

Synthesis and evaluation of alkylated analogues of azagalactofagomine – potential pharmacological chaperones for Krabbe disease

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Supporting Information

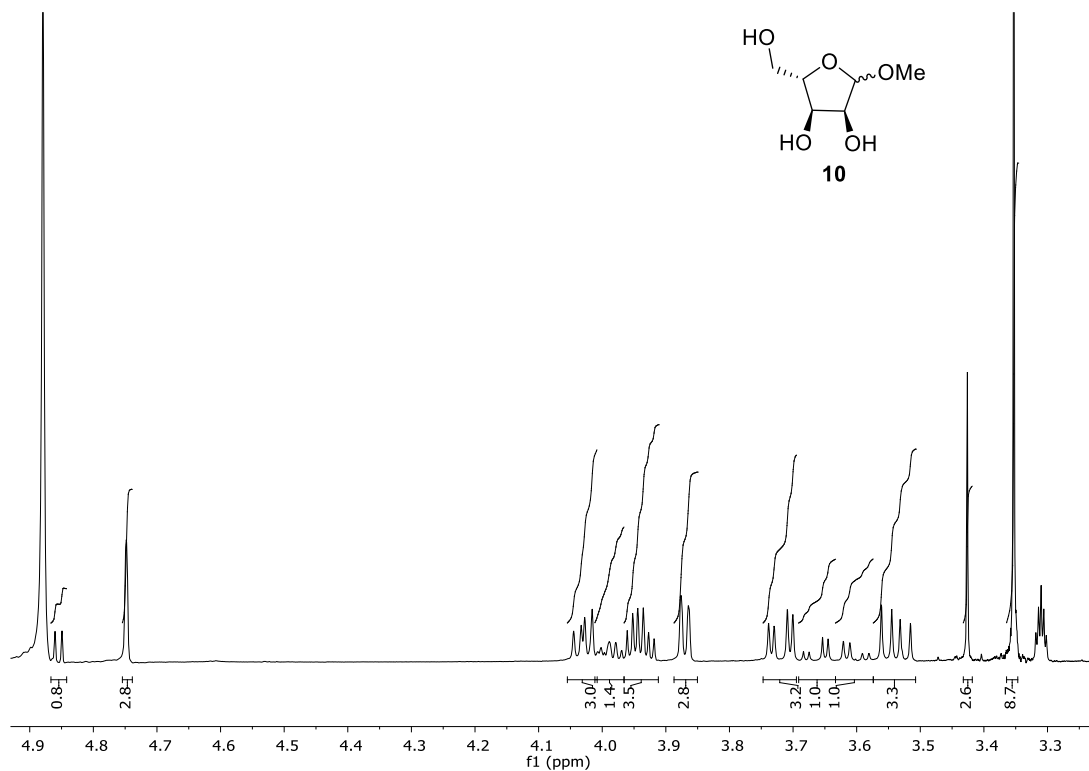
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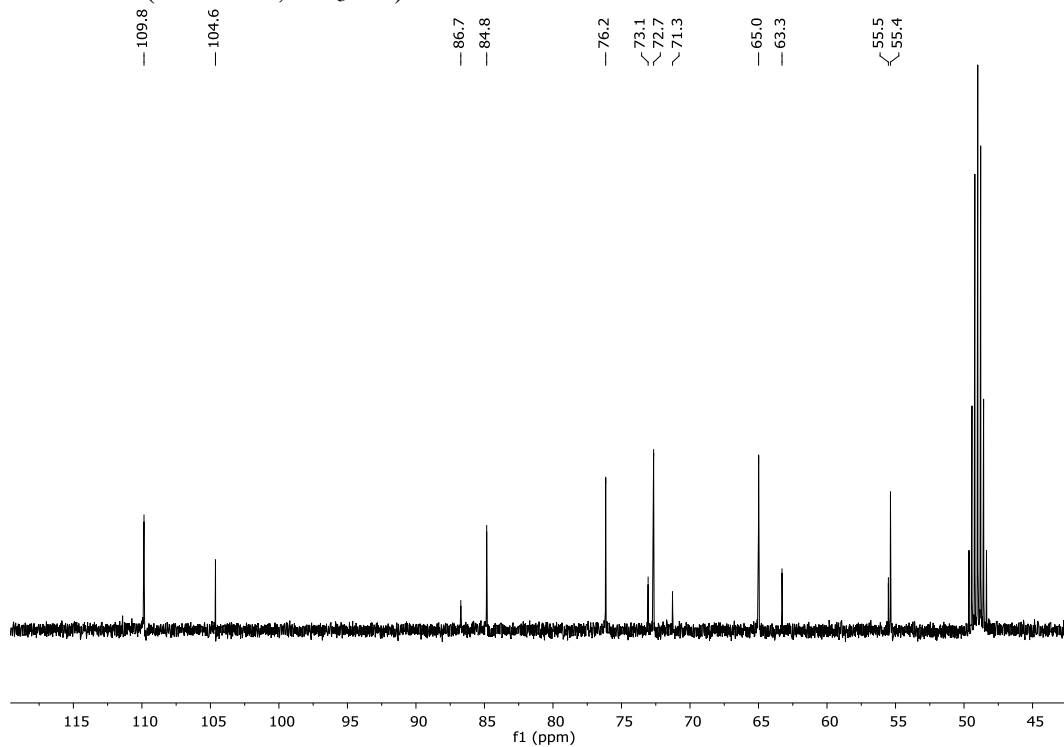
$^1\text{H-NMR}$ and $^{13}\text{C-NMR}$ spectra for compounds **10-41**:

Methyl L-ribofuranoside (10):

$^1\text{H-NMR}$ (400 MHz, CD_3OD)

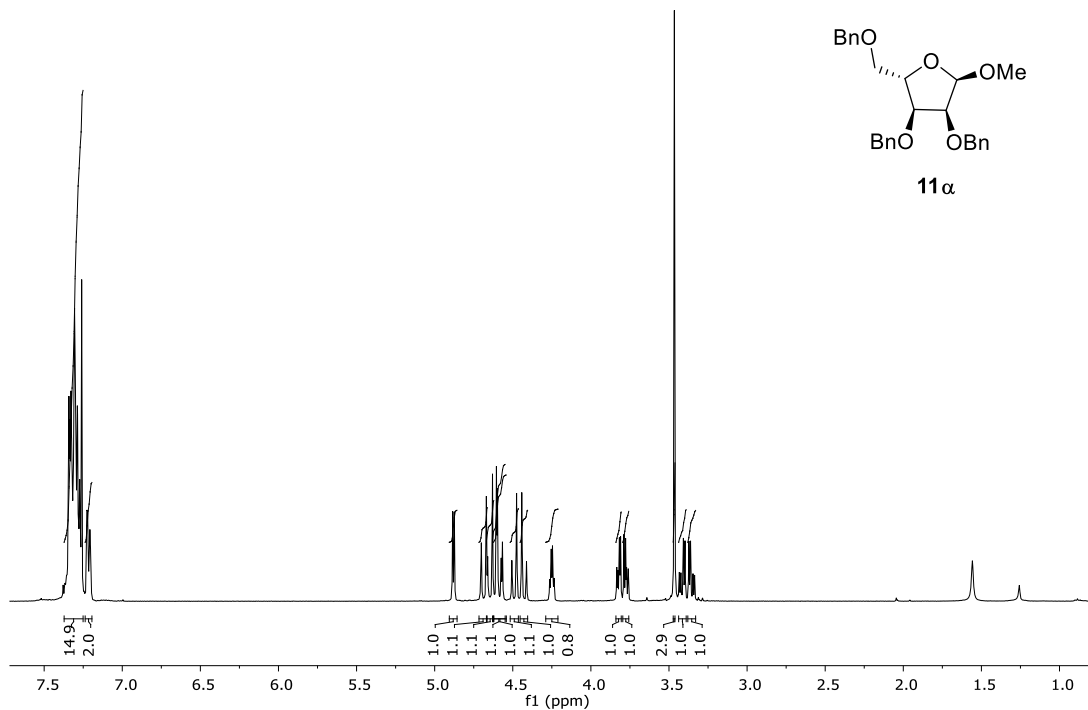


$^{13}\text{C-NMR}$ (100 MHz, CD_3OD):

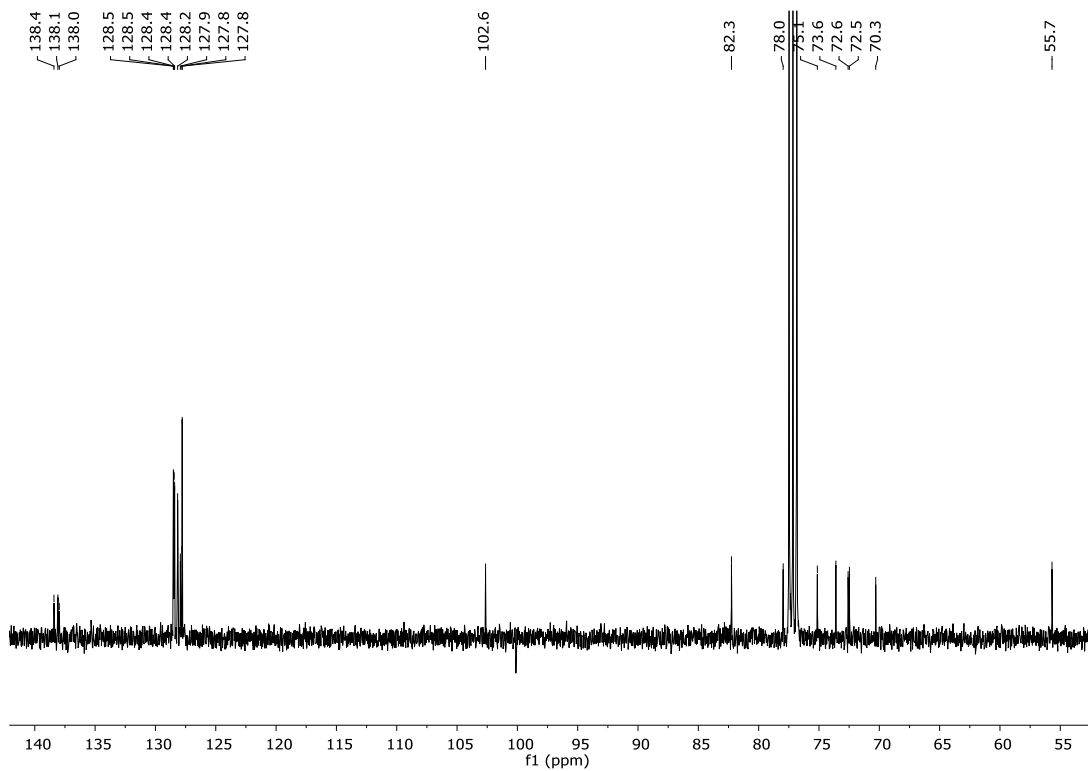


Methyl- α -2,3,5-tri-*O*-benzyl-L-ribofuranoside (11 α)

$^1\text{H-NMR}$ (400 MHz, CDCl_3)

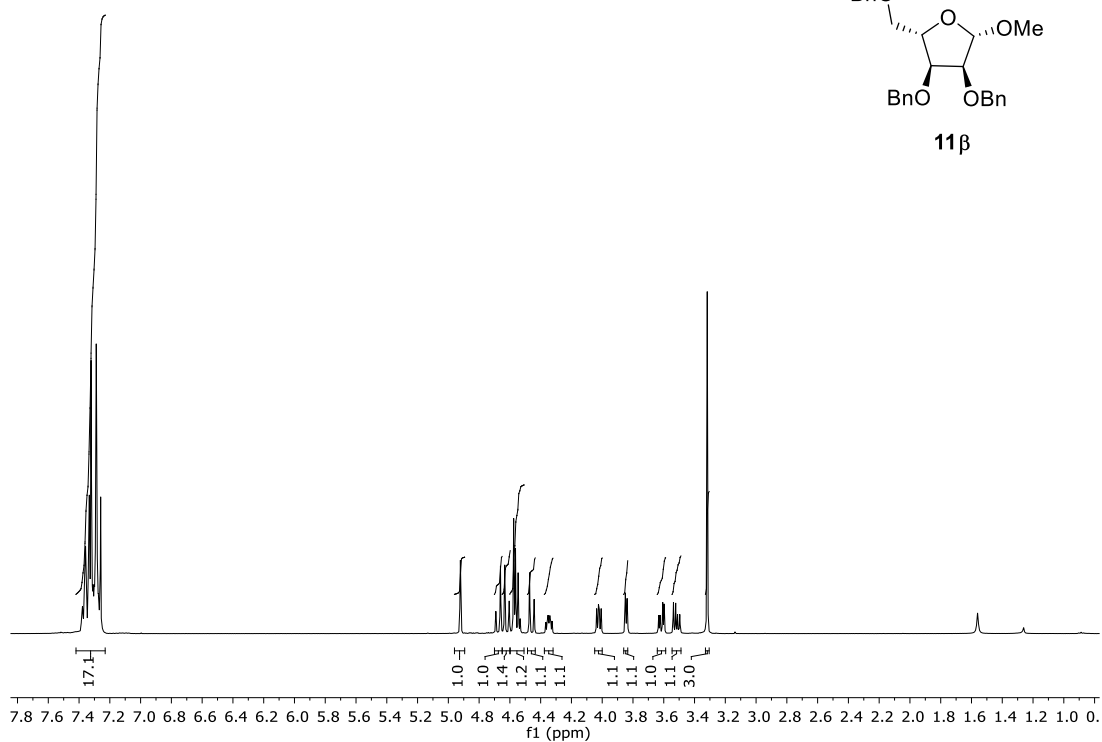
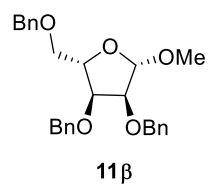


$^{13}\text{C-NMR}$ (100 MHz, CDCl_3):

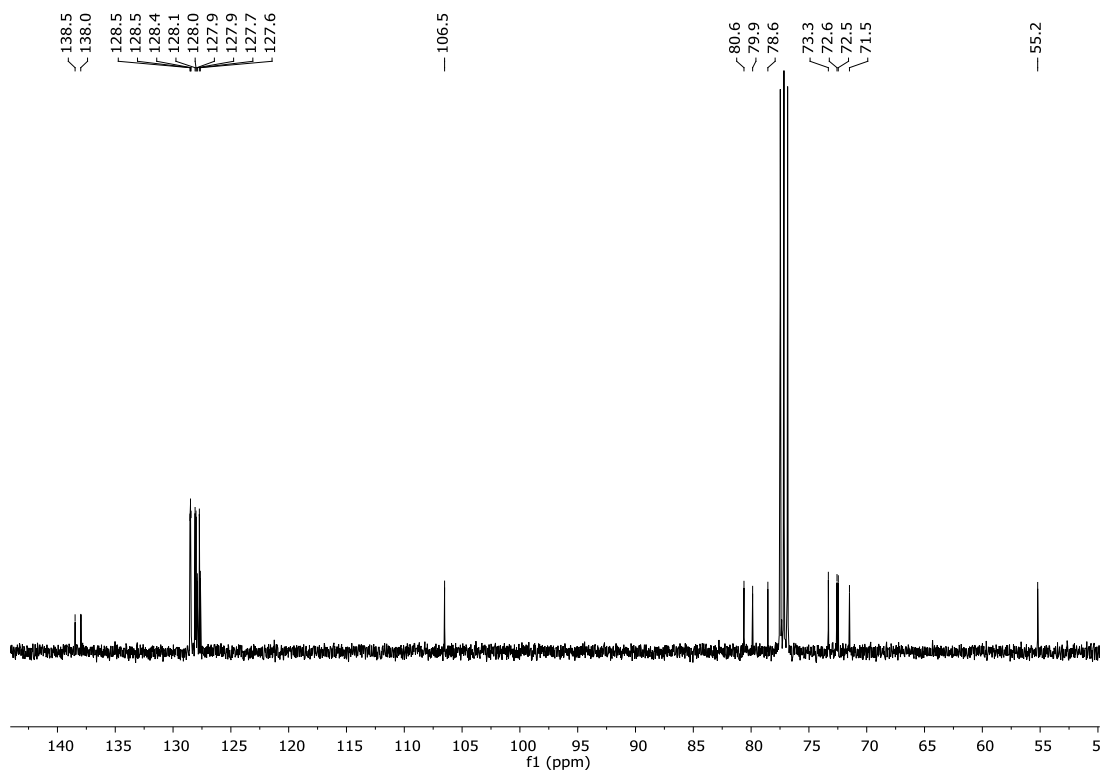


Methyl- β -2,3,5-tri-*O*-benzyl-L-ribofuranoside (11 β):

$^1\text{H-NMR}$ (400 MHz, CDCl_3)

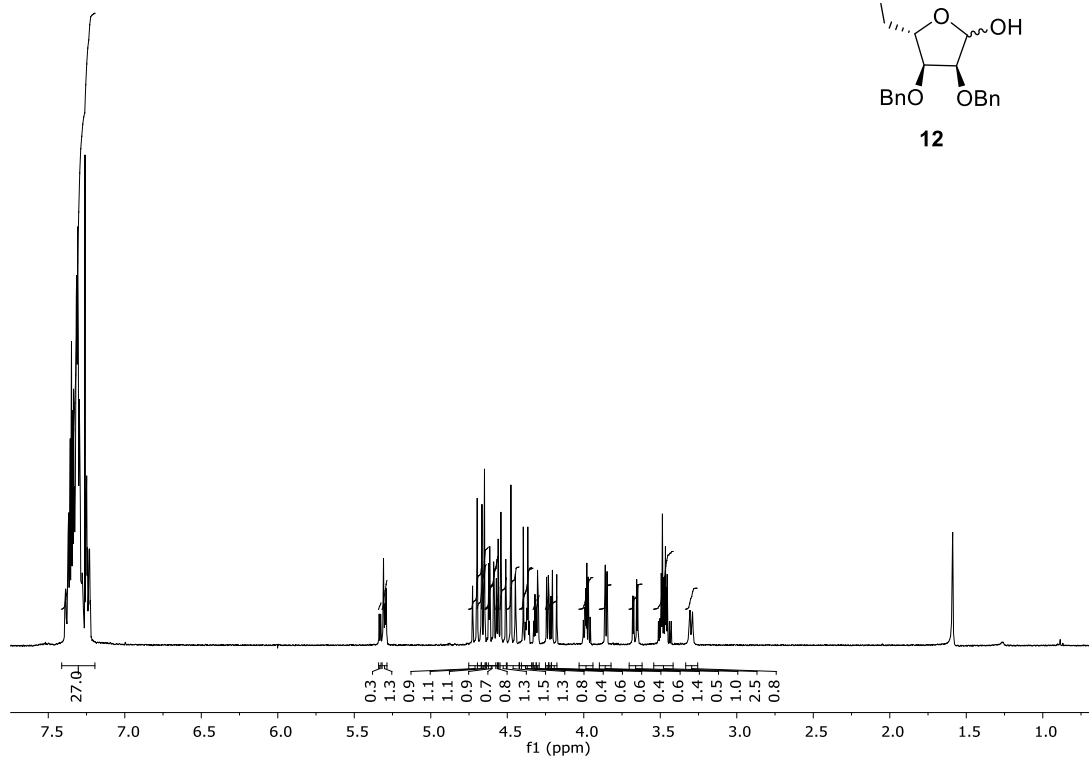
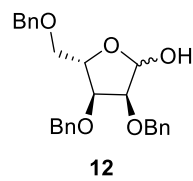


$^{13}\text{C-NMR}$ (100 MHz, CDCl_3):

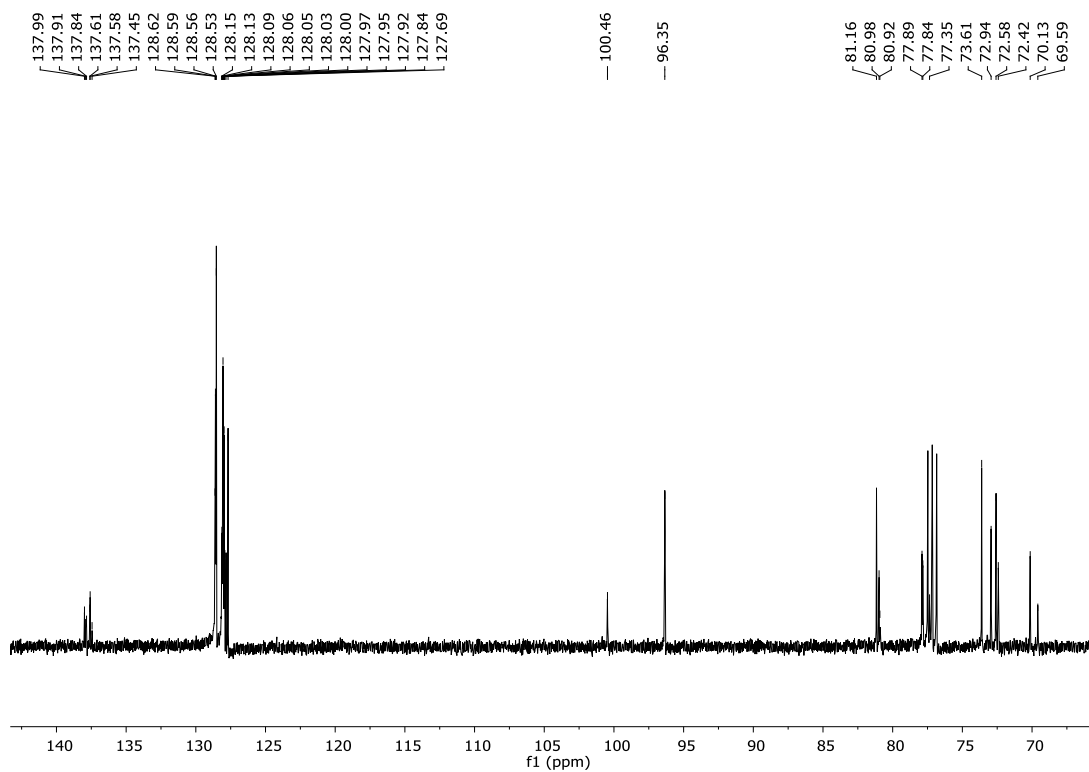


2,3,5-tri-*O*-benzyl-L-ribofuranose (12):

$^1\text{H-NMR}$ (400 MHz, CDCl_3)

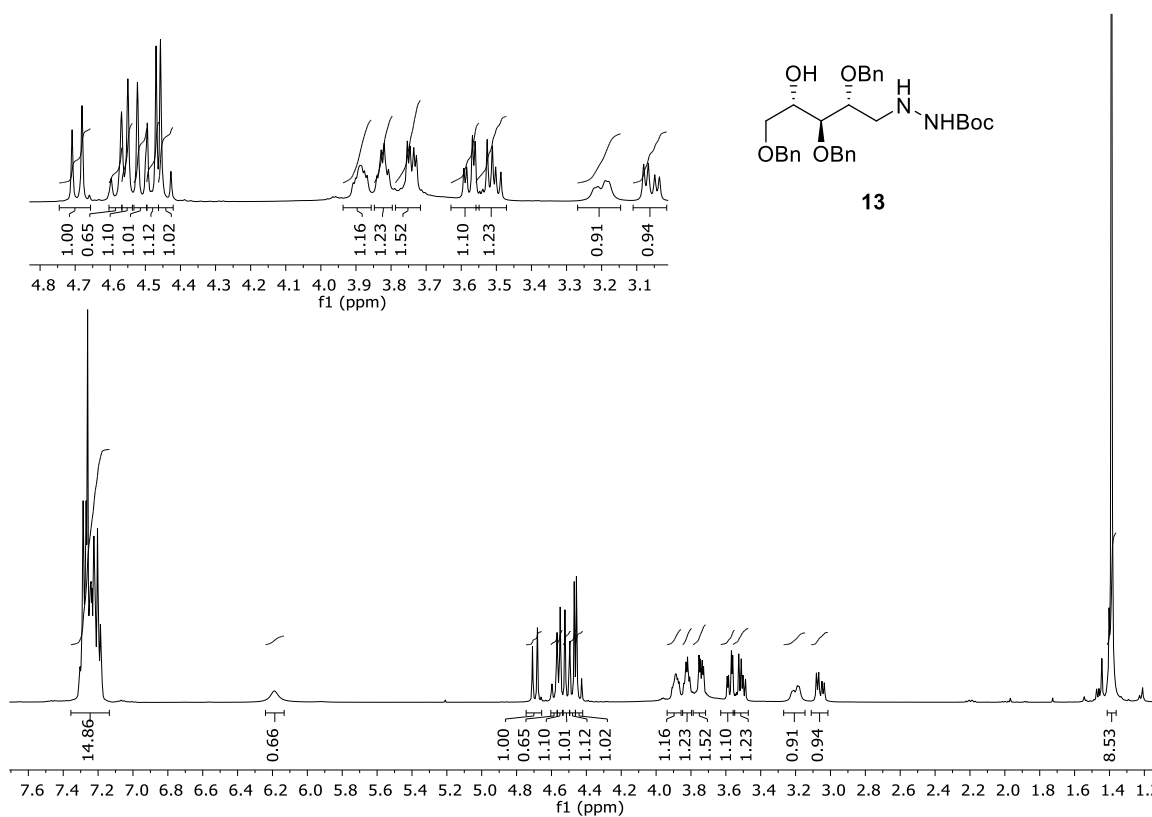


$^{13}\text{C-NMR}$ (100 MHz, CDCl_3):

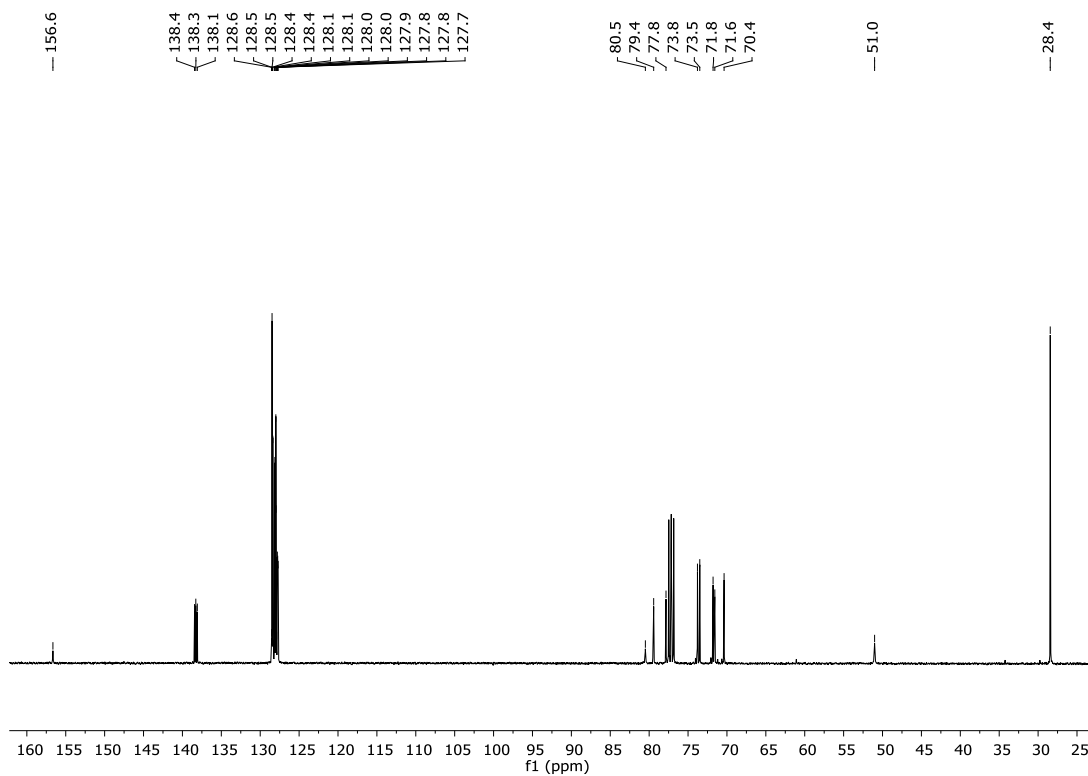


1-(*tert*-butyloxycarbonyl)hydrazino-1-deoxy-2,3,5-tri-*O*-benzyl-L-ribose (13):

¹H-NMR (400 MHz, CDCl₃)

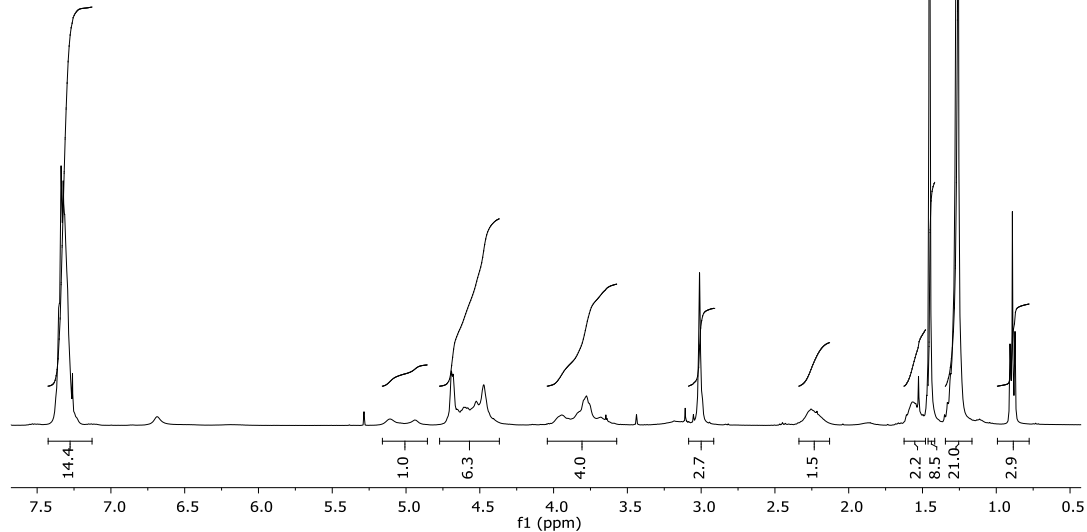
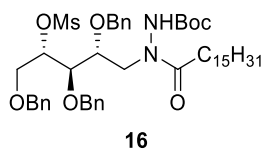


¹³C-NMR (100 MHz, CDCl₃)

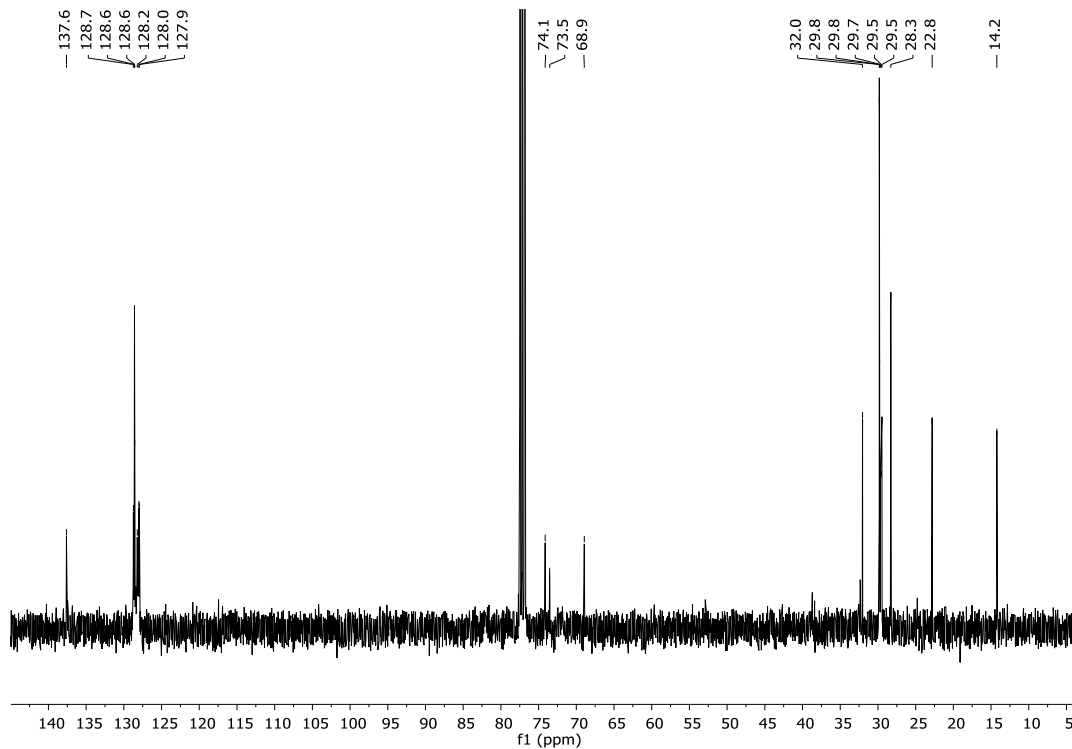


1-(1-Acetyl-2-hexadecyl)hydrazino-1-deoxy-2,3,5-tri-O-benzyl-4-methanesulfonyl-L-ribose (16):

¹H NMR (400 MHz, CDCl₃):

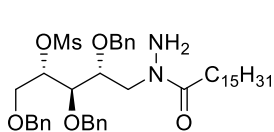


¹³C NMR (100 MHz, CDCl₃):

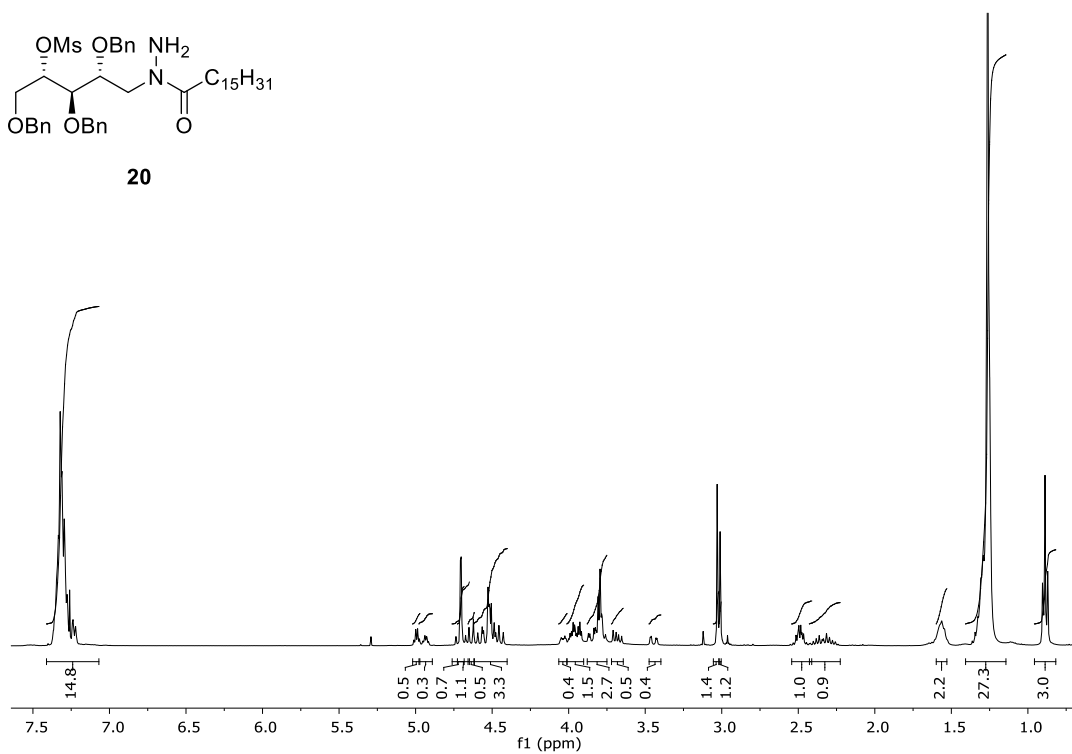


1-(2-palmitoyl)hydrazino-1-deoxy-2,3,5-tri-O-benzyl-4-methanesulfonyl-L-ribose (20):

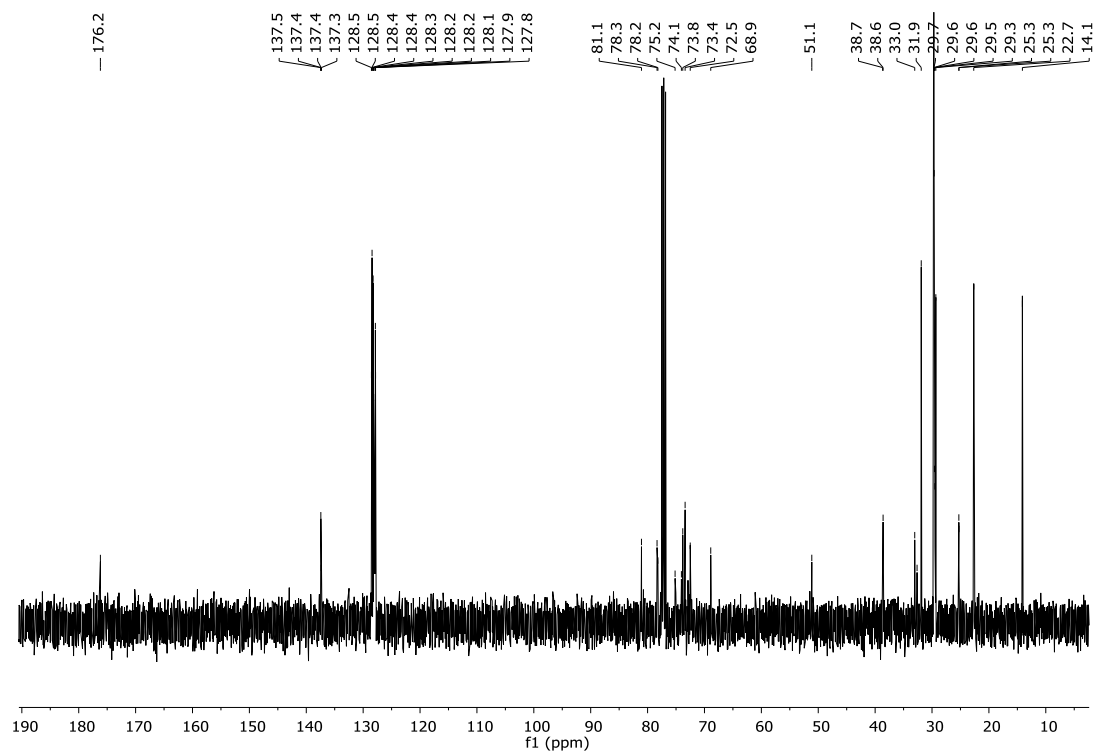
^1H NMR (400 MHz, CDCl_3):



20

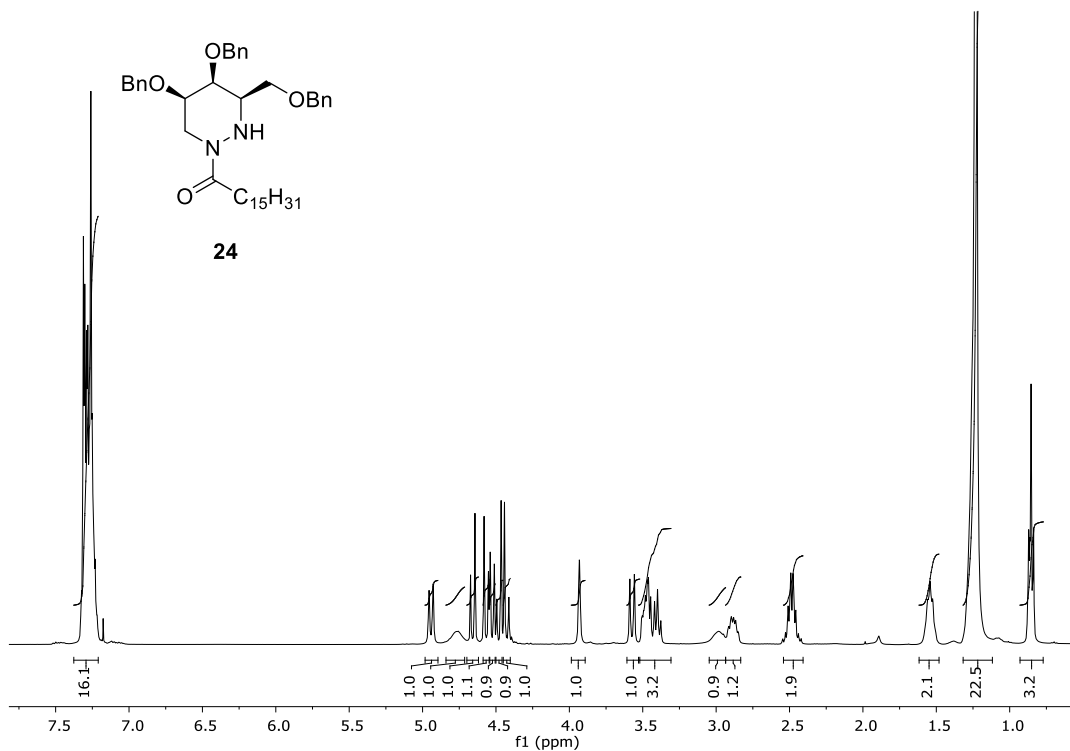


^{13}C NMR (100 MHz, CDCl_3):

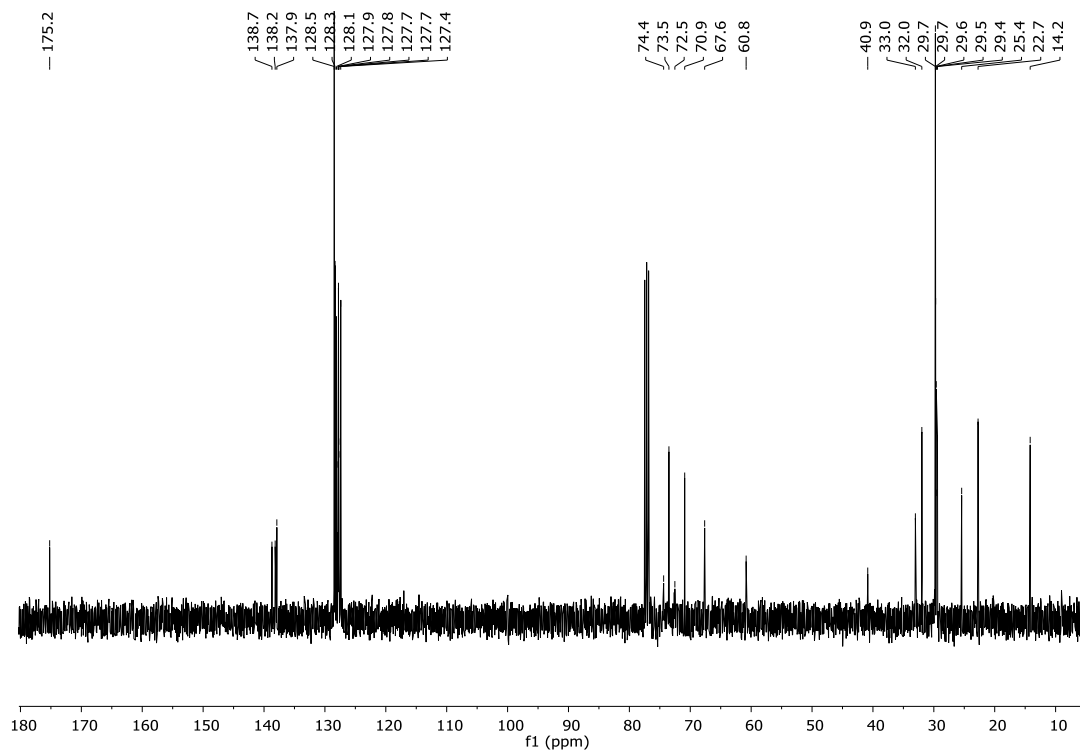


(3R,4S,5R)-1-N-palmitoyl-3-benzoxymethyl-4,5-di-O-benzyl-4,5-dihydroxyhexahydropyridazine (24):

¹H NMR (400 MHz, CDCl₃):

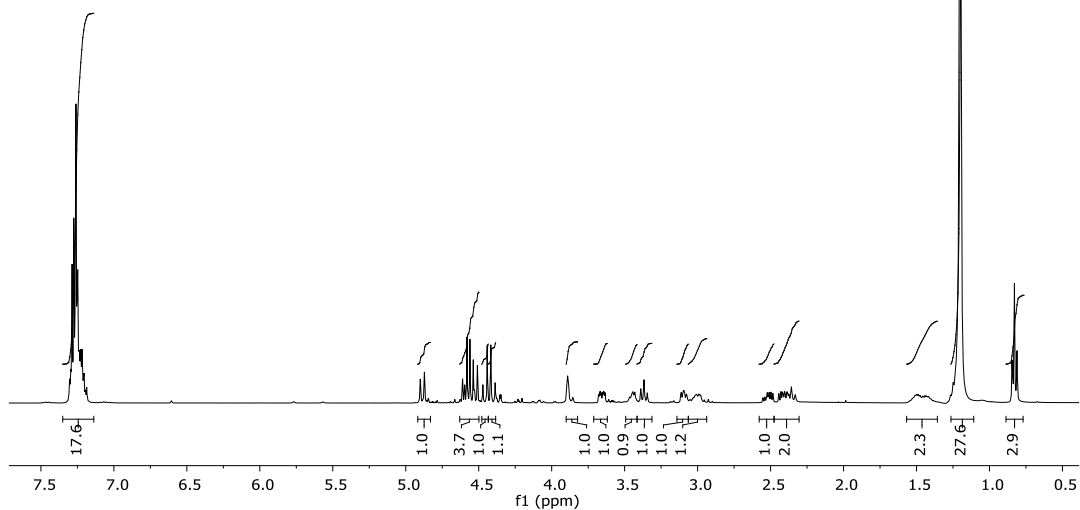
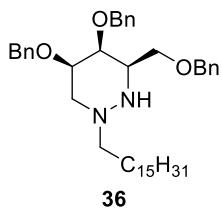


¹³C NMR (100 MHz, CDCl₃):

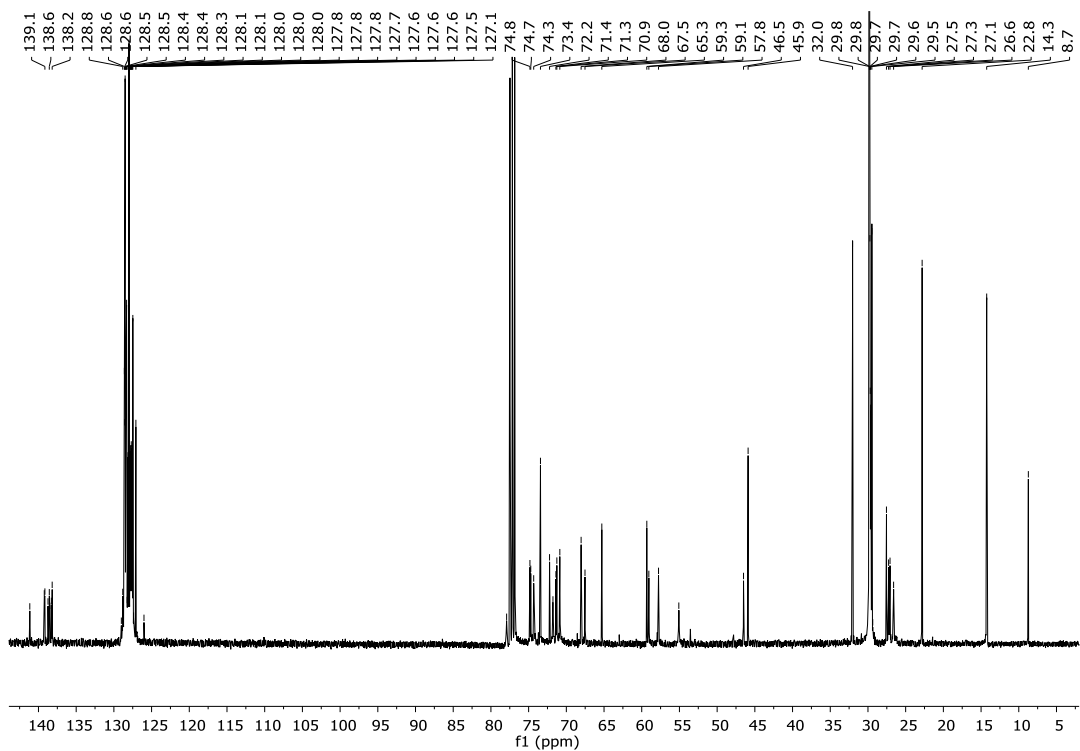


(3R,4S,5R)-1-N-palmityl-3-benzyloxymethyl-4,5-di-O-benzyl-4,5-dihydroxyhexahydropyridazine (36):

¹H NMR (400 MHz, CDCl₃):

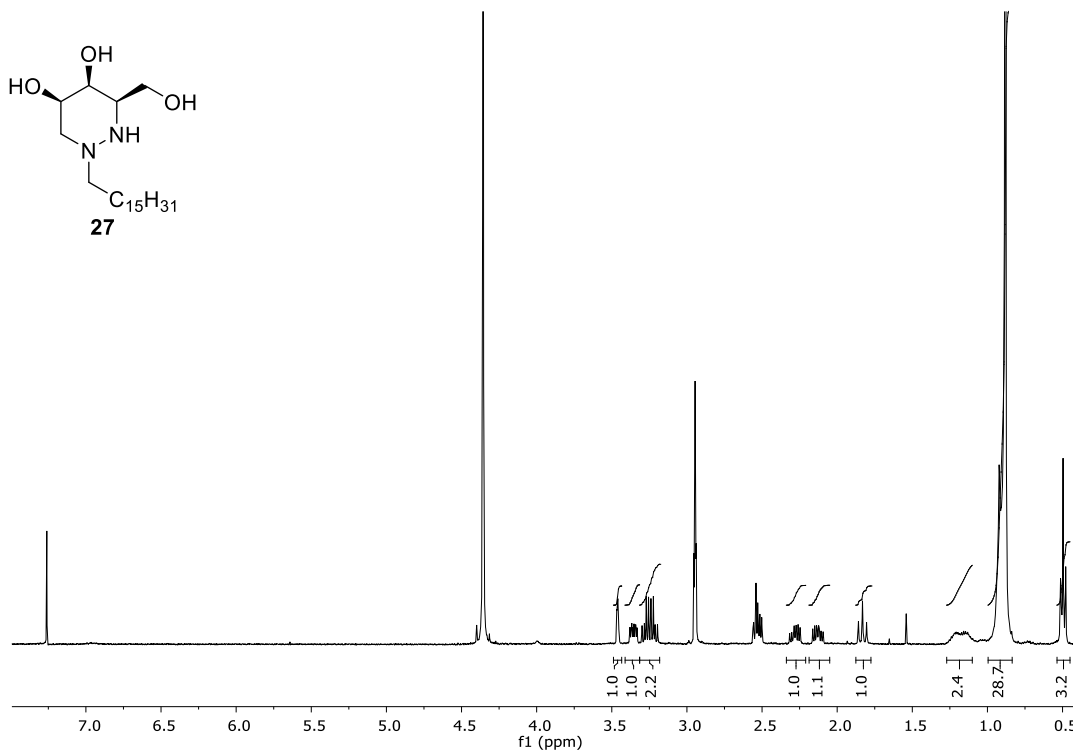


¹³C NMR (100 MHz, CDCl₃):

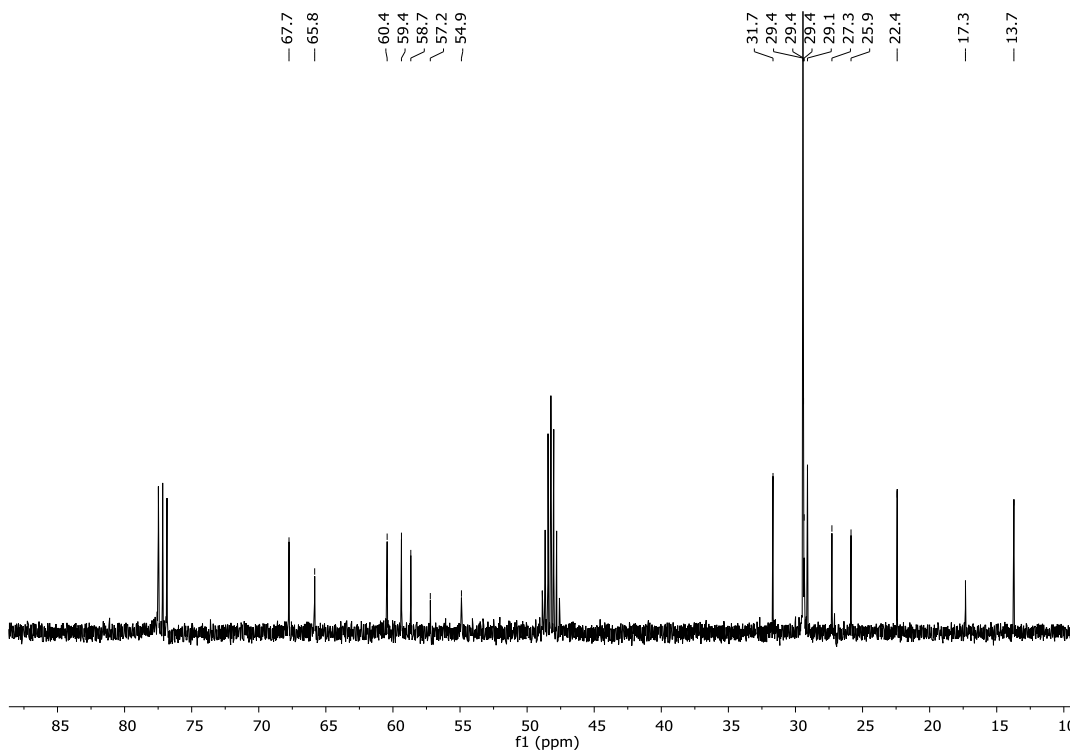


***N*-1-palmityl-azagalactofagomine (27):**

¹H NMR (400 MHz, 6:4 CD₃OD:CDCl₃):

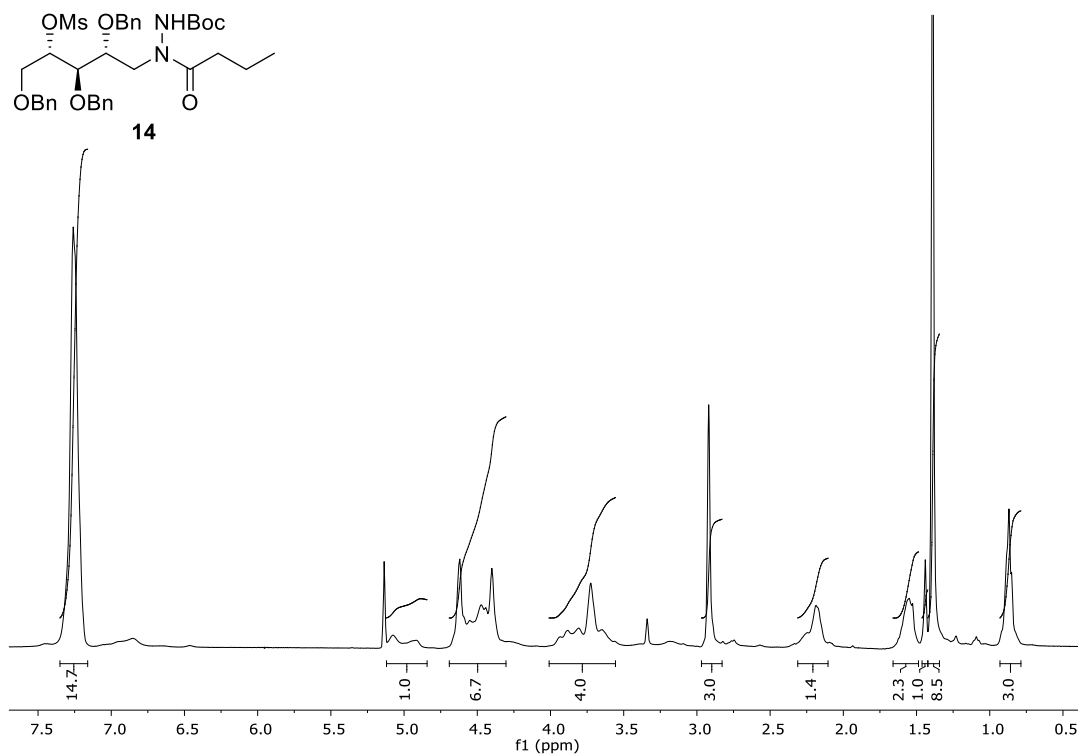


¹³C NMR (100 MHz, 6:4:1 CDCl₃:CD₃OD:D₂O):

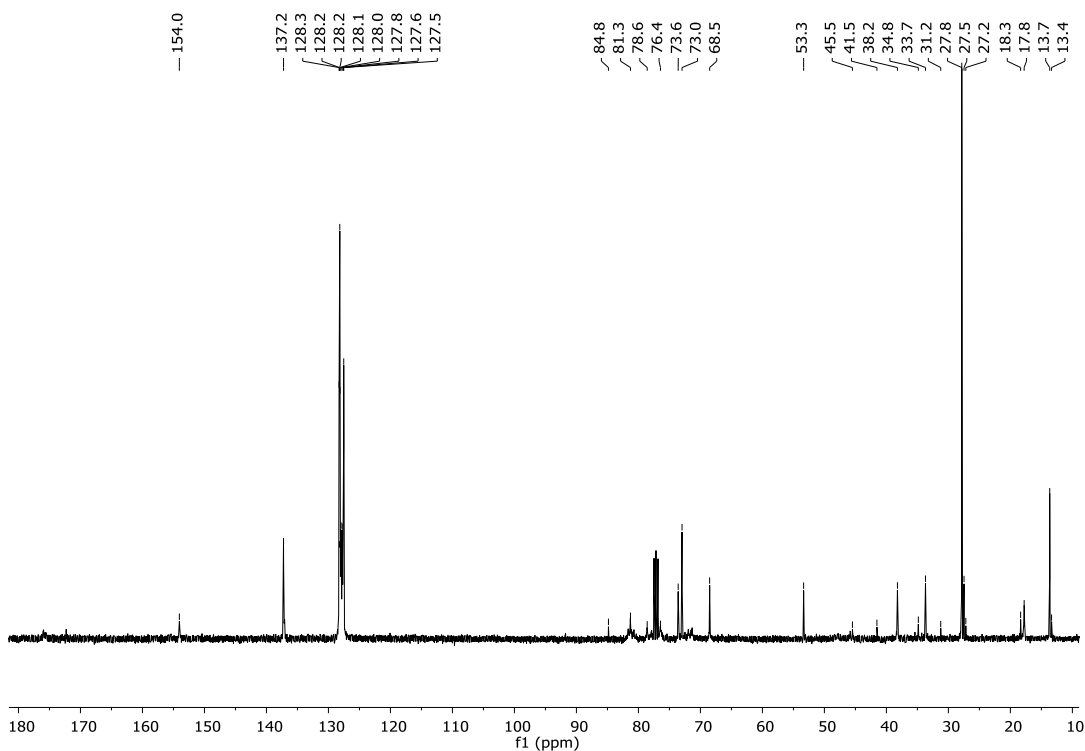


1-(1-Acetyl-2-butanoyl)hydrazino-1-deoxy-2,3,5-tri-O-benzyl-4-methanesulfonyl-L-ribose (14):

¹H NMR (400 MHz, CDCl₃):

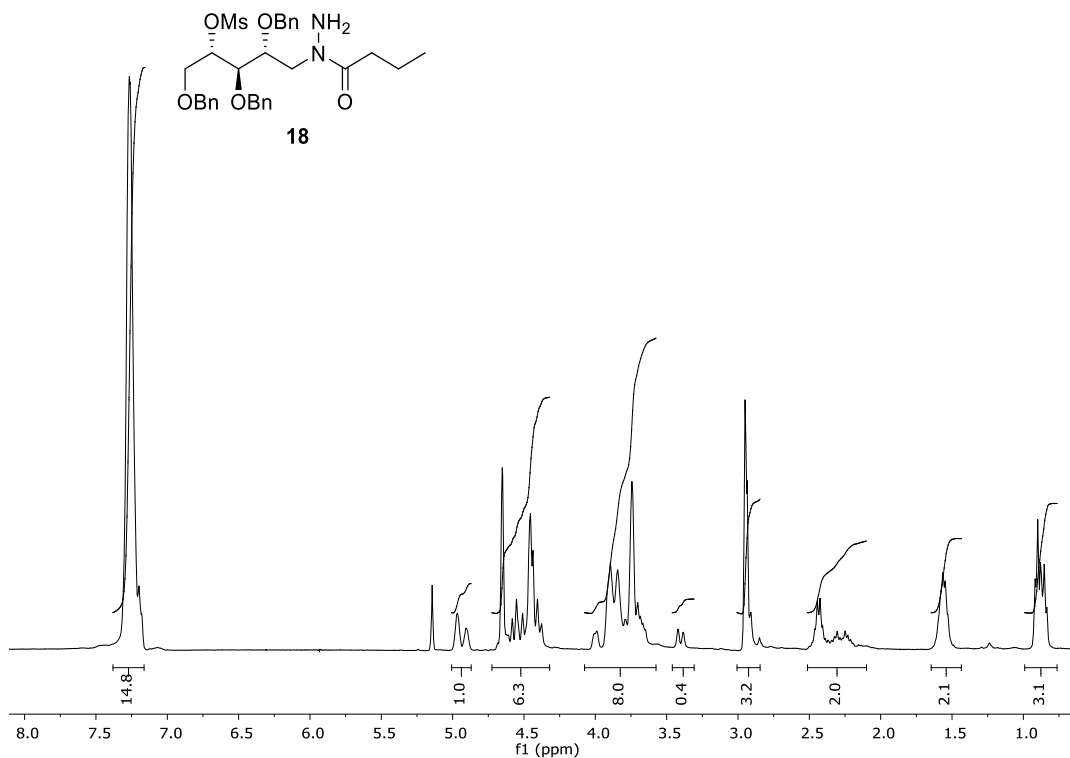


¹³C NMR (100 MHz, CDCl₃):

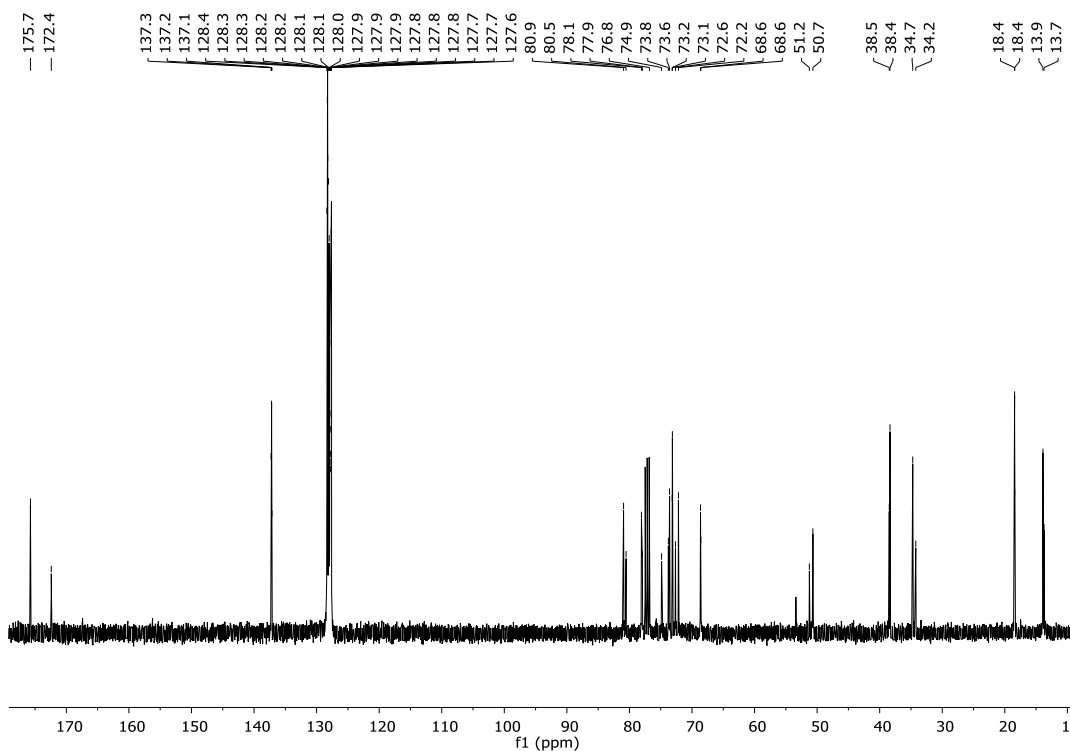


1-(1-butanoyl)hydrazino-1-deoxy-2,3,5-tri-O-benzyl-4-methanesulfonyl-L-ribose (18):

¹H NMR (400 MHz, CDCl₃):

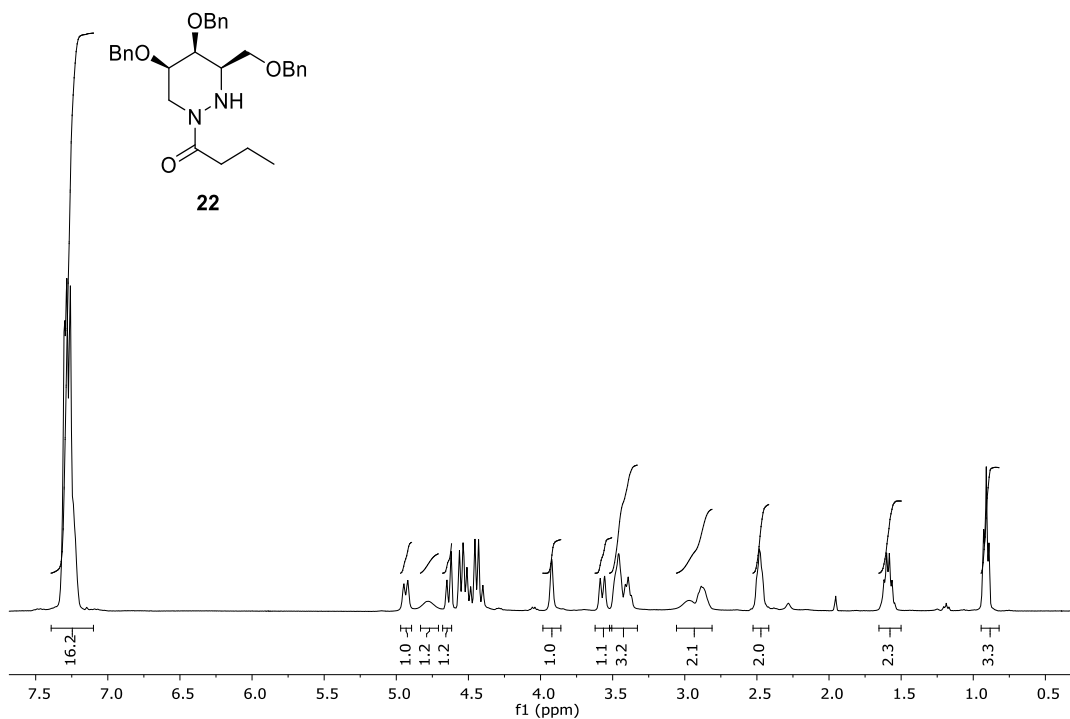


¹³C NMR (100 MHz, CDCl₃):

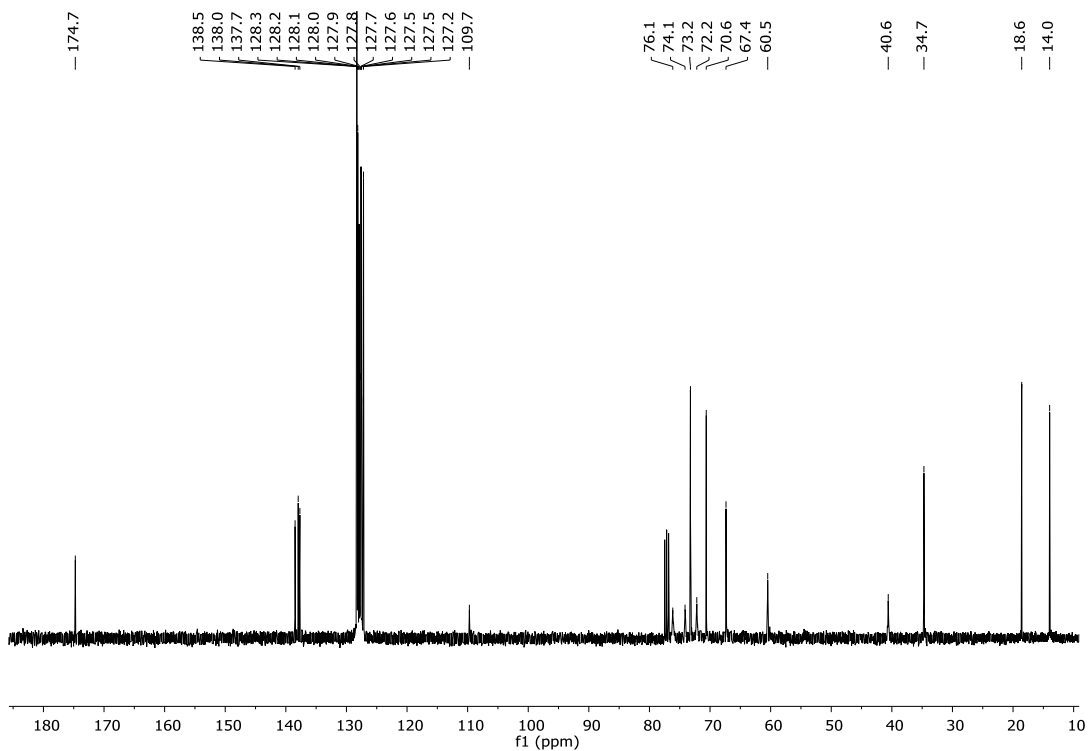


(3R,4S,5R)-1-N-butanoyl-3-benzyloxymethyl-4,5-di-O-benzyl-4,5-dihydroxyhexahydropyridazine (22):

¹H-NMR (400 MHz, CDCl₃):

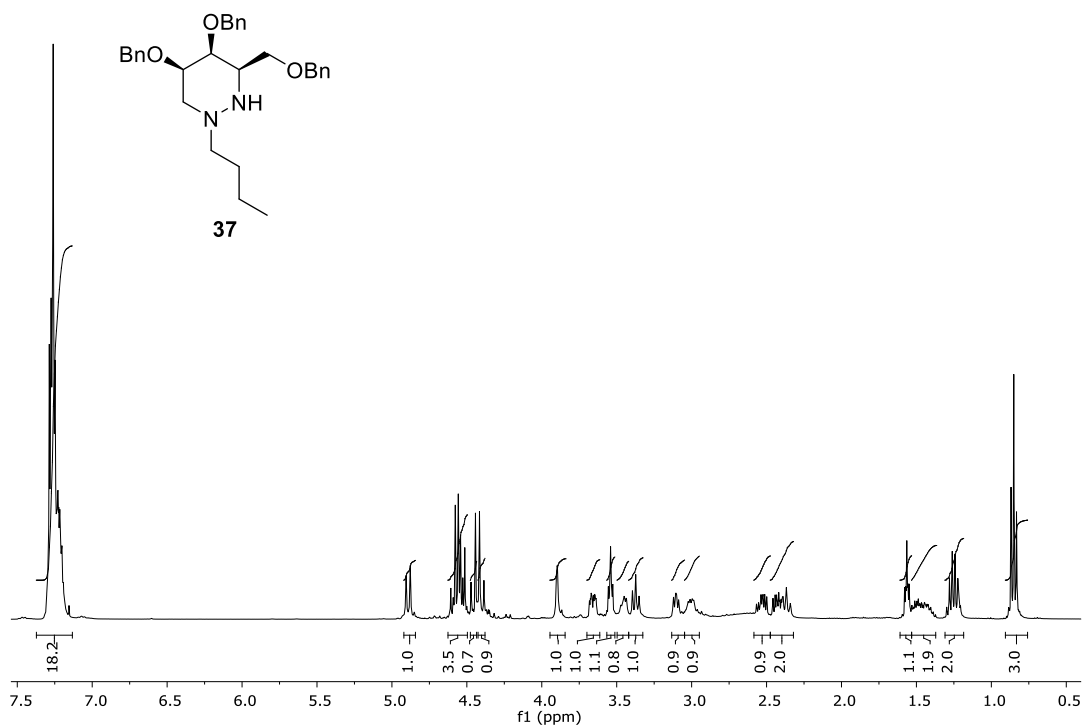


¹³C-NMR (100 MHz, CDCl₃):

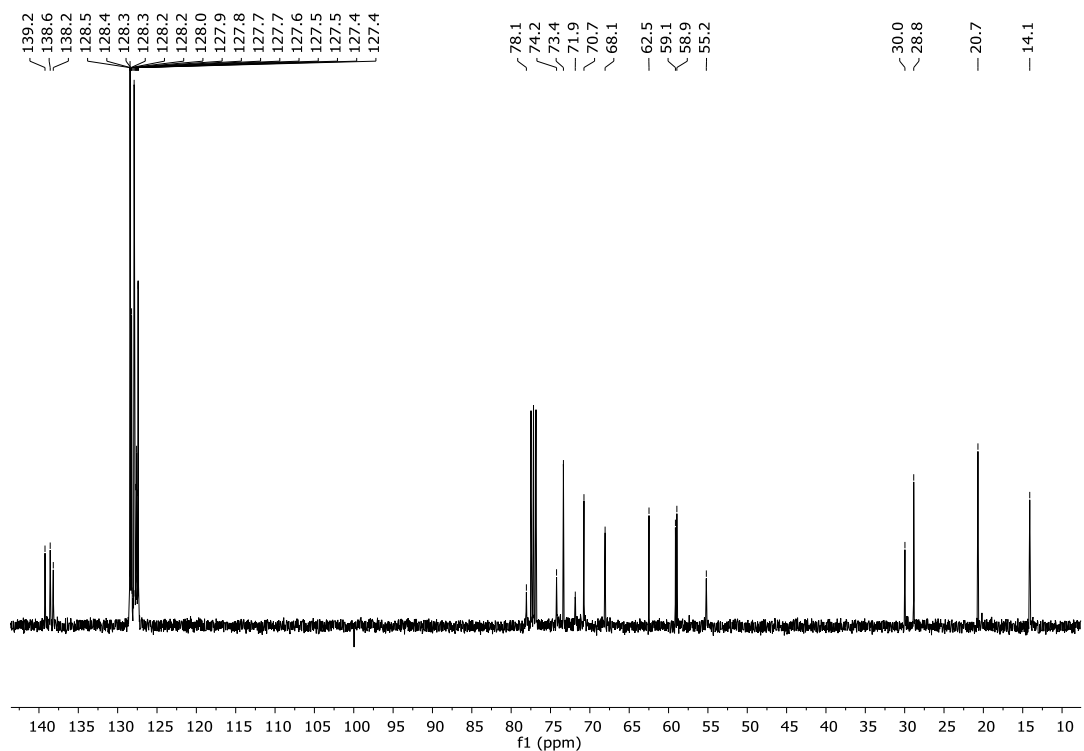


(3R,4S,5R)-1-N-butanyl-3-benzyloxymethyl-4,5-di-O-benzyl-4,5-dihydroxyhexahydropyridazine (37):

¹H NMR (400 MHz, CDCl₃):

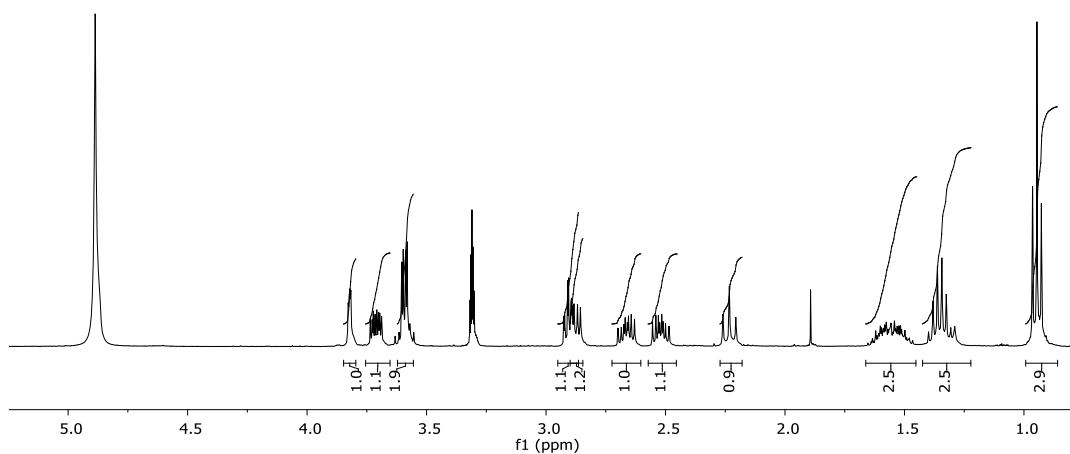
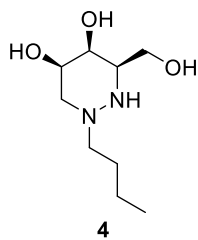


¹³C-NMR (100 MHz, CDCl₃):

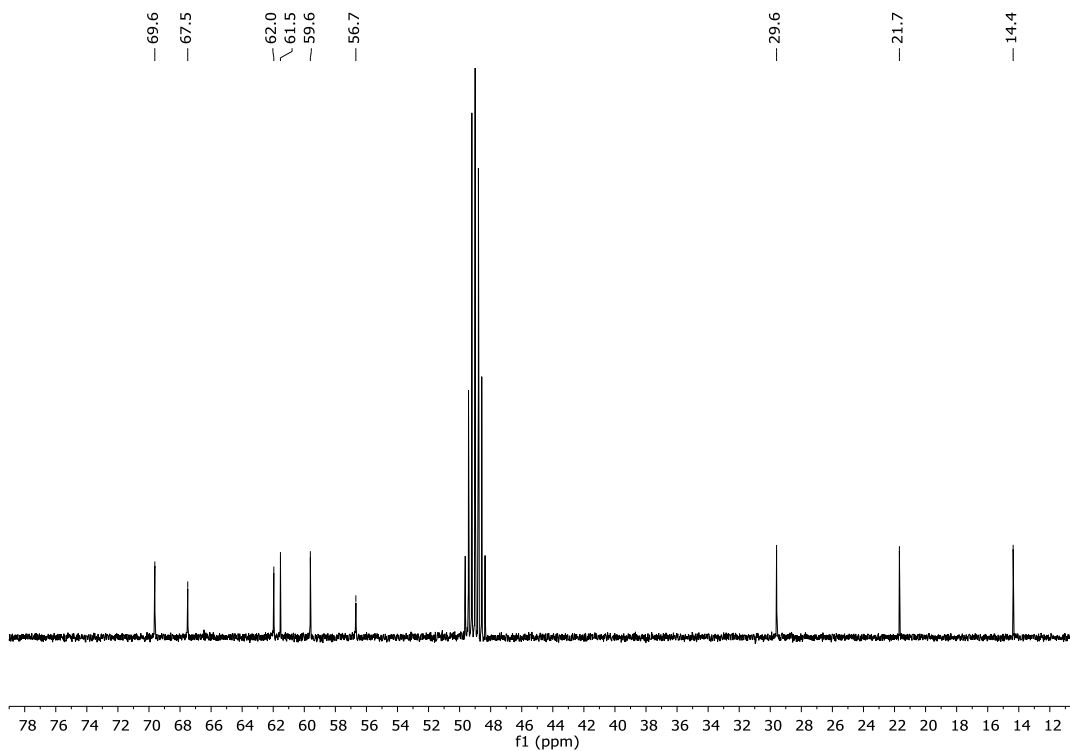


***N*-1-butyl-azagalactofagomine (4):**

¹H-NMR (400 MHz, CD₃OD):

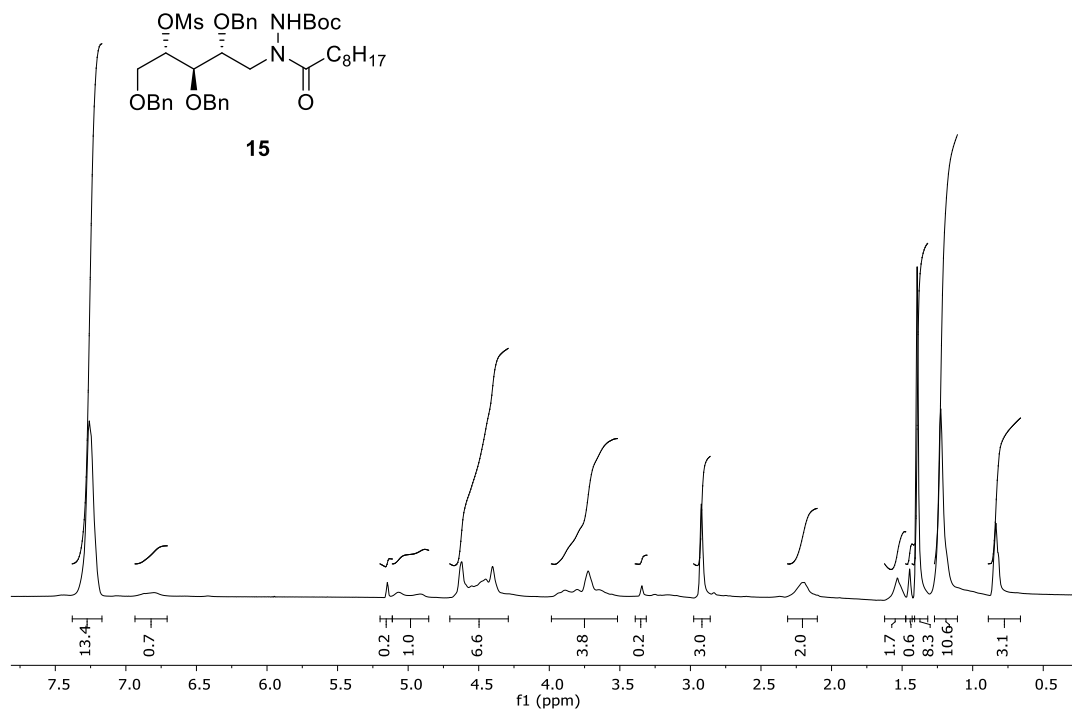


¹³C-NMR (100 MHz, CD₃OD):

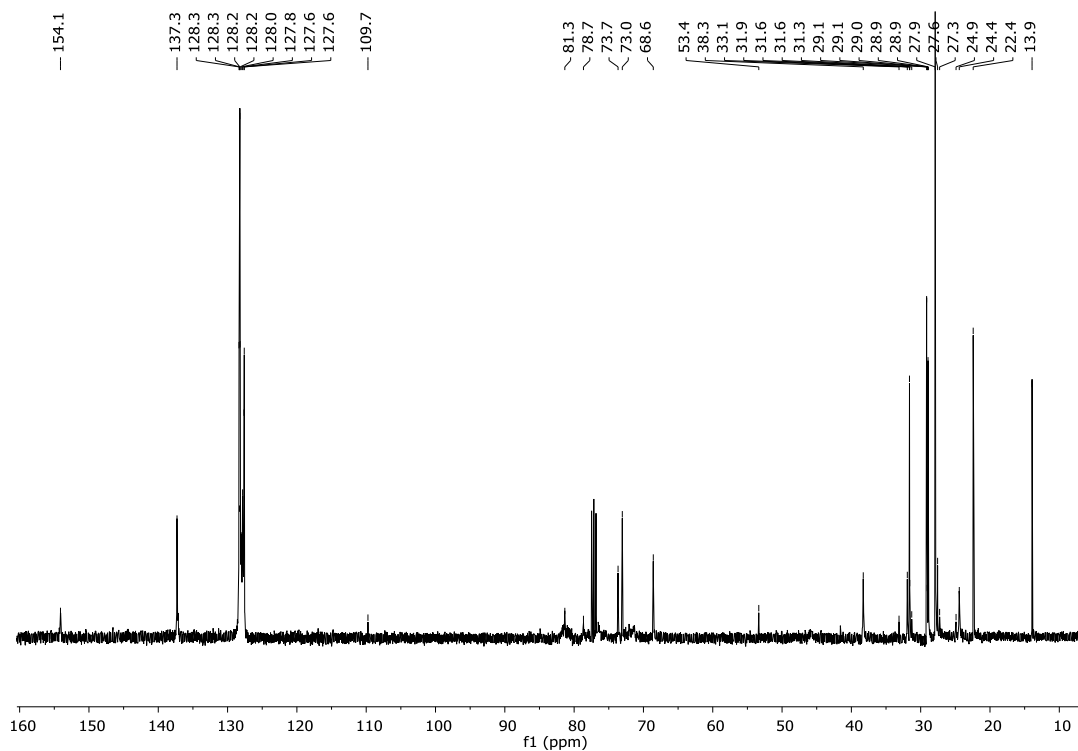


1-(1-octanoyl-2-*tert*-butyloxycarbonyl)hydrazino-1-deoxy-2,3,5-tri-*O*-benzyl-4-methanesulfonyl-L-ribose (15):

¹H-NMR (400 MHz, CDCl₃):

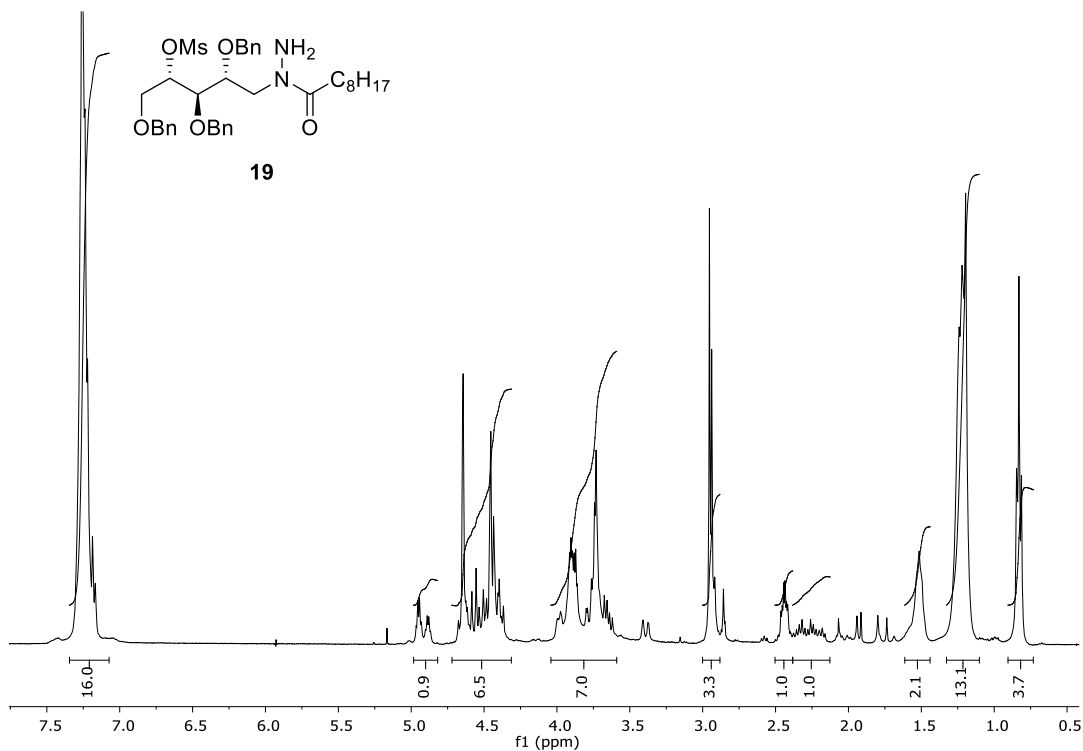


¹³C-NMR (100 MHz, CDCl₃):

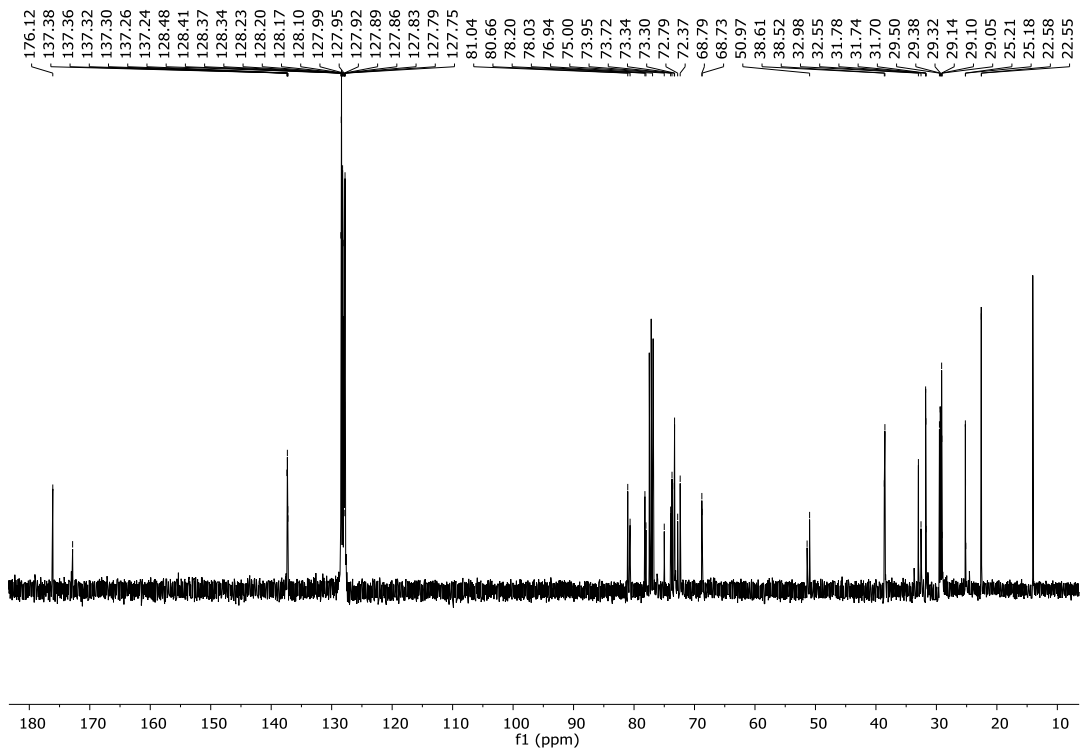


1-(1-nonanoyl)hydrazino-1-deoxy-2,3,5-tri-O-benzyl-4-methanesulfonyl-L-ribose (19):

¹H-NMR (400 MHz, CDCl₃):

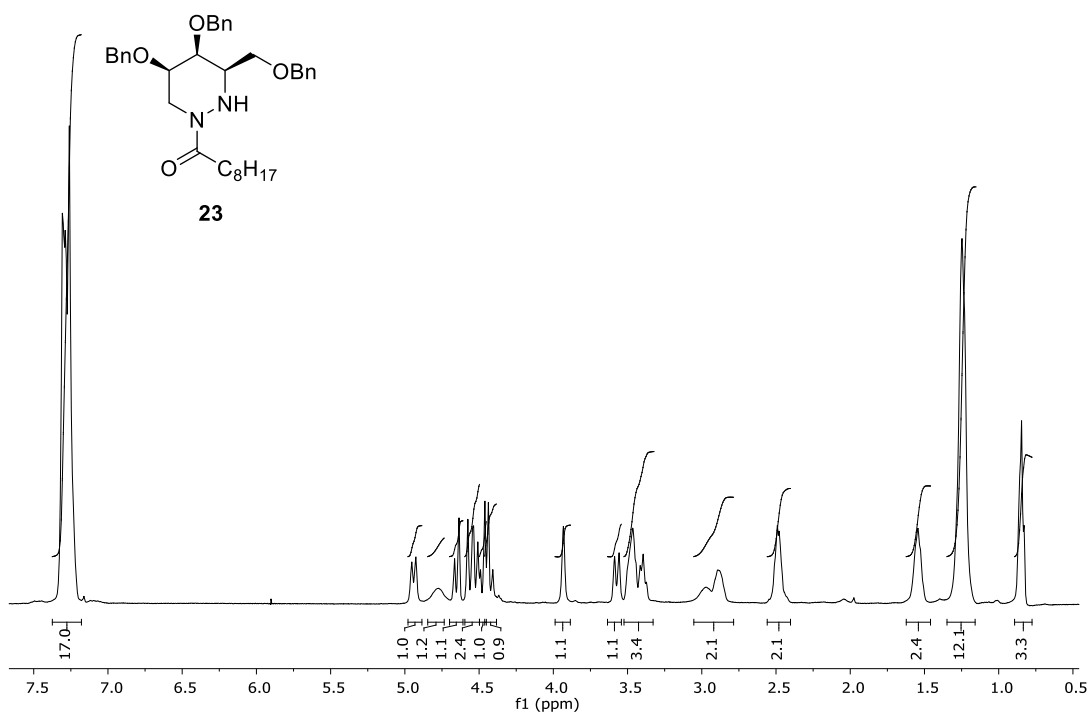


¹³C-NMR (100 MHz, CDCl₃):

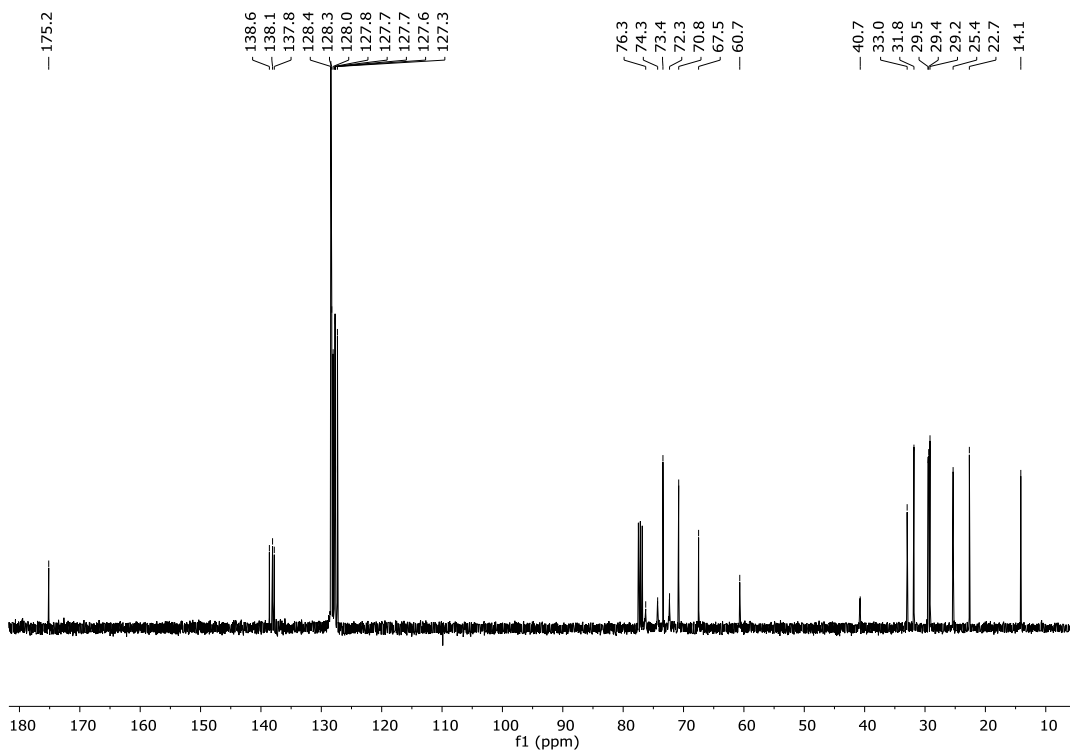


(3*R*,4*S*,5*R*)-1-*N*-nonanoyl-3-benzyloxymethyl-4,5-di-*O*-benzyl-4,5-dihydroxyhexahydropyridazine (23):

¹H-NMR (400 MHz, CDCl₃):

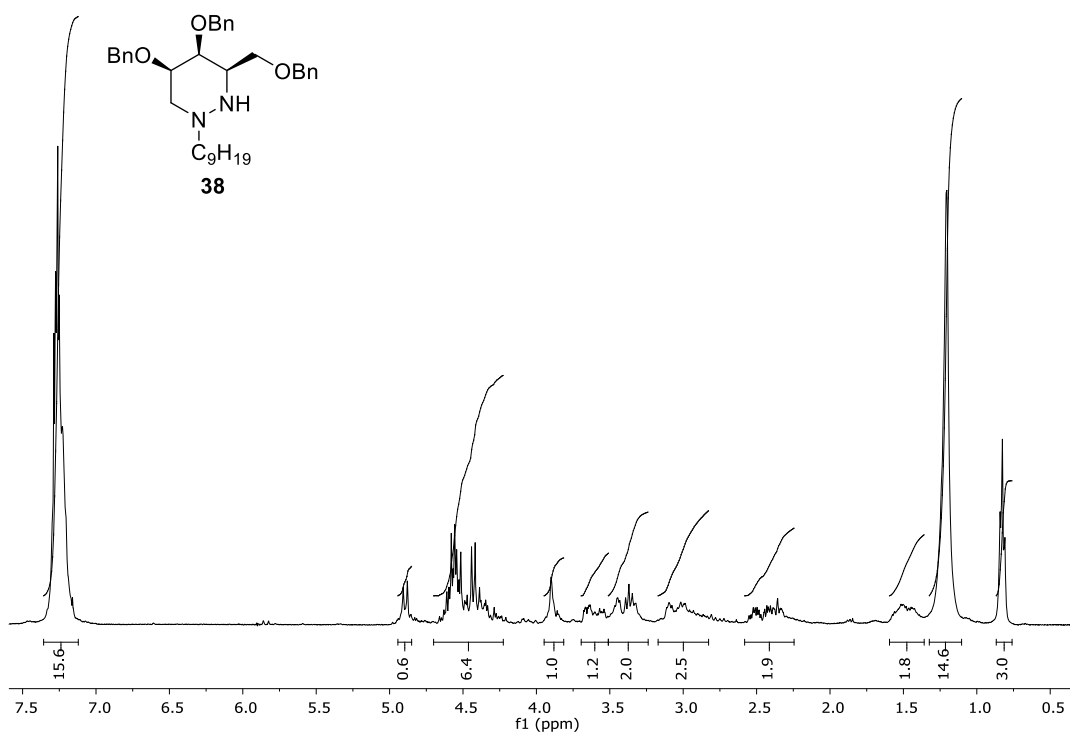


¹³C-NMR (100 MHz, CDCl₃):

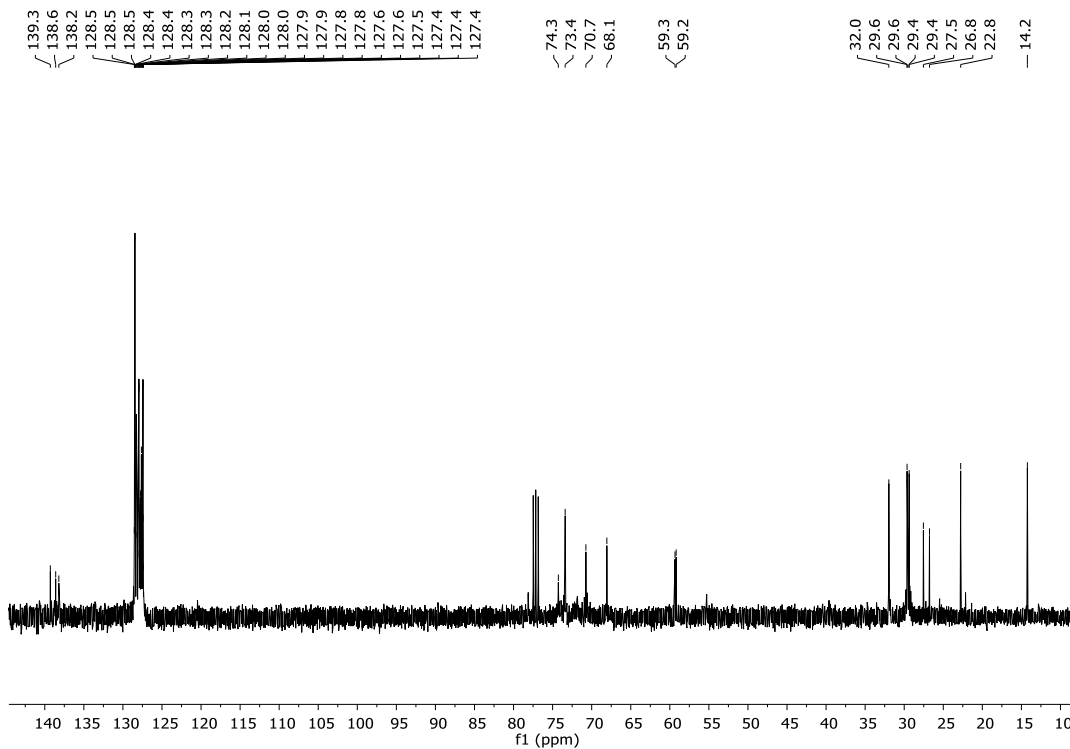


(3R,4S,5R)-1-N-nonyl-3-benzyloxymethyl-4,5-di-O-benzyl-4,5-dihydroxyhexahydropyridazine (38):

¹H-NMR (400 MHz, CDCl₃):

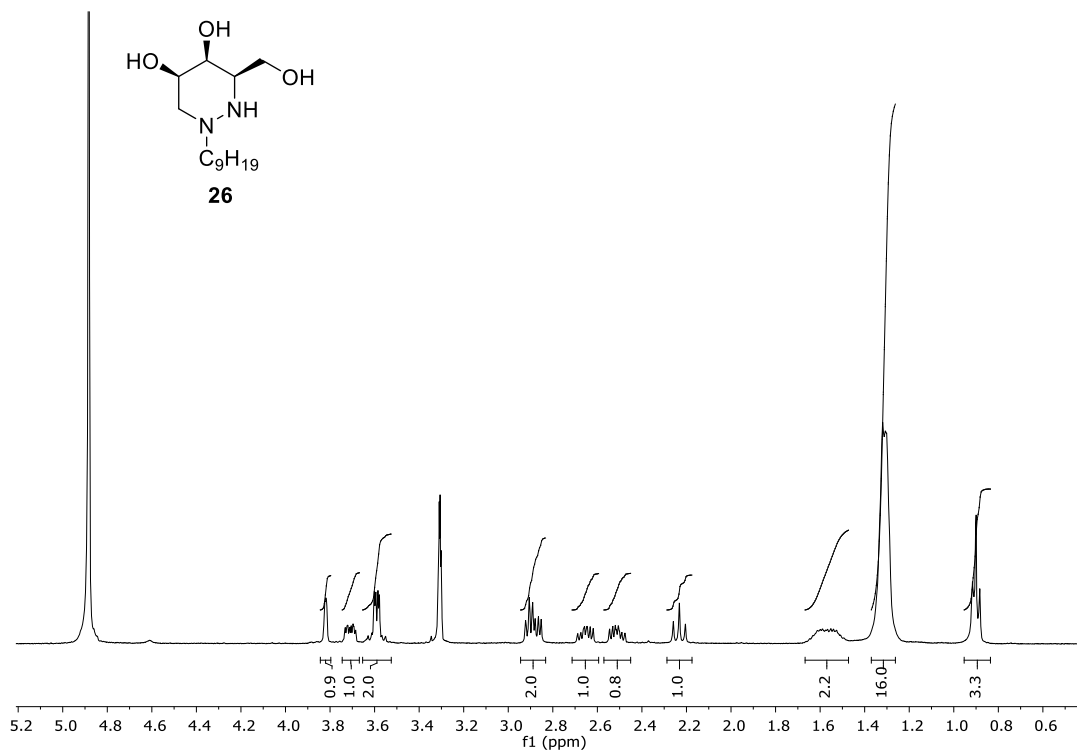


¹³C-NMR (100 MHz, CDCl₃):

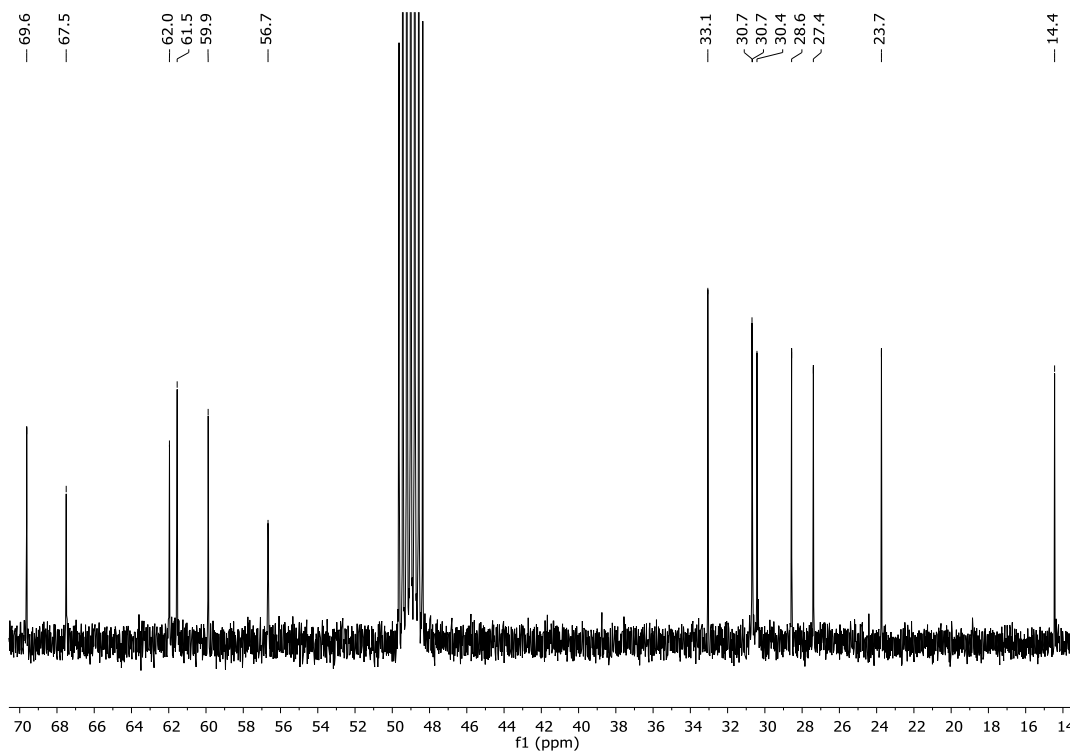


***N*-1-nonyl-azagalactofagomine (26):**

¹H-NMR (400 MHz, CD₃OD):

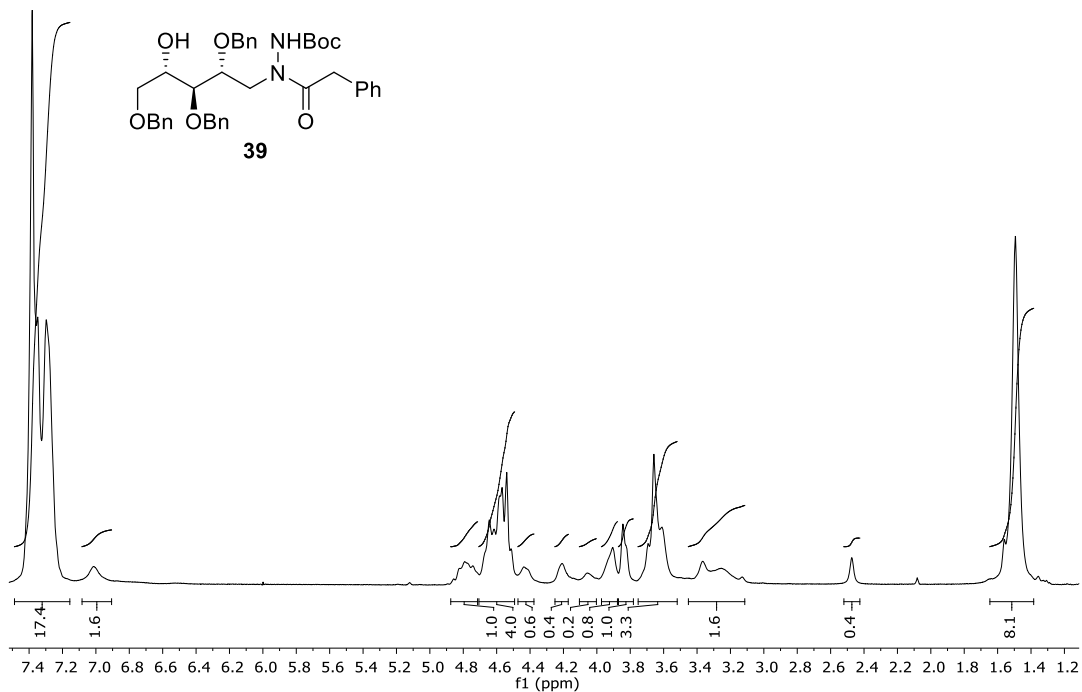


¹³C NMR (100 MHz, CD₃OD):

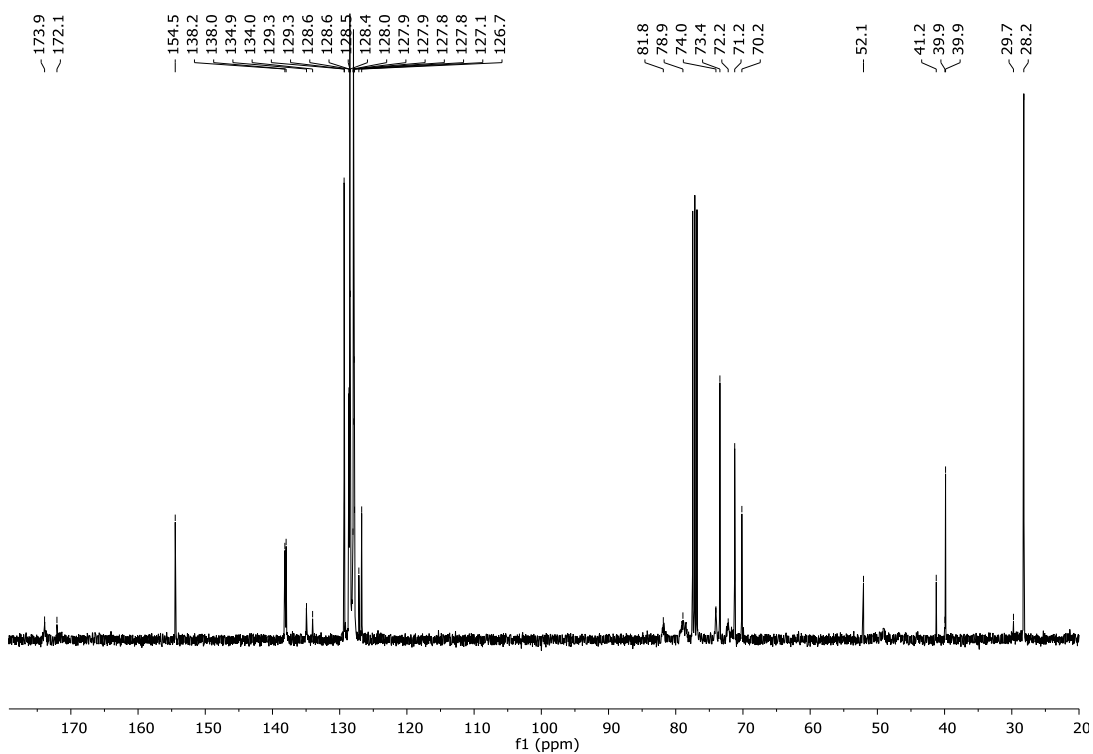


1-(1-phenethanoyl-2-*tert*-butyloxycarbonyl)hydrazino-1-deoxy-2,3,5-tri-*O*-benzyl-4-hydroxy-L-ribose (39):

¹H-NMR (400 MHz, CDCl₃):

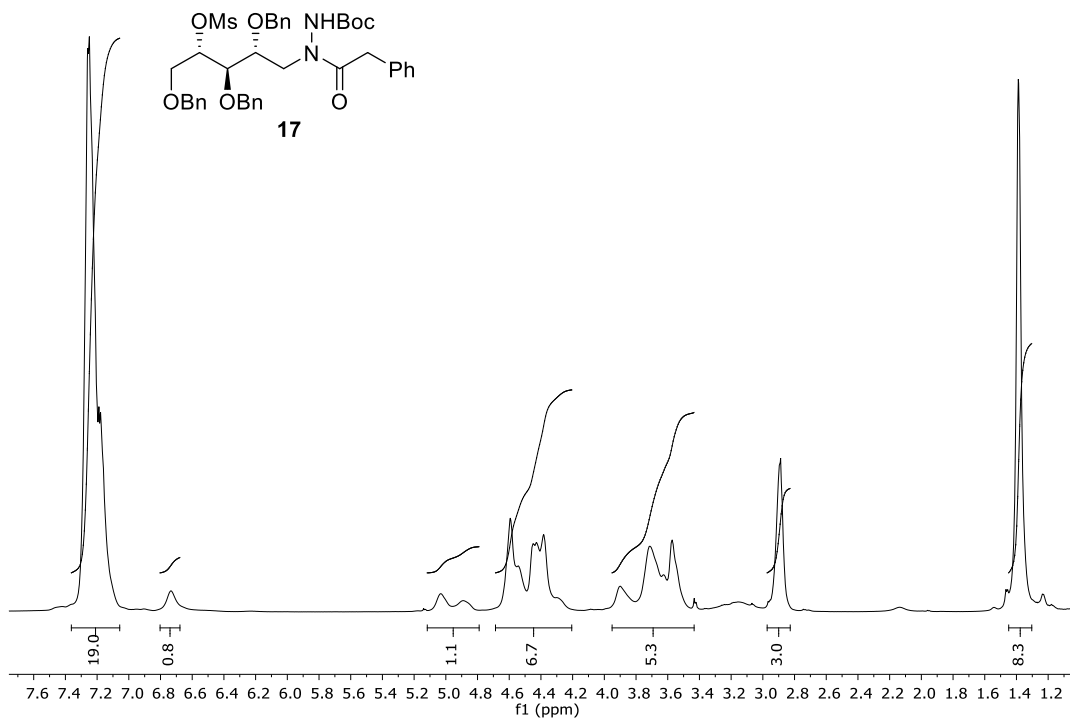


¹³C-NMR (100 MHz, CDCl₃):

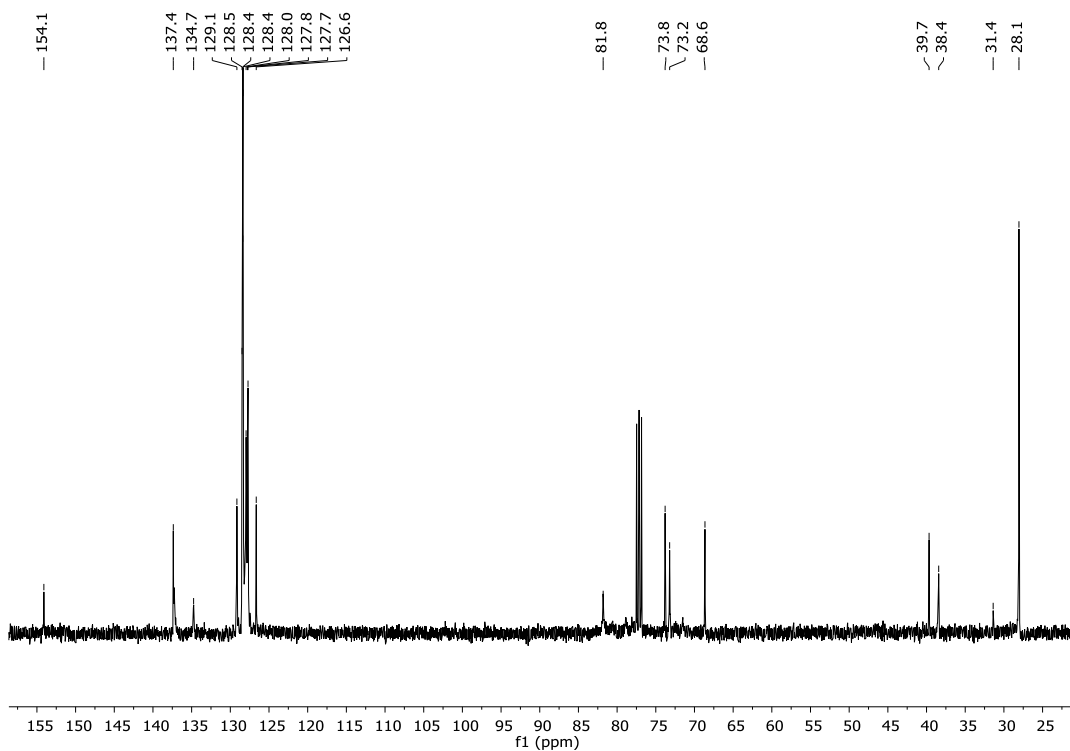


1-(1-phenethanoyl-2-*tert*-butyloxycarbonyl)hydrazino-1-deoxy-2,3,5-tri-*O*-benzyl-4-methanesulfonyl-L-ribose (17):

$^1\text{H-NMR}$ (400 MHz, CDCl_3):

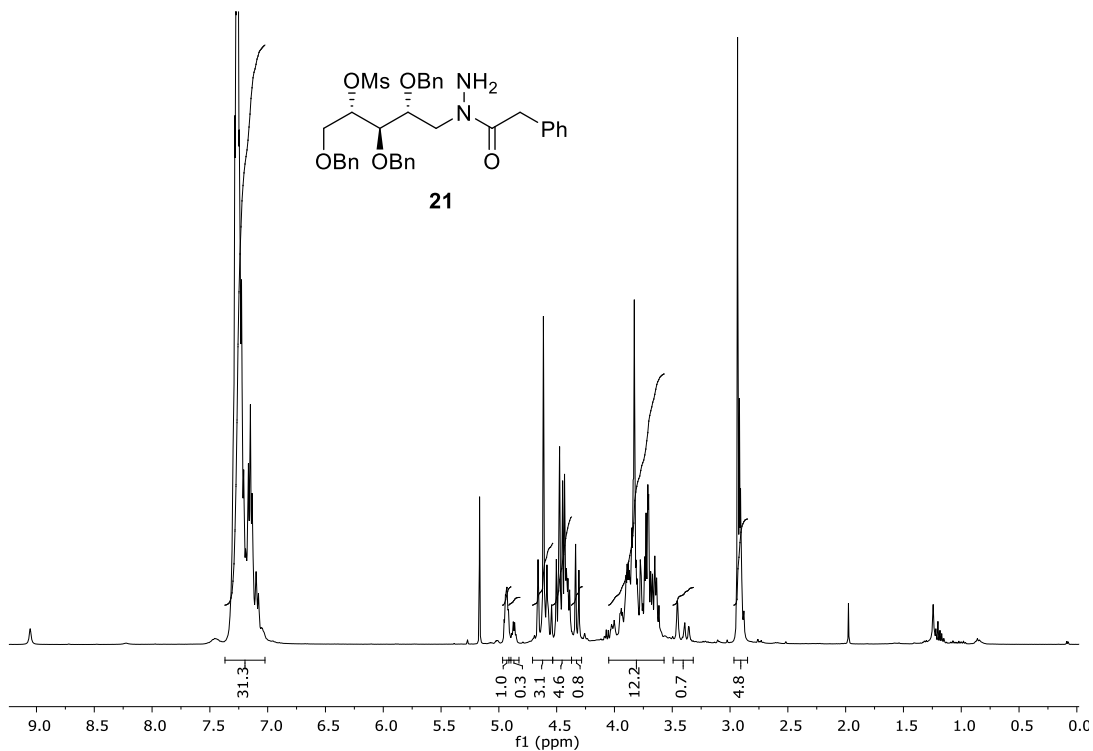


$^{13}\text{C-NMR}$ (100 MHz, CDCl_3):

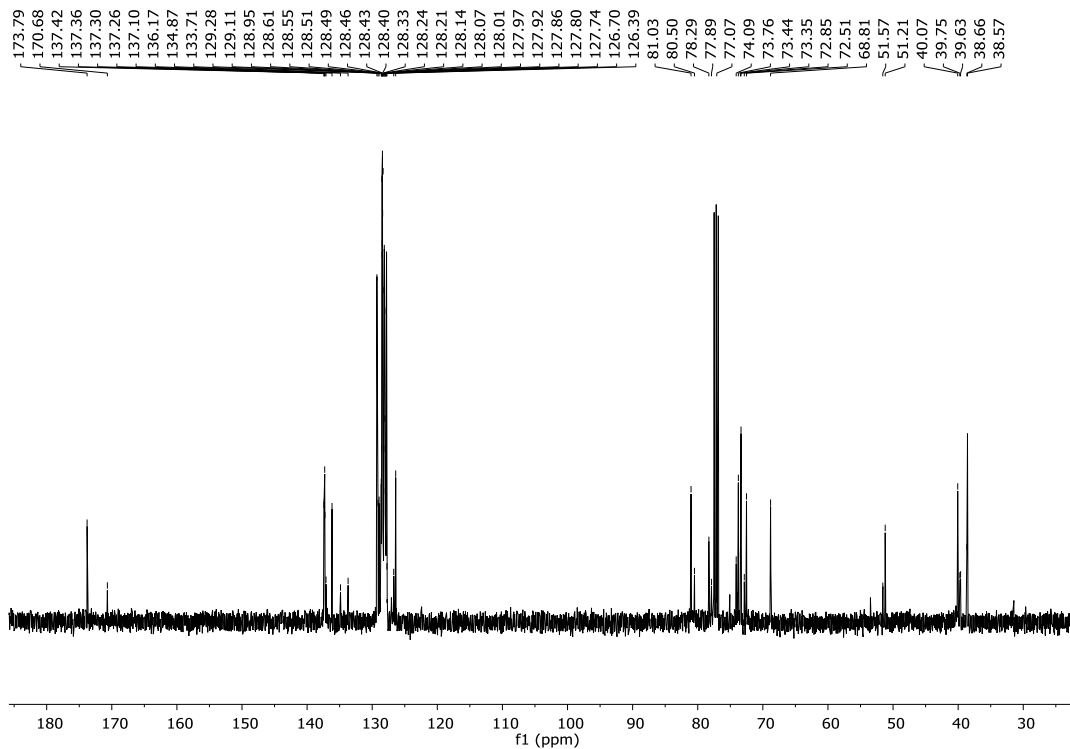


1-(1-phenethanoyl)hydrazino-1-deoxy-2,3,5-tri-O-benzyl-4-methanesulfonyl-L-ribose (21):

¹H-NMR (400 MHz, CDCl₃):

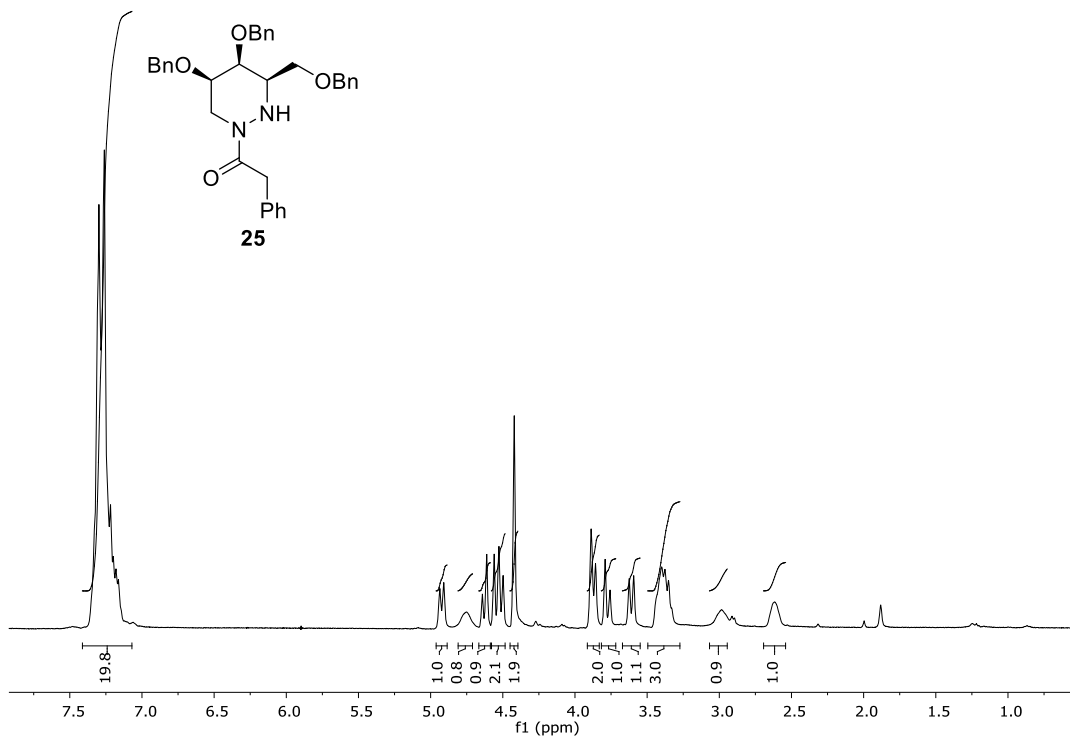


¹³C NMR (100 MHz, CDCl₃):

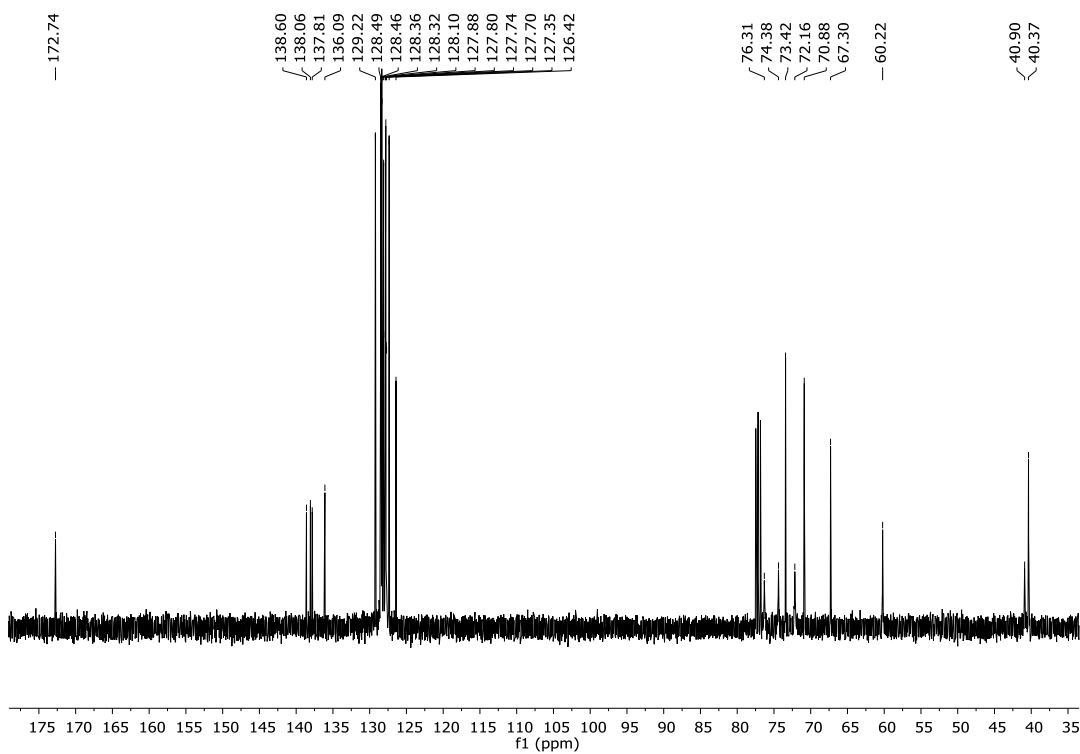


(3R,4S,5R)-1-N-phenethanoyl-3-benzyloxymethyl-4,5-di-O-benzyl-4,5-dihydroxyhexahydropyridazine (25):

¹H-NMR (400 MHz, CDCl₃):

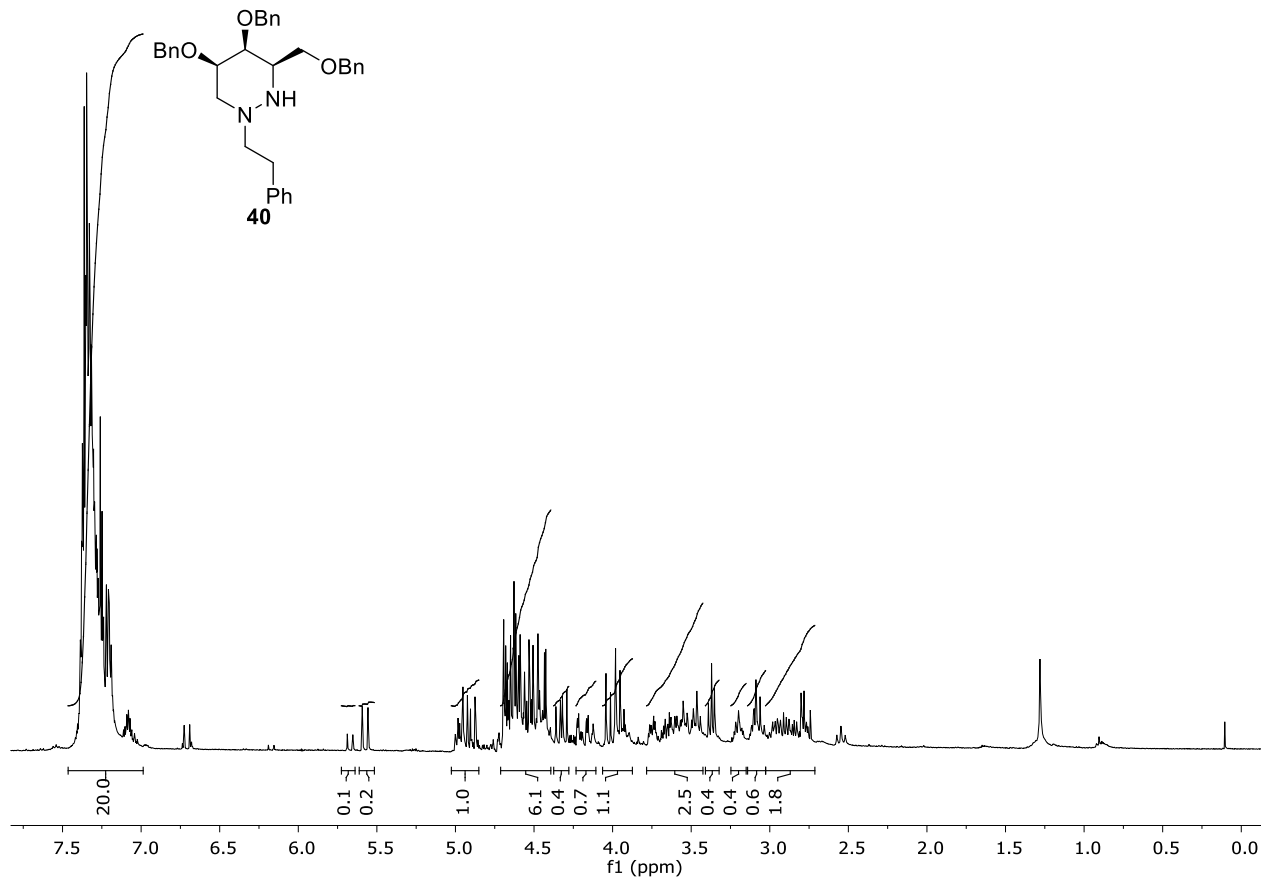


¹³C NMR (100 MHz, CDCl₃):



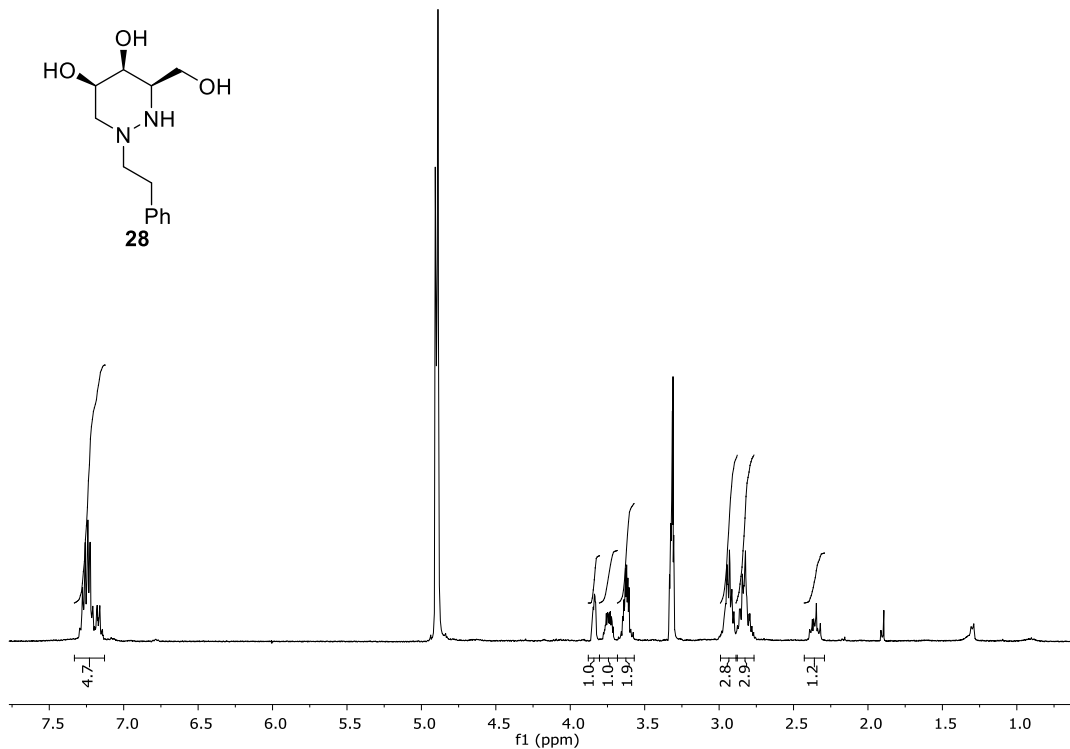
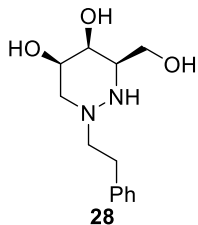
(3*R*,4*S*,5*R*)-1-*N*-phenethyl-3-benzyloxymethyl-4,5-di-*O*-benzyl-4,5-dihydroxyhexahydropyridazine (40):

¹H-NMR (400 MHz, CDCl₃):

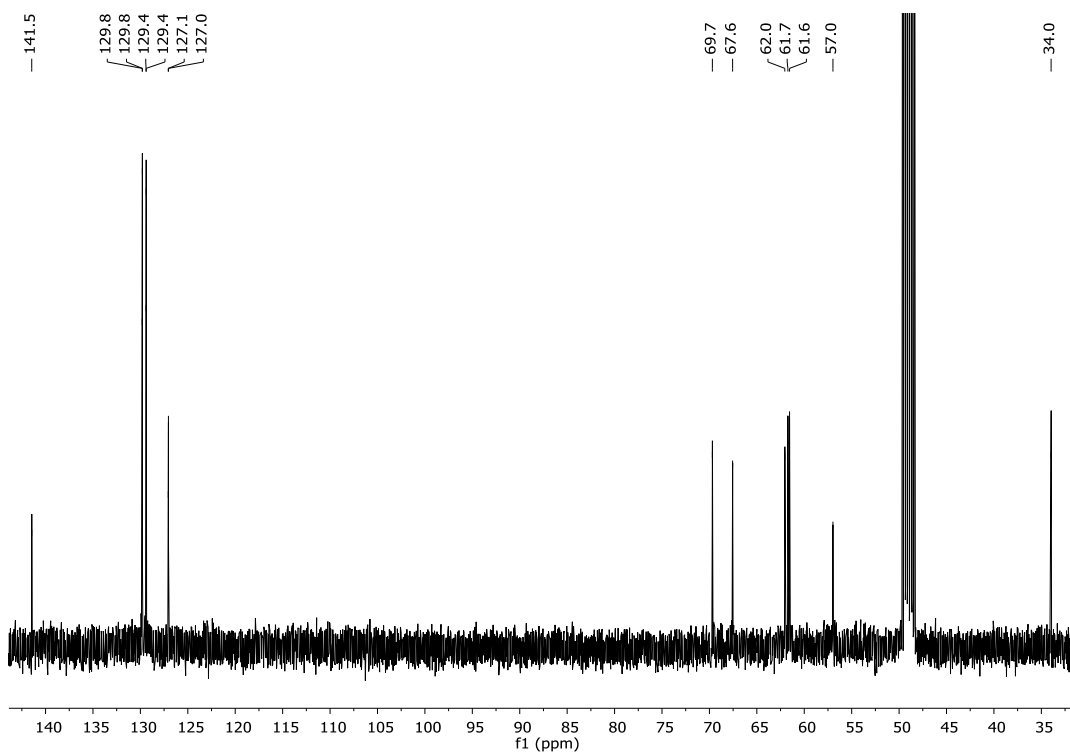


1-N-phenethyl-azagalactofagomine (28):

¹H-NMR (400 MHz, CD₃OD):

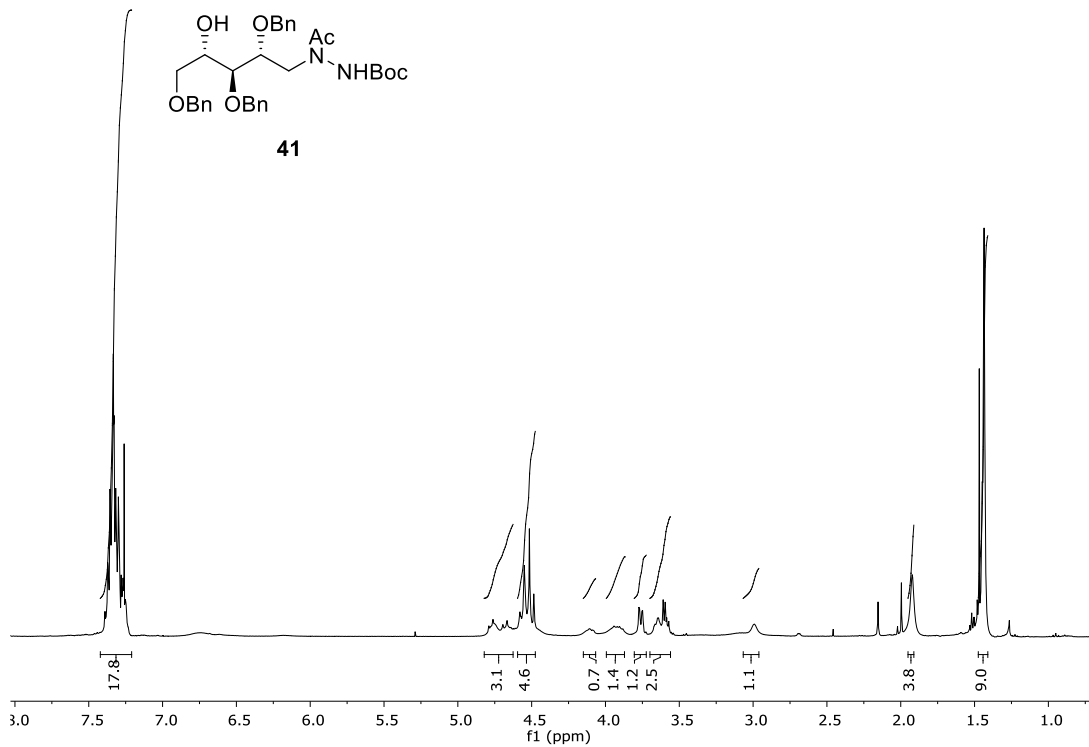


¹³C-NMR (100 MHz, CD₃OD):

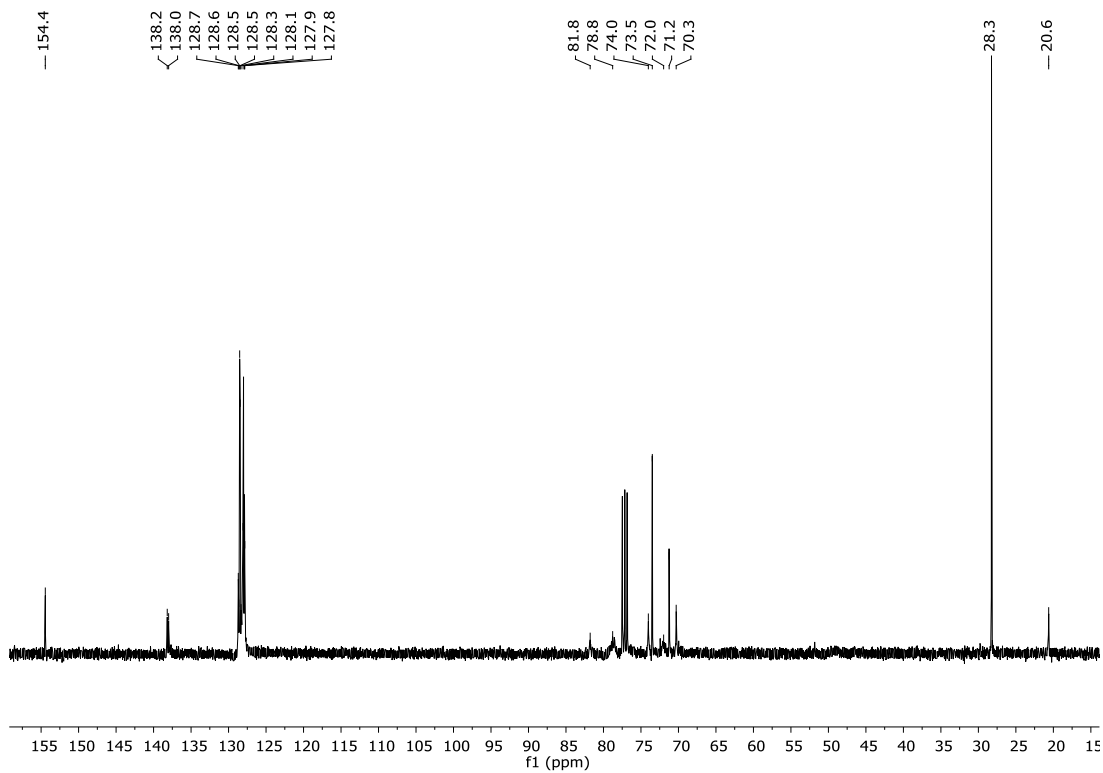


1-(1-Acetyl-2-*tert*-butyloxycarbonyl)hydrazino-1-deoxy-2,3,5-tri-*O*-benzyl-L-ribose (41)

¹H-NMR (400 MHz, CDCl₃)

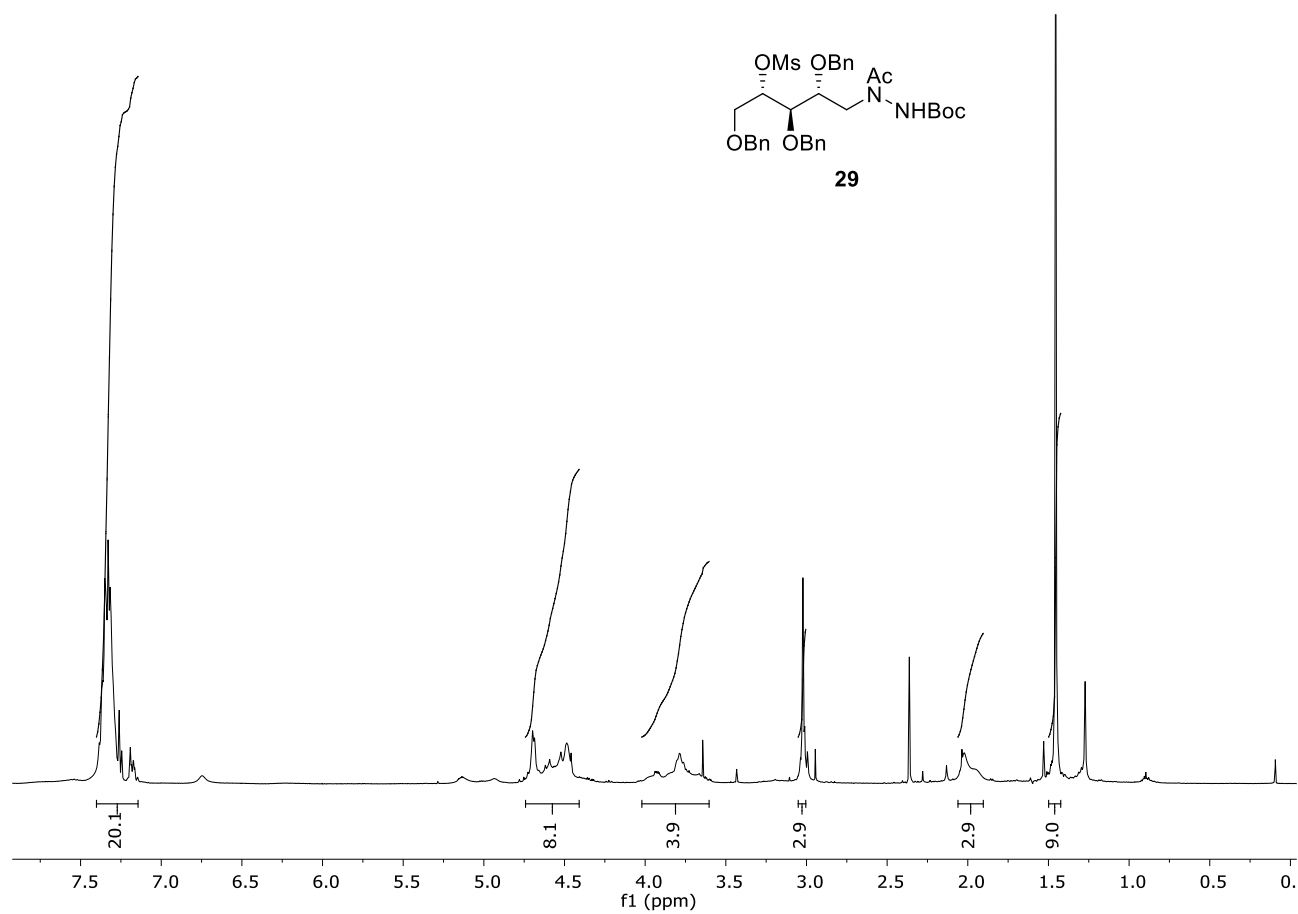


¹³C-NMR (100 MHz, CDCl₃)



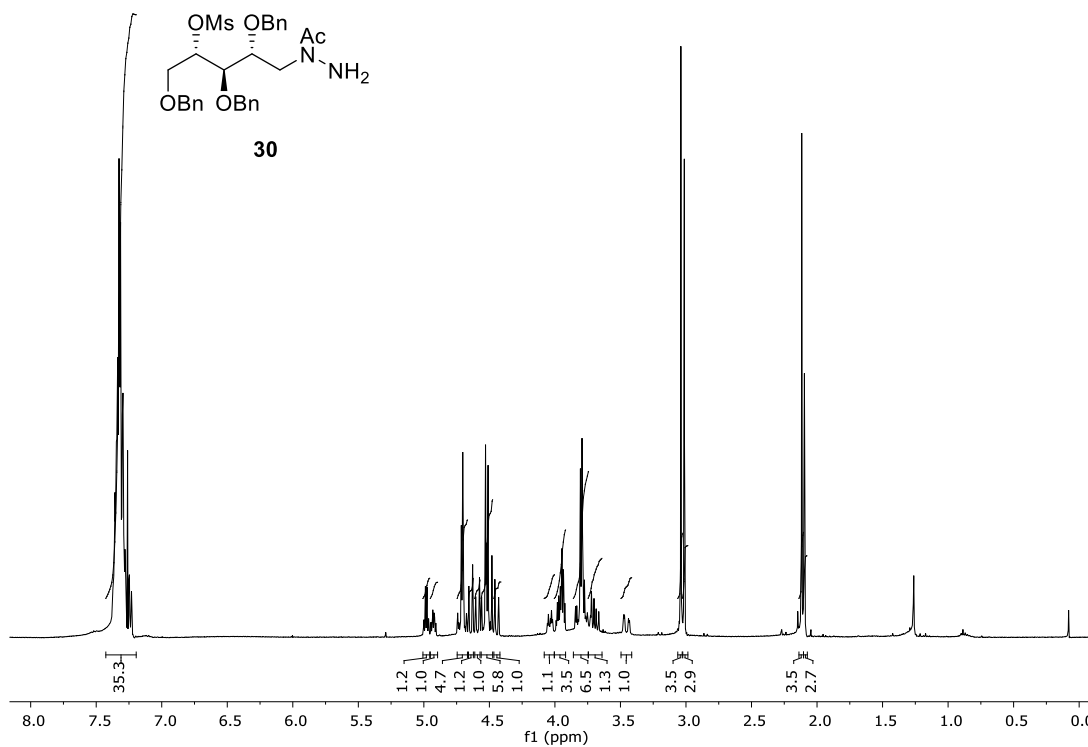
1-(1-Acetyl-2-*tert*-butyloxycarbonyl)hydrazino-1-deoxy-2,3,5-tri-*O*-benzyl-4-methanesulfonyl-L-ribose (29):

¹H-NMR (400 MHz, CDCl₃)

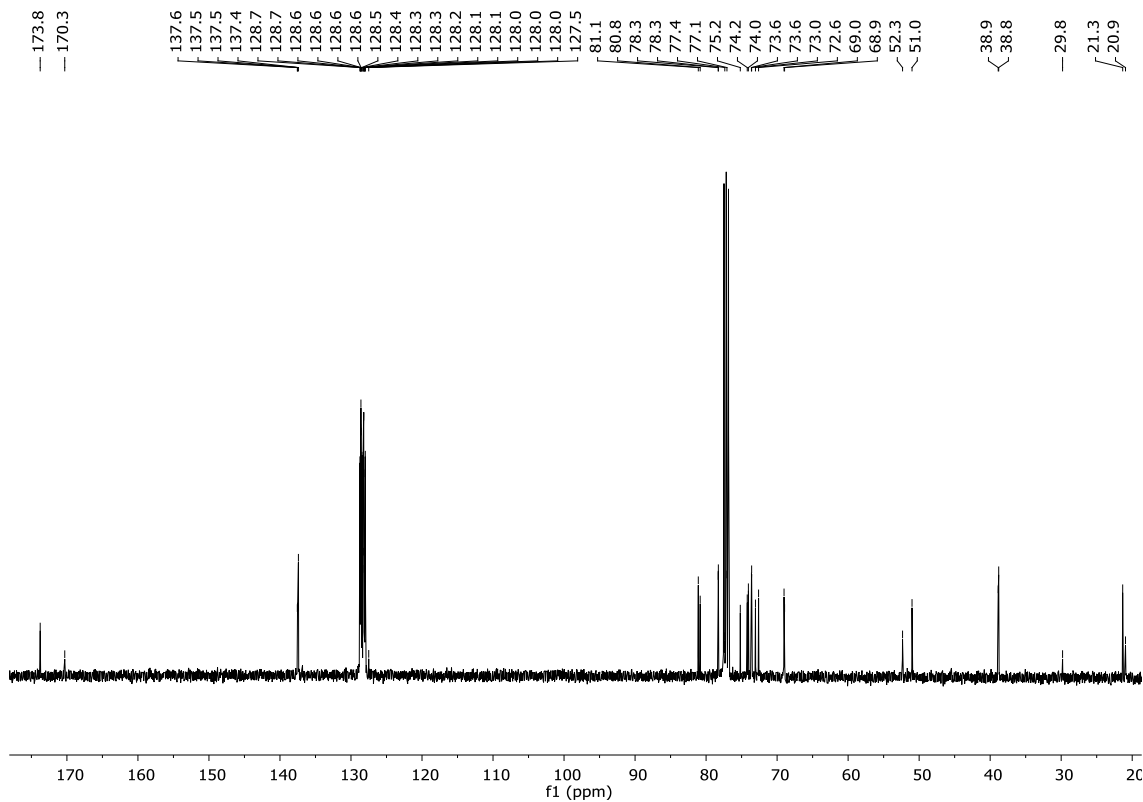


1-(1-Acetyl)hydrazino-1-deoxy-2,3,5-tri-O-benzyl-4-methanesulfonyl-L-ribose (30):

¹H-NMR (400 MHz, CDCl₃)

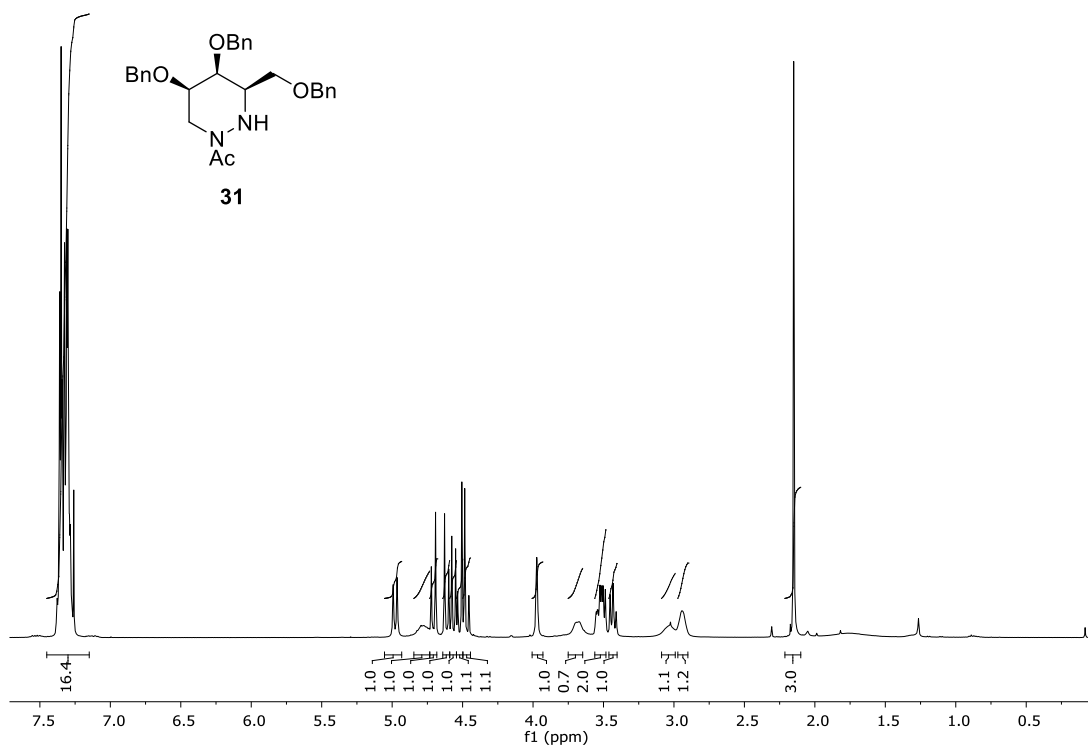


¹³C-NMR (100 MHz, CDCl₃)

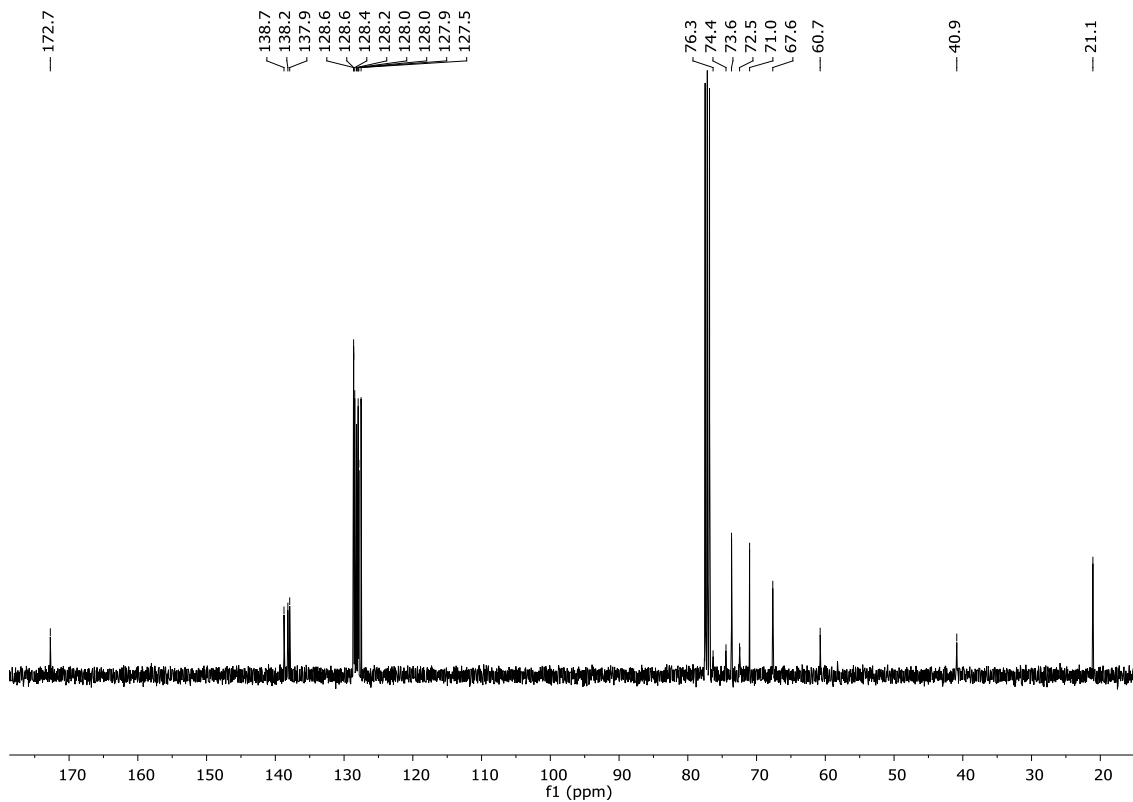


(3R,4S,5R)-1-N-acetyl-3-benzyloxymethyl-4,5-di-O-benzyl-4,5-dihydroxyhexahydropyridazine (31):

¹H-NMR (400 MHz, CDCl₃)

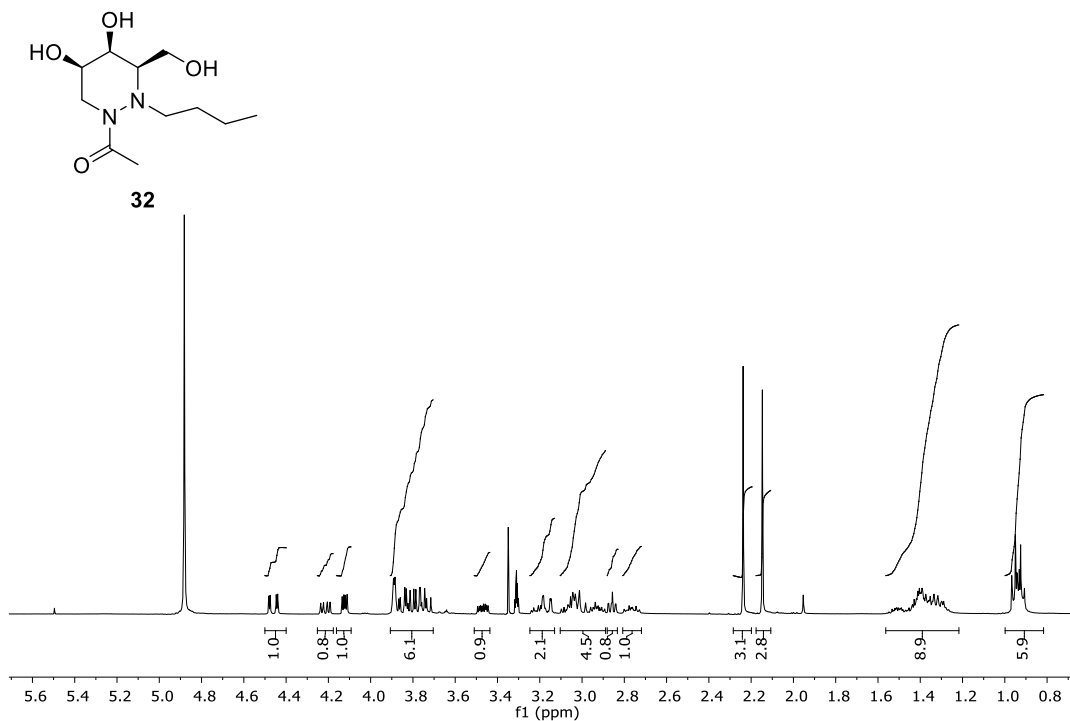


¹³C-NMR (100 MHz, CDCl₃)

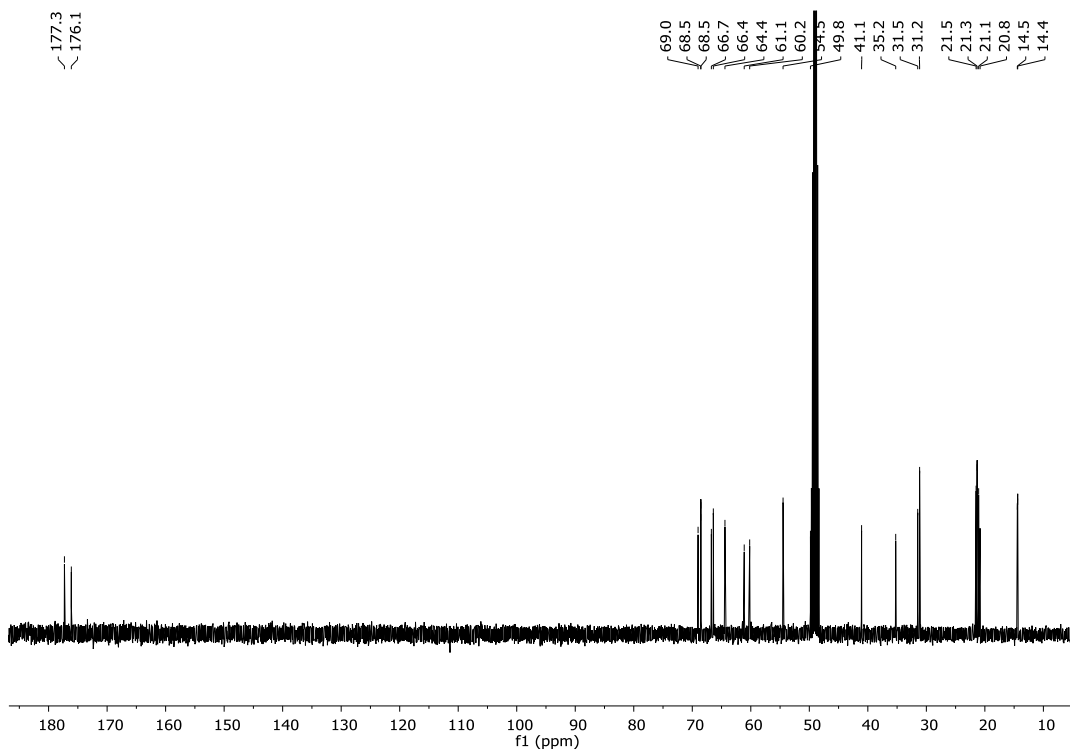


1-*N*-Acetyl-2-*N*-butyl-azagalactofagomine (32):

¹H-NMR (400 MHz, CD₃OD):

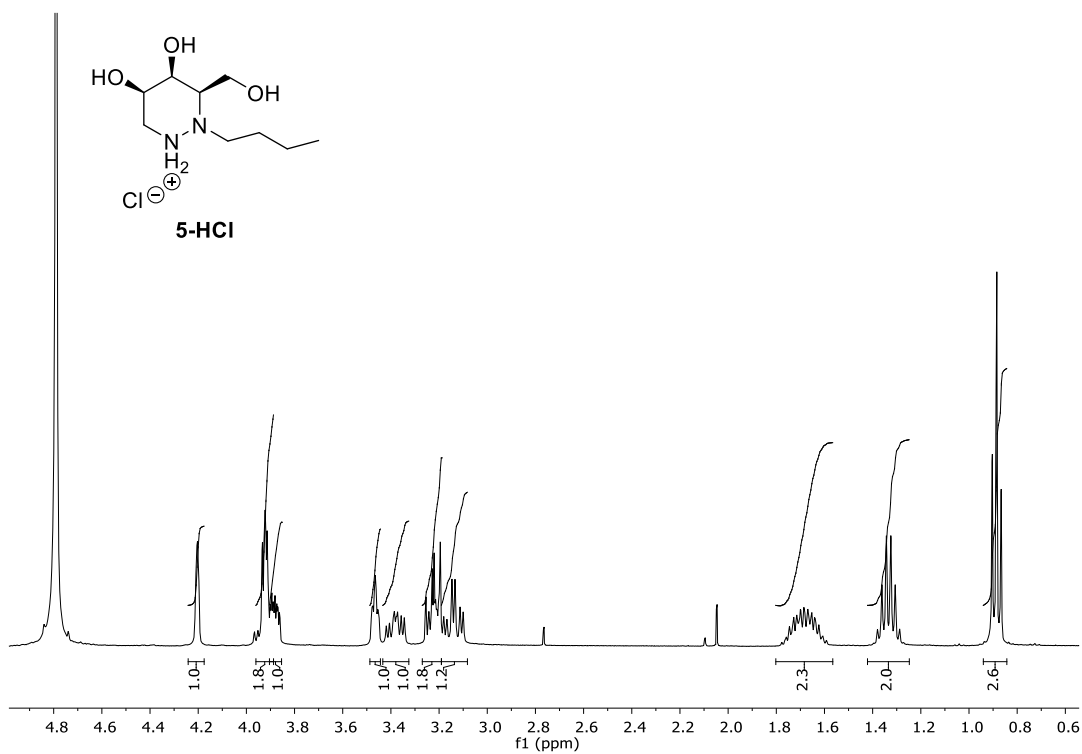


¹³C-NMR (100 MHz, CD₃OD): δ_c

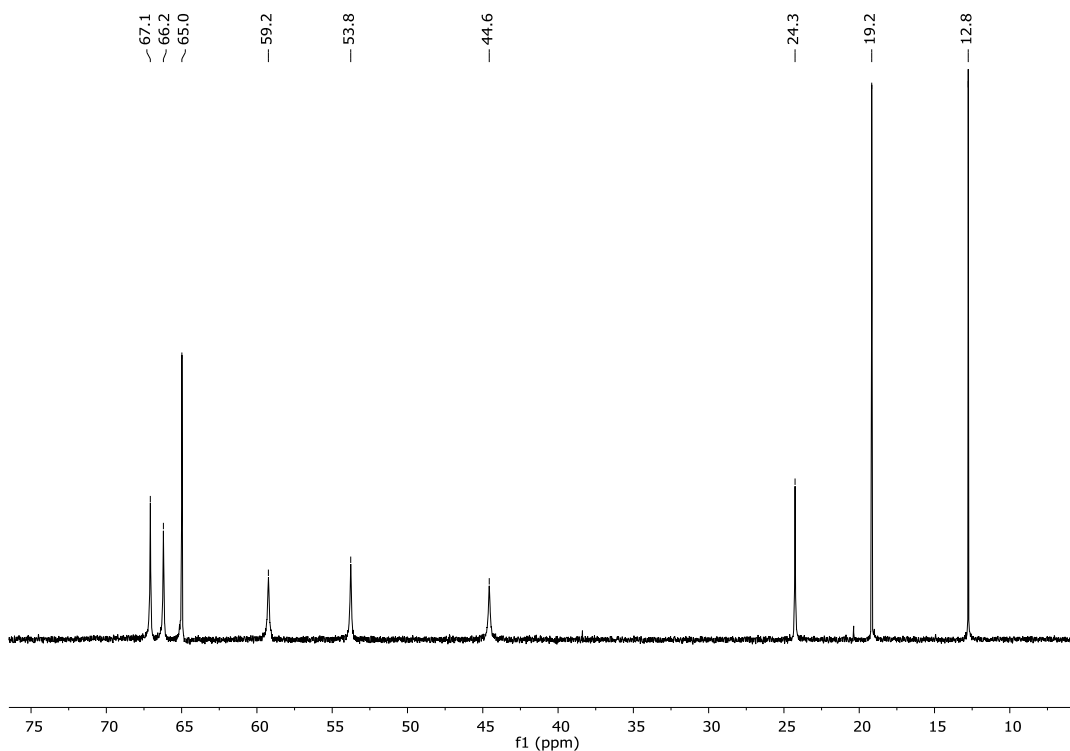


2-N-butyl-azagalactofagomine (5-HCl):

¹H-NMR (400 MHz, D₂O):

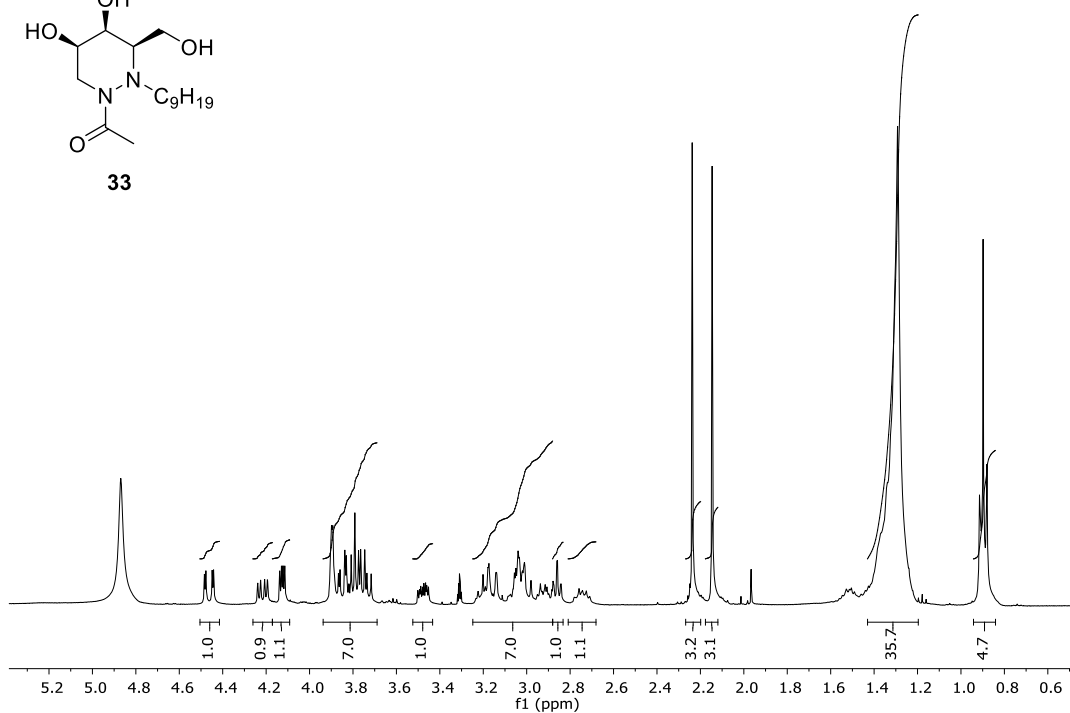
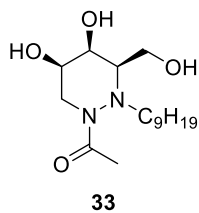


¹³C-NMR (100 MHz, D₂O):

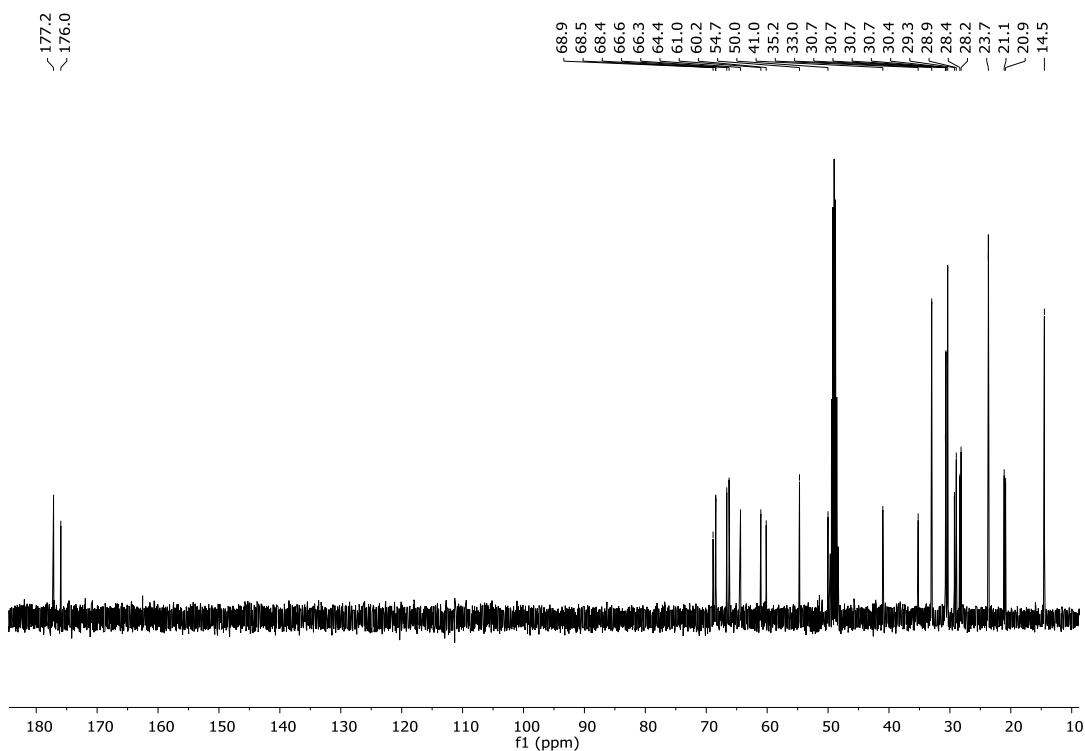


1-*N*-Acetyl-2-*N*-nonyl-azagalactofagomine (33):

¹H-NMR (400 MHz, CD₃OD):

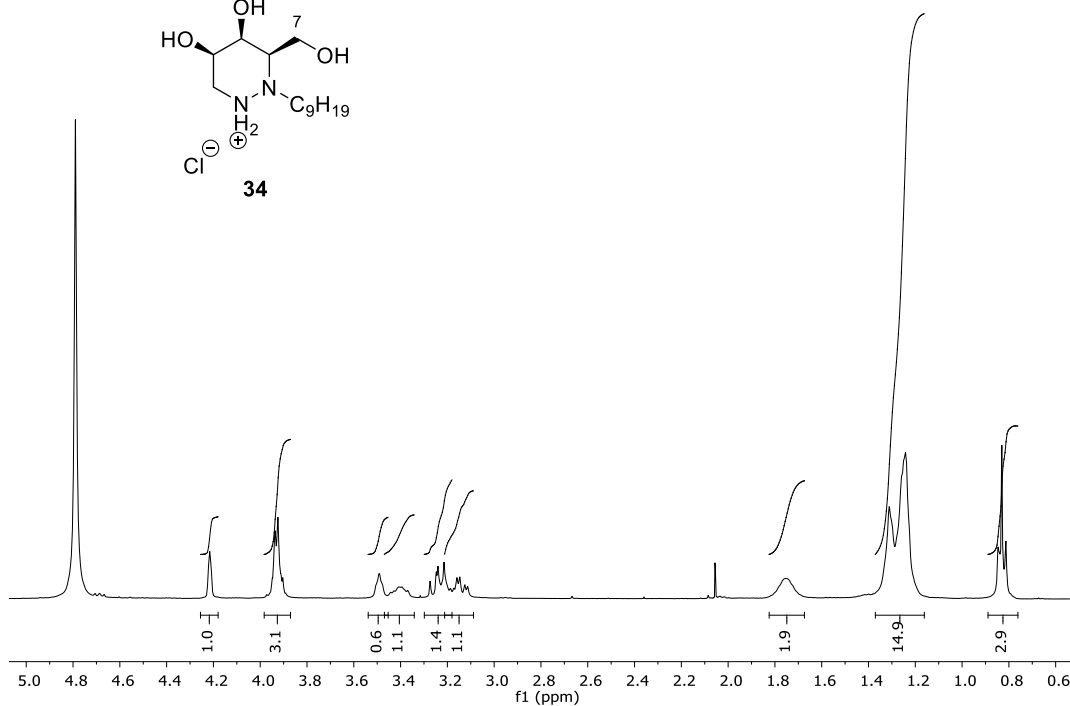
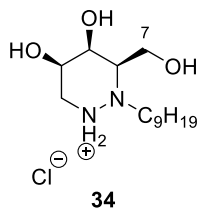


¹³C-NMR (100 MHz, CD₃OD):



2-N-nonyl-azagalactofagomine (34):

¹H-NMR (400 MHz, D₂O):



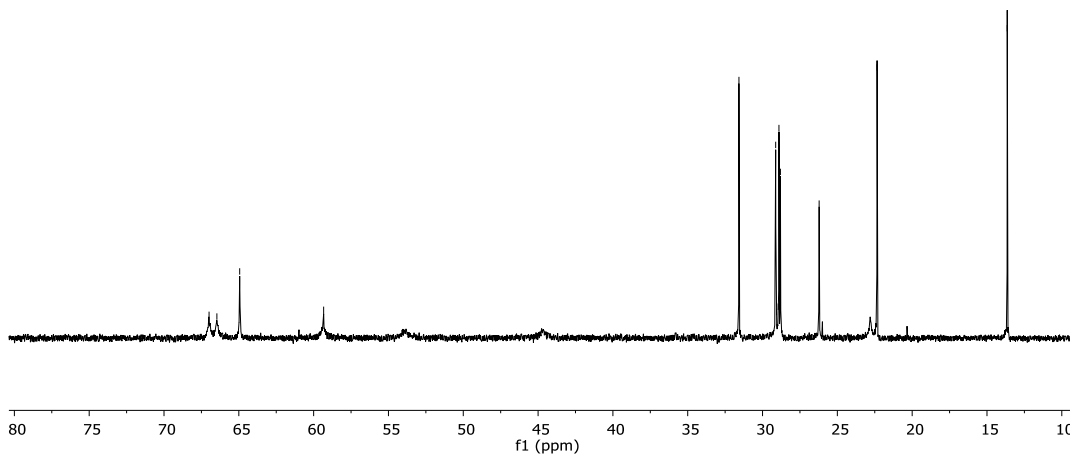
¹³C-NMR (100 MHz, D₂O):

67.0
66.5
64.9
59.3

31.6
29.1
29.1
29.0
28.9
28.8
26.2

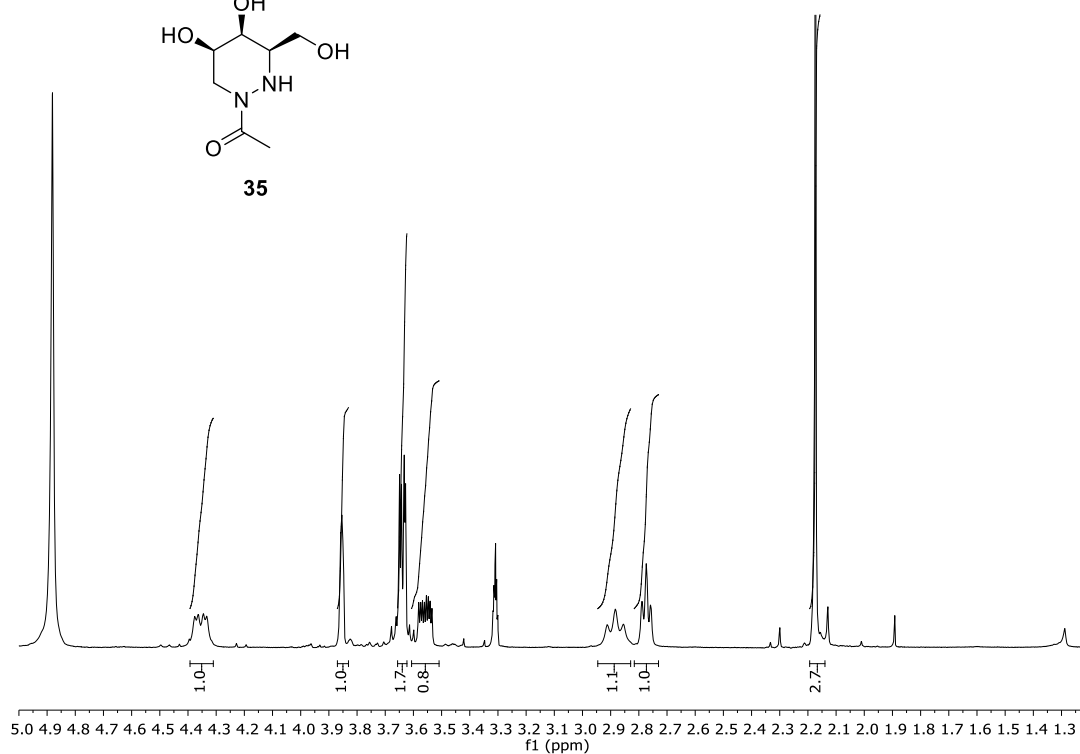
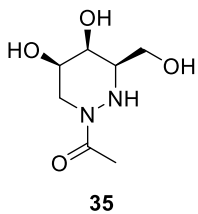
22.3

13.6

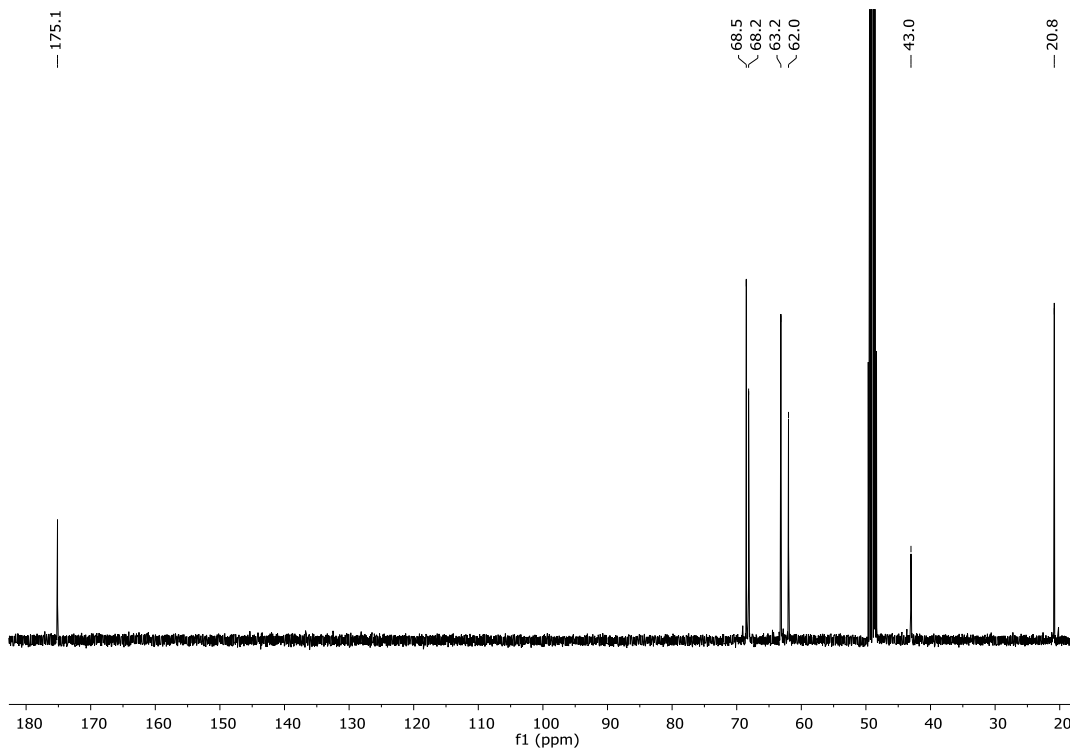


1-N-acetyl-azagalactofagmine (35):

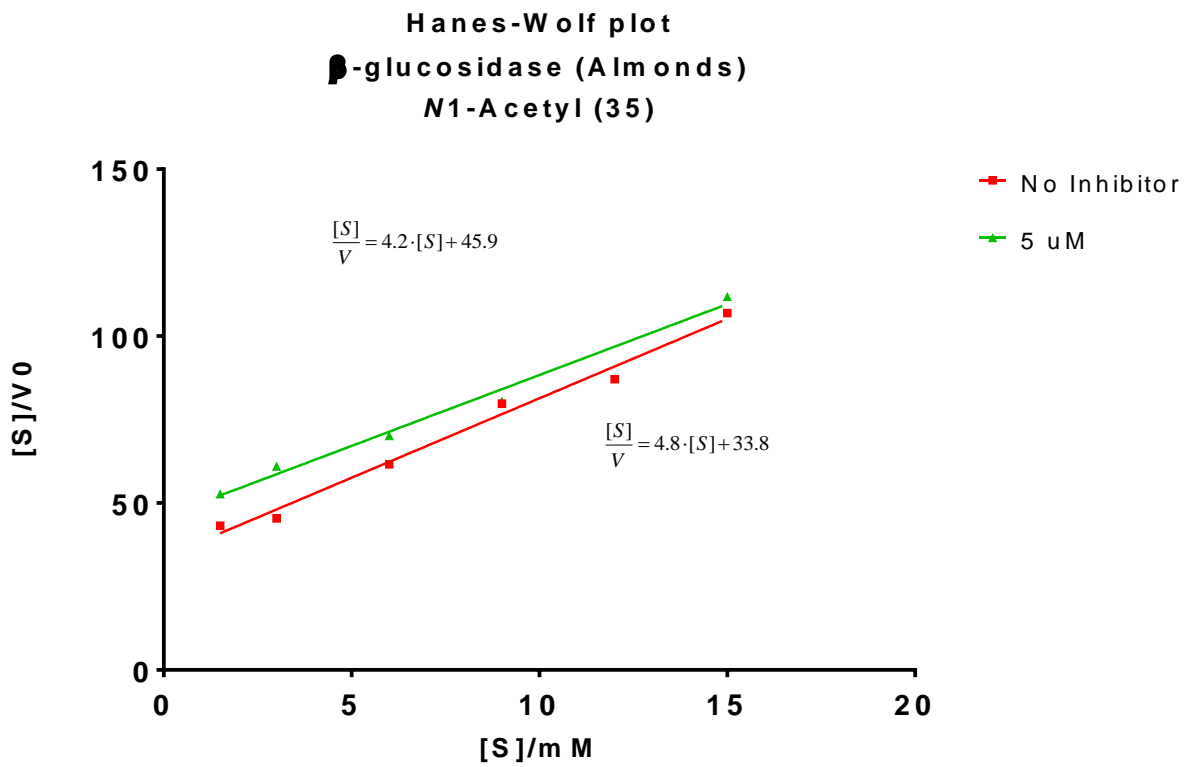
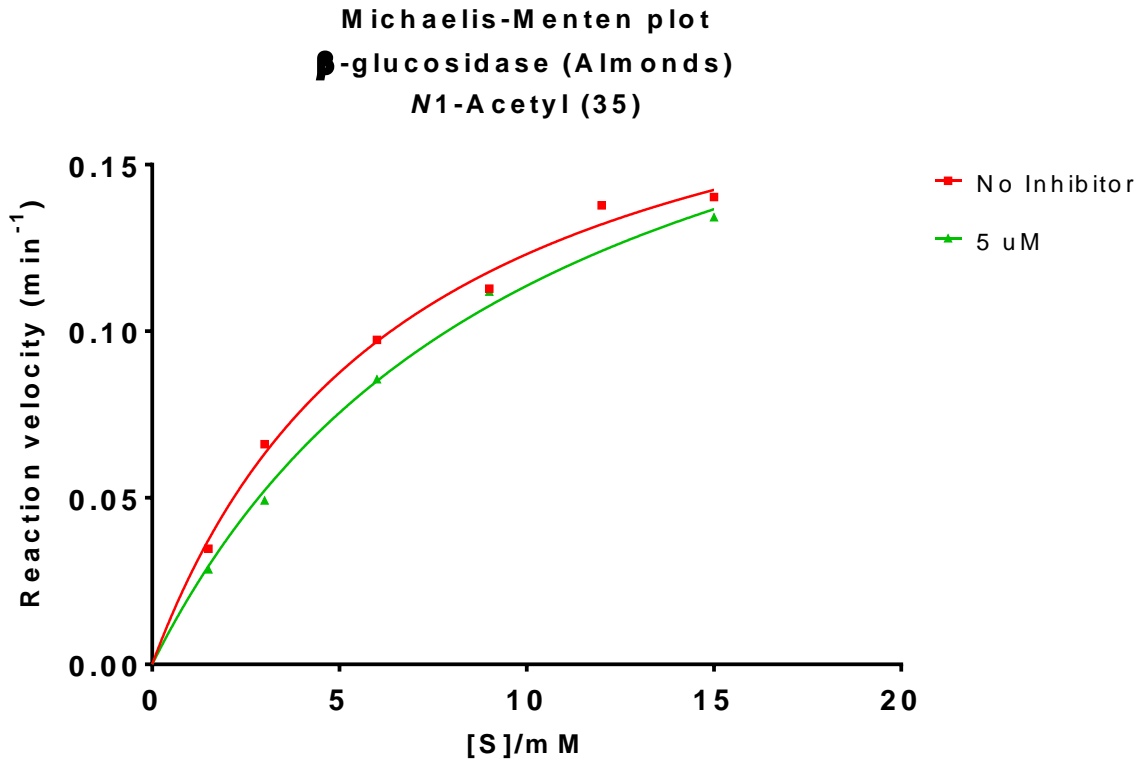
¹H-NMR (400 MHz, CD₃OD):



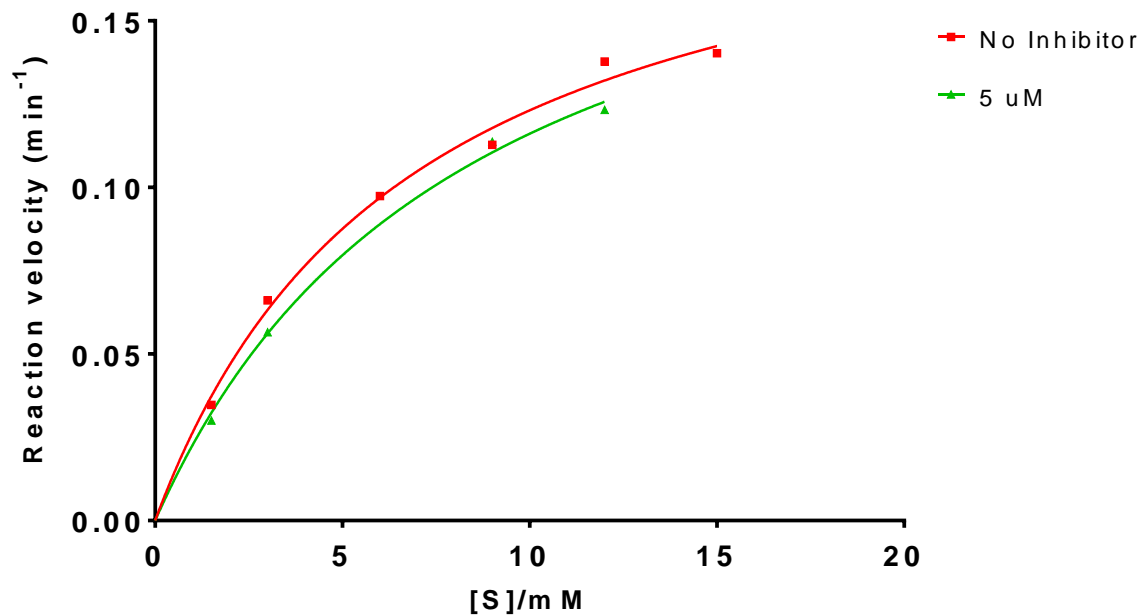
¹³C-NMR (100 MHz, CD₃OD):



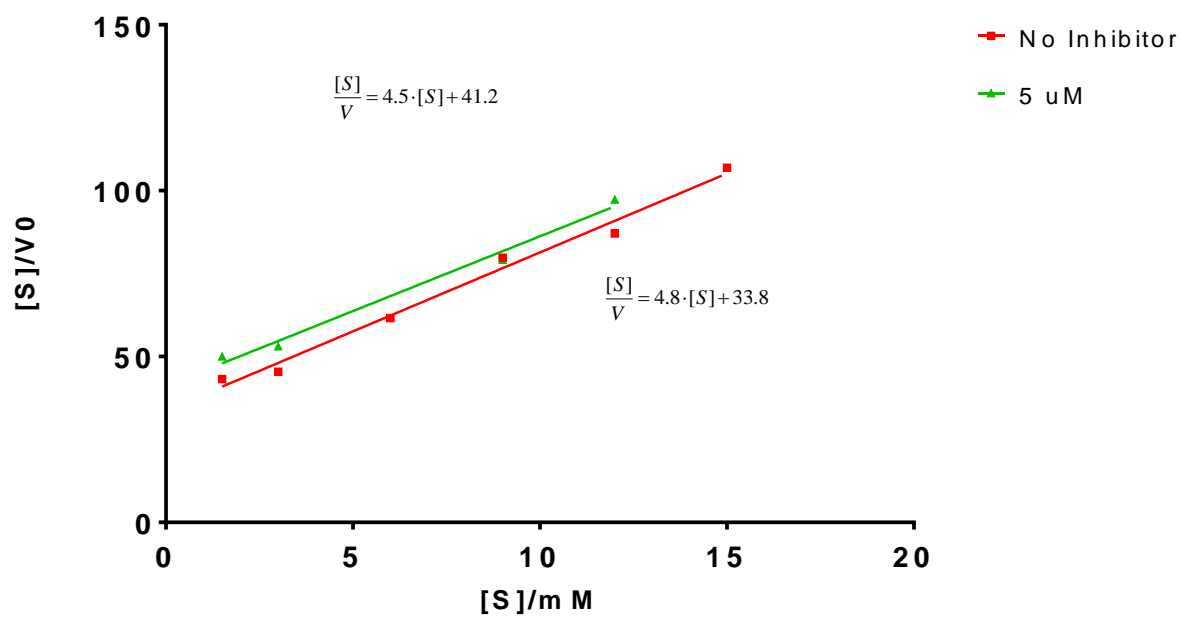
Michaelis-Menten and Hanes plots:



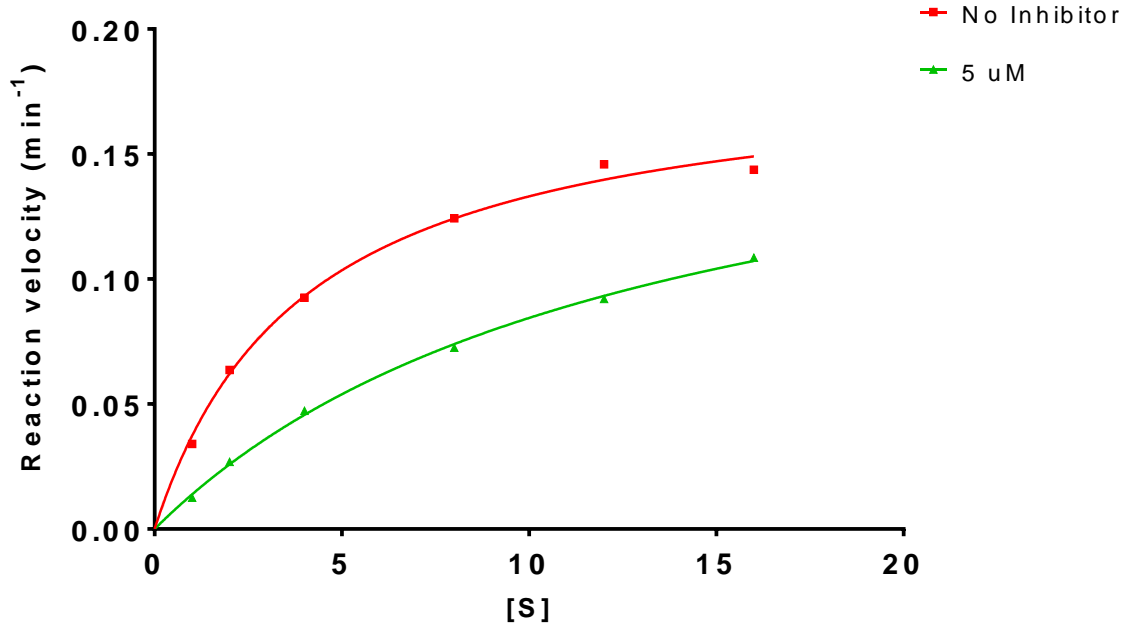
Michaelis-Menten plot
 β -glucosidase (Almonds)
N1-Phenethyl (28)



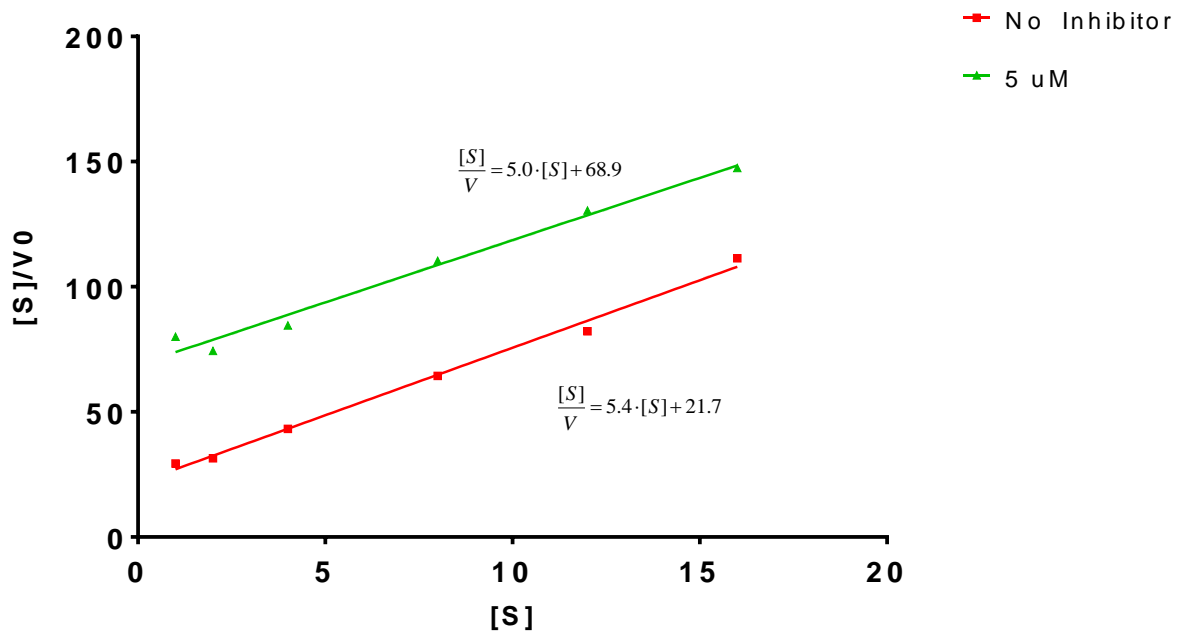
Hanes-Wolf plot
 β -glucosidase (Almonds)
N1-Phenethyl (28)



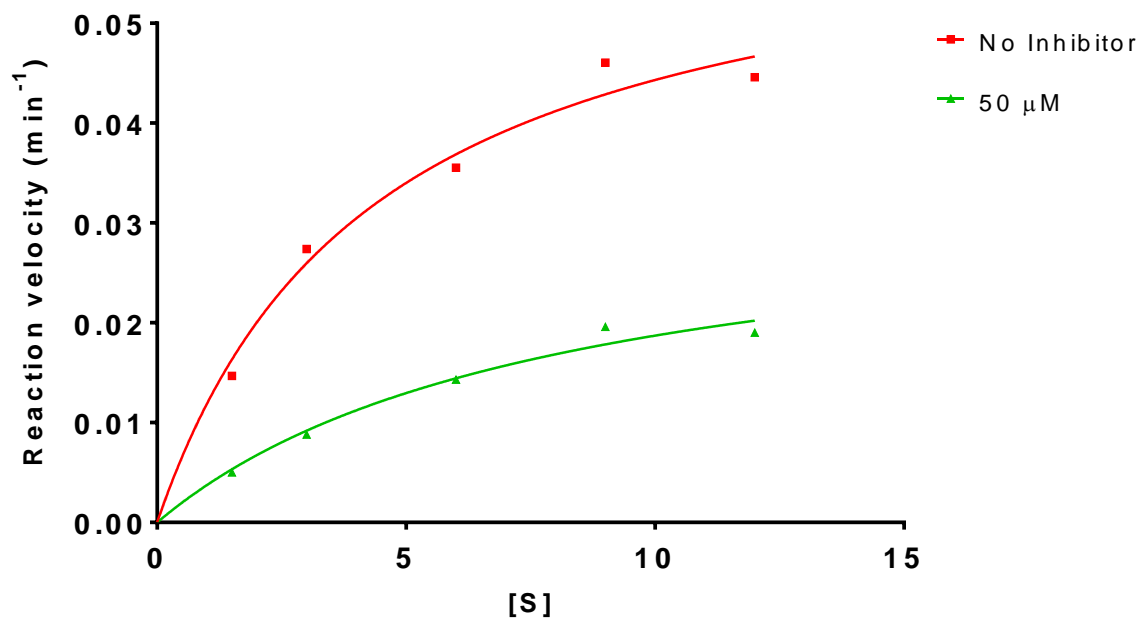
Michaelis Menten plot
 β -glucosidase (Almonds)
*N*2-Butyl (5-HCl)



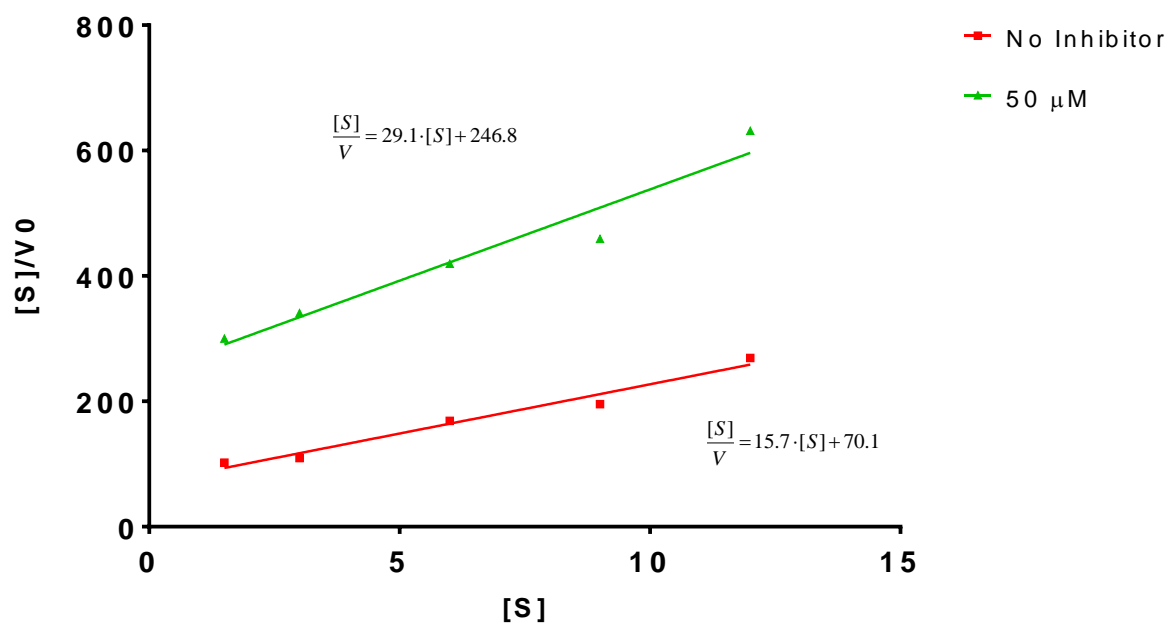
Hanes-Wolf
 β -glucosidase (Almonds)
*N*2-Butyl (5-HCl)



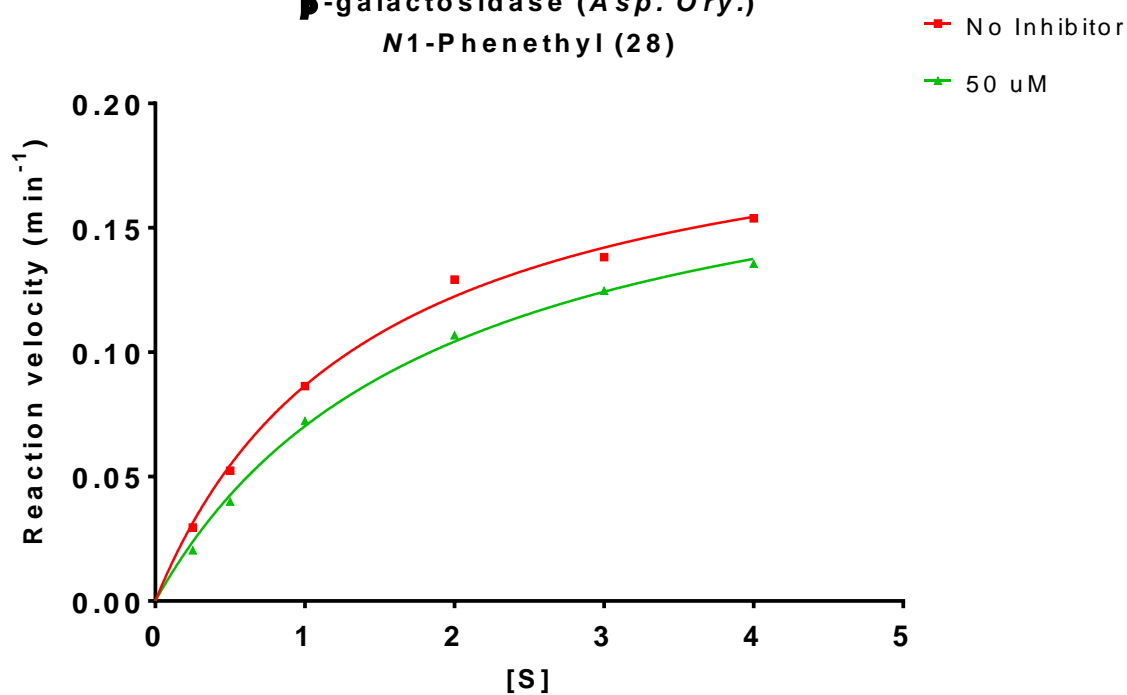
Michaelis-Menten plot
 β -glucosidase (Almonds)
 N2-Nonyl (34)



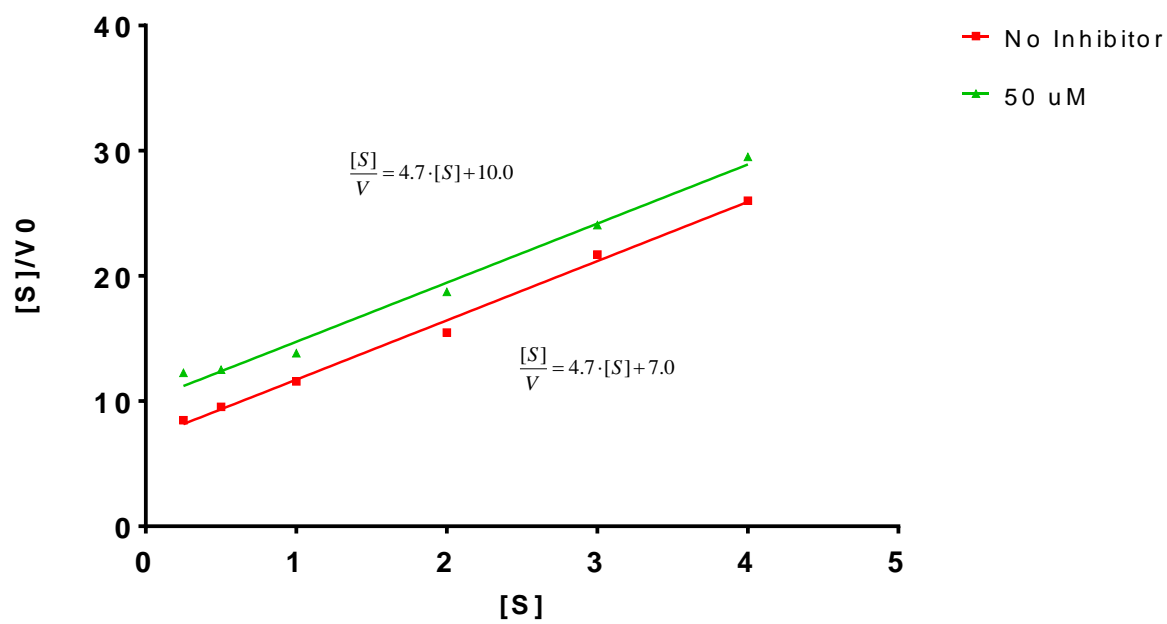
Hanes-Wolf plot
 β -glucosidase (Almonds)
 N2-Nonyl (34)



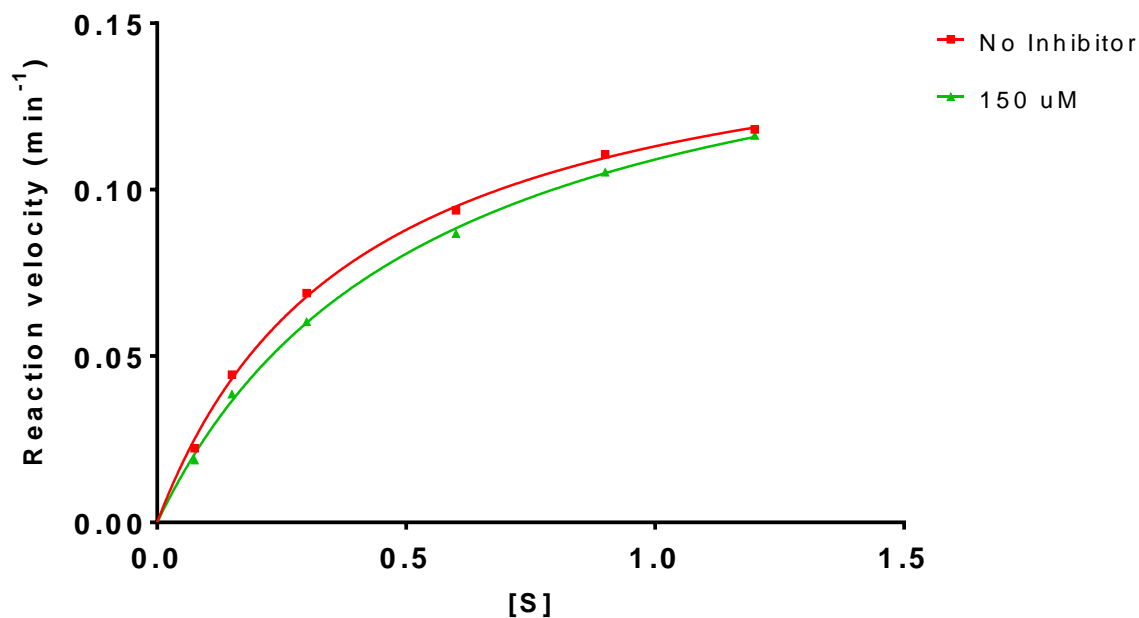
Hanes-Wolf plot
 β -galactosidase (*Asp. Ory.*)
*N*1-Phenethyl (28)



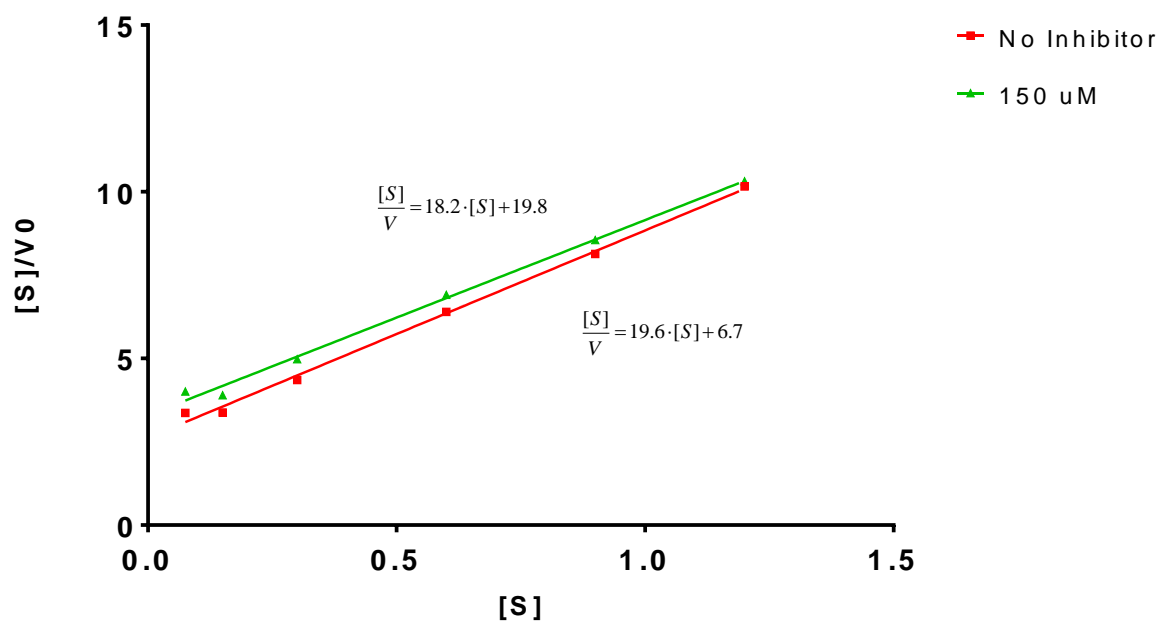
Hanes-Wolf
 β -galactosidase (*Asp. Ory.*)
*N*1-Phenethyl (28)



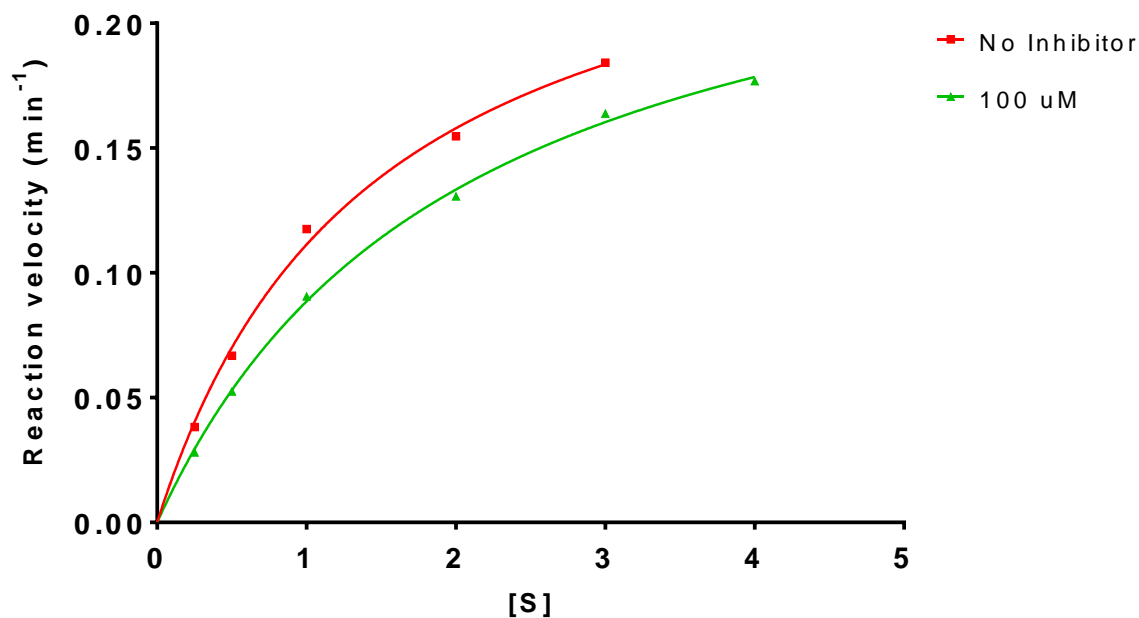
Michaelis-Menten plot
 β -galactosidase (*A. sp. Ory.*)
 N1-Butyl (4)



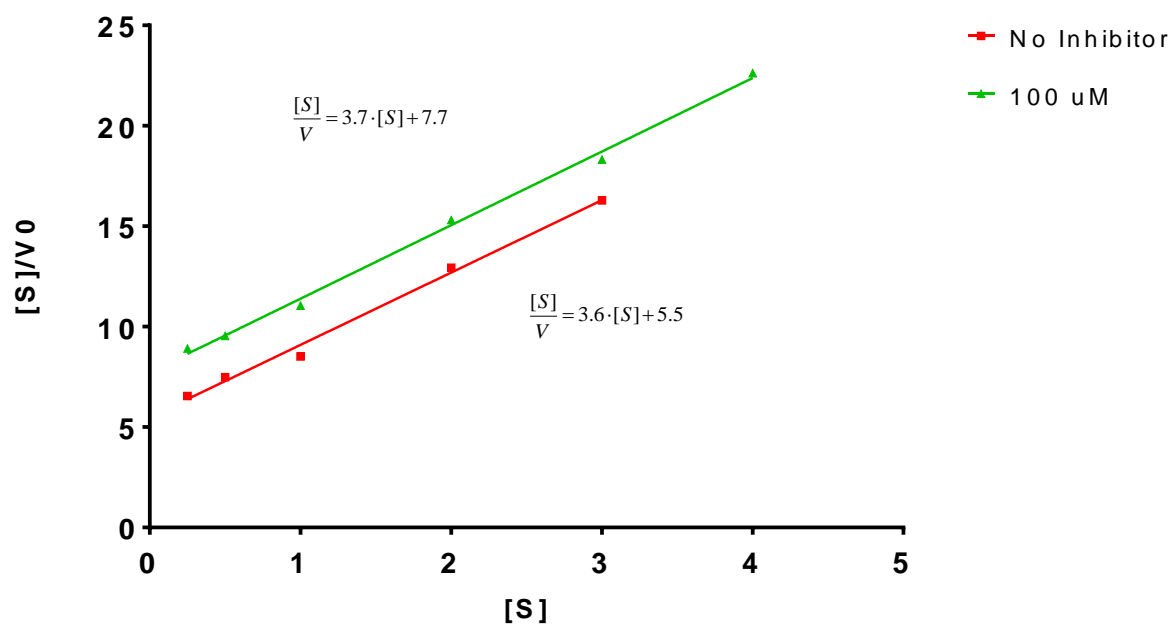
Hanes-Wolf plot
 β -galactosidase (*A. sp. Ory.*)
 N1-Butyl (4)



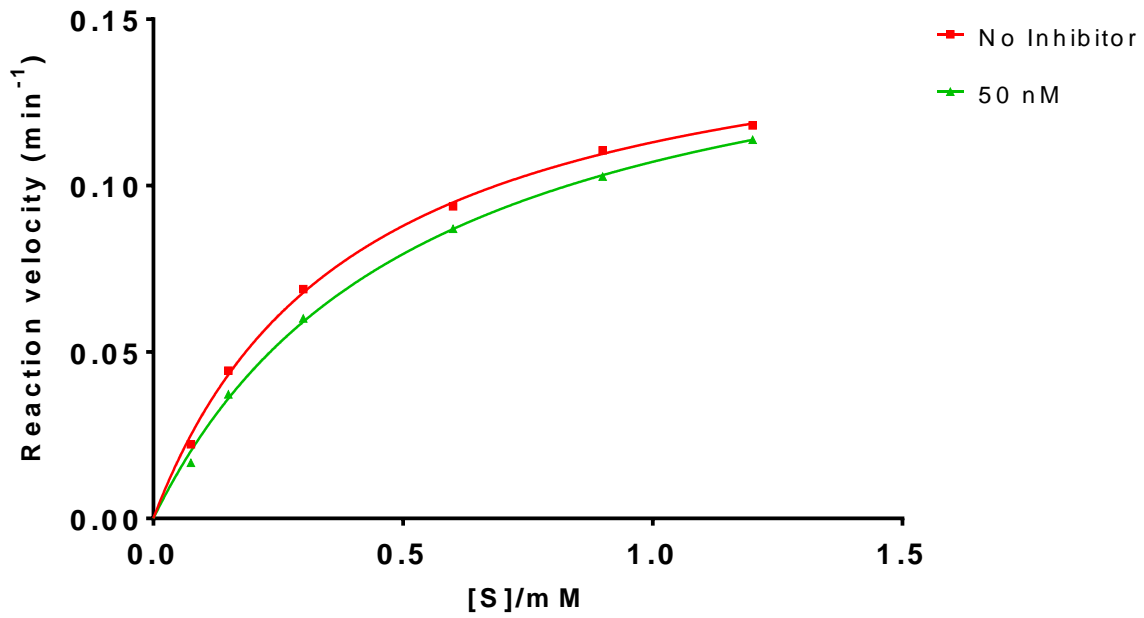
Michaelis-Menten plot
 β -galactosidase (*Asp. ory.*)
 N1-Nonyl (26)



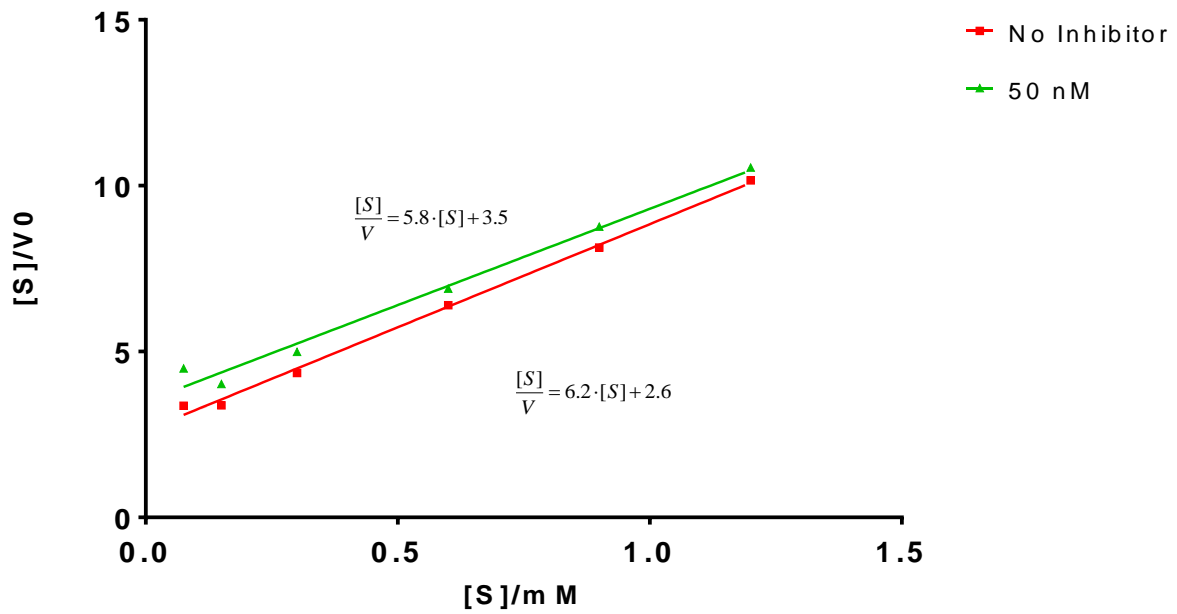
Hanes-Wolf plot
 β -galactosidase (*Asp. ory.*)
 N1-Nonyl (26)



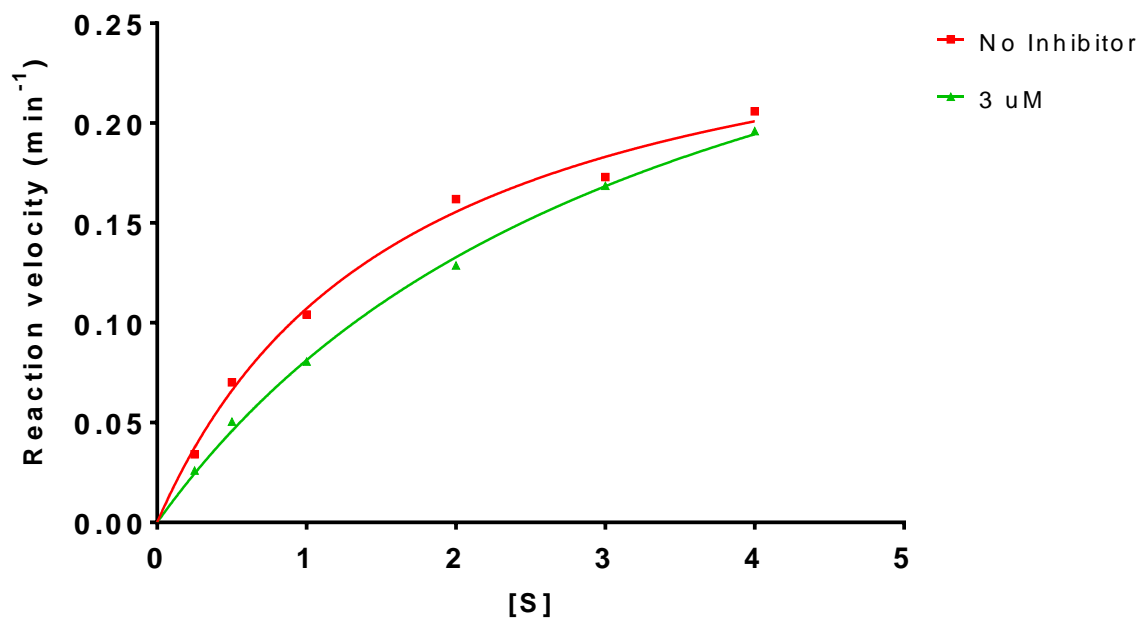
Michaelis-Menten plot
 β -galactosidase (*Asp. Ory.*)
 N2-Butyl (5-HCl)



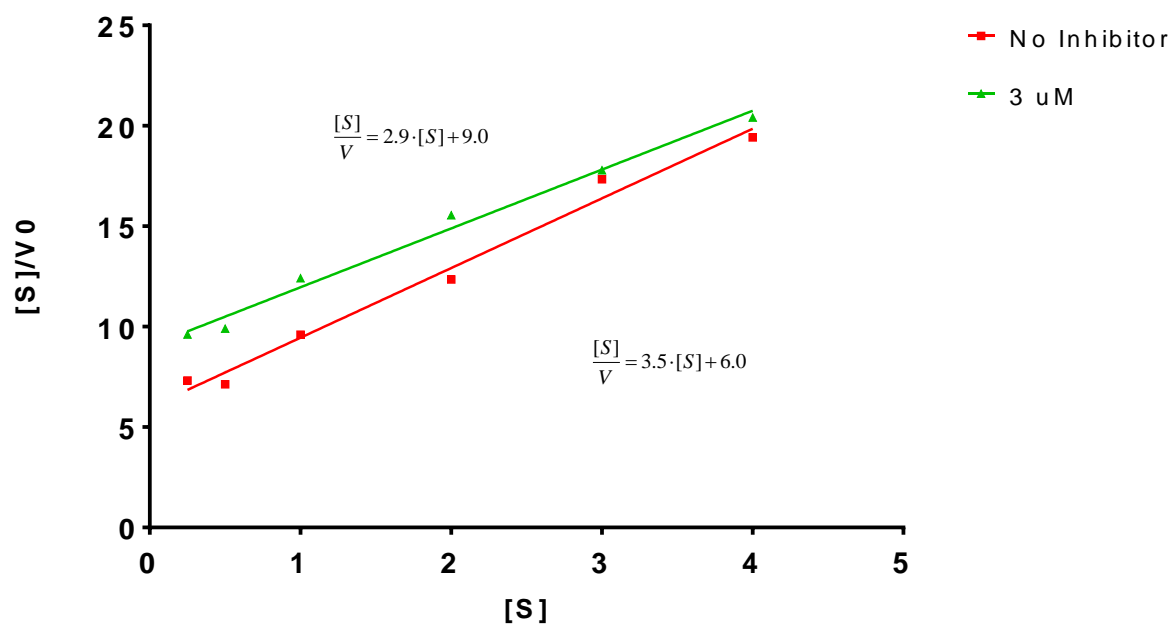
Hanes-Wolf plot
 β -galactosidase (*Asp. Ory.*)
 N2-Butyl (5-HCl)

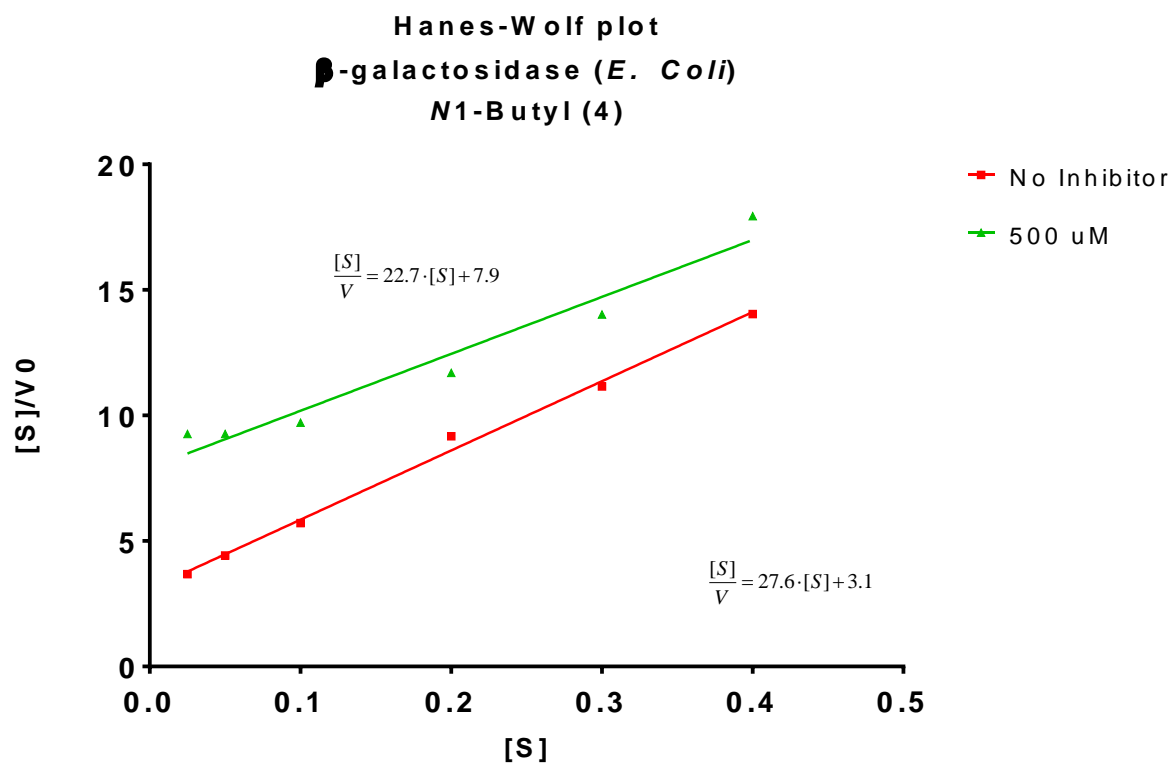
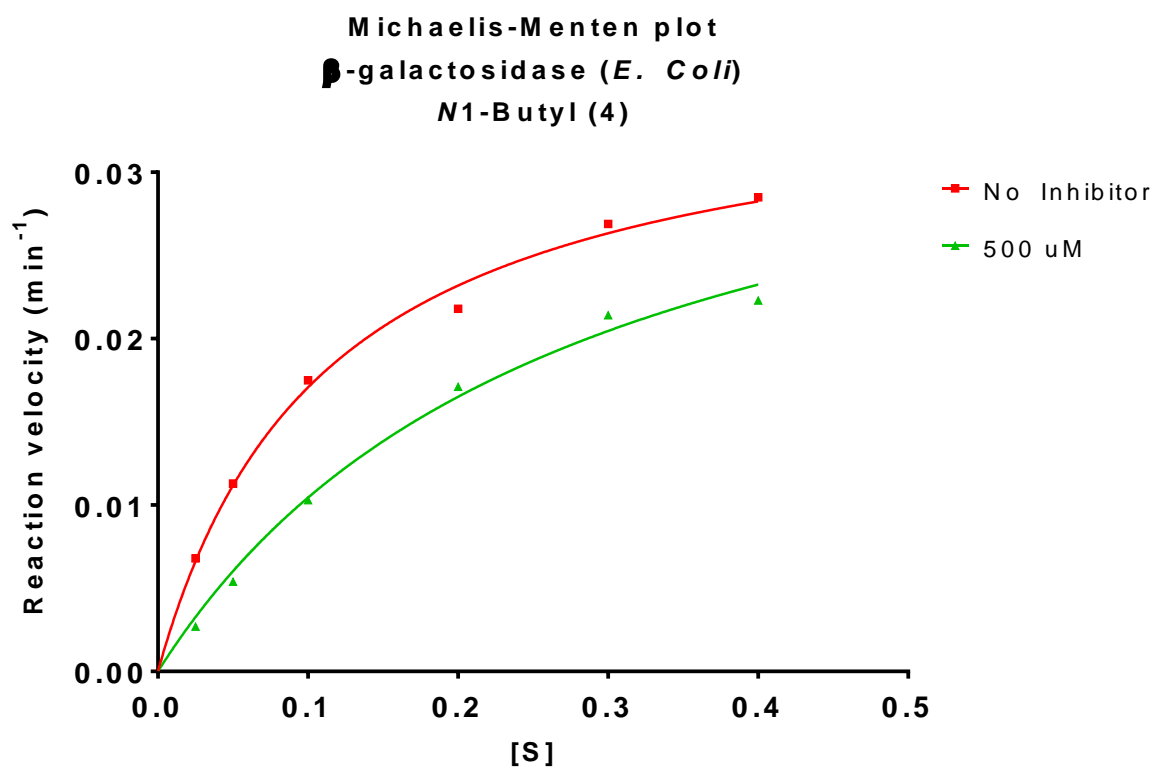


Michaelis-Menten plot
 β -galactosidase (*Asp. Ory.*)
 N2-Nonyl (34)

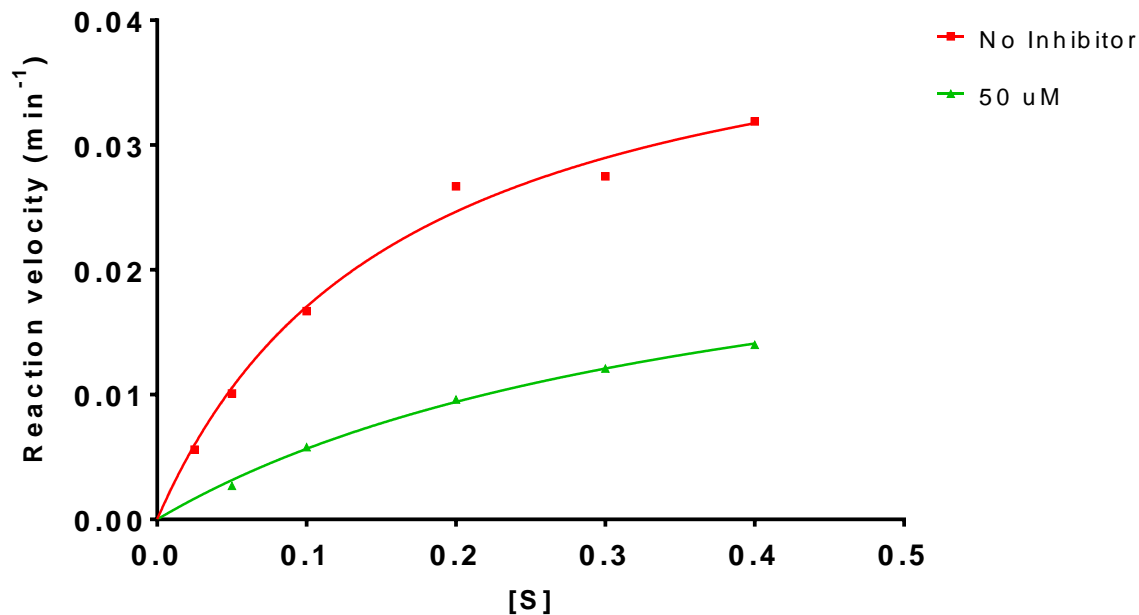


Hanes-Wolf plot
 β -galactosidase (*Asp. Ory.*)
 N2-Nonyl (34)

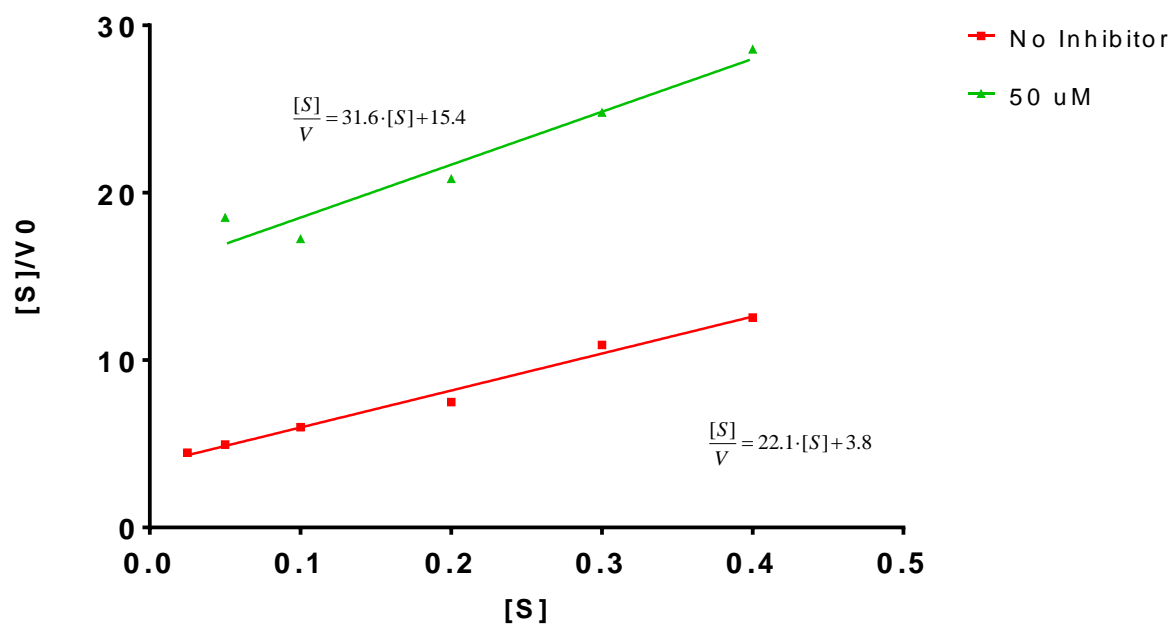




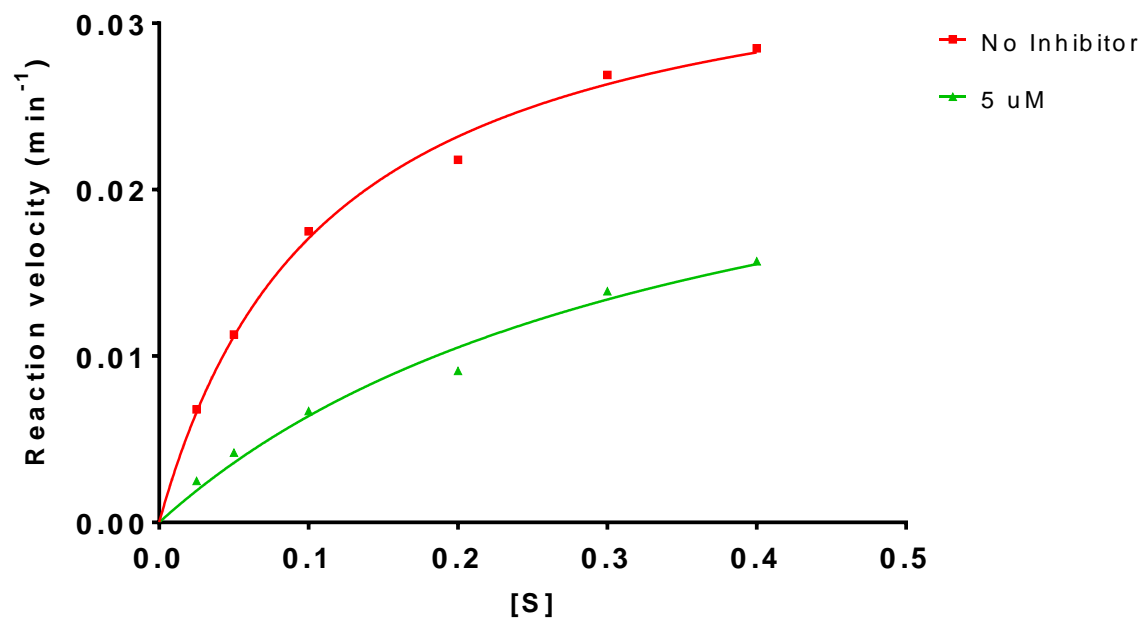
Michaelis-Menten plot
 β -galactosidase (*E. Coli*)
 N1-Nonyl (26)



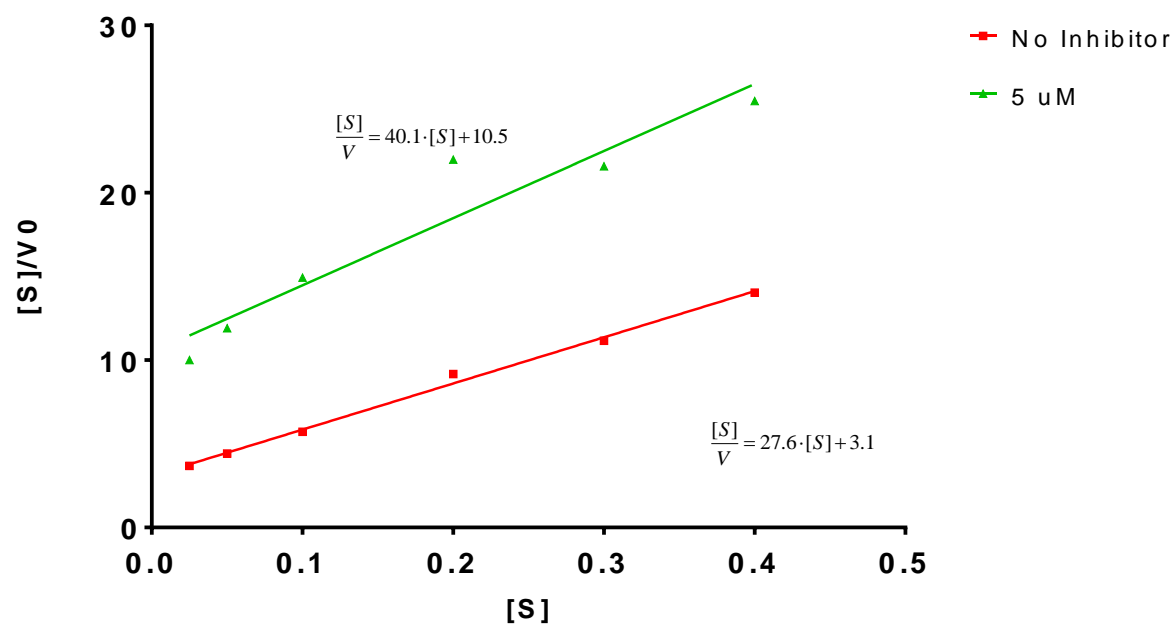
Hanes-Wolf plot
 β -galactosidase (*E. Coli*)
 N1-Nonyl (26)



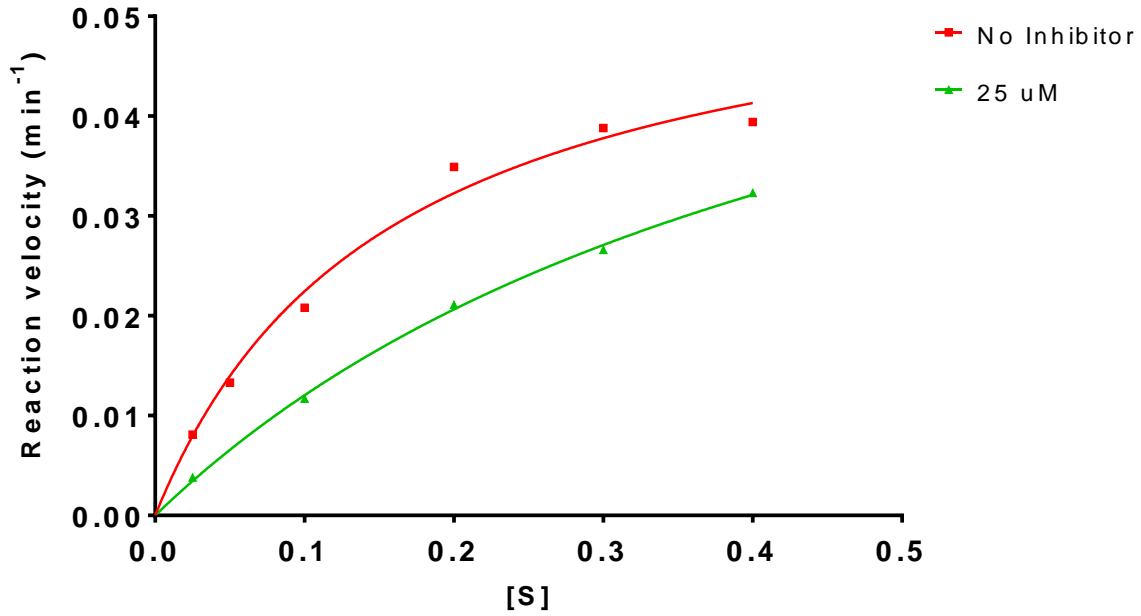
Michaelis-Menten plot
 β -galactosidase (*E. Coli*)
 N2-Butyl (5-HCl)



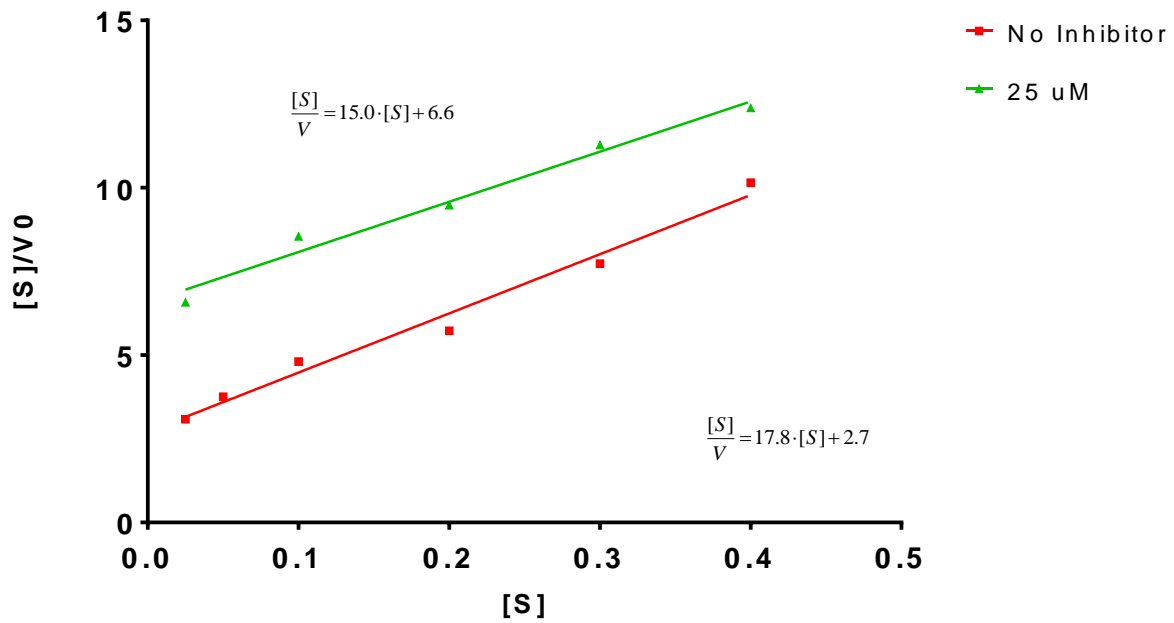
Hanes-Wolf plot
 β -galactosidase (*E. Coli*)
 N2-Butyl (5-HCl)



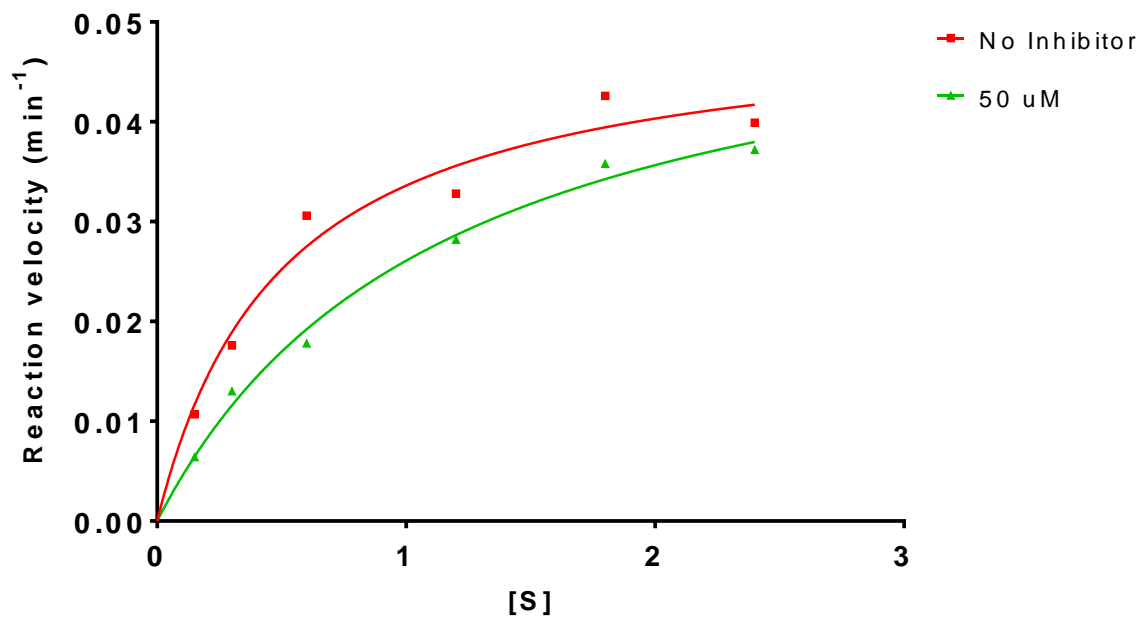
Michaelis-Menten plot
 β -galactosidase (*E. coli*)
 N2-Nonyl (34)



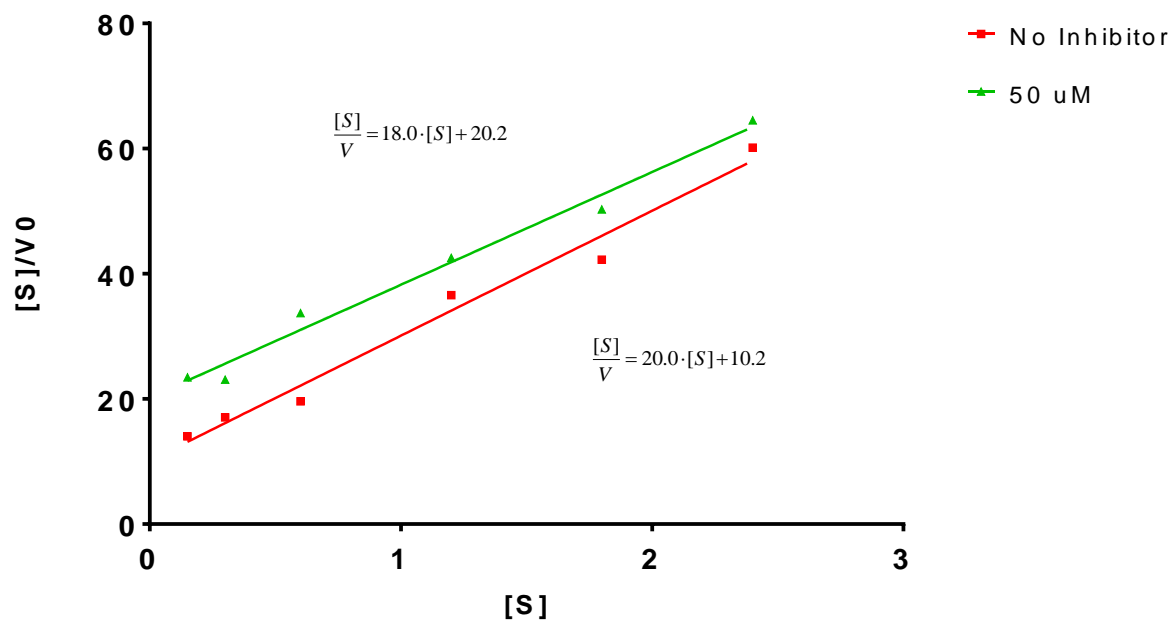
Hanes-Wolf plot
 β -galactosidase (*E. coli*)
 N2-Nonyl (34)



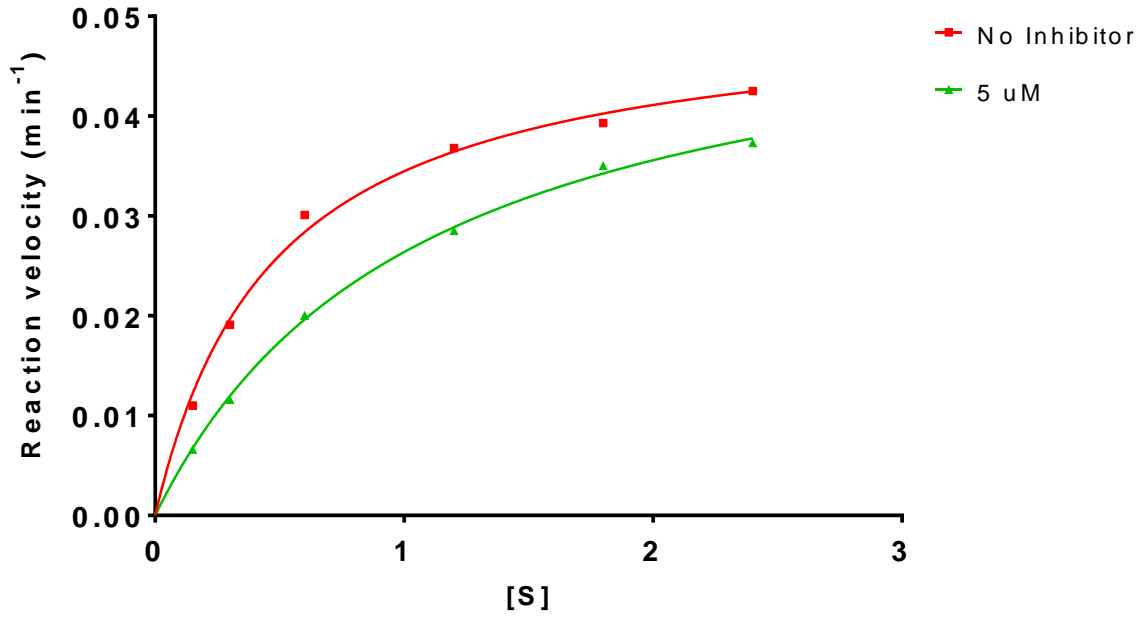
Michaelis-Menten plot
 ●-galactosidase (Coffee)
 N1-Phenethyl (28)



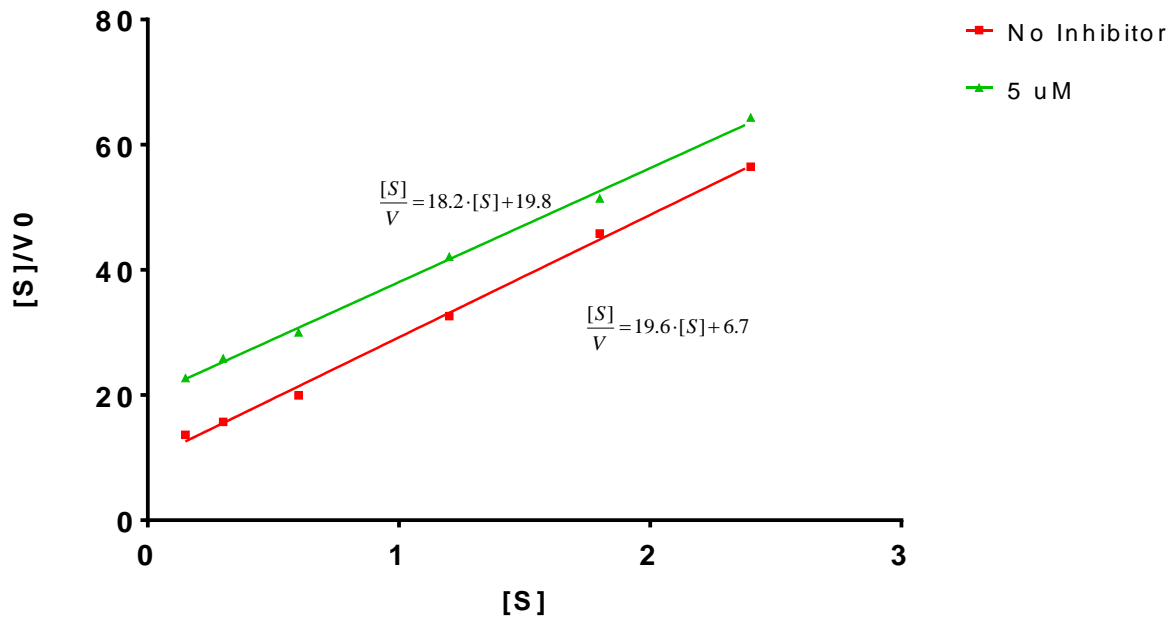
Hanes-Wolf plot
 ●-galactosidase (Coffee)
 N1-Phenethyl (28)



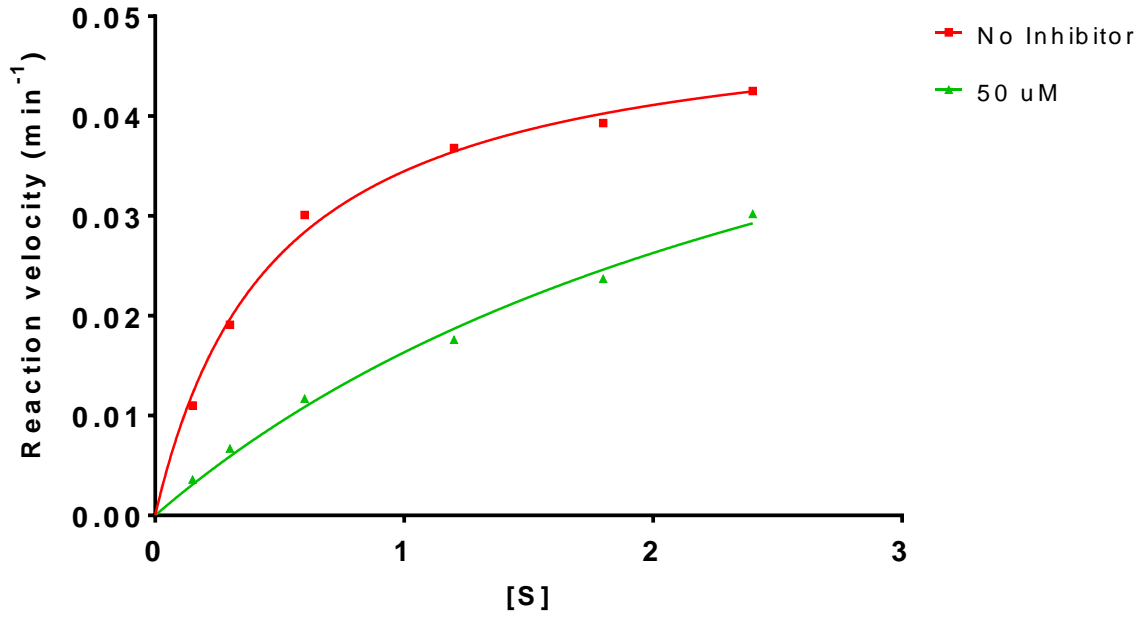
Michaelis-Menten plot
 ●-galactosidase (Coffee)
 N1-Butyl (4)



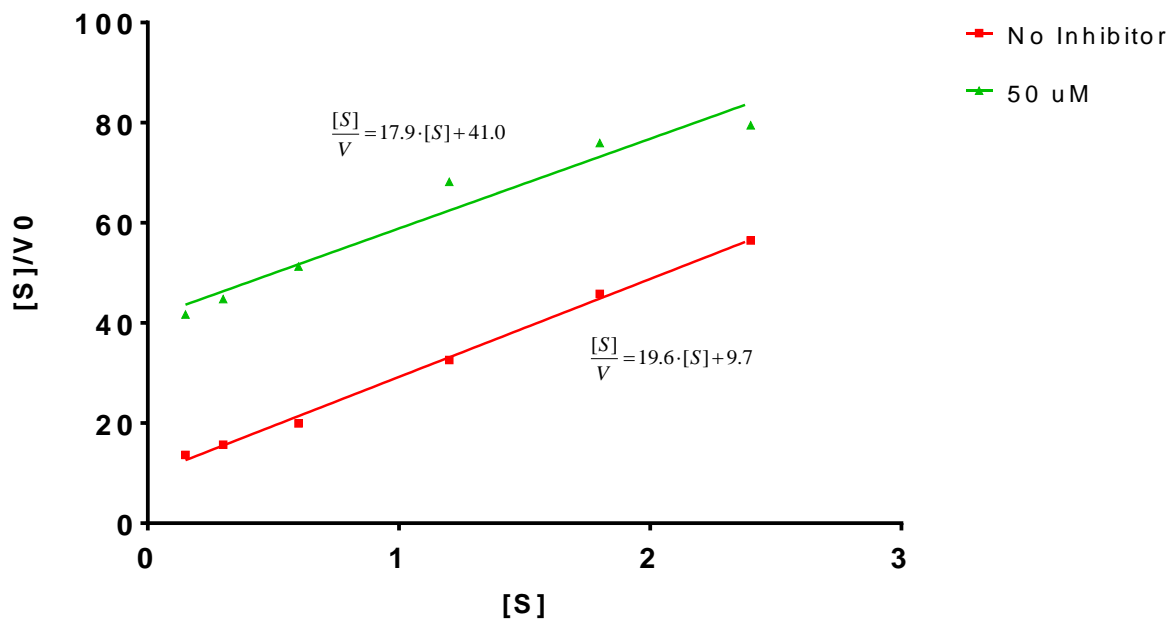
Hanes-Wolf plot
 ●-galactosidase (Coffee)
 N1-Butyl (4)



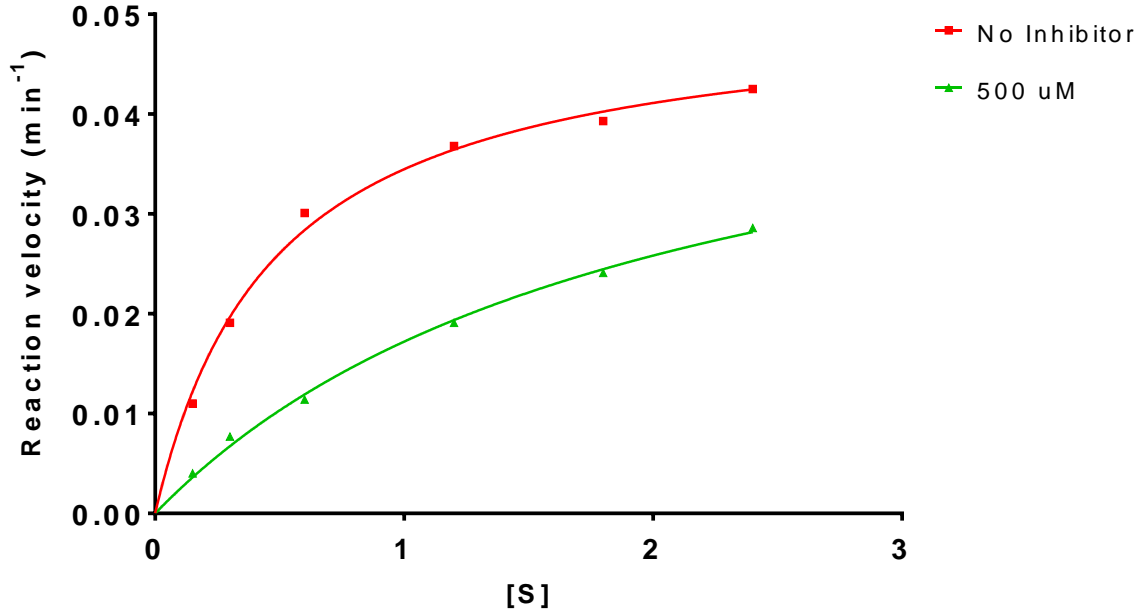
Michaelis-Menten plot
 ●-galactosidase (Coffee)
 N1-Nonyl (26)



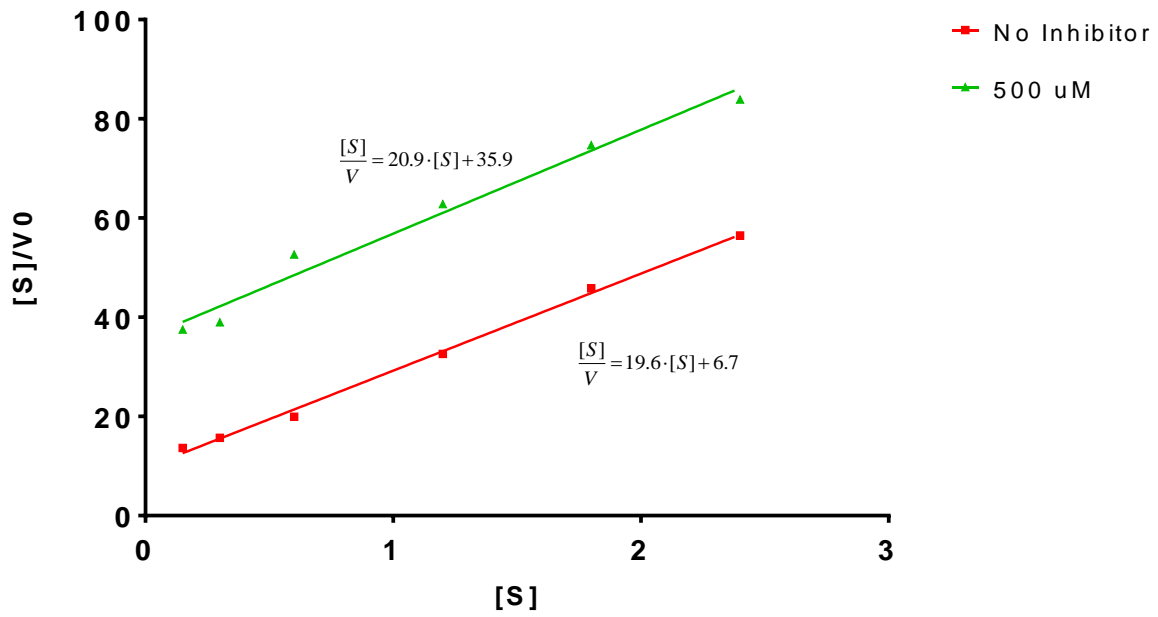
Hanes-Wolf plot
 ●-galactosidase (Coffee)
 N1-Nonyl (26)



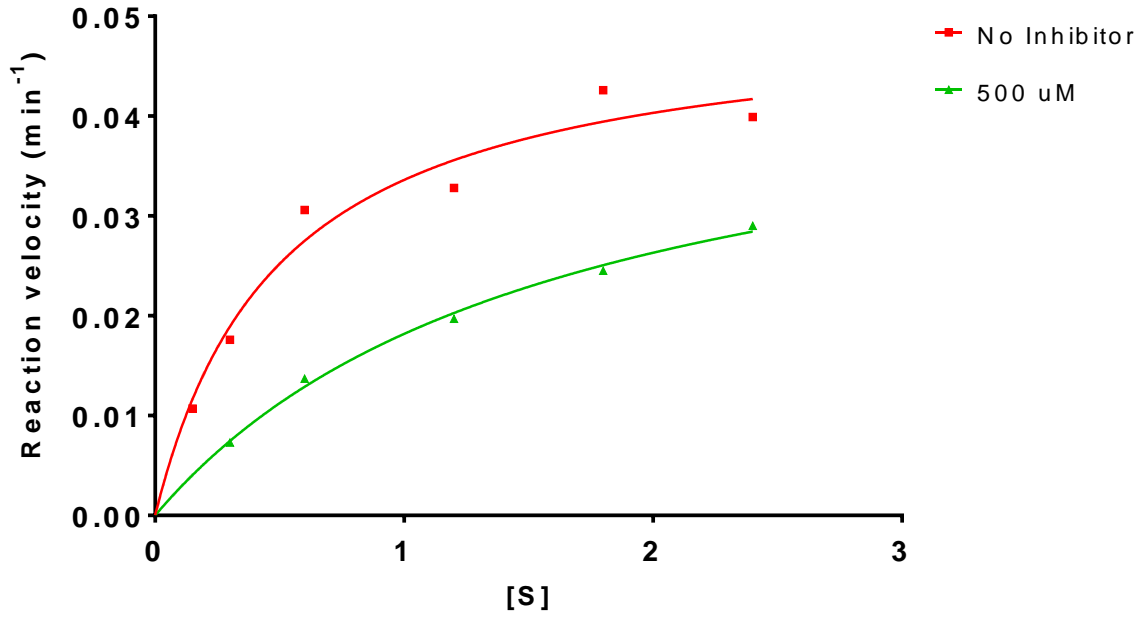
Michaelis-Menten plot
 ●-galactosidase (Coffee)
 N2-Butyl (5-HCl)



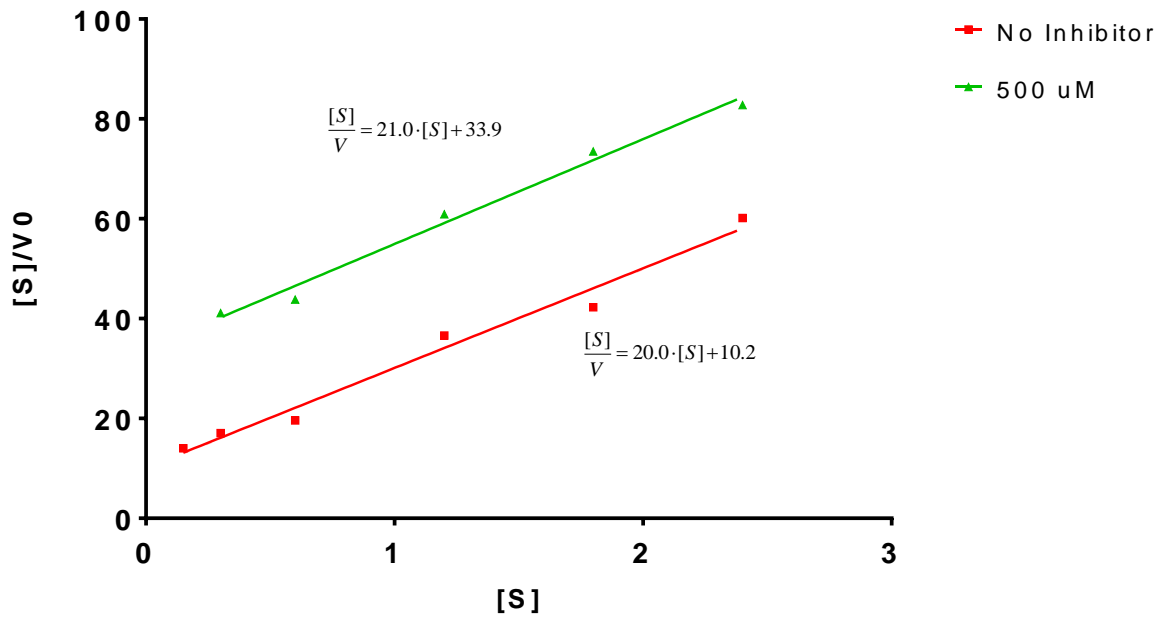
Hanes-Wolf plot
 ●-galactosidase (Coffee)
 N2-Butyl (5-HCl)



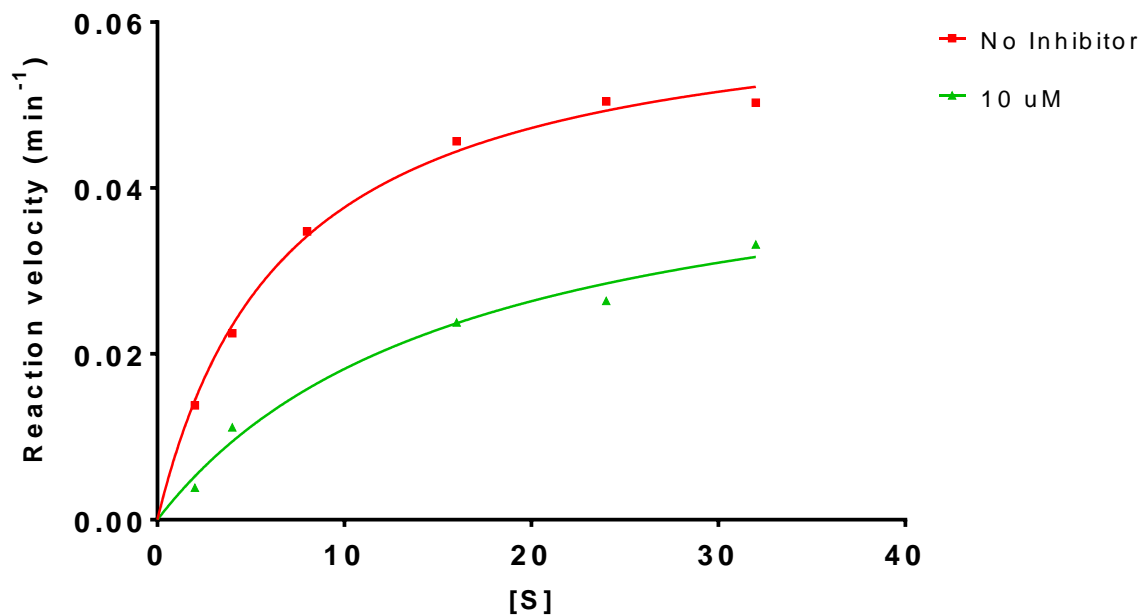
Michaelis-Menten plot
 ●-galactosidase (Coffee)
 N2-Nonyl (34)



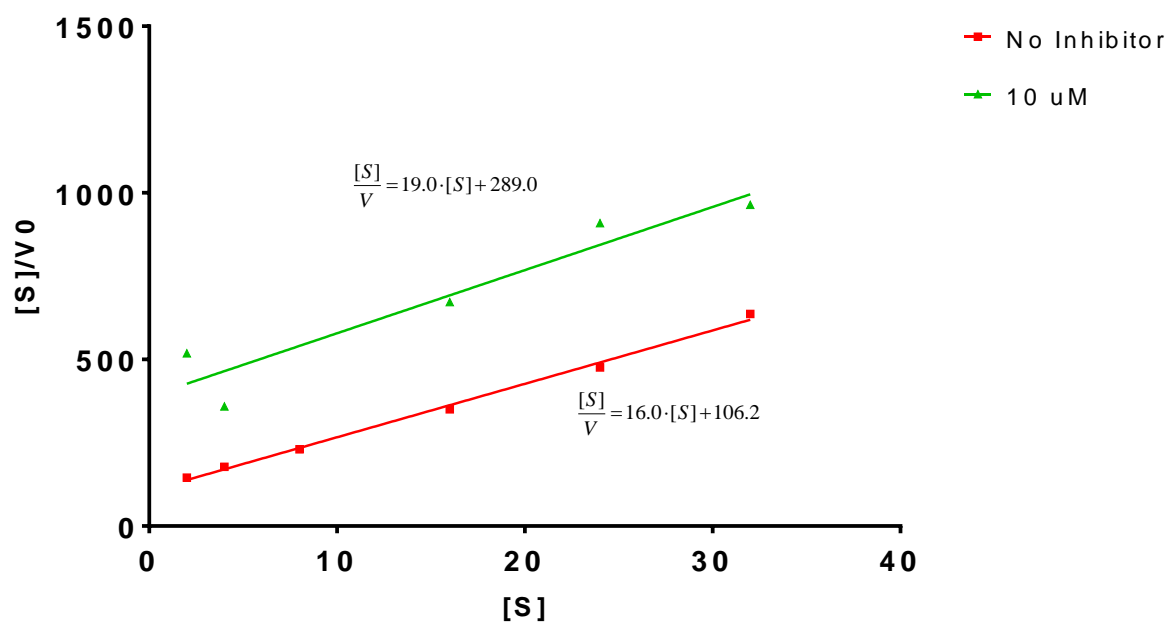
Hanes-Wolf plot
 ●-galactosidase (Coffee)
 N2-Nonyl (34)



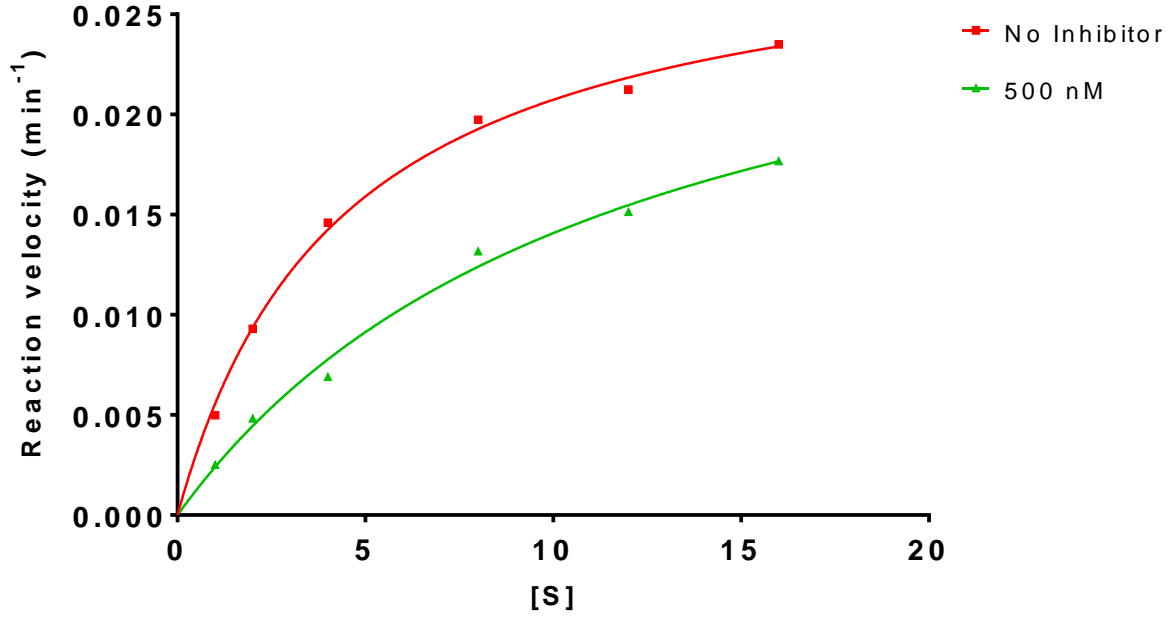
Michaelis-Menten plot
Galactocerebrosidase (mouse)
N1-Phenethyl (28)



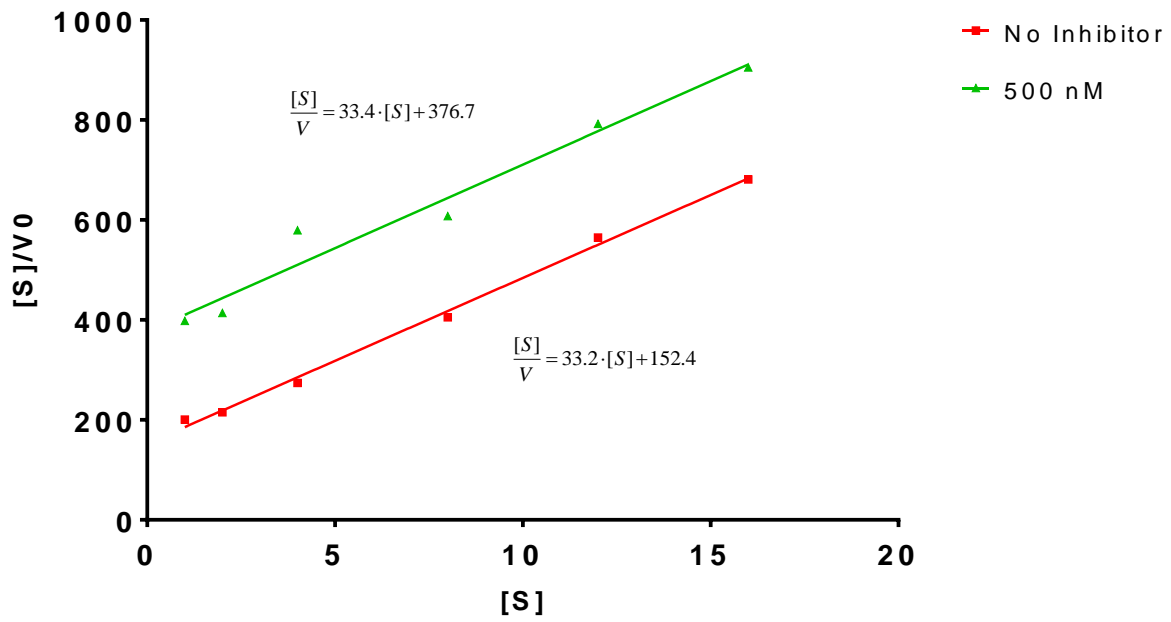
Hanes-Wolf plot
Galactocerebrosidase (mouse)
N1-Phenethyl (28)



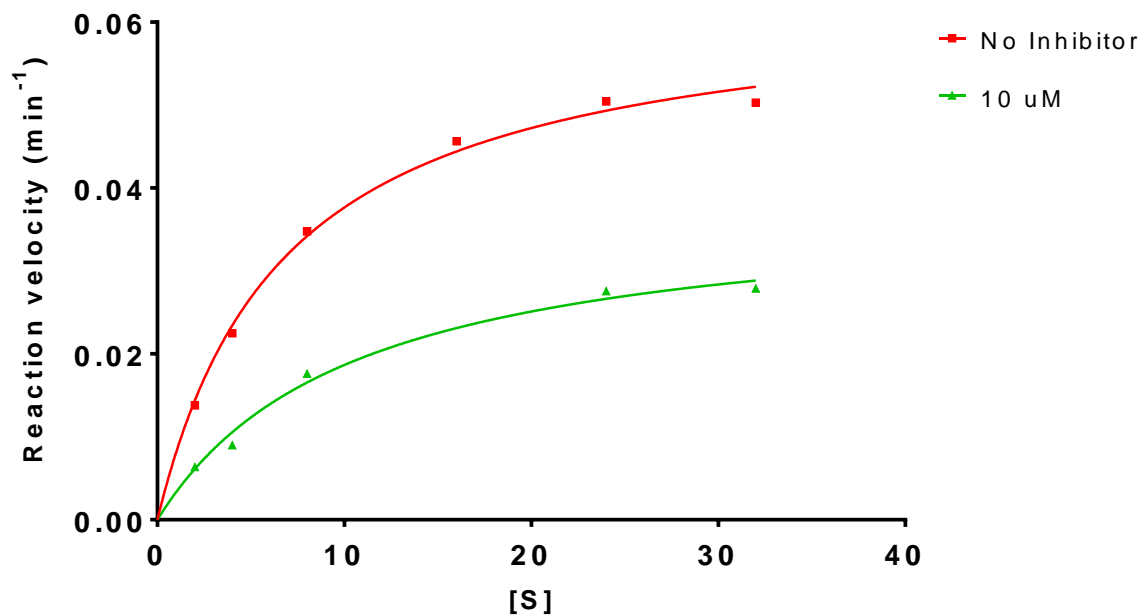
Michaelis-Menten plot
Galactocerebrosidase (mouse)
N2-Butyl (5-HCl)



Hanes-Wolf plot
Galactocerebrosidase (mouse)
N2-Butyl (5-HCl)



Michaelis-Menten plot
Galactocerebrosidase (mouse)
N2-Nonyl (34)



Hanes-Wolf plot
Galactocerebrosidase (mouse)
N2-Nonyl (34)

