A New Ring Closure Approach to Enantiopure 3,6-Dihydro-2*H*-pyrans – Stereodivergent Access to Carbohydrate Mimetics

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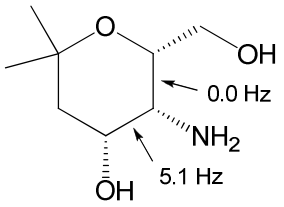
General methods:

Reactions were generally performed under argon in flame-dried flasks, and the components were added by syringe. Methanol was purchased in p. a. quality and stored under argon over molecular sieves (4 Å). Tetrahydrofuran and dichloromethane were obtained from a solvent purification system MB-SPS-800 (M. Braun). Products were purified by flash chromatography on silica gel (230–400 mesh, Merck). Unless otherwise stated, yields refer to analytically pure samples. ^{1}H NMR [$CHCl_3$ (δ = 7.26 ppm), TMS (δ = 0.00 ppm), CD_3OD (δ = 3.31 ppm) or D_2O (δ = 4.79 ppm) as internal standards] and ^{13}C NMR spectra [$CDCl_3$ (δ = 77.0 ppm) or CD_3OD (δ = 49.0 ppm) as internal standards] were recorded on Bruker AC 250, ECP 400, AC 500, AVIII 700, or Joel Eclipse 500 instruments in $CDCl_3$, CD_3OD or D_2O solution. Integrals are in accordance with assignments; coupling constants are given in Hz. IR spectra were measured with an FT-IR spectrometer Nicolet 5 SXC or with a Nexus FT-IR equipped with a Nicolet Smart DuraSamplIR ATR. MS and HRMS analyses were performed on Finnigan MAT 711 (EI, 80 eV, 8 kV), MAT CH7A (EI, 80 eV, 3 kV), CH5DF (FAB, 80 eV, 3 kV), Varian Ionspec QFT-7 (ESI-FT-ICR) and Agilent ESI-TOF 6210 (4 μL/min, 1 bar, 4000 V) instruments. The elemental analyses were

recorded with "Elemental-Analyzers" (Perkin–Elmer or Carlo Erba). Melting points were measured with a Reichert apparatus (Thermovar) and are uncorrected. Optical rotations ($[\alpha]_D$) were determined with Perkin–Elmer 241 polarimeter at the temperatures given. Commercially available chemicals were used without further purification.

Characteristic $^3J_{H\text{-}H}$ coupling constants in carbohydrate mimetics 14, 16, 19 and 22:



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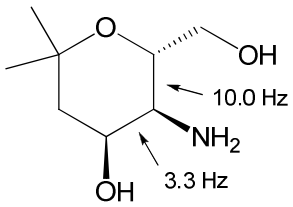

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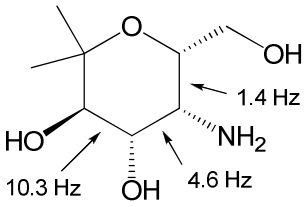

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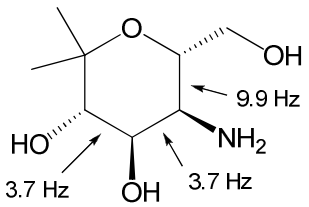

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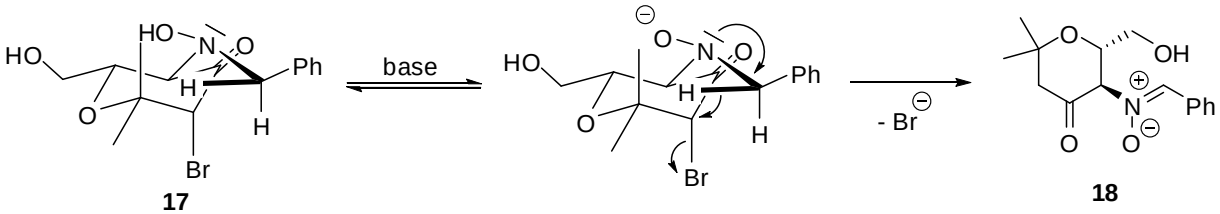
Mechanistic suggestion for the transformation of hydroxylamine (17) into nitrone (18)



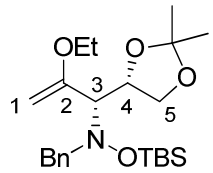
17 **18**

After deprotonation of the hydroxylamine moiety by azide, a hydride shift occurs from the benzylic position to the 3-position of the pyran ring providing nitrone **18** in an intramolecular S_N2-like reaction. The transformation might be facilitated by the suitable geometry of compound **17**. Different approaches to further clarify the reaction mechanism are currently under investigation (e.g. reaction without base or with sterically demanding bases).

Experimental procedures and characterization data:

Due to hindered rotation of the bulky -N(OTBS)Bn moiety some signals in the ^{1}H- or ^{13}C-NMR spectra of the compounds containing this group are broadened and in several cases these signals can not be clearly recognized.

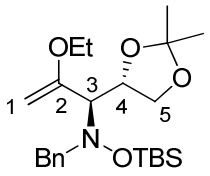
***N*-Benzyl-*O*-(*tert*-butyldimethylsilyl)-*N*-((*S*)-1-((*S*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2-ethoxyallyl)hydroxylamine (*syn*-10)**



Ethyl vinyl ether (445 µL, 4.62 mmol) was dissolved in THF (8 mL) and cooled to -78 °C. *t*BuLi (1.6 M in pentane, 2.89 mL, 4.62 mmol) was added and the reaction mixture was stirred for 1 h until it reached 0 °C. After further stirring for 1 h at this temperature, it was cooled down to -78 °C again. A solution of nitrone **1a** (725 mg, 3.08 mmol) in THF (2 mL) was added dropwise over a period of 15 min. Then, the mixture was stirred at this temperature for 1 h and quenched by addition of H_2O. After the mixture reached room temperature it was extracted 3 times with Et_2O. The combined organic phases were dried (Na_2SO_4) and the solvent was removed in vacuo. The crude product (844 mg) was dissolved in CH_2Cl_2 (7 mL) and 2,6-lutidine (641 µL, 5.50 mmol) and TBSOTf (946 µL, 4.13 mmol) were added slowly at 0 °C. The mixture was stirred at room temperature for 30 min and was then quenched by the addition of a sat. NH_4Cl solution. The layers were separated and the aqueous phase was extracted three times with CH_2Cl_2. The combined organic phases were dried (Na_2SO_4) and the solvent was removed in vacuo. Purification by column chromatography (silica gel, hexane/EtOAc = 20:1) yielded *syn*-**10** (800 mg, 61%) and *anti*-**10** (115 mg, 9%) as colorless oils. *syn*-**10**: $[\alpha]_D^{22}$ = -27.2 (c = 0.20, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.10 (s, 6 H, $SiMe_2$), 0.88 (s, 9 H, *t*Bu), 1.28 (t, *J* = 7.0 Hz, 3 H, Et), 1.33, 1.36 (2 s, 3 H each, Me), 3.29 (s_{br}, 1 H, 3-H), 3.57 (t, *J* = 7.9 Hz, 1 H, 5-H), 3.66, 3.72 (2 td, *J* = 7.0, 9.4 Hz, 1 H each, Et), 3.85 (s_{br}, 1 H, NCH_2), 3.99 (dd, *J* = 6.8, 7.9 Hz, 1 H, 5-H), 4.03 (d, *J* = 1.6 Hz, 1 H, 1-H), 4.12 (d, *J* = 13.2 Hz, 1 H, NCH_2), 4.16 (d, *J* = 1.6 Hz, 1 H, 1-H), 4.40 (td, *J* = 6.8, 7.9 Hz, 1 H, 4-H), 7.20-7.42 (m, 5 H, Ph) ppm. ^{13}C-NMR (176 MHz, $CDCl_3$): δ = -5.2, -4.8 (2 q, $SiMe_2$), 14.6 (q, Et), 17.9, 26.2 (s, q, *t*Bu), 25.6, 26.7 (2 q, Me), 60.5 (t, NCH_2),

62.2 (t, Et), 67.6 (t, C-5), 71.5 (d, C-3), 74.1 (d, C-4), 87.4 (t, C-1), 109.2 (s, C-2'), 126.9, 127.9, 129.8, 138.0 (3 d, s, Ph), 157.3 (s, C-2) ppm. IR (film): 3100-2850 cm^{-1} (=C-H, C-H). ESI-TOF: *m/z* calc. for $[M + Na]^+$ 444.2541, found 444.2546. Anal. calc. for $C_{23}H_{39}NO_4Si$ (421.7): C 65.52, H 9.32, N 3.32, found: C 65.39, H 9.37, N 3.36.

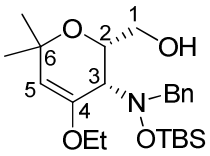
_N_-Benzyl-_O_-(_tert_-butyldimethylsilyl)-_N_-((_R_)-1-((_S_)-2,2-dimethyl-1,3-dioxolan-4-yl)-2-ethoxyallyl)hydroxylamine (_anti_-10)



Ethyl vinyl ether (409 µL, 4.25 mmol) was dissolved in THF (8 mL) and cooled to -78 °C. *t*BuLi (1.6 M in pentane, 2.66 mL, 4.25 mmol) was added and the reaction mixture was stirred for 1 h until it reached 0 °C. After further stirring for 3 h at this temperature, it was cooled down to -78 °C again. A solution of nitrone **1a** (200 mg, 0.850 mmol) in THF (2 mL) was treated with Et_2AlCl (1 M in hexane, 850 µL, 0.850 mmol) for 5 min. The prepared solution was added dropwise over a period of 15 min. Then, the mixture was stirred at this temperature for another 15 min and quenched by addition of 2 M NaOH solution. After the mixture reached room temperature it was extracted 3 times with Et_2O. The combined organic phases were dried (Na_2SO_4) and the solvent was removed in vacuo. The crude product (250 mg) was dissolved in CH_2Cl_2 (3 mL) and 2,6-lutidine (180 µL, 1.22 mmol) and TBSOTf (268 µL, 1.63 mmol) were added slowly at 0 °C. The mixture was stirred at room temperature for 30 min and then quenched by the addition of sat. NH_4Cl solution. The phases were separated and the aeqeuous phase was extracted three times with CH_2Cl_2. The combined organic phases were dried (Na_2SO_4) and the solvent was removed in vacuo. Purification by column chromatography (silica gel, hexane/EtOAc = 20:1) yielded *syn*-**10** (14 mg, 4%) and *anti*-**10** (171 mg, 48%) as colorless oils. *anti*-**10**: $[\alpha]_D^{22}$ = +26.7 (c = 0.22, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = -0.40 (s_{br}, 3 H, $SiMe_2$), -0.01 (s, 3 H, $SiMe_2$), 0.85 (s, 9 H, *t*Bu), 1.34 (m_c, 3 H, Et), 1.35 (s, 6 H, Me), 3.31 (s_{br}, 1 H, 3-H), 3.80-3.90 (m, 4 H, NCH_2, OCH_2, 3-H), 4.01 (m_c, 1 H, 5-H), 4.11 (dd, *J* = 5.8, 8.4 Hz, 1 H, 5-H), 4.16 (d, *J* = 1.9 Hz, 1 H, 1-H), 4.31 (d, *J* = 1.9 Hz, 1 H, 1-H), 4.42 (td, *J* = 5.8, 9.9 Hz, 1 H, 4-H), 7.20-7.34 (m, 5 H, Ph) ppm. ^{13}C-NMR (126 MHz, $CDCl_3$): δ = -4.8, -4.6 (2 q, $SiMe_2$), 14.6 (q, Et), 17.8, 26.1 (s, q, *t*Bu), 25.7, 26.9 (2 q, Me), 60.8 (t, NCH_2), 62.4 (t, Et), 67.9 (t, C-5), 74.0 (d, C-4), 88.1

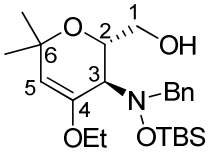
(t, C-1), 108.2 (s, C-2'), 127.2, 128.0, 130.2, 138.1 (3 d, s, Ph), 157.3 (s, C-2) ppm. IR (film): 3120-2840 cm^{-1} (=C-H, C-H). ESI-TOF: *m/z* calc. for $[M + Na]^+$ 444.2541, found 444.2523. Anal. calc. for $C_{23}H_{39}NO_4Si$ (421.7): C 65.52, H 9.32, N 3.32, found: C 64.93, H 8.60, N 3.52.

((2*S*,3*S*)-3-(Benzyl(*tert*-butyldimethylsiloxy)amino)-4-ethoxy-6,6-dimethyl-3,6-dihydro-2*H*-pyran-2-yl)methanol (11)



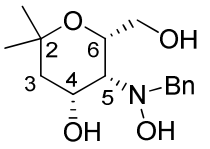
To a solution of *syn*-**10** (135 mg, 0.321 mmol) in CH_2Cl_2 (2 mL) at -30 °C was added TMSOTf (119 µL, 0.643 mmol), and the resulting solution was stirred until it slowly reached rt (6 h). Then the mixture was quenched by water. After separation of the layers, the aqueous phase was extracted 3 times with CH_2Cl_2. The combined organic phases were dried (Na_2SO_4) and the solvent was removed in vacuo. Purification by column chromatography (silica gel, hexane/EtOAc = 6:1) yielded **11** (106 mg, 79%) as colorless oil. $[\alpha]_D^{22}$ = -118.6 (c = 0.25, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = -0.05, 0.03 (2 s, 3 H each, $SiMe_2$), 0.79 (s, 9 H, *t*Bu), 1.24, 1.31 (2 s, 3 H each, Me), 1.37 (t, *J* = 7.0 Hz, 3 H, Et), 3.55 (dd, *J* = 2.1, 7.1 Hz, 1 H, 3-H), 3.75 (q, *J* = 7.0 Hz, 2 H, Et), 3.89-3.98 (m, 3 H, 2-H, OH), 4.11 (m_c, 2 H, 1-H), 4.73 (s, 1 H, 5-H), 7.21-7.26 (m, 5 H, Ph) ppm. ^{13}C-NMR (101 MHz, $CDCl_3$): δ = -5.0 (q, $SiMe_3$), 14.9 (q, Et), 17.8, 26.1 (s, q, *t*Bu), 25.9, 30.3 (2 q, Me), 62.0 (t, C-1), 62.3 (t, Et), 64.2 (d, C-3), 73.0 (s, C-6), 73.4 (d, C-2), 106.7 (d, C-5), 127.2, 128.0, 130.6, 139.0 (3 d, s, Ph), 149.8 (s, C-4) ppm. IR (film): 3450 cm^{-1} (OH), 3090-2840 (=C-H, C-H), 1660 (C=C). ESI-TOF: *m/z* calc. for $[M + H]^+$ 422.2727, found 422.2753. Anal. calc. for $C_{23}H_{39}NO_4Si$ (421.7): C 65.52, H 9.32, N 3.32, found: C 65.12, H 9.54, N 3.37.

((2*S*,3*R*)-3-[Benzyl(*tert*-butyldimethylsiloxy)amino]-4-ethoxy-6,6-dimethyl-3,6-dihydro-2*H*-pyran-2-yl)methanol (12)



To a solution of *anti*-**10** (1.83 g, 4.34 mmol) in CH_2Cl_2 (25 mL) at -30 °C was added TMSOTf (1.60 µL, 8.27 mmol), and the resulting solution was stirred until it slowly reached rt (6 h). Then the mixture was quenched by water. After separation of the layers, the aqueous phase was extracted 3 times with CH_2Cl_2. The combined organic phases were dried ($MgSO_4$) and the solvent was removed in vacuo. Purification by column chromatography (silica gel, hexane/EtOAc = 6:1) yielded **12** (1.53 g, 84%) as colorless oil. $[\alpha]_D^{22}$ = +69.7 (c = 0.66, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = -0.16, 0.01 (2 s, 3 H each, $SiMe_2$), 0.82 (s, 9 H, *t*Bu), 1.23, 1.29 (2 s, 3 H each, Me), 1.41 (t, *J* = 7.0 Hz, 3 H, Et), 2.81 (s_{br}, 1 H, OH), 3.36 (m_c, 1 H, 3-H), 3.53 (m_c, 1 H, 1-H), 3.65-3.78 (m, 2 H, Et), 3.82 (td, *J* = 5.5, 10.6 Hz, 1 H, 1-H), 3.95 (d, *J* = 12.5 Hz, 1 H, NCH_2), 4.00 (s_{br}, 1 H, 2-H), 4.34 (m_c, 1 H, NCH_2), 4.69 (d, *J* = 1.1 Hz, 1 H, 5-H), 7.18-7.35 (m, 5 H, Ph) ppm. ^{13}C-NMR (126 MHz, $CDCl_3$): δ = -4.9, -4.7 (2 q, $SiMe_2$), 14.9 (q, Et), 17.8, 26.0 (s, q, *t*Bu), 26.7, 31.2 (2 q, Me), 61.0 (d, C-3), 62.2 (t, Et), 64.9 (t, C-1), 70.2 (d, C-2), 72.5 (s, C-6), 105.7 (d, C-5), 127.3, 128.1, 130.3, 137.9 (3 d, s, Ph), 151.5 (s, C-4) ppm. IR (film): 3400 cm^{-1} (OH), 3090-2840 (=C-H, C-H), 1660 (C=C). ESI-TOF: *m/z* calc. for $[M + H]^+$ 422.2727, found 422.2744. Anal. calc. for $C_{23}H_{39}NO_4Si$ (421.7): C 65.52, H 9.32, N 3.32, found: C 65.32, H 9.28, N 3.39.

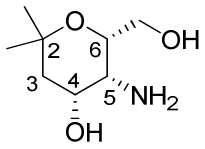
(4*R*,5*R*,6*S*)-5-[Benzyl(hydroxy)amino]-6-(hydroxymethyl)-2,2-dimethyltetrahydro-2*H*-pyran-4-ol via intermediate (13)



To compound **11** (350 mg, 0.830 mmol) was added satd. methanolic HCl (20 mL) and the resulting mixture was stirred for 12 h at rt. Then the solvent was removed in vacuo and the residue was dissolved in sat. $NaHCO_3$-solution and CH_2Cl_2. The layers were separated and the

aqueous phase was extracted 2 times with CH_2Cl_2. The combined organic layers were dried (Na_2SO_4) and the solvent was removed in vacuo to yield (5*S*,6*S*)-5-[benzyl(hydroxy)amino]-6-(hydroxymethyl)-2,2-dimethyldihydro-2*H*-pyran-4(3*H*)-one **13** as a brownish oil (180 mg, 84%). The crude product (180 mg, 0.645 mmol) was dissolved in ethanol (1 mL) and cooled to 0 °C. $NaBH_4$ (36 mg, 0.966 mmol) was added and the mixture was stirred for 1 h at 0 °C. Then the solvent was removed in vacuo and the residue was dissolved in CH_2Cl_2 and H_2O. The layers were separated and the aqueous phase was extracted 2 times with CH_2Cl_2. The combined organic layers were dried (Na_2SO_4) and the solvent was removed in vacuo. Purification by recrystallization (hexane/EtOAc) yielded the product (160 mg, 69% over two steps) as colorless crystals. M.p. 86-88 °C. $[\alpha]_D^{22}$ = +26.7 (c = 0.61, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.20, 1.25 (2 s, 3 H each, Me), 1.76 (dd, *J* = 5.6, 12.8 Hz, 1 H, 3-H), 1.96 (t, *J* = 12.8 Hz, 1 H, 3-H), 3.16 (dd, *J* = 2.9, 5.6 Hz, 1 H, 5-H), 3.70 (dt, *J* = 2.9, 5.1 Hz, 1 H, 6-H), 3.79 (dd, *J* = 5.1, 11.6 Hz, 1 H, 6-CH_2), 3.89 (dd, *J* = 5.1, 11.6 Hz, 1 H, 6-CH_2), 4.04 (dt, *J* = 5.6, 11.8 Hz, 1 H, 4-H), 4.24 (s, 2 H, NCH_2), 6.42 (s_{br}, 1 H, OH), 7.24-7.36 (m, 5 H, Ph) ppm. ^{13}C-NMR (101 MHz, $CDCl_3$): δ = 23.1, 31.4 (2 q, Me), 42.3 (t, C-3), 63.2 (d, C-5), 63.7 (t, 6-CH_2), 64.0 (t, NCH_2), 67.9 (d, C-4), 71.9 (d, C-6), 73.4 (s, C-2), 127.5, 128.4, 129.3, 138.0 (3 d, s, Ph) ppm. IR (KBr): 3390-3200 cm^{-1} (OH), 3090-2840 (=C-H, C-H). ESI-TOF: *m/z* calc. for $C_{15}H_{23}NO_4$ $[M + H]^+$ 282.1700, found 282.1713. Anal. calc. for $C_{15}H_{23}NO_4$ (281.3): C 64.03, H 8.24, N 4.98, found: C 63.77, H 7.86, N 4.98.

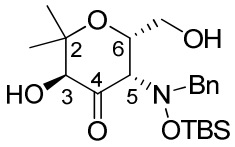
(4*R*,5*R*,6*S*)-5-Amino-6-(hydroxymethyl)-2,2-dimethyltetrahydro-2*H*-pyran-4-ol (14)



A suspension of palladium on charcoal (10% Pd, 50 mg) in MeOH (4 mL) was saturated with hydrogen for 1 h. After addition of the above described compound (50 mg, 0.178 mmol) in MeOH (2 mL), hydrogen was bubbled through the mixture for another 30 min and finally the reaction mixture was stirred under an atmosphere of hydrogen for 24 h. Filtration through a short pad of celite and concentration of the solution to dryness yielded **14** (28 mg, 90%) as colorless oil. $[\alpha]_D^{22}$ = +70.9 (c = 0.47, MeOH). ^{1}H NMR (500 MHz, CD_3OD): δ = 1.20, 1.25 (2 s, Me), 1.49 (t, *J* = 13.1 Hz, 1 H, 3-H), 1.70 (dd, *J* = 5.1, 13.1 Hz, 1 H, 3-H), 3.23 (d, *J* = 5.1 Hz, 1 H, 5-H), 3.62

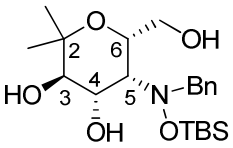
(dd, *J* = 5.3 Hz, 11.5, 1 H, 6-CH_2), 3.89 (dd, *J* = 5.3, 11.5 Hz, 1 H, 6-CH_2), 3.76 (t, *J* = 5.3 Hz, 1 H, 6-H), 4.07 (td, 5.1, 13.1 Hz, 1 H, 4-H) ppm. ^{13}C-NMR (126 MHz, CD_3OD): δ = 23.1, 31.3 (2 q, Me), 39.6 (t, C-3), 53.2 (d, C-5), 63.5 (t, 6-CH_2), 65.9 (d, C-4), 71.5 (d, C-6), 74.5 (s, C-2) ppm. IR (film): 3400-3100 cm^{-1} (OH), 2950-2840 (C-H). ESI-TOF: *m/z* calc. for $C_8H_{17}NO_3$ $[M + H]^+$ 176.1281, found 176.1277.

(3*S*,5*S*,6*S*)-5-[Benzyl(*tert*-butyldimethylsilyl)amino]-3-hydroxy-6-(hydroxymethyl)-2,2-dimethyldihydro-2*H*-pyran-4(3*H*)-one (15)



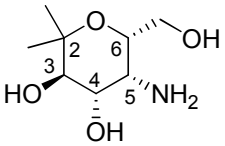
To a solution of **11** (260 mg, 0.616 mmol) in acetone (3 mL) were added H_2O (300 µL), K_2OsO_4•$2H_2O$ (16 mg, 0.043 mmol) and *N*-methylmorpholine-*N*-oxide (50 wt.% in H_2O, 170 µL, 0.840 mmol). The reaction mixture was stirred for 3 d at rt. Then solid Na_2SO_3 (106 mg, 0.840 mmol) was added and the mixture was stirred for 1 h. The mixture was filtrated over a pad of celite, dried (Na_2SO_4) and the solvent was removed in vacuo. Purification by column chromatography (silica gel, hexane/EtOAc = 3:1) yielded **15** (193 mg, 76%) as colorless oil. $[\alpha]_D^{22}$ = -6.0 (c = 0.52, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.30 (s_{br}, 6 H, $SiMe_2$), 0.90 (s, 9 H, *t*Bu), 1.06, 1.42 (2 s, 3 H each, Me), 1.94 (s_{br}, 1 H, OH), 3.36 (s_{br}, 1 H), 3.63 (s_{br}, 2 H), 3.79 (d, *J* = 12.1 Hz, 1 H), 3.85-4.01 (m, 2 H), 4.12 (s_{br}, 1 H), 4.40 (d, *J* = 3.3 Hz, 1 H), 7.24-7.41 (m, 5 H, Ph) ppm. ^{13}C-NMR (126 MHz, $CDCl_3$): δ = -4.7 (q, $SiMe_2$), 18.0, 28.2 (2 q, Me), 18.6, 25.9 (s, q, *t*Bu), 62.3, 63.6, 73.0, 83.6, 128.2, 128.8, 130.0 ppm. IR (film): 3480 cm^{-1} (OH), 3090-2820 (=C-H, C-H). ESI-TOF: *m/z* calc. for $C_{21}H_{35}NO_5Si$ $[M + Na]^+$432.2177, found 432.2184.

(3*R*,4*S*,5*R*,6*S*)-5-[Benzyl(*tert*-butyldimethylsiloxy)amino]-6-(hydroxymethyl)-2,2-dimethyltetrahydro-2*H*-pyran-3,4-diol



Compound **15** (90 mg, 0.220 mmol) was dissolved in ethanol (1.5 mL) and cooled to -40 °C. $CeCl_3$ (164 mg, 0.440 mmol) and then $NaBH_4$ (17 mg, 0.440 mmol) were added and the mixture was stirred until it slowly reached rt (5 h). Then CH_2Cl_2 and H_2O were added. The layers were separated and the aqueous phase was extracted 2 times with CH_2Cl_2. The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Purification by column chromatography (silica gel, hexane/EtOAc = 2:1) yielded the product (81 mg, 86%) as colorless crystals. M.p. 94-96 °C. $[\alpha]_D^{22}$ = +85.7 (c = 1.1, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = -0.78, -0.03 (2 s_{br}, 3 H each, $SiMe_2$), 0.80 (s, 9 H, *t*Bu), 1.20, 1.34 (2 s, 3 H each, Me), 2.56 (s_{br}, 1 H), 3.11 (s_{br}, 1 H), 3.67-4.09 (m, 6 H), 4.25 (m_c, 1 H), 4.43 (s_{br}, 1 H) 7.21-7.34 (m, 5 H, Ph) ppm. ^{13}C-NMR (126 MHz, $CDCl_3$): δ = -4.6 (q, $SiMe_2$), 17.3, 28.6 (2 q, Me), 17.6, 26.0 (s, q, *t*Bu), 63.4, 63.7, 64.9, 71.4, 127.8, 128.3, 130.5, 137.5 (3 d, s, Ph) ppm. IR (KBr): 3080 cm^{-1} (OH), 30700-2830 (=C-H, C-H). ESI-TOF: *m/z* calc. for $C_{21}H_{37}NO_5Si$ $[M + (2H) – (TBS)]^+$ 298.1649, found 298.1414.

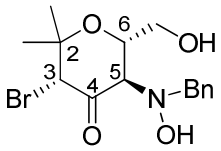
(3*R*,4*S*,5*R*,6*S*)-5-Amino-6-(hydroxymethyl)-2,2-dimethyltetrahydro-2*H*-pyran-3,4-diol (16)



A suspension of palladium on charcoal (10% Pd, 50 mg) in MeOH (3 mL) was saturated with hydrogen for 1 h. After addition of the above described compound (50 mg, 0.121 mmol) in MeOH (2 mL), hydrogen was bubbled through the mixture for another 30 min and finally the reaction mixture was stirred under an atmosphere of hydrogen for 24 h. Filtration through a short pad of celite and concentration of the solution to dryness yielded **16** (21 mg, 91%) as colorless oil. $[\alpha]_D^{22}$ = +85.6 (c = 0.36, MeOH). ^{1}H NMR (500 MHz, D_2O): δ = 1.23, 1.31 (2 s, Me), 3.41 (d, *J* = 10.3 Hz, 1 H, 3-H), 3.69 (dd, *J* = 1.4, 4.6 Hz, 1 H, 5-H), 3.72 (m_c, 2 H, 6-CH_2), 4.02 (m_c, 1 H, 6-H), 4.04 (dd, *J* = 4.6, 10.3 Hz, 1 H, 4-H) ppm. ^{13}C-NMR (101 MHz, D_2O): δ = 16.9, 26.9 (2 q,

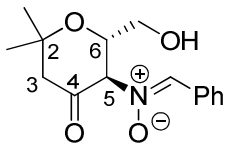
Me), 53.8 (d, C-5), 61.3 (t, 6-CH_2), 67.2 (d, C-4), 68.3 (d, C-6), 73.2 (d, C-3) ppm. IR (film): 3400-3100 cm^{-1} (OH), 2950-2800 (C-H). ESI-TOF: *m/z* calc. for $C_8H_{17}NO_3$ $[M + H]^+$ 192.1230, found 192.1233.

(3*R*,5*R*,6*S*)-5-[Benzyl(hydroxy)amino]3-bromo-6-(hydroxymethyl)-2,2-dimethyldihydro-2*H*-pyran-4(3*H*)-one (17)



To a solution of **12** (500 mg, 1.19 mmol) in MeCN (8 mL) were added H_2O (800 µL) and *N*-bromosuccinimide (211 mg, 1.19 mmol). After stirring the reaction mixture for 15 min, it was added further H_2O and the mixture was extracted 3 times with CH_2Cl_2. The combined organic phases were dried (Na_2SO_4) and the solvent was removed in vacuo. Purification by column chromatography (silica gel, hexane/EtOAc = 2:1) yielded **17** (298 mg, 70%) as colorless crystals. M.p. 109-111 °C. $[\alpha]_D^{22}$ = -144.5 (c = 0.38, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.40, 1.42 (2 s, 3 H each, Me), 3.77 (dd, *J* = 3.6, 11.6 Hz, 1 H, 6-CH_2), 3.80 (dd, *J* = 3.5, 11.6 Hz, 1 H, 6-CH_2), 4.04 (s, 1 H, 3-H), 4.17 (m, 1 H, 6-H), 4.20 (d, *J* = 12.8 Hz, 1 H, NCH_2), 4.25 (d, *J* = 9.6 Hz, 1 H, 5-H), 4.55 (d, *J* = 12.8 Hz, 1 H, NCH_2), 5.63 (s_{br}, 1 H, OH), 7.26-7.37 (m, 5 H, Ph) ppm. ^{13}C-NMR (126 MHz, $CDCl_3$): δ = 22.7, 28.0 (2 q, Me), 59.2 (d, C-3), 62.5 (t, NCH_2), 63.6 (d, C-5), 63.7 (t, 6-CH_2), 73.6 (d, C-6), 74.8 (s, C-2), 127.8, 128.5, 129.1, 136.7 (3 d, s, Ph), 202.1 (s, C-4) ppm. IR (KBr): 3260 cm^{-1} (OH), 3090-2820 (=C-H, C-H), 1730 (C=O). ESI-TOF: *m/z* calc. for $C_{15}H_{20}BrNO_4$ $[M + Na]^+$ 380.0462, found 380.0453.

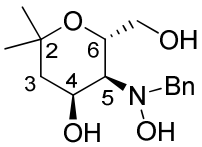
(2*S*,3*R*,*Z*)-*N*-Benzylidene-2-(hydroxymethyl)-6,6-dimethyl-4-oxotetrahydropyran-3-amine oxide (18)



To a solution of **17** (110 mg, 0.307 mmol) in DMF (3 mL) was added NaN_3 (99 mg, 1.52 mmol) and the reaction mixture was stirred for 12 h at rt. H_2O was added and the resulting mixture was

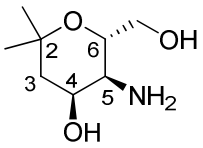
extracted 3 times with ethyl acetate. The combined organic phases were dried (Na_2SO_4) and the solvent was removed in vacuo. Purification by column chromatography (silica gel, CH_2Cl_2/EtOAc = 1:1) yielded **18** (74 mg, 87%) as colorless crystals. M.p. 156 °C. $[\alpha]_D^{22}$ = +73.8 (c = 0.13, $CHCl_3$). ^{1}H NMR (700 MHz, $CDCl_3$): δ = 1.39, 1.41 (2 s, 3 H each, Me), 2.50, 2.57 (AB-system, J_{AB} = 14.5 Hz, 1 H each, 3-H), 2.57 (s_{br}, 1 H, OH), 3.70 (dd, *J* = 2.2, 12.3 Hz, 1 H, 6-CH_2), 3.94 (dd, J = 2.2, 12.3 Hz, 1 H, 6-CH_2), 4.79 (dt, J = 2.2, 9.7 Hz, 1 H, 6-H), 4.83 (d, *J* = 9.7 Hz, 1 H, 5-H), 7.39 (s, 1 H, N=C<u>H</u>Ph), 7.40-7.45 (m, 3 H, Ph), 8.23-8.26 (m, 2 H, Ph) ppm. ^{13}C-NMR (176 MHz, $CDCl_3$): δ = 24.3, 30.3 (2 s, Me), 51.8 (t, C-3), 62.1 (t, 6-CH_2), 72.4 (d, C-6), 75.4 (s, C-2), 77.8 (d, C-5), 128.4, 128.9, 129.7, 131.0 (3 d, s, Ph), 138.2 (d, N=<u>C</u>HPh), 199.5 (s, C-4) ppm. IR (KBr): 3280 cm^{-1} (OH), 3090-2860 (=C-H, C-H), 1720 (C=O). ESI-TOF: *m/z* calc. for $C_{15}H_{19}NO_4$ $[M + Na]^+$ 300.1212, found 300.1256.

(4*S*,5*S*,6*S*)-5-[Benzyl(hydroxy)amino]-6-(hydroxymethyl)-2,2-dimethyltetrahydro-2*H*-pyran-4-ol



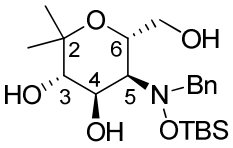
To a solution of **18** (70 mg, 0.252 mmol) in EtOH (2 mL) was added $NaBH_4$ (24 mg, 0.631 mmol) at 0 °C and the mixture was stirred for 1 h at rt. Then the solvent was removed in vacuo and the residue was dissolved in CH_2Cl_2 and H_2O. The layers were separated and the aqueous phase was extracted 2 times with CH_2Cl_2. The combined organic layers were dried (Na_2SO_4) and the solvent was removed in vacuo. Purification by column chromatography (silica gel, hexane/EtOAc = 1:1) yielded the product (63 mg, 89%) as colorless crystals. M.p. 128-129 °C. $[\alpha]_D^{22}$ = +40.0 (c = 0.08, $CHCl_3$). ^{1}H NMR (700 MHz, $CDCl_3$): δ = 1.18, 1.51 (2 s, 3 H each, Me), 1.51 (dd, *J* = 3.1, 14.3 Hz, 1 H, 3-H), 1.88 (dd, *J* = 3.1, 14.3 Hz, 1 H, 3-H), 2.61 (dd, *J* = 3.1, 10.3 Hz, 1 H, 5-H), 3.69 (dd, *J* = 5.3, 11.2 Hz, 1 H, 6-CH_2), 3.83 (dd, *J* = 5.3, 11.2 Hz, 1 H, 6-CH_2), 4.00, 4.27 (2 d, *J* = 13.1 Hz, 1 H each, NCH_2), 4.34 (td, *J* = 5.3, 10.3 Hz, 1 H, 6-H), 4.79 (q, *J* = 3.1 Hz, 1 H, 4-H), 7.27-7.43 (m, 5 H, Ph) ppm. ^{13}C-NMR (176 MHz, $CDCl_3$): δ = 25.3, 32.1 (2 q, Me), 42.5 (t, C-3), 61.2 (t, NCH_2), 65.0 (d, C-5), 65.8 (t, 6-CH_2), 65.8 (d, C-6), 65.8 (d, C-4), 71.8 (s, C-2), 127.7, 128.5, 129.0, 136.9 (3 d, s, Ph) ppm. IR (KBr): 3440 cm^{-1} (OH), 3130-2850 (=C-H, C-H). ESI-TOF: *m/z* calc. for $C_{15}H_{23}NO_4$ $[M + Na]^+$ 304.1519, found 304.1523.

(4*S*,5*S*,6*S*)-5-Amino-6-(hydroxymethyl)-2,2-dimethyltetrahydro-2*H*-pyran-4-ol (19)



A suspension of palladium on charcoal (10% Pd, 60 mg) in MeOH (4 mL) was saturated with hydrogen for 1 h. After addition of the above described compound (60 mg, 0.214 mmol) in MeOH (2 mL), hydrogen was bubbled through the mixture for another 30 min and finally the reaction mixture was stirred under an atmosphere of hydrogen for 24 h. Filtration through a short pad of celite and concentration of the solution to dryness yielded **19** (35 mg, 94%) as colorless oil. $[\alpha]_D^{22}$ = +173.8 (c = 1.80, MeOH). ^{1}H NMR (700 MHz, CD_3OD): δ = 1.19, 1.44 (2 s, Me), 1.66 (dd, *J* = 3.3, 14.4 Hz, 1 H, 3-H), 1.87 (dd, *J* = 3.3, 14.4 Hz, 1 H, 3-H), 2.84 (dd, *J* = 3.3, 10.0 Hz, 1 H, 5-H), 3.70-3.72 (m, 2 H, 6-CH_2), 3.80 (td, *J* = 4.5, 10.0 Hz, 1 H, 6-H), 4.06 (q, 3.3 Hz, 1 H, 4-H) ppm. ^{13}C-NMR (176 MHz, CD_3OD): δ = 25.4, 32.3 (2 q, Me), 43.3 (t, C-3), 52.8 (d, C-5), 64.5 (t, 6-CH_2), 67.5 (d, C-4), 70.2 (d, C-6), 72.7 (s, C-2) ppm. IR (film): 3350 cm^{-1} (OH), 2990-2850 (C-H). ESI-TOF: *m/z* calc. for $C_8H_{17}NO_3$ $[M + H]^+$ 176.1281, found 176.1278.

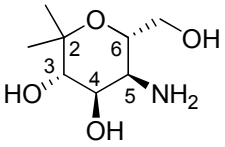
(3*S*,4*R*,5*S*,6*S*)-5-[Benzyl(*tert*-butyldimethylsiloxy)amino]-6-(hydroxymethyl)-2,2-dimethyltetrahydro-2*H*-pyran-3,4-diol (21) via intermediate (20)



To a solution of **12** (165 mg, 0.391 mmol) in acetone (2 mL) were added H_2O (200 µL), K_2OsO_4•$2H_2O$ (24 mg, 0.065 mmol) and *N*-methylmorpholine-*N*-oxide (50 wt.% in H_2O, 167 µL, 0.825 mmol). The reaction mixture was stirred for 3 d at rt. Then solid Na_2SO_3 (50 mg, 0.391 mmol) was added and the mixture was stirred for 1 h. The mixture was filtrated over a pad of celite, dried (Na_2SO_4) and the solvent was removed in vacuo. Purification by column chromatography (silica gel, hexane/EtOAc = 3:1) yielded starting material (50 mg) and the desired α-hydroxyketone **20** together with the hydroxylated hemiacetal (108 mg, 1:1, 64%) in spectroscopically pure form as colorless oil. 230 mg of the obtained mixture were dissolved in ethanol (5 mL) and cooled to 0 °C. $NaBH_4$ (42 mg, 1.13 mmol) was added and the mixture was

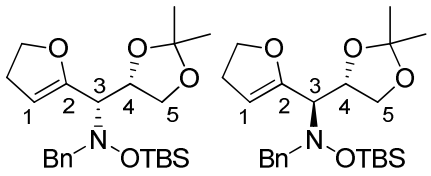
stirred for 1 h at rt. Then the solvent was removed in vacuo and the residue was dissolved in CH_2Cl_2 and H_2O. The layers were separated and the aqueous phase was extracted 2 times with CH_2Cl_2. The combined organic layers were dried (Na_2SO_4) and the solvent was removed in vacuo. Purification by recrystallization (Et_2O) yielded **21** (190 mg, 52% over 2 steps) as colorless crystals. M.p. 127-128 °C. $[\alpha]_D^{22}$ = +89.2 (c = 0.44, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.21, 0.22 (2 s_{br}, 3 H each, $SiMe_2$), 0.91 (s, 9 H, *t*Bu), 1.12, 1.47 (2 s, 3 H each, Me), 2.10 (s_{br}, 1 H, OH), 2.26 (s_{br}, 1 H, OH), 2.72 (dd, *J* = 2.6, 10.8 Hz, 1 H, 5-H), 3.39-3.47 (m, 2 H, 3-H, 6-CH_2), 3.84 (d, *J* = 11.3 Hz, 1 H, 6-CH_2), 4.09 (ddd, *J* = 2.8, 6.5, 10.5 Hz, 1 H, 6-H), 4.17, 4.27 (2 d, *J* = 12.4 Hz, 1 H each, NCH_2), 4.66 (m_c, 1 H, 4-H), 5.18 (s_{br}, 1 H, OH), 7.19-7.31 (m, 5 H, Ph) ppm. ^{13}C-NMR (126 MHz, $CDCl_3$): δ = -5.1, -4.1 (2 q, $SiMe_2$), 17.7, 25.8 (s, q, *t*Bu), 23.0, 26.6 (2 q, Me), 56.3 (d, C-5), 61.7 (t, NCH_2), 63.8 (t, 6-CH_2), 67.3 (d, C-6), 70.2 (d, C-4), 74.1 (d, C-3), 74.3 (s, C-2), 128.0, 128.7, 129.2, 135.9 (3 d, s, Ph) ppm. IR (KBr): 3440 cm^{-1} (OH), 3080-2830 (=C-H, C-H). ESI-TOF: *m/z* calc. for $C_{21}H_{37}NO_5Si$ $[M + Na]^+$ 434.2333, found 434.2341.

(3*S*,4*R*,5*R*,6*S*)-5-Amino-6-(hydroxymethyl)-2,2-dimethyltetrahydropyran-3,4-diol (22)



A suspension of palladium on charcoal (10% Pd, 60 mg) in MeOH (3 mL) was saturated with hydrogen for 1 h. After addition of compound **21** (60 mg, 0.146 mmol) in MeOH (2 mL), hydrogen was bubbled through the mixture for another 30 min and finally the reaction mixture was stirred under an atmosphere of hydrogen for 24 h. Filtration through a short pad of celite and concentration of the solution to dryness yielded **22** (29 mg, quant.) as colorless crystals. M.p. 148-149 °C. $[\alpha]_D^{22}$ = +64.4 (c = 0.23, MeOH). ^{1}H NMR (400 MHz, D_2O): δ = 1.09, 1.30 (2 s, Me), 3.01 (dd, *J* = 3.7, 9.9 Hz, 1 H, 5-H), 3.47 (d, *J* = 3.7 Hz, 1 H, 3-H), 3.58 (dd, *J* = 5.3, 11.9 Hz, 1 H, 6-CH_2), 3.65-3.75 (m, 2 H, 6-H, 6-CH_2), 3.90 (t, *J* = 3.7 Hz, 1 H, 4-H) ppm. ^{13}C-NMR (101 MHz, D_2O): δ = 22.0, 25.8 (2 q, Me), 46.6 (d, C-5), 61.3 (t, 6-CH_2), 67.2 (d, C-4), 68.3 (d, C-6), 73.2 (d, C-3) ppm. IR (film): 3460-3240 cm^{-1} (OH), 2990-2830 (C-H). ESI-TOF: *m/z* calc. for $C_8H_{17}NO_3$ $[M + H]^+$ 192.1230, found 192.1225.

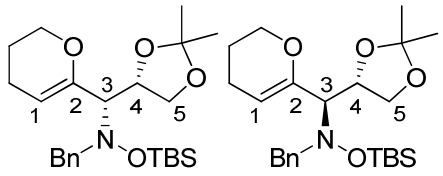
***N*-Benzyl-*O*-(*tert*-butyldimethylsilyl)-*N*-[(*S*)-(4,5-dihydrofuran-2-yl)((*S*)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl]hydroxylamine (*syn*-25) and *N*-Benzyl-*O*-(*tert*-butyldimethylsilyl)-*N*-[(*R*)-(4,5-dihydrofuran-2-yl)((*S*)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl]hydroxylamine (*anti*-25)**



2,3-Dihydrofuran (726 µL, 9.60 mmol) was dissolved in THF (10 mL) and cooled to -78 °C. *t*BuLi (1.6 M in pentane, 6.00 mL, 9.60 mmol) was added and the reaction mixture was stirred for 1 h until it reached 0 °C. After further stirring for 1 h at this temperature, it was cooled down to -78 °C again. A solution of nitrone **1a** (1.50 g, 6.40 mmol) in THF (4 mL) was added dropwise over a period of 15 min. Then, the mixture was stirred at this temperature for 1 h and quenched by addition of H_2O. After the mixture reached room temperature it was extracted 3 times with Et_2O. The combined organic phases were dried ($MgSO_4$) and the solvent was removed in vacuo. The crude product (1.91 g) was dissolved in CH_2Cl_2 (15 mL) and 2,6-lutidine (1.46 mL, 12.5 mmol) and TBSOTf (2.15 mL, 9.39 mmol) were added slowly at 0 °C. The mixture was stirred at room temperature for 30 min and was then quenched by the addition of sat. NH_4Cl solution. The phases were separated and the aqueous phase was extracted three times with CH_2Cl_2. The combined organic phases were dried ($MgSO_4$) and the solvent was removed in vacuo. Purification by column chromatography (silica gel, hexane/EtOAc = 20:1) yielded *syn*-**25** (1.57 g, 58%) and *anti*-**25** (260 mg, 10%) as colorless oils. *syn*-**25**: $[\alpha]_D^{22}$ = -63.7 (c = 0.19, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = -0.30 (s_{br}, 3 H, $SiMe_2$), 0.10 (s, 3 H, $SiMe_2$), 0.88 (s, 9 H, *t*Bu), 1.28, 1.33 (2 s, 3 H each, Me), 2.65 (m_c, 2 H, DHF), 3.36 (s_{br}, 1 H, 3-H), 3.61 (t, *J* = 7.5 Hz, 1 H, 5-H), 3.86, 4.06 (2 m_c, 1 H each, NCH_2), 3.98 (m_c, 1 H, 5-H), 4.22-4.36 (m, 3 H, DHF, 4-H), 4.89 (t, *J* = 2.1 Hz, 1 H, 1-H), 7.15-7.48 (m, 5 H, Ph) ppm. ^{13}C-NMR (126 MHz, $CDCl_3$): δ = -4.8 (s, $SiMe_2$), 17.8, 26.1 (s, q, *t*Bu), 25.5, 26.7 (2 q, Me), 30.0 (t, DHF), 61.1 (t, NCH_2), 67.5 (t, C-5), 69.0 (t, DHF), 74.2 (d, C-4), 99.9 (d, C-1), 109.2 (s, C-2'), 127.0, 128.0, 129.7 (3 d, Ph) ppm. IR (film): 3100-2820 cm^{-1} (=C-H, C-H). ESI-TOF: *m/z* calc. for $C_{23}H_{37}NO_4Si$ $[M + Na]^+$ 442.2379, found 442.2380. *anti*-**25**: $[\alpha]_D^{22}$ = +46.8 (c = 0.41, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = -0.24 (s_{br}, 3 H, $SiMe_2$), -0.19 (s, 3 H, $SiMe_2$), 0.85 (s, 9 H, *t*Bu), 1.31, 1.33 (2 s, 3 H

each, Me), 2.73 (m_c, 2 H, DHF), 3.39 (s_{br}, 1 H, 3-H), 3.83 (m_c, 1 H, 5-H), 3.83, 3.94 (2 m_c, 1 H each, NCH_2), 4.06 (dd, *J* = 8.5, 5.9 Hz, 1 H, 5-H), 4.32-4.39 (m, 2 H, DHF, 4-H) 4.42 (q, *J* = 8.9 Hz, 1 H, DHF), 4.97 (t, *J* = 2.4 Hz, 1 H, 1-H), 7.19-7.37 (m, 5 H, Ph) ppm. ^{13}C-NMR (126 MHz, $CDCl_3$): δ = -4.6 (s, $SiMe_2$), 17.8, 26.0 (s, q, *t*Bu), 25.7, 26.9 (2 q, Me), 30.2 (t, DHF), 67.9 (t, C-5), 69.3 (t, DHF), 74.3 (d, C-4), 109.1 (s, C-2'), 127.3, 128.1, 130.2, 137.8 (3 d, s, Ph) ppm. IR (film): 3100-2820 cm^{-1} (=C-H, C-H). ESI-TOF: *m/z* calc. for $C_{23}H_{37}NO_4Si$ $[M + Na]^+$ 442.2379, found 442.2377.

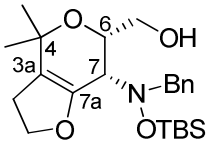
_N_-Benzyl-_O_-(_tert_-butyldimethylsilyl)-_N_-[(_S_)-(3,4-dihydro-2_H_-pyran-6-yl)((_S_)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl]hydroxylamine (_syn_-26) and _N_-Benzyl-_O_-(_tert_-butyldimethylsilyl)-_N_-[(_R_)-(3,4-dihydro-2_H_-pyran-6-yl)((_S_)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl]hydroxylamine (_anti_-26)



3,4-Dihydropyran (444 µL, 5.37 mmol) was dissolved in THF (5 mL) and cooled to -78 °C. *t*BuLi (1.6 M in pentane, 3.04 mL, 4.86 mmol) was added and the reaction mixture was stirred for 1 h until it reached 0 °C. After further stirring for 1 h at this temperature the mixture was cooled down to -78 °C again. A solution of nitrone **1a** (840 mg, 3.58 mmol) in THF (2 mL) was added dropwise over a period of 15 min. Then, the mixture was stirred at this temperature for 1 h and quenched by addition of H_2O. After the mixture reached rt it was extracted 3 times with Et_2O. The combined organic phases were dried (Na_2SO_4) and the solvent was removed in vacuo. The crude product (980 mg) was dissolved in CH_2Cl_2 (8 mL) and 2,6-lutidine (1.07 mL, 9.18 mmol) and TBSOTf (1.40 mL, 6.11 mmol) were added slowly at 0 °C. The mixture was stirred at room temperature for 30 min and was then quenched by the addition of sat. NH_4Cl solution. The phases were separated and the aqueous phase was extracted three times with CH_2Cl_2. The combined organic phases were dried (Na_2SO_4) and the solvent was removed in vacuo. Purification by column chromatography (silica gel, hexane/EtOAc = 20:1) yielded *syn*-**26** (682 mg, 44%) and *anti*-**26** (276 mg, 18%) as colorless oils. *syn*-**26**: $[\alpha]_D^{22}$ = -39.5 (c = 2.3, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = -0.08 (s_{br}, 3 H, $SiMe_2$), 0.09 (s, 3 H, $SiMe_2$), 0.87 (s, 9 H, *t*Bu), 1.32, 1.35 (2 s,

3 H each, Me), 1.72-1.82 (m, 2 H, DHP), 2.02-2.10 (m, 2 H, DHP), 3.17 (s_{br}, 1 H, 3-H), 3.62 (dd, *J* = 6.9, 7.9 Hz, 1 H, 5-H), 3.84-3.95 (m, 3 H, DHP, NCH_2), 4.00 (dd, *J* = 6.9, 7.9 Hz, 1 H, 5-H), 4.09 (d, *J* = 13.1 Hz, 1 H, NCH_2), 4.36 (td, *J* = 6.9, 8.9 Hz, 1 H, 4-H), 4.69 (m_c, 1 H, 1-H), 7.16-7.41 (m, 5 H, Ph) ppm. ^{13}C-NMR (126 MHz, $CDCl_3$): δ = -5.2, -4.8 (2 s, $SiMe_2$), 17.8, 26.1 (s, q, *t*Bu), 20.2, 22.3 (2 t, DHP), 25.6, 26.7 (2 q, Me), 60.6 (t, NCH_2), 65.3 (t, DHP), 67.6 (t, C-5), 74.2 (d, C-4), 102.8 (d, C-1), 109.1 (s, C-2'), 126.8, 127.9, 129.8 (3 d, Ph), 149.4 (s, C-2) ppm. IR (film): 3090-2820 cm^{-1} (=C-H, C-H). ESI-TOF: *m/z* calc. for $[M + Na]^+$ 456.2541, found 456.2538. Anal. calc. for $C_{24}H_{39}NO_4Si$ (433.7): C 66.47, H 9.06, N 3.23; found: C 66.51, H 9.06, N 3.31. *anti*-**26**: $[\alpha]_D^{22}$ = +39.1 (c = 0.80, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = -0.37 (s_{br}, 3 H, $SiMe_2$), -0.03 (s, 3 H, $SiMe_2$), 0.84 (s, 9 H, *t*Bu), 1.33, 1.35 (2 s, 3 H each, Me), 1.81-1.94 (m, 2 H, DHP), 2.06-2.21 (m, 2 H, DHP), 3.18 (s_{br}, 1 H, 3-H), 3.81 (s_{br}, 1 H, NCH_2), 3.85 (d, *J* = 11.5 Hz, 1 H, NCH_2), 3.95-4.11 (m, 4 H, DHP, 5-H), 4.36 (dt, *J* = 5.7, 9.4 Hz, 1 H, 4-H), 4.77 (t, *J* = 3.6 Hz, 1 H, 1-H), 7.20-7.32 (m, 5 H, Ph) ppm. ^{13}C-NMR (126 MHz, $CDCl_3$): δ = -4.8, -4.5 (2 s, $SiMe_2$), 17.8, 26.1 (s, q, *t*Bu), 20.4, 22.5 (2 t, DHP), 25.9, 27.0 (2 q, Me), 61.0 (t, NCH_2), 65.4 (t, DHP), 67.9 (t, C-5), 73.6 (d, C-4), 103.2 (d, C-1), 108.8 (s, C-2'), 127.2, 128.0, 130.2, 138.1 (3 d, s, Ph), 148.5 (s, C-2) ppm. IR (film): 3090-2800 cm^{-1} (=C-H, C-H). ESI-TOF: *m/z* calc. for $[M + Na]^+$ 456.2541, found 456.2523. Anal. calc. for $C_{24}H_{39}NO_4Si$ (433.7): C 66.47, H 9.06, N 3.23; found: C 66.12, H 8.90, N 3.32.

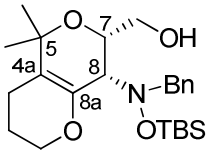
((6*S*,7*S*)-7-[Benzyl(*tert*-butyldimethylsiloxy)amino]-4,4-dimethyl-3,4,6,7-tetrahydro-2*H*-furo[3,2-*c*]pyran-6-yl)methanol (27)



To a solution of *syn*-**25** (1.52 g, 3.62 mmol) in CH_2Cl_2 (15 mL) at -30 °C was added TMSOTf (1.32 mL, 7.24 mmol), and the resulting solution was stirred until it slowly reached rt (6 h). Then the mixture was quenched by water. The resulting mixture was extracted 3 times with CH_2Cl_2. The combined organic phases were dried ($MgSO_4$) and the solvent was removed in vacuo. Purification by column chromatography (silica gel, hexane/EtOAc = 6:1) yielded **27** (1.29 g, 85%) as colorless oil. $[\alpha]_D^{22}$ = -130.0 (c = 0.61, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = -0.51, -0.25 (2 s_{br}, 3 H each, $SiMe_2$), 0.80 (s, 9 H, *t*Bu), 1.26, 1.32 (2 s, 3 H each, Me), 2.53-2.66 (m, 2 H,

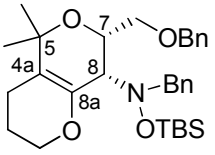
DHF), 3.28 (s_{br}, 1 H, OH), 3.64 (s_{br}, 1 H, 6-H), 3.84 (s_{br}, 1 H, NCH_2), 3.91 (s_{br}, 1 H, 6-CH_2), 3.96 (m_c, 1 H, 4-H), 4.10 (d, J = 13.4 Hz, 1 H, NCH_2), 4.13 (m_c, 1 H, 6-CH_2), 4.37-4.45 (m, 2 H, DHF), 7.17-7.32 (m, 5 H, Ph) ppm. ^{13}C-NMR (101 MHz, $CDCl_3$): δ = -5.3, -5.1 (2 q, $SiMe_2$), 17.7, 26.0 (s, q, *t*Bu), 23.1, 27.8 (2 q, Me), 29.6 (t, DHF), 60.8 (t, NCH_2), 62.6 (d, C-7), 63.8 (t, 6-CH_2), 69.1 (t, DHF), 73.1 (d, C-6), 74.1 (s, C-4), 117.4 (s, C-3a), 127.1, 127.9, 130.6, 138.6 (3 d, s, Ph), 146.8 (s, C-7a) ppm. IR (film): 3460 cm^{-1} (OH), 3100-2800 (=C-H, C-H), 1690 (C=C). ESI-TOF: *m/z* calc. for $C_{23}H_{37}NO_4Si$ $[M + Na]^+$ 442.2379, found 442.2377.

((7*S*,8*S*)-8-[Benzyl(*tert*-butyldimethylsiloxy)amino]-5,5-dimethyl-2,3,4,5,6,7,8-hexahydropyrano[4,3-*b*]pyran-7-yl)methanol (28)



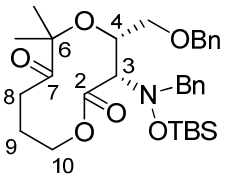
To a solution of *syn*-**26** (590 mg, 1.36 mmol) in CH_2Cl_2 (6 mL) at -30 °C was added TMSOTf (501 µL, 2.72 mmol), and the resulting solution was stirred until it slowly reached rt (6 h). Then the mixture was quenched by water. The resulting mixture was extracted 3 times with CH_2Cl_2. The combined organic phases were dried (Na_2SO_4) and the solvent was removed in vacuo. Purification by column chromatography (silica gel, hexane/EtOAc = 6:1) yielded **28** (434 mg, 74%) as colorless oil. $[\alpha]_D^{22}$ = -130.2 (c = 0.58, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = -0.37 (s_{br}, 6 H, $SiMe_2$), 0.79 (s, 9 H, *t*Bu), 1.26, 1.30 (2 s, 3 H each, Me), 1.81-1.92 (m, 3 H, DHP), 2.06 (m_c, 1 H, DHP), 3.49 (s_{br}, 1 H, 8-H), 3.64 (s_{br}, 1 H, 7-CH_2), 3.87-3.97 (m, 3 H, 7-H, 7-CH_2, NCH_2), 4.01-4.18 (m, 3 H, DHP, NCH_2), 7.16-7.32 (m, 5 H, Ph) ppm. ^{13}C-NMR (101 MHz, $CDCl_3$): δ = -5.3 (q, $SiMe_2$), 17.7, 26.0 (s, q, *t*Bu), 20.6, 22.6 (2 t, DHP), 23.5, 27.7 (2 q, Me), 64.0 (t, 7-CH_2), 65.2 (t, DHP), 72.6 (d, C-7), 75.2 (s, C-5), 115.4 (s, C-4a), 127.0, 127.9, 130.6, 139.2 (3 d, s, Ph), 143.2 (s, C-8a) ppm. IR (film): 3450 cm^{-1} (OH), 3100-2850 (=C-H, C-H), 1660 (C=C). ESI-TOF: *m/z* calc. for $C_{24}H_{39}NO_4Si$ $[M + H]^+$ 434.2721, found 434.2724.

***N*-Benzyl-*N*-((7*S*,8*S*)-7-(benzyloxymethyl)-5,5-dimethyl-2,3,4,5,6,7,8-hexahydropyrano[4,3-*b*]pyran-8-yl)-*O*-(*tert*-butyldimethylsilyl)hydroxylamine**



To a solution of **28** (600 mg, 1.38 mmol) in THF (13 mL) was added NaH (60% in paraffin oil, 84 mg, 2.16 mmol) at 0 °C. The reaction mixture was stirred for 1 h at rt, was then cooled to 0 °C and BnBr (247 µL, 1.98 mmol) was added. The mixture was stirred for 12 h at rt. Sat. NH_4Cl solution was added and the mixture was extracted 3 times with CH_2Cl_2. The combined organic phases were dried ($MgSO_4$) and concentrated. Purification by column chromatography (silica gel, hexane/EtOAc = 15:1) yielded the product (560 mg, 78%) as colorless oil. $[\alpha]_D^{22}$ = -103.9 (c = 0.44, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.07, 0.08 (2 s, 3 H each, $SiMe_2$), 0.91 (s, 9 H, *t*Bu), 1.25, 1.26 (2 s, 3 H each, Me), 1.86-1.97 (m, 3 H, DHP), 2.04-2.13 (m, 1 H, DHP), 3.44 (s_{br}, 1 H, 8-H), 3.69 (dd, *J* = 10.5, 3.8 Hz, 1 H, 7-CH_2), 3.78-3.89 (m, 3 H, 7-H, 7-CH_2, NCH_2), 3.97 (m_c, 1 H, DHP), 4.11-4.17 (m, 2 H, DHP, NCH_2), 4.24 (d, *J* = 11.1 Hz, 1 H, O$\underline{C}H_2$Ph), 4.40 (d, *J* = 11.1 Hz, 1 H, O$\underline{C}H_2$Ph), 7.04-7.10 (m, 2 H, Ph), 7.15-7.42 (m, 8 H, Ph) ppm. ^{13}C-NMR (126 MHz, $CDCl_3$): δ = -5.1, -4.9 (2 q, $SiMe_2$), 18.3, 26.0 (s, q, *t*Bu), 20.5, 22.7 (2 t, DHP), 23.4, 28.0 (2 q, Me), 61.1 (t, NCH_2), 61.6 (d, C-8), 64.1 (t, 7-CH_2), 65.1 (t, DHP), 73.4 (d, C-7), 74.8 (t, O$\underline{C}H_2$Ph), 75.6 (s, C-5), 115.3 (s, C-4a), 126.8, 127.3, 127.9, 128.0, 128.8, 129.9, 137.9, 139.4 (6 d, 2 s, Ph), 143.4 (s, C-8a) ppm. IR (film): 3100-2850 cm^{-1} (=C-H, C-H), 1670 (C=C). ESI-TOF:*m/z* calc. for $[M + H]^+$ 546.3005, found 546.2981. Anal. calc. for $C_{31}H_{45}NO_4Si$ (523.8): C 71.09, H 8.66, N 2.67, found: C 71.21, H 8.65, N 2.82.

(3*S*,4*S*)-3-[Benzyl(*tert*-butyldimethylsiloxy)amino]-4-(benzyloxymethyl)-6,6-dimethyl-1,5-dioxecane-2,7-dione (29)

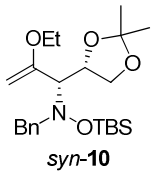


To a solution of the above described compound (100 mg, 0.191 mmol) in H_2O:CCl_4:MeCN (1.5:1:1, 1.4 mL) was added $RuCl_3$ (0.1M in H_2O, 57 µL, 5.73 µmol) and $NaIO_4$ (168 mg, 0.783 mmol). The reaction mixture was stirred at rt for 2 h and then quenched by the addition of sat. $Na_2S_2O_3$ solution. The resulting mixture was extracted 3 times with CH_2Cl_2. The combined organic phases were dried (Na_2SO_4) and concentrated to dryness giving 94 mg of **29** (94 mg, 88%) in analytically pure form as yellow oil. $[\alpha]_D^{22}$ = -43.8 (c = 0.96, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.10, 0.11 (2 s, 3 H each, $SiMe_2$), 0.92 (s, 9 H, *t*Bu), 1.31, 1.35 (2 s, 3 H each, Me), 1.82 (m_c, 1 H, 9-H), 2.01 (ddd, *J* = 1.3, 11.6, 16.7 Hz, 1 H, 8-H), 2.58 (m_c, 1 H, 9-H), 2.94 (ddd, *J* = 1.5, 11.6, 16.7 Hz, 1 H, 8-H), 3.72 (dd, *J* = 5.0, 9.4 Hz, 1 H, 4-CH_2), 3.81 (ddd, *J* = 2.0, 7.3, 10.9 Hz, 1 H, 10-H), 3.96 (m_c, 1 H, 4-H), 4.11 (t, *J* = 9.4 Hz, 1 H, 4-CH_2), 4.22 (d, *J* = 3.3 Hz, 1 H, 3-H), 4.29-4.40 (m, 3 H, O$C\underline{H}_2$Ph, NCH_2), 4.69 (d, *J* = 13.8 Hz, 1 H, NCH_2), 4.91 (dt, *J* = 6.0, 10.9 Hz, 1 H, 10-H), 6.98-7.49 (m, 10 H, Ph) ppm. ^{13}C-NMR (101 MHz, $CDCl_3$): δ = -5.1 (q, $SiMe_2$), 18.4, 26.1 (s, q, *t*Bu), 21.7 (t, C-9), 21.8, 26.0 (2 q, Me), 31.4 (t, C-8), 60.0 (t, NCH_2), 61.0 (t, C-10), 62.7 (t, 4-CH_2), 66.7 (d, C-3), 75.7 (t, O$C\underline{H}_2$Ph), 75.8 (d, C-4), 80.9 (s, C-6), 127.2, 127.6, 128.1, 128.2, 128.7, 129.8, 137.2, 139.3 (6 d, 2 s, Ph), 169.9 (s, C-2), 209.3 (s, C-7) ppm. IR (film): 3100-2830 cm^{-1} (=C-H, C-H), 1750, 1710 (C=O). ESI-TOF: *m/z* calc. for $C_{31}H_{45}NO_6Si$ $[M + Na]^+$ 578.2903, found 578.2911.

^{1}H- and ^{13}C-NMR spectra:

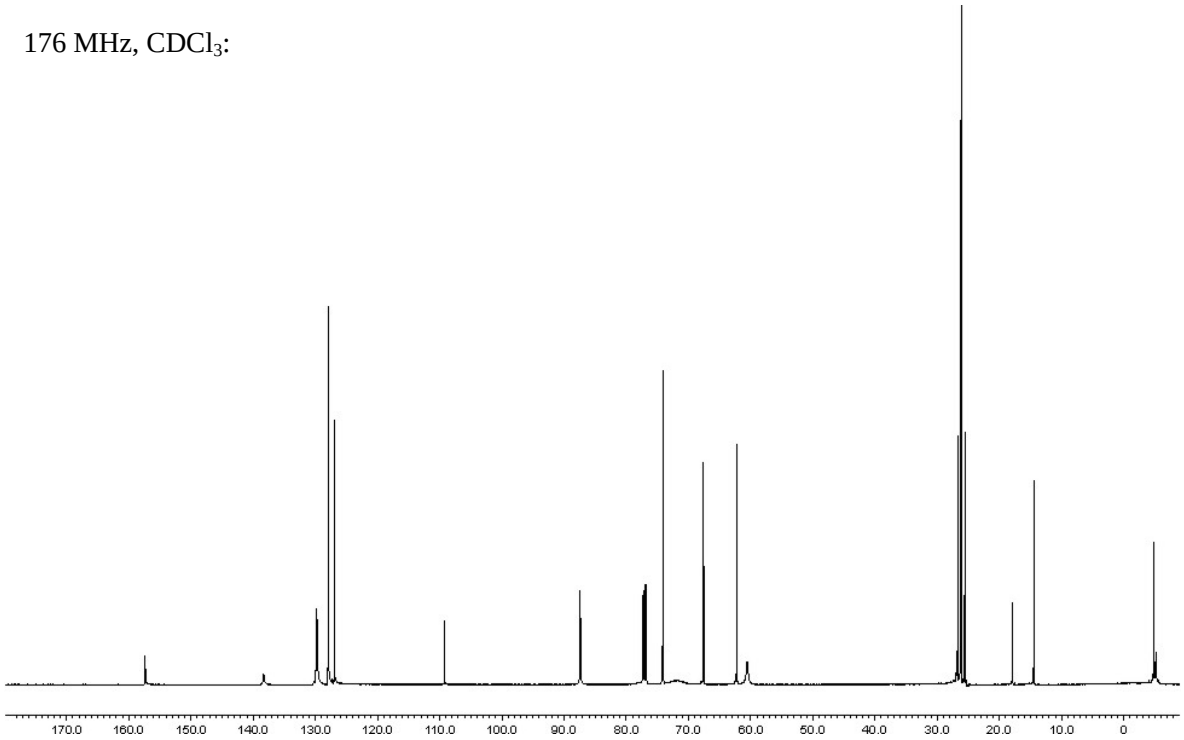
^{13}C-NMR spectra recorded at 101 MHz show signals at 27.5, 103.5 and 179.1 ppm, which are caused by external electromagnetic interference.

500 MHz, $CDCl_3$:

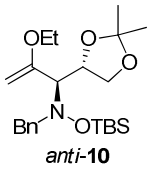


syn-**10**

176 MHz, $CDCl_3$:

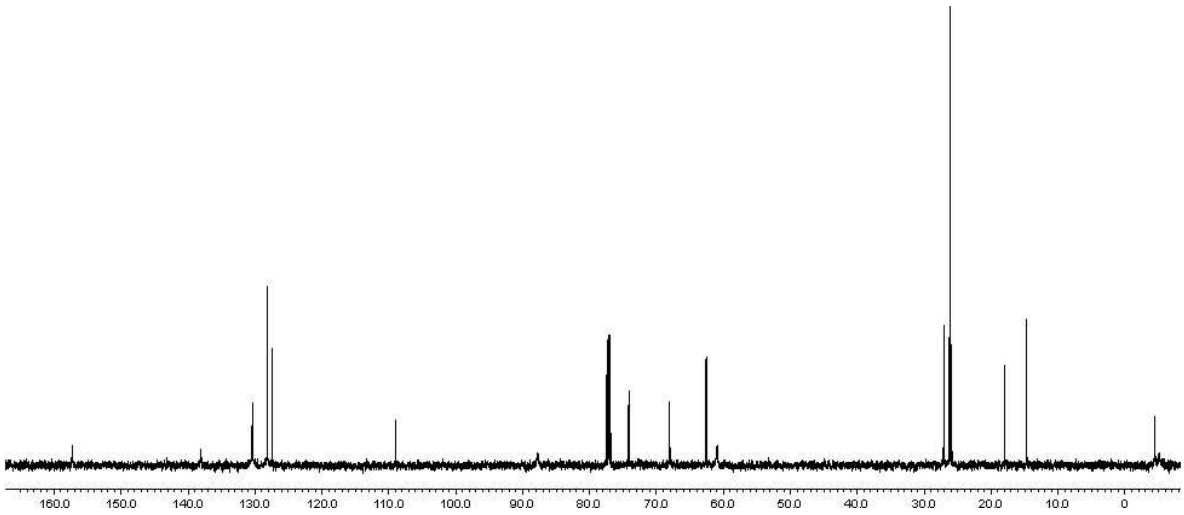


500 MHz, $CDCl_3$:

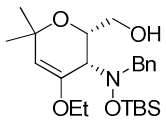


anti-**10**

126 MHz, $CDCl_3$:

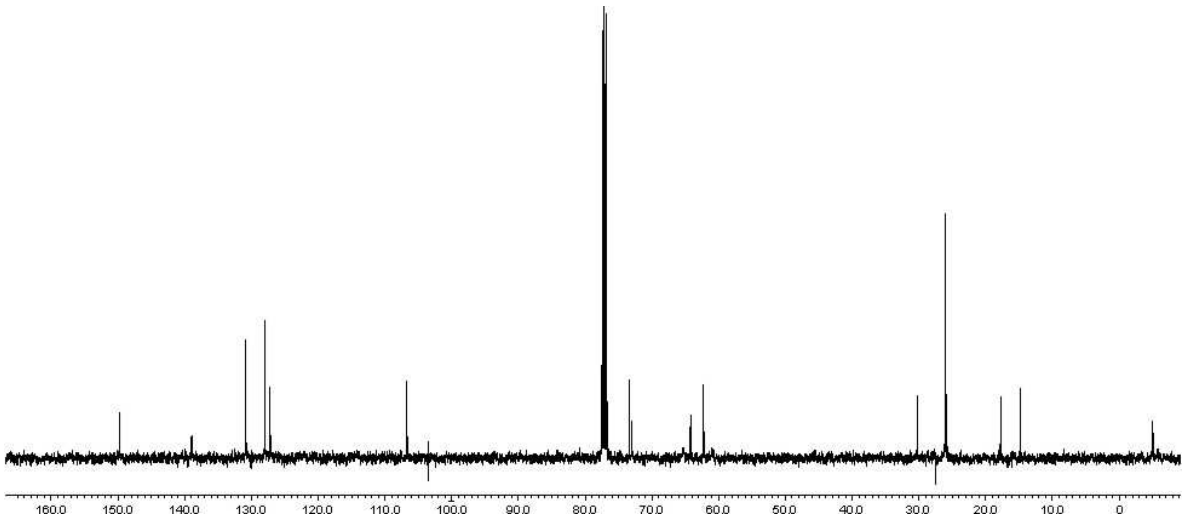


400 MHz, $CDCl_3$:

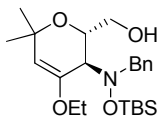


11

101 MHz, $CDCl_3$:

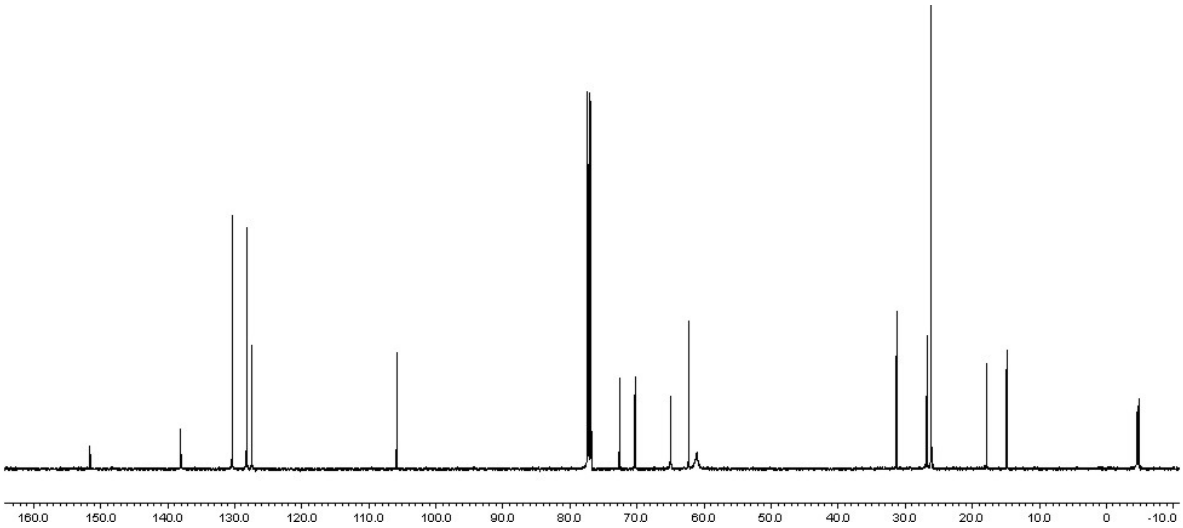


500 MHz, $CDCl_3$:

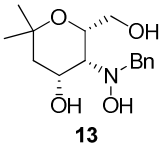


12

126 MHz, $CDCl_3$:

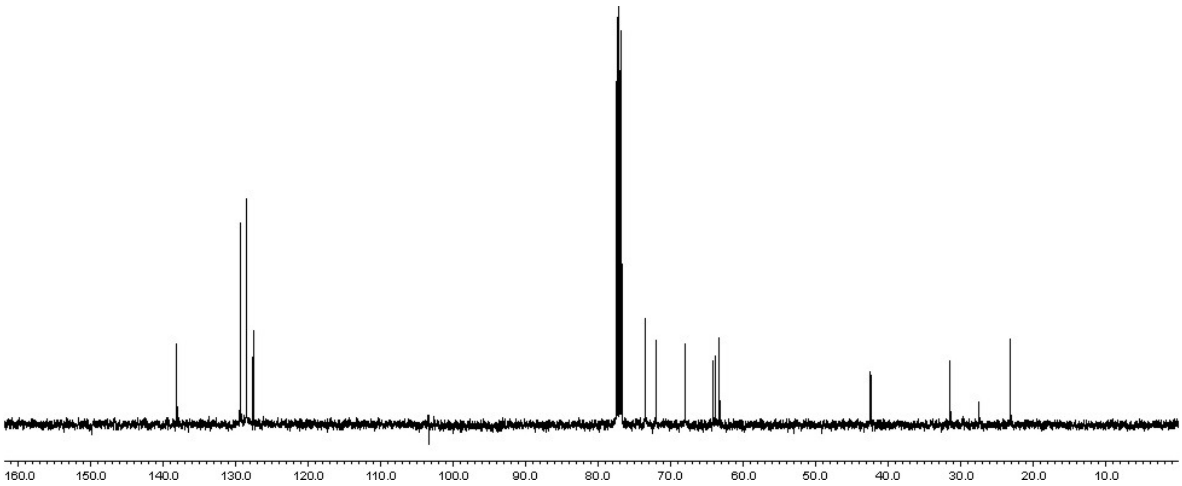


500 MHz, $CDCl_3$:

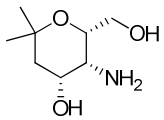


13

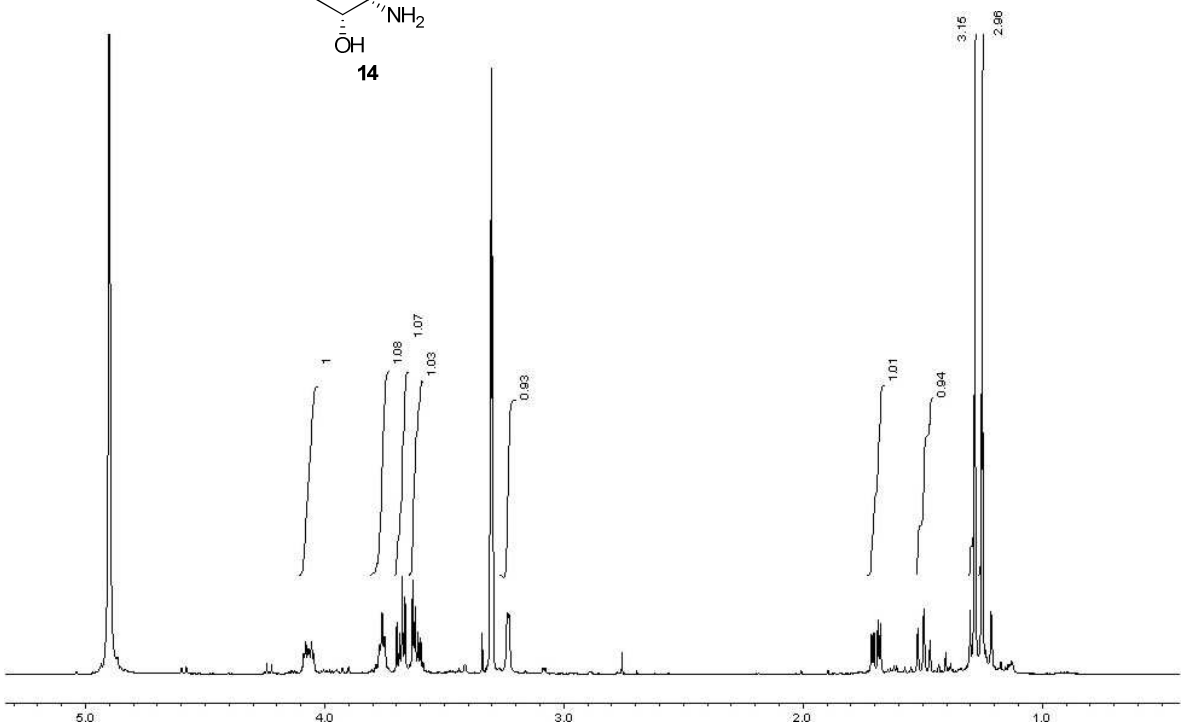
101 MHz, $CDCl_3$:



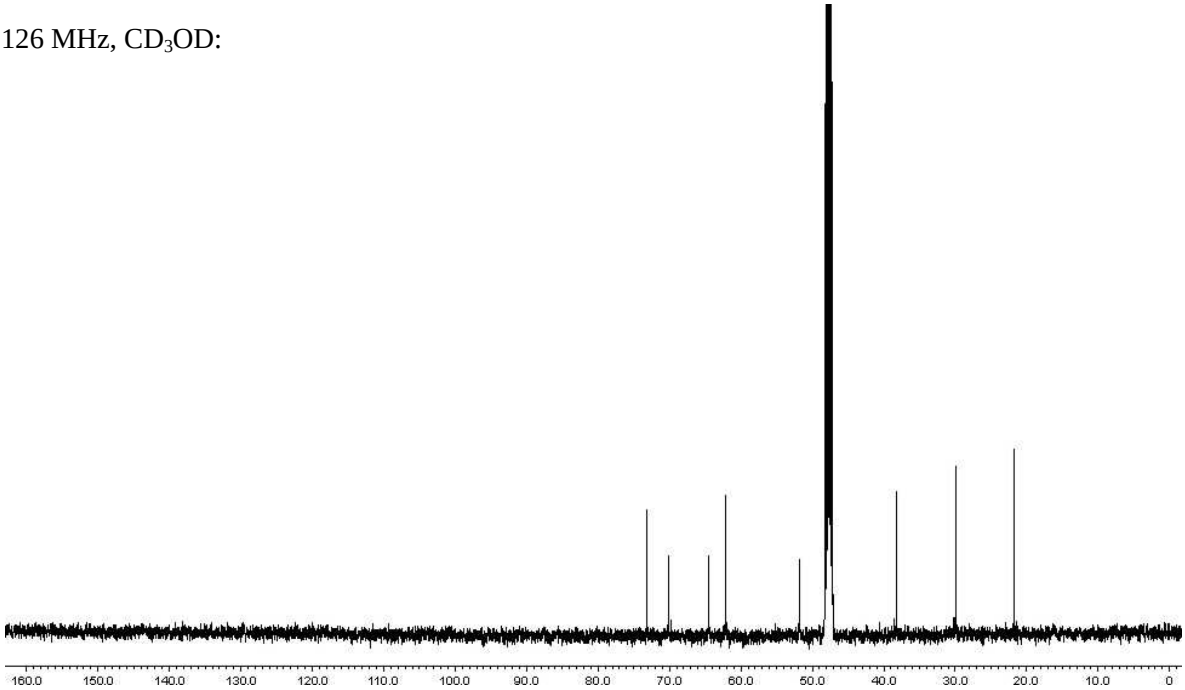
500 MHz, CD_3OD:



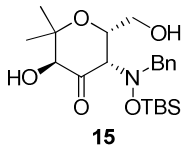
14



126 MHz, CD_3OD:

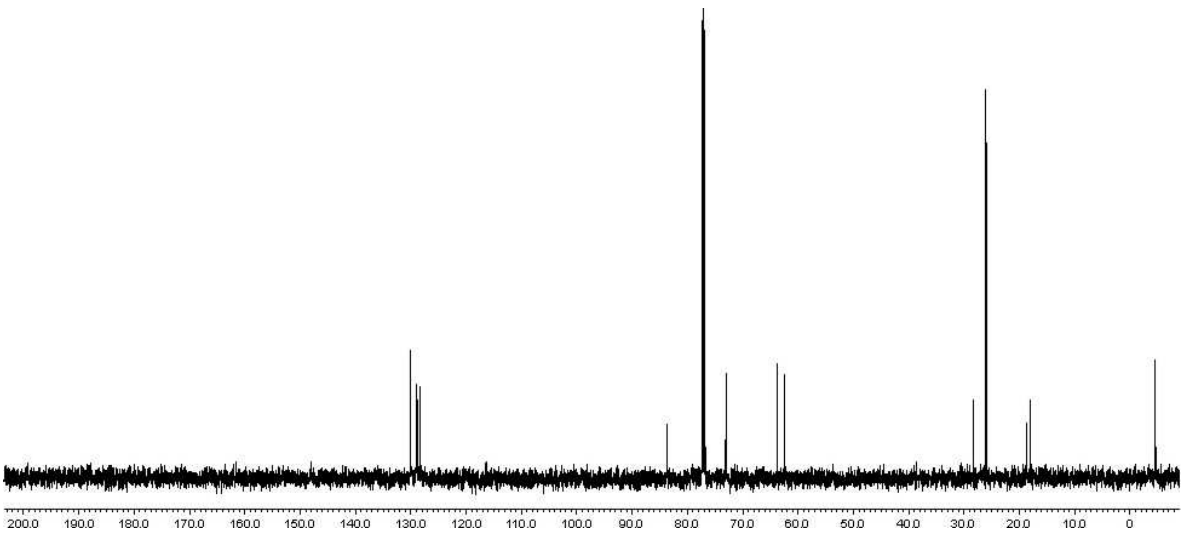


500 MHz, $CDCl_3$:

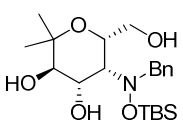


15

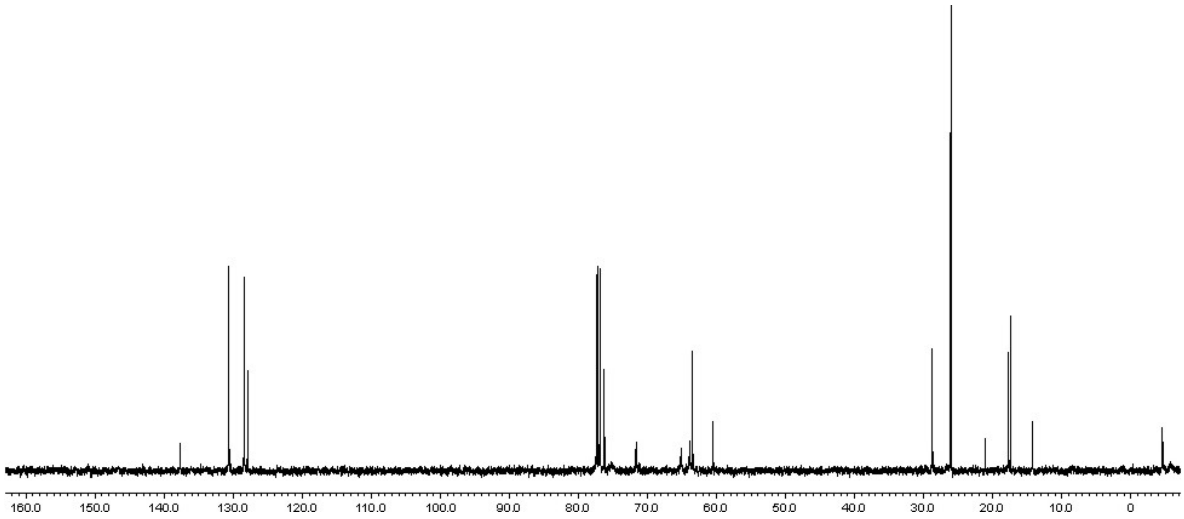
126 MHz, $CDCl_3$:



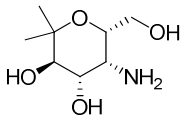
500 MHz, $CDCl_3$:



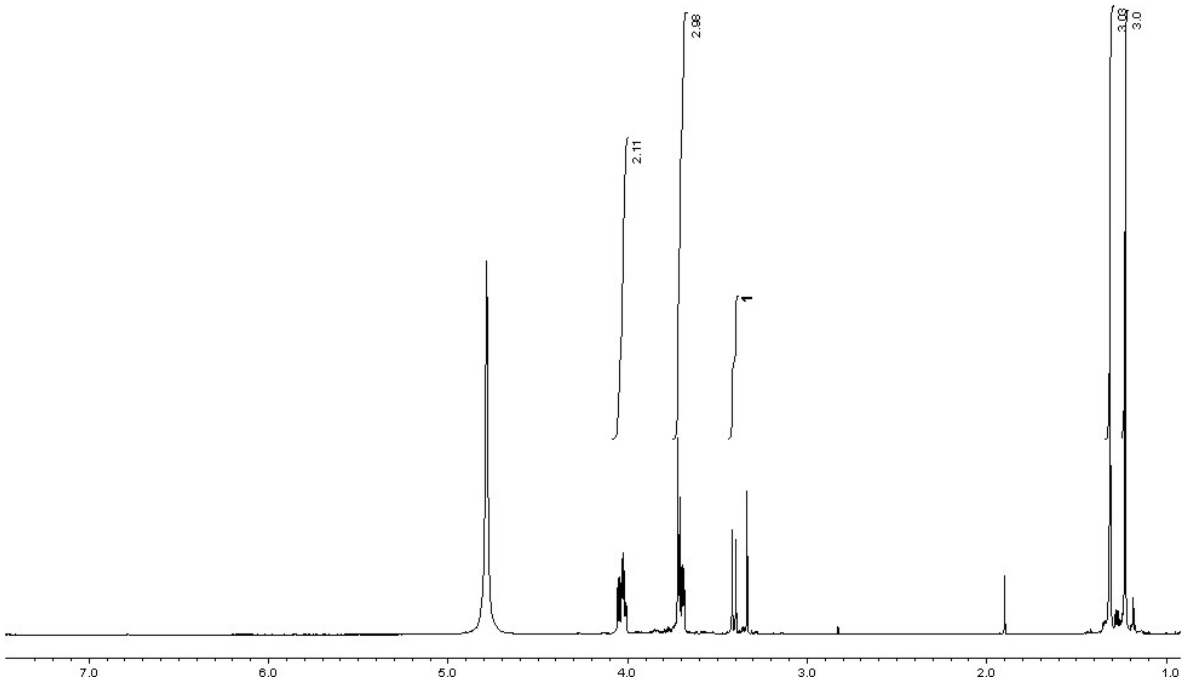
126 MHz, $CDCl_3$:



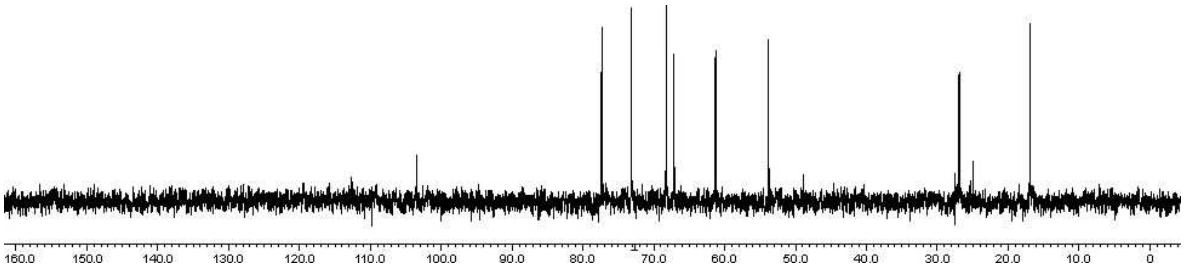
500 MHz, D_2O:



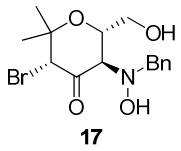
16



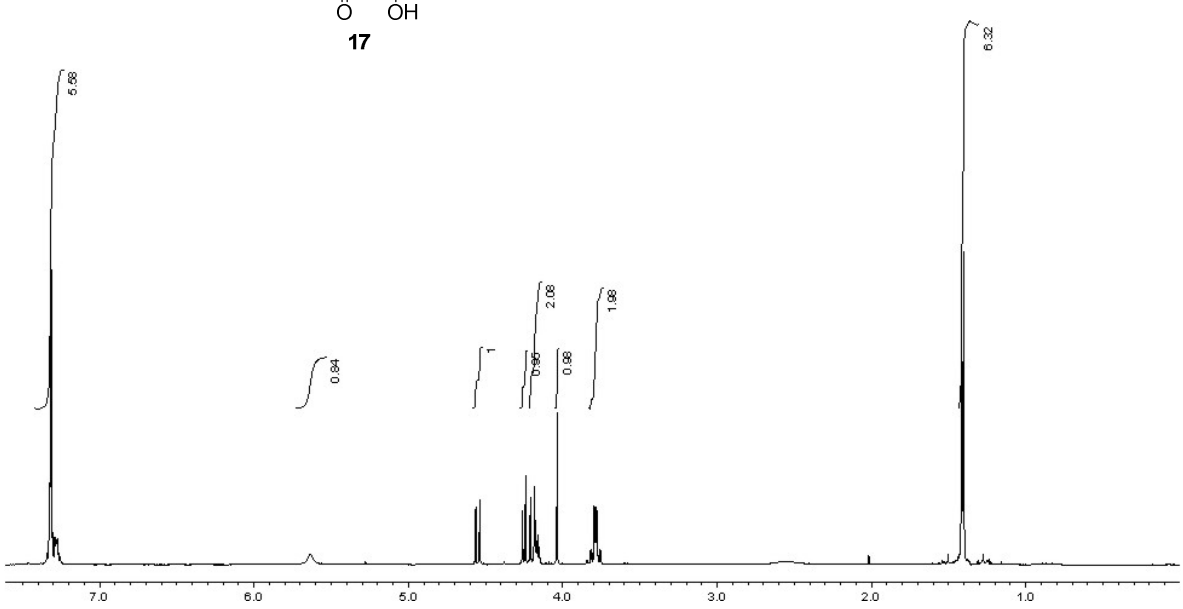
101 MHz, D_2O:



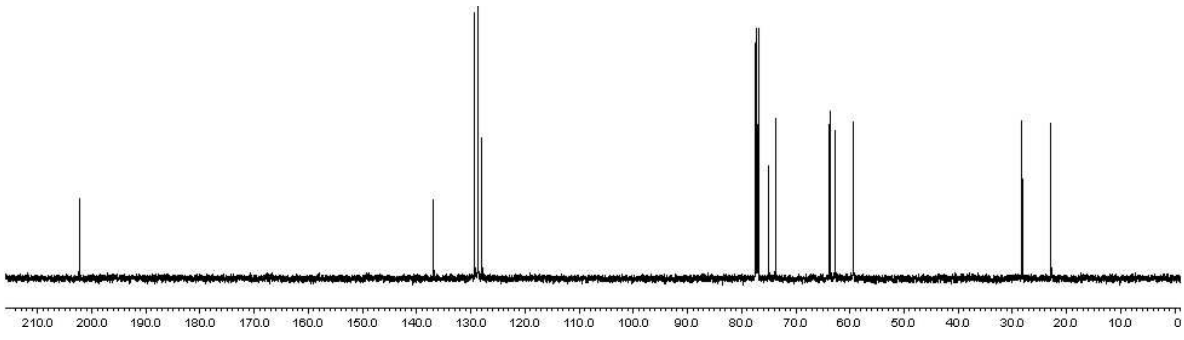
500 MHz, $CDCl_3$:



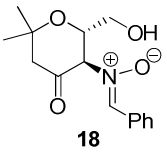
17



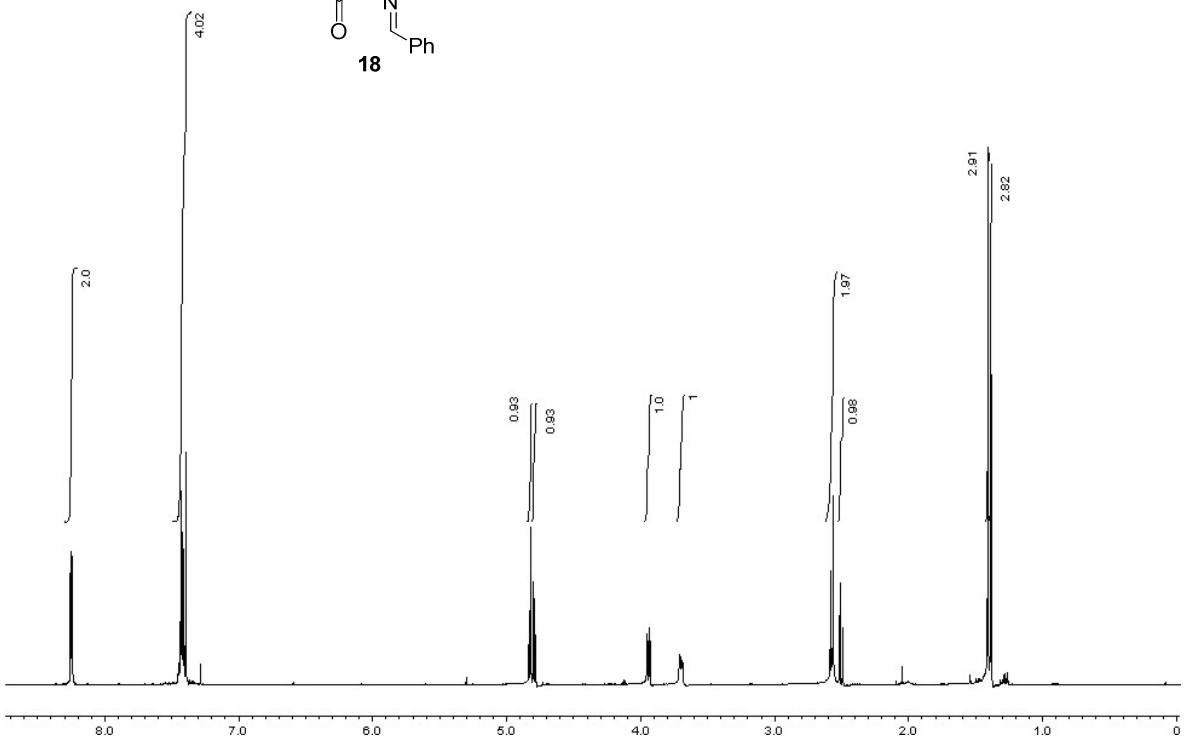
126 MHz, $CDCl_3$:



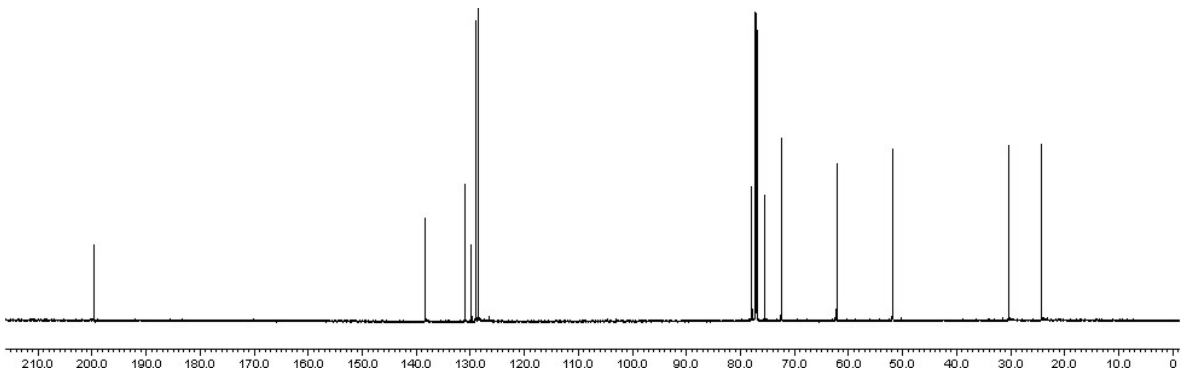
700 MHz, $CDCl_3$:



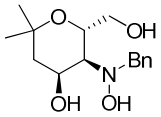
18

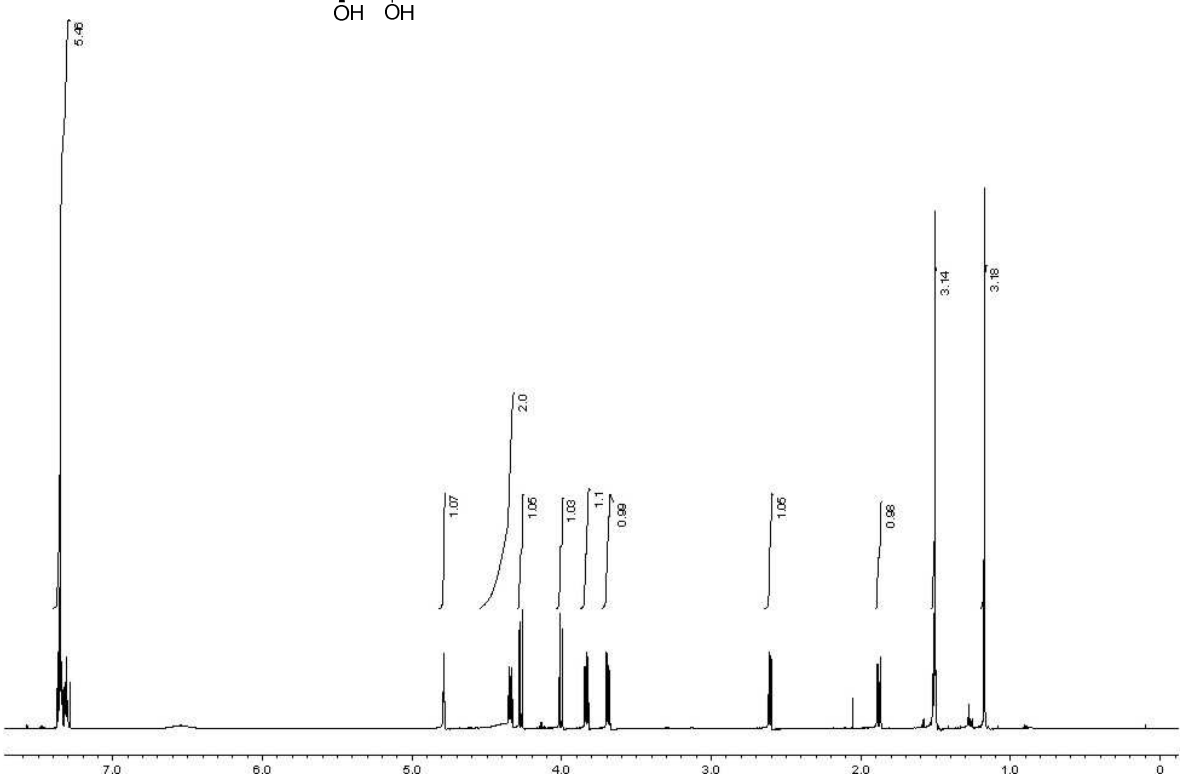


176 MHz, $CDCl_3$:

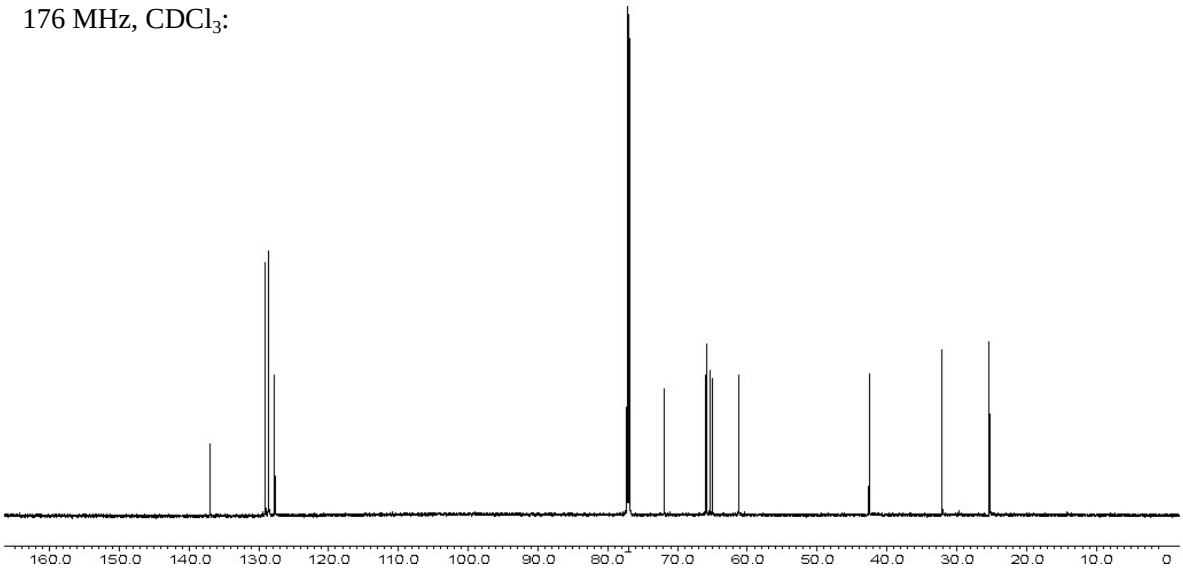


700 MHz, $CDCl_3$:

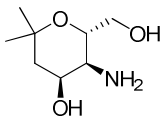




176 MHz, $CDCl_3$:

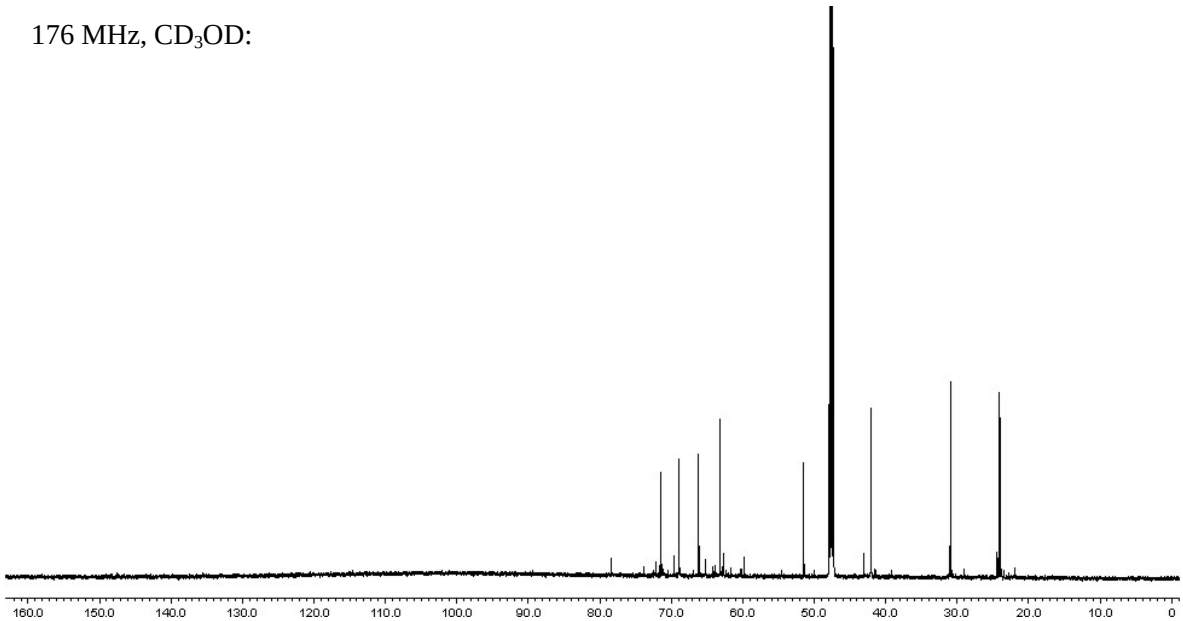


700 MHz, CD_3OD:

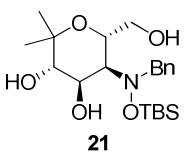


19

176 MHz, CD_3OD:

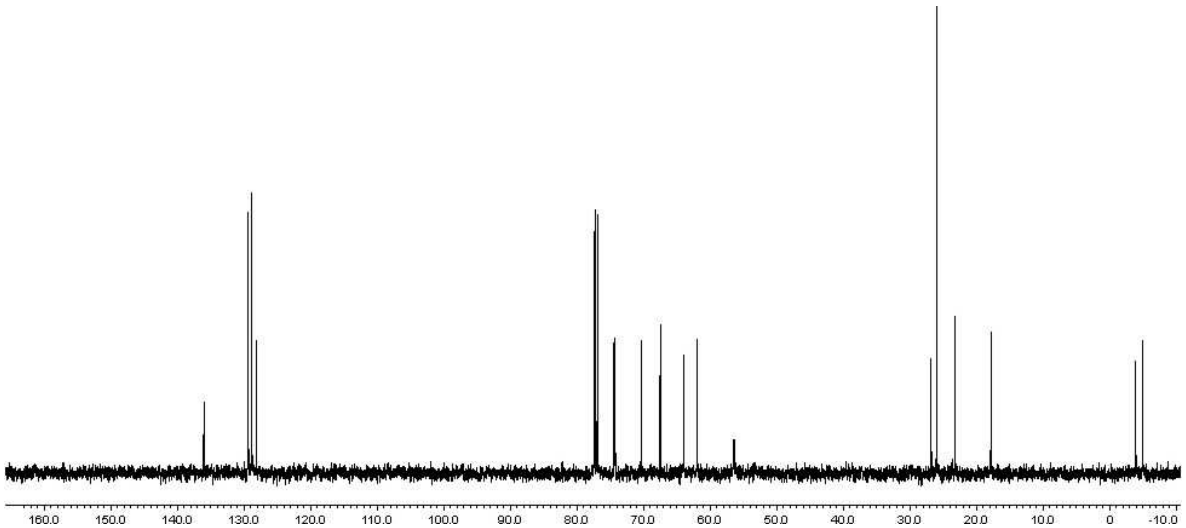


500 MHz, $CDCl_3$:

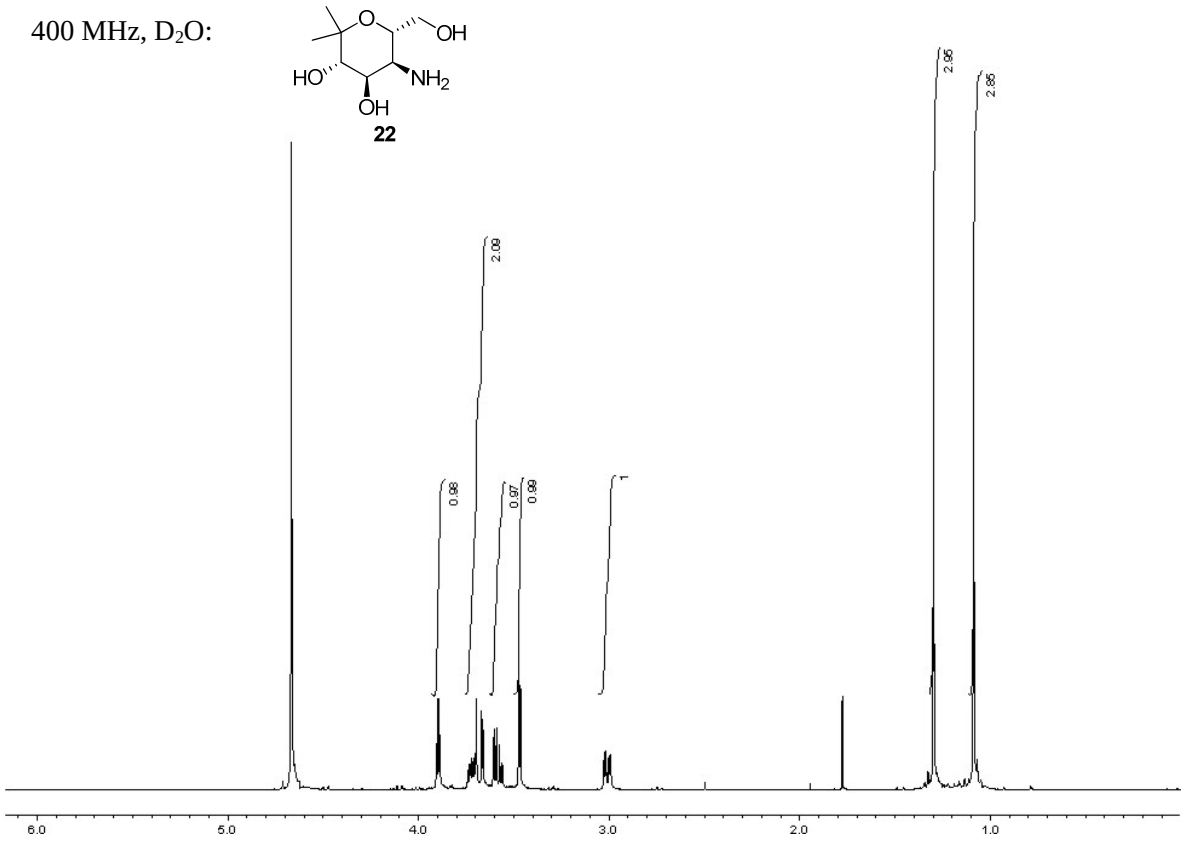


21

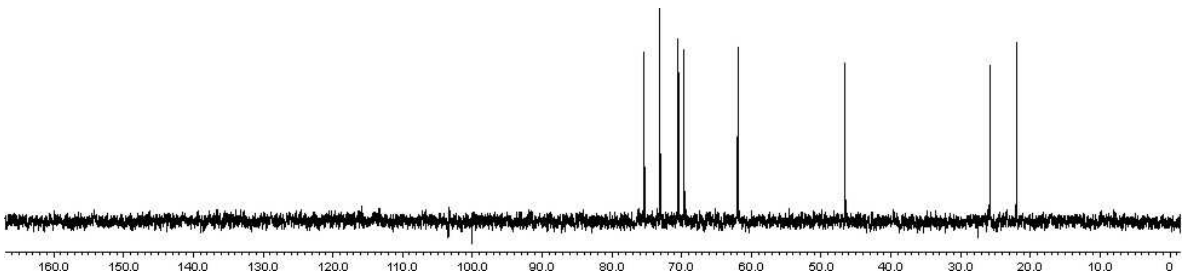
126 MHz, $CDCl_3$:



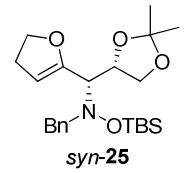
400 MHz, D_2O:



101 MHz, D_2O:

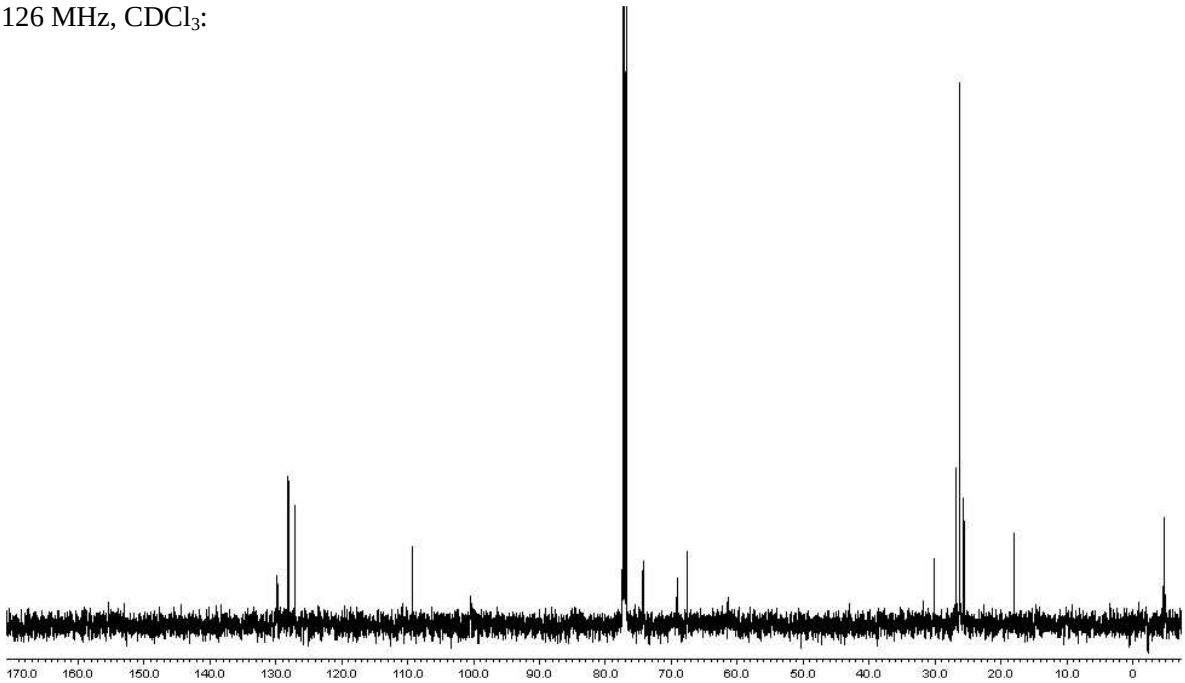


500 MHz, $CDCl_3$:

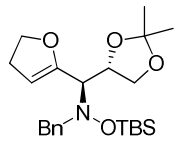


syn-**25**

126 MHz, $CDCl_3$:

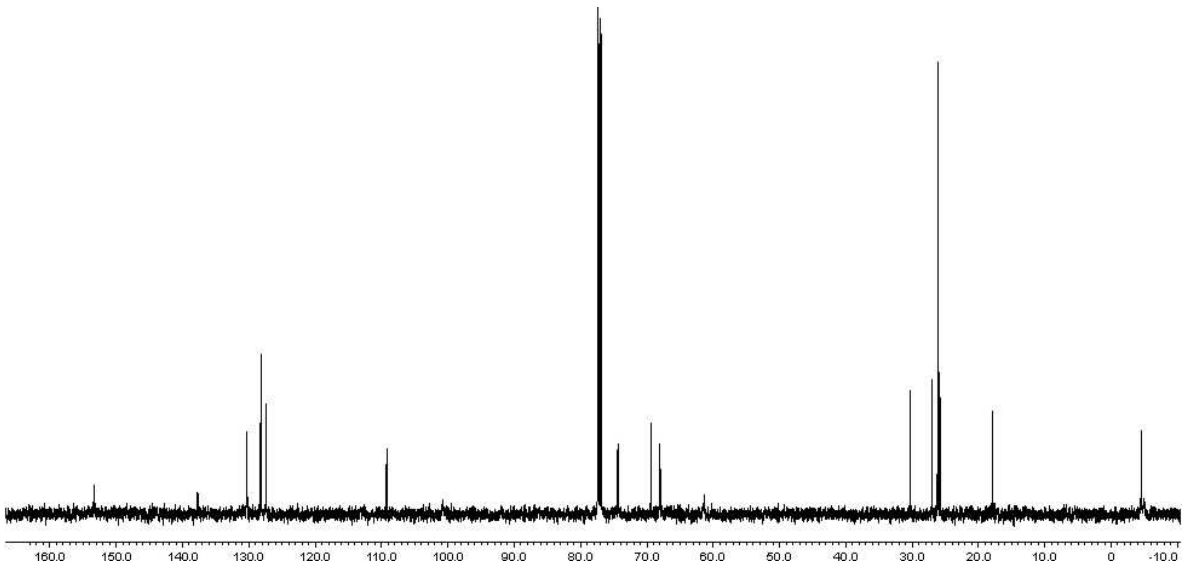


500 MHz, $CDCl_3$:

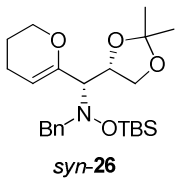


anti-**25**

126 MHz, $CDCl_3$:

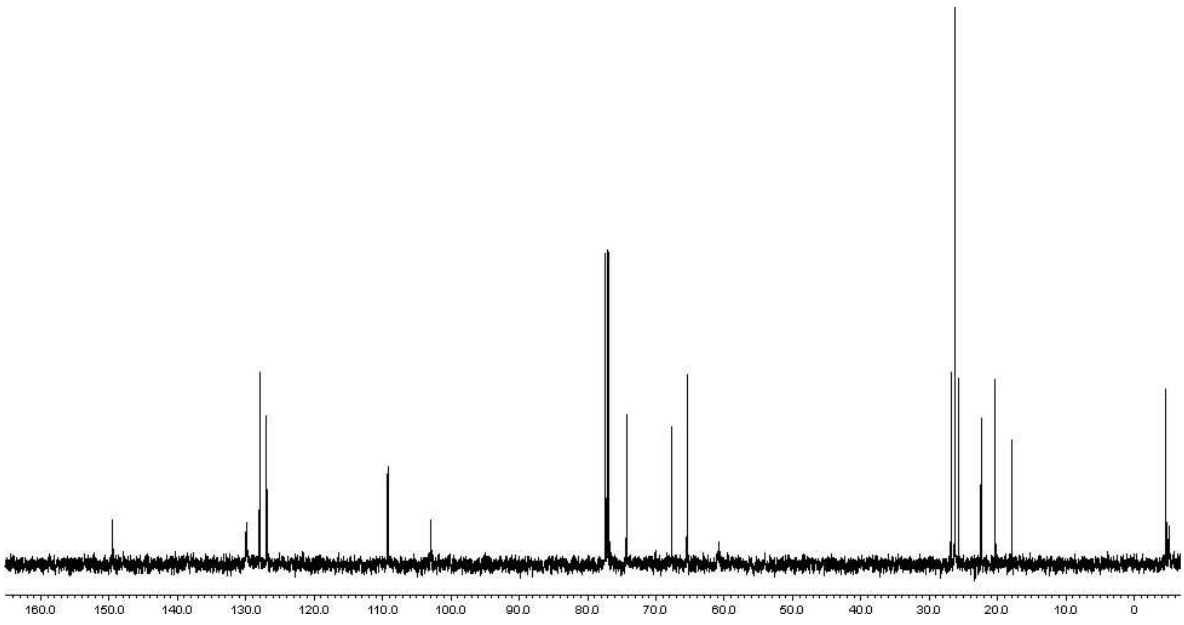


500 MHz, $CDCl_3$:

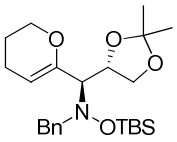


syn-**26**

126 MHz, $CDCl_3$:

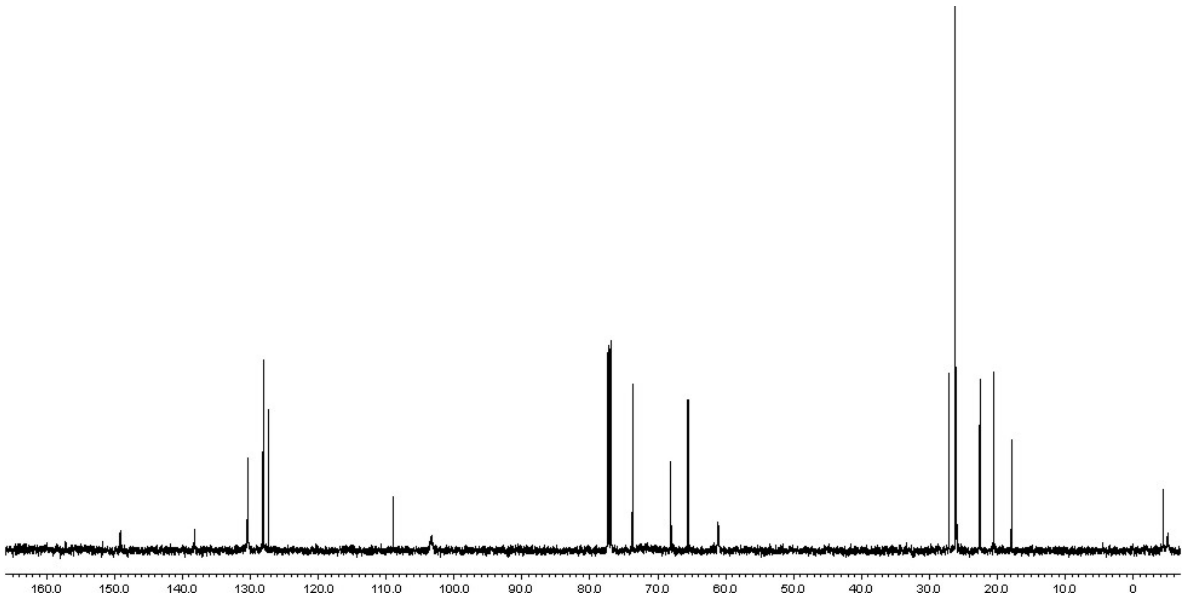


500 MHz, $CDCl_3$:

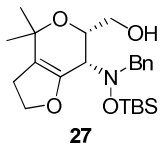


anti-**26**

126 MHz, $CDCl_3$:

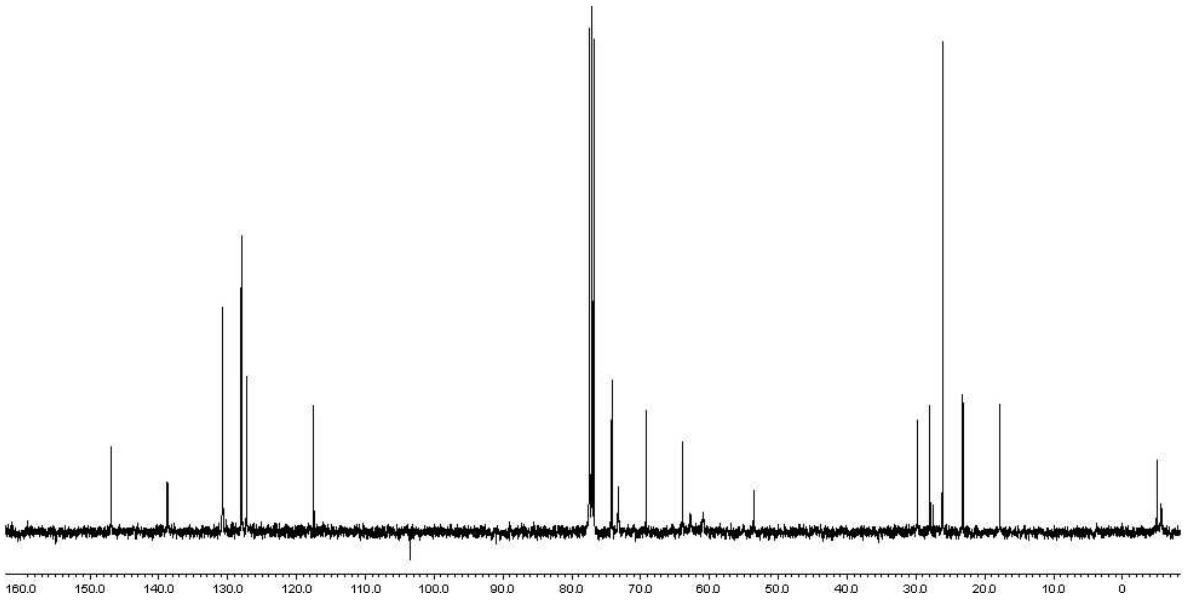


500 MHz, $CDCl_3$:

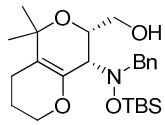


27

101 MHz, $CDCl_3$:

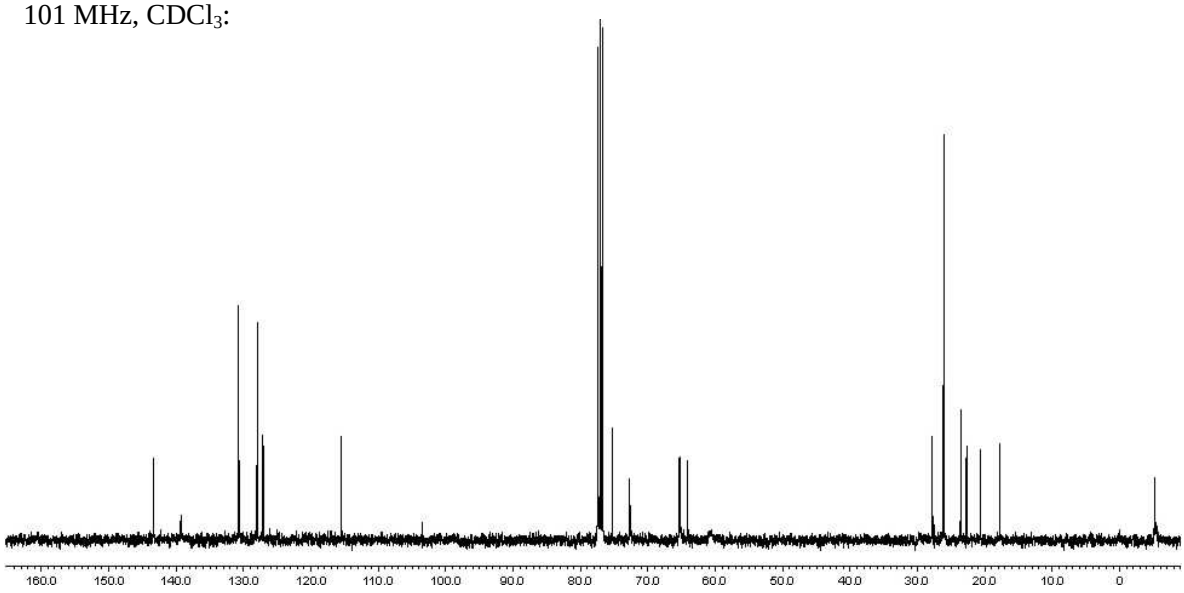


500 MHz, $CDCl_3$:

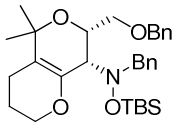


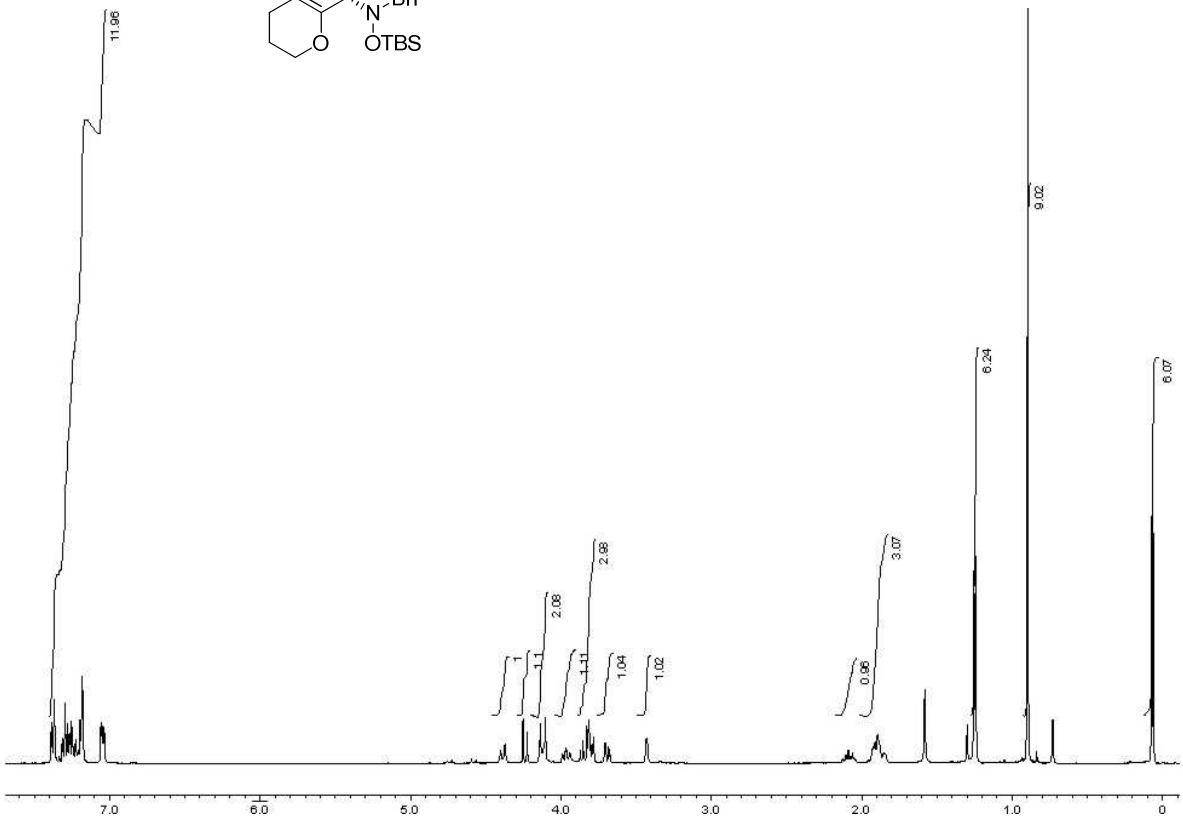
28

101 MHz, $CDCl_3$:

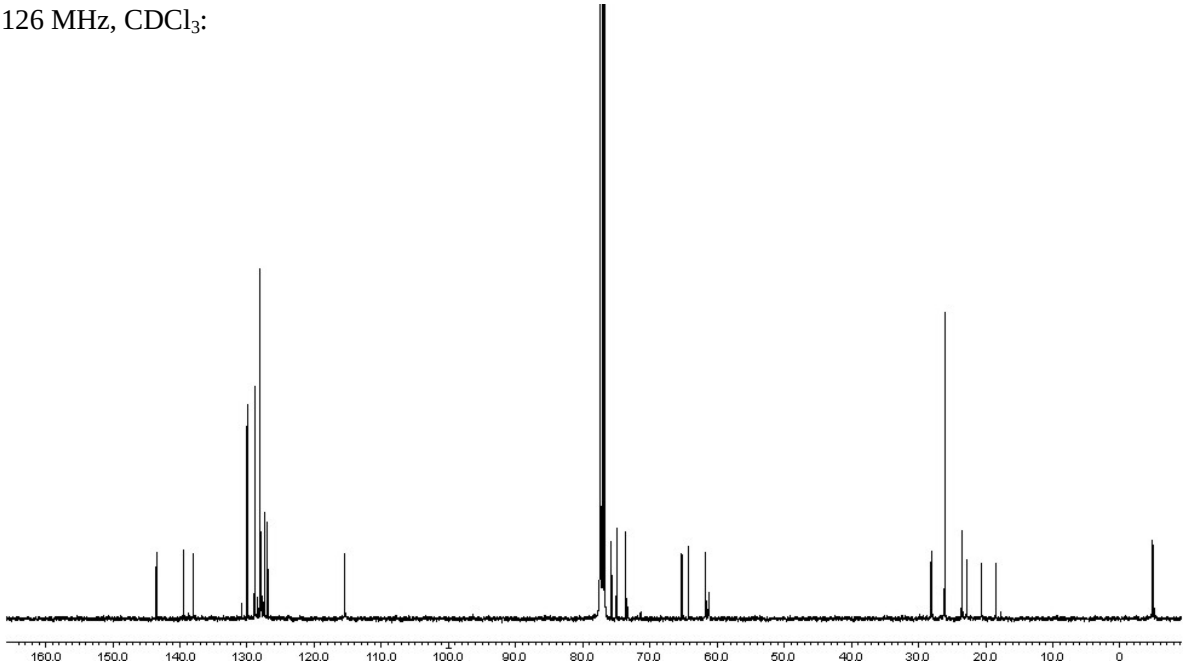


500 MHz, $CDCl_3$:

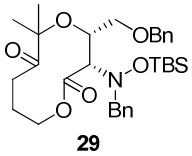




126 MHz, $CDCl_3$:



500 MHz, $CDCl_3$:



29

101 MHz, $CDCl_3$: