

Supporting information

Synthesis of novel N-9 substituted 6-(4-(4-propoxyphenyl)piperazin-1-yl)-9H-purine derivatives as inducers of apoptosis in MCF-7 breast cancer cells

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Table 3. Cytotoxicity of 6-(4-(4-propoxyphenyl)piperazin-1-yl)-9H-purine derivatives (PP05-PP21) against a HeLa cancer cell line in triplicate experiments

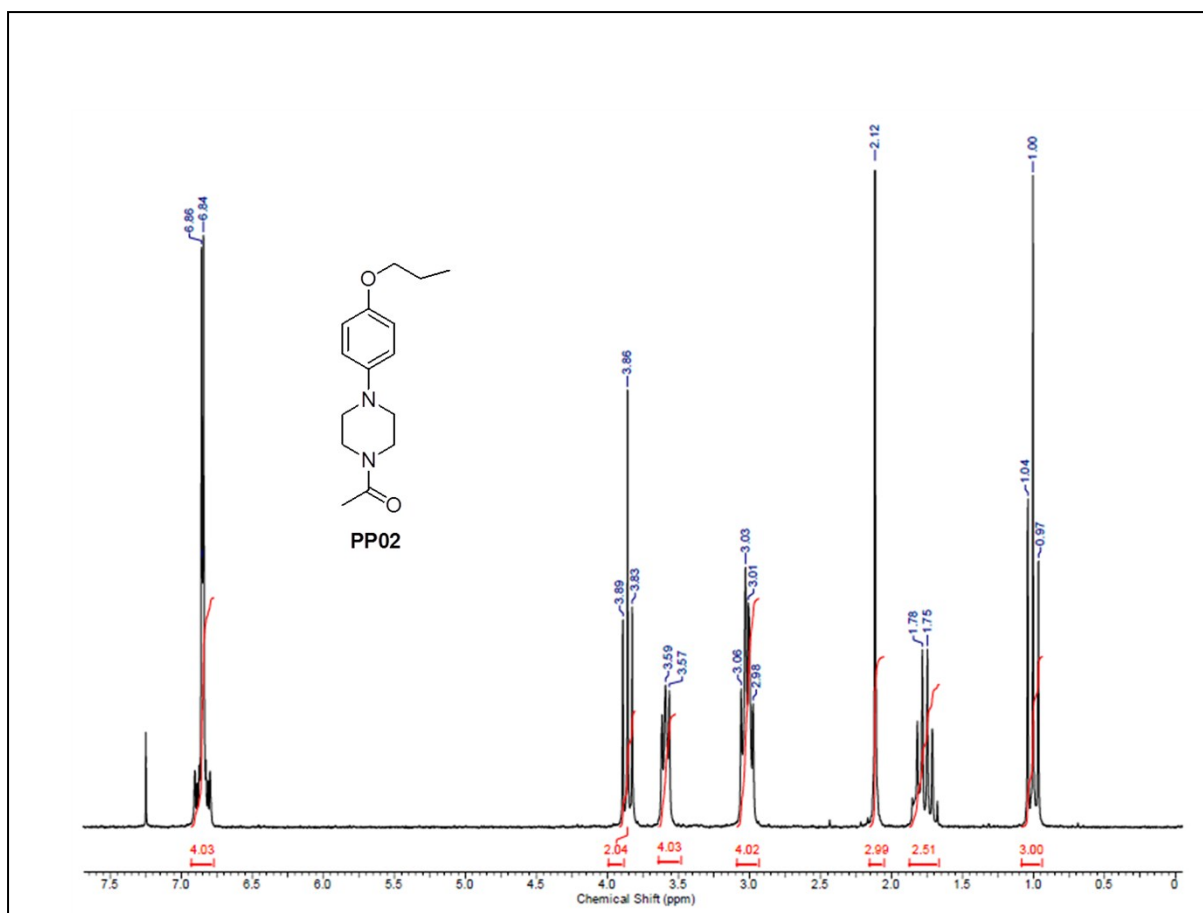
Compounds	Human Cervix Cancer Cell Line HeLa															
	% Control Growth															
	Drug Concentrations (µg/mL)															
	Experiment 1				Experiment 2				Experiment 3				Average Values			
	10	20	40	80	10	20	40	80	10	20	40	80	10	20	40	80
PP-5	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
PP-6	99.2	98.1	96.1	93.2	96.3	92.2	90.0	89.1	95.1	93.4	92.1	89.9	96.8	94.5	92.7	90.7
PP-7	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
PP-8	100.0	100.0	100.0	94.8	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	98.3
PP-9	71.5	62.5	46.8	32.9	87.6	81.8	61.1	44.2	77.0	68.2	47.8	37.1	78.7	70.8	51.9	38.1
PP-10	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
PP-11	98.8	97.2	80.1	75.7	100.0	100.0	97.3	86.2	100.0	100.0	97.6	78.4	99.6	99.1	91.7	80.1
PP-12	100.0	100.0	100.0	92.2	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	97.4
PP-13	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
PP-14	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
PP-15	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
PP-16	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
PP-17	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
PP-18	100.0	100.0	98.3	97.1	100.0	100.0	99.2	98.4	99.1	97.3	96.8	95.7	99.7	99.1	98.1	97.0
PP19	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
PP-20	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
PP-21	100.0	100.0	99.5	97.2	100.0	99.1	96.2	94.1	99.2	97.5	94.6	92.1	99.7	98.8	96.7	94.4
ADR	-76.3	-77.5	-79.3	-81.0	-71.4	-74.7	-79.4	-80.2	-72.5	-75.5	-78.2	-80.6	-73.4	-75.9	-79.0	-80.6

Table 4. Cytotoxicity of 6-(4-(4-propoxyphenyl)piperazin-1-yl)-9H-purine derivatives (PP05-PP21) against a HCT-15 cancer cell line in triplicate experiments

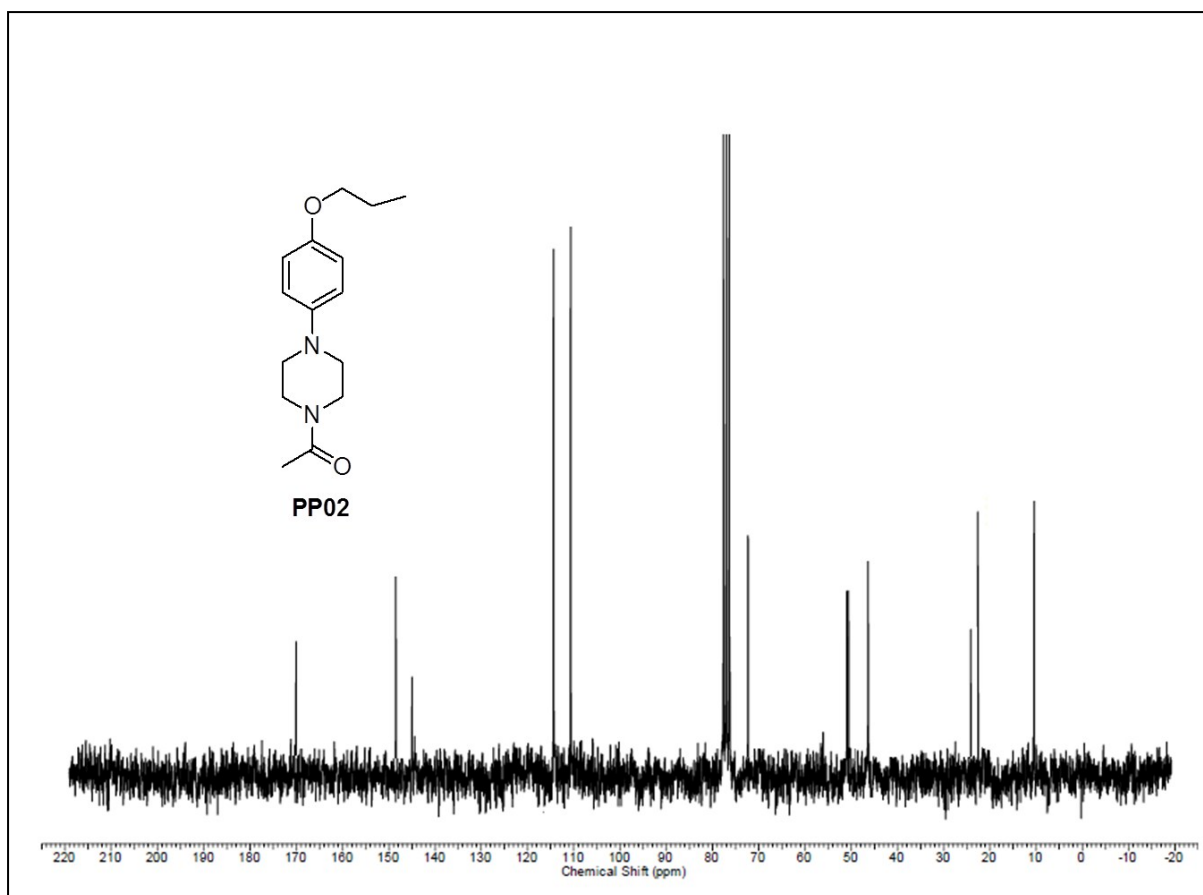
Human Colon Cancer Cell Line HCT-15																
Compounds	% Control Growth															
	Drug Concentrations (µg/mL)															
	Experiment 1				Experiment 2				Experiment 3				Average Values			
	10	20	40	80	10	20	40	80	10	20	40	80	10	20	40	80
PP-5	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
PP-6	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
PP-7	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
PP-8	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
PP-9	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
PP-10	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
PP-11	100.0	100.0	97.7	96.7	100.0	98.9	91.2	88.2	100.0	100.0	100.0	96.5	100.0	99.6	96.3	93.8
PP-12	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
PP-13	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
PP-14	100.0	100.0	100.0	100.0	100.0	100.0	96.6	97.4	100.0	100.0	100.0	100.0	100.0	100.0	98.9	99.1
PP-15	100.0	100.0	100.0	95.8	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	98.6
PP-16	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
PP-17	100.0	100.0	100.0	98.2	100.0	100.0	100.0	100.0	100.0	100.0	100.0	93.9	100.0	100.0	100.0	97.4
PP-18	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
PP-19	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
PP-20	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
PP-21	99.5	98.8	98.2	97.6	99.1	98.8	97.9	97.1	99.3	98.7	97.9	97.4	99.3	98.7	98.0	97.3
ADR	-26.7	-27.9	-29.3	-32.0	-19.2	-20.5	-25.0	-34.4	-19.6	-27.3	-28.4	-29.9	-21.8	-25.2	-27.6	-32.1

Table 5. Cytotoxicity of 6-(4-(4-propoxyphenyl)piperazin-1-yl)-9H-purine derivatives (PP05-PP21) against a MCF-7 cancer cell line in triplicate experiments

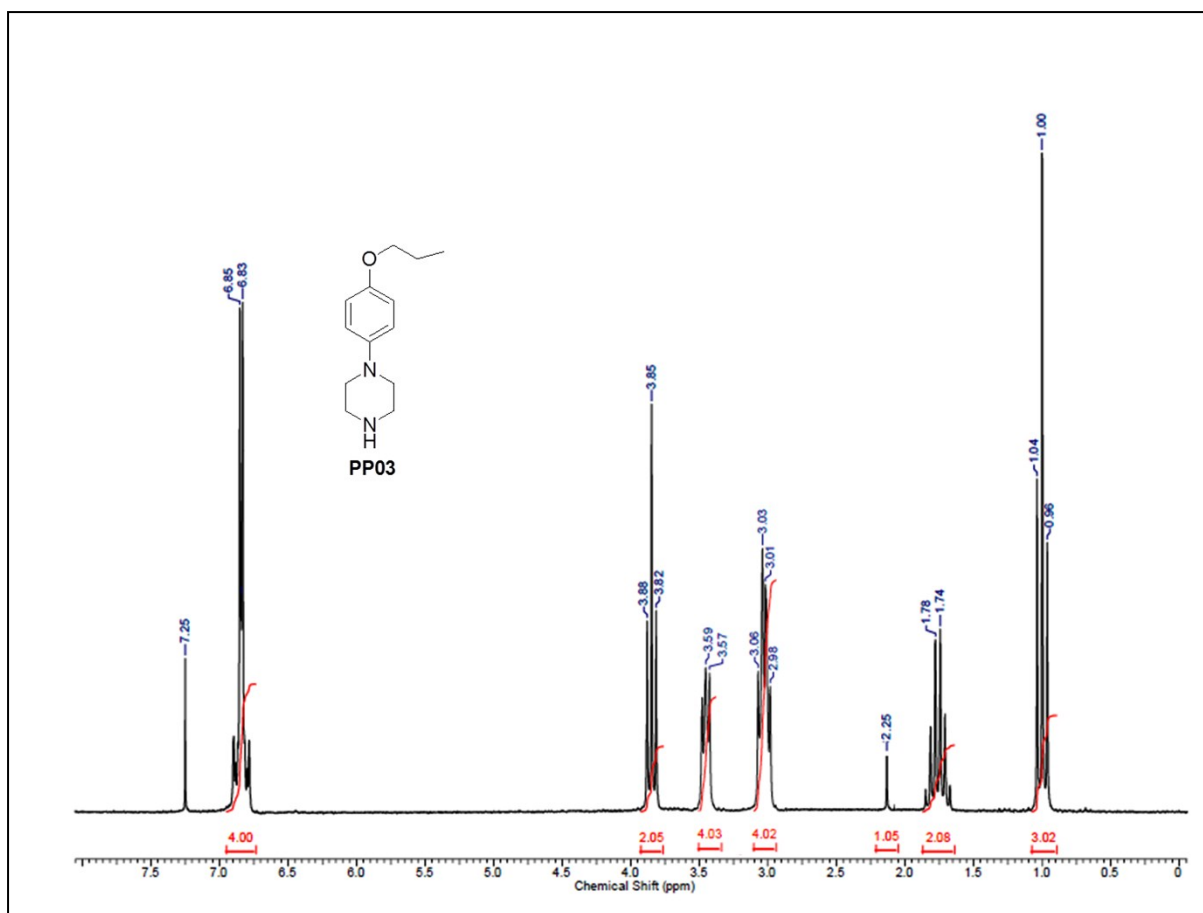
Human Breast Cancer Cell Line MCF7																
Compounds	% Control Growth															
	Drug Concentrations (µg/mL)															
	Experiment 1				Experiment 2				Experiment 3				Average Values			
	10	20	40	80	10	20	40	80	10	20	40	80	10	20	40	80
PP-5	98.1	95.2	94.4	93.6	97.1	96.2	94.3	92.1	97.3	95.7	92.4	90.0	97.5	95.7	93.6	91.9
PP-6	100.0	99.8	96.1	94.7	99.2	97.1	94.3	93.1	98.2	97.2	95.1	92.1	99.1	98.0	95.1	93.3
PP-7	100.8	98.6	97.1	95.6	106.7	98.0	89.8	98.9	104.6	100.4	98.7	94.8	104.0	99.0	95.2	96.4
PP-8	98.2	90.7	83.4	83.1	102.1	90.7	91.5	97.0	101.2	99.8	94.7	94.8	100.5	93.7	89.9	91.6
PP-9	53.1	41.0	33.3	31.1	64.3	42.5	31.1	34.2	58.4	50.5	41.6	32.3	58.6	44.6	35.4	32.5
PP-10	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
PP-11	88.8	79.3	74.9	78.3	100.5	84.5	81.3	79.8	98.5	90.0	89.4	80.1	95.9	84.6	81.9	79.4
PP-12	95.3	88.3	88.6	96.9	103.8	92.4	93.4	98.2	103.9	97.9	96.1	99.2	101.0	92.9	92.7	98.1
PP-13	97.6	92.4	96.6	93.0	104.9	96.4	97.1	103.2	104.4	100.5	99.7	99.0	102.3	96.4	97.8	98.4
PP-14	96.6	91.9	91.4	96.3	96.2	95.5	97.3	96.4	99.9	95.6	92.3	93.6	97.6	94.3	93.7	95.4
PP-15	99.6	95.1	94.5	96.9	94.6	94.1	100.4	101.2	99.2	92.0	93.5	104.1	97.8	93.7	96.1	100.8
PP-16	91.1	88.4	87.6	85.6	96.6	92.4	91.2	91.6	97.2	89.8	85.4	90.1	95.0	90.2	88.1	89.1
PP-17	34.8	30.9	28.3	28.8	32.4	30.7	28.0	31.2	38.0	31.4	26.2	29.2	35.0	31.0	27.5	29.8
PP-18	96.1	93.5	91.6	89.8	94.3	92.1	90.0	88.5	95.1	93.2	90.1	87.0	85.1	92.9	90.5	88.4
PP-19	96.0	93.4	91.1	88.0	94.1	93.7	90.8	86.3	96.8	94.3	92.8	90.8	95.6	93.8	91.5	88.3
PP-20	89.6	86.4	84.5	82.1	88.3	87.6	83.4	81.6	88.9	86.3	82.5	80.0	88.9	86.7	83.4	81.2
PP-21	86.8	82.1	79.3	74.4	84.3	80.1	78.4	75.1	80.2	83.8	80.1	77.3	85.4	82.0	79.2	75.6
ADR	-0.8	-7.9	-23.6	-56.0	-7.0	-5.6	-17.1	-40.8	-8.1	-5.5	-7.1	-41.5	-5.3	-6.3	-15.9	-46.1



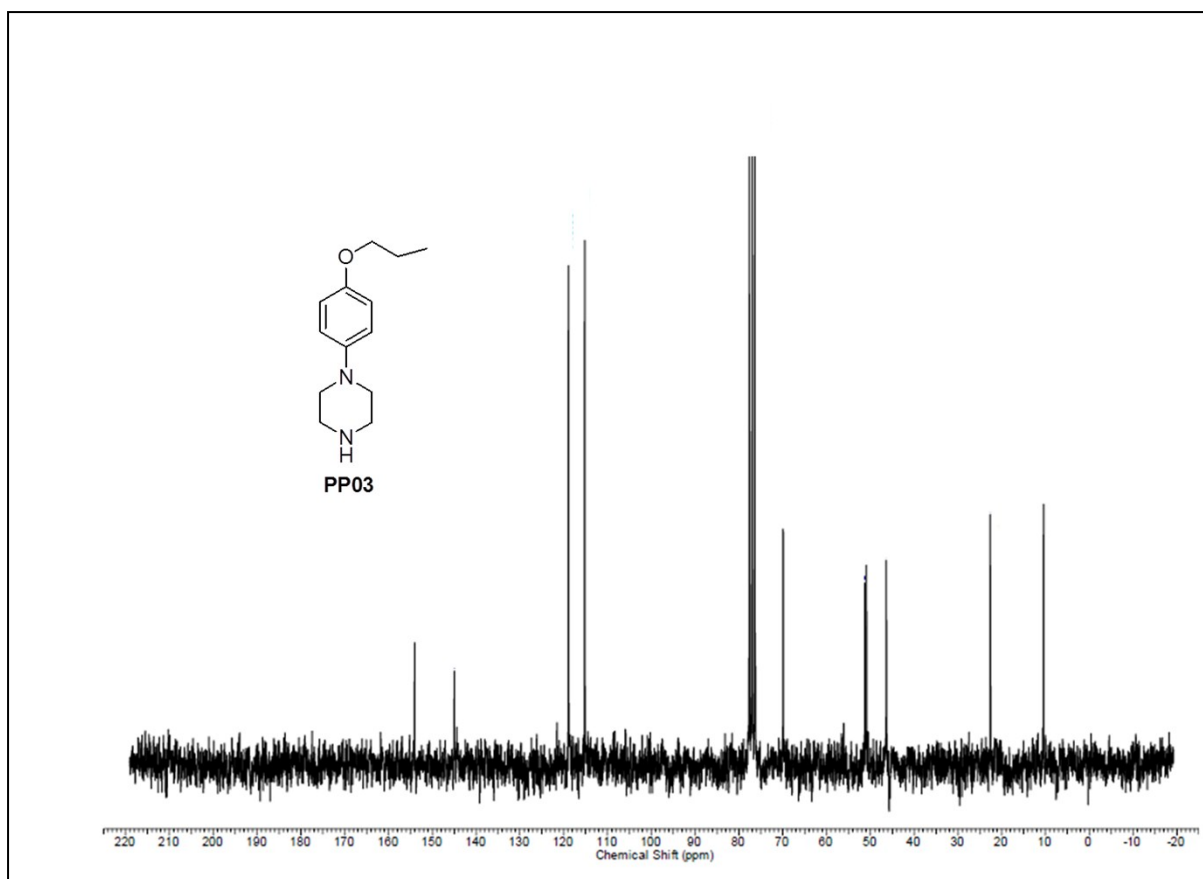
¹H NMR SPECTRUM OF COMPOUND PP02



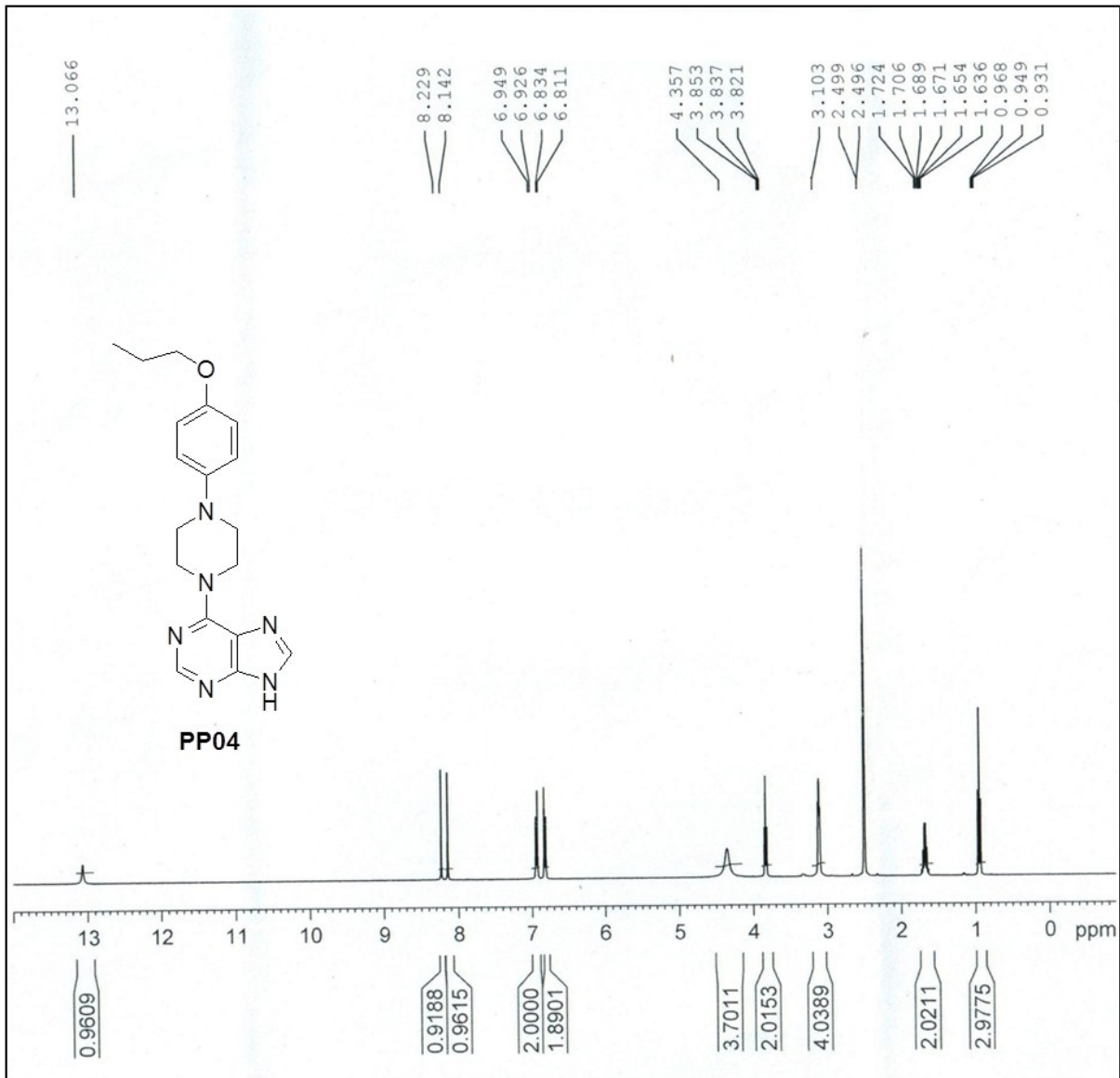
^{13}C NMR SPECTRUM OF COMPOUND PP02



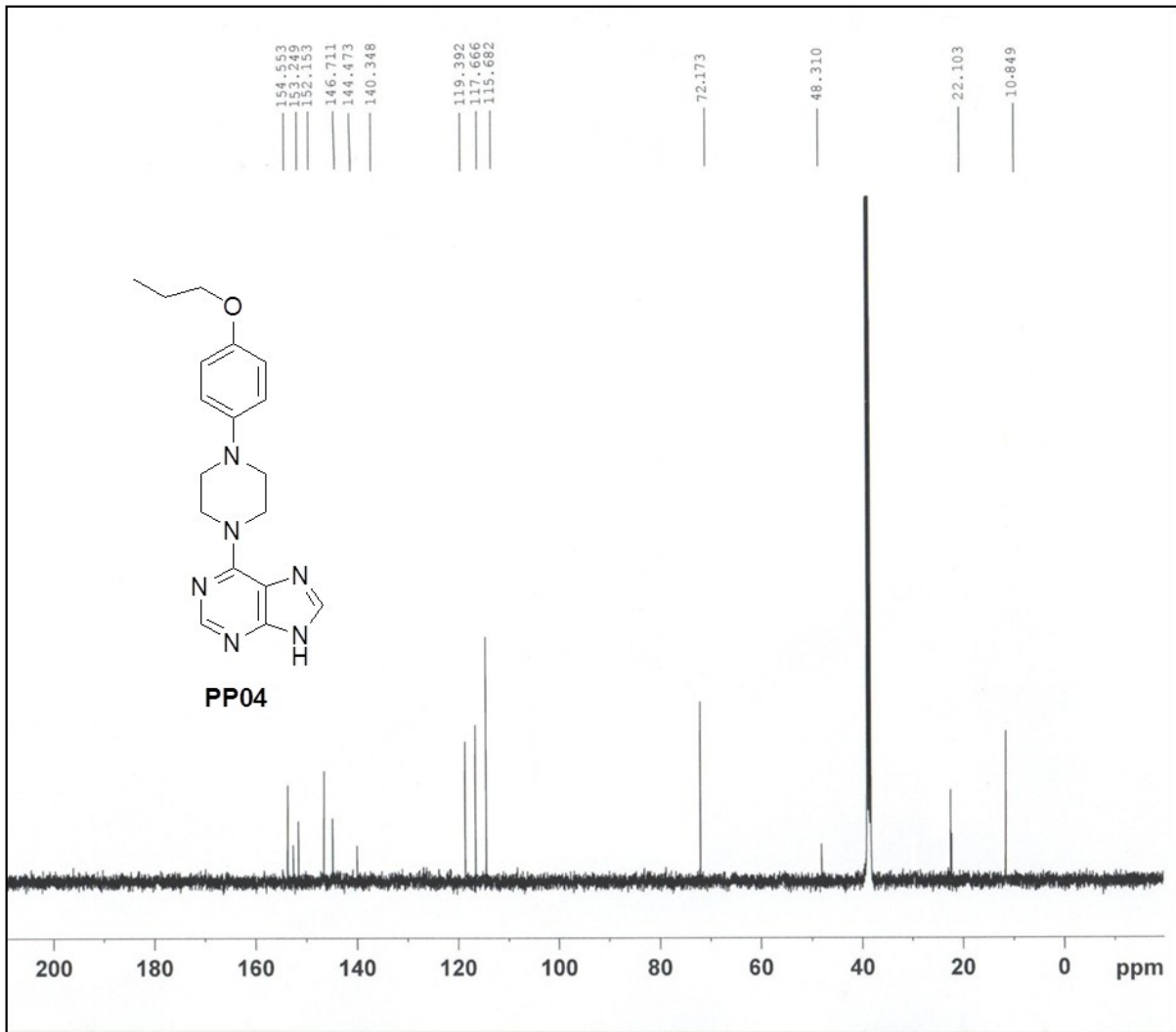
¹H NMR SPECTRUM OF COMPOUND PP03



^{13}C NMR SPECTRUM OF COMPOUND PP03

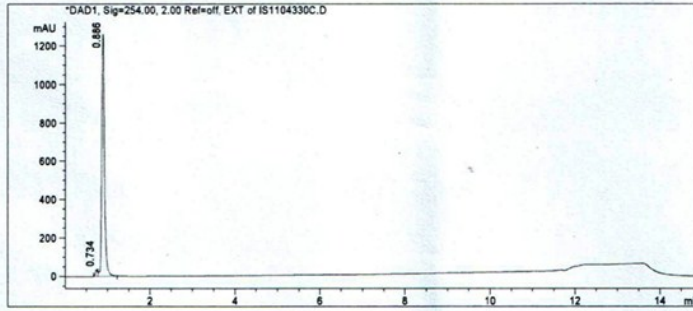


¹H NMR SPECTRUM OF COMPOUND PP04

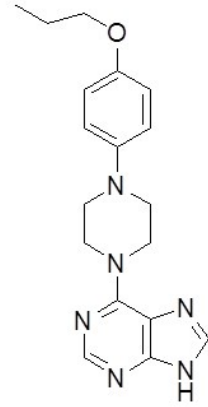


¹³C NMR SPECTRUM OF COMPOUND PP04

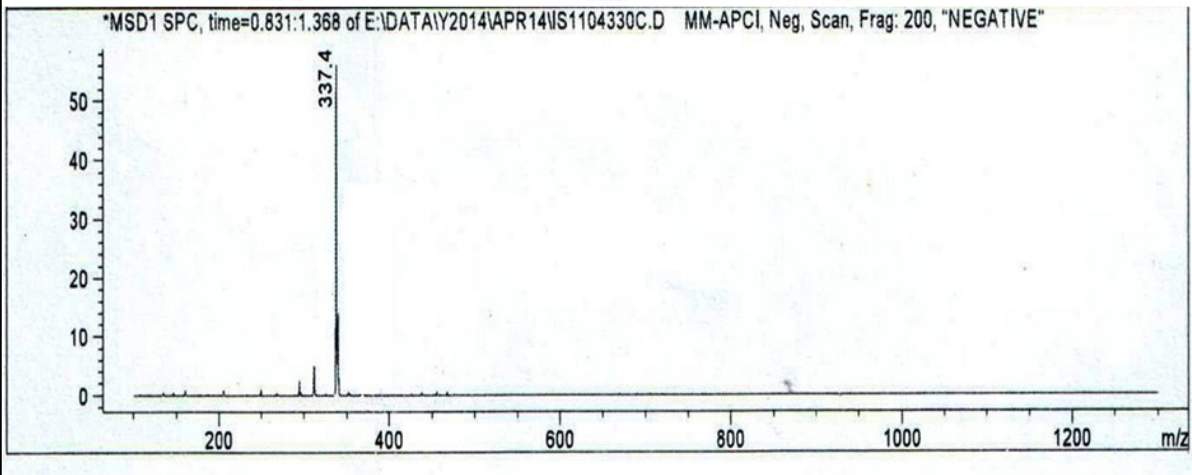
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 Time (min.): %A %B %C
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 10 50 48 2
 10.1 0 98 2
 12 0 98 2
 12.1 95 3 2
 17 95 3 2



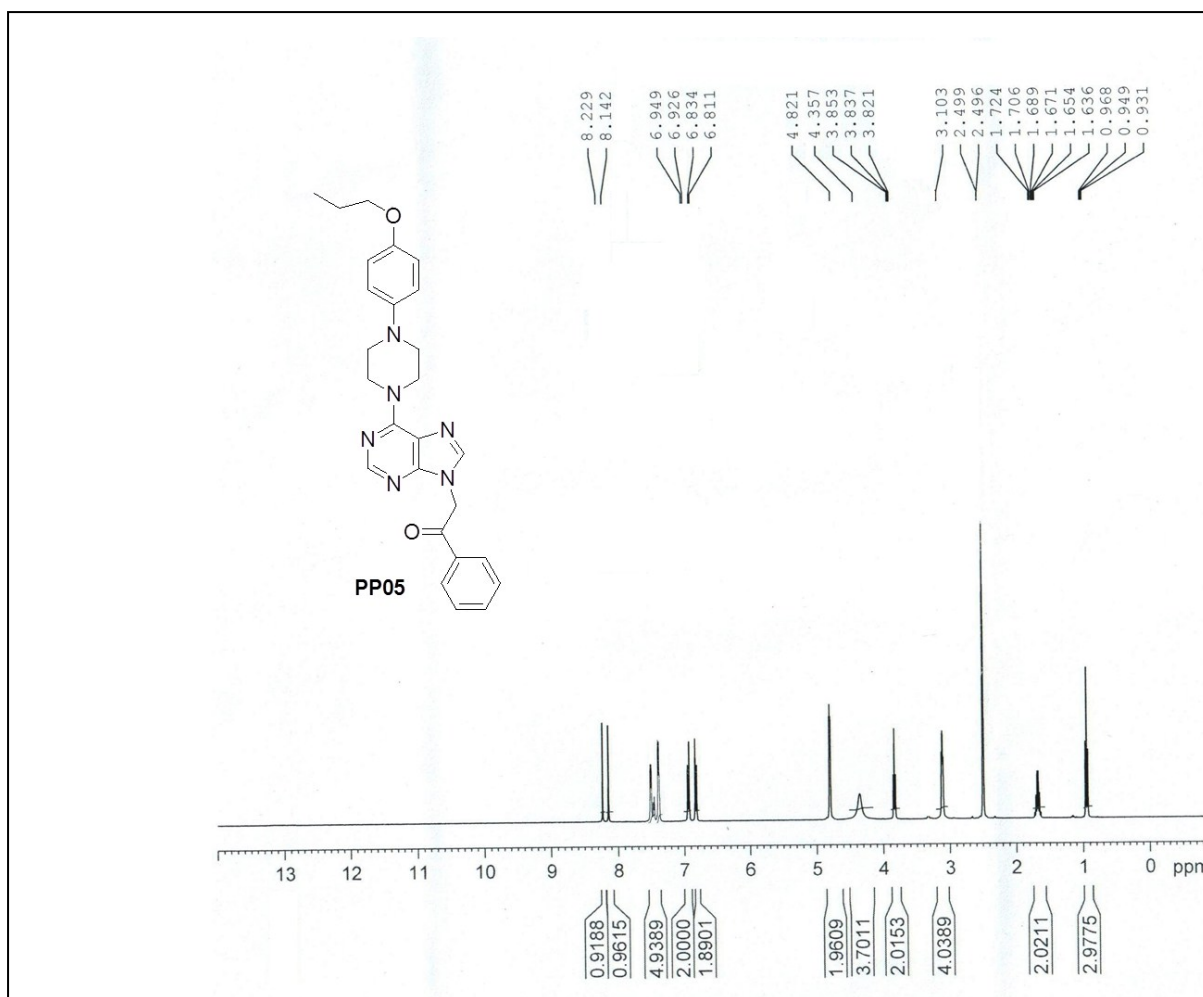
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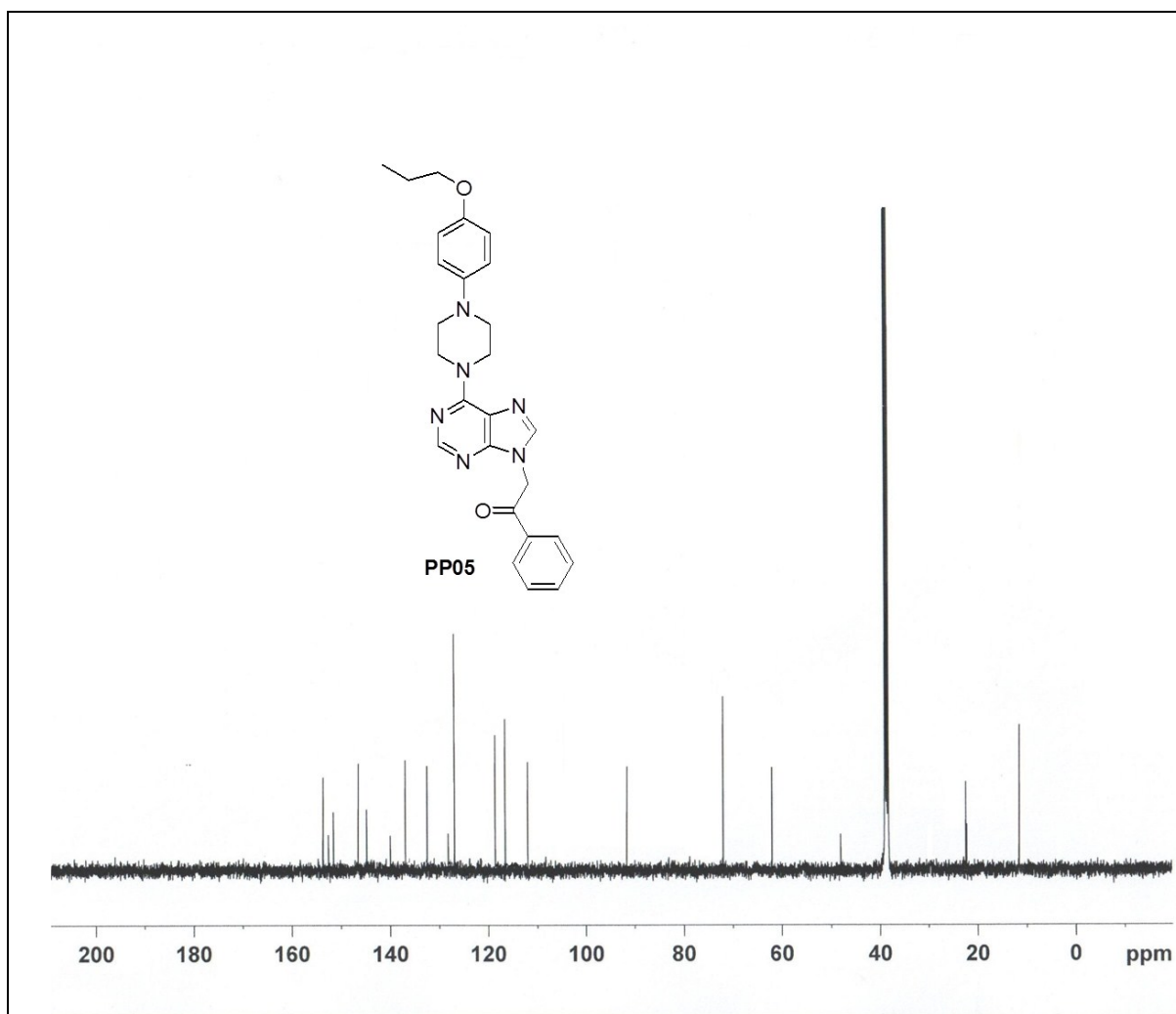
PP04



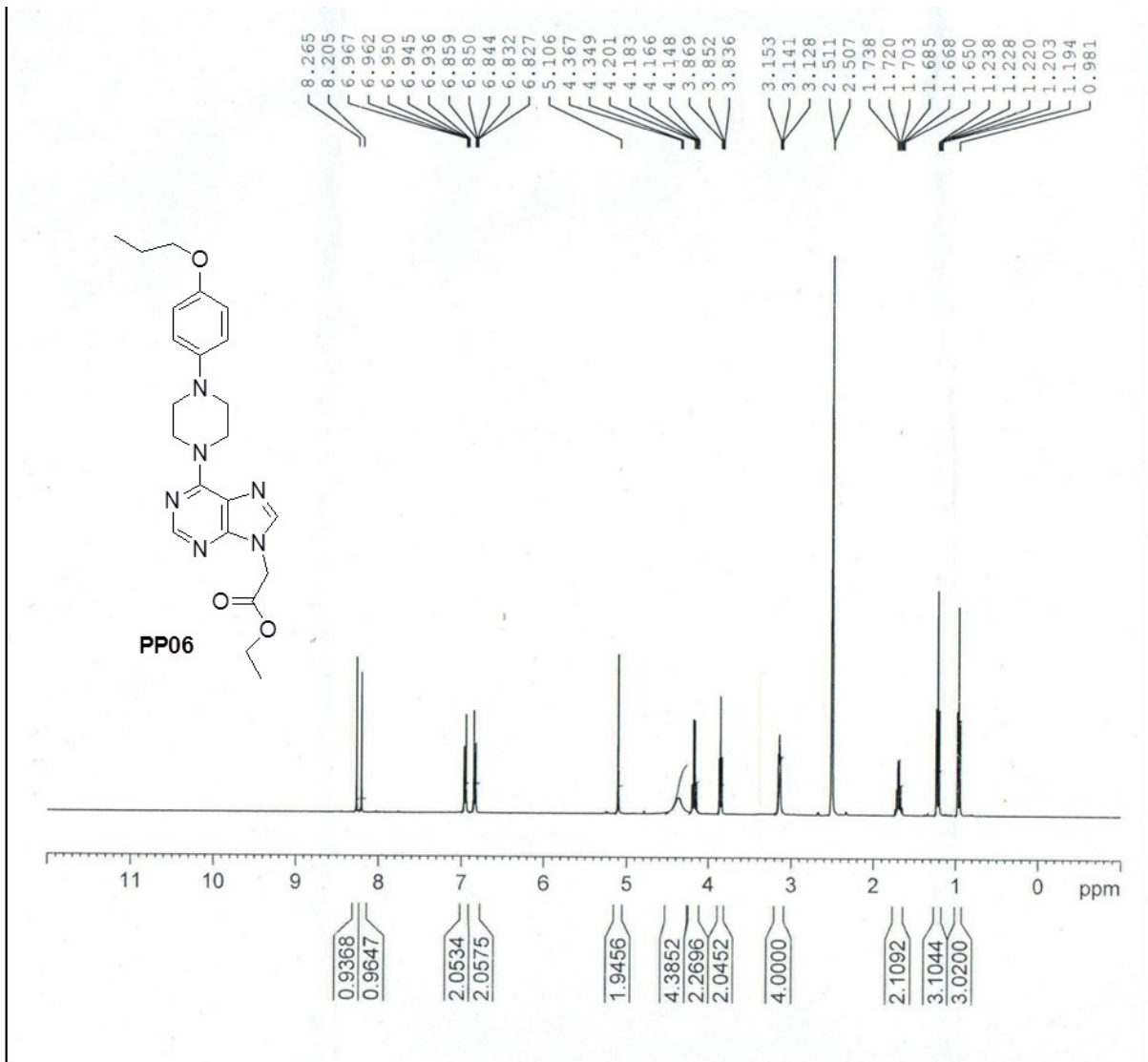
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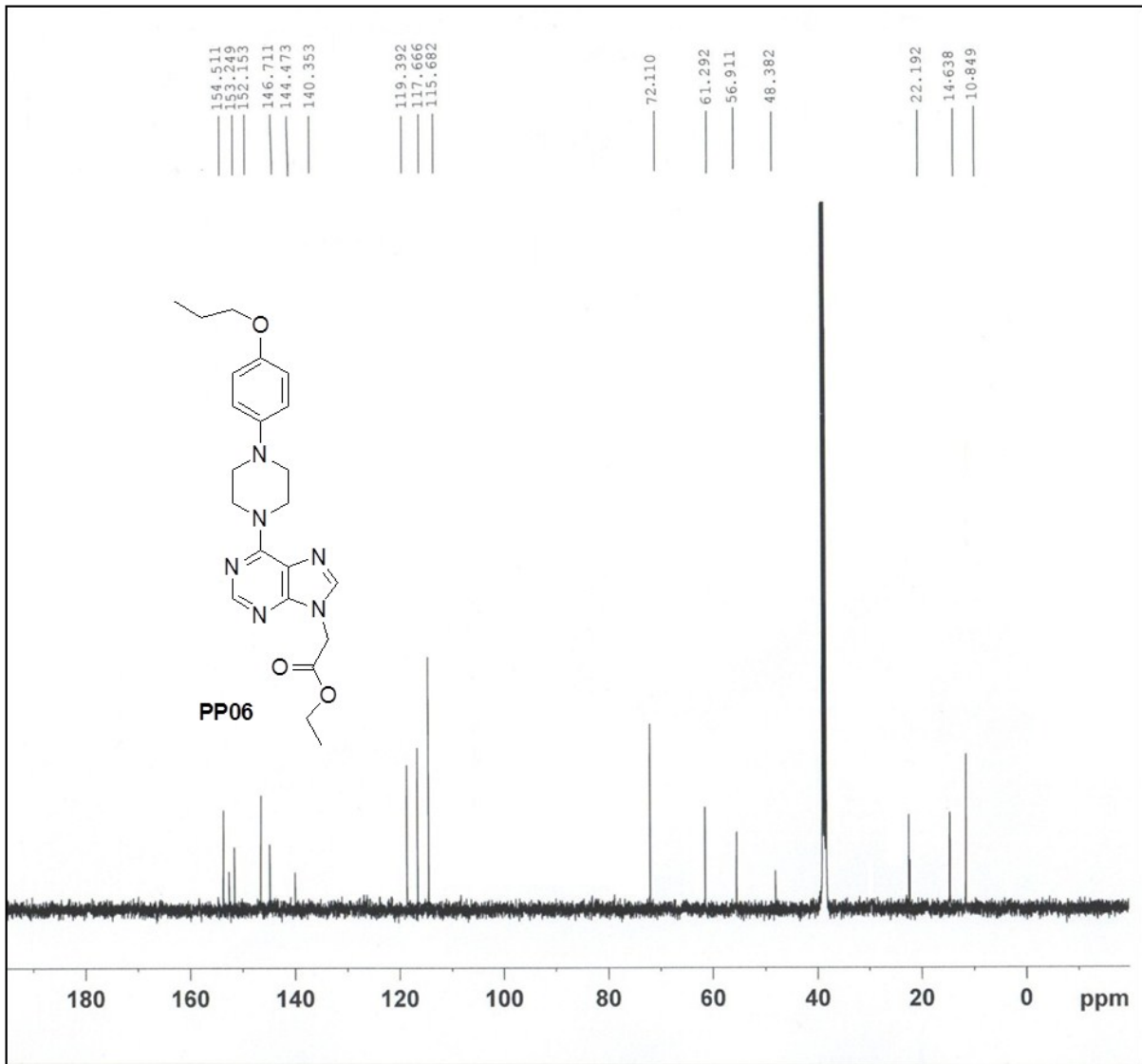
¹H NMR SPECTRUM OF COMPOUND PP05



¹³C NMR SPECTRUM OF COMPOUND PP05

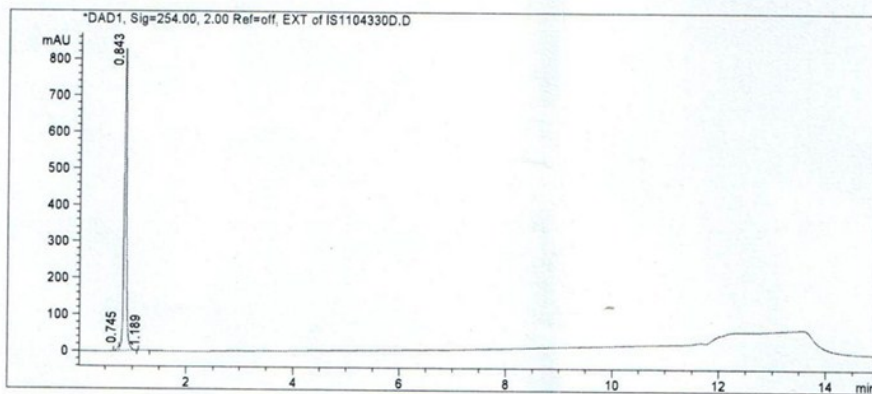


¹H NMR SPECTRUM OF COMPOUND PP06

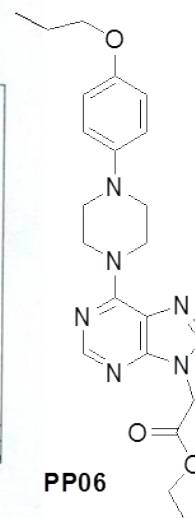


¹³C NMR SPECTRUM OF COMPOUND PP06

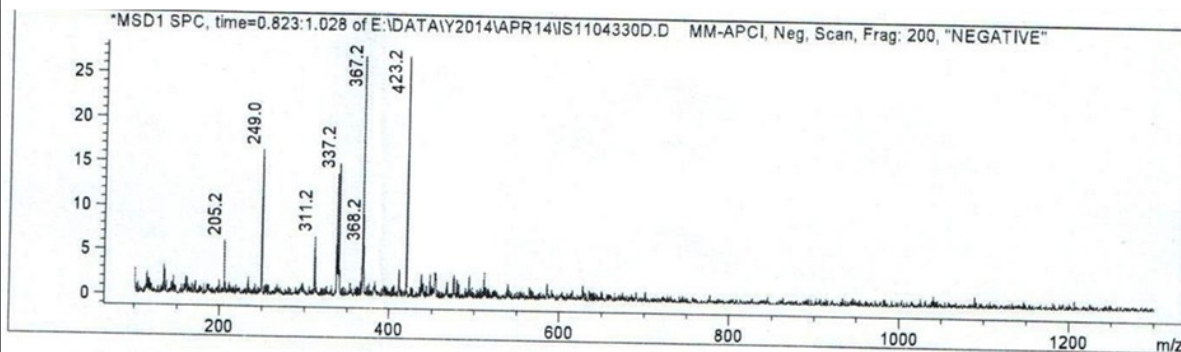
Method info : Column-Ascentis C18 (75X4.6mm) 2.7micron,
 Mobile phase A: ACN B :THF C :0.1%HCOOH in water Flow = 1.0ml/min,
 Time (min.): %A %B %C
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 5 80 18 2
 10 50 48 2
 10.1 0 98 2
 12 0 98 2
 12.1 95 3 2
 17 95 3 2



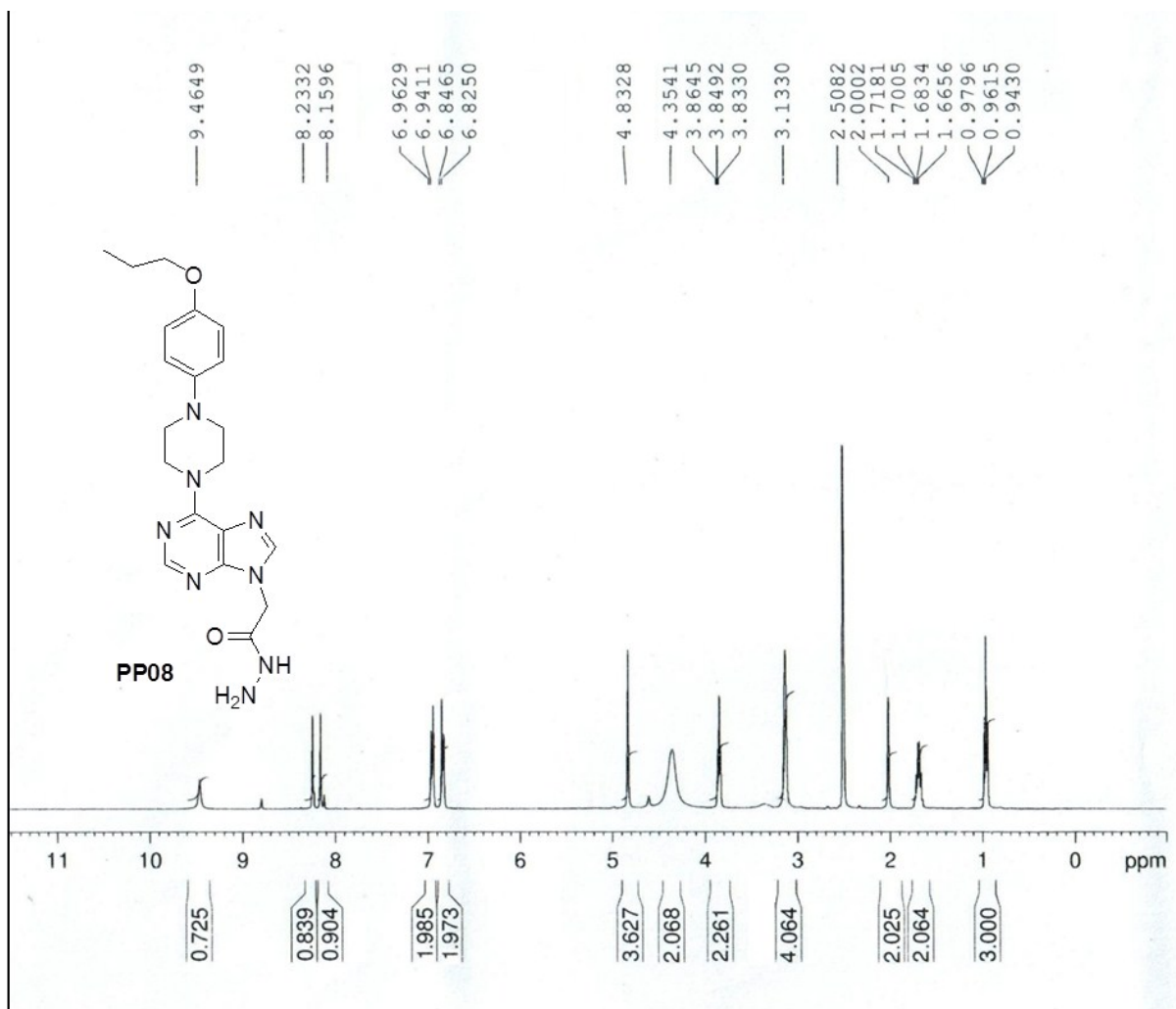
Peak No	RT min	Area	Area %
1	0.745	138.893	1.414
2	0.843	2701.412	98.217
3	1.189	110.158	0.369



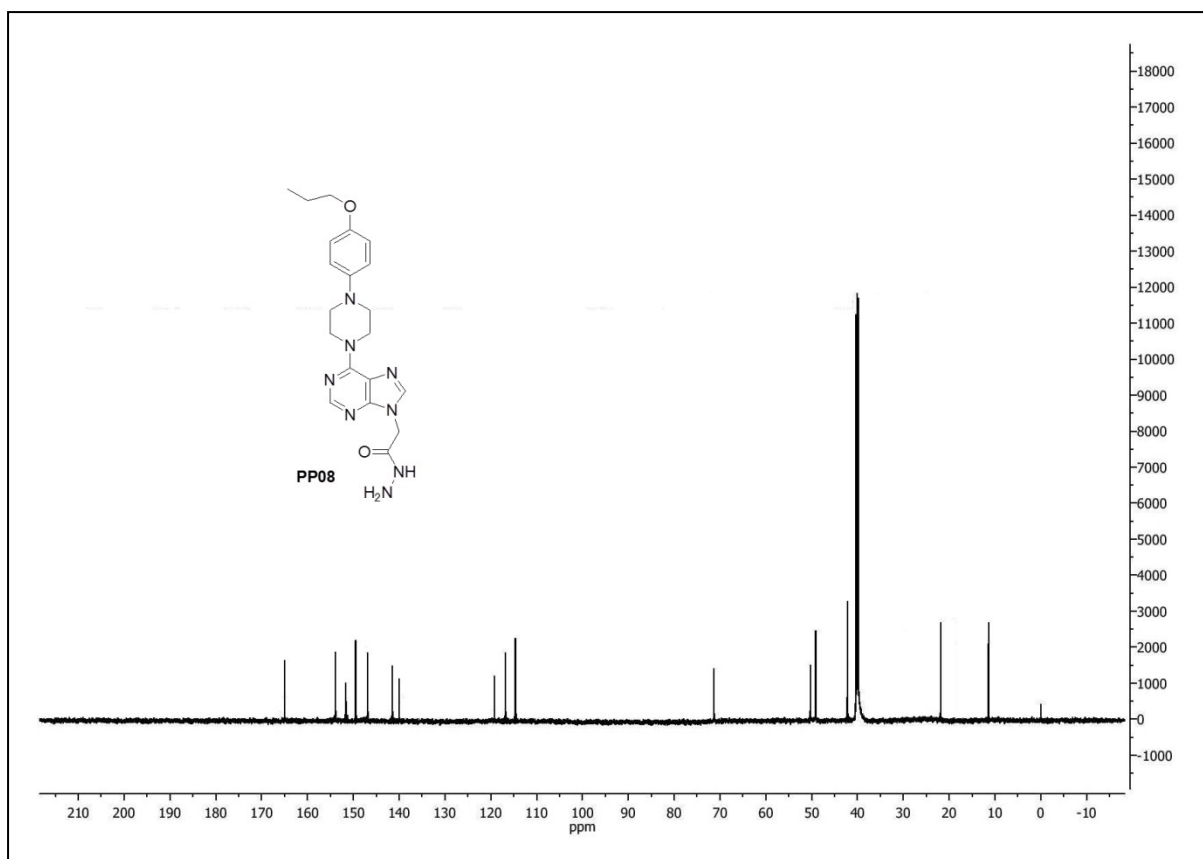
PP06



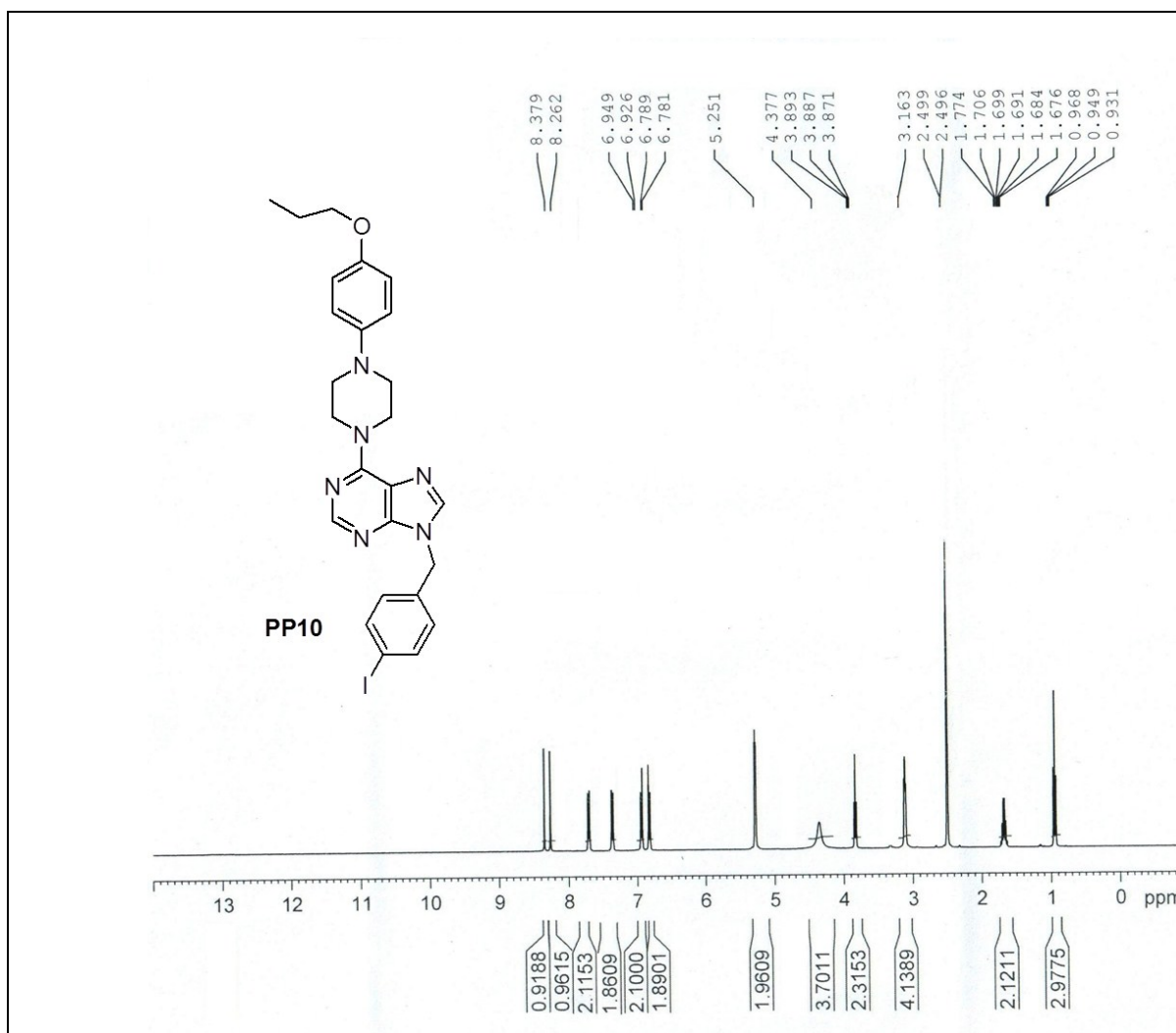
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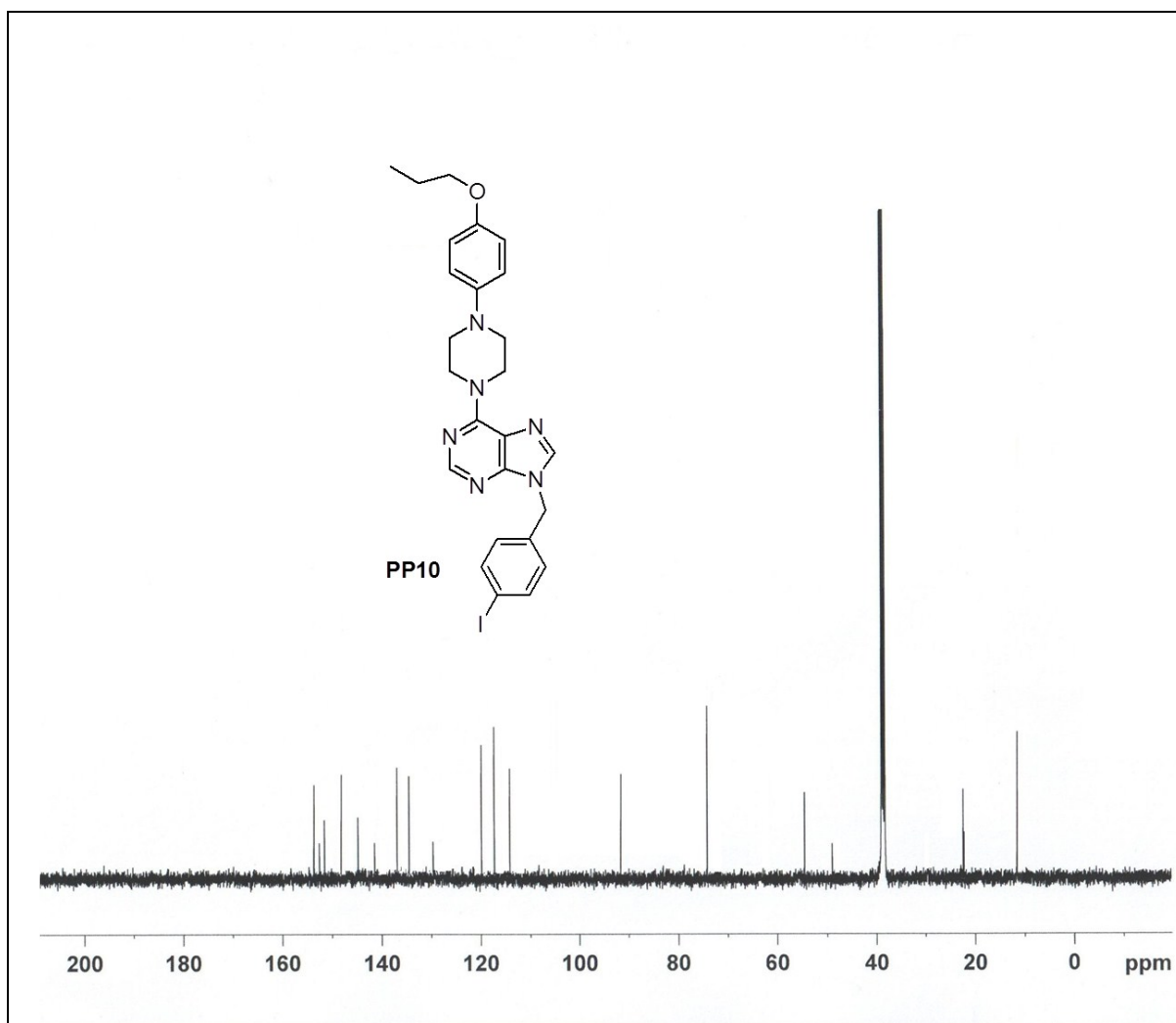
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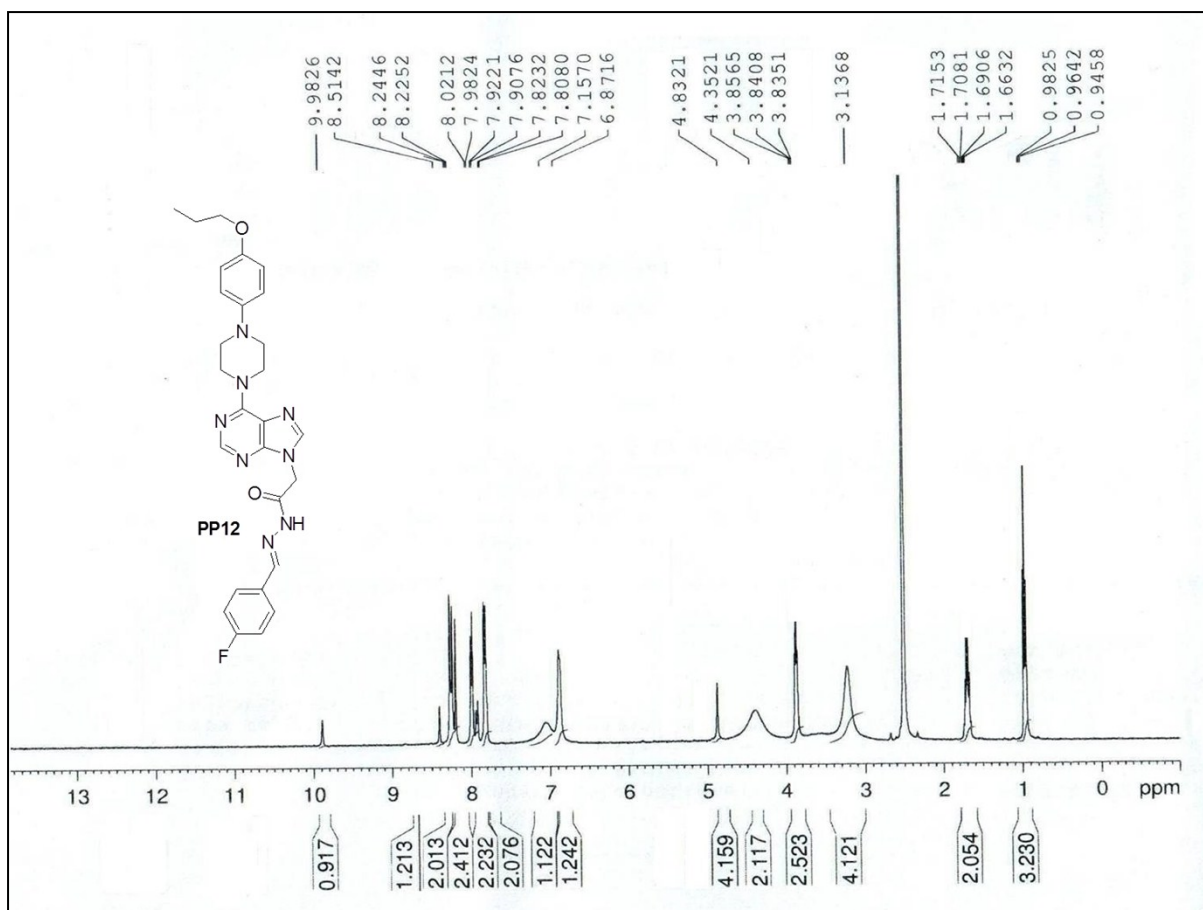
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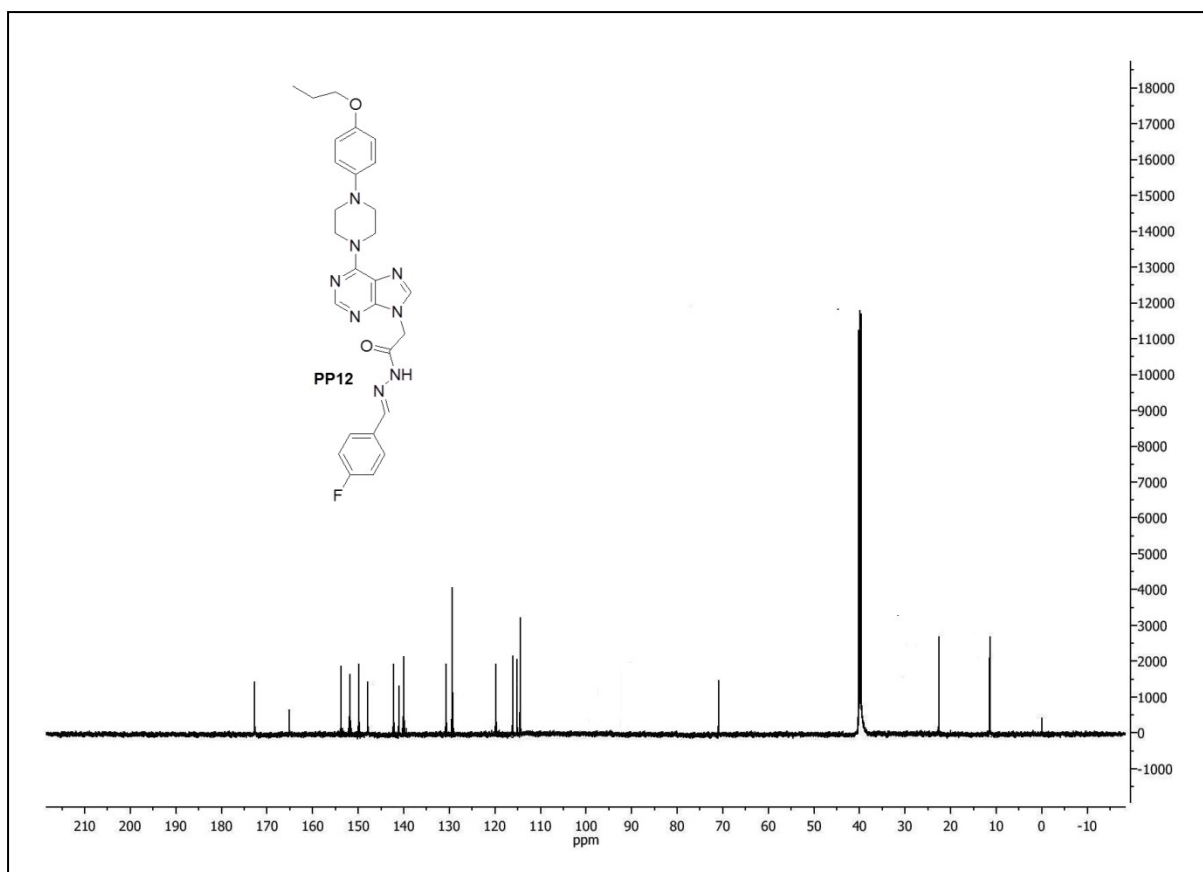
¹H NMR SPECTRUM OF COMPOUND PP10



¹³C NMR SPECTRUM OF COMPOUND PP10

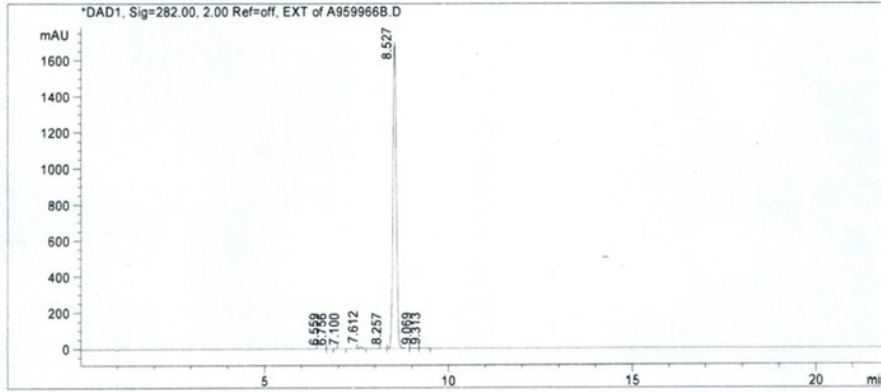


¹H NMR SPECTRUM OF COMPOUND PP12

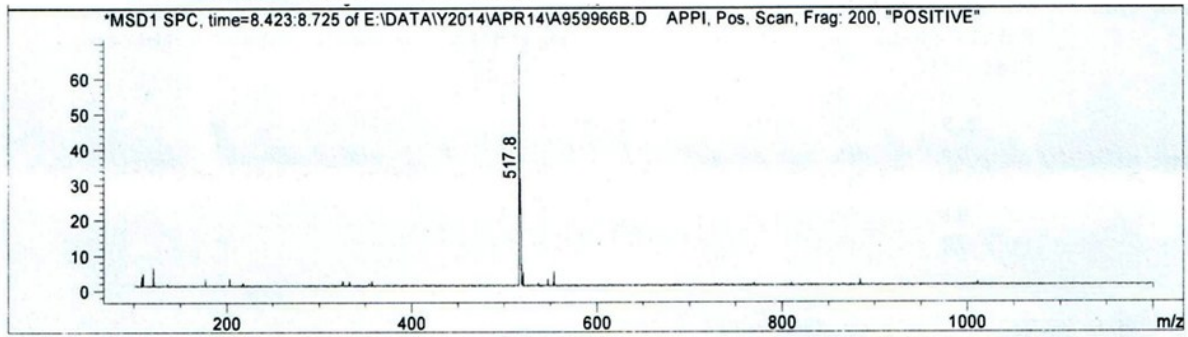
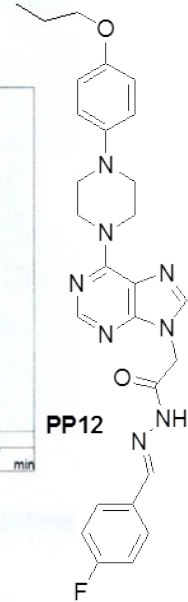


^{13}C NMR SPECTRUM OF COMPOUND PP12

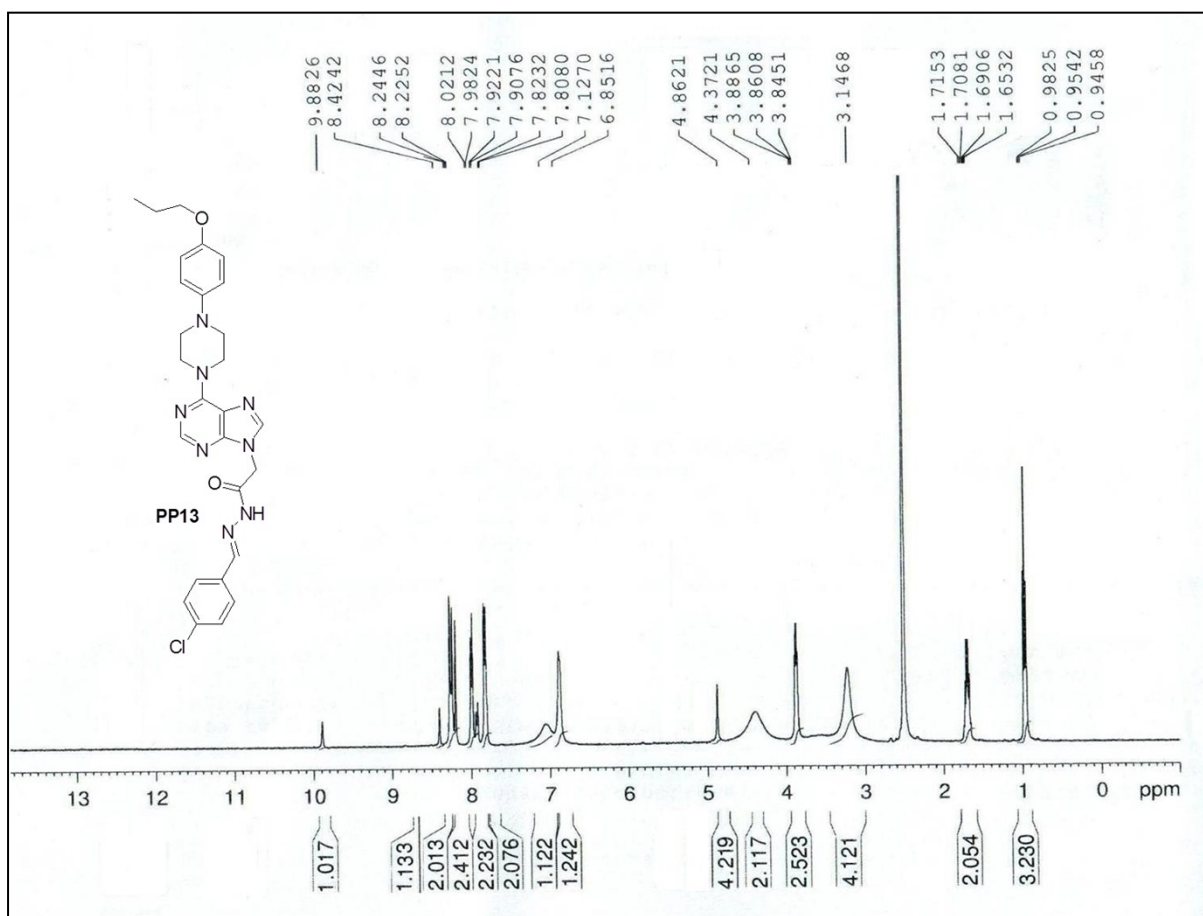
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 Mobile phase A: 0.1%CH₃COOH in 10mM NH₄OAC B :ACN Flow = 1.0ml/min,
 Time (min.): %B
 0 30
 2.5 30
 10 95
 16 95
 18 30
 22 30



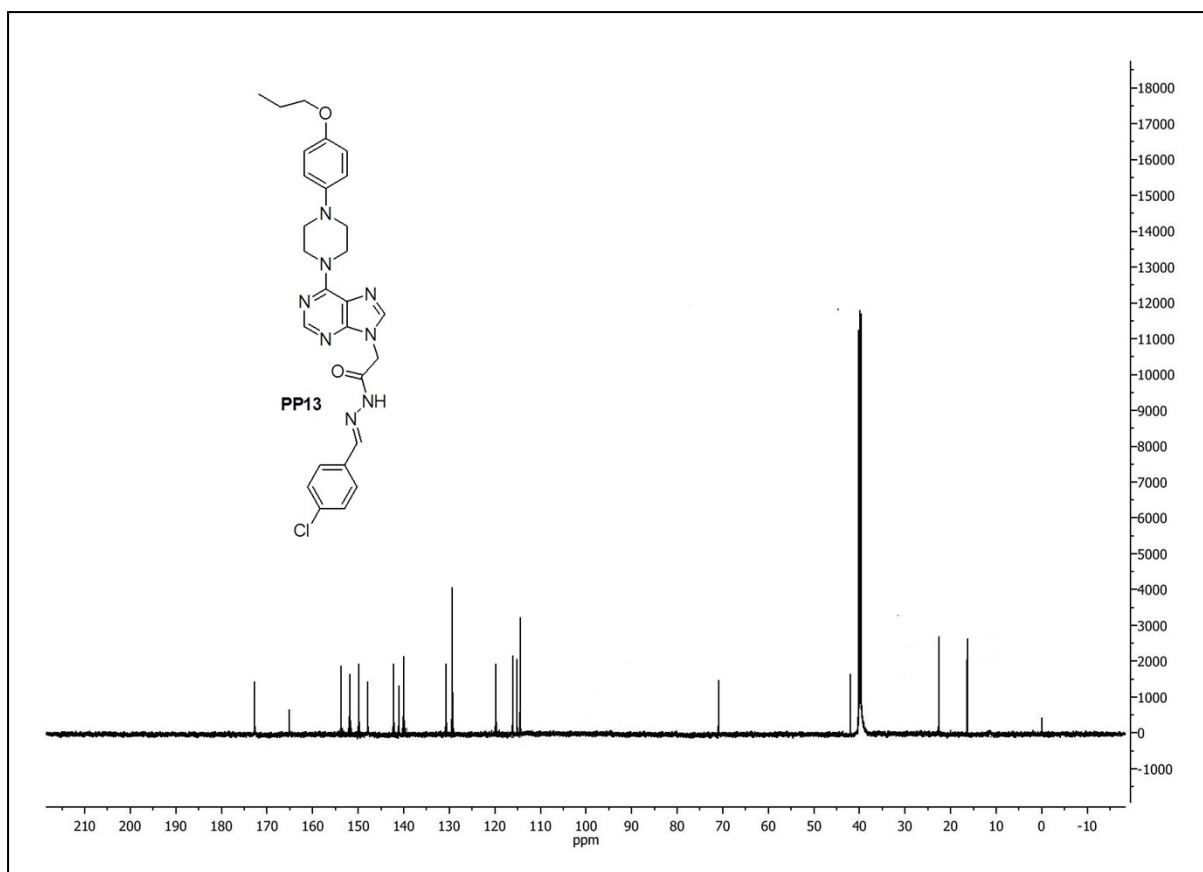
Peak No	RT min	Area	Area %
1	6.559	15.959	0.054
2	6.756	13.796	0.034
3	7.100	12.961	0.027
4	7.612	153.360	0.483
5	8.257	14.559	0.041
6	8.527	10956.800	99.228
7	9.069	16.190	0.056
8	9.313	18.407	0.076



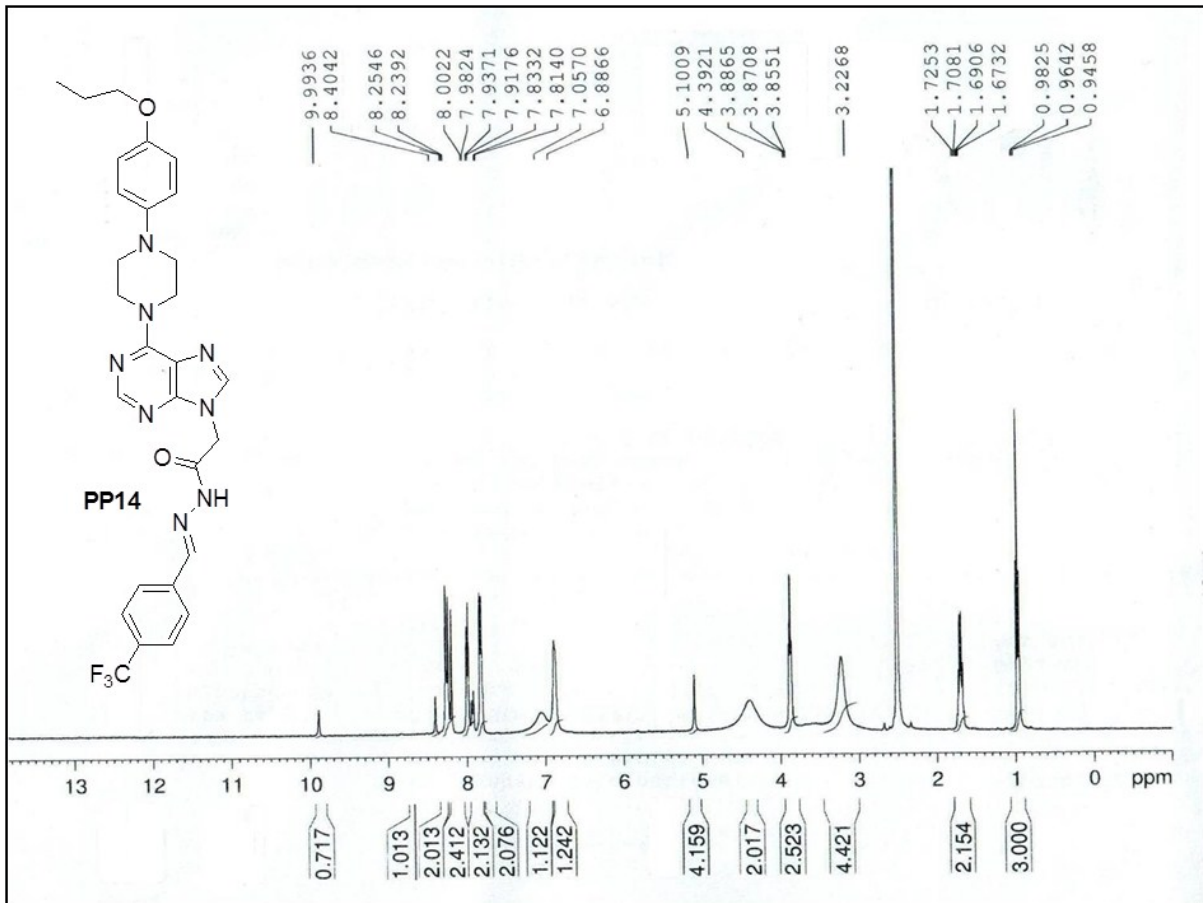
LC-MS SPECTRUM OF COMPOUND PP12



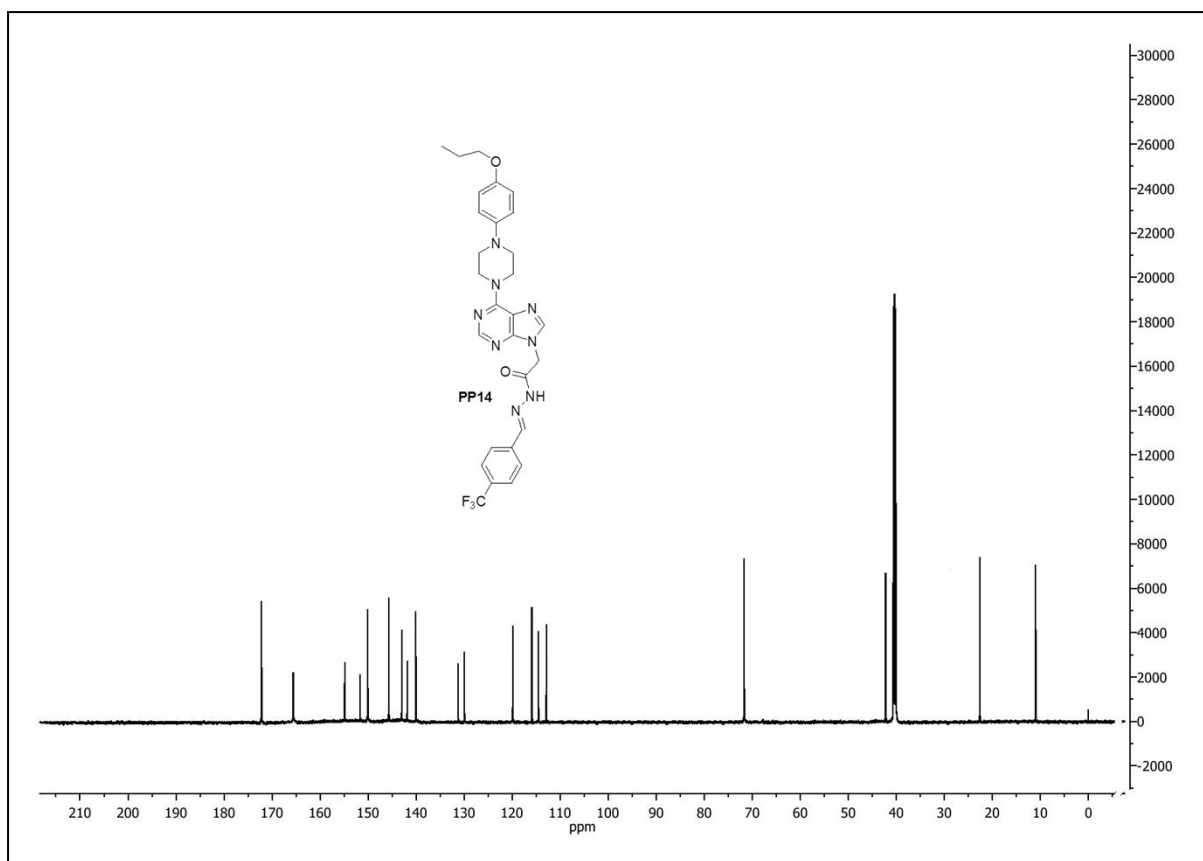
¹H NMR SPECTRUM OF COMPOUND PP13



¹³C NMR SPECTRUM OF COMPOUND PP13

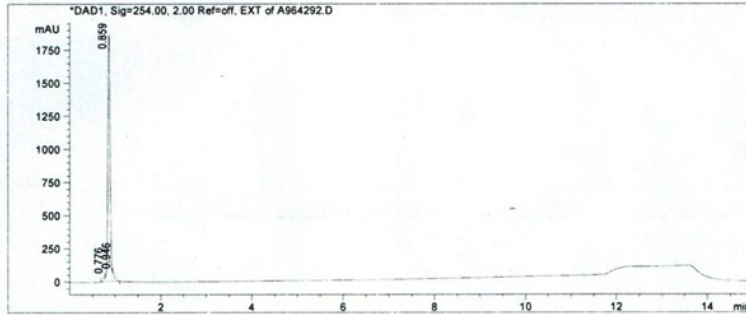


¹H NMR SPECTRUM OF COMPOUND PP14

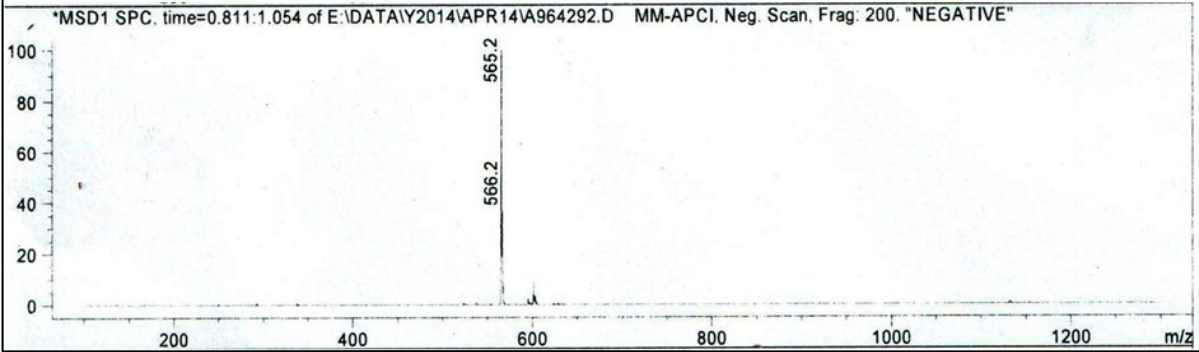
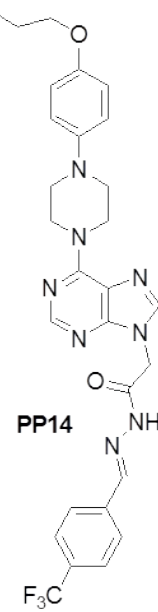


¹³C NMR SPECTRUM OF COMPOUND PP14

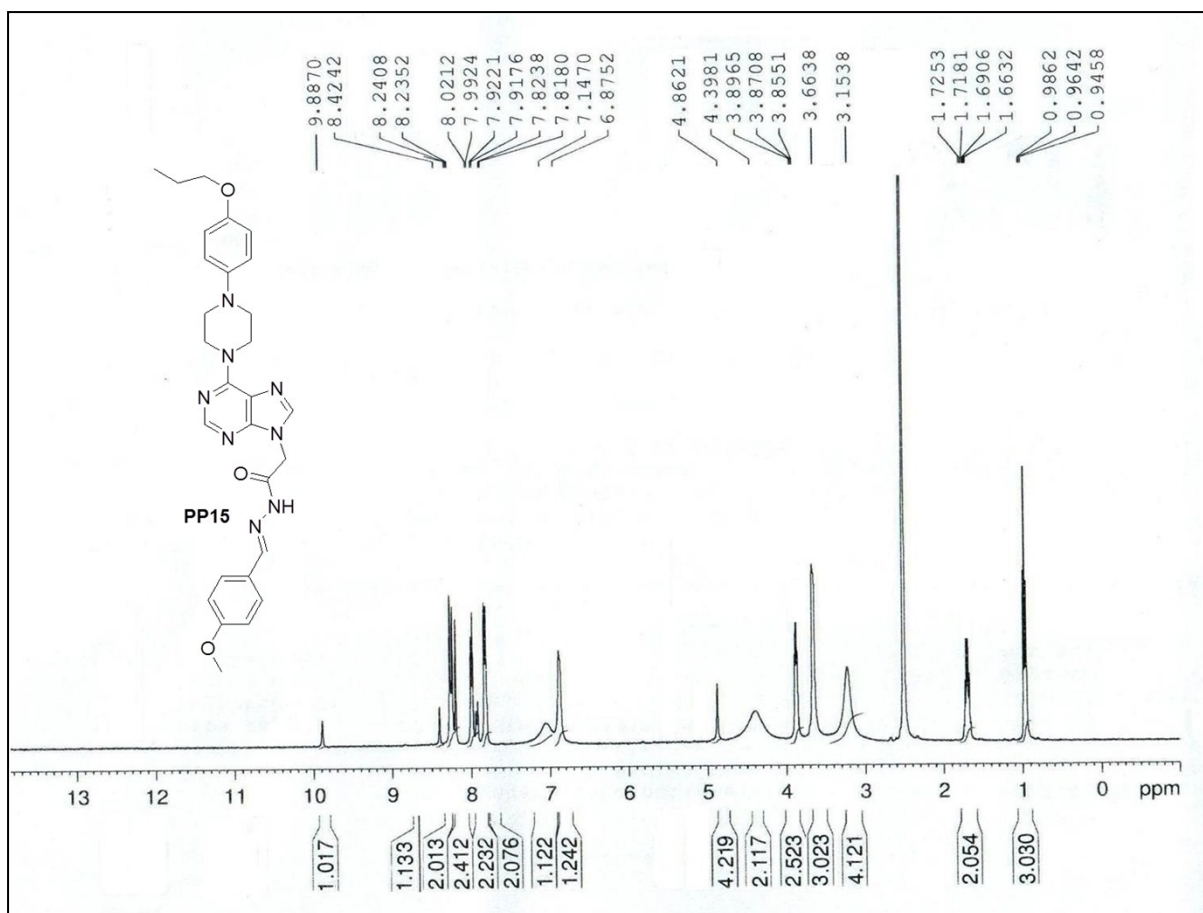
Method info : Column-Ascentis C18 (75X4.6mm) 2.7micron,
Mobile phase A: ACN B: THF C: 0.1% HCOOH in water Flow = 1.0ml/min,
Time (min.): %A %B %C
0 95 3 2
5 80 18 2
10 50 48 2
10.1 0 98 2
12 0 98 2
12.1 95 3 2
17 95 3 2



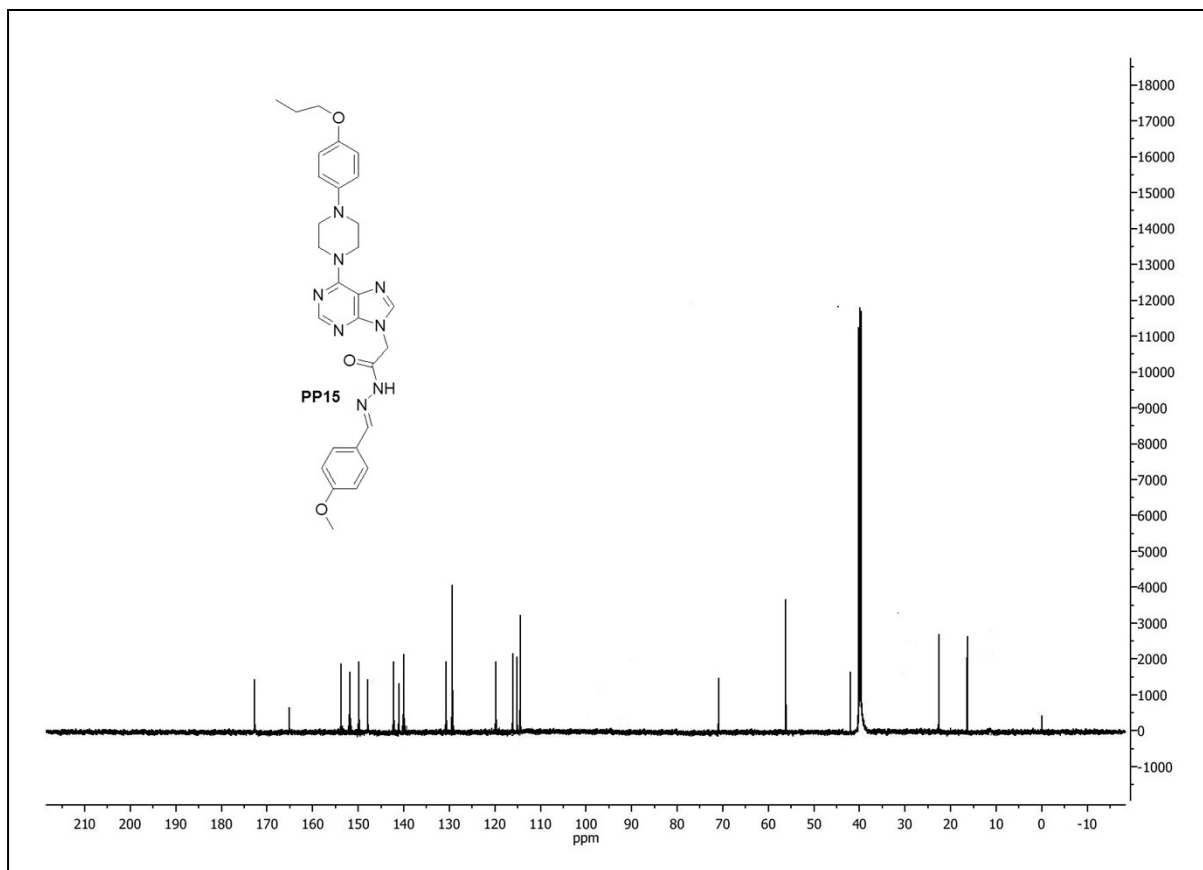
Peak No	RT min	Area	Area %
1	10.776	115.664	1.746
2	10.859	16311.900	95.295
3	10.946	1195.961	2.959



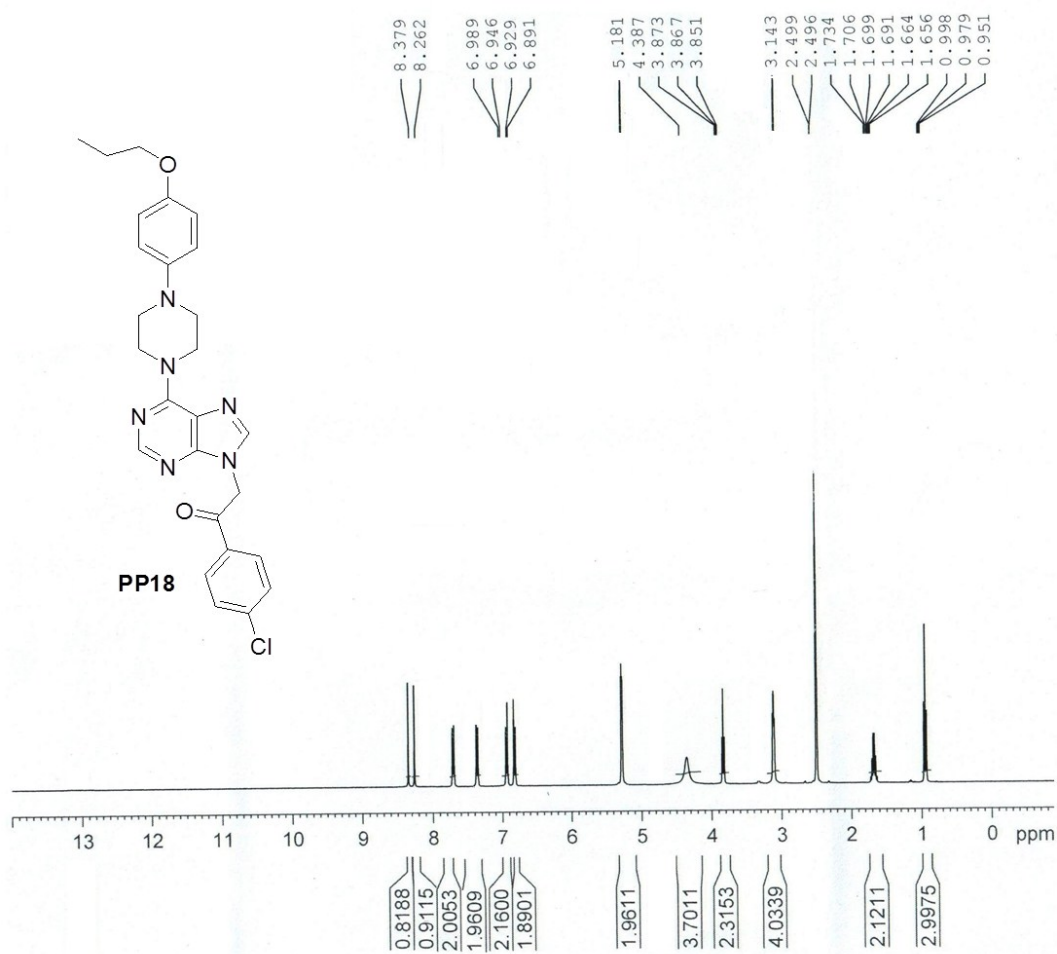
LC-MS SPECTRUM OF COMPOUND PP14



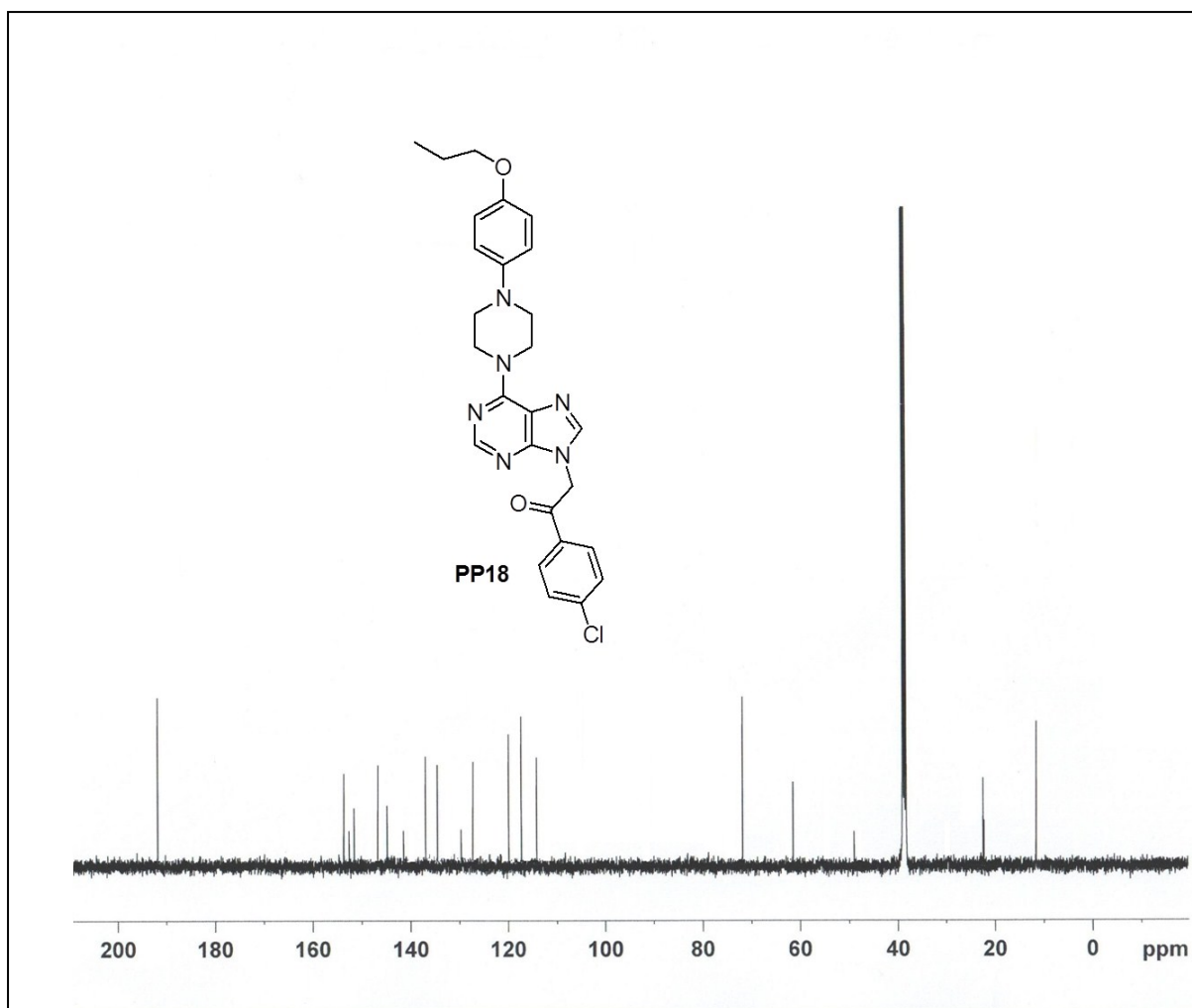
¹H NMR SPECTRUM OF COMPOUND PP15



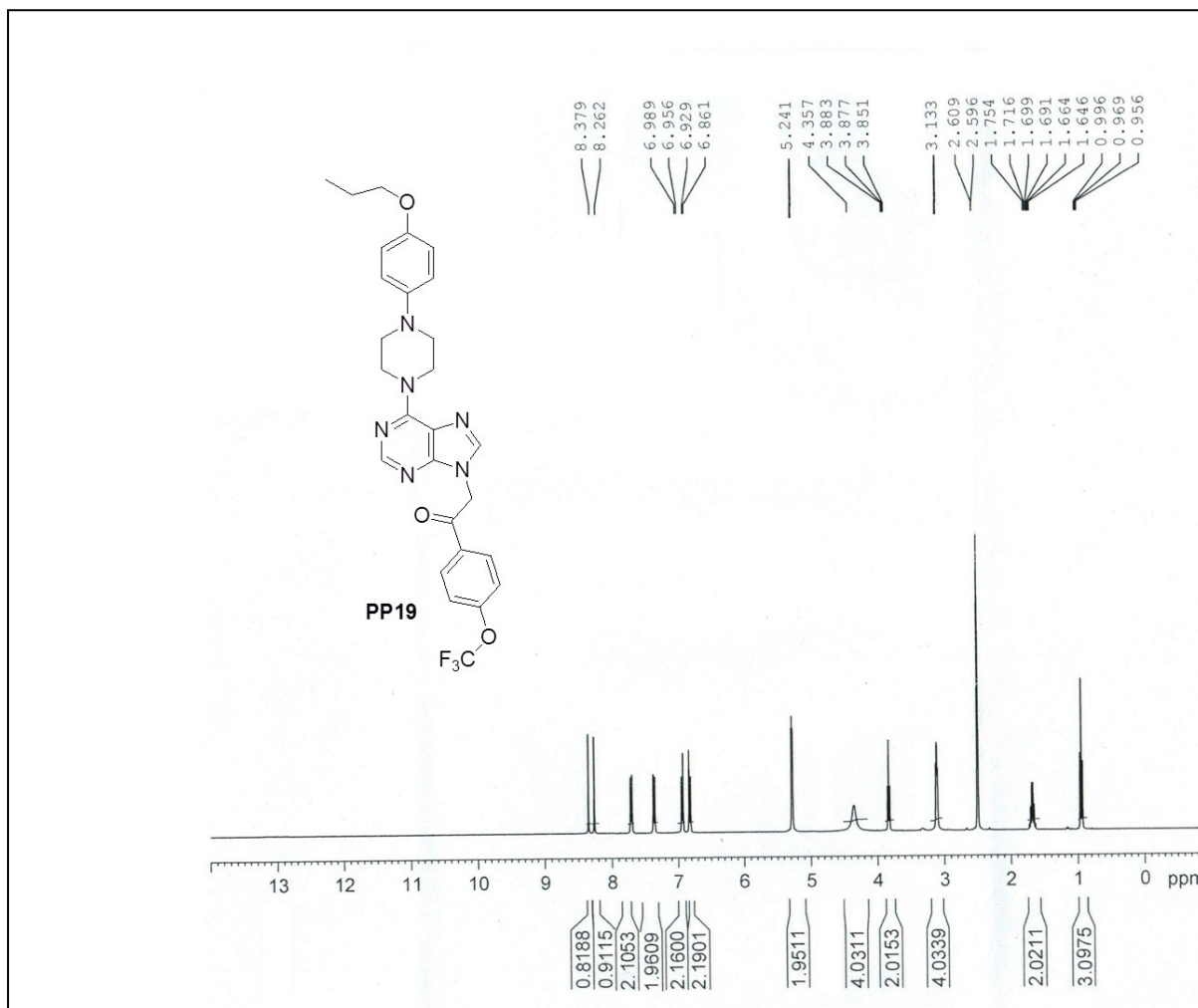
¹³C NMR SPECTRUM OF COMPOUND PP15



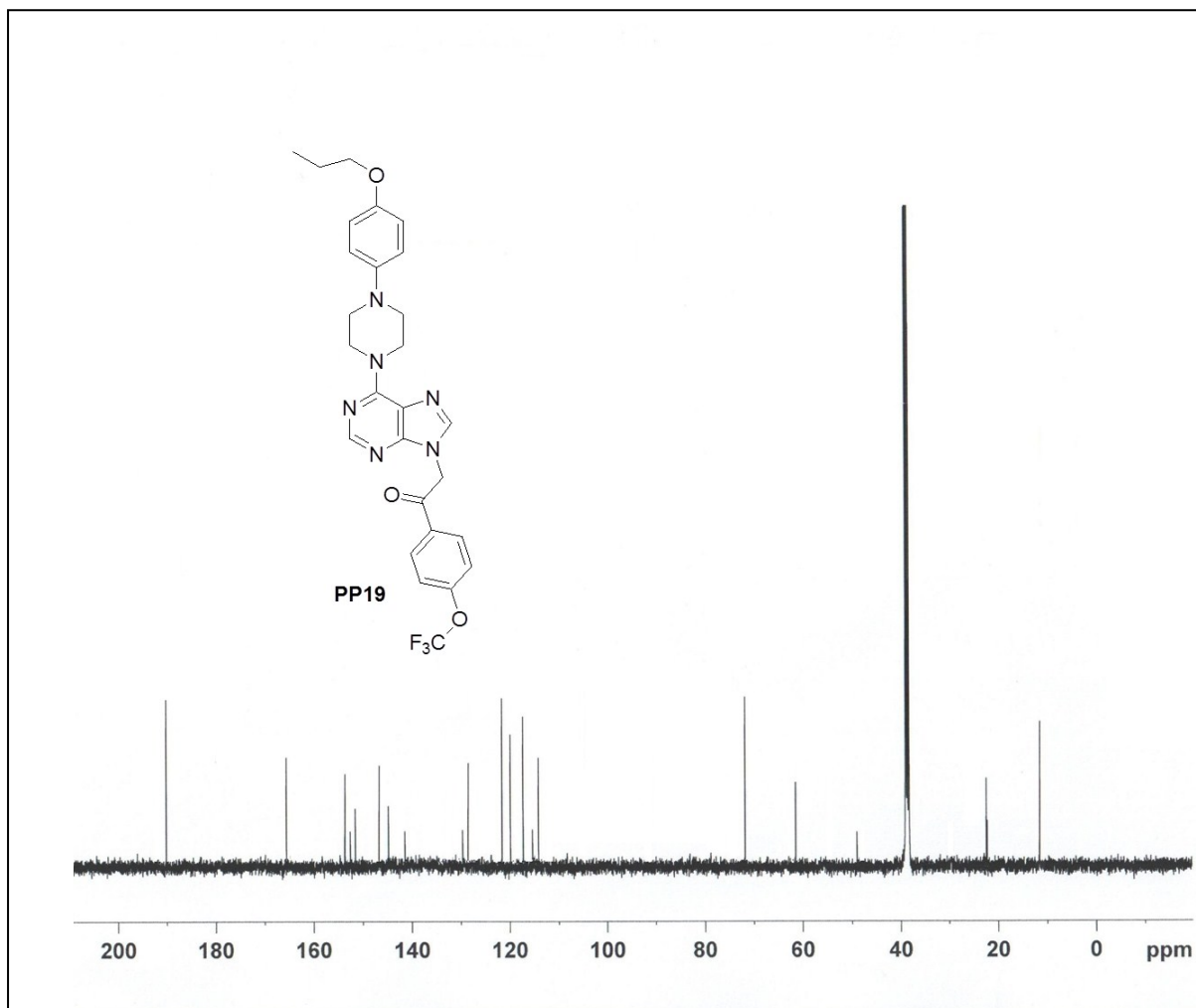
¹H NMR SPECTRUM OF COMPOUND PP18



^{13}C NMR SPECTRUM OF COMPOUND PP18



¹H NMR SPECTRUM OF COMPOUND PP19



^{13}C NMR SPECTRUM OF COMPOUND PP19