Design, synthesis and in vitro evaluations of new cyclotriphosphazenes as safe drug candidates

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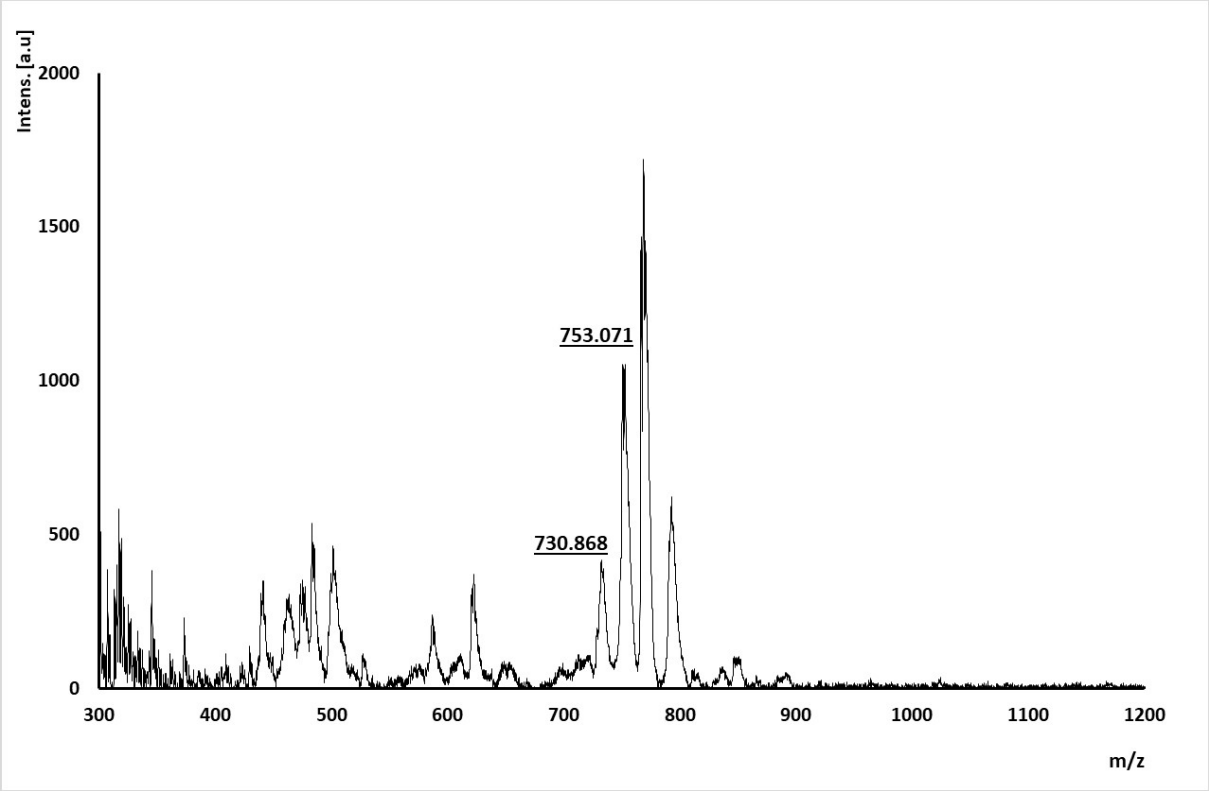


Fig S1. The MALDI TOF mass spectrum of compound **1**

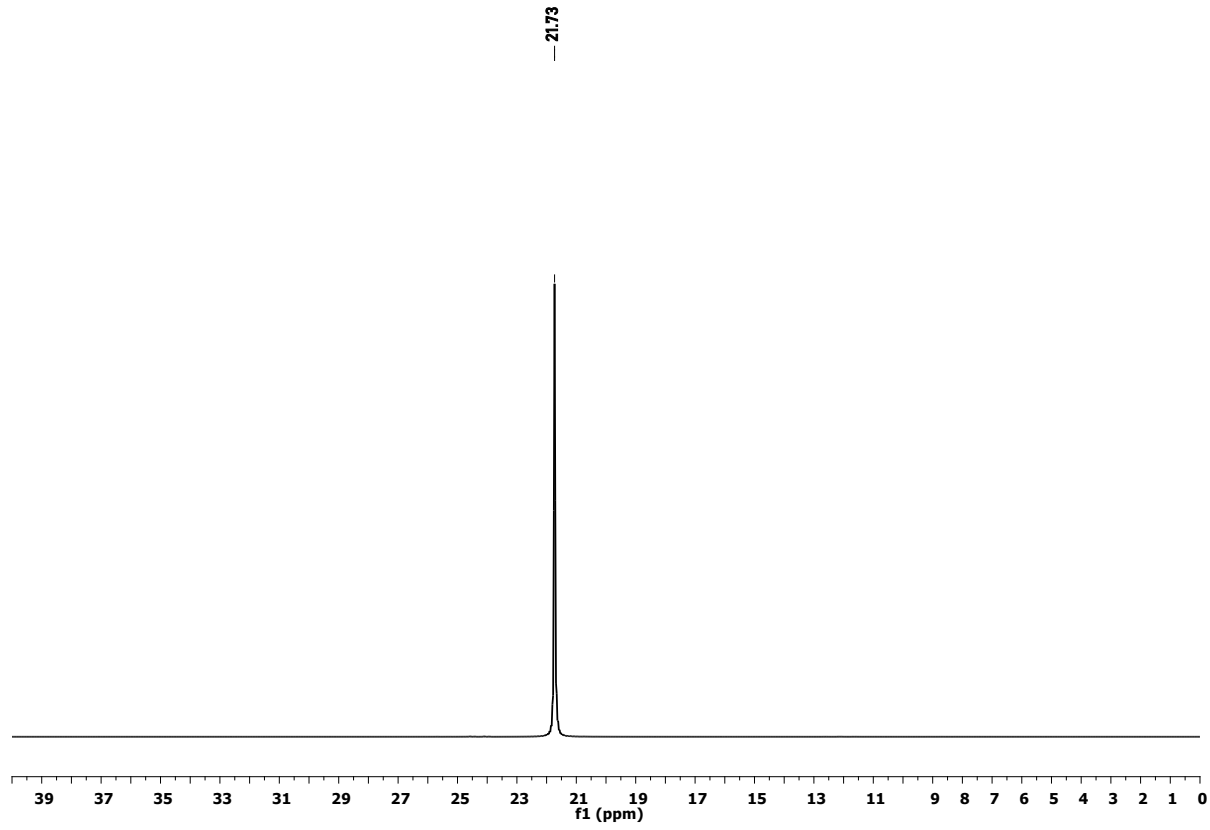


Fig S2. The proton decoupled ^{31}P NMR spectrum of compound **1**

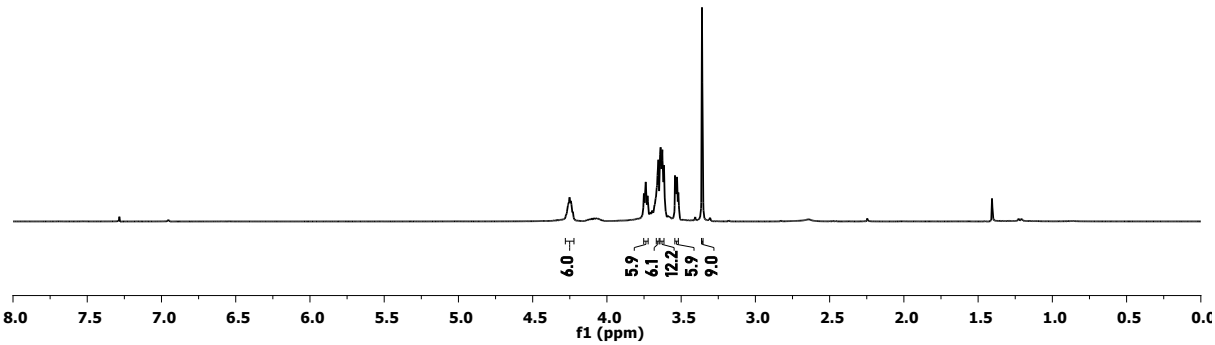


Fig S3. The ^{1}H NMR spectrum of compound **1**

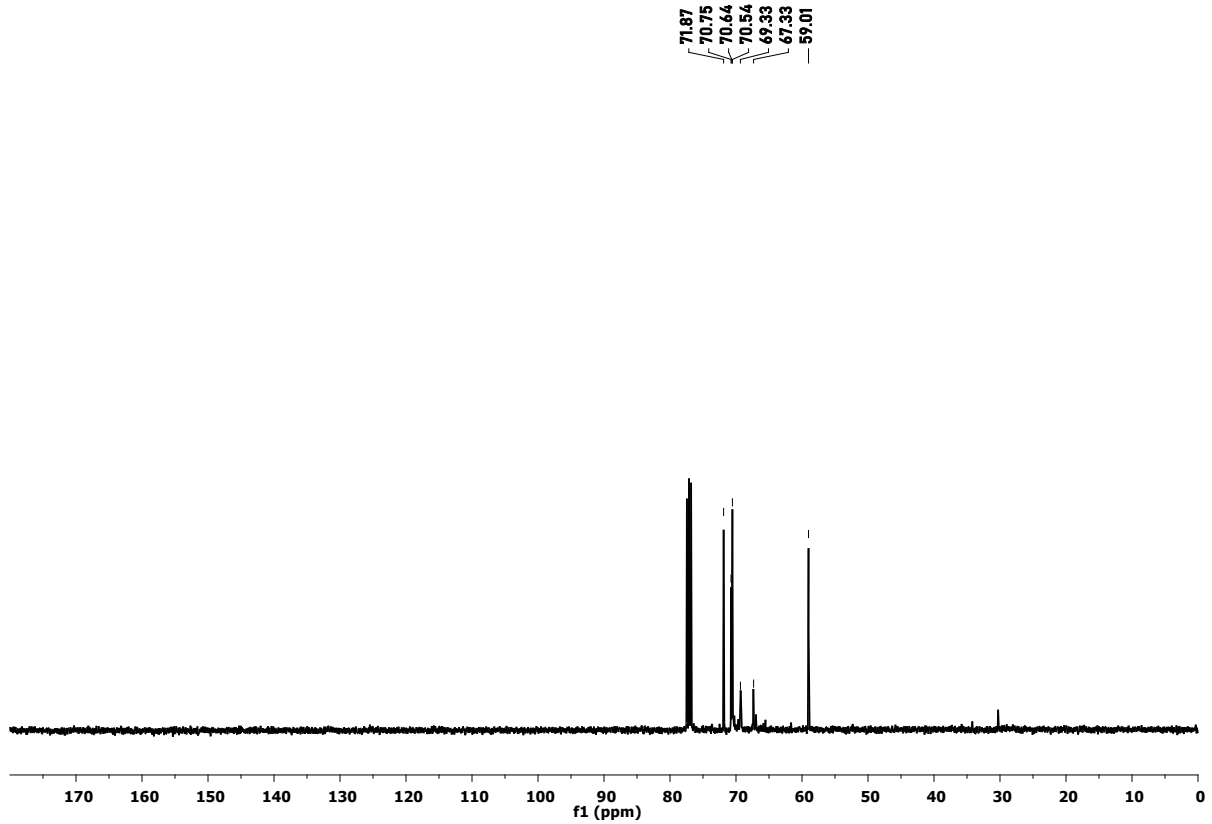


Fig S4. The ^{13}C NMR spectrum of compound **1**

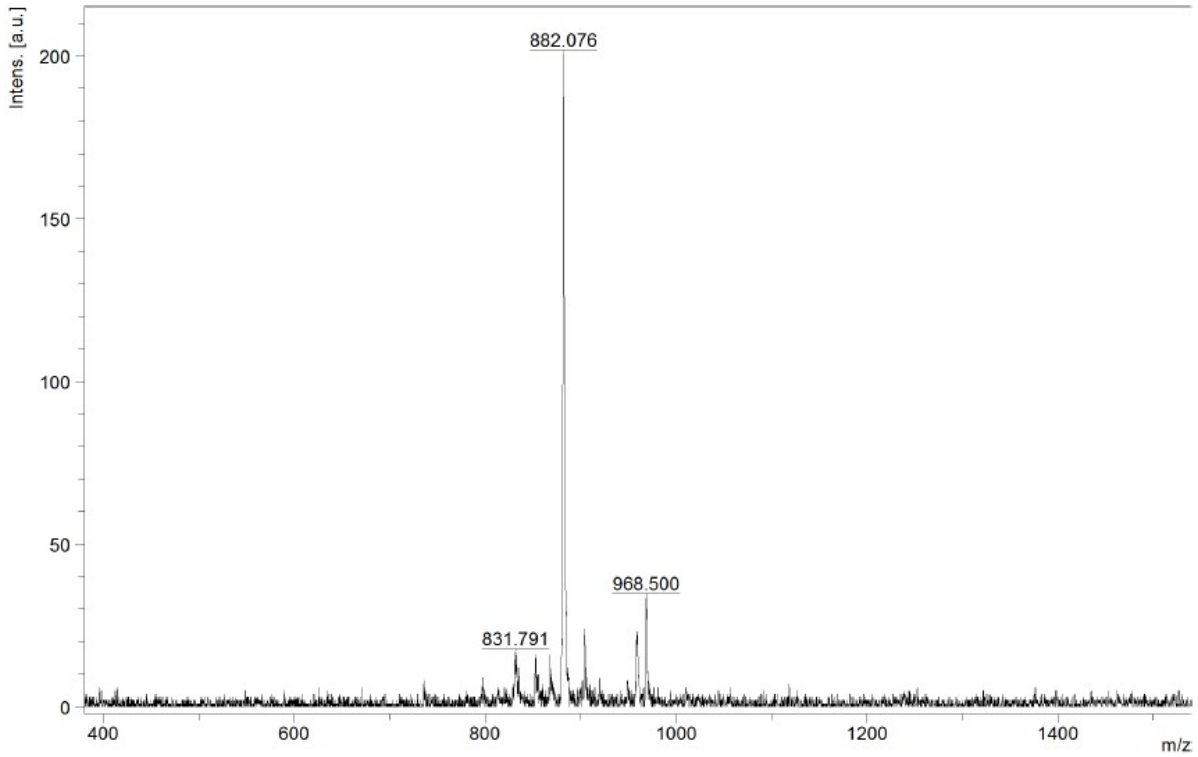


Fig S5. The MALDI TOF mass spectrum of compound **2**

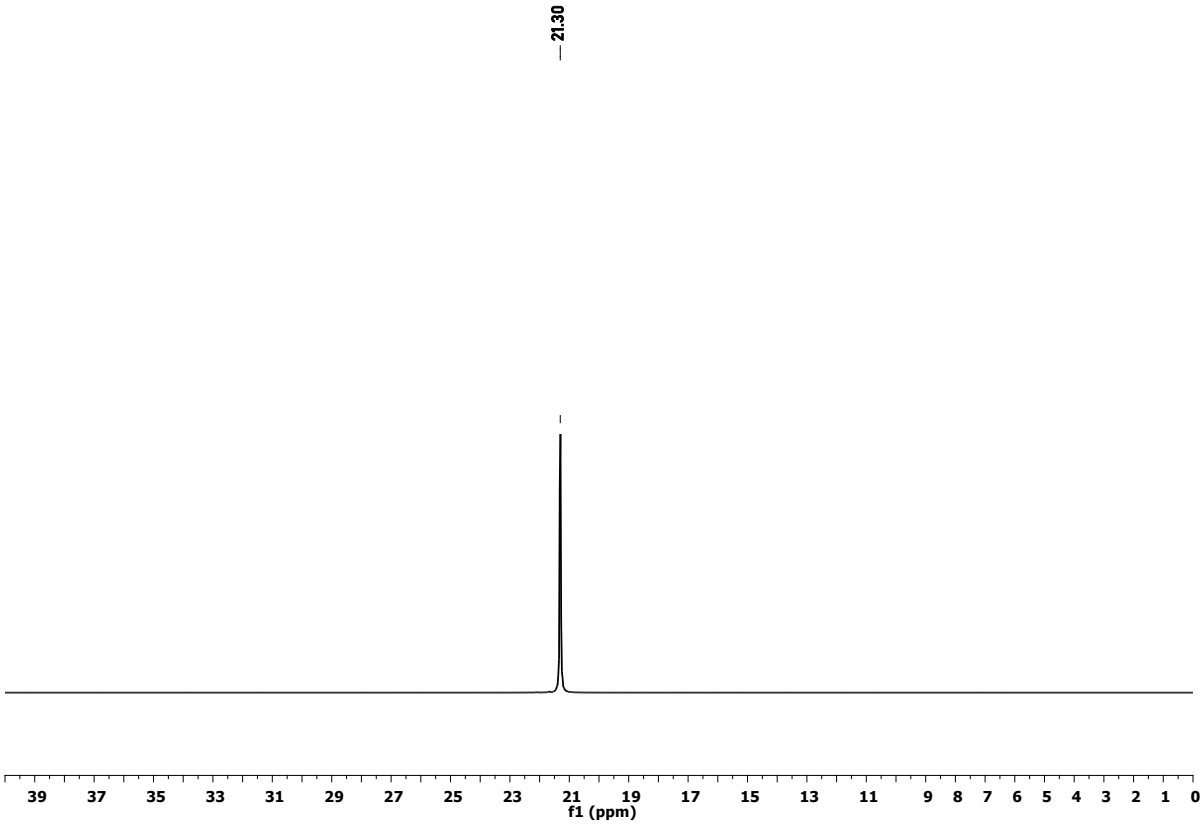


Fig S6. The proton decoupled ^{31}P NMR spectrum of compound **2**

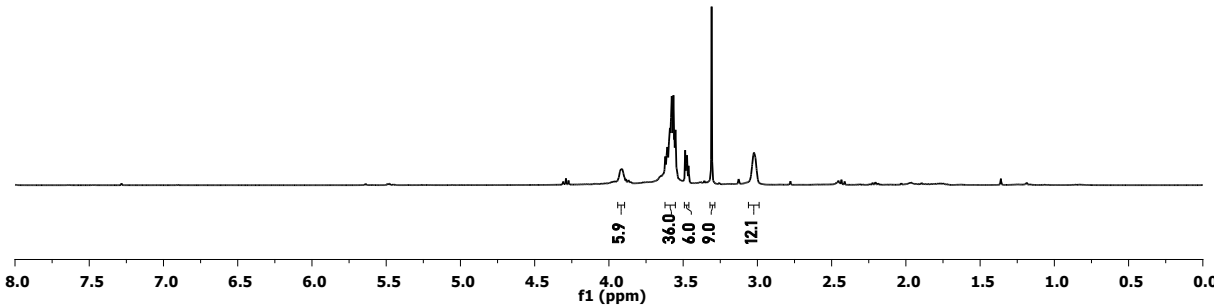


Fig S7. The ^{1}H NMR spectrum of compound **2**

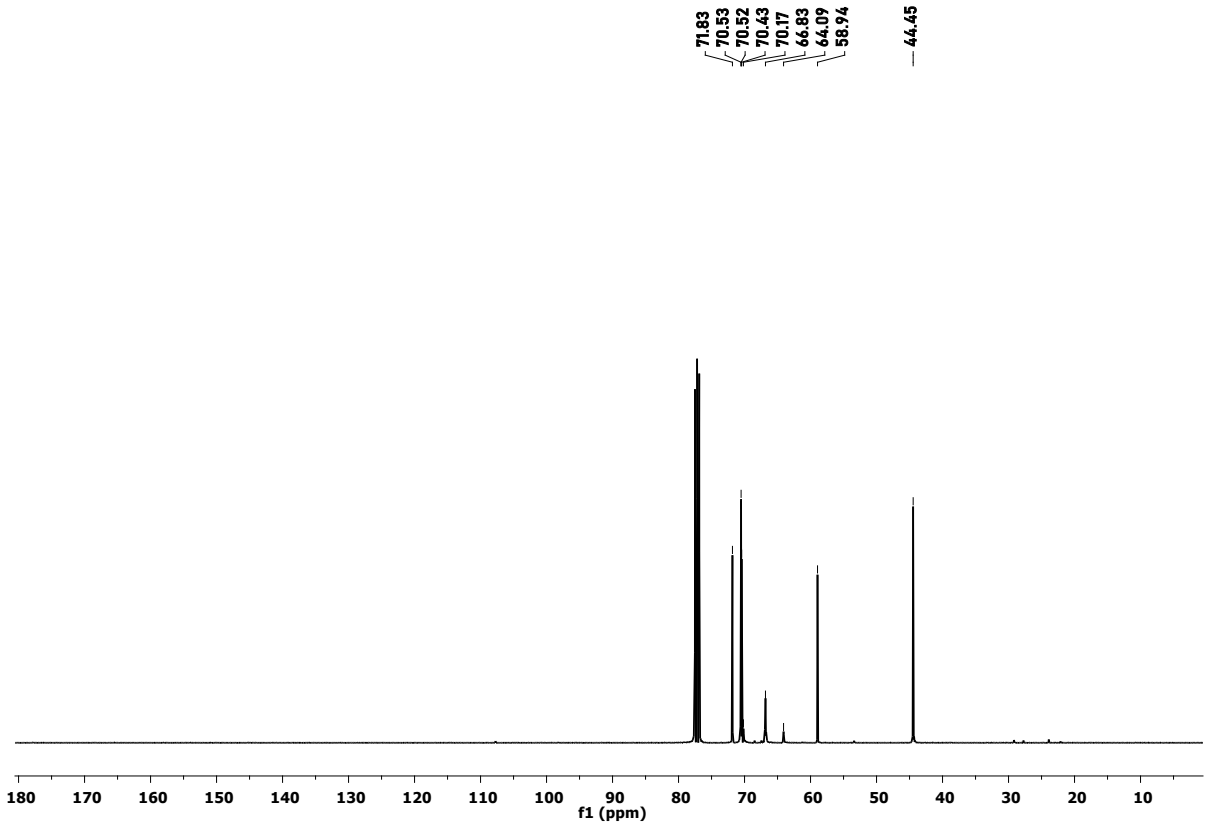


Fig S8. The ^{13}C NMR spectrum of compound **2**

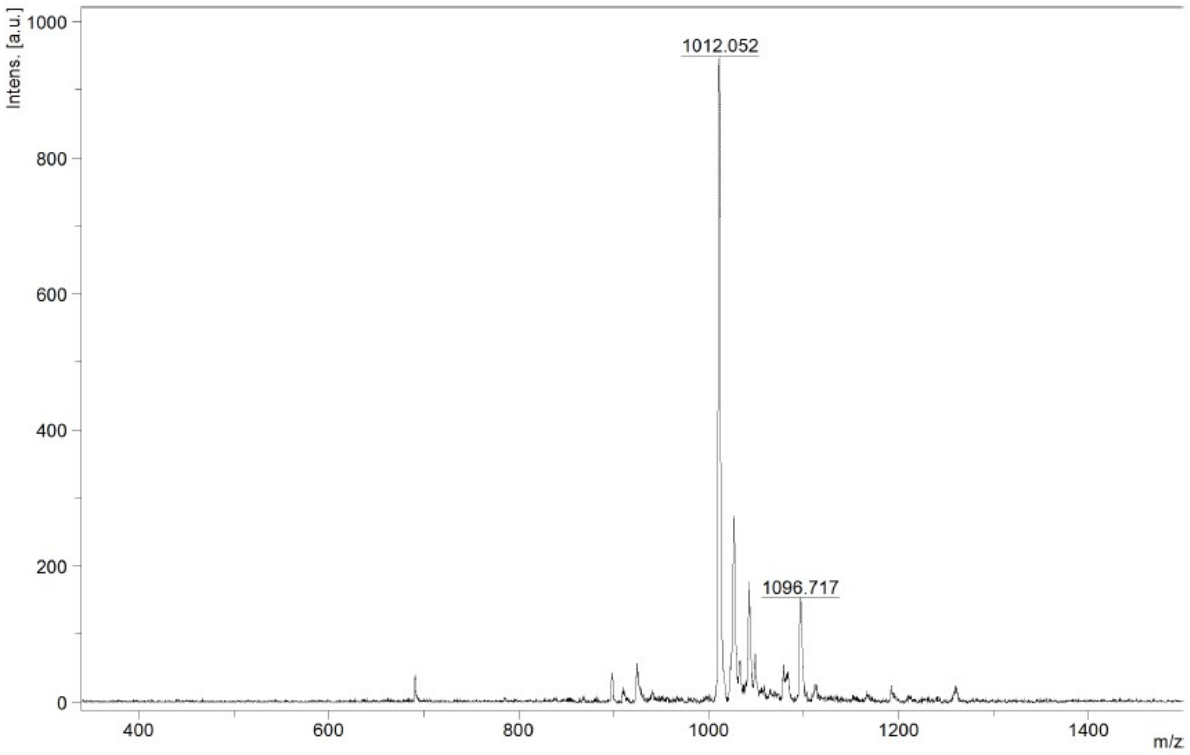


Fig S9. The MALDI TOF mass spectrum of compound **3**

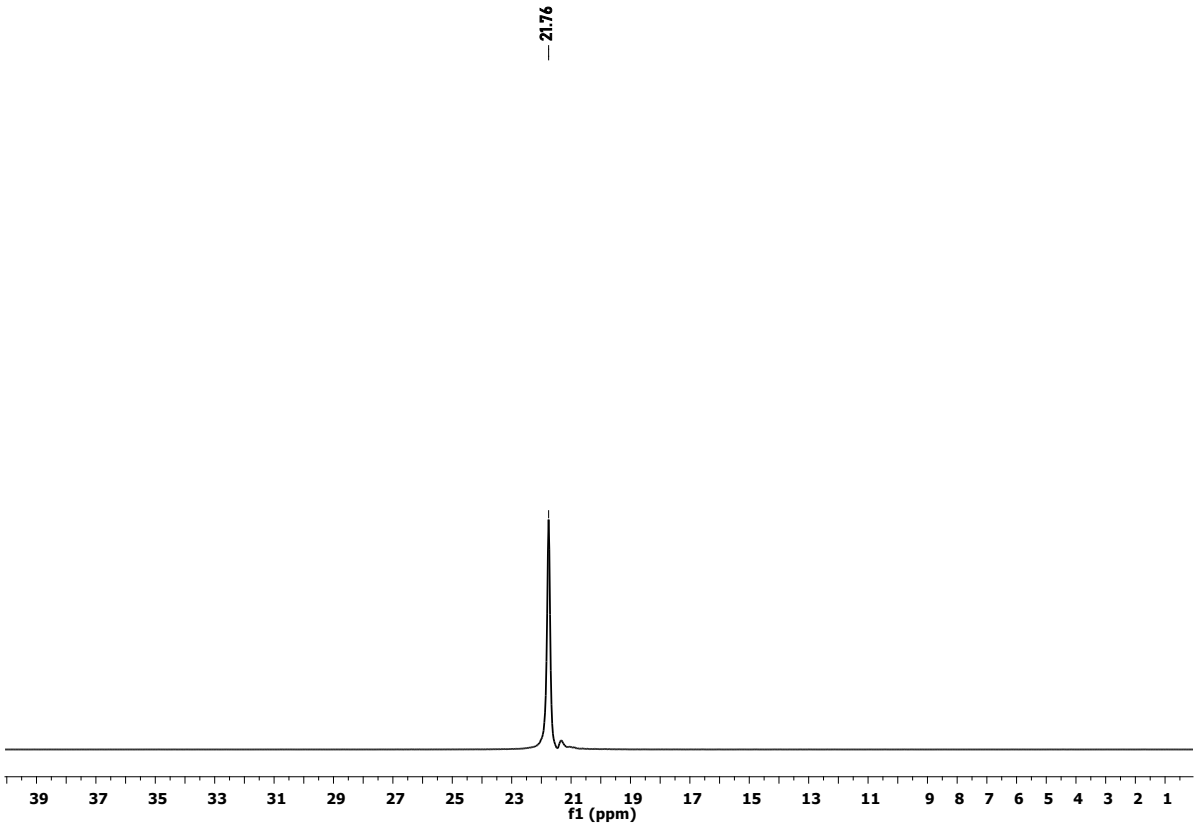


Fig S10. The proton decoupled ^{31}P NMR spectrum of compound **3**

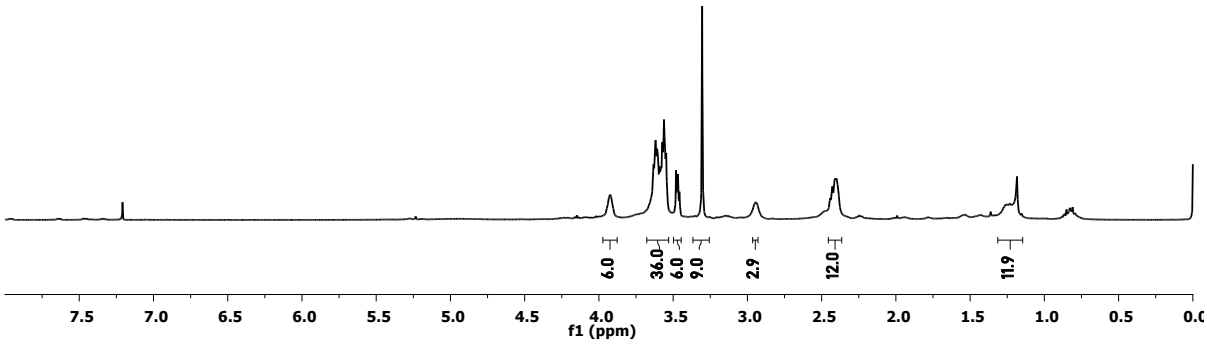


Fig S11. The ^{1}H NMR spectrum of compound **3**

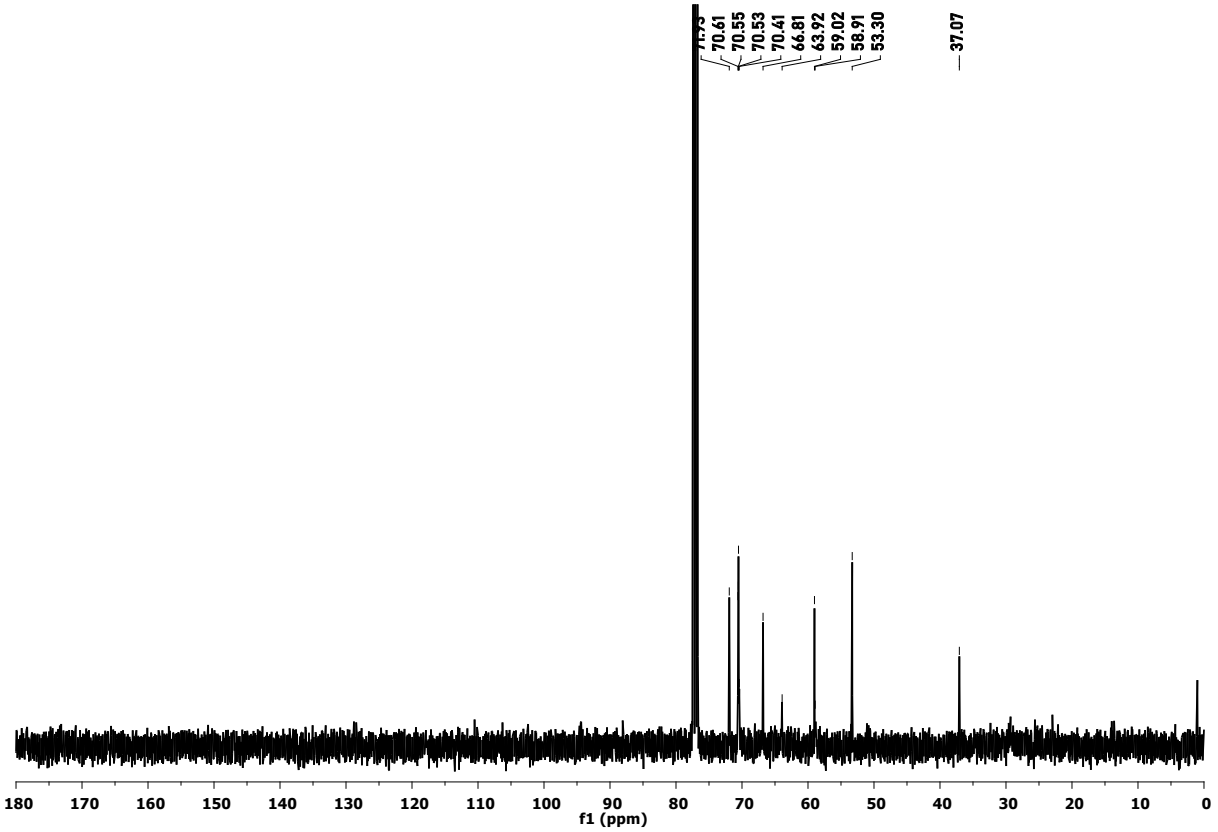


Fig S12. The ^{13}C NMR spectrum of compound **3**

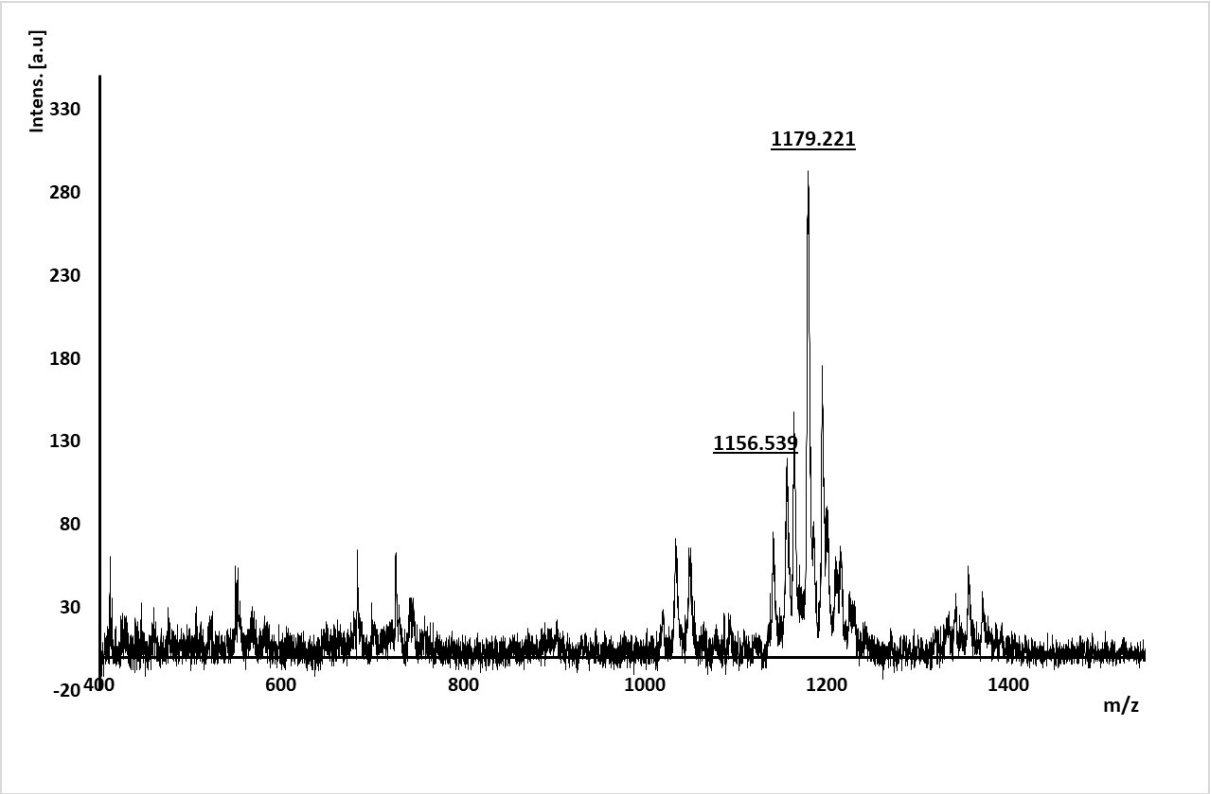


Fig S13. The MALDI TOF mass spectrum of compound **4**

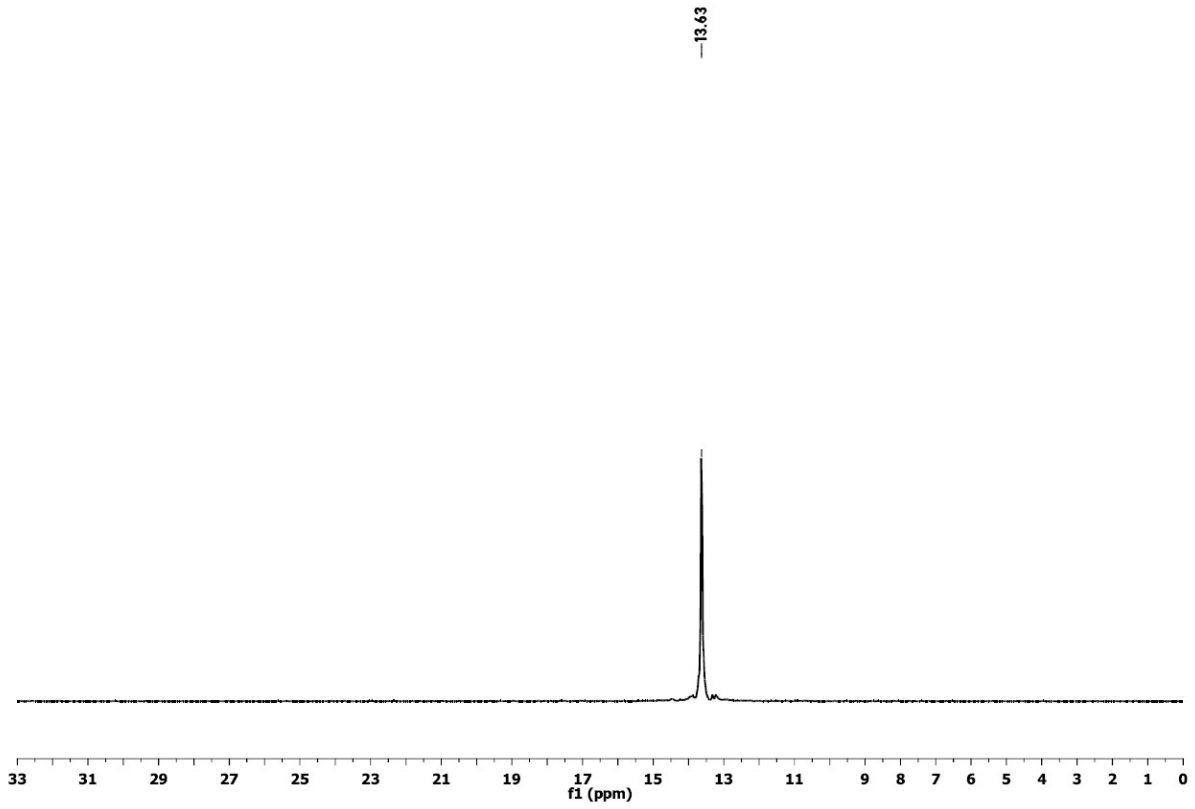


Fig S14. The proton decoupled ^{31}P NMR spectrum of compound **4**

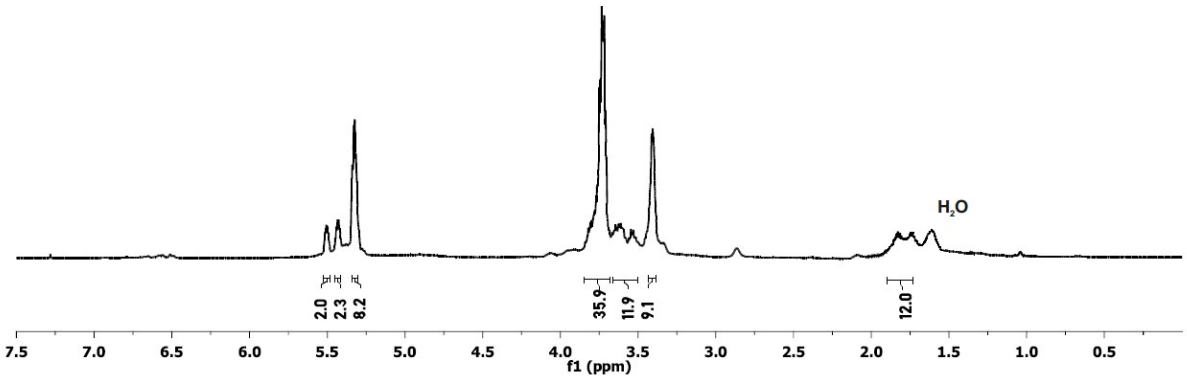


Fig S15. The ^{1}H NMR spectrum of compound **4**

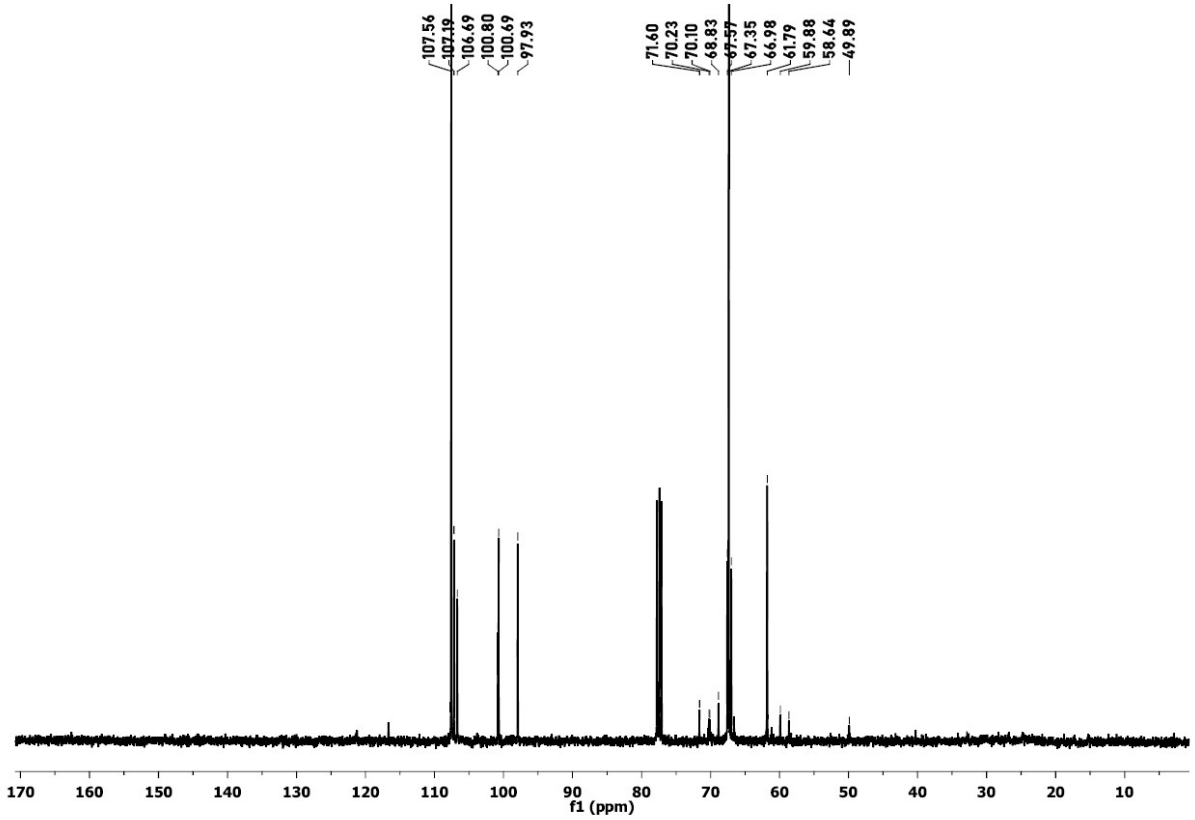


Fig S16. The ^{13}C NMR spectrum of compound **4**

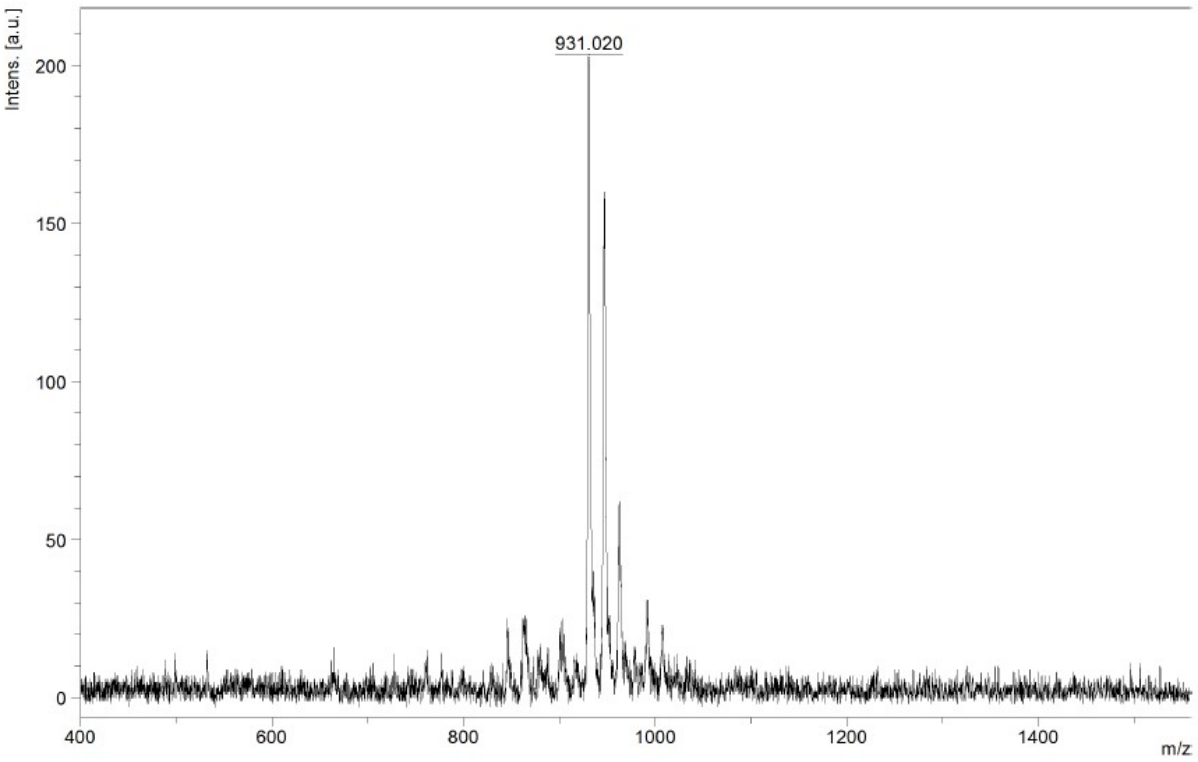


Fig S17. The MALDI TOF mass spectrum of compound **5**

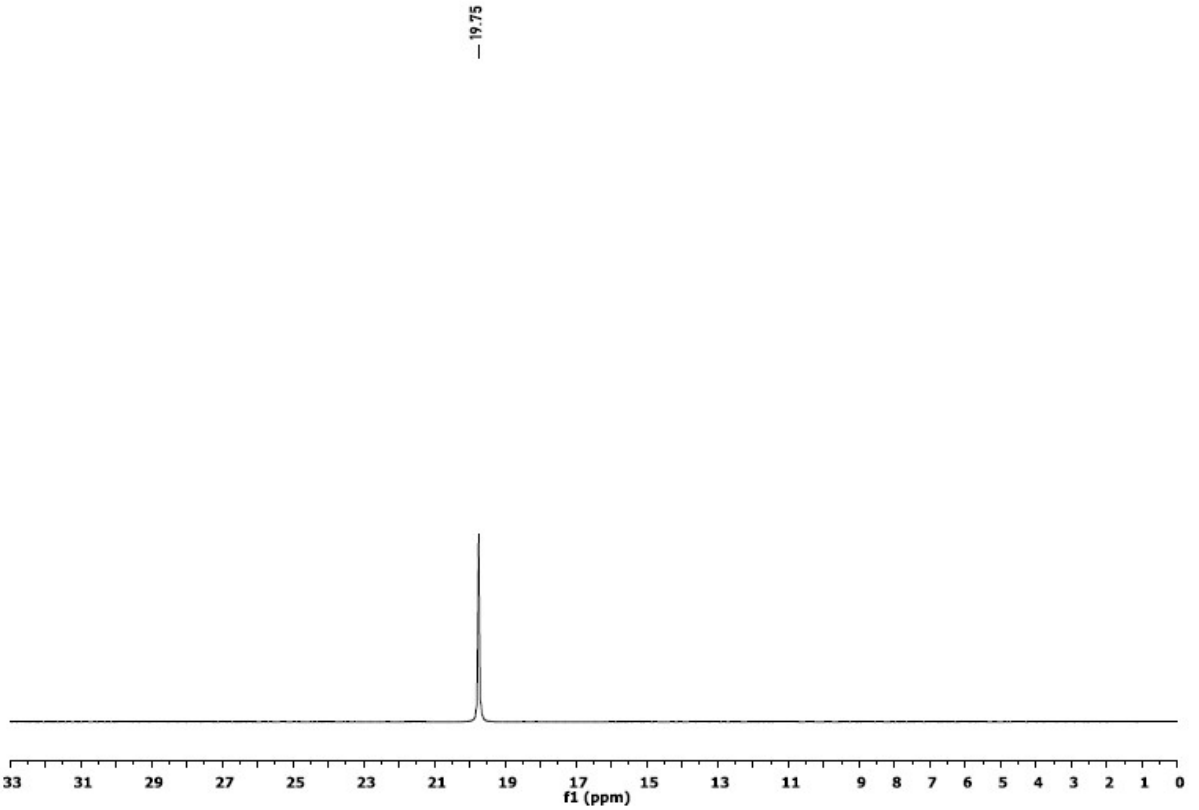


Fig S18. The proton decoupled ^{31}P NMR spectrum of compound **5**

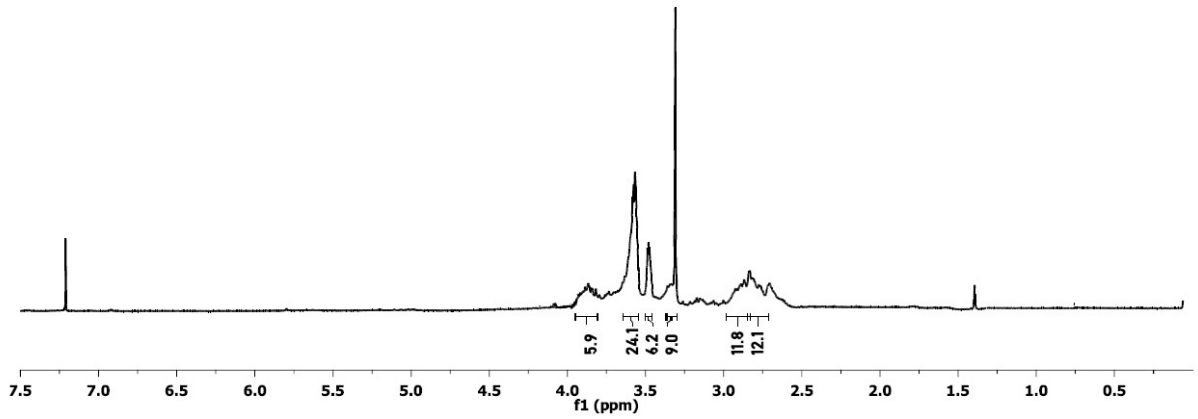


Fig S19. The ^{1}H NMR spectrum of compound **5**

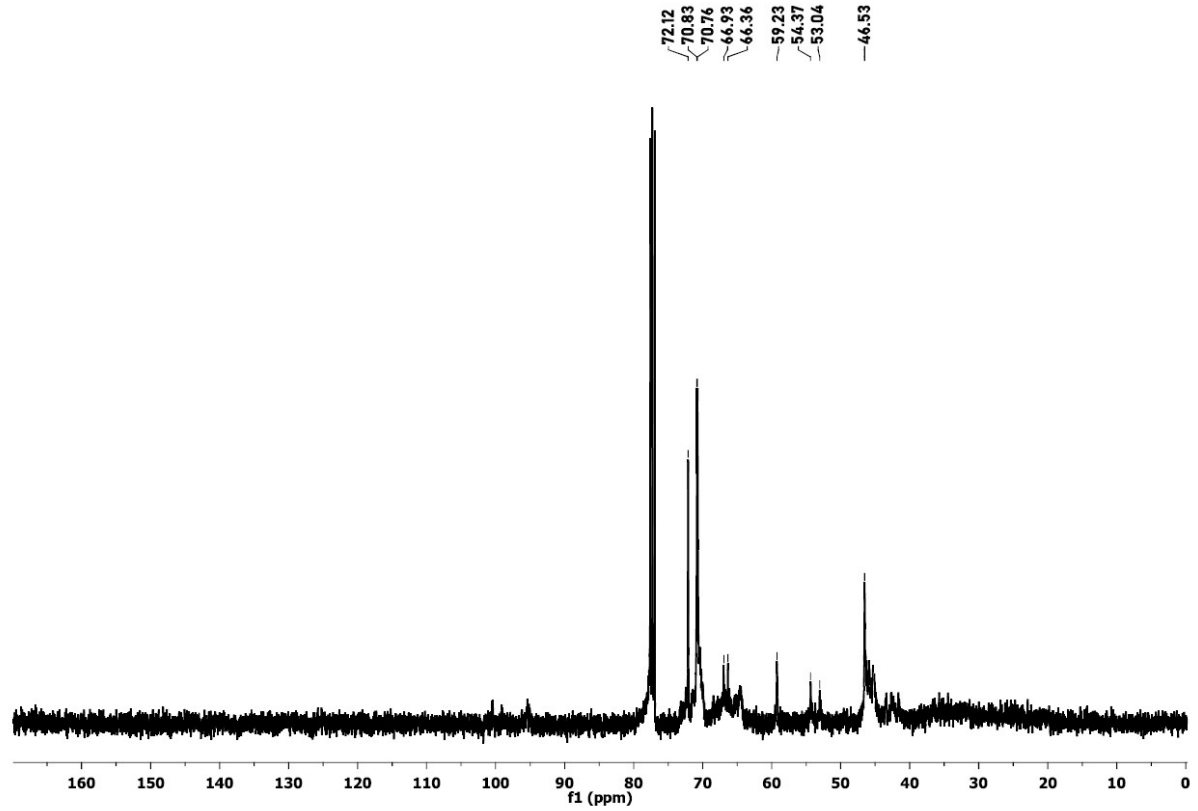


Fig S20. The ^{13}C NMR spectrum of compound **5**

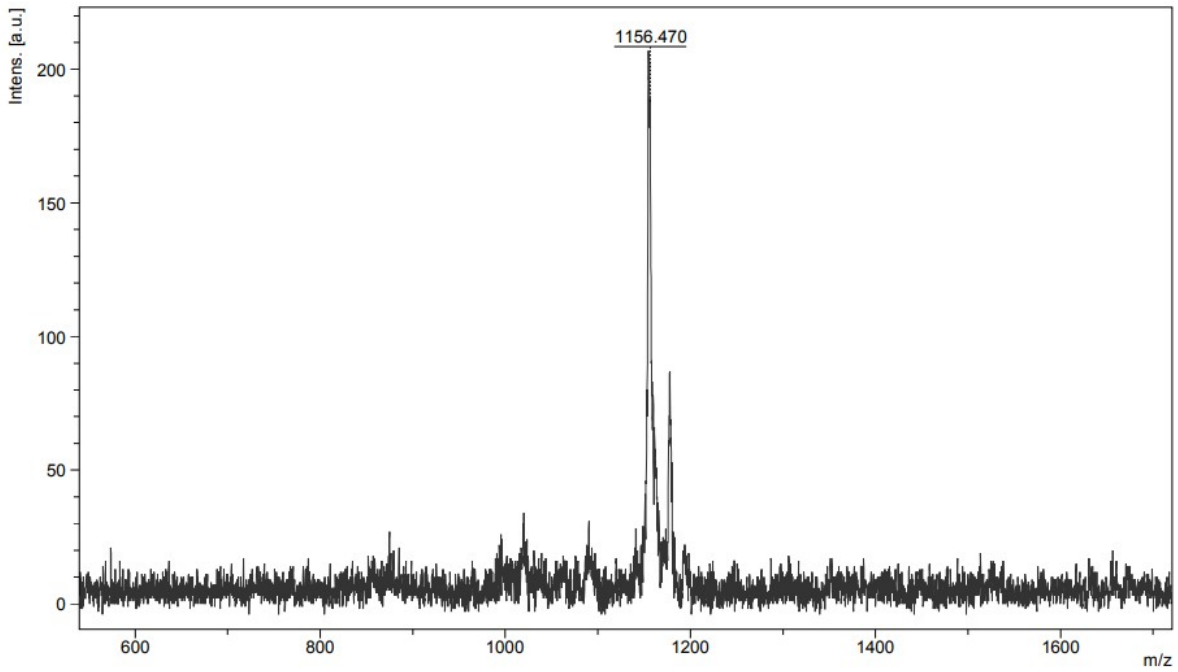


Fig S21. The MALDI TOF mass spectrum of compound **6**

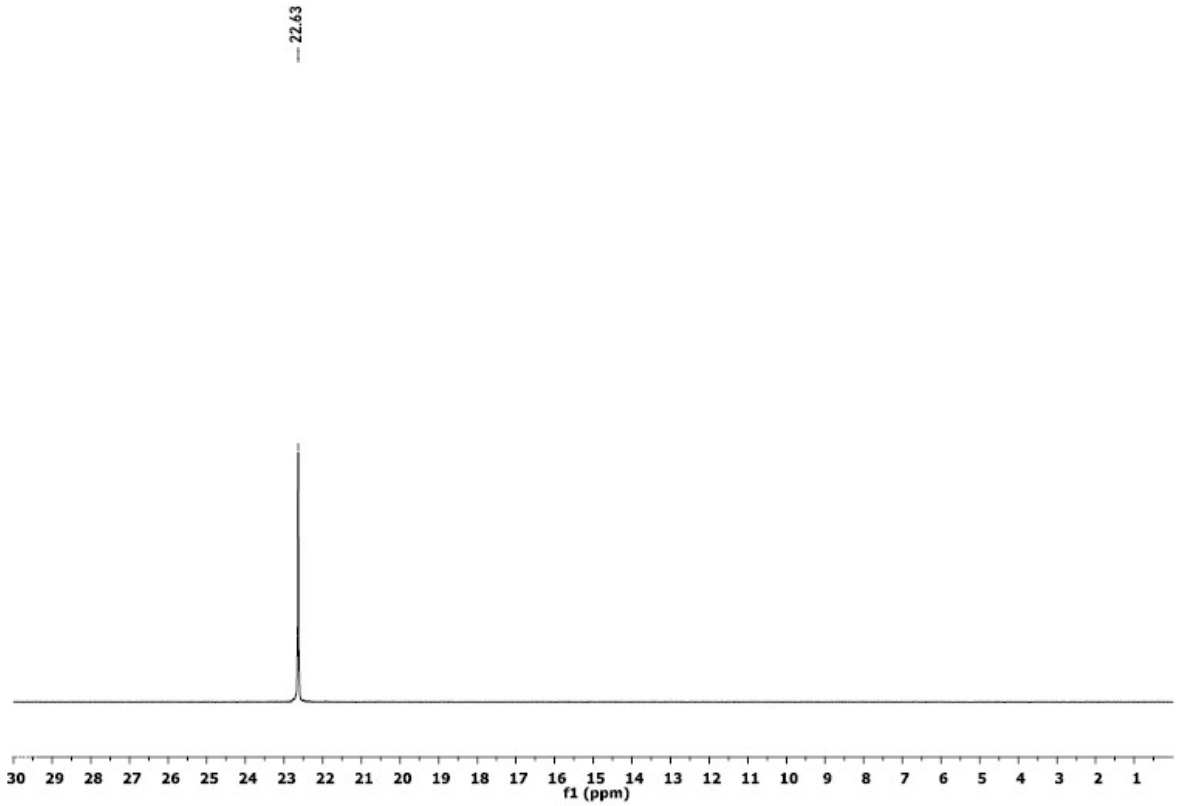


Fig S22. The proton decoupled ^{31}P NMR spectrum of compound **6**

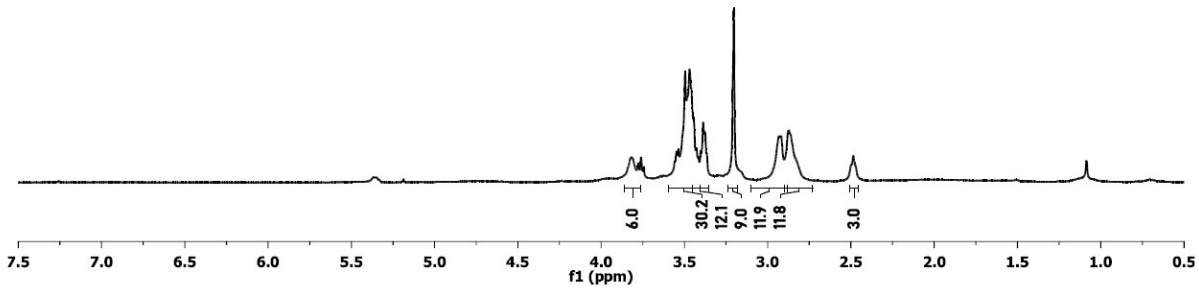


Fig S23. The ^{1}H NMR spectrum of compound **6**

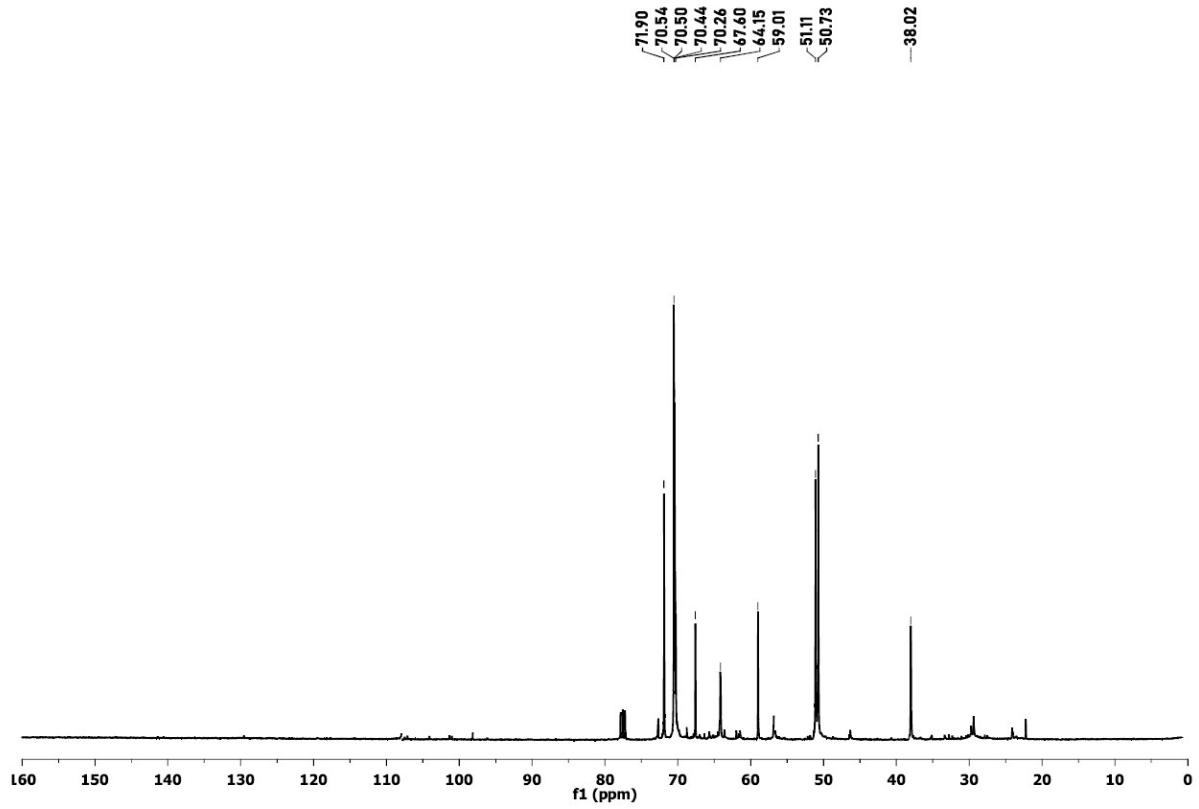


Fig S24. The ^{13}C NMR spectrum of compound **6**

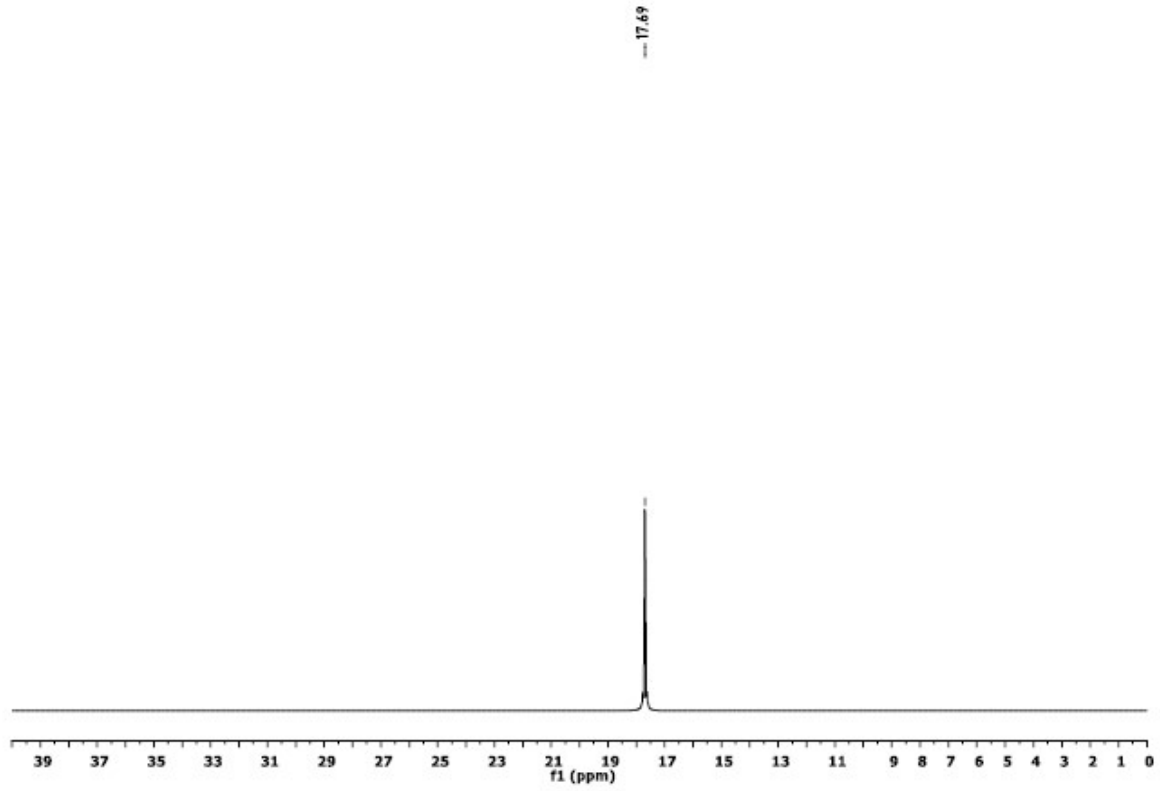


Fig S25. The proton decoupled ^{31}P NMR spectrum of compound **7**

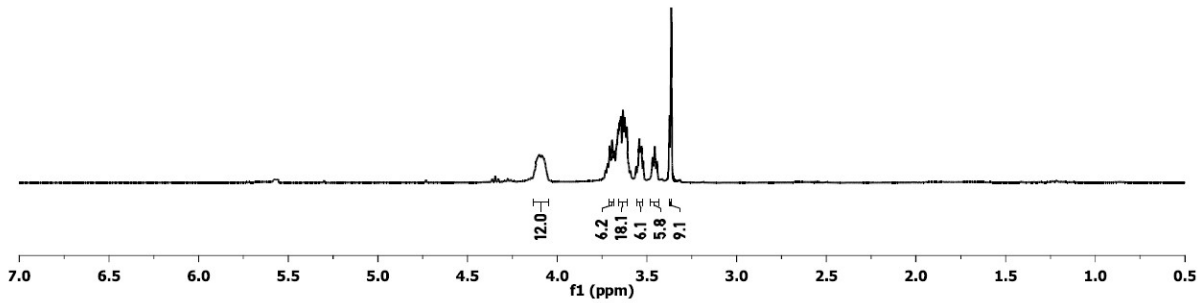


Fig S26. The ^{1}H NMR spectrum of compound **7**

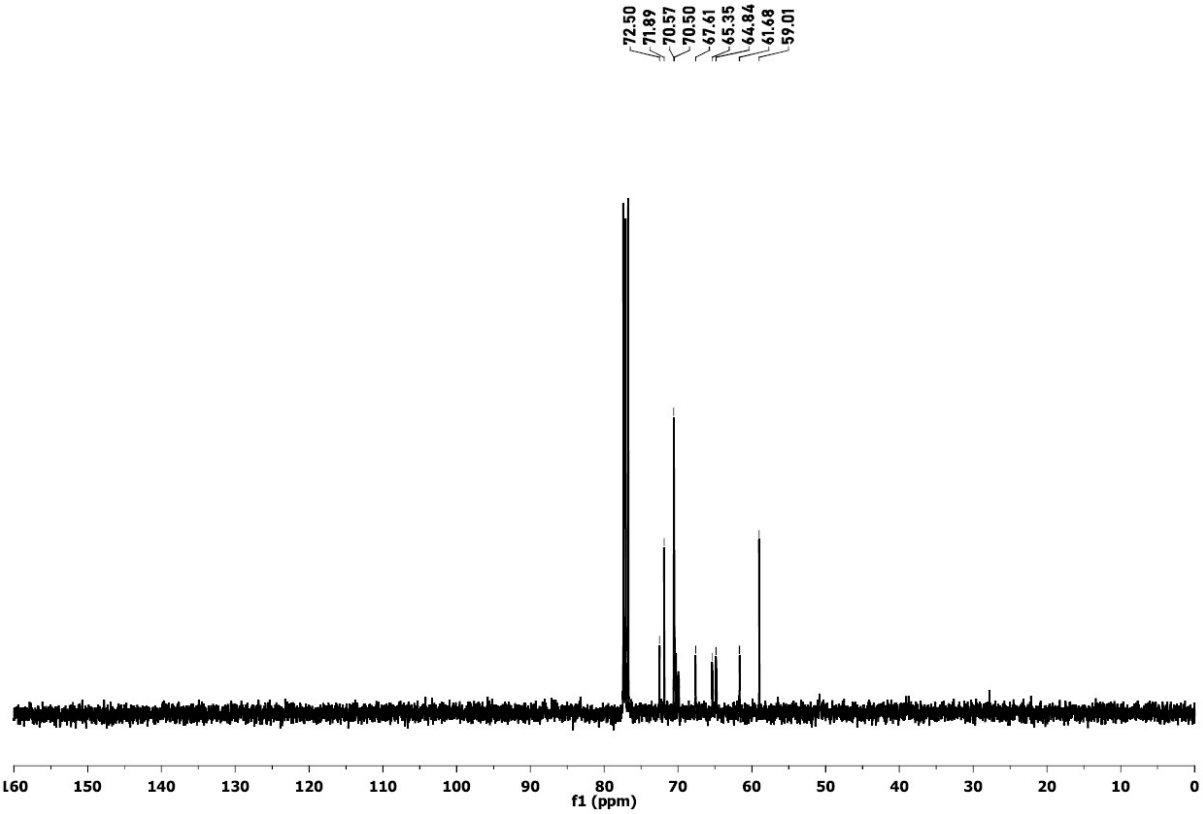


Fig S27. The ^{13}C NMR spectrum of compound **7**

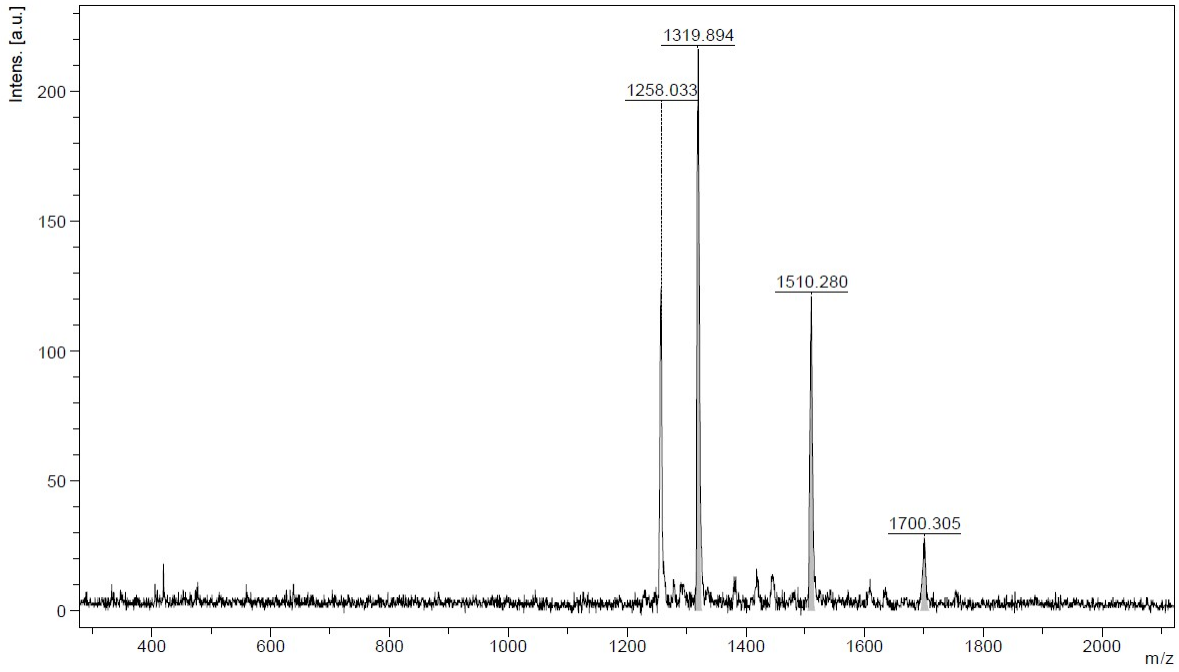


Fig S28. The MALDI TOF mass spectrum of compound **8**

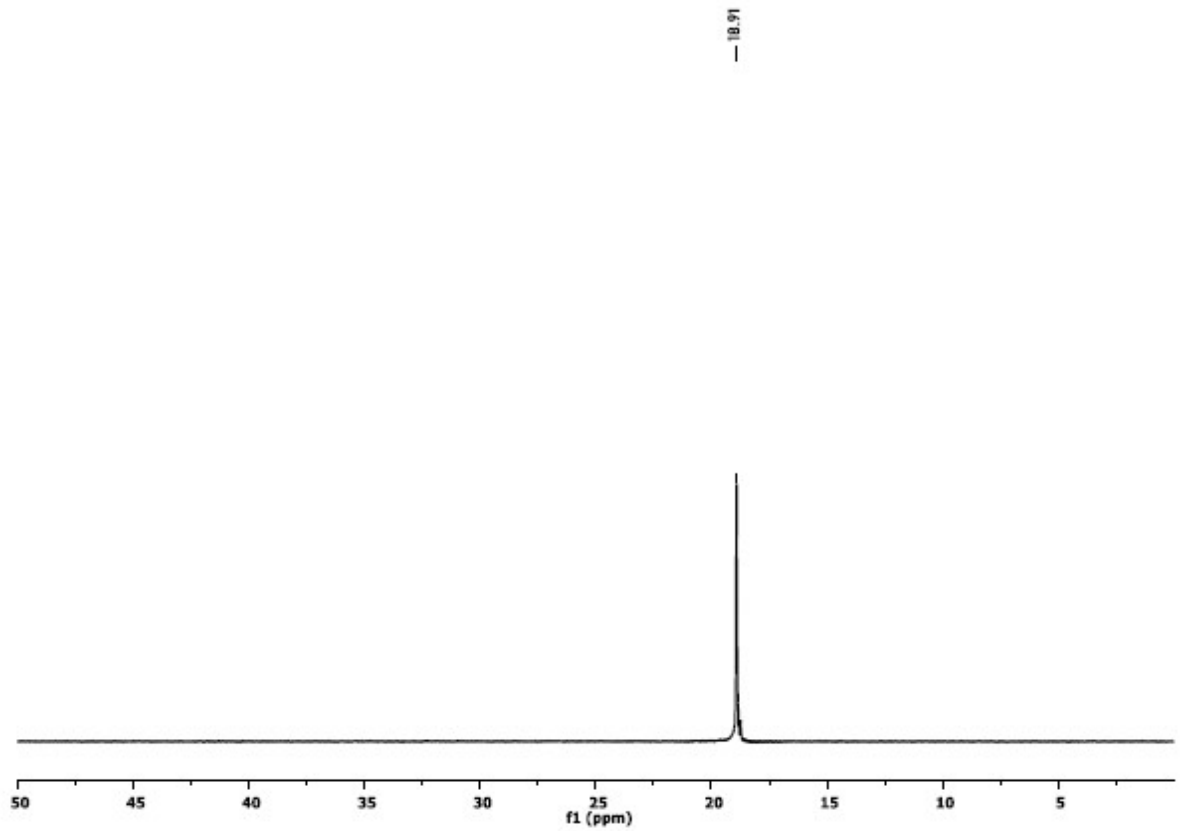


Fig S29. The proton decoupled ^{31}P NMR spectrum of compound **8**

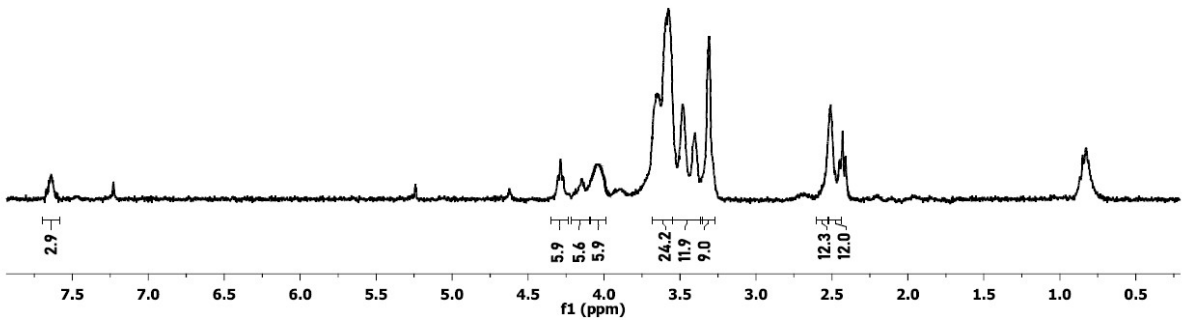


Fig S30. The ^{1}H NMR spectrum of compound **8**

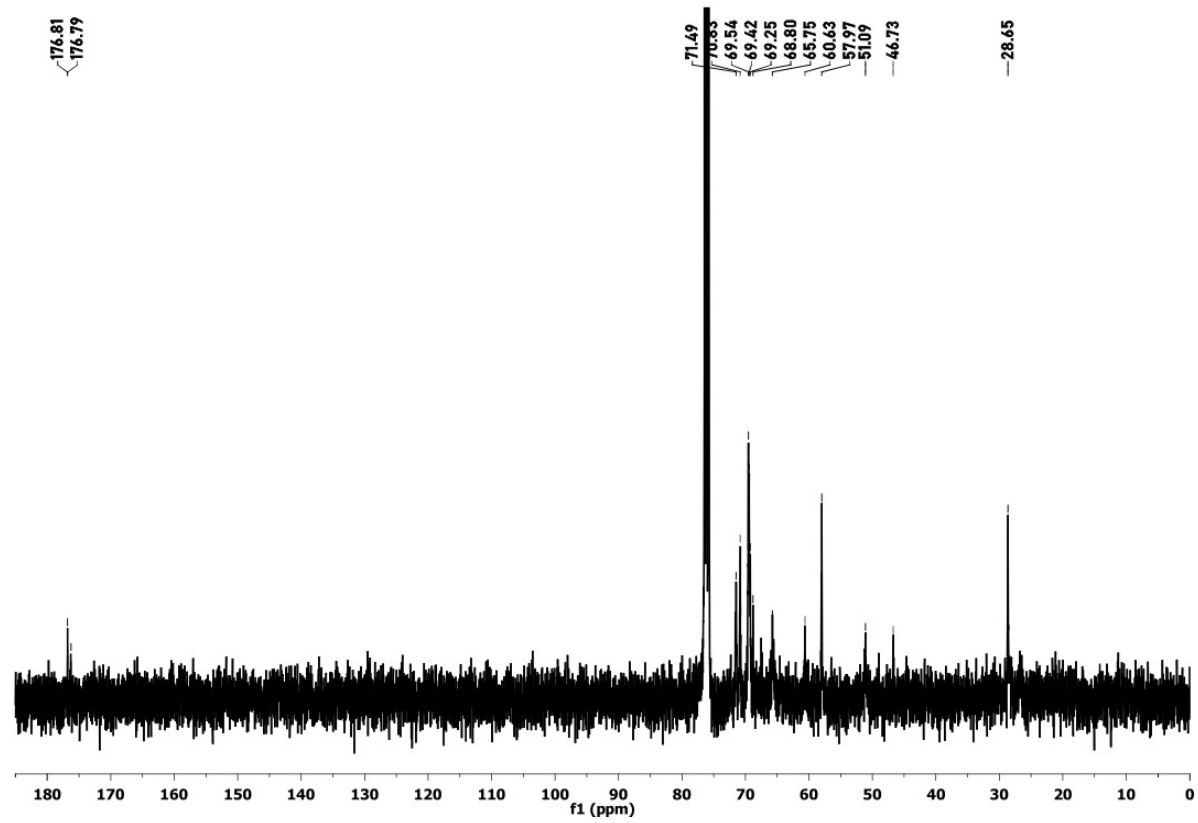


Fig S31. The ^{13}C NMR spectrum of compound **8**

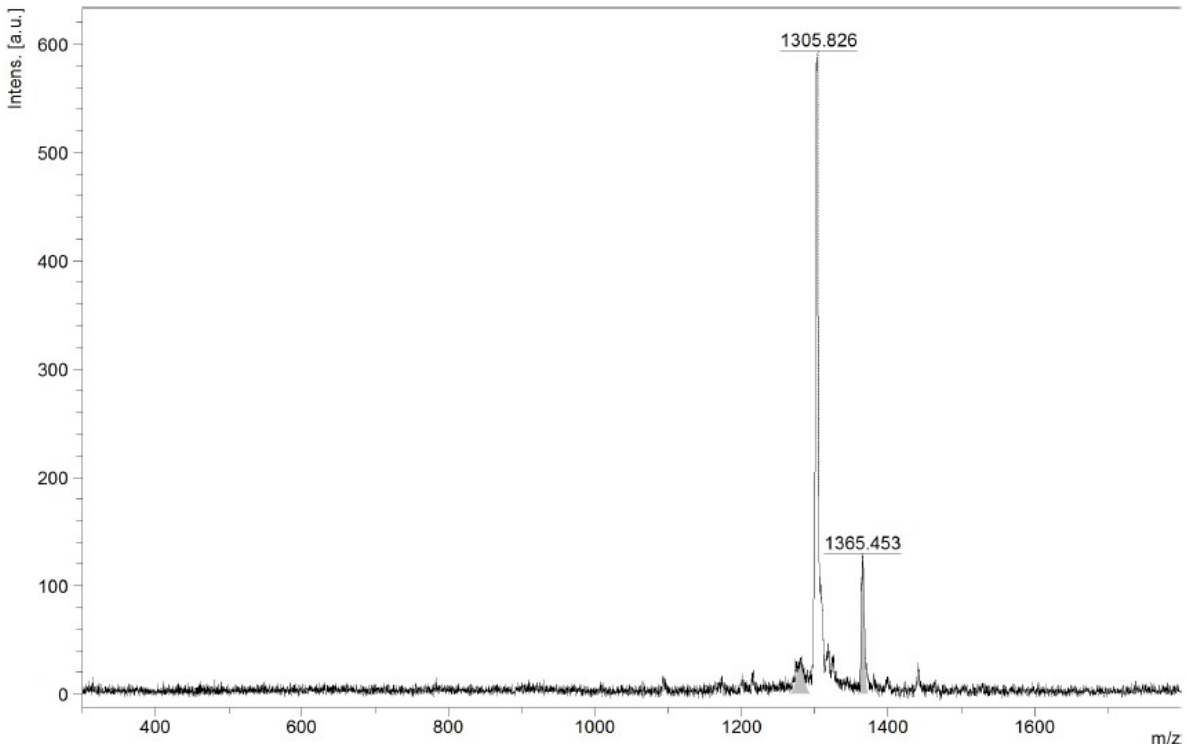


Fig S32. The MALDI TOF mass spectrum of compound **9**

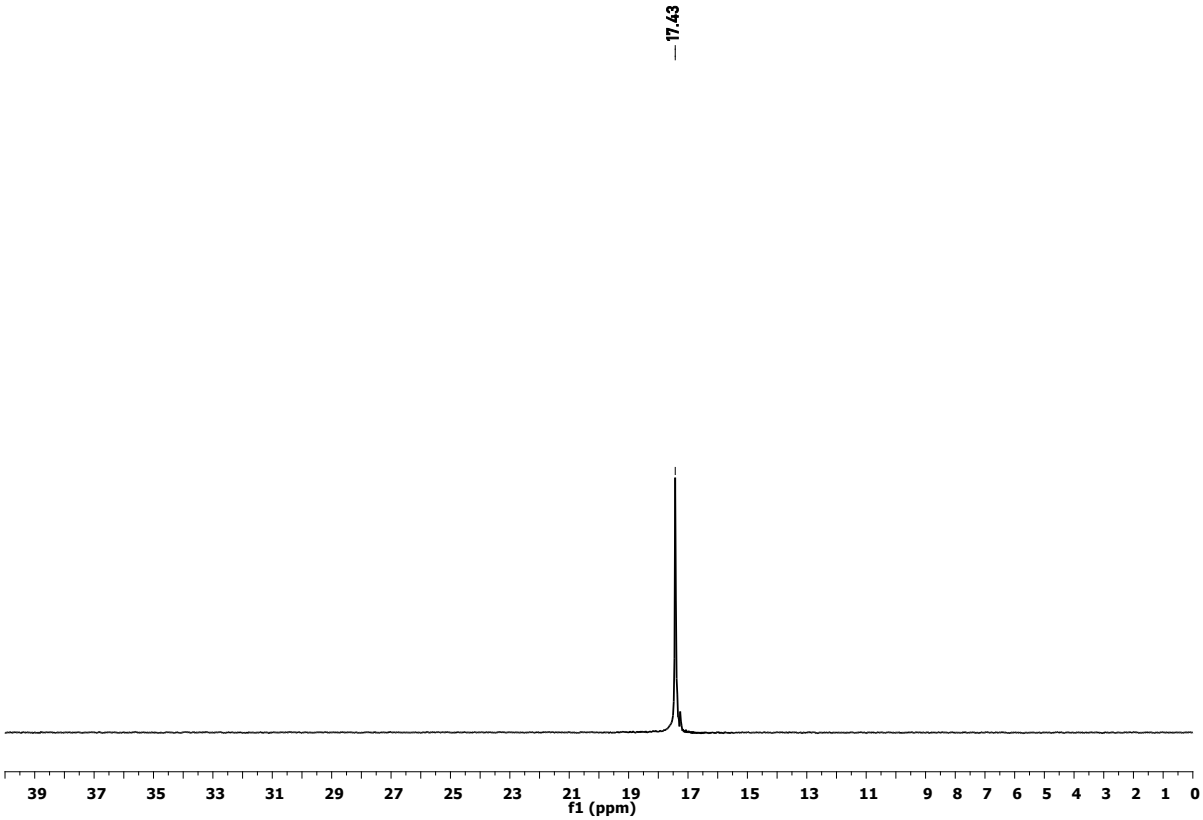


Fig S33. The proton decoupled ^{31}P NMR spectrum of compound **9**

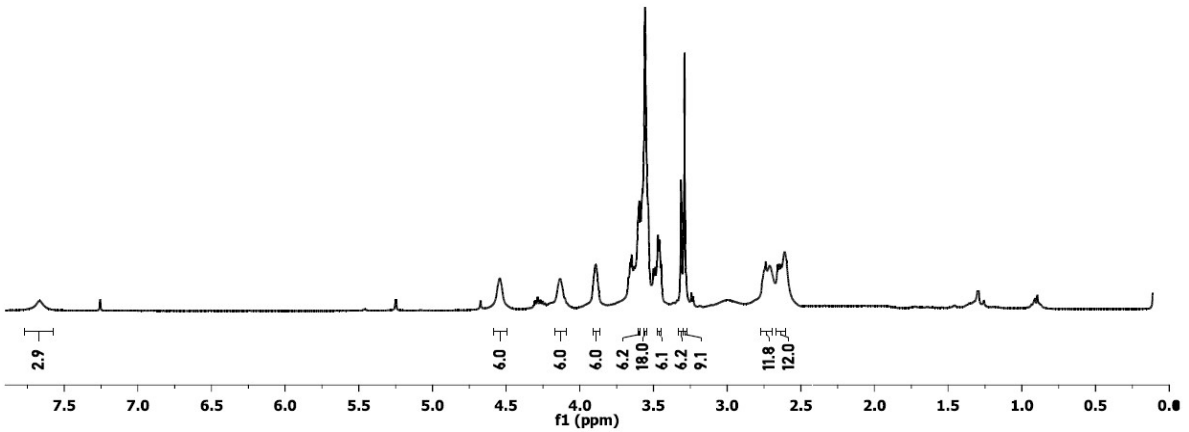


Fig S34. The ^{1}H NMR spectrum of compound **9**

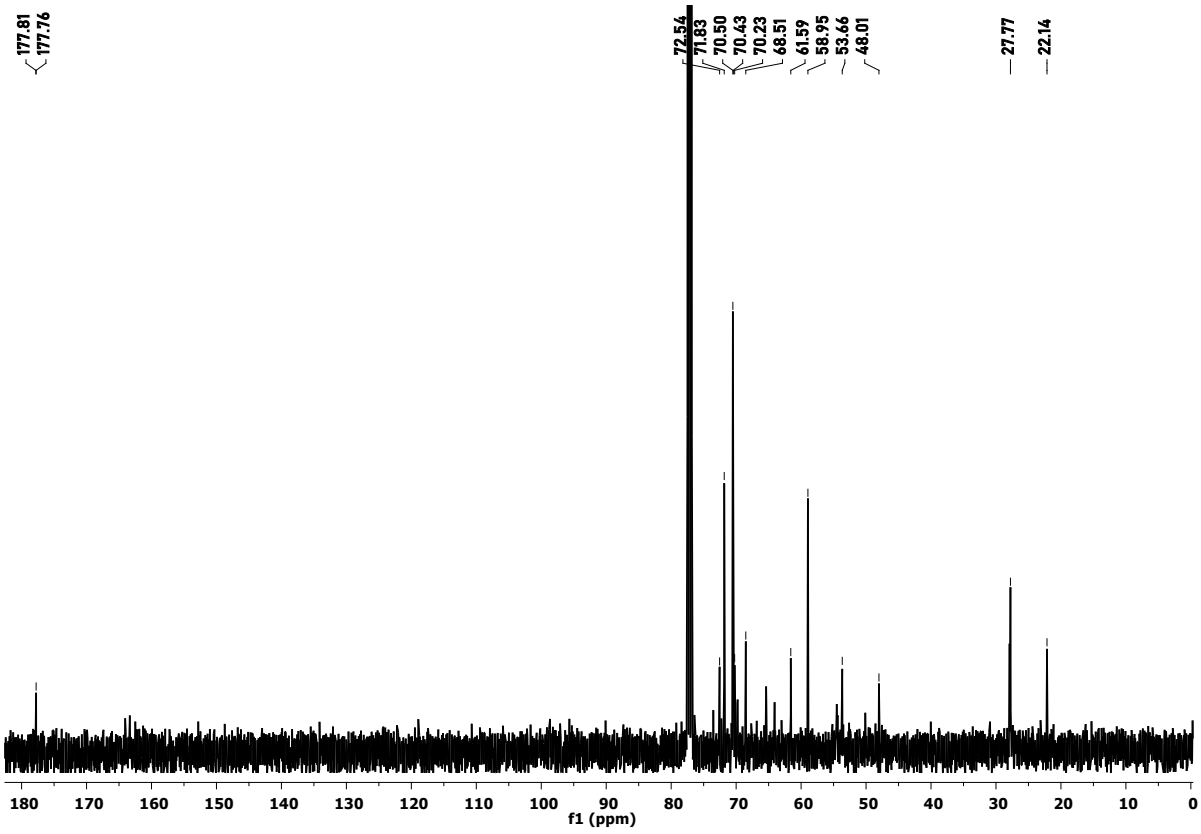
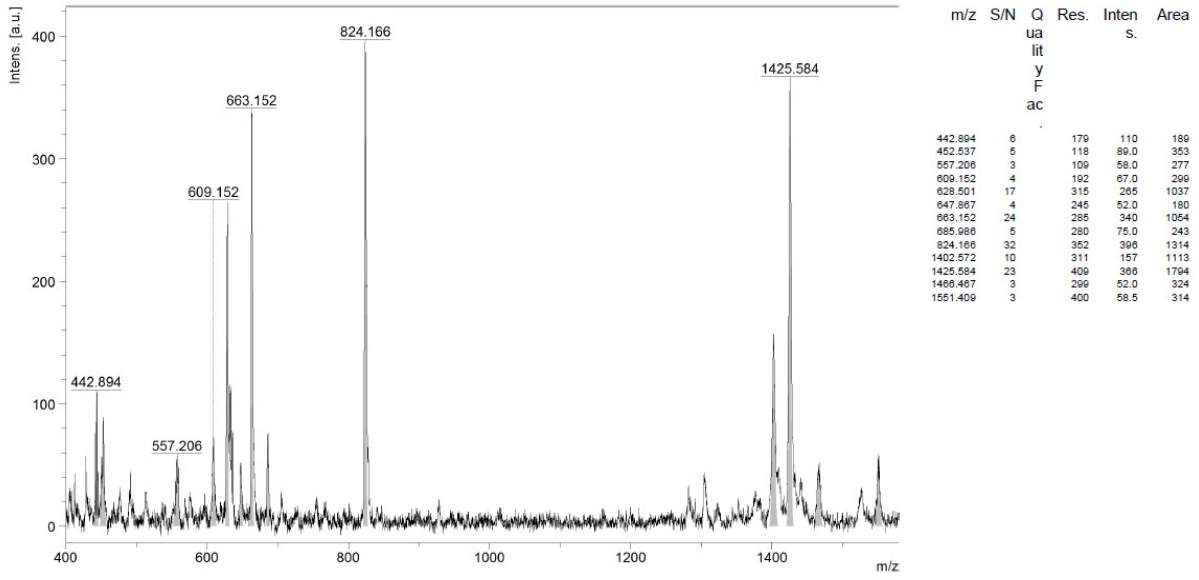


Fig S35. The ^{13}C NMR spectrum of compound **9**



m/z	S/N	Quality Fac.	Res.	Intens.	Area
442.894	6		179	110	189
452.537	5		118	89.0	353
557.206	3		109	58.0	277
609.152	4		192	67.0	299
628.501	17		315	265	1037
647.867	4		245	52.0	180
663.152	24		285	340	1054
685.986	5		280	75.0	243
824.166	32		352	396	1314
1402.572	10		311	157	1113
1425.584	23		409	366	1794
1466.467	3		299	52.0	324
1551.409	3		400	58.5	314

Fig S36. The MALDI TOF mass spectrum of compound **10**

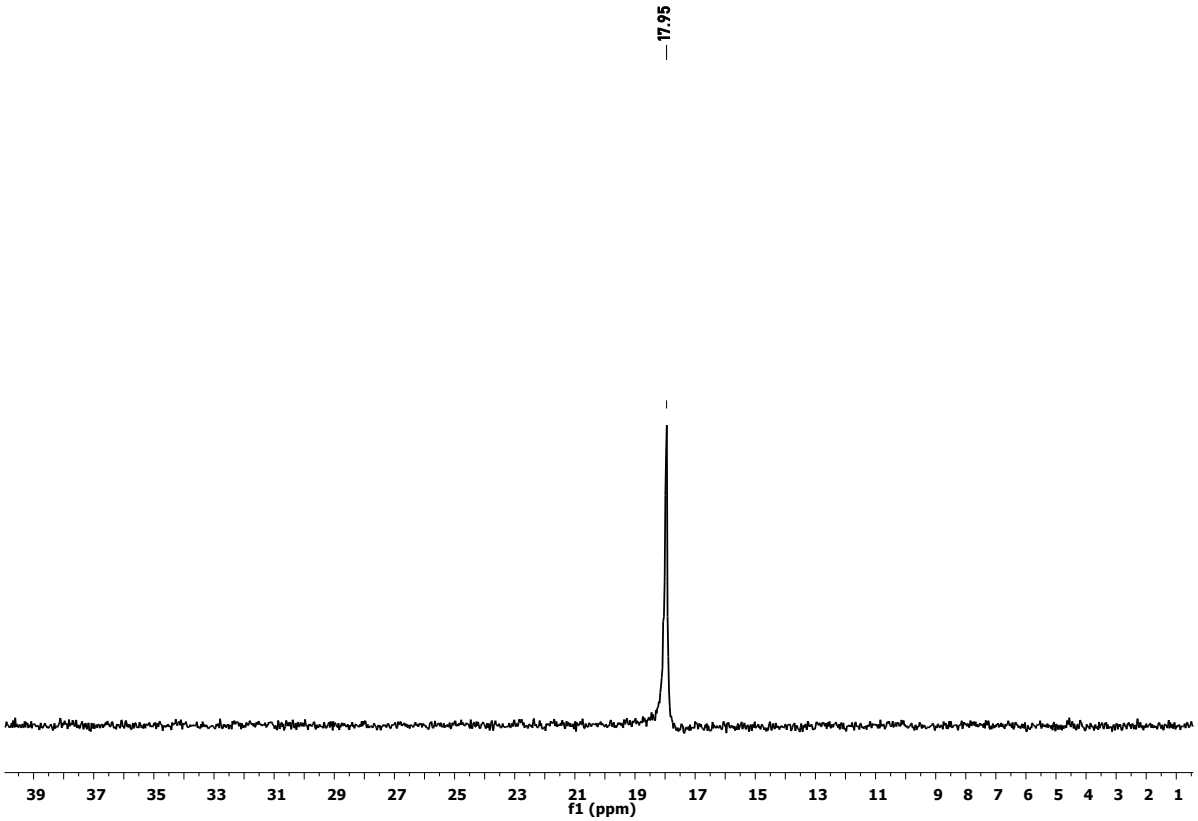


Fig S37. The proton decoupled ^{31}P NMR spectrum of compound **10**

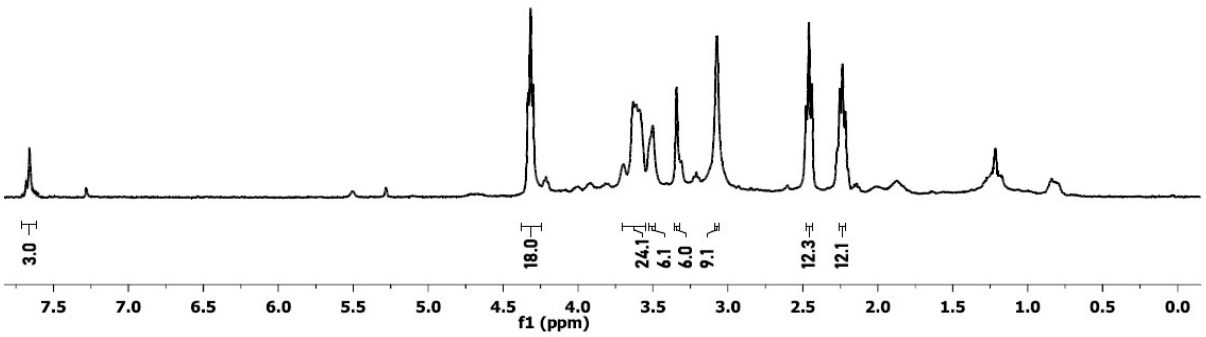


Fig S38. The ^{1}H NMR spectrum of compound **10**

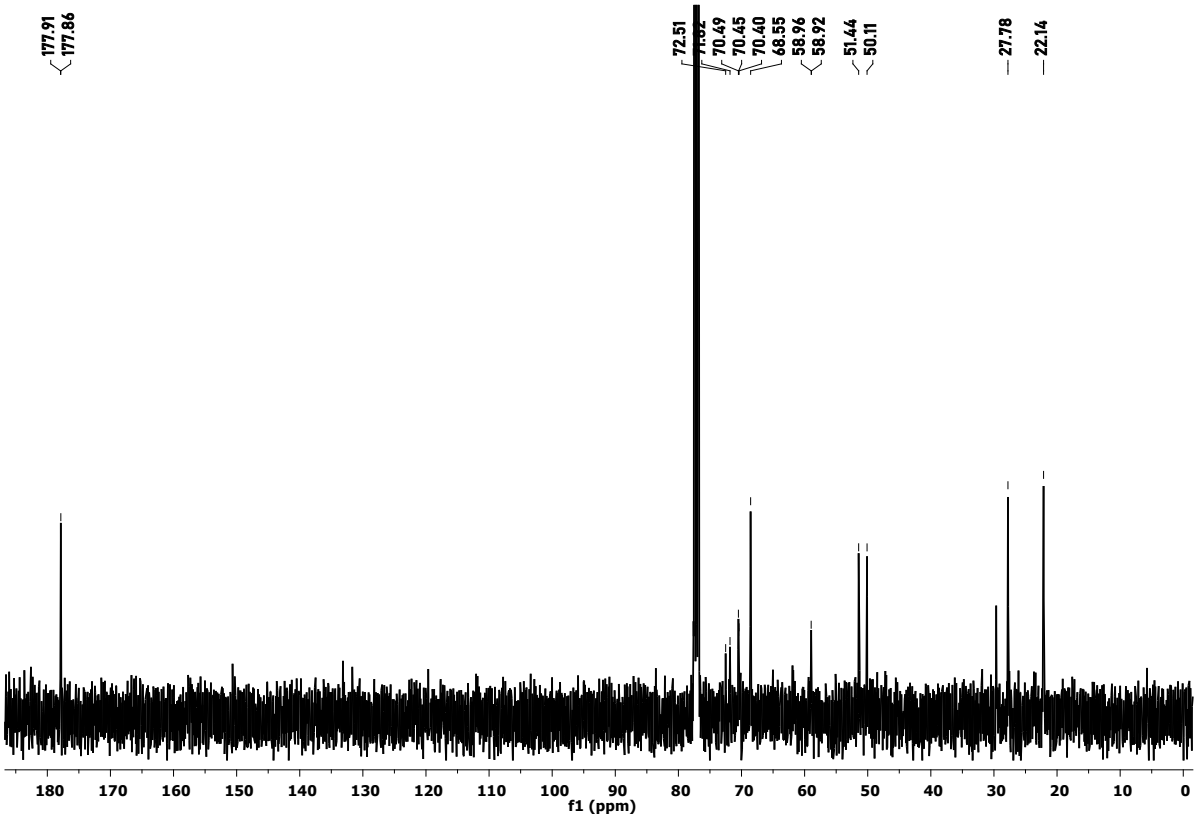


Fig S39. The ^{13}C NMR spectrum of compound **10**

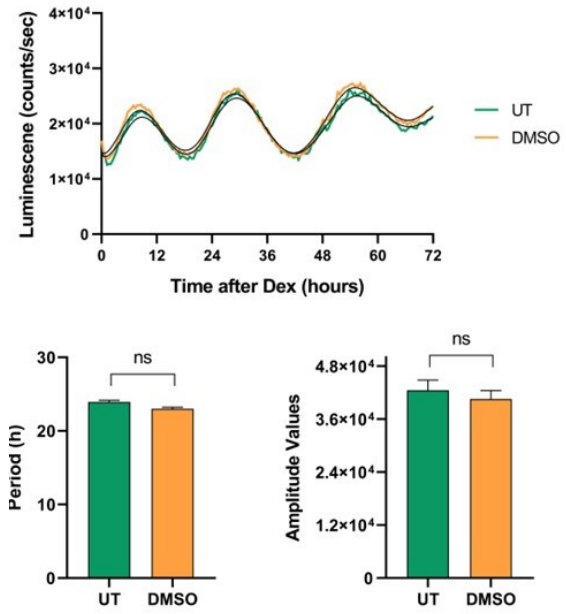


Fig S40. Real-time bioluminescence graph representing circadian oscillations in untreated (UT) and 0.5% DMSO treated U2OS cells. Graphs represented raw data were illustrated with GraphPad. Period and amplitude data were analyzed using Student's-t test, revealing no significant differences between groups. Period and amplitude values are represented mean ± SD (n = 3). Statistical significance was set at *p < 0.01.

Table S1. XLOGP values computed by SwissADME web server.

Compound	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
XLOGP	1.75	-1.03	-0.59	5.39	1.36	0.84	4.77	-2.56	-1.39	-5.21

Table S2. Colony Formation values.

		Colony Numbers		Average		Plating Efficiency		Plating Efficiency (%)		Plating Efficiency (%)Normalized to DMSO		Plating Efficiency Normalized to DMSO	
Compound No	**Replicates**	**Min Dose**	**Max Dose**	**Min Dose**	**Max Dose**	**Min Dose**	**Max Dose**	**Min Dose**	**Max Dose**	**Min Dose**	**Max Dose**	**Min Dose**	**Max Dose**
1	R1	165,00	152,00	179,33	162,33	0,36	0,32	35,87	32,47	61,91	56,04	0,62	0,56
	R2	191,00	169,00										
	R3	182,00	166,00										
2	R1	153,00	76,00	167,67	84,67	0,34	0,17	33,53	16,93	57,88	29,23	0,58	0,29
	R2	195,00	92,00										
	R3	155,00	86,00										
3	R1	189,00	150,00	182,67	152,00	0,37	0,30	36,53	30,40	63,06	52,47	0,63	0,52
	R2	194,00	158,00										
	R3	165,00	148,00										
4	R1	153,00	57,00	169,67	62,67	0,34	0,13	33,93	12,53	58,57	21,63	0,59	0,22
	R2	180,00	68,00										
	R3	176,00	63,00										
5	R1	176,00	107,00	163,67	114,33	0,33	0,23	32,73	22,87	56,50	39,47	0,57	0,39
	R2	170,00	122,00										
	R3	145,00	114,00										
6	R1	219,00	187,00	209,00	190,33	0,42	0,38	41,80	38,07	72,15	65,71	0,72	0,66
	R2	216,00	195,00										
	R3	192,00	189,00										
7	R1	190,00	127,00	196,67	129,33	0,39	0,26	39,33	25,87	67,89	44,65	0,68	0,45
	R2	208,00	141,00										
	R3	192,00	120,00										
8	R1	193,00	132,00	180,33	134,33	0,36	0,27	36,07	26,87	62,26	46,38	0,62	0,46
	R2	175,00	135,00										
	R3	173,00	136,00										
9	R1	215,00	161,00	207,67	173,33	0,42	0,35	41,53	34,67	71,69	59,84	0,72	0,60
	R2	228,00	185,00										
	R3	180,00	174,00										
10	R1	153,00	77,00	166,33	67,33	0,33	0,13	33,27	13,47	57,42	23,25	0,57	0,23
	R2	185,00	75,00										
	R3	161,00	50,00										
DMSO Control	R1	280,00	280,00	289,67	289,67	0,58	0,58	57,93	57,93	100,00	100,00	1,00	1,00
	R2	291,00	291,00										
	R3	298,00	298,00										