

Electronic Supplementary Information for

**Polyhydroxylated pyrrolizidine alkaloids from transannular iodoaminations:
application to the asymmetric syntheses of (–)-hyacinthacine A1,
(–)-7a-*epi*-hyacintahcine, (–)-hyacinthacine A2, and (–)-1-*epi*-alexine**

E. Anne Brock, Stephen G. Davies,* James A. Lee,

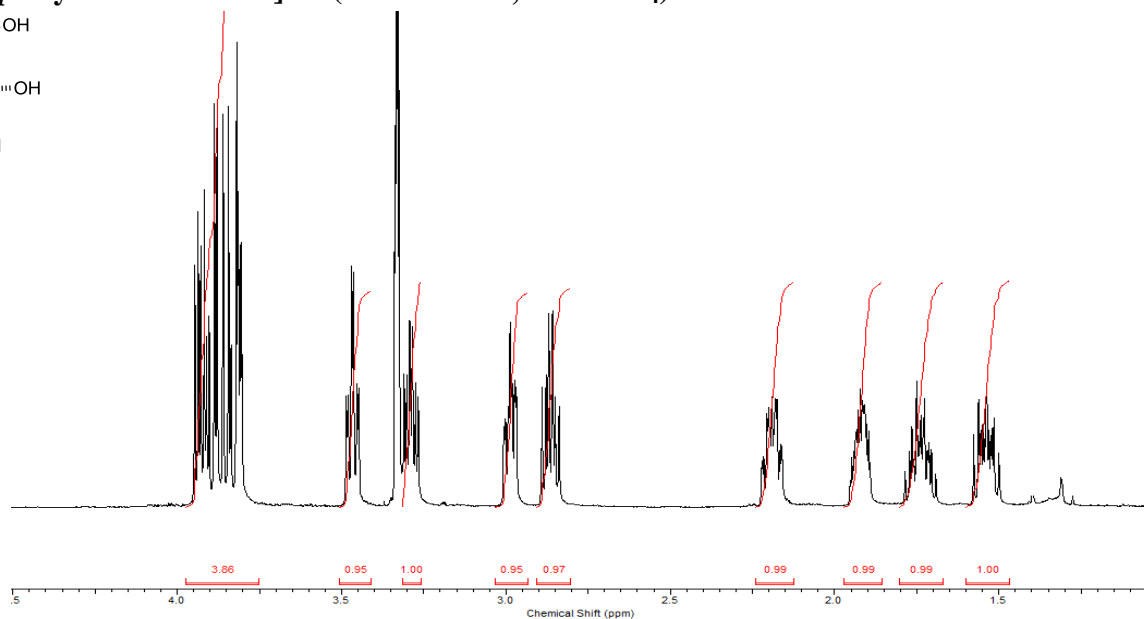
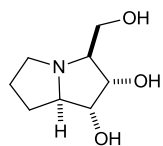
Paul M. Roberts and James E. Thomson

*Department of Chemistry, Chemistry Research Laboratory,
University of Oxford, Mansfield Road, Oxford OX1 3TA, U.K.*

steve.davies@chem.ox.ac.uk

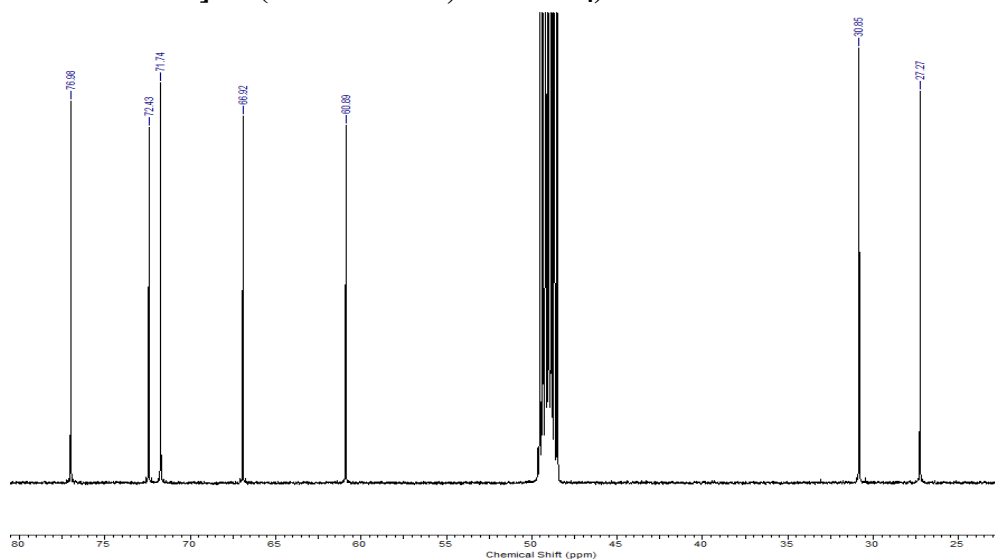
(1*R*,2*S*,3*S*,7*aR*)-1,2-Dihydroxy-3-(hydroxymethyl)hexahydro-1*H*-pyrrolizidine

[(-)-7*a-epi*-hyacinthacine A1] 10 (500 MHz ¹H, MeOH-*d*₄)

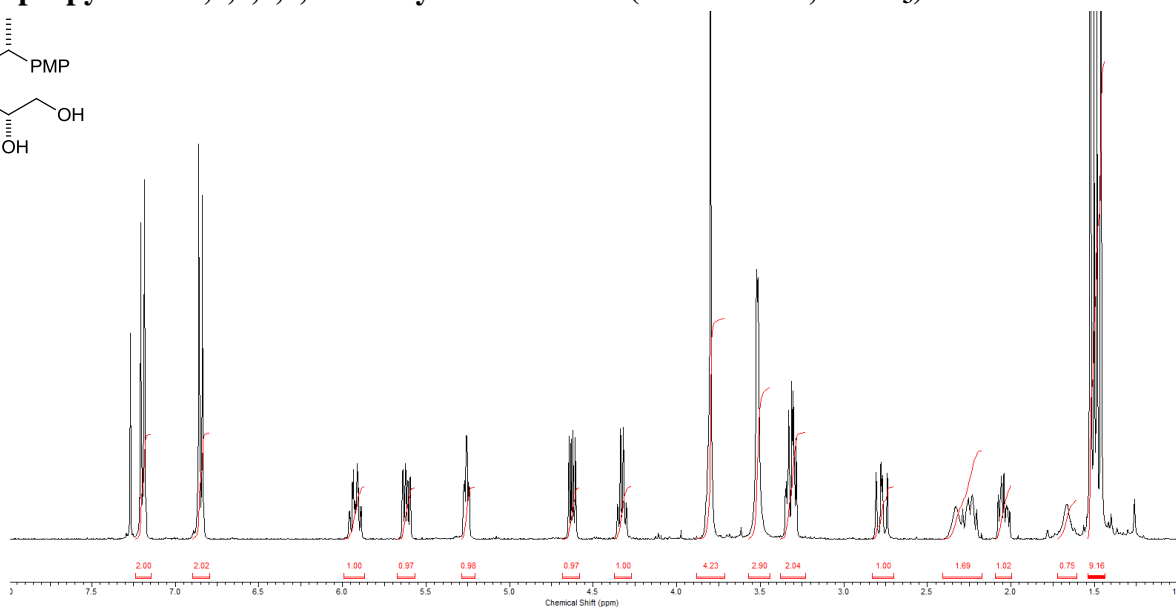
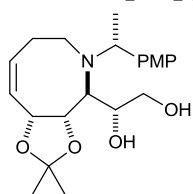


(1*R*,2*S*,3*S*,7*aR*)-1,2-Dihydroxy-3-(hydroxymethyl)hexahydro-1*H*-pyrrolizidine

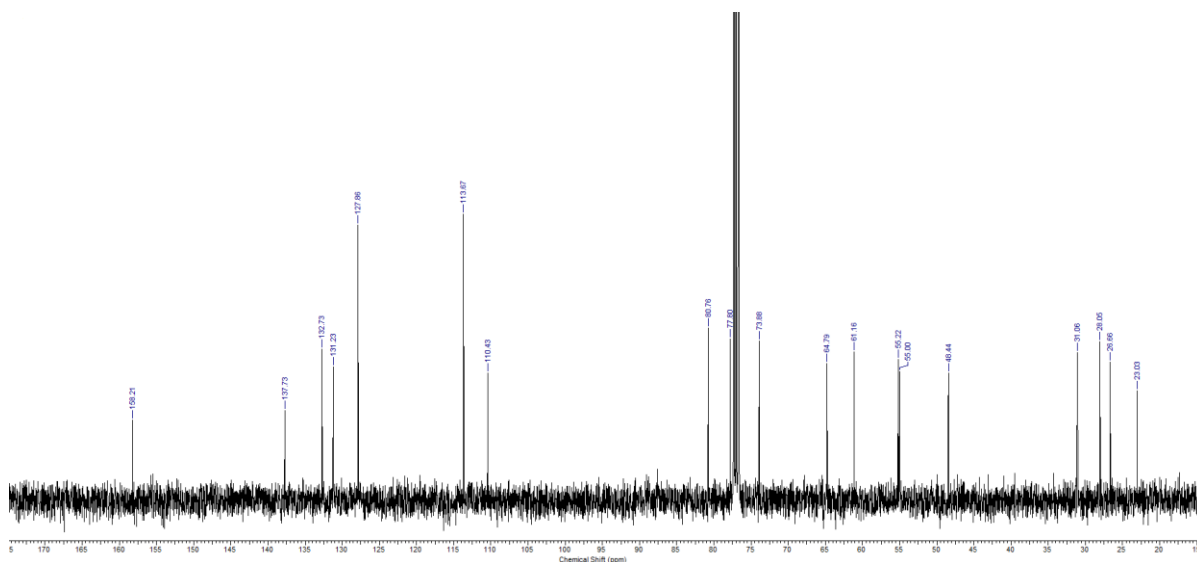
[(-)-7*a-epi*-hyacinthacine A1] 10 (125 MHz ¹³C, MeOH-*d*₄)



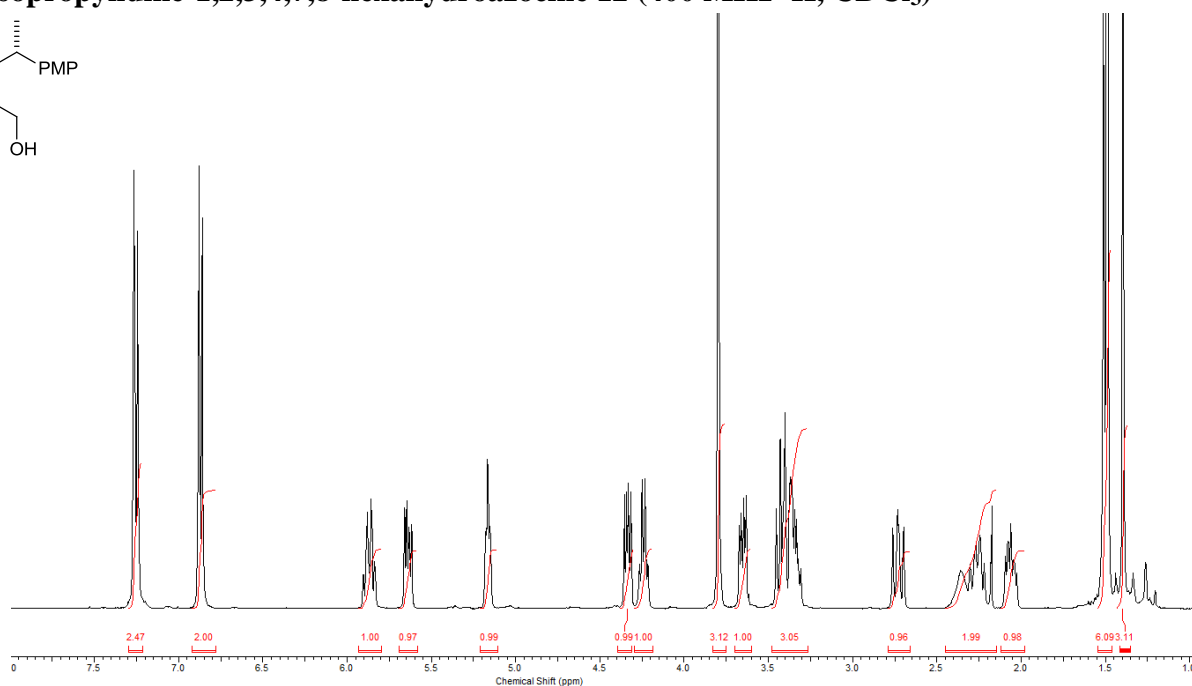
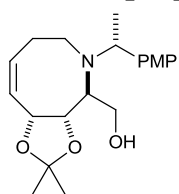
(2*S*,3*S*,4*R*,1'*R*,*aR*,*Z*)-*N*(1)-(*α*-Methyl-*p*-methoxybenzyl)-2-(1',2'-dihydroxyethyl)-3,4-dihydroxy-3,4-*O*-isopropylidene-1,2,3,4,7,8-hexahydroazocine 11 (400 MHz ¹H, CDCl₃)



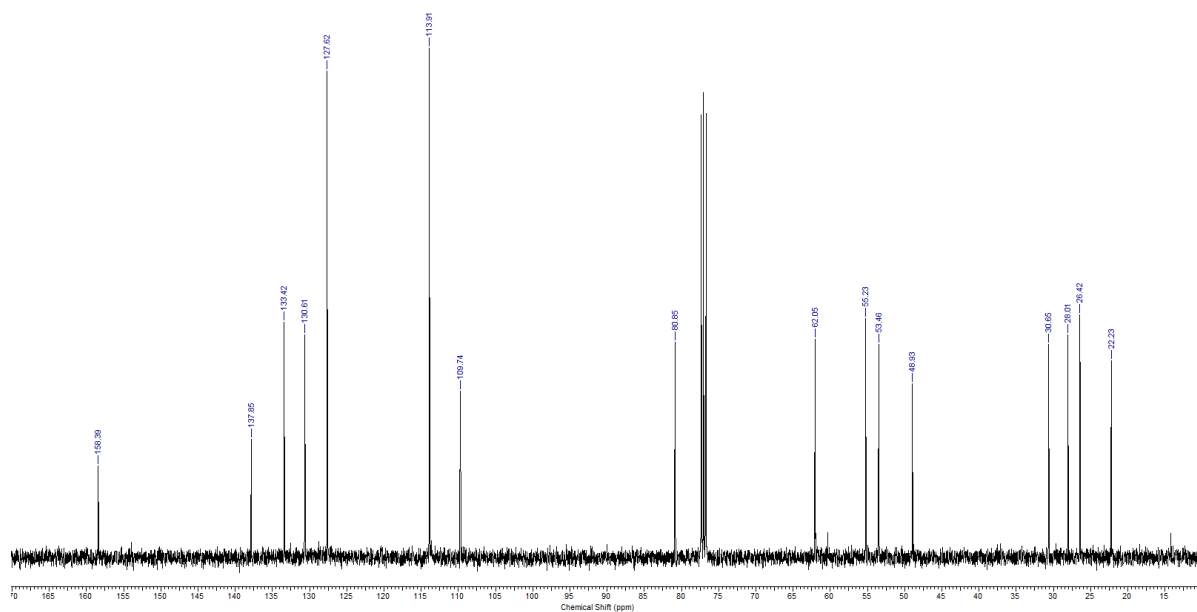
(2*S*,3*S*,4*R*,1'*R*,*aR*,*Z*)-*N*(1)-(*α*-Methyl-*p*-methoxybenzyl)-2-(1',2'-dihydroxyethyl)-3,4-dihydroxy-3,4-*O*-isopropylidene-1,2,3,4,7,8-hexahydroazocine 11 (100 MHz ¹³C, CDCl₃)



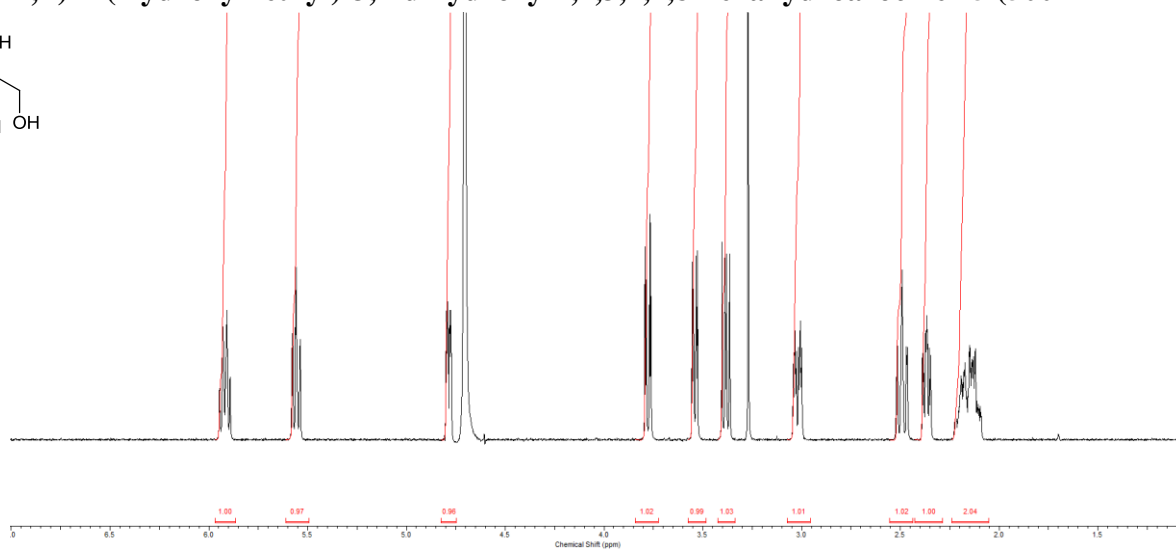
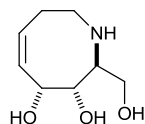
(2*S*,3*S*,4*R*, α *R*,*Z*)-*N*(1)-(α -Methyl-*p*-methoxybenzyl)-2-(hydroxymethyl)-3,4-dihydroxy-3,4-*O*-isopropylidene-1,2,3,4,7,8-hexahydroazocine 12 (400 MHz ^1H , CDCl_3)



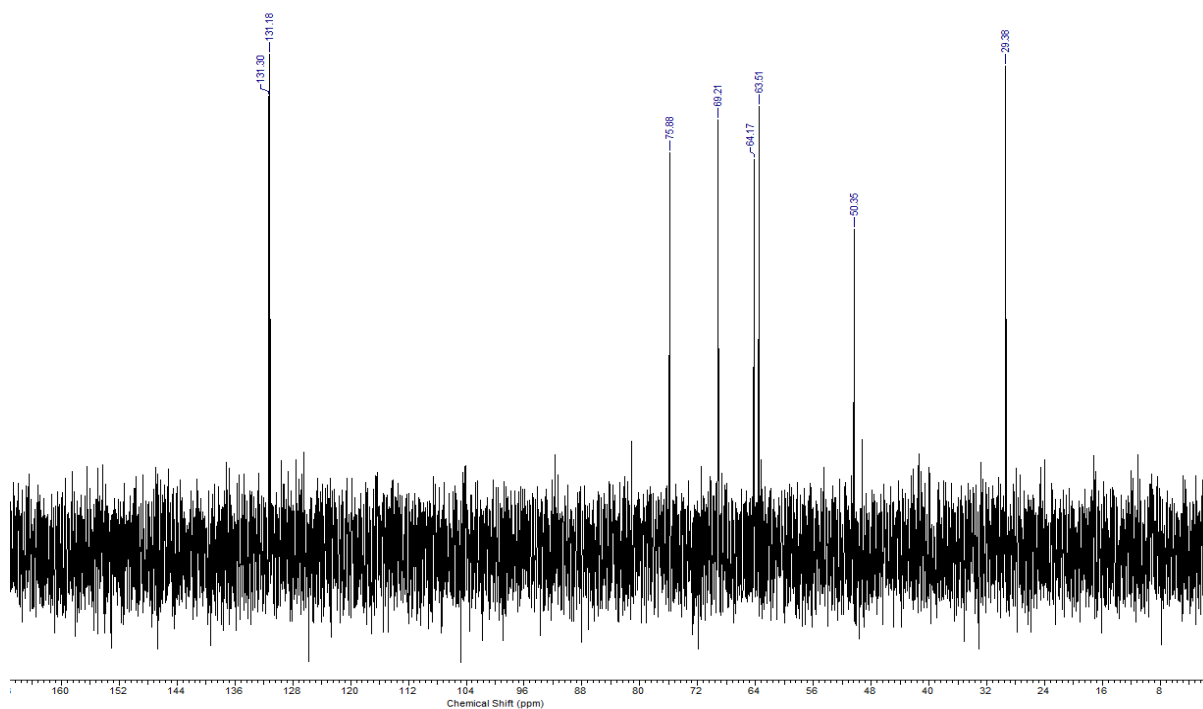
(2*S*,3*S*,4*R*, α *R*,*Z*)-*N*(1)-(α -Methyl-*p*-methoxybenzyl)-2-(hydroxymethyl)-3,4-dihydroxy-3,4-*O*-isopropylidene-1,2,3,4,7,8-hexahydroazocine 12 (100 MHz ^{13}C , CDCl_3)



(2*S*,3*S*,4*R*,*Z*)-2-(Hydroxymethyl)-3,4-dihydroxy-1,2,3,4,7,8-hexahydroazocine 15 (500 MHz ¹H, D₂O)

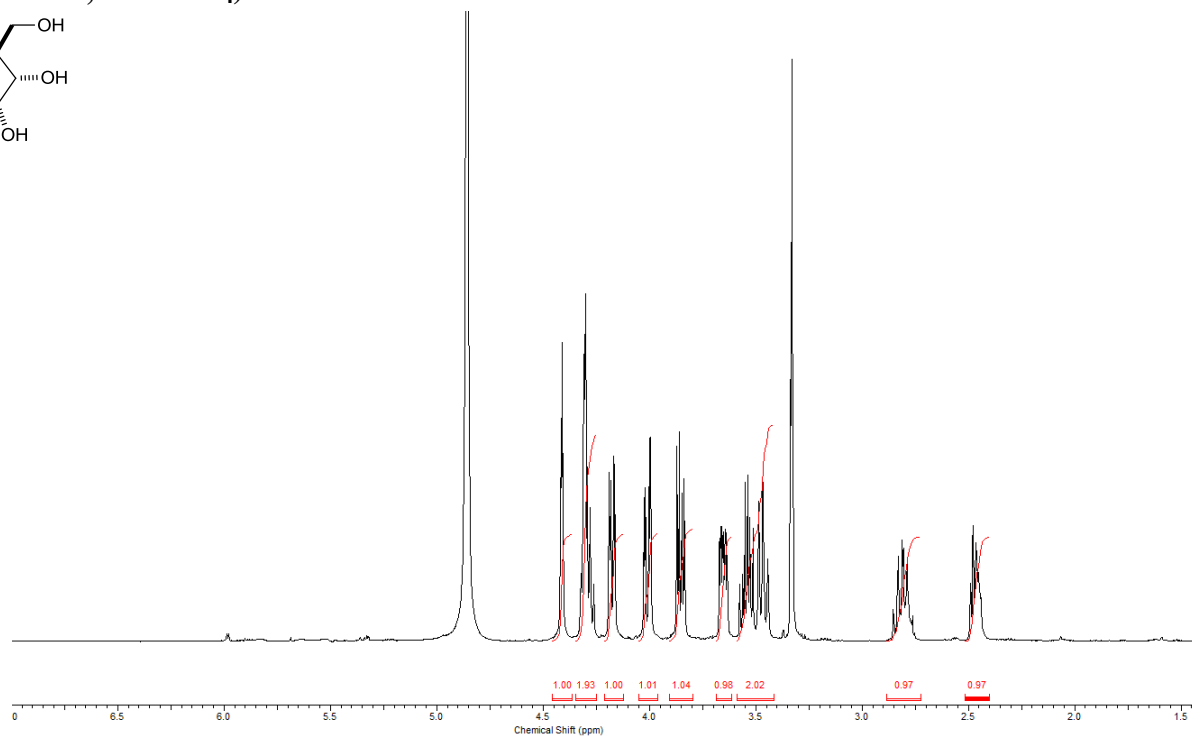
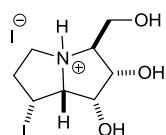


(2*S*,3*S*,4*R*,*Z*)-2-(Hydroxymethyl)-3,4-dihydroxy-1,2,3,4,7,8-hexahydroazocine 15 (125 MHz ¹³C, D₂O)



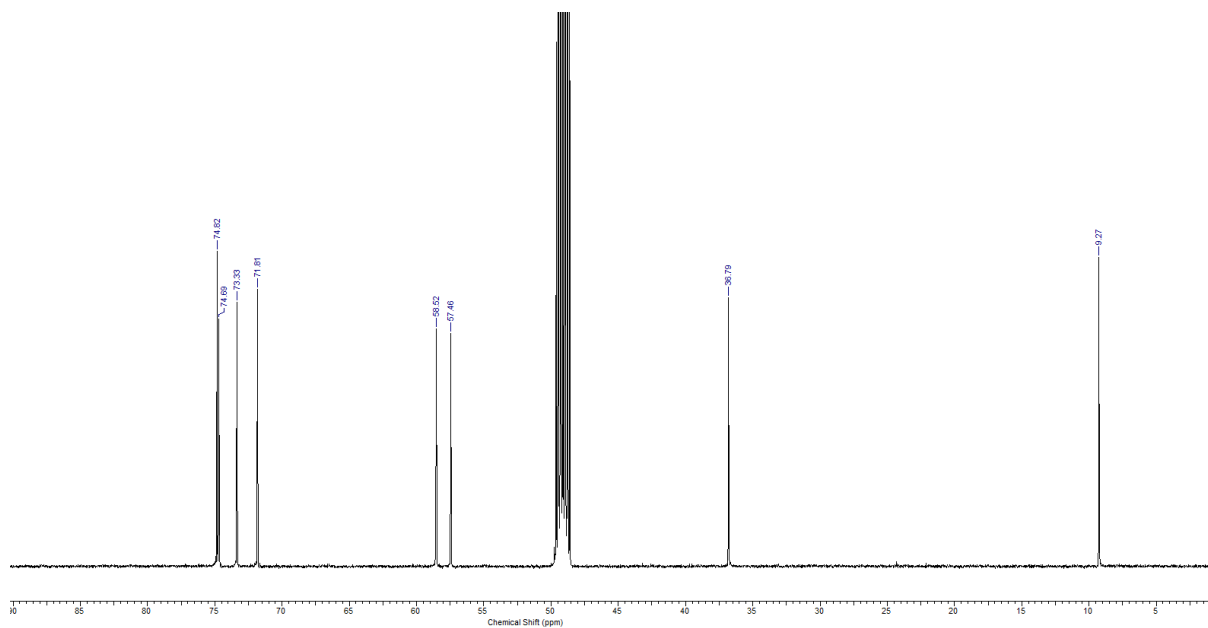
(1*R*,2*S*,3*S*,4*R*,7*R*,7*aR*)-1,2-Dihydroxy-3-hydroxymethyl-7-iodohexahydropyrrolizidinium iodide 17•HI

(500 MHz ¹H, MeOH-*d*₄)



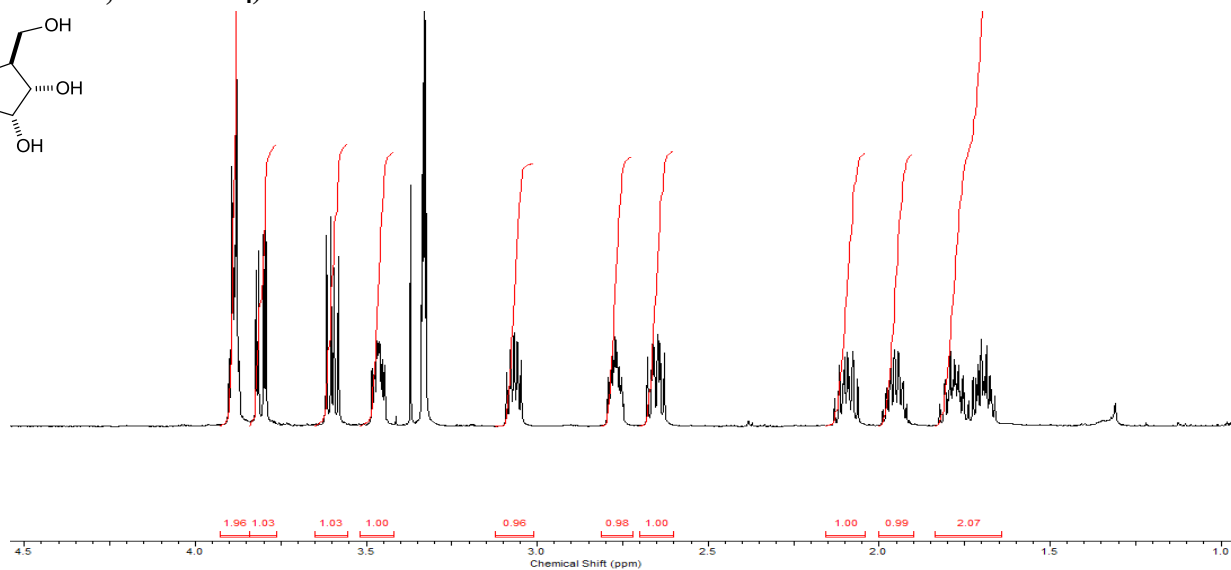
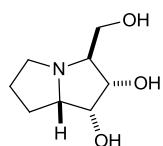
(1*R*,2*S*,3*S*,4*R*,7*R*,7*aR*)-1,2-Dihydroxy-3-hydroxymethyl-7-iodohexahydropyrrolizidinium iodide 17•HI

(125 MHz ¹³C, MeOH-*d*₄)



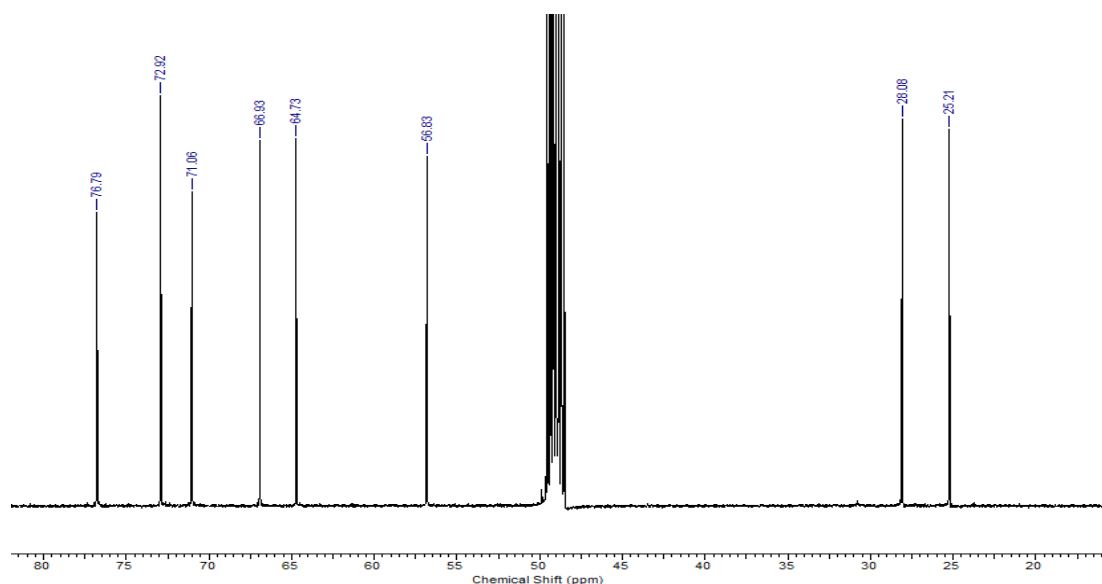
(1*R*,2*S*,3*S*,7*aR*)-1,2-Dihydroxy-3-hydroxymethylhexahydro-1*H*-pyrrolizidine [(-)-hyacinthacine A1] 18

(500 MHz ^1H , MeOH- d_4)

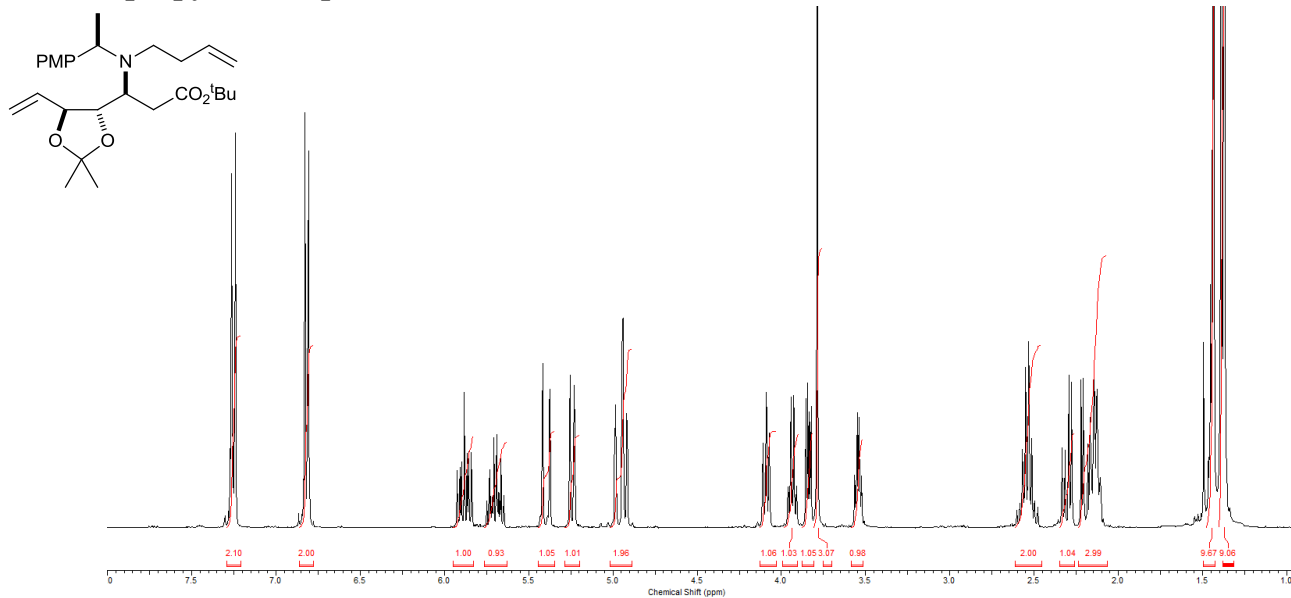


(1*R*,2*S*,3*S*,7*aR*)-1,2-Dihydroxy-3-hydroxymethylhexahydro-1*H*-pyrrolizidine [(-)-hyacinthacine A1] 18

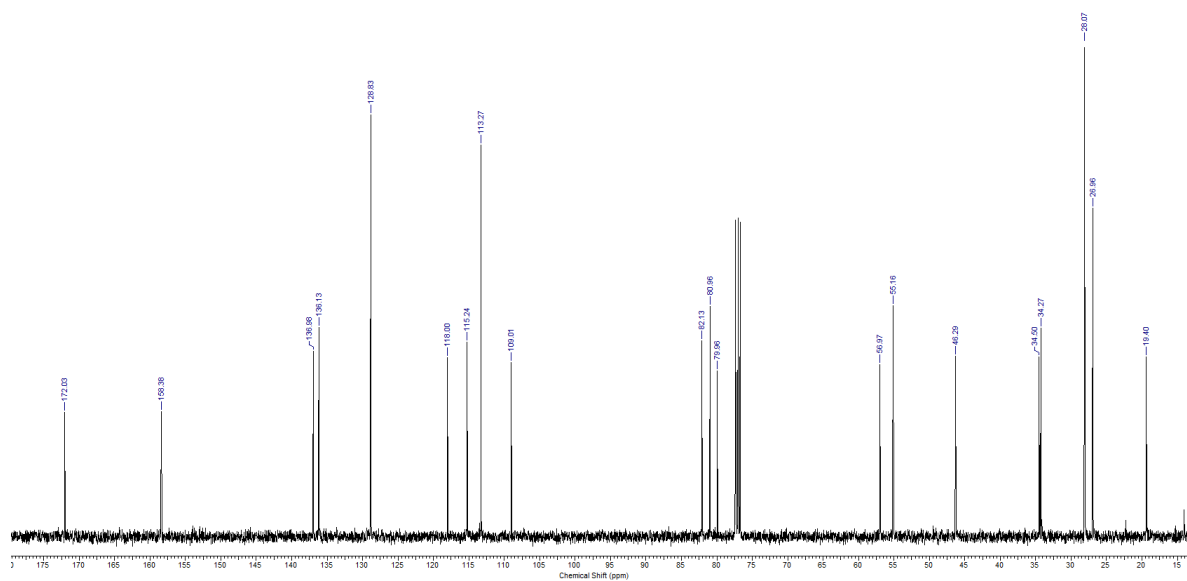
(125 MHz ^1H , MeOH- d_4)



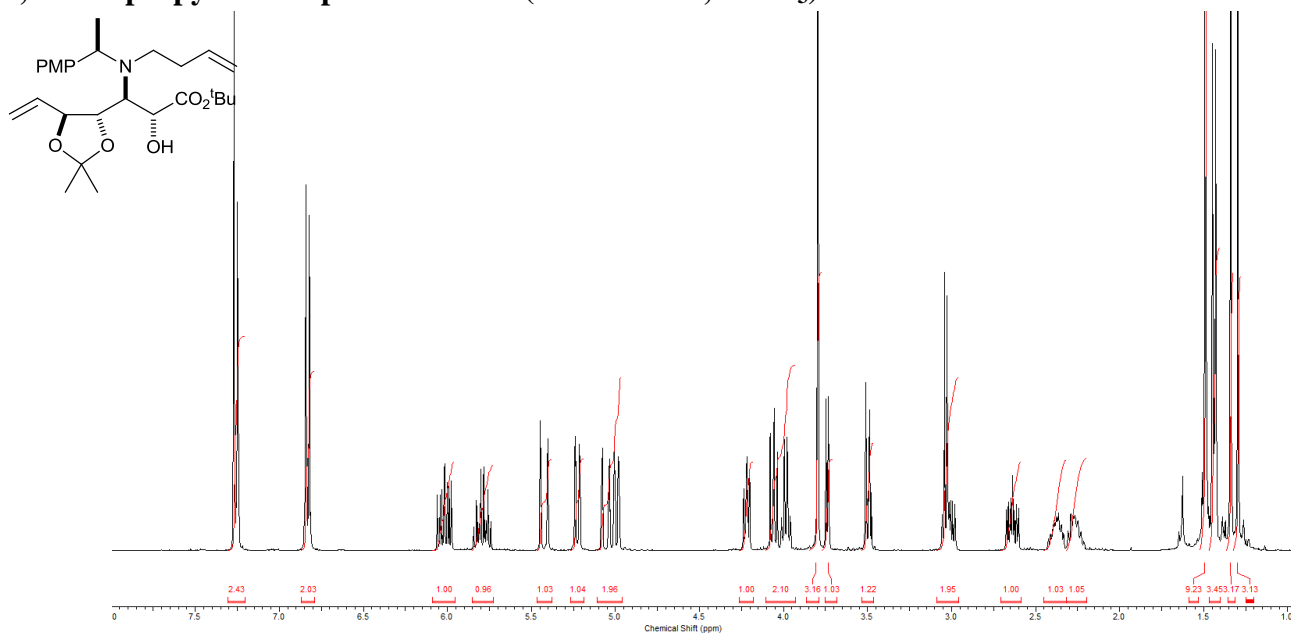
***tert*-Butyl (3*S*,4*S*,5*S*, α *R*)-3-[*N*-but-3'-enyl-*N*-(α -methyl-*p*-methoxybenzyl)amino]-4,5-dihydroxy-4,5-*O*-isopropylidenehept-6-enoate 27 (400 MHz, CDCl₃)**



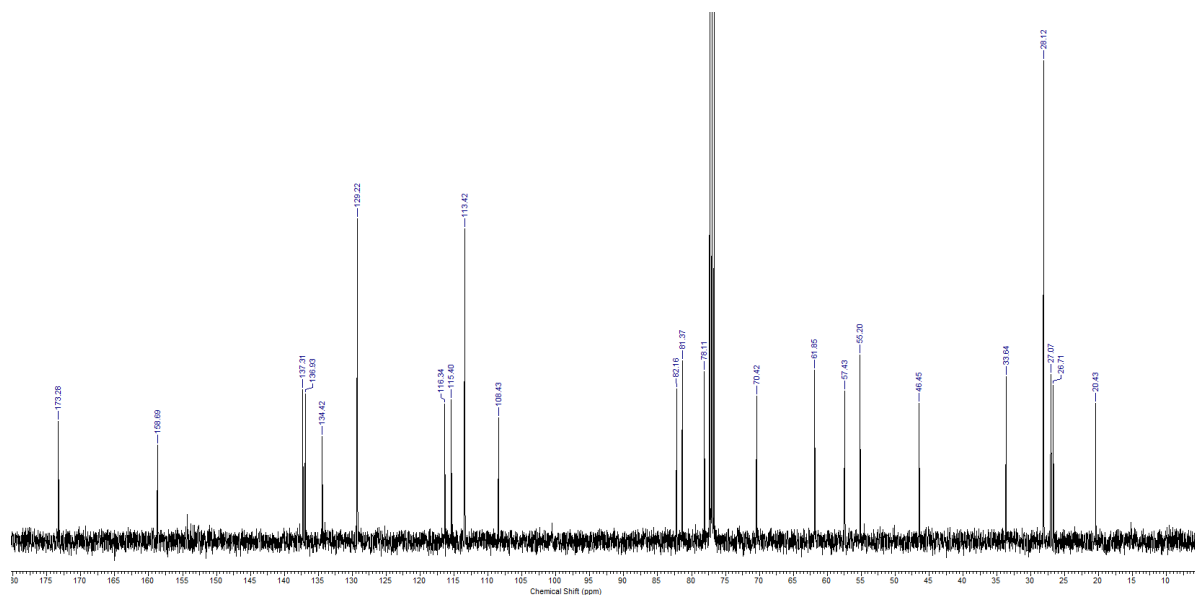
***tert*-Butyl (3*S*,4*S*,5*S*, α *R*)-3-[*N*-but-3'-enyl-*N*-(α -methyl-*p*-methoxybenzyl)amino]-4,5-dihydroxy-4,5-*O*-isopropylidenehept-6-enoate 27 (100 MHz ¹³C, CDCl₃)**



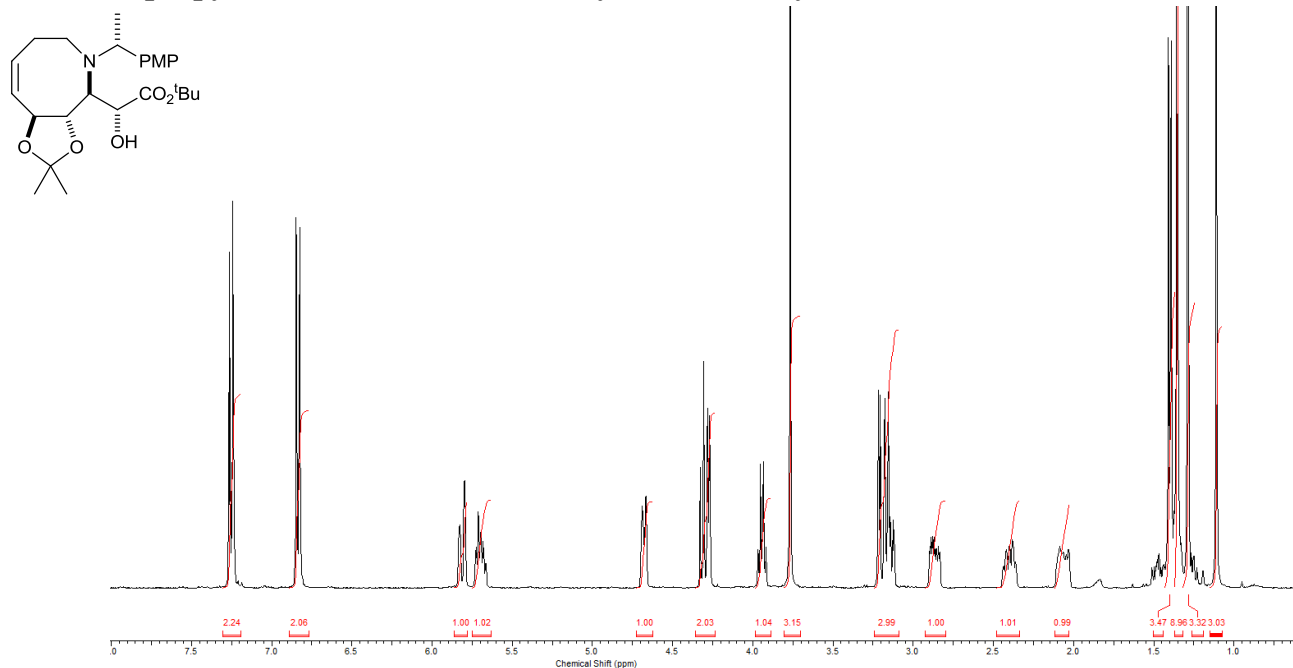
***tert*-Butyl (2*R*,3*S*,4*S*,5*S*, α *R*)-2,4,5-trihydroxy-3-[*N*-but-3'-enyl-*N*-(α -methyl-*p*-methoxybenzyl)amino]-4,5-*O*-isopropylidenehept-6-enoate 28 (400 MHz ^1H , CDCl_3)**



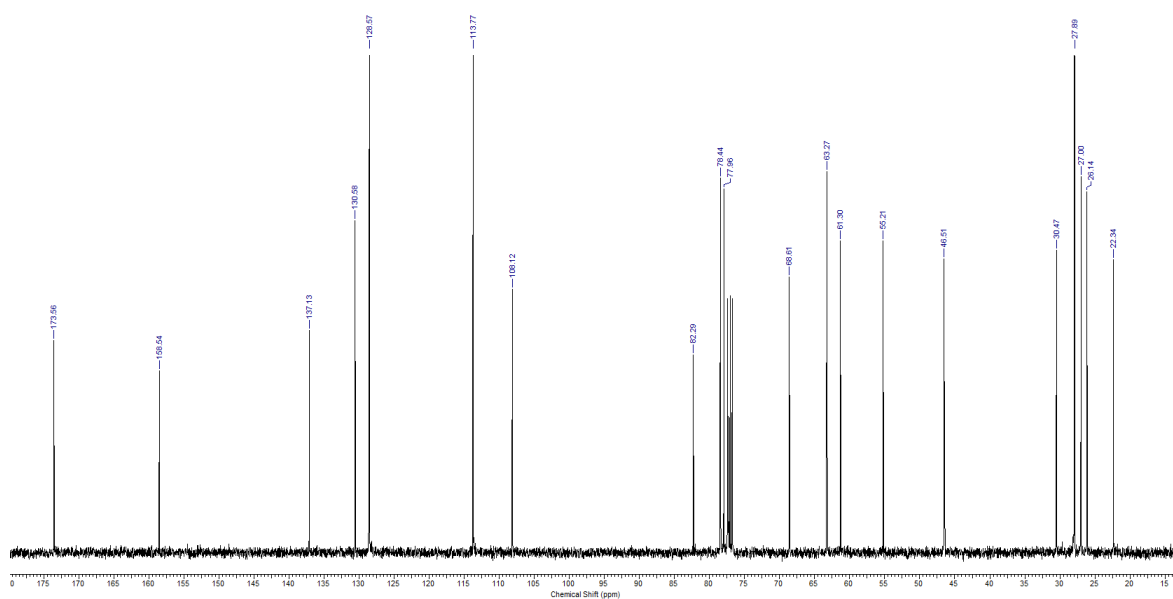
***tert*-Butyl (2*R*,3*S*,4*S*,5*S*, α *R*)-2,4,5-trihydroxy-3-[*N*-but-3'-enyl-*N*-(α -methyl-*p*-methoxybenzyl)amino]-4,5-*O*-isopropylidenehept-6-enoate 28 (100 MHz ^{13}C , CDCl_3)**



***tert*-Butyl (2*R*,2'*S*,3'*S*,4'*S*, α *R*,*Z*)-2-hydroxy-2-[*N*(1')-(α -methyl-*p*-methoxybenzyl)-3',4'-dihydroxy-3',4'-*O*-isopropylidene-1',2',3',4',7',8'-hexahydroazocin-2'-yl]ethanoate 29 (400 MHz ^1H , CDCl_3)**

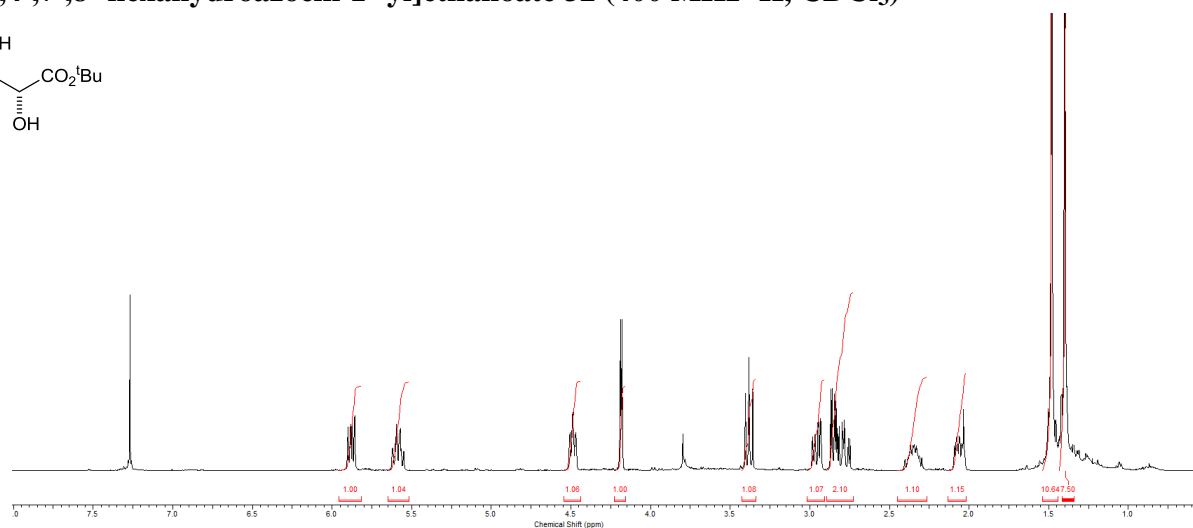
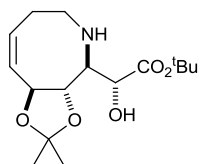


***tert*-Butyl (2*R*,2'*S*,3'*S*,4'*S*, α *R*,*Z*)-2-hydroxy-2-[*N*(1')-(α -methyl-*p*-methoxybenzyl)-3',4'-dihydroxy-3',4'-*O*-isopropylidene-1',2',3',4',7',8'-hexahydroazocin-2'-yl]ethanoate 29 (100 MHz ^{13}C , CDCl_3)**



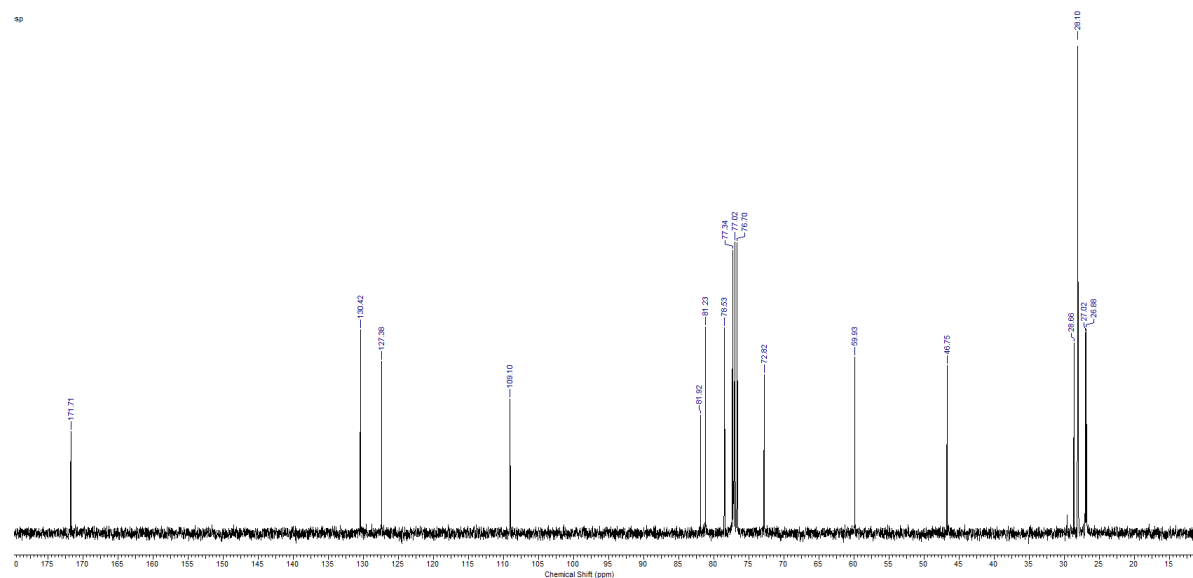
***tert*-Butyl (2*R*,2'*S*,3'*S*,4'*S*,*Z*)-2-hydroxy-2-[3',4'-dihydroxy-3',4'-*O*-isopropylidene-**

1',2',3',4',7',8'-hexahydroazocin-2'-yl]ethanoate 32 (400 MHz ¹H, CDCl₃)



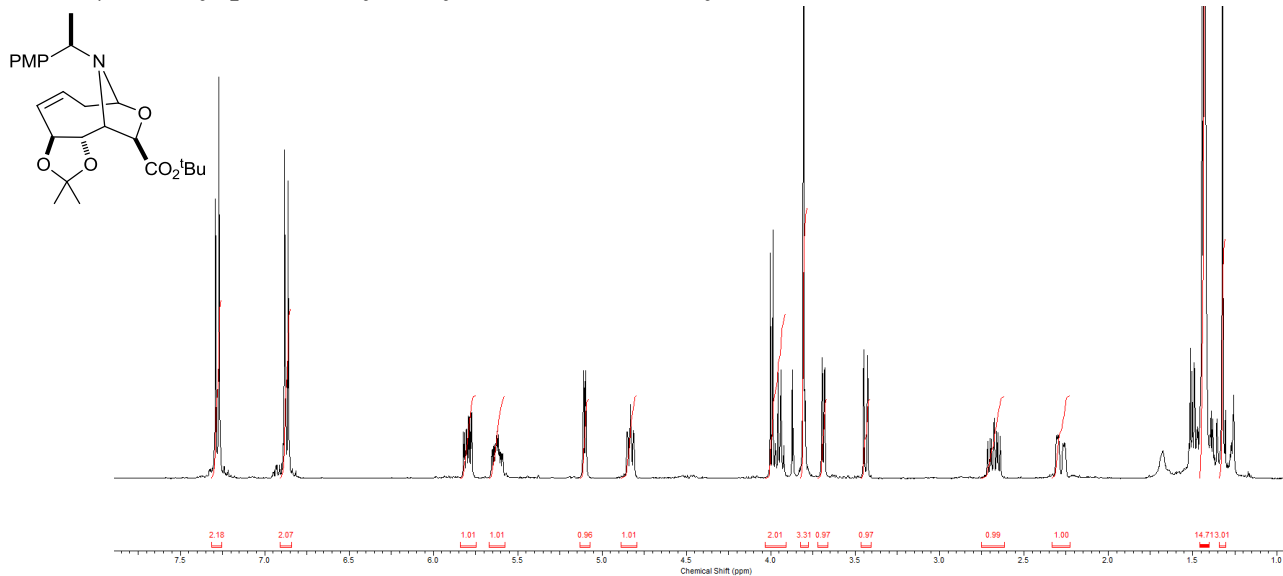
***tert*-Butyl (2*R*,2'*S*,3'*S*,4'*S*,*Z*)-2-hydroxy-2-[3',4'-dihydroxy-3',4'-*O*-isopropylidene-**

1',2',3',4',7',8'-hexahydroazocin-2'-yl]ethanoate 32 (100 MHz ¹³C, CDCl₃)



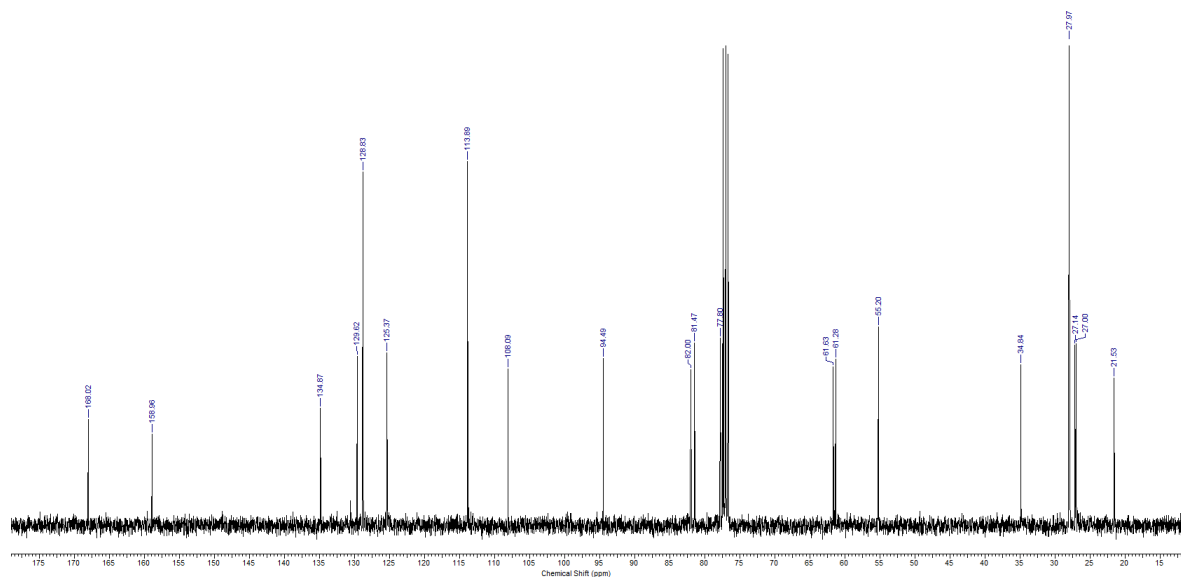
(1*R*,2*S*,3*S*,7*S*,9*R*, α *R*,*Z*)-2,3-dihydroxy-2,3-*O*-isopropylidene-9-(*tert*-butoxycarbonyl)-

***N*(10)-(α -methyl-*p*-methoxybenzyl)-8-oxa-10-azabicyclo[5.2.1]dec-4-ene 33 (400 MHz ^1H , CDCl_3)**

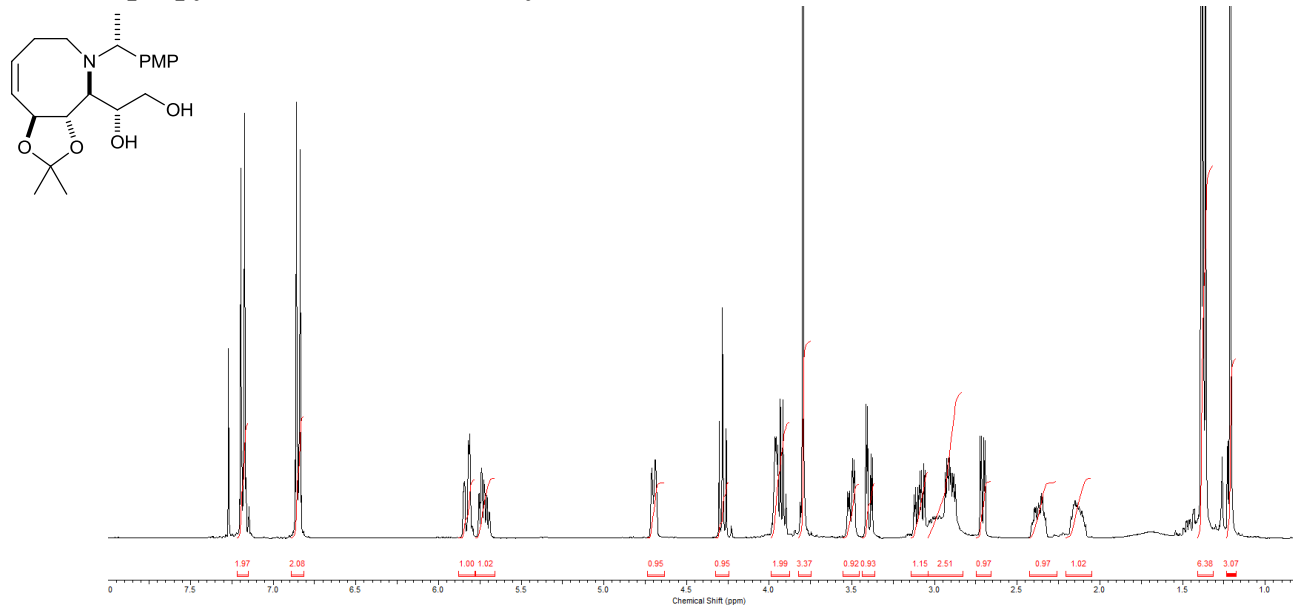


(1*R*,2*S*,3*S*,7*S*,9*R*, α *R*,*Z*)-2,3-dihydroxy-2,3-*O*-isopropylidene-9-(*tert*-butoxycarbonyl)-

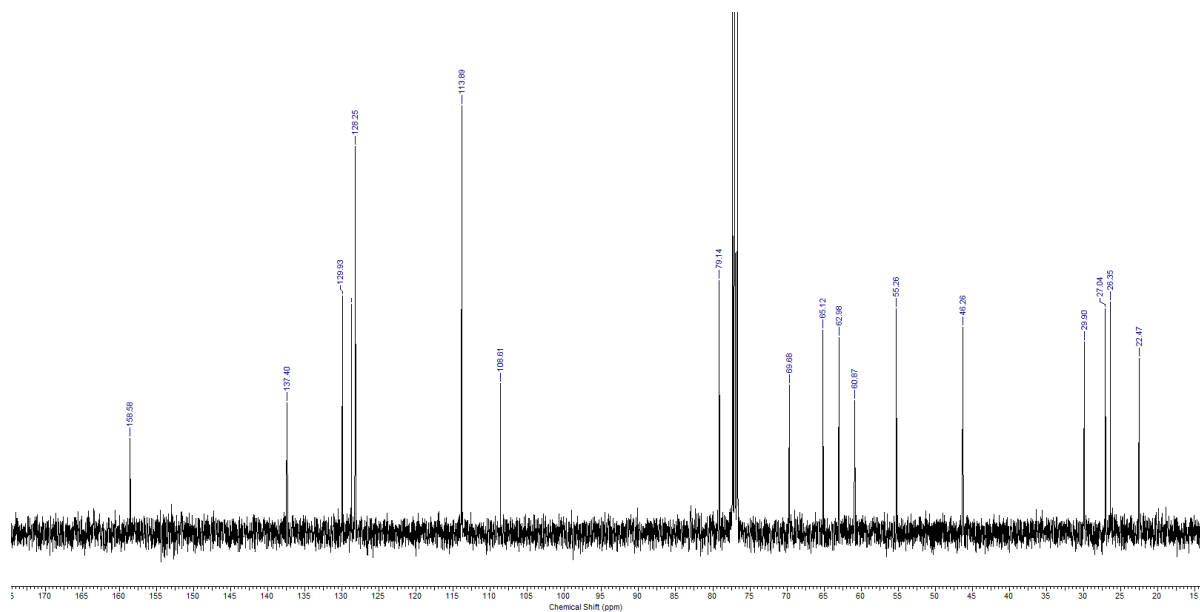
***N*(10)-(α -methyl-*p*-methoxybenzyl)-8-oxa-10-azabicyclo[5.2.1]dec-4-ene 33 (100 MHz ^{13}C , CDCl_3)**



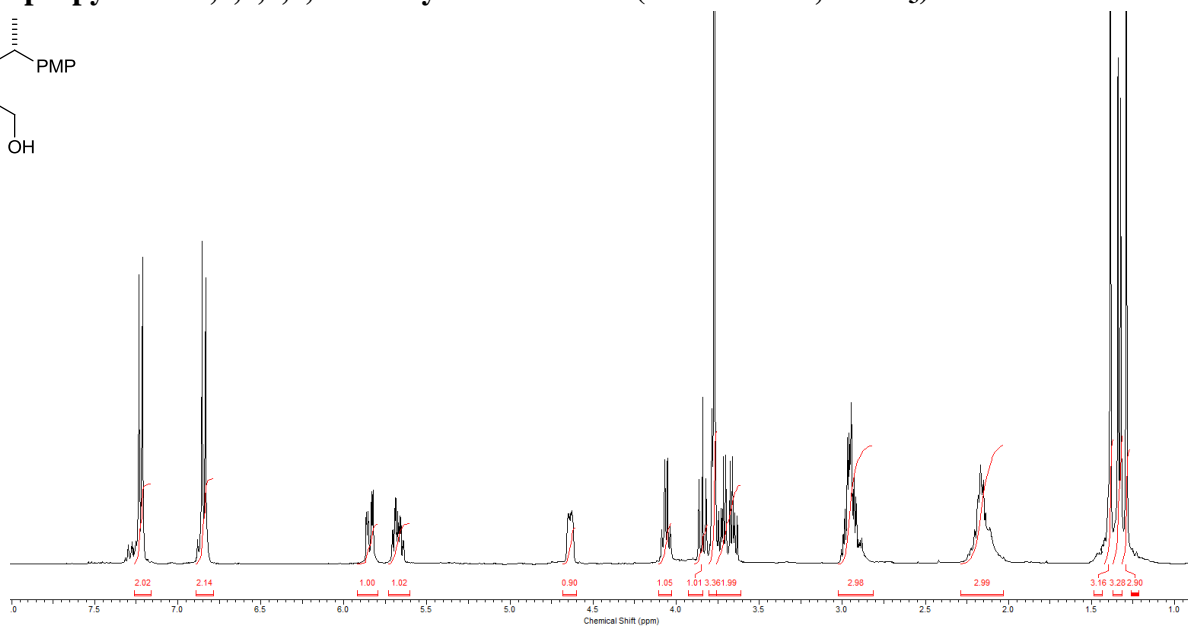
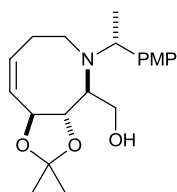
(2*S*,3*S*,4*S*,1'*R*, α *R*,*Z*)-*N*(1)-(α -Methyl-*p*-methoxybenzyl)-2-(dihydroxyethyl)-3,4-dihydroxy-3,4-*O*-isopropylidene-1,2,3,4,7,8-hexahydroazocine 35 (400 MHz ^1H , CDCl_3)



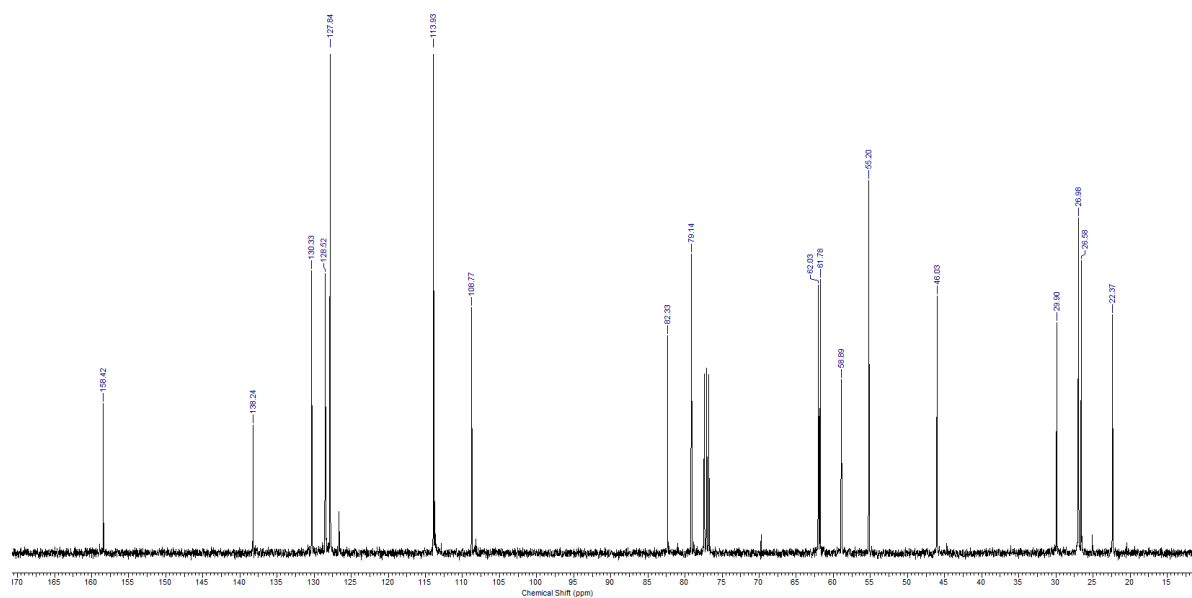
(2*S*,3*S*,4*S*,1'*R*, α *R*,*Z*)-*N*(1)-(α -Methyl-*p*-methoxybenzyl)-2-(dihydroxyethyl)-3,4-dihydroxy-3,4-*O*-isopropylidene-1,2,3,4,7,8-hexahydroazocine 35 (100 MHz ^{13}C , CDCl_3)



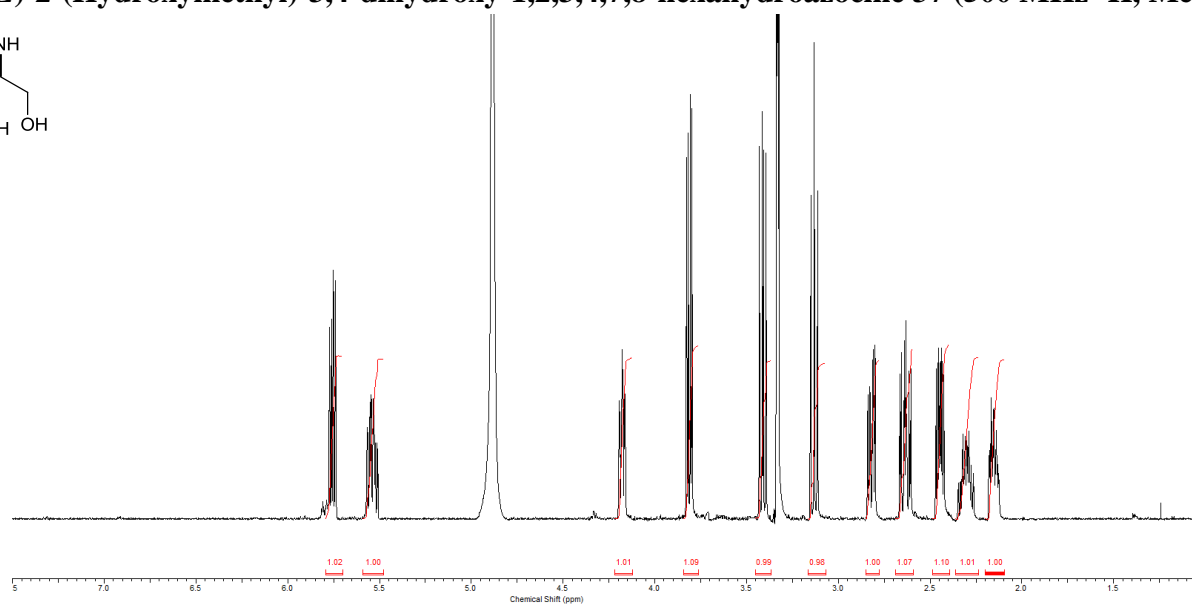
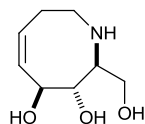
(2*S*,3*S*,4*S*,*aR*,*Z*)-*N*(1)-(*α*-Methyl-*p*-methoxybenzyl)-2-(hydroxymethyl)-3,4-dihydroxy-3,4-*O*-isopropylidene-1,2,3,4,7,8-hexahydroazocine 36 (400 MHz ¹H, CDCl₃)



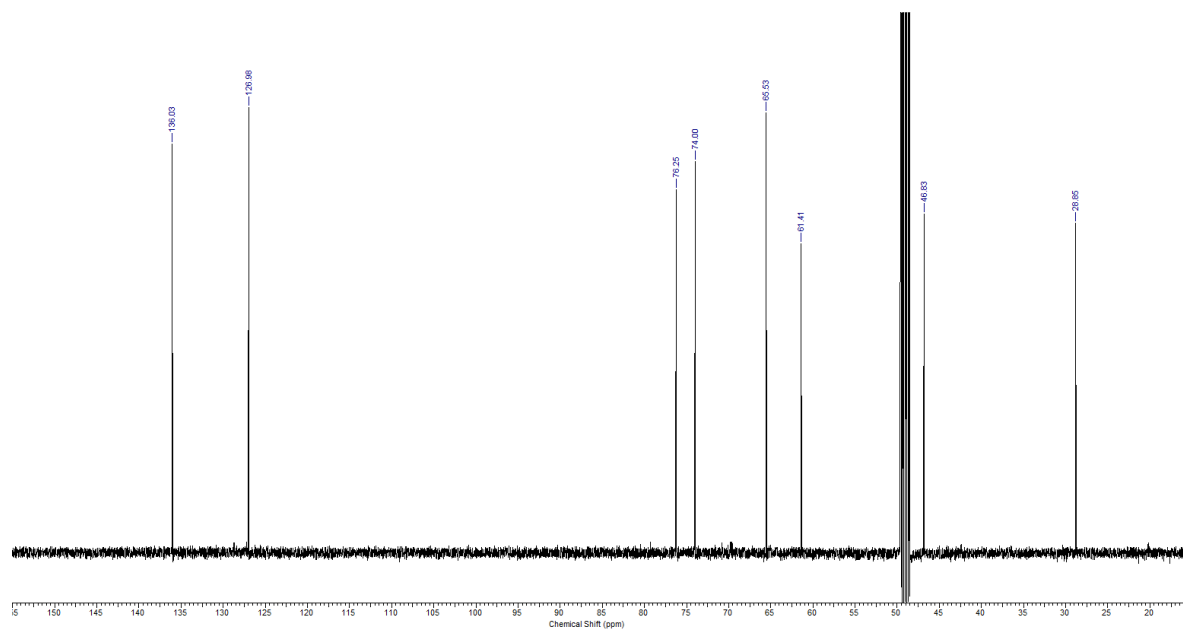
(2*S*,3*S*,4*S*,*aR*,*Z*)-*N*(1)-(*α*-Methyl-*p*-methoxybenzyl)-2-(hydroxymethyl)-3,4-dihydroxy-3,4-*O*-isopropylidene-1,2,3,4,7,8-hexahydroazocine 36 (100 MHz ¹³C, CDCl₃)



(S,S,S,Z)-2-(Hydroxymethyl)-3,4-dihydroxy-1,2,3,4,7,8-hexahydroazocine 37 (500 MHz ^1H , MeOH- d_4)

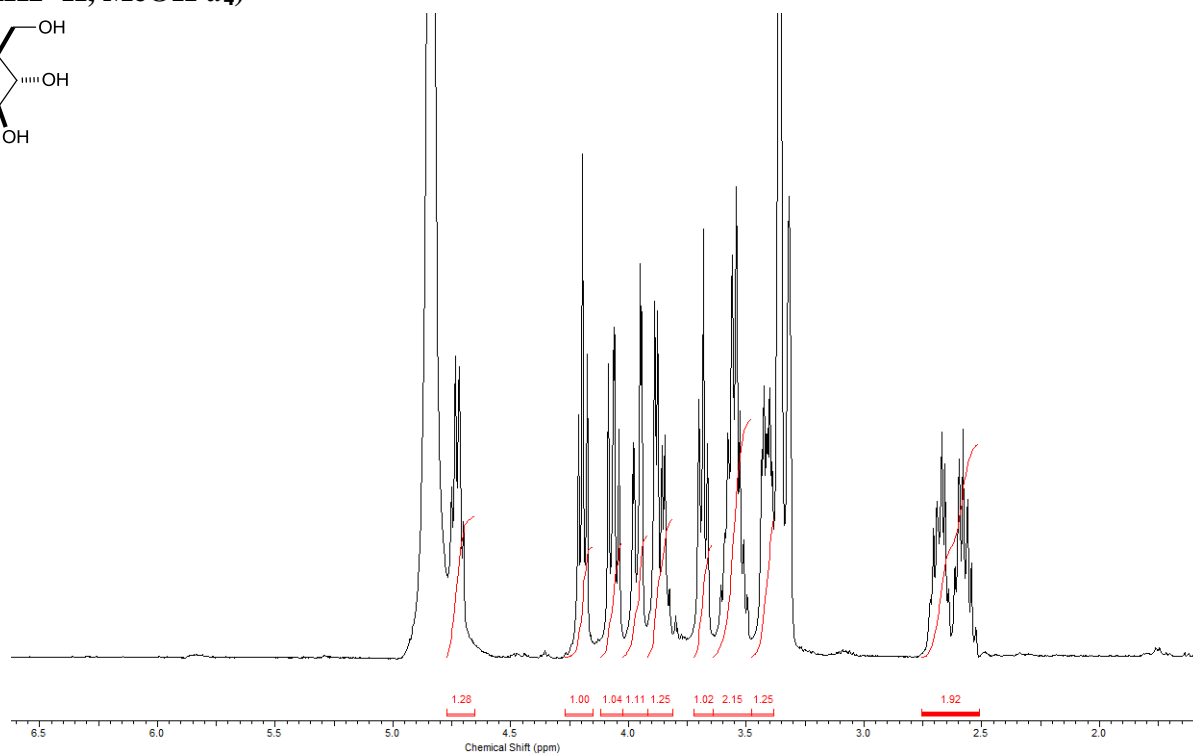
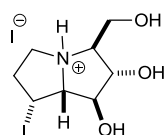


(S,S,S,Z)-2-(Hydroxymethyl)-3,4-dihydroxy-1,2,3,4,7,8-hexahydroazocine 37 (125 MHz ^{13}C , MeOH- d_4)



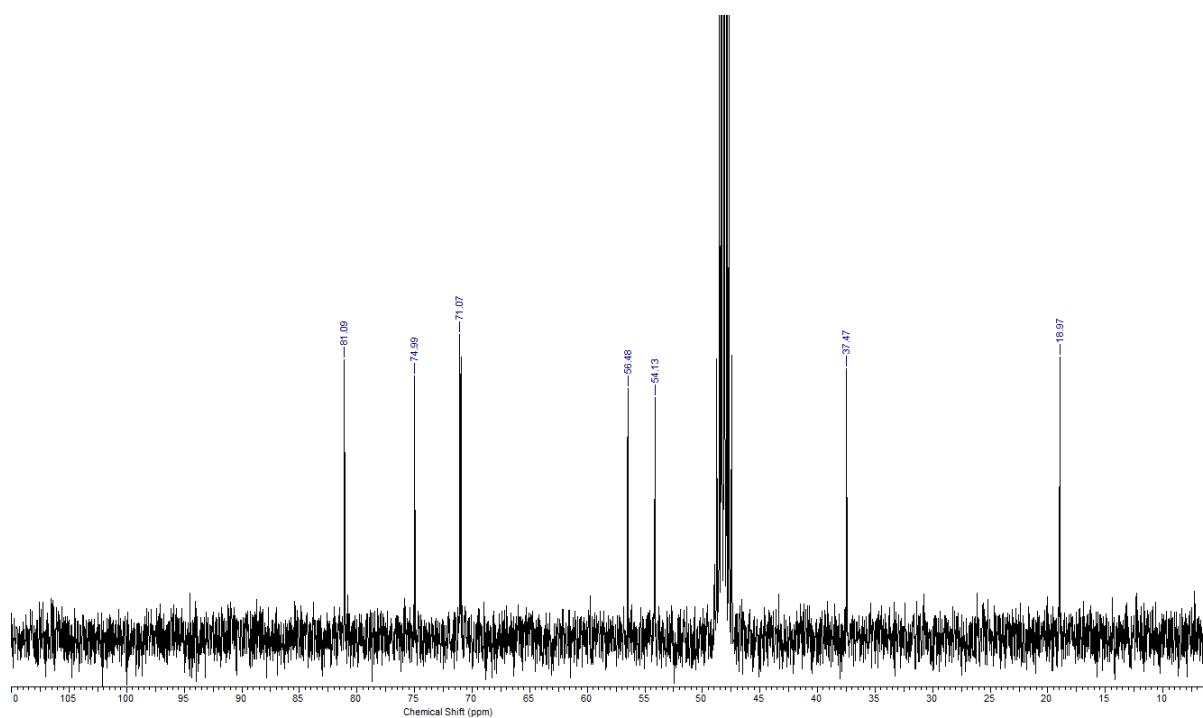
(1*S*,2*S*,3*S*,4*R*,7*R*,7*aR*)-1,2-Dihydroxy-3-hydroxymethyl-7-iodohexahydropyrrolizidinium iodide 39•HI

(400 MHz ^1H , MeOH- d_4)



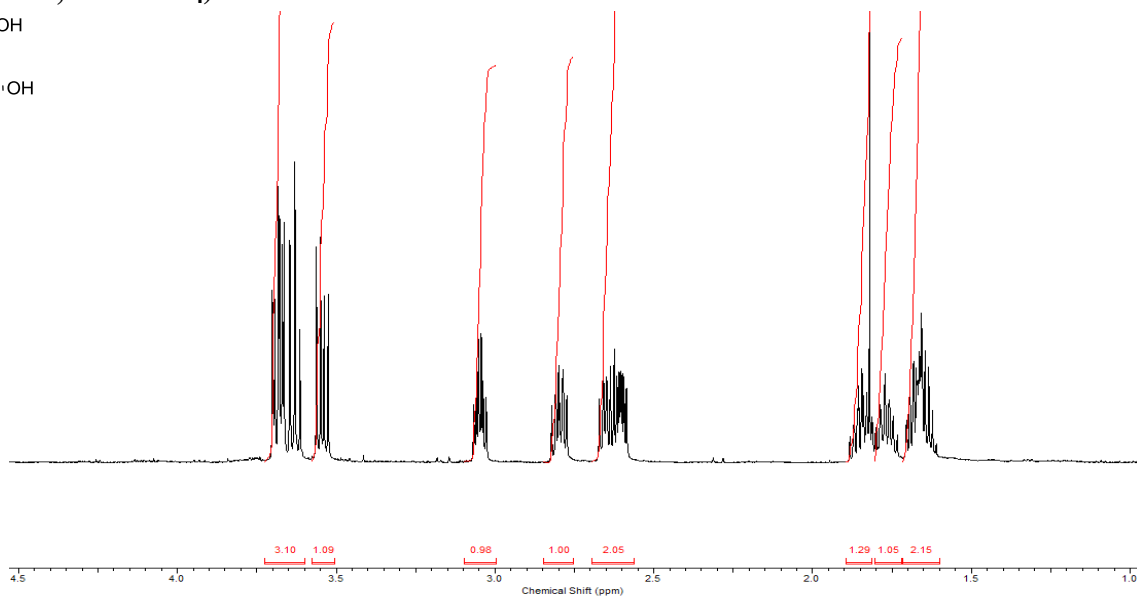
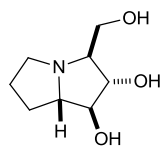
(1*S*,2*S*,3*S*,4*R*,7*R*,7*aR*)-1,2-Dihydroxy-3-hydroxymethyl-7-iodohexahydropyrrolizidinium iodide 39•HI

(100 MHz ^{13}C , MeOH- d_4)



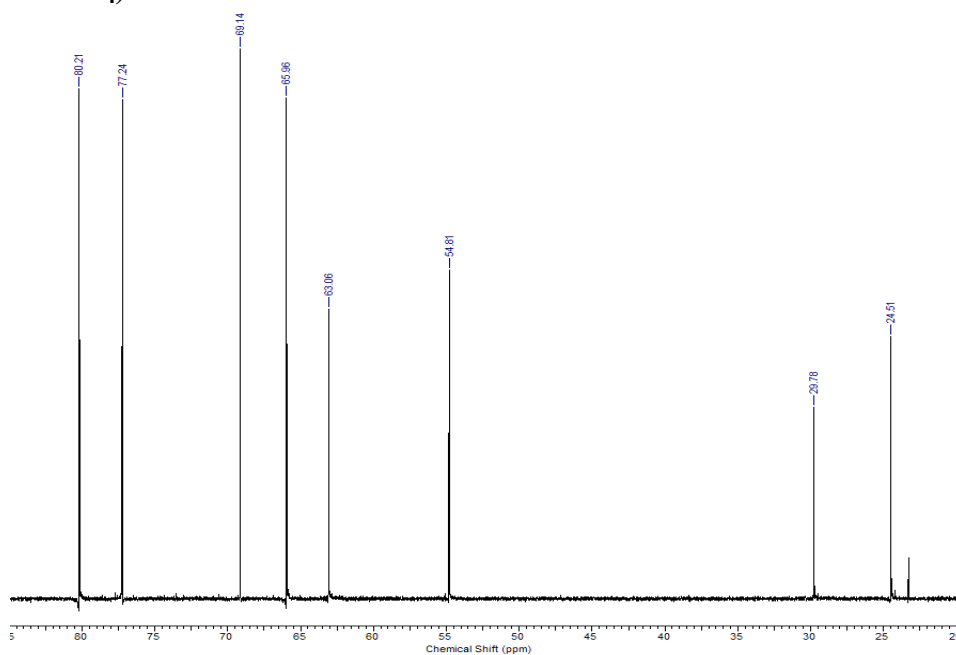
(*S,S,S,S*)-1,2-Dihydroxy-3-(hydroxymethyl)hexahydro-1*H*-pyrrolizidine [(–)-hyacinthacine A2] 40

(400 MHz ^1H , MeOH- d_4)



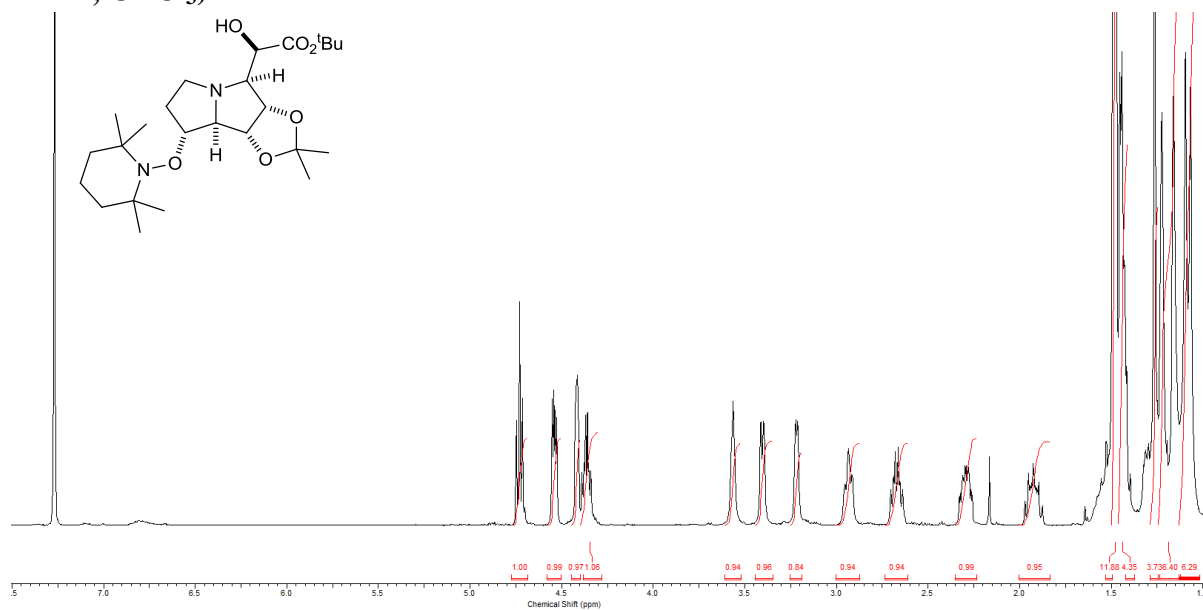
(*S,S,S,S*)-1,2-Dihydroxy-3-(hydroxymethyl)hexahydro-1*H*-pyrrolizidine [(–)-hyacinthacine A2] 40

(100 MHz ^1H , MeOH- d_4)



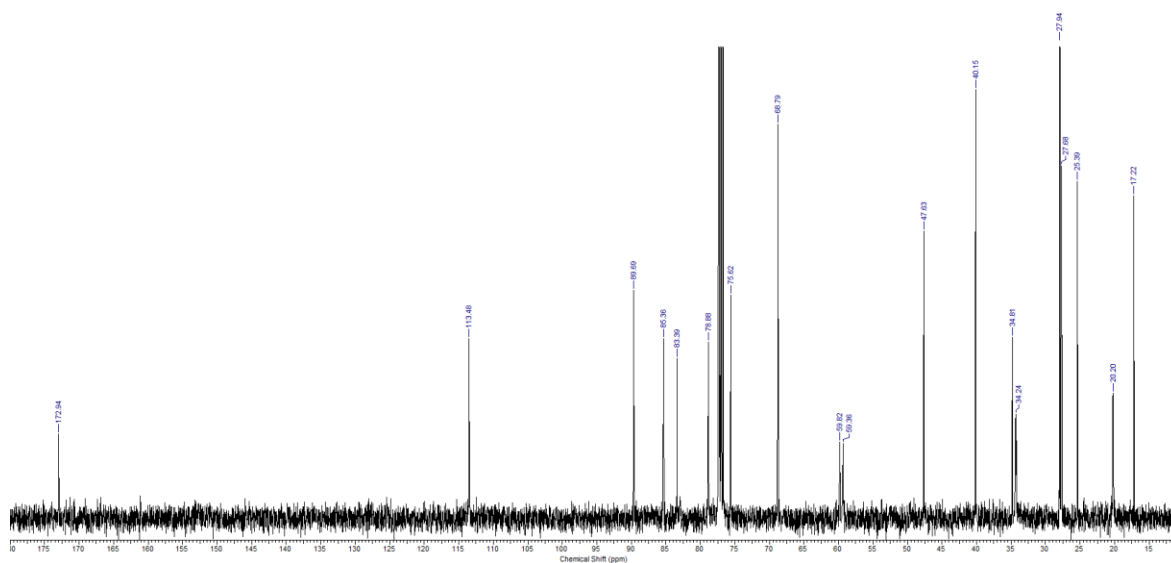
(1*R*,2*S*,3*S*,7*R*,7*aS*,1'*R*)-1,2-Dihydroxy-1,2-*O*-isopropylidene-3-(1'-hydroxy-2'-*tert*-butoxy-2'-oxoethyl)-7-[[2'',2'',6'',6''-tetramethylpiperidin-*N*(1'')-yl]oxy}hexahydro-1*H*-pyrrolizidine 45

(400 MHz ¹H, CDCl₃)

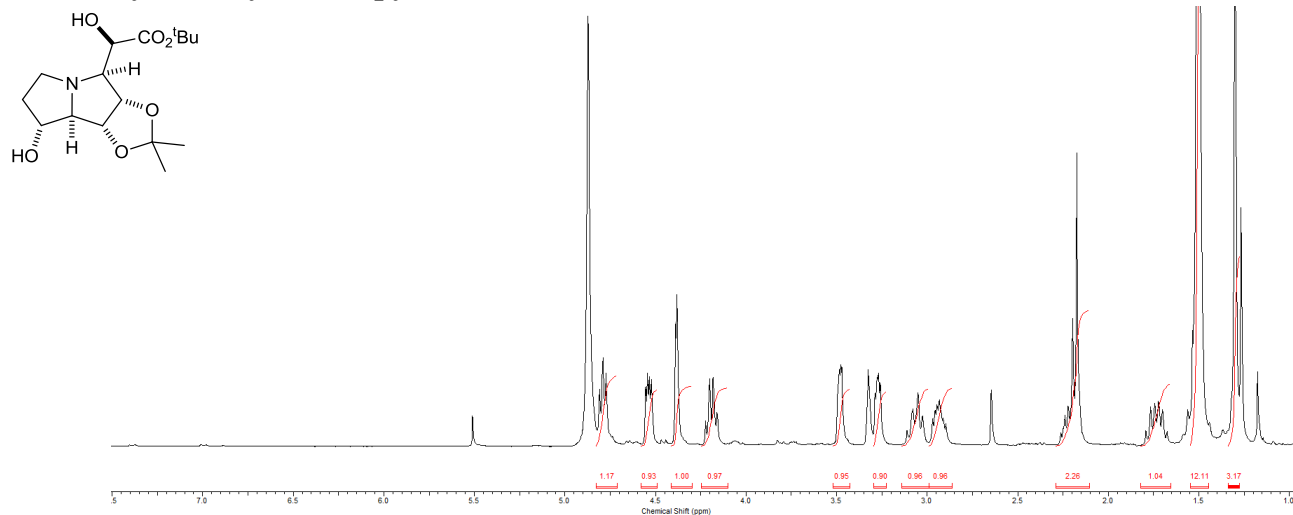


(1*R*,2*S*,3*S*,7*R*,7*aS*,1'*R*)-1,2-Dihydroxy-1,2-*O*-isopropylidene-3-(1'-hydroxy-2'-*tert*-butoxy-2'-oxoethyl)-7-[[2'',2'',6'',6''-tetramethylpiperidin-*N*(1'')-yl]oxy}hexahydro-1*H*-pyrrolizidine 45

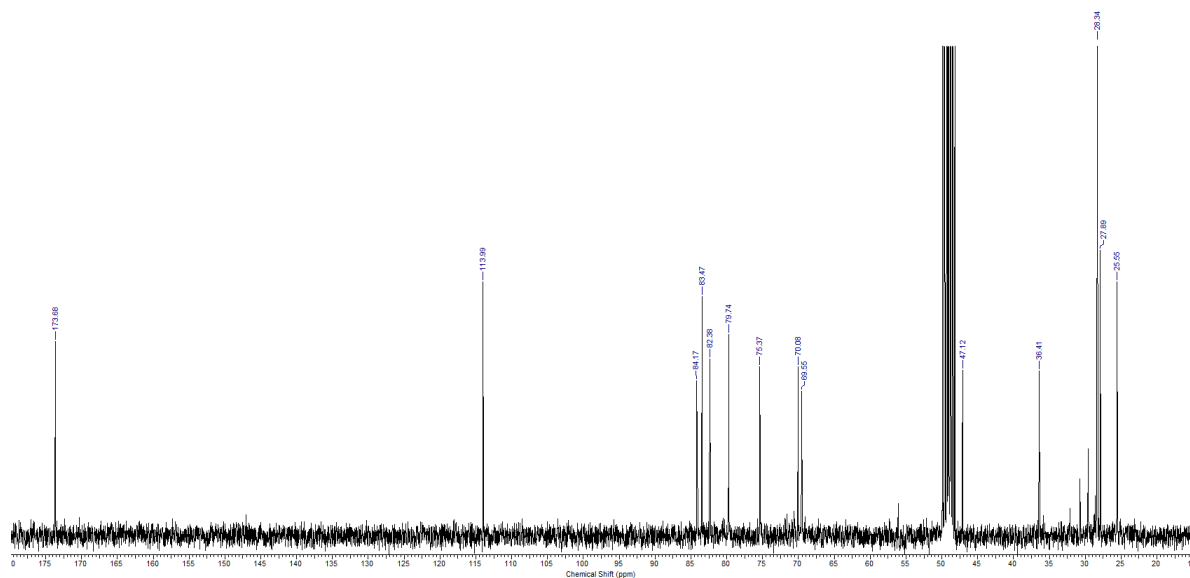
(100 MHz ¹³C, CDCl₃)



(1*R*,2*S*,3*S*,7*R*,7*aS*,1'*R*)-1,2,7-Trihydroxy-1,2-*O*-isopropylidene-3-(1'-hydroxy-2'-*tert*-butoxy-2'-oxoethyl)hexahydro-1*H*-pyrrolizidine 47 (300 MHz ¹H, MeOH-*d*₄)

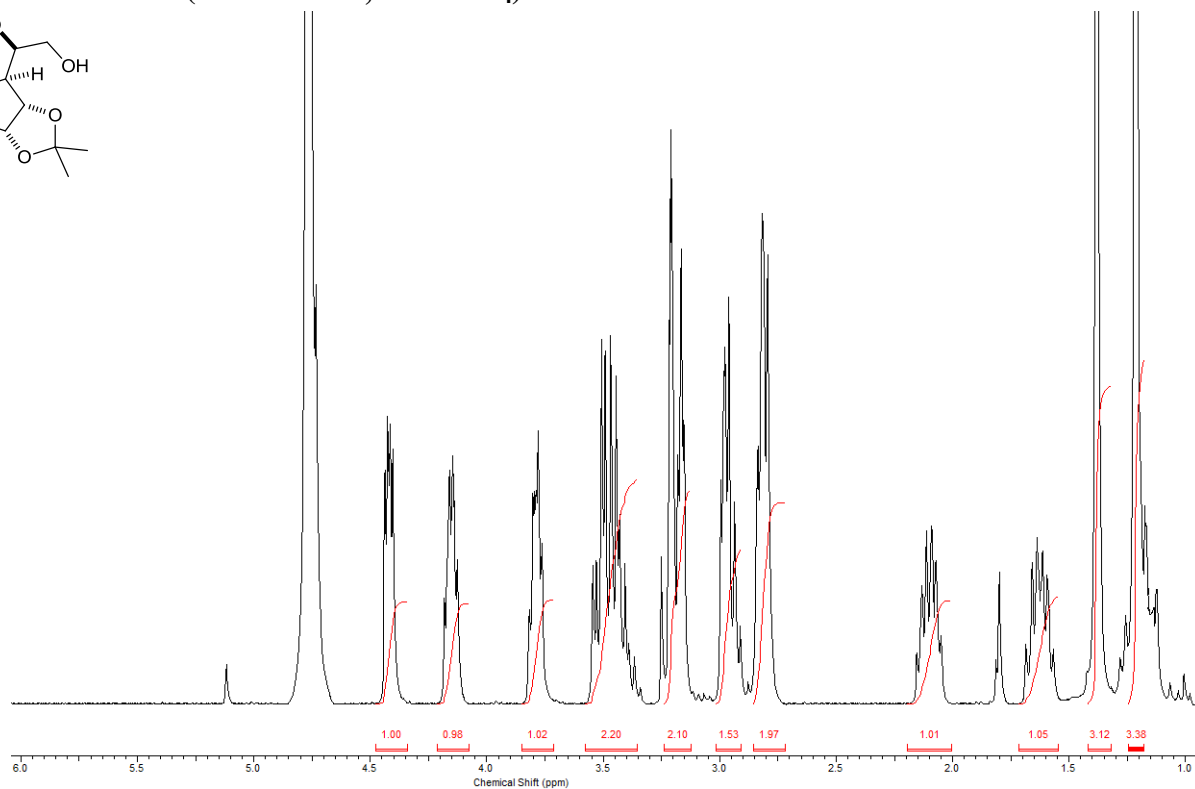
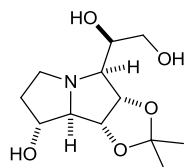


(1*R*,2*S*,3*S*,7*R*,7*aS*,1'*R*)-1,2,7-Trihydroxy-1,2-*O*-isopropylidene-3-(1'-hydroxy-2'-*tert*-butoxy-2'-oxoethyl)hexahydro-1*H*-pyrrolizidine 47 (75 MHz ¹³C, MeOH-*d*₄)



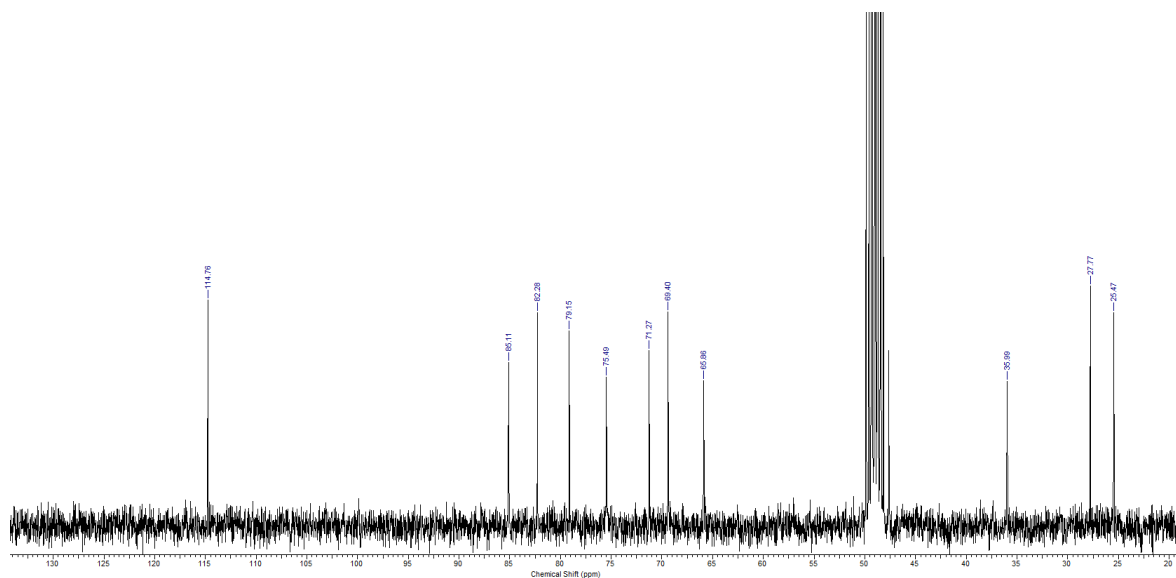
(1*R*,2*S*,3*S*,7*R*,7*aR*,1'*R*)-1,2,7-Trihydroxy-1,2-*O*-isopropylidene-3-(1',2'-dihydroxyethyl)hexahydro-

1*H*-pyrrolizidine 48 (300 MHz ¹H, MeOH-*d*₄)



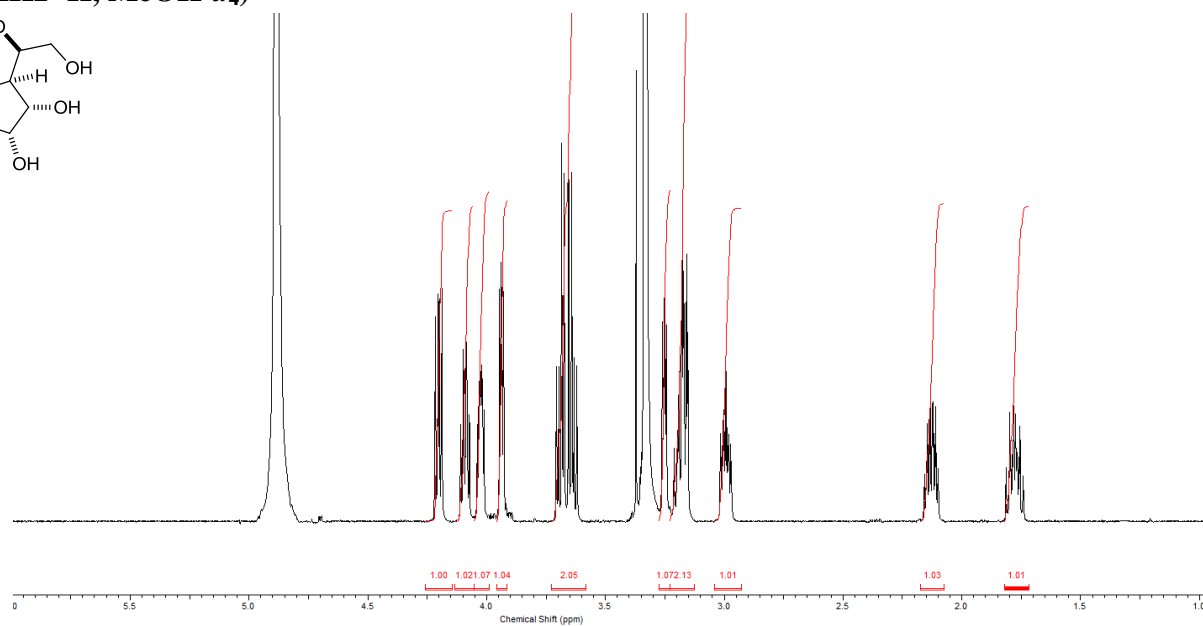
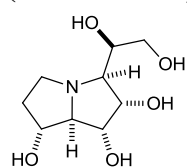
(1*R*,2*S*,3*S*,7*R*,7*aR*,1'*R*)-1,2,7-Trihydroxy-1,2-*O*-isopropylidene-3-(1',2'-dihydroxyethyl)hexahydro-

1*H*-pyrrolizidine 48 (75 MHz ¹³C, MeOH-*d*₄)



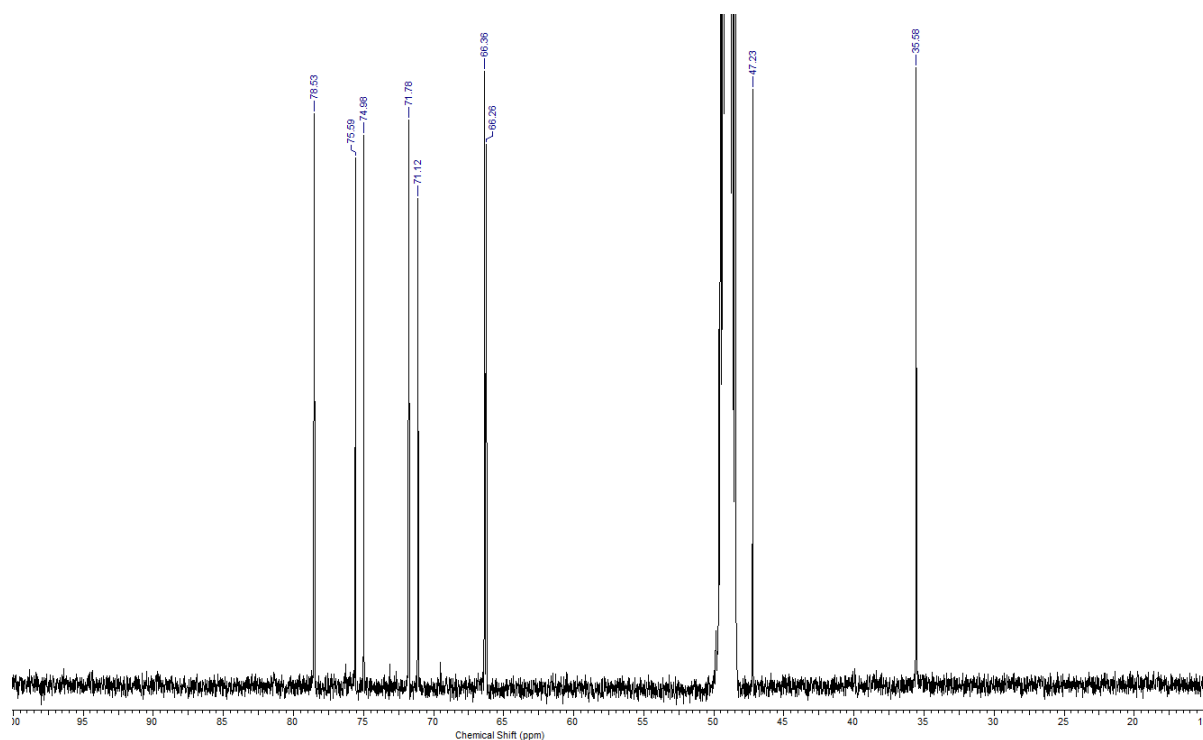
(1*R*,2*S*,3*S*,7*R*,7*aR*,1'*R*)-1,2,7-Trihydroxy-3-(1',2'-dihydroxyethyl)hexahydro-1*H*-pyrrolizidine 49

(500 MHz ¹H, MeOH-*d*₄)



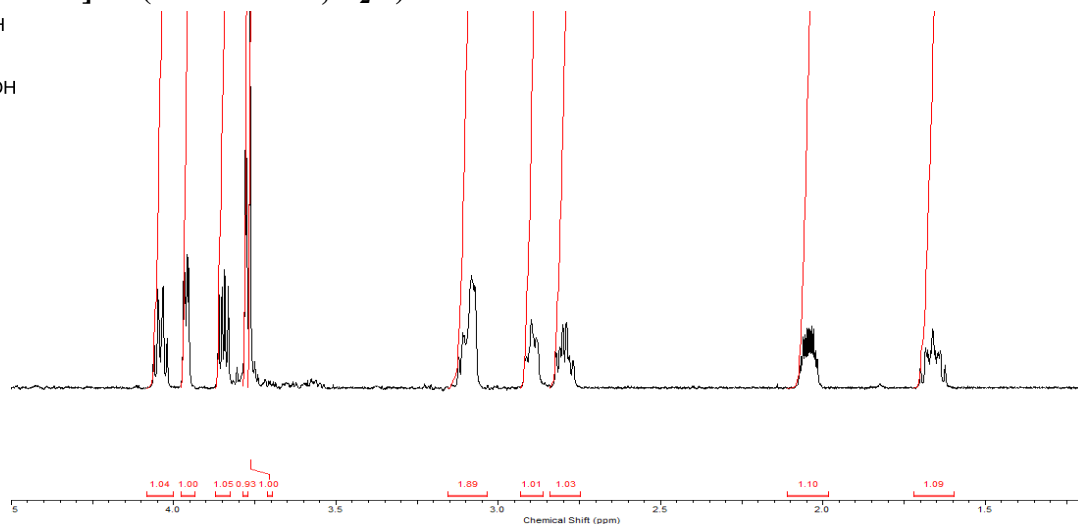
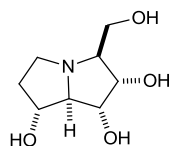
(1*R*,2*S*,3*S*,7*R*,7*aR*,1'*R*)-1,2,7-Trihydroxy-3-(1',2'-dihydroxyethyl)hexahydro-1*H*-pyrrolizidine 49

(125 MHz ¹³C, MeOH-*d*₄)



(1*R*,2*S*,3*S*,7*R*,7*aR*)-1,2,7-Trihydroxy-3-hydroxymethylhexahydro-1*H*-pyrrolizidine

[(-)-1-*epi*-alexine] 51 (500 MHz ¹H, D₂O)



(1*R*,2*S*,3*S*,7*R*,7*aR*)-1,2,7-Trihydroxy-3-hydroxymethylhexahydro-1*H*-pyrrolizidine

[(-)-1-*epi*-alexine] 51 (100 MHz ¹³C, D₂O)

