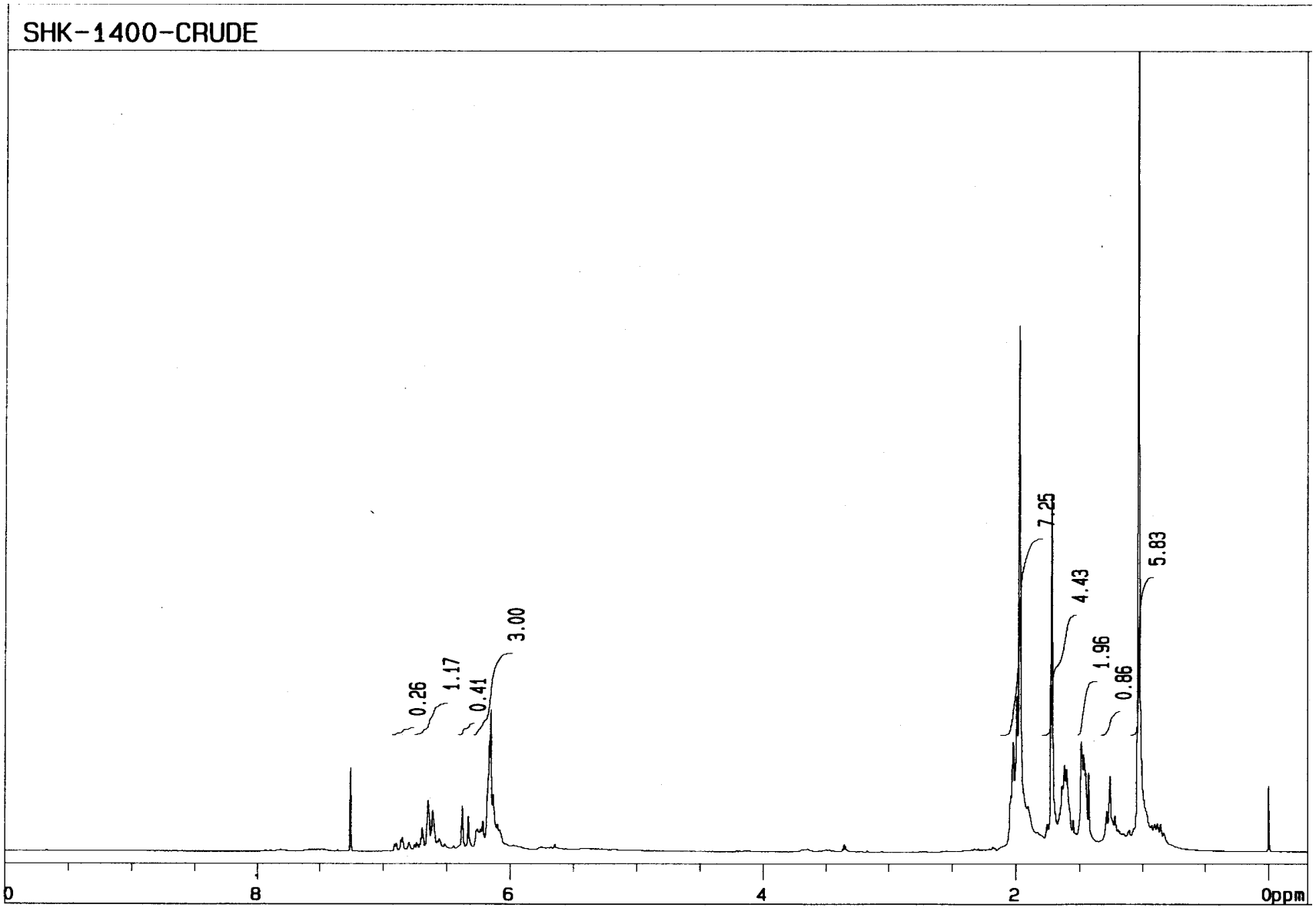
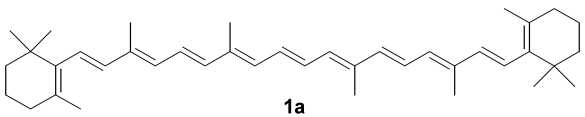
8
6
4
2
0ppm

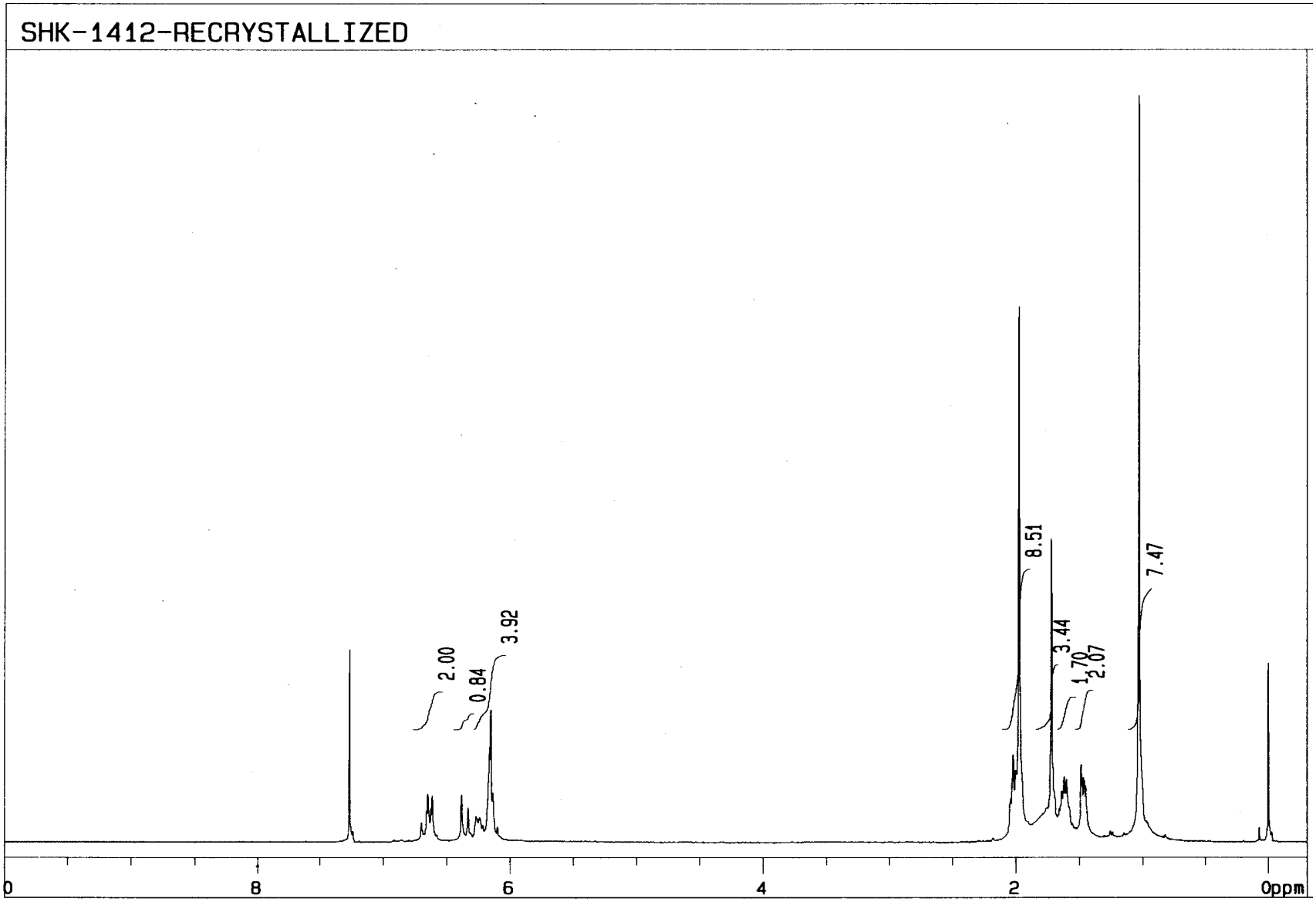

PhO2S
SO2Ph

10





1a


SHK-1412-RECRYSTALLIZED
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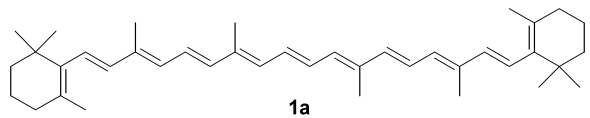
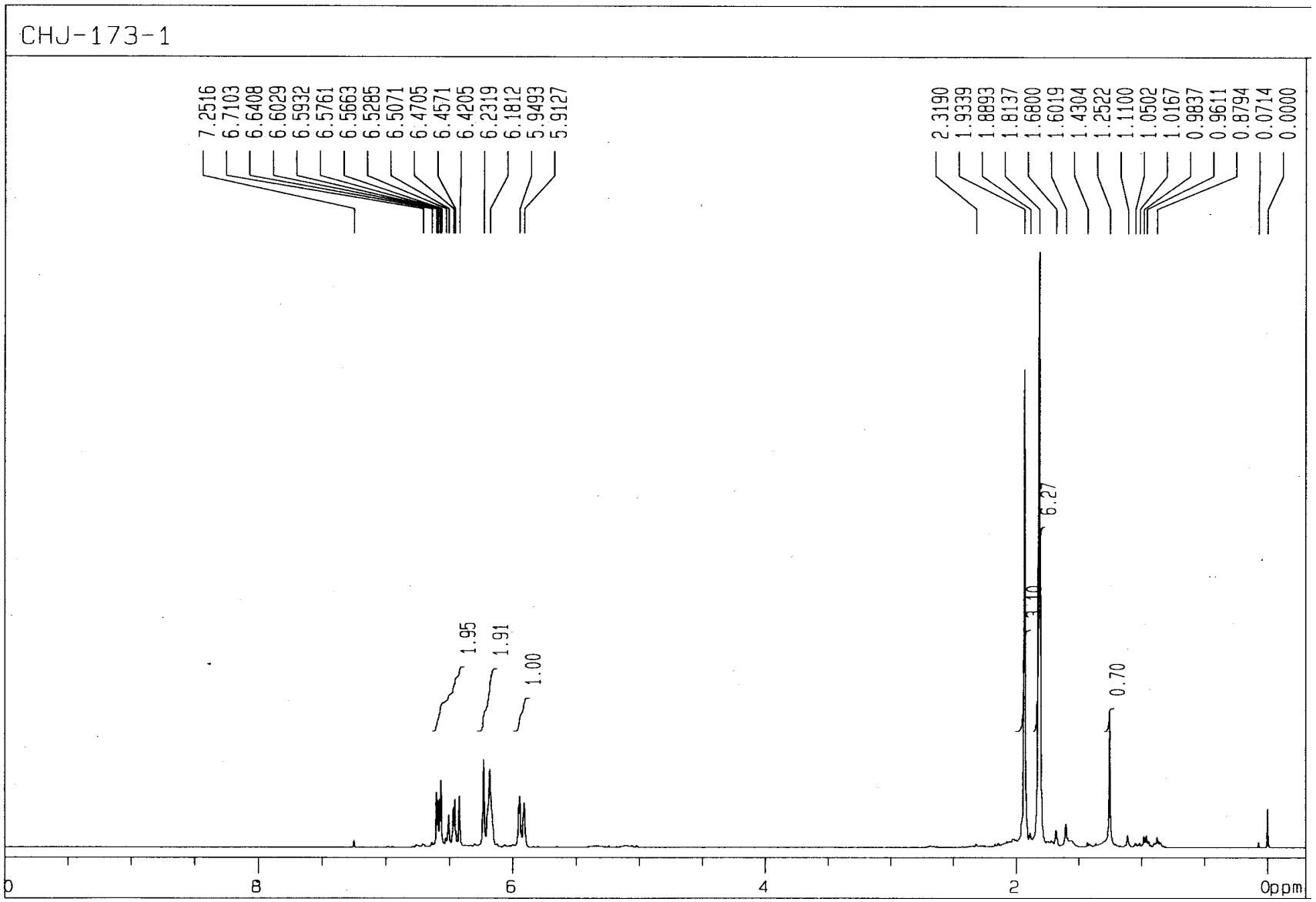
0.84
3.92
8.51
3.44
1.70
2.07
7.47
0
8
6
4
2
0ppm



1a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6.6408
6.6029
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6.5761
6.5663
6.5285
6.5071
6.4705
6.4571
6.4205
6.2319
6.1812
5.9493
5.9127
2.3190
1.9339
1.8893
1.8137
1.6800
1.6019
1.4304
1.2522
1.1100
1.0502
1.0167
0.9837
0.9611
0.8794
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1.91
1.00
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6
4
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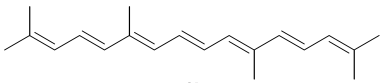
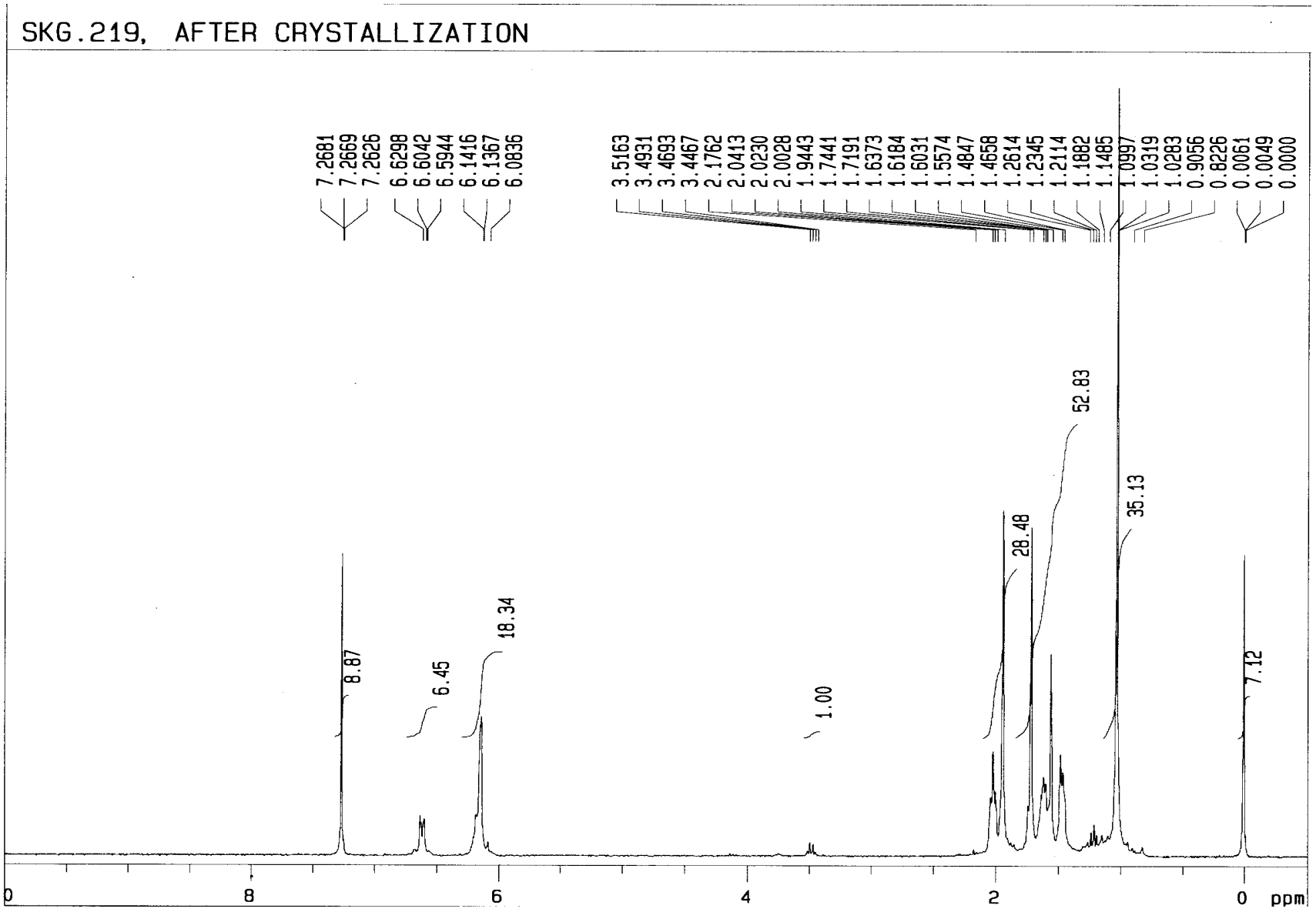
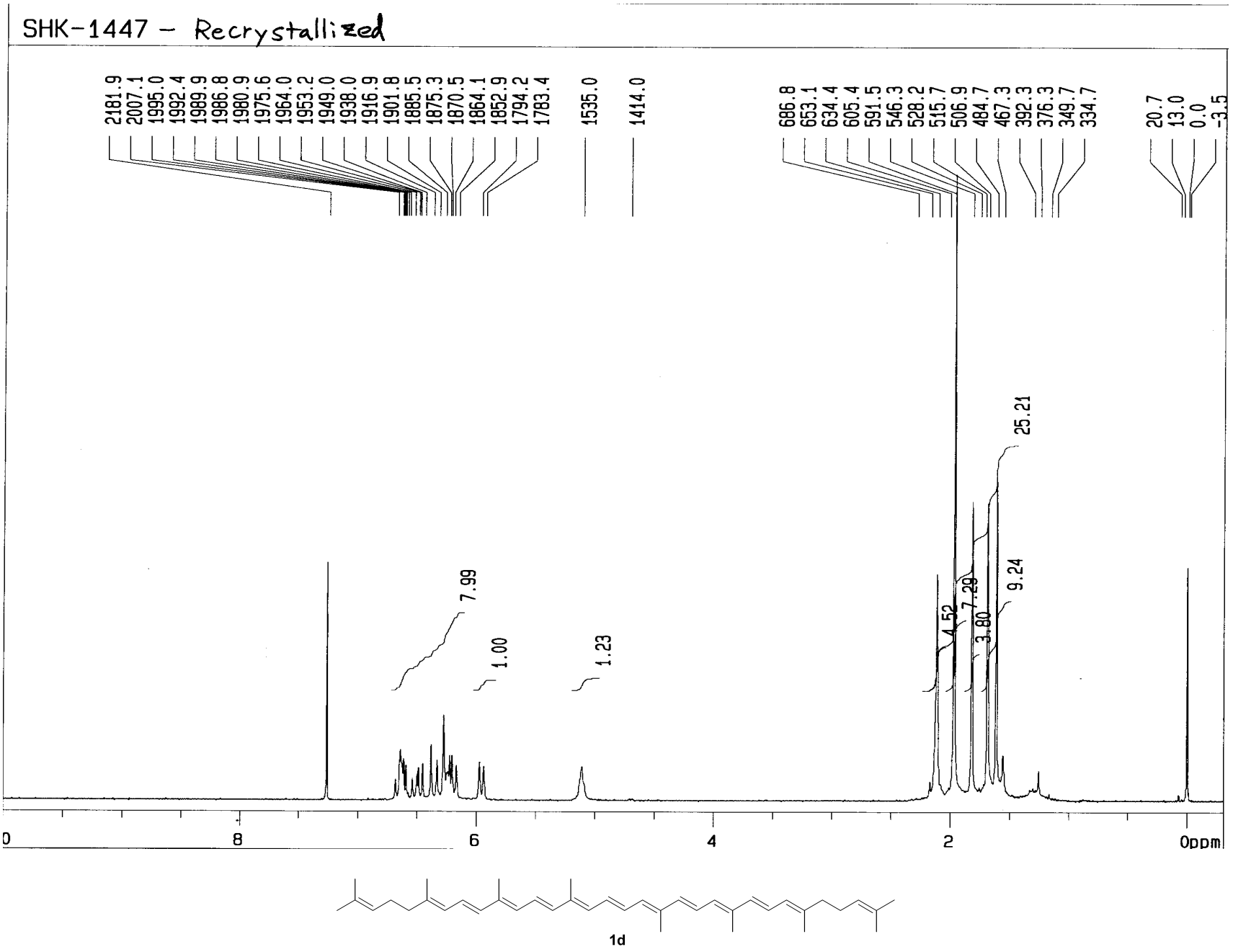


1b


SKG.219, AFTER CRYSTALLIZATION
7.2681
7.2669
7.2626
6.6298
6.6042
6.5944
6.1416
6.1367
6.0836
3.5163
3.4931
3.4693
3.4467
2.1762
2.0413
2.0230
2.0028
1.9443
1.7441
1.7191
1.6373
1.6184
1.6031
1.5574
1.4847
1.4658
1.2614
1.2345
1.2114
1.1882
1.1485
1.0997
1.0319
1.0283
0.9056
0.8226
0.0061
0.0049
0.0000
8.87
6.45
18.34
1.00
28.48
52.83
35.13
7.12
0
8
6
4
2
0
ppm

1c


SHK-1447 – Recrystallized
2181.9
2007.1
1995.0
1992.4
1989.9
1986.8
1980.9
1975.6
1964.0
1953.2
1949.0
1938.0
1916.9
1901.8
1885.5
1875.3
1870.5
1864.1
1852.9
1794.2
1783.4
1535.0
1414.0
686.8
653.1
634.4
605.4
591.5
546.3
528.2
515.7
506.9
484.7
467.3
392.3
376.3
349.7
334.7
20.7
13.0
0.0
-3.5
25.21
9.24
7.99
7.29
4.52
3.80
1.00
1.23
8
6
4
2
0ppm

1d