Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Discovery of 3-chlorobenzyl linked 1,9-diazaspiro[5.5]undecane derivatives, a lead for Dengue virus type 2 infection.

Supporting Information.

Table S1. Computed inhibition constant (Ki) and binding free energy (kcal/mol) from the docking calculations.

Compound	NS5 protein (RDRP) (PDB ID: 2J7U)		dengue envelope (PDB ID: 1OKE)		Protease (PDB ID: 3U1i)		NS3/NS2B protein (PDB ID: 2FOM)		NS5 Methyltransferase (PDB ID: 1L9K)	
	Ki (μM)	kcal/ mol	Ki (μM)	kcal/ mol	Ki (μM)	kcal/ mol	Ki (μM)	kcal/ mol	Ki (μM)	kcal/mol
SPO-6	0.81	-8.31	0.37	-8.76	2.69	-7.60	0.26	8.96	0.20	-9.12
SPO-7	0.92	-8.23	1.07	-8.14	1.47	-7.96	0.30	-8.88	0.23	-9.03
SPO-13	1.28	-8.04	1.80	-7.84	1.97	-7.78	0.23	-9.04	0.15	-9.30
co-crystalized ligands	2.41	-3.57	103.0	-5.26	41.43	-5.98	11.50 mM	-2.65	0.663	-8.43

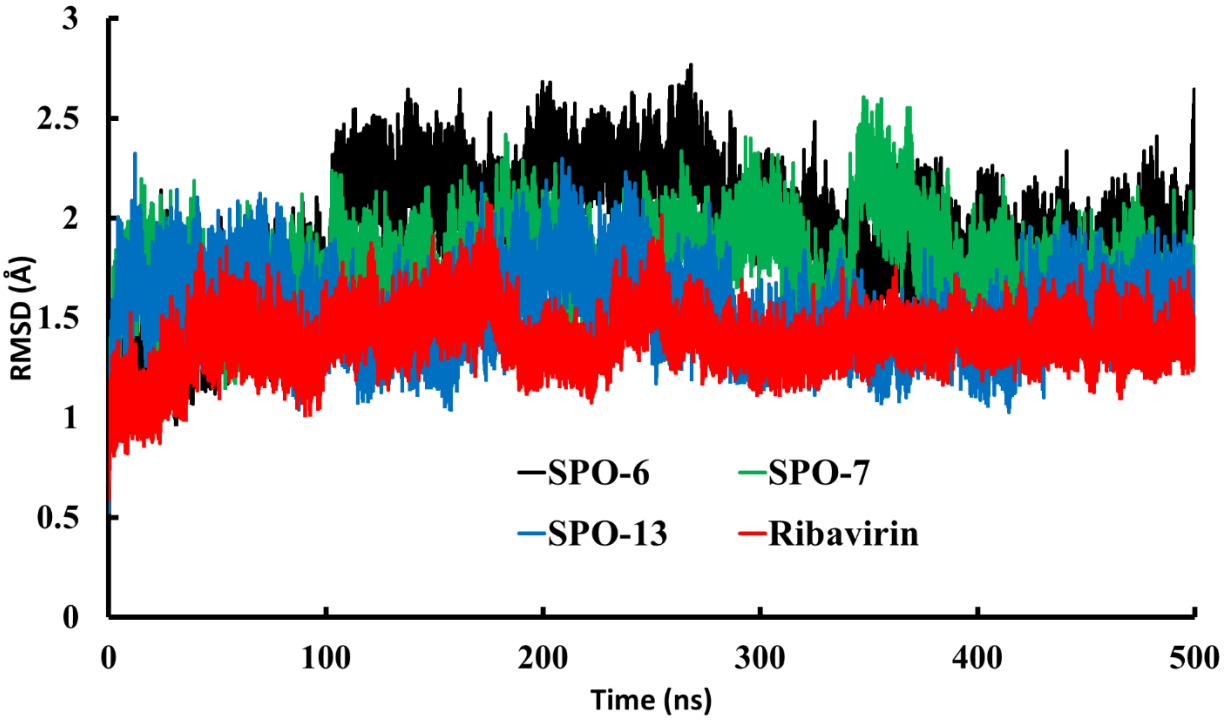


Figure S1. Root-mean-square deviation (RMSD) plots of the protein backbone atoms (N, C_α, and C) for the respective MD simulations relative to the first frame.

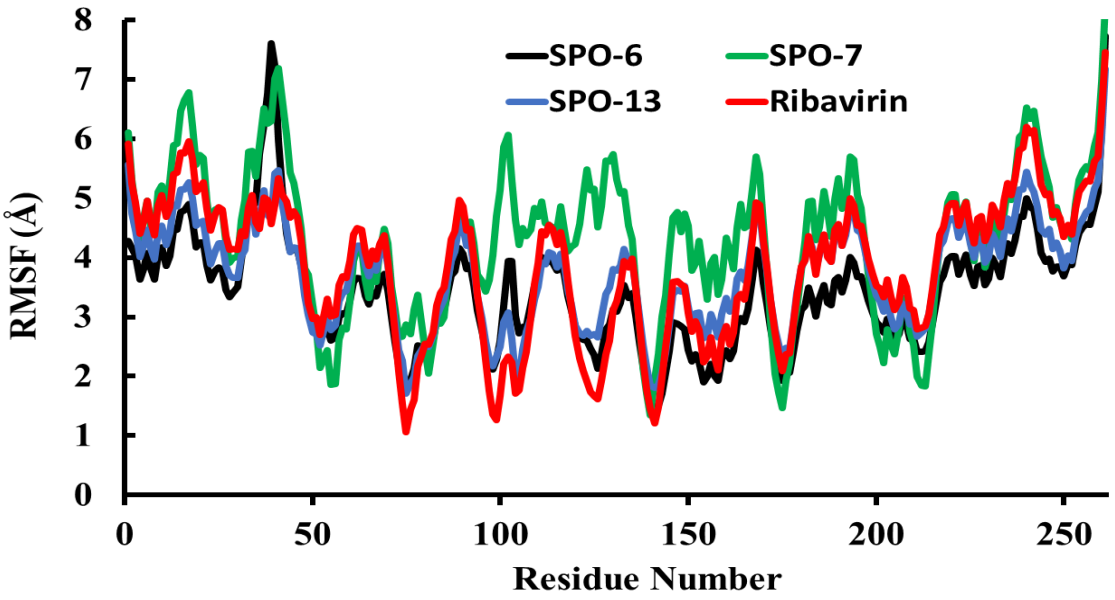
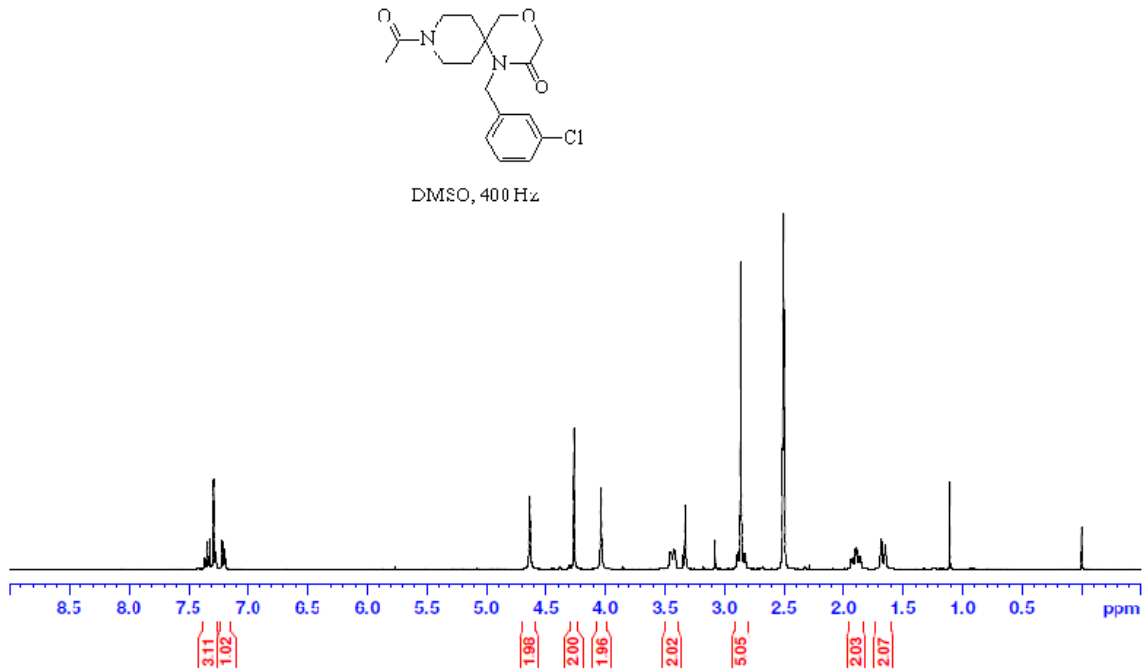
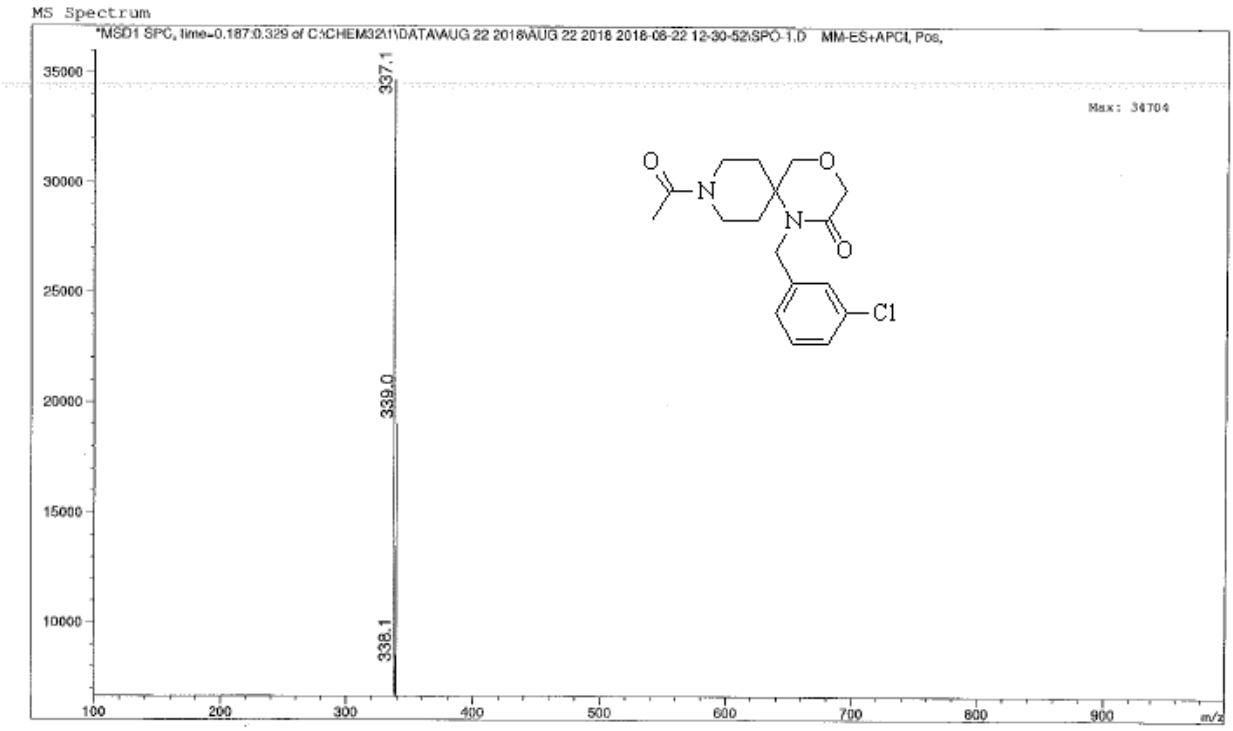


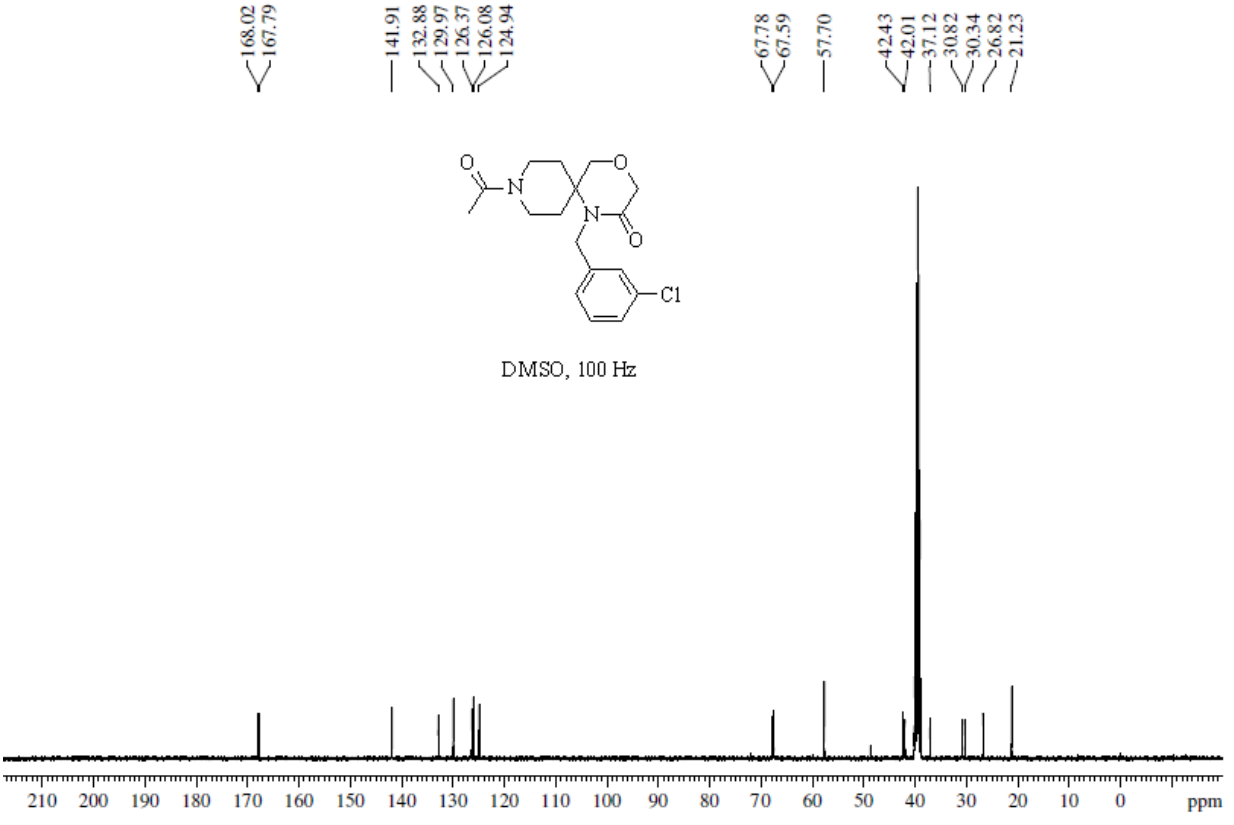
Figure S2. Root-mean-square fluctuation (RMSF) plot by residue for the NS5-methyltransferase-ligand complexes using backbone atoms (C, C_α, and N) relative to the lowest energy structure from MD simulations.



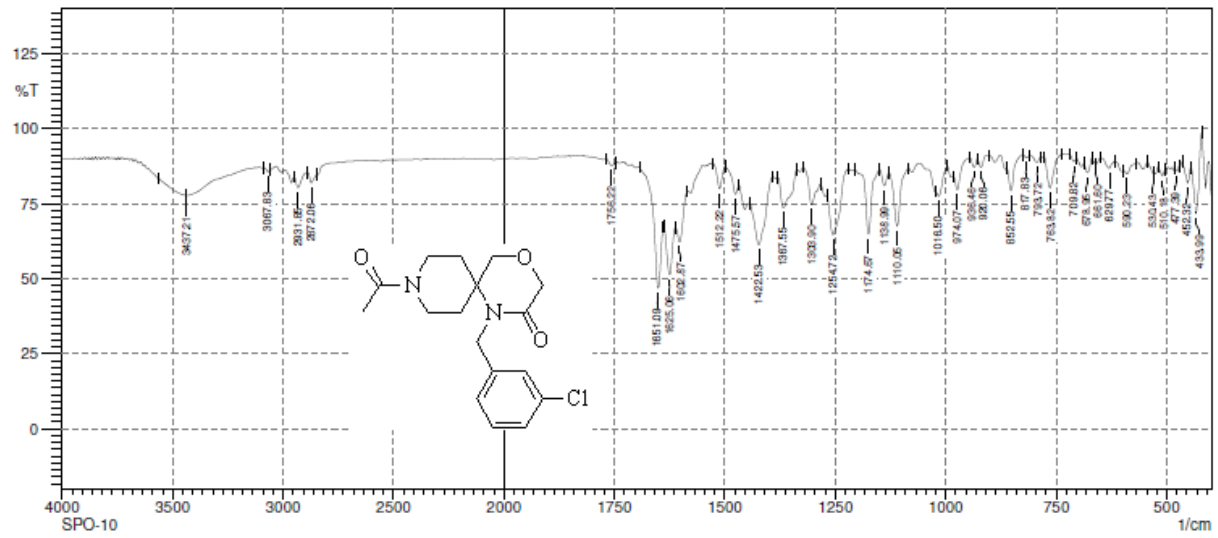
^{1}H NMR spectrum of **SPO-1**



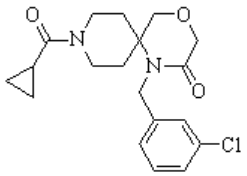
MS spectrum of **SPO-1**



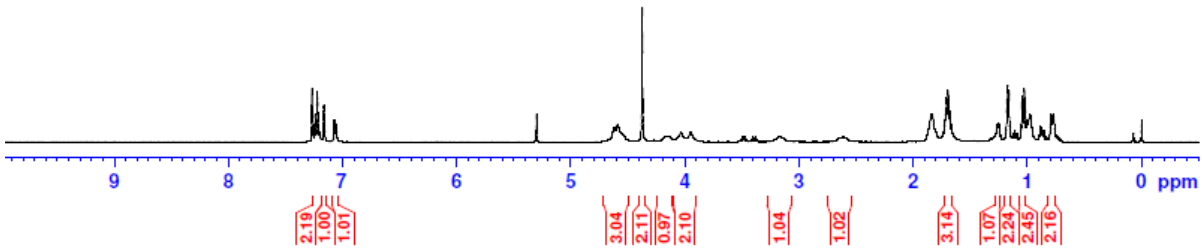
^{13}C-NMR spectrum of **SPO-1**



IR spectrum of **SPO-1**



$CDCl_3$, 400 Hz



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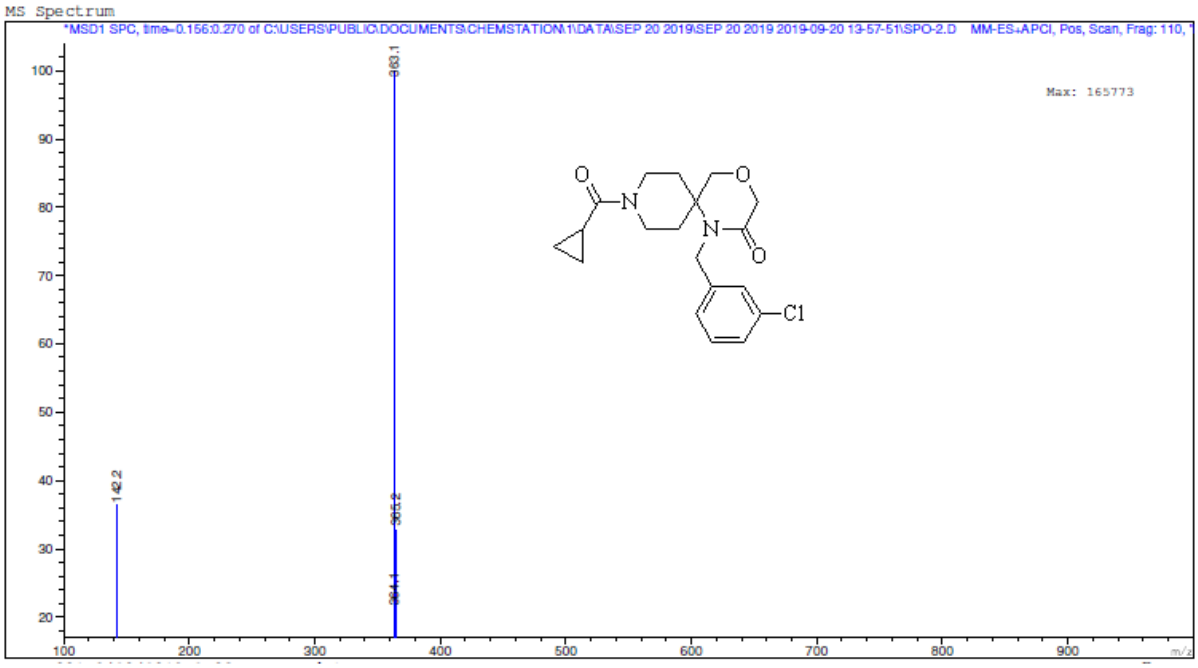
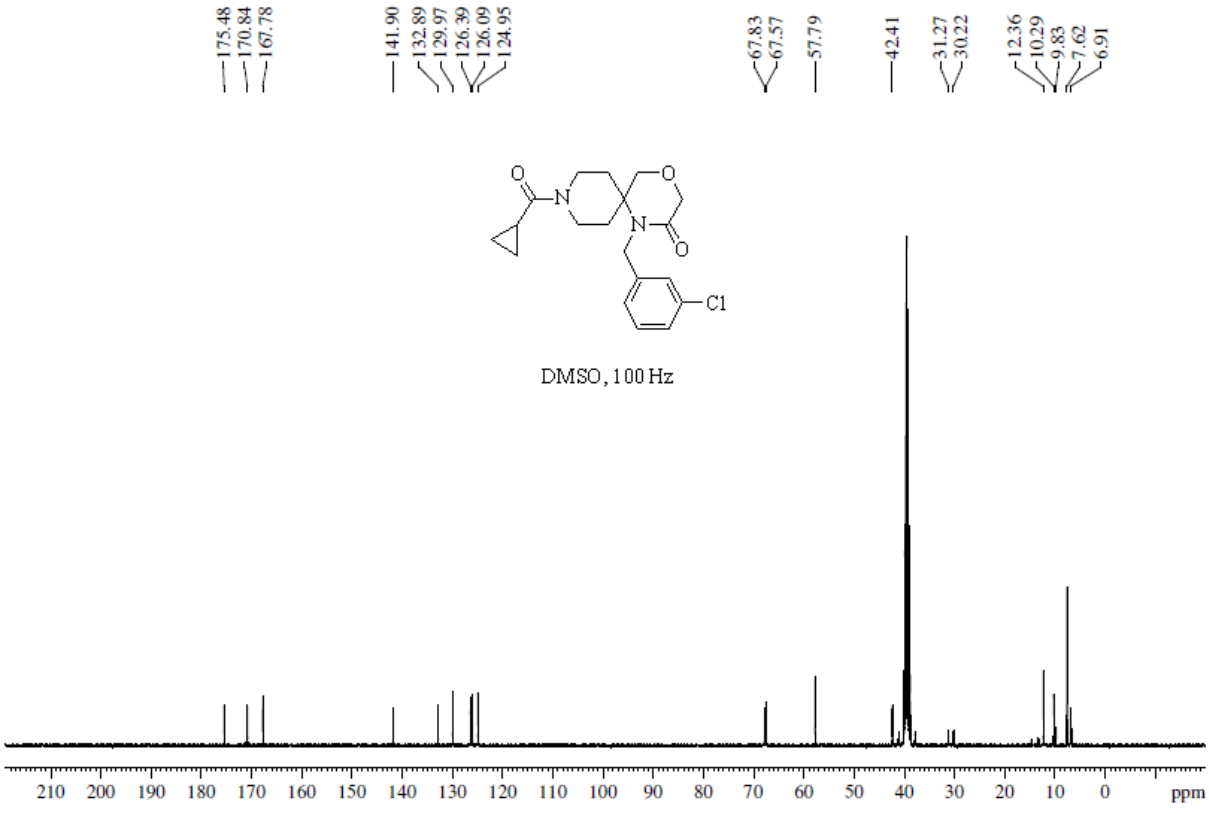
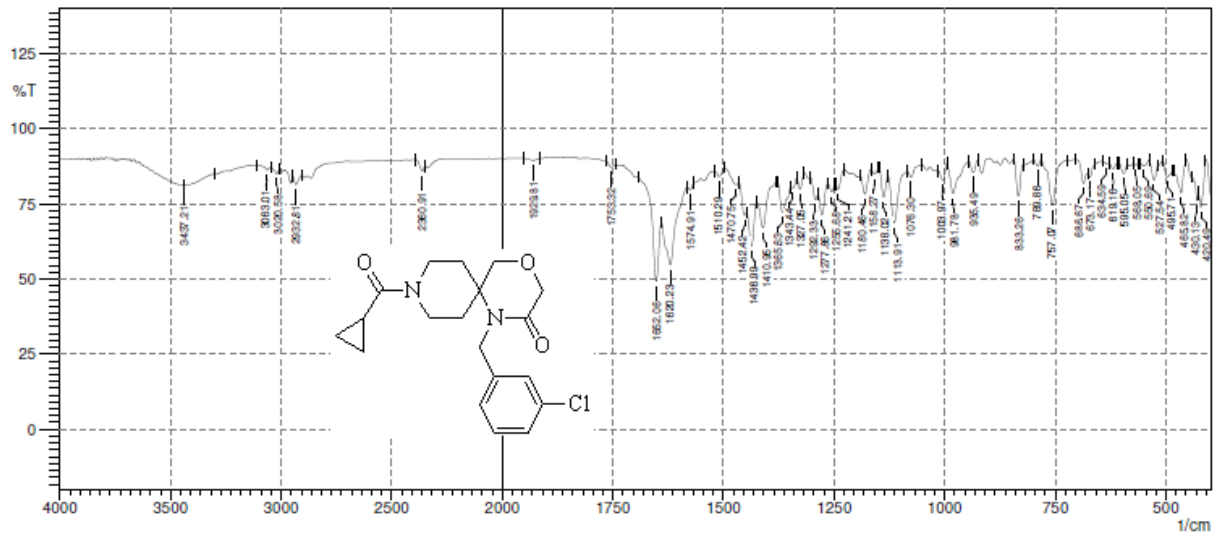


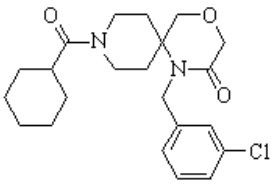
MS spectrum of **SPO-2**



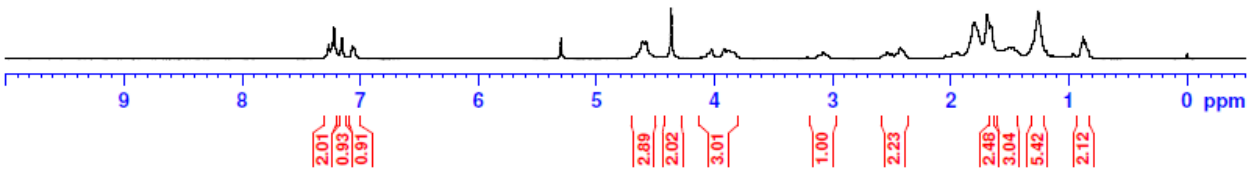
^{13}C-NMR spectrum of **SPO-2**



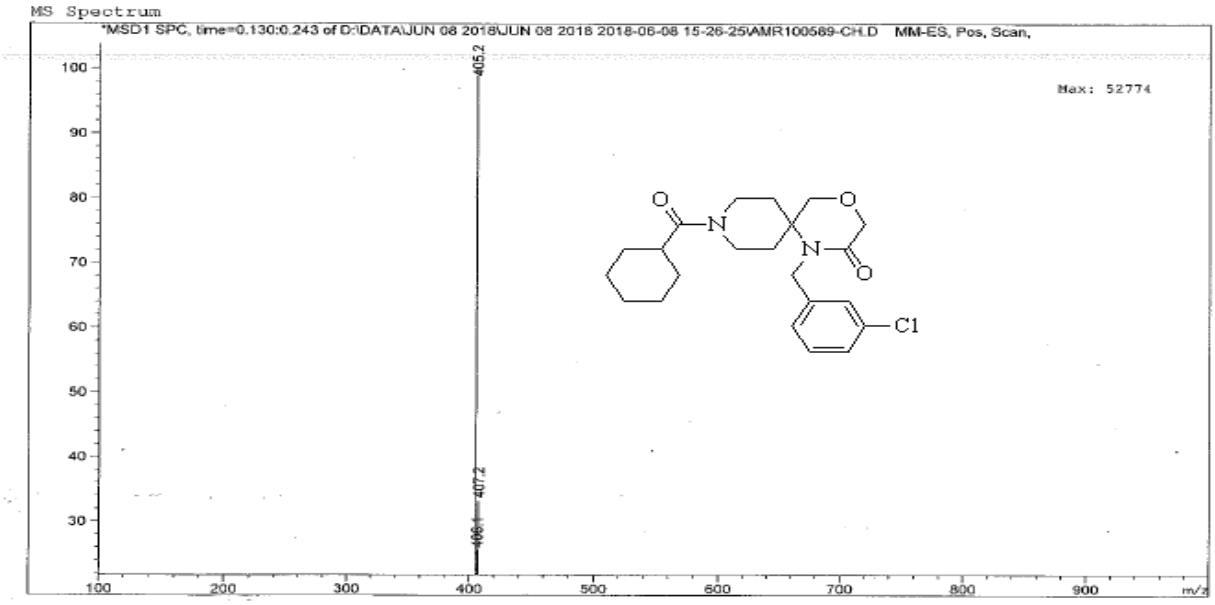
IR spectrum of **SPO-2**



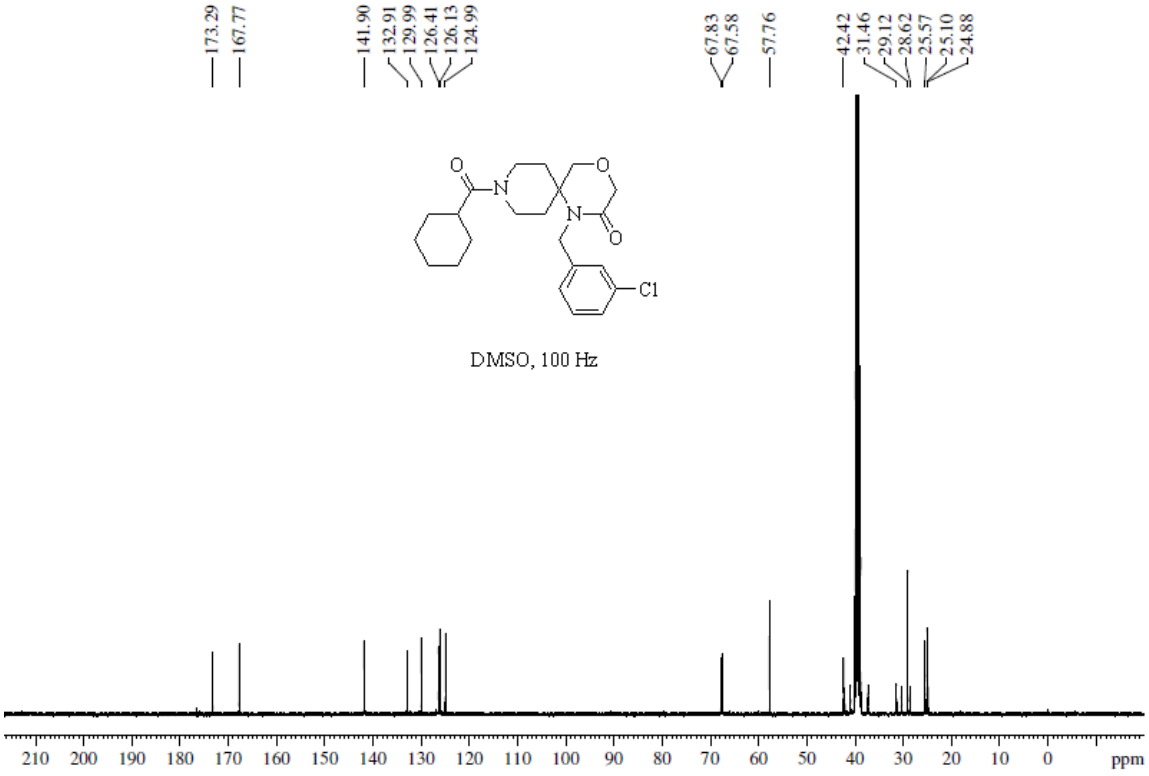
$CDCl_3$, 400 Hz



^{1}H-NMR spectrum of **SPO-3**



MS spectrum of **SPO-3**



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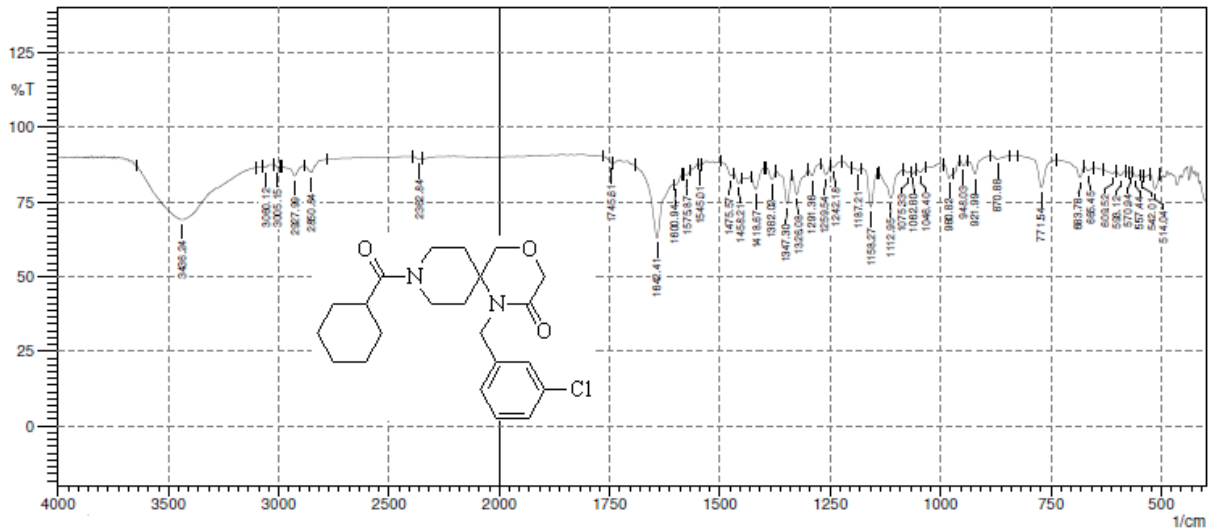
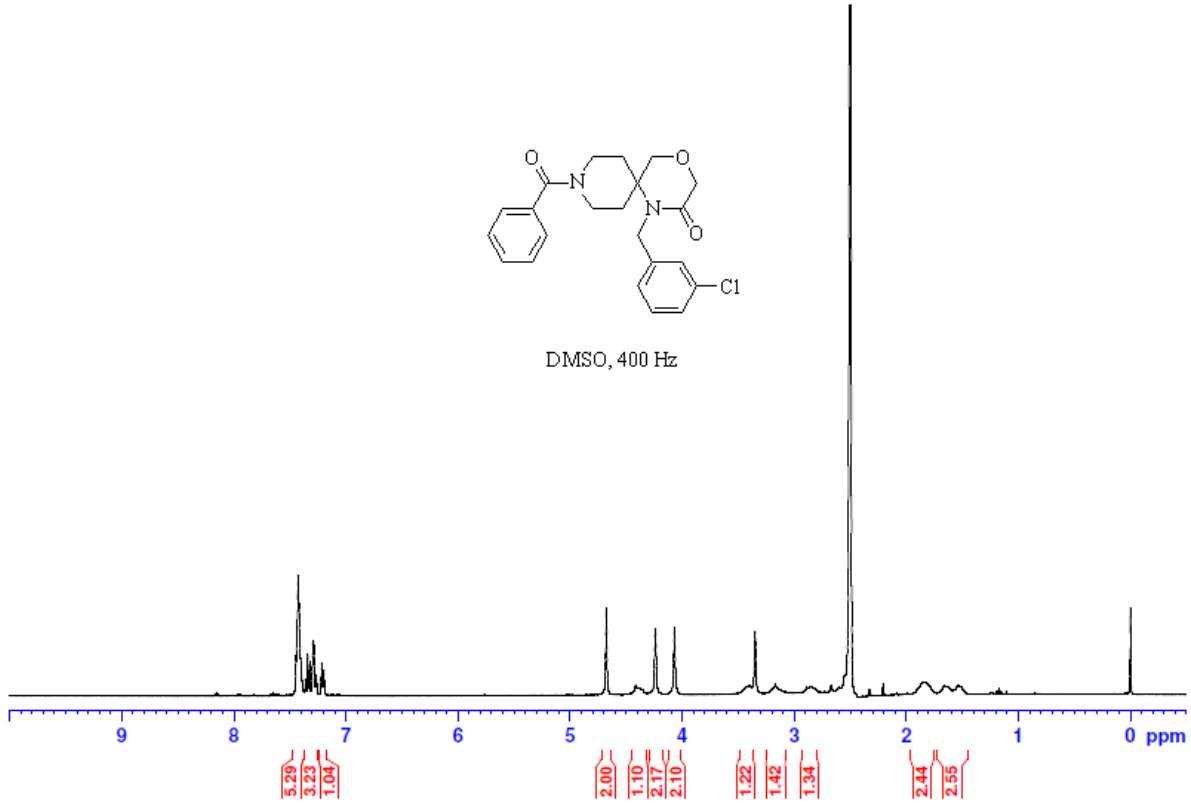
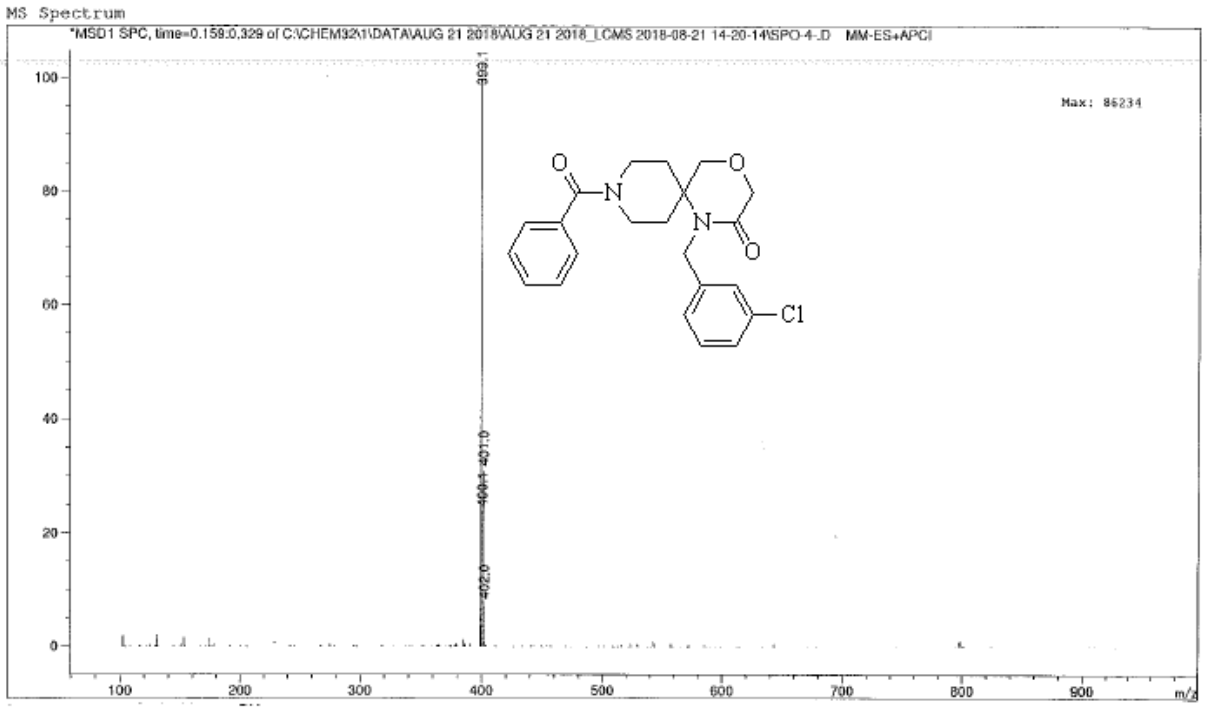


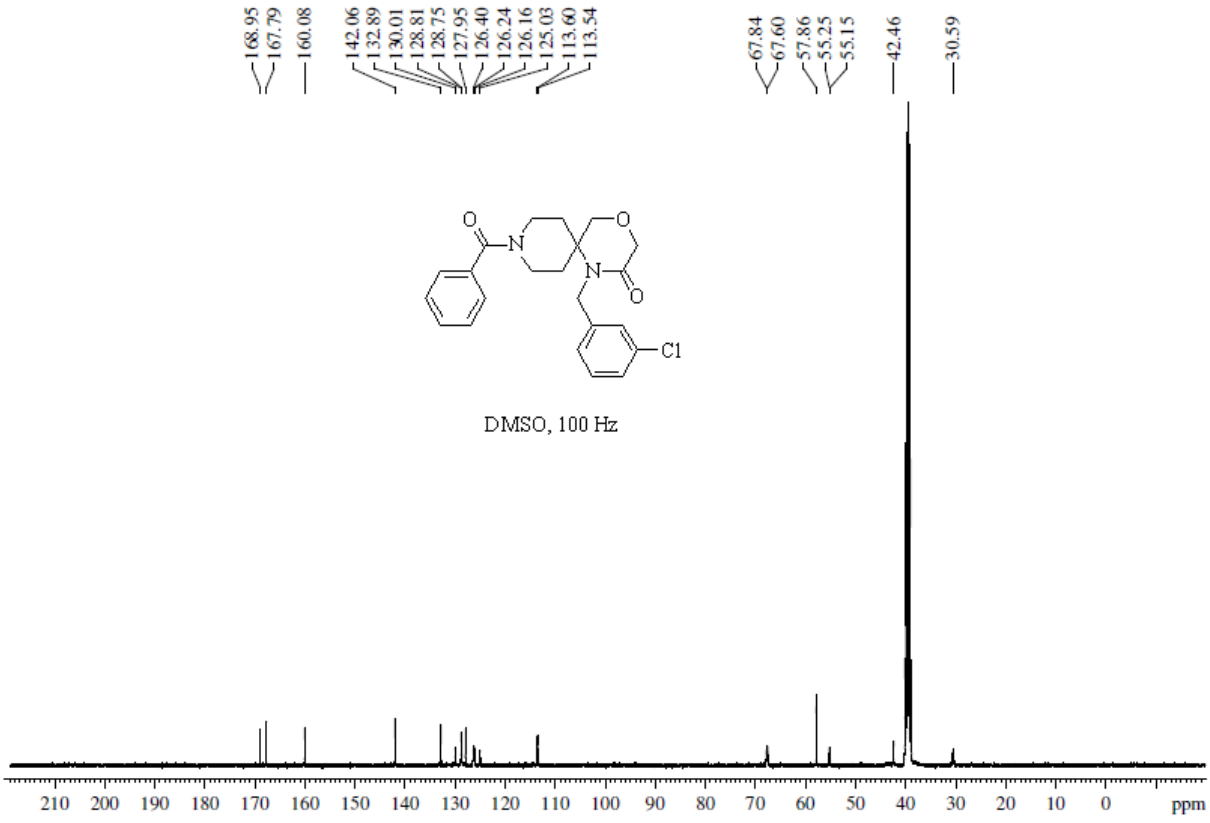
IR spectrum of **SPO-3**



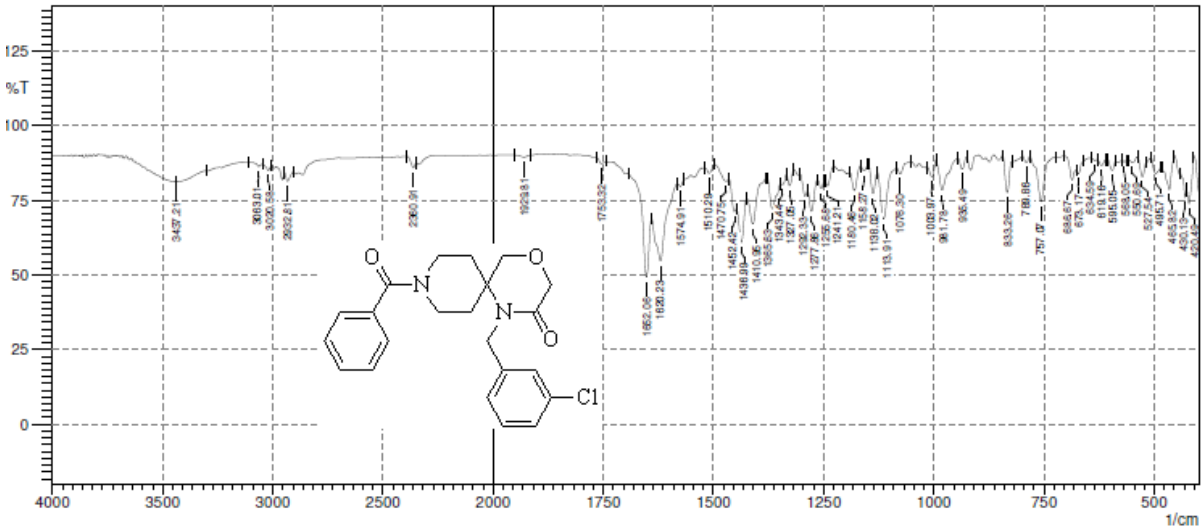
^{1}H-NMR spectrum of **SPO-4**



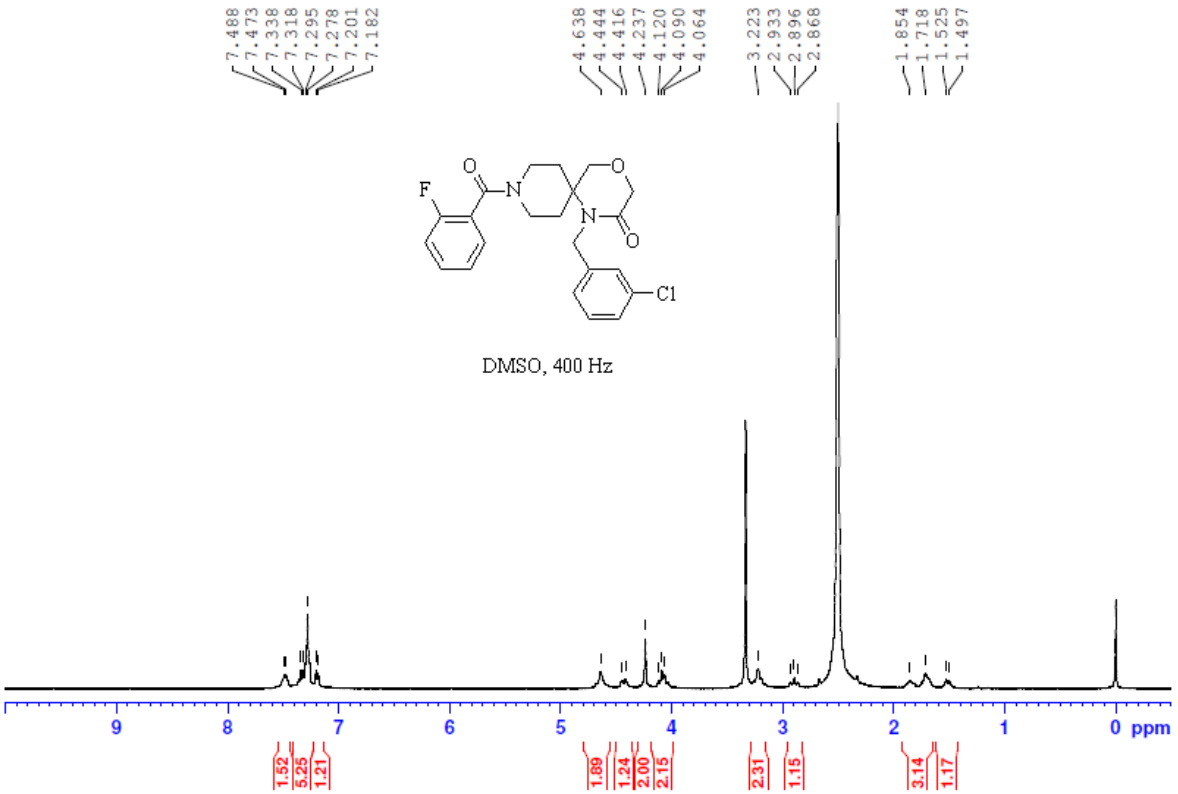
MS spectrum of **SPO-4**



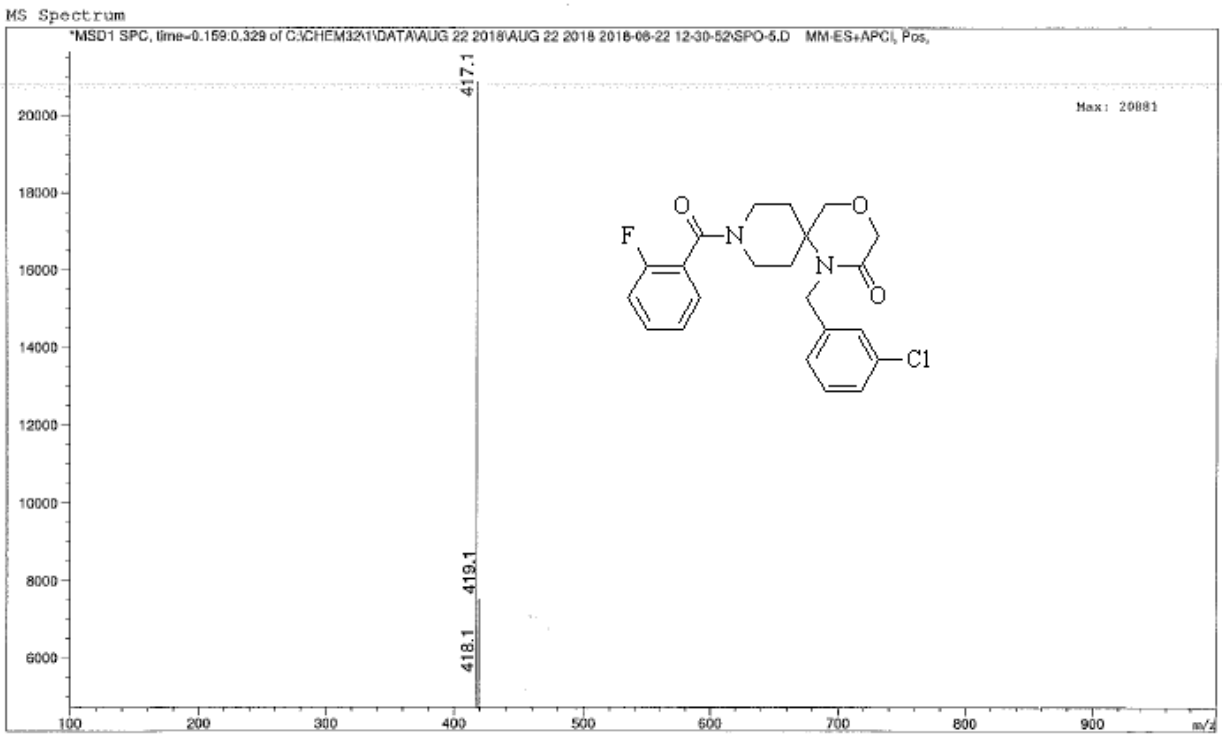
^{13}C-NMR spectrum of **SPO-4**



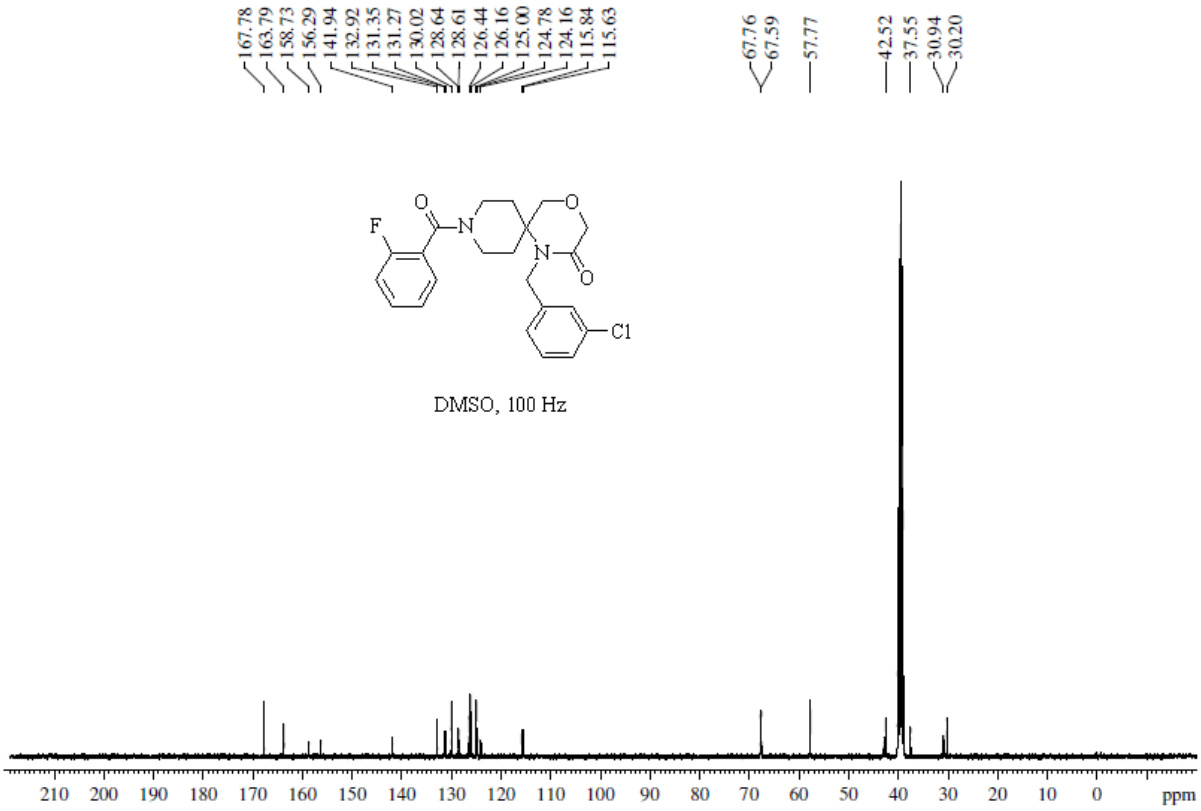
IR spectrum of **SPO-4**



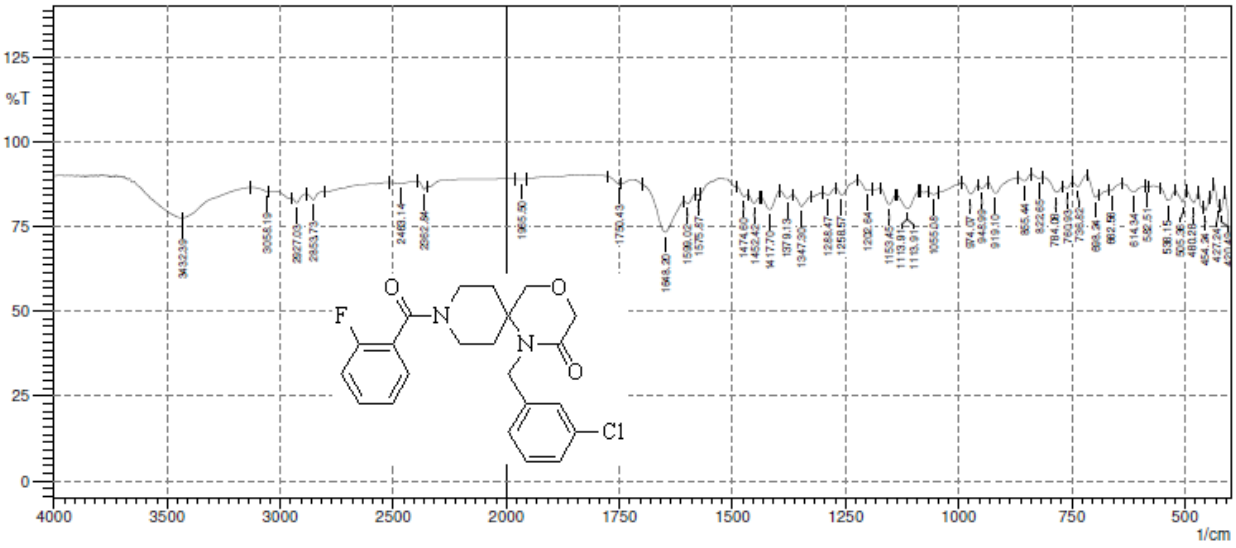
^{1}H-NMR spectrum of **SPO-5**



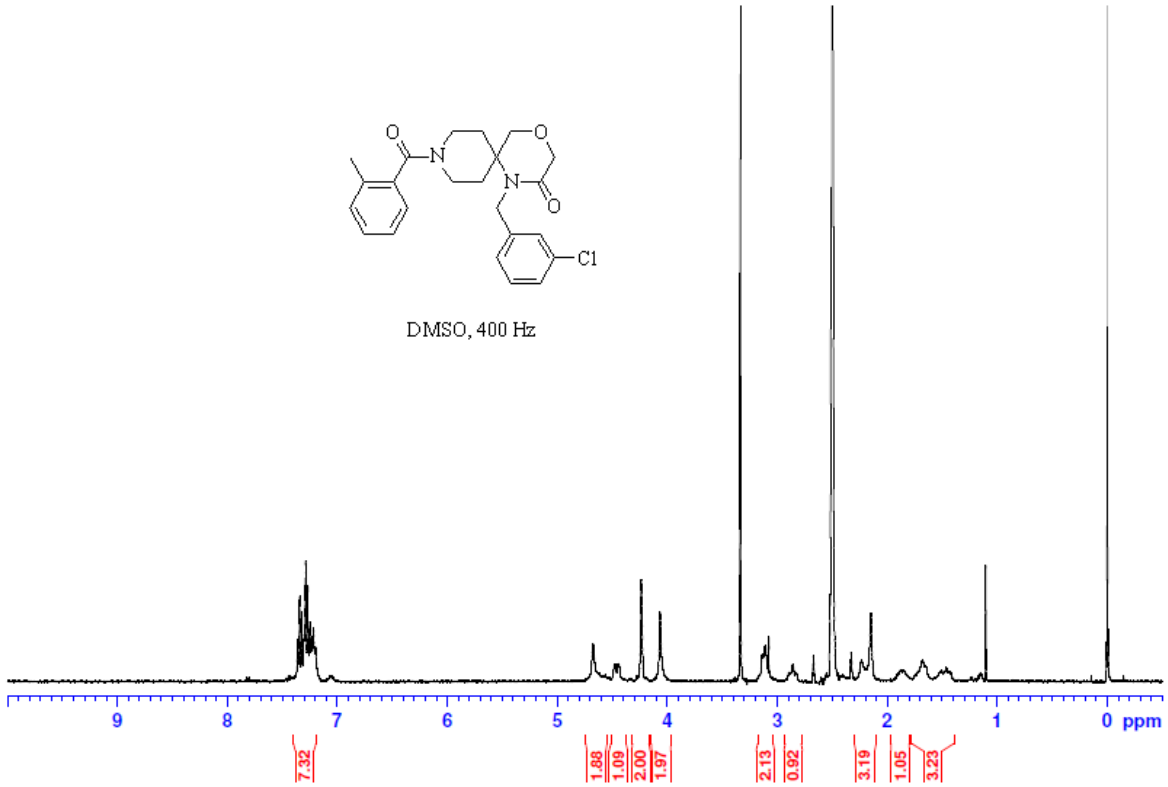
MS spectrum of **SPO-5**



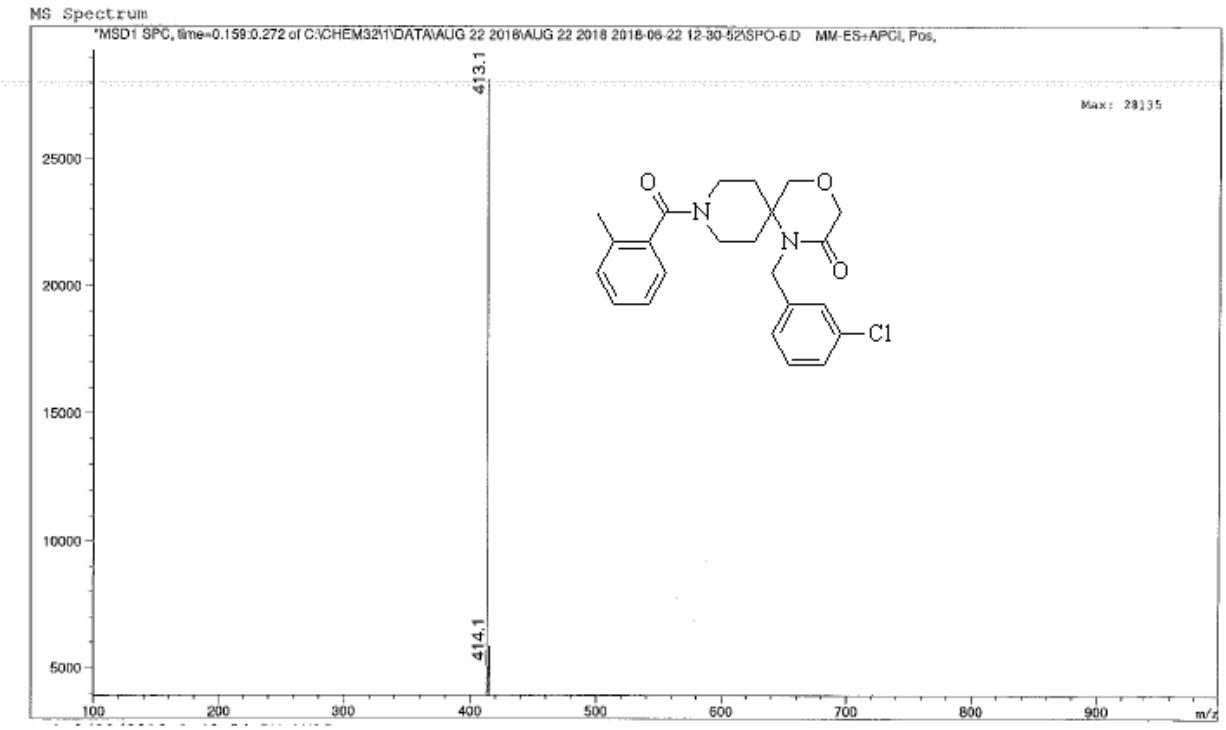
^{13}C-NMR spectrum of **SPO-5**



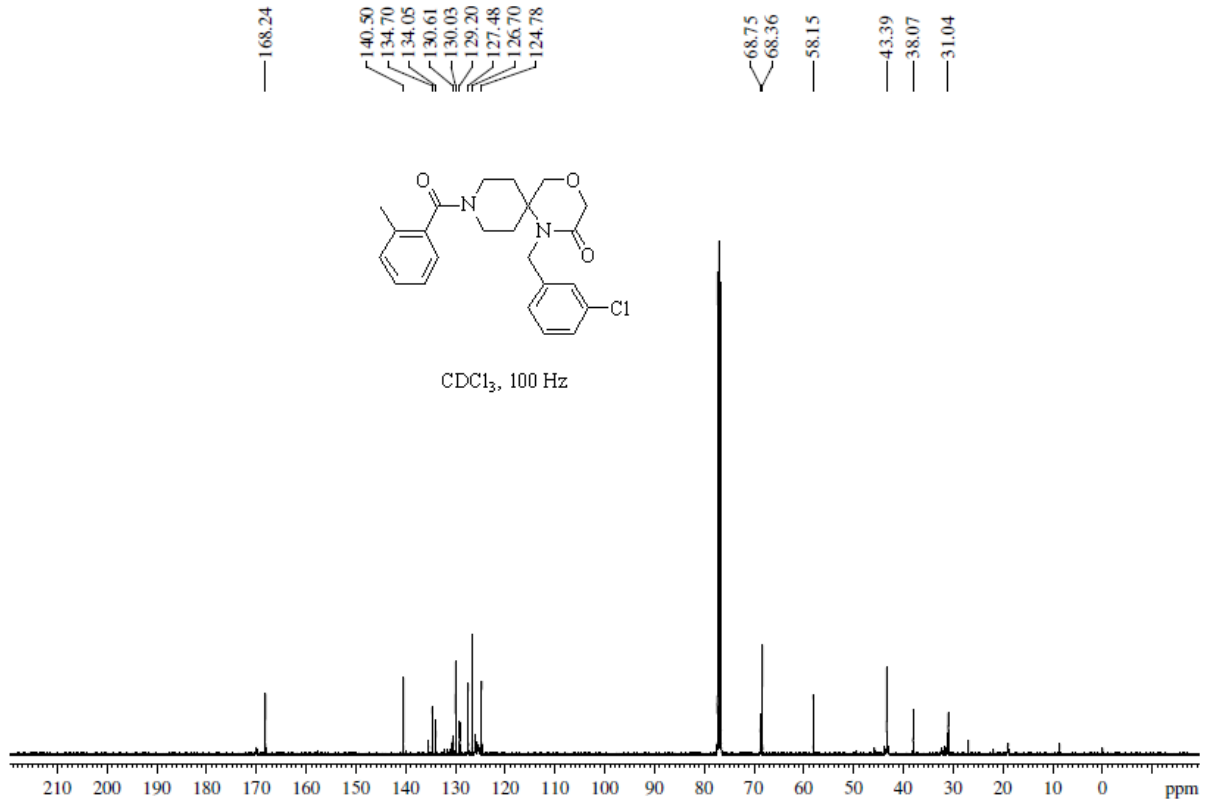
IR spectrum of **SPO-5**



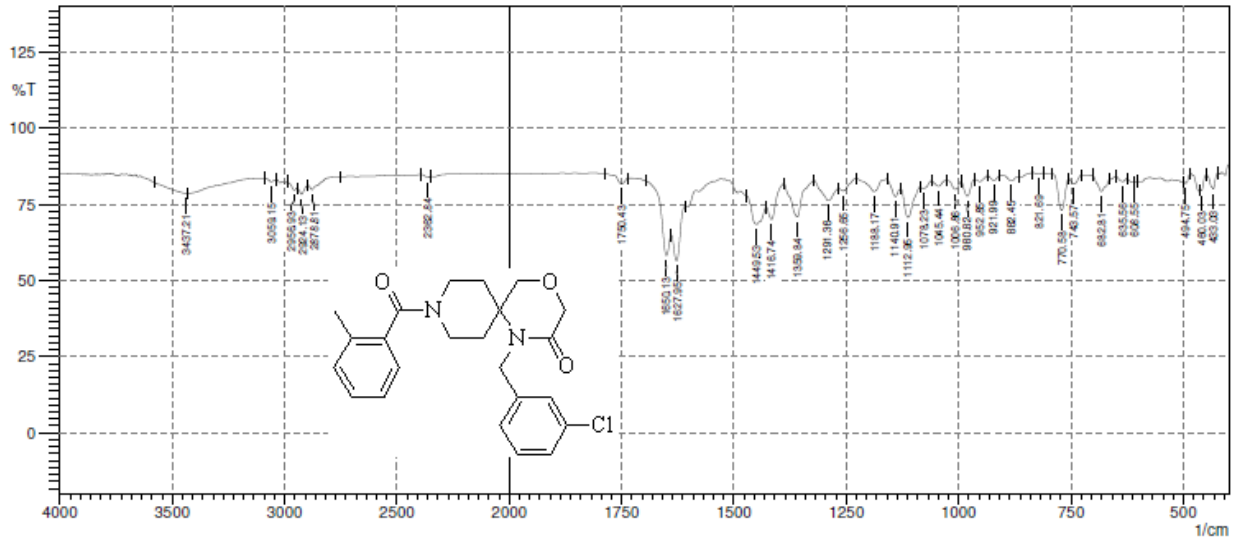
^{1}H-NMR spectrum of **SPO-6**



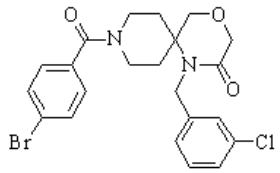
MS spectrum of **SPO-6**



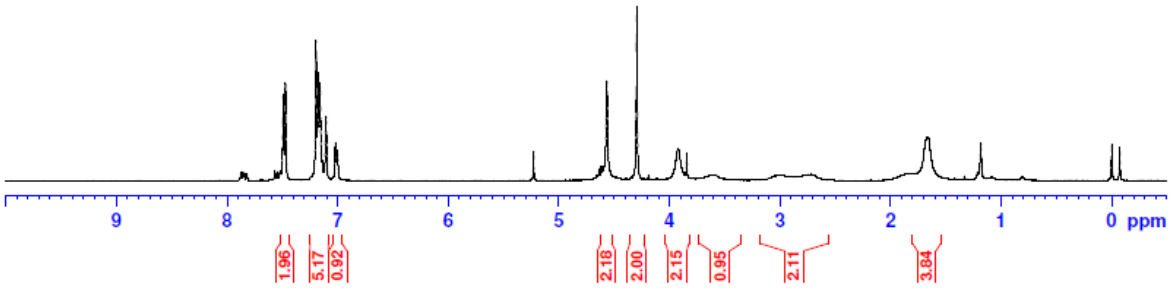
^{13}C-NMR spectrum of **SPO-6**



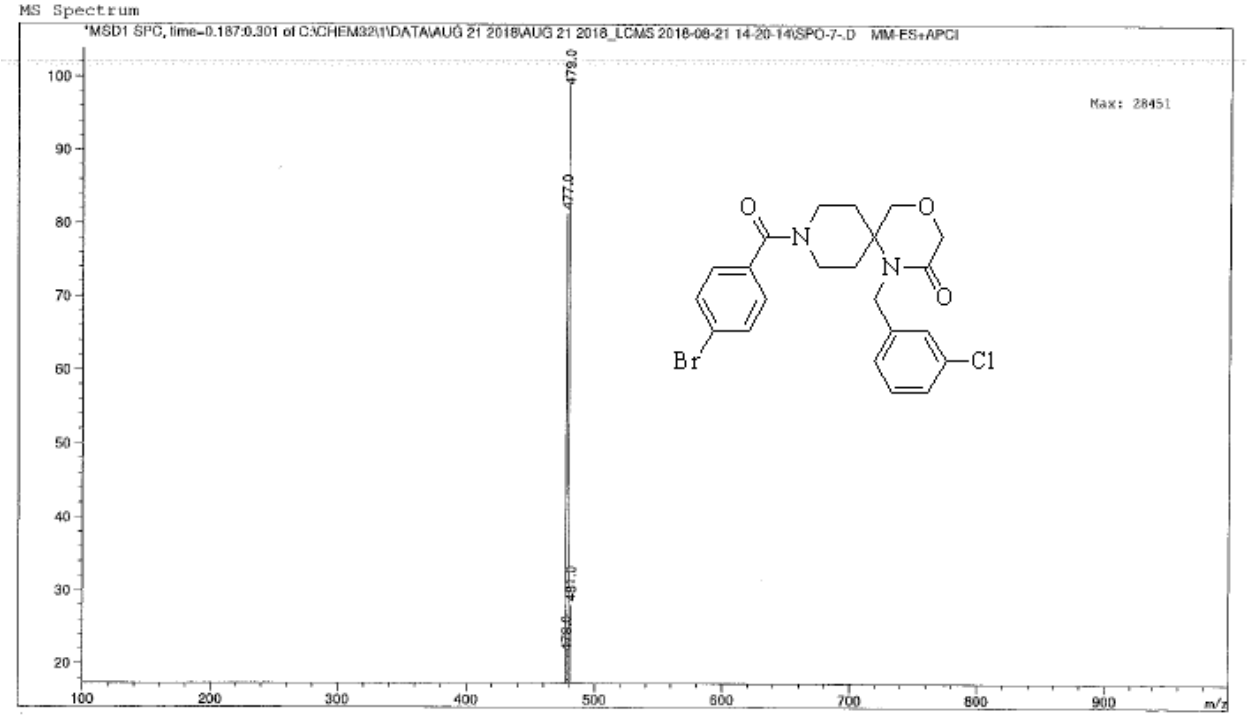
IR spectrum of **SPO-6**



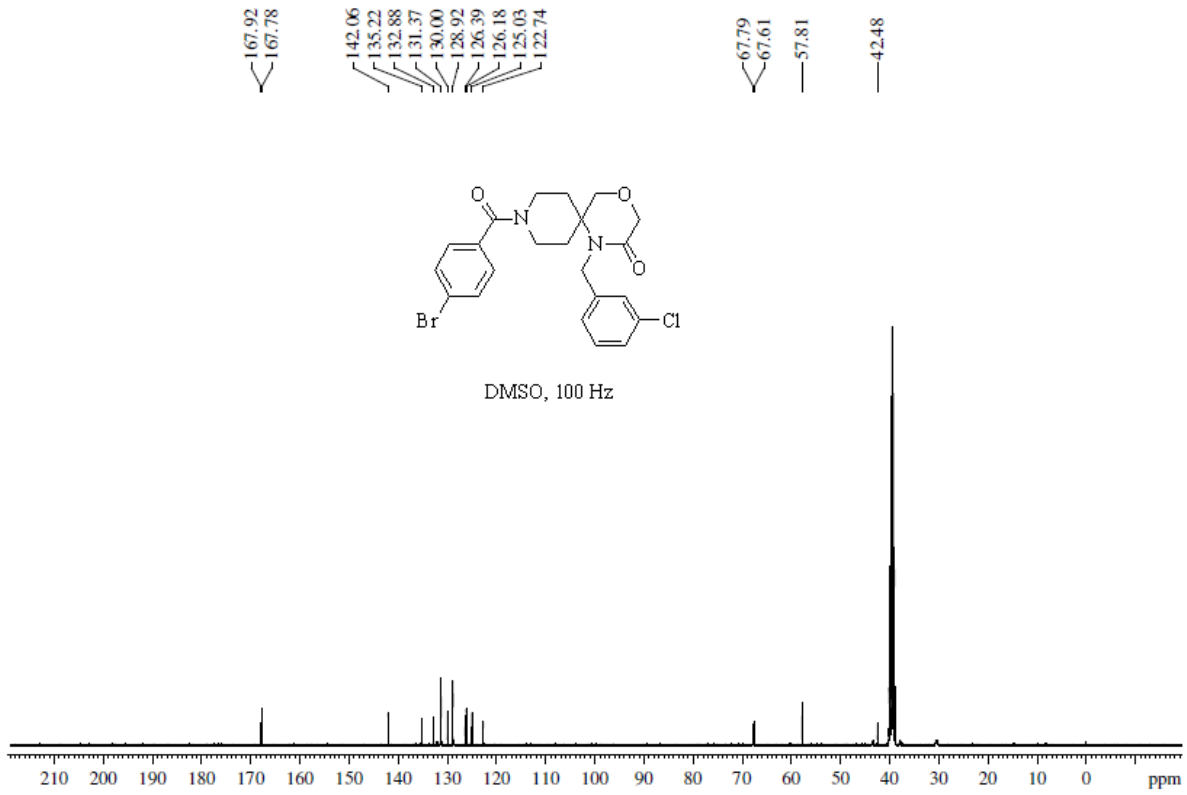
$CDCl_3$, 400 Hz



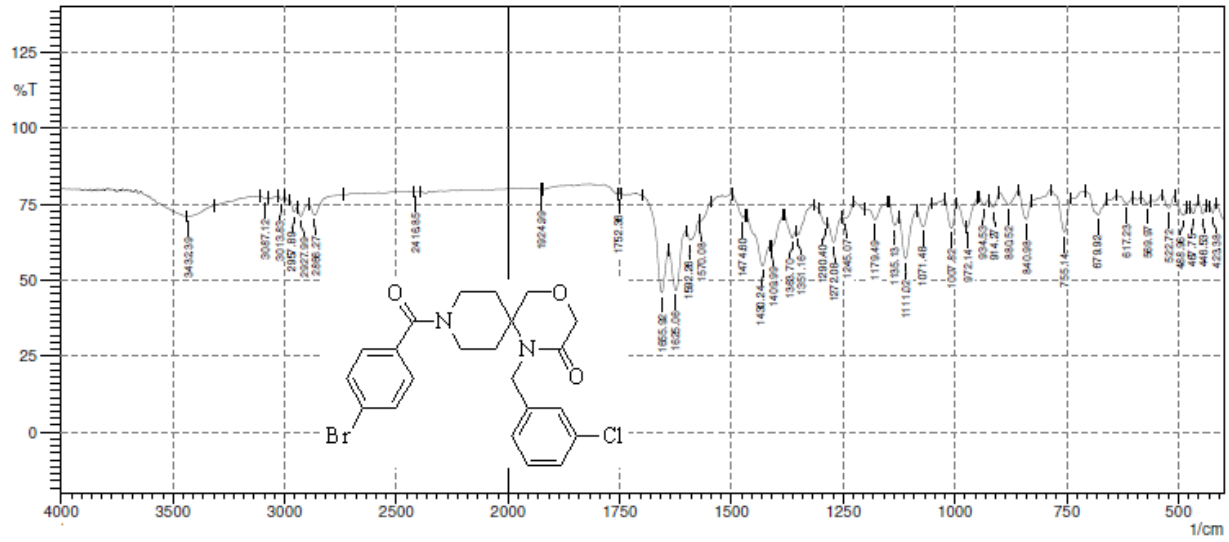
^{1}H-NMR spectrum of **SPO-7**



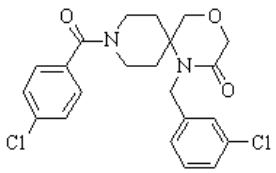
MS spectrum of **SPO-7**



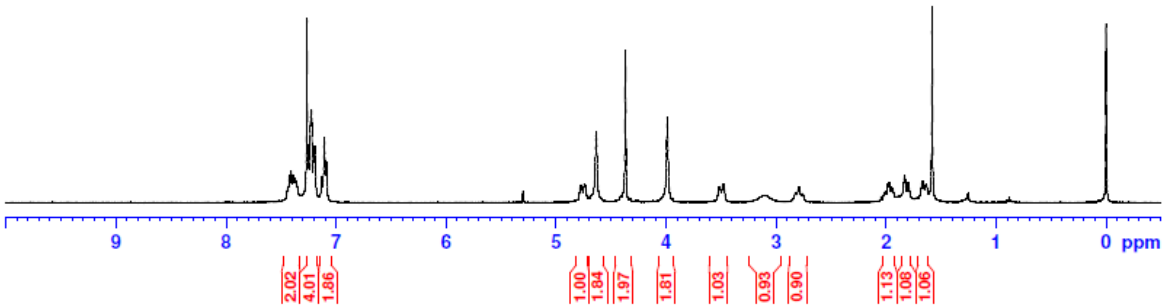
^{13}C-NMR spectrum of **SPO-7**



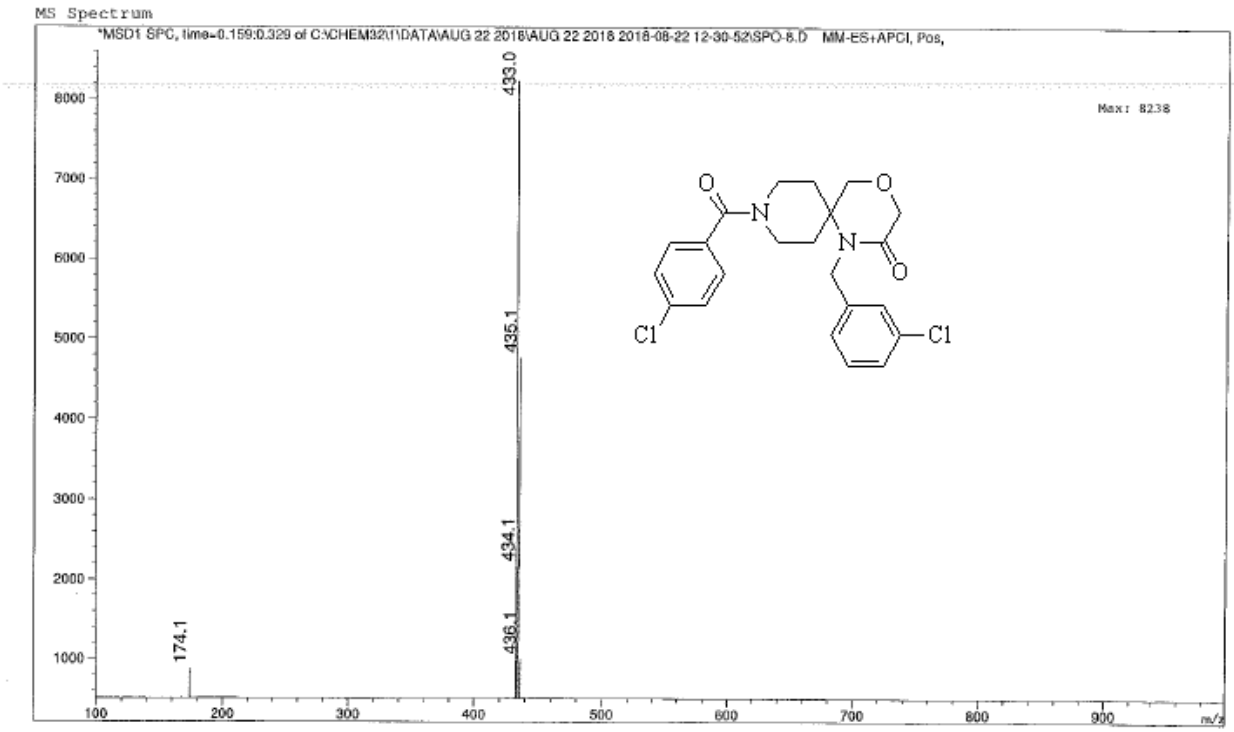
IR spectrum of **SPO-7**



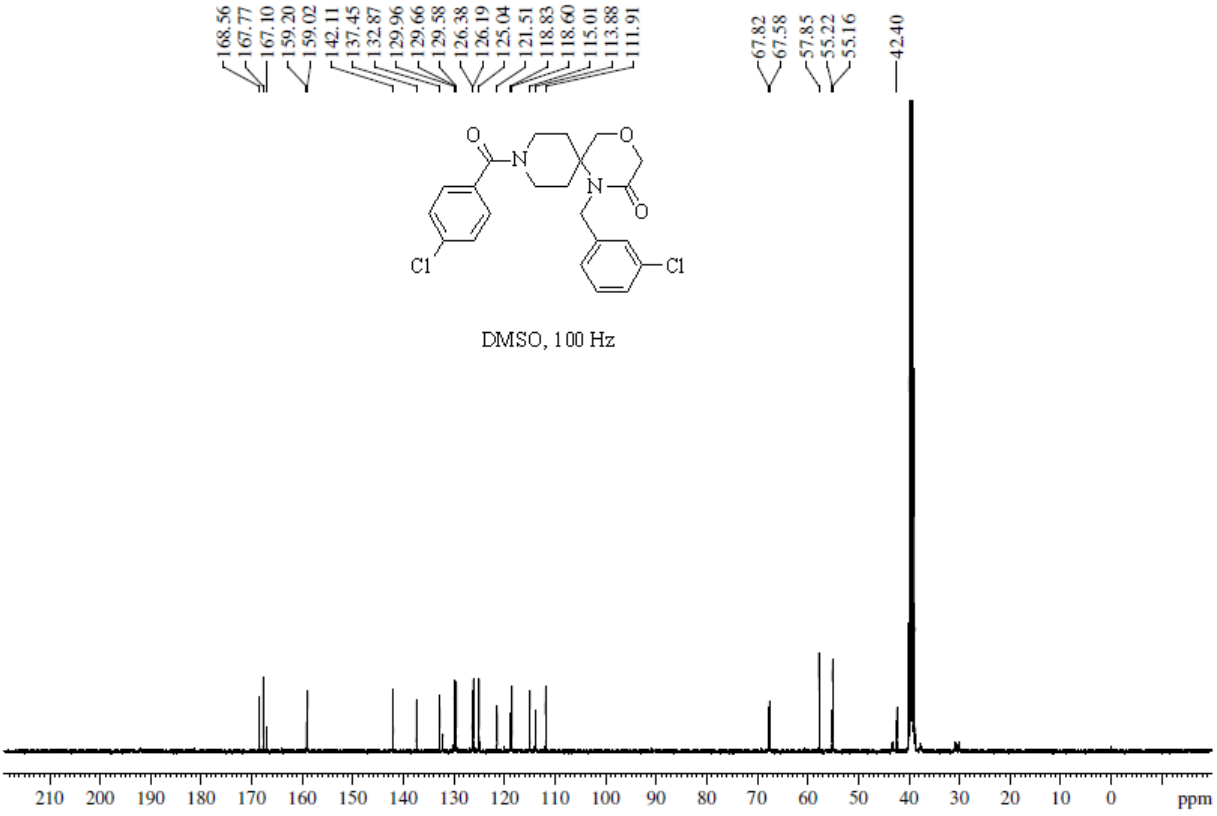
$CDCl_3$, 400 Hz



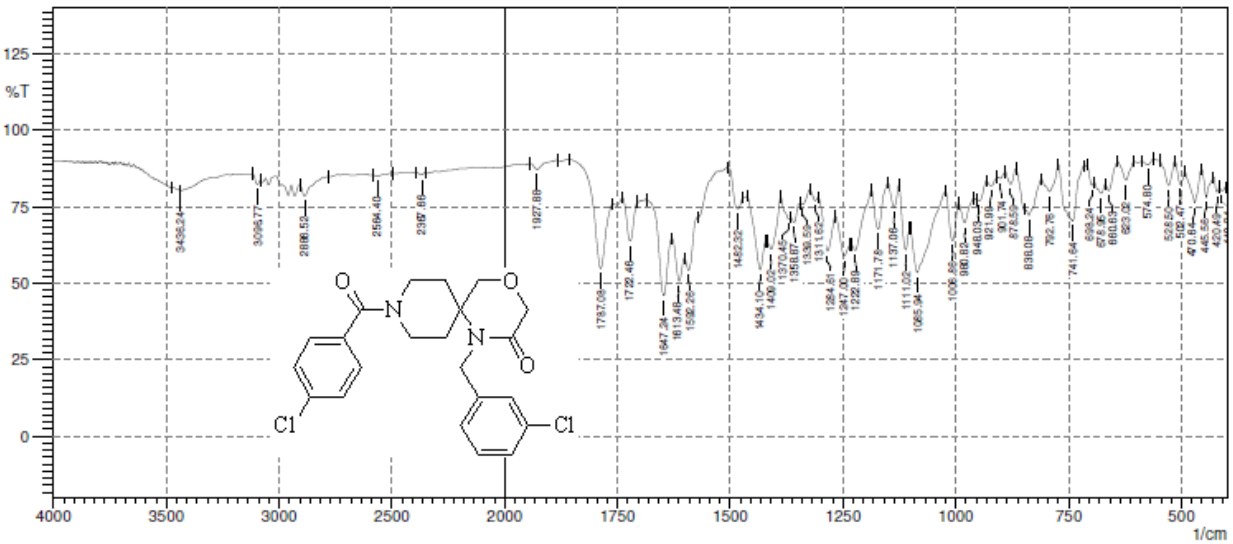
^{1}H-NMR spectrum of **SPO-8**



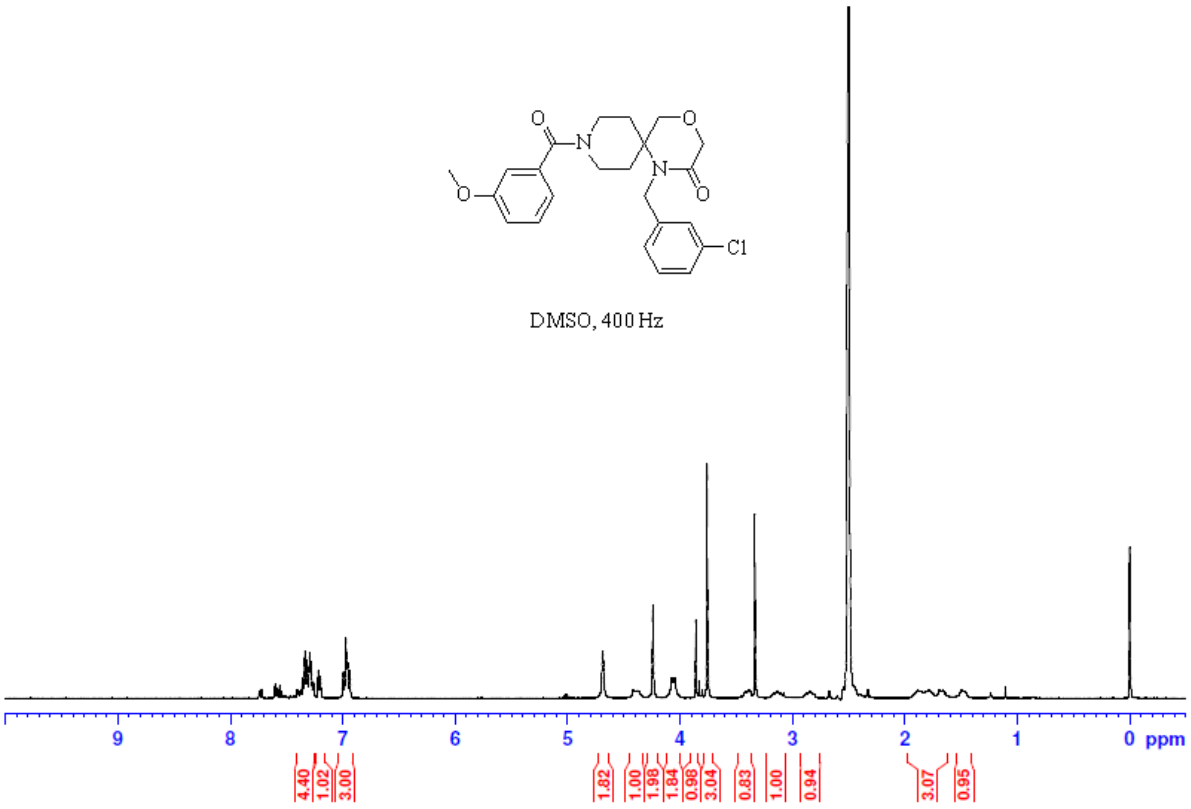
MS spectrum of **SPO-8**



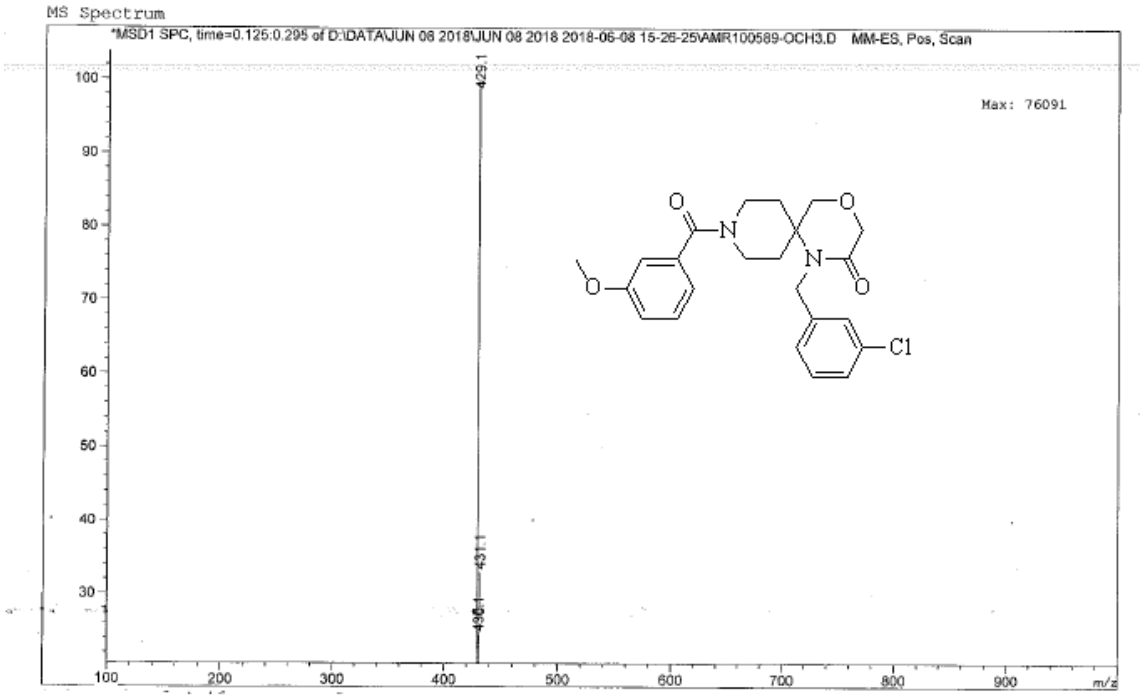
^{13}C-NMR spectrum of **SPO-8**



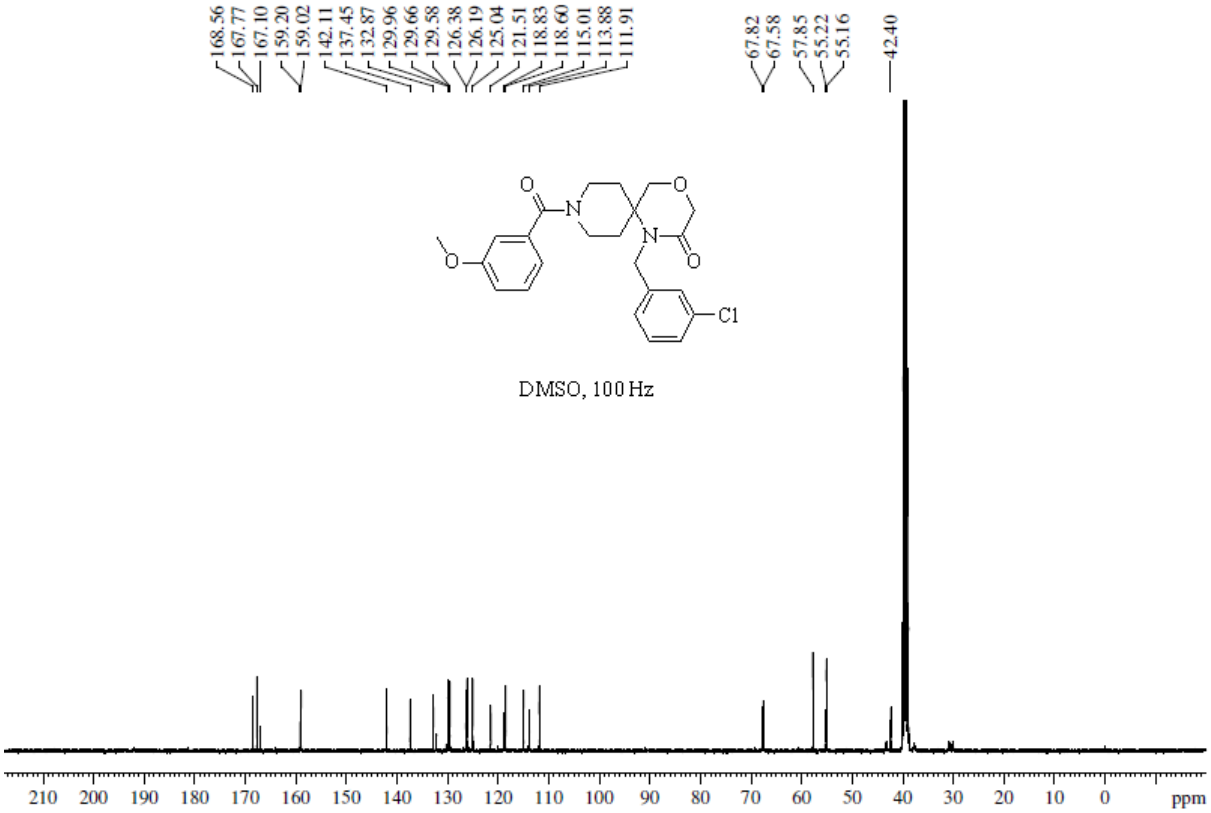
IR spectrum of **SPO-8**



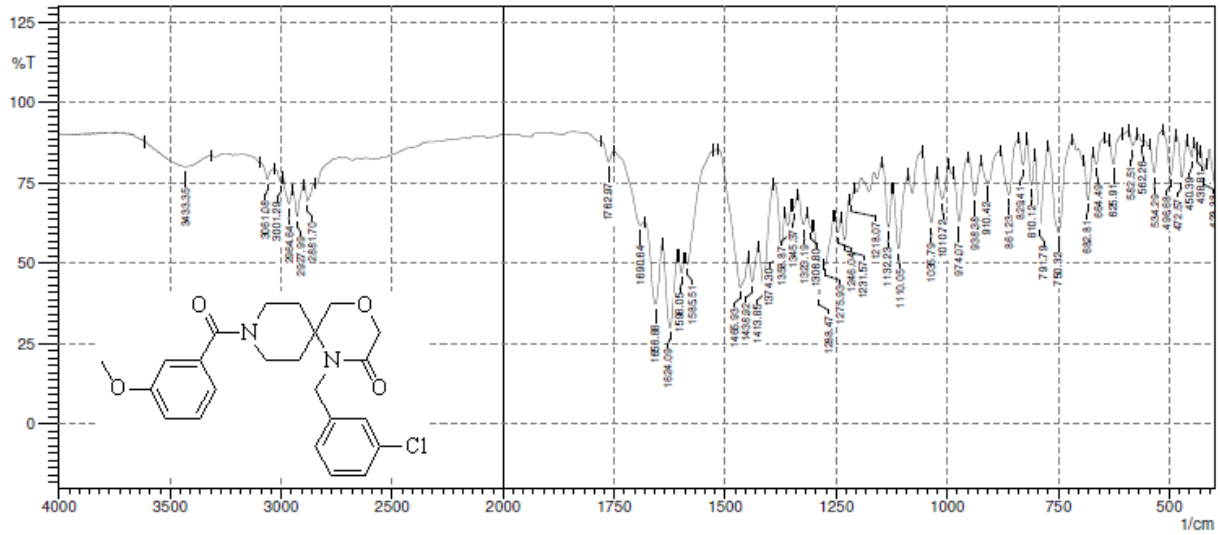
^{1}H-NMR spectrum of **SPO-9**



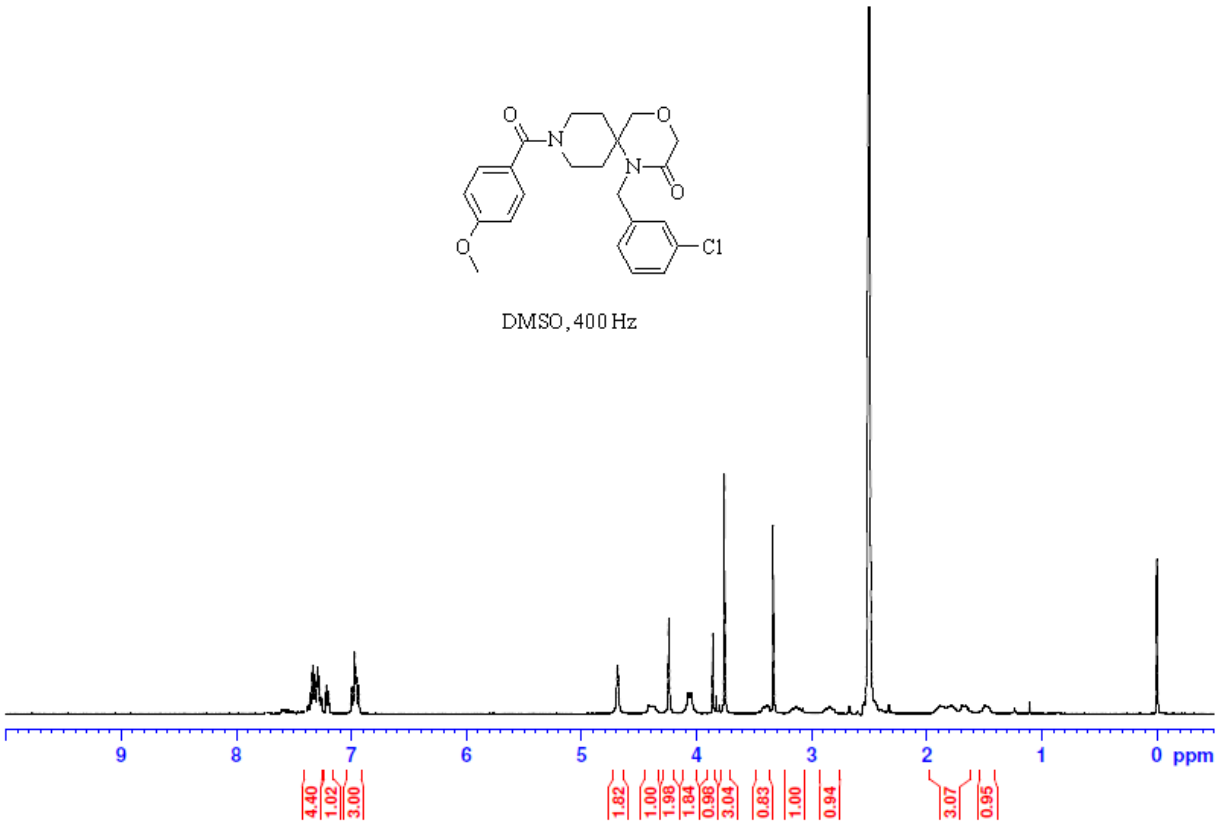
MS spectrum of **SPO-9**



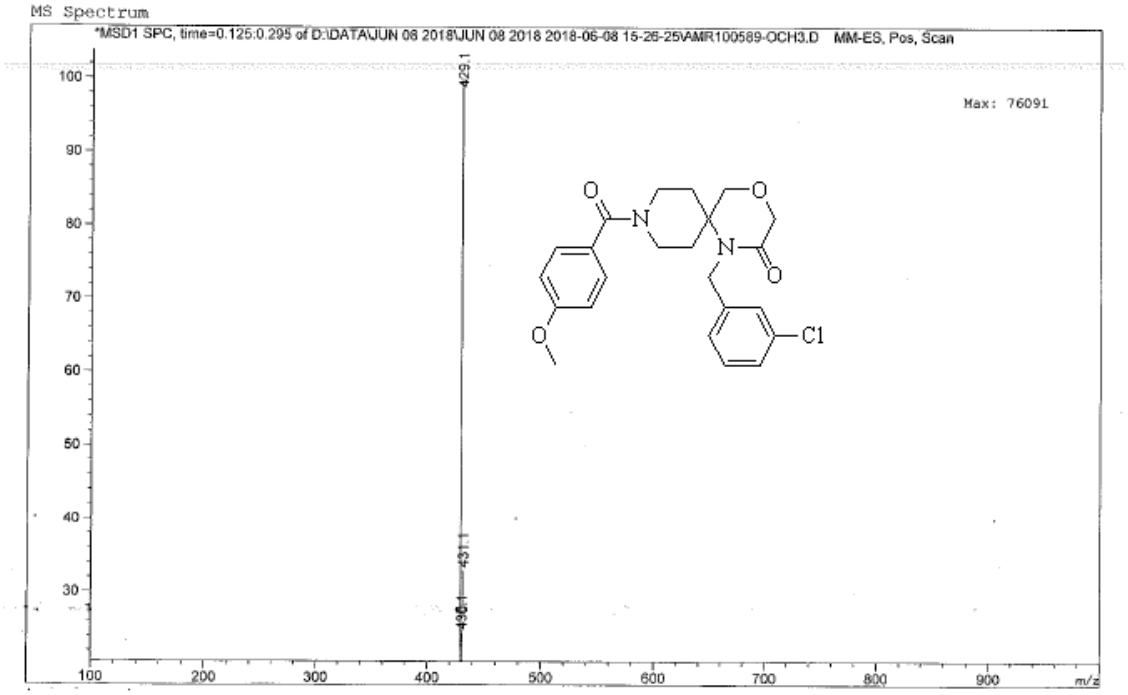
^{13}C-NMR spectrum of **SPO-9**



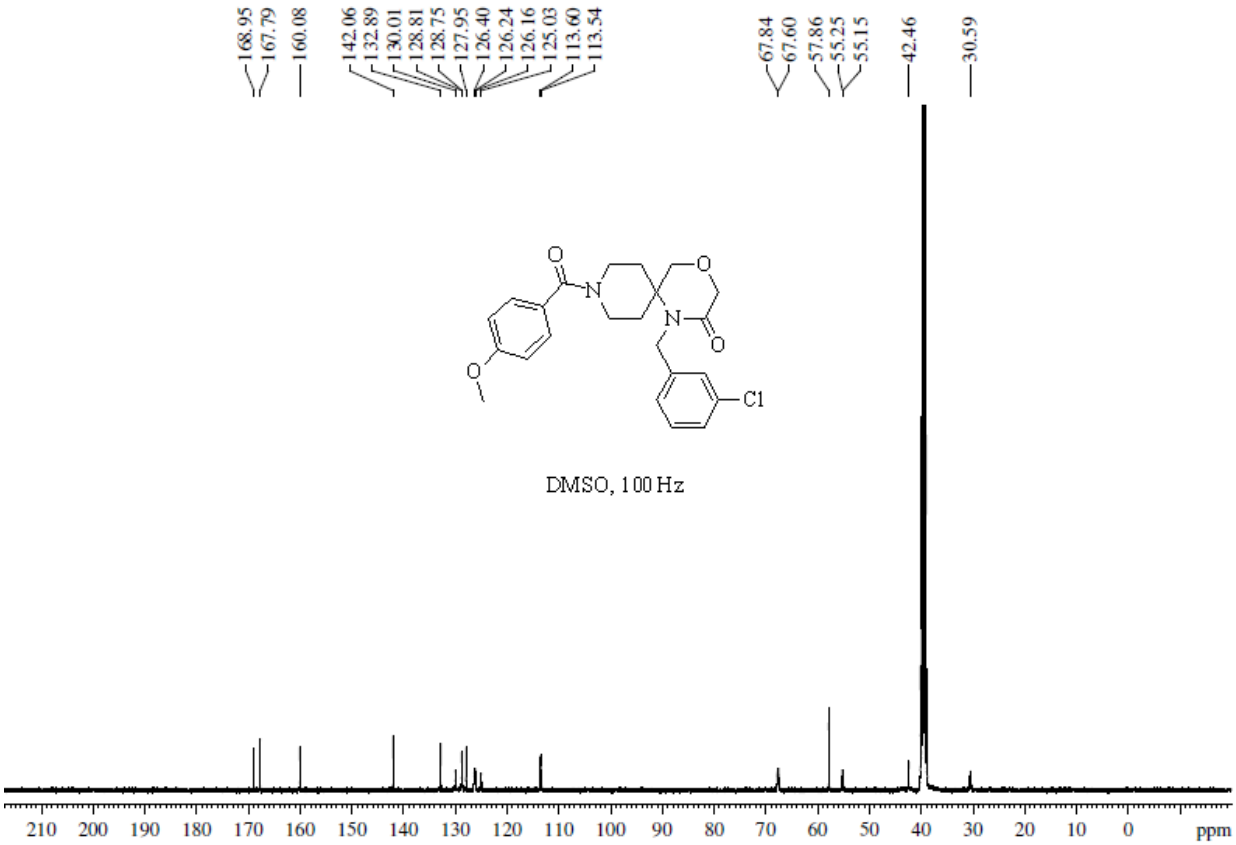
IR spectrum of **SPO-9**



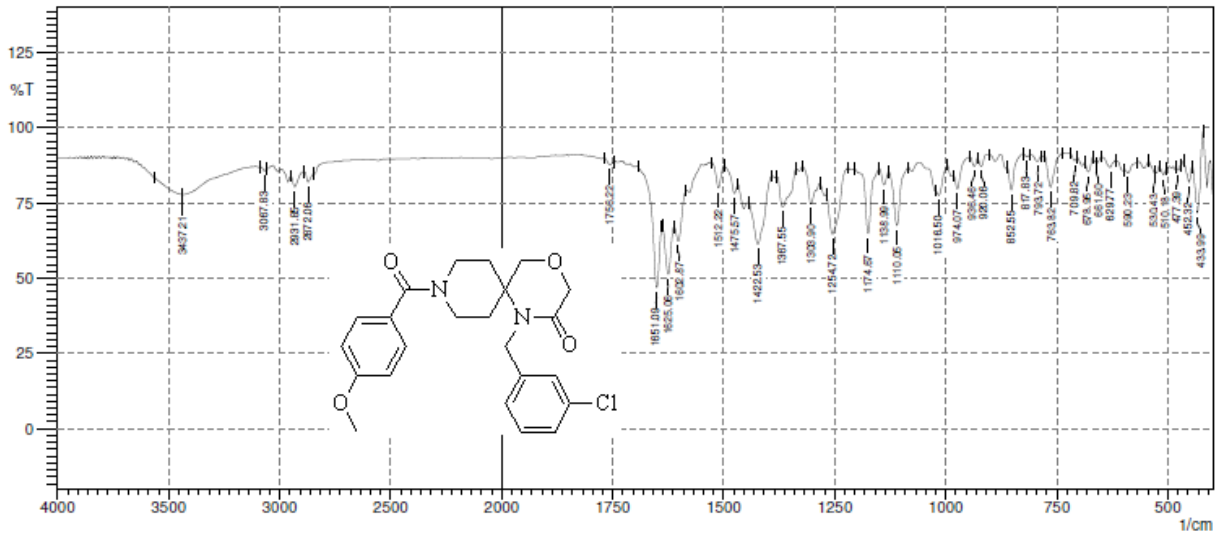
^{1}H-NMR spectrum of **SPO-10**



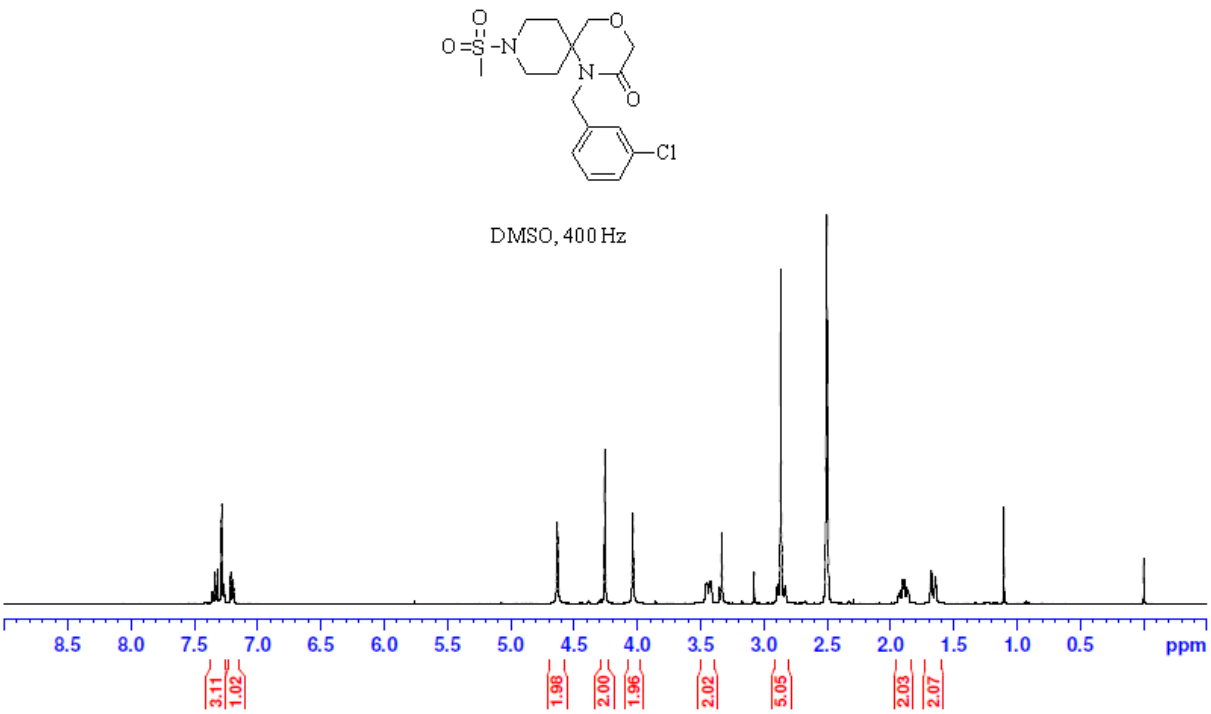
MS spectrum of **SPO-10**



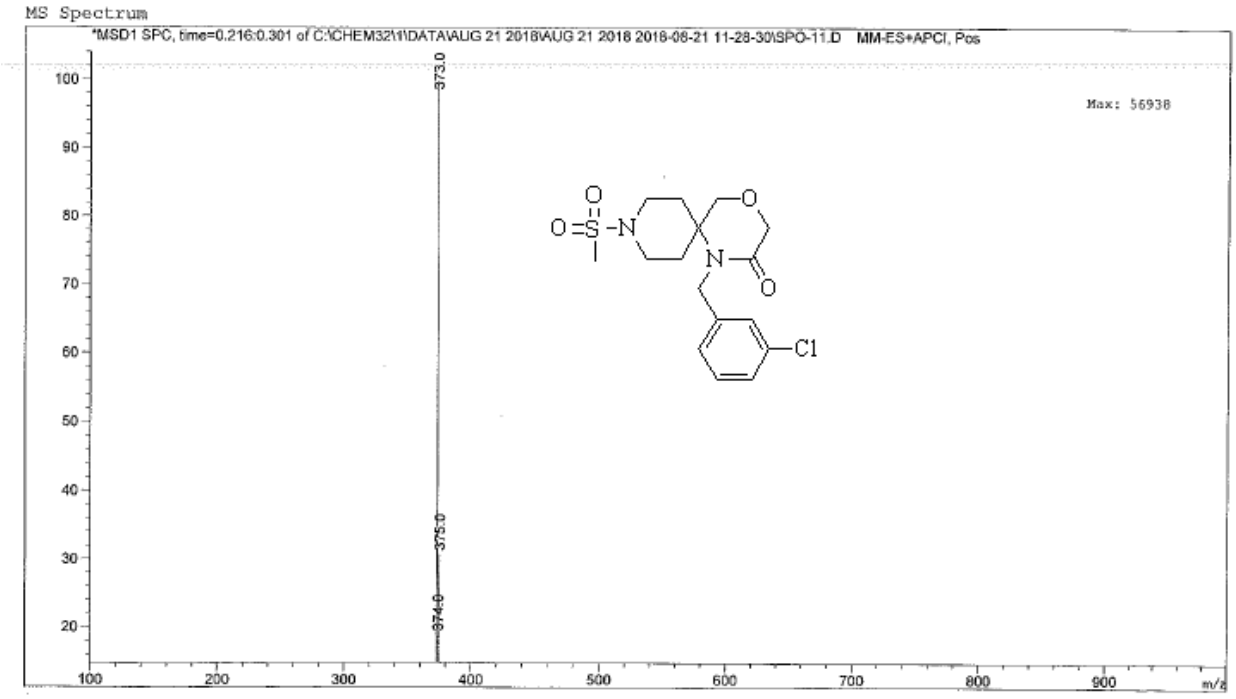
^{13}C-NMR spectrum of **SPO-10**



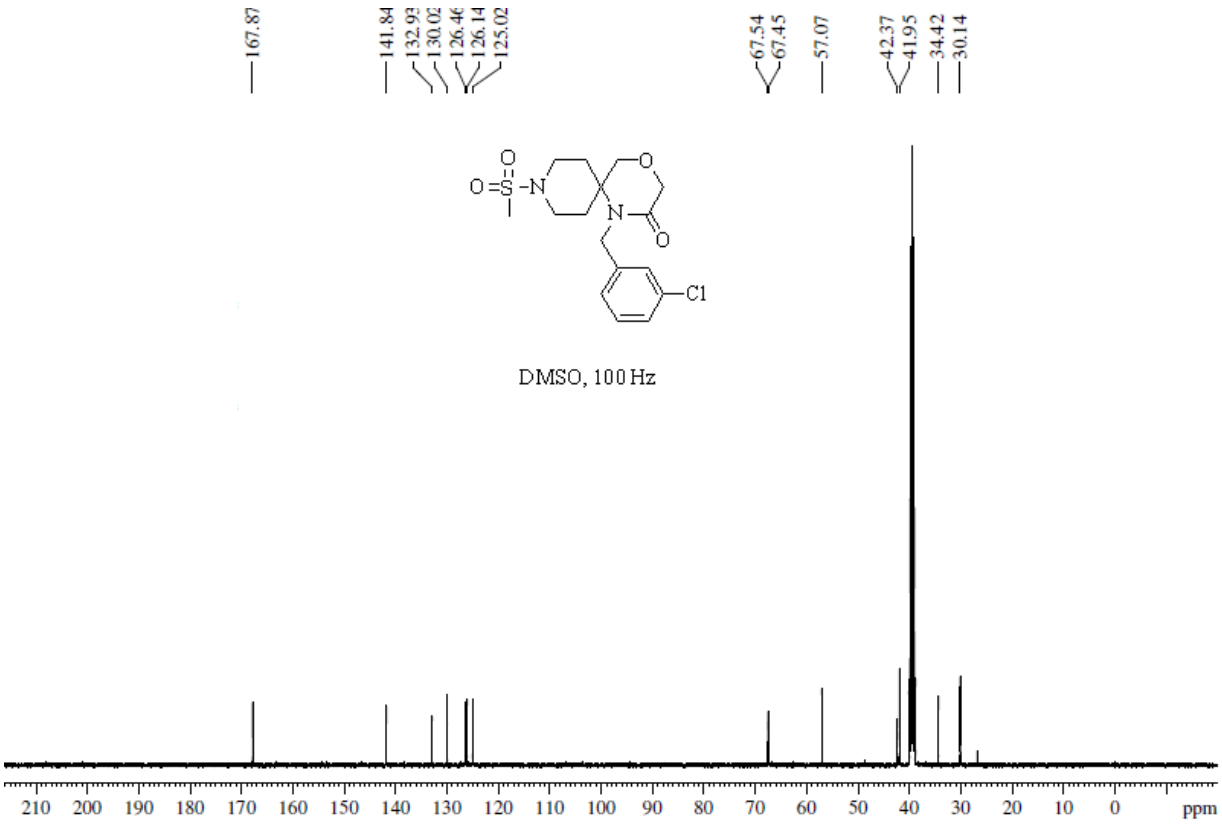
IR spectrum of **SPO-10**



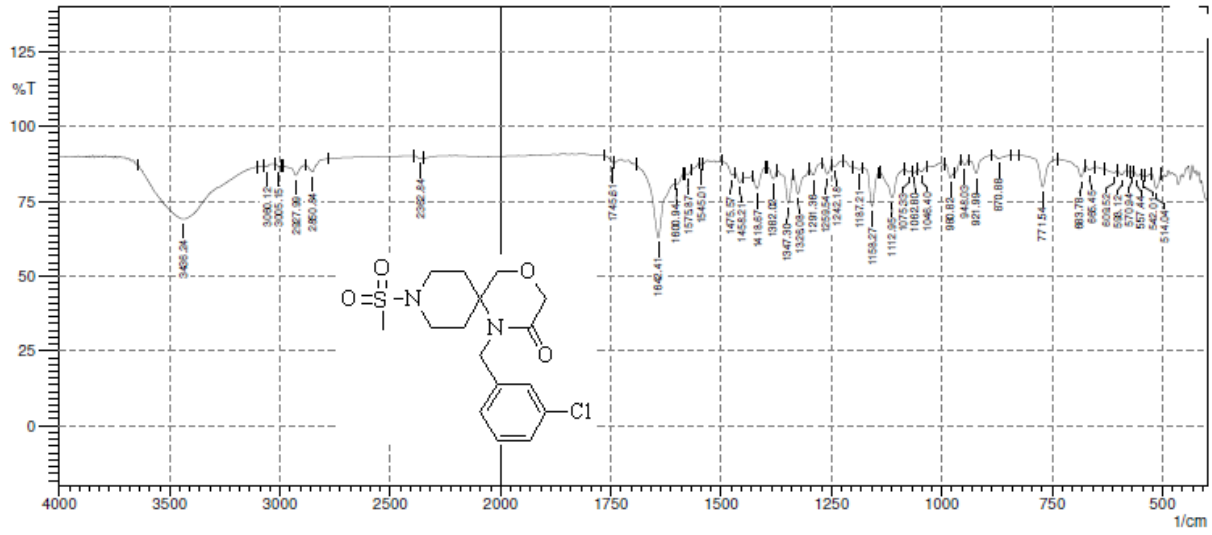
^{1}H-NMR spectrum of **SPO-11**



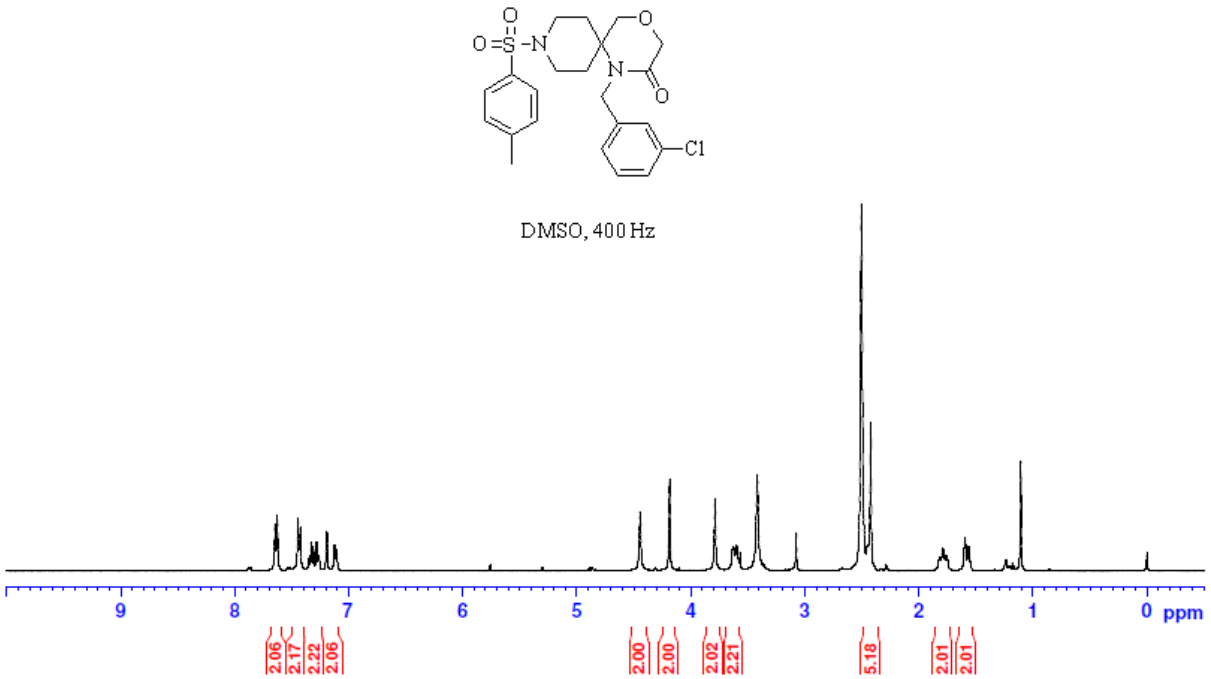
MS spectrum of **SPO-11**



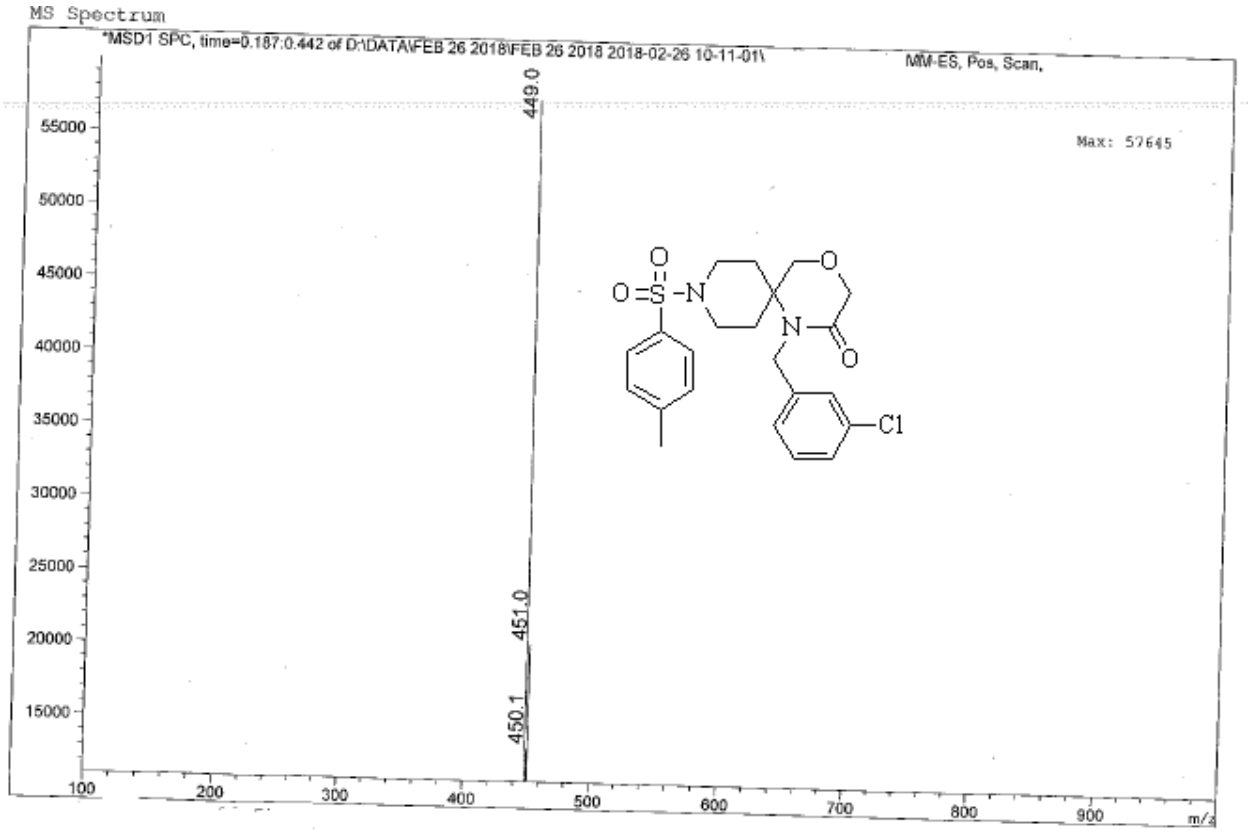
^{13}C-NMR spectrum of **SPO-11**



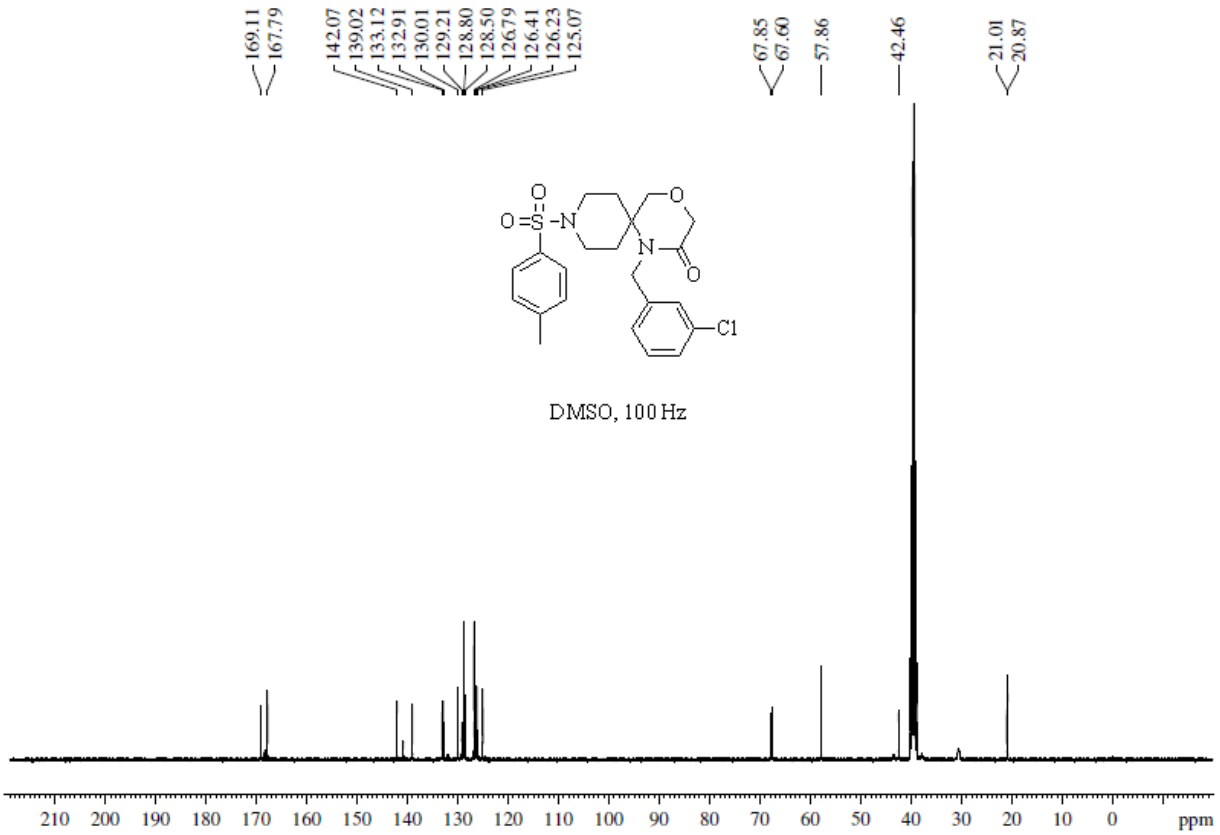
IR spectrum of **SPO-11**



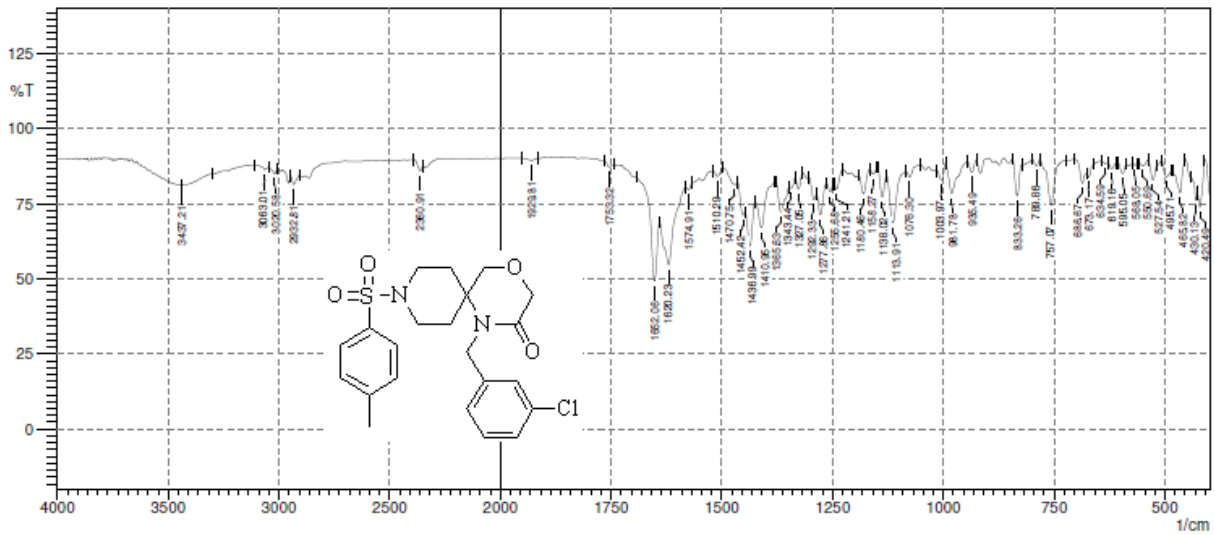
^{1}H-NMR spectrum of **SPO-12**



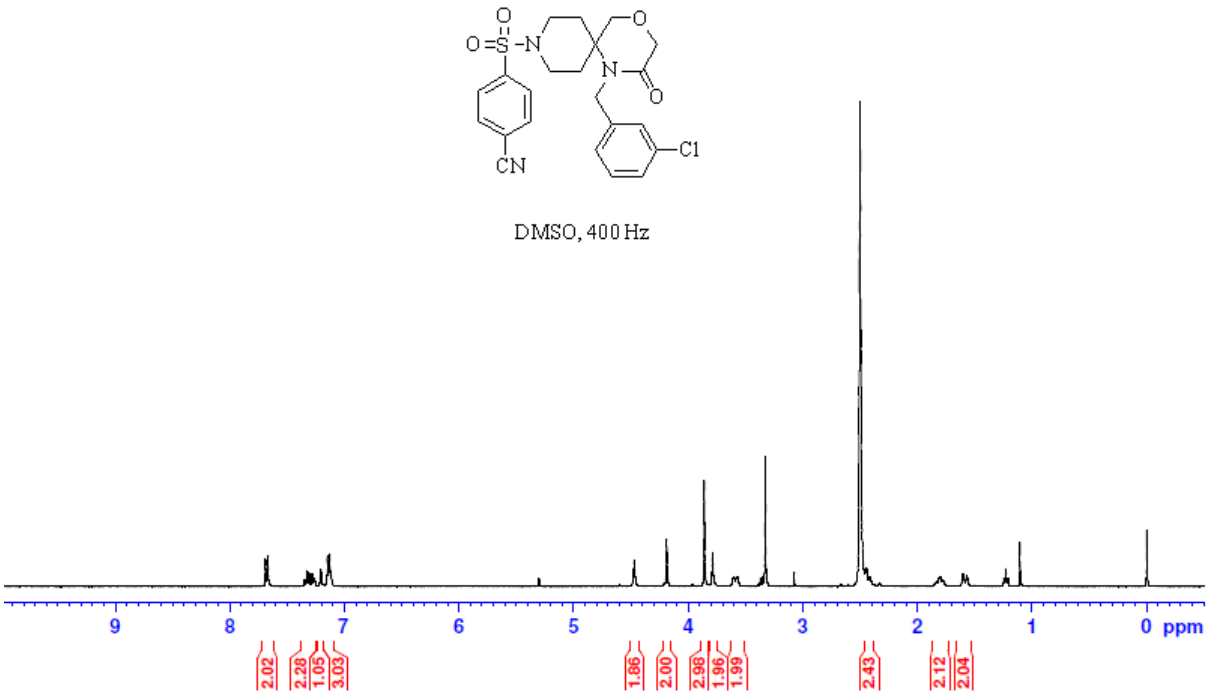
MS spectrum of **SPO-12**

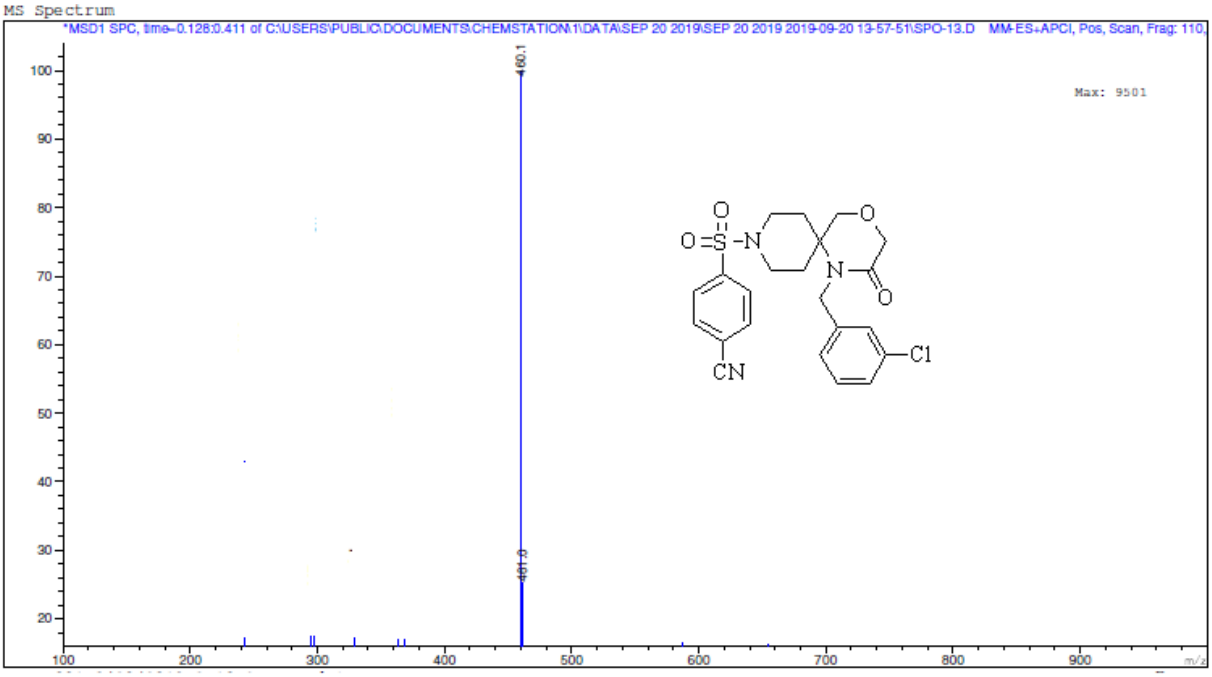


^{13}C-NMR spectrum of **SPO-12**

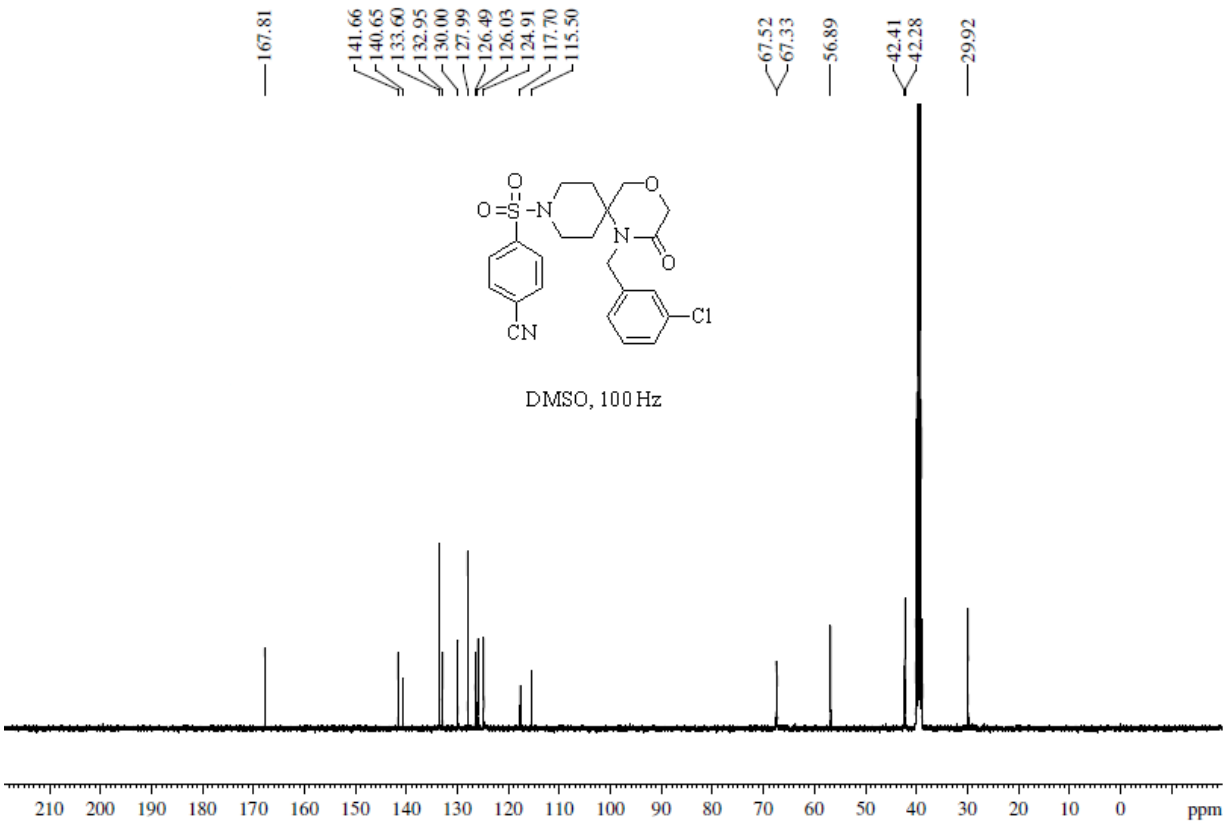


IR spectrum of **SPO-12**

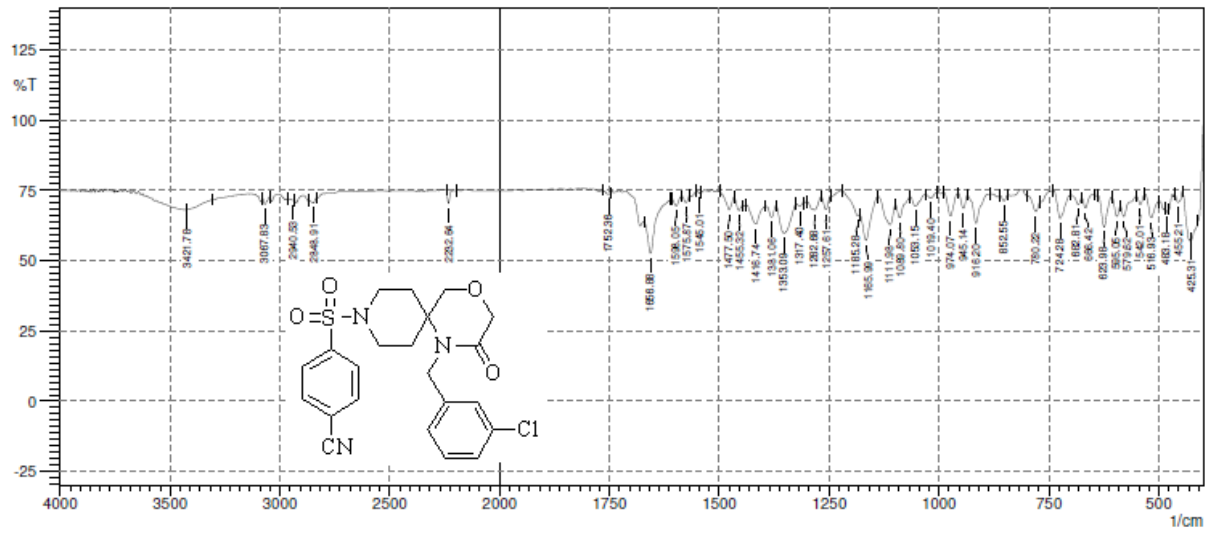




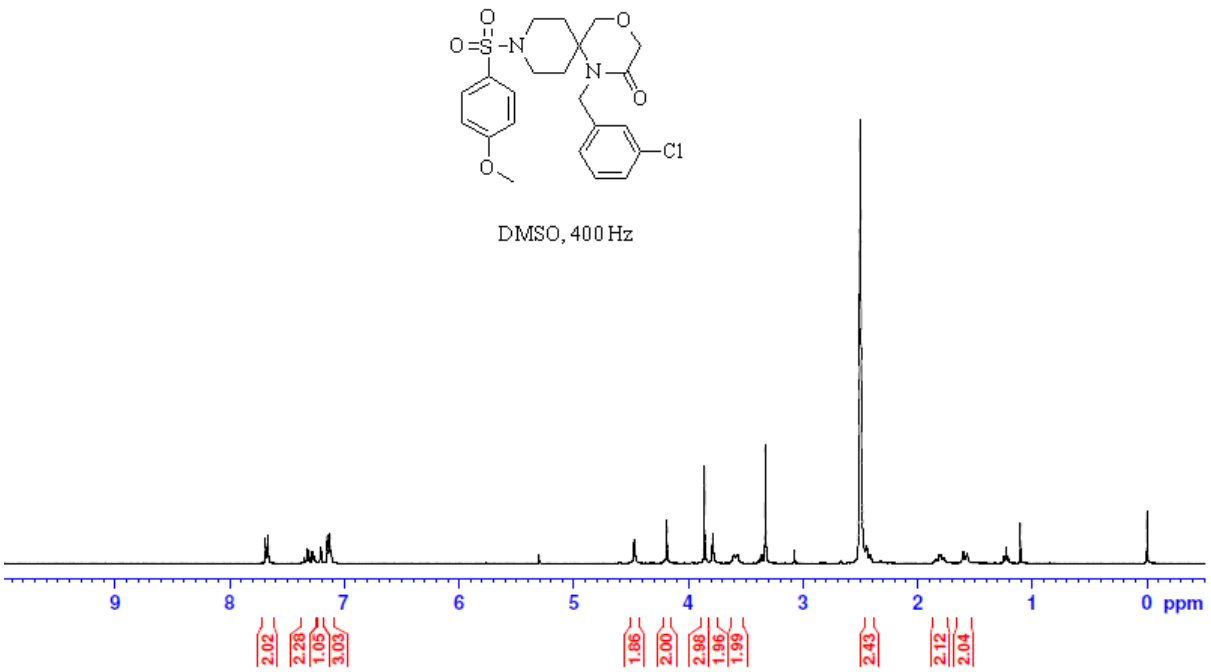
MS spectrum of **SPO-13**



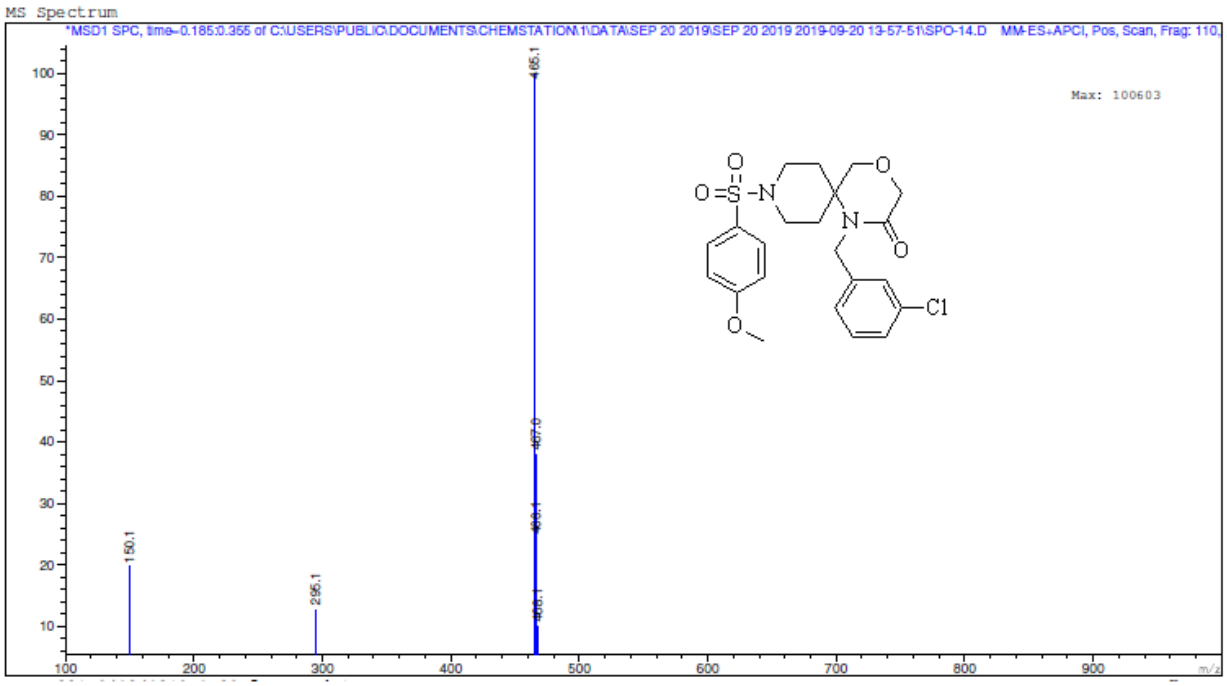
^{13}C-NMR spectrum of **SPO-13**



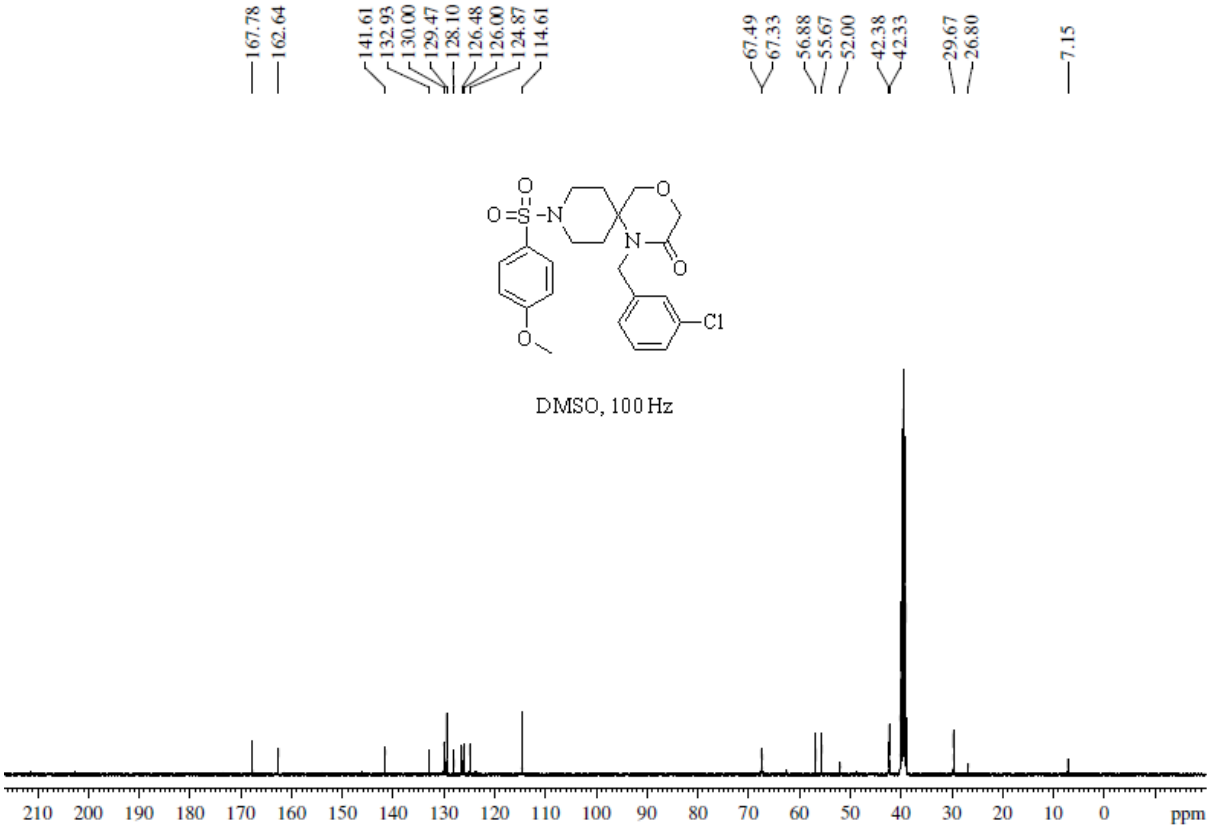
IR spectrum of **SPO-13**



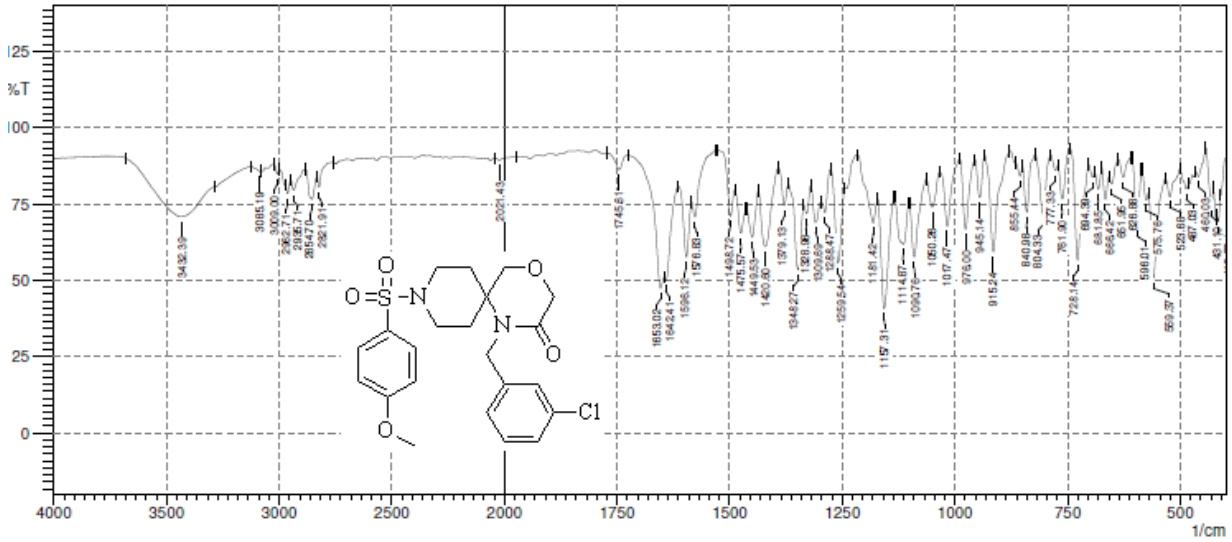
^{1}H-NMR spectrum of **SPO-14**



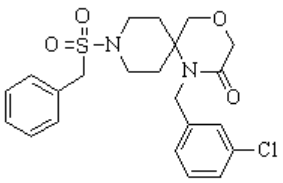
MS spectrum of **SPO-14**



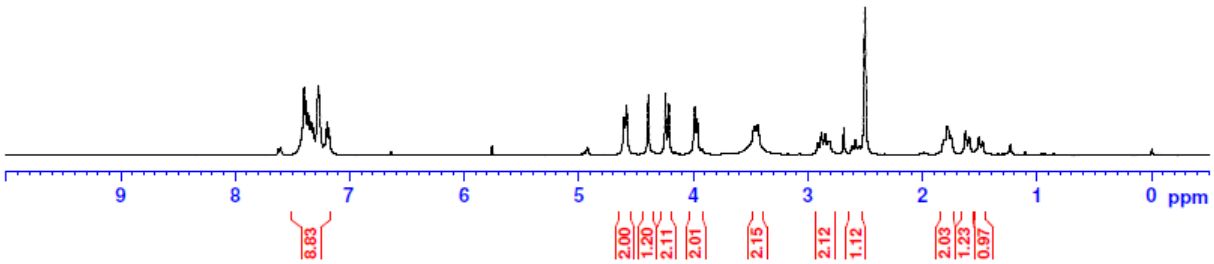
^{13}C-NMR spectrum of **SPO-14**



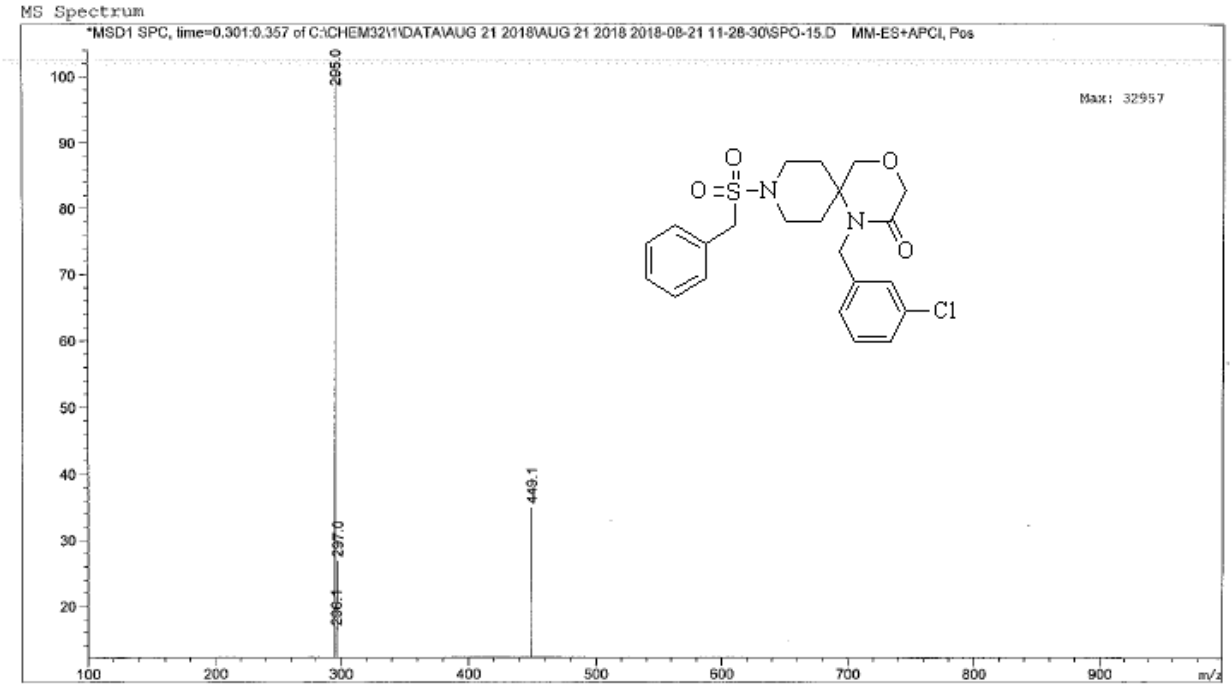
IR spectrum of **SPO-14**



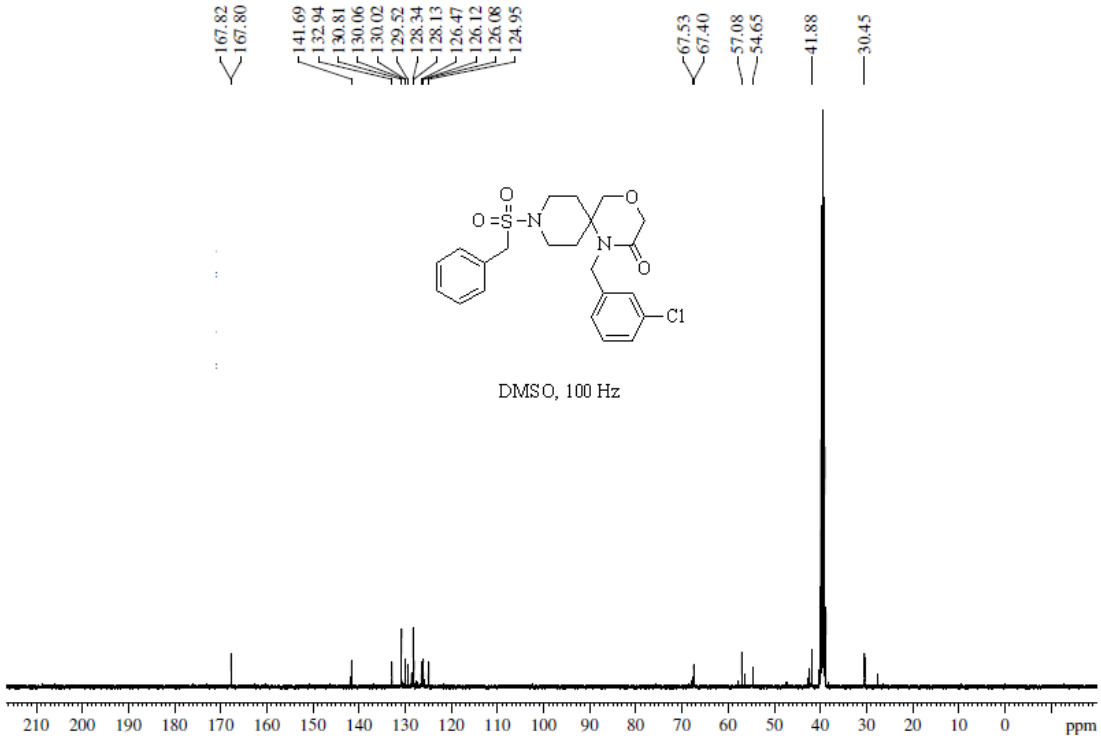
DMSO, 400 Hz



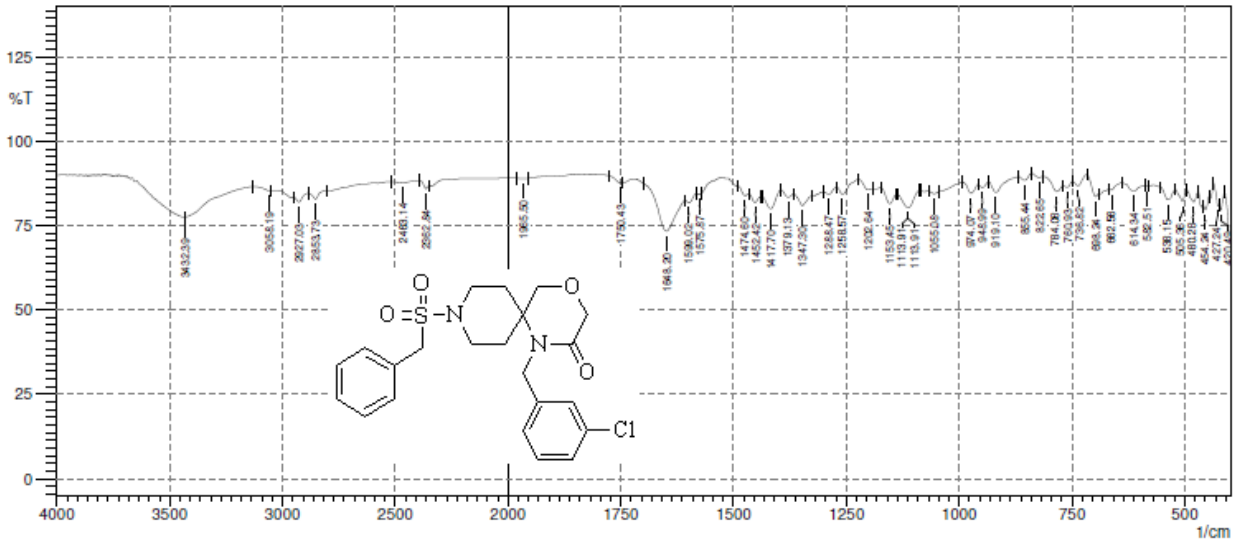
^{1}H-NMR spectrum of **SPO-15**



MS spectrum of **SPO-15**



^{13}C-NMR spectrum of **SPO-15**



IR spectrum of **SPO-15**