

SUPPLEMENTARY INFORMATION

Quinoline and Coumarin Isoxazole Derivatives: Synthesis, Antitumor Evaluation and Molecular Docking Studies with Bcl-2

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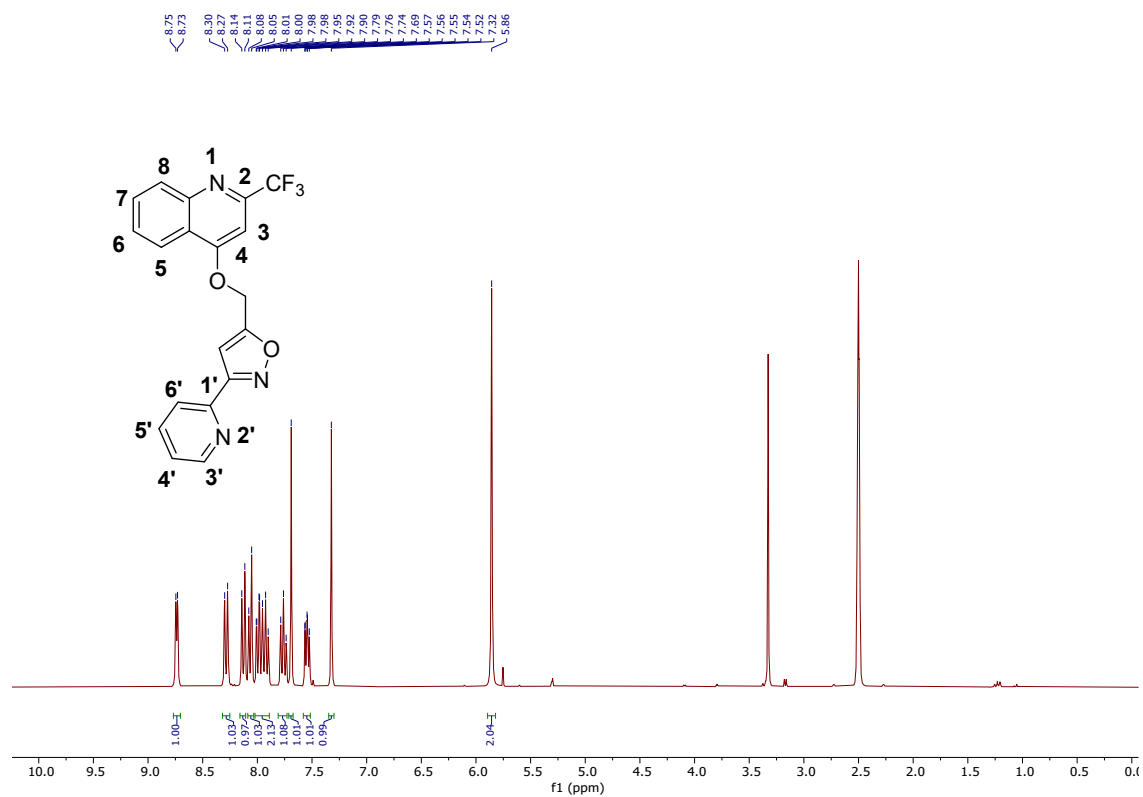
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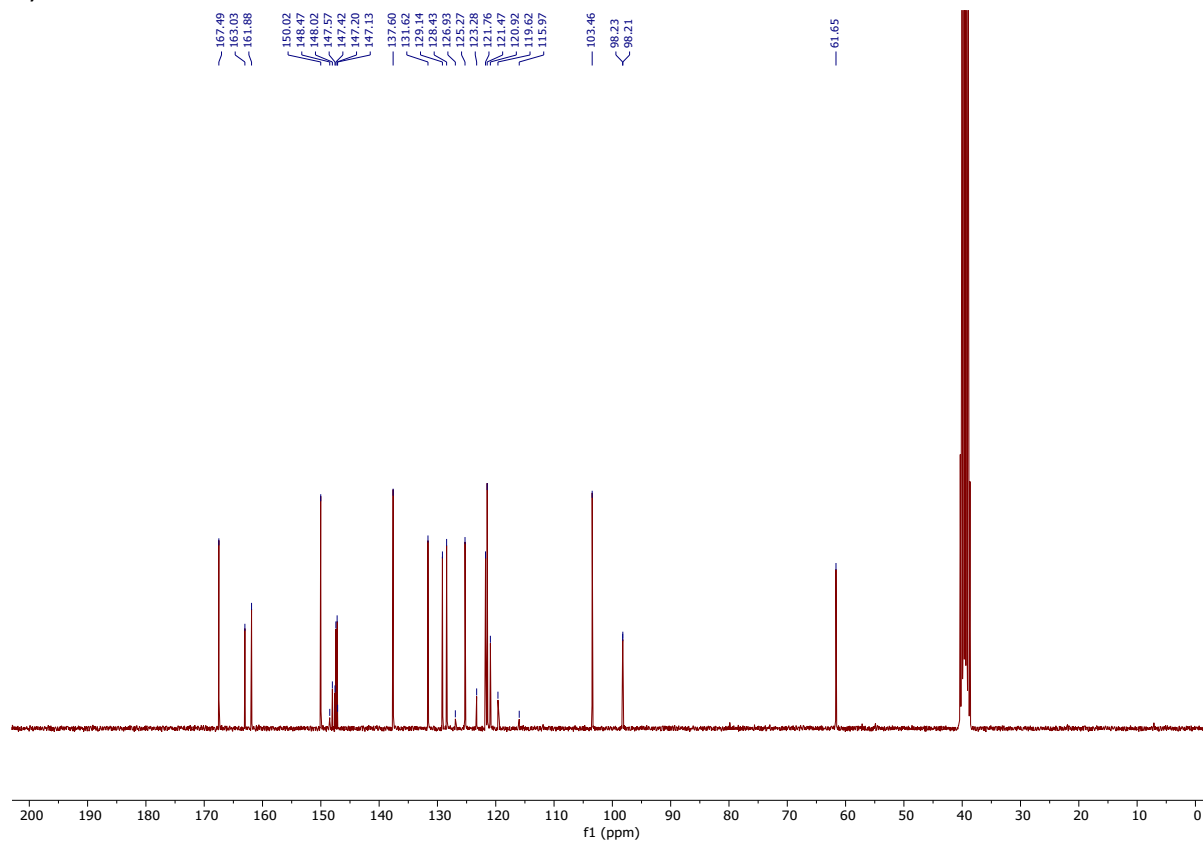
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Figure S2: a) ^1H NMR and b) ^{13}C NMR c) COSY of compd. **7b** in $\text{DMSO}-d_6$.

a)



b)



c)

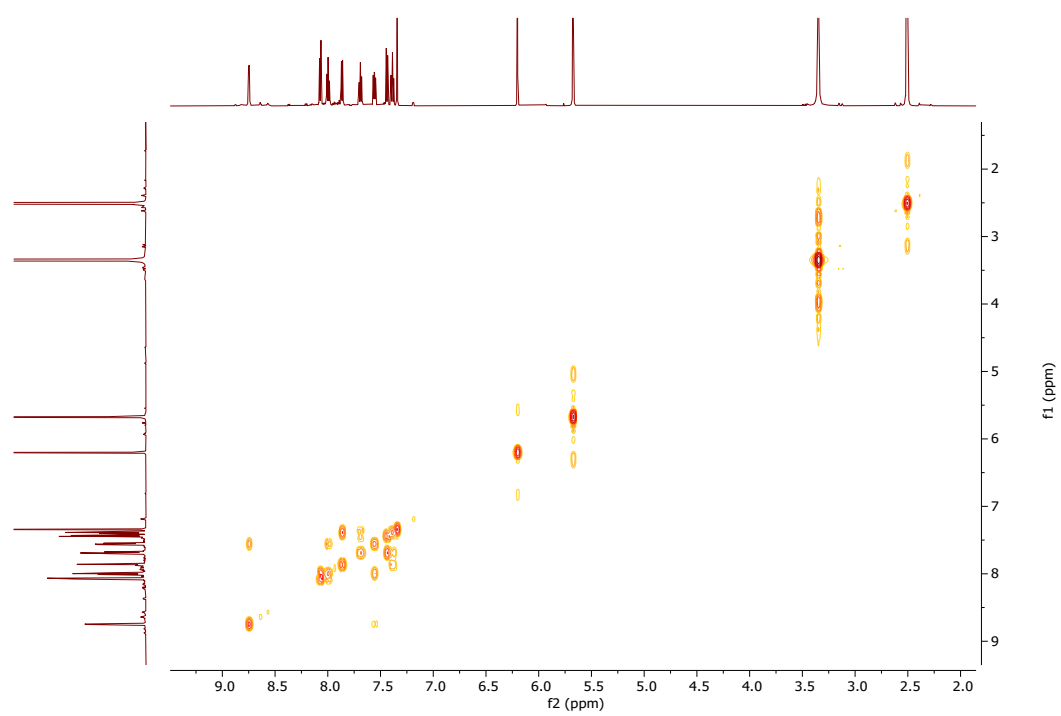
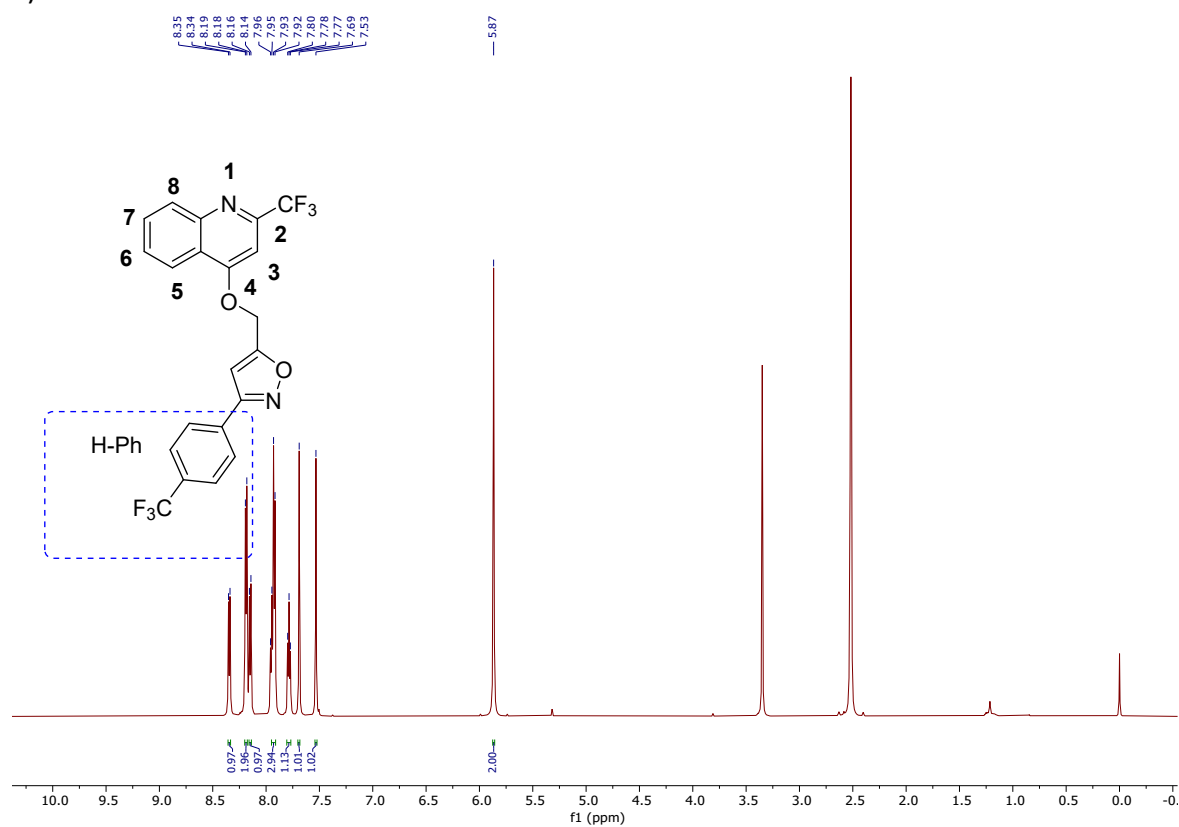


Figure S3: a) ^1H NMR and b) ^{13}C NMR of compd. **7c** in $\text{DMSO}-d_6$.

a)



b)

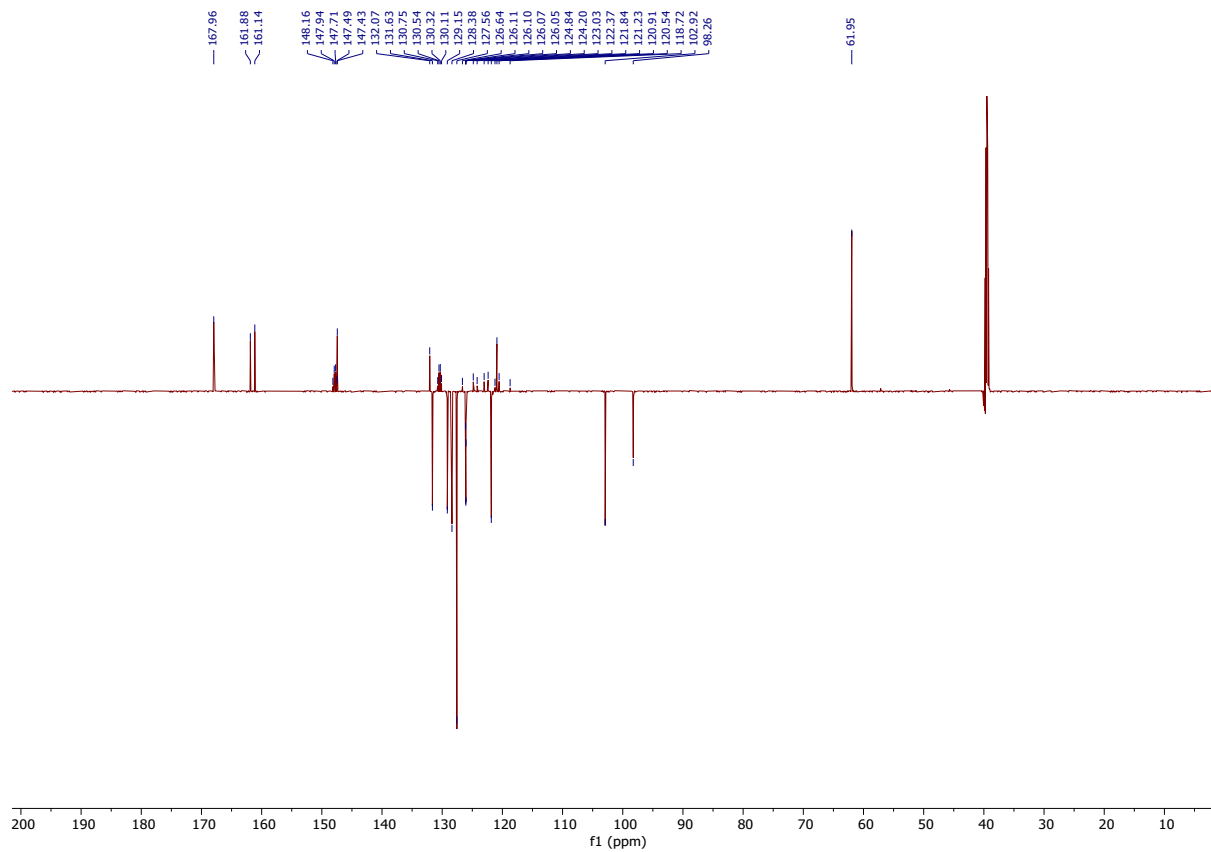
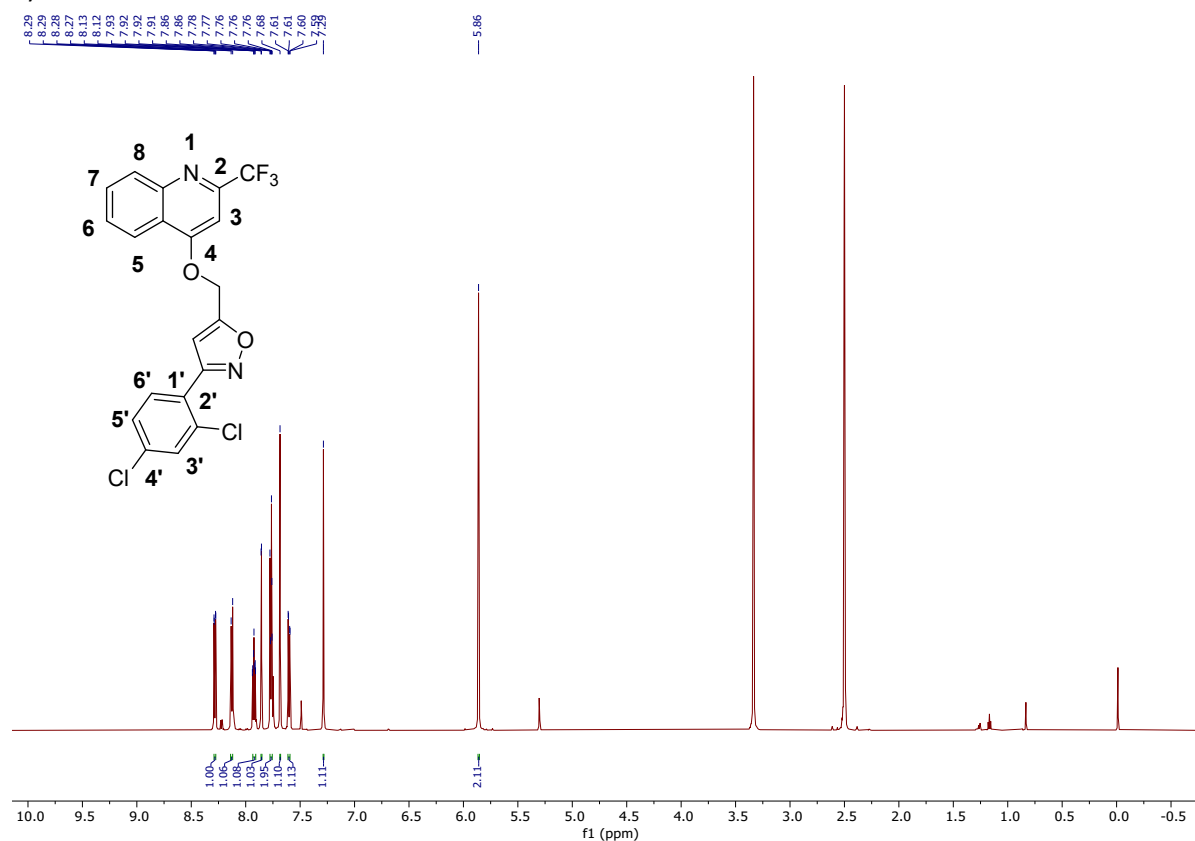
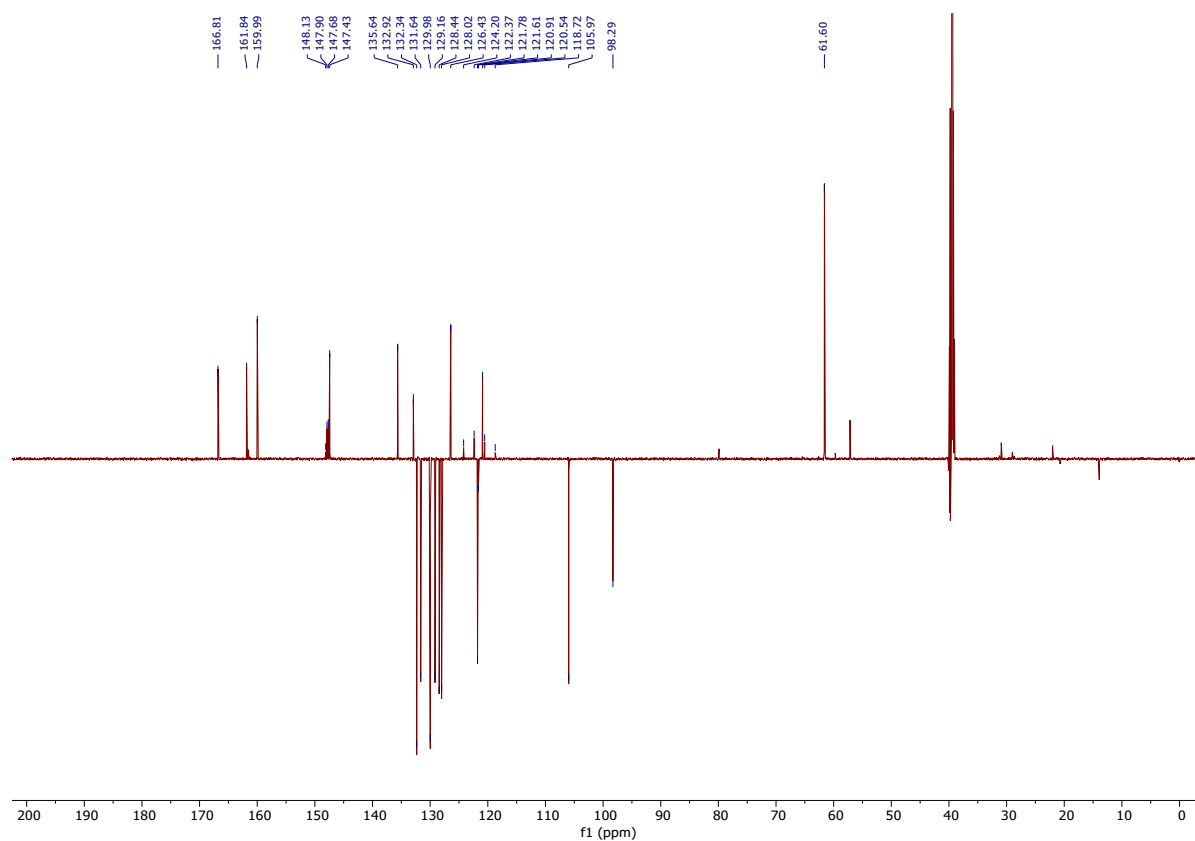


Figure S4: a) ^1H NMR and b) ^{13}C NMR of compd. **7d** in $\text{DMSO}-d_6$.

a)



b)



The figure displays the chemical structure of compound 10 and its corresponding ¹H and ¹³C NMR spectra.

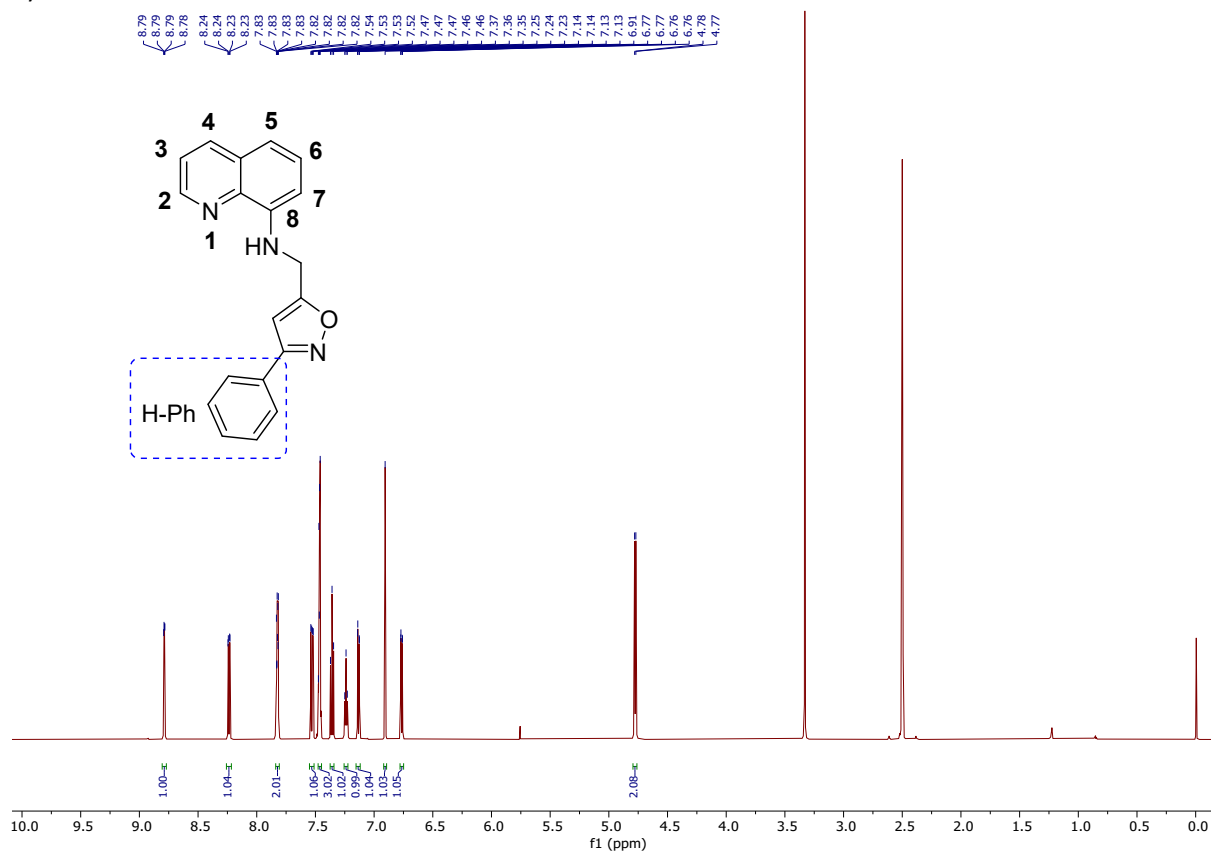
Chemical Structure: The structure shows a quinoline ring system. The nitrogen atom is substituted with a trifluoromethyl group (CF₃). The quinoline ring is numbered 1 through 8. A methylene group (CH₂) is attached to the quinoline ring at position 4, which is further connected to an isoxazole ring. The isoxazole ring is numbered 1' and 2'. The isoxazole ring is also connected to a phenyl ring, which is numbered 1' through 4'. The phenyl ring has a cyano group (NC) attached at position 4'.

¹H NMR Spectrum: The spectrum shows peaks in the aromatic region (7.5-8.3 ppm) and a peak in the aliphatic region (2.5 ppm). The x-axis is labeled f1 (ppm) and ranges from 10.0 to -0.5. Integration values are provided for several peaks: 1.00, 2.85, 1.95, 0.97, 1.01, 0.97, and 2.02.

¹³C NMR Spectrum: The spectrum shows peaks in the aromatic region (118-168 ppm) and a peak in the aliphatic region (61.99 ppm). The x-axis is labeled f1 (ppm) and ranges from 200 to 0. The peak at 61.99 ppm corresponds to the methylene group (CH₂) attached to the quinoline ring.

Figure S6: a) ^1H NMR and b) ^{13}C NMR of compd. **8a**.

a)



b)

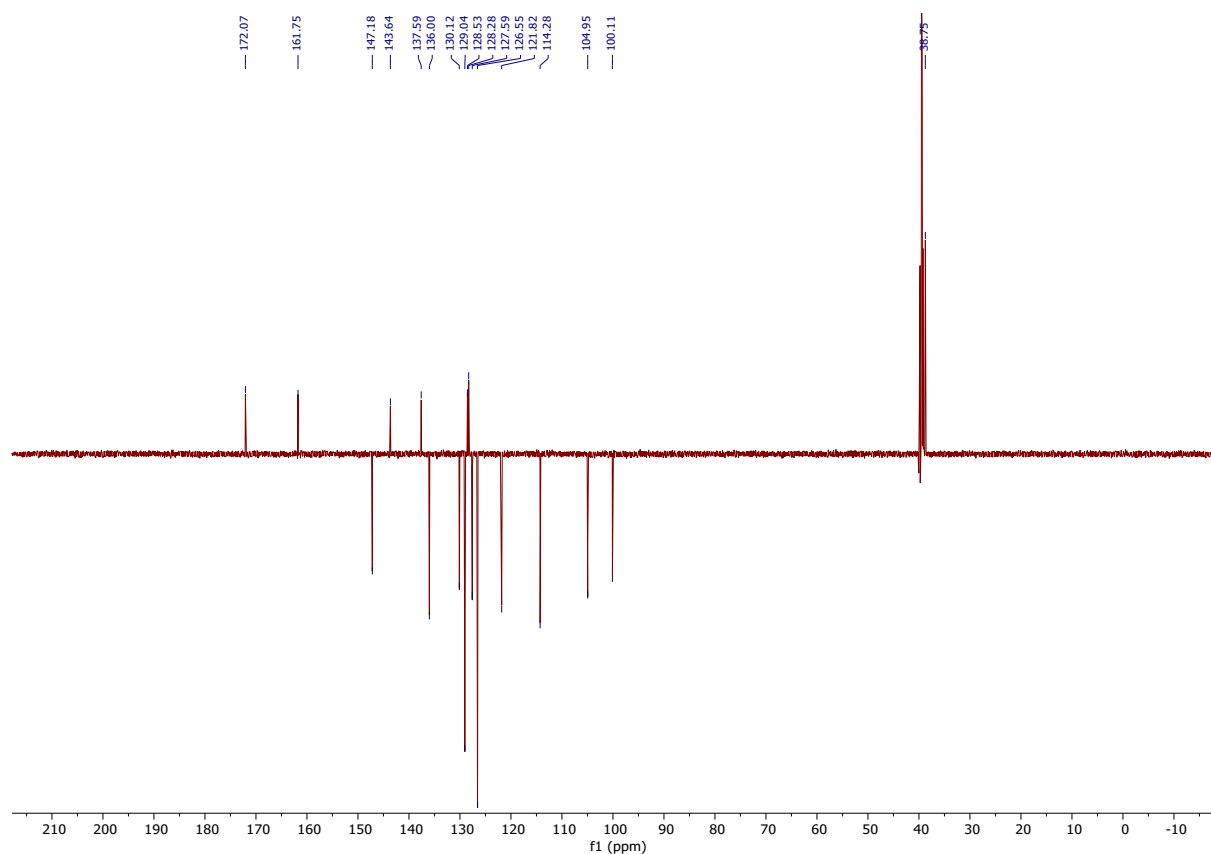
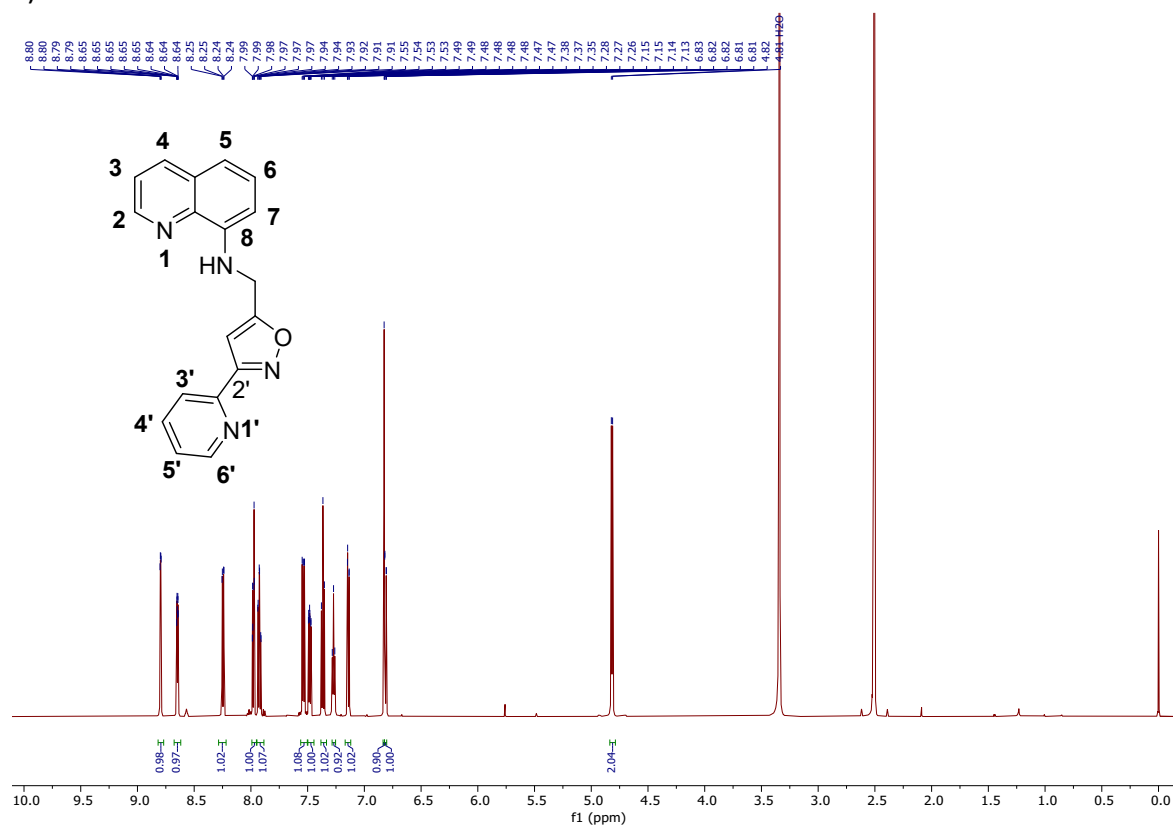


Figure S7: a) ^1H NMR and b) ^{13}C NMR of compd. **8b**.

a)



b)

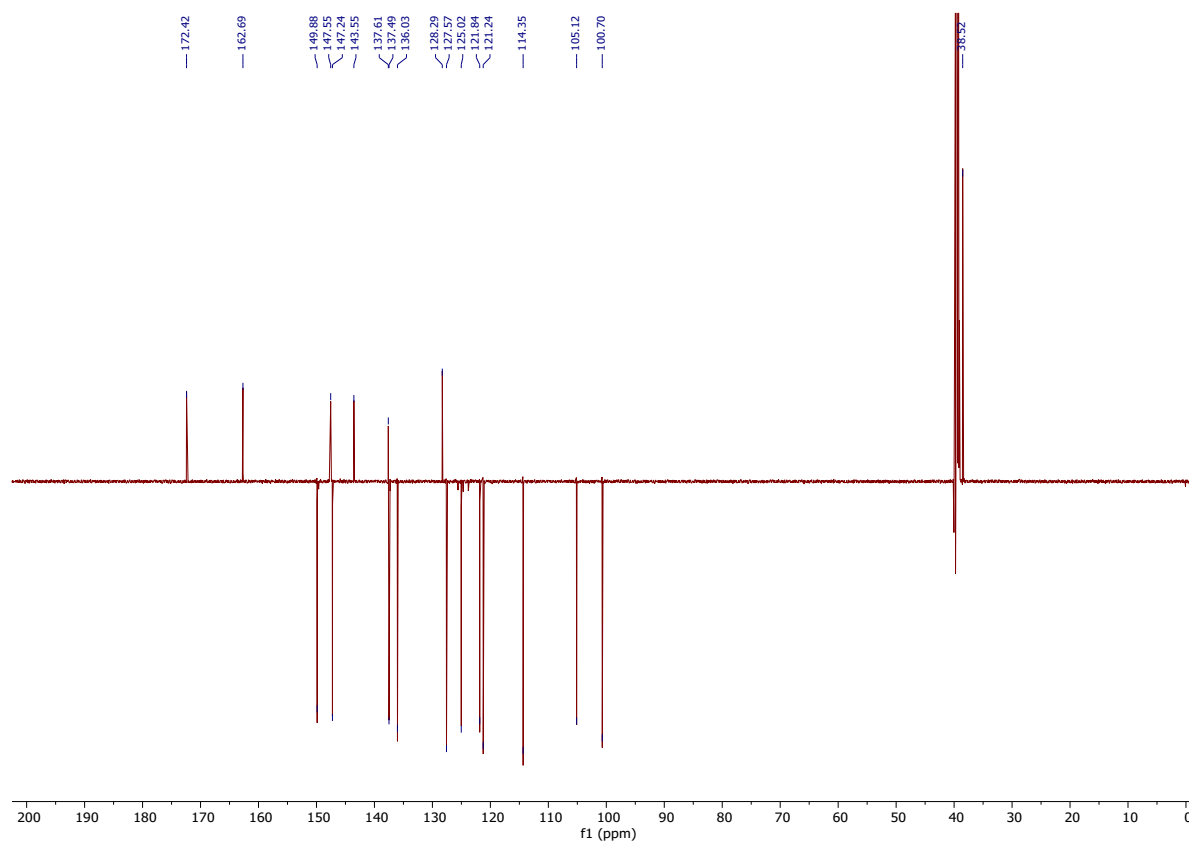
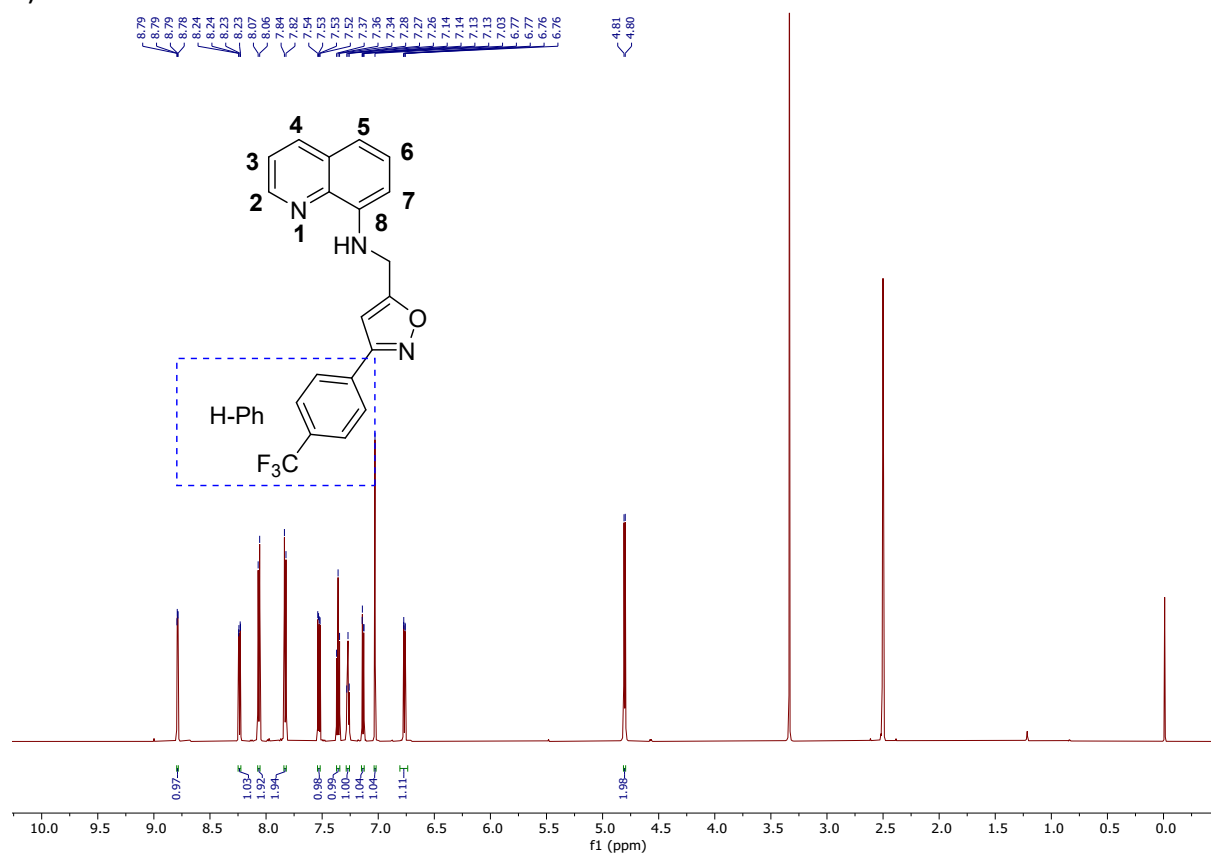


Figure S8: a) ^1H NMR and b) ^{13}C NMR of compd. **8c**.

a)



b)

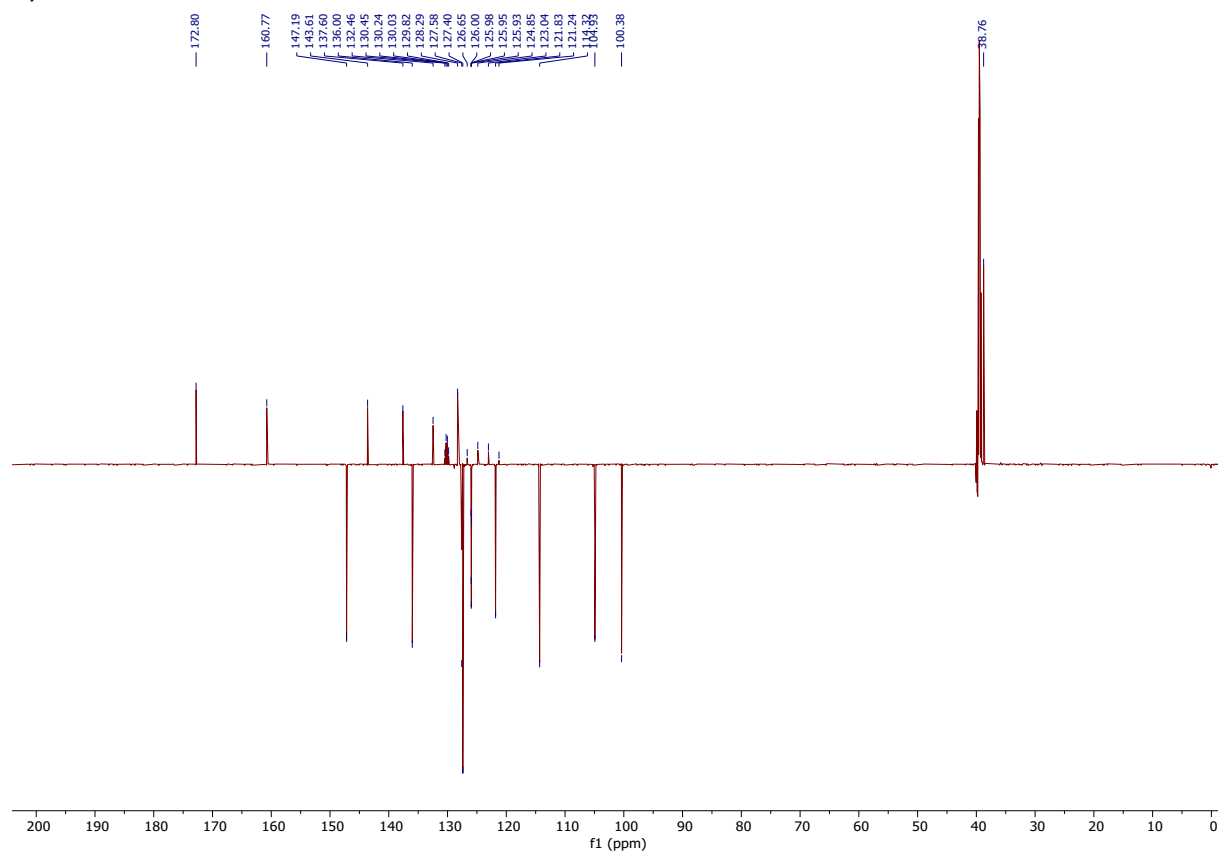
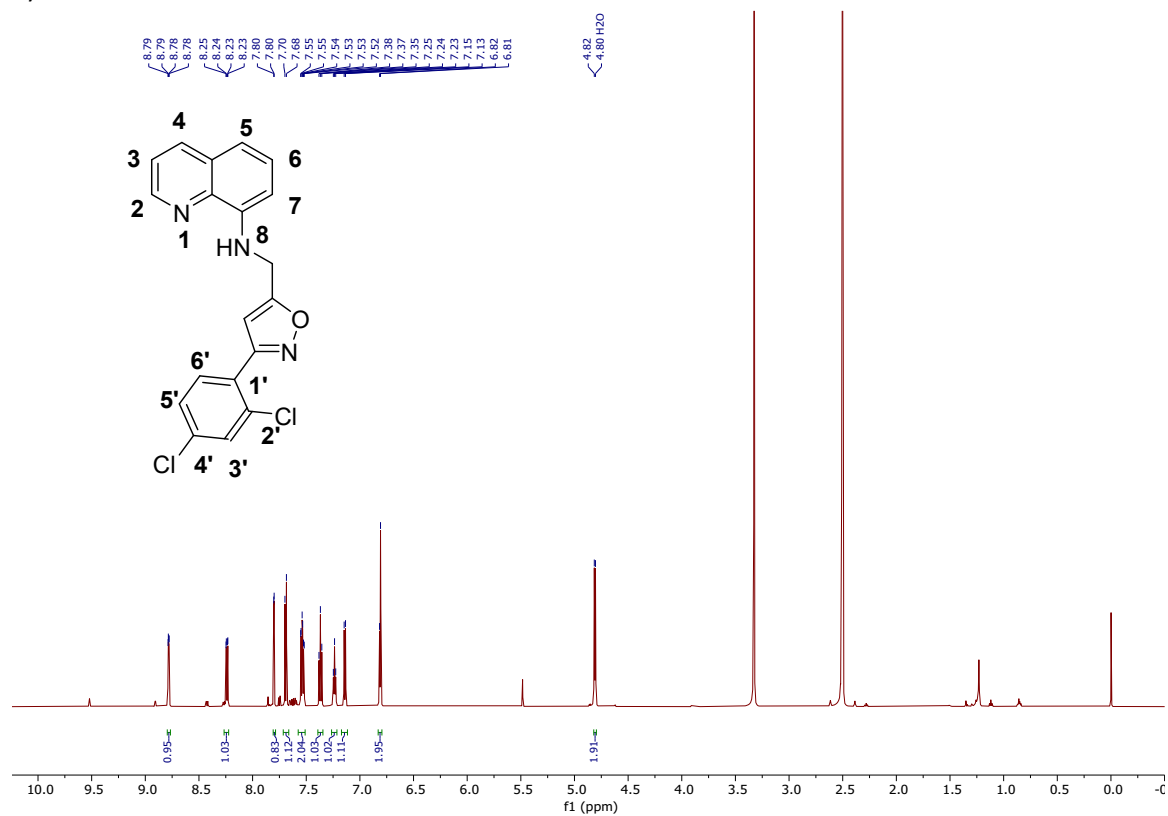


Figure S9: a) ^1H NMR and b) ^{13}C NMR of compd. **8d**.

a)



b)

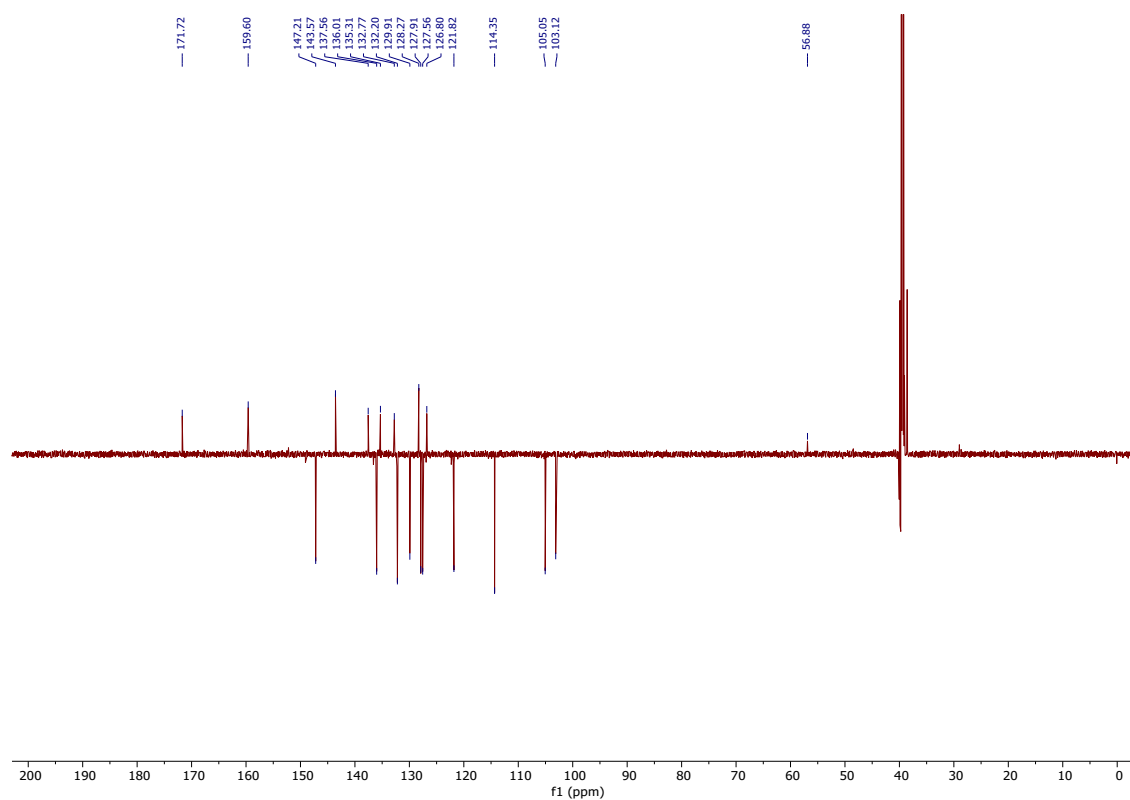
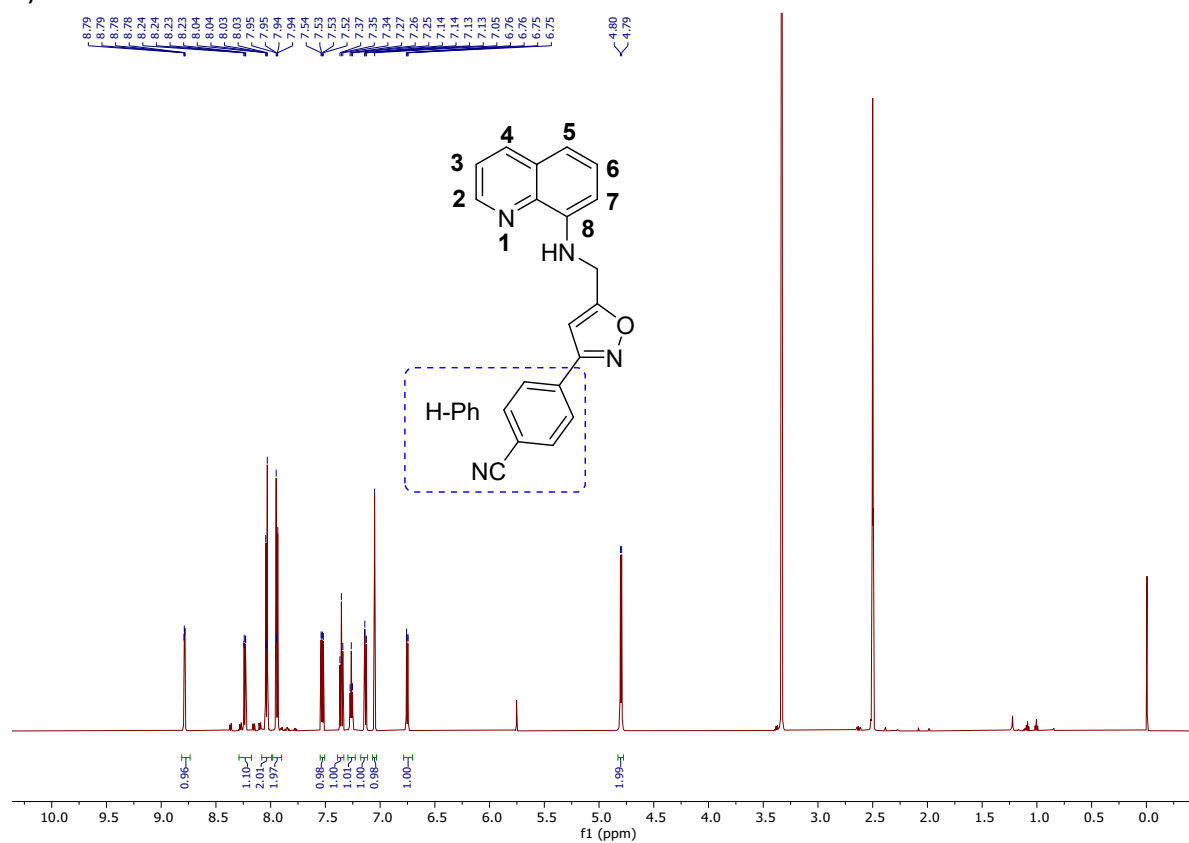


Figure S10: a) ^1H NMR and b) ^{13}C NMR of compd. **8e**.

a)



b)

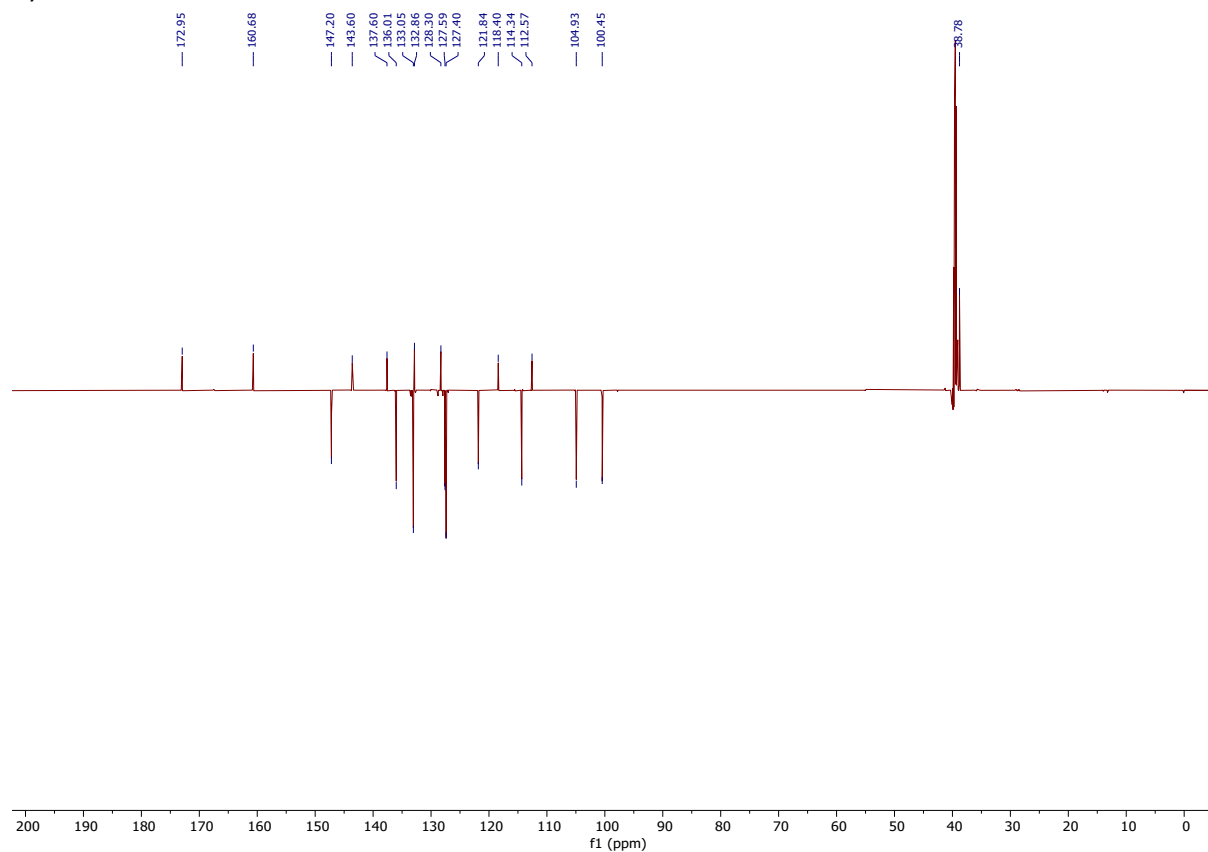
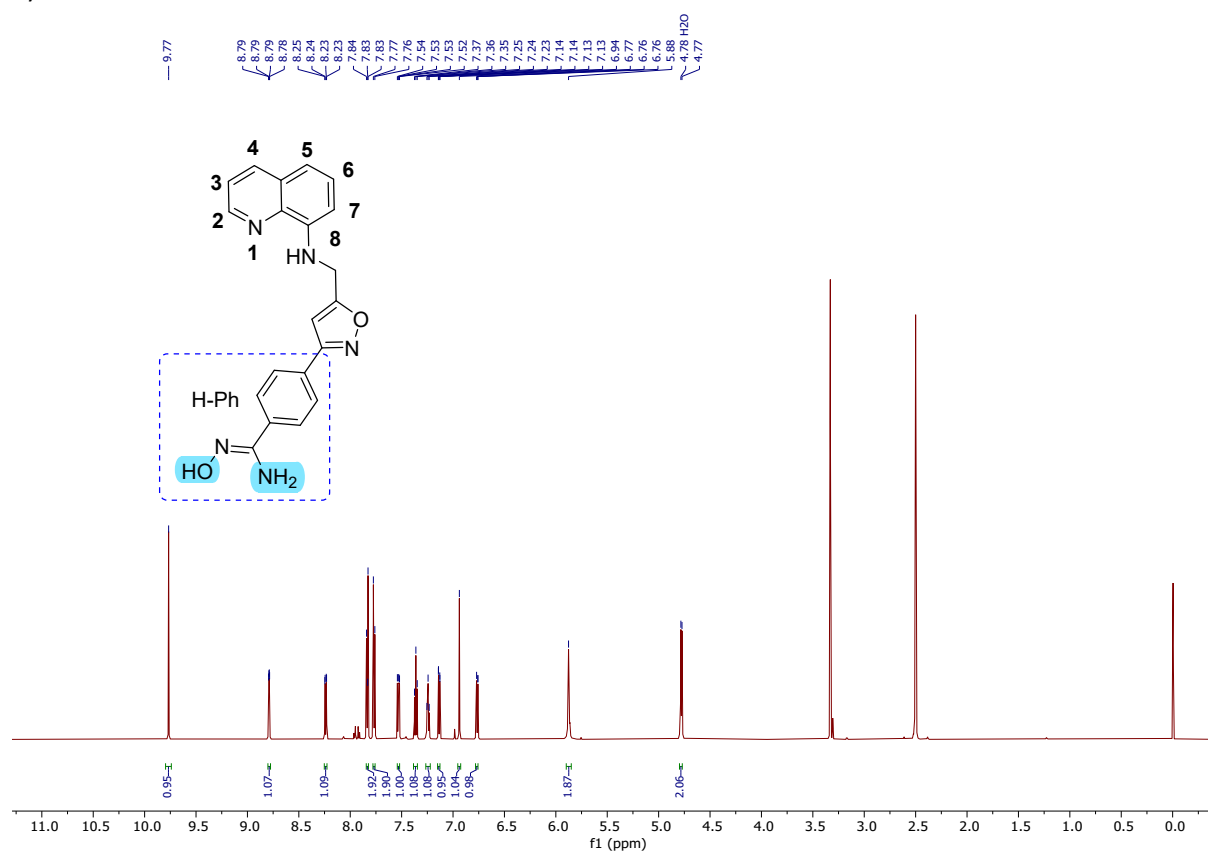


Figure S11: a) ^1H NMR and b) ^{13}C NMR of compd. **8f**.

a)



b)

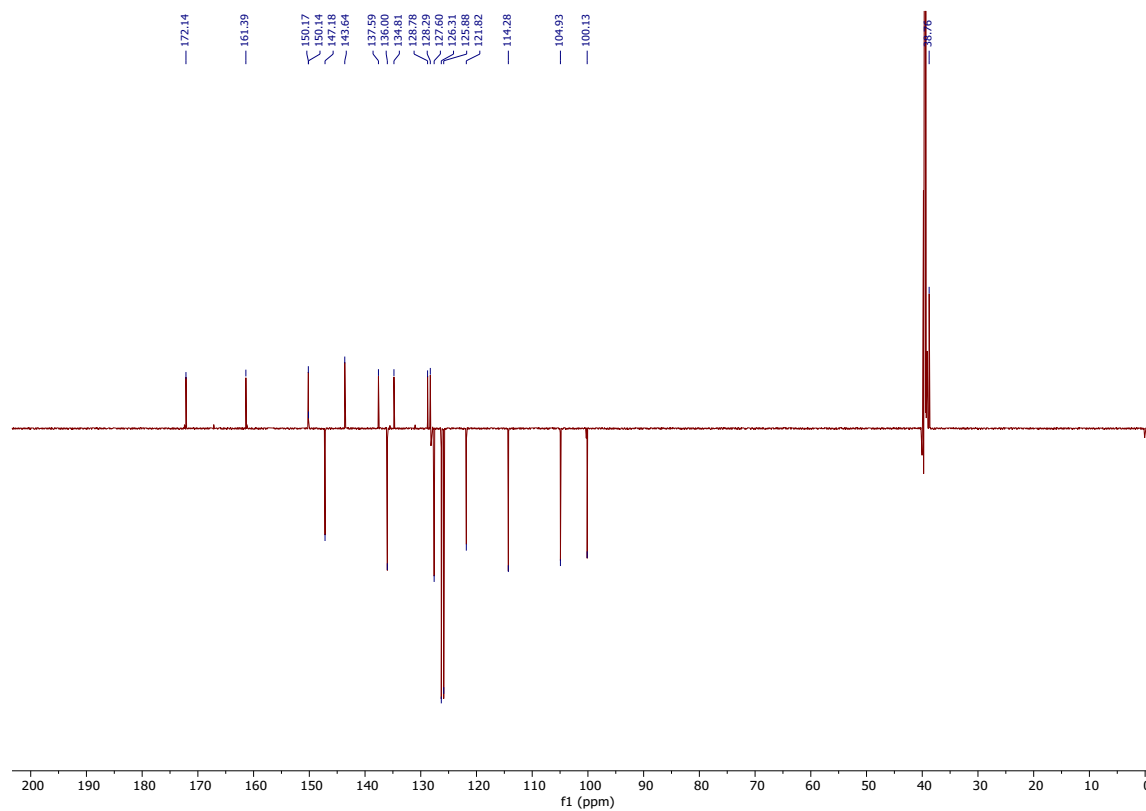
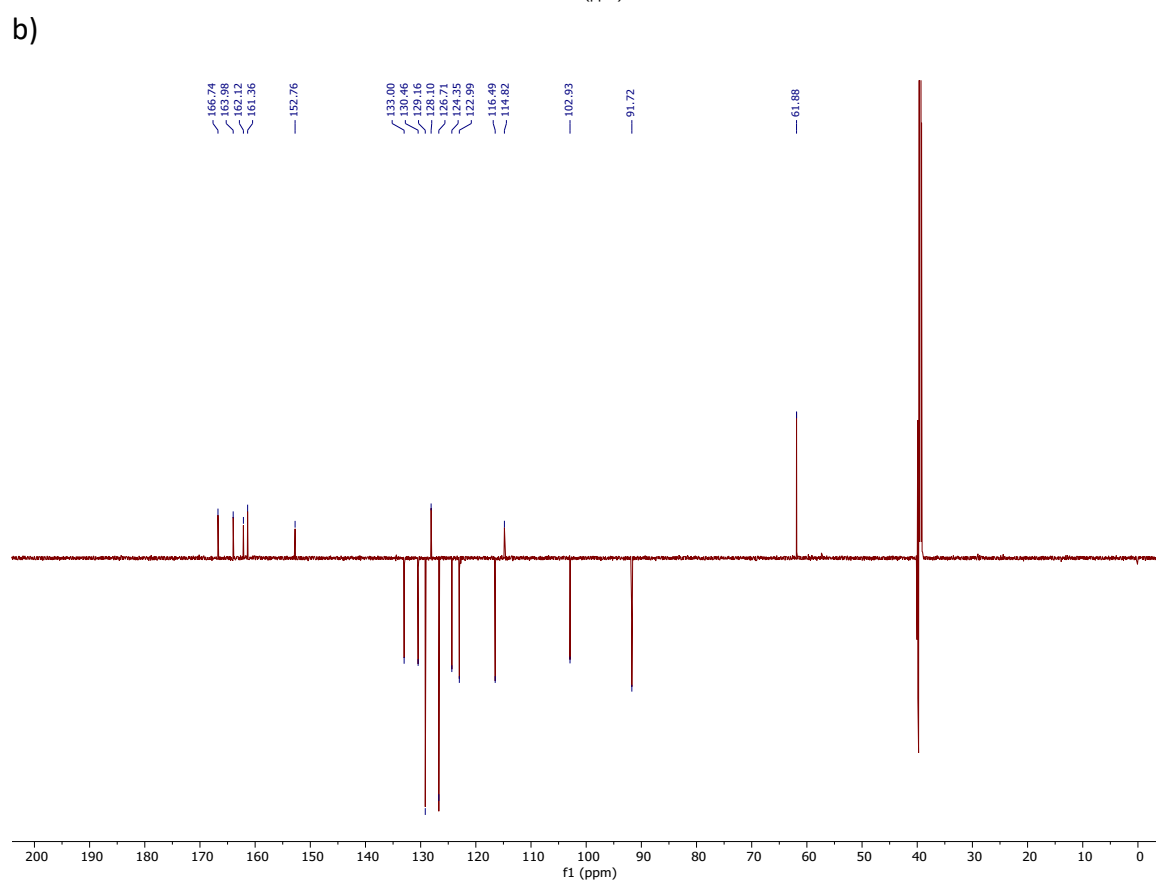
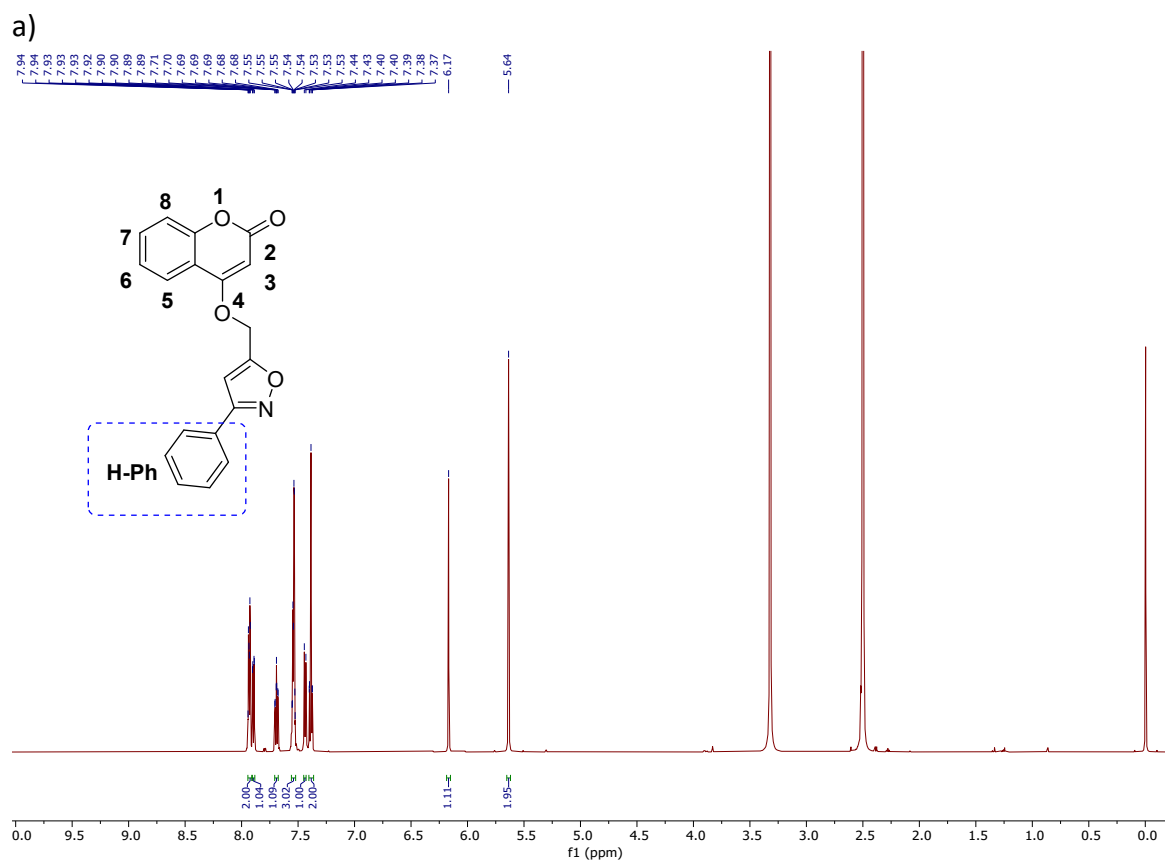


Figure S12: a) ^1H NMR and b) ^{13}C NMR of compd. **9a**.



a)

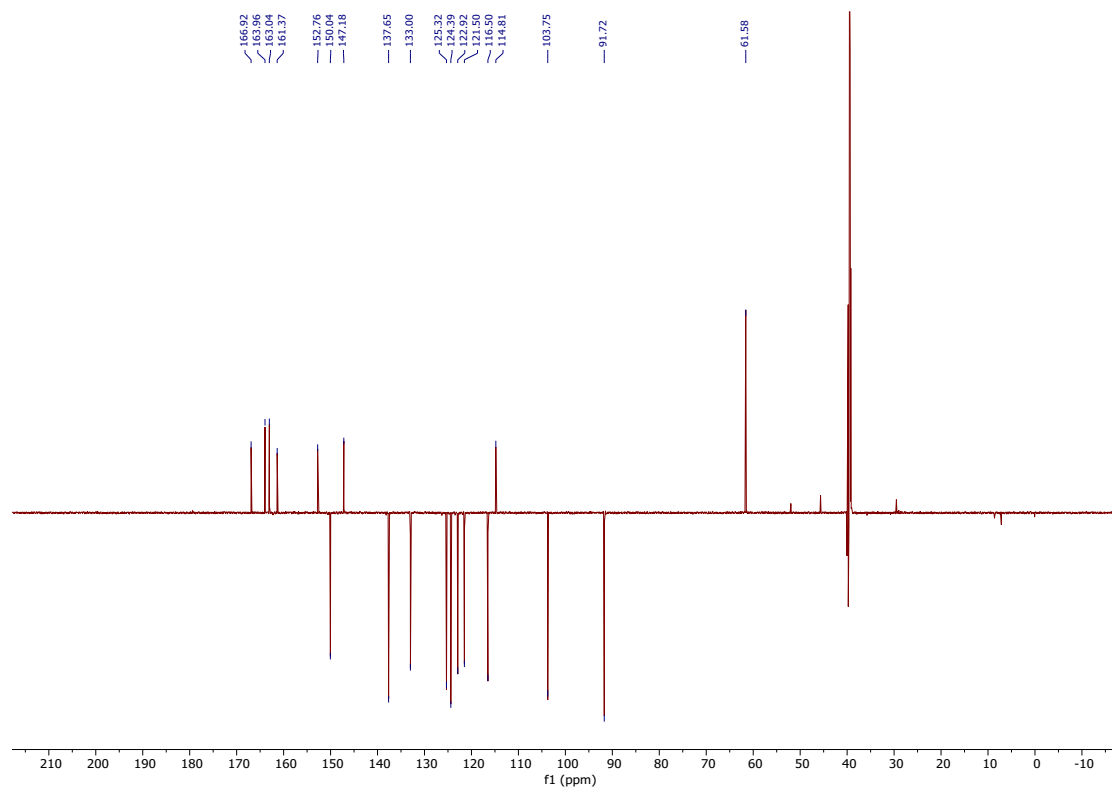
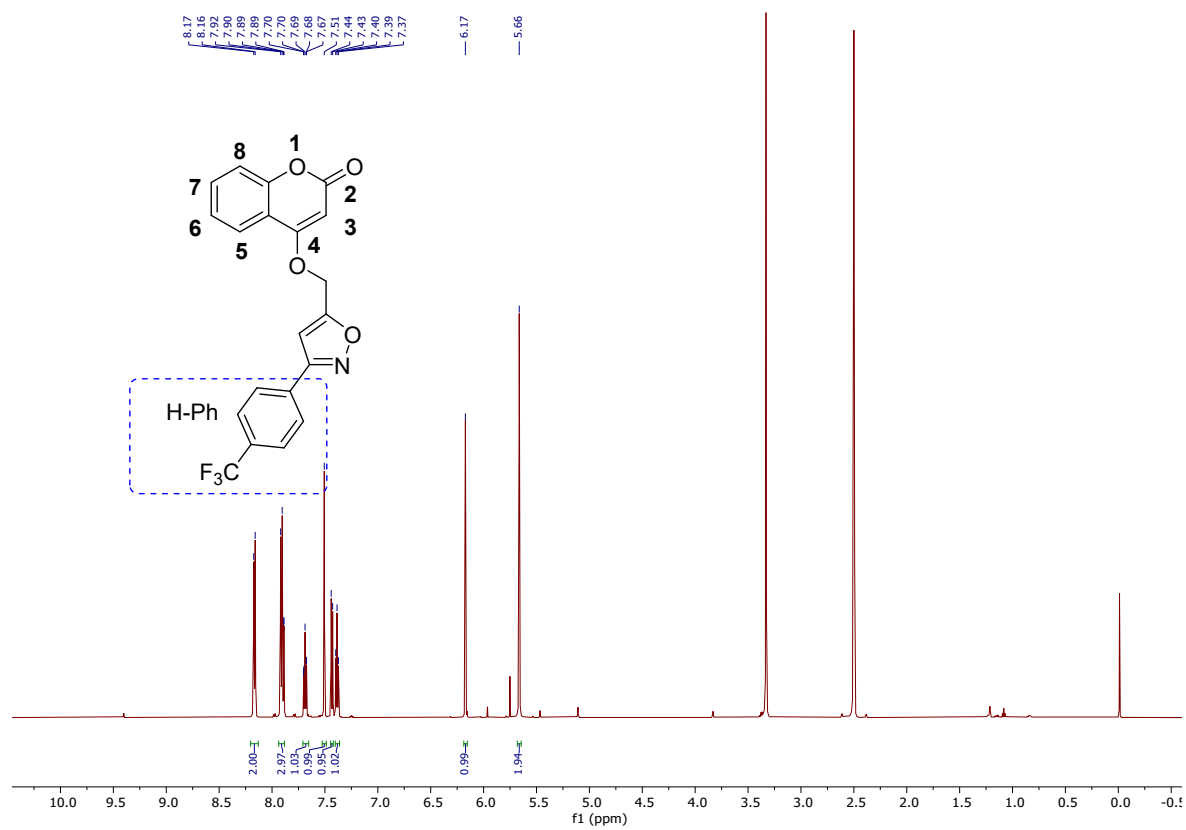


Figure S14: a) ^1H NMR and b) ^{13}C NMR of compd. **9c**.

a)



b)

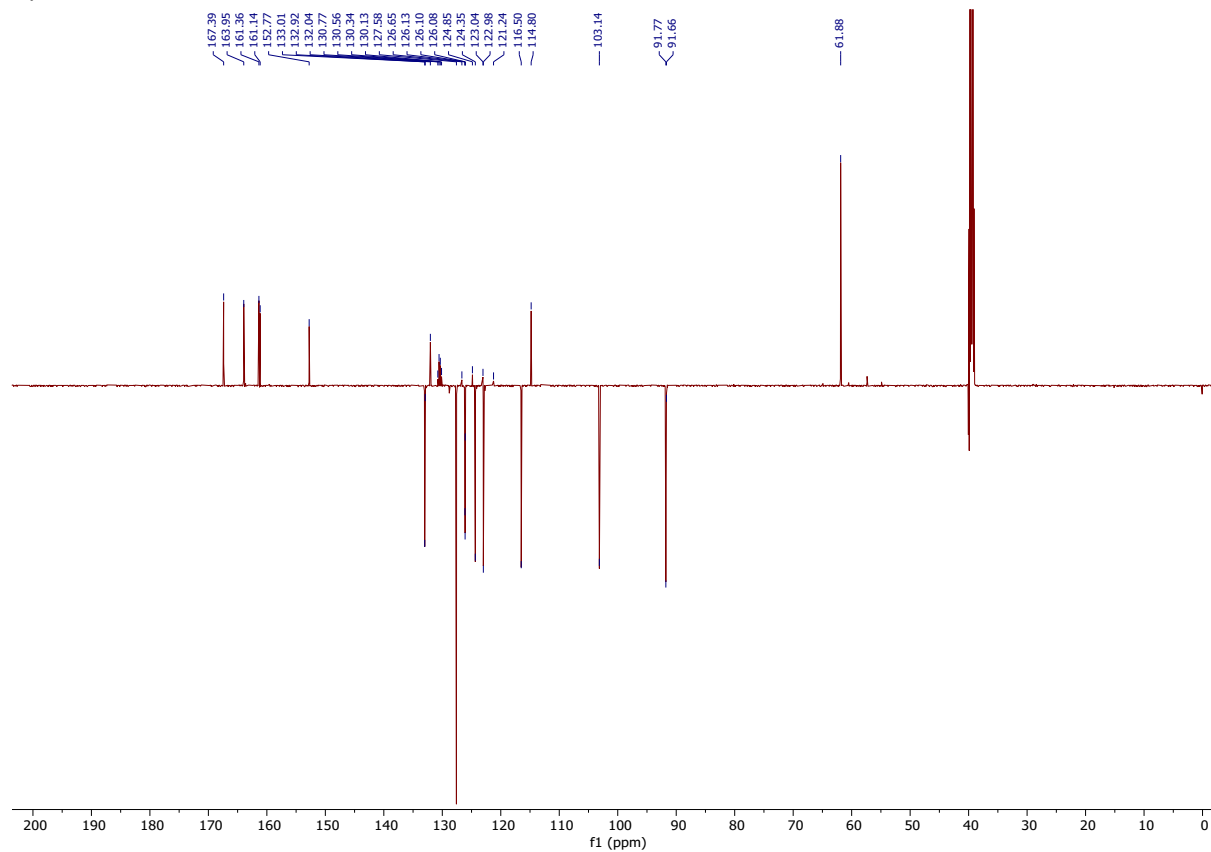


Figure S15: a) ^1H NMR and b) ^{13}C NMR of compd. **9d**.

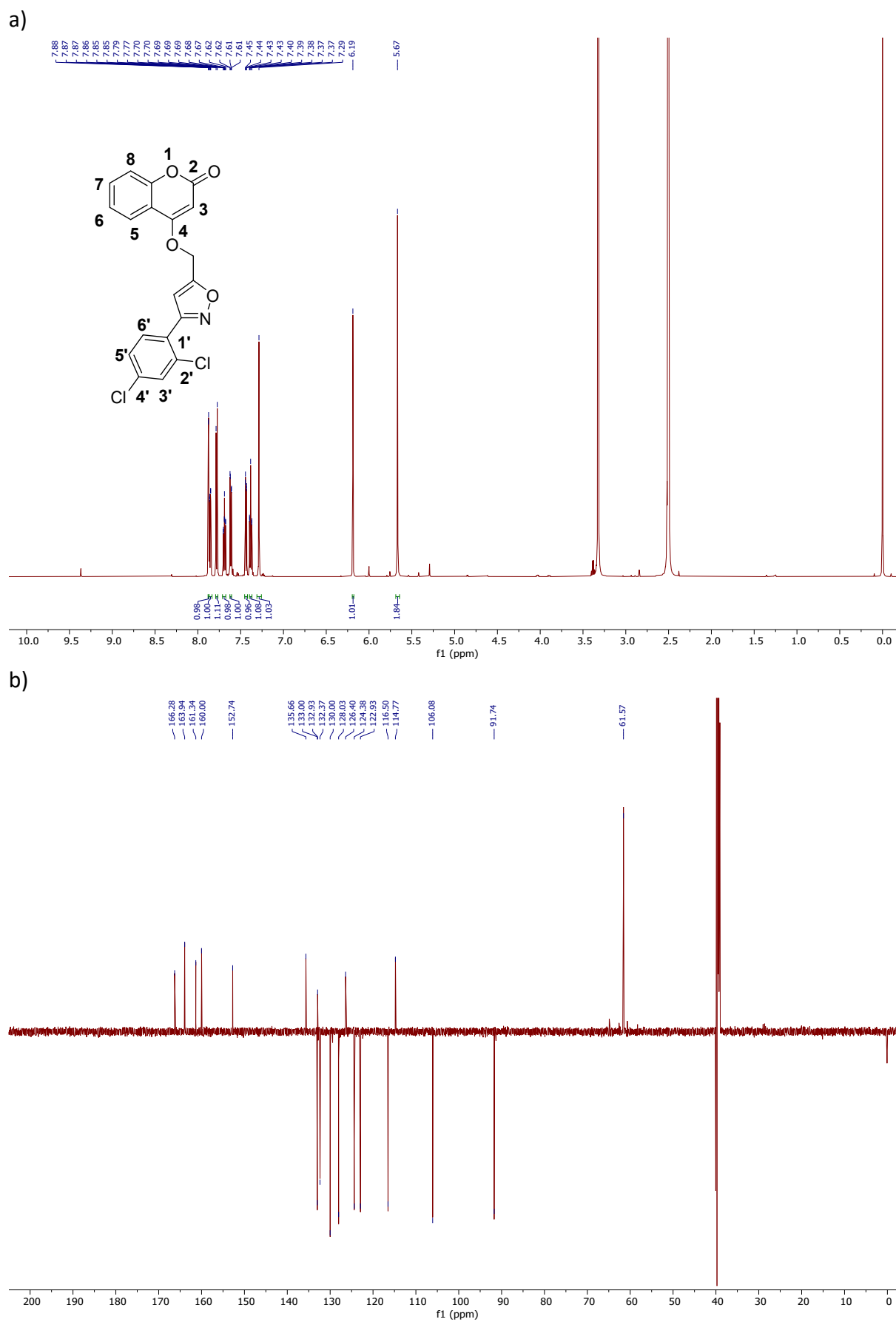
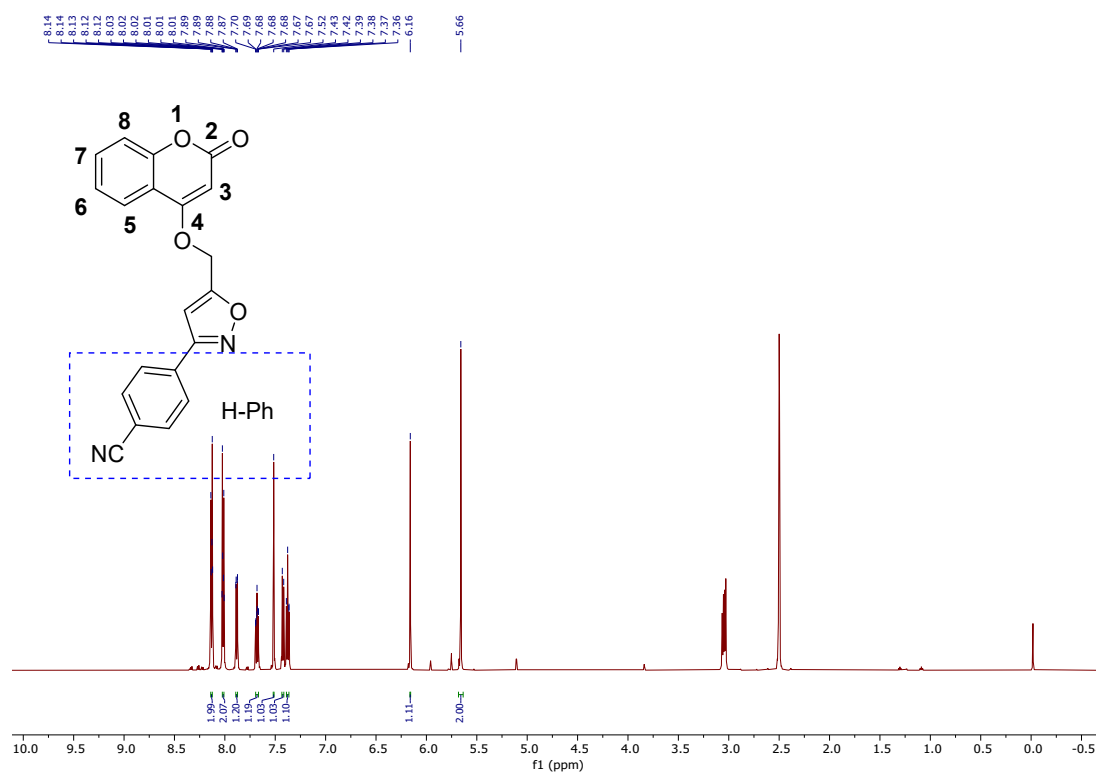
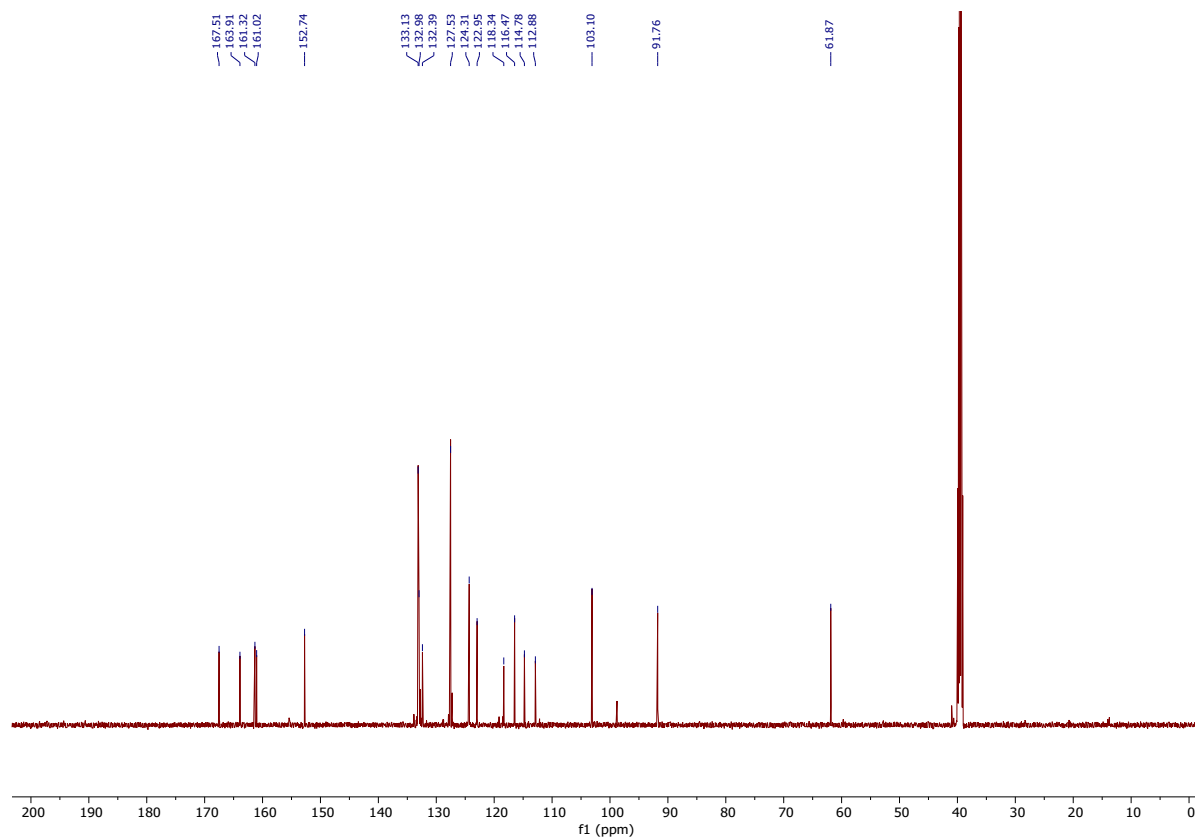


Figure S16: a) ^1H NMR and b) ^{13}C NMR of compd. **9e**.

a)



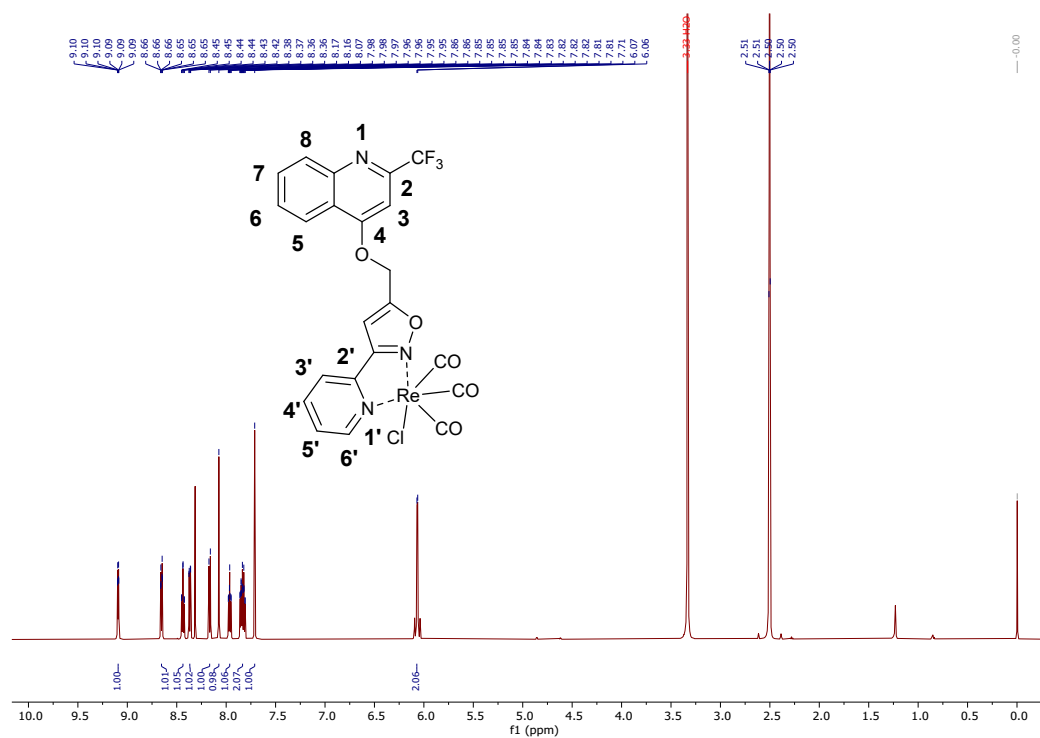
b)



1.2. ^1H and ^{13}C NMR spectra of Re(I) (**7b_{Re}**, **9b_{Re}**) and Ru(II) (**7b_{Ru}**, **9b_{Ru}**) complexes

Figure S17: a) ^1H NMR and b) ^{13}C NMR of compd **7b_{Re}**.

a)



b)

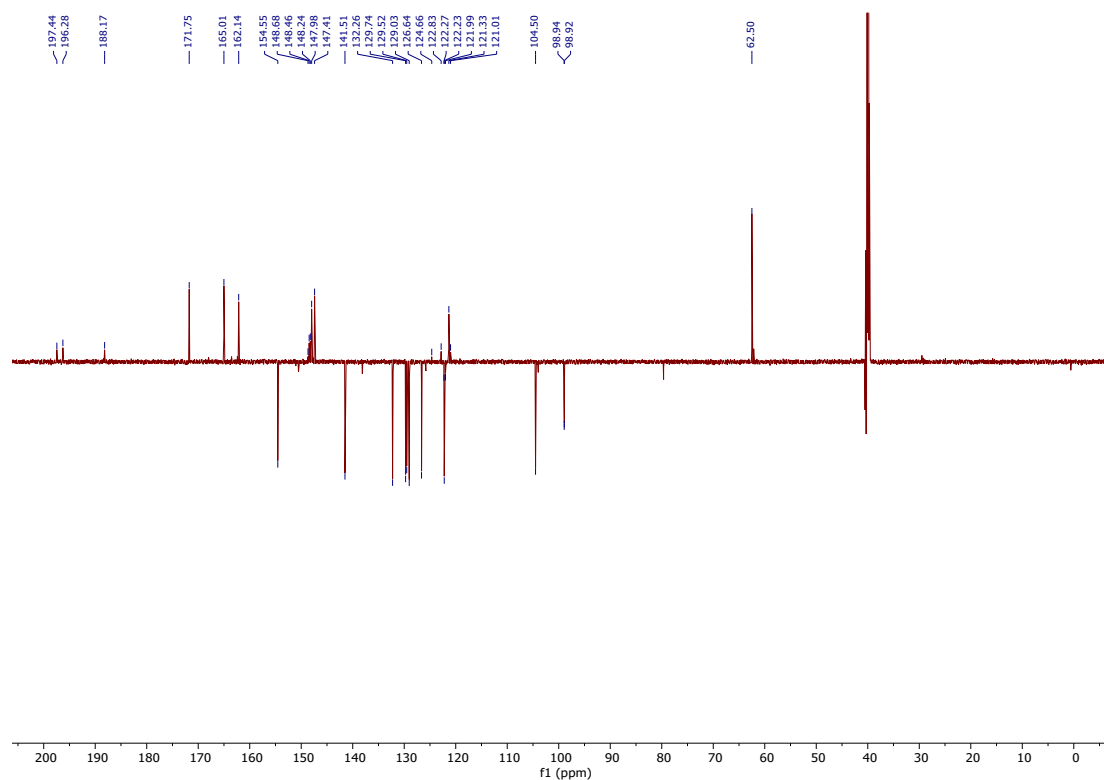
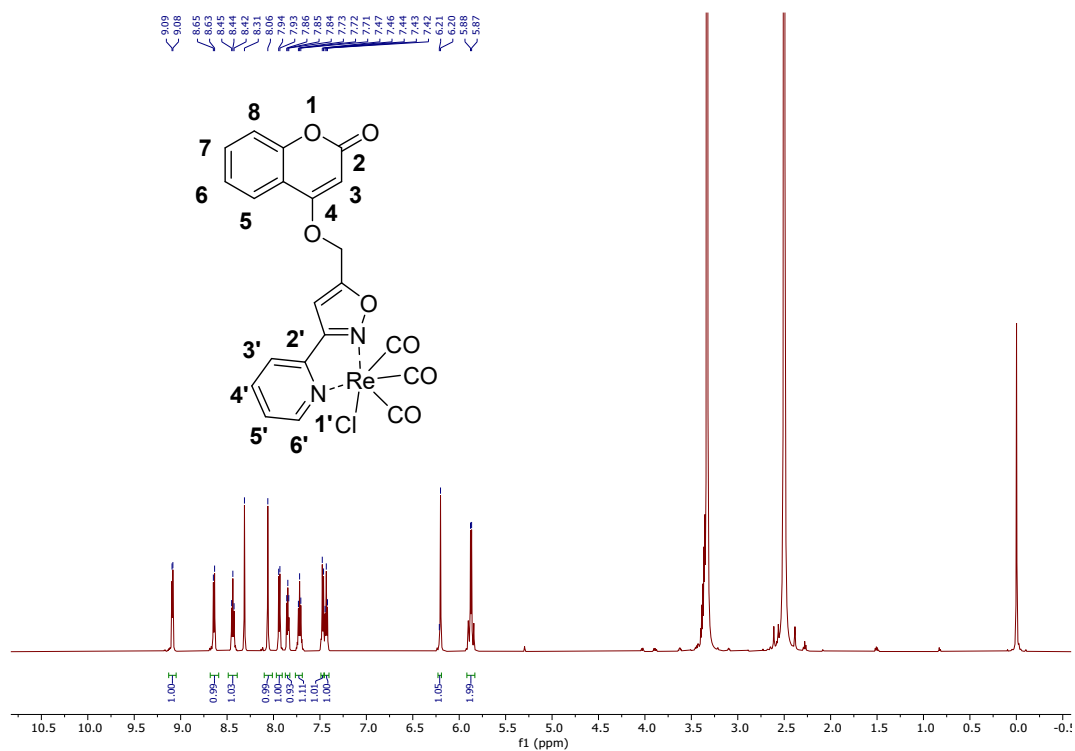


Figure S18: a) ^1H NMR and b) ^{13}C NMR of compd **9b_{Re}**.

a)



b)

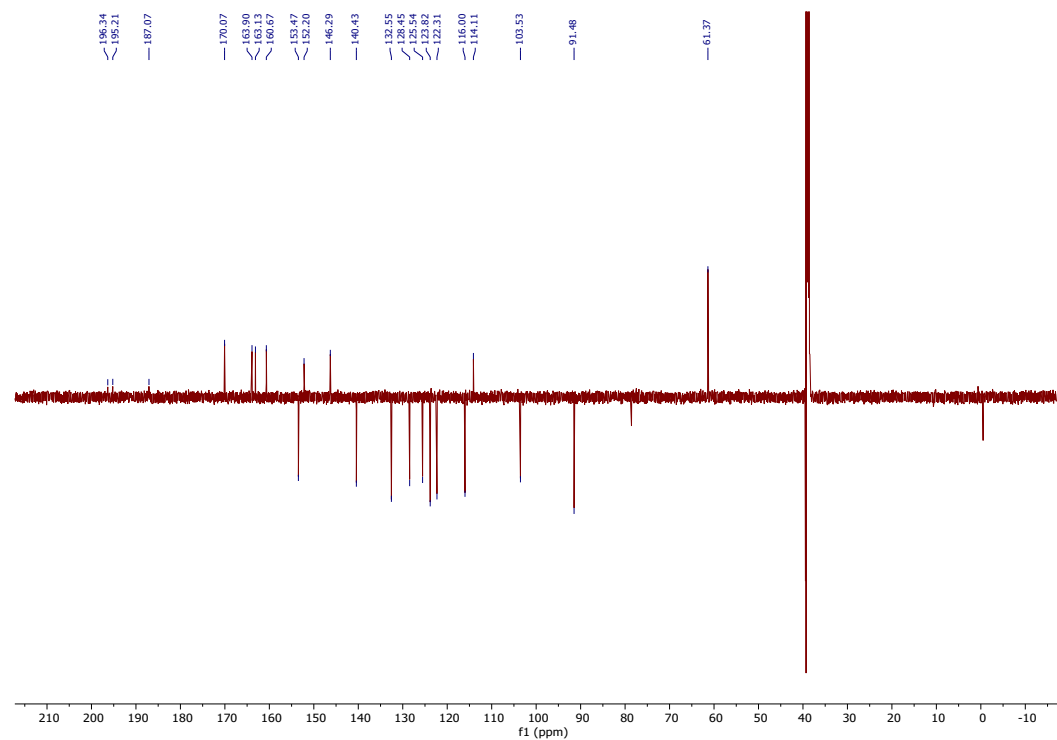
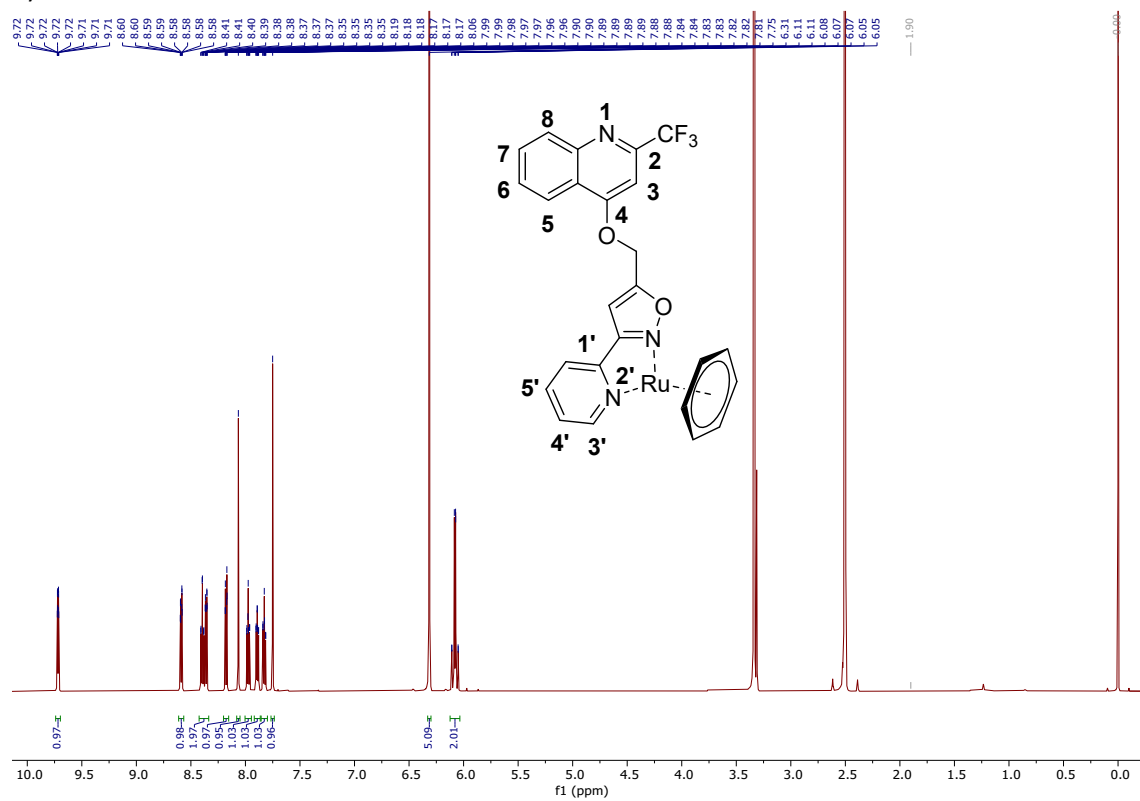


Figure S19: a) ^1H NMR and b) ^{13}C NMR of compd. **7b_{Ru}**.

a)



b)

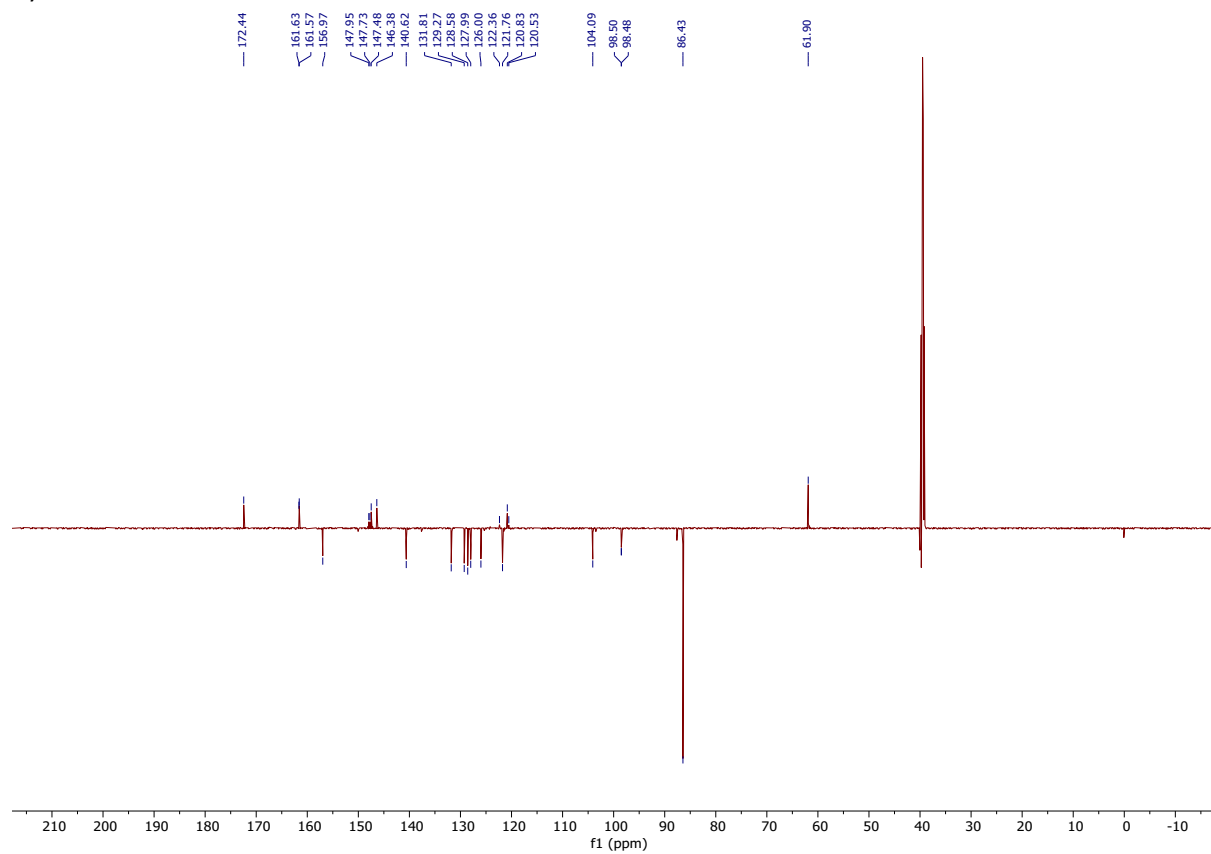
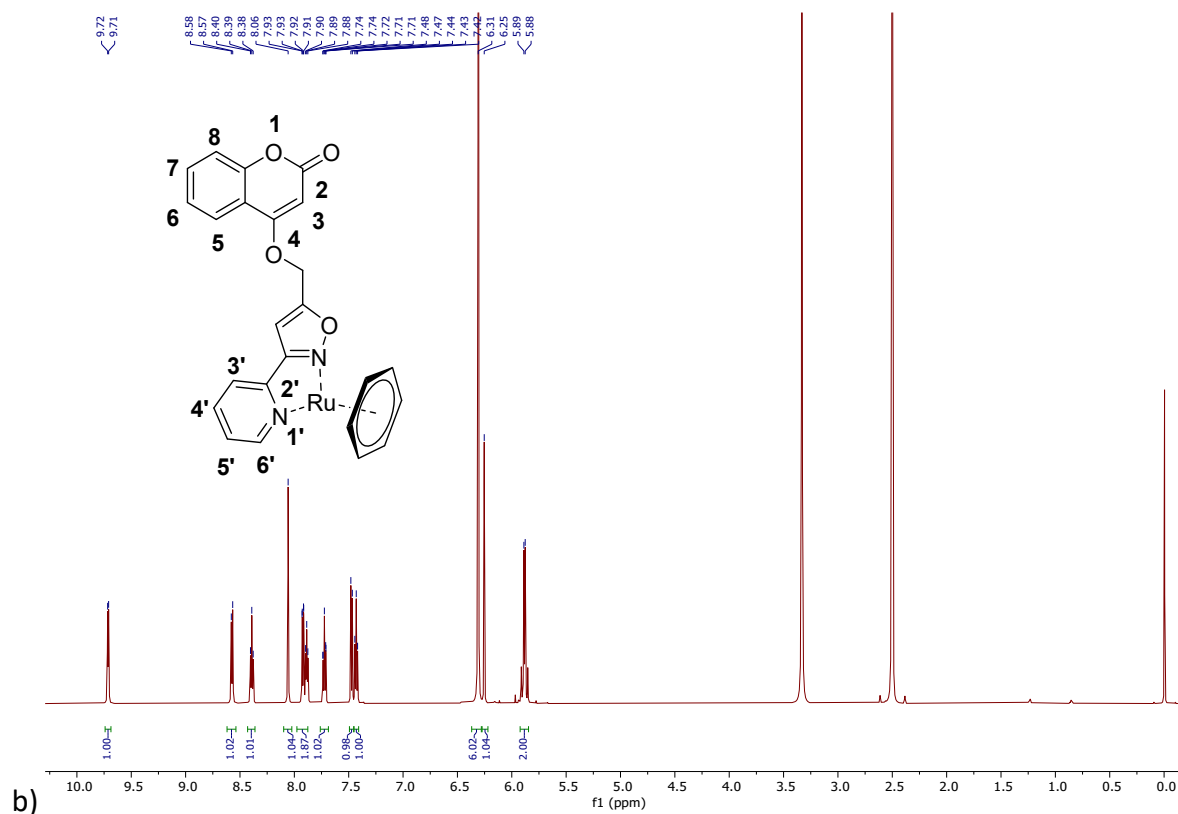
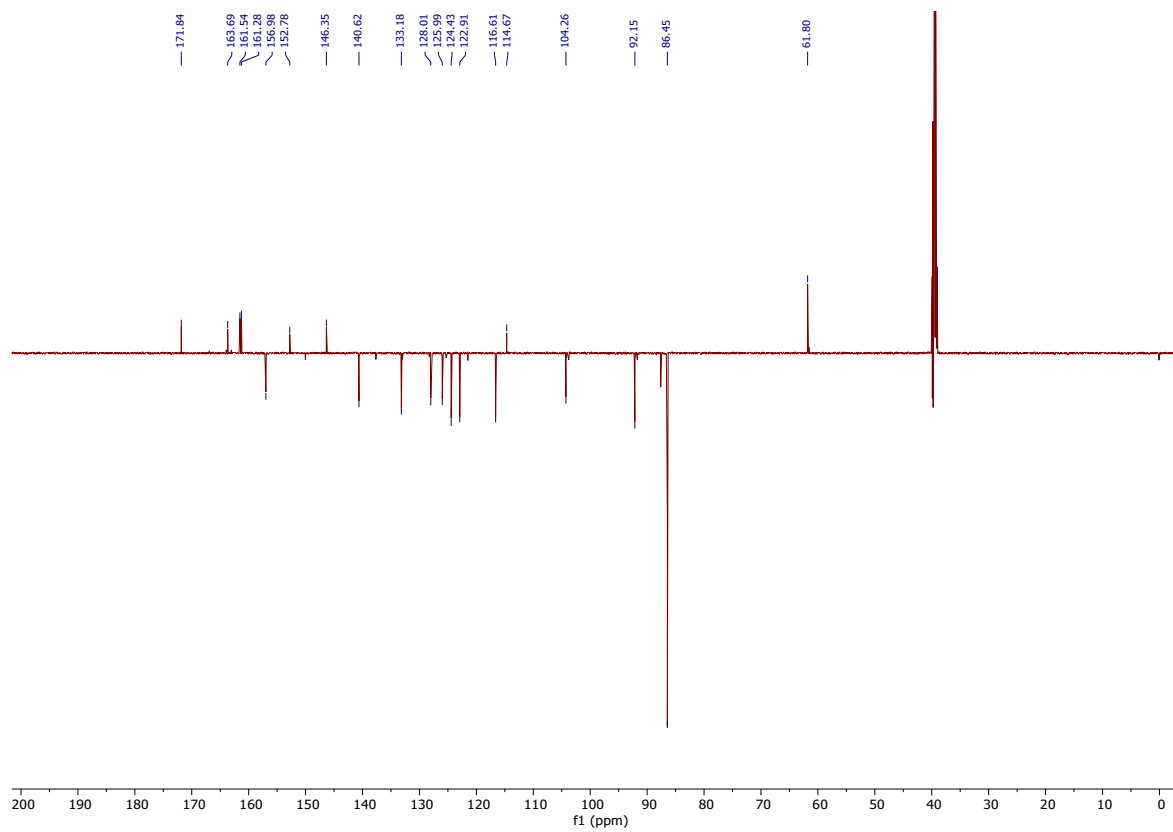


Figure S20: a) ^1H NMR and b) ^{13}C NMR of compd. **9b_{Ru}**.

a)



b)



2. FTIR spectra of ligands (**7b**, **9b**) and complexes (**7b_{Re}**, **7b_{Ru}**, **9b_{Re}**, **9b_{Ru}**)

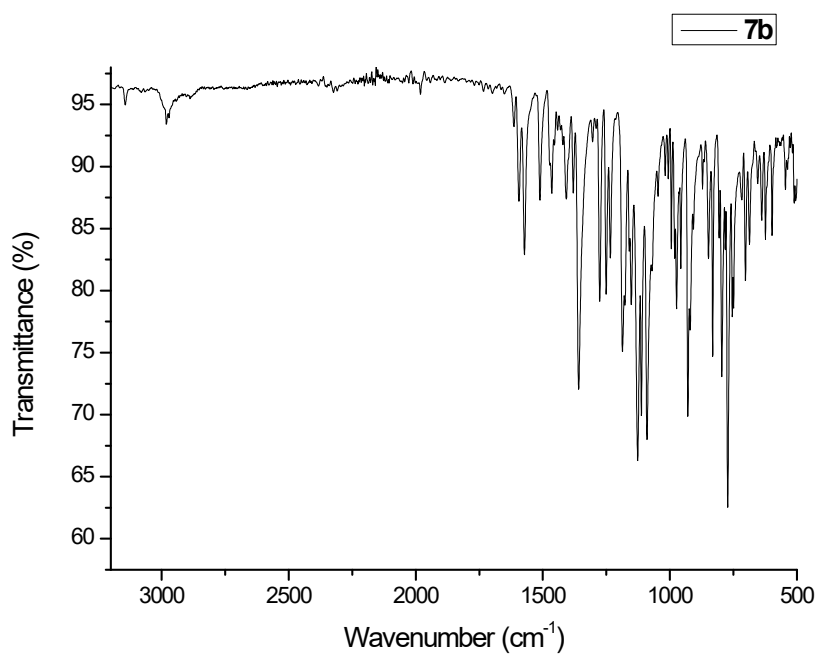


Figure S21. FTIR spectrum of **7b**.

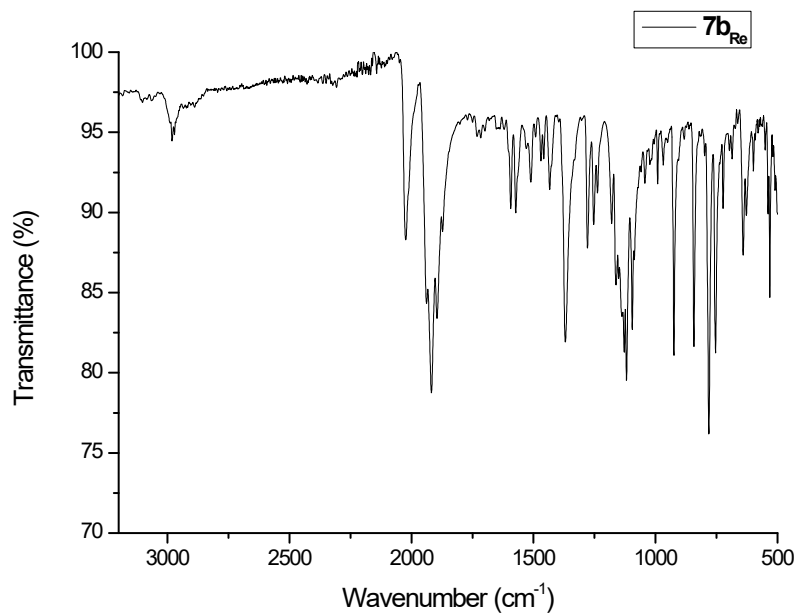


Figure S22. FTIR spectrum of **7b_{Re}**.

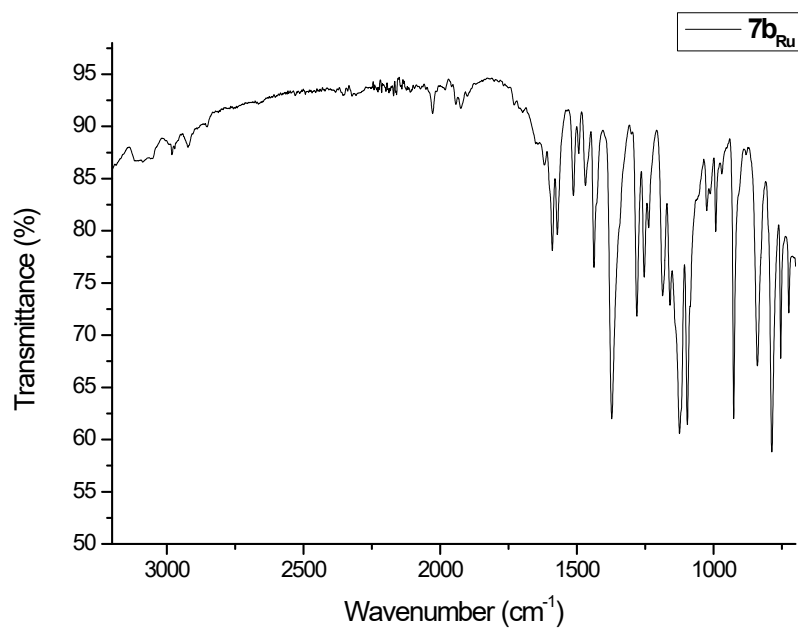


Figure S23. FTIR spectrum of 7b_{Ru}.

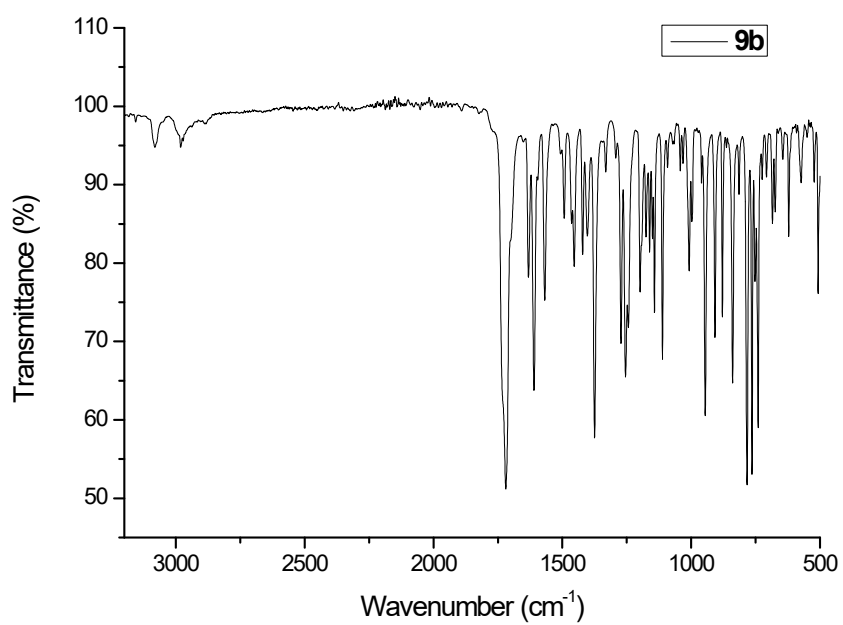


Figure S24. FTIR spectrum of 9b.

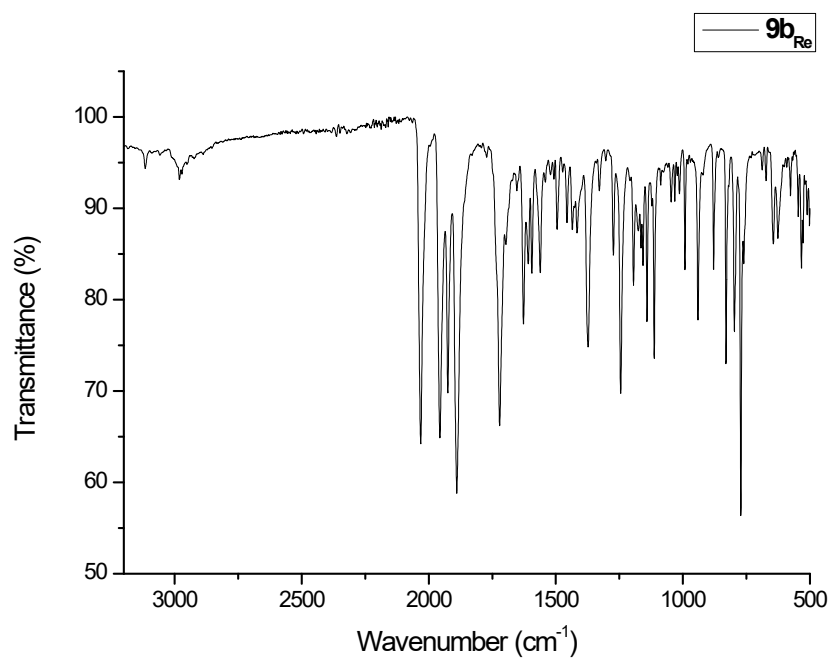


Figure S25. FTIR spectrum of **9b_{Re}**.

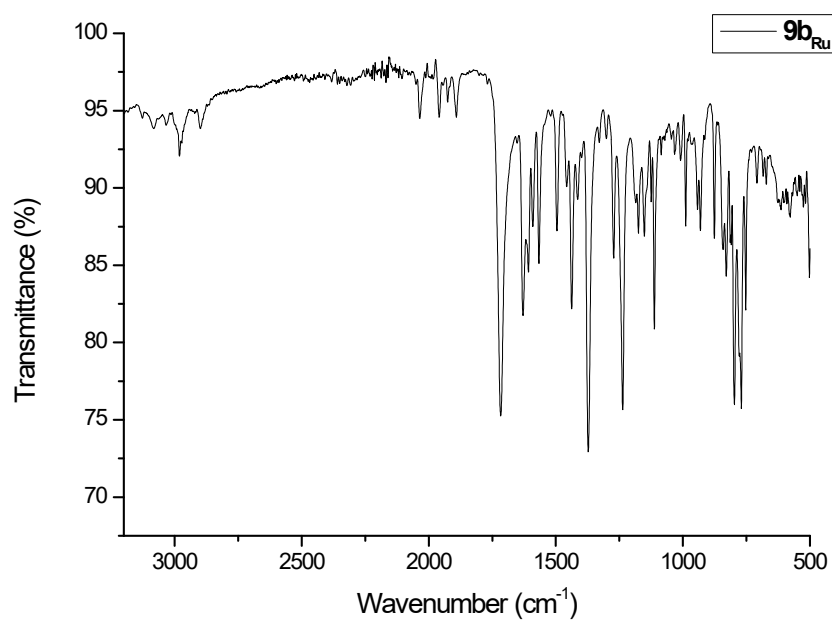


Figure S26. FTIR spectrum of **9b_{Ru}**.

3. UV-Vis spectra of ligands (**7b**, **9b**) and complexes (**7b_{Re}**, **7b_{Ru}**, **9b_{Re}**, **9b_{Ru}**)

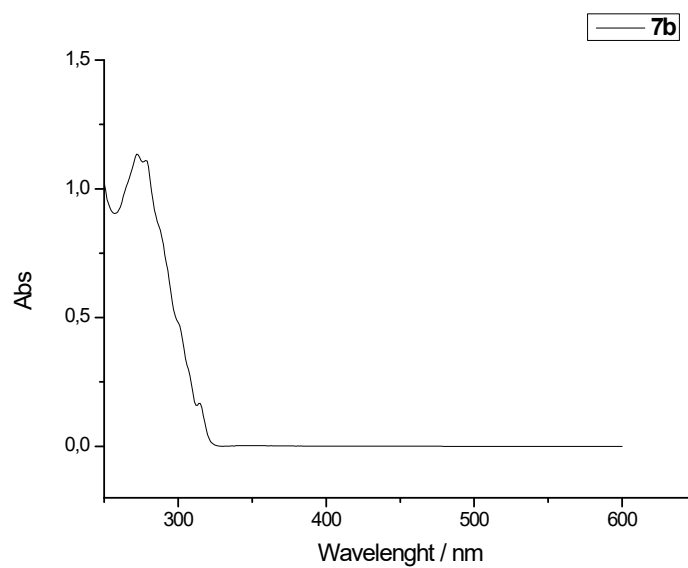


Figure S27. Absorption spectrum of derivative **7b** ($c(\text{ACN}) = 10^{-4}$).

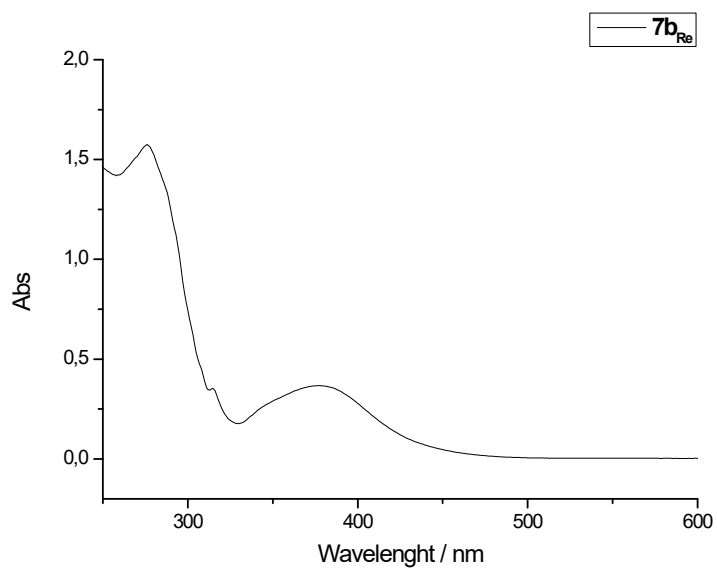


Figure S28. Absorption spectrum of derivative **7b_{Re}** ($c(\text{ACN}) = 10^{-4} \text{ mol/dm}^3$).

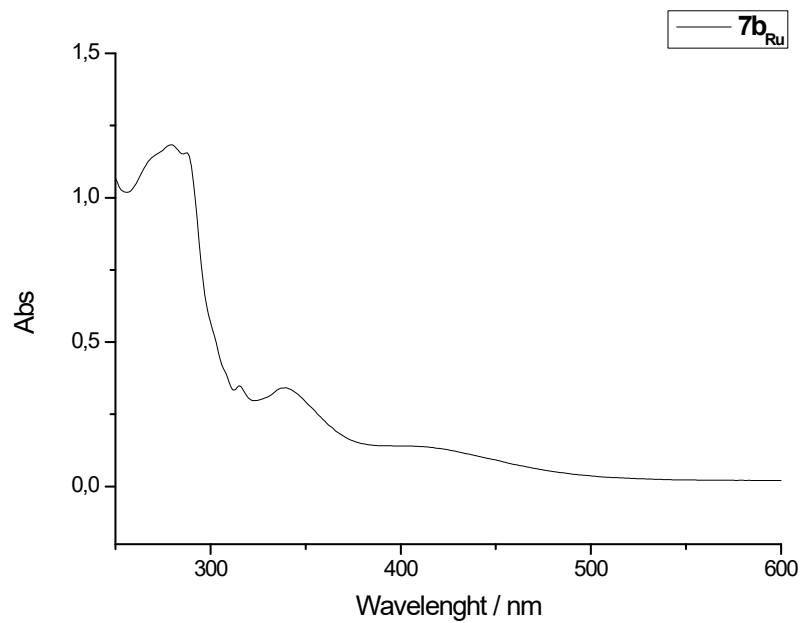


Figure S29. Absorption spectrum of derivative **7b_{Ru}** ($c(\text{ACN}) = 10^{-4} \text{ mol/dm}^3$).

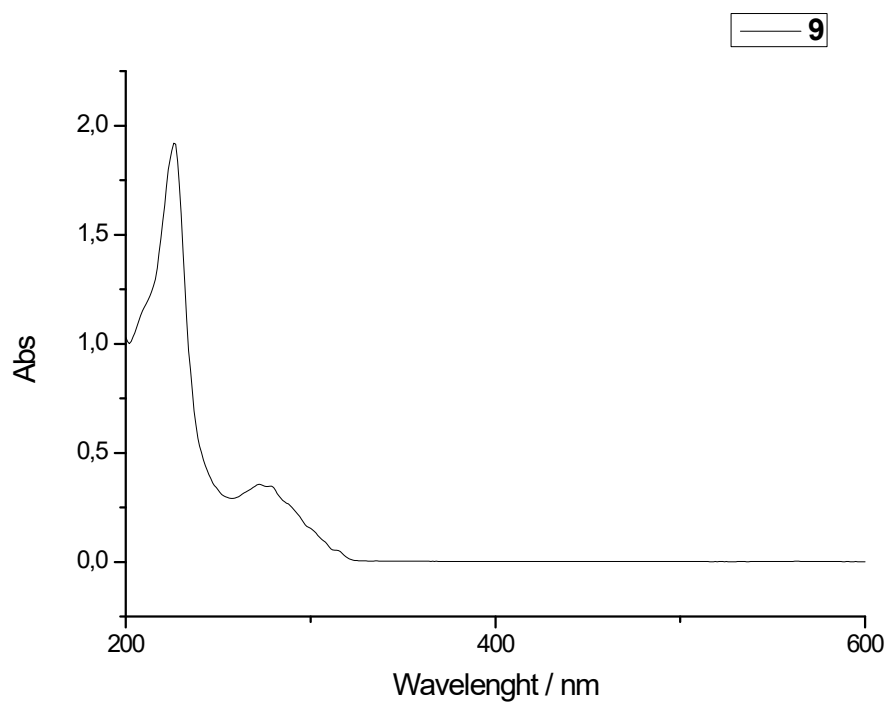


Figure S30. Absorption spectrum of derivative **9** ($c(\text{ACN}) = 10^{-4} \text{ mol/dm}^3$).

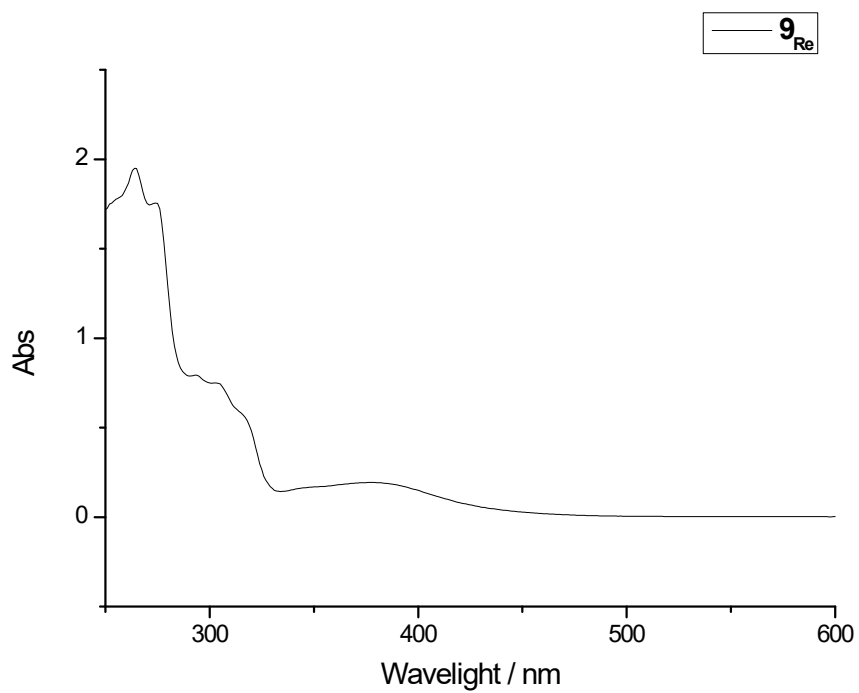


Figure S31. Absorption spectrum of derivative **9_{Re}** ($c(\text{ACN}) = 10^{-4} \text{ mol/dm}^3$).

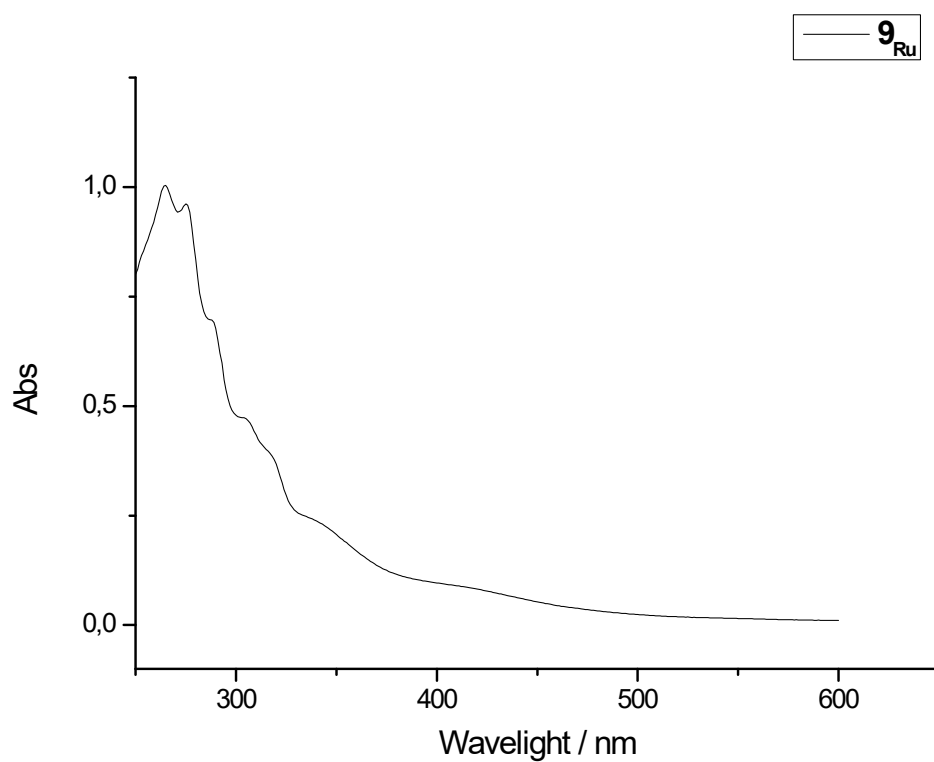


Figure S32. Absorption spectrum of derivative **9_{Ru}** ($c(\text{ACN}) = 10^{-4} \text{ mol/dm}^3$).

4. Molecular Docking Studies with Bcl-2

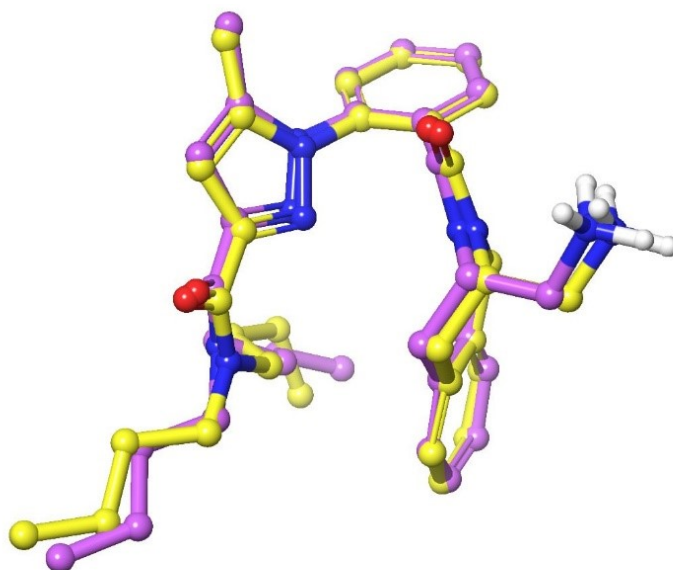


Figure S33. Comparison between the docked pose of the Bcl-2 inhibitor J1Q produced by the docking study (yellow) and the original crystallographic structure of the same inhibitor within the Bcl-2 binding pocket (Purple, PDB: 6QGK).

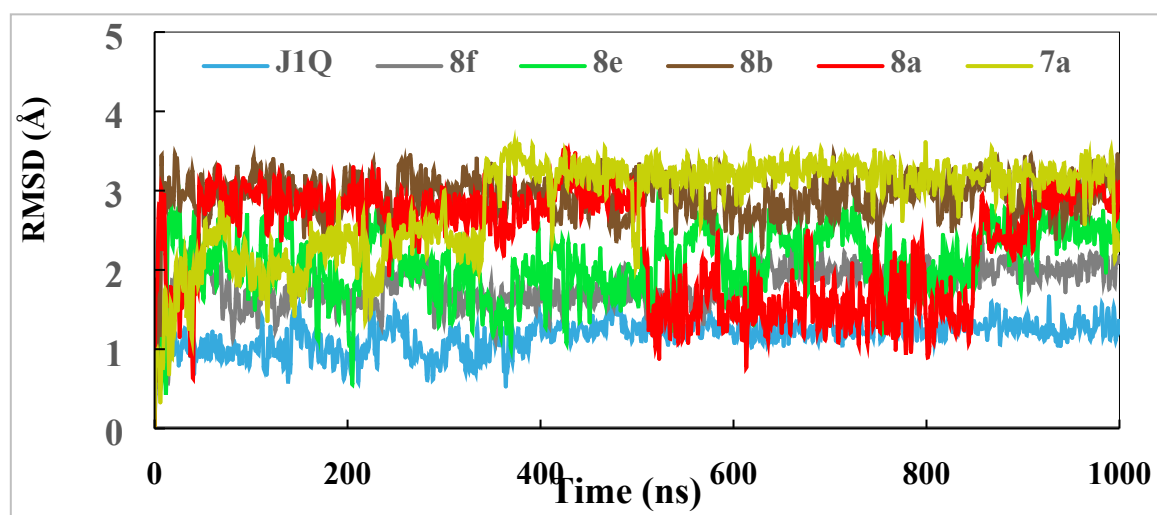


Figure 34. The RMSD of the backbone of Bcl-2 and complexes during the simulation period.

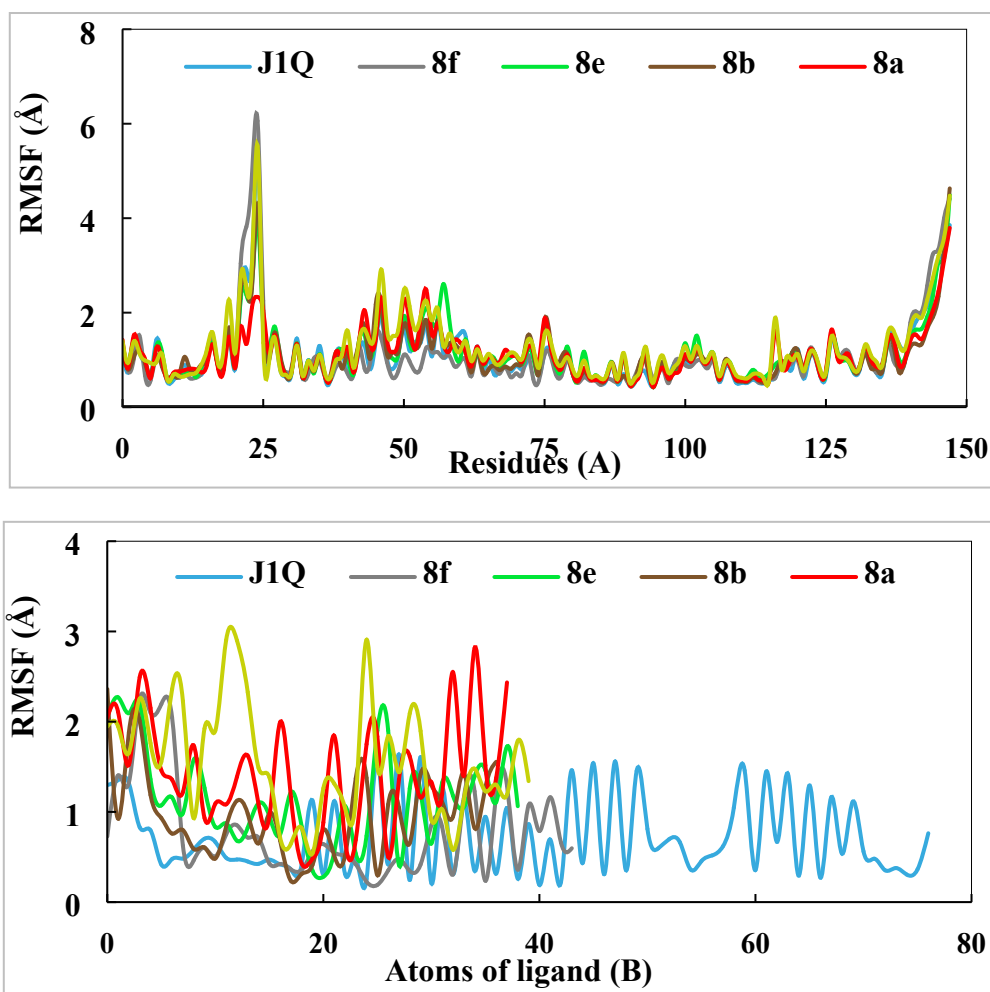


Figure 35. (A) The RMSF of Cα atoms of Bcl-2 in the absence and presence of ligands. (B) The average RMSF value of each atom of the ligands during MD simulation.

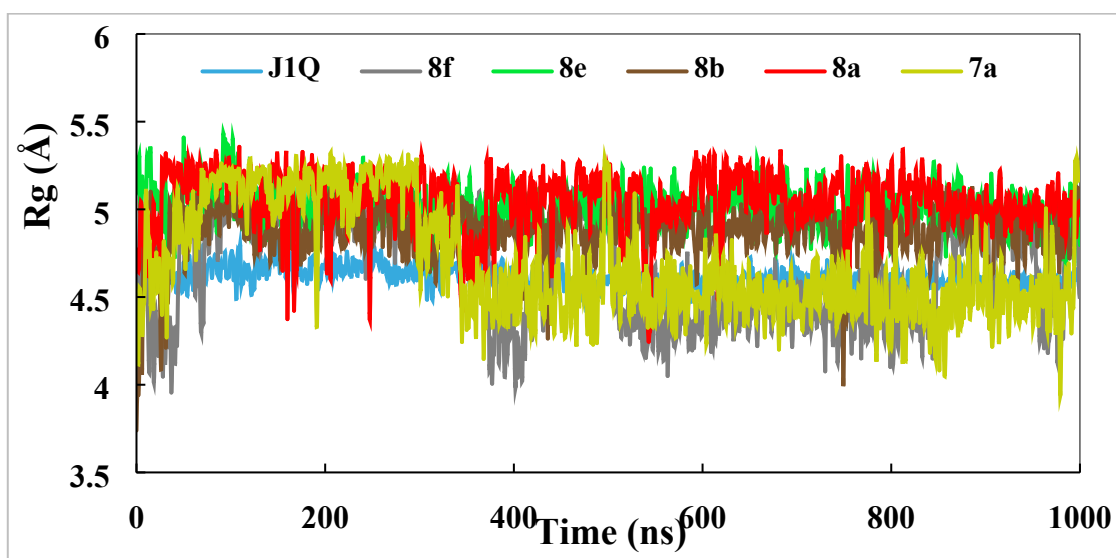


Figure S36. Radius gyration of the backbone of Bcl-2 and complexes during simulation.

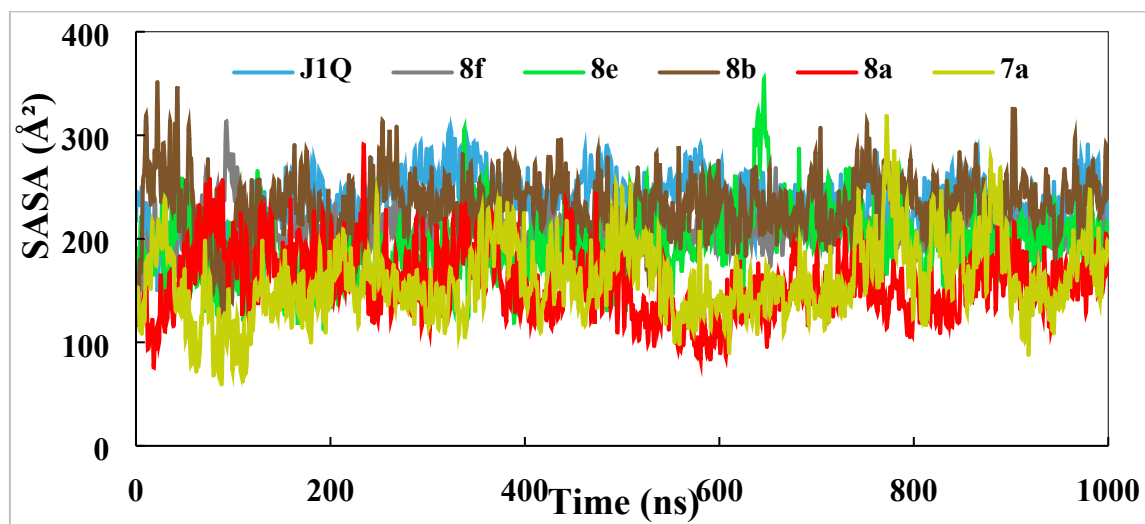


Figure S37. Solvent accessible surface area (SASA) of Bcl-2 and complexes during simulation.

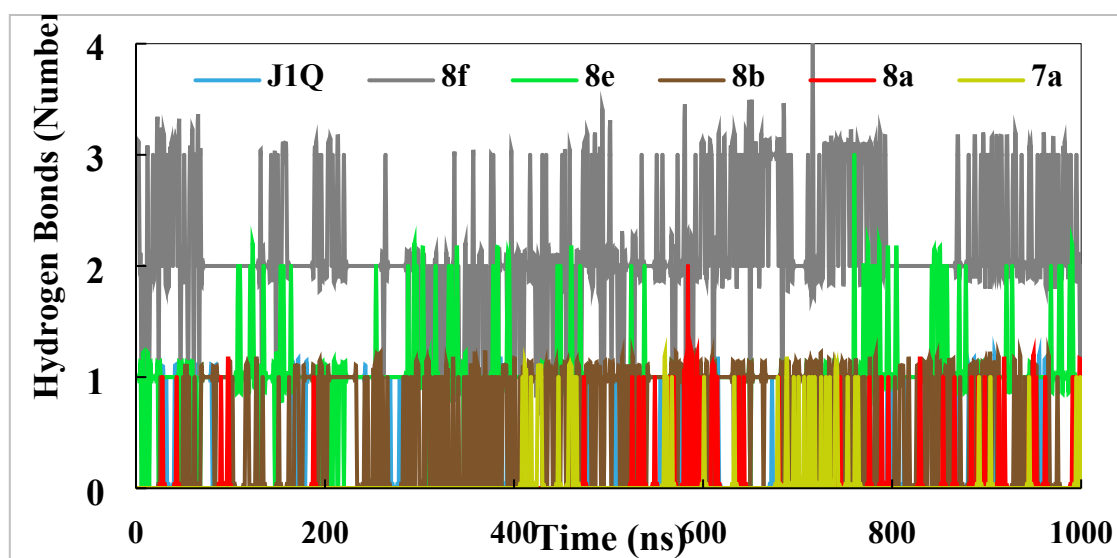


Figure S38. Number of hydrogen bonds between ligands and Bcl-2 during the simulation.