Universitat Autònoma de Barcelona

Rational Design and Synthesis of New Nucleoside Analogues Bearing a Cyclohexane Core

Beatriz Domínguez Pérez

Ph.D. Thesis

Ph.D. in Chemistry

Supervisors:

Dr. Ramon Alibés Arqués

Dr. Félix Busqué Sánchez

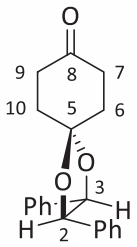
Dr. Jean-Didier Márechal

Departament de Química

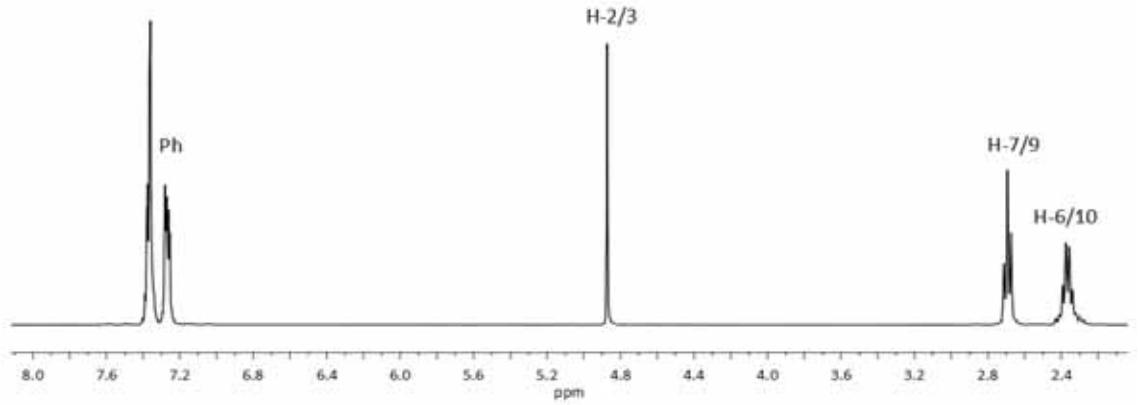
Facultat de Ciències

2015

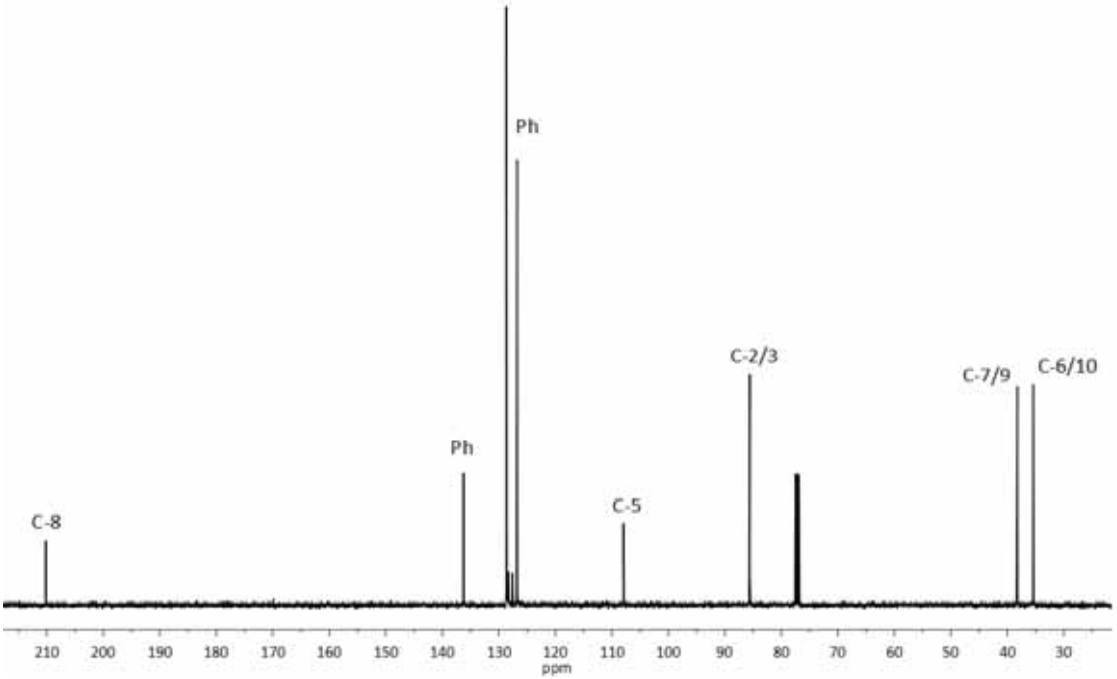
NMR spectra of selected compounds



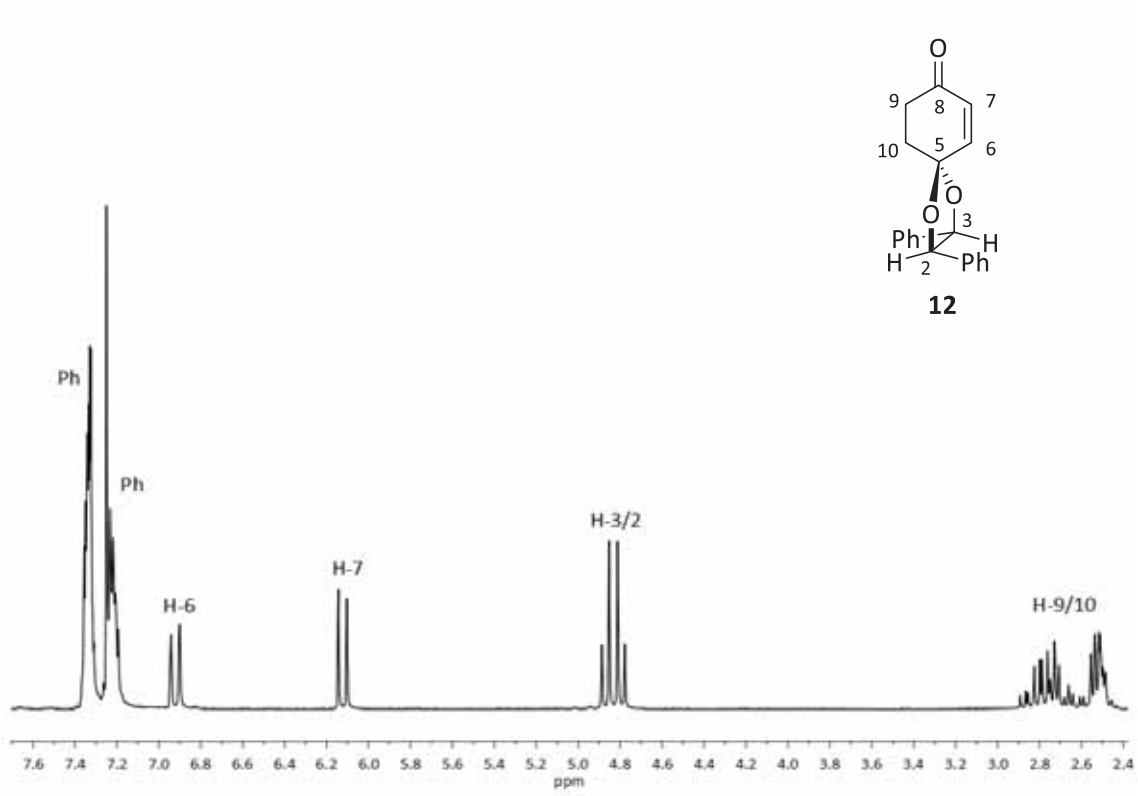
11



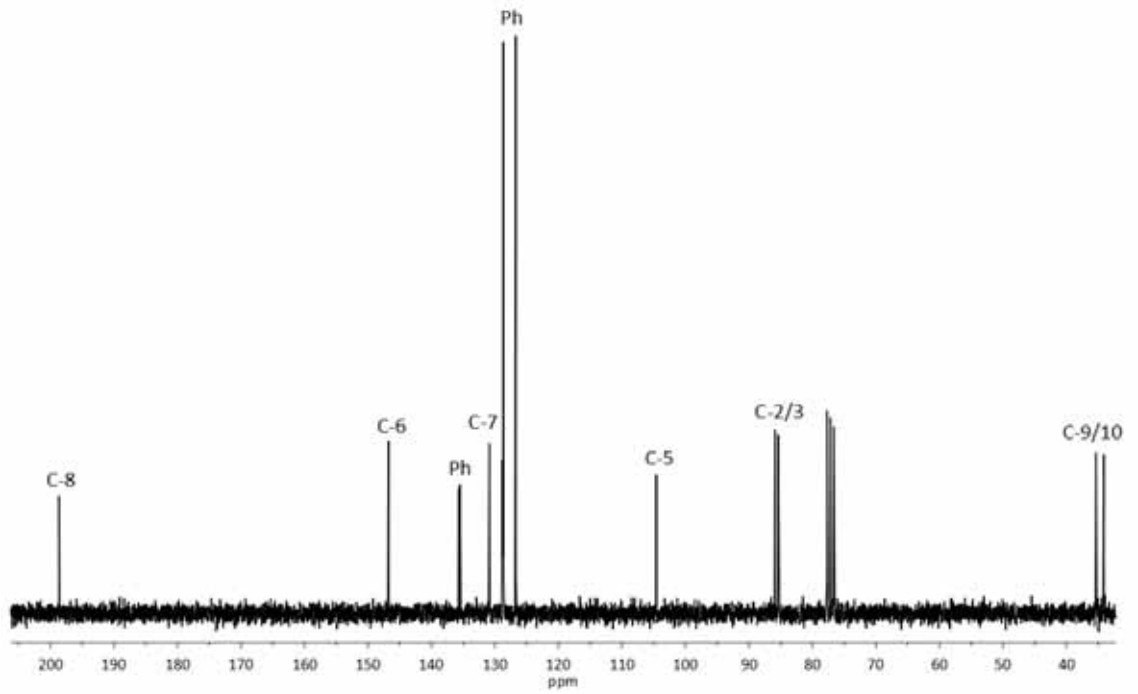
^{1}H-NMR (360 MHz, $CDCl_3$)



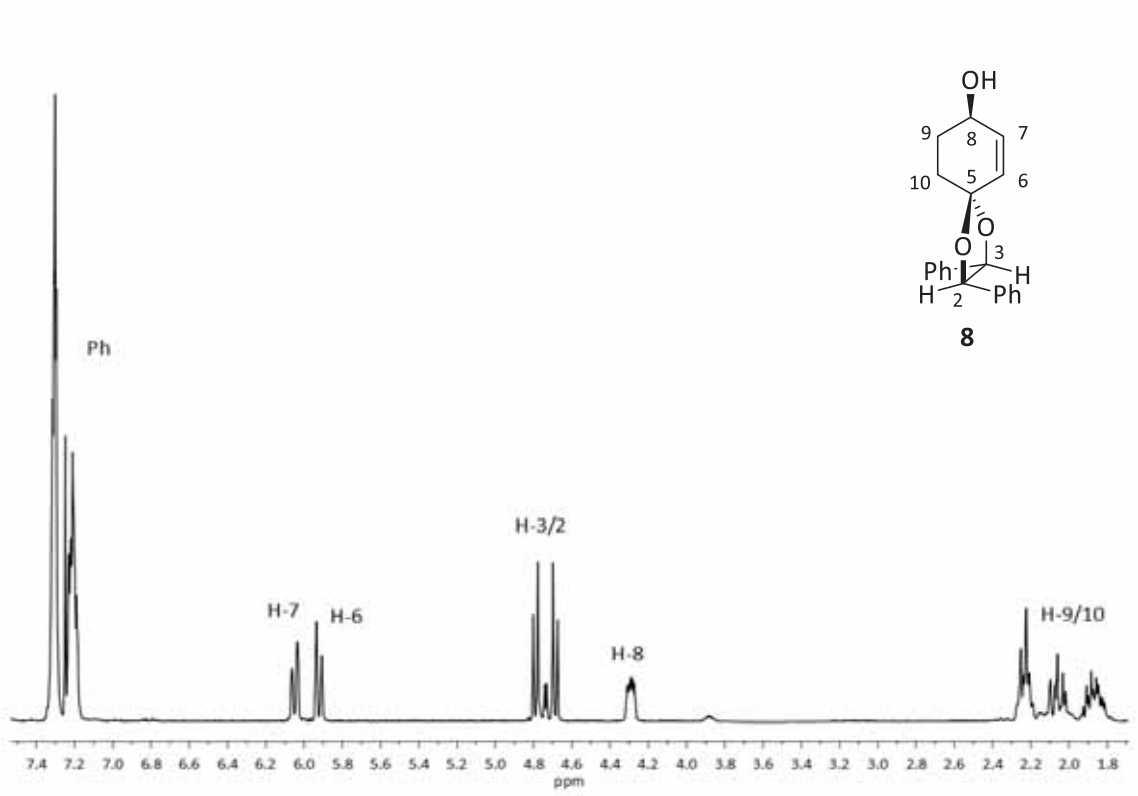
^{13}C-NMR (100 MHz, $CDCl_3$)



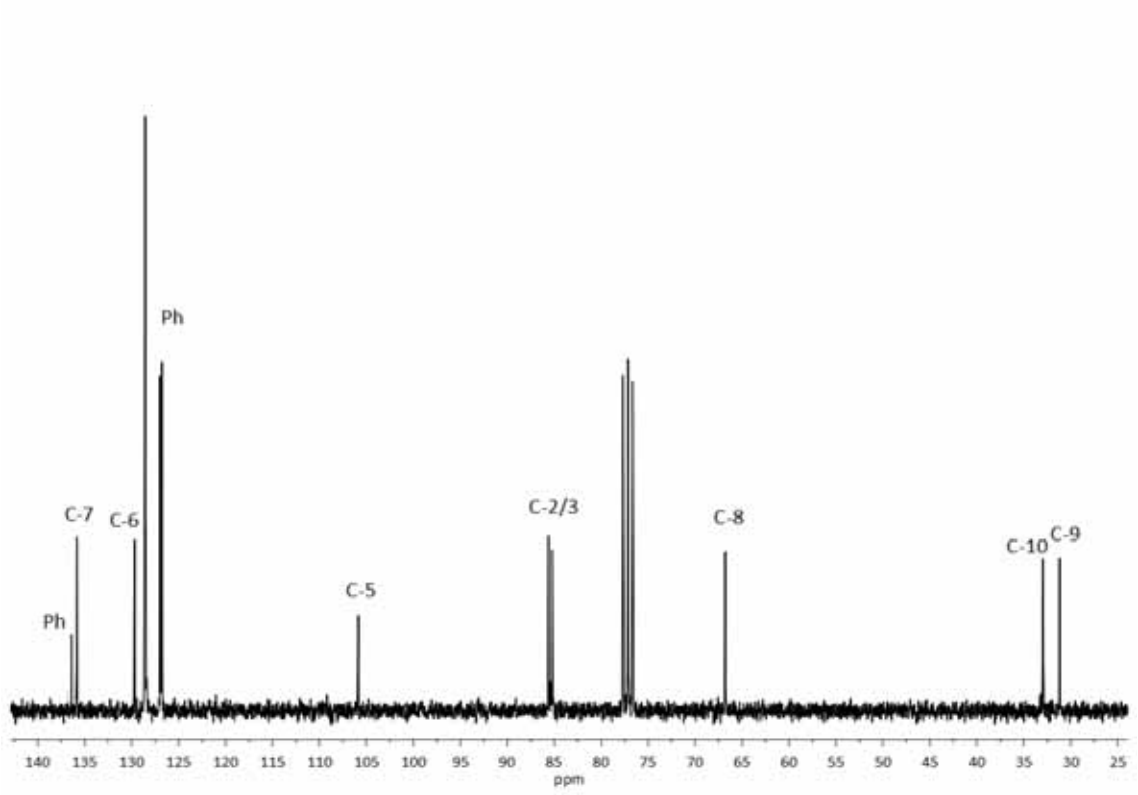
^{1}H-NMR (250 MHz, $CDCl_3$)



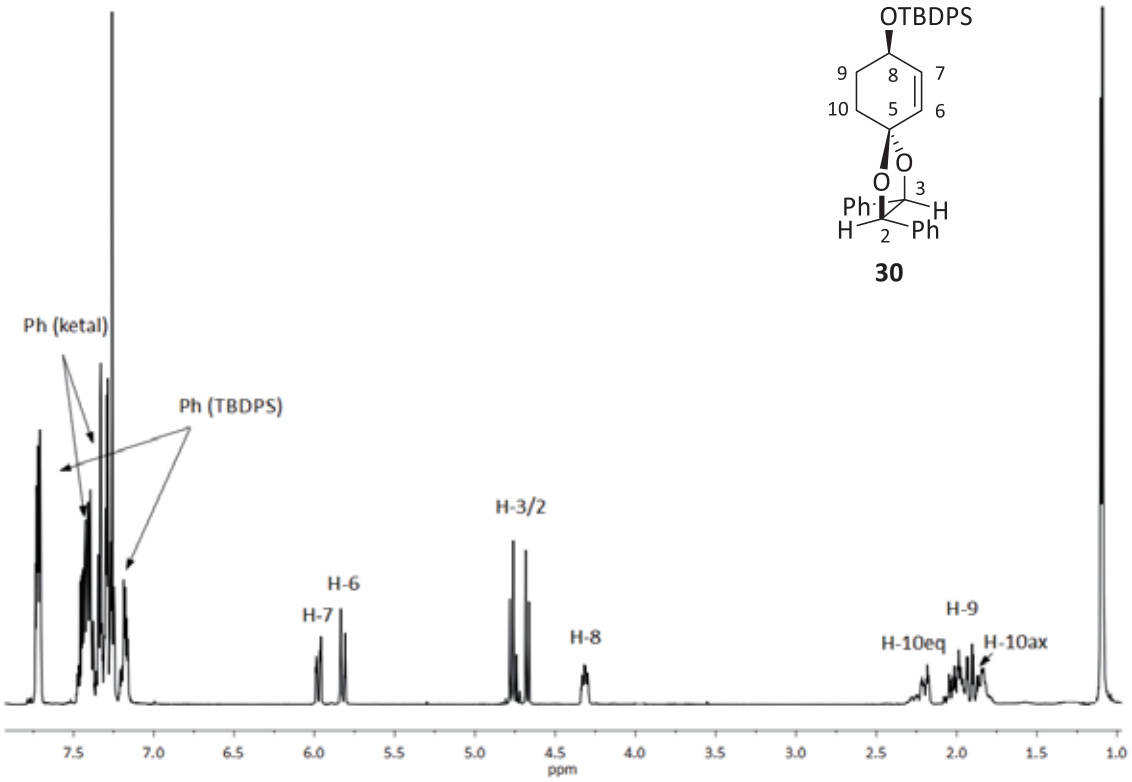
^{13}C-NMR (63 MHz, $CDCl_3$)



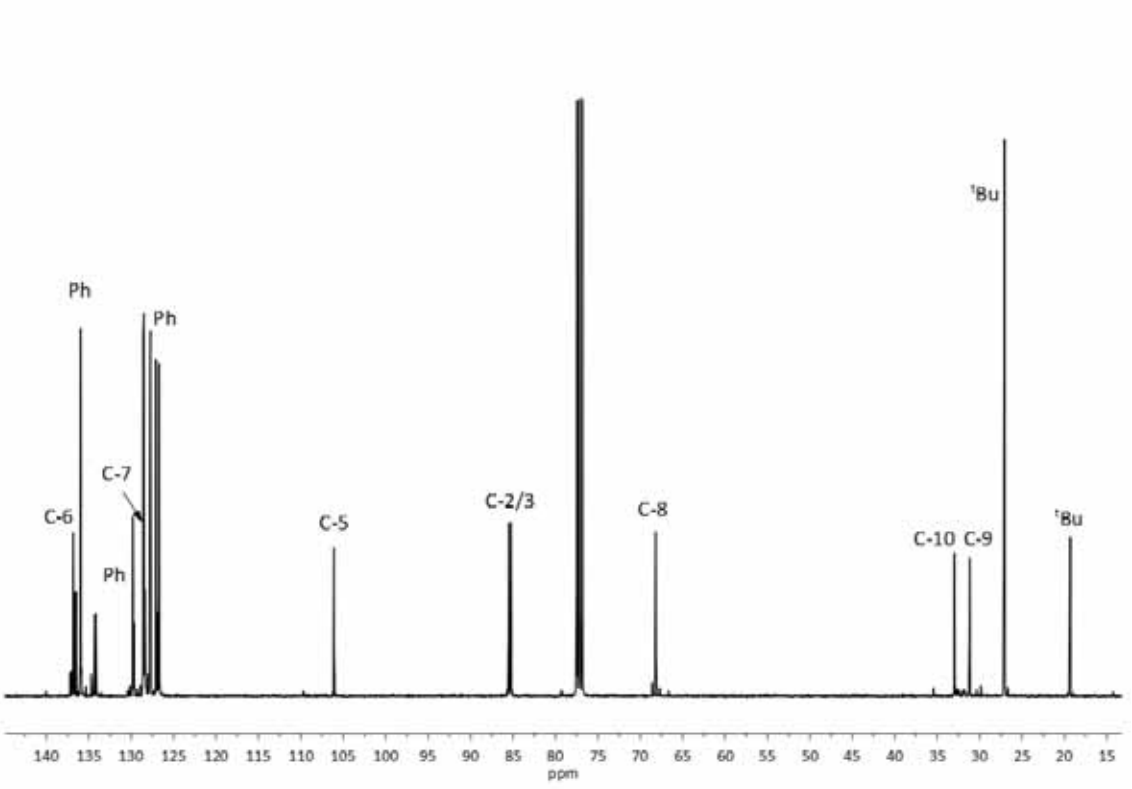
^{1}H-NMR (400 MHz, $CDCl_3$)



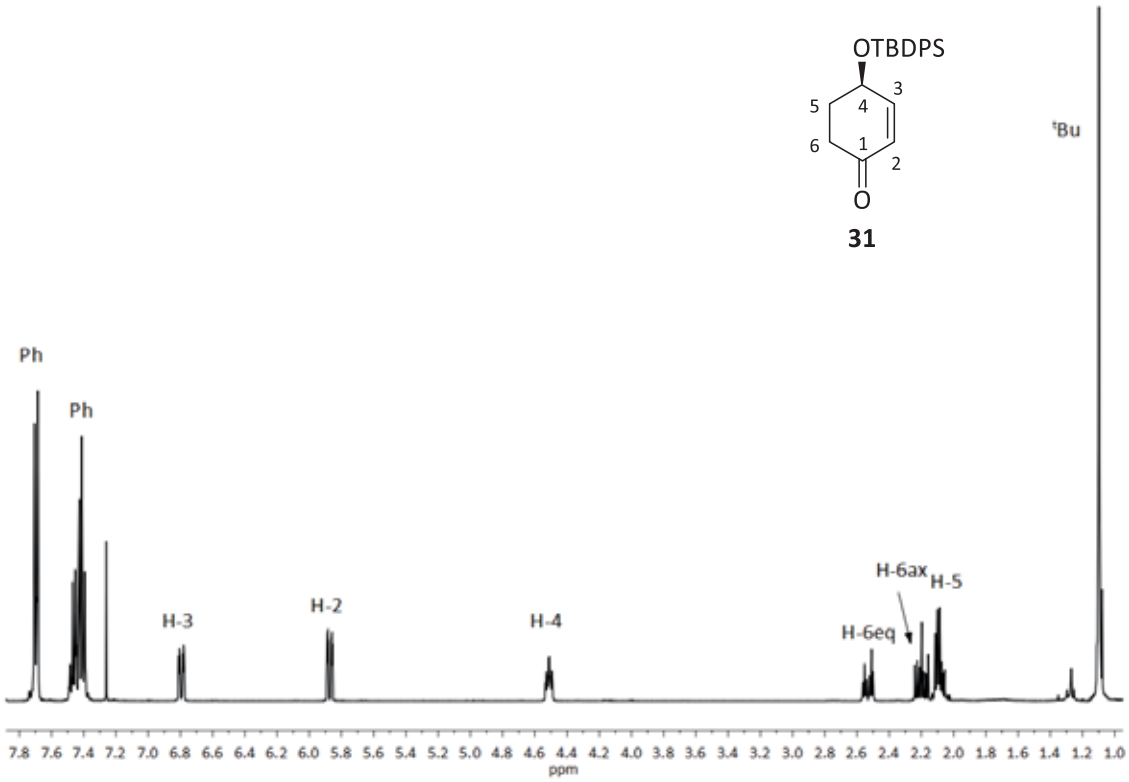
^{13}C-NMR (100 MHz, $CDCl_3$)



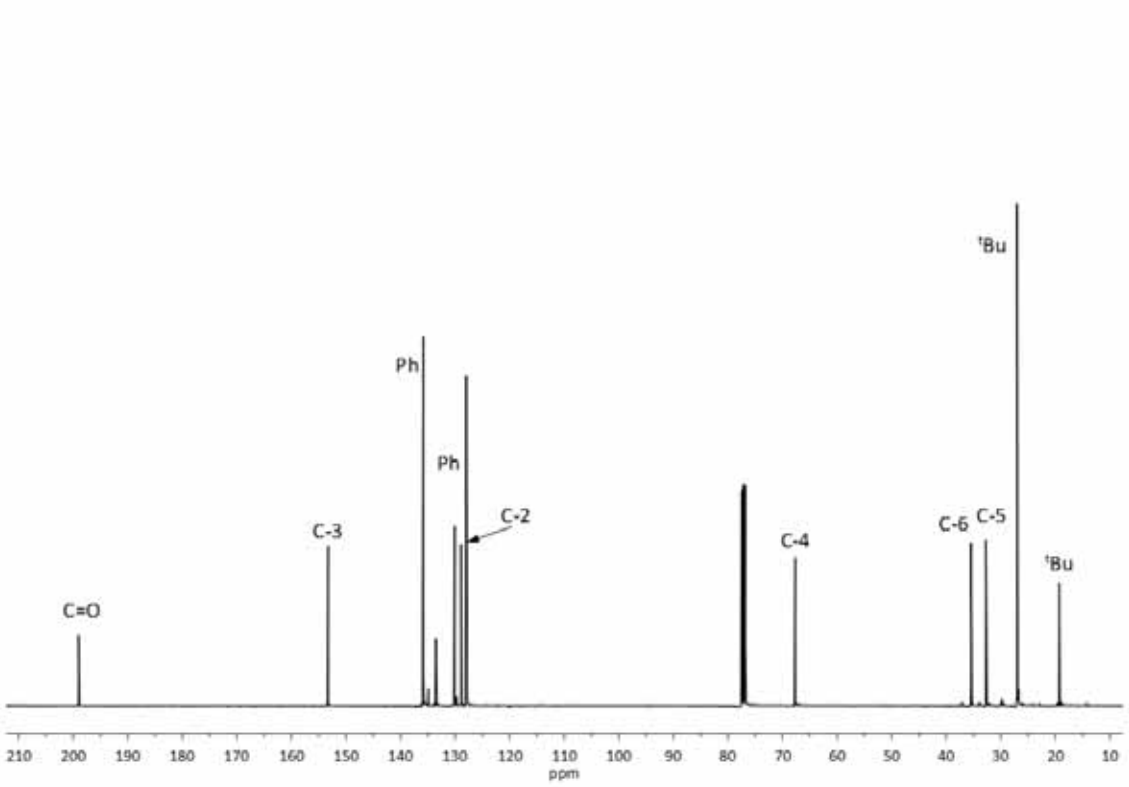
^{1}H-NMR (400 MHz, $CDCl_3$)



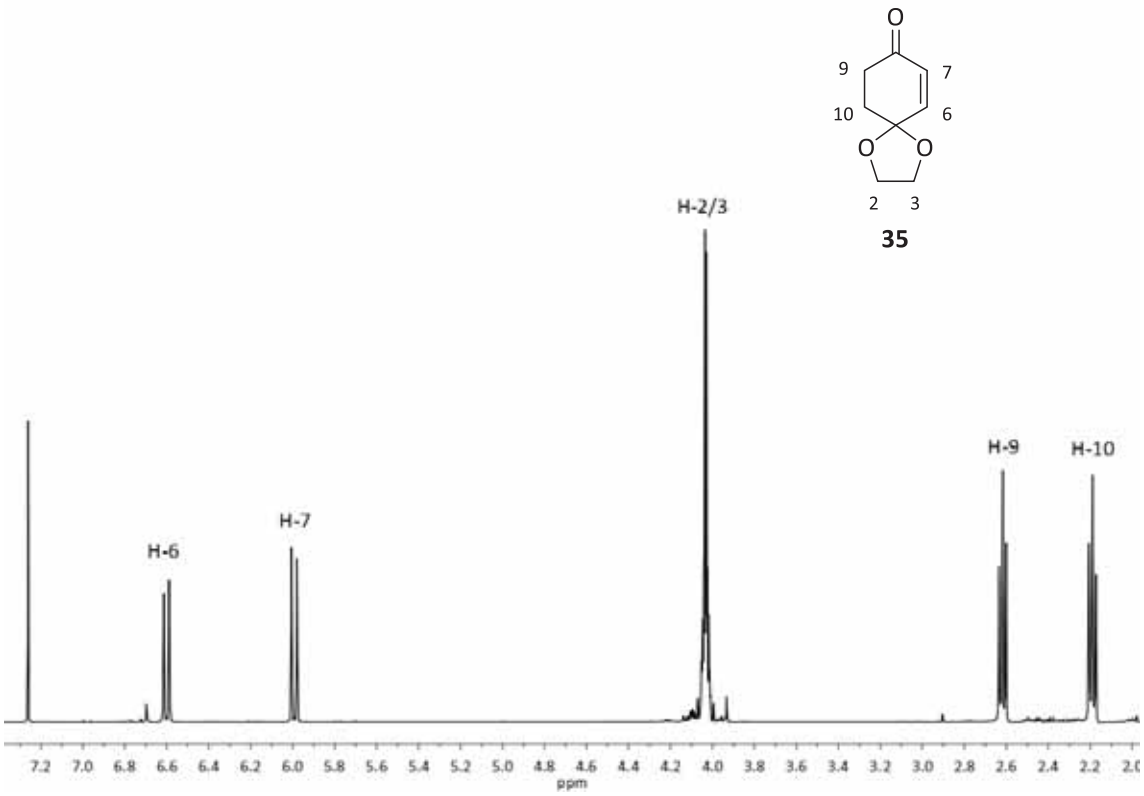
^{13}C-NMR (100 MHz, $CDCl_3$)



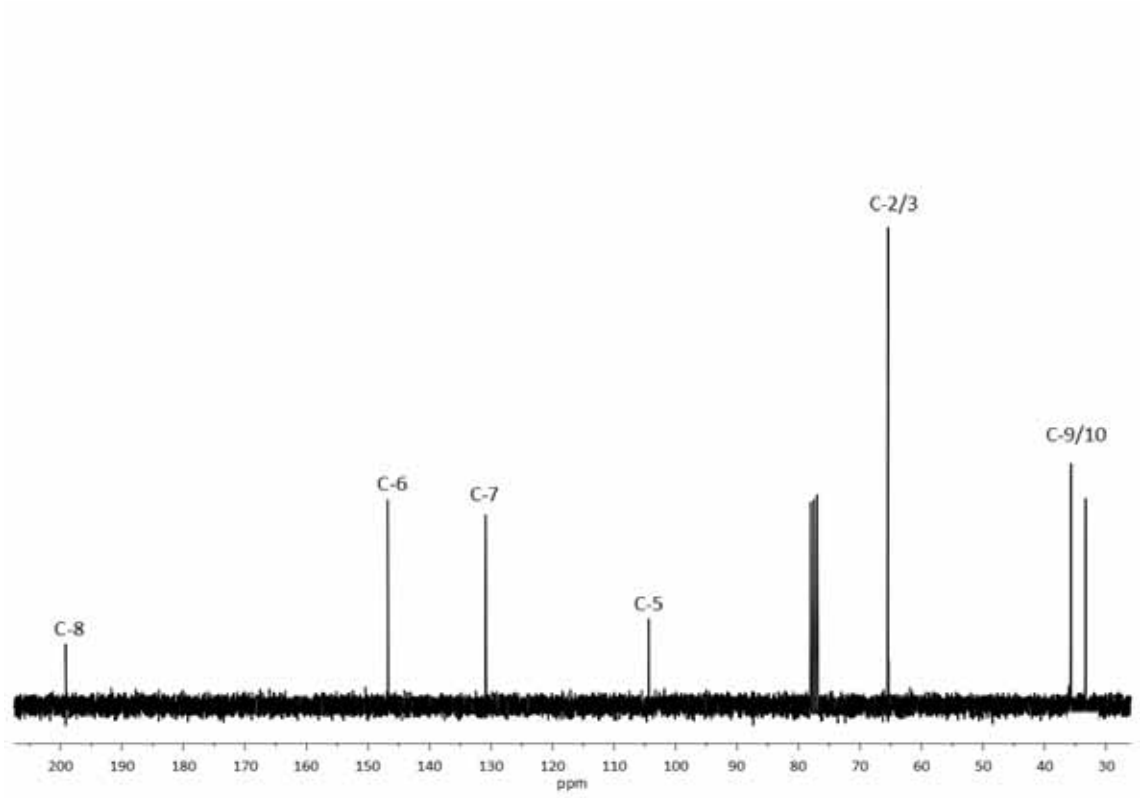
^{1}H-NMR (400 MHz, $CDCl_3$)



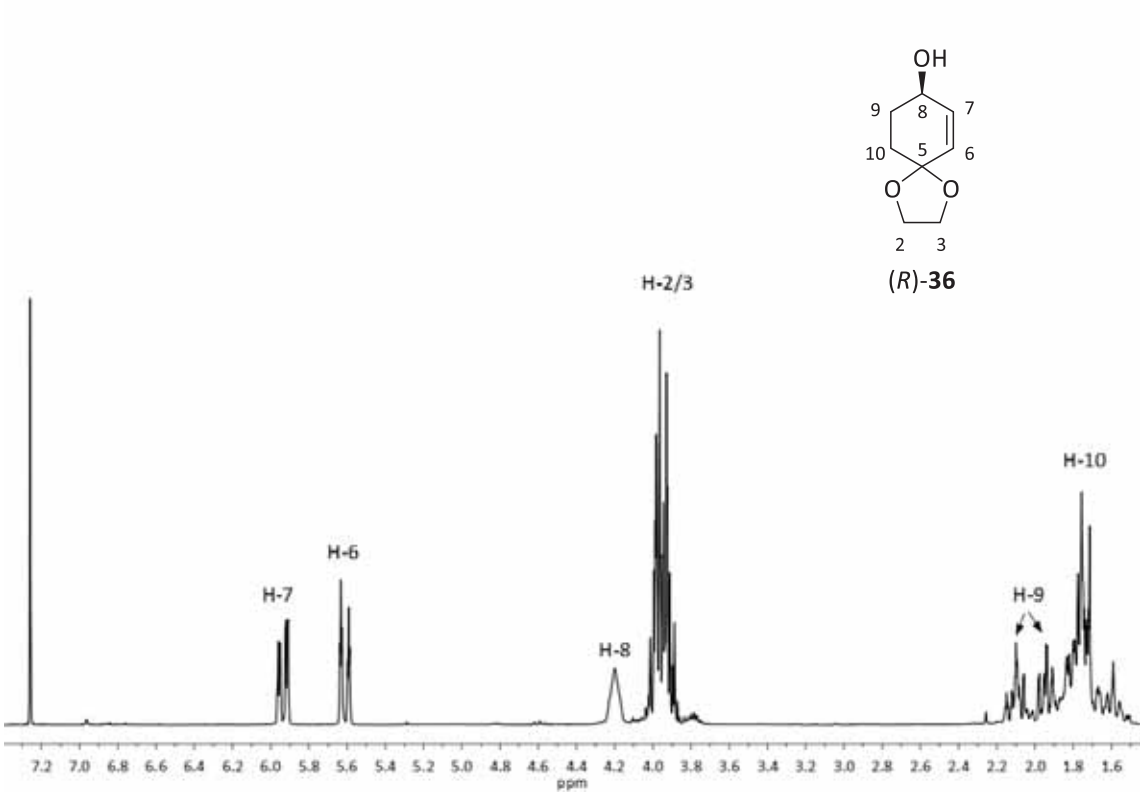
^{13}C-NMR (100 MHz, $CDCl_3$)



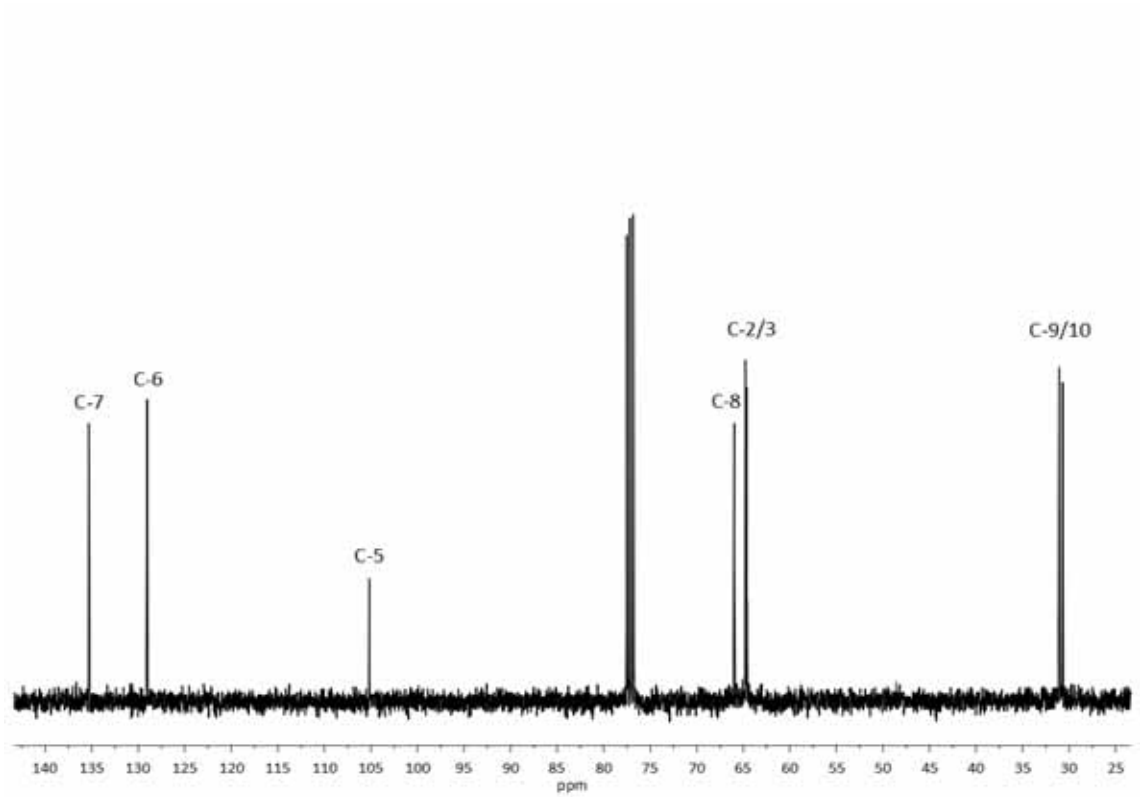
^{1}H-NMR (250 MHz, $CDCl_3$)



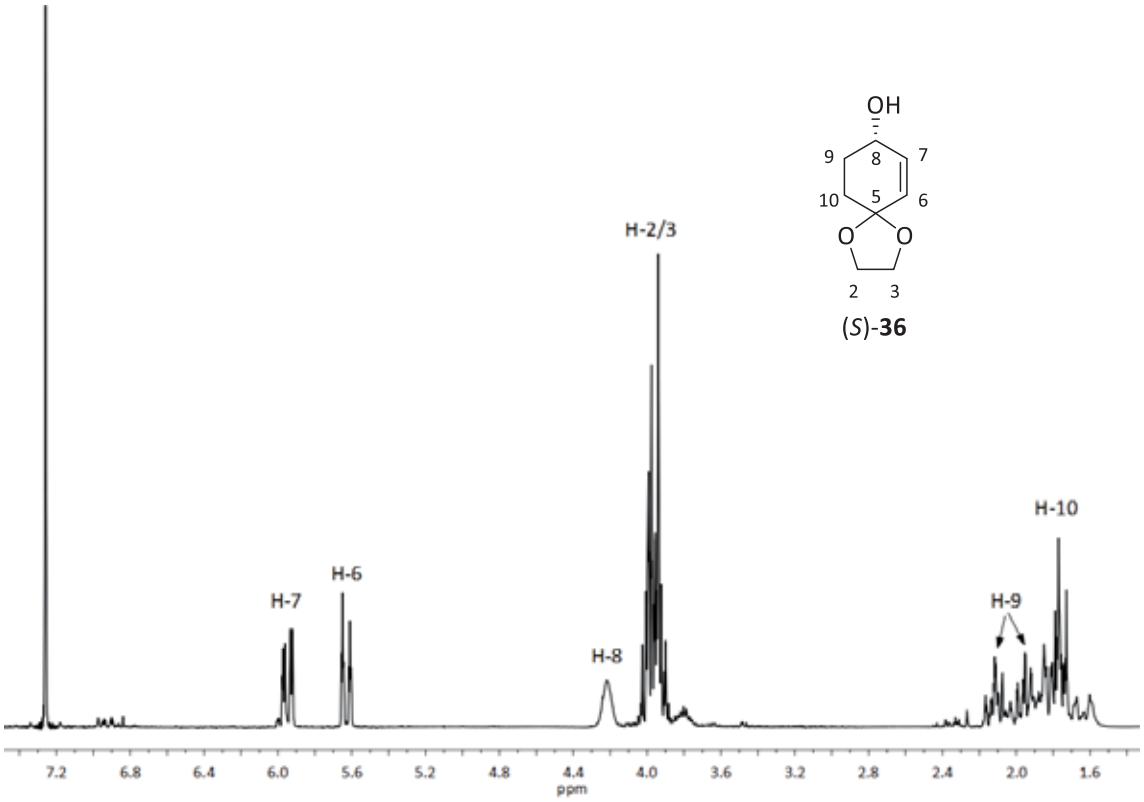
^{13}C-NMR (90 MHz, $CDCl_3$)



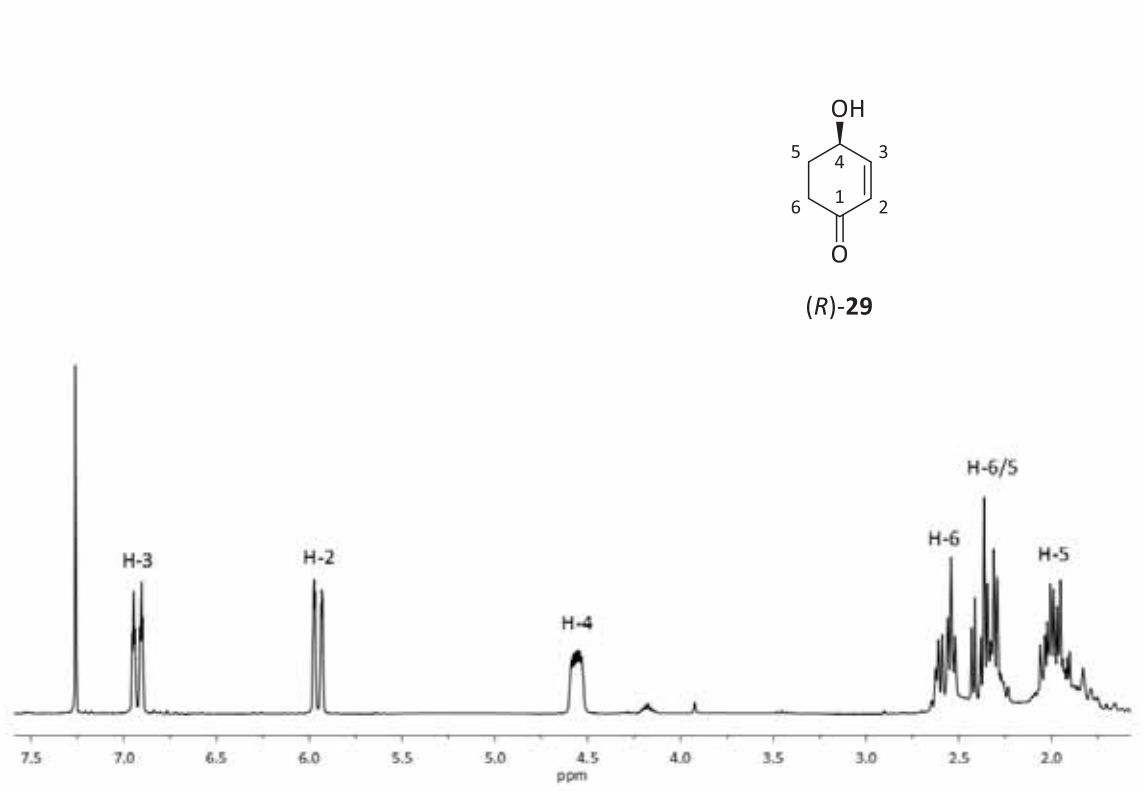
^{1}H-NMR (250 MHz, $CDCl_3$)



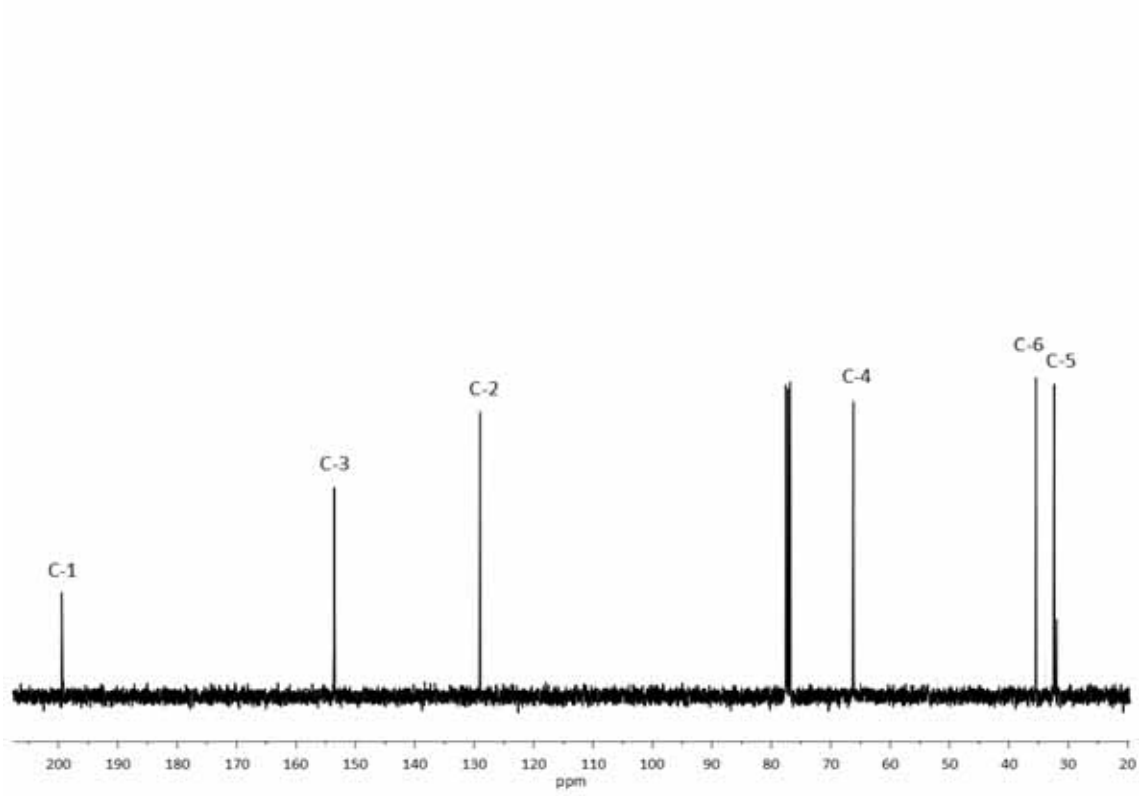
^{13}C-NMR (90 MHz, $CDCl_3$)



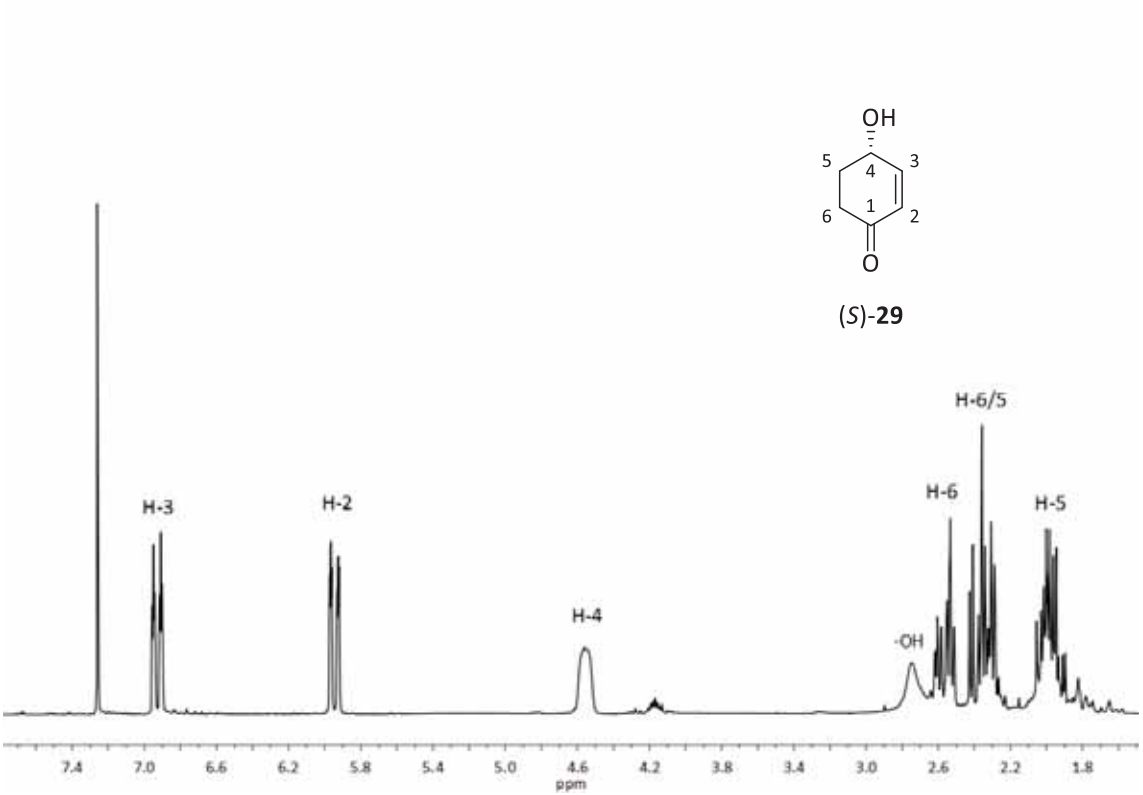
^{1}H-NMR (250 MHz, $CDCl_3$)



^{1}H-NMR (250 MHz, $CDCl_3$)

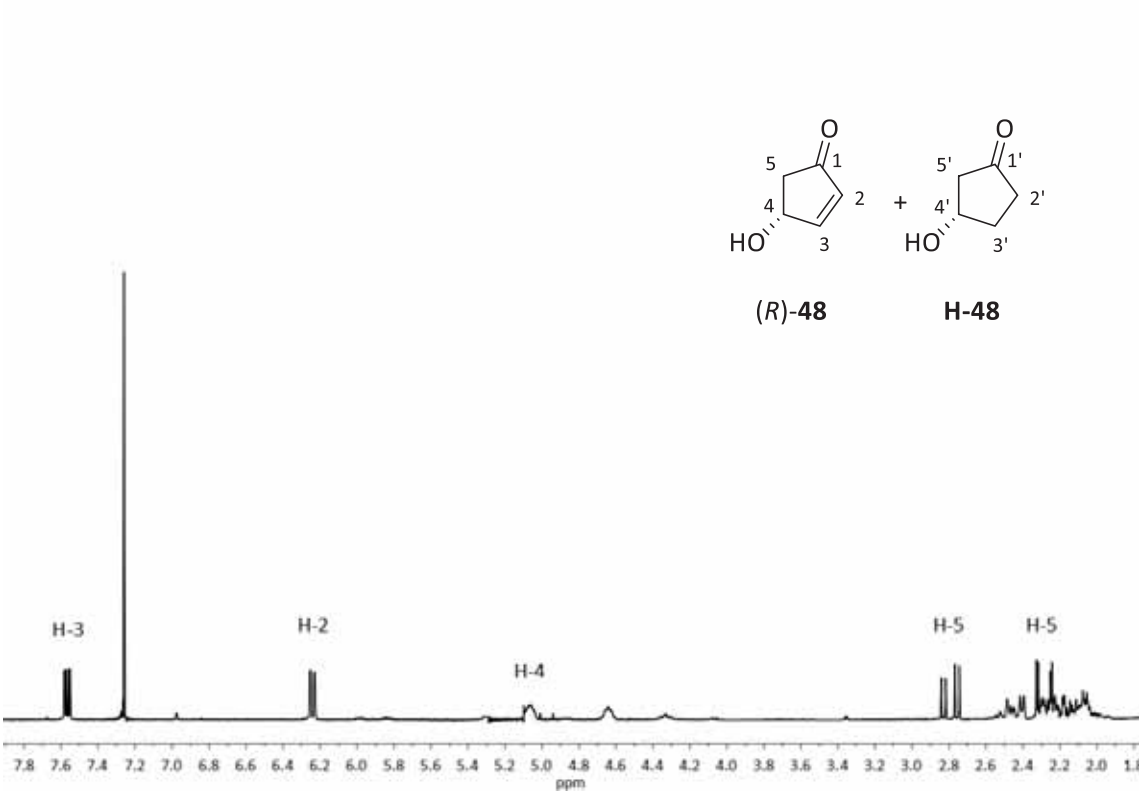


^{13}C-NMR (90 MHz, $CDCl_3$)

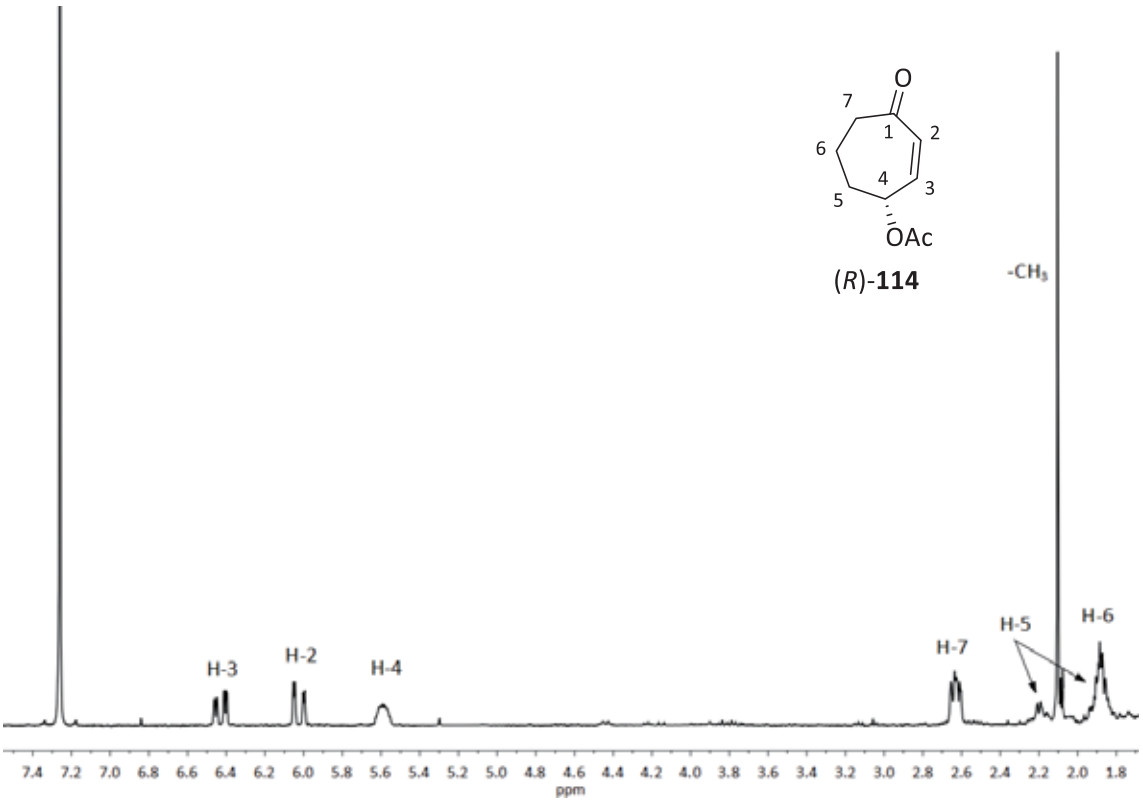


(*S*)-**29**

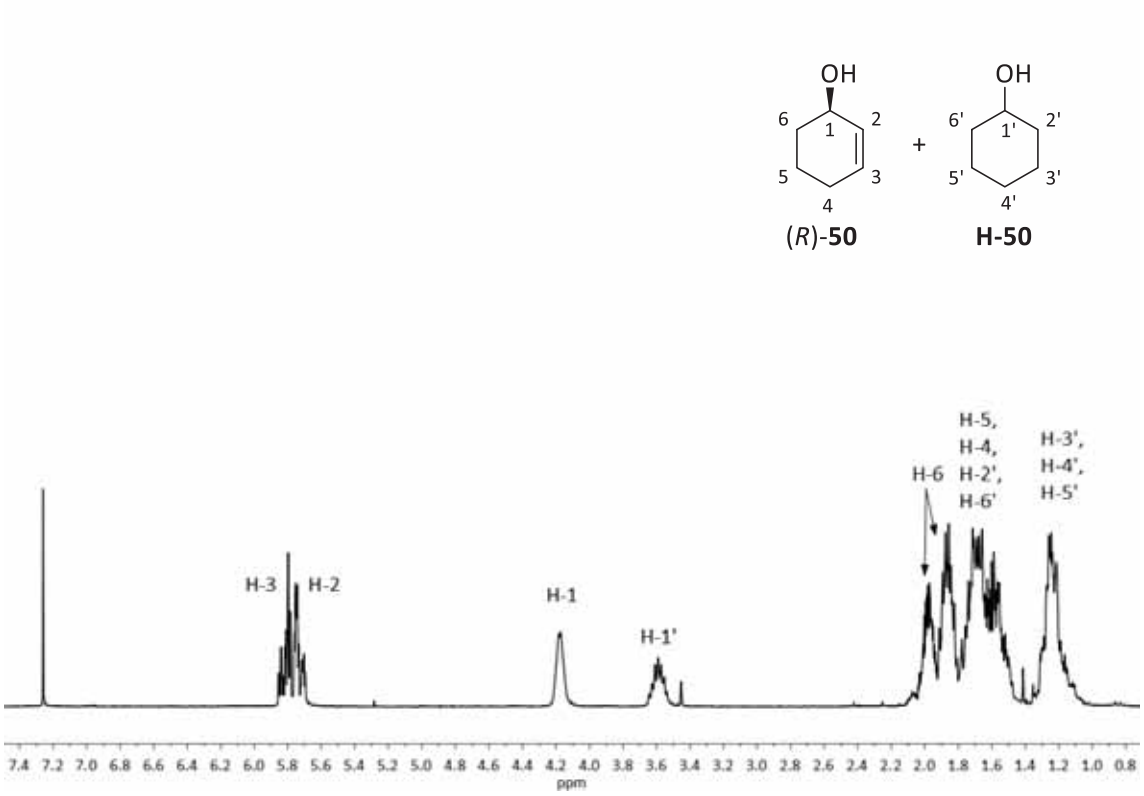
^{1}H-NMR (250 MHz, $CDCl_3$)



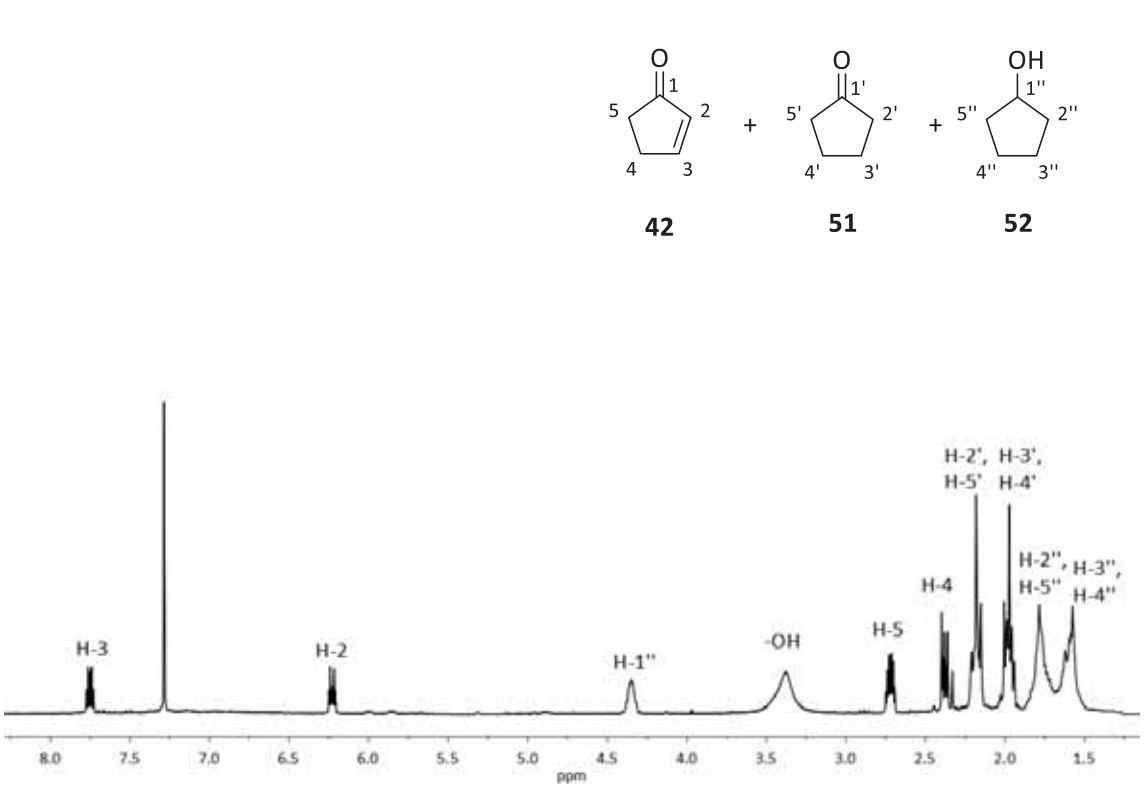
^{1}H-NMR (250 MHz, $CDCl_3$)



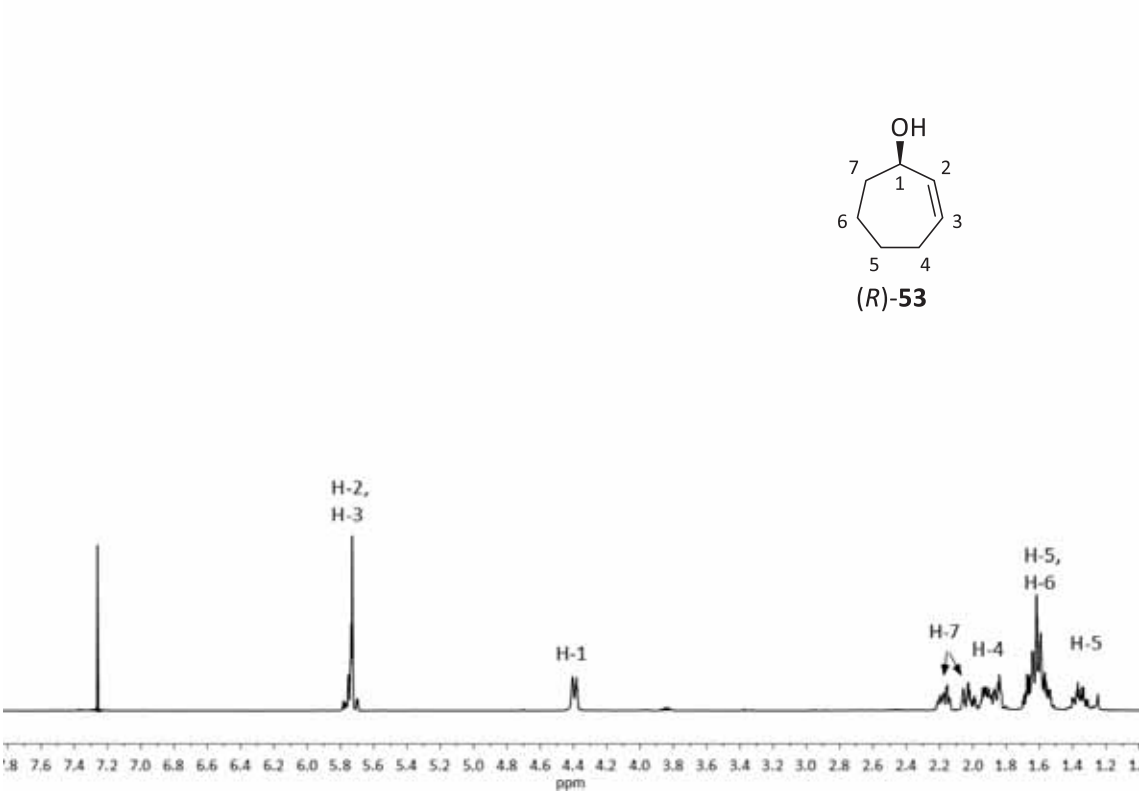
^{1}H-NMR (250 MHz, $CDCl_3$)



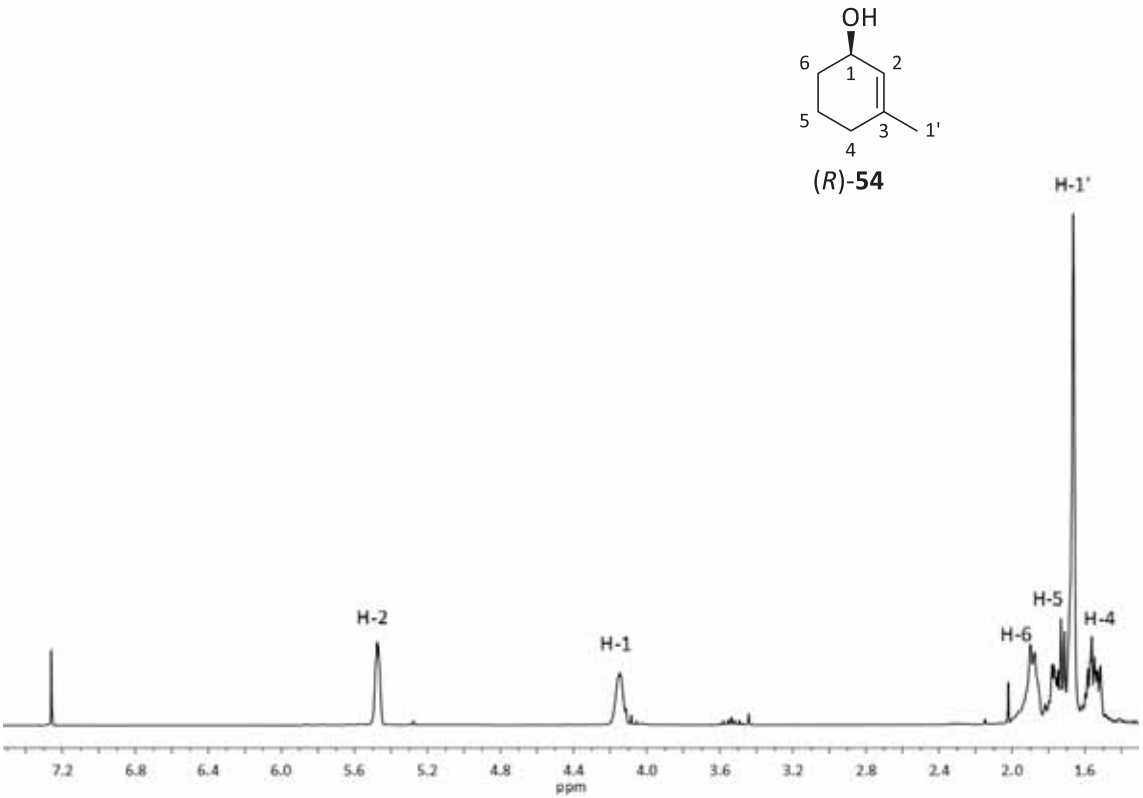
^{1}H-NMR (400 MHz, $CDCl_3$)



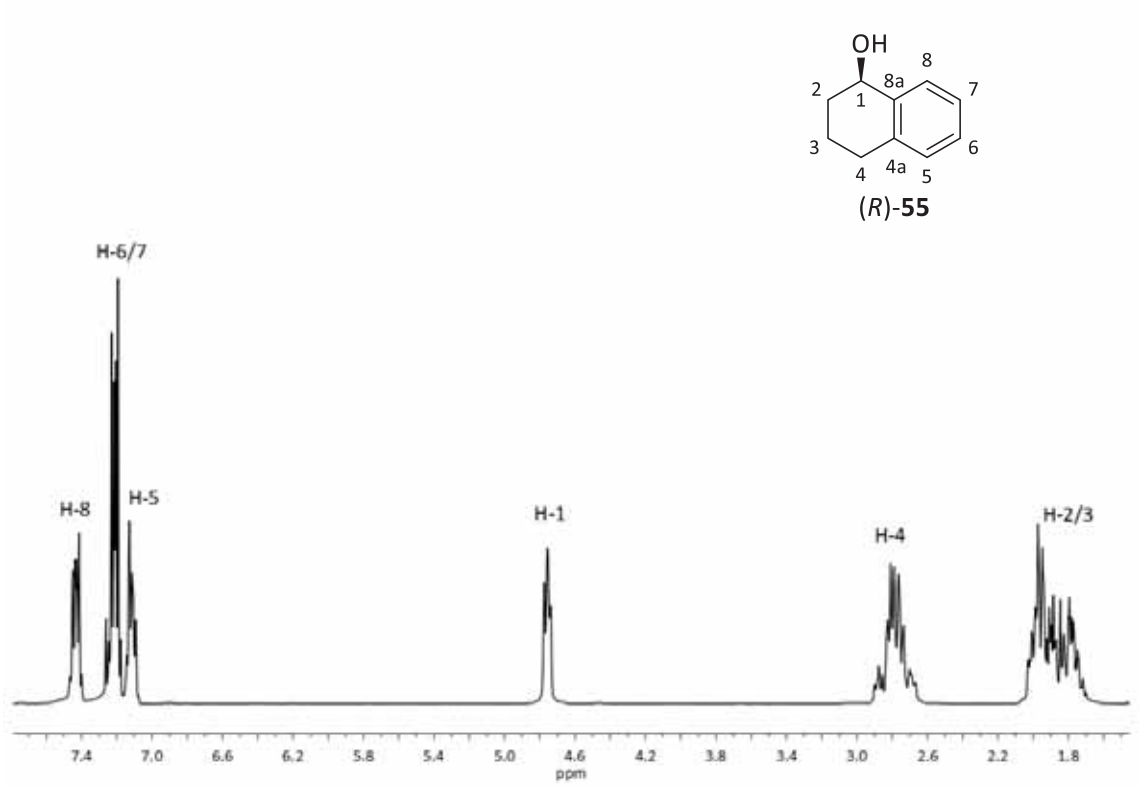
^{1}H-NMR (250 MHz, $CDCl_3$)



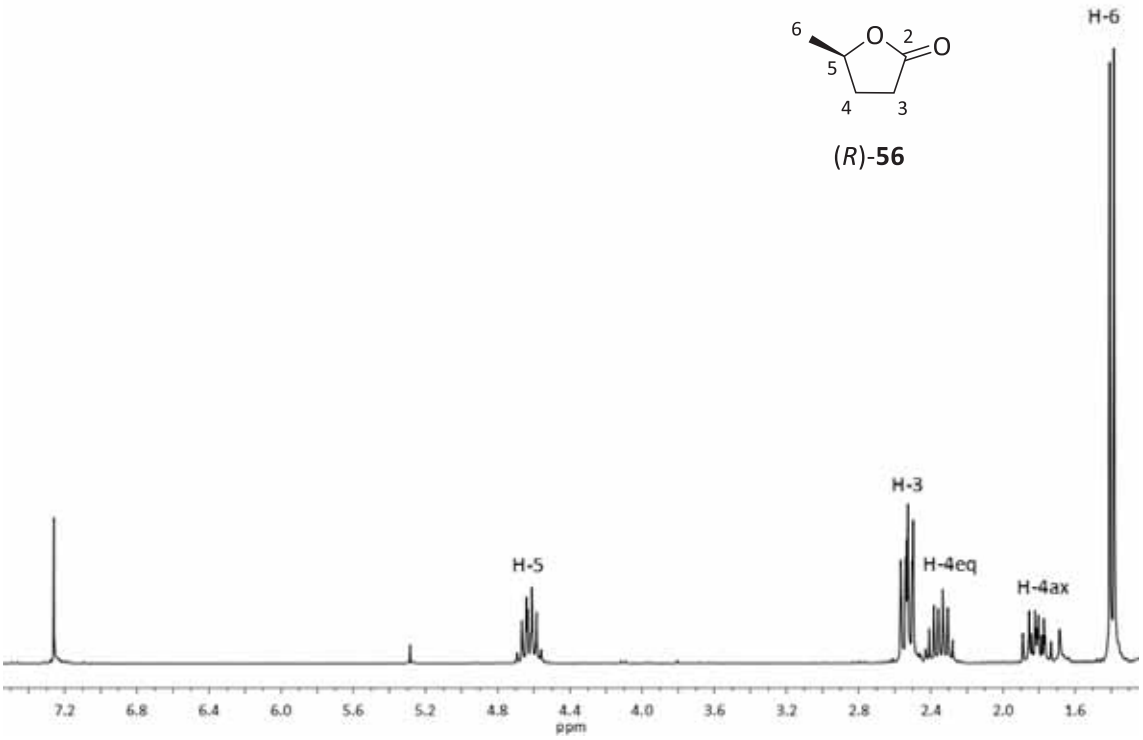
^{1}H-NMR (400 MHz, $CDCl_3$)



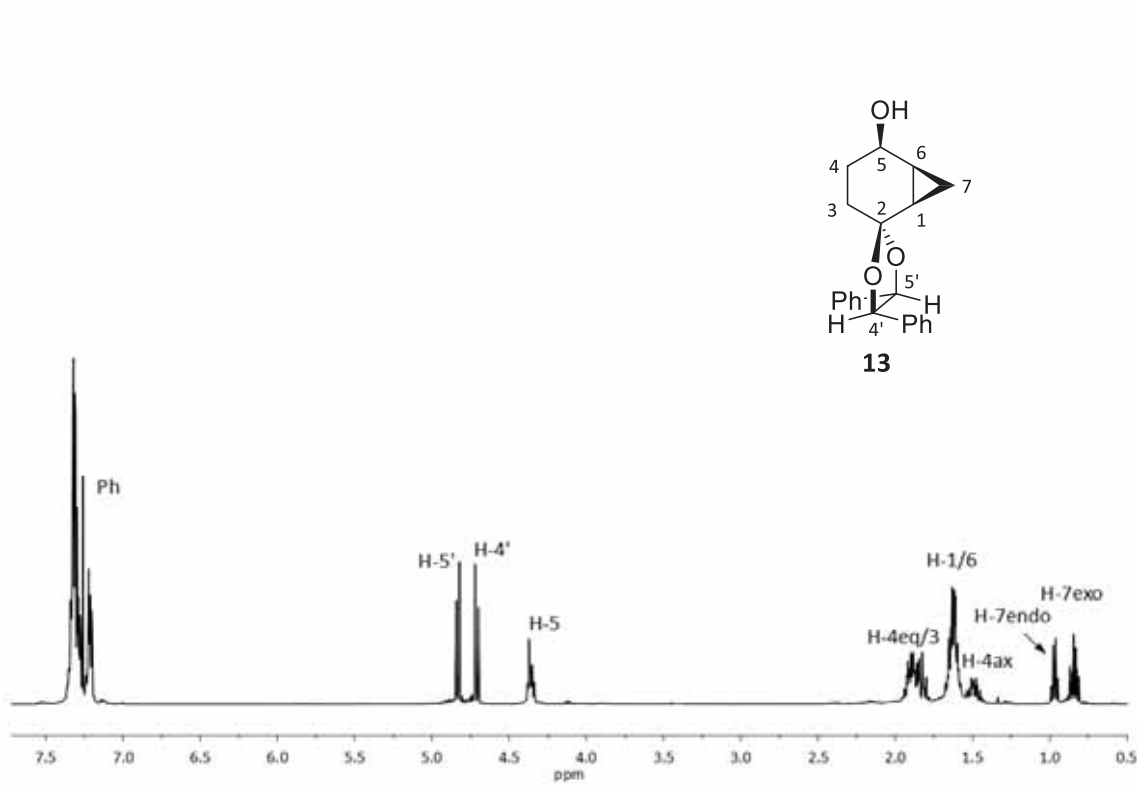
^{1}H-NMR (250 MHz, $CDCl_3$)



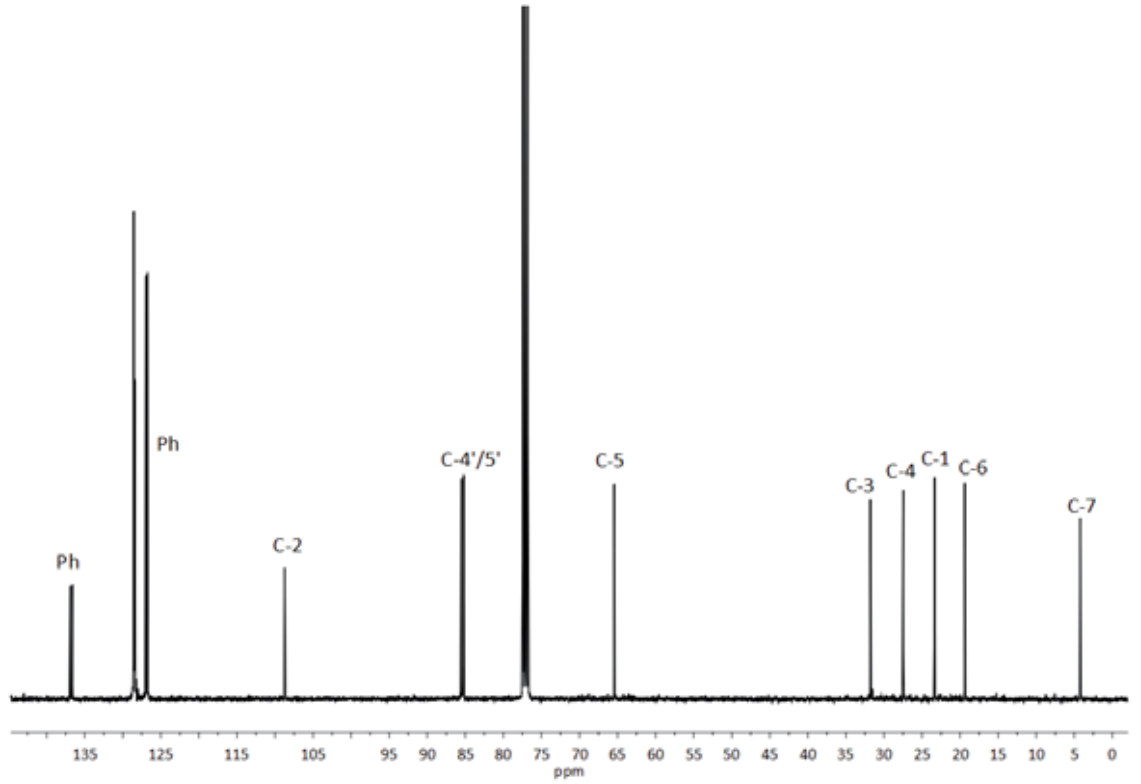
^{1}H-NMR (250 MHz, $CDCl_3$)



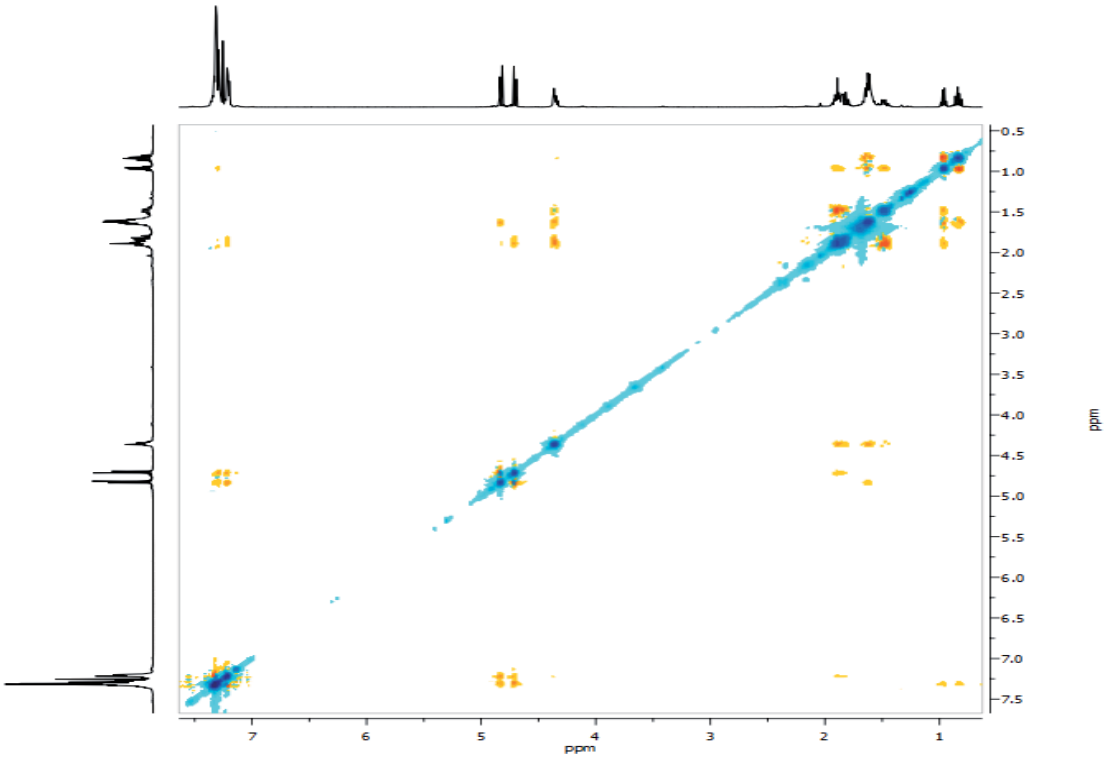
^{1}H-NMR (250 MHz, $CDCl_3$)



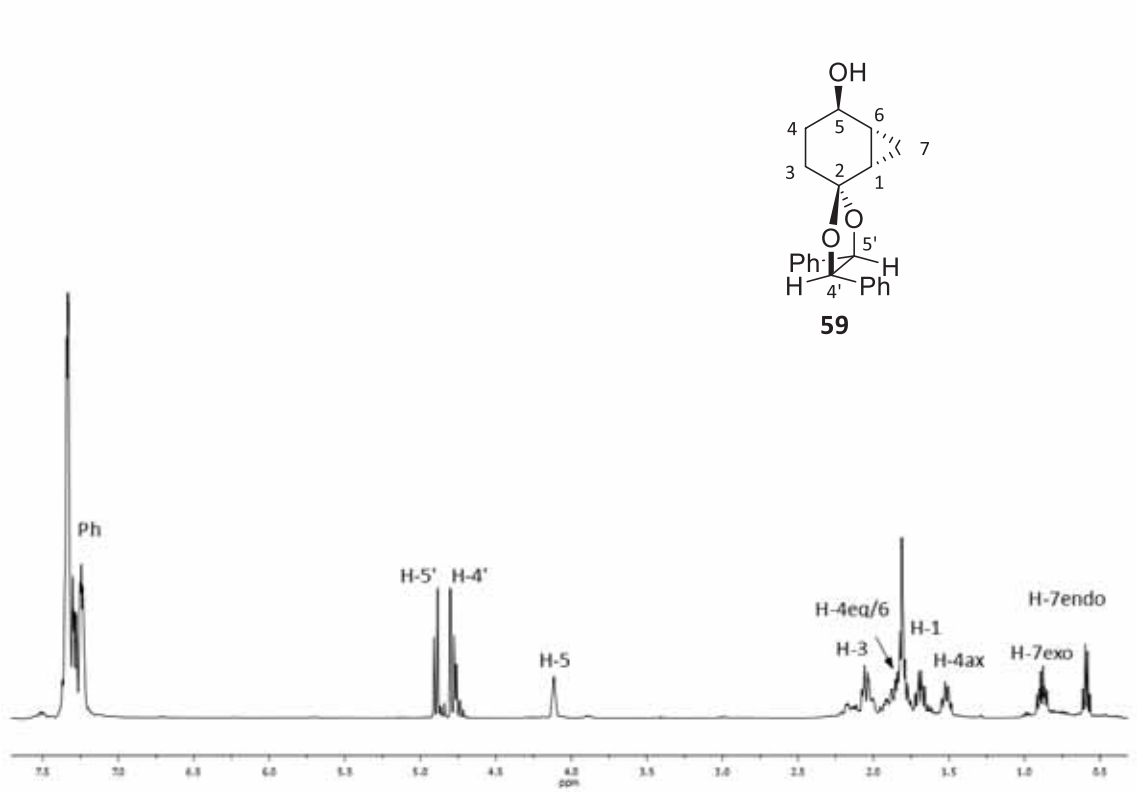
^{1}H-NMR (400 MHz, $CDCl_3$)



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

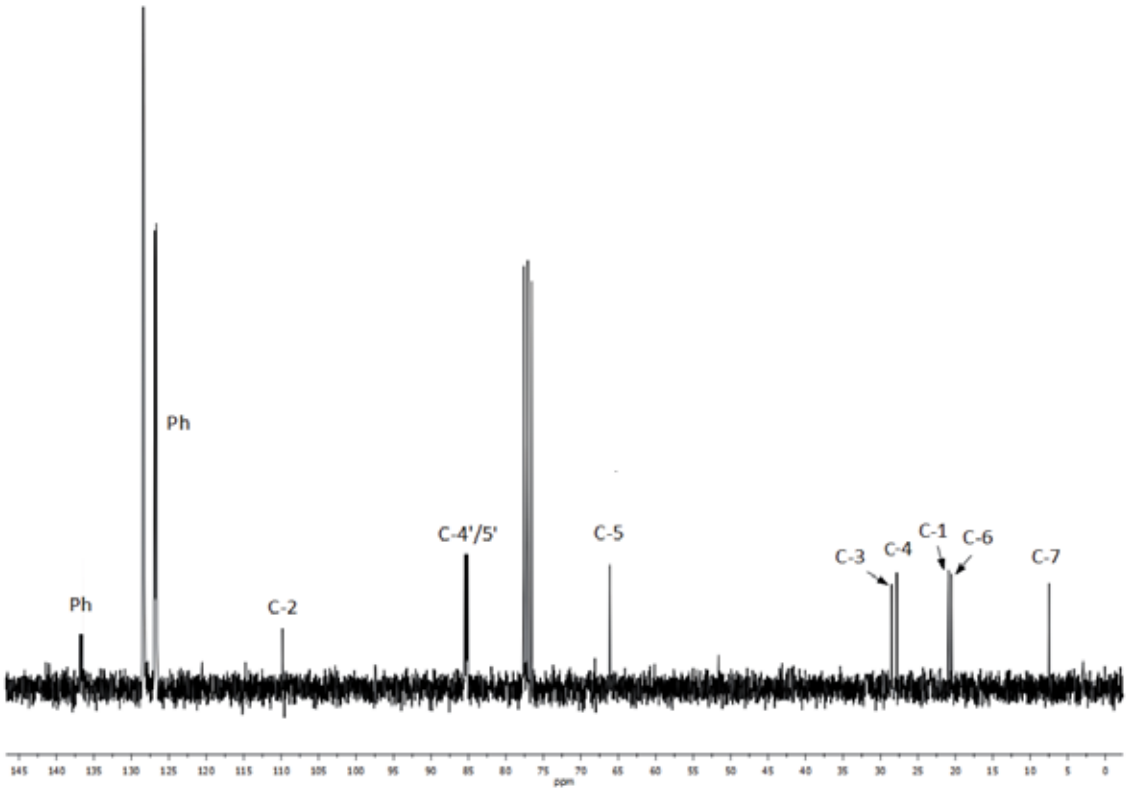


NOESY (400 MHz, $CDCl_3$)

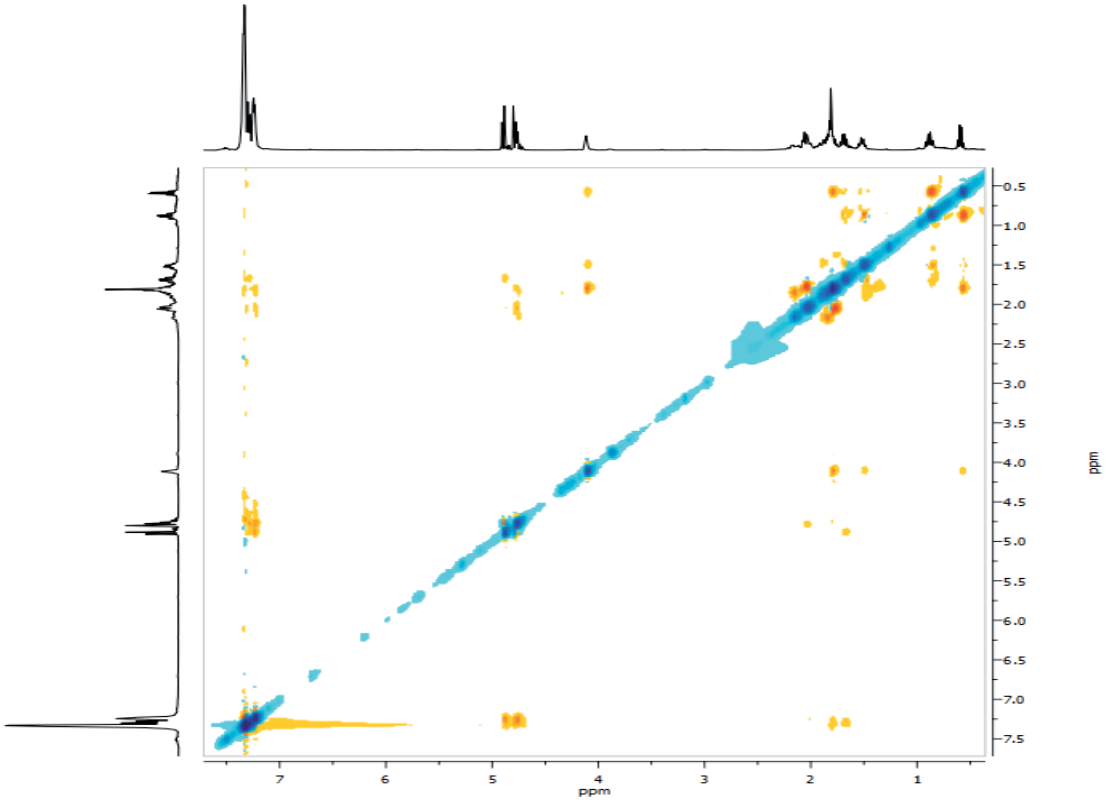


59

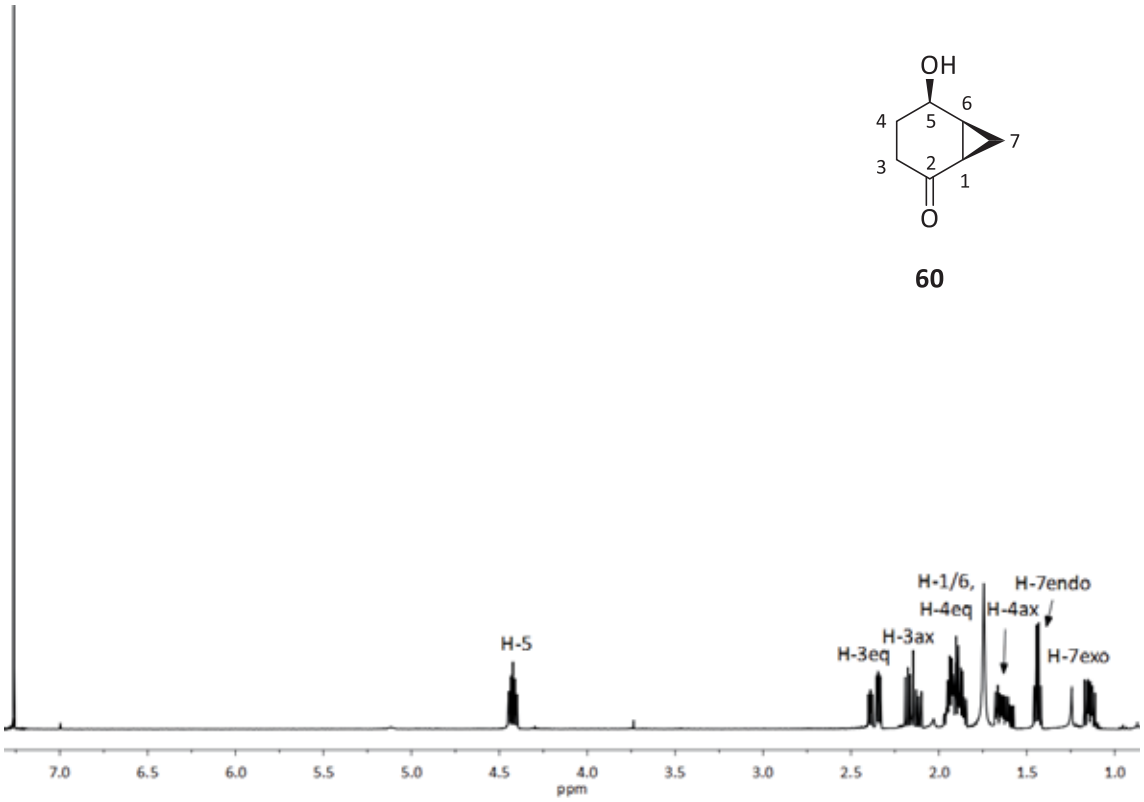
^{1}H-NMR (360 MHz, $CDCl_3$)



^{13}C-NMR (90 MHz, $CDCl_3$)

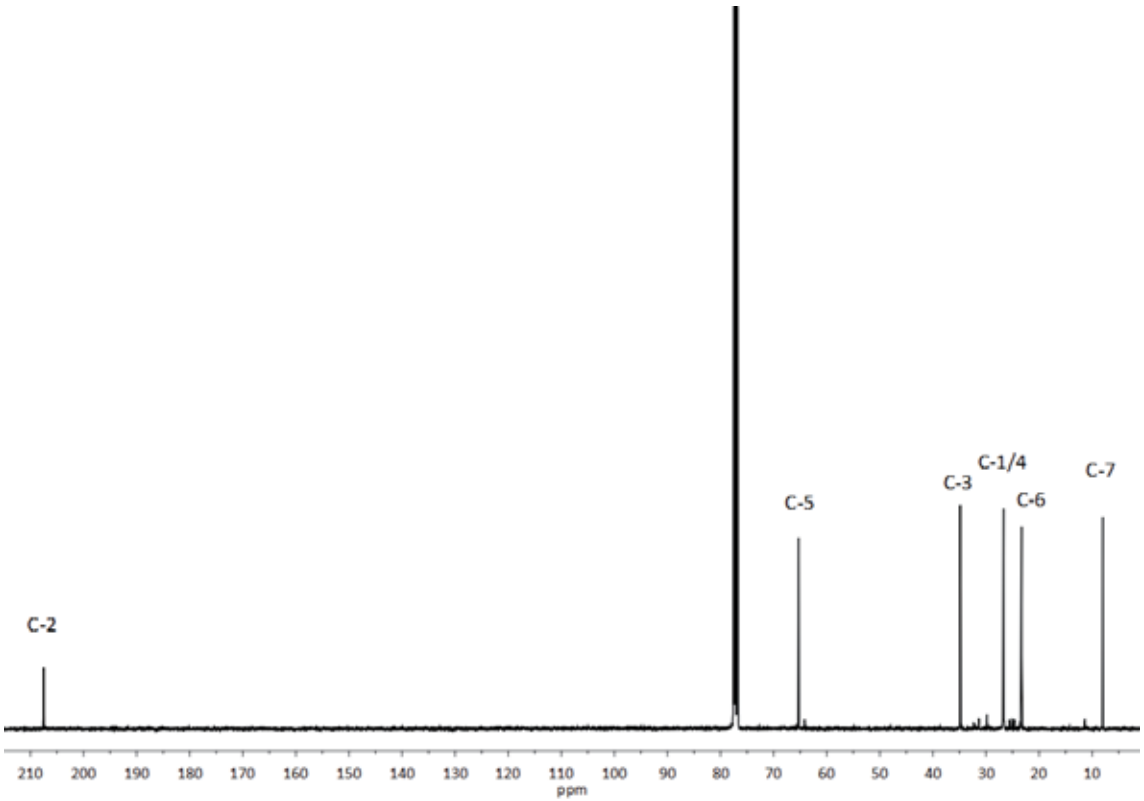


NOESY (360 MHz, $CDCl_3$)

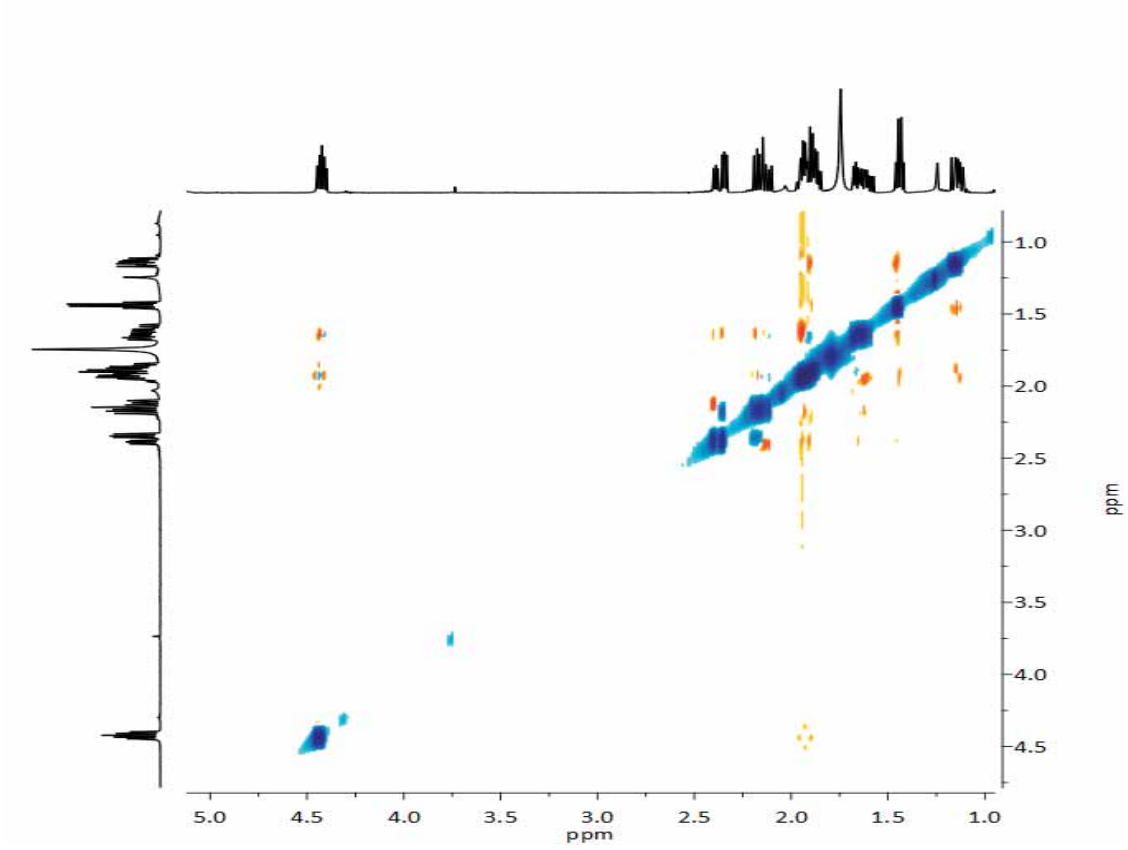


60

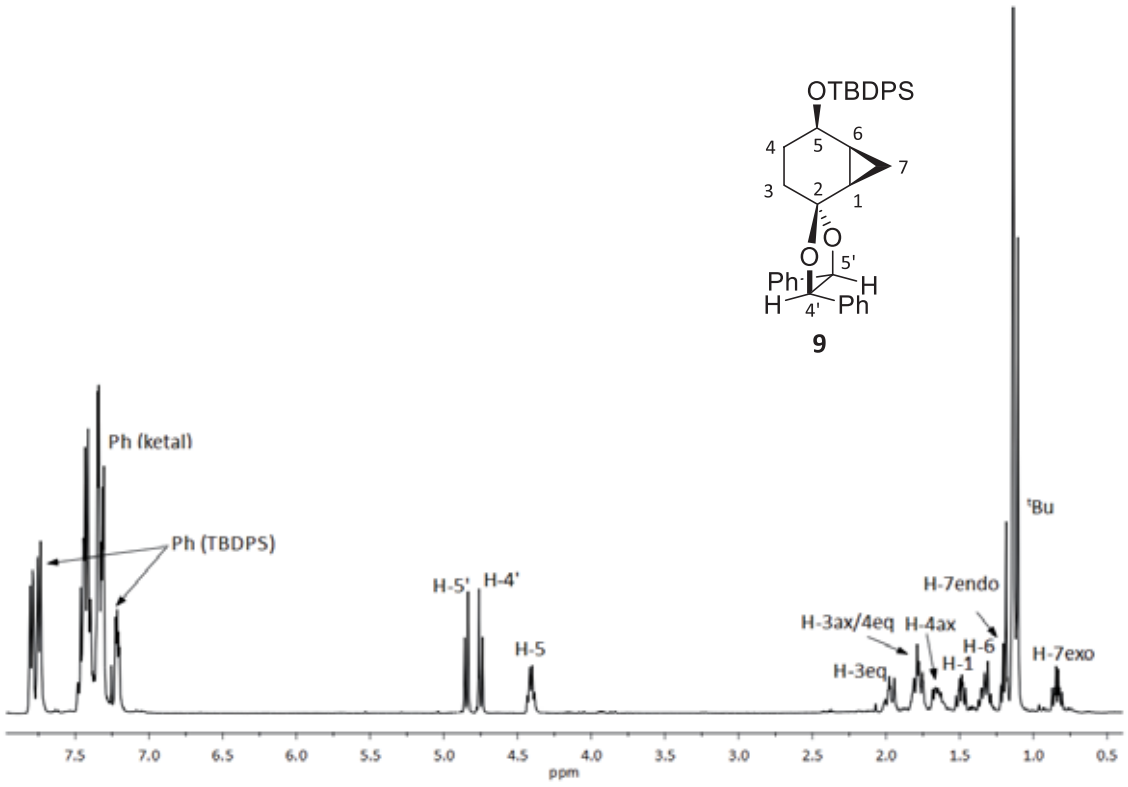
^{1}H-NMR (400 MHz, $CDCl_3$)



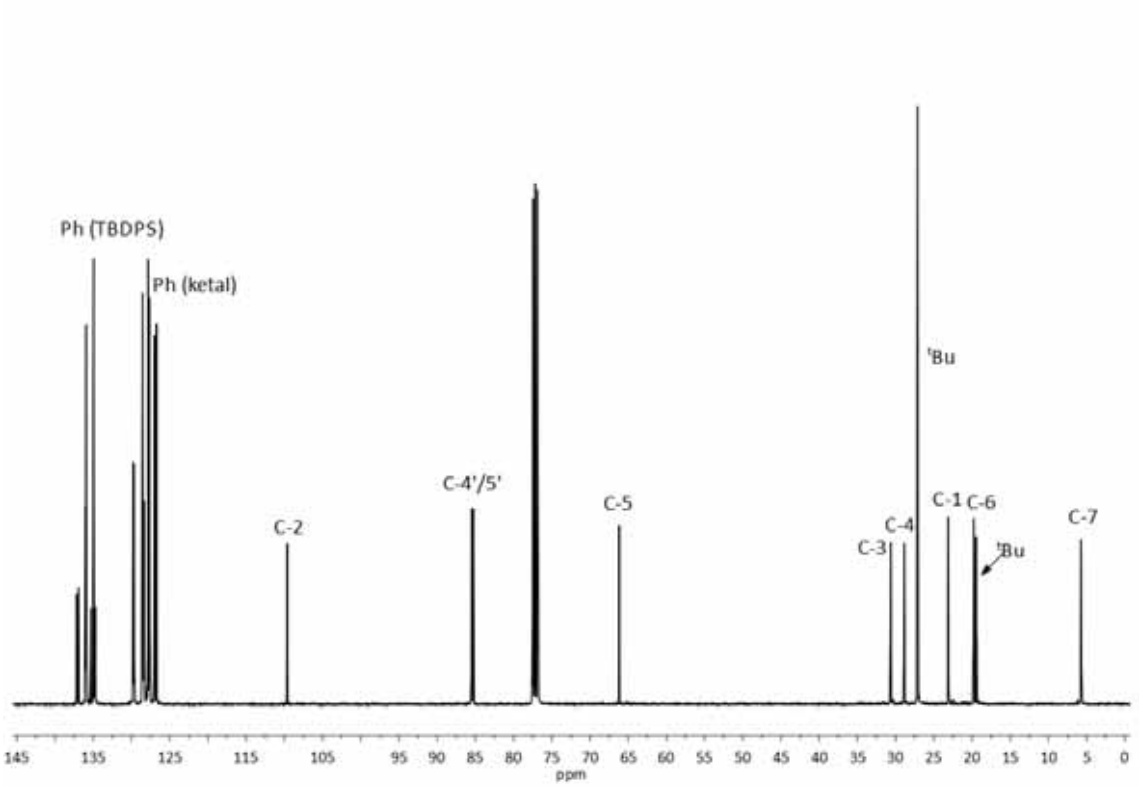
^{13}C-NMR (100 MHz, $CDCl_3$)



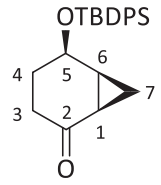
NOESY (400 MHz, $CDCl_3$)



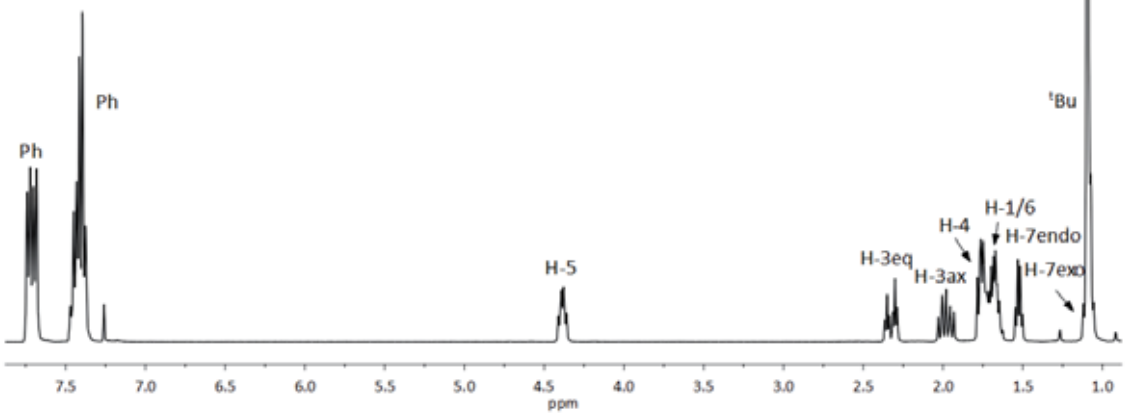
^{1}H-NMR (400 MHz, $CDCl_3$)



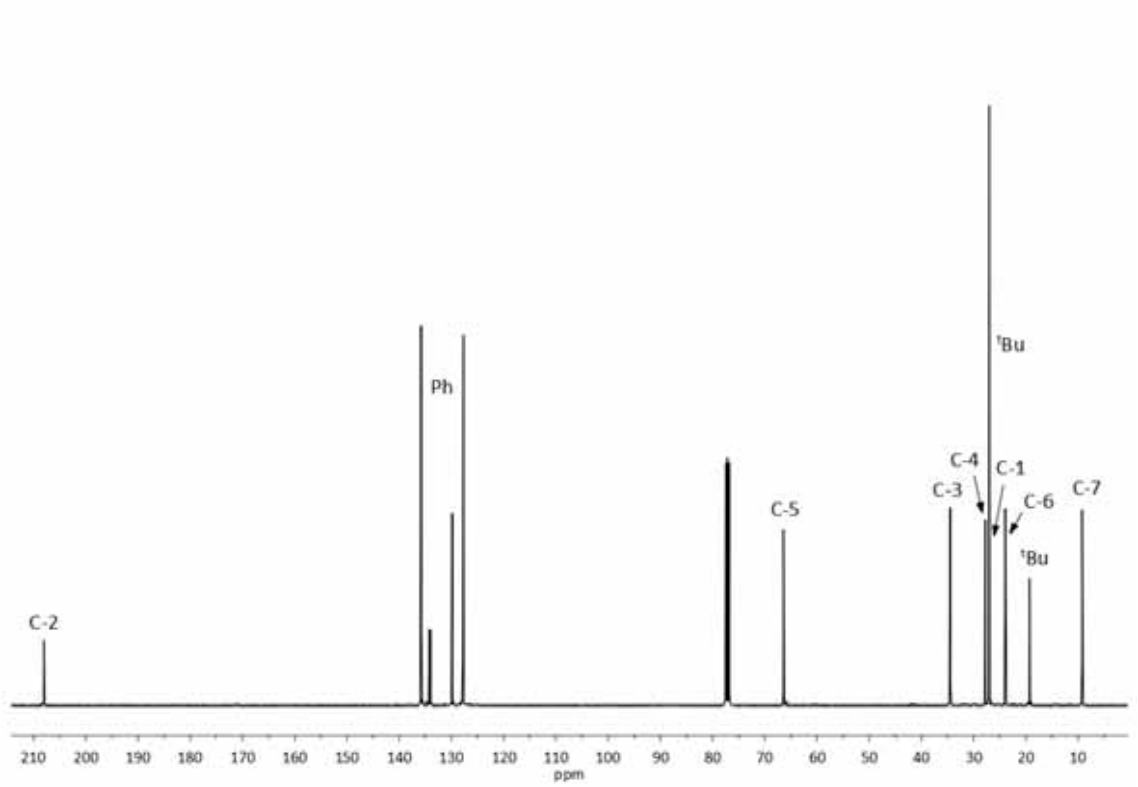
^{13}C-NMR (100 MHz, $CDCl_3$)



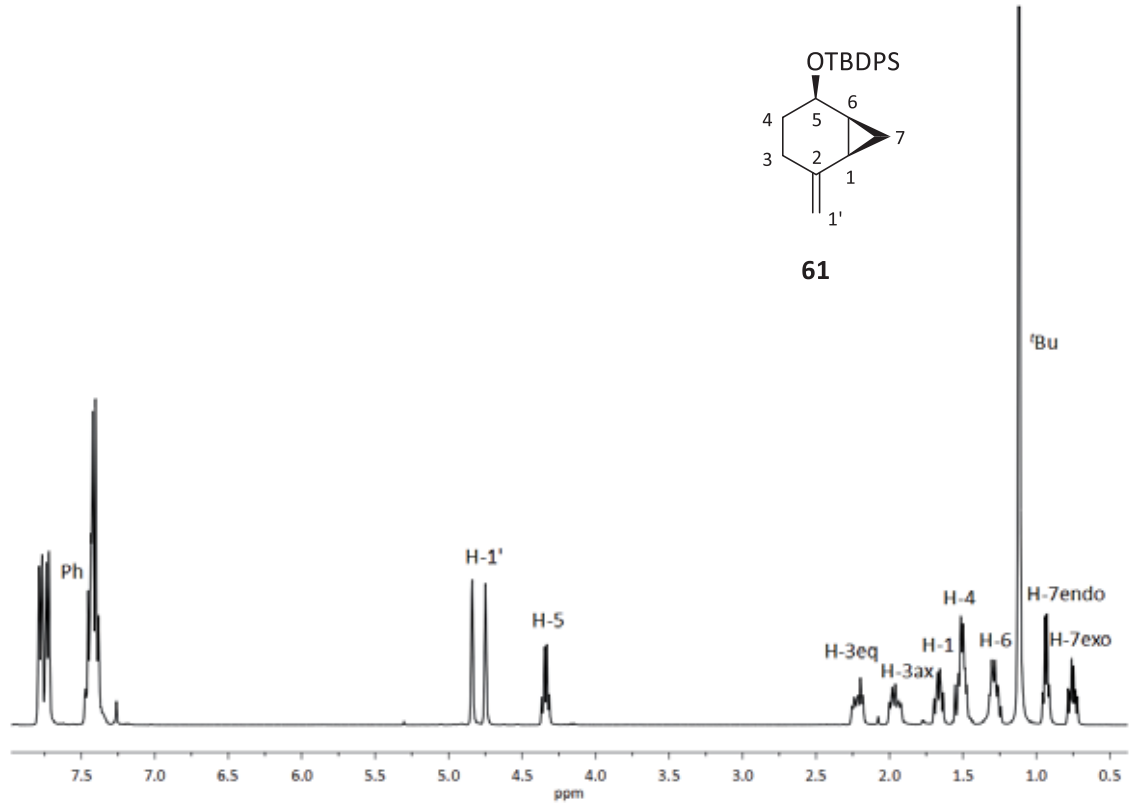
10



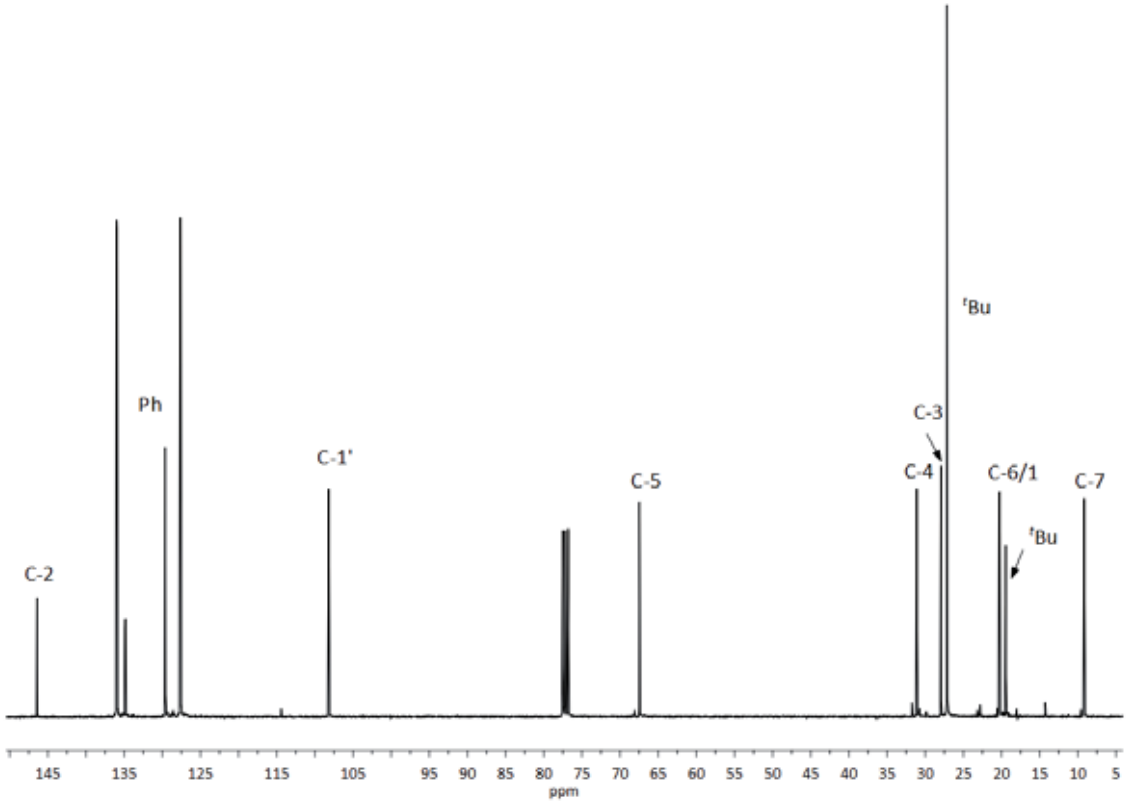
^{1}H-NMR (400 MHz, $CDCl_3$)



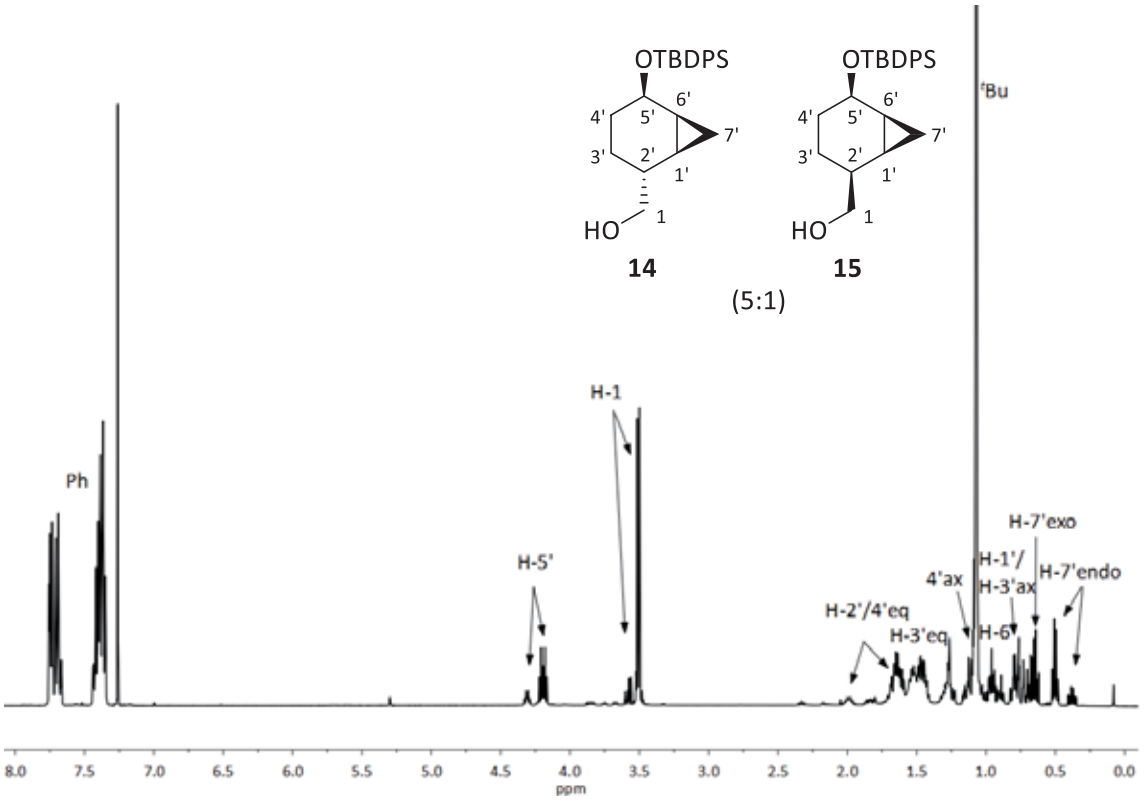
^{13}C-NMR (100 MHz, $CDCl_3$)



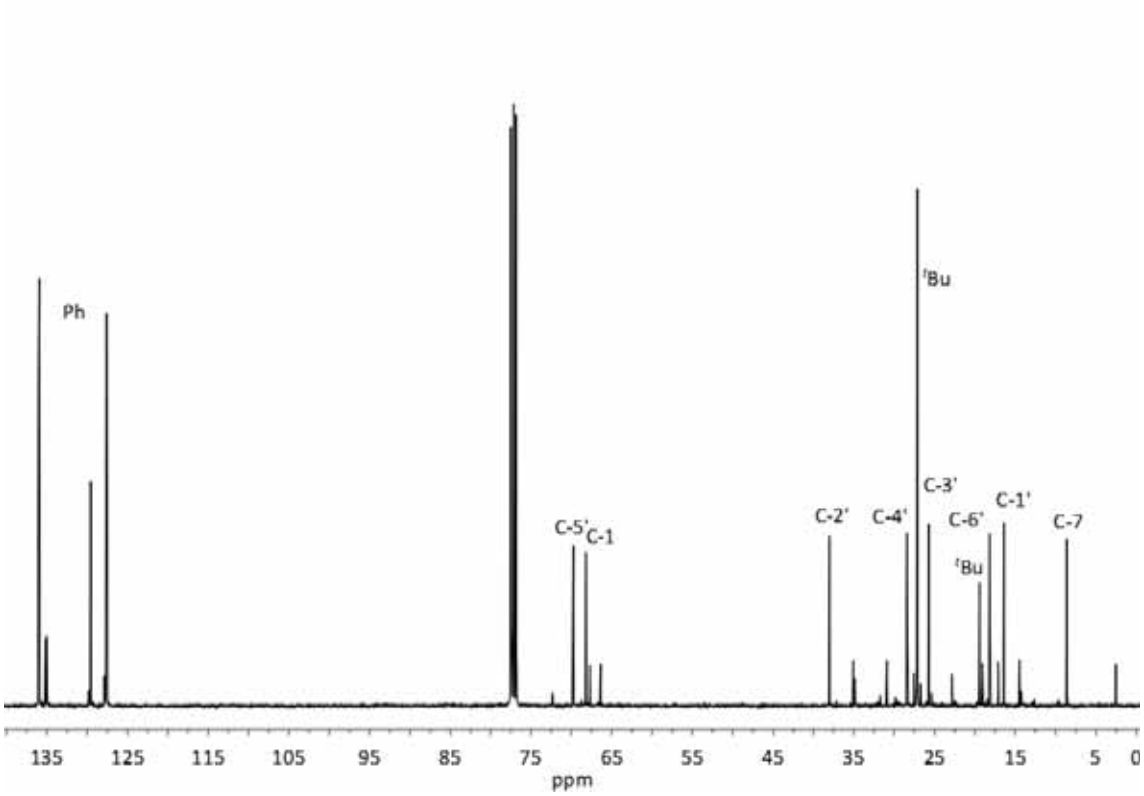
^{1}H-NMR (360 MHz, $CDCl_3$)



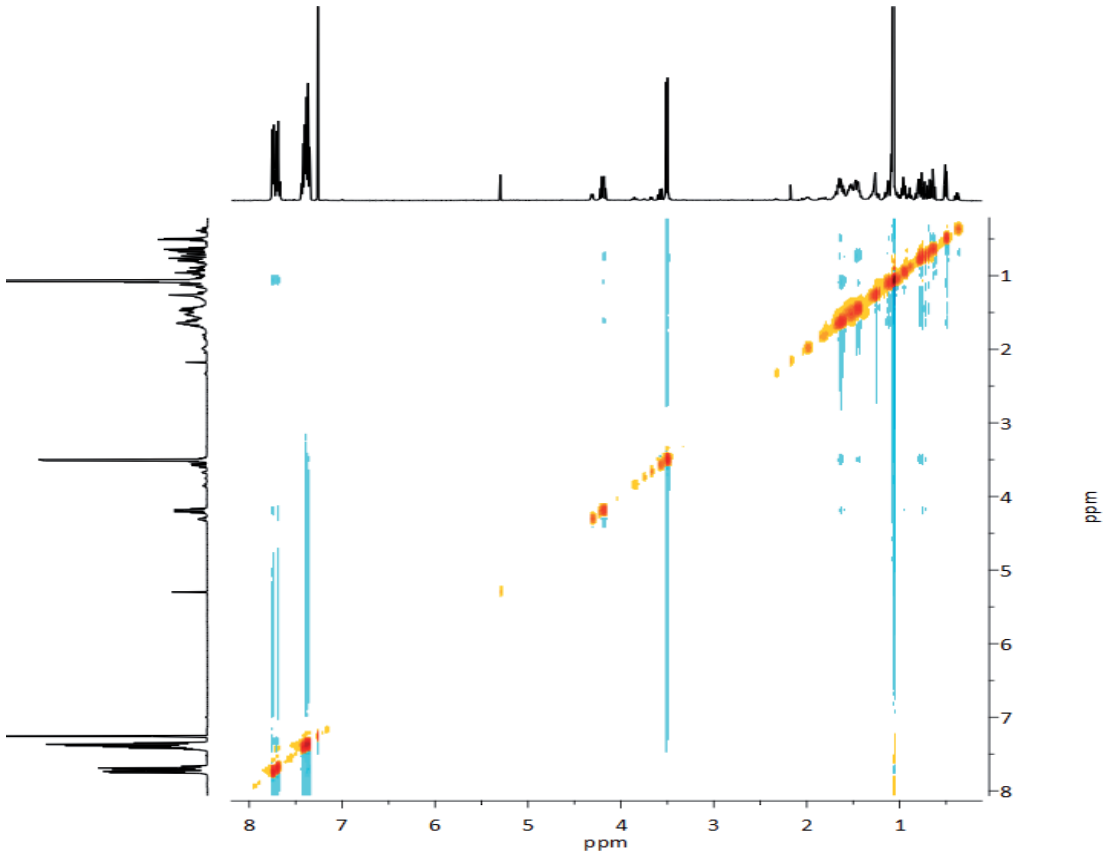
^{13}C-NMR (90 MHz, $CDCl_3$)



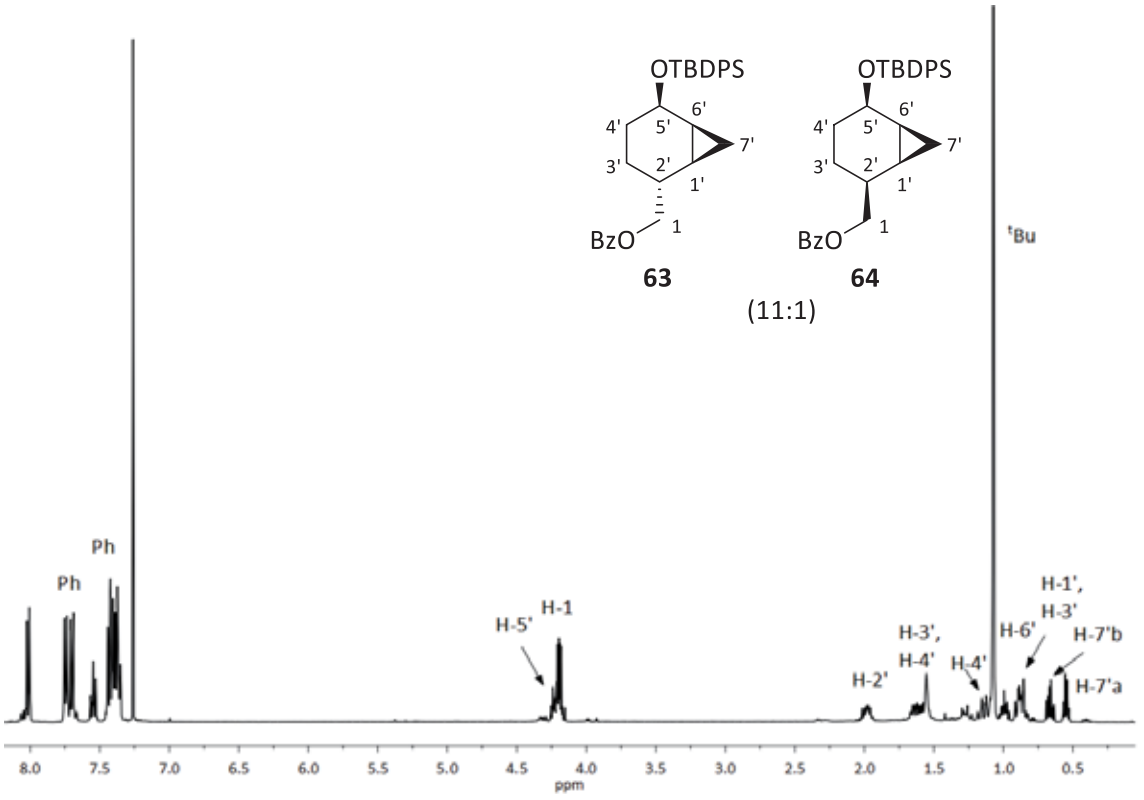
^{1}H-NMR (400 MHz, $CDCl_3$)



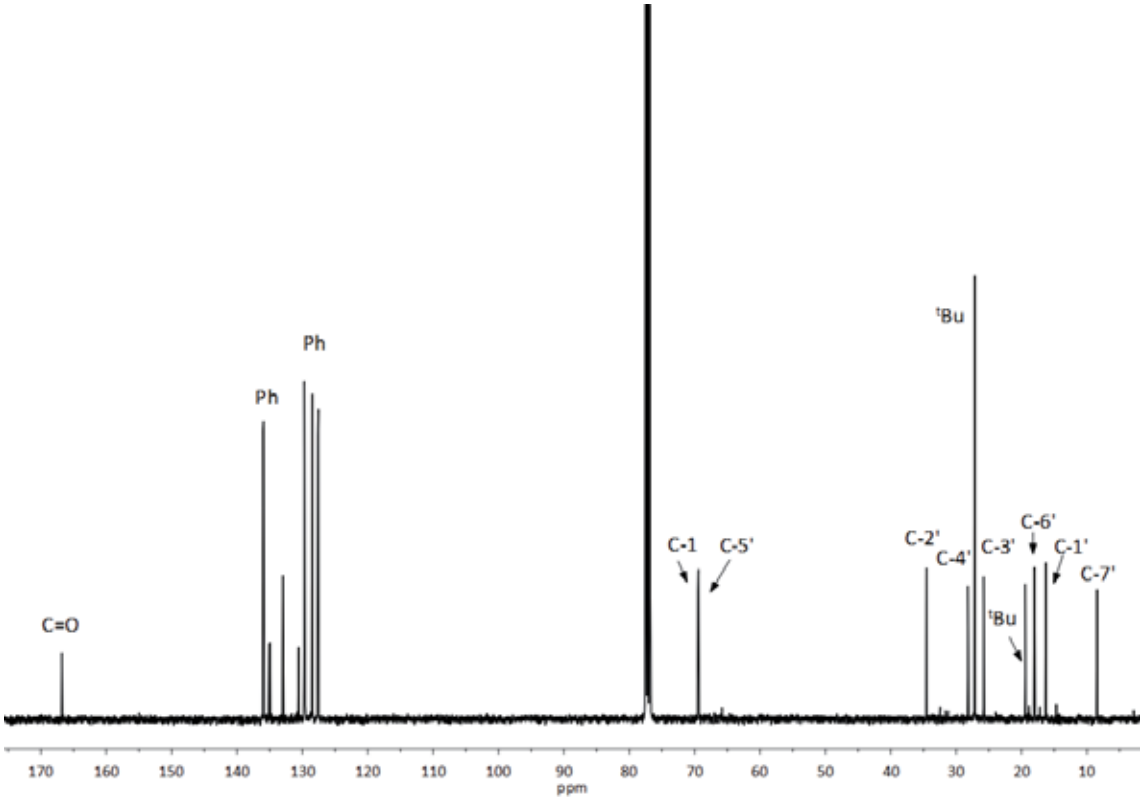
^{13}C-NMR (100 MHz, $CDCl_3$)



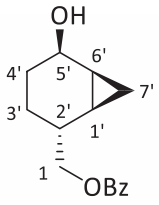
NOESY (400 MHz, $CDCl_3$)



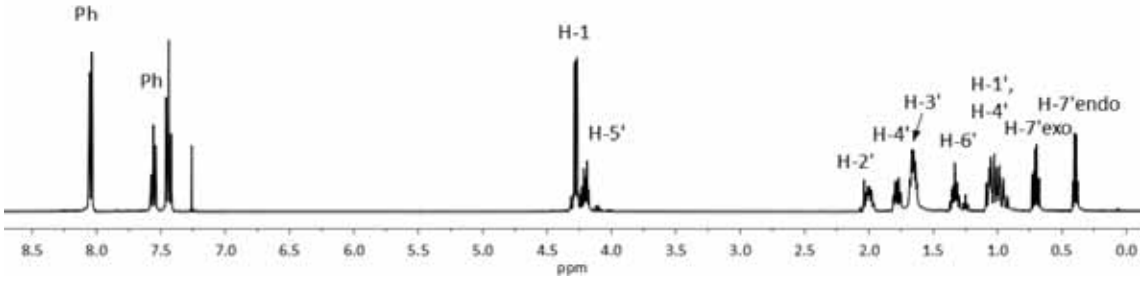
^{1}H-NMR (400 MHz, $CDCl_3$)



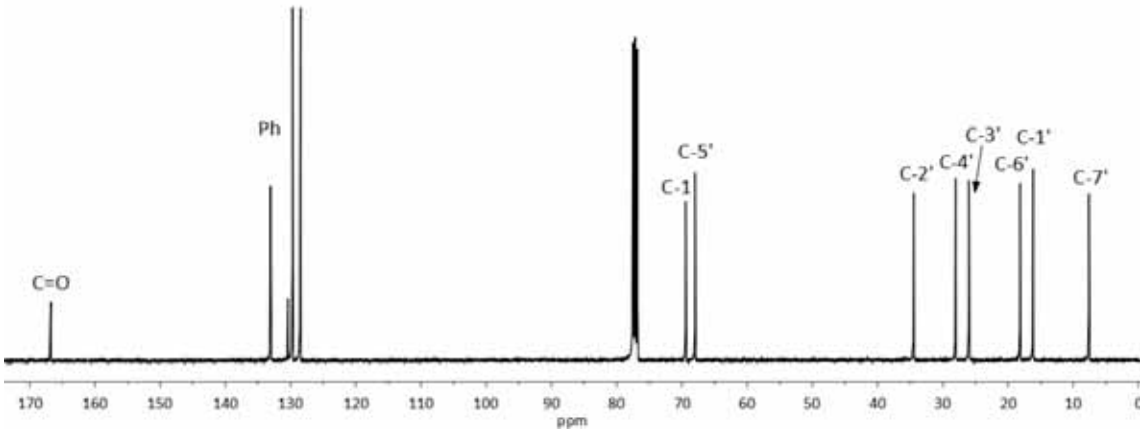
^{13}C-NMR (100 MHz, $CDCl_3$)



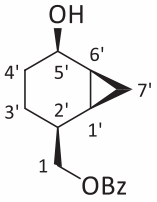
16



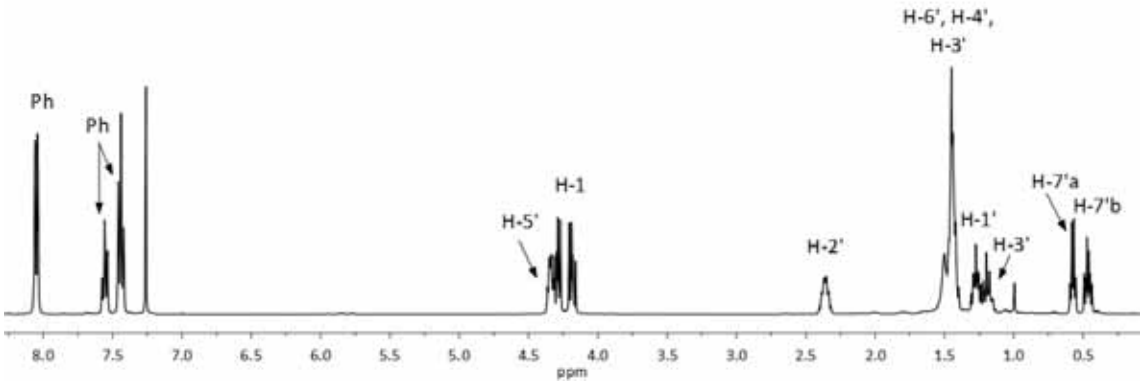
^{1}H-NMR (400 MHz, $CDCl_3$)



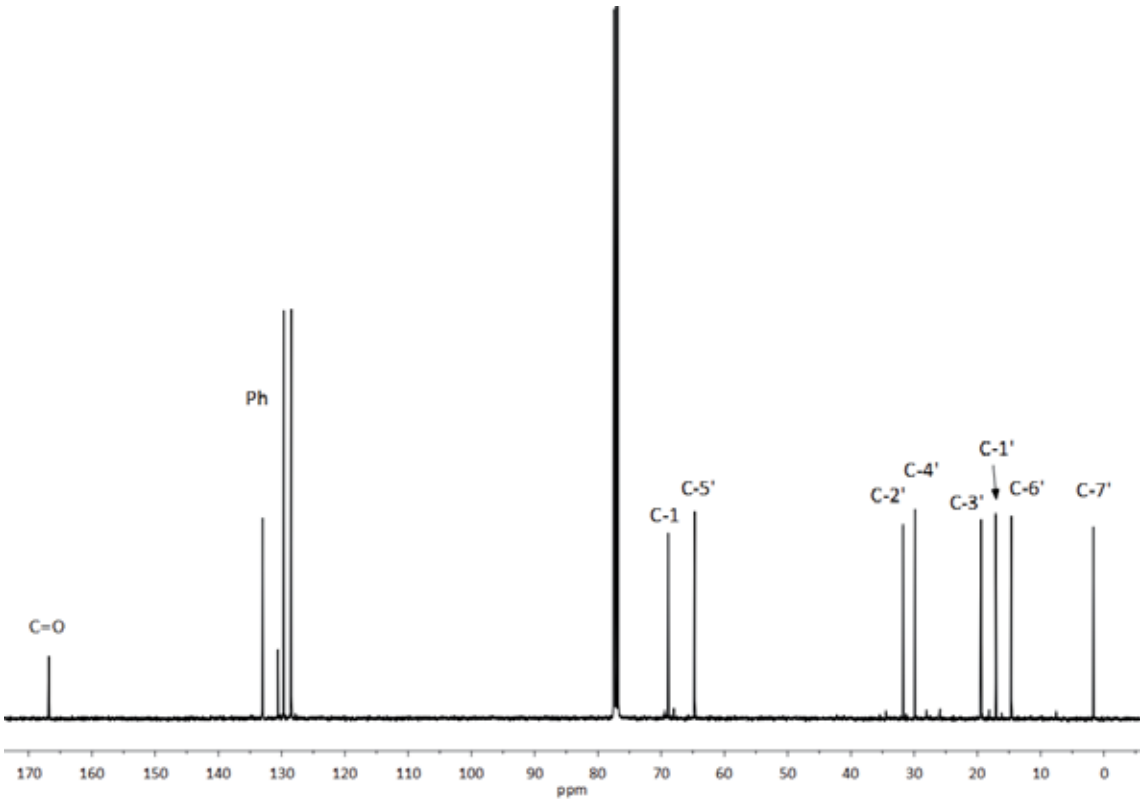
^{13}C-NMR (100 MHz, $CDCl_3$)



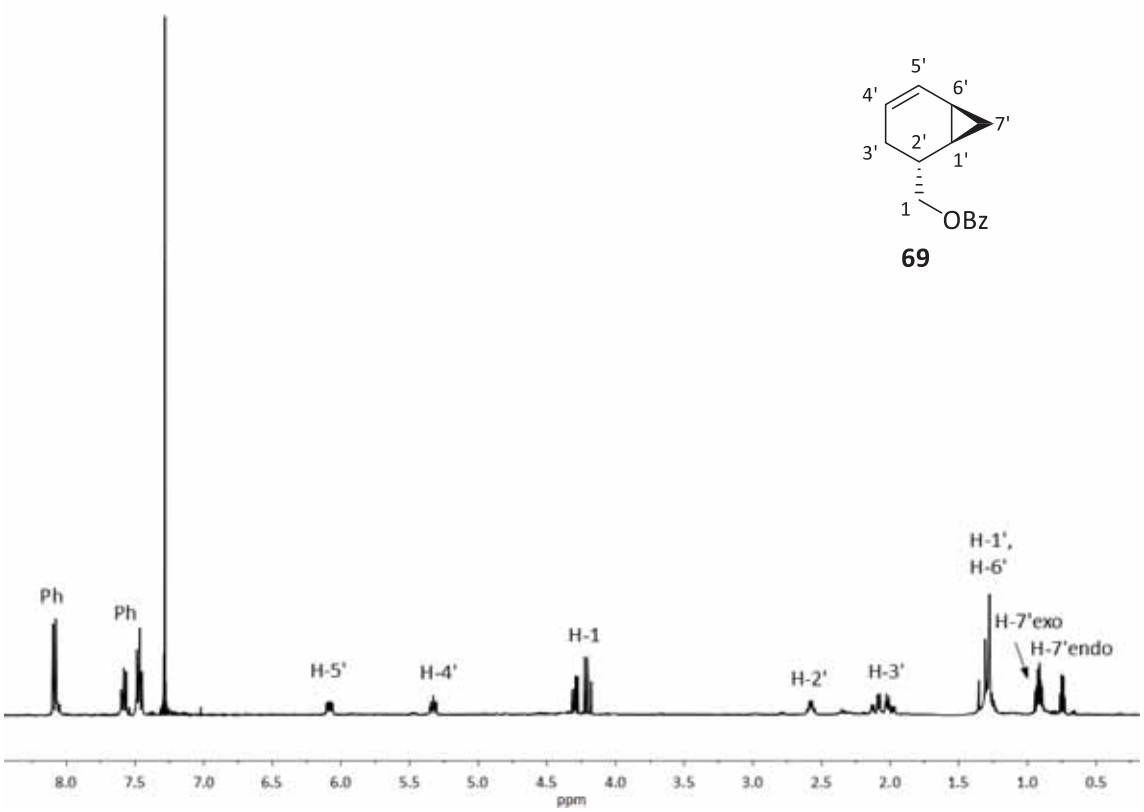
65



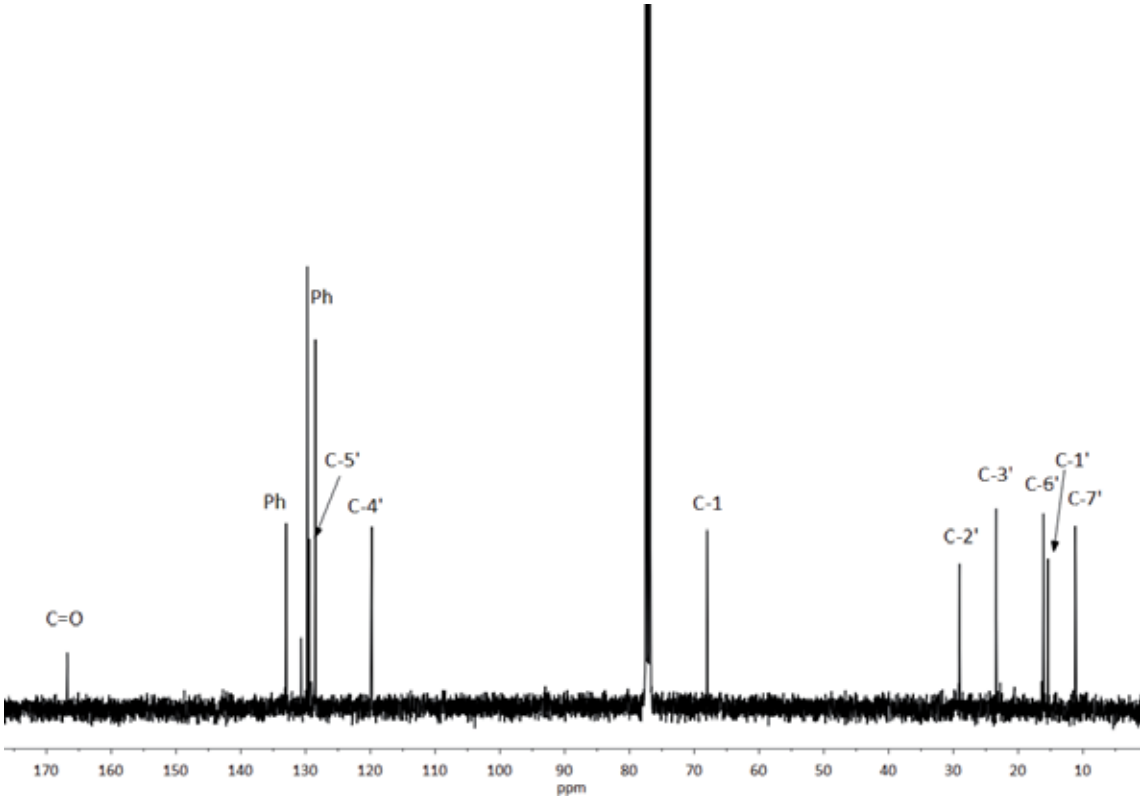
^{1}H-NMR (400 MHz, $CDCl_3$)



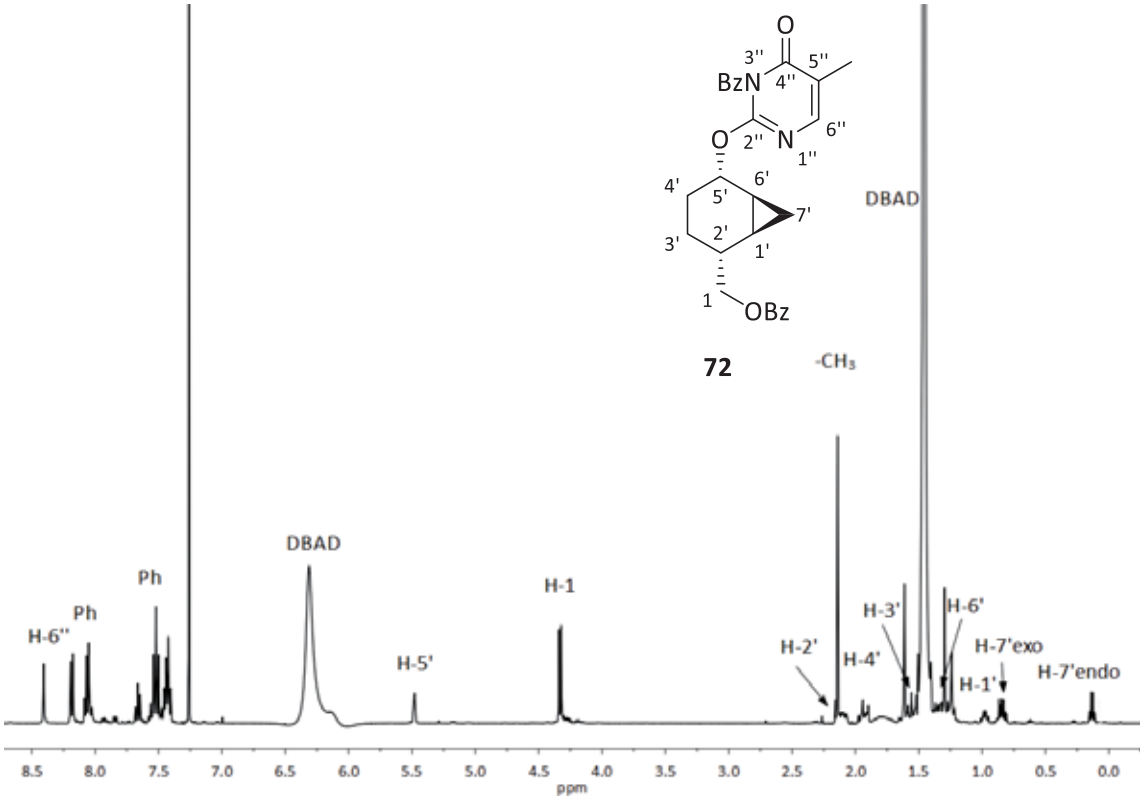
^{13}C-NMR (100 MHz, $CDCl_3$)



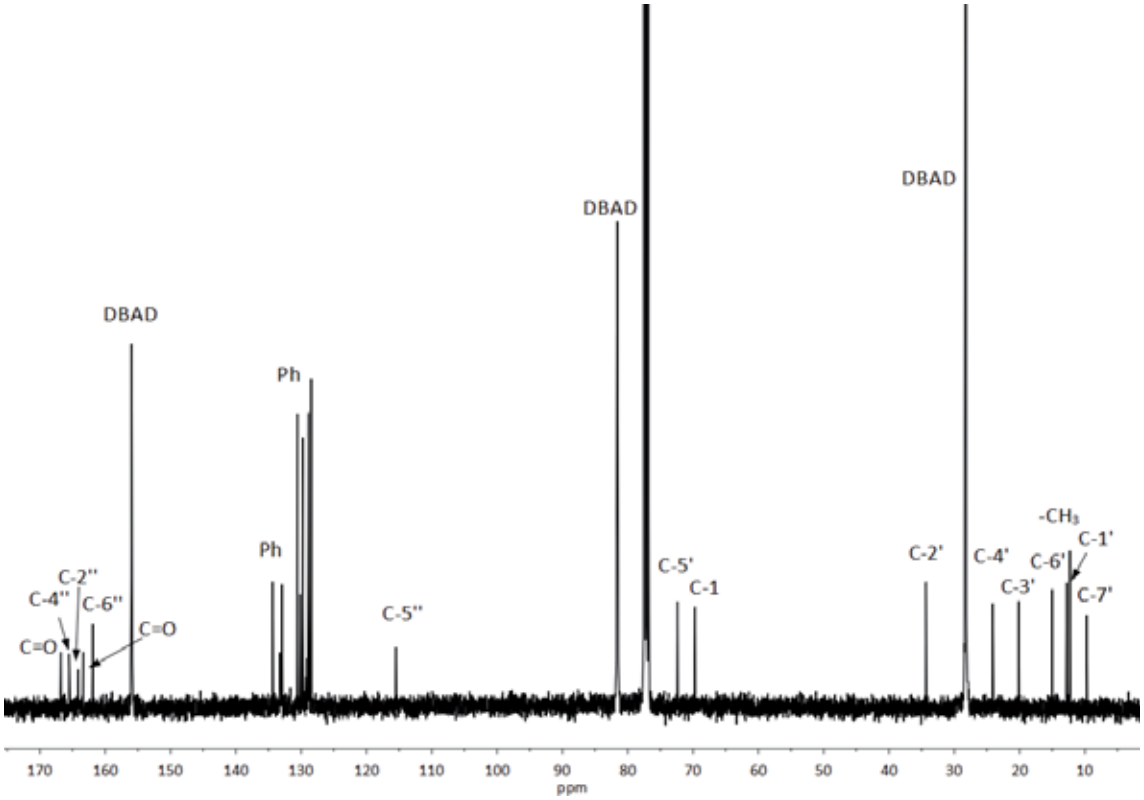
^{1}H-NMR (400 MHz, $CDCl_3$)



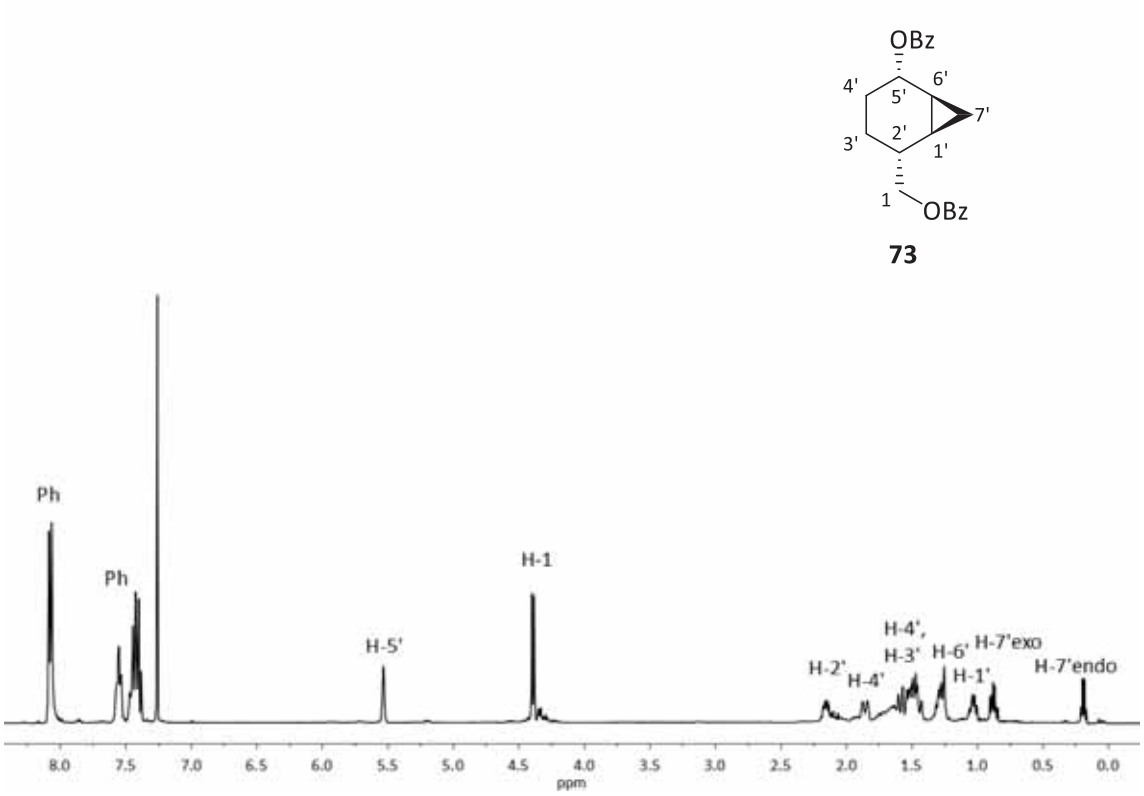
^{13}C-NMR (100 MHz, $CDCl_3$)



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

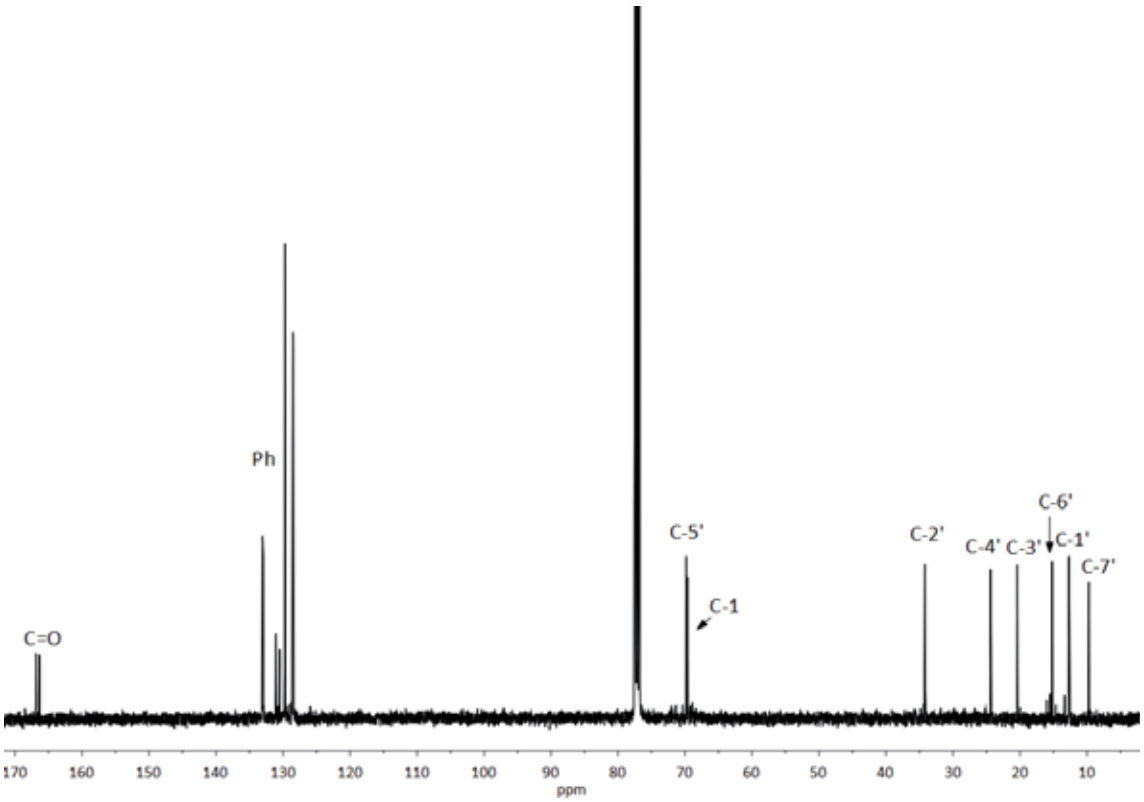


^{13}C-NMR (100 MHz, $CDCl_3$)

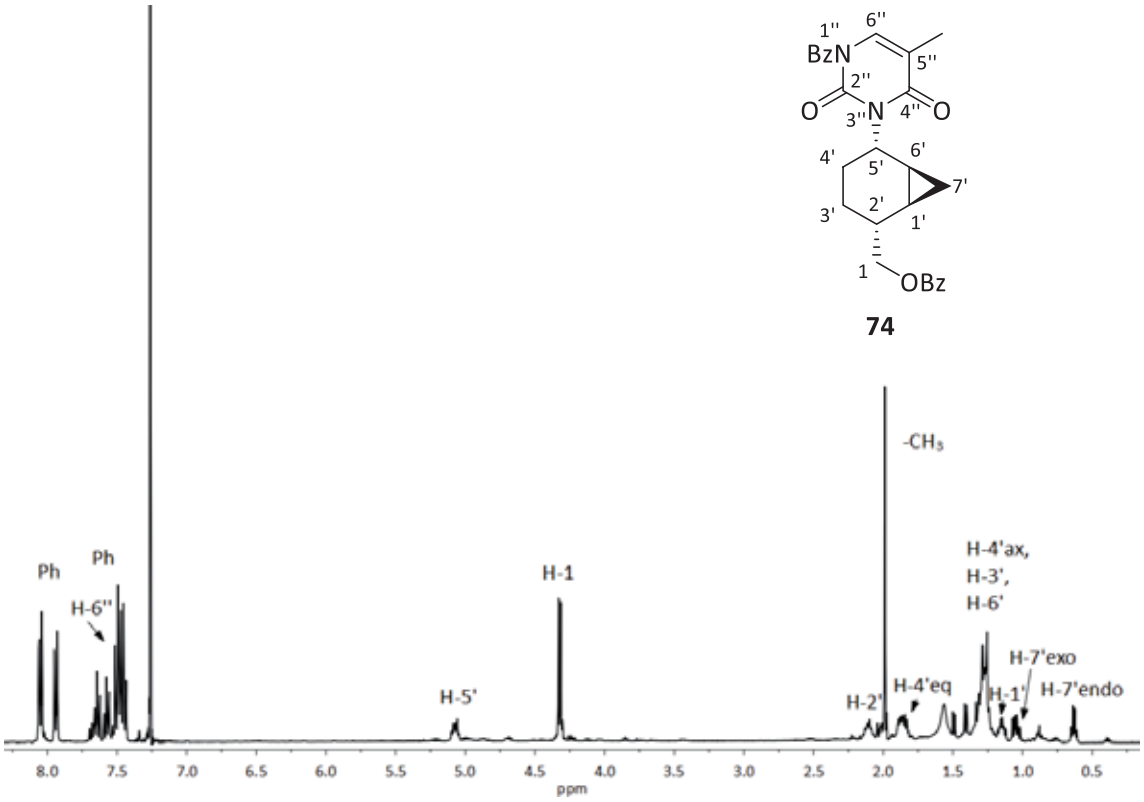


73

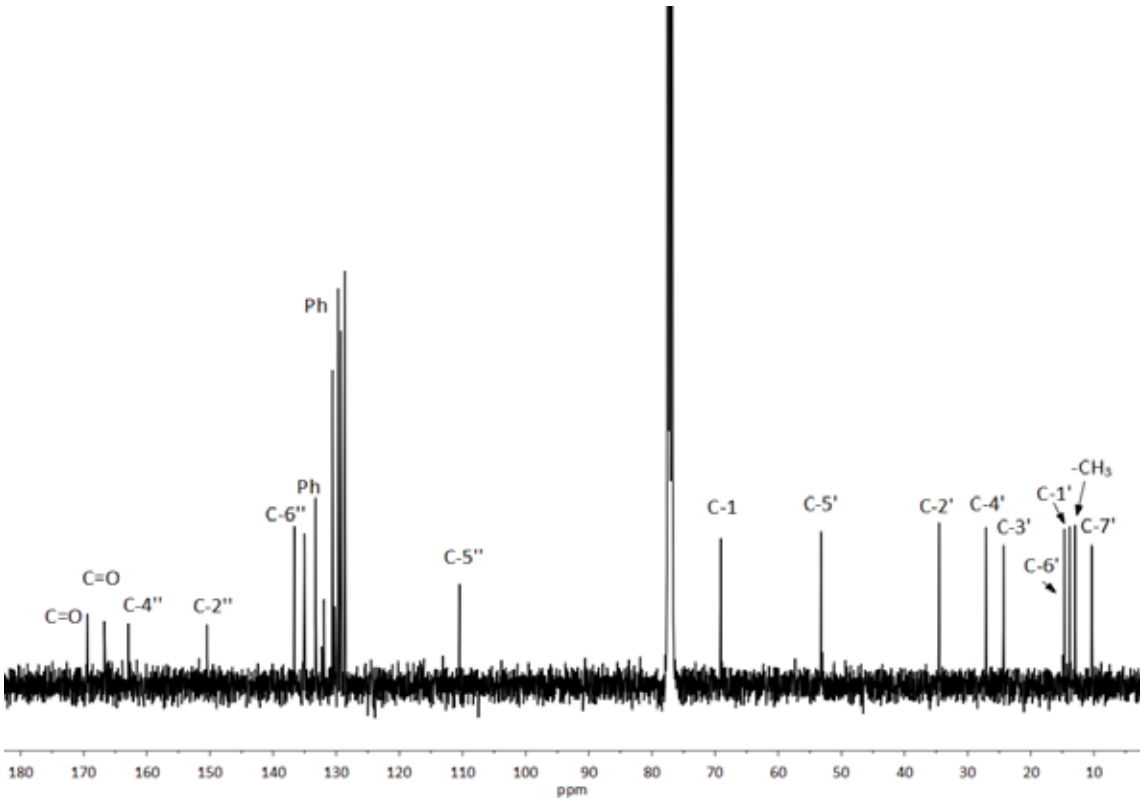
^{1}H-NMR (400 MHz, $CDCl_3$)



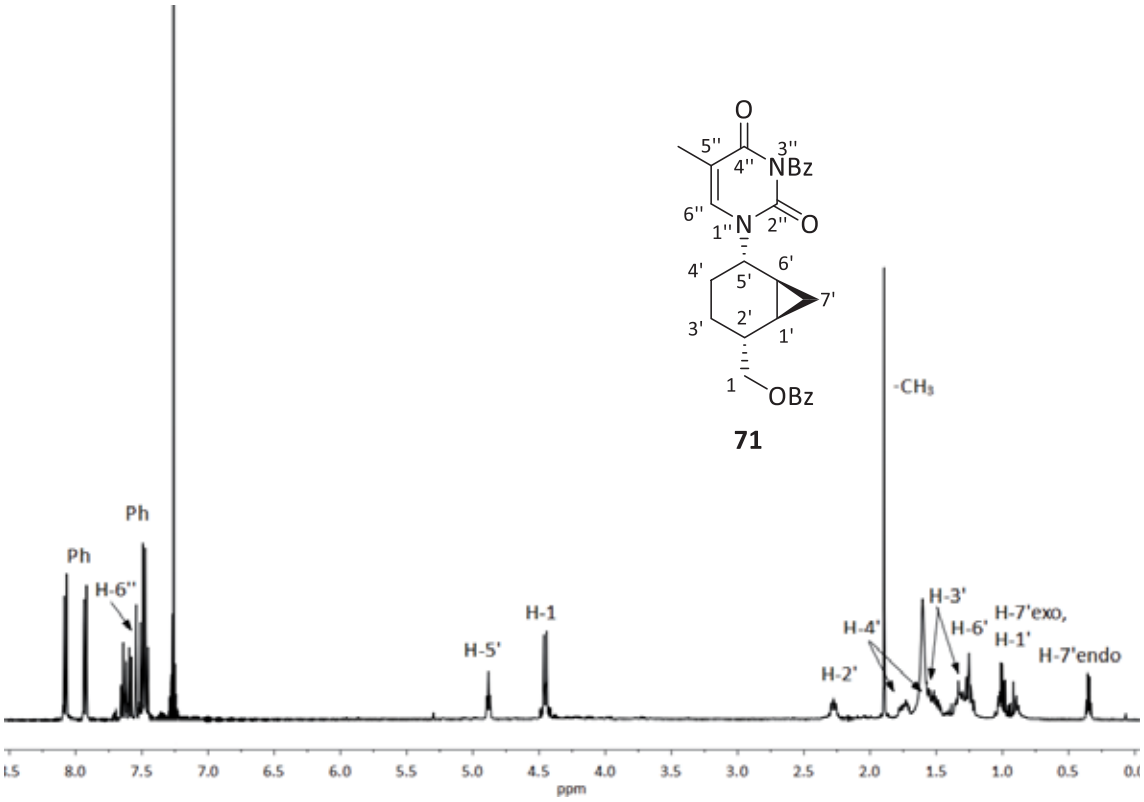
^{13}C-NMR (100 MHz, $CDCl_3$)



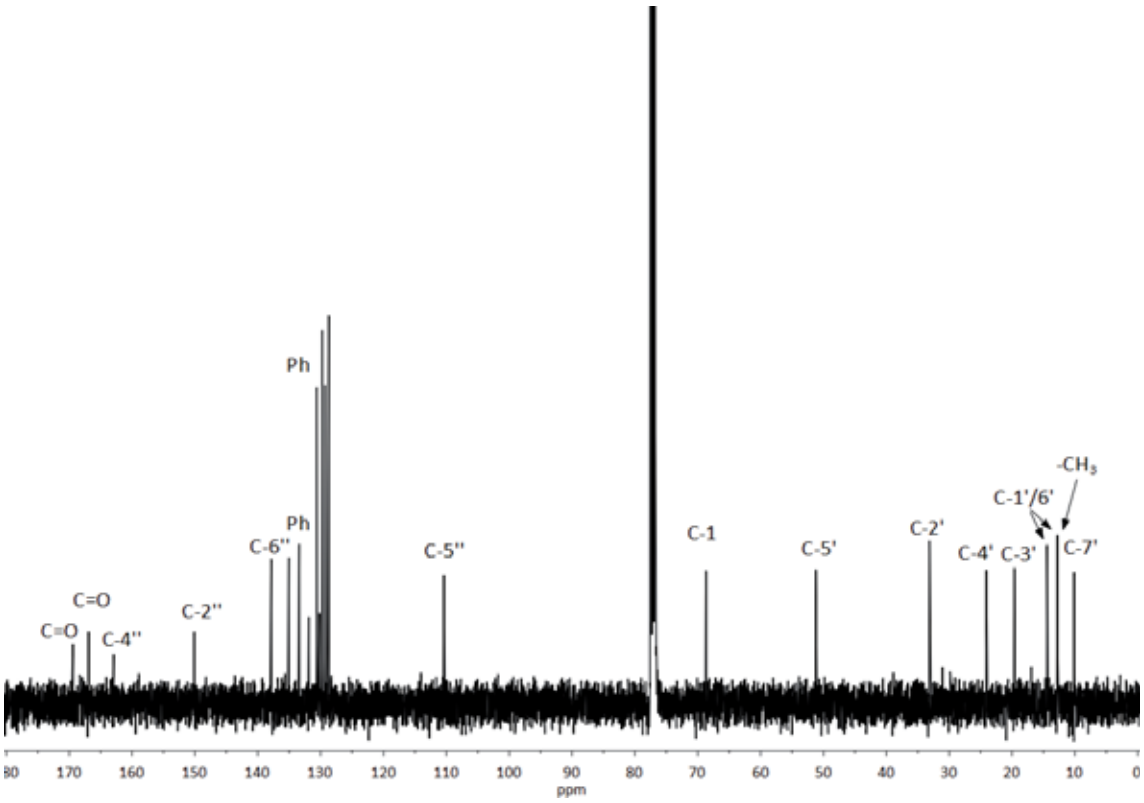
^{1}H-NMR (400 MHz, $CDCl_3$)



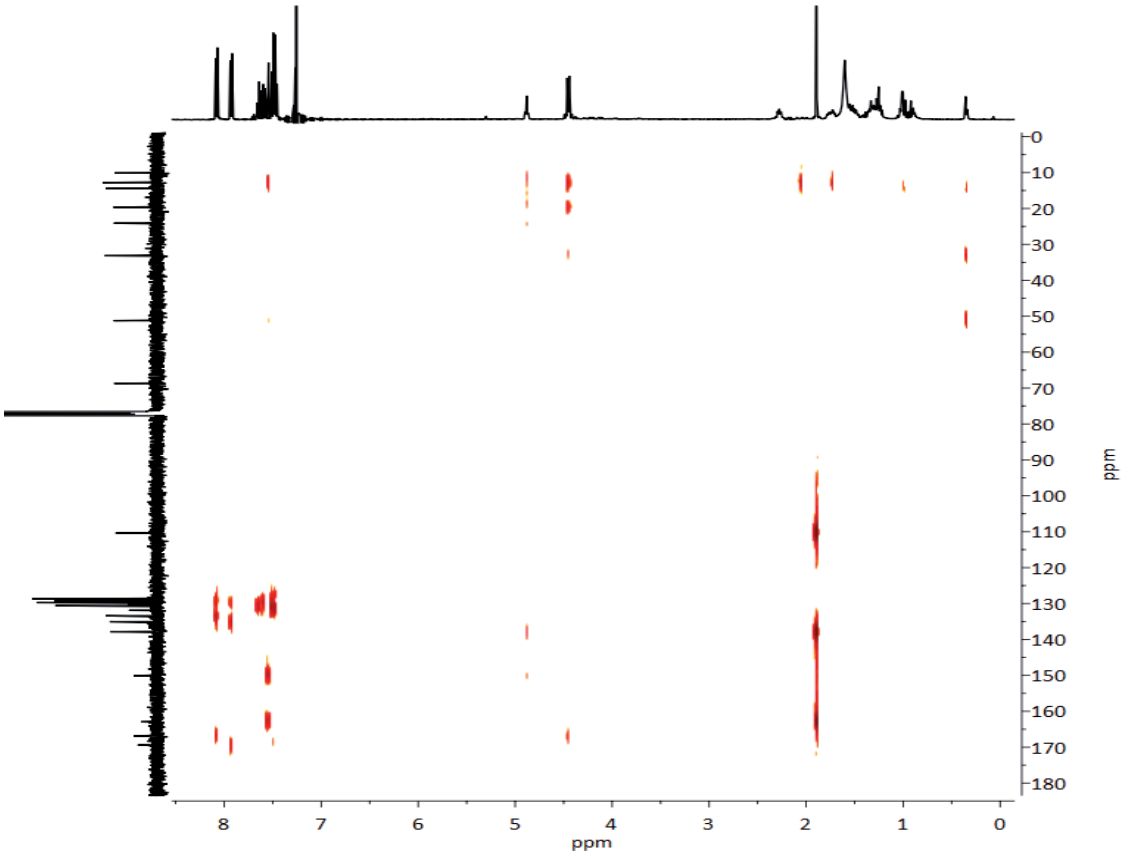
^{13}C-NMR (100 MHz, $CDCl_3$)



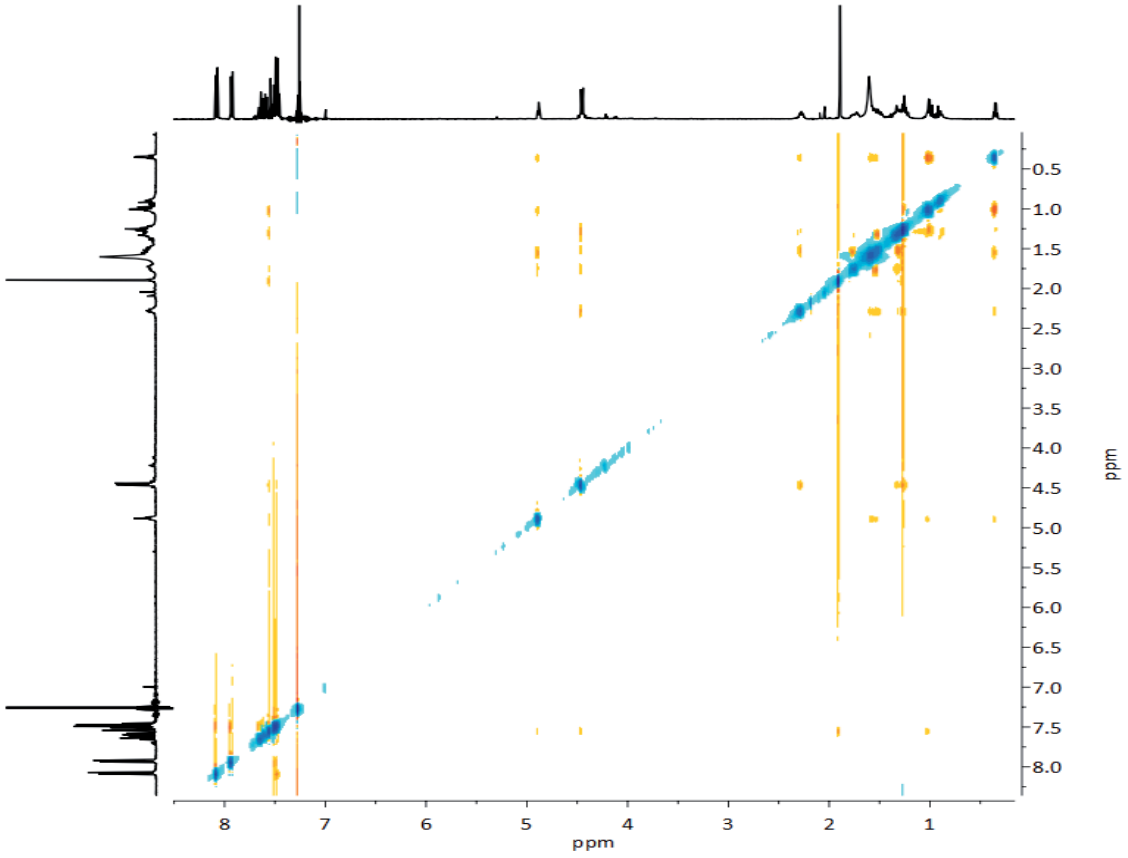
^{1}H-NMR (400 MHz, $CDCl_3$)



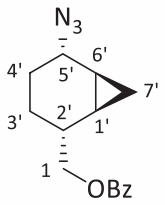
^{13}C-NMR (100 MHz, $CDCl_3$)



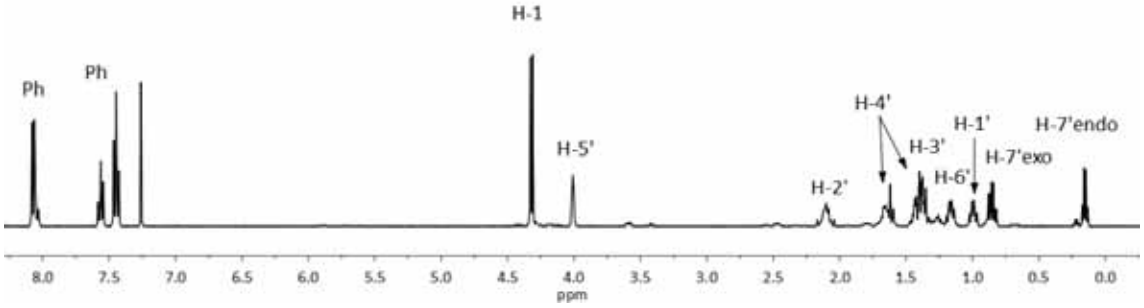
HMBC (400 MHz, $CDCl_3$)



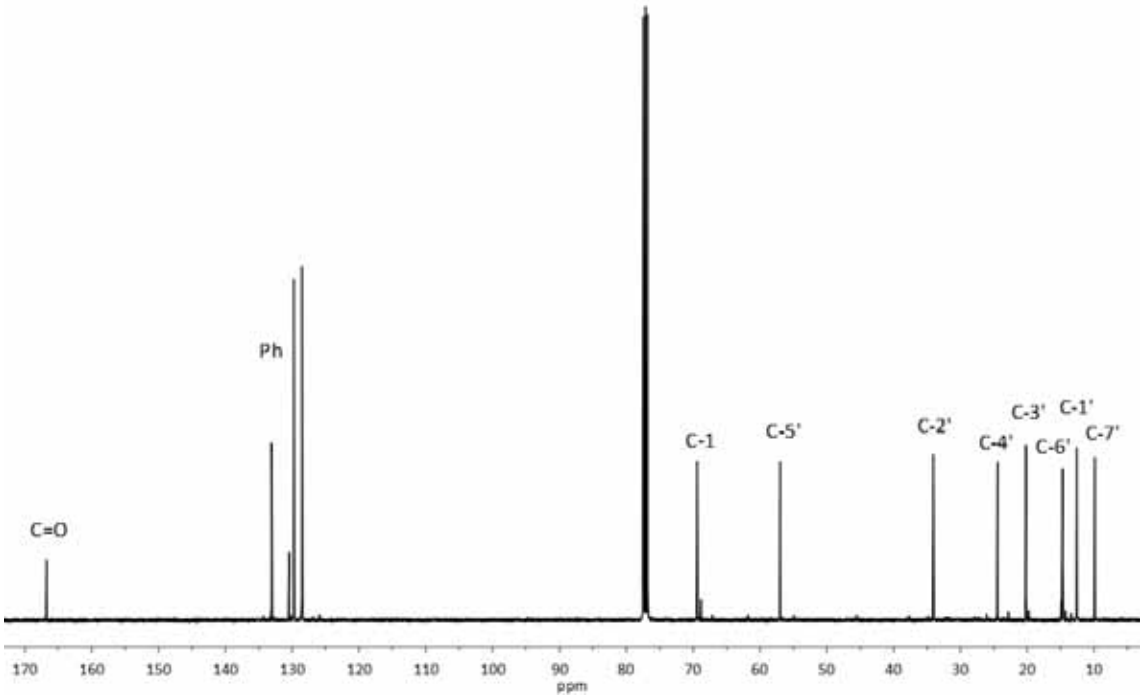
NOESY (400 MHz, $CDCl_3$)



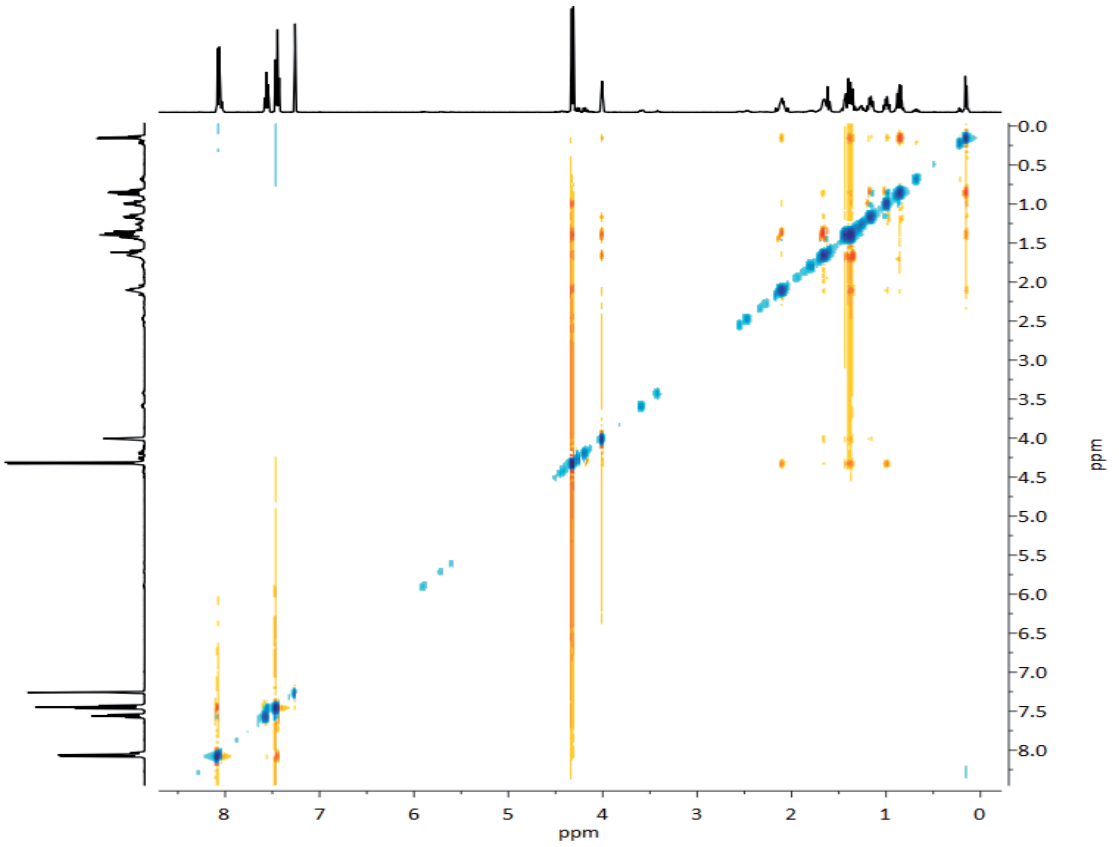
75



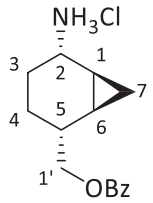
^{1}H-NMR (400 MHz, $CDCl_3$)



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

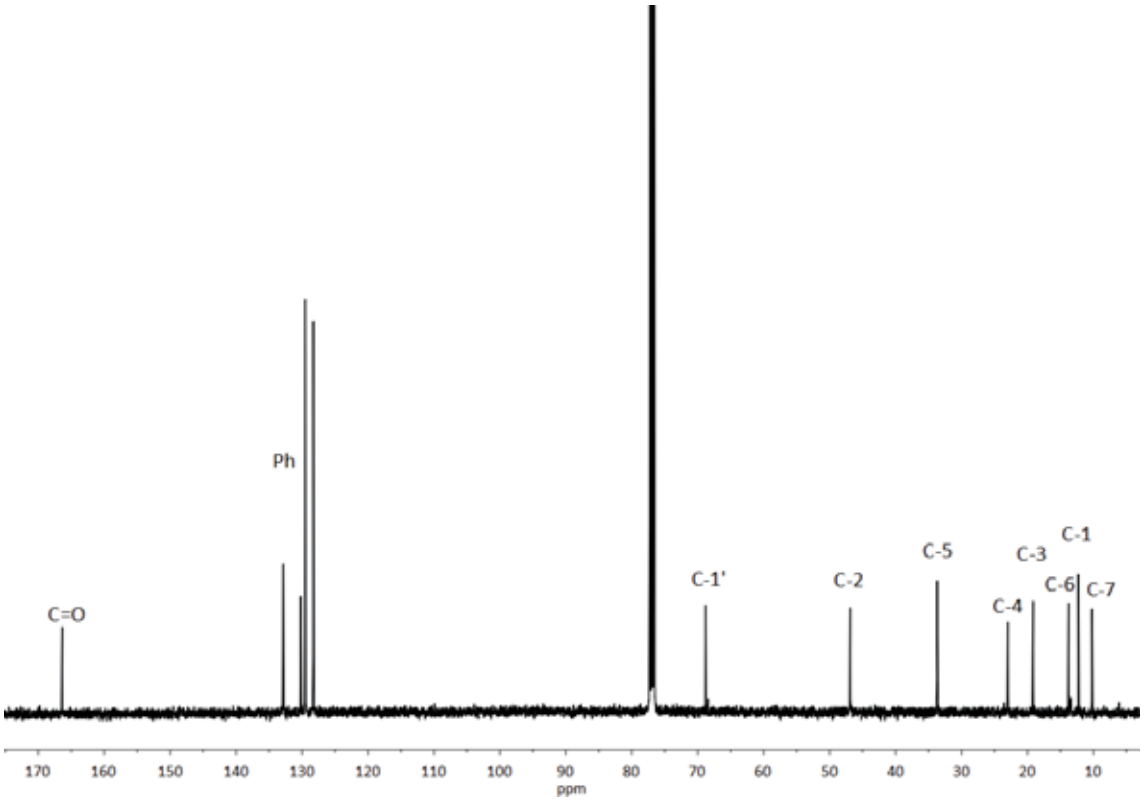


NOESY (400 MHz, $CDCl_3$)

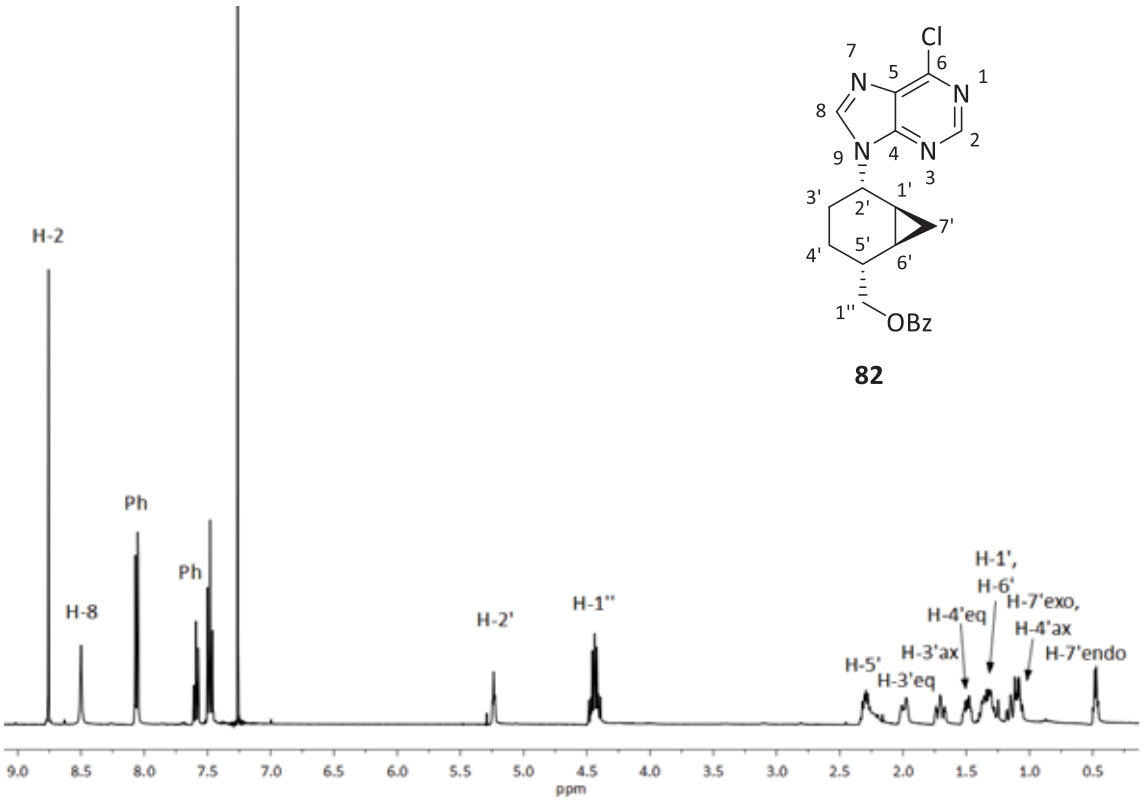


76

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

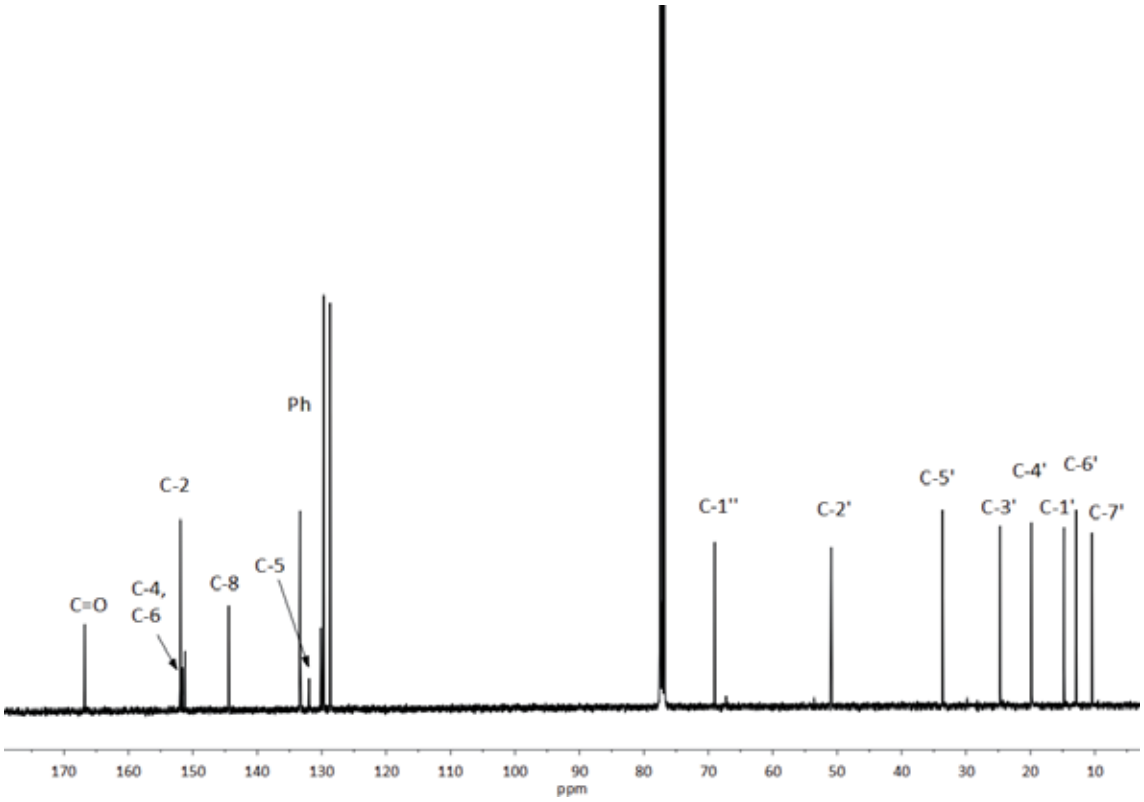


^{13}C-NMR (400 MHz, $CDCl_3$)

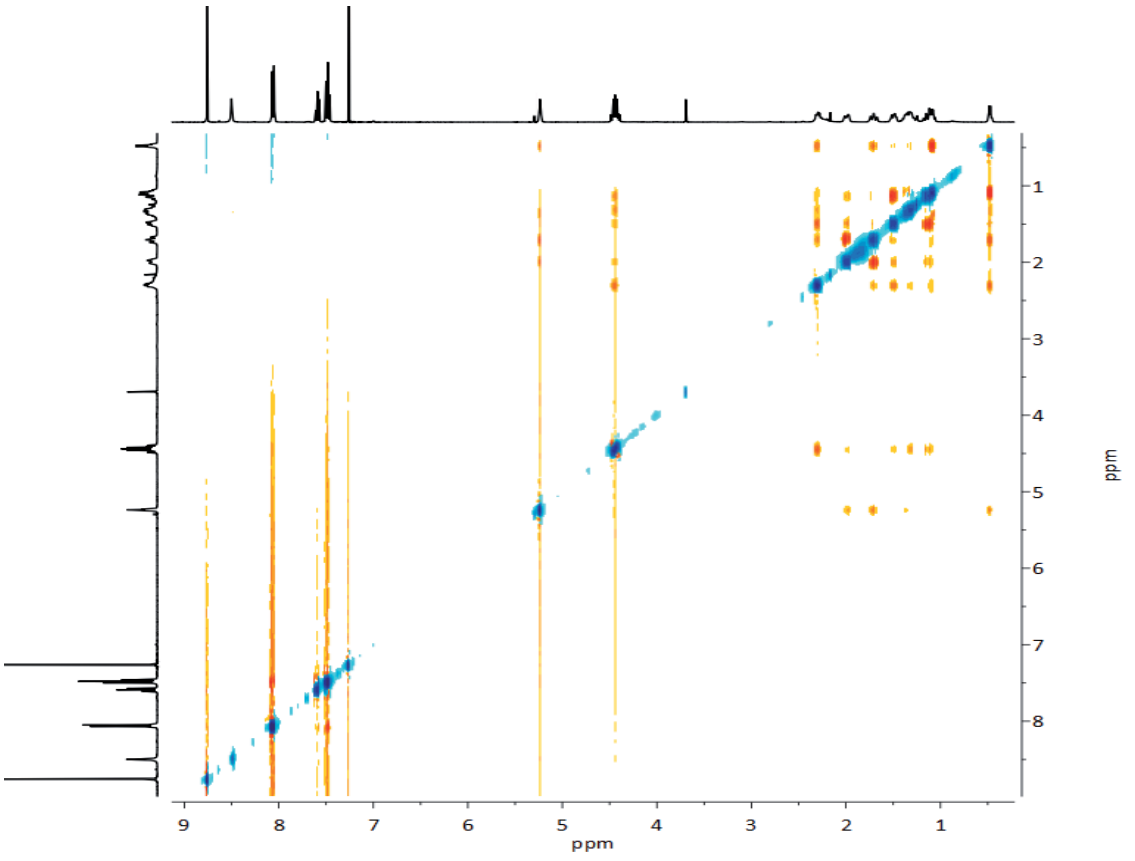


82

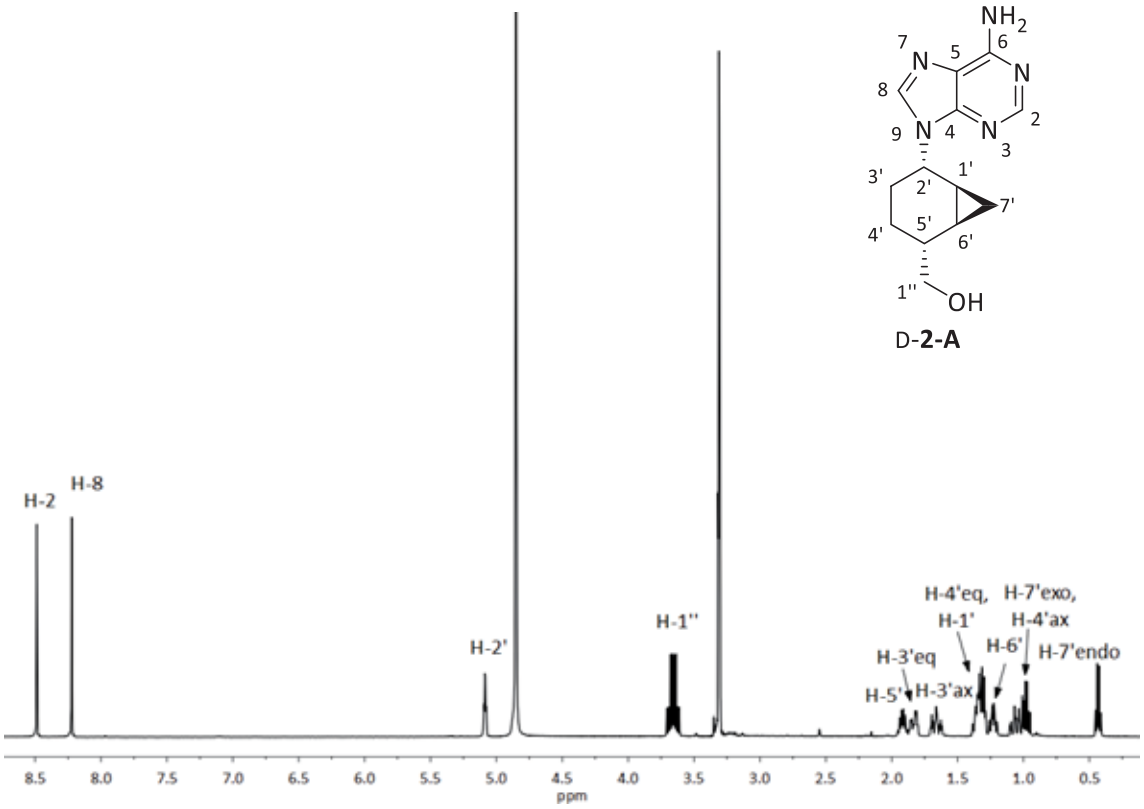
^{1}H-NMR (400 MHz, $CDCl_3$)



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

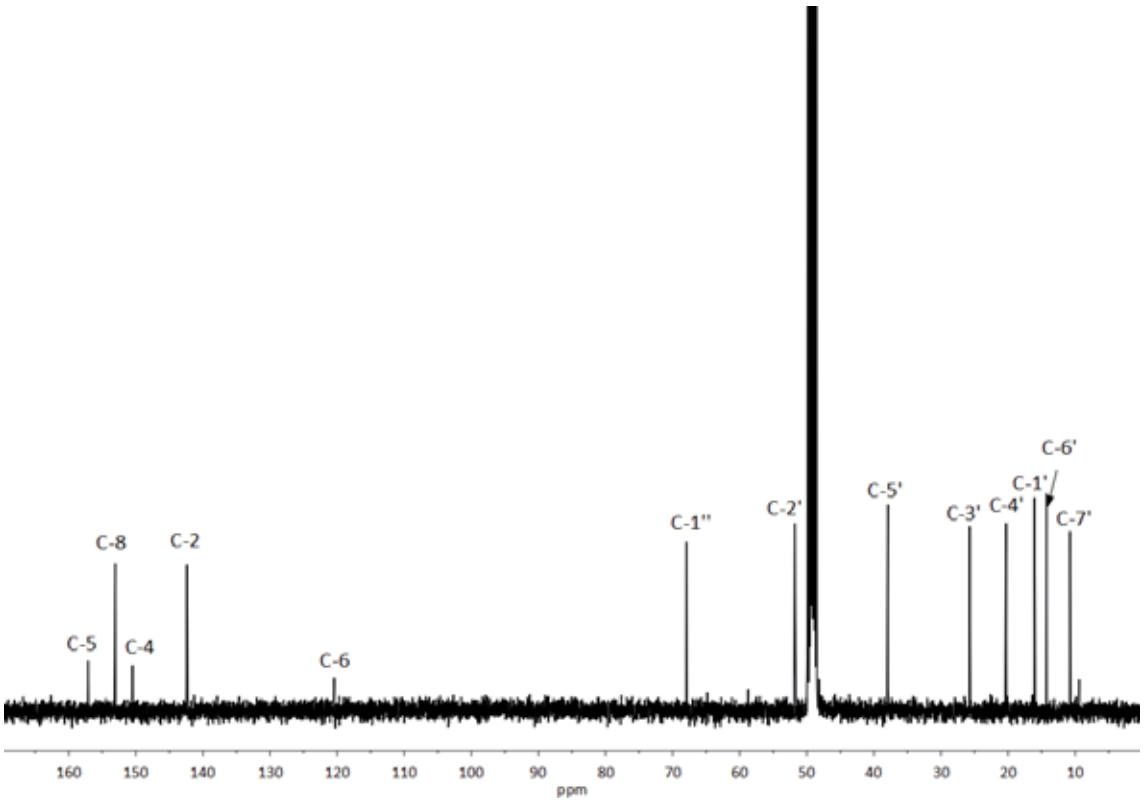


NOESY (400 MHz, $CDCl_3$)

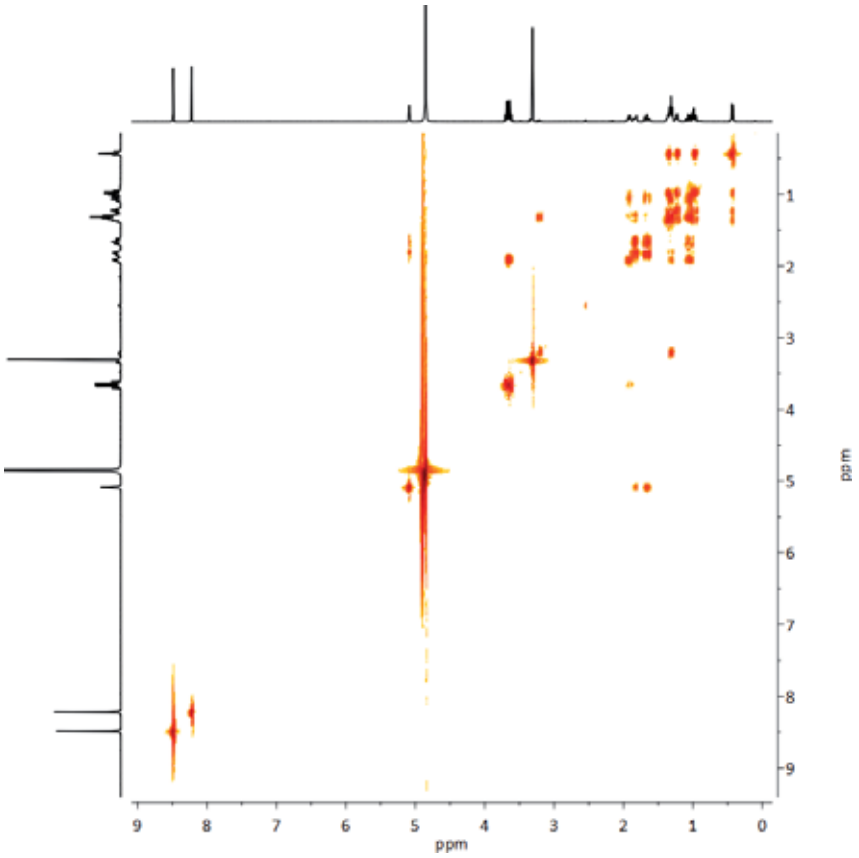


D-**2-A**

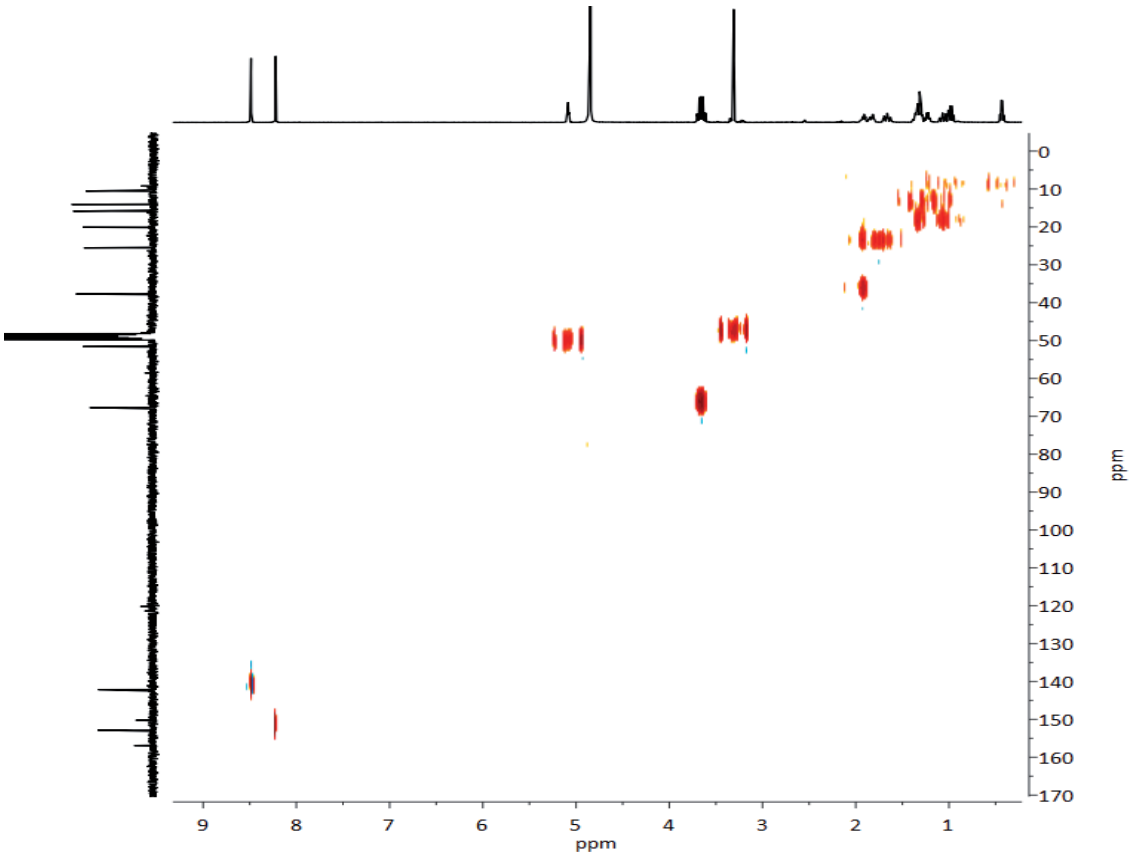
^{1}H-NMR (400 MHz, MeOD)



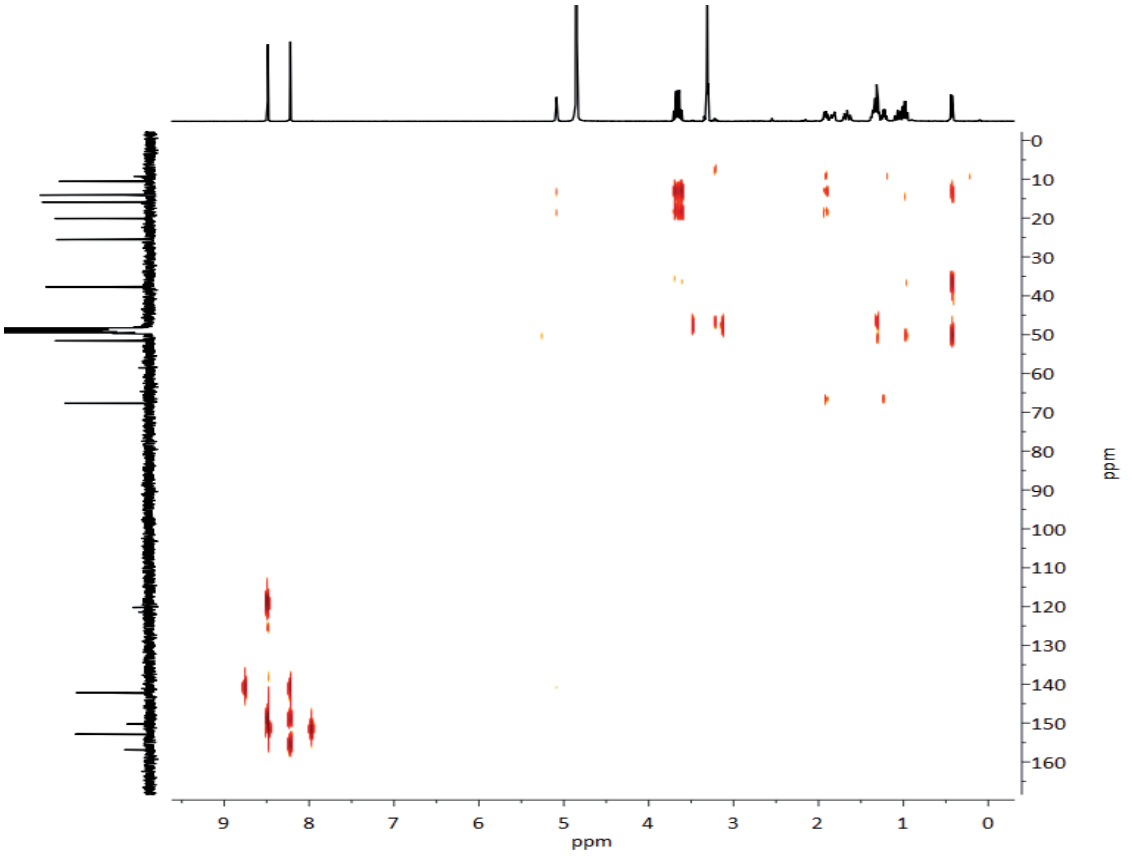
^{13}C-NMR (100 MHz, MeOD)



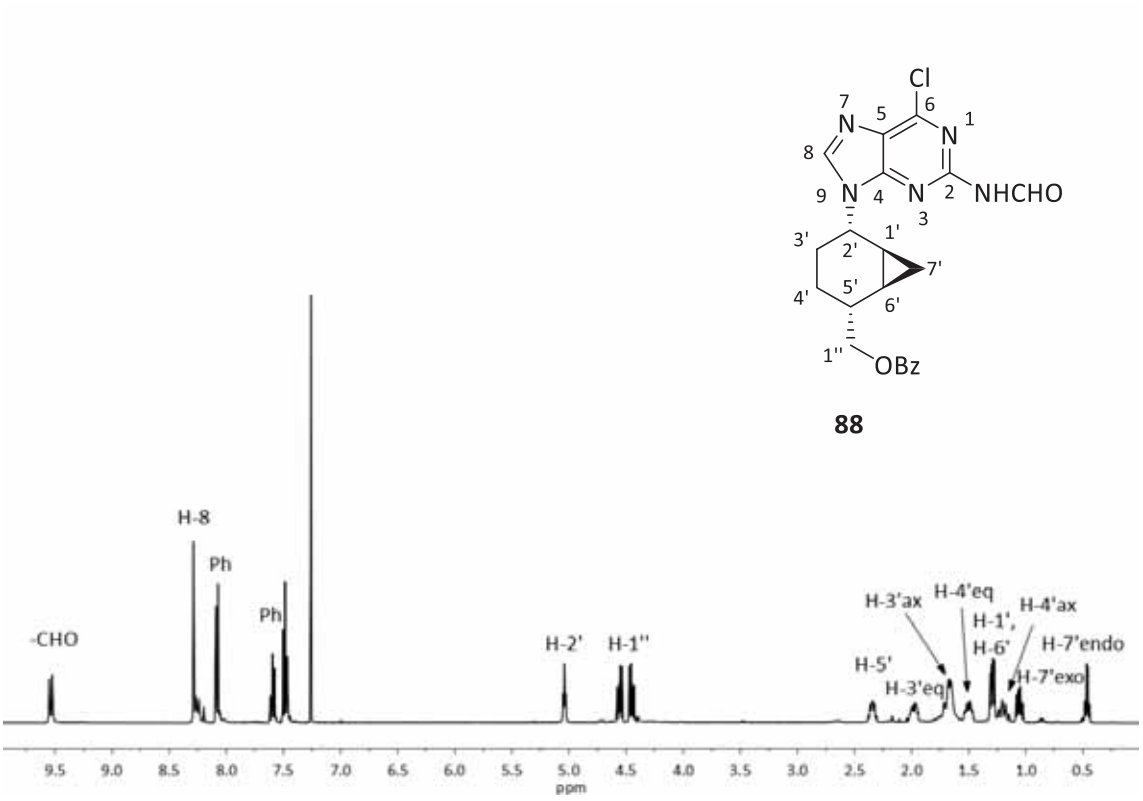
COSY (400 MHz, MeOD)



HSQC (400 MHz, MeOD)

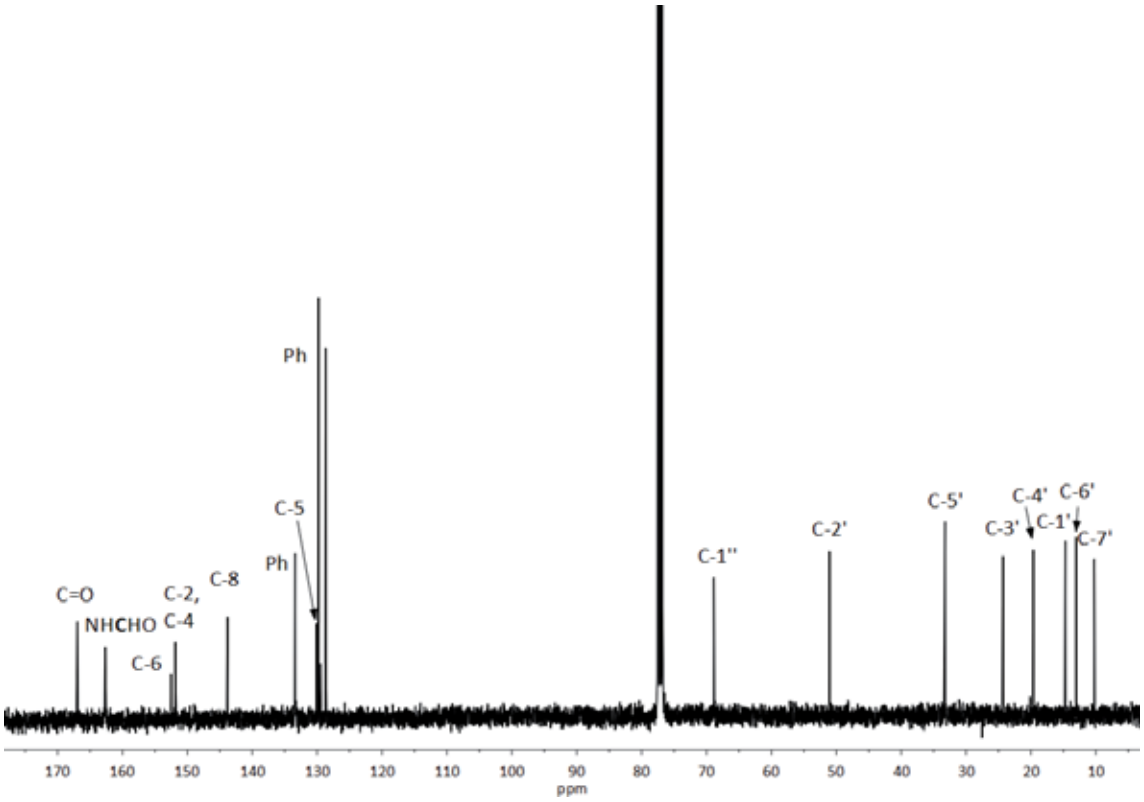


HMBC (400 MHz, MeOD)

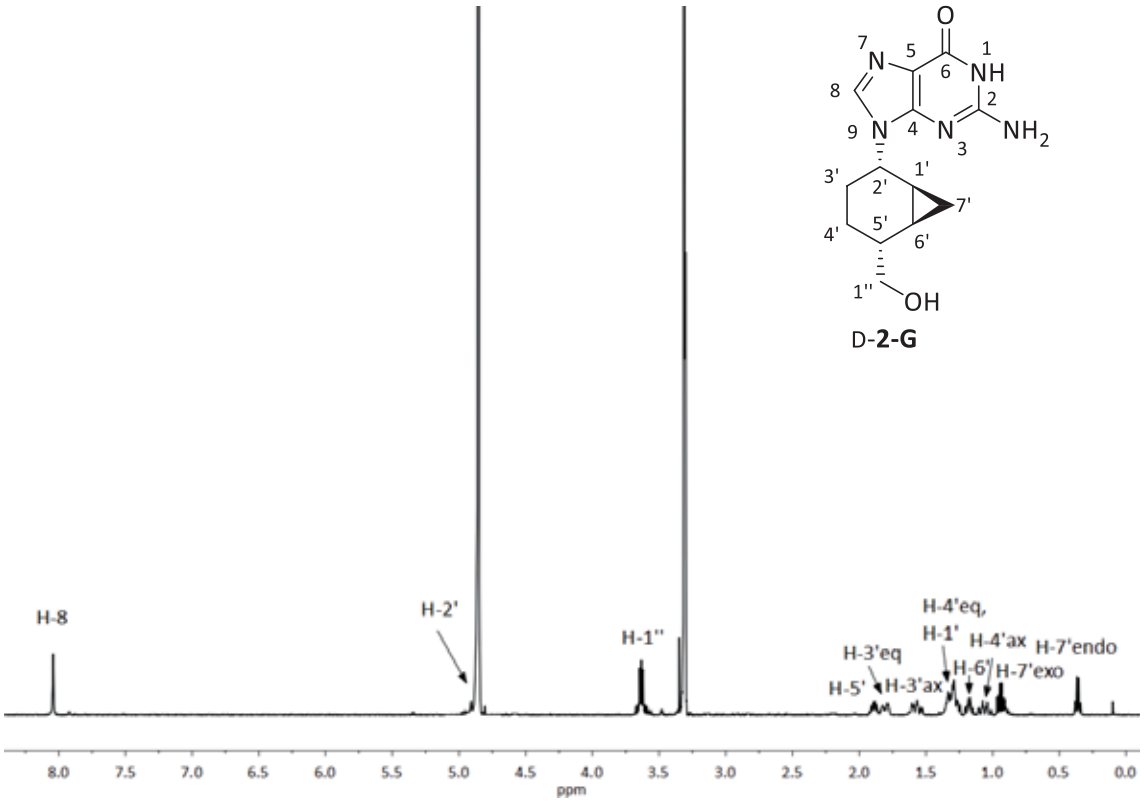


88

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

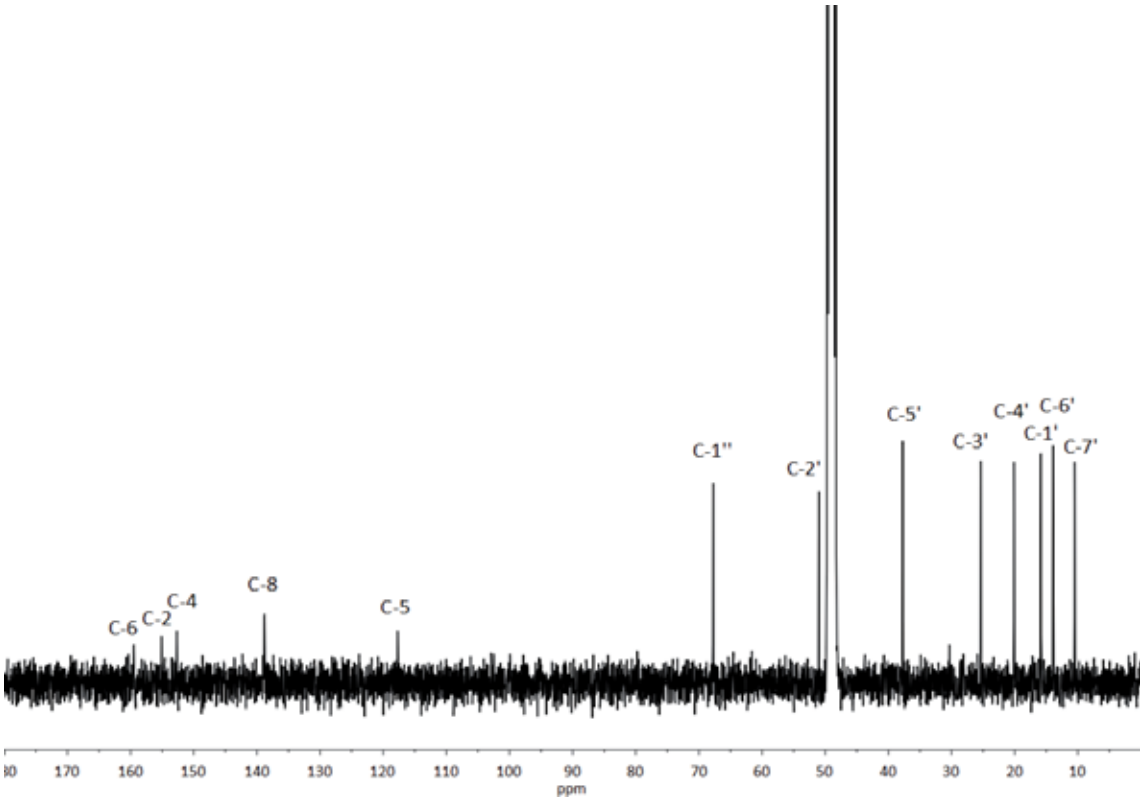


^{13}C-NMR (100 MHz, $CDCl_3$)

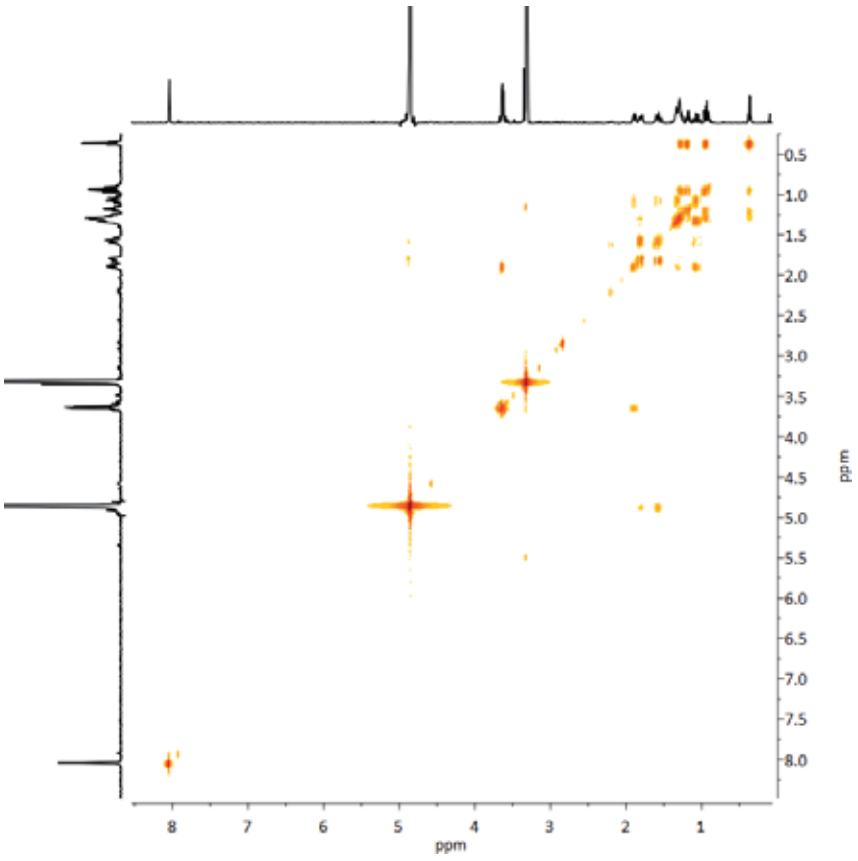


^{1}H-NMR (400 MHz, MeOD)

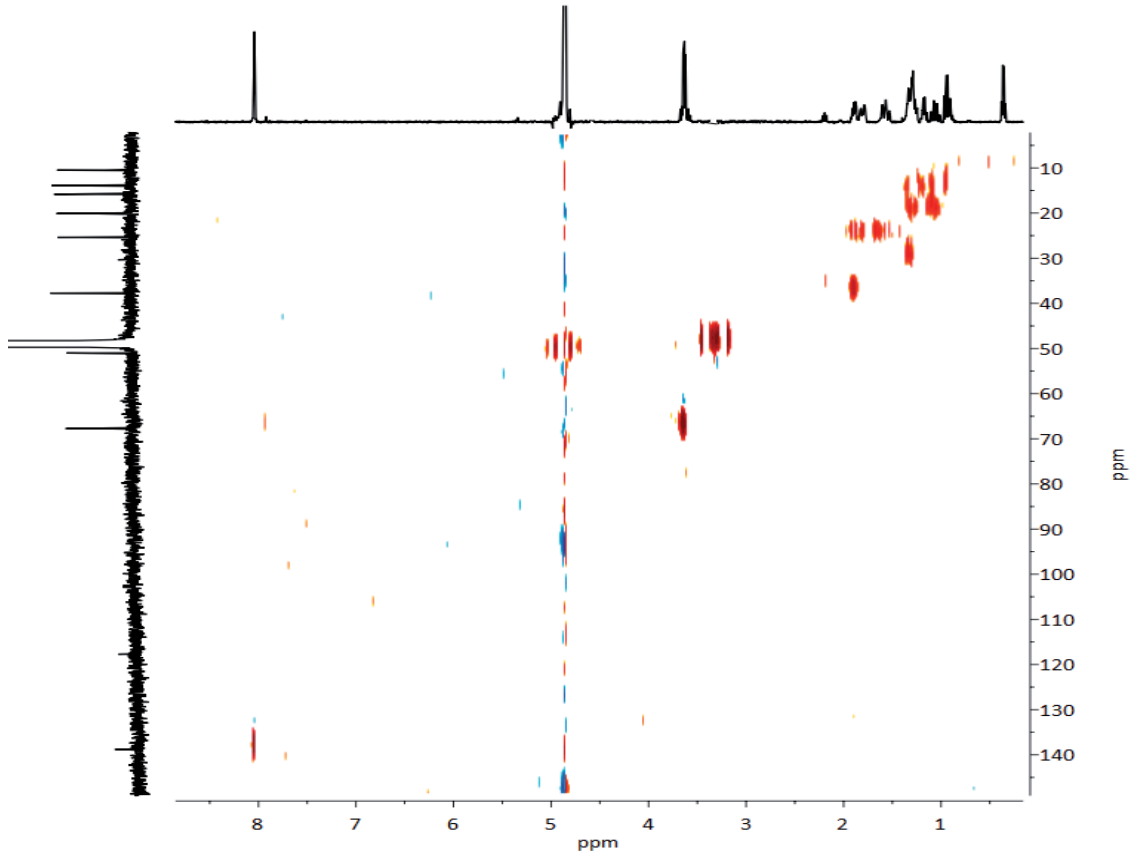
D-**2-G**



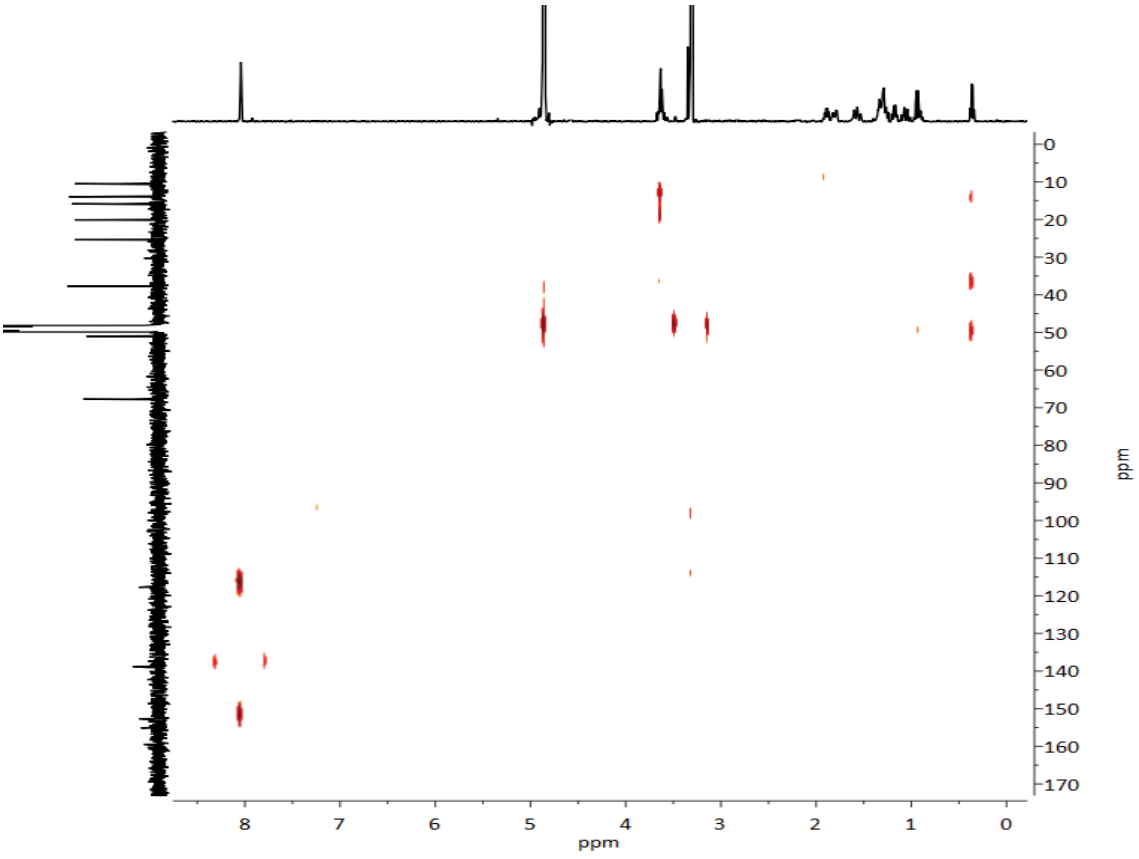
^{13}C-NMR (100 MHz, MeOD)



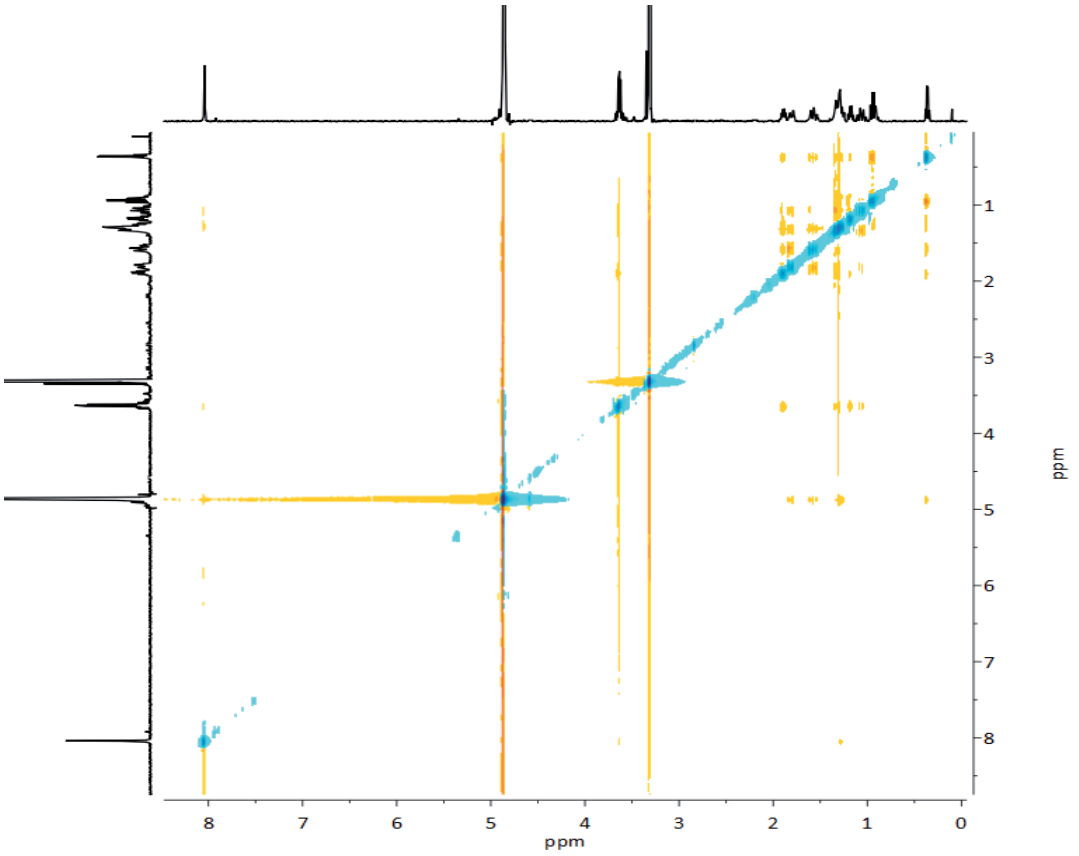
COSY (400 MHz, MeOD)



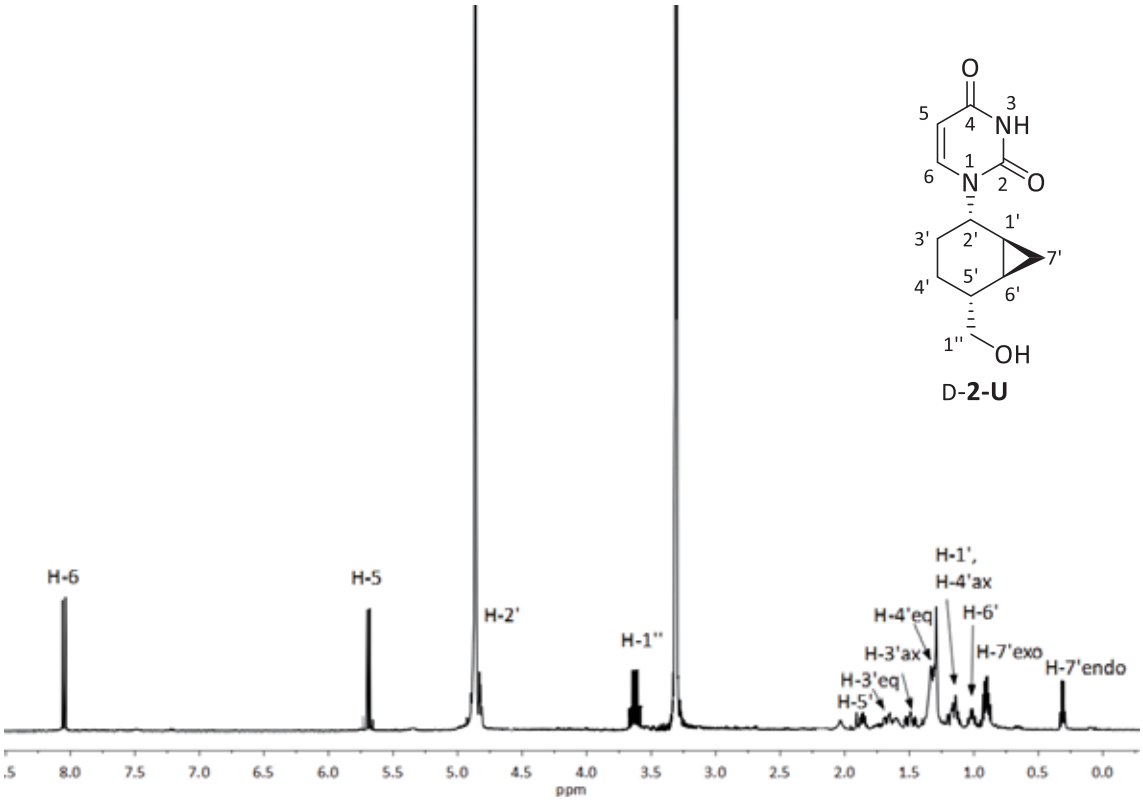
HSQC (400 MHz, MeOD)



HMBC (400 MHz, MeOD)

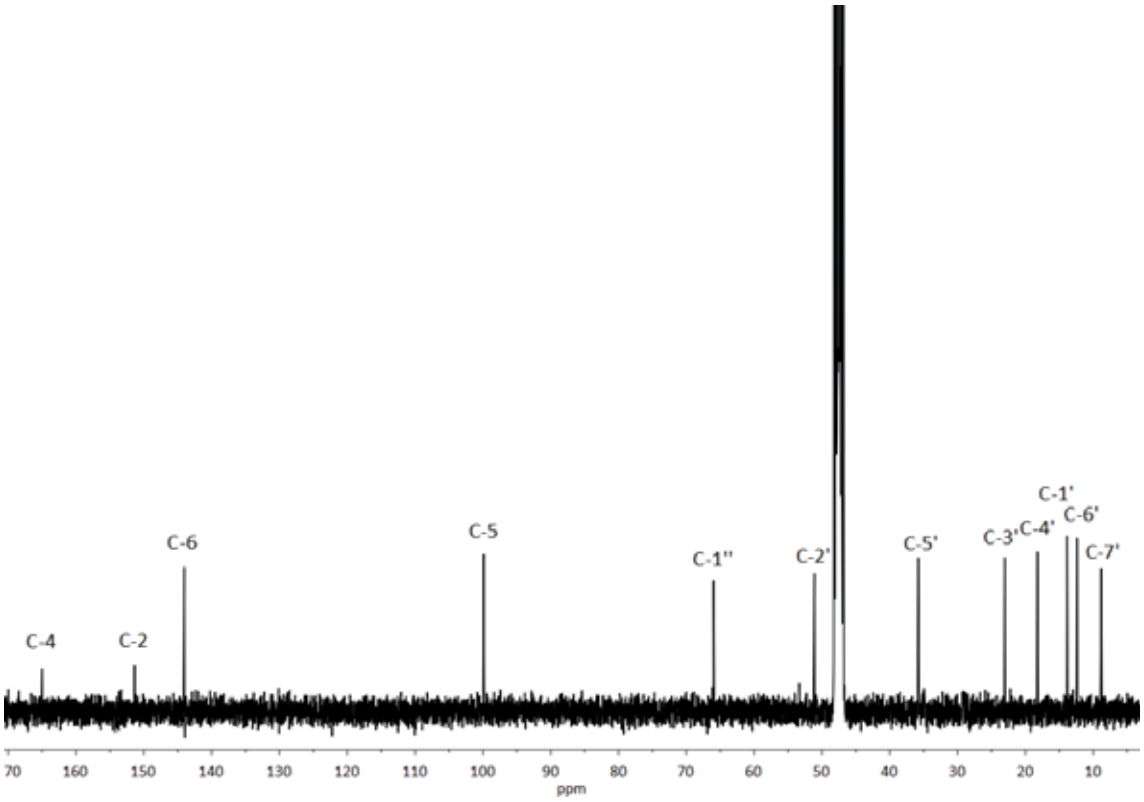


NOESY (400 MHz, MeOD)

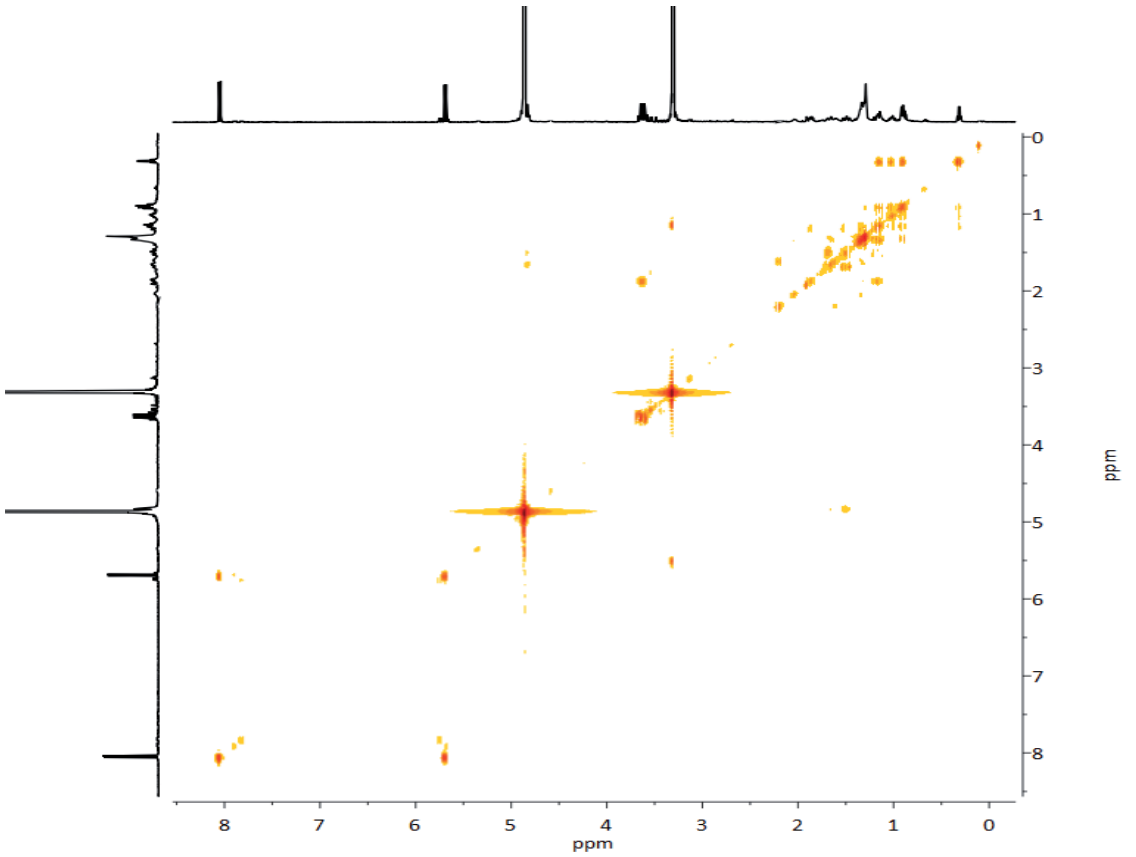


D-**2-U**

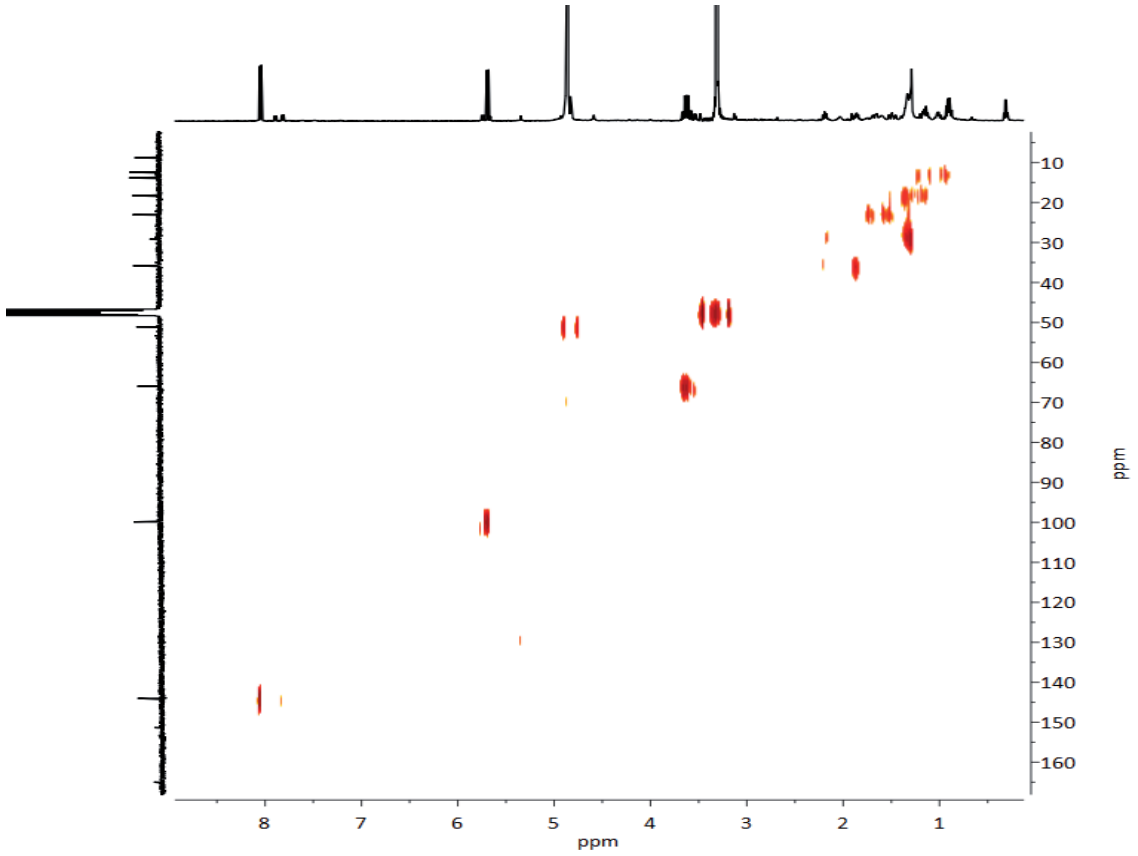
^{1}H-NMR (400 MHz, MeOD)



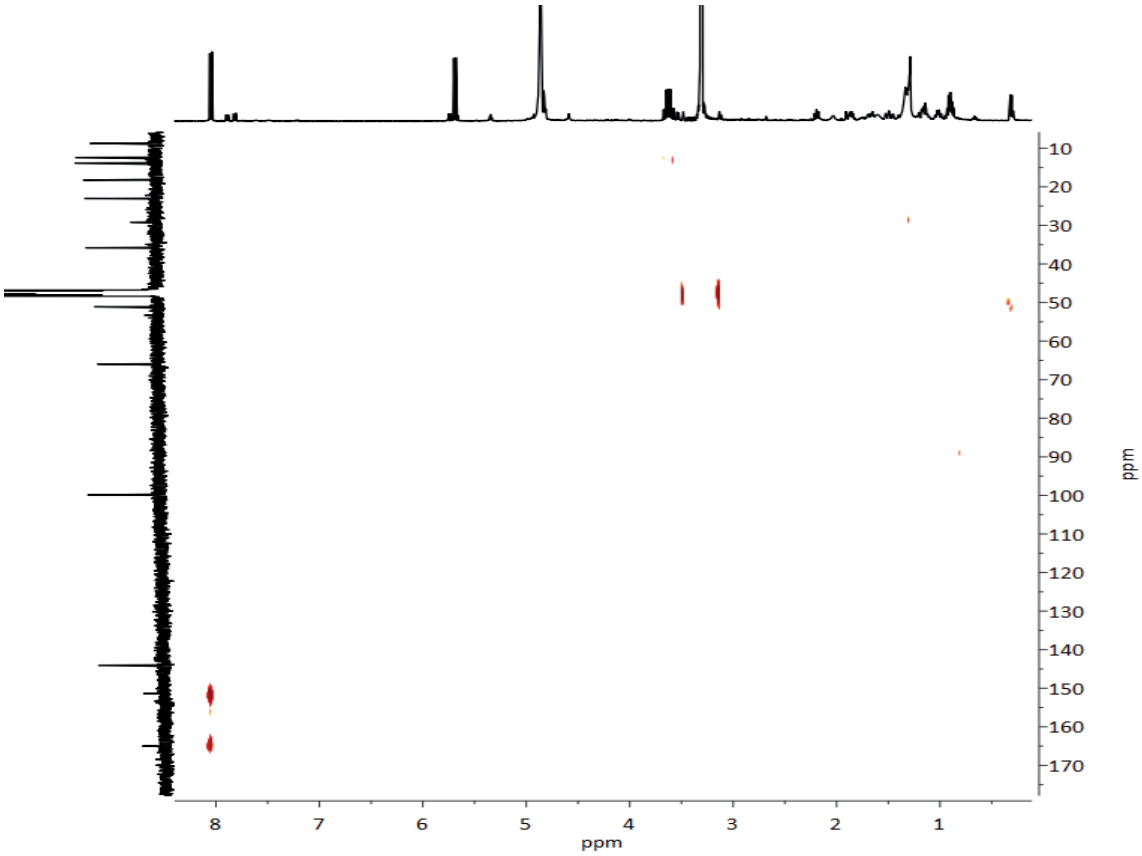
^{13}C-NMR (100 MHz, MeOD)



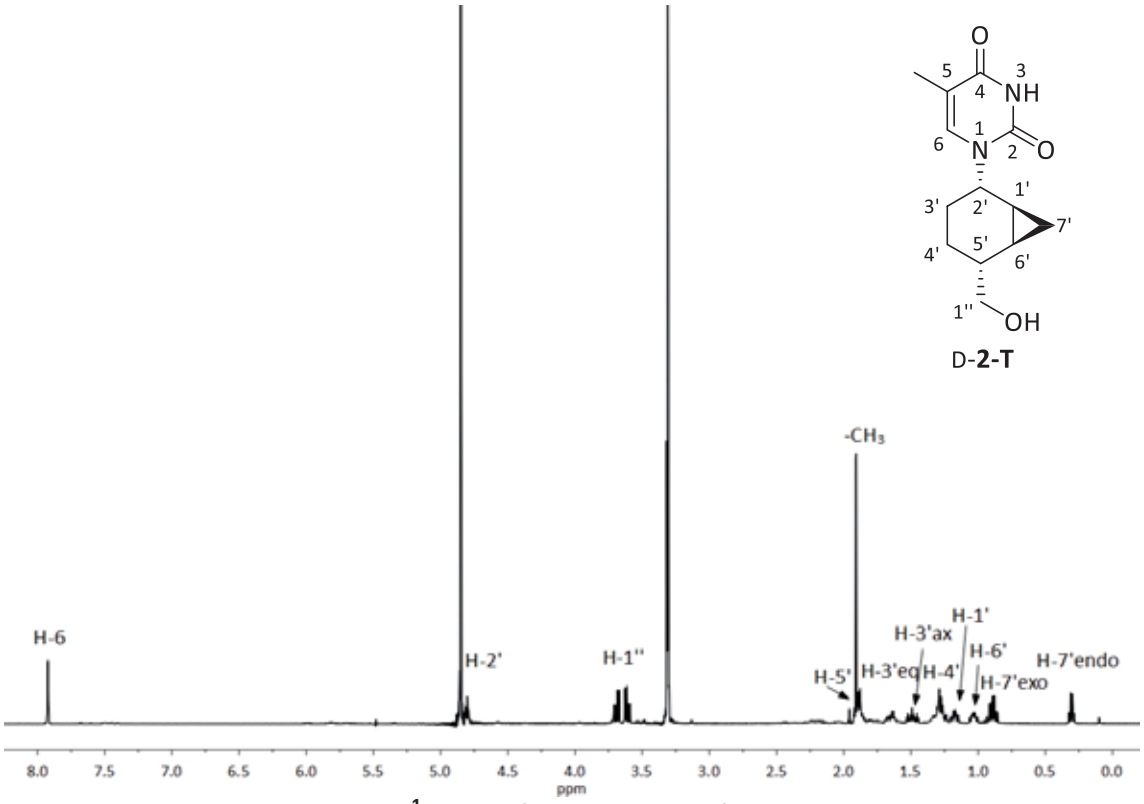
COSY (400 MHz, MeOD)



HSQC (400 MHz, MeOD)

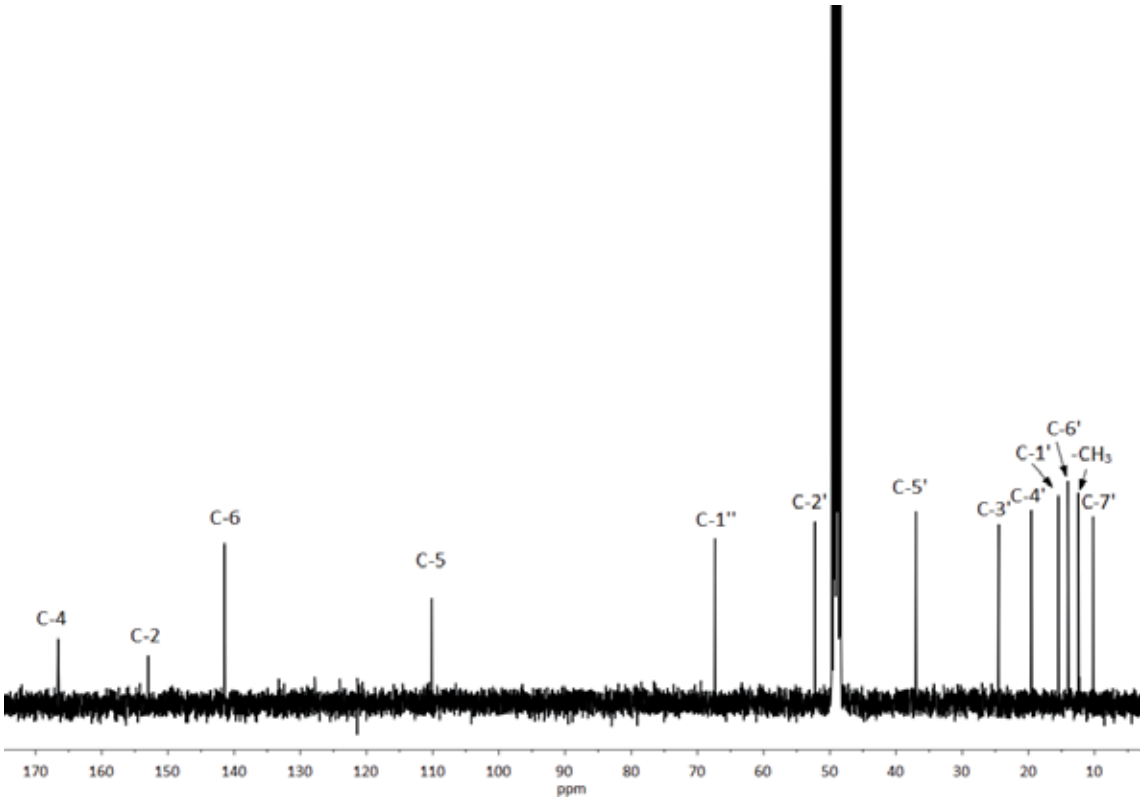


HMBC (400 MHz, MeOD)

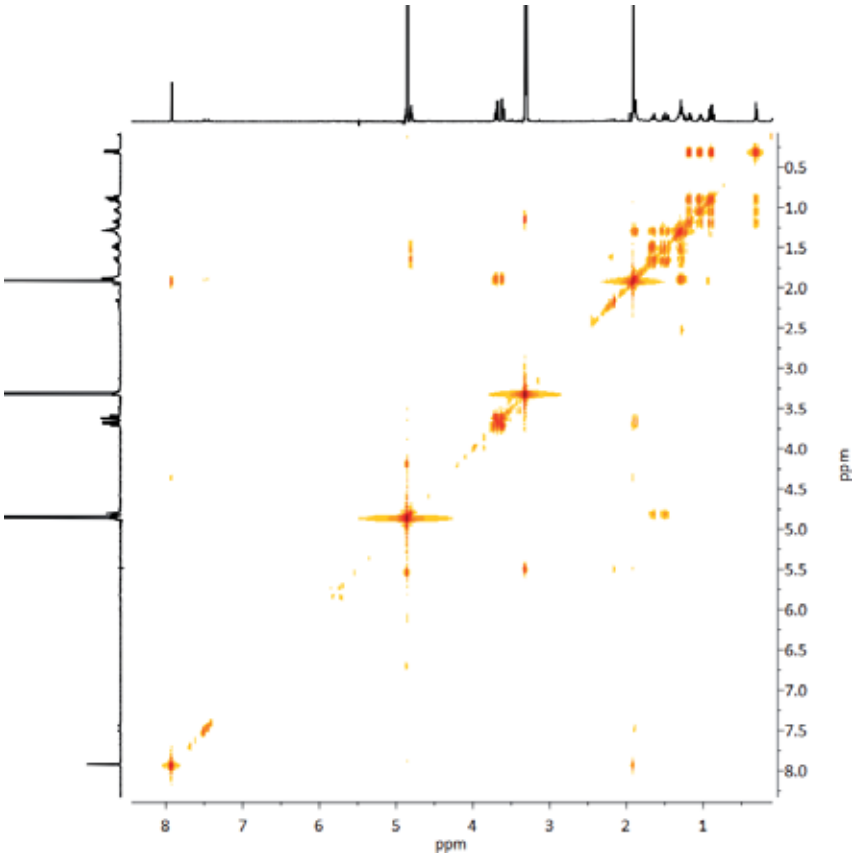


D-**2-T**

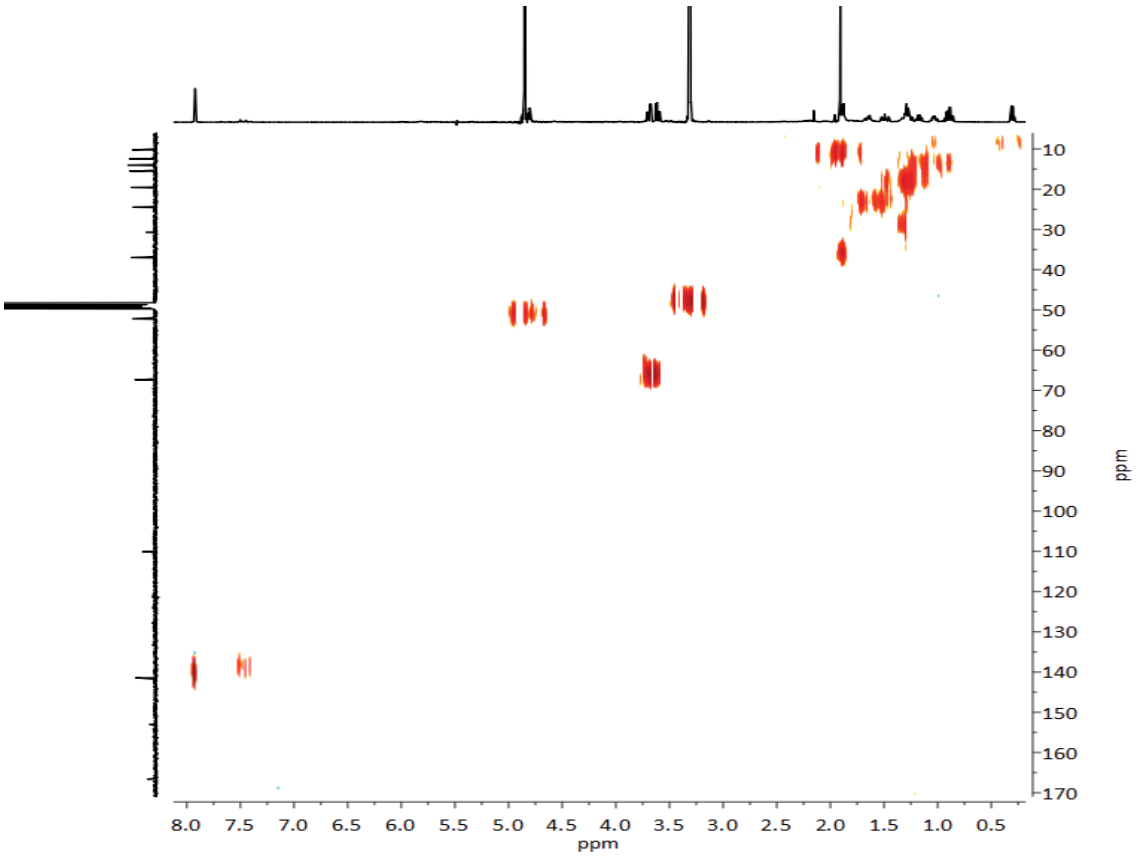
^{1}H-NMR (400 MHz, MeOD)



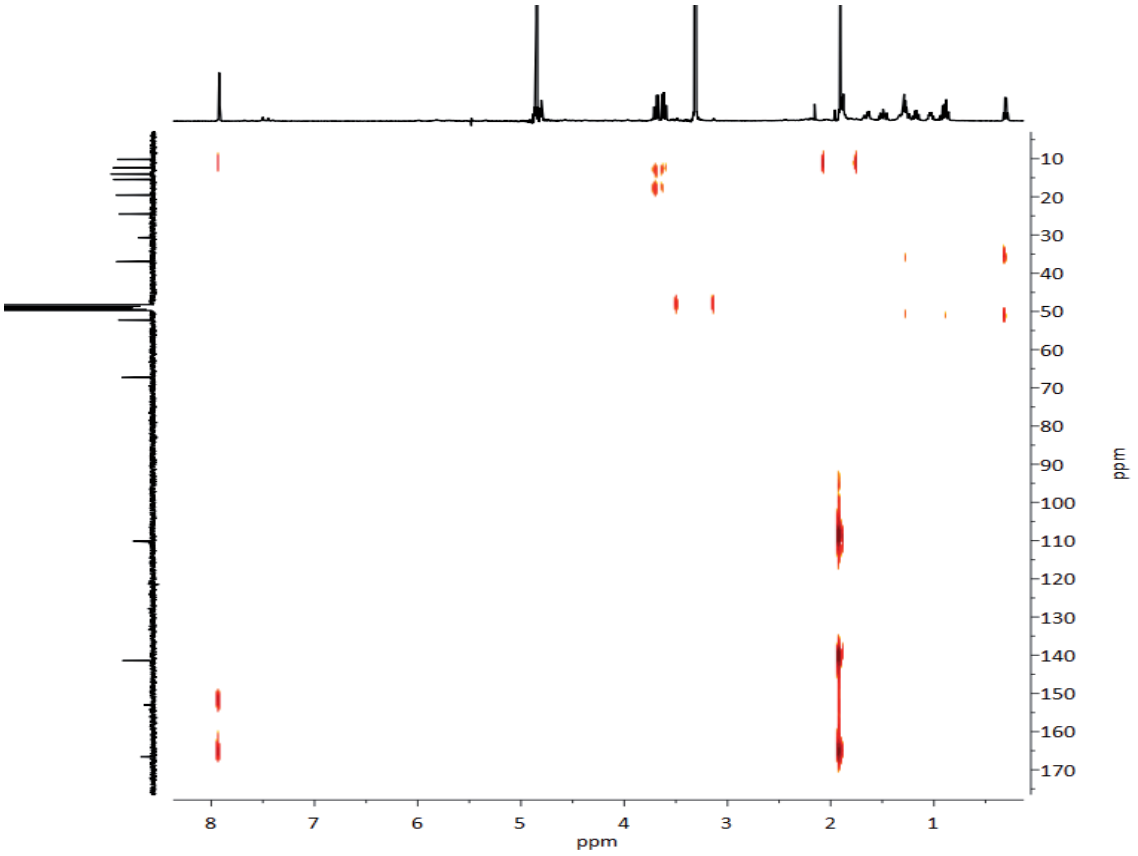
^{13}C-NMR (100 MHz, MeOD)



COSY (400 MHz, MeOD)



HSQC (400 MHz, MeOD)



HMBC (400 MHz, MeOD)

Universitat Autònoma de Barcelona

Appendix A

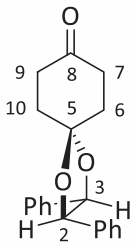
NMR spectra

Beatriz Domínguez Pérez

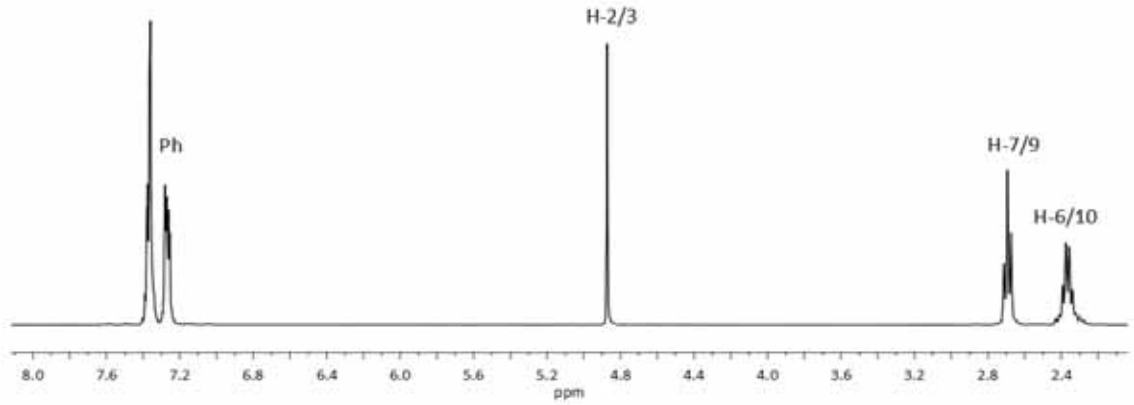
Ph.D. Thesis
Ph.D. in Chemistry

Supervisors:
Dr. Ramon Alibés Arqués
Dr. Félix Busqué Sánchez
Dr. Jean-Didier Márechal

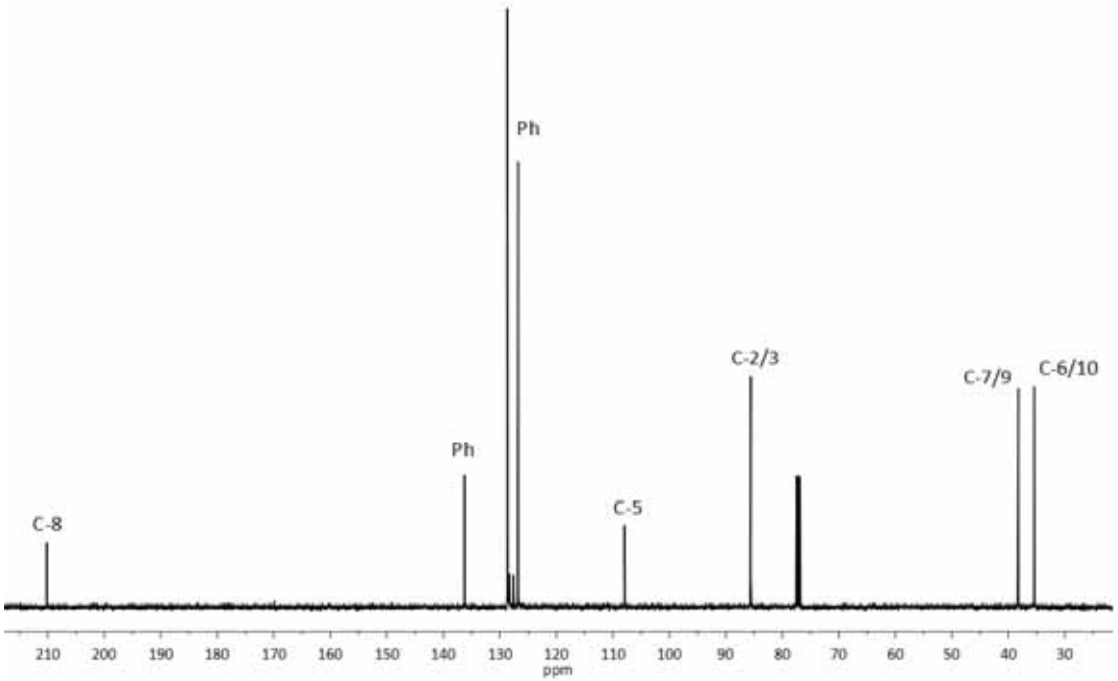
Departament de Química
Facultat de Ciències
2015



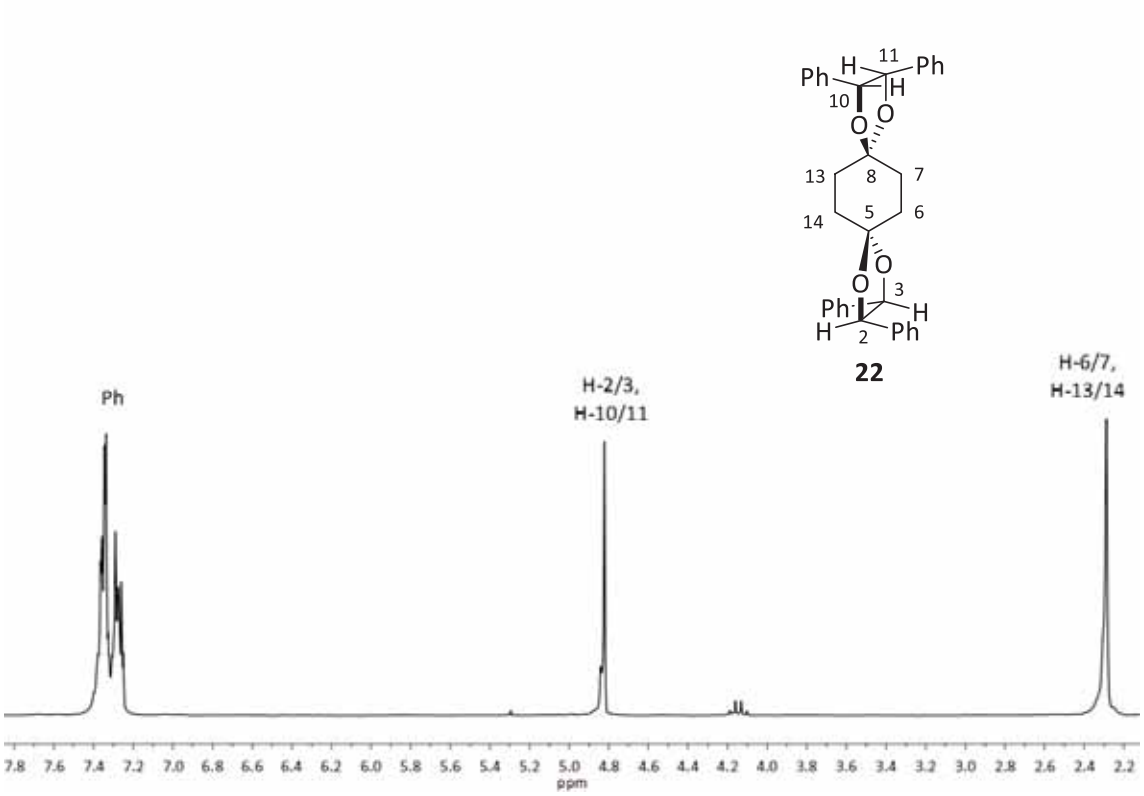
11



^{1}H-NMR (360 MHz, $CDCl_3$)

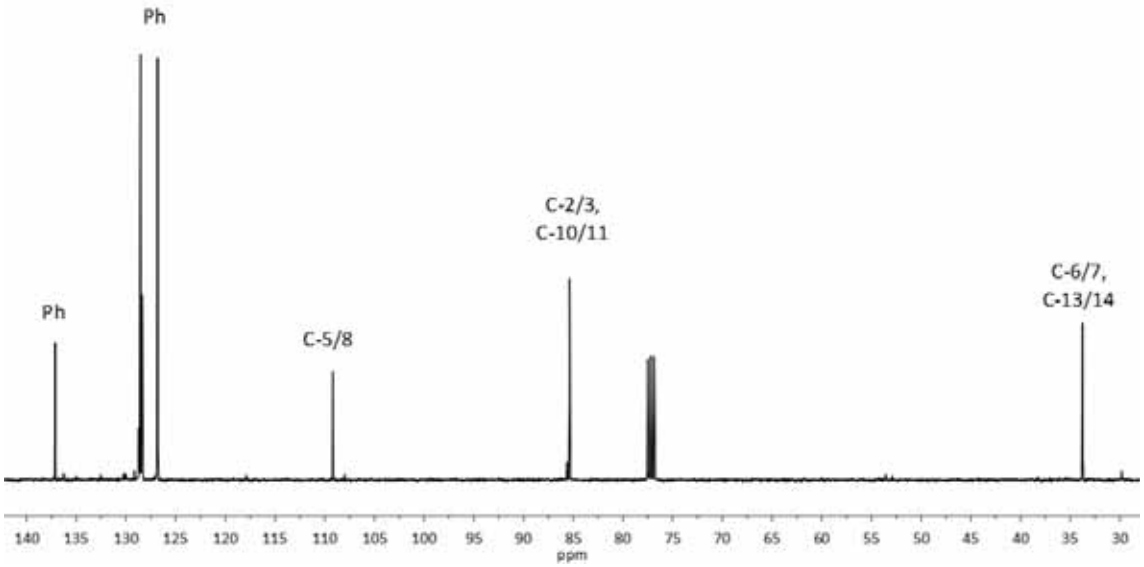


^{13}C-NMR (100 MHz, $CDCl_3$)

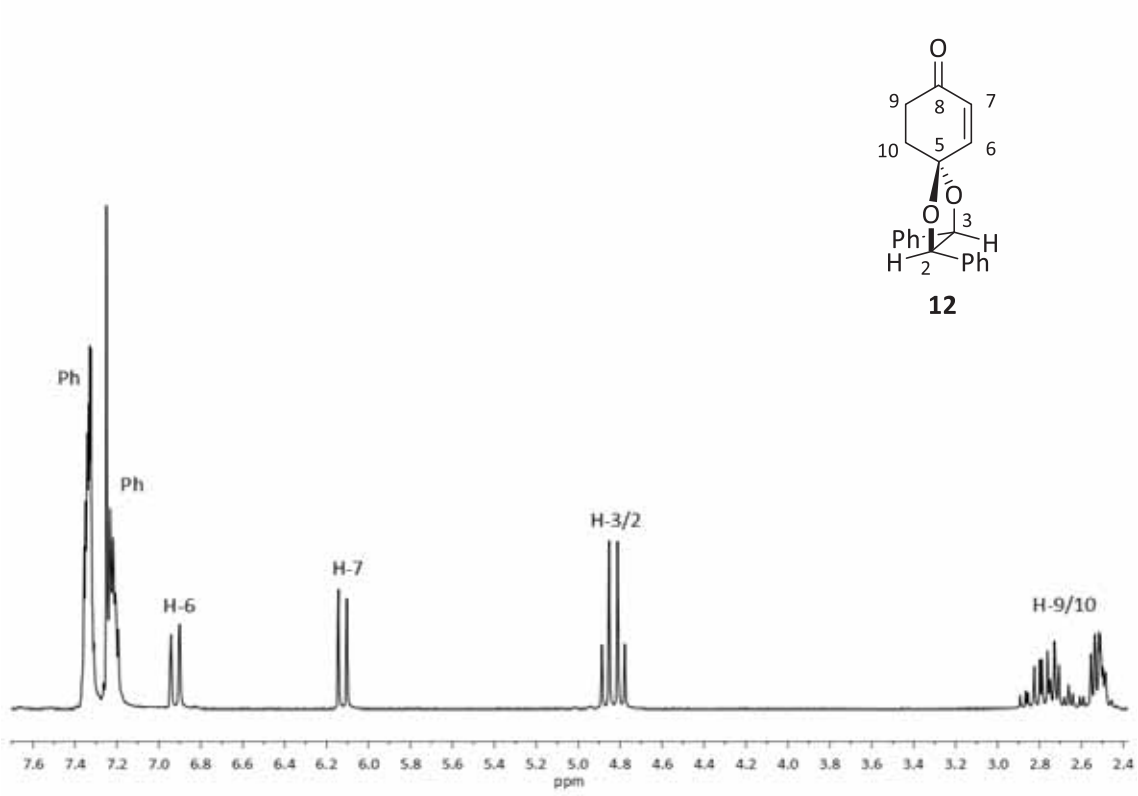


22

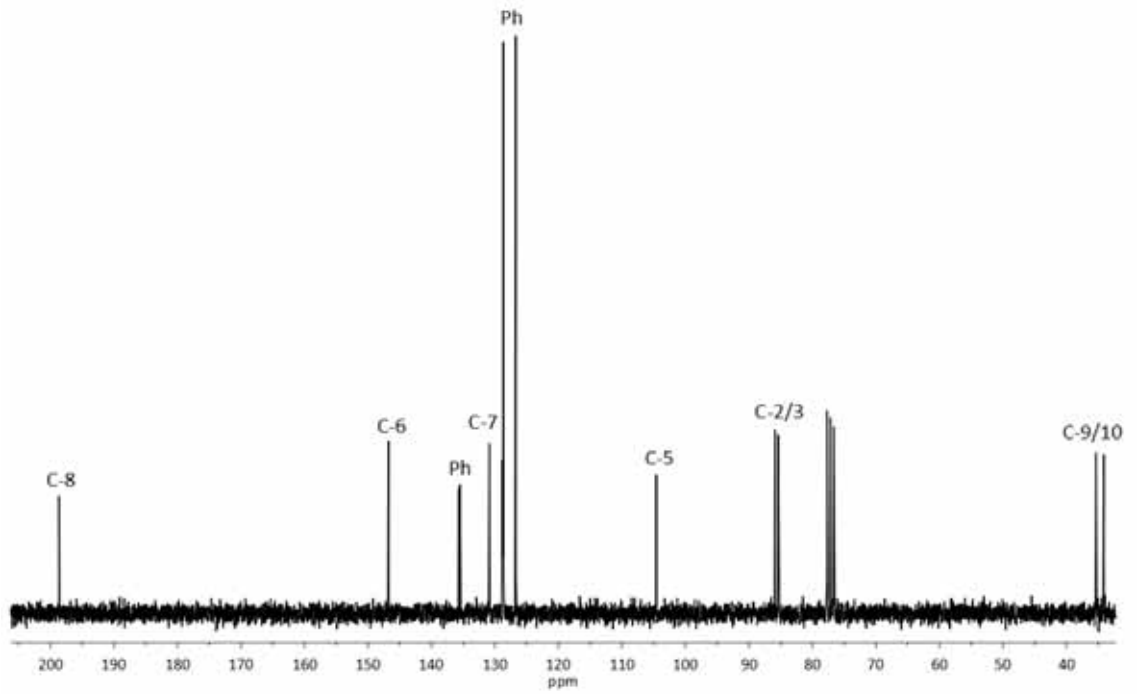
^{1}H-NMR (250 MHz, $CDCl_3$)



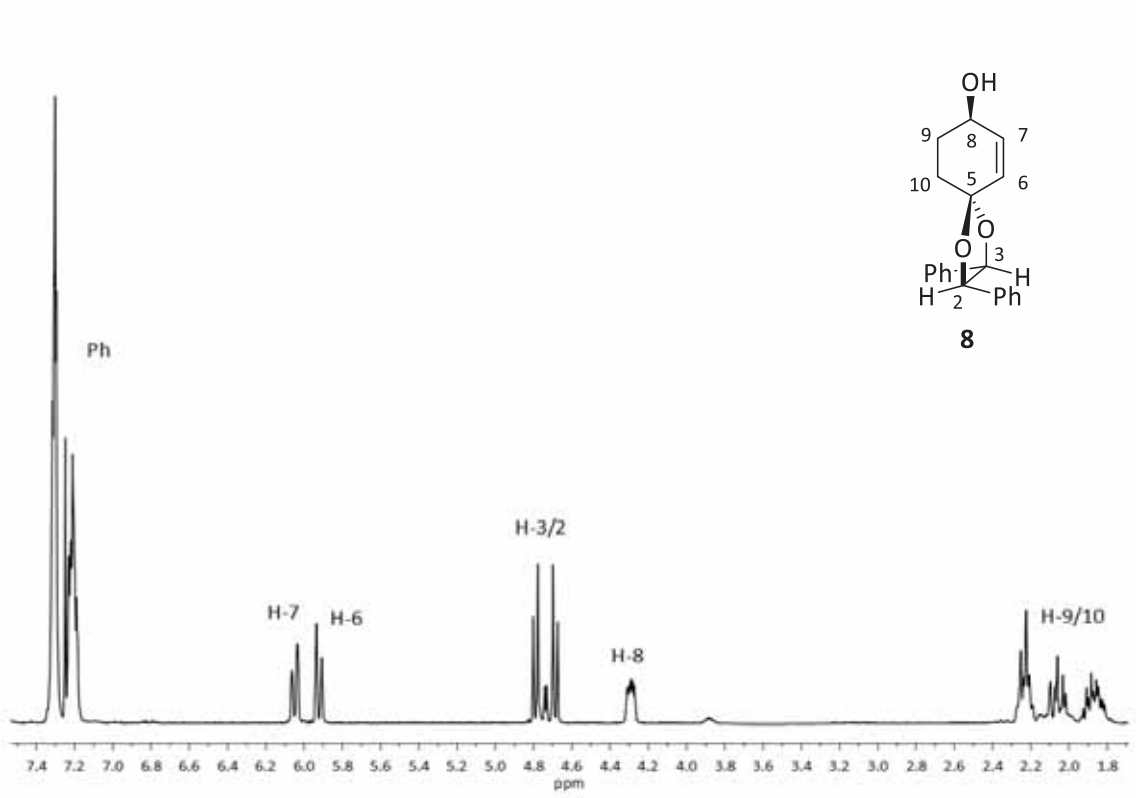
^{13}C-NMR (400 MHz, $CDCl_3$)



^{1}H-NMR (250 MHz, $CDCl_3$)

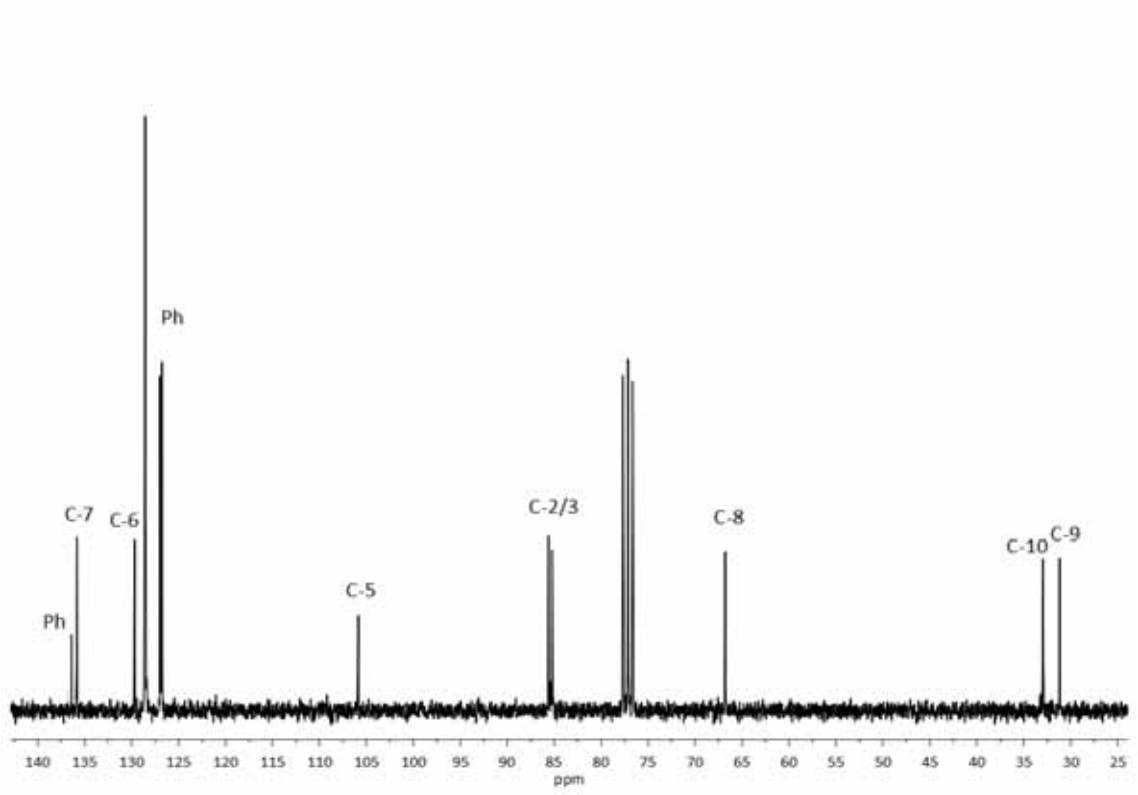


^{13}C-NMR (63 MHz, $CDCl_3$)

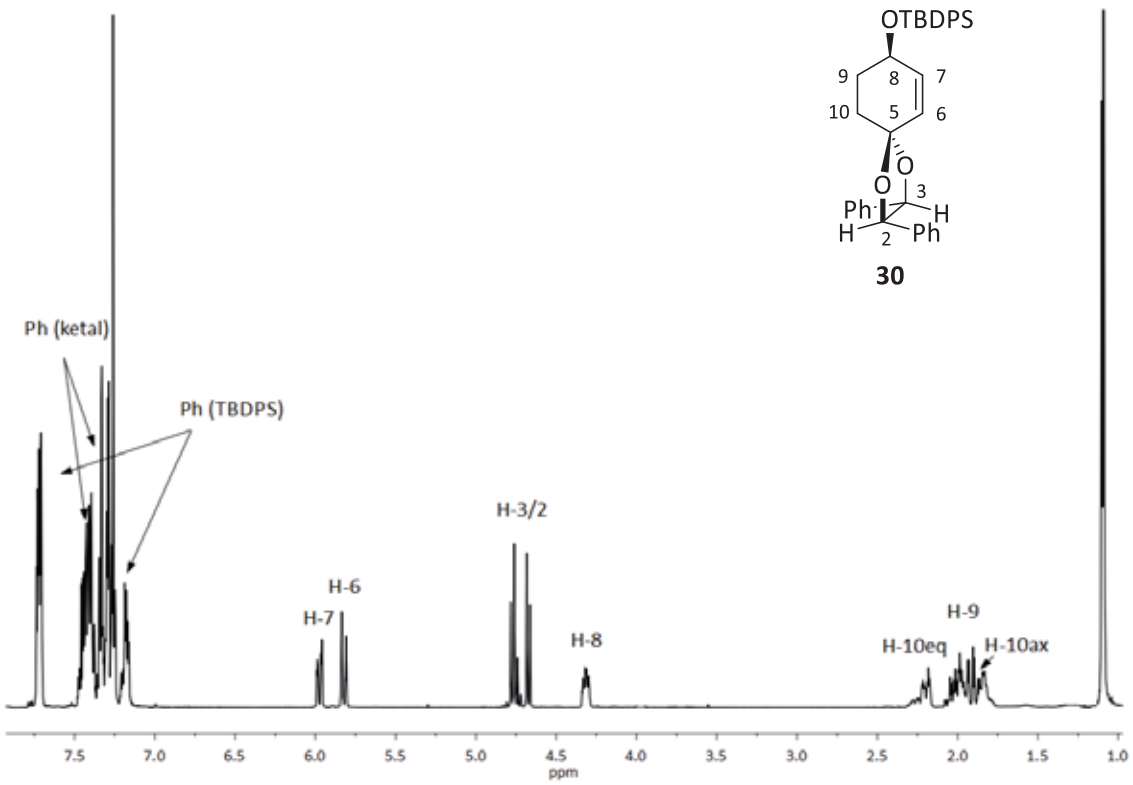


8

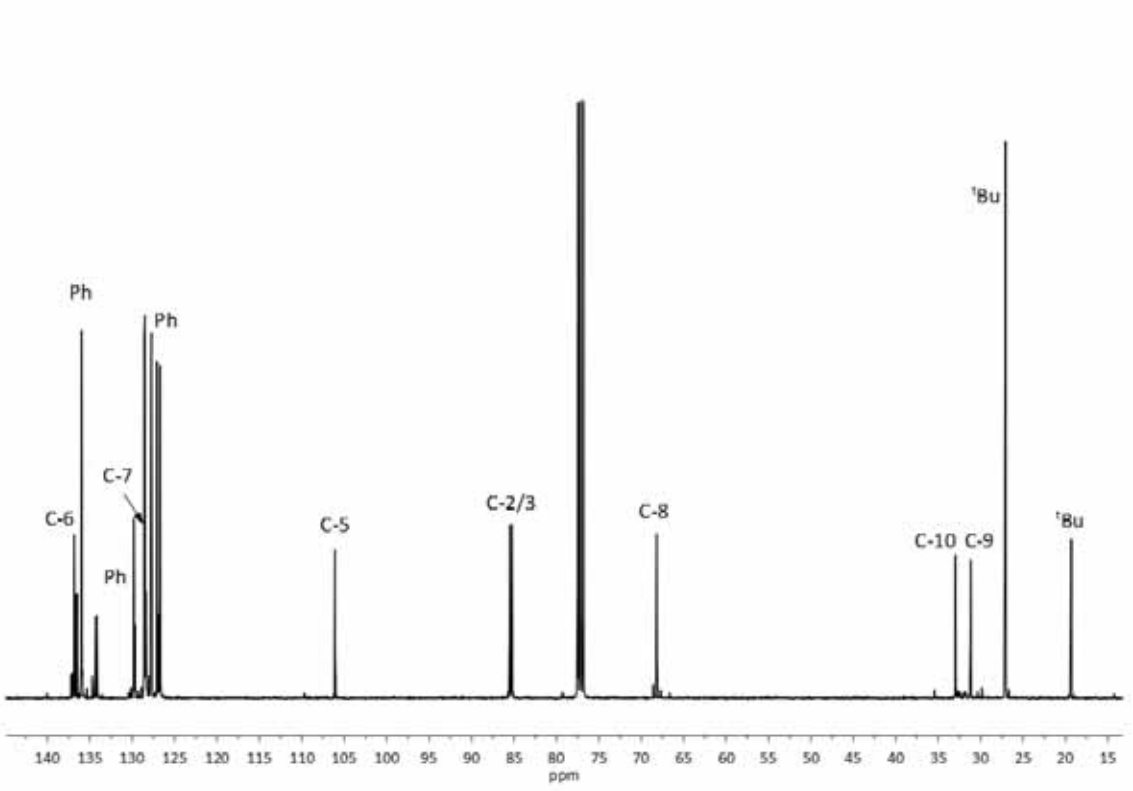
^{1}H-NMR (400 MHz, $CDCl_3$)



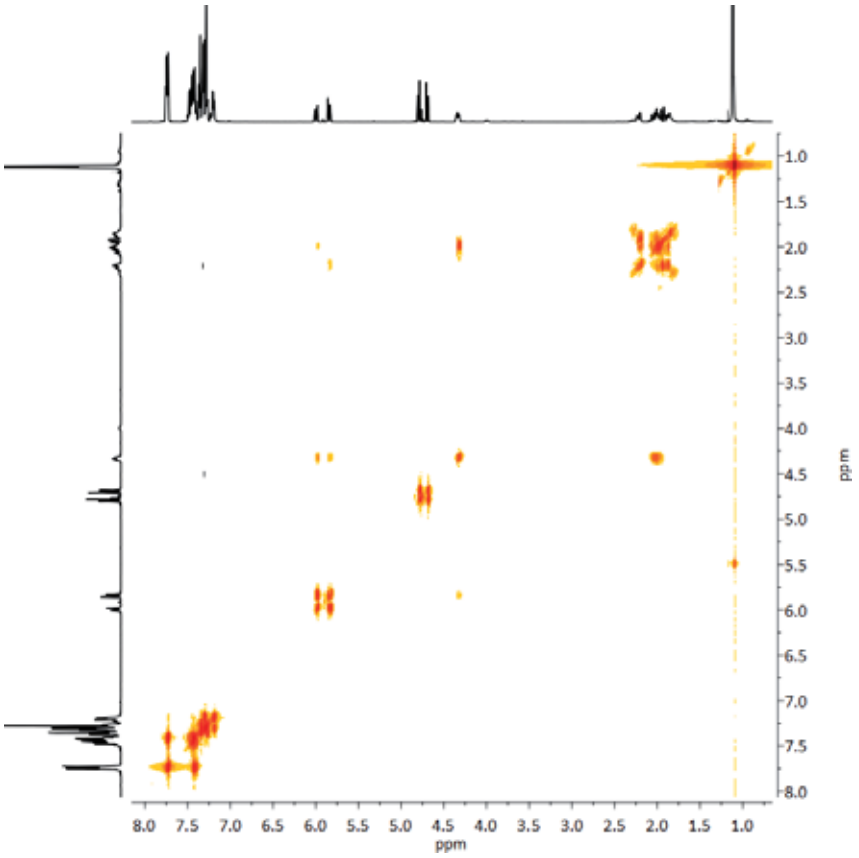
^{13}C-NMR (100 MHz, $CDCl_3$)



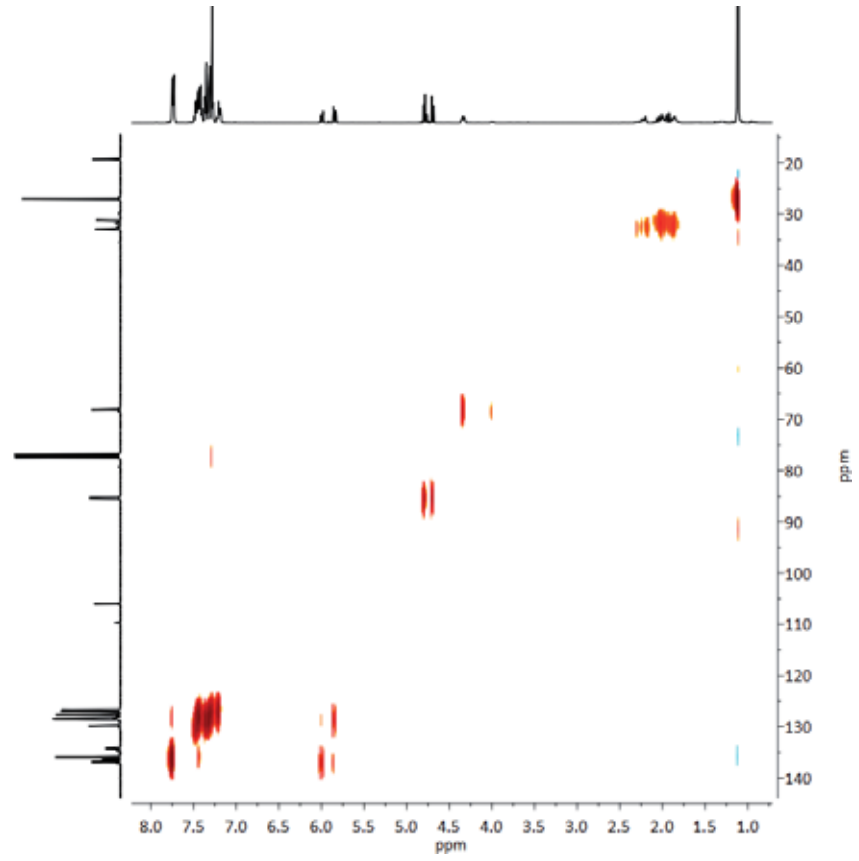
^{1}H-NMR (400 MHz, $CDCl_3$)



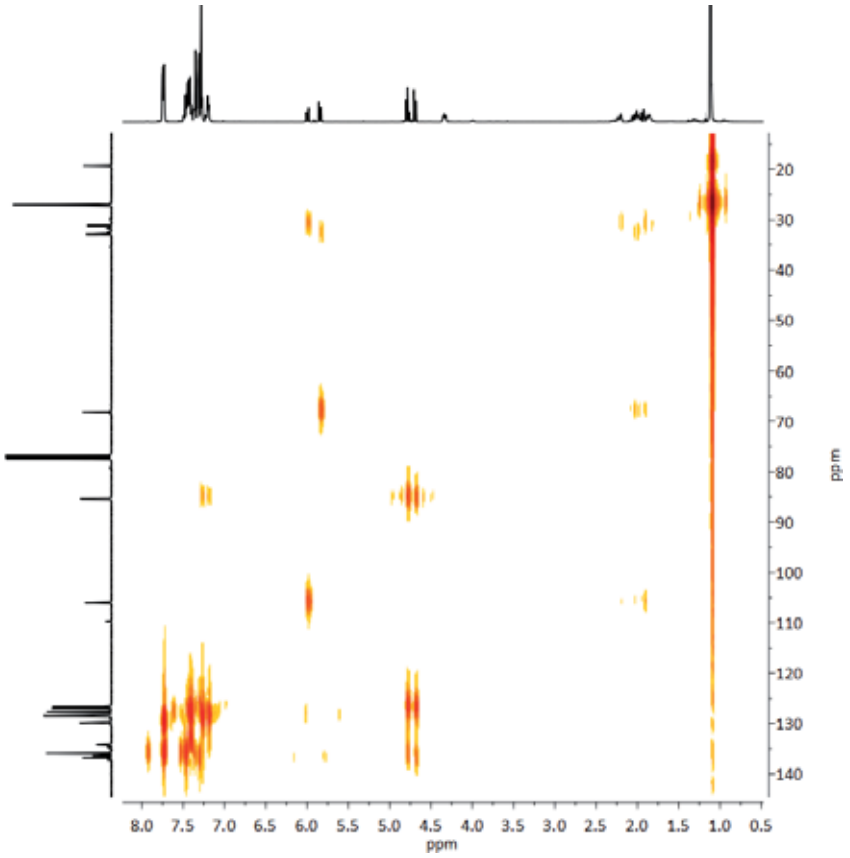
^{13}C-NMR (100 MHz, $CDCl_3$)



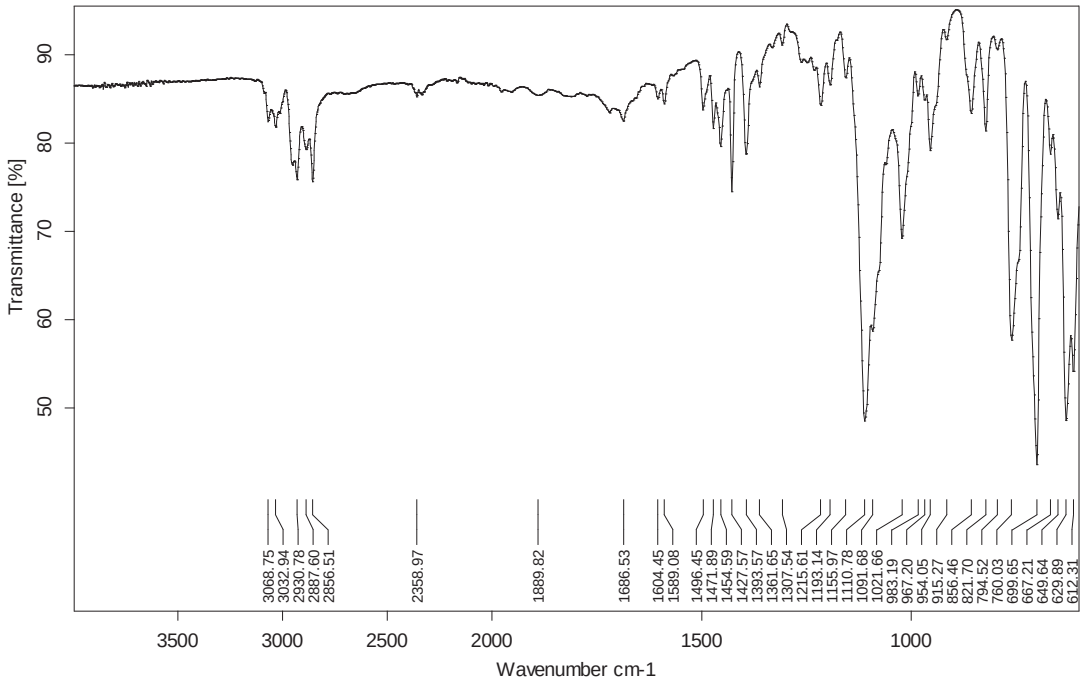
COSY (400 MHz, $CDCl_3$)



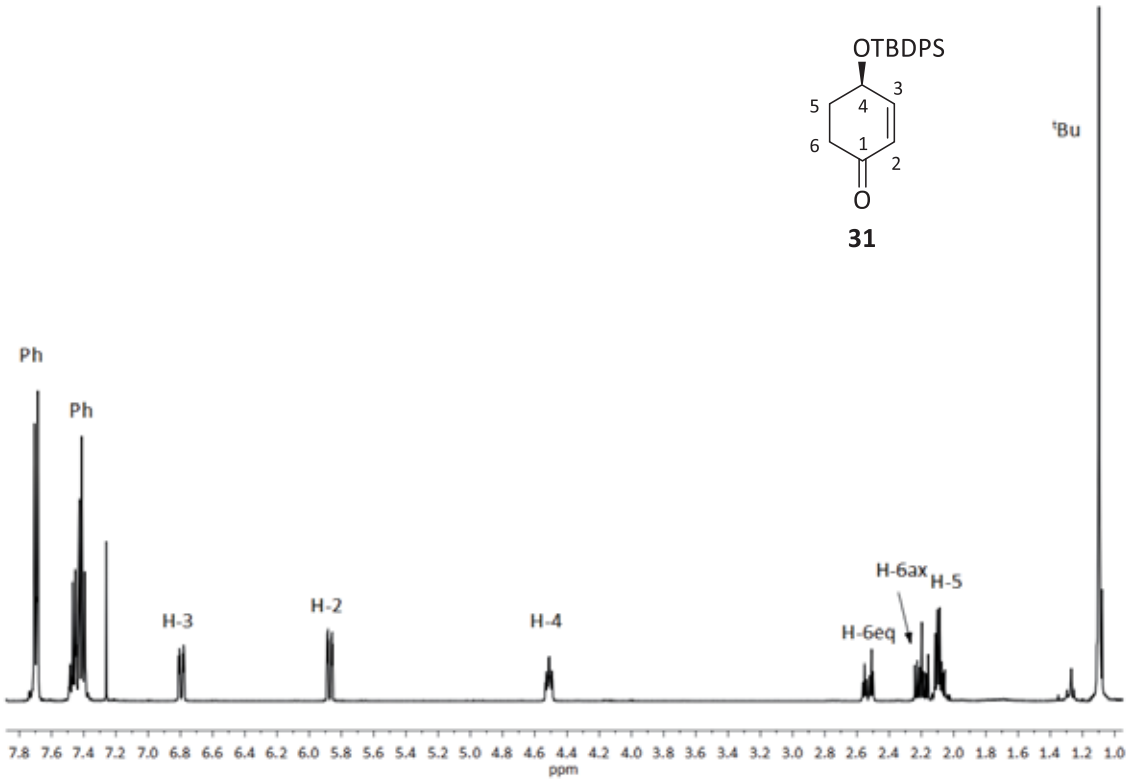
HSQC (400 MHz, $CDCl_3$)



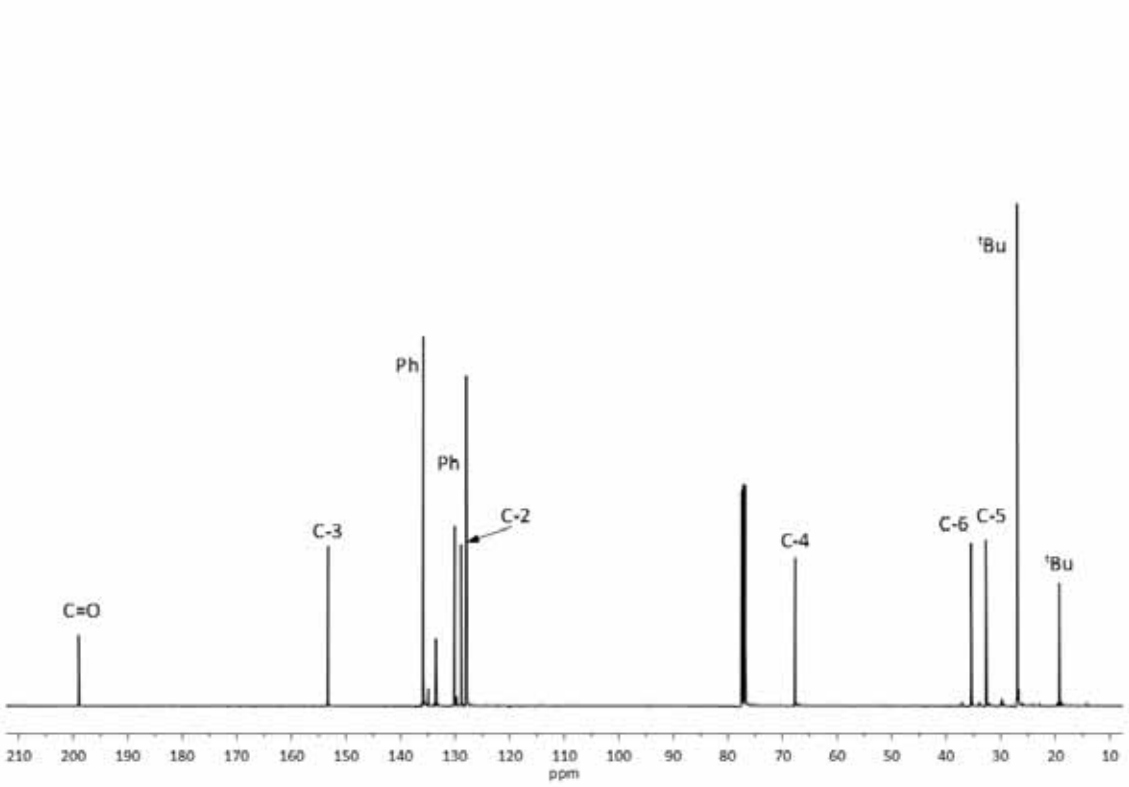
HMBC (400 MHz, $CDCl_3$)



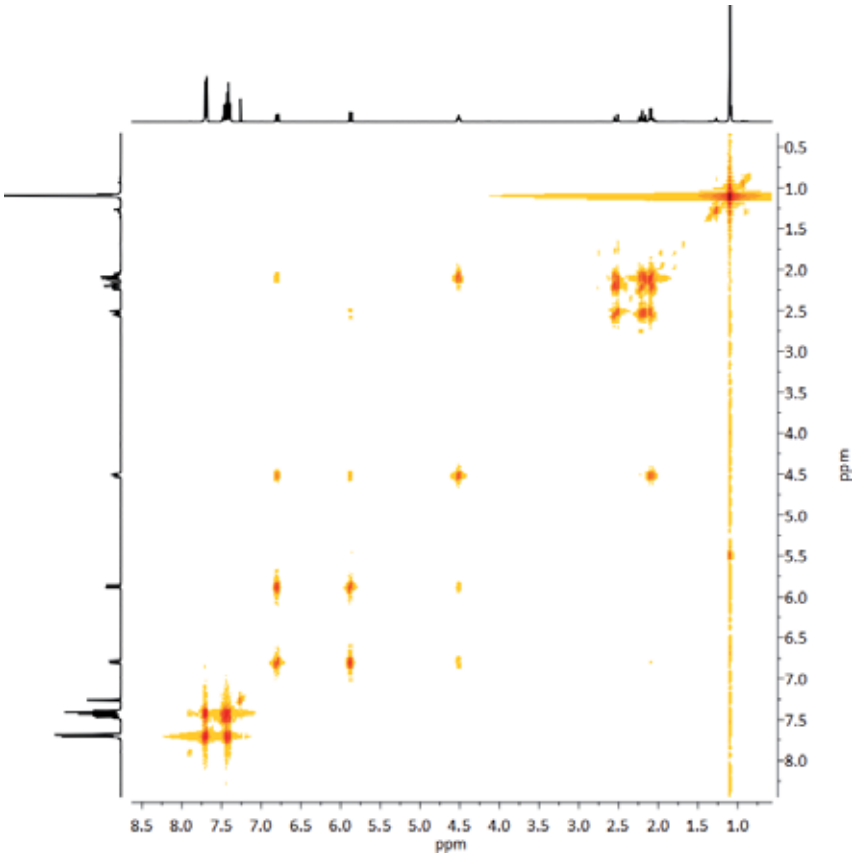
IR (ATR)



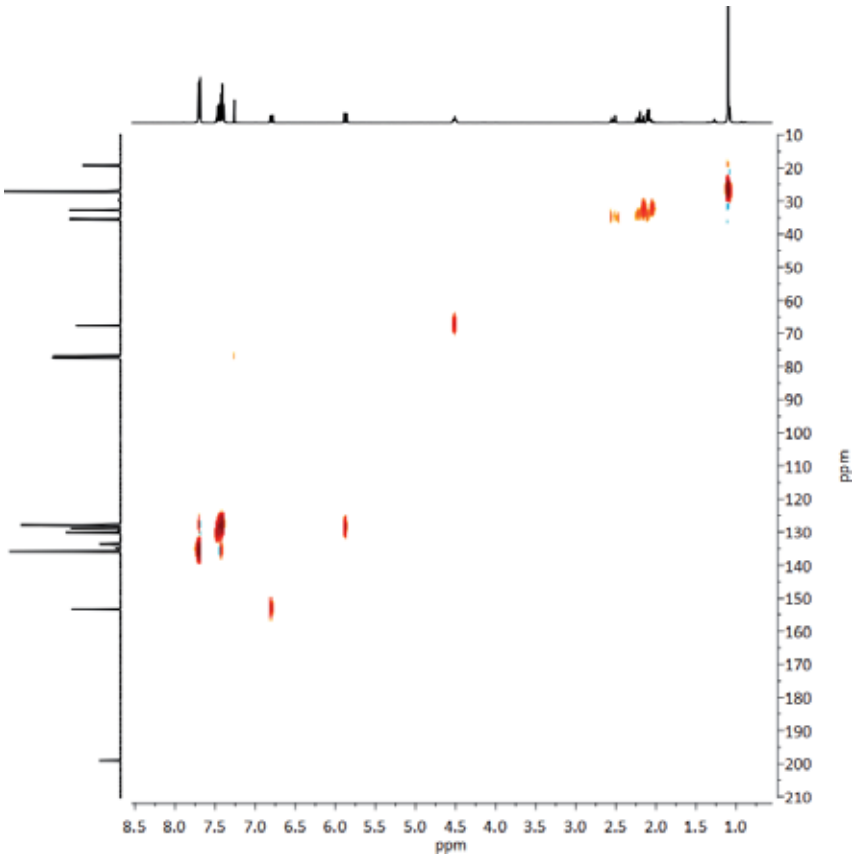
^{1}H-NMR (400 MHz, $CDCl_3$)



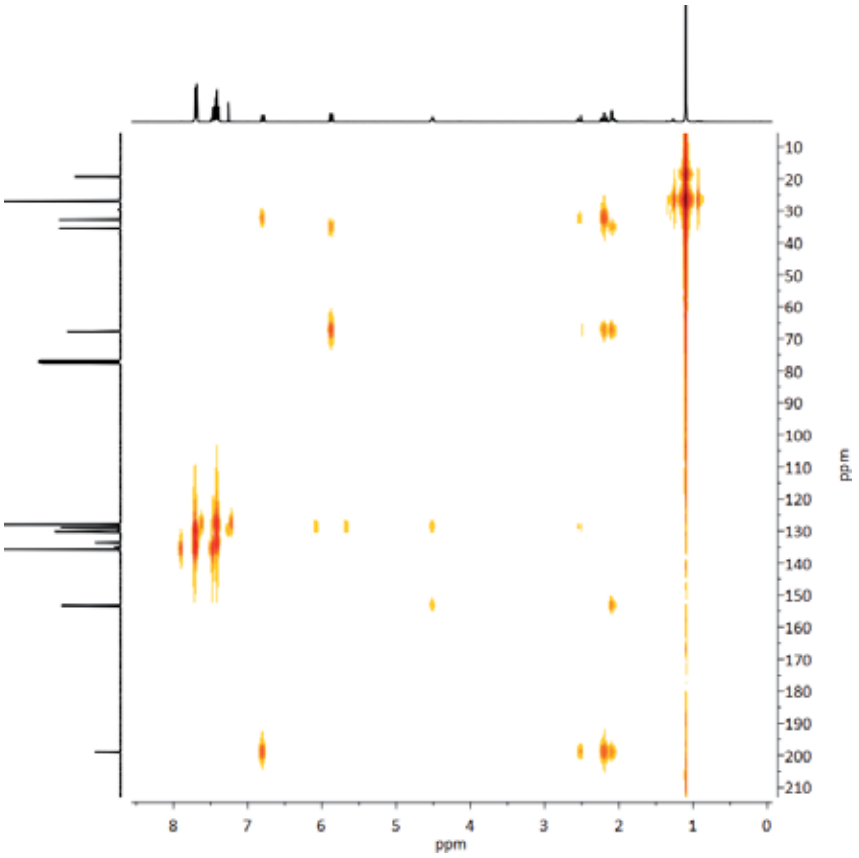
^{13}C-NMR (100 MHz, $CDCl_3$)



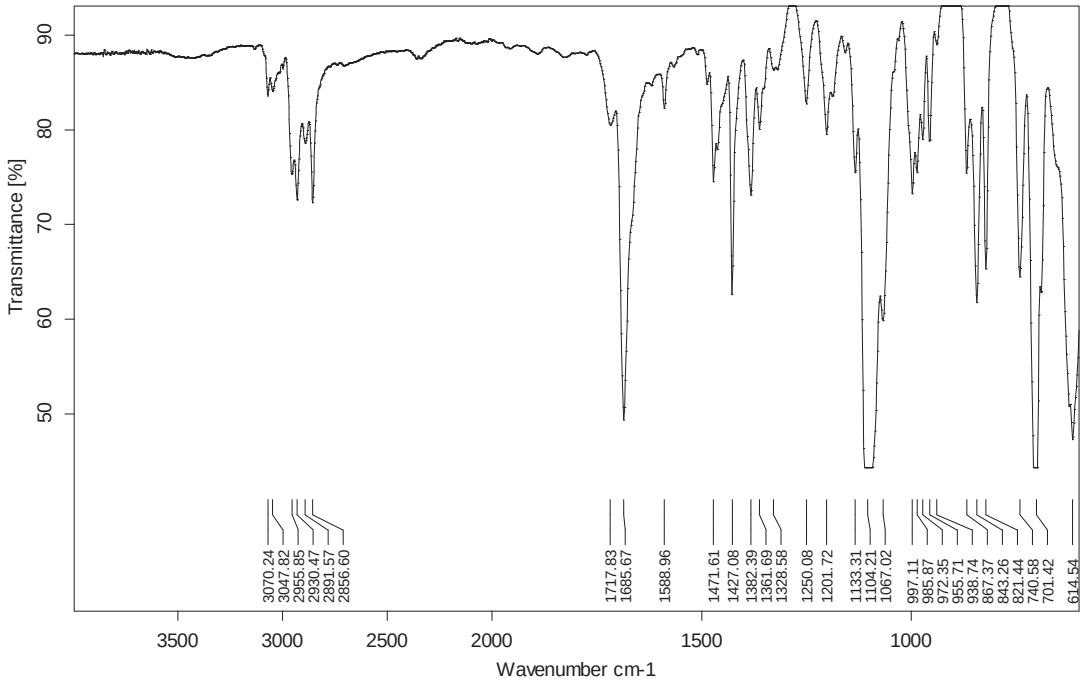
COSY (400 MHz, $CDCl_3$)



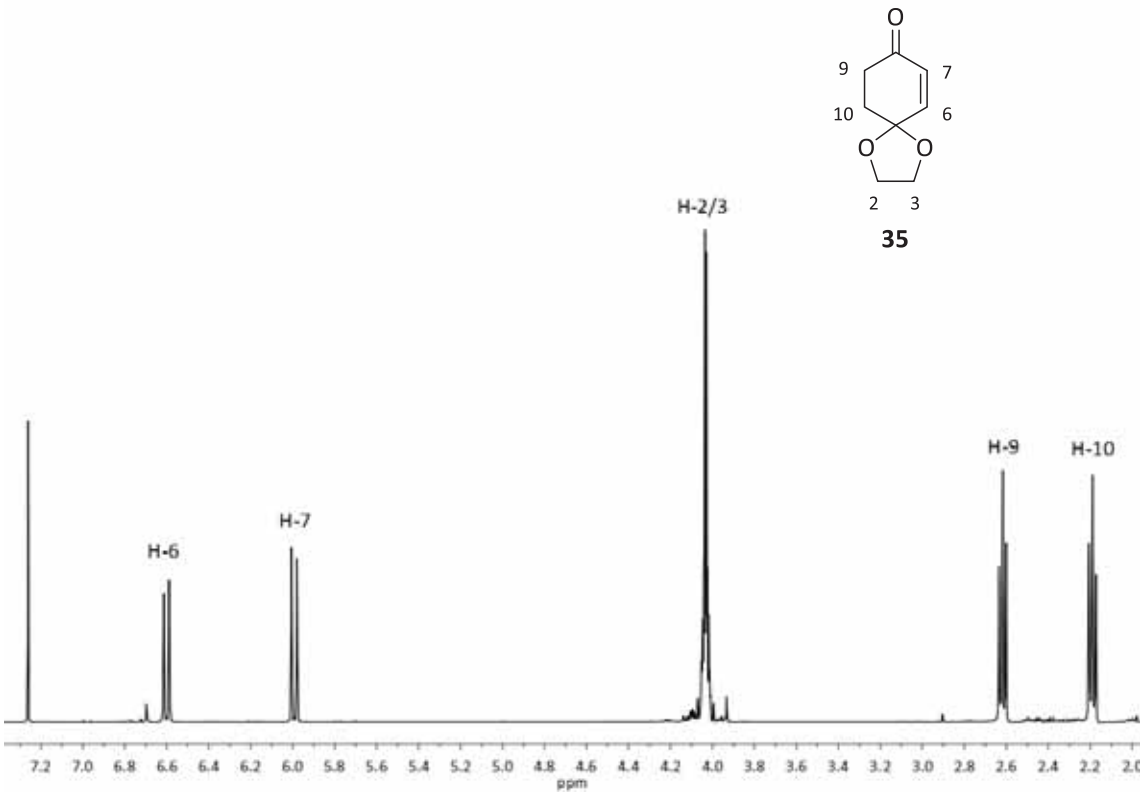
HSQC (400 MHz, $CDCl_3$)



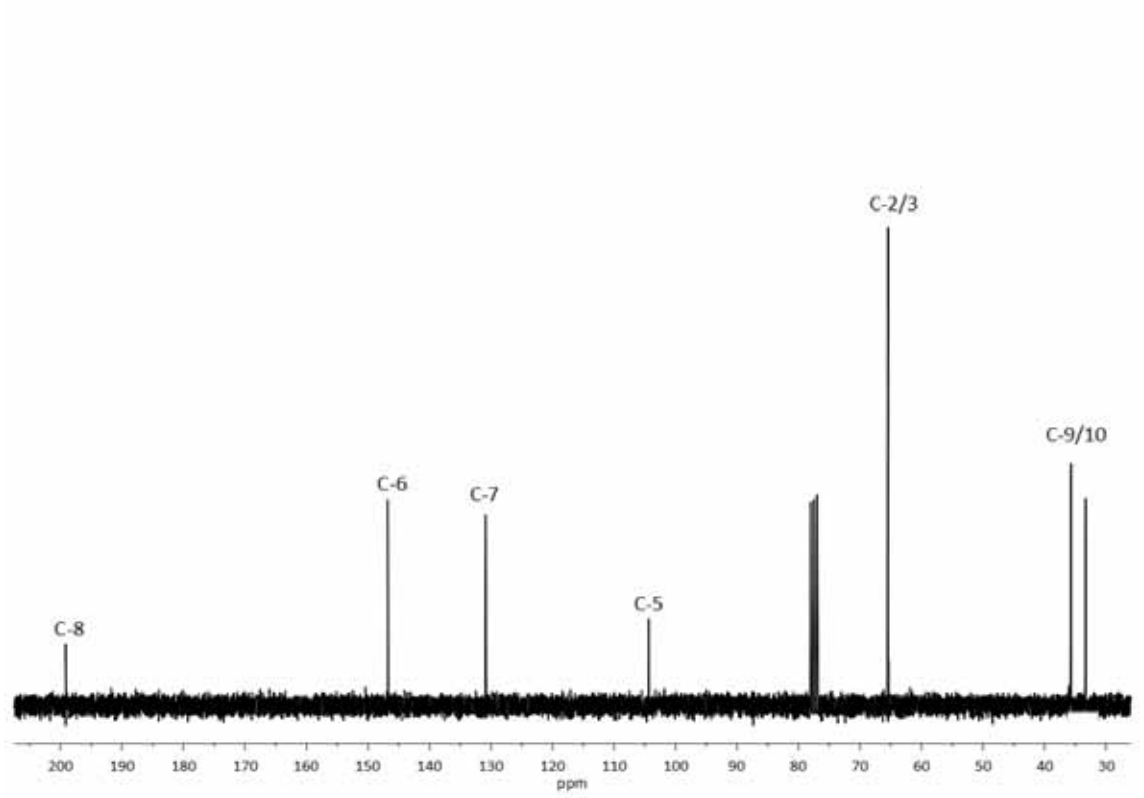
HMBC (400 MHz, $CDCl_3$)



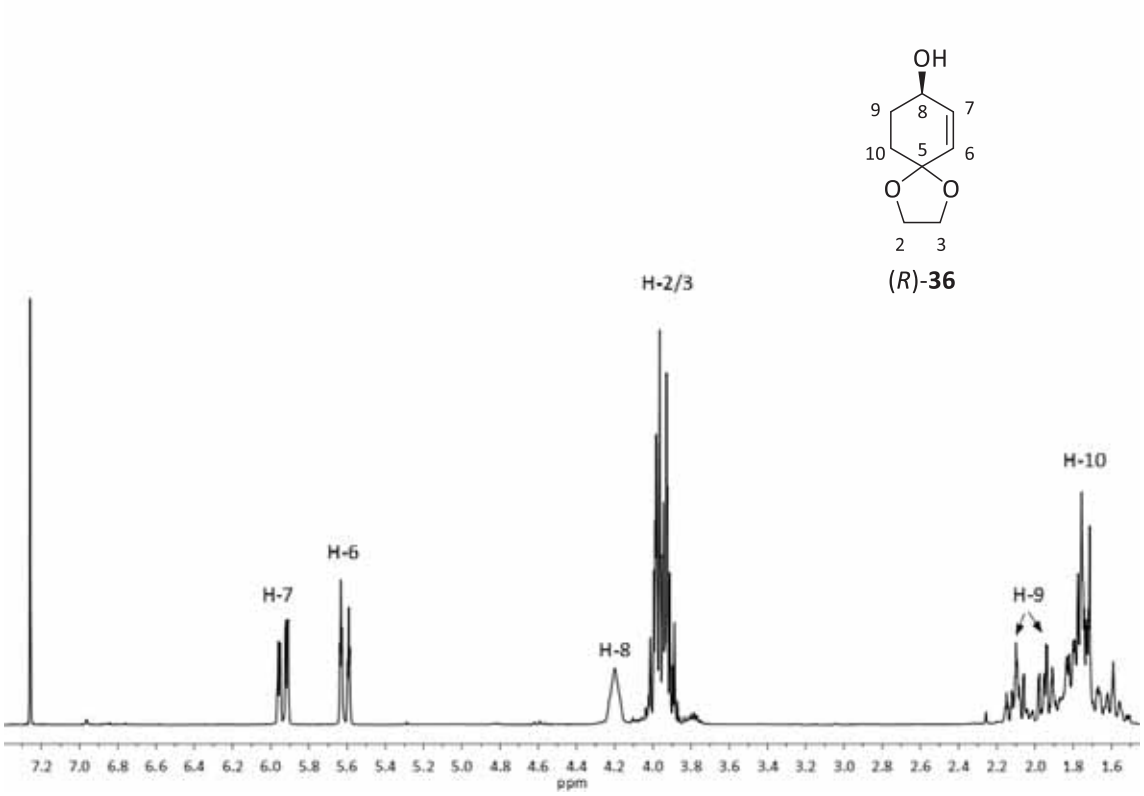
IR (ATR)



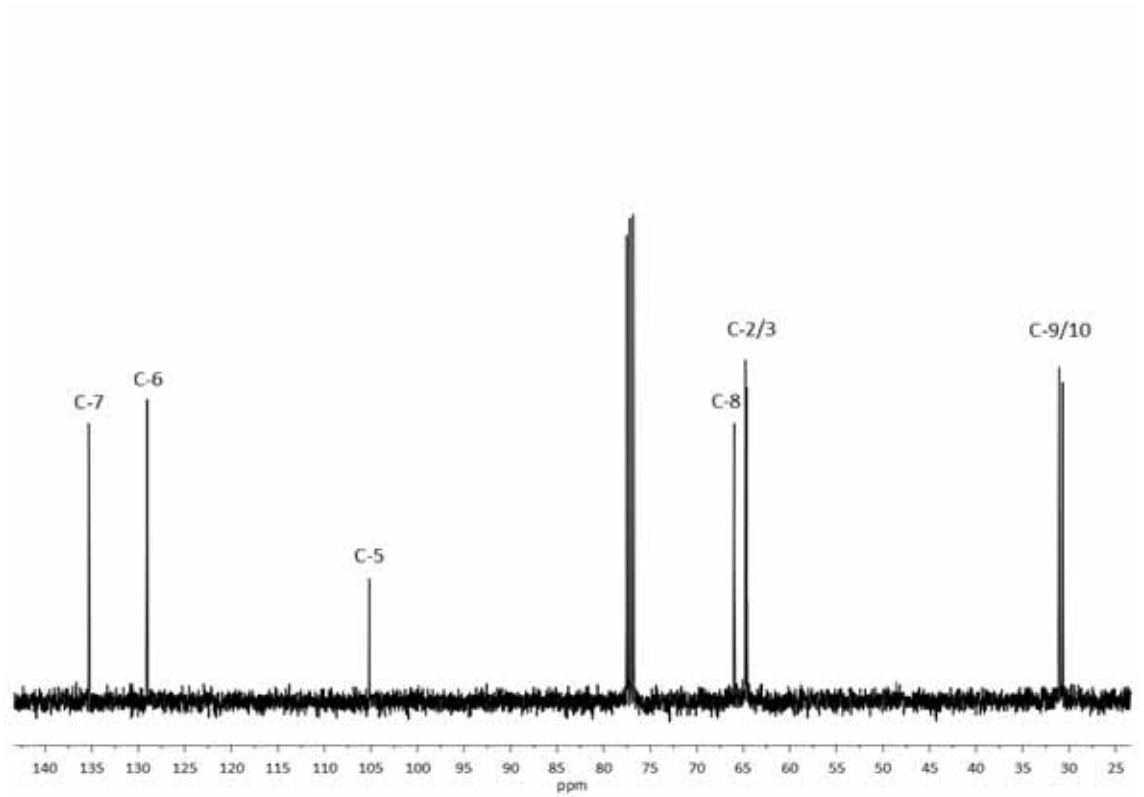
^{1}H-NMR (250 MHz, $CDCl_3$)



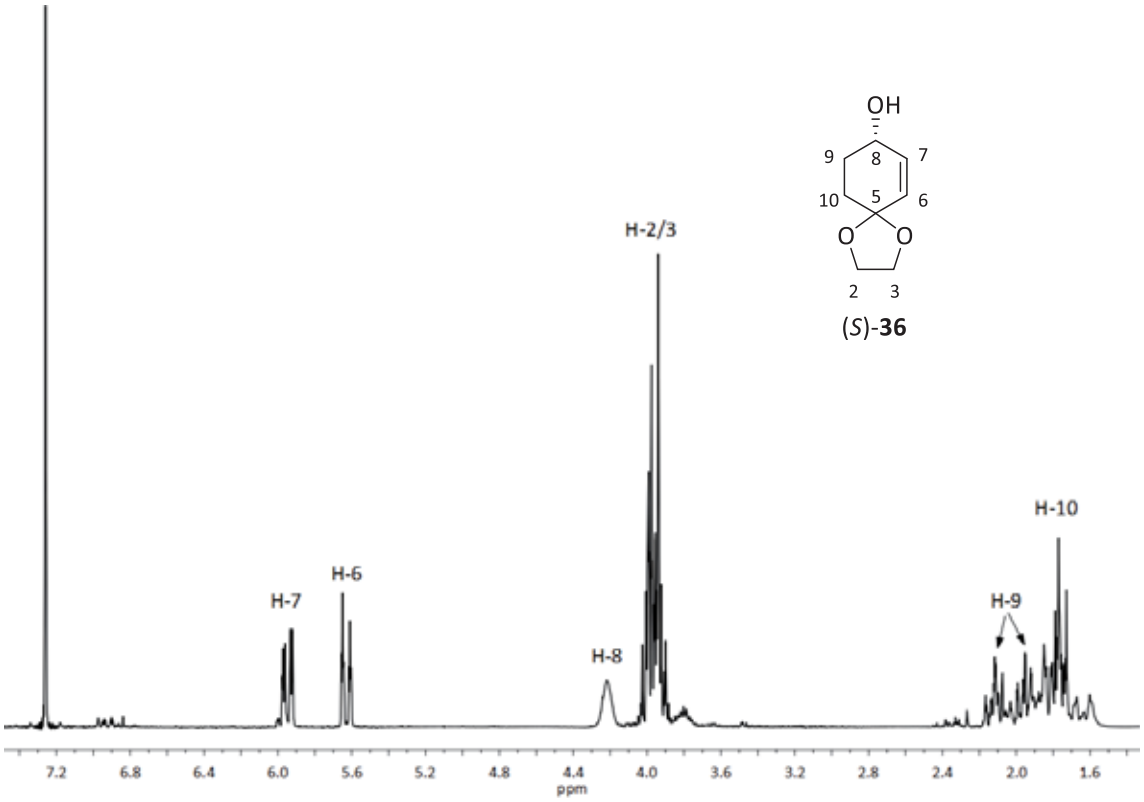
^{13}C-NMR (90 MHz, $CDCl_3$)



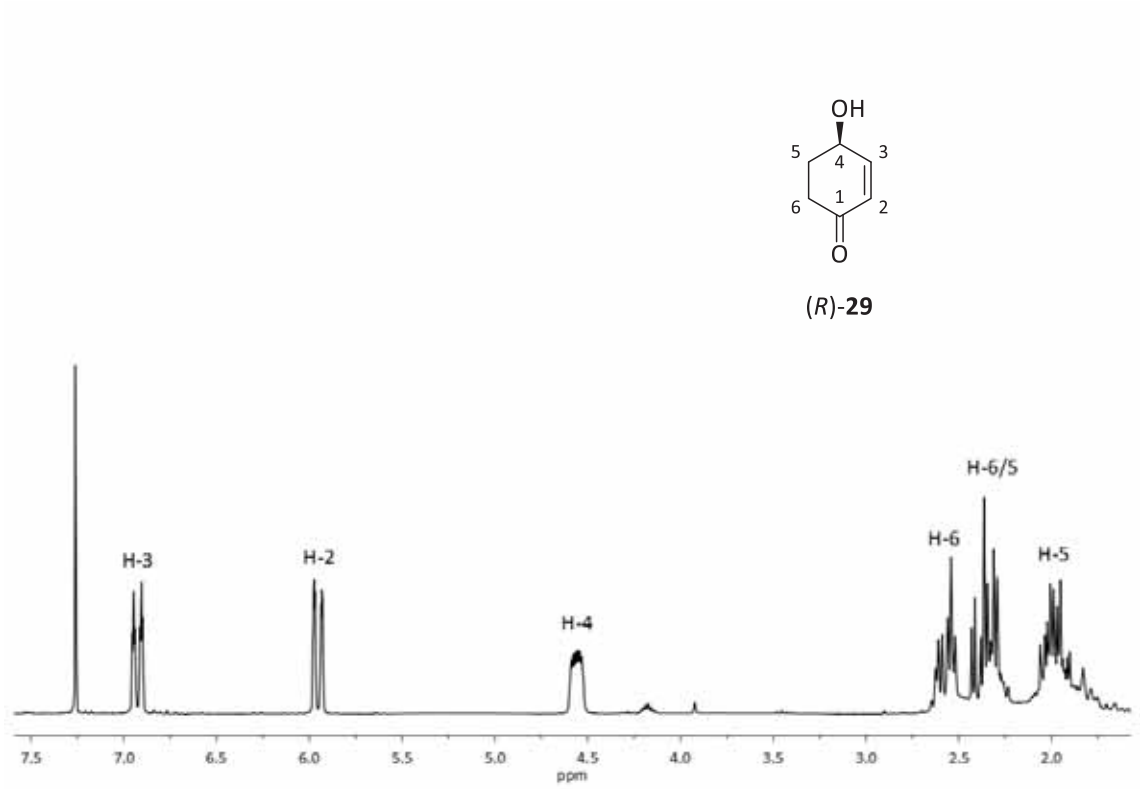
^{1}H-NMR (250 MHz, $CDCl_3$)



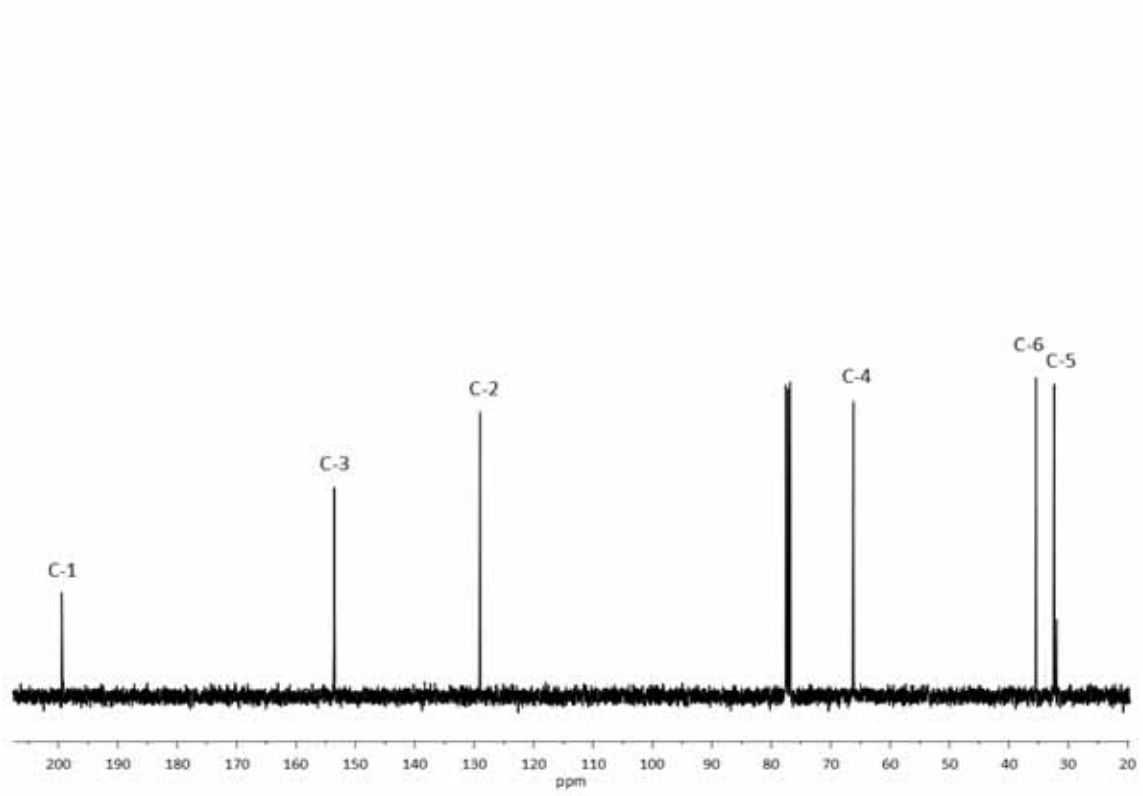
^{13}C-NMR (90 MHz, $CDCl_3$)



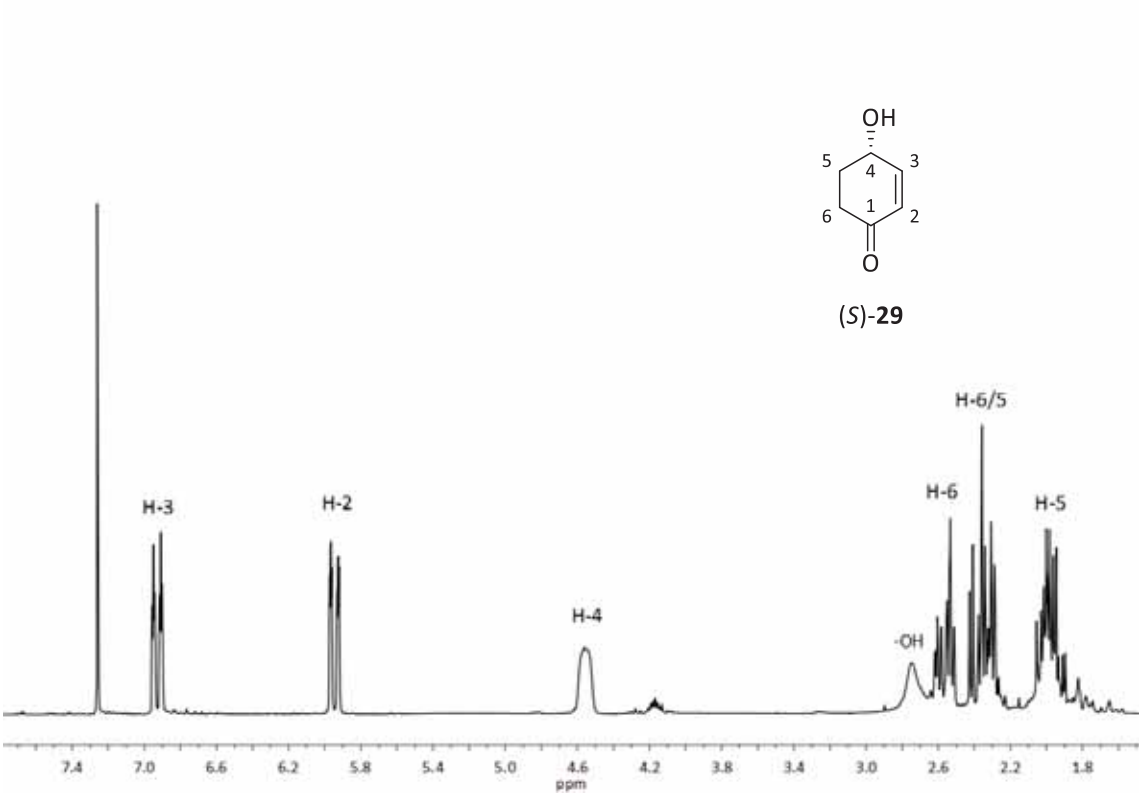
^{1}H-NMR (250 MHz, $CDCl_3$)



^{1}H-NMR (250 MHz, $CDCl_3$)

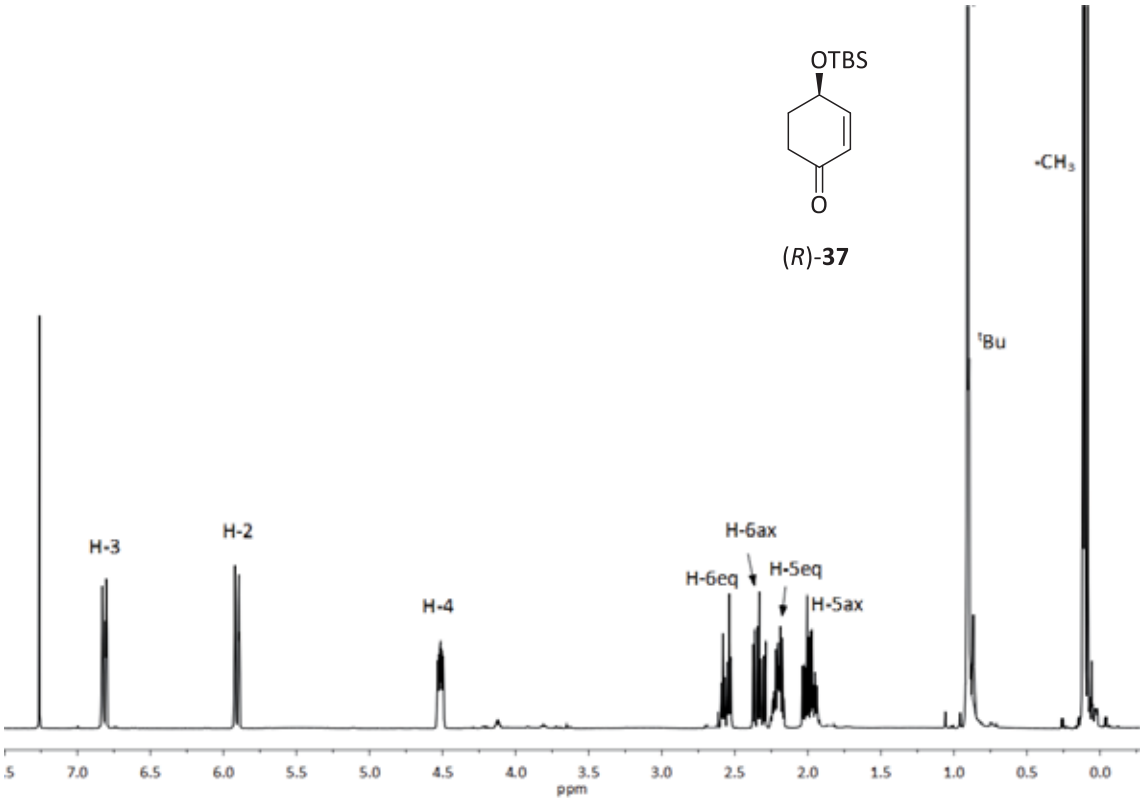


^{13}C-NMR (90 MHz, $CDCl_3$)

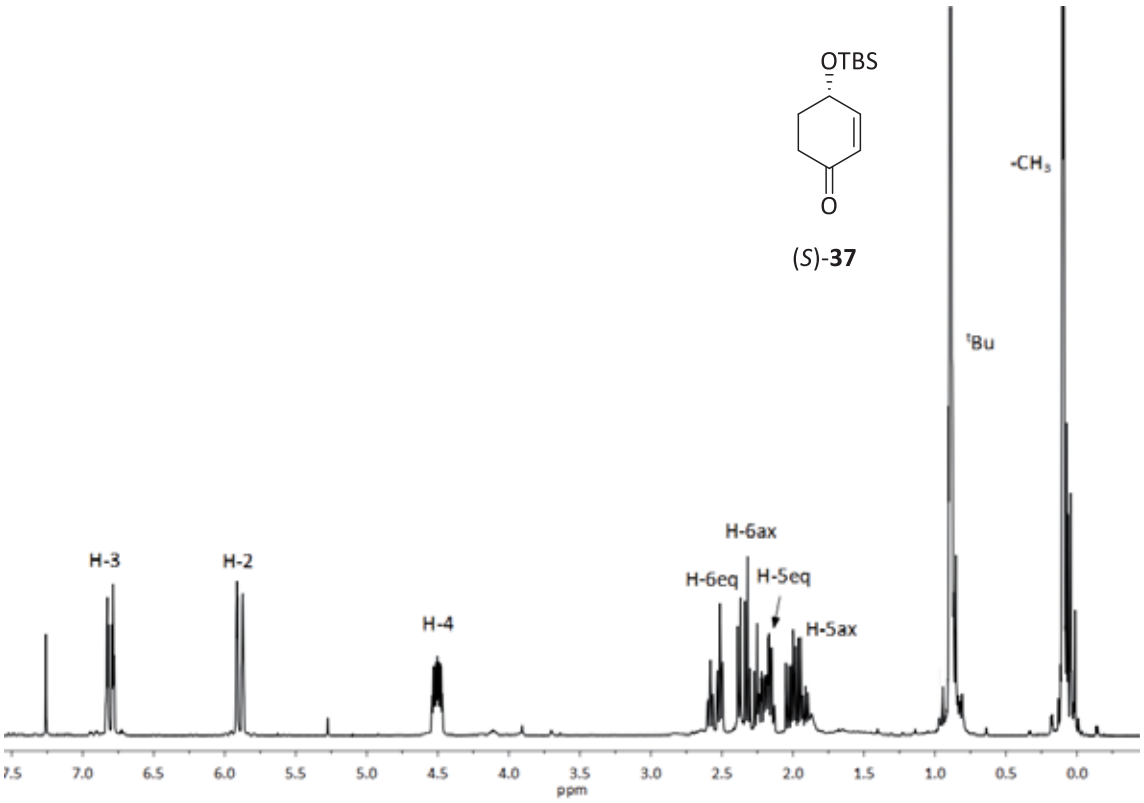


(*S*)-**29**

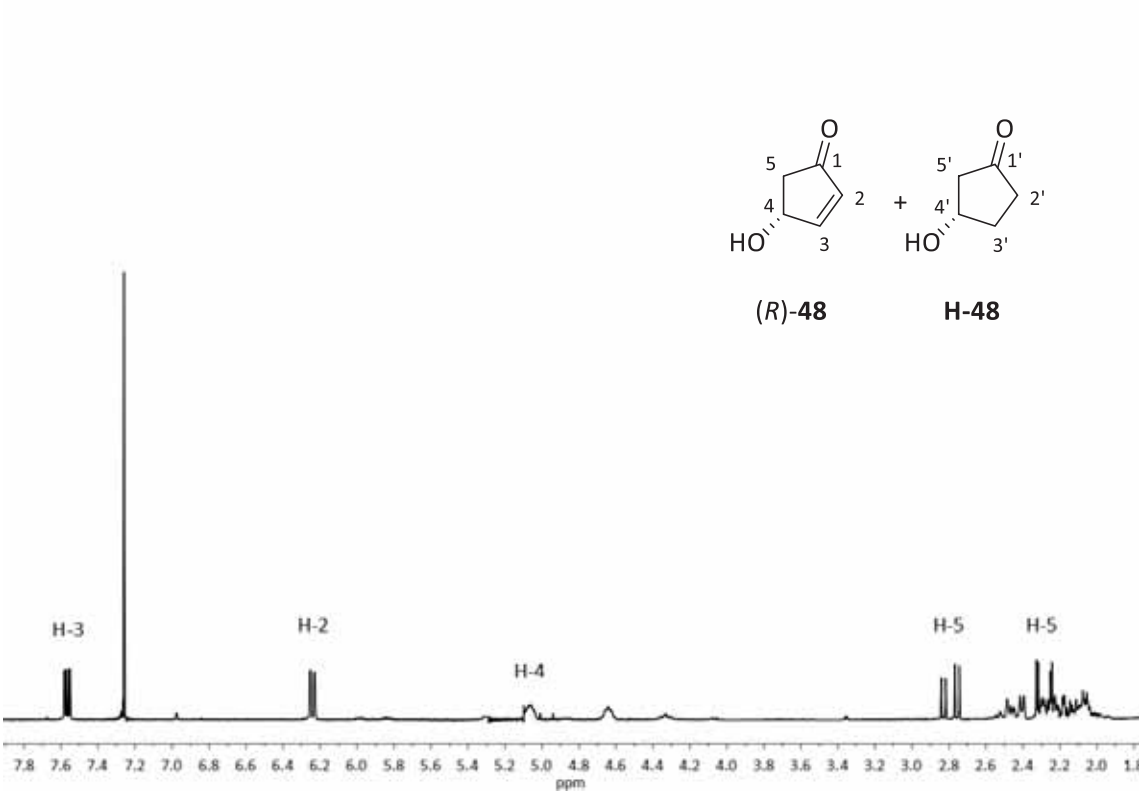
^{1}H-NMR (250 MHz, $CDCl_3$)



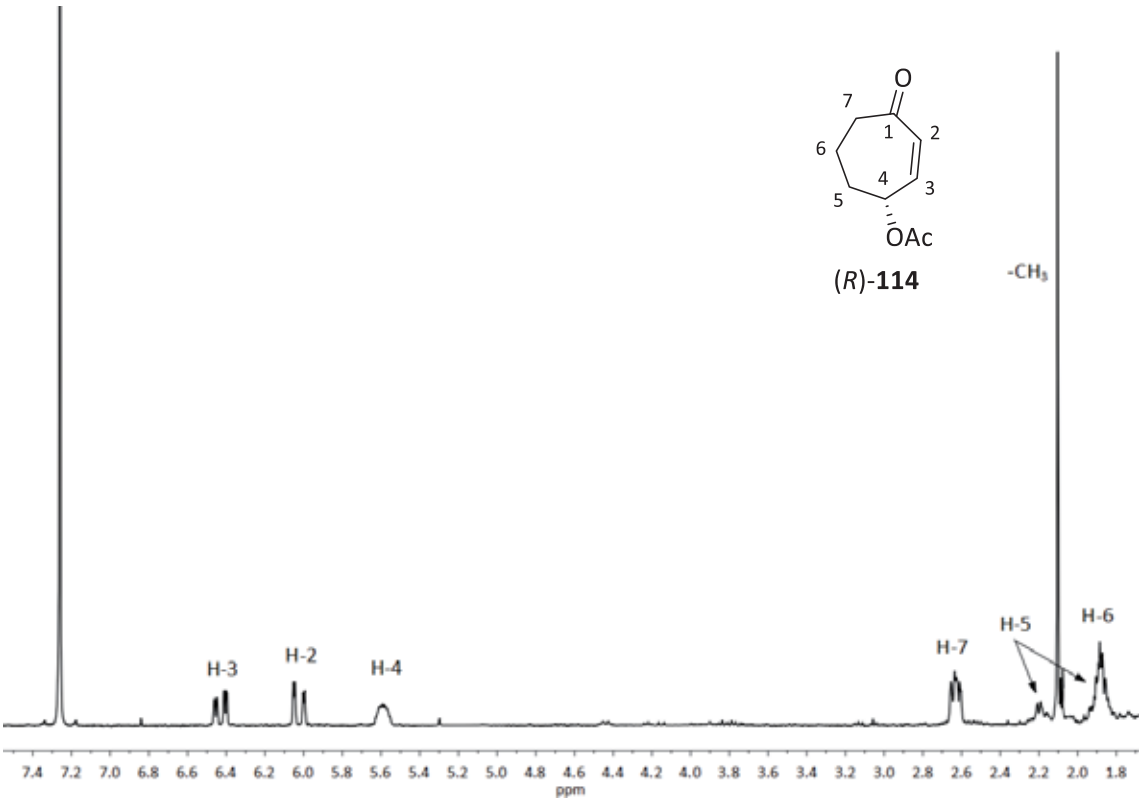
^{1}H-NMR (400 MHz, $CDCl_3$)



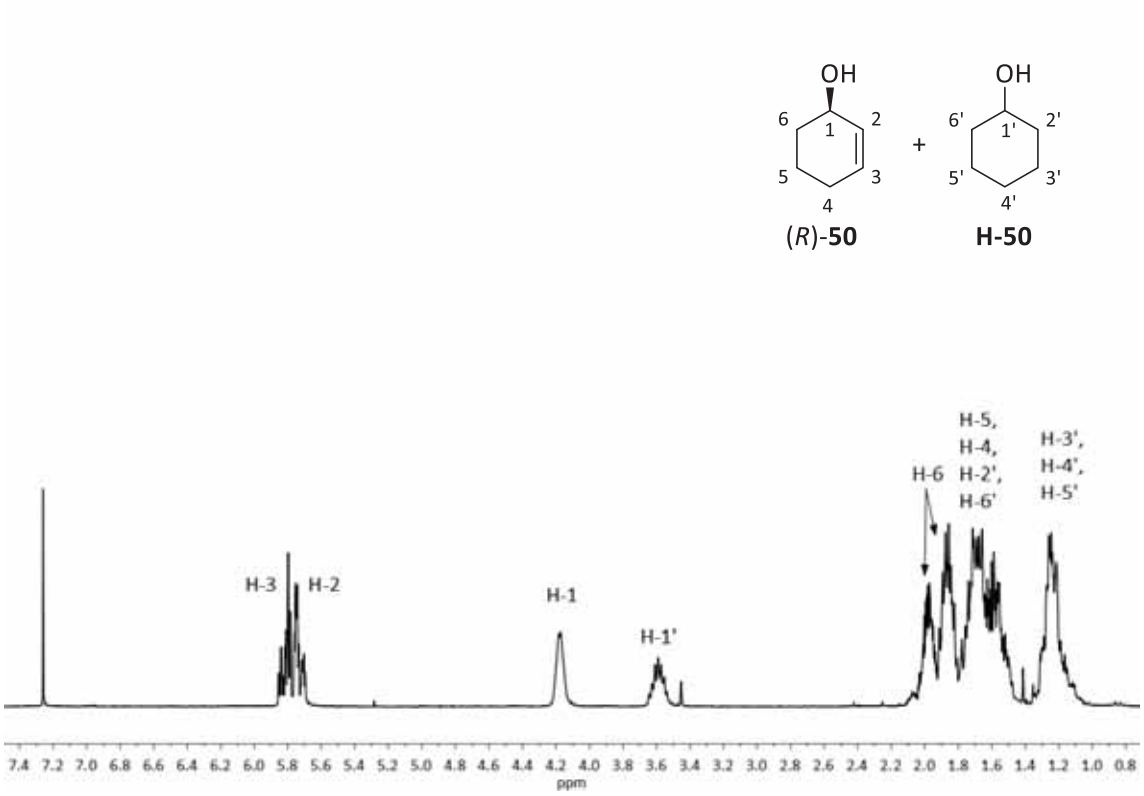
^{1}H-NMR (400 MHz, $CDCl_3$)



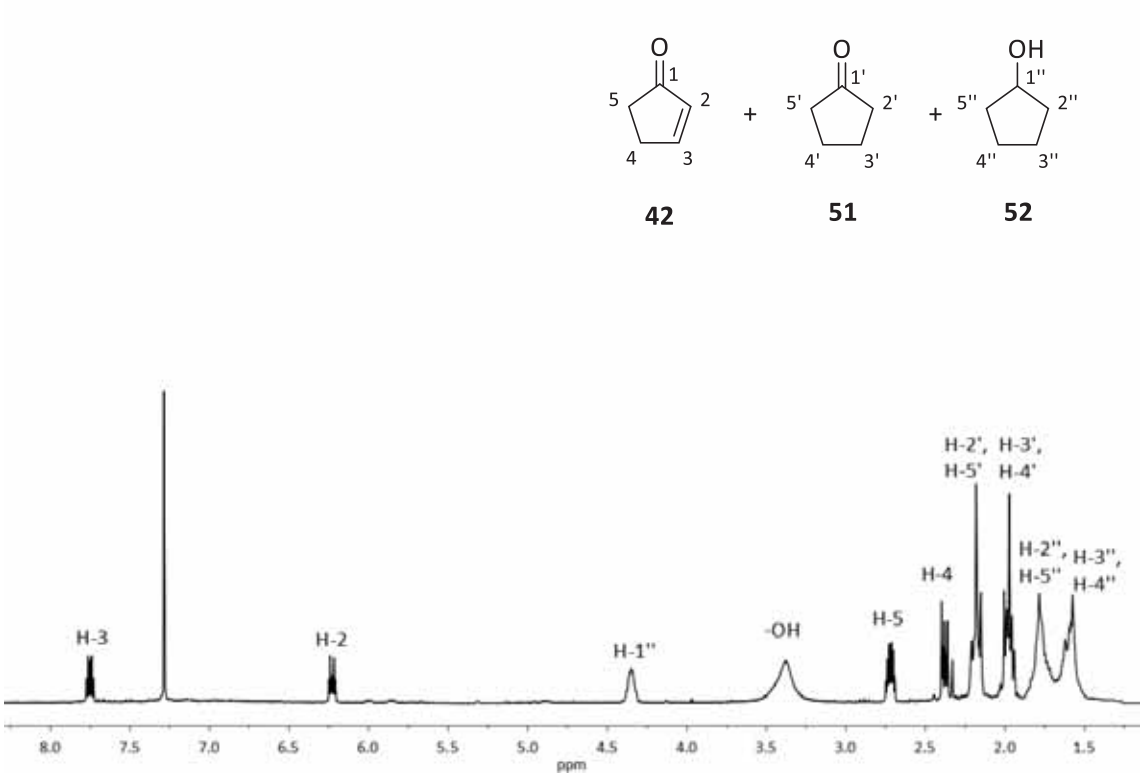
^{1}H-NMR (250 MHz, $CDCl_3$)



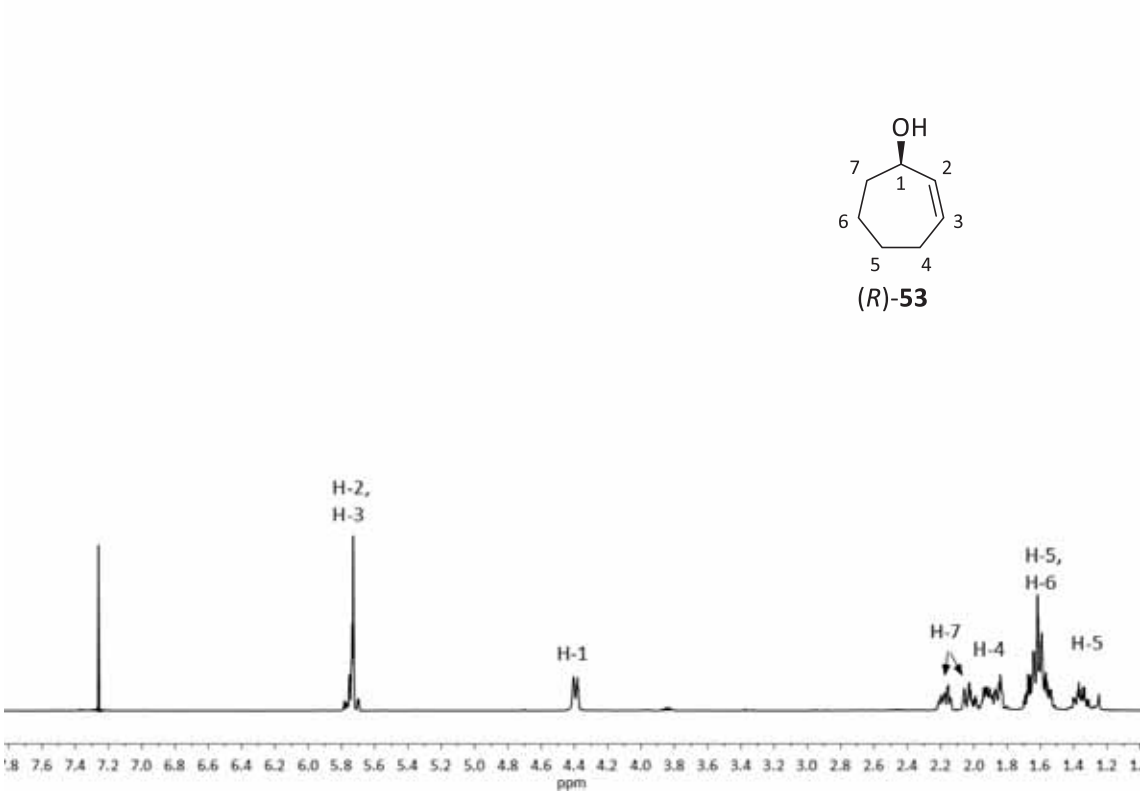
^{1}H-NMR (250 MHz, $CDCl_3$)



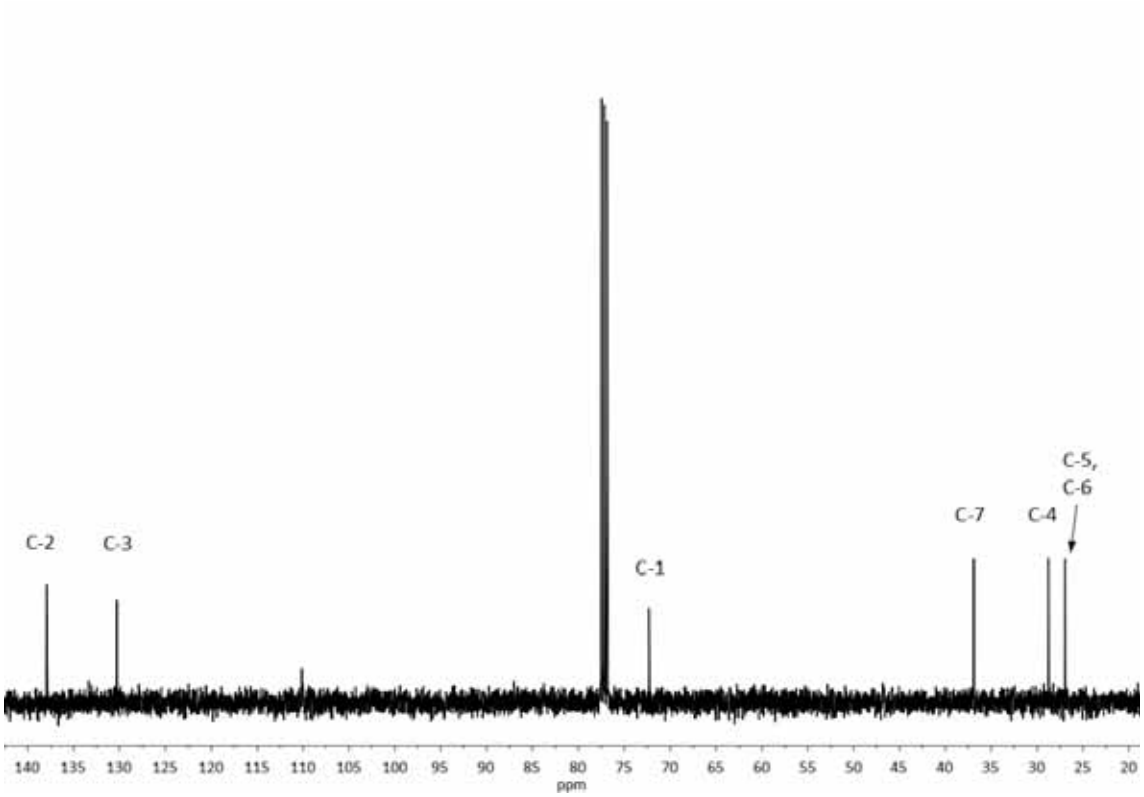
^{1}H-NMR (400 MHz, $CDCl_3$)



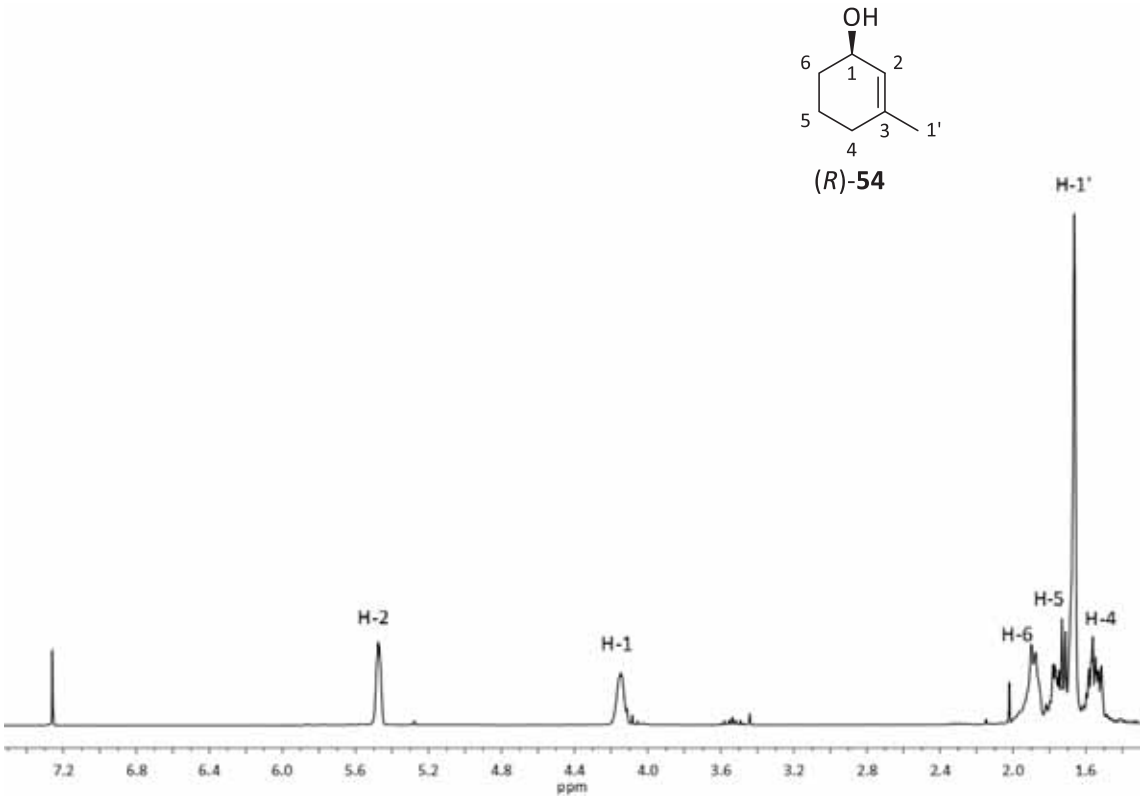
^{1}H-NMR (250 MHz, $CDCl_3$)



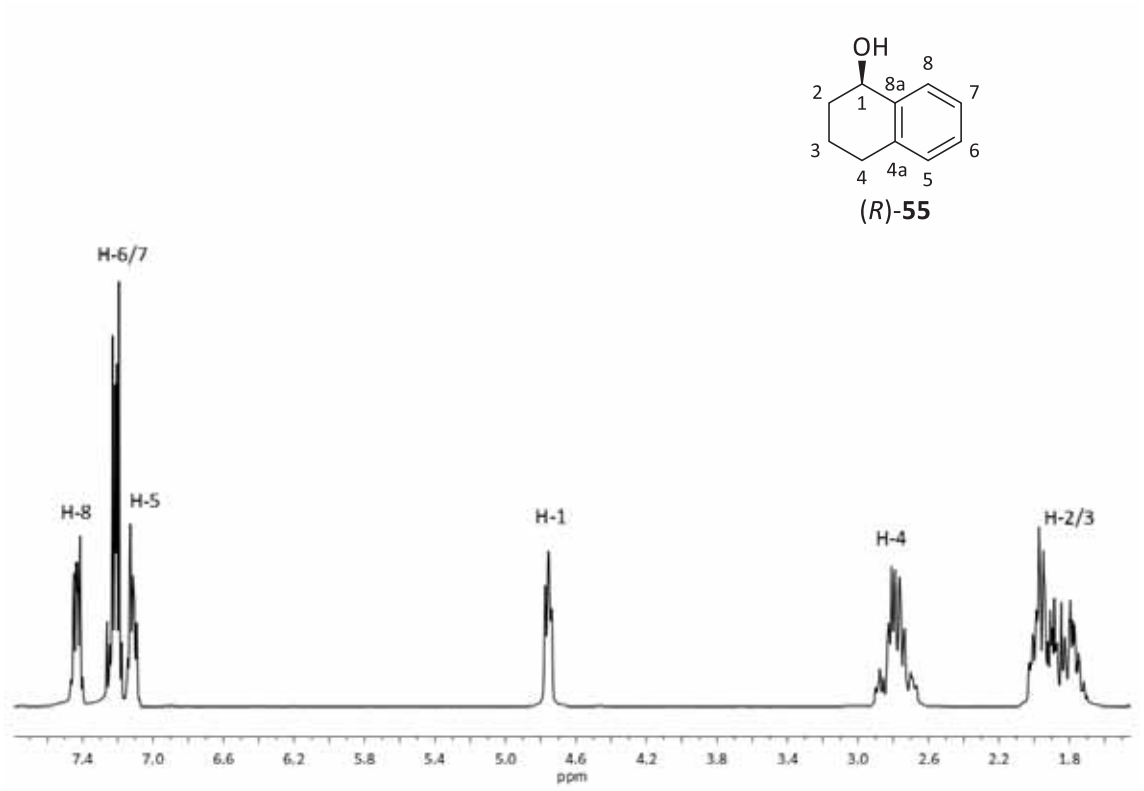
^{1}H-NMR (400 MHz, $CDCl_3$)



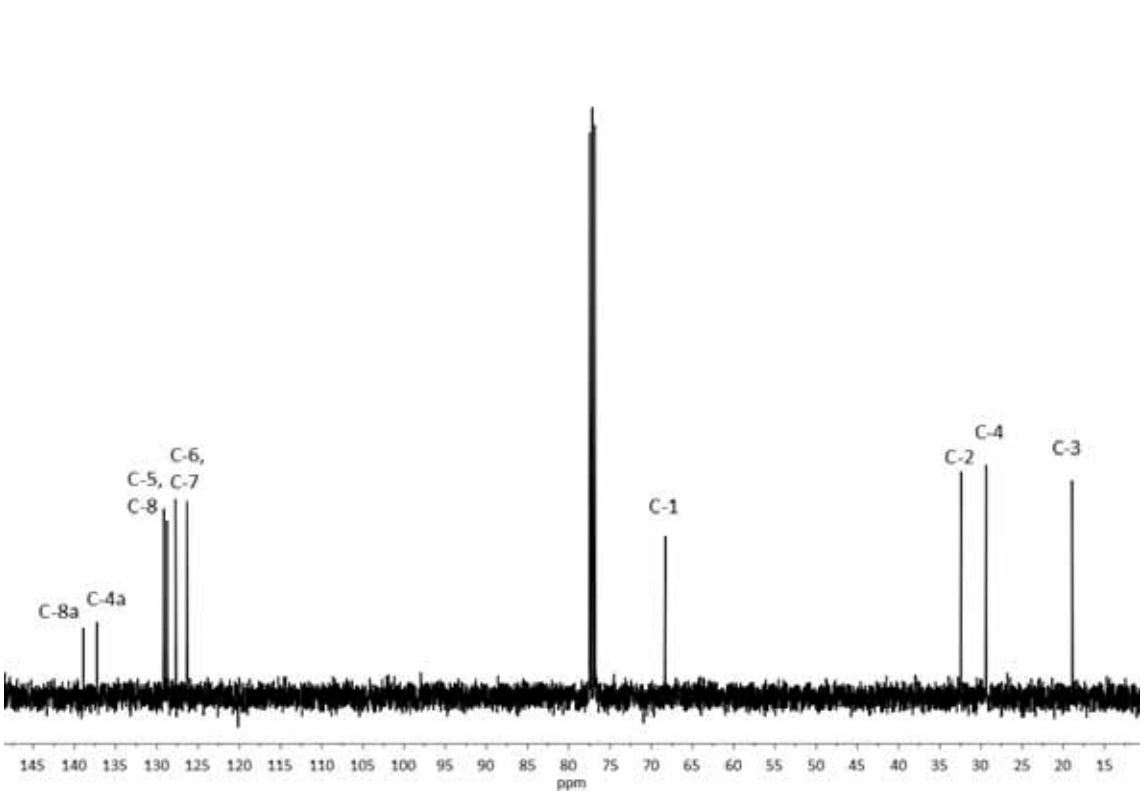
^{13}C-NMR (100 MHz, $CDCl_3$)



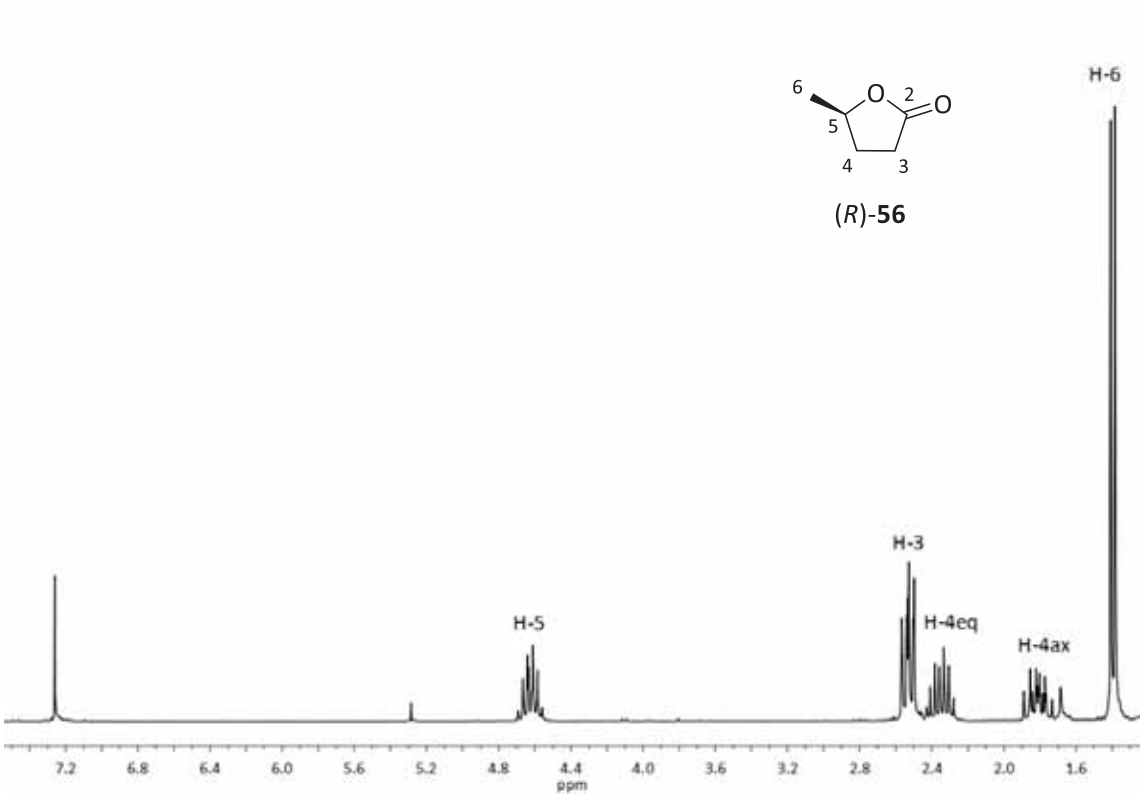
^{1}H-NMR (250 MHz, $CDCl_3$)



^{1}H-NMR (250 MHz, $CDCl_3$)

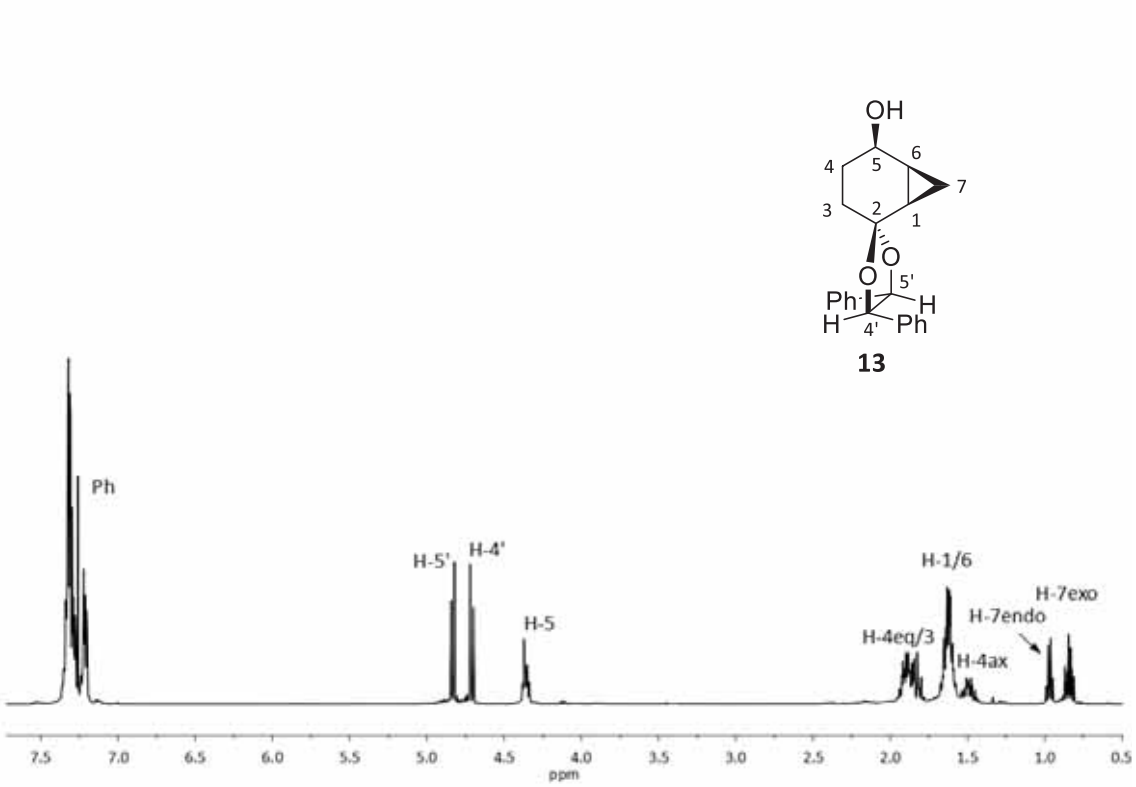


^{13}C-NMR (100 MHz, $CDCl_3$)

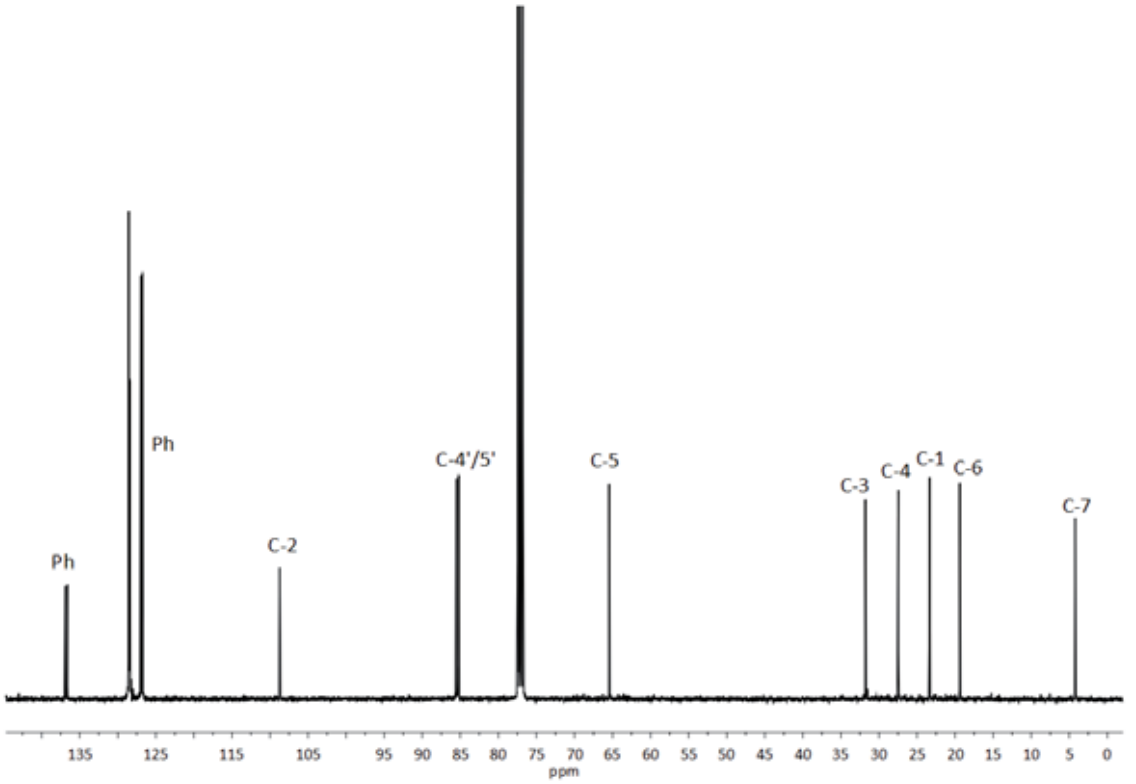


(*R*)-**56**

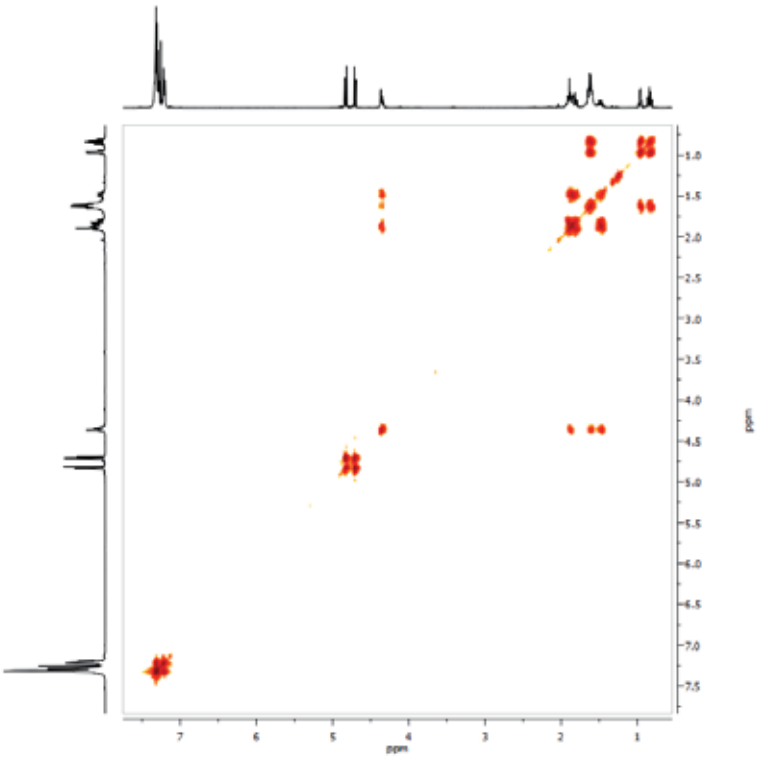
^{1}H-NMR (250 MHz, $CDCl_3$)



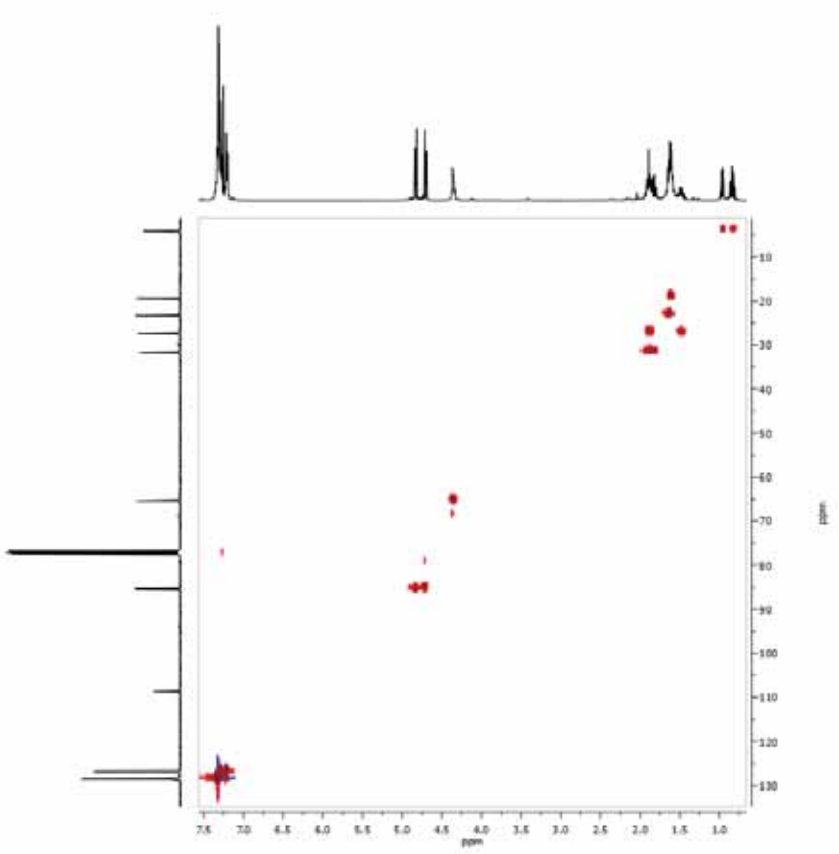
^{1}H-NMR (400 MHz, $CDCl_3$)



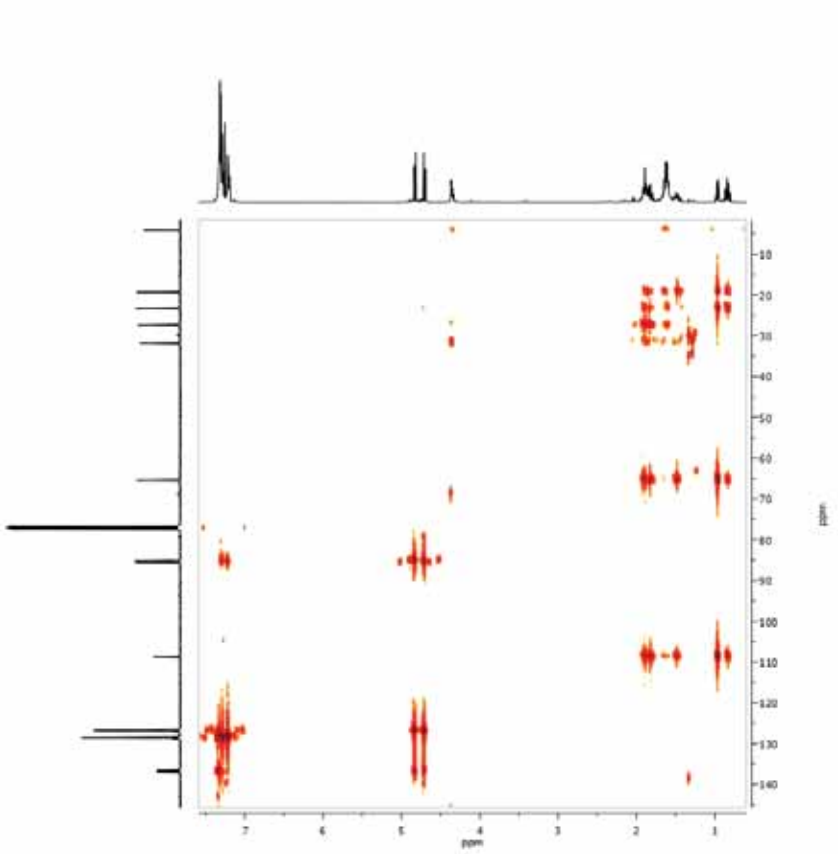
^{13}C-NMR (100 MHz, $CDCl_3$)



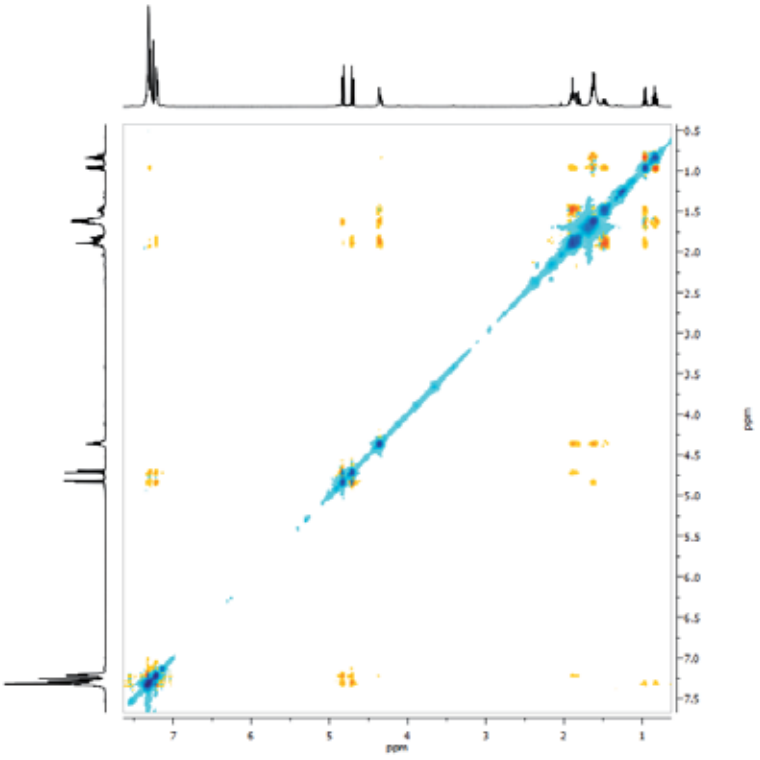
COSY (400 MHz, $CDCl_3$)



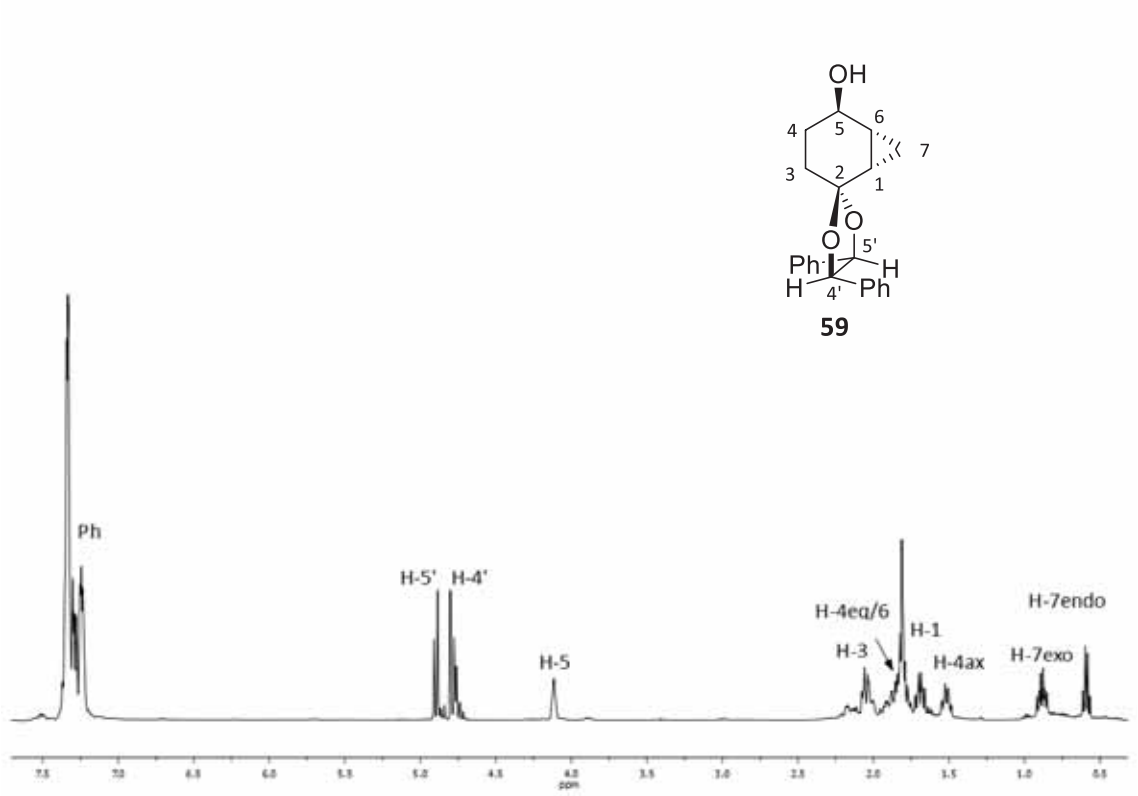
HSQC (400 MHz, $CDCl_3$)



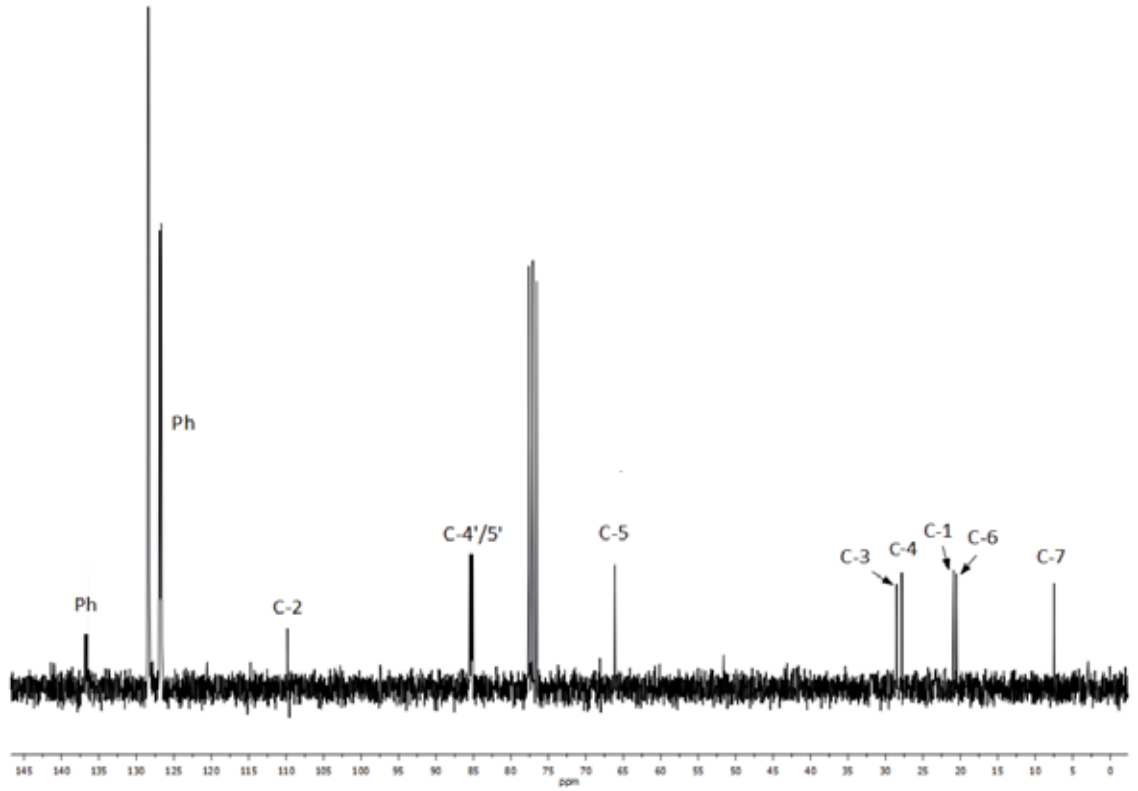
HMBC (400 MHz, $CDCl_3$)



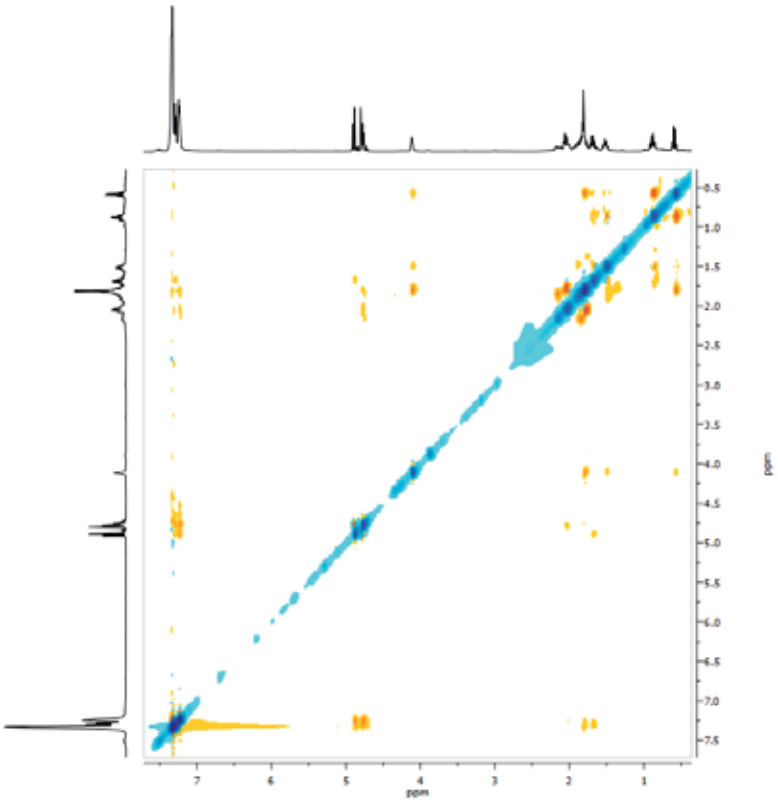
NOESY (400 MHz, $CDCl_3$)



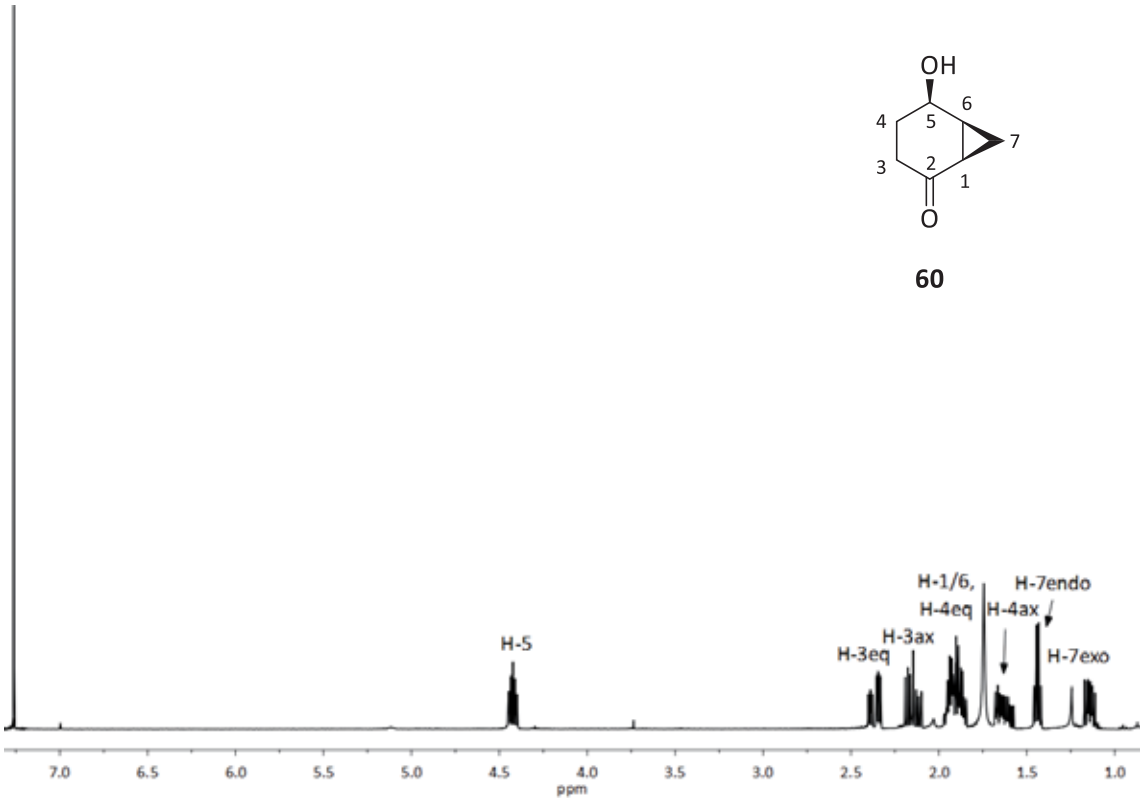
^{1}H-NMR (360 MHz, $CDCl_3$)



^{13}C-NMR (90 MHz, $CDCl_3$)

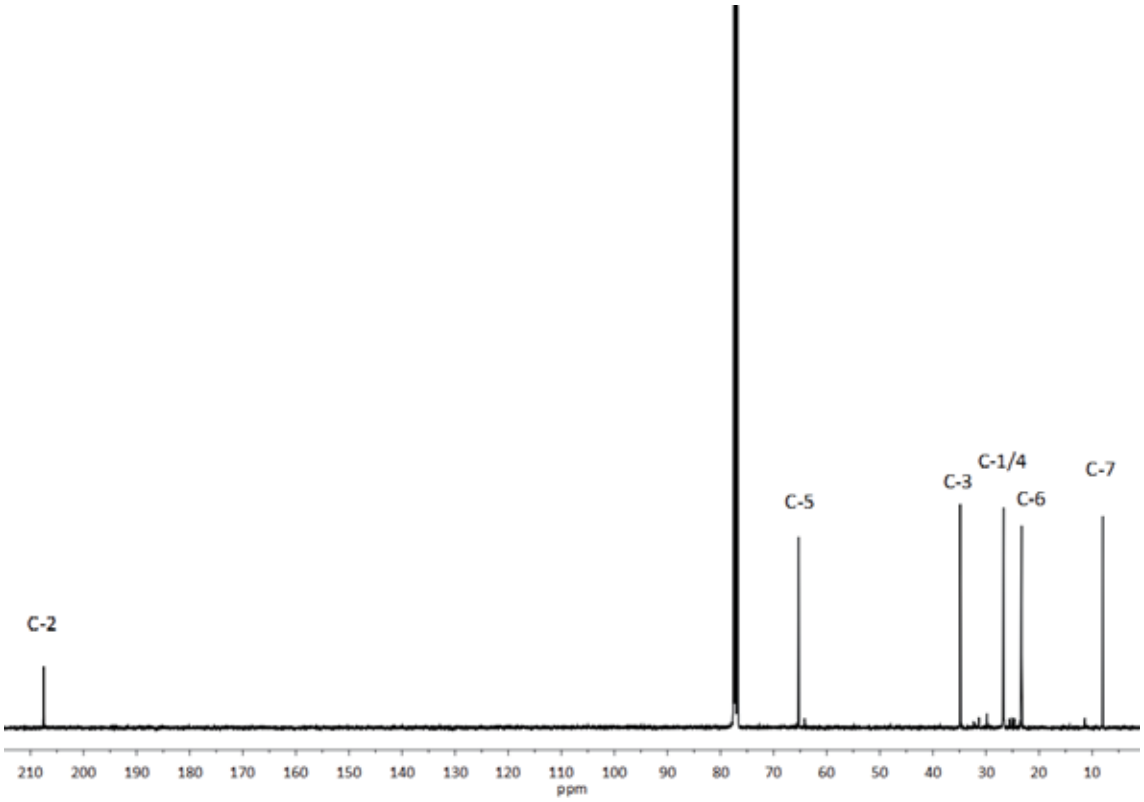


NOESY (360 MHz, $CDCl_3$)

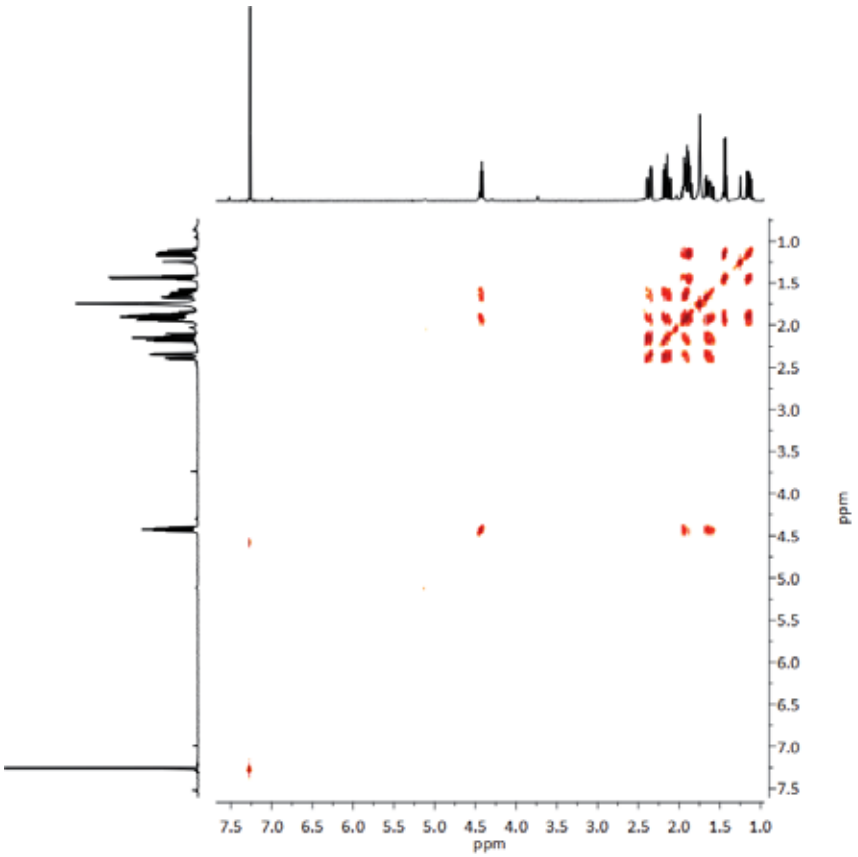


^{1}H-NMR (400 MHz, $CDCl_3$)

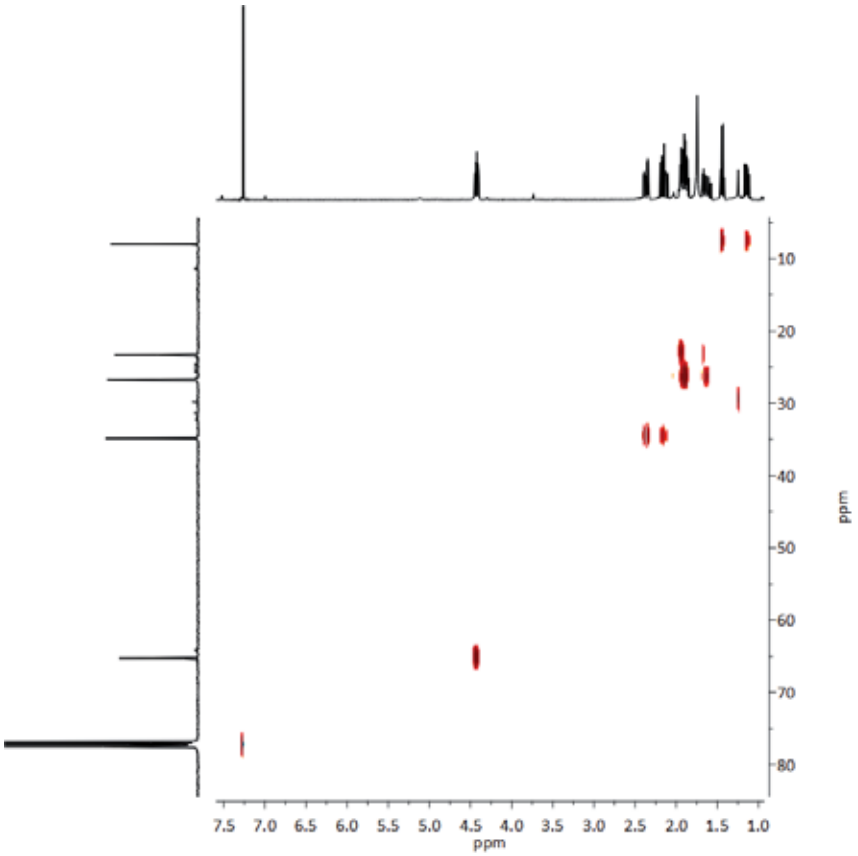
60



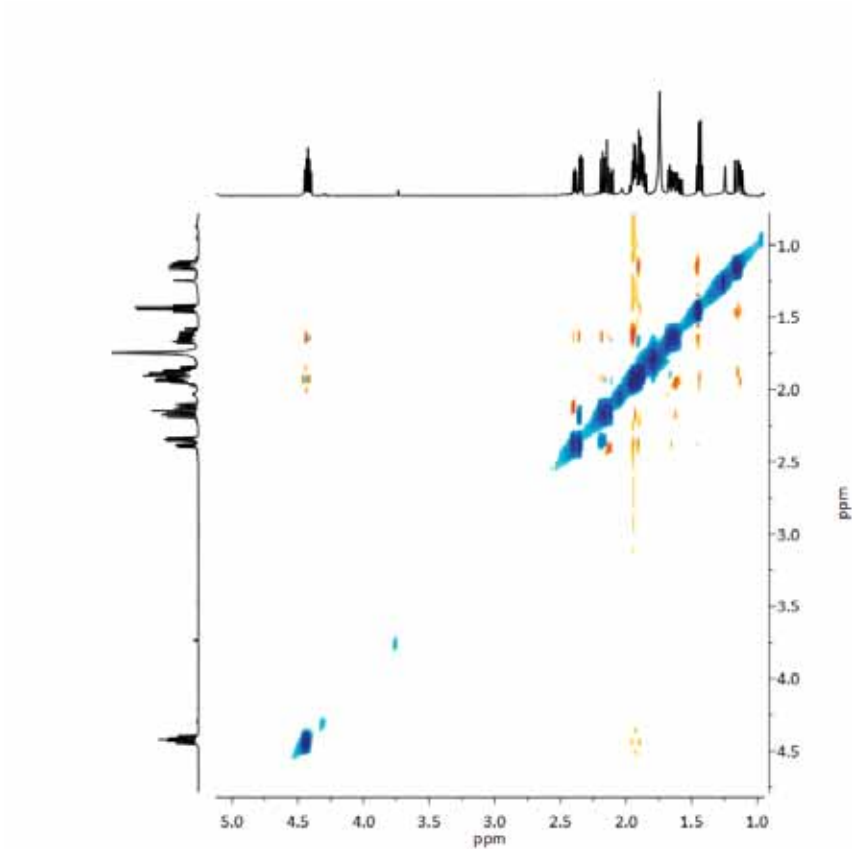
^{13}C-NMR (100 MHz, $CDCl_3$)



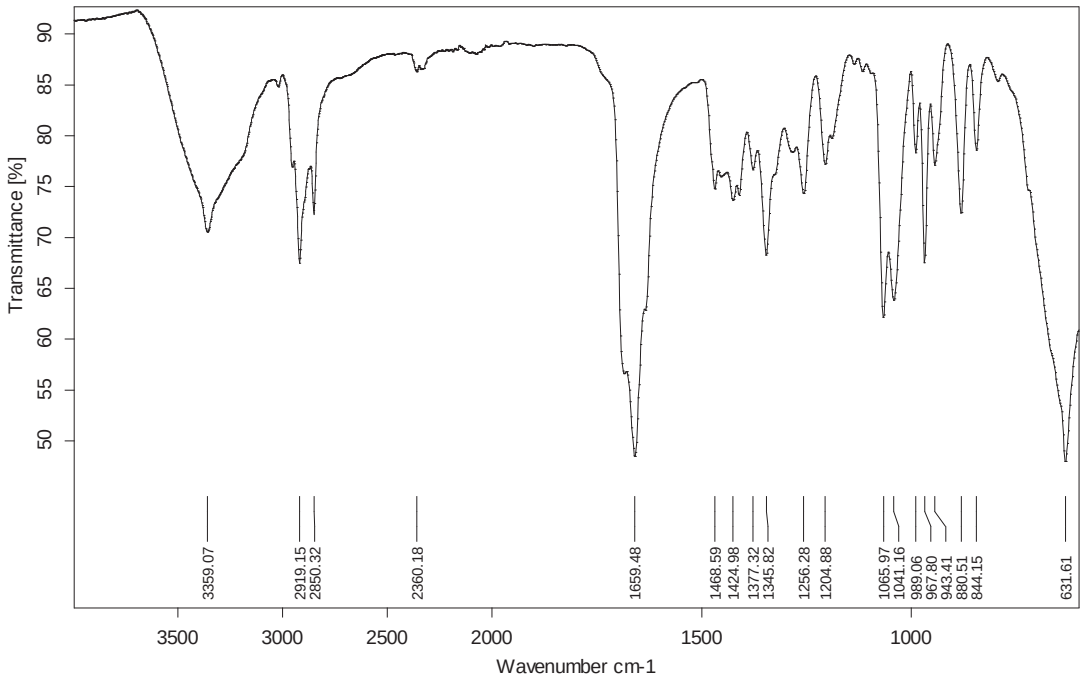
COSY (400 MHz, $CDCl_3$)



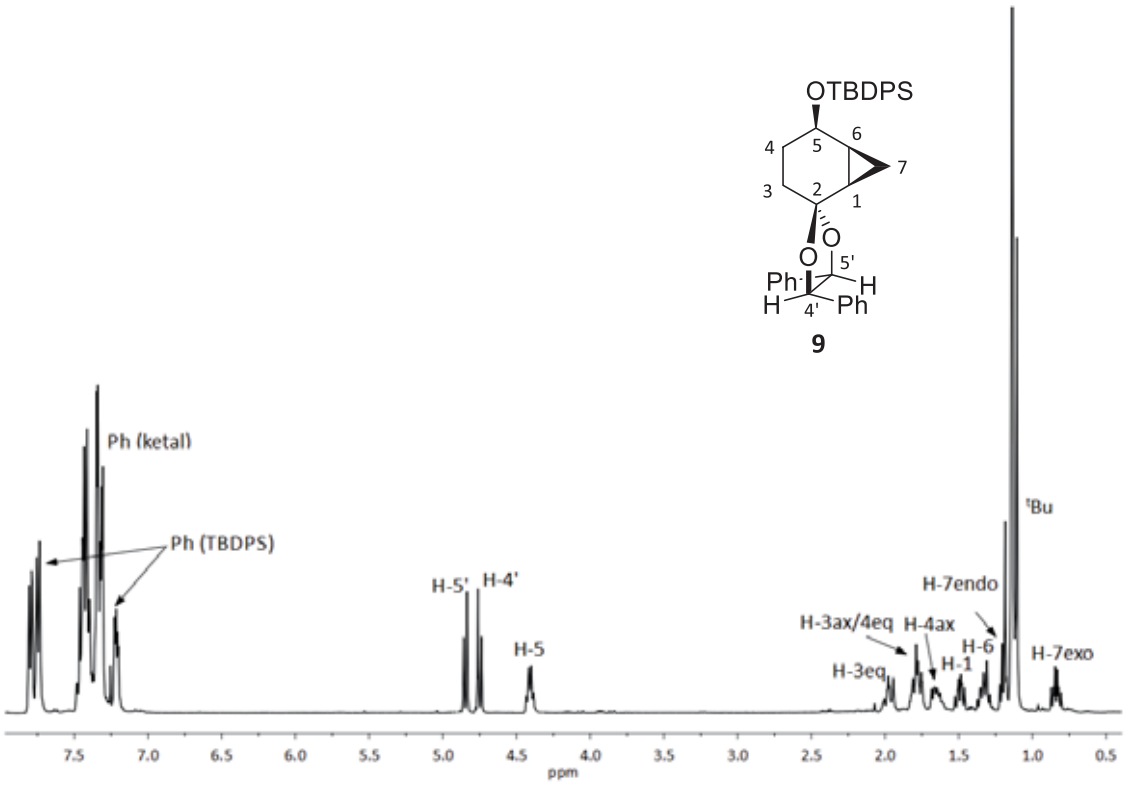
HSQC (400 MHz, $CDCl_3$)



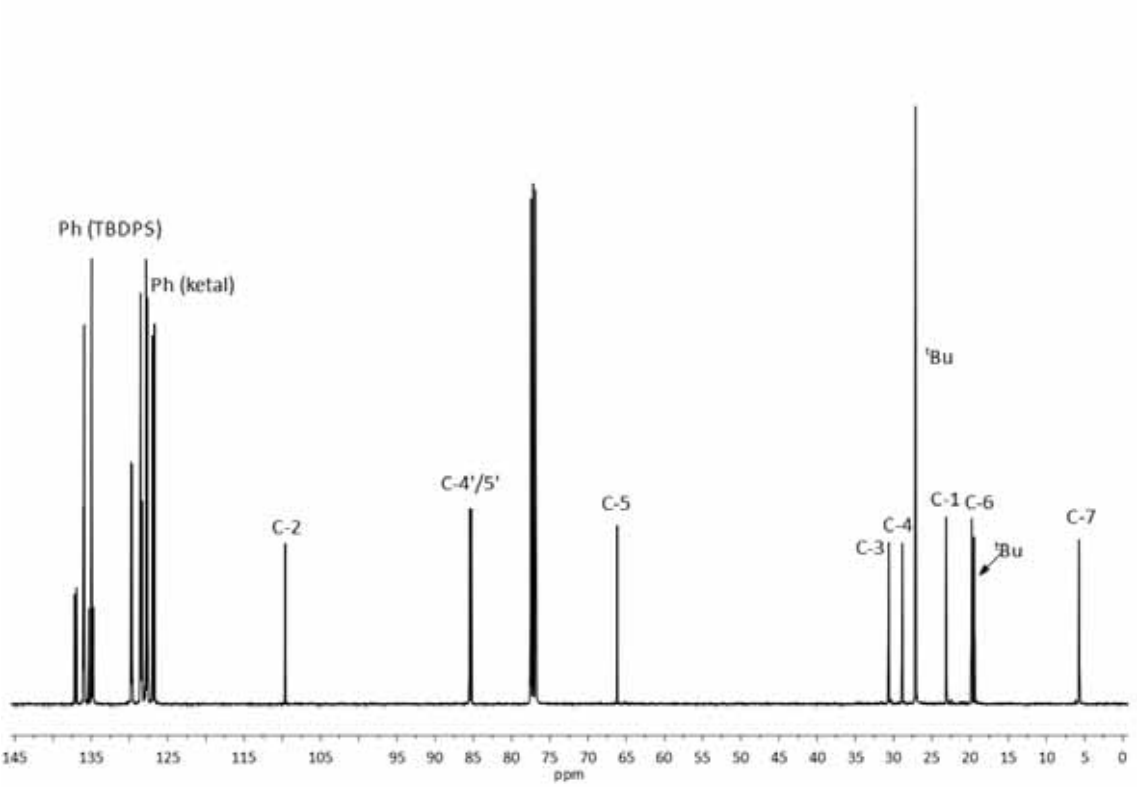
NOESY (400 MHz, $CDCl_3$)



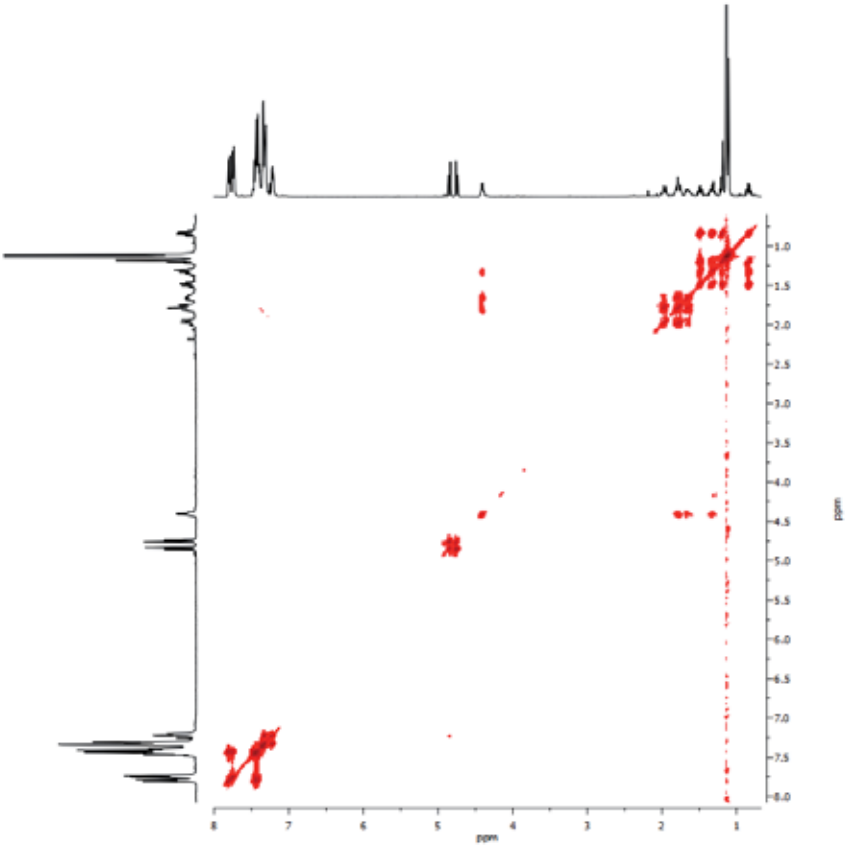
IR (ATR)



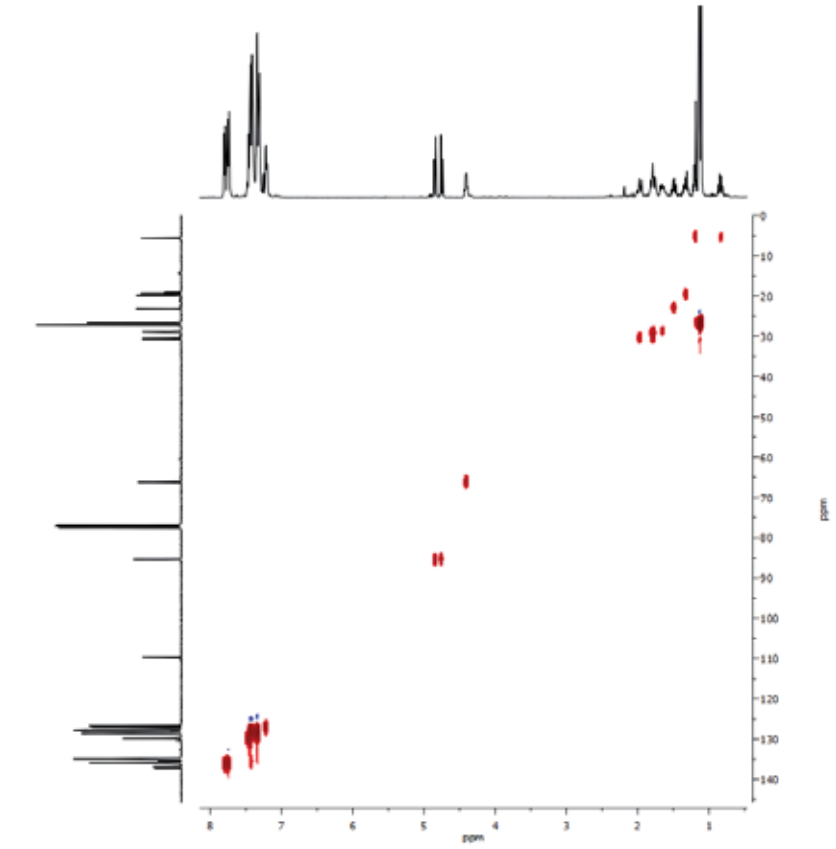
^{1}H-NMR (400 MHz, $CDCl_3$)



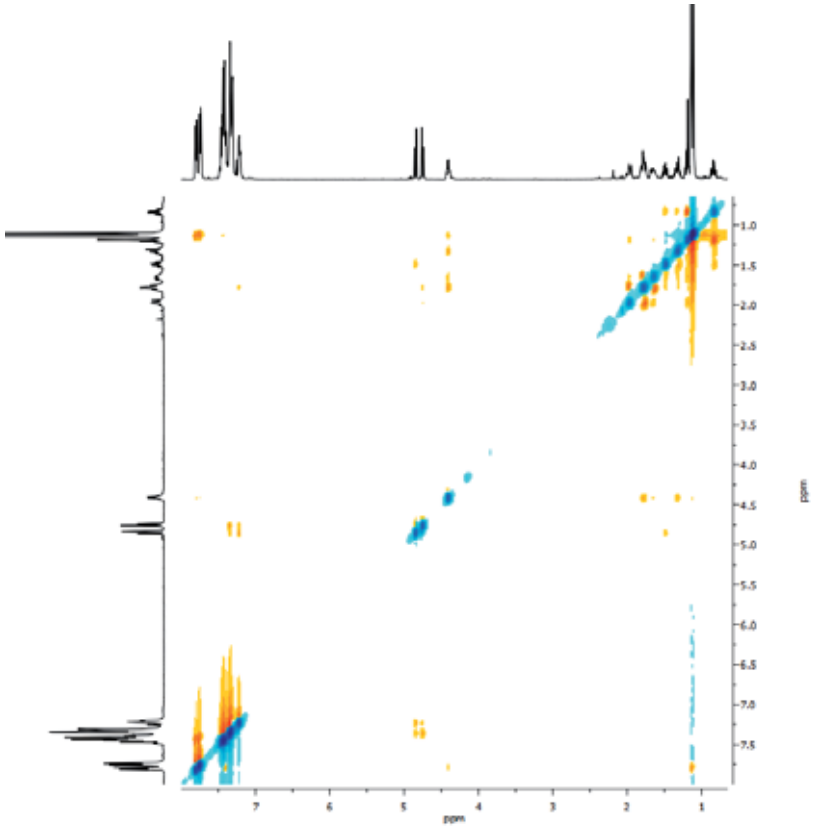
^{13}C-NMR (100 MHz, $CDCl_3$)



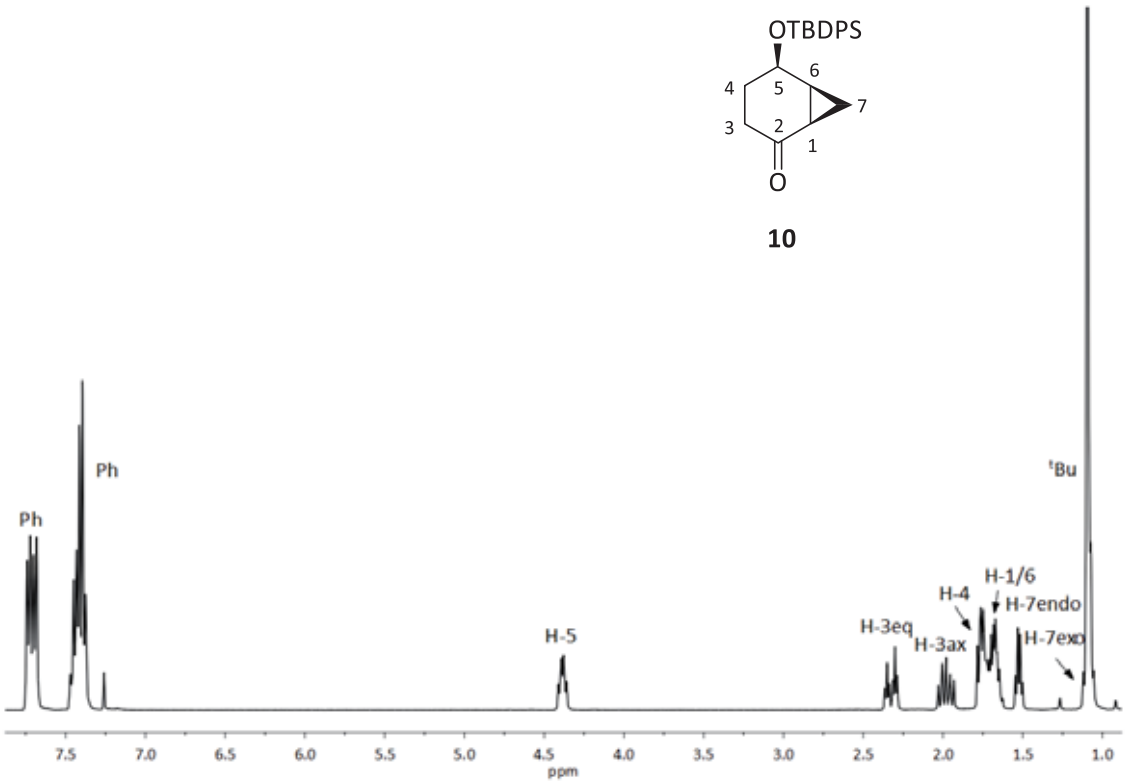
COSY (400 MHz, $CDCl_3$)



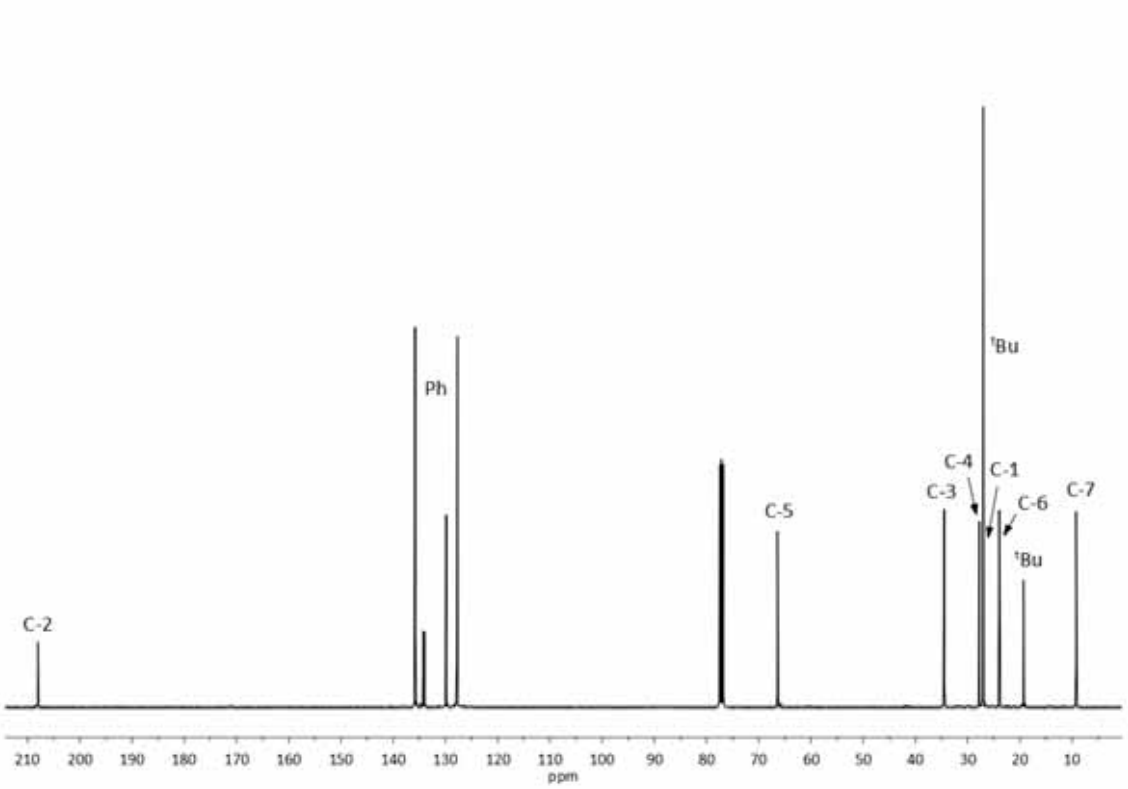
HSQC (400 MHz, $CDCl_3$)



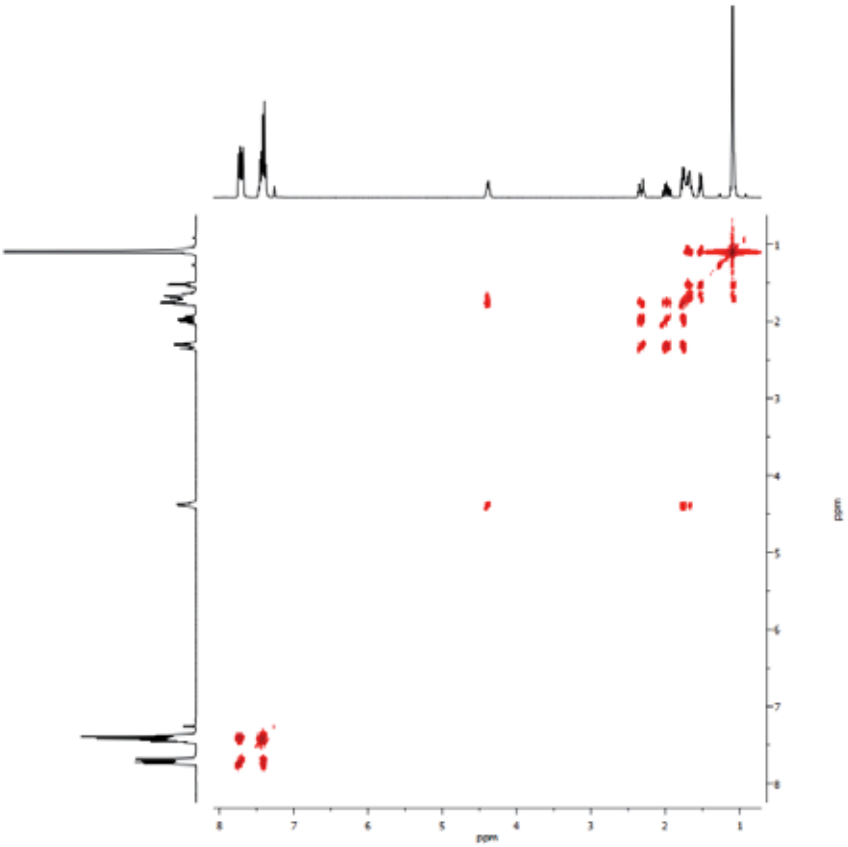
NOESY (400 MHz, $CDCl_3$)



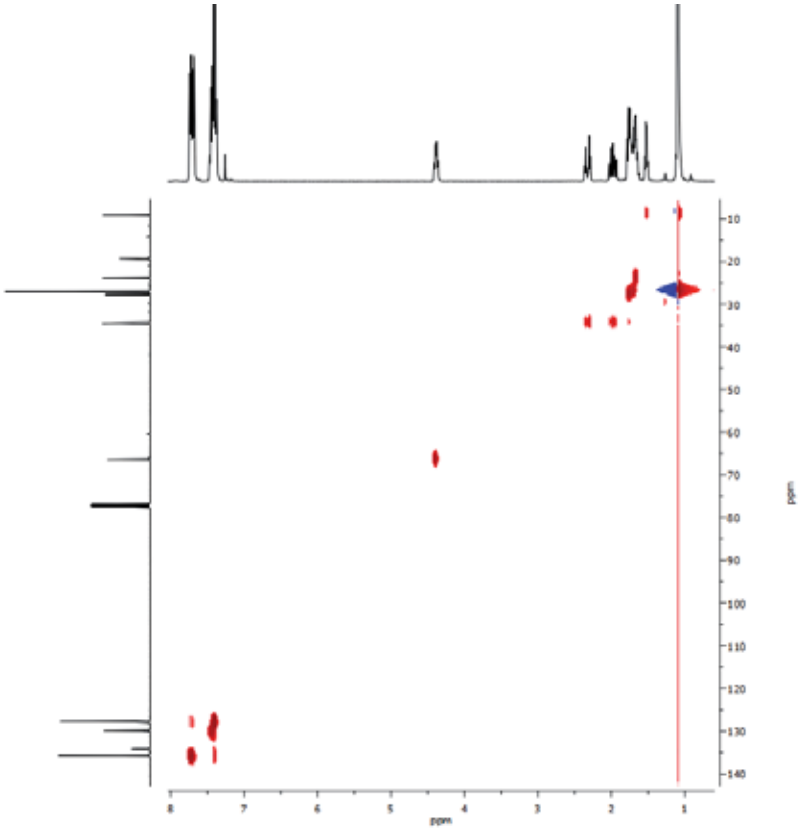
^{1}H-NMR (400 MHz, $CDCl_3$)



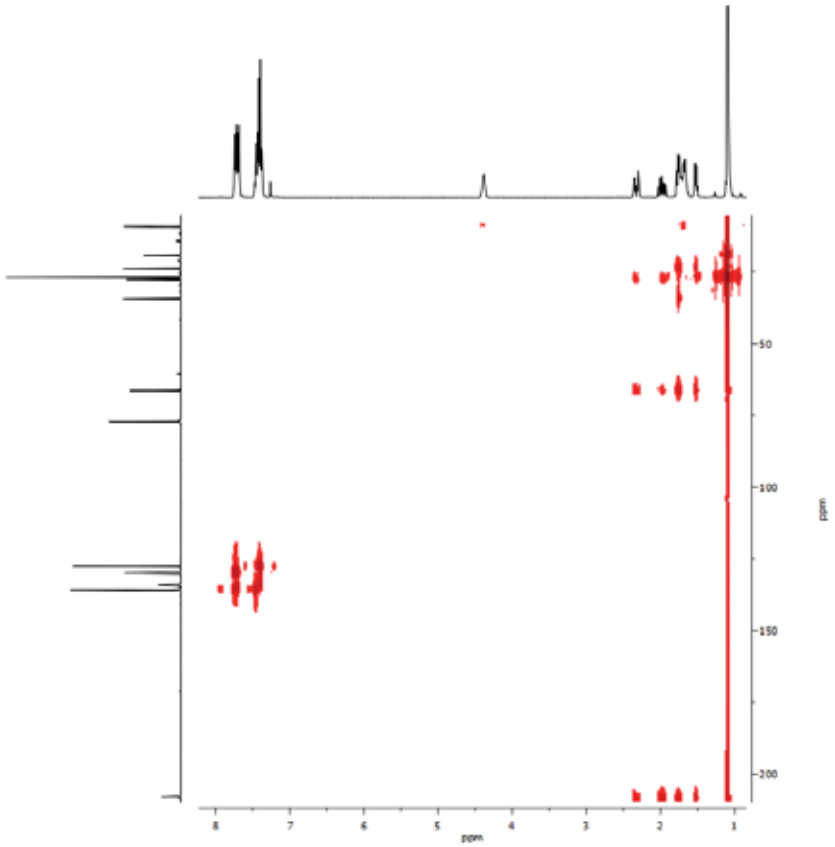
^{13}C-NMR (100 MHz, $CDCl_3$)



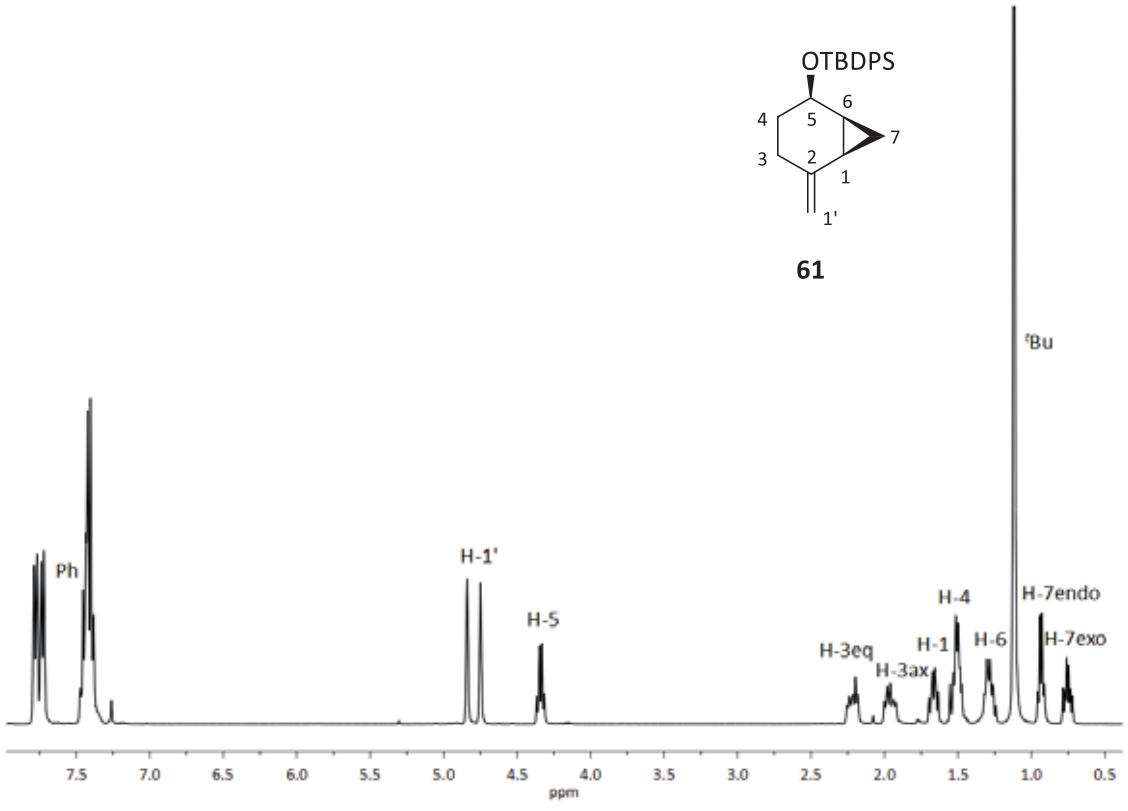
COSY (400 MHz, $CDCl_3$)



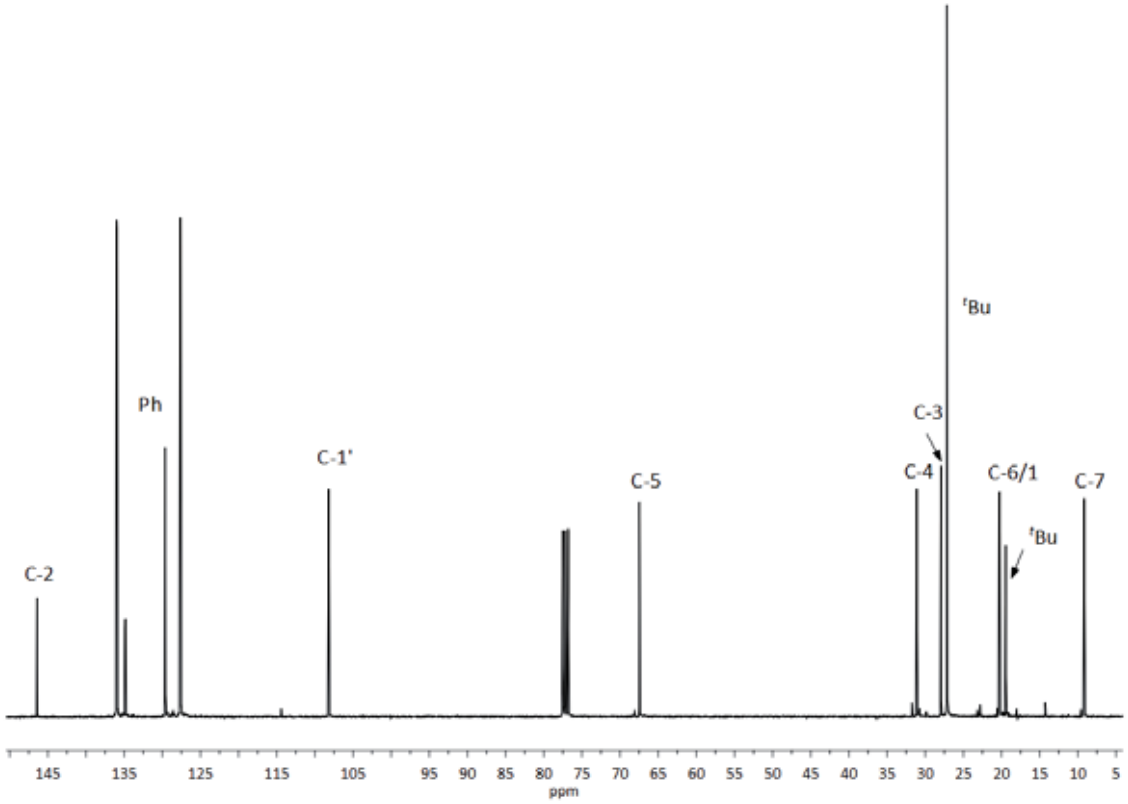
HSQC (400 MHz, $CDCl_3$)



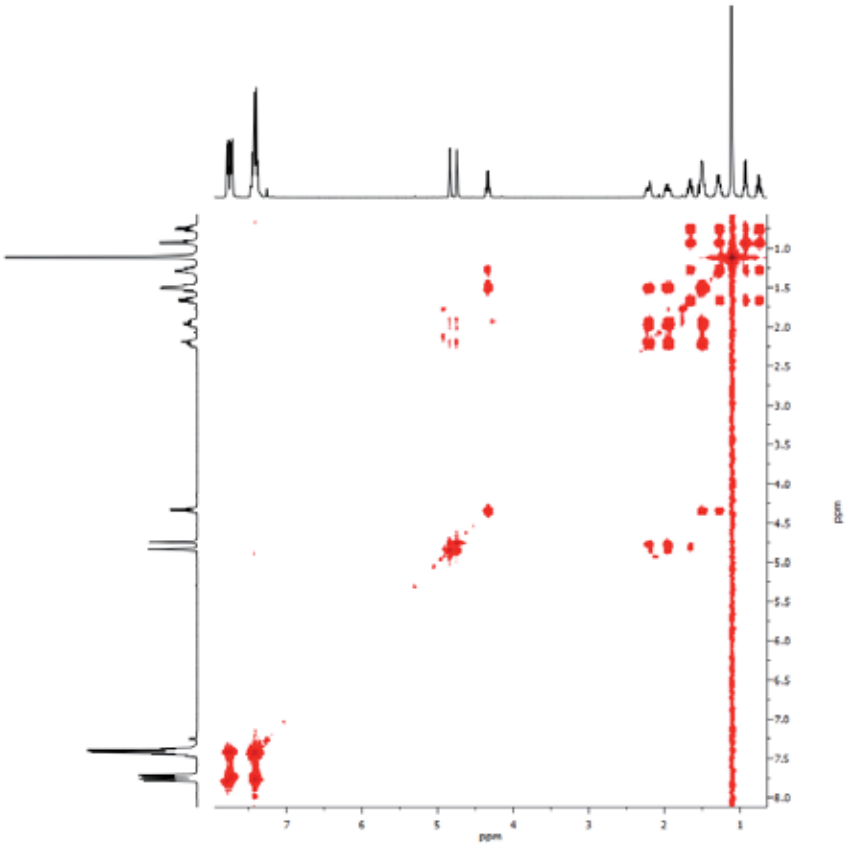
HMBC (400 MHz, $CDCl_3$)



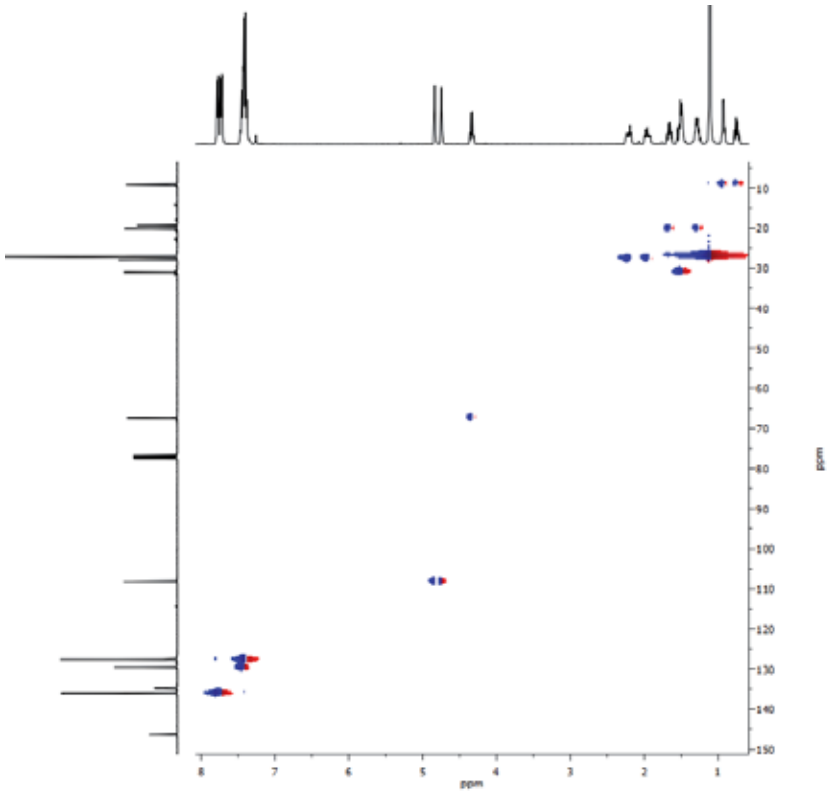
^{1}H-NMR (360 MHz, $CDCl_3$)



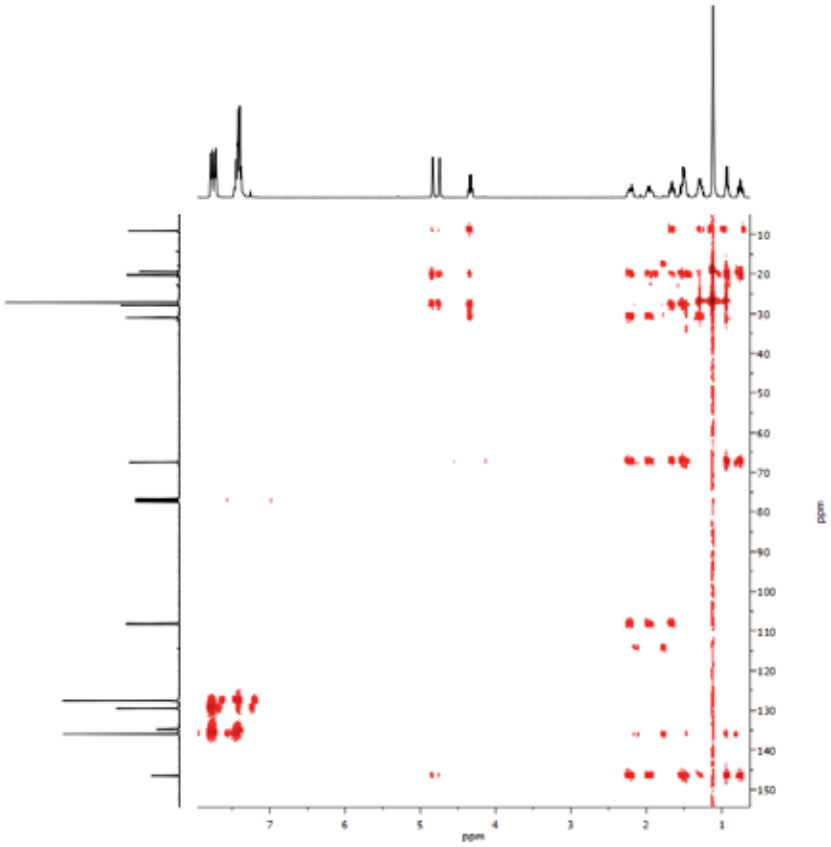
^{13}C-NMR (90 MHz, $CDCl_3$)



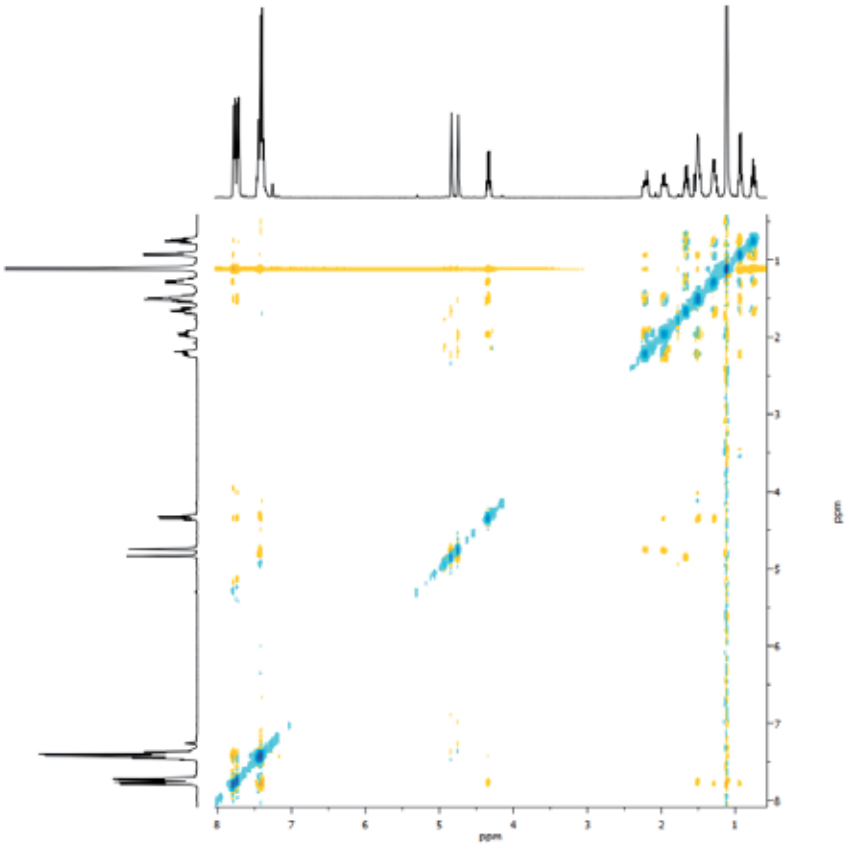
COSY (360 MHz, $CDCl_3$)



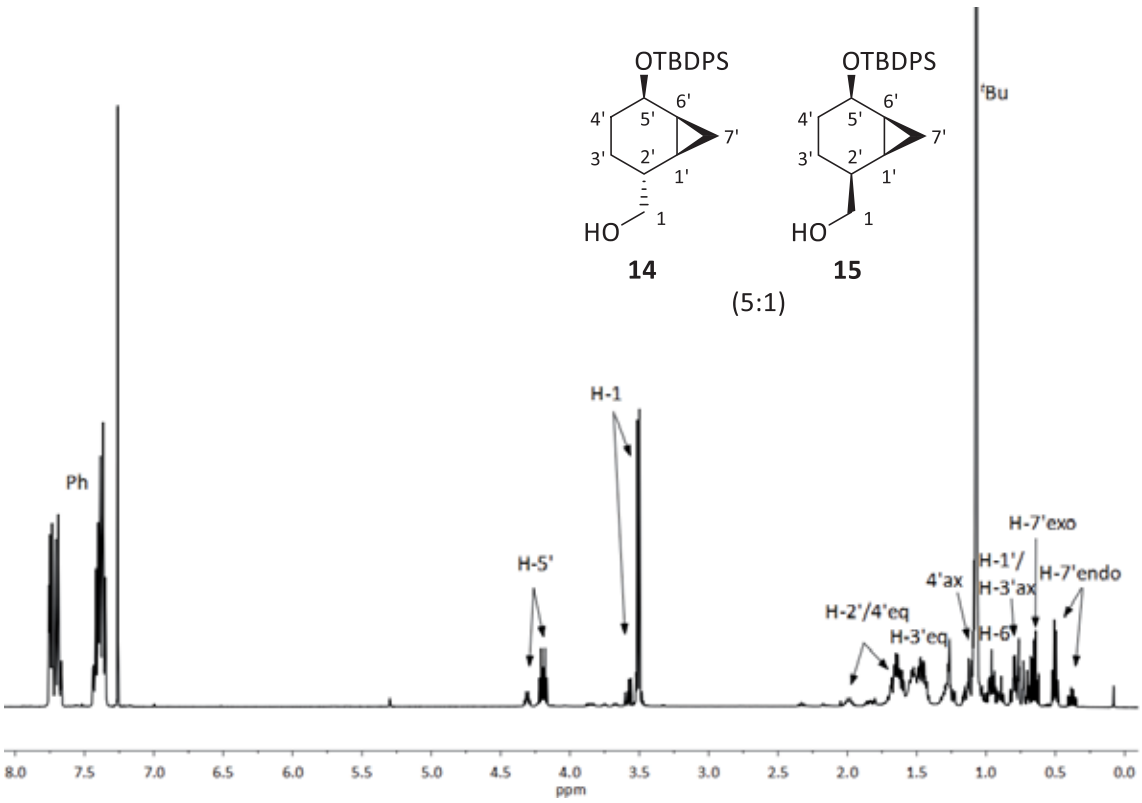
HSQC (360 MHz, $CDCl_3$)



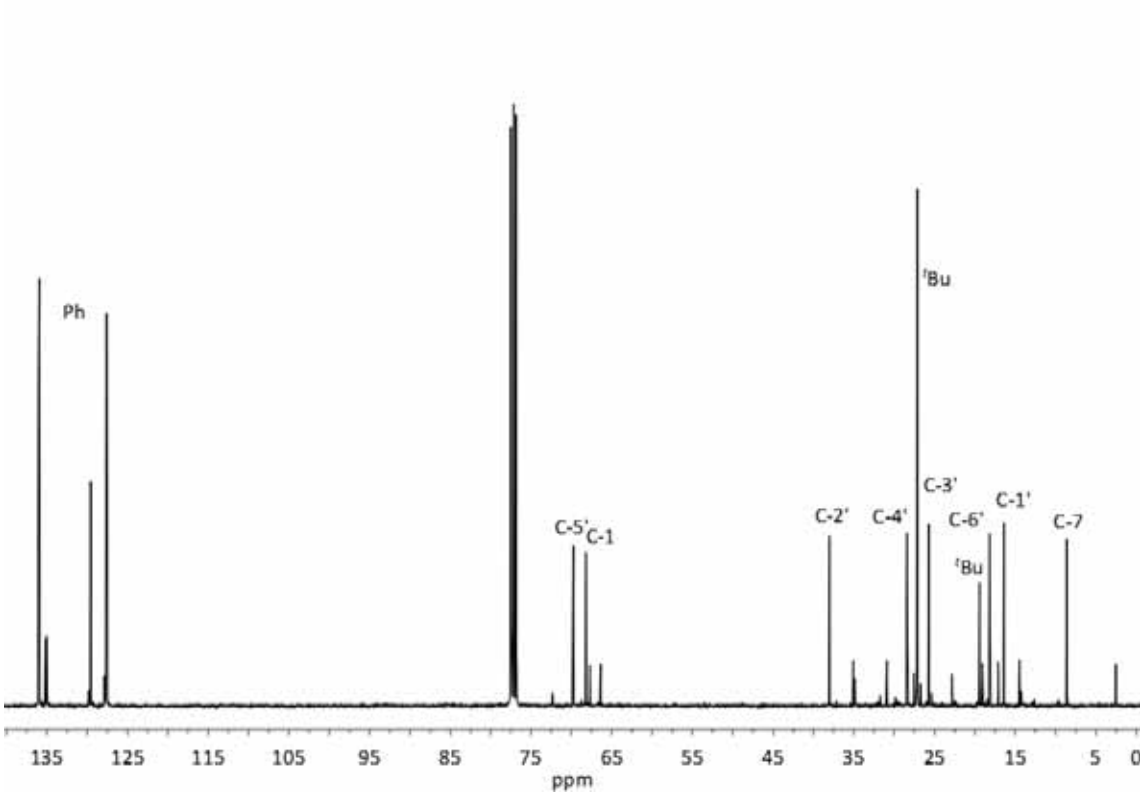
HMBC (360 MHz, $CDCl_3$)



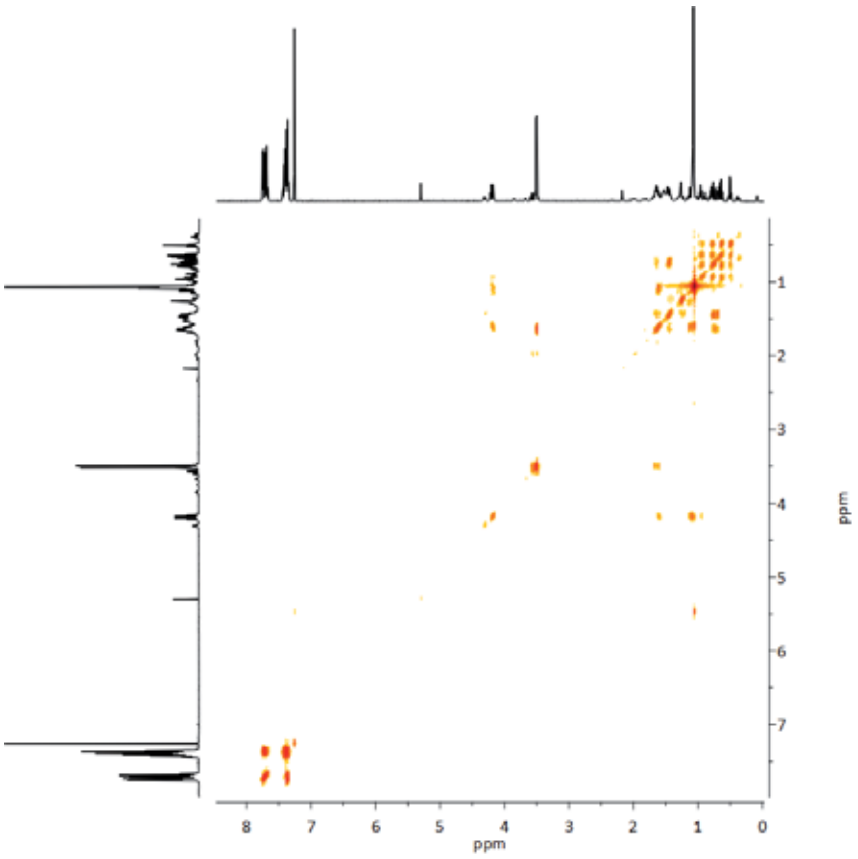
NOESY (360 MHz, $CDCl_3$)



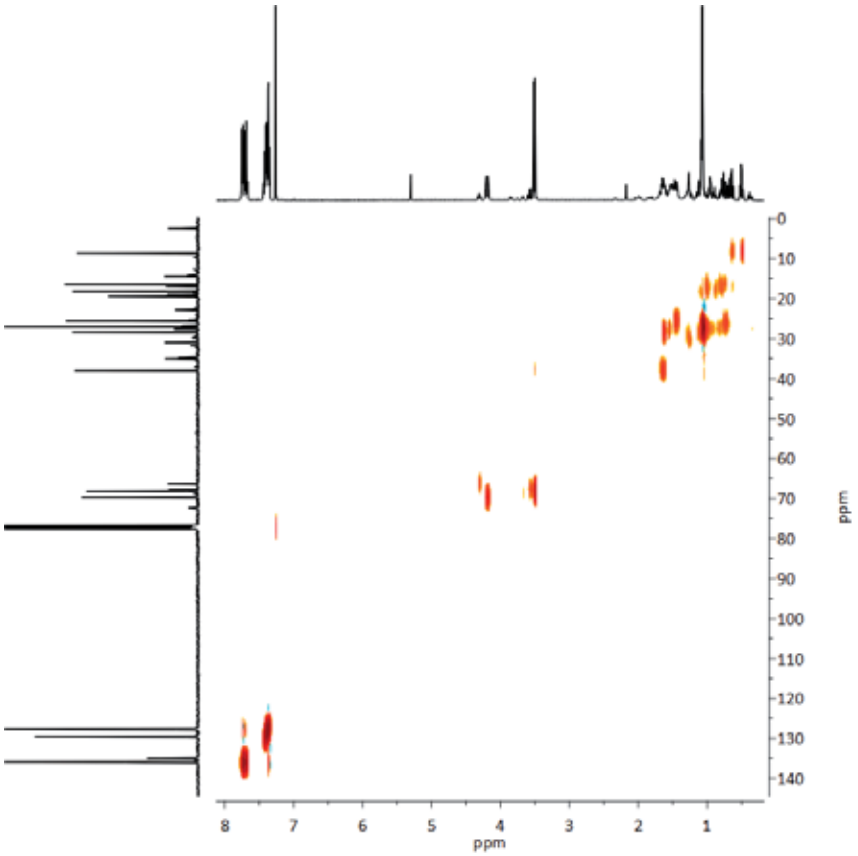
^{1}H-NMR (400 MHz, $CDCl_3$)



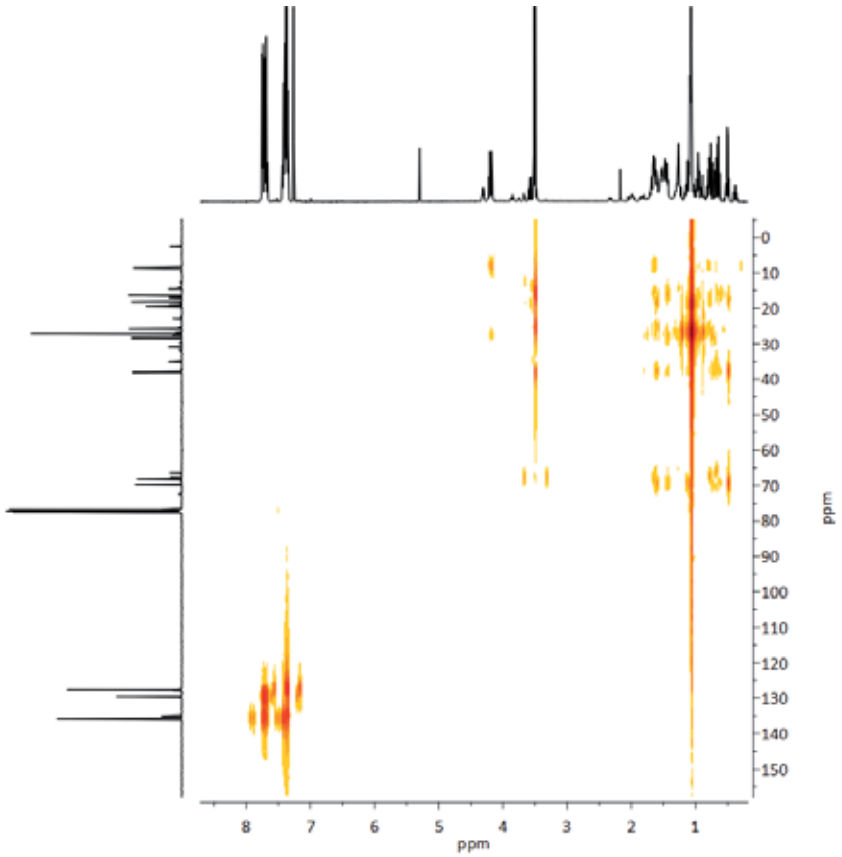
^{13}C-NMR (100 MHz, $CDCl_3$)



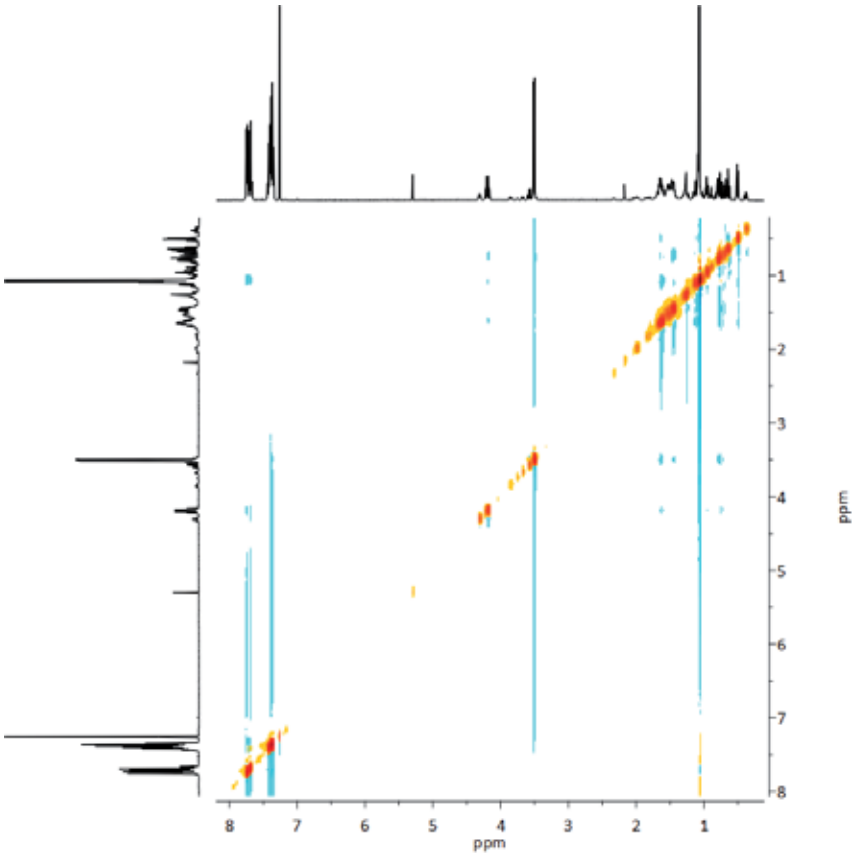
COSY (400 MHz, $CDCl_3$)



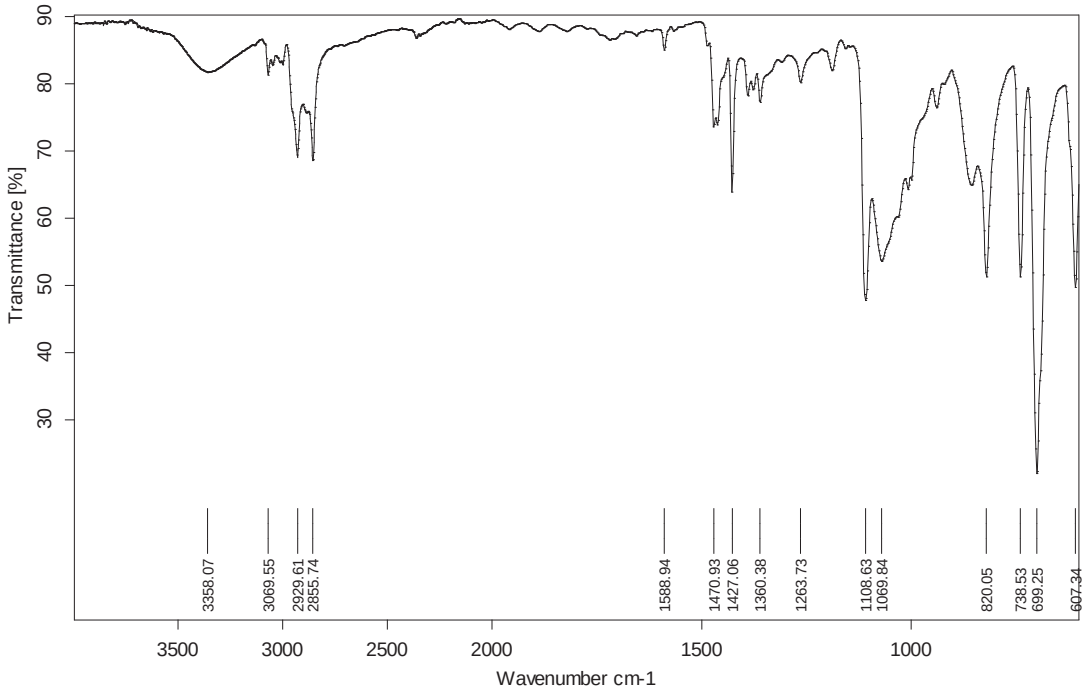
HSQC (400 MHz, $CDCl_3$)



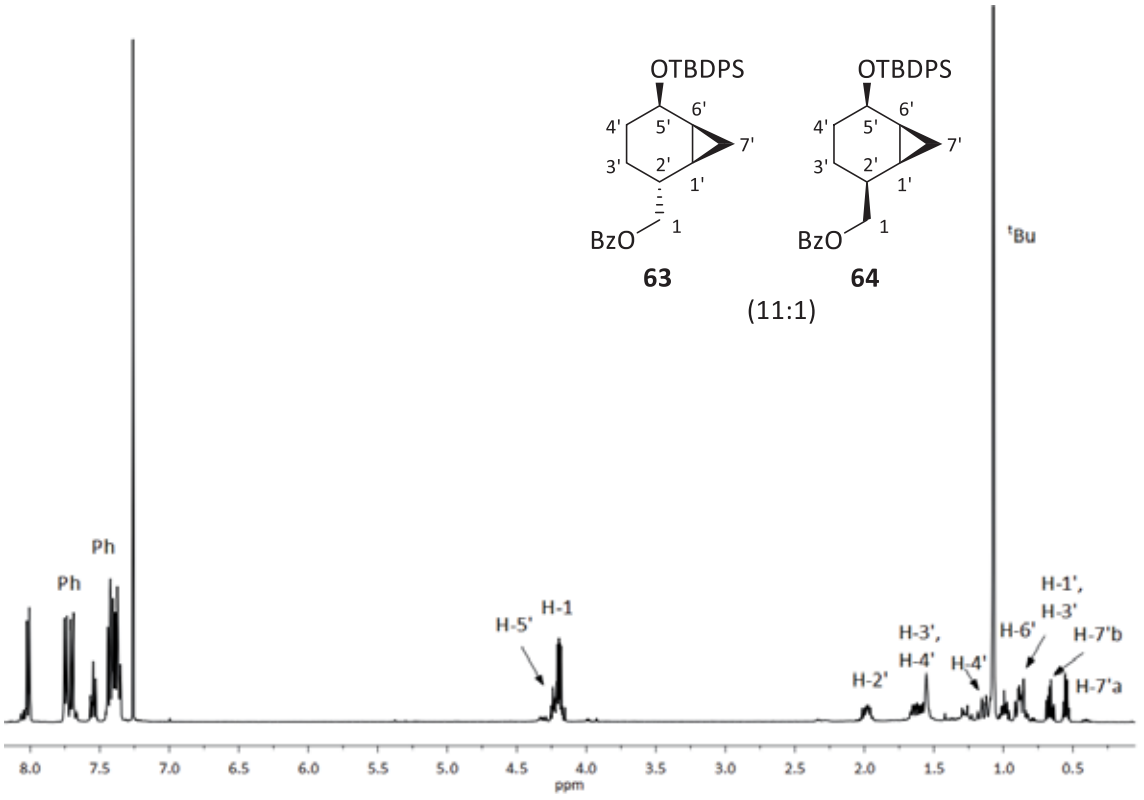
HMBC (400 MHz, $CDCl_3$)



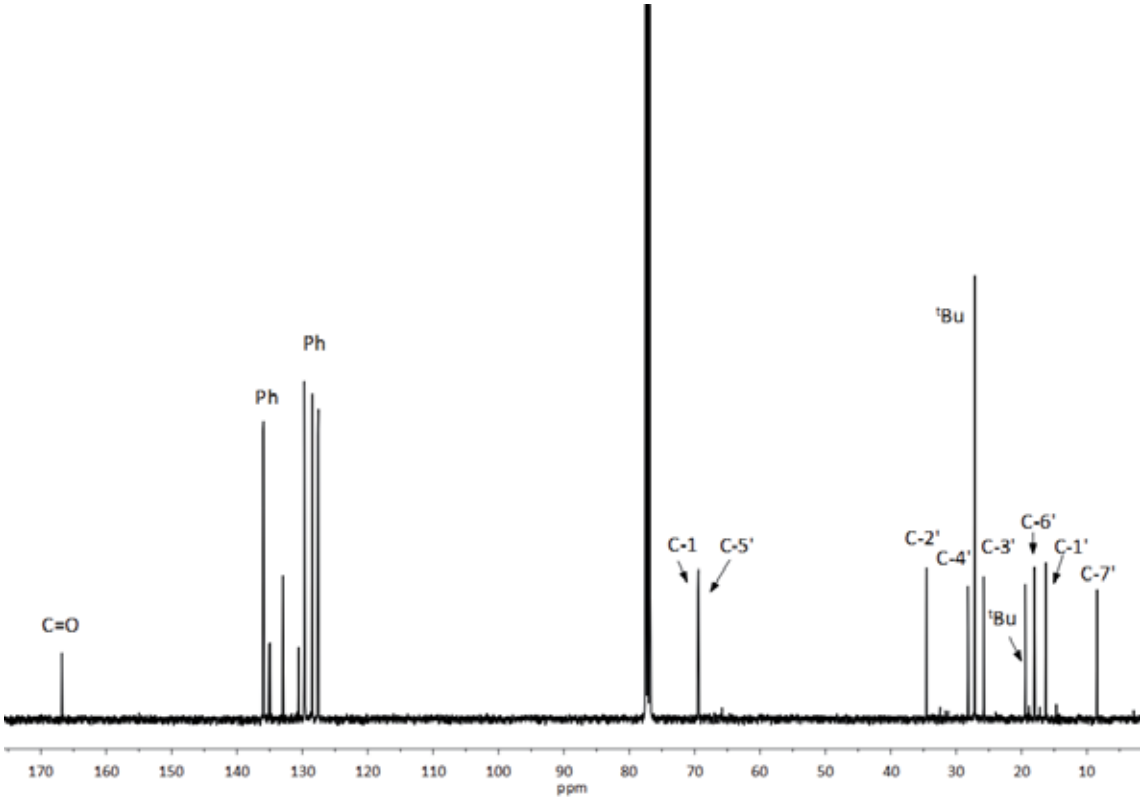
NOESY (400 MHz, $CDCl_3$)



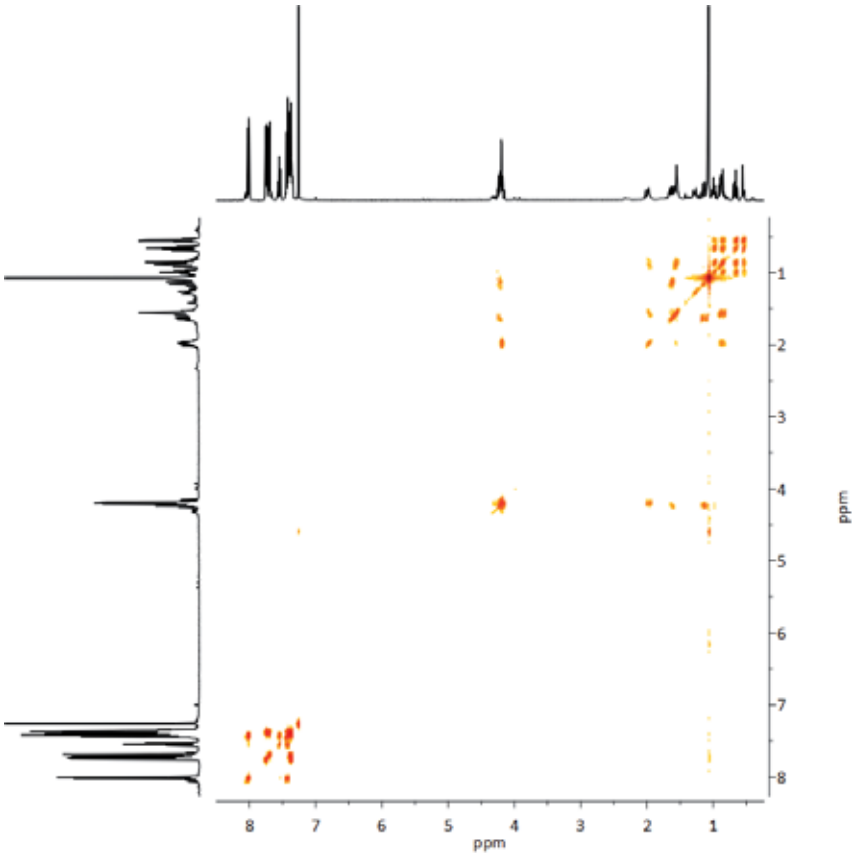
IR (ATR)



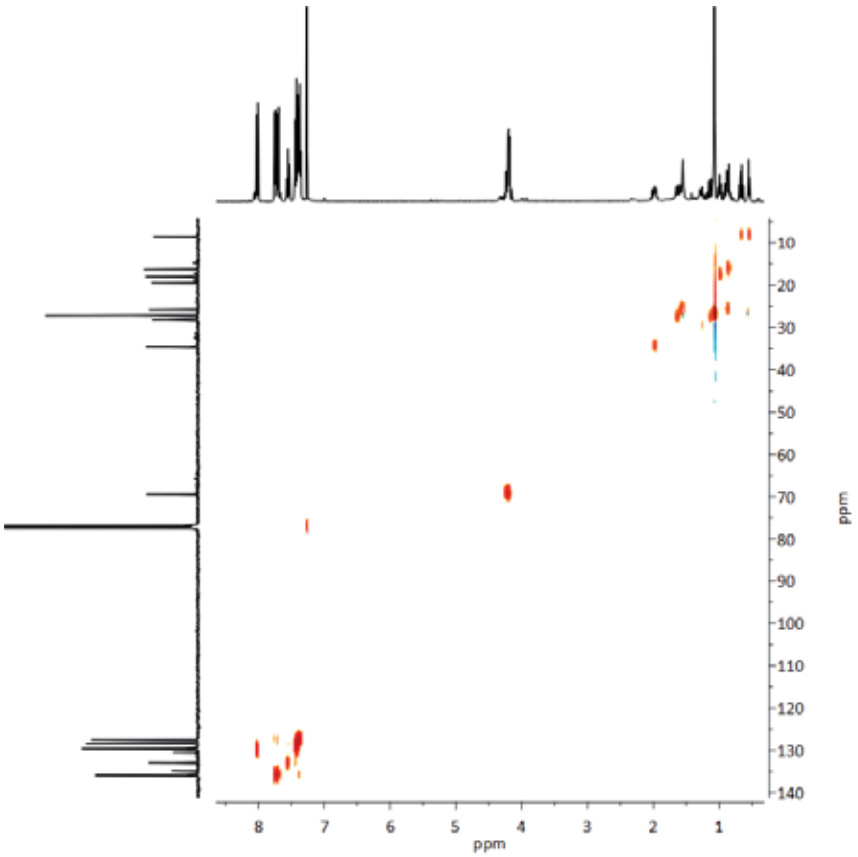
^{1}H-NMR (400 MHz, $CDCl_3$)



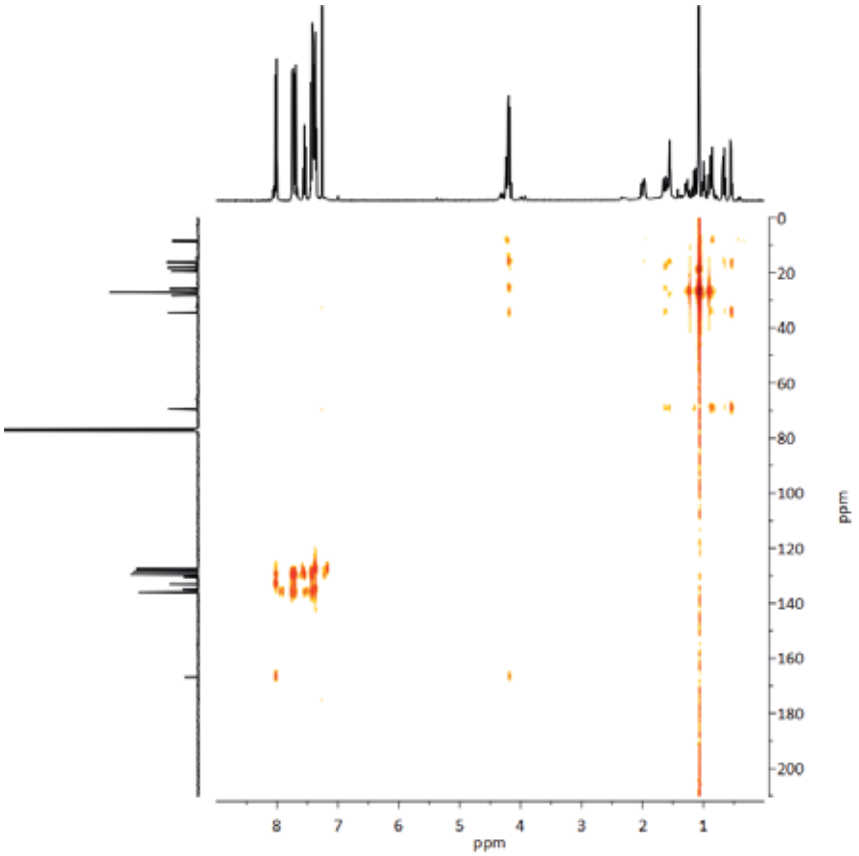
^{13}C-NMR (100 MHz, $CDCl_3$)



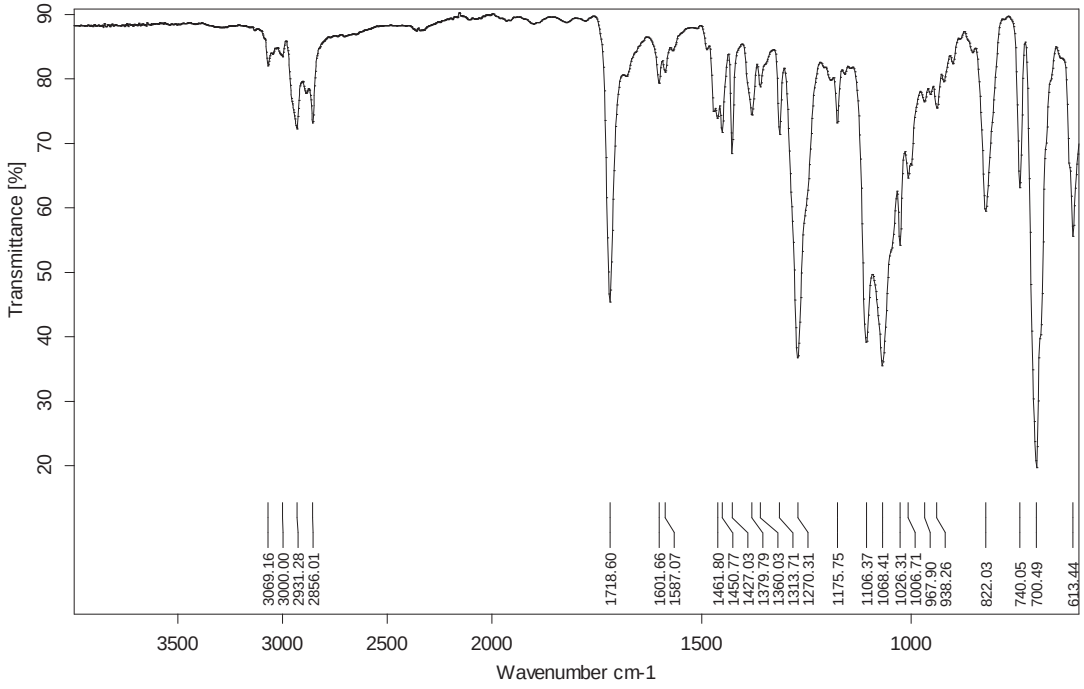
COSY (400 MHz, $CDCl_3$)



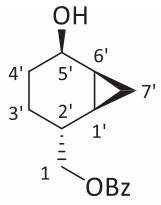
HSQC (400 MHz, $CDCl_3$)



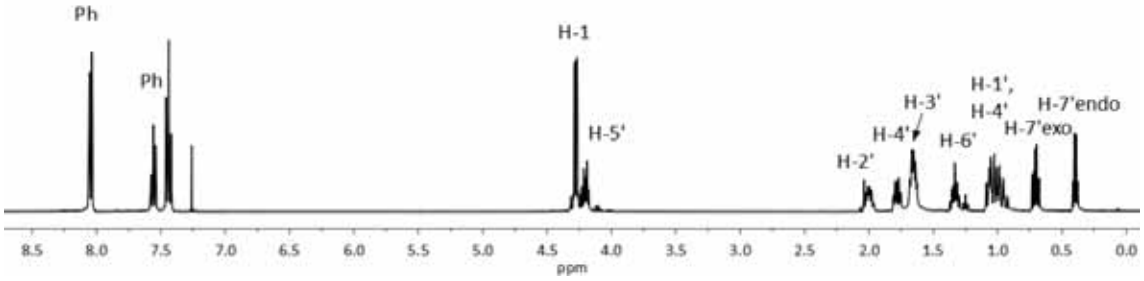
HMBC (400 MHz, $CDCl_3$)



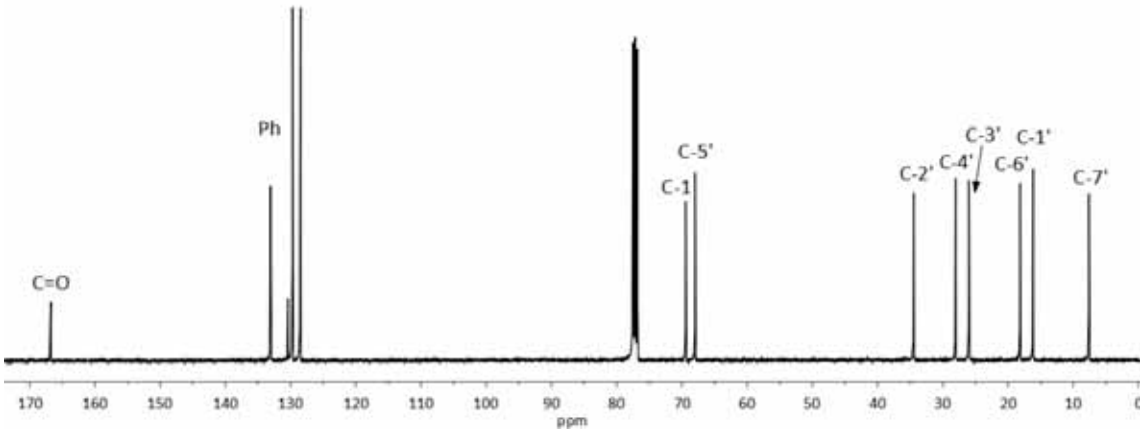
IR (ATR)



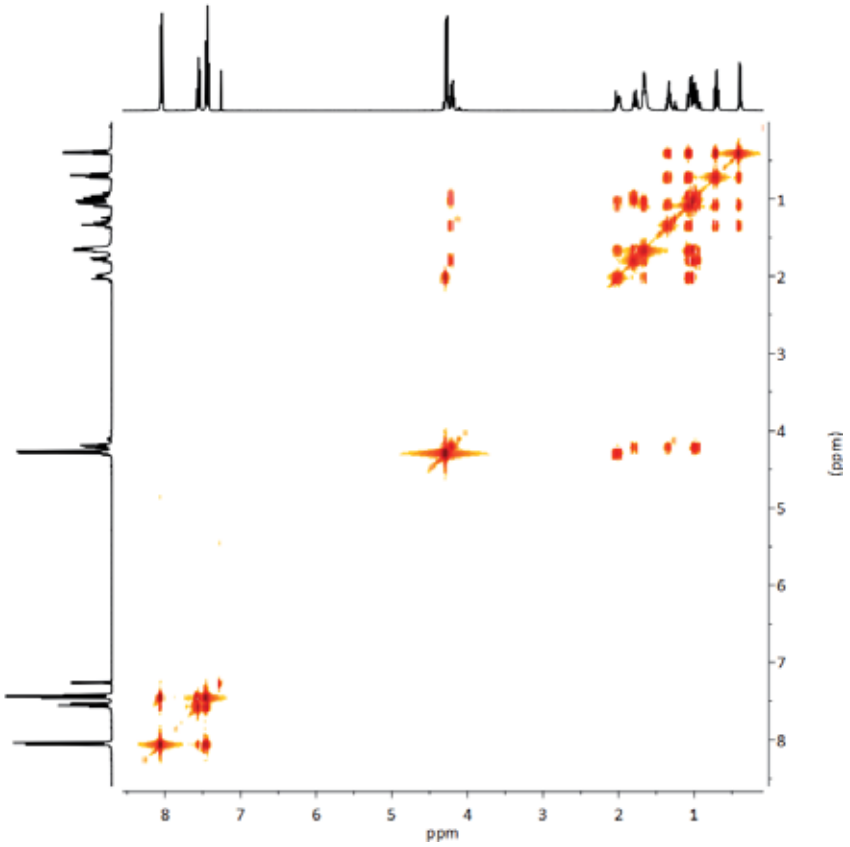
16



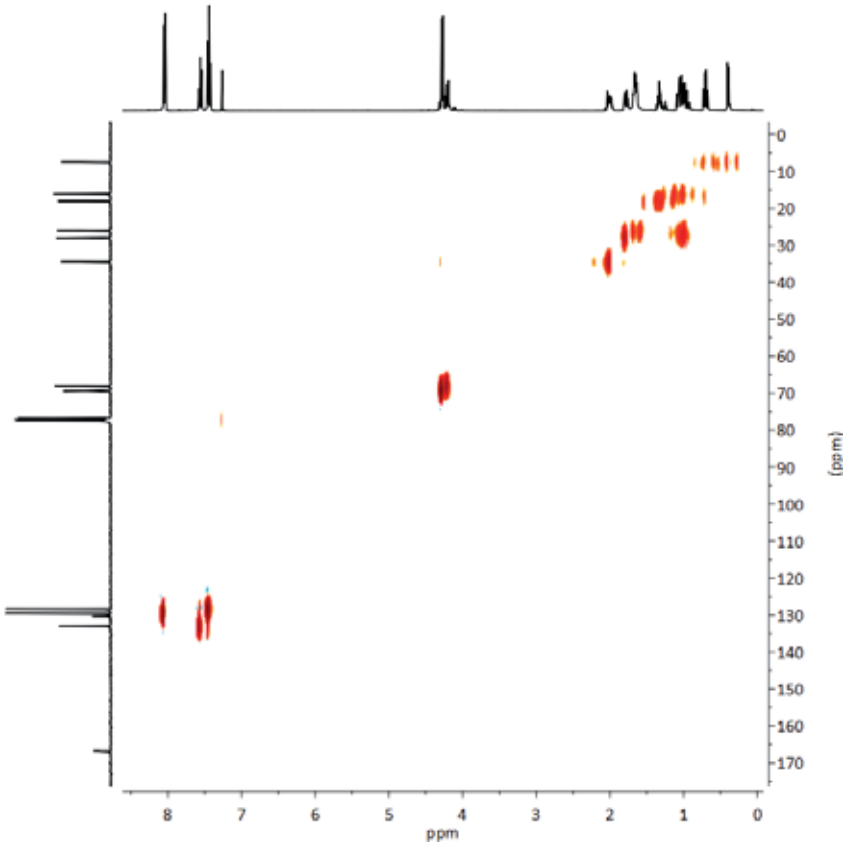
^{1}H-NMR (400 MHz, $CDCl_3$)



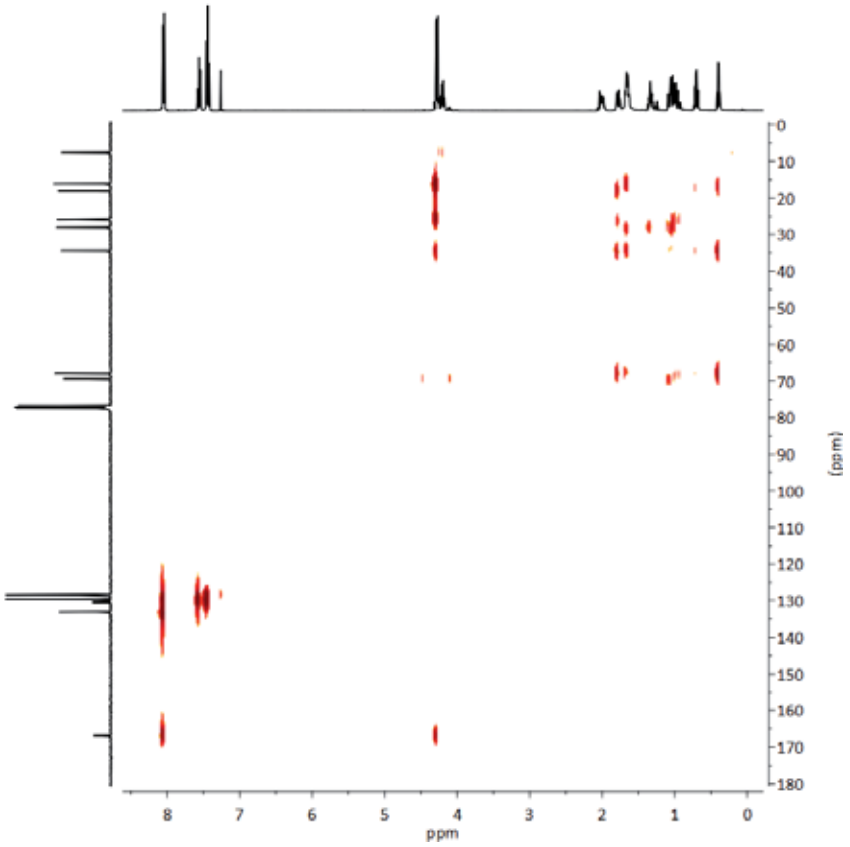
^{13}C-NMR (100 MHz, $CDCl_3$)



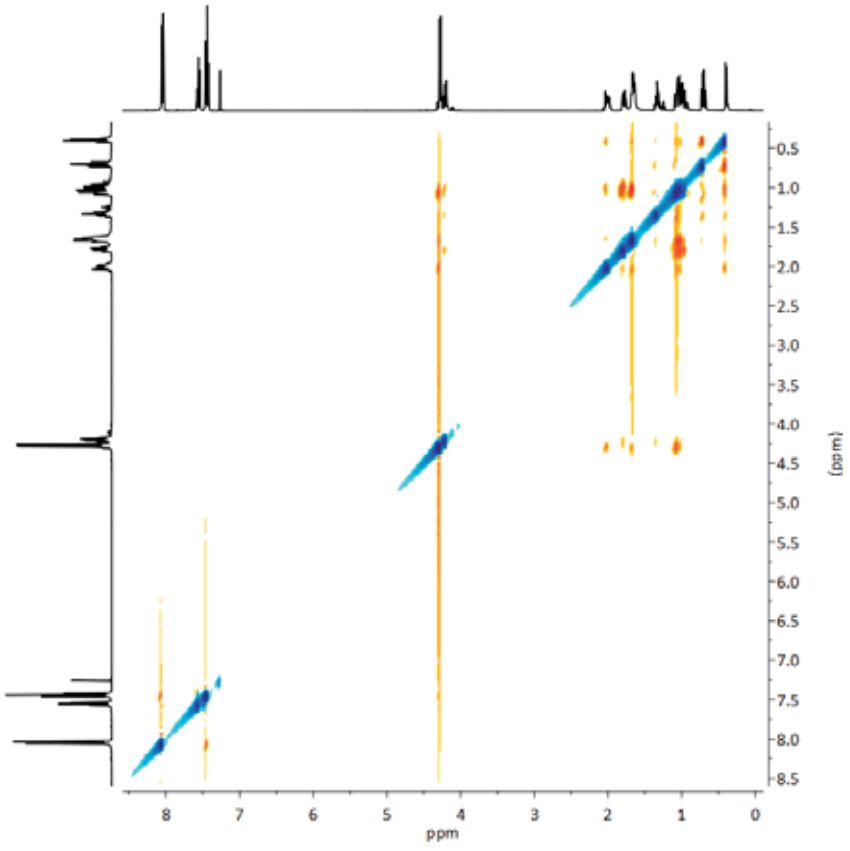
COSY (400 MHz, $CDCl_3$)



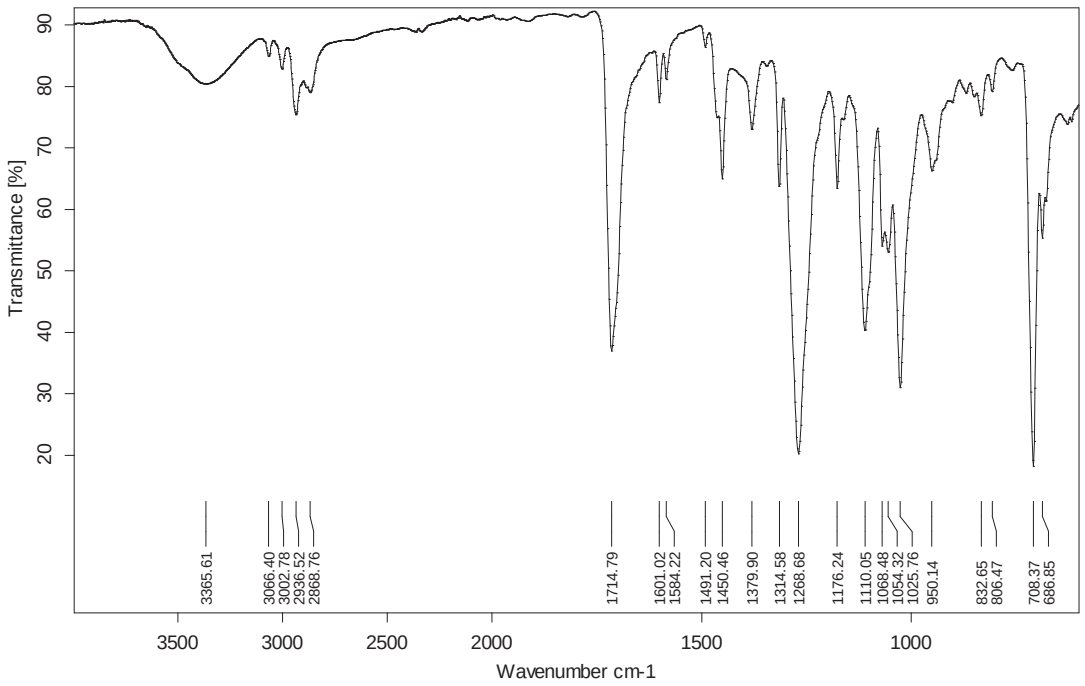
HSQC (400 MHz, $CDCl_3$)



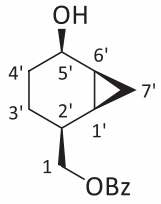
HMBC (400 MHz, $CDCl_3$)



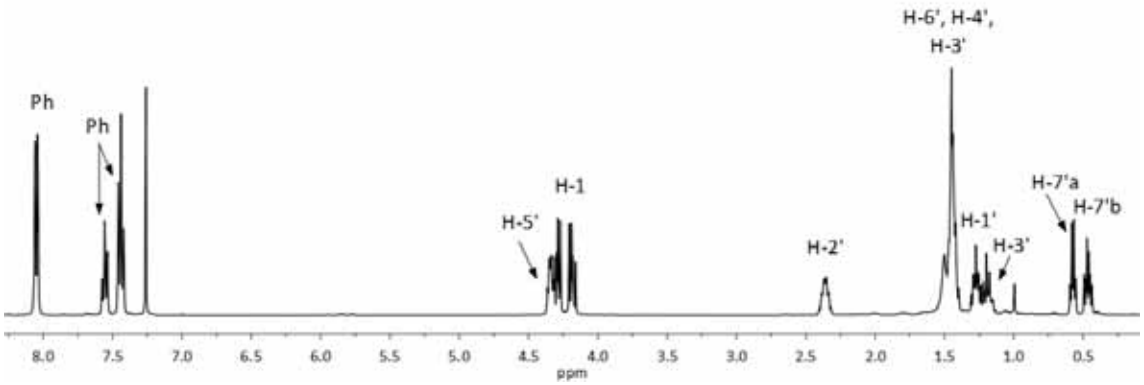
NOESY (400 MHz, $CDCl_3$)



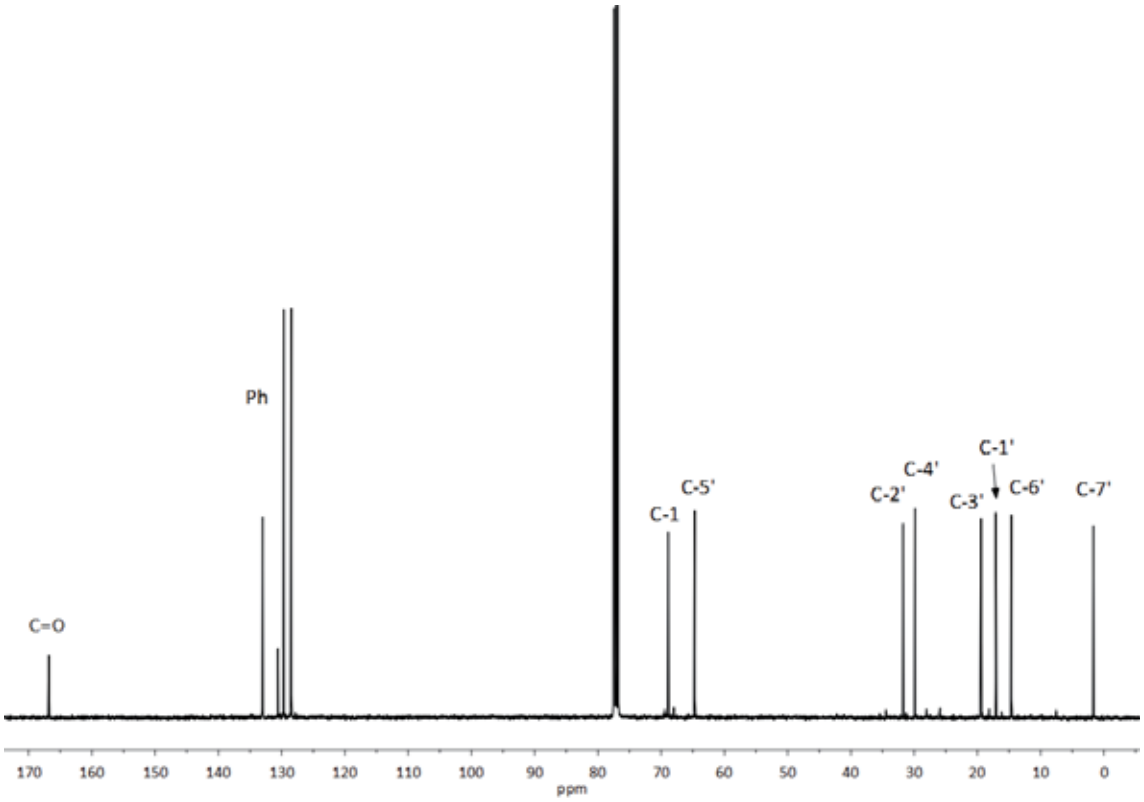
IR (ATR)



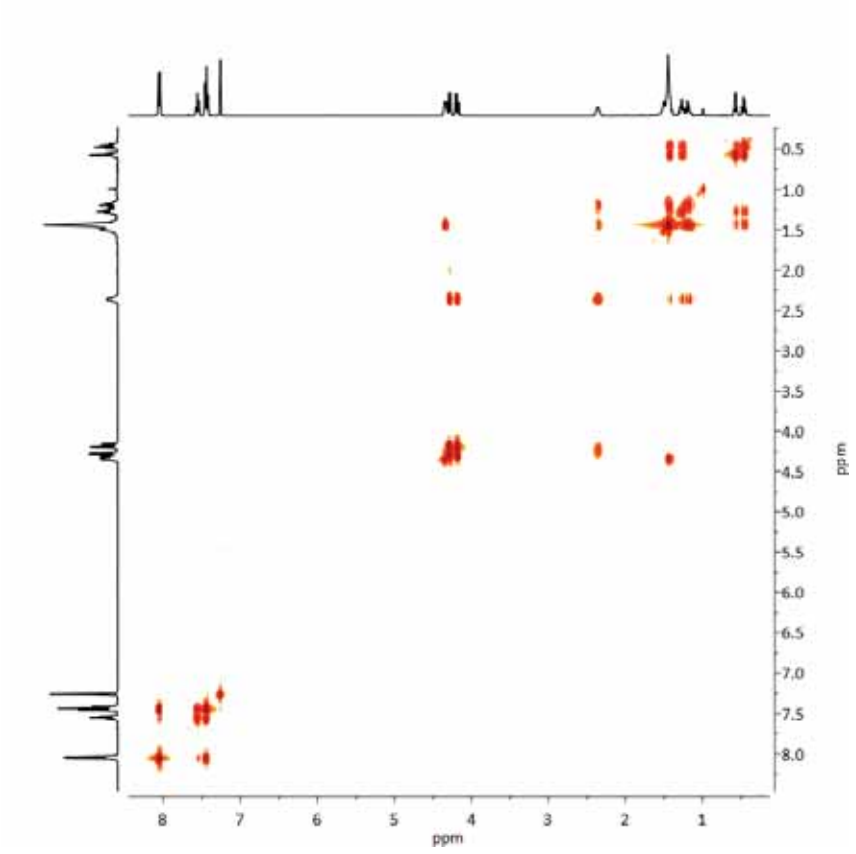
65



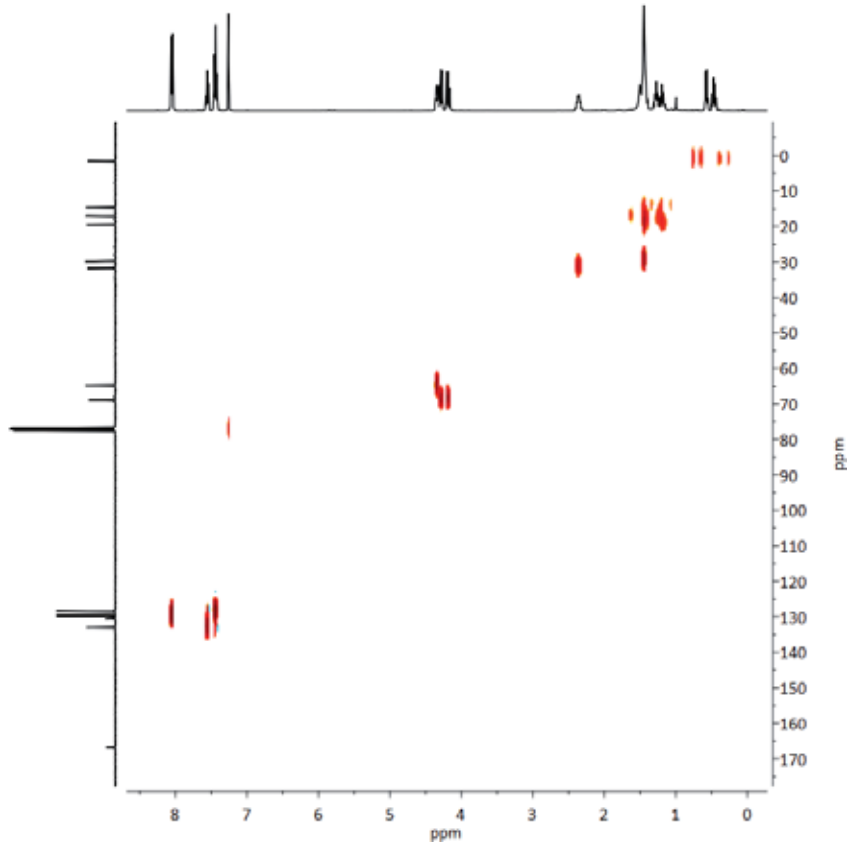
^{1}H-NMR (400 MHz, $CDCl_3$)



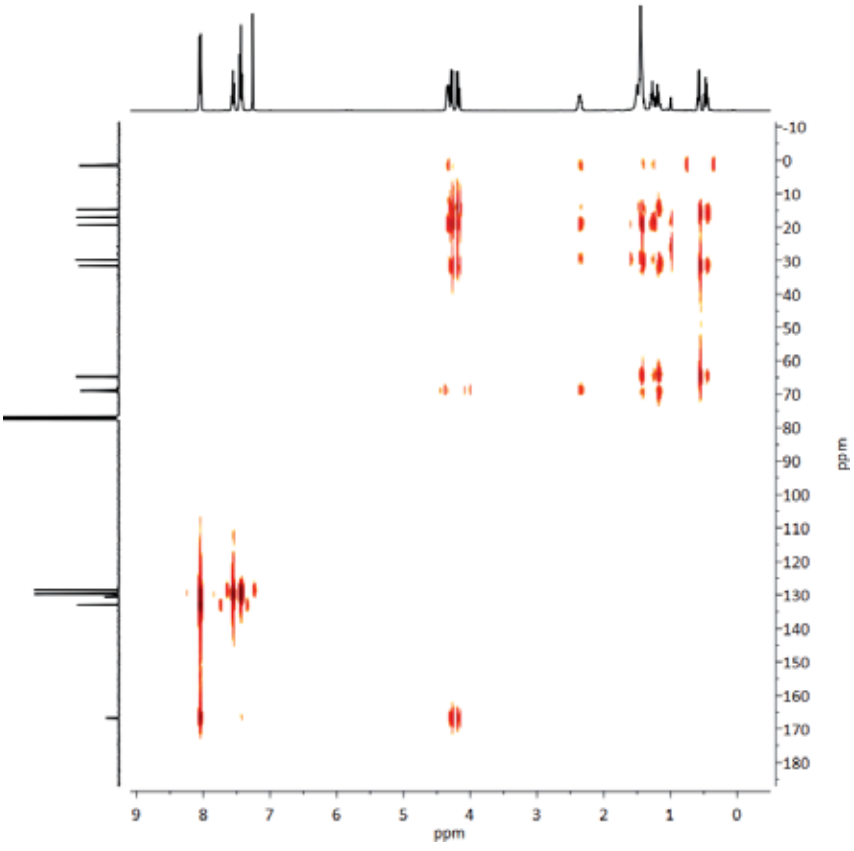
^{13}C-NMR (100 MHz, $CDCl_3$)



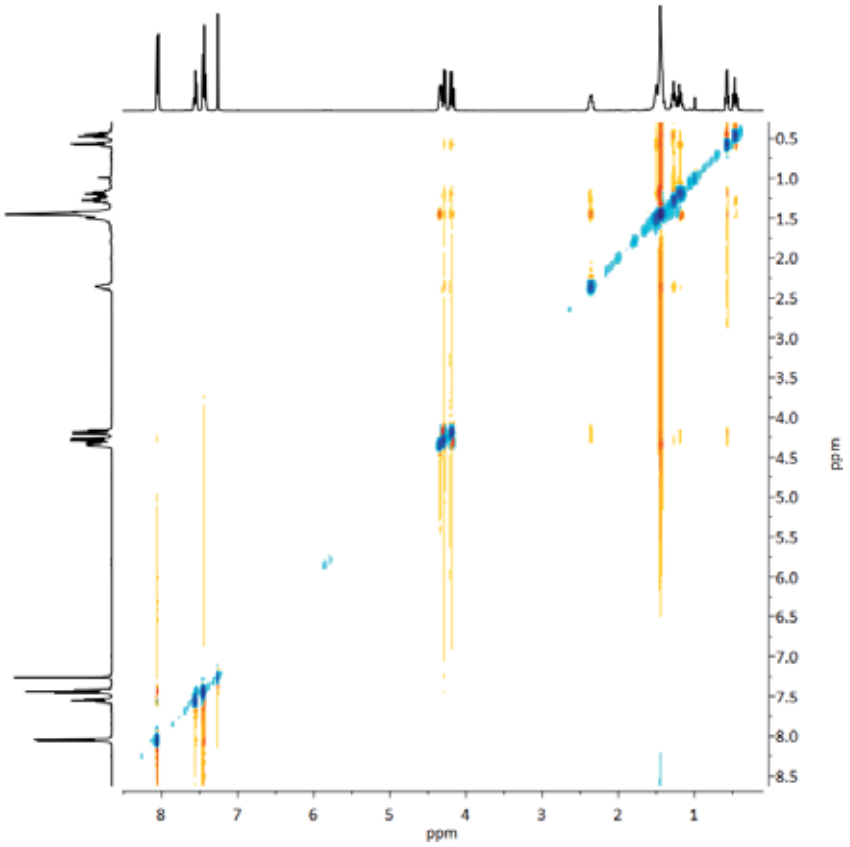
COSY (400 MHz, $CDCl_3$)



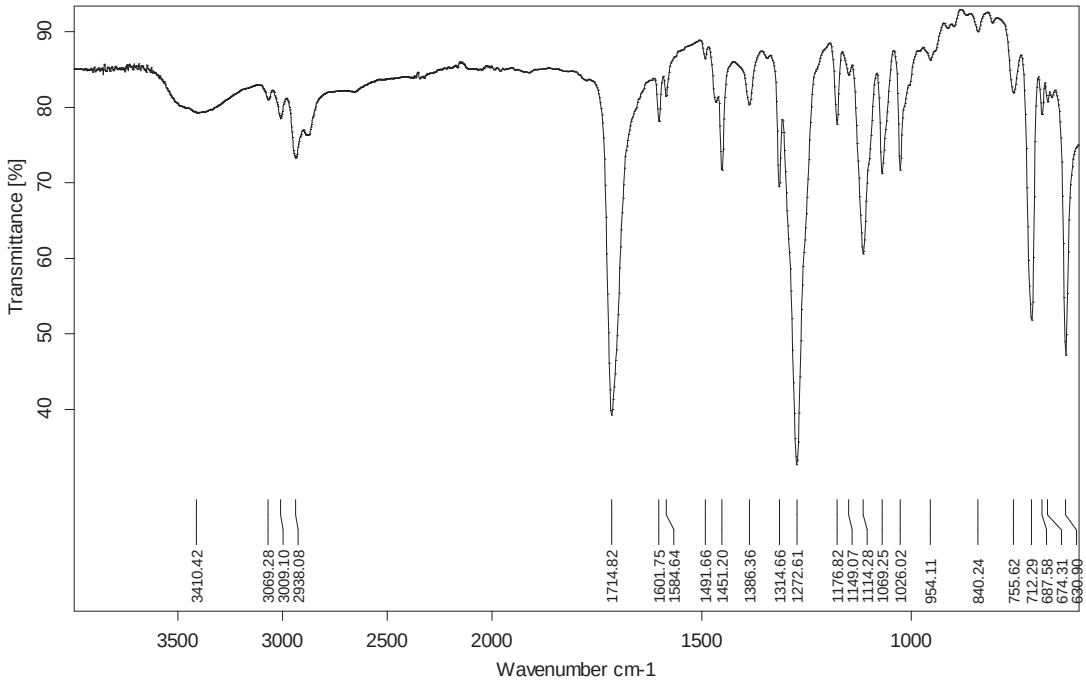
HSQC (400 MHz, $CDCl_3$)



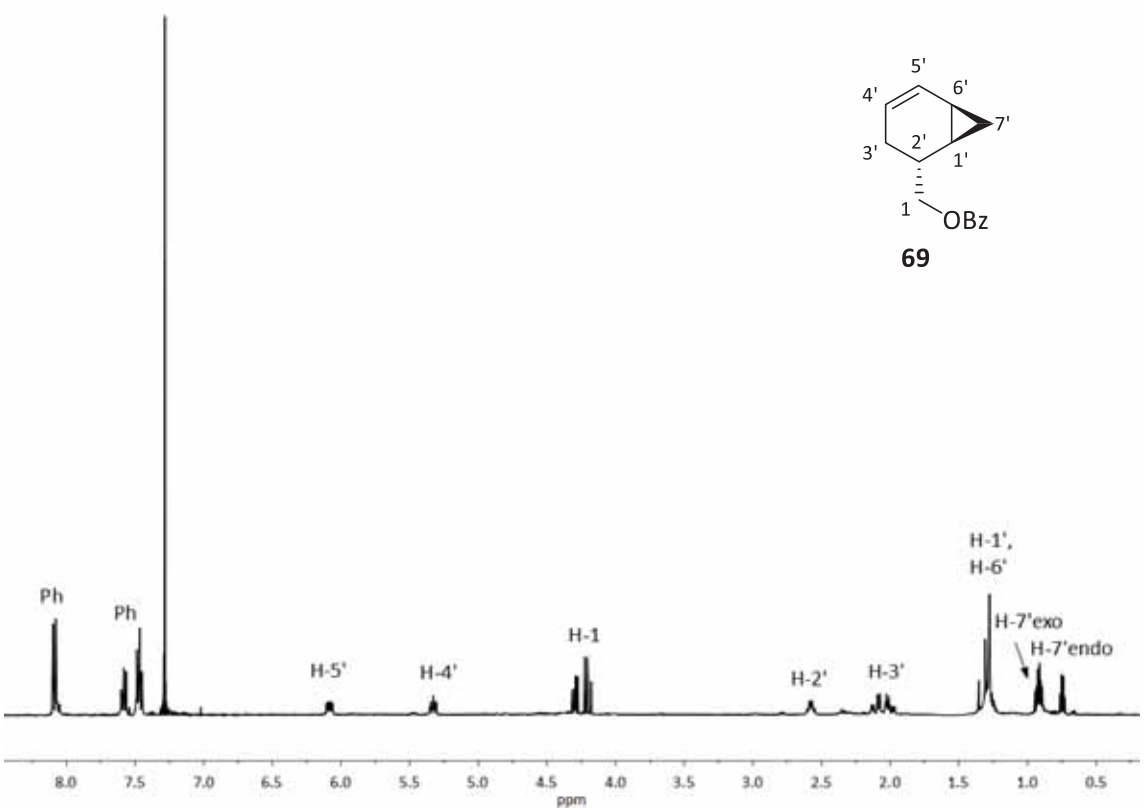
HMBC (400 MHz, $CDCl_3$)



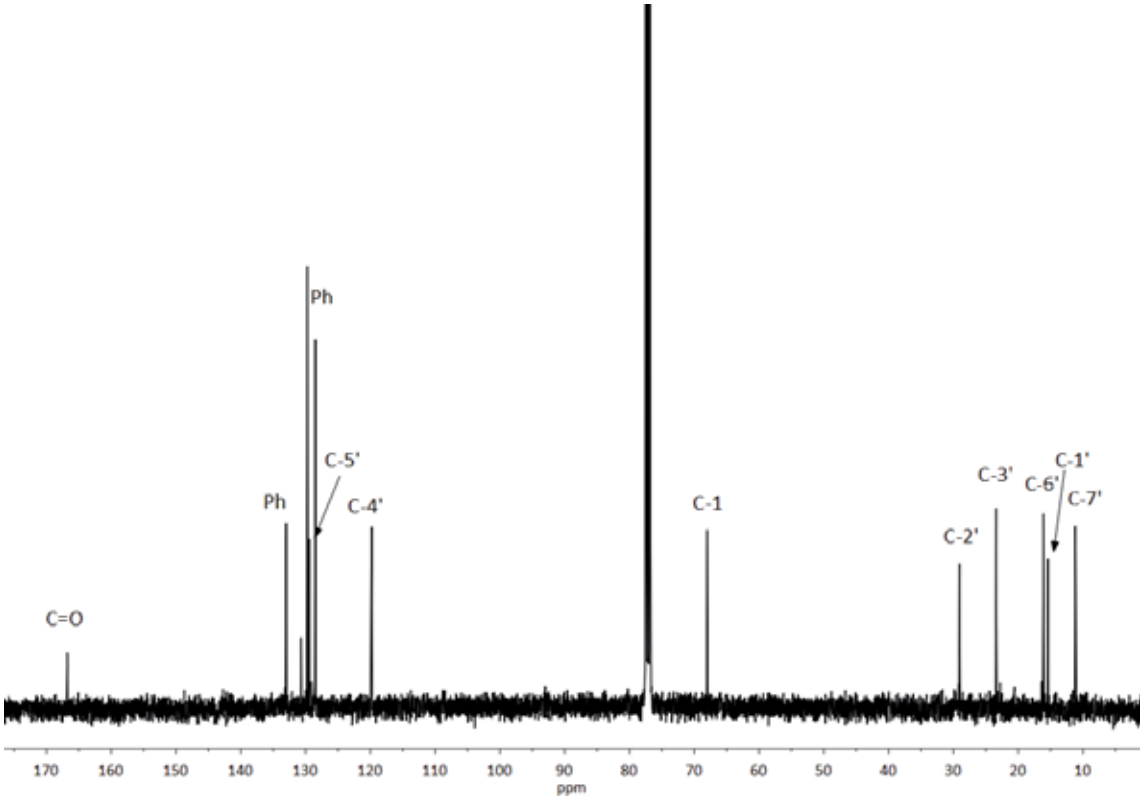
NOESY (400 MHz, $CDCl_3$)



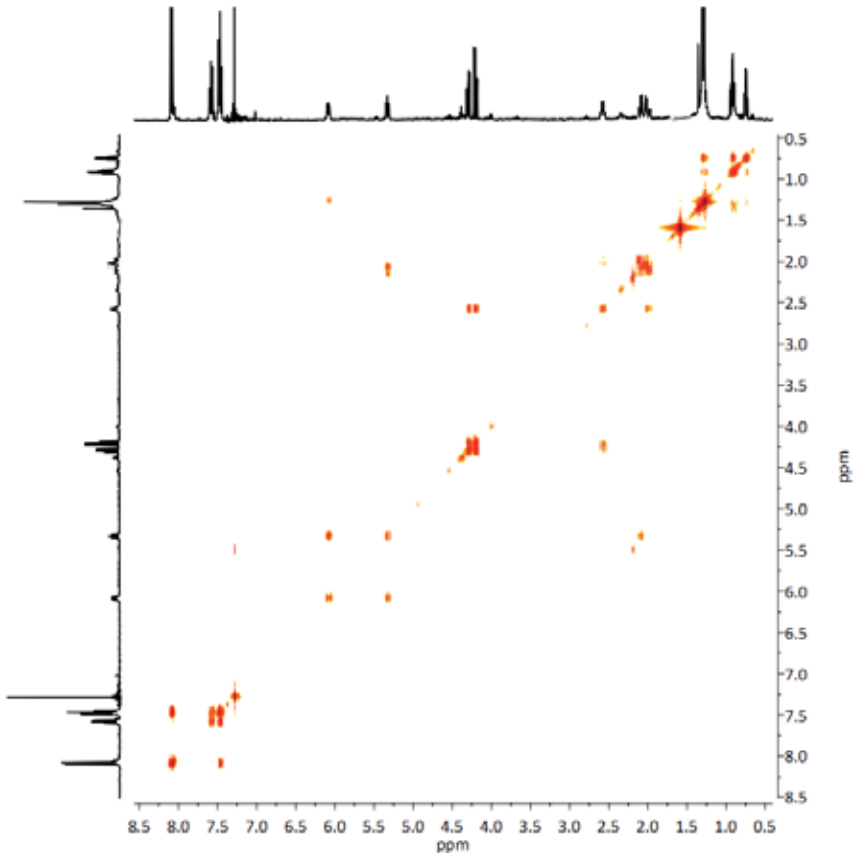
IR (ATR)



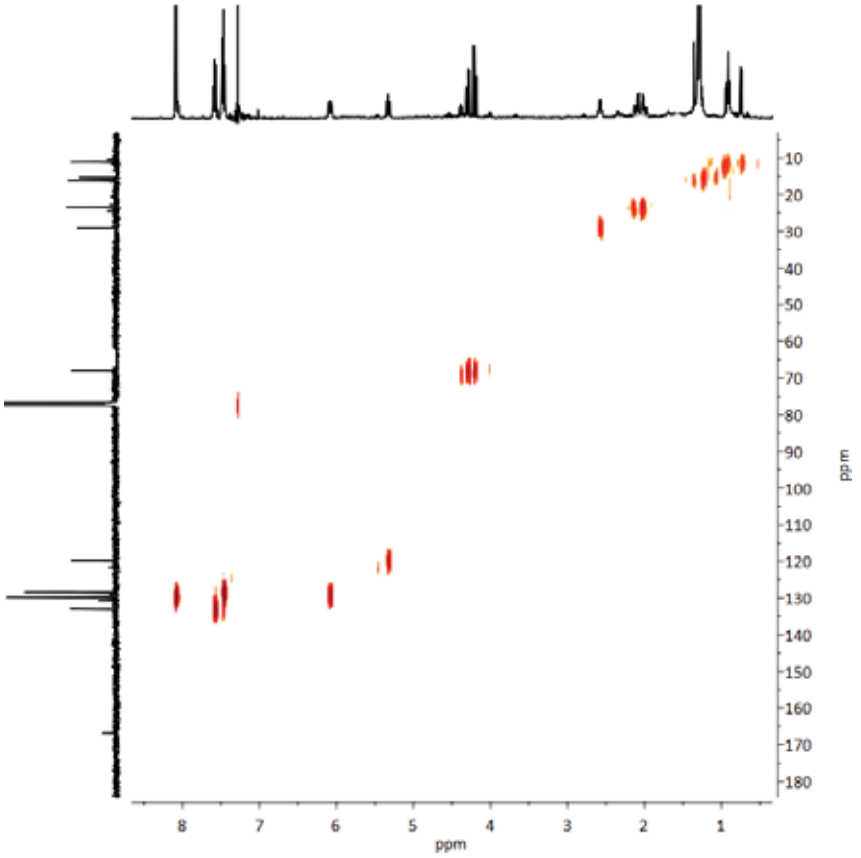
^{1}H-NMR (400 MHz, $CDCl_3$)



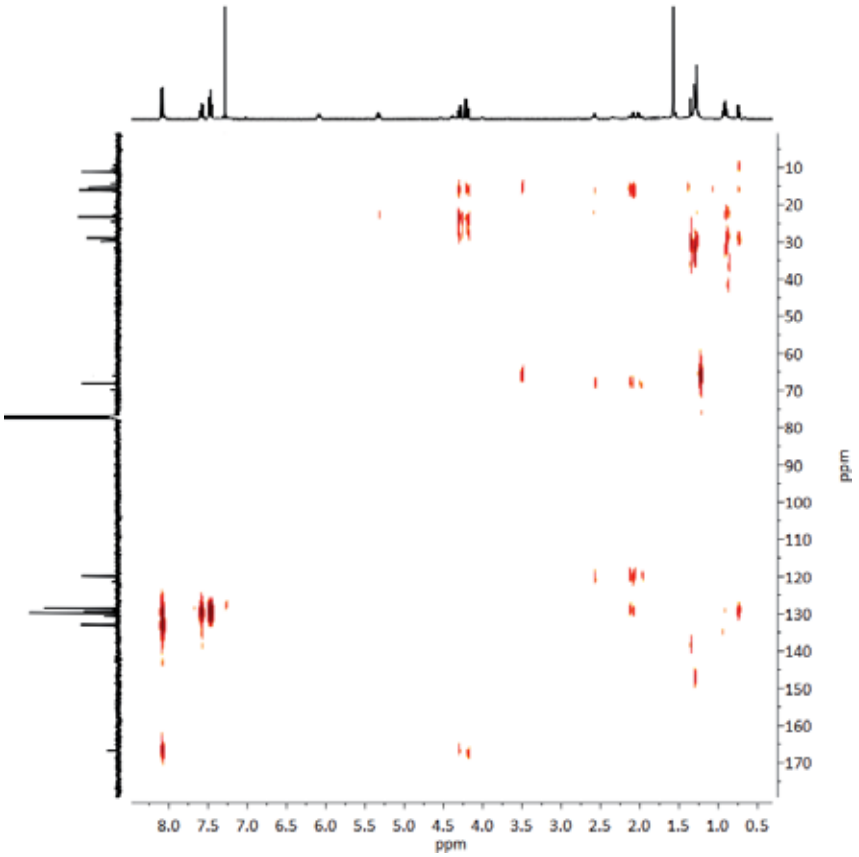
^{13}C-NMR (100 MHz, $CDCl_3$)



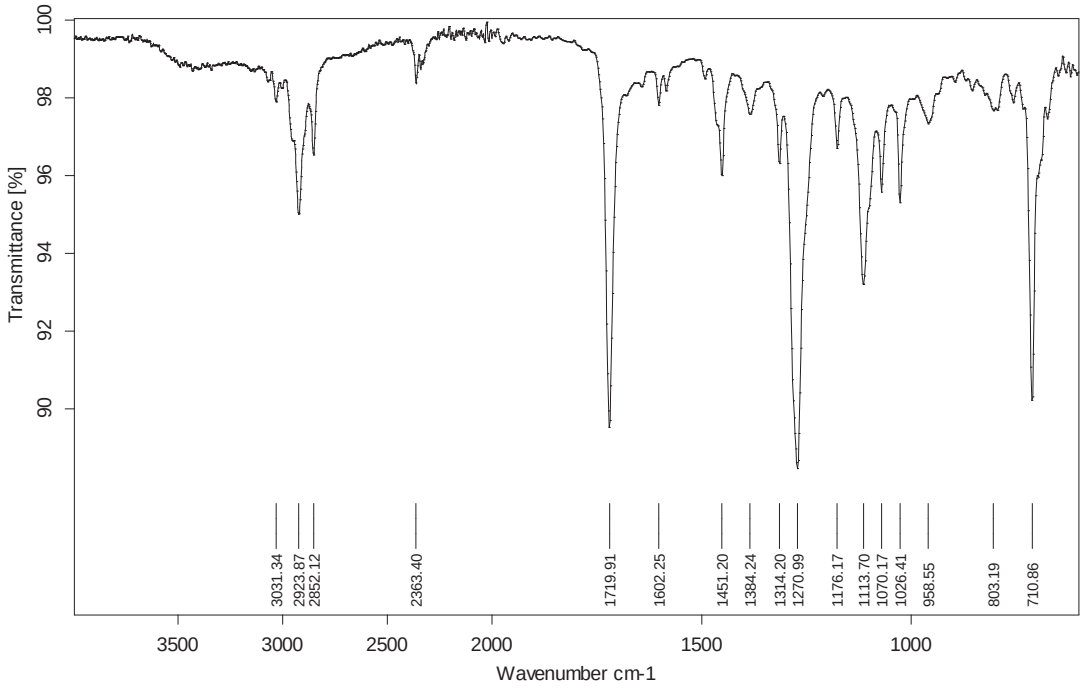
COSY (400 MHz, $CDCl_3$)



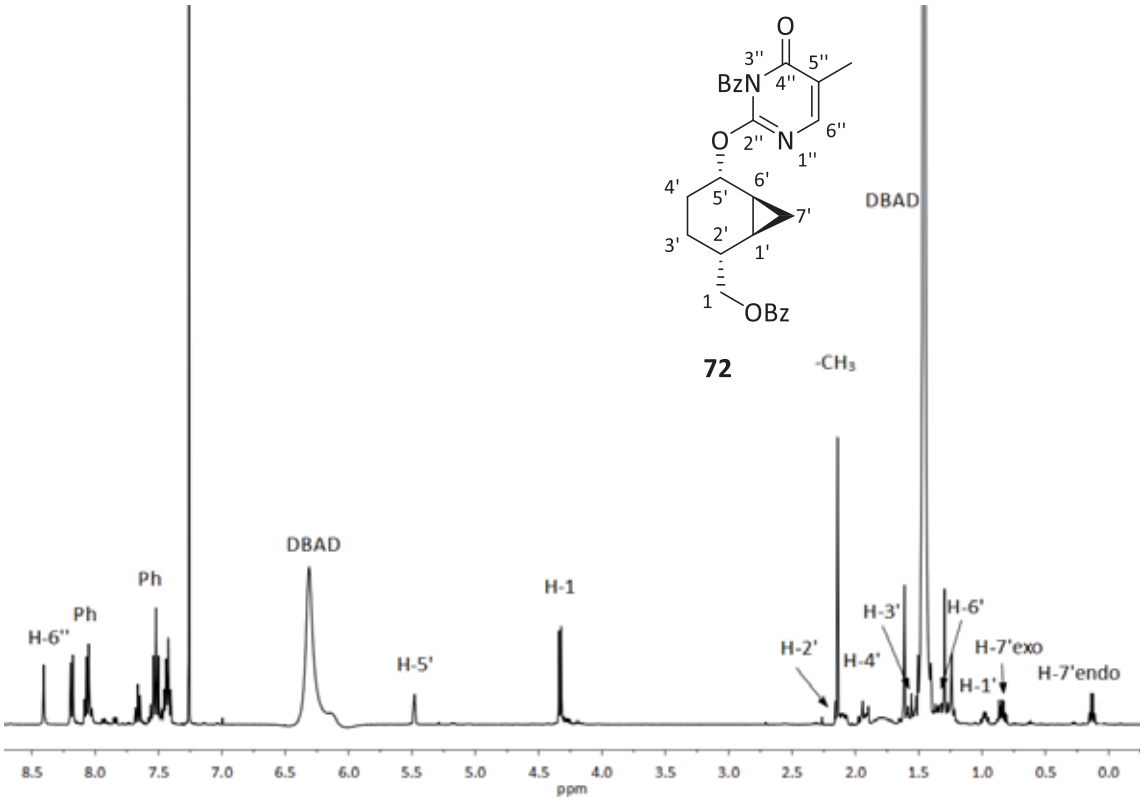
HSQC (400 MHz, $CDCl_3$)



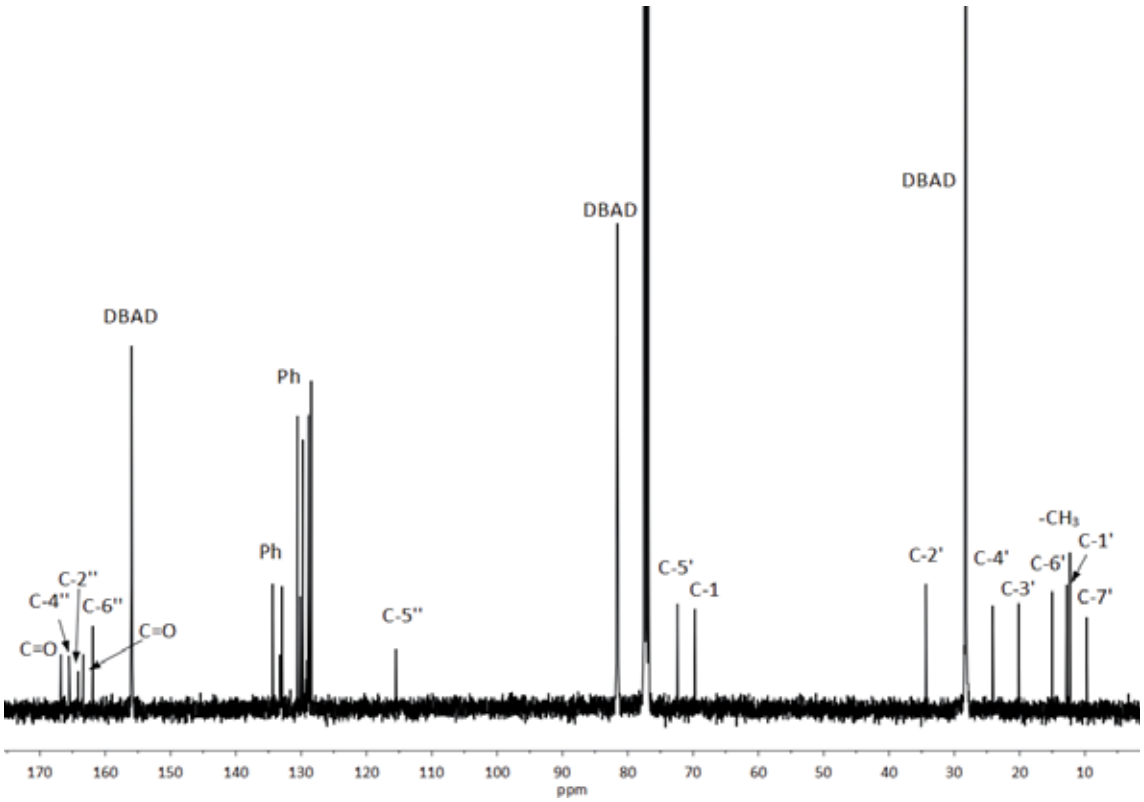
HMBC (400 MHz, $CDCl_3$)



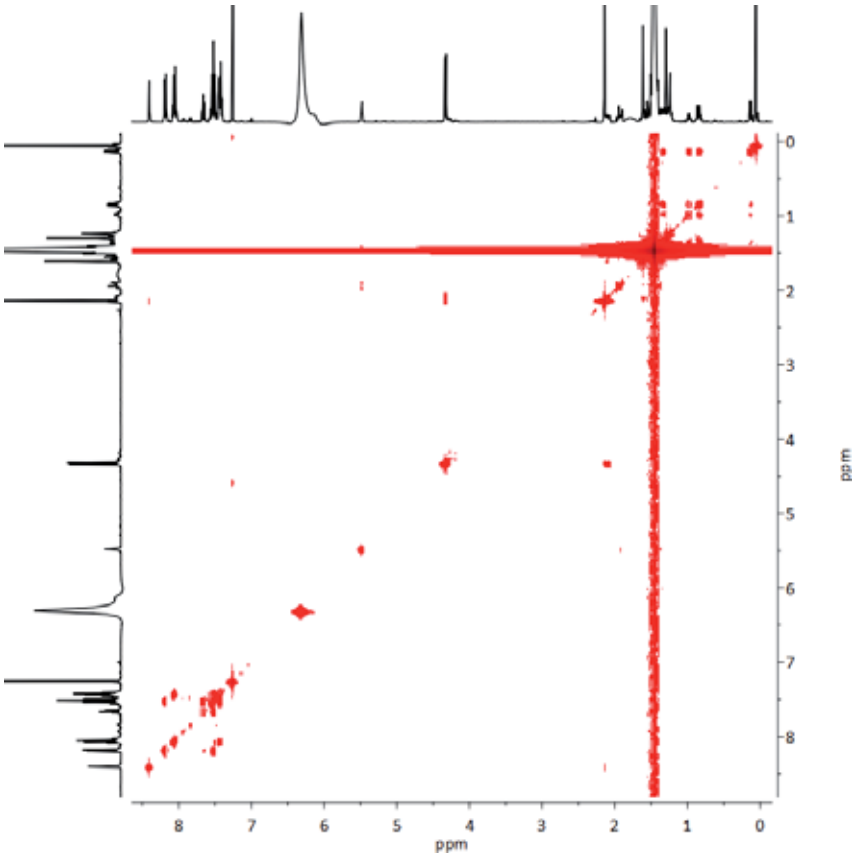
IR (ATR)



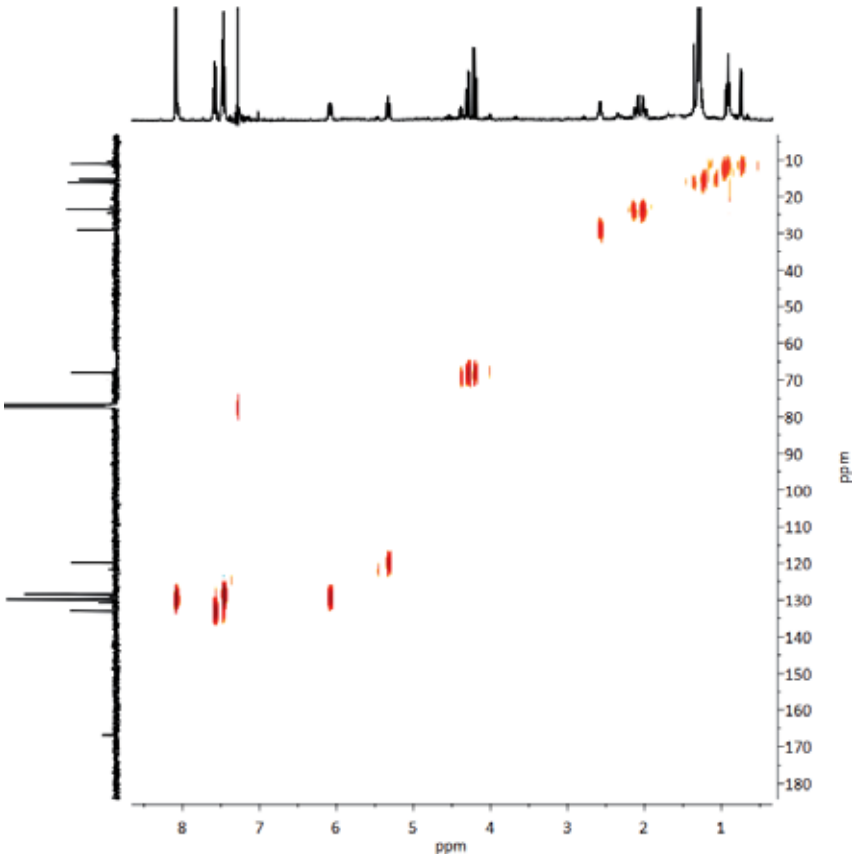
^{1}H-NMR (400 MHz, $CDCl_3$)



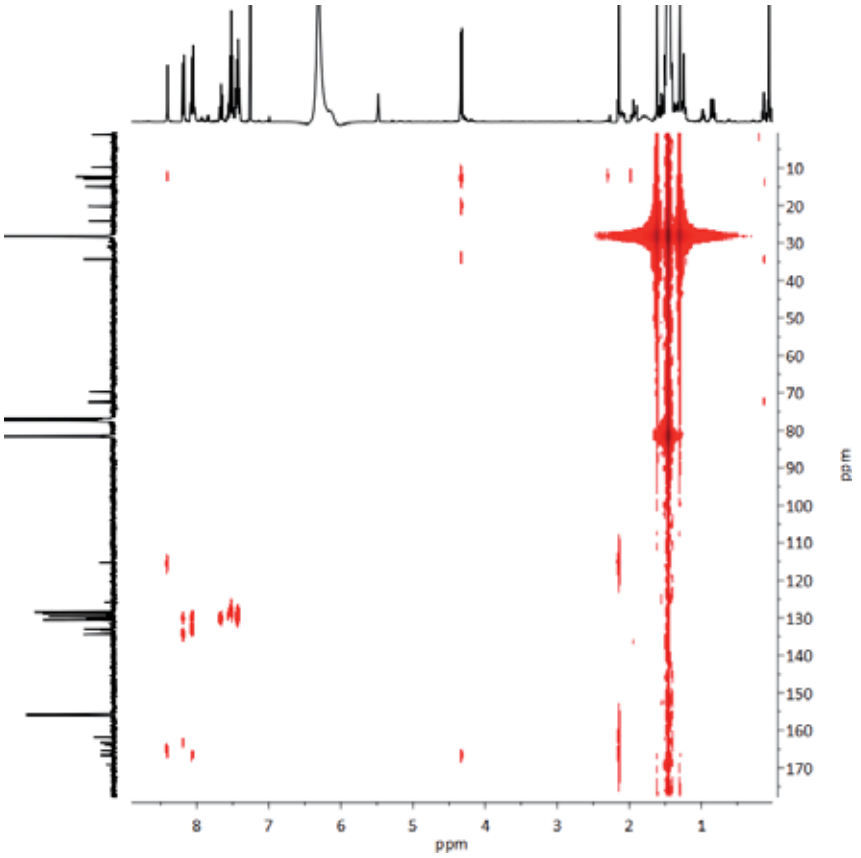
^{13}C-NMR (100 MHz, $CDCl_3$)



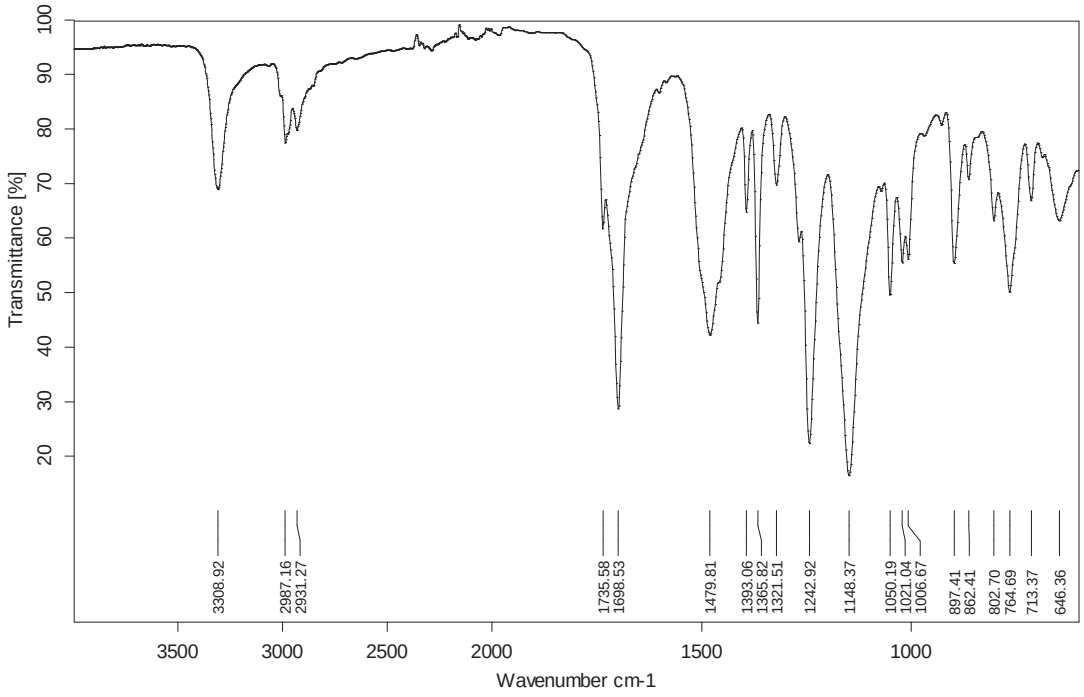
COSY (400 MHz, $CDCl_3$)



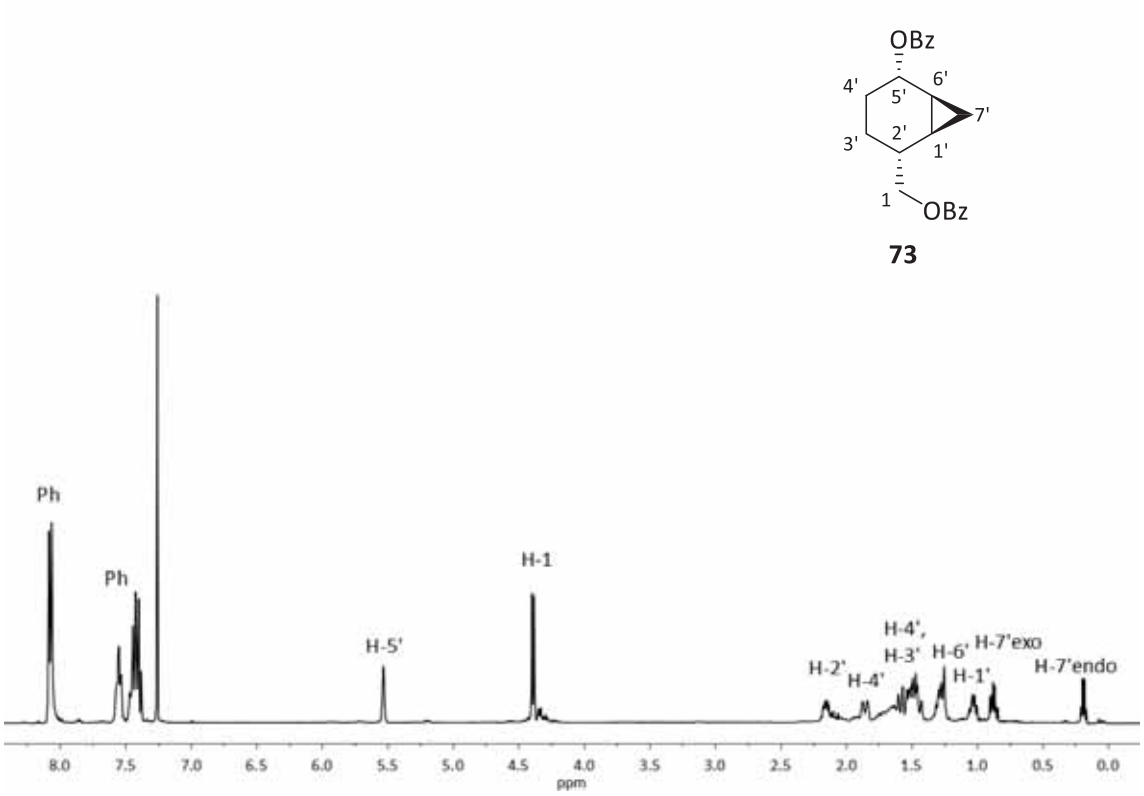
HSQC (400 MHz, $CDCl_3$)



HMBC (400 MHz, $CDCl_3$)

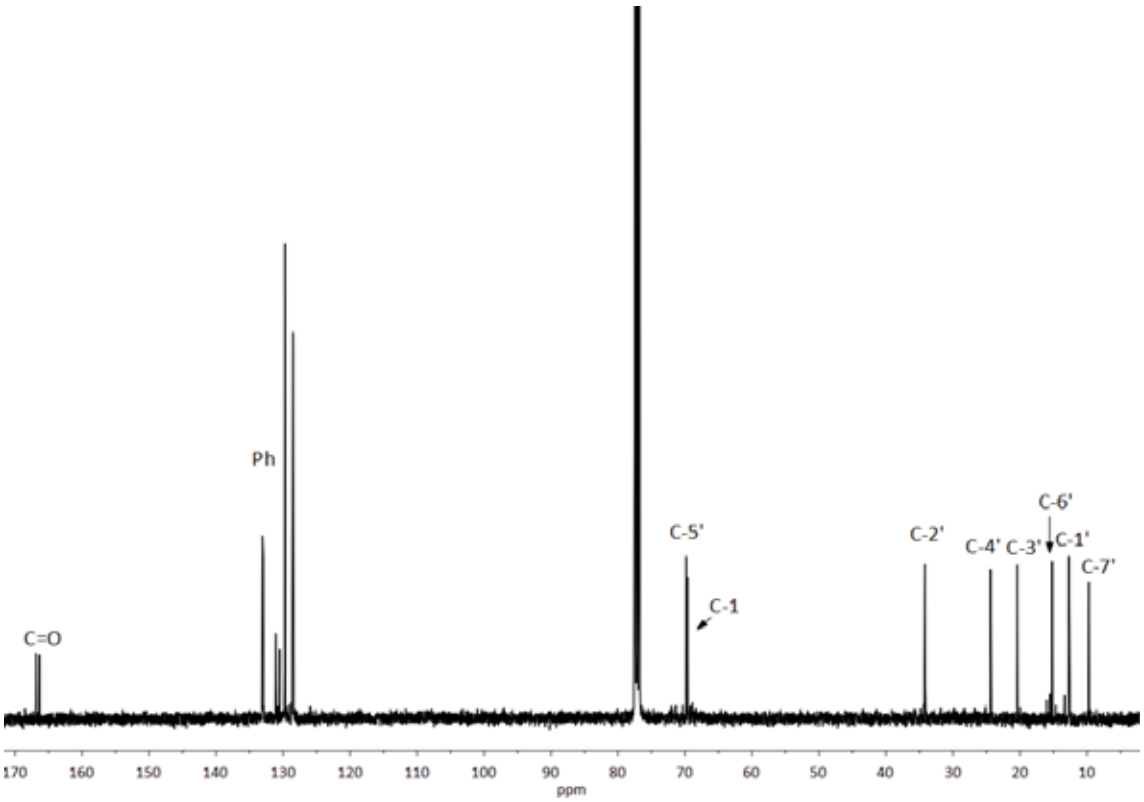


IR (ATR)

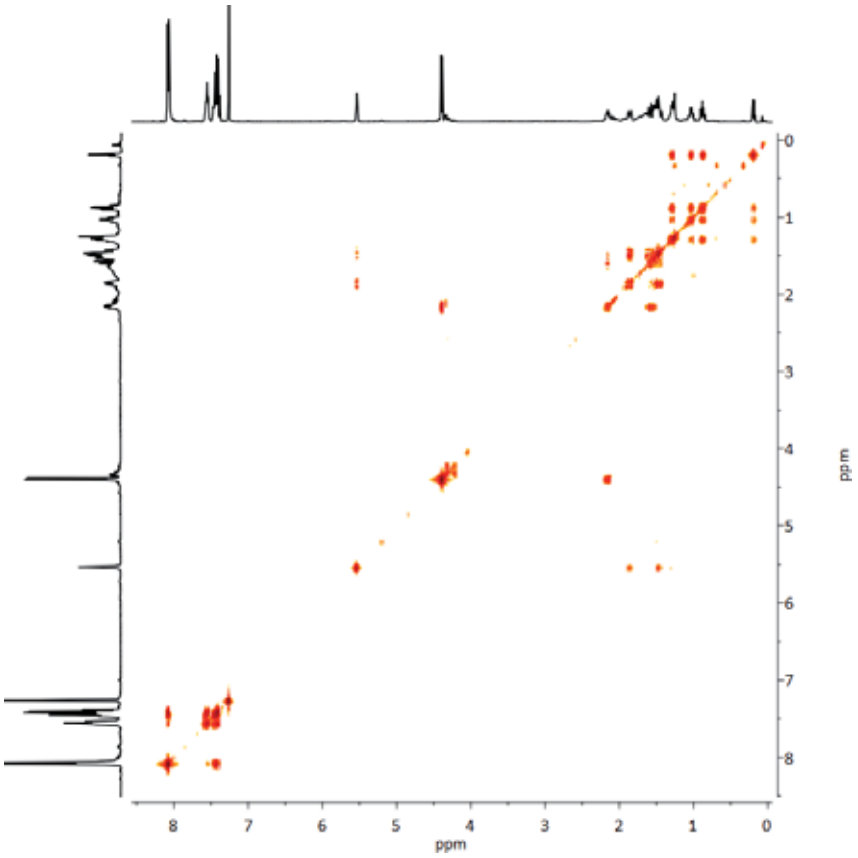


73

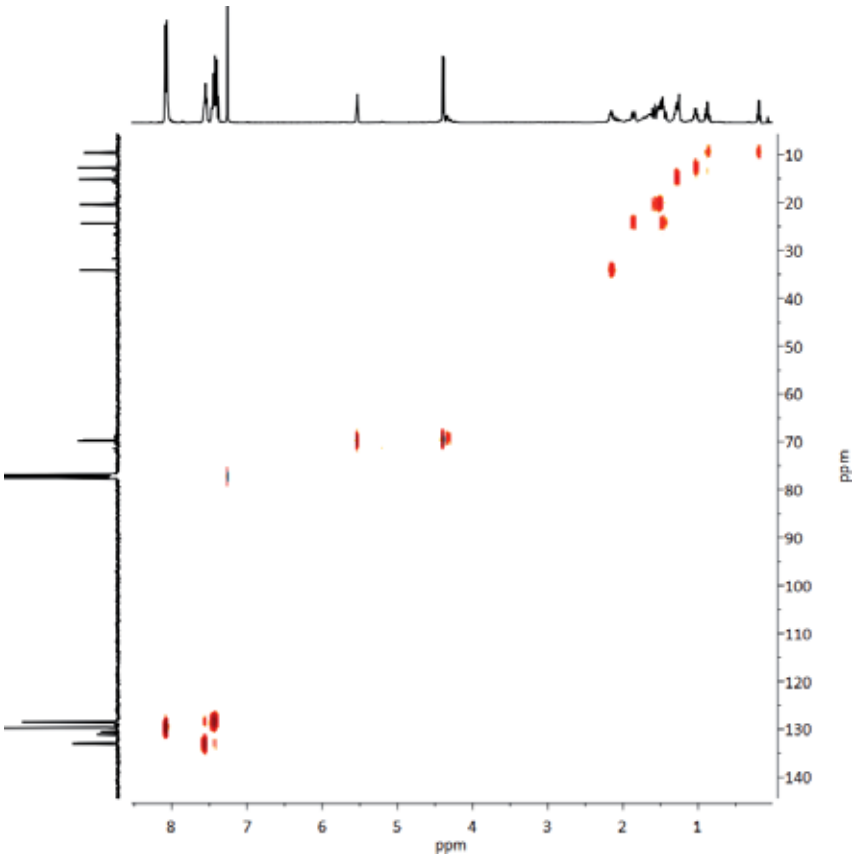
^{1}H-NMR (400 MHz, $CDCl_3$)



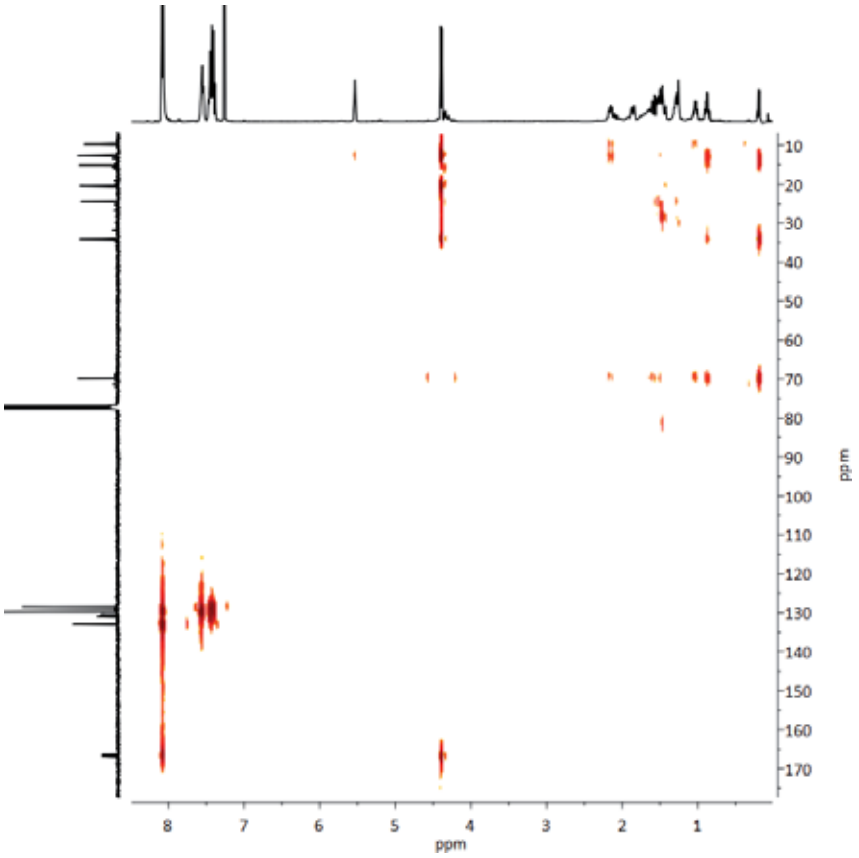
^{13}C-NMR (100 MHz, $CDCl_3$)



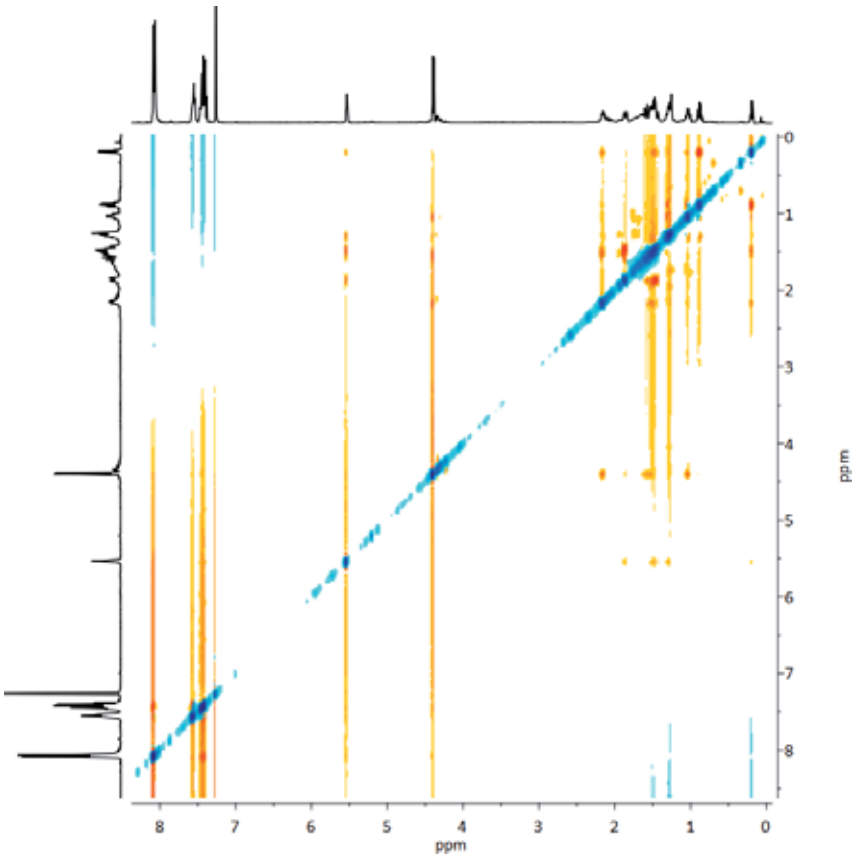
COSY (400 MHz, $CDCl_3$)



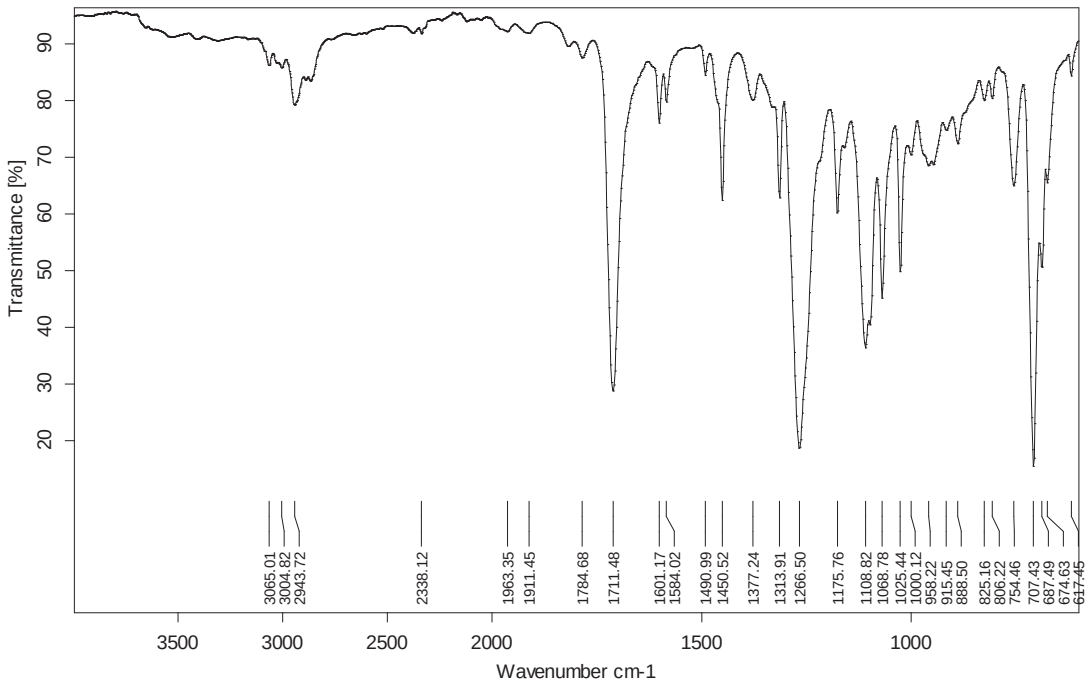
HSQC (400 MHz, $CDCl_3$)



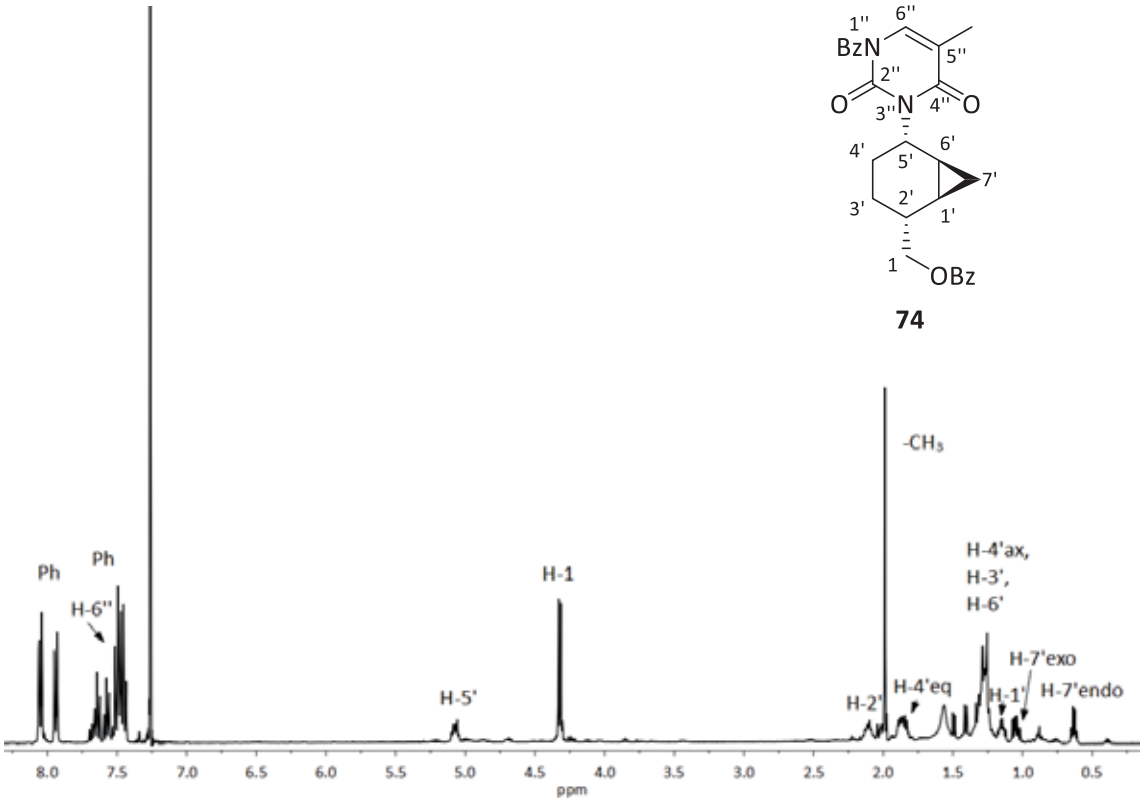
HMBC (400 MHz, $CDCl_3$)



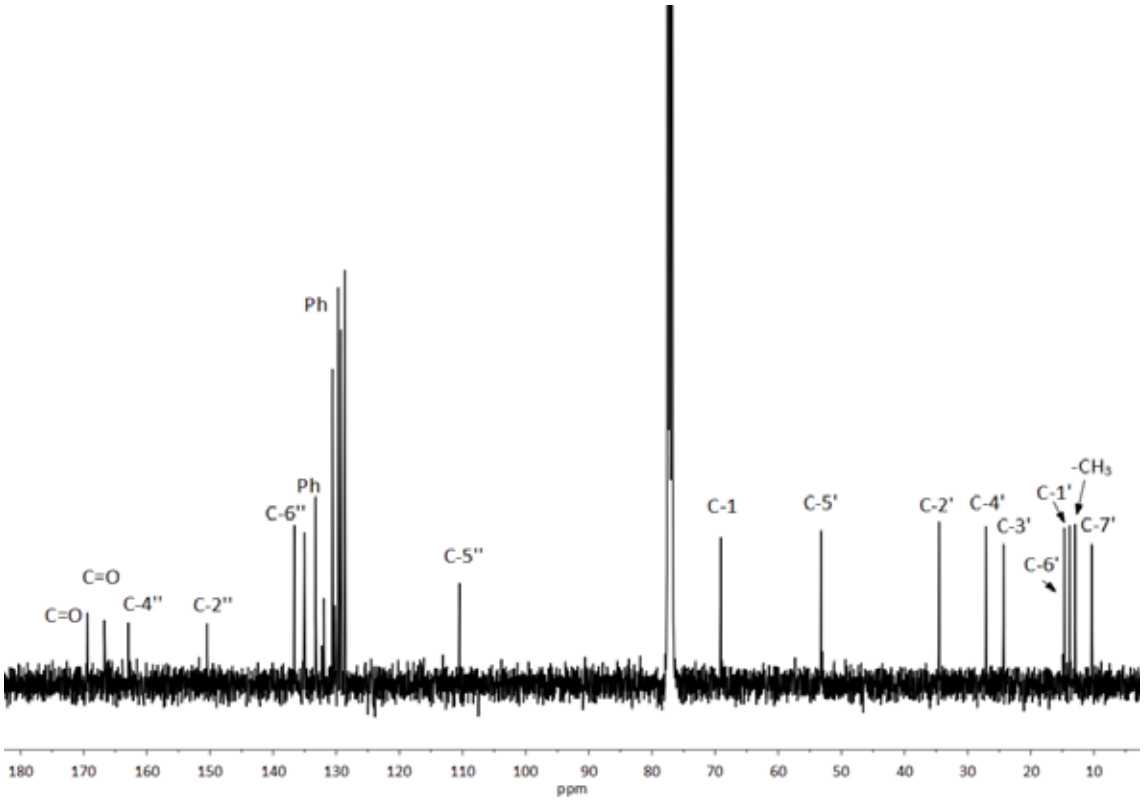
NOESY (400 MHz, $CDCl_3$)



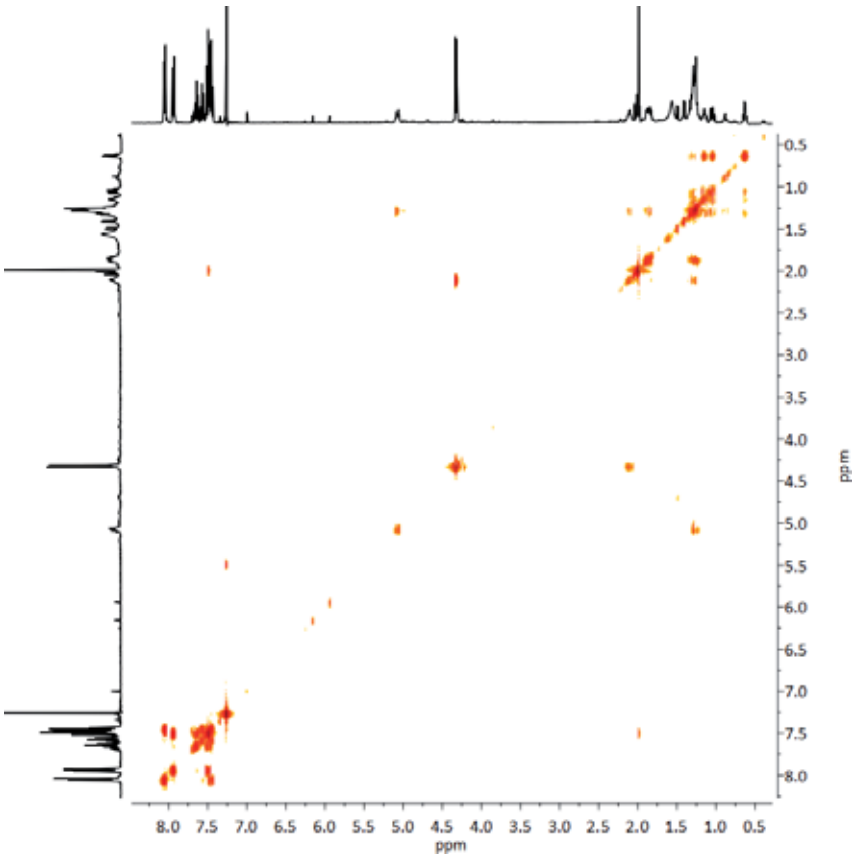
IR (ATR)



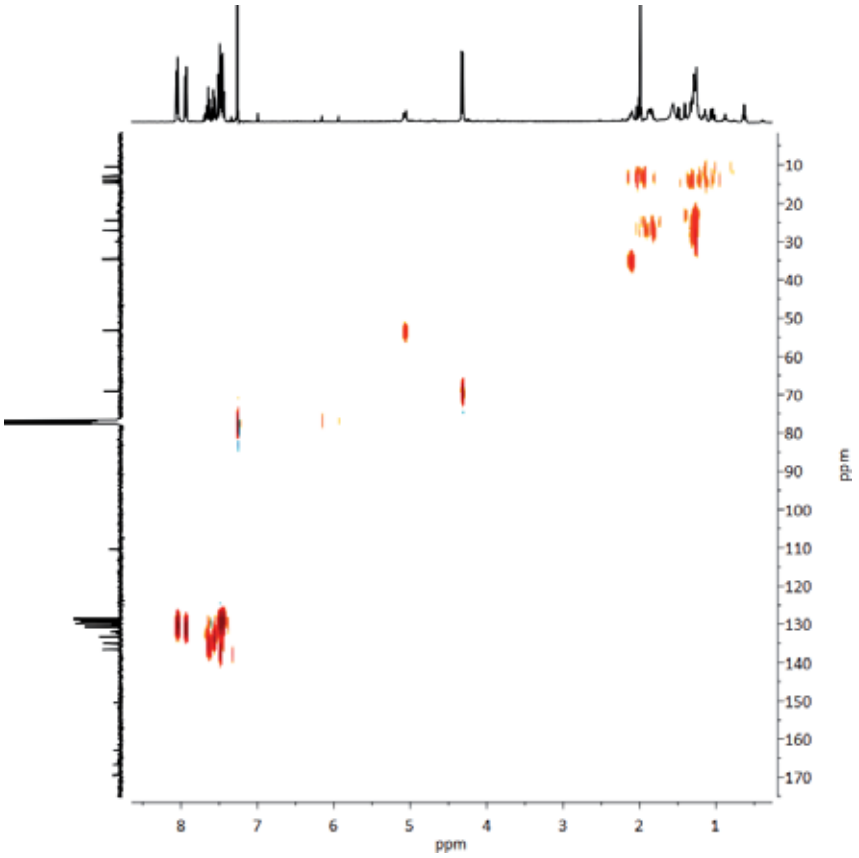
^{1}H-NMR (400 MHz, $CDCl_3$)



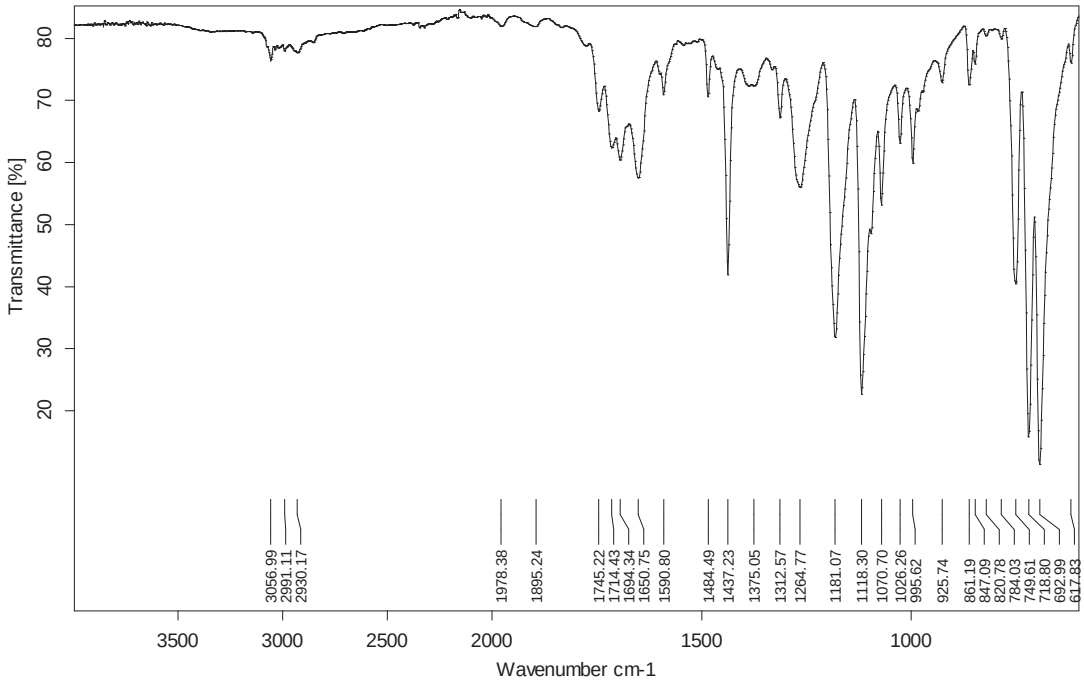
^{13}C-NMR (100 MHz, $CDCl_3$)



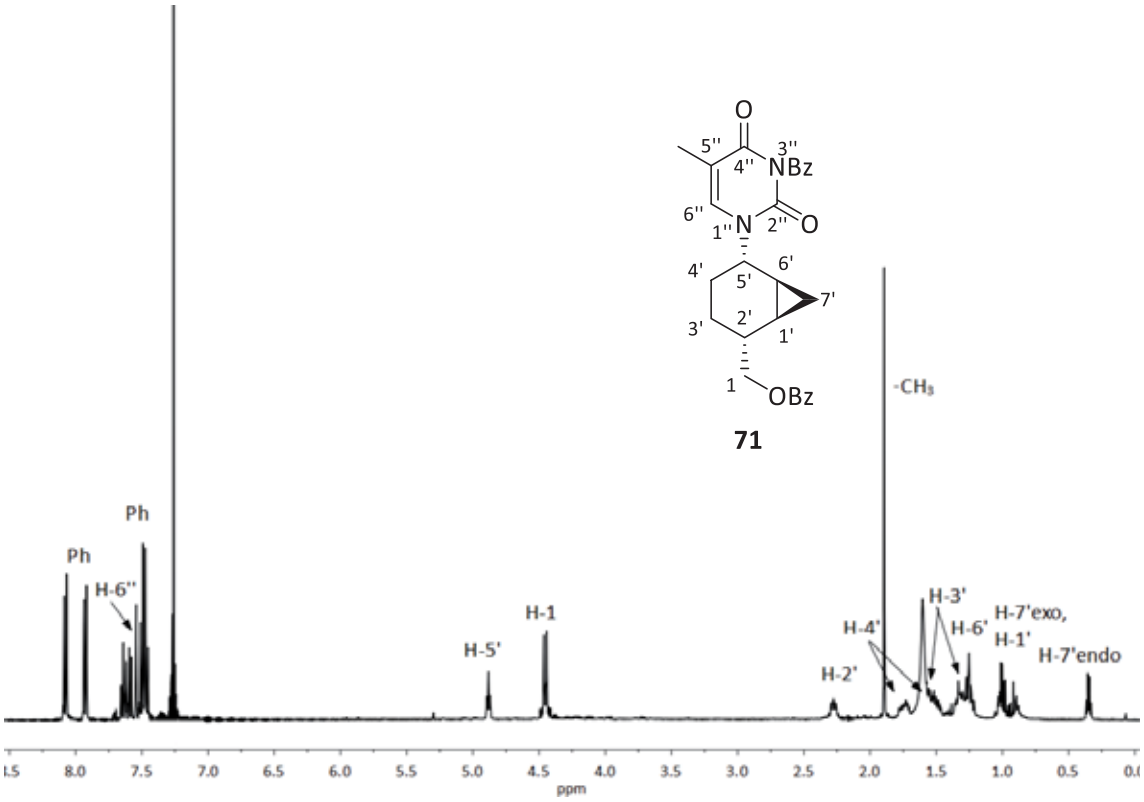
COSY (400 MHz, $CDCl_3$)



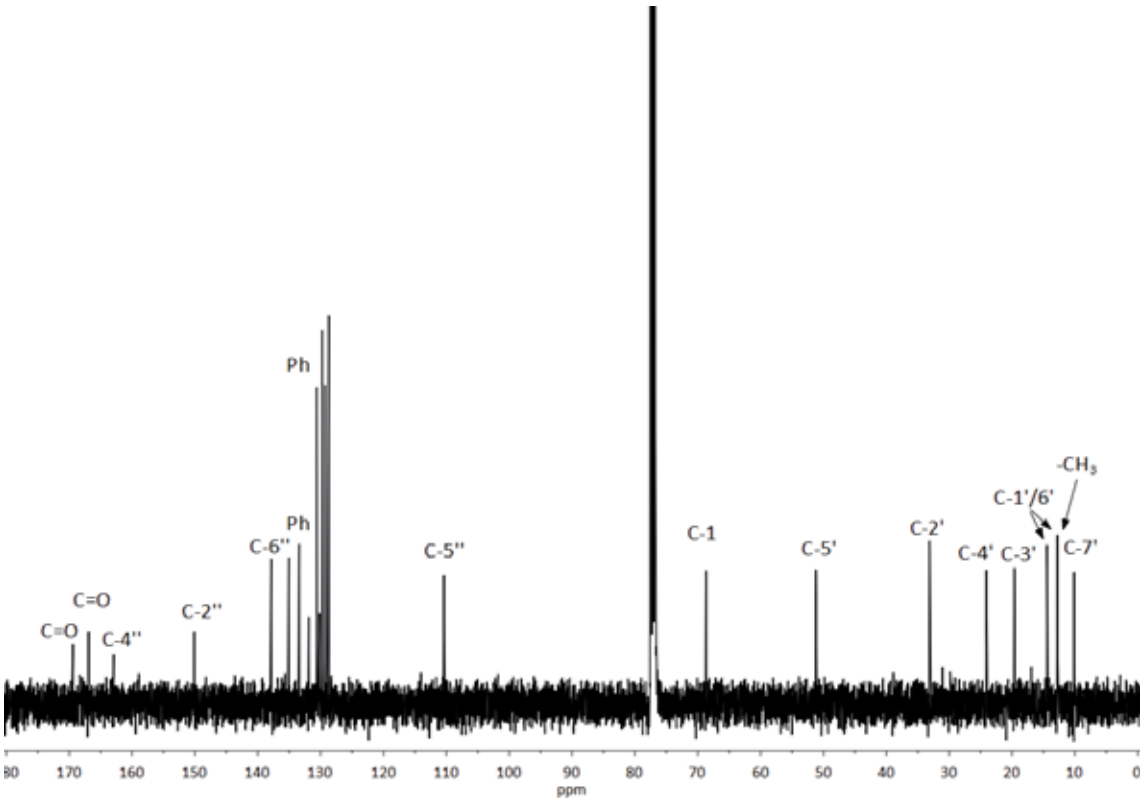
HSQC (400 MHz, $CDCl_3$)



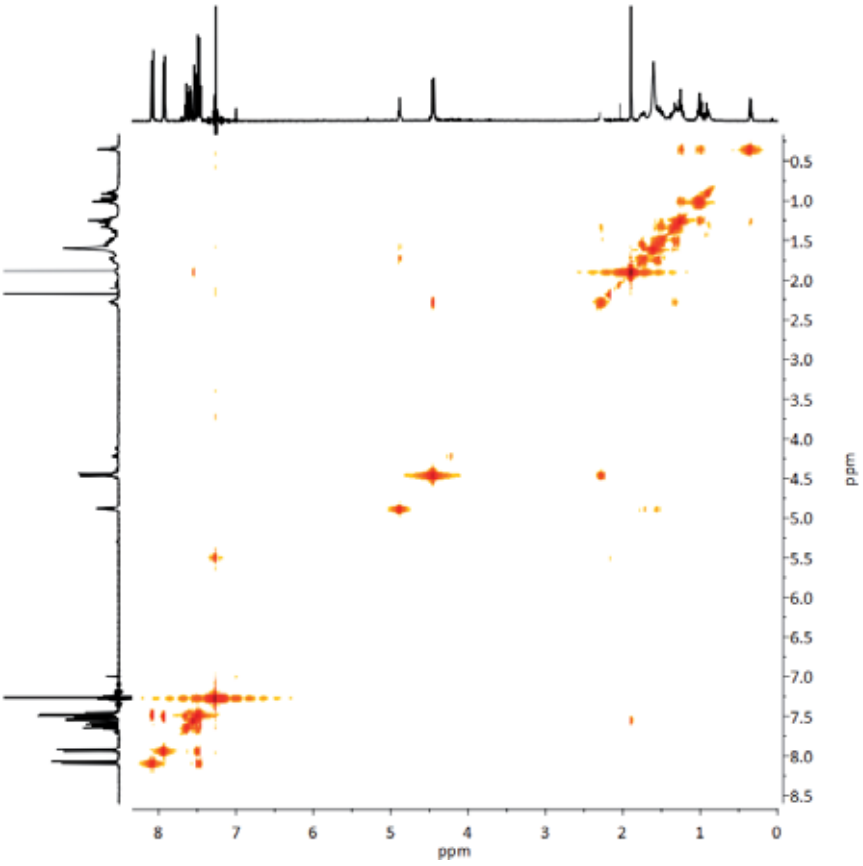
IR (ATR)



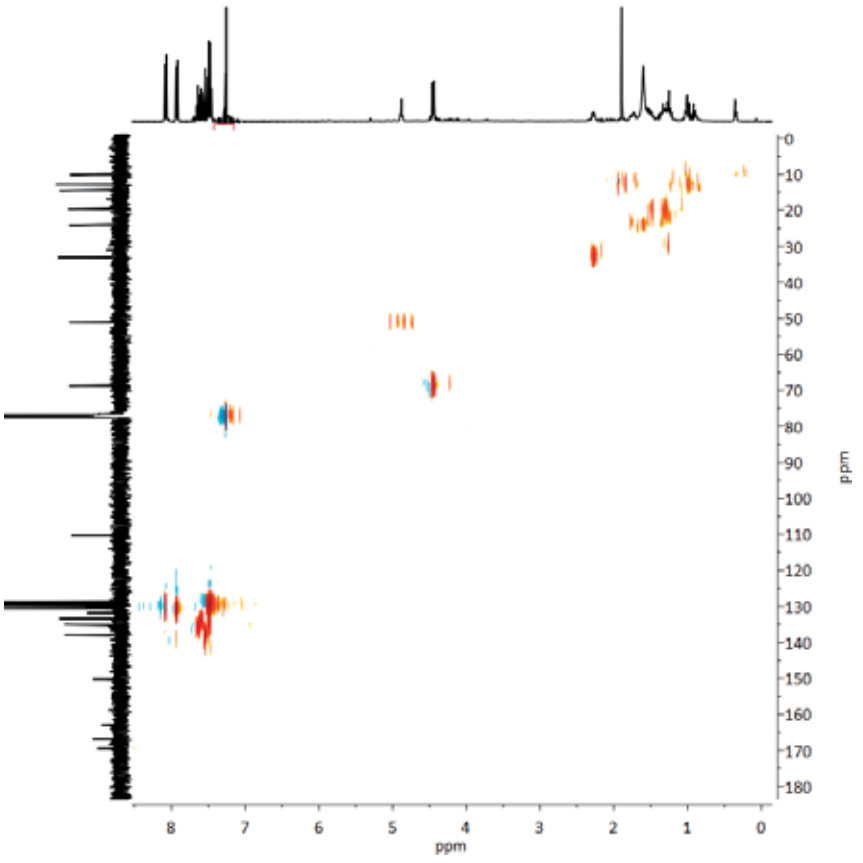
^{1}H-NMR (400 MHz, $CDCl_3$)



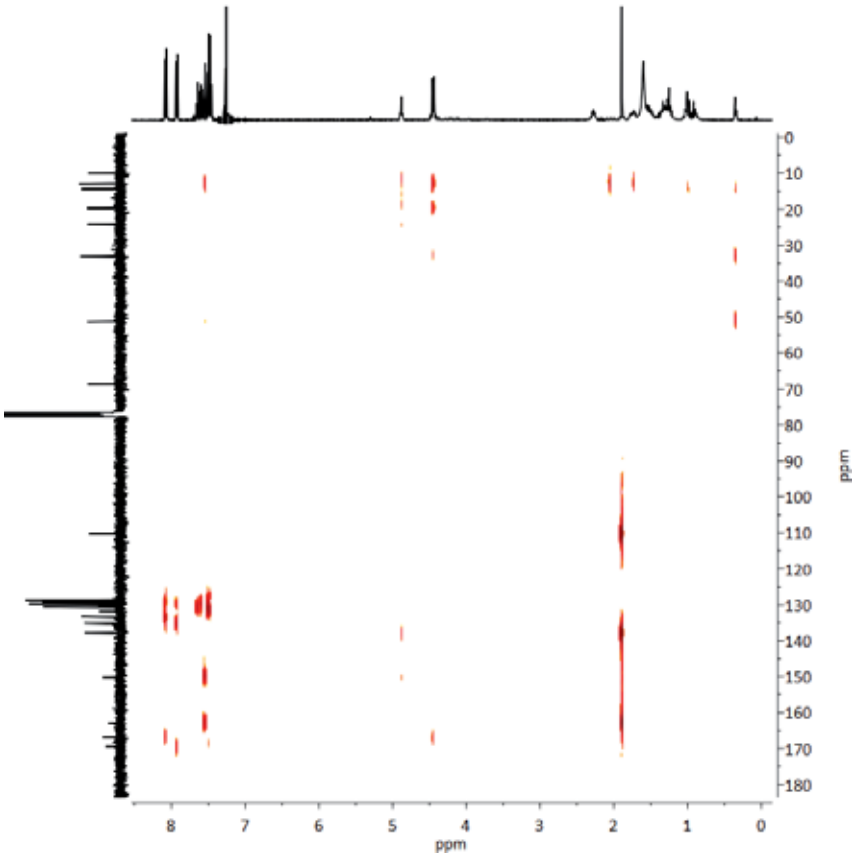
^{13}C-NMR (100 MHz, $CDCl_3$)



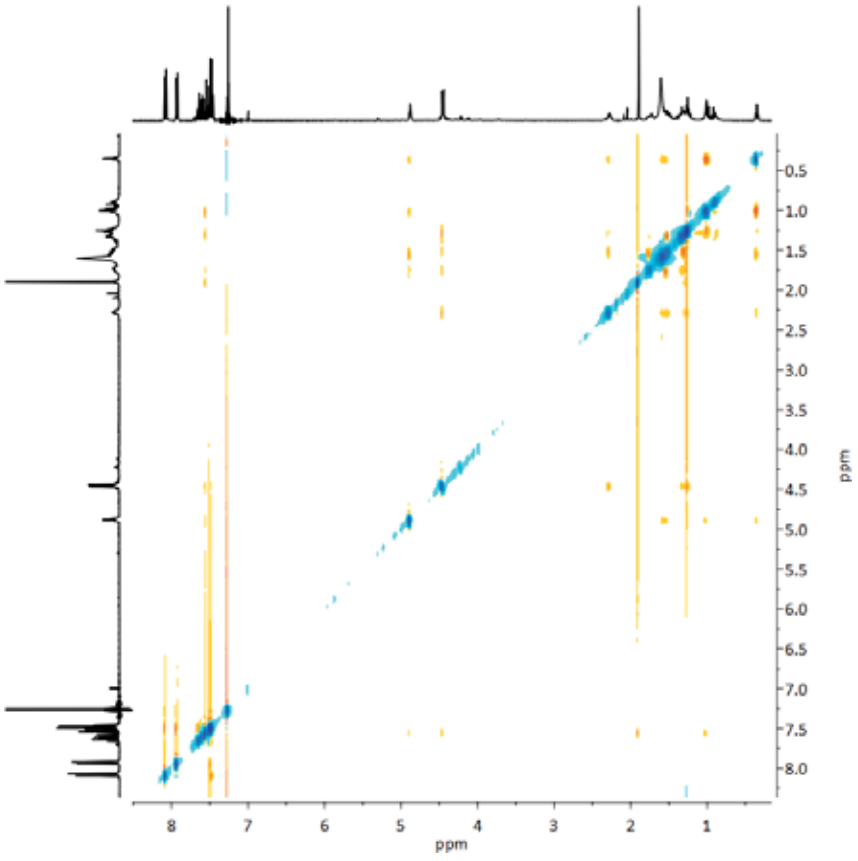
COSY (400 MHz, $CDCl_3$)



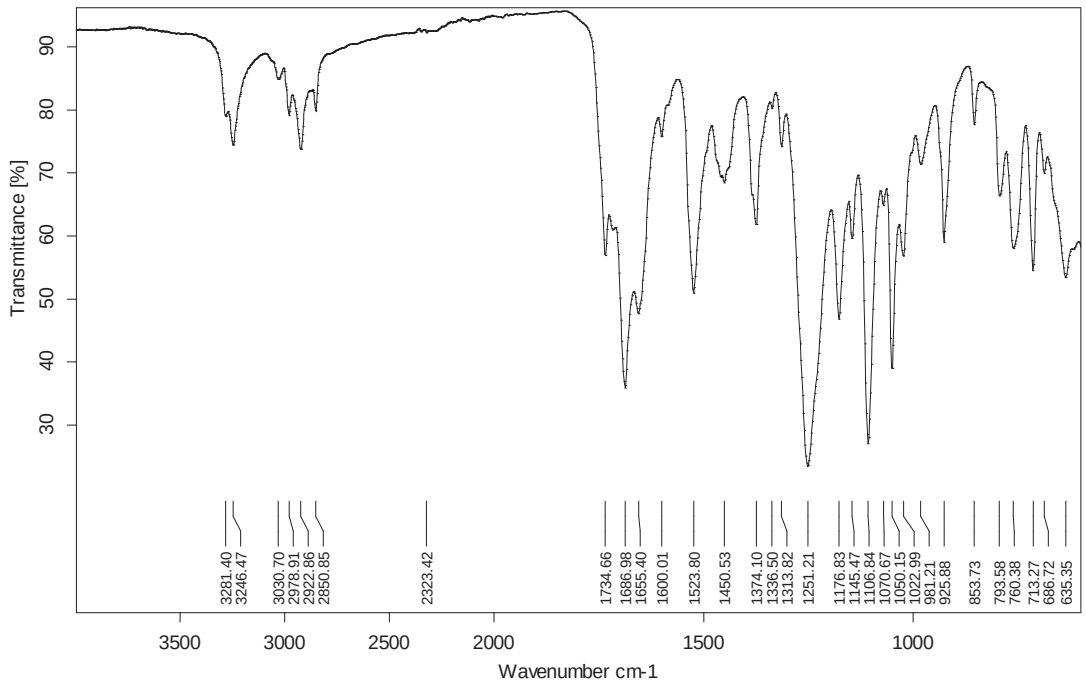
HSQC (400 MHz, $CDCl_3$)



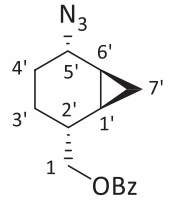
HMBC (400 MHz, $CDCl_3$)



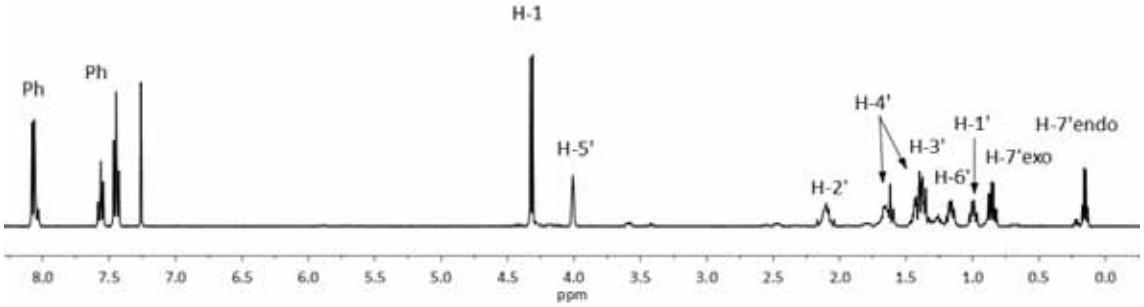
NOESY (400 MHz, $CDCl_3$)



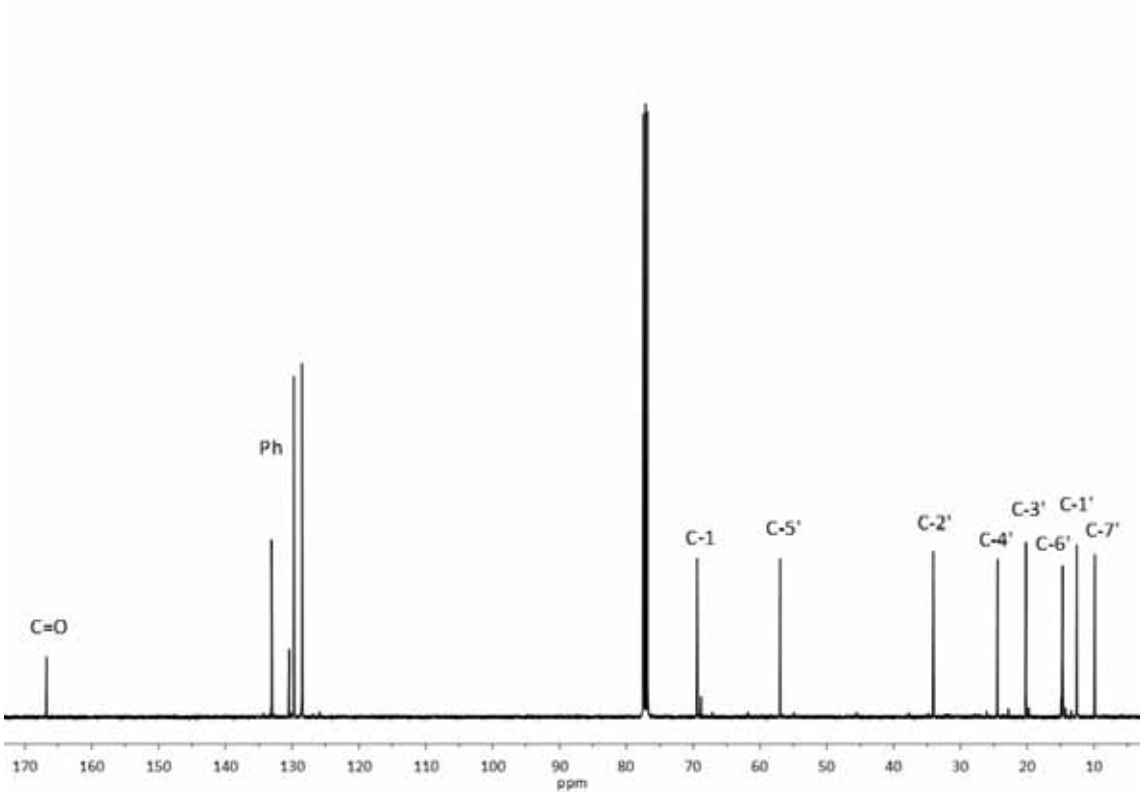
IR (ATR)



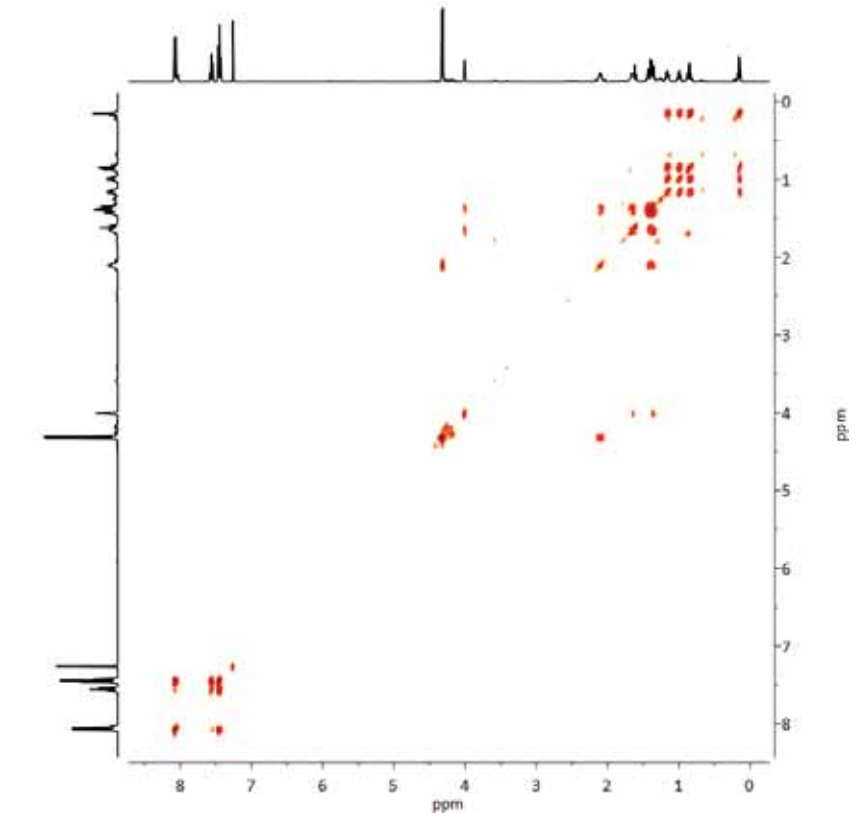
75



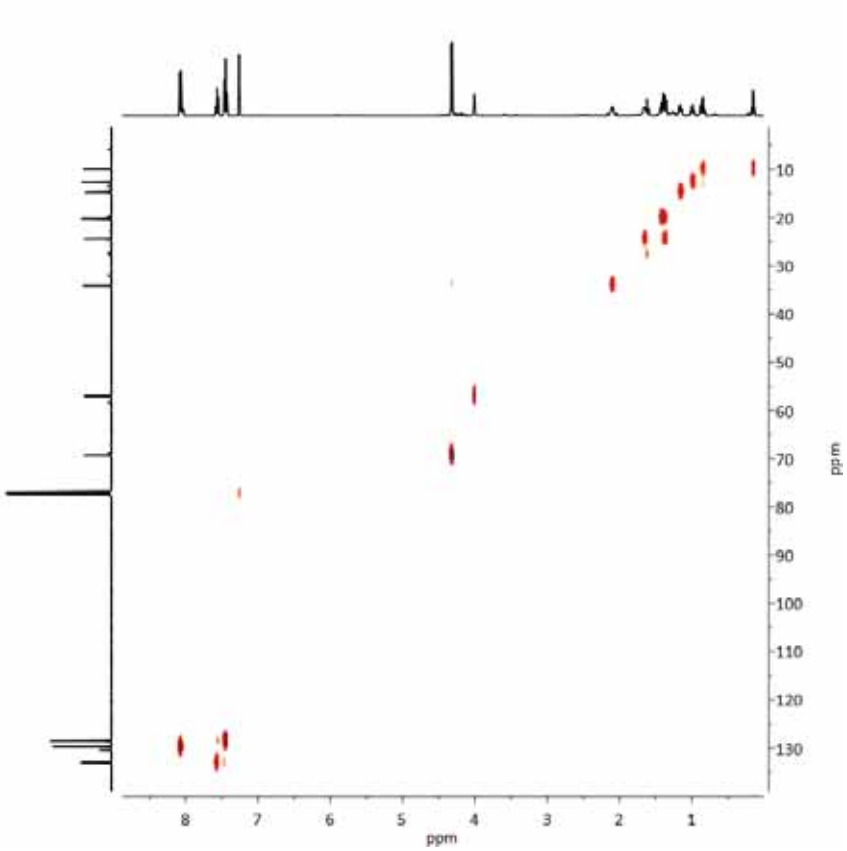
^{1}H-NMR (400 MHz, $CDCl_3$)



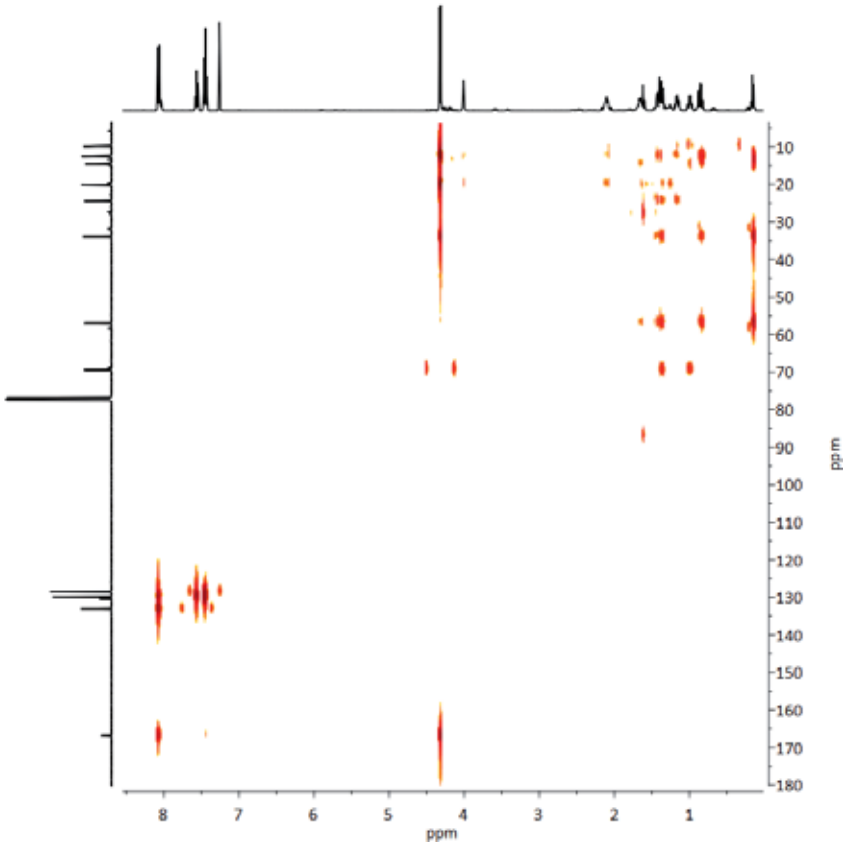
^{13}C-NMR (100 MHz, $CDCl_3$)



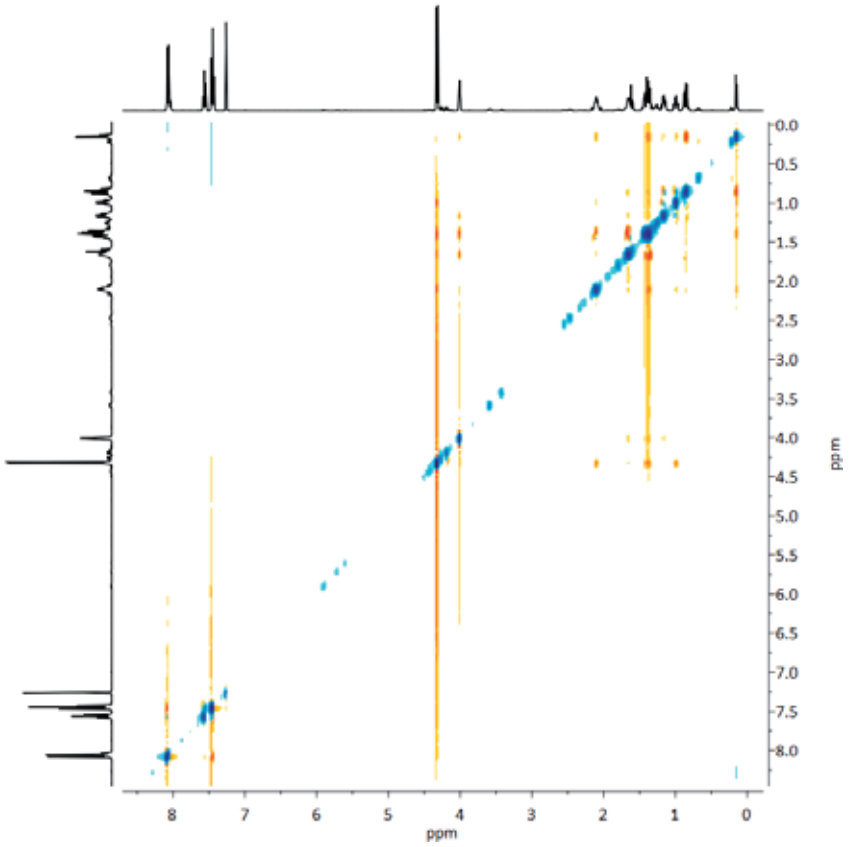
COSY (400 MHz, $CDCl_3$)



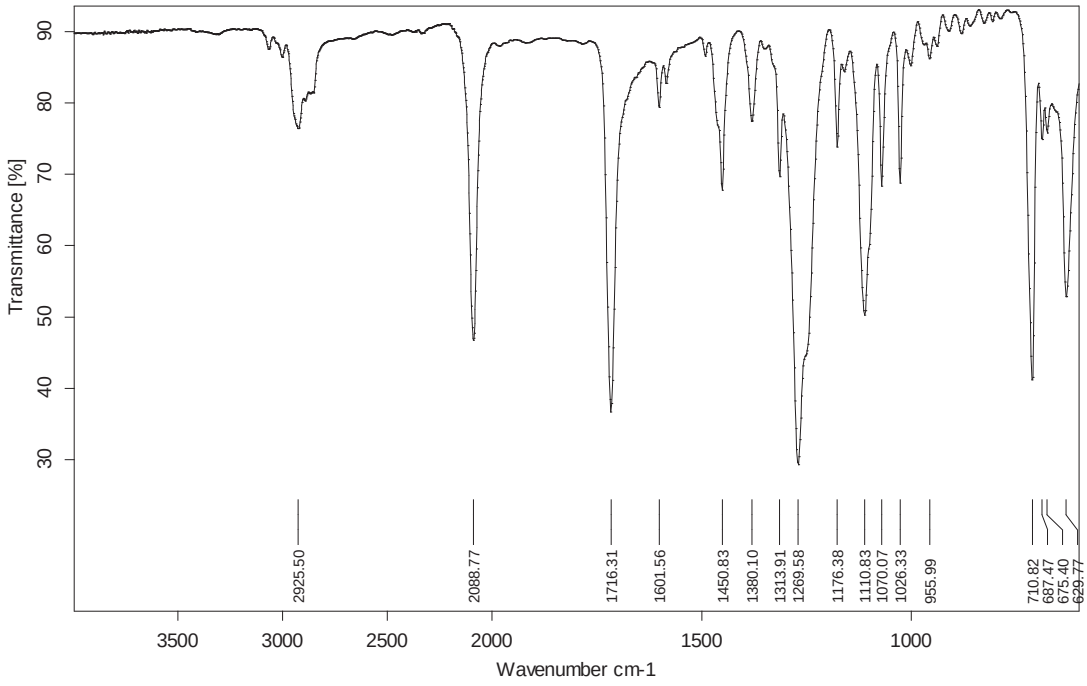
HSQC (400 MHz, $CDCl_3$)



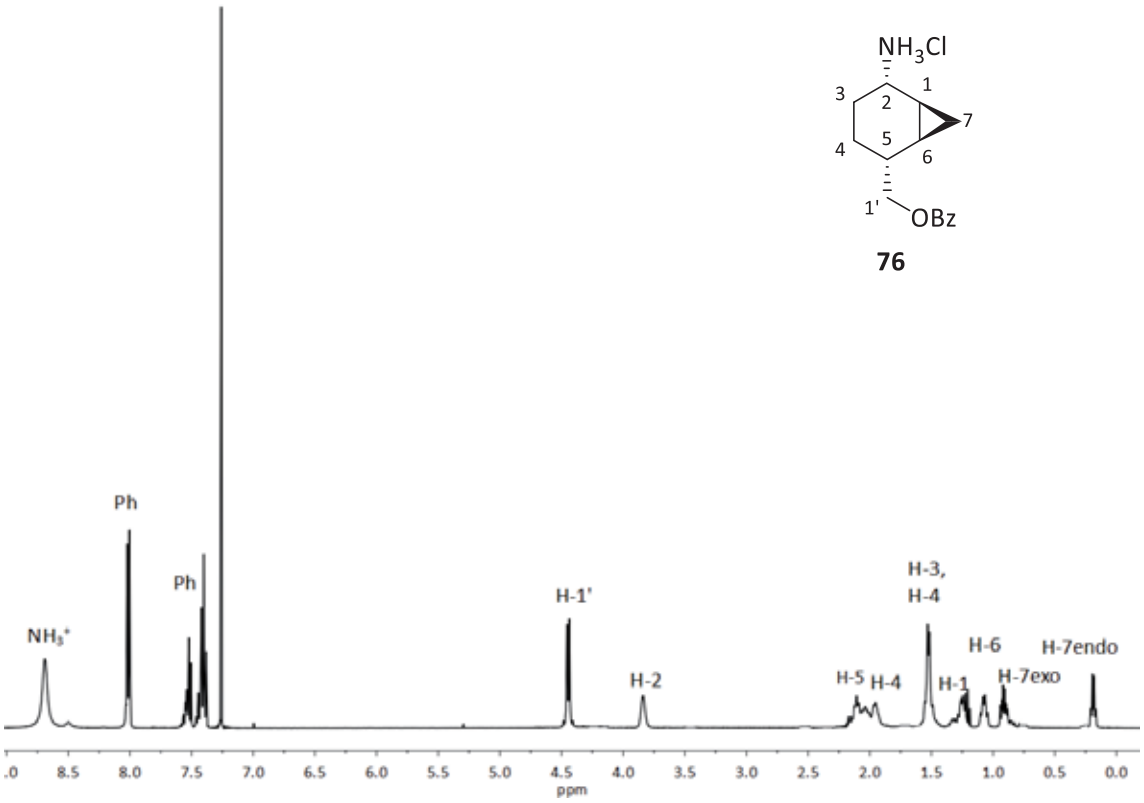
HMBC (400 MHz, $CDCl_3$)



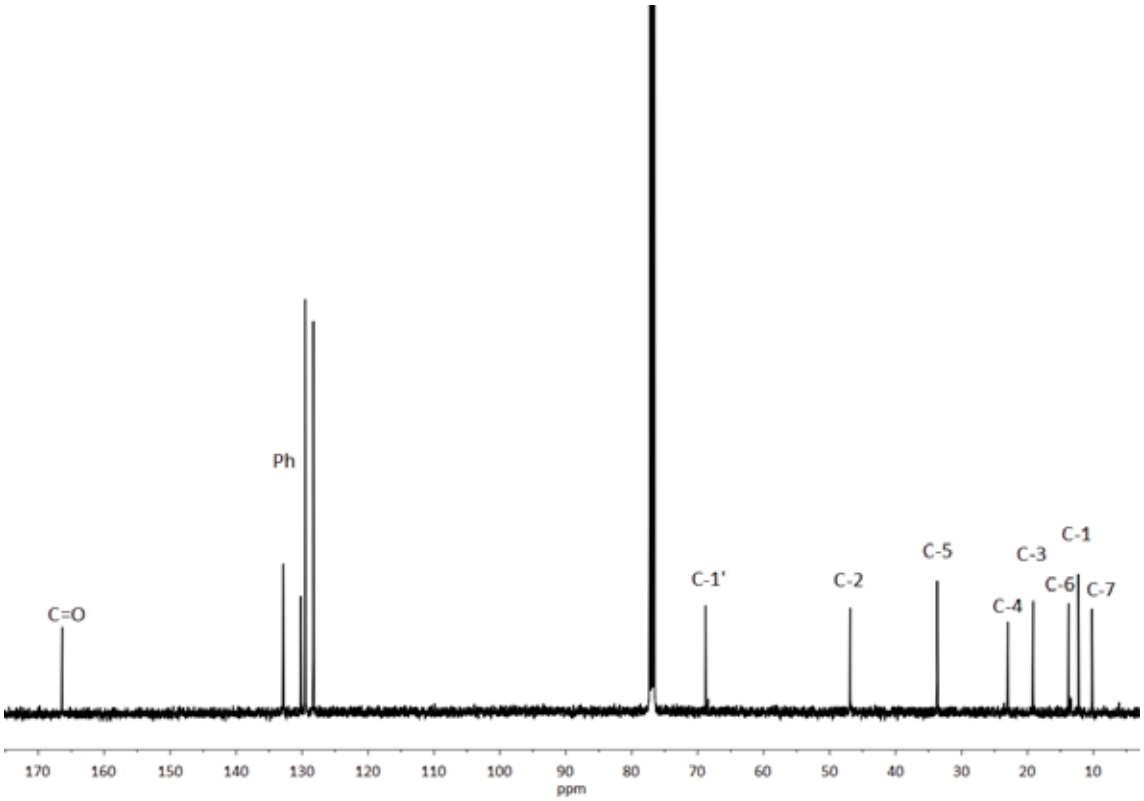
NOESY (400 MHz, $CDCl_3$)



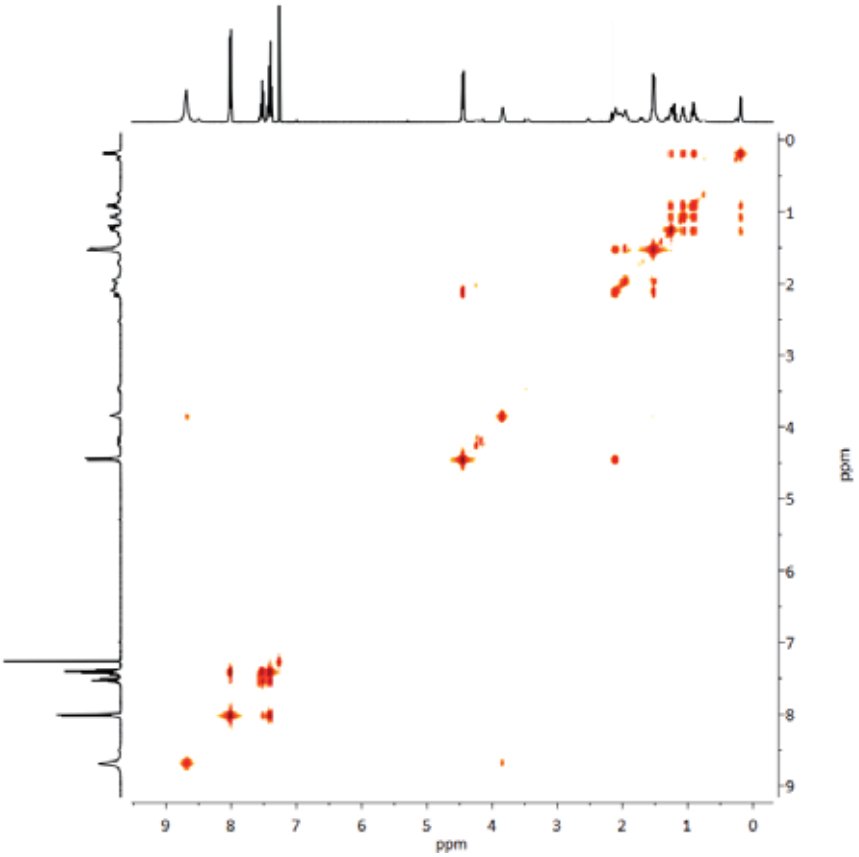
IR (ATR)



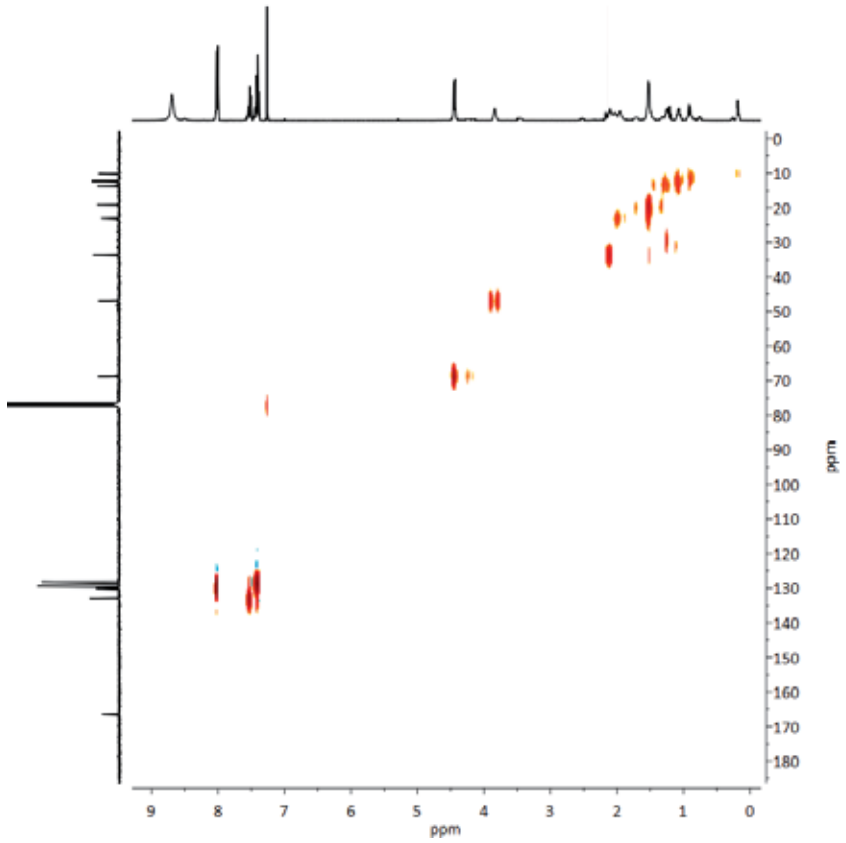
^{1}H-NMR (400 MHz, $CDCl_3$)



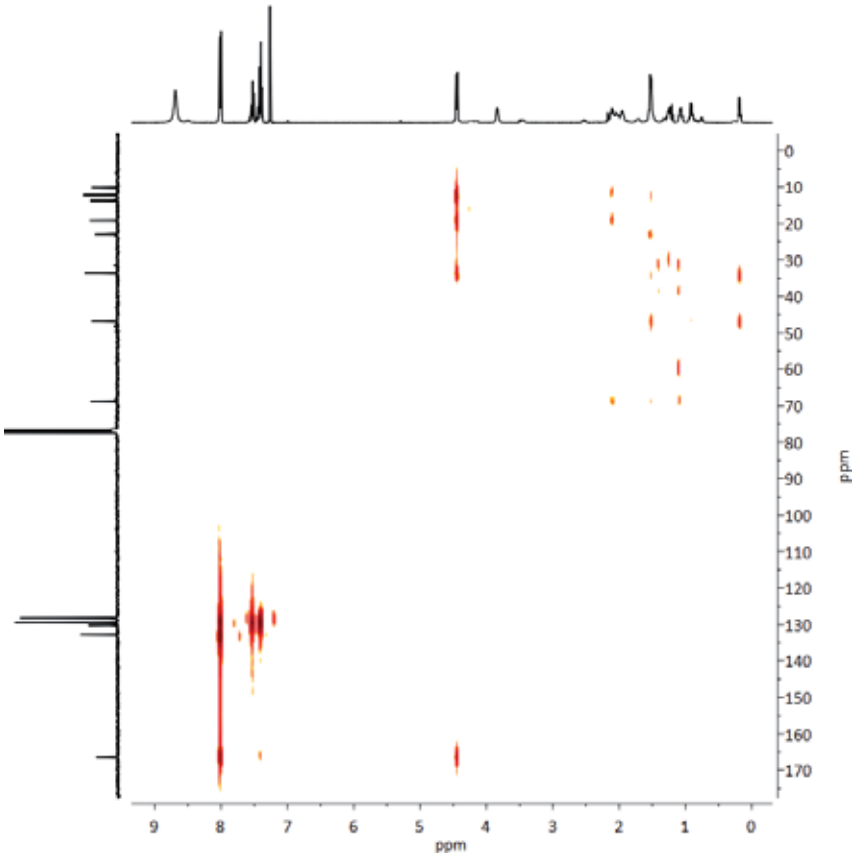
^{13}C-NMR (400 MHz, $CDCl_3$)



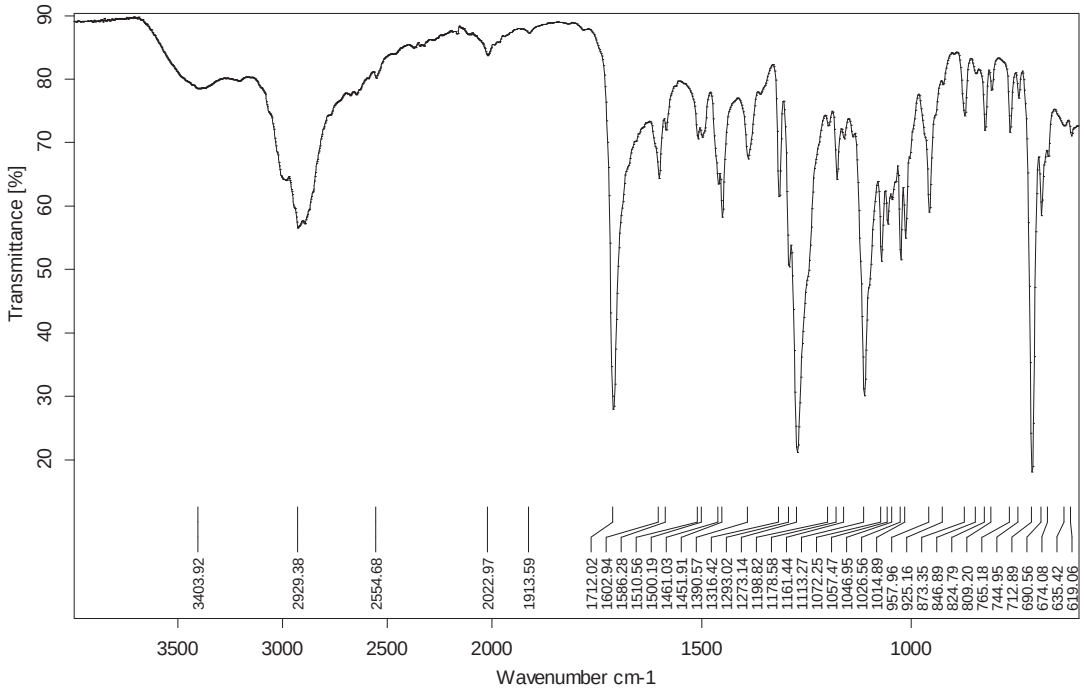
COSY (400 MHz, $CDCl_3$)



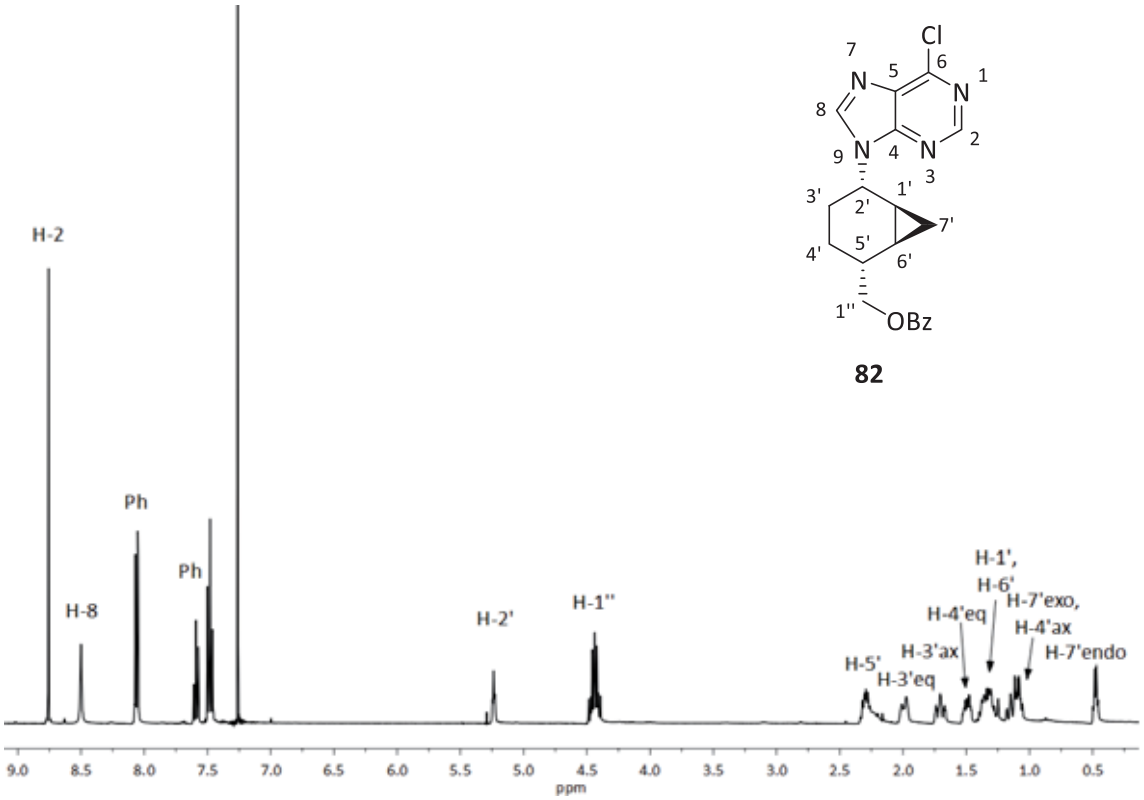
HSQC (400 MHz, $CDCl_3$)



HMBC (400 MHz, $CDCl_3$)

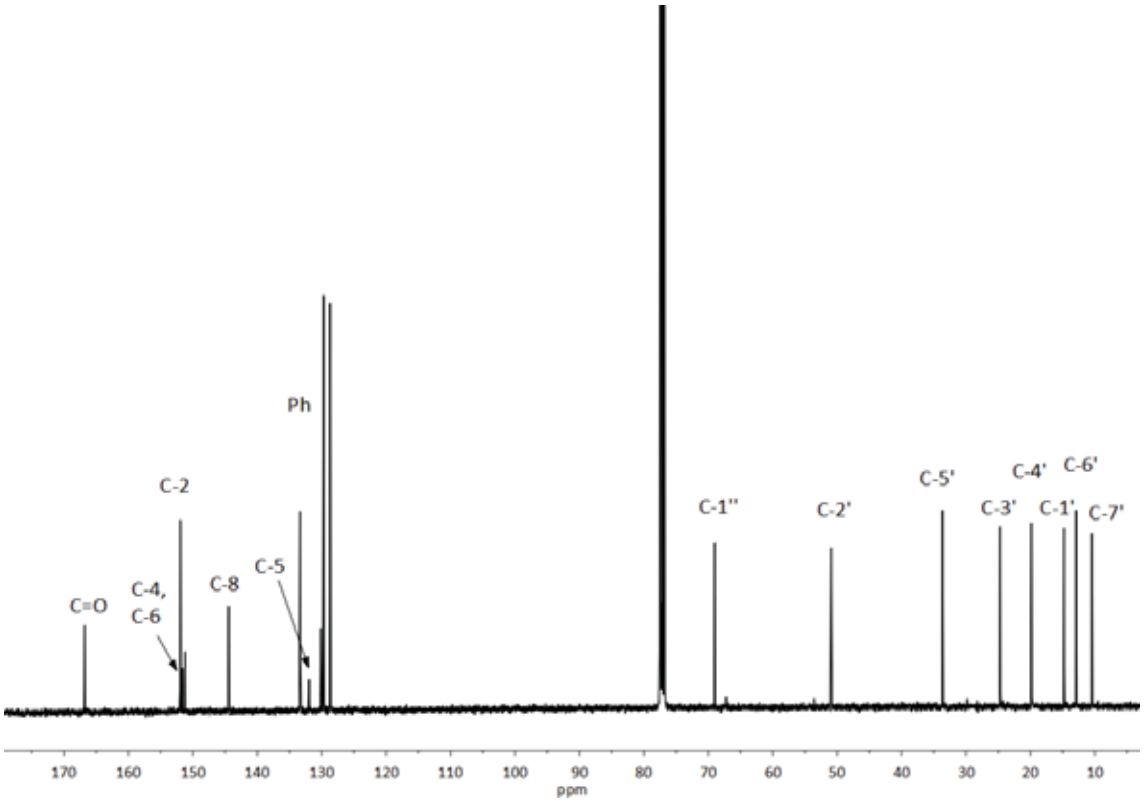


IR (ATR)

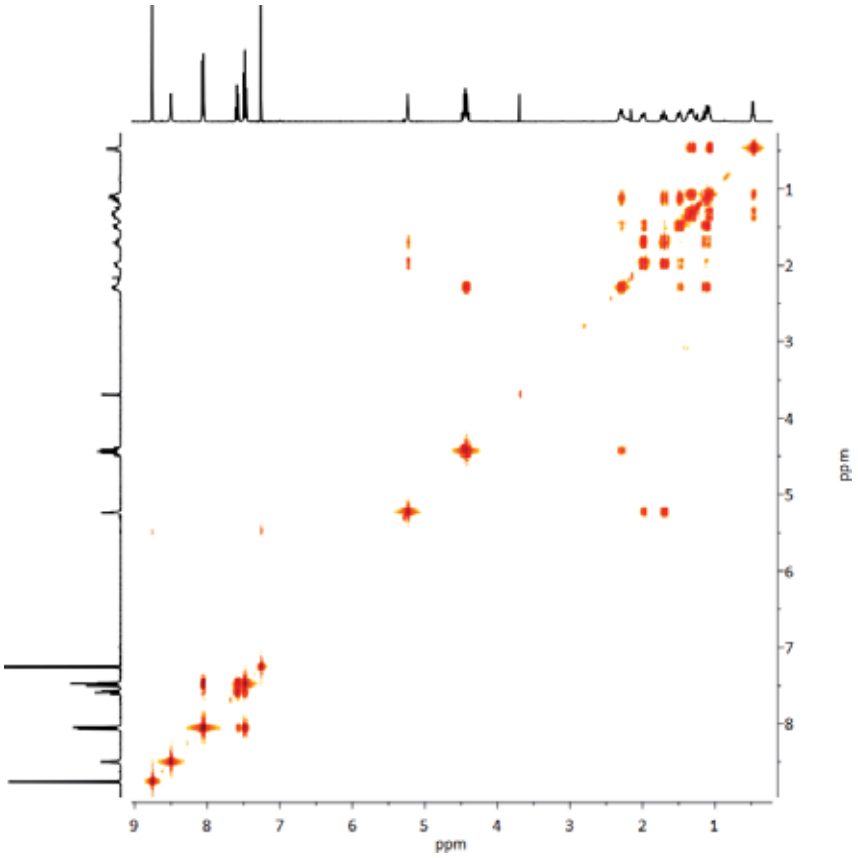


82

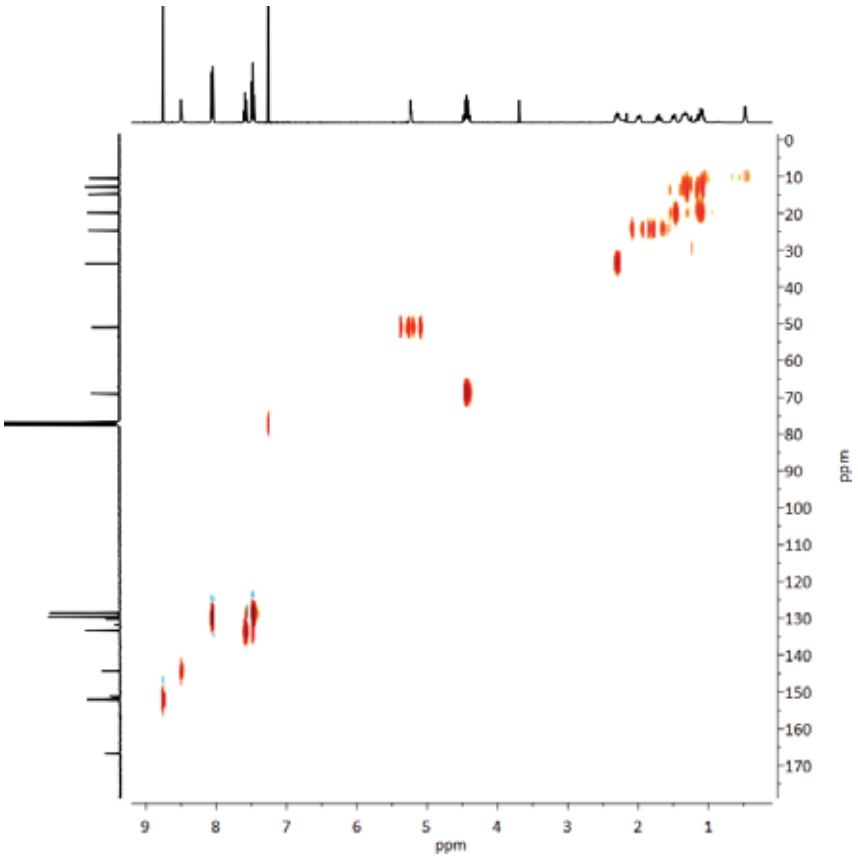
^{1}H-NMR (400 MHz, $CDCl_3$)



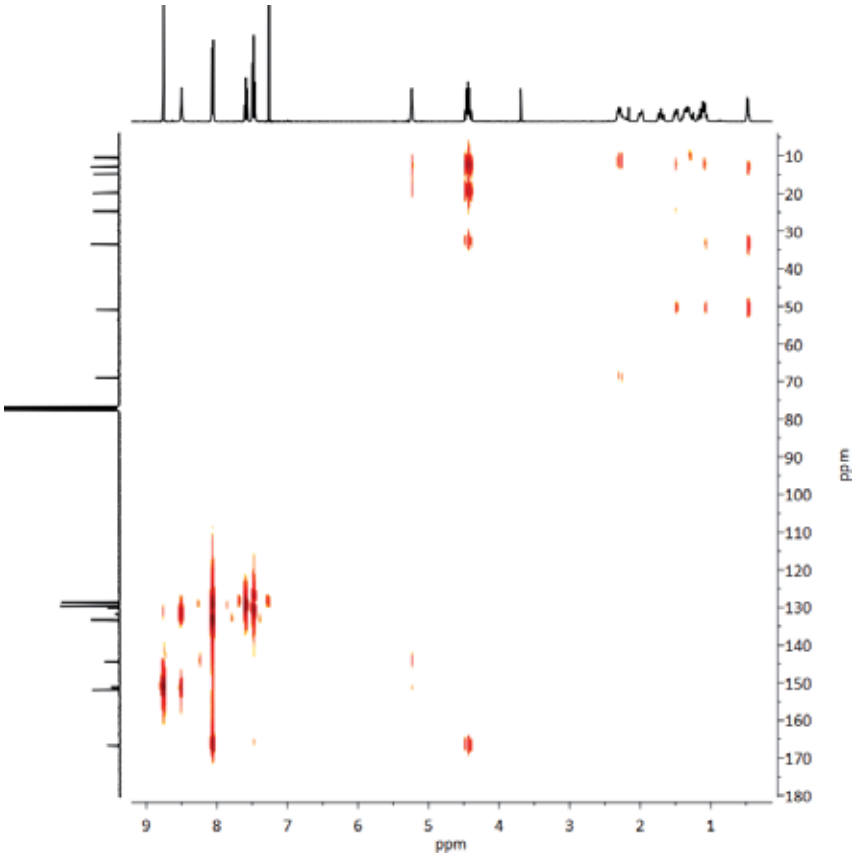
^{13}C-NMR (100 MHz, $CDCl_3$)



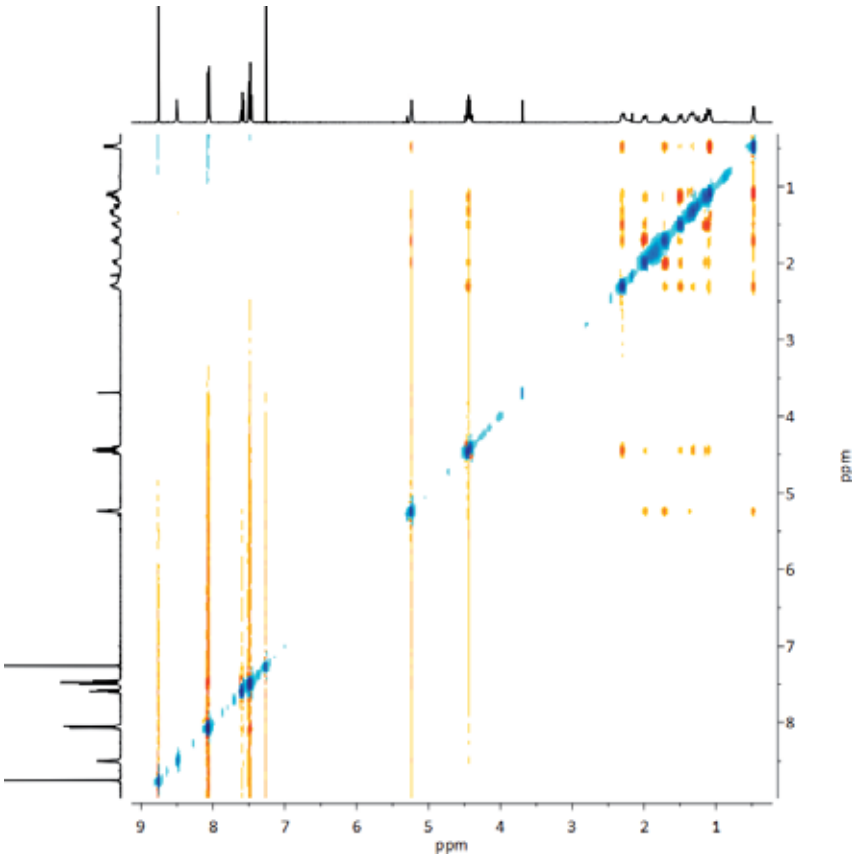
COSY (400 MHz, $CDCl_3$)



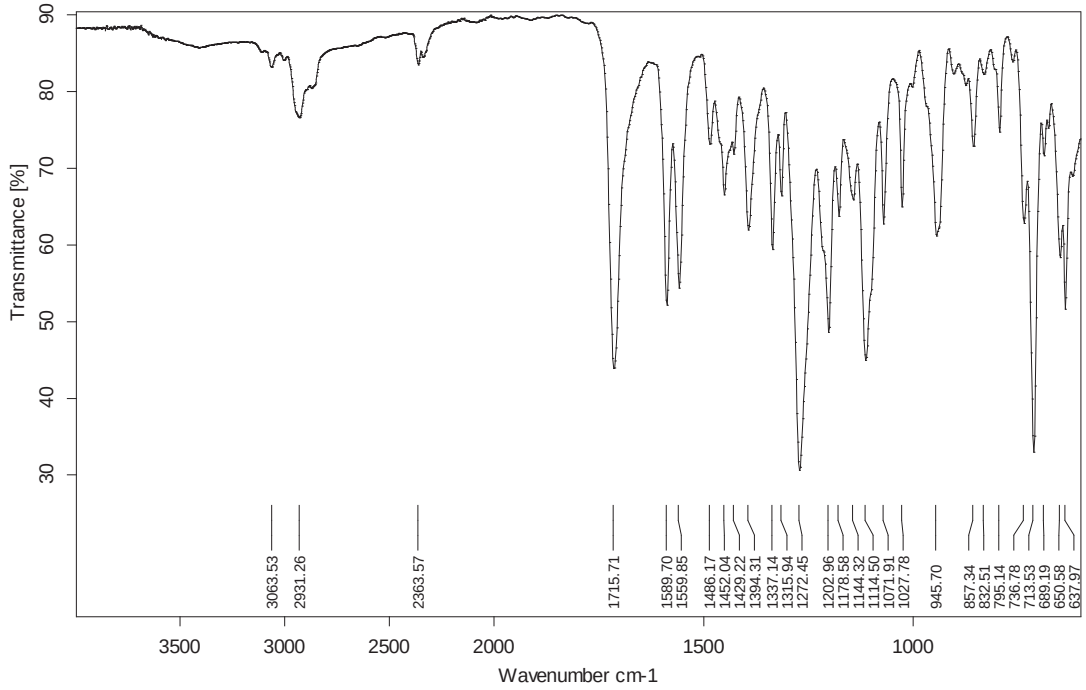
HSQC (400 MHz, $CDCl_3$)



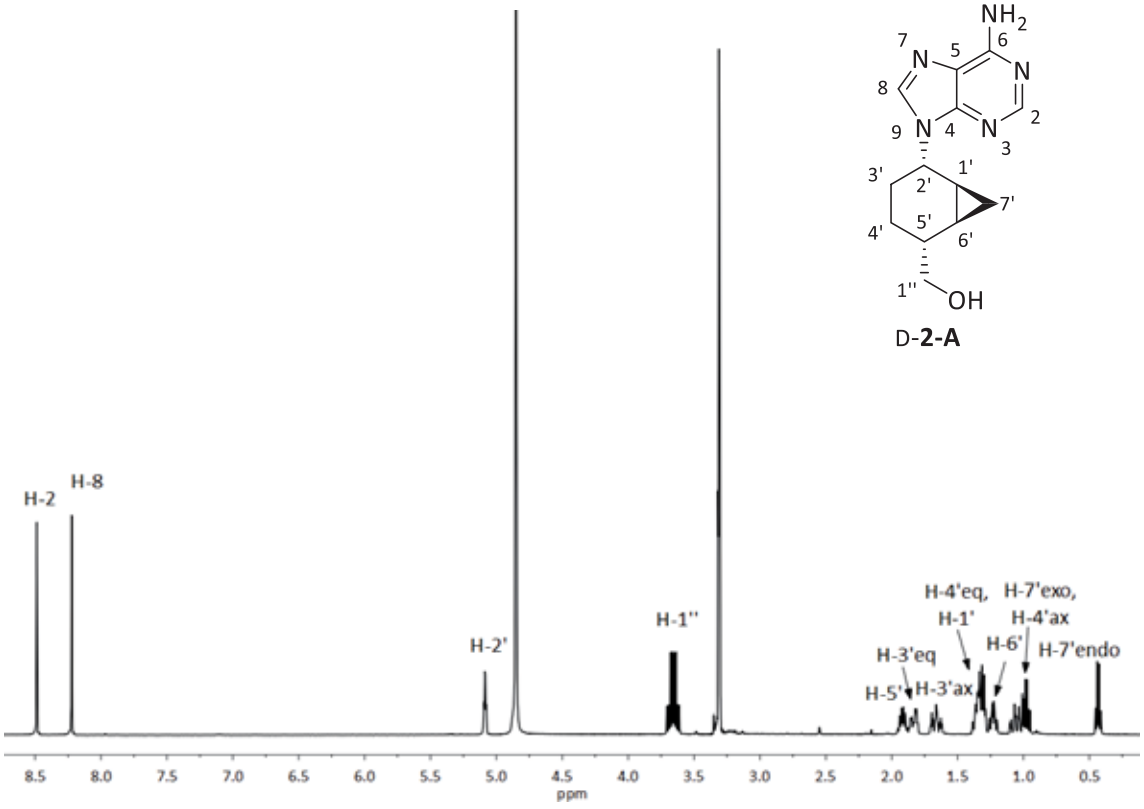
HMBC (400 MHz, $CDCl_3$)



NOESY (400 MHz, $CDCl_3$)

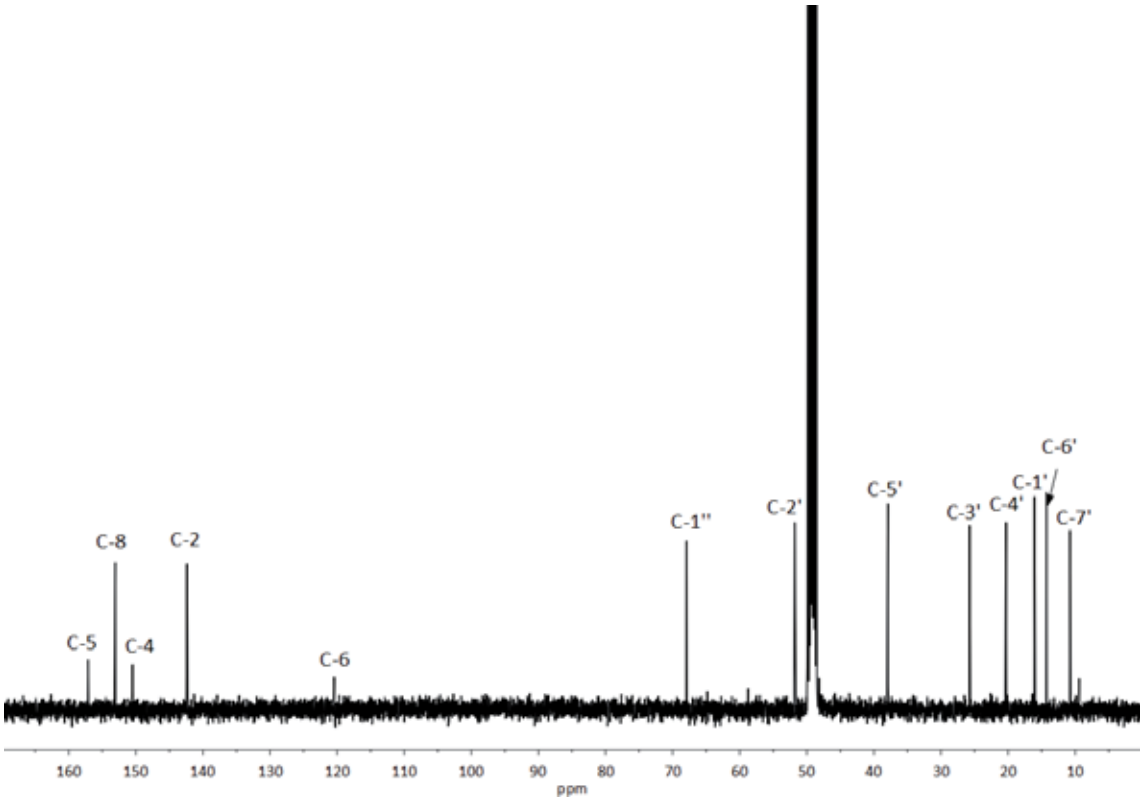


IR (ATR)

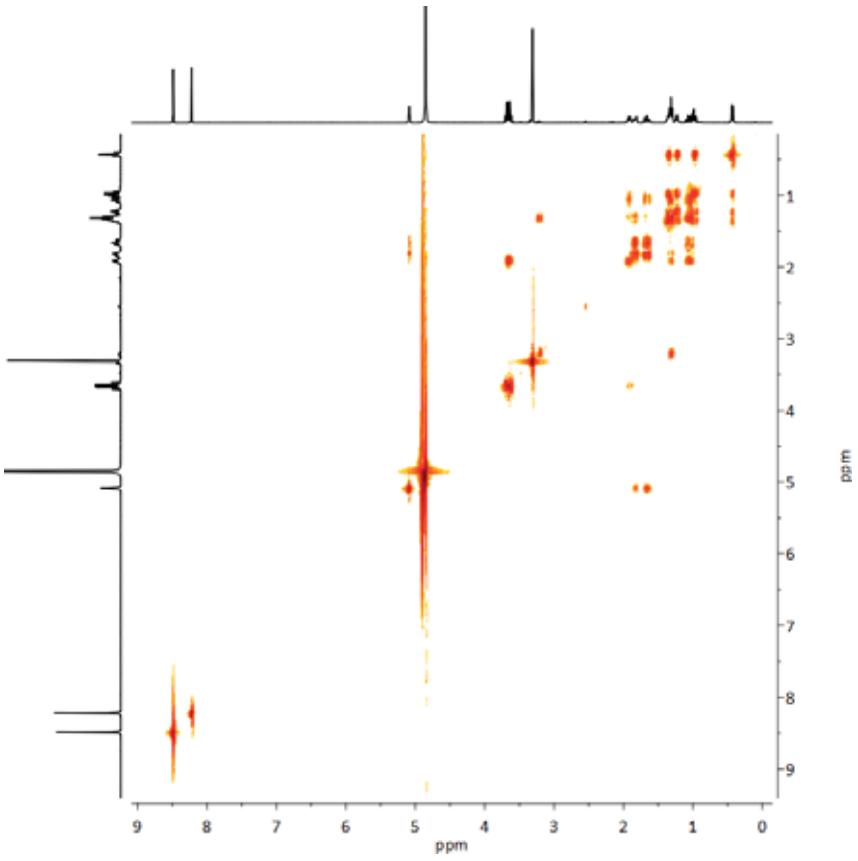


D-**2-A**

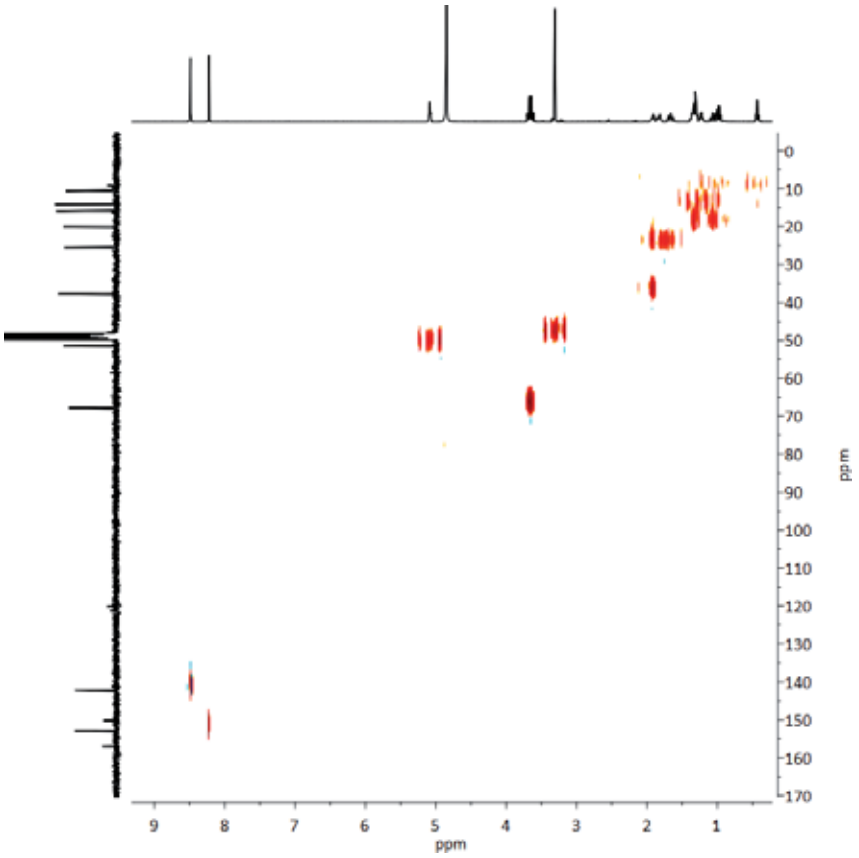
^{1}H-NMR (400 MHz, MeOD)



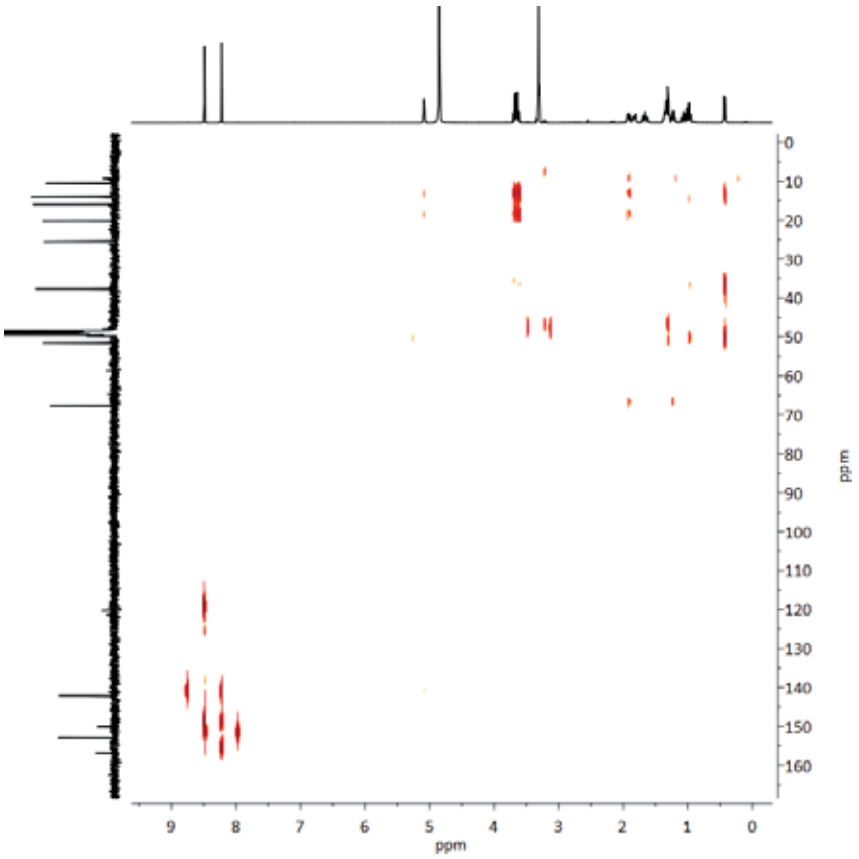
^{13}C-NMR (100 MHz, MeOD)



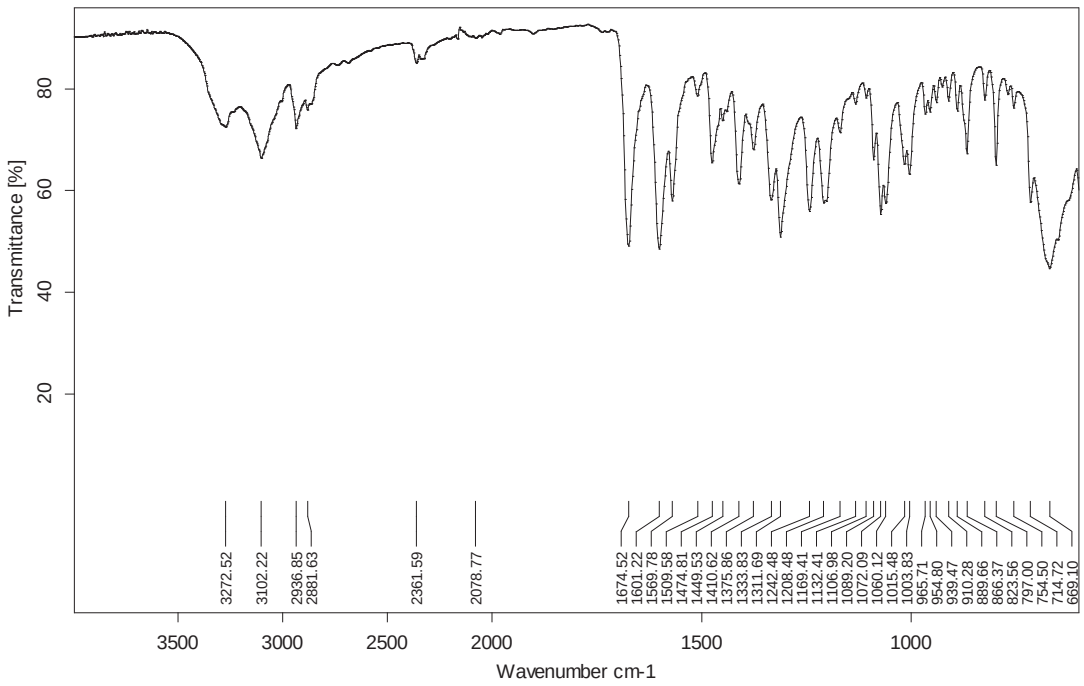
COSY (400 MHz, MeOD)



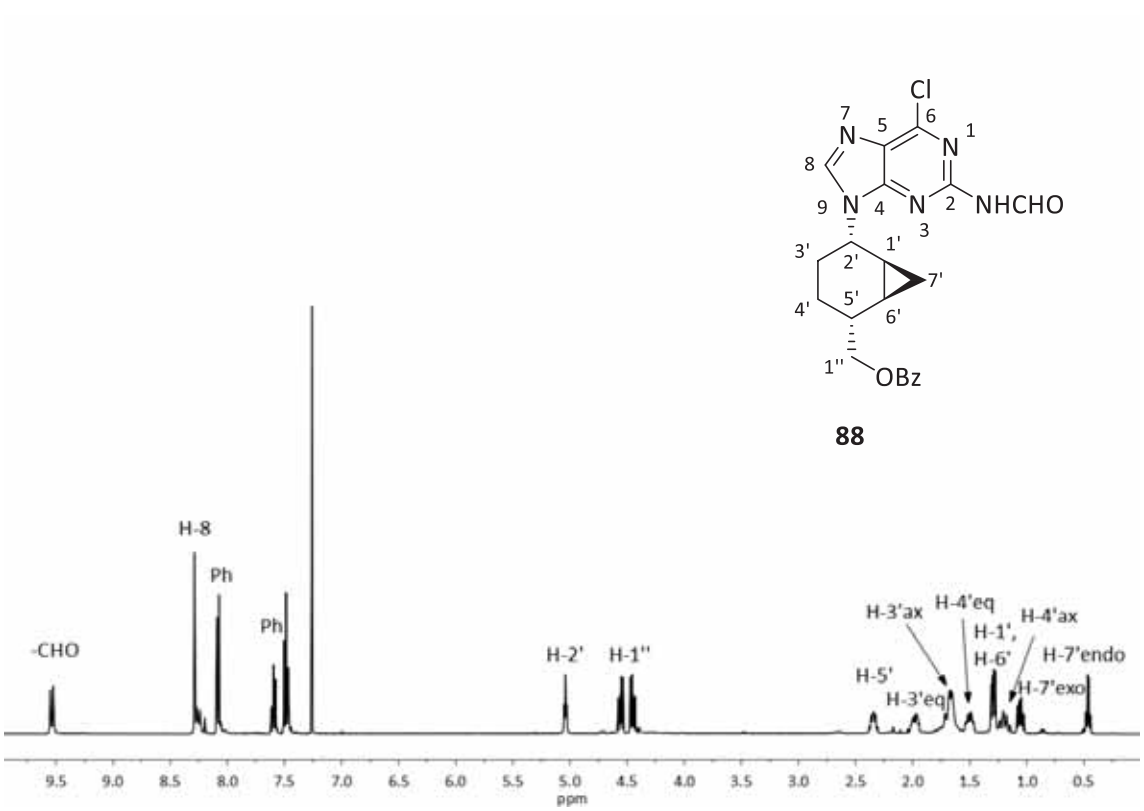
HSQC (400 MHz, MeOD)



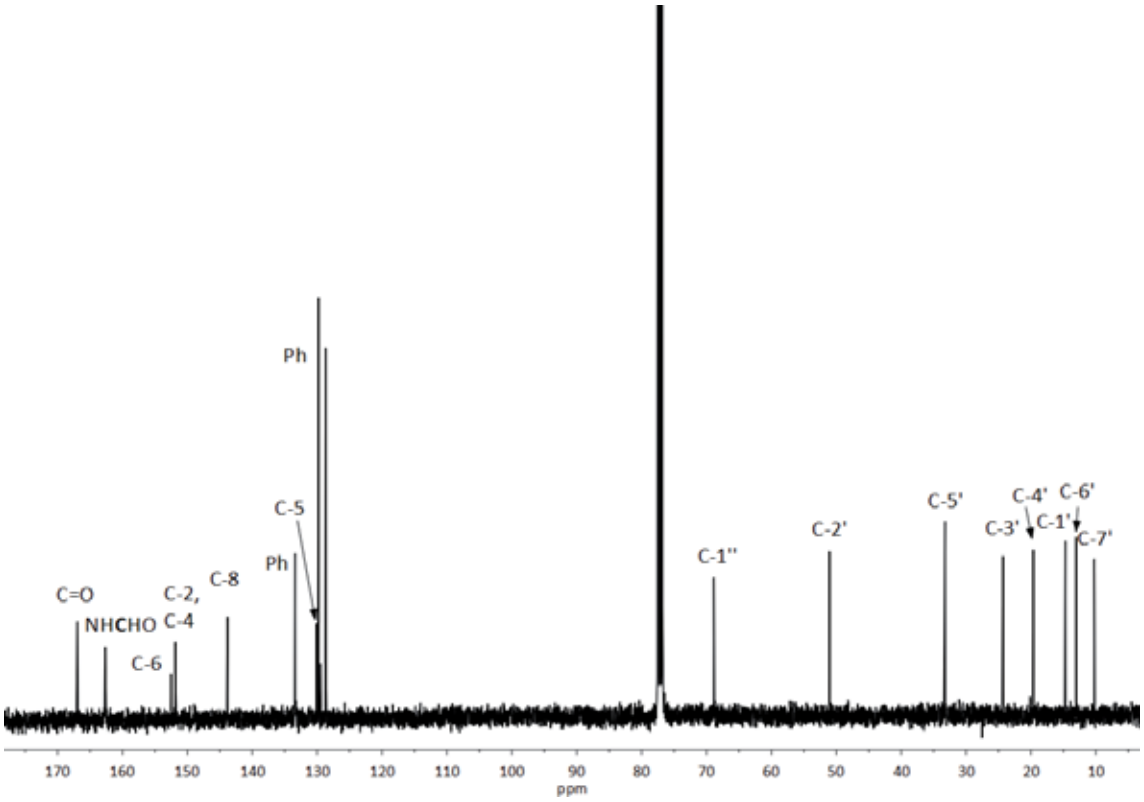
HMBC (400 MHz, MeOD)



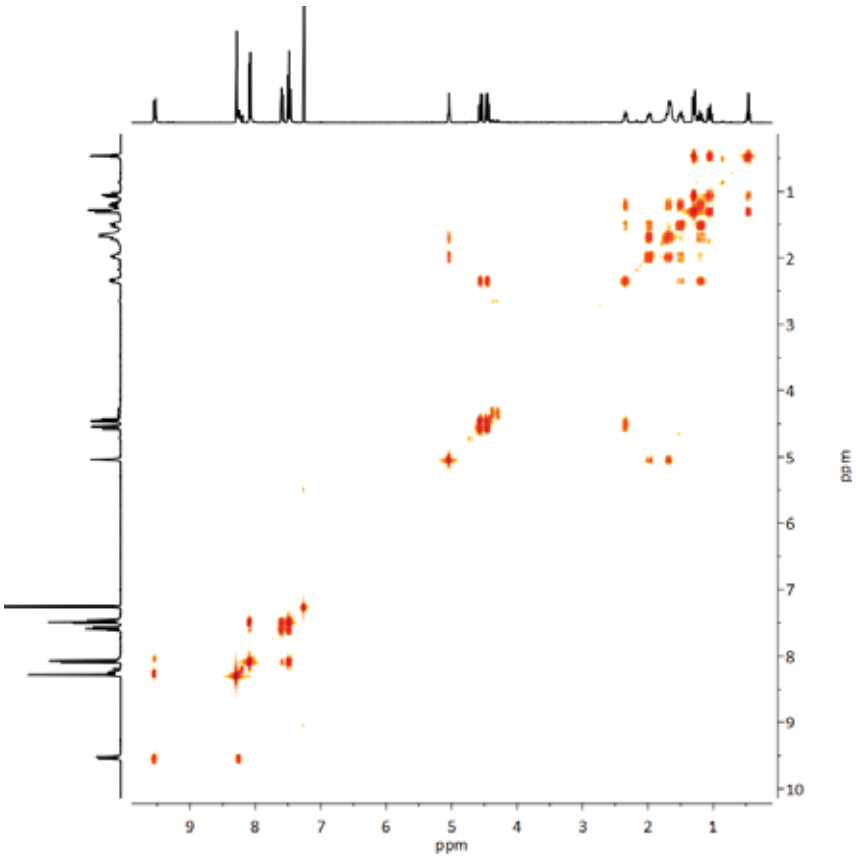
IR (ATR)



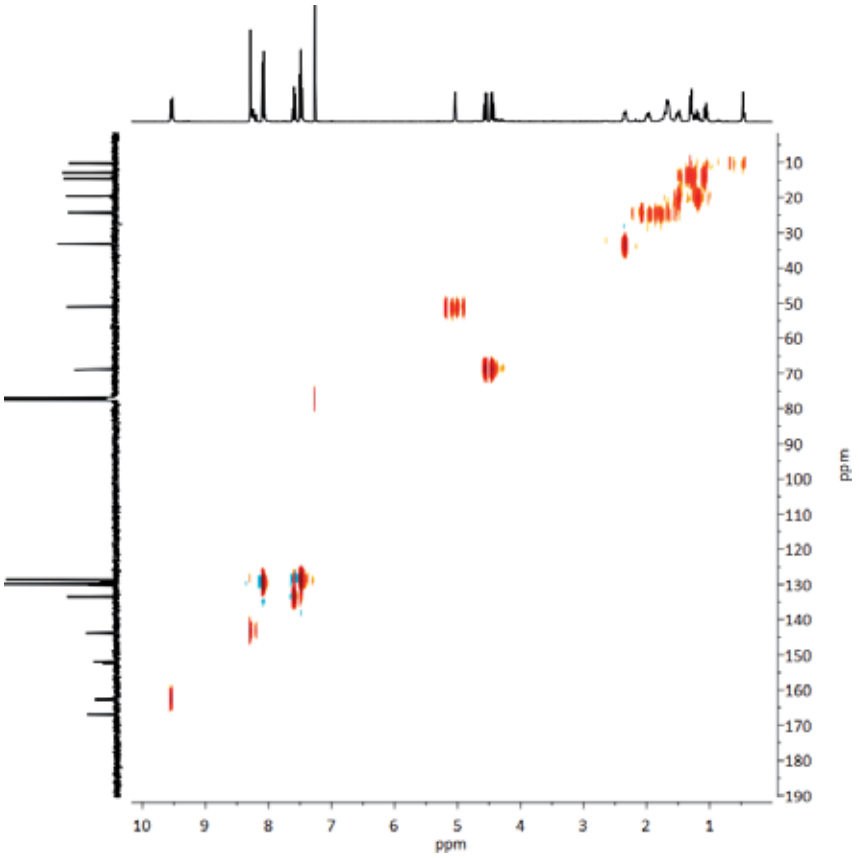
^{1}H-NMR (400 MHz, $CDCl_3$)



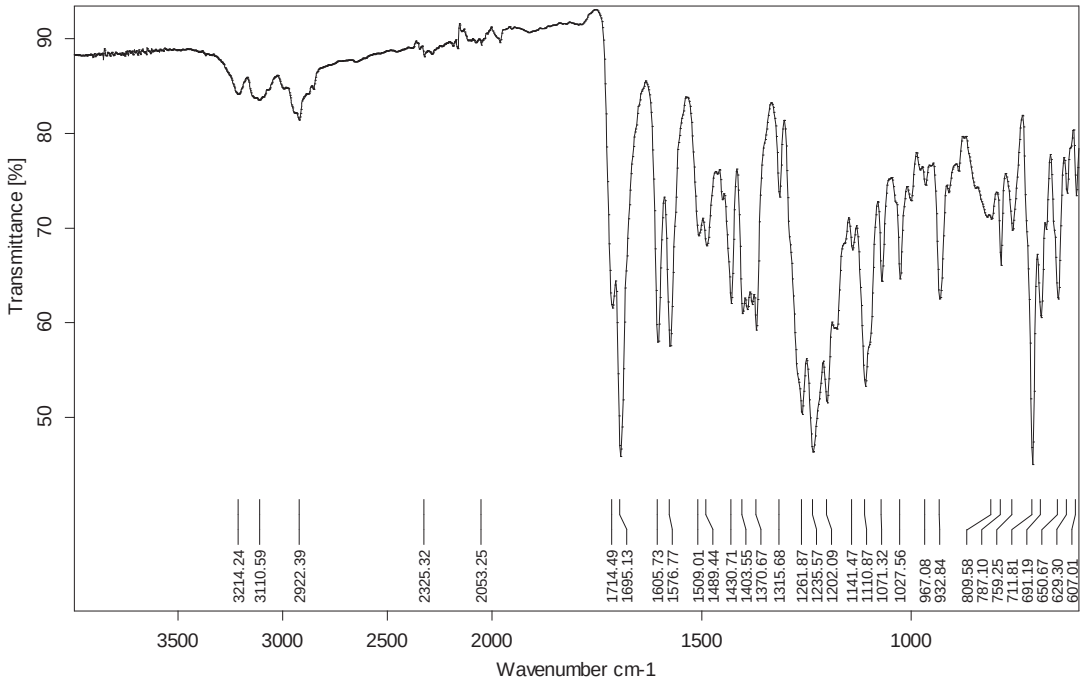
^{13}C-NMR (100 MHz, $CDCl_3$)



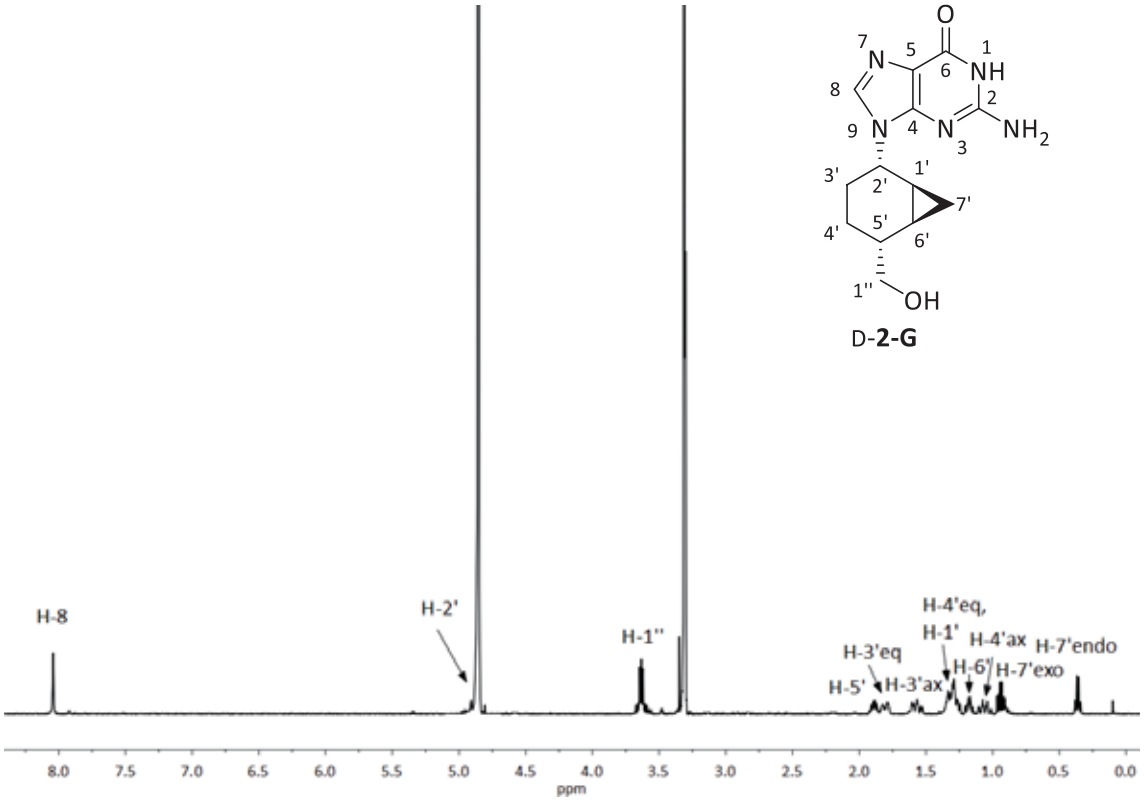
COSY (400 MHz, $CDCl_3$)



HSQC(400 MHz, $CDCl_3$)

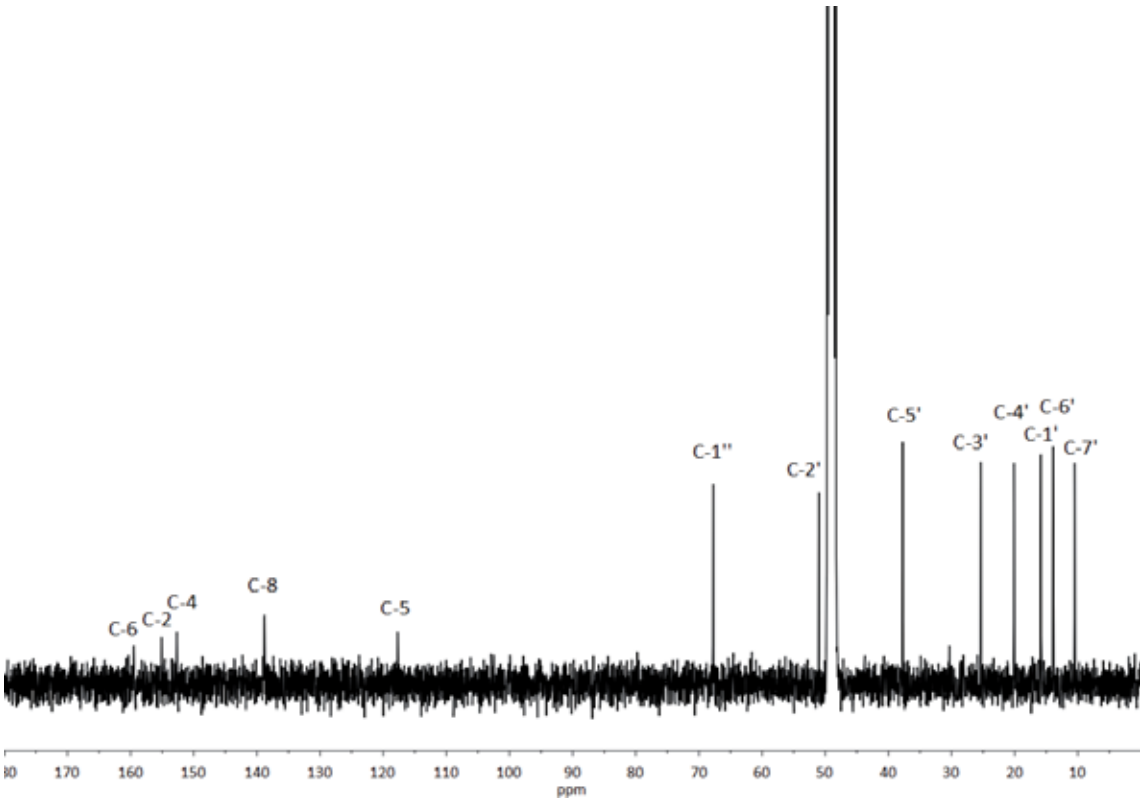


IR (ATR)

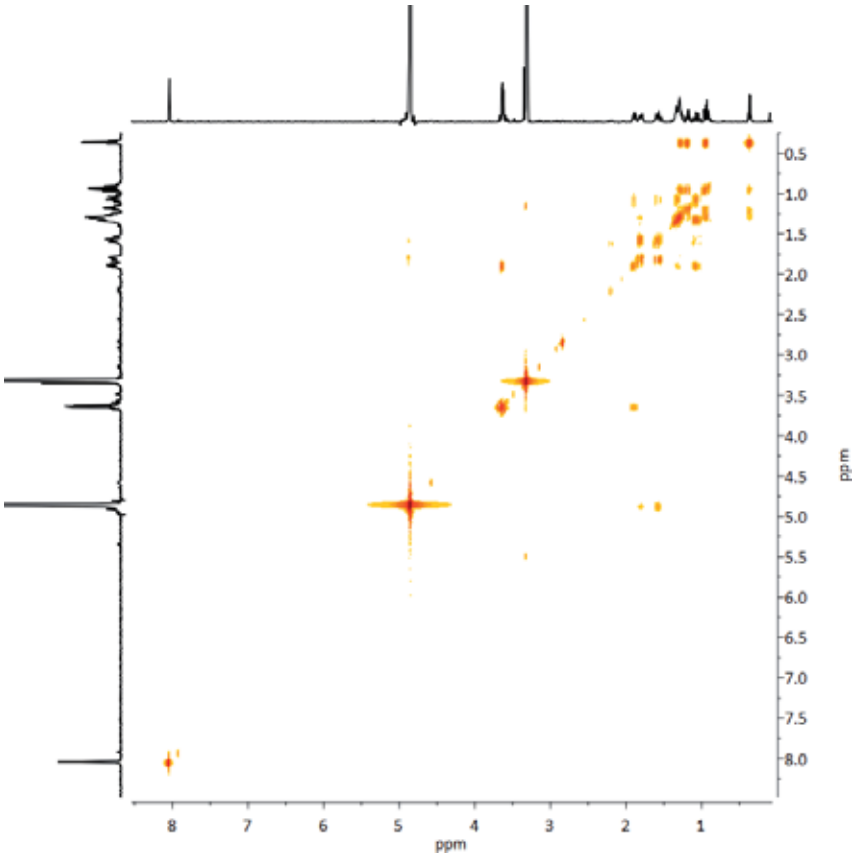


D-**2-G**

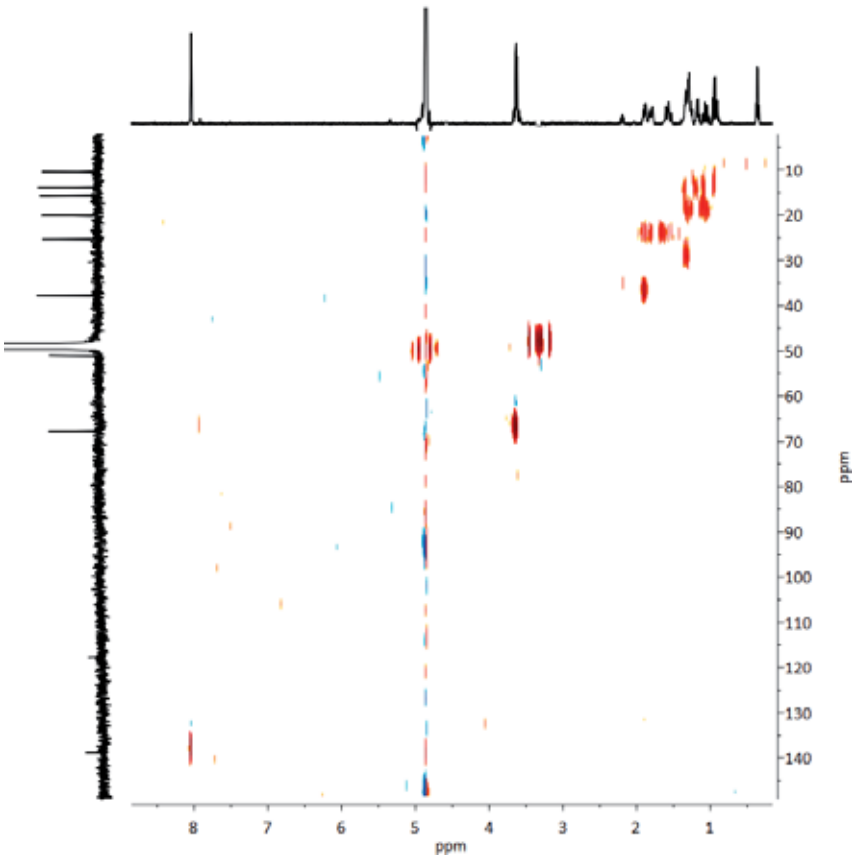
^{1}H-NMR (400 MHz, MeOD)



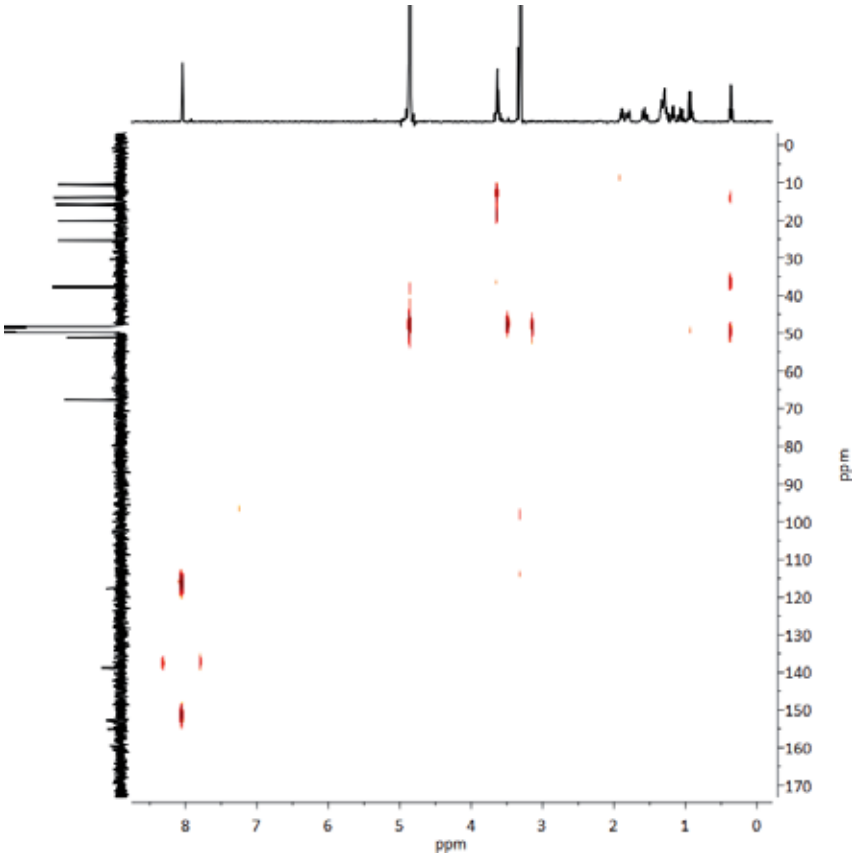
^{13}C-NMR (100 MHz, MeOD)



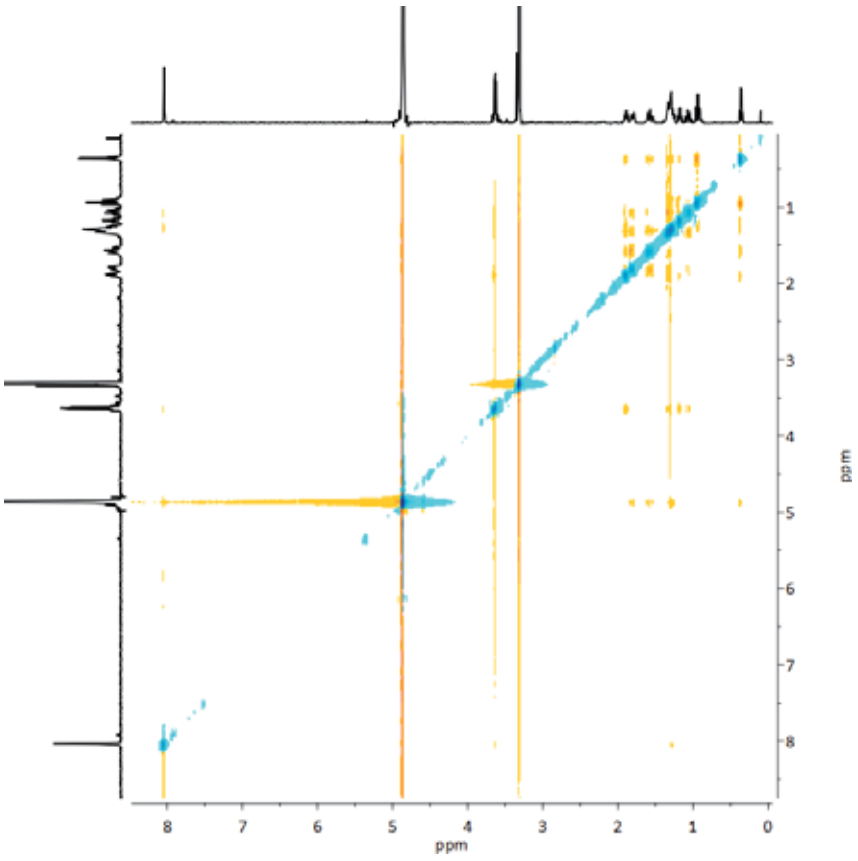
COSY (400 MHz, MeOD)



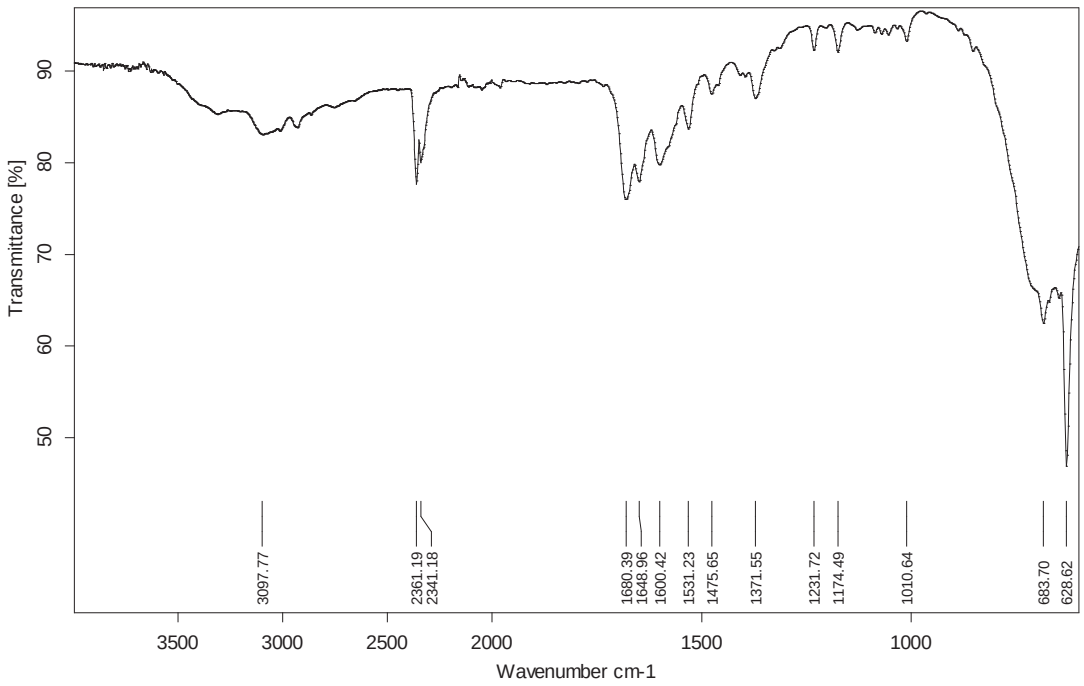
HSQC (400 MHz, MeOD)



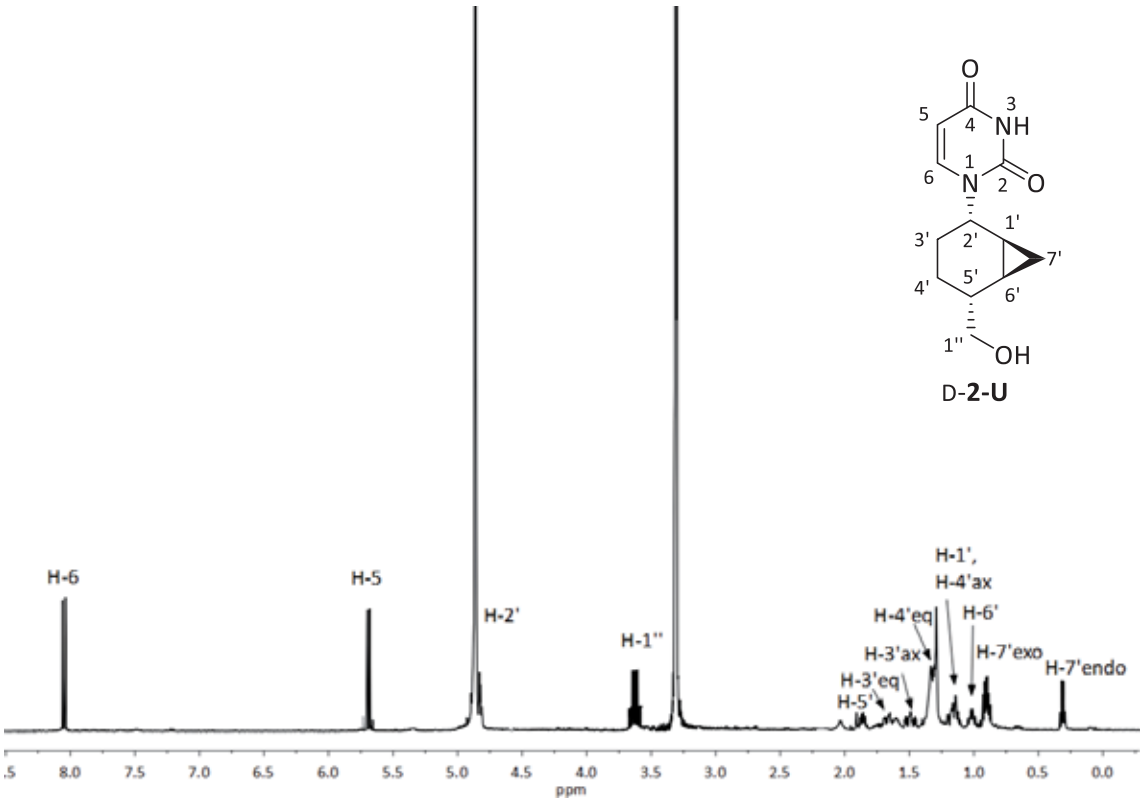
HMBC (400 MHz, MeOD)



NOESY (400 MHz, MeOD)

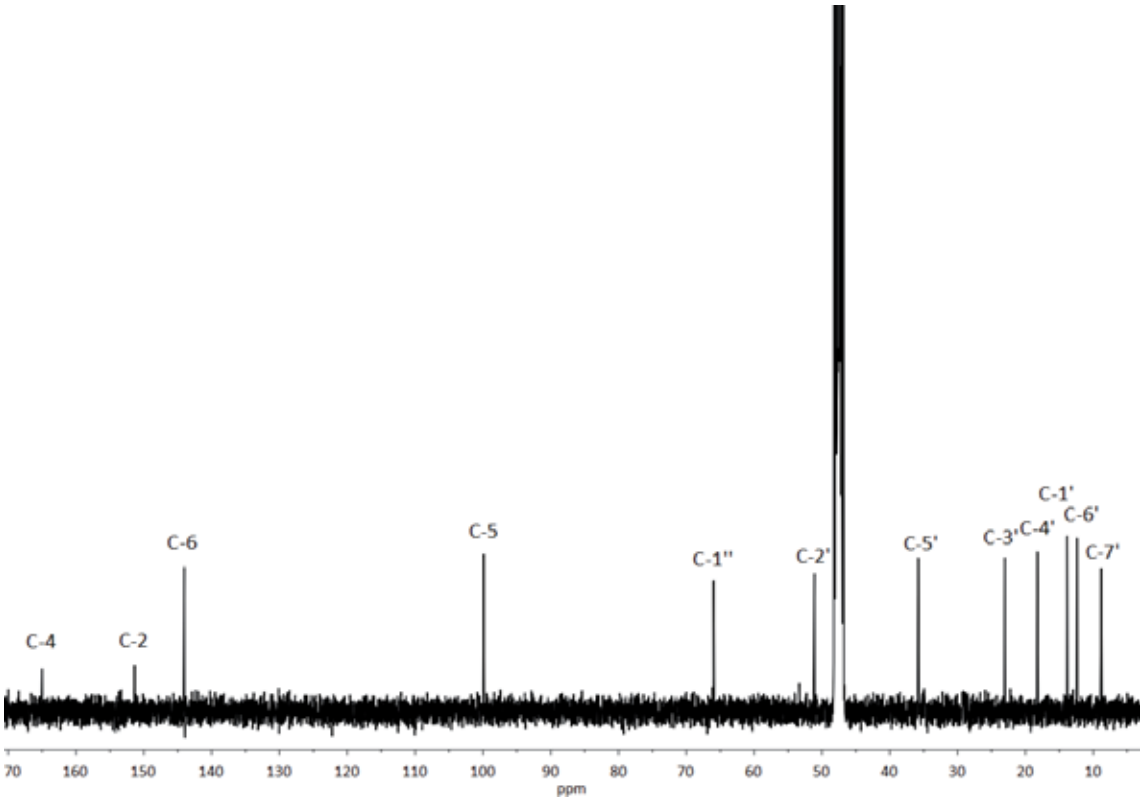


IR (ATR)

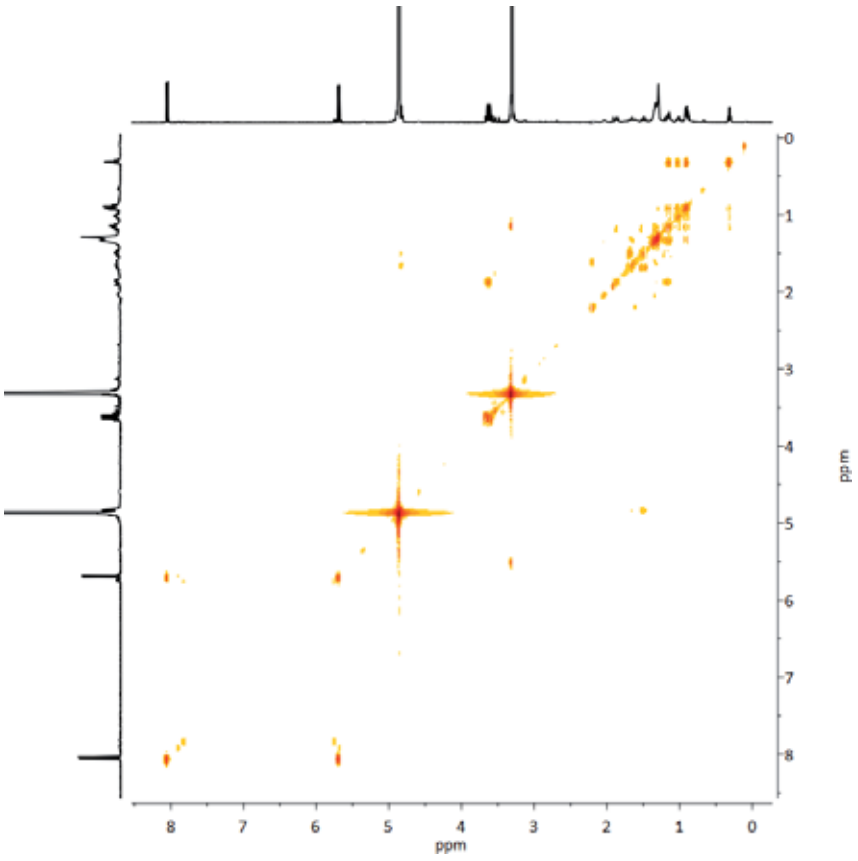


D-**2-U**

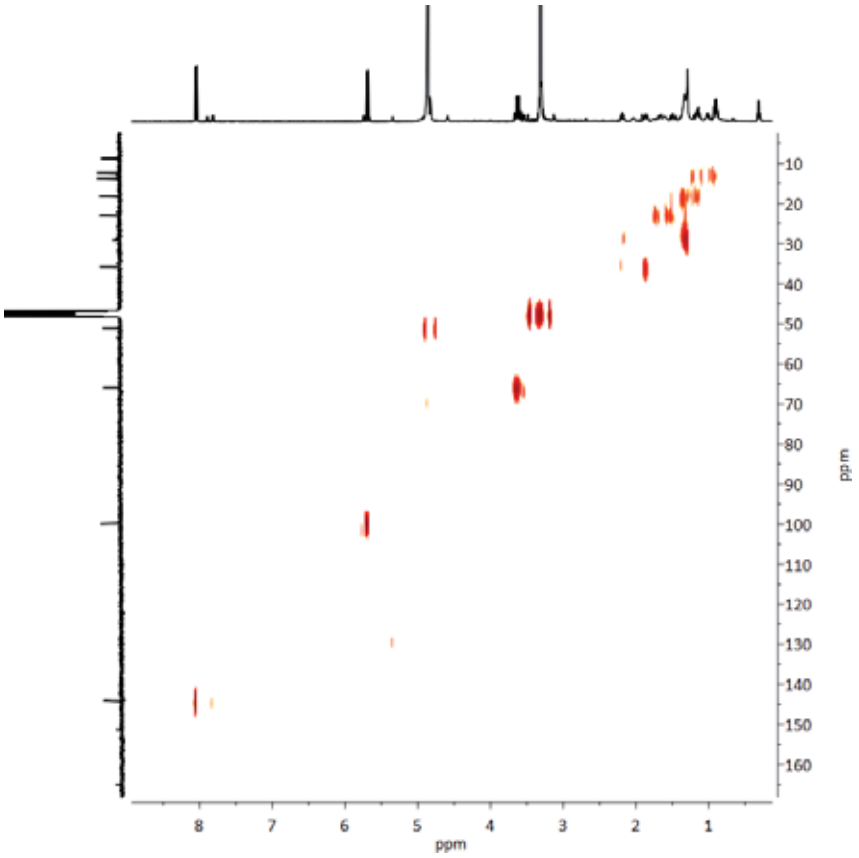
^{1}**H-NMR** (400 MHz, MeOD)



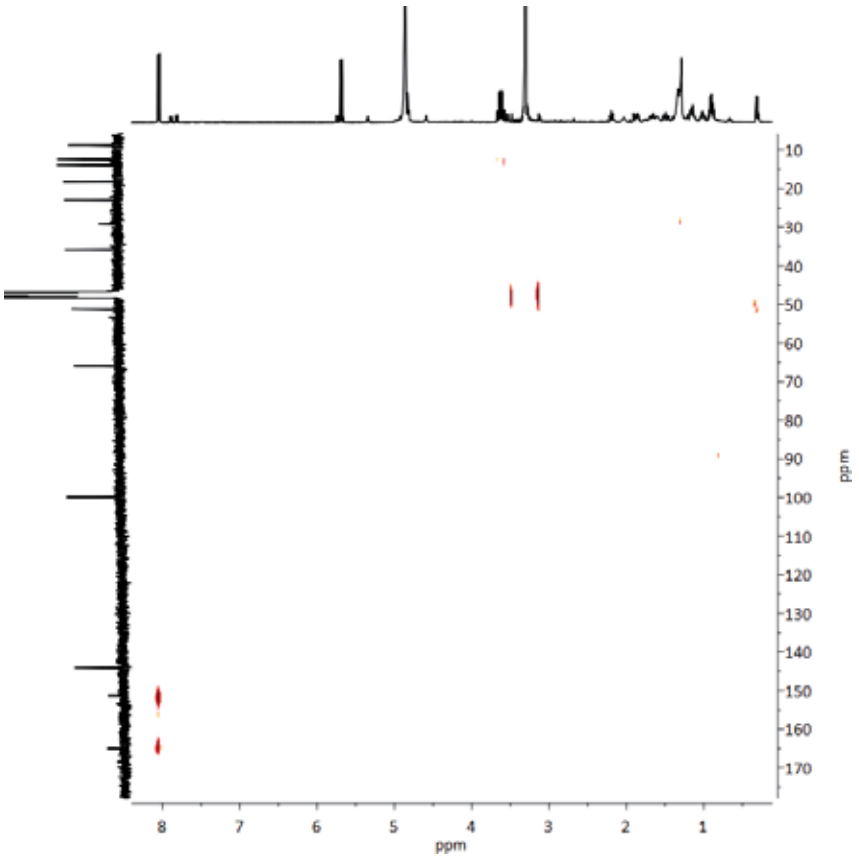
^{13}C-NMR (100 MHz, MeOD)



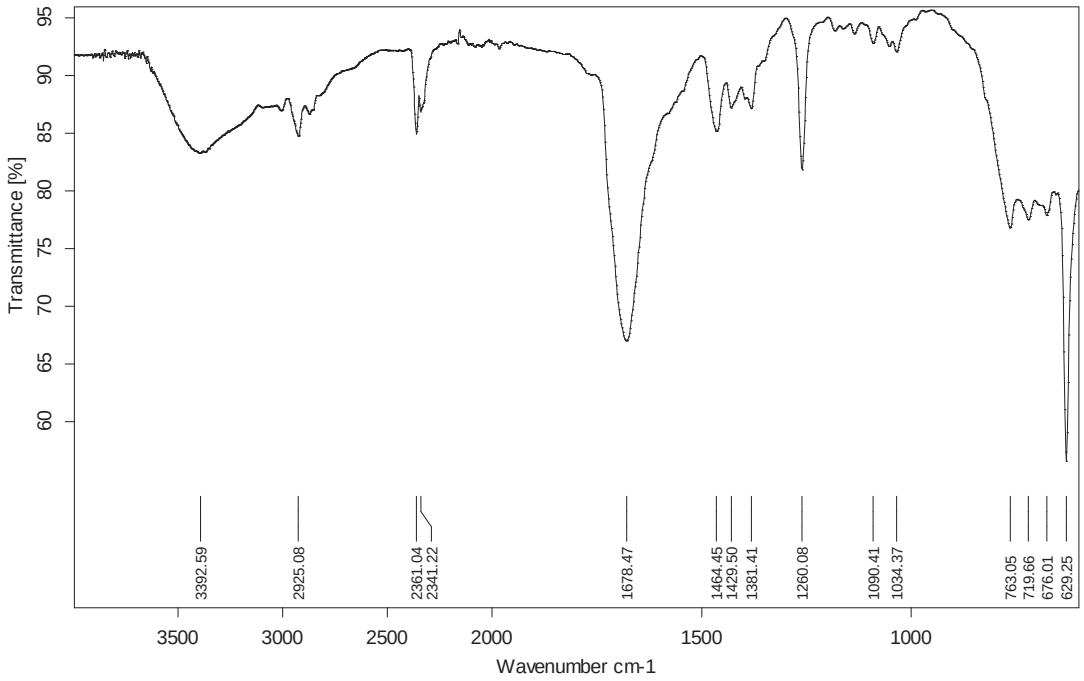
COSY (400 MHz, MeOD)



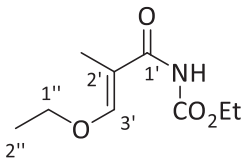
HSQC (400 MHz, MeOD)



HMBC (400 MHz, MeOD)

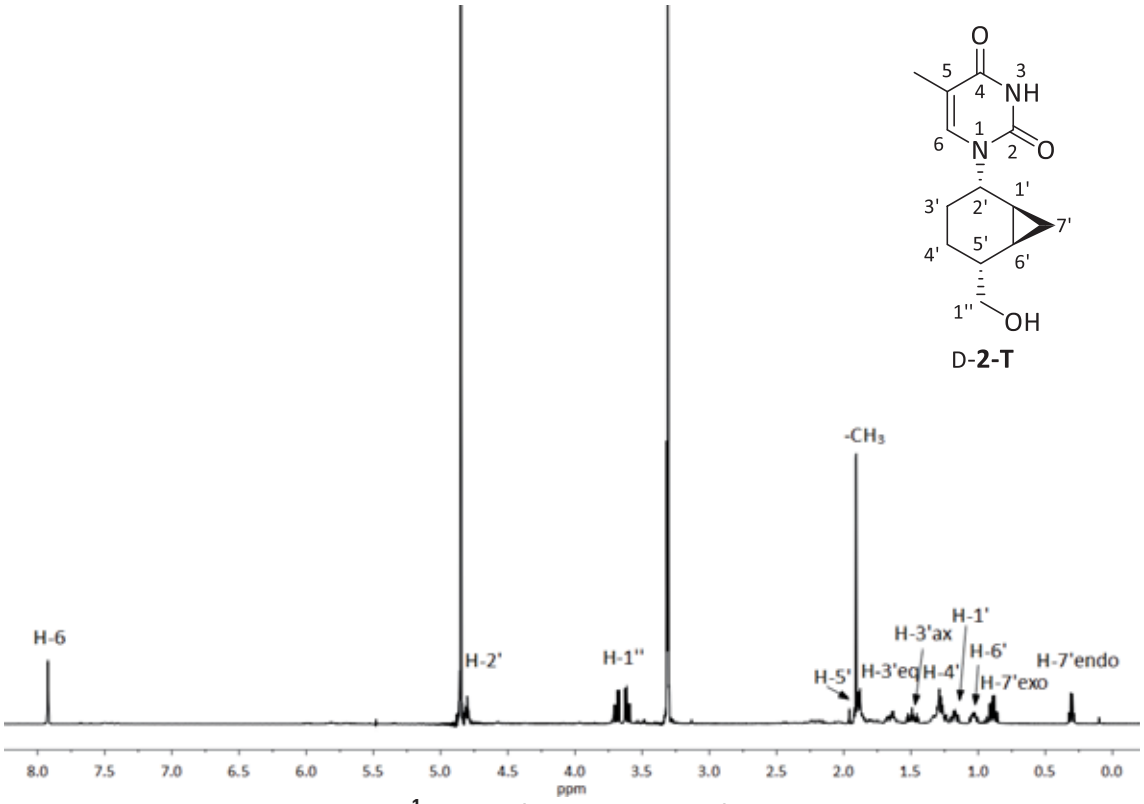


IR (ATR)

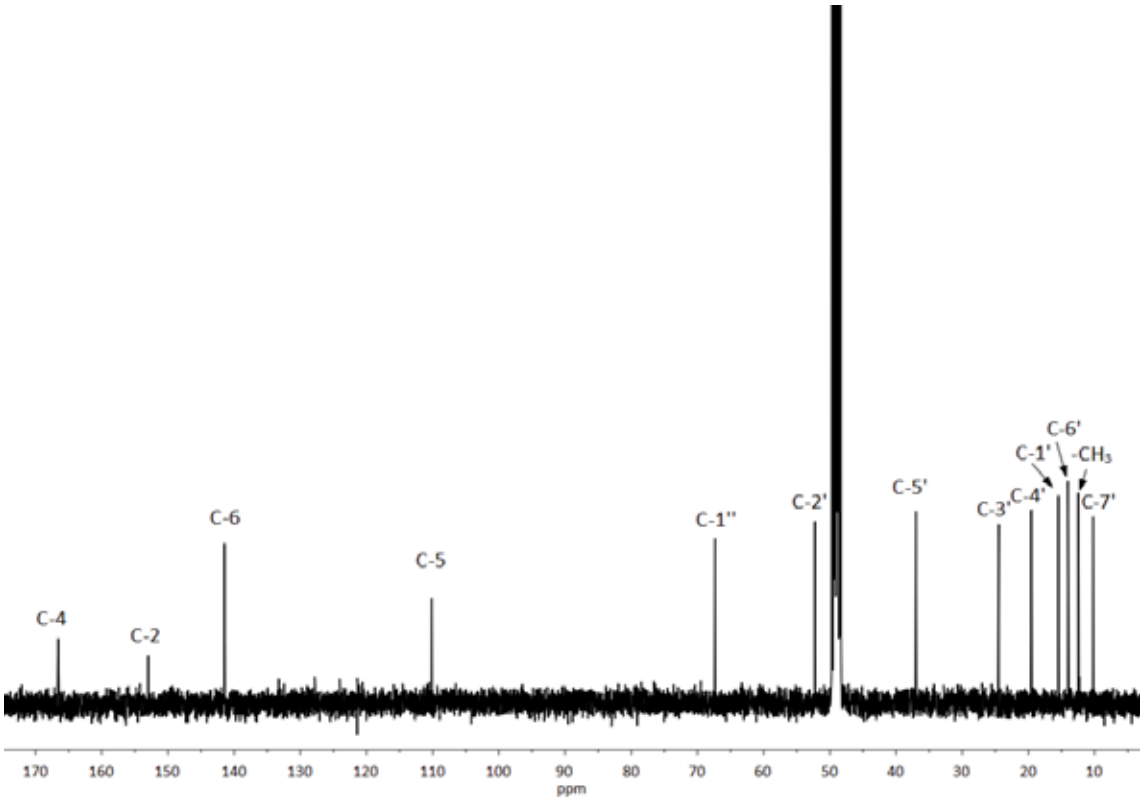


101

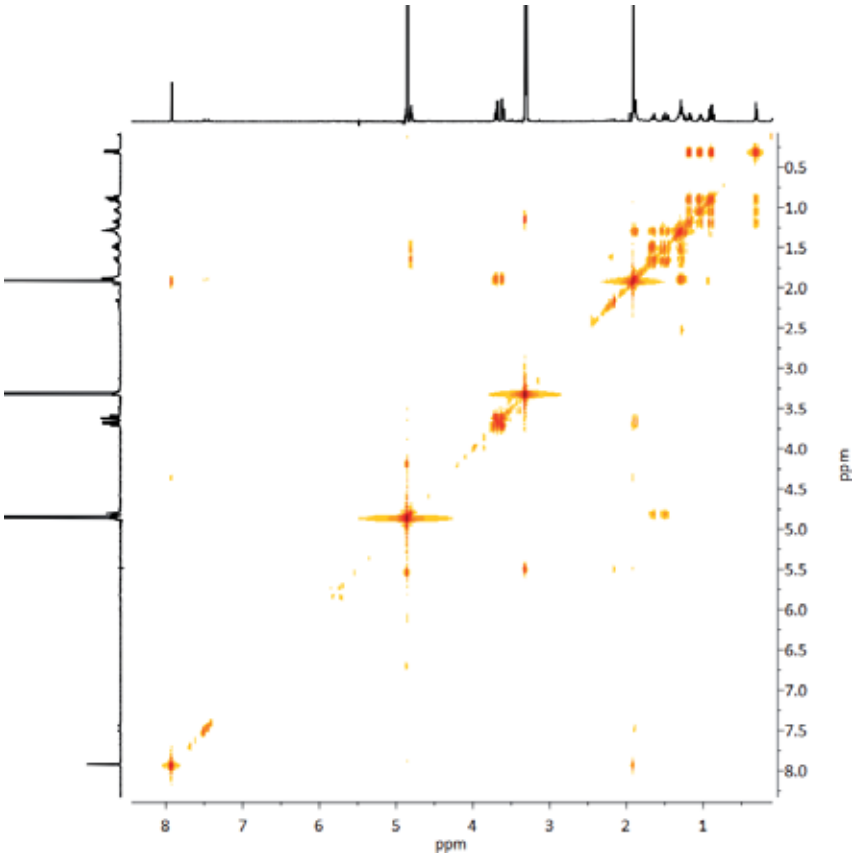
^{1}H-NMR (400 MHz, $CDCl_3$)



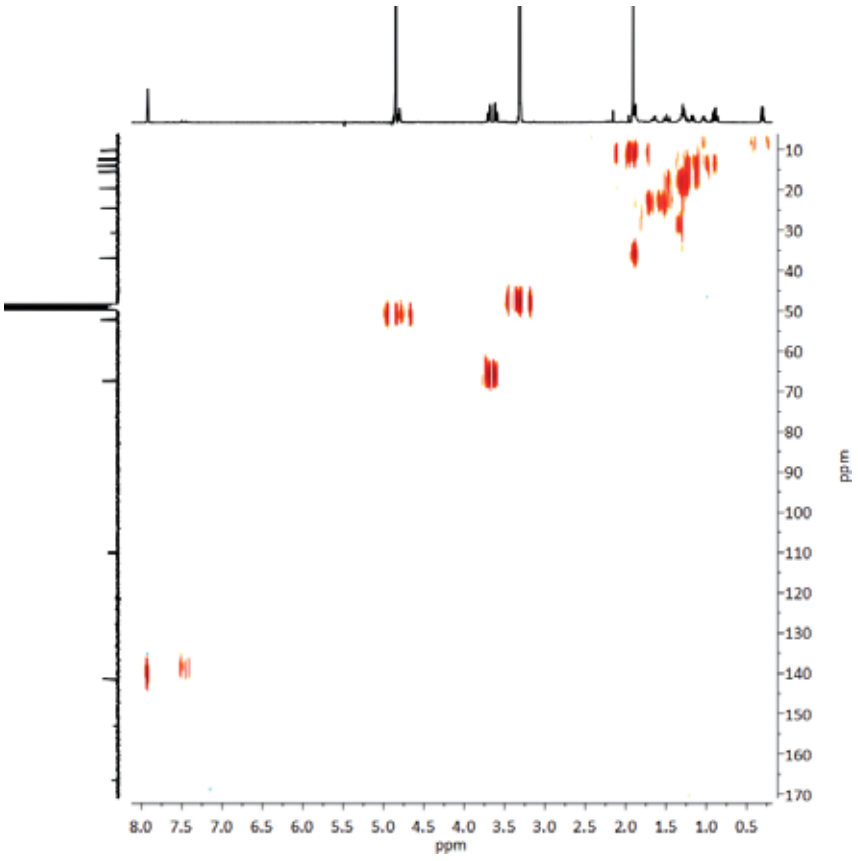
^{1}H-NMR (400 MHz, MeOD)



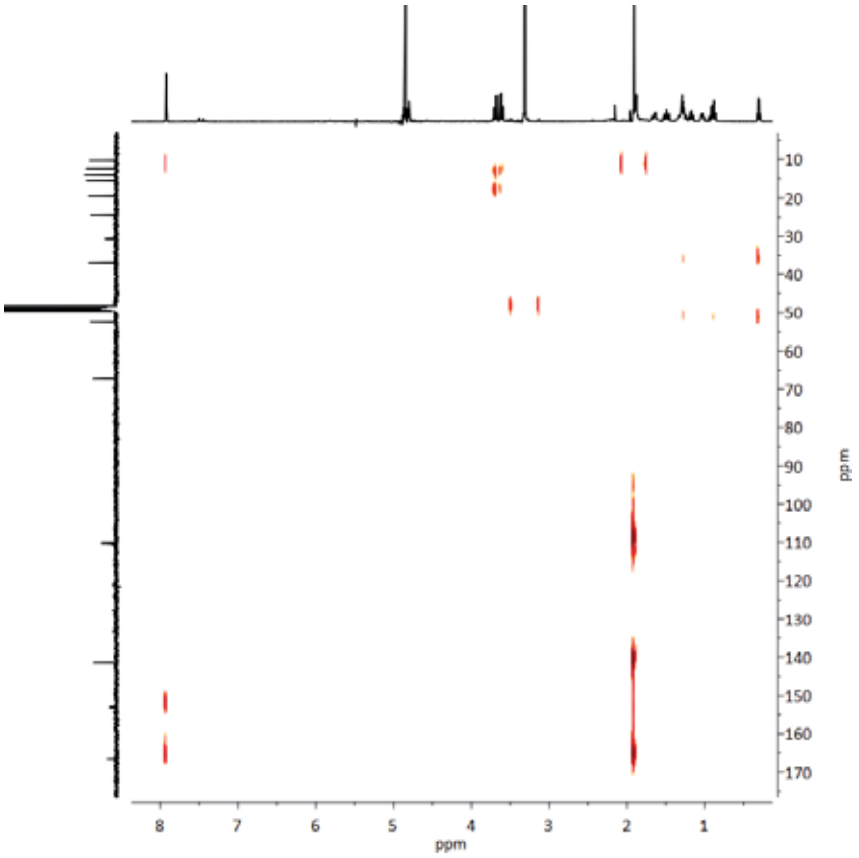
^{13}C-NMR (100 MHz, MeOD)



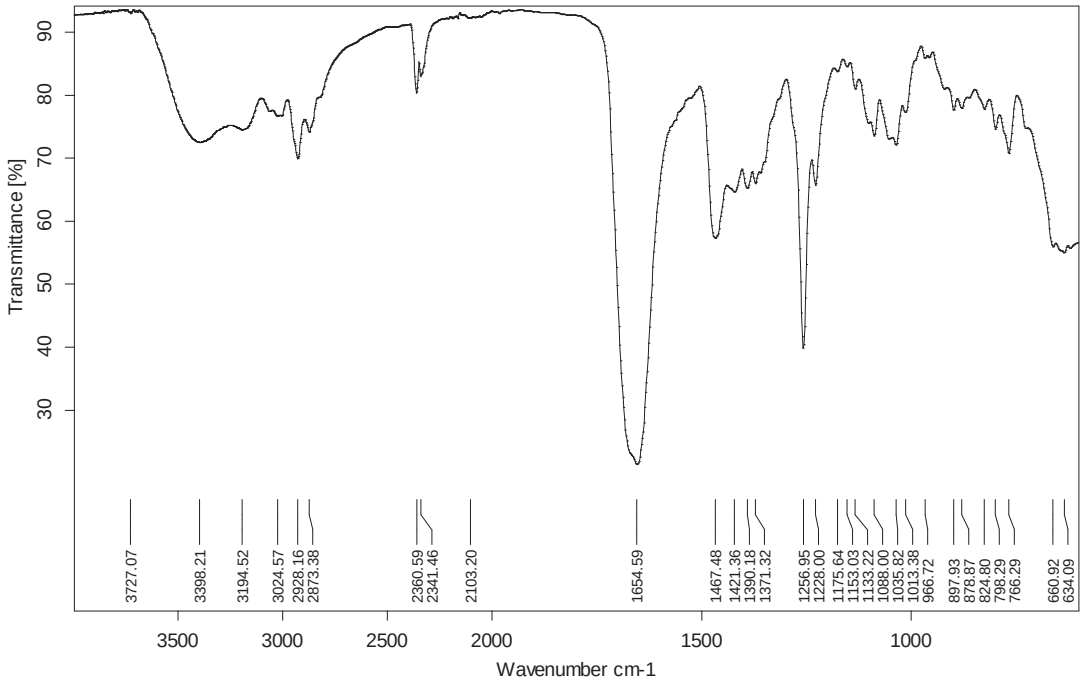
COSY (400 MHz, MeOD)



HSQC (400 MHz, MeOD)



HMBC (400 MHz, MeOD)



IR (ATR)

Universitat Autònoma de Barcelona

Appendix B

Figures not included in the manuscript

Beatriz Domínguez Pérez

Ph.D. Thesis
Ph.D. in Chemistry

Supervisors:
Dr. Ramon Alibés Arqués
Dr. Félix Busqué Sánchez
Dr. Jean-Didier Márechal

Departament de Química
Facultat de Ciències
2015

1. Molecular modelling study of novel carbocyclic nucleoside analogues as anti-HSV

1.1. 1st phosphorylation step

1.1.1. Docking results

- **Pyrimidine nucleoside analogues**

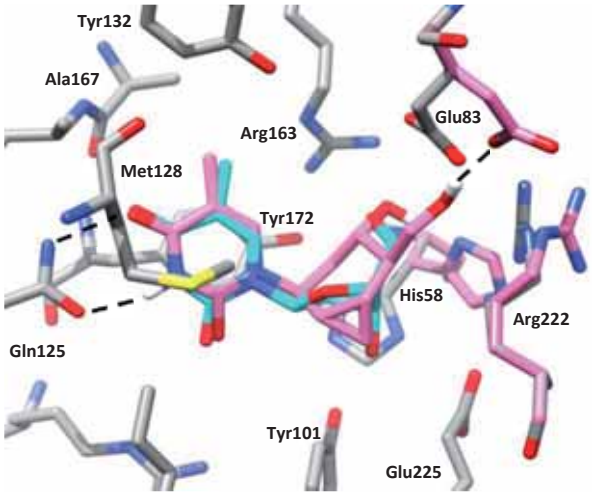


Figure B-1. D-**3-T** (pink) superimposed to crystallographic **dT** (blue) in HSV-1 TK (PDB:1KIM, X-ray residues shown in grey). Hydrogen bonds are depicted as dotted lines. For the sake of clarity, crystallographic waters are not shown and hydrogen atoms are only shown when bound to a heteroatom of the ligand.

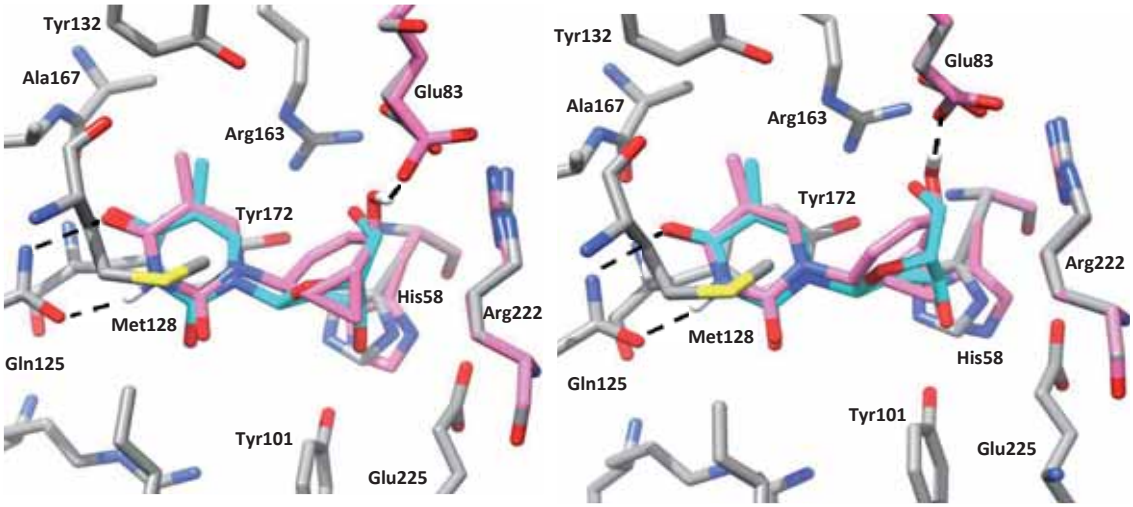


Figure B-2. D-**5-T** (left) and L-**5-T** (right) in pink superimposed to crystallographic **dT** (blue) in HSV-1 TK (PDB:1KIM, X-ray residues shown in grey). Hydrogen bonds are depicted as dotted lines. For the sake of clarity, crystallographic waters are not shown and hydrogen atoms are only shown when bound to a heteroatom of the ligand.

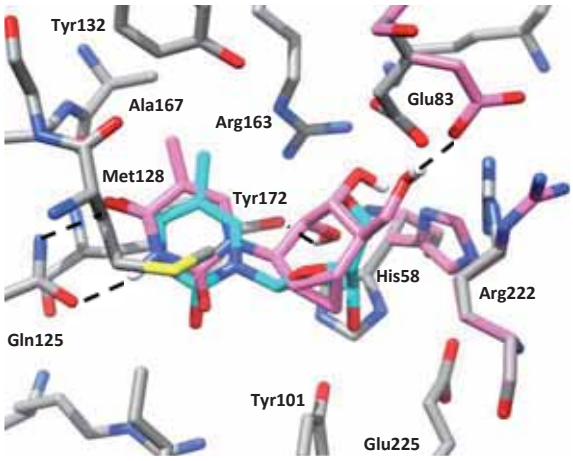


Figure B-3. D-**6-T** (pink) superimposed to crystallographic **dT** (blue) in HSV-1 TK (PDB:1KIM, X-ray residues shown in grey). Hydrogen bonds are depicted as dotted lines. For the sake of clarity, crystallographic waters are not shown and hydrogen atoms are only shown when bound to a heteroatom of the ligand.

- **Purine nucleoside analogues**

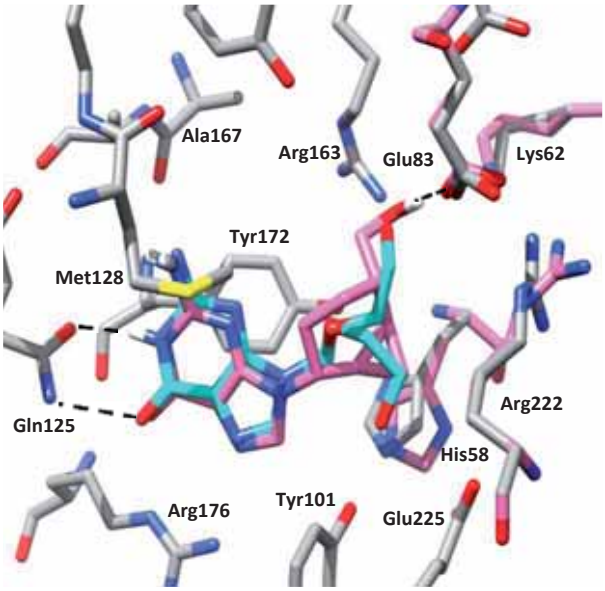


Figure B-4. L-**2-G** (pink) superimposed to crystallographic ACV (blue) in HSV-1 TK (PDB: 2KI5, X-ray residues shown in grey). Hydrogen bonds are depicted as dotted lines. For the sake of clarity, crystallographic waters are not shown and hydrogen atoms are only shown when bound to a heteroatom of the ligand.

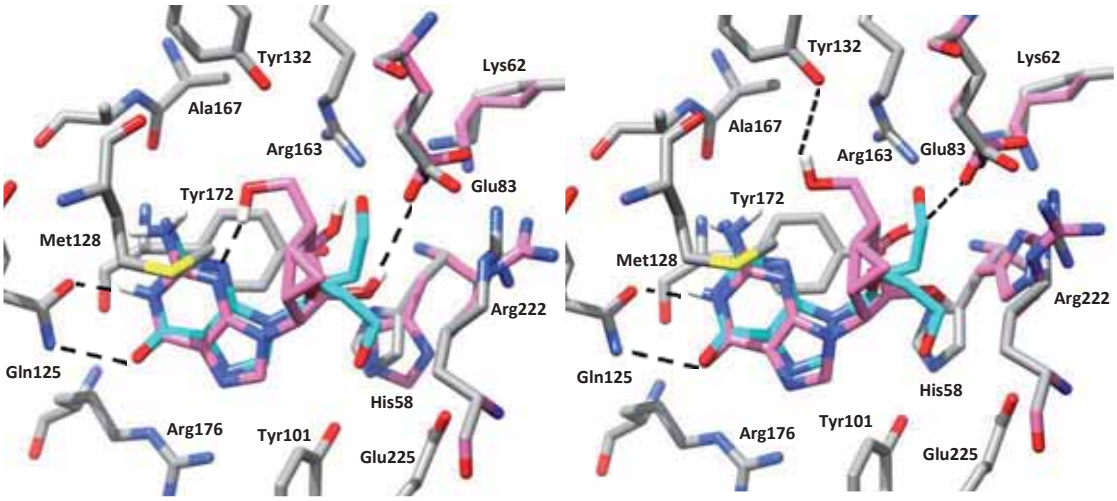
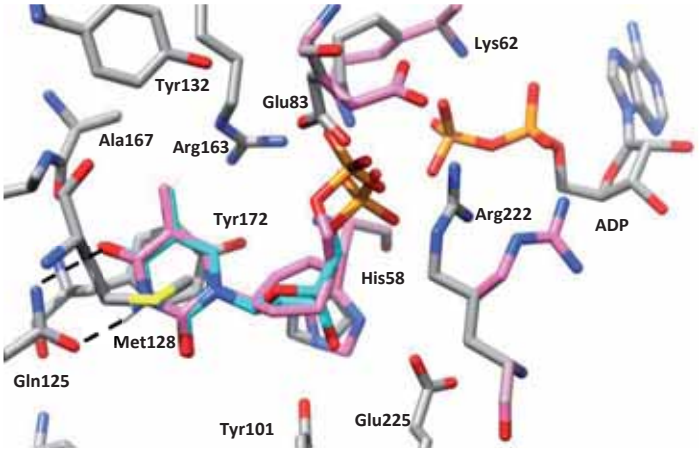


Figure B-5. D-**6-G** orientations with an internal hydrogen bond and 3'-OH pointing towards Glu-83 (left) and D-**6-G** orientations with 4'-OH pointing towards Glu-83 (right) in pink superimposed to crystallographic ACV (blue) in HSV-1 TK (PDB: 2KI5, X-ray residues shown in grey). Hydrogen bonds are depicted as dotted lines. For the sake of clarity, crystallographic waters are not shown and hydrogen atoms are only shown when bound to a heteroatom of the ligand.

1.2. 2nd phosphorylation step

1.2.1. Docking results

- **Pyrimidine nucleoside analogues**



a)

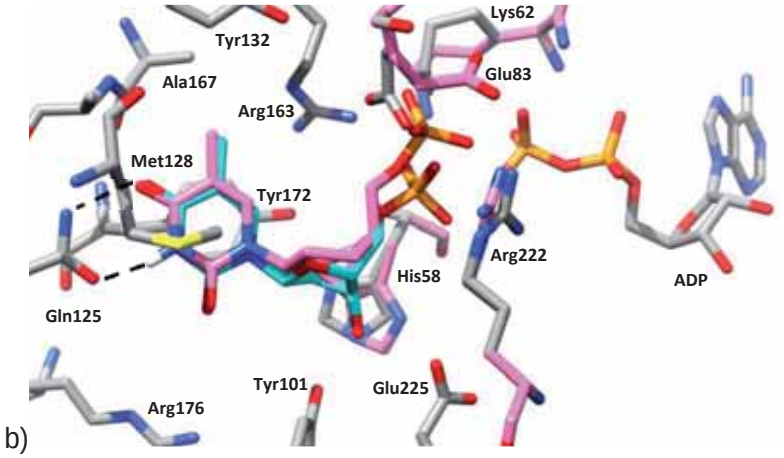


Figure B-6. a) L-**1-TMP** (pink) superimposed to crystallographic dTMP (blue) in HSV-1 TK (PDB: 1VTK, X-ray residues shown in grey). b) L-**2-TMP** (pink) superimposed to crystallographic dTMP (blue) in HSV-1 TK (PDB: 1VTK, X-ray residues shown in grey). Hydrogen bonds are depicted as dotted lines. For the sake of clarity, crystallographic waters are not shown and hydrogen atoms are only shown when bound to a heteroatom of the ligand.

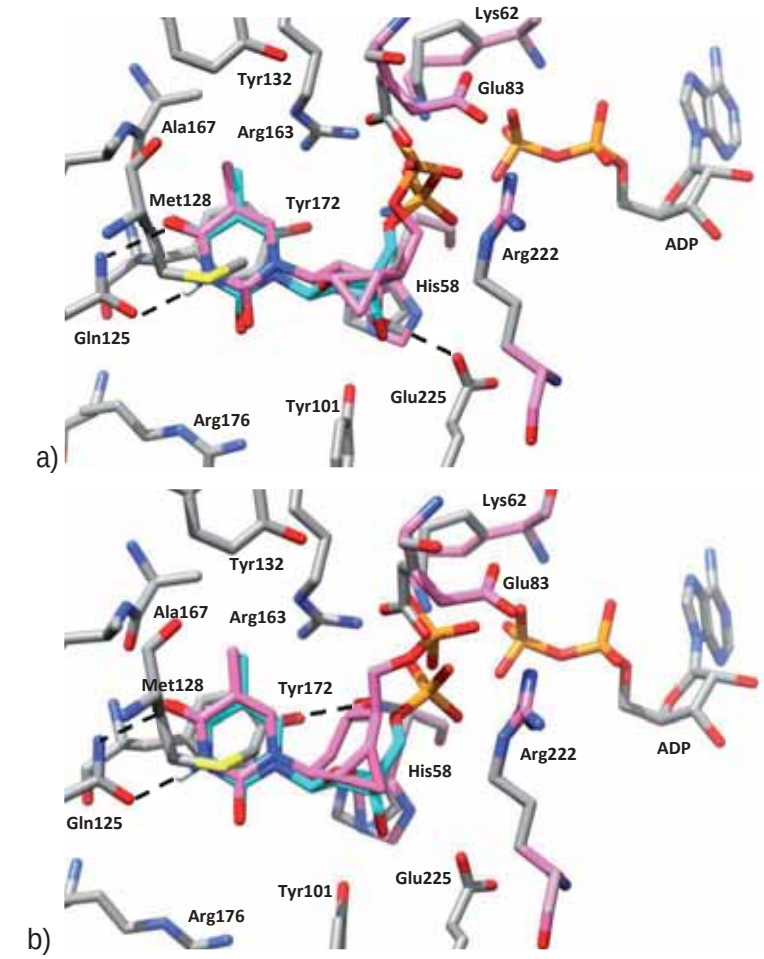


Figure B-7. a) D-**3-TMP** (pink) in pseudo-equatorial conformation superimposed to crystallographic dTMP (blue) in HSV-1 TK (PDB: 1VTK, X-ray residues shown in grey). b) D-**3-TMP** (pink) in pseudo-axial conformation superimposed to crystallographic dTMP (blue) in HSV-1 TK (PDB: 1VTK, X-ray residues shown in grey). Hydrogen bonds are depicted as dotted lines. For the sake of clarity, crystallographic waters are not shown and hydrogen atoms are only shown when bound to a heteroatom of the ligand.

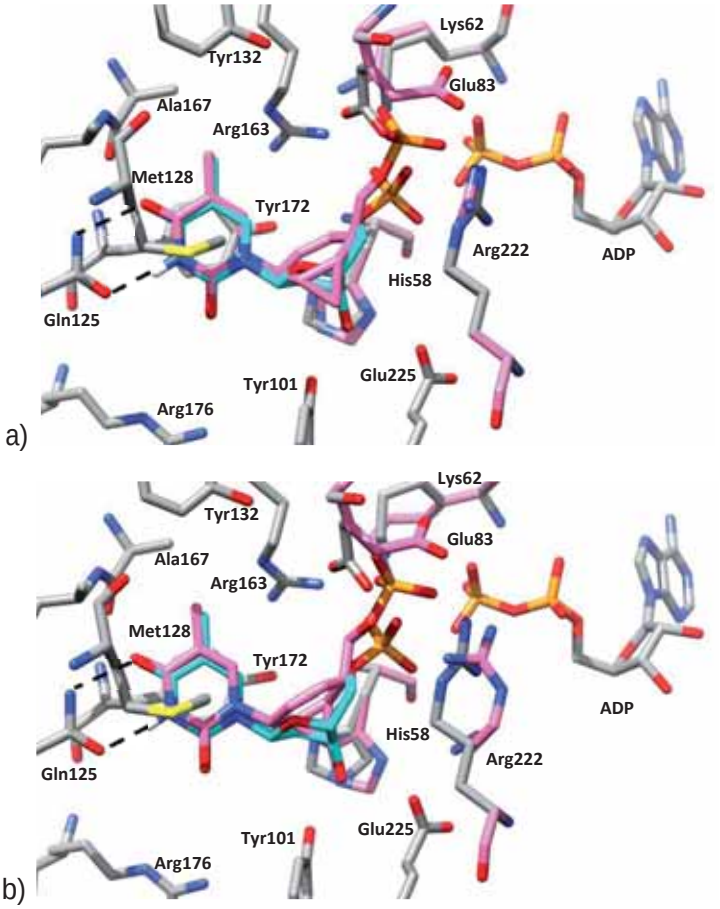


Figure B-8. a) D-**4-TMP** (pink) superimposed to crystallographic dTMP (blue) in HSV-1 TK (PDB: 1VTK, X-ray residues shown in grey). b) L-**4-TMP** (pink) superimposed to crystallographic dTMP (blue) in HSV-1 TK (PDB: 1VTK, X-ray residues shown in grey). Hydrogen bonds are depicted as dotted lines. For the sake of clarity, crystallographic waters are not shown and hydrogen atoms are only shown when bound to a heteroatom of the ligand.

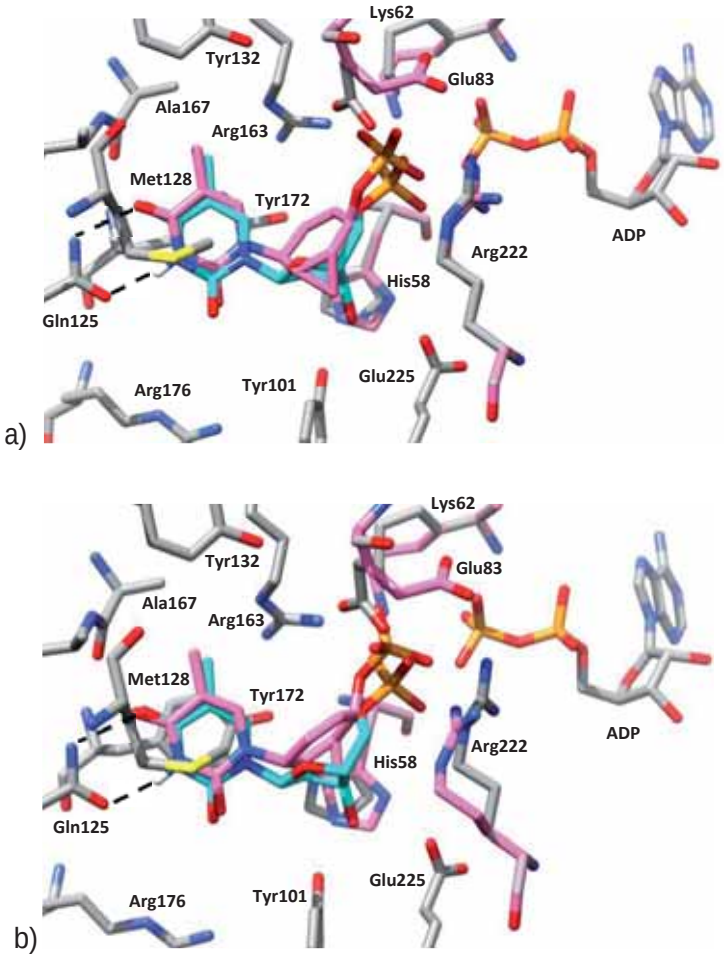


Figure B-9. a) D-**5-TMP** (pink) superimposed to crystallographic dTMP (blue) in HSV-1 TK (PDB: 1VTK, X-ray residues shown in grey). b) L-**5-TMP** (pink) superimposed to crystallographic dTMP (blue) in HSV-1 TK (PDB: 1VTK, X-ray residues shown in grey). Hydrogen bonds are depicted as dotted lines. For the sake of clarity, crystallographic waters are not shown and hydrogen atoms are only shown when bound to a heteroatom of the ligand.

- **Purine nucleoside analogues**

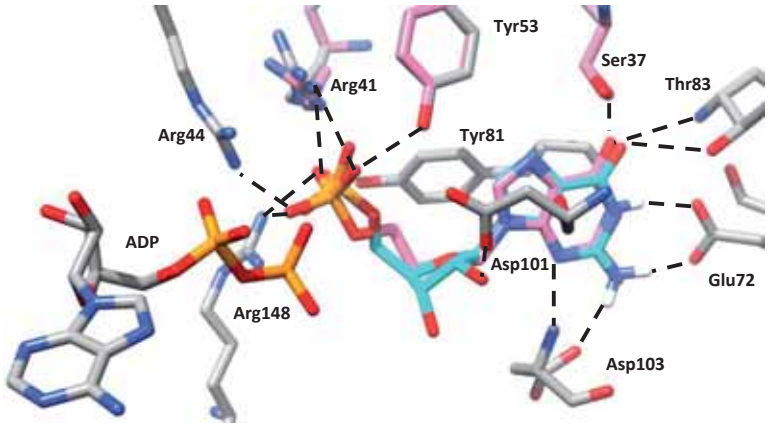


Figure B-10. ACVMP (pink) superimposed to crystallographic GMP (blue) in mGMPK (PDB: 1LVG, X-ray residues shown in grey). Hydrogen bonds are depicted as dotted lines. For the sake of clarity, crystallographic waters are not shown and hydrogen atoms are only shown when bound to a heteroatom of the ligand.

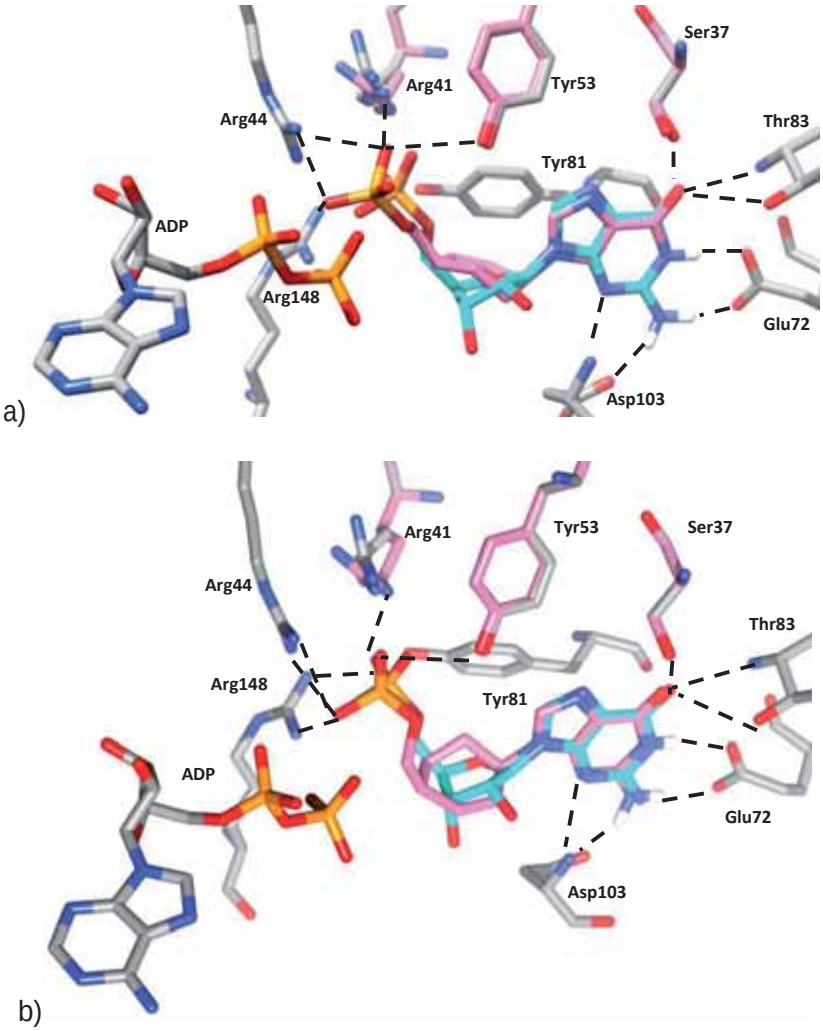
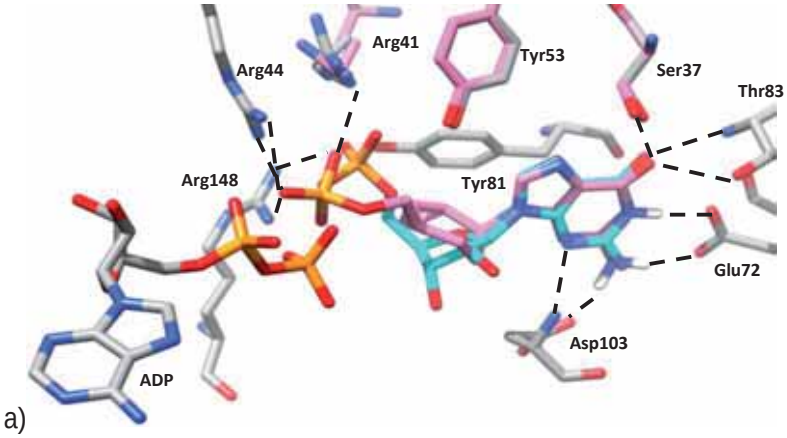


Figure B-11. a) D-**1-GMP** (pink) superimposed to crystallographic GMP (blue) in mGMPK (PDB: 1LVG, X-ray residues shown in grey). b) L-**1-GMP** (pink) superimposed to crystallographic GMP (blue) in mGMPK (PDB: 1LVG, X-ray residues shown in grey). Hydrogen bonds are depicted as dotted lines. For the sake of clarity, crystallographic waters are not shown and hydrogen atoms are only shown when bound to a heteroatom of the ligand.



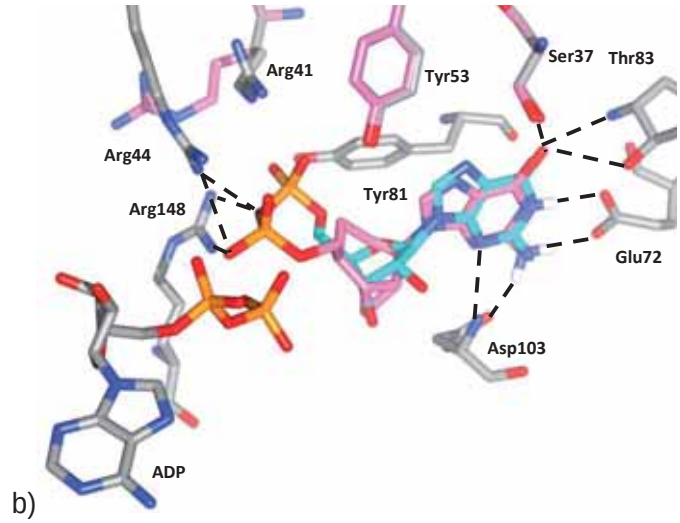


Figure B-12. a) D-**2-GMP** (pink) superimposed to crystallographic GMP (blue) in mGMPK (PDB: 1LVG, X-ray residues shown in grey). b) L-**2-GMP** (pink) superimposed to crystallographic GMP (blue) in mGMPK (PDB: 1LVG, X-ray residues shown in grey). Hydrogen bonds are depicted as dotted lines. For the sake of clarity, crystallographic waters are not shown and hydrogen atoms are only shown when bound to a heteroatom of the ligand.

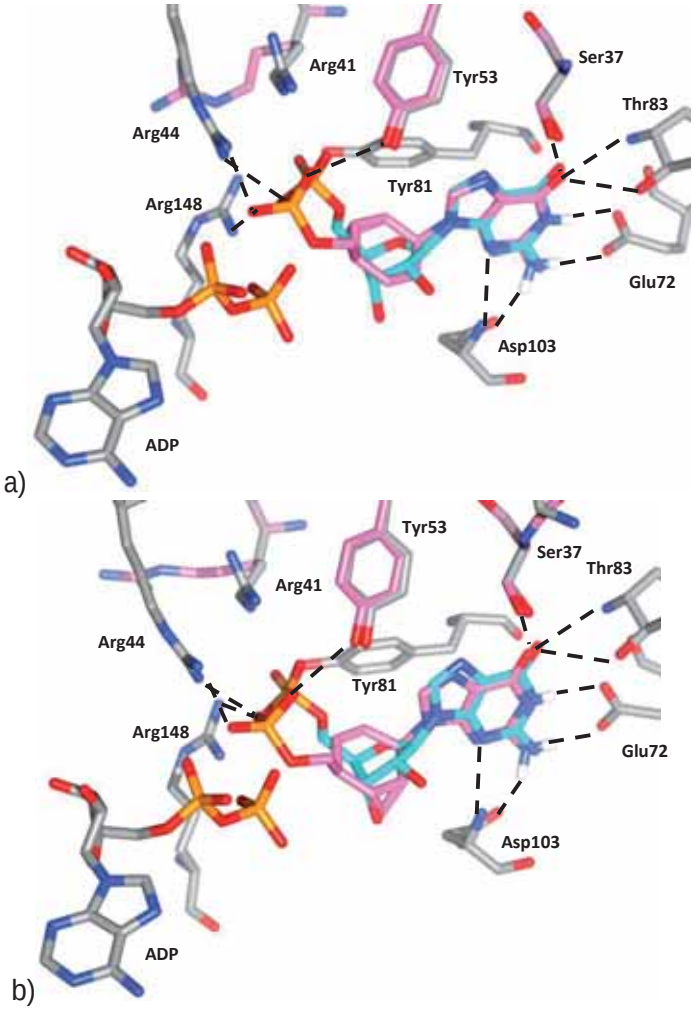


Figure B-13. a) D-**4-GMP** (pink) superimposed to crystallographic GMP (blue) in mGMPK (PDB: 1LVG, X-ray residues shown in grey). b) L-**4-GMP** (pink) superimposed to crystallographic GMP (blue) in mGMPK (PDB: 1LVG, X-ray residues shown in grey). Hydrogen bonds are depicted as dotted lines. For the sake of clarity, crystallographic waters are not shown and hydrogen atoms are only shown when bound to a heteroatom of the ligand.

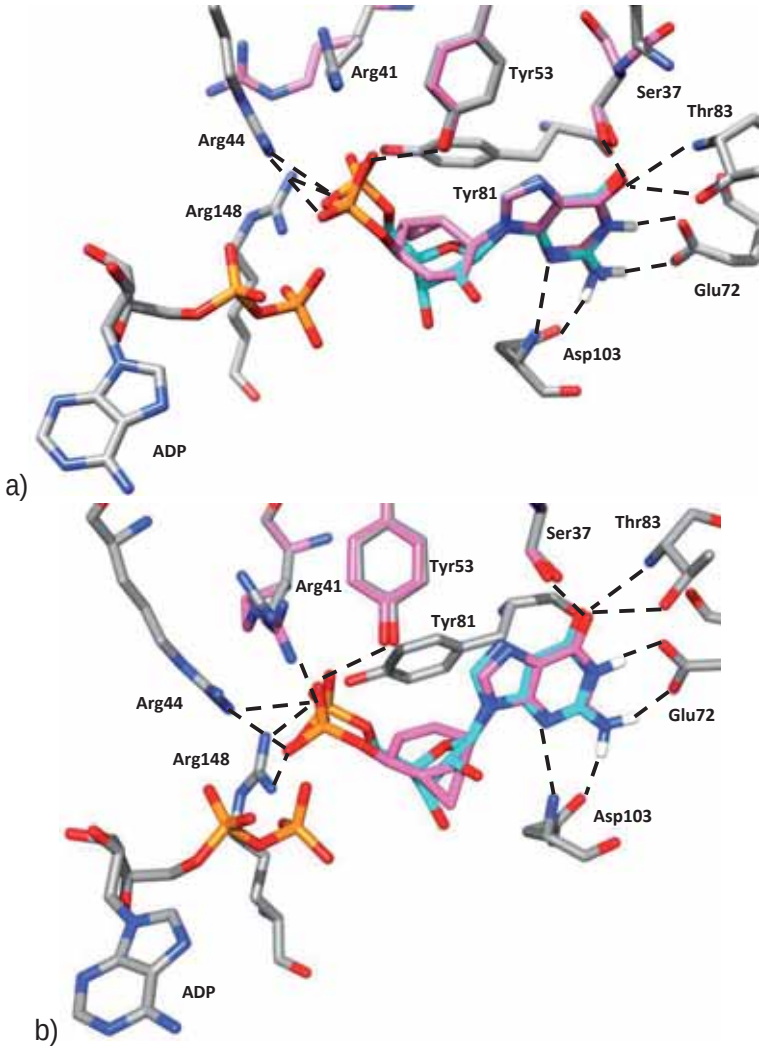


Figure B-14. a) D-**5-GMP** (pink) superimposed to crystallographic GMP (blue) in mGMPK (PDB: 1LVG, X-ray residues shown in grey). b) L-**5-GMP** (pink) superimposed to crystallographic GMP (blue) in mGMPK (PDB: 1LVG, X-ray residues shown in grey). Hydrogen bonds are depicted as dotted lines. For the sake of clarity, crystallographic waters are not shown and hydrogen atoms are only shown when bound to a heteroatom of the ligand.

1.3. 3rd phosphorylation step

1.3.1. Docking results

- **Pyrimidine nucleoside analogues**

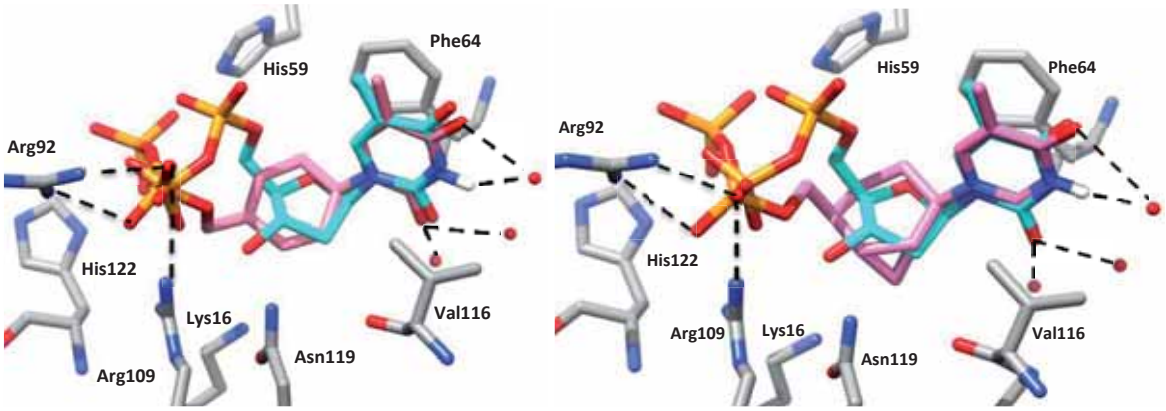


Figure B-15. L-**1-TDP** (left) and L-**2-TDP** (right) in pink superimposed to crystallographic dTDP (blue) in NDPK (PDB: 1NDC, X-ray residues shown in grey). Hydrogen bonds are depicted as dotted lines. For the sake of clarity, crystallographic waters are not shown and hydrogen atoms are only shown when bound to a heteroatom of the ligand.

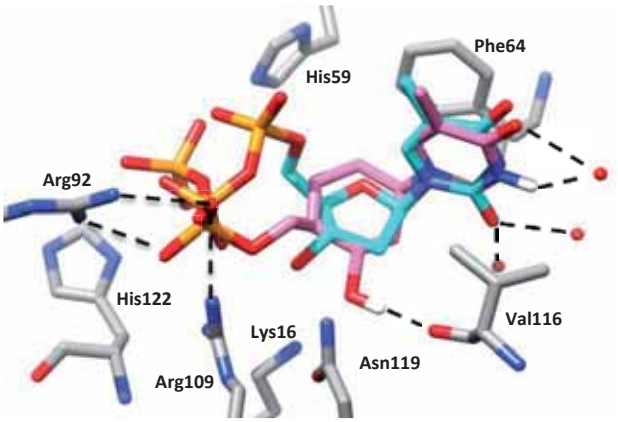


Figure B-16. D-**3-TDP** (pink) superimposed to crystallographic dTDP (blue) in NDPK (PDB: 1NDC, X-ray residues shown in grey). Hydrogen bonds are depicted as dotted lines. For the sake of clarity, crystallographic waters are not shown and hydrogen atoms are only shown when bound to a heteroatom of the ligand.

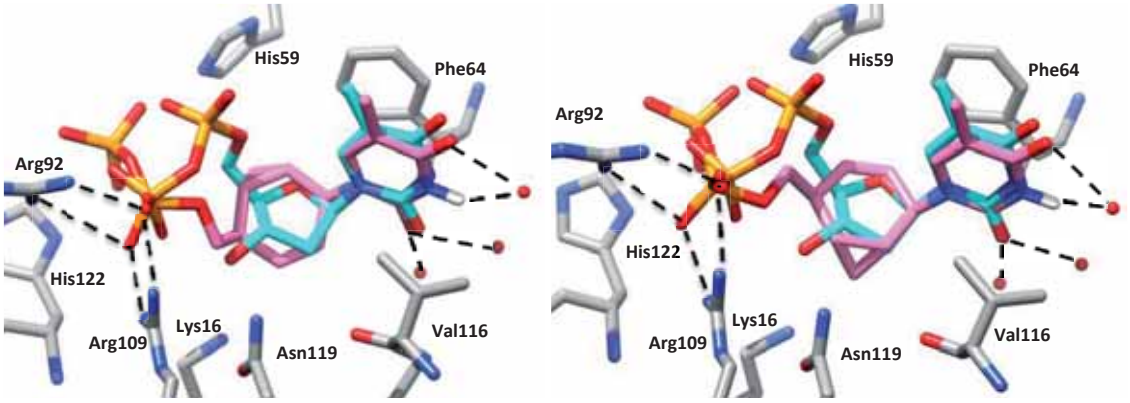


Figure B-17. D-**4-TDP** (left) and L-**4-TDP** (right) in pink superimposed to crystallographic dTDP (blue) in NDPK (PDB: 1NDC, X-ray residues shown in grey). Hydrogen bonds are depicted as dotted lines. For the sake of clarity, crystallographic waters are not shown and hydrogen atoms are only shown when bound to a heteroatom of the ligand.

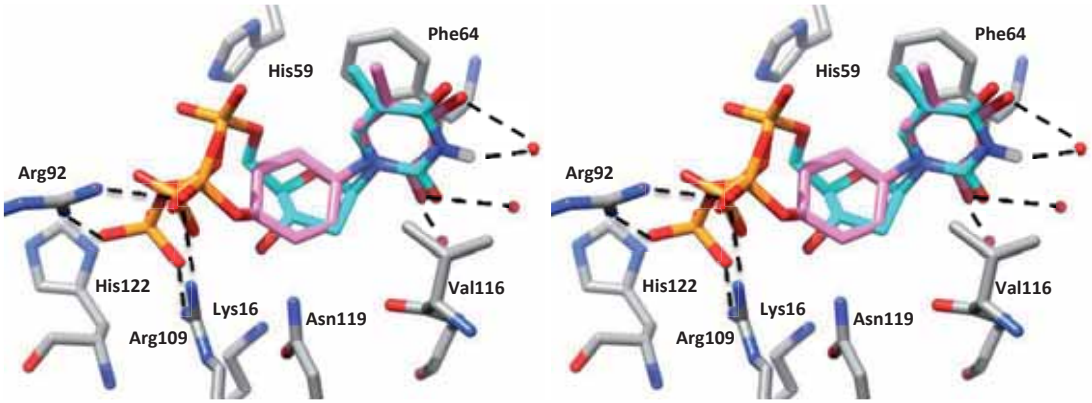


Figure B-18. D-**5-TDP** (left) and L-**5-TDP** (right) in pink superimposed to crystallographic dTDP (blue) in NDPK (PDB: 1NDC, X-ray residues shown in grey). Hydrogen bonds are depicted as dotted lines. For the sake of clarity, crystallographic waters are not shown and hydrogen atoms are only shown when bound to a heteroatom of the ligand.

- **Purine nucleoside analogues**

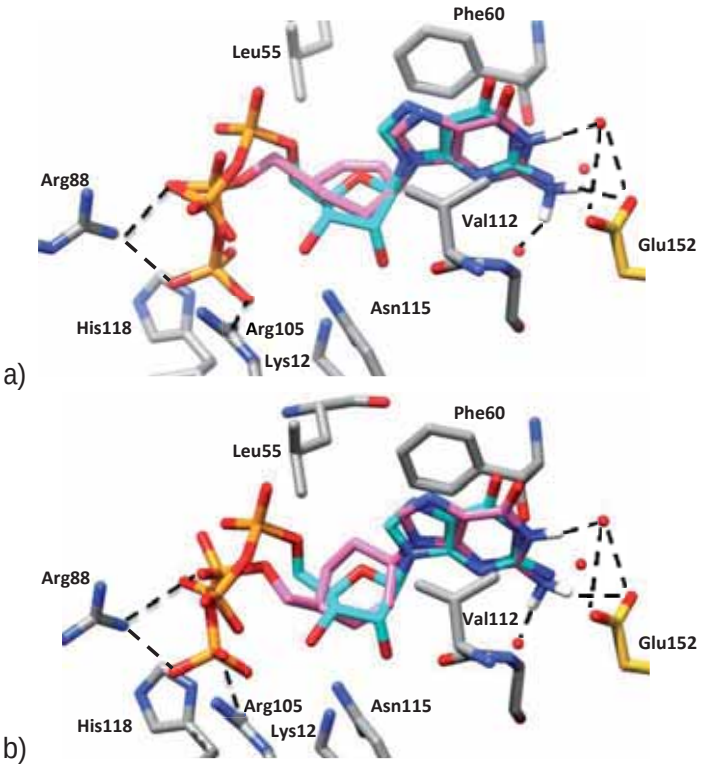


Figure B-19. D-**1-GDP** (left) and L-**1-GDP** (right) in pink superimposed to crystallographic GDP (blue) in NDPK (PDB: 1NUE, X-ray residues shown in grey). Hydrogen bonds are depicted as dotted lines. For the sake of clarity, crystallographic waters are only shown when interacted with the ligand and hydrogen atoms are only shown when bound to a heteroatom of the ligand.

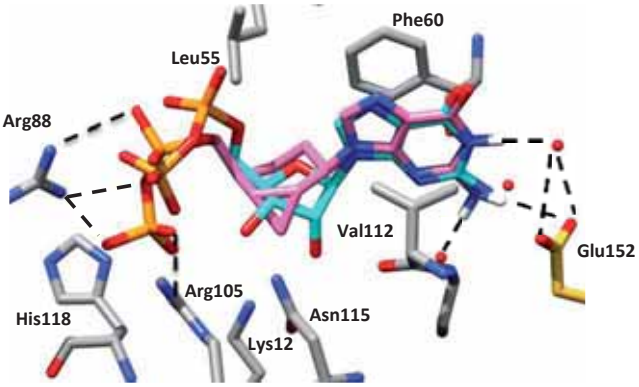


Figure B-1. L-**2-GDP** (pink) superimposed to crystallographic GDP (blue) in NDPK (PDB: 1NUE, X-ray residues shown in grey). Hydrogen bonds are depicted as dotted lines. For the sake of clarity, crystallographic waters are only shown when interacted with the ligand and hydrogen atoms are only shown when bound to a heteroatom of the ligand.

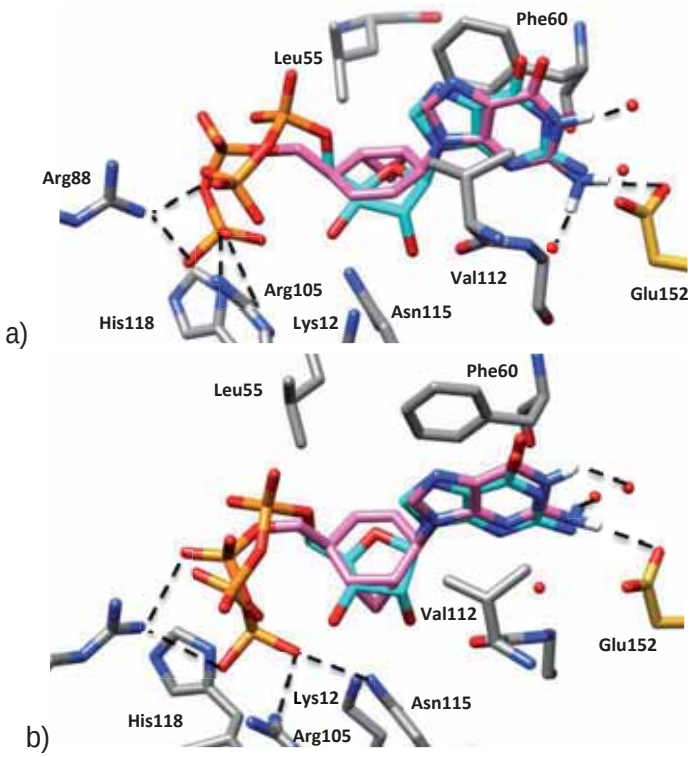


Figure B-21. D-**4-GDP** (left) and L-**4-GDP** (right) in pink superimposed to crystallographic GDP (blue) in NDPK (PDB: 1NUE, X-ray residues shown in grey). Hydrogen bonds are depicted as dotted lines. For the sake of clarity, crystallographic waters are only shown when interacted with the ligand and hydrogen atoms are only shown when bound to a heteroatom of the ligand.

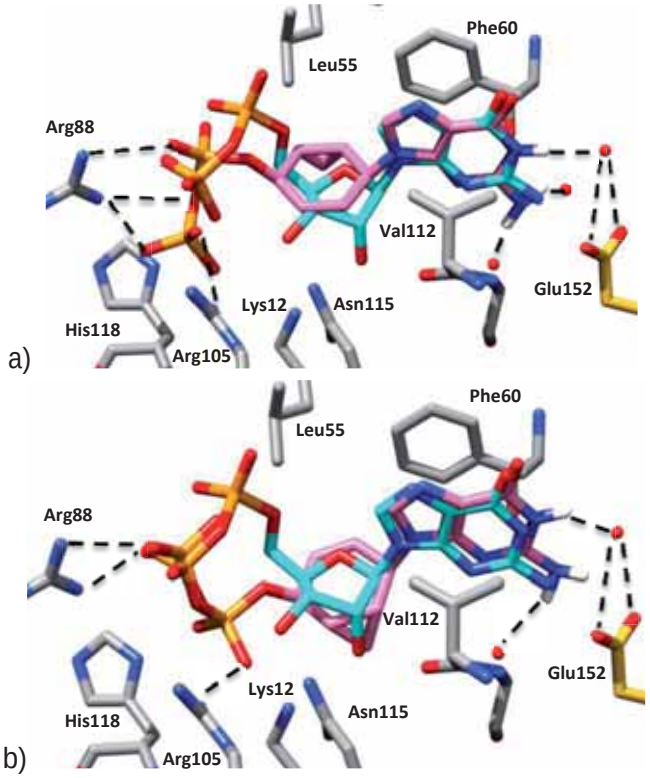


Figure B-22. D-**5-GDP** (left) and L-**5-GDP** (right) in pink superimposed to crystallographic GDP (blue) in NDPK (PDB: 1NUE, X-ray residues shown in grey). Hydrogen bonds are depicted as dotted lines. For the sake of clarity, crystallographic waters are only shown when interacted with the ligand and hydrogen atoms are only shown when bound to a heteroatom of the ligand.