Stereo/regio-selective access to substituted 3-hydroxy-oxindoles with anti-proliferative assessment and *in-silico* validation†

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Contents

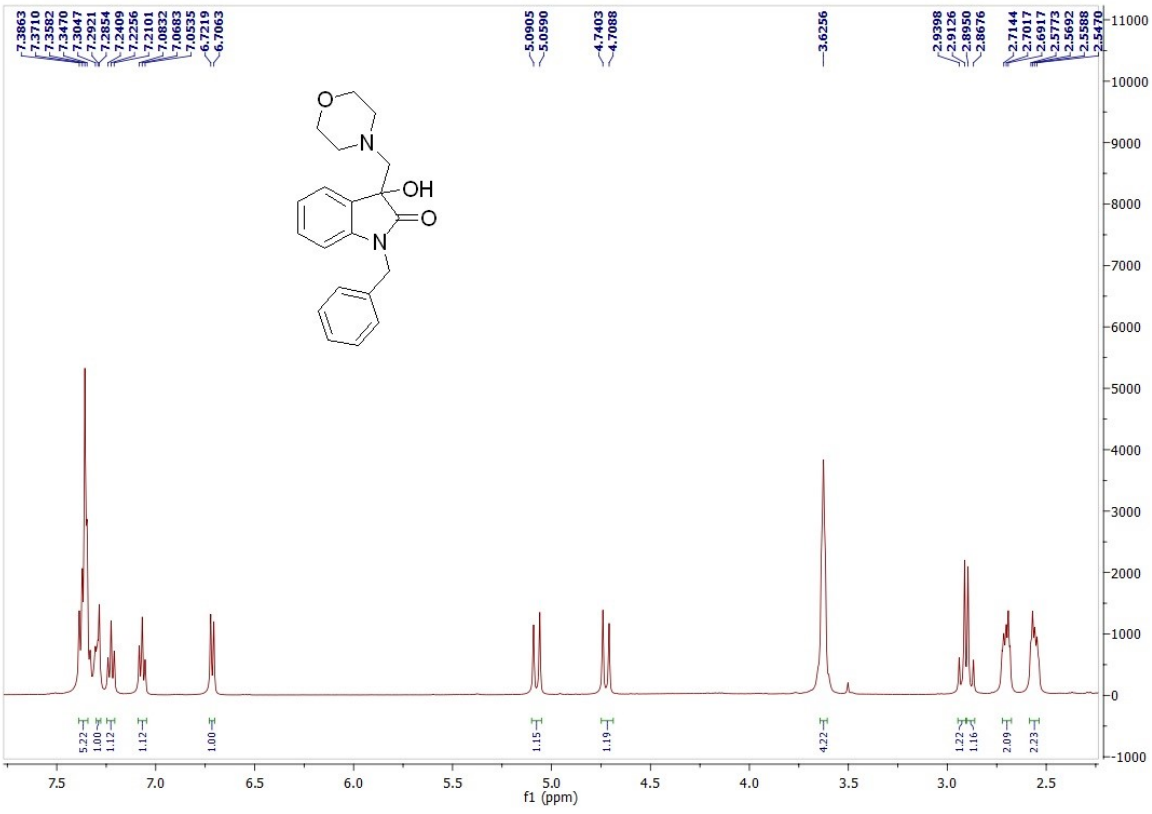
Table S1: Physicochemical and ADMET properties of compounds **4a, 4d, 4j** and **4m**.

	4a	**4d**	**4j**	**4m**
Absorption				
Water solubility (log mol/L)	-2.855	-3.124	-3.411	-2.252
Caco2 permeability (log Papp in 10-6 cm/s)	1.189	0.886	0.885	1.117
Intestinal absorption (human) (% Absorbed)	93.868	92.941	91.328	86.619
Skin permeability (log Kp)	-2.745	-2.746	-2.746	-2.745
P-glycoprotein substrate	Yes	Yes	Yes	No
P-glycoprotein I inhibitor	No	No	Yes	No
P-glycoprotein II inhibitor	Yes	Yes	Yes	No
Metabolism				
CYP2D6 inhibitor	Yes	Yes	Yes	Yes
CYP3A4 inhibitor	Yes	Yes	Yes	No
CYP1A2 inhibitor	Yes	No	No	No
CYP2C19 Inhibitor	No	No	No	No
CYP2C9 inhibitor	No	No	No	No
CYP2D6 inhibitor	Yes	Yes	No	No
CYP3A4 inhibitor	No	No	No	No
Excretion				
Total Clearance (log ml/min/kg)	1.059	0.972	0.591	1.093
Renal OCT2 substrate	No	No	No	No
Distribution				
VDss (human) (log L/kg)	1.066	1.098	1.065	0.08
BBB permeability (log BB)	0.042	0.011	-0.04	-0.244
Fraction unbound (human) (Fu)	0.206	0.23	0.261	0.728
CNS permeability (log PS)	-2.55	-2.414	-2.266	-2.965
Toxicity				

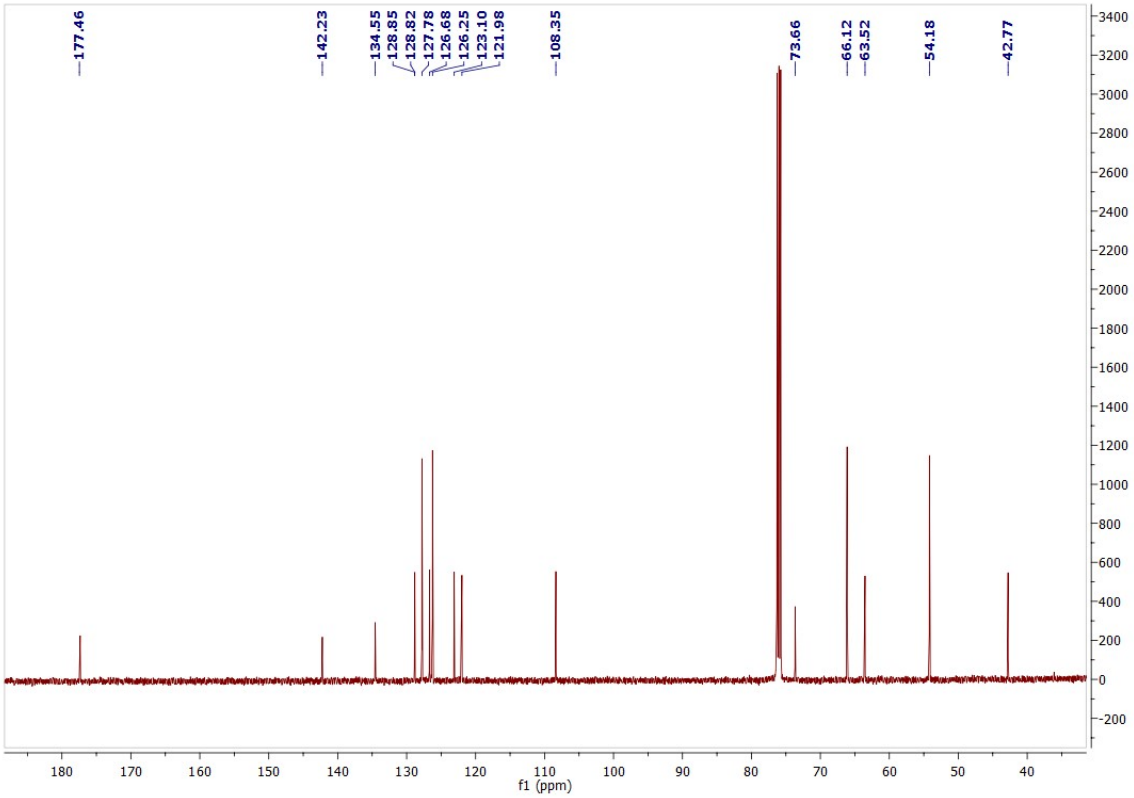
Oral Rat Acute Toxicity (LD50) (mol/kg)	2.772	2.866	2.942	2.851
Hepatotoxicity	Yes	No	Yes	No
Skin Sensitisation	No	No	No	No
T.Pyriformis toxicity (log ug/L)	0.305	0.31	0.312	0.258
Minnow toxicity (log mM)	1.762	1.123	0.616	2.401
Molecular weight	338.40	417.30	496.19	248.28
Log$P_{o/w}$	1.7532	2.5157	3.2782	0.1585
TPSA (Å)	53.01	53.01	53.01	61.80
No. of rotatable bonds	4	4	4	2
No. of HBA	4	4	4	4
No. of HBD	1	1	1	1
Molar refractivity	101.98	109.68	117.38	72.60

2. Scanned copies of ^{1}H and ^{13}C NMR spectra:

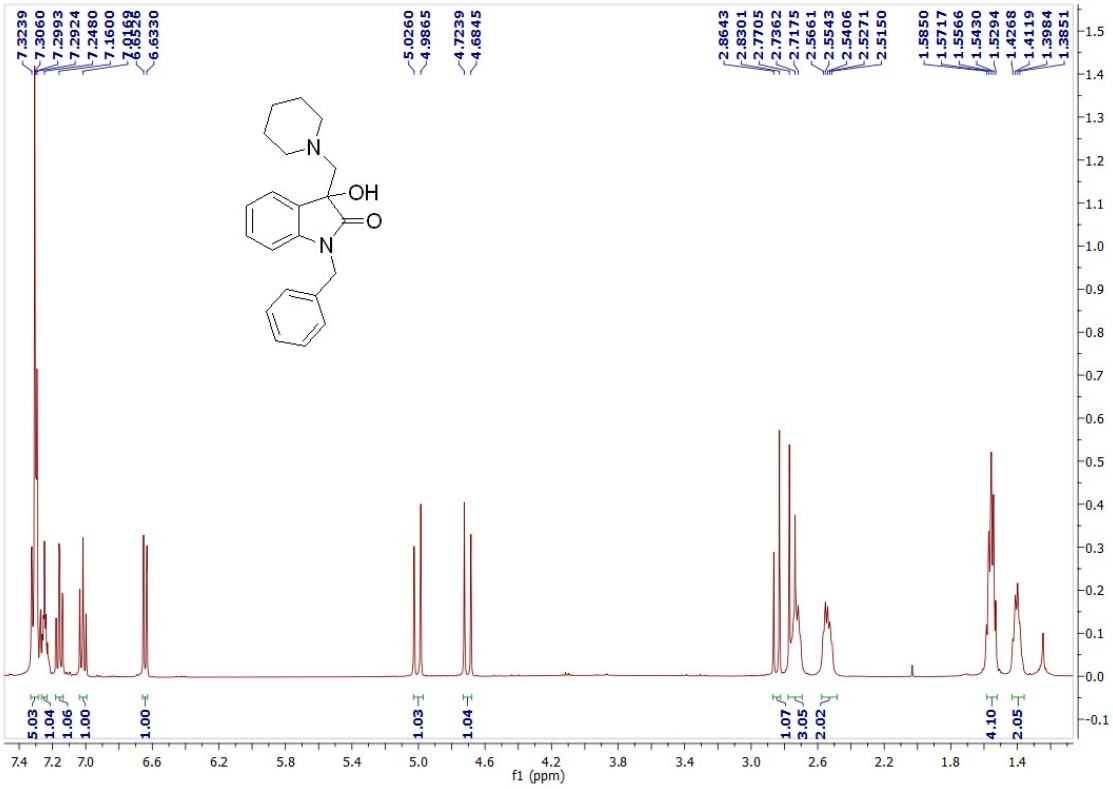
1. **^{1}H NMR** 1-Benzyl-3-hydroxy-3-(morpholinomethyl)indolin-2-one (**4a**).



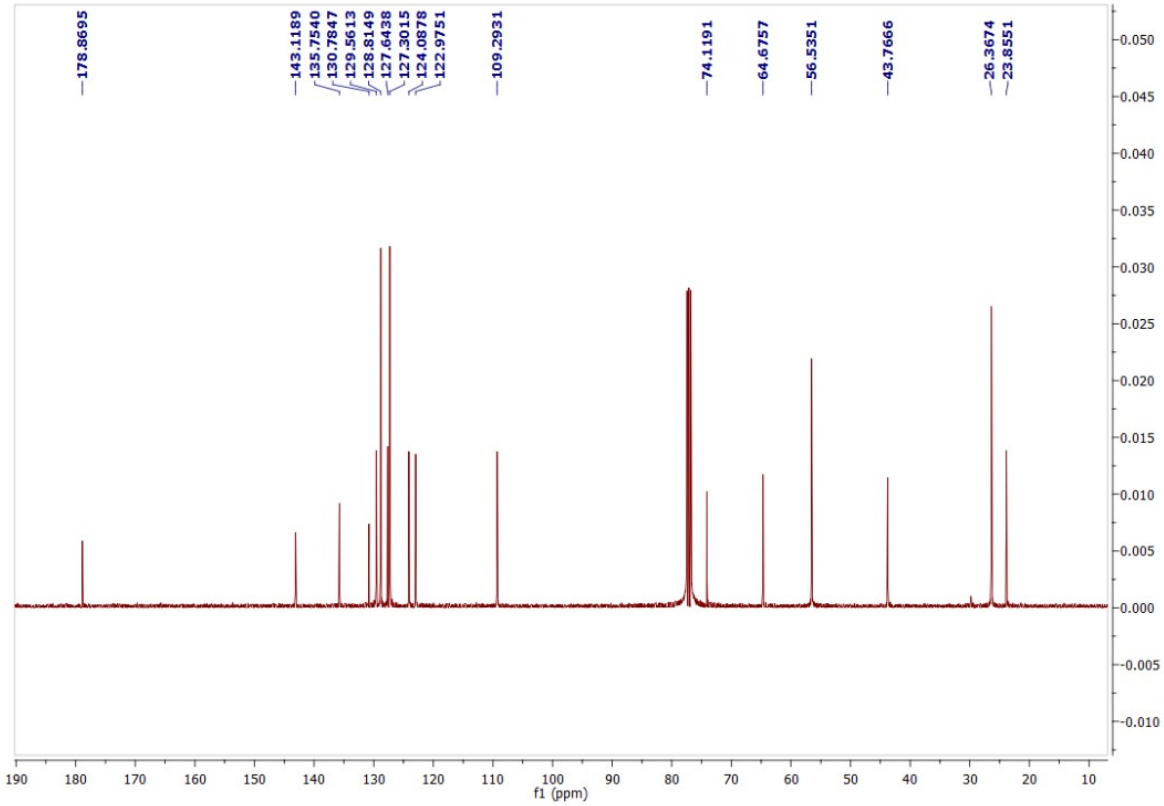
2. **^{13}C NMR** 1-Benzyl-3-hydroxy-3-(morpholinomethyl)indolin-2-one (**4a**)



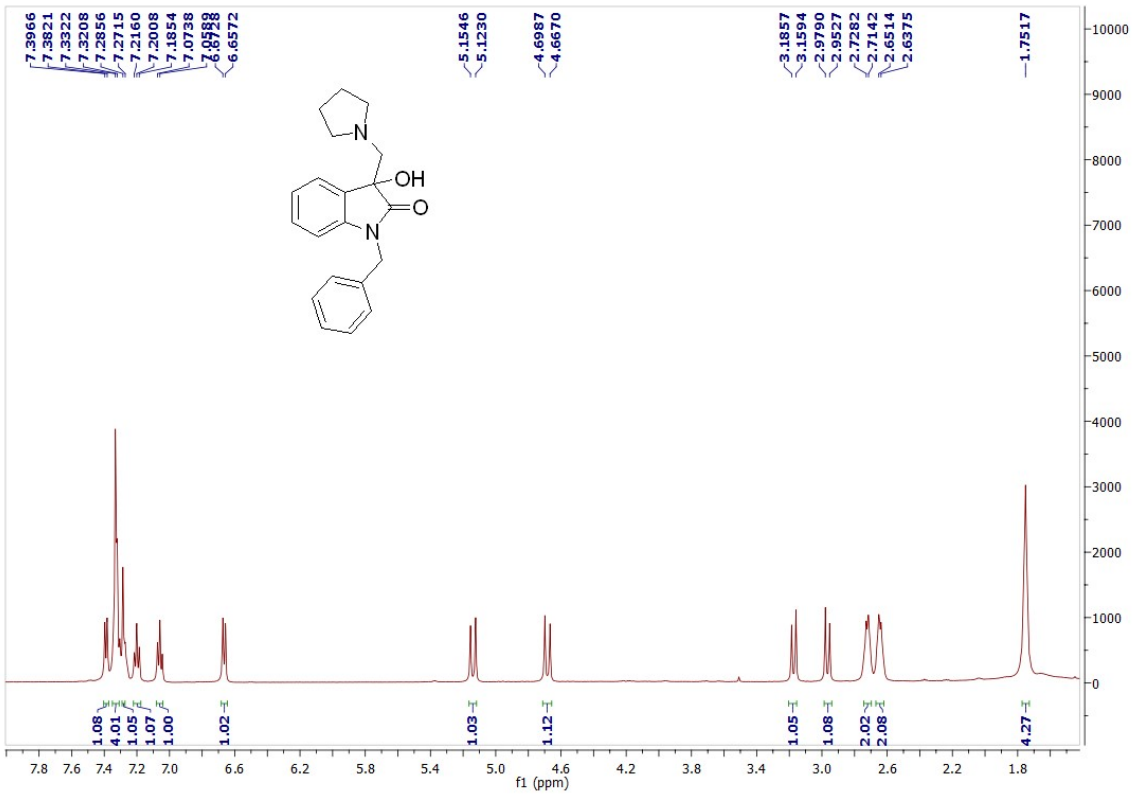
3. **^{1}H NMR** 1-Benzyl-3-hydroxy-3-(piperidin-1-ylmethyl)indolin-2-one (**4b**)



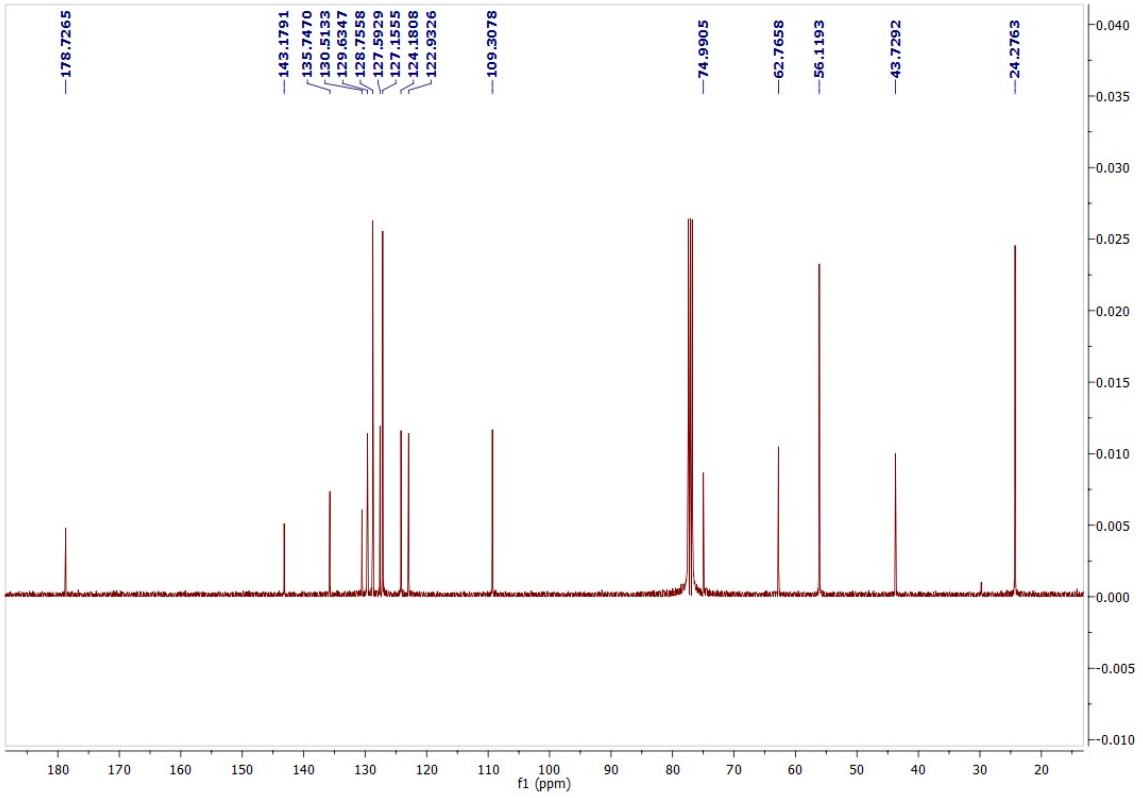
4. **^{13}C NMR** 1-Benzyl-3-hydroxy-3-(piperidin-1-ylmethyl)indolin-2-one (**4b**)



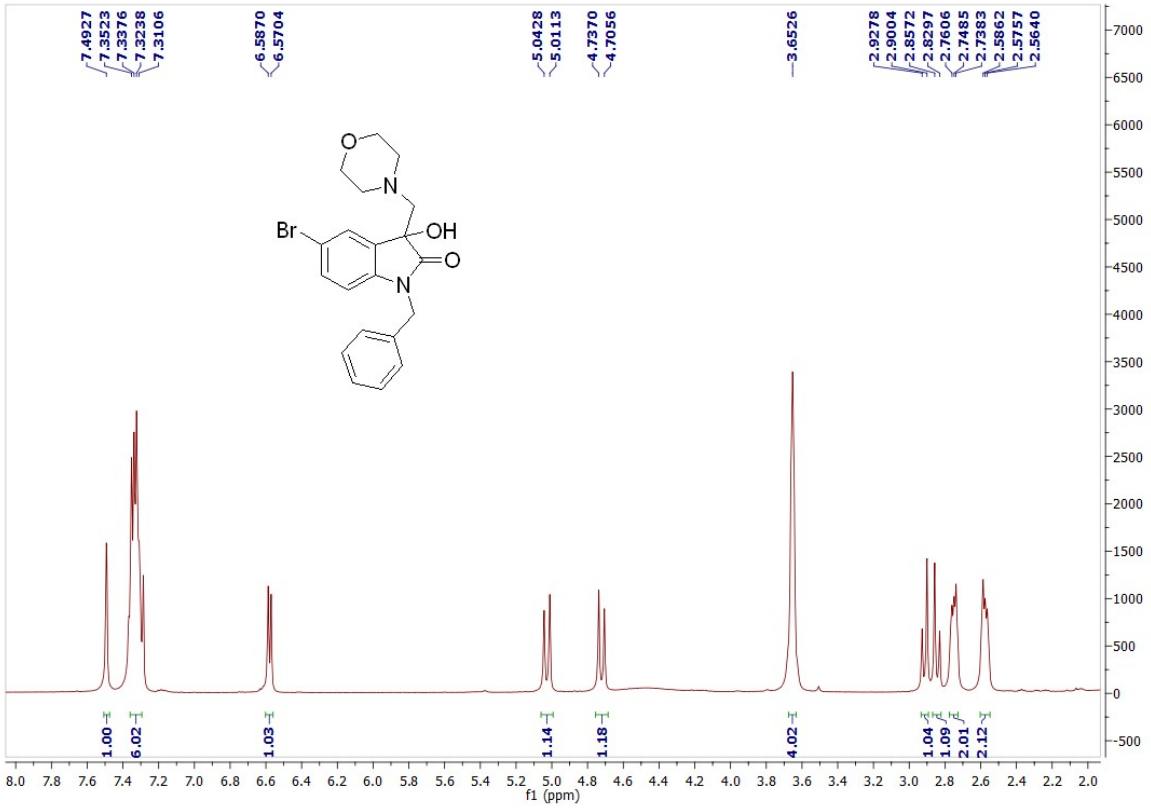
5. **^{1}H NMR** 1-Benzyl-3-hydroxy-3-(pyrrolidin-1-ylmethyl)indolin-2-one(**4c**)



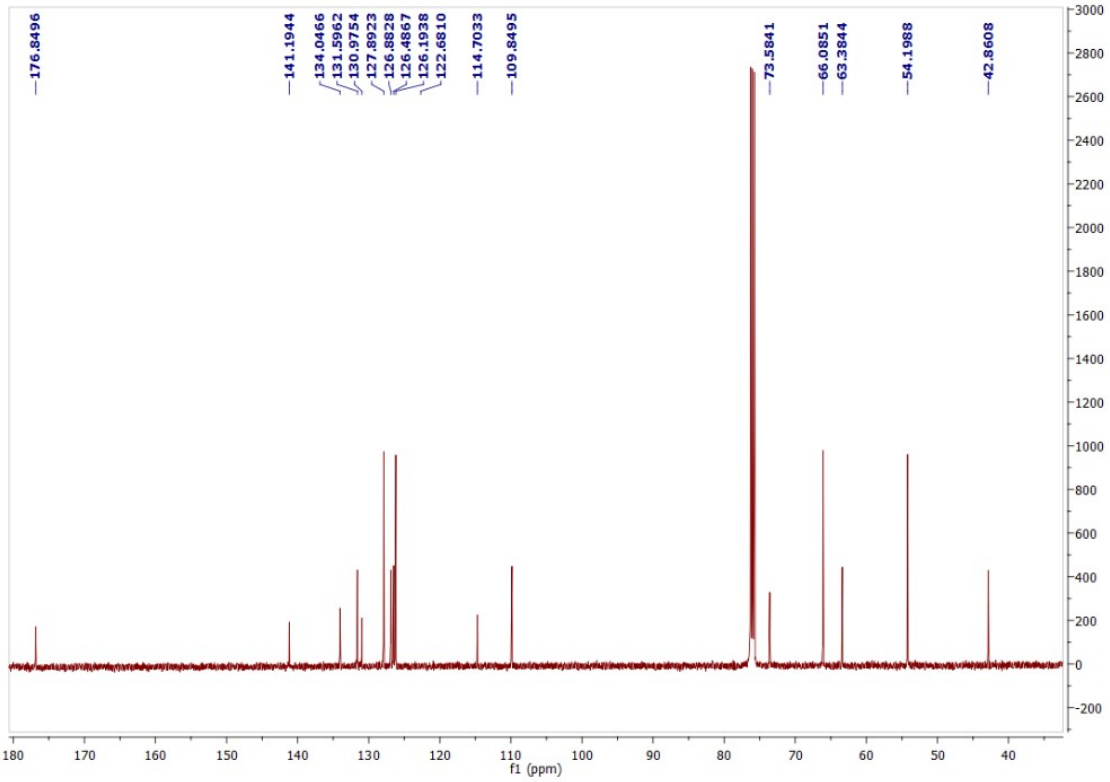
6. **^{13}C NMR** 1-Benzyl-3-hydroxy-3-(pyrrolidin-1-ylmethyl)indolin-2-one (**4c**)



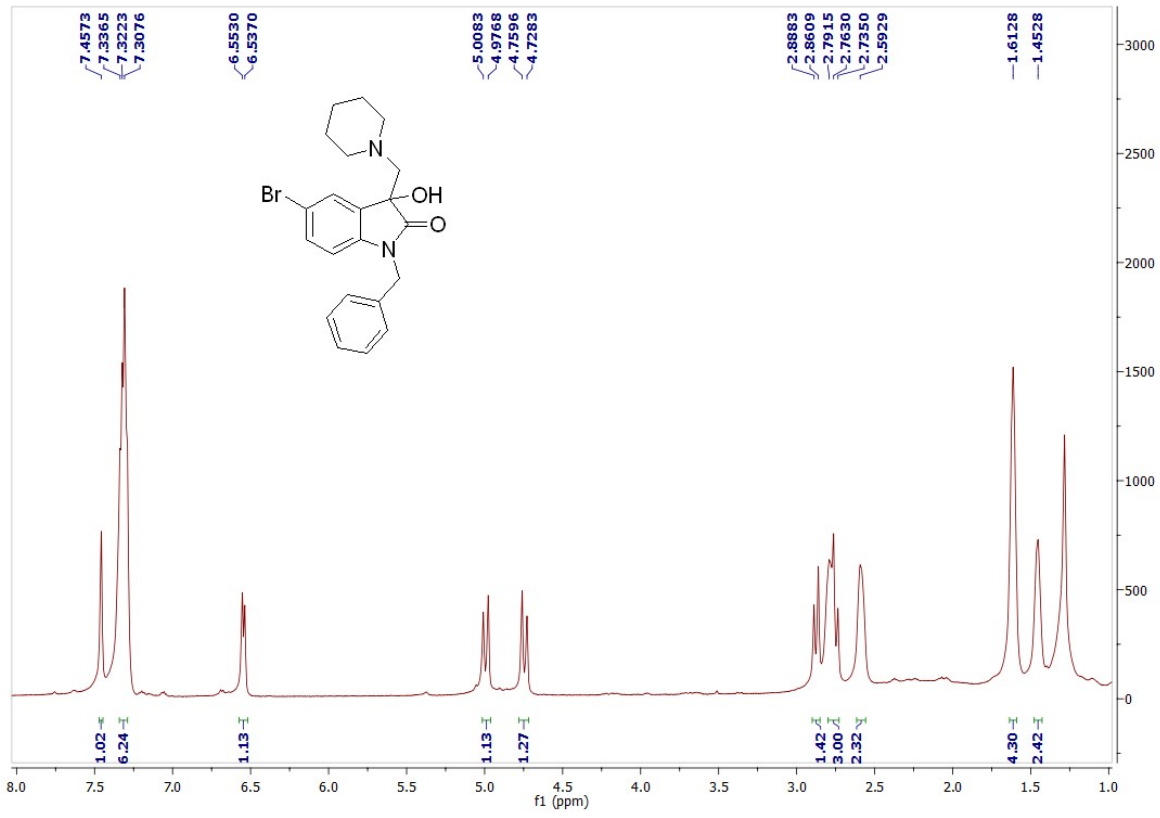
7. **^{1}H NMR** 1-Benzyl-5-bromo-3-hydroxy-3-(morpholinomethyl)indolin-2-one (**4d**)



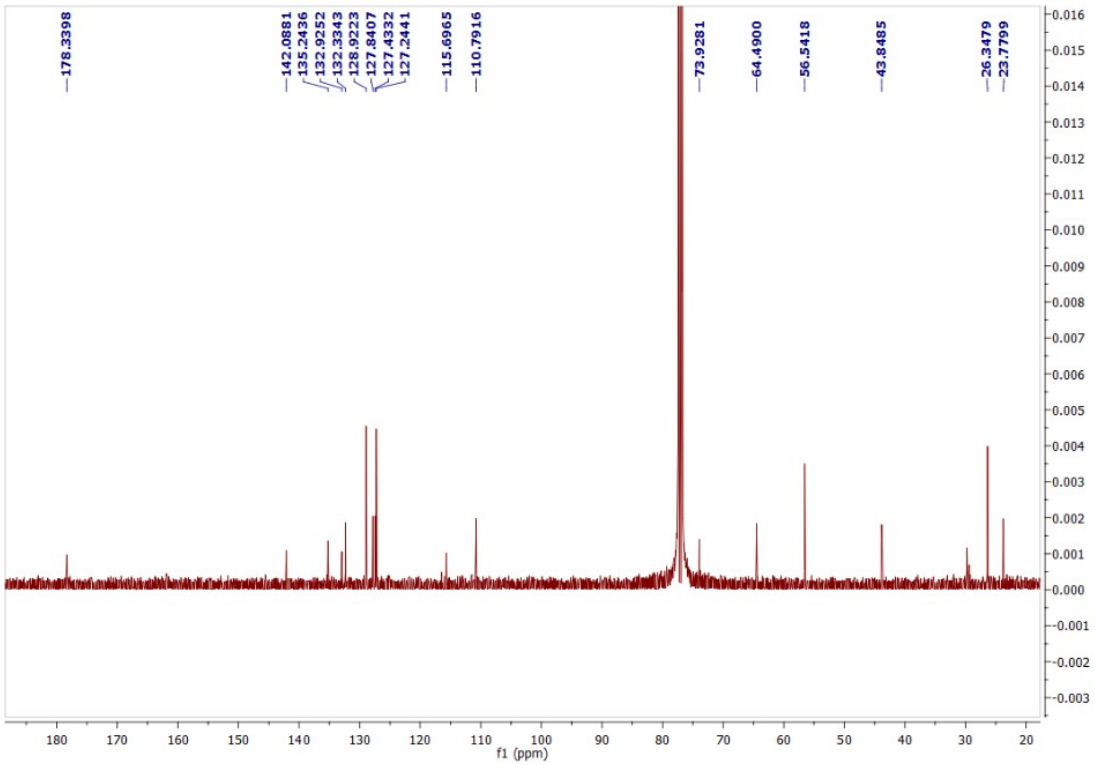
8. **^{13}C NMR** 1-Benzyl-5-bromo-3-hydroxy-3-(morpholinomethyl)indolin-2-one (**4d**)



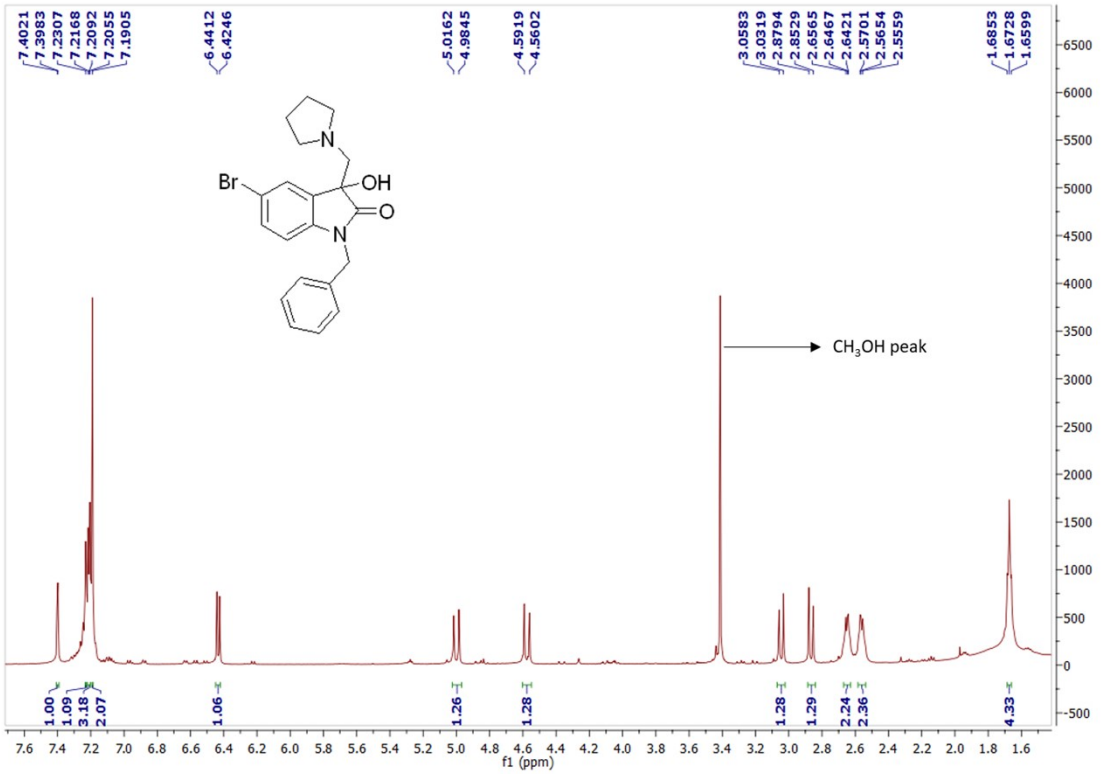
9. **^{1}H NMR** 1-Benzyl-5-bromo-3-hydroxy-3-(piperidin-1-ylmethyl)indolin-2-one (**4e**)



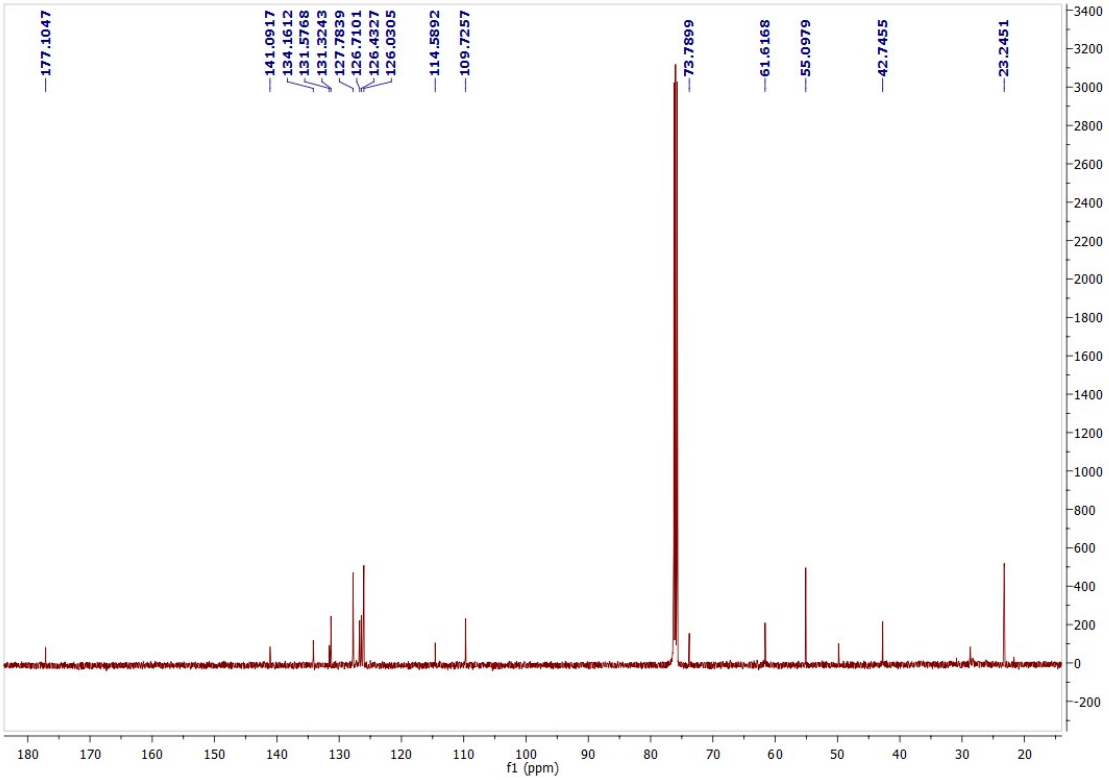
10. **^{13}C NMR** 1-Benzyl-5-bromo-3-hydroxy-3-(piperidin-1-ylmethyl)indolin-2-one (**4e**)



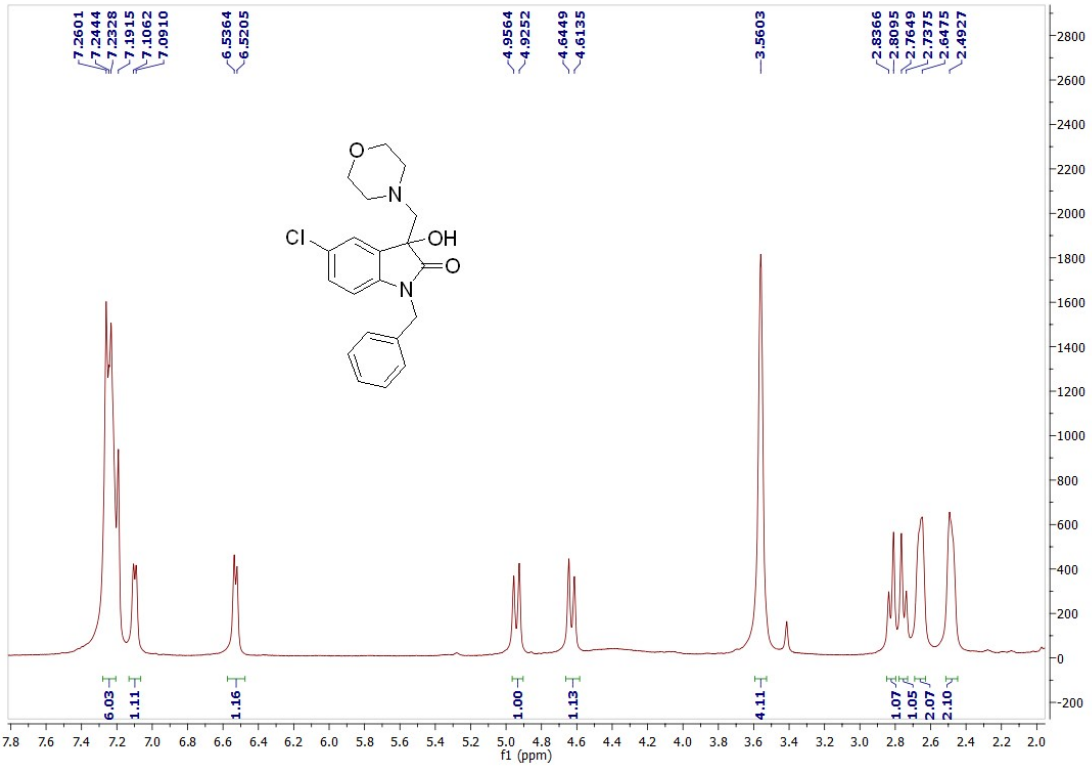
11. **^{1}H NMR** 1-Benzyl-5-bromo-3-hydroxy-3-(pyrrolidin-1-ylmethyl)indolin-2-one (**4f**)



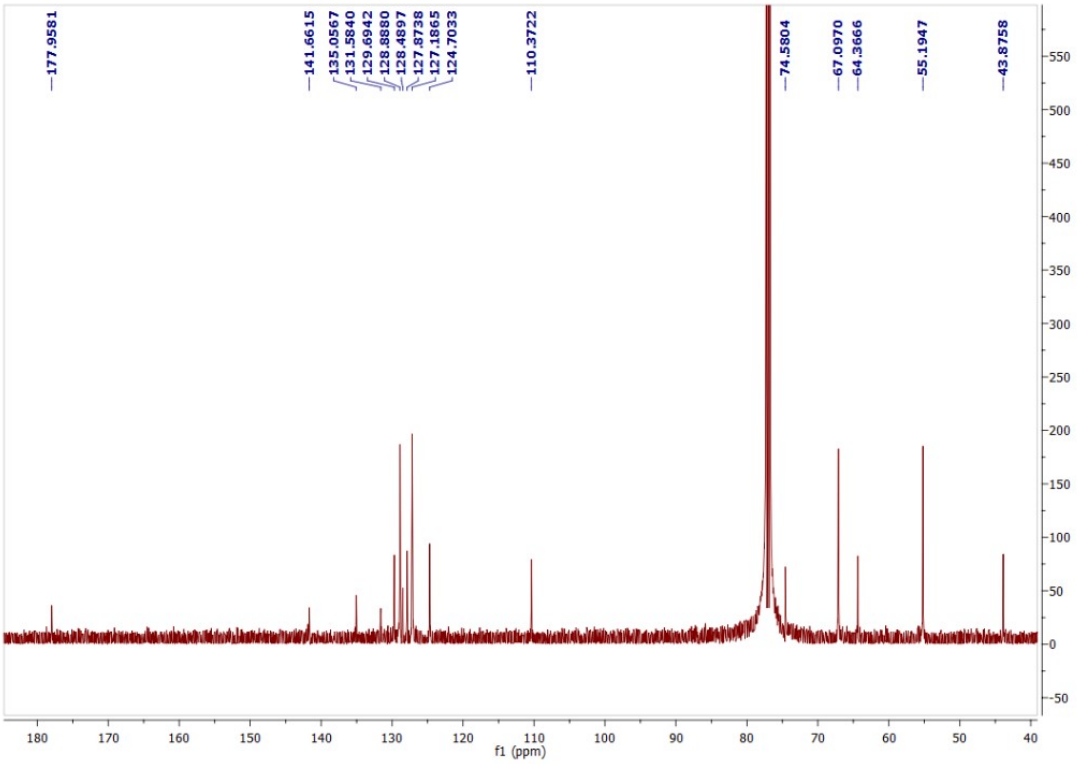
12. **^{13}C NMR** 1-Benzyl-5-bromo-3-hydroxy-3-(pyrrolidin-1-ylmethyl)indolin-2-one (**4f**)



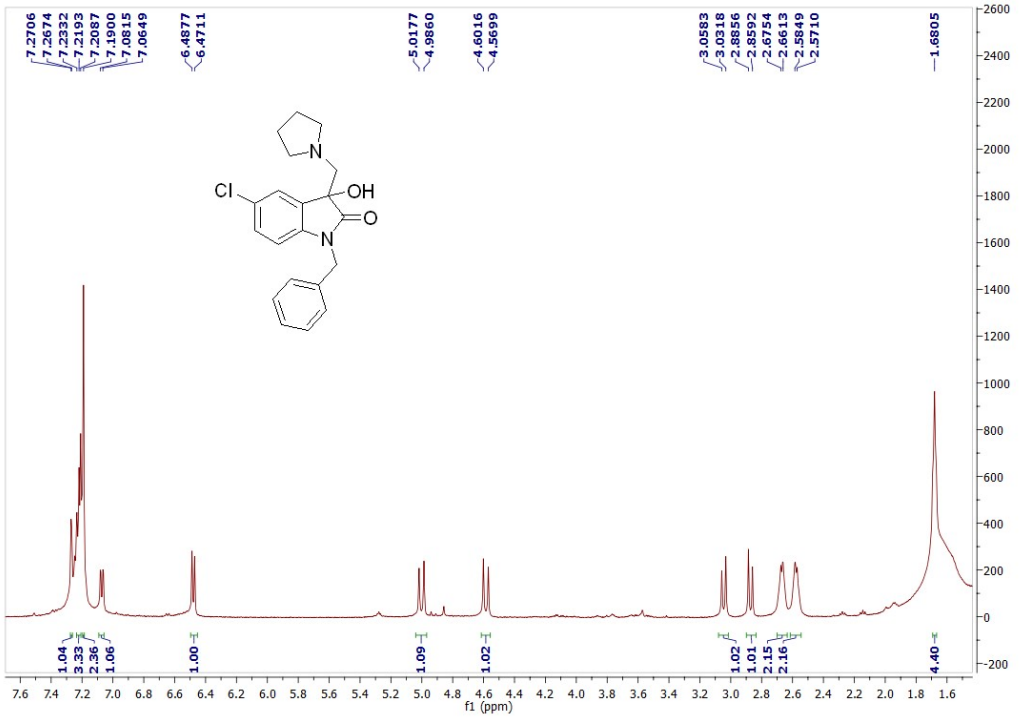
13. **^{1}H NMR** 1-Benzyl-5-chloro-3-hydroxy-3-(morpholinomethyl)indolin-2-one (**4g**)



14. **^{13}C NMR** 1-Benzyl-5-chloro-3-hydroxy-3-(morpholinomethyl)indolin-2-one (**4g**)



15. **^{1}H NMR** 1-Benzyl-5-chloro-3-hydroxy-3-(pyrrolidin-1-ylmethyl)indolin-2-one (**4i**)



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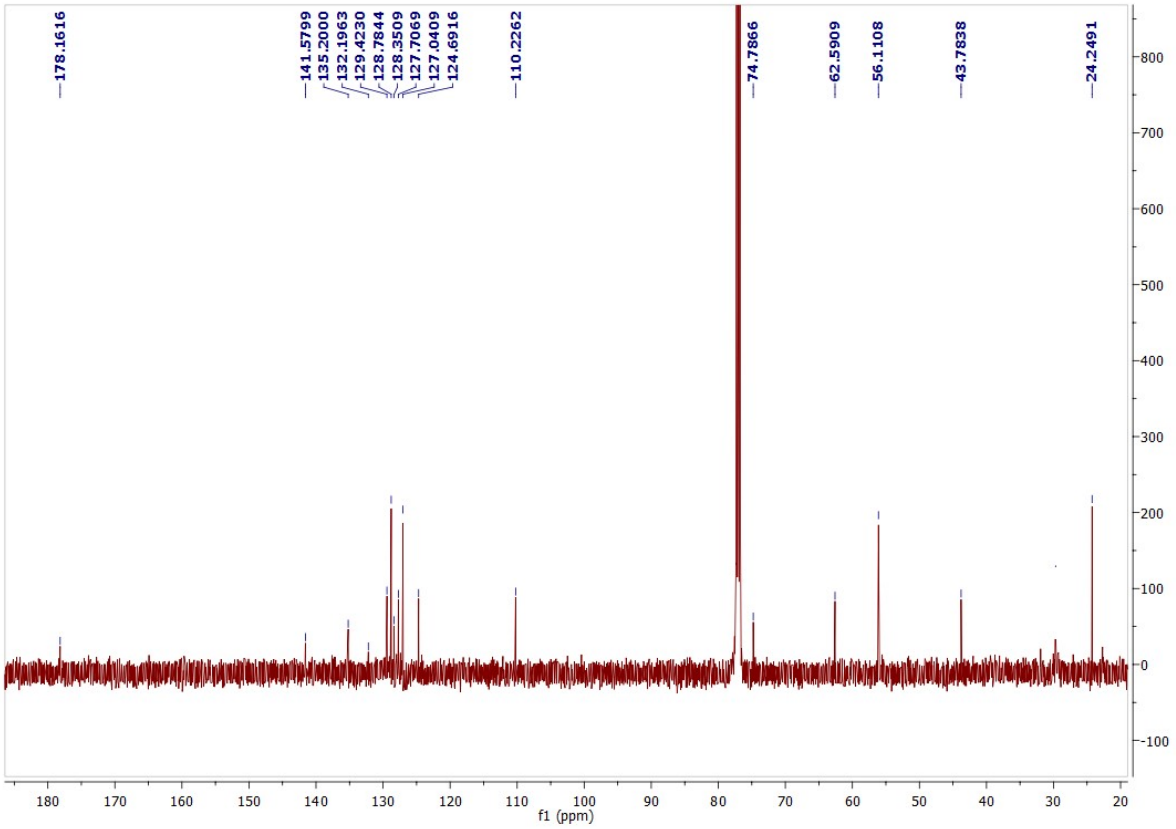
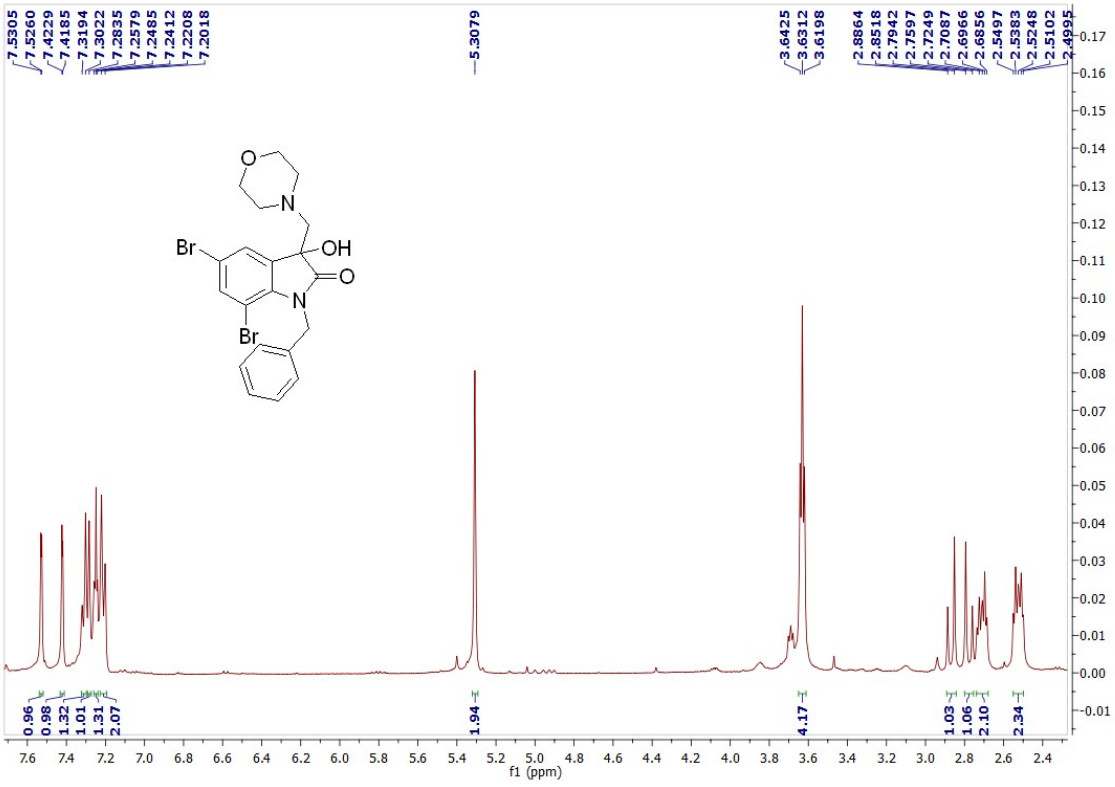
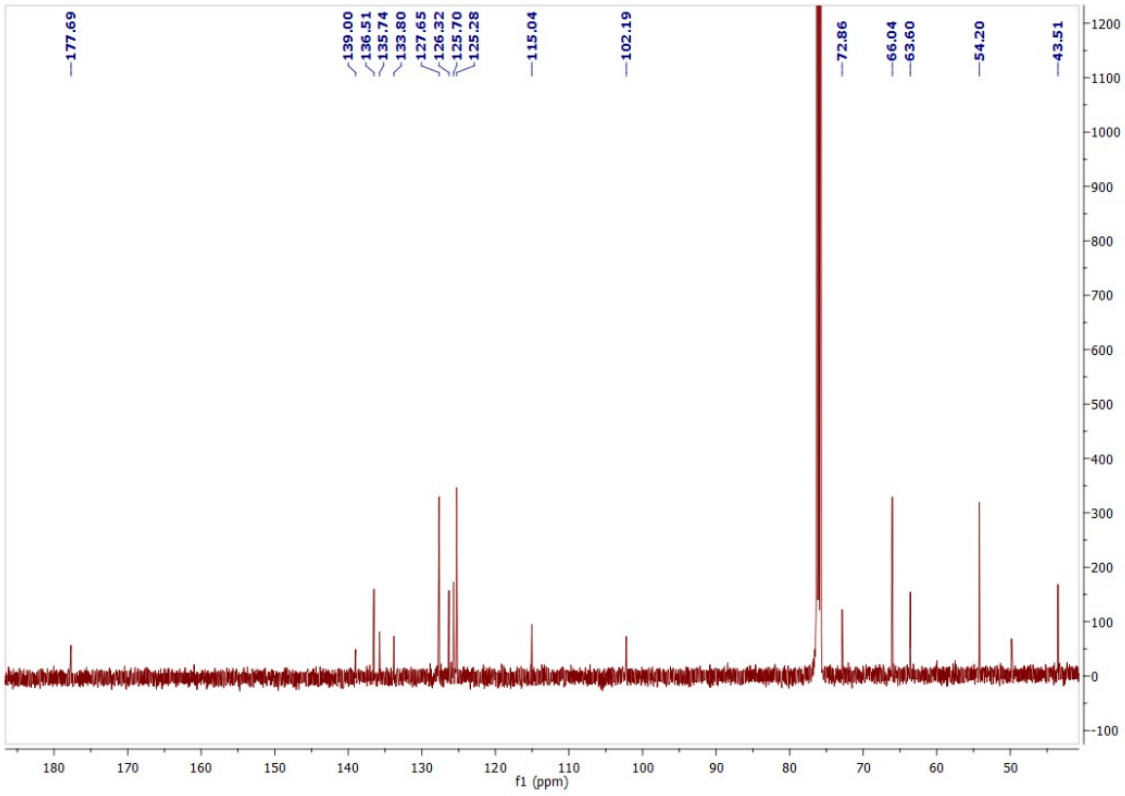
16. **^{13}C NMR** 1-Benzyl-5-chloro-3-hydroxy-3-(pyrrolidin-1-ylmethyl)indolin-2-one (**4i**)



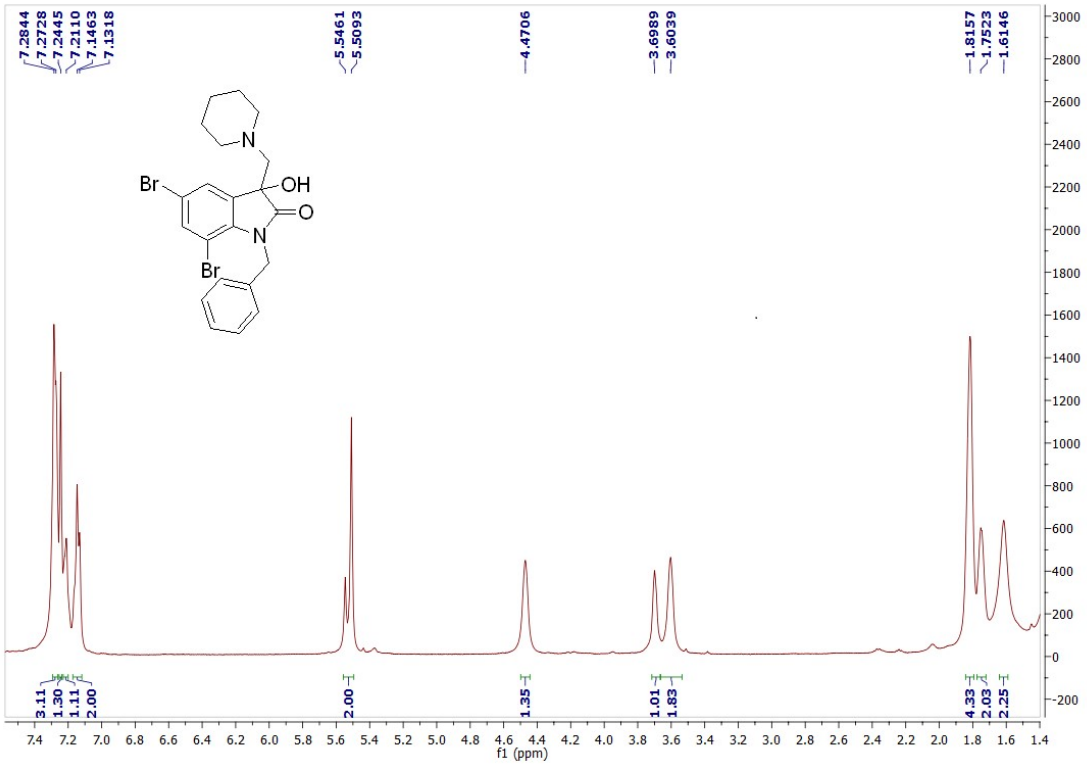
17. **^{1}H NMR** 1-Benzyl-5,7-dibromo-3-hydroxy-3-(morpholinomethyl)indolin-2-one (**4j**)



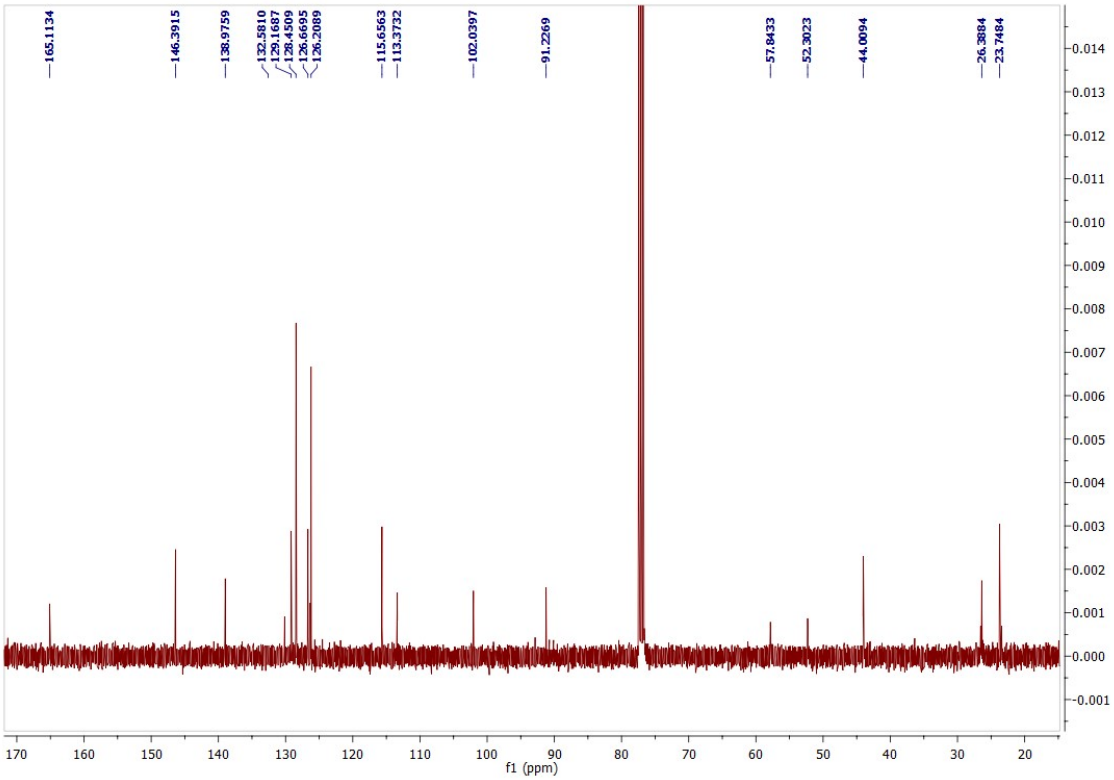
18. **^{13}C NMR** 1-Benzyl-5,7-dibromo-3-hydroxy-3-(morpholinomethyl)indolin-2-one (**4j**)



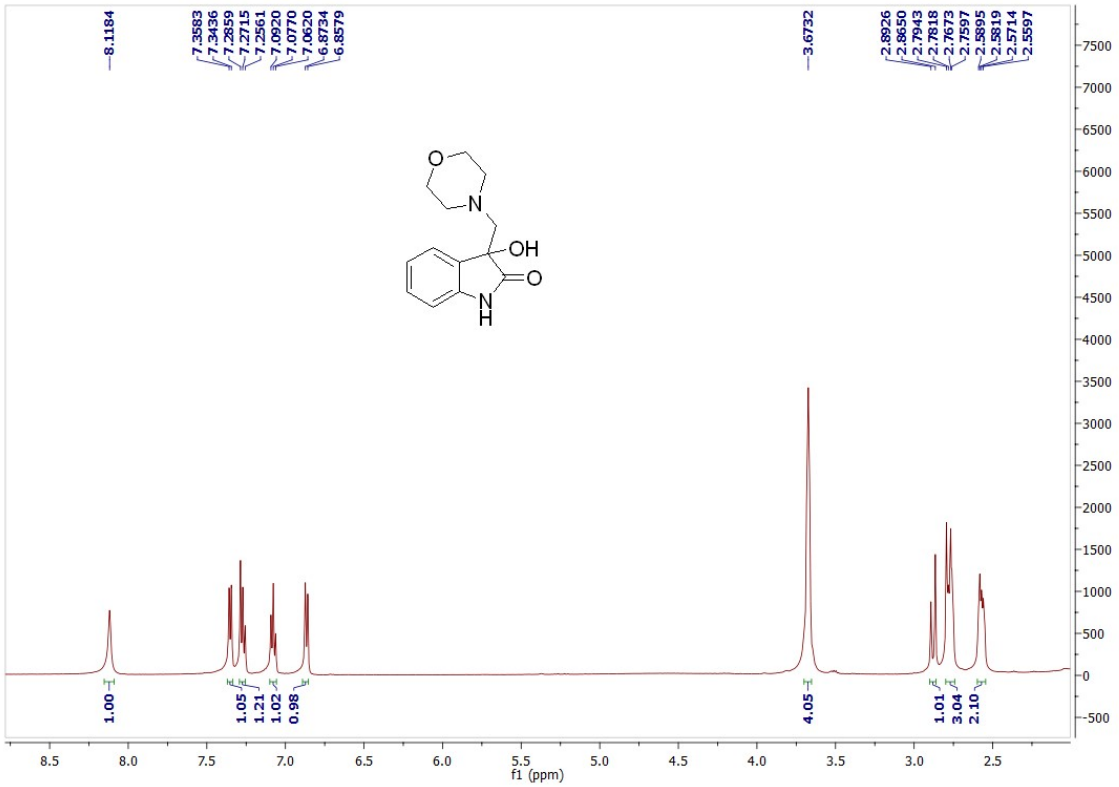
19. **^{1}H NMR** 1-Benzyl-5,7-dibromo-3-hydroxy-3-(piperidin-1-ylmethyl)indolin-2-one (**4k**)



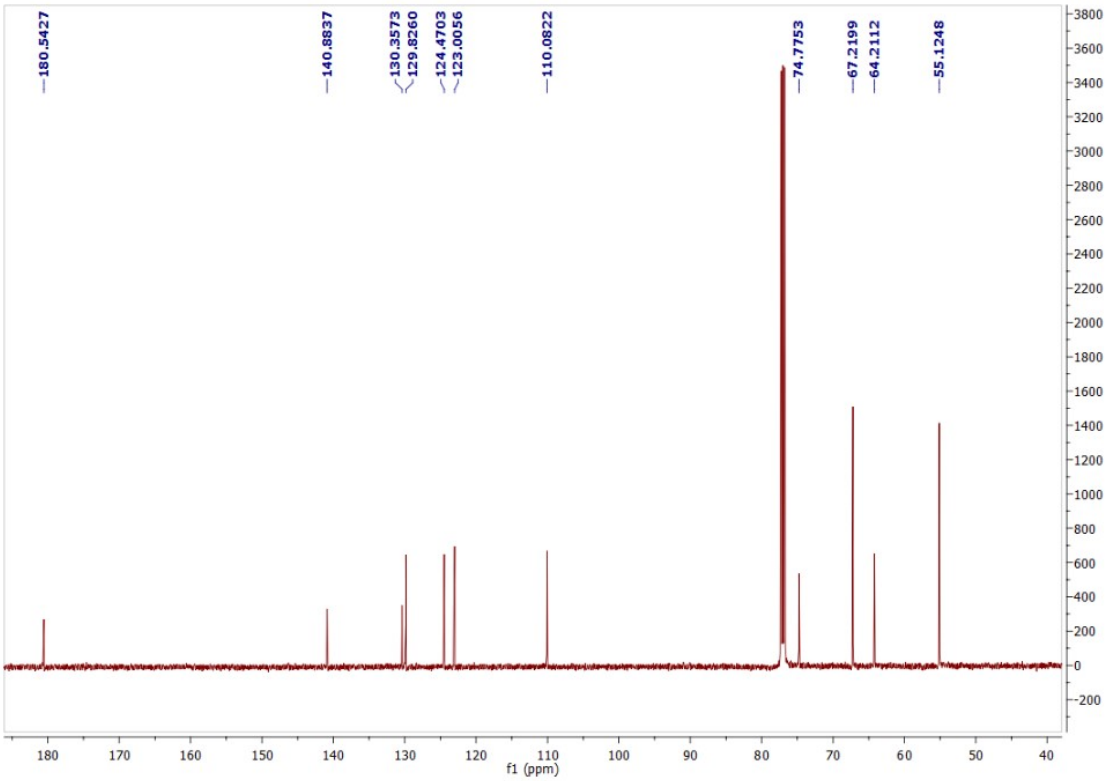
20. **^{13}C NMR** 1-Benzyl-5,7-dibromo-3-hydroxy-3-(piperidin-1-ylmethyl)indolin-2-one (**4k**)



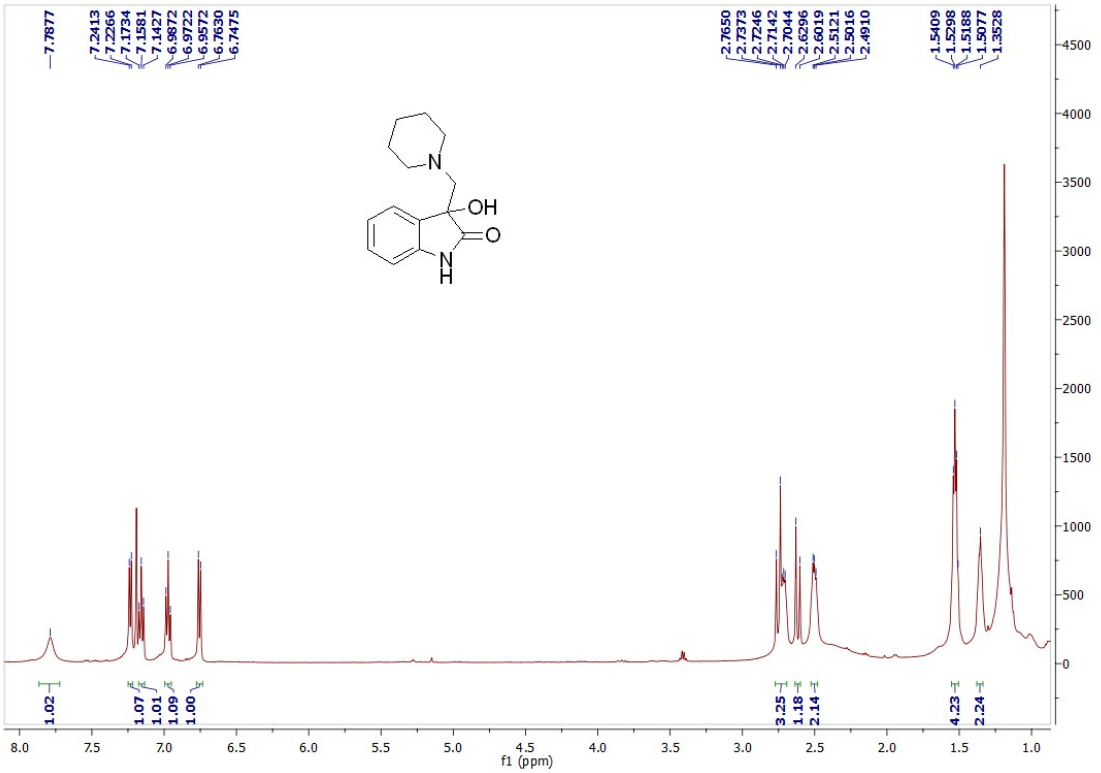
21. **^{1}H NMR** 3-Hydroxy-3-(morpholinomethyl)indolin-2-one (**4m**)



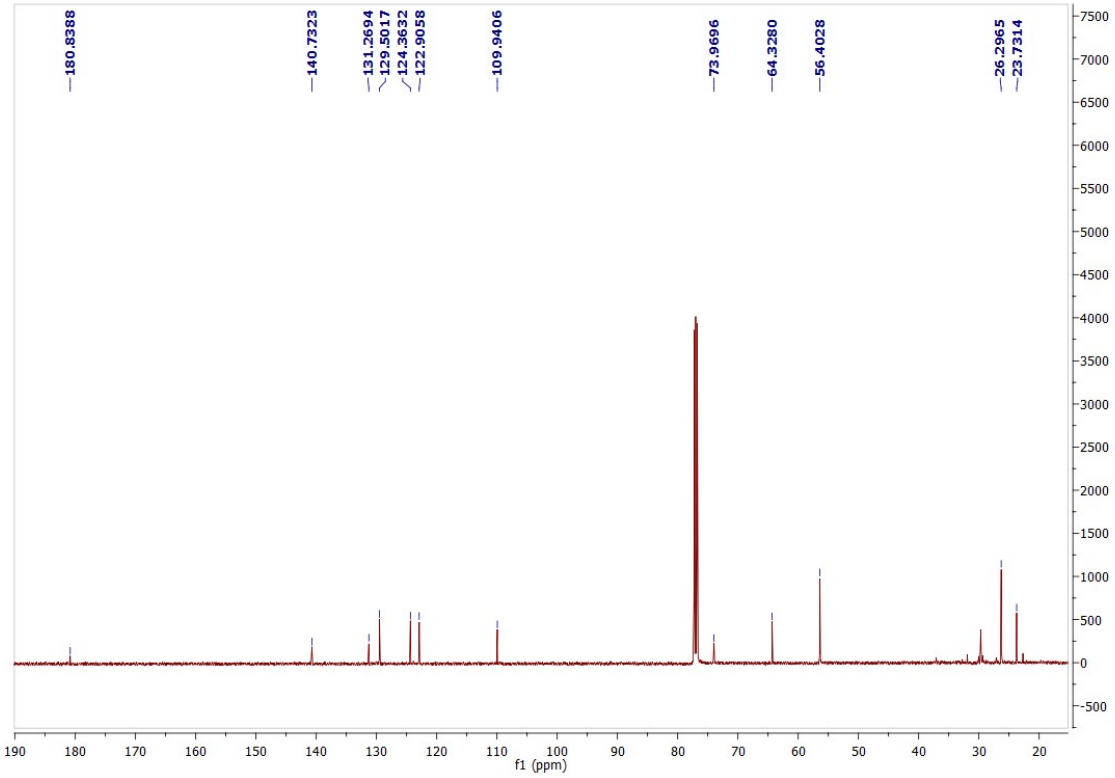
22. **^{13}C NMR** 3-Hydroxy-3-(morpholinomethyl)indolin-2-one (**4m**)



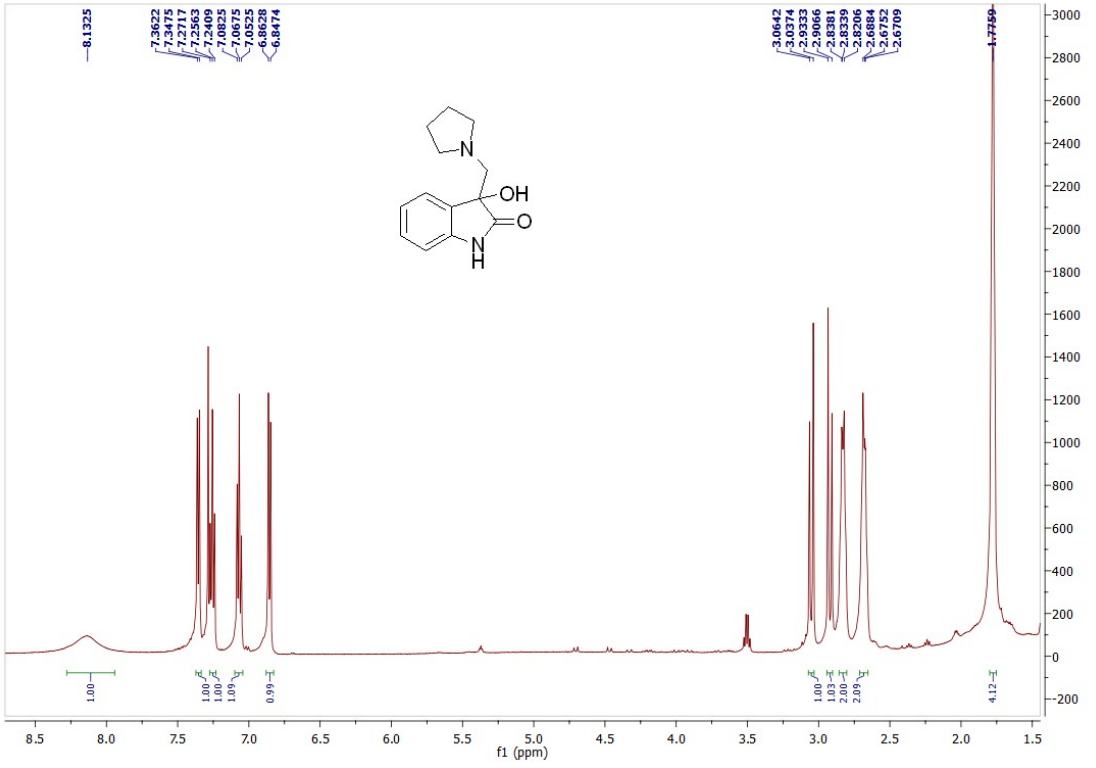
23. **^{1}H NMR** 3-Hydroxy-3-(piperidin-1-ylmethyl)indolin-2-one (**4n**)



24. **^{13}C NMR** 3-Hydroxy-3-(piperidin-1-ylmethyl)indolin-2-one (**4n**)



25. **^{1}H NMR** 3-Hydroxy-3-(pyrrolidin-1-ylmethyl)indolin-2-one (**4o**)



26. **^{13}C NMR** 3-ydroxy-3-(pyrrolidin-1-ylmethyl)indolin-2-one (**4o**)