Supplementary Information

Screening of a virtual mirror-image library of natural products

Taro Noguchi, Shinya Oishi,* Kaori Honda, Yasumitsu Kondoh, Tamio Saito, Hiroaki Ohno, Hiroyuki Osada, and Nobutaka Fujii*

Graduate School of Pharmaceutical Sciences, Kyoto University
RIKEN CSRS

Contents

Experimental Procedures

General Methods. ^{1}H NMR and ^{13}C NMR spectra were recorded using a JEOL ECA-500 spectrometer. Chemical shifts are reported in δ (ppm) relative to Me_4Si (in $CDCl_3$) and residual THF (in THF-d_8). ^{13}C NMR spectra were referenced to the residual $CHCl_3$ (in $CDCl_3$) and THF (in THF-d_8). ^{1}H NMR spectra were tabulated as follows: chemical shift, multiplicity (br: broad, s: singlet, d: doublet, t: triplet, q: quartet, m: multiplet), number of protons, and coupling constants. Exact mass (HRMS) spectra were recorded on a JMS-HX/HX 110A mass spectrometer or Shimadzu LC-ESI-IT-TOF-MS equipment. Melting points were measured by a hot stage melting point apparatus (uncorrected). For flash chromatography, Wakogel C-300E (Wako) was employed. For analytical HPLC for MDM2 proteins, Cosmosil 5C18-AR300 (4.6 × 250 mm, Nacalai Tesque Inc.) was employed with a linear gradient of CH_3CN containing 0.1% (v/v) TFA aq. at a flow rate of 1 cm^3 min^{-1}. Cosmosil 5C18-ARII column (4.6 × 250 mm, Nacalai Tesque Inc.) was employed for the analysis of the other peptides.

Synthesis of MDM2$^{25–109}$ and MDM2^{TMR} Proteins

L-MDM2$^{25–109}$, L-MDM2^{TMR}, D-MDM2$^{25–109}$ and D-MDM2^{TMR} proteins were synthesized by the identical protocol in our previous report.[1] Briefly, protected MDM2$^{25–109}$ was synthesized by a standard protocol of Fmoc-based SPPS using automatic peptide synthesizer (PSSM-8, Shimadzu Corporation Ltd.) on H-Rink Amide-ChemMatrix resin (0.4-0.6 mmol g^{-1}) using HBTU/HOBt/ (^{i}Pr)$_2$NEt activation. The resulting protected peptide resin was treated with TFA/thioanisole/ *m*-cresol/1,2-ethanedithiol/H_2O (80:5:5:5:5) at room temperature for 2 h. After removal of the resin by filtration, the filtrate was poured into ice-cold dry Et_2O. The resulting powder was collected by centrifugation and then washed with ice-cold dry Et_2O three times. The crude product was purified by HPLC to provide MDM2$^{25–109}$ proteins as white powder.

For the synthesis of MDM2^{TMR} proteins, two glycines and 5-hexynoic acid were coupled with HBTU/HOBt/(^{i}Pr)$_2$NEt. The resulting protected peptides were treated with the deprotection cocktail as above to provide alkyne-conjugated proteins. Subsequently, treatment of the proteins with TMR-$(PEG)_3$-azide in the presence of Cu(I) provided TMR-labeled MDM2^{TMR} proteins as pink powder.

ESI-TOF MS for L-MDM2$^{25–109}$: Calcd for $C_{462}H_{739}N_{117}O_{123}S_4$: 10027.42; observed: $[M+12H]^{12+}$ *m/z* = 836.74, $[M+11H]^{11+}$ *m/z* = 912.76, $[M+10H]^{10+}$ *m/z* = 1003.86, $[M+9H]^{9+}$ *m/z* = 1115.39, $[M+8H]^{8+}$ *m/z* = 1254.76, $[M+7H]^{7+}$ *m/z* = 1434.00.[1]

ESI-TOF MS for D-MDM2$^{25–109}$: Calcd for $C_{462}H_{739}N_{117}O_{123}S_4$: 10027.42; observed: $[M+12H]^{12+}$ *m/z* = 836.68, $[M+11H]^{11+}$ *m/z* = 912.77, $[M+10H]^{10+}$ *m/z* = 1003.94, $[M+9H]^{9+}$ *m/z* = 1115.46, $[M+8H]^{8+}$ *m/z* = 1254.85, $[M+7H]^{7+}$ *m/z* = 1433.42.

ESI-TOF MS for L-MDM2^{TMR}: Calcd for $C_{505}H_{789}N_{125}O_{133}S_4$: 10865.79; observed: $[M+13H]^{13+}$ *m/z* = 836.94, $[M+12H]^{12+}$ *m/z* = 906.78, $[M+11H]^{11+}$ *m/z* = 989.03, $[M+10H]^{10+}$ *m/z* = 1087.90, $[M+9H]^{9+}$ *m/z* = 1208.38, $[M+8H]^{8+}$ *m/z* = 1359.59.[1]

ESI-TOF MS for D-MDM2^{TMR}: Calcd for $C_{505}H_{789}N_{125}O_{133}S_4$: 10865.79; observed: $[M+13H]^{13+}$ *m/z* = 836.65, $[M+12H]^{12+}$ *m/z* = 906.65, $[M+11H]^{11+}$ *m/z* = 989.11, $[M+10H]^{10+}$ *m/z* = 1088.17, $[M+9H]^{9+}$ *m/z* = 1208.45, $[M+8H]^{8+}$ *m/z* = 1359.80.

Folding of Synthetic MDM2$^{25–109}$ and MDM2^{TMR} Proteins

Folding of synthetic MDM2 proteins were carried out by the identical protocol in our previous report.[1] Lyophilized polypeptide was dissolved in 6 M Gu·HCl (1 mg cm^{-3}) followed by 100-fold dilution with PBS (pH 7.4) containing 0.5 mmol dm^{-3} TCEP·HCl and 0.005% Tween-20 at 4 °C. The solution was stored at 4 °C overnight, and the solution was concentrated using a MWCO 3000 centrifugal filtration membrane (Millipore, Amicon-Ultra 3 kDa) (3 times).

Synthesis of p53 Peptides and Their Derivatives

p53 peptides were synthesized by Fmoc-SPPS on Rink-amide resin (0.66 mmol g^{-1}, 45.5 mg, 0.025 mmol) according to the identical protocol in our previous report.[1] Fmoc-protected amino acids (3 eq) were coupled by using DIC (3 eq) and HOBt (3 eq) in DMF. The Fmoc-protecting group was removed by treatment of the resin with 20% piperidine in DMF. Coupling of biotin (0.125 mmol) was carried out with HBTU (5 eq), HOBt (5 eq) and (^{i}Pr)$_2$NEt (10 eq) in DMF. Coupling of 5-carboxyfluorescein (5 eq) was carried out with DIC (5 eq) and HOBt (10 eq) in DMF. The resulting protected peptide resin was treated with TFA/thioanisole/*m*-cresol/1,2-ethanedithiol/H_2O (80:5:5:5:5) at room temperature for 2 h. After removal of the resin by filtration, the filtrate was poured into ice-cold dry Et_2O. The resulting powder was collected by centrifugation and then washed with ice-cold dry Et_2O three times. The crude product was purified by HPLC on a Cosmosil 5C18-ARII preparative column (Nacalai Tesque, 20 × 250 mm). All peptides were characterized by ESI-MS or MALDI-TOF-MS.

Biotin-labeled L-p53 peptide (biotinyl-aminocaproyl-GSGSSQETFSDLWKLLPEN-NH_2): MS (MALDI-TOF) calcd for $C_{108}H_{166}N_{27}O_{35}S$ $[M+H]^+$ 2434.19; found: 2434.13.[1]

Biotin-labeled D-p53 peptide: MS (MALDI-TOF) calcd for $C_{108}H_{166}N_{27}O_{35}S$ $[M+H]^+$ 2434.19; found: 2434.12.

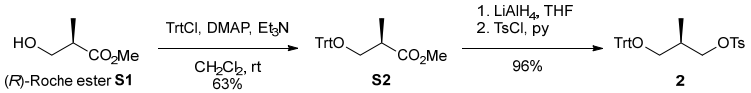
L-P4 (H-LTFEHYWAQLTS-NH_2): MS (MALDI-TOF) calcd for $C_{71}H_{100}N_{17}O_{19}$ $[M+H]^+$ 1494.74; found: 1494.75.[1]

D-P4: MS (MALDI-TOF) calcd for $C_{71}H_{100}N_{17}O_{19}$ $[M+H]^+$ 1494.74; found: 1494.73.[1]

5-Carboxyfluorescein-labeled L-P4 (5-FAM-LTFEHYWAQLTS-NH_2): MS (MALDI-TOF) calcd for $C_{92}H_{110}N_{17}O_{25}$ $[M+H]^+$ 1852.79; found: 1852.80.[1]

5-Carboxyfluorescein-labeled D-P4: MS (MALDI-TOF) calcd for $C_{92}H_{110}N_{17}O_{25}$ $[M+H]^+$ 1852.79; found: 1852.76.

Synthesis of NP843 Derivatives 12a-d



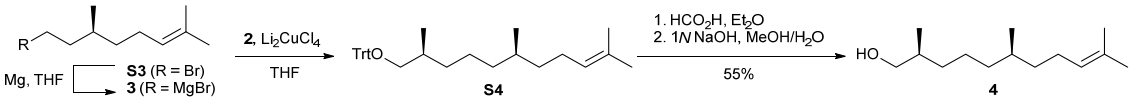
Methyl (*R*)-2-Methyl-3-(trityloxy)propanoate (S2).[2] To a stirred solution TrtCl (23.5 g, 169 mmol) in CH_2Cl_2 (150 cm^3) were added Et_3N (17.9 cm^3, 186 mmol), DMAP (1.03 g, 16.9 mmol), (*R*)-Roche ester (**S1**, 4.69 cm^3, 42.3 mmol) at room temperature. After the mixture was stirred overnight, saturated NH_4Cl was added. The whole was extracted with $CHCl_3$ and the extract was washed with H_2O and brine, and dried over $MgSO_4$. The filtrate was concentrated under reduced pressure. Recrystallization from EtOH gave the title compound **S2** as colorless crystals (9.55 g, 63%): mp 96–98 °C (from EtOH); $[\alpha]^{25}_D$ –16.8 (*c* 1.10, $CHCl_3$); IR (neat) ν_{max}/cm^{-1}: 1737 (C=O); δ_H (500 MHz, $CDCl_3$) 1.15 (3H, d, *J* 6.9, CH_3), 2.71-2.77 (1H, m, CH), 3.17 (1H, dd, J_1 8.9, J_2 6.0, CH_2), 3.30 (1H, dd, J_1 8.6, J_2 6.9, CH_2), 3.70 (3H, s, CH_3) 7.21-7.42 (15H, m, Ar); δ_C(125 MHz, $CDCl_3$) 14.0, 40.4, 51.6, 65.3, 86.3, 127.0 (3C), 127.7 (6C), 128.7 (6C), 143.9 (3C), 175.4. *Anal*. calcd. for $C_{24}H_{24}O_3$: C, 79.97; H, 6.71. Found: C, 79.76; H, 6.86.

Methyl (*S*)-2-Methyl-3-(trityloxy)propanoate (*ent*-S2). According to the procedure described for the preparation of **S2**, (*S*)-Roche ester (*ent*-**S1**, 4.69 cm^3, 42.3 mmol) was converted into *ent*-**S2** as colorless crystals (9.56 g, 63%): mp 96–98 °C (from EtOH); $[\alpha]^{25}_D$ +16.6 (*c* 1.05, $CHCl_3$); IR (neat) ν_{max}/cm^{-1}: 1739 (C=O); δ_H(500 MHz, $CDCl_3$) 1.15 (3H, d, *J* 6.9, CH_3), 2.71-2.77 (1H, m, CH), 3.17 (1H, dd, J_1 8.6, J_2 5.7, CH_2), 3.30 (1H, dd, J_1 8.6, J_2 6.9, CH_2), 3.70 (3H, s, CH_3), 7.21-7.42 (15H, m, Ar); δ_C(125 MHz, $CDCl_3$) 14.0, 40.4, 51.6, 65.3, 86.3, 127.0 (3C), 127.7 (6C), 128.7 (6C), 143.9 (3C), 175.4. *Anal*. calcd. for $C_{24}H_{24}O_3$: C, 79.97; H, 6.71. Found: C, 80.05; H, 6.77.

(*R*)-2-Methyl-3-(trityloxy)propyl 4-Methylbenzenesulfonate (2).[2] To a stirred solution of compound **S2** (9.00 g, 25.0 mmol) in THF (200 cm^3) under argon was added $LiAlH_4$ (1.42 g, 37.4 mmol) at 0 °C. After the mixture was stirred for 30 min, saturated aqueous solution of sodium potassium tartrate was slowly added at 0 °C, and the mixture was stirred overnight at room temperature. The whole was extracted with Et_2O and the extract was washed with H_2O and brine, and dried over $MgSO_4$. Filtration through a short pad of silica gel and concentration under reduced pressure gave a crude alcohol, which was used without further purification. TsCl (5.96 g, 31.3 mmol) was added to a solution of the alcohol in pyridine (18.2 cm^3) at 0 °C. After the mixture was stirred overnight, the reaction was quenched with H_2O at 0 °C. The whole was extracted with $CHCl_3$, and the extract was washed with H_2O and brine, and dried over $MgSO_4$. Filtration through a short pad of silica gel and concentration gave a crude sulfonate. Recrystallization from $CHCl_3$/hexane gave the title compound **2** as colorless crystals (11.6 g, 96%): mp 146–148 °C (from $CHCl_3$/hexane); $[\alpha]^{25}_D$ –11.4 (*c* 1.15, $CHCl_3$); IR (neat) ν_{max}/cm^{-1}: 1360 (OSO_2), 1176 (OSO_2); δ_H(500 MHz, $CDCl_3$) 0.89 (3H, d, *J* 8.6, CH_3), 2.01-2.08 (1H, m, CH), 2.43 (3H, s, CH_3), 2.93 (1H, dd, J_1 9.2, J_2 6.9, CH_2), 3.02 (1H, dd, J_1 9.2, J_2 5.2, CH_2), 3.99 (1H, dd, J_1 9.2, J_2 6.3, CH_2), 4.12 (1H, dd, J_1 9.5, J_2 5.4, CH_2), 7.21-7.34 (17H, m, Ar), 7.74-7.76 (2H, m, Ar); δ_C(125 MHz, $CDCl_3$) 13.9, 21.6, 34.0, 64.2, 72.5, 86.4, 127.0 (3C),

127.7 (6C), 127.9 (2C), 128.6 (6C), 129.8 (2C), 133.0, 143.9 (3C), 144.6. *Anal*. calcd. for $C_{30}H_{30}O_4S$: C, 74.05; H, 6.21. Found: C, 73.91; H, 6.26.

(*S*)-2-Methyl-3-(trityloxy)propyl 4-Methylbenzenesulfonate (*ent*-2). According to the procedure described for the preparation of **2**, compound *ent*-**S2** (8.00 g, 22.2 mmol) was converted into *ent*-**2** as colorless crystals (9.05 g, 84%): mp 145–148 °C (from $CHCl_3$/hexane); $[\alpha]^{25}_D$ +11.4 (*c* 1.08, $CHCl_3$); IR (neat) ν_{max}/cm^{-1}: 1361 (OSO_2), 1175 (OSO_2); δ_H(500 MHz, $CDCl_3$) 0.89 (3H, d, *J* 8.6, CH_3), 2.01-2.08 (1H, m, CH), 2.43 (3H, s, CH_3), 2.93 (1H, dd, J_1 9.2, J_2 6.9, CH_2), 3.02 (1H, dd, J_1 9.2, J_2 5.2, CH_2), 3.99 (1H, dd, J_1 9.2, J_2 6.3, CH_2), 4.12 (1H, dd, J_1 9.5, J_2 5.4, CH_2), 7.21-7.34 (17H, m, Ar), 7.74-7.76 (2H, m, Ar); δ_C(125 MHz, $CDCl_3$) 13.9, 21.6, 34.0, 64.2, 72.5, 86.4, 127.0 (3C), 127.7 (6C), 127.9 (2C), 128.6 (6C), 129.8 (2C), 133.0, 143.9 (3C), 144.6. *Anal*. calcd. for $C_{30}H_{30}O_4S$: C, 74.05; H, 6.21. Found: C, 73.86; H, 6.33.



(2*S*,6*R*)-2,6,10-Trimethylundec-9-en-1-ol (4). To a stirred mixture of Mg (1.00 g, 41.2 mmol) in THF (6.6 cm^3) was added dropwise (*S*)-citronellyl bromide (**S3**, 6.00 g, 27.4 mmol) in THF (16.8 cm^3) over 2 h using syringe pump at 60 °C to give Grignard reagent **3**. To a stirred solution of **2** (6.9 g, 14.2 mmol) in THF (31.0 cm^3) were added the reagent **3** and Li_2CuCl_4 in THF (0.1 mol dm^{-3}, 27.0 cm^3, 2.70 mmol) at –40 °C. The resulting mixture was stirred at –40 °C overnight and the reaction was quenched with saturated NH_4Cl at 0 °C. The whole was extracted with Et_2O and the extract was washed with H_2O and brine, and dried over $MgSO_4$. The filtrate was concentrated under reduced pressure. The oily residue was dissolved in hexane and the solution was filtrated through a short pad of silica gel to give crude **S4**. To a stirred solution of the compound **S4** in dry Et_2O (120 cm^3) was added HCO_2H (120 cm^3) dropwise at 0 °C under argon, and the stirring was continued for 1 h. After toluene (150 cm^3) was added, the solution was concentrated under reduced pressure. 1*N* NaOH in MeOH/H_2O (1:1, 100 cm^3) was added to the residue and the mixture was stirred for 10 min. The mixture was concentrated under reduced pressure. The residue was extracted with Et_2O and the extract was dried over $MgSO_4$. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography to give the title compound **4** as a colorless oil (1.67 g, 55%). $[\alpha]^{25}_D$ –7.5 (*c* 1.10, $CHCl_3$); IR (neat) ν_{max}/cm^{-1}: 3319 (OH), 1035 (C-O); δ_H(500 MHz, $CDCl_3$) 0.86 (3H, d, *J* 6.3, CH_3), 0.93 (3H, d, *J* 6.3, CH_3), 1.04-1.42 (9H, m), 1.60 (3H, s, CH_3), 1.58-1.65 (1H , m), 1.68 (3H, s, CH_3), 1.89-2.03 (2H, m, CH_2), 3.42 (1H, dd, J_1 10.3, J_2 6.3, CH_2), 3.51 (1H, dd, J_1 10.6, J_2 6.0, CH_2), 5.09-5.11 (1H, m, CH); δ_C(125 MHz, $CDCl_3$) 16.6, 17.6, 19.6, 24.3, 25.5, 25.7, 32.4, 33.4, 35.8, 37.1, 37.2, 68.4, 125.0, 131.0. HRMS (FAB) calcd for $C_{14}H_{29}O$ (MH^+): 213.2213; found: 213.2217.

(2*R*,6*S*)-2,6,10-Trimethylundec-9-en-1-ol (*ent*-4). According to the procedure described for the preparation of **4**, compound *ent*-**2** (5.00 g, 10.3 mmol) was converted into *ent*-**4** with (*R*)-citronellyl bromide (6.40 g, 29.2 mmol) as a colorless oil (996 mg, 46%). $[\alpha]^{25}_D$ +7.4 (*c* 1.17, $CHCl_3$); IR

(neat) ν_{max}/cm^{-1}: 3357 (OH), 1034 (C-O); δ_H(500 MHz, $CDCl_3$) 0.86 (3H, d, *J* 6.9, CH_3), 0.92 (3H, d, *J* 6.3, CH_3), 1.03-1.41 (m, 9H), 1.60 (3H, s, CH_3), 1.58-1.65 (1H, m), 1.68 (3H, s, CH_3), 1.89-2.03 (2H, m, CH_3), 3.42 (1H, dd, J_1 10.3, J_2 6.3, CH_2), 3.51 (1H, dd, J_1 10.6, J_2 6.3, CH_2), 5.09-5.11 (1H, m, CH); δ_C(125 MHz, $CDCl_3$) 16.6, 17.6, 19.6, 24.3, 25.5, 25.7, 32.4, 33.4, 35.8, 37.1, 37.2, 68.4, 125.0, 131.0. HRMS (FAB) calcd for $C_{14}H_{29}O$ (MH^+): 213.2213; found: 213.2223.

(3*S*,7*R*)-3,7,11-Trimethyldodec-10-enenitrile (5). To a stirred solution of compound **4** (1.26 g, 5.93 mmol) in pyridine (4.3 cm^3) was added TsCl (1.40 g, 7.72 mmol) at 0 °C. After the mixture was stirred for 2 h, saturated aqueous solution of citric acid was added. The whole was extracted with Et_2O and the extract was washed with H_2O and brine, and dried over $MgSO_4$. The extract was concentrated under reduced pressure after filtration through a short pad of silica gel to give a crude sulfonate. To a stirred solution of the sulfonate in DMSO (13.0 cm^3) was added NaCN (0.581 g, 11.8 mmol) at room temperature. After the mixture was stirred overnight, saturated aqueous solution of NH_4Cl was added. The whole was extracted with $CHCl_3$ and the extract was washed with H_2O and brine, and dried over $MgSO_4$. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography to give the title cyanide **5** as a colorless oil (1.17 g, 89%). $[\alpha]^{25}_D$ +5.2 (*c* 1.02, $CHCl_3$); IR (neat) ν_{max}/cm^{-1}: 2247 (C≡N); δ_H(500 MHz, $CDCl_3$) 0.87 (3H, d, *J* 6.3, CH_3), 1.07 (3H, d, *J* 6.9, CH_3), 1.07-1.17 (2H , m), 1.23-1.43 (7H, m), 1.60 (3H, s, CH_3), 1.69 (3H, s, CH_3), 1.81-1.89 (1H, m), 1.89-2.03 (2H, m, CH_2), 2.23 (1H, dd, J_1 16.6, J_2 6.9, CH_2), 2.32 (1H, dd, J_1 16.6, J_2 5.7, CH_2), 5.09-5.11 (1H, m, CH); δ_C(125 MHz, $CDCl_3$) δ 17.6, 19.5 (2C), 24.2, 24.4, 25.5, 25.7, 30.5, 32.3, 36.2, 36.8, 37.0, 119.0, 124.9, 131.1. HRMS (FAB) calcd for $C_{15}H_{28}N$ (MH^+): 222.2216; found: 222.2224.

(3*R*,7*S*)-3,7,11-Trimethyldodec-10-enenitrile (*ent*-5). According to the procedure described for the preparation of **5**, compound *ent*-**4** (950 mg, 4.47 mmol) was converted into *ent*-**5** as a colorless oil (948 mg, 96%). $[\alpha]^{25}_D$ –5.3 (*c* 1.08, $CHCl_3$); IR (neat) ν_{max}/cm^{-1}: 2247 (C≡N); δ_H(500 MHz, $CDCl_3$) 0.87 (3H, d, *J* 6.3, CH_3), 1.07 (3H, d, *J* 6.9, CH_3), 1.09-1.17 (2H, m), 1.21-1.43 (7H, m), 1.61 (3H, s, CH_3), 1.69 (3H, s, CH_3), 1.81-1.89 (1H, m), 1.89-2.03 (2H, m, CH_2), 2.24 (1H, dd, J_1 16.6, J_2 6.9, CH_2), 2.32 (1H, dd, J_1 16.6, J_2 5.7, CH_2), 5.08-5.11 (1H, m, CH); δ_C(125 MHz, $CDCl_3$) 17.6, 19.5 (2C), 24.2, 24.4, 25.5, 25.7, 30.5, 32.3, 36.2, 36.8, 37.0, 119.0, 124.9, 131.1. HRMS (FAB) calcd for $C_{15}H_{28}N$ (MH^+): 222.2216; found: 222.2224.

(3*S*,7*R*)-3,7,11-Trimethyldodec-10-en-1-ol (6).[3] To a stirred solution of **5** (1.00 g, 4.52 mmol) in CH_2Cl_2 (5.0 cm^3) was added dropwise DIBAL-H in THF (1.0 mol dm^{-3}, 4.97 cm^3, 4.97 mmol) at –78 °C under argon. After the mixture was stirred for 2 h, saturated aqueous solution of sodium potassium tartrate was added and the mixture was warmed to room temperature. The whole was extracted with Et_2O and the extract was dried over $MgSO_4$. The extract was concentrated under reduced pressure after filtration through a short pad of silica gel to give crude aldehyde. To a stirred solution of the aldehyde in CH_2Cl_2 (5.0 cm^3) was added dropwise DIBAL-H in THF (1.0 mol dm^{-3}, 4.97 cm^3, 4.97 mmol) at –78 °C under argon. After the mixture was stirred for 2 h, saturated aqueous solution of sodium potassium tartrate was added. The whole was extracted with Et_2O and the extract was dried

over $MgSO_4$. The extract was concentrated under reduced pressure, and the residue was purified by column chromatography to give the title alcohol **6** as a colorless oil (0.848 g, 83%). $[\alpha]^{25}_D$ –2.3 (*c* 0.90, $CHCl_3$); IR (neat) ν_{max}/cm^{-1}: 3299 (OH), 1058 (C-O); δ_H(500 MHz, $CDCl_3$) 0.86 (3H, d, *J* 6.3, CH_3), 0.90 (3H, d, *J* 6.3, CH_3), 1.07-1.41 (11H, m), 1.54-1.64 (1H, m), 1.61 (3H, s, CH_3), 1.69 (3H, s, CH_3), 1.89-2.03 (2H, m, CH_2), 3.64-3.73 (2H, m, CH_2), 5.09-5.11 (1H, m, CH); δ_C(125 MHz, $CDCl_3$) 17.6, 19.6, 19.7, 24.3, 25.6, 25.7, 29.5, 32.4, 37.0, 37.2, 37.5, 40.0, 61.3, 125.0, 124.9, 131.0. HRMS (FAB) calcd for $C_{15}H_{31}O$ (MH^+): 227.2369; found: 227.2363.

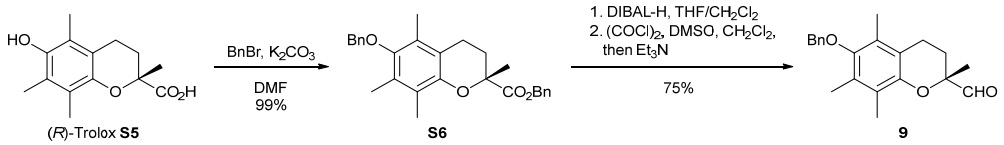
(3*R*,7*S*)-3,7,11-Trimethyldodec-10-en-1-ol (*ent*-6). According to the procedure described for the preparation of **6**, compound *ent*-**5** (900 mg, 4.07 mmol) was converted into *ent*-**6** as a colorless oil (606 mg, 66%). $[\alpha]^{25}_D$ +2.0 (*c* 1.05, $CHCl_3$); IR (neat) ν_{max}/cm^{-1}: 3299 (OH), 1055 (C-O); δ_H(500 MHz, $CDCl_3$) 0.86 (3H, d, *J* 6.3, CH_3), 0.90 (3H, d, *J* 6.3, CH_3), 1.04-1.41 (11H, m), 1.52-1.63 (1H, m), 1.60 (3H, s, CH_3), 1.68 (3H, s, CH_3), 1.89-2.03 (2H, m, CH_2), 3.64-3.73 (2H, m, CH_2), 5.08-5.12 (1H, m, CH); δ_C(125 MHz, $CDCl_3$) 17.6, 19.6, 19.7, 24.3, 25.6, 25.7, 29.5, 32.4, 37.0, 37.2, 37.5, 39.9, 61.3, 125.0, 124.9, 131.0. HRMS (FAB) calcd for $C_{15}H_{31}O$ (MH^+): 227.2369; found: 227.2363.

(6*R*,10*S*)-12-Bromo-2,6,10-trimethyldodec-2-ene (7). To a stirred solution of compound **6** (800 mg, 3.53 mmol) in pyridine (2.70 cm^3) was added TsCl (876 mg, 4.60 mmol) at 0 °C. After the mixture was stirred for 2 h, saturated aqueous solution of citric acid was added. The whole was extracted with Et_2O and the extract was washed with H_2O and brine, and dried over $MgSO_4$. The extract was concentrated under reduced pressure after filtration through a short pad of silica gel to give a crude sulfonate. To a stirred solution of the sulfonate in acetone (5 cm^3) was added LiBr (1.80 g, 17.7 mmol). After the mixture was stirred for 1 h under reflux, the whole was concentrated under reduced pressure. To the residue was added H_2O and the whole was extracted with Et_2O and dried over $MgSO_4$. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography to give the title bromide **7** as a colorless oil (923 mg, 90%). $[\alpha]^{25}_D$ +5.8 (*c* 1.00, $CHCl_3$); δ_H(500 MHz, $CDCl_3$) 0.86 (3H, d, *J* 6.9, CH_3), 0.89 (3H, d, *J* 6.9, CH_3), 1.04-1.41 (9H, m), 1.61 (3H, s, CH_3), 1.68 (3H, s, CH_3), 1.61-1.68 (2H, m), 1.85-2.03 (3H, m), 3.38-3.49 (2H, m, CH_2), 5.09-5.11 (1H, m, CH); δ_C(125 MHz, $CDCl_3$) 17.6, 19.0, 19.6, 24.1, 25.6, 25.7, 31.6, 32.3, 32.4, 36.8, 37.1 (2C), 40.0, 125.0, 131.0. *Anal*. calcd. for $C_{15}H_{29}Br$: C, 62.28; H, 10.10. Found: C, 62.31; H, 10.32.

(6*S*,10*R*)-12-Bromo-2,6,10-trimethyldodec-2-ene (*ent*-7). According to the procedure described for the preparation of **7**, compound *ent*-**6** (580 mg, 2.56 mmol) was converted into *ent*-**7** as a colorless oil (669 mg, 90%). $[\alpha]^{25}_D$ –5.8 (*c* 1.01, $CHCl_3$); δ_H(500 MHz, $CDCl_3$) 0.86 (3H, d, *J* 6.9, CH_3), 0.89 (3H, d, *J* 6.9, CH_3), 1.07-1.41 (9H, m), 1.61 (3H, s, CH_3), 1.68 (3H, s, CH_3), 1.61-1.68 (2H, m), 1.84-2.03 (3H, m), 3.38-3.49 (2H, m, CH_2), 5.09-5.11 (1H, m, CH); δ_C(125 MHz, $CDCl_3$) 17.6, 19.0, 19.6, 24.1, 25.6, 25.7, 31.6, 32.2, 32.4, 36.8, 37.1 (2C), 40.0, 125.0, 131.0. *Anal*. calcd. for $C_{15}H_{29}Br$: C, 62.28; H, 10.10. Found: C, 62.22; H, 10.08.

Triphenyl[(3*S*,7*R*)-3,7,11-trimethyldodec-10-en-1-yl]phosphonium Bromide (8). A mixture of the bromide **7** (757 mg, 2.61 mmol) and PPh_3 (750 mg, 2.87 mmol) was heated to 100 °C and the mixture was stirred for 15 h. After cooling, Et_2O was added to the mixture and the resulting white precipitate was washed with Et_2O to remove the excess PPh_3. The residue was dried under vacuum to give the title phosphonium salt **8**, which was used without further purification.

Triphenyl((3*R*,7*S*)-3,7,11-trimethyldodec-10-en-1-yl)phosphonium Bromide (*ent*-8). According to the procedure described for the preparation of **8**, compound *ent*-**7** (600 mg, 2.07 mmol) was converted into *ent*-**8**.



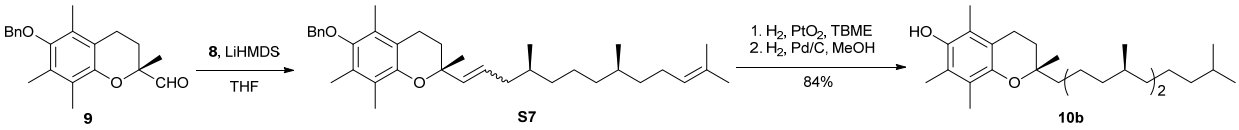
Benzyl (*R*)-6-(Benzyloxy)-2,5,7,8-tetramethylchromane-2-carboxylate (S6).[4] To a stirred solution of (*R*)-Trolox (**S5**, 1.90 g, 7.59 mmol) in DMF (13.0 cm^3) were added K_2CO_3 (8.38 g, 60.8 mmol) and BnBr (3.61 cm^3, 30.4 mmol) at room temperature. After the mixture was stirred overnight, the reaction was quenched with H_2O. The whole was extracted with Et_2O and the extract was washed with H_2O and brine, and dried over $MgSO_4$. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography to give the title compound **S6** as a colorless oil (3.24 g, 99%). $[\alpha]^{25}_D$ +38.6 (*c* 1.05, $CHCl_3$); IR (neat) ν_{max}/cm^{-1}: 1731 (C=O); δ_H(500 MHz, $CDCl_3$) 1.64 (3H, s, CH_3), 1.83-1.91 (1H, m, CH_2), 2.09 (3H, s, CH_3), 2.15 (3H, s, CH_3), 2.23 (3H, s, CH_3), 2.38-2.48 (2H, m, CH_2), 2.54-2.62 (1H, m, CH_2), 4.68 (2H, dd, J_1 13.2, J_2 11.5, CH_2), 5.04 (1H, d, *J* 12.6, CH_2), 5.15 (1H, d, *J* 12.6, CH_2), 7.09-7.51 (10H, m, Ar); δ_C(125 MHz, $CDCl_3$) 11.8, 11.9, 12.9, 20.9, 25.5, 30.6, 66.6, 74.7, 77.2, 117.3, 123.0, 126.0, 127.6 (2C), 127.7 (2C), 127.8, 128.0, 128.2, 128.4 (2C), 128.5 (2C), 135.7, 137.9, 148.0, 148.9, 173.7. HRMS (ESI) calcd for $C_{28}H_{30}NaO_4$ (MNa^+): 453.2036; found: 453.2039.

Benzyl (*S*)-6-(Benzyloxy)-2,5,7,8-tetramethylchromane-2-carboxylate (*ent*-S6). According to the procedure described for the preparation of **S6**, (*S*)-Trolox (*ent*-**S5**, 2.5 g, 10.0 mmol) was converted into *ent*-**S6** as a colorless oil (4.28 g, 99%). $[\alpha]^{25}_D$ –38.4 (*c* 1.27, $CHCl_3$); IR (neat) ν_{max}/cm^{-1}: 1731 (C=O); δ_H(500 MHz, $CDCl_3$) 1.64 (3H, s, CH_3), 1.83-1.91 (1H, m, CH_2), 2.09 (3H, s, CH_3), 2.15 (3H, s, CH_3), 2.23 (3H, s, CH_3), 2.38-2.48 (2H, m, CH_2), 2.54-2.62 (1H, m, CH_2), 4.68 (2H, dd, J_1 13.2, J_2 11.2 Hz, CH_2), 5.04 (1H, d, *J* 12.6, CH_2), 5.15 (1H, d, *J* 12.6, CH_2), 7.09-7.51 (10H, m, Ar); δ_C(125 MHz, $CDCl_3$) 11.8, 11.9, 12.9, 20.9, 25.5, 30.6, 66.6, 74.7, 77.2, 117.3, 123.0, 126.0, 127.6 (2C), 127.7 (2C), 127.8, 128.0, 128.2, 128.4 (2C), 128.5 (2C), 135.7, 137.9, 148.0, 148.9, 173.7. HRMS (ESI) calcd for $C_{28}H_{30}NaO_4$ (MNa^+): 453.2036; found: 453.2026.

(*R*)-6-(Benzyloxy)-2,5,7,8-tetramethylchromane-2-carbaldehyde (9).[4] To a stirred solution of compound **S6** (3.24 g, 7.53 mmol) in CH_2Cl_2 (8.2 cm^3) was added dropwise DIBAL-H in THF (1.0 M,

15.2 cm^3, 15.2 mmol) at –78 °C under argon. After the mixture was stirred for 2 h, saturated aqueous solution of sodium potassium tartrate was added. The whole was extracted with Et_2O and the extract was dried over $MgSO_4$. Filtration through a short pad of silica gel and concentration under reduced pressure gave a crude alcohol. To a stirred solution of $(COCl)_2$ (0.881 cm^3, 15.2 mmol) in CH_2Cl_2 (60.0 cm^3) was slowly added DMSO (1.97 cm^3, 30.4 mmol) in CH_2Cl_2 (9.0 cm^3) at –78 °C under argon. After the mixture was stirred for 15 min, the above alcohol in CH_2Cl_2 (41.5 cm^3) was added dropwise, and stirred for 30 min. Et_3N (6.36 cm^3, 45.6 mmol) was slowly added to the mixture and the mixture was warmed to 0 °C. After the mixture was stirred for 30 min, saturated NH_4Cl aq. was added. The whole was extracted with Et_2O, the extract was washed with H_2O and brine, and was dried over Na_2SO_4. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography. Recrystallization from $CHCl_3$/hexane at –20 °C gave the title compound **9** as white solid (1.85 g, 75%): mp 60–61 °C (from $CHCl_3$/hexane); $[\alpha]^{25}_D$ –13.6 (*c* 0.90, $CHCl_3$); IR (neat) ν_{max}/cm^{-1}: 1737 (C=O); δ_H(500 MHz, $CDCl_3$) 1.41 (3H, s, CH_3), 1.80-1.86 (1H, m, CH_2), 2.13 (3H, s, CH_3), 2.20 (3H, s, CH_3), 2.24 (3H, s, CH_3), 2.25-2.29 (1H, m, CH_2), 2.50-2.63 (2H, m, CH_2), 4.68 (2H, s, CH_2), 7.33-7.50 (5H, m, Ar), 9.64 (1H, d, *J* 1.1, CHO); δ_C(125 MHz, $CDCl_3$) 11.9, 12.0, 12.9, 20.2, 21.6, 27.7, 74.7, 80.4, 117.7, 123.1, 126.4, 127.7 (2C), 127.9, 128.5 (2C), 128.6, 137.7, 147.4, 149.1, 204.4. *Anal*. calcd. for $C_{21}H_{24}O_3$: C, 77.75; H, 7.46. Found: C, 77.50; H, 7.49.

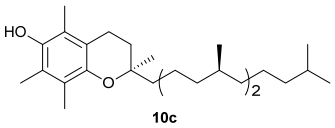
(*S*)-6-(Benzyloxy)-2,5,7,8-tetramethylchromane-2-carbaldehyde (*ent*-9). According to the procedure described for the preparation of **9**, *ent*-**S6** (3.90 g, 9.06 mmol) was converted into *ent*-**9** as white solid (2.10 g, 71%): mp 59–61 °C (from $CHCl_3$/hexane); $[\alpha]^{25}_D$ +12.5 (*c* 1.00, $CHCl_3$); IR (neat) ν_{max}/cm^{-1}: 1737 (C=O); δ_H(500 MHz, $CDCl_3$) 1.41 (3H, s, CH_3), 1.80-1.86 (1H, m, CH_2), 2.13 (3H, s, CH_3), 2.20 (3H, s, CH_3), 2.24 (3H, s, CH_3), 2.25-2.29 (1H, m, CH_2), 2.50-2.63 (2H, m, CH_2), 4.68 (2H, s, CH_2), 7.34-7.50 (5H, m, Ar), 9.64 (1H, d, *J* 1.1, CHO); δ_C(125 MHz, $CDCl_3$) 11.9, 12.0, 12.9, 20.3, 21.6, 27.7, 74.7, 80.4, 117.7, 123.1, 126.4, 127.7 (2C), 127.9, 128.5 (2C), 128.6, 137.7, 147.4, 149.1, 204.4. *Anal*. calcd. for $C_{21}H_{24}O_3$: C, 77.75; H, 7.46. Found: C, 77.52; H, 7.55.



9 **S7** **10b**

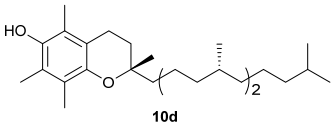
(*S*)-2,5,7,8-Tetramethyl-2-((4*S*,8*S*)-4,8,12-trimethyltridecyl)chroman-6-ol (10b).[5] To a stirred solution of phosphonium salt **8** (ca. 2.61 mmol) in THF (15.0 cm^3) was added LiHMDS (1.0 mol dm^{-3}, 2.30 cm^3, 2.30 mmol) in THF dropwise at –40 °C under argon. After the mixture was stirred for 30 min, the aldehyde **9** (675 mg, 2.08 mmol) in THF (5.0 cm^3) was added to the mixture. The stirring was continued for 30 min at the same temperature and for 1 h at 0 °C. After the reaction was quenched with saturated aqueous solution of NH_4Cl, the whole was extracted with Et_2O and the extract was washed with H_2O and brine, and dried over Na_2SO_4. The filtrate was concentrated under reduced pressure. The oily residue was dissolved in hexane and the solution was filtrated through a short pad of silica gel and concentrated down to give crude **S7**. To a stirred solution of **S7** in TBME (9.5 cm^3) was added PtO_2 (37.8 mg, 0.167 mmol). The mixture was stirred under an atmosphere of H_2 at room temperature. After

30 min, the reaction mixture was filtrated through Celite and the filtrate was concentrated. To a stirred solution of the residue in MeOH (35.0 cm^3) was added 10% Pd/C (222 mg, 0.208 mmol). The mixture was stirred under an atmosphere of H_2 at room temperature. After 30 min, the reaction mixture was filtrated through Celite. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography to give the title compound **10b** as a pale yellow oil (759 mg, 84%). $[\alpha]^{25}_D$ –0.7 (*c* 1.01, $CHCl_3$); δ_H(500 MHz, $CDCl_3$) 0.83-0.87 (12H, m, $4CH_3$), 1.02-1.53 (21H, m), 1.23 (3H, s, CH_3), 1.73-1.84 (2H, m, CH_2), 2.11 (6H, s, $2CH_3$), 2.16 (3H, s, CH_3), 2.60 (2H, t, *J* 6.9, CH_2), 4.17 (1H, s, OH); δ_C(125 MHz, $CDCl_3$) 11.3, 11.8, 12.2, 19.6, 19.7, 20.7, 21.0, 22.6, 22.7, 23.8, 24.4, 24.8, 28.0, 31.5, 32.7, 32.9, 37.3, 37.4 (3C), 39.4, 39.8, 74.5, 117.3, 118.4, 121.0, 122.6, 144.5, 145.5. HRMS (ESI) calcd for $C_{29}H_{50}O_2$ (M^+): 430.3811; found: 430.3806.



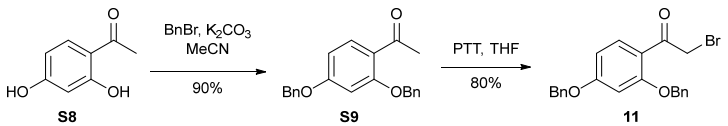
10c

(*R*)-2,5,7,8-Tetramethyl-2-((4*S*,8*S*)-4,8,12-trimethyltridecyl)chroman-6-ol (10c). According to the procedure described for the preparation of **10b**, compound *ent*-**9** (675 mg, 2.07 mmol) was converted into compound **10c** by the reaction with **8** (ca. 2.61 mmol) as a pale yellow oil (573 mg, 57%). $[\alpha]^{25}_D$ +1.0 (*c* 1.10, $CHCl_3$); δ_H(500 MHz, $CDCl_3$) 0.83-0.87 (12H, m, $4CH_3$), 1.03-1.58 (21H, m), 1.23 (3H, s, CH_3), 1.73-1.84 (2H, m, CH_2), 2.11 (6H, s, $2CH_3$), 2.16 (3H, s, CH_3), 2.60 (2H, t, *J* 6.9, CH_2), 4.17 (1H, s, OH); δ_C(125 MHz, $CDCl_3$) 11.3, 11.8, 12.2, 19.7 (2C), 20.8, 21.0, 22.6, 22.7, 23.8, 24.4, 24.8, 28.0, 31.4, 32.7, 32.8, 37.3, 37.4 (2C), 37.5, 39.4, 39.8, 74.5, 117.3, 118.4, 121.0, 122.6, 144.5, 145.5. HRMS (ESI) calcd for $C_{29}H_{50}O_2$ (M^+): 430.3811; found: 430.3803.



10d

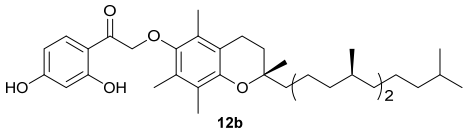
(*S*)-2,5,7,8-Tetramethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecy)chroman-6-ol (10d). According to the procedure described for the preparation of **10b**, compound **9** (540 mg, 1.66 mmol) was converted into compound **10d** by the reaction with *ent*-**8** (ca. 2.08 mmol) as a pale yellow oil (573 mg, 80%). $[\alpha]^{25}_D$ –1.0 (*c* 1.00, $CHCl_3$); δ_H(500 MHz, $CDCl_3$) 0.83-0.87 (12H, m, $4CH_3$), 1.03-1.58 (21H, m), 1.23 (3H, s, CH_3), 1.73-1.84 (2H, m, CH_2), 2.11 (6H, s, $2CH_3$), 2.16 (3H, s, CH_3), 2.60 (2H, t, *J* 6.9, CH_2), 4.17 (1H, s, OH); δ_C(125 MHz, $CDCl_3$) 11.3, 11.8, 12.2, 19.7 (2C), 20.8, 21.0, 22.6, 22.7, 23.8, 24.4, 24.8, 28.0, 31.5, 32.7, 32.9, 37.3, 37.4 (2C), 37.5, 39.4, 39.8, 74.5, 117.3, 118.4, 121.0, 122.6, 144.5, 145.5. HRMS(ESI) calcd for $C_{29}H_{50}O_2$ (M^+): 430.3811; found: 430.3801.



1-[2,4-Bis(benzyloxy)phenyl]ethan-1-one (S9).[6] To a stirred solution of 2,4-dihydroxyaceto-phenone (**S8**, 5.00 g, 32.9 mmol) in MeCN (100 cm^3) were added K_2CO_3 (13.6 g, 98.7 mmol) and

BnBr (8.59 cm^3, 72.3 mmol). The mixture was stirred under reflux. After the mixture was stirred overnight, the reaction mixture was filtrated through Celite. After concentration, the residue was dissolved in Et_2O. The whole was washed with H_2O and brine, and dried over $MgSO_4$. The filtrate was concentrated under reduced pressure. Recrystallization from $CHCl_3$/hexane gave the title compound **S9** as colorless crystals (9.5 g, 90%): mp 75–77 °C (from $CHCl_3$/hexane); IR (neat) ν_{max}/cm^{-1}: 1661 (C=O); δ_H(500 MHz, $CDCl_3$) 2.55 (3H, s, CH_3), 5.09 (2H, s, CH_2), 5.11 (2H, s, CH_2), 6.60-6.63 (2H, m, Ar), 7.34-7.44 (10H, m, Ar), 7.85 (1H, dd, J_1 7.7, J_2 1.4, Ar); δ_C(125 MHz, $CDCl_3$) 32.2, 70.2, 70.7, 100.3, 106.2, 121.7, 127.5 (2C), 127.6 (2C), 128.3 (2C), 128.7 (4C), 132.7, 136.0, 136.1, 160.1, 163.5, 197.8. *Anal*. calcd. for $C_{22}H_{20}O_3$: C, 79.50; H, 6.07. Found: C, 79.56; H, 6.13.

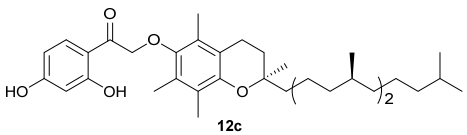
1-[2,4-Bis(benzyloxy)phenyl]-2-bromoethan-1-one (11).[7] A solution of phenyltrimethylammonium tribromide (PTT; 4.51 g, 12.0 mmol) in THF (14.6 cm^3) was slowly added to compound **S9** (4.00 g, 12.0 mmol) at 0 °C. After the mixture was stirred for 2.5 h at room temperature, the reaction was quenched with H_2O. The whole was extracted with Et_2O and the extract was washed with H_2O and brine, and dried over $MgSO_4$. The filtrate was concentrated under reduced pressure. Recrystallization from $CHCl_3$/hexane gave the title compound **11** as pink crystals (3.98 g, 80%): mp 78–80 °C (from $CHCl_3$/hexane); IR (neat) ν_{max}/cm^{-1}: 1671 (C=O); δ_H(500 MHz, $CDCl_3$) 4.50 (2H, s, CH_2), 5.09 (2H, s, CH_2), 5.13 (2H, s, CH_2), 6.61 (1H, d, *J* 2.3, Ar), 6.65 (1H, dd, J_1 8.6, J_2 2.3, Ar), 7.34-7.45 (10H, m, Ar), 7.91 (1H, d, *J* 8.6, Ar); δ_C(125 MHz, $CDCl_3$) 37.8, 70.4, 71.1, 100.1, 107.0, 118.3, 127.5 (2C), 127.8 (2C), 128.4, 128.6, 128.7 (2C), 128.9 (2C), 133.9, 135.4, 135.9, 160.0, 164.3. *Anal*. calcd. for $C_{22}H_{19}BrO_3$: C, 64.25; H, 4.66. Found: C, 64.32; H, 4.75.



12b

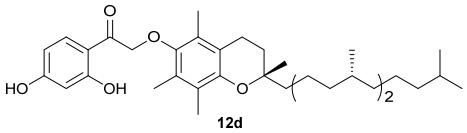
1-(2,4-Dihydroxyphenyl)-2-{[(*S*)-2,5,7,8-tetramethyl-2-((4*S*,8*S*)-4,8,12-trimethyltridecyl)-chroman-6-yl]oxy}ethan-1-one (12b). To a stirred solution of compound **10b** (600 mg, 1.39 mmol) in DMF (1.4 cm^3) were added K_2CO_3 (385 mg, 2.78 mmol) and compound **11** (745 mg, 1.81 mmol) at room temperature. After the mixture was stirred overnight, the reaction was quenched with H_2O. The whole was extracted with Et_2O and the extract was washed with H_2O and brine, and dried over $MgSO_4$. The filtrate was concentrated under reduced pressure. To a stirred solution of the residue in EtOAc (15.0 cm^3) was added 10% Pd/C (149 mg, 0.140 mmol). The mixture was stirred under an atmosphere of H_2 at room temperature. After the reaction was completed, the reaction mixture was filtrated through Celite. Purification by column chromatography gave the title compound **12b** as pale yellow solid (583 mg, 72%): mp 87–88 °C (from EtOAc/hexane); $[\alpha]^{25}_D$ –4.0 (*c* 1.01, $CHCl_3$); IR (neat) ν_{max}/cm^{-1}: 3315 (OH), 1627 (C=O); δ_H(500 MHz, $CDCl_3$) 0.84-0.87 (12H, m, 4CH_3), 1.04-1.57 (21H, m), 1.24 (3H, s, CH_3), 1.73-1.85 (2H, m, CH_2), 2.09 (3H, s, CH_3), 2.14 (3H, s, CH_3), 2.18 (3H, s, CH_3), 2.58 (2H, t, *J* 6.6, CH_2), 4.92 (2H, s, CH_2), 5.80 (1H, br s, OH), 6.36 (1H, dd, J_1 8.6, J_2 2.3 Hz, Ar), 6.42 (1H, d, *J* 2.3, Ar), 7.52 (1H, d, *J* 7.7, Ar), 12.40 (1H, s, OH); δ_C(125 MHz, $CDCl_3$) 11.8, 11.9, 12.8, 19.7 (2C), 20.6, 21.0, 22.6, 22.7, 23.8, 24.4, 24.8, 28.0, 31.2, 32.7, 32.8, 37.3, 37.4 (3C), 39.4, 40.0, 74.0, 75.0,

103.8, 108.0, 111.9, 117.8, 123.2, 125.7, 127.6, 130.9, 147.8, 148.3, 162.8, 165.3, 198.0. *Anal*. calcd. for $C_{37}H_{56}O_5$: C, 76.51; H, 9.72. Found: C, 76.41; H, 9.89.



12c

1-(2,4-Dihydroxyphenyl)-2-{[(*R*)-2,5,7,8-tetramethyl-2-((4*S*,8*S*)-4,8,12-trimethyltridecyl)chroman-6-yl]oxy}ethan-1-one (12c). According to the procedure described for the preparation of **12b**, compound **10c** (100 mg, 0.232 mmol) was converted into compound **12c** as pale yellow solid (88.9 mg, 66%): mp 86–87 °C (from EtOAc/hexane); $[\alpha]^{25}_D$ +3.7 (*c* 0.55, $CHCl_3$); IR (neat) ν_{max}/cm^{-1}: 3351 (OH), 1626 (C=O); δ_H(500 MHz, $CDCl_3$) 0.84-0.87 (12H, m, $4CH_3$), 1.04-1.61 (21H, m), 1.24 (3H, s, CH_3), 1.73-1.85 (2H, m, CH_2), 2.08 (3H, s, CH_3), 2.14 (3H, s, CH_3), 2.18 (3H, s, CH_3), 2.58 (2H, t, *J* 6.6, CH_2), 4.92 (2H, s, CH_2), 6.36 (1H, dd, J_1 8.9, J_2 2.6, Ar), 6.42 (1H, d, *J* 2.3, Ar), 7.51 (1H, d, *J* 7.7, Ar), 12.40 (1H, s, OH); δ_C(125 MHz, $CDCl_3$) 11.8, 11.9, 12.8, 19.7 (2C), 20.6, 21.0, 22.6, 22.7, 23.8, 24.4, 24.8, 28.0, 31.1, 32.7, 32.8, 37.3, 37.4 (2C), 37.5, 39.4, 40.1, 74.0, 75.0, 103.8, 108.1, 111.9, 117.8, 123.2, 125.7, 127.6, 130.9, 147.8, 148.3, 162.9, 165.3, 198.0. *Anal*. calcd. for $C_{37}H_{56}O_5$: C, 76.51; H, 9.72. Found: C, 76.35; H, 9.79.



12d

1-(2,4-Dihydroxyphenyl)-2-{[(*S*)-2,5,7,8-tetramethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl)chroman-6-yl]oxy}ethan-1-one (12d). According to the procedure described for the preparation of **12b**, compound **10d** (500 mg, 1.16 mmol) was converted into compound **12d** as pale yellow solid (483 mg, 72%): mp 86–87 °C (from EtOAc/hexane); $[\alpha]^{25}_D$ –3.9 (*c* 1.11, $CHCl_3$); IR (neat) ν_{max}/cm^{-1}: 3350 (OH), 1626 (C=O); δ_H(500 MHz, $CDCl_3$) 0.84-0.87 (12H, m, $4CH_3$), 1.04-1.61 (21H, m), 1.24 (3H, s, CH_3), 1.73-1.85 (2H, m, CH_2), 2.08 (3H, s, CH_3), 2.14 (3H, s, CH_3), 2.18 (3H, s, CH_3), 2.58 (2H, t, *J* 6.9, CH_2), 4.92 (2H, s, CH_2), 6.36 (1H, dd, J_1 8.9, J_2 2.6, Ar), 6.42 (1H, d, *J* 2.9, Ar), 7.51 (1H, d, *J* 9.2, Ar), 12.40 (1H, s, OH); δ_C(125 MHz, $CDCl_3$) 11.8, 11.9, 12.8, 19.7 (2C), 20.6, 21.0, 22.6, 22.7, 23.8, 24.4, 24.8, 28.0, 31.1, 32.7, 32.8, 37.3, 37.4 (2C), 37.5, 39.4, 40.1, 74.0, 75.0, 103.8, 108.1, 111.8, 117.8, 123.2, 125.7, 127.6, 130.9, 147.7, 148.3, 163.0, 165.3, 198.0. HRMS (ESI) calcd for $C_{37}H_{57}O_5$ (MH^+): 581.4201; found: 581.4207.

7-Hydroxy-3-{[(*S*)-2,5,7,8-tetramethyl-2-((4*S*,8*S*)-4,8,12-trimethyltridecyl)chroman-6-yl]oxy}-4*H*-chromen-4-one (1b: *ent*-NP843). To a stirred solution of compound **12b** (100 mg, 0.172 mmol) in THF (0.76 cm^3) was added DMF-DMA (0.0277 cm^3, 0.260 mmol) under argon, and the mixture was stirred under reflux for 4 h. Then, aqueous 1*N* HCl (1 cm^3) and MeOH (1 cm^3) were added and the mixture was stirred overnight. The whole was extracted with Et_2O and dried over Na_2SO_4. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography to give the title compound **1b** as white solid (23.3 mg, 23%): mp 228–229 °C (from

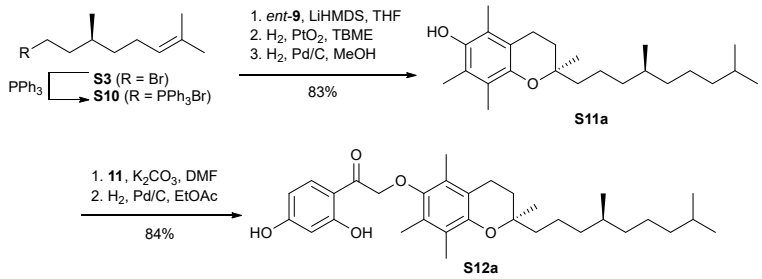
EtOAc); $[\alpha]^{25}_D$ –5.3 (*c* 1.00, $CHCl_3$); IR (neat) ν_{max}/cm^{-1}: 3133 (OH); δ_H(500 MHz, $CDCl_3$) 0.84-0.87 (12H, m, $4CH_3$), 1.03-1.59 (21H, m), 1.25 (3H, s, CH_3), 1.75-1.85 (2H, m, CH_2), 2.02 (3H, s, CH_3), 2.06 (3H, s, CH_3), 2.09 (3H, s, CH_3), 2.58 (2H, t, *J* 6.9, CH_2), 6.86 (1H, d, *J* 2.3, Ar), 7.07-7.10 (2H, m, Ar), 8.22 (1H, d, *J* 9.2, Ar), 8.55 (1H, br s, OH); δ_C(125 MHz, $CDCl_3$) 11.8 (2C), 12.6, 19.6, 19.7, 20.6, 21.0, 22.6, 22.7, 23.8, 24.4, 24.8, 28.0, 31.2, 32.7, 32.8, 37.3, 37.4 (3C), 39.4, 40.0, 75.2, 102.7, 115.5, 117.0, 118.2, 123.7, 125.3, 127.1, 127.6, 140.0, 142.8, 143.4, 149.0, 157.8, 162.1, 172.6. *Anal*. calcd. for $C_{38}H_{54}O_5$: C, 77.25; H, 9.21. Found: C, 77.22; H, 9.43.

7-Hydroxy-3-{[(*R*)-2,5,7,8-tetramethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl)chroman-6-yl]oxy}-4*H*-chromen-4-one (1a, NP843). mp 228–229 °C (from EtOAc); $[\alpha]^{25}_D$ +5.0 (*c* 1.00, $CHCl_3$); IR (neat) ν_{max}/cm^{-1}: 3163 (OH); δ_H(500 MHz, $CDCl_3$) 0.84-0.87 (12H, m, $4CH_3$), 1.03-1.59 (21H, m), 1.25 (3H, s, CH_3), 1.75-1.85 (2H, m, CH_2), 2.02 (3H, s, CH_3), 2.06 (3H, s, CH_3), 2.09 (3H, s, CH_3), 2.58 (2H, t, *J* 6.9, CH_2), 6.86 (1H, d, *J* 2.3, Ar), 7.07-7.10 (2H, m, Ar), 8.22 (1H, d, *J* 9.2, Ar), 8.67 (1H, br s, OH); δ_C(125 MHz, $CDCl_3$) 11.8 (2C), 12.6, 19.6, 19.7, 20.6, 21.0, 22.6, 22.7, 23.7, 24.4, 24.8, 28.0, 31.2, 32.7, 32.8, 37.3, 37.4 (3C), 39.4, 40.0, 75.3, 102.7, 115.5, 117.0, 118.2, 123.7, 125.3, 127.1, 127.6, 140.0, 142.8, 143.4, 149.0, 157.8, 162.2, 172.6. *Anal*. calcd. for $C_{38}H_{54}O_5$: C, 77.25; H, 9.21. Found: C, 77.13; H, 9.40.

7-Hydroxy-3-{[(*R*)-2,5,7,8-tetramethyl-2-((4*S*,8*S*)-4,8,12-trimethyltridecyl)chroman-6-yl]oxy}-4*H*-chromen-4-one (1c). According to the procedure described for the preparation of **1b**, compound **12c** (50.0 mg, 0.0861 mmol) was converted into compound **1c** as white solid (12.2 mg, 24%): mp 229–231 °C (from EtOAc); $[\alpha]^{25}_D$ +5.4 (*c* 1.01, $CHCl_3$); IR (neat) ν_{max}/cm^{-1}: 3125 (OH); δ_H(500 MHz, $CDCl_3$) 0.84-0.87 (12H, m, $4CH_3$), 1.03-1.64 (21H, m), 1.25 (3H, s, CH_3), 1.75-1.85 (2H, m, CH_2), 2.02 (3H, s, CH_3), 2.06 (3H, s, CH_3), 2.09 (3H, s, CH_3), 2.58 (2H, t, *J* 6.9, CH_2), 6.86 (1H, d, *J* 2.3, Ar), 7.07-7.10 (2H, m, Ar), 8.22 (1H, d, *J* 9.2, Ar), 8.57 (1H, br s, OH); δ_C(125 MHz, $CDCl_3$) 11.8 (2C), 12.6, 19.7 (2C), 20.6, 21.0, 22.6, 22.7, 23.7, 24.4, 24.8, 28.0, 31.1, 32.7, 32.8, 37.3, 37.4 (3C), 39.4, 40.0, 75.3, 102.7, 115.5, 117.0, 118.3, 123.7, 125.3, 127.1, 127.6, 140.0, 142.8, 143.4, 149.1, 157.8, 162.1, 172.6. *Anal*. calcd. for $C_{38}H_{54}O_5 \cdot 0.15$EtOAc: C, 76.75; H, 9.21. Found: C, 76.40; H, 9.21.

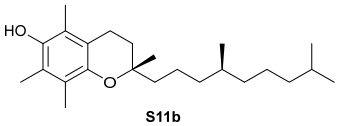
7-Hydroxy-3-{[(*S*)-2,5,7,8-tetramethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl)chroman-6-yl]oxy}-4*H*-chromen-4-one (1d). According to the procedure described for the preparation of **1b**, compound **12d** (100 mg, 0.172 mmol) was converted into compound **1d** as white solid (23.5 mg, 23%): mp 229–231 °C (from EtOAc); $[\alpha]^{25}_D$ –5.4 (*c* 0.95, $CHCl_3$); IR (neat) ν_{max}/cm^{-1}: 3126 (OH); δ_H(500 MHz, $CDCl_3$) 0.84-0.87 (12H, m, $4CH_3$), 1.03-1.64 (21H, m), 1.25 (3H, s, CH_3), 1.75-1.85 (2H, m, CH_2), 2.02 (3H, s, CH_3), 2.06 (3H, s, CH_3), 2.09 (3H, s, CH_3), 2.58 (2H, t, *J* 6.9, CH_2), 6.86 (1H, d, *J* 2.3, Ar), 7.07-7.10 (2H, m, Ar), 8.22 (1H, d, *J* 9.2, Ar), 8.51 (1H, br s, OH); δ_C(125 MHz, $CDCl_3$) 11.8 (2C), 12.6, 19.7 (2C), 20.6, 21.0, 22.6, 22.7, 23.8, 24.4, 24.8, 28.0, 31.1, 32.7, 32.8, 37.3, 37.4 (3C), 39.4, 40.0, 75.3, 102.7, 115.4, 117.0, 118.3, 123.7, 125.3, 127.1, 127.6, 139.9, 142.8, 143.4, 149.1, 157.8, 162.1, 172.6. *Anal*. calcd. for $C_{38}H_{54}O_5$: C, 77.25; H, 9.21. Found: C, 77.36; H, 9.32.

Synthesis of Compounds 13a,b



(*S*)-(3,7-Dimethyloct-6-en-1-yl)triphenylphosphonium Bromide (S10). According to the procedure described for the preparation of **8**, (*S*)-citronellyl bromide (3.99 g, 18.2 mmol) was converted into compound **S10**, which was used without further purification.

(*R*)-2-((*S*)-4,8-Dimethylnonyl)-2,5,7,8-tetramethylchroman-6-ol (S11a). According to the procedure described for the preparation of **10b**, compound *ent*-**9** (800 mg, 2.47 mmol) was converted into compound **S11a** using the phosphonium salt **S10** (ca. 4.93 mmol) as a pale yellow oil (735 mg, 83%). $[\alpha]^{25}_{D}$ +0.4 (*c* 1.00, $CHCl_3$); δ_H(500 MHz, $CDCl_3$) 0.83-0.88 (9H, m, $3CH_3$), 1.05-1.53 (14H, m), 1.23 (3H, s, CH_3), 1.73-1.84 (2H, m, CH_2), 2.11 (6H, s, $2CH_3$), 2.16 (3H, s, CH_3), 2.60 (2H, t, *J* 6.9, CH_2), 4.18 (1H, s, OH); δ_C(125 MHz, $CDCl_3$) 11.3, 11.8, 12.2, 19.7 (2C), 21.0, 22.6, 22.7, 23.8, 24.7, 28.0, 31.5, 32.7, 37.2, 37.5, 39.3, 39.8, 74.5, 117.3, 118.4, 121.0, 122.6, 144.5, 145.5. HRMS (ESI) calcd for $C_{24}H_{40}O_2$ (M^+): 360.3028; found: 360.3026.

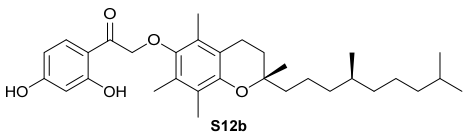


S11b

(*S*)-2-((*S*)-4,8-Dimethylnonyl)-2,5,7,8-tetramethylchroman-6-ol (S11b). According to the procedure described for the preparation of **10b**, compound **9** (800 mg, 2.47 mmol) was converted into compound **S11b** using phosphonium salt **S10** (ca. 4.93 mmol) as a pale yellow oil (730 mg, 82%). $[\alpha]^{25}_{D}$ +1.5 (*c* 1.00, $CHCl_3$); δ_H(500 MHz, $CDCl_3$) 0.83-0.88 (m, 9H), 1.04-1.53 (m, 14H), 1.23 (s, 3H), 1.73-1.84 (m, 2H), 2.11 (s, 6H), 2.16 (s, 3H), 2.60 (t, *J* = 6.9 Hz, 2H), 4.18 (s, 1H); δ_C(125 MHz, $CDCl_3$) 11.3, 11.8, 12.2, 19.6, 20.7, 21.0, 22.6, 22.7, 23.8, 24.8, 28.0, 31.5, 32.7, 37.3, 37.5, 39.3, 39.7, 74.5, 117.3, 118.4, 121.0, 122.6, 144.5, 145.5. HRMS (ESI) calcd for $C_{24}H_{40}O_2$ (M^+): 360.3028; found: 360.3035.

1-(2,4-Dihydoxyphenyl)-2-{[(*R*)-2-((*S*)-4,8-dimethylnonyl)-2,5,7,8-tetramethylchroman-6-yl]-oxy}ethan-1-one (S12a). According to the procedure described for the preparation of **12b**, compound **S11a** (700 mg, 1.94 mmol) was converted into compound **S12a** as a pale yellow solid (916 mg, 84%): mp 89–91 °C (from EtOAc/hexane); $[\alpha]^{25}_{D}$ +3.8 (*c* 0.70, $CHCl_3$); IR (neat) ν_{max}/cm^{-1}: 3341 (OH), 1626 (C=O); δ_H(500 MHz, $CDCl_3$) 0.84-0.87 (9H, m, $3CH_3$), 1.06-1.61 (14H, m), 1.24 (3H, s, CH_3), 1.73-1.85 (2H, m, CH_2), 2.09 (3H, s, CH_3), 2.14 (3H, s, CH_3), 2.18 (3H, s, CH_3), 2.57 (2H, t, *J* 6.6, CH_2), 4.93 (2H, s, CH_2), 6.37 (1H, dd, J_1 8.9, J_2 2.6, Ar), 6.42 (1H, d, *J* 2.9, Ar), 7.49 (1H, d, *J* 8.6, Ar), 12.37 (1H, s, OH); δ_C(125 MHz, $CDCl_3$) 11.8, 11.9, 12.8, 19.6, 20.6, 21.0, 22.6, 22.7, 23.8, 24.7, 28.0,

31.1, 32.7, 37.2, 37.5, 39.3, 40.0, 73.9, 75.0, 103.8, 108.2, 111.7, 117.8, 123.2, 125.7, 127.6, 130.8, 147.7, 148.3, 163.2, 165.3, 198.0. HRMS (ESI) calcd for $C_{32}H_{47}O_5$ (MH^+): 511.3418; found: 511.3414.



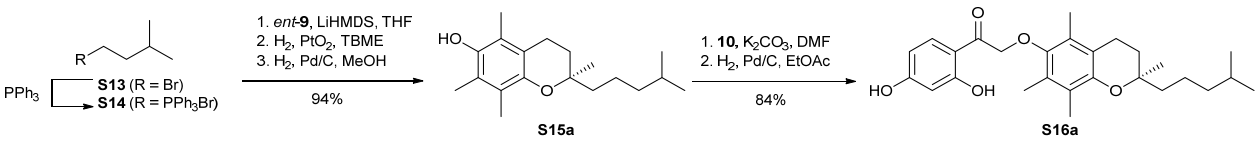
S12b

1-(2,4-Dihydroxyphenyl)-2-{[(*S*)-2-((*S*)-4,8-dimethylnonyl)-2,5,7,8-tetramethylchroman-6-yl-]oxy}ethan-1-one (S12b). According to the procedure described for the preparation of **12b**, compound **S11b** (700 mg, 1.94 mmol) was converted into compound **S12b** as a pale yellow solid (766 mg, 79%): mp 89–91 °C (from EtOAc/hexane); $[\alpha]^{25}_D$ –3.7 (*c* 0.62, $CHCl_3$); IR (neat) ν_{max}/cm^{-1}: 3363 (OH), 1626 (C=O); δ_H(500 MHz, $CDCl_3$) 0.84-0.87 (9H, m, $3CH_3$), 1.03-1.60 (14H, m), 1.24 (3H, s, CH_3), 1.73-1.85 (2H, m, CH_2), 2.09 (3H, s, CH_3), 2.14 (3H, s, CH_3), 2.18 (3H, s, CH_3), 2.57 (2H, t, *J* 6.6, CH_2), 4.93 (2H, s, CH_2), 6.26 (s, 1H), 6.37 (1H, dd, J_1 9.2, J_2 2.3, Ar), 6.42 (1H, d, *J* 2.9, Ar), 7.50 (1H, d, *J* 9.2, Ar), 12.38 (1H, s, OH); δ_C(125 MHz, $CDCl_3$) 11.8, 11.9, 12.8, 19.6, 20.6, 21.0, 22.6, 22.7, 23.8, 24.7, 28.0, 31.2, 32.7, 37.3, 37.5, 39.3, 40.0, 73.9, 75.0, 103.8, 108.2, 111.7, 117.8, 123.2, 125.7, 127.6, 130.9, 147.7, 148.3, 163.1, 165.3, 198.0. HRMS (ESI) calcd for $C_{32}H_{47}O_5$ (MH^+): 511.3418; found: 511.3419.

3-{[(*R*)-2-((*S*)-4,8-Dimethylnonyl)-2,5,7,8-tetramethylchroman-6-yl]oxy}-7-hydroxy-4*H*-chromen-4-one (13a). According to the procedure described for the preparation of **1b**, compound **S12a** (100 mg, 0.196 mmol) was converted into compound **13a** as a white solid (20.5 mg, 20%): mp 239–241 °C (from EtOAc); $[\alpha]^{25}_D$ +5.4 (*c* 0.33, $CHCl_3$); IR (neat) ν_{max}/cm^{-1}: 3116 (OH); δ_H(500 MHz, $CDCl_3$) 0.84-0.87 (9H, m, $3CH_3$), 1.06-1.61 (14H, m), 1.25 (3H, s, CH_3), 1.75-1.85 (2H, m, CH_2), 2.02 (3H, s, CH_3), 2.05 (3H, s, CH_3), 2.09 (3H, s, CH_3), 2.58 (2H, t, *J* 6.7, CH_2), 6.86 (1H, d, *J* 2.3, Ar), 7.07-7.10 (2H, m, Ar), 8.22 (1H, d, *J* 8.7, Ar), 8.59 (1H, br s, OH); δ_C(125 MHz, $CDCl_3$) 11.8 (2C), 12.7, 19.6, 20.6, 21.0, 22.6, 22.7, 23.8, 24.7, 28.0, 31.1, 32.7, 37.2, 37.5, 39.3, 39.9, 75.3, 102.7, 115.5, 117.0, 118.3, 123.7, 125.3, 127.1, 127.6, 140.0, 142.8, 143.4, 149.0, 157.8, 162.1, 172.6. *Anal*. calcd. for $C_{33}H_{44}O_5 \cdot 0.25$EtOAc: C, 75.24; H, 8.54. Found: C, 75.08; H, 8.60.

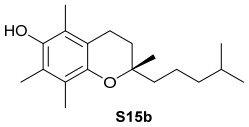
3-{[(*S*)-2-((*S*)-4,8-Dimethylnonyl)-2,5,7,8-tetramethylchroman-6-yl]oxy}-7-hydroxy-4*H*-chromen-4-one (13b). According to the procedure described for the preparation of **1b**, compound **S12b** (100 mg, 0.196 mmol) was converted into compound **13b** as a white solid (23.4 mg, 23%): mp 239–241 °C (from EtOAc); $[\alpha]^{25}_D$ –5.6 (*c* 0.39, $CHCl_3$); IR (neat) ν_{max}/cm^{-1}: 3131 (OH); δ_H(500 MHz, $CDCl_3$) 0.86 (9H, d, *J* 6.3, $3CH_3$), 1.05-1.59 (14H, m), 1.25 (3H, s, CH_3), 1.76-1.84 (2H, m, CH_2), 2.02 (3H, s, CH_3), 2.06 (3H, s, CH_3), 2.09 (3H, s, CH_3), 2.58 (2H, t, *J* 6.9, CH_2), 6.85 (1H, d, *J* 1.7, Ar), 7.07 (1H, dd, J_1 9.2, J_2 2.3, Ar), 7.09 (1H, s, Ar), 8.22 (1H, d, *J* 8.6, Ar), 8.38 (1H, br s, OH); δ_C(125 MHz, $CDCl_3$) 11.8 (2C), 12.6, 19.6, 20.6, 21.0, 22.6, 22.7, 23.7, 24.7, 28.0, 31.2, 32.7, 37.3, 37.5, 39.3, 39.9, 75.3, 102.7, 115.7, 116.7, 118.3, 123.6, 125.3, 127.1, 127.4, 140.2, 142.8, 143.3, 149.0, 157.9, 162.5, 172.7. *Anal*. calcd. for $C_{33}H_{44}O_5 \cdot 0.1$EtOAc: C, 75.76; H, 8.53. Found: C, 75.65; H, 8.58.

Synthesis of Compounds 14a,b



(Isopentyl)triphenylphosphonium Bromide (S14). According to the procedure described for the preparation of **8**, 1-bromo-3-methylbutane (**S13**, 1.99 g, 13.2 mmol) was converted into compound **S14**, which was used without further purification.

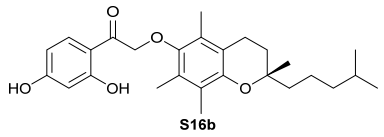
(*R*)-2,5,7,8-Tetramethyl-2-(4-methylpentyl)chroman-6-ol (S15a). According to the procedure described for the preparation of **10b**, compound *ent*-**9** (800 mg, 2.47 mmol) was converted into compound **S15a** using the phosphonium salt **S14** (ca. 4.93 mmol) as a pale yellow oil (675 mg, 94%). $[\alpha]^{25}_{D}$ –0.9 (*c* 1.00, $CHCl_3$); δ_H(500 MHz, $CDCl_3$) 0.87 (6H, d, *J* 6.9, $2CH_3$), 1.14-1.19 (2H, m), 1.22 (3H, s, CH_3), 1.37-1.58 (5H, m), 1.73-1.84 (2H, m, CH_2), 2.11 (6H, s, $2CH_3$), 2.16 (3H, s, CH_3), 2.60 (2H, t, *J* 6.9, CH_2), 4.17 (1H, s, OH); δ_C(125 MHz, $CDCl_3$) 11.3, 11.8, 12.2, 20.7, 21.4, 22.6 (2C), 23.8, 27.9, 31.5, 39.4, 39.7, 74.5, 117.3, 118.4, 121.0, 122.6, 144.5, 145.5. HRMS (ESI) calcd for $C_{19}H_{30}O_2$ (M^+): 290.2246; found: 290.2245.



S15b

(*S*)-2,5,7,8-Tetramethyl-2-(4-methylpentyl)chroman-6-ol (S15b). According to the procedure described for the preparation of **10b**, compound **9** (800 mg, 2.47 mmol) was converted into compound **S15b** using compound **S14** (ca. 4.93 mmol) as a pale yellow oil (621 mg, 86%). $[\alpha]^{25}_{D}$ +0.9 (*c* 1.00, $CHCl_3$); δ_H(500 MHz, $CDCl_3$) 0.87 (6H, d, *J* 6.9, $2CH_3$), 1.14-1.19 (2H, m), 1.22 (3H, s, CH_3), 1.37-1.58 (5H, m), 1.73-1.84 (2H, m, CH_2), 2.11 (6H, s, $2CH_3$), 2.16 (3H, s, CH_3), 2.60 (2H, t, *J* 6.9, CH_2), 4.17 (1H, s, OH); δ_C(125 MHz, $CDCl_3$) 11.3, 11.8, 12.2, 20.7, 21.4, 22.6 (2C), 23.8, 27.9, 31.5, 39.4, 39.7, 74.5, 117.3, 118.4, 121.0, 122.6, 144.5, 145.5. HRMS (ESI) calcd for $C_{19}H_{30}O_2$ (M^+): 290.2246; found: 290.2239.

(*R*)-1-(2,4-Dihydroxyphenyl)-2-{[2,5,7,8-tetramethyl-2-(4-methylpentyl)chroman-6-yl]oxy}ethan-1-one (S16a). According to the procedure described for the preparation of **12b**, compound **S15a** (600 mg, 2.07 mmol) was converted into compound **S16a** as a pale yellow solid (765 mg, 84%): mp 86–87 °C (from EtOAc/hexane); $[\alpha]^{25}_{D}$ +3.5 (*c* 0.78, $CHCl_3$); IR (neat) ν_{max}/cm^{-1}: 3351 (OH), 1626 (C=O); δ_H(500 MHz, $CDCl_3$) 0.87 (6H, d, *J* 6.9, $2CH_3$), 1.18 (2H, dd, J_1 14.9, J_2 6.9, CH_2), 1.24 (3H, s, CH_3), 1.37-1.61 (5H, m), 1.73-1.85 (2H, m, CH_2), 2.08 (3H, s, CH_3), 2.14 (3H, s, CH_3), 2.18 (3H, s, CH_3), 2.57 (2H, t, *J* 6.6, CH_2), 4.93 (2H, s, CH_2), 6.36 (1H, dd, J_1 8.9, J_2 2.3, Ar), 6.42 (1H, d, *J* 2.3, Ar), 6.52 (1H, br s, OH), 7.49 (1H, d, *J* 9.2 Hz, Ar), 12.37 (1H, s, OH); δ_C(125 MHz, $CDCl_3$) 11.8, 11.9, 12.8, 20.6, 21.3, 22.6 (2C), 23.8, 27.8, 31.1, 39.3, 39.9, 73.9, 75.0, 103.8, 108.1, 111.7, 117.8, 123.2, 125.7, 127.6, 130.8, 147.7, 148.3, 163.3, 165.3, 198.0. HRMS (ESI) calcd for $C_{27}H_{37}O_5$ (MH^+): 441.2636; found: 441.2633.



S16b

(*S*)-1-(2,4-Dihydroxyphenyl)-2-{[2,5,7,8-tetramethyl-2-(4-methylpentyl)chroman-6-yl]oxy}ethan-1-one (S16b). According to the procedure described for the preparation of **12b**, compound **S15b** (600 mg, 2.07 mmol) was converted into compound **S16b** as pale yellow solid (505 mg, 55%): mp 86–87 °C (from EtOAc/hexane); $[\alpha]^{25}_{D}$ –3.9 (*c* 1.11, $CHCl_3$); IR (neat) ν_{max}/cm^{-1}: 3351 (OH), 1626 (C=O); δ_H(500 MHz, $CDCl_3$) 0.87 (6H, d, *J* 6.9, $2CH_3$), 1.17 (2H, dd, J_1 14.9, J_2 6.9, CH_2), 1.24 (3H, s, CH_3), 1.37-1.61 (5H, m), 1.73-1.85 (2H, m, CH_2), 2.09 (3H, s, CH_3), 2.14 (3H, s, CH_3), 2.18 (3H, s, CH_3), 2.57 (2H, t, *J* 6.6, CH_2), 4.93 (2H, s, CH_2), 6.28 (1H, br s, OH), 6.37 (1H, dd, J_1 8.9, J_2 2.3, Ar), 6.42 (1H, d, *J* 2.3, Ar), 7.50 (1H, d, *J* 9.2 Hz, Ar), 12.38 (1H, s, OH); δ_C(125 MHz, $CDCl_3$) 11.8, 11.9, 12.8, 20.6, 21.3, 22.6 (2C), 23.8, 27.8, 31.1, 39.3, 39.9, 73.9, 75.0, 103.8, 108.1, 111.7, 117.8, 123.2, 125.7, 127.6, 130.8, 147.7, 148.3, 163.1, 165.3, 198.0. *Anal*. calcd. for $C_{27}H_{36}O_5$: C, 73.61; H, 8.24. Found: C, 73.39; H, 8.49.

(*R*)-7-Hydroxy-3-{[2,5,7,8-tetramethyl-2-(4-methylpentyl)chroman-6-yl]oxy}-4*H*-chromen-4-one (14a). According to the procedure described for the preparation of **1b**, compound **S16a** (100 mg, 0.227 mmol) was converted into compound **14a** as white solid (23.0 mg, 23%): mp 255–258 °C (from EtOAc); $[\alpha]^{25}_{D}$ +5.3 (*c* 0.40, THF); IR (neat) ν_{max}/cm^{-1}: 3265 (OH); δ_H(500 MHz, THF-d_8) 2.69 (3H, d, *J* 2.9, CH_3), 2.70 (3H, d, *J* 2.9, CH_3), 3.01 (2H, dd, J_1 14.9, J_2 6.9, CH_2), 3.06 (3H, s, CH_3), 3.26-3.43 (5H, m), 3.56-3.68 (2H, m, CH_2), 3.82 (3H, s, CH_3), 3.86 (3H, s, CH_3), 3.89 (3H, s, CH_3), 4.44 (2H, t, *J* 6.9, CH_2), 8.47 (1H, d, *J* 2.3, Ar), 8.64 (1H, dd, J_1 8.6, J_1 2.3, Ar), 8.84 (1H, s, Ar), 9.87 (1H, d, *J* 8.6, Ar), 11.19 (1H, s, OH); δ_C(125 MHz, THF-d_8) 10.9, 11.1, 11.8, 20.4, 21.4, 22.0 (2C), 23.2, 27.9, 31.1, 39.5, 39.9, 74.9, 101.9, 114.1, 117.5, 118.0, 123.2, 125.2, 126.9, 127.3, 139.2, 143.4, 143.8, 148.9, 157.6, 162.4, 170.0. *Anal*. calcd. for $C_{28}H_{34}O_5 \cdot 0.1$EtOAc: C, 74.25; H, 7.64. Found: C, 74.12; H, 7.61.

(*S*)-7-Hydroxy-3-{[2,5,7,8-tetramethyl-2-(4-methylpentyl)chroman-6-yl]oxy}-4*H*-chromen-4-one (14b). According to the procedure described for the preparation of **1b**, compound **S16b** (100 mg, 0.227 mmol) was converted into compound **14b** as white solid (22.7 mg, 22%): mp 255–258 °C (from EtOAc); $[\alpha]^{25}_{D}$ –5.1 (*c* 0.52, THF); IR (neat) ν_{max}/cm^{-1}: 3147 (OH); δ_H(500 MHz, THF-d_8) 2.69 (3H, d, *J* 2.9, CH_3), 2.70 (3H, d, *J* 2.9, CH_3), 3.01 (2H, dd, J_1 14.9, J_2 6.9, CH_2), 3.06 (3H, s, CH_3), 3.26-3.43 (5H, m), 3.56-3.68 (2H, m, CH_2), 3.82 (3H, s, CH_3), 3.86 (3H, s, CH_3), 3.89 (3H, s, CH_3), 4.44 (2H, t, *J* 6.9, CH_2), 8.47 (1H, d, *J* 2.3, Ar), 8.64 (1H, dd, J_1 8.6, J_1 2.3, Ar), 8.84 (1H, s, Ar), 9.87 (1H, d, *J* 8.6, Ar), 11.20 (1H, s, OH); δ_C(125 MHz, THF-d_8) 10.9, 11.1, 11.8, 20.4, 21.4, 22.0 (2C), 23.2, 27.9, 31.1, 39.5, 39.9, 74.9, 101.9, 114.1, 117.5, 118.0, 123.2, 125.2, 126.9, 127.3, 139.2, 143.3, 143.8, 148.9, 157.6, 162.4, 170.0. *Anal*. calcd. for $C_{28}H_{34}O_5$: C, 74.64; H, 7.61. Found: C, 74.33; H, 7.74.

Screening by the Chemical Array

Photoaffinity linker-coated (PALC) slides were prepared according to previous reports using amine-coated slides and the photoaffinity proline linker.[8-10] A solution of compounds (2.5 mg cm^{-3} in DMSO) from the in-house chemical library (NPDepo, RIKEN) was immobilized onto the PALC glass slides with a chemical arrayer equipped with 24 stamping pins. The slides were exposed to UV irradiation of 4 J cm^{-2} at 365 nm using a CL-1000L UV crosslinker (UVP, CA). The slides were washed successively with DMSO, DMF, acetonitrile, THF, dichloromethane, EtOH, and ultra-pure water (5 min, 3 times each), and dried. D- or L-$MDM2^{TMR}$ (3 μmol dm^{-3} in 1% skim-milk-TBS-T) was incubated with the glass slide for 1 h, and then washed with TBS-T (10 mmol dm^{-3} Tris-HCl (pH 8.0), 150 mmol dm^{-3} NaCl, 0.05% Tween-20) (5 min, 3 times). The slides were dried and scanned at 532 nm on a GenePix scanner. The fluorescence signals were quantified with GenePixPro (Table S1).

Fluorescent Polarization Assay

Fluorescence polarization (FP) assays were carried out in PBS containing 2% DMSO and 0.005% Tween-20 using a fluorescein-labeled p53 (P4) peptide (0.5-1.0 nmol dm^{-3}) and $MDM2^{25-109}$ (10 nmol dm^{-3}) in black 96-well non-binding surface assay plates (Corning).[1] The potential inhibitors and fluorescein-labeled P4 peptide in DMSO were diluted five-fold with PBS in advance. The protein (0.090 cm^3) was preincubated with the compound solution (0.005 cm^3) for 30 min. Then, the fluorescein-labeled P4 peptide (0.005 cm^3) was added and incubated for 30 min. The P4 peptide was used as the positive control. FP signals were analyzed using an EnVision Xcite plate reader (Perkin Elmer) with a 480-nm excitation filter and a 535-nm emission filter. The mP values of the assay were calculated according to the report by Czarna *et al* (Table 1, Table S2, Figure S6).[11]

SPR Analysis

SPR Analyses of p53 binding to synthetic $MDM2^{25–109}$ and $MDM2^{TMR}$ were carried out using Biacore T200 SPR instrument. PBS (Nacalai Tesque, pH 7.4) containing 0.05 % Tween-20 was used as the running buffer at 25 °C. Biotinylated wild-type p53 peptides (biotinyl-aminocaproyl-GSGS-SQETFSDLWKLLPEN-NH_2) were immobilized on a SA sensor chip (L-p53: 45.1 RU, D-p53: 46.4 RU). All analytes were evaluated for 2 min as contact time, followed by 2 min dissociation at a flow rate of 30 μL min^{-1} (Figure S4).

For competitive inhibition assays, L-$MDM2^{25-109}$ (30 nmol dm^{-3}) in the presense of varying concentration of inhibitors in PBS containing 0.05% Tween-20 and 1% DMSO were injected on SA sensor chip, where biotinylated wild-type L-p53 peptide was immobilized (127.3 RU) (Table S3, Figure S6).

Competitive Binding Inhibition Assay by a Standard ELISA

ELISA assays were carried out in HEPES buffer [20 mmol dm^{-3} HEPES (pH7.4), 100 mmol dm^{-3} NaCl, 0.05% Tween-20, 0.1% BSA]. Precoated streptavidin 96-well plates (Nunc) were incubated with HEPES buffer containing 3% BSA (0.300 cm^3 $well^{-1}$) for 1h. After three washes, biotinylated wild-type p53 peptide (100 nmol dm^{-3}) in HEPES buffer (0.100 cm^3 $well^{-1}$) was added and incubated for 2 h. After three washes, 100 nmol dm^{-3} MDM2 (recombinant human MDM2, untagged, Sigma) in

the presence of varying concentration of inhibitors in HEPES buffer containg 1% DMSO (0.100 cm^3 $well^{-1}$) was added and incubated for 1 h. After three washes, 1:1000 dilution of anti-MDM2 rabbit IgG antibody (N-20, Santa Cruz] in HEPES buffer (0.100 cm^3 $well^{-1}$) was added and incubated for 1 h. After three washes, 1:5000 dilution of HRP-conjugated anti-rabbit IgG antibody (Promega) in HEPES buffer (0.100 cm^3 $well^{-1}$) was added and incubated for 1 h. After three washes, TMB (3,3',5,5'-Tetramethylbenzidine) solution (WAKO, 0.100 cm^3 $well^{-1}$) was added and incubated for 1 h. Then, aqueous 2 N H_2SO_4 (0.010 cm^3 $well^{-1}$) was added. Absorbance at 450 nm was measured for each well using an EnVision Xcite plate reader. The IC_{50} values were calculated by using GraphPad Prizm (GraphPad software, San Diego, CA) (Table S3, Figure S6).

Cell Growth Inhibition Assay

SJSA-1 and H1299 cells were cultured in RPMI-1640 medium (high glucose) (WAKO) supplemented with 10% (v/v) FBS at 37 °C in a 5% CO_2-incubator. Cell-based assays using SJSA-1 and H1299 cells were performed in 96-well plates (BD Falcon). Both cells were seeded at 500 cells $well^{-1}$ in 0.050 cm^3 of DMEM, and placed for 6 h. Chemical compounds in DMSO were diluted 250-fold with the culture medium in advance. Following the addition of the fresh culture medium (0.040 cm^3), the chemical diluents (0.030 cm^3) were also added to the cell cultures. The final volume of DMSO in the medium was equal to 0.1% (v/v). The cells under chemical treatment were incubated for a further 72 h. The wells in the plates were washed with the cultured medium without phenol-red twice. After 1 h of incubation with 0.10 cm^3 of the medium, the cell culture in each well was supplemented with the MTS reagent (0.020 cm^3, Promega), followed by incubation for an additional 40 min. Absorbance at 490 nm was measured for each well using an EnVision Xcite plate reader. The GI_{50} values were calculated by using GraphPad Prizm (GraphPad software, San Diego, CA) (Figure S8).

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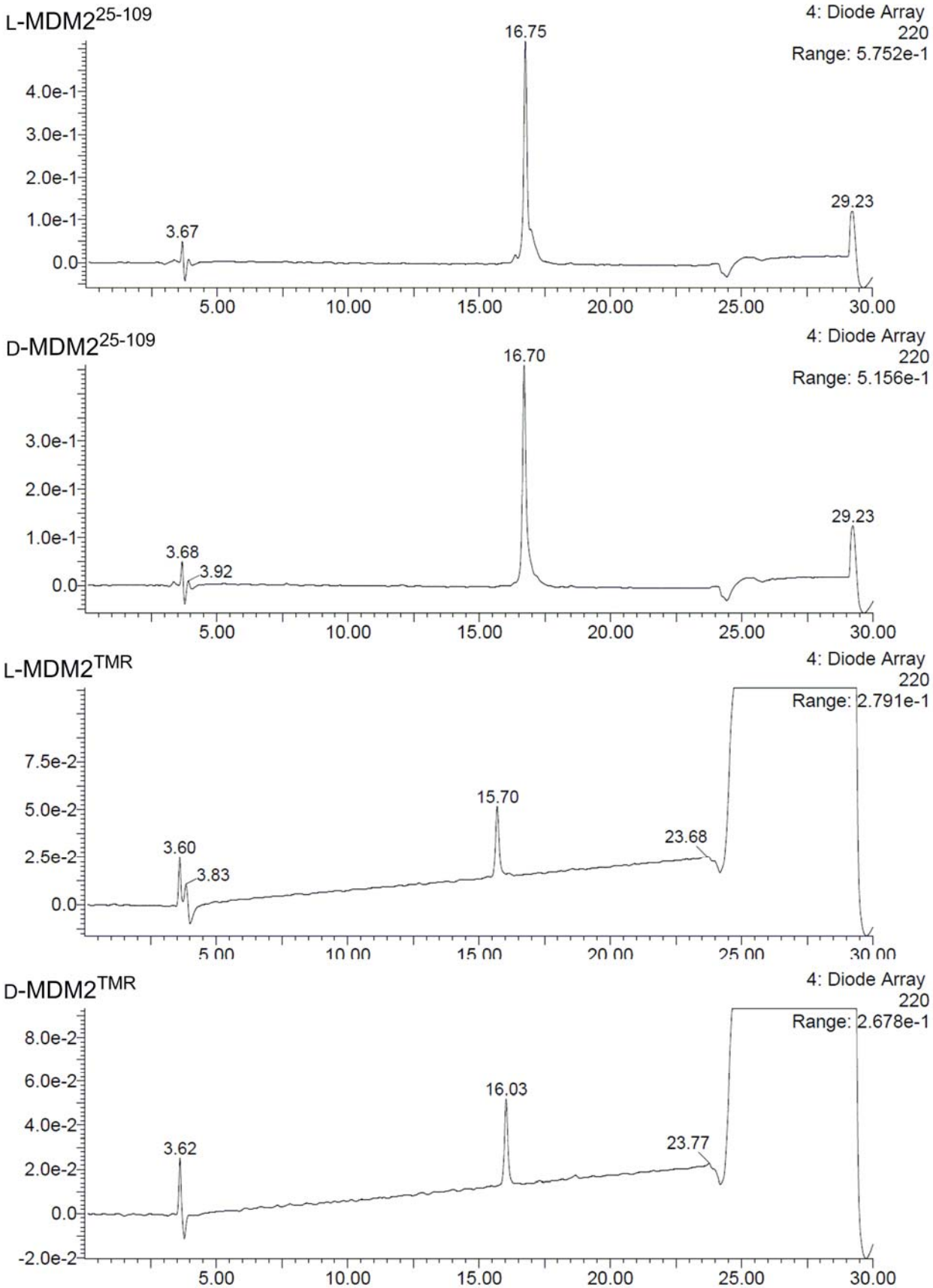
Fig. S1. LC–MS Chromatograms of Purified Synthetic MDM2$^{25–109}$ and MDM2^{TMR} Proteins.



HPLC Conditions: HPLC analysis was performed at 25 °C on a Cosmosil 5C18-AR300 preparative column (Nacalai Tesque, 4.5 × 250 mm) with a linear gradient of 30–50% CH_3CN containing 0.1% TFA at a flow rate of 1 cm^3 min^{-1} over 20min.

Fig. S2. Mass Spectrometry Data of Synthetic MDM2$^{25–109}$ and MDM2^{TMR} Proteins.

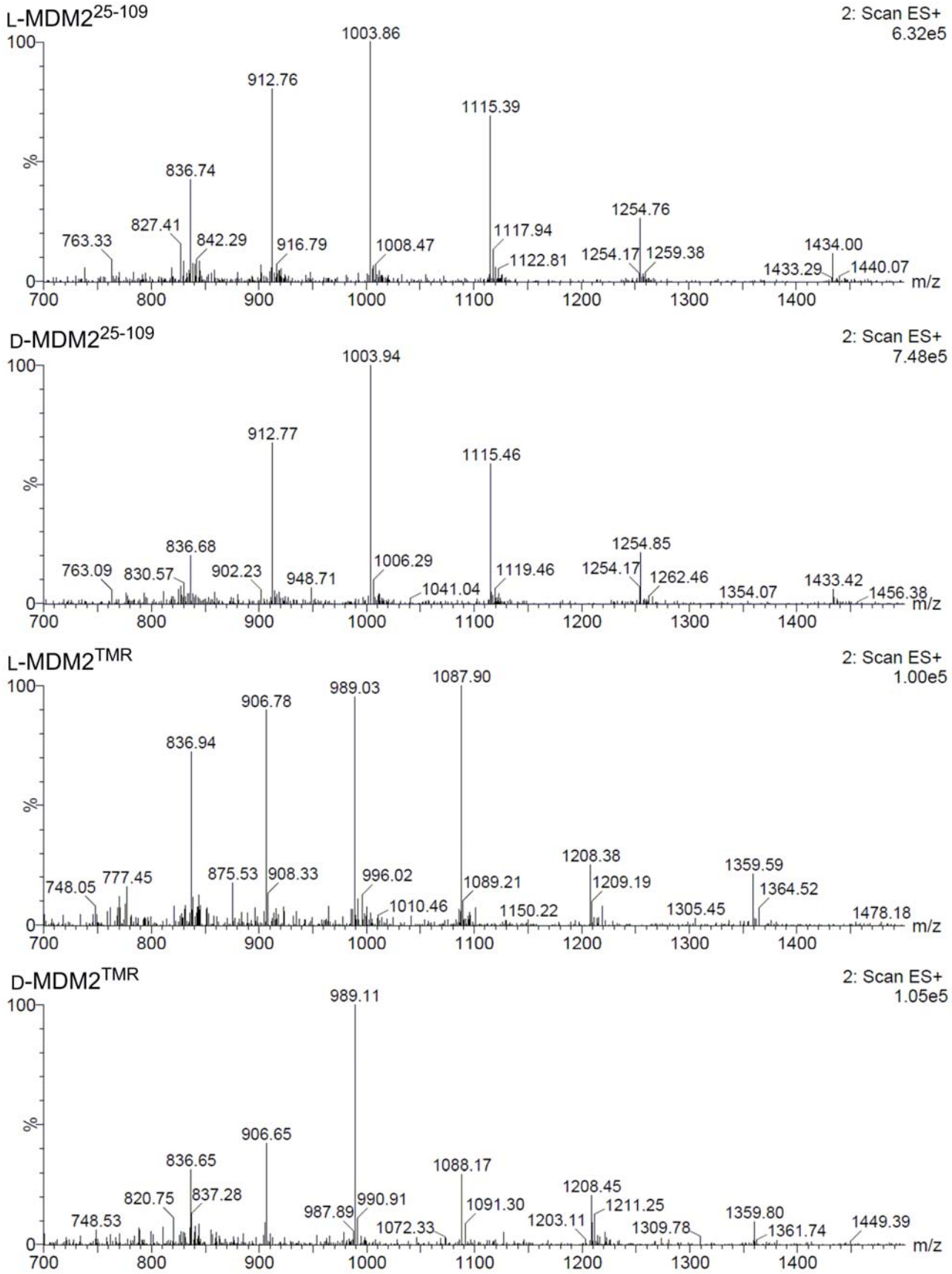


Fig. S3. CD Spectra of Synthetic L-MDM2 and D-MDM2 Proteins. Spectra of L-MDM2$^{25–109}$ and D-MDM2$^{25–109}$ were measured at 25 °C in PBS containing 0.5 mmol dm^{-3} TCEP and 0.005% Tween-20 (pH 7.4).

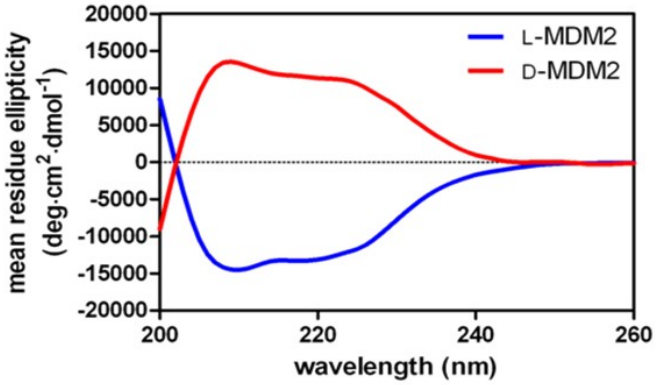
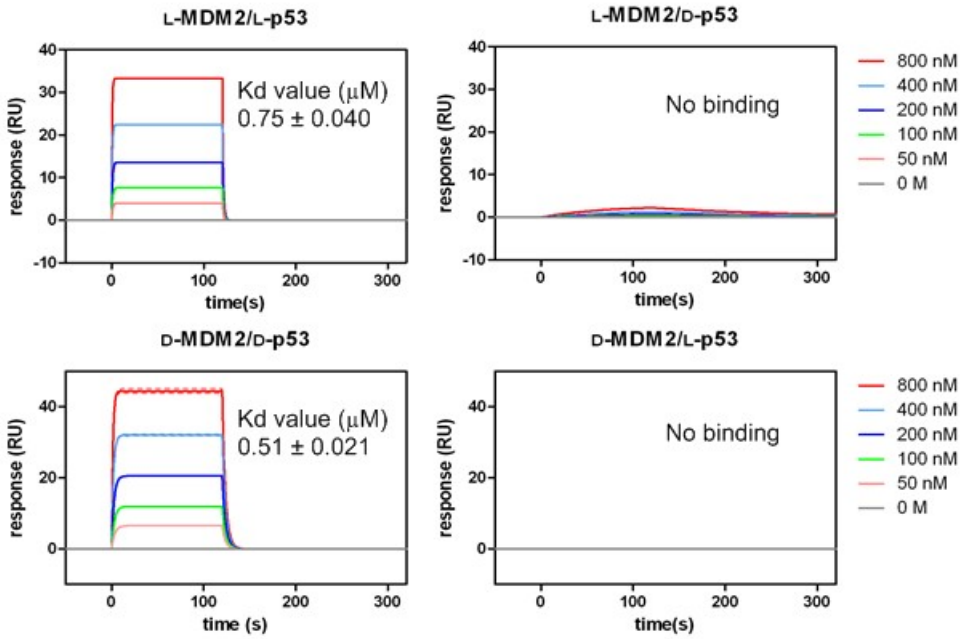


Fig. S4. SPR Analysis of p53 Binding to Synthetic MDM2$^{25–109}$.



Analyte/Ligand	k_a (1 Ms^{-1})	k_d (1 s^{-1})	K_d (mol dm^{-3})
L-MDM2$^{25-109}$/L-p53	1.1 ± 0.75 E^{+6}	8.5 ± 0.16 E^{-1}	7.5 ± 0.40 E^{-7}
D-MDM2$^{25-109}$/D-p53	5.6 ± 0.69 E^{+5}	2.8 ± 0.24 E^{-1}	5.1 ± 0.21 E^{-7}

Table S1. Data of the Initial Chemical Array Screening.

Code name	L-MDM2	D-MDM2	Code name	L-MDM2	D-MDM2
NPD5176	+	–	NPD9453	–	++
NPD5180	+	–	NPD9481	–	++
NPD5494	+	–	NPD9515	–	++
NPD6517	+	–	NPD10099	–	++
NPD7843	+	–	Cromolyn	–	+
NPD8361	+	–	NP507	–	+
NPD8439	+	–	NP653	–	+
NPD12476	+	–	NP699	–	+
NPD12691	+	–	NP783	–	+
NP843 (1)	–	+++	NP846	–	+
NPD6370	–	+++	NP891	–	+
NPD9234	–	+++	NP897	–	+
Nystatin Al	–	++	NPD1967	–	+
Curcumin	–	++	NPD8611	–	+
NP627	–	++	NPD9100	–	+
NP637	–	++	NPD9120	–	+
NPD6878	–	++	NPD9150	–	+
NPD8700	–	++	NPD9399	–	+
NPD8908	–	++	**NPD9580**	–	+
NPD9098	–	++	NPD9657	–	+
NPD9268	–	++	NPD10038	–	+
NPD9315	–	++			

Hit compounds by chemical array screening had selective binding activity to L-MDM2^{TMR} or D-MDM2^{TMR} protein. Fluorescent intensity I of each spot was measured at 532 nm. The relative intensities (ΔI) of each compound were calculated from the difference between the fluorescence signals of L-MDM2^{TMR} and D-MDM2^{TMR} ($\Delta I = |I_L - I_D|$). The average (ΔI_{ave}) and standard deviation (SD) for all spots were also calculated. The compounds with a larger ΔI value than 'ΔI_{ave} + 1SD' were determined to be selective compounds for L-MDM2 or D-MDM2. [+: >+1SD; ++: >+2SD; +++: >+3SD]. Because of the heterogeneous system of chemical array screening, the result of chemical array screening was not always consistent with that of homogeneous fluorescence polarization assay. Therefore, we should consider the possibilities that false positive signals (non-specific binding between the protein and array surface) and false negative signals (weak binding of the protein to randomly immobilized compounds) occurred in chemical array screening.

Fig. S5. Structures of Hit Compounds.

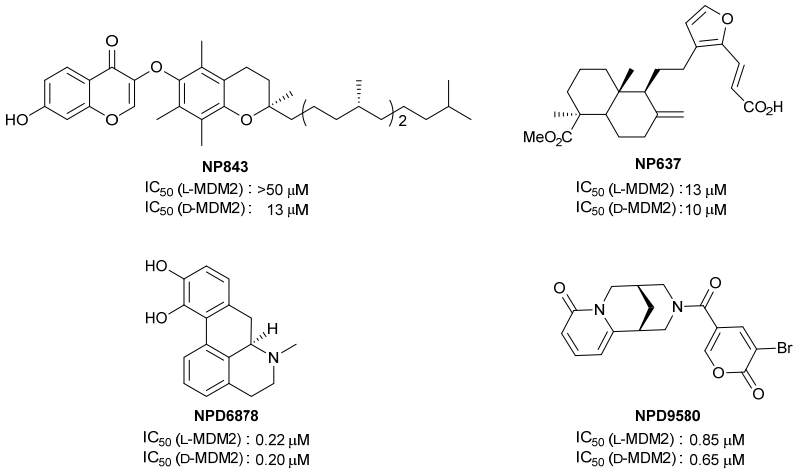


Table S2. Inhibitory Activities of Reference Compounds by a Fluorescence Polarization Assay.

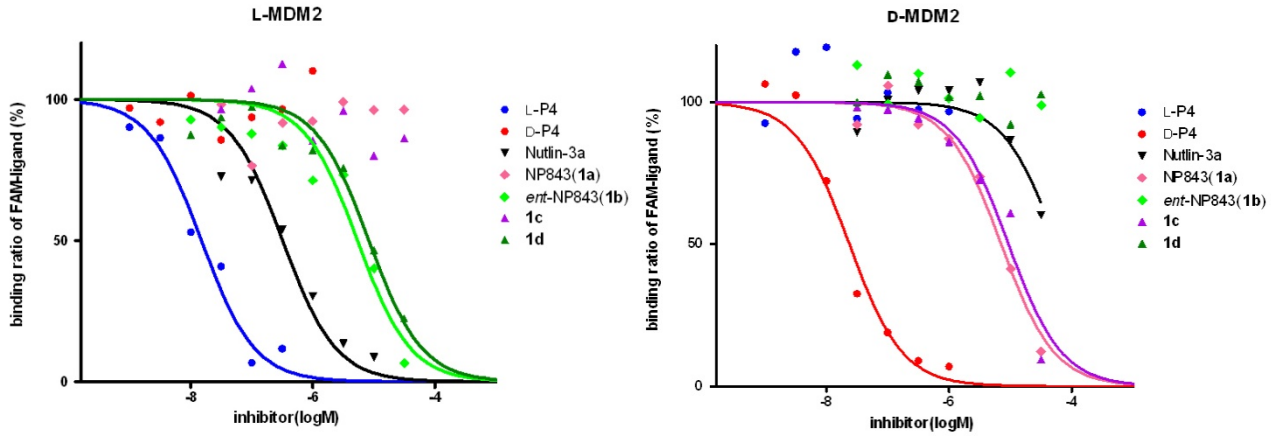
Compound	IC_{50} (μM)	
	L-MDM2	D-MDM2
L-P4	0.030 ± 0.016	>1.0
D-P4	>1.0	0.019 ± 0.004
Nutlin-3a	0.32 ± 0.03	>30

Table S3. Inhibitory Activities of NP843 (**1a**) and *ent*-NP843 (**1b**) by SPR Analysis and ELISA.

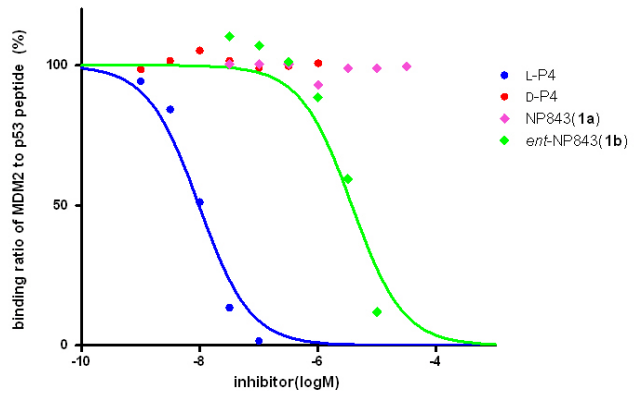
Compound	IC_{50} (μM)	
	SPR	ELISA
L-P4	0.011 ± 0.001	0.066 ± 0.007
D-P4	>1.0	>1.0
NP843 (**1a**)	>30	>30
ent-NP843 (**1b**)	3.1 ± 0.5	16.7 ± 1.1

Fig. S6. The Representative Dose-response Curves in the Binding Inhibition Assays: (A) FP Assay; (B) SPR Analysis; (C) ELISA.

(A)



(B)



(C)

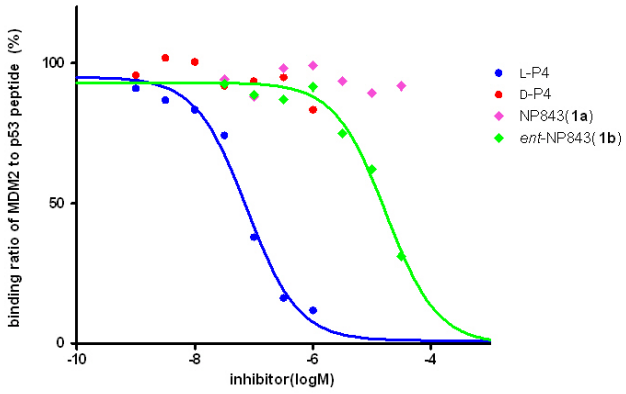
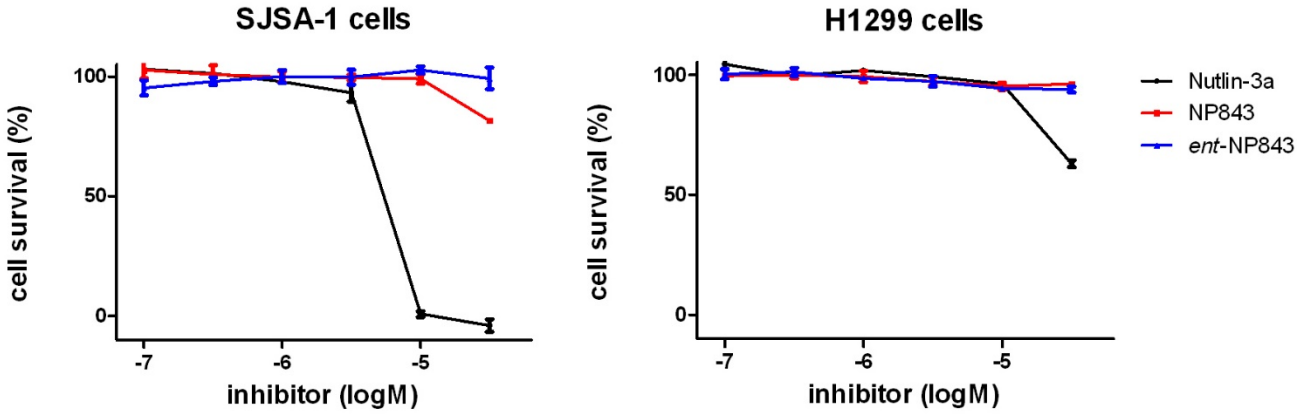
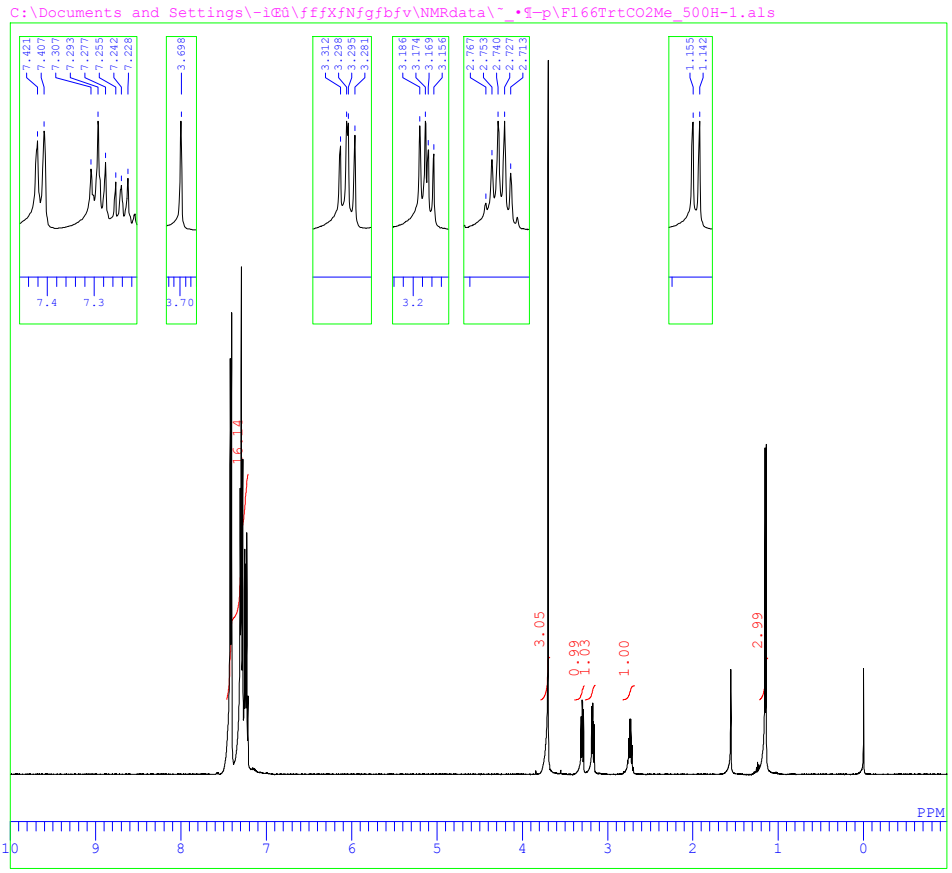


Fig. S7. Results of Cell Growth Inhibition Assay.



Compounds	GI_{50} (μM)	
	SJSA-1 cells[12]	H1299 cells[13]
Nutlin-3a	5.2 ± 0.19	>30
NP843 (**1a**)	>30	>30
ent-NP843 (**1b**)	>30	>30



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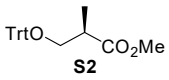
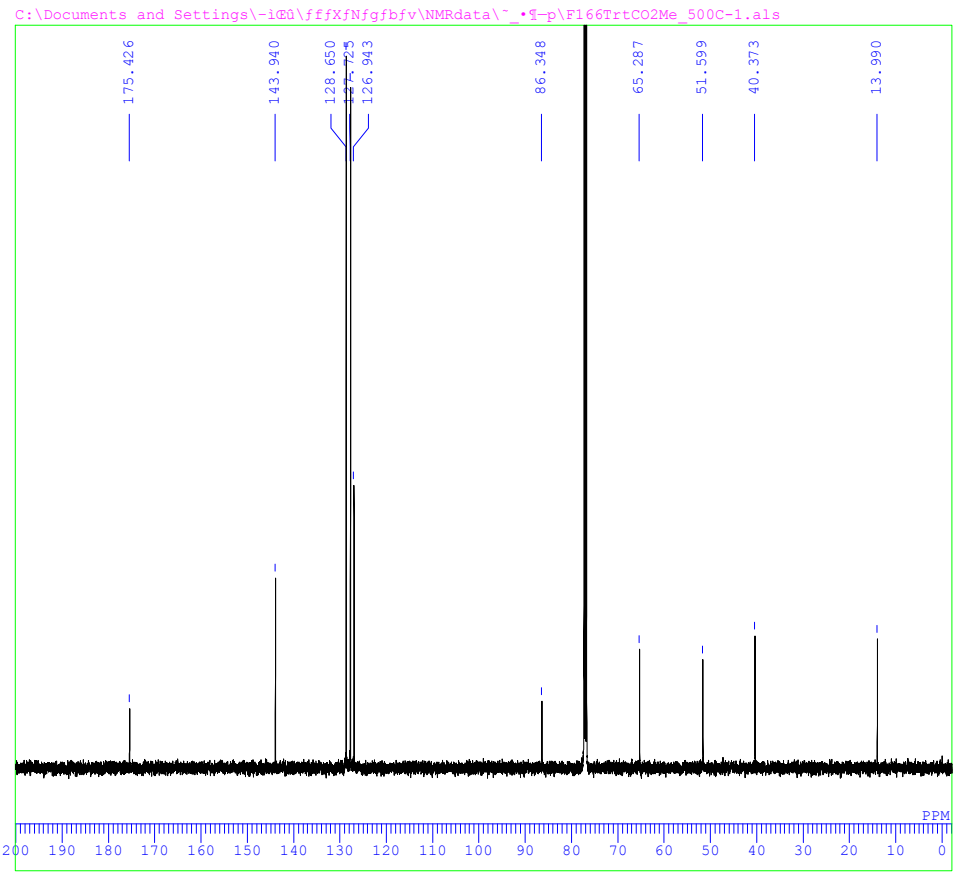
OBSET 2.41 KHz
OBFIN 6.01 Hz
POINT 13107
FREQU 7507.39 Hz
SCANS 8
ACQTM 1.7459 sec
PD 5.0000 sec
PW1 6.82 usec
IRNUC 1H
CTEMP 21.9 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 0.12 Hz
RGAIN 44



S2



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EXMOD single_pulse_dec
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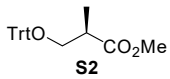
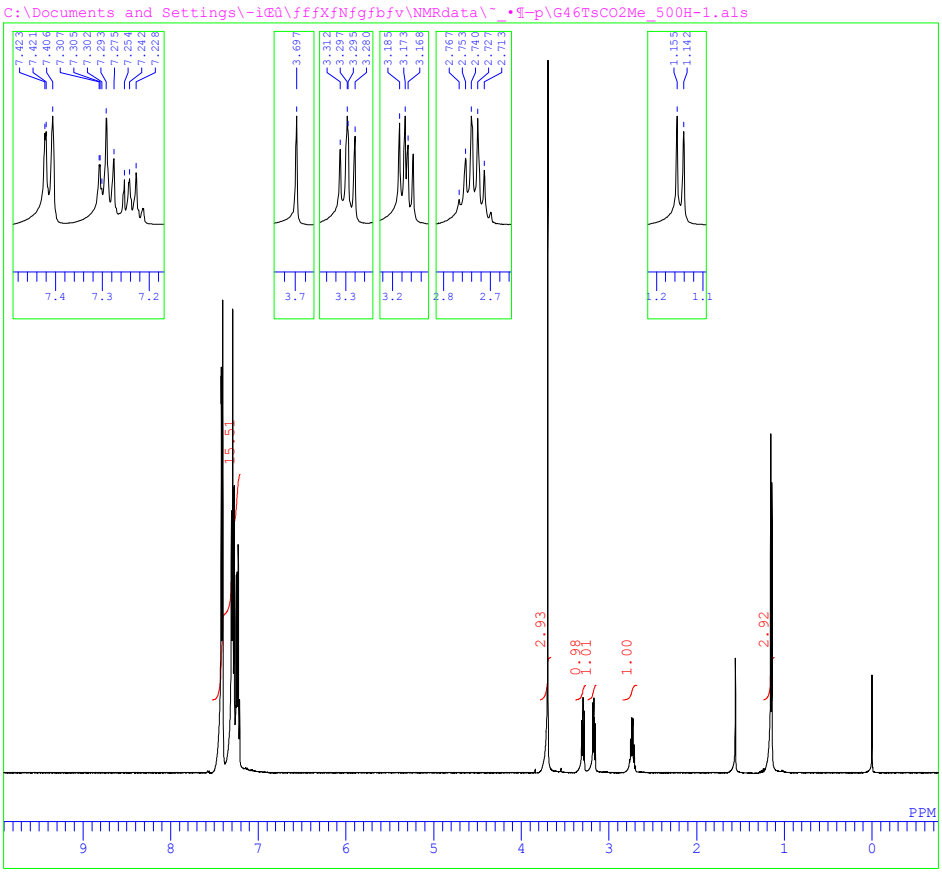
OBSET 7.87 KHz
OBFIN 4.21 Hz
POINT 26214
FREQU 31446.06 Hz
SCANS 1000
ACQTM 0.8336 sec
PD 2.0000 sec
PW1 3.50 usec
IRNUC 1H
CTEMP 22.2 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 1.20 Hz
RGAIN 54



S2

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EXMOD  single_pulse.ex2
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OBSET          2.41 KHz
OBFIN          6.01 Hz
POINT         13107
FREQU       7507.39 Hz
SCANS             8
ACQTM        1.7459 sec
PD           5.0000 sec
PW1            6.82 usec
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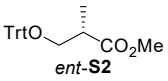
CTEMP         21.6 c
SLVNT  CDCL3
EXREF          0.00 ppm
BF             0.12 Hz
RGAIN            44
```



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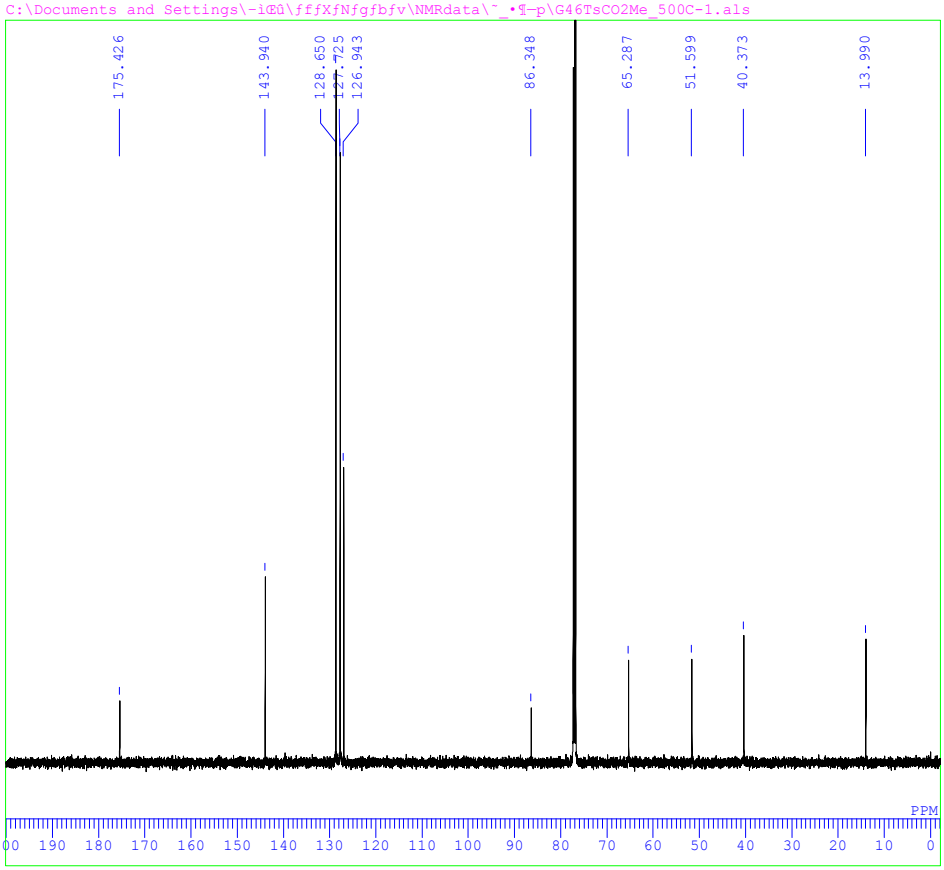


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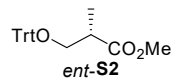
OBFIN          4.21 Hz
POINT         26214
FREQU       31446.06 Hz
SCANS           1000
ACQTM         0.8336 sec
PD            2.0000 sec
PW1             3.50 usec
IRNUC  1H
CTEMP          22.4 c
SLVNT  CDCL3
EXREF          77.00 ppm
BF             1.20 Hz
RGAIN            52
```



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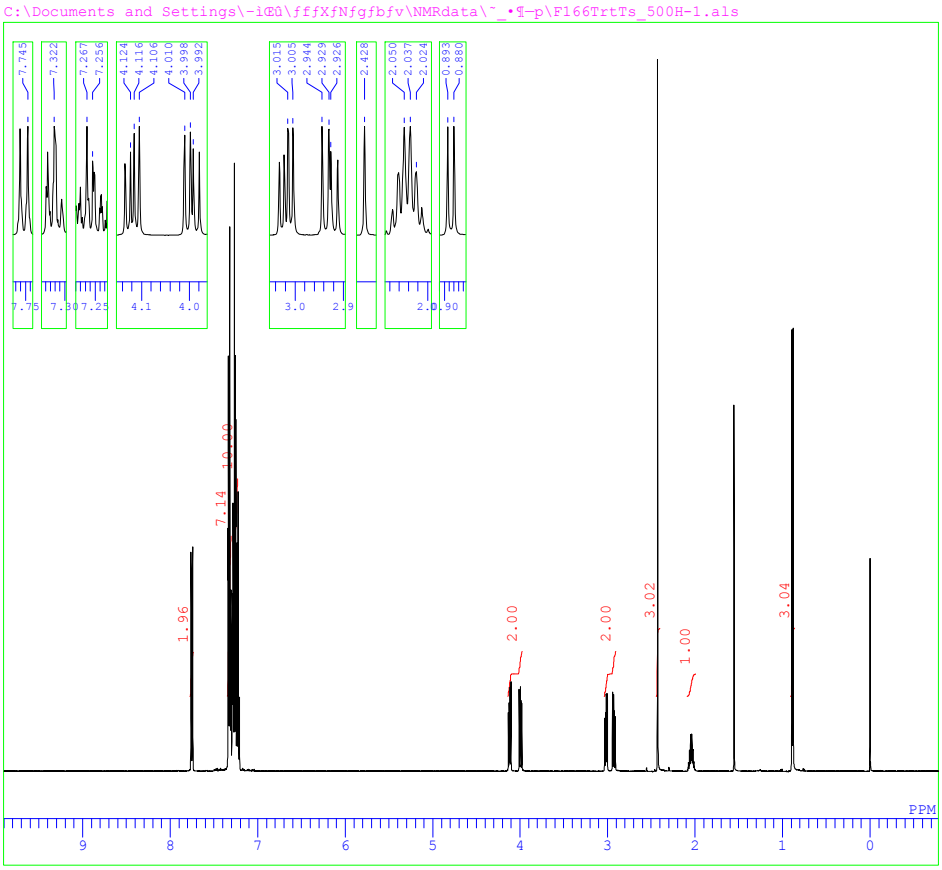

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EXMOD single_pulse.ex2
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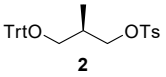
OBSET 2.41 KHz
OBFIN 6.01 Hz
POINT 13107
FREQU 7507.39 Hz
SCANS 8
ACQTM 1.7459 sec
PD 5.0000 sec
PW1 6.82 usec
IRNUC 1H
CTEMP 21.9 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 0.12 Hz
RGAIN 44



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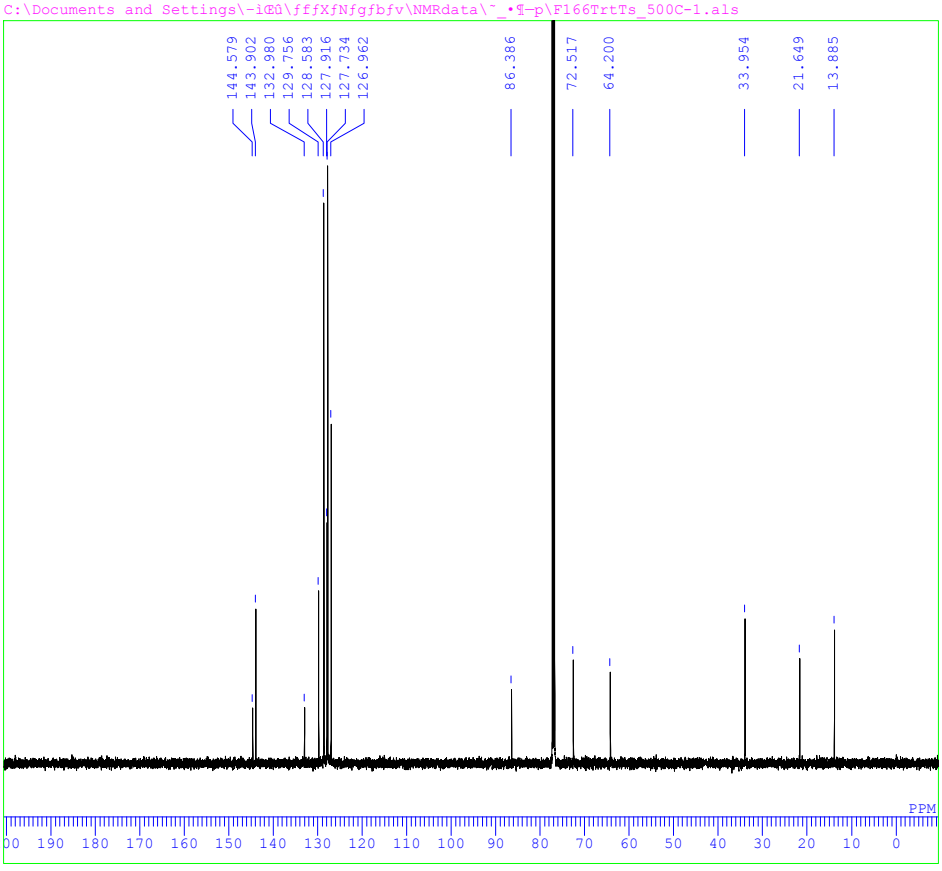

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EXMOD single_pulse_dec
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OBSET 7.87 KHz
OBFIN 4.21 Hz
POINT 26214
FREQU 31446.06 Hz
SCANS 1000
ACQTM 0.8336 sec
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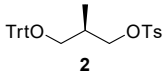
IRNUC 1H
CTEMP 22.4 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 1.20 Hz
RGAIN 52



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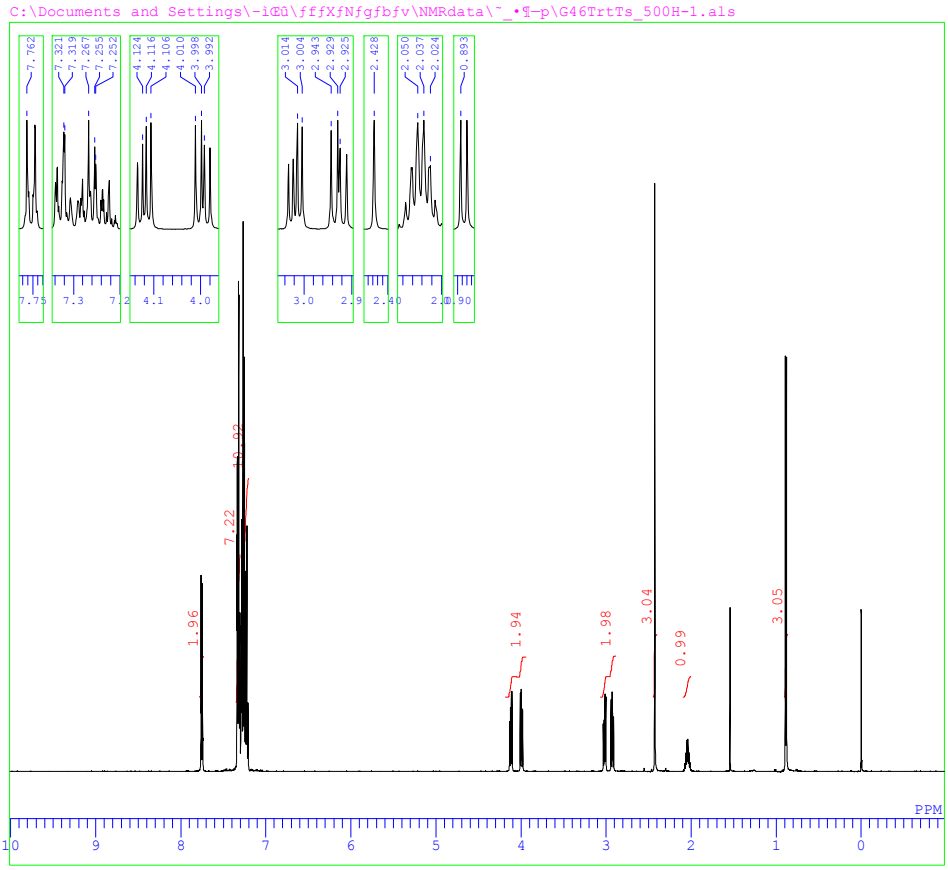


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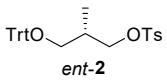
OBFIN          6.01 Hz
POINT         13107
FREQU       7507.39 Hz
SCANS             8
ACQTM        1.7459 sec
PD           5.0000 sec
PW1            6.82 usec
IRNUC  1H
CTEMP         21.4 c
SLVNT  CDCL3
EXREF         0.00 ppm
BF            0.12 Hz
RGAIN           46
```



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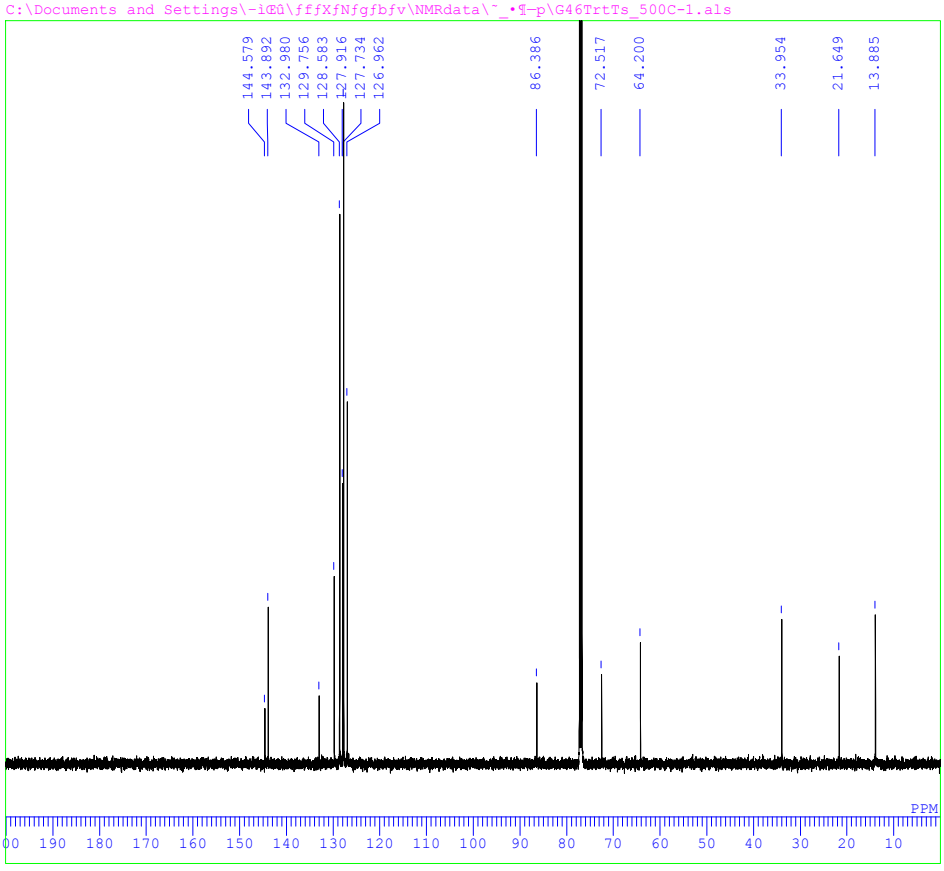


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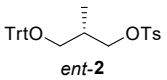
OBFRQ        125.77 MHz
OBSET          7.87 KHz
OBFIN          4.21 Hz
POINT         26214
FREQU      31446.06 Hz
SCANS          1000
ACQTM        0.8336 sec
PD           2.0000 sec
PW1            3.50 usec
IRNUC  1H
CTEMP         21.9 c
SLVNT  CDCL3
EXREF         77.00 ppm
BF            1.20 Hz
RGAIN           52
```



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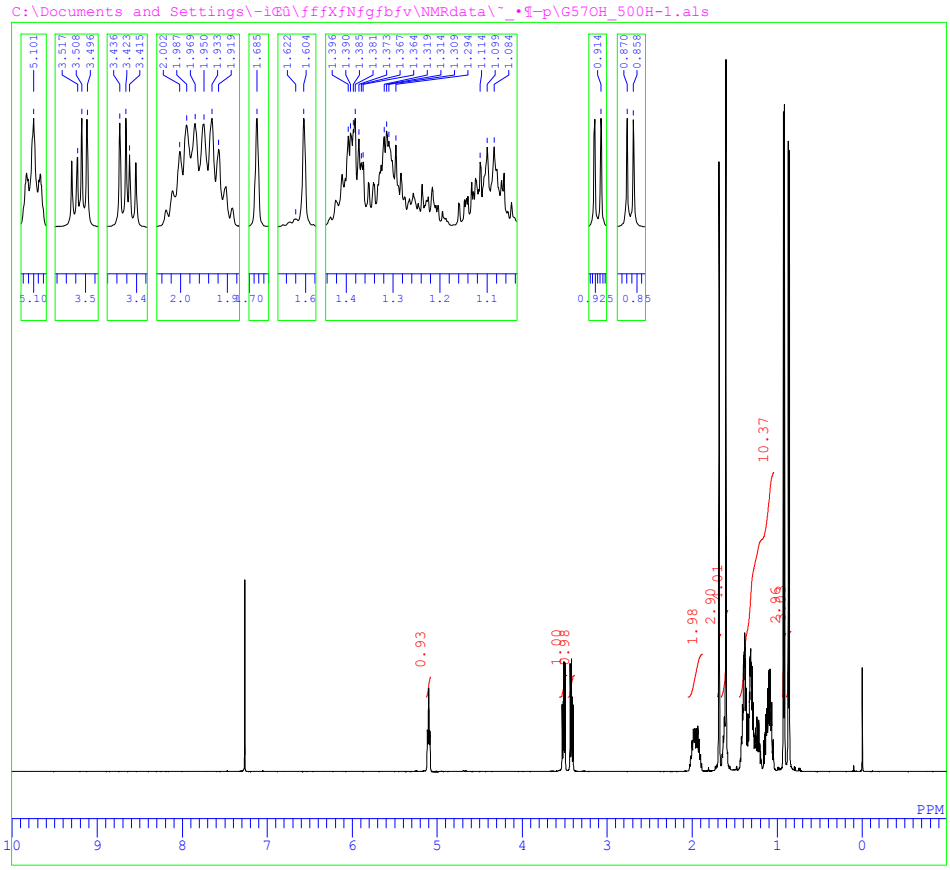


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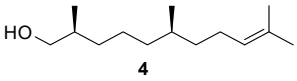
EXMOD  single_pulse.ex2
OBFRQ        500.16 MHz
OBSET          2.41 KHz
OBFIN          6.01 Hz
POINT         13107
FREQU       7507.39 Hz
SCANS             8
ACQTM        1.7459 sec
PD           5.0000 sec
PW1             6.82 usec
IRNUC  1H
CTEMP          20.5 c
SLVNT  CDCL3
EXREF          0.00 ppm
BF             0.12 Hz
RGAIN            38
```



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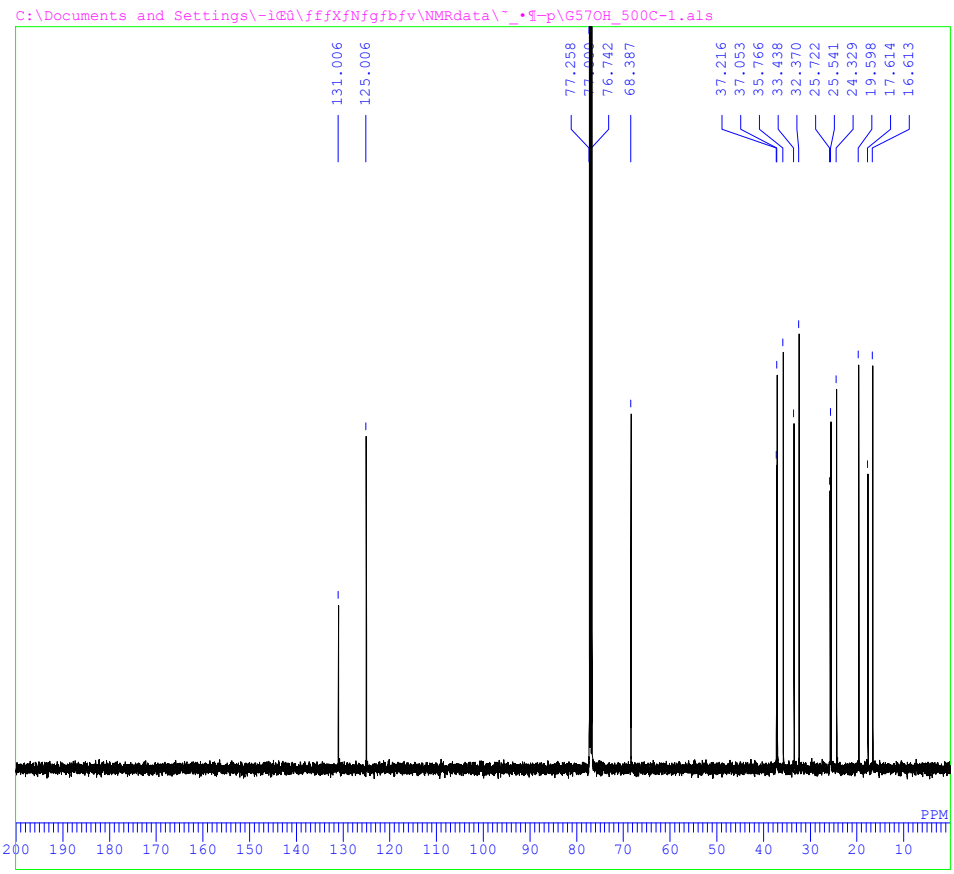


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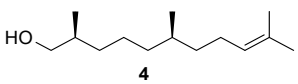
EXMOD  single_pulse_dec
OBFRQ        125.77 MHz
OBSET          7.87 KHz
OBFIN          4.21 Hz
POINT         26214
FREQU      31446.06 Hz
SCANS          1000
ACQTM        0.8336 sec
PD           2.0000 sec
PW1             3.50 usec
IRNUC  1H
CTEMP          21.1 c
SLVNT  CDCL3
EXREF         77.00 ppm
BF             1.20 Hz
RGAIN            52
```



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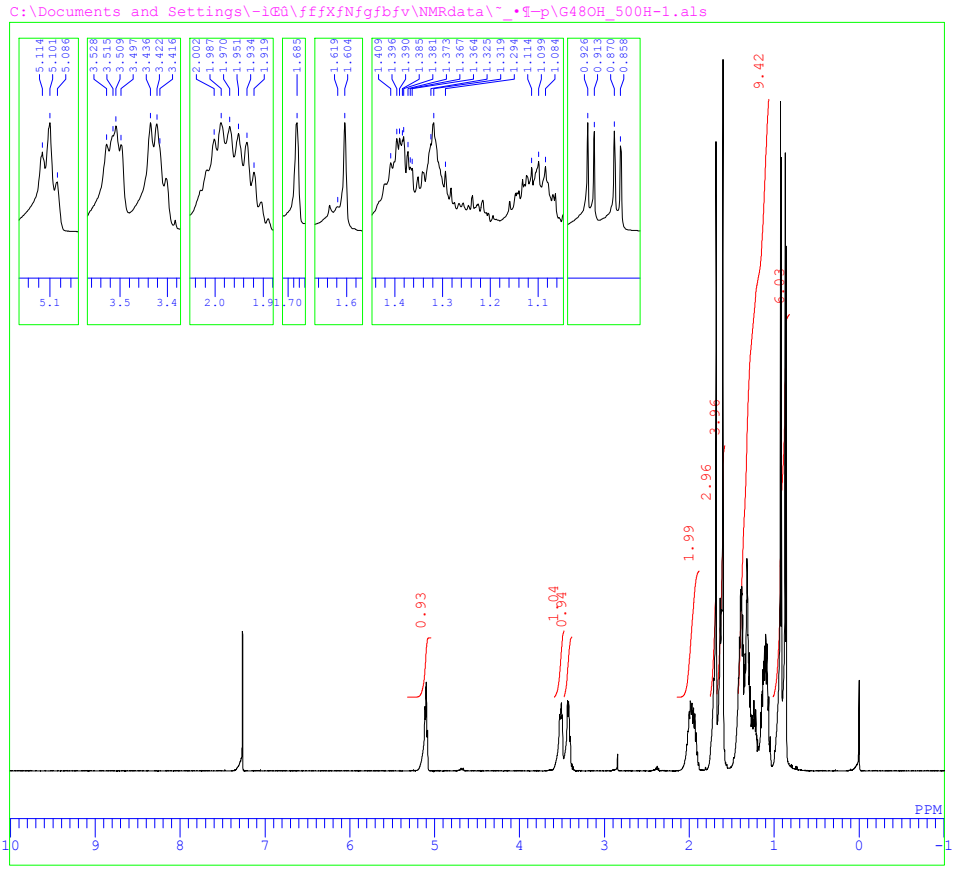


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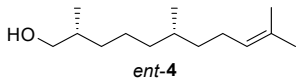
EXMOD  single_pulse.ex2
OBFRQ        500.16 MHz
OBSET          2.41 KHz
OBFIN          6.01 Hz
POINT         13107
FREQU       7507.39 Hz
SCANS             8
ACQTM        1.7459 sec
PD           5.0000 sec
PW1            6.82 usec
IRNUC  1H
CTEMP         20.8 c
SLVNT  CDCL3
EXREF         0.00 ppm
BF            0.12 Hz
RGAIN           38
```



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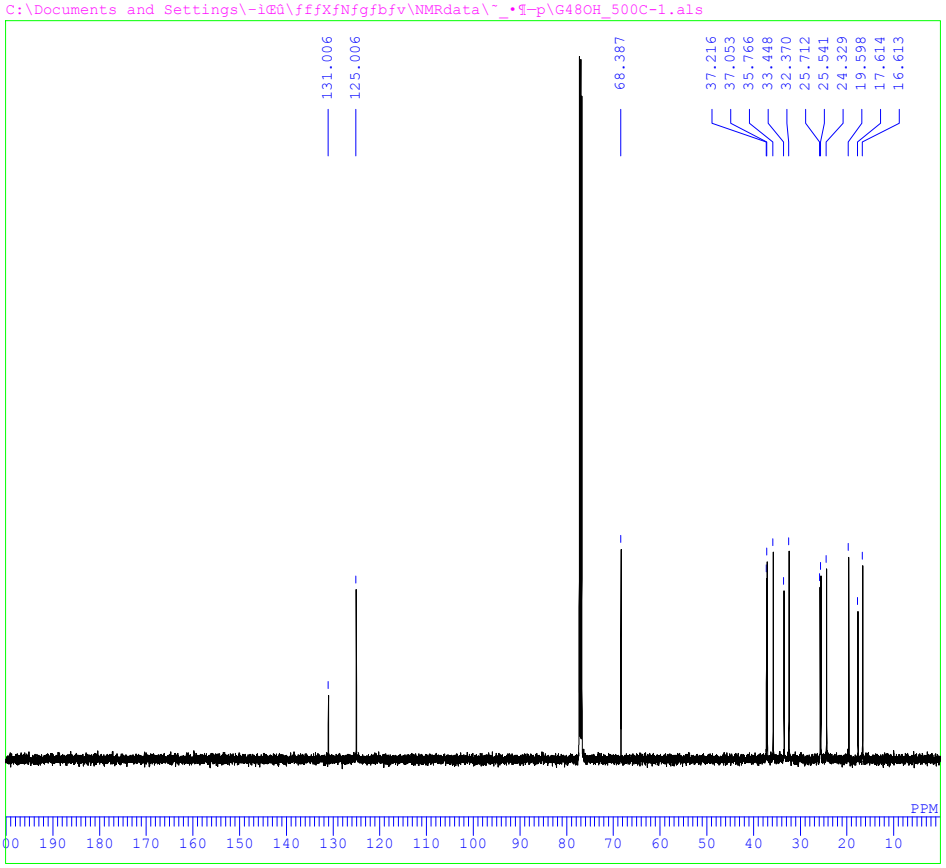


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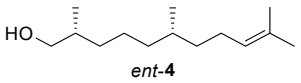
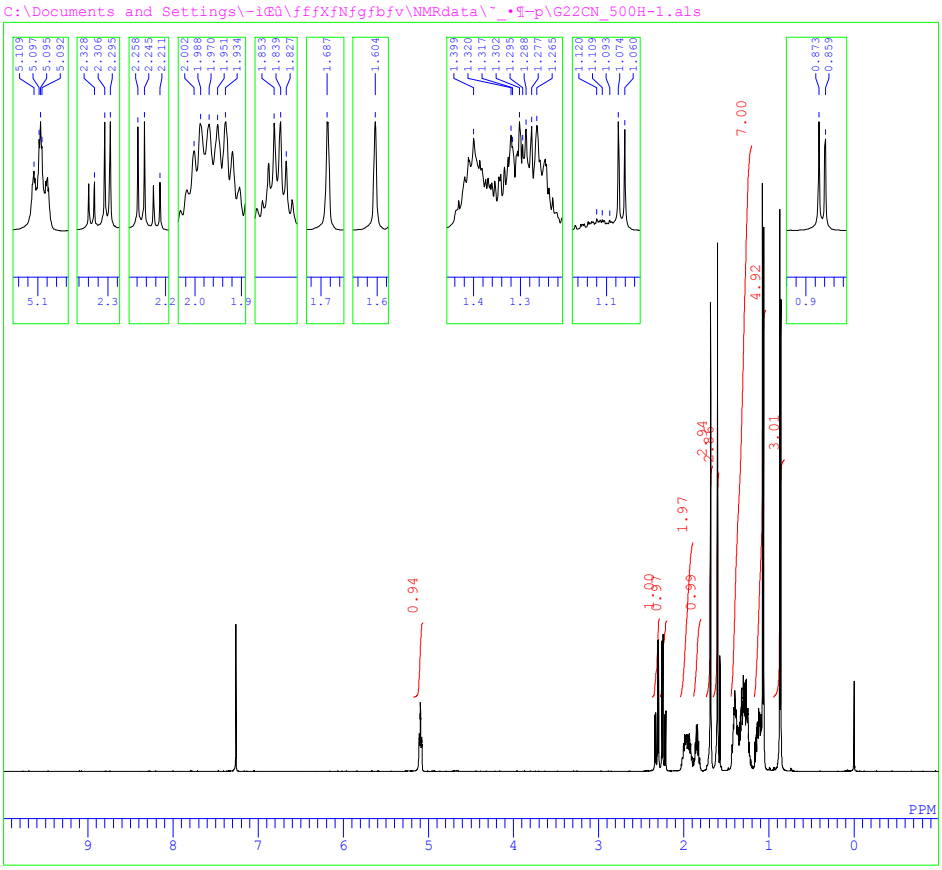
OBSET          7.87 KHz
OBFIN          4.21 Hz
POINT         26214
FREQU      31446.06 Hz
SCANS           1000
ACQTM         0.8336 sec
PD            2.0000 sec
PW1             3.50 usec
IRNUC  1H
CTEMP          21.5 c
SLVNT  CDCL3
EXREF         77.00 ppm
BF             1.20 Hz
RGAIN            54
```



ent-**4**

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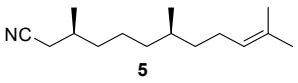
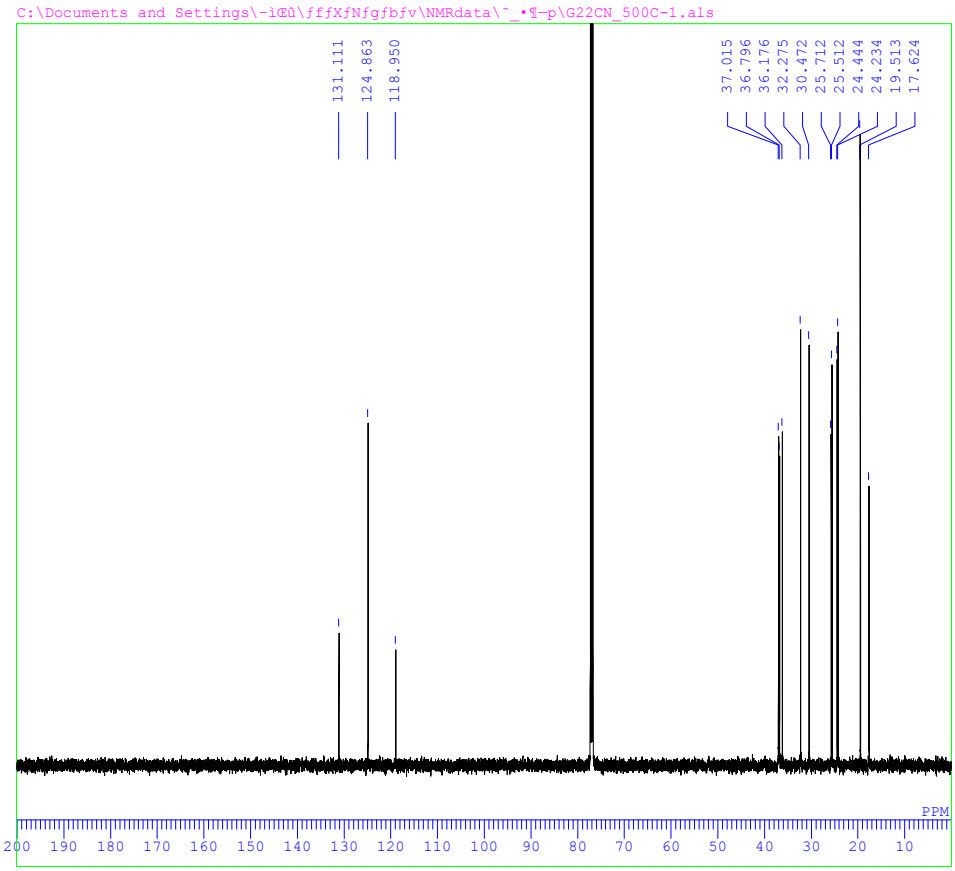
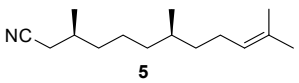
OBNUC   1H
EXMOD   single_pulse.ex2
OBFRQ         500.16 MHz
OBSET           2.41 KHz
OBFIN           6.01 Hz
POINT          13107
FREQU        7507.39 Hz
SCANS               8
ACQTM         1.7459 sec
PD            5.0000 sec
PW1             6.82 usec
IRNUC   1H
CTEMP          22.2 c
SLVNT   CDCL3
EXREF          0.00 ppm
BF             0.12 Hz
RGAIN            40
```



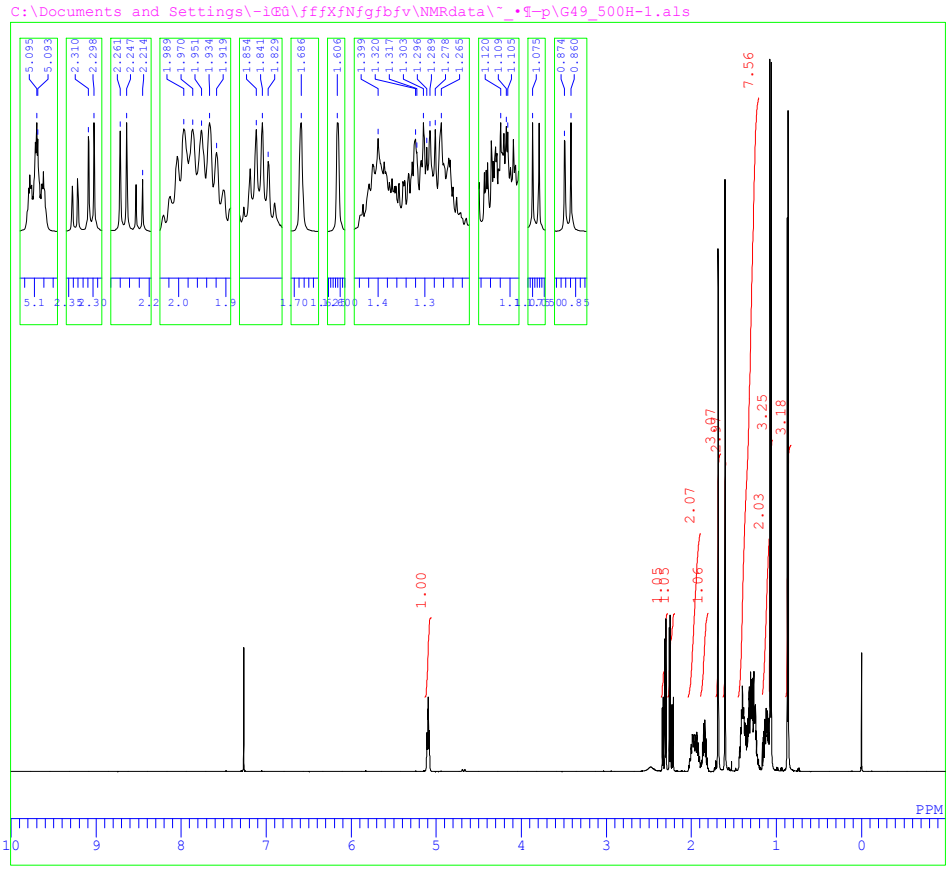
5



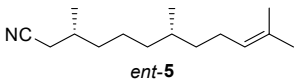

```
DFILE   G22CN_500C-1.als
COMNT   single pulse decoupled gated NOE
DATIM   2014-10-31 11:22:20
OBNUC   13C
EXMOD   single_pulse_dec
OBFRQ         125.77 MHz
OBSET           7.87 KHz
OBFIN           4.21 Hz
POINT          26214
FREQU       31446.06 Hz
SCANS           1000
ACQTM         0.8336 sec
PD            2.0000 sec
PW1             3.50 usec
IRNUC   1H
CTEMP          23.1 c
SLVNT   CDCL3
EXREF          77.00 ppm
BF              1.20 Hz
RGAIN            52
```



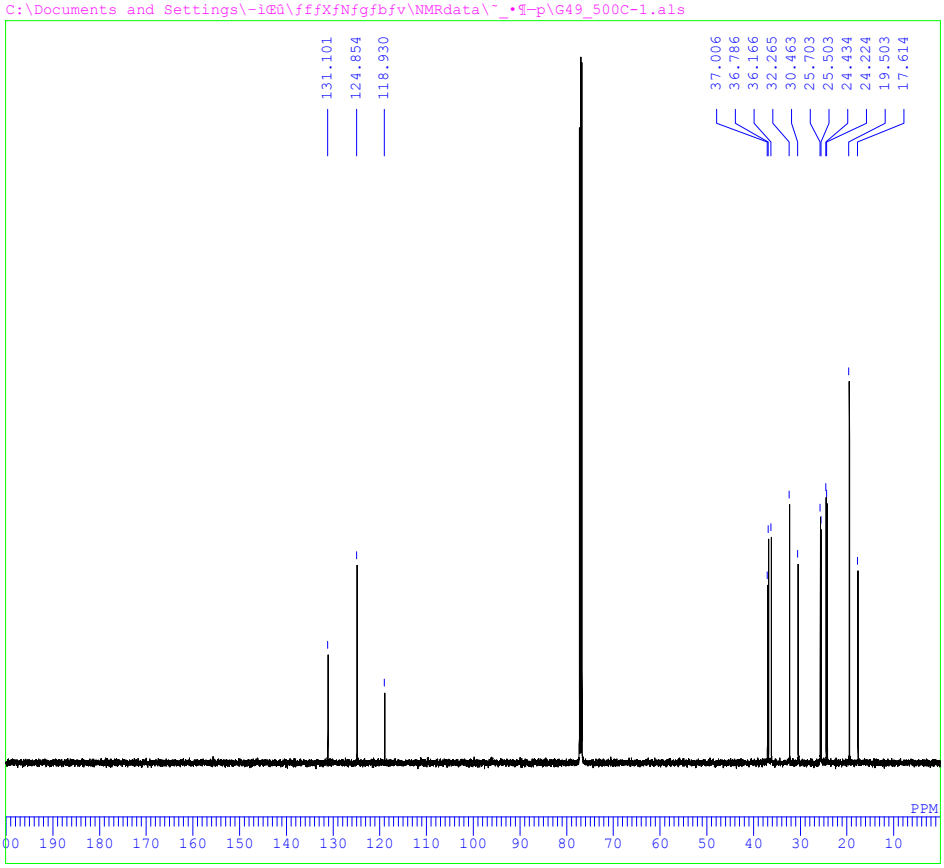
5



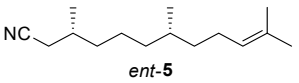

```
DFILE  G49_500H-1.als
COMNT  single_pulse
DATIM  2015-04-13 10:19:11
OBNUC  1H
EXMOD  single_pulse.ex2
OBFRQ        500.16 MHz
OBSET          2.41 KHz
OBFIN          6.01 Hz
POINT         13107
FREQU       7507.39 Hz
SCANS             8
ACQTM        1.7459 sec
PD           5.0000 sec
PW1            6.82 usec
IRNUC  1H
CTEMP         21.9 c
SLVNT  CDCL3
EXREF          0.00 ppm
BF             0.12 Hz
RGAIN            38
```



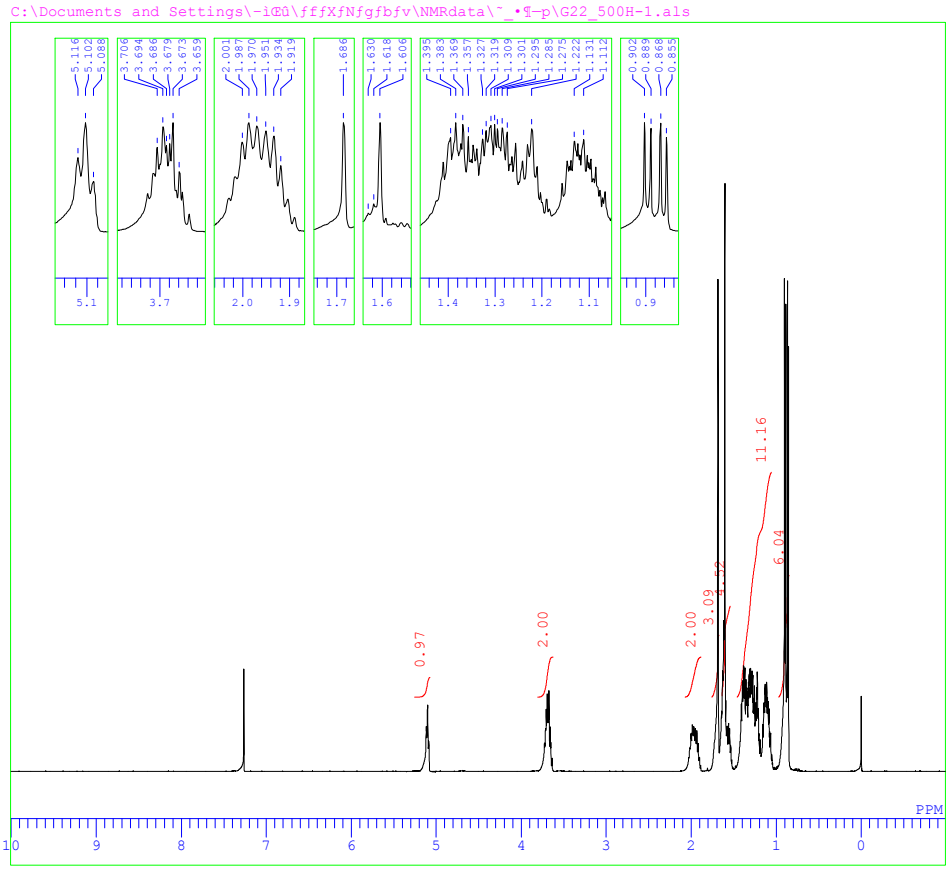
***ent*-5**



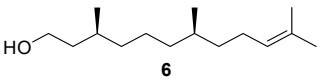

```
DFILE  G49_500C-1.als
COMNT  single pulse decoupled gated NOE
DATIM  2015-04-13 11:07:11
OBNUC  13C
EXMOD  single_pulse_dec
OBFRQ        125.77 MHz
OBSET          7.87 KHz
OBFIN          4.21 Hz
POINT         26214
FREQU      31446.06 Hz
SCANS          1000
ACQTM        0.8336 sec
PD           2.0000 sec
PW1            3.50 usec
IRNUC  1H
CTEMP         22.4 c
SLVNT  CDCL3
EXREF         77.00 ppm
BF             1.20 Hz
RGAIN            54
```



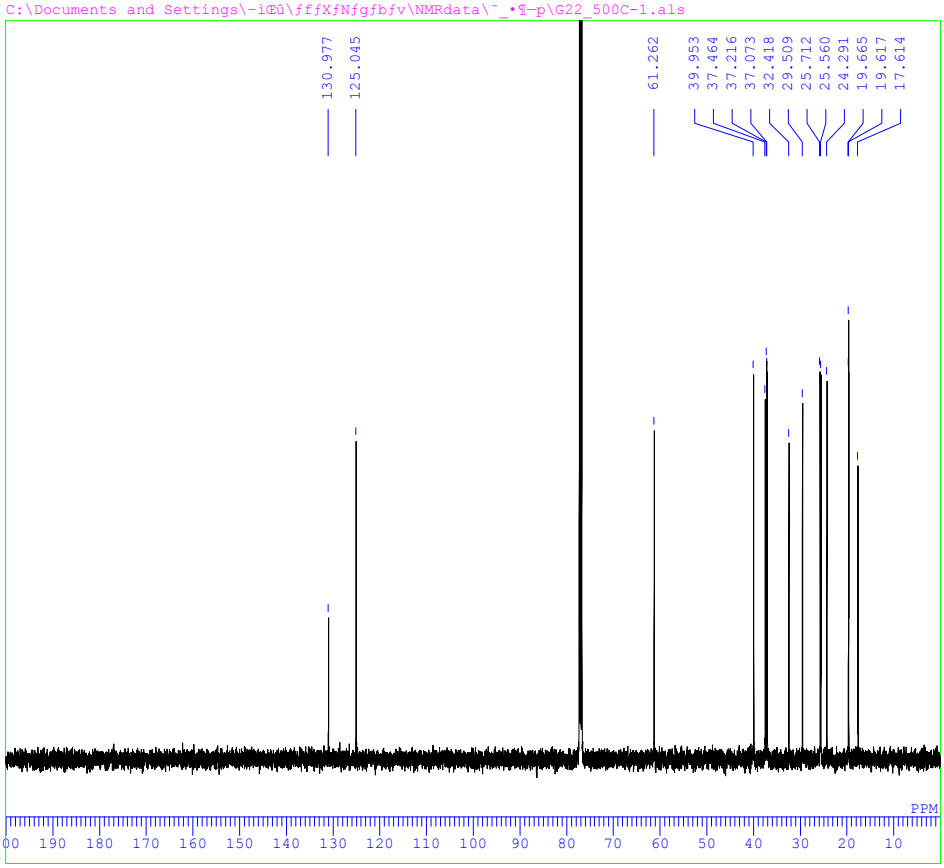
***ent*-5**



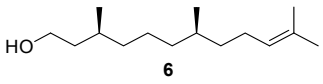

```
DFILE   G22_500H-1.als
COMNT   single_pulse
DATIM   2014-09-06 15:21:14
OBNUC   1H
EXMOD   single_pulse.ex2
OBFRQ         500.16 MHz
OBSET           2.41 KHz
OBFIN           6.01 Hz
POINT          13107
FREQU        7507.39 Hz
SCANS               8
ACQTM         1.7459 sec
PD            5.0000 sec
PW1             6.82 usec
IRNUC   1H
CTEMP           23.5 c
SLVNT   CDCL3
EXREF           0.00 ppm
BF              0.12 Hz
RGAIN             38
```



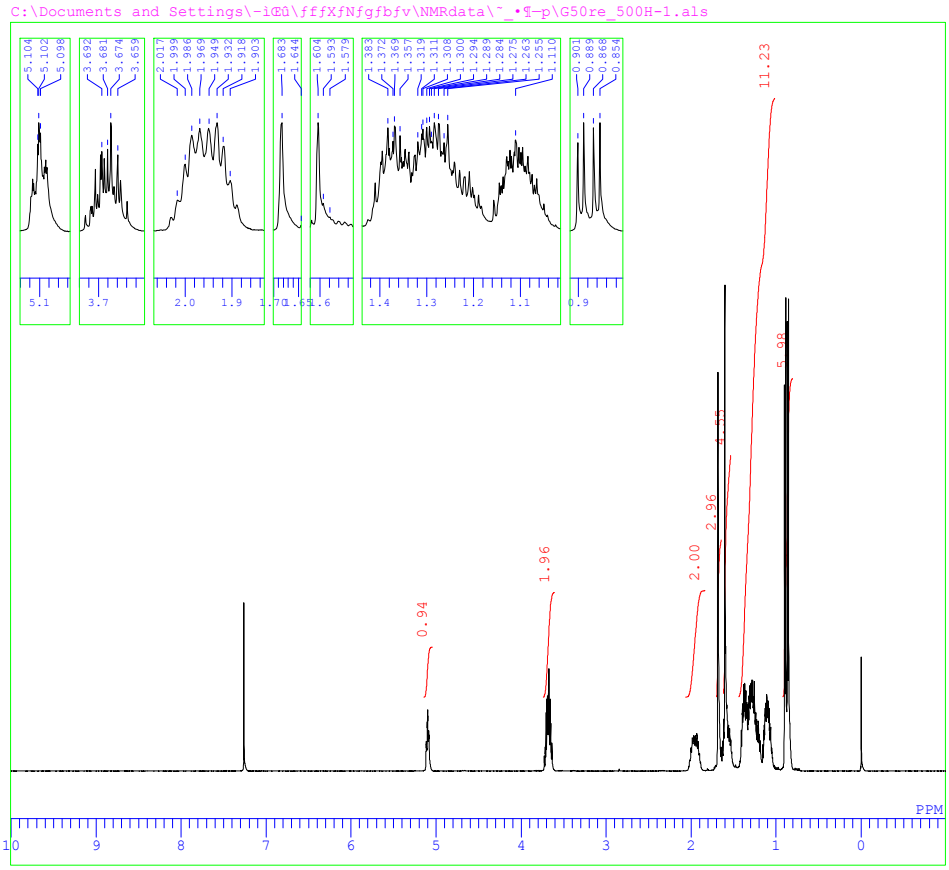
6



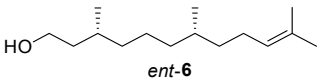

```
DFILE   G22_500C-1.als
COMNT   single pulse decoupled gated NOE
DATIM   2014-09-06 16:09:23
OBNUC   13C
EXMOD   single_pulse_dec
OBFRQ         125.77 MHz
OBSET           7.87 KHz
OBFIN           4.21 Hz
POINT          26214
FREQU       31446.06 Hz
SCANS           1000
ACQTM         0.8336 sec
PD            2.0000 sec
PW1             3.50 usec
IRNUC   1H
CTEMP           23.7 c
SLVNT   CDCL3
EXREF          77.00 ppm
BF              1.20 Hz
RGAIN             54
```



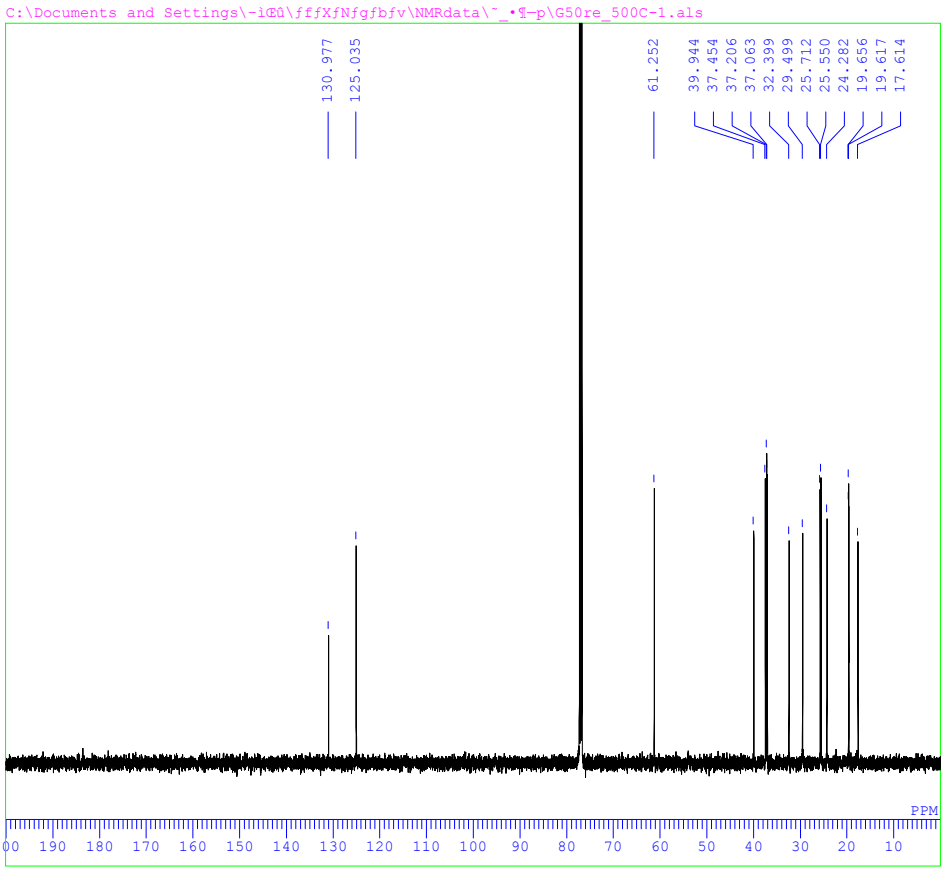
6



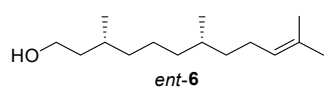

```
DFILE   G50re_500H-1.als
COMNT   single_pulse
DATIM   2015-04-13 15:08:10
OBNUC   1H
EXMOD   single_pulse.ex2
OBFRQ         500.16 MHz
OBSET           2.41 KHz
OBFIN           6.01 Hz
POINT          13107
FREQU        7507.39 Hz
SCANS               8
ACQTM         1.7459 sec
PD            5.0000 sec
PW1             6.82 usec
IRNUC   1H
CTEMP          22.0 c
SLVNT   CDCL3
EXREF          0.00 ppm
BF             0.12 Hz
RGAIN            40
```



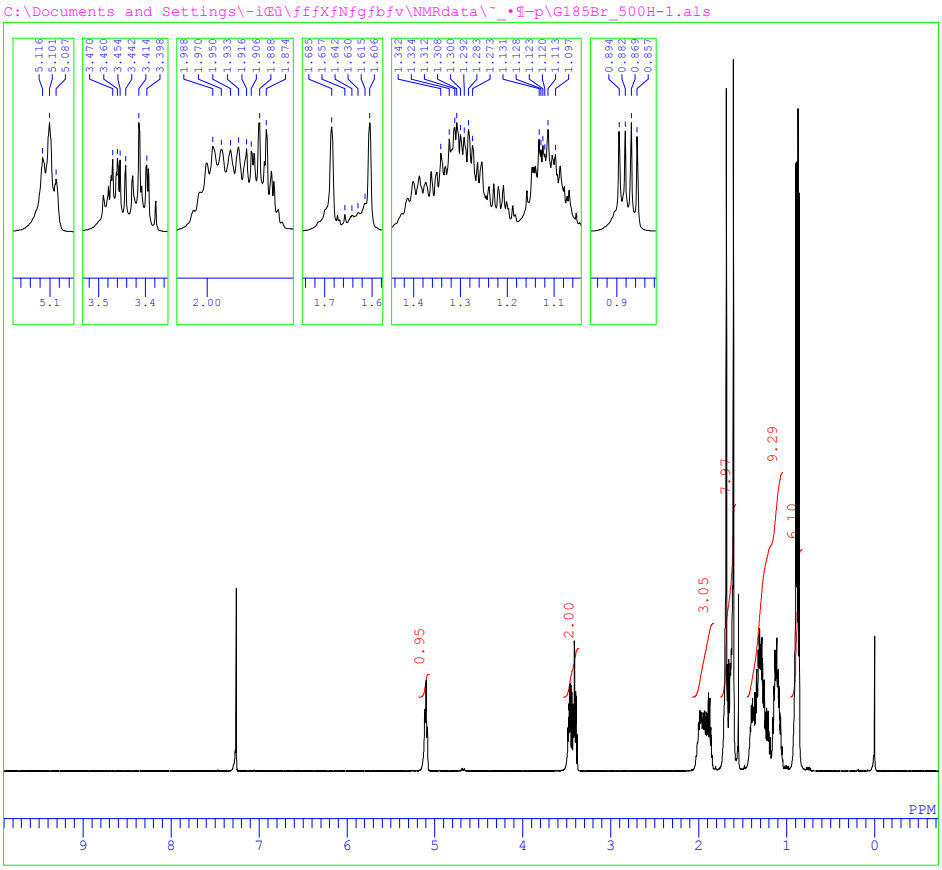
ent-**6**



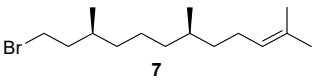

```
DFILE   G50re_500C-1.als
COMNT   single pulse decoupled gated NOE
DATIM   2015-04-13 15:56:05
OBNUC   13C
EXMOD   single_pulse_dec
OBFRQ         125.77 MHz
OBSET           7.87 KHz
OBFIN           4.21 Hz
POINT          26214
FREQU       31446.06 Hz
SCANS           1000
ACQTM         0.8336 sec
PD            2.0000 sec
PW1             3.50 usec
IRNUC   1H
CTEMP          22.4 c
SLVNT   CDCL3
EXREF          77.00 ppm
BF             1.20 Hz
RGAIN            58
```



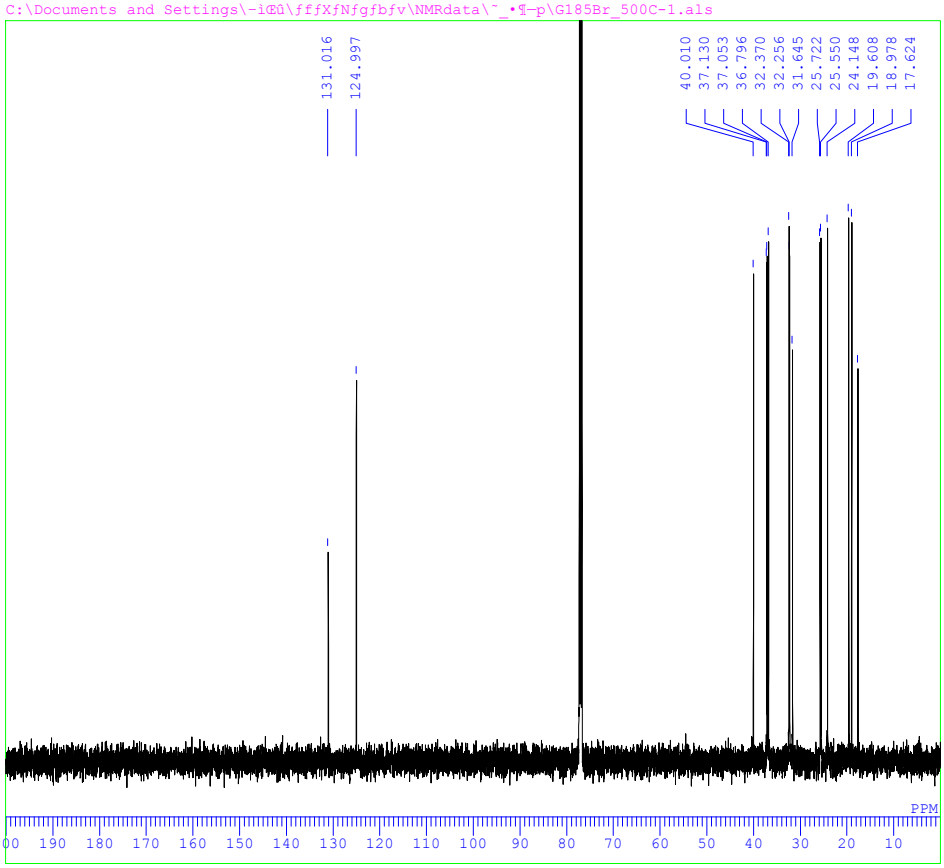
ent-**6**



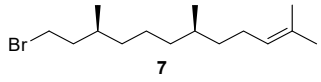

```
DFILE  G185Br_500H-1.als
COMNT  single_pulse
DATIM  2015-04-13 18:13:38
OBNUC  1H
EXMOD  single_pulse.ex2
OBFRQ        500.16 MHz
OBSET          2.41 KHz
OBFIN          6.01 Hz
POINT         13107
FREQU       7507.39 Hz
SCANS             8
ACQTM        1.7459 sec
PD           5.0000 sec
PW1            6.82 usec
IRNUC  1H
CTEMP         21.8 c
SLVNT  CDCL3
EXREF          0.00 ppm
BF             0.12 Hz
RGAIN            42
```



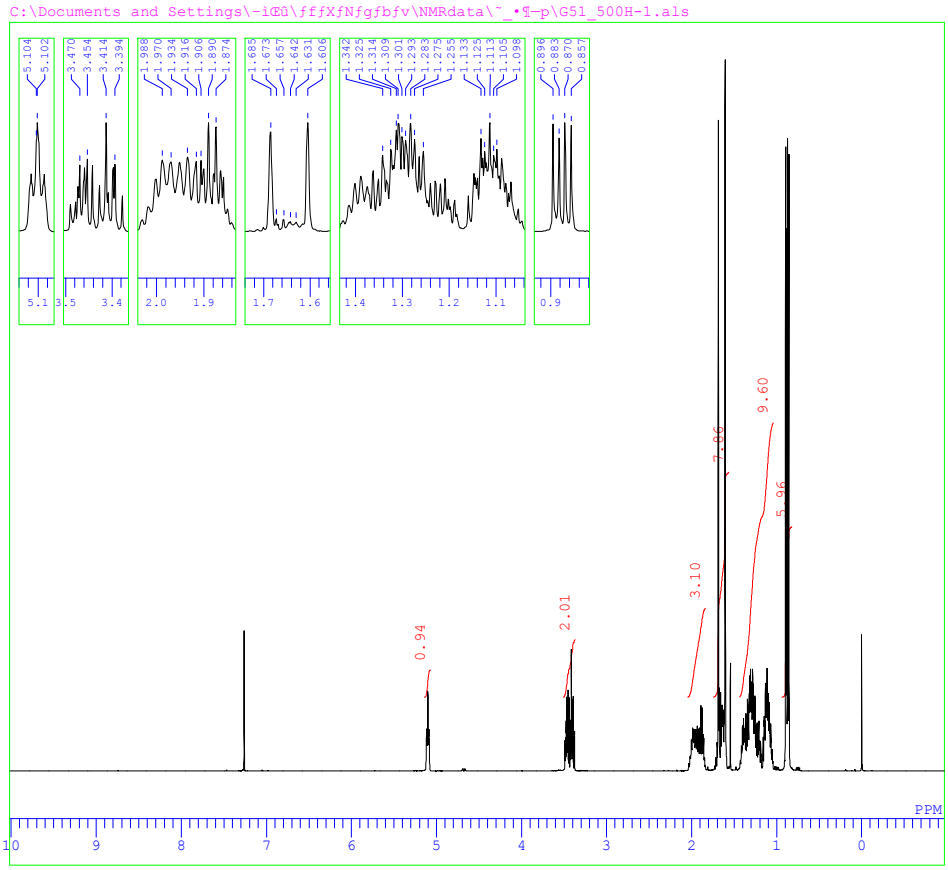
7



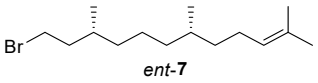

```
DFILE  G185Br_500C-1.als
COMNT  single pulse decoupled gated NOE
DATIM  2015-04-13 19:01:31
OBNUC  13C
EXMOD  single_pulse_dec
OBFRQ        125.77 MHz
OBSET          7.87 KHz
OBFIN          4.21 Hz
POINT         26214
FREQU      31446.06 Hz
SCANS          1000
ACQTM        0.8336 sec
PD           2.0000 sec
PW1            3.50 usec
IRNUC  1H
CTEMP         22.4 c
SLVNT  CDCL3
EXREF         77.00 ppm
BF             1.20 Hz
RGAIN            54
```



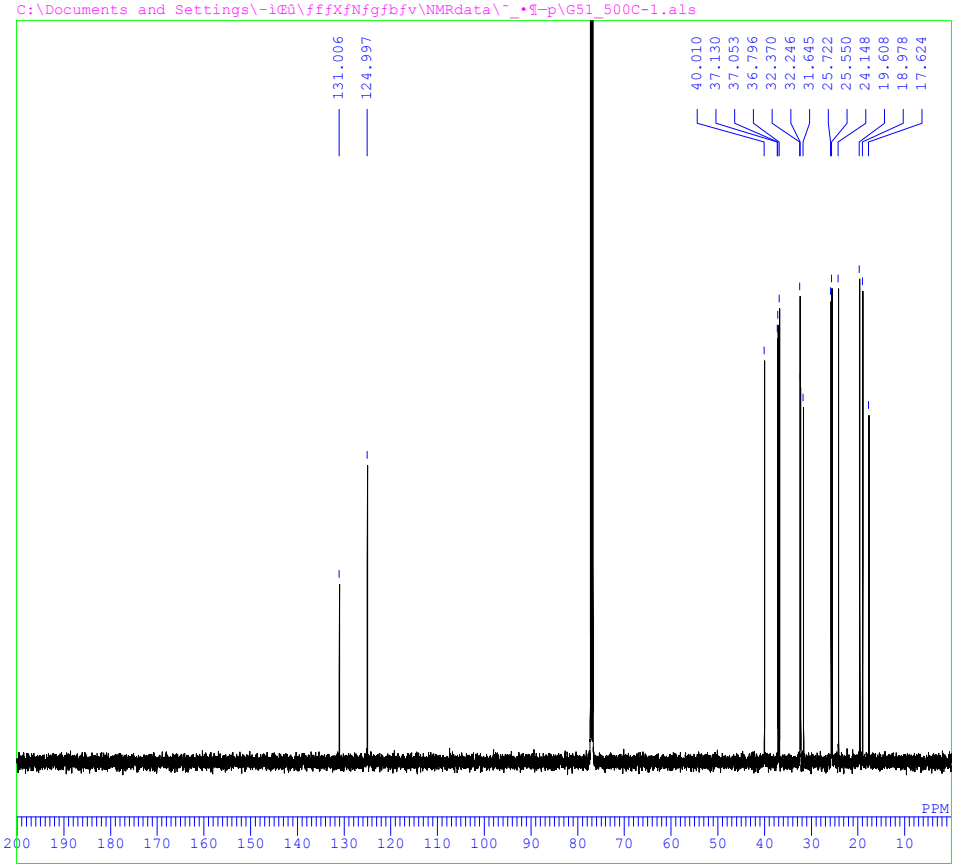
7



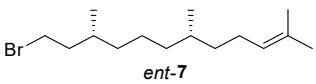

```
DFILE   G51_500H-1.als
COMNT   single_pulse
DATIM   2015-04-13 12:26:57
OBNUC   1H
EXMOD   single_pulse.ex2
OBFRQ         500.16 MHz
OBSET           2.41 KHz
OBFIN           6.01 Hz
POINT          13107
FREQU        7507.39 Hz
SCANS               8
ACQTM         1.7459 sec
PD            5.0000 sec
PW1             6.82 usec
IRNUC   1H
CTEMP          21.8 c
SLVNT   CDCL3
EXREF          0.00 ppm
BF             0.12 Hz
RGAIN            38
```



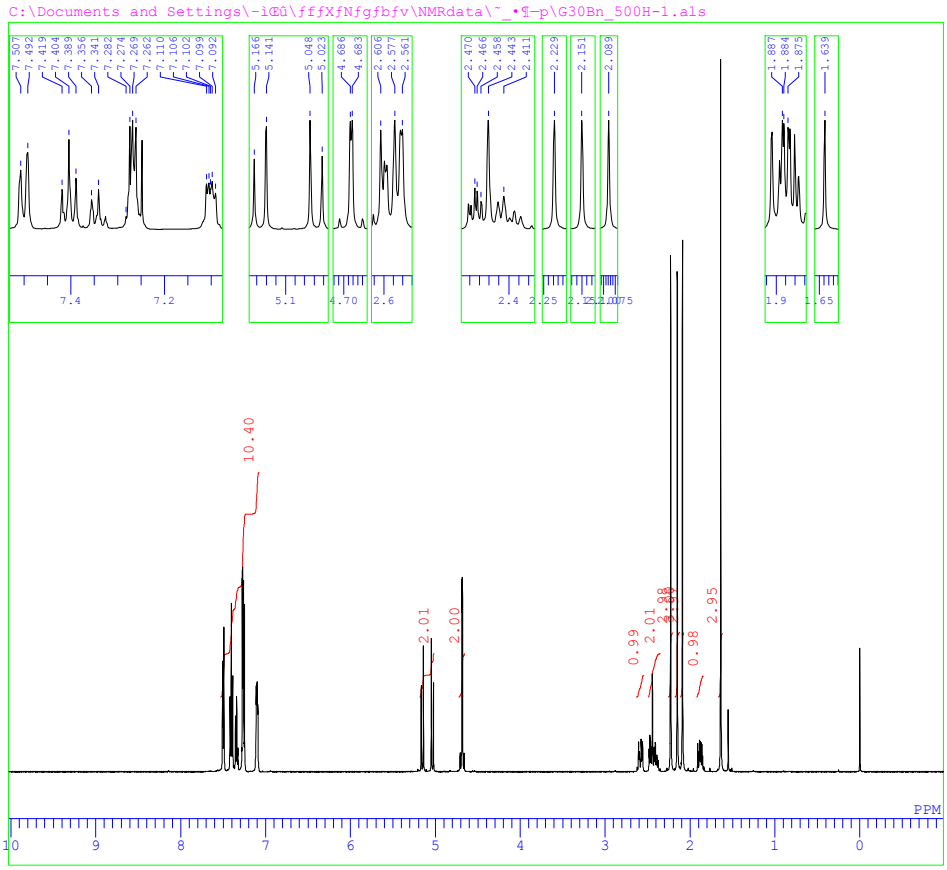
ent-**7**



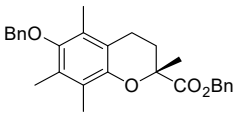

```
DFILE   G51_500C-1.als
COMNT   single pulse decoupled gated NOE
DATIM   2015-04-13 13:05:58
OBNUC   13C
EXMOD   single_pulse_dec
OBFRQ         125.77 MHz
OBSET           7.87 KHz
OBFIN           4.21 Hz
POINT          26214
FREQU       31446.06 Hz
SCANS            800
ACQTM         0.8336 sec
PD            2.0000 sec
PW1             3.50 usec
IRNUC   1H
CTEMP          22.3 c
SLVNT   CDCL3
EXREF         77.00 ppm
BF             1.20 Hz
RGAIN            56
```



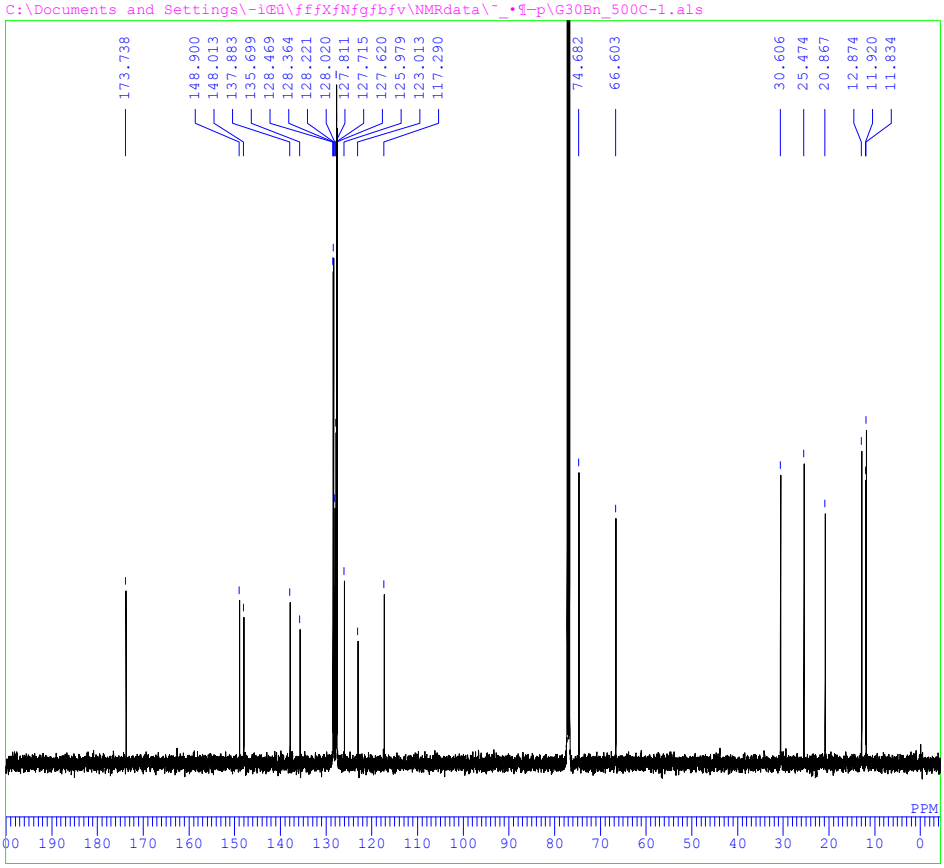
ent-**7**



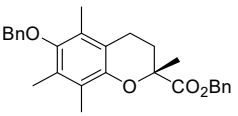

```
DFILE  G30Bn_500H-1.als
COMNT  single_pulse
DATIM  2015-04-09 01:51:20
OBNUC  1H
EXMOD  single_pulse.ex2
OBFRQ        500.16 MHz
OBSET          2.41 KHz
OBFIN          6.01 Hz
POINT         13107
FREQU       7507.39 Hz
SCANS             8
ACQTM        1.7459 sec
PD           5.0000 sec
PW1            6.82 usec
IRNUC  1H
CTEMP         21.5 c
SLVNT  CDCL3
EXREF         0.00 ppm
BF            0.12 Hz
RGAIN           42
```



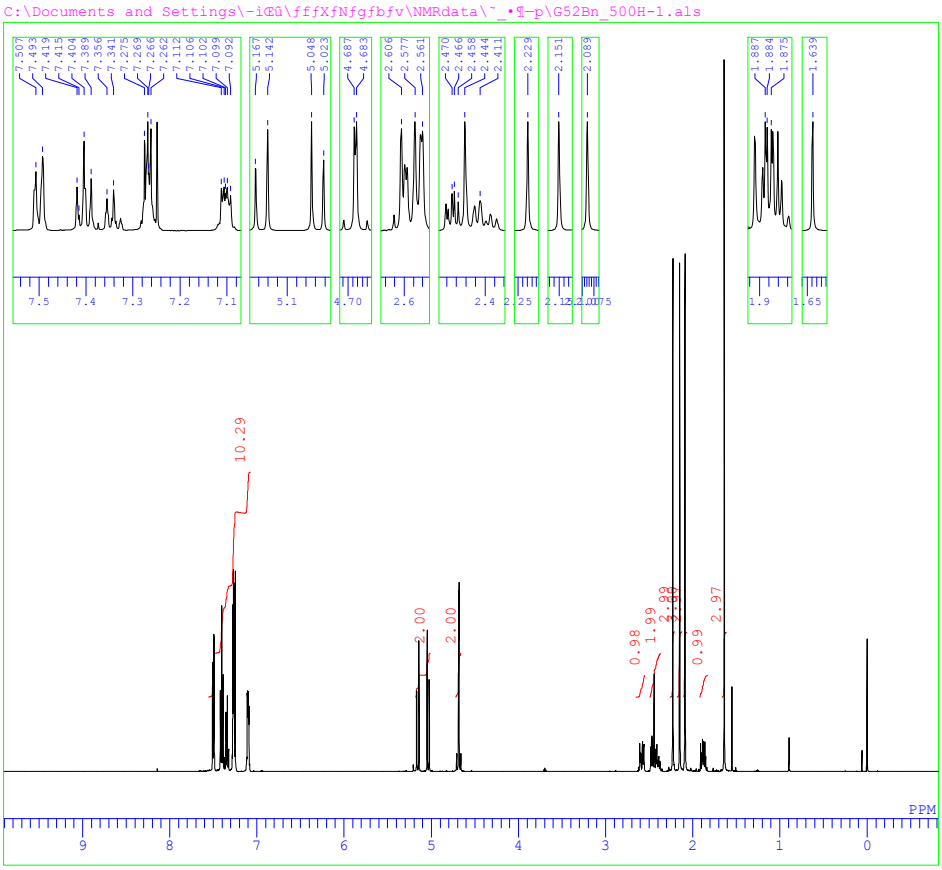
S6



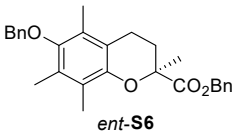

```
DFILE  G30Bn_500C-1.als
COMNT  single pulse decoupled gated NOE
DATIM  2015-04-09 02:39:17
OBNUC  13C
EXMOD  single_pulse_dec
OBFRQ        125.77 MHz
OBSET          7.87 KHz
OBFIN          4.21 Hz
POINT         26214
FREQU       31446.06 Hz
SCANS           1000
ACQTM         0.8336 sec
PD            2.0000 sec
PW1             3.50 usec
IRNUC  1H
CTEMP         21.9 c
SLVNT  CDCL3
EXREF         77.00 ppm
BF            1.20 Hz
RGAIN           58
```



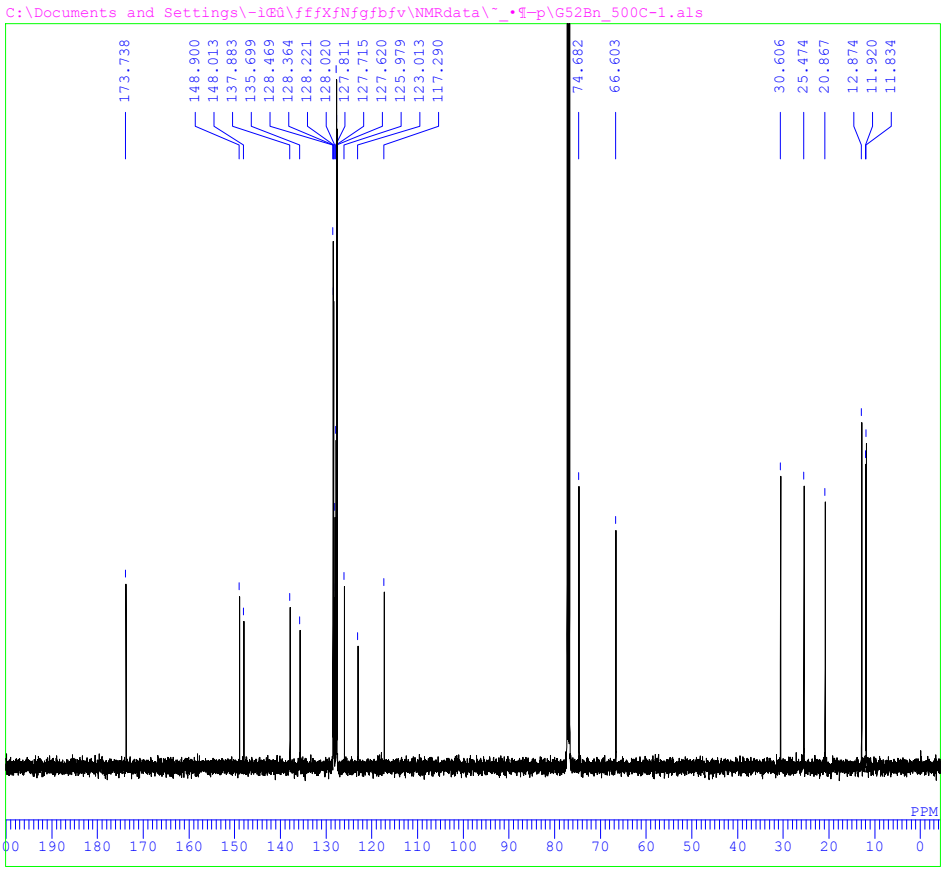
S6



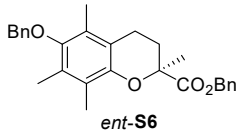

```
DFILE  G52Bn_500H-1.als
COMNT  single_pulse
DATIM  2015-04-09 02:49:50
OBNUC  1H
EXMOD  single_pulse.ex2
OBFRQ        500.16 MHz
OBSET          2.41 KHz
OBFIN          6.01 Hz
POINT         13107
FREQU       7507.39 Hz
SCANS             8
ACQTM        1.7459 sec
PD           5.0000 sec
PW1            6.82 usec
IRNUC  1H
CTEMP         21.5 c
SLVNT  CDCL3
EXREF          0.00 ppm
BF             0.12 Hz
RGAIN            40
```



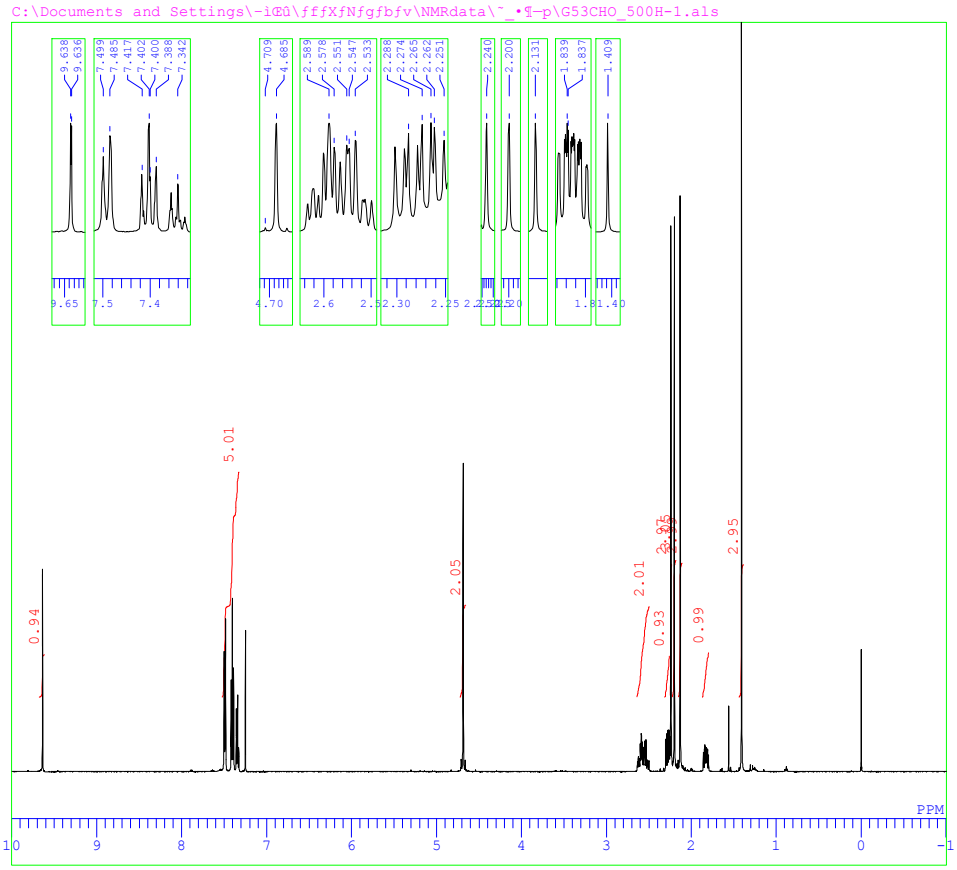
ent-**S6**



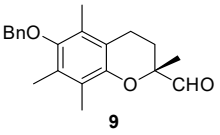

```
DFILE  G52Bn_500C-1.als
COMNT  single pulse decoupled gated NOE
DATIM  2015-04-09 03:37:48
OBNUC  13C
EXMOD  single_pulse_dec
OBFRQ        125.77 MHz
OBSET          7.87 KHz
OBFIN          4.21 Hz
POINT         26214
FREQU      31446.06 Hz
SCANS           1000
ACQTM         0.8336 sec
PD            2.0000 sec
PW1             3.50 usec
IRNUC  1H
CTEMP          21.8 c
SLVNT  CDCL3
EXREF         77.00 ppm
BF             1.20 Hz
RGAIN            58
```



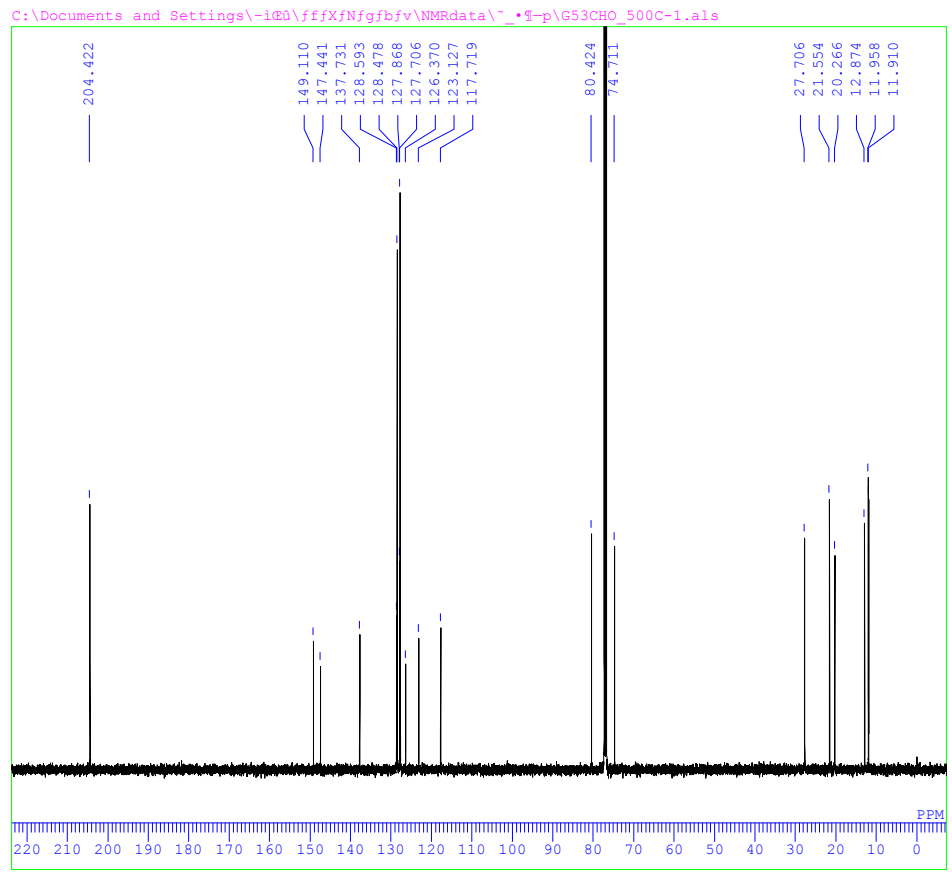
ent-**S6**



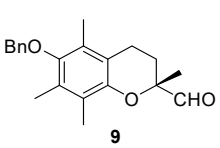

```
DFILE  G53CHO_500H-1.als
COMNT  single_pulse
DATIM  2015-04-09 04:44:00
OBNUC  1H
EXMOD  single_pulse.ex2
OBFRQ        500.16 MHz
OBSET          2.41 KHz
OBFIN          6.01 Hz
POINT         13107
FREQU       7507.39 Hz
SCANS             8
ACQTM        1.7459 sec
PD           5.0000 sec
PW1            6.82 usec
IRNUC  1H
CTEMP         21.5 c
SLVNT  CDCL3
EXREF          0.00 ppm
BF             0.12 Hz
RGAIN            40
```



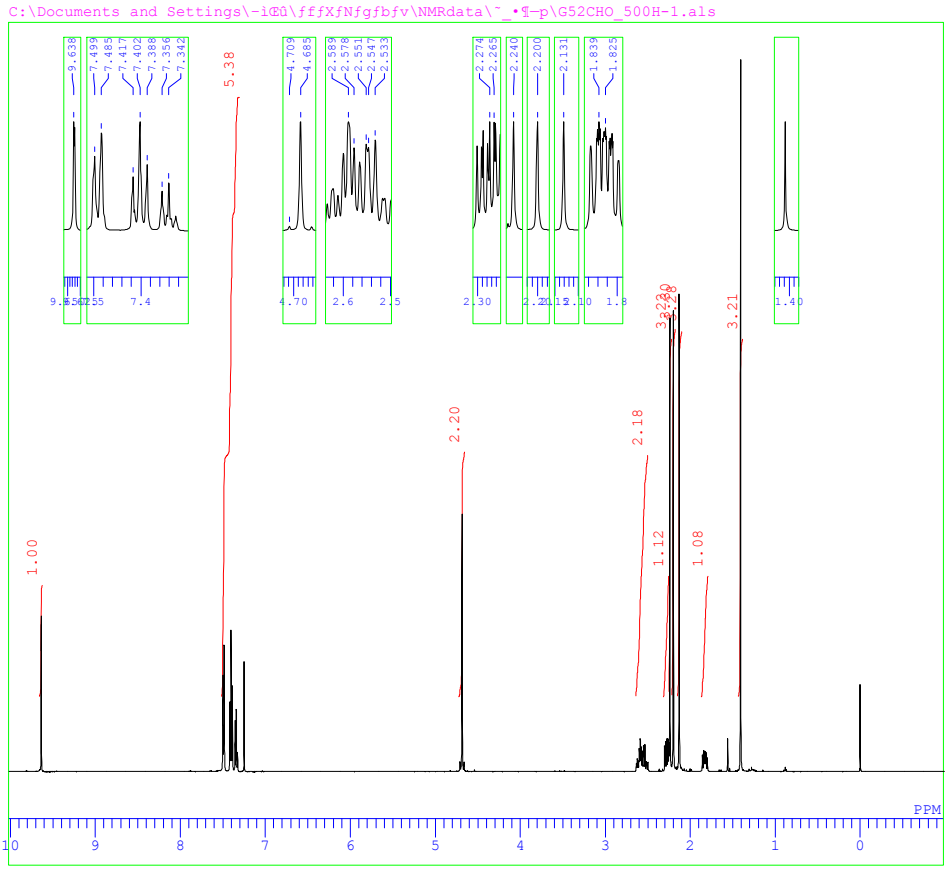
9



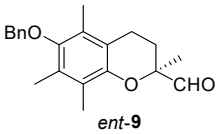

```
DFILE  G53CHO_500C-1.als
COMNT  single pulse decoupled gated NOE
DATIM  2015-04-09 05:31:57
OBNUC  13C
EXMOD  single_pulse_dec
OBFRQ        125.77 MHz
OBSET          7.87 KHz
OBFIN          4.21 Hz
POINT         26214
FREQU       31446.06 Hz
SCANS           1000
ACQTM         0.8336 sec
PD            2.0000 sec
PW1             3.50 usec
IRNUC  1H
CTEMP          21.9 c
SLVNT  CDCL3
EXREF         77.00 ppm
BF             1.20 Hz
RGAIN            58
```



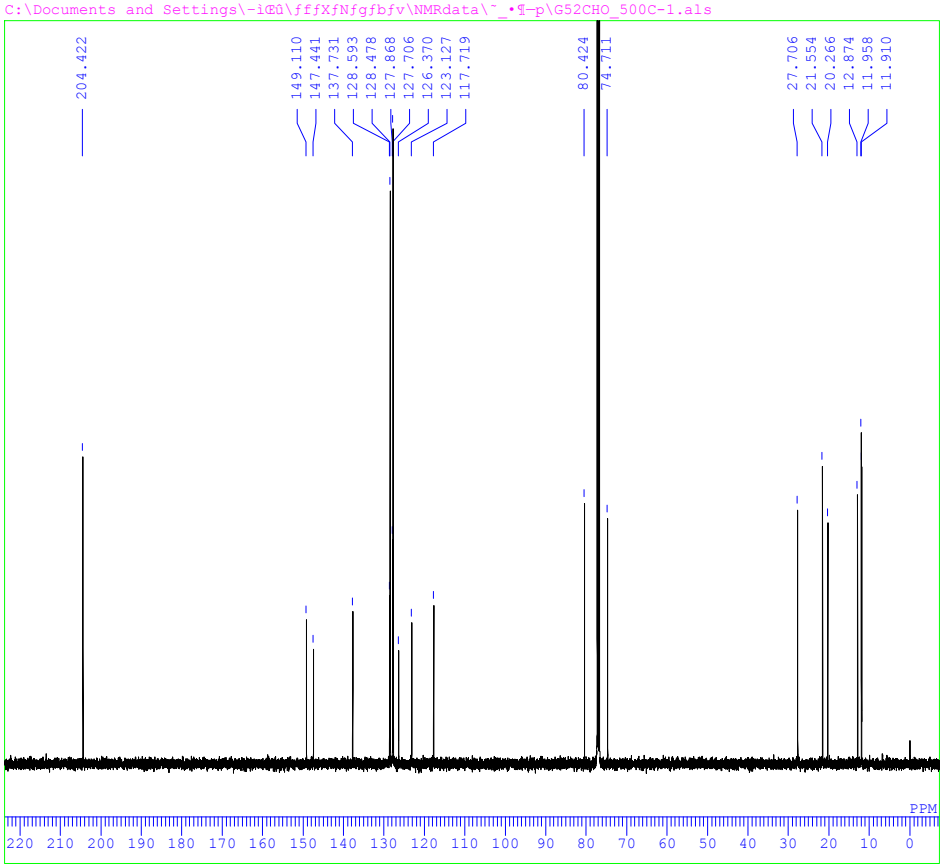
9



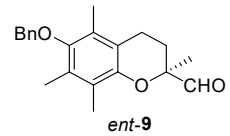

```
DFILE   G52CHO_500H-1.als
COMNT   single_pulse
DATIM   2015-04-09 03:48:19
OBNUC   1H
EXMOD   single_pulse.ex2
OBFRQ         500.16 MHz
OBSET           2.41 KHz
OBFIN           6.01 Hz
POINT          13107
FREQU        7507.39 Hz
SCANS                8
ACQTM         1.7459 sec
PD            5.0000 sec
PW1             6.82 usec
IRNUC   1H
CTEMP          21.6 c
SLVNT   CDCL3
EXREF          0.00 ppm
BF             0.12 Hz
RGAIN            40
```



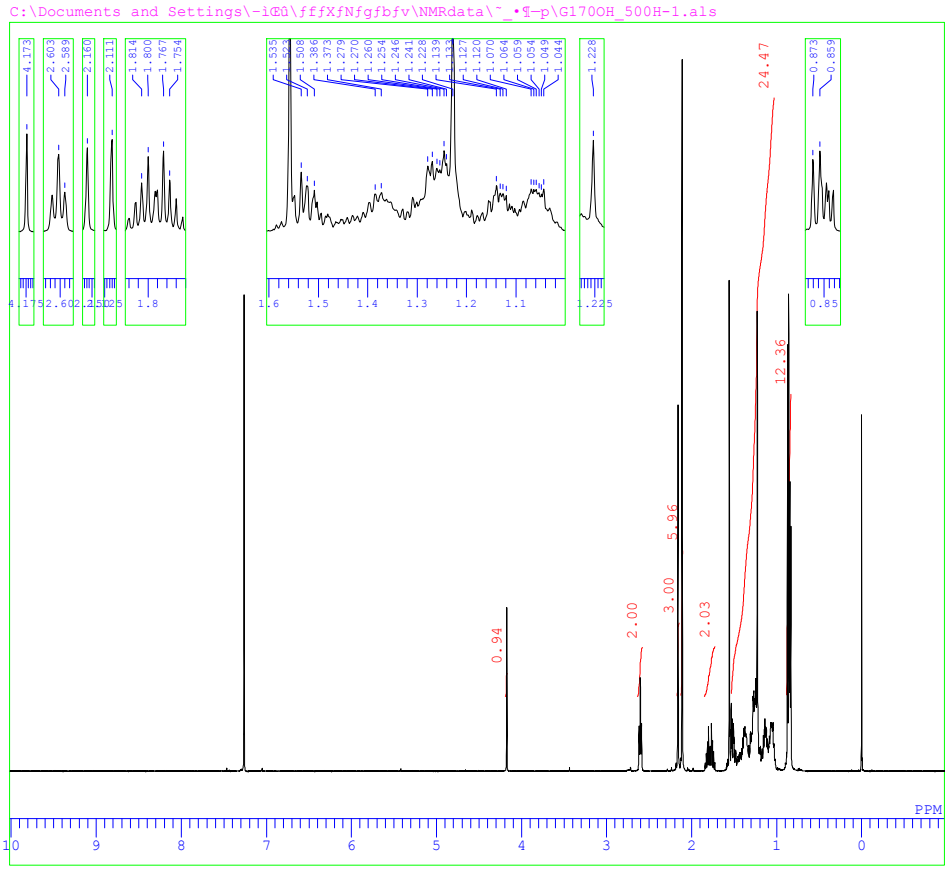
ent-**9**



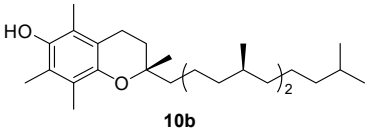

```
DFILE   G52CHO_500C-1.als
COMNT   single pulse decoupled gated NOE
DATIM   2015-04-09 04:36:16
OBNUC   13C
EXMOD   single_pulse_dec
OBFRQ         125.77 MHz
OBSET           7.87 KHz
OBFIN           4.21 Hz
POINT          26214
FREQU       31446.06 Hz
SCANS            1000
ACQTM         0.8336 sec
PD            2.0000 sec
PW1             3.50 usec
IRNUC   1H
CTEMP          21.8 c
SLVNT   CDCL3
EXREF          77.00 ppm
BF             1.20 Hz
RGAIN            58
```



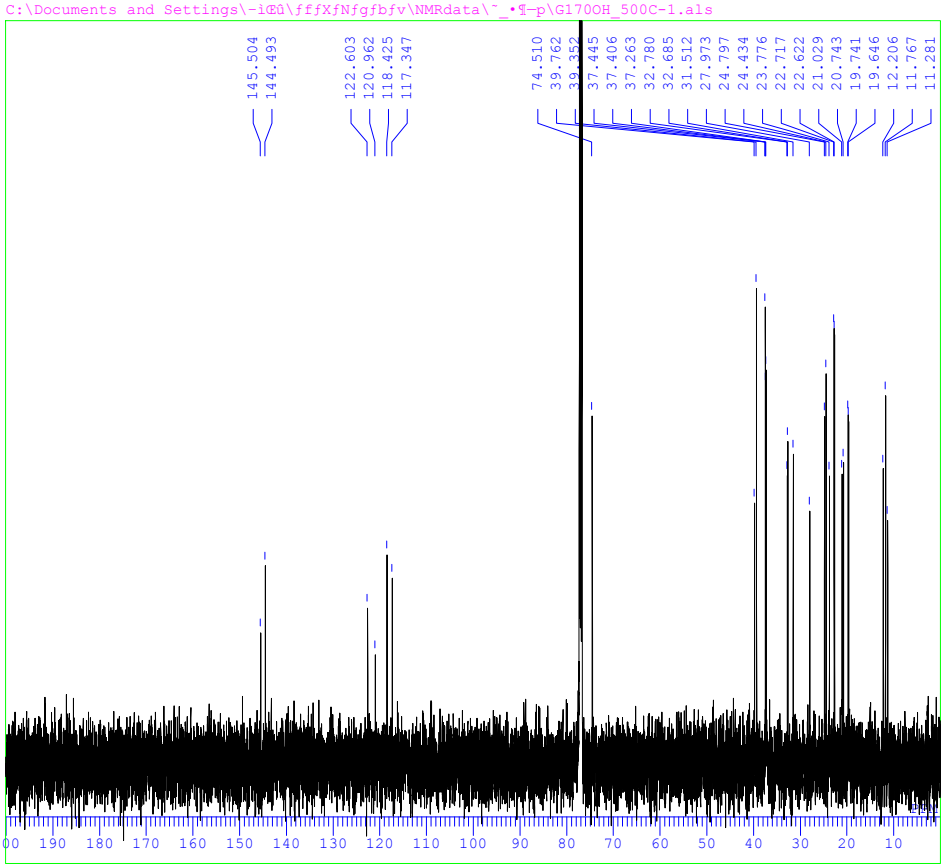
ent-**9**



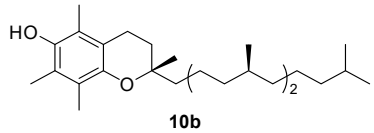

```
DFILE   G170OH_500H-1.als
COMNT   single_pulse
DATIM   2015-02-23 13:30:55
OBNUC   1H
EXMOD   single_pulse.ex2
OBFRQ         500.16 MHz
OBSET           2.41 KHz
OBFIN           6.01 Hz
POINT          13107
FREQU        7507.39 Hz
SCANS                8
ACQTM         1.7459 sec
PD            5.0000 sec
PW1             6.82 usec
IRNUC   1H
CTEMP          21.1 c
SLVNT   CDCL3
EXREF          0.00 ppm
BF             0.12 Hz
RGAIN            48
```



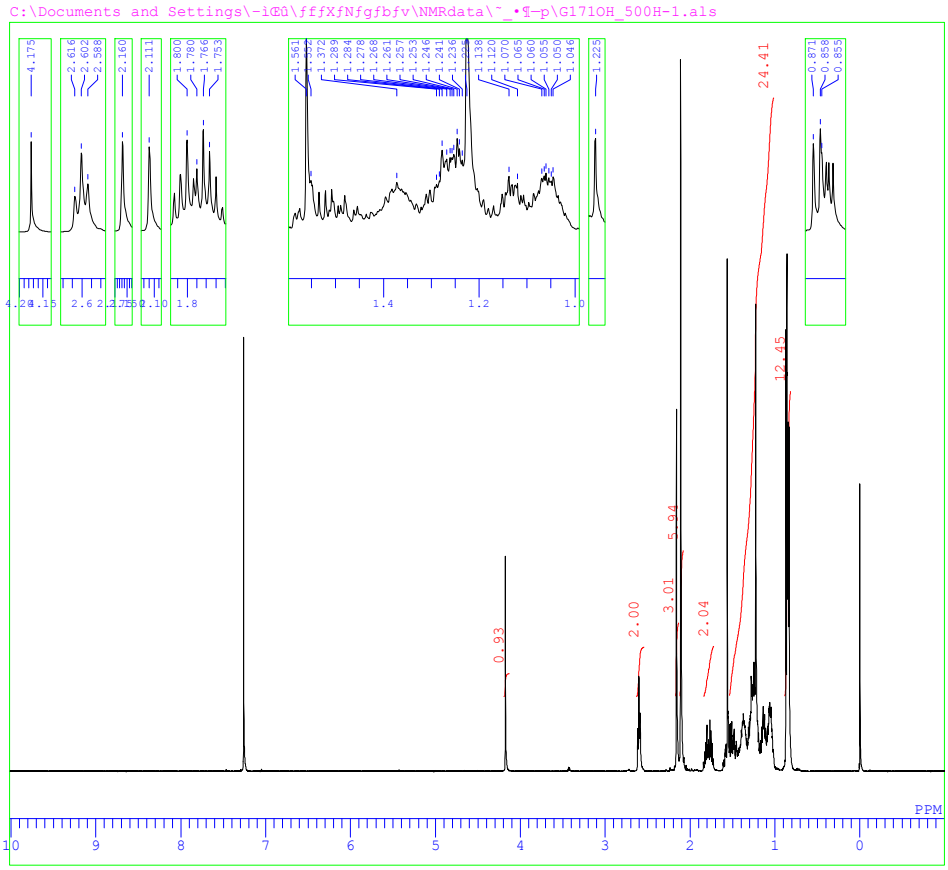
10b



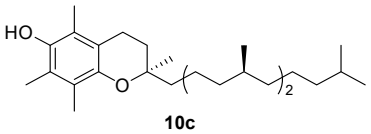

```
DFILE   G170OH_500C-1.als
COMNT   single pulse decoupled gated NOE
DATIM   2015-02-23 14:18:53
OBNUC   13C
EXMOD   single_pulse_dec
OBFRQ         125.77 MHz
OBSET           7.87 KHz
OBFIN           4.21 Hz
POINT          26214
FREQU       31446.06 Hz
SCANS            1000
ACQTM         0.8336 sec
PD            2.0000 sec
PW1             3.50 usec
IRNUC   1H
CTEMP          21.6 c
SLVNT   CDCL3
EXREF          77.00 ppm
BF             1.20 Hz
RGAIN            50
```



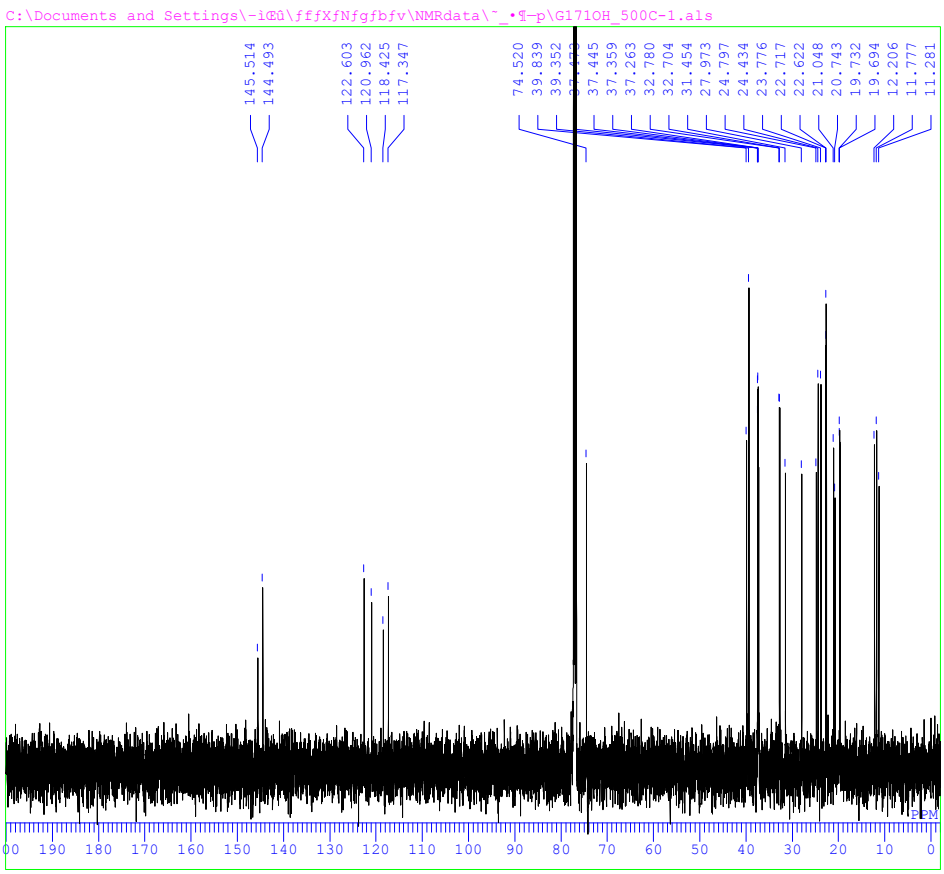
10b



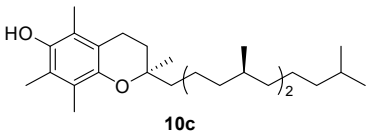
DFILE G171OH_500H-1.als
COMNT single_pulse
DATIM 2015-02-23 17:12:57
OBNUC 1H
EXMOD single_pulse.ex2
OBFRQ 500.16 MHz
OBSET 2.41 KHz
OBFIN 6.01 Hz
POINT 13107
FREQU 7507.39 Hz
SCANS 8
ACQTM 1.7459 sec
PD 5.0000 sec
PW1 6.82 usec
IRNUC 1H
CTEMP 21.2 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 0.12 Hz
RGAIN 44



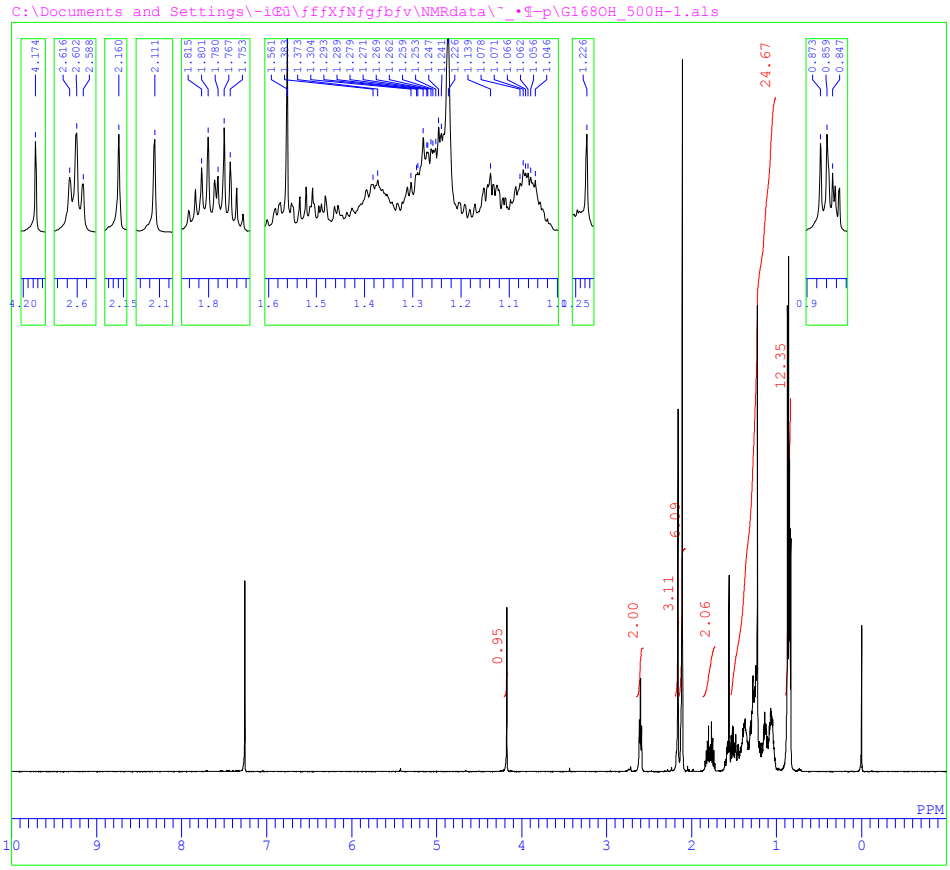
10c



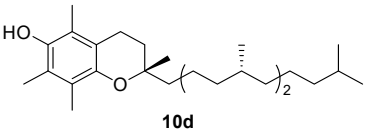
DFILE G171OH_500C-1.als
COMNT single pulse decoupled gated NOE
DATIM 2015-02-23 18:01:08
OBNUC 13C
EXMOD single_pulse_dec
OBFRQ 125.77 MHz
OBSET 7.87 KHz
OBFIN 4.21 Hz
POINT 26214
FREQU 31446.06 Hz
SCANS 1000
ACQTM 0.8336 sec
PD 2.0000 sec
PW1 3.50 usec
IRNUC 1H
CTEMP 21.7 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 1.20 Hz
RGAIN 56



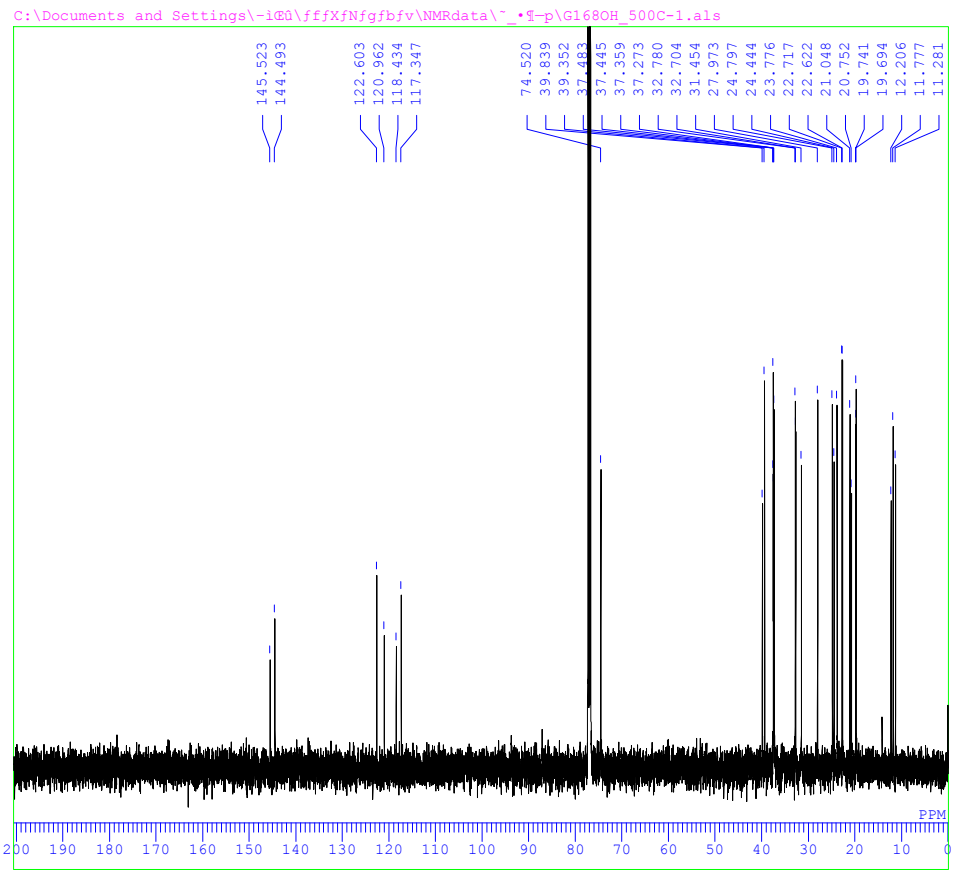
10c



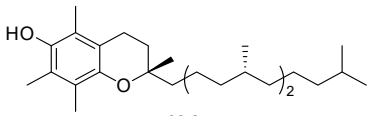

```
DFILE  G168OH_500H-1.als
COMNT  single_pulse
DATIM  2015-02-23 11:31:56
OBNUC  1H
EXMOD  single_pulse.ex2
OBFRQ        500.16 MHz
OBSET          2.41 KHz
OBFIN          6.01 Hz
POINT         13107
FREQU       7507.39 Hz
SCANS             8
ACQTM        1.7459 sec
PD           5.0000 sec
PW1             6.82 usec
IRNUC  1H
CTEMP          21.0 c
SLVNT  CDCL3
EXREF          0.00 ppm
BF             0.12 Hz
RGAIN            42
```



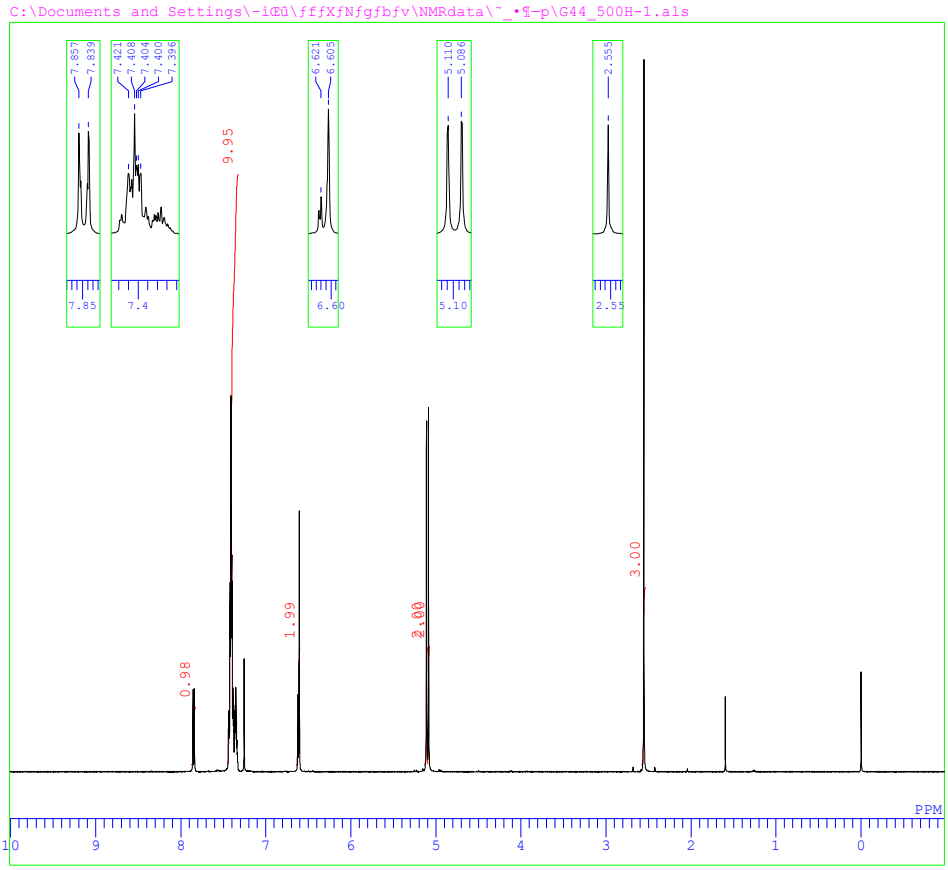
10d



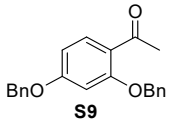

```
DFILE  G168OH_500C-1.als
COMNT  single pulse decoupled gated NOE
DATIM  2015-02-23 12:19:56
OBNUC  13C
EXMOD  single_pulse_dec
OBFRQ        125.77 MHz
OBSET          7.87 KHz
OBFIN          4.21 Hz
POINT         26214
FREQU      31446.06 Hz
SCANS          1000
ACQTM        0.8336 sec
PD           2.0000 sec
PW1             3.50 usec
IRNUC  1H
CTEMP          21.5 c
SLVNT  CDCL3
EXREF         77.00 ppm
BF             1.20 Hz
RGAIN            54
```



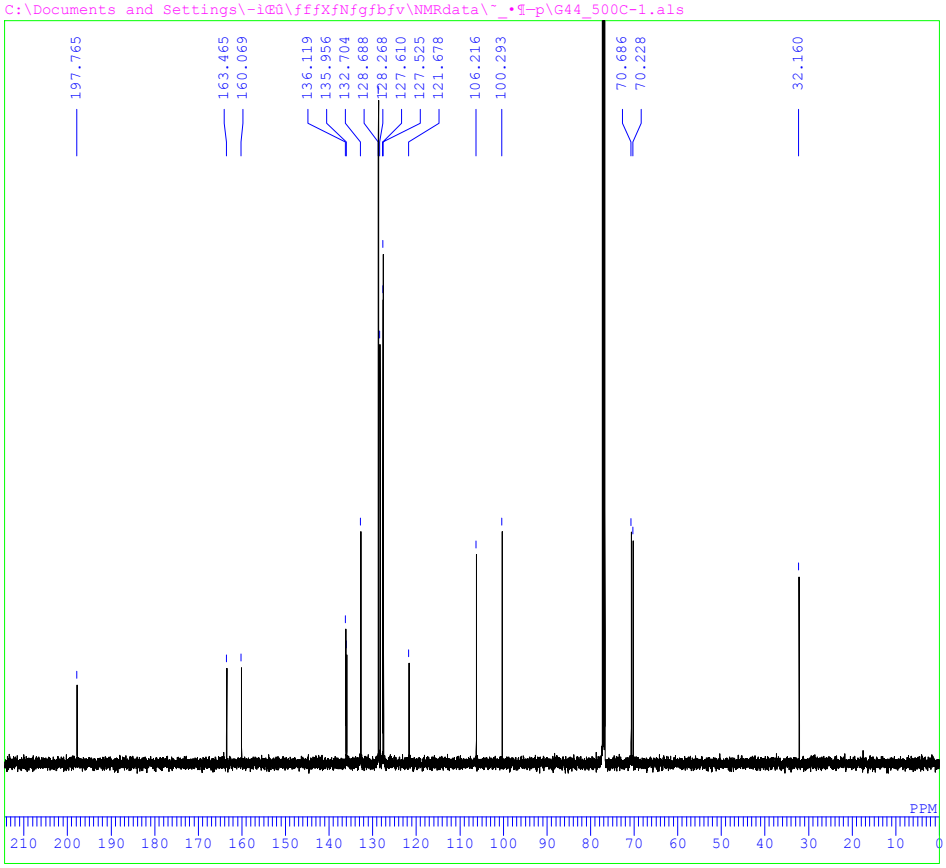
10d



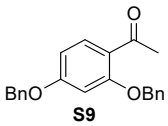
DFILE G44_500H-1.als
COMNT single_pulse
DATIM 2015-04-08 23:50:41
OBNUC 1H
EXMOD single_pulse.ex2
OBFRQ 500.16 MHz
OBSET 2.41 KHz
OBFIN 6.01 Hz
POINT 13107
FREQU 7507.39 Hz
SCANS 8
ACQTM 1.7459 sec
PD 5.0000 sec
PW1 6.82 usec
IRNUC 1H
CTEMP 21.5 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 0.12 Hz
RGAIN 44



S9

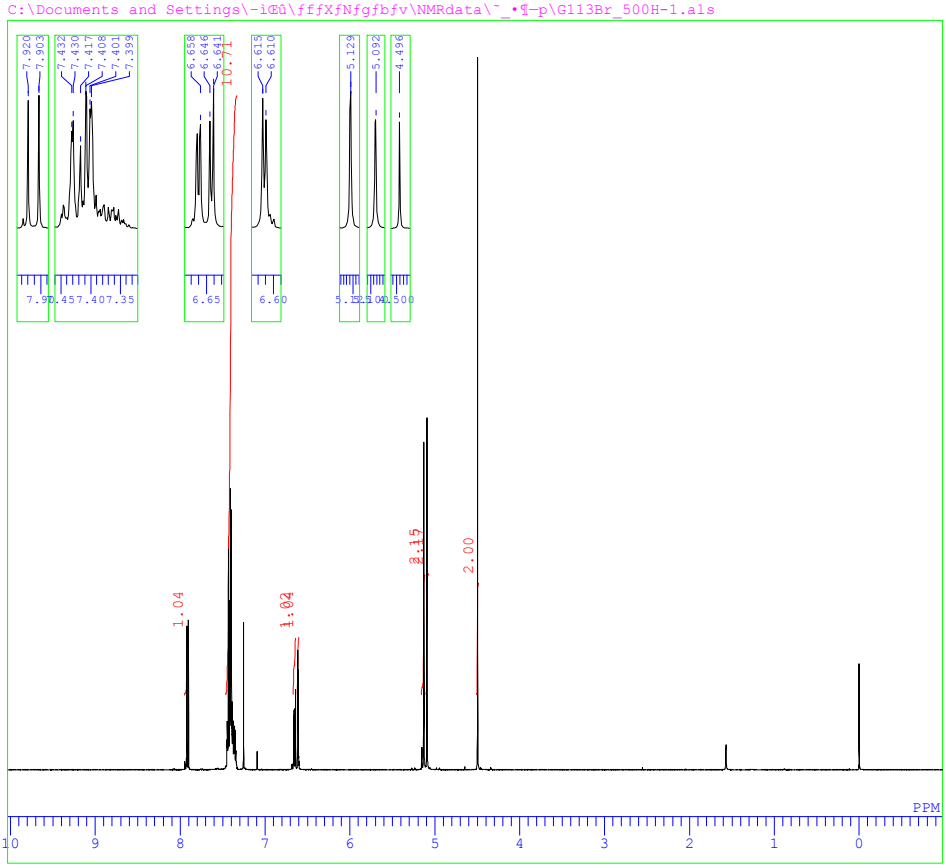


DFILE G44_500C-1.als
COMNT single pulse decoupled gated NOE
DATIM 2015-04-09 00:38:38
OBNUC 13C
EXMOD single_pulse_dec
OBFRQ 125.77 MHz
OBSET 7.87 KHz
OBFIN 4.21 Hz
POINT 26214
FREQU 31446.06 Hz
SCANS 1000
ACQTM 0.8336 sec
PD 2.0000 sec
PW1 3.50 usec
IRNUC 1H
CTEMP 21.8 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 1.20 Hz
RGAIN 54

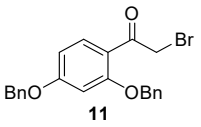


S9

C:\Documents and Settings\~iŒ0\ƒfƒXfNfgfbfv\NMRdata\˜_•¶—p\G113Br_500H-1.als

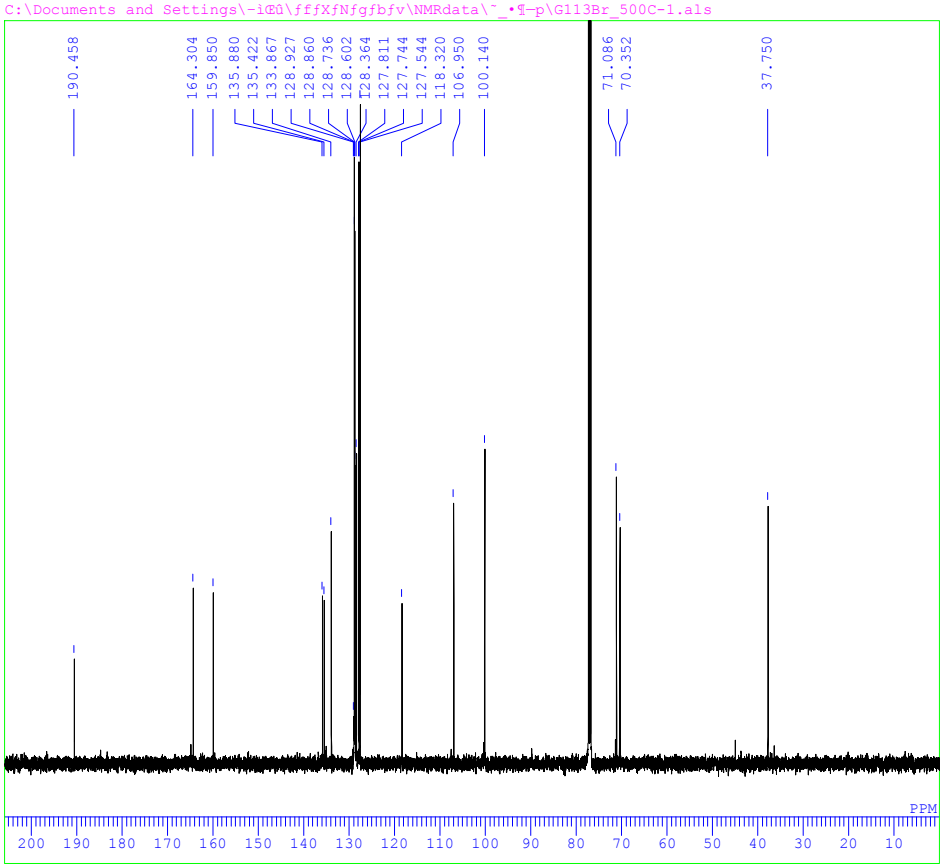



```
DFILE   G113Br_500H-1.als
COMNT   single_pulse
DATIM   2015-04-09 00:51:17
OBNUC   1H
EXMOD   single_pulse.ex2
OBFRQ         500.16 MHz
OBSET           2.41 KHz
OBFIN           6.01 Hz
POINT          13107
FREQU        7507.39 Hz
SCANS               8
ACQTM         1.7459 sec
PD            5.0000 sec
PW1              6.82 usec
IRNUC   1H
CTEMP           21.4 c
SLVNT   CDCL3
EXREF           0.00 ppm
BF              0.12 Hz
RGAIN             44
```

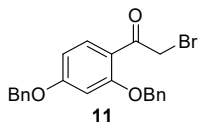


11

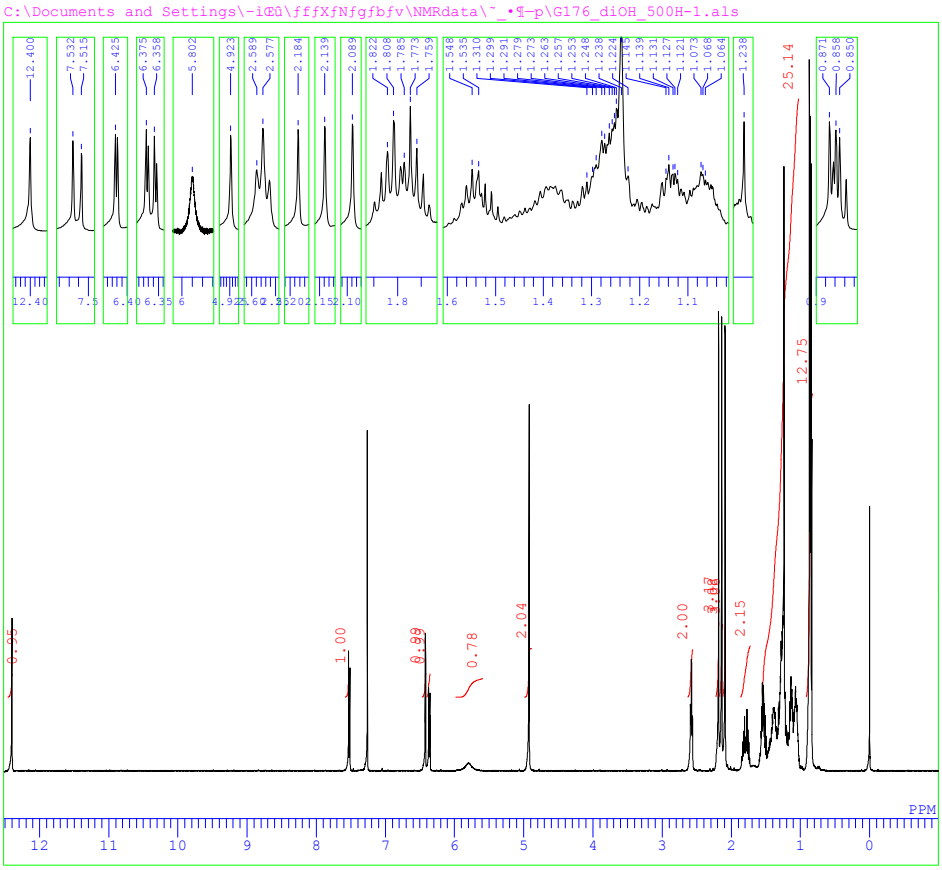
C:\Documents and Settings\~iŒ0\ƒfƒXfNfgfbfv\NMRdata\˜_•¶—p\G113Br_500C-1.als



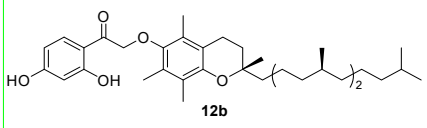

```
DFILE   G113Br_500C-1.als
COMNT   single pulse decoupled gated NOE
DATIM   2015-04-09 01:39:14
OBNUC   13C
EXMOD   single_pulse_dec
OBFRQ         125.77 MHz
OBSET           7.87 KHz
OBFIN           4.21 Hz
POINT          26214
FREQU       31446.06 Hz
SCANS           1000
ACQTM         0.8336 sec
PD            2.0000 sec
PW1              3.50 usec
IRNUC   1H
CTEMP           21.9 c
SLVNT   CDCL3
EXREF          77.00 ppm
BF              1.20 Hz
RGAIN             58
```



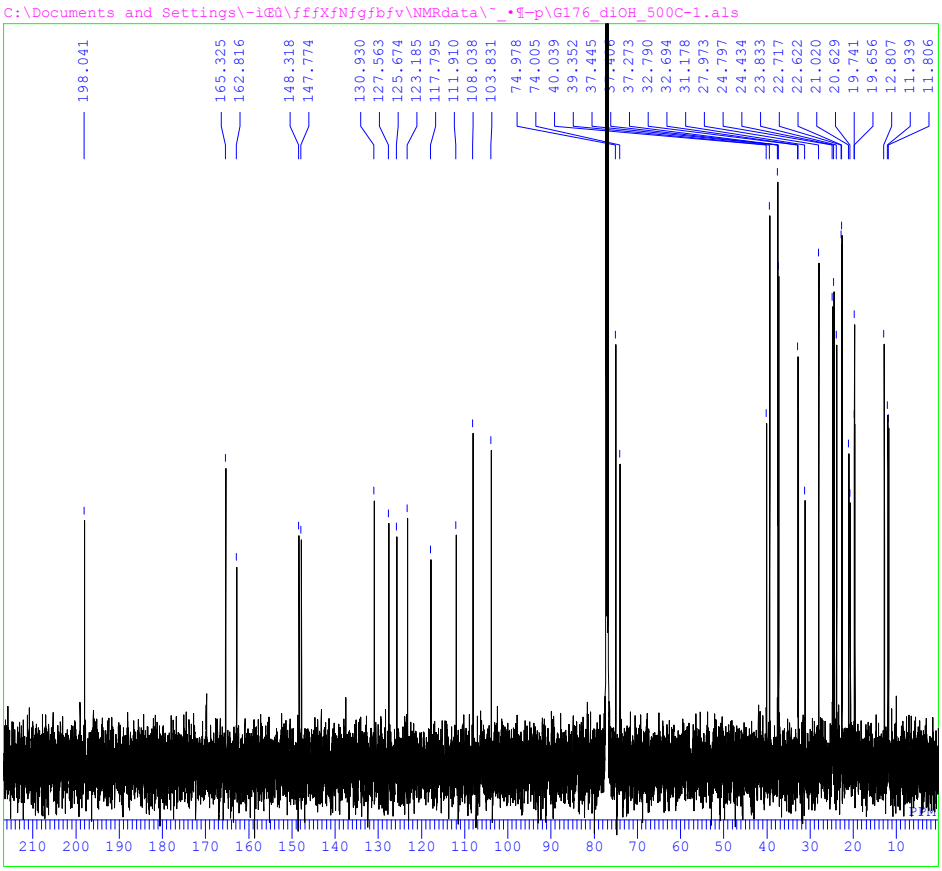
11



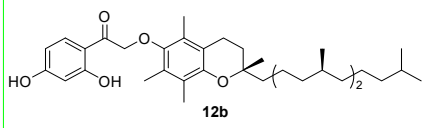

```
DFILE  G176_diOH_500H-1.als
COMNT  single_pulse
DATIM  2015-03-03 12:45:18
OBNUC  1H
EXMOD  single_pulse.ex2
OBFRQ        500.16 MHz
OBSET          2.41 KHz
OBFIN          6.01 Hz
POINT         13107
FREQU       7507.39 Hz
SCANS             8
ACQTM        1.7459 sec
PD           5.0000 sec
PW1            6.82 usec
IRNUC  1H
CTEMP         20.8 c
SLVNT  CDCL3
EXREF          0.00 ppm
BF             0.12 Hz
RGAIN            44
```



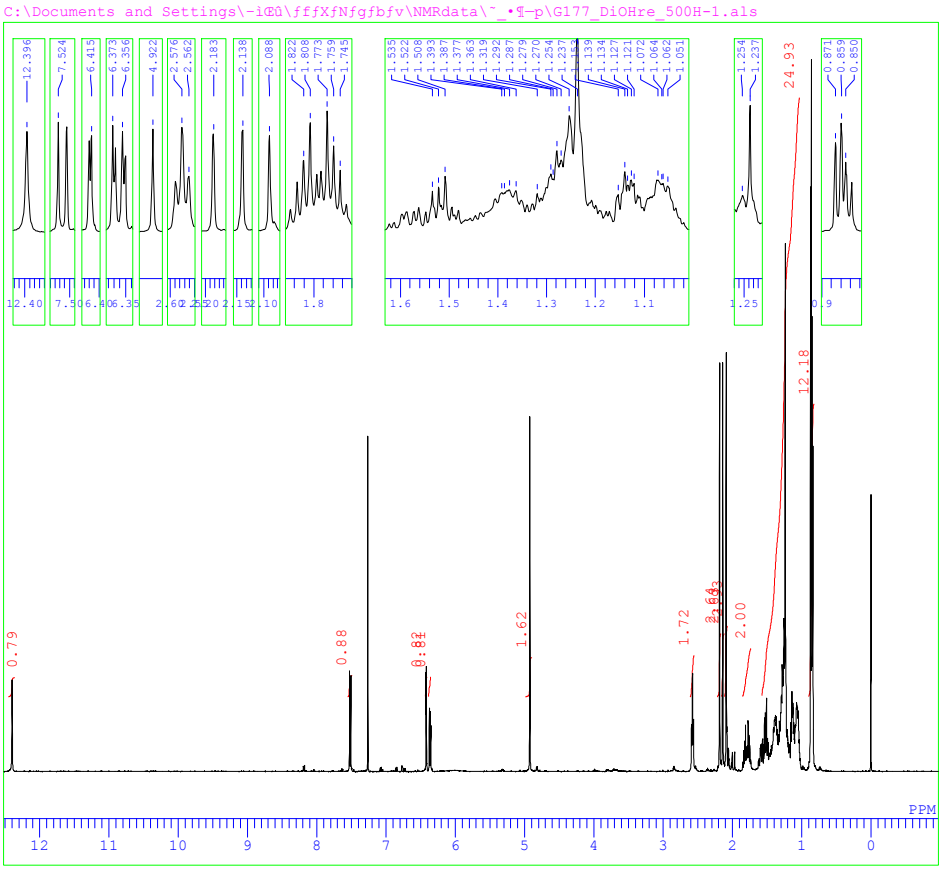
12b



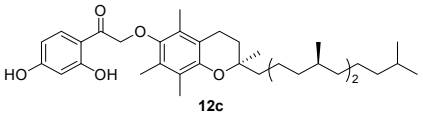

```
DFILE  G176_diOH_500C-1.als
COMNT  single pulse decoupled gated NOE
DATIM  2015-03-03 13:33:12
OBNUC  13C
EXMOD  single_pulse_dec
OBFRQ        125.77 MHz
OBSET          7.87 KHz
OBFIN          4.21 Hz
POINT         26214
FREQU      31446.06 Hz
SCANS          1000
ACQTM        0.8336 sec
PD           2.0000 sec
PW1            3.50 usec
IRNUC  1H
CTEMP         21.3 c
SLVNT  CDCL3
EXREF         77.00 ppm
BF             1.20 Hz
RGAIN            50
```



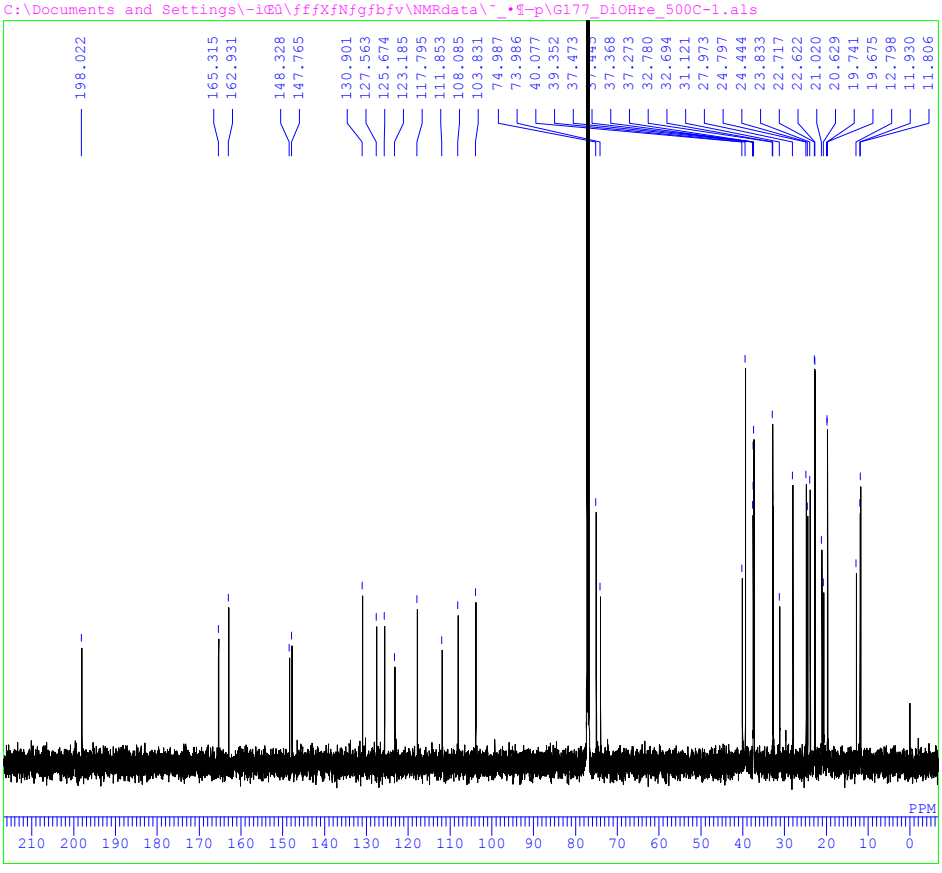
12b



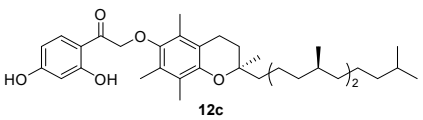

```
DFILE  G177_DiOHre_500H-1.als
COMNT  single_pulse
DATIM  2015-03-06 11:09:42
OBNUC  1H
EXMOD  single_pulse.ex2
OBFRQ        500.16 MHz
OBSET          2.41 KHz
OBFIN          6.01 Hz
POINT         13107
FREQU       7507.39 Hz
SCANS             8
ACQTM        1.7459 sec
PD           5.0000 sec
PW1            6.82 usec
IRNUC  1H
CTEMP         21.5 c
SLVNT  CDCL3
EXREF          0.00 ppm
BF             0.12 Hz
RGAIN            40
```



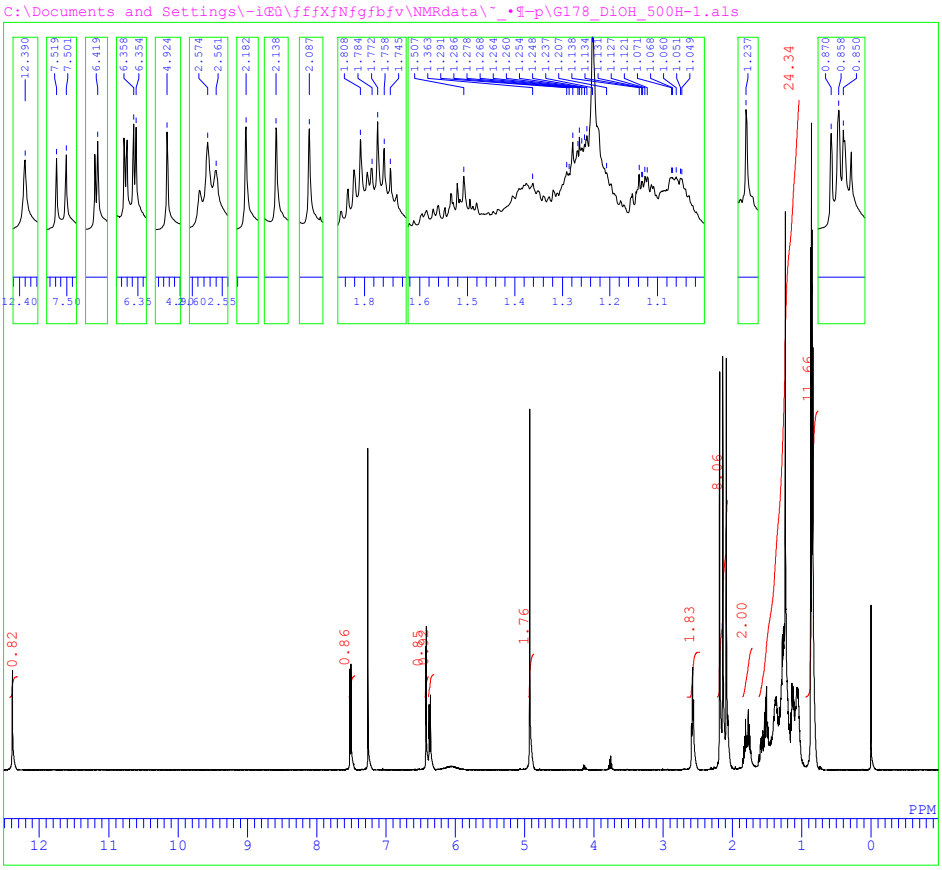
12c



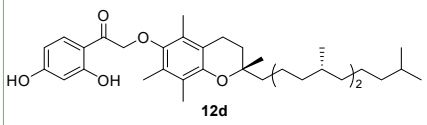

```
DFILE  G177_DiOHre_500C-1.als
COMNT  single pulse decoupled gated NOE
DATIM  2015-03-06 11:57:37
OBNUC  13C
EXMOD  single_pulse_dec
OBFRQ        125.77 MHz
OBSET          7.87 KHz
OBFIN          4.21 Hz
POINT         26214
FREQU      31446.06 Hz
SCANS          1000
ACQTM        0.8336 sec
PD           2.0000 sec
PW1            3.50 usec
IRNUC  1H
CTEMP         21.8 c
SLVNT  CDCL3
EXREF         77.00 ppm
BF             1.20 Hz
RGAIN            52
```



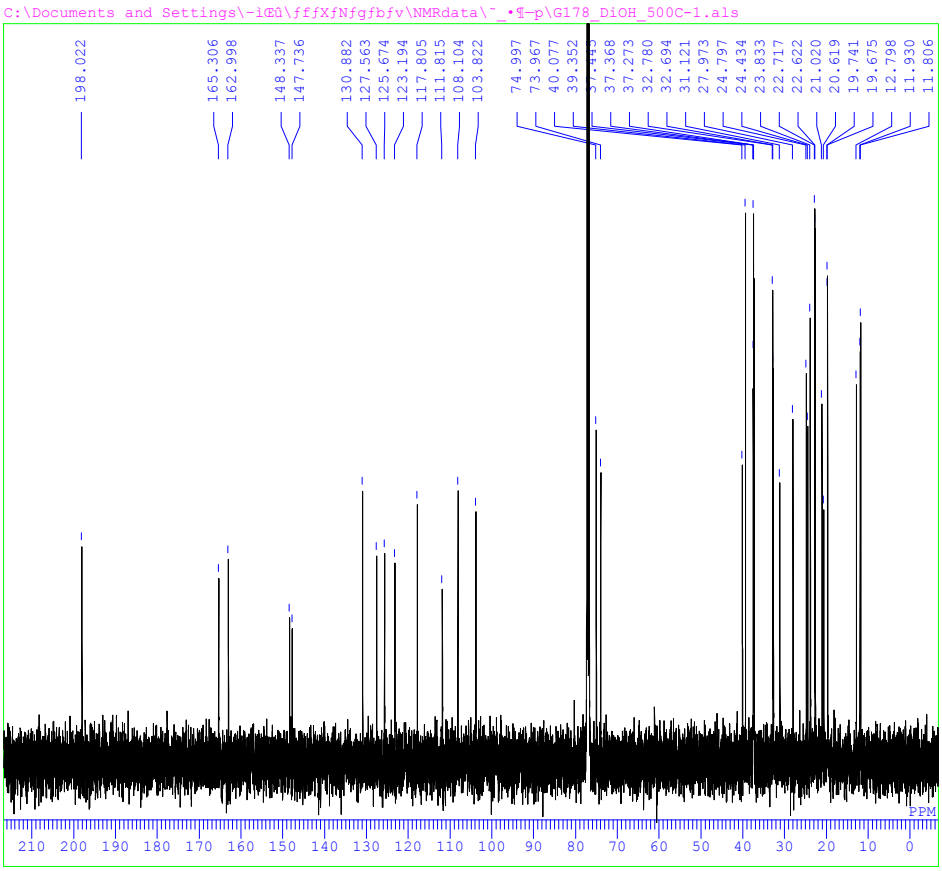
12c



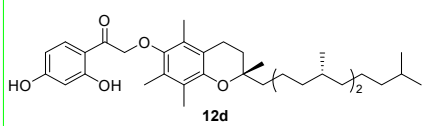

```
DFILE  G178_DiOH_500H-1.als
COMNT  single_pulse
DATIM  2015-03-04 15:27:13
OBNUC  1H
EXMOD  single_pulse.ex2
OBFRQ        500.16 MHz
OBSET          2.41 KHz
OBFIN          6.01 Hz
POINT         13107
FREQU       7507.39 Hz
SCANS             8
ACQTM        1.7459 sec
PD           5.0000 sec
PW1            6.82 usec
IRNUC  1H
CTEMP         21.3 c
SLVNT  CDCL3
EXREF          0.00 ppm
BF             0.12 Hz
RGAIN            42
```



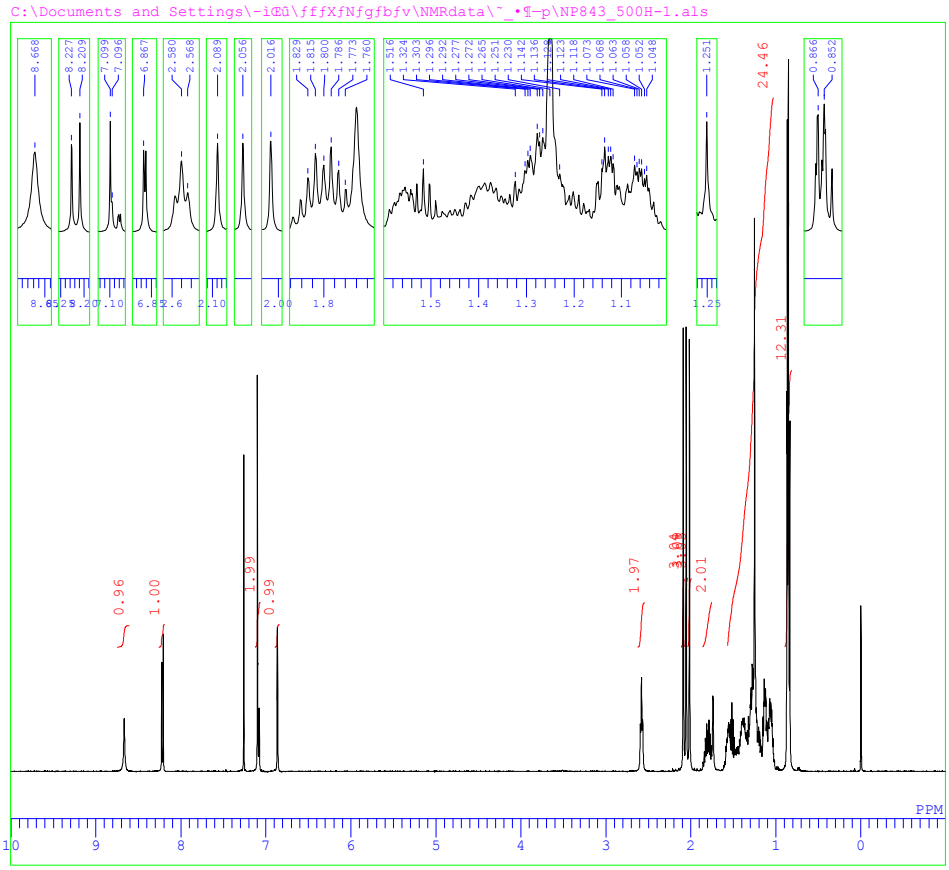
12d



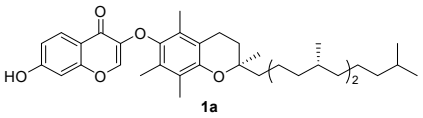

```
DFILE  G178_DiOH_500C-1.als
COMNT  single pulse decoupled gated NOE
DATIM  2015-03-04 16:06:06
OBNUC  13C
EXMOD  single_pulse_dec
OBFRQ        125.77 MHz
OBSET          7.87 KHz
OBFIN          4.21 Hz
POINT         26214
FREQU      31446.06 Hz
SCANS            800
ACQTM         0.8336 sec
PD            2.0000 sec
PW1             3.50 usec
IRNUC  1H
CTEMP         21.7 c
SLVNT  CDCL3
EXREF         77.00 ppm
BF             1.20 Hz
RGAIN            52
```



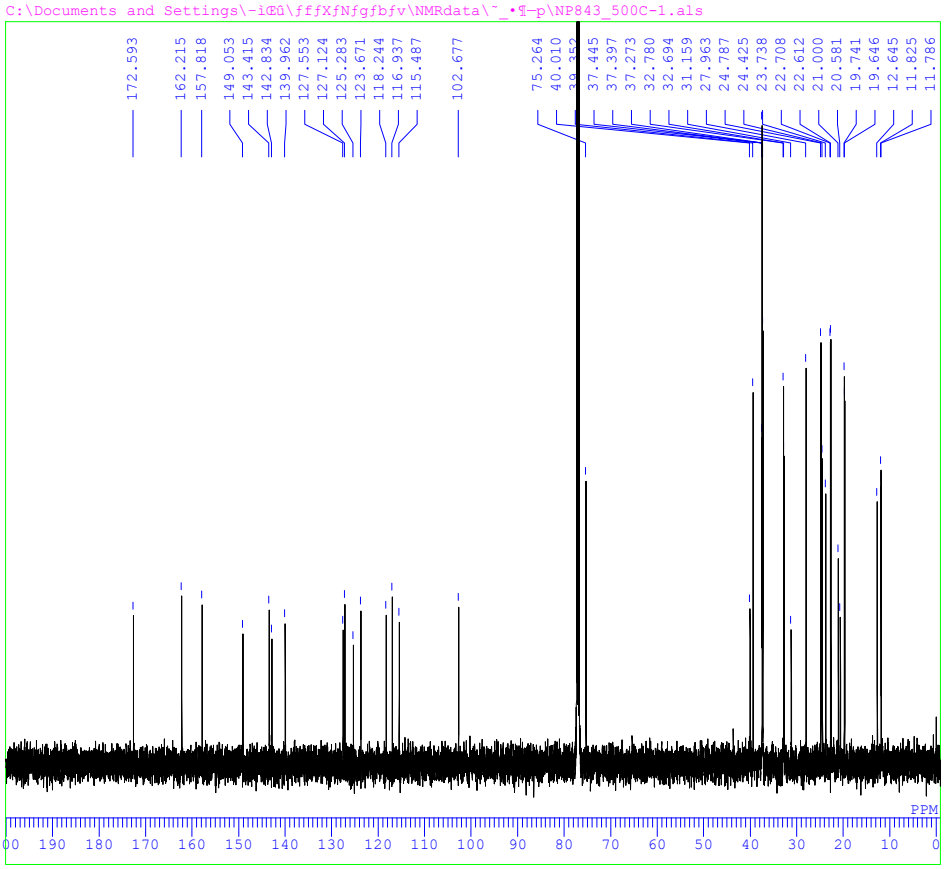
12d



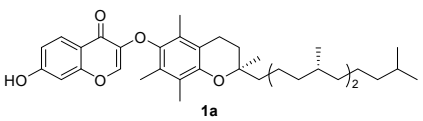

```
DFILE  NP843_500H-1.als
COMNT  single_pulse
DATIM  2015-04-28 15:10:48
OBNUC  1H
EXMOD  single_pulse.ex2
OBFRQ        500.16 MHz
OBSET          2.41 KHz
OBFIN          6.01 Hz
POINT         13107
FREQU       7507.39 Hz
SCANS             8
ACQTM        1.7459 sec
PD           5.0000 sec
PW1            6.82 usec
IRNUC  1H
CTEMP         21.7 c
SLVNT  CDCL3
EXREF          0.00 ppm
BF             0.12 Hz
RGAIN            42
```



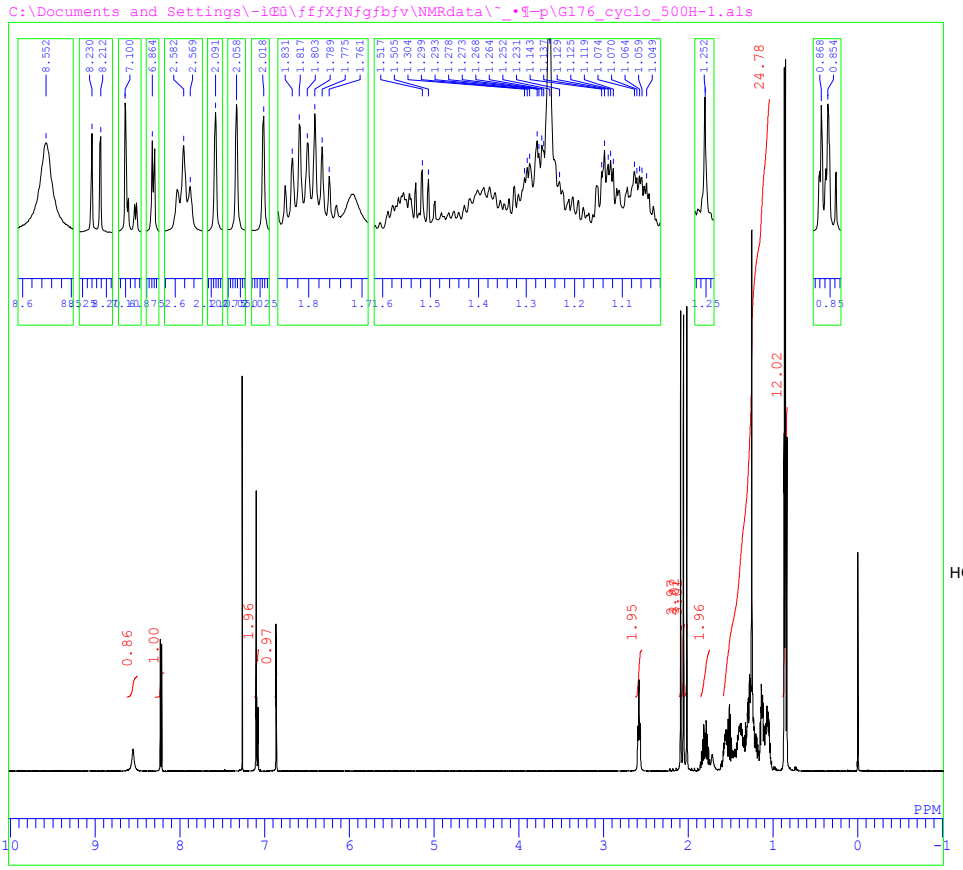
1a



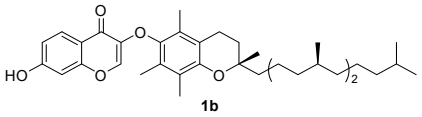

```
DFILE  NP843_500C-1.als
COMNT  single pulse decoupled gated NOE
DATIM  2015-04-28 15:59:35
OBNUC  13C
EXMOD  single_pulse_dec
OBFRQ        125.77 MHz
OBSET          7.87 KHz
OBFIN          4.21 Hz
POINT         26214
FREQU      31446.06 Hz
SCANS          1000
ACQTM        0.8336 sec
PD           2.0000 sec
PW1            3.50 usec
IRNUC  1H
CTEMP         22.2 c
SLVNT  CDCL3
EXREF         77.00 ppm
BF             1.20 Hz
RGAIN            52
```



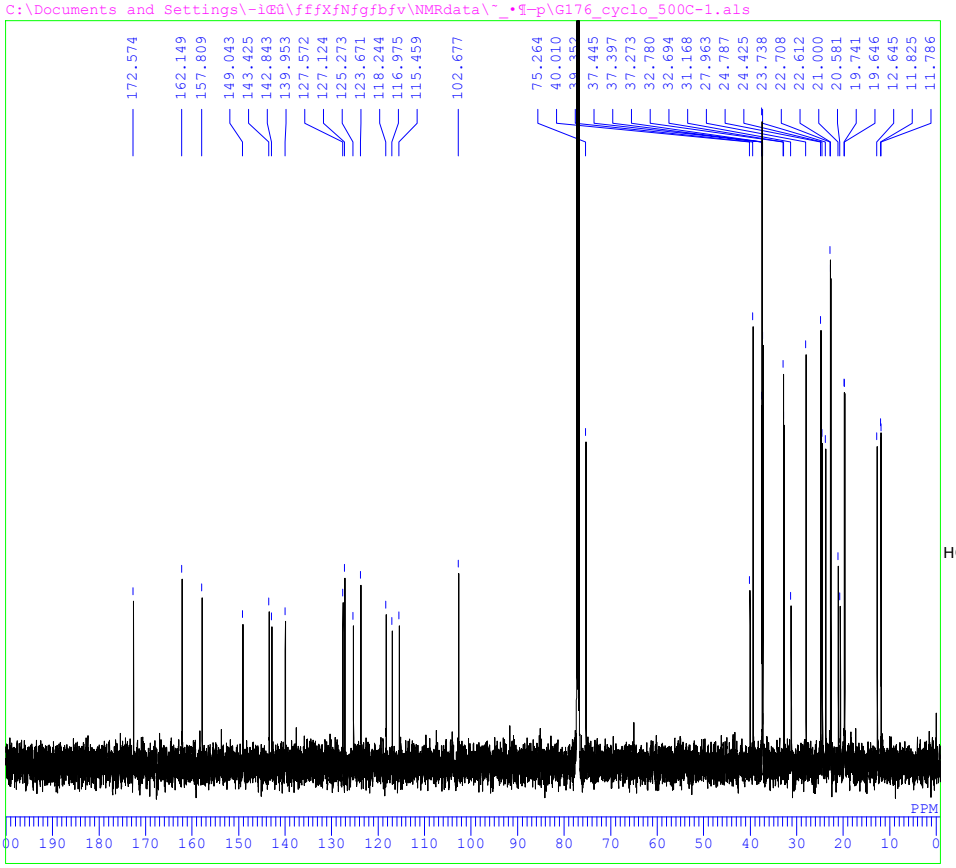
1a



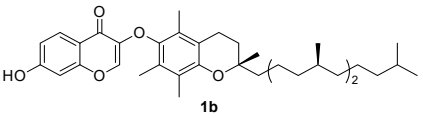

```
DFILE  G176_cyclo_500H-1.als
COMNT  single_pulse
DATIM  2015-04-22 13:17:41
OBNUC  1H
EXMOD  single_pulse.ex2
OBFRQ        500.16 MHz
OBSET          2.41 KHz
OBFIN          6.01 Hz
POINT         13107
FREQU       7507.39 Hz
SCANS             8
ACQTM        1.7459 sec
PD           5.0000 sec
PW1            6.82 usec
IRNUC  1H
CTEMP         22.1 c
SLVNT  CDCL3
EXREF         0.00 ppm
BF            0.12 Hz
RGAIN           42
```



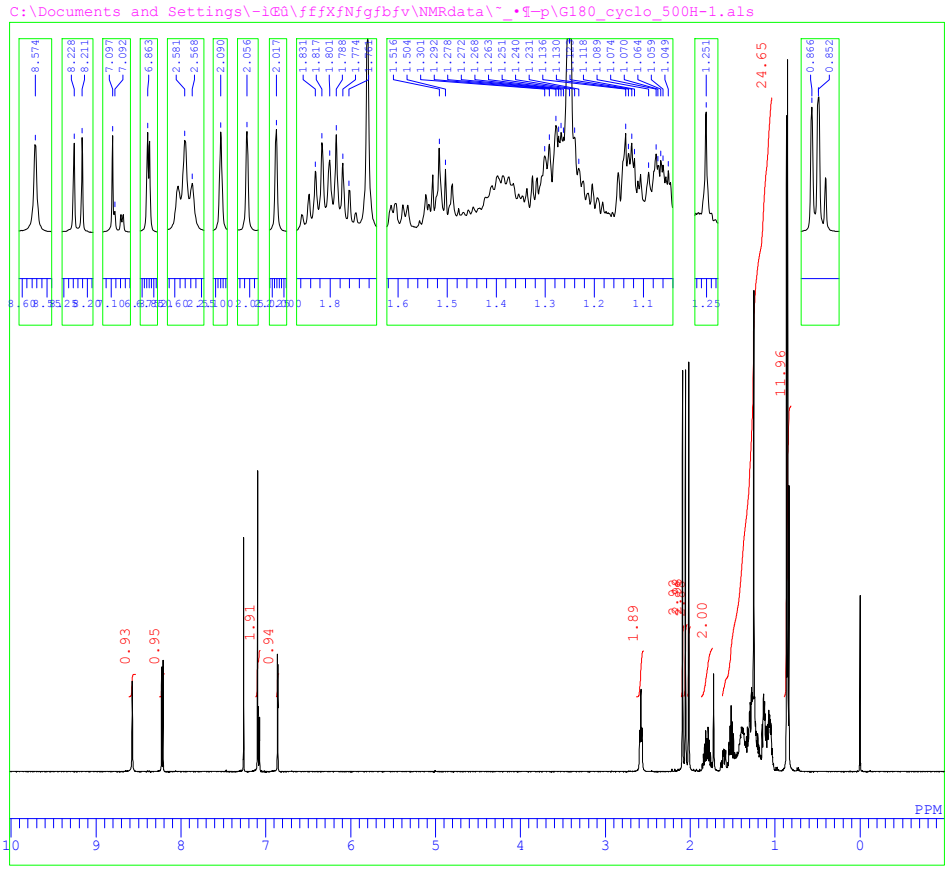
1b



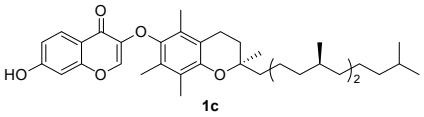

```
DFILE  G176_cyclo_500C-1.als
COMNT  single pulse decoupled gated NOE
DATIM  2015-04-22 14:05:47
OBNUC  13C
EXMOD  single_pulse_dec
OBFRQ        125.77 MHz
OBSET          7.87 KHz
OBFIN          4.21 Hz
POINT         26214
FREQU      31446.06 Hz
SCANS          1000
ACQTM        0.8336 sec
PD           2.0000 sec
PW1            3.50 usec
IRNUC  1H
CTEMP         22.5 c
SLVNT  CDCL3
EXREF         77.00 ppm
BF            1.20 Hz
RGAIN           58
```



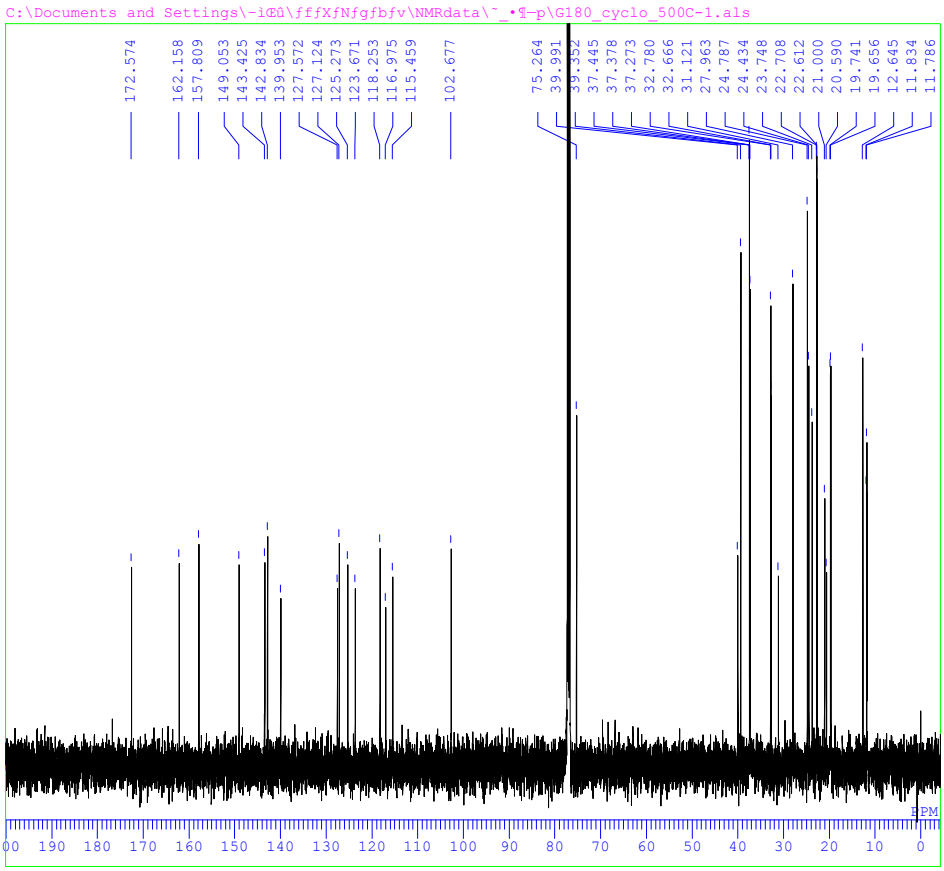
1b



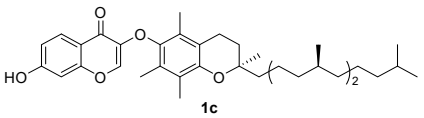

```
DFILE   G180_cyclo_500H-1.als
COMNT   single_pulse
DATIM   2015-04-22 19:05:57
OBNUC   1H
EXMOD   single_pulse.ex2
OBFRQ         500.16 MHz
OBSET           2.41 KHz
OBFIN           6.01 Hz
POINT          13107
FREQU        7507.39 Hz
SCANS                8
ACQTM         1.7459 sec
PD            5.0000 sec
PW1             6.82 usec
IRNUC   1H
CTEMP          22.0 c
SLVNT   CDCL3
EXREF          0.00 ppm
BF             0.12 Hz
RGAIN            42
```



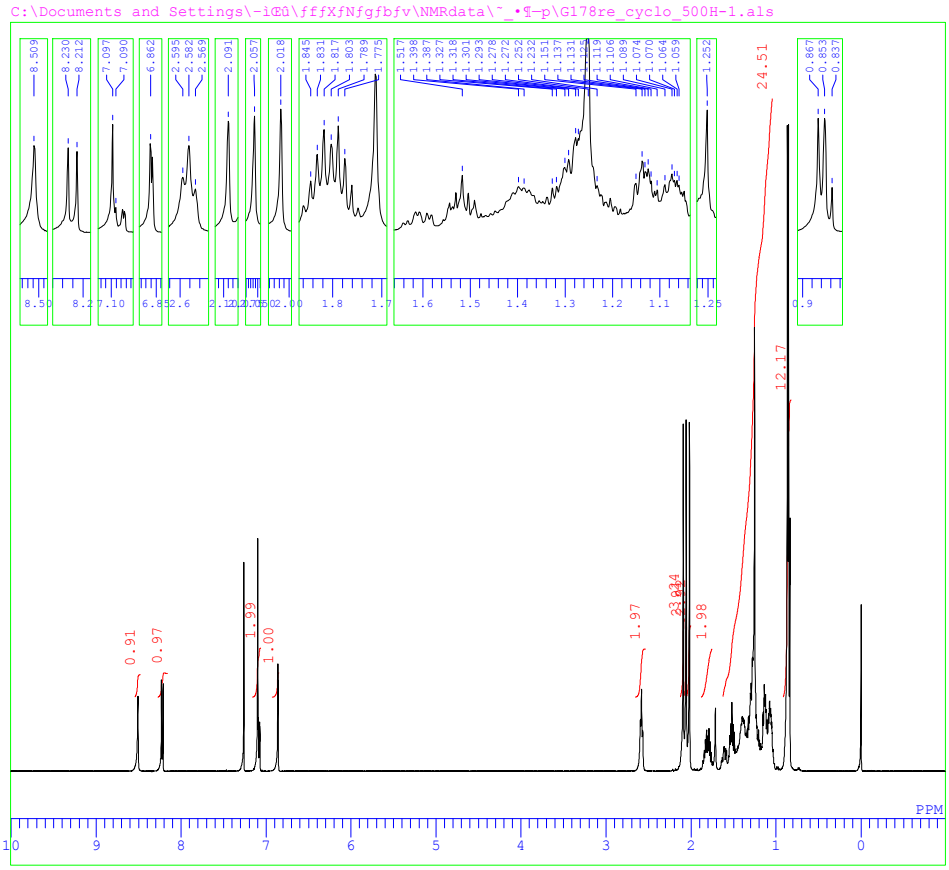
1c



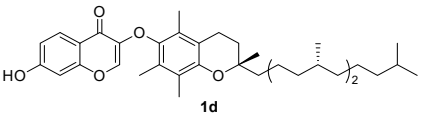

```
DFILE   G180_cyclo_500C-1.als
COMNT   single pulse decoupled gated NOE
DATIM   2015-04-22 19:54:17
OBNUC   13C
EXMOD   single_pulse_dec
OBFRQ         125.77 MHz
OBSET           7.87 KHz
OBFIN           4.21 Hz
POINT          26214
FREQU       31446.06 Hz
SCANS            1000
ACQTM         0.8336 sec
PD            2.0000 sec
PW1             3.50 usec
IRNUC   1H
CTEMP          22.5 c
SLVNT   CDCL3
EXREF          77.00 ppm
BF             1.20 Hz
RGAIN            54
```



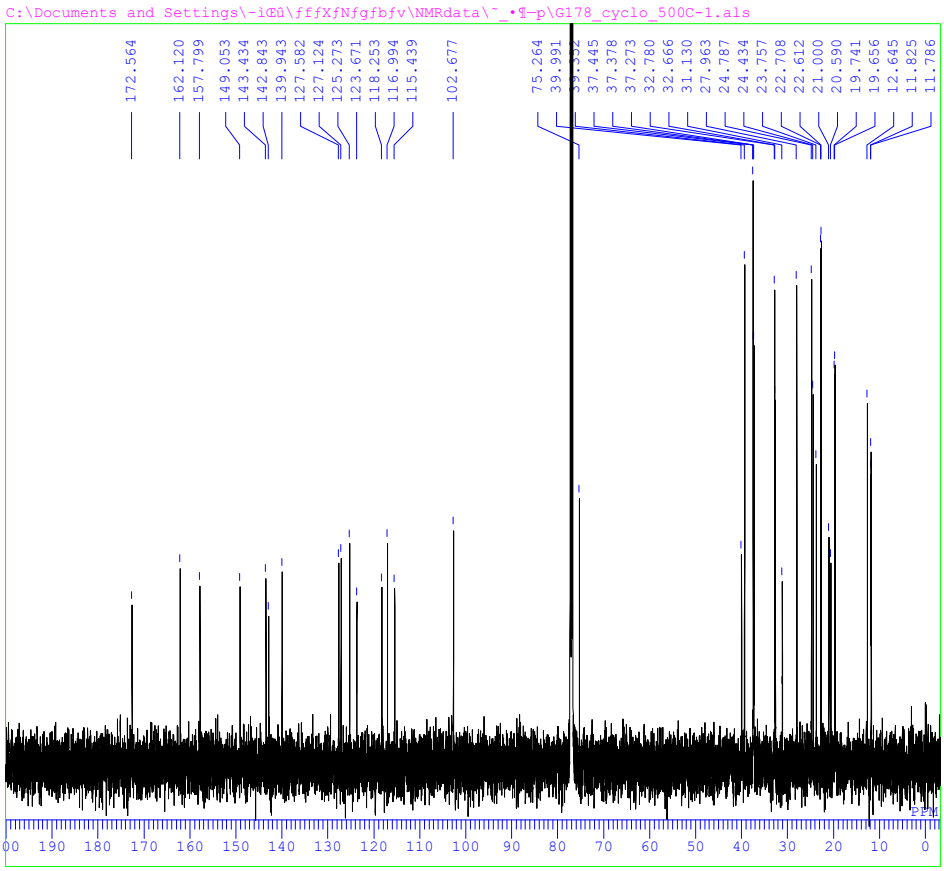
1c



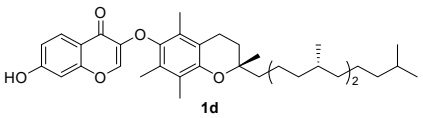

```
DFILE  G178re_cyclo_500H-1.als
COMNT  single_pulse
DATIM  2015-04-22 17:13:06
OBNUC  1H
EXMOD  single_pulse.ex2
OBFRQ        500.16 MHz
OBSET          2.41 KHz
OBFIN          6.01 Hz
POINT         13107
FREQU       7507.39 Hz
SCANS             8
ACQTM        1.7459 sec
PD           5.0000 sec
PW1            6.82 usec
IRNUC  1H
CTEMP         22.1 c
SLVNT  CDCL3
EXREF         0.00 ppm
BF            0.12 Hz
RGAIN           42
```



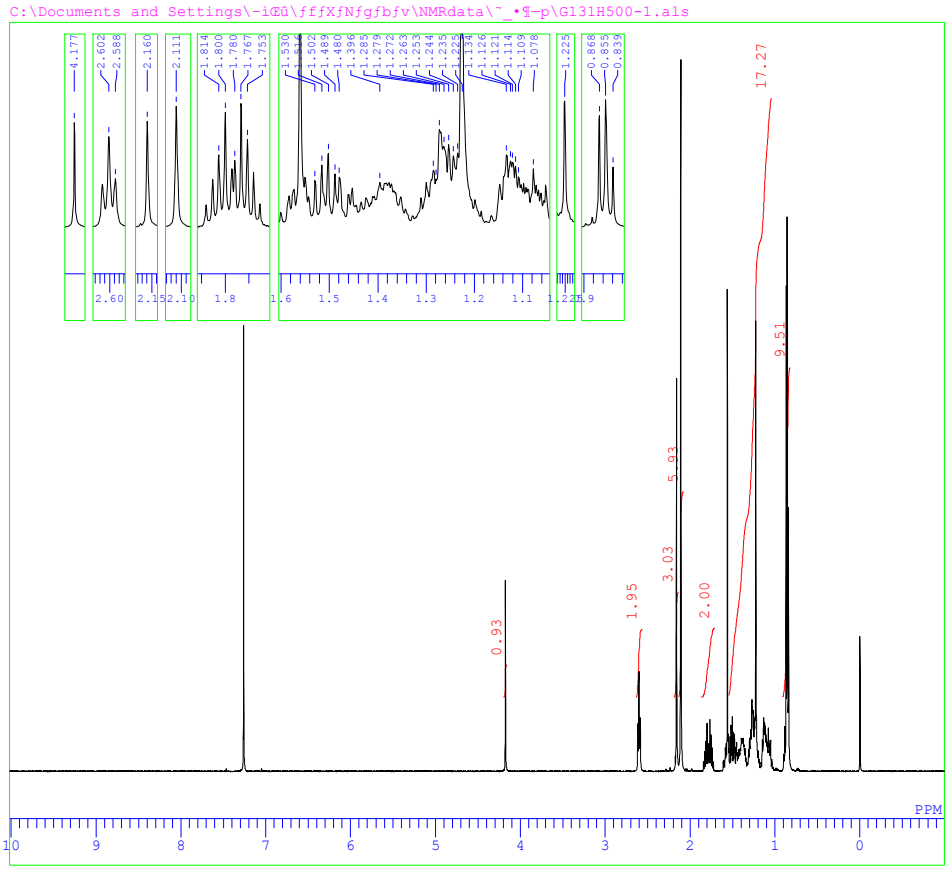
1d



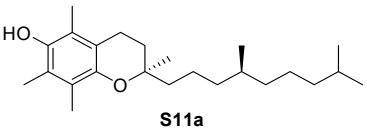

```
DFILE  G178_cyclo_500C-1.als
COMNT  single pulse decoupled gated NOE
DATIM  2015-04-22 18:01:04
OBNUC  13C
EXMOD  single_pulse_dec
OBFRQ        125.77 MHz
OBSET          7.87 KHz
OBFIN          4.21 Hz
POINT         26214
FREQU      31446.06 Hz
SCANS          1000
ACQTM        0.8336 sec
PD           2.0000 sec
PW1            3.50 usec
IRNUC  1H
CTEMP         22.6 c
SLVNT  CDCL3
EXREF         77.00 ppm
BF            1.20 Hz
RGAIN           54
```



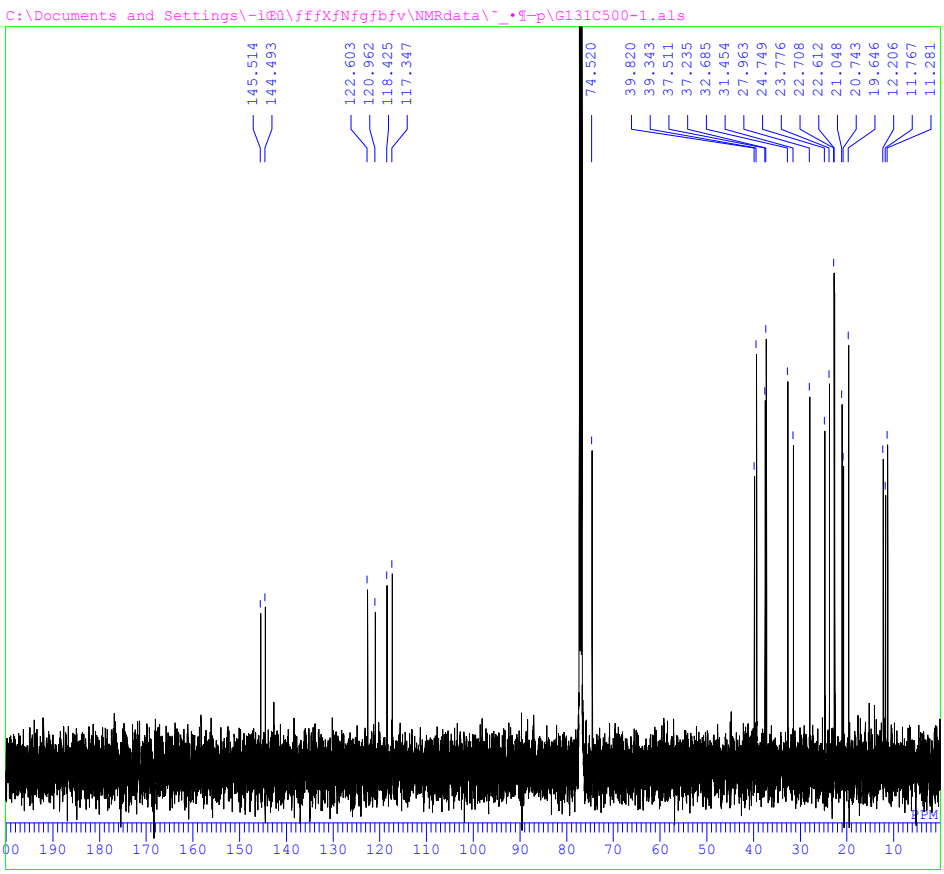
1d



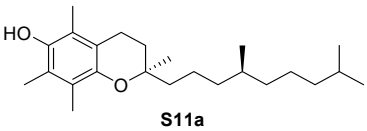

```
DFILE   G131H500-1.als
COMNT   single_pulse
DATIM   2015-01-16 11:26:33
OBNUC   1H
EXMOD   single_pulse.ex2
OBFRQ         500.16 MHz
OBSET           2.41 KHz
OBFIN           6.01 Hz
POINT          13107
FREQU        7507.39 Hz
SCANS               8
ACQTM         1.7459 sec
PD            5.0000 sec
PW1             6.82 usec
IRNUC   1H
CTEMP          21.2 c
SLVNT   CDCL3
EXREF          0.00 ppm
BF             0.12 Hz
RGAIN            46
```



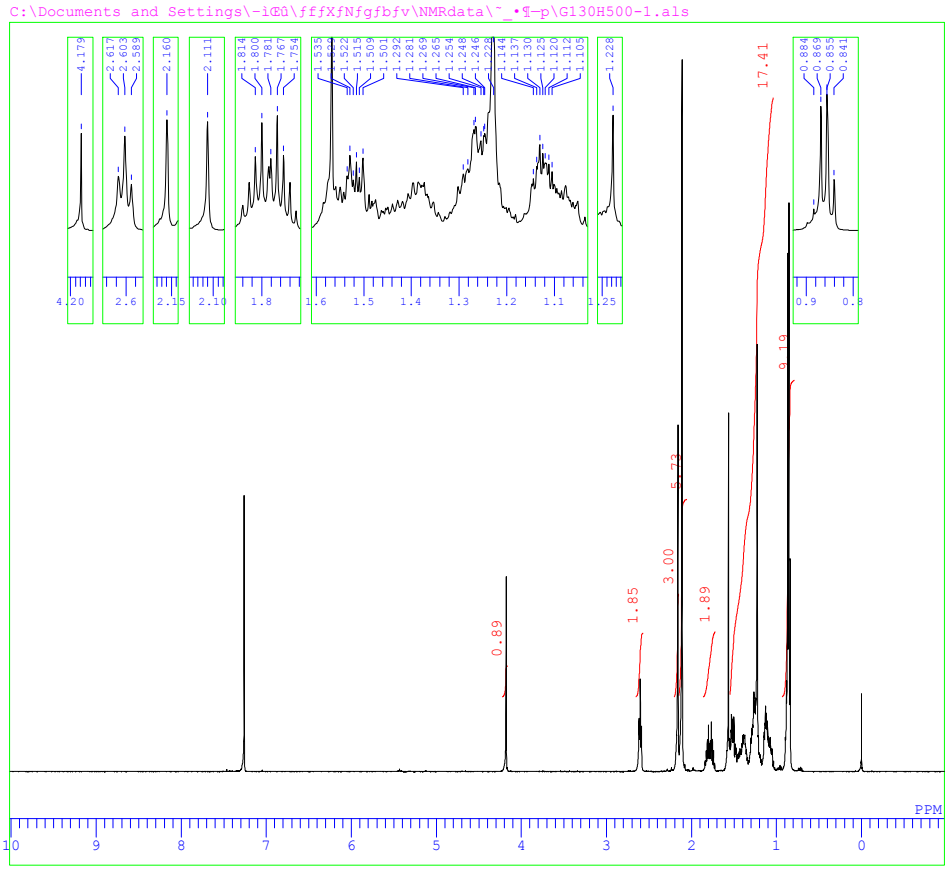
S11a



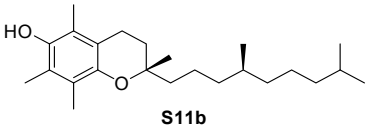

```
DFILE   G131C500-1.als
COMNT   single pulse decoupled gated NOE
DATIM   2015-01-16 12:14:41
OBNUC   13C
EXMOD   single_pulse_dec
OBFRQ         125.77 MHz
OBSET           7.87 KHz
OBFIN           4.21 Hz
POINT          26214
FREQU       31446.06 Hz
SCANS           1000
ACQTM         0.8336 sec
PD            2.0000 sec
PW1             3.50 usec
IRNUC   1H
CTEMP          21.5 c
SLVNT   CDCL3
EXREF          77.00 ppm
BF             1.20 Hz
RGAIN            56
```



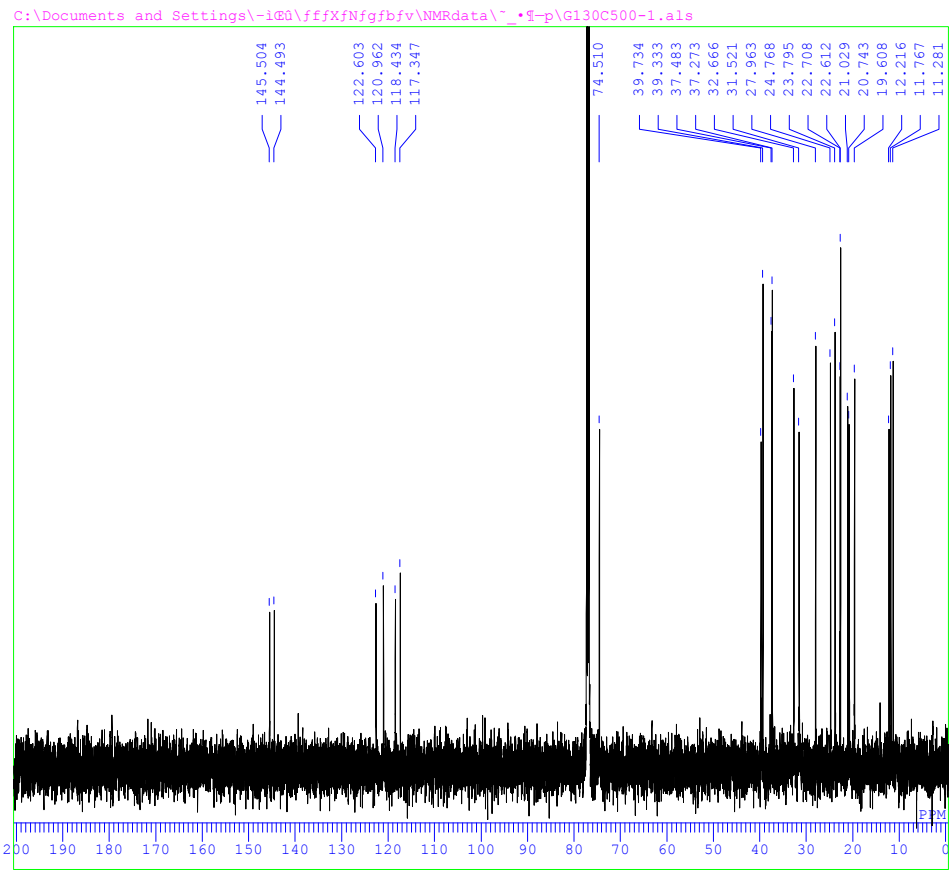
S11a



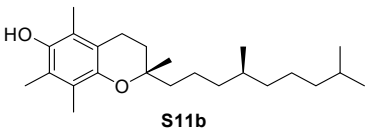
DFILE G130H500-1.als
COMNT single_pulse
DATIM 2015-01-16 10:26:14
OBNUC 1H
EXMOD single_pulse.ex2
OBFRQ 500.16 MHz
OBSET 2.41 KHz
OBFIN 6.01 Hz
POINT 13107
FREQU 7507.39 Hz
SCANS 8
ACQTM 1.7459 sec
PD 5.0000 sec
PW1 6.82 usec
IRNUC 1H
CTEMP 21.0 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 0.12 Hz
RGAIN 44



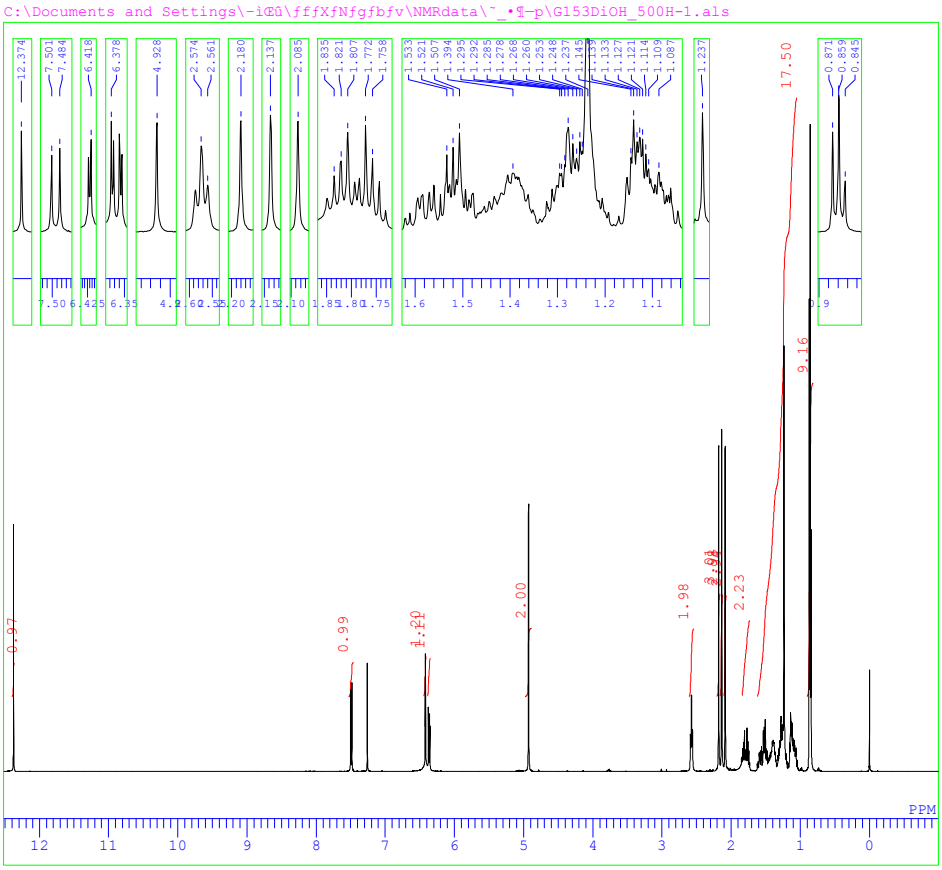
S11b



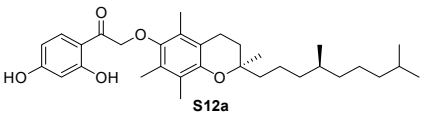
DFILE G130C500-1.als
COMNT single pulse decoupled gated NOE
DATIM 2015-01-16 11:14:25
OBNUC 13C
EXMOD single_pulse_dec
OBFRQ 125.77 MHz
OBSET 7.87 KHz
OBFIN 4.21 Hz
POINT 26214
FREQU 31446.06 Hz
SCANS 1000
ACQTM 0.8336 sec
PD 2.0000 sec
PW1 3.50 usec
IRNUC 1H
CTEMP 21.5 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 1.20 Hz
RGAIN 52



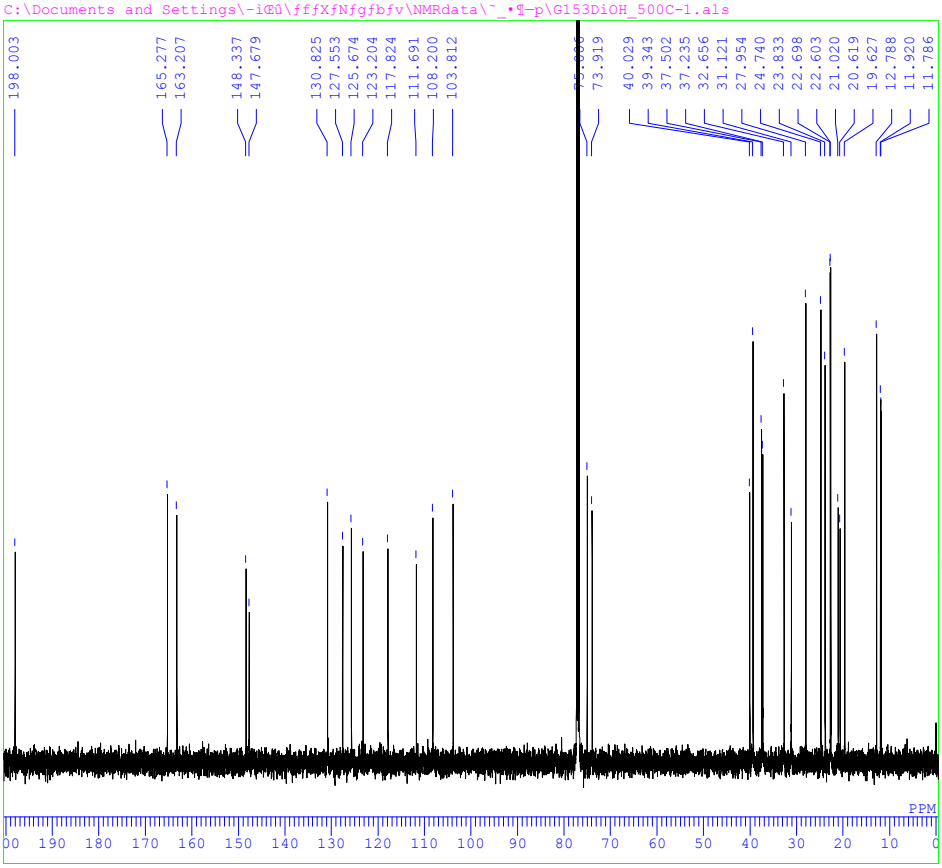
S11b



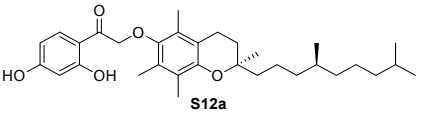

```
DFILE   G153DiOH_500H-1.als
COMNT   single_pulse
DATIM   2015-04-14 17:11:31
OBNUC   1H
EXMOD   single_pulse.ex2
OBFRQ         500.16 MHz
OBSET           2.41 KHz
OBFIN           6.01 Hz
POINT          13107
FREQU        7507.39 Hz
SCANS               8
ACQTM         1.7459 sec
PD            5.0000 sec
PW1             6.82 usec
IRNUC   1H
CTEMP          22.2 c
SLVNT   CDCL3
EXREF          0.00 ppm
BF             0.12 Hz
RGAIN            38
```



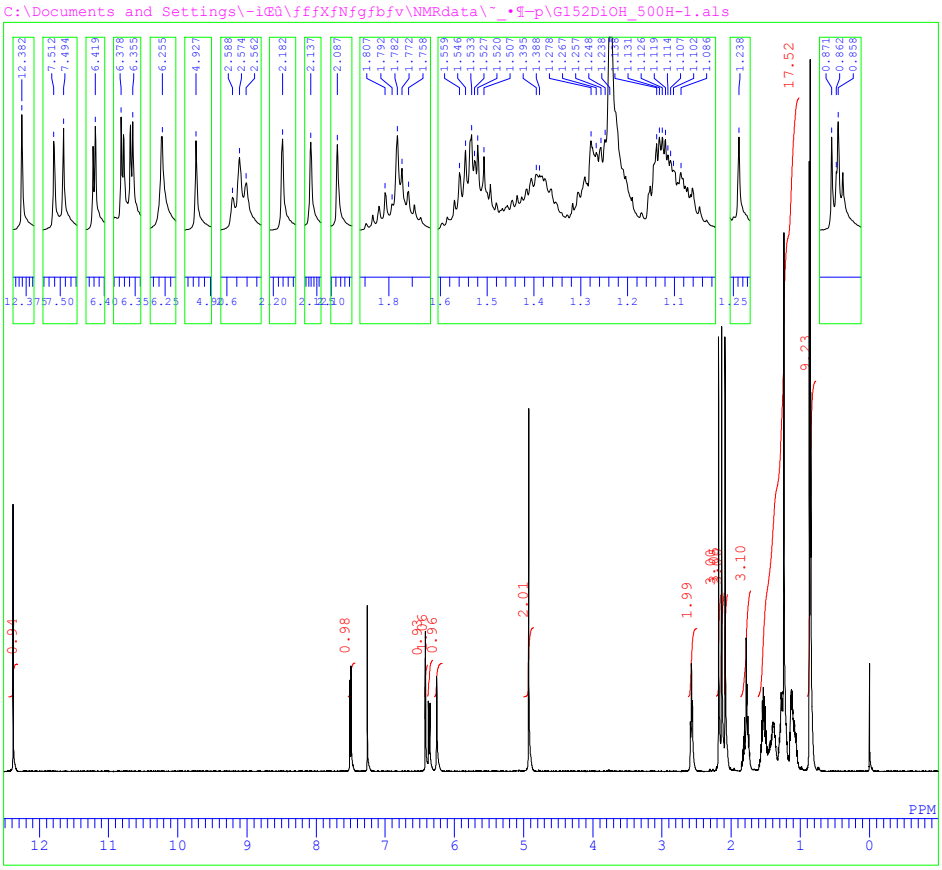
S12a



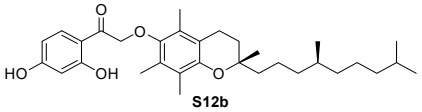

```
DFILE   G153DiOH_500C-1.als
COMNT   single pulse decoupled gated NOE
DATIM   2015-04-14 17:59:37
OBNUC   13C
EXMOD   single_pulse_dec
OBFRQ         125.77 MHz
OBSET           7.87 KHz
OBFIN           4.21 Hz
POINT          26214
FREQU        31446.06 Hz
SCANS            1000
ACQTM         0.8336 sec
PD            2.0000 sec
PW1             3.50 usec
IRNUC   1H
CTEMP          22.7 c
SLVNT   CDCL3
EXREF          77.00 ppm
BF             1.20 Hz
RGAIN            54
```



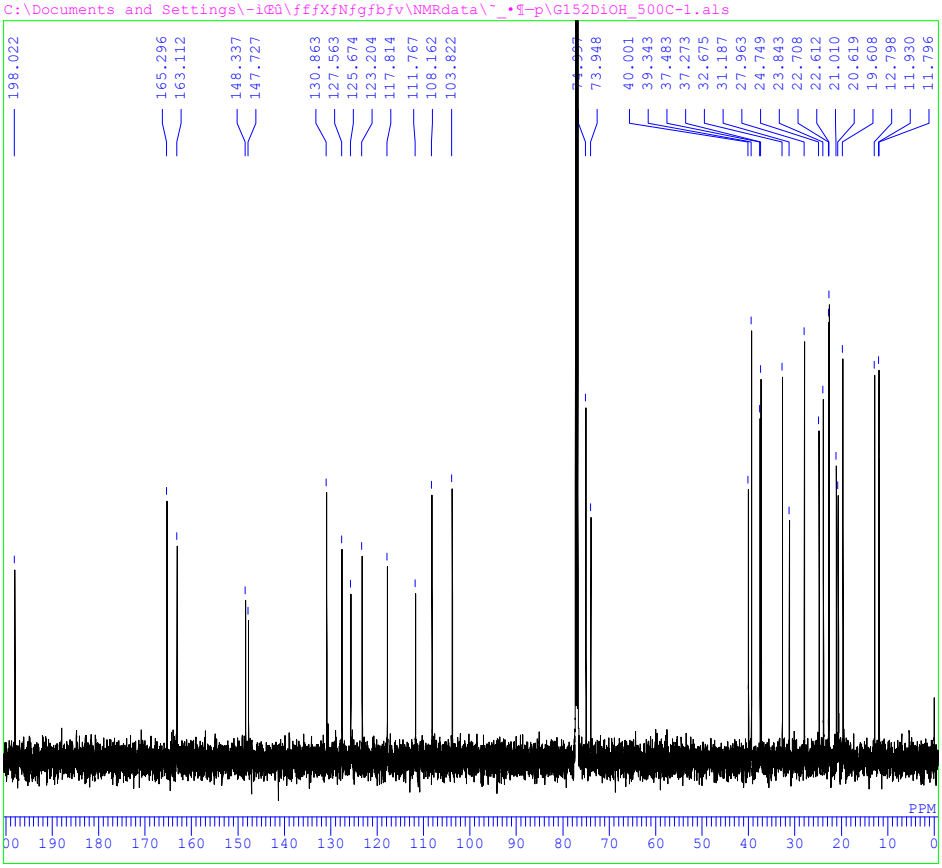
S12a



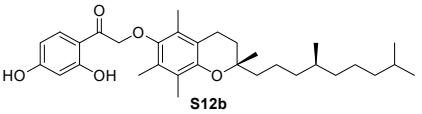

```
DFILE   G152DiOH_500H-1.als
COMNT   single_pulse
DATIM   2015-04-14 15:14:27
OBNUC   1H
EXMOD   single_pulse.ex2
OBFRQ         500.16 MHz
OBSET           2.41 KHz
OBFIN           6.01 Hz
POINT          13107
FREQU        7507.39 Hz
SCANS               8
ACQTM          1.7459 sec
PD             5.0000 sec
PW1              6.82 usec
IRNUC   1H
CTEMP           22.2 c
SLVNT   CDCL3
EXREF           0.00 ppm
BF              0.12 Hz
RGAIN             40
```



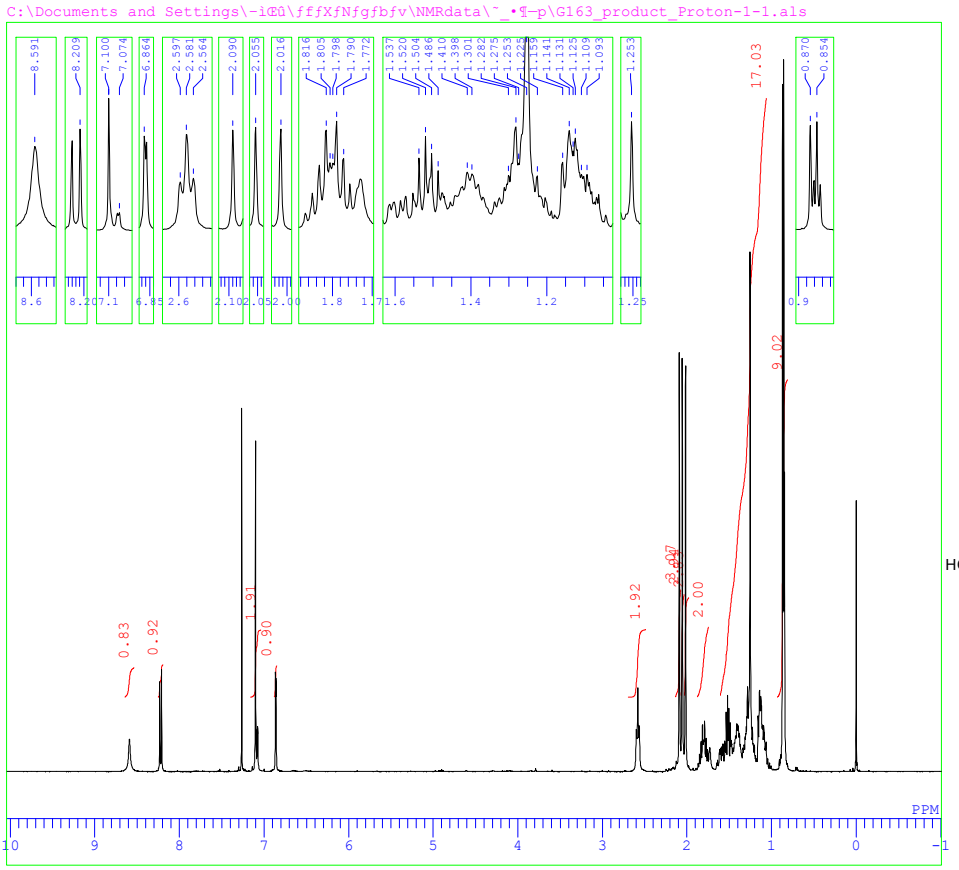
S12b



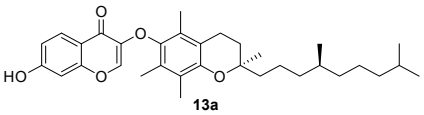

```
DFILE   G152DiOH_500C-1.als
COMNT   single pulse decoupled gated NOE
DATIM   2015-04-14 16:02:28
OBNUC   13C
EXMOD   single_pulse_dec
OBFRQ         125.77 MHz
OBSET           7.87 KHz
OBFIN           4.21 Hz
POINT          26214
FREQU       31446.06 Hz
SCANS           1000
ACQTM         0.8336 sec
PD            2.0000 sec
PW1              3.50 usec
IRNUC   1H
CTEMP           22.8 c
SLVNT   CDCL3
EXREF          77.00 ppm
BF              1.20 Hz
RGAIN             52
```



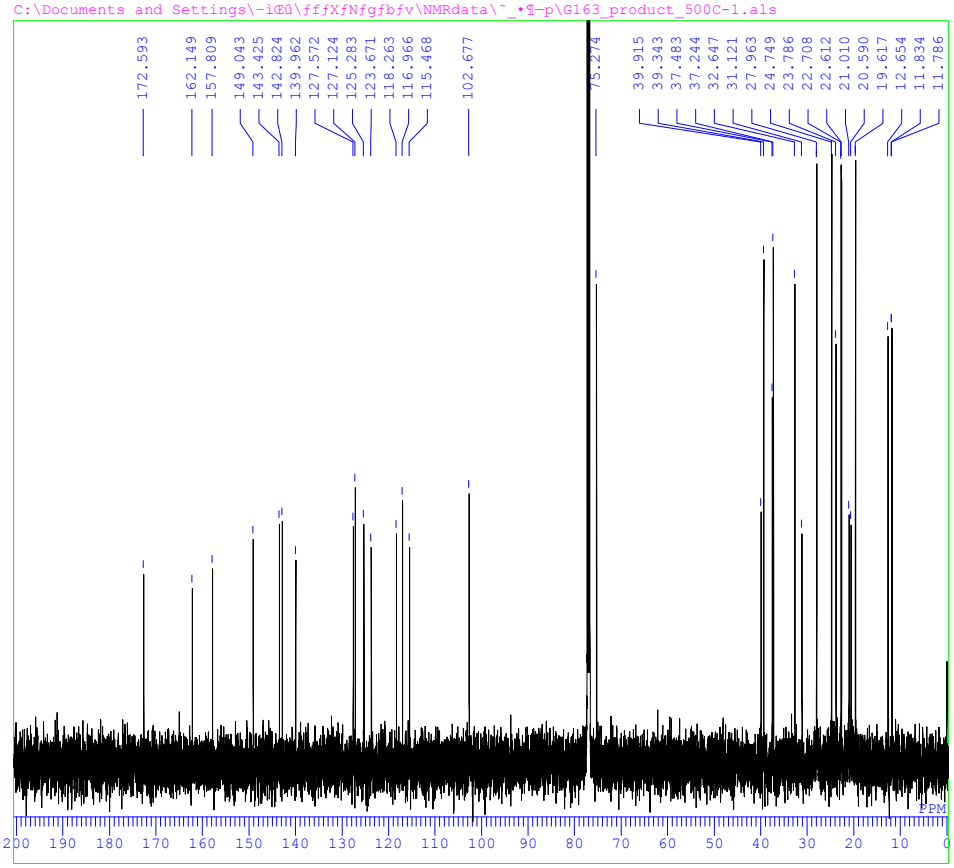
S12b



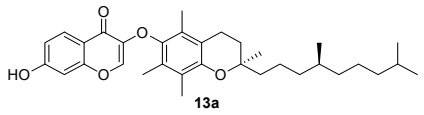

```
DFILE  G163_product_Proton-1-1.als
COMNT  single_pulse
DATIM  2015-02-12 10:57:34
OBNUC  1H
EXMOD  proton.jxp
OBFRQ        399.78 MHz
OBSET          4.19 KHz
OBFIN          7.29 Hz
POINT         13107
FREQU       7598.78 Hz
SCANS             8
ACQTM        1.7249 sec
PD           5.0000 sec
PW1            3.06 usec
IRNUC  1H
CTEMP         18.4 c
SLVNT  CDCL3
EXREF         0.00 ppm
BF            0.12 Hz
RGAIN           34
```



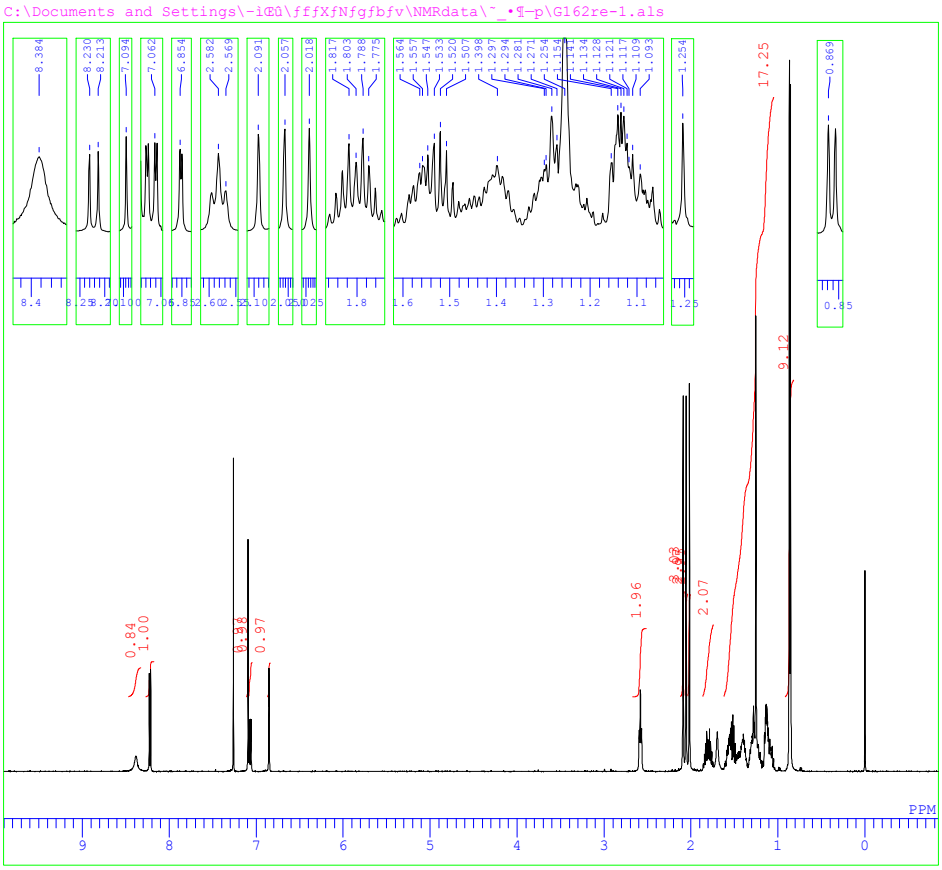
13a



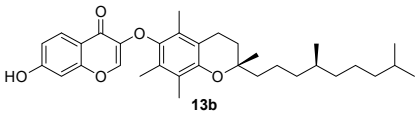

```
DFILE  G163_product_500C-1.als
COMNT  single pulse decoupled gated NOE
DATIM  2015-02-12 21:19:32
OBNUC  13C
EXMOD  single_pulse_dec
OBFRQ        125.77 MHz
OBSET          7.87 KHz
OBFIN          4.21 Hz
POINT         26214
FREQU      31446.06 Hz
SCANS          1000
ACQTM        0.8336 sec
PD           2.0000 sec
PW1            3.50 usec
IRNUC  1H
CTEMP         21.5 c
SLVNT  CDCL3
EXREF         77.00 ppm
BF            1.20 Hz
RGAIN           52
```



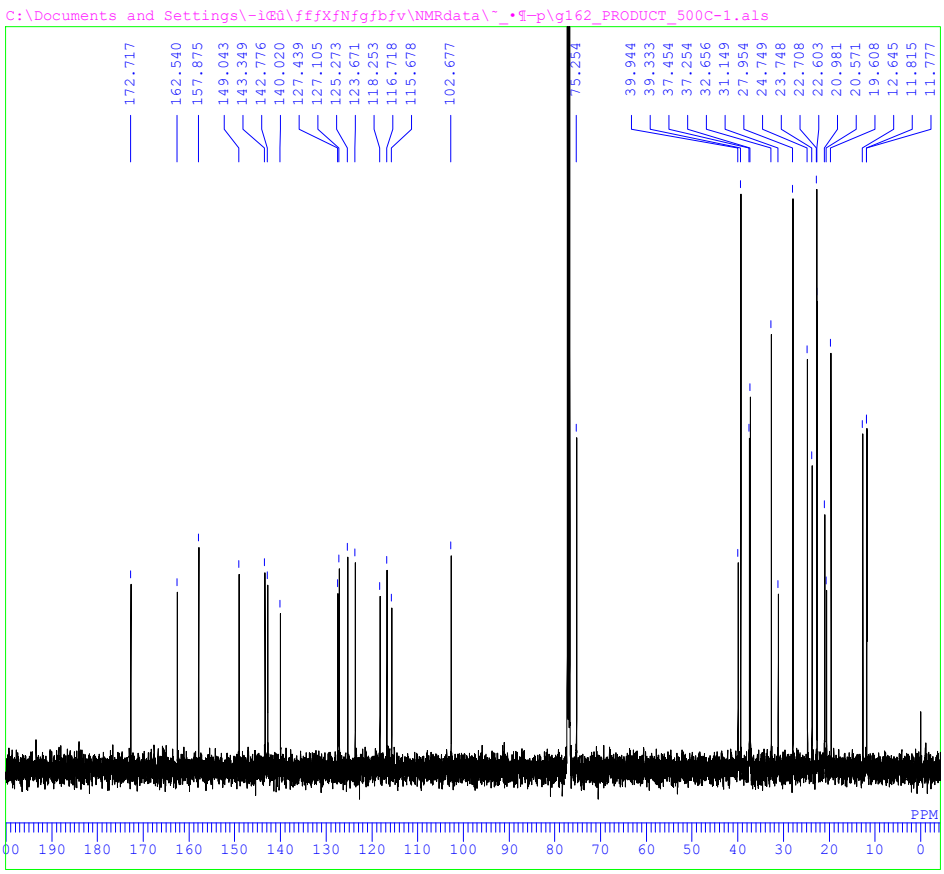
13a



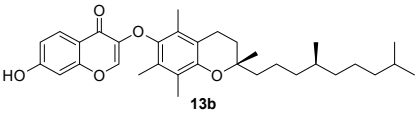

```
DFILE  G162re-1.als
COMNT  single_pulse
DATIM  2015-05-07 18:52:37
OBNUC  1H
EXMOD  single_pulse.ex2
OBFRQ        500.16 MHz
OBSET          2.41 KHz
OBFIN          6.01 Hz
POINT         13107
FREQU       7507.39 Hz
SCANS             8
ACQTM        1.7459 sec
PD           5.0000 sec
PW1            6.82 usec
IRNUC  1H
CTEMP         21.4 c
SLVNT  CDCL3
EXREF          0.00 ppm
BF             0.12 Hz
RGAIN            44
```



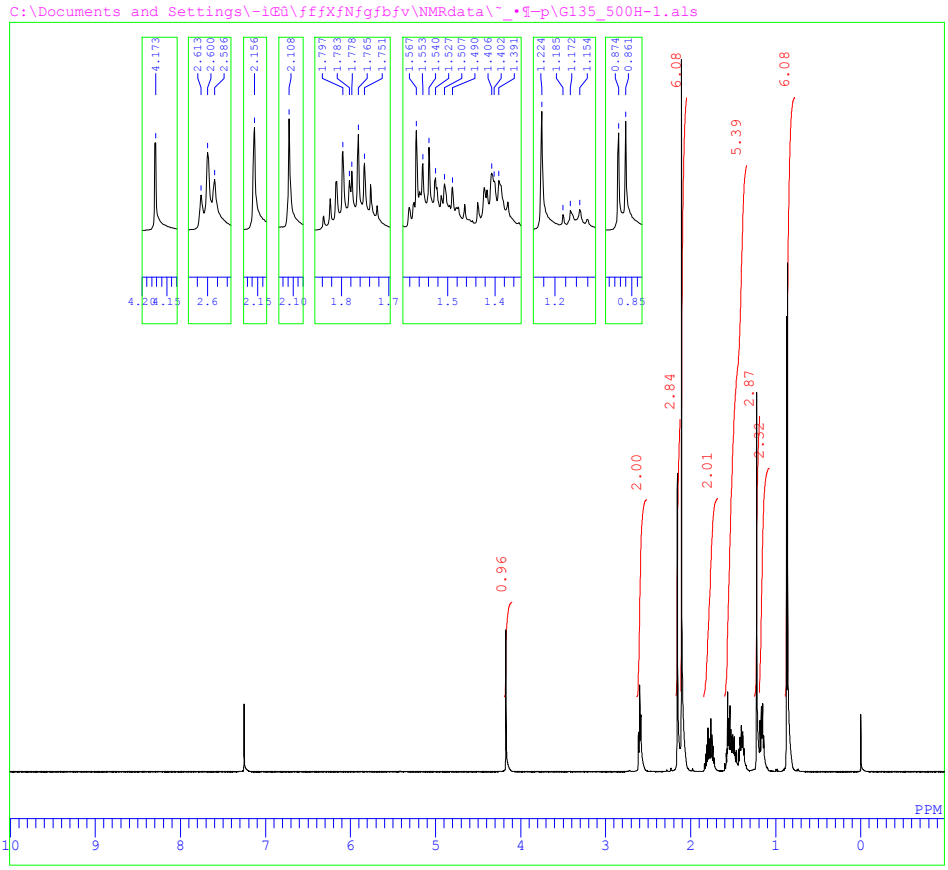
13b



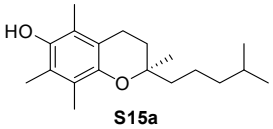

```
DFILE  g162_PRODUCT_500C-1.als
COMNT  single pulse decoupled gated NOE
DATIM  2015-02-12 12:31:47
OBNUC  13C
EXMOD  single_pulse_dec
OBFRQ        125.77 MHz
OBSET          7.87 KHz
OBFIN          4.21 Hz
POINT         26214
FREQU      31446.06 Hz
SCANS          1000
ACQTM        0.8336 sec
PD           2.0000 sec
PW1            3.50 usec
IRNUC  1H
CTEMP         21.1 c
SLVNT  CDCL3
EXREF         77.00 ppm
BF             1.20 Hz
RGAIN            54
```



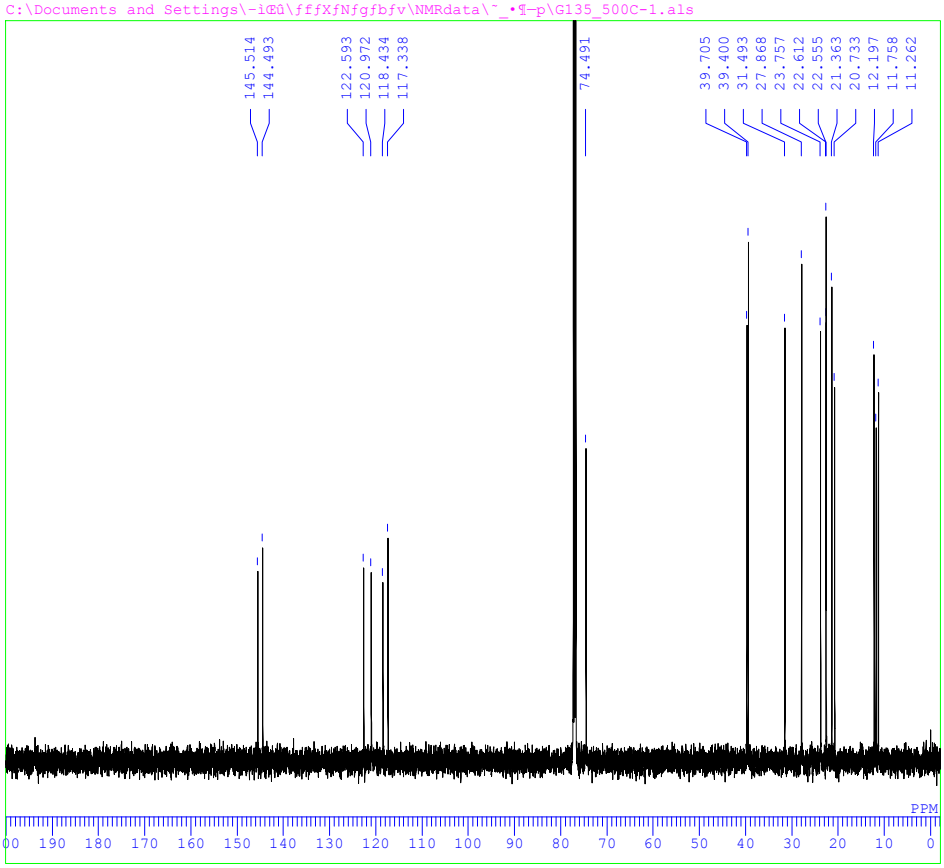
13b



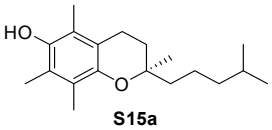

```
DFILE   G135_500H-1.als
COMNT   single_pulse
DATIM   2015-04-14 12:08:18
OBNUC   1H
EXMOD   single_pulse.ex2
OBFRQ         500.16 MHz
OBSET           2.41 KHz
OBFIN           6.01 Hz
POINT          13107
FREQU        7507.39 Hz
SCANS                8
ACQTM         1.7459 sec
PD            5.0000 sec
PW1             6.82 usec
IRNUC   1H
CTEMP          22.2 c
SLVNT   CDCL3
EXREF          0.00 ppm
BF             0.12 Hz
RGAIN            40
```



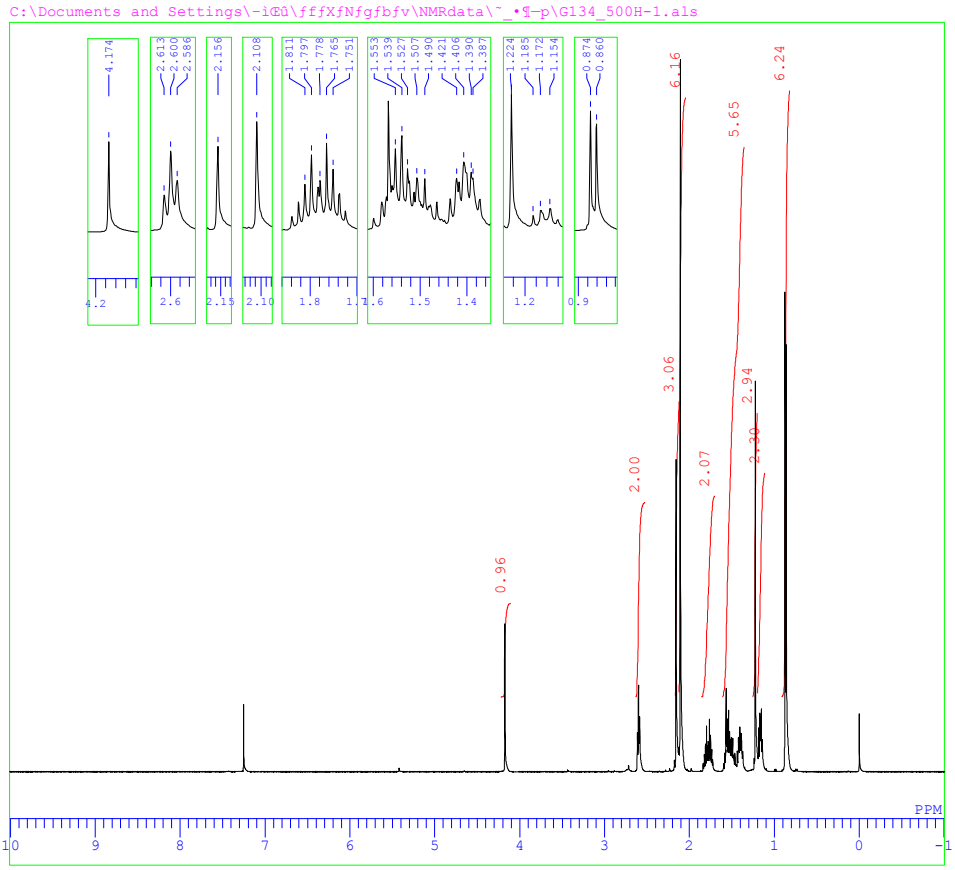
S15a



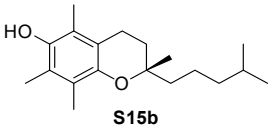

```
DFILE   G135_500C-1.als
COMNT   single pulse decoupled gated NOE
DATIM   2015-04-14 12:56:10
OBNUC   13C
EXMOD   single_pulse_dec
OBFRQ         125.77 MHz
OBSET           7.87 KHz
OBFIN           4.21 Hz
POINT          26214
FREQU       31446.06 Hz
SCANS            1000
ACQTM         0.8336 sec
PD            2.0000 sec
PW1             3.50 usec
IRNUC   1H
CTEMP          22.5 c
SLVNT   CDCL3
EXREF          77.00 ppm
BF             1.20 Hz
RGAIN            52
```



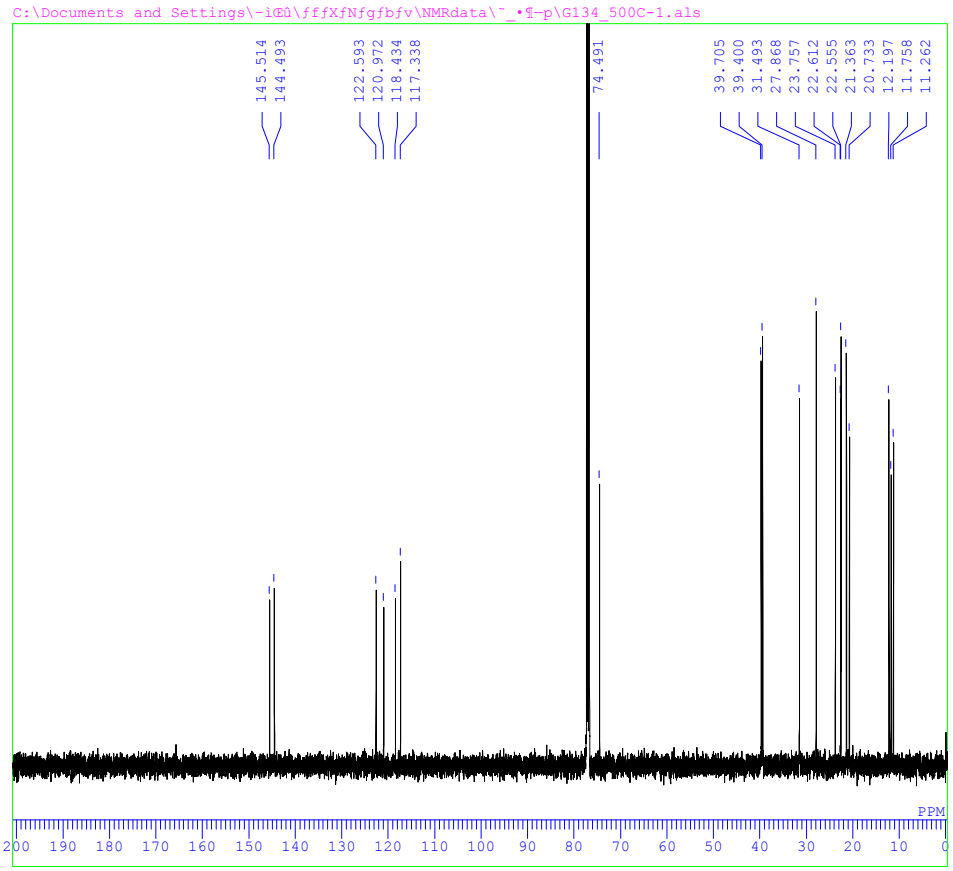
S15a



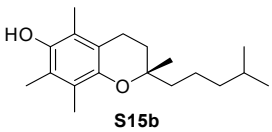

```
DFILE  G134_500H-1.als
COMNT  single_pulse
DATIM  2015-04-14 10:19:00
OBNUC  1H
EXMOD  single_pulse.ex2
OBFRQ        500.16 MHz
OBSET          2.41 KHz
OBFIN          6.01 Hz
POINT         13107
FREQU       7507.39 Hz
SCANS             8
ACQTM        1.7459 sec
PD           5.0000 sec
PW1            6.82 usec
IRNUC  1H
CTEMP         22.1 c
SLVNT  CDCL3
EXREF          0.00 ppm
BF             0.12 Hz
RGAIN            40
```



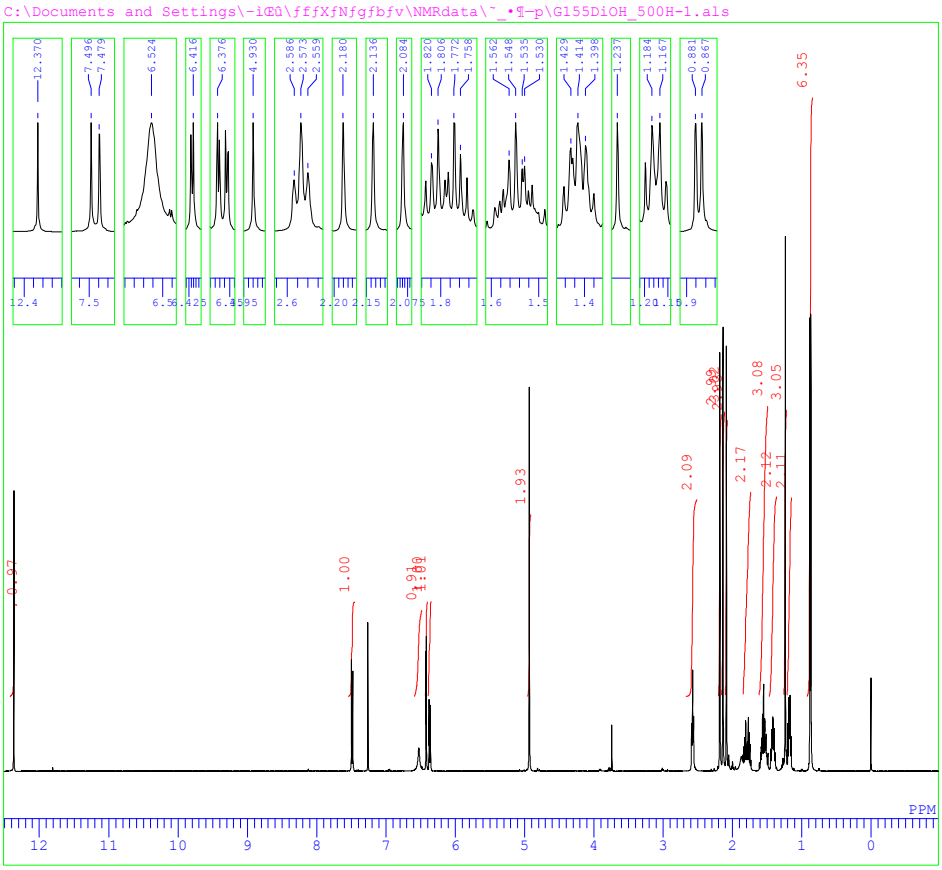
S15b



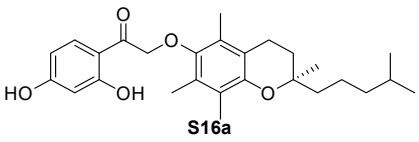

```
DFILE  G134_500C-1.als
COMNT  single pulse decoupled gated NOE
DATIM  2015-04-14 11:06:53
OBNUC  13C
EXMOD  single_pulse_dec
OBFRQ        125.77 MHz
OBSET          7.87 KHz
OBFIN          4.21 Hz
POINT         26214
FREQU       31446.06 Hz
SCANS           1000
ACQTM         0.8336 sec
PD            2.0000 sec
PW1             3.50 usec
IRNUC  1H
CTEMP         22.6 c
SLVNT  CDCL3
EXREF         77.00 ppm
BF             1.20 Hz
RGAIN            54
```



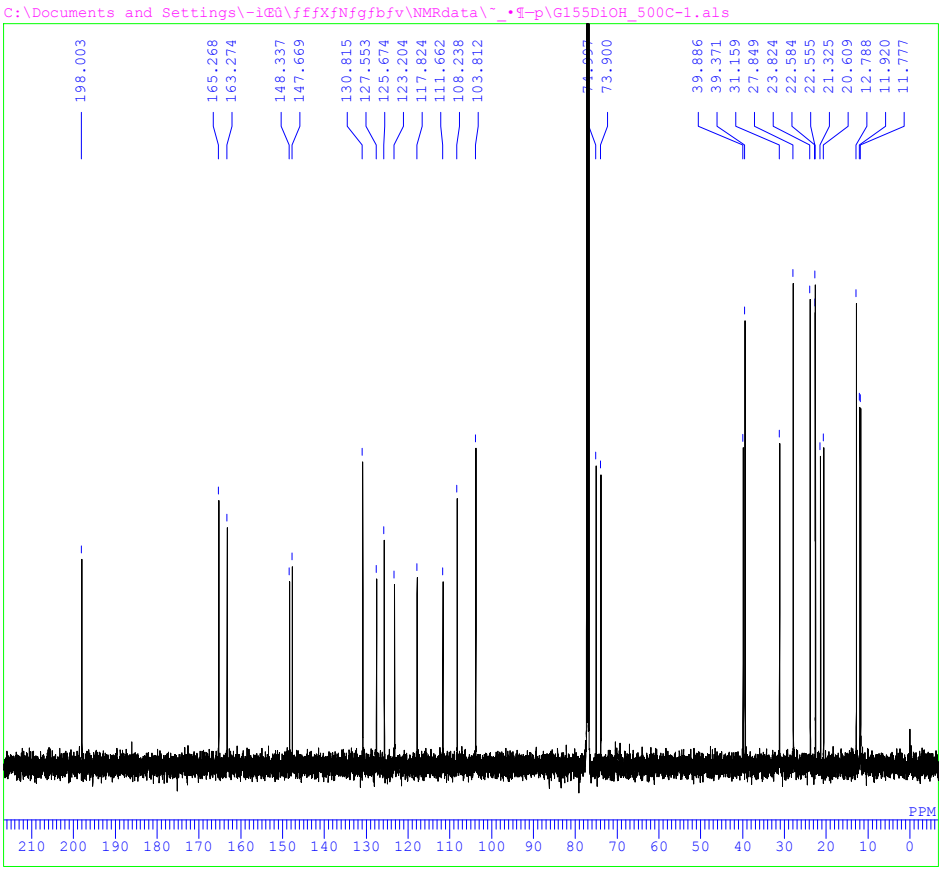
S15b



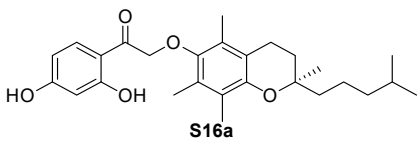

```
DFILE  G155DiOH_500H-1.als
COMNT  single_pulse
DATIM  2015-04-14 19:09:53
OBNUC  1H
EXMOD  single_pulse.ex2
OBFRQ        500.16 MHz
OBSET          2.41 KHz
OBFIN          6.01 Hz
POINT         13107
FREQU       7507.39 Hz
SCANS             8
ACQTM        1.7459 sec
PD           5.0000 sec
PW1            6.82 usec
IRNUC  1H
CTEMP         22.2 c
SLVNT  CDCL3
EXREF         0.00 ppm
BF            0.12 Hz
RGAIN           40
```



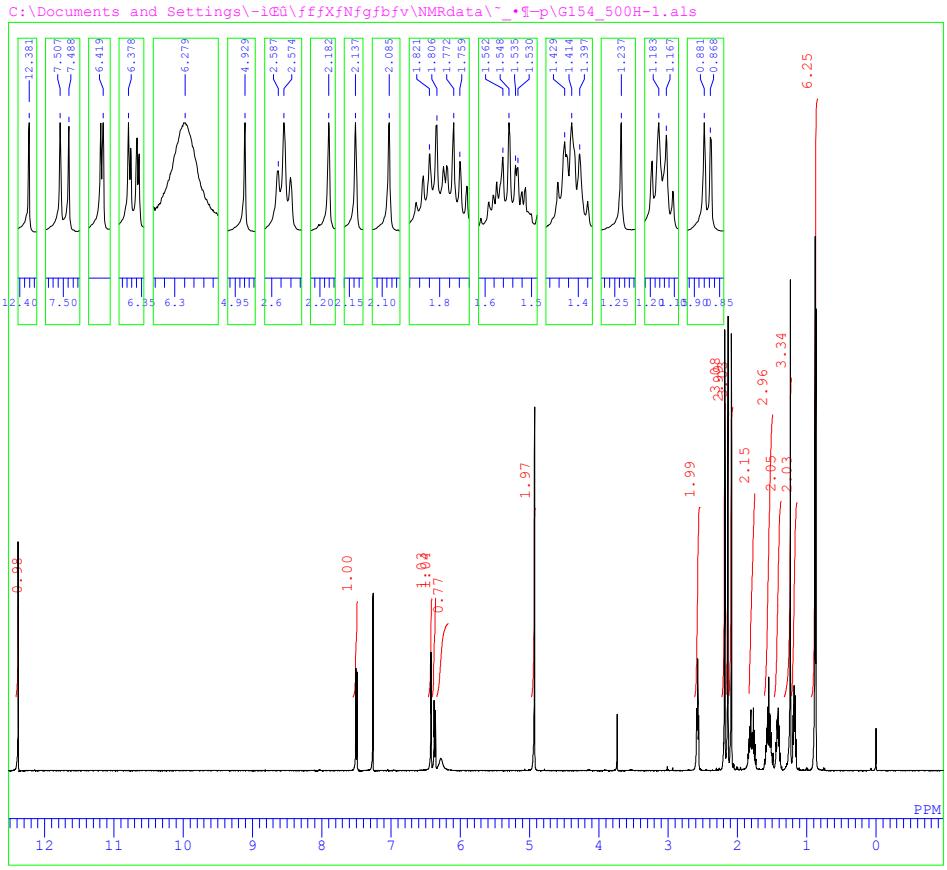
S16a



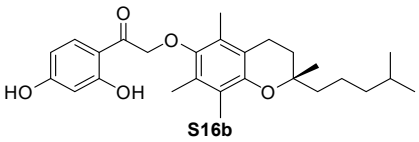

```
DFILE  G155DiOH_500C-1.als
COMNT  single pulse decoupled gated NOE
DATIM  2015-04-14 19:58:11
OBNUC  13C
EXMOD  single_pulse_dec
OBFRQ        125.77 MHz
OBSET          7.87 KHz
OBFIN          4.21 Hz
POINT         26214
FREQU      31446.06 Hz
SCANS           1000
ACQTM         0.8336 sec
PD            2.0000 sec
PW1             3.50 usec
IRNUC  1H
CTEMP         22.8 c
SLVNT  CDCL3
EXREF         77.00 ppm
BF            1.20 Hz
RGAIN           54
```



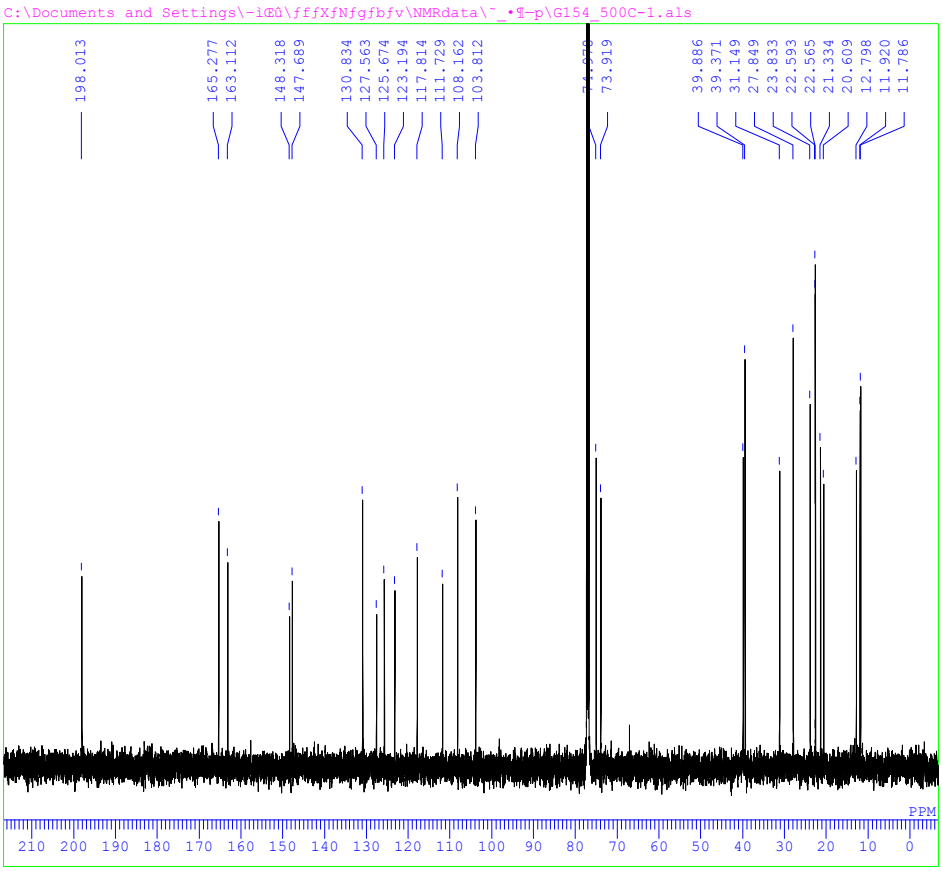
S16a



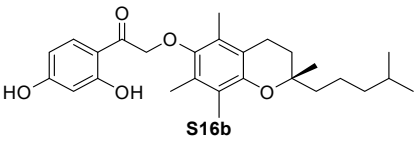
DFILE G154_500H-1.als
COMNT single_pulse
DATIM 2015-02-04 14:19:13
OBNUC 1H
EXMOD single_pulse.ex2
OBFRQ 500.16 MHz
OBSET 2.41 KHz
OBFIN 6.01 Hz
POINT 13107
FREQU 7507.39 Hz
SCANS 8
ACQTM 1.7459 sec
PD 5.0000 sec
PW1 6.82 usec
IRNUC 1H
CTEMP 20.6 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 0.12 Hz
RGAIN 42



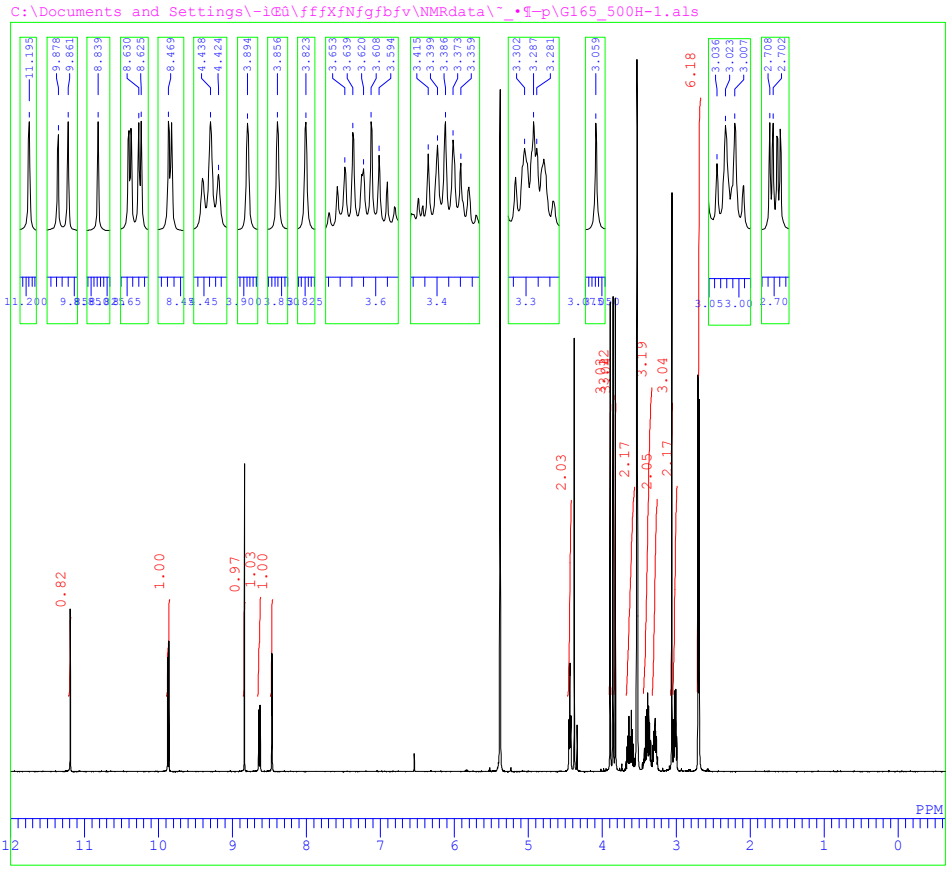
S16b



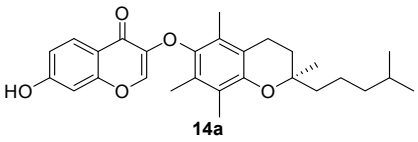
DFILE G154_500C-1.als
COMNT single pulse decoupled gated NOE
DATIM 2015-02-04 15:08:05
OBNUC 13C
EXMOD single_pulse_dec
OBFRQ 125.77 MHz
OBSET 7.87 KHz
OBFIN 4.21 Hz
POINT 26214
FREQU 31446.06 Hz
SCANS 1000
ACQTM 0.8336 sec
PD 2.0000 sec
PW1 3.50 usec
IRNUC 1H
CTEMP 21.1 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 1.20 Hz
RGAIN 54



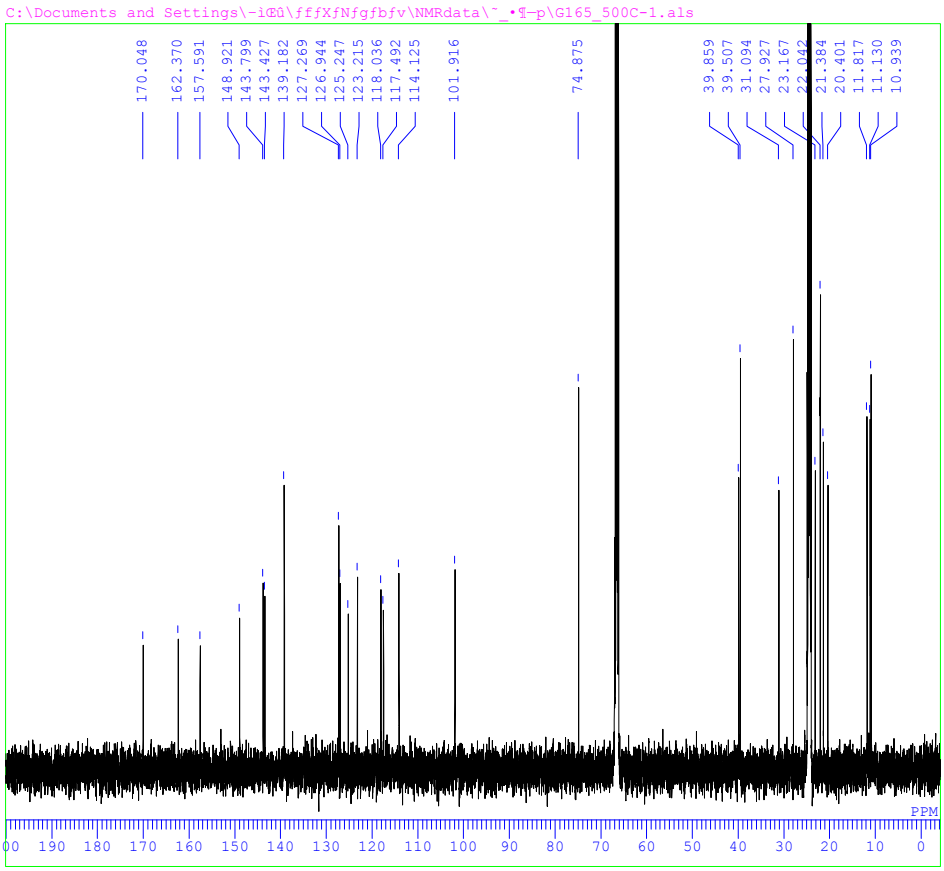
S16b



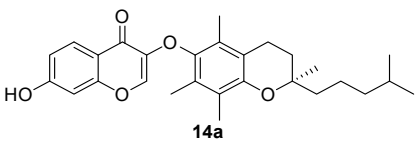

```
DFILE  G165_500H-1.als
COMNT  single_pulse
DATIM  2015-04-03 13:47:26
OBNUC  1H
EXMOD  single_pulse.ex2
OBFRQ        500.16 MHz
OBSET          2.41 KHz
OBFIN          6.01 Hz
POINT         13107
FREQU       7507.39 Hz
SCANS             8
ACQTM        1.7459 sec
PD           5.0000 sec
PW1            6.82 usec
IRNUC  1H
CTEMP         22.0 c
SLVNT  C4D8O
EXREF          3.53 ppm
BF             0.12 Hz
RGAIN            44
```



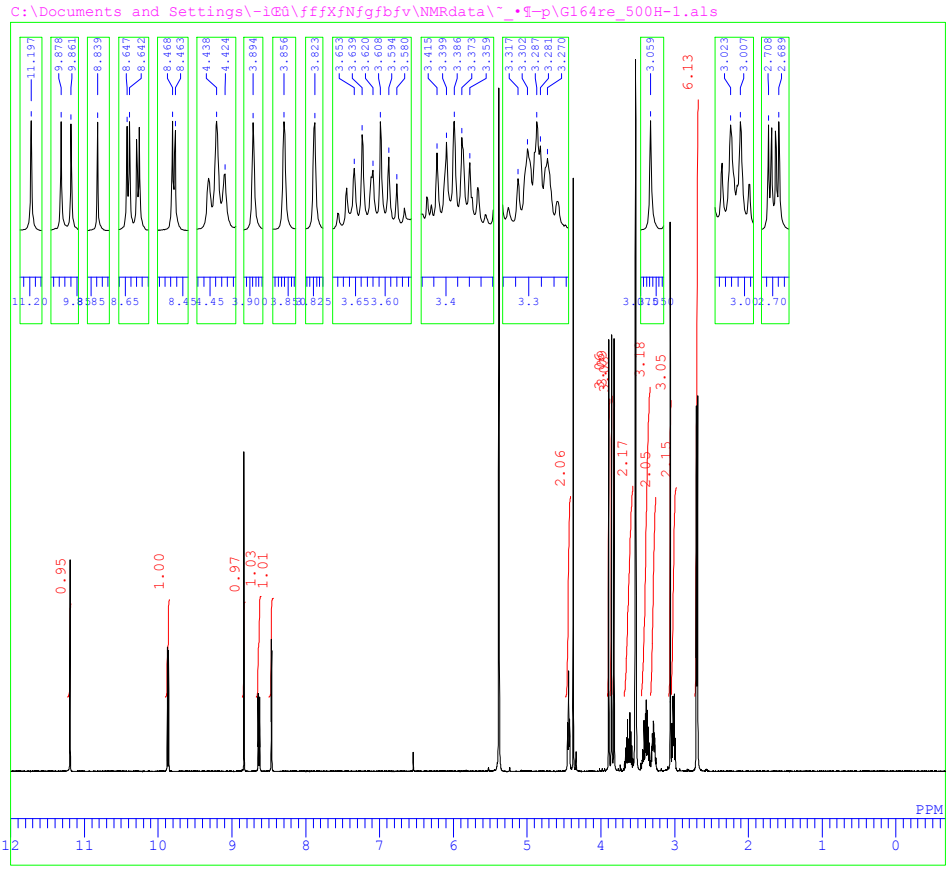
14a



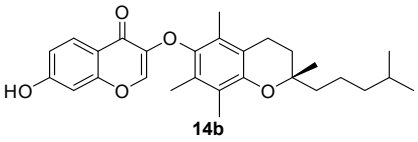

```
DFILE  G165_500C-1.als
COMNT  single pulse decoupled gated NOE
DATIM  2015-04-03 14:35:40
OBNUC  13C
EXMOD  single_pulse_dec
OBFRQ        125.77 MHz
OBSET          7.87 KHz
OBFIN          4.21 Hz
POINT         26214
FREQU      31446.06 Hz
SCANS          1000
ACQTM        0.8336 sec
PD           2.0000 sec
PW1            3.50 usec
IRNUC  1H
CTEMP         22.5 c
SLVNT  C4D8O
EXREF         66.50 ppm
BF             1.20 Hz
RGAIN            52
```



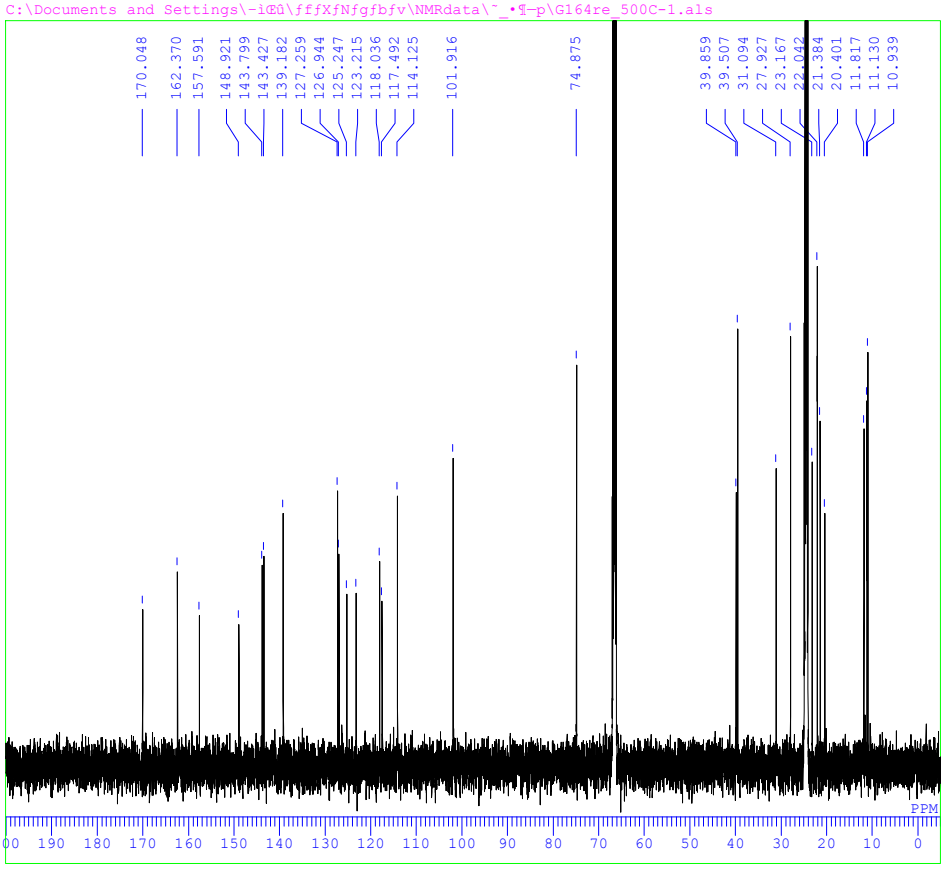
14a



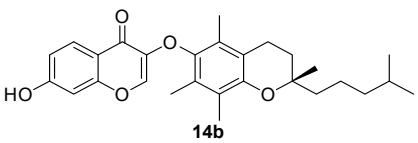

```
DFILE   G164re_500H-1.als
COMNT   single_pulse
DATIM   2015-04-03 16:14:27
OBNUC   1H
EXMOD   single_pulse.ex2
OBFRQ         500.16 MHz
OBSET           2.41 KHz
OBFIN           6.01 Hz
POINT          13107
FREQU        7507.39 Hz
SCANS                8
ACQTM         1.7459 sec
PD            5.0000 sec
PW1             6.82 usec
IRNUC   1H
CTEMP          22.0 c
SLVNT   C4D8O
EXREF          3.53 ppm
BF             0.12 Hz
RGAIN            44
```



14b




```
DFILE   G164re_500C-1.als
COMNT   single pulse decoupled gated NOE
DATIM   2015-04-03 17:02:37
OBNUC   13C
EXMOD   single_pulse_dec
OBFRQ         125.77 MHz
OBSET           7.87 KHz
OBFIN           4.21 Hz
POINT          26214
FREQU       31446.06 Hz
SCANS            1000
ACQTM         0.8336 sec
PD            2.0000 sec
PW1             3.50 usec
IRNUC   1H
CTEMP          22.5 c
SLVNT   C4D8O
EXREF          66.50 ppm
BF             1.20 Hz
RGAIN            50
```



14b