Supplementary Material (ESI) for Chemical Communications

– Electronic Supplementary Information (ESI) –

(Experimental Procedures, Characterization Data, and Copies of ^{1}H and ^{13}C NMR Spectra)

Total Synthesis of Spiruchostatin B, a Potent Histone Deacetylase Inhibitor, from a Microorganism

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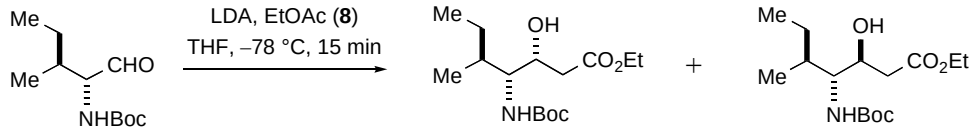
General Techniques.

All reactions involving air- and moisture-sensitive reagents were carried out using oven dried glassware and standard syringe-septum cap techniques. Routine monitorings of reaction were carried out using glass-supported Merck silica gel 60 F_{254} TLC plates. Flash column chromatography was performed on Kanto Chemical Silica Gel 60N (spherical, neutral 40–50 μm) with the solvents indicated.

All solvents and reagents were used as supplied with following exceptions. Tetrahydrofuran (THF) and Et_2O were freshly distilled from Na metal/benzophenone under argon. Toluene was distilled from Na metal under argon. *N*,*N*-Dimethylformamide (DMF), dimethyl sulfoxide (DMSO), CH_2Cl_2, MeCN, pyridine, *N*,*N*-diisopropylamine, and hexane were distilled from calcium hydride under argon.

Measurements of optical rotations were performed with a JASCO DIP-370 automatic digital polarimeter. Melting points were taken on a Yanaco MP-3 micro melting point apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were measured with a JEOL AL-400 (400 MHz) spectrometer. Chemical shifts were expressed in ppm using Me_4Si (δ=0) as an internal standard. The following abbreviations are used: singlet (s), doublet (d), triplet (t), quartet (q), sextet (sext), multiplet (m), and broad (br). Infrared (IR) spectral measurements were carried out with a JASCO FT/IR-4100 spectrometer. Low- and High-resolution mass (HRMS) spectra were measured on a JEOL JMS-DX 303/JMA-DA 5000 SYSTEM high resolution mass spectrometer.

(3*R*,4*R*,5*S*)-Ethyl 4-(*tert*-butoxycarbonylamino)-3-hydroxy-5-methylheptanoate (13) and its (3*S*,4*R*,5*S*)-isomer (14).



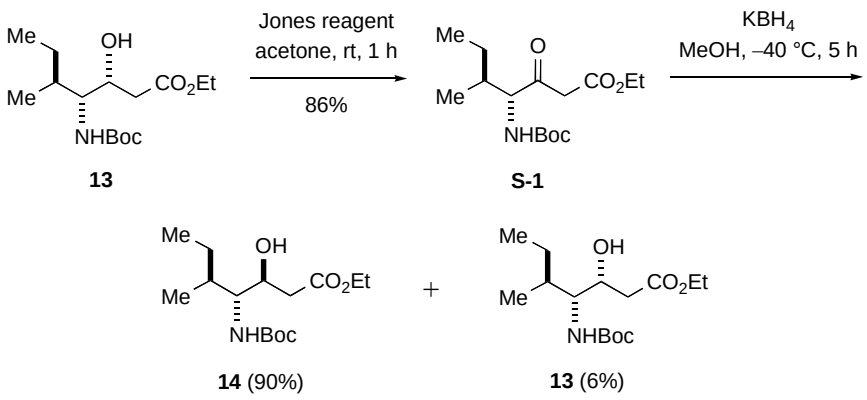
7 **13** (62%) **14** (31%)

A solution of EtOAc (**8**) (2.1 mL, 19 mmol) was added slowly to a stirred solution of lithium diisopropylamide (LDA) (19 mmol) [prepared from *n*-BuLi in hexane (1.6 M solution, 12.6 mL, 21 mmol) and *i*-Pr_2NH (2.74 mL, 19 mmol)] in dry THF (7 mL) at −78˚C. After 10 min, (2*R*,3*S*)-*N*-(*tert*-butoxycarbonyl)-D-allo-isoleucinal (**7**) (2.46 g, 11 mmol) in dry THF (10 mL) was added to the above mixture at −78˚C. After 15 min, the reaction was quenched with 2 M HCl (10 mL) at −78˚C, and the resulting mixture was extracted with Et_2O (2 x 40 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$ (2 x 20 mL) and brine (2 x 20 mL), then dried over Na_2SO_4. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane/EtOAc, 5:1□4:1) to **13** (3.57 g, 62%, less polar) and **14** (1.79 g, 31%, more polar).

13: colorless oil, $[\alpha]_D^{25}$ +26.9 (*c* 2.00, MeOH); IR (neat): 3447, 1734, 1686, 1076 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 0.91 (6H, t, *J* = 6.8 Hz), 1.16–1.22 (1H, m), 1.27 (3H, t, *J* = 7.3 Hz), 1.44 (9H, s), 1.48–1.73 (2H, m), 2.45 (1H, dd, *J* = 2.9, 16.5 Hz), 2.55 (1H, dd, *J* = 9.8, 16.5 Hz), 3.32 (2H, d, *J* = 3.4 Hz), 4.16 (2H, dd, *J* = 7.3, 14.1 Hz), 4.21–4.24 (1H, m), 4.87 (1H, d, *J* = 10.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.0, 14.1, 15.3, 26.2, 28.4 (3 C), 36.7, 39.2, 57.6, 60.8, 67.6, 79.1, 156.4, 173.5; HRMS (EI) calcd for $C_{15}H_{29}NO_5$ (M^+), 303.2046, found 303.2032.

14: colorless oil, $[\alpha]_D^{25}$ −6.4 (*c* 0.99, MeOH); IR (neat): 3451, 1714, 1695, 1073 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 0.86 (3H, d, *J* = 6.8 Hz), 0.92 (3H, t, *J* = 7.3 Hz), 1.21–1.46 (2H, m), 1.28 (3H, t, *J* = 7.3 Hz), 1.44 (9H, s), 1.91–1.98 (1H, m), 2.47 (1H, dd, *J* = 9.2, 17.5 Hz), 2.61 (1H, dd, *J* = 2.9, 16.5 Hz), 3.31 (1H, d, *J* = 4.9 Hz), 3.62–3.67 (1H, m), 3.88–3.94 (1H, m), 4.14–4.22 (2H, m), 4.43 (1H, d, *J* = 10.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.7, 13.2, 14.1, 27.1, 28.3 (3 C), 33.9, 38.6, 56.6, 60.7, 69.1, 79.4, 156.1, 173.4; HRMS (EI) calcd for $C_{15}H_{29}NO_5$ (M^+), 303.2046, found 303.2032.

Conversion of 13 to 14.

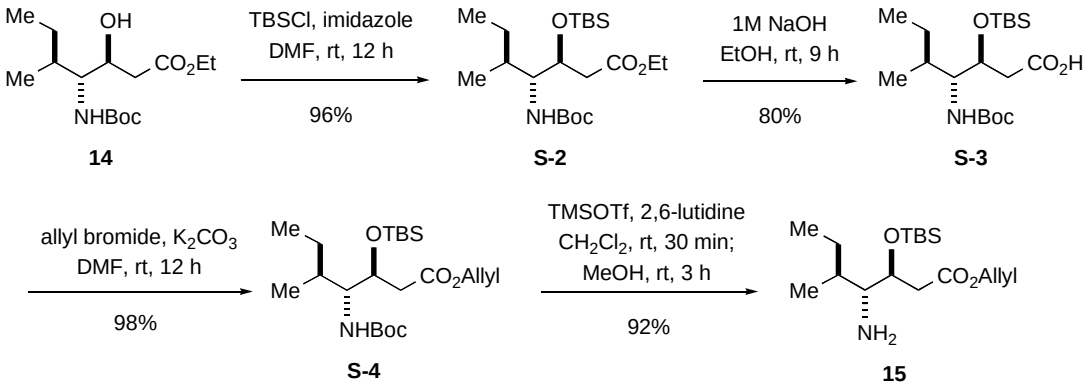


13 **S-1** **14** (90%) **13** (6%)

2.6 M Jones reagent (4.95 mL, 13 mmol) was added dropwise to a stirred solution of **13** (2.67 g, 8.8 mmol) in acetone (90 mL) at room temperature. After 1 h, the mixture was diluted with Et_2O (160 mL). The organic layer was washed with saturated aqueous $NaHCO_3$ (2 x 30 mL) and brine (2 x 30 mL), then dried over Na_2SO_4. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane/EtOAc, 10:1□8:1) to give **S-1** (2.28 g, 86%) as a colorless oil.

KBH_4 (1.84 g, 34 mmol) was added in small portions to a stirred solution of **S-1** (2.06 g, 6.8 mmol) in MeOH (70 mL) at −40°C. After 5 h, the reaction was quenched with 10% aqueous citric acid at 0°C (adjusted pH 3). After concentration of the solvent *in vacuo*, water (30 mL) was added, and the resulting mixture was extracted with CH_2Cl_2 (4 x 20 mL). The combined extracts were washed with brine (2 x 20 mL), then dried over Na_2SO_4. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane/EtOAc, 5:1□4:1) to give **14** (1.86 g, 90%) and **13** (124 mg, 6%). The IR, ^1H and ^{13}C NMR, mass spectra of these samples were identical with those recorded for **13** and **14**.

(3*S*,4*R*,5*S*)-Allyl 4-amino-3-(*tert*-butyldimethylsilyloxy)-5-methylheptanoate (15).



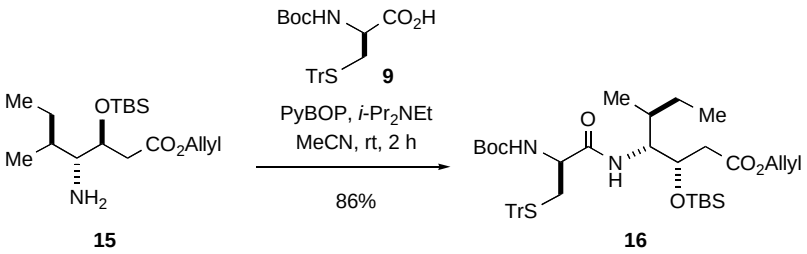
tert-Butyldimethylsilyl chloride (TBSCl) (2.76 g, 18 mmol) was added to stirred solution of **14** (1.86 g, 6.1 mmol) in dry DMF (50 mL) containing imidazole (2.50 g, 36 mmol) at room temperature. After 12 h, the reaction mixture was diluted with Et_2O (120 mL), and the organic layer was washed with brine (2 x 30 mL), then dried over Na_2SO_4. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane/EtOAc, 15:1□10:1) to give **S-2** (2.47 g, 96%) as a colorless oil.

1 M NaOH (30.0 mL, 30 mmol) was added dropwise to a stirred solution of **S-2** (2.47 g, 5.9 mmol) in EtOH (60 mL) at room temperature. After 9 h, the reaction was quenched 10% aqueous HCl (50 mL) at 0°C, and the resulting mixture was extracted with EtOAc (3 x 50 mL). The combined extracts were washed with brine (2 x 30 mL), then dried over Na_2SO_4. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane/EtOAc, 10:1□2:1) to give **S-3** (1.84 g, 80%) as a white amorphous solid.

Allyl bromide (0.79 mL, 9.5 mmol) was added to stirred solution of **S-3** (1.84 g, 4.7 mmol) in dry DMF (50 mL) containing K_2CO_3 (1.96 g, 14 mmol) at room temperature. After 12 h, the reaction was quenched with water (20 mL) at room temperature, and the resulting mixture was extracted with Et_2O (4 x 40 mL). The combined extracts were washed with saturated aqueous NH_4Cl (2 x 30 mL) and brine (2 x 30 mL), then dried over Na_2SO_4. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane/EtOAc, 10:1) to give **S-4** (1.99 g, 98%) as a pale yellow oil.

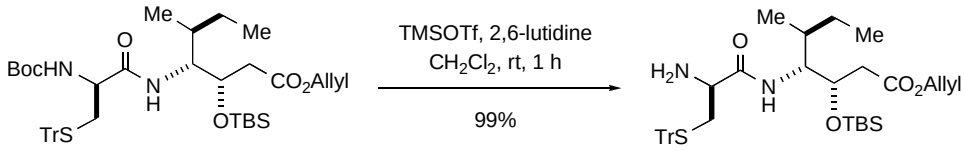
Trimethylsilyl trifluoromethanesulfonate (TMSOTf) (0.87 mL, 4.8 mmol) was added to a stirred solution of **S-4** (208 mg, 0.48 mmol) in dry CH_2Cl_2 (5 mL) in the presence of 2,6-lutidine (0.68 mL, 5.8 mmol) at room temperature. After 30 min, MeOH (1.0 mL) was added to the reaction mixture at 0°C. After stirring at room temperature for 3 h, the reaction mixture was concentrated *in vacuo* to afford a residue, which was purified by column chromatography (hexane–EtOAc, 3:1) to give **15** (145.4 mg, 92%) as a colorless oil. This material was immediately used for the next reaction due to its instability (prone to form a γ-lactam ring).

(3*S*,4*R*,5*S*)-Allyl 4-[(*S*)-2-(*tert*-butoxycarbonylamino)-3-(tritylthio)propanamido]-3-(*tert*-butyldimethylsilyloxy)-5-methylheptanoate (16).



N,*N*-Diisopropylethylamine (0.19 mL, 1.1 mmol) was added dropwise to a stirred solution of *N*-(*tert*-butoxycarbonyl)-*S*-trityl-D-cysteine (**9**)[9] (241 mg, 0.52 mmol) and **15** (159 mg, 0.43 mmol) in dry MeCN (5 mL) containing (benzotriazol-1-yloxy)tripyrrolidinophosphonium hexafluorophosphate (PyBOP) (293 mg, 0.56 mmol) at room temperature under argon. After 2 h, the mixture was diluted with Et_2O (60 mL), and the organic layer was washed with 3% aqueous HCl (2 x 20 mL), saturated aqueous $NaHCO_3$ (2 x 20 mL) and brine (2 x 20 mL), then dried over Na_2SO_4. Concentration of the solvent *in vacuo* to afford a residue, which was purified by column chromatography (hexane/EtOAc, 8:1) to give **16** (289 mg, 86%) as a colorless oil. $[\alpha]_D^{25}$ +5.7 (*c* 1.01, $CHCl_3$); IR (neat) : 1734, 1693, 1671, 1594, 776, 743 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 0.01 (3H, s), 0.06 (3H, s), 0.84 (9H, s), 0.81–0.86 (6H, m), 1.04–1.14 (1H, m), 1.18–1.26 (1H, m), 1.39 (9H, s), 1.77–1.82 (1H, m), 2.43 (1H, dd, *J* = 6.8, 16.1 Hz), 2.54 (2H, dd, *J* = 4.8, 16.1 Hz), 2.70 (1H, dd, *J* = 7.3, 12.6 Hz), 3.74 (1H, dd, *J* = 6.8, 13.1 Hz), 3.90–3.96 (1H, m), 4.12 (1H, dd, *J* = 6.8, 11.6 Hz), 4.50 (2H, ddd, *J* = 5.8, 13.1, 24.4 Hz), 4.67 (1H, br d, *J* = 6.8 Hz), 5.20 (1H, d, *J* = 10.2 Hz), 5.28 (1H, d, *J* = 17.1 Hz), 5.82–5.91 (1H, m), 6.07 (1H, br d, *J* = 9.3 Hz), 7.19–7.45 (15H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ −4.8, −4.5, 11.8, 13.5, 17.9 (2 C), 25.8 (3 C), 27.3, 28.3 (3 C), 32.9, 34.0, 40.3, 53.7, 55.8, 65.2, 67.1, 69.8, 80.3, 118.4, 126.8 (3 C), 128.0 (6 C), 129.6 (6 C), 132.0, 144.5 (2 C), 155.5, 170.5, 171.5; HRMS (FAB^+) calcd for $C_{44}H_{63}N_2O_6SSi$ (M^++1), 775.4176, found 775.4162.

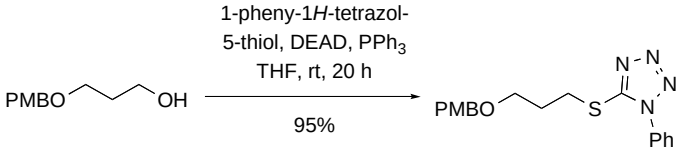
(3*S*,4*R*,5*S*)-Allyl 4-[(*S*)-2-amino-3-(tritylthio)propanamido]-3-(*tert*-butyldimethylsilyloxy)-5-methylheptanoate (5).



16 **5**

Trimethylsilyl trifluoromethanesulfonate (TMSOTf) (1.26 mL, 6.9 mmol) was added dropwise to a stirred solution of **16** (675 mg, 0.87 mmol) in CH_2Cl_2 (20 mL) containing 2,6-lutidine (1.01 mL, 8.7 mmol) at room temperature. After 1 h, MeOH (1.2 mL) was added to the reaction mixture at 0°C. After 1 h, the mixture was concentrated *in vacuo* to afford a residue, which was purified by column chromatography (hexane/EtOAc, 2:1→1:1) to give **5** (581 mg, 99%) as a white amorphous solid. $[\alpha]_D^{25}$ +1.87 (*c* 0.97, $CHCl_3$); IR (neat) : 1734, 1675, 1594, 1255, 777, 743 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 0.02 (3H, s), 0.05 (3H, s), 0.85 (9H, s), 0.79–0.88 (6H, m), 1.00–1.12 (1H, m), 1.16–1.26 (2H, m), 1.39 (2H, brs), 1.75–1.81 (1H, m), 2.43 (1H, dd, *J* = 5.8, 16.0 Hz), 2.49–2.57 (2H, m), 2.69 (1H, dd, *J* = 3.9, 12.1 Hz), 3.08 (1H, dd, *J* = 3.9, 8.1 Hz), 3.87–3.92 (1H, m), 4.13 (1H, dd, *J* = 5.8, 13.2 Hz), 4.51 (2H, d, *J* = 5.8 Hz), 5.24 (1H, d, *J* = 16.0 Hz), 5.29 (1H, d, *J* = 16.0 Hz), 5.83–5.93 (1H, m), 7.18–7.47 (15H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ −4.9, −4.5, 11.8, 13.8, 17.9, 25.8 (3 C), 27.5, 29.7, 34.1, 37.3, 40.6, 53.9, 55.6, 65.2, 66.9, 69.9, 118.4, 126.7 (3 C), 127.9 (6 C), 129.6 (6 C), 132.0, 144.6 (2 C), 171.5, 172.7; HRMS (FAB^+) calcd for $C_{39}H_{55}N_2O_4SSi$ (M^++1), 675.3652, found 675.3664.

5-[3-(4-Methoxybenzyloxy)propylthio]-1-phenyl-1*H*-tetrazole (18).

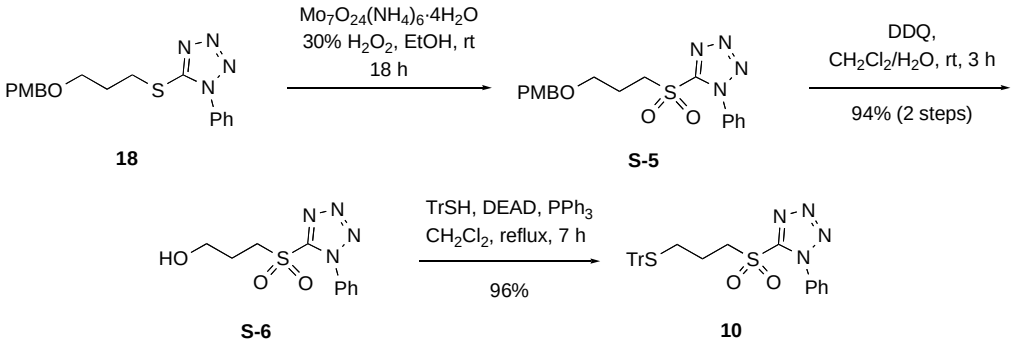


17 **18**

Diethyl azodicarboxylate (DEAD) in THF (2.2M in solution, 23.4 mL, 52 mmol) was added dropwise to a stirred solution of 3-(4-methoxybenzyloxy)propan-1-ol (**17**) (9.18 g, 47 mmol) in dry THF (500 mL) containing Ph_3P (13.5 g, 52 mmol) and 1-phenyl-1*H*-tetrazol-5-thiol (9.17 g, 52 mmol) at room temperature under argon. After 5 h, the reaction mixture was concentrated *in vacuo* to afford a residue, which was purified by column chromatography (hexane/EtOAc, 2:1) to give **18** (15.8 g, 95%) as a white amorphous solid. IR (neat): 2857, 2546, 2347, 1596, 761, 694, 636 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.13 (2H, ddd, *J* = 5.8, 6.9, 13.2 Hz), 3.49 (2H, t, *J* = 6.9 Hz), 3.58 (2H, t, *J* = 5.8 Hz), 3.79 (3H, s), 4.43 (2H, s), 6.85–6.88 (2H, m), 7.23–7.26 (2H, m), 7.52–7.59 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ

29.2, 30.3, 55.2, 67.6, 72.6, 77.2, 113.8, 123.8, 129.3 (3 C), 129.7 (2 C), 130.0, 130.2, 133.7, 154.3, 159.2; HRMS (EI) calcd for $C_{18}H_{20}N_4O_2S$ (M), 356.1307, found 356.1320.

1-Phenyl-5-[3-(tritylthio)propylsulfonyl]-1*H*-tetrazole (10).

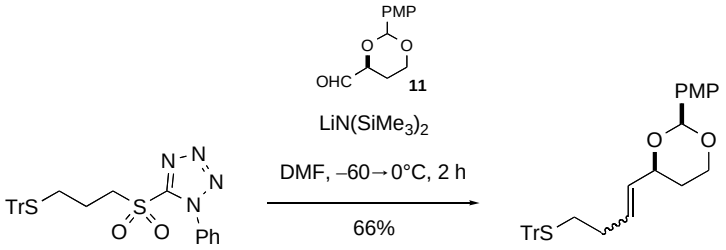


Hexaammonium heptamolybdate tetrahydrate [$Mo_7O_{24}(NH_4)_6{\cdot}4H_2O$] (1.08 g, 0.9 mmol) in 30% aqueous H_2O_2 (9.38 mL, 83 mmol)] was added dropwise to a stirred solution of **18** (3.10 g, 8.7 mmol) in EtOH (90 mL) at 0°C, and the mixture was allowed to warm up to room temperature. After 18 h, the reaction was quenched with water (20 mL) at room temperature, and the resulting mixture was extracted with EtOAc (3 x 40 mL). The organic layer was washed with saturated aqueous $Na_2S_2O_3$ (2 x 20 mL) and brine (2 x 20 mL), then dried over $MgSO_4$. Concentration of the solvent *in vacuo* afforded a residue, which was purified by short-pass column chromatography (hexane/EtOAc, 3:1) to give **S-5** (3.30 g), which was used for the next reaction without further purification.

2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (3.51 g, 16 mmol) was added in small portions to a stirred solution of **S-5** (3.30 g, 7.8 mmol) in CH_2Cl_2/H_2O (9:1, 150 mL) at room temperature under argon. After 3 h, the mixture was diluted with CH_2Cl_2 (50 mL), and the organic layer was washed with saturated aqueous $NaHCO_3$ (2 x 40 mL) and brine (2 x 40 mL), then dried over Na_2SO_4. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane/EtOAc, 2:1) to give **S-6** (655 mg, 94%, two steps) as a colorless oil.

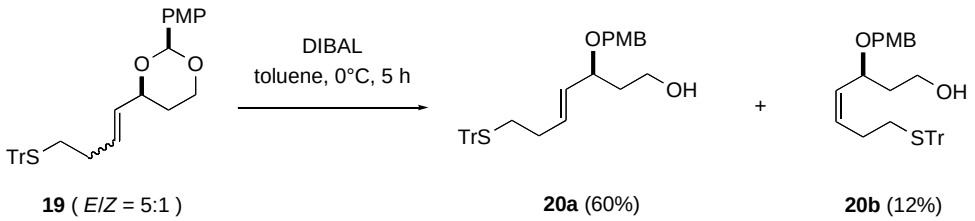
Diethyl azodicarboxylate (DEAD) in toluene (2.2 M in solution, 0.68 mL, 1.5 mmol) was added dropwise to a stirred solution of **S-6** (200 mg, 0.75 mmol) in dry CH_2Cl_2 (10 mL) containing Ph_3P (391 mg, 1.5 mmol) and triphenylmethyl thiol (412 mg, 1.5 mmol) at room temperature under argon. The mixture was heated at reflux for 7 h under argon. After cooling, the reaction mixture was concentrated *in vacuo* to afford a residue, which was purified by column chromatography (hexane/EtOAc, 6:1) to give **10** (377 mg, 96%) as a white solid. Recrystallization from hexane/AcOEt afforded white needles, mp 117–119 ºC. IR (neat): 2360, 1593, 1339, 761, 744, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.82–1.89 (2H, m), 2.39 (2H, t, J = 6.8 Hz), 3.56 (2H, dd, J = 5.4, 10.2 Hz), 7.18–7.65 (20H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.5, 30.0, 54.9, 67.2, 77.2, 125.1, 126.9 (3 C), 128.0 (8 C), 129.5 (4 C), 129.7 (2 C), 131.4, 132.9, 144.4 (3 C), 153.3; HRMS (FAB^+) calcd for $C_{29}H_{27}N_4O_2S_2$ (M^++1), 527.1575, found 527.1578.

(2*S*,4*S*)-2-(4-Methoxyphenyl)-4-[(*E*/*Z*)-4-(tritylthio)but-1-enyl]-1,3-dioxane (19).



Lithium bis(trimethylsilyl)amide in THF (1.0 M solution, 8.9 mL, 8.9 mmol) was added dropwise to a stirred solution of **10** (4.26 g, 8.1 mmol) and (4*S*)-2-(4-methoxyphenyl)-1,3-dioxane-4-carbaldehyde (**11**) (2.68 g, 12 mmol) in dry DMF (200 mL) at −60°C under argon. After 2 h, the mixture was gradually warmed up to 0°C over 2 h. The reaction was quenched with saturated aqueous NH_4Cl (20 mL) at 0°C . The resulting mixture was extracted with Et_2O (3 x 150 mL), and the combined extracts were washed with brine (2 x 100 mL), then dried over Na_2SO_4. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane/EtOAc, 6:1) to give **19** (2.77 g, 66%) as an olefinic isomers (*E*/*Z* = 5:1) as a colorless oil. IR (neat) : 2955, 2849, 2025, 1954, 1615, 1372, 1302, 747, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.51 (1H, t, *J* = 12.1 Hz), 1.86 (1H, ddd, *J* = 5.3, 12.1, 24.4 Hz), 2.09 (2H, t, *J* = 6.8 Hz), 2.19 (2H, d, *J* = 6.8 Hz), 3.78 (3H, s), 3.93 (1H, dt, *J* = 2.4, 12.1 Hz), 4.21–4.26 (2H, m), 5.45–5.50 (1H, m), 5.61 (1H, t, *J* = 6.8 Hz), 6.85 (1H, dd, *J* = 1.9, 4.8 Hz), 7.17–7.44 (20H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.3, 31.4, 55.3, 66.5, 66.9, 77.1, 77.2, 101.2, 113.5, 113.6, 126.5, 126.6, 127.4, 127.8, 128.0 (7 C), 129.6 (6 C), 130.3, 131.1, 131.2, 144.9 (3 C), 159.9; HRMS (FAB$^+$) calcd for $C_{34}H_{35}O_3S$ (M^++1), 522.2229, found 523.2162.

(*S*,*E*)-3-(4-Methoxybenzyloxy)-7-(tritylthio)hept-4-en-1-ol (20a) and its (*S*,*Z*)-isomer (20b).



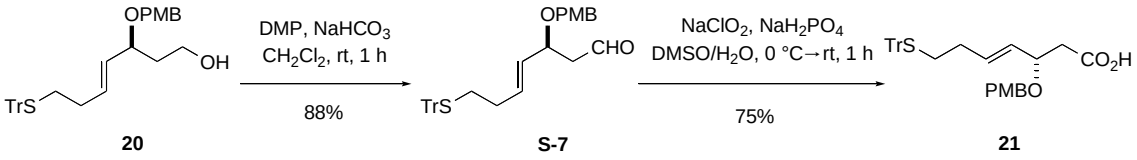
Diisobutylaluminum hydride (DIBAL) in toluene (1.0 M solution, 6.74 mL, 6.7 mmol) was added dropwise to a stirred solution of **19** (*E*/*Z* = 5:1) (1.53 g, 2.9 mmol) in dry toluene (40 mL) at 0°C under argon. After 5 h, the reaction mixture was quenched 10% aqueous NaOH (10 mL) at 0°C. The resulting mixture was extracted with Et_2O (3 x 60 mL), and the combined extracts were washed with brine (3 x 50 mL), then dried over Na_2SO_4. Concentration of the solvent

in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc, 3:1) to give **20a** (921 mg, 60%, more polar) and **20b** (184 mg, 12%, less polar).

20a: colorless oil, $[\alpha]_D^{25}$ −33.1 (*c* 1.02, $CHCl_3$); IR (neat) : 3418, 1666, 1612, 1034, 972, 767, 743, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.66–1.74 (1H, m), 1.78–1.86 (1H, m), 2.14 (2H, t, *J* = 6.8 Hz), 2.22 (2H, d, *J* = 6.8 Hz), 3.66–3.76 (2H, m), 3.79 (3H, s), 3.89 (1H, dt, *J* = 4.4, 8.2 Hz), 4.23 (1H, d, *J* = 11.2 Hz), 4.51 (1H, d, *J* = 11.2 Hz), 5.33 (1H, dd, *J* = 8.2, 15.5 Hz), 5.53 (1H, dd, *J* = 6.8, 13.6 Hz), 6.84 (1H, dd, *J* = 1.9, 6.8 Hz), 7.18–7.43 (19H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.2, 31.6, 37.9, 55.3, 60.8, 66.5, 69.6, 77.2, 79.1, 113.8 (2 C), 126.6, 127.8 (8 C), 129.4 (3 C), 129.6 (4 C), 130.3, 131.5, 132.2, 144.9 (3 C), 159.1; HRMS (FAB^+) calcd for $C_{34}H_{35}O_3S$ (M^+−1), 523.2307, found 523.2298.

20b: colorless oil, $[\alpha]_D^{25}$ −10.2 (*c* 0.94, $CHCl_3$); IR (neat) : 3397, 2865, 1716, 1612, 1443, 1034, 743, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.57–1.64 (1H, m), 1.76–1.85 (1H, m), 2.04–2.25 (4H, m), 2.46 (1H, d, *J* = 4.4 Hz), 3.64–3.76 (2H, m), 3.78 (3H, s), 4.17 (1H, d, *J* = 11.2 Hz), 4.23 (1H, d, *J* = 4.4 Hz), 4.45 (1H, d, *J* = 11.2 Hz), 5.37 (1H, dd, *J* = 9.2, 10.6 Hz), 5.46–5.52 (1H, m), 6.84 (2H, dd, *J* = 1.9, 6.3 Hz), 7.15–7.46 (17H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.9, 31.8, 37.7, 55.2, 60.8, 66.6, 69.8, 73.6, 113.8 (2 C), 126.5, 126.6, 127.8 (8 C), 129.3 (2 C), 129.4 (2 C), 129.5, 129.6 (2 C), 130.4, 131.2, 131.6, 144.8 (3 C), 159.2; HRMS (FAB^+) calcd for $C_{34}H_{35}O_3S$ (M^+−1), 523.2307, found 523.2298.

(*S*,*E*)-3-(4-Methoxybenzyloxy)-7-(tritylthio)hept-4-enoic acid (21).



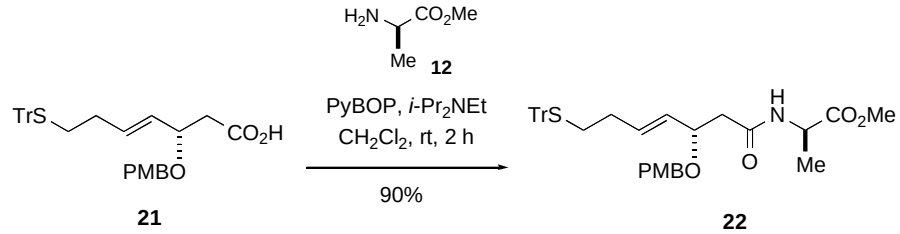
20 **S-7** **21**

Dess-Martin periodinane (DMP) (1.07 g, 2.5 mmol) was added in small portions to a stirred solution of **20** (660 mg, 1.3 mmol) in CH_2Cl_2 (60 mL) containing $NaHCO_3$ (1.06 g, 13 mmol) at room temperature. After 1 h, the reaction was quenched with saturated aqueous $Na_2S_2O_3$ (10 mL) at 0°C, and the resulting mixture was extracted with $CHCl_3$ (3 x 50 mL). The combined extracts were washed with brine (2 x 30 mL), then dried over Na_2SO_4. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane/EtOAc, 3:1) to give **S-7** (575 mg, 88%) as a colorless oil.

A solution of 80% $NaClO_2$ (635 mg, 5.6 mmol) and $NaH_2PO_4{\cdot}2H_2O$ (876 mg, 5.6 mmol) in water (10 mL) were added dropwise to a stirred solution of **S-7** (575 mg, 1.1 mmol) in DMSO (40 mL) at 0°C, and stirring was continued for 1 h at room temperature. The reaction was quenched with saturated aqueous $Na_2S_2O_3$ (20 mL) at 0°C. The resulting mixture was extracted with Et_2O (3 x 100 mL), and the combined extracts were washed with brine (2 x 50 mL), then dried over Na_2SO_4. Concentration of the solvent *in vacuo* afforded **21** (443 mg, 75%), which was used for the next reaction without further purification. $[\alpha]_D^{25}$ −17.8 (*c* 1.25, $CHCl_3$); IR (neat) : 2835, 1738, 1713, 1668, 1644, 1594, 743, 700, 676 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.12–2.19 (2H, m), 2.21–2.25 (2H, m), 2.48 (1H, dd, *J* = 4.8, 15.5 Hz), 2.61 (1H, dd, *J* = 8.2, 15.5 Hz), 3.78 (3H, s), 4.12 (1H, dt, *J* = 4.8, 8.2 Hz), 4.29 (1H, d, *J* = 11.2 Hz), 4.52 (1H, d, *J* = 11.2 Hz), 5.31 (1H, dd, *J* = 8.2, 15.0 Hz), 5.56–5.63 (1H, m), 6.82 (2H, d, *J* = 8.8 Hz), 7.13–7.45 (19H, m); ^{13}C

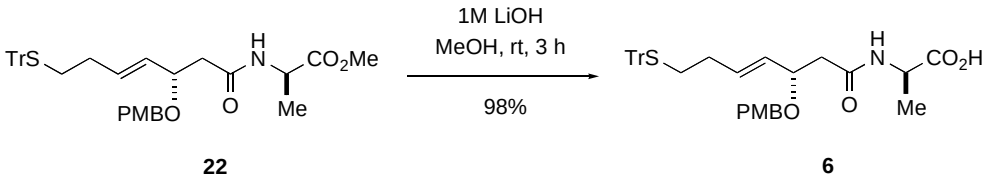
NMR (100 MHz, $CDCl_3$): δ 31.2, 31.4, 40.9, 55.2, 66.6, 69.8, 75.5, 77.2, 113.8 (x2), 126.6 (x3), 127.8, 127.9 (x8), 129.4, 129.5 (x3), 129.8, 129.9, 133.3, 144.9 (x3), 159.2, 175.9; HRMS (FAB^+) calcd for $C_{34}H_{35}O_4S$ (M^+), 539.2256, found 539.2273.

(*R*)-Methyl 2-[(*S*,*E*)-3-(4-methoxybenzyloxy)-7-(tritylthio)hept-4-enamido]propanoate (22).



N,*N*-Diisopropylethylamine (1.12 mL, 6.6 mmol) was added dropwise to a stirred solution of **21** (507 mg, 0.9 mmol) in dry MeCN (20 mL) and D-alanine methyl ester (**12**) (261 mg, 1.9 mmol) containing (benzotriazol-1-yloxy)tripyrrolidinophosphonium hexafluorophosphate (PyBOP) (981 mg, 1.88 mmol) at room temperature under argon. After 2 h, the reaction mixture was diluted with EtOAc (100 mL). The organic layer was washed successively with 10% aqueous HCl (2 x 20 mL), saturated aqueous $NaHCO_3$ (2 x 20 mL) and brine (2 x 20 mL), then dried over Na_2SO_4. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane/EtOAc, 1:1) to give **22** (528 mg, 90%) as a colorless oil. $[\alpha]_D^{25}$ −7.9 (*c* 1.00, $CHCl_3$); IR (neat) : 3318, 2867, 2836, 1745, 1659, 1513, 1247, 973, 744, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.30 (3H, d, *J* = 7.3 Hz), 2.09–2.17 (2H, m), 2.22 (2H, t, *J* = 6.7 Hz), 2.35 (1H, dd, *J* = 3.8, 15.3 Hz), 2.48 (1H, dd, *J* = 8.6, 15.3 Hz), 3.72 (3H, s), 3.79 (3H, s), 4.08 (1H, dt, *J* = 3.3, 8.2 Hz), 4.30 (1H, d, *J* = 10.6 Hz), 4.49–4.59 (2H, m), 5.30 (1H, q, *J* = 7.7 Hz), 5.54–5.61 (1H, m), 6.82 (2H, d, *J* = 8.6 Hz), 6.89 (1H, d, *J* = 7.7 Hz), 7.19–7.42 (17H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 18.2, 31.2, 31.4, 42.7 (2 C), 47.8, 52.2, 55.2, 66.5, 69.9, 76.5, 77.2, 113.8 (2 C), 126.6 (3 C), 127.8 (8 C), 129.5, 129.6 (2 C), 129.7, 129.9, 130.3, 132.8, 144.8 (3 C), 159.2, 170.2, 173.3; HRMS (FAB^+) calcd for $C_{38}H_{42}NO_5S$ (M^++1), 624.2783, found 624.2776.

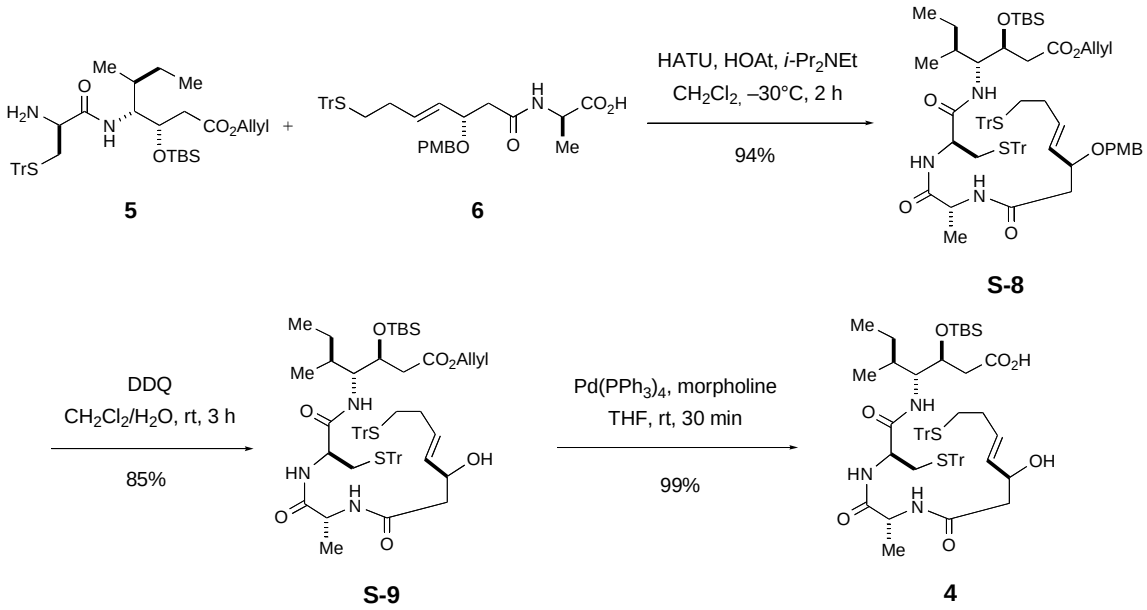
(*R*)-2-[(*S*,*E*)-3-(4-Methoxybenzyloxy)-7-(tritylthio)hept-4-enamido]propanoic acid (6).



1 M LiOH (3.0 mL, 3.0 mmol) was added dropwise to a stirred solution of **22** (470 mg, 0.8 mmol) in MeOH (15 mL) at room temperature. After 3 h, 10% aqueous HCl was added to the mixture at 0°C until pH was 6. The resulting mixture was extracted with EtOAc (3 x 30 mL), and the combined extracts were washed with brine (2 x 30 mL), then dried over Na_2SO_4. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column

chromatography ($CHCl_3$/MeOH, 9:1) to give **6** (450 mg, 98%) as a white amorphous solid. $[\alpha]_D^{25}$ −1.8 (*c* 1.00, $CHCl_3$); IR (neat) : 2931, 2868, 1730, 1632, 1614, 744, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.32 (3H, d, *J* = 6.8 Hz), 2.10–2.15 (2H, m), 2.21 (2H, d, *J* = 6.8 Hz), 2.40 (1H, dd, *J* = 3.4, 15.6 Hz), 2.49 (1H, dd, *J* = 8.8, 15.6 Hz), 3.78 (3H, s), 4.08 (1H, dt, *J* = 3.4, 8.2 Hz), 4.25 (1H, d, *J* = 10.7 Hz), 4.44 (1H, t, *J* = 6.8 Hz), 4.49 (1H, d, *J* = 11.2 Hz), 5.29 (1H, dd, *J* = 8.2, 15.6 Hz), 5.59 (1H, dd, *J* = 6.8, 15.6 Hz), 6.82 (2H, d, *J* = 8.2 Hz), 7.00 (1H, d, *J* = 6.8 Hz), 7.17–7.42 (17H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 18.1, 31.5, 31.7, 42.6 (2 C), 48.5, 55.5, 66.9, 70.3, 77.5, 77.6, 114.1 (2 C), 126.9 (3 C), 128.1 (8 C), 129.8 (5 C), 130.0, 133.3, 145.1 (3 C), 159.5, 171.7, 176.4; HRMS (FAB^+) calcd for $C_{37}H_{40}NO_5S$ (M^++1), 610.2627, found 610.2627.

(3*S*,4*R*,5*R*)-3-(*tert*-Butyldimethylsilyloxy)-4-[(*S*)-2-[(*R*)-2-[(*S*,*E*)-3-hydroxy-7-(tritylthio)hept-4-enoylamino]propionylamino]-3-(tritylthio)propionylamino]-5-metylheptanoic acid (4)

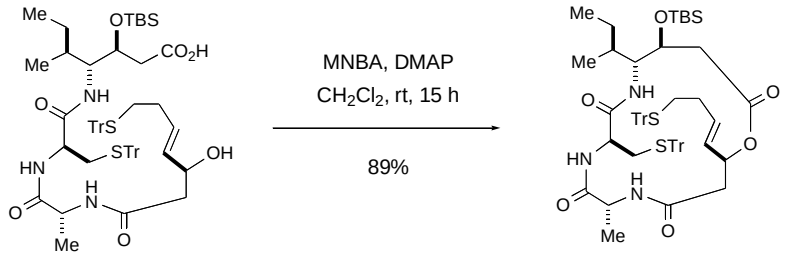


N,*N*-Diisopropylethylamine (0.30 mL, 1.8 mmol) was added dropwise to a stirred solution of **5** (465 mg, 0.7 mmol) and **6** (419 mg, 0.7 mmol) in dry CH_2Cl_2 (14 mL) containing *O*-(7-azabenzotriazol-1-yl)-*N*,*N*,*N*',*N*'-tetramethyluronium hexafluorophosphate (HATU) (340 mg, 0.9 mmol) and 1-hydroxy-7-azabenzotriazol (HOAt) (122 mg, 0.9 mmol) at −30°C under argon. After 2 h, the reaction mixture was diluted with $CHCl_3$ (80 mL). The organic layer was washed successibly with 10% aqueous HCl (2 x 20 mL), saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL), then dried over Na_2SO_4. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane/EtOAc, 1:1) to give **S-8** (819 mg, 94%) as a colorless viscous liquid.

DDQ (276 mg, 1.2 mmol) was added in small portions to a stirred solution of **S-8** (769 mg, 0.61 mmol) in CH_2Cl_2/H_2O 9:1 (12mL) at room temperature under argon. After 3 h, the mixture was diluted with $CHCl_3$ (100 mL), and the organic layer was washed with saturated aqueous $NaHCO_3$ (2 x 25 mL) and brine (2 x 25 mL), then dried over Na_2SO_4. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane/EtOAc, 3:2) to give **S-9** (592 mg, 85%) as a colorless viscous liquid.

Morpholine (69 μL, 0.79 mmol) was added dropwise to a stirred solution of **S-9** (450 mg, 0.39 mmol) in dry THF (10 mL) containing $Pd(PPh_3)_4$ (45.4 mg, 39 μmol) at room temperature under argon. After 30 min, the reaction mixture diluted with EtOAc (100 mL), and the organic layer was washed successively with 10% aqueous HCl (2 x 25 mL), saturated aqueous $NaHCO_3$ (2 x 25 mL) and brine (2 x 25 mL), then dried over Na_2SO_4. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography ($CHCl_3$/MeOH, 9:1) to give **4** (430 mg, 99%) as a white amorphous solid. $[\alpha]_D^{26}$ −3.9 (*c* 1.03, $CHCl_3$); IR (neat) : 3284, 1712, 1635, 1595, 1095, 1033, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 0.05 (6H, s), 0.80 (3H, d, *J* = 6.8 Hz), 0.85 (9H, s), 0.83–0.87 (3H, m), 1.07–1.16 (1H, m), 1.20–1.28 (4H, m), 1.31 (3H, d, *J* = 6.8 Hz), 1.79–1.83 (1H, m), 2.04 (2H, dd, *J* = 6.8, 14.1 Hz), 2.17–2.25 (3H, m), 2.32 (1H, dd, *J* = 2.9, 13.6 Hz), 2.38–2.46 (2H, m), 2.54 (1H, dd, *J* = 6.8, 16.5 Hz), 2.81 (1H, dd, *J* = 7.3, 12.6 Hz), 3.91–3.96 (1H, m), 4.05–4.17 (2H, m), 4.36–4.43 (2H, m), 5.32 (1H, dd, *J* = 5.9, 15.5 Hz), 5.42–5.48 (1H, m), 6.30 (1H, d, *J* = 10.2 Hz), 6.47 (1H, d, *J* = 7.3 Hz), 6.99 (1H, d, *J* = 7.8 Hz), 7.16–7.44 (30H, m); ^{13}C NMR (100 MHz, $CDCl_3$):δ −4.9, −4.3, 11.8, 13.3, 17.5, 17.9, 25.7, 27.2, 29.7, 31.3, 31.4, 33.0, 34.1, 40.2, 44.1 (4 C), 49.3, 53.1, 57.0, 66.6, 66.9, 68.8, 69.7, 77.2, 126.6 (3 C), 126.9 (3 C), 127.9 (6 C), 128.1 (8 C), 129.4 (6 C), 129.6 (3 C), 130.0, 132.2, 144.2 (3 C), 144.8, 170.3, 171.8, 172.7, 173.9; HRMS (FAB^+) calcd for $C_{65}H_{79}N_3O_7S_2Si$ (M^++Na), 1128.5027, found 1128.5020.

(2*S*,6*R*,9*S*,12*R*,13*S*)-13-(*tert*-Butyldimethylsiloxy)-12-[(*S*)-isobutyl]-6-methyl-2-[(*E*)-4-(tritylthio)but-1-enyl]-9-(tritylthio)methyl-1-oxa-5,8,11-triazacyclopentadecane-4,7,10,15-tetraone (23).

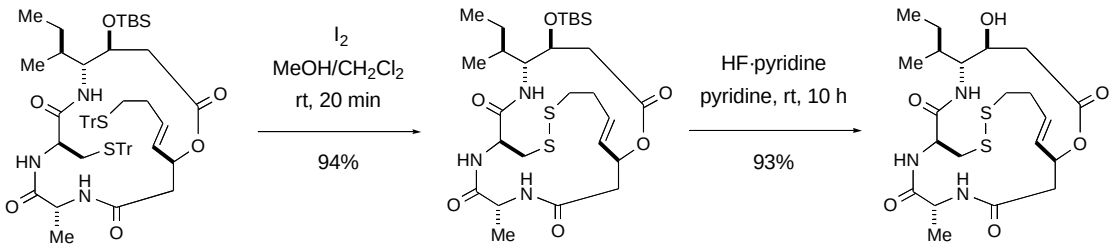


4 **23**

A solution of **4** (151 mg, 0.14 mmol) in dry CH_2Cl_2 (10 mL) was added very slowly to a stirred solution of 2-methyl-6-nitrobenzoic anhydride (MNBA) (61.1 mg, 0.18 mmol) in dry CH_2Cl_2 (120 mL, 1 mM concentration) containing *N*,*N*-dimethylamino pyridine (DMAP) (50.1 mg, 0.41 mmol) at toom temperature over 14 hours. After 1 h, the mixture was diluted with CH_2Cl_2 (30 mL), and the organic layer was washed with saturated aqueous $NaHCO_3$ (2 x 30 mL), water (2 x 30 mL), and brine (2 x 30 mL), then dried over Na_2SO_4. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography ($CHCl_3$/MeOH, 20:1) to give **23** (132 mg, 89%) as a white amorphous solid. $[\alpha]_D^{25}$ −5.4 (*c* 1.00, $CHCl_3$); IR (neat) : 1733, 1647, 1594, 1101, 1001, 751, 700, 666, 616 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ −0.06 (3H,s), 0.01 (3H,s), 0.76 (3H, d, *J* = 6.8 Hz), 0.82 (9H, s), 0.85–0.97 (3H, m), 1.00–1.11 (1H, m), 1.13–1.23 (1H, m), 1.34 (3H, d, *J* = 7.3 Hz), 1.79–1.87 (1H, m), 1.97–2.09 (2H, m), 2.16 (2H, t, *J* = 7.3 Hz), 2.31–2.45 (4H, m), 2.60 (1H, dd, *J* = 6.8, 15.0 Hz), 5.54–5.65 (2H, m), 6.46 (1H, br s), 6.86 (1H, br s), 7.04 (1H, d, *J* = 10.2 Hz), 7.14–7.48 (30H, m); ^{13}C NMR (100 MHz, $CDCl_3$):δ −4.9, −4.0, 12.0, 13.1, 16.5, 17.9, 25.7,

27.4, 31.0, 31.3, 32.0, 34.3, 41.9, 42.3 (4 C), 49.8, 56.7, 57.3, 66.6, 66.7, 68.4, 71.2, 77.2, 126.6 (3 C), 126.7 (2 C), 126.8, 127.9 (6 C), 128.2 (10 C), 129.5 (6 C), 129.8 (3 C), 132.9, 144.5 (3 C), 144.8, 169.9, 170.1, 170.2, 172.4; HRMS (FAB^+) calcd for $C_{65}H_{77}N_3O_6S_2SiNa$ (M^++Na), 1110.4921, found 1110.4928.

Spiruchostatin B (2).

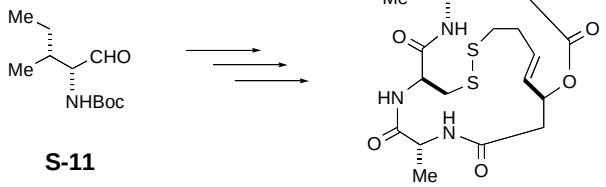


23 **S-10** spiruchostatin B (**2**)

A solution of **23** (131 mg, 120 μmol) in CH_2Cl_2/MeOH 9:1 (30 mL) was added dropwise to a vigorously stirring solution of I_2 (306 mg, 1.2 mmol) in CH_2Cl_2/MeOH 9:1 (170 mL, 0.5 mM concentration) over 10 min at room temperature. After 10 min, the reaction was quenched with 0.01M $Na_2S_3O_2$ (10 mL) at room temperature. The resulting mixture was diluted with CH_2Cl_2 (50 mL), and the organic layer was washed with saturated aqueous $NaHCO_3$ (2 x 30 mL) and brine (2 x 30 mL), then dried over Na_2SO_4. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography ($CHCl_3$/MeOH, 20:1) to give **S-10** (68.3 mg, 94%) as a white amorphous solid.

HF·pyridine (1.0 mL) was added to a stirring solution of **S-10** (68.3 mg, 114 μmol) in pyridine (2 mL) at room temperature. After 10 h, the reaction mixture was diluted with EtOAc (60 mL), and the organic layer was washed successively with 3% aqueous HCl (2 x 20 mL), saturated aqueous $NaHCO_3$ (2 x 20 mL) and brine (2 x 20 mL), then dried over Na_2SO_4. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography ($CHCl_3$/MeOH, 10:1) to give **2** (spiruchostatin B) (51.3 mg, 93%) as a white amorphous solid. $[\alpha]_D^{25}$ −58.6 (*c* 0.11, MeOH); IR (neat) : 3374, 3332, 1731, 1660, 1539, 1273, 990 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 0.89 (3H, t, *J* = 7.5 Hz), 0.90 (3H, d, *J* = 7.0 Hz), 1.18–1.29 (2H, m), 1.50 (3H, d, *J* = 7.3 Hz), 1.54–1.59 (1H, m), 2.04–2.11 (1H, m), 2.42-2.51 (1H, m), 2.61 (1H, d, *J* = 13.2 Hz), 2.69–2.78 (4H, m), 2.93 (1H, m), 2.94 (1H, ddd, *J* = 4.0, 7.0, 9.0 Hz), 3.11–3.24 (2H, m), 3.33 (2H, dd, *J* = 7.3, 13.1 Hz), 4.22 (1H, dq, *J* = 3.9, 7.3 Hz), 4.60–4.65 (1H, m), 4.87 (1H, dt, *J* = 3.4, 9.2 Hz), 5.50–5.51 (1H, m), 5.68 (1H, d, *J* = 15.6 Hz), 6.27 (1H, s), 6.37–6.42 (1H, m), 6.78 (1H, d, *J* = 9.7 Hz), 7.29 (1H, d, *J* = 9.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$):δ 11.5, 15.4, 16.6, 27.1, 33.3, 36.3, 39.5, 40.5, 40.7, 41.3, 52.2, 54.5, 61.7, 68.2, 70.6, 128.6, 133.4, 169.2, 170.6, 171.2, 171.8; HRMS (FAB^+) calcd for $C_{21}H_{34}N_3O_6S_2$ (M^++1), 488.1889, found 488.1886. The IR, ^1H and ^{13}C NMR, and HRMS spectrum are essentially identical with those reported for natural spiruchostatin B.

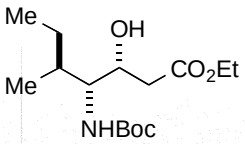
5”-*epi*-Spiruchostatin B (5”-*epi*-2)



S-11

5”-*epi*-spiruchostatin B (5”-*epi*-**2**)

5”-*epi*-Spiruchostatin B (5”-*epi*-**2**) was synthesized in the same manner as described for the synthetic pathway to spiruchostatin B (**2**) by employing (2*R*,3*R*)-*N*-(*tert*-butoxycarbonyl)-D-isoleucinal (**S-11**) instead of (2*R*,3*S*)-*N*-(*tert*-butoxycarbonyl)-D-allo-isoleucinal (**7**). $[\alpha]_D^{25}$ −51.9 (*c* 0.10, MeOH); IR (KBr) : 3375, 3320, 2964, 1731, 1660, 1652, 1539, 1040, 891, 753 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 0.82 (3H, t, *J* = 7.3 Hz), 0.97 (3H, d, *J* = 6.8 Hz), 1.02–1.11 (1H, m), 1.46 (3H, d, *J* = 7.3 Hz), 1.50–1.56 (1H, m), 2.07 (1H, q, *J* = 7.3 Hz), 2.41–2.49 (1H, m), 2.68 (1H, d, *J* = 12.6 Hz), 2.64-2.78 (4H, m), 2.95 (1H, q, *J* = 7.8 Hz), 3.24 (2H, dd, *J* = 6.8, 13.2 Hz), 4.13–4.19 (1H, m), 4.45–4.47 (1H, m), 4.72 (1H, dd, *J* = 8.3, 13.2 Hz), 5.50 (1H, br s), 5.75 (1H, d, *J* = 15.6 Hz), 6.16–6.18 (1H, m), 6.98 (1H, d, *J* = 8.7 Hz), 7.07 (1H, s), 7.42 (1H, d, *J* = 7.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$):δ 10.8, 16.3, 16.4, 25.8, 32.6, 35.8, 39.5, 39.7, 39.9, 40.9, 52.2, 55.8, 61.7, 69.1, 71.0, 129.5, 132.8, 169.2, 171.1, 171.4, 171.9; HRMS (FAB^+) calcd for $C_{21}H_{34}N_3O_6S_2$ (M^++1), 488.1889, found 488.1886. The ^1H and ^{13}C NMR spectrum did not match those reported for natural spiruchostatin B.


Me
OH
Me
CO_2Et
NHBoc

13

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OBSET 124.00 KHz
OBFIN 10500.00 Hz
POINT 16384
FREQU 7992.01 Hz
SCANS 16
ACQTM 2.0501 sec
PD 4.9500 sec
PW1 5.40 usec
IRNUC 1H
CTEMP 26.5 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 0.24 Hz
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PPM
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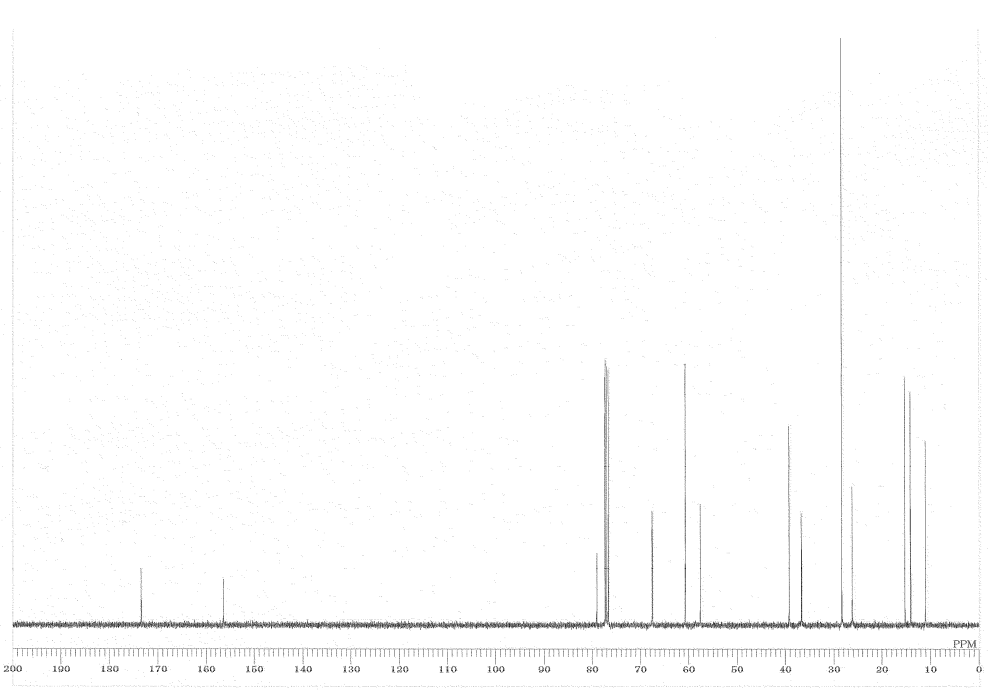
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0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OBSET 125.00 KHz
OBFIN 10500.00 Hz
POINT 32768
FREQU 27118.64 Hz
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ACQTM 1.2083 sec
PD 1.7920 sec
PW1 5.60 usec
IRNUC 1H
CTEMP 29.1 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 0.24 Hz
RGAIN 24
PPM
200
190
180
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150
140
130
120
110
100
90
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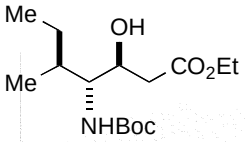
70
60
50
40
30
20
10
0


Me
OH
Me
CO_2Et
NHBoc

14

DFILE KK-6041-15-18-下のス
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OBNUC 1H
EXMOD NON
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OBSET 124.00 KHz
OBFIN 10500.00 Hz
POINT 16384
FREQU 7992.01 Hz
SCANS 16
ACQTM 2.0501 sec
PD 4.9500 sec
PW1 5.40 usec
IRNUC 1H
CTEMP 23.0 c
SLVNT CDCL3
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BF 0.24 Hz
RGAIN 10
PPM
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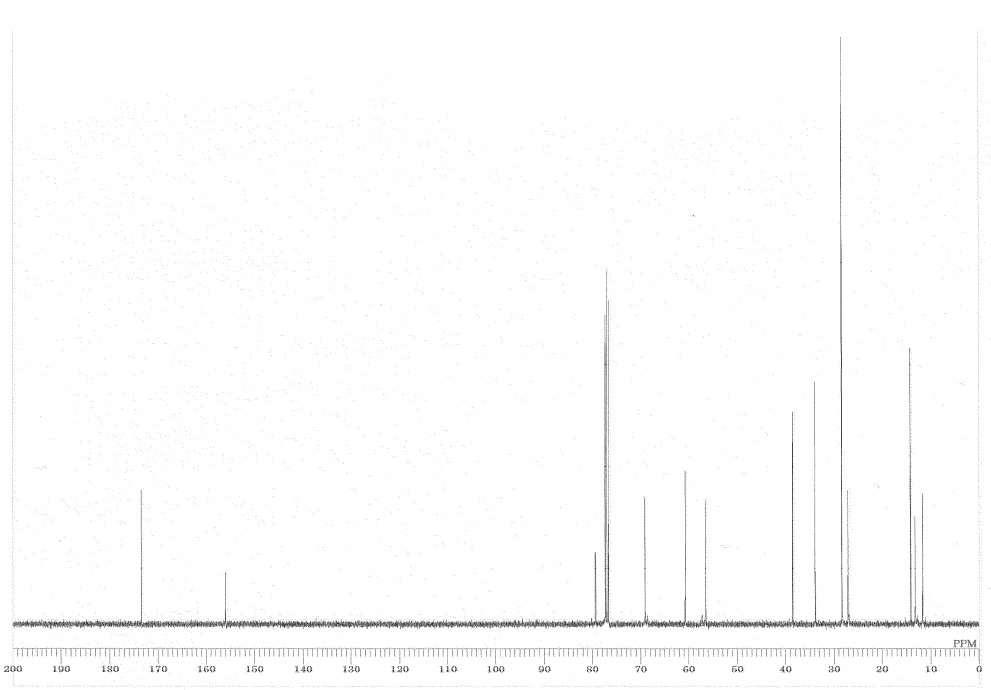
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FREQU 27118.64 Hz
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PD 1.7920 sec
PW1 5.60 usec
IRNUC 1H
CTEMP 25.7 c
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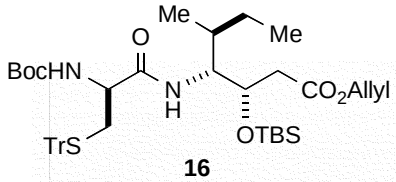
Me
Me
O
BocHN
N
H
CO2Allyl
TrS
OTBS

16

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DATIM Tue Nov 06 19:43:59 2
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EXMOD NON
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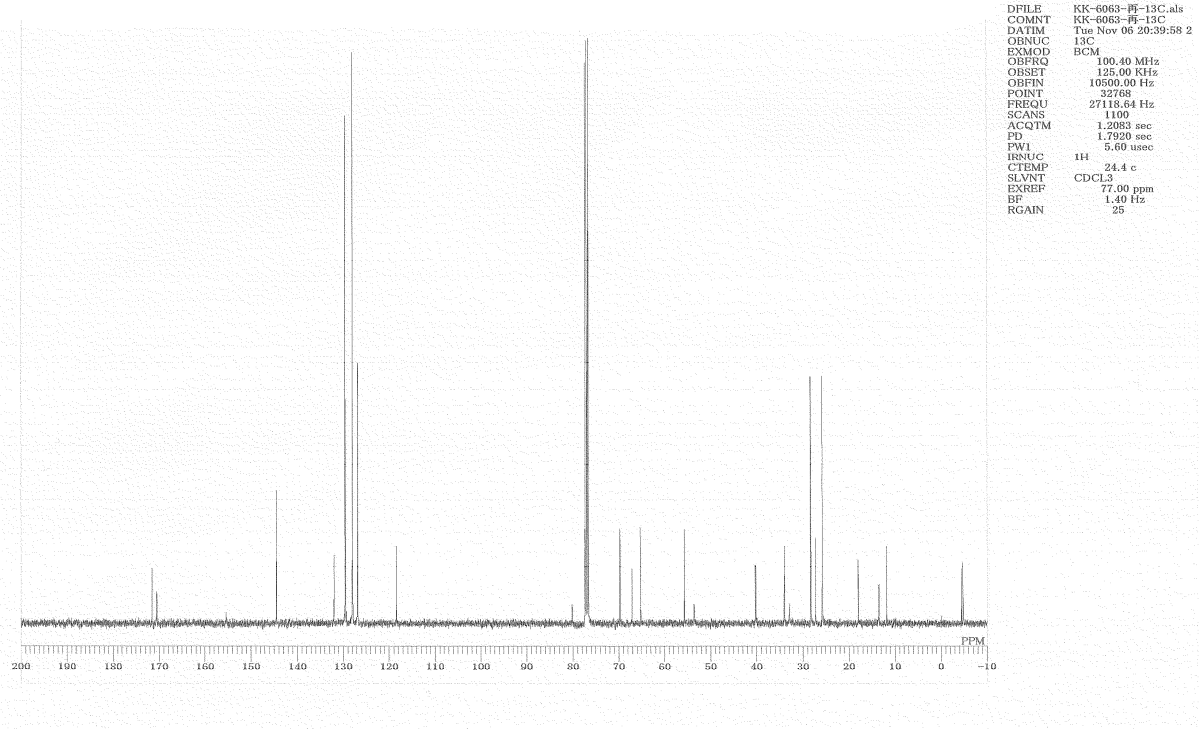
OBSET 124.00 KHz
OBFIN 10500.00 Hz
POINT 16384
FREQU 7992.01 Hz
SCANS 16
ACQTM 2.0501 sec
PD 4.9500 sec
PW1 5.40 usec
IRNUC 1H
CTEMP 22.1 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 1.40 Hz
RGAIN 12
PPM
8 7 6 5 4 3 2 1 0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OBSET 125.00 KHz
OBFIN 10500.00 Hz
POINT 32768
FREQU 27118.64 Hz
SCANS 1100
ACQTM 1.2083 sec
PD 1.7920 sec
PW1 5.60 usec
IRNUC 1H
CTEMP 24.4 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 1.40 Hz
RGAIN 25
PPM
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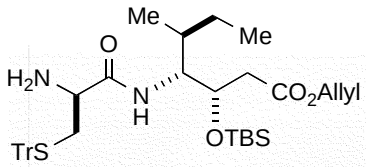
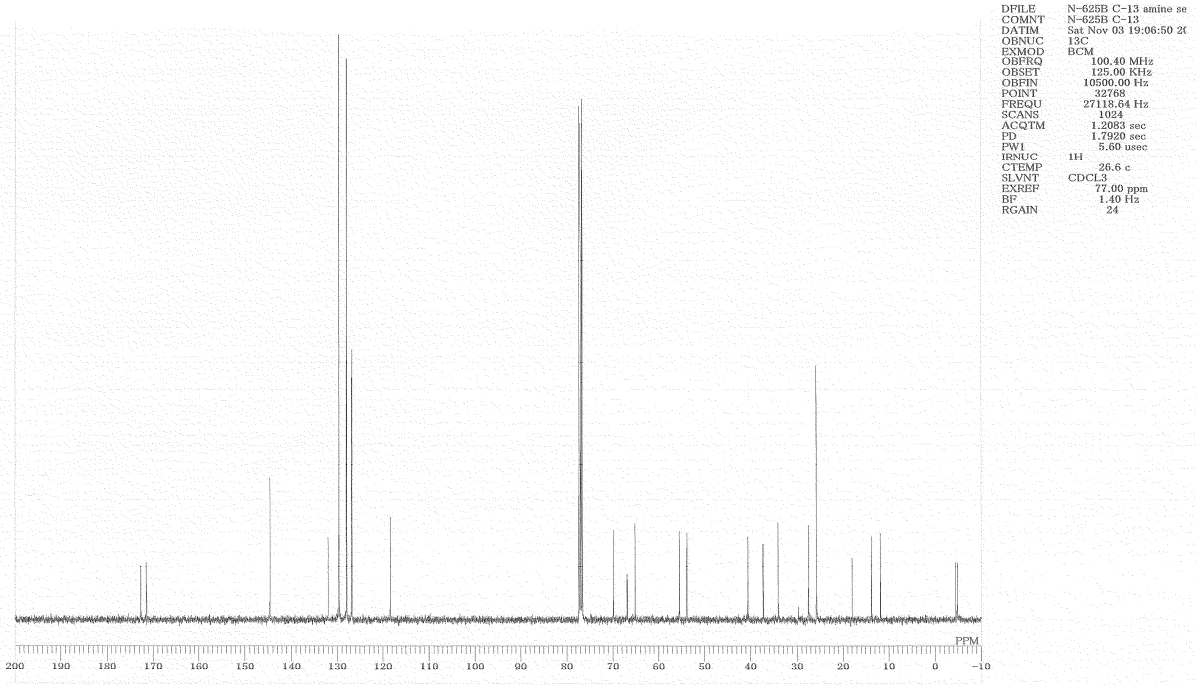

Me
Me
O
H2N
N
H
CO2Allyl
TrS
OTBS

5

DFILE N-625B amine segment
COMNT N-625B
DATIM Sat Nov 03 17:49:03 2
OBNUC 1H
EXMOD NON
OBFRQ 399.65 MHz
OBSET 124.00 KHz
OBFIN 10500.00 Hz
POINT 16384
FREQU 7992.01 Hz
SCANS 8
ACQTM 2.0501 sec
PD 4.9500 sec
PW1 5.40 usec
IRNUC 1H
CTEMP 24.3 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 1.40 Hz
RGAIN 13
PPM
8 7 6 5 4 3 2 1 0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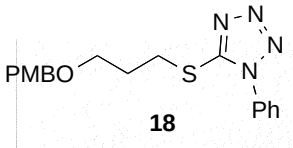
COMNT N-625B C-13
DATIM Sat Nov 03 19:06:50 2
OBNUC 13C
EXMOD BCM
OBFRQ 100.40 MHz
OBSET 125.00 KHz
OBFIN 10500.00 Hz
POINT 32768
FREQU 27118.64 Hz
SCANS 1024
ACQTM 1.2083 sec
PD 1.7920 sec
PW1 5.60 usec
IRNUC 1H
CTEMP 26.6 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 1.40 Hz
RGAIN 24
PPM
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10



18


```
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EXMOD     NON
OBFRQ       399.65 MHz
OBSET       124.00 KHz
OBFIN     10500.00 Hz
POINT       16384
FREQU      7992.01 Hz
SCANS          16
ACQTM       2.0501 sec
PD          4.9500 sec
PW1          5.40 usec
IRNUC     1H
CTEMP       23.6 c
SLVNT     CDCL3
EXREF       0.00 ppm
BF          0.24 Hz
RGAIN          17
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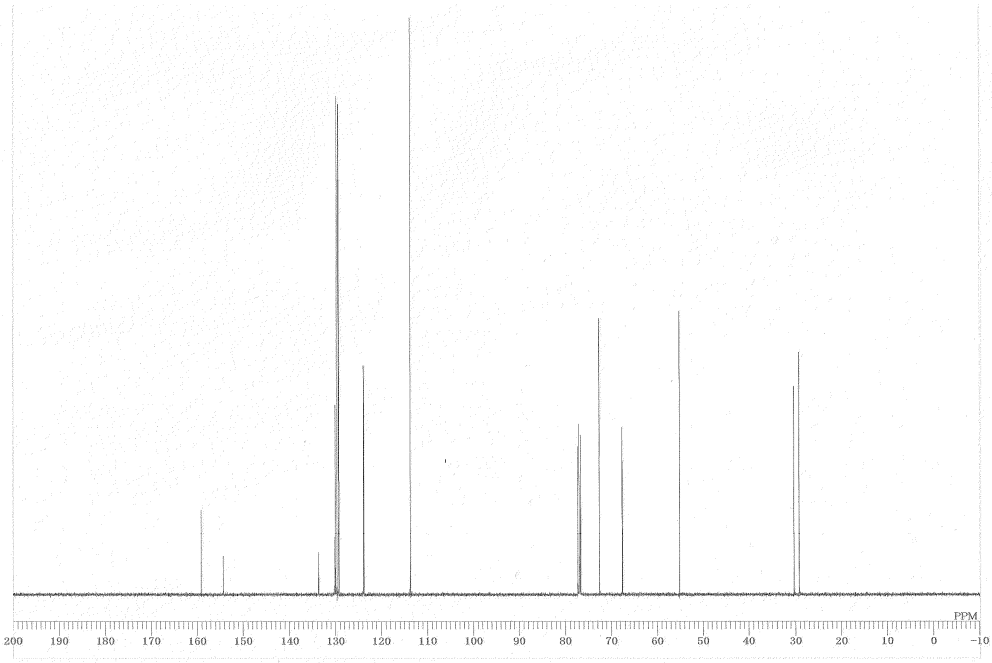


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COMNT     N-FK-2 C-13
DATIM     Sat Apr 14 23:54:42 20
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EXMOD     BCM
OBFRQ       100.40 MHz
OBSET       125.00 KHz
OBFIN     10500.00 Hz
POINT       32768
FREQU      27118.64 Hz
SCANS          925
ACQTM       1.2083 sec
PD          1.7920 sec
PW1          5.60 usec
IRNUC     1H
CTEMP       25.9 c
SLVNT     CDCL3
EXREF       77.00 ppm
BF          0.24 Hz
RGAIN          25
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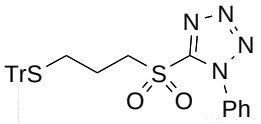
TrS
S
O
O
N
N
N
Ph

10

DFILE N-464RE.als
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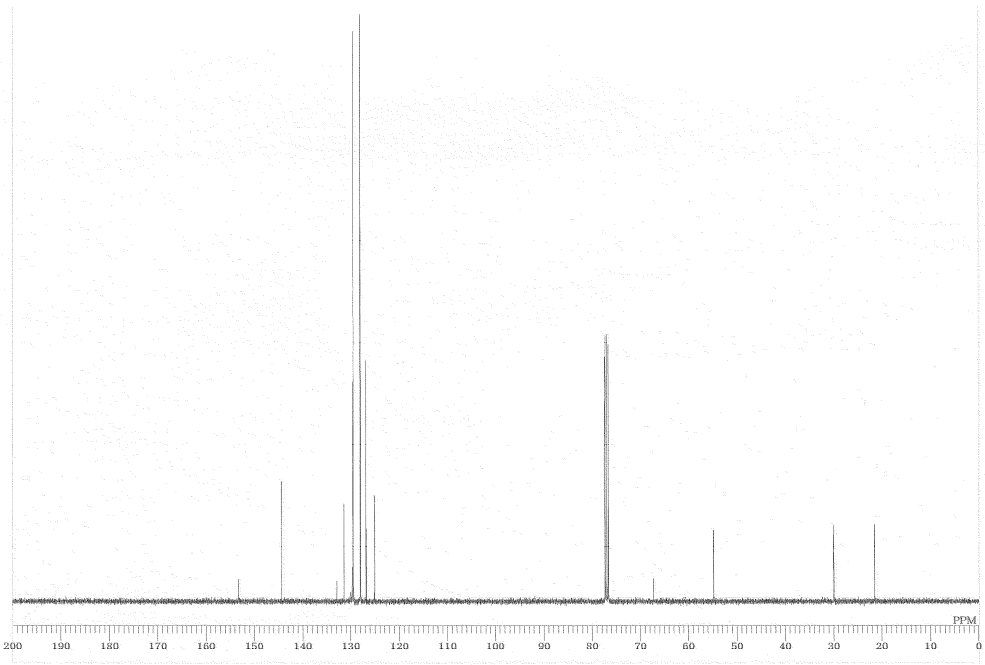
DATIM Wed Apr 11 17:18:07 2
OBNUC 1H
EXMOD NON
OBFRQ 399.65 MHz
OBSET 124.00 KHz
OBFIN 10500.00 Hz
POINT 16384
FREQU 7992.01 Hz
SCANS 16
ACQTM 2.0501 sec
PD 4.9500 sec
PW1 5.40 usec
IRNUC 1H
CTEMP 23.3 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 0.24 Hz
RGAIN 14
PPM
10 9 8 7 6 5 4 3 2 1 0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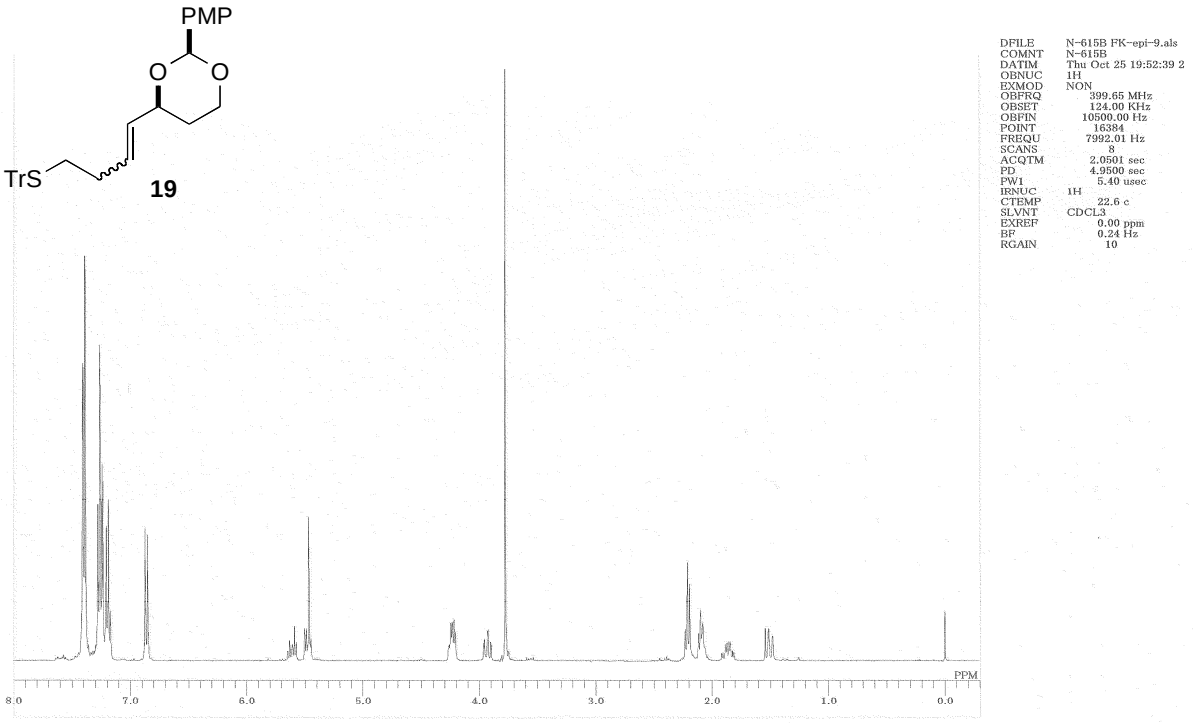
COMNT N-464RE
DATIM Wed Apr 11 18:07:23 2
OBNUC 13C
EXMOD BCM
OBFRQ 100.40 MHz
OBSET 125.00 KHz
OBFIN 10500.00 Hz
POINT 32768
FREQU 27118.64 Hz
SCANS 906
ACQTM 1.2083 sec
PD 1.7920 sec
PW1 5.60 usec
IRNUC 1H
CTEMP 25.4 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 0.24 Hz
RGAIN 25
PPM
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0


PMP
O
O
TrS
19
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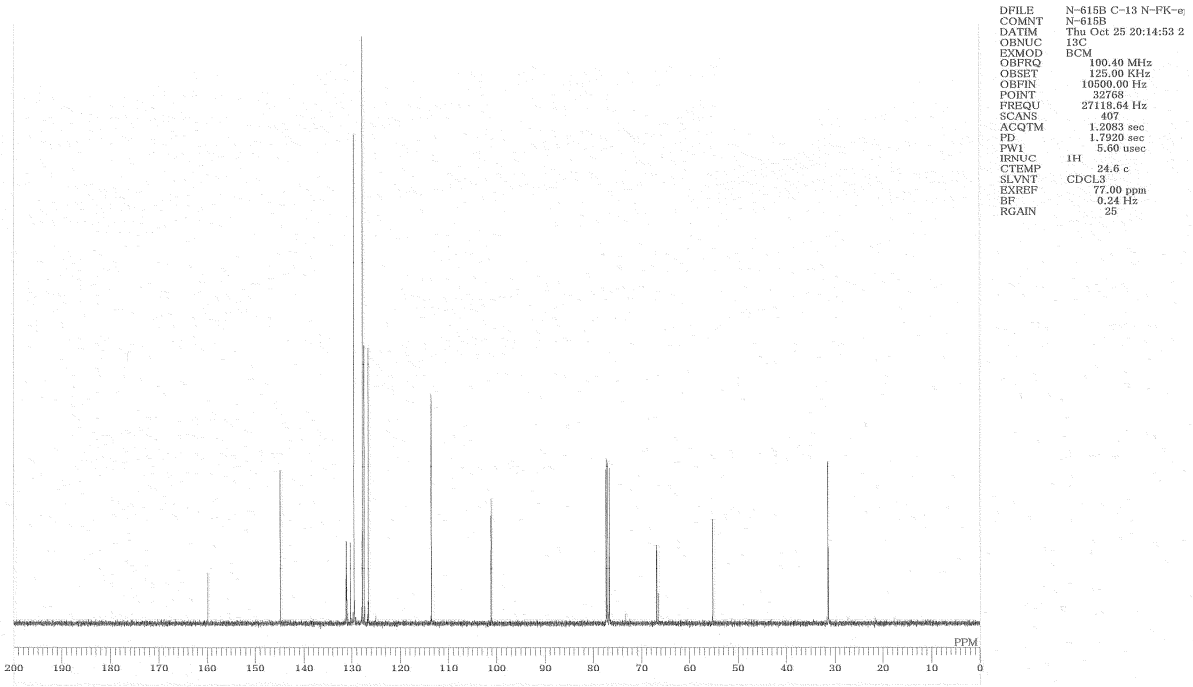
COMNT N-615B
DATIM Thu Oct 25 19:52:39 2
OBNUC 1H
EXMOD NON
OBFRQ 399.65 MHz
OBSET 124.00 KHz
OBFIN 10500.00 Hz
POINT 16384
FREQU 7992.01 Hz
SCANS 8
ACQTM 2.0501 sec
PD 4.9500 sec
PW1 5.40 usec
IRNUC 1H
CTEMP 22.6 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 0.24 Hz
RGAIN 10
PPM
8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0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COMNT N-615B
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EXMOD BCM
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OBSET 125.00 KHz
OBFIN 10500.00 Hz
POINT 32768
FREQU 27118.64 Hz
SCANS 407
ACQTM 1.2083 sec
PD 1.7920 sec
PW1 5.60 usec
IRNUC 1H
CTEMP 24.6 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 0.24 Hz
RGAIN 25
PPM
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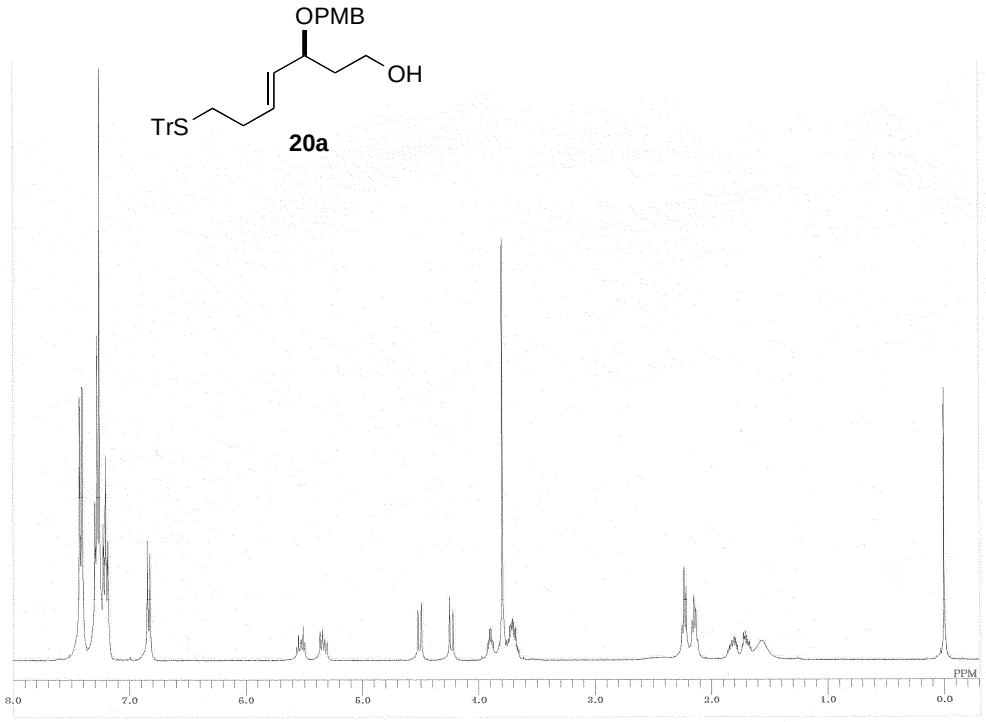


```
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EXMOD     NON
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OBSET       124.00 KHz
OBFIN     10500.00 Hz
POINT       16384
FREQU      7992.01 Hz
SCANS         16
ACQTM       2.0501 sec
PD          4.9500 sec
PW1         5.40 usec
IRNUC     1H
CTEMP       24.3 c
SLVNT     CDCL3
EXREF       0.00 ppm
BF          0.24 Hz
RGAIN         18
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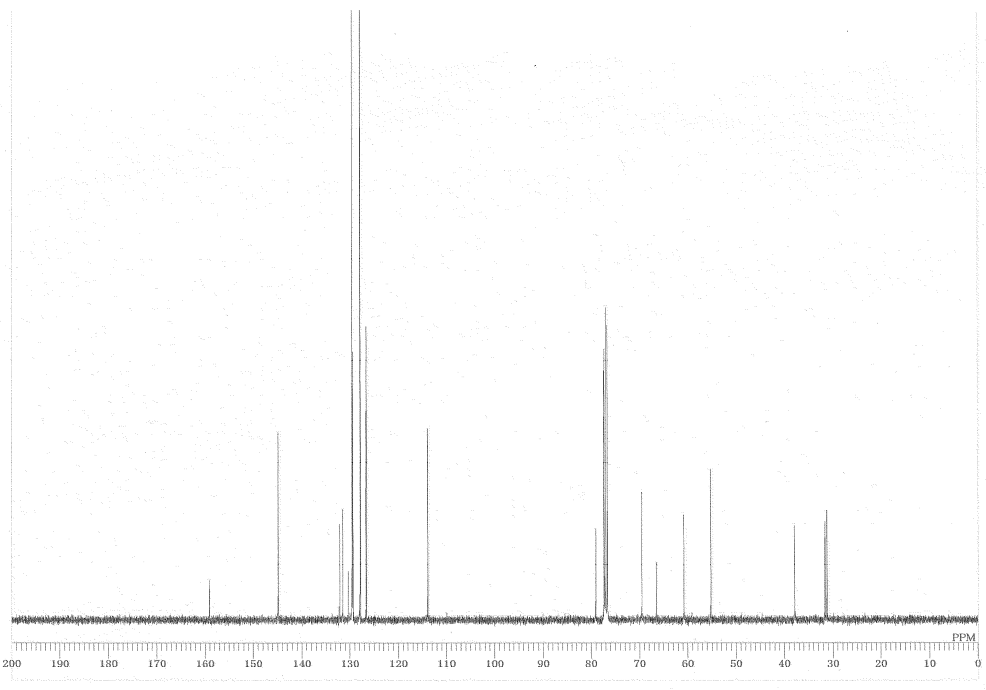


```
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OBSET       125.00 KHz
OBFIN     10500.00 Hz
POINT       32768
FREQU      27118.64 Hz
SCANS        1024
ACQTM       1.2083 sec
PD          1.7920 sec
PW1         5.60 usec
IRNUC     1H
CTEMP       25.4 c
SLVNT     CDCL3
EXREF       77.00 ppm
BF          0.24 Hz
RGAIN         25
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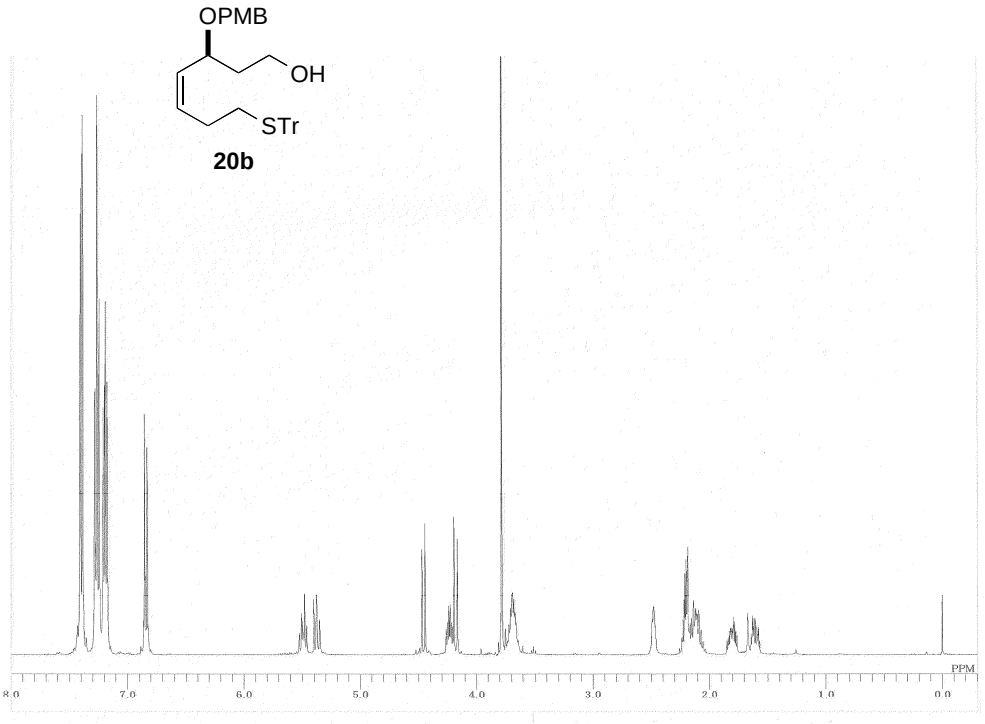
OPMB
OH
STr
20b
DFILE DIBAL-Z-isomer.als
COMNT DIBAL-Z-isomer
DATIM Mon Oct 22 20:25:23 2
OBNUC 1H
EXMOD NON
OBFRQ 399.65 MHz
OBSET 124.00 KHz
OBFIN 10500.00 Hz
POINT 16384
FREQU 7992.01 Hz
SCANS 8
ACQTM 2.0501 sec
PD 4.9500 sec
PW1 5.40 usec
IRNUC 1H
CTEMP 23.0 c
SLVNT CDCL3
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BF 0.24 Hz
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PPM
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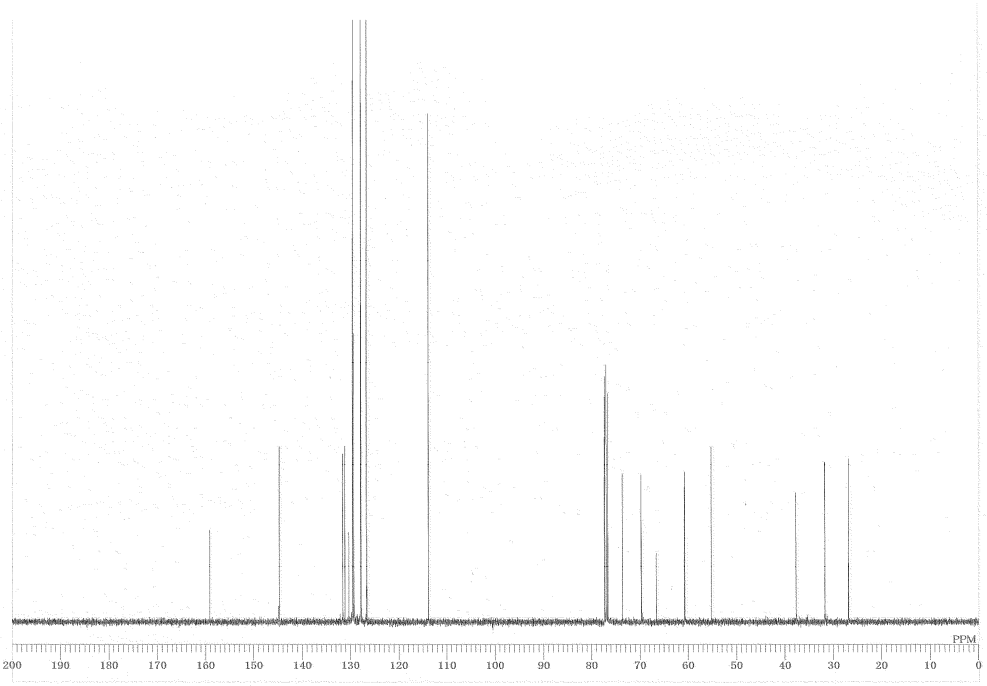
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OBFIN 10500.00 Hz
POINT 32768
FREQU 27118.64 Hz
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ACQTM 1.2083 sec
PD 1.7920 sec
PW1 5.60 usec
IRNUC 1H
CTEMP 25.1 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 0.24 Hz
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PPM
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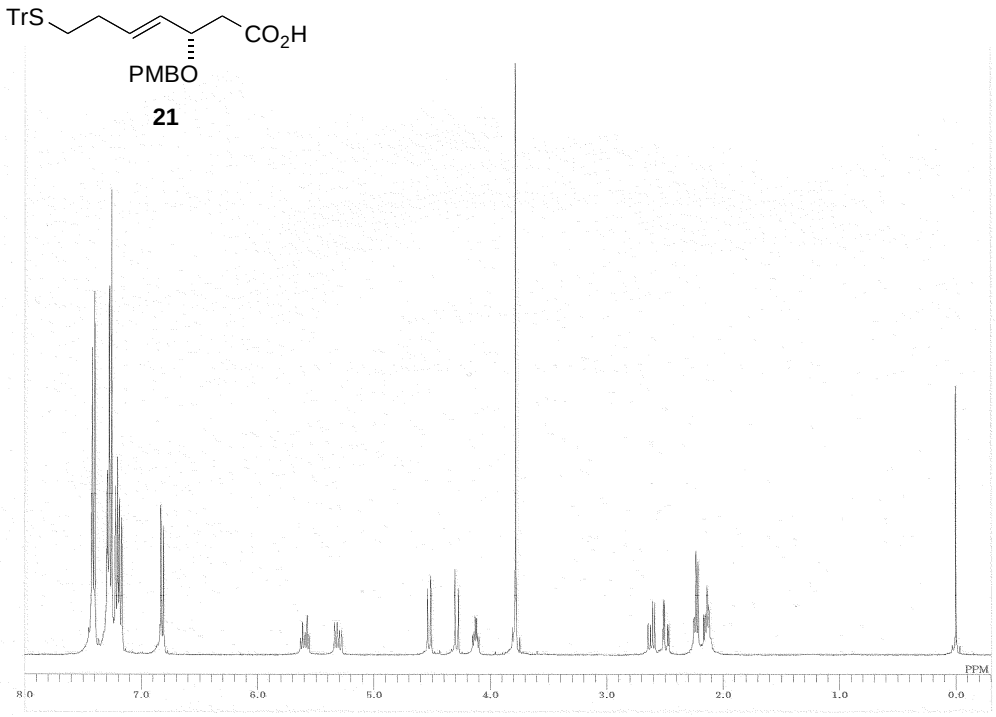
TrS
CO2H
PMBO
21
DFILE N-619RE.als
COMNT N-619RE
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OBNUC 1H
EXMOD NON
OBFRQ 399.65 MHz
OBSET 124.00 KHz
OBFIN 10500.00 Hz
POINT 16384
FREQU 7992.01 Hz
SCANS 8
ACQTM 2.0501 sec
PD 4.9500 sec
PW1 5.40 usec
IRNUC 1H
CTEMP 27.3 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 0.24 Hz
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PPM
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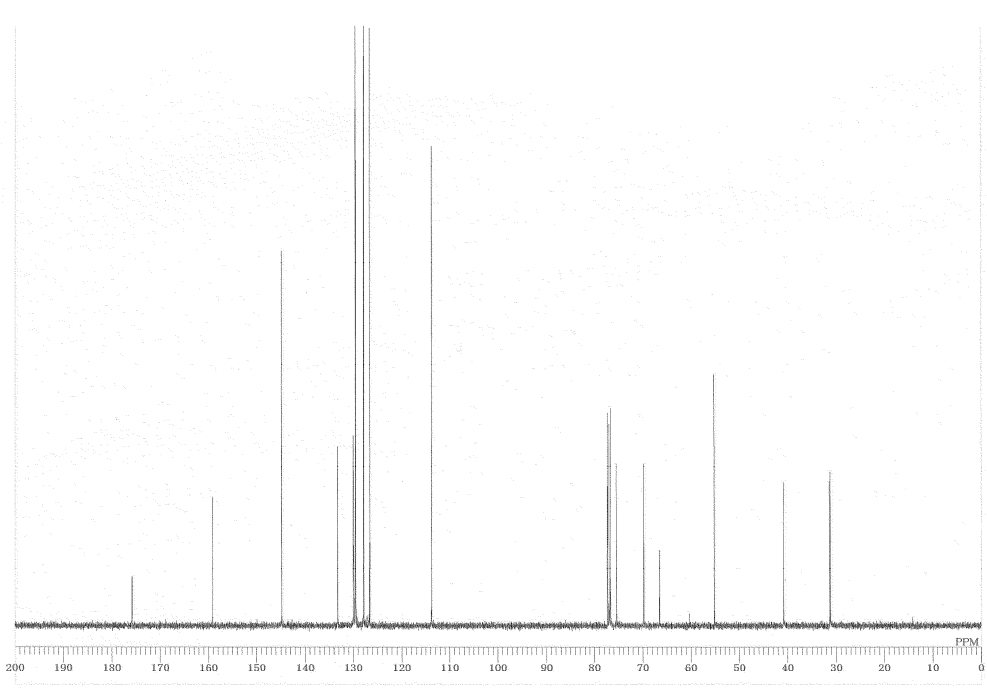
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0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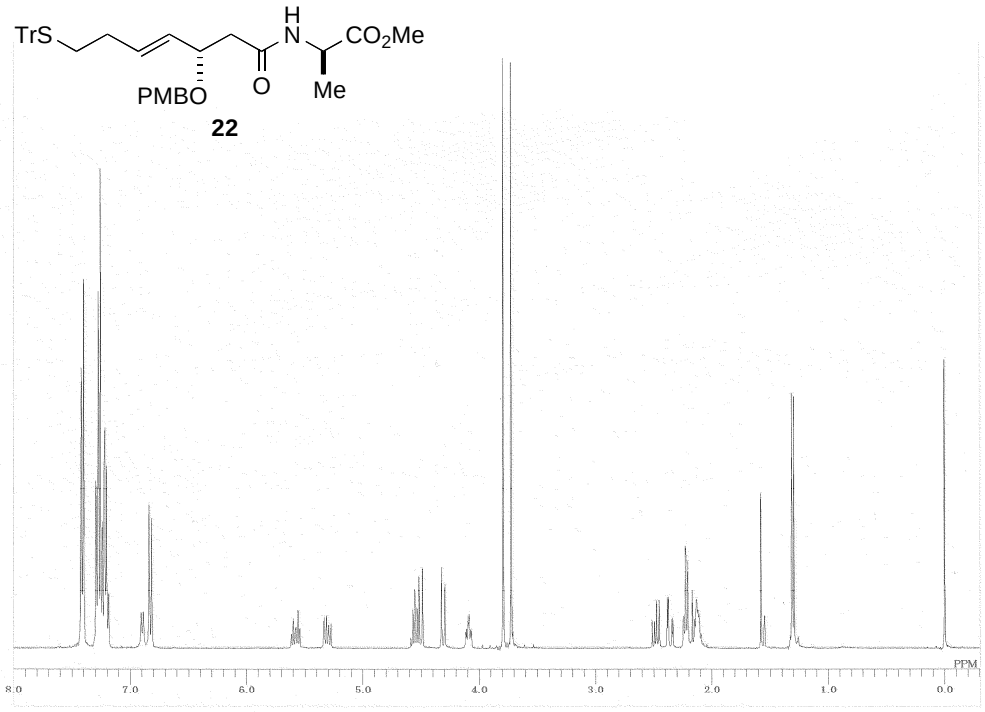
OBFRQ 100.40 MHz
OBSET 125.00 KHz
OBFIN 10500.00 Hz
POINT 32768
FREQU 27118.64 Hz
SCANS 622
ACQTM 1.2083 sec
PD 1.7920 sec
PW1 5.60 usec
IRNUC 1H
CTEMP 25.3 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 0.24 Hz
RGAIN 24
PPM
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


TrS
H
N
CO2Me
PMBO
O
Me
22
DFILE N-620 Jilia segment D-
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DATIM Tue Oct 30 01:22:32 2
OBNUC 1H
EXMOD NON
OBFRQ 395.75 MHz
OBSET 124.00 KHz
OBFIN 10277.00 Hz
POINT 16384
FREQU 7912.96 Hz
SCANS 8
ACQTM 2.0705 sec
PD 4.9290 sec
PW1 5.20 usec
IRNUC 1H
CTEMP 24.5 c
SLVNT CDCL3
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BF 0.20 Hz
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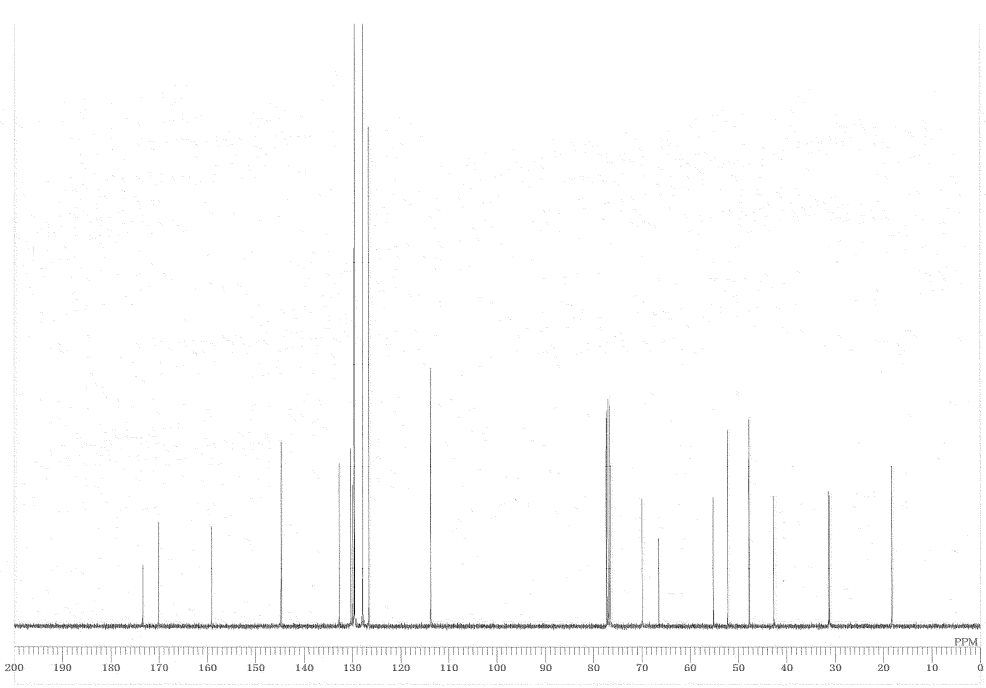
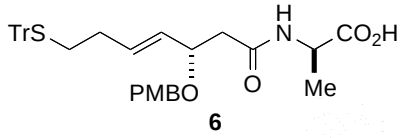
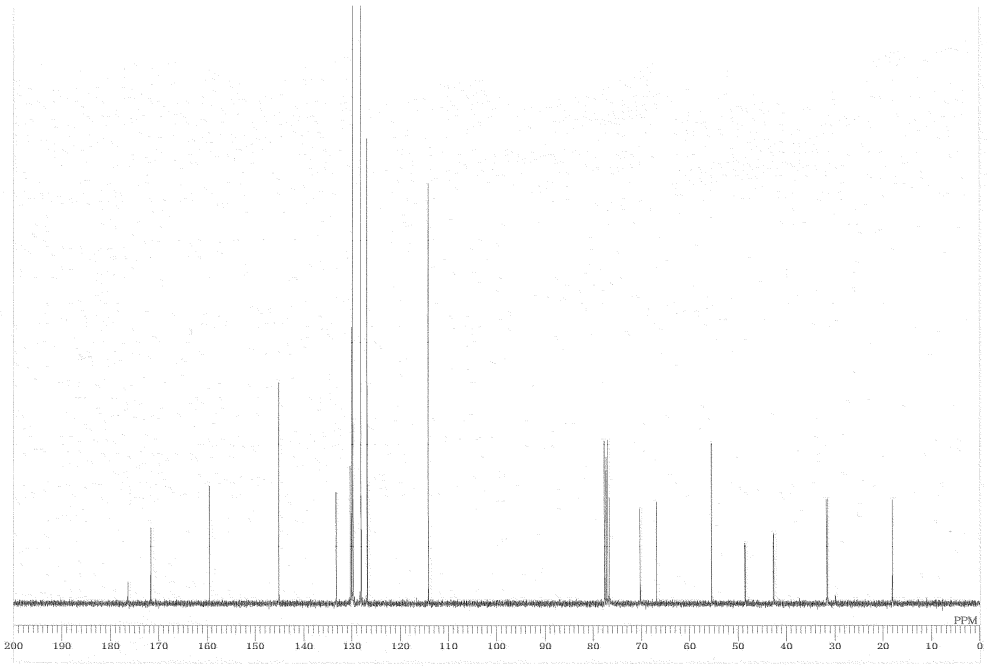

DFILE N-620 C-13 Jilia segm
COMNT N-620 C-13
DATIM Tue Oct 30 02:37:14 2
OBNUC 13C
EXMOD BCM
OBFRQ 99.45 MHz
OBSET 94.00 KHz
OBFIN 10309.00 Hz
POINT 32768
FREQU 26845.64 Hz
SCANS 1024
ACQTM 1.2206 sec
PD 1.7790 sec
PW1 5.20 usec
IRNUC 1H
CTEMP 25.0 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 0.20 Hz
RGAIN 23
PPM
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

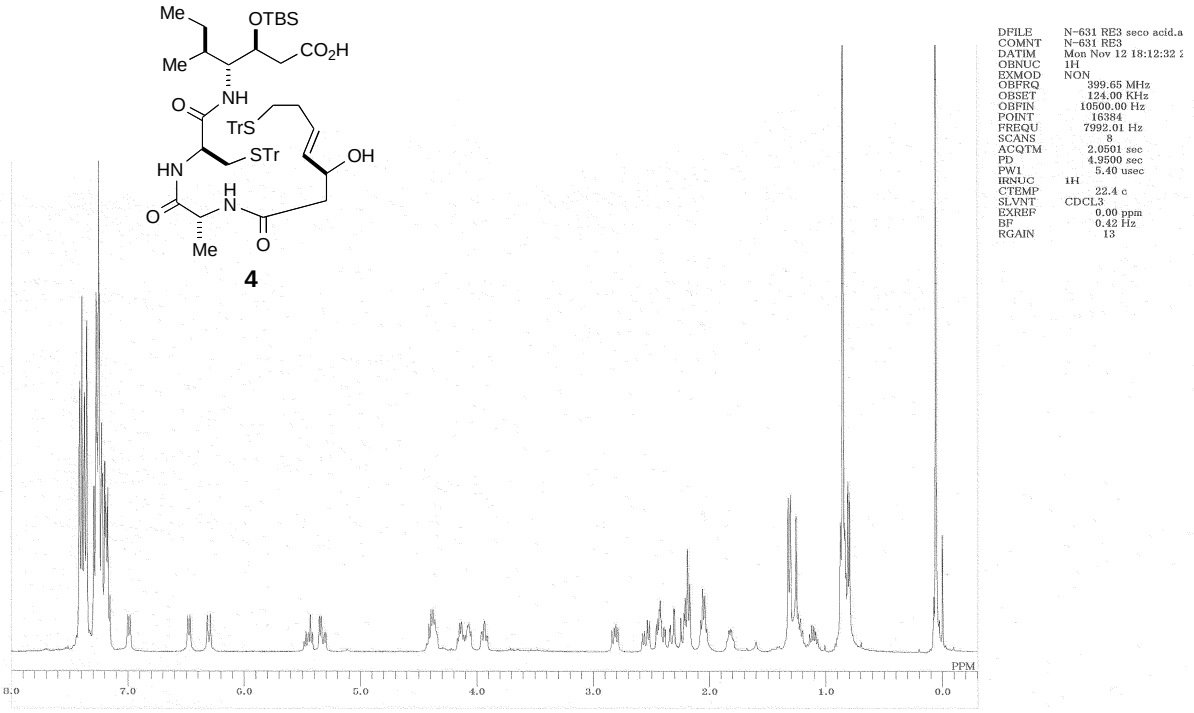


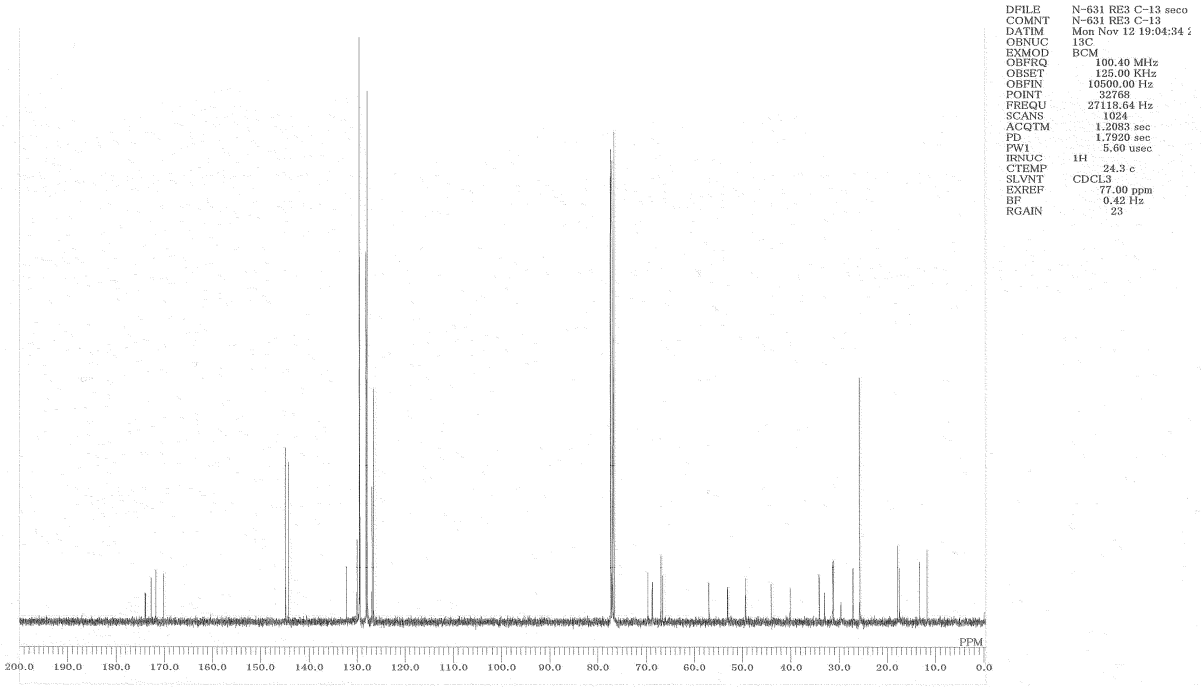
6

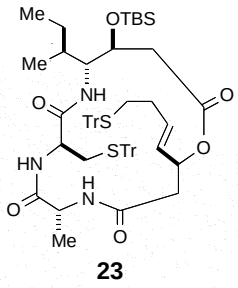

```
DFILE     N-624 Julia D-Ala-OH
COMNT     N-624
DATIM     Wed Oct 31 21:01:15 2
OBNUC     1H
EXMOD     NON
OBFRQ       399.65 MHz
OBSET       124.00 KHz
OBFIN     10500.00 Hz
POINT       16384
FREQU      7992.01 Hz
SCANS           8
ACQTM       2.0501 sec
PD          4.9500 sec
PW1          5.40 usec
IRNUC     1H
CTEMP       24.4 c
SLVNT     CDCL3
EXREF       0.00 ppm
BF          0.00 Hz
RGAIN         20
```




```
DFILE     N-624 C-13 Julia D-A
COMNT     N-624 C-13
DATIM     Wed Oct 31 21:37:58 2
OBNUC     13C
EXMOD     BCM
OBFRQ       100.40 MHz
OBSET       125.00 KHz
OBFIN     10500.00 Hz
POINT       32768
FREQU     27118.64 Hz
SCANS         566
ACQTM       1.2083 sec
PD          1.7920 sec
PW1          5.60 usec
IRNUC     1H
CTEMP       27.0 c
SLVNT     CDCL3
EXREF       77.00 ppm
BF          0.00 Hz
RGAIN         23
```

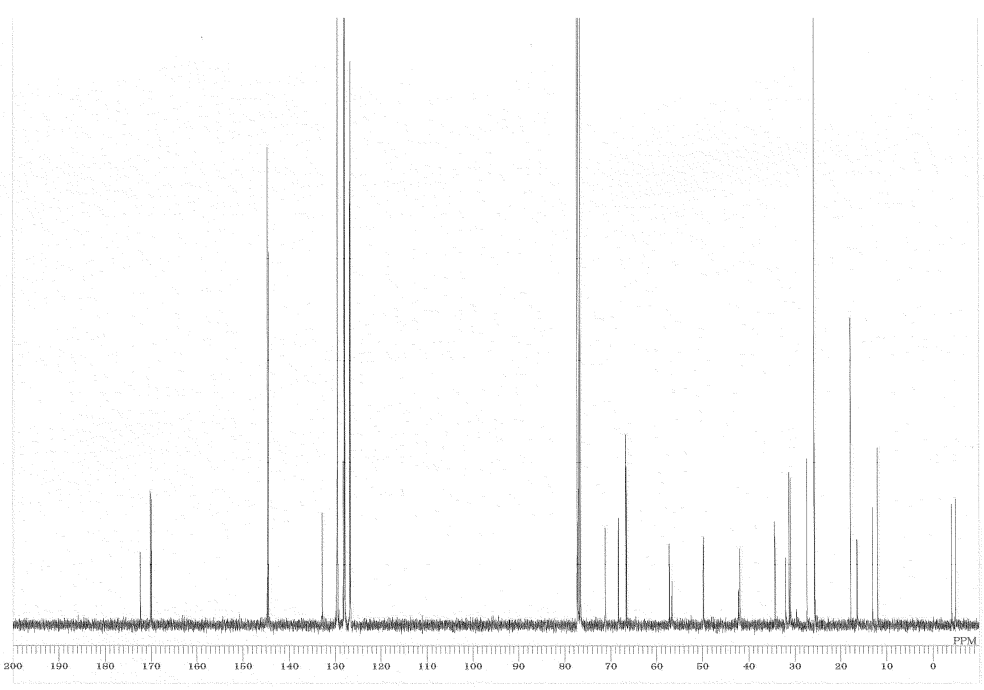

Me
OTBS
Me
CO_2H
O
NH
TrS
STr
OH
HN
H
N
O
Me
O
4
DFILE N-631 RE3 seco acid.a
COMNT N-631 RE3
DATIM Mon Nov 12 18:12:32
OBNUC 1H
EXMOD NON
OBFRQ 399.65 MHz
OBSET 124.00 KHz
OBFIN 10500.00 Hz
POINT 16384
FREQU 7992.01 Hz
SCANS 8
ACQTM 2.0501 sec
PD 4.9500 sec
PW1 5.40 usec
IRNUC 1H
CTEMP 22.4 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 0.42 Hz
RGAIN 13
PPM
8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0

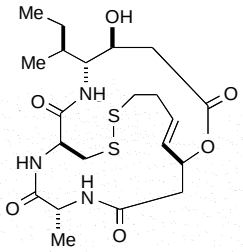

DFILE N-631 RE3 C-13 seco
COMNT N-631 RE3 C-13
DATIM Mon Nov 12 19:04:34
OBNUC 13C
EXMOD BCM
OBFRQ 100.40 MHz
OBSET 125.00 KHz
OBFIN 10500.00 Hz
POINT 32768
FREQU 27118.64 Hz
SCANS 1024
ACQTM 1.2083 sec
PD 1.7920 sec
PW1 5.60 usec
IRNUC 1H
CTEMP 24.3 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 0.42 Hz
RGAIN 23
PPM
200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0.0


Me
OTBS
Me
NH
O
TrS
O
STr
HN
H
N
O
O
Me
O

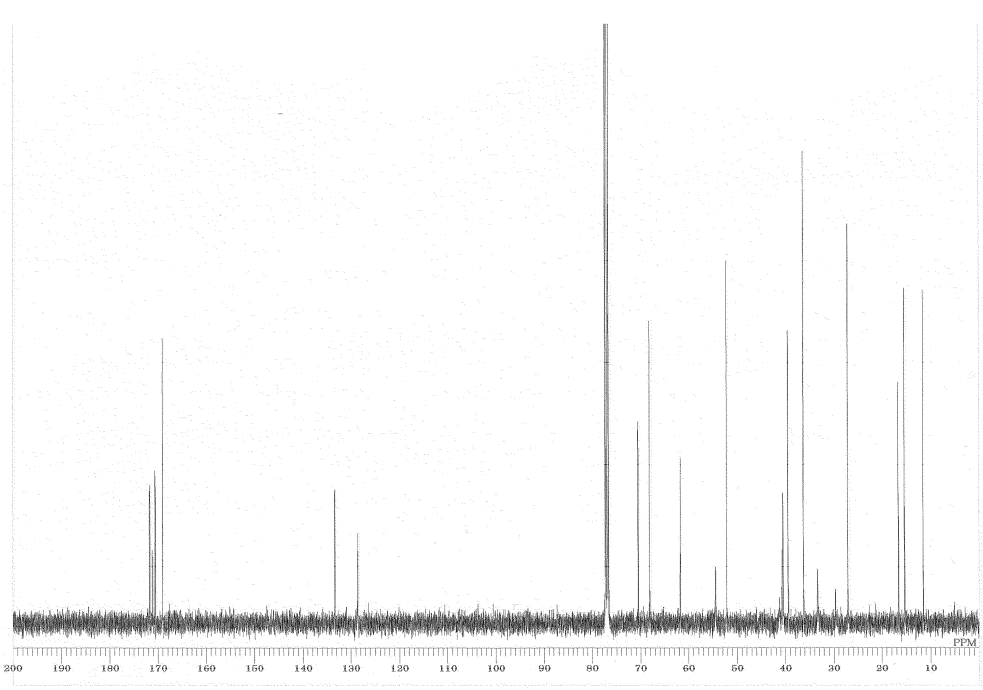
23

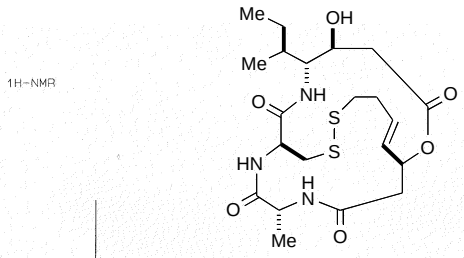
DFILE N-632 MNBA.als
COMNT N-632
DATIM Tue Nov 13 12:46:21 2
OBNUC 1H
EXMOD NON
OBFRQ 399.65 MHz
OBSET 124.00 KHz
OBFIN 10500.00 Hz
POINT 16384
FREQU 7992.01 Hz
SCANS 8
ACQTM 2.0501 sec
PD 4.9500 sec
PW1 5.40 usec
IRNUC 1H
CTEMP 22.6 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 0.42 Hz
RGAIN 10
PPM
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0


DFILE N-632 C-13 MNBA.als
COMNT N-632 C-13
DATIM Tue Nov 13 13:40:13 2
OBNUC 13C
EXMOD BCM
OBFRQ 100.40 MHz
OBSET 125.00 KHz
OBFIN 10500.00 Hz
POINT 32768
FREQU 27118.64 Hz
SCANS 1024
ACQTM 1.2083 sec
PD 1.7920 sec
PW1 5.60 usec
IRNUC 1H
CTEMP 25.2 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 0.42 Hz
RGAIN 23
PPM
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



spiruchostatin B (**2**) (synthetic)





spiruchostatin B (**2**) (natural)

[These charts were provided by Dr. K. Shin-ya.]


```
17-SEP-1998 18:16:57.31

DFILE : ALPHA
SFILE : XO9Q71576BH

COMNT : 1H-NMR
EXMOD : SINGL
IRMOD : NON
POINT :     16384
FREQU :  5000.00 Hz
SCANS :        16
DUMMY :         2
ACQTM :    3.2768 sec
PD    :    2.0000 sec
RGAIN :        19

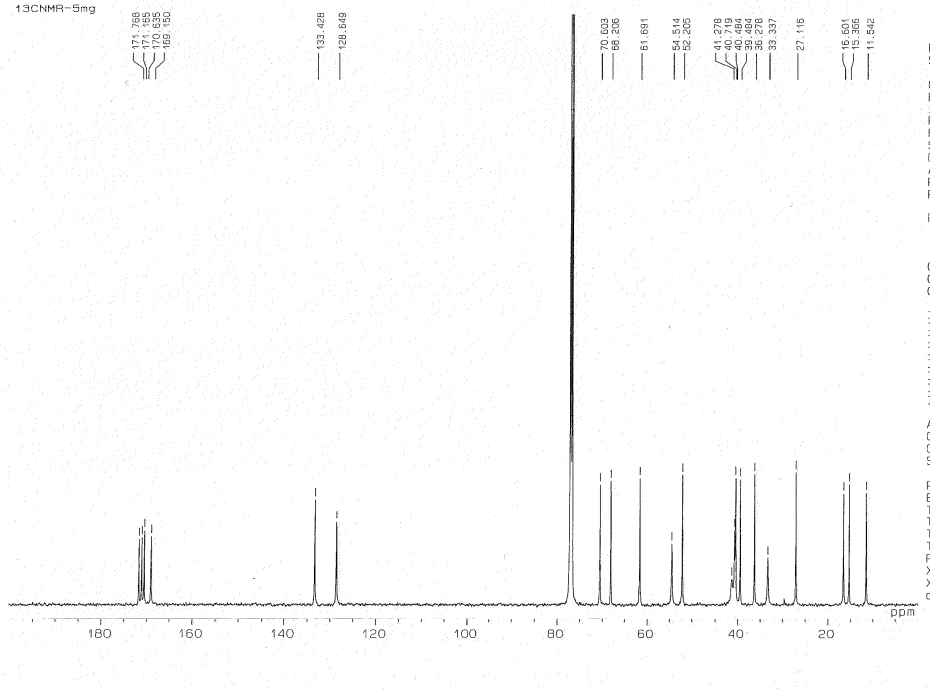
PW1   :    11.00 usec


OBNUC : 1H
OBFRQ :   500.00 MHz
OBSET : 162300.00 Hz

IRNUC : 1H
IRFRQ :   500.00 MHz
IRSET : 162300.00 Hz
IRATN :       160
IRRPW :    50.0 usec
IRBP1 :        25
IRBP2 :         4
IRRNS :         0

ADBIT :        16
CTEMP :      25.9 c
CSPED :        13 Hz
SLVNT : CDCL3

RESOL :      0.31 Hz
BF    :      0.20 Hz
T1    :      0.00 %
T2    :      0.00 %
T3    :     90.00 %
T4    :    100.00 %
REFVL :      7.24 ppm
XE    :   3901.06 Hz
XS    :    320.59 Hz
operator
```




```
18-SEP-1998 09:55:21.53

DFILE : ALPHA
SFILE : XO9Q71576BC

COMNT : 13CNMR-5mg
EXMOD : SINGL
IRMOD : BCM
POINT :     16384
FREQU : 30303.03 Hz
SCANS :     16220
DUMMY :         2
ACQTM :    0.5407 sec
PD    :    2.0000 sec
RGAIN :        23

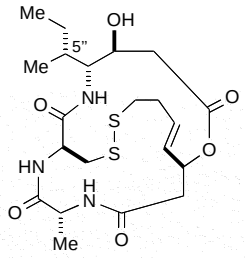
PW1   :     5.00 usec


OBNUC : 13C
OBFRQ :   125.65 MHz
OBSET : 129800.00 Hz

IRNUC : 1H
IRFRQ :   500.00 MHz
IRSET : 162300.00 Hz
IRATN :       160
IRRPW :    50.0 usec
IRBP1 :        25
IRBP2 :         4
IRRNS :         0

ADBIT :        16
CTEMP :      26.1 c
CSPED :        13 Hz
SLVNT : CDCL3

RESOL :      1.85 Hz
BF    :     10.00 Hz
T1    :      0.00 %
T2    :      0.00 %
T3    :     90.00 %
T4    :    100.00 %
REFVL :     77.00 ppm
XE    :  25150.18 Hz
XS    :   1910.59 Hz
operator
```



5”-*epi*-spiruchostatin B (5”-*epi*-**2**)