# Phenylthiomethyl Glycosides: Convenient Synthons for the Formation of Azidomethyl and Glycosylmethyl Glycosides and Their Derivatives

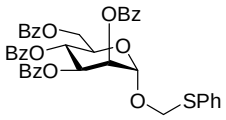
*David Crich*[a,b,*] *and Fan Yang*[a]

Supporting Information

*a) Department of Chemistry, Wayne State University, 5101 Cass Avenue, Detroit, MI 48202, USA, and b) Centre de Recherche de Gif, Institut de Chimie des Substances Naturelles, Centre National de la Recherche Scientifique, Avenue de la Terrasse, Gif-sur-Yvette, France*

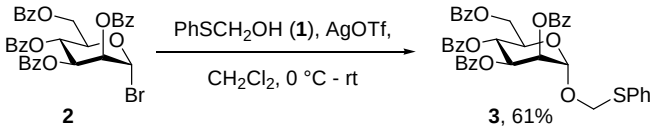
**Table of Contents**

**General Methods.** All reagents were purchased from commercial sources and used as received, unless otherwise indicated. All reactions were conducted under an atmosphere of dry nitrogen. Organic extracts were dried over sodium sulfate and concentrated under aspirator vacuum at room temperature. Experiments conducted using microwave irradiation were carried out with a Biotage Initiator Exp US operating at a high absorbance level and with temperature determination by means of an infrared sensor.



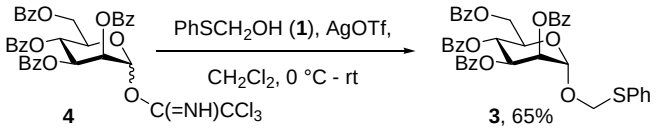

**Phenylthiomethyl 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranoside (3).**

Method A:

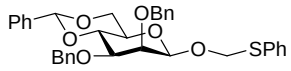



2,3,4,6-Tetra-*O*-benzoyl-α-D-mannopyranosyl bromide[2] (2.24 g, 3.41 mmol), phenythiomethanol[3] (1.91 g, 13.6 mmol) and activated 4Å powdered molecular sieves (900 mg) were mixed in dichloromethane (17 mL) and stirred at room temperature for 10 min before AgOTf (964 mg, 3.75 mmol) was added at 0 ºC. The reaction mixture was allowed to warm to room temperature, and was stirred for 2-4 h. When TLC showed the donor had been consummed, saturated aqueous $NaHCO_3$ was added at 0 ºC, and the reaction mixture was filtered, and the filtrate was washed with brine. The organic layer was dried and concentrated under reduced pressure and the product was isolated by silica gel column chromatography (eluent: hexane/ethyl acetate from 20/1 to 10/1) to give **3** (1.58 g, 61%) as a white foam.

Method B:

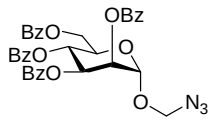



2,3,4,6-Tetra-*O*-benzoyl-α-D-mannopyranosyl trichloroacetimidate[4] (1 g, 1.35 mmol), phenythiomethanol[3] (378 mg, 2.7 mmol) and activated 4Å powdered molecular sieves (900 mg) were mixed in dichloromethane (10 mL) and stirred at room temperature for 10 min before AgOTf (28 mg, 0.11 mmol) was added at 0 ºC. The reaction mixture was allowed to warm to room temperature, and stirred for 1 h. When TLC showed the donor had been consummed, saturated aqueous $NaHCO_3$ was added at 0 ºC, and the reaction mixture was filtered, and the filtrate was washed with brine. The organic layer was dried and concentrated under reduced pressure and the glycosides were isolated by silica gel column chromatography (eluent: hexane/ethyl acetate from 20/1 to 10/1) to give **3** (633 mg, 65%) as a white foam. $[\alpha]_D^{23}$ +42.0 $^{o}$ (*c*, 2.6, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) δ: 8.15-8.13 (m, 2H), 8.11-8.10 (m, 2H), 7.99-7.97 (m, 2H), 7.88-7.86 (m, 2H), 7.64-7.59 (m, 4H), 7.54-7.51 (m, 1H), 7.47-7.43 (m, 5H), 7.41-7.37 (m, 4H), 7.34-7.29 (m, 3H), 6.17 (t, *J* = 10.0 Hz, 1H), 5.96 (dd, *J* = 3.5, *J* = 10.5 Hz, 1H), 5.75 (m, 1H), 5.62 (d, *J* = 1.5 Hz, 1H), 5.27 (d, *J* = 12.0 Hz, 1H), 5.18 (d, *J* = 12.0 Hz, 1H), 4.72 (dd, *J* = 2.5, *J* = 12.5 Hz, 1H), 4.50 (dd, *J* = 4.5, *J* = 12.0 Hz, 1H), 4.41 (m, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 166.4, 165.74, 165.68, 165.6, 134.8, 133.81, 133.75, 133.5, 133.4, 131.3, 130.2, 130.1, 130.0, 129.5, 129.3, 129.2, 128.9, 128.8, 128.7, 128.6, 127.8, 94.9, 72.6, 70.6, 70.2, 69.9, 67.1, 63.0; ESIHRMS Calcd. for $C_{41}H_{34}O_{10}S$ $[M+Na]^+$ 741.1770, found 741.1738.

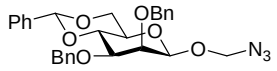



**Phenylthiomethyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-mannopyranoside (6).**

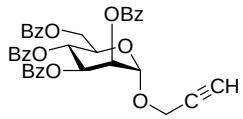
To a stirred mixture of ethyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-1-thio-α-D-mannopyranoside[5] (161 mg, 0.3 mmol), TTBP (81 mg, 0.6 mmol), BSP (68 mg, 0.3 mmol), and activated 5Å powdered molecular sieves in dichloromethane (4 mL) was added $Tf_2O$ (55 μL, 0.3 mmol) at 60 ºC under $N_2$. After 30 min, **1** was slowly added. The reaction mixture was stirred at – 78 ºC for 1 h and then was quenched by the addition of triethyl phosphate (59 μL, 0.3 mmol) and stirred for a further 1 h at – 78 ºC before it was allowed to reach room temperature. The reaction mixture was diluted with dichloromethane and the molecular sieves were filtered off and washed with saturated $NaHCO_3$. The organic layer was separated, dried, and concentrated. The crude product was purified by silica gel column chromatography (eluent: hexane/ethyl acetate, 17/1) to give **6** (75 mg, 40%, β only) as a syrup. $[\alpha]_D^{24}$ –180.7 $^{o}$ (*c*, 1.1, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) δ: 7.52-7.50 (m, 2H), 7.44-7.37 (m, 7H), 7.34-7.26 (m, 11H), 5.63 (s, 1H), 5.33 (d, *J* = 12.0 Hz, 1H), 5.22 (d, *J* = 12.0 Hz, 1H), 4.96-4.93 (m, 2H), 4.85 (d, *J* = 12.5 Hz, 1H), 4.69 (d, *J* = 12.5 Hz, 1H), 4.58 (d, *J* = 12.5 Hz, 1H), 4.27 (dd, *J* = 4.5, *J* = 10.0 Hz, 1H), 4.22 (t, *J* = 10.0 Hz, 1H), 3.94-3.90 (m, 2H), 3.63 (dd, *J* = 3.0, *J* = 10.0 Hz, 1H), 3.28 (dt, *J* = 5.0, *J* = 10.0 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 138.5, 138.4, 137.7, 135.6, 129.8, 129.3, 129.1, 128.9, 128.6, 128.44, 128.40, 127.9, 127.81, 127.77, 127.1, 126.3, 101.7 ($^1J_{C\text{-}H}$, 163.9 Hz), 97.4, 78.8, 78.3, 75.8, 75.0, 72.8, 72.6, 68.7, 67.9; ESIHRMS Calcd. for $C_{34}H_{34}O_6S$ $[M+Na]^+$ 593.1974, found 593.1967.




**Azidomethyl 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranoside (7).** Phenylthiomethyl 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranoside (299 mg, 0.4 mmol), $TMSN_3$ (175 μL, 1.2 mmol) and activated acid washed 3Å powdered molecular sieves (300 mg) were mixed in dichloromethane (4 mL) and stirred at room temperature for 10 min before NIS (198 mg, 0.8 mmol) was added, followed by TfOH (38 μL, 0.4 mmol) at 0 ºC. The reaction mixture was stirred at 0 ºC for 1 h. When TLC showed the donor had been consummed, saturated aqueous $NaHCO_3$ was added at 0 ºC, and the reaction mixture was filtered, and the filtrate was washed with $NaS_2O_3$ and brine. The organic layer was dried and concentrated under reduced pressure and the product was isolated by silica gel column chromatography (eluent: hexane/ethyl acetate from 10/1 to 8/1) to give **7** (233 mg, 86%) as a white foam. $[\alpha]_D^{23}$ –13.8 $^{o}$ (*c*, 2.1, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) δ: 8.13-8.11 (m, 2H), 8.09-8.07 (m, 2H), 7.99-7.97 (m, 2H), 7.88-7.86 (m, 2H), 7.64-7.58 (m, 2H), 7.54-7.51 (m, 1H), 7.47-7.37 (m, 7H), 7.31-7.27 (m, 1H), 6.19 (t, *J* = 10.0 Hz, 1H), 5.95 (dd, *J* = 3.0, *J* = 10.0 Hz, 1H), 5.78 (m, 1H), 5.42 (d, *J* = 2.0 Hz, 1H), 4.99 (d, *J* = 9.0 Hz, 1H), 4.90 (d, *J* = 9.0 Hz, 1H), 4.75 (m, 1H), 4.53 (m, 2H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 166.4, 165.74, 165.66, 165.57, 133.9, 133.8, 133.5, 133.4, 130.13, 130.07, 130.01, 129.98, 129.4, 129.2, 129.1, 128.9, 128.7, 128.6, 96.4, 80.0, 70.4, 70.1, 70.0, 66.8, 62.9; IR: 2135.9, 2102.9, 1728.3; ESIHRMS Calcd. for $C_{35}H_{29}N_3O_{10}$ $[M+Na]^+$ 674.1751, found 674.1742.

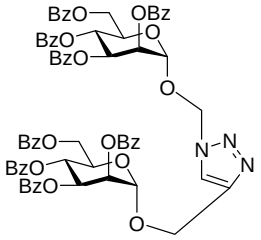



**Azidomethyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-mannopyranoside (8).** White foam, eluted from silica gel with hexane/ethyl acetate (10:1) in 66% yield. $[\alpha]_D^{23}$ –138.9 $^o$ (*c*, 1.1, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) δ: 7.52-7.47 (m, 4H), 7.41-7.29 (m, 11H), 5.64 (s, 1H), 5.00 (d, *J* = 9.0 Hz, 1H), 4.97 (s, 1H), 4.90 (d, *J* = 12.5 Hz, 1H), 4.77-4.72 (m, 3H), 4.63 (d, *J* = 12.5 Hz, 1H), 4.33 (m, 1H), 4.24 (t, *J* = 10.0 Hz, 1H), 3.99 (d, *J* = 3.0 Hz, 1H), 3.95 (t, *J* = 10.0 Hz, 1H), 3.66 (dd, *J* = 3.0, *J* = 10.0 Hz, 1H), 3.39 (dt, *J* = 4.5, *J* = 9.5 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 138.4, 138.3, 137.7, 129.2, 128.8, 128.6, 128.5, 127.95, 127.90, 127.8, 126.3, 101.7, 98.9, 80.0, 78.7, 78.1, 76.0, 75.3, 72.8, 68.6, 68.1; IR: 2869.9, 2104.5; ESIHRMS Calcd. for $C_{28}H_{29}N_3O_6$ $[M+Na]^+$ 526.1954, found 526.1931.



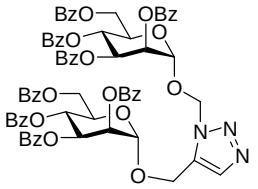

**2-Propynyl 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranoside (9).** 2,3,4,6-Tetra-*O*-benzoyl-α-D-mannopyranosyl bromide (3.3 g, 5.0 mmol), propargyl alcohol (5.89 mL, 100 mmol) and activated 4Å powdered molecular sieves (1.5 g) were mixed in dichloromethane (10 mL) and stirred at room temperature for 10 min before AgOTf (1.93 g, 7.5 mmol) was added at 0 ºC. The reaction mixture was allowed to warm to room temperature, and stirred for 4 h. When TLC showed the donor had been consummed, saturated aqueous $NaHCO_3$ was added at 0 ºC, and the reaction mixture was filtered, and the filtrate was washed with brine. The organic layer was dried and

concentrated under reduced pressure and the product was isolated by silica gel column chromatography (eluent: hexane/ethyl acetate from 15/1 to 6/1) to give **9** (2.43 g, 77%) as white foam. $[\alpha]_D^{22}$ –40.0 $^{o}$ (*c*, 1.1, $CHCl_3$); $^{1}H$ NMR (500 MHz, $CDCl_3$) δ: 8.13-8.11 (m, 2H), 8.09-8.07 (m, 2H), 7.98-7.96 (m, 2H), 7.86-7.84 (m, 2H), 7.63-7.58 (m, 2H), 7.54-7.50 (m, 1H), 7.46-7.37 (m, 7H), 7.36-7.26 (m, 1H), 6.16 (t, *J* = 10.0 Hz, 1H), 5.94 (dd, *J* = 3.5, *J* = 10.5 Hz, 1H), 5.75 (m, 1H), 5.33 (d, *J* = 2.0 Hz, 1H), 4.73 (m, 1H), 4.50 (m, 2H), 4.44 (d, *J* = 2.5 Hz, 2H), 2.53 (t, *J* = 2.5 Hz, 1H); $^{13}C$ NMR (125 MHz, $CDCl_3$) δ: 166.4, 165.7, 165.6, 133.8, 133.7, 133.4, 133.3, 130.0, 129.5, 129.3, 129.2, 128.9, 128.8, 128.7, 128.5, 96.8, 78.3, 75.9, 70.5, 70.1, 69.6, 67.0, 63.0, 55.6; ESIHRMS Calcd. for $C_{37}H_{30}O_{10}$ $[M+Na]^+$ 657.1737, found 657.1756.



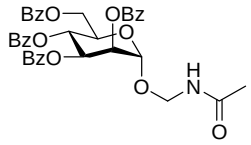

**1-(2',3',4',6',-Tetra-*O*-benzoyl-α-D-mannopyranosyloxymethyl)-4-(2'',3'',4'',6''-tetra-*O*-benzoyl-α-D-mannopyranosyloxymethyl)-1*H*-[1,2,3]-triazole (10).** The azide **7** (109 mg, 0.17 mmol) and alkyne **9** (107 mg, 0.17 mmol) were suspended in a 1:1 mixture of $H_2O$ (0.34 mL) and $^{t}$BuOH (0.34 mL). (+)-Sodium L-ascorbate (3.3 mg, 0.016 mmol, 1M solution in $H_2O$) was added, followed by $CuSO_4 \cdot 5H_2O$ (0.4 mg, 0.0016mmol). The heterogeneous mixture was stirred vigorously overnight, then heated to 50 ºC for few hours at which point it cleared and TLC analysis indicated complete consumption of the reactants. The reaction mixture was diluted with water, cooled in ice and the white

precipitate was collected by filtration. The 1,4-disubstituted product was isolated by silica gel column chromatography (eluent: hexane/ethyl acetate from 5/1 to 1.5/1) to give **10** (196 mg, 92%) as a white foam. $[\alpha]_D^{24}$ –25.8 $^{o}$ (*c*, 1.0, $CHCl_3$); $^{1}H$ NMR (500 MHz, $CDCl_3$) δ: 8.13-8.10 (m, 4H), 8.05-8.00 (m, 5H), 7.97-7.95 (m, 4H), 7.97-7.95 (m, 4H), 7.84-7.80 (m, 2H), 7.79-7.78 (m, 2H), 7.60-7.54 (m, 4H), 7.50-7.46 (m, 2H), 7.44-7.33 (m, 15H), 7.29-7.23 (m, 3H), 6.20 (d, *J* = 8.5 Hz, 1H), 6.17 (m, 1H), 6.14 (d, *J* = 7.0 Hz, 1H), 5.93 (m, 2H), 5.90 (dd, *J* = 3.0, *J* = 10.0 Hz, 1H), 5.76 (m, 1H), 5.72 (m, 1H), 5.40 (d, *J* = 2.0 Hz, 1H), 5.30 (d, *J* = 1.5 Hz, 1H), 5.09 (d, *J* = 12.5 Hz, 1H), 4.91 (d, *J* = 12.5 Hz, 1H), 4.72 (m, 1H), 4.70 (m, 1H), 4.56 (m, 1H), 4.50 (dd, *J* = 4.0, *J* = 12.5 Hz, 1H), 4.45 (dd, *J* = 4.0, *J* = 12.5 Hz, 1H), 4.34 (m, 1H); $^{13}C$ NMR (125 MHz, $CDCl_3$) δ: 166.4, 166.3, 165.71, 165.67, 165.64, 165.59, 165.4, 145.1, 133.8, 133.74, 133.69, 133.6, 133.5, 133.4, 133.3, 130.1, 130.0, 129.5, 129.3, 129.2, 129.1, 129.0, 128.84, 128.81, 128.72, 128.66, 128.6, 128.5, 124.2, 97.7, 97.1, 75.5, 70.6, 70.2, 70.0, 69.9, 69.4, 67.0, 66.6, 62.9, 62.4, 61.8; ESIHRMS Calcd. for $C_{73}H_{59}N_3O_{20}$ $[M+Na]^+$ 1308.3590, found 1308.3563.




**1-(2',3',4',6'-Tetra-*O*-benzoyl-α-D-mannopyranosyloxymethyl)-5-(2'',3'',4'',6''-tetra-*O*-benzoyl-α-D-mannopyranosyloxymethyl)-1*H*-[1,2,3]-triazole (11).** To a solution of azide **6** (166 mg, 0.25 mmol) and alkyne **9** (170 mg, 0.27 mmol) in anhydrous DMF (1.5 mL) was added $[Cp^*RuCl]_4$. The vial was purged with nitrogen, sealed and irradiated to 110 ºC by microwave for 20 min. When TLC showed the azide **7** had been

consumed, the mixture was concentrated under reduced pressure. The 1,5-disubstitued product was isolated by silica gel column chromatography (eluent: hexane/ethyl acetate from 5/1 to 1.5/1) to give **11** (240 mg, 75%) as a white foam. $[\alpha]_D^{23}$ –19.7 $^{o}$ (*c*, 1.0, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) δ: 8.13 (m, 4H), 8.00-7.94 (m, 8H), 7.80 (m, 2H), 7.79 (s, 1H), 7.71 (m, 2H), 7.60-7.55 (m, 4H), 7.48 (m, 1H), 7.45-7.29 (m, 14H), 7.23-7.18 (m, 4H), 6.25 (d, *J* = 11.0 Hz, 1H), 6.19 (t, *J* = 10.0 Hz, 1H), 6.13 (d, *J* = 11.0 Hz, 1H), 5.92 (m, 2H), 5.77 (m, 1H), 5.71 (m, 1H), 5.40 (d, *J* = 2.0 Hz, 1H), 5.23 (d, *J* = 1.5 Hz, 1H), 5.17 (d, *J* = 13.5 Hz, 1H), 5.04 (d, *J* = 13.5 Hz, 1H), 4.79-4.72 (m, 2H), 4.59 (dd, *J* = 4.0, *J* = 12.0 Hz, 1H), 4.52-4.47 (m, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 166.3, 165.8, 165.7, 165.63, 165.59, 165.5, 165.4, 135.5, 133.8, 133.7, 133.5, 133.4, 133.3, 133.0, 130.11, 130.06, 129.98, 129.95, 128.8, 128.75, 128.66, 128.5, 128.45, 97.0, 96.4, 73.8, 70.3, 70.2, 70.1, 70.02, 69.91, 66.8, 66.5, 62.9, 62.6, 57.6; ESIHRMS Calcd. for $C_{73}H_{59}N_3O_{20}$ $[M+Na]^+$ 1308.3590, found 1308.3541.

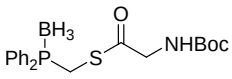



**Acetamidomethyl 2',3',4',6'-tetra-*O*-benzoyl-α-D-mannopyranoside (12).** To a stirred solution of azide **7** (101 mg, 0.16 mmol) in $CHCl_3$ (0.55 mL) was added 2,6-lutidine (27 μL, 0.23 mmol) followed by thiolacetic acid (15 μL, 0.2 mmol). The vial was purged with nitrogen, sealed and heated to 60 ºC by microwave for 14 h. The mixture was concentrated under reduced pressure and the product was isolated by silica gel column chromatography (eluent: hexane/ethyl acetate from 10/1 to 1.5/1) to give **12** (52 mg, 51%) as a white foam. $[\alpha]_D^{23}$ –46.8 $^{o}$ (*c*, 1.1, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) δ: 8.11-8.10

(m, 2H), 8.06-8.04 (m, 2H), 7.97-7.95 (m, 2H), 7.85-7.83 (m, 2H), 7.62-7.56 (m, 2H), 7.51 (m, 1H), 7.50-7.35 (m, 7H), 7.29-7.26 (m, 2H), 6.50 (t, *J* = 7.0 Hz, 1H), 6.14 (t, *J* = 10.0 Hz, 1H), 5.90 (dd, *J* = 3.0, *J* = 10.0 Hz, 1H), 5.69 (m, 1H), 5.30 (d, *J* = 2.0 Hz, 1H), 5.00 (d, *J* = 7.0 Hz, 1H), 4.73 (dd, *J* = 2.5, *J* = 11.5 Hz, 1H), 4.57-4.51 (m, 2H), 2.09 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 171.0, 166.5, 165.8, 165.7, 165.6, 133.8, 133.7, 133.5, 133.3, 130.10, 130.07, 129.99, 129.5, 129.3, 129.2, 128.8, 128.71, 128.68, 128.5, 96.3, 70.6, 70.2, 69.4, 68.2, 67.1, 63.2, 23.6; ESIHRMS Calcd. for $C_{37}H_{33}NO_{11}$ $[M+Na]^+$ 690.1951, found 690.1919.

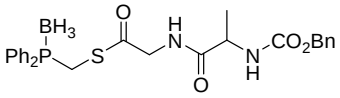
**General Procedure for the Synthesis of Thioesters.**

Diphenylphosphino(borane)methanethiyl acetate[7] (144 mg, 0.5 mmol) was dissolved in methanol (2.5 mL), followed by addition of sodium methoxide (25% w.t., 148 μL, 0.65 mmol). After stirring under nitrogen for 10 min, the solution was neutralized by Amberlyst® 15. The filtrate was concentrated under reduced pressure. The crude product was dissolved in dichloromethane (2 mL), followed by addition of the amino acid (0.5 mmol), 1,3-dicyclohexylcarbodiimide (116 mg, 0.55 mmol), and *N*,*N*'-dimethyl-4-aminopyridine (6 mg, 0.05 mmol). The solution was stirred under nitrogen for 4 h, and the solution was filtered through a pad of Celite. The solvent was removed under reduced pressure. The crude product was purified by flash chromatography on silica gel to give the thioester.




**Diphenylphosphino(borane)methanethiyl *N*-(*tert*-butoxycarbonyl)glycinate.** White foam, eluted from silica gel with hexane/ethyl acetate (10:1) in 88% yield. $^1$H NMR (500

MHz, $CDCl_3$) δ: 7.72-7.68 (m, 4H), 7.55-7.51 (m, 2H), 7.48-7.45 (m, 4H), 5.02 (br s, 1H), 3.9 (d, *J* = 6.0 Hz, 2H), 3.71 (d, *J* = 7.0 Hz, 2H), 1.44 (s, 9H), 1.31-0.85 (m, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$) δ: 196.9, 155.6, 132.8, 132.7, 132.1, 132.0, 129.2, 129.1, 128.0, 127.5, 80.9, 50.3, 28.5, 23.6, 23.3; $^{31}P$ NMR ($CDCl_3$) δ:19.9; ESIHRMS Calcd. for $C_{20}H_{27}NO_3PS$ $[M+Na]^+$ 426.1440, found 426.1443.

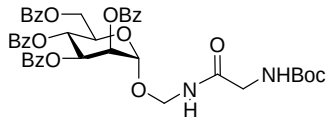



**Diphenylphosphino(borane)methanethiyl *N*-(benzyloxycarbonyl)-L-alanyl-glycinate.** White foam, eluted from silica gel with hexane/ethyl acetate (2:1) in 94% yield. $^1H$ NMR (500 MHz, $CDCl_3$) δ: 7.69-7.66 (m, 4H), 7.53-7.50 (m, 2H), 7.46-7.43 (m, 4H), 7.36-7.27 (m, 5H), 7.07 (br s, 1H), 5.51 (d, *J* = 7.5 Hz, 1H), 5.08 (m, 2H), 4.30 (br s, 1H), 4.08-3.97 (m, 2H), 1.36 (d, *J* = 7.0Hz, 3H), 1.26-0.88 (m, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$) δ: 195.4 (d, *J* = 2.8Hz), 173.1, 156.4, 136.3, 132.7, 132.6, 132.13, 132.12, 129.3, 129.2, 128.8, 128.5, 128.3, 127.9, 127.4, 67.4, 50.6, 49.0, 23.5 (d, *J* = 35.1Hz), 18.4; $^{31}P$ NMR ($CDCl_3$) δ: 19.9; ESIHRMS Calcd. for $C_{26}H_{30}BN_2O_4PS$ $[M+Na]^+$ 531.1655, found 531.1643.

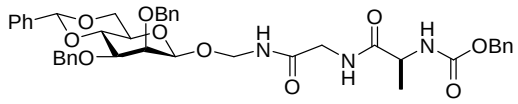
**General Procedure for Staudinger Ligation.**

Glycosyl azide (68 mg, 0.1 mmol) and the diphenylphosphino(borane)thioester (84 mg, 0.2 mmol) were dissolved in DMF (0.8 mL) and degassed by ultrasonic for 20 min. A solution of 1,4-diazabicyclo[2.2.2]octane in DMF (0.2 mL) was transferred via cannula under nitrogen to the above solution. The mixture was stirred under nitrogen at 50 ºC for 12 h, before water (200 μL) was added. The solution was stirred for addition 30 min, and

the solvent was removed under high vacuum. The crude product was purified by flash chromatography.




***N*-[(2,3,4,6-Tetra-*O*-benzoyl-α-D-mannopyranosyl)oxymethyl] $N_\alpha$-(*tert*-butoxycarbonyl)glycinamide (13).** White foam, eluted from silica gel with hexane/ethyl acetate (10:1) in 89% yield. $[\alpha]_D^{24}$ –46.4 $^o$ (*c*, 1.6, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) δ: 8.09 (m, 2H), 8.03 (m, 2H), 7.95 (m, 2H), 7.84 (m, 2H), 7.58 (m, 2H), 7.50 (m, 1H), 7.44 (m, 1H), 7.40-7.34 (m, 6H), 7.29-7.26 (m, 2H), 6.14 (t, *J* = 10.0 Hz, 1H), 5.88 (dd, *J* = 3.5, *J* = 10.5 Hz, 1H), 5.67 (m, 1H), 5.40 (br s, 1H), 5.30 (d, *J* = 1.5 Hz, 1H), 5.05 (m, 2H), 4.73 (m, 1H), 4.53 (m, 2H), 3.93 (d, *J* = 10.5 Hz, 2H), 1.46 (s, 9H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 170.8, 166.5, 165.8, 165.7, 165.6, 133.74, 133.67, 133.4, 133.3, 96.5, 80.8, 70.6, 70.2, 69.4, 68.2, 67.2, 63.2, 44.8, 28.5; ESIHRMS Calcd. for $C_{42}H_{42}N_2O_{13}$ $[M+Na]^+$ 805.2585, found 805.2595.

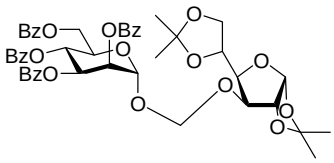



***N*-[(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-mannopyranosyl)oxymethyl] $N_\alpha$-(benzyloxycarbonyl)-L-alanyl-glycinamide (14).** White foam, eluted from silica gel with hexane/ethyl acetate (1:1) in 80% yield. $[\alpha]_D^{24}$ –27.4 $^o$ (*c*, 0.8, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) δ: 7.77 (m, 1H), 7.50-7.48 (m, 2H), 7.45-7.38 (m, 2H), 7.38-7.28 (m, 15H), 6.83 (br s, 1H), 5.60 (s, 1H), 5.37 (br s, 1H), 5.14-5.05 (m, 3H), 5.00 (d, *J* = 9.0 Hz, 1H), 4.91 (m, 1H), 4.84 (d, *J* = 11.5 Hz, 2H), 4.71-4.68 (m, 2H), 4.59 (d, *J* = 12.5 Hz,

1H), 4.29 (m, 1H), 4.19-4.15 (m, 2H), 3.94-3.87 (m, 4H), 3.63 (d, *J* = 9.5 Hz, 1H), 3.36 (m, 1H), 1.40 (d, *J* = 6.5 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 173.2, 138.6, 137.8, 129.1, 128.9, 128.7, 128.5, 128.41, 128.36, 127.8, 126.3, 101.7, 100.3, 78.8, 78.2, 76.6, 75.3, 72.6, 68.7, 67.9, 67.6, 51.4, 43.5, 18.2; ESIHRMS Calcd. for $C_{41}H_{45}N_3O_{10}$ $[M+Na]^+$ 762.3003, found 762.2969.

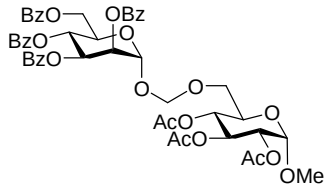
**General Procedure for Coupling Reaction.**

A mixture of azidomethyl glycoside, acceptor (1.5 eq.) and activated acid washed 3Å powdered molecular sieves were stirred in dichloromethane (10 mL per mmol of donor) and stirred at room temperature for 10 min before NIS (2 eq.) was added, followed by catalytic TfOH (0.1 eq.) at – 30 ˚C. The reaction mixture was stirred at – 30 ˚C for 1 h. When TLC showed the donor had been consummed, saturated aqueous $NaHCO_3$ was added at 0 ºC, and the reaction mixture was filtered, and the filtrate was washed with $NaS_2O_3$ and brine. The organic layer was dried and concentrated under reduced pressure and the glycoside was isolated by silica gel column chromatography.



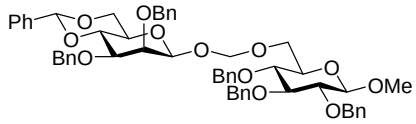

**3-*O*-(2,3,4,6-Tetra-*O*-benzoyl-α-D-mannopyranosyloxymethyl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (15).** White foam, eluted from silica gel with hexane/ethyl acetate (4:1) in 90% yield. $[\alpha]_D^{24}$ -4.3 º (*c*, 1.1, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) δ: 8.10-8.07 (m, 4H), 7.97 (m, 2H), 7.87 (m, 2H), 7.60 (m, 2H), 7.52 (m, 1H), 7.47-7.36 (m, 7H), 7.29 (m, 2H), 6.18 (t, *J* = 10.0 Hz, 1H), 5.99 (dd, *J* = 3.5, *J* = 10.5 Hz, 1H), 5.94 (d, *J* = 3.5 Hz, 1H), 5.64 (m, 1H), 5.51 (d, *J* = 1.5 Hz, 1H), 5.15 (d, *J* = 7.0 Hz,

1H), 5.00 (d, *J* = 7.5 Hz, 1H), 4.81 (d, *J* = 3.5 Hz, 1H), 4.70 (d, *J* = 9.5 Hz, 1H), 4.51-4.45 (m, 2H), 4.34 (d, *J* = 2.5 Hz, 1H), 4.25 (m, 1H), 4.15-4.12 (m, 2H), 4.03 (m, 1H), 1.54 (s, 3H), 1.46 (s, 3H), 1.40 (s, 3H), 1.35 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 166.4, 165.8, 165.71, 165.69, 133.8, 133.7, 133.5, 133.3, 130.1, 130.04, 130.02, 130.00, 129.95, 129.5, 129.25, 129.16, 128.9, 128.70, 128.68, 128.6, 112.4, 109.5, 105.6, 93.5, 91.9, 84.0, 81.9, 81.3, 72.7, 71.0, 69.8, 69.7, 67.9, 67.1, 63.0, 27.2, 27.1, 26.3, 25.6; ESIHRMS Calcd. for $C_{47}H_{48}O_{16}$ $[M+Na]^+$ 891.2840, found 891.2796.

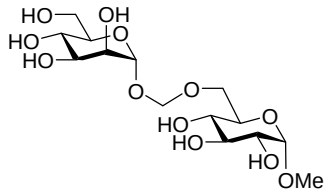



**Methyl 6-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyloxymethyl)-2,3,4-tri-*O*-acetyl-α-D-glucopyranoside (16).** Syrup, eluted from silica gel with hexane/ethyl acetate (2:1) in 88% yield. $[\alpha]_D^{25}$ +34.9 $^o$ (*c*, 1.0, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) δ: 8.10 (m, 2H), 8.05 (m, 2H), 7.95 (m, 2H), 7.84 (m, 2H), 7.60 (m, 2H), 7.51 (m, 1H), 7.46-7.35 (m, 7H), 7.29-7.26 (m, 2H), 6.10 (t, *J* = 10.0 Hz, 1H), 5.91 (dd, *J* = 3.0, *J* = 10.0 Hz, 1H), 5.71 (m, 1H), 5.49 (t, *J* = 10.0 Hz, 1H), 5.44 (d, *J* = 1.5 Hz, 1H), 5.16 (t, *J* = 10.0 Hz, 1H), 5.11 (d, *J* = 7.0 Hz, 1H), 4.97 (d, *J* = 4.0 Hz, 1H), 4.89 (dd, *J* = 3.5, *J* = 10.0 Hz, 1H), 4.84 (d, *J* = 6.5 Hz, 1H), 4.70 (m, 1H), 4.51-4.45 (m, 2H), 3.94 (m, 1H), 3.86 (dd, *J* = 4.0, *J* = 11.0 Hz, 1H), 3.72 (dd, *J* = 2.5, *J* = 11.5 Hz, 1H), 3.41 (s, 3H), 2.07 (s, 3H), 2.02 (s, 3H), 1.98 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 170.4, 170.3, 169.9, 166.4, 165.8, 165.6, 165.5, 133.6, 133.4, 133.3, 130.1, 130.0, 129.98, 129.6, 129.3, 129.2, 128.8, 128.72, 128.67, 128.5, 97.0, 94.2, 91.7, 71.1, 70.5, 70.3, 69.6, 68.9, 68.3, 67.1, 66.9, 63.1,

55.7, 21.0, 20.9, 20.8; ESIHRMS Calcd. for $C_{48}H_{48}O_{19}$ $[M+Na]^+$ 951.2687, found 951.2723.

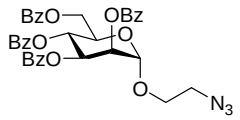


**Methyl 6-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-mannopyranosyloxymethyl)-2,3,4-tri-*O*-benzyl-β-D-glucopyranoside (17).** White foam, eluted from silica gel with hexane/ethyl acetate (10:1) in 80% yield. $[\alpha]_D^{24}$ –41.0 $^o$ (*c,* 1.2, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) δ: 7.50 (m, 4H), 7.41-7.29 (m, 26H), 5.63 (s, 1H), 5.07 (d, *J* = 6.5 Hz, 1H), 5.00-4.88 (m, 4H), 4.88 (d, *J* = 4.5 Hz, 1H), 4.84-4.78 (m, 3H), 4.73-4.70 (m, 2H), 4.62 (m, 2H), 4.32-4.29 (m, 2H), 4.24 (t, *J* = 9.5 Hz, 1H), 3.96 (d, *J* = 3.0 Hz, 1H), 3.93-3.86 (m, 2H), 3.72-3.65 (m, 3H), 3.59 (t, *J* = 9.5 Hz, 1H), 3.49 (s, 3H), 3.42 (m, 2H), 3.38 (m, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 138.8, 138.7, 138.3, 137.8, 129.1, 128.74, 128.69, 128.64, 128.55, 128.44, 128.36, 128.3, 128.19, 128.16, 128.1, 127.94, 127.90, 127.8, 127.7, 126.3, 105.0, 101.7, 97.2, 92.8, 84.8, 82.6, 79.0, 78.7, 77.8, 76.6, 75.9, 75.3, 75.2, 74.6, 72.9, 68.9, 67.8, 67.3, 57.4; ESIHRMS Calcd. for $C_{56}H_{60}O_{12}$ $[M+Na]^+$ 947.3982, found 947.3950.



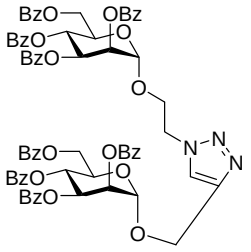
**Methyl 6-*O*-(α-D-mannopyranosyloxymethyl)-α-D-glucopyranoside (18).** The disaccharide (**16**) (30 mg, 0.032 mmol) was dissolved in dichloromethane (0.3 mL) and

methanol (0.7 mL) at 0 ºC, and treated with sodium methoxide (25 wt. % in methanol, 2.9 μL). The reaction mixture was stirred for 4-5 h at room temperature, at which point TLC analysis indicated complete consumption of the reactant. The pH of the solution was adjusted to 7 with Amberlyst® 15. Evaporation of the filtrate followed by flash chromatography on silica gel (eluent: dichloromethane/methanol, 2:1) gave the product **18** (11 mg, 91%) as a white foam. $[\alpha]_D^{24}$ +186.0 $^{o}$ (*c*, 0.9, $CH_3OH$); $^1$H NMR (500 MHz, $CD_3OD$) δ: 5.11 (d, *J* = 1.5 Hz, 1H), 4.99 (d, *J* = 7.0 Hz, 1H), 4.70 (d, *J* = 6.5 Hz, 1H), 4.67 (d, *J* = 4.0 Hz, 1H), 3.87-3.78 (m, 4H), 3.73-3.69 (m, 2H), 3.67-3.61 (m, 3H), 3.59-3.55 (m, 1H), 3.41 (s, 3H), 3.38 (m, 1H), 3.29 (m, 1H); $^{13}$C NMR (125 MHz, $CD_3OD$) δ: 100.1, 96.6, 91.2, 74.0, 72.3, 71.3, 71.05, 70.95, 70.6, 67.40, 67.38, 61.7, 54.5; ESIHRMS Calcd. for $C_{14}H_{26}O_{12}$ $[M+Na]^+$ 409.1322, found 409.1313.



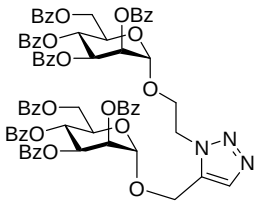

**2-Azidoethyl 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranoside (19).** 2,3,4,6-Tetra-*O*-benzoyl-α-D-mannopyranosyl bromide (1.32 g, 2.0 mmol), 2-azidoethanol[1] (522 mg, 6 mmol) and activated 4Å powdered molecular sieves (600 mg) were mixed in dichloromethane (10 mL) and stirred at room temperature for 10 min before AgOTf (1.03 g, 4 mmol) was added at 0 ºC. The reaction mixture was allowed to warm to room temperature, and stirred for 4 h. When TLC showed the donor had been consummed, saturated aqueous $NaHCO_3$ was added at 0 ºC, and the reaction mixture was filtered, and the filtrate was washed with brine. The organic layer was dried and concentrated under reduced pressure and the product was isolated by silica gel column chromatography

(eluent: hexane/ethyl acetate from 10/1 to 3/1) to give the product (1.2 g, 90%) as a white foam. $[\alpha]_D^{22}$ –61.3 $^{o}$ (*c,* 1.2, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) δ: 8.14-8.12 (m, 2H), 8.08-8.06 (m, 2H), 7.99-7.98 (m, 2H), 7.88-7.85 (m, 2H), 7.63-7.58 (m, 2H), 7.54-7.51 (m, 1H), 7.46-7.37 (m, 7H), 7.30-7.27 (m, 1H), 6.17 (t, *J* = 10.0 Hz, 1H), 5.97 (dd, *J* = 3.5, *J* = 10.5 Hz, 1H), 5.76 (m, 1H), 5.18 (d, *J* = 2.0 Hz, 1H), 4.75 (m, 1H), 4.52 (m, 2H), 4.05 (m, 1H), 3.81 (m, 1H), 3.63 (m, 1H), 3.51 (m, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 166.4, 165.72, 165.78, 165.65, 133.8, 133.7, 133.5, 133.4, 130.1, 130.00, 129.99, 129.5, 129.3, 129.2, 128.9, 128.8, 128.6, 98.0, 70.5, 70.1, 69.5, 67.6, 66.9, 63.0, 50.7; ESIHRMS Calcd. for $C_{36}H_{31}N_3O_{10}$ $[M+Na]^+$ 688.1907, found 688.1937.




**1-(2',3',4',6'-Tetra-*O*-benzoyl-α-D-mannopyranosyloxyethyl)-4-(2'',3'',4'',6''-tetra-*O*-benzoyl-α-D-mannopyranosyloxymethyl)-1*H*-[1,2,3]-triazole (20).** To a solution of alkyne **9** (133 mg, 0.2 mmol) and 2-azidoethyl 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranoside (127 mg, 0.2 mmol) in anhydrous acetonitrile (2 mL) were added CuI (78 mg, 0.4 mmol) and *N*,*N*-diisopropylethylamine (105 μL, 0.6 mmol) at room temperature, and the mixture was stirred for 2h. When TLC showed the azide and alkyne had been consummed, the reaction mixture was diluted using water (5 mL) and saturated aqueous $NH_4Cl$ (2 mL). The aqueous layer was extracted with ethyl acetate, and the combined organic layer was washed brine. The organic layer was dried and concentrated

under reduced pressure and the product was isolated by silica gel column chromatography (eluent: hexane/ethyl acetate from 10/1 to 1/1) to give the product (247 mg, 95%) as a white foam. $[\alpha]_D^{22}$ –52.0 $^{o}$ (*c*, 1.1, $CHCl_3$); $^{1}$H NMR (500 MHz, $CDCl_3$) δ: 8.15-8.14 (m, 2H), 8.11-8.10 (m, 2H), 8.05-8.03 (m, 2H), 8.01-8.00 (m, 3H), 7.97 (d, *J* = 8.5 Hz, 4H), 7.84-7.82 (m, 2H), 7.75-7.73 (m, 2H), 7.60-7.53 (m, 4H), 7.51-7.43 (m, 2H), 7.43-7.32 (m, 14H), 7.22-7.17 (m, 4H), 6.19 (t, *J* = 10.0 Hz, 1H), 6.14 (t, *J* = 10.0 Hz, 1H), 5.94 (dd, *J* = 3.5, *J* = 10.5 Hz, 1H), 5.86 (dd, *J* = 3.5, *J* = 10.5 Hz, 1H), 5.79 (m, 1H), 5.71 (m, 1H), 5.34 (s, 1H), 5.17 (s, 1H), 5.12 (d, *J* = 12.0 Hz, 1H), 4.93 (t, *J* = 12.0 Hz, 1H), 4.84-4.76 (m, 2H), 4.71 (m, 2H), 4.59 (m, 1H), 4.51 (m, 2H), 4.35 (m, 1H), 4.17 (m, 1H), 4.06 (m, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 166.4, 166.3, 165.8, 165.70, 165.68, 165.6, 165.5, 144.4, 133.8, 133.73, 133.65, 133.6, 133.4, 133.3, 130.2, 130.08, 130.05, 130.02, 129.99, 129.96, 129.9, 129.6, 129.34, 129.3, 129.2, 129.1, 128.8, 128.75, 128.72, 128.65, 128.5, 128.4, 124.9, 97.8, 97.6, 70.7, 70.5, 70.4, 70.0, 69.6, 69.3, 67.0, 66.7, 66.6, 62.9, 62.8, 61.9, 50.1; ESIHRMS Calcd. for $C_{73}H_{61}N_3O_{20}$ $[M+Na]^+$ 1322.3746, found 1322.3757.



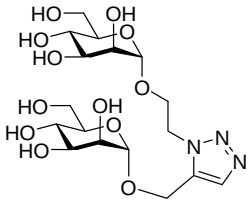

**1-(2',3',4',6'-Tetra-*O*-benzoyl-α-D-mannopyranosyloxyethyl)-5-(2'',3'',4'',6''-tetra-*O*-benzoyl-α-D-mannopyranosyloxymethyl)-1*H*-[1,2,3]-triazole (21).** A solution of azide 2-azidoethyl 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranoside (333 mg, 0.5 mmol) and alkyne **9** (343 mg, 0.54 mmol) in anhydrous DMF (0.6 mL) was added into the

solution of Cp*RuCl($PPh_3$)$_2$[6] in anhydrous DMF (3 mL). The vial was purged with nitrogen, sealed and heated in an oil bath at 100 ºC for 11h. When TLC showed the azide had been consummed, the mixture was concentrated under reduced pressure. The 1,5-disubstitued product was isolated by silica gel column chromatography (eluent: hexane/ethyl acetate from 10/1 to 1/1) to give the product (533 mg, 82%) as a white foam. $[\alpha]_D^{22}$ –39.4$^o$ (*c*, 1.3, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) δ: 8.14-8.12 (m, 2H), 8.03-8.01 (m, 2H), 8.00-7.98 (m, 2H), 7.97-7.95 (m, 2H), 7.92-7.90 (m, 2H), 7.84-7.81 (m, 5H), 7.61-7.52 (m, 4H), 7.47-7.20 (m, 20H), 6.19 (t, *J* = 10.0 Hz, 1H), 6.14 (t, *J* = 10.0 Hz, 1H), 5.94 (dd, *J* = 3.5, *J* = 10.5 Hz, 1H), 5.81 (m, 1H), 5.70 (dd, *J* = 3.5, *J* = 10.5 Hz, 1H), 5.64 (m, 1H), 5.32 (d, *J* = 13.5 Hz, 1H), 5.27 (d, *J* = 2.0 Hz, 1H), 5.13 (m, 2H), 4.96-4.85 (m, 2H), 4.79 (dd, *J* = 2.5, *J* = 12.5 Hz, 1H), 4.70 (dd, *J* = 2.5, *J* = 12.5 Hz, 1H), 4.58 (dd, *J* = 4.5, *J* = 12.5 Hz, 1H), 4.55-4.52 (m, 1H), 4.48 (dd, *J* = 4.0, *J* = 12.5 Hz, 1H), 4.43 (m, 1H), 4.04 (m, 2H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 166.4, 166.3, 165.9, 165.8, 165.7, 165.6, 165.51, 165.46, 134.8, 133.8, 133.7, 133.5, 133.4, 133.3, 130.12, 130.09, 130.03, 130.00, 129.32, 129.29, 129.16, 129.1, 129.0, 128.81, 128.76, 128.74, 128.7, 128.64, 128.56, 97.6, 96.8, 70.3, 70.2, 69.8, 69.6, 66.9, 66.8, 66.3, 63.0, 62.7, 57.6, 48.3; ESIHRMS Calcd. for $C_{73}H_{61}N_3O_{20}$ $[M+Na]^+$ 1322.3746, found 1322.3776.

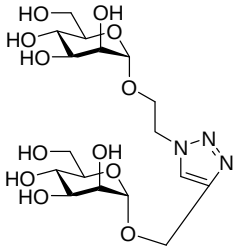
**General Procedure for Deprotection of Benzoylated Adducts.**

The substrate (0.15 mmol) was dissolved in dichloromethane (0.3 mL) and methanol (1.3 mL) at 0 ºC, and treated with sodium methoxide (25 wt. % in methanol, 10.3 μL). The reaction mixture was stirred for 4-5 h at room temperature, at which point TLC analysis indicated complete consumption of the reactant. The pH of the solution was adjusted to 7

with Amberlyst® 15. Evaporation of the filtrate followed by chromatographic purification over silica gel gave the products.

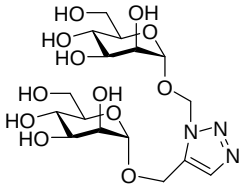


**1-(α-D-Mannopyranosyloxyethyl)-5-(α-D-mannopyranosyloxymethyl)-1*H*-[1,2,3]-triazole (22).** White foam, eluted from silica gel with dichloromethane/methanol (2:1) in 95% yield. $[\alpha]_D^{24}$ +79.1 $^{o}$ (*c*, 1.2, $CH_3OH$); $^{1}H$ NMR (500 MHz, $CH_3OH$) δ: 7.75 (s, 1H), 4.93 (d, *J* = 13.5 Hz, 1H), 4.84 (d, *J* = 1.5 Hz, 1H), 4.77 (d, *J* = 13.0 Hz, 1H), 4.73-4.63 (m, 3H), 4.17 (m, 1H), 3.93-3.87 (m, 2H), 3.84 (m, 1H), 3.78 (dd, *J* = 2.5, *J* = 11.5 Hz, 1H), 3.74-3.70 (m, 2H), 3.68-3.64 (m, 2H), 3.62-3.58 (m, 3H), 3.56-3.51 (m, 1H), 3.22 (m, 1H); $^{13}C$ NMR (125 MHz, $CH_3OH$) δ: 134.9, 133.5, 100.5, 99.9, 74.4, 73.8, 71.3, 71.2, 70.7, 67.3, 67.1, 65.8, 61.8, 61.6, 56.7; ESIHRMS Calcd. for $C_{17}H_{29}N_3O_{12}$ $[M+Na]^+$ 490.1649, found 490.1626.

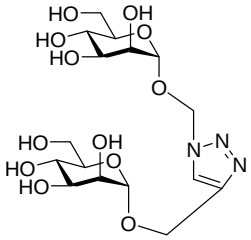


**1-(α-D-Mannopyranosyloxyethyl)-4-(α-D-mannopyranosyloxymethyl)-1*H*-[1,2,3]-triazole (23).** White foam, eluted from silica gel with dichloromethane/methanol (2:1) in 91% yield. $[\alpha]_D^{24}$ +70.4 $^{o}$ (*c*, 1.0, $CH_3OH$); $^{1}H$ NMR (500 MHz, $CH_3OH$) δ: 8.06 (s, 1H), 4.84 (d, *J* = 1.5 Hz, 1H), 4.81 (d, *J* = 12.5 Hz, 1H), 4.73 (d, *J* = 1.5 Hz, 1H), 4.70-4.60

(m, 3H), 4.14 (m, 1H), 3.90-3.88 (m, 1H), 3.87-3.86 (m, 1H), 3.81-3.77 (m, 2H), 3.75-3.73 (m, 2H), 3.70 (m, 1H), 3.68-3.64 (m, 1H), 3.62-3.56 (m, 4H), 3.25 (m, 1H); $^{13}$C NMR (125 MHz, $CH_3OH$) δ: 144.1, 125.0, 100.5, 99.4, 73.9, 73.8, 71.3, 70.8, 70.7, 67.5, 67.2, 65.6, 61.8, 61.6, 59.4, 50.1; ESIHRMS Calcd. for $C_{17}H_{29}N_3O_{12}$ $[M+Na]^+$ 490.1649, found 490.1627.




**1-(α-D-Mannopyranosyloxymethyl)-5-(α-D-mannopyranosyloxymethyl)-1*H*-[1,2,3]-triazole (24).** White foam, eluted from silica gel with dichloromethane/methanol (2:1) in 95% yield. $[\alpha]_D^{23}$ +116.3 $^{o}$ (*c*, 1.0, $CH_3OH$ ); $^1$H NMR (500 MHz, $CH_3OH$) δ: 7.80 (s, 1H), 6.02 (d, *J* = 11.5 Hz, 1H), 5.90 (d, *J* = 11.5 Hz, 1H), 4.97 (d, *J* = 13.0 Hz, 1H), 4.94 (d, *J* = 1.5 Hz, 1H), 4.81 (d, *J* = 13.5 Hz, 1H), 3.87 (dd, *J* = 2.5, *J* = 12.0 Hz, 1H), 3.84 (m, 1H), 3.78 (dd, *J* = 2.0, *J* = 12.0 Hz, 1H), 3.75 (m, 1H), 3.74-3.68 (m, 5H), 3.65 (d, *J* = 9.5 Hz, 1H), 3.62 (d, *J* = 9.5 Hz, 1H), 3.58-3.54 (m, 1H), 3.49-3.46 (m, 1H); $^{13}$C NMR (125 MHz, $CH_3OH$) δ: 135.0, 134.1, 100.1, 98.9, 74.6, 74.2, 73.1, 71.2, 71.0, 70.7, 70.4, 67.3, 66.9, 61.7, 61.4, 56.6; ESIHRMS Calcd. for $C_{16}H_{27}N_3O_{12}$ $[M+Na]^+$ 476.1492, found 476.1475.



**1-(α-D-Mannopyranosyloxymethyl)-4-(α-D-mannopyranosyloxymethyl)-1*H*-[1,2,3]-triazole (25).** White foam, eluted from silica gel with dichloromethane/methanol (2:1) in 92% yield. $[\alpha]_D^{23}$ +103.3 $^{o}$ (*c*, 0.5, $CH_3OH$ ); $^{1}H$ NMR (500 MHz, $CH_3OH$) δ: 8.24 (s, 1H), 5.98 (d, *J* = 11.5 Hz, 1H), 5.83 (d, *J* = 11.0 Hz, 1H), 4.95 (d, *J* = 1.5 Hz, 1H), 4.84 (d, *J* = 12.5 Hz, 1H), 4.68 (d, *J* = 12.5 Hz, 1H), 3.86 (dd, *J* = 1.5, *J* = 11.5 Hz, 1H), 3.81-3.77 (m, 2H), 3.75 (m, 1H), 3.73-3.69 (m, 2H), 3.68-3.63 (m, 4H), 3.60-3.56 (m, 2H), 3.43 (m, 1H); $^{13}C$ NMR (125 MHz, $CH_3OH$) δ: 144.8, 125.0, 99.7, 99.3, 74.7, 74.6, 73.9, 71.3, 71.0, 70.8, 70.5, 67.4, 67.0, 61.8, 61.5, 59.5; ESIHRMS Calcd. for $C_{16}H_{27}N_3O_{12}$ $[M+Na]^+$ 476.1492, found 476.1477.

**Isothermal Titration Microcalorimetry**

Concanavalin A (type IV, lyophilized powder) from *Canavalia ensiformis* (Jack bean) was purchased from Sigma-Aldrich chemical company. The concentration of Con A was determined spectrophotometrically at 280 nm using $E^{1\%}$ = 13.7 at pH 7.2 and expressed in terms of tetramer ($M_r$ = 25,500).

Methyl α-D-mannopyranoside was purchased from Sigma-Aldrich chemical company. All of the sugar solutions were prepared by weight in Hepes buffer.

The buffer was 0.1 M Hepes containing 0.9 M NaCl, 1 nM $Mn^{2+}$, and 1 nM $Ca^{2+}$ at pH 7.2. Water was purified with a Millipore purification system.

A VP-ITC titration calorimeter (MicroCal, Inc.) was used for all measurements. In individual titrations, injections of 4 μL of carbohydrate were added by computer-controlled 250 μL microsyringe at intervals of 4 min into a Con A solution (cell volume = 1.4 mL) in the same buffer as the saccharide, while stirring at 351 rpm.

The raw thermogram data were integrated and normalized, resulting in a plot of $\Delta H$ (kcal/mole of saccharide) versus molar ratio (Fig. 1). In each experiment, a long baseline was collected after binding transition was saturated, which ensured the materials were exactly the same as those that were used to collect the primary data. The terminal 10 points of the upper baseline in each experiment were fit to a straight line, which was subsequently subtracted from the entire data to remove contributions from background heats of mixing and dilution. The experiment data were obtained by fitting the data to a single binding site model using ORIGIN software (MicroCal Inc., ver. 7.0), with $n$ (number of biding sites per monomer), $\Delta H$ (enthalpy change in kcal $mol^{-1}$); $K_a$ (association constant in $M^{-1}$). From the measurement of $K_a$, the free energy of binding, $\Delta G$, and the entropy of binding, $\Delta S$ can be calculated using Eq. 1 and Eq. 2, where $T$ is the absolute temperature , and $R$ = 1.98 $calmol^{-1}K^{-1}$.

$$\Delta G = -RT \ln K_a \qquad (1)$$

$$\Delta G = \Delta H - T\Delta S \qquad (2)$$

The quantity $c = n K_a$ [P] is important in titration microcalorimeter, [P] is the initial concentration of the protein. All experiments were performed with $c$ values $1 < c < 20$.

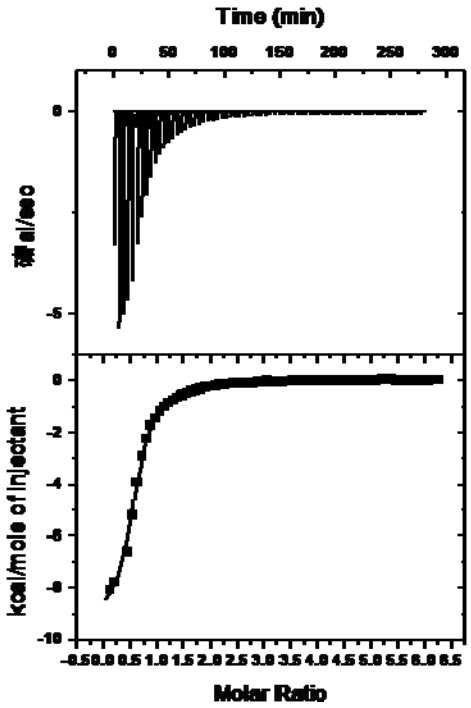



**Fig.1**. Calorimetric titration of Con A (0.2 mM) with **25** (6 mM) at 300 K.

**Table 1**. Thermodynamics of binding for Con A with carbohydrates[a]

| | Carbohydrate | $K_a$ | $n$[b] | $-\Delta G$ | $-\Delta H$ | $-T\Delta S$ |
|---|---|---|---|---|---|---|
| | | $M^{-1} \times 10^3$ | | Kcal $mol^{-1}$ | Kcal $mol^{-1}$ | Kcal $mol^{-1}$ |
| 1 | MeαMan | 15.4 ± 0.5 | 0.75 | 5.7 ± 0.1 | 7.5 ± 0.1 | 1.8 ± 0.2 |
| 2 | **22** | 19.2 ± 0.3 | 0.75 | 5.91 ± 0.3 | 6.81 ± 0.3 | 0.9 ± 0.3 |
| 3 | **23** | 61.0 ± 1.8 | 0.61 | 6.55 ± 0.5 | 9.55 ± 1.3 | 3.0 ± 0.2 |
| 4 | **24** | 13.7 ± 0.07 | 0.72 | 5.65 ± 0.2 | 6.25 ± 0.2 | 0.6 ± 0.2 |
| 5 | **25** | 80.0 ± 0.01 | 0.60 | 6.8 ± 0.1 | 9.4 ± 0.1 | 2.6 ± 0.2 |

a: In 0.1 M Hepes buffer containing 0.9 M NaCl, 1 nm $Mn^{2+}$, and 1 nm $Ca^{2+}$ at *pH* 7.2; $T$ = 300 K, $R$ = 1.98 cal $mol^{-1}$ $K^{-1}$.
b: Errors in $n$ values were 0.01 to 0.1.
c: Data taken from Brewer *et al.*[8] and included here for comparison.

**References**


(1) Lu, X.; Bittman, R. *J. Org. Chem.* **2005**, *70*, 4746-4750.

(2) Dowlut, M.; Hall, D. G.; Hindsgaul, O. *J. Org. Chem.* **2005**, *70*, 9809-9813.

(3) Gundersen, L. L.; Benneche, T. *Acta Chem. Scand.* **1991**, *45*, 975-977.

(4) Bien, F.; Ziegler, T. *Tetrahedron: Asymmetry* **1998**, *9*, 781-790.

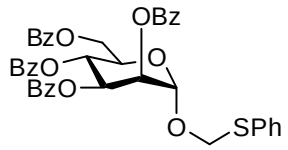
(5) Garegg, P. J.; Kvarnstrom, I.; Niklasson, A.; Niklasson, G.; Svensson, S. C. T. *J. Carbohydr. Chem.* **1993**, *12*, 933-953.

(6) Boren, B. C.; Narayan, S.; Rasmussen, L. K.; Zhang, L.; Zhao, H.; Lin, Z.; Jia, G.; Fokin, V. V. *J. Am. Chem. Soc.* **2008**, *130*, 8923-8930.

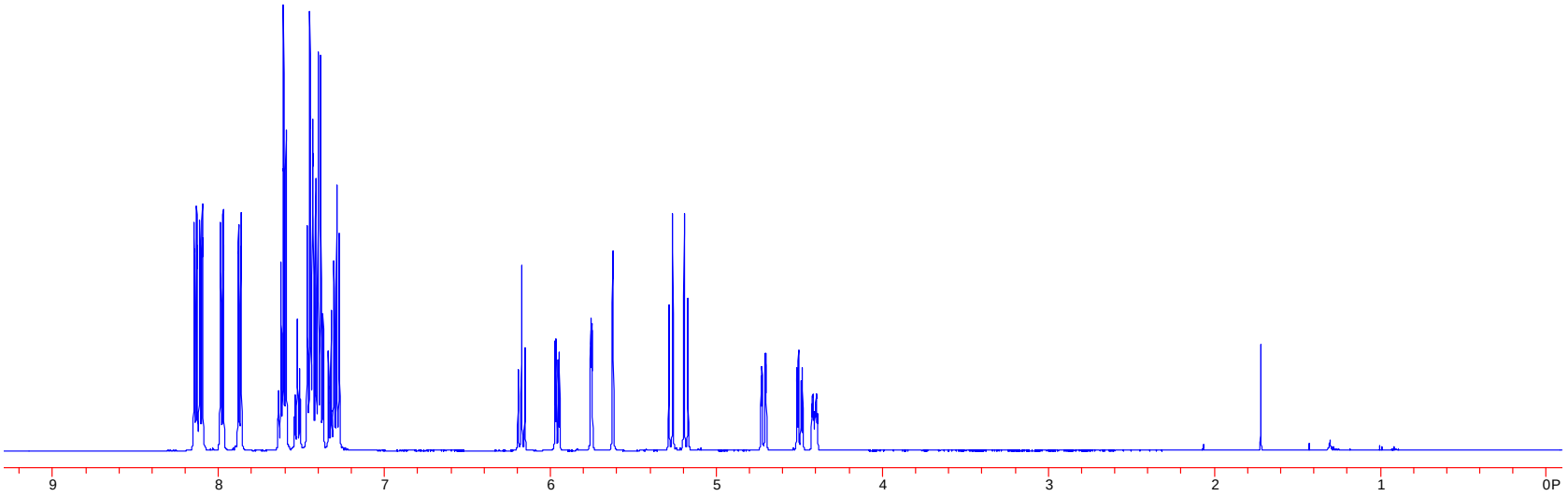
(7) He, Y.; Hinklin, R. J.; Chang, J.; Kiessling, L. L. *Org. Lett.* **2004**, *6*, 4479-4482.

(8) Dam, T. K.; Oscarson, S.; Brewer, C. F. *J. Biol. Chem.* **1998**, *273*, 32812-32817.

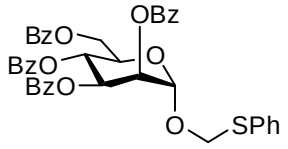
**Phenylthiomethyl 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranoside (3)**



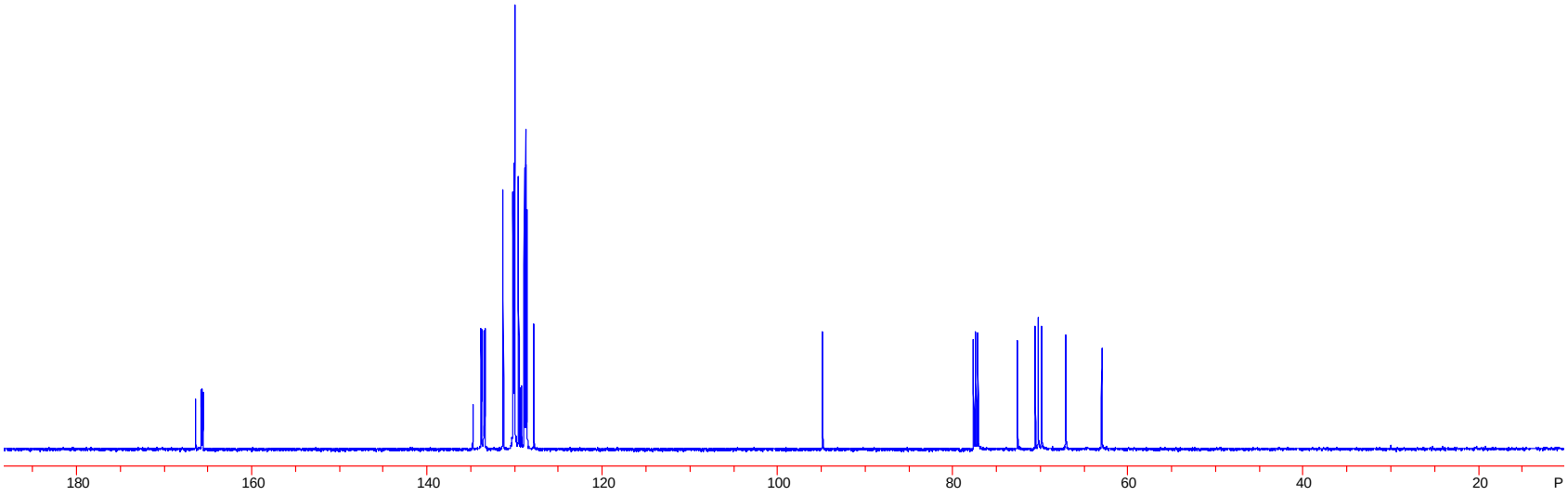

$^{1}$H NMR (500 MHz, $CDCl_3$)



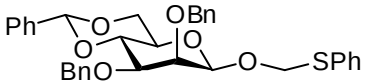
**Phenylthiomethyl 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranoside (3)**



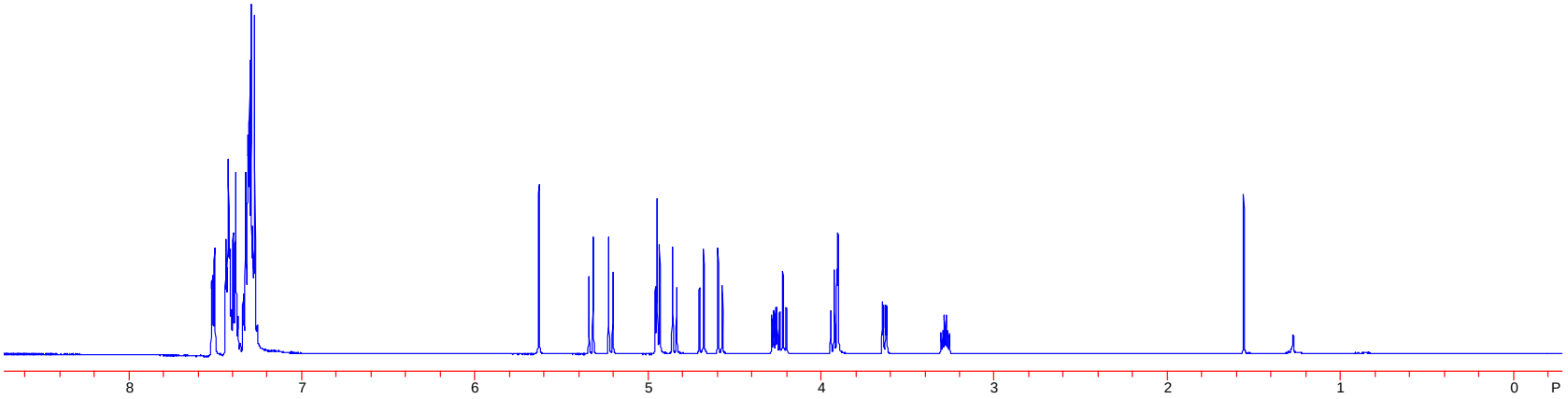

$^{13}$C NMR (125 MHz, $CDCl_3$)



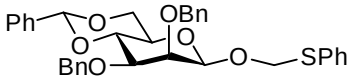
**Phenylthiomethyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-mannopyranoside (6)**



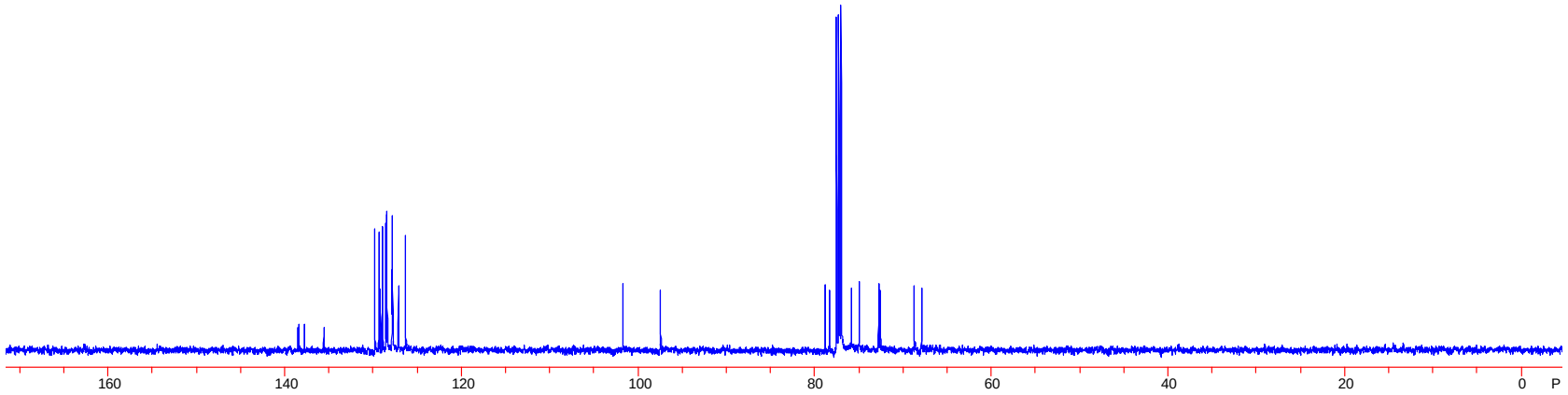

$^{1}$H NMR (500 MHz, $CDCl_3$)



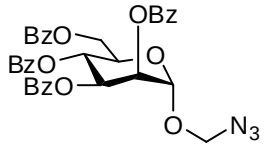
**Phenylthiomethyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-mannopyranoside (6)**



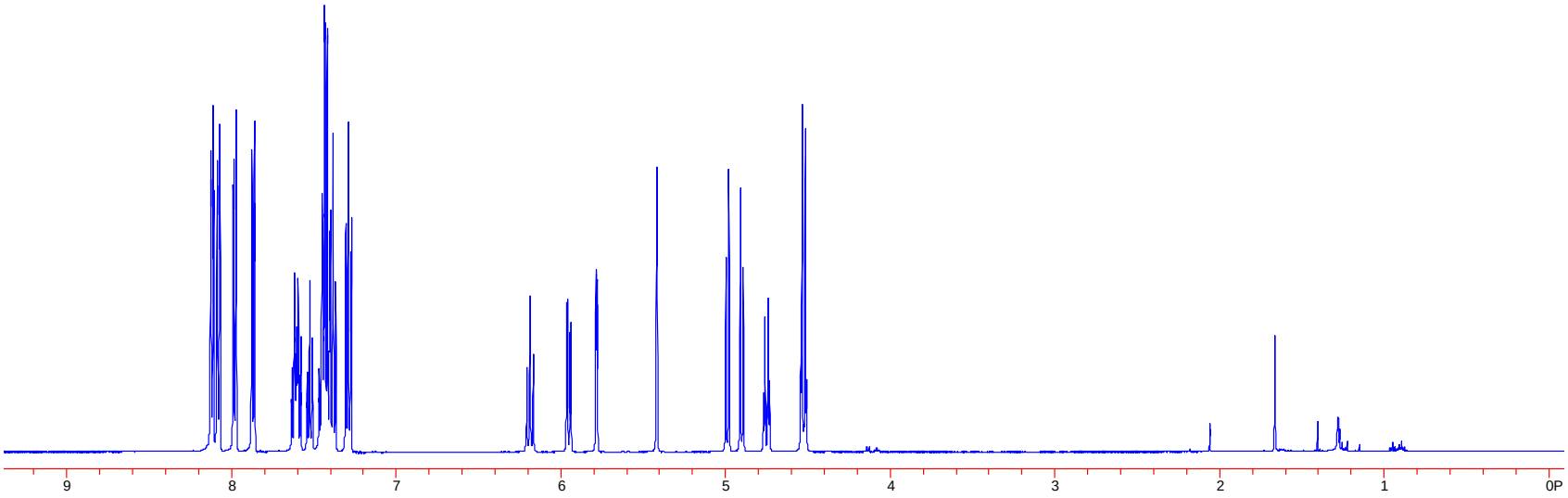

$^{13}$C NMR (125 MHz, $CDCl_3$)



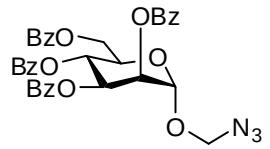
**Azidomethyl 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranoside (7)**



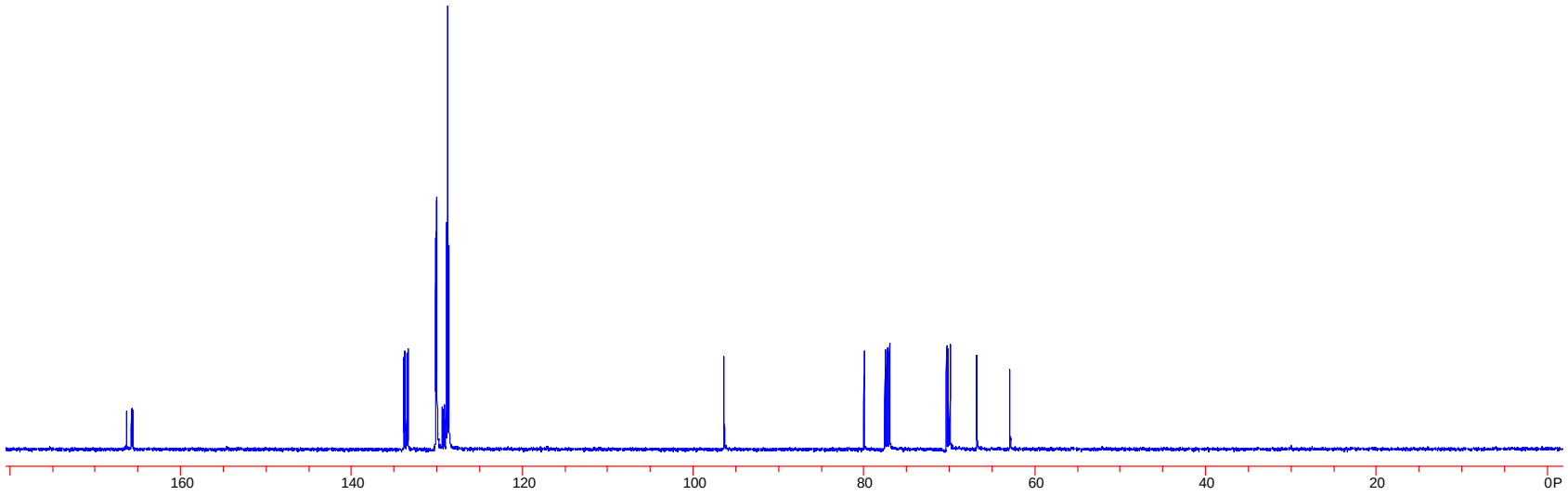

$^1$H NMR (500 MHz, $CDCl_3$)



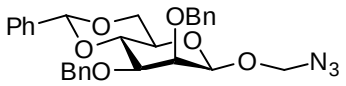
**Azidomethyl 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranoside (7)**



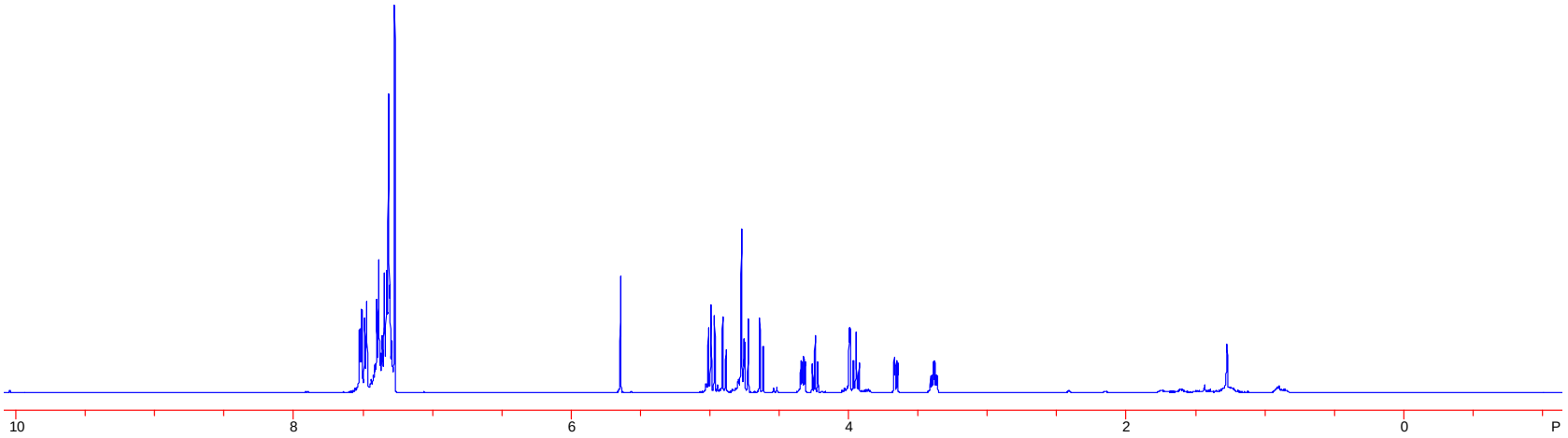

$^{13}$C NMR (125 MHz, $CDCl_3$)



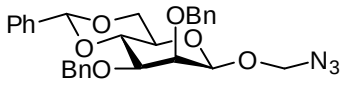
**Azidomethyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-mannopyranoside (8)**



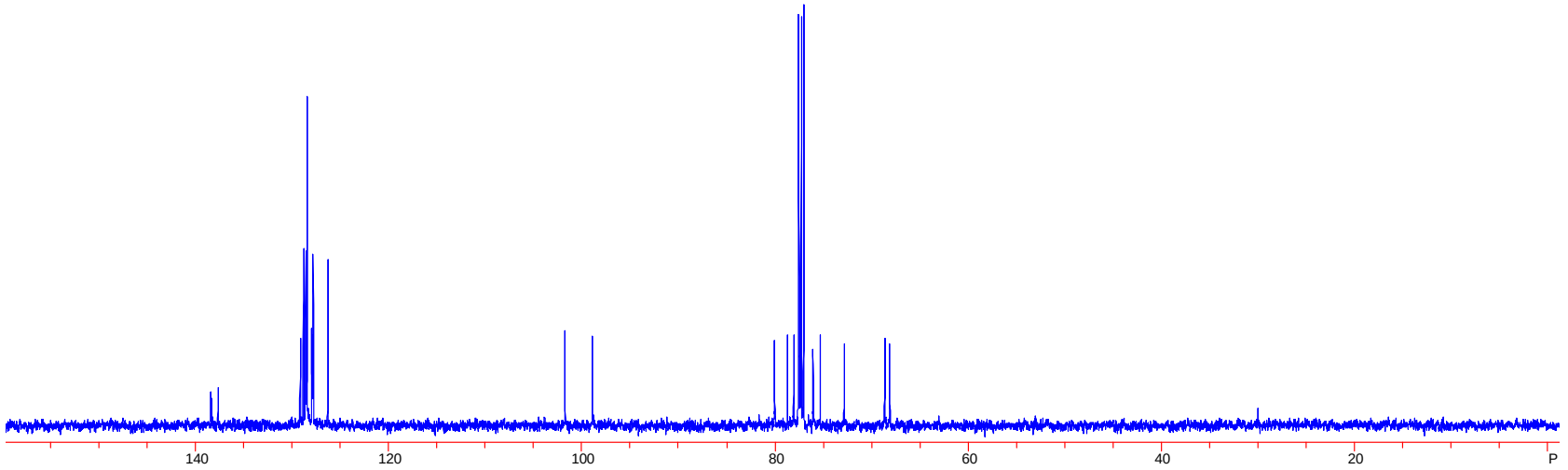

$^1$H NMR (500 MHz, $CDCl_3$)



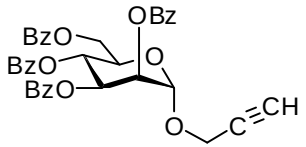
**Azidomethyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-mannopyranoside (8)**



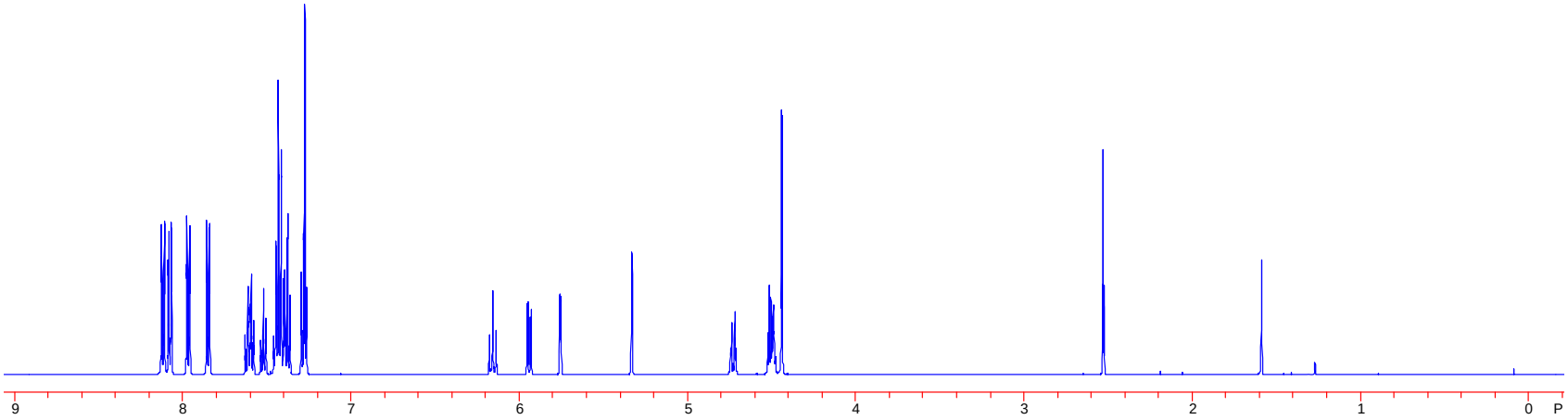

$^{13}C$ NMR (125 MHz, $CDCl_3$)



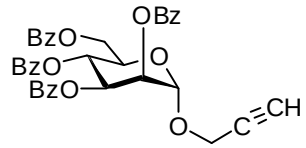
**2-Propynyl 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranoside (9)**



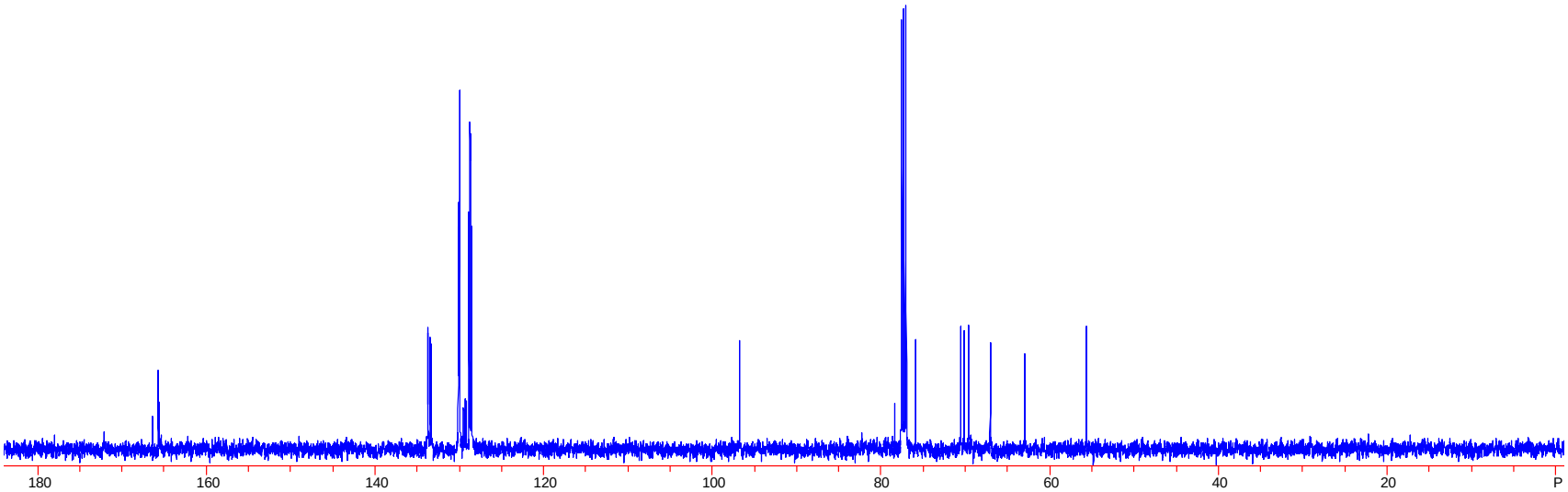

$^{1}$H NMR (500 MHz, $CDCl_3$)



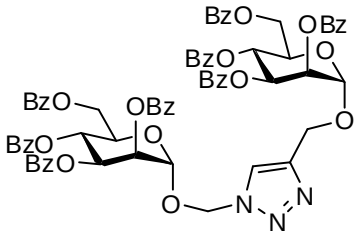
**2-Propynyl 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranoside (9)**



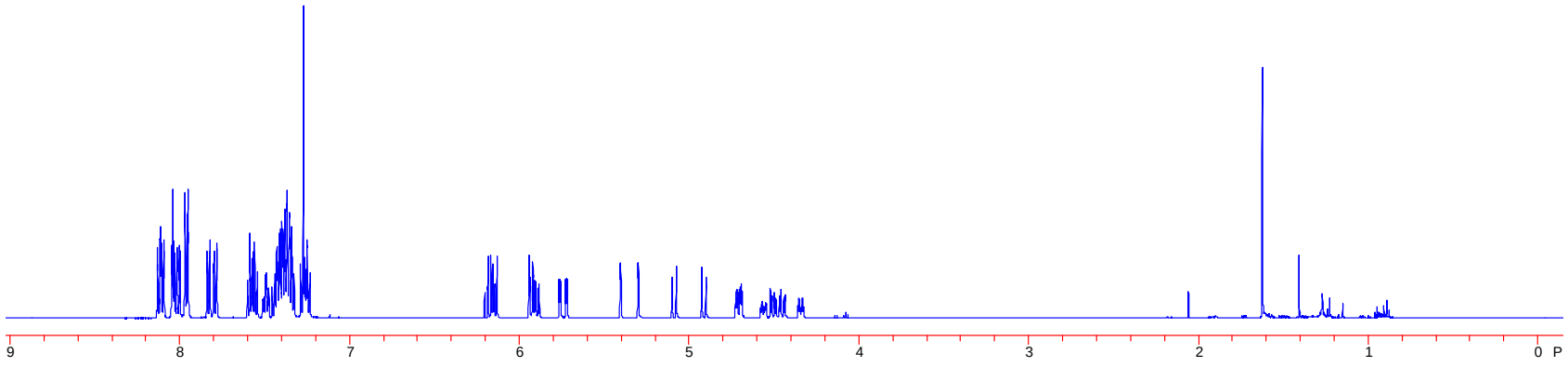

$^{13}$C NMR (125 MHz, $CDCl_3$)



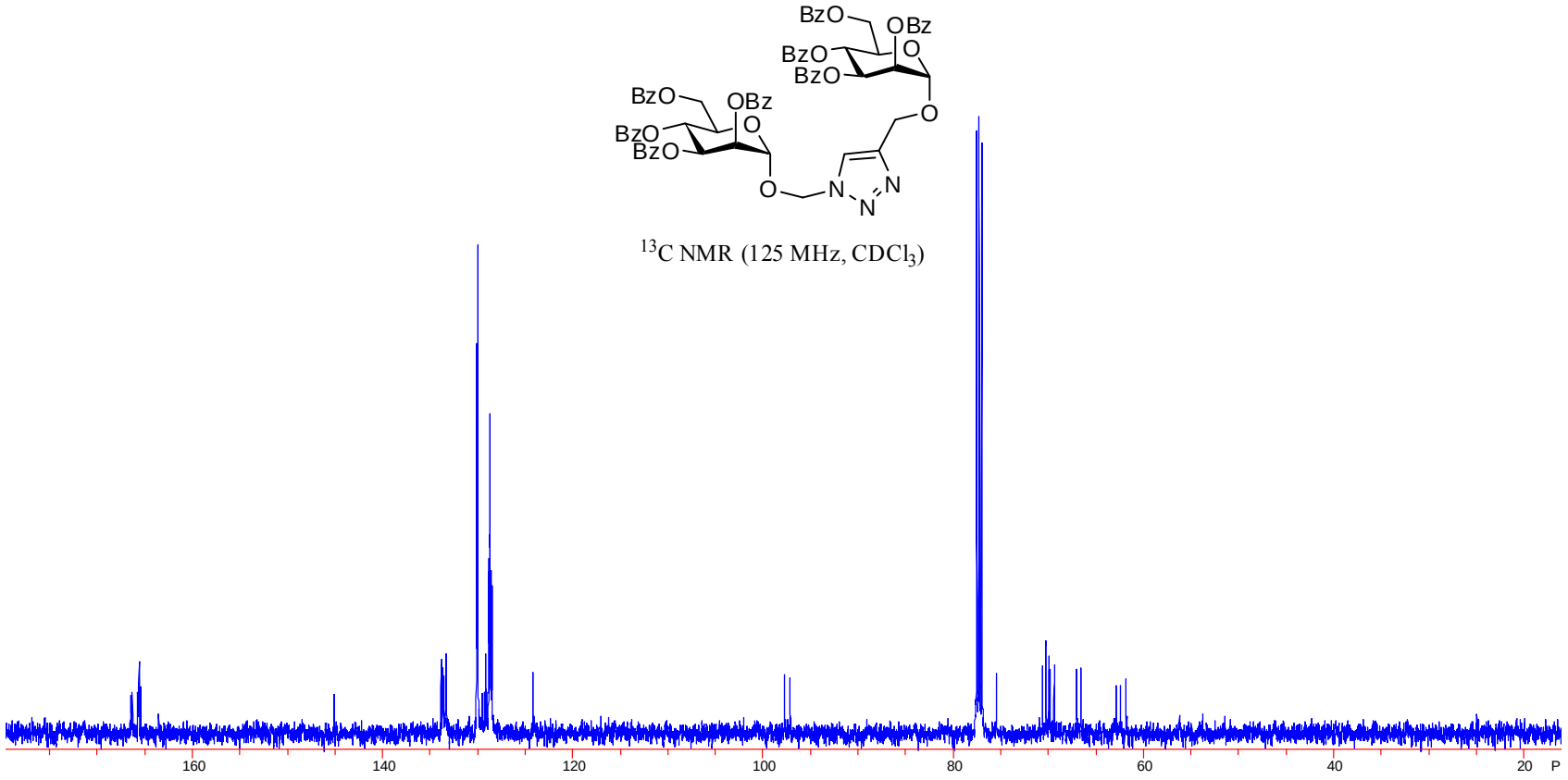
**1-(2',3',4',6',-Tetra-*O*-benzoyl-α-D-mannopyranosyloxymethyl)-4-(2'',3'',4'',6''-tetra-*O*-benzoyl-α-D-mannopyranosyloxymethyl)-1*H*-[1,2,3]-triazole (10)**




$^1$H NMR (500 MHz, $CDCl_3$)

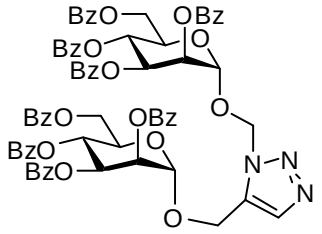


**1-(2',3',4',6',-Tetra-*O*-benzoyl-α-D-mannopyranosyloxymethyl)-4-(2'',3'',4'',6''-tetra-*O*-benzoyl-α-D-mannopyranosyloxymethyl)-1*H*-[1,2,3]-triazole (10)**



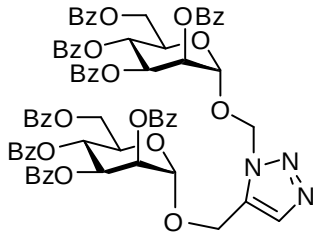

$^{13}$C NMR (125 MHz, $CDCl_3$)

**1-(2',3',4',6'-Tetra-*O*-benzoyl-α-D-mannopyranosyloxymethyl)-5-(2'',3'',4'',6''-tetra-*O*-benzoyl-α-D-mannopyranosyloxymethyl)-1*H*-[1,2,3]-triazole (11)**

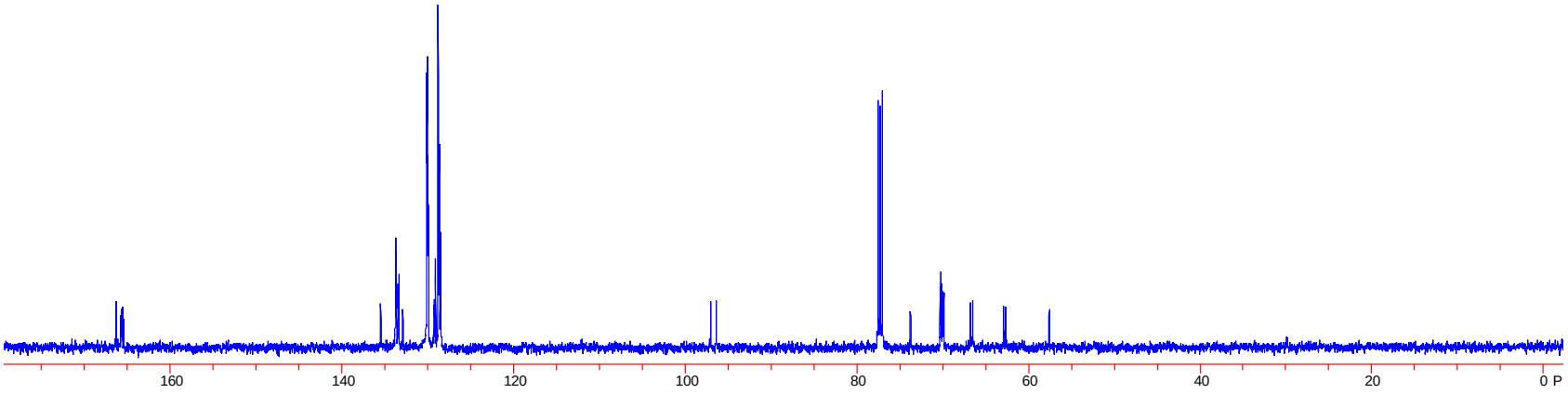



$^1$H NMR (500 MHz, $CDCl_3$)

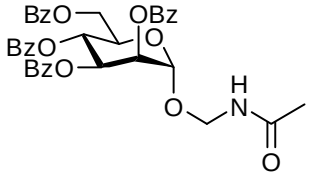
**1-(2',3',4',6'-Tetra-*O*-benzoyl-α-D-mannopyranosyloxymethyl)-5-(2'',3'',4'',6''-tetra-*O*-benzoyl-α-D-mannopyranosyloxymethyl)-1*H*-[1,2,3]-triazole (11)**



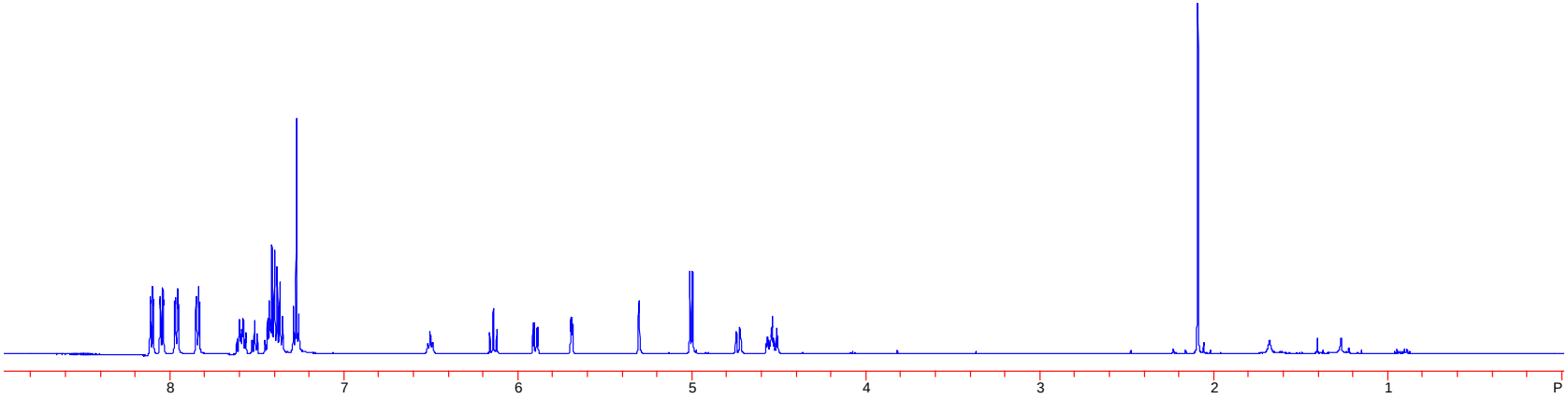

$^{13}$C NMR (125 MHz, $CDCl_3$)



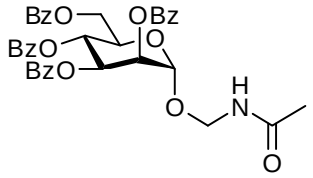
**Acetamidomethyl 2',3',4',6'-tetra-*O*-benzoyl-α-D-mannopyranoside (12)**



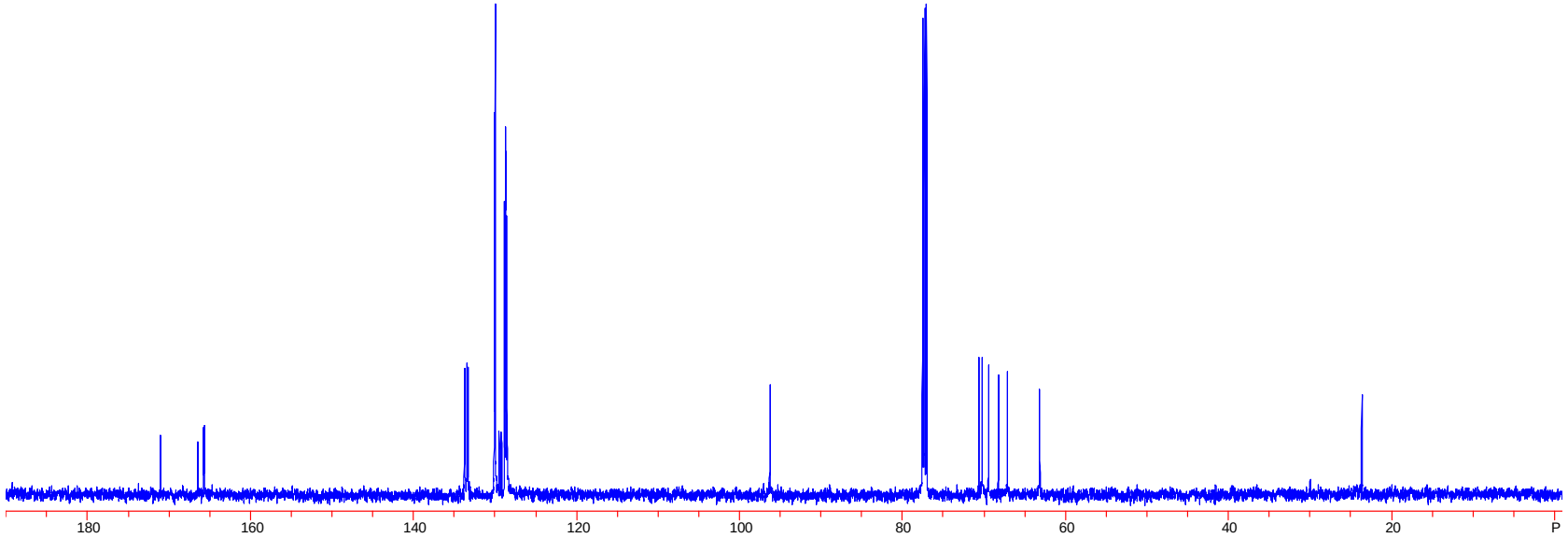

$^1$H NMR (500 MHz, $CDCl_3$)



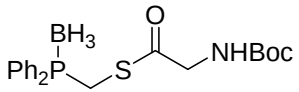
**Acetamidomethyl 2',3',4',6'-tetra-*O*-benzoyl-α-D-mannopyranoside (12)**




$^{13}C$ NMR (125 MHz, $CDCl_3$)

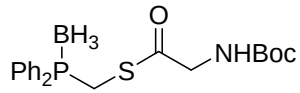


**Diphenylphosphino(borane)methanethiyl *N*-(*tert*-butoxycarbonyl)glycinate**



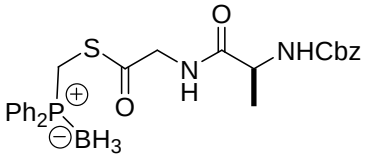

$^{1}$H NMR (500 MHz, $CDCl_3$)

**Diphenylphosphino(borane)methanethiyl *N*-(*tert*-butoxycarbonyl)glycinate**

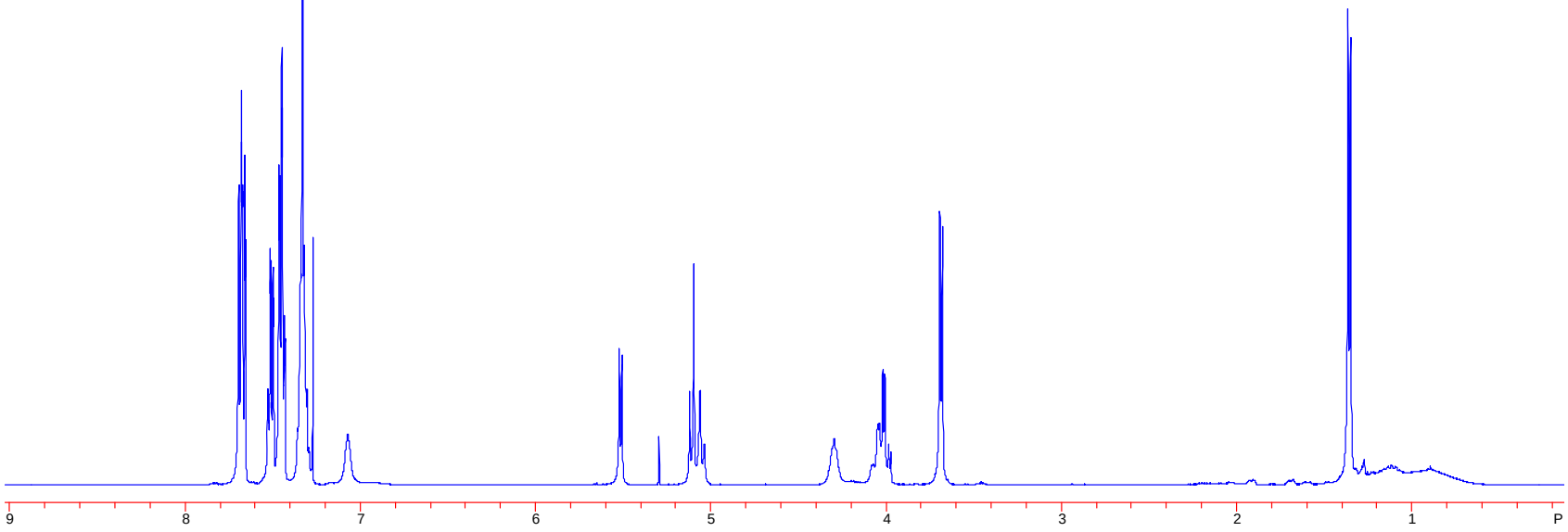



$^{13}$C NMR (125 MHz, $CDCl_3$)

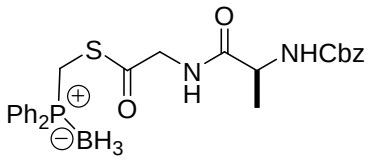
**Diphenylphosphino(borane)methanethiyl *N*-(benzyloxycarbonyl)-L-alanyl-glycinate**




$^{1}$H NMR (500 MHz, $CDCl_3$)

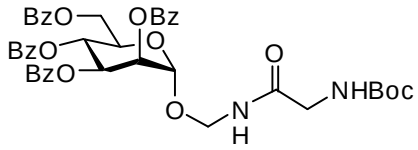


**Diphenylphosphino(borane)methanethiyl *N*-(benzyloxycarbonyl)-L-alanyl-glycinate**



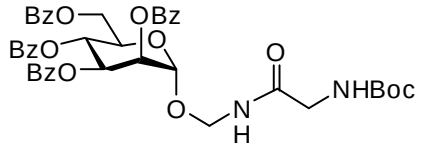

$^{13}$C NMR (125 MHz, $CDCl_3$)

**_N_-[(2,3,4,6-Tetra-_O_-benzoyl-α-D-mannopyranosyl) oxymethyl] _N_-(_tert_-butoxycarbonyl)glycinamide (13)**

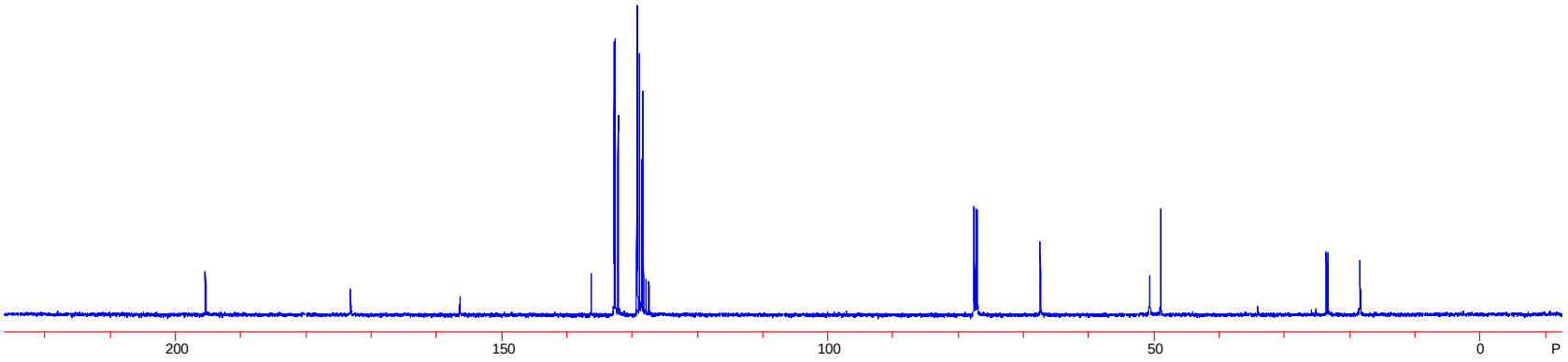



$^{1}$H NMR (500 MHz, $CDCl_3$)

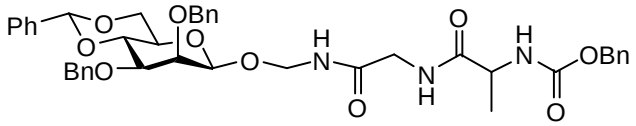
**_N_-[(2,3,4,6-Tetra-_O_-benzoyl-α-D-mannopyranosyl) oxymethyl] _N_-(tert-butoxycarbonyl)glycinamide (13)**




$^{13}$C NMR (125 MHz, $CDCl_3$)

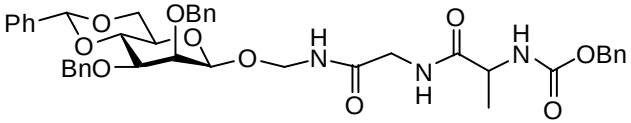


**_N_-[(2,3-di-_O_-benzyl-4,6-_O_-benzylidene-β-D-mannopyranosyl) oxymethyl] _N_$_{\alpha}$-(benzyloxycarbonyl)-L-alanyl-glycinamide (14)**



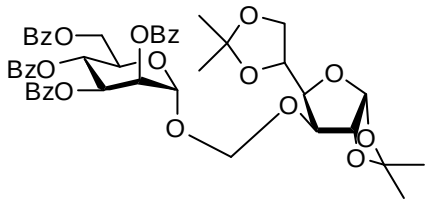

$^{1}$H NMR (500 MHz, $CDCl_3$)

**_N_-[(2,3-di-_O_-benzyl-4,6-_O_-benzylidene-β-D-mannopyranosyl) oxymethyl] _N_$^{1}$-(benzyloxycarbonyl)-L-alanyl-glycinamide (14)**

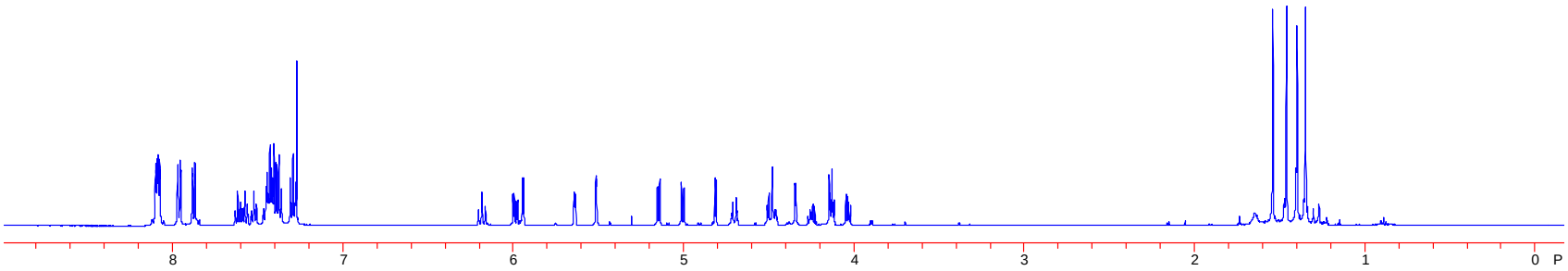



$^{13}$C NMR (125 MHz, $CDCl_3$)

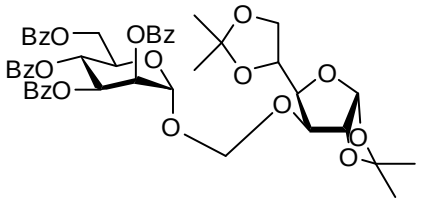
**3-*O*-(2,3,4,6-Tetra-*O*-benzoyl-α-D-mannopyranosyloxymethyl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (15)**



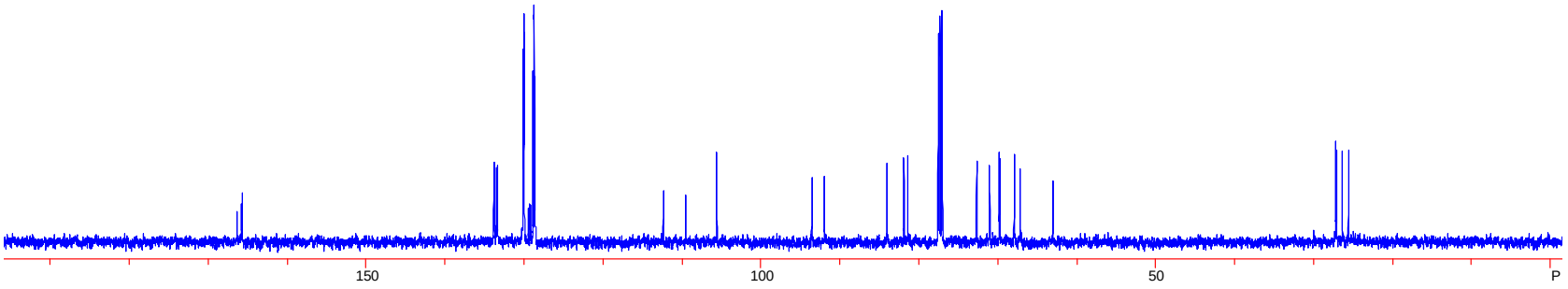

$^1$H NMR (500 MHz, $CDCl_3$)



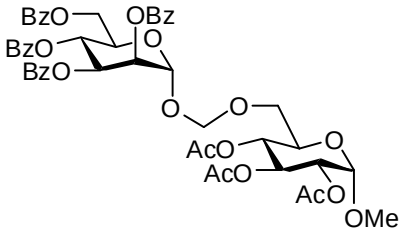
**3-*O*-(2,3,4,6-Tetra-*O*-benzoyl-α-D-mannopyranosyloxymethyl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (15)**



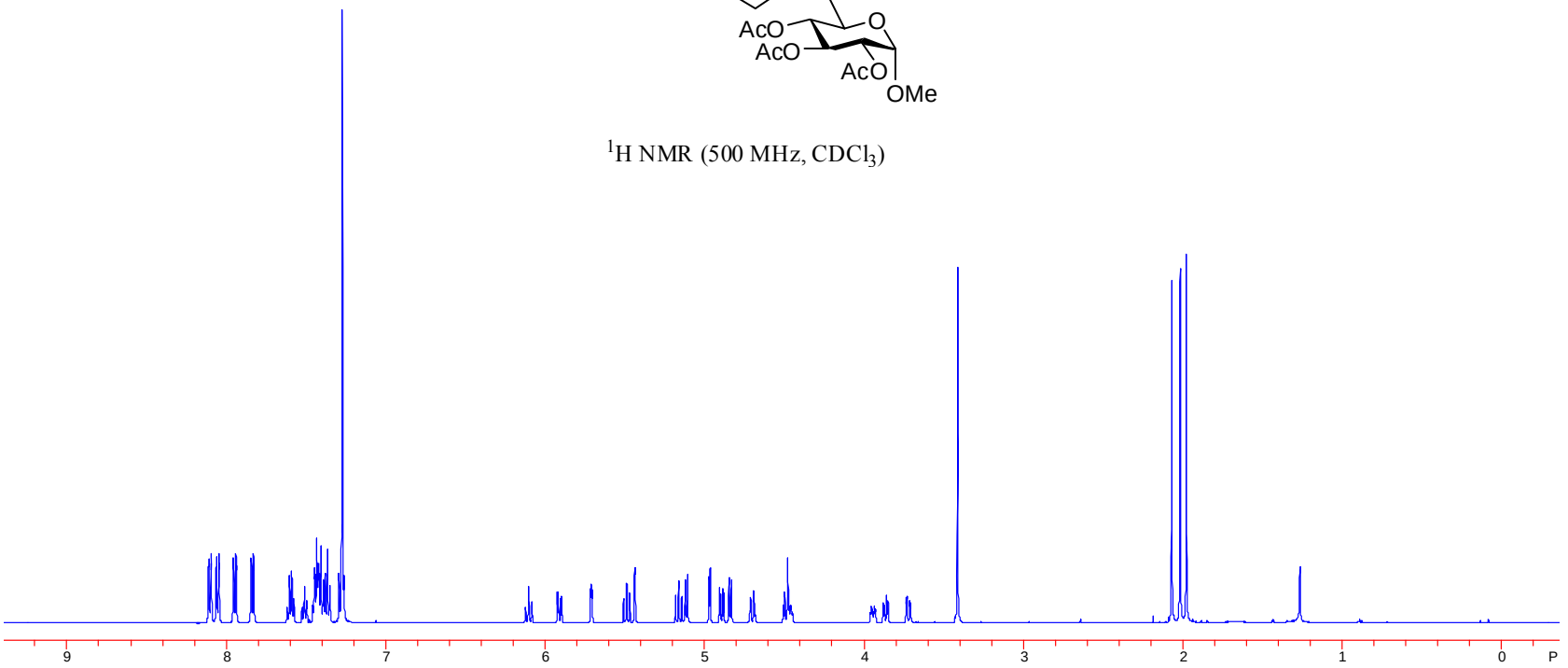

$^{13}$C NMR (125 MHz, $CDCl_3$)



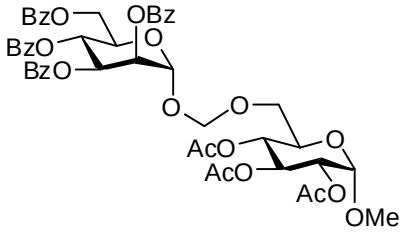
**Methyl 6-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyloxymethyl)-2,3,4-tri-*O*-acetyl-α-D-glucopyranoside (16)**



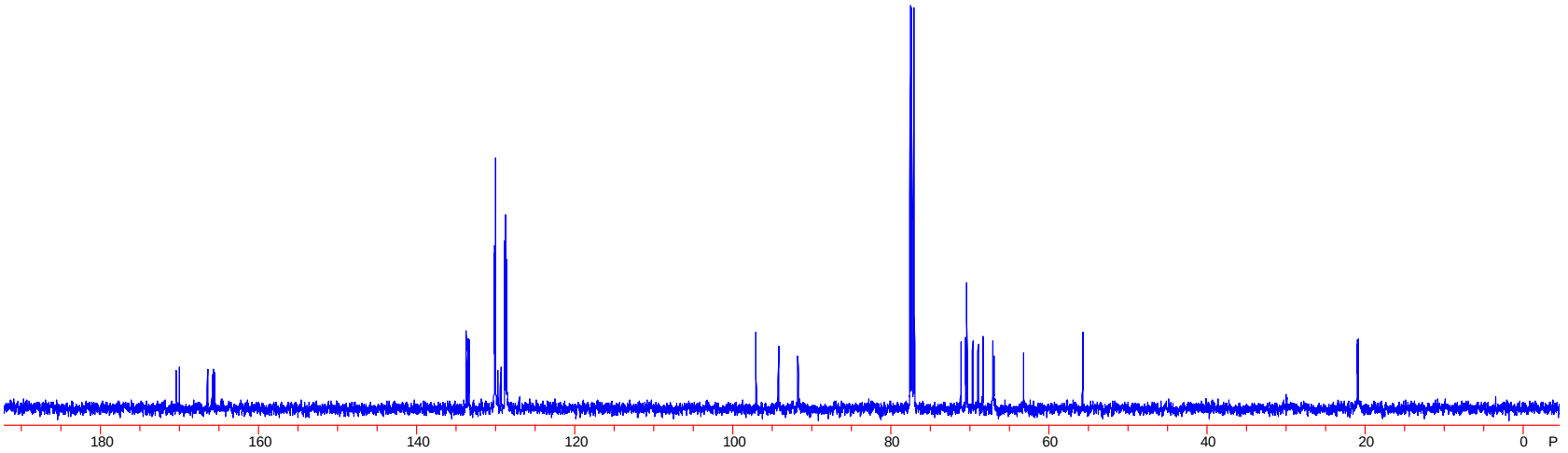

$^{1}$H NMR (500 MHz, $CDCl_3$)



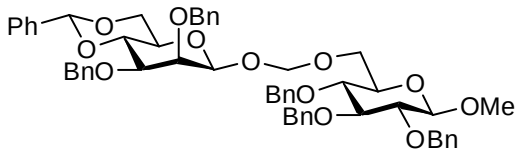
**Methyl 6-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyloxymethyl)-2,3,4-tri-*O*-acetyl-α-D-glucopyranoside (16)**




$^{13}$C NMR (125 MHz, $CDCl_3$)

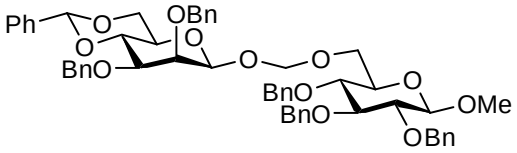


**Methyl 6-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-mannopyranosyloxymethyl)-2,3,4-tri-*O*-benzyl-β-D-glucopyranoside (17)**

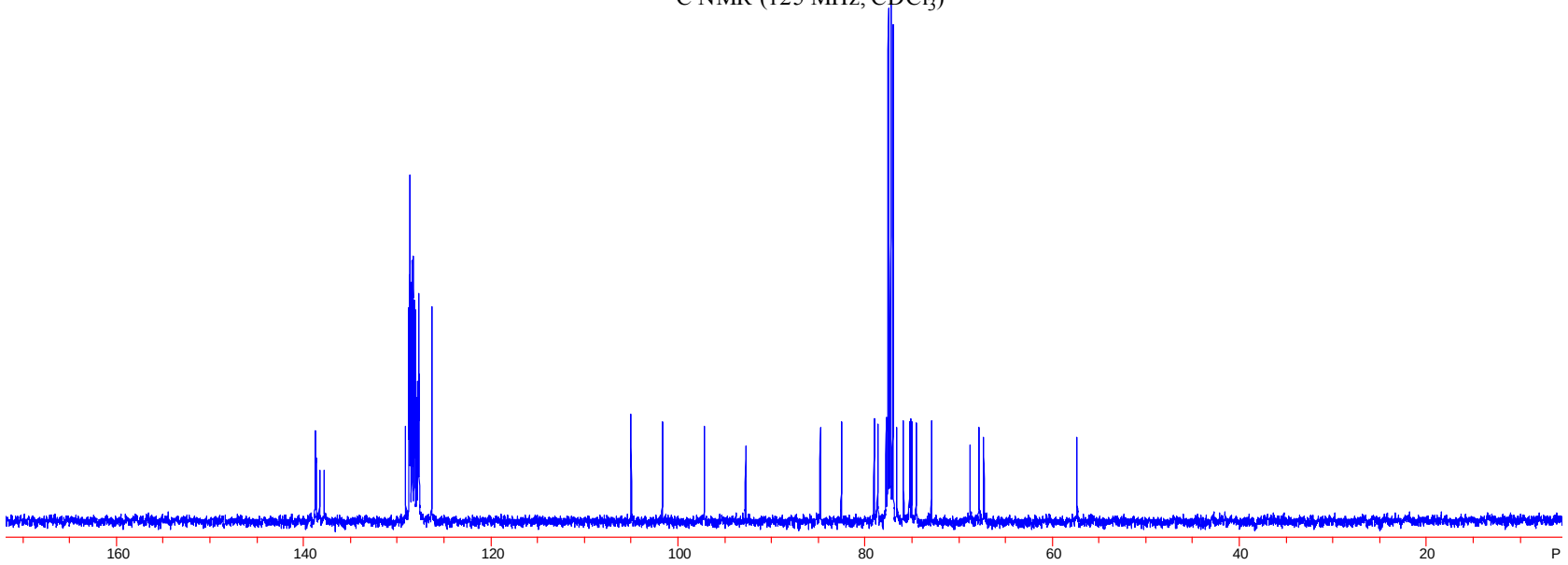



$^1$H NMR (500 MHz, $CDCl_3$)

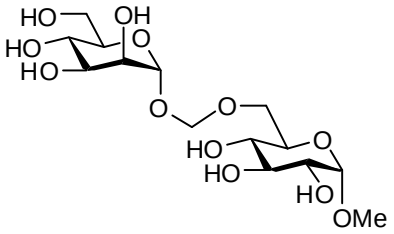
**Methyl 6-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-mannopyranosyloxymethyl)-2,3,4-tri-*O*-benzyl-β-D-glucopyranoside (17)**




$^{13}$C NMR (125 MHz, $CDCl_3$)

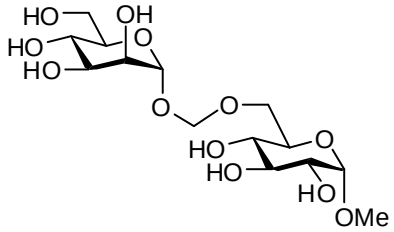


**Methyl 6-*O*-(α-D-mannopyranosyloxymethyl)-α-D-glucopyranoside (18)**



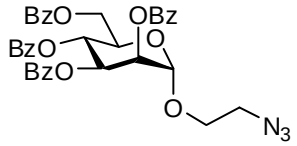

$^1$H NMR (500 MHz, $CD_3OD$)

**Methyl 6-*O*-(α-D-mannopyranosyloxymethyl)-α-D-glucopyranoside (18)**

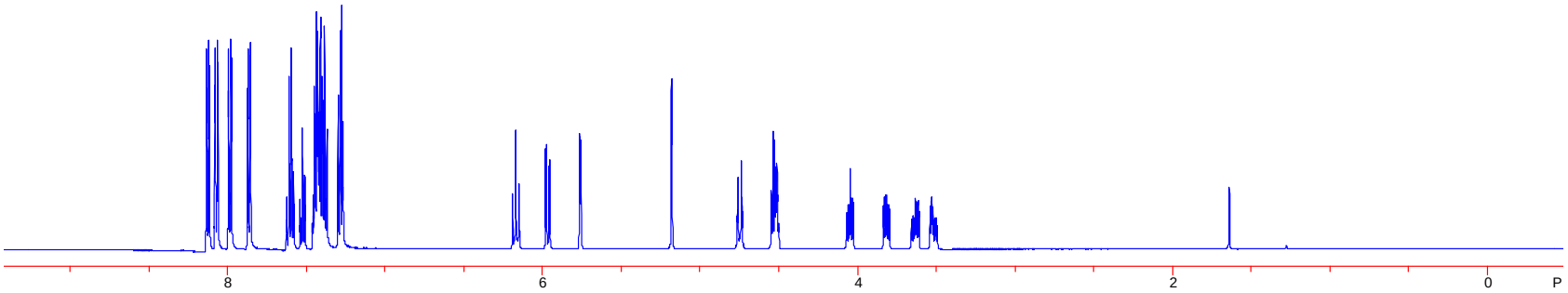



$^{13}$C NMR (125 MHz, $CD_3OD$)

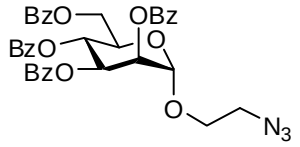
**2-Azidoethyl 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranoside (19)**



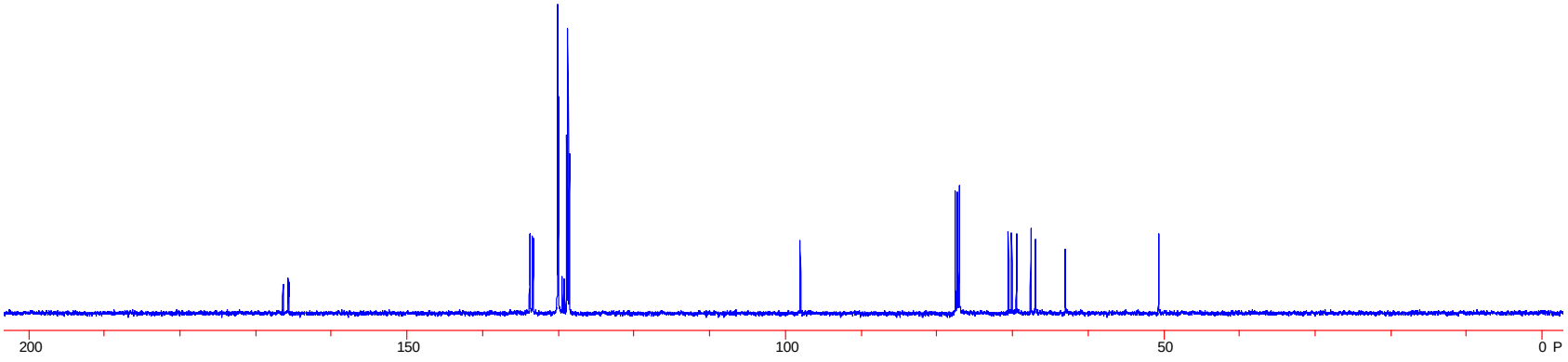

$^{1}$H NMR (500 MHz, $CDCl_3$)



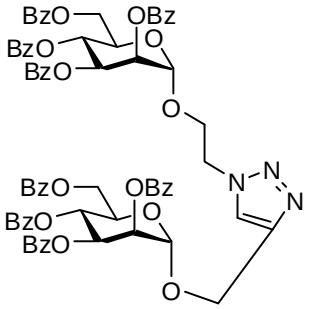
**2-Azidoethyl 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranoside (19)**



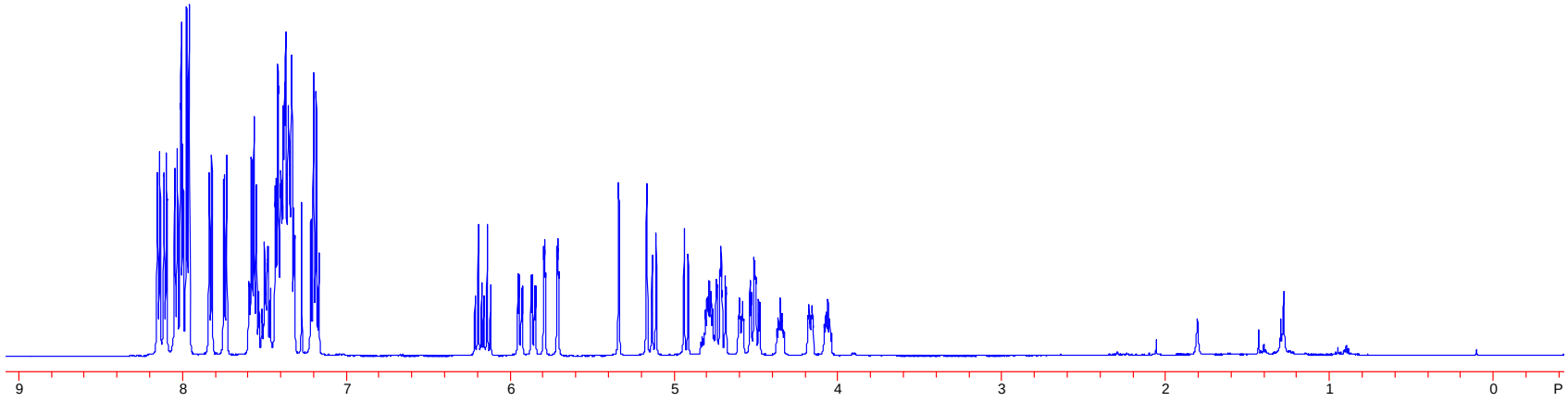

$^{13}$C NMR (125 MHz, $CDCl_3$)



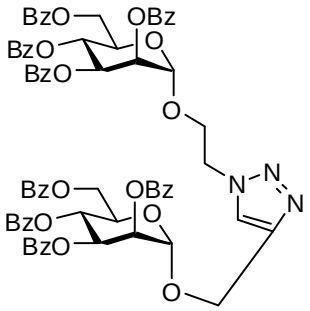
**1-(2',3',4',6'-Tetra-*O*-benzoyl-α-D-mannopyranosyloxyethyl)-4-(2'',3'',4'',6''-tetra-*O*-benzoyl-α-D-mannopyranosyloxymethyl)-1*H*-[1,2,3]-triazole (20)**



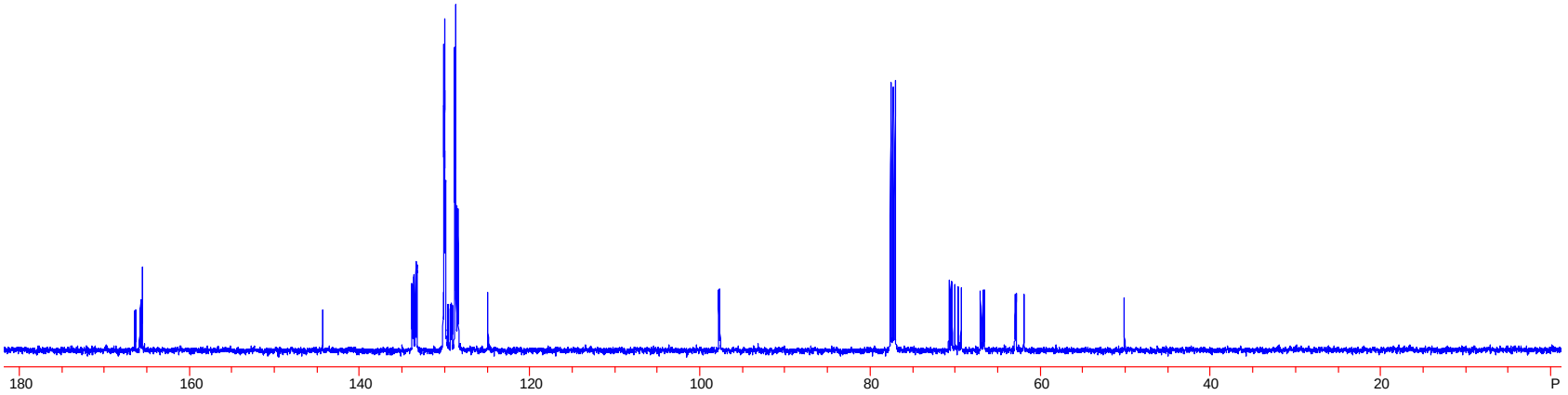

$^1$H NMR (500 MHz, $CDCl_3$)



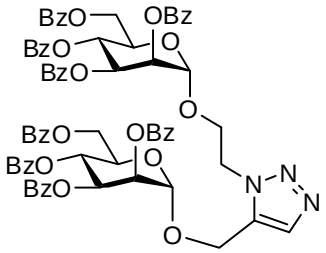
**1-(2',3',4',6'-Tetra-*O*-benzoyl-α-D-mannopyranosyloxyethyl)-4-(2'',3'',4'',6''-tetra-*O*-benzoyl-α-D-mannopyranosyloxymethyl)-1*H*-[1,2,3]-triazole (20)**



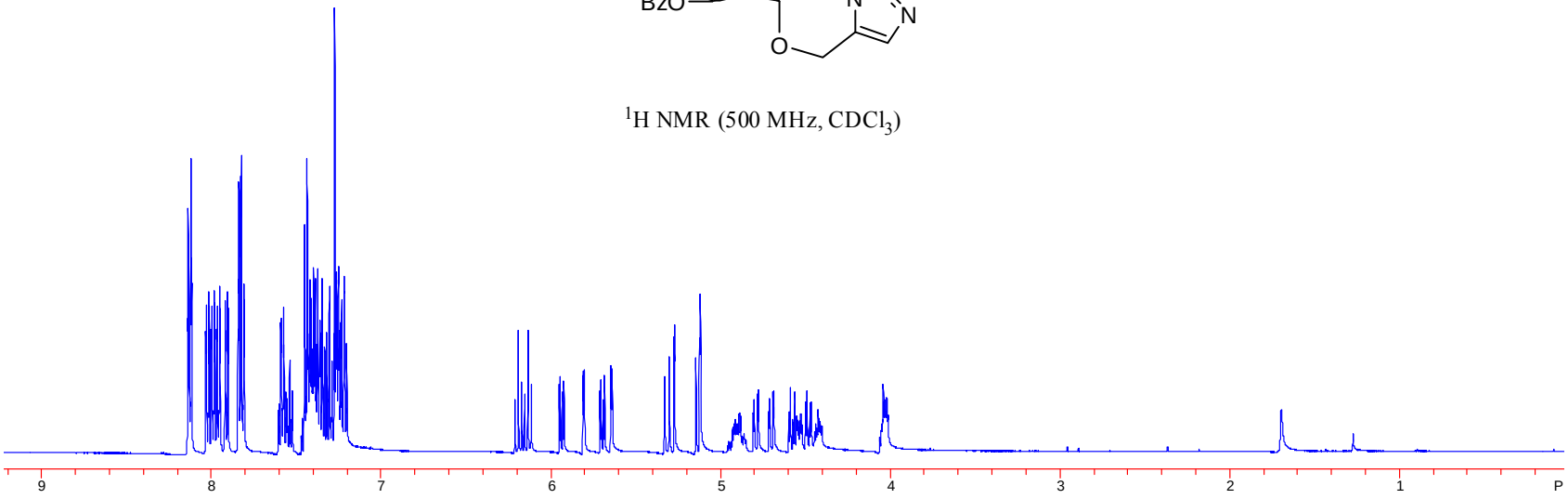

$^{13}$C NMR (125 MHz, $CDCl_3$)



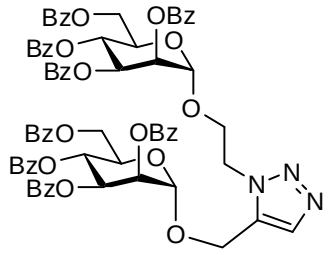
**1-(2',3',4',6'-Tetra-*O*-benzoyl-α-D-mannopyranosyloxyethyl)-5-(2'',3'',4'',6''-tetra-*O*-benzoyl-α-D-mannopyranosyloxymethyl)-1*H*-[1,2,3]-triazole (21)**



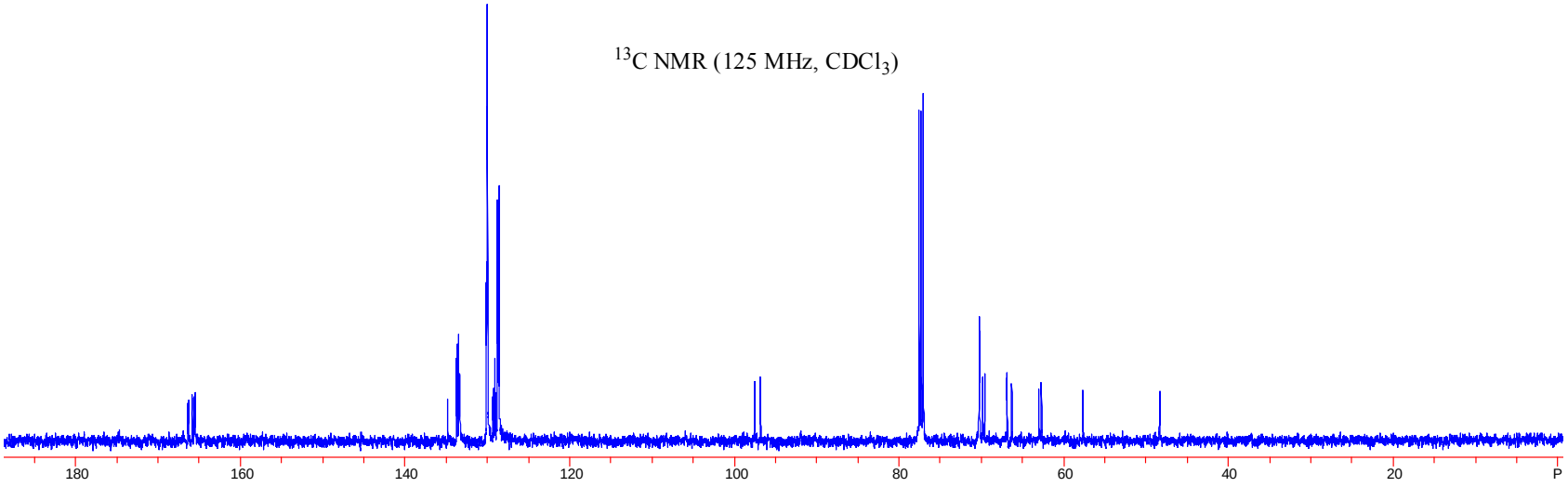

$^1$H NMR (500 MHz, $CDCl_3$)



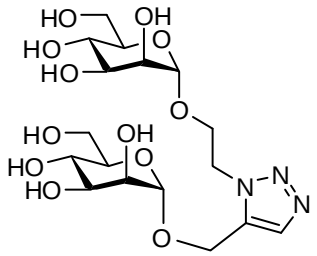
**1-(2',3',4',6'-Tetra-*O*-benzoyl-α-D-mannopyranosyloxyethyl)-5-(2'',3'',4'',6''-tetra-*O*-benzoyl-α-D-mannopyranosyloxymethyl)-1*H*-[1,2,3]-triazole (21)**



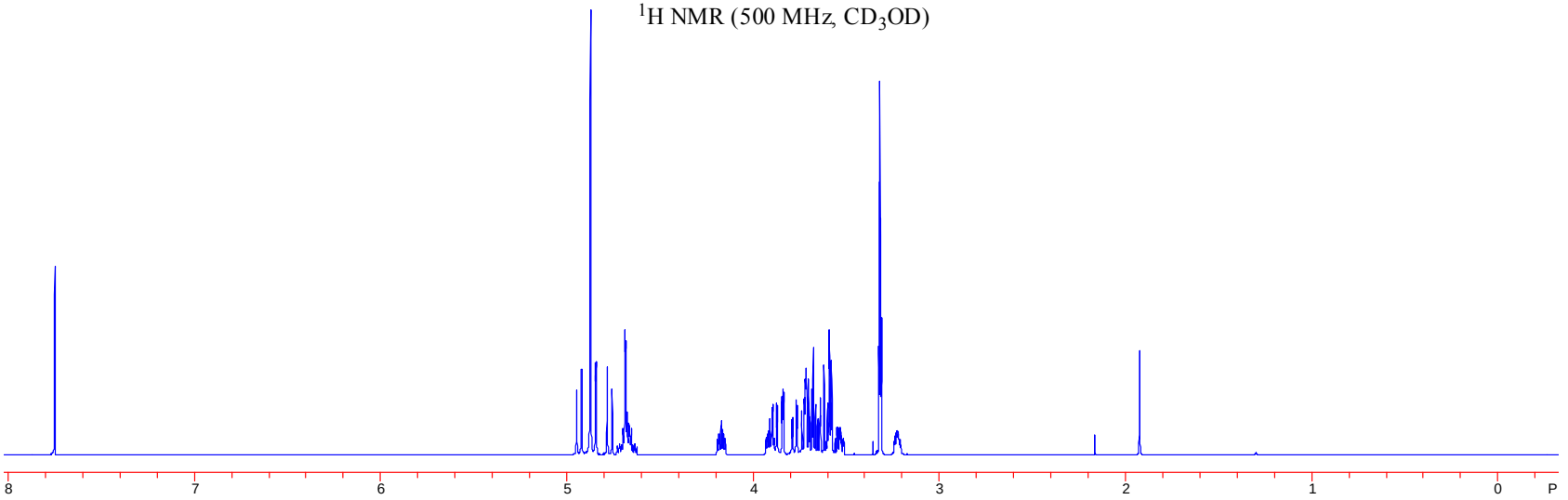

$^{13}$C NMR (125 MHz, $CDCl_3$)



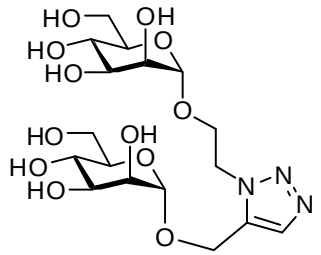
**1-(α-D-Mannopyranosyloxyethyl)-5-(α-D-mannopyranosyloxymethyl)-1*H*-[1,2,3]-triazole (22)**




$^1$H NMR (500 MHz, $CD_3OD$)

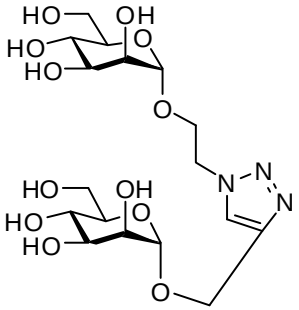


**1-(α-D-Mannopyranosyloxyethyl)-5-(α-D-mannopyranosyloxymethyl)-1*H*-[1,2,3]-triazole (22)**

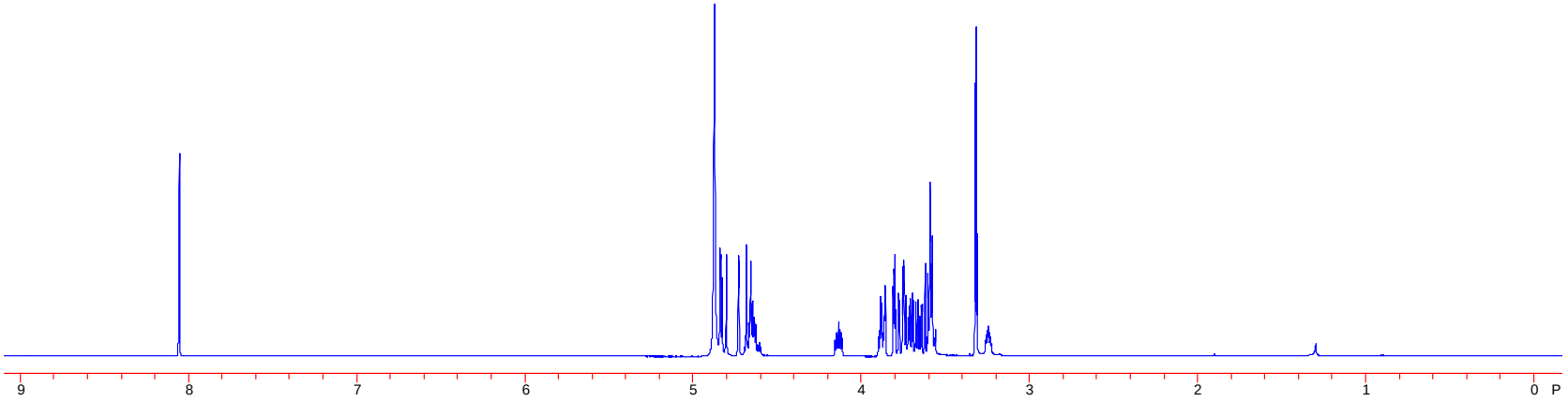


$^{13}$C NMR (125 MHz, $CD_3OD$)

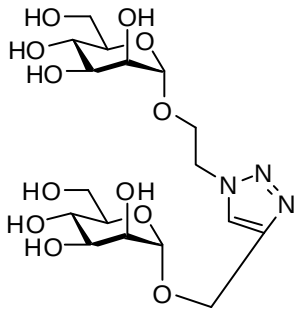
**1-(α-D-Mannopyranosyloxyethyl)-4-(α-D-mannopyranosyloxymethyl)-1*H*-[1,2,3]-triazole (23)**




$^{1}$H NMR (500 MHz, $CD_3OD$)

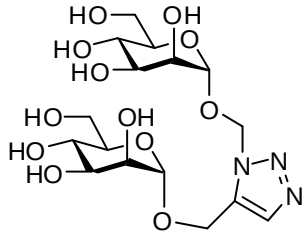


**1-(α-D-Mannopyranosyloxyethyl)-4-(α-D-mannopyranosyloxymethyl)-1*H*-[1,2,3]-triazole (23)**

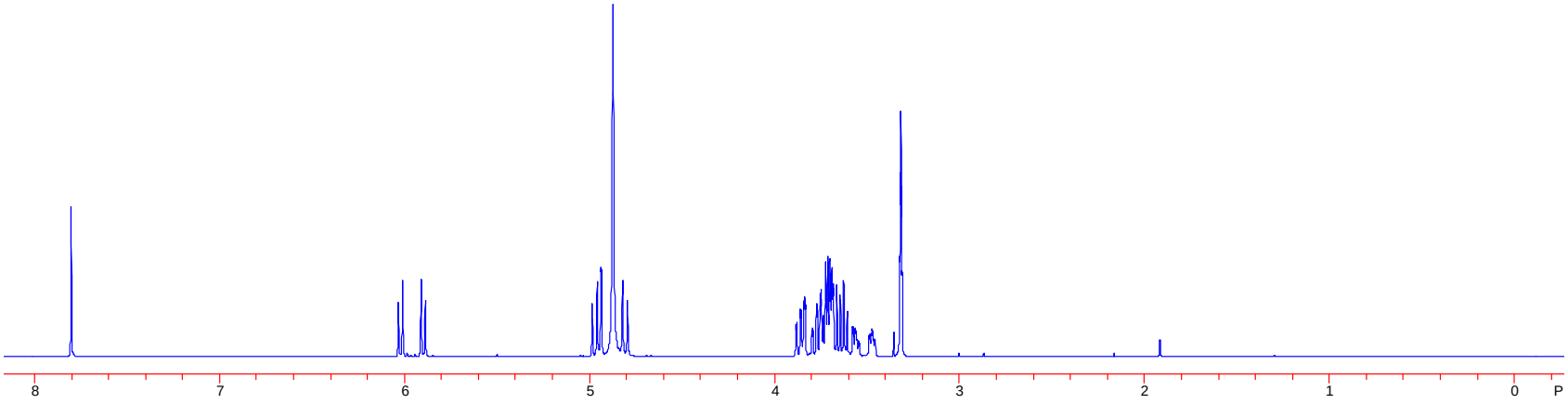



$^{13}$C NMR (125 MHz, $CD_3OD$)

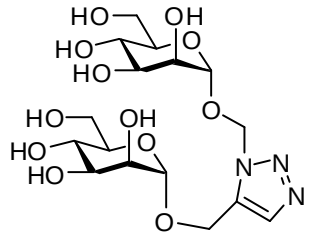
**1-(α-D-Mannopyranosyloxymethyl)-5-(α-D-mannopyranosyloxymethyl)-1*H*-[1,2,3]-triazole (24)**




$^1$H NMR (500 MHz, $CD_3OD$)

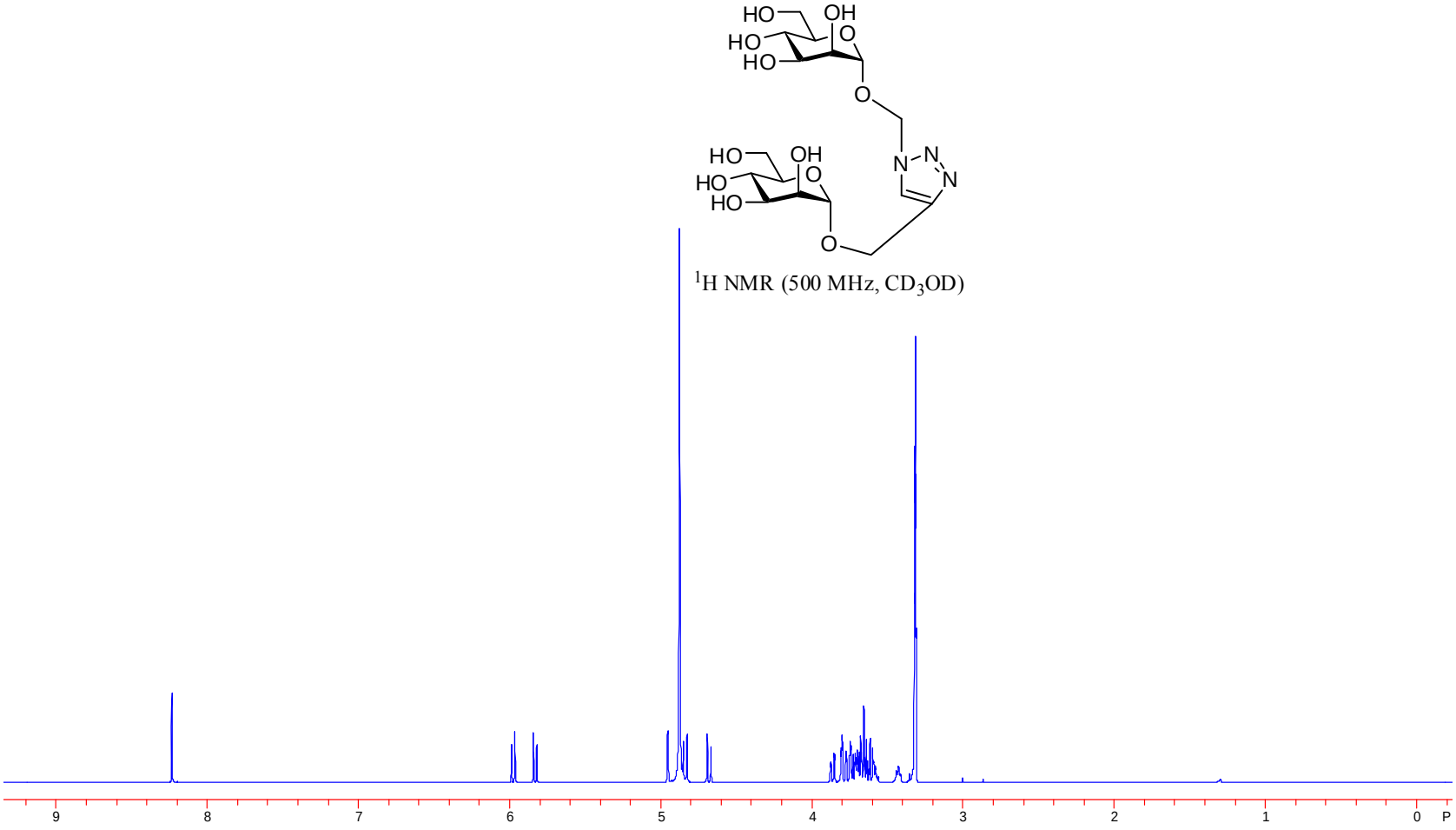


**1-(α-D-Mannopyranosyloxymethyl)-5-(α-D-mannopyranosyloxymethyl)-1*H*-[1,2,3]-triazole (24)**

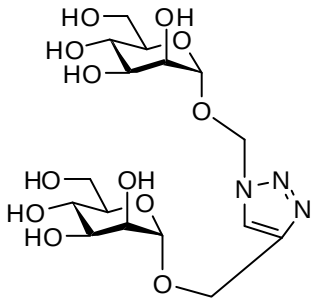


$^{13}$C NMR (125 MHz, $CD_3OD$)

**1-(α-D-Mannopyranosyloxymethyl)-4-(α-D-mannopyranosyloxymethyl)-1*H*-[1,2,3]-triazole (25)**



**1-(α-D-Mannopyranosyloxymethyl)-4-(α-D-mannopyranosyloxymethyl)-1*H*-[1,2,3]-triazole (25)**




$^{13}$C NMR (125 MHz, $CD_3OD$)