

Supplementary Information

Synthesis and Biological Evaluation of Selective CXCR4 Antagonists Containing Alkene Dipeptide Isosteres

Tetsuo Narumi,^{a,b} Ryoko Hayashi,^a Kenji Tomita,^a Kazuya Kobayashi,^a Noriko Tanahara,^a Hiroaki Ohno,^a Takeshi Naito,^a Eiichi Kodama,^c Masao Matsuoka,^c Shinya Oishi,^{*a} and Nobutaka Fujii^{*a}

^a Graduate School of Pharmaceutical Sciences, Kyoto University, Sakyo-ku, Kyoto 606-8501, Japan. Fax: +81-75-753-4570; Tel: +81-75-753-4551

E-mail: soishi@pharm.kyoto-u.ac.jp (S.O.); nfujii@pharm.kyoto-u.ac.jp (N.F.)

^b Institute of Biomaterials and Bioengineering, Tokyo Medical and Dental University, Chiyoda-ku, Tokyo 101-0062, Japan

^c Laboratory of Virus Control, Institute for Virus Research, Kyoto University, Sakyo-ku, Kyoto 606-8507, Japan

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General Information

¹H NMR spectra were recorded using a JEOL AL-400 and JEOL ECA-500 spectrometer. Chemical shifts are reported in δ (ppm) relative to Me₄Si (in CDCl₃) as internal standard. ¹³C NMR spectra were recorded using a JEOL AL-400 and JEOL ECA-500, and referenced to the residual CHCl₃ signal. ¹⁹F NMR spectra were recorded using a JEOL AL-400 and JEOL ECA-500, and referenced to the residual CFCl₃ signal (δ_F 0.00 ppm). Exact mass (HRMS) spectra were recorded on a JMS-HX/HX 110A mass spectrometer. Optical rotations were measured with a JASCO sodium automatic polarimeter P-1020. Infrared (IR) spectra were obtained on a JASCO FT/IR-4100 FT-IR spectrometer with JASCO ATR PRO410-S. Melting points (uncorrected) were measured by a hot stage melting point apparatus. For flash chromatography, Wakosil C-300, C-300E and silica gel 60 H (silica gel for thin-layer chromatography, Merck) were employed. For analytical HPLC, a Cosmosil 5C18-ARII column (4.6 x 250 mm, Nacalai Tesque, Inc., Kyoto, Japan) was employed with a linear gradient of CH₃CN containing 0.1% (v/v) TFA at a flow rate of 1 cm³ min⁻¹ on a Shimadzu LC-10ADvp (Shimadzu Corp., Ltd., Kyoto, Japan), and eluting products were detected by UV at 220 nm. Preparative HPLC was performed using a Cosmosil 5C18-ARII column (20 x 250 mm, Nacalai Tesque, Inc.) on a Shimadzu LC-6AD (Shimadzu corporation, Ltd.) in an isocratic mode of CH₃CN solution containing 0.1% (v/v) TFA at a flow rate of 10 cm³ min⁻¹.

Experimental Procedures

(3S,4S)-7-[N-(Benzyloxycarbonyl)amino]-4-[N-(tert-butoxycarbonyl)amino]hept-1-en-3-ol (6a).

To a stirred solution of **5** (9.51 g, 27.0 mmol) in CH₂Cl₂/toluene (1/2, 90 cm³) was added dropwise a solution of DIBAL-H in toluene (0.99 M, 55.6 cm³, 55.0 mmol) at -78 °C under argon, and the mixture was stirred at -78 °C for 1 h. To a stirred solution of ZnCl₂ (10.2 g, 75.0 mmol) and LiCl (3.18 g, 75.0 mmol) in THF (50 cm³) was added dropwise vinyl magnesium chloride in THF (1.1 M, 68.2 cm³, 75.0 mmol) at -78 °C. After being stirred at this temperature for 30 min, the mixture was stirred at 0 °C for 30 min. To this solution was added dropwise the above solution of aldehyde at -78 °C, and the mixture was stirred for 3 h with warming to 0 °C, followed by quenching with 0.25 M Rochelle salt and saturated NH₄Cl. The mixture was concentrated under reduced pressure, and the residue was extracted with EtOAc. The extract was washed with saturated citric acid, saturated NaHCO₃ and brine, and dried over MgSO₄. Concentration under reduced pressure followed by flash chromatography over silica gel with EtOAc/*n*-hexane (1/4) gave the diastereomixture of allyl alcohol **6** (4.28 g, 42%). Recrystallization from EtOAc/*n*-hexane (1/10) gave the title compound **6a** as a colorless solid: mp 67-68 °C; $[\alpha]_D^{24}$ -27.6 (*c* 1.13, CHCl₃); δ_H (500 MHz, CDCl₃, Me₄Si) 1.42 (9 H, s), 1.54–1.61 (4 H, m), 2.52–2.65 (1 H, m), 3.10–3.30 (2 H, m), 3.50–3.65 (1 H, m), 4.04–4.15 (1 H, m), 4.70–4.82 (1 H, m), 4.90–5.00 (1 H, m), 5.09 (2 H, s), 5.19 (1 H, d, *J* 10.8), 5.30 (1 H, d, *J* 16.8), 5.86 (1 H, ddd, *J* 16.8, 10.8 and 5.7) and 7.30–7.35 (5 H, m); δ_C (125 MHz, CDCl₃, Me₄Si) 26.6, 28.3 (3 C), 28.9, 40.8, 54.3, 66.6, 74.3, 79.3, 116.2, 128.0 (3 C), 128.4 (2 C), 136.6, 138.0, 156.4 and 156.5; HRMS (FAB), *m/z* calcd for C₂₀H₃₁N₂O₅ ([M+H]⁺) 379.2227, found 379.2228.

(3S,4S)-7-[N-(Benzyloxycarbonyl)amino]-4-[N-(*o*-nitrobenzenesulfonyl)amino]hept-1-en-3-ol

(7). To a stirred solution of allyl alcohol **6a** (3.92 g, 10.3 mmol) in CH₂Cl₂ (60 cm³) at 0 °C was added TFA (40 cm³), and the mixture was stirred for 1 h. The reaction mixture was diluted with toluene (30 cm³) and concentrated under reduced pressure, and the residue was extracted with EtOAc. The extract was washed with saturated NaHCO₃ and brine, and dried over MgSO₄. Concentration under reduced pressure gave an oily residue of a crude amine, which was dissolved in CH₂Cl₂ (80 cm³). To this solution were added Et₃N (0.740 cm³, 10.3 mmol) and nosyl chloride (2.28 g, 10.3 mmol) at room temperature, and the mixture was stirred at the same temperature for 9 h. After concentration under reduced pressure, the residue was extracted with EtOAc. The extract was washed with saturated citric acid, saturated NaHCO₃ and brine, and dried over MgSO₄. Concentration under reduced pressure followed by flash chromatography over silica gel with EtOAc/*n*-hexane (1/4) gave the title compound **7** (3.51 g, 74%) as a yellow oil: [α]_D²⁴ -70.1 (*c* 1.00, CHCl₃); δ _H (500 MHz, CDCl₃, Me₄Si) δ 1.53–1.81 (4 H, m), 2.45 (1 H, s), 3.13–3.17 (2 H, m), 3.44–3.59 (1 H, m), 4.02–4.12 (1 H, m), 4.84–4.86 (2 H, m), 5.07–5.14 (3 H, m), 5.56 (1 H, ddd, *J* 17.2, 10.3 and 5.2), 5.76 (1 H, d, *J* 9.2), 7.33–7.36 (5 H, m), 7.64–7.70 (2 H, m), 7.78–7.87 (1 H, m) and 8.04–8.15 (1H, m); δ _C (125 MHz, CDCl₃, Me₄Si) 26.1, 29.4, 40.4, 58.8, 66.6, 73.8, 116.9, 125.1, 128.0 (2 C), 128.1, 128.5 (2 C), 130.4, 132.8, 133.2, 135.2, 136.5, 137.0, 147.6 and 156.6; HRMS (FAB), *m/z* calcd for C₂₁H₂₆N₃O₇S ([M+H]⁺) 464.1486, found 464.1483.

(3R,4S)-7-[N-(Benzyloxycarbonyl)amino]-3,4-[N-(*o*-nitrobenzenesulfonyl)epimino]hept-1-ene

(8). To a stirred solution of allyl alcohol **7** (905 mg, 1.95 mmol) in dry THF (20 cm³) at 0 °C were added triphenylphosphine (767 mg, 2.93 mmol) and diethyl azodicarboxylate in toluene solution (2.2 M, 975 cm³, 2.15 mmol), and the reaction mixture was stirred at room temperature for 4 h. The mixture was concentrated under reduced pressure and purified by flash chromatography over silica gel with CHCl₃ to give the title compound **8** (806 mg, 93%) as a yellow oil: [α]_D²⁴ +4.0 (*c* 1.00, CHCl₃); δ _H (500 MHz, CDCl₃, Me₄Si) 1.55–1.60 (4 H, m), 3.09–3.16 (1 H, m), 3.17–3.25 (2 H, m), 3.56 (1 H, t, *J* 6.9), 5.00 (1 H, br s), 5.07 (2 H, s), 5.34 (1 H, d, *J* 10.3), 5.48 (1 H, d, *J* 17.2 Hz), 5.58–5.65 (1 H, m), 7.29–7.34 (5 H, m), 7.71–7.79 (3 H, m) and 8.16 (1H, d, *J* 7.5); δ _C (125 MHz, CDCl₃, Me₄Si) 24.0, 27.1, 40.1, 46.0, 46.5, 47.6, 66.4, 122.0, 124.2, 127.9, 127.9, 128.4 (2 C), 129.0, 131.0, 131.7, 132.1, 134.4, 136.5, 148.4 and 156.3; HRMS (FAB), *m/z* calcd for C₂₁H₂₂N₃O₆S ([M-H]⁻) 444.1235, found 444.1235.

tert-Butyl (4R,5S,2E)-8-[N-(benzyloxycarbonyl)amino]-4,5-[N-(*o*-nitrobenzenesulfonyl)epimino]oct-2-enoate (9). Ozone gas was bubbled through a solution of aziridine **8** (2.79 g, 6.26 mmol) in EtOAc (60 cm³) at -78 °C until a blue color persisted. To the above solution was added Me₂S (4.90 cm³, 63.0 mmol), and the mixture was stirred at -78 °C for 10 min. Concentration under reduced pressure gave an oily residue of a crude aldehyde, which was used immediately in the next step without further purification. To a stirred suspension of LiCl (398 mg, 9.39 mmol) in MeCN (40 cm³)

under argon, were added (EtO)₂P(O)CH₂CO₂*t*-Bu (2.37 g, 9.39 mmol) in MeCN (10 cm³) and (*i*-Pr)₂NEt (1.64 cm³, 9.39 mmol) at 0 °C. After 30 min, the above aldehyde in MeCN (20 cm³) was added to the mixture at 0 °C, and the mixture was stirred at this temperature for 4 h followed by quenching with saturated NH₄Cl. The mixture was concentrated under reduced pressure, and the residue was extracted with EtOAc. The extract was washed successively with saturated citric acid, saturated NaHCO₃ and brine, and dried over MgSO₄. Concentration under reduced pressure followed by flash chromatography over silica gel with EtOAc/*n*-hexane (1/4) gave the title compound **9** (1.93 g, 57%) as a yellow oil: [α]_D²⁴ -24.3 (*c* 1.01, CHCl₃); δ_H (500 MHz, CDCl₃, Me₄Si) 1.46 (9 H, s), 1.59–1.67 (4 H, m), 3.22–3.24 (3 H, m), 3.67 (1 H, t, *J* 6.9), 4.93 (1 H, br s), 5.08 (2 H, s), 6.12 (1 H, d, *J* 16.0), 6.56 (1 H, dd, *J* 16.0 and 7.4), 7.29–7.37 (5 H, m), 7.71–7.78 (3 H, m) and 8.19 (1 H, d, *J* 7.5); δ_C (125 MHz, CDCl₃, Me₄Si) 24.3, 27.3, 28.0 (3 C), 40.1, 46.0, 46.9, 66.6, 81.1, 124.4, 128.0 (3 C), 128.5 (2 C), 129.0, 131.4, 131.6, 132.3, 134.7, 136.5, 136.9, 148.5, 156.4 and 164.5; HRMS (FAB), *m/z* calcd for C₂₆H₃₀N₃O₈S ([M-H]⁻) 544.1759, found 544.1763.

***tert*-Butyl (2*R*,5*S*,3*E*)-8-[*N*-(benzyloxycarbonyl)amino]-2-(3-hydroxyprop-1-yl)-5-[*N*-(*o*-nitrobenzenesulfonyl)amino]oct-3-enoate (11).** To a stirred solution of **10** (101 mg, 0.140 mmol) in dry THF (2 cm³) at 0 °C were added 1 M tetrabutylammonium fluoride in THF solution (0.210 cm³, 0.210 mmol), and the reaction mixture was stirred at this temperature for 14 h followed by quenching with saturated aqueous NH₄Cl. The mixture was concentrated under reduced pressure, and the residue was extracted with EtOAc. The extract was washed successively with saturated citric acid, saturated NaHCO₃ and brine twice, and dried over MgSO₄. Concentration under reduced pressure followed by flash chromatography over silica gel with EtOAc/*n*-hexane (1/2) gave the title compound **11** (62.0 mg, 85%) as a yellow oil: [α]_D²⁴ -96.1 (*c* 1.00, CHCl₃); δ_H (500 MHz, CDCl₃, Me₄Si) 1.26–1.35 (2 H, m), 1.37 (9 H, s), 1.40–1.56 (6 H, m), 2.12 (1 H, br s), 2.63–2.71 (1 H, m), 3.10–3.20 (2 H, m), 3.48–3.56 (2 H, m), 3.87–3.97 (1 H, m), 4.94–5.03 (1 H, m), 5.09 (2 H, s), 5.29 (1 H, dd, *J* 15.5 and 7.4), 5.40 (1 H, dd, *J* 15.5 and 8.6), 5.63 (1 H, d, *J* 8.0), 7.32–7.34 (5 H, m), 7.66–7.71 (2 H, m), 7.81 (1 H, d, *J* 6.7) and 8.07 (1 H, d, *J* 7.5); δ_C (125 MHz, CDCl₃, Me₄Si) 25.9, 27.9 (3 C), 28.4, 29.8, 32.9, 40.3, 49.0, 56.4, 62.0, 66.5, 80.8, 125.3, 127.9 (2 C), 128.0, 128.4 (2 C), 130.8, 130.9, 131.2, 132.8, 133.4, 134.6, 136.5, 147.7, 156.4 and 172.7; HRMS (FAB), *m/z* calcd for C₂₉H₃₈N₃O₉S ([M-H]⁻) 604.2334, found 604.2343.

***tert*-Butyl (2*R*,5*S*,3*E*)-8-[*N*-(benzyloxycarbonyl)amino]-2-{3-[*N*-(benzyloxycarbonyl)-*N*-(*o*-nitrobenzenesulfonyl)amino]prop-1-yl}-5-[*N*-(*o*-nitrobenzenesulfonyl)amino]oct-3-enoate (12).** To a stirred solution of alcohol **11** (255 mg, 0.490 mmol) in dry THF (5 cm³) at 0 °C were added triphenylphosphine (170 mg, 0.640 mmol), 2.2 M diethyl azodicarboxylate in toluene solution (0.270 cm³, 0.590 mmol) and benzyl *N*-(2-nitrophenylsulfonyl)carbamate (180 mg, 0.540 mmol), and the reaction mixture was stirred at this temperature for 24 h. The mixture was concentrated under reduced pressure and purified by flash chromatography over silica gel with CHCl₃ to give the title compound **12** (421 mg, 93%) as a yellow oil: [α]_D²⁴ -71.0 (*c* 1.01, CHCl₃); δ_H (500 MHz, CDCl₃,

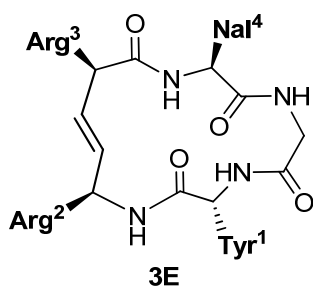
Me₄Si) 1.24–1.29 (2 H, m), 1.38 (9 H, s), 1.53–1.59 (6 H, m), 2.61–2.70 (1 H, m), 3.18–3.20 (2 H, m), 3.70–3.75 (2 H, m), 3.93 (1 H, br s), 4.87 (1 H, br s), 5.09 (2 H, s), 5.11 (2 H, s), 5.27 (1 H, dd, *J* 15.5 and 7.5), 5.35 (1 H, dd, *J* 15.5 and 8.0), 5.41 (1 H, d, *J* 8.6), 7.19–7.23 (2 H, m), 7.29–7.43 (9 H, m), 7.63–7.72 (4 H, m), 7.82–7.86 (1 H, m) and 8.03–8.08 (2H, m); δ_{C} (125 MHz, CDCl₃, Me₄Si) 26.0, 27.1, 27.9 (3 C), 29.0, 33.1, 40.4, 47.6, 48.5, 56.6, 66.6, 69.5, 81.0, 124.3, 125.5, 128.0 (3 C), 128.5 (2 C), 128.6 (2 C), 128.7 (2 C), 128.9, 130.7, 130.8, 131.3, 131.6, 132.6, 132.9, 133.6, 134.0, 134.1, 134.4, 134.7, 136.6, 147.7, 147.8, 151.6, 156.4 and 172.2; HRMS (FAB), *m/z* calcd for C₄₃H₄₈N₅O₁₅S₂ ([M–H][−]) 922.2645, found 922.2650.

***tert*-Butyl (2*R*,5*S*,3*E*)-8-[*N*-(benzyloxycarbonyl)amino]-2-{3-[*N*-(benzyloxycarbonyl)amino]-prop-1-yl}-5-[*N*-(fluorenylmethoxycarbonyl)amino]oct-3-enoate (13).** To a stirred solution of **12** (750 mg, 0.810 mmol) in DMSO/MeCN (1/49, 10 cm³) were added thiophenol (0.330 cm³, 3.24 mmol) and K₂CO₃ (0.67 g, 4.86 mmol) at room temperature, and the mixture was stirred at 50 °C for 2 h. The solution was filtered, and the filtrate was concentrated under reduced pressure. The residue was extracted with CHCl₃, washed with saturated NaHCO₃ and brine, and dried over MgSO₄. Concentration under reduced pressure gave an oily residue, which was dissolved in THF/H₂O (1/1, 8 cm³). Fmoc-OSu (330 mg, 0.970 mmol) and Et₃N (0.120 cm³, 1.62 mmol) were added to the above solution at 0 °C. After being stirred for 4 h, the mixture was concentrated under reduced pressure, and the residue was extracted with EtOAc. The extract was washed successively with saturated citric acid and saturated NaHCO₃ and brine, and dried over MgSO₄. Concentration under reduced pressure followed by flash chromatography over silica gel with EtOAc/*n*-hexane (1/4) gave the title compound **13** (664 mg, quant.) as a colorless oil: $[\alpha]_{\text{D}}^{24}$ −15.6 (*c* 0.51, CHCl₃); δ_{H} (500 MHz, CDCl₃, Me₄Si) 1.41 (9 H, s), 1.44–1.54 (7 H, m), 1.67–1.74 (1 H, m), 2.84–2.86 (1 H, br s), 3.12–3.17 (4 H, m), 4.12 (1 H, br s), 4.17–4.20 (1 H, m), 4.35–4.37 (1 H, m), 4.40–4.46 (1 H, m), 4.92–5.00 (2 H, m), 5.05 (2 H, s), 5.27–5.12 (3 H, m), 5.40–5.45 (1 H, m), 5.52–5.58 (1 H, m), 7.28–7.39 (14 H, m), 7.58 (2 H, d, *J* 6.9) and 7.75 (2 H, d, *J* 7.5); δ_{C} (125 MHz, CDCl₃, Me₄Si) 26.2, 27.3, 28.0 (3 C), 29.2, 32.1, 40.6, 47.2, 49.2, 52.4, 66.4, 66.5, 80.8, 119.9, 120.0, 124.9 (2 C), 125.0 (2 C), 127.0 (2 C), 127.6 (2 C), 128.0 (3 C), 128.1 (3 C), 128.4 (2 C), 128.4 (2 C), 129.3 (2 C), 132.6, 136.5 (2 C), 141.3, 143.8, 143.9, 155.7, 156.3, 156.4 and 172.9; HRMS (FAB), *m/z* calcd for C₄₆H₅₄N₃O₈ ([M+H]⁺) 776.3905, found 776.3911.

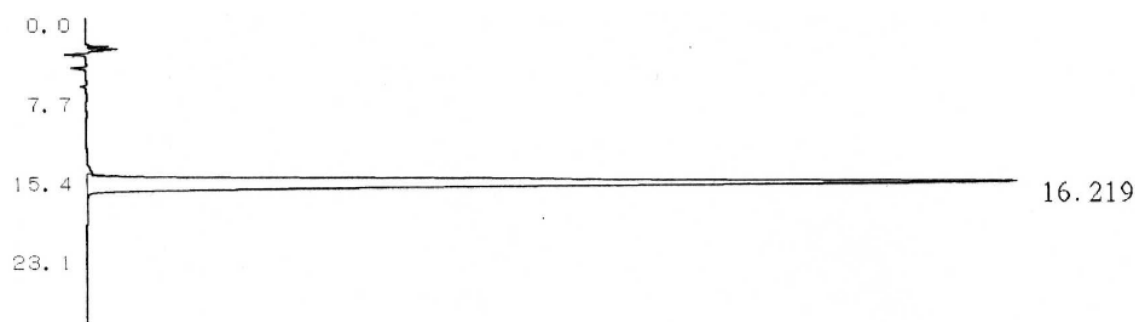
(2*R*,5*S*,3*Z*)-8-[*N*-(*tert*-Butoxycarbonyl)-*N*-(*o*-nitrobenzenesulfonyl)amino]-5-[(*tert*-butoxycarbonyl)amino]-4-fluoro-2-(2-naphthylmethyl)oct-3-enoyl (*S*)-sultam (17). To a solution of the TBS ether **16** (1.32 g, 1.78 mmol) in MeCN/H₂O (1/1, 20 cm³) at 0 °C under argon was added aqueous H₂SiF₆ (3.26 N, 0.546 cm³), and the mixture was stirred at room temperature for 1 h. After dilution with EtOAc (300 cm³), the reaction mixture was washed with aqueous 5% K₂CO₃ and dried over MgSO₄. Concentration under reduced pressure gave the corresponding alcohol, which was used in the next step without purification. To a solution of the alcohol, triphenylphosphine (934 mg, 3.56 mmol), *tert*-butyl *N*-(2-nitrophenylsulfonyl)carbamate (1.15 g, 3.92 mmol) in THF (18 cm³) a

solution of diethyl azodicarboxylate in toluene (2.2 M, 1.62 cm³, 3.56 mmol) were added at 0 °C under argon. After being stirred at room temperature for 12 h, concentration under reduced pressure followed by flash chromatography over silica gel with EtOAc/*n*-hexane (1/2) gave the title compound **17** (1.59 g, 98%) as a colorless semisolid: $[\alpha]_D^{25} -52.4$ (*c* 1.10, CHCl₃); δ_H (500 MHz, CDCl₃, Me₄Si) 0.27 (3 H, s), 0.75 (3 H, s), 1.15–1.26 (2 H, m), 1.35 (9 H, s), 1.44 (9 H, s), 1.53–1.81 (8 H, m), 1.90 (1 H, dd, *J* 13.2 and 8.0), 2.99 (1 H, dd, *J* 13.2 and 6.3), 3.25–3.36 (3 H, m), 3.68–3.77 (3 H, m), 4.49–4.59 (1 H, m), 4.67 (1 H, d, *J* 9.2), 5.08 (1 H, dd, *J* 36.1 and 8.6), 6.38–6.51 (1 H, m), 7.38–7.44 (3 H, m), 7.65 (1 H, s), 7.70–7.78 (6 H, m) and 8.24–8.29 (1 H, m); δ_C (125 MHz, CDCl₃, Me₄Si) 14.4, 19.6, 19.8, 26.3, 26.4, 27.8 (3 C), 28.3 (3 C), 32.7, 38.1, 40.5 (d, *J* 2.4), 43.0, 44.6, 47.3, 47.5, 48.0, 52.8, 62.2, 64.9, 79.7, 84.9, 104.2 (d, *J* 12.0), 124.3, 125.3, 125.8, 127.5, 127.6, 127.6, 127.8, 127.9, 131.7, 132.4, 133.1, 133.4, 133.6, 134.0, 135.1, 147.6, 150.3, 154.8, 158.3 (d, *J* 260.3) and 175.2; δ_F (125 MHz, CDCl₃, CFCl₃) –119.8; HRMS (FAB), *m/z* calcd for C₄₅H₅₇FN₄NaO₁₁S₂ ([M+Na]⁺) 935.3347, found: 935.3358.

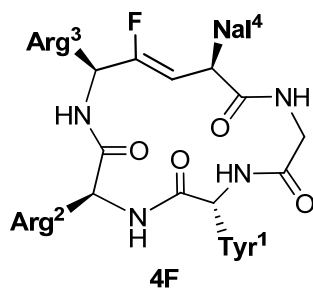
HPLC chart of 3E and 4F.



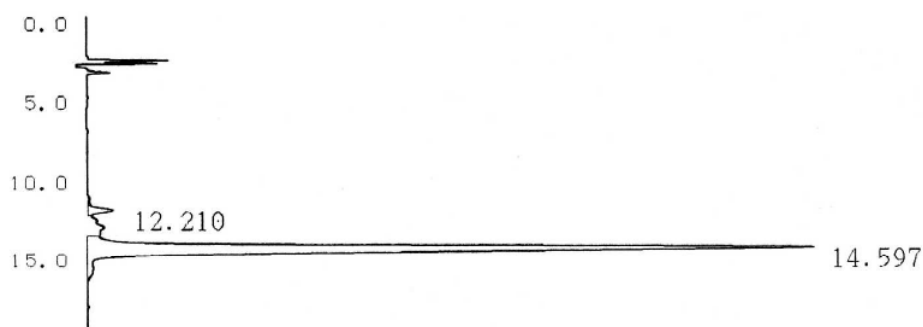
Peptide 3E



HPLC condition: isocratic MeCN (22%) in 0.1% TFA aq., flow rate 1 cm³ min⁻¹



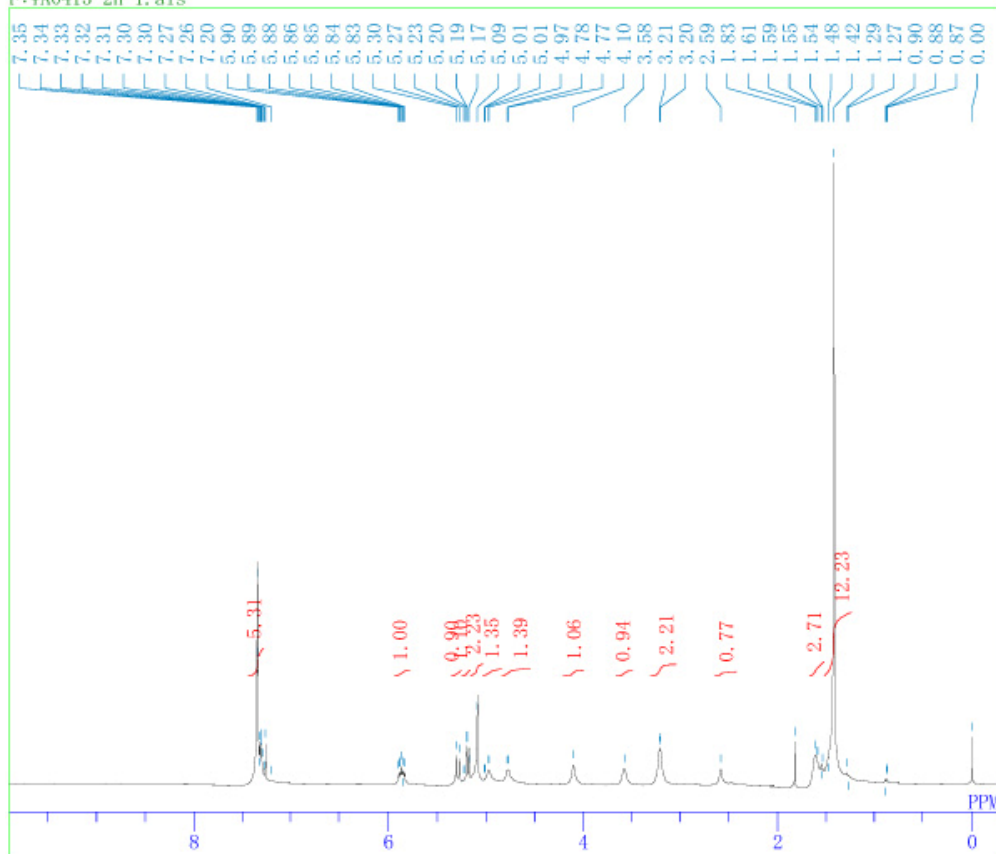
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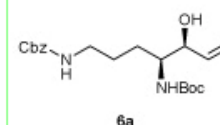
HPLC condition: isocratic MeCN (26%) in 0.1% TFA aq., flow rate 1 cm³ min⁻¹

6a

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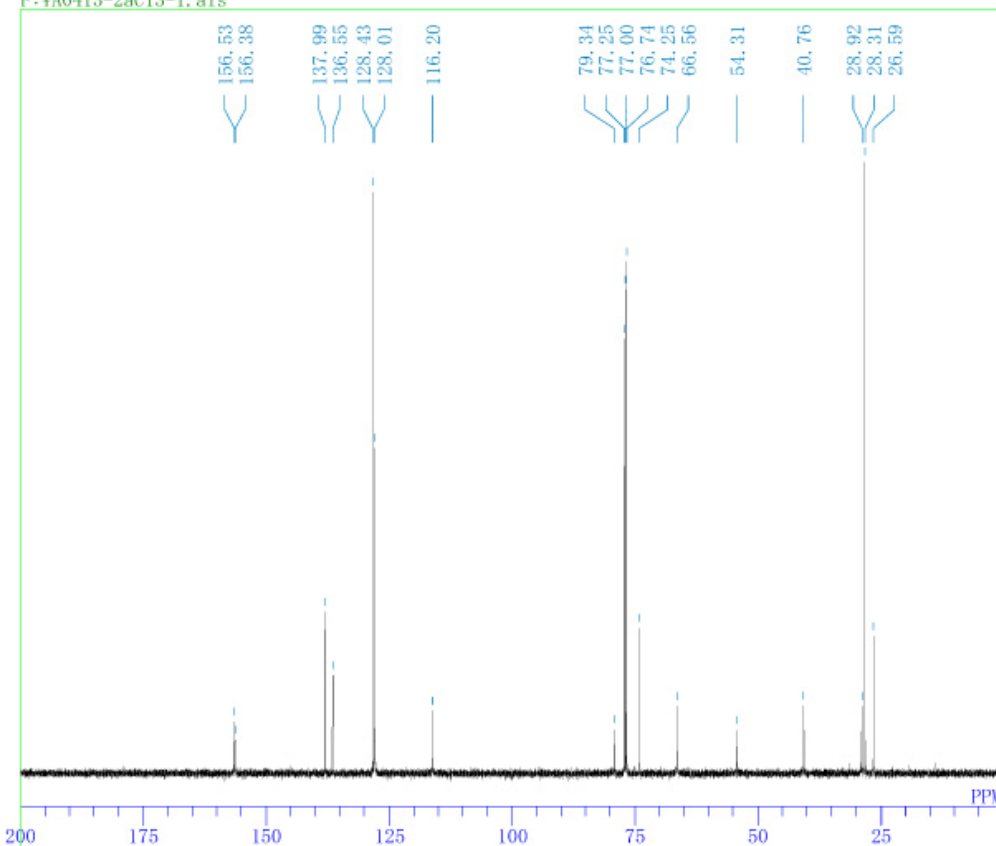


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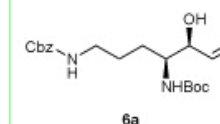


6a

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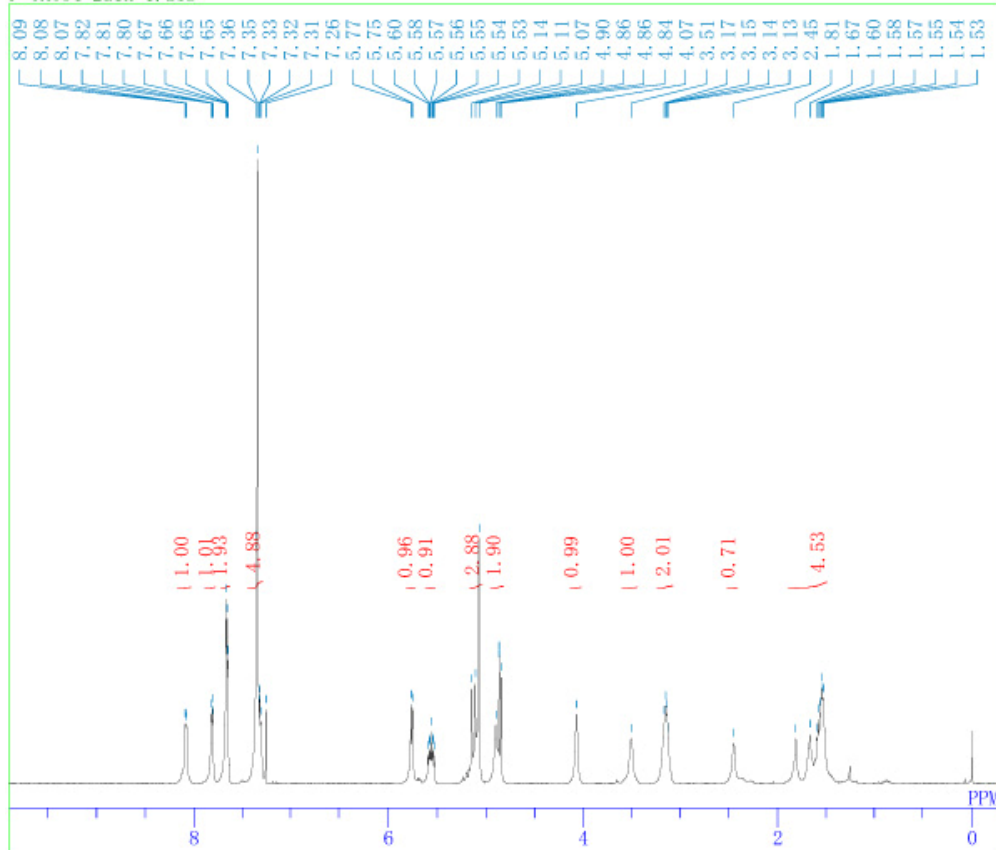


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 BF 0.12 Hz
 RGAIN 58

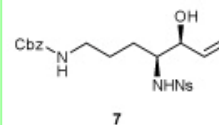


7

F:\A054-2a1h-1.als

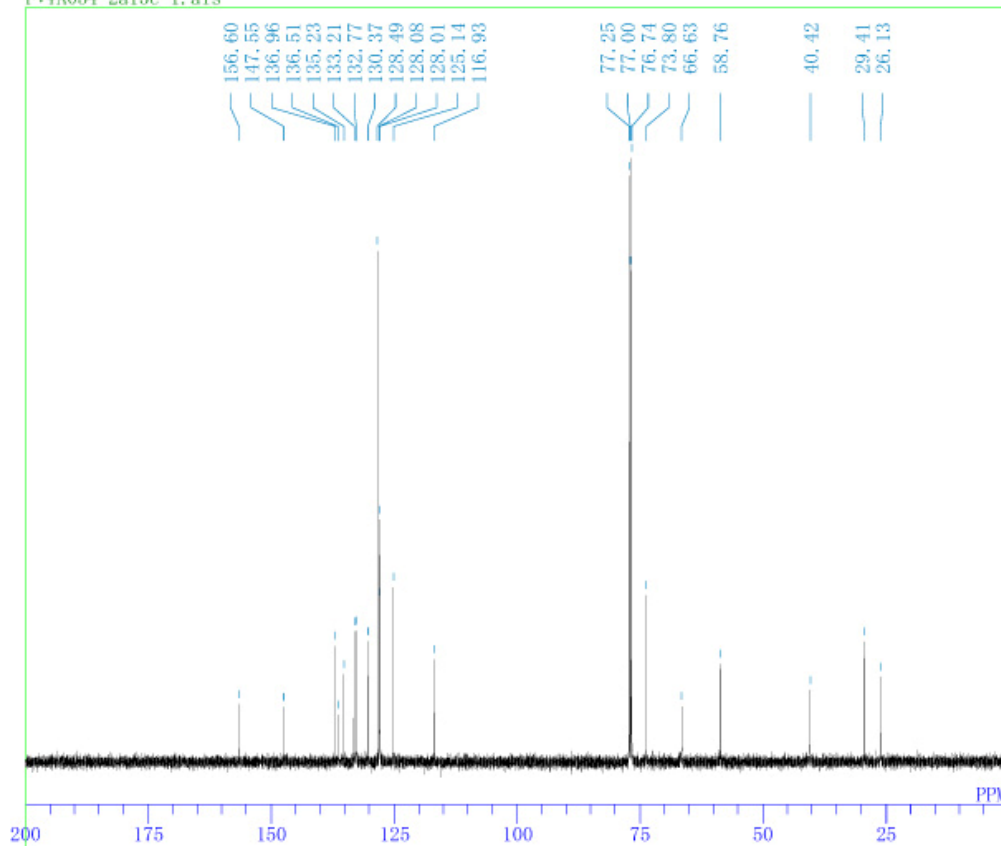


DFILE A054-2a1h-1.als
COMNT 7
DATIM 12-06-2008 14:27:28
OBNUC 1H
EXMOD single_pulse_ex2
OBFREQ 500.16 MHz
OBSET 2.41 KHz
OBFIN 6.01 Hz
POINT 13107
FREQU 7507.39 Hz
SCANS 32
ACQTM 1.7459 sec
PD 5.0000 sec
PW1 6.05 usec
IRNUC 1H
CTEMP 26.4 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 0.12 Hz
RGAIN 40

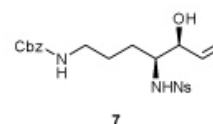


7

F:\A054-2a13c-1.als

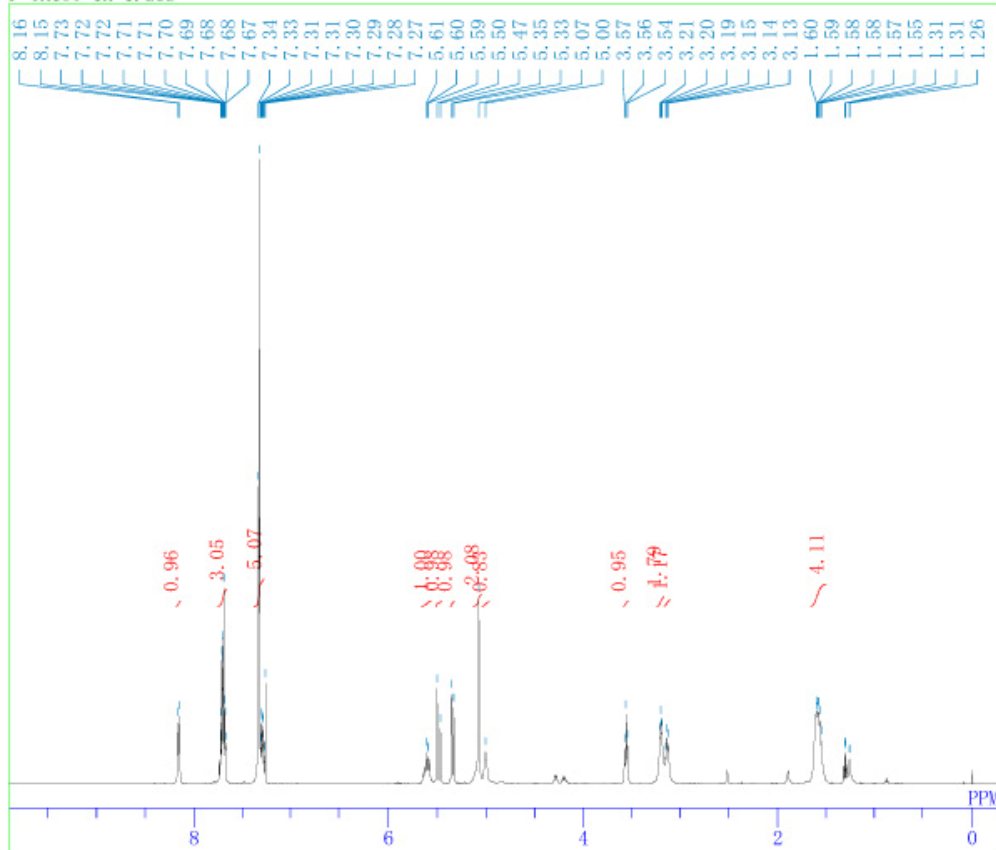


DFILE A054-2a13c-1.als
COMNT 7
DATIM 12-06-2008 15:13:17
OBNUC 13C
EXMOD single_pulse_dec
OBFREQ 125.77 MHz
OBSET 7.87 KHz
OBFIN 4.21 Hz
POINT 26214
FREQU 31446.06 Hz
SCANS 800
ACQTM 0.8336 sec
PD 2.0000 sec
PW1 3.83 usec
IRNUC 1H
CTEMP 26.7 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 0.12 Hz
RGAIN 60

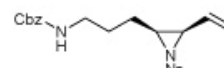


8

F:\A150-1H-1.als



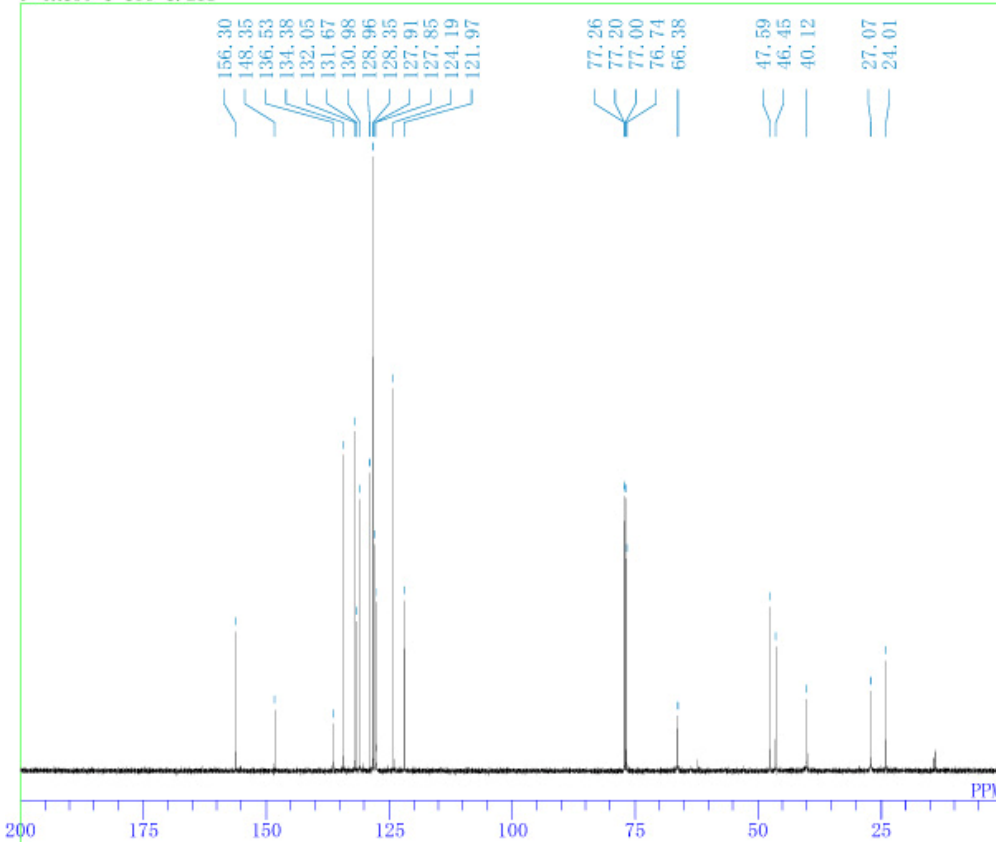
DFILE A150-1H-1.als
COMNT 8
DATIM 22-10-2008 09:13:19
OBNUC 1H
EXMOD single_pulse_ex2
OBFRQ 500.16 MHz
OBSET 2.41 KHz
OBFIN 6.01 Hz
POINT 13107
FREQU 7507.39 Hz
SCANS 16
ACQTM 1.7459 sec
PD 5.0000 sec
PW1 6.05 usec
IRNUC 1H
CTEMP 28.9 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 0.12 Hz
RGAIN 28



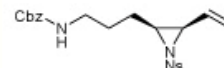
8

8

F:\A150-1 13c-1.als



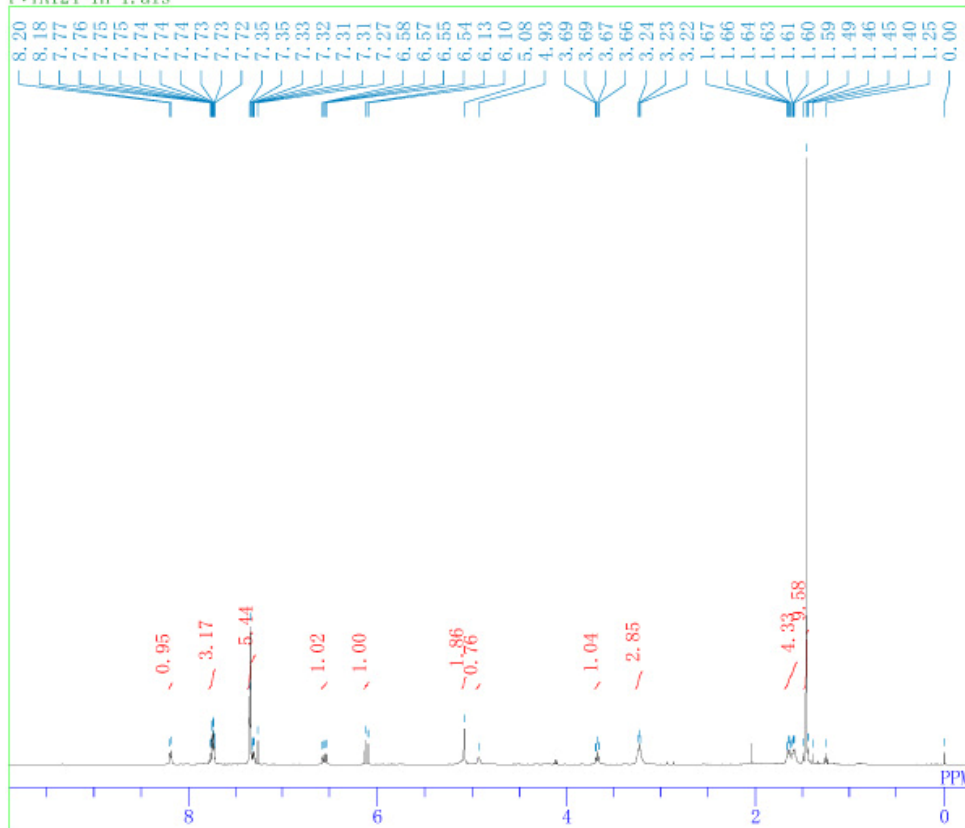
DFILE A150-1 13c-1.als
COMNT 8
DATIM 22-10-2008 09:47:51
OBNUC 13C
EXMOD single_pulse_dec
OBFRQ 125.77 MHz
OBSET 7.87 KHz
OBFIN 4.21 Hz
POINT 26214
FREQU 31446.06 Hz
SCANS 560
ACQTM 0.8336 sec
PD 2.0000 sec
PW1 3.83 usec
IRNUC 1H
CTEMP 29.4 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 0.12 Hz
RGAIN 60



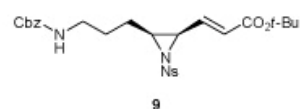
8

9

F:\A124-1H-1.als

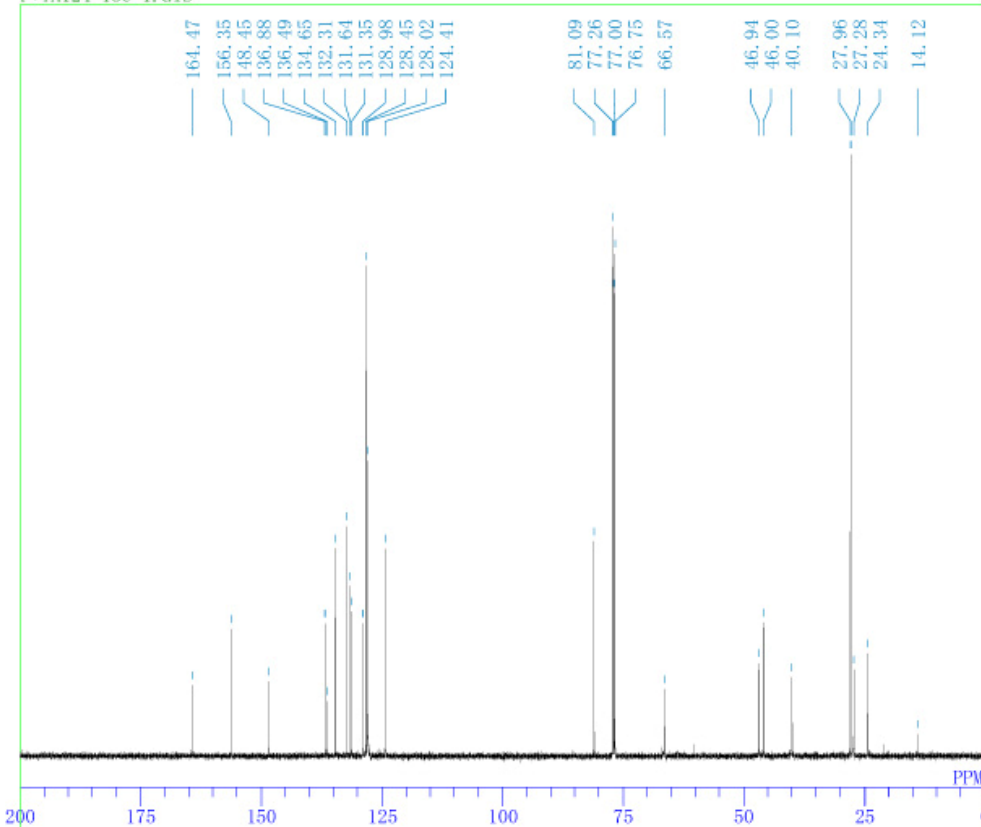


DFILE A124-1H-1.als
COMNT 9
DATIM 11-09-2008 08:49:29
OBNUC 1H
EXMOD single_pulse.ex2
OBFRQ 500.16 MHz
OBSET 2.41 KHz
OBFIN 6.01 Hz
POINT 13107
FREQU 7507.39 Hz
SCANS 32
ACQTM 1.7459 sec
PD 5.0000 sec
PW1 6.05 usec
IRNUC 1H
CTEMP 22.9 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 0.12 Hz
RGAIN 34

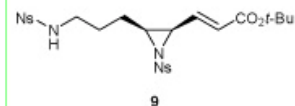


9

F:\A124-13C-1.als

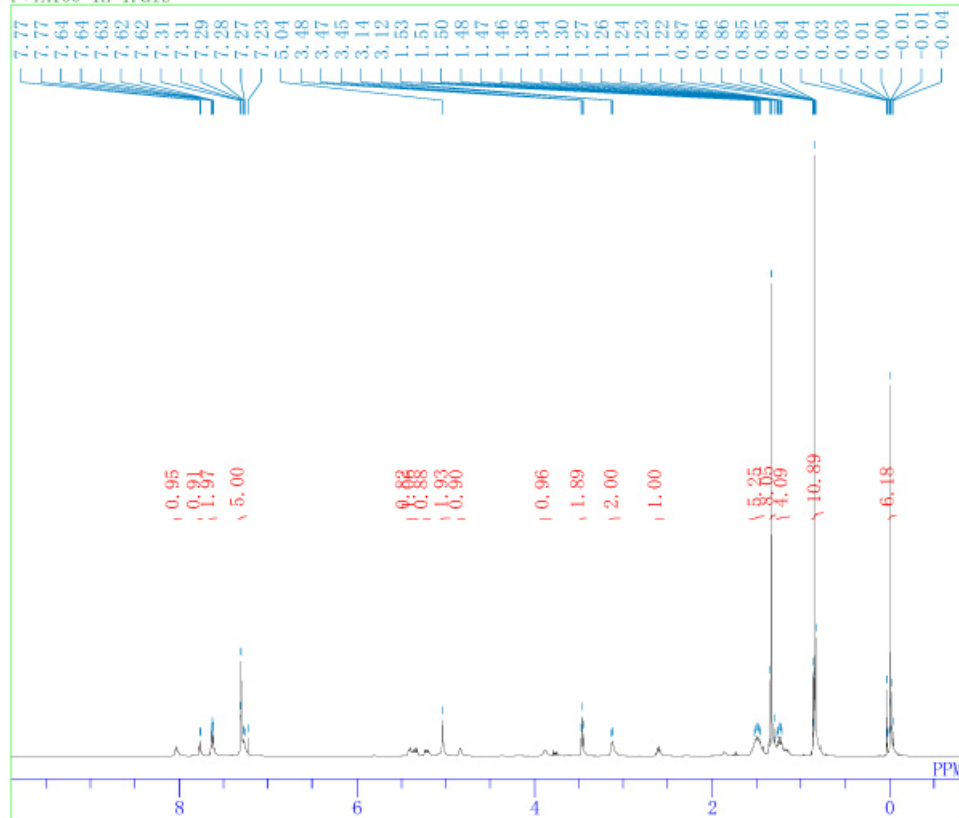


DFILE A124-13C-1.als
COMNT 9
DATIM 11-09-2008 10:07:27
OBNUC 13C
EXMOD single_pulse_dec
OBFRQ 125.77 MHz
OBSET 7.87 KHz
OBFIN 4.21 Hz
POINT 26214
FREQU 31446.06 Hz
SCANS 1480
ACQTM 0.8336 sec
PD 2.0000 sec
PW1 3.83 usec
IRNUC 1H
CTEMP 23.6 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 0.12 Hz
RGAIN 58

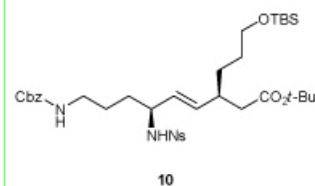


10

F:\A100-1b-1.als

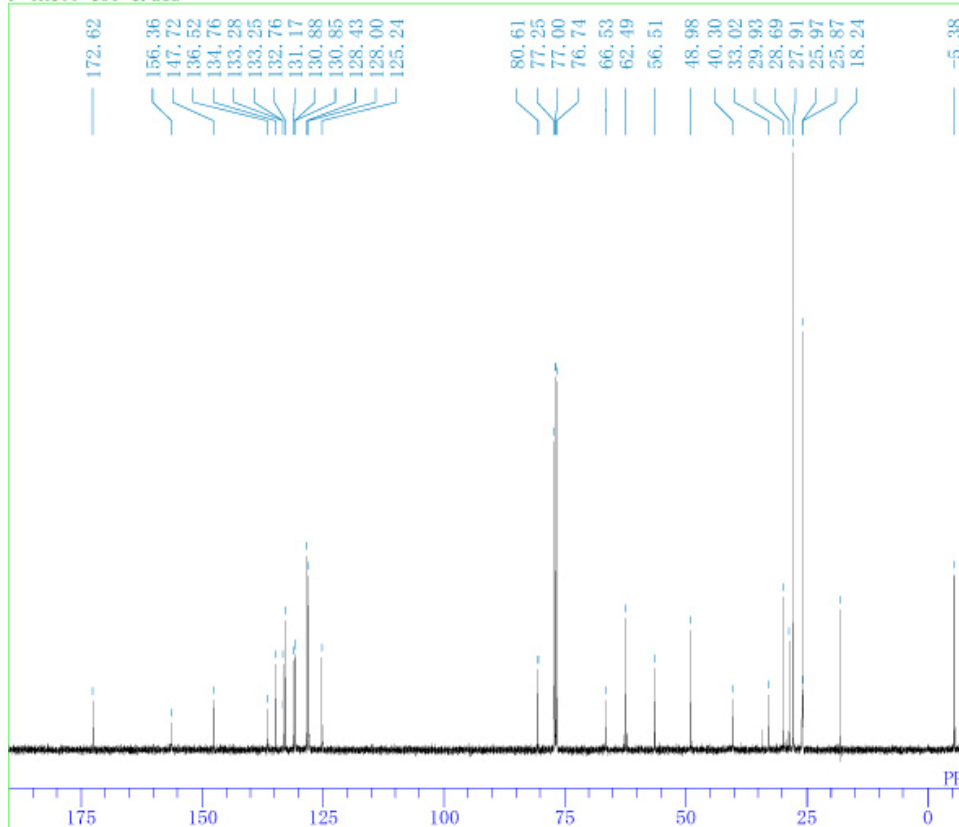


DFILE A100-1b-1.als
COMNT 10
DATIM 30-08-2008 12:29:39
OBNUC 1H
EXMOD single_pulse_ex2
OBFREQ 500.16 MHz
OBSET 2.41 KHz
OBFIN 6.01 Hz
POINT 13107
FREQU 7507.39 Hz
SCANS 16
ACQTM 1.7459 sec
PD 5.0000 sec
PW1 6.05 usec
IRNUC 1H
CTEMP 25.3 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 0.12 Hz
RGAIN 30

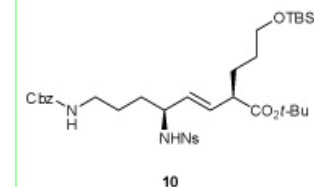


10

F:\A100-13c-1.als

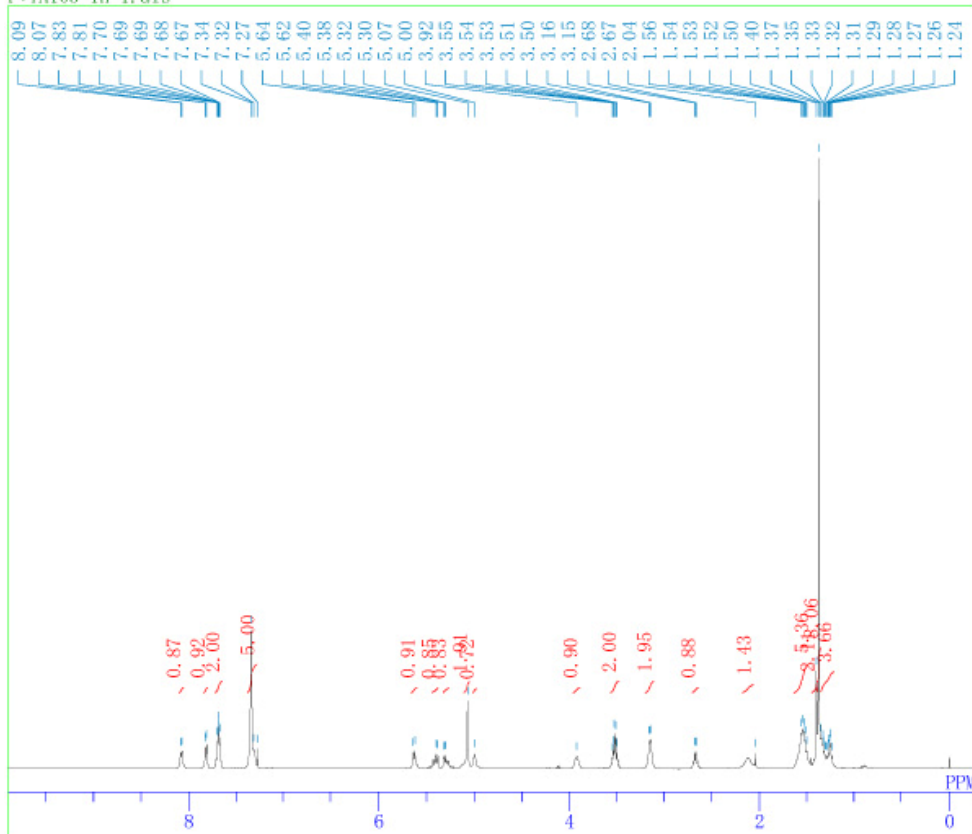


DFILE A100-13c-1.als
COMNT 10
DATIM 30-08-2008 13:15:31
OBNUC 13C
EXMOD single_pulse_dec
OBFREQ 125.77 MHz
OBSET 7.87 KHz
OBFIN 4.21 Hz
POINT 26214
FREQU 31446.06 Hz
SCANS 800
ACQTM 0.8336 sec
PD 2.0000 sec
PW1 3.83 usec
IRNUC 1H
CTEMP 25.6 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 0.12 Hz
RGAIN 60

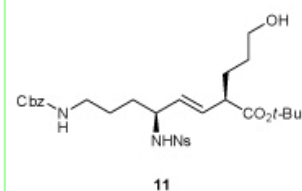


11

F:\A103-1h-1.als

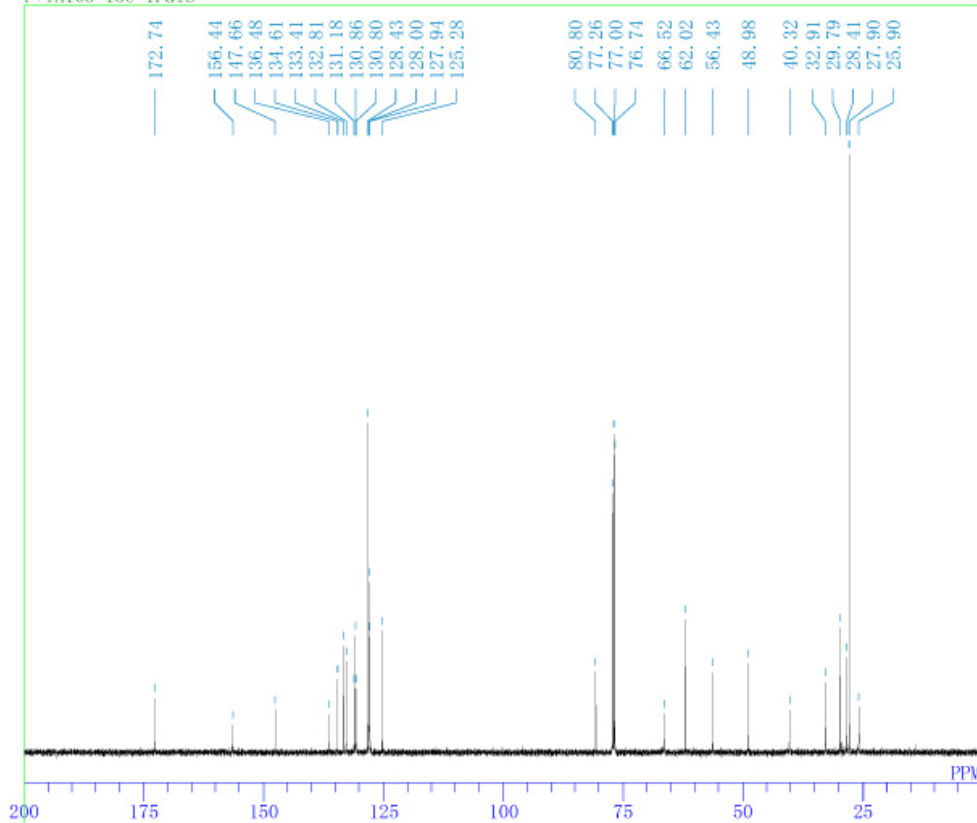


DFILE A103-1h-1.als
 COMNT 11
 DATIM 01-09-2008 09:23:56
 OBNUC 1H
 EXMOD single_pulse_ex2
 OBFREQ 500.16 MHz
 OBSET 2.41 KHz
 OBFIN 6.01 Hz
 POINT 13107
 FREQU 7507.39 Hz
 SCANS 16
 ACQTM 1.7459 sec
 PD 5.0000 sec
 PW1 6.05 usec
 IRNUC 1H
 CTEMP 25.1 c
 SLVNT CDCL3
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 32

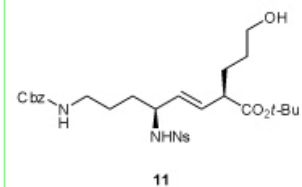


11

F:\A103-13c-1.als

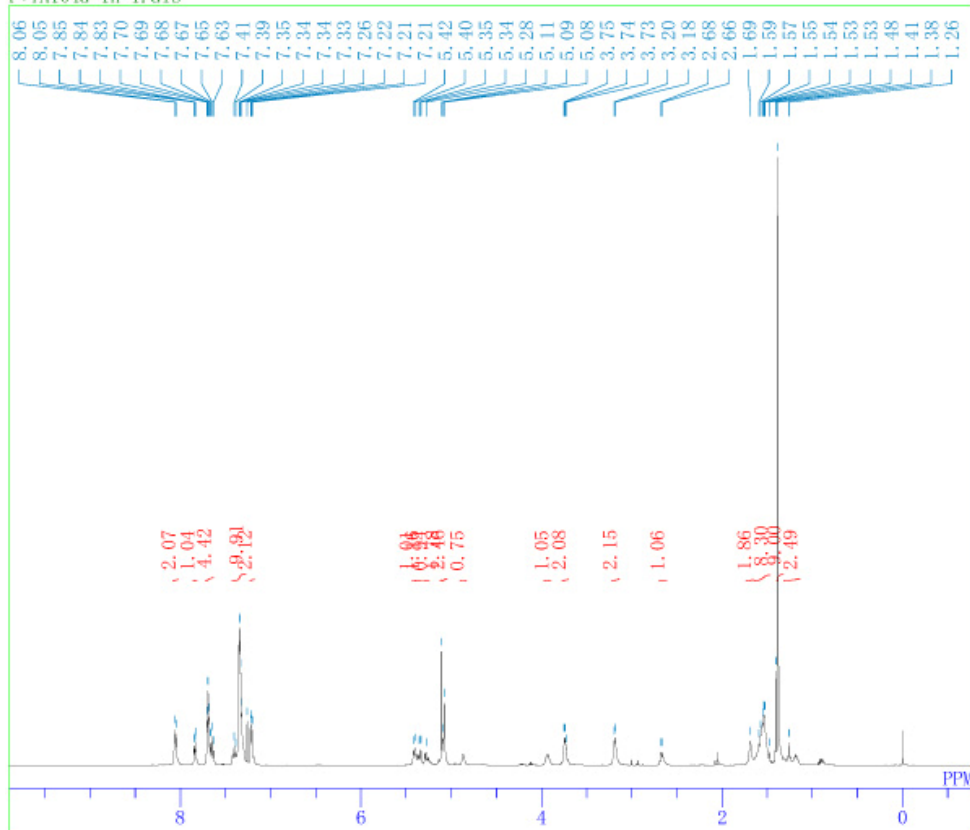


DFILE A103-13c-1.als
 COMNT 11
 DATIM 01-09-2008 10:05:06
 OBNUC 13C
 EXMOD single_pulse_dec
 OBFREQ 125.77 MHz
 OBSET 7.87 KHz
 OBFIN 4.21 Hz
 POINT 26214
 FREQU 31446.06 Hz
 SCANS 700
 ACQTM 0.8336 sec
 PD 2.0000 sec
 PW1 3.83 usec
 IRNUC 1H
 CTEMP 25.4 c
 SLVNT CDCL3
 EXREF 77.00 ppm
 BF 0.12 Hz
 RGAIN 58

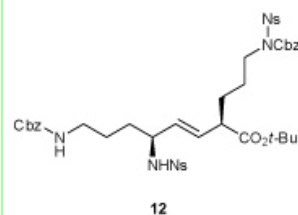


12

F:\A104a-1h-1.als

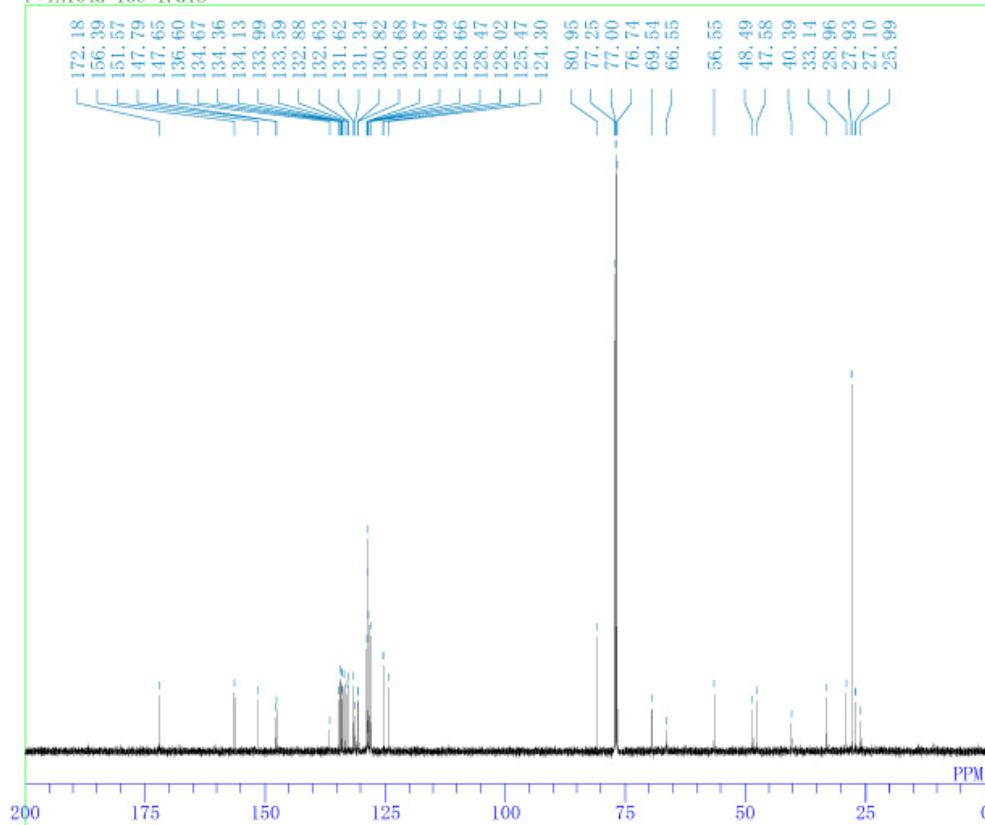


DFILE A104a-1h-1.als
COMNT 12
DATIM 06-09-2008 10:10:23
OBNUC 1H
EXMOD single_pulse_ex2
OBFRQ 500.16 MHz
OBSET 2.41 KHz
OBFIN 6.01 Hz
POINT 13107
FREQU 7507.39 Hz
SCANS 32
ACQTM 1.7459 sec
PD 5.0000 sec
PW1 6.05 usec
IRNUC 1H
CTEMP 25.3 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 0.12 Hz
RGAIN 40

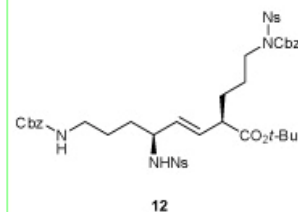


12

F:\A104a-13c-1.als

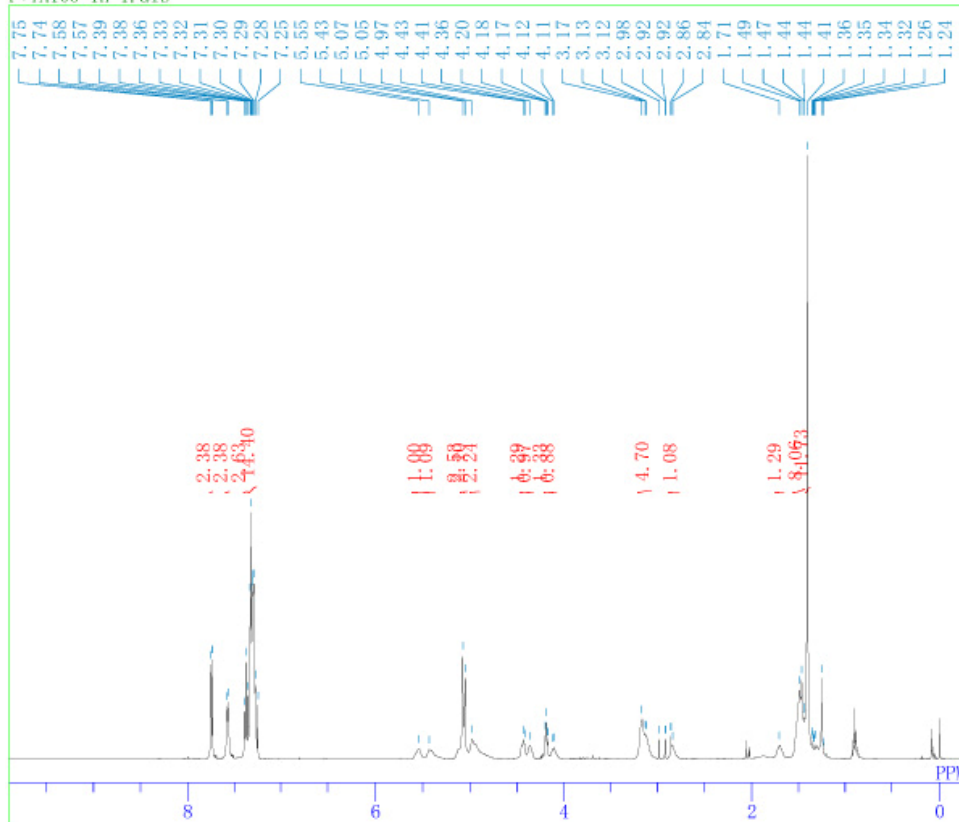


DFILE A104a-13c-1.als
COMNT 12
DATIM 06-09-2008 11:29:19
OBNUC 13C
EXMOD single_pulse_dec
OBFRQ 125.77 MHz
OBSET 7.87 KHz
OBFIN 4.21 Hz
POINT 26214
FREQU 31446.06 Hz
SCANS 1500
ACQTM 0.8336 sec
PD 2.0000 sec
PW1 3.83 usec
IRNUC 1H
CTEMP 25.6 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 0.12 Hz
RGAIN 60

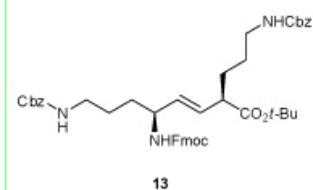


13

F:\A106-1b-1. als

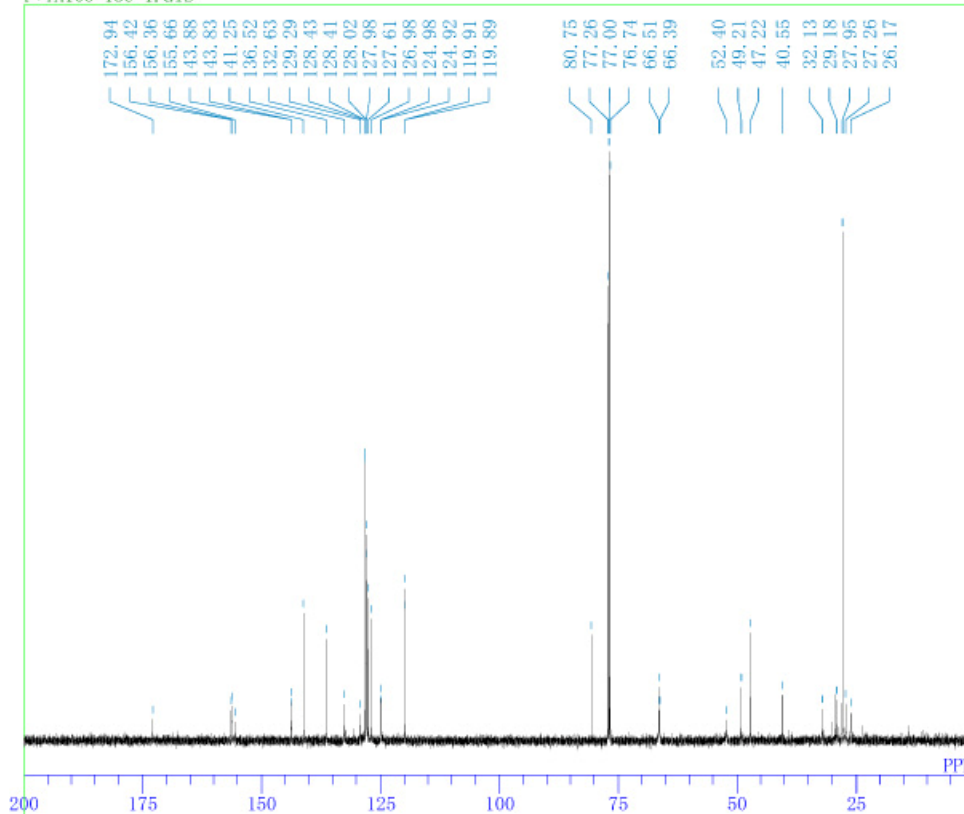


D1FILE A106-1b-1. als
COMNT 13
DATIM 21-08-2008 21:44:01
OBNUC 1H
EXMOD single_pulse.ex2
OBFREQ 500.16 MHz
OBSET 2.41 KHz
OBFIN 6.01 Hz
POINT 13107
FREQU 7507.39 Hz
SCANS 8
ACQTM 1.7459 sec
PD 5.0000 sec
PW1 6.05 usec
IRNUC 1H
CTEMP 22.7 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 0.12 Hz
RGAIN 34

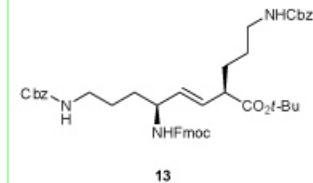


13

F:\A106-13c-1. als

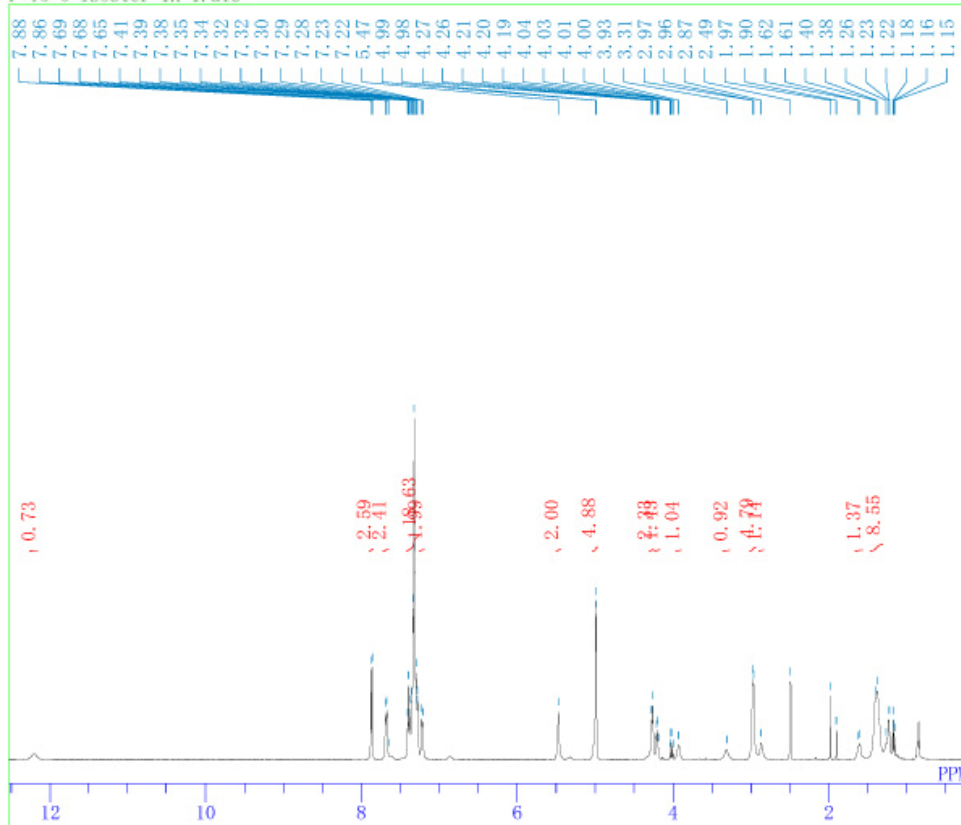


D1FILE A106-13c-1. als
COMNT 13
DATIM 21-08-2008 22:27:60
OBNUC 13C
EXMOD single_pulse_dec
OBFREQ 125.77 MHz
OBSET 7.87 KHz
OBFIN 4.21 Hz
POINT 26214
FREQU 31446.06 Hz
SCANS 760
ACQTM 0.8336 sec
PD 2.0000 sec
PW1 3.83 usec
IRNUC 1H
CTEMP 22.8 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 0.12 Hz
RGAIN 56

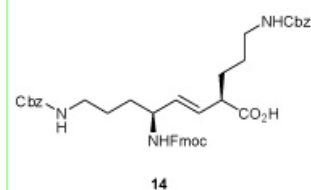


14

F:\0-0 isoster 1H-1.als

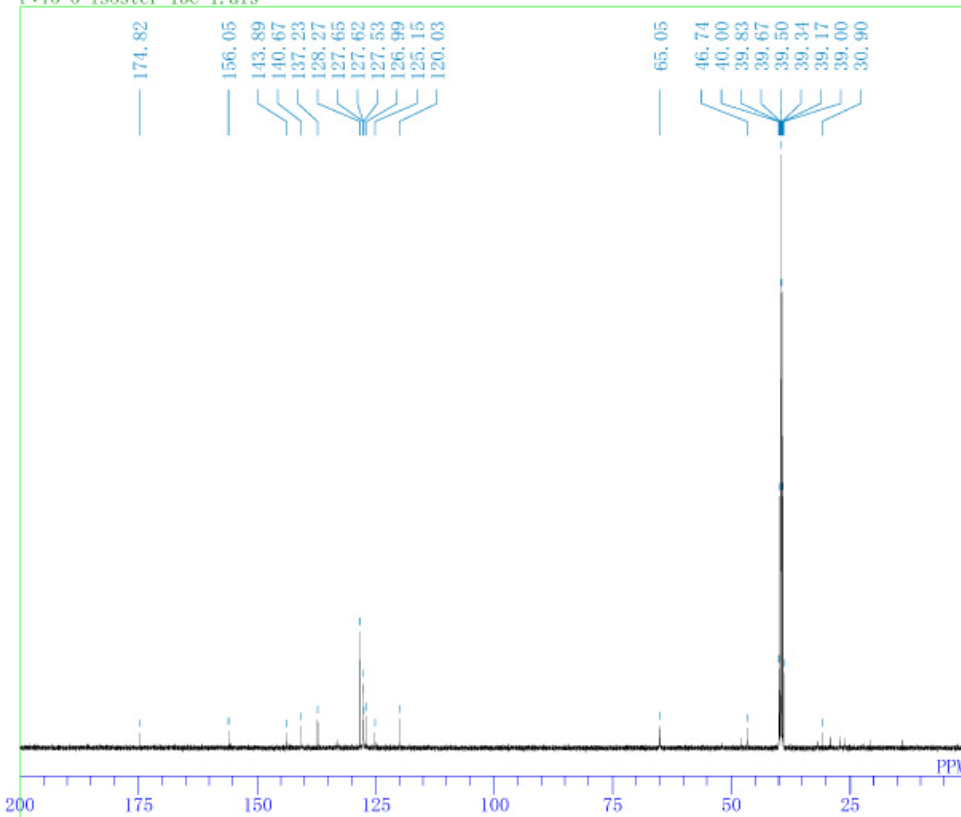


DFILE 0-0 isoster 1H-1.als
 COMNT 14
 DATIM 07-10-2008 18:39:10
 OBNUC 1H
 EXMOD single_pulse.ex2
 OBFREQ 500.16 MHz
 OBSSET 2.41 KHz
 OBFIN 6.01 Hz
 POINT 13107
 FREQU 7507.39 Hz
 SCANS 16
 ACQTM 1.7459 sec
 PD 5.0000 sec
 PW1 6.05 usec
 IRNUC 1H
 CTEMP 28.0 c
 SLVNT DMSO
 EXREF 2.49 ppm
 BF 0.12 Hz
 RGAIN 40

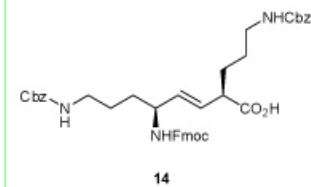


14

F:\0-0 isoster 13C-1.als

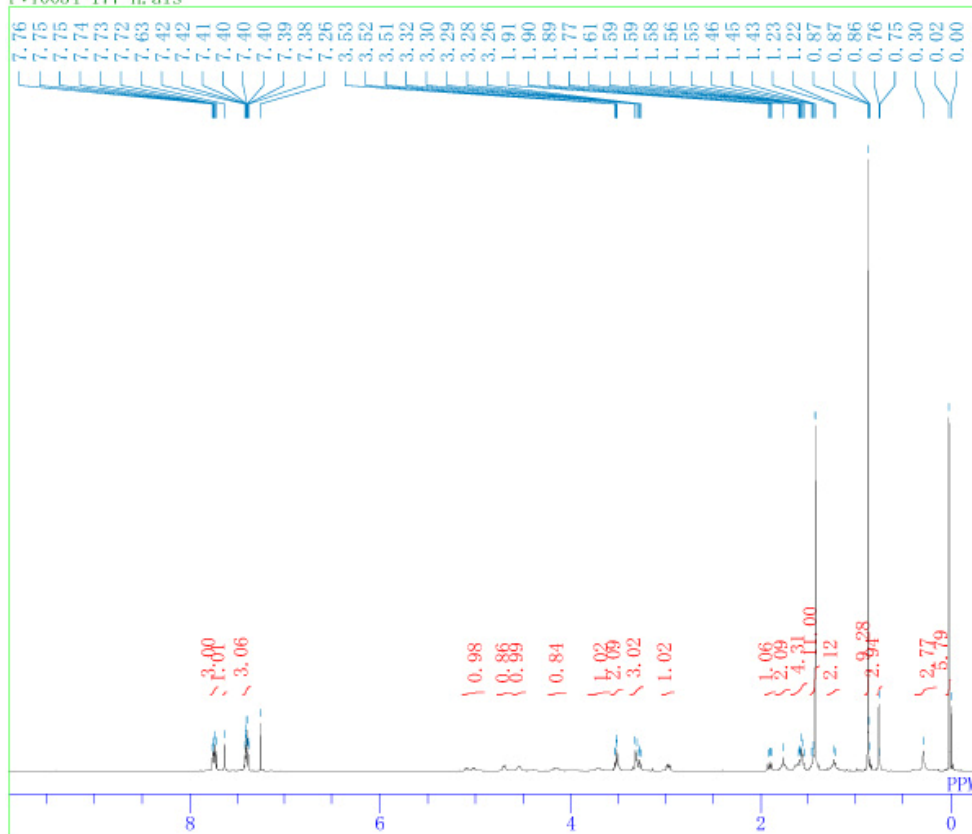


DFILE 0-0 isoster 13C-1.als
 COMNT 14
 DATIM 07-10-2008 19:23:00
 OBNUC 13C
 EXMOD single_pulse_dec
 OBFREQ 125.77 MHz
 OBSSET 7.87 KHz
 OBFIN 4.21 Hz
 POINT 26214
 FREQU 31446.06 Hz
 SCANS 760
 ACQTM 0.8336 sec
 PD 2.0000 sec
 PW1 3.83 usec
 IRNUC 1H
 CTEMP 28.3 c
 SLVNT DMSO
 EXREF 39.50 ppm
 BF 0.12 Hz
 RGAIN 60

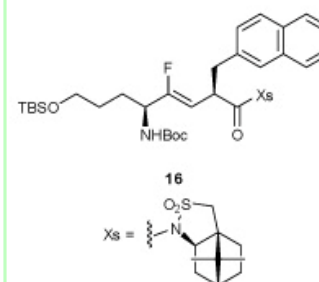


16

F:\0034-177-H.als

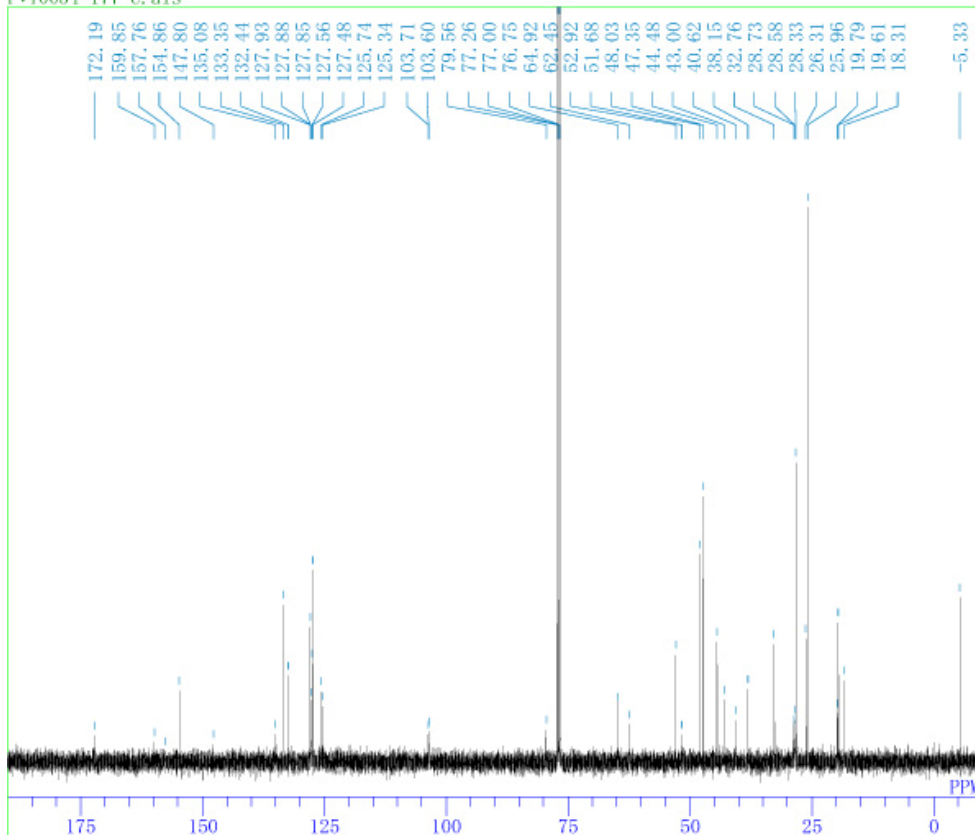


DFILE 0034-177-H.als
COMNT 16
DATIM 29-12-2008 12:30:11
OBNUC 1H
EXMOD single_pulse.ex2
OBFRQ 500.16 MHz
OBSET 2.41 KHz
OBFIN 6.01 Hz
POINT 13107
FREQU 7507.39 Hz
SCANS 32
ACQTM 1.7459 sec
PD 5.0000 sec
PW1 6.05 usec
IRNUC 1H
CTEMP 21.6 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 0.12 Hz
RGAIN 38

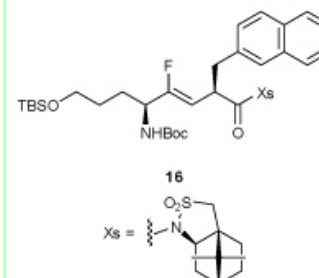


16

F:\0034-177-C.als

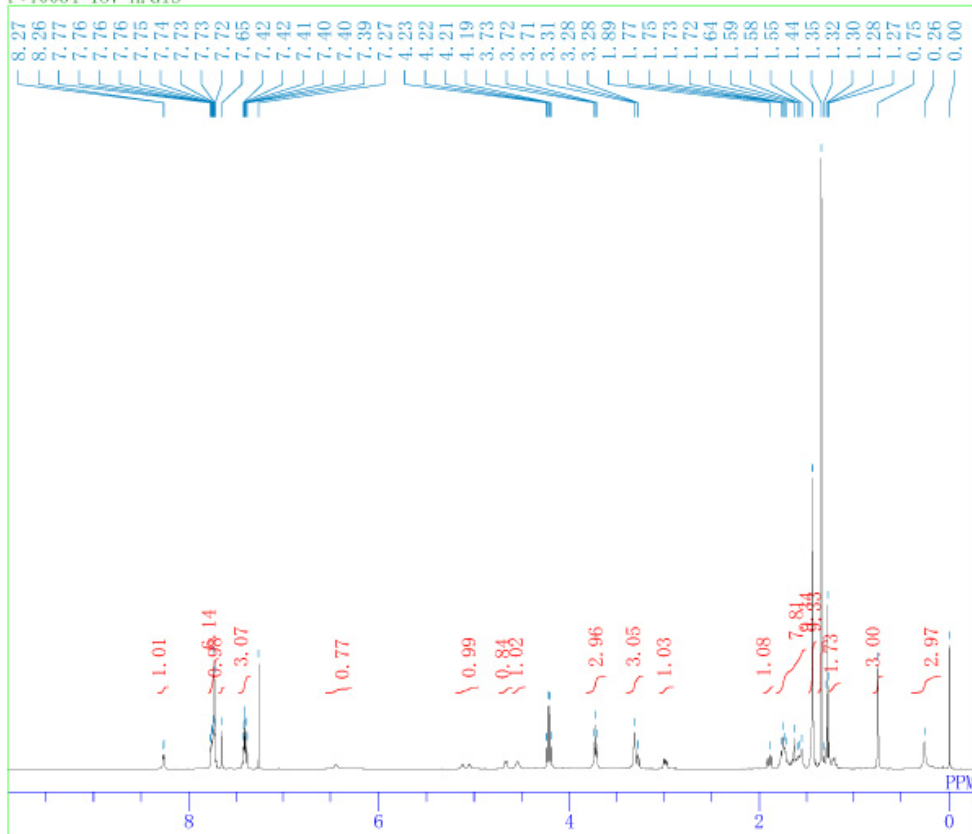


DFILE 0034-177-C.als
COMNT 16
DATIM 29-12-2008 13:02:27
OBNUC 13C
EXMOD single_pulse_dec
OBFRQ 125.77 MHz
OBSET 7.87 KHz
OBFIN 4.21 Hz
POINT 26214
FREQU 31446.06 Hz
SCANS 512
ACQTM 0.8336 sec
PD 2.0000 sec
PW1 3.83 usec
IRNUC 1H
CTEMP 22.0 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 0.12 Hz
RGAIN 58

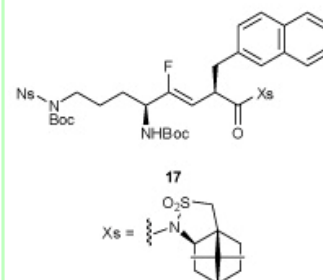


17

F:\0034-187-H.als

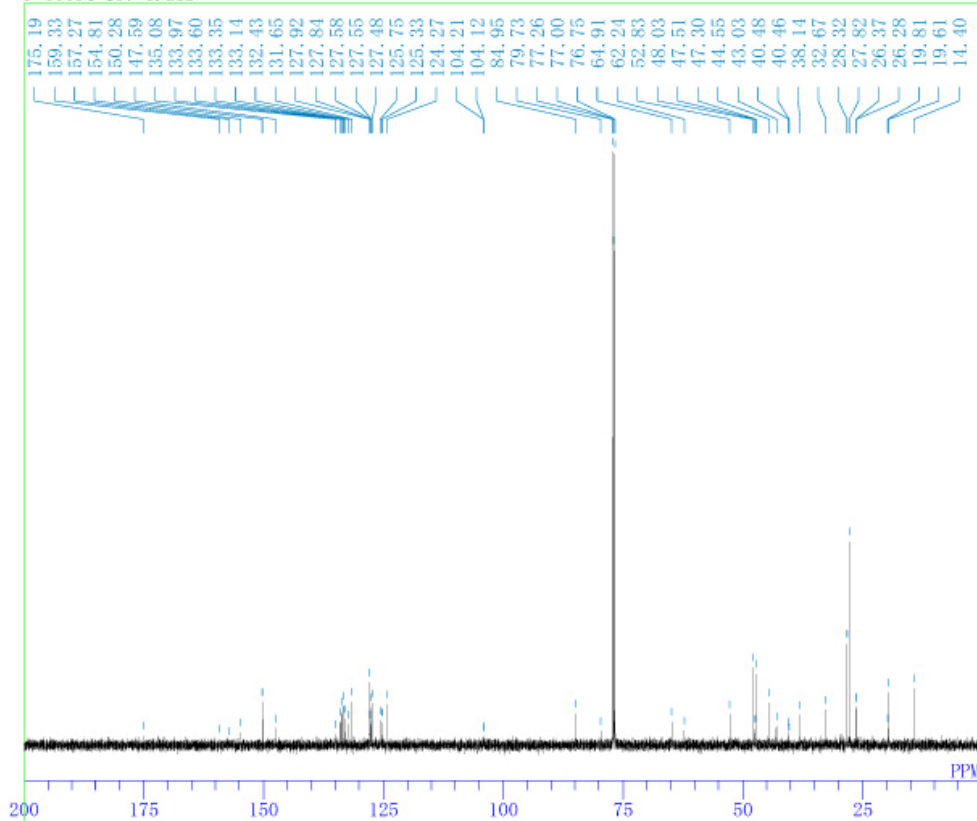


DFILE 0034-187-H.als
COMNT 17
DATIM 29-12-2008 14:31:12
OBNUC 1H
EXMOD single_pulse.ex2
OBFRQ 500.16 MHz
OBSET 2.41 KHz
OBFIN 6.01 Hz
POINT 13107
FREQU 7507.39 Hz
SCANS 32
ACQTM 1.7459 sec
PD 5.0000 sec
PW1 6.05 usec
IRNUC 1H
CTEMP 21.9 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 0.12 Hz
RGAIN 40

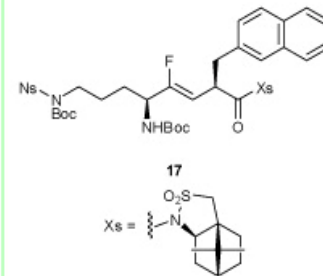


17

F:\0034-187-C.als

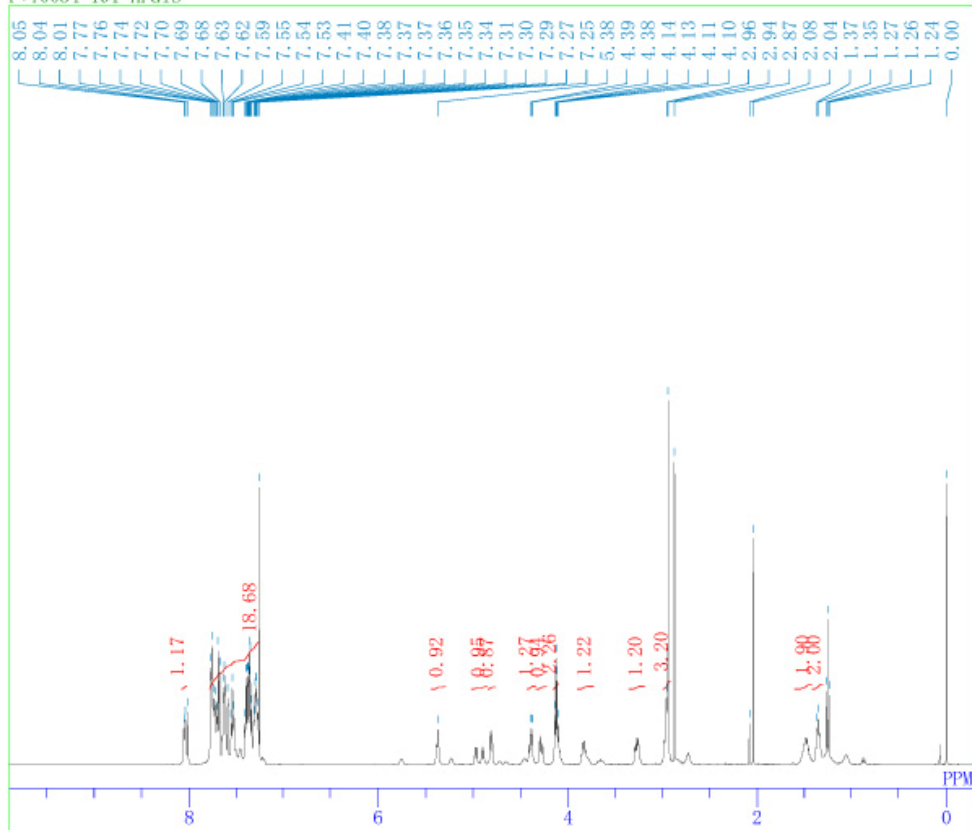


DFILE 0034-187-C.als
COMNT 17
DATIM 29-12-2008 15:03:30
OBNUC 13C
EXMOD single_pulse_dec
OBFRQ 125.77 MHz
OBSET 7.87 KHz
OBFIN 4.21 Hz
POINT 26214
FREQU 31446.06 Hz
SCANS 512
ACQTM 0.8336 sec
PD 2.0000 sec
PW1 3.83 usec
IRNUC 1H
CTEMP 22.4 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 0.12 Hz
RGAIN 58

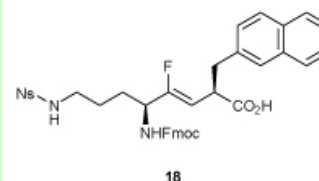


18

F:\0034-191-H.als

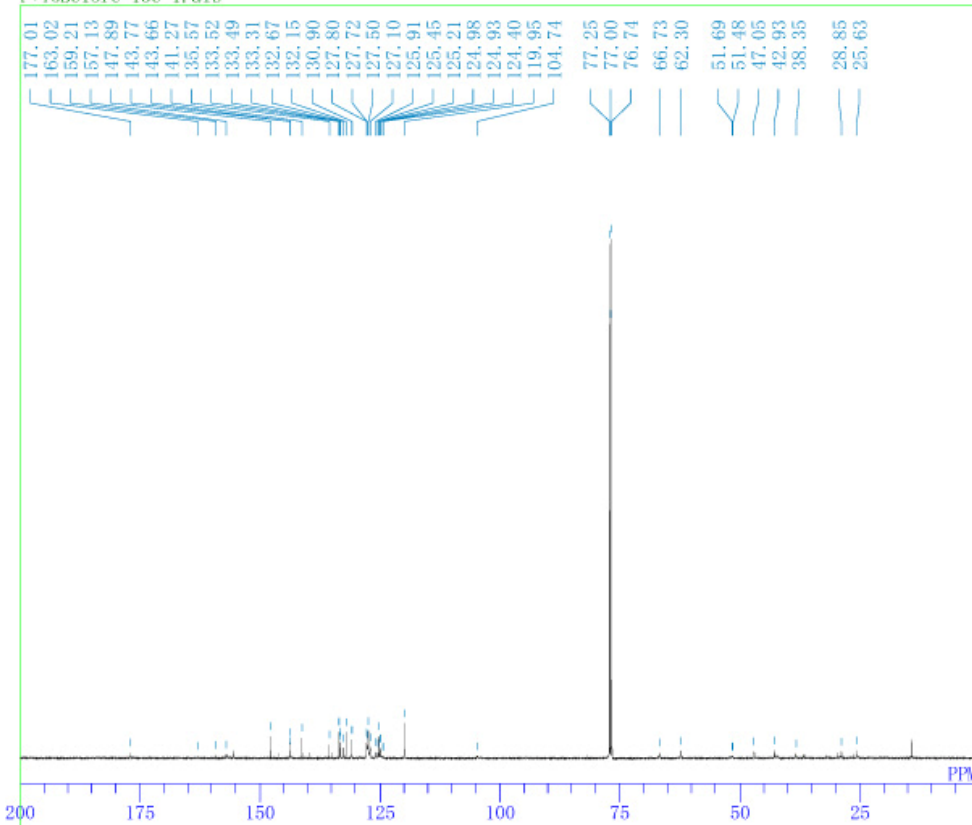


DFILE 0034-191-H.als
 COMNT 18
 DATIM 29-12-2008 16:32:44
 OBNUC 1H
 EXMOD single_pulse_ex2
 OBFREQ 500.16 MHz
 OBSET 2.41 KHz
 OBFIN 6.01 Hz
 POINT 13107
 FREQU 7507.39 Hz
 SCANS 32
 ACQTM 1.7459 sec
 PD 5.0000 sec
 PW1 6.05 usec
 IRNUC 1H
 CTEMP 22.3 c
 SLVNT CDCL3
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 40



18

F:\OBC18re-13C-1.als



DFILE OBC18re-13C-1.als
 COMNT 18
 DATIM 15-08-2009 08:31:27
 OBNUC 13C
 EXMOD single_pulse_dec
 OBFREQ 125.77 MHz
 OBSET 7.87 KHz
 OBFIN 4.21 Hz
 POINT 26214
 FREQU 31446.06 Hz
 SCANS 12000
 ACQTM 0.8336 sec
 PD 2.0000 sec
 PW1 3.50 usec
 IRNUC 1H
 CTEMP 26.5 c
 SLVNT CDCL3
 EXREF 77.00 ppm
 BF 0.12 Hz
 RGAIN 60

