Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

69451 Weinheim, Germany

Total Synthesis of Peribysin E: Necessitates Revision of the Assignment of its Absolute Configuration

Angie R. Angeles, David C. Dorn, Cynthia A. Kou, Malcolm A. S. Moore and Samuel J. Danishefsky*

Prof. S. J. Danishefsky, Dr. A. R. Angeles
The Laboratory for Bioorganic Chemistry
Sloan-Kettering Institute for Cancer Research
1275 York Avenue, New York, NY 10021 (USA)
Fax: (+1) 212-772-8691
E-mail: s-danishefsky@ski.mskcc.org

Dr. M. A. S. Moore, Dr. D. C. Dorn, C. A. Kou
The Laboratory of Developmental Hematopoiesis
Sloan-Kettering Institute for Cancer Research
1275 York Avenue, New York, NY 10021 (USA)

Prof. S. J. Danishefsky
The Department of Chemistry
Columbia University
Havemeyer Hall, New York, NY 10027 (USA)

[**] This work was supported by the National Institutes of Health (CA28824 to SJD, HL61401 and CA59350 to MASM, and CA062948 to ARA). We thank Dr. Louis Todaro (Hunter College) for X-ray structure analyses and Professor Shahin Rafii (Weill Cornell) for the HUVEC.

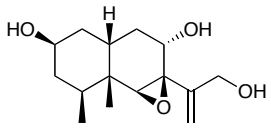
Materials and Methods:

Unless otherwise stated, all non-aqueous reactions were carried out under an atmosphere of dry argon in dried glassware. When necessary, solvents and reagents were dried prior to use. Toluene, benzene, tetrahydrofuran, diethyl ether, and dichloromethane were dried and using a Solv-Tek, Inc. solvent purification system. All other solvents were of anhydrous quality purchased from Aldrich Chemical Co. and used as received. Triethylamine was distilled from calcium hydride under an inert atmosphere prior to use. Commercially available starting materials and reagents were purchased from Aldrich and were used as received.

Analytical thin layer chromatography (TLC) was performed on Sigma-Aldrich 0.25 mm silica gel plates with UV indicator. Visualization was accomplished by either irradiation under a 254 nm UV lamp or by staining with an aqueous solution of ceric ammonium molybdate (CAM). Chromatography on silica gel was performed using a forced flow of the indicated solvent system on Aldrich Silica Gel (60 Å).

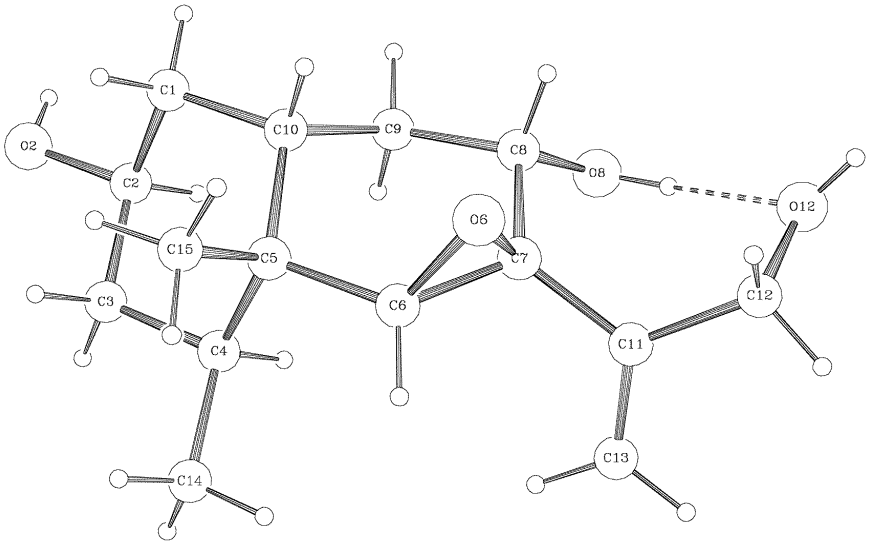
^{1}H NMR spectra were recorded on a Bruker AMX-400 (400 MHz) and Bruker AMX-500 (500 MHz) spectrometers. ^{13}C NMR spectra were recorded on a Bruker AMX-400 (100 MHz) and Bruker AMX-500 (125 MHz) spectrometers. Chemical shifts are reported in ppm from tetramethylsilane (0 ppm) or with the solvent resonance as the internal standard ($CDCl_3$ 7.26 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants, and number of protons. Infrared spectra were taken on an Perkin-Elmer 1600 FT-IR spectrometer using thin neat film deposition on NaCl plates. Infrared peaks are reported in cm^{1}. Mass spectra were acquired using a Perkin-Elmer Sciex API 100 in ionspray (a version of electron spray) mode. Melting points were obtained on an Electrothermal series IA9100 digital melting point apparatus.

Preparative Experiments:

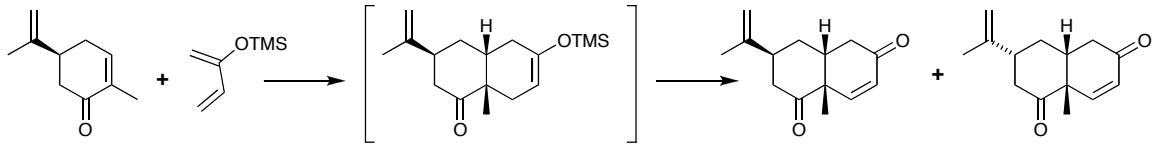


S1

Epoxy triol S1. To a solution of epoxy diol **S5** (Page 12) (20.7 mg, 0.054 mmol) in anhydrous THF (2 mL) was added TBAF (1M in THF, 0.08 mL, 0.081 mmol). The resultant mixture was stirred at ambient temperature for 30 min. and concentrated. Flash chromatography using MeOH:CH_2Cl_2 5:95 as eluent furnished 13.7 mg (94%) of (+)-**S1** as a crystalline solid, mp 150-152 °C; $[\alpha]_D^{25}$ +35.00 (c = 0.042, CH_2Cl_2); IR (neat) 3322 (br), 2925 (s), 2360 (s), 1730 (m), 1540 (m), 1458 (m), 1028 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.33 (s, 1 H), 5.21 (s, 1 H), 4.38 (d, J = 11.9, 1 H), 4.17 (d, J = 11.6, 1 H), 3.97 (m, 1 H), 3.84 (m, 1 H), 3.18 (s, 1 H), 2.08 (m, 1 H), 1.79-1.60 (m, 6 H), 1.54 (br s, 3 H), 1.31 (app q, J = 11.7, 1 H), 1.09 (s, 3 H), 1.02 (d, J = 6.7 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.3, 117.7, 69.4, 68.5, 67.3, 66.2, 64.5, 40.1, 36.4, 35.5, 34.7, 33.4, 30.7, 16.7, 16.5; mass spectrum (ES, Na) m/z 291.1 [$(M + Na)^+$; calcd for $C_{15}H_{24}O_4$ Na: 291.0].



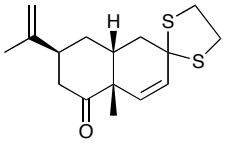
X-Ray Structure of S1



8 **9** **10** **11** **S2**

Enone 11. To a stirred solution of (*S*)-carvone (5.0 g, 33.3 mmol) in anhydrous toluene (100 mL) was added $EtAlCl_2$ (1M in hexanes, 16.7 mL, 16.7 mmol). The mixture was stirred at ambient temperature for 15 min. The reaction was cooled to 0 °C and 2-silyloxy diene (8.7 mL, 50.0 mmol) was added. The resultant reaction mixture was gradually warmed to room temperature, stirred for 4 h, and quenched with saturated sodium bicarbonate (100 mL) at –78 °C. The mixture was stirred until the ice melted and extracted with diethyl ether (3 x 100 mL). The organic extracts were washed with Rochelle's salt (100 mL), saturated $NaHCO_3$ (3 x 100 mL), brine (2 x 100 mL), dried over Na_2SO_4, and concentrated. The crude material was placed on the pump for 12 h and used without further purification.

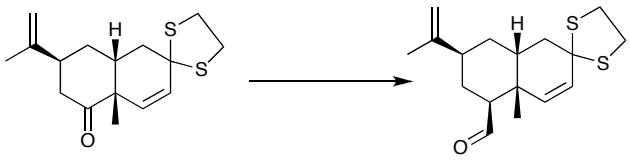
To the above crude silyl enol ether (8.35 g, 28.6 mmol) in anhydrous DMSO (100 mL) was added $Pd(OAc)_2$ (6.4 g, 28.6 mmol) at 0 °C. The reaction was stirred at rt for 4.5 h, then filtered through a pad of Celite and concentrated. Flash chromatography using ethyl acetate-hexanes 20:80 as eluent furnished 4.6 g (64% over 2 steps) of a 19:1 (**12** and **S2**) diastereomeric mixtures of enone (+)-**11** as a clear oil. All characterization data were identical with the reported[1]



12

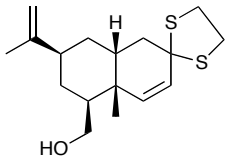
Ketone 12. To a cold solution of enone **11** (4.0 g, 18.4 mmol) in anhydrous MeOH (60 mL) at 0 °C was added ethanedithiol (1.78 mL, 21.1 mmol) followed by $BF_3{\cdot}OEt_2$ (2.54 mL, 20.2 mmol). The resultant mixture was stirred at 0 °C for 30 h, quenched with saturated sodium bicarbonate (20 mL) and extracted with ethyl acetate (3 x 20 mL). The organic extracts were washed with brine, dried over Na_2SO_4, and concentrated. Flash

chromatography using ethyl acetate-hexanes 20:80 as eluent furnished 4.5 g (83%) of thioketal as a white solid. All characterization data were identical with the reported.[1]



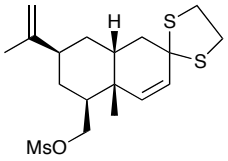
12 **14**

Aldehyde **14**. To a stirred cold (–30 °C) solution of (methoxymethyl)triphenylphosphonium chloride (1.9 g, 5.6 mmol) in anhydrous THF (19 mL) was added KHMDS (0.5 M in toluene, 9.4 mL, 4.7 mmol). The reaction mixture was warmed to 0 °C and stirred for 15 minutes. Then, a solution of ketone **12** (550 mg, 1.87 mmol) in THF (5 mL) was added. The mixture was gradually warmed to room temperature and stirred for 24 h. A THF:MeOH (1:1, 5 mL) solution was added to the reaction mixture at 0 °C followed by the additon of 4N HCl (5 mL). The mixture was gradually warmed to room temperature and stirred for an additional 36 h. Then, water (20 mL) was added and extracted with ether (3 x 20 mL). The organic extracts were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. Flash chromatography using ethyl acetate-hexanes 3:97 as eluent furnished 513.2 mg (89%) of a 13:1 (β/α) mixture of aldehydes. The β-aldehyde (+)-**14** was isolated as a clear oil, which solidified upon standing mp = 77-80 °C; $[\alpha]_D^{26}$ +151.8 (*c* = 0.478, CH_2Cl_2); IR (neat) 2924 (m), 2864 (w), 1717 (s), 1645 (w), 1436 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.81 (d, *J* = 1.0 Hz, 1 H), 5.87 (dd, *J* = 9.8, 1.5 Hz, 1 H), 5.76 (d, *J* = 9.8 Hz, 1 H), 4.74 (s, 2 H), 3.45-3.36 (m, 3 H), 3.28-3.22 (m, 1 H), 2.63 (dd, *J* = 12.9, 3.2 Hz, 1 H), 2.52 (t, *J* = 13.6 Hz, 1 H), 2.11 (dt, *J* = 12.8, 3.1, 1 H), 2.04 (dt, *J* = 13.7, 1.8, 1 H), 1.91-1.87 (m, 1 H), 1.86-1.73 (m, 2 H), 1.69 (s, 3 H), 1.54-1.45 (m, 2 H), 1.09 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.5, 149.0, 135.4, 131.3, 109.2, 65.4, 55.1, 43.8, 41.9, 40.2, 39.8, 38.6, 36.3, 32.7, 26.4, 21.5, 20.8; mass spectrum (ES, Na) *m*/z 331.1 $[(M + Na)]^+$; calcd for $C_{17}H_{24}OS_2Na$: 331.0].



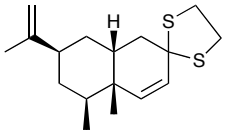
15

Alcohol 15. To a solution of aldehyde **14** (220 mg, 0.713 mmol) in anhydrous MeOH (4 mL) and dry THF (0.8 mL) at 0 °C was added $NaBH_4$ (54 mg, 1.4 mmol) in small portions. The reaction mixture was warmed to rt, stirred for 2.5 h, quenched with saturated ammonium chloride (2 mL) at 0 °C and extracted with ethyl acetate (3 x 3 mL). The combined organic layers were washed with brine (3 mL), dried over sodium sulfate, filtered and concentrated. Flash chromatography using ethyl acetate-hexanes 10:90 as eluent furnished 200 mg (90%) of (+)-**15**; $[\alpha]_D^{23}$ +91.16 (*c* = 0.215, CH_2Cl_2) as a clear oil; IR (neat) 3380 (br), 2921 (s), 2866 (m), 1642 (m), 1434 (m), 1372 (w), 1275 (w), 1220 (w), 1071 (w), 1017 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.76 (dd, *J* = 9.8, 1.3 Hz, 1 H), 5.67 (d, *J* = 9.8 Hz, 1 H), 4.71 (s, 2 H), 3.82 (dd, *J* = 10.5, 4.1 Hz, 1 H), 3.45-3.34 (m, 4 H), 3.28-3.20 (m, 1 H), 2.55 (t, *J* = 13.2 Hz, 1 H), 2.10 (m, 1 H), 1.90 (dt, *J* = 13.7, 2.0 Hz, 1 H), 1.80 (m, 4 H), 1.70 (s, 3 H), 1.50 (d, *J* = 12.4, 1 H), 1.12 (app q, *J* = 12.4, 1 H), 0.98 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.0, 137.2, 130.3, 108.5, 65.9, 64.2, 44.6, 43.9, 42.2, 40.2, 39.7, 39.4, 35.7, 33.3, 30.4, 21.0, 20.9; mass spectrum (ES, Na) *m*/z 332.9 [$(M + Na)^+$; calcd for $C_{17}H_{26}OS_2Na$: 333.1].



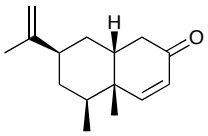
S3

Mesylate **S3**. To a cold (0 °C) mixture of alcohol **15** (200 mg, 0.64 mmol) and triethylamine (0.18 mL, 1.28 mmol) in anhydrous CH_2Cl_2 (4 mL) was added methanesulfonyl chloride (0.09 mL, 1.22 mmol). The resultant mixture was warmed to room temperature, stirred for 1.5 h, and washed with water (5 mL) and brine (5 mL). The organic layer was dried over sodium sulfate, filtered and concentrated. The crude mesylate was used directly into the next reaction without further purification.



S4

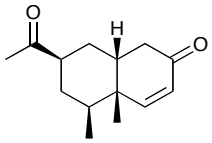
Thioketal S4. To a stirred solution of the above mesylate **S3** (249 mg, 0.64 mmol) in anhydrous THF (3 mL) at 0 °C was added super hydride (1M in THF, 1.4 mL, 1.4 mmol). The reaction mixture was gradually warmed to room temperature and stirred for 24 h, quenched with water (5 mL) and extracted with diethyl ether (3 x 5 mL). The combined organic layers were washed with brine (5 mL), dried over anhydrous sodium sulfate, filtered and concentrated. Flash chromatography using ethyl acetate-hexanes 20:80 as eluent provided 133.7 mg (71% yield over 2 steps) of (+)-**S4** as a white solid, mp 90-92 °C; $[\alpha]_D^{24}$ +91.00 (*c* = 1.0, CH_2Cl_2); IR (neat) 2961 (s), 2921 (s), 2871 (m), 1643 (w), 1457 (m), 1436 (w), 1371 (w), 1275 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.73 (dd, *J* = 9.8, 1.5 Hz, 1 H), 5.63 (d, *J* = 9.8 Hz, 1 H), 4.68 (s, 2 H), 3.42-3.35 (m, 3 H), 3.26-3.22 (m, 1 H), 2.54 (app t, *J* = 13.4 Hz, 1 H), 2.14-2.07 (m, 1 H), 1.96 (dt, *J* = 13.7, 2.0 Hz, 1 H), 1.89-1.85 (m, 1 H), 1.79-1.73 (m, 2 H), 1.71 (s, 3 H), 1.45 (m, 2 H), 1.17 (app q, *J* = 12.6, 1 H), 0.95 (s, 3 H), 0.85 (d, *J* = 6.7, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.3, 138.1, 129.5, 108.2, 66.1, 43.9, 41.7, 40.09, 40.07, 39.7, 36.5, 35.9, 35.8, 33.4, 20.9, 19.8, 16.1; mass spectrum (ES, Na) *m*/z 317.1 [$(M + Na)^+$; calcd for $C_{17}H_{26}S_2Na$: 317.1]



16

***Cis* dimethyl enone 16**. To a solution of thioketal **S4** (530 mg, 1.8 mmol) in MeOH (24 mL), H_2O (3 mL) and CH_2Cl_2 (12 mL) was added tetrahydrofuran (2 mL) was added bis(trifluoroacetoxy)iodobenzene (1.2 g, 2.7 mmol) at room temperature. After 10 minutes, the solution was poured into saturated aqueous sodium bicarbonate (10 mL) and extracted with dietyl ether (3 x 10 mL). The combined organic layers were washed with

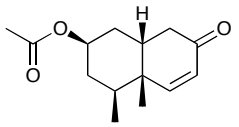
brine (10 mL), dried over anhydrous sodium sulfate, filtered and concentrated. Flash chromatography using ethyl acetate-hexanes 20:80 as eluent provided 340 mg (87%) of (+)-**16** as a clear oil; $[\alpha]_D^{24}$ +53.40 (*c* = 1.0, CH_2Cl_2); IR (neat) 2965 (m), 2925 (m), 2874 (m), 1681 (s), 1644 (w), 1460 (w), 1376 (w), 1258 (w), 1126 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.87 (d, *J* = 10.2, 1 H), 5.90 (d, *J* = 10.2 Hz, 1 H), 4.70 (d, *J* = 2.9 Hz, 2 H), 2.74 (dd, *J* = 17.6, 15.5 Hz, 1 H), 2.19-2.10 (m, 3 H), 1.92-1.88 (m, 1 H), 1.74 (dd, *J* = 13.5, 4.8 Hz, 1 H), 1.70 (s, 3 H), 1.52-1.48 (m, 1 H), 1.43-1.39 (m, 1 H), 1.21 (app q, *J* = 12.9, 1 H), 1.10 (s, 3 H), 0.92 (d, *J* = 6.8, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.3, 160.9, 149.3, 127.2, 108.9, 41.2, 39.5, 39.1, 38.5, 35.2, 35.1, 32.0, 20.9, 19.2, 16.2; mass spectrum (ES, Na) *m*/z 241.1 [$(M + Na)^+$; calcd for $C_{15}H_{22}ONa$: 241.0].



17

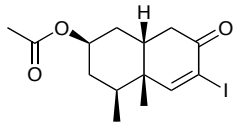
Diketone 17. To a solution of *cis* dimethyl enone **16** (1.3 g, 5.96 mmol) in dioxane (45 mL) and H_2O (18 mL) was added 2,6-lutidine (1.4 mL, 11.92 mmol), $NaIO_4$ (5.1 g, 23.8 mmol) and 4 % aqueous solution of osmium tetroxide (0.7 mL, 0.119 mmol). The mixture was stirred at room temperature for 5 h, quenched with water (20 mL) and extracted with dichloromethane (4 x 10 mL). The combined organic layers were washed with brine (20 mL), dried over anhydrous sodium sulfate, filtered and concentrated. Flash chromatography using ethyl acetate-hexanes 40:60 as eluent furnished 1.11 g (85%) of (+)-**17** as a clear oil, which solidified upon standing, mp 66-67 °C; $[\alpha]_D^{24}$ +42.70 (*c* = 1.0, CH_2Cl_2); IR (neat) 2964 (m), 2935 (m), 2876 (m), 1706 (s), 1682 (s), 1464 (m), 1380 (m), 1355 (m), 1269 (w), 1182 (m), 1126 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.84 (d, *J* = 10.2 Hz, 1 H), 5.92 (d, *J* = 10.2 Hz, 1 H), 2.69-2.59 (m, 2 H), 2.20-2.16 (m, 2 H), 2.13 (s, 3 H), 1.93-1.82 (m, 2 H), 1.67-1.62 (m, 1 H), 1.56-1.51 (m, 1 H), 1.37 (app q, *J* = 12.7 Hz, 1 H), 1.07 (s, 3 H), 0.93 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.9, 199.6, 160.5, 127.3, 45.9, 40.5, 39.1, 38.4, 38.4, 31.7, 28.7, 28.2,

19.0, 16.1; mass spectrum (ES, Na) *m*/z 243.0 [(M + Na)$^+$; calcd for $C_{14}H_{20}O_2Na$: 243.1].



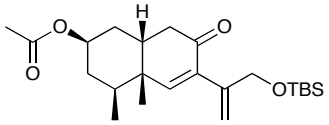
18

Acetate 18. To a solution of diketone **17** (200 mg, 0.909 mmol) in CH_2Cl_2 (5 mL) was added MCPBA (77 % wt, 290 mg, 1.4 mmol) in CH_2Cl_2 (5 mL) at room temperature. The mixture was stirred for 12 h. The reaction was poured into saturated sodium bicarbonate (10 mL) and the aqueous layer was extracted with methylene chloride (3 x 10 mL). The organic extracts were washed with brine (10 mL), dried over Na_2SO_4, and concentrated. Flash chromatography using ethyl acetate-hexanes 40:60 as eluent furnished 96 mg (45%) of (+)-**18,** as a light yellow oil; $[\alpha]_D^{26}$ +52.10 (*c* = 1.0, CH_2Cl_2); IR (neat) 2962 (m), 2877 (m), 1730 (s), 1684 (s), 1676 (s), 1364 (m), 1242 (s), 1027 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.82 (d, *J* = 10.2 Hz, 1 H), 5.93 (d, *J* = 10.2 Hz, 1 H), 4.99-4.91 (m, 1 H), 2.65 (dd, *J* = 16.7, 14.3 Hz, 1H), 2.31-2.20 (m, 2 H), 2.05 (s, 3 H), 2.02-1.96 (m, 1 H), 1.88-1.80 (m, 2 H), 1.73-1.69 (m, 1 H), 1.40 (app q, *J* = 12.4 Hz, 1 H), 1.14 (s, 3 H), 0.96 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.6, 170.8, 160.0, 127.9, 69.6, 41.5, 39.9, 38.5, 35.5, 34.2, 32.7, 21.7, 19.7, 16.6; mass spectrum (ES, Na) *m*/z 259.1 [(M + Na)$^+$; calcd for $C_{14}H_{20}O_3Na$: 258.9].



19

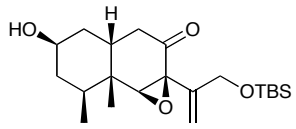
Enone iodide 19. To a cold solution of acetate (+)-**18** (108 mg, 0.457 mmol) in anhydrous methylene chloride (1 mL) at 0 °C was added $TMSN_3$ (0.121 mL, 0.915 mmol). The reaction mixture was stirred under argon at 0 °C for 2 h before the addition of I_2 (231 mg, 0.914 mmol) in methylene chloride (1 mL) and pyridine (0.7 mL). The resultant mixture was gradually warmed to room temperature and stirred for 12 h, diluted with ether (5 mL), washed with H_2O (5 mL), followed by $Na_2S_2O_3$ (5 mL) and brine (5 mL). The organic layer was dried over magnesium sulfate, filtered and concentrated. Flash chromatography using ethyl acetate-hexanes 20:80 as eluent furnished 116.0 mg (71%, 100% BORSM) of (+)-**19**, as a light yellow oil, which solidified upon standing, mp 117-119 °C; $[\alpha]_D^{24}$ +30.80 (c = 1.0, CH_2Cl_2); IR (neat) 2963 (m), 2877 (m), 1732 (s), 1685 (s), 1363 (m), 1244 (s), 1149 (m), 1028 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.62 (s, 1 H), 4.97-4.89 (m, 1 H), 2.82 (dd, J = 16.9, 14.6 Hz, 1H), 2.60 (dd, J = 17.0, 4.3, 1 H), 2.33-2.28 (m, 1 H), 2.08-2.03 (m, 1 H), 2.02 (s, 3 H), 1.88-1.78 (m, 2 H), 1.74-1.69 (m, 1 H), 1.39 (app q, J = 12.6 Hz, 1 H), 1.17 (s, 3 H), 0.99 (d, J = 6.8 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.7, 170.4, 167.7, 102.5, 68.7, 43.2, 41.1, 38.5, 35.0, 33.6, 32.0, 21.3, 19.2, 16.3; mass spectrum (ES, Na) m/z 385.0 [$(M + Na)^+$; calcd for $C_{14}H_{19}O_3INa$: 385.0].



21

Dienone 21. To a mixture of enone iodide **19** (128 mg, 0.354), alkenyl boronate **20**[2] (158 mg, 0.530 mmol), Ag_2O (132 mg, 0.570 mmol), triphenyl arsine (12.2 mg, 0.040 mmol) in THF (4 mL) and H_2O (0.5 mL) was added $Pd(PhCN)_2Cl_2$ at room temperature and stirred for 14 h under nitrogen in the dark. The reaction mixture was quenched with saturated aqueous ammonium chloride (2 mL) and stirred for 30 minutes. The reaction

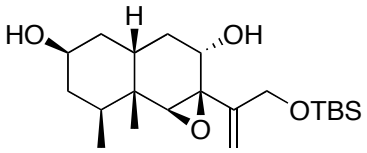
mixture was filtered through a pad of *celite* followed by extraction with ethyl acetate (3 x 5 mL). The organic extracts were washed with brine (5 mL), dried over Na_2SO_4, and concentrated. Flash chromatography using ethyl acetate-hexanes 10:90 as eluent furnished 128 mg (89%) of (+)-**21,** as a light yellow oil; $[\alpha]_D^{24}$ +17.60 (*c* = 1.0, CH_2Cl_2); IR (neat) 2955 (m), 2929 (m), 2856 (m), 1734 (s), 1681 (s), 1362 (m), 1242 (s), 1098 (m), 1028 (m) cm^1; ^1H NMR (400 MHz, $CDCl_3$) δ 6.73 (s, 1 H), 5.24 (s, 1 H), 5.07 (s, 1 H), 4.98-4.90 (m, 1 H), 4.32 (dd, *J* = 13.6, 6.0 Hz, 2H), 2.71 (dd, *J* = 14.5, 2.1, 1 H), 2.28 (dd, *J* = 12.4, 4.3, 1 H), 2.28 (m, 1 H), 2.09 (m, 1 H), 2.02 (s, 3 H), 1.86-1.79 (m, 2 H), 1.78-1.70 (m, 1 H), 1.40 (app q, *J* = 12.5 Hz, 1 H), 1.15 (s, 3 H), 0.97 (d, *J* = 6.8 Hz, 3 H), 0.88 (s, 9 H), 0.04 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.7, 170.4, 156.6, 146.0, 137.4, 114.2, 69.2, 65.1, 40.9, 40.2, 38.3, 35.1, 33.8, 32.1, 25.9, 21.3, 19.6, 18.3, 16.2, –5.37, –5.39; mass spectrum (ES, Na) *m*/z 429.2 [$(M + Na)^+$; calcd for $C_{23}H_{38}O_4SiNa$: 429.0].



22

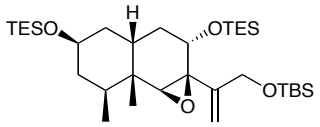
Epoxy ketone 22. To a mixture of dienone **21** (148 mg, 0.485 mmol) in MeOH (9 mL) and hydrogen peroxide (30% in H_2O, 0.458 mL**,** 4.04 mmol) at 0 °C was added sodium hydroxide (10% in H_2O, 193 μL). The reaction mixture was allowed to warm gradually to rt. After 2 d, the reaction was filtered, followed by addition of 4 mL saturated aqueous $NaHCO_3$ and extraction with EtOAc (3 x 3 mL). The organic extracts were washed with brine (3 mL), dried over Na_2SO_4, and concentrated. Flash chromatography using ethyl acetate-hexanes 20:80 as eluent furnished 117.6 mg (85%) of (–)-**22,** as a white solid, mp 80-82 °C; $[\alpha]_D^{24}$ –18.90 (*c* = 1.0, CH_2Cl_2); IR (neat) 3398 (br), 2956 (s), 2930 (s), 2859 (s), 1708 (s), 1465 (m), 1253 (m), 1111 (m), 1078 (s), 838 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.24 (d, *J* = 1.4 Hz, 1 H), 5.16 (d, *J* = 1.0 Hz, s, 1 H), 4.35 (d, *J* = 12.9 Hz, 1 H), 4.26 (d, *J* = 13.6 Hz, 1 H), 3.82-3.74 (m, 1H), 3.22 (s, 1 H), 2.33 (d, *J* = 9.3, 2 H), 2.21-2.15 (m, 1 H), 1.87-1.79 (m, 1 H), 1.78-1.70 (m, 2 H), 1.58 (ddd, *J* = 17.9, 13.4, 4.6

Hz, 2 H), 1.34 (app q, J = 12.5 Hz, 1 H), 1.20 (s, 3 H), 0.99 (d, J = 6.8 Hz, 3 H), 0.88 (s, 9 H), 0.044 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.6, 143.1, 112.4, 71.5, 65.9, 64.1, 63.3, 39.7, 39.4, 35.8, 35.0, 34.8, 31.3, 26.0, 18.6, 17.3, 16.2, –5.38, –5.44; mass spectrum (ES, Na) m/z 403.2 [$(M + Na)^+$; calcd for $C_{21}H_{36}O_4SiNa$: 403.2].



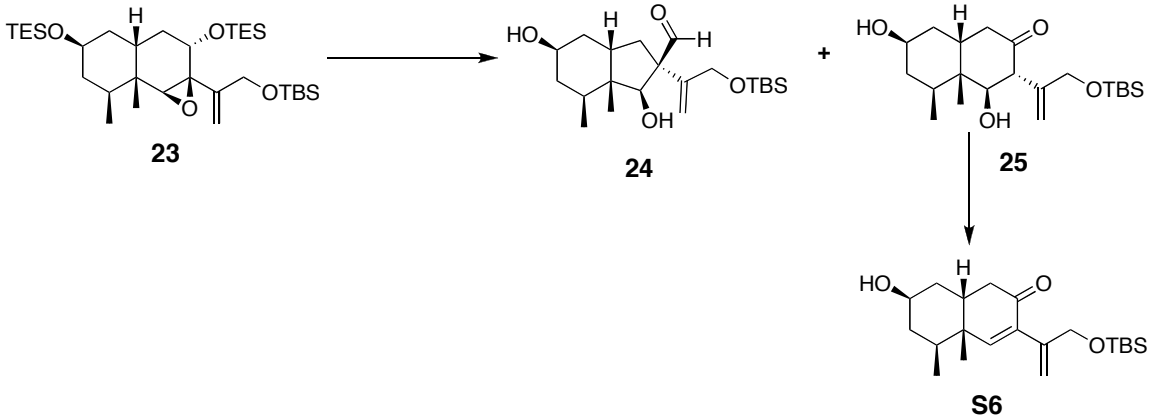
S5

Epoxy diol S5. To a cold solution of epoxy ketone **22** (72.4 mg, 0.190 mmol) in MeOH (3 mL) and THF (0.6 mL) 0 °C was added $NaBH_4$ (18 mg, 0.476 mmol) in small portions. The reaction mixture was stirred for 45 min, quenched with saturated ammonium chloride (1 mL) at 0 °C and extracted with ethyl acetate (3 x 2 mL). The combined organic layers were washed with brine (2 mL), dried over sodium sulfate, filtered and concentrated. Flash chromatography using ethyl acetate-hexanes 10:90 as eluent furnished 66.0 mg (91%) of of a 7:1 mixture of diastereomers of (+)-**S5,** as a clear oil; $[\alpha]_D^{25}$ +34.52 (c = 0.42, CH_2Cl_2); IR (neat) 3045 (br), 2930 (s), 2858 (s), 1466 (m), 1364 (w), 1256 (m), 1064 (m), 1075 (m), 838 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.29 (s, 1 H), 5.14 (s, 1 H), 4.34 (d, J = 10.7 Hz, 1H), 4.07 (d, J = 10.7 Hz, 1 H), 3.91-3.80 (m, 3 H), 3.19 (s, 1 H), 2.10-2.04 (m, 1 H), 1.78-1.75 (m, 6 H), 1.63 (app q, J = 12.6 Hz, 1 H), 1.42 (br s, 1 H), 1.08 (s, 3 H), 1.01 (d, J = 6.8 Hz, 3 H), 0.93 (s, 9 H), 0.14 (d, J = 1.3, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.6, 119.0, 69.9, 68.1, 67.8, 66.2, 65.0, 40.2, 36.4, 35.5, 34.7, 33.0, 30.8, 25.8, 18.2, 16.7, 16.6, –5.50, –5.60; mass spectrum (ES, Na) m/z 405.3 [$(M + Na)^+$; calcd for $C_{21}H_{38}O_4SiNa$: 405.2].



23

Epoxide 23. To a solution of epoxy diol **S5** (105 mg, 0.275 mmol) in anhydrous DMF (10 mL) was added imidazole (112 mg, 1.65 mmol) at 0 °C, followed by chlorotriethylsilane (0.138 mL, 0.824 mmol). The resultant mixture was gradually warmed to room temperature and stirred for 12 h. The mixture was quenched with H_2O (5 mL) and extracted with ethyl acetate (3 x 5 mL). The organic extracts were washed with brine (5 mL), dried over Na_2SO_4, and concentrated. Flash chromatography using ethyl acetate-hexanes 10:90 as eluent furnished 155 mg (93%) of (+)-**23**, as a clear oil; $[\alpha]_D^{25}$ +45.26 (*c* = 0.19, CH_2Cl_2); IR (neat) 2954 (s), 2933 (s), 2876 (s), 1462 (m), 1415 (w), 1378 (w), 1253 (m), 1101 (s), 1061 (m), 1006 (m), 835 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.30 (s, 1 H), 5.24 (s, 1 H), 5.13 (s, 1 H), 4.38 (d, *J* = 14.2 Hz, 1H), 4.16 (d, *J* = 14.0 Hz, 1 H), 3.91 (m, 1 H), 3.79 (m, 1 H), 2.97 (s, 1 H), 2.01 (m, 1 H), 1.68-1.60 (m, 4 H), 1.45 (dd, *J* = 6.71, 4.9 Hz, 1 H), 1.34 (app q, *J* = 12.4, 1 H), 1.04 (s, 3 H), 0.98-0.91 (m, 30 H), 0.61-0.55 (m, 12 H), 0.06 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.0, 110.4, 70.4, 69.1, 66.7, 66.2, 64.1, 40.6, 37.1, 36.0, 35.2, 34.9, 30.9, 25.9, 18.4, 16.9, 16.7, 6.9, 6.8, 4.92, 4.86, –5.4 (2 C); mass spectrum (ES, Na) *m*/z 633.3 [$(M + Na)^+$; calcd for $C_{33}H_{66}O_4Si_3Na$: 633.3].



Aldehyde 24. To a solution of epoxide **23** (62.5 mg, 0.102 mmol) in anhydrous CH_2Cl_2 (5 mL) at –78 °C was added $TiCl_4$ (1M in CH_2Cl_2, 0.123 mL, 0.123 mmol). The

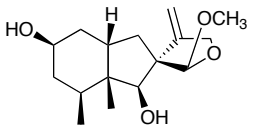
resultant mixture was stirred for 10 minutes, quenched with saturated sodium bicarbonate (1 mL), and extracted with CH_2Cl_2 (3 x 3 mL). The organic extracts were dried over Na_2SO_4, concentrated and the crude was used directly into the next reaction. For characterization purposes, the crude was purified via flash chromatography using ethyl acetate-hexanes 40:60 as eluant and furnished 19.5 mg (50% combined yield) of a 10:1 mixture of unstable aldehyde **24** and ketone **25.** The unstable ketone dehydrates to dienone **S6**.

Aldehyde **24** was isolated as a clear oil; IR (neat) 3382 (br), 2928 (s), 2856 (s), 2615 (w), 1715 (s), 1450 (m), 1254 (m), 1099 (s), 835 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.36 (s, 1 H), 5.35 (s, 1 H), 5.15 (s, 1 H), 4.27 (d, J = 13.2 Hz, 1H), 4.19 (d, J = 13.4 Hz, 1 H), 3.96 (s, 1 H), 3.83 (m, 1 H), 2.00-1.86 (m, 3 H), 1.69 (m, 2 H), 1.52 (ddd, J = 17.1, 11.6, 5.5 Hz, 2 H), 1.39 (m, 2 H), 1.22 (app q, J = 12.5, 2 H), 0.93 (s, 3 H), 0.88 (s, 9 H), 0.86 (d, J = 6.8 Hz, 3 H), 0.06 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.5, 146.6, 113.7, 86.0, 67.1, 64.9, 64.0, 45.4, 43.7, 40.1, 35.9, 34.1, 32.2, 25.9, 18.3, 15.9, 13.9, –5.4 (2 C); mass spectrum (ES, Na) m/z 405.25 [$(M + Na)^+$; calcd for $C_{21}H_{31}O_4SiNa$: 405.3].

Ketone **25** was isolated as a clear oil ^1H NMR (500 MHz, $CDCl_3$) δ 5.41 (s, 1 H), 5.05 (s, 1 H), 4.16 (d, J = 11.5, 1 H), 4.12 (d, J = 11.6 Hz, 1H), 4.00 (d, J = 11.2 Hz, 1 H), 3.98 (m, 1 H), 3.42 (d, J = 11.0, 1 H), 2.57 (dd, J = 15.5, 4.2, 1 H), 2.34 (m, 1 H), 2.25 (dd, J = 15.5, 7.3, 1 H), 2.07 (m, 1 H), 1.89 (dt, J = 10.7, 3.9 Hz, 1 H), 1.70-1.64 (m, 5 H), 1.18 (d, J = 5.6, 3 H), 1.17 (s, 3 H), 0.89 (s, 9 H), 0.093 (d, J = 5.3, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.2, 157.2, 142.3, 120.8, 114.1, 72.7, 67.0, 66.0, 60.4, 43.2, 39.5, 37.0, 34.3, 33.8, 25.8, 18.2, 16.3, –5.4 (2C); mass spectrum (ES, Na) m/z 405.25 [$(M + Na)^+$; calcd for $C_{21}H_{31}O_4SiNa$: 405.2].

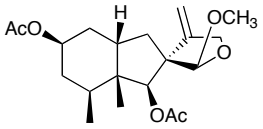
Dienone (+)-**S6** was isolated as a clear oil; $[\alpha]_D^{25}$ +13.43 (c = 0.73, CH_2Cl_2); IR (neat) 3420 (br), 2956 (s), 2929 (s), 2857 (s), 1676 (s), 1471 (m), 1362 (m), 1252 (m), 1083 (m), 836 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.75 (s, 1 H), 5.25 (s, 1 H), 5.07 (s, 1 H), 4.32 (d, J = 13.7 Hz, 1H), 4.28 (d, J = 13.8 Hz, 1 H), 3.90 (m, 1 H), 2.71 (app t, J = 14.8, 1 H), 2.25 (m, 2 H), 1.98 (m, 1 H), 1.78 (m, 3 H), 1.36 (br s, 1 H), 1.33 (app q, J = 12.4 Hz, 1 H), 1.14 (s, 3 H), 0.98 (d, J = 6.8, 3 H), 0.88 (s, 9 H), 0.041 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.0, 157.2, 146.1, 137.3, 114.1, 66.4, 65.1, 41.4, 40.5, 39.3,

38.3, 36.0, 33.9, 25.9, 19.5, 18.3, 16.3, –5.4 (2C); mass spectrum (ES, Na) *m*/z 387.2 [(M + Na)$^+$; calcd for $C_{21}H_{36}O_3Si_3Na$: 387.1].



1

(–)-Peribysin E 1. To a solution of crude aldehyde **xx** (20 mg, 0.052 mmol) in MeOH (2 mL) at 0 °C was added HCl (5 μL). The resultant mixture was stirred for 1 h, quenched with saturated sodium bicarbonate (1 mL) and extracted with ethyl acetate (3 x 2 mL). The organic extracts were washed with brine (5 mL), dried over Na_2SO_4, and concentrated. Flash chromatography using ethyl acetate-hexanes 40:60 as eluent furnished 11.7 mg (80%) of (–)-**1,** as a clear oil, whose spectroscopic data are identical to the natural product reported by Yamada and coworkers. However, there is a large discrepancy in the optical rotation; $[\alpha]_D^{25}$ –52.17 (*c* = 0.11, EtOH).



S7

Bis acetate peribysin E S7. To a solution of peribysin E (3.5 mg, 0.012 mmol) in freshly distilled pyridine (2 mL) was added acetic anhydride (2 mL). The resultant mixture was stirred for 12 h at ambient temperature and concentrated. Flash chromatography using ethyl acetate-hexanes 40:60 as eluant furnished 3.5 mg (78%) of (–)-**S7,** as a light yellow oil, which is spectroscopically identical with the bis-acetylated natural peribysin E. However, the optical rotation is the opposite of what is reported; $[\alpha]_D^{25}$ –34.783 (*c* = 0.069, EtOH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 169.8, 152.0, 105.0, 103.5, 85.7, 69.6, 68.9, 59.3, 54.8, 45.9, 45.5, 35.8, 33.8, 33.1, 29.7, 21.4, 21.0,

16.2, 14.4,; mass spectrum (ES, Na) *m*/z 389.2 [(M + Na)$^+$; calcd for $C_{20}H_{30}O_6$ Na: 389.2].

Biological Evaluation:

Material and Methods

Cell culture

Human umbilical vein endothelial cells (HUVEC) (a generous gift of Professor Shahin Rafii) were isolated from umbilical cord veins with collagenase and were cultured in M199 medium containing 10% (vol/vol) fetal calf serum (FCS), 20 μg/ml endothelial cell growth factor, 50 μg/ml heparin, 100 μg/ml penicillin, and 100 μg/ml streptomycin in a humidified incubator at 37°C with air/5% CO_2 as previousely described.[3] HUVEC monolayers from passages 4–5 were used in all studies. The acute myeloid leukemia cell line HL60 (ATCC) was cultured in RPMI 1640 medium with 10% FCS.

Adhesion of leukemia cells to HUVEC

Adhesion assays of the leukemic cell line HL60 to HUVEC were performed as previously described.[4] HUVEC were cultured until confluent in collagen coated 96-well plates (0.1mg/ml, (Cellmatrix Type I-C, Nitta Gelatin, Osaka) for 1h at 37°C). Adhered HUVEC were subsequently washed with PBS containing 20% FCS and stimulated with LPS in RPMI 1640 medium containing 10% FCS for 4h in the presence and absence of various concentrations of the enantiomers of Peribysin E. After 4h of drug treatment HL60 cells were added (2x10e5 cells/well) for 40 min at 37°C with air/5% CO2. Unbound cells were gently washed away by 3 consecutive washes with PBS with 10% FCS. Wells were photographed and individually evaluated for HL60 stromal adhesion.

[1] T. Harayama, H. Cho, Y. Inubushi, *Chem. Pharm. Bull*. **1978**, *26*, 1201-1214.

[2] K. Takahashi, T. Ishiyama, N. Miyaura, *J. Organomet. Chem*. **2001**, *625,* 47-53.

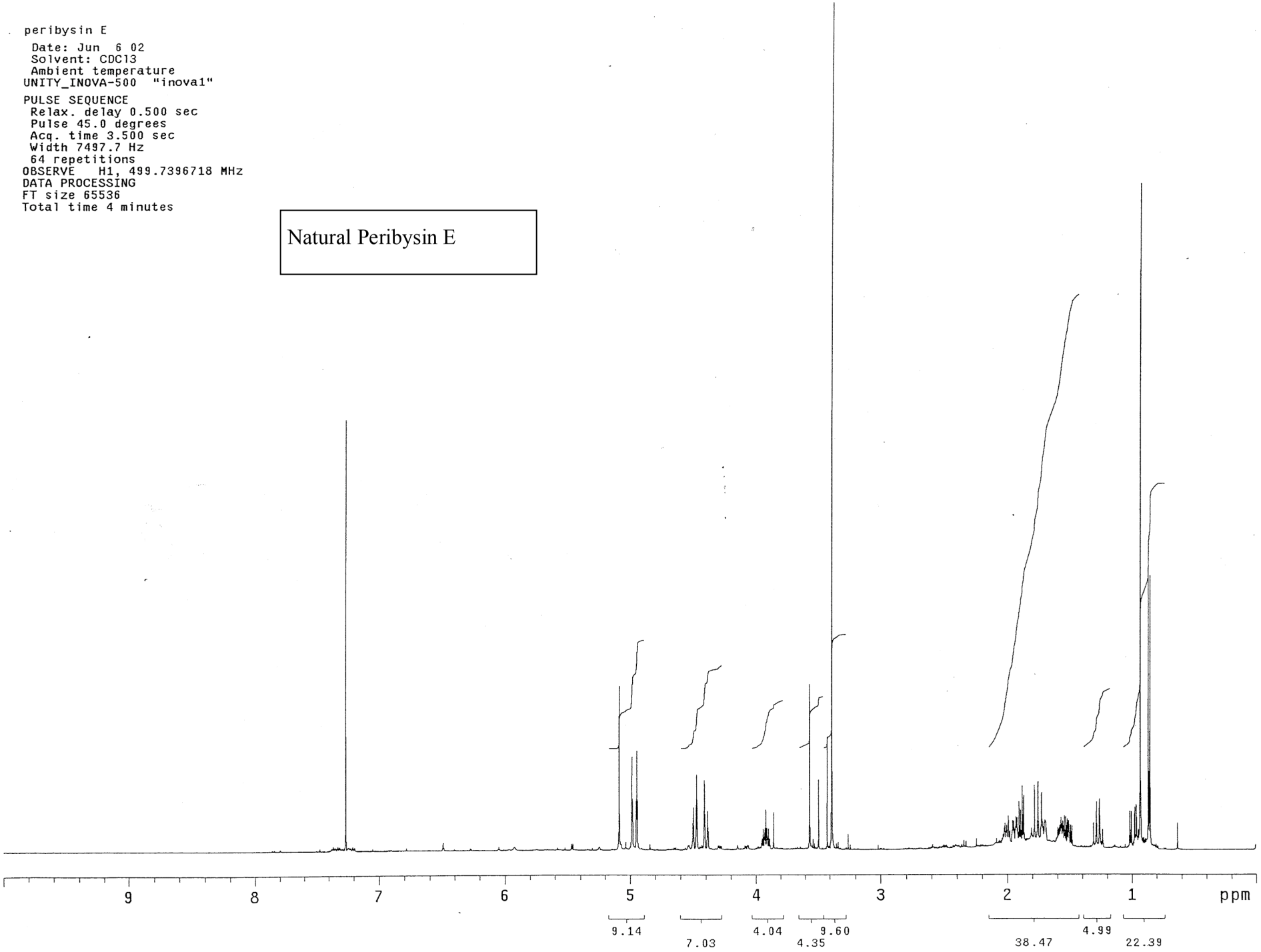
[3] L. Vincent, P. Kermani, L. M. Young, J. Cheng, F. Zhang, K. Shido, G. Lam, H. Bompais-Vincent, Z. Zhu, D. J. Hicklin, P. Bohlen, D. J. Chaplin, C. May, and S. Rafii, *J Clin Invest*. **2005**, *115*, 2992–3006.

[4] T. Yamada, M. Doi, A. Miura, W. Harada, Hiramura M, K. Minoura, R. Tanaka, A. Numata, *J Antibiot.* **2005**, *58*, 185-191.

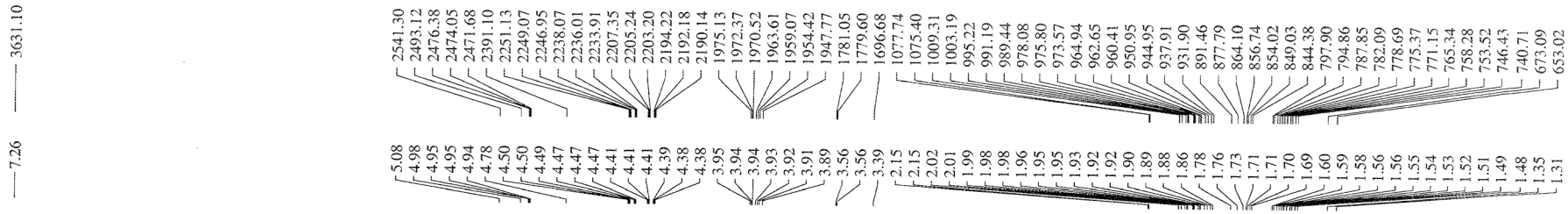
^{1}H and ^{13}C Spectra

peribysin E
Date: Jun 6 02
Solvent: CDCl3
Ambient temperature
UNITY_INOVA-500 "inova1"
PULSE SEQUENCE
Relax. delay 0.500 sec
Pulse 45.0 degrees
Acq. time 3.500 sec
Width 7497.7 Hz
64 repetitions
OBSERVE H1, 499.7396718 MHz
DATA PROCESSING
FT size 65536
Total time 4 minutes

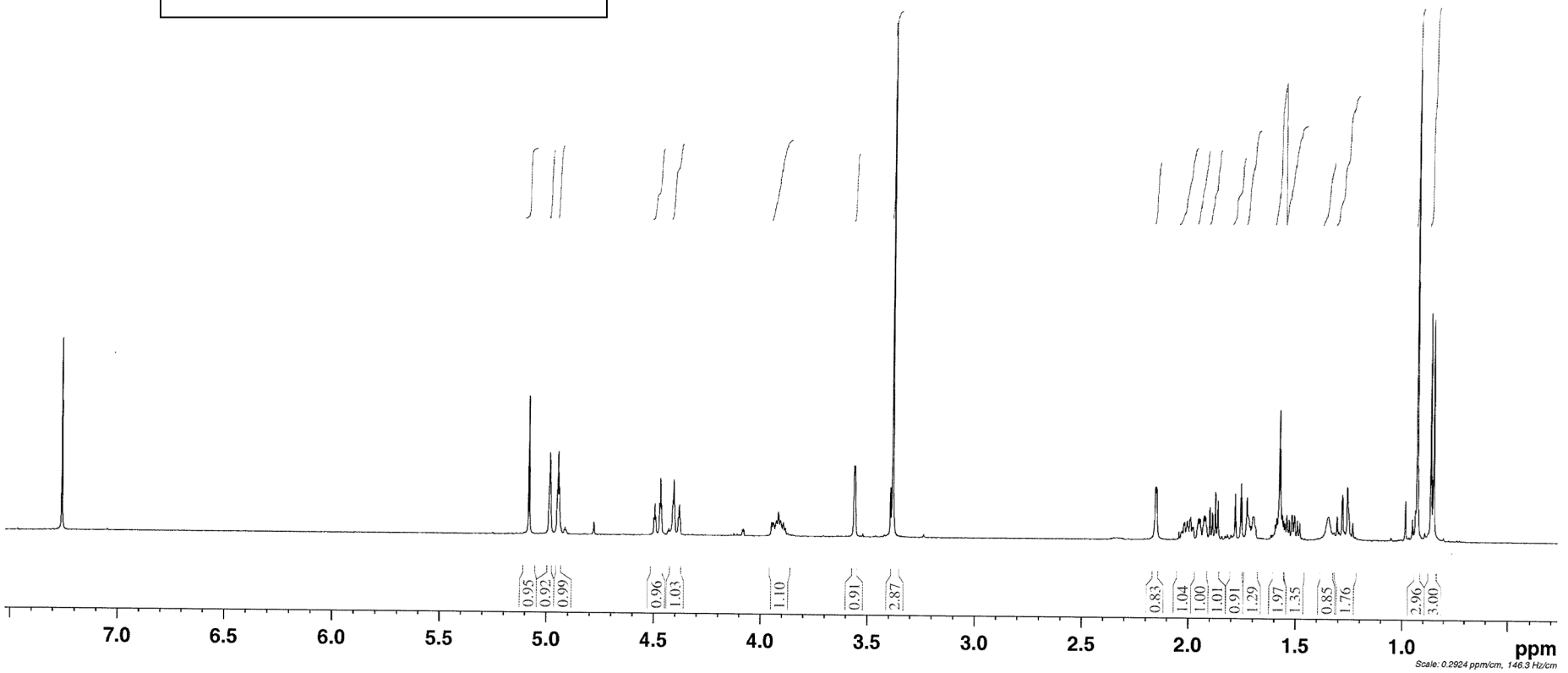
Natural Peribysin E



Proton24 .* angelesa aa2peribysinE (1 1) CDCl3 24.0C August_30,2006_11:35 DRX 500MHz zg30 1H *.

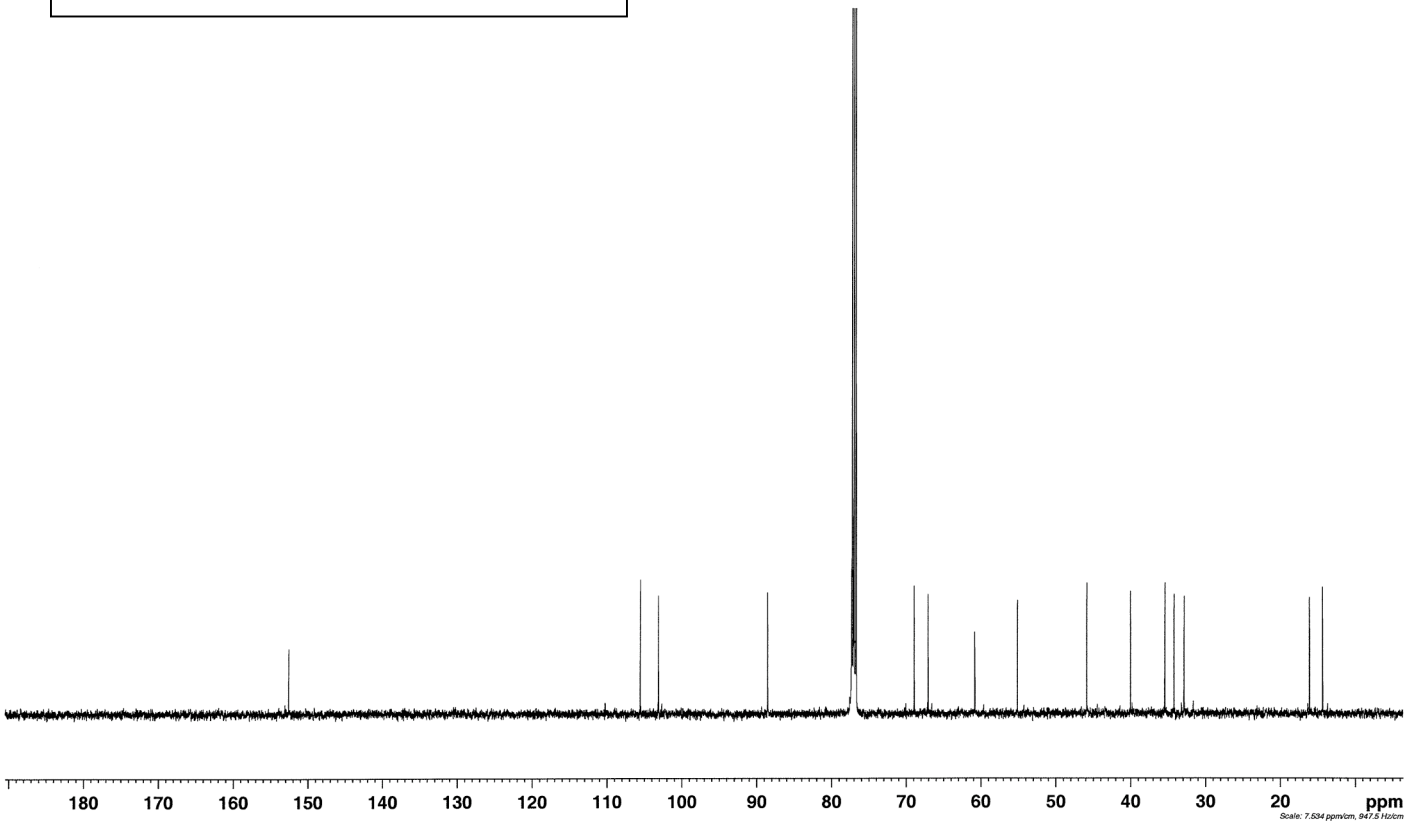


Synthetic Peribysin E



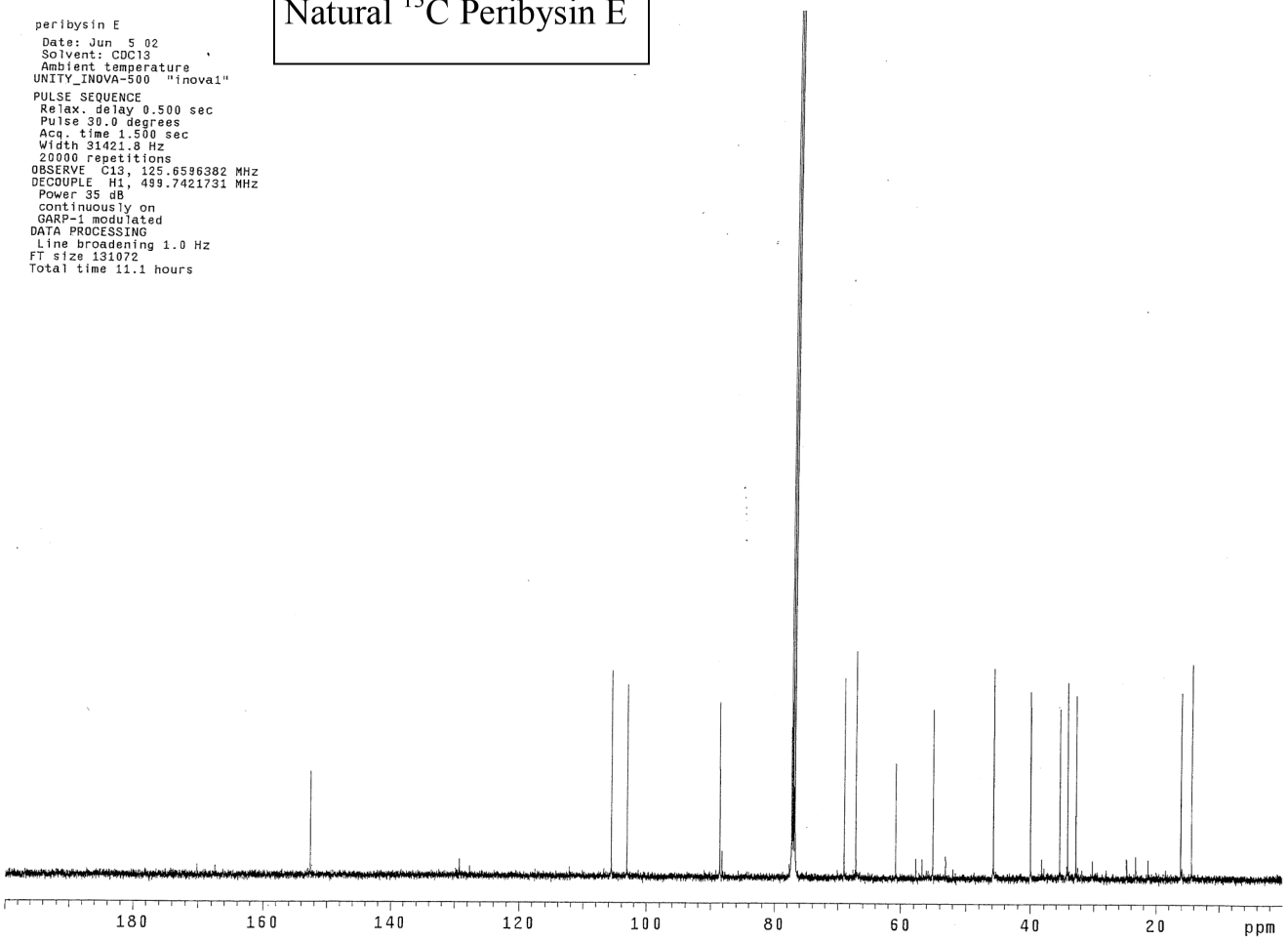
Carbon .* angelesa aa2peribysinc13 (1 1) CDCl3 24.0C August_30,2006_11:38 DRX 500MHz zgpg30 13C; 1H O2=4.000 *.

Synthetic ^{13}C Peribysin E

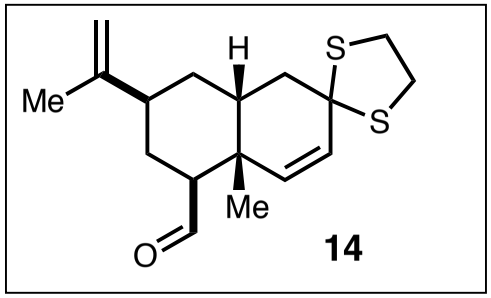


Natural ^{13}C Peribysin E

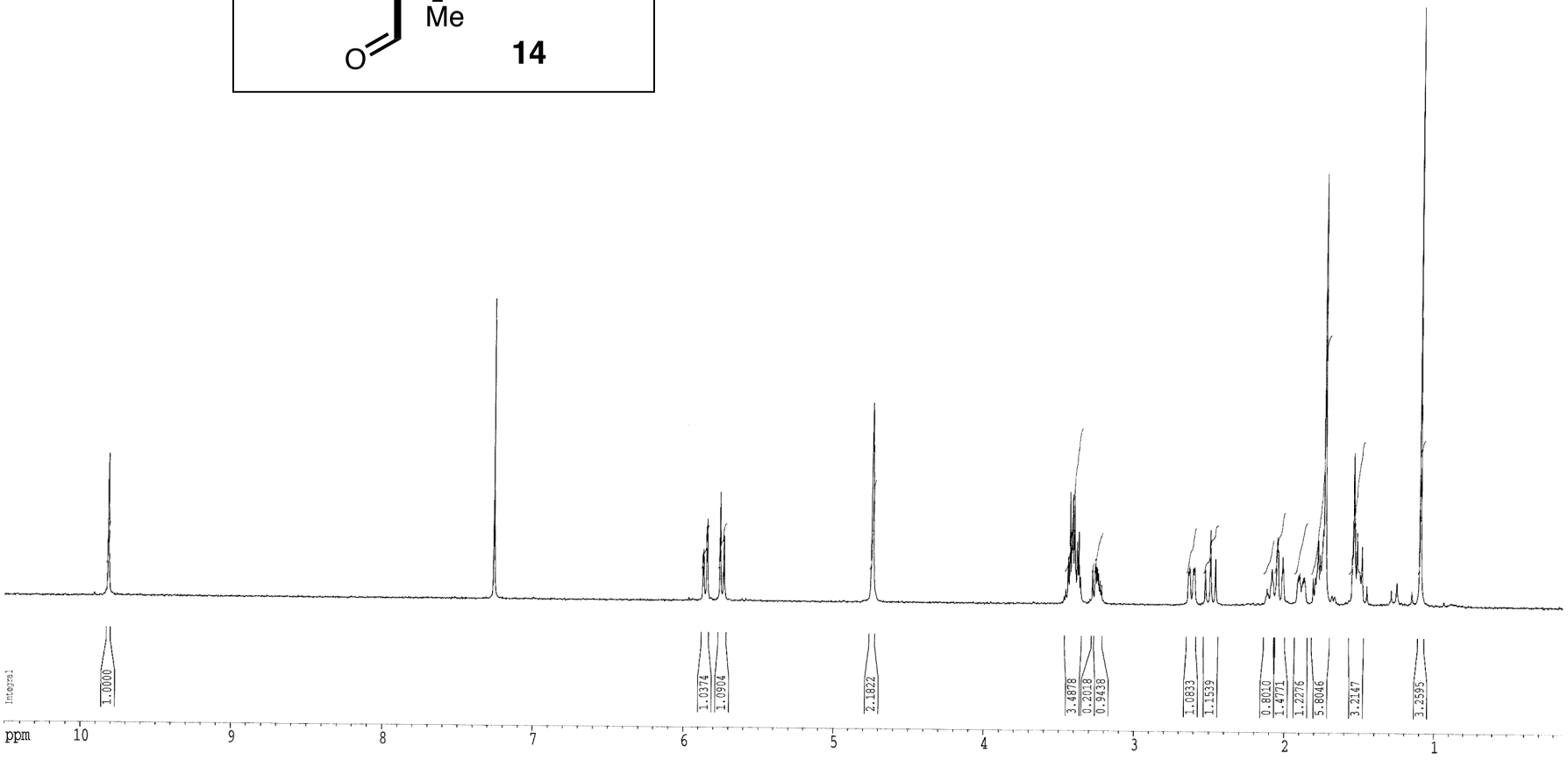
peribysin E
Date: Jun 5 02
Solvent: CDCl3
Ambient temperature
UNITY_INOVA-500 "inova1"
PULSE SEQUENCE
Relax. delay 0.500 sec
Pulse 30.0 degrees
Acq. time 1.500 sec
Width 31421.8 Hz
20000 repetitions
OBSERVE C13, 125.6596382 MHz
DECOUPLE H1, 499.7421731 MHz
Power 35 dB
continuously on
GARP-1 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 11.1 hours



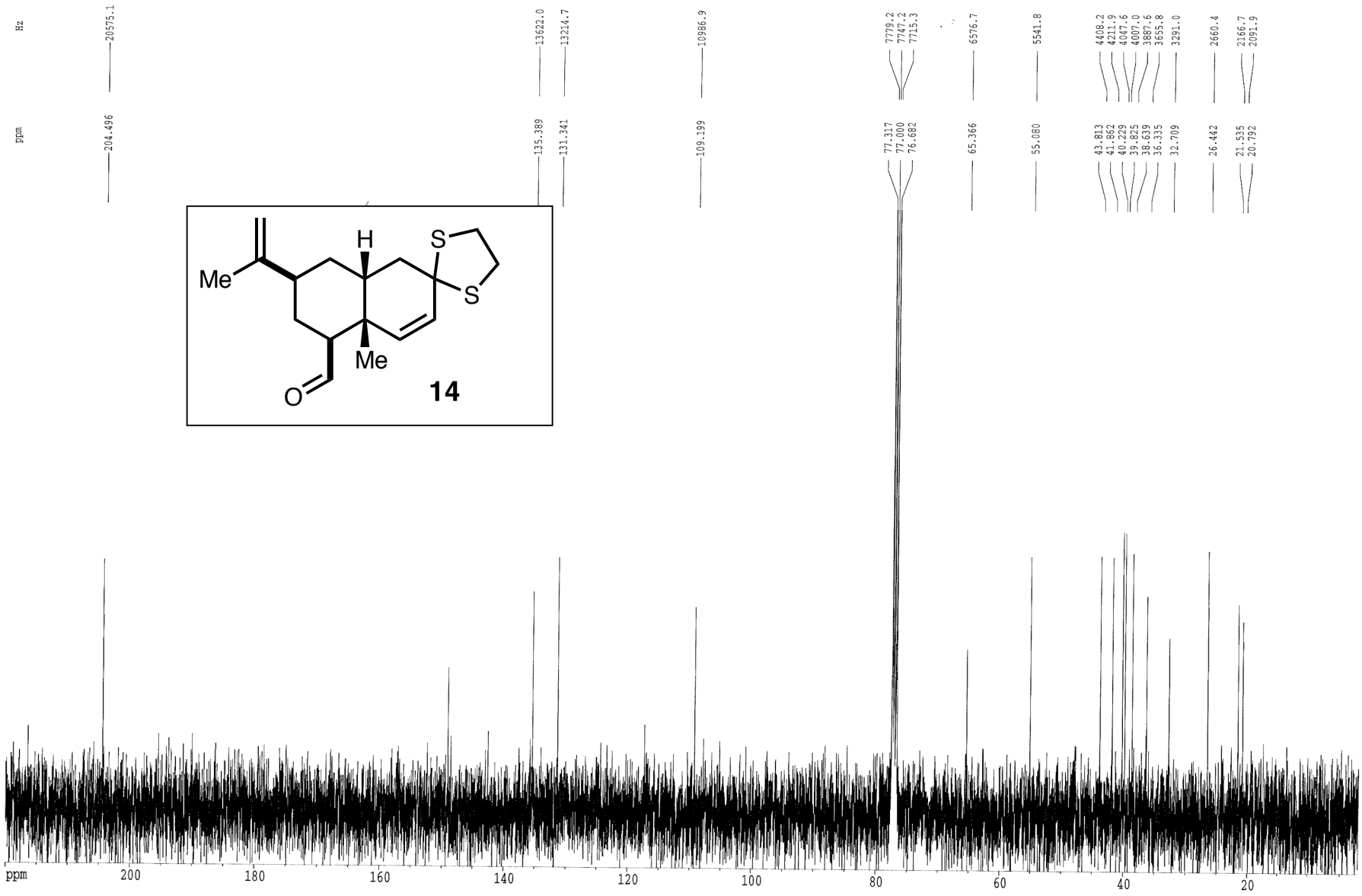
Proton .* angelesa aa1073ag (1 1) CDCl3 25.0C March_24,2006_10:53 AMX 400MHz zg30 1H *.



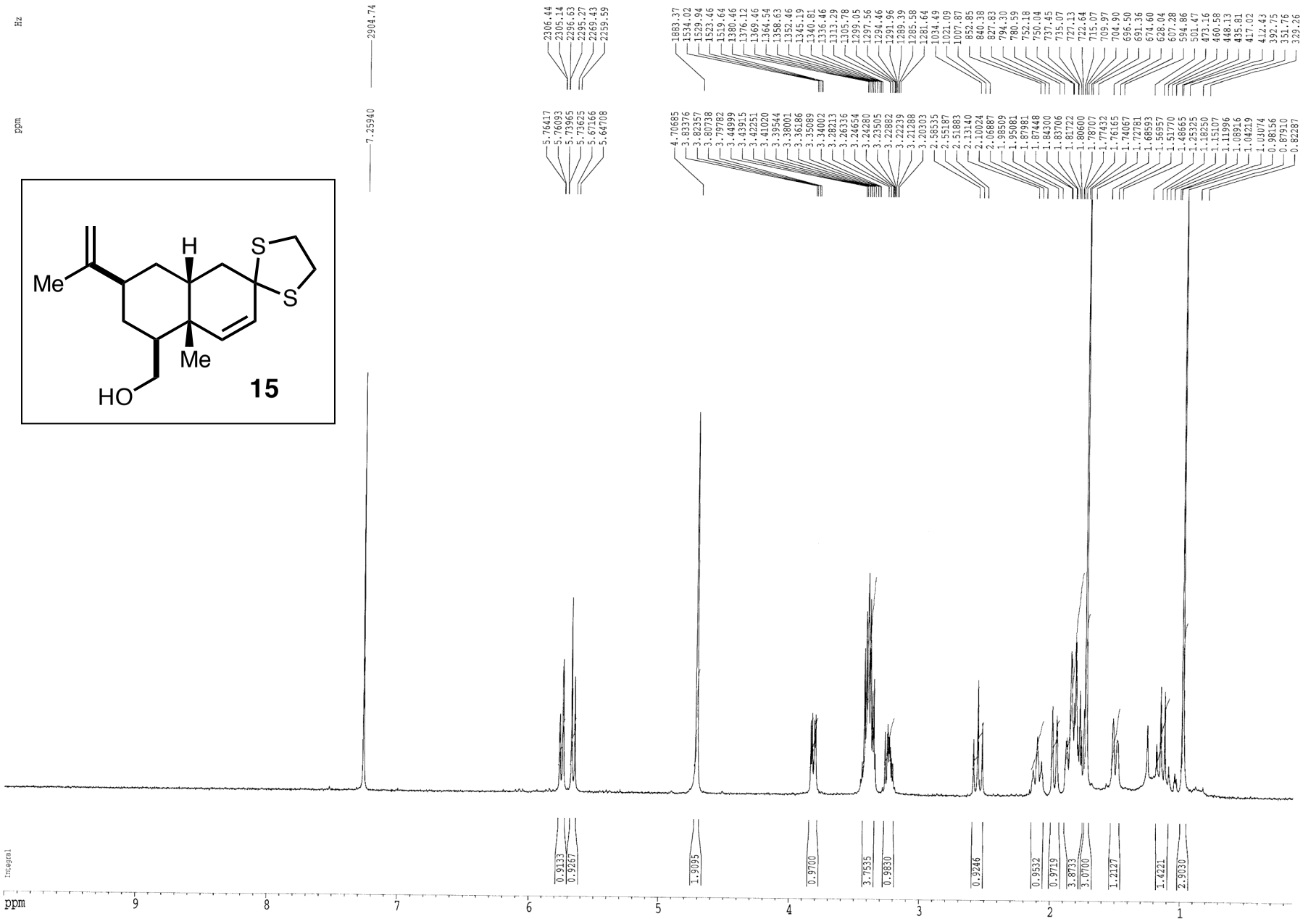
14



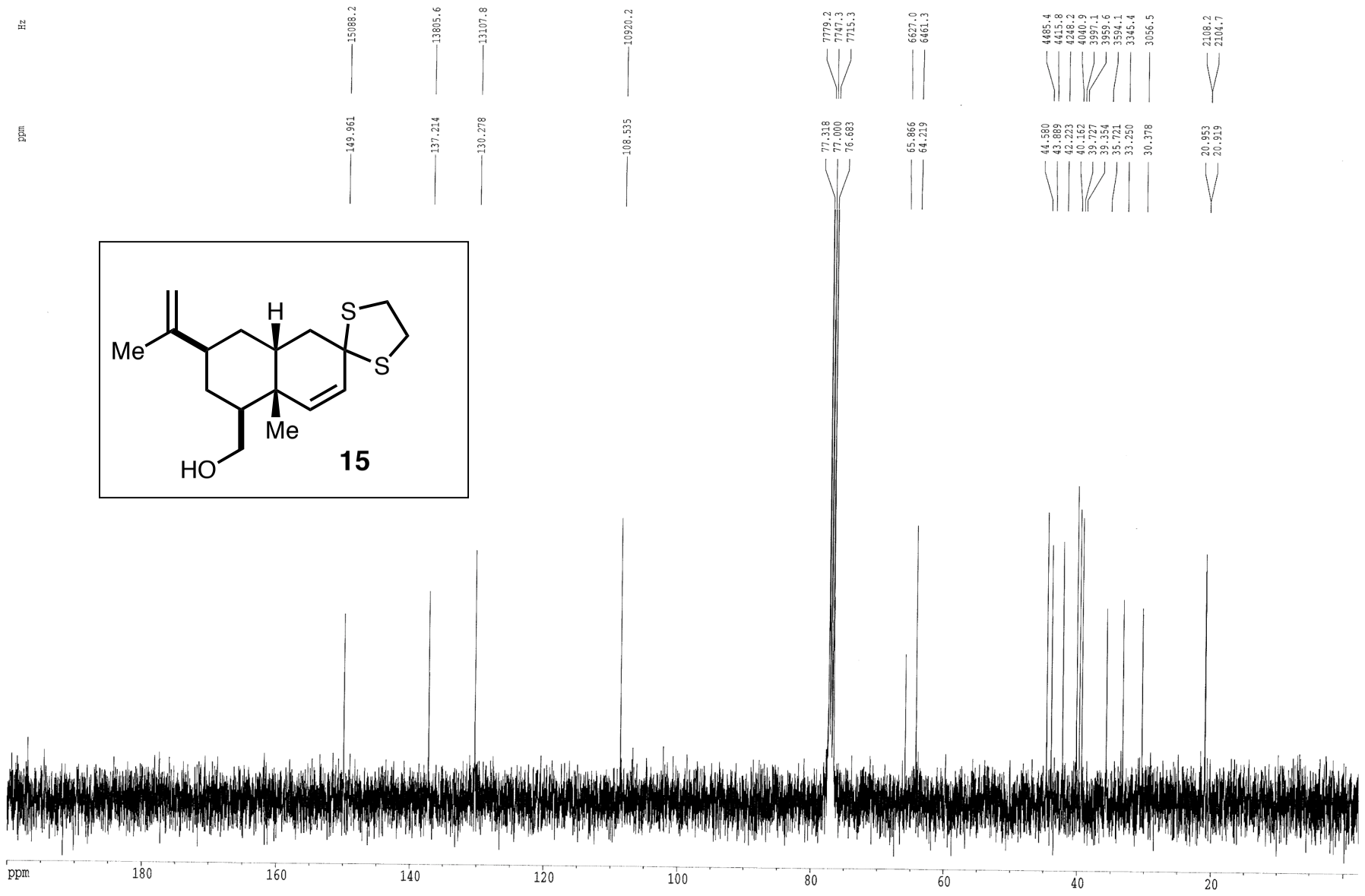
Carbon .* angelesa aa1073carbon (1 1) CDCl3 25.0C March_24,2006_10:55 AMX 400MHz zgpg30 13C; 1H O2=7020.000 *.



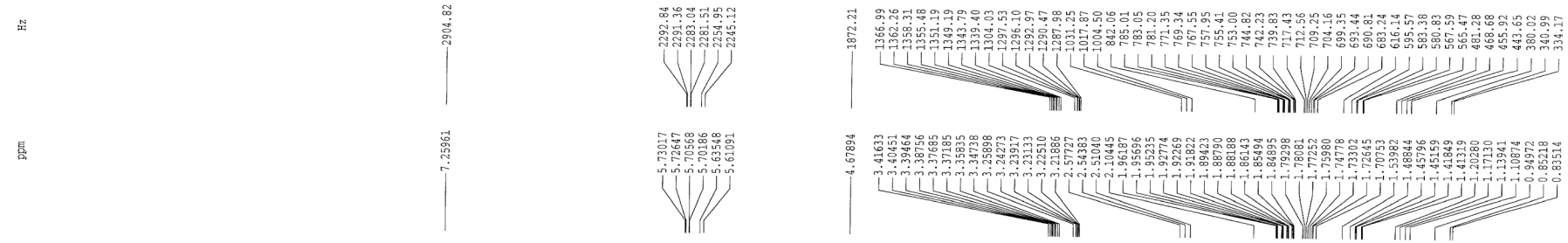
Proton .* angelesa aa10hb (1 1) CDCl3 25.0C March_28,2006_13:48 AMX 400MHz zg30 1H *.

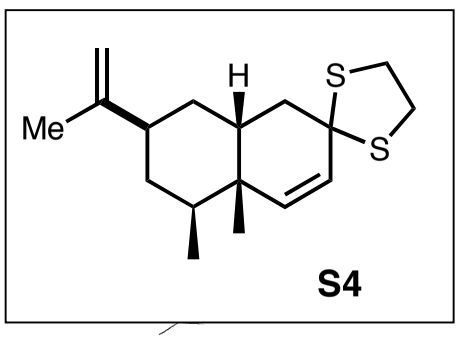


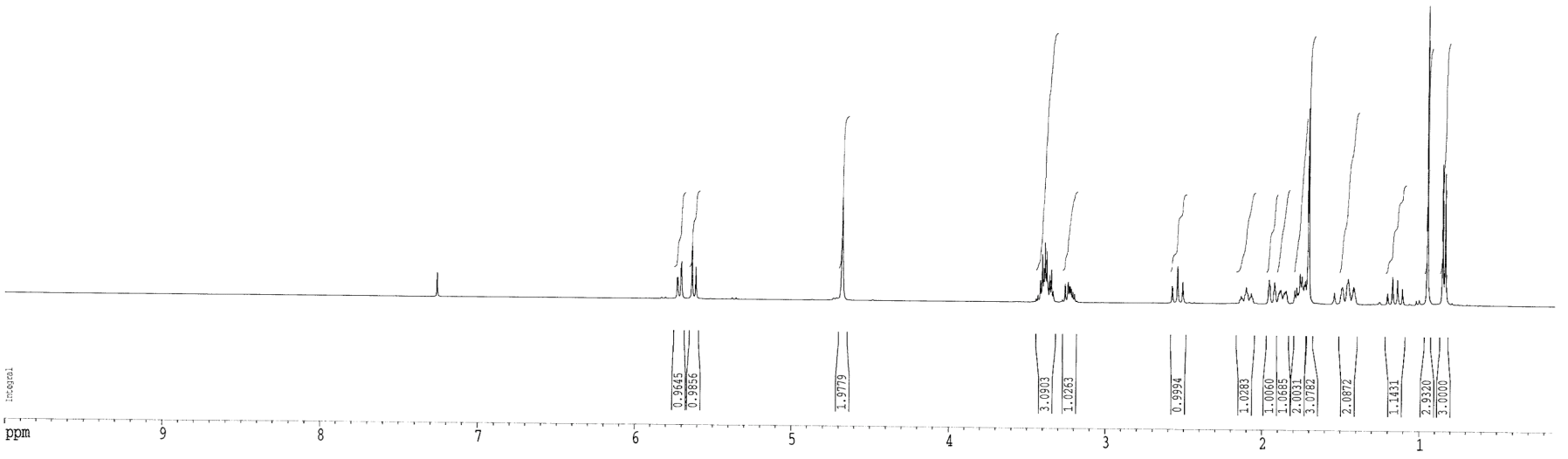
Carbon .* angelesa aa1ohbcarbon (1 1) CDCl3 25.0C March_28,2006_13:51 AMX 400MHz zgpg30 13C; 1H O2=7020.000 *.



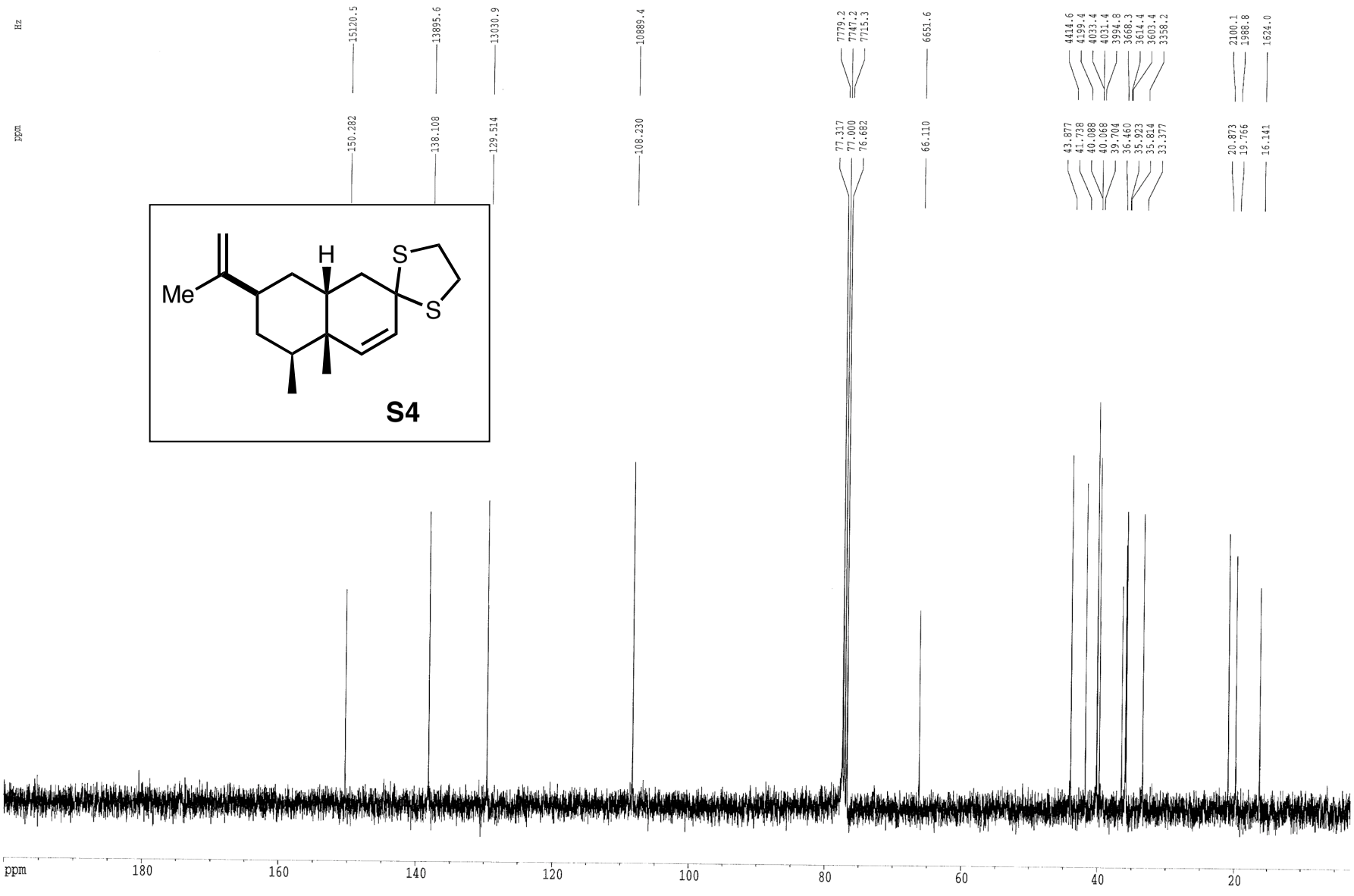
Proton .* angelesa aa1224proton (1 1) CDCl3 25.0C March_31,2006_12:30 AMX 400MHz zg30 1H *.



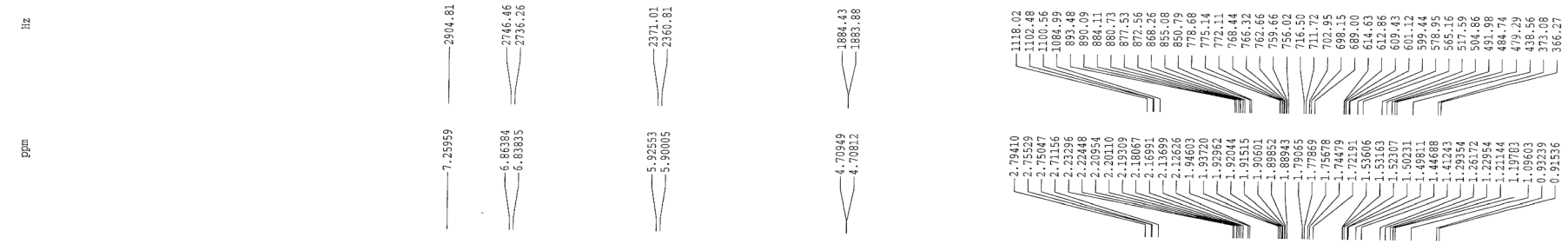


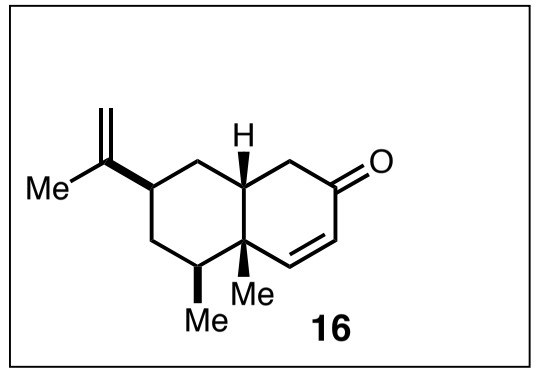


Carbon .* angelesa aa1224carbon (1 1) CDCl3 25.0C March_31,2006_12:32 AMX 400MHz zgpg30 13C; 1H O2=7020.000 *.



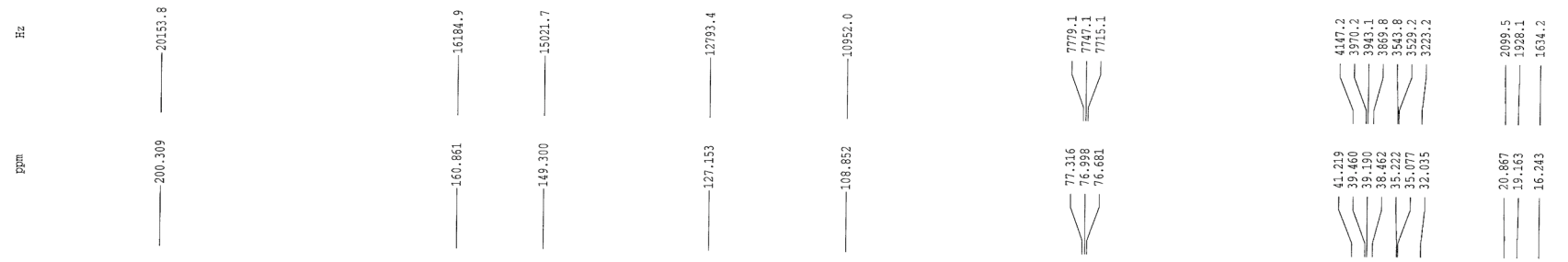
Proton .* angelesa aa1185final (1 1) CDCl3 25.0C March_23,2006_14:39 AMX 400MHz zg30 1H *.

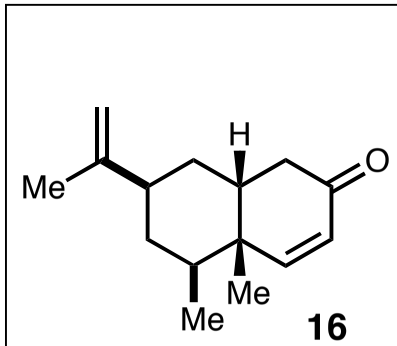




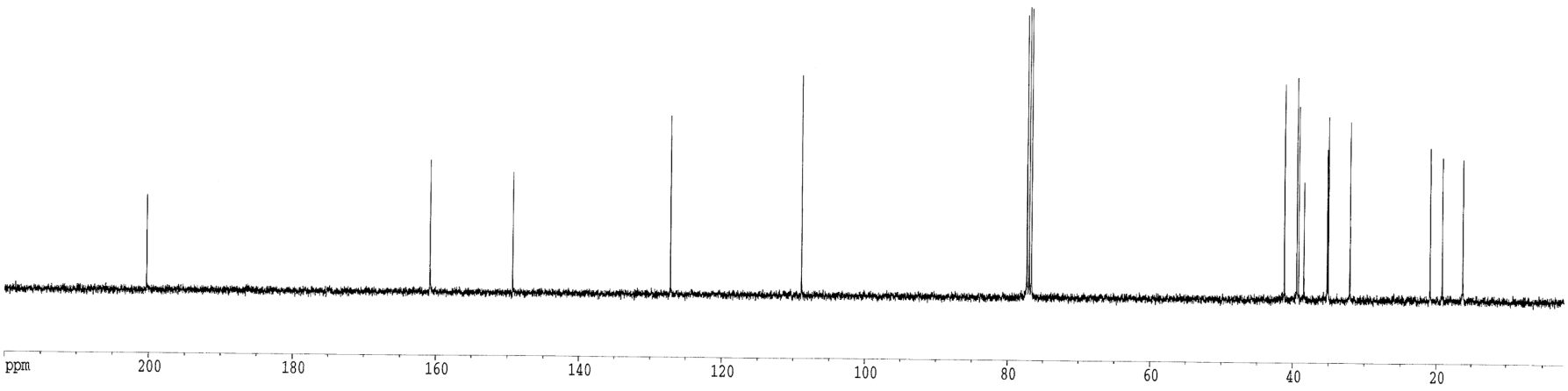
16

Carbon .* angelesa aa1185carbon (1 1) CDCl3 25.0C March_23,2006_14:41 AMX 400MHz zgpg30 13C; 1H O2=7020.000 *.

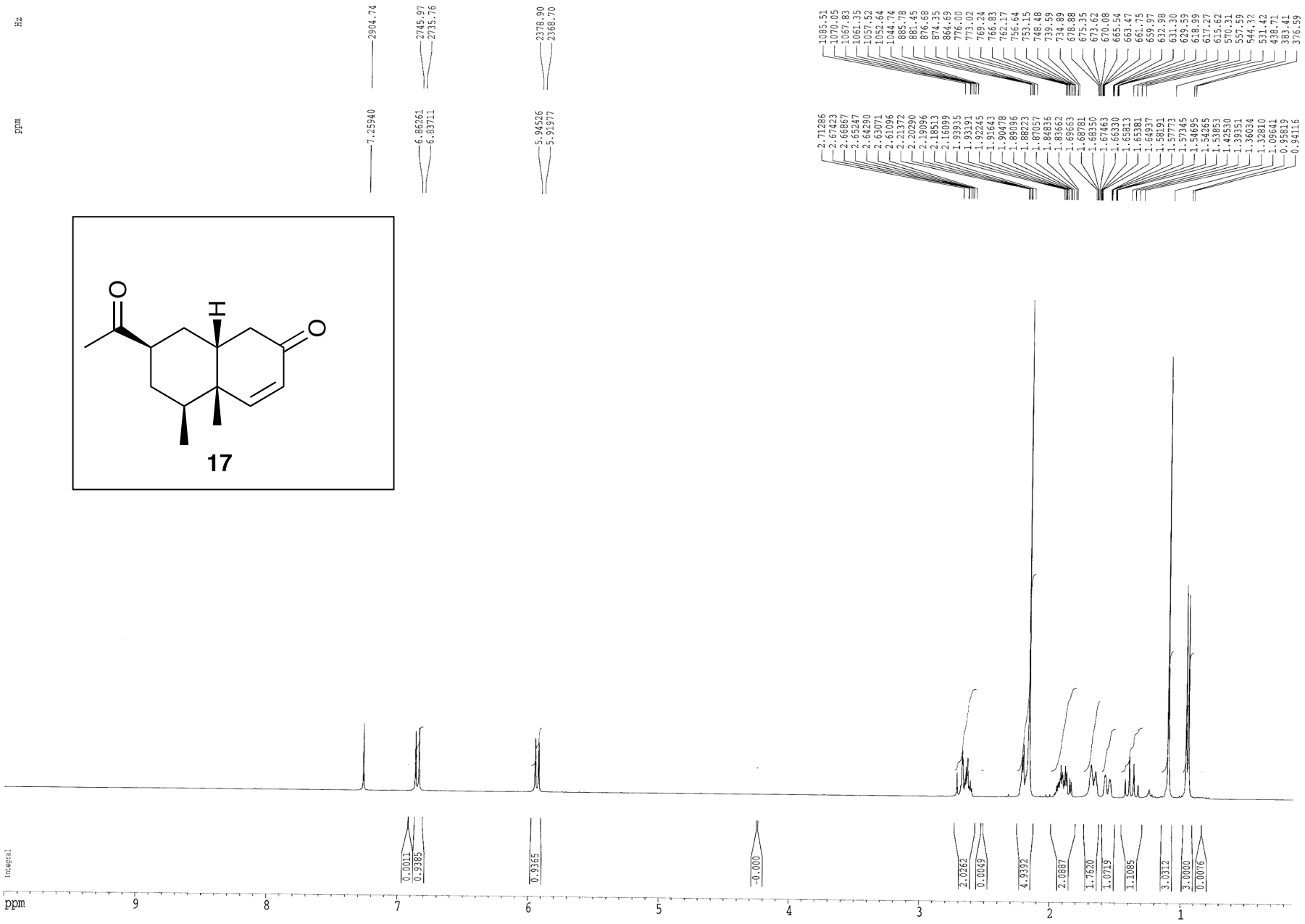




16

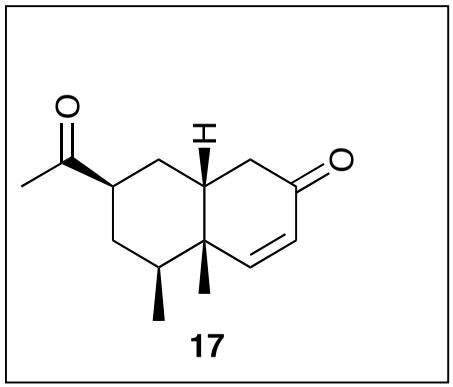


Proton .* angelesa aa1084 (1 1) CDCl3 25.1C July_19,2005_15:17 AMX 400MHz zg30 1H *.

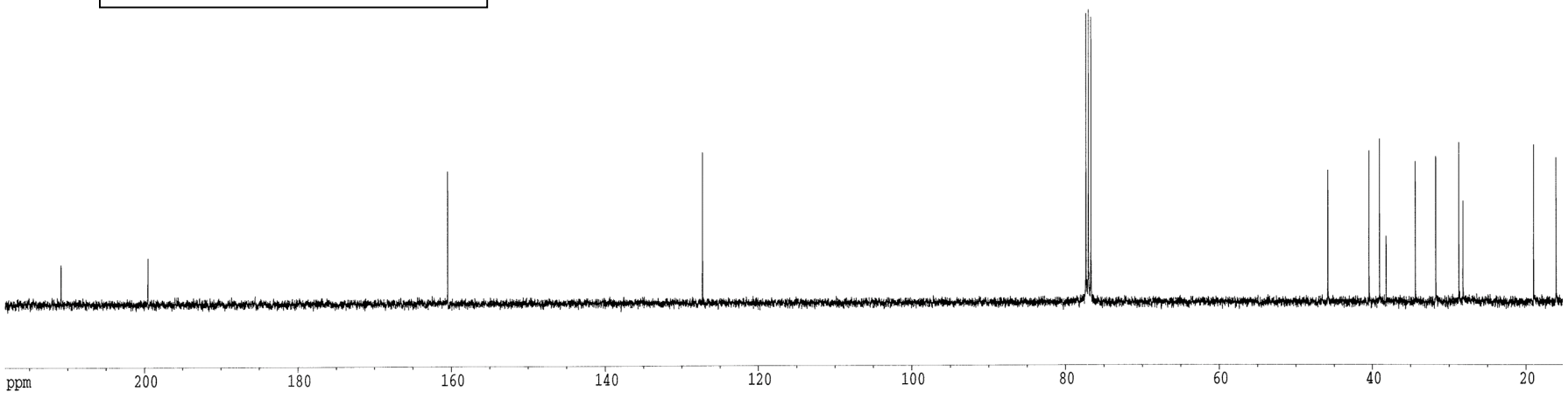


Carbon .* angelesa aa1084carbon (1 1) CDCl3 25.1C July_19,2005_15:26 AMX 400MHz zgpg30 13C; 1H O2=5999.783 *.

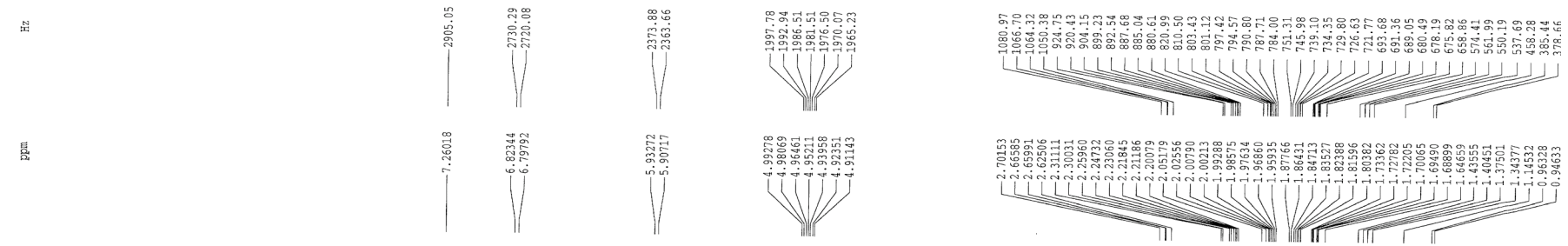
Hz	ppm
21219.6	210.902
20077.6	199.551
16144.3	160.458
12812.2	127.340
7779.2	77.317
7747.2	77.000
7715.3	76.682
4614.9	45.867
4072.0	40.472
3934.6	39.106
3847.6	38.241
3463.2	34.421
3193.8	31.743
2891.9	28.743
2838.0	28.207
1913.2	19.015
1619.2	16.093

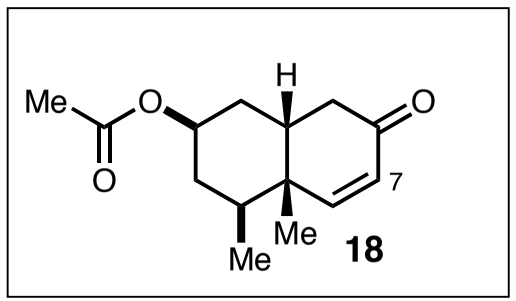


17



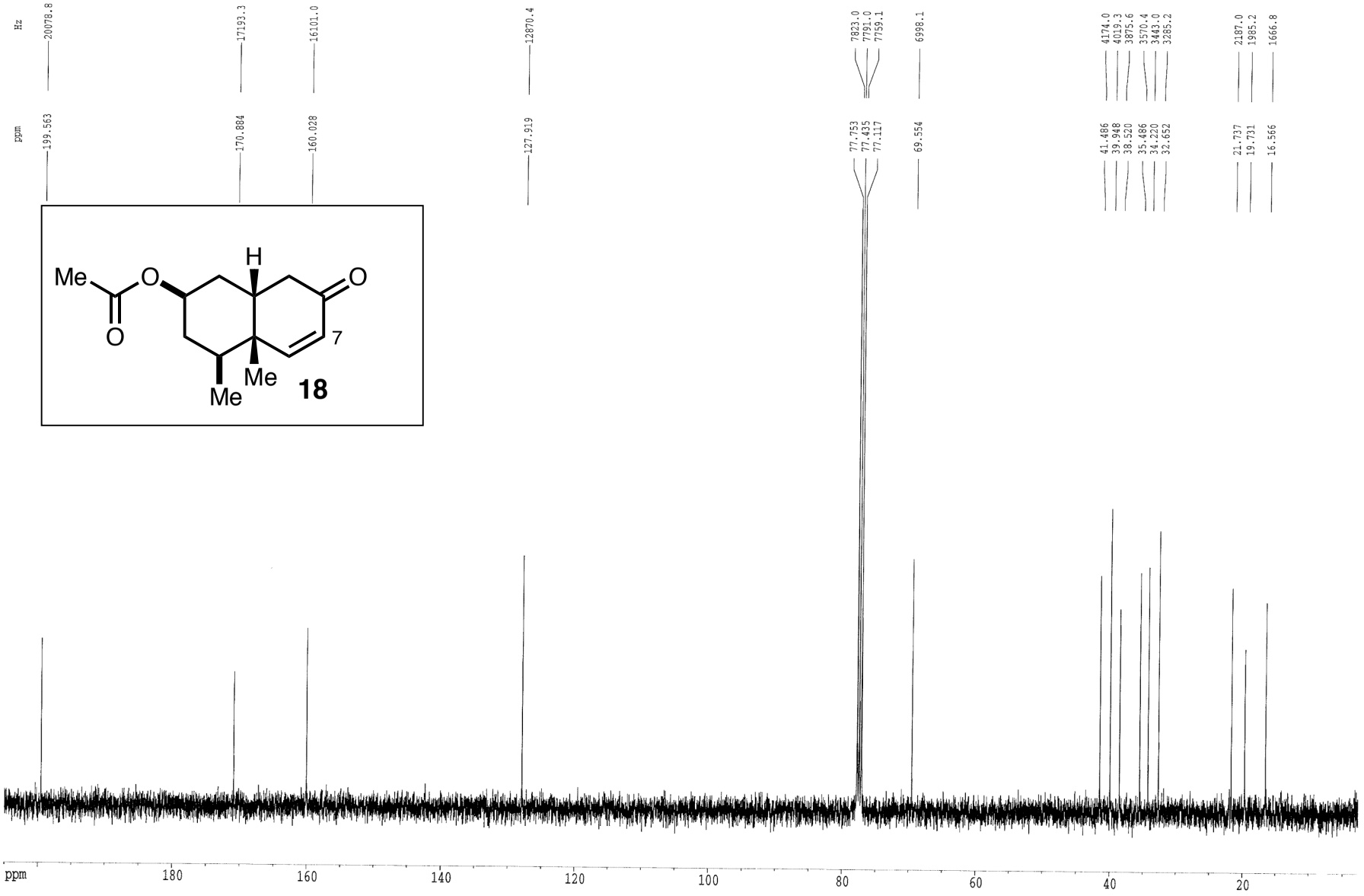
Proton .* angelesa aa1098ag (1 1) CDCl3 25.0C March_24,2006_11:16 AMX 400MHz zg30 1H *.



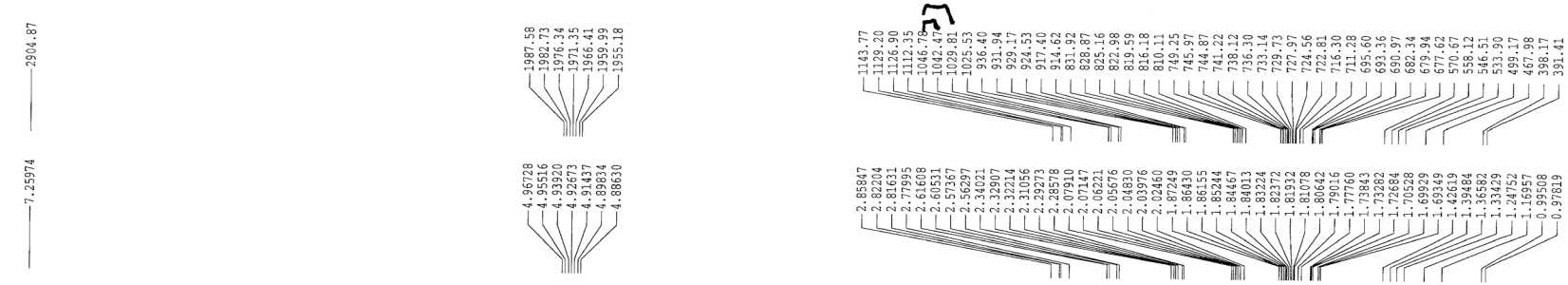


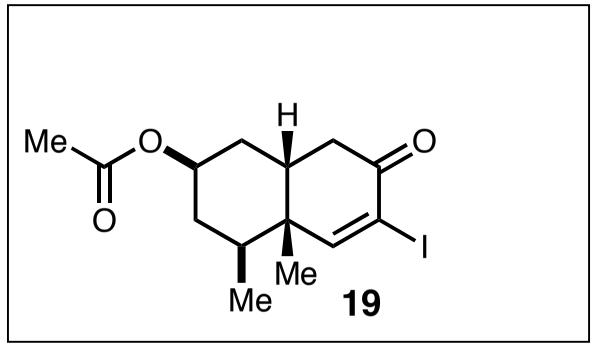
18

Carbon .* angelesa aa1098carbon (1 1) CDCl3 25.0C March_24,2006_11:18 AMX 400MHz zgpg30 13C; 1H O2=7020.000 *.



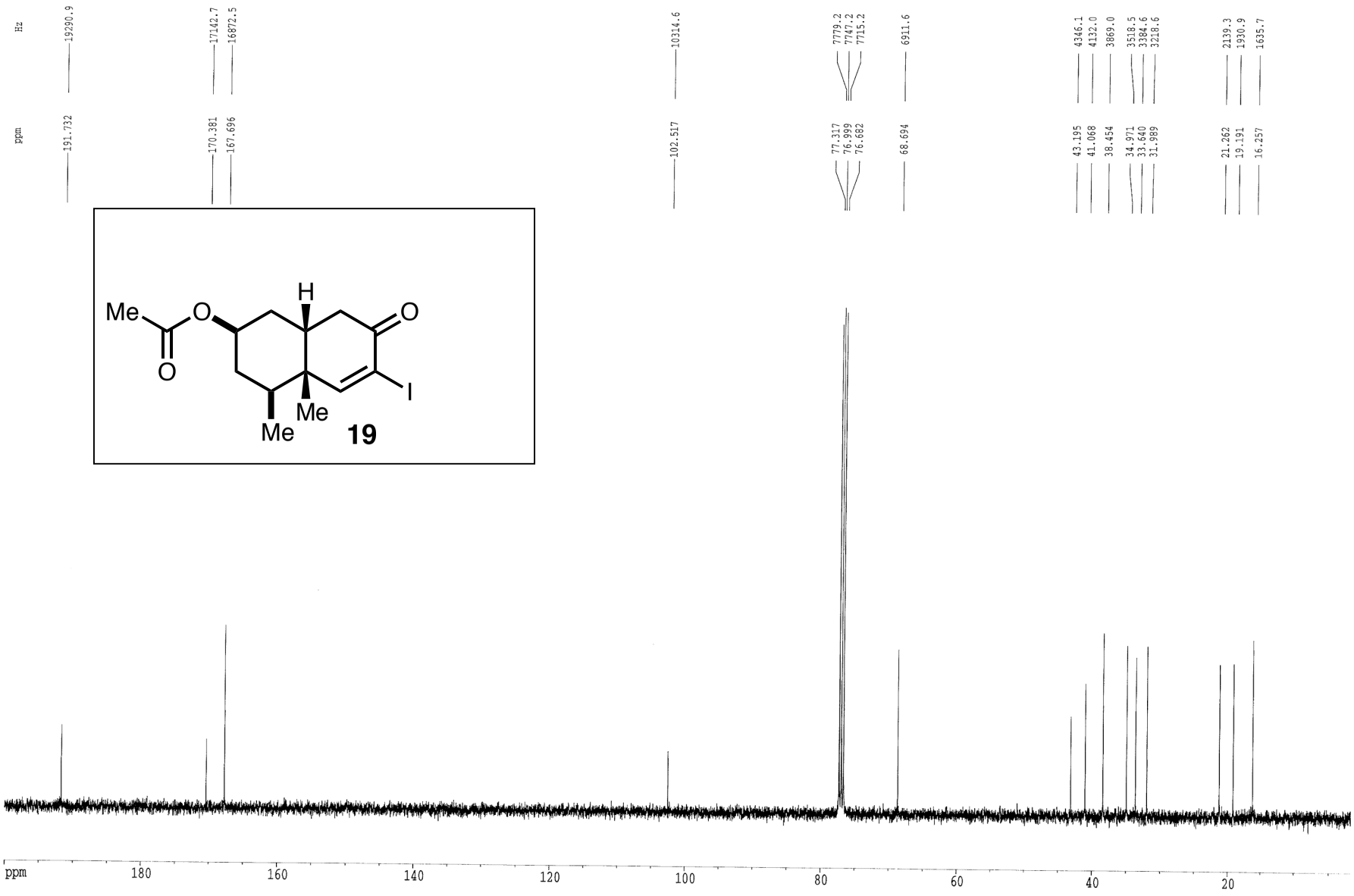
Proton .* angelesa aa1eniodide (1 1) CDCl3 25.0C March_23,2006_10:40 AMX 400MHz zg30 1H *.



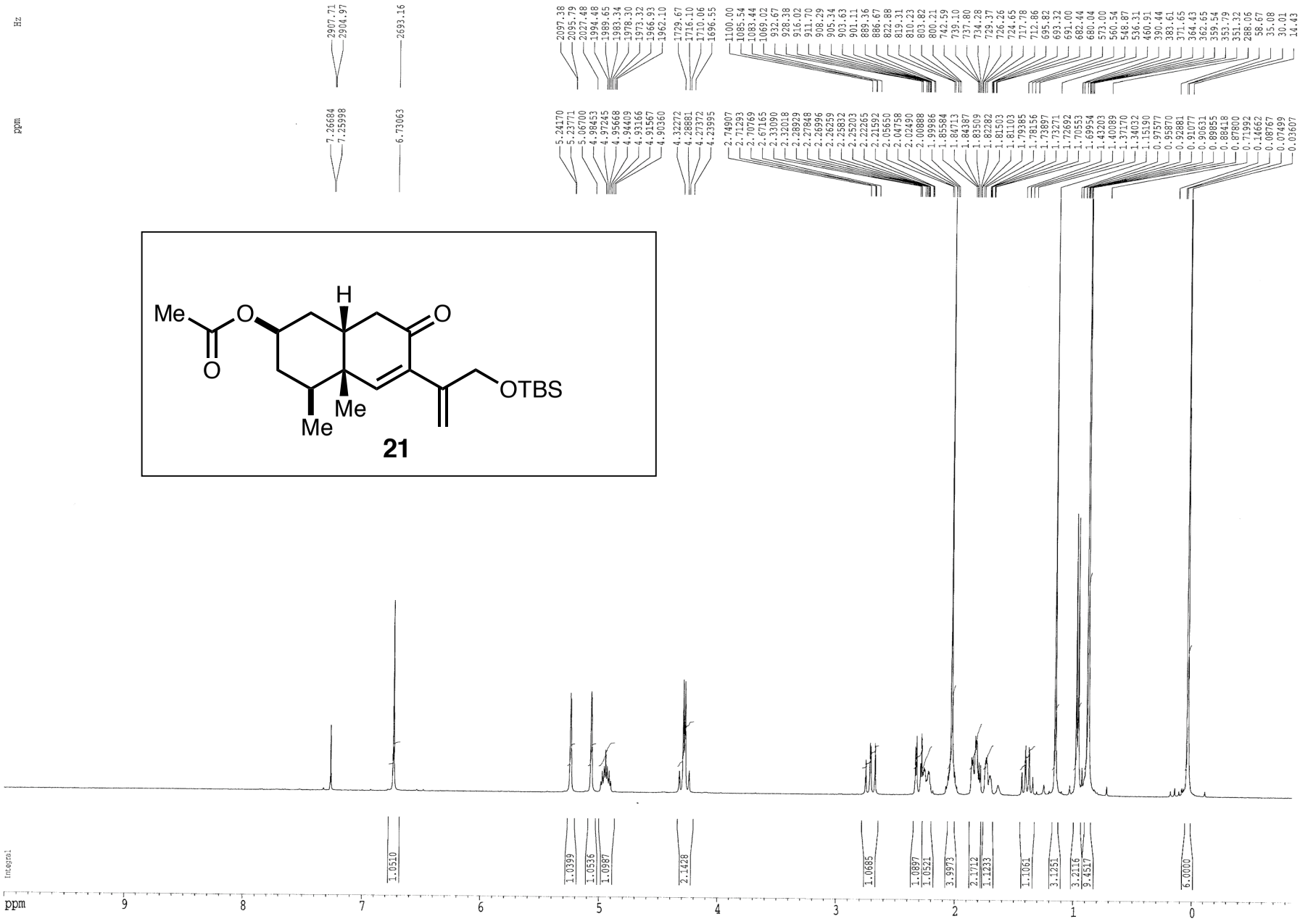


19

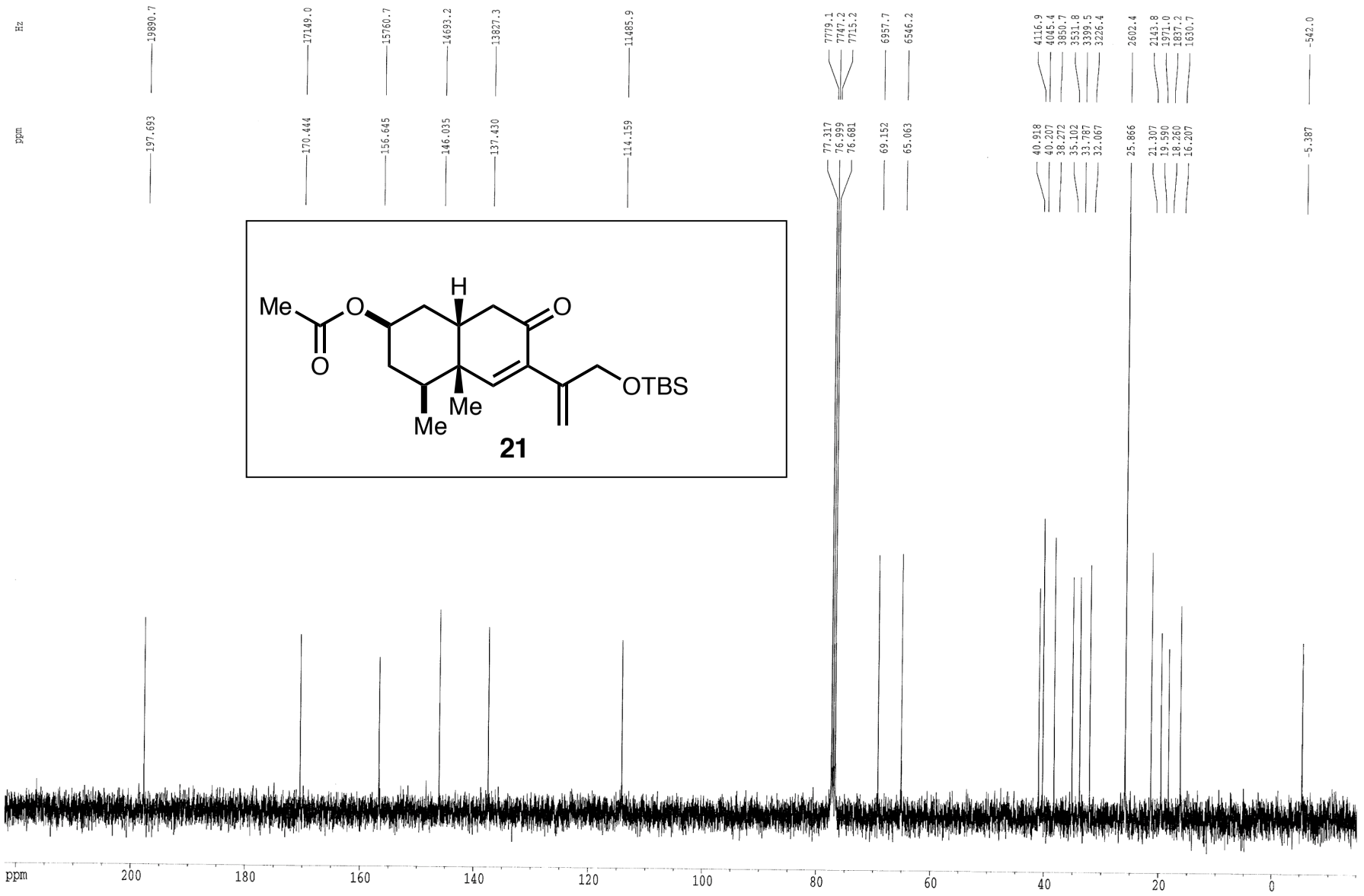
Carbon .* angelesa aa1eniocarbon (1 1) CDCl3 25.0C March_23,2006_10:45 AMX 400MHz zgpg30 13C; 1H O2=5999.783 *.



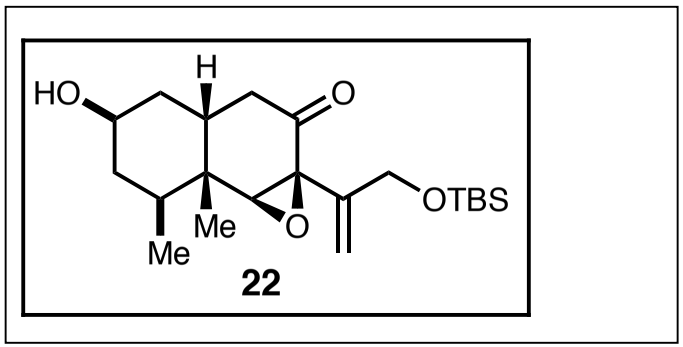
Proton .* angelesa aa1217proton (1 1) CDCl3 25.0C March_31,2006_12:46 AMX 400MHz zg30 1H *.



Carbon .* angelesa aa1217carbon (1 1) CDCl3 25.1C March_31,2006_12:48 AMX 400MHz zgpg30 13C; 1H O2=7020.000 *.

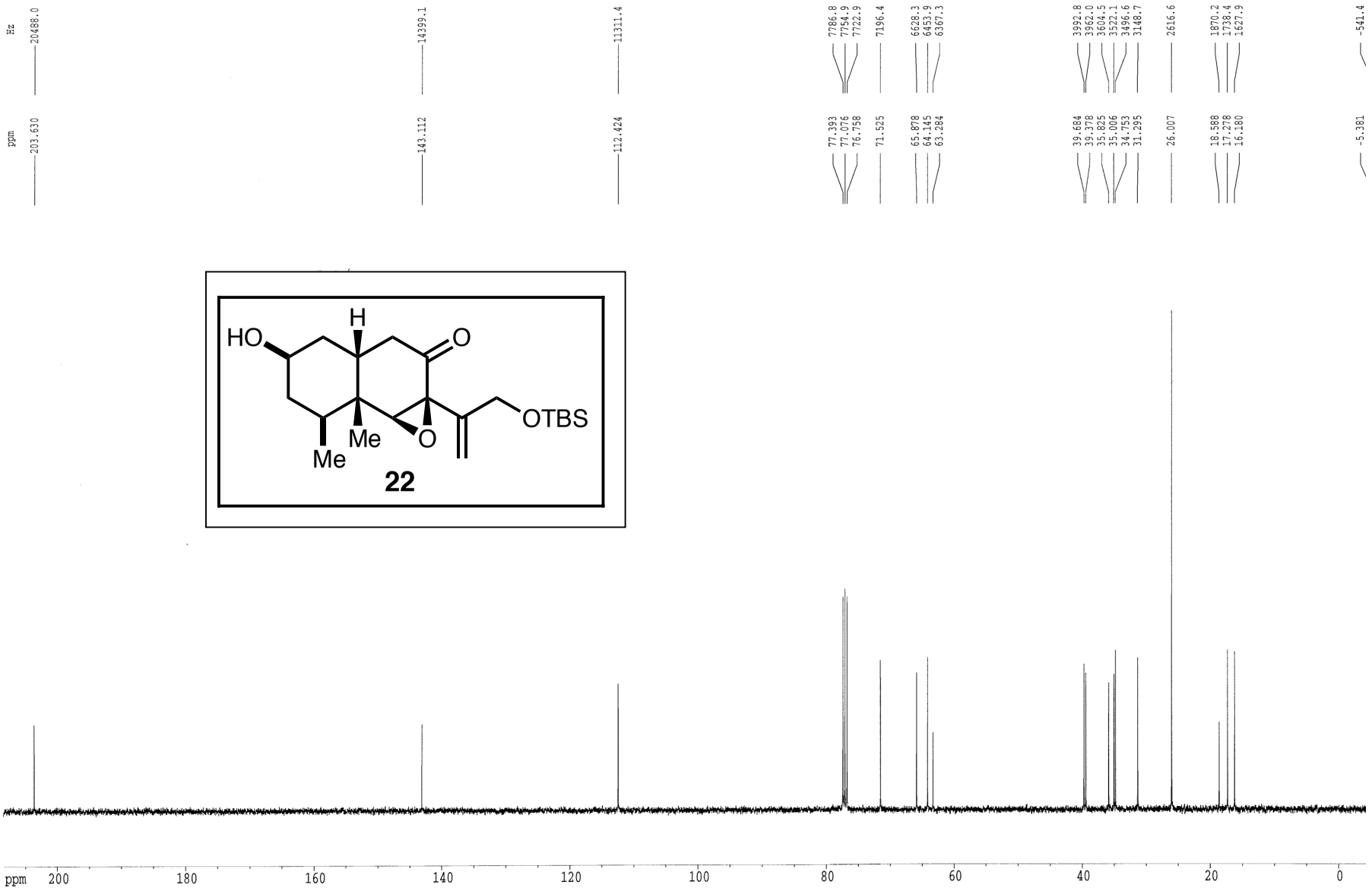


Proton .* angelesa aa1158proton (1 1) CDCl3 25.0C November_06,2005_14:11 AMX 400MHz zg30 1H *.



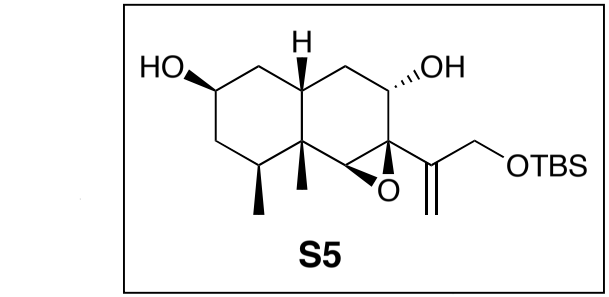
22

Carbon .* angelesa aa1158carbon (1 1) CDCl3 25.0C November_06,2005_14:19 AMX 400MHz zgpg30 13C; 1H O2=5999.783 *.



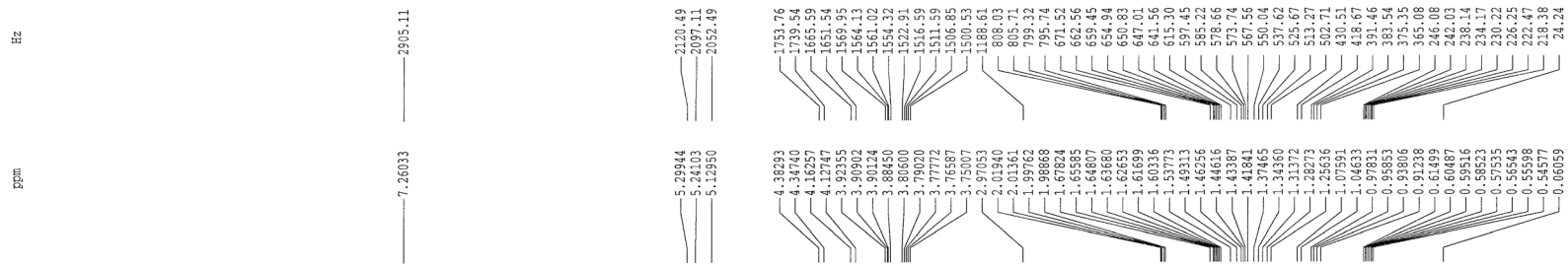
ppm
Integral
Hz
S5
OH
H
O
OH
OTBS
0.9514
0.9287
0.9869
0.9660
2.9644
0.9457
1.0197
1.1284
5.3128
0.9254
1.4155
3.0230
3.1281
8.9279
5.7955
3635.04
3634.39
3630.91
2647.68
2598.28
2581.86
2571.20
2570.07
2555.71
2171.75
2161.09
2089.23
2074.68
2033.71
2022.96
1950.56
1940.13
1935.01
1930.33
1923.46
1918.68
1913.87
1907.23
1902.54
1598.96
1586.87
1573.98
1039.59
1035.77
1033.45
1029.65
1026.77
888.20
878.95
875.63
844.14
838.27
831.44
829.06
826.79
821.82
818.77
814.95
811.84
807.89
799.31
796.01
787.81
663.26
650.68
638.96
626.20
539.77
504.69
497.89
477.33
474.19
473.55
472.94
465.16
462.63
458.69
458.08
457.54
456.92
454.57
74.18
72.25
46.36
39.53
32.14

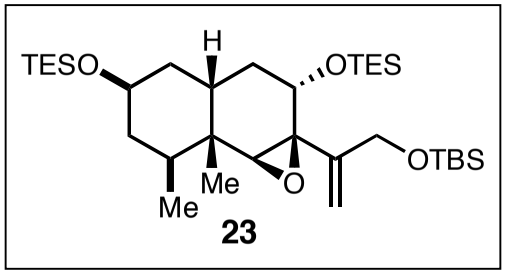
Carbon .* angelesa aaepohcarbon (1 1) CDCl3 25.0C March_25,2006_12:09 AMX 400MHz zgpg30 13C; 1H O2=7020.000 *.



S5

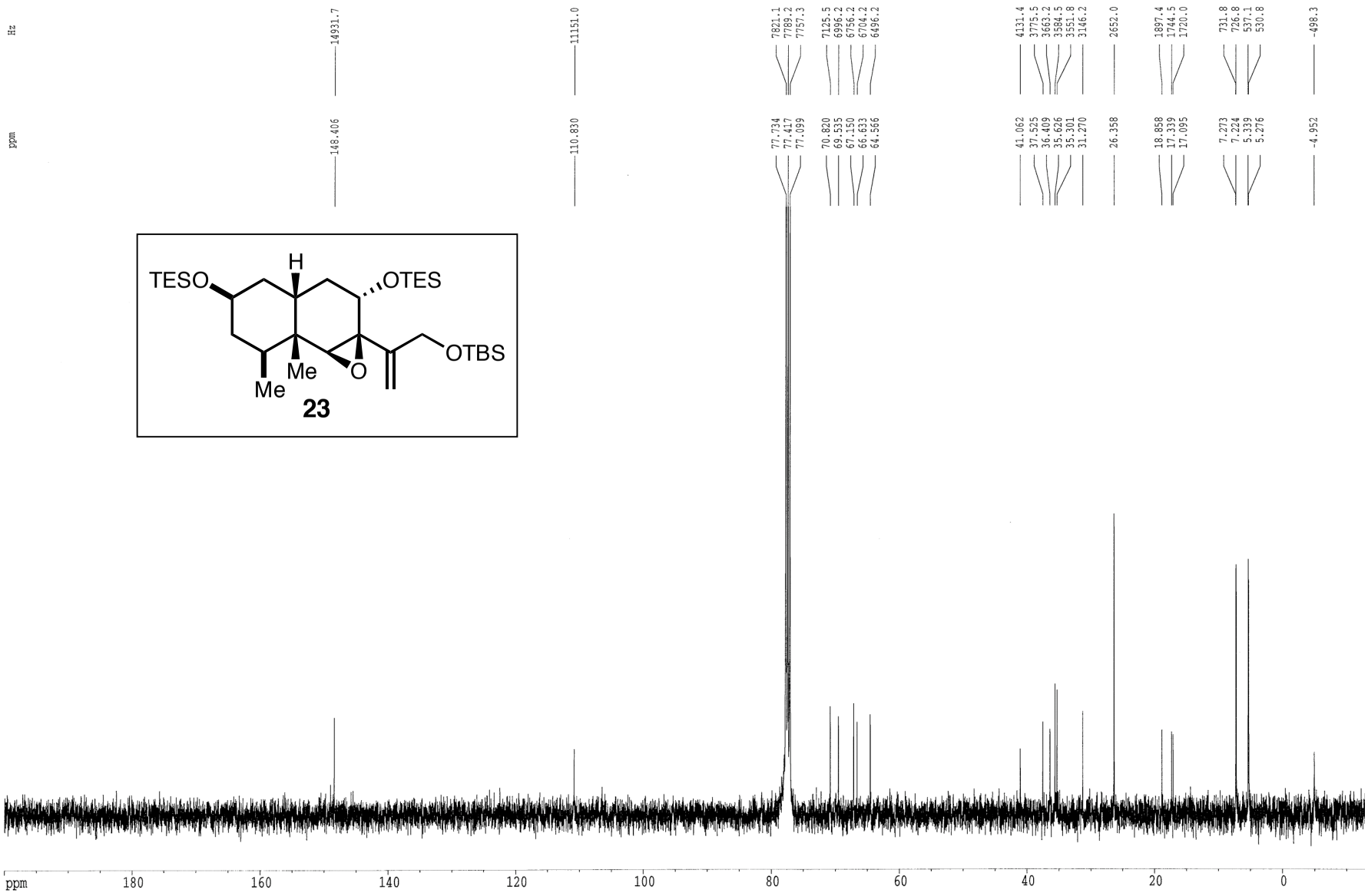
Proton .* angelesa aa1tess (1 1) CDCl3 25.0C March_25,2006_13:07 AMX 400MHz zg30 1H *.



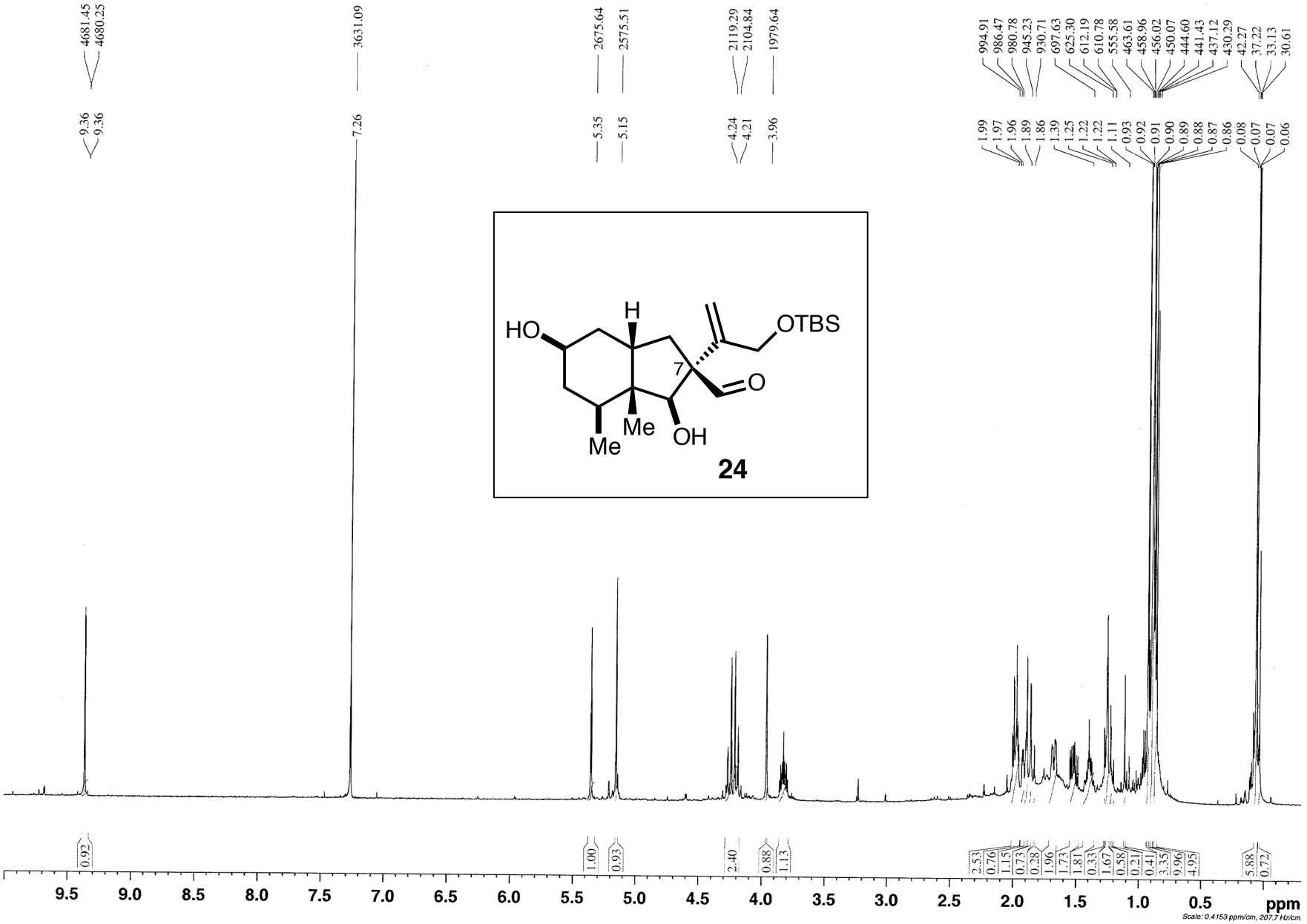


23

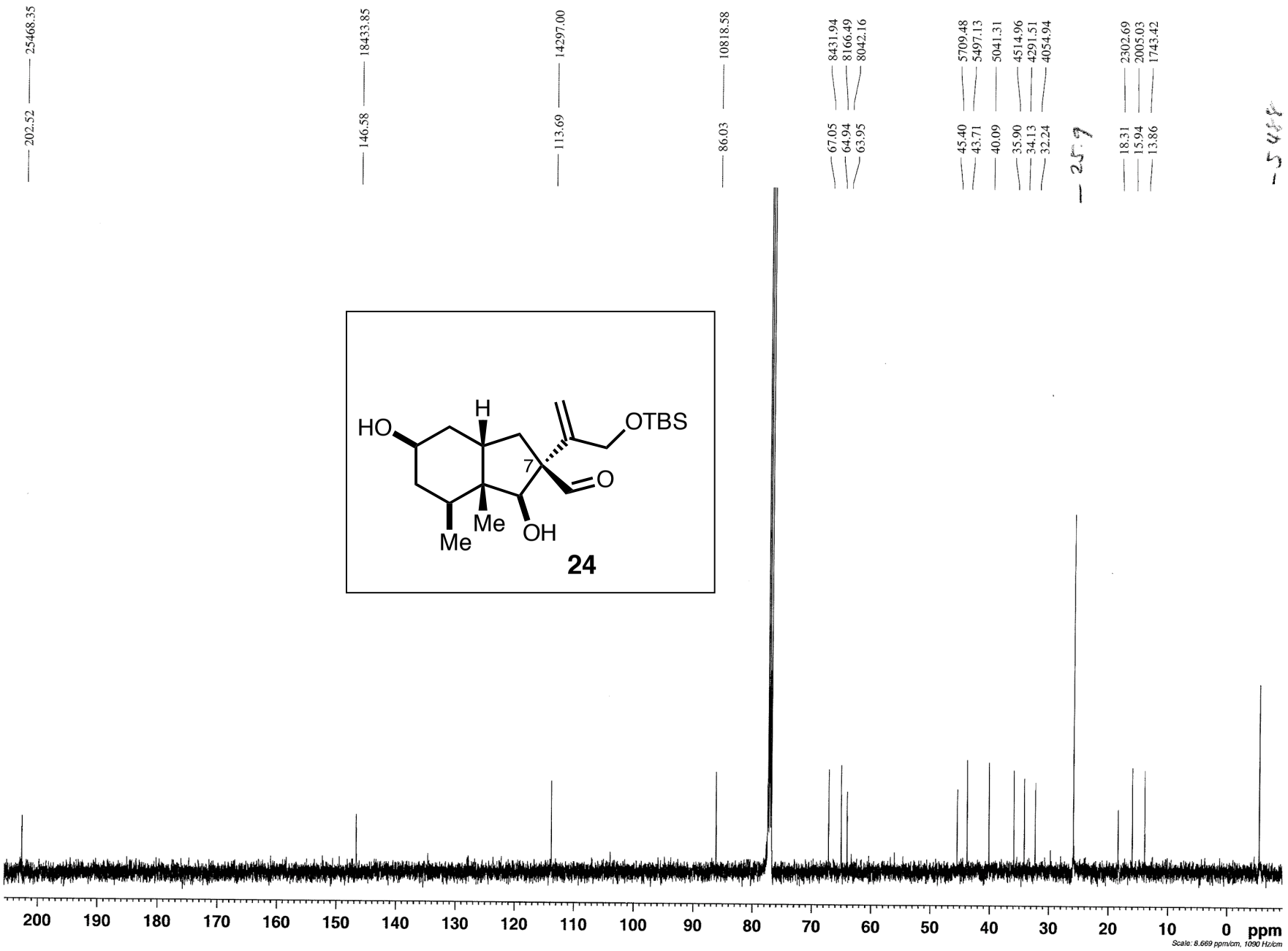
Carbon .* angelesa aa1tesscarbon (1 1) CDCl3 25.0C March_25,2006_13:12 AMX 400MHz zgpg30 13C; 1H O2=7020.000 *.



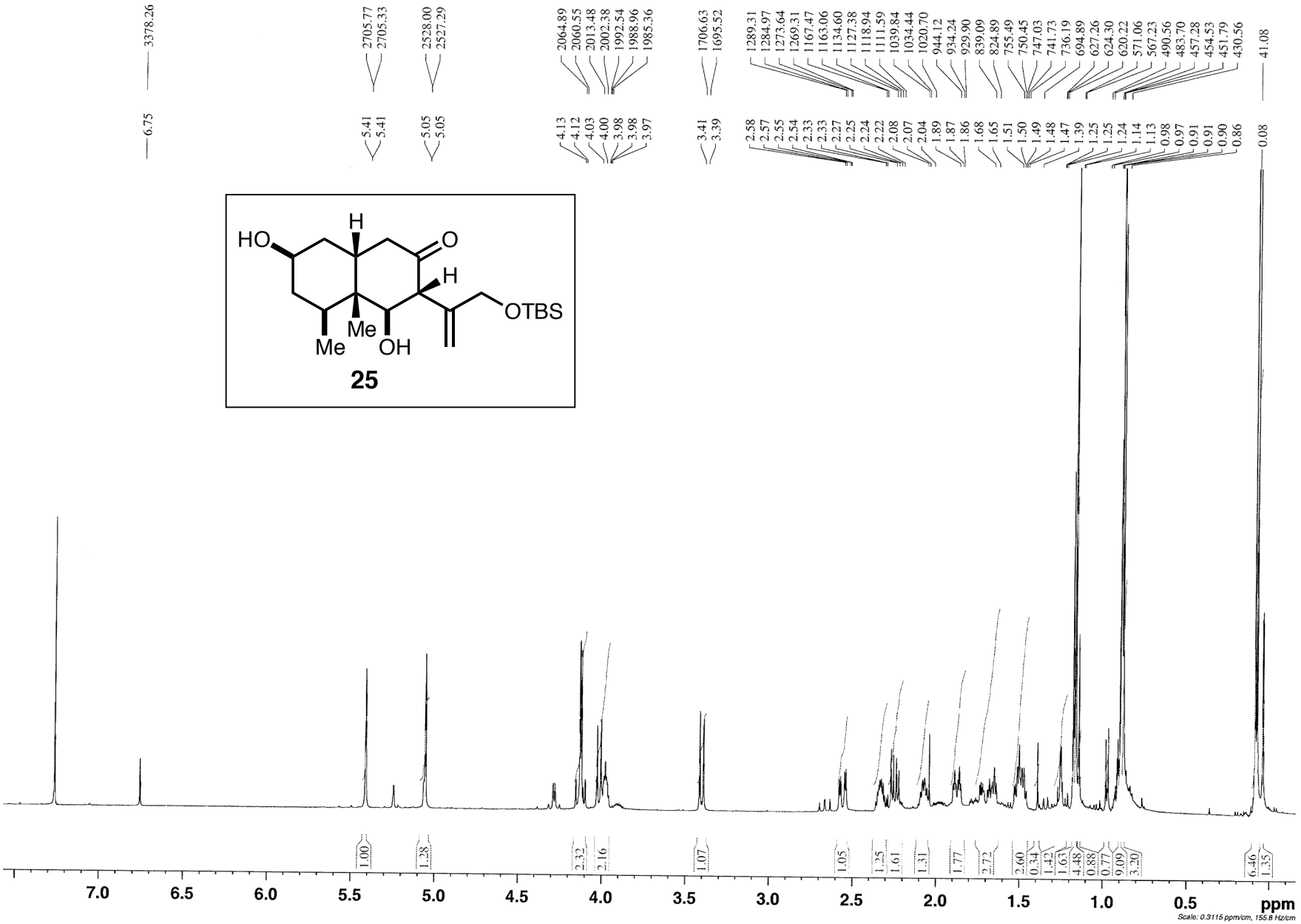
Proton24 .* angelesa aa2148aproton (1 1) CDCl3 24.0C August_15,2006_13:21 DRX 500MHz zg30 1H *.



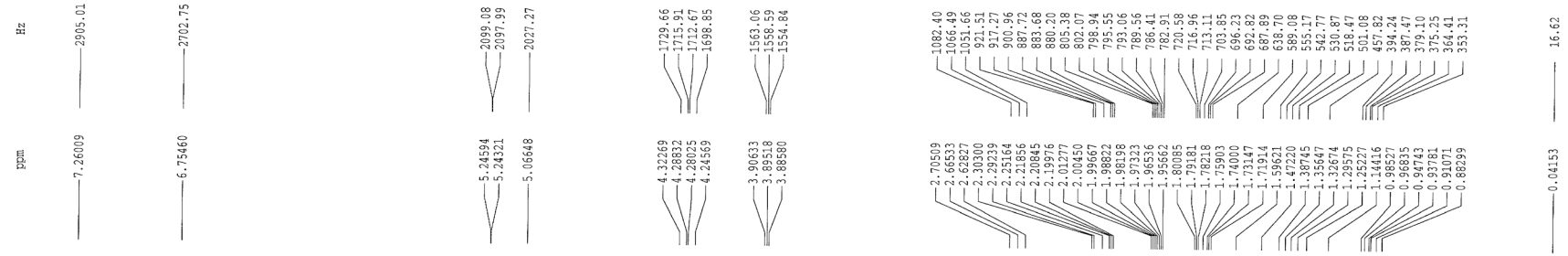
Carbon .* angelesa aa2148ac13 (1 1) MeOD 24.0C August_15,2006_13:23 DRX 500MHz zgpg30 13C; 1H O2=4.000 *.

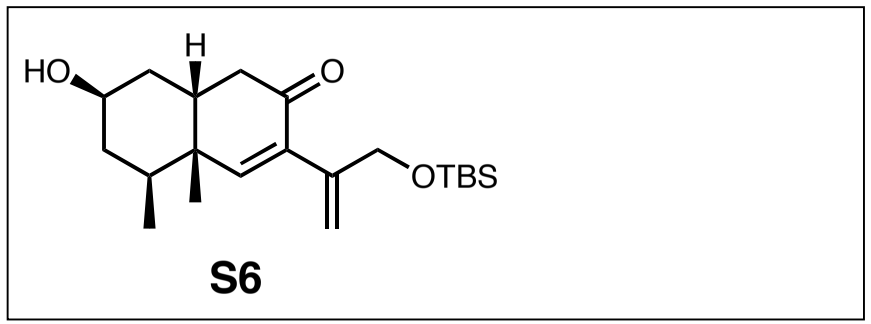


Proton24 .* angelesa aa2148b (1 1) CDCl3 24.0C August_15,2006_11:02 DRX 500MHz zg30 1H *.



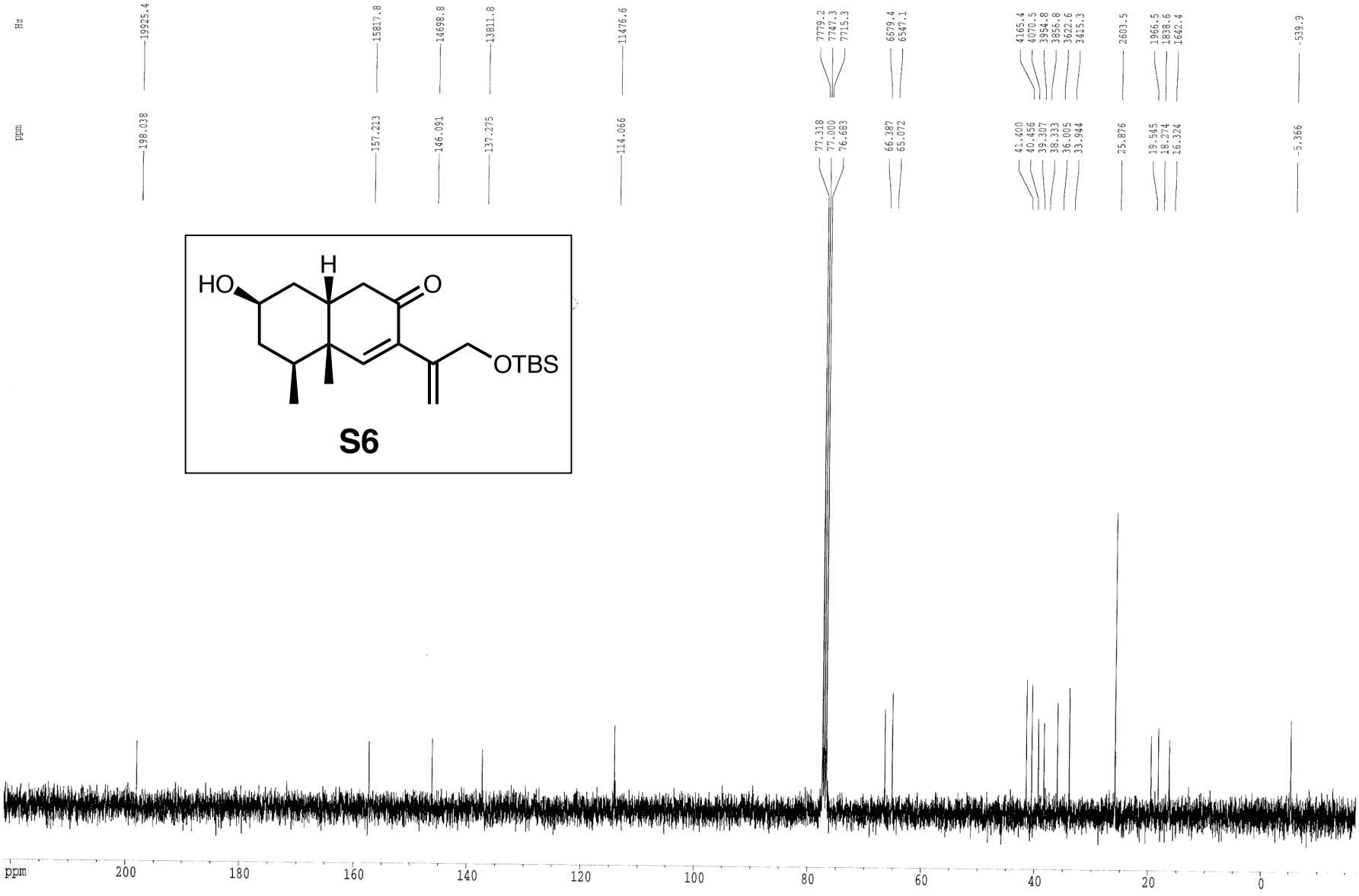
Proton .* angelesa aa1269b (1 1) CDCl3 25.0C April_24,2006_14:46 AMX 400MHz zg30 1H *.



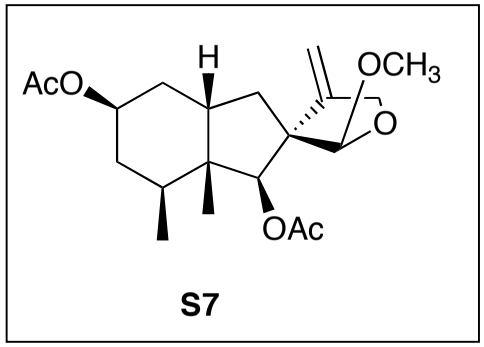


S6

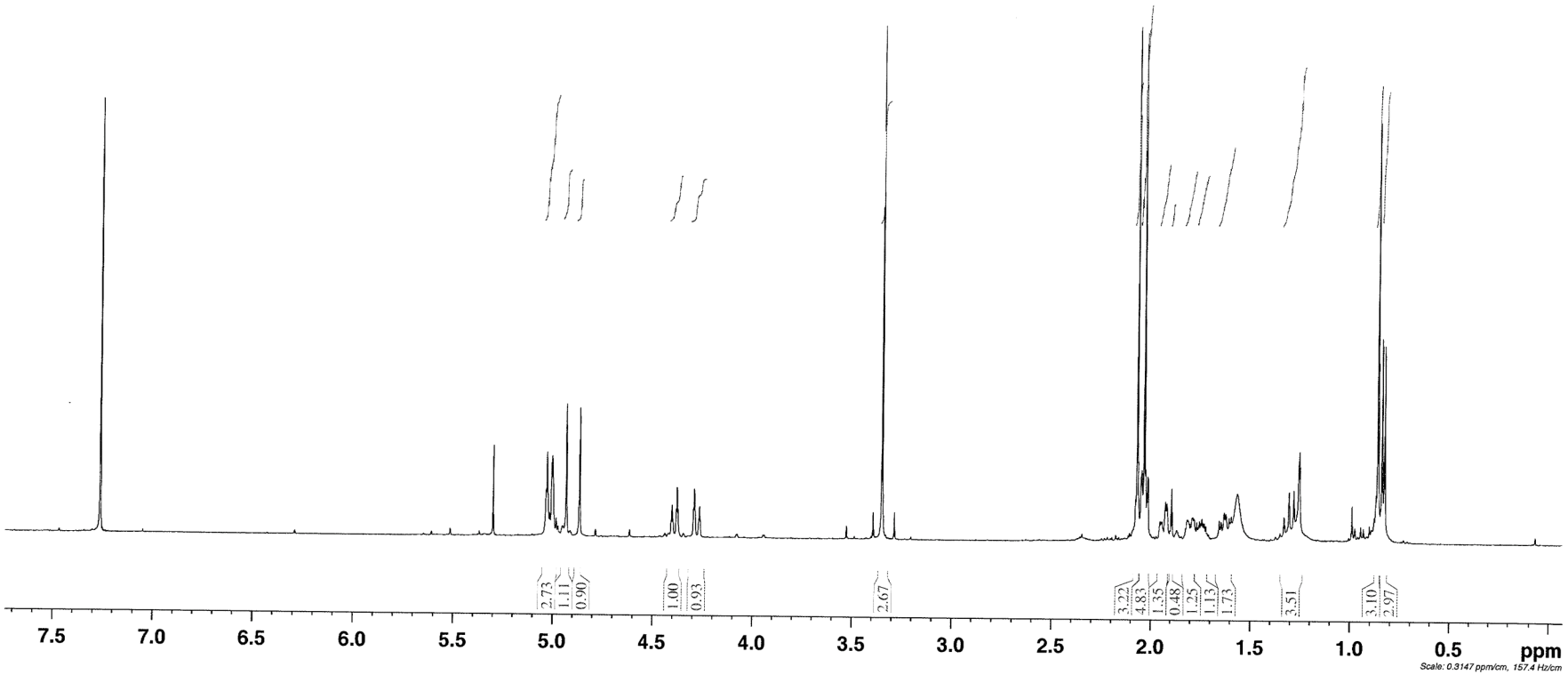
Carbon .* angelesa aa1263cc13 (1 1) CDCl3 25.0C May_02,2006_16:57 AMX 400MHz zgpg30 13C; 1H O2=7020.000 *.



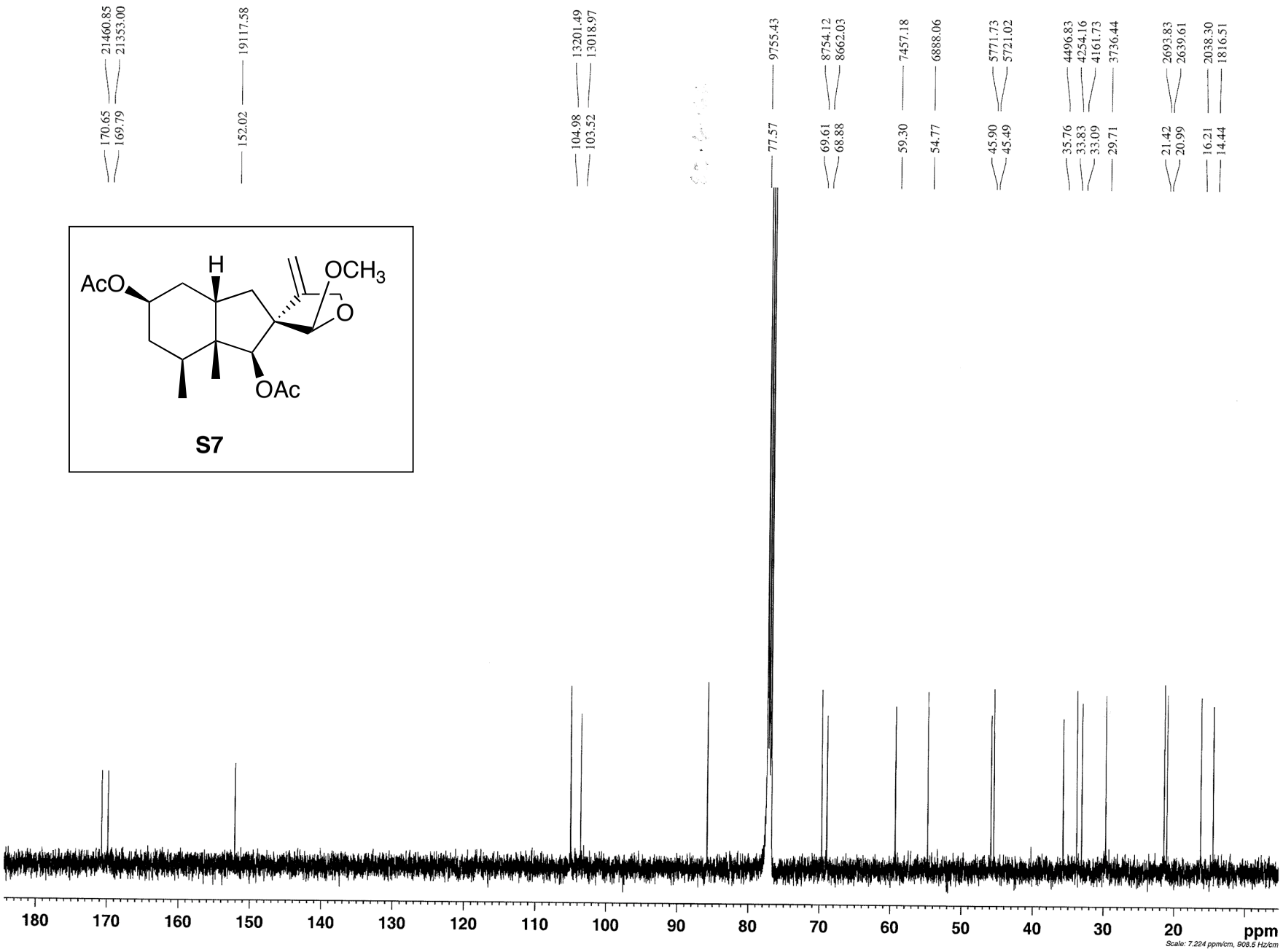
Proton24 .* angelesa aa2bisacetate (1 1) CDCl3 24.0C August_31,2006_15:02 DRX 500MHz zg30 1H *.



S7



Carbon .* angelesa aa2bisacetatec13 (1 1) CDCl3 24.0C August_31,2006_15:05 DRX 500MHz zgpg30 13C; 1H O2=4.000 *.



\