Organocatalytic asymmetric assembly reactions for syntheses of carbohydrate derivatives by intermolecular Michael-Henry reactions

*Hisatoshi Uehara, Ritsuo Imashiro, Gloria Hernández-Torres, and Carlos F. Barbas III**

Supporting Information

Table of Contents

1. General Experimental

^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker DRX-600 (600 MHz), Bruker DRX-500 (500 MHz), Bruker AMX-400 (400 MHz), Varian Inova-300 or 400 (300 or 400 MHz) spectrometers in $CDCl_3$. Spectra were referenced to tetramethylsilane (δ 0.00 ppm, ^{1}H) or residual chloroform (δ 7.26 ppm, ^{1}H; δ 77.23 ppm, ^{13}C). Chemical shifts were reported in parts per million (ppm) on the δ scale from an internal standard (NMR descriptions: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad). Coupling constants, *J*, are reported in Hertz.

Mass spectroscopy was performed by the Scripps Research Institute Mass Spectrometer Center. Analytical thin-layer chromatography and flash column chromatography were performed on Merck Kieselgel 60 F254 silica gel plates and Silica Gel ZEOprep 60 ECO 40-63 Micron, respectively. Visualization was accomplished with I_2 or anisaldehyde.

High performance liquid chromatography (HPLC) was performed on Hitachi L-7400 UV detector (λ = 220 nm) and Hitachi L-2490 RI detector using Daicel Chiralpak IC and AD-H columns. Retention times (t_R) and peak areas for HPLC were obtained from reporting integrators.

Unless otherwise noted, all the materials were obtained from commercial suppliers, and were used without further purification. All solvents were commercially available grade.

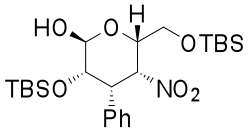
Catalysts **3** (ref. S1) and **8** (ref. S2) were prepared according to published procedures.

2. Experimental procedure

General procedure for 3,4-dideoxy-D-talose derivatives 6 (Table 2).

(*tert*-Butyldimethylsilyloxy)acetaldehyde **1** (152 μL, 0.8 mmol) was added to the solution of thiourea catalyst **3** (15.4 mg, 40 μmol) and nitroolefin **2** (0.2 mmol) in CH_2Cl_2 (0.2 mL). The resulting solution was stirred at 30 °C for T_1, and then triethylamine (13.9 μL, 0.1 mmol) was added. After T_2 at 30 °C, Et_2O and 1N HCl (0.2 mL) was added to the solution at rt. The aqueous layer was separated and extracted three times with Et_2O. The combined organic layers were dried over $MgSO_4$, concentrated, and purified by flash column chromatography to afford 3,4-dideoxy-D-talose derivative **6**.

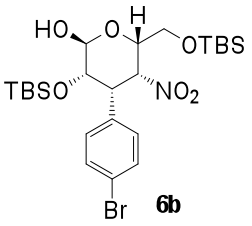
2,6-Bis-*O*-(*tert*-butyldimethylsilyl)-3,4-dideoxy-4-nitro-3-phenyl-α-D-talopyranose (6a)



6a

Colorless oil, yield 68%; Equilibrium mixture of **6a** and **5a** (3:1) in $CDCl_3$; ^1H NMR (500 MHz, $CDCl_3$) major (**6a**): δ 7.40 – 7.24 (m, 5H), 5.29 (brs, 1H), 4.79 (dd, *J* = 4.6, 2.5 Hz, 1H), 4.47 (ddd, *J* = 8.5, 6.2, 2.3 Hz, 1H), 3.90 (dd, *J* = 2.8, 1.4 Hz, 1H), 3.88 (dd, *J* = 9.9, 6.2 Hz, 1H), 3.84 (dd, *J* = 9.9, 8.6 Hz, 1H), 3.55 (dd, *J* = 4.7, 2.7 Hz, 1H), 3.03 (brs, 1H), 0.93 (s, 9H), 0.84 (s, 9H), 0.03 (s, 3H), 0.01 (s, 6H), -0.22 (s, 3H); minor (**5a**): δ 9.48 (brd, *J* = 1.1 Hz, 1H), 7.40 – 7.24 (m, 5H), 5.30 – 5.26 (m, 1H), 4.16 – 4.12 (m, 2H), 3.57 (dd, *J* = 9.3, 4.7 Hz, 1H), 3.55 – 3.51 (m, 1H), 3.46 (dd, *J* = 9.2, 6.0 Hz, 1H), 2.65 (brs, 1H), 0.96 (s, 9H), 0.86 (s, 9H), 0.02 (s, 3H), 0.01 (s, 3H), 0.00 (s, 3H), -0.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) major (**6a**): δ 137.19, 129.95, 128.38, 128.11, 95.08, 81.65, 69.98, 68.85, 62.44, 43.47, 26.00, 25.95, 18.41, 18.29, -4.43, -4.98, -5.46, -5.55; minor (**5a**): δ 202.86, 137.47, 129.33, 128.85, 128.46, 87.27, 80.13, 69.44, 63.51, 49.33, 25.93, 25.91, 18.33, 18.29, -4.26, -4.85, -5.51, -5.55; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{24}H_{44}NO_6Si_2^+$ 498.2702, found 498.2700; Enantiomeric excess: 98%, determined by HPLC after reduction to corresponding alcohol (Chiralpak IC, hexane/*i*-PrOH = 97:3, flow rate 1.00 mL/min, λ = 220 nm, rt): t_R (major) = 13.6 min, t_R (minor) = 15.2 min.

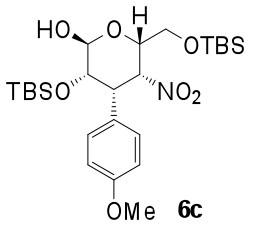
2,6-Bis-*O*-(*tert*-butyldimethylsilyl)-3-(4-bromophenyl)-3,4-dideoxy-4-nitro-α-D-talopyranose (6b)



6b

Colorless oil, yield 62%; Equilibrium mixture of **6b** and **5b** (4:1) in $CDCl_3$; ^1H NMR (**6b**, 400 MHz, $CDCl_3$) δ 7.46 – 7.42 (m, 2H), 7.27 – 7.23 (m, 2H), 5.28 (brs, 1H), 4.73 (dd, *J* = 4.5, 2.5 Hz, 1H), 4.48 – 4.41 (m, 1H), 3.91 – 3.81 (m, 3H), 3.52 (dd, *J* = 4.5, 2.8 Hz, 1H), 2.78 (brs, 1H), 0.93 (s, 9H), 0.84 (s, 9H), 0.03 (s, 6H), 0.00 (s, 3H), -0.18 (s, 3H); ^{13}C NMR (**6b**, 100 MHz, $CDCl_3$) δ 136.23, 131.64, 131.49, 122.32, 94.82, 81.25, 69.78, 68.71, 62.32, 42.89, 25.97, 25.90, 18.39, 18.27, -4.35, -4.82, -5.48, -5.59; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{24}H_{43}BrNO_6Si_2^+$ 576.1807, found 576.1812; Enantiomeric excess: 98%, determined by HPLC after reduction to corresponding alcohol (Chiralpak IC, hexane/*i*-PrOH = 97:3, flow rate 1.00 mL/min, λ = 220 nm, rt): t_R (major) = 12.4 min, t_R (minor) = 21.0 min.

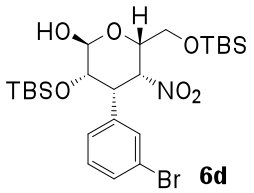
2,6-Bis-*O*-(*tert*-butyldimethylsilyl)-3,4-dideoxy-3-(4-methoxyphenyl)-4-nitro-α-D-talopyranose (6c)



6c

Colorless oil, yield 76%; Equilibrium mixture of **6c** and **5c** (3:1) in $CDCl_3$; ^{1}H NMR (**6c**, 500 MHz, $CDCl_3$) δ 7.29 – 7.25 (m, 2H), 6.86 – 6.80 (m, 2H), 5.27 (brs, 1H), 4.73 (dd, *J* = 4.7, 2.6 Hz, 1H), 4.45 (ddd, *J* = 8.6, 6.1, 2.4 Hz, 1H), 3.89 – 3.80 (m, 3H), 3.79 (s, 3H), 3.50 (dd, *J* = 4.6, 2.8 Hz, 1H), 3.29 (brs, 1H), 0.93 (s, 9H), 0.84 (s, 9H), 0.03 (s, 3H), 0.01 (s, 3H), 0.00 (s, 3H), -0.21 (s, 3H); ^{13}C NMR (**6c**, 100 MHz, $CDCl_3$) δ 159.38, 131.11, 129.33, 113.67, 95.05, 81.98, 70.27, 68.67, 62.40, 55.37, 42.67, 25.98, 25.94, 18.38, 18.25, -4.47, -4.90, -5.51, -5.59; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{25}H_{46}NO_7Si_2^+$ 528.2807, found 528.2807; Enantiomeric excess: 97%, determined by HPLC after reduction to corresponding alcohol (Chiralpak IC, hexane/*i*-PrOH = 95:5, flow rate 1.00 mL/min, λ = 220 nm, rt): t_R (major) = 15.5 min, t_R (minor) = 23.7 min.

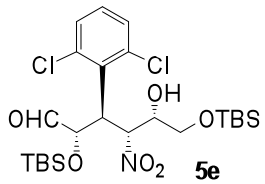
2,6-Bis-*O*-(*tert*-butyldimethylsilyl)-3-(3-bromophenyl)-3,4-dideoxy-4-nitro-α-D-talopyranose (6d)



6d

Colorless oil, yield 68%; Equilibrium mixture of **6d** and **5d** (6:1) in $CDCl_3$; H NMR (**6d**, 500 MHz, $CDCl_3$) δ 7.56 (t, *J* = 1.8 Hz, 1H), 7.45 (ddd, *J* = 8.0, 1.9, 1.0 Hz, 1H), 7.30 (m, 1H), 7.19 (t, *J* = 7.9 Hz, 1H), 5.28 (s, 1H), 4.74 (dd, *J* = 4.7, 2.5 Hz, 1H), 4.45 (td, *J* = 7.7, 2.5 Hz, 1H), 3.91 (dd, *J* = 2.5, 1.5 Hz, 1H), 3.89 – 3.85 (m, 2H), 3.53 (dd, *J* = 4.6, 2.7 Hz, 1H), 2.82 (brs, 1H), 0.95 (s, 9H), 0.84 (s, 9H), 0.05 (s, 3H), 0.03 (s, 3H), 0.01 (s, 3H), -0.13 (s, 3H); ^{13}C NMR (**6d**, 100 MHz, $CDCl_3$) δ 139.58, 132.83, 131.28, 129.93, 128.64, 122.52, 94.87, 81.17, 69.78, 68.90, 62.42, 43.14, 26.03, 25.95, 18.44, 18.33, -4.32, -4.82, -5.42, -5.54; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{24}H_{43}BrNO_6Si_2^+$ 576.1807, found 576.1807; Enantiomeric excess: 97%, determined by HPLC after reduction to corresponding alcohol (Chiralpak IC, hexane/*i*-PrOH = 98:2, flow rate 1.00 mL/min, λ = 220 nm, rt): t_R (major) = 34.0 min, t_R (minor) = 37.6 min.

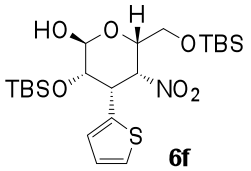
(2*S*,3*S*,4*R*,5*S*)-2,6-Bis(*tert*-butyldimethylsilyloxy)-3-(2,6-dichlorophenyl)-5-hydroxy-4-nitrohexanal (5e)



5e

White solid, yield 37%; ^{1}H NMR (500 MHz, $CDCl_3$) δ9.45 (d, *J* = 3.4 Hz, 1H), 7.40 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.32 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.23 (t, *J* = 8.0 Hz, 1H), 5.71 (dd, *J* = 10.1, 2.1 Hz, 1H), 5.21 (t, *J* = 10.2 Hz, 1H), 4.58 (dd, *J* = 10.1, 3.5 Hz, 1H), 3.61 (dd, *J* = 9.8, 5.4 Hz, 1H), 3.58 – 3.52 (m, 1H), 3.45 (dd, *J* = 9.8, 6.9 Hz, 1H), 2.39 (d, *J* = 8.1 Hz, 1H), 0.90 (s, 9H), 0.88 (s, 9H), 0.15 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.04, 138.50, 135.15, 131.46, 130.37, 130.04, 129.69, 86.67, 77.96, 70.48, 63.37, 43.71, 25.96, 18.33, 18.32, -4.45, -4.68, -5.42, -5.50; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{24}H_{42}Cl_2NO_6Si_2^+$ 566.1922, found 566.1936; Enantiomeric excess: 99%, determined by HPLC (Chiralpak AD-H, hexane/*i*-PrOH = 97:3, flow rate 1.00 mL/min, λ = 220 nm, rt): t_R (major) = 7.5 min, t_R (minor) = 9.2min.

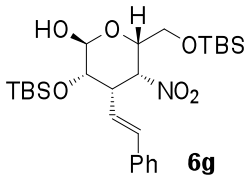
2,6-Bis-*O*-(*tert*-butyldimethylsilyl)-3,4-dideoxy-4-nitro-3-(thiophen-2-yl)-α-D-talopyranose (6f)



6f

Colorless oil, yield 63%; Equilibrium mixture of **6f** and **5f** (13:1) in $CDCl_3$; ^{1}H NMR (**6f**, 500 MHz, $CDCl_3$) δ 7.24 (dd, *J* = 5.1, 1.1 Hz, 1H), 7.08 (d, *J* = 3.0 Hz, 1H), 6.99 (dd, *J* = 5.2, 3.6 Hz, 1H), 5.32 (s, 1H), 4.76 (dd, *J* = 4.6, 2.5 Hz, 1H), 4.46 – 4.40 (m, 1H), 3.97 – 3.93 (m, 1H), 3.92 (dd, *J* = 2.7, 1.4 Hz, 1H), 3.89 – 3.84 (m, 2H), 2.87 (brs, 1H), 0.93 (s, 9H), 0.85 (s, 9H), 0.05 (s, 3H), 0.03 (s, 3H), 0.01 (s, 3H), -0.08 (s, 3H); ^{13}C NMR (**6f**, 100 MHz, $CDCl_3$) δ 138.39, 127.59, 126.90, 124.99, 94.67, 81.94, 70.26, 68.71, 62.45, 39.54, 26.01, 18.42, 18.36, -4.23, -4.64, -5.45, -5.54; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{22}H_{42}NO_6SSi_2^+$ 504.2266, found 504.2270; Enantiomeric excess: 97%, determined by HPLC after reduction to corresponding alcohol (Chiralpak AD-H, hexane/*i*-PrOH = 97:3, flow rate 1.00 mL/min, λ = 220 nm, rt): t_R (major) = 27.1 min, t_R (minor) = 20.2 min.

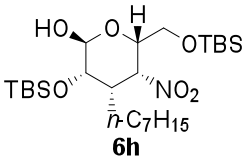
2,6-Bis-*O*-(*tert*-butyldimethylsilyl)-3,4-dideoxy-4-nitro-3-styryl-α-D-talopyranose (6g)



6g

Colorless oil, yield 68%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 – 7.37 (m, 2H), 7.32 (m, 3H), 6.61 (d, *J* = 15.9 Hz, 1H), 6.46 (dd, *J* = 15.9, 9.4 Hz, 1H), 5.19 (s, 1H), 4.54 (dd, *J* = 4.7, 2.0 Hz, 1H), 4.34 (ddd, *J* = 8.5, 6.2, 2.1 Hz, 1H), 4.00 (t, *J* = 9.2 Hz, 1H), 3.89 (dd, *J* = 9.8, 6.2 Hz, 1H), 3.75 – 3.70 (m, 1H), 3.15 (ddd, *J* = 9.3, 4.7, 2.6 Hz, 1H), 2.77 (brs, 1H), 0.90 (s, 9H), 0.85 (s, 9H), 0.04 (s, 6H), 0.02 (s, 3H), -0.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.98, 133.18, 128.89, 128.01, 126.73, 126.58, 94.94, 79.86, 70.65, 68.67, 62.48, 42.60, 26.04, 25.75, 18.45, 18.18, -4.44, -5.01, -5.38, -5.51; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{26}H_{46}NO_6Si_2^+$ 524.2858, found 524.2859; Enantiomeric excess: 93%, determined by HPLC after reduction to corresponding alcohol (Chiralpak IC, hexane/*i*-PrOH = 97:3, flow rate 1.00 mL/min, λ = 220 nm, rt): t_R (major) = 14.9 min, t_R (minor) = 12.1 min.

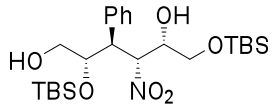
2,6-Bis-*O*-(*tert*-butyldimethylsilyl)-3,4-dideoxy-3-(*n*-heptyl)-4-nitro-α-D-talopyranose (6h)



6h

Colorless oil, yield 44%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.16 (s, 1H), 4.50 (d, *J* = 2.5 Hz, 1H), 4.22 (t, *J* = 8.4 Hz, 1H), 3.92 (t, *J* = 9.1 Hz, 1H), 3.84 (dd, *J* = 9.8, 6.2 Hz, 1H), 3.65 (s, 1H), 2.69 (brs, 1H), 2.24 (ddd, *J* = 8.8, 5.8, 3.5 Hz, 1H), 1.55 – 1.42 (m, 1H), 1.39 – 1.20 (m, 11H), 0.87 (t, *J* = 6.2 Hz, 3H), 0.86 (s, 9H), 0.86 (s, 9H), 0.05 (s, 3H), 0.03 (s, 3H), 0.02 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 94.97, 78.82, 69.14, 62.51, 38.68, 32.01, 29.77, 29.43, 29.15, 26.72, 26.00, 25.71, 22.85, 18.40, 18.16, 14.29, -4.31, -5.01, -5.39, -5.54; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{25}H_{54}NO_6Si_2^+$ 520.3484, found 520.3487; Enantiomeric excess: 96%, determined by HPLC after transformation into corresponding O-benzyl aldoxime (Chiralpak AD-H, hexane/*i*-PrOH = 99.5:0.5, flow rate 1.00 mL/min, λ = 220 nm, rt): t_R (major) = 19.9 min, t_R (minor) = 17.0 min.

Typical experimental procedure for (2*S*,3*S*,4*R*,5*S*)-2,6-Bis(*tert*-butyldimethylsilyloxy)-4-nitro-3-phenylhexane-1,5-diol (6a', for HPLC analysis)



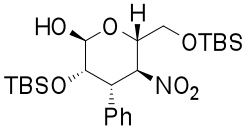
6a'

To a solution of 3,4-dideoxy-D-talose derivative **6a** (33.3 mg, 67 μmol) in MeOH (1.3 mL) was added $NaBH_4$ (12.7 mg, 340 μmol) at 0 °C. After stirring for 30 min, aqueous NH_4Cl and Et_2O were added. The aqueous layer was separated and extracted three times with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, concentrated, and purified by flash column chromatography to afford corresponding alcohol **6a'** as a colorless oil (18.2 mg, 34 μmol, yield 54%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.23 (m, 5H), 5.22 (dd, *J* = 11.4, 2.5 Hz, 1H), 4.07 (dd, *J* = 11.4, 6.1 Hz, 1H), 3.97 (ddd, *J* = 6.0, 5.3, 4.0 Hz, 1H), 3.57 – 3.44 (m, 3H), 3.43 – 3.33 (m, 2H), 2.54 (d, *J* = 8.5 Hz, 1H), 0.90 (s, 9H), 0.87 (s, 9H), 0.16 (s, 3H), 0.08 (s, 3H), 0.01 (s, 3H), -0.01 (s, 3H); ^{13}C NMR(100 MHz, $CDCl_3$) δ 137.09, 129.64, 129.11, 128.03, 88.73, 75.16, 70.02, 64.05, 63.57, 48.43, 26.10, 25.93, 18.34, 18.30, -4.37, -4.47, -5.48, -5.50; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{24}H_{46}NO_6Si_2^+$ 500.2858, found 500.2856.

General procedure for 3,4-dideoxy-D-mannose derivatives 7 (Table 3).

(*tert*-Butyldimethylsilyloxy)acetaldehyde **1** (152 μL, 0.8 mmol) was added to the solution of thiourea catalyst **3** (15.4 mg, 40 μmol) and nitroolefin **2** (0.2 mmol) in CH_2Cl_2 (0.2 mL). The resulting solution was stirred at 30 °C for T_1, and then DBU (15.0 μL, 0.1 mmol) was added. After T_2 at 30 °C, Et_2O and 1N HCl (0.2 mL) was added to the solution at rt. The aqueous layer was separated and extracted three times with Et_2O. The combined organic layers were dried over $MgSO_4$, concentrated, and purified by flash column chromatography to afford 3,4-dideoxy-D-mannose derivative **7**.

2,6-Bis-*O*-(*tert*-butyldimethylsilyl)-3,4-dideoxy-4-nitro-3-phenyl-α-D-mannopyranose (7a)

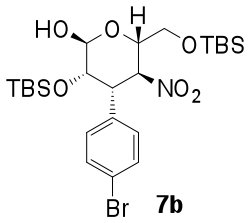


7a

Colorless oil, yield 51%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.21 (m, 5H), 5.47 (dd, *J* = 12.0, 9.8 Hz, 1H), 5.13 (d, *J* = 1.3 Hz, 1H), 4.47 (dt, *J* = 9.8, 3.5 Hz, 1H), 3.94 (dd, *J* = 12.0, 2.5 Hz, 1H), 3.82 – 3.77 (m, 2H), 3.74 (dd, *J* = 11.5, 3.9 Hz, 1H), 3.14 (brs, 1H), 0.93 (s, 9H), 0.83 (s, 9H), 0.08 (s, 3H),

0.08 (s, 3H), -0.21 (s, 3H), -0.57 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.18, 129.08, 128.60, 127.92, 94.33, 82.45, 72.45, 71.32, 63.15, 45.66, 26.07, 25.95, 18.53, 18.13, -5.22, -5.24, -5.47, -5.73; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{24}H_{44}NO_6Si_2^+$ 498.2702, found 498.2705; Enantiomeric excess: 98%, determined by HPLC (Chiralpak AD-H, hexane/*i*-PrOH = 99:1, flow rate 1.00 mL/min, λ = 220 nm, rt): t_R (major) = 11.6 min, t_R (minor) = 8.8 min.

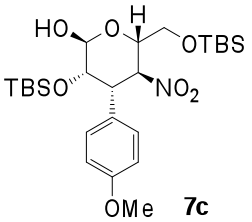
2,6-Bis-*O*-(*tert*-butyldimethylsilyl)-3-(4-bromophenyl)-3,4-dideoxy-4-nitro-α-D-mannopyranose (7b)



7b

Colorless oil, yield 65% ; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (m, 2H), 7.18 (m, 2H), 5.40 (dd, *J* = 12.0, 9.8 Hz, 1H), 5.13 (s, 1H), 4.47 – 4.40 (m, 1H), 3.89 (dd, *J* = 12.0, 2.4 Hz, 1H), 3.78 (dd, *J* = 11.4, 3.3 Hz, 1H), 3.77 (m, 1H), 3.72 (dd, *J* = 11.4, 3.6 Hz, 1H), 2.95 (brs, 1H), 0.92 (s, 9H), 0.84 (s, 9H), 0.07 (s, 3H), 0.07 (s, 3H), -0.16 (s, 3H), -0.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.23, 131.74, 130.84, 122.00, 94.15, 82.33, 72.09, 71.17, 63.03, 45.30, 26.05, 25.93, 18.51, 18.13, -5.12, -5.24, -5.50; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{24}H_{43}BrNO_6Si_2^+$ 576.1807, found 576.1803; Enantiomeric excess: 96%, determined by HPLC (Chiralpak AD-H, hexane/*i*-PrOH = 99:1, flow rate 1.00 mL/min, λ = 220 nm, rt): t_R (major) = 25.1 min, t_R (minor) = 15.7 min.

2,6-Bis-*O*-(*tert*-butyldimethylsilyl)-3,4-dideoxy-3-(4-methoxyphenyl)-4-nitro-α-D-mannopyranose (7c)

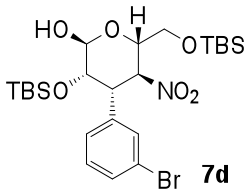


7c

Colorless oil, yield 48%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23-7.20 (m, 2H), 6.85-6.82 (m, 2H), 5.41 (dd, *J* = 11.9, 9.8 Hz, 1H), 5.13 (d, *J* = 1.0 Hz, 1H), 4.45 (dt, *J* = 9.6, 3.5 Hz, 1H), 3.86 (dd, *J* = 12.1, 2.4 Hz, 1H), 3.82 – 3.68 (m, 3H), 3.75 (s, 3H), 2.76 (d, *J* = 3.2 Hz, 1H), 0.92 (s, 9H), 0.85 (s, 9H), 0.07 (s, 6H), -0.18 (s, 3H), -0.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.32, 130.16, 128.10,

113.97, 94.35, 82.74, 72.32, 71.31, 63.10, 55.45, 44.93, 26.03, 25.95, 18.49, 18.12, -5.21, -5.52; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{25}H_{46}NO_7Si_2^+$ 528.2807, found 528.2627; Enantiomeric excess: 95%, determined by HPLC (Chiralpak AD-H, hexane/*i*-PrOH = 95:5, flow rate 1.00 mL/min, λ = 220 nm, rt): t_R (major) = 12.7 min, t_R (minor) = 9.4 min.

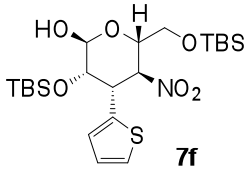
2,6-Bis-*O*-(*tert*-butyldimethylsilyl)-3-(3-bromophenyl)-3,4-dideoxy-4-nitro-α-D-mannopyranose (7d)



7d

Colorless oil, yield 57%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (brs, 1H), 7.40 (brd, *J* = 7.8 Hz, 1H), 7.34 – 7.12 (m, 2H), 5.40 (d, *J* = 10.7 Hz, 1H), 5.13 (brs, 1H), 4.45 (d, *J* = 9.2 Hz, 1H), 3.90 (d, *J* = 13.5 Hz, 1H), 3.79 – 3.74 (m, 3H), 2.79 (brs, 1H), 0.92 (s, 9H), 0.86 (s, 9H), 0.07 (s, 6H), -0.15 (s, 3H), -0.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.49, 132.11, 131.12, 130.15, 127.84, 122.66, 94.11, 82.33, 72.04, 71.11, 63.06, 45.44, 26.02, 25.89, 18.49, 18.11, -5.19, -5.26, -5.52, -5.61; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{24}H_{43}BrNO_6Si_2^+$ 576.1801, found 576.1801; Enantiomeric excess: 98%, determined by HPLC (Chiralpak AD-H, hexane/*i*-PrOH = 95:5, flow rate 1.00 mL/min, λ = 220 nm, rt): t_R (major) = 10.0 min, t_R (minor) = 8.7 min.

2,6-Bis-*O*-(*tert*-butyldimethylsilyl)-3,4-dideoxy-4-nitro-3-(thiophen-2-yl)-α-D-mannopyranose (7f)

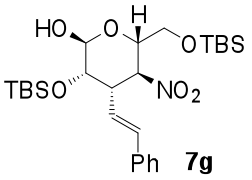


7f

Colorless oil, yield 59%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (d, *J* = 5.1 Hz, 1H), 6.99 – 6.86 (m, 2H), 5.27 (dd, *J* = 11.7, 9.9 Hz, 1H), 5.16 (s, 1H), 4.44 (dt, *J* = 9.8, 3.5 Hz, 1H), 4.24 (dd, *J* = 11.8, 2.4 Hz, 1H), 3.88 (s, 1H), 3.77 (dd, *J* = 11.5, 3.3 Hz, 1H), 3.72 (dd, *J*= 11.4, 3.8 Hz, 1H), 2.84 (brs, 1H), 0.91 (s, 9H), 0.88 (s, 9H), 0.06 (s, 6H), -0.09 (s, 3H), -0.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.08, 126.99, 126.83, 125.20, 94.02, 84.26, 72.05, 71.33, 63.15, 41.59, 26.05, 18.52, 18.22, -4.95, -5.25, -5.50; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{22}H_{42}NO_6SSi_2^+$ 504.2266, found 504.2267; Enantiomeric

excess: 96%, determined by HPLC (Chiralpak AD-H, hexane/*i*-PrOH = 99:1, flow rate 1.00 mL/min, λ = 220 nm, rt): t_R (major) = 33.7 min, t_R (minor) = 19.6 min.

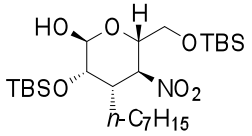
2,6-Bis-*O*-(*tert*-butyldimethylsilyl)-3,4-dideoxy-4-nitro-3-styryl-α-D-mannopyranose (7g)



7g

Colorless oil, yield 66% ; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 – 7.18 (m, 5H), 6.49 (d, *J* = 16.0 Hz, 1H), 6.19 (dd, *J* = 16.0, 9.3 Hz, 1H), 5.08 (d, *J* = 1.3 Hz, 1H), 4.94 (dd, *J* = 11.2, 10.2 Hz, 1H), 4.43 (dt, *J* = 10.1, 3.6 Hz, 1H), 3.87 – 3.82 (m, 1H), 3.76 – 3.69 (m, 2H), 3.36 (ddd, *J* = 11.7, 9.5, 2.5 Hz, 1H), 0.95 (s, 9H), 0.90 (s, 9H), 0.06 (s, 3H), 0.05 (s, 6H) , 0.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.64, 134.74, 128.78, 128.06, 126.71, 124.36, 94.09, 84.04, 71.37, 70.32, 63.32, 44.59, 26.07, 25.96, 18.53, 18.27, -4.52, -4.58, -5.25, -5.51. HRMS (*m/z*): $[M+H]^+$ calcd for $C_{26}H_{46}NO_6Si_2^+$ 524.2858, found 524.2860; Enantiomeric excess: 93%, determined by HPLC (Chiralpak AD-H, hexane/*i*-PrOH = 99:1, flow rate 1.00 mL/min, λ = 220 nm, rt): t_R (major) = 20.4 min, t_R (minor) = 16.9 min.

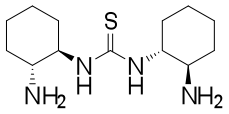
2,6-Bis-*O*-(*tert*-butyldimethylsilyl)-3,4-dideoxy-3-(*n*-heptyl)-4-nitro-α-D-mannopyranose (7h)



7h

Colorless oil, yield 50% ; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.08 (s, 1H), 4.67 (t, *J* = 11.3 Hz, 1H), 4.33 (dt, *J* = 10.0, 3.7 Hz, 1H), 3.84 (t, *J* = 2.0 Hz, 1H), 3.68 – 3.64 (m, 2H), 2.82 (brs, 1H), 2.51 (tt, *J* = 11.3, 2.8 Hz, 1H), 1.59 – 1.50 (m, 1H), 1.40 – 1.06 (m, 11H), 0.90 (s, 9H), 0.88 (s, 9H), 0.86 (t, *J* = 7.1 Hz, 3H), 0.08 (s, 3H), 0.07 (s, 3H), 0.03 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 94.00, 85.63, 70.81, 68.21, 63.40, 39.16, 31.96, 29.60, 29.39, 26.79, 26.15, 26.04, 25.91, 22.81, 18.51, 18.25, 14.26, -4.20, -4.70, -5.31, -5.54; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{25}H_{54}NO_6Si_2^+$ 520.3484, found 520.3483; Enantiomeric excess: 96%, determined by HPLC (Chiralpak AD-H, hexane/*i*-PrOH = 99:1, flow rate 0.50 mL/min, rt, RI): t_R (major) = 15.6 min, t_R (minor) = 11.1 min.

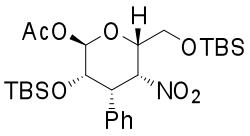
1,3-Bis((1*R*,2*R*)-2-aminocyclohexyl)thiourea (11)



11

A mixture of 1,3-bis((1*R*,2*R*)-2-(1,3-dioxoisoindolin-2-yl)cyclohexyl)thiourea (1.06 g, 2 mmol) (ref. S3) and hydrazine hydrate (485 μL, 10 mmol) in EtOH (10.6 mL) was refluxed for 1 h. After the reaction mixture was cooled to rt and filtered. The filtrate was evaporated and the residue was purified by flash column chromatography to afford **11** as colorless crystals (266 mg, 0.983 mmol, yield 49%).^{1}H NMR (300 MHz, $CDCl_3$) δ 2.60-2.52 (m, 2H), 2.13 – 2.03 (m, 2H), 1.98 – 1.84 (m, 2H), 1.84 – 1.35 (m, 10H), 1.32 – 1.14 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.92, 62.06, 56.20, 32.62, 25.07, 25.00; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{13}H_{27}N_4S^+$ 271.1951, found 271.1949.

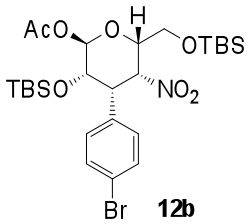
Acetylation of 3,4-dideoxy-D-talose derivatives 6: 1-*O*-Acetyl-2,6-bis-*O*-(*tert*-butyldimethylsilyl)-3,4-dideoxy-4-nitro-3-phenyl-α-D-talopyranose (12a)



12a

To a solution of 3,4-dideoxy-D-talose derivative **6a** (192 mg, 0.39 mmol) in pyridine (0.5 mL) was added Ac_2O (0.5 mL) at rt. After stirring for 40 min, toluene was added to the mixture and resulting solution was concentrated in vacuo. The residue was purified by flash column chromatography to afford acetyl talopyranose derivative **12a** as a colorless oil (128 mg, 0.24 mmol, yield 61%).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.30 (m, 5H), 6.19 (brs, 1H), 4.85 (dd, *J* = 4.6, 2.6 Hz, 1H), 4.31 (ddd, *J* = 8.6, 6.1, 2.5 Hz, 1H), 3.94 – 3.83 (m, 3H), 3.47 (dd, *J* = 4.6, 2.8 Hz, 1H), 2.16 (s, 3H), 0.94 (s, 9H), 0.84 (s, 9H), 0.10 (s, 3H), 0.03 (s, 3H), 0.01 (s, 3H), -0.18 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.95, 136.62, 129.79, 128.47, 128.35, 93.98, 80.91, 71.07, 68.91, 62.05, 44.03, 25.95, 25.89, 21.36, 18.35, 18.27, -4.38, -5.05, -5.51, -5.63; HRMS (*m/z*): $[M+Na]^+$ calcd for $C_{26}H_{45}NNaO_7Si_2^+$ 562.2627, found 562.2626.

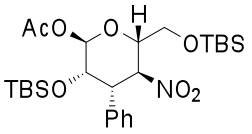
1-*O*-Acetyl-2,6-bis-*O*-(*tert*-butyldimethylsilyl)-3-(4-bromophenyl)-3,4-dideoxy-4-nitro-α-D-talopyranose (12b)



12b

Colorless oil, yield 56%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.44 (m, 2H), 7.29 – 7.24 (m, 2H), 6.17 (brs, 1H), 4.79 (dd, *J* = 4.5, 2.6 Hz, 1H), 4.29 (ddd, *J* = 8.6, 6.2, 2.5 Hz, 1H), 3.93 – 3.83 (m, 3H), 3.43 (dd, *J* = 4.5, 2.8 Hz, 1H), 2.16 (s, 3H), 0.93 (s, 9H), 0.83 (s, 9H), 0.11 (s, 3H), 0.03 (s, 3H), -0.00 (s, 3H), -0.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.86, 135.66, 131.59, 131.49, 122.57, 93.71, 80.61, 70.94, 68.76, 61.97, 43.51, 25.93, 25.86, 21.34, 18.33, 18.27, -4.33, -4.90, -5.51, -5.66; HRMS (*m/z*): $[M+Na]^+$ calcd for $C_{26}H_{44}BrNNaO_7Si_2^+$ 618.1732, found 618.1732.

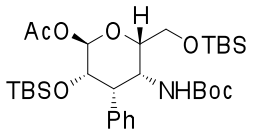
Epimerization of 12a: 1-*O*-Acetyl-2,6-bis-*O*-(*tert*-butyldimethylsilyl)-3,4-dideoxy-4-nitro-3-phenyl-α-D-mannopyranose (13a)



13a

To a solution of acetyl talopyranose derivative **12a** (28 mg, 52 μmol) in CH_2Cl_2 (0.1 mL) was added DBU (3.9 μL, 26 μmol) at 30 °C. After 0.5 h at 30 °C, Et_2O and 1N HCl (0.1 mL) was added to the solution at rt. The aqueous layer was separated and extracted three times with Et_2O. The combined organic layers were dried over $MgSO_4$, concentrated, and purified by flash column chromatography to afford acetyl mannopyranose derivative **13a** as a colorless oil (22 mg, 40 μmol, yield 77%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.23 (m, 5H), 5.99 (d, *J* = 1.6 Hz, 1H), 5.56 (dd, *J* = 12.0, 9.9 Hz, 1H), 4.30 (dt, *J* = 9.8, 3.3 Hz, 1H), 3.82 (dd, *J* = 11.4, 3.5 Hz, 1H), 3.81 (dd, *J* = 12.0, 2.7 Hz, 1H), 3.77 – 3.74 (m, 1H), 3.72 (dd, *J* = 11.6, 3.3 Hz, 1H), 2.23 (s, 3H), 0.92 (s, 9H), 0.84 (s, 9H), 0.07 (s, 6H), -0.13 (s, 3H), -0.57 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.18, 135.45, 129.03, 128.70, 128.20, 93.36, 81.77, 73.35, 71.23, 62.71, 46.41, 26.00, 25.91, 21.41, 18.43, 18.09, -5.24, -5.28, -5.54, -5.84; HRMS (*m/z*): $[M+Na]^+$ calcd for $C_{26}H_{45}NNaO_7Si_2^+$ 562.2627, found 562.2620.

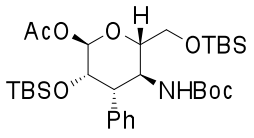
Reduction of 12a: 1-*O*-Acetyl-4-(*tert*-butoxycarbonylamino)-2,6-bis-*O*-(*tert*-butyldimethylsilyl)-3,4-dideoxy-3-phenyl-α-D-talopyranose (14)



14

A solution of acetyl talopyranose derivative **12a** (7.0 mg, 13 μmol) in AcOH (0.3 mL) was added to Zn (24mg, 0.37 mmol, activated by 1N HCl then washed with H_2O, EtOH, Et_2O) at rt. After stirring for 1 h, Et_2O, saturated aqueous $NaHCO_3$ and Na_2CO_3 were added to the solution at rt. The aqueous layer was separated and extracted three times with Et_2O. The combined organic layers were dried over $MgSO_4$, concentrated, and purified by short column chromatography to afford corresponding primary amine, which was used to the next reaction without further purification. To a solution of the amine in Et_2O (0.5 mL), Boc_2O (15 mg, 68 μmol) was added at rt. After stirring for 16 h, the mixture was concentrated, and purified by flash column chromatography to afford 4-amino-3,4-dideoxy-3-phenyl-D-talose derivative **14** as a colorless oil (4.3 mg, 7.1 μmol, yield 54%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.35 (m, 2H), 7.32 – 7.18 (m, 3H), 6.24 (d, J = 9.9 Hz, 1H), 6.07 (d, J = 1.3 Hz, 1H), 4.25 (brd, J = 9.5 Hz, 1H), 4.09 (ddd, J = 6.5, 5.0, 1.5 Hz, 1H), 4.00 (dt, J = 2.5, 1.3 Hz, 1H), 3.84 (dd, J = 10.9, 4.9 Hz, 1H), 3.69 (dd, J = 10.9, 6.8 Hz, 1H), 3.20 (t, J = 2.6 Hz, 1H), 2.15 (s, 3H), 1.40 (s, 9H), 0.89 (s, 9H), 0.85 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H), -0.30 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.37, 155.77, 138.96, 128.56, 128.40, 127.10, 94.51, 78.95, 76.55, 71.42, 63.48, 48.26, 42.34, 28.61, 26.13, 25.92, 21.40, 18.56, 17.96, -4.36, -5.11, -5.14, -5.55; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{31}H_{56}NO_7Si_2^+$ 610.3590, found 610.3592.

Reduction of 13a: 1-*O*-Acetyl-4-(*tert*-butoxycarbonylamino)-2,6-bis-*O*-(*tert*-butyldimethylsilyl)-3,4-dideoxy-3-phenyl-α-D-mannopyranose (15)

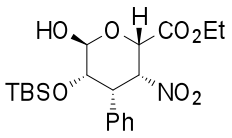


15

To a solution of acetyl mannopyranose derivative **13a** (12.3 mg, 23 μmol) in EtOH (0.3 mL) was added Raney Ni (c.a. 50mg, washed with EtOH) in EtOH (0.3 mL) at rt. After stirring for 24 h under hydrogen atmosphere at rt, Boc_2O (15 mg, 68 μmol) was added to the solution. After stirring for 24 h at rt, the mixture was filtered through Celite. The filtrate was concentrated, and purified by flash

column chromatography to afford 4-amino-3,4-dideoxy-3-phenyl-D-mannose derivative **15** as a colorless oil (11.0 mg, 18 μmol, yield 79%).^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30 – 7.19 (m, 5H), 5.96 (brs, 1H), 4.28 (brq, *J* = 10.4 Hz, 1H), 4.17 (brd, *J* = 9.5 Hz, 1H), 3.88 (brd, *J* = 10.4 Hz, 1H), 3.85 – 3.77 (m, 2H), 3.72 (brs, 1H), 3.19 (brd, *J* = 11.6 Hz, 1H), 2.16 (s, 3H), 1.28 (brs, 9H), 0.91 (s, 9H), 0.81 (brs, 9H), 0.08 (s, 3H), 0.08 (s, 3H), -0.15 (s, 3H), -0.63 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.01, 156.18, 138.89, 130.17, 128.92, 127.71, 94.43, 80.14, 77.82, 72.52, 64.90, 48.25, 45.54, 29.02, 26.84, 26.60, 22.08, 19.26, 18.74, -4.27, -4.41, -4.53, -5.26; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{31}H_{56}NO_7Si_2^+$ 610.3590, found 610.3591.

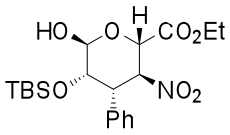
Tandem *anti*-Michael–Henry reaction: (2*S*,3*R*,4*S*,5*S*,6*S*)-Ethyl 5-((*tert*-butyldimethylsilyl)oxy)-6-hydroxy-3-nitro-4-phenyltetrahydro-2*H*-pyran-2-carboxylate (17)



17

(*tert*-Butyldimethylsilyloxy)acetaldehyde **1** (304 μL, 1.6 mmol) was added to the solution of thiourea catalyst **3** (31 mg, 0.08 mmol) and β-nitrostyrene **2a** (60 mg, 0.4 mmol) in CH_2Cl_2 (0.4 mL). The resulting solution was stirred at 30 °C for 8 h. To the reaction mixture was added 50% ethyl glyoxylate in toluene solution (317 μl, 1.6 mmol), and then triethylamine (28 μL, 0.2 mmol) at rt. After 0.5 h at rt, sat NH_4Claq. was added to the solution at rt. The mixture was extracted three times with AcOEt. The combined organic layers were dried over Na_2SO_4, concentrated, and purified by flash column chromatography to afford **17** as a colorless oil (91.6 mg, 215 mmol, yield 54%). Equilibrium mixture of **17** and its open form (3:1) in $CDCl_3$. ^{1}H NMR (**17**, 300 MHz, $CDCl_3$) δ 7.49 – 7.29 (m, 5H), 5.48 (m, 1H), 5.13 (m, 1H), 4.93 (d, *J* = 2.3 Hz, 1H), 4.47 – 4.11 (m, 3H), 4.06 (*J* = 3.2 Hz, 1H), 3.83 (d, *J* = 3.6 Hz, 1H), 1.25 (t, *J* = 7.1 Hz, 3H), 0.91 (9H), 0.13 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (**17**, 100 MHz, $CDCl_3$) δ 168.50, 137.74, 129.11, 128.34, 127.81, 94.72, 81.34, 69.69, 68.17, 43.01, 25.81, 18.31, 14.18, -3.66, -4.61; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{20}H_{32}NO_7Si^+$ 426.1942, found 426.1946. Enantiomeric excess: 98%, determined by HPLC after reduction to corresponding alcohol (Chiralpak AD-H, hexane/*i*-PrOH = 90:10, flow rate 1.00 mL/min, λ = 220 nm, rt): t_R (major) = 24.4 min, t_R (minor) = 22.0 min.

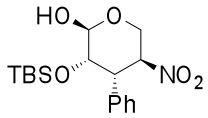
(2*S*,3*S*,4*S*,5*S*,6*S*)-Ethyl 5-((*tert*-butyldimethylsilyl)oxy)-6-hydroxy-3-nitro-4-phenyltetrahydro-2*H*-pyran-2-carboxylate (18)



18

(*tert*-Butyldimethylsilyloxy)acetaldehyde **1** (152 μL, 0.8 mmol) was added to the solution of thiourea catalyst **3** (15.8 mg, 0.04 mmol) and β-nitrostyrene **2a** (30 mg, 0.2 mmol) in CH_2Cl_2 (0.2 mL). The resulting solution was stirred at 30 °C for 5 h. To the reaction mixture was added 50% ethyl glyoxylate in toluene solution (159 μl, 0.8 mmol), and then DBU (60 μL, 0.4 mmol) at 30 °C. After 1 h at rt, sat NH_4Claq. was added to the solution at rt. The mixture was extracted three times with AcOEt. The combined organic layers were dried over Na_2SO_4, concentrated, and purified by flash column chromatography to afford **18** as a colorless oil (62.0 mg, 148 mmol, yield 74%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.29 (m, 5H), 5.43 (dd, *J* = 11.9, 10.2 Hz, 1H), 5.23 (dd, *J* = 3.4, 1.2 Hz, 1H), 5.09 (d, *J* = 10.2 Hz, 1H), 4.42 – 4.17 (m, 2H), 4.39 – 4.19 (m, 2H), 3.91 (dd, *J* = 11.9, 2.5 Hz, 1H), 3.85 – 3.79 (m, 1H), 3.20 (d, *J* = 3.7 Hz, 1H), 1.29 (t, *J* = 7.1 Hz, 1H), 0.85 (s, 9H), -0.20 (s, 3H), -0.54 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.02, 135.16, 129.16, 128.65, 128.22, 94.50, 82.29, 72.03, 69.61, 62.61, 46.02, 25.96, 18.08, 14.06, -5.19, -5.72; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{20}H_{32}NO_7Si^+$ 426.1944, found 426.1946. Enantiomeric excess: 98%, determined by HPLC after reduction to corresponding alcohol (Chiralpak AD-H, hexane/*i*-PrOH = 95:5, flow rate 1.00 mL/min, λ = 220 nm, rt): t_R (major) = 9.3 min, t_R (minor) = 11.1 min.

(2*S*,3*S*,4*S*,5*S*)-3-((*tert*-Butyldimethylsilyl)oxy)-5-nitro-4-phenyltetrahydro-2*H*-pyran-2-ol (19)

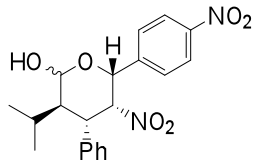


19

To a solution of chiral aldehyde **4a** (58 mg, 0.18 mmol) in CH_2Cl_2 (0.2 mL) was added 37% aqueous formaldehyde (9.9 μl, 0.358 mmol), and then triethylamine (13.9 μL, 0.1 mmol) was added to the mixture. After 1 h at rt, 37% aqueous formaldehyde (15 μl, 0.537 mmol) was further added. The readtion mixture was stirred for further 3 h at rt. To the mixture was added sat NH_4Claq at rt. The mixture was extracted three times with AcOEt. The combined organic layers were dried over Na_2SO_4, concentrated, and purified by flash column chromatography to afford **19** as a colorless oil (21.4 mg, 0.0605 mmol, yield 34%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.28 (m, 5H), 5.50 (dt, *J* = 5.0, 11.4

Hz, 1H), 5.09 (brs, 1H), 4.35 (t, *J* = 10.5 Hz, 1H), 4.17 (d, *J* = 4.7 Hz, 1H), 4.15 (brs, 1H), 2.73 (brs, 1H), 0.83 (s, 9H), -0.22 (s, 3H), -0.57 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.49, 128.72, 128.64, 127.86, 94.04, 81.12, 72.61, 61.53, 44.74, 25.91, 18.11, -5.33, -5.77; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{17}H_{28}NO_5Si^+$ 376.1551, found 376.1555. Enantiomeric excess: 97%, determined by HPLC after reduction to corresponding alcohol (Chiralpak AD-H, hexane/*i*-PrOH = 95:5, flow rate 1.00 mL/min, λ = 220 nm, rt): t_R (major) = 21.7 min, t_R (minor) = 15.5 min.

Tandem *syn*-Michael–Henry reaction: (3*R*,4*S*,5*R*,6*R*)-3-Isopropyl-5-nitro-6-(4-nitrophenyl)-4-phenyltetrahydro-2*H*-pyran-2-ol (24)

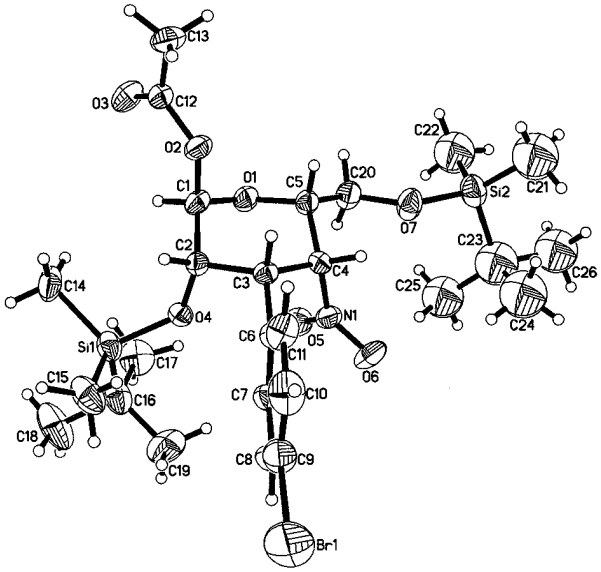


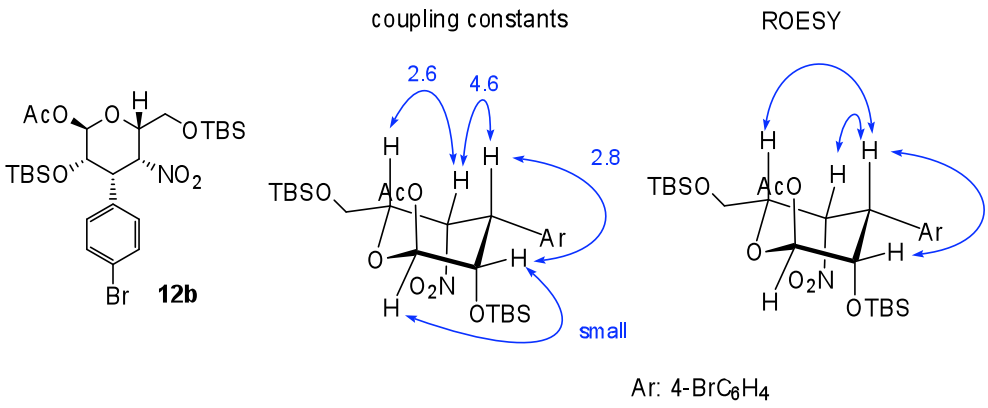
24

Isovaleraldehyde **20** (64 μL, 0.6 mmol) was added to a solution of diphenylprolinol TMS ether **21** (6.5 mg, 20 μmol) and β-nitrostyrene **2a** (29.8 mg, 0.2 mmol) in CH_2Cl_2 (0.2 mL). The resulting solution was stirred at rt for 18 h, and then 4-nitrobenzaldehyde (90.7 mg, 0.6 mmol) and triethylamine (13.9 μL, 0.1 mmol) were added. After 4 h at rt, the reaction mixture was directly subjected to flash column chromatography to afford (3*R*,4*S*,5*R*,6*R*)-3-isopropyl-5-nitro-6-(4-nitrophenyl)-4-phenyltetrahydro-2H-pyran-2-ol **24** as a white solid (59.5 mg, 154 μmol, yield 77%). Anomeric mixture (4:1) in $CDCl_3$; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 – 8.10 (m, 2H), 7.53 – 7.48 (m, 2H), 7.34 – 7.25 (m, 3H), 7.22 – 7.16 (m, 2H), 5.79 (d, *J* = 2.7 Hz, 1H), 5.72 (d, *J* = 2.9 Hz, 1H), 5.01 – 4.95 (m, 1H), 3.82 (dd, *J* = 12.9, 4.5 Hz, 1H), 3.21 – 3.14 (m, 1H), 3.10 (brs, 1H), 1.84 – 1.77 (m, 1H), 1.04 (d, *J* = 7.1 Hz, 3H), 0.83 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.87, 143.77, 136.29, 129.28, 128.38, 128.31, 126.98, 123.90, 93.84, 91.56, 68.84, 41.97, 38.72, 26.35, 20.32, 16.92; HRMS (*m/z*): $[M+Na]^+$ calcd for $C_{20}H_{22}N_2NaO_6^+$ 409.1370, found 409.1369; Enantiomeric excess: 99%, determined by HPLC (Chiralpak AD-H, hexane/*i*-PrOH = 80:20, flow rate 0.80 mL/min, λ = 220 nm, rt): t_R (major) = 27.8 min, t_R (minor) = 15.1 min.

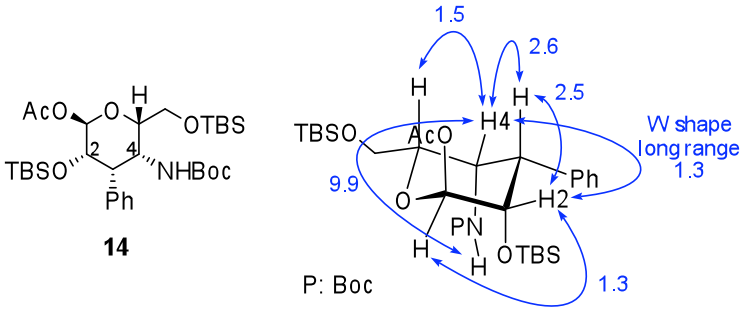
3. Determination of the absolute and relative configurations

The absolute and relative structure of D-talopyranose derivative **12b** was unambiguously determined by X-ray crystallography as shown below. For reference, coupling constants (Hz) and important ROESY crosspeaks of **12b** are depicted. In its chair-like conformation, there was no axial-axial orientation of *gem*-protons, which resulted in relatively small coupling constants.

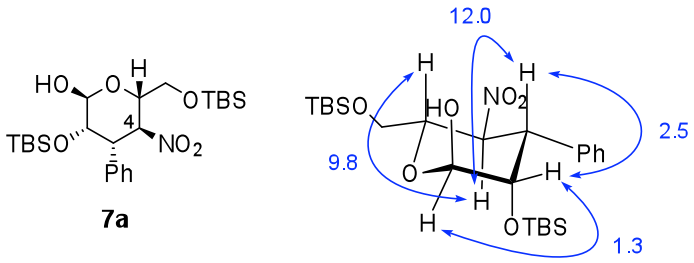




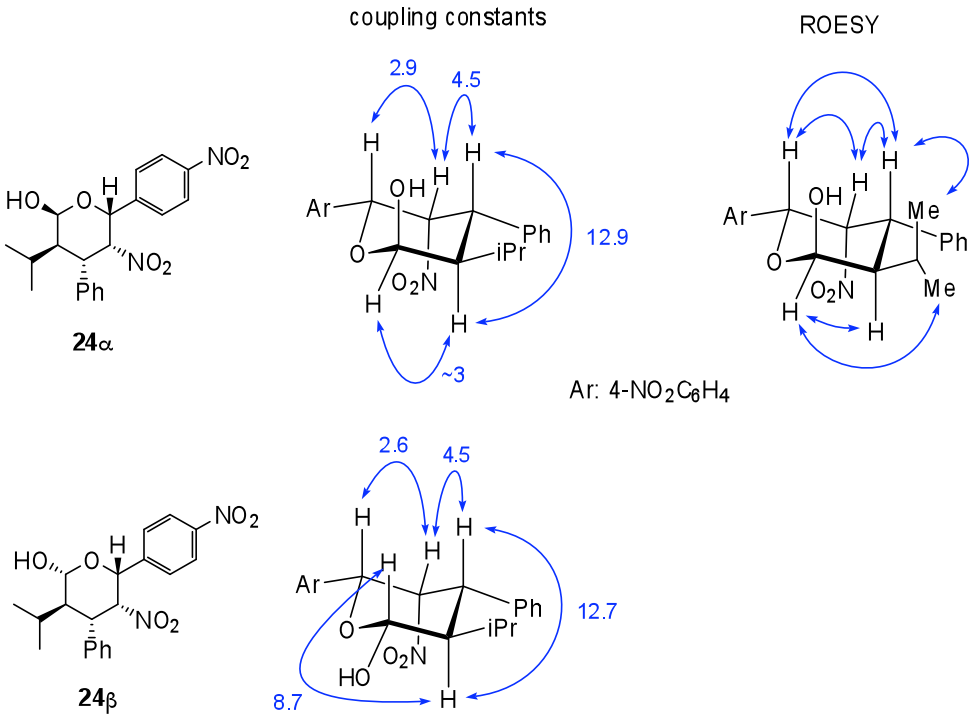
This talo-configuration was completely preserved during the transformation into Boc-protected amine **14**. The sharp signal of NH proton with a large (9.9 Hz) coupling constant implies intramolecular hydrogen bonding between NHBoc and OTBS. This hydrogen bonding decreases ring strain by releasing 1,3-diaxial repulsion between C2 and C4, and the undistorted chair-like conformation results in a ”W-shape” long range coupling between H2 and H4.



On the other hand, D-mannopyranose derivative **7a**, which has opposite configuration at C4 to talo-type compounds, has large axial-axial coupling constants around H4 with small H1-H2 and H2-H3 coupling constants. These constants provide good support for the structure below.



Similar coupling patterns can be observed in **24** produced through *syn*-Michael–Henry tandem process. **24** contains mainly two compounds, which were determined as anomeric diastereomers (**24α**: **24β** = ~4 : 1).



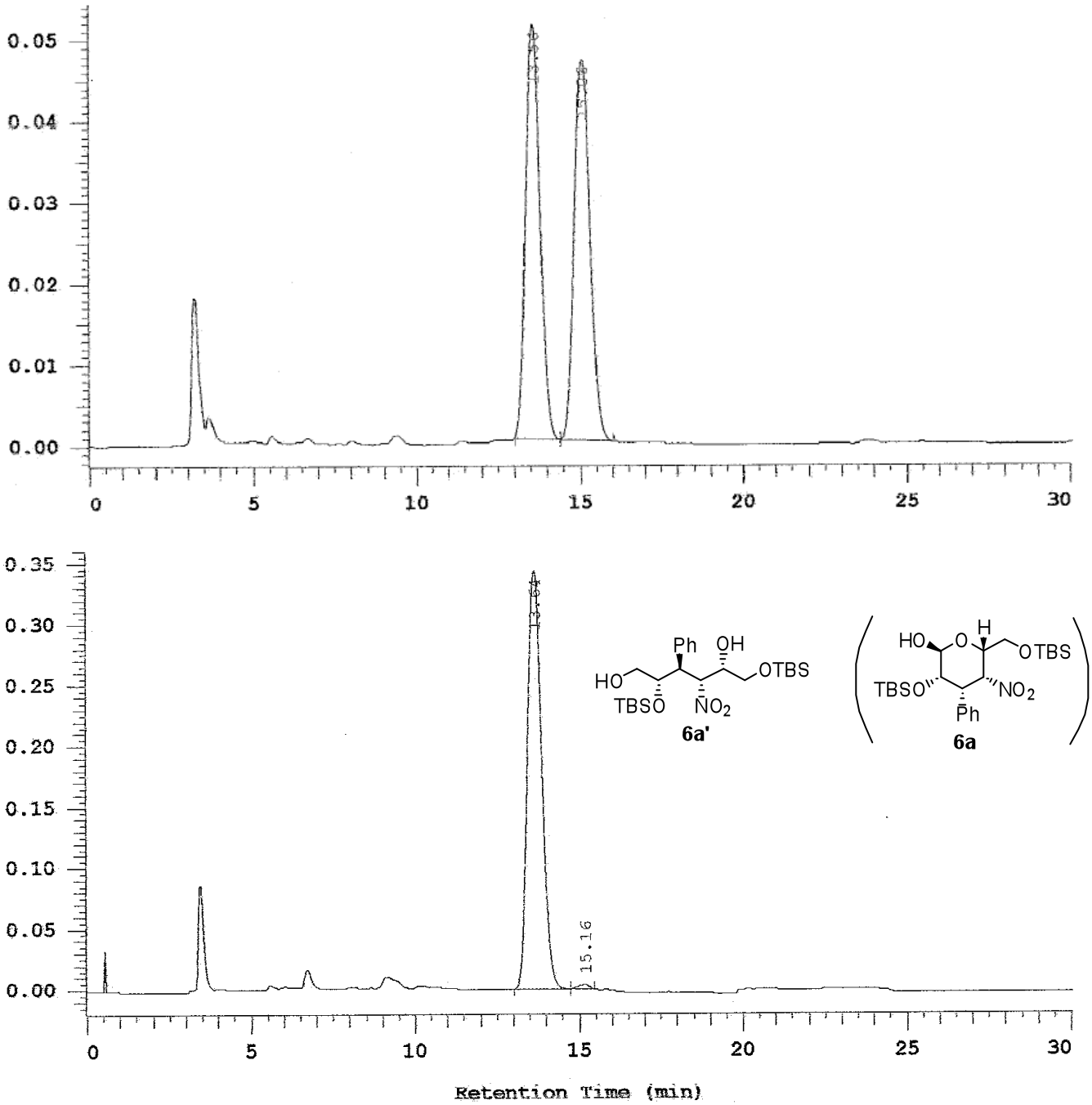
4. Reference

S1. Xue F, Zhang S, Duan W, Wang W (2008) A Novel Bifunctional Sulfonamide Primary Amine-Catalyzed Enantioselective Conjugate Addition of Ketones to Nitroolefins *Adv. Synth. Catal.* 350:2194-2198.

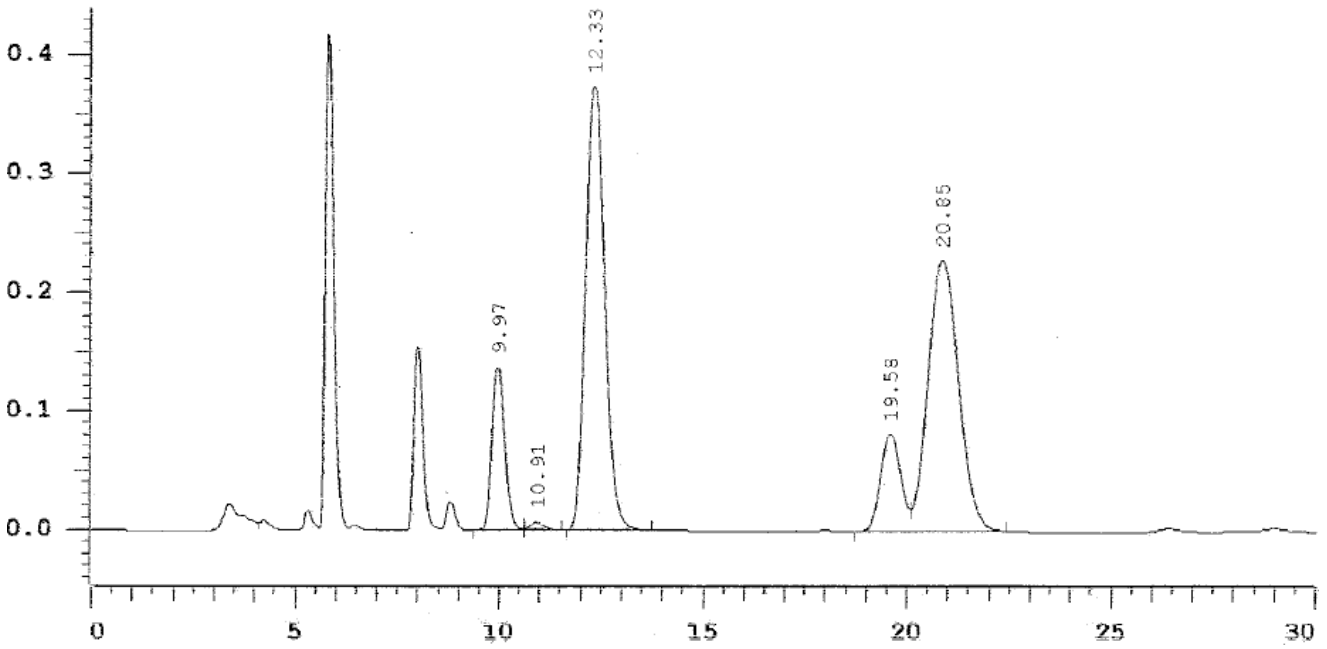
S2. Okino T, Hoashi Y, Takemoto Y (2003) Enantioselective Michael Reaction of Malonates to Nitroolefins Catalyzed by Bifunctional Organocatalysts *J. Am. Chem. Soc.* 125:12672-12673.

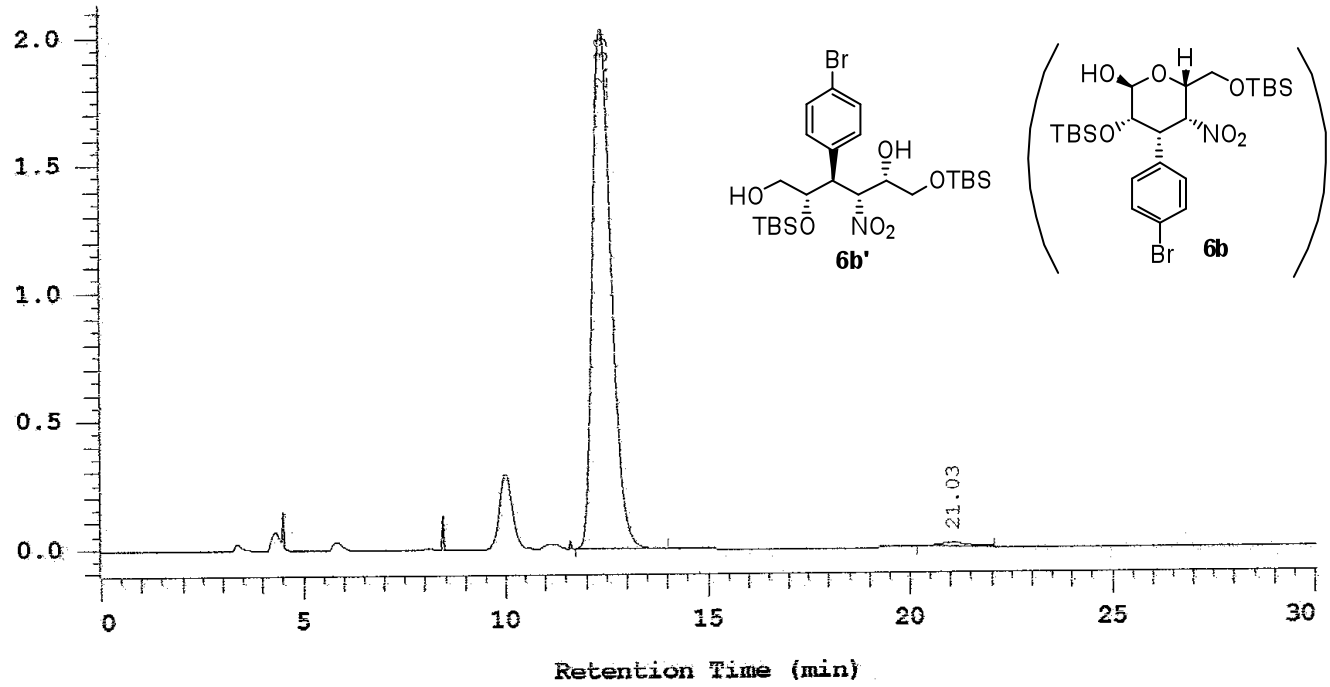
S3. Gawronski J, Kwit M, Skowronek P (2009) Thiourea and isothiocyanate – two useful chromophores for stereochemical studies. A comparison of experiment and computation. *Org. Biomol. Chem.* 7:1562-1572.

5. HPLC traces



No.	RT	Height	Area	Conc 1	BC
1	13.64	171157	4840842	98.998	BV
2	15.16	2327	49001	1.002	VB
		173484	4889843	100.000	

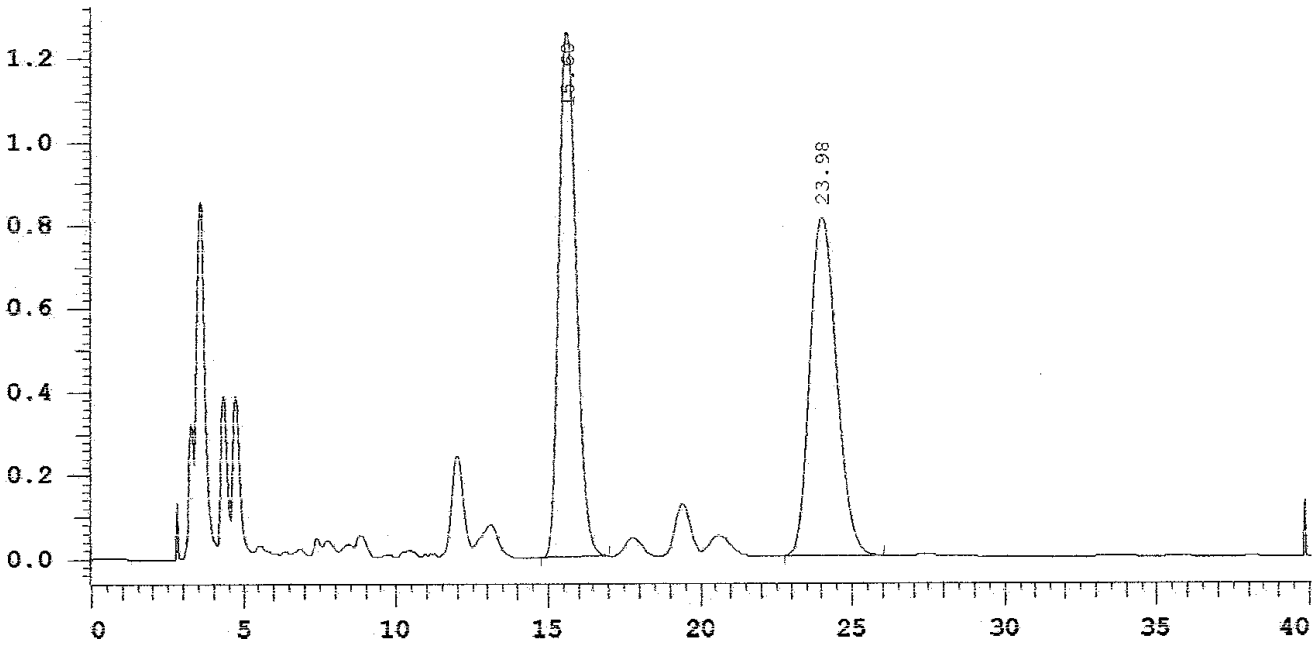


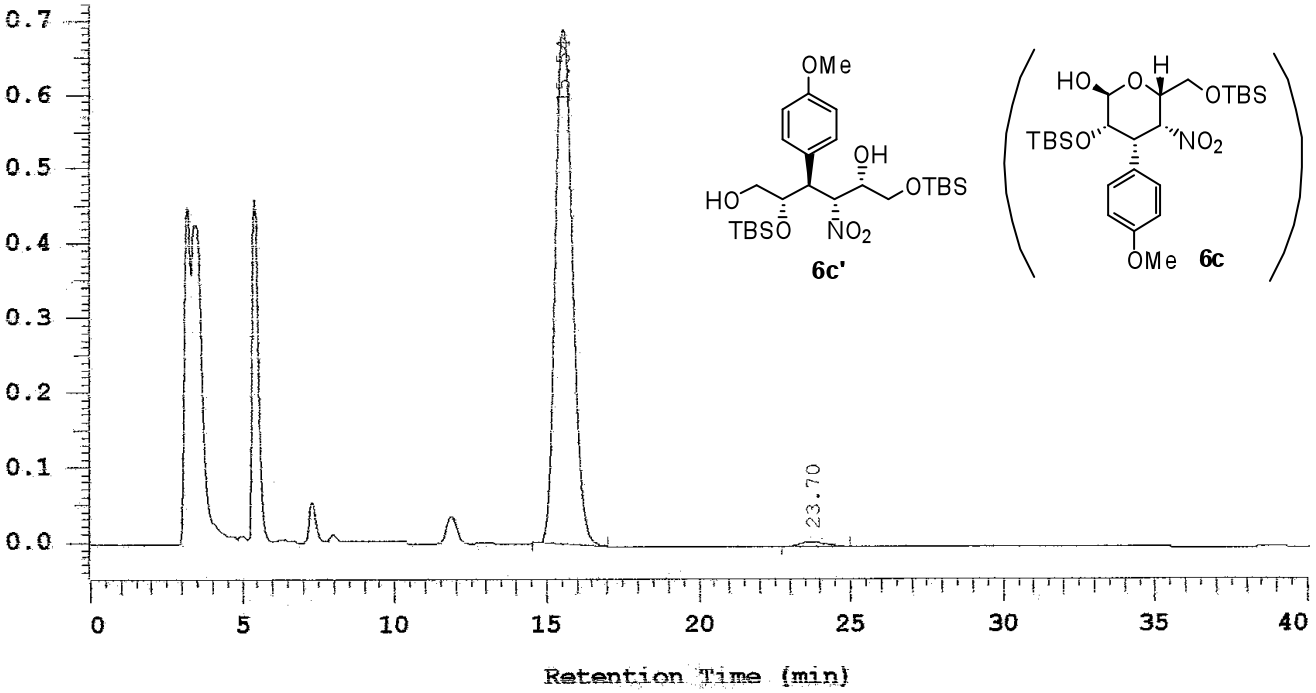


6b'

6b

No.	RT	Height	Area	Conc 1	BC
1	12.39	1015036	30931616	98.890	BB
2	21.03	7273	347102	1.110	BB
		1022309	31278718	100.000	

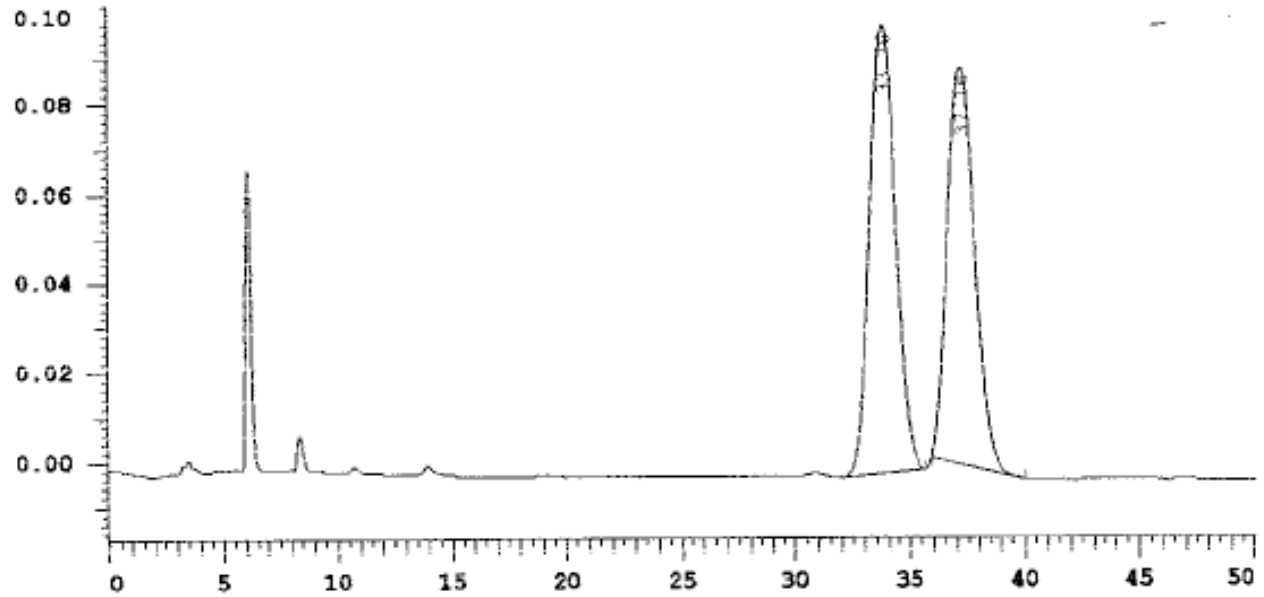


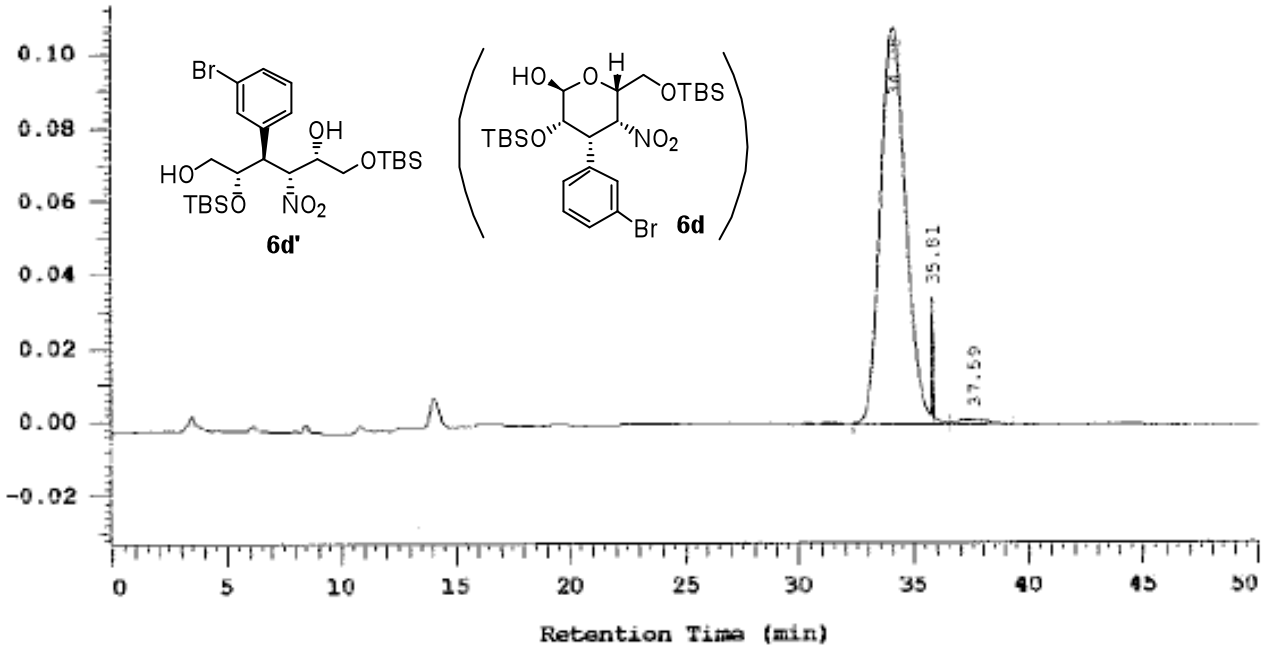


6c'

6c

No.	RT	Height	Area	Conc 1	BC
1	15.54	343868	12624355	98.571	BB
2	23.70	3276	183011	1.429	BB
		347144	12807366	100.000	

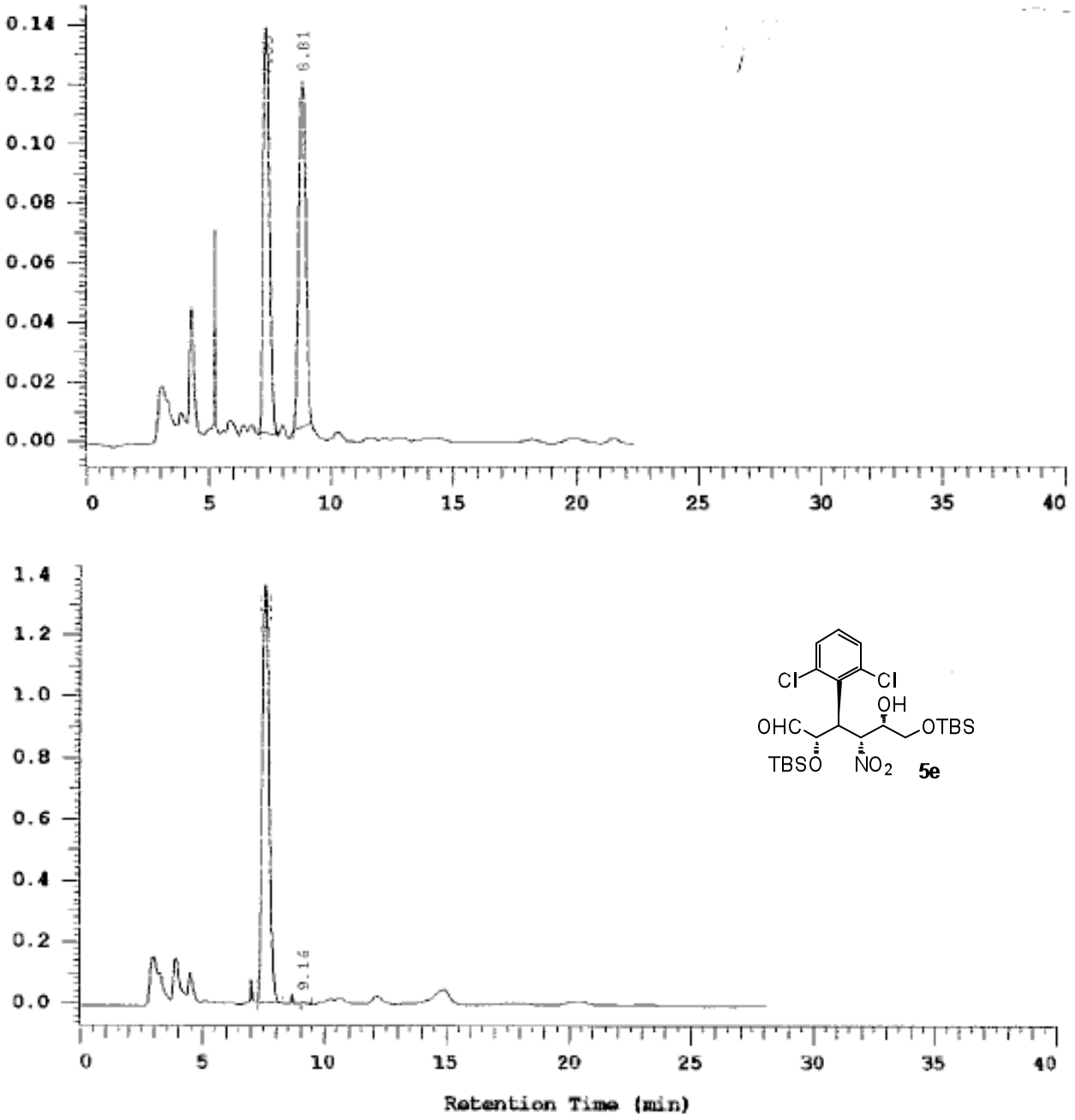




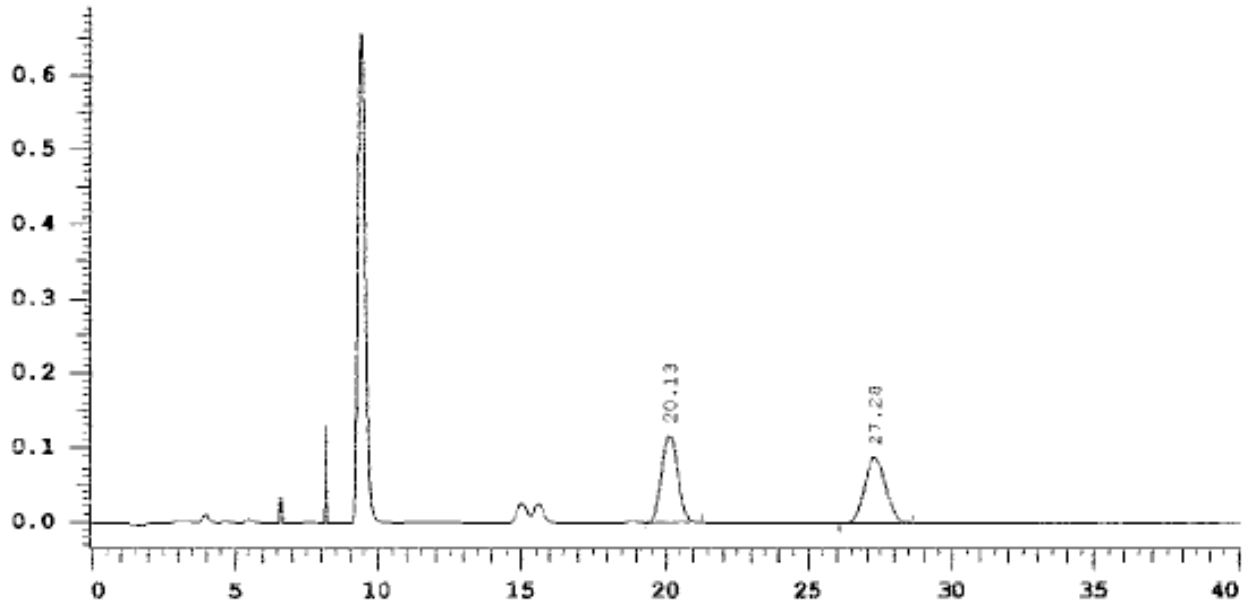
6d'

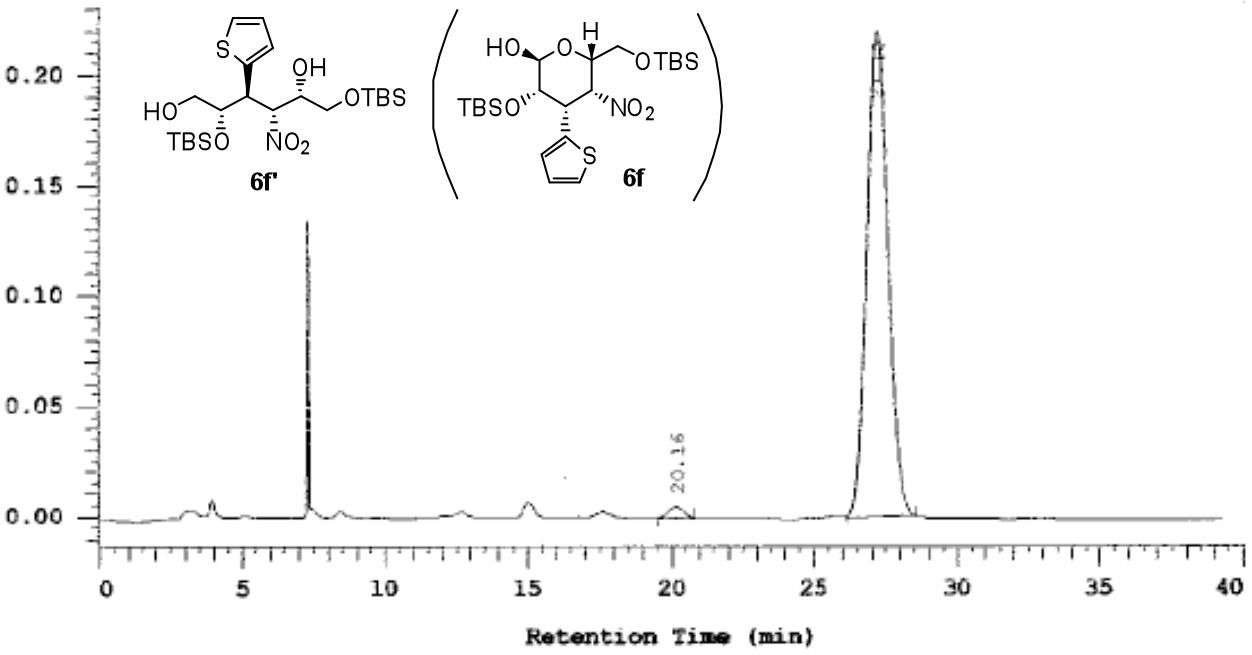
6d

No.	RT	Height	Area	Conc 1	BC
1	34.05	53665	3951594	97.780	VV
2	35.81	17244	31331	0.775	VV
3	37.59	587	58383	1.445	VB
		71496	4041308	100.000	

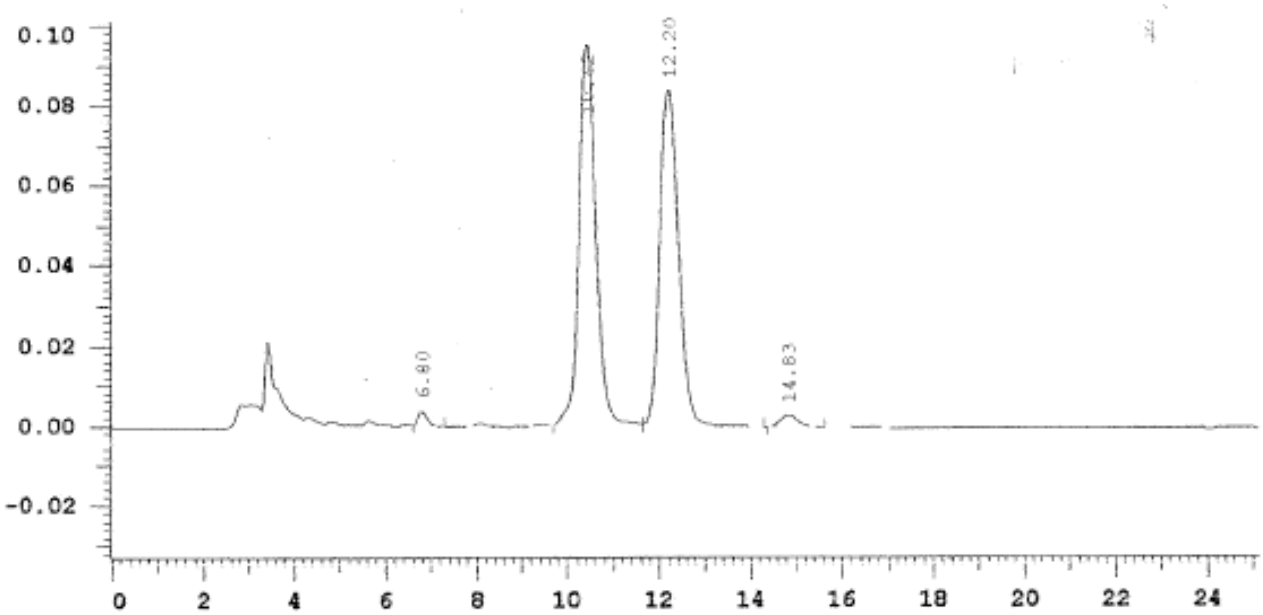


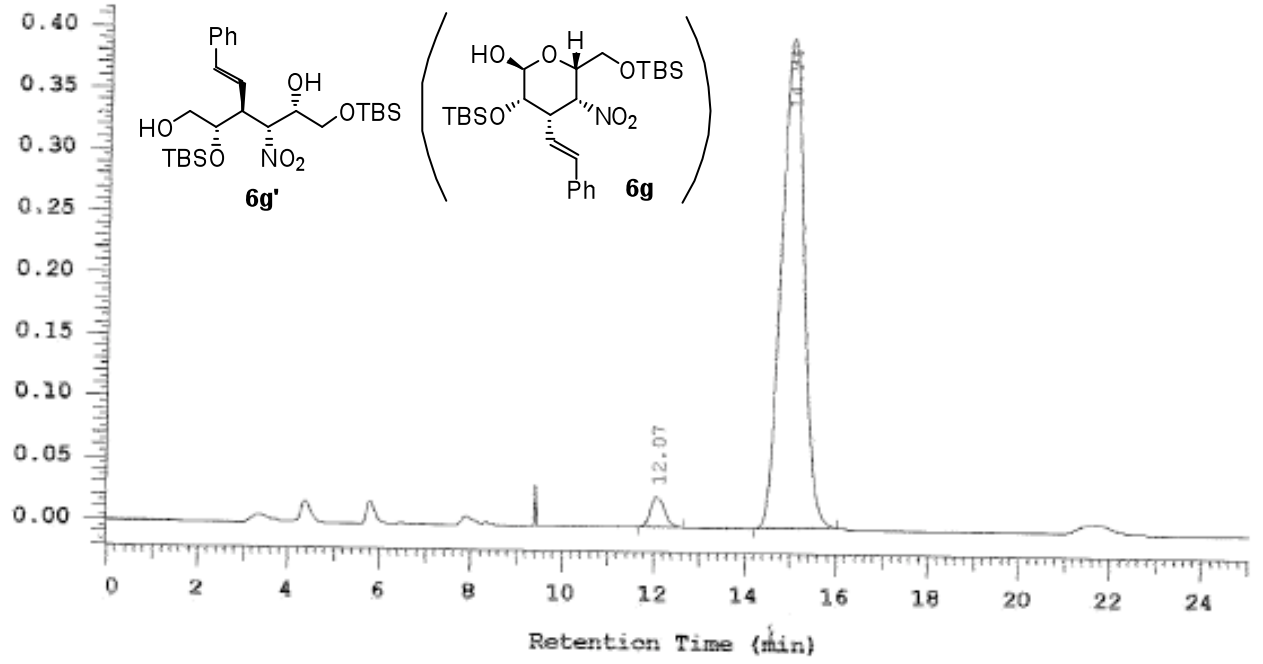
No.	RT	Area	Area %	Conc 1	BC
1	7.55	11236176	99.686	99.686	BB
2	9.16	35342	0.314	0.314	BB
		11271518	100.000	100.000	





No.	RT	Area	Area %	Conc 1	BC
1	20.16	85929	1.547	1.547	BB
2	27.15	5467618	98.453	98.453	VB
		5553547	100.000	100.000	

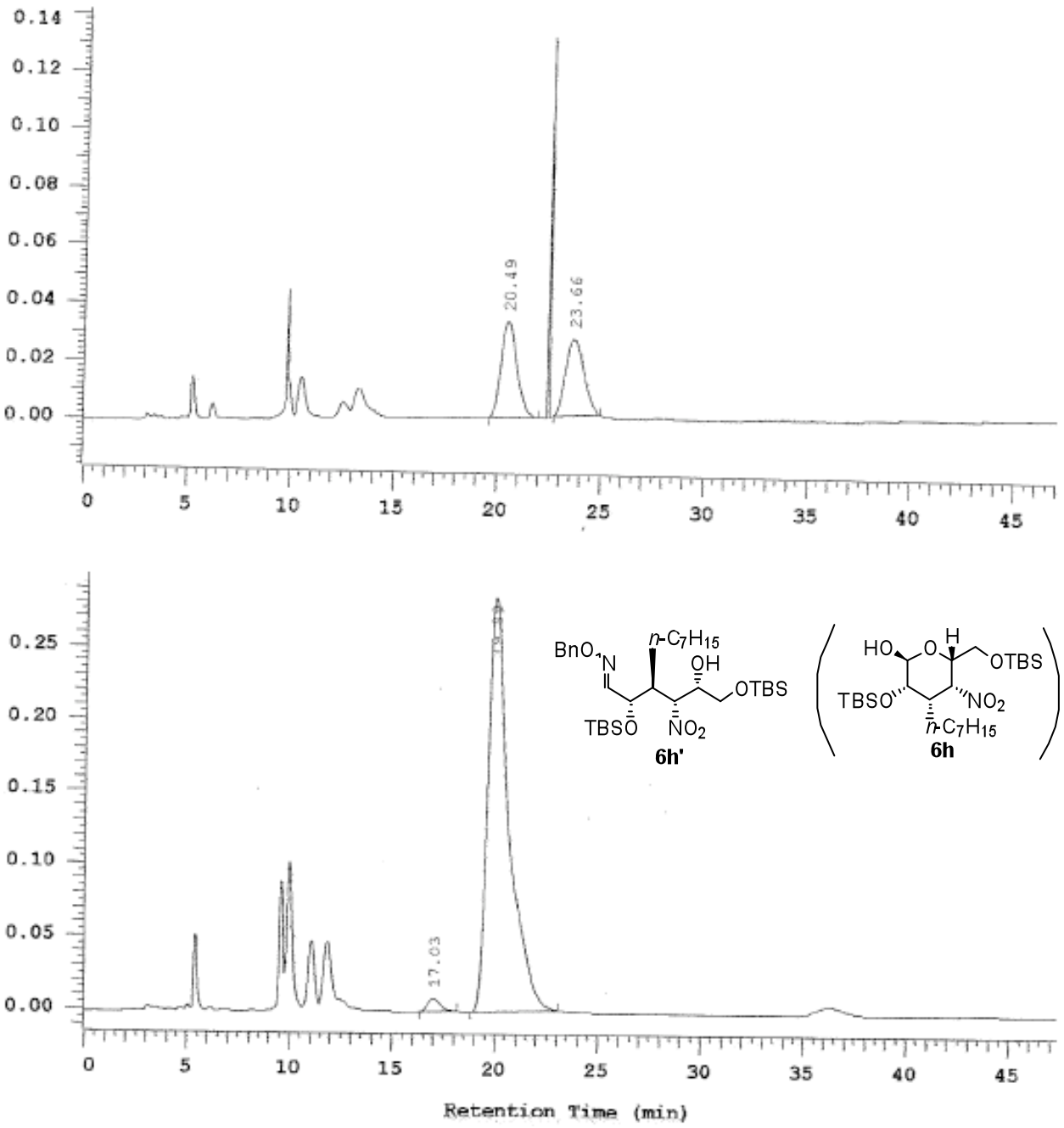




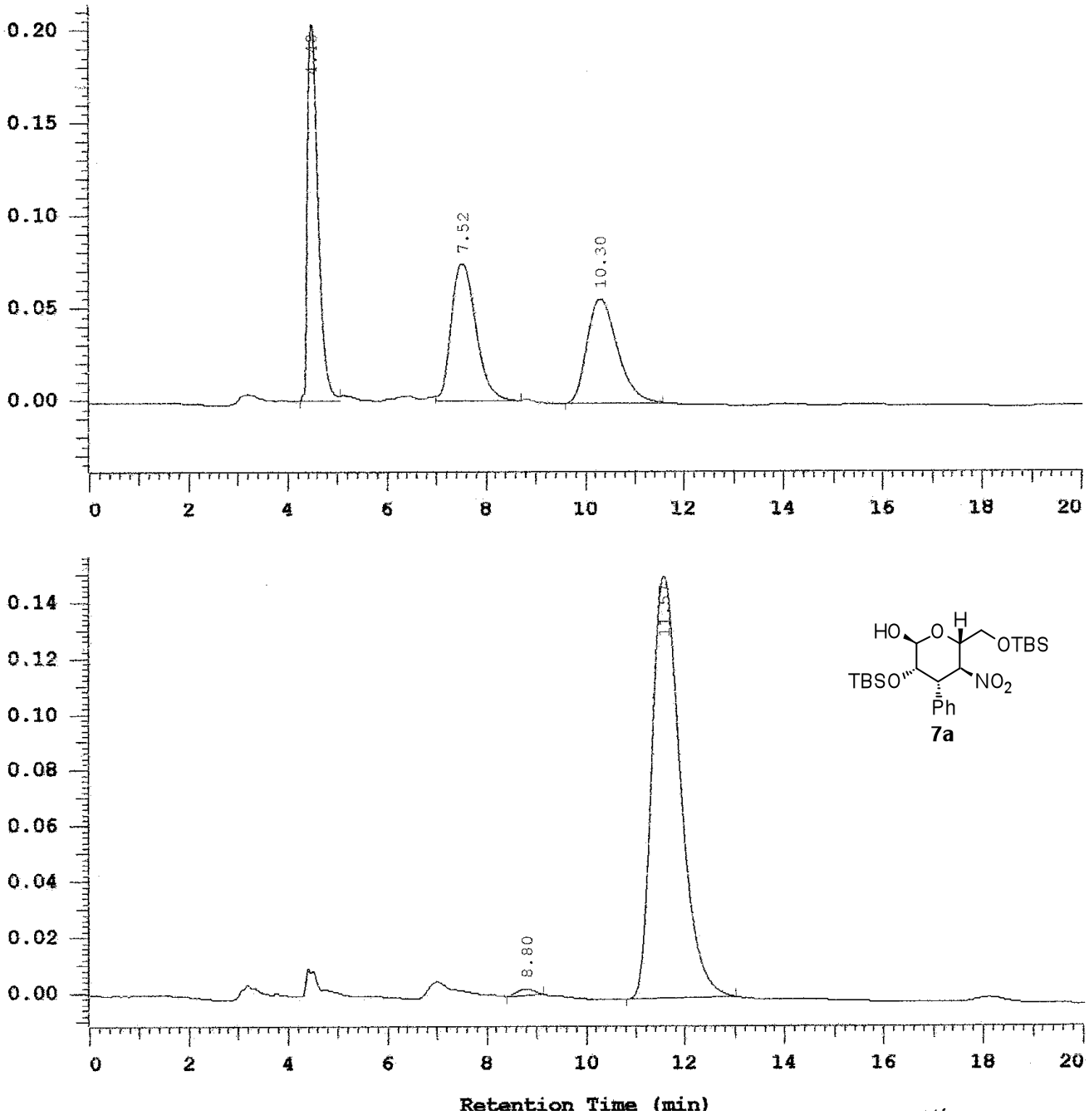
6g'

6g

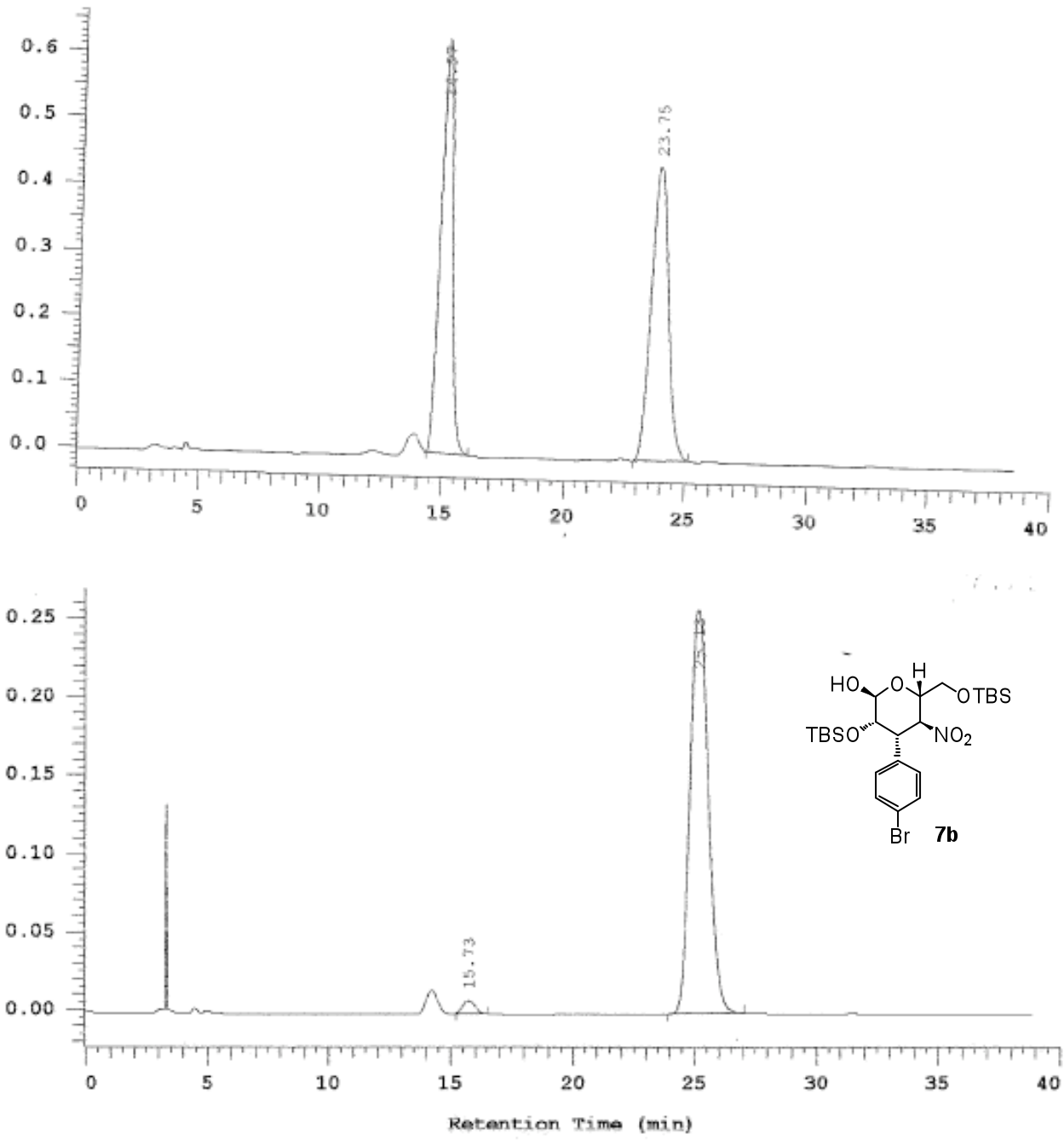
No.	RT	Height	Area	Conc 1	BC
1	12.07	11671	237355	3.503	BB
2	14.94	197779	6538372	96.497	BB
		209450	6775727	100.000	



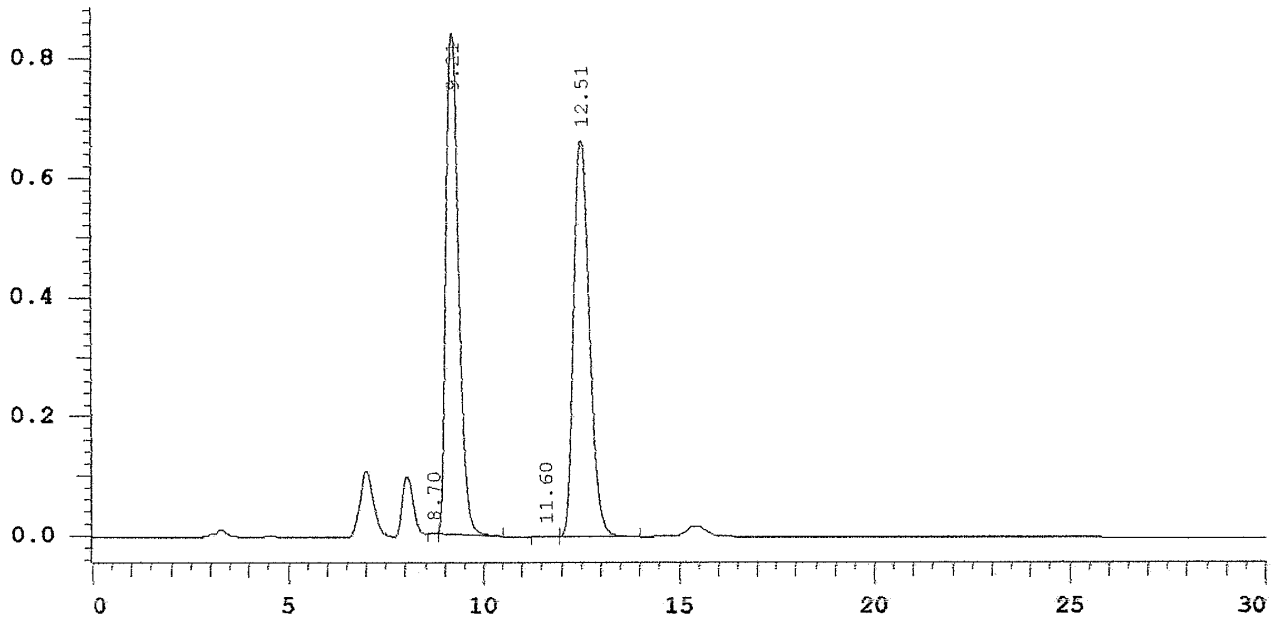
No.	RT	Area	Area %	Conc 1	BC
1	17.03	180020	1.819	1.819	BB
2	19.89	9716007	98.181	98.181	BB
		9896027	100.000	100.000	

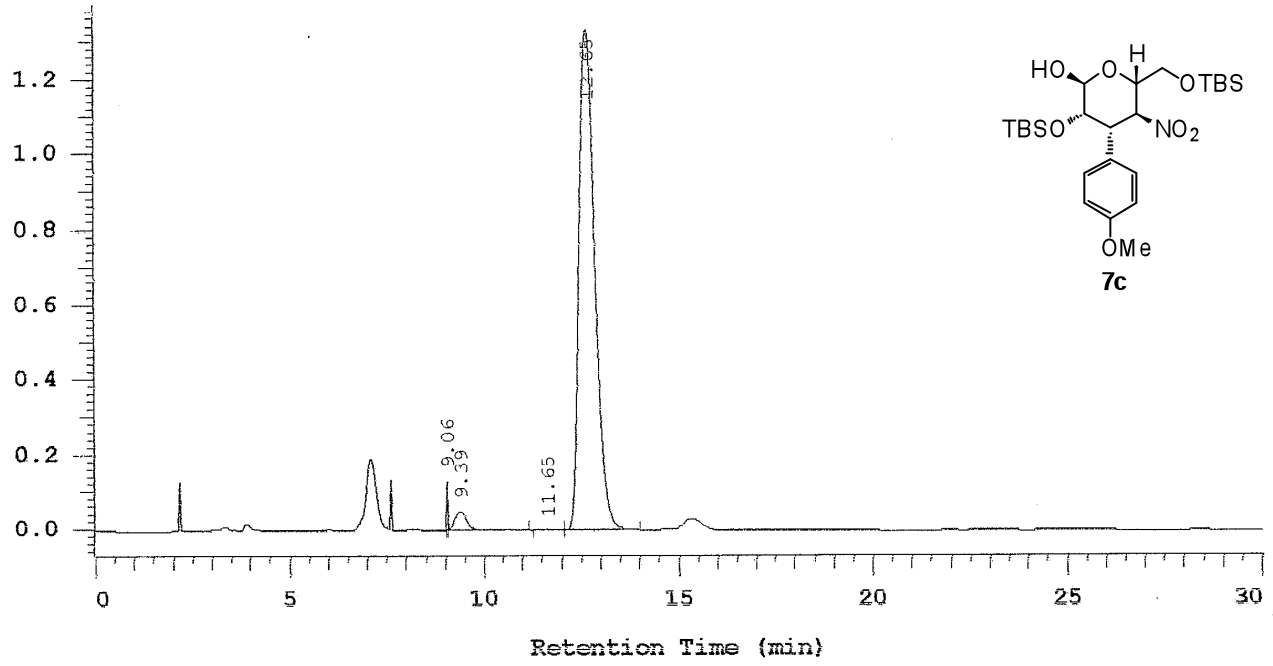


No.	RT	Area	Area %	Conc 1	BC
1	8.80	26247	0.897	0.897	BB
2	11.57	2898391	99.103	99.103	BB
		2924638	100.000	100.000	



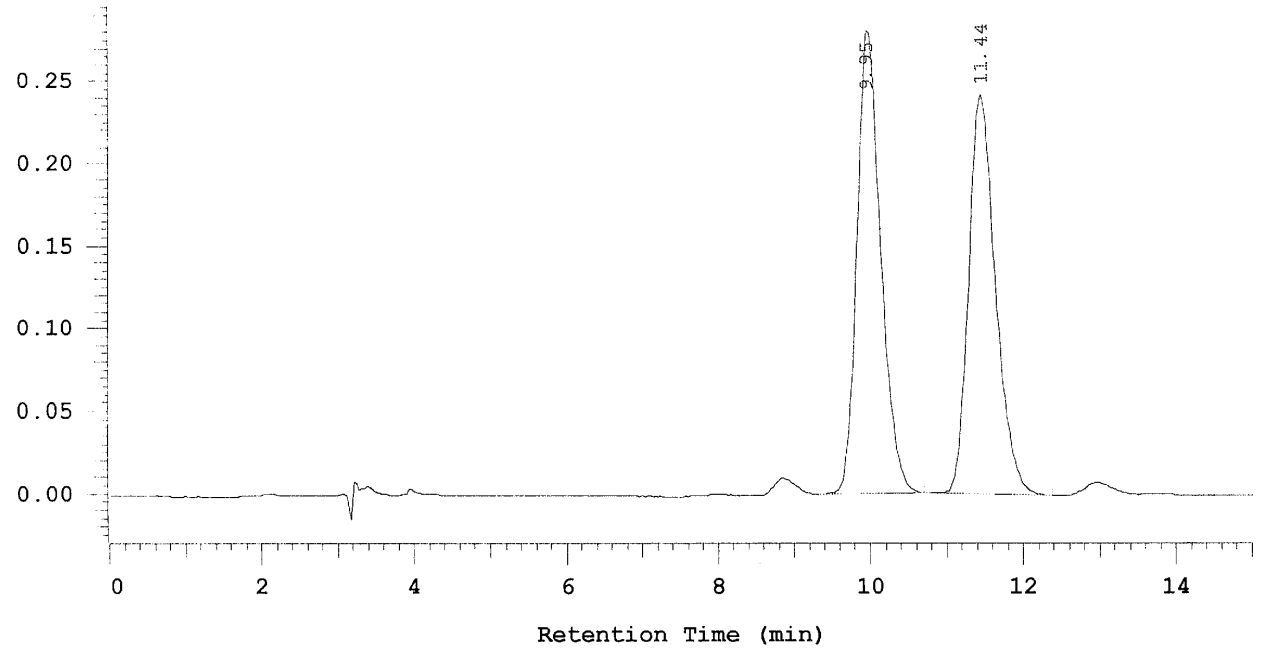
No.	RT	Area	Area %	Conc 1	BC
1	15.73	134538	2.070	2.070	BB
2	25.13	6365444	97.930	97.930	BB
		6499982	100.000	100.000	

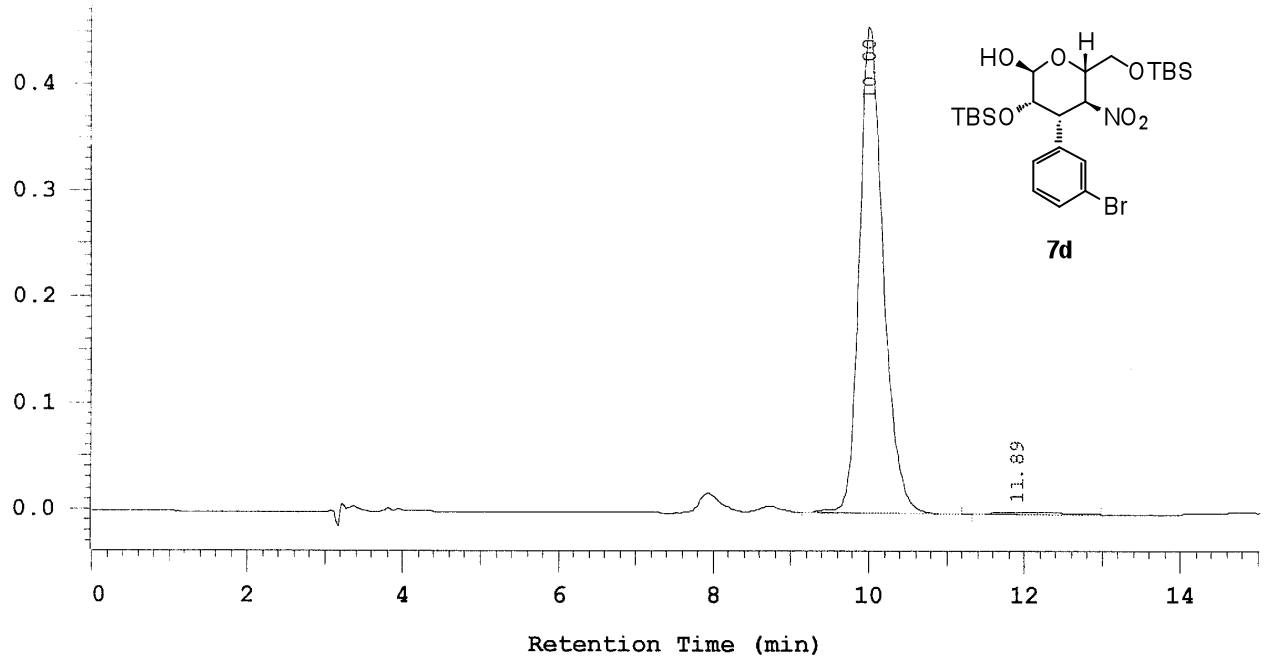




7c

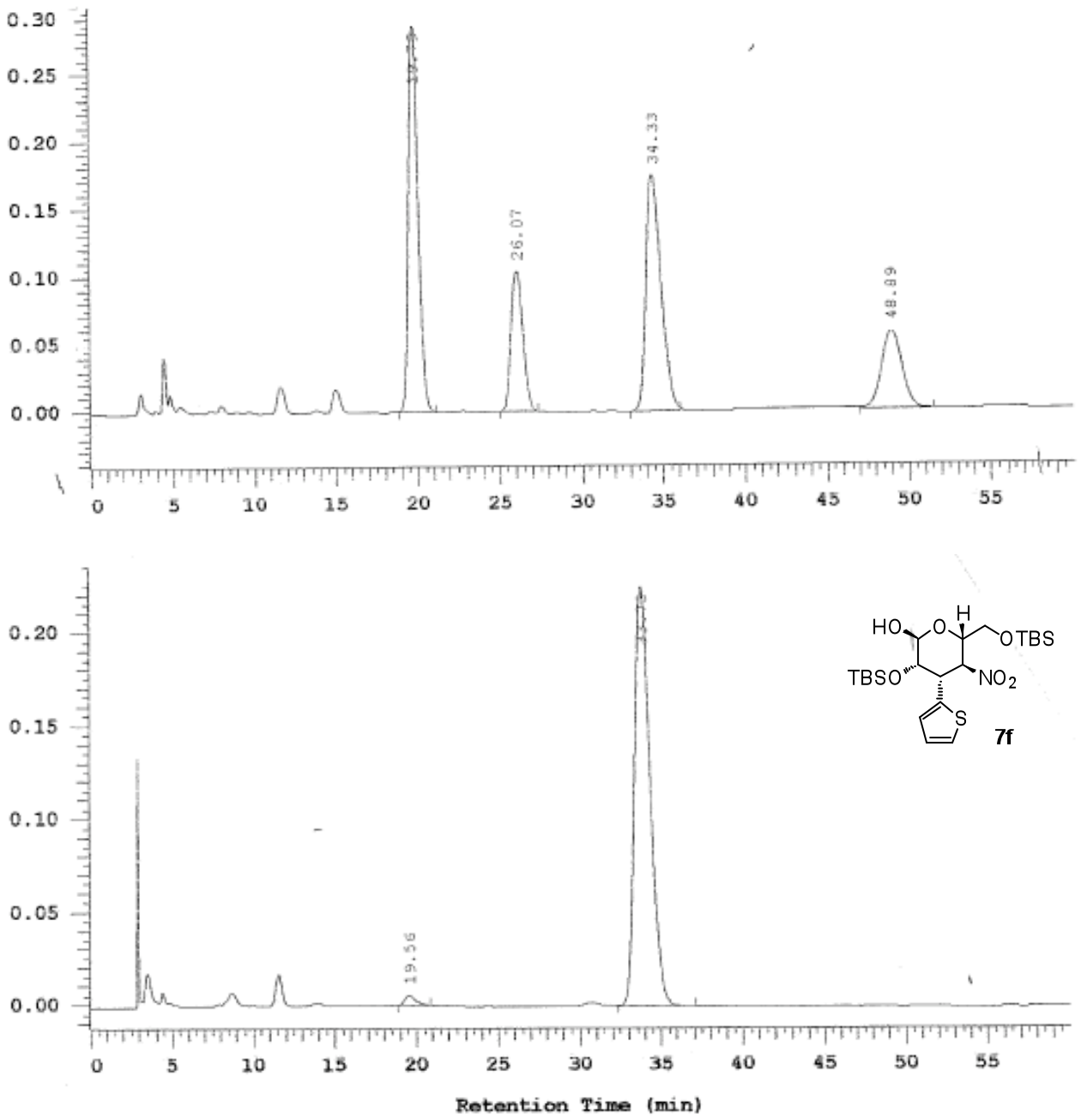
No.	RT	Area	Area %	Conc 1	BC
1	9.06	27432	0.153	0.153	BV
2	9.39	493888	2.749	2.749	TBB
3	11.65	8640	0.048	0.048	BB
4	12.65	17435817	97.050	97.050	BB
		17965777	100.000	100.000	



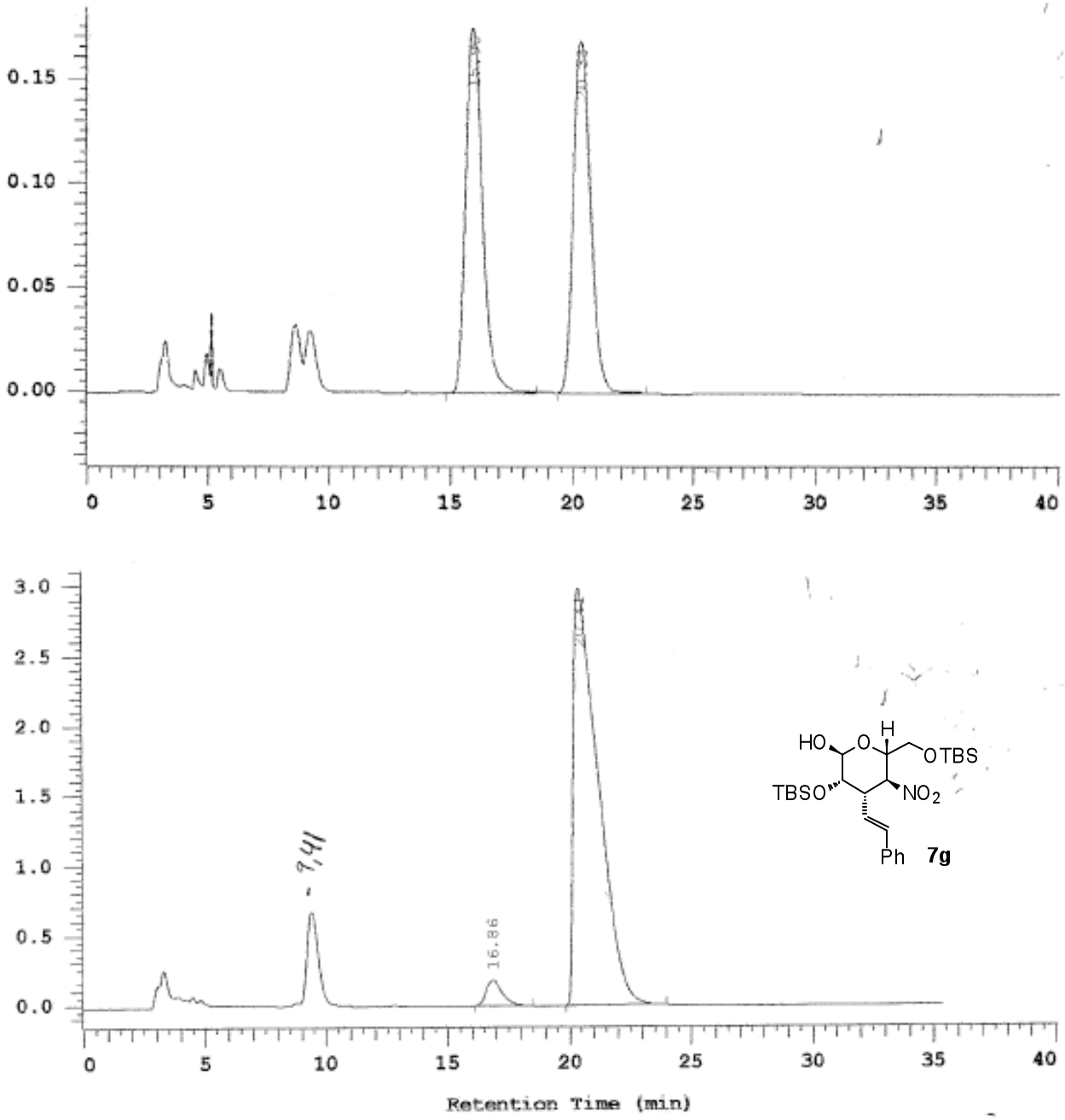


7d

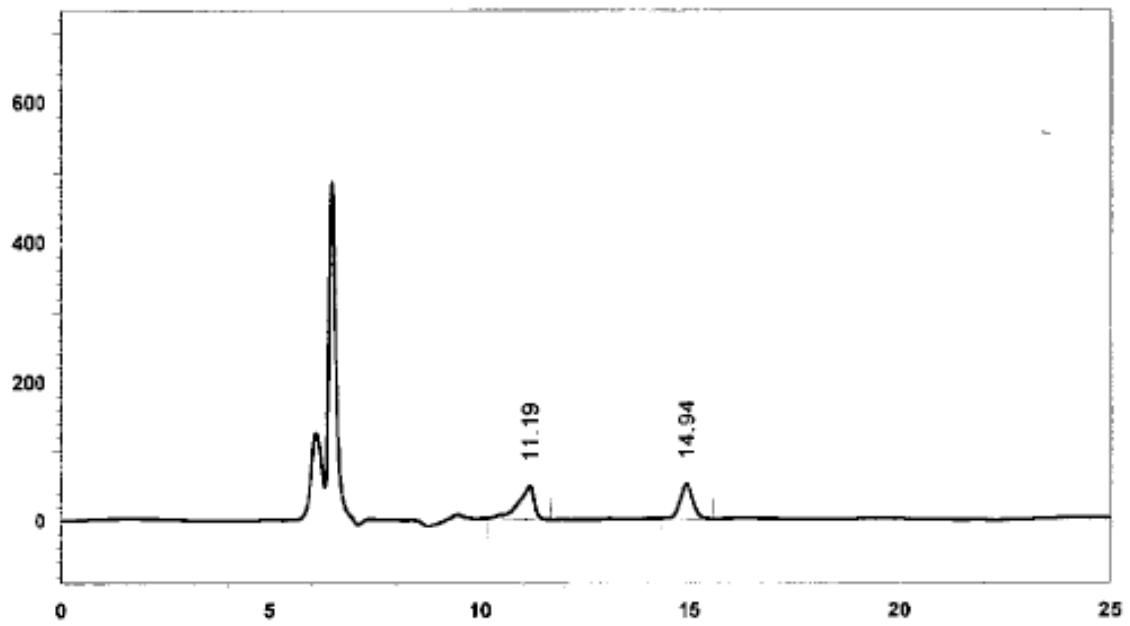
No.	RT	Area	Area %	Conc 1	BC
1	10.00	4890060	98.808	98.808	BB
2	11.89	59000	1.192	1.192	BB
		4949060	100.000	100.000	

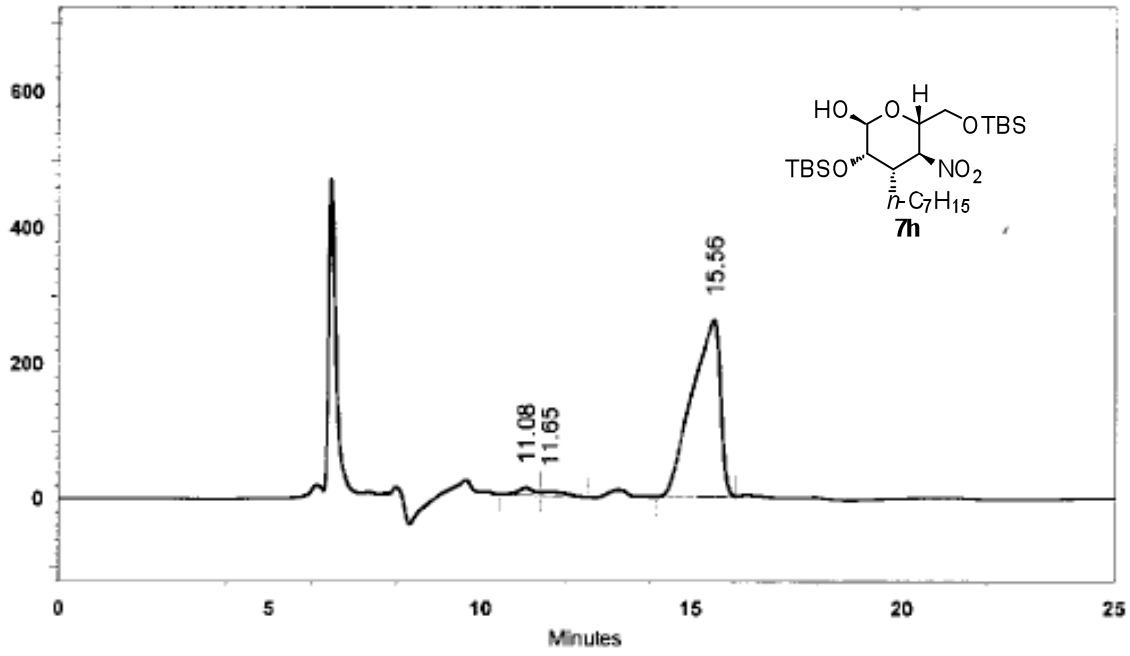


No.	RT	Area	Area %	Conc 1	BC
1	19.56	133516	1.834	1.834	BV
2	33.73	7147768	98.166	98.166	BB
		7281284	100.000	100.000	



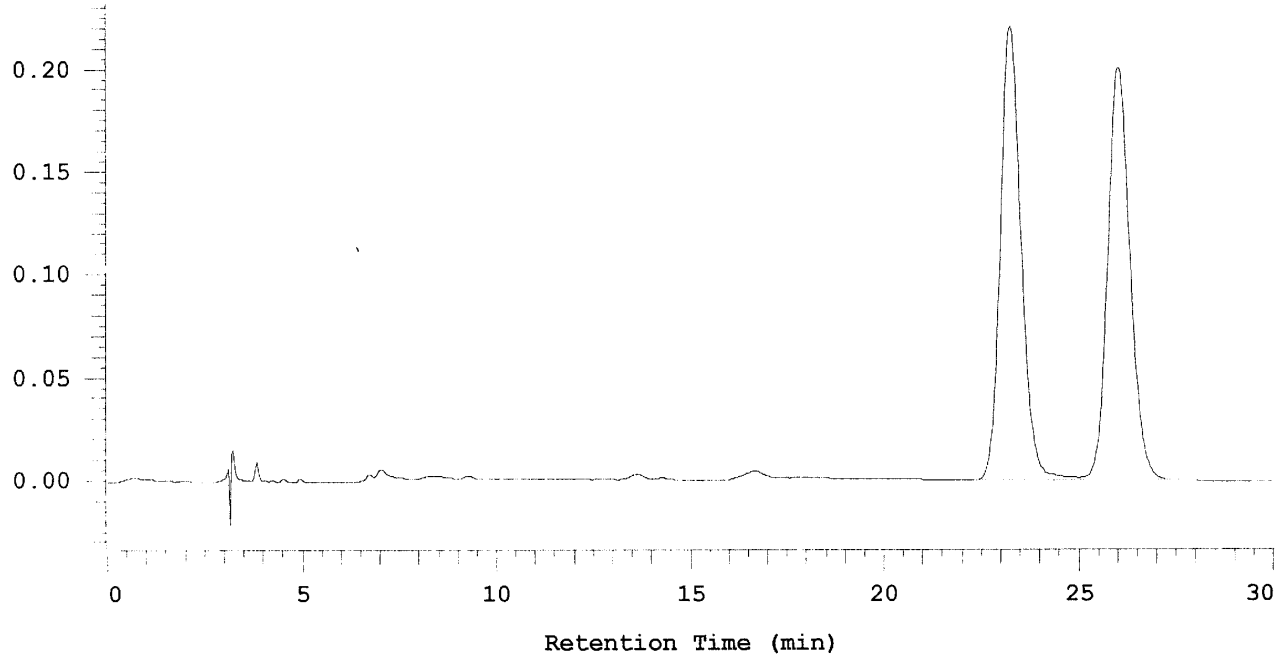
No.	RT	Area	Area %	Conc 1	BC
1	16.86	3956663	3.718	3.718	BB
2	20.41	1.024E+08	96.282	96.282	BB
		1.064E+08	100.000	100.000	

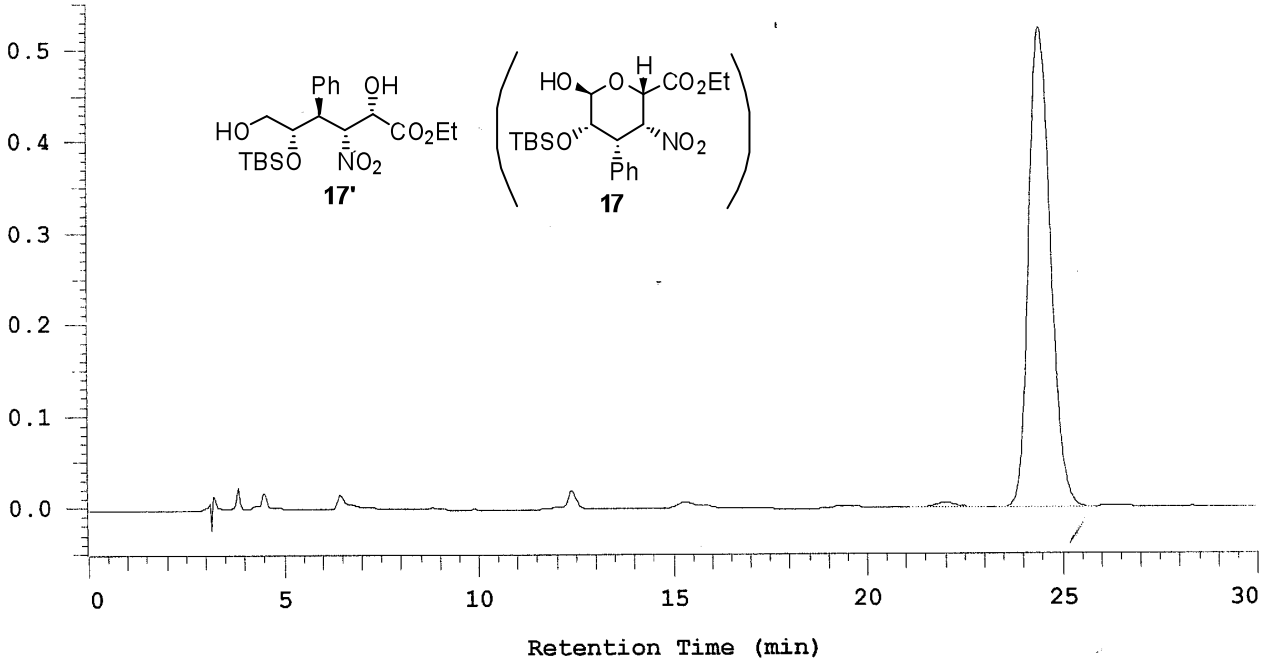




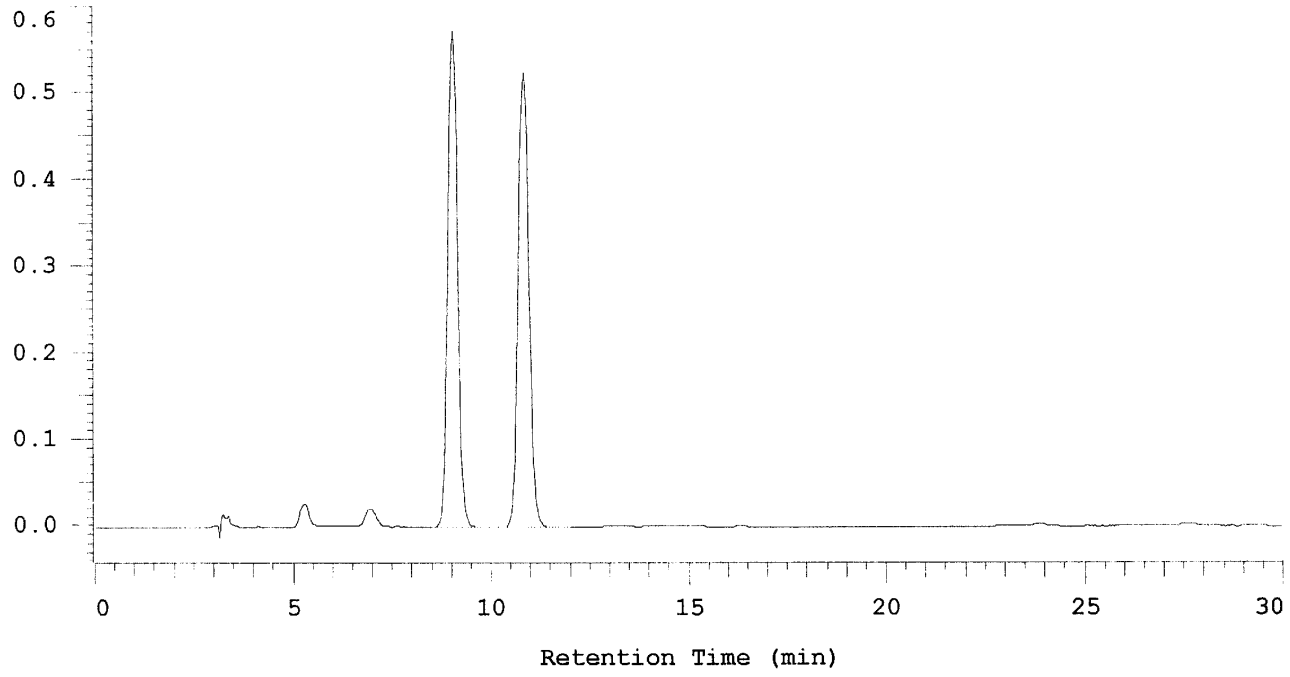
RI Results

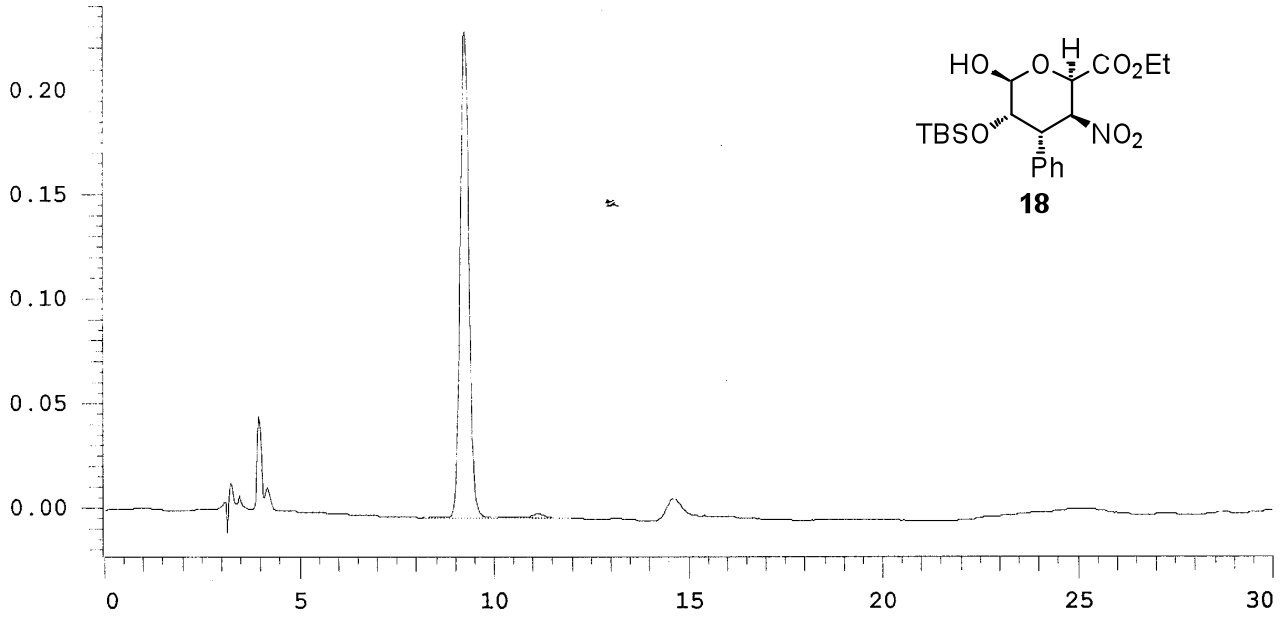
Pk #	RT	Area	Area %
1	11.077	2214903	2.2
2	11.647	2021711	2.0
3	15.557	96503496	95.8
Totals		100740110	100.0





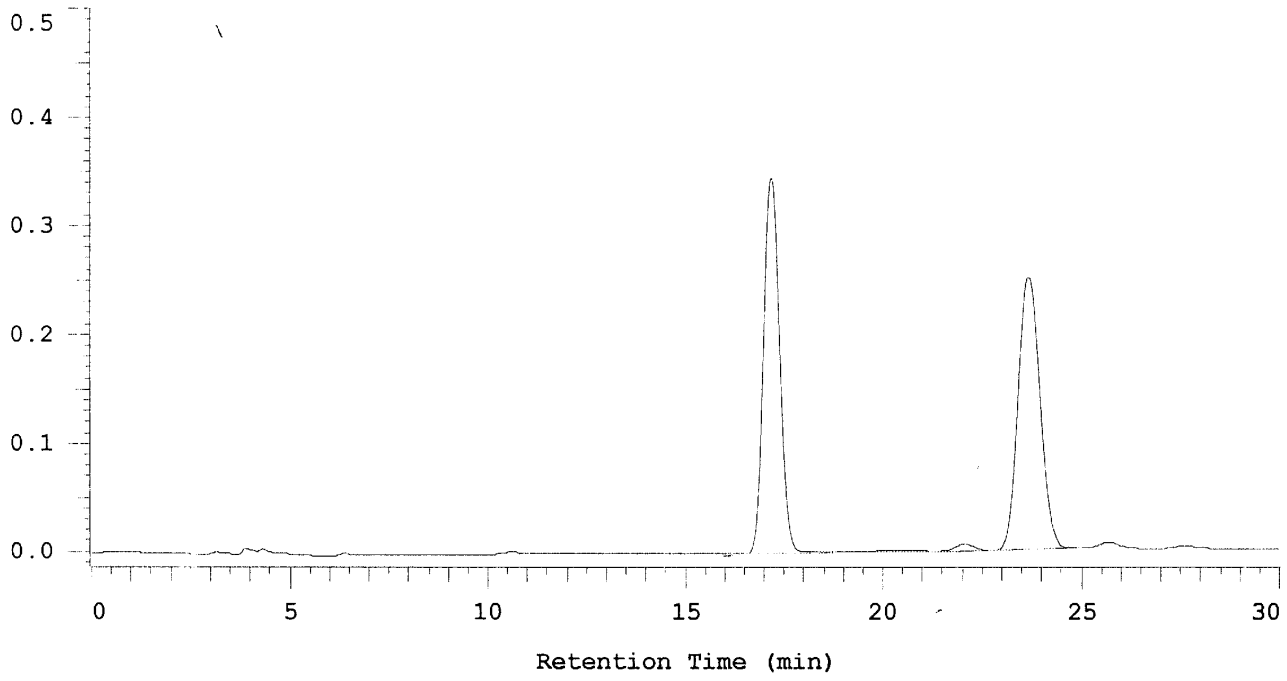
No.	RT	Area	Area %	Conc 1	BC
1	22.00	103560	1.029	1.029	BB
2	24.40	9956000	98.971	98.971	BB
		10059560	100.000	100.000	

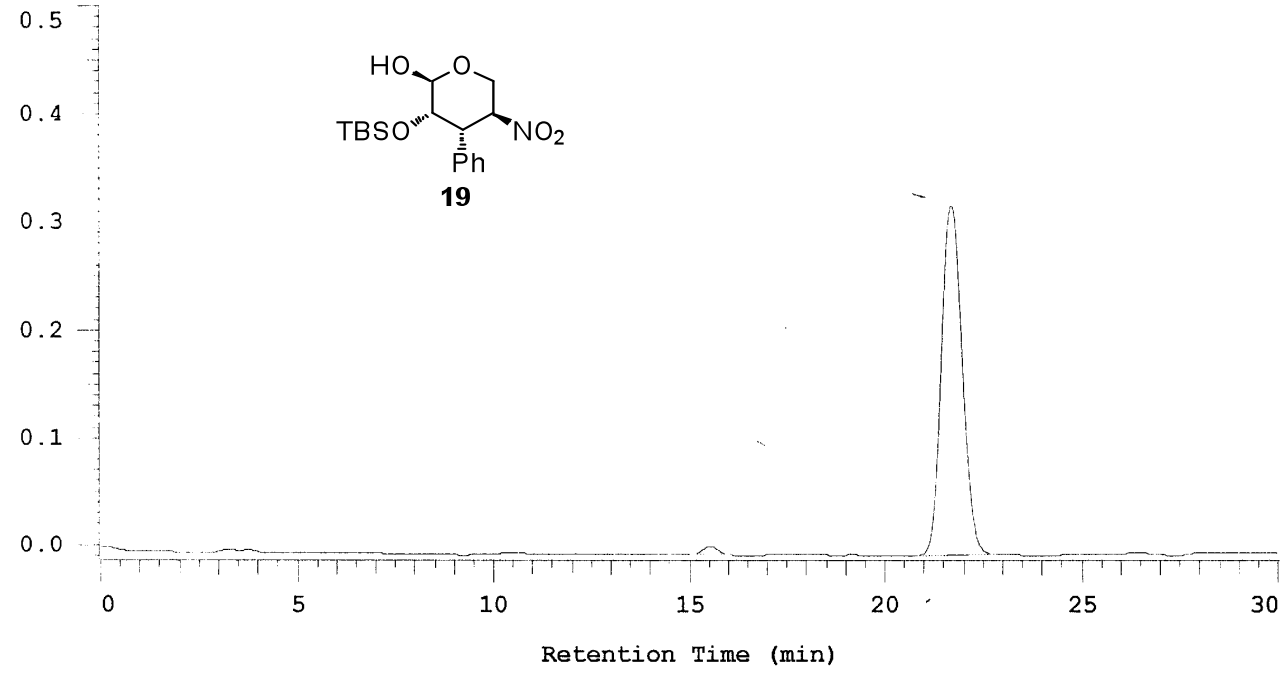




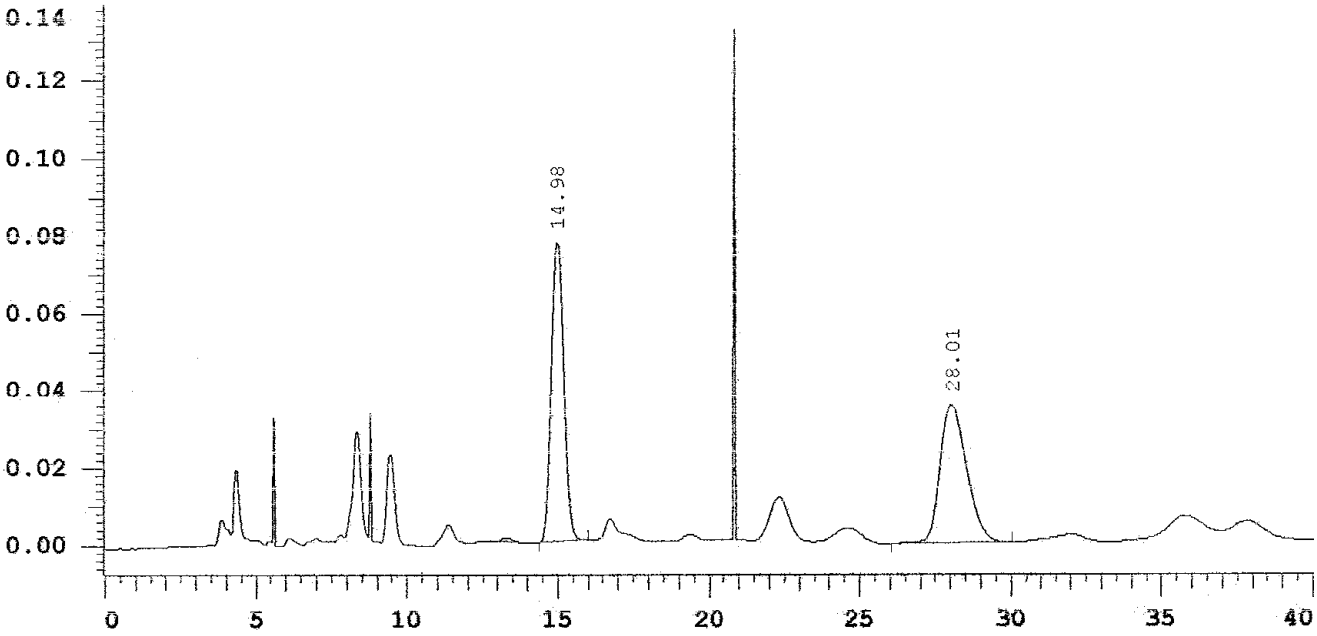
18

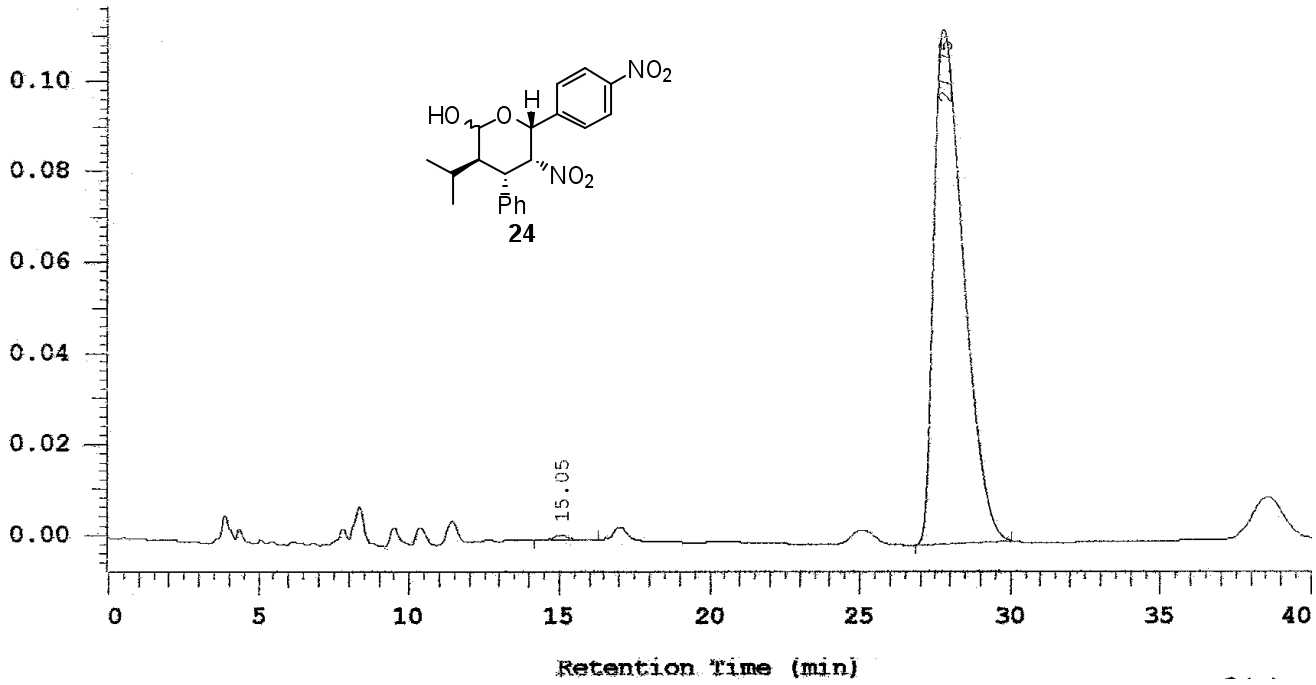
No.	RT	Area	Area %	Conc 1	BC
1	9.25	1752720	98.478	98.478	BV
2	10.67	7280	0.409	0.409	TBB
3	11.12	19799	1.112	1.112	TBB
		1779799	100.000	100.000	





No.	RT	Area	Area %	Conc 1	BC
1	15.53	99630	1.726	1.726	BB
2	21.69	5674177	98.274	98.274	BB
		5773807	100.000	100.000	

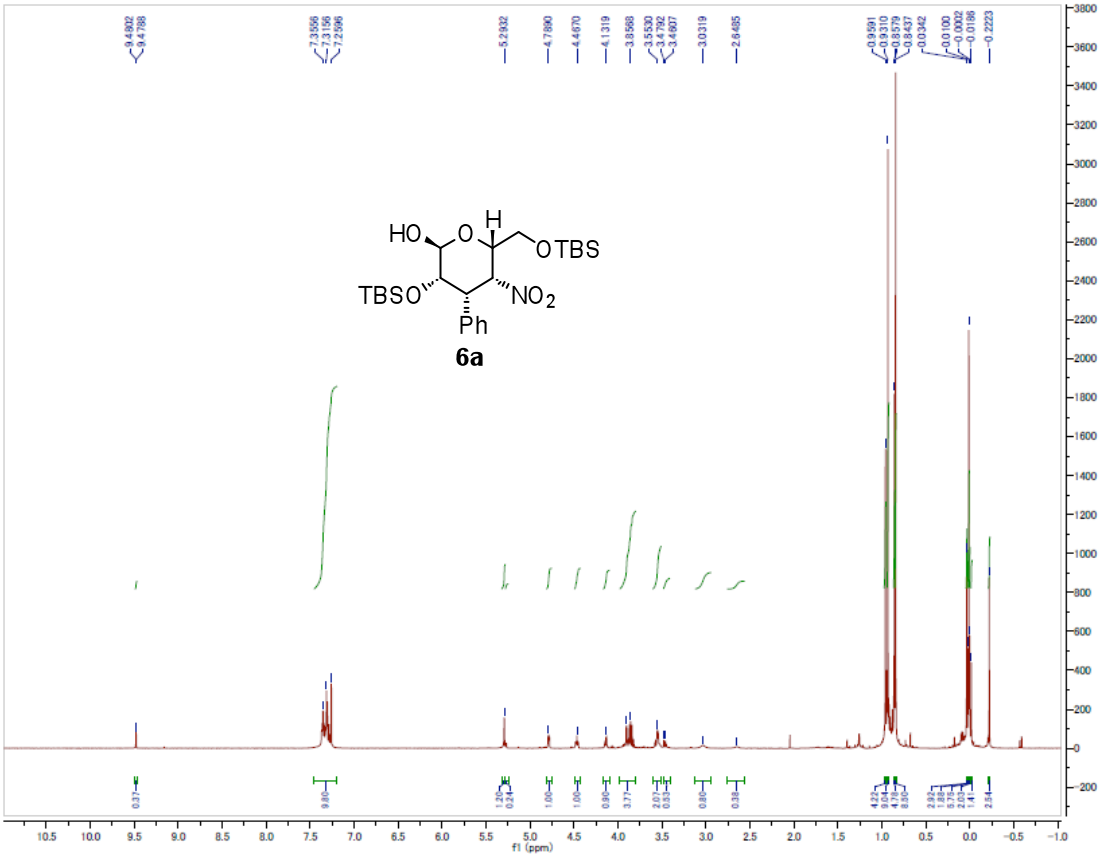


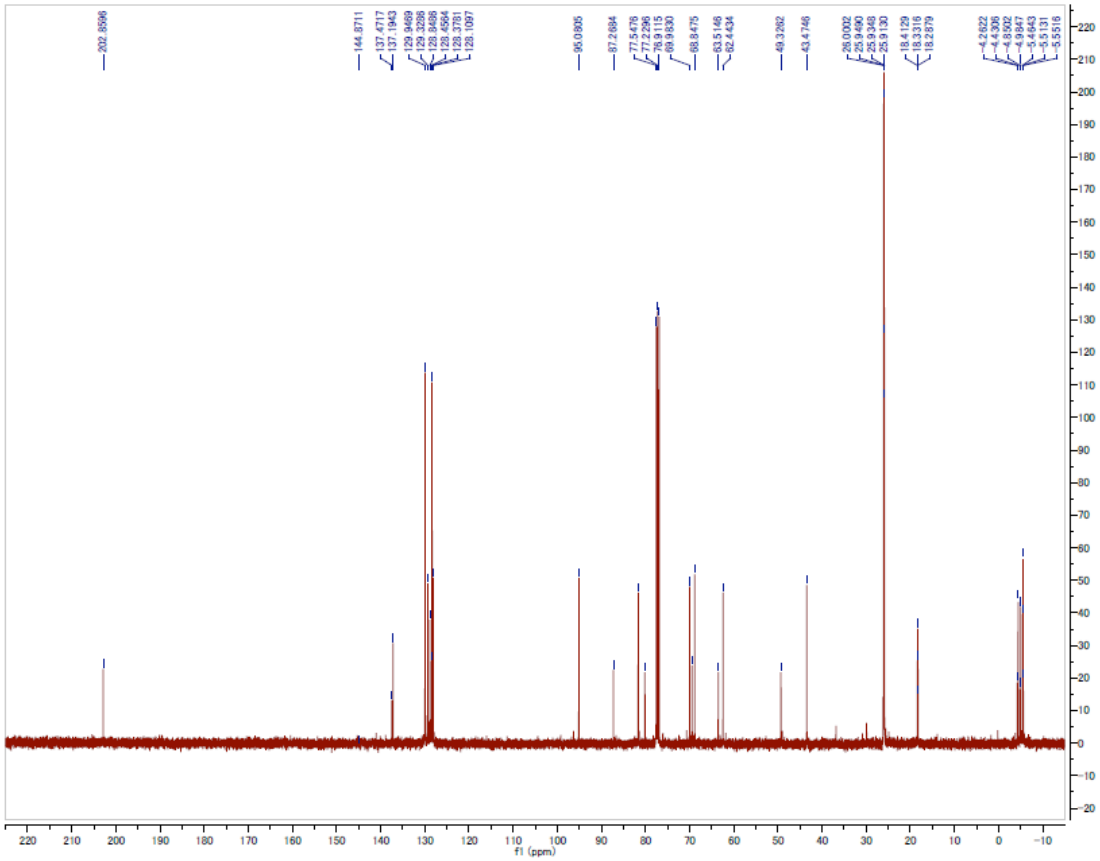


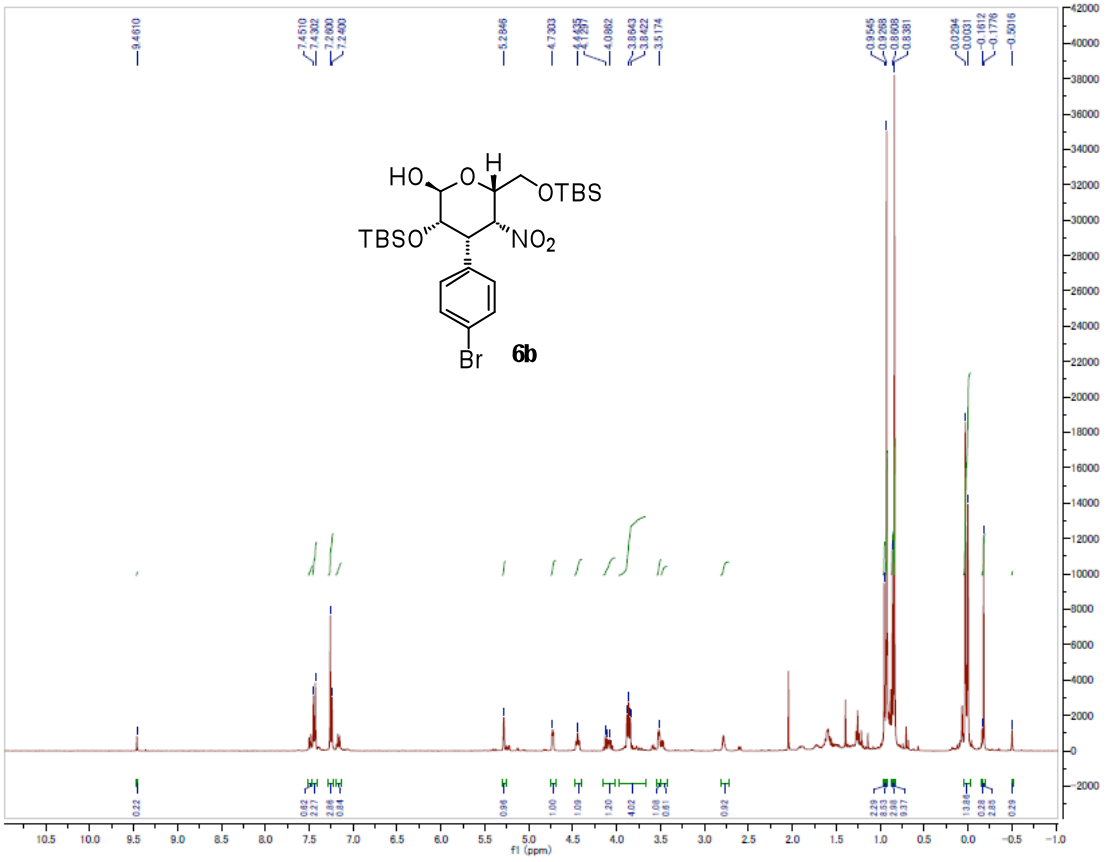
24

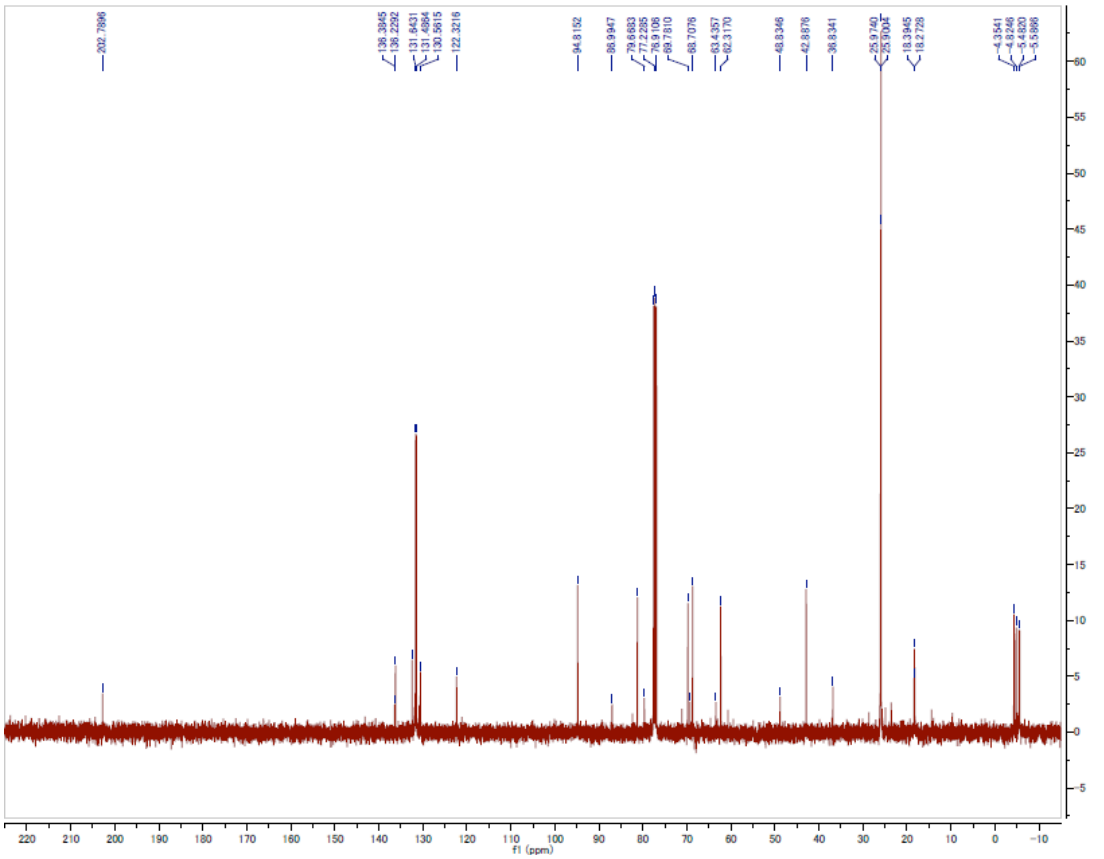
No.	RT	Area	Area %	Conc 1	BC
1	15.05	18552	0.497	0.497	BB
2	27.75	3717638	99.503	99.503	BB
		3736190	100.000	100.000	

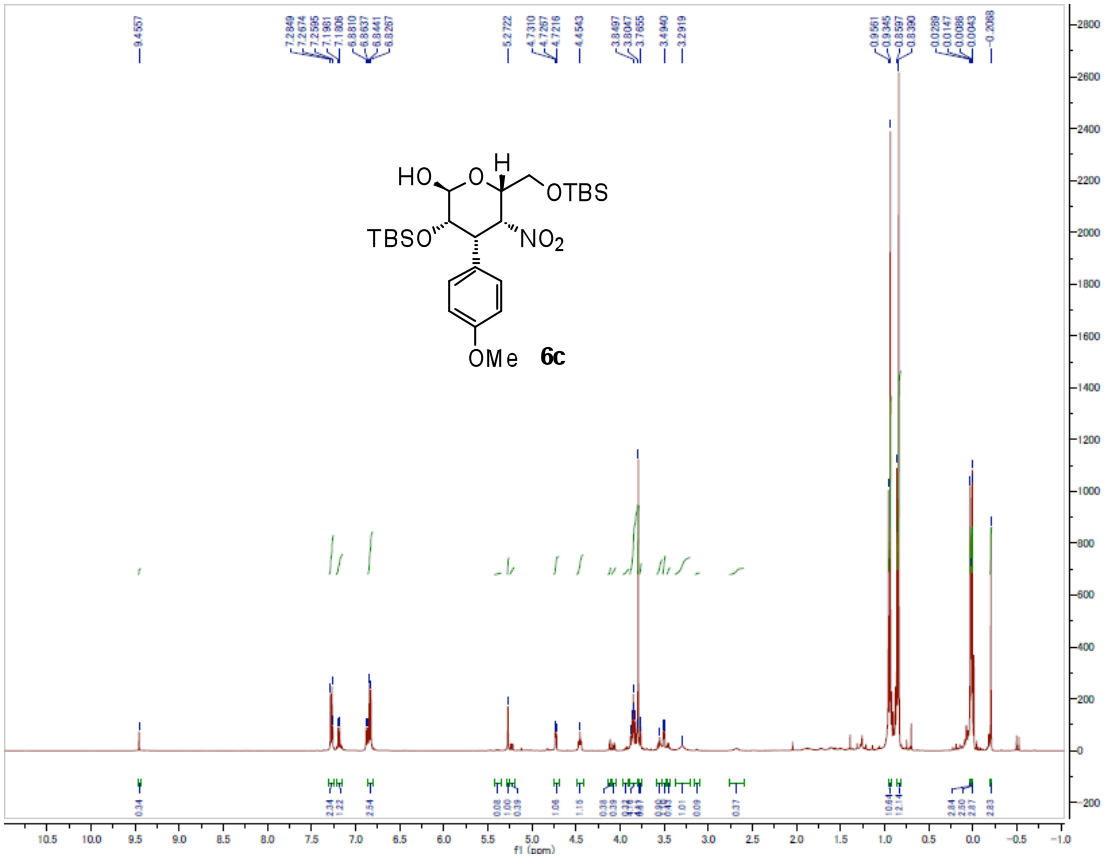
6. NMR charts

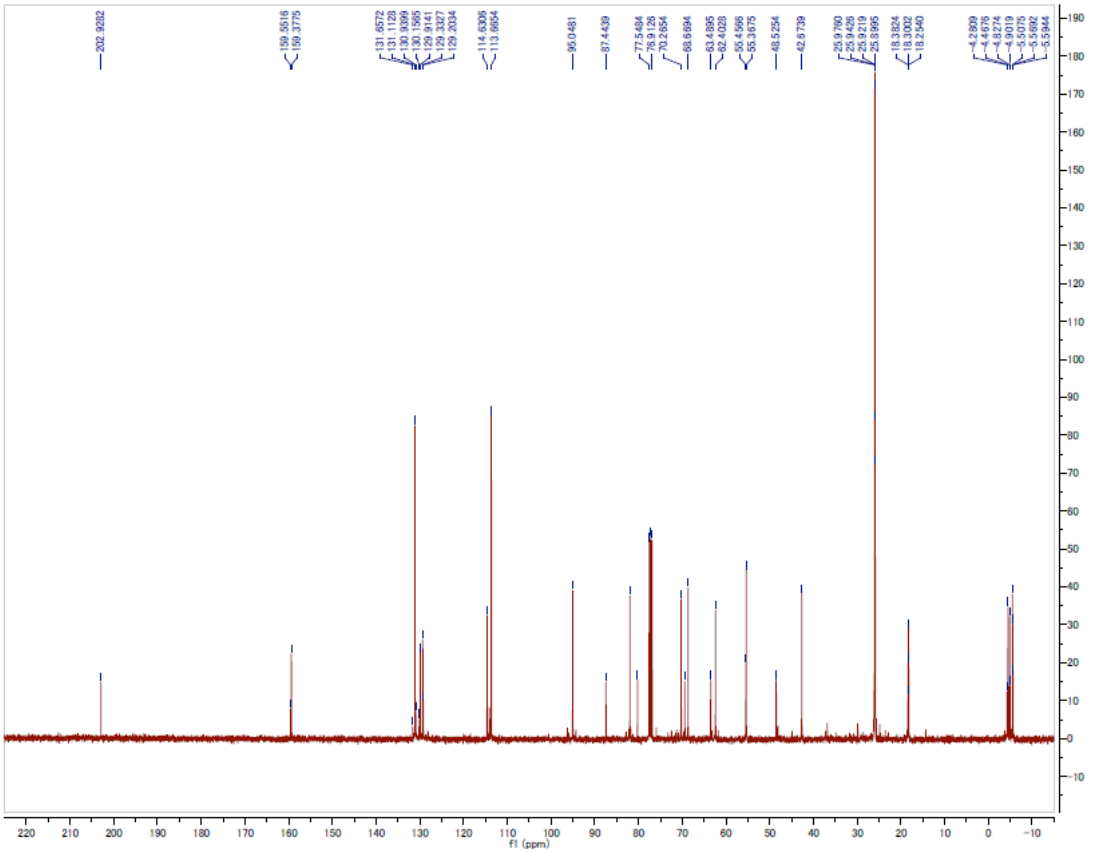


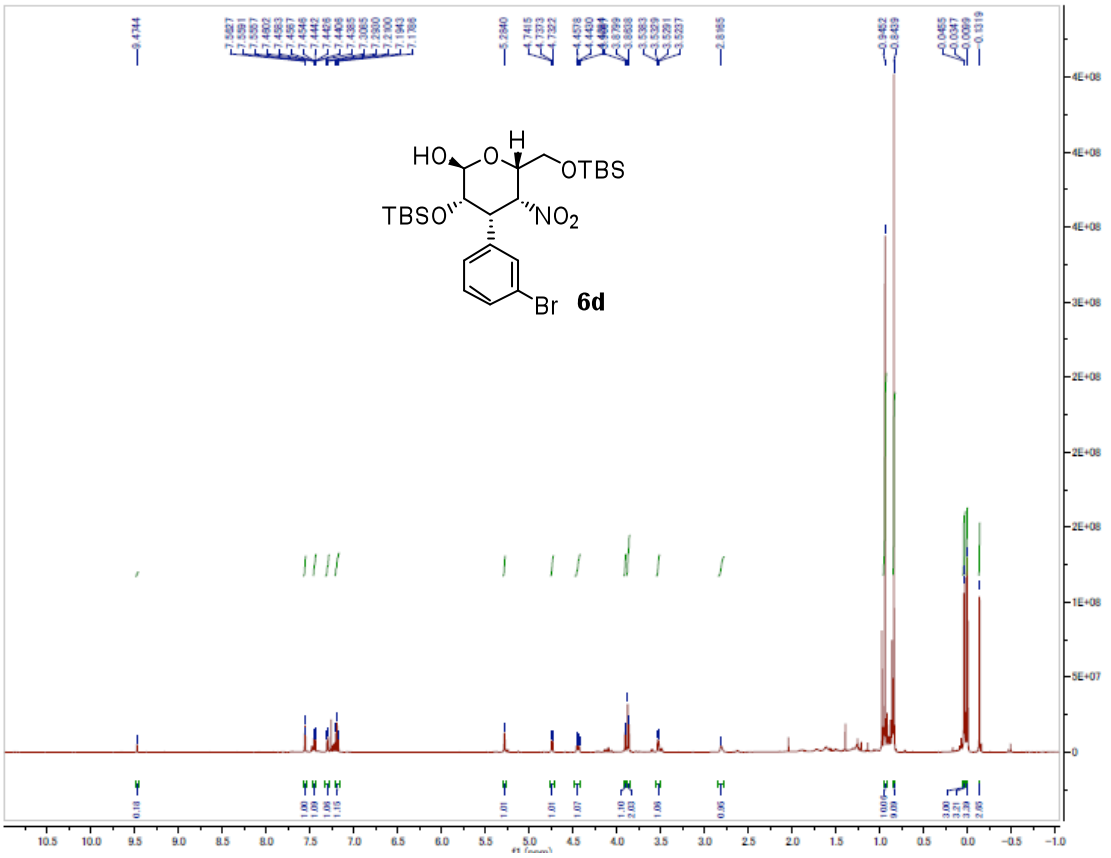


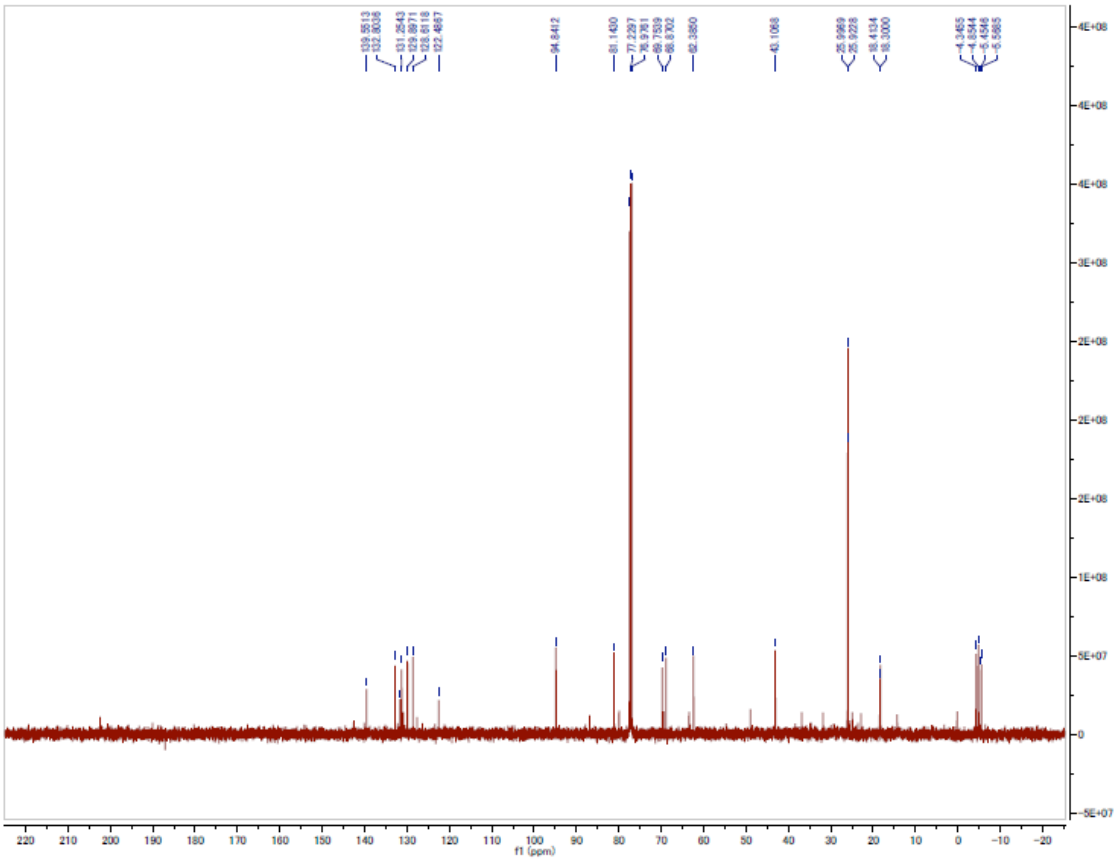

HO
O
H
OTBS
TBSO
NO2
Br
6b
f1 (ppm)

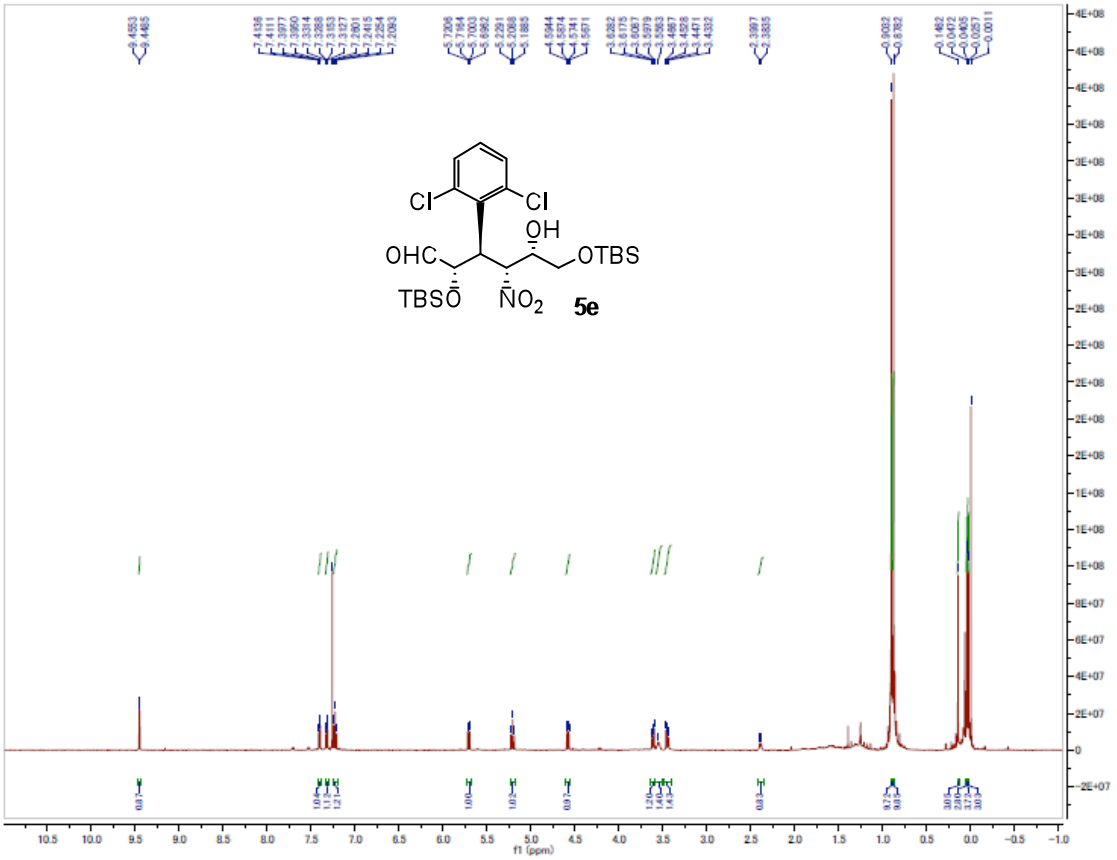

f1 (ppm)

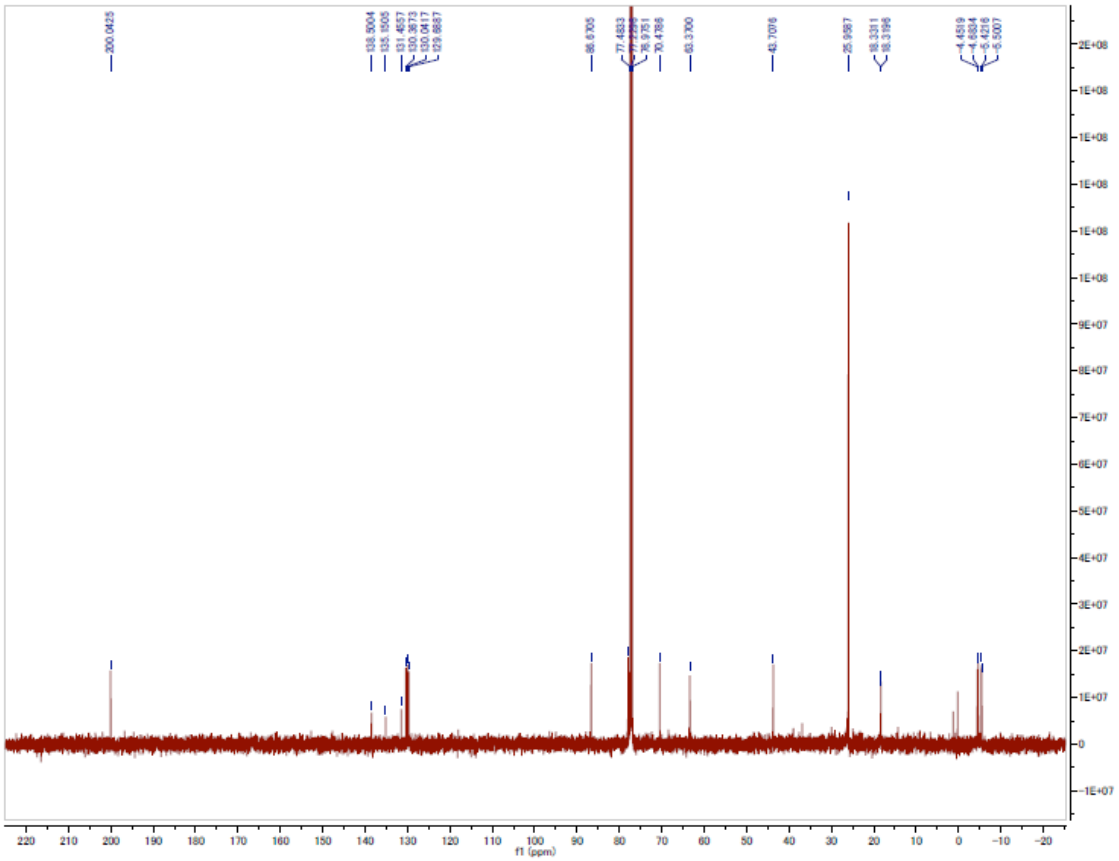

HO
O
H
OTBS
TBSO
NO2
OMe
6c

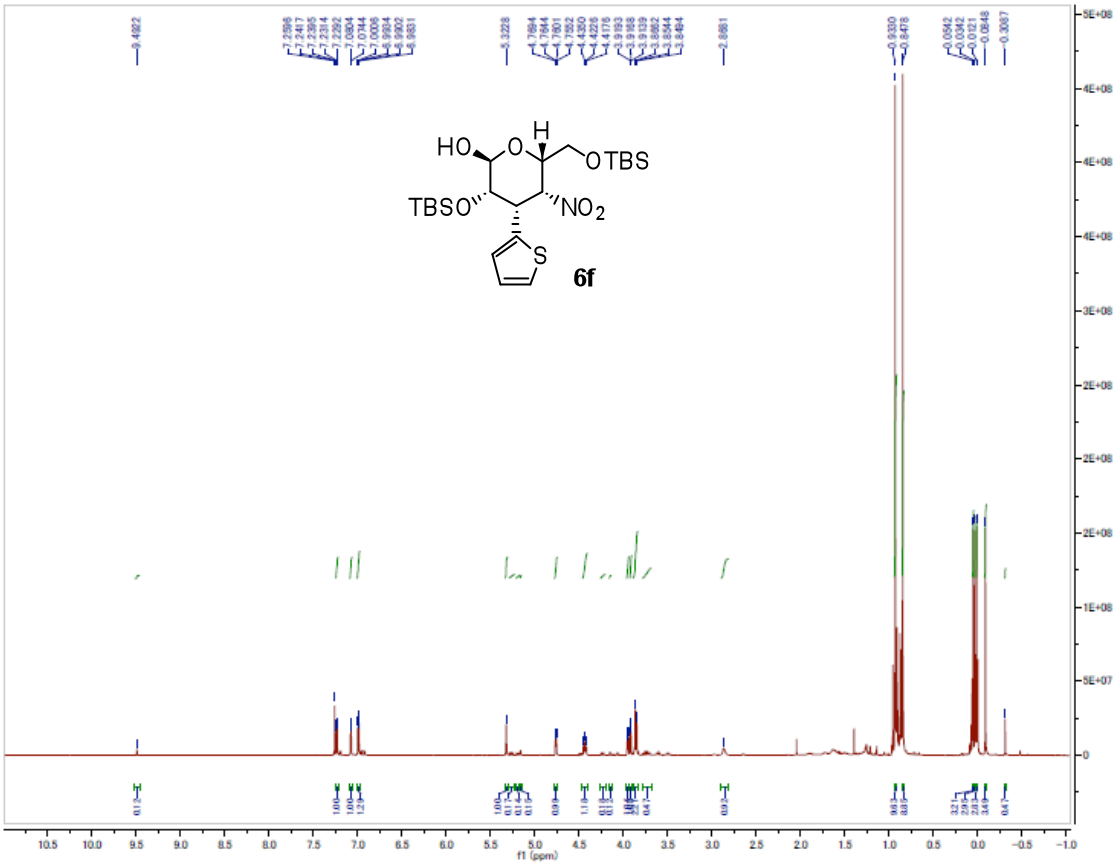


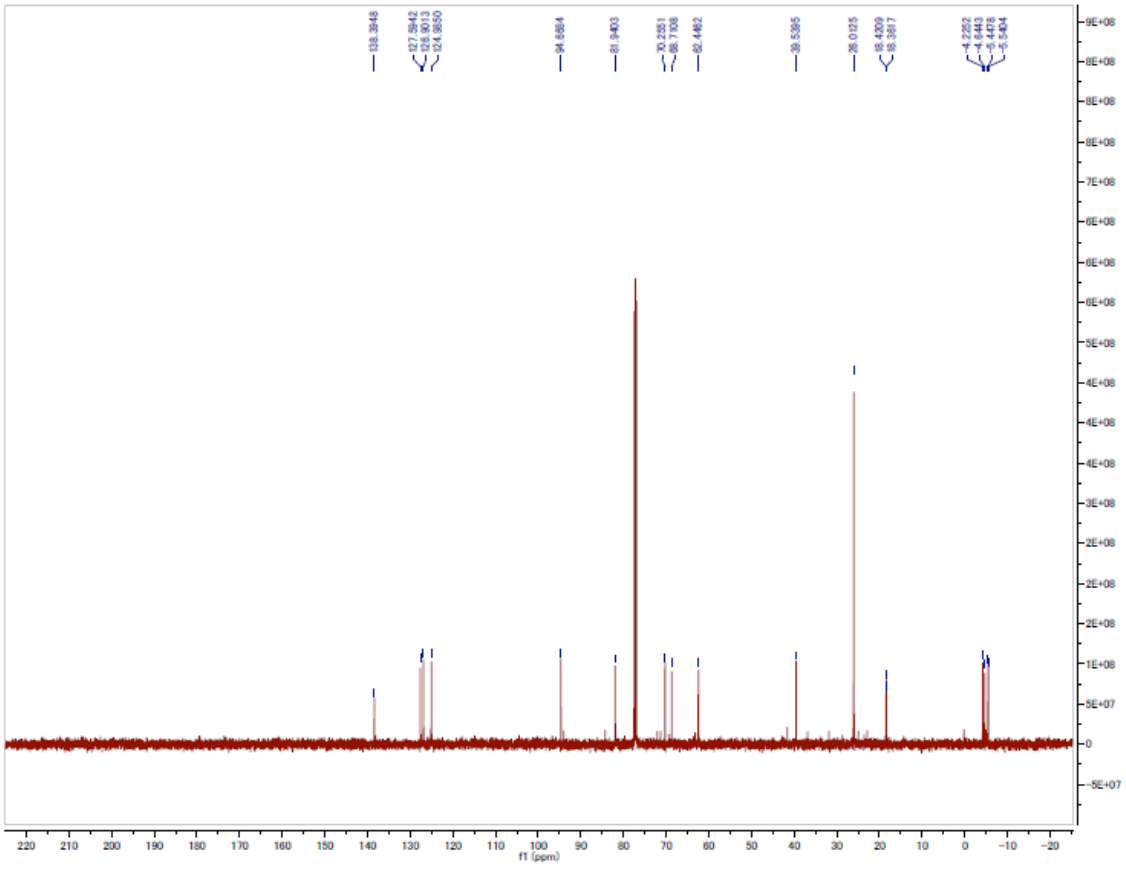

HO
O
H
OTBS
TBSO
NO2
Br
6d

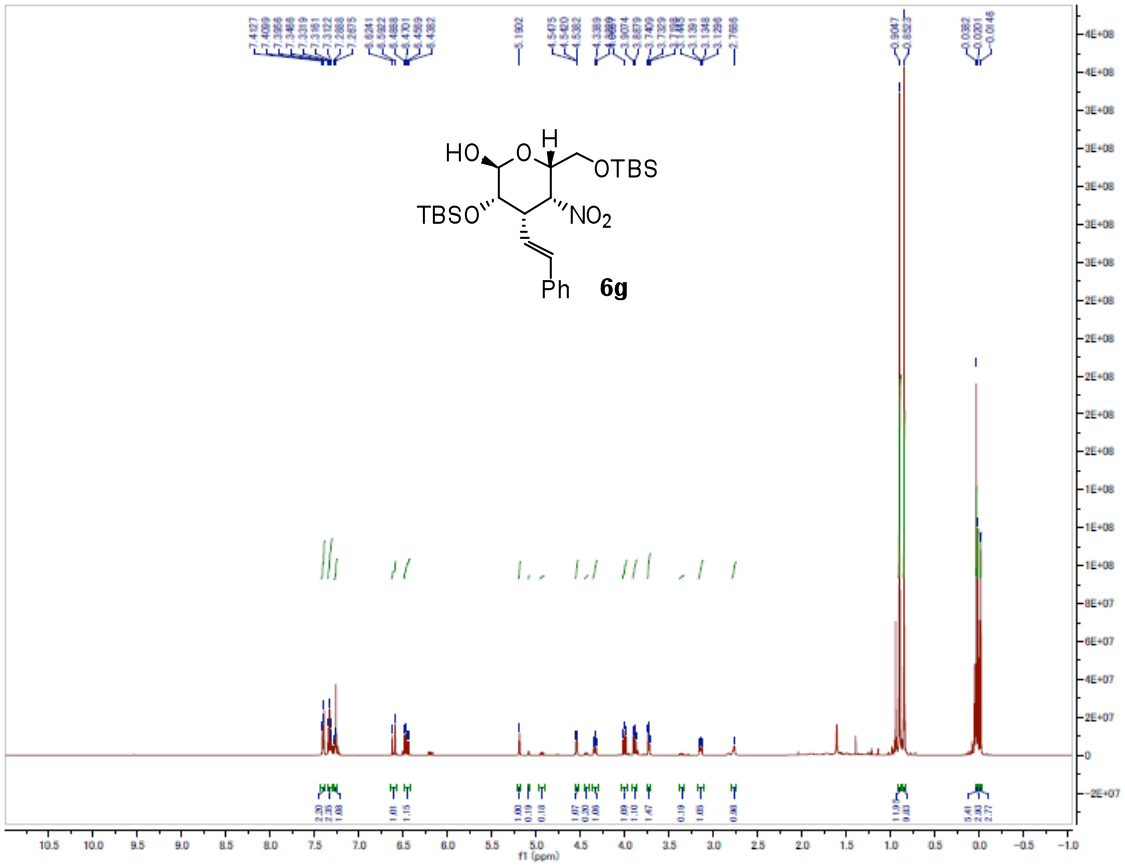


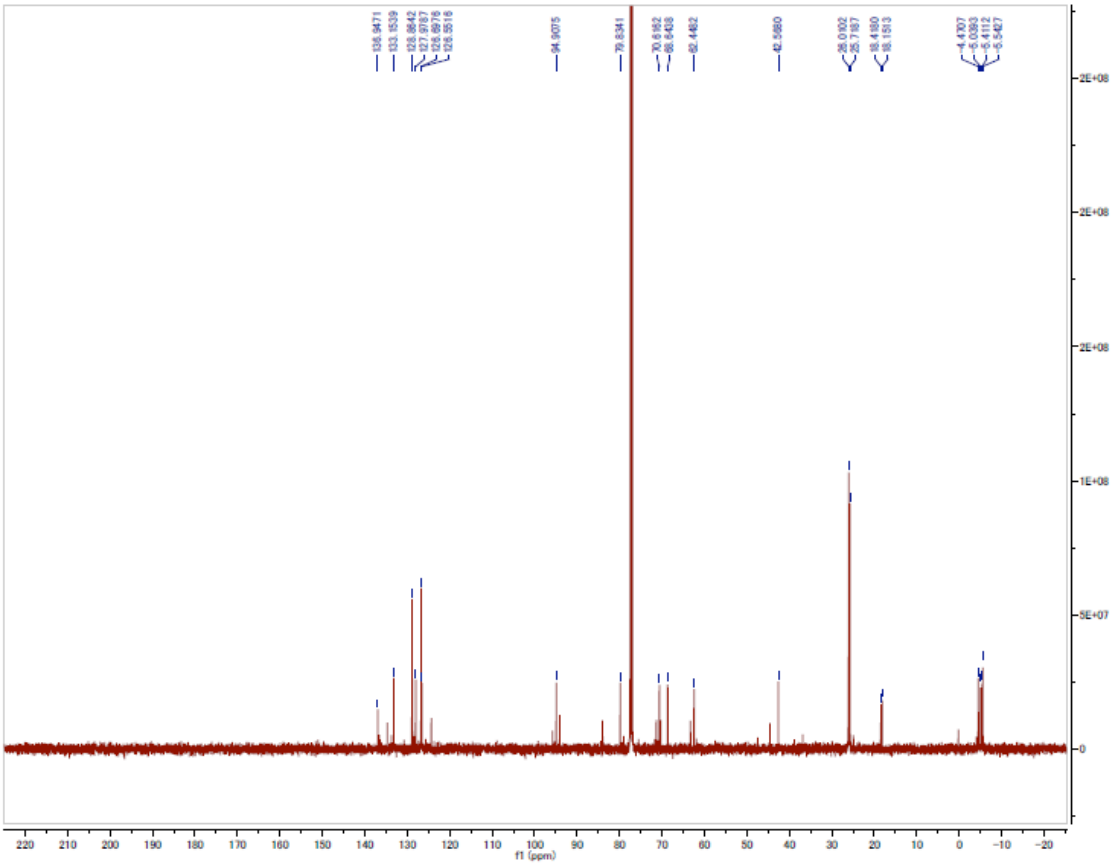

Cl
Cl
OH
OHC
OTBS
TBSO
NO2
5e

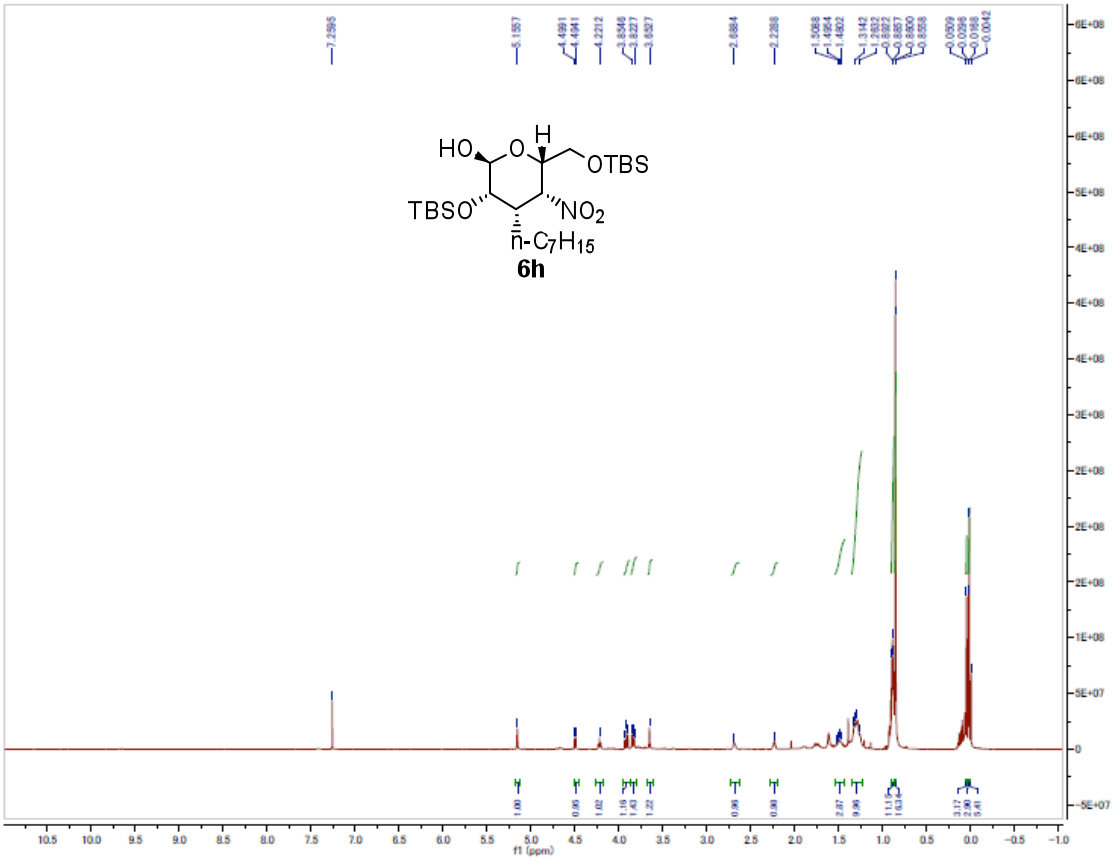


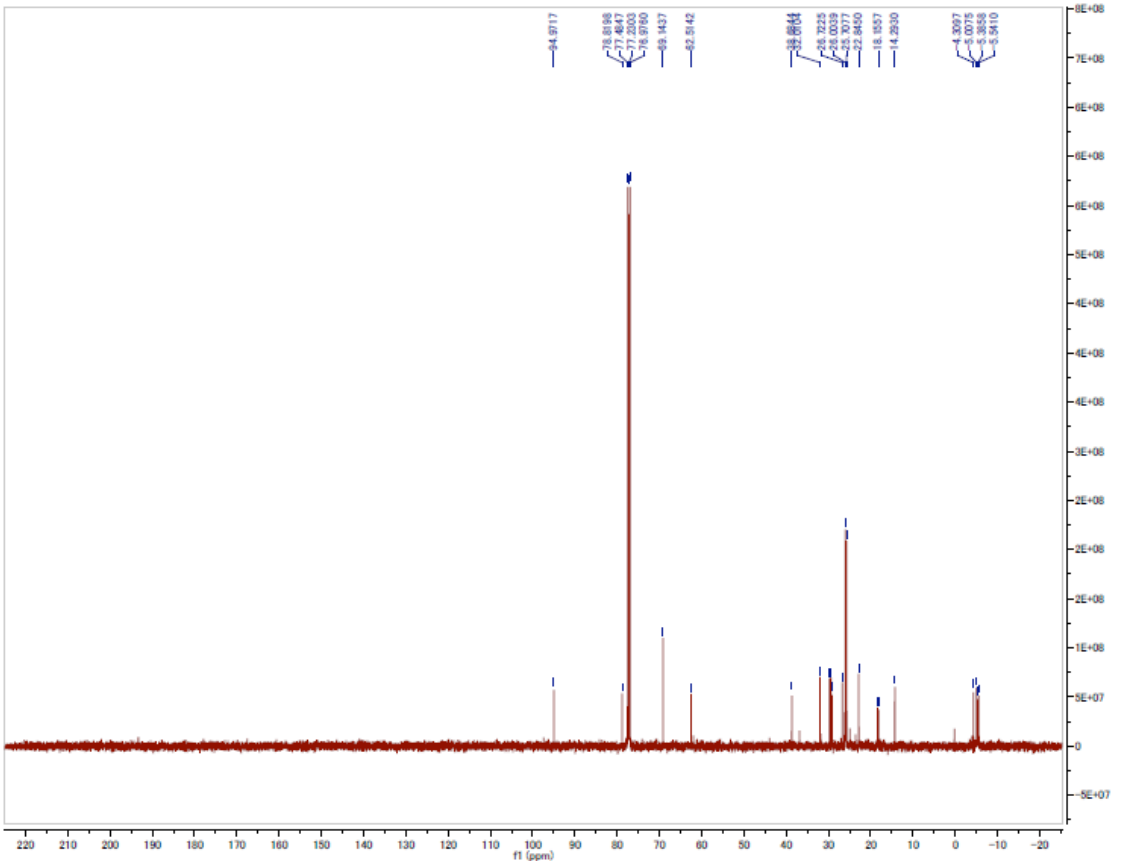

HO
O
H
OTBS
TBSO
NO2
S
6f

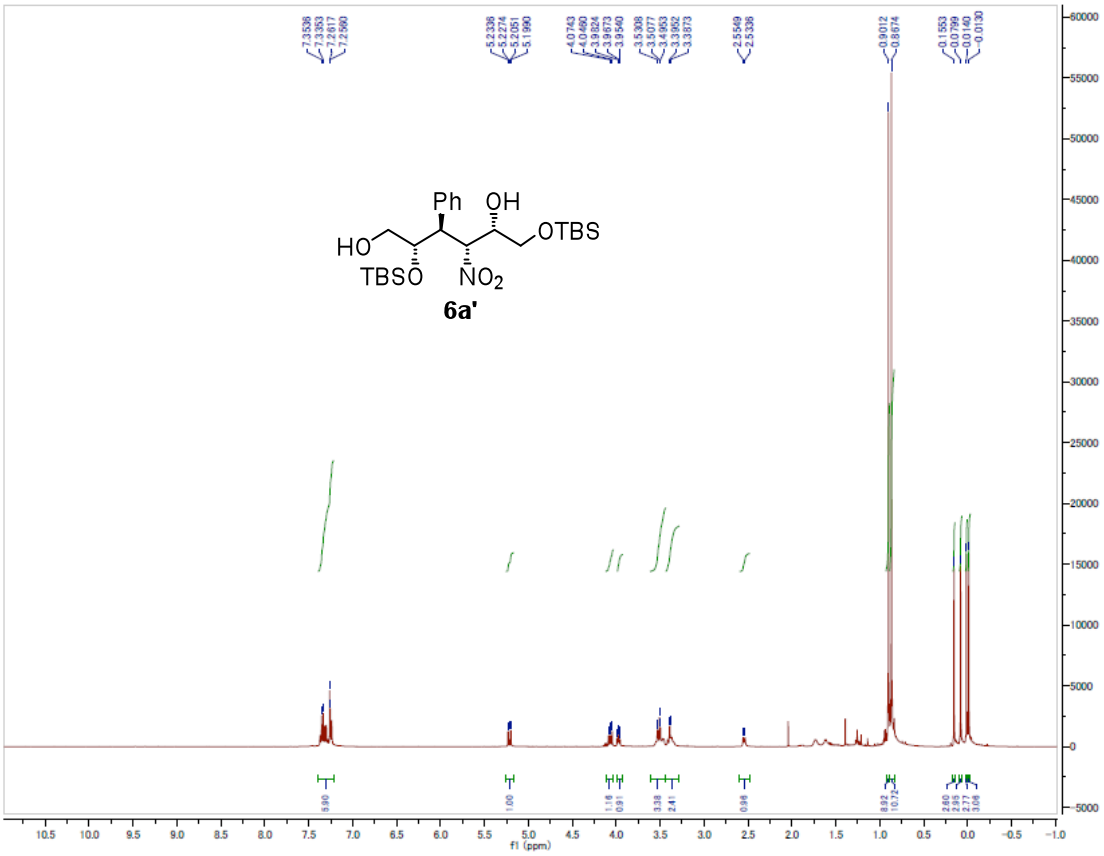


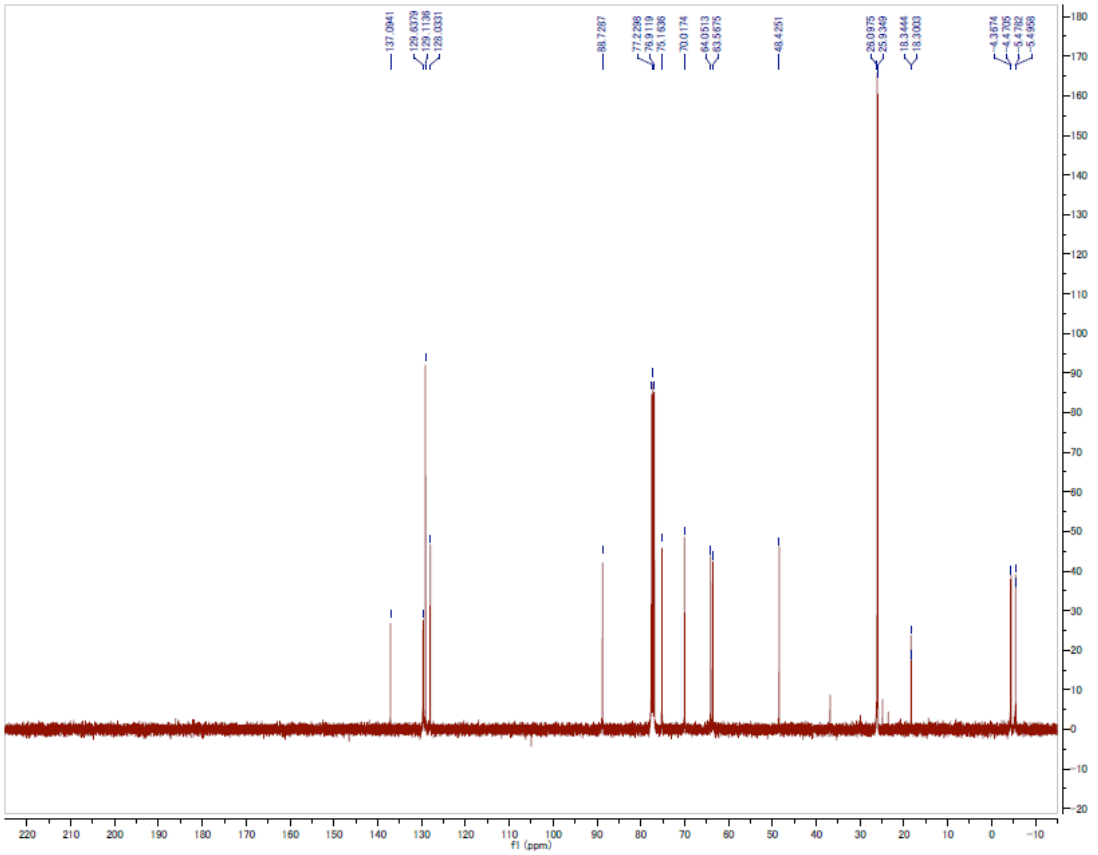

HO
O
H
OTBS
TBSO
NO2
Ph
6g

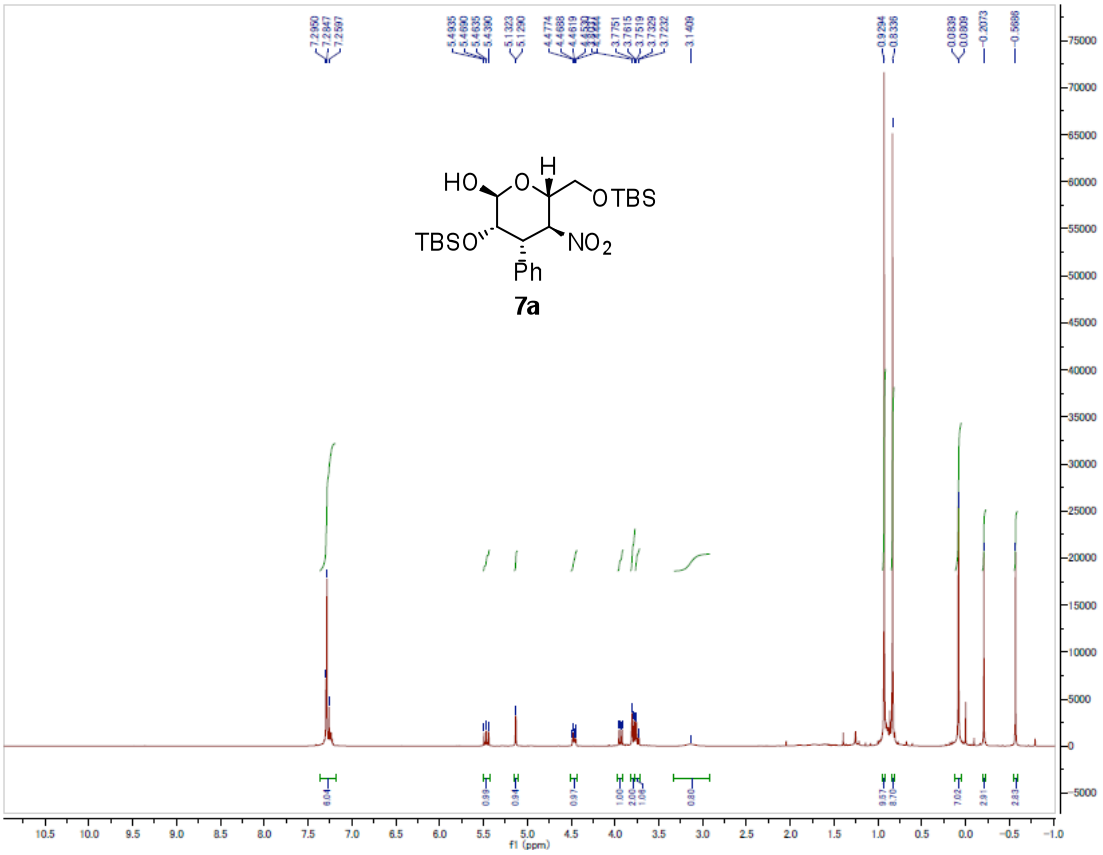


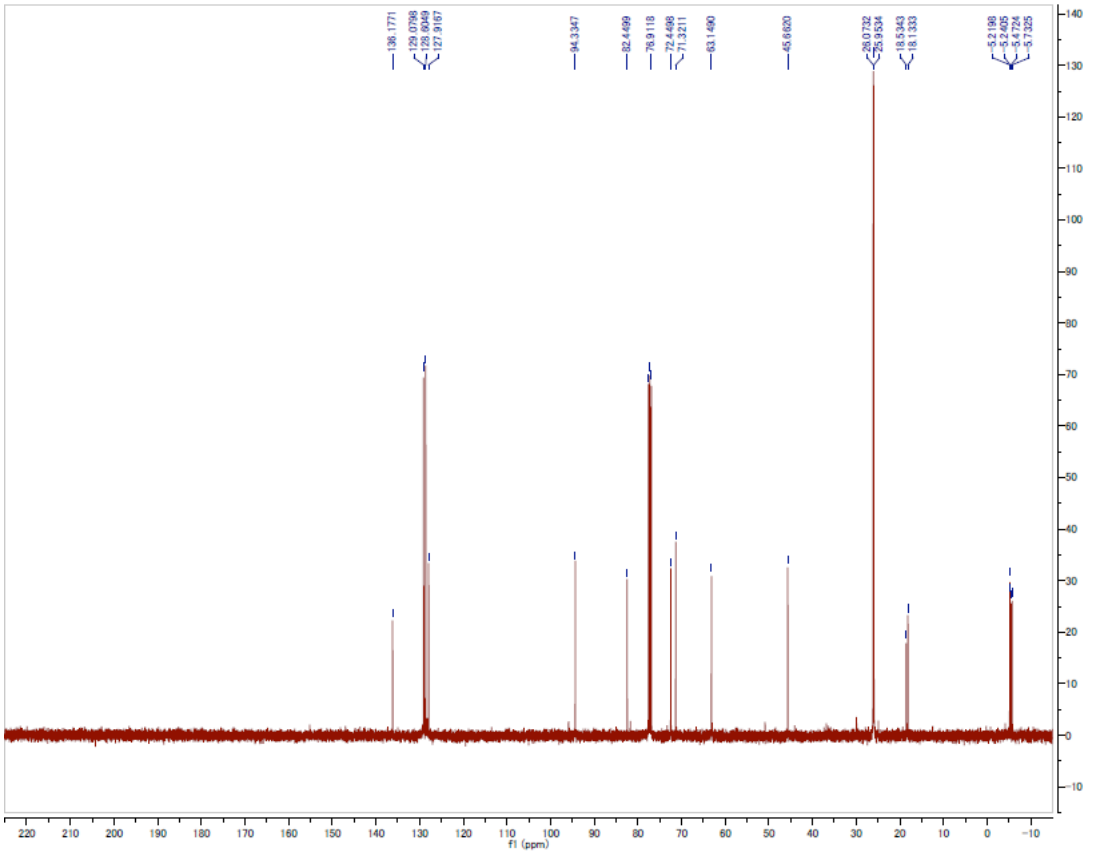

HO
O
H
OTBS
TBSO
NO2
n-C7H15
6h
f1 (ppm)

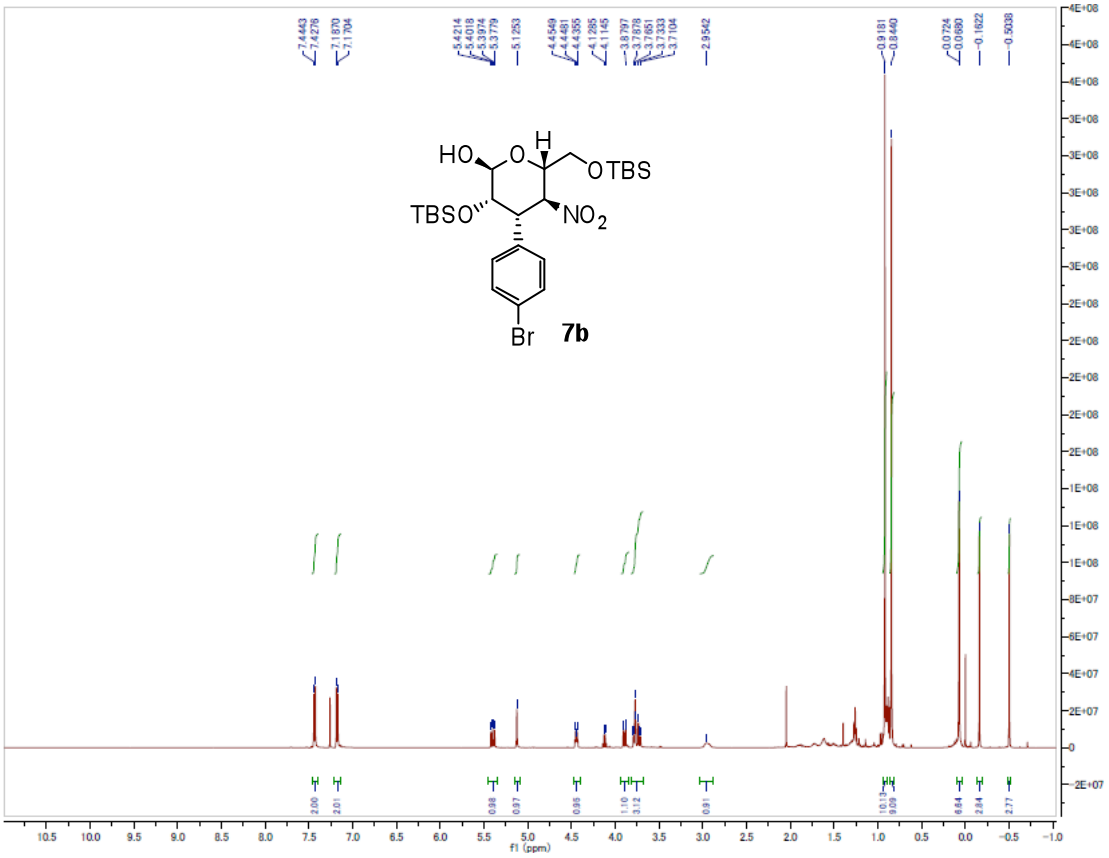

f1 (ppm)

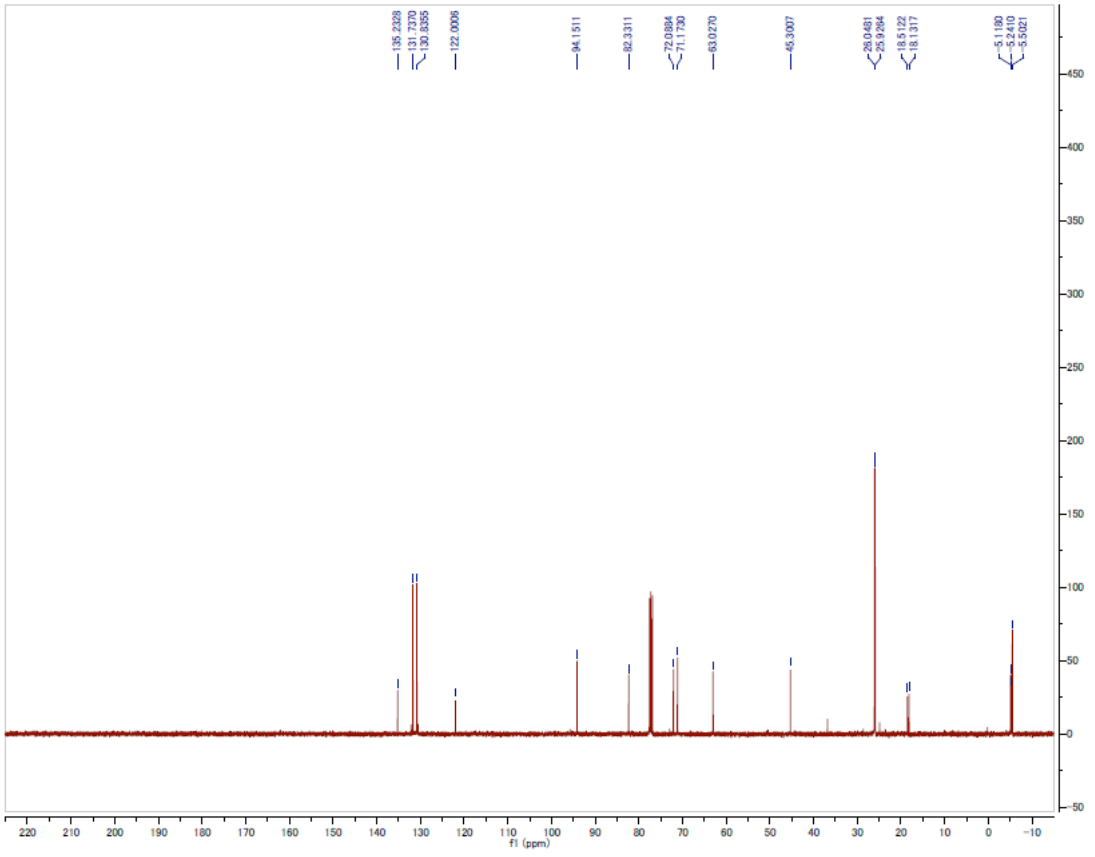

Ph
OH
HO
OTBS
TBSO
NO2
6a'

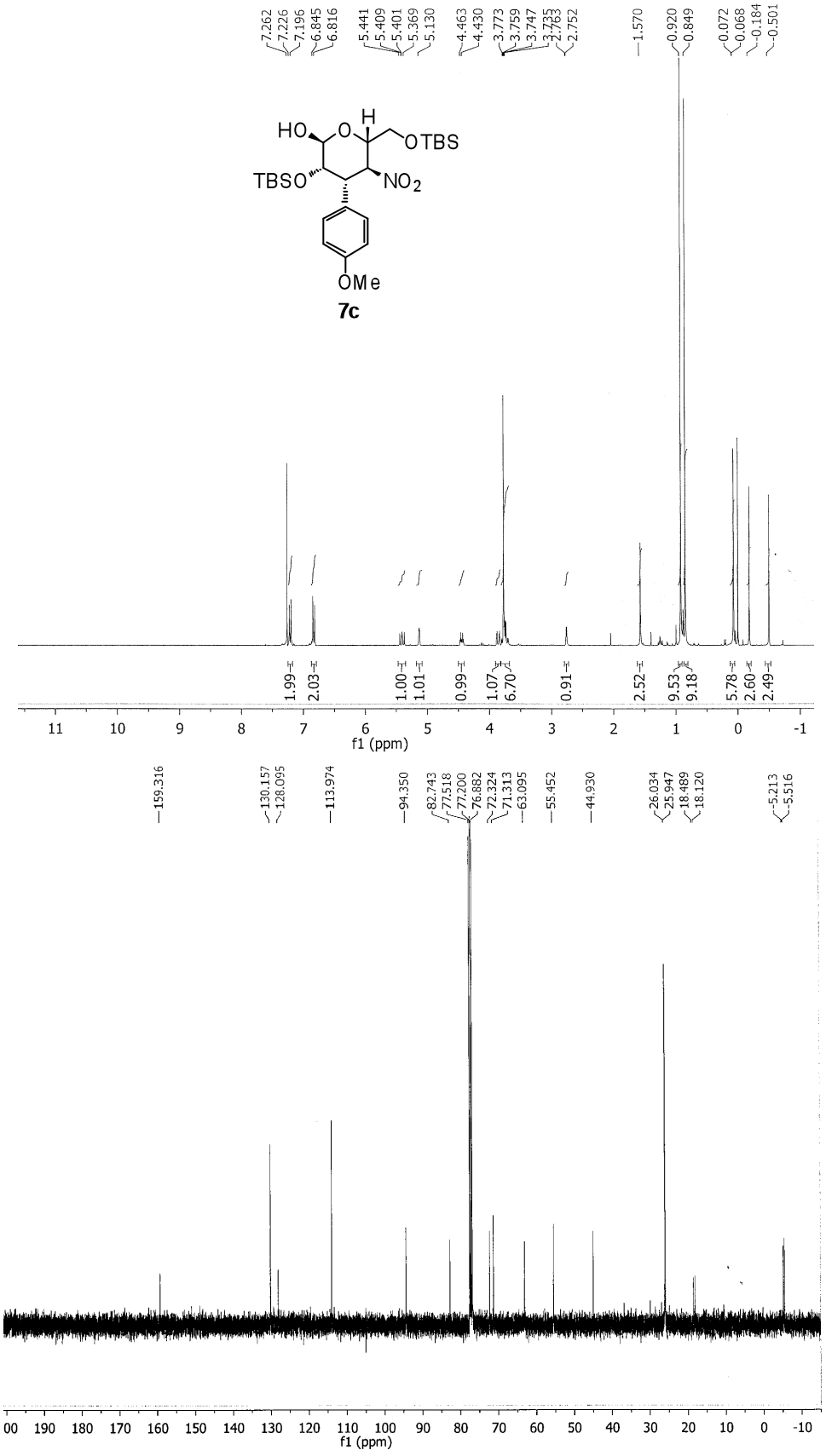


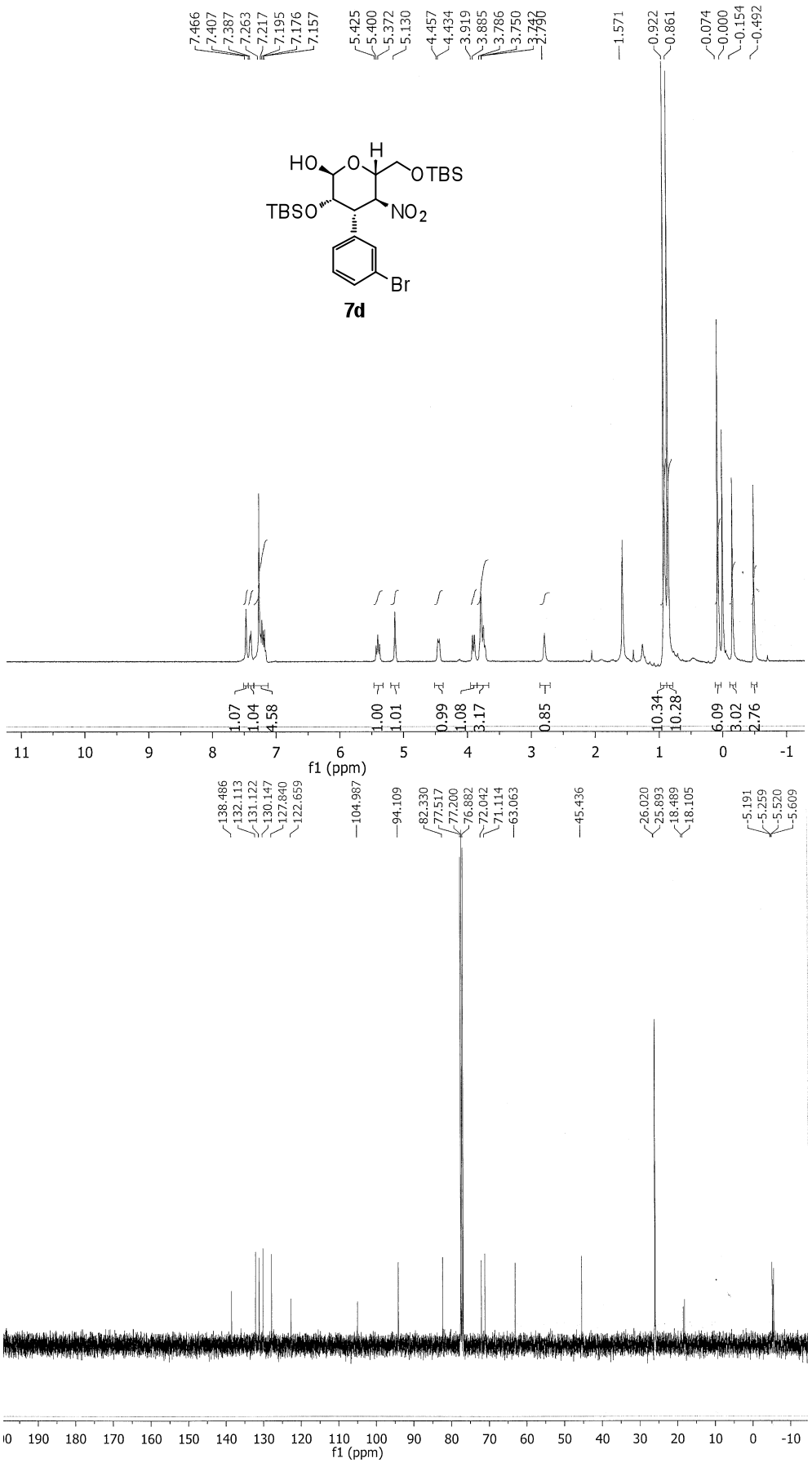

HO
O
H
OTBS
TBSO
NO2
Ph
7a
f1 (ppm)

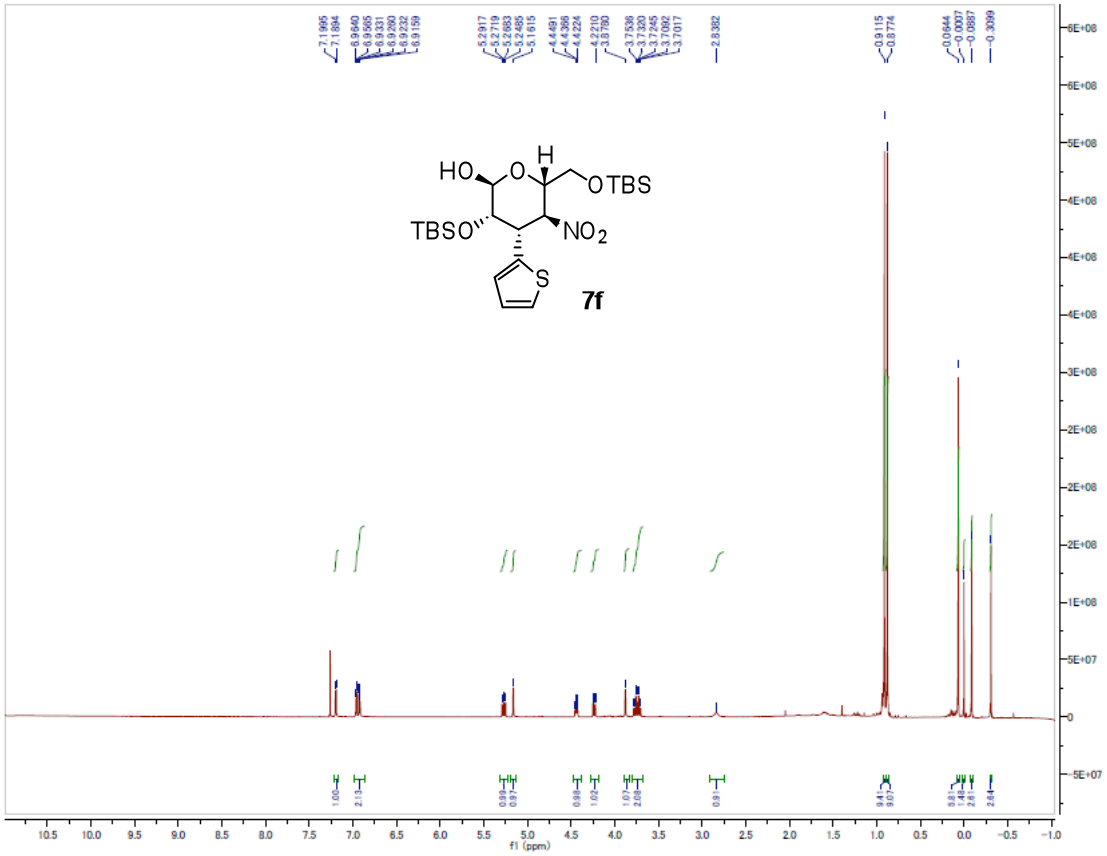

f1 (ppm)

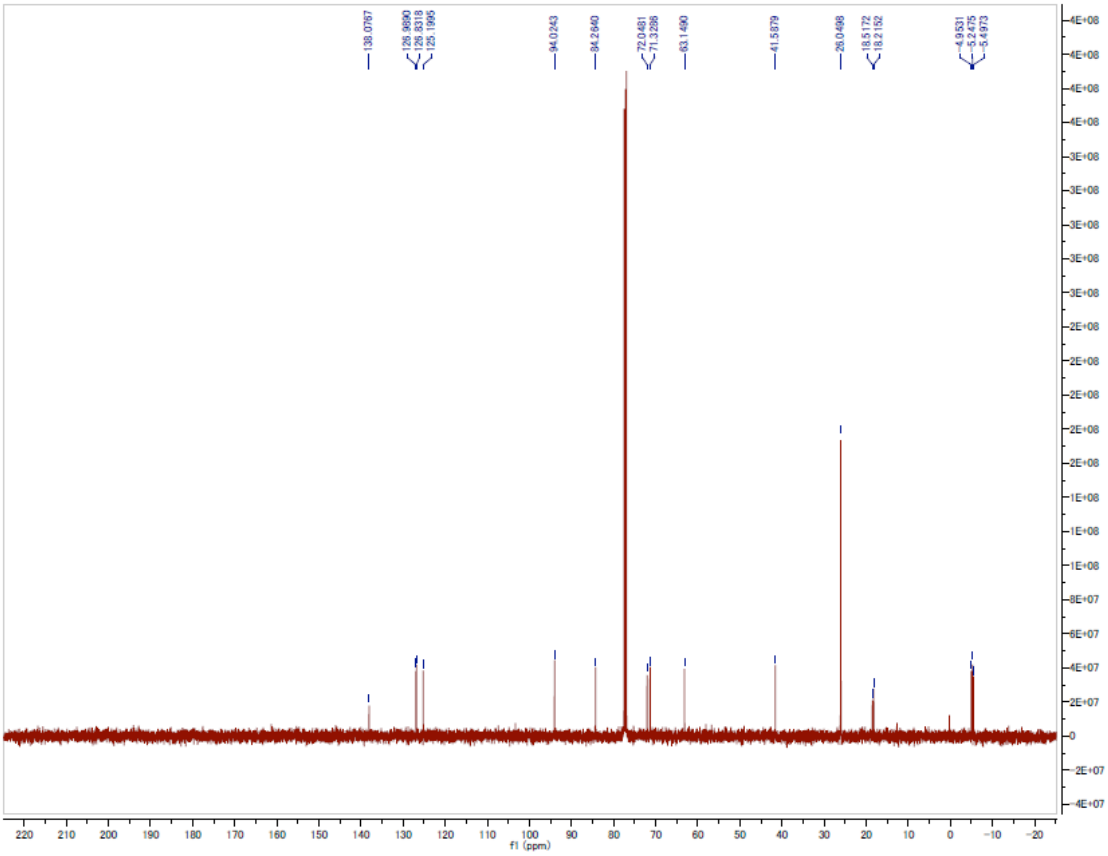

HO
O
H
OTBS
TBSO
NO2
Br
7b
f1 (ppm)

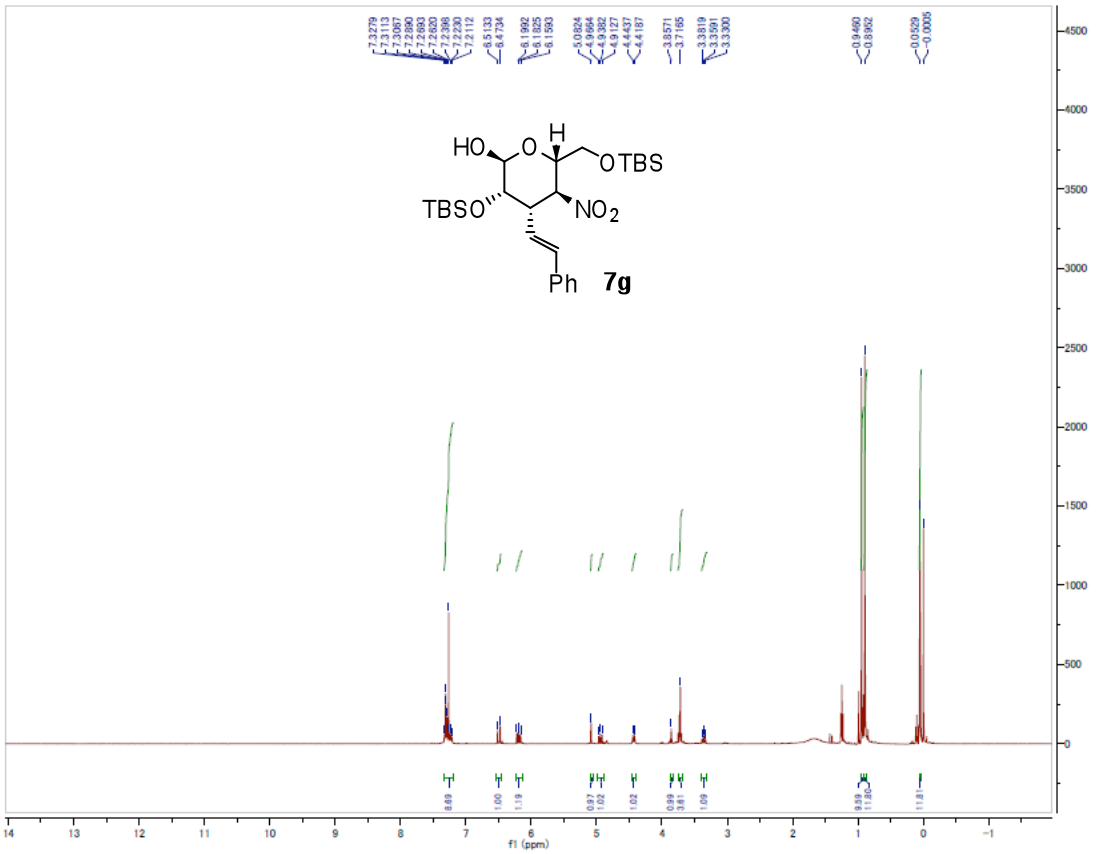

f1 (ppm)


7.262
7.226
7.196
6.845
6.816
5.441
5.409
5.401
5.369
5.130
4.463
4.430
3.773
3.759
3.747
3.735
2.763
2.752
1.570
0.920
0.849
0.072
0.068
-0.184
-0.501
HO
O
H
OTBS
TBSO
NO2
OMe
7c
1.99
2.03
1.00
1.01
0.99
1.07
6.70
0.91
2.52
9.53
9.18
5.78
2.60
2.49
f1 (ppm)
159.316
130.157
128.095
113.974
94.350
82.743
77.518
77.200
76.882
72.324
71.313
63.095
55.452
44.930
26.034
25.947
18.489
18.120
-5.213
-5.516
f1 (ppm)

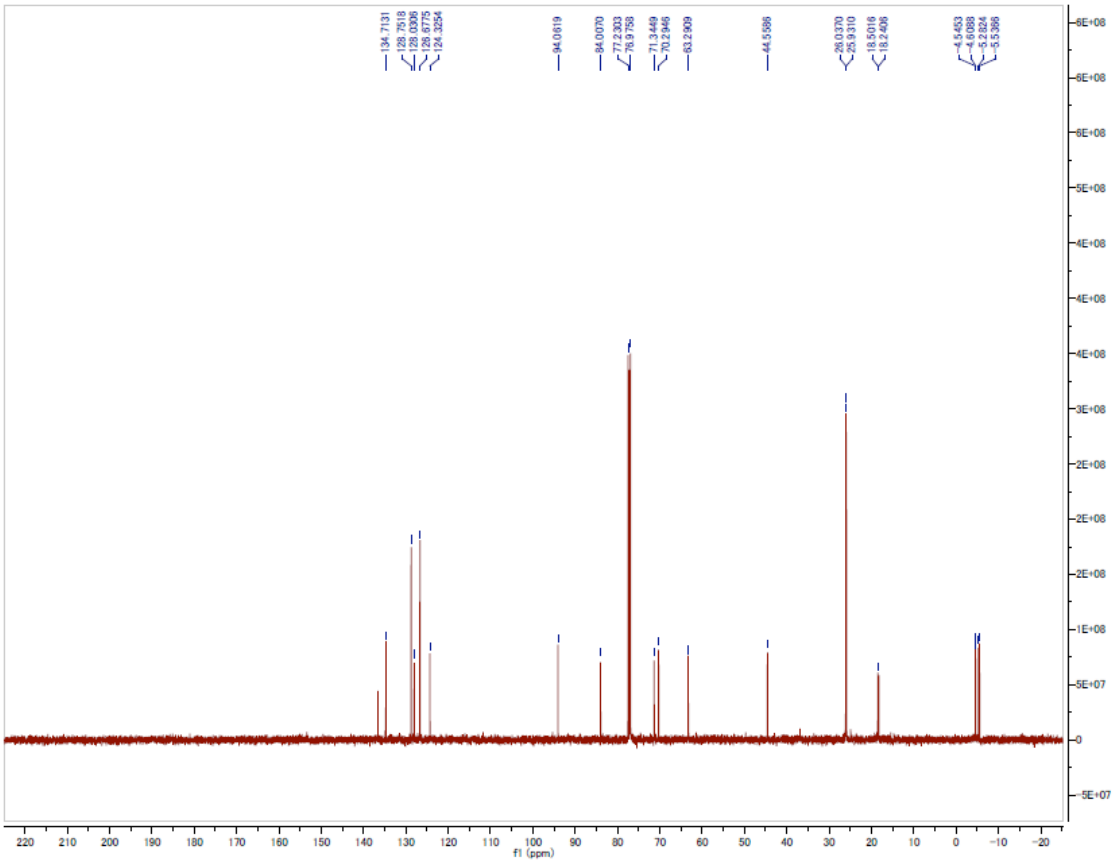

HO
O
H
OTBS
TBSO
NO2
Br
7d
f1 (ppm)
f1 (ppm)

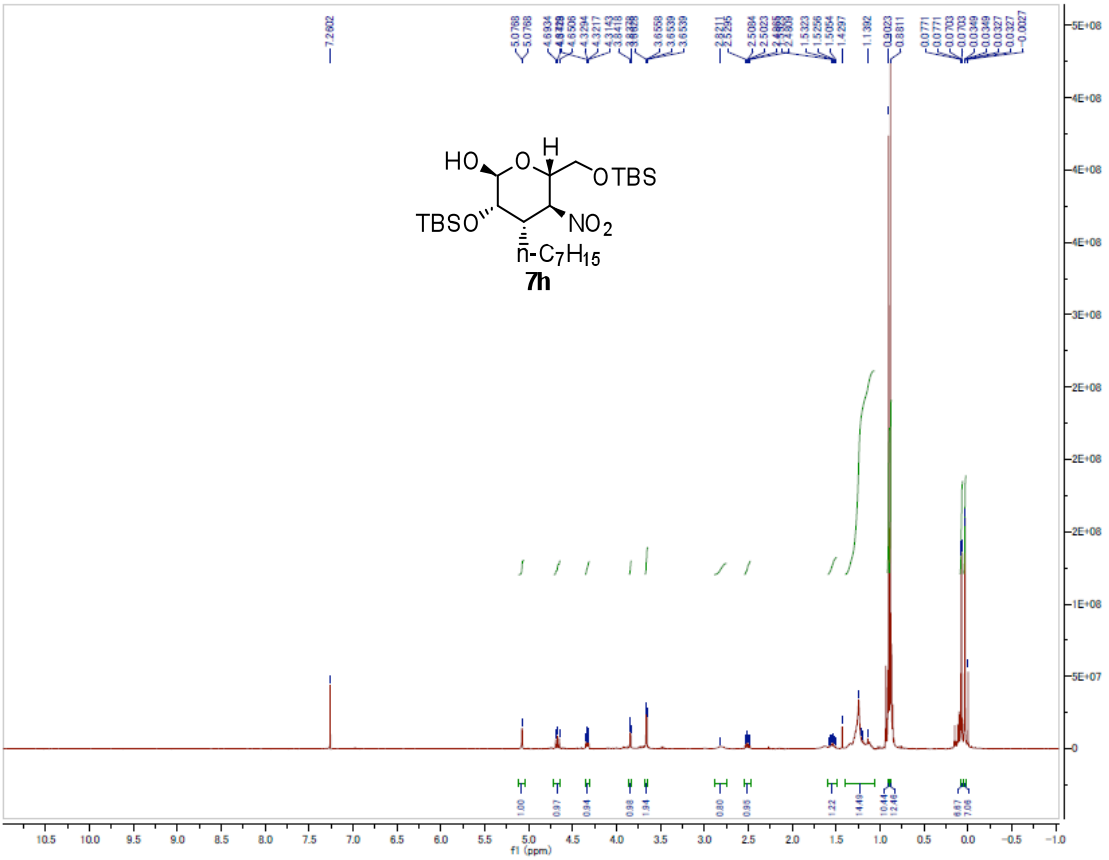

HO
O
H
OTBS
TBSO
NO2
S
7f
f1 (ppm)

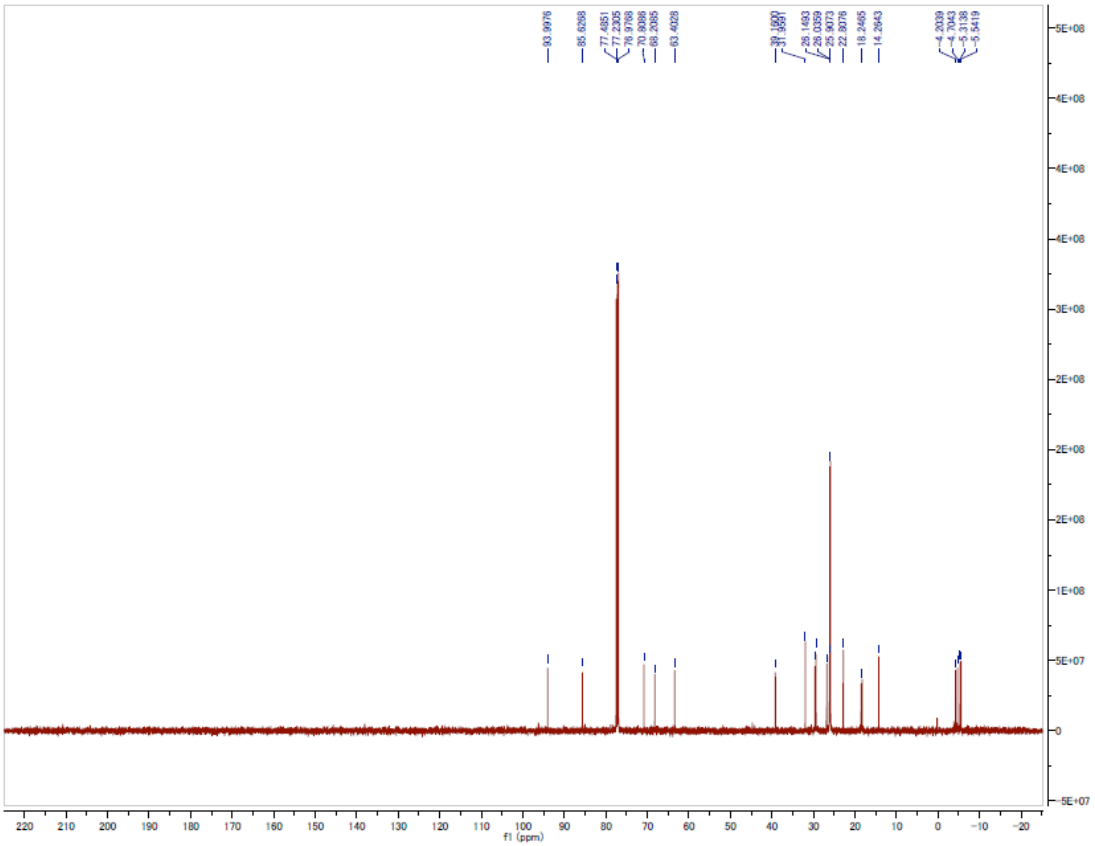

f1 (ppm)

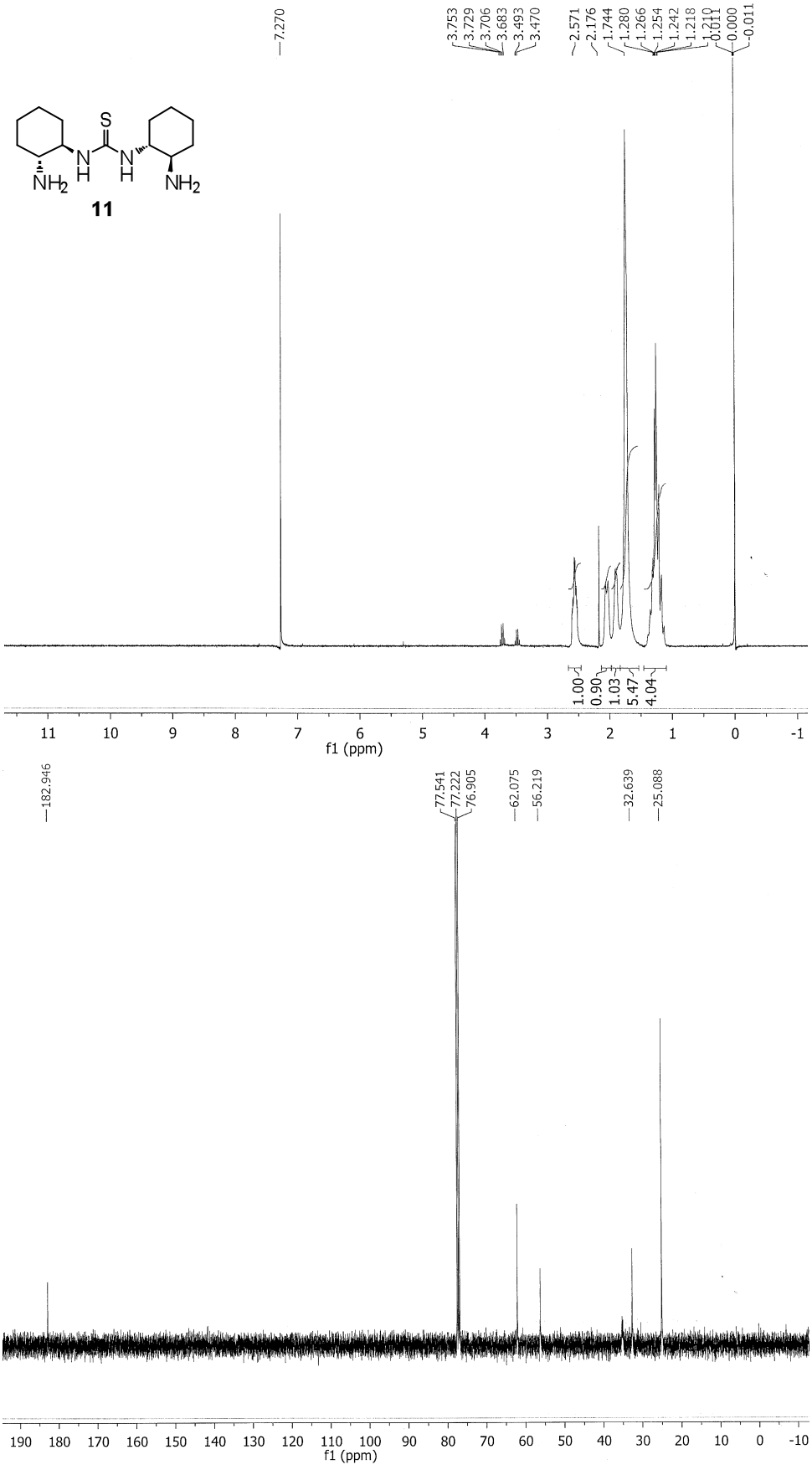


CAMBIAR sin Et2O

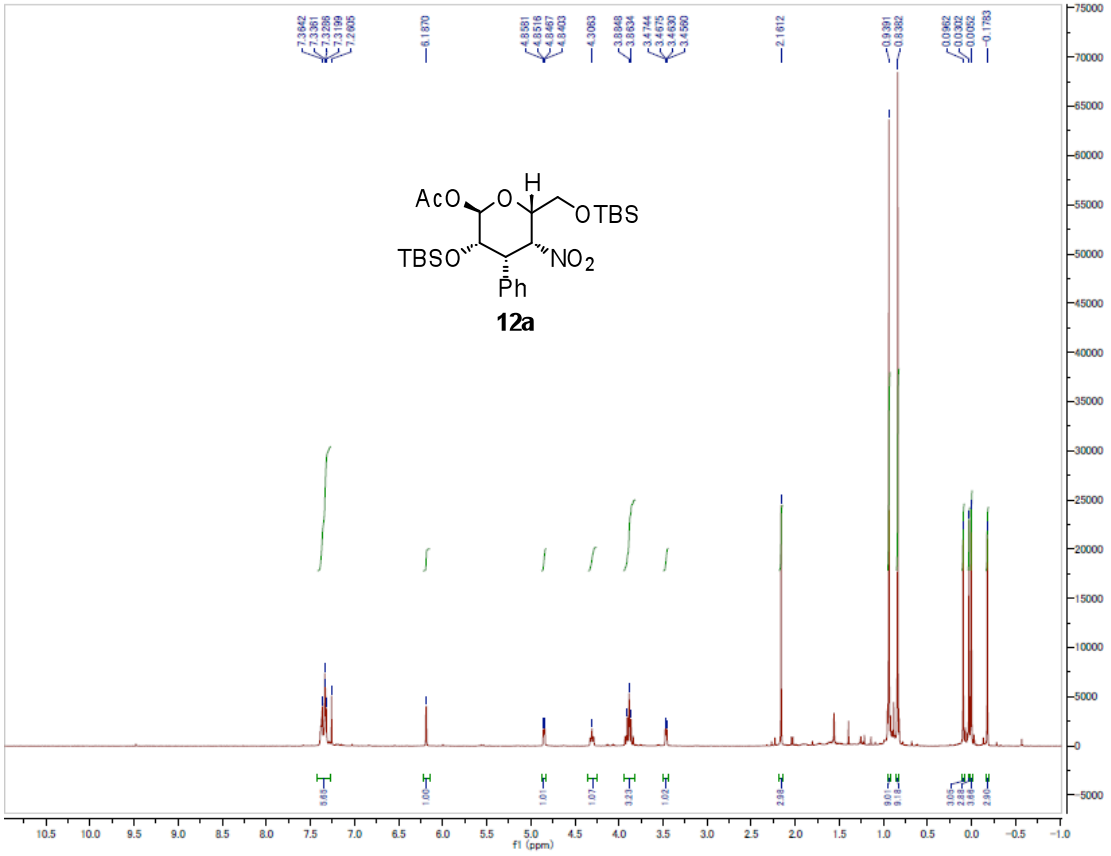


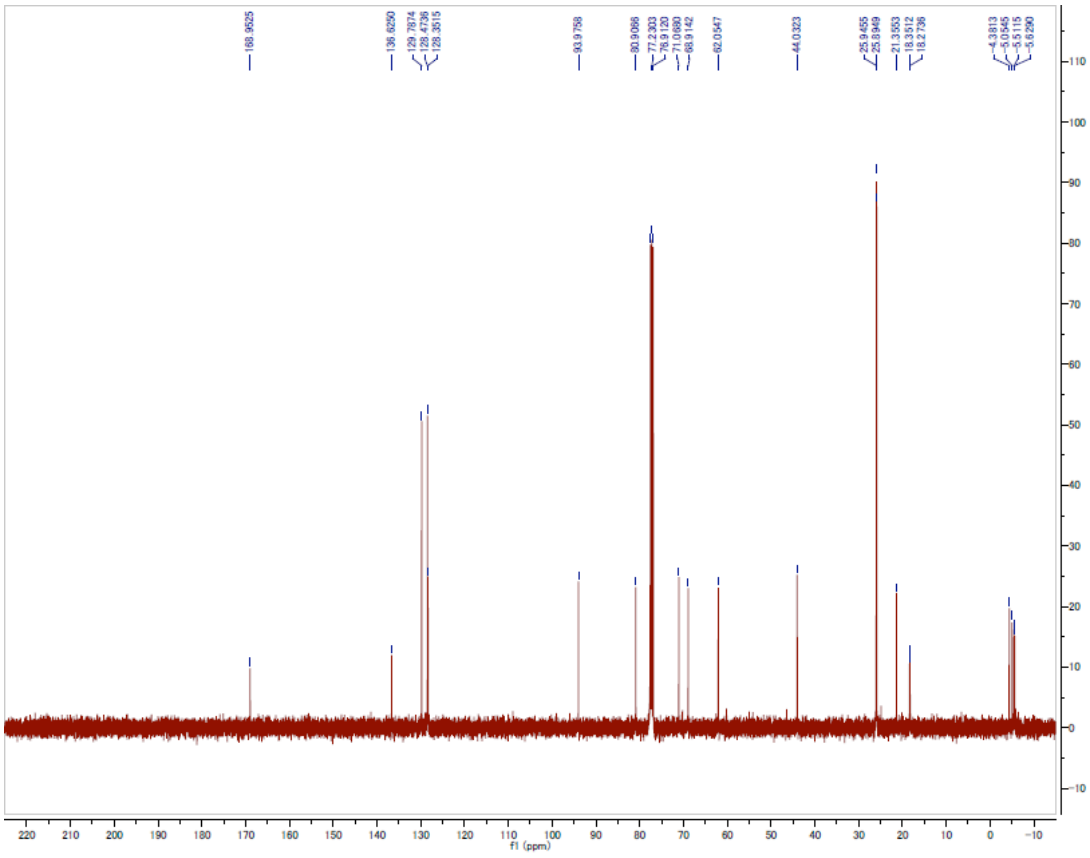

HO
O
H
OTBS
TBSO
NO2
n-C7H15
7h
f1 (ppm)

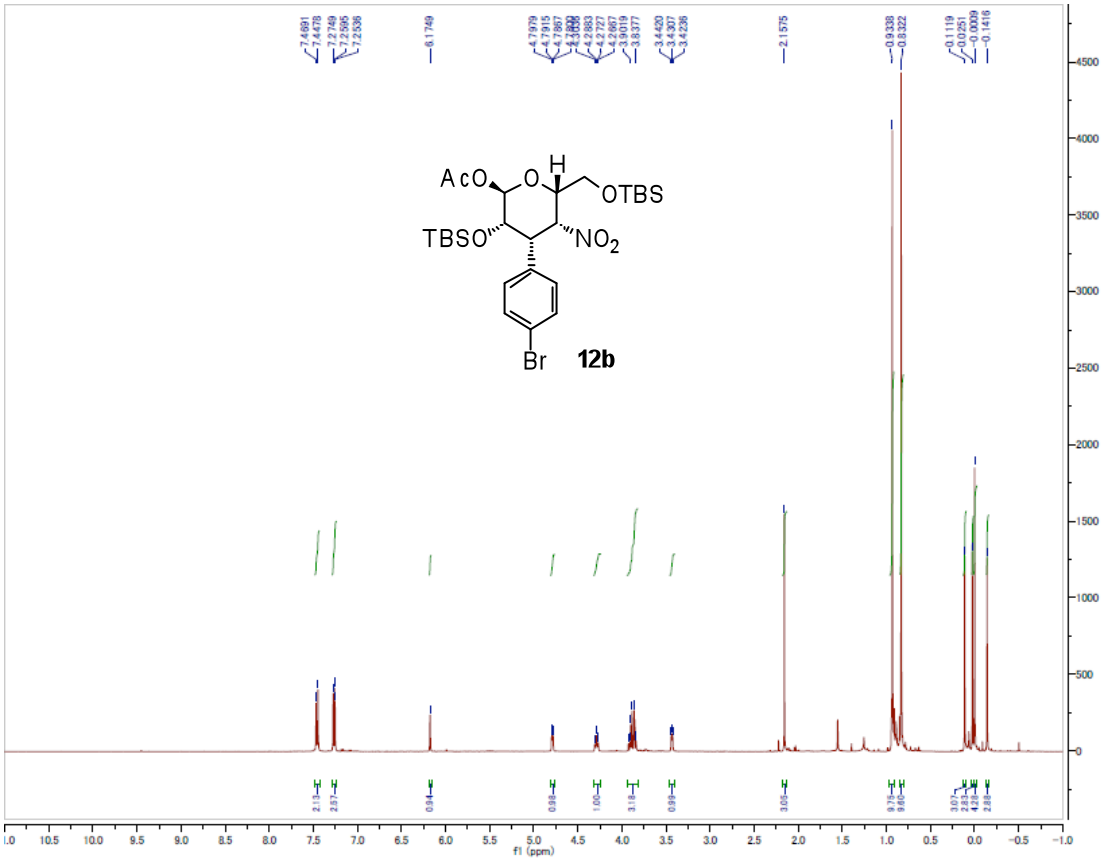

f1 (ppm)

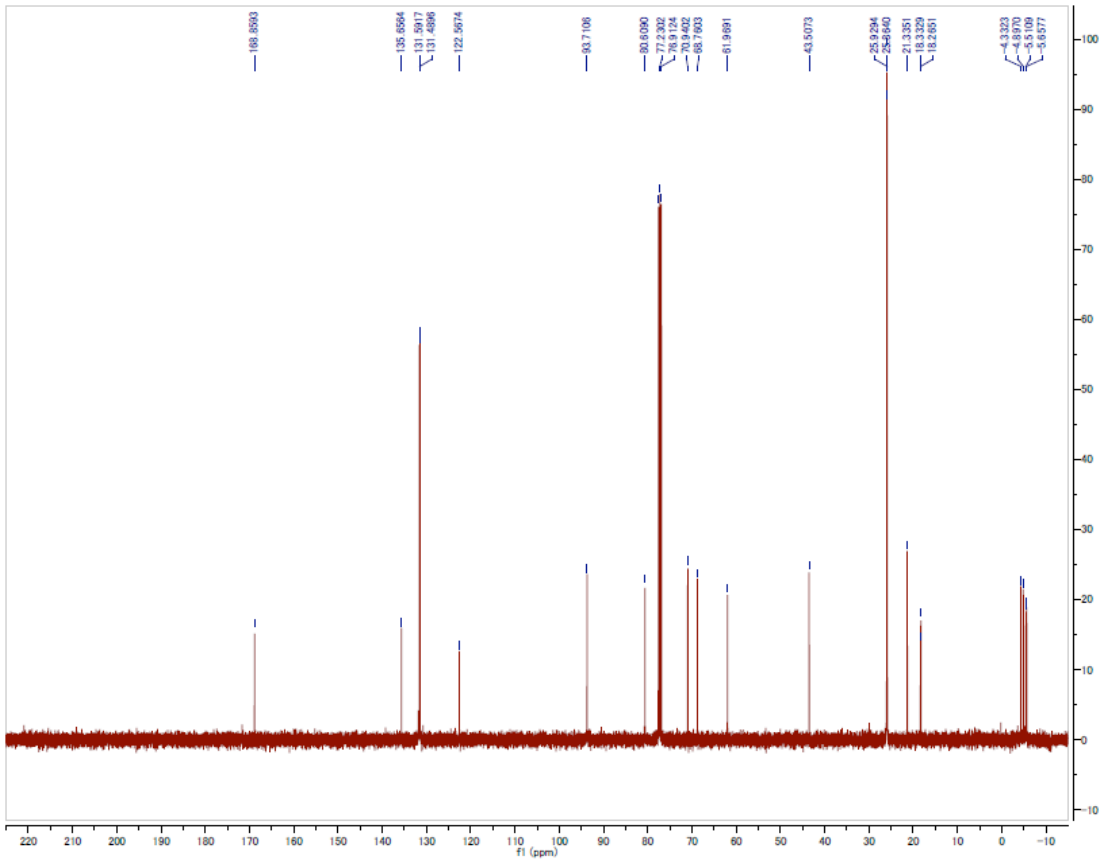

7.270
3.753
3.729
3.706
3.683
3.493
3.470
2.571
2.176
1.744
1.280
1.266
1.254
1.242
1.218
1.210
0.011
0.000
-0.011
1.00
0.90
1.03
5.47
4.04
f1 (ppm)
182.946
77.541
77.222
76.905
62.075
56.219
32.639
25.088
f1 (ppm)

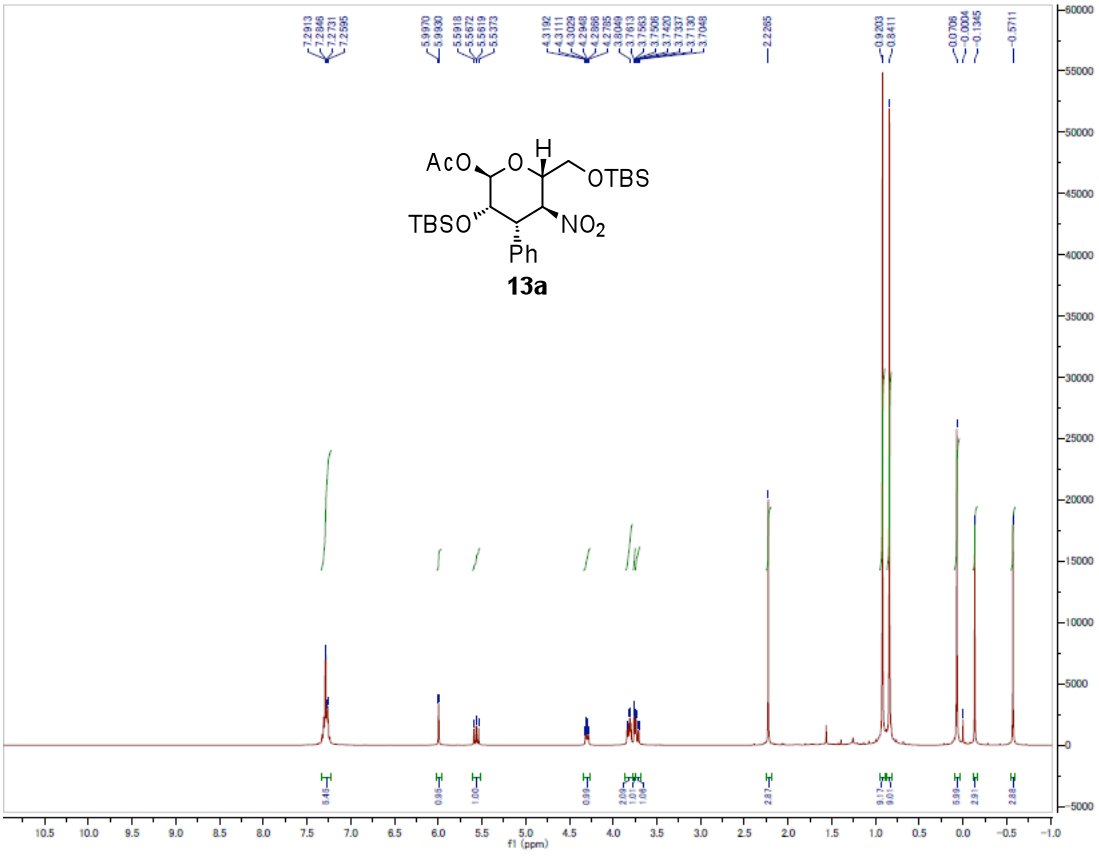
11

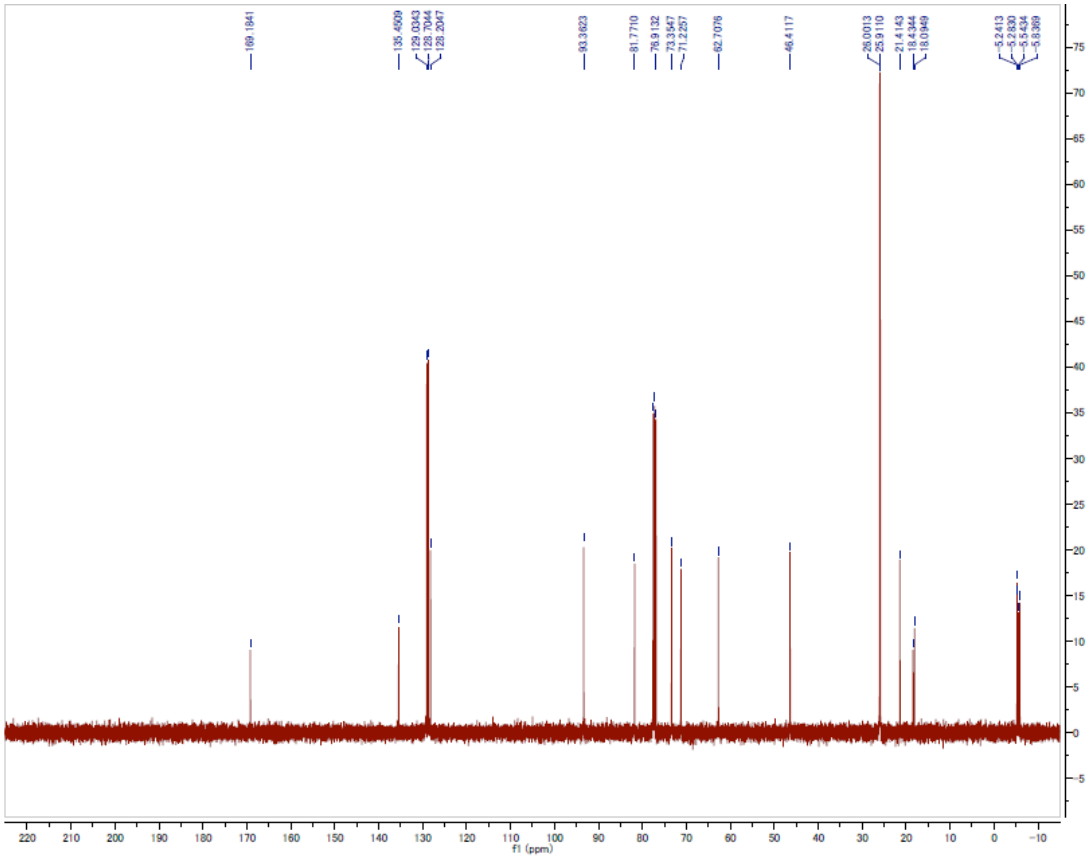

AcO
O
H
OTBS
TBSO
NO2
Ph
12a

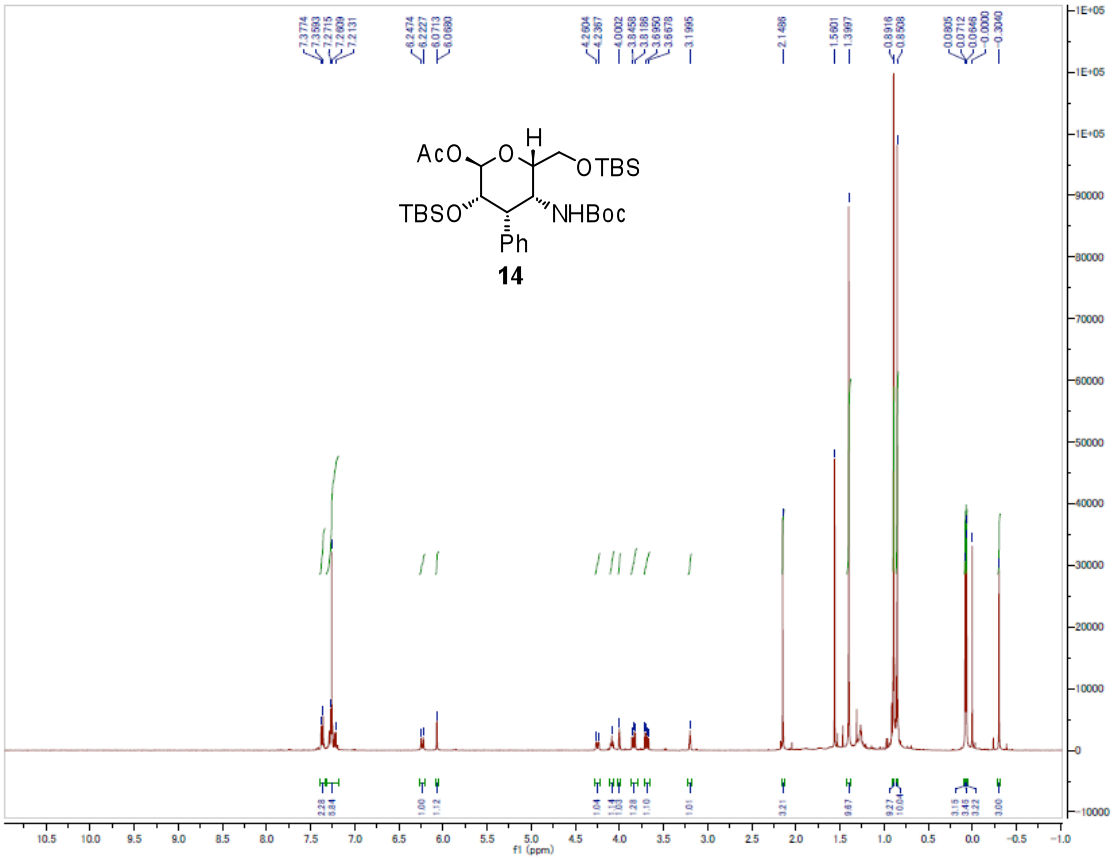


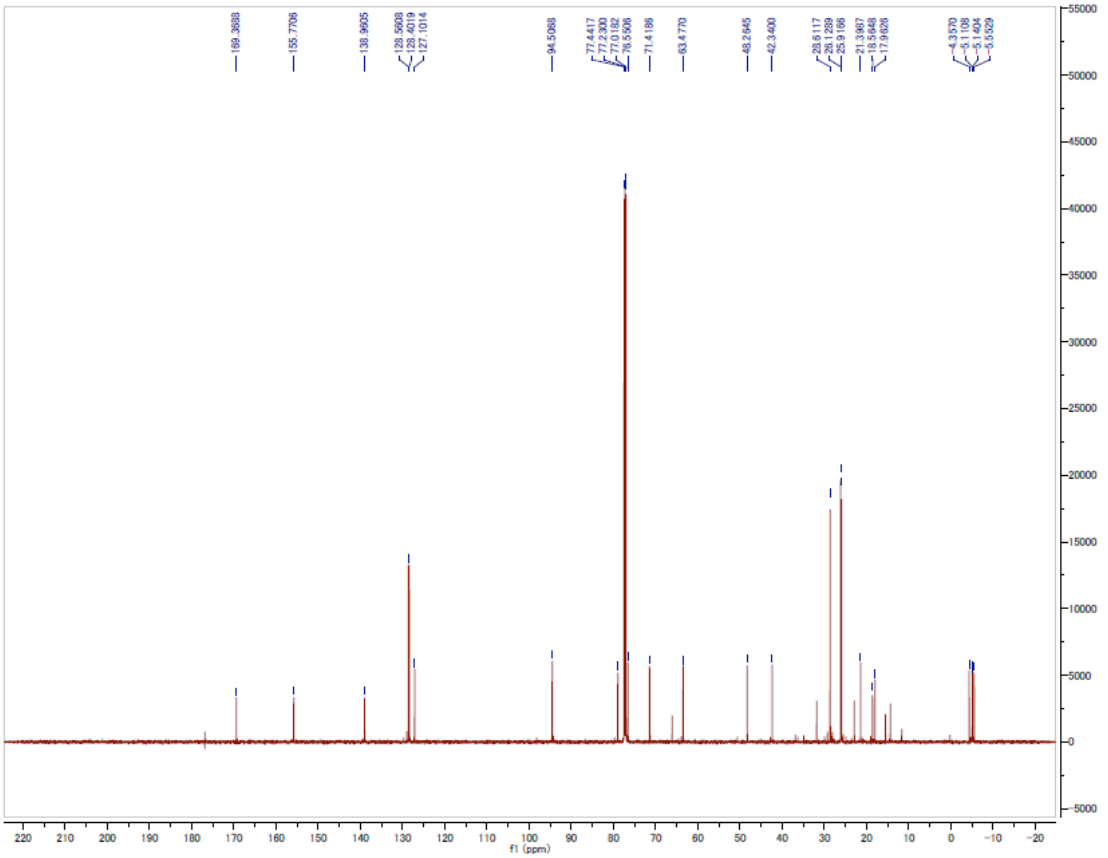

AcO
O
H
OTBS
TBSO
NO2
Br
12b
f1 (ppm)

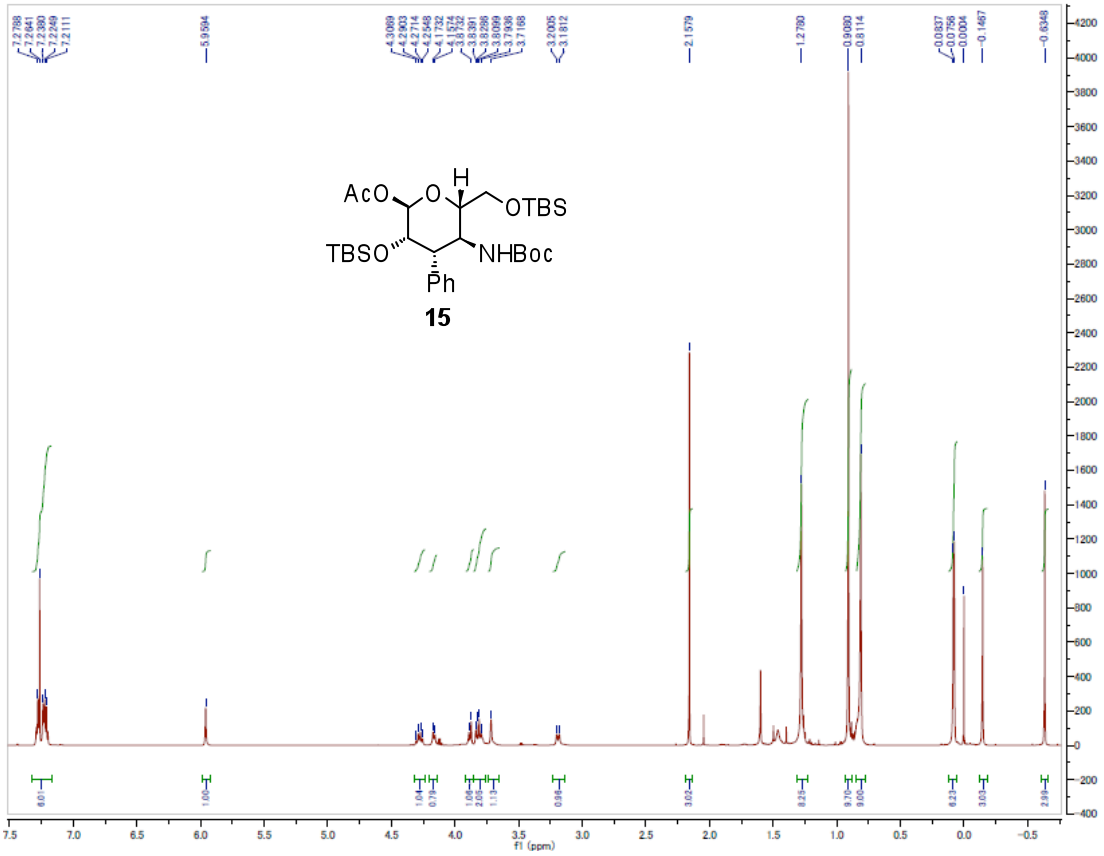

f1 (ppm)

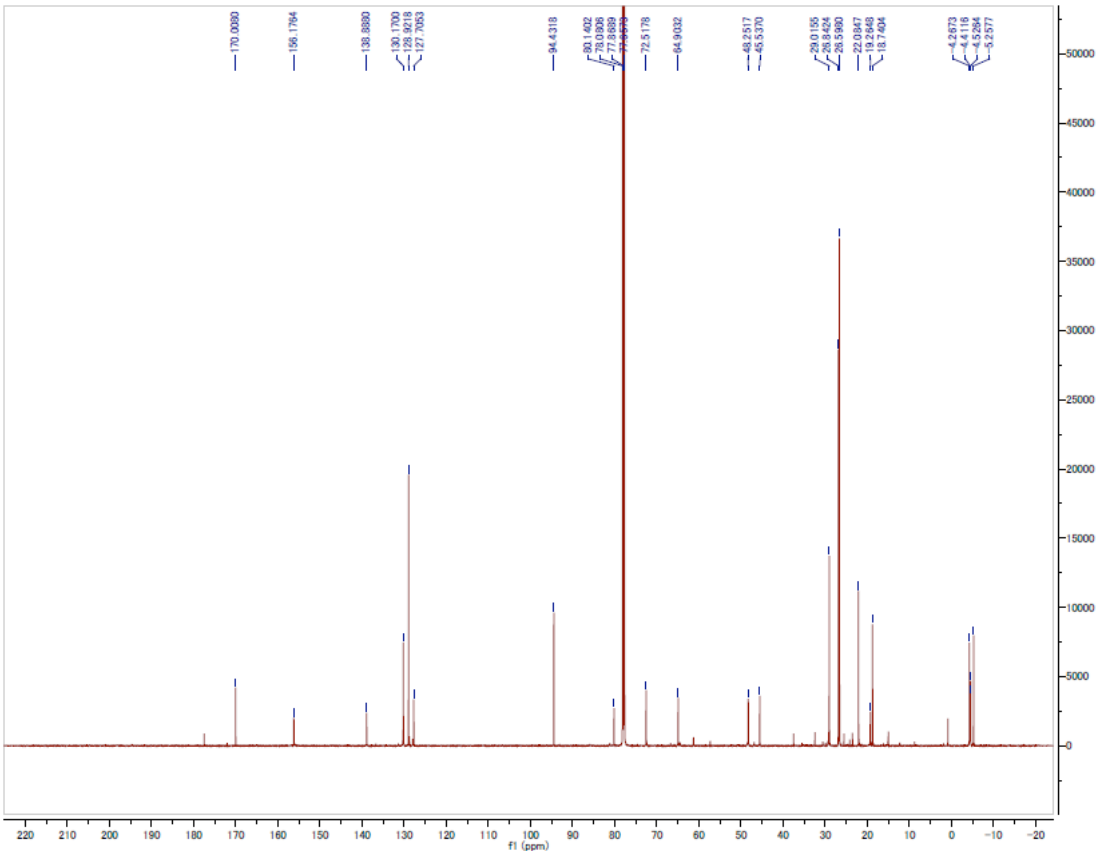

AcO
O
H
OTBS
TBSO
NO2
Ph
13a

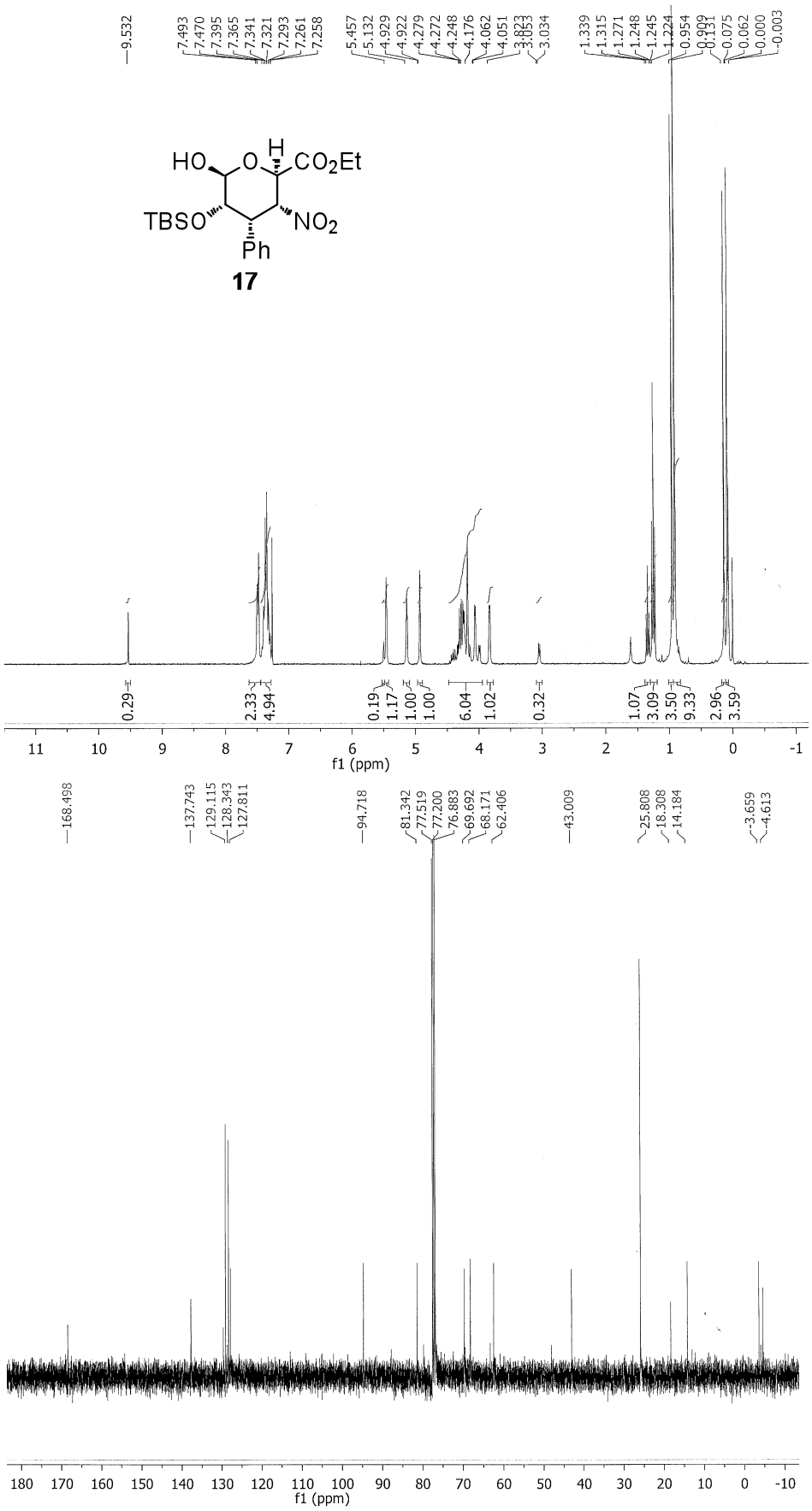


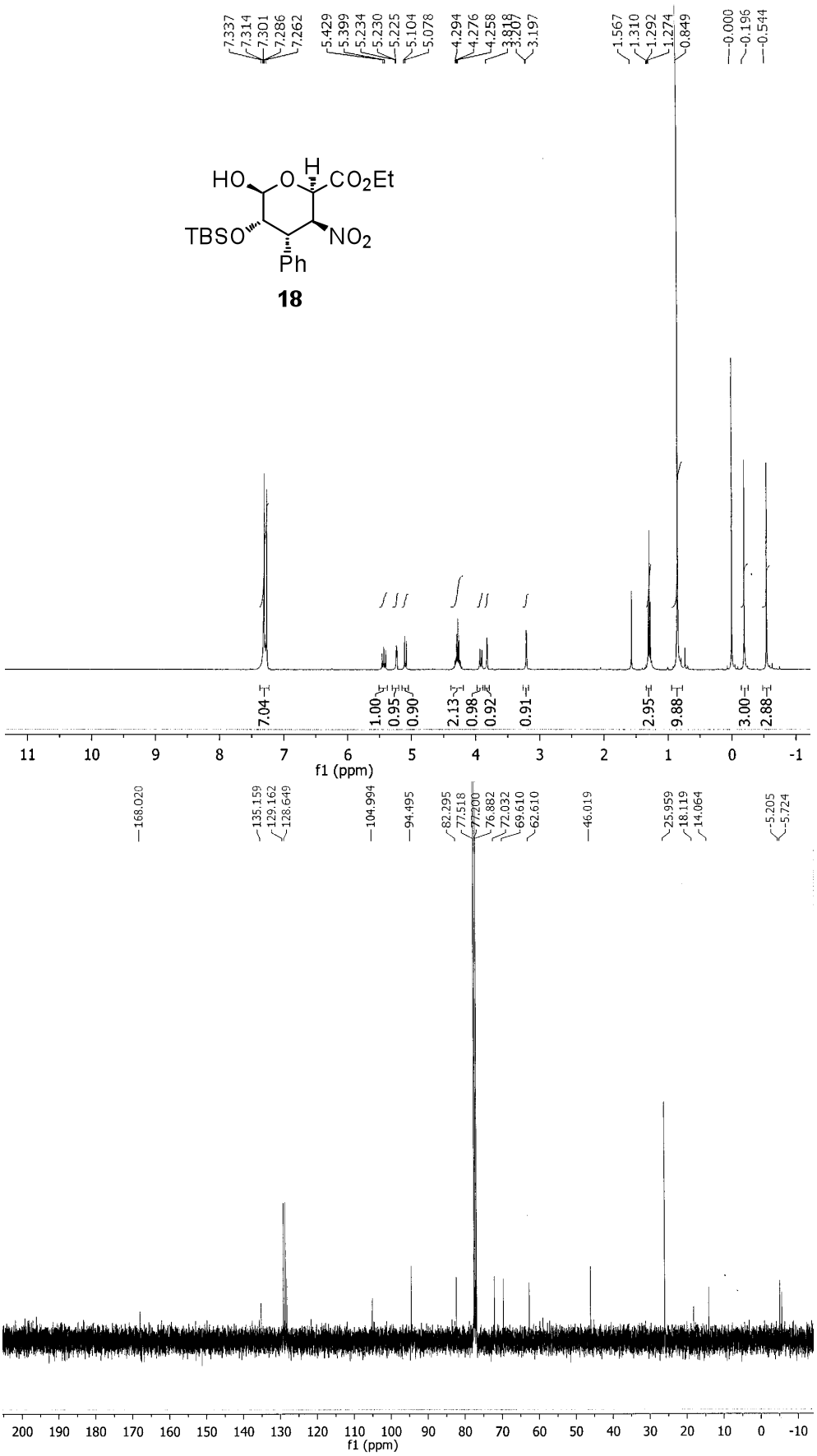

AcO
O
H
OTBS
TBSO
NHBoc
Ph
14

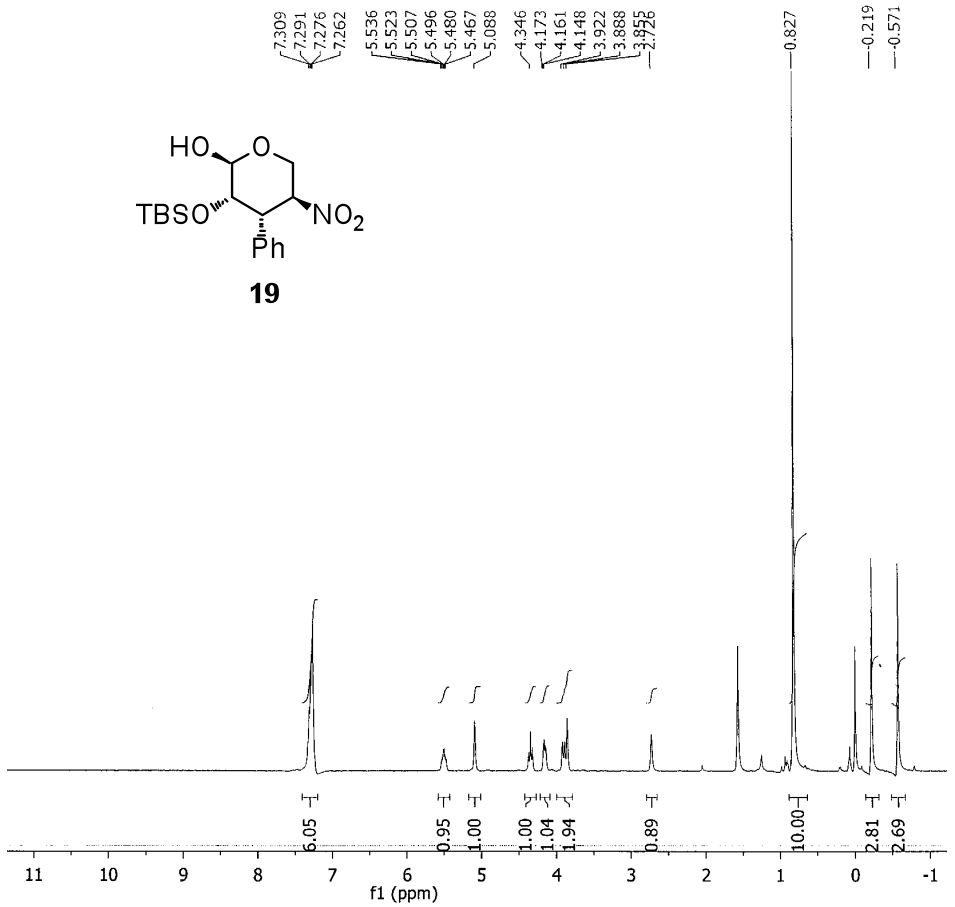


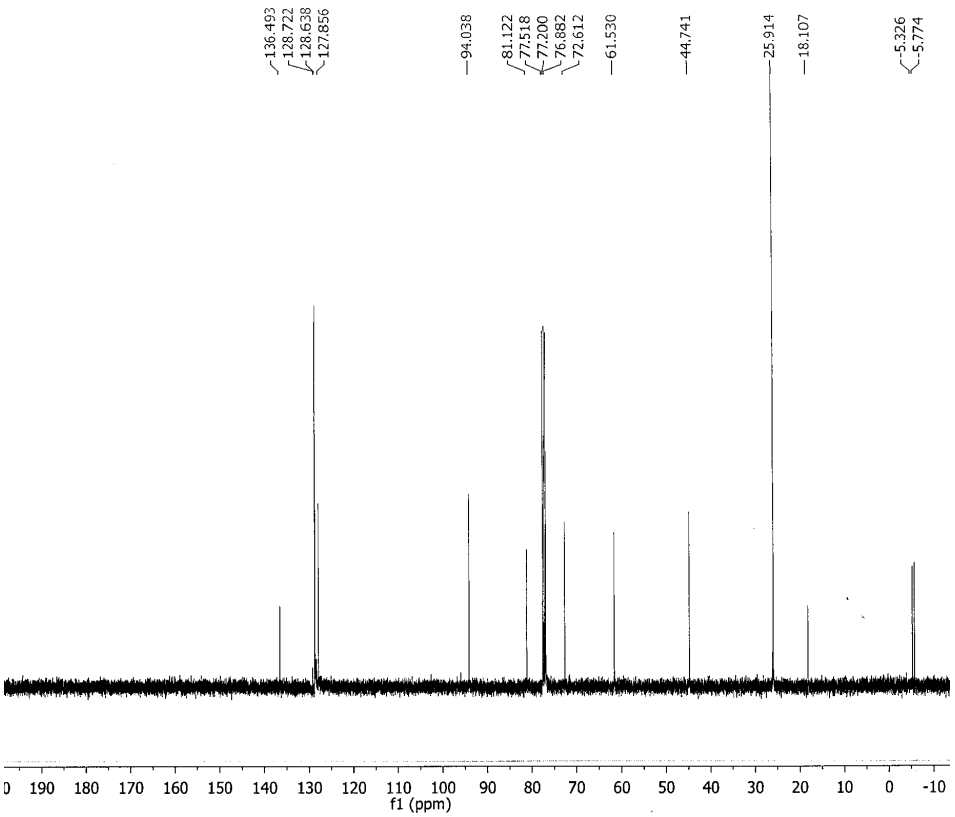

AcO
O
H
OTBS
TBSO
NHBoc
Ph
15
f1 (ppm)

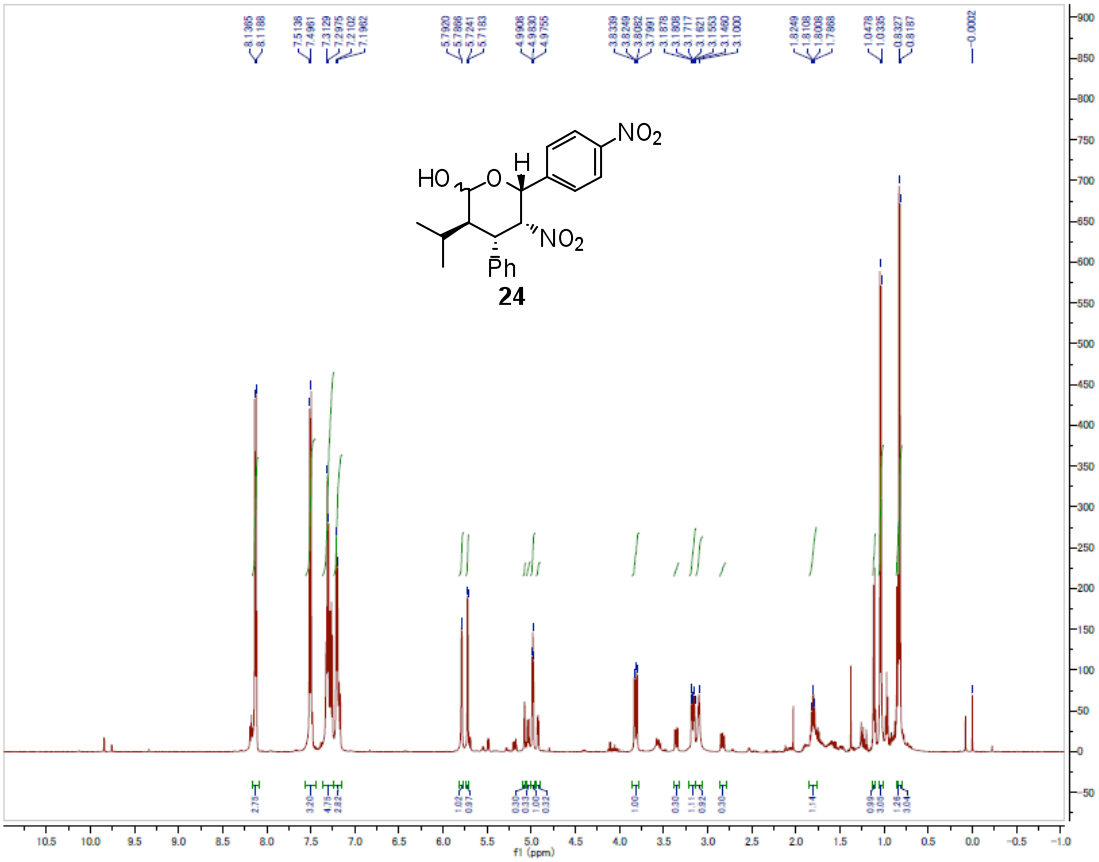

f1 (ppm)

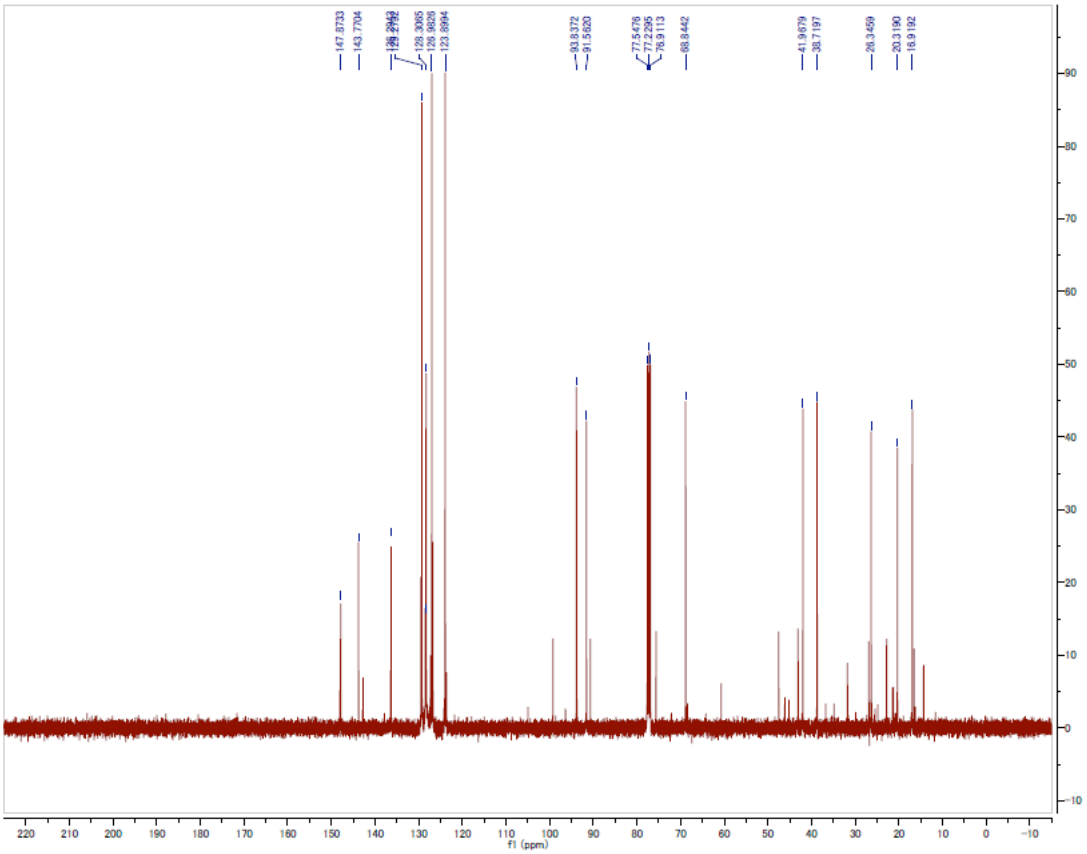

HO
O
H
CO2Et
TBSO
NO2
Ph
17
f1 (ppm)
f1 (ppm)


HO
O
H
CO2Et
TBSO
NO2
Ph
18
f1 (ppm)
f1 (ppm)

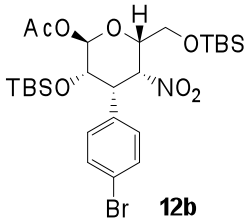

7.309
7.291
7.276
7.262
5.536
5.523
5.507
5.496
5.480
5.467
5.088
4.346
4.173
4.161
4.148
3.922
3.888
3.855
3.726
0.827
0.219
0.571
HO
O
TBSO
NO2
Ph
19
6.05
0.95
1.00
1.00
1.04
1.94
0.89
10.00
2.81
2.69
f1 (ppm)


136.493
128.722
128.638
127.856
94.038
81.122
77.518
77.200
76.882
72.612
61.530
44.741
25.914
18.107
5.326
5.774
f1 (ppm)


HO
O
H
NO2
NO2
Ph
24
f1 (ppm)


f1 (ppm)

7. X-ray crystallographic data of 12b



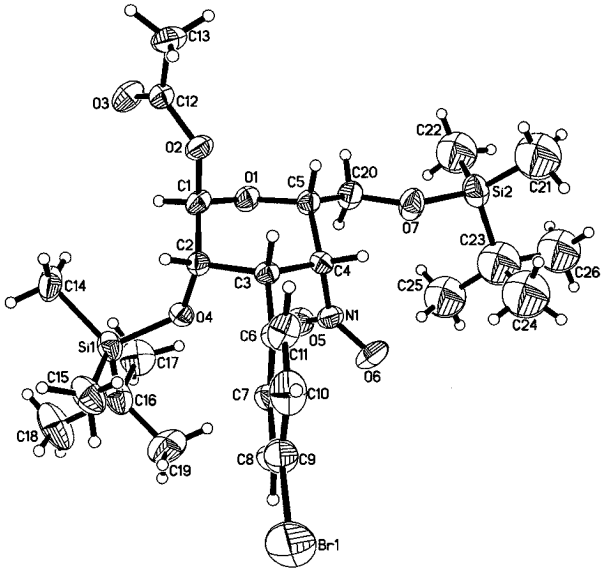


Table S1. Crystal data and structure refinement for 12b.

Empirical formula	C26 H44 Br N O7 Si2	
Formula weight	618.71	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 7.3567(15) Å	α= 90°.
	b = 18.732(4) Å	β= 90°.
	c = 24.448(5) Å	γ = 90°.
Volume	3369.1(12) Å^3	
Z	4	
Density (calculated)	1.220 Mg/m^3	
Absorption coefficient	1.329 mm^{-1}	
F(000)	1304	
Crystal size	0.27 x 0.22 x 0.18 mm^3	
Theta range for data collection	1.37 to 24.99°.	
Index ranges	-8<=h<=8, -22<=k<=20, -29<=l<=29	
Reflections collected	24869	
Independent reflections	5931 [R(int) = 0.0356]	
Completeness to theta = 24.99°	100.0 %	
Absorption correction	Semi-empirical from equivalents	

Max. and min. transmission	0.7959 and 0.7155
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5931 / 0 / 325
Goodness-of-fit on F^2	1.068
Final R indices [I>2sigma(I)]	R1 = 0.0823, wR2 = 0.2324
R indices (all data)	R1 = 0.1183, wR2 = 0.2637
Absolute structure parameter	0.05(2)
Largest diff. peak and hole	0.915 and -0.538 e.Å^{-3}

Table S2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for 12b. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br(1)	1716(4)	10824(1)	8897(1)	232(1)
Si(1)	4727(2)	7623(1)	7579(1)	83(1)
Si(2)	6760(16)	10593(4)	4871(3)	110(3)
Si(2')	7790(30)	10401(7)	5092(7)	111(7)
O(1)	4558(6)	8371(2)	5890(2)	75(1)
O(2)	1482(6)	8093(2)	5984(2)	79(1)
O(3)	1766(8)	6980(3)	5668(2)	106(2)
O(4)	4637(5)	8251(2)	7109(2)	67(1)
O(5)	7222(7)	9213(3)	6546(2)	96(1)
O(6)	6368(8)	10281(3)	6730(2)	109(2)
O(7)	5769(8)	10058(3)	5321(2)	101(2)
N(1)	6071(9)	9680(3)	6547(2)	77(2)
C(1)	3299(8)	8059(3)	6225(3)	70(2)
C(2)	3110(8)	8417(3)	6792(2)	61(1)
C(3)	2866(7)	9231(3)	6718(2)	57(1)
C(4)	4264(8)	9557(3)	6306(2)	66(2)
C(5)	4313(9)	9106(3)	5788(2)	68(2)
C(6)	2637(8)	9625(3)	7255(2)	63(1)
C(7)	4007(11)	9689(4)	7628(3)	84(2)
C(8)	3784(17)	10044(4)	8121(3)	115(3)
C(9)	2100(20)	10317(5)	8234(4)	118(3)
C(10)	702(15)	10292(5)	7871(5)	122(3)
C(11)	1007(10)	9940(4)	7376(4)	93(2)
C(12)	940(10)	7508(4)	5707(2)	75(2)
C(13)	-903(11)	7642(5)	5461(4)	103(2)

C(14)	3850(12)	6778(4)	7296(5)	118(3)
C(15)	3334(12)	7894(6)	8173(4)	126(3)
C(16)	7201(10)	7575(5)	7755(4)	103(3)
C(17)	8260(11)	7393(6)	7247(4)	127(3)
C(18)	7484(15)	6969(8)	8178(6)	180(6)
C(19)	7807(15)	8289(6)	7982(6)	155(5)
C(20)	5830(12)	9317(4)	5395(3)	89(2)
C(21)	5470(30)	11248(11)	4568(9)	245(9)
C(22)	8050(20)	10044(10)	4349(8)	214(7)
C(23)	8680(30)	11011(14)	5235(9)	235(8)
C(24)	7400(30)	11566(12)	5617(11)	268(10)
C(25)	9800(30)	10438(10)	5572(9)	217(7)
C(26)	9630(30)	11550(12)	4806(8)	241(9)

Table S3. Bond lengths [Å] and angles [°] for 12b.

Br(1)-C(9)	1.899(8)
Si(1)-O(4)	1.645(4)
Si(1)-C(14)	1.843(9)
Si(1)-C(15)	1.848(10)
Si(1)-C(16)	1.873(8)
Si(2)-O(7)	1.658(7)
Si(2)-C(21)	1.72(3)
Si(2)-C(23)	1.85(3)
Si(2)-C(22)	1.891(19)
O(1)-C(1)	1.368(8)
O(1)-C(5)	1.410(7)
O(2)-C(12)	1.349(8)
O(2)-C(1)	1.462(7)
O(3)-C(12)	1.164(8)
O(4)-C(2)	1.400(7)
O(5)-N(1)	1.218(7)
O(6)-N(1)	1.230(7)
O(7)-C(20)	1.399(9)
N(1)-C(4)	1.473(8)
C(1)-C(2)	1.546(8)
C(2)-C(3)	1.547(8)
C(3)-C(6)	1.516(8)

C(3)-C(4)	1.563(8)
C(4)-C(5)	1.523(8)
C(5)-C(20)	1.525(9)
C(6)-C(7)	1.364(9)
C(6)-C(11)	1.369(9)
C(7)-C(8)	1.386(10)
C(8)-C(9)	1.368(15)
C(9)-C(10)	1.360(15)
C(10)-C(11)	1.397(13)
C(12)-C(13)	1.504(11)
C(16)-C(19)	1.514(14)
C(16)-C(17)	1.505(13)
C(16)-C(18)	1.550(12)
C(23)-C(25)	1.58(3)
C(23)-C(26)	1.61(3)
C(23)-C(24)	1.69(3)

O(4)-Si(1)-C(14)	109.7(3)
O(4)-Si(1)-C(15)	109.3(4)
C(14)-Si(1)-C(15)	109.7(5)
O(4)-Si(1)-C(16)	103.5(3)
C(14)-Si(1)-C(16)	112.7(4)
C(15)-Si(1)-C(16)	111.8(5)
O(7)-Si(2)-C(21)	118.2(10)
O(7)-Si(2)-C(23)	105.9(10)
C(21)-Si(2)-C(23)	109.2(11)
O(7)-Si(2)-C(22)	109.8(8)
C(21)-Si(2)-C(22)	112.0(11)
C(23)-Si(2)-C(22)	99.9(11)
C(1)-O(1)-C(5)	115.9(5)
C(12)-O(2)-C(1)	115.9(5)
C(2)-O(4)-Si(1)	125.3(4)
C(20)-O(7)-Si(2)	132.1(5)
O(5)-N(1)-O(6)	122.3(6)
O(5)-N(1)-C(4)	120.9(5)
O(6)-N(1)-C(4)	116.7(7)
O(1)-C(1)-O(2)	111.0(5)
O(1)-C(1)-C(2)	114.4(5)
O(2)-C(1)-C(2)	105.0(5)

O(4)-C(2)-C(3)	112.2(5)
O(4)-C(2)-C(1)	109.1(5)
C(3)-C(2)-C(1)	109.5(4)
C(6)-C(3)-C(2)	113.0(4)
C(6)-C(3)-C(4)	116.2(5)
C(2)-C(3)-C(4)	112.6(5)
N(1)-C(4)-C(5)	113.5(5)
N(1)-C(4)-C(3)	113.4(4)
C(5)-C(4)-C(3)	109.5(5)
O(1)-C(5)-C(4)	113.5(5)
O(1)-C(5)-C(20)	105.7(5)
C(4)-C(5)-C(20)	113.4(5)
C(7)-C(6)-C(11)	117.7(6)
C(7)-C(6)-C(3)	122.7(5)
C(11)-C(6)-C(3)	119.6(6)
C(6)-C(7)-C(8)	122.4(8)
C(9)-C(8)-C(7)	117.5(9)
C(10)-C(9)-C(8)	122.7(7)
C(10)-C(9)-Br(1)	117.4(9)
C(8)-C(9)-Br(1)	119.6(9)
C(9)-C(10)-C(11)	117.4(8)
C(6)-C(11)-C(10)	122.0(9)
O(3)-C(12)-O(2)	125.2(6)
O(3)-C(12)-C(13)	125.4(7)
O(2)-C(12)-C(13)	109.4(6)
C(19)-C(16)-C(17)	110.5(9)
C(19)-C(16)-C(18)	111.3(10)
C(17)-C(16)-C(18)	108.4(9)
C(19)-C(16)-Si(1)	109.2(6)
C(17)-C(16)-Si(1)	108.9(6)
C(18)-C(16)-Si(1)	108.6(6)
O(7)-C(20)-C(5)	108.4(6)
C(25)-C(23)-C(26)	122.5(18)
C(25)-C(23)-C(24)	115.0(18)
C(26)-C(23)-C(24)	102.4(19)
C(25)-C(23)-Si(2)	111.2(17)
C(26)-C(23)-Si(2)	106.4(14)
C(24)-C(23)-Si(2)	95.7(14)

Symmetry transformations used to generate equivalent atoms:

Table S4. Anisotropic displacement parameters ($Å^2 x 10^3$) for 12b. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2} U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	410(3)	172(1)	114(1)	-57(1)	81(1)	47(2)
Si(1)	70(1)	84(1)	94(1)	25(1)	-4(1)	3(1)
Si(2)	129(6)	101(3)	101(3)	25(3)	17(4)	-5(3)
Si(2')	125(11)	96(6)	111(9)	13(5)	40(8)	-10(6)
O(1)	95(3)	57(2)	73(2)	-13(2)	4(2)	0(2)
O(2)	84(3)	62(2)	92(3)	-14(2)	-23(2)	-3(2)
O(3)	116(4)	73(3)	128(4)	-36(3)	0(4)	-7(3)
O(4)	67(2)	68(2)	65(2)	4(2)	-9(2)	4(2)
O(5)	81(3)	99(4)	108(4)	2(3)	-10(3)	-1(3)
O(6)	116(4)	93(3)	117(4)	-39(3)	-2(3)	-34(3)
O(7)	137(4)	78(3)	89(3)	-3(2)	36(3)	-16(3)
N(1)	88(4)	82(4)	60(3)	-8(3)	0(3)	-23(3)
C(1)	70(4)	55(3)	84(4)	-13(3)	-6(3)	-2(3)
C(2)	62(3)	57(3)	64(3)	3(2)	-4(3)	-1(3)
C(3)	49(3)	61(3)	63(3)	-3(2)	-6(2)	3(2)
C(4)	83(4)	63(3)	51(3)	3(2)	-4(3)	-3(3)
C(5)	82(4)	59(3)	61(3)	-4(3)	7(3)	-4(3)
C(6)	74(4)	54(3)	60(3)	4(2)	-3(3)	2(3)
C(7)	111(5)	78(4)	62(3)	-7(3)	-2(4)	13(4)
C(8)	187(10)	93(5)	65(4)	-19(4)	-15(5)	30(6)
C(9)	190(11)	90(5)	73(5)	-16(4)	33(6)	8(7)
C(10)	121(7)	112(7)	133(8)	0(6)	55(7)	27(6)
C(11)	80(4)	81(4)	117(5)	-15(4)	30(4)	10(4)
C(12)	92(4)	67(4)	66(3)	-1(3)	-5(3)	-13(4)
C(13)	95(5)	105(6)	108(5)	-25(5)	-31(4)	-5(4)
C(14)	110(6)	74(5)	169(9)	41(5)	-30(6)	-20(4)
C(15)	94(5)	181(9)	102(6)	49(6)	23(5)	2(6)
C(16)	70(4)	113(6)	127(6)	43(5)	-8(4)	6(4)
C(17)	72(4)	150(8)	161(8)	5(7)	6(5)	23(5)
C(18)	109(7)	235(14)	195(12)	123(11)	-8(7)	63(8)
C(19)	102(7)	139(9)	224(13)	-17(9)	-83(8)	-2(6)
C(20)	123(6)	74(4)	71(4)	-12(3)	27(4)	-11(4)

Table S5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for 12b.

	x	y	z	U(eq)
H(1)	3629	7557	6278	84
H(2)	2027	8225	6973	73
H(3)	1688	9281	6535	69
H(4)	3790	10026	6200	79
H(5)	3151	9167	5598	81
H(7)	5131	9487	7549	101
H(8)	4743	10094	8366	138
H(10)	-415	10501	7950	147
H(11)	74	9920	7119	111
H(13A)	-1464	7194	5371	123
H(13B)	-773	7923	5135	123
H(13C)	-1648	7893	5719	123
H(14A)	4465	6673	6959	141
H(14B)	2569	6822	7229	141
H(14C)	4060	6399	7553	141
H(15A)	2559	8283	8070	151
H(15B)	4117	8040	8466	151
H(15C)	2604	7498	8290	151
H(17A)	7709	6991	7069	153
H(17B)	9489	7278	7345	153
H(17C)	8257	7795	7004	153
H(18A)	8741	6951	8284	216
H(18B)	7141	6521	8018	216
H(18C)	6747	7058	8495	216
H(19A)	7939	8624	7688	186
H(19B)	8951	8233	8166	186
H(19C)	6915	8461	8237	186
H(20A)	7000	9179	5545	107
H(20B)	5669	9077	5047	107
H(21A)	5483	11669	4792	294
H(21B)	4237	11082	4530	294
H(21C)	5954	11357	4214	294

H(22A)	7202	9766	4138	257
H(22B)	8876	9731	4534	257
H(22C)	8711	10356	4111	257
H(24A)	8009	12016	5654	322
H(24B)	7214	11360	5972	322
H(24C)	6246	11637	5441	322
H(25A)	10546	10676	5838	261
H(25B)	10563	10170	5327	261
H(25C)	8979	10120	5754	261
H(26A)	10126	11283	4507	289
H(26B)	10587	11808	4986	289
H(26C)	8740	11881	4671	289

Table S6. Torsion angles [°] for 12b.

C(14)-Si(1)-O(4)-C(2)	50.1(6)
C(15)-Si(1)-O(4)-C(2)	-70.2(6)
C(16)-Si(1)-O(4)-C(2)	170.6(5)
C(21)-Si(2)-O(7)-C(20)	135.1(11)
C(23)-Si(2)-O(7)-C(20)	-102.1(11)
C(22)-Si(2)-O(7)-C(20)	4.9(14)
C(5)-O(1)-C(1)-O(2)	62.6(6)
C(5)-O(1)-C(1)-C(2)	-56.1(7)
C(12)-O(2)-C(1)-O(1)	96.0(6)
C(12)-O(2)-C(1)-C(2)	-139.8(5)
Si(1)-O(4)-C(2)-C(3)	139.3(4)
Si(1)-O(4)-C(2)-C(1)	-99.2(5)
O(1)-C(1)-C(2)-O(4)	-73.0(6)
O(2)-C(1)-C(2)-O(4)	165.0(4)
O(1)-C(1)-C(2)-C(3)	50.1(7)
O(2)-C(1)-C(2)-C(3)	-71.9(6)
O(4)-C(2)-C(3)-C(6)	-59.7(6)
C(1)-C(2)-C(3)-C(6)	179.0(5)
O(4)-C(2)-C(3)-C(4)	74.4(6)
C(1)-C(2)-C(3)-C(4)	-46.9(6)
O(5)-N(1)-C(4)-C(5)	-37.7(8)
O(6)-N(1)-C(4)-C(5)	139.8(6)
O(5)-N(1)-C(4)-C(3)	88.2(7)

O(6)-N(1)-C(4)-C(3)	-94.3(6)
C(6)-C(3)-C(4)-N(1)	52.7(7)
C(2)-C(3)-C(4)-N(1)	-79.9(6)
C(6)-C(3)-C(4)-C(5)	-179.3(5)
C(2)-C(3)-C(4)-C(5)	48.1(6)
C(1)-O(1)-C(5)-C(4)	56.9(7)
C(1)-O(1)-C(5)-C(20)	-178.2(5)
N(1)-C(4)-C(5)-O(1)	76.9(6)
C(3)-C(4)-C(5)-O(1)	-51.0(7)
N(1)-C(4)-C(5)-C(20)	-43.8(7)
C(3)-C(4)-C(5)-C(20)	-171.7(5)
C(2)-C(3)-C(6)-C(7)	68.1(7)
C(4)-C(3)-C(6)-C(7)	-64.2(7)
C(2)-C(3)-C(6)-C(11)	-112.8(6)
C(4)-C(3)-C(6)-C(11)	114.8(6)
C(11)-C(6)-C(7)-C(8)	1.5(10)
C(3)-C(6)-C(7)-C(8)	-179.4(7)
C(6)-C(7)-C(8)-C(9)	1.9(12)
C(7)-C(8)-C(9)-C(10)	-4.2(15)
C(7)-C(8)-C(9)-Br(1)	-178.9(6)
C(8)-C(9)-C(10)-C(11)	3.0(15)
Br(1)-C(9)-C(10)-C(11)	177.8(6)
C(7)-C(6)-C(11)-C(10)	-2.8(11)
C(3)-C(6)-C(11)-C(10)	178.1(7)
C(9)-C(10)-C(11)-C(6)	0.6(13)
C(1)-O(2)-C(12)-O(3)	3.6(10)
C(1)-O(2)-C(12)-C(13)	-177.0(6)
O(4)-Si(1)-C(16)-C(19)	61.4(8)
C(14)-Si(1)-C(16)-C(19)	179.9(8)
C(15)-Si(1)-C(16)-C(19)	-56.1(9)
O(4)-Si(1)-C(16)-C(17)	-59.3(7)
C(14)-Si(1)-C(16)-C(17)	59.2(8)
C(15)-Si(1)-C(16)-C(17)	-176.8(7)
O(4)-Si(1)-C(16)-C(18)	-177.1(8)
C(14)-Si(1)-C(16)-C(18)	-58.6(10)
C(15)-Si(1)-C(16)-C(18)	65.4(10)
Si(2)-O(7)-C(20)-C(5)	-167.1(8)
O(1)-C(5)-C(20)-O(7)	-174.2(6)
C(4)-C(5)-C(20)-O(7)	-49.3(8)

O(7)-Si(2)-C(23)-C(25)	45.9(16)
C(21)-Si(2)-C(23)-C(25)	174.2(15)
C(22)-Si(2)-C(23)-C(25)	-68.2(16)
O(7)-Si(2)-C(23)-C(26)	-178.5(13)
C(21)-Si(2)-C(23)-C(26)	-50.2(17)
C(22)-Si(2)-C(23)-C(26)	67.5(17)
O(7)-Si(2)-C(23)-C(24)	-73.7(15)
C(21)-Si(2)-C(23)-C(24)	54.6(17)
C(22)-Si(2)-C(23)-C(24)	172.2(14)

Symmetry transformations used to generate equivalent atoms: