D-Glucosamine as a novel chiral auxiliary for the stereoselective synthesis of P-stereogenic phosphines oxides.

Alice D'Onofrio,[a] Laurent Copey,[a] Ludivine Jean-Gérard,[a] Catherine Goux-Henry,[a] Guillaume Pilet,[b] Bruno Andrioletti[a] and Eric Framery*[a]

[a] Institut de Chimie et Biochimie Moléculaires et Supramoléculaires (ICBMS-UMR CNRS 5246), Université Claude Bernard Lyon 1, 43 Bd du 11 Novembre 1918, 69622 Villeurbanne cedex, France.

[b] Laboratoire des Multimatériaux et Interfaces (LMI-UMR CNRS 5615), Université Claude Bernard Lyon 1, 43 Bd du 11 Novembre 1918, 69622 Villeurbanne cedex, France.

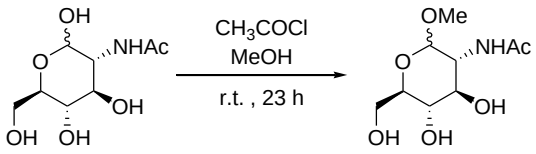
I. Synthesis of compounds.

All reactions were performed under an argon atmosphere using Schlenk techniques. THF was freshly distilled over sodium/benzophenone. Dry dichloromethane stabilized on amylene was purchased from Aldrich and used as received. Phenylphosphonic dichloride and *N*-methylimidazole were freshly distilled under reduced pressure before use. Organometallics reagents were ordered from Aldrich or Acros® as solutions in THF unless otherwise specified, and used as received.

Analytical TLC was performed on ready-made plates coated with silica gel on aluminium (Merck 60 F_{254}). Products were visualized by ultraviolet light and treatment with permanganate stain followed by gentle heating. Flash chromatography was performed using silica gel (60 Å, particle size 40-63µm).

NMR spectra were recorded on a Bruker ALS-300 MHz spectrometer with a QNP probe in $CDCl_3$. ^1H and ^{13}C chemical shifts are reported in parts per million (ppm) downfield to tetramethylsilane using the residual solvent signal as internal standard. ^{31}P spectra are decoupled ^1H and referenced to H_3PO_4. Proton (^1H) NMR information is given in the following format: multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad signal), coupling constant (*J*) in Hertz (Hz), number of protons. UV spectra were recorded on a Shimadzu UVmini-1240. High resolution mass spectrometry spectra are recorded on BruckerMicrOQTOF-Q II XL. The enantiomeric excess was determined by chiral HPLC using a Chiralpack AD column (4.6mm x 25cm) or a Cellulose OD-H column (4.6mm x 20cm).

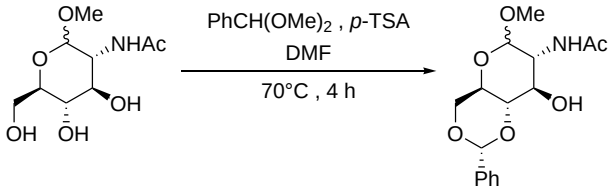
I-1. Synthesis of methyl 2-*N*-acetamido-2-deoxy-D-glucopyranoside.



In a Schlenk tube, *N*-acetyl-D-glucosamine (3.60 g, 16.27 mmol) was added on a cooled solution of acetyl chloride (5.75 g, 73.00 mmol) in freshly dried methanol (70 mL). The resulting mixture was stirred at room temperature for 23 hours. After concentration methyl *N*-acetyl-D-glucosamine was obtained in quantitative yield as a white solid in α/β anomeric ratio of 3/2. ^1H NMR (300 MHz, MeOH-d4), δ(ppm) = 4.70 (d, *J* = 3.6 Hz, 0.6H), 4.35 (d, *J* = 8.4 Hz, 0.4H), 3.95 (dd, *J* = 10.6, 3.4 Hz, 0.6H), 3.90 (dd, *J* = 11.9, 1.9 Hz, 0.4H), 3.85 (dd, *J* = 11.9, 2.4 Hz, 0.6H), 3.76 – 3.65 (m, 2H), 3.60 – 3.45 (m, 2H), 3.40 (s, 1.8H), 3.36 (s, 1.2H), 3.25 – 3.20 (m, 0.4H), 2.14 (s, 1.2H), 2.12 (s, 1.8H); ^{13}C NMR (75 MHz, MeOH-d4), δ (ppm)

= 173.9 (C), 173.5 (C), 101.7 (CH), 98.0 (CH), 76.6 (CH), 74.5 (CH), 72.3 (CH), 71.3 (CH), 70.8 (CH), 70.6 (CH), 61.2 (CH_2), 61.1 (CH_2), 56.7 (CH), 55.7 (CH), 54.7 (CH_3), 54.1 (CH_3), 20.6 (CH_3), 20.3 (CH_3). The NMR data are in agreement with the literature.[1]

I-2. Synthesis of methyl 2-*N*-acetamido-4,6-*O*-benzylidene-2-deoxy-D-glucopyranoside.

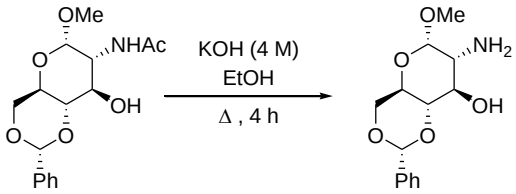


In a Schlenk tube, to a solution of methyl *N*-acetyl-D-glucosamine (3.62 g, 16.27 mmol) in anhydrous DMF (40 mL), benzaldehyde dimethylacetal (4.95 g, 32.54 mmol) and *p*-toluene sulfonic acid (0.06 g, 0.32 mmol) were added. The mixture was stirred at 70°C for 4 hours. Then, the solvent was evaporated under reduced pressure, and the residue was partitioned between chloroform (100 mL) and aqueous solution of saturated $NaHCO_3$ (50 mL). The organic layer was extracted, washed with brine (30 mL), and dried over Na_2SO_4. After filtration, and concentration, the two anomers were isolated by flash chromatography on silica gel using a mixture of $CHCl_3$ / MeOH (98/2) as eluent.

Methyl 2-N-acetamido-4,6-O-benzylidene-2-deoxy-α-D-glucopyranoside: white solid in 60% yield, m.p.= 290°C. Rf = 0.40 ($CHCl_3$ / MeOH 9/1). ^{1}H NMR (300 MHz, $CDCl_3$), δ(ppm) = 7.53 – 7.46 (m, 2H), 7.40 – 7.32 (m, 3H), 5.89 (br d, *J* = 8.8 Hz, 1H), 5.56 (s, 1H), 4.72 (d, *J* = 4.0 Hz, 1H), 4.28 (dd, *J* = 8.1, 2.9 Hz, 1H), 4.23 (ddd, *J* = 9.2, 8.8, 4.0 Hz, 1H), 3.90 (br dd, *J* = 9.2, 9.1 Hz, 1H), 3.83 – 3.74 (m, 2H), 3.59 (dd, *J* = 9.1, 9.0 Hz, 1H), 3.41 (s, 3H), 3.12 (br s, 1H), 2.14 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ(ppm) = 171.5 (C), 137.1 (C), 129.2 (CH), 128.3 (2 x CH), 126.4 (2 x CH), 102.0 (CH), 98.8 (CH), 82.1 (CH), 71.0 (CH), 68.6 (CH_2), 62.3 (CH), 55.1 (CH_3), 54.0 (CH), 23.4 (CH_3). $[\alpha]^{25}_D$ = +46.3 (c = 1.00, MeOH), lit.[1] $[\alpha]^{25}_D$ = +90 (c = 0.11, MeOH). The NMR data are in agreement with the literature.[1]

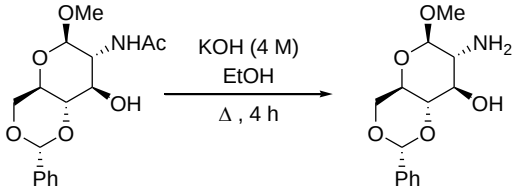
Methyl 2-N-acetamido-4,6-O-benzylidene-2-deoxy-β-D-glucopyranoside: white solid in 26% yield, m.p.= 285°C. Rf = 0.30 ($CHCl_3$ / MeOH 9/1). ^{1}H NMR (300 MHz, MeOH-d4), δ(ppm) = 7.56 – 7.45 (m, 2H), 7.41 - 7.28 (m, 3H), 5.61 (s, 1H), 4.45 (d, *J* = 8.4 Hz, 1H), 4.31 (dd, *J* = 10.2, 4.8 Hz, 1H), 3.88 – 3.70 (m, 3H), 3.59 – 3.34 (m, 2H), 3.46 (s, 3H), 1.99 (s, 3H); ^{13}C NMR (75 MHz, MeOH-d4), δ(ppm) = 172.9 (C), 138.3 (C), 129.1 (CH), 128.2 (2 x CH), 126.7 (2 x CH), 103.3 (CH), 102.1 (CH), 82.0 (CH), 71.8 (CH), 68.8 (CH_2), 66.8 (CH), 57.0 (CH_3), 56.4 (CH), 22.1 (CH_3). $[\alpha]^{25}_D$ = -59.7 (c = 0.21, MeOH), lit.[1] $[\alpha]^{25}_D$ = -57 (c = 0.21, MeOH). The NMR data are in agreement with the literature.[1]

I-3. Synthesis of methyl 2-amino-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside.



The corresponding benzylidene acetal (1.14 g, 3.52 mmol) was added to a solution of KOH (4M, 30 mL) in ethanol. The mixture was heated under reflux for 4 hours. After TLC ($CHCl_3$ / MeOH 9/1) showed completion of the reaction, most of ethanol was evaporated. After dilution with dichloromethane (30 mL), the organic phase was washed twice with water (2 x 20 mL), dried over Na_2SO_4, and concentrated to give crude product as an orange solid in 97% yield. No further purification was necessary. m.p.= 155°C. ^{1}H NMR (300 MHz, $CDCl_3$), δ(ppm) = 7.54 – 7.45 (m, 2H), 7.42 – 7.32 (m, 3H), 5.53 (s, 1H), 4.67 (d, *J* = 3.7 Hz, 1H), 4.27 (dd, *J* = 8.6, 3.5 Hz, 1H), 3.84 – 3.57 (m, 3H), 3.46 (dd, *J* = 8.6, 8.6 Hz, 1H), 3.41 (s, 3H), 2.76 (dd, *J* = 9.4, 3.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$), δ(ppm): 137.4 (C), 129.4 (CH), 128.5 (2 x CH), 126.5 (2 x CH), 102.1 (CH), 101.4 (CH), 82.2 (CH), 71.9 (CH), 69.2 (CH_2), 62.7 (CH), 56.8 (CH), 55.6 (CH_3). $[\alpha]^{25}_D$ = +47.4 (c = 0.27, $CHCl_3$), lit.[1] $[\alpha]^{25}_D$ = +103.1 (c = 0.905, $CHCl_3$). The NMR data are in agreement with the literature.[1]

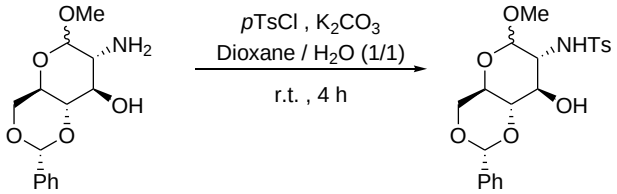
I-4. Synthesis of methyl 2-amino-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside.



The corresponding benzylidene acetal (0.20 g, 0.22 mmol) was added to a solution of KOH (4M, 6 mL) in ethanol. The mixture was heated under reflux for 4 hours. After TLC ($CHCl_3$ / MeOH 9/1) showed completion of the reaction, most of ethanol was evaporated. After dilution with dichloromethane (10 mL), the organic phase was washed twice with water (2 x 5 mL), dried over Na_2SO_4, and concentrated to give crude product as an orange solid in 73% yield. No further purification was necessary. m.p.= 155°C. ^{1}H NMR (300 MHz, $CDCl_3$), δ(ppm) = 7.55 – 7.45 (m, 2H), 7.42 – 7.32 (m, 3H), 5.54 (s, 1H), 4.33 (dd, *J* = 10.4, 4.8 Hz, 1H), 4.23 (d, *J* = 8.4 Hz, 1H), 3.78 (dd, *J* = 10.2, 10.2 Hz, 1H), 3.66 (dd, *J* = 9.2, 9.2 Hz, 1H), 3.57 – 3.40 (m, 2H), 3.54 (s, 3H), 2.79 (dd, *J* = 8.4, 8.4 Hz, 1H), 2.49 (br s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$), δ(ppm) = 137.0 (C), 129.2 (CH), 128.2 (2 x CH), 126.2 (2 x CH), 105.0 (CH), 101.8 (CH), 81.2 (CH), 72.8 (CH), 68.6 (CH_2), 66.3 (CH), 57.7 (CH), 57.3 (CH_3).

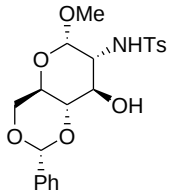
$[\alpha]^{25}_D$ = -39.3 (c = 0.22, $CHCl_3$), lit.[1] $[\alpha]^{25}_D$ = -55.6 (c = 0.90, $CHCl_3$). The NMR data are in agreement with the literature.[1]

I-5. Sulfonylation of methyl 2-amino-4,6-*O*-benzylidene-2-deoxy-D-glucopyranoside.



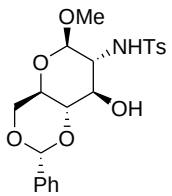
α- or β-anomer of methyl 2-amino-4,6-benzylidine-2-deoxy-2-glucopyranoside (200 mg, 0.71 mmol) and K_2CO_3 (118 mg, 0.85 mmol) were dissolved in a 1/1 water / dioxane mixture (5 mL). *p*-Toluenesulfonyl chloride (149 mg, 0.78 mmol) was then added, and the mixture was stirred at room temperature for 4 hours. After concentration, the residue was dissolved in chloroform (10 mL), and washed successively with a saturated aqueous Na_2CO_3 solution (10 mL) and brine (10 mL). The organic phase was dried over $MgSO_4$, and concentrated. Purification was performed by column chromatography on silica gel using a mixture of Cyclohexane / EtOAc (7/3) as eluent.

Methyl 4,6-O-benzylidene-2-deoxy-2-N-p-toluenesulfonamido-α-D-glucopyranoside ***1***: white



solid in 64% yield, m.p.= 182°C. Rf = 0.17 (Cyclohexane / EtOAc 7/3). ^{1}H NMR (300 MHz, $CDCl_3$), δ(ppm) = 7.81 (d, *J* = 8.3 Hz, 2H), 7.48 – 7.40 (m, 2H), 7.38 – 7.29 (m, 5H), 5.50 (s, 1H), 5.04 (br d, *J* = 9.5 Hz, 1H), 4.38 (d, *J* = 3.8 Hz, 1H), 4.23 (dd, *J* = 9.0, 3.6 Hz, 1H), 3.84 (dd, *J* = 9.5, 9.5 Hz, 1H), 3.75 – 3.66 (m, 2H), 3.53 – 3.45 (m, 1H), 3.39 (ddd, *J* = 9.5, 9.5, 3.8 Hz, 1H), 3.29 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ(ppm) = 143.6 (C), 137.3 (C), 136.6 (C), 129.5 (2 x CH), 128.9 (CH), 128.0 (2 x CH), 126.8 (2 x CH), 126.0 (2 x CH), 101.6 (CH), 98.4 (CH), 80.9 (CH), 69.1 (CH), 68.4 (CH_2), 61.9 (CH), 57.9 (CH), 55.2 (CH_3), 21.3 (CH_3). $[\alpha]^{25}_D$ = +36.0 (c = 0.97, $CHCl_3$), lit.[2] $[\alpha]^{25}_D$ = +34.4 (c = 0.77, $CHCl_3$). The NMR data are in agreement with the literature.[2,3]

Methyl 4,6-O-benzylidene-2-deoxy-2-N-p-toluenesulfonamido-α-D-glucopyranoside ***2***: white



solid in 56% yield, m.p.= 180°C. Rf = 0.19 (Cyclohexane / EtOAc 7/3). ^{1}H NMR (300 MHz, $CDCl_3$), δ(ppm) = 7.79 (d, *J* = 8.3 Hz, 2H), 7.52 – 7.42 (m, 2H), 7.40 - 7.28 (m, 5H), 5.51 (s, 1H), 5.26 (br s, 1H, NH), 4.29 (dd, *J* = 10.5, 4.9 Hz, 1H), 4.16 (d, *J* = 8.2 Hz, 1H), 3.90 (br dd, *J* = 9.3, 9.3 Hz, 1H), 3.72 (dd, *J* = 10.5, 10.5 Hz, 1H), 3.52 (dd, *J* = 9.3, 9.3 Hz, 1H), 3.43 – 3.32 (m, 2H), 3.22 – 3.12 (m, 4H), 2.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ(ppm) = 143.6 (C), 137.4 (C), 136.9 (C),

129.5 (2 x CH), 129.2 (CH), 128.3 (2 x CH), 127.5 (2 x CH), 126.3 (2 x CH), 102.5 (CH), 101.9 (CH), 80.9 (CH), 71.6 (CH), 68.5 (CH_2), 66.2 (CH), 61.0 (CH), 57.0 (CH_3), 21.6 (CH_3). $[\alpha]^{25}_D$ = -58.0 (c = 0.965, $CHCl_3$), lit.[4] $[\alpha]^{25}_D$ = -56.9 (c = 0.56, $CHCl_3$). The NMR data are in agreement with the literature.[4]

I-6. References.

[1] D. P. G. Emmerson, W. P. Hems, B. G. Davis, *Tetrahedron: Asymmetry* **2005**, *16*, 213.

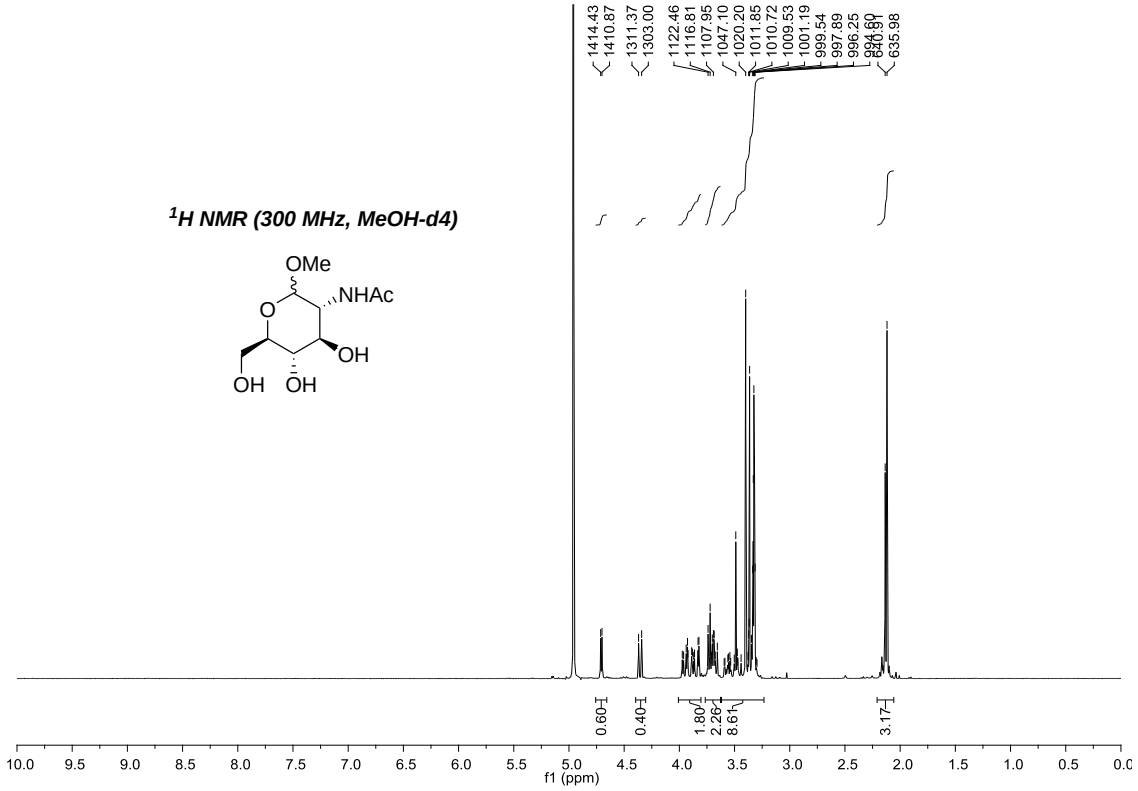
[2] T. Bauer, J. Tarasiuk, K. Pasniczek, *Tetrahedron: Asymmetry* **2002**, *13*, 77.

[3] D. P. G. Emmerson, R. Villard, C. Mugnaini, A. Batsanov, J. A. K. Howard, W. P. Hems, R. P. Tooze, B. G. Davis, *Org. Biomol. Chem.* **2003**, *1*, 3826.

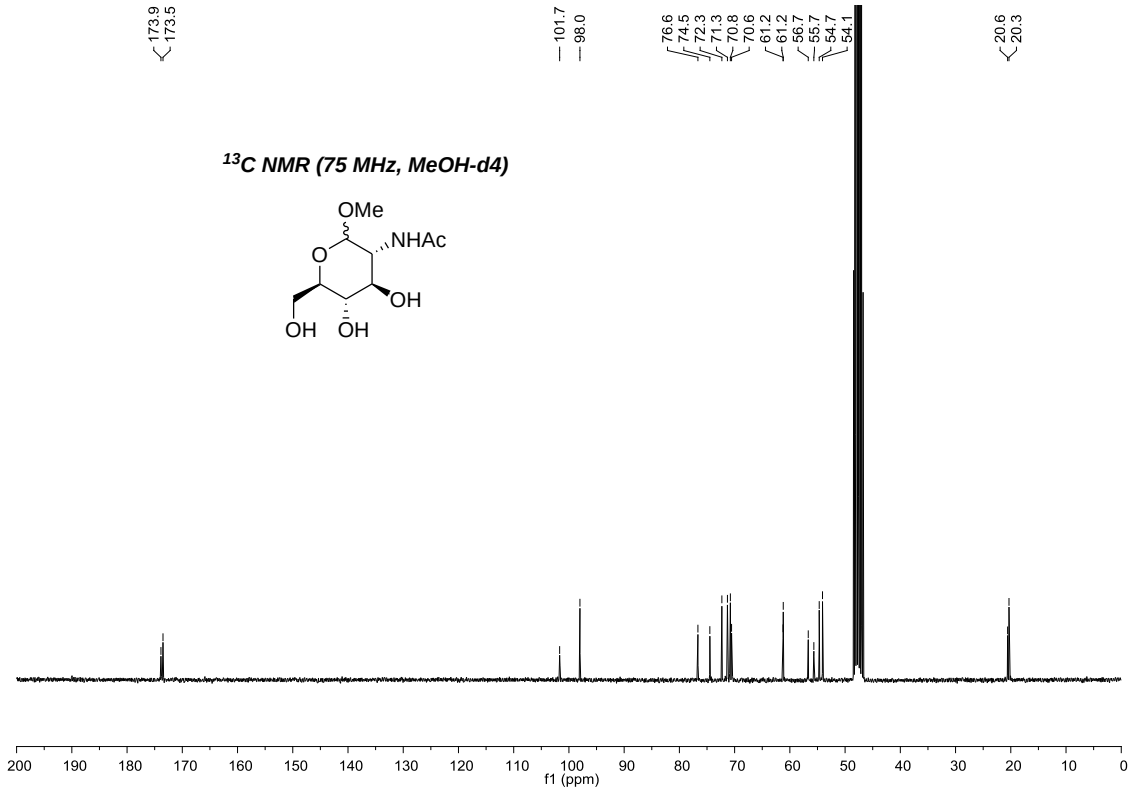
[4] T. Bauer, S. Smolinski, *Applied Catal. A: General* **2010**, *375*, 247.

II. NMR data.

^{1}H & ^{13}C NMR of methyl 2-N-acetamido-2-deoxy-D-glucopyranoside.

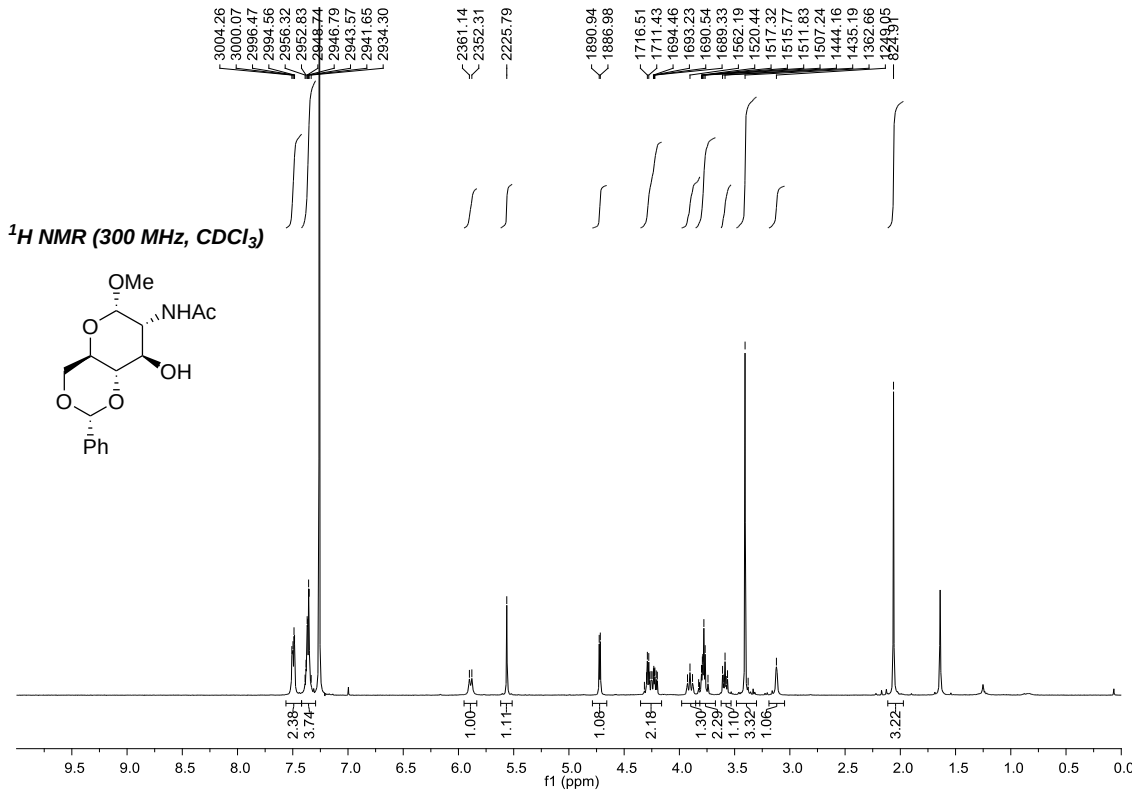


^{1}H NMR (300 MHz, MeOH-d4)

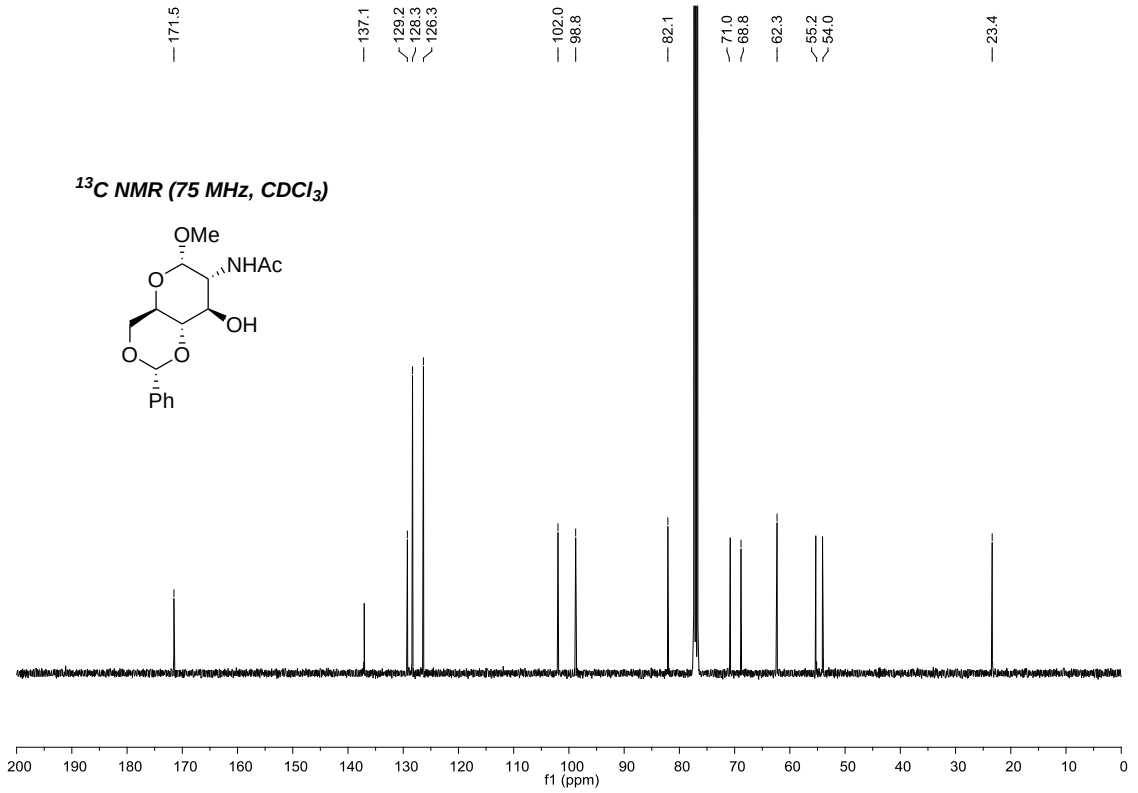


^{13}C NMR (75 MHz, MeOH-d4)

^{1}H & ^{13}C NMR of methyl 2-N-acetamido-4,6-O-benzylidene-2-deoxy-α-D-glucopyranoside.

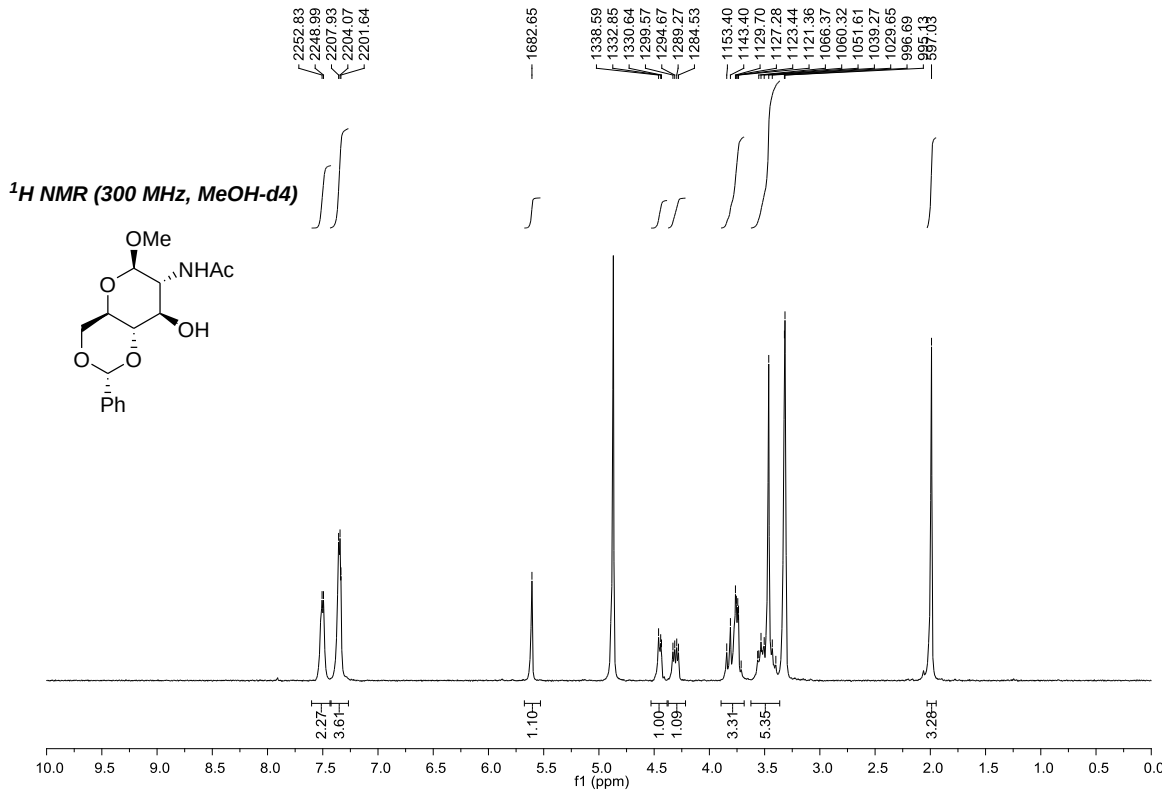


^{1}H NMR (300 MHz, $CDCl_3$)

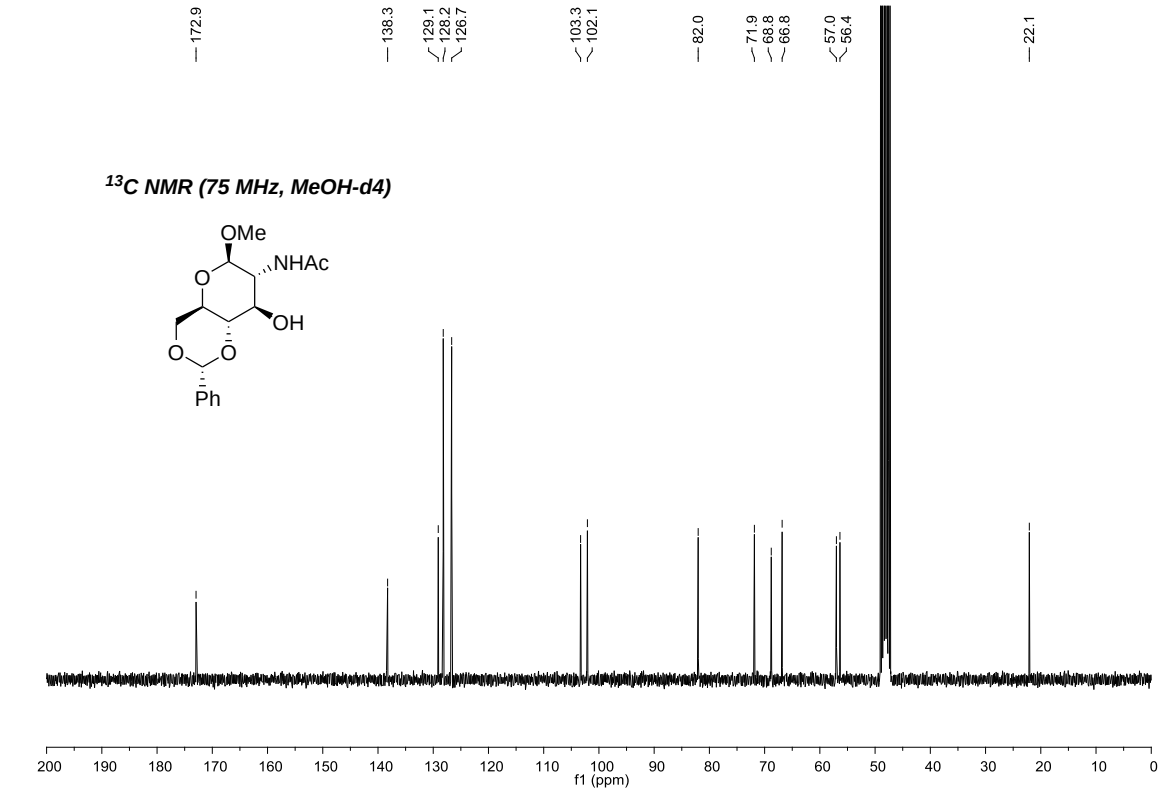


^{13}C NMR (75 MHz, $CDCl_3$)

^{1}H & ^{13}C NMR of methyl 2-N-acetamido-4,6-O-benzylidene-2-deoxy-β-D-glucopyranoside.

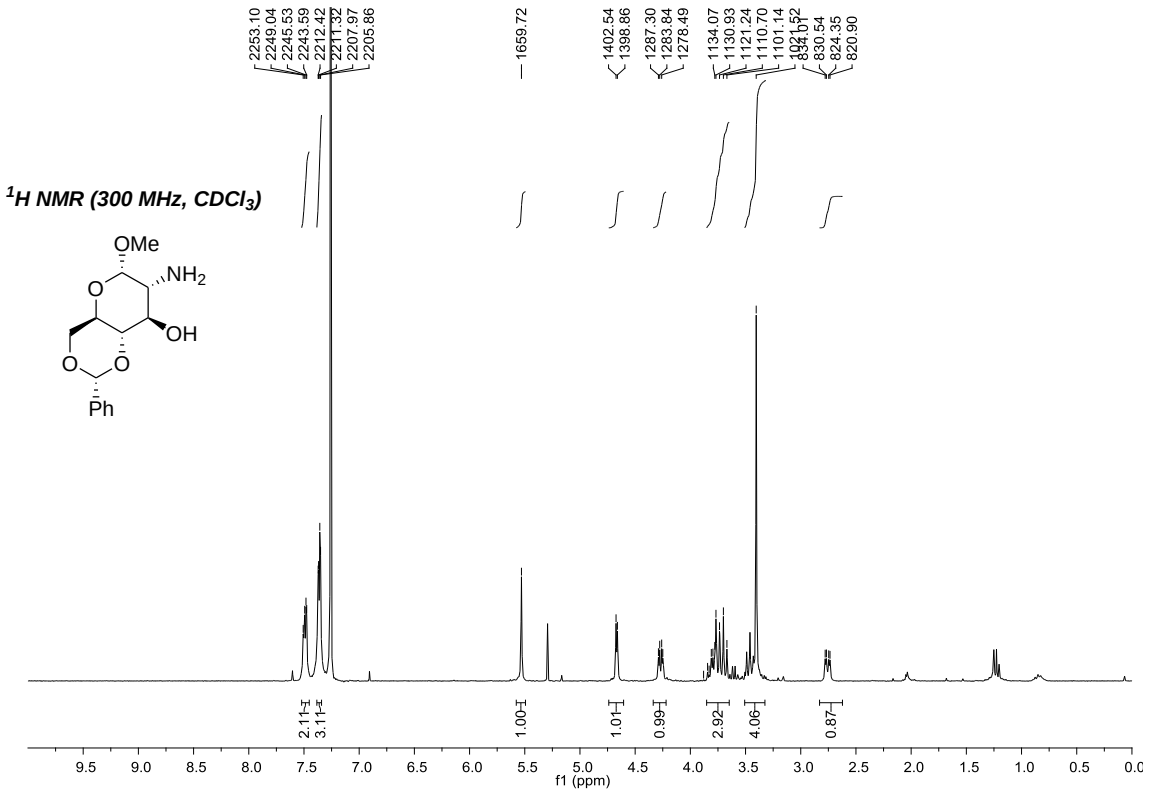


^{1}H NMR (300 MHz, MeOH-d4)

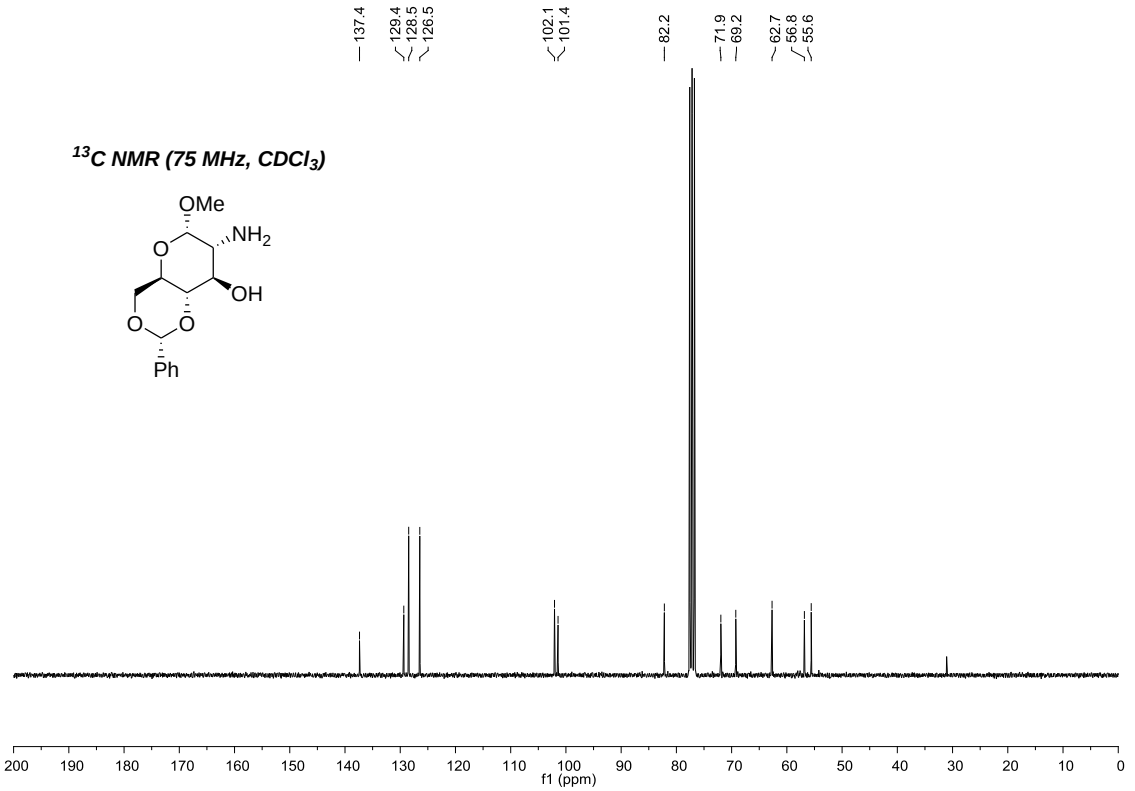


^{13}C NMR (75 MHz, MeOH-d4)

^{1}H & ^{13}C NMR of methyl 2-amino-4,6-O-benzylidene-2-deoxy-α-D-glucopyranoside.

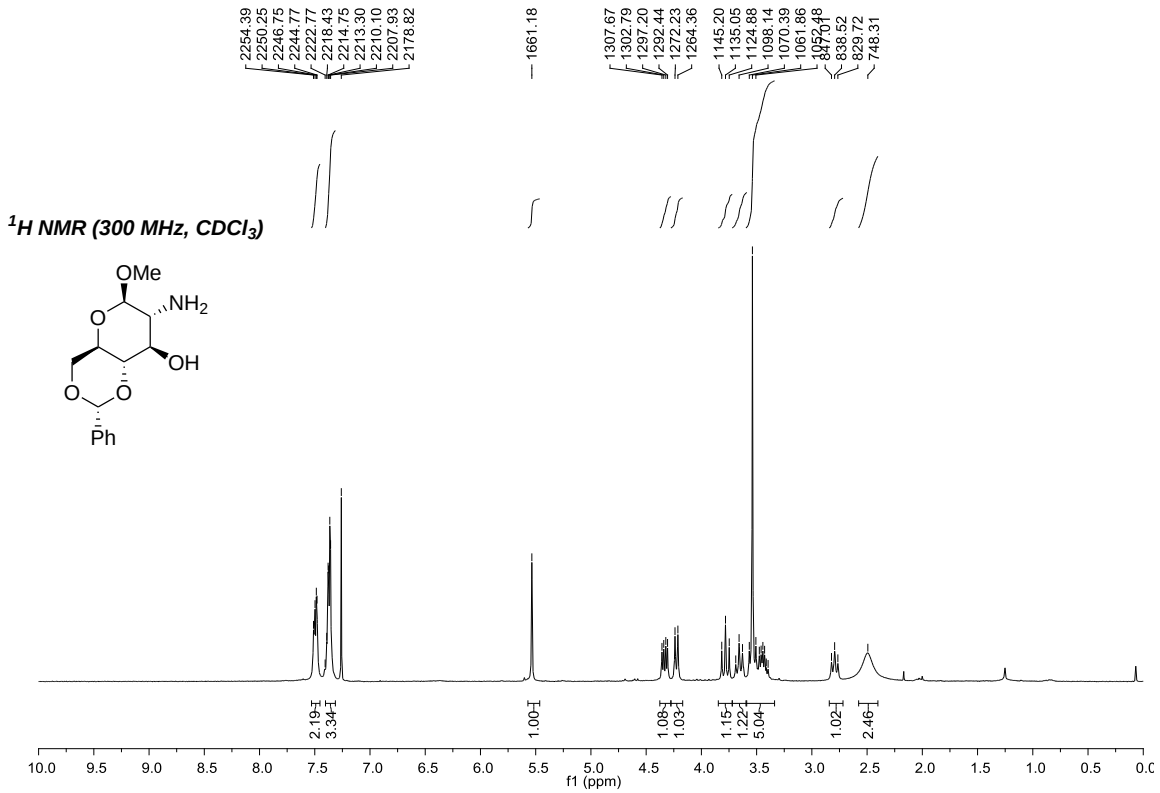


^{1}H NMR (300 MHz, $CDCl_3$)

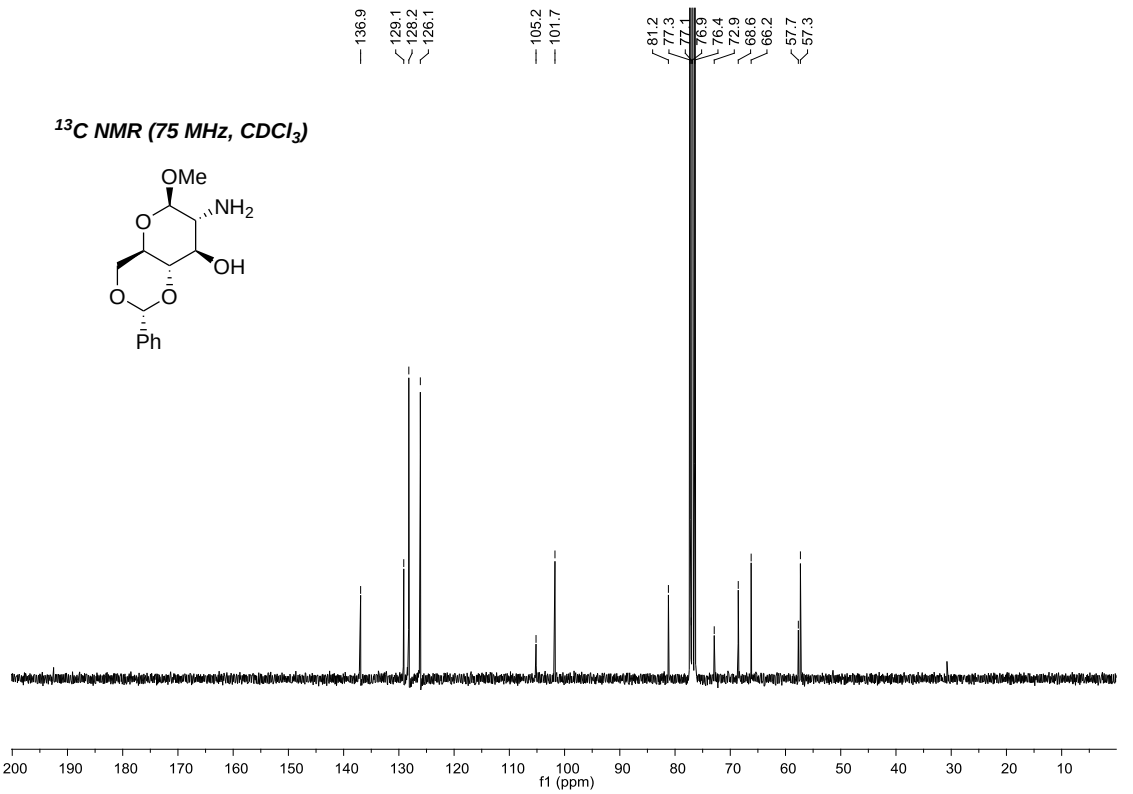


^{13}C NMR (75 MHz, $CDCl_3$)

^{1}H & ^{13}C NMR of methyl 2-amino-4,6-O-benzylidene-2-deoxy-β-D-glucopyranoside.

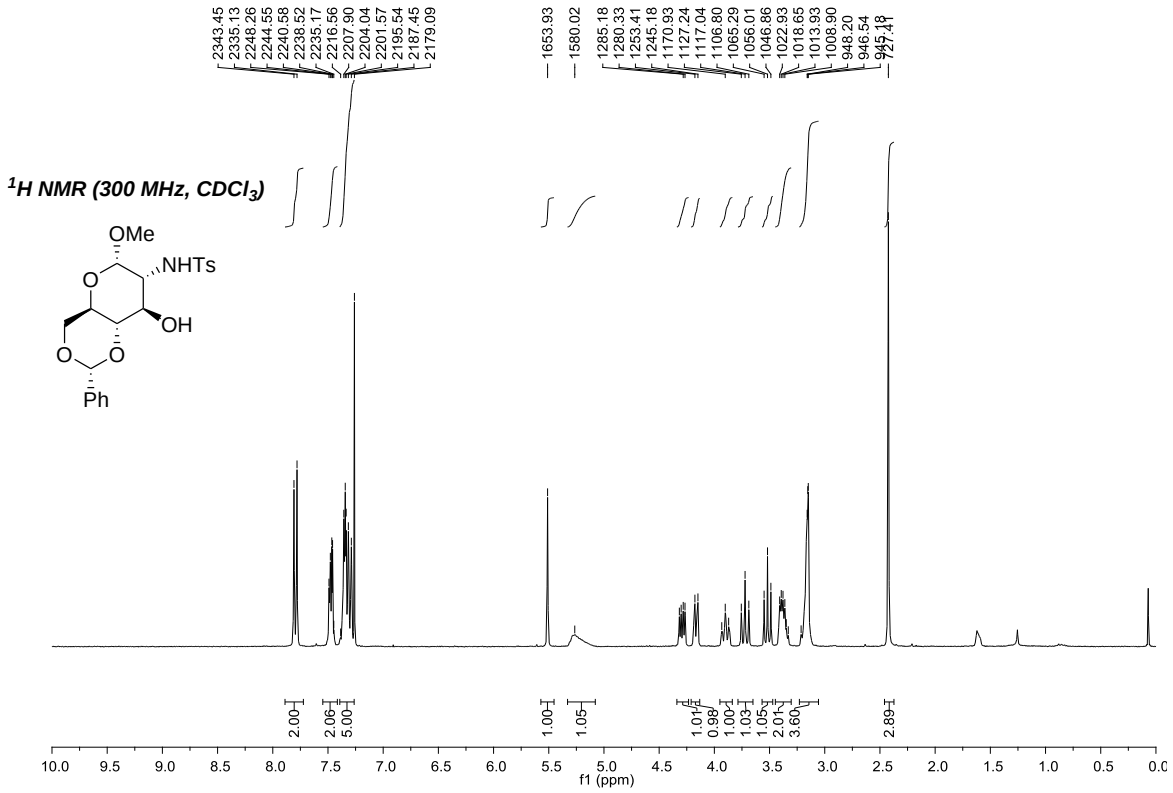


^{1}H NMR (300 MHz, $CDCl_3$)

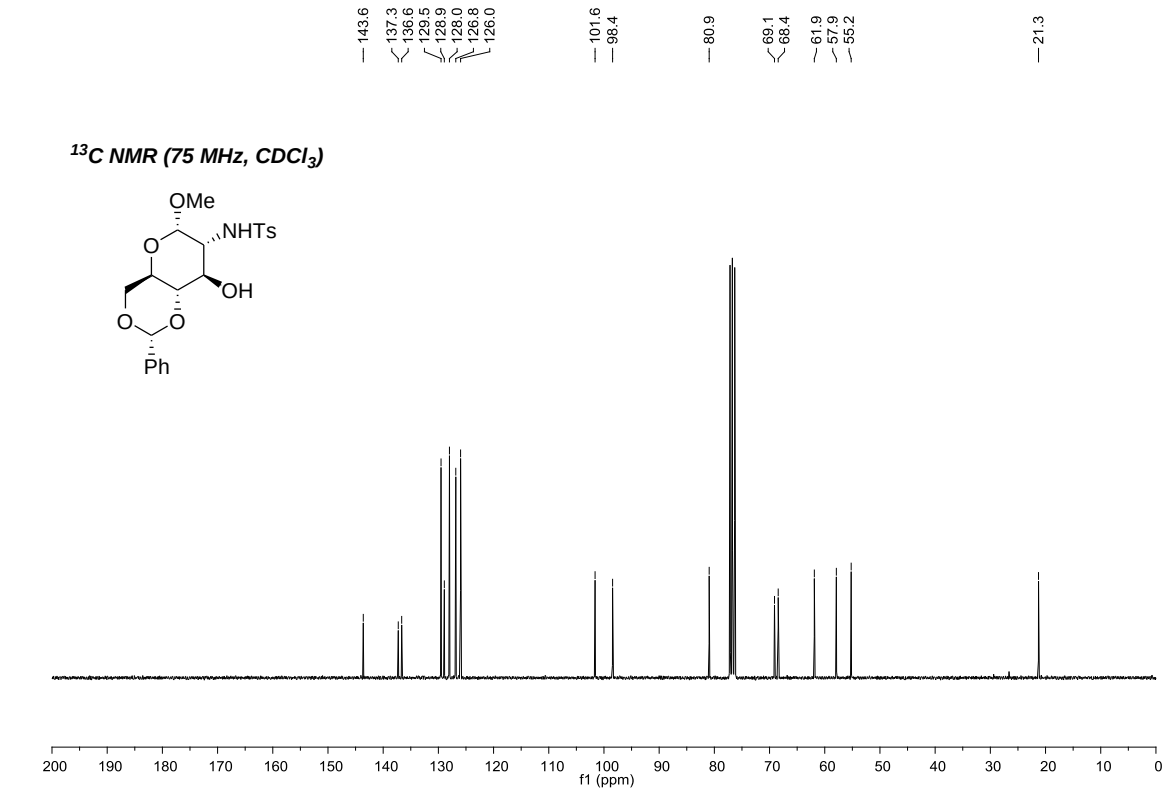


^{13}C NMR (75 MHz, $CDCl_3$)

^{1}H & ^{13}C NMR of methyl 4,6-O-benzylidene-2-deoxy-2-N-p-toluenesulfonamido-α-D-glucopyranoside 1.

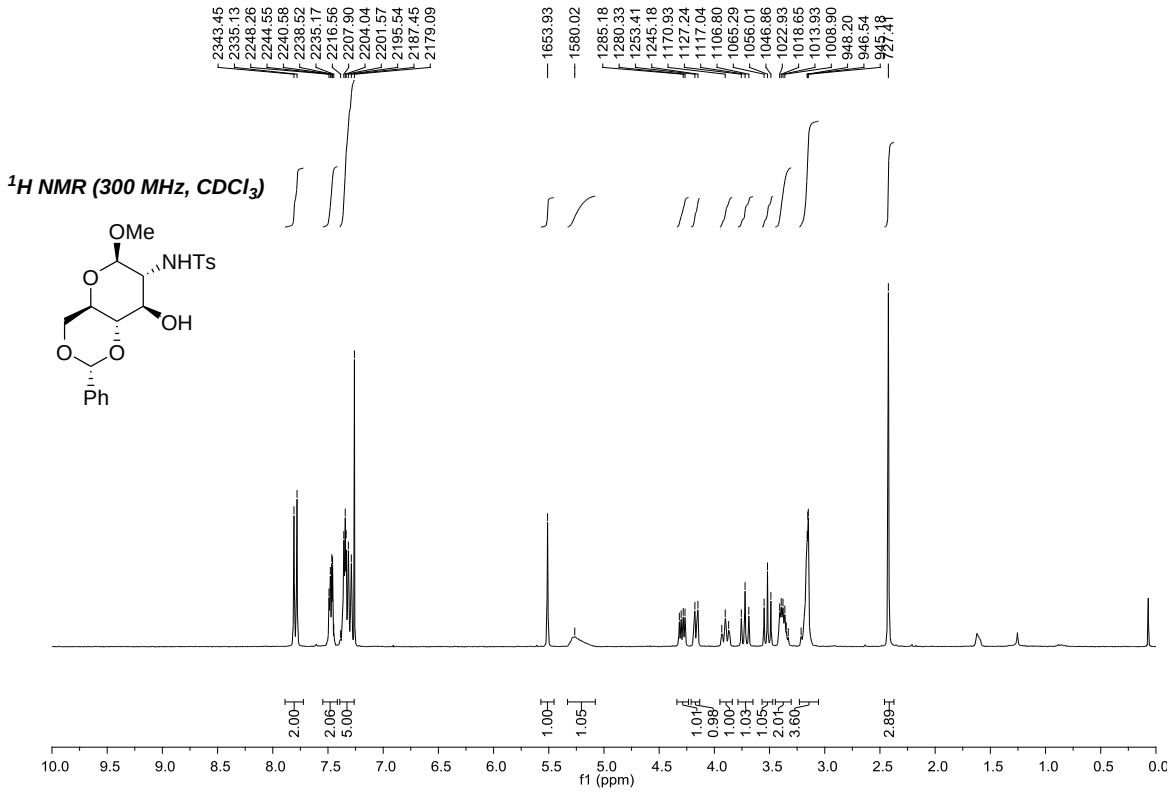


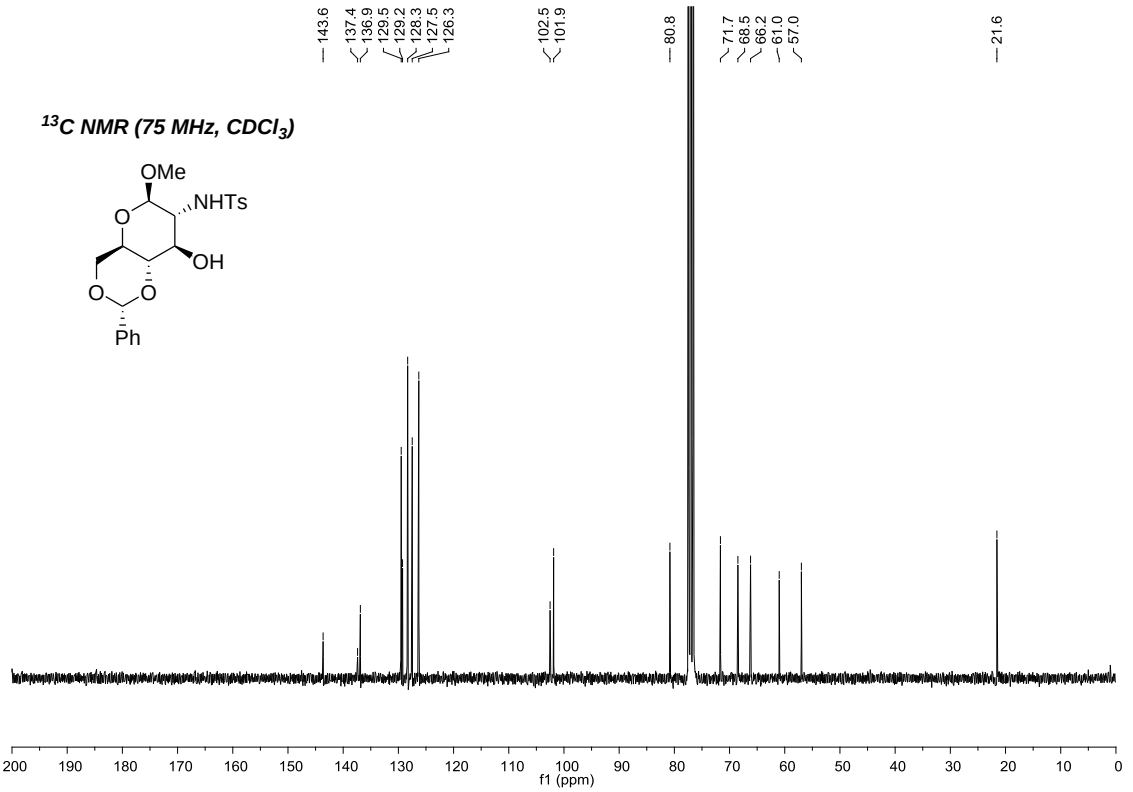
^{1}H NMR (300 MHz, $CDCl_3$)



^{13}C NMR (75 MHz, $CDCl_3$)

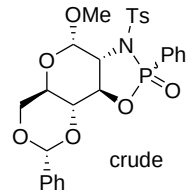
^{1}H & ^{13}C NMR of methyl 4,6-O-benzylidene-2-deoxy-2-N-p-toluenesulfonamido-β-D-glucopyranoside 2.





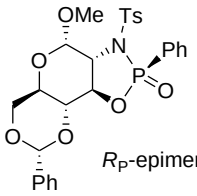
^{31}P NMR of oxazaphospholidine derivative R_P-3.

^{31}P NMR (121 MHz, $CDCl_3$)



crude

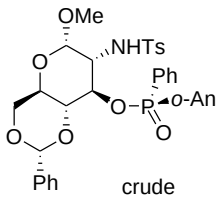
^{31}P NMR (121 MHz, $CDCl_3$)



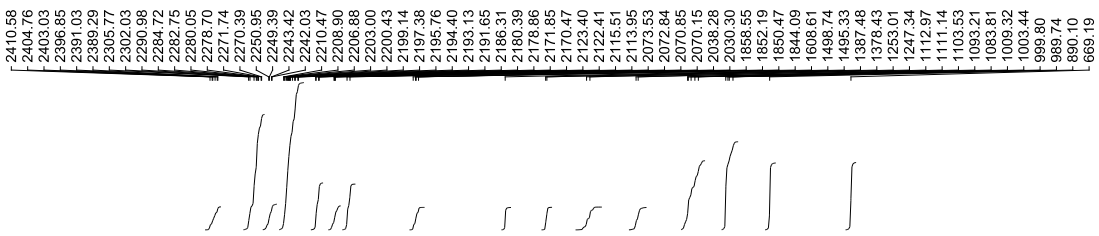
R_P-epimer (from obtained crystal)

^{1}H, ^{31}P & ^{13}C NMR of methyl 3-O-[(S)-(2-methoxyphenyl)phenylphosphinate]-4,6-O-benzylidene-2-deoxy-2-N-p-toluenesulfonamido-α-D-glucopyranoside S_P-5.

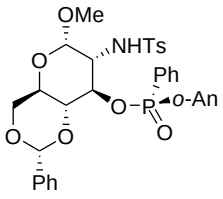
^{31}P NMR (121 MHz, $CDCl_3$)

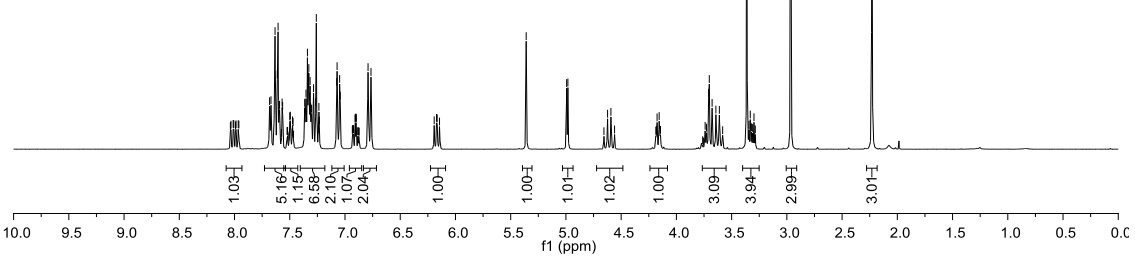


crude

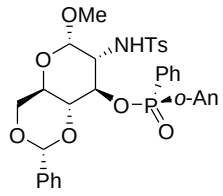


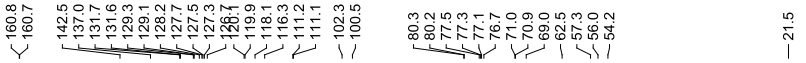
^{1}H NMR (300 MHz, $CDCl_3$)



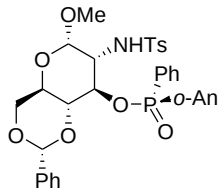


^{31}P NMR (121 MHz, $CDCl_3$)

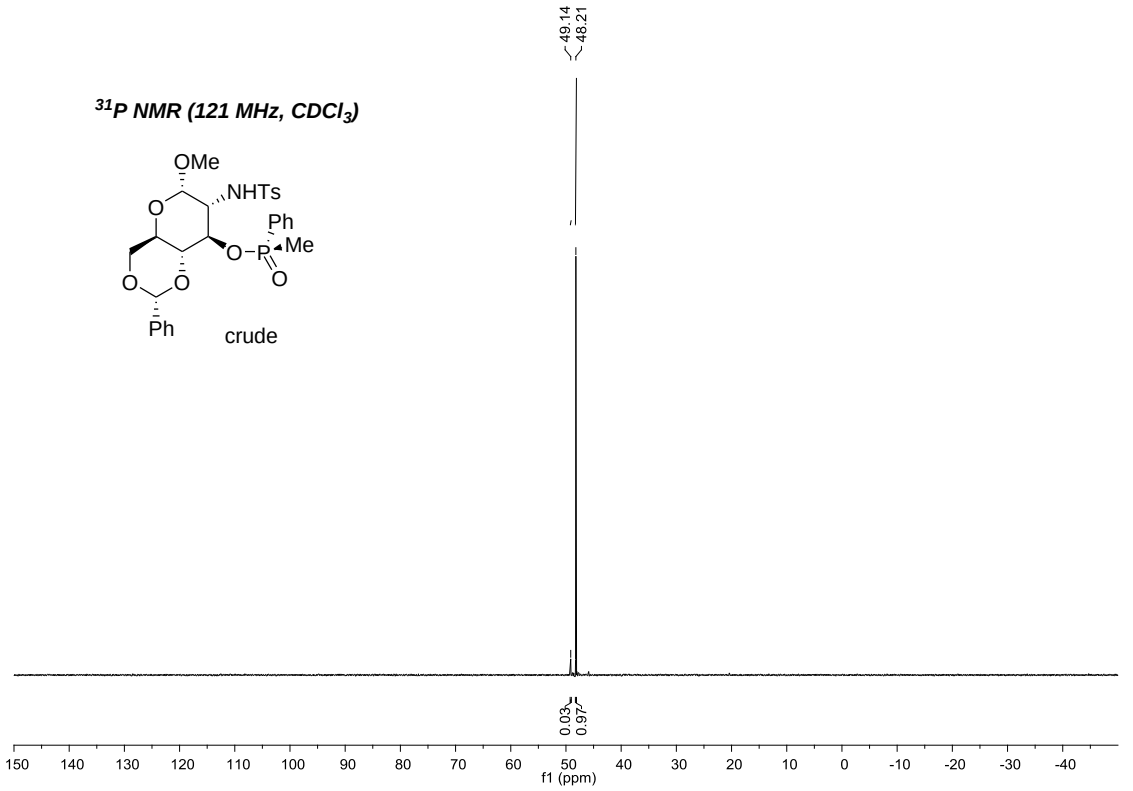


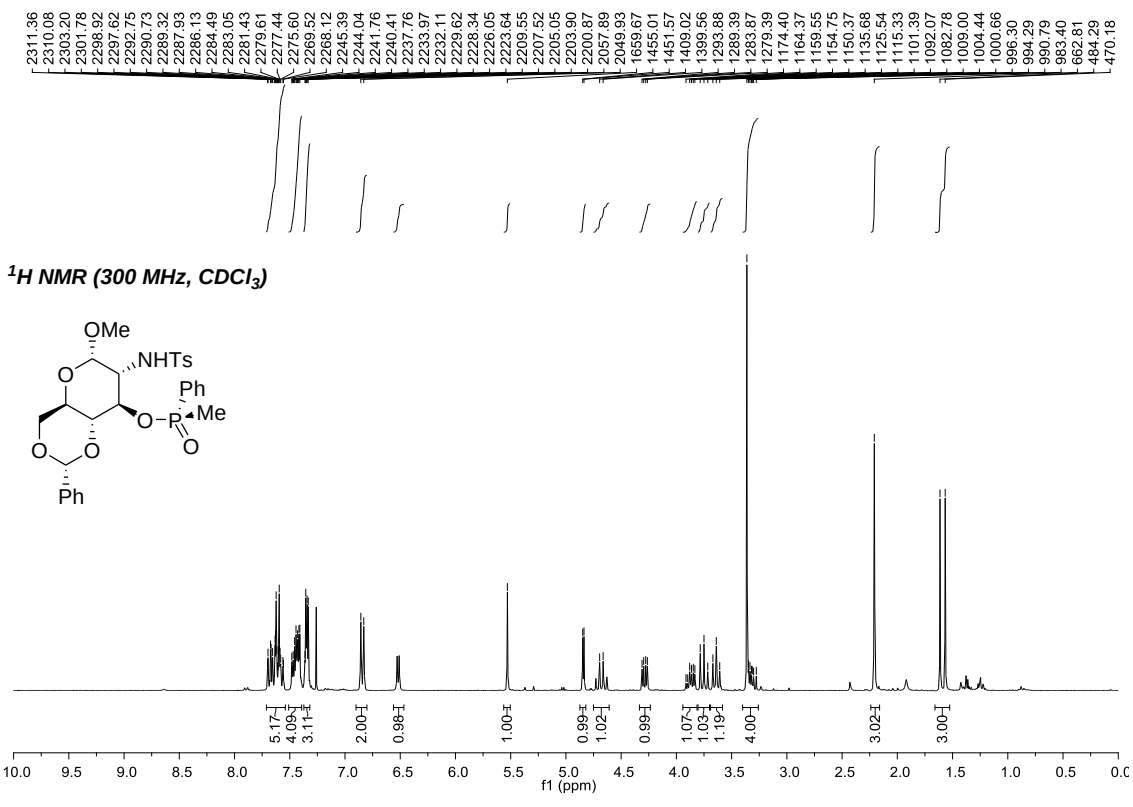


^{13}C NMR (75 MHz, $CDCl_3$)

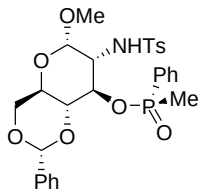


^{1}H, ^{31}P & ^{13}C NMR of methyl 3-O-[(R)-methylphenylphosphinate]-4,6-O-benzylidene-2-deoxy-2-N-p-toluenesulfonamido-α-D-glucopyranoside R_P-6.

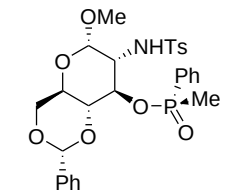




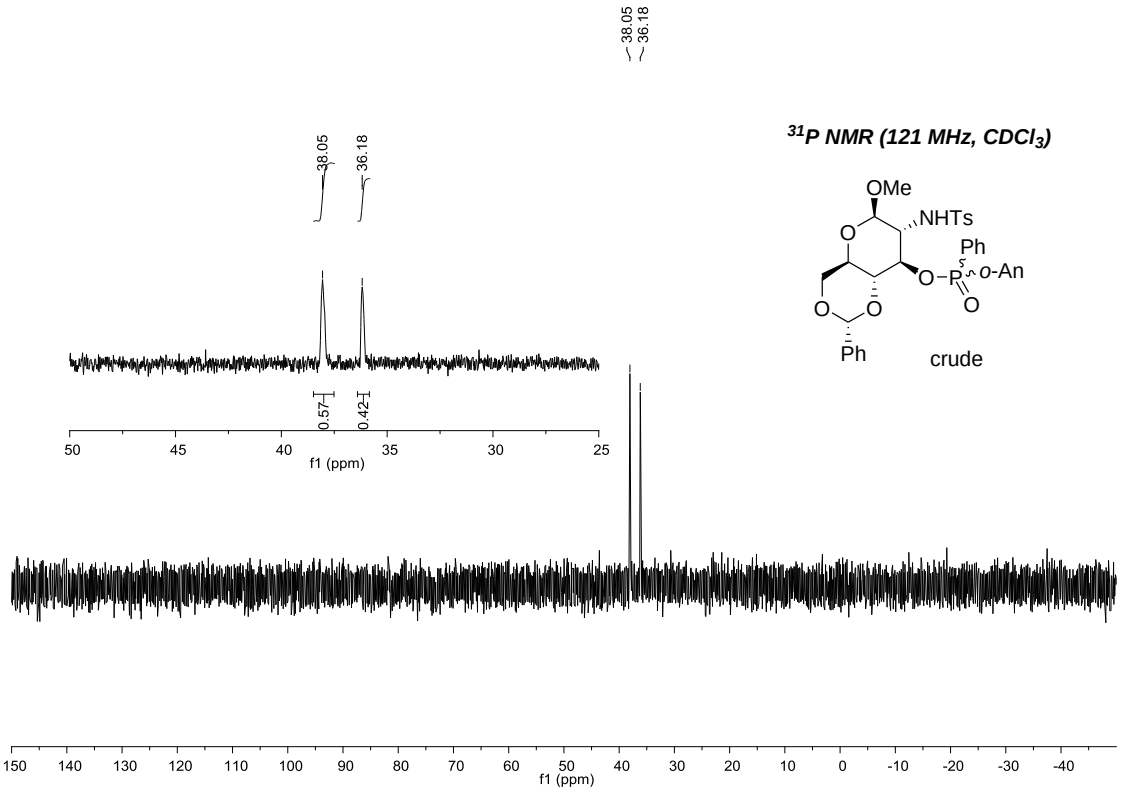
^{31}P NMR (121 MHz, $CDCl_3$)



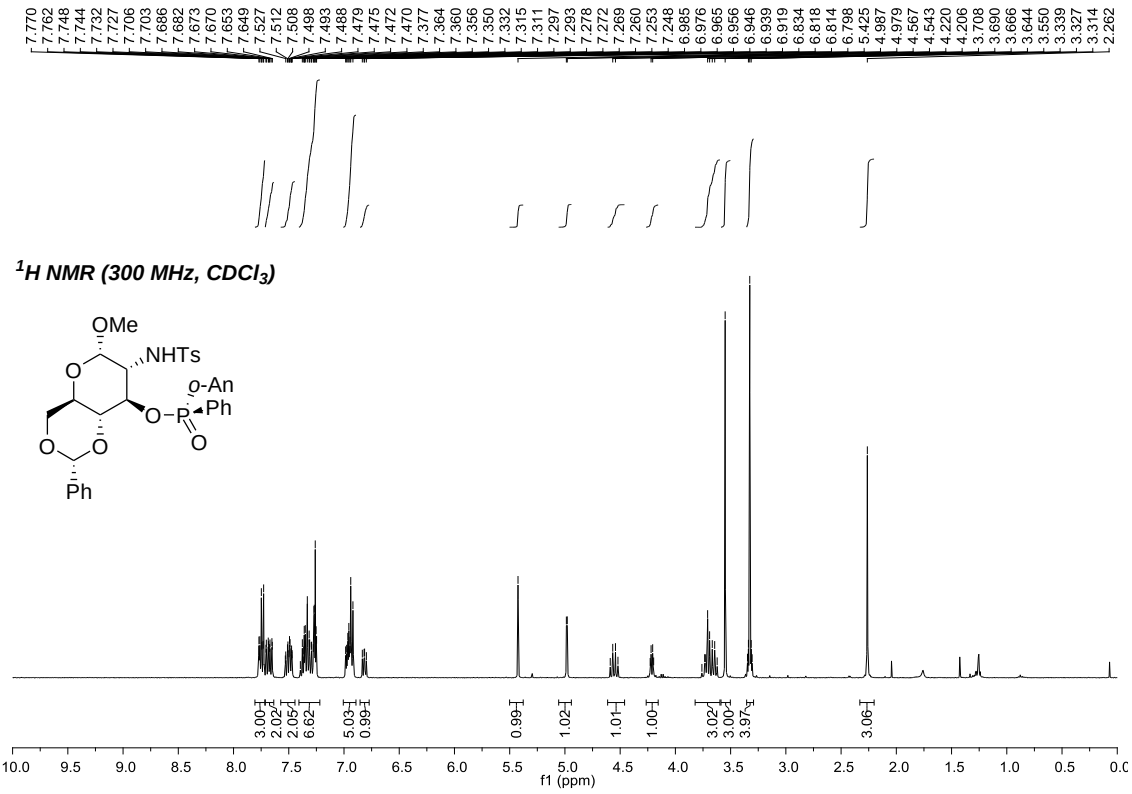
^{13}C NMR (75 MHz, $CDCl_3$)



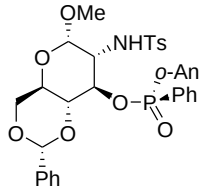
^{31}P NMR of not purified methyl 3-O-[(2-methoxyphenyl)phenylphosphinate]-4,6-O-benzylidene-2-deoxy-2-N-p-toluenesulfonamido-β-D-glucopyranoside 7.



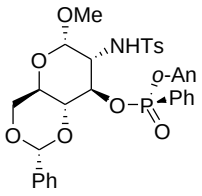
^{1}H, ^{31}P & ^{13}C NMR of methyl 3-O-[(R)-(2-methoxyphenyl)phenylphosphinate]-4,6-O-benzylidene-2-deoxy-2-N-p-toluenesulfonamido-α-D-glucopyranoside R_P-5.



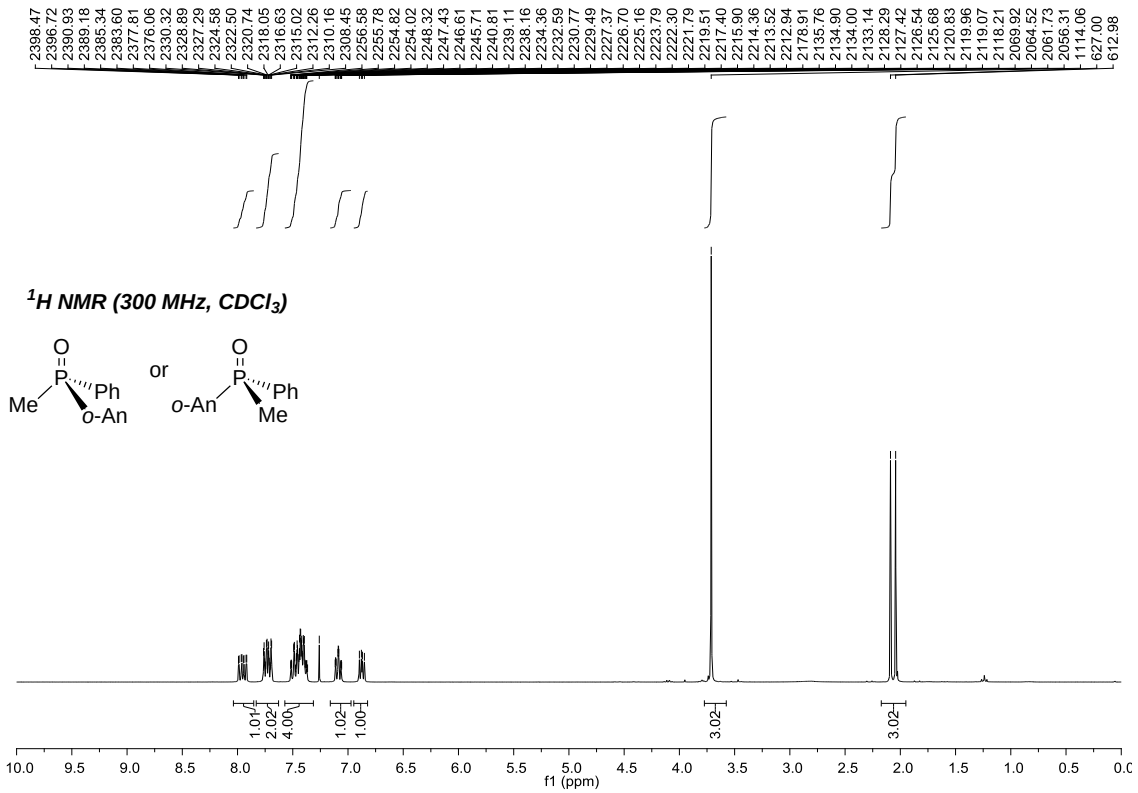
^{31}P NMR (121 MHz, $CDCl_3$)

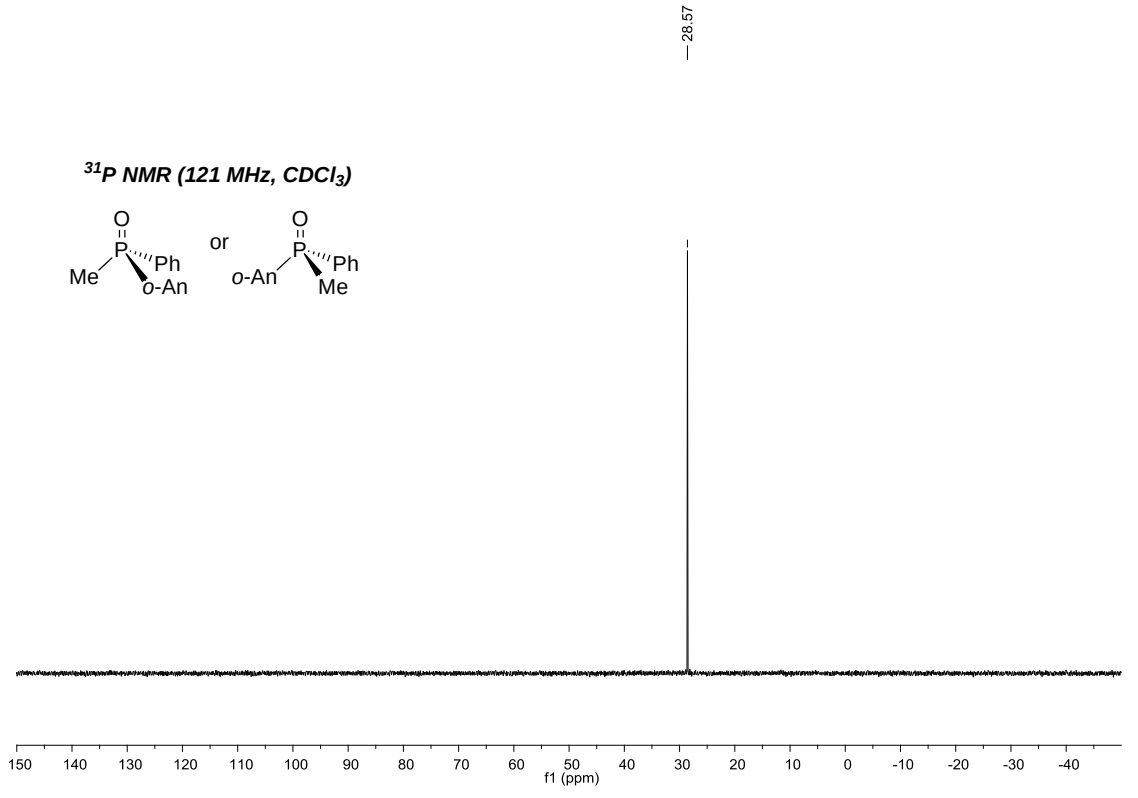


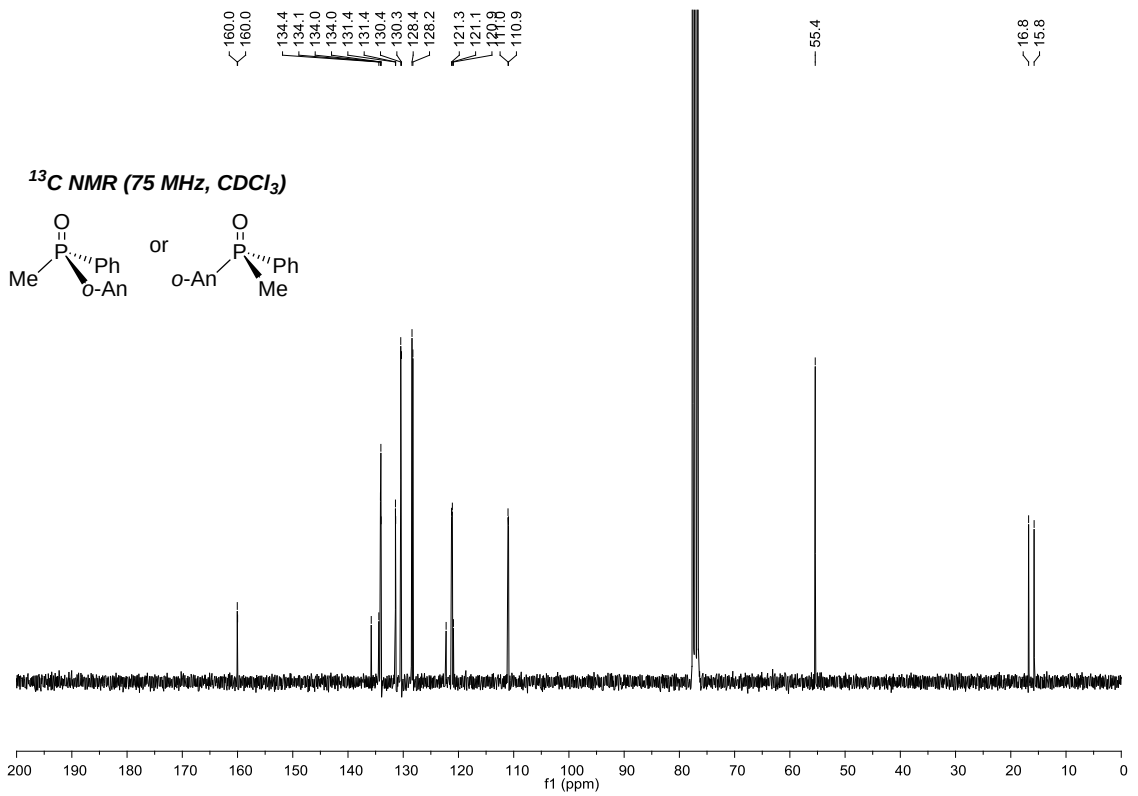
^{13}C NMR (75 MHz, $CDCl_3$)



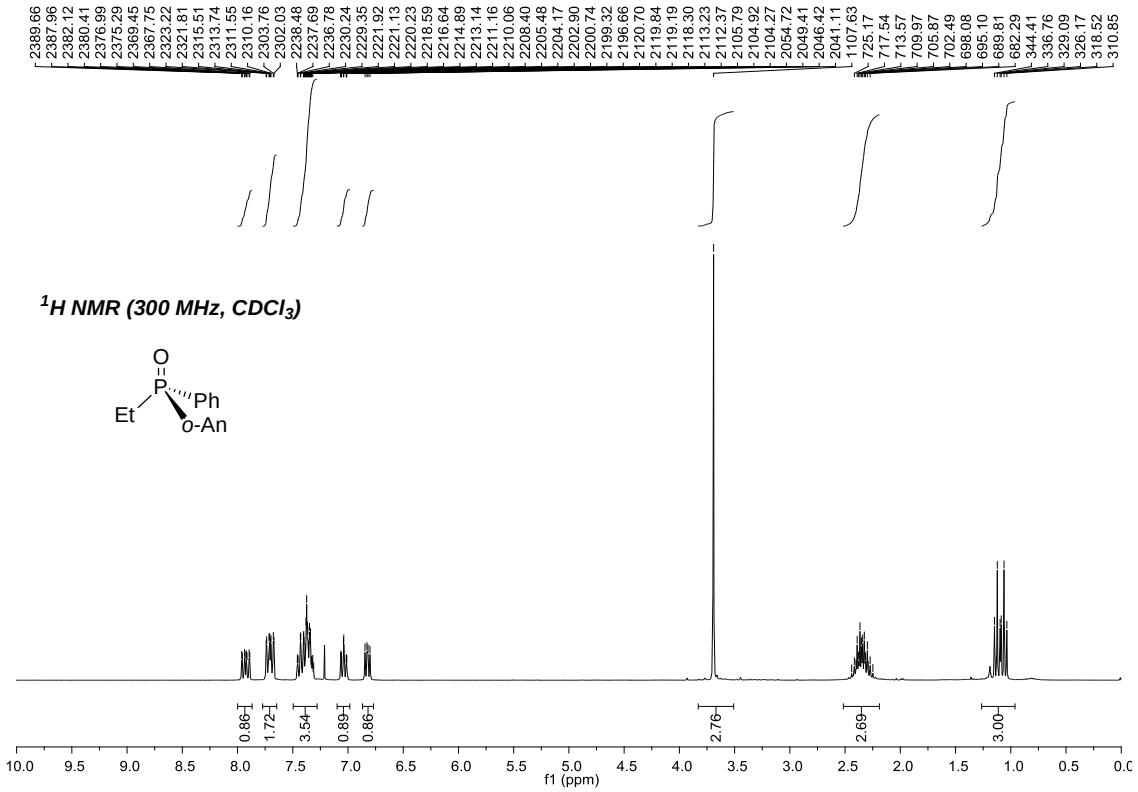
^{1}H, ^{31}P & ^{13}C NMR of o-anisylmethylphenylphosphine oxide R_P- or S_P-8.



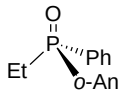




^{1}H, ^{31}P & ^{13}C NMR of o-anisylethylphenylphosphine oxide S_P-9.



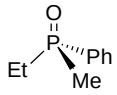
^{31}P NMR (121 MHz, $CDCl_3$)



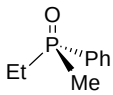
^{13}C NMR (75 MHz, $CDCl_3$)

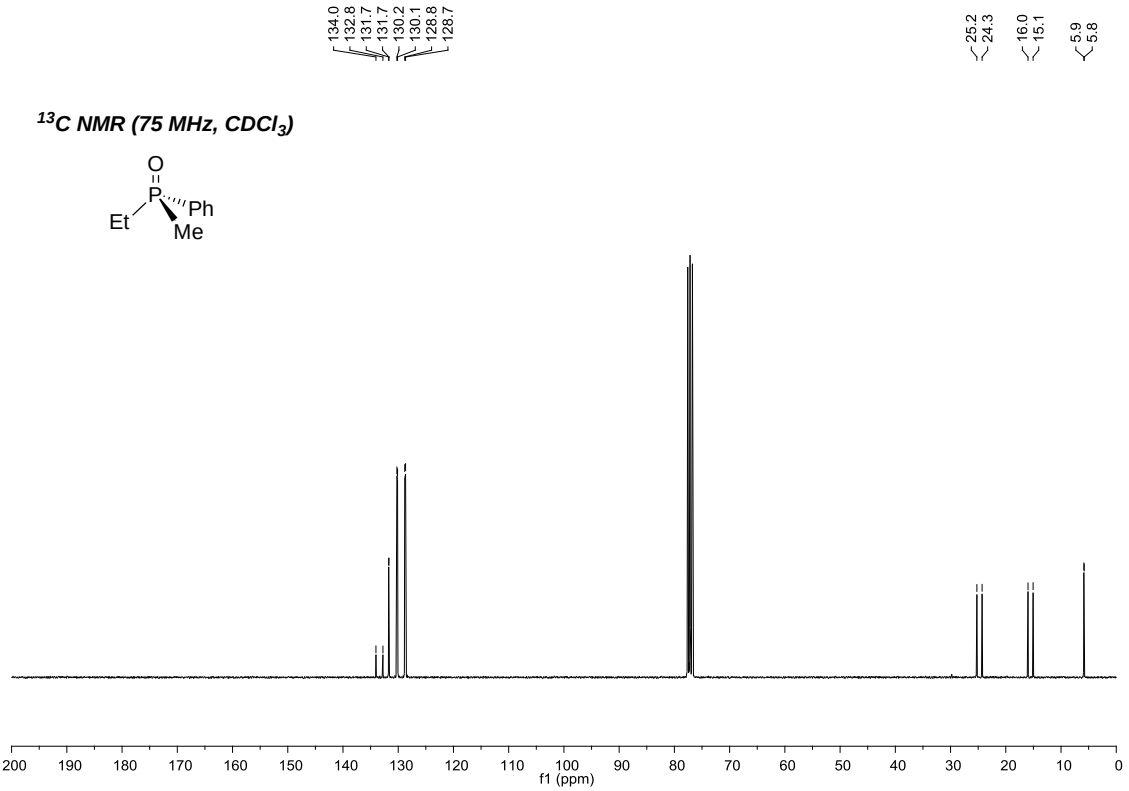
^{1}H, ^{31}P & ^{13}C NMR of ethylmethylphenylphosphine oxide S_P-10.

^{1}H NMR (300 MHz, $CDCl_3$)



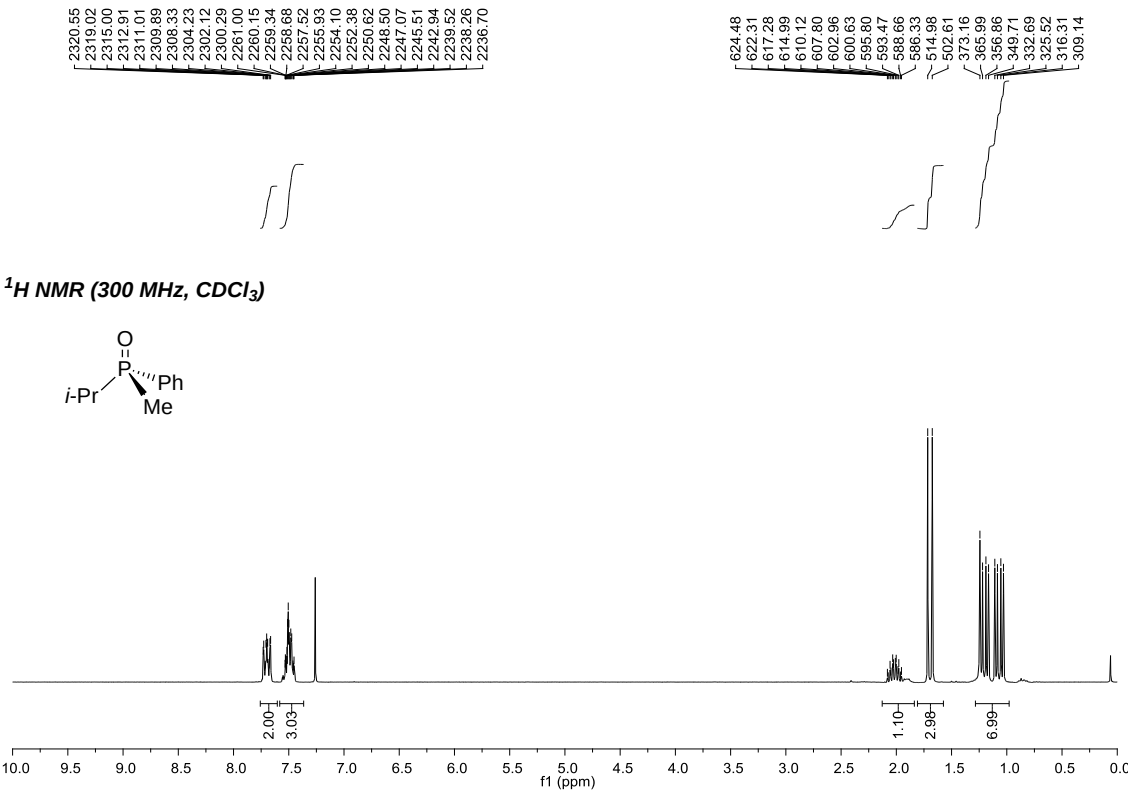
^{31}P NMR (121 MHz, $CDCl_3$)





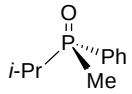
^{13}C NMR (75 MHz, CDCl$_3$)

^{1}H, ^{31}P & ^{13}C NMR of i-propylmethylphenylphosphine oxide S_P-11.

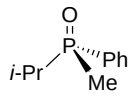


^{1}H NMR (300 MHz, CDCl$_3$)

^{31}P NMR (121 MHz, $CDCl_3$)



^{13}C NMR (75 MHz, $CDCl_3$)

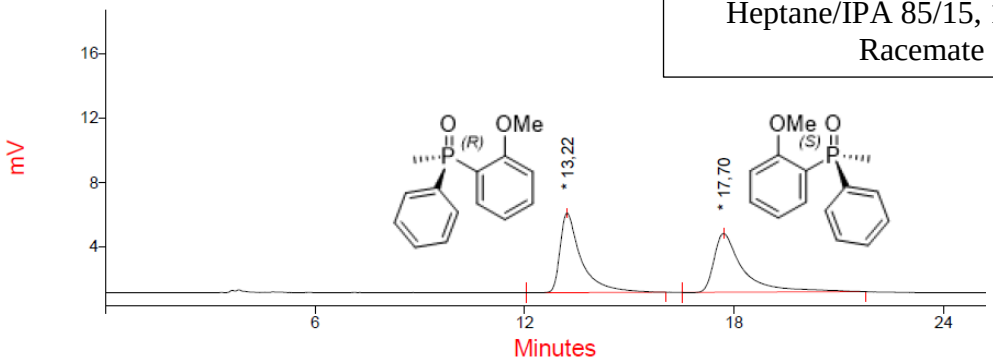


III. HPLC data.

HPLC of racemic and enriched o-anisylmethylphenylphosphine oxide 8.

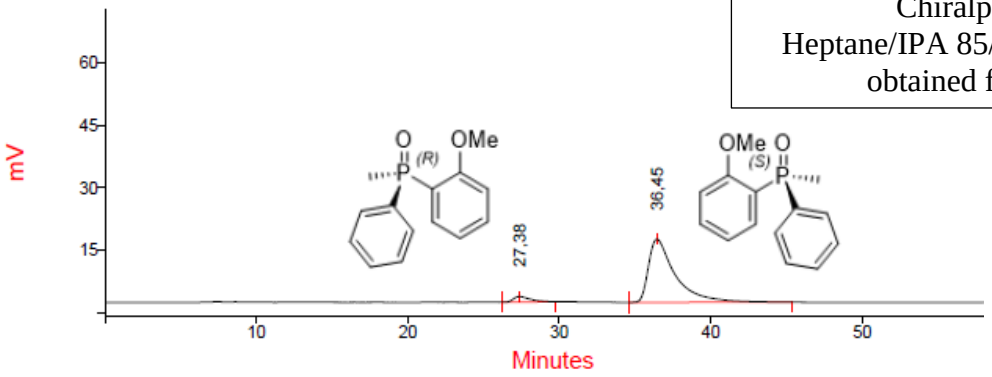
#	Nom du pic	Tr.	Aire	% Aire
1		13,22	207,94	**49,60**
2		17,70	211,30	**50,40**
SOMME			**419,23**	**100,00**

ChiralpackAD
Heptane/IPA 85/15, 1 mL/min
Racemate



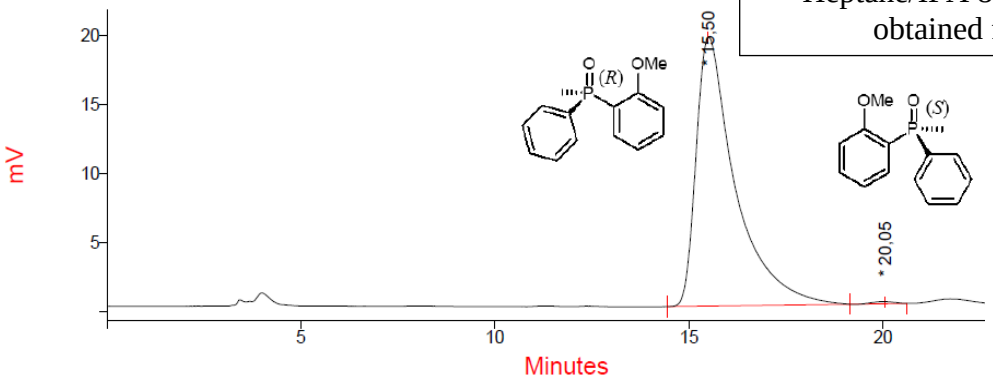
#	Nom du pic	Tr.	Aire	% Aire
1		27,38	102,43	**5,19**
2		36,45	1869,72	**94,81**
SOMME			**1972,15**	**100,00**

ChiralpackAD
Heptane/IPA 85/15, 0,5 mL/min
obtained from ***S*P-5**



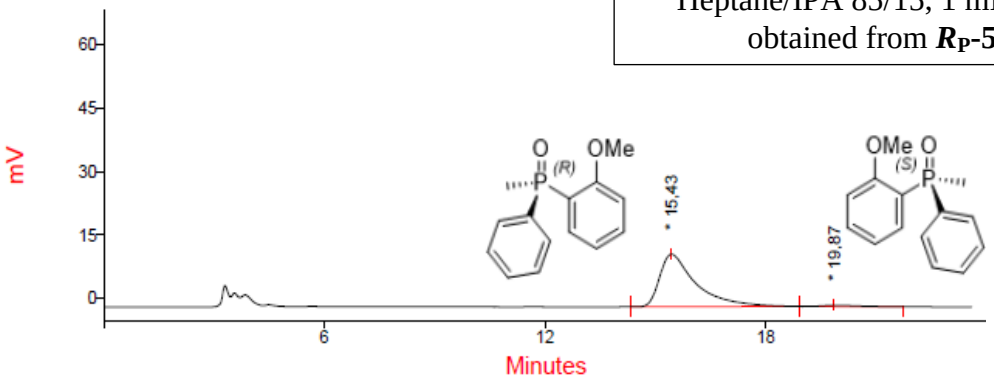
#	Nom du pic	Tr.	Aire	% Aire
1		15,50	1363,55	**99,59**
2		20,05	5,68	**0,41**
SOMME			**1369,23**	**100,00**

ChiralpackAD
Heptane/IPA 85/15, 1 mL/min
obtained from ***R*P-6**



#	Nom du pic	Tr.	Aire	% Aire
1		15,43	851,66	97,84
2		19,87	18,79	2,16
SOMME			870,45	100,00

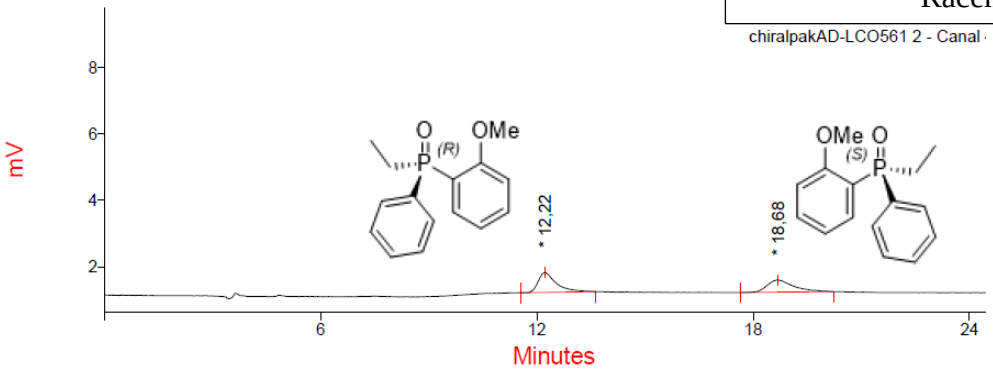
ChiralpackAD
Heptane/IPA 85/15, 1 mL/min
obtained from $\boldsymbol{R_P}$**-5**



HPLC of racemic and enriched o-anisylethylphenylphosphine oxide 9.

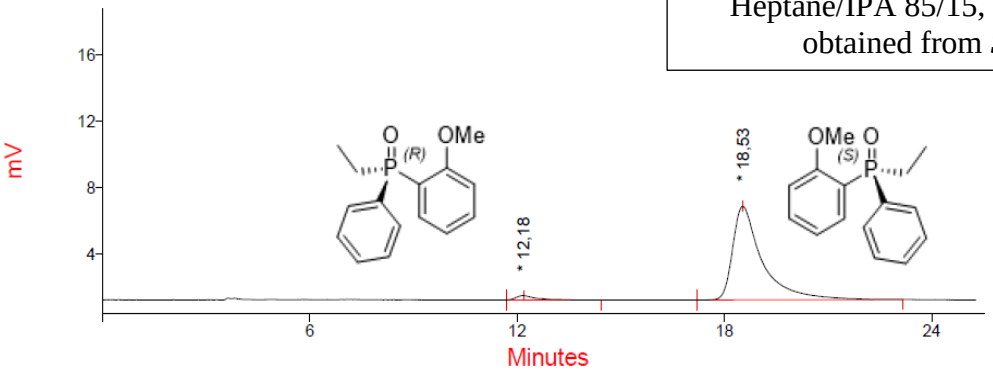
#	Nom du pic	Tr.	Aire	% Aire
1		12,22	20,93	53,34
2		18,68	18,31	46,66
SOMME			39,24	100,00

ChiralpackAD
Heptane/IPA 85/15, 1 mL/min
Racemate



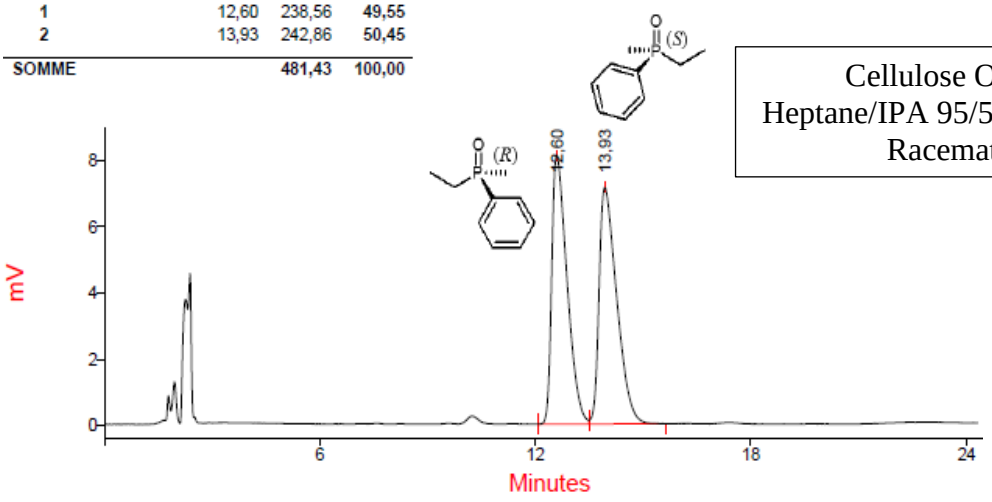
#	Nom du pic	Tr.	Aire	% Aire
1		12,18	11,30	3,27
2		18,53	334,44	96,73
SOMME			345,74	100,00

ChiralpackAD
Heptane/IPA 85/15, 1 mL/min
obtained from $\boldsymbol{S_P}$**-5**



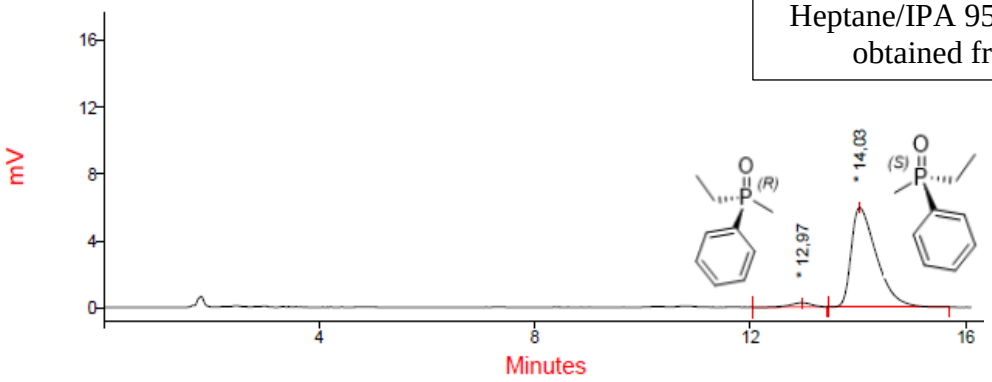
HPLC of racemic and enriched ethylmethylphenylphosphine oxide 10.

#	Nom du pic	Tr.	Aire	% Aire
1		12,60	238,56	49,55
2		13,93	242,86	50,45
SOMME			481,43	100,00



Cellulose OD-H
Heptane/IPA 95/5, 1 mL/min
Racemate

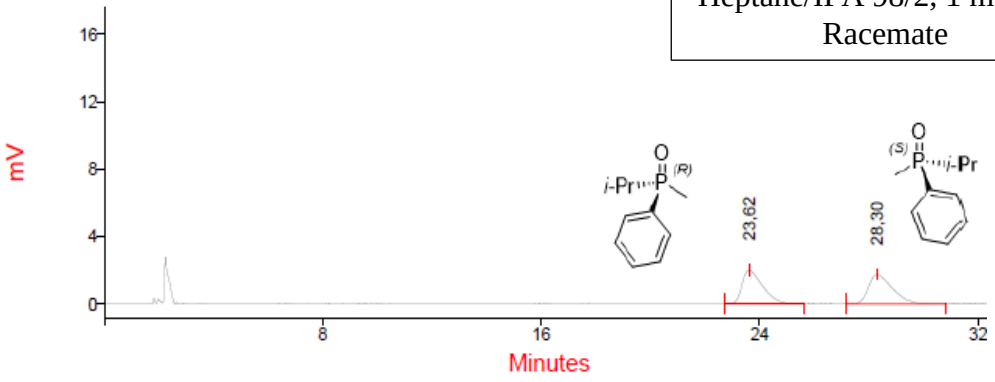
#	Nom du pic	Tr.	Aire	% Aire
1		12,97	7,10	3,53
2		14,03	194,30	96,47
SOMME			201,40	100,00



Cellulose OD-H
Heptane/IPA 95/5, 1 mL/min
obtained from $\boldsymbol{R_P}$**-6**

HPLC of racemic and enriched i-propylmethylphenylphosphine oxide 11.

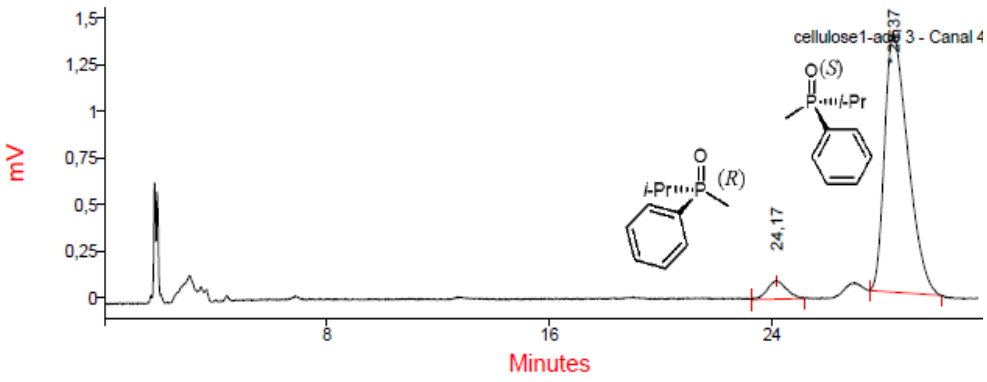
#	Nom du pic	Tr.	Aire	% Aire
1		23,62	105,57	49,49
2		28,30	107,73	50,51
SOMME			213,30	100,00



Cellulose OD-H
Heptane/IPA 98/2, 1 mL/min
Racemate

#	Nom du pic	Tr.	Aire	% Aire
1		24,17	4,76	5,55
2		28,37	81,05	94,45
SOMME			85,81	100,00

Cellulose OD-H
Heptane/IPA 98/2, 1 mL/min
obtained from ***R*P-6**



IV. X-ray data.

Crystal data of ***R*P-3**, ***S*P-5** and ***R*P-6** were collected at room temperature using a Geminini Oxford Diffractometer (MoKα radiation, λ = 0.71069 Å) equipped with a CCD camera and by using the related software.[i] An absorption correction (analytical) has been applied to all the data sets.[ii] All the structures were solved by direct methods using the SIR97 program [iii] combined with Fourier Difference and the refined against F using the CRYSTALS program.[iv] In each structure, all atomic displacements for non-hydrogen atoms were refined using an anisotropic model. Hydrogen atoms have been placed by Fourier Difference account the hybridization of the supporting atoms and for the possible presence of hydrogen bonds in the case of donor atoms. Hydrogen atoms have been finally refined using a riding mode.

CCDC 1400048, 1400046 and 1400047 references contain the supplementary crystallographic data for ***R*P-3**, ***S*P-5** and ***R*P-6**, respectively. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif

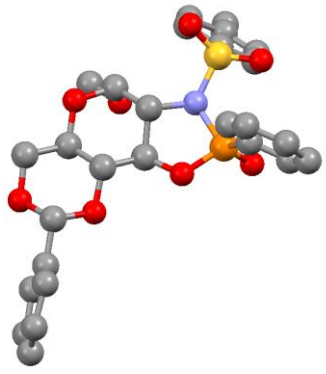
[i] CrysAlisPro, version 1.171.34.40 (rel. 27-08-2010, CrysAlis171.NET), Oxford Diffraction Ltd.

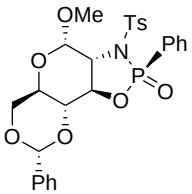
[ii] O. D. L. CrysAlisPro, version 1.171.34.40 (rel. 27-08-2010, CrysAlis1 171.NET), (compiled Aug. 27, 2010, 11:50:40). Analytical numeric absorption correction using a multifaceted crystal model based on expressions derived by: R. C. Clark, J. S. Reid, Acta Crystallogr., Sect. A 1995, 51, 887-897.

[iii] G. Cascarano, A. Altomare, C. Giacovazzo, A. Guagliardi, A. G. G. Moliterni, D. Siliqi, M. C. Burla, G. Polidori, M. Camalli, Acta Crystallogr., Sect. A 1996, A52.

[iv] D. J. Watkin, C. K. Prout, J. R. Carruthers, P. W. Betteridge, Chemical CrystallographyLaboratory, Oxford, 1999.

***X-ray of oxazaphospholidine derivative R*P-3.**

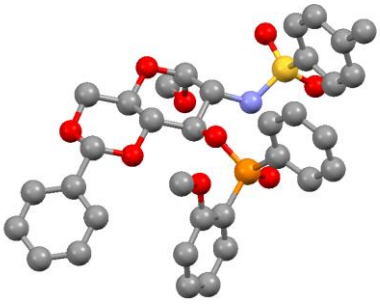


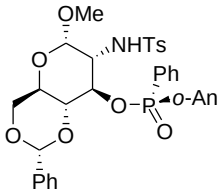


X-ray diffraction analysis: CCDC 1400048; Empirical formula: $C_{27}H_{28}NO_8PS$; molecular weight = 557.6 g.mol^{-1}; crystal system: orthorhombic; space group: $P2_12_12_1$;

a = 11.8008(5) Å; b = 14.3566(8) Å; c = 16.680(1) Å; V = 2825.9(3) $Å^3$; crystal description: needle; crystal color: colorless; crystal size: 0.133×0.135×0.232 mm^3; Z = 4 ; T = 293 K; d = 1.310; μ = 0.219 mm^{-1}; Number of independent reflections: 6417; R_{int} = 0.054; R(F) = 0.0562; $R_w(F)$ = 0.0536; S = 1.12; $\Delta\rho_{min}$ = -0.48 $e^-.Å^{-3}$; $\Delta\rho_{max}$ = +0.48 $e^-.Å^{-3}$; Flack parameter = -0.2(2); Number of reflections used: 2690; Number of refined parameters: 343; absorption correction: analytical.

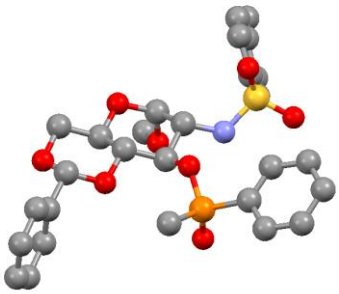
X-ray of phosphinate derivative S_P-5.

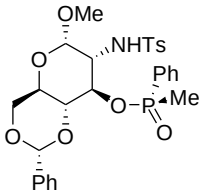




X-ray diffraction analysis: CCDC 1400046; Empirical formula: $C_{34}H_{36}NO_9PS$; molecular weight = 665.7 $g.mol^{-1}$; crystal system: orthorhombic; space group: $P2_12_12_1$; a = 16.3644(6) Å; b = 15.9689(6) Å; c = 12.8284(5) Å; V = 3352.4(2) $Å^3$; crystal description: needle; crystal color: colorless; crystal size: 0.229×0.273×0.729 mm^3; Z = 4 ; T = 293 K; d = 1.331; μ = 0.119 mm^{-1}; Number of independent reflections: 7801; R_{int} = 0.021; R(F) = 0.0422; $R_w(F)$ = 0.0511; S = 1.07; $\Delta\rho_{min}$ = -0.17 $e^-.Å^{-3}$; $\Delta\rho_{max}$ = +0.21 $e^-.Å^{-3}$; Flack parameter = -0.04(8); Number of reflections used: 4899; Number of refined parameters: 416; absorption correction: analytical.

X-ray of phosphinate derivative R_P-6.





X-ray diffraction analysis: CCDC 1400047; Empirical formula: $C_{31}H_{40}NO_9PS$; molecular weight = 633.7 $g.mol^{-1}$; crystal system: monoclinic; space group: $P2_1$;

a = 10.2628(5) Å; b = 8.9164(4) Å; c = 18.5939(9) Å; β = 105.023(5); V = 1643.3(1) $Å^3$; crystal description: needle; crystal color: colorless; crystal size: 0.142×0.175×0.515 mm^3; Z = 2 ; T = 293 K; d = 1.289; μ = 0.200 mm^{-1}; Number of independent reflections: 6292; R_{int} = 0.026; R(F) = 0.0409; R_w(F) = 0.0406; S = 1.15; $\Delta\rho_{min}$ = -0.23 $e^-.Å^{-3}$; $\Delta\rho_{max}$ = +0.19 $e^-.Å^{-3}$; Flack parameter = 0.08(8); Number of reflections used: 3953; Number of refined parameters: 389; absorption correction: analytical.