

Design, Synthesis, Crystal Structure, in vitro cytotoxicity evaluation, Density Functional Theory calculations and docking studies of 2-(benzamido) benzohydrazide derivatives as Potent AChE and BChE inhibitors:

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Spectral data of Methyl 2-benzamidobenzoate (3)

M.F: C₁₅H₁₃NO₃; Yield: 75%; m.p. 104±1°C; ¹H-NMR (300 MHz, DMSO-*d*₆): δ = 11.17 (1H, br, s, NHCO), 7.35-8.38 (9H, m, Aromatic CH), 3.47 (3H, s, CH₃O). ¹³C NMR (75 MHz, DMSO-*d*₆): δ = 167.6 (COO), 165.9 (CONH), 142.6, 138.4, 135.7 (2), 131.5 (2), 129.3, 126.8 (2), 124.7, 121.6, 120.5 (benzene rings), 52.6 (CH₃O). FTIR (cm⁻¹): 3263 (NH, stretch), 3023 (C-H Stretch), 1691 (ester C=O, stretch), 1667 (C=O, stretch), 1267 (C-O, stretch). MS (ESI): m/z (%), (254 (30), [M]⁻), 224(12), 196 (24), 178 (27).

Spectral data of *N*-(2-(hydrazinecarbonyl)phenyl)benzamide (4)

M.F: C₁₄H₁₃N₃O₂; Yield: 71%; m.p. 192±1°C; ¹H-NMR (300 MHz, DMSO-*d*₆): δ = 12.57 (1H, s, NH-CO), 10.21 (1H, br, NH-NH₂), 7.17-8.68 (8H, m, Aromatic CH), 4.70 (2H, br, NH₂, amine). ¹³C NMR (75 MHz, DMSO-*d*₆): δ = 167.9 (CONHNH₂), 164.6 (NHCO), 139.7, 134.9, 132.5 (2), 129.4 (2), 128.1, 127.4 (2), 123.3, 120.6, 119.5 (benzene rings). FTIR (cm⁻¹): 3316 (NH₂ stretch), 3204 (CON-H, Stretch), 3054 (C-H, stretch), 1646 (C=O, stretch). MS (ESI): m/z (%), 254 (40, [M]⁻), 240 (35), 236 (11), 196(10).

Table S1: Bond Lengths for compound 10

Table S1 Bond Lengths for compound 10					
Atom	Atom	Length/Å	Atom	Atom	Length/Å
C1	C6	1.388(3)	C12	C13	1.377(3)
C1	N1	1.404(3)	C14	O2	1.224(3)
C1	C2	1.407(3)	C14	N2	1.348(3)
C2	C3	1.382(3)	C15	N3	1.276(3)
C2	C14	1.490(3)	C15	C16	1.436(3)
C3	C4	1.383(3)	C16	C21	1.395(3)
C4	C5	1.377(3)	C16	C17	1.406(3)
C5	C6	1.367(3)	C17	O3	1.365(3)
C7	O1	1.228(2)	C17	C18	1.382(3)
C7	N1	1.354(2)	C18	C19	1.390(3)
C7	C8	1.484(3)	C19	O4	1.357(2)
C8	C13	1.384(3)	C19	C20	1.389(3)
C8	C9	1.385(3)	C20	C21	1.369(3)

C9	C10	1.370(3)	C22	O5	1.397(3)
C10	C11	1.372(3)	N2	N3	1.374(2)
C11	C12	1.374(4)			

Table S2: Bond Angles for compound 10

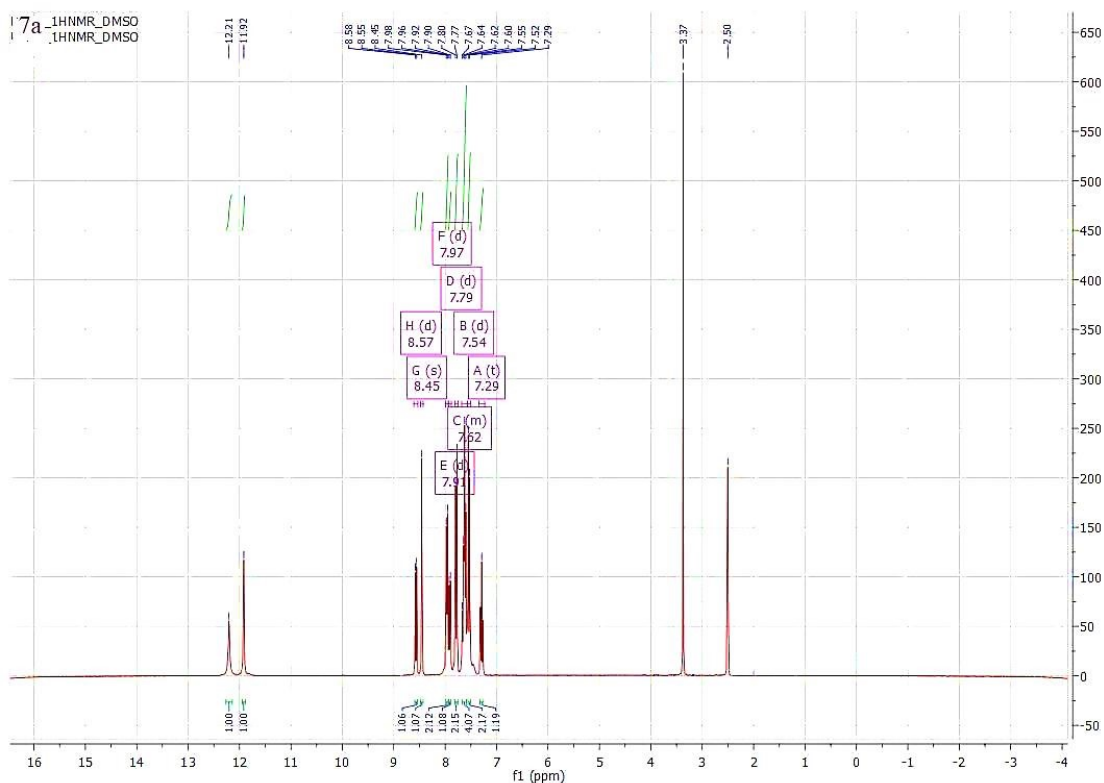
Table S2 Bond Angles for compound 10							
Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C6	C1	N1	122.06(19)	C12	C13	C8	120.1(2)
C6	C1	C2	119.2(2)	O2	C14	N2	122.47(18)
N1	C1	C2	118.68(16)	O2	C14	C2	123.50(19)
C3	C2	C1	118.84(17)	N2	C14	C2	114.03(19)
C3	C2	C14	120.69(18)	N3	C15	C16	121.7(2)
C1	C2	C14	120.45(18)	C21	C16	C17	117.46(19)
C2	C3	C4	121.2(2)	C21	C16	C15	120.1(2)
C5	C4	C3	119.3(2)	C17	C16	C15	122.5(2)
C6	C5	C4	120.64(19)	O3	C17	C18	118.1(2)
C5	C6	C1	120.7(2)	O3	C17	C16	120.86(18)
O1	C7	N1	123.4(2)	C18	C17	C16	121.0(2)
O1	C7	C8	121.47(18)	C17	C18	C19	119.5(2)
N1	C7	C8	115.09(17)	O4	C19	C20	122.4(2)
C13	C8	C9	118.7(2)	O4	C19	C18	117.0(2)
C13	C8	C7	119.1(2)	C20	C19	C18	120.6(2)
C9	C8	C7	122.09(19)	C21	C20	C19	119.0(2)
C10	C9	C8	120.8(2)	C20	C21	C16	122.4(2)
C9	C10	C11	120.3(2)	C7	N1	C1	128.60(17)
C10	C11	C12	119.6(2)	C14	N2	N3	119.55(18)
C11	C12	C13	120.6(2)	C15	N3	N2	116.58(19)

Table S3: Torsion Angles for compound 10

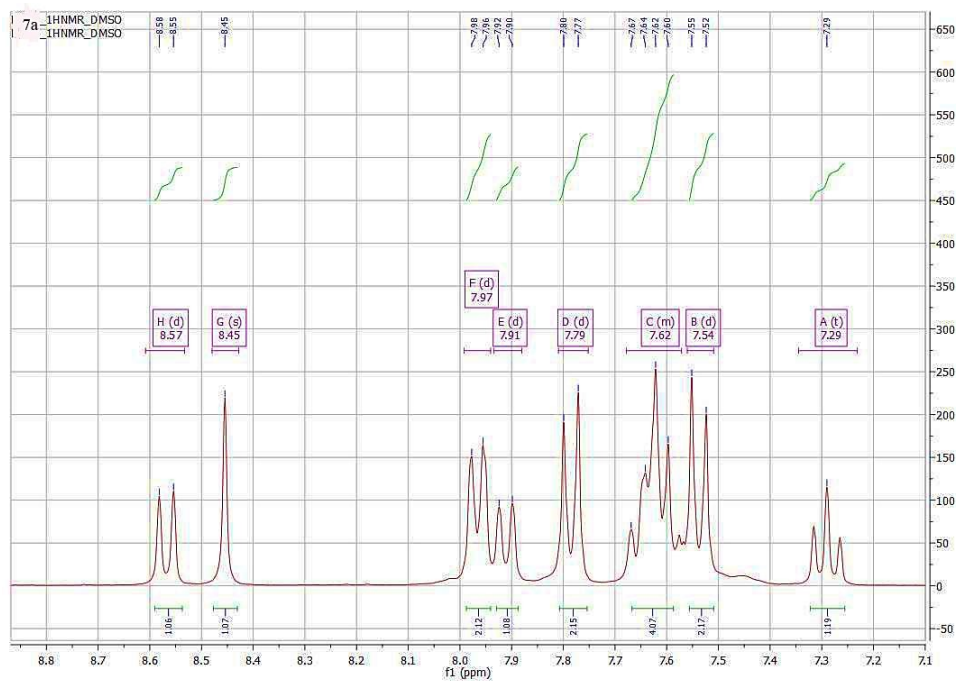
Table S3 Torsion Angles for compound 10										
A	B	C	D	Angle/°	A	B	C	D	Angle/°	
C6	C1	C2	C3	-1.5(3)	C3	C2	C14	N2	33.3(3)	
N1	C1	C2	C3	176.44(19)	C1	C2	C14	N2	-148.28(19)	
C6	C1	C2	C14	-179.92(19)	N3	C15	C16	C21	-179.63(19)	
N1	C1	C2	C14	-2.0(3)	N3	C15	C16	C17	-0.6(3)	
C1	C2	C3	C4	1.0(3)	C21	C16	C17	O3	-179.55(19)	
C14	C2	C3	C4	179.5(2)	C15	C16	C17	O3	1.3(3)	
C2	C3	C4	C5	0.1(4)	C21	C16	C17	C18	1.3(3)	
C3	C4	C5	C6	-0.7(4)	C15	C16	C17	C18	-177.80(18)	
C4	C5	C6	C1	0.3(4)	O3	C17	C18	C19	-179.42(19)	

N1	C1	C6	C5	-177.0(2)	C16	C17	C18	C19	-0.3(3)
C2	C1	C6	C5	0.9(3)	C17	C18	C19	O4	178.30(19)
O1	C7	C8	C13	-24.7(3)	C17	C18	C19	C20	-1.4(3)
N1	C7	C8	C13	155.54(19)	O4	C19	C20	C21	-177.77(19)
O1	C7	C8	C9	152.3(2)	C18	C19	C20	C21	1.9(3)
N1	C7	C8	C9	-27.4(3)	C19	C20	C21	C16	-0.8(3)
C13	C8	C9	C10	0.2(3)	C17	C16	C21	C20	-0.8(3)
C7	C8	C9	C10	-176.9(2)	C15	C16	C21	C20	178.35(19)
C8	C9	C10	C11	-0.3(4)	O1	C7	N1	C1	-5.4(4)
C9	C10	C11	C12	-0.3(4)	C8	C7	N1	C1	174.35(19)
C10	C11	C12	C13	1.0(4)	C6	C1	N1	C7	-25.9(3)
C11	C12	C13	C8	-1.0(4)	C2	C1	N1	C7	156.2(2)
C9	C8	C13	C12	0.4(3)	O2	C14	N2	N3	-1.1(3)
C7	C8	C13	C12	177.6(2)	C2	C14	N2	N3	178.73(16)
C3	C2	C14	O2	-146.8(2)	C16	C15	N3	N2	179.15(17)
C1	C2	C14	O2	31.6(3)	C14	N2	N3	C15	179.73(18)

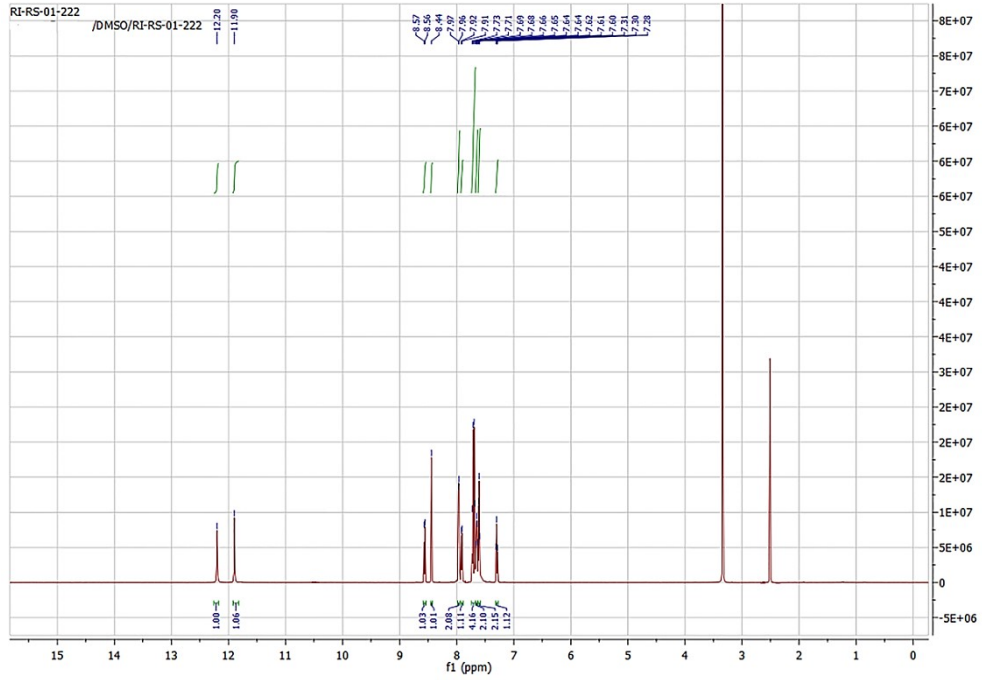
1H NMR of Compound 5



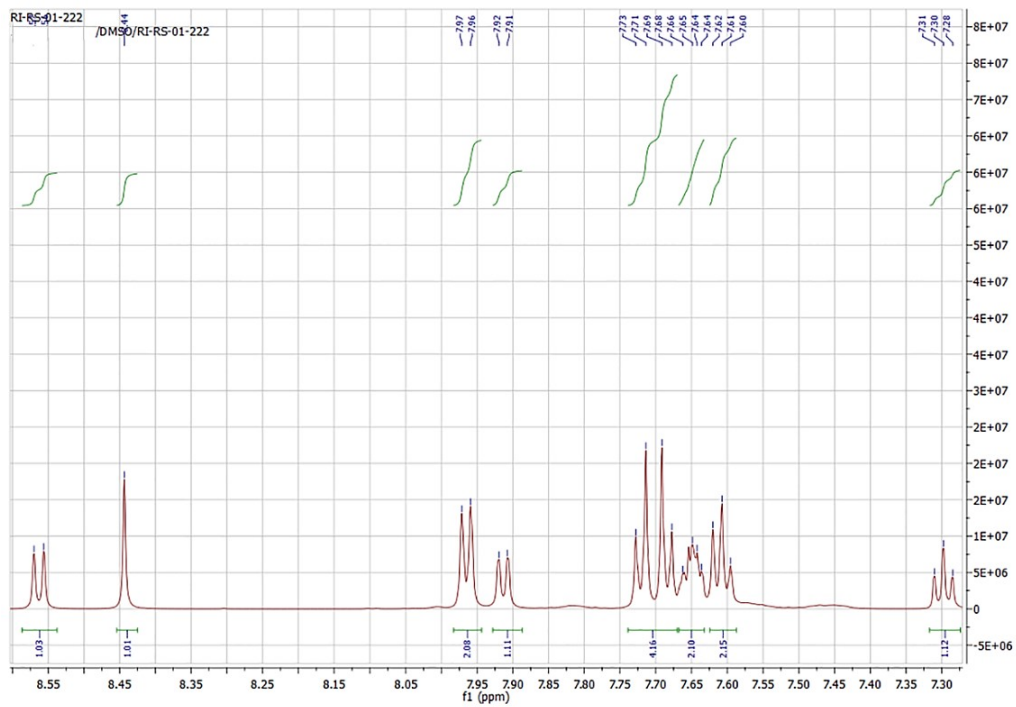
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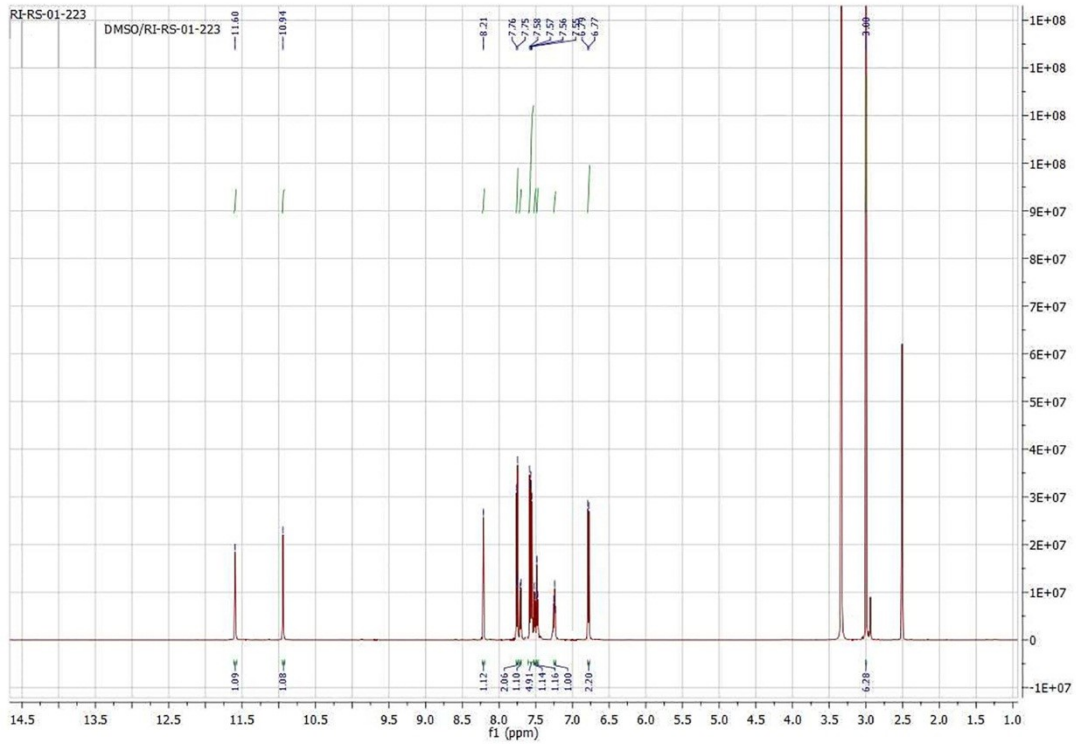
1HNMR Compound 6



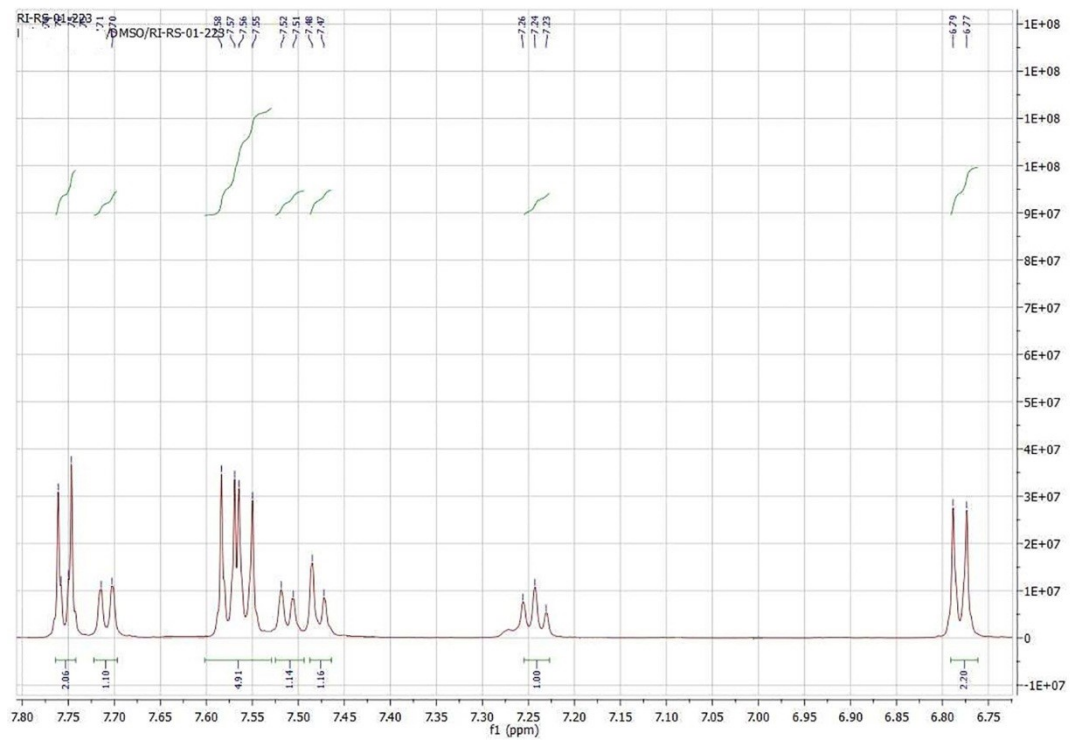
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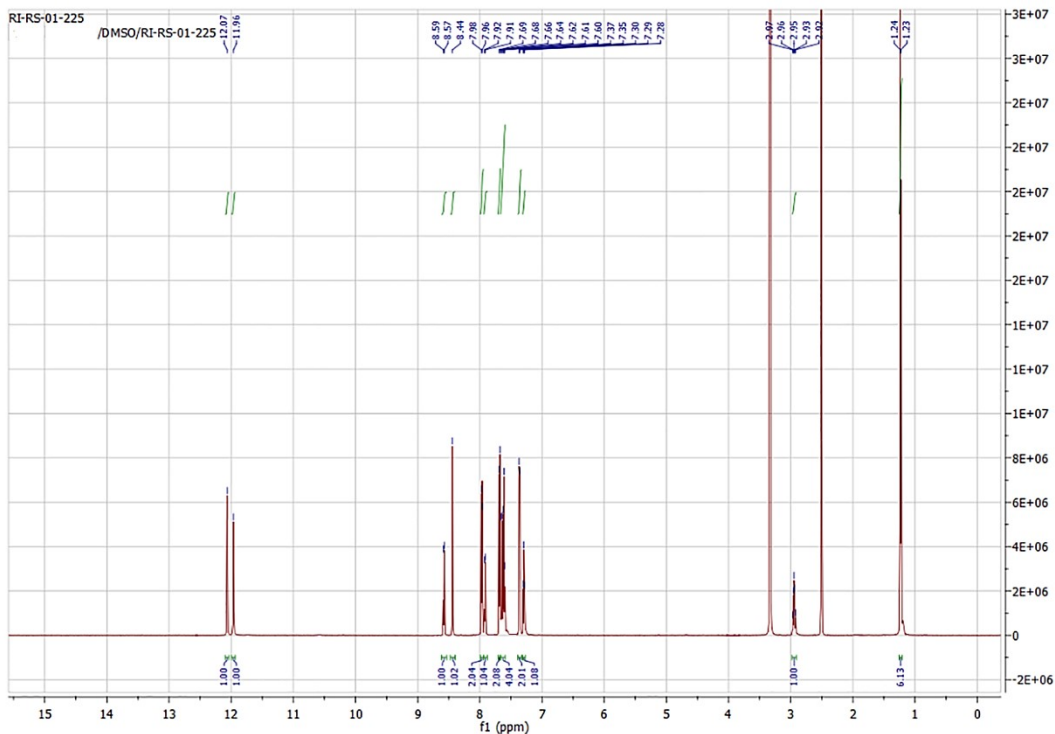
1HNMR Compound 7



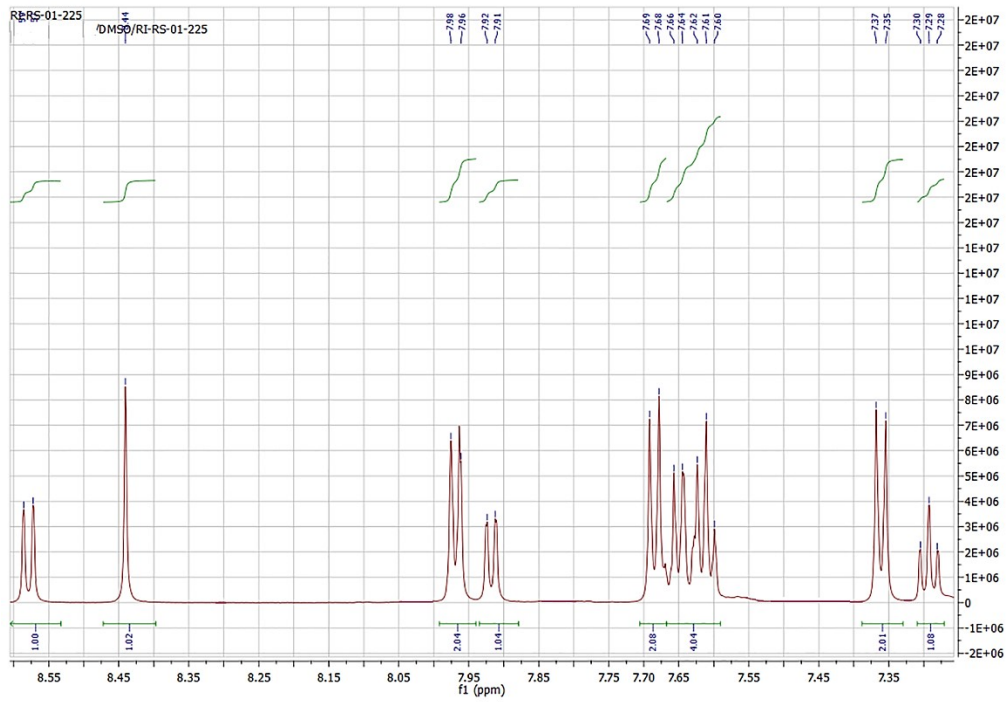
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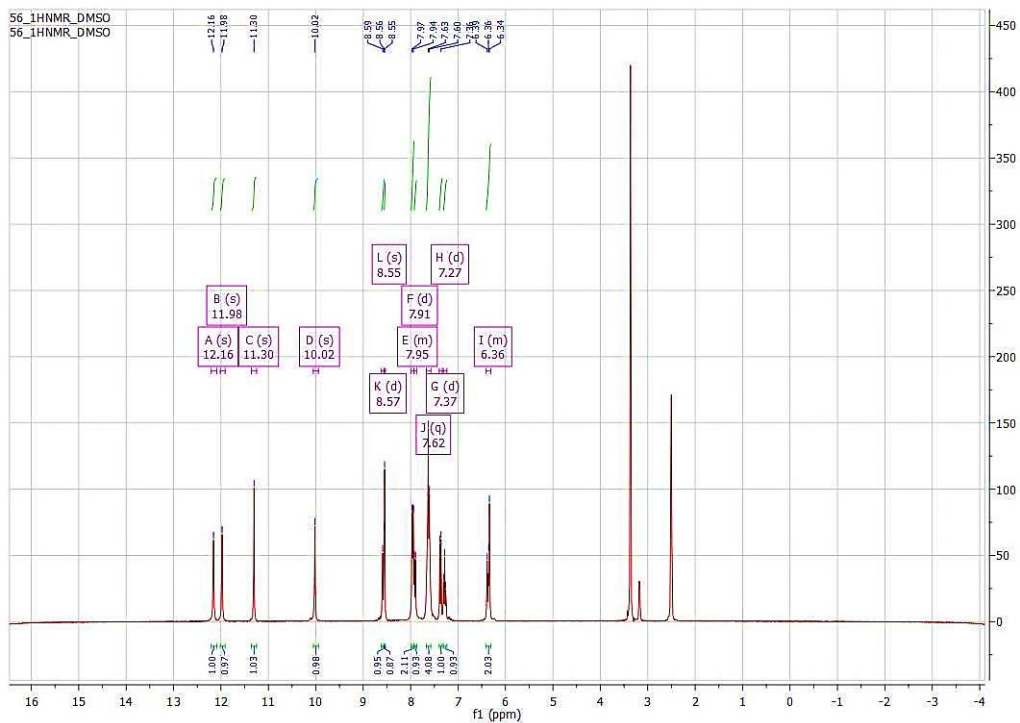
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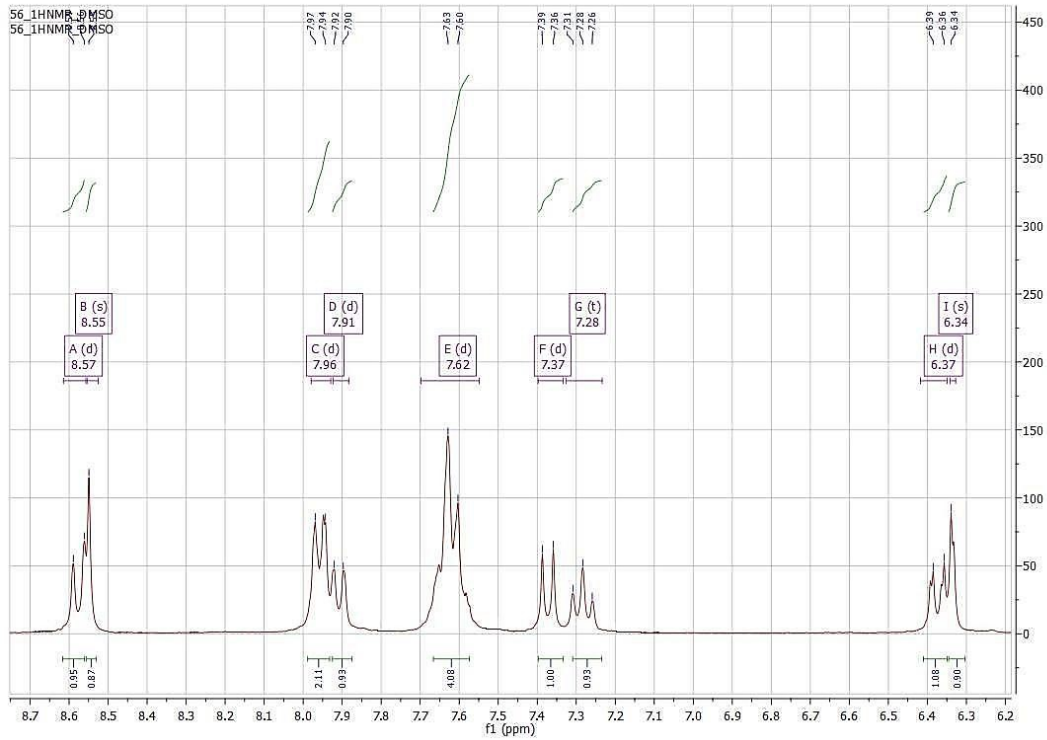
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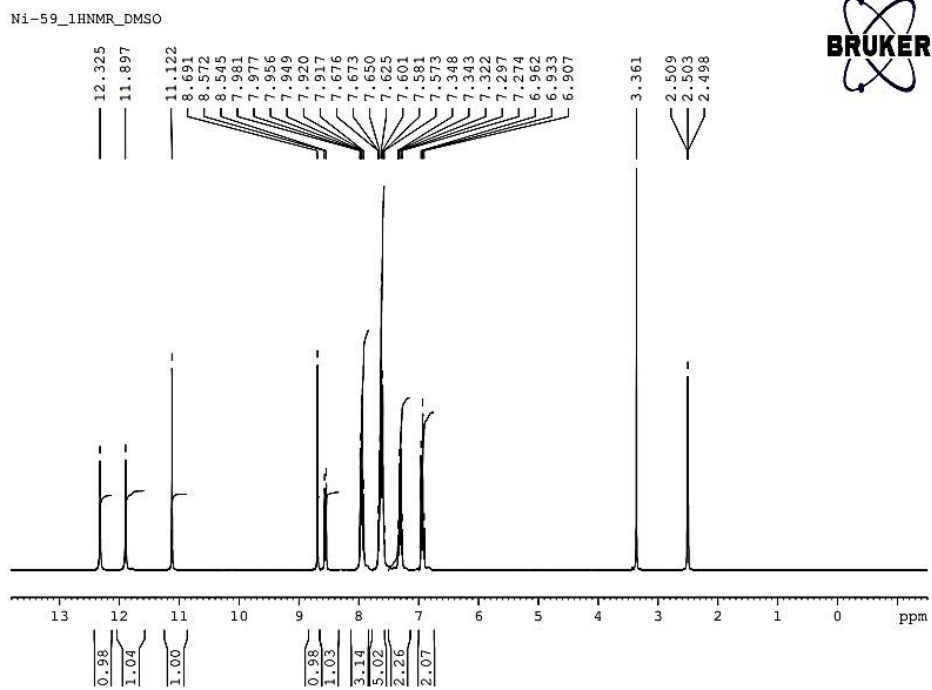
1HNMR Compound 10



1HNMR Compound 10

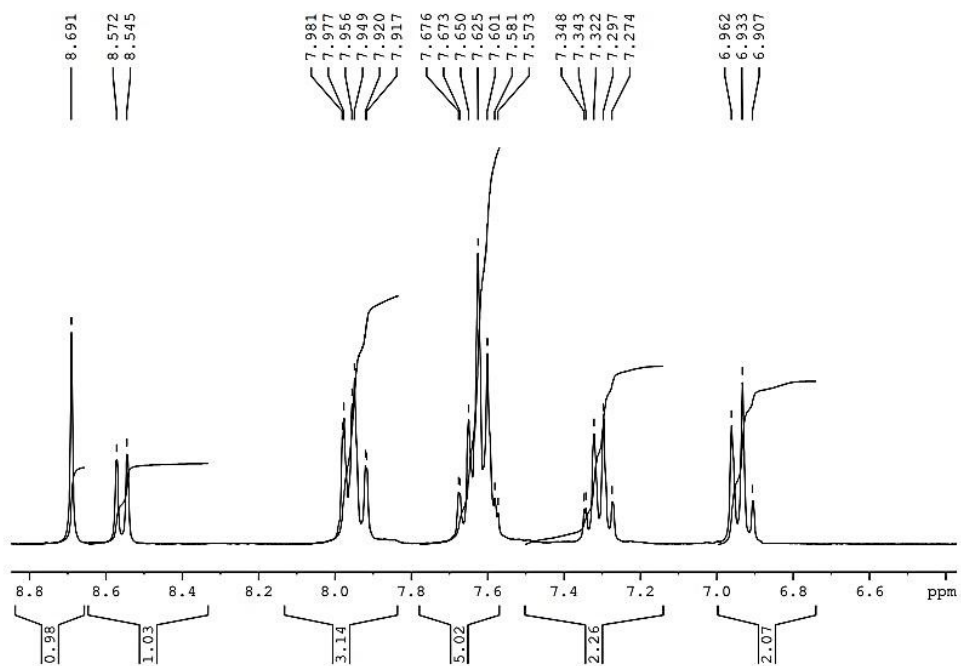


1HNMR Compound 11



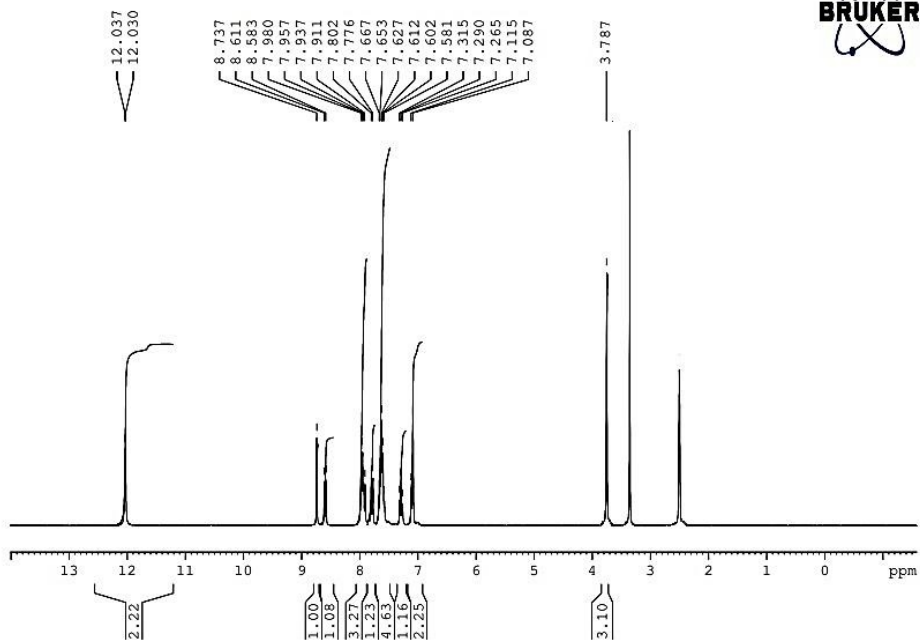
1HNMR Compound 11

Ni-59_1HNMR_DMSO

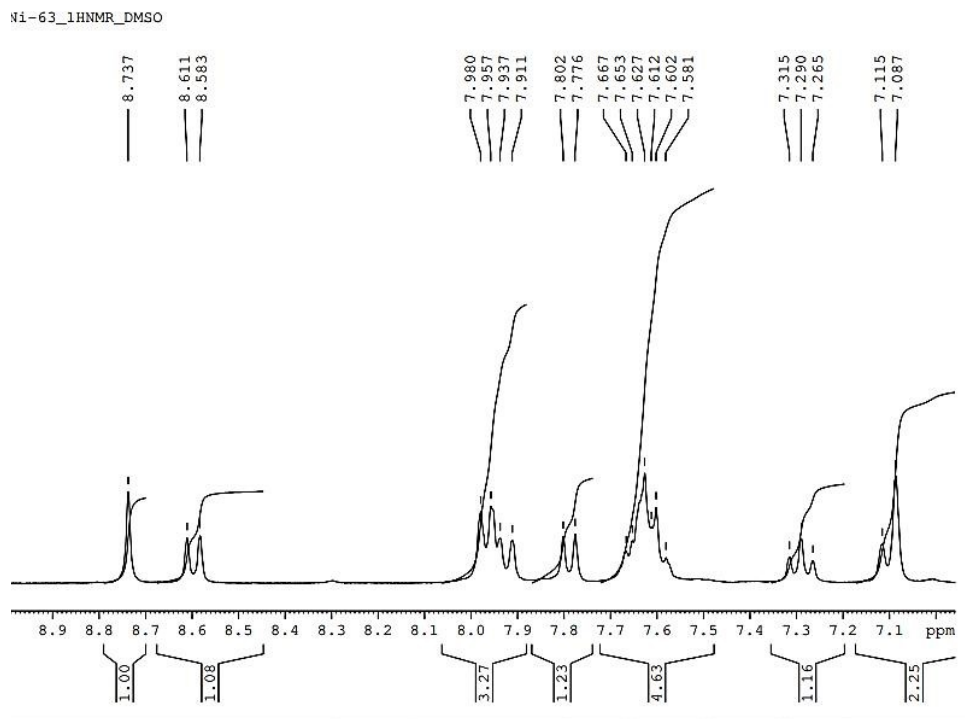


1HNMR Compound 12

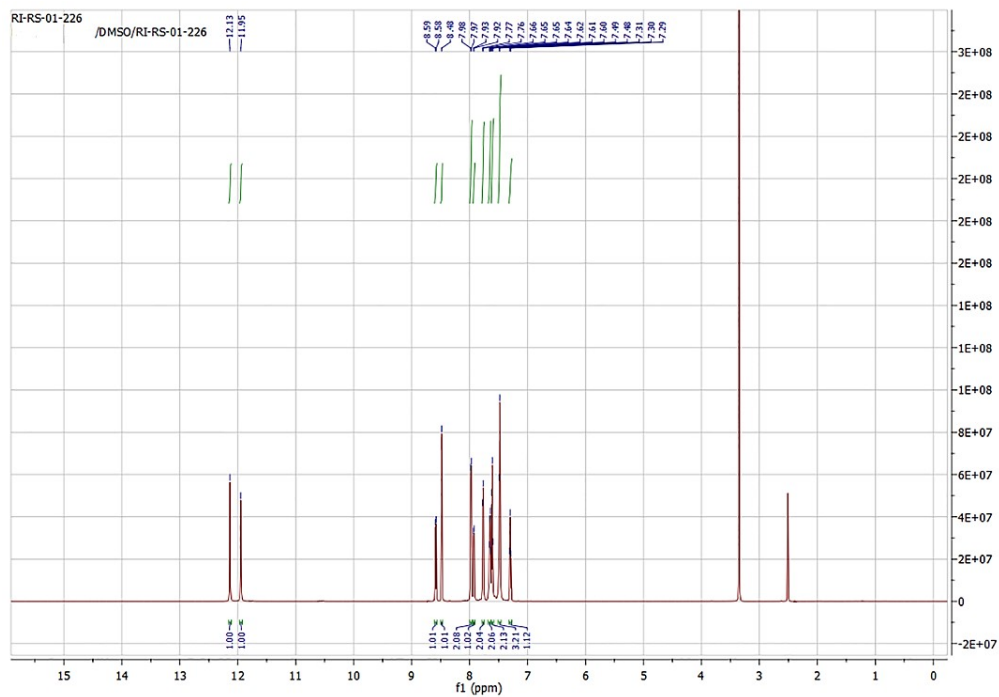
Ni-63_1HNMR_DMSO



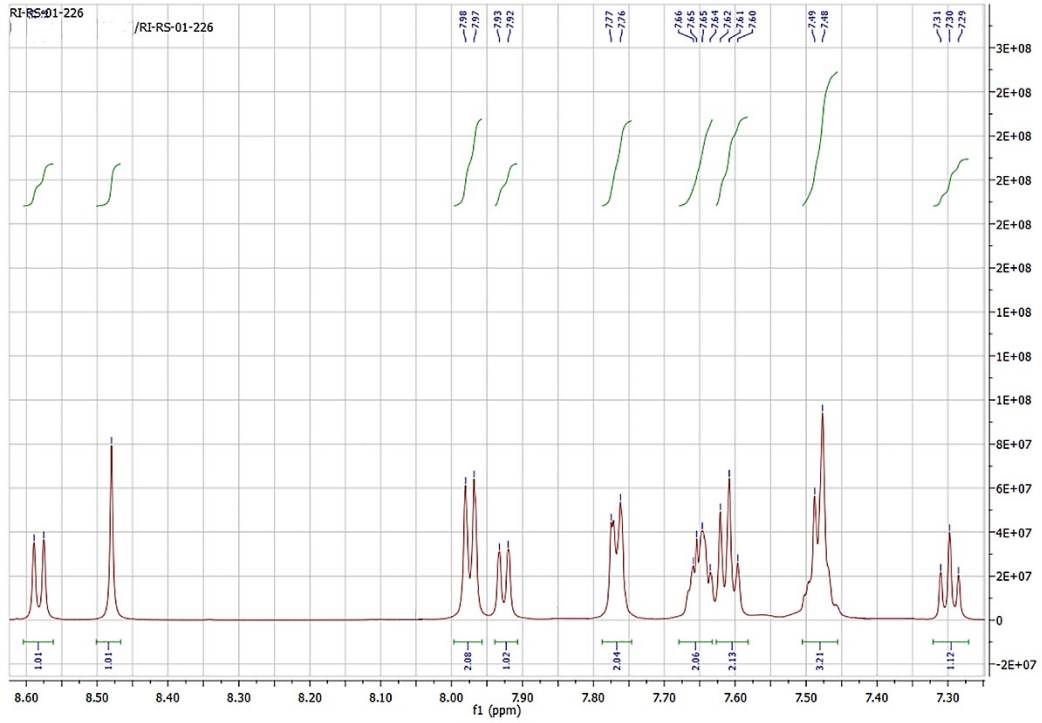
1HNMR Compound 12



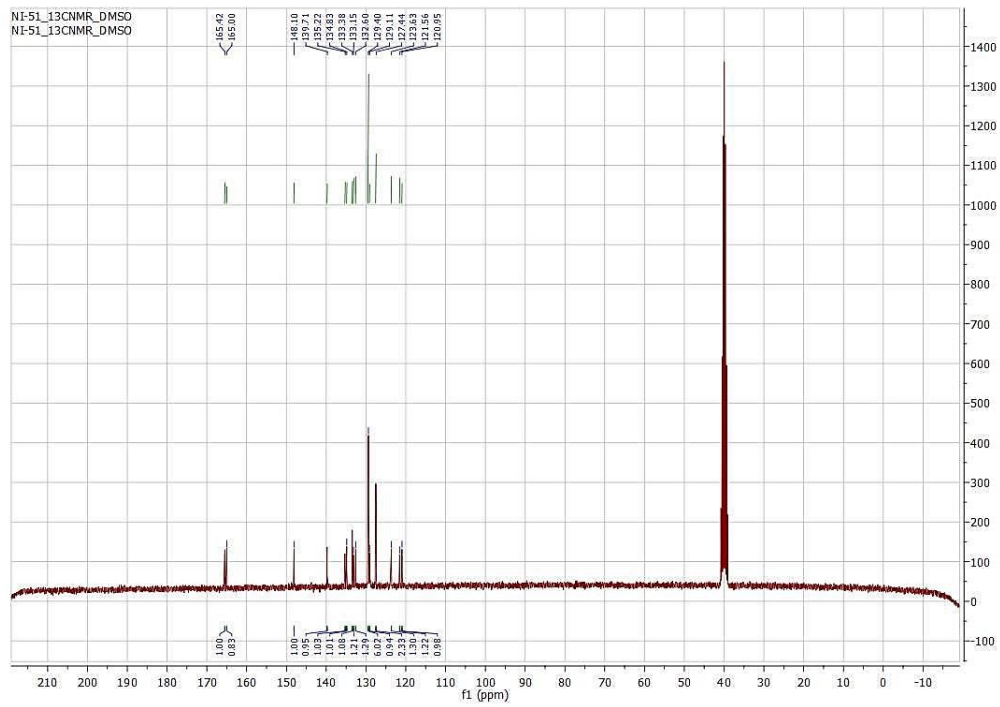
1HNMR Compound 13



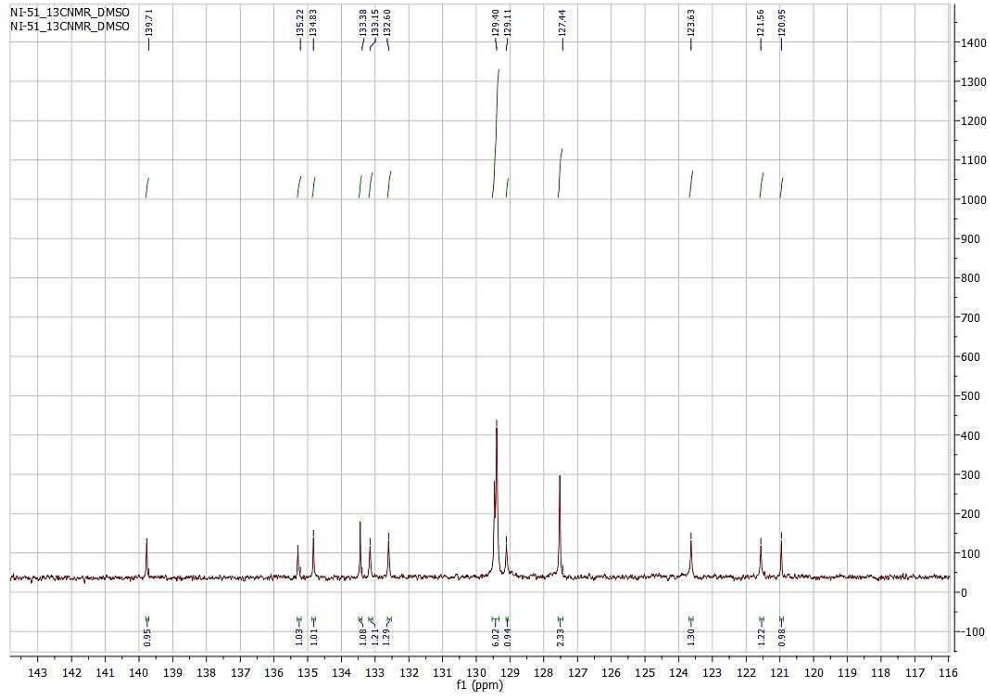
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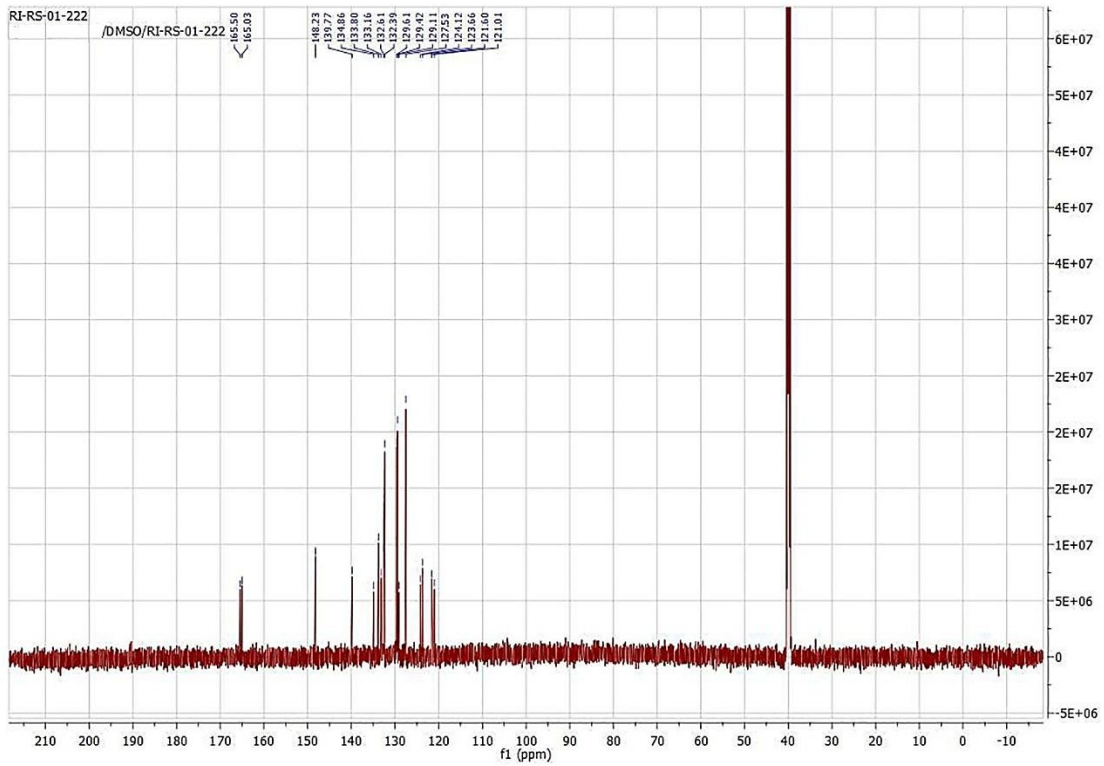
13C NMR Compound 5



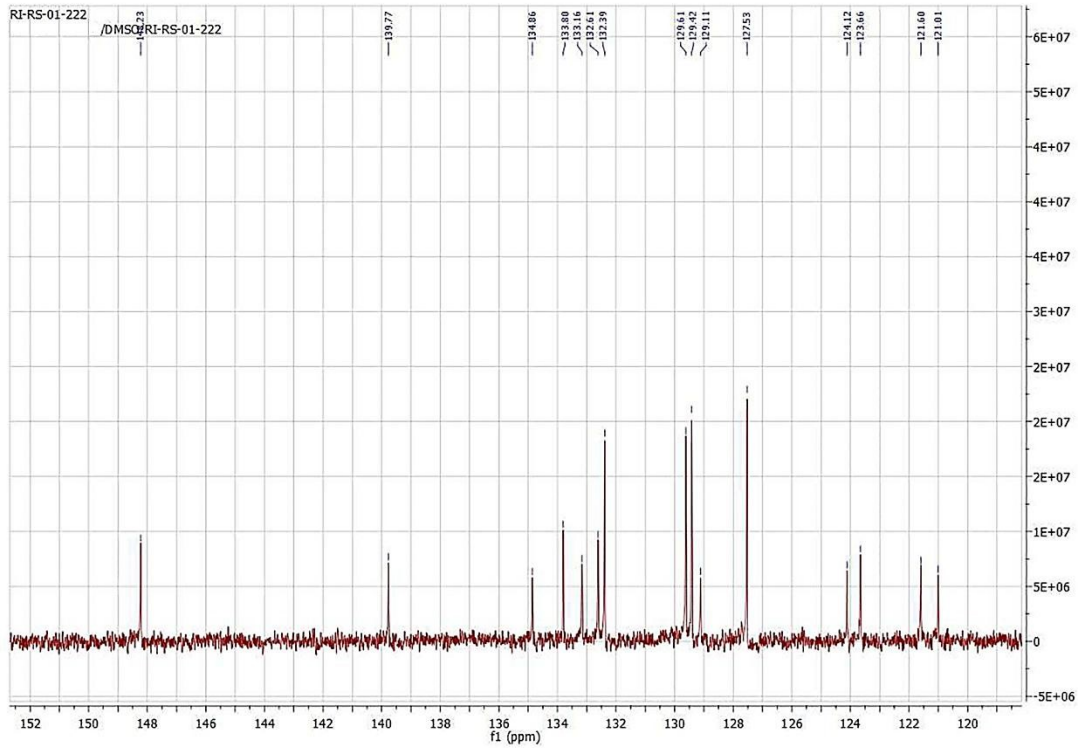
13C NMR Compound 5



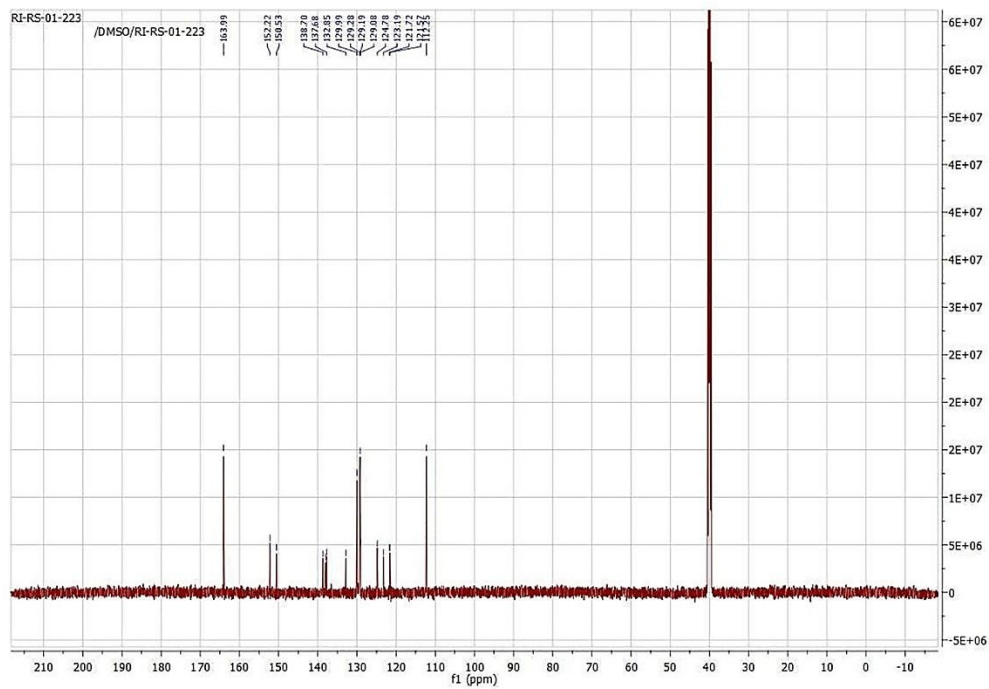
13C NMR Compound 6



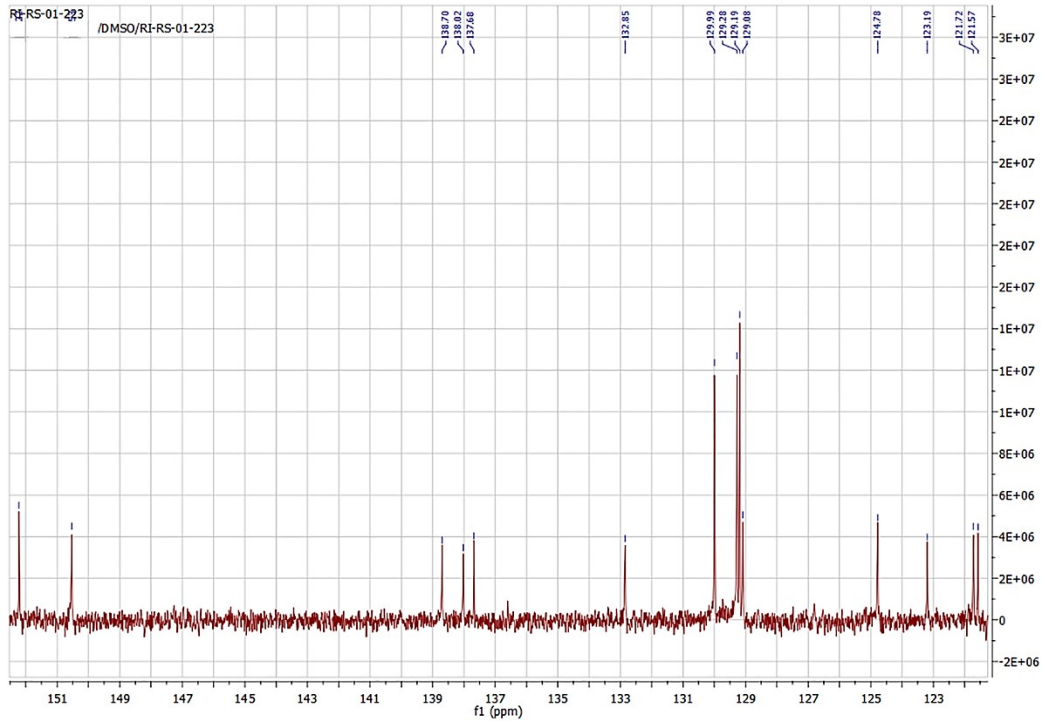
13C NMR Compound 6



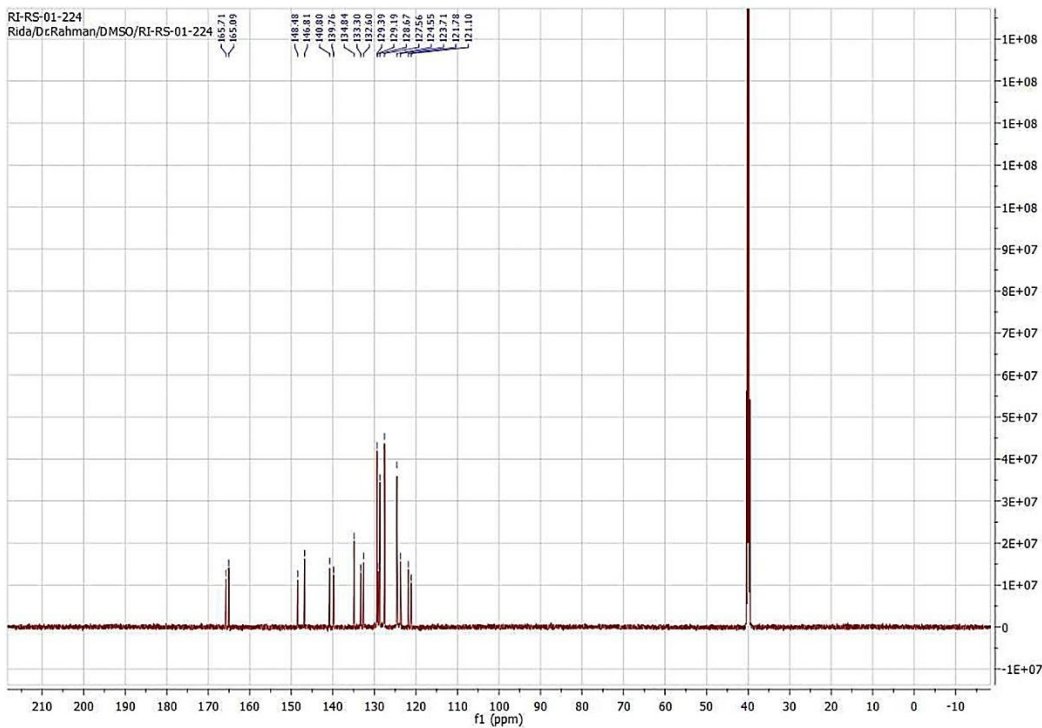
13C NMR Compound 7



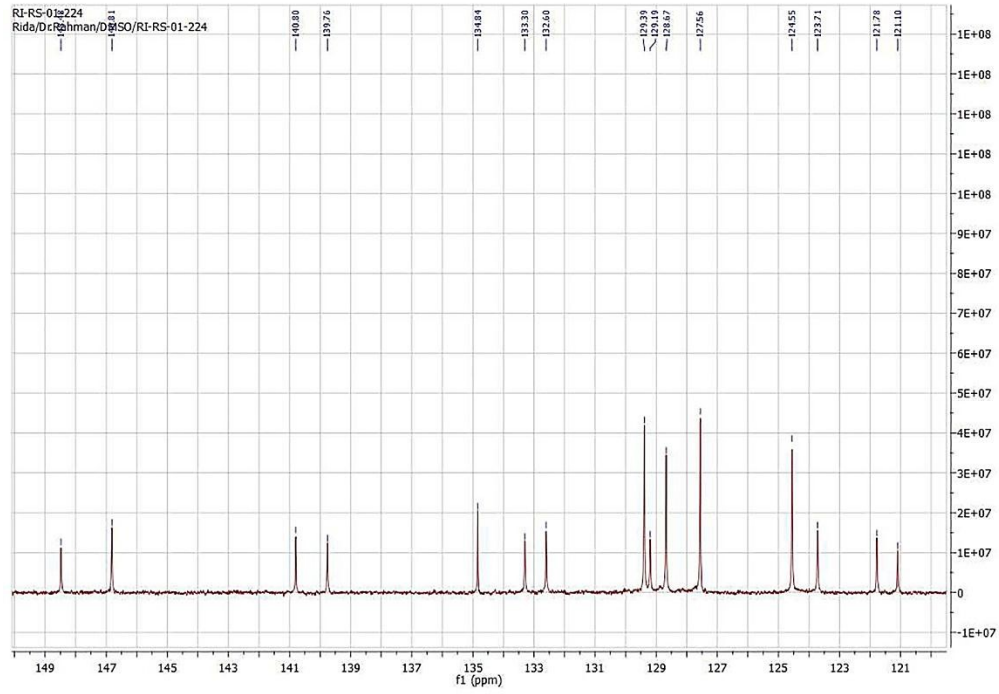
13C NMR Compound 7



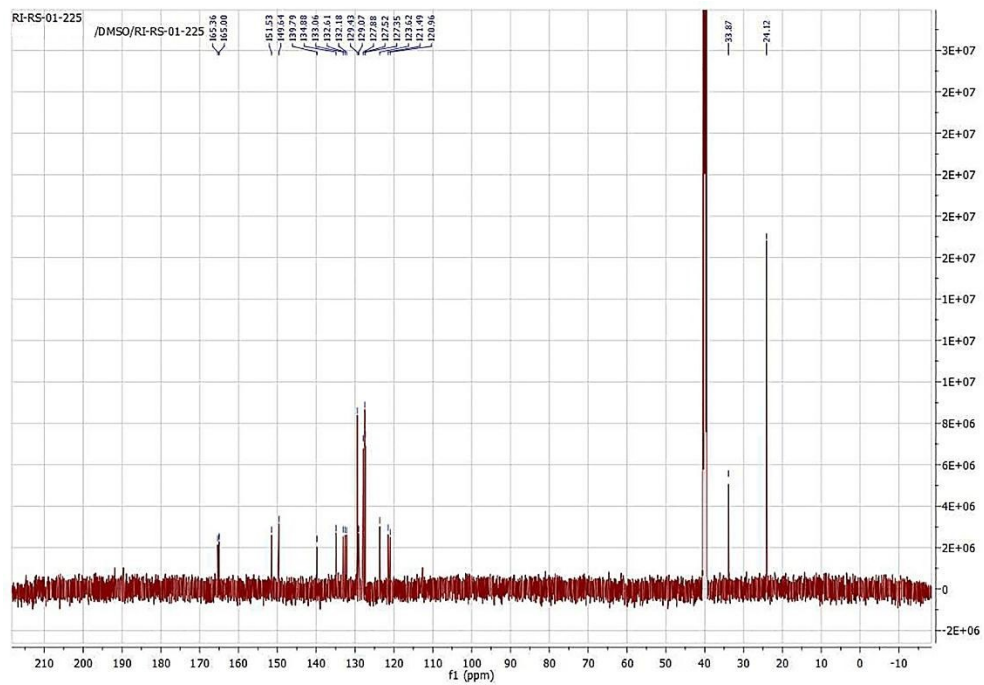
13C NMR Compound 8



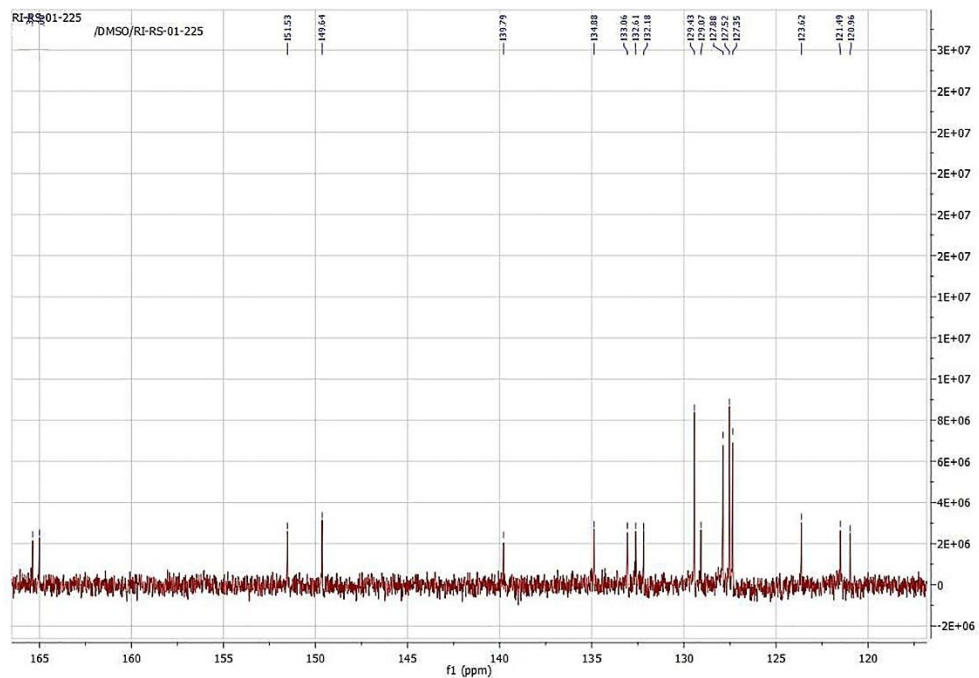
13C NMR Compound 8



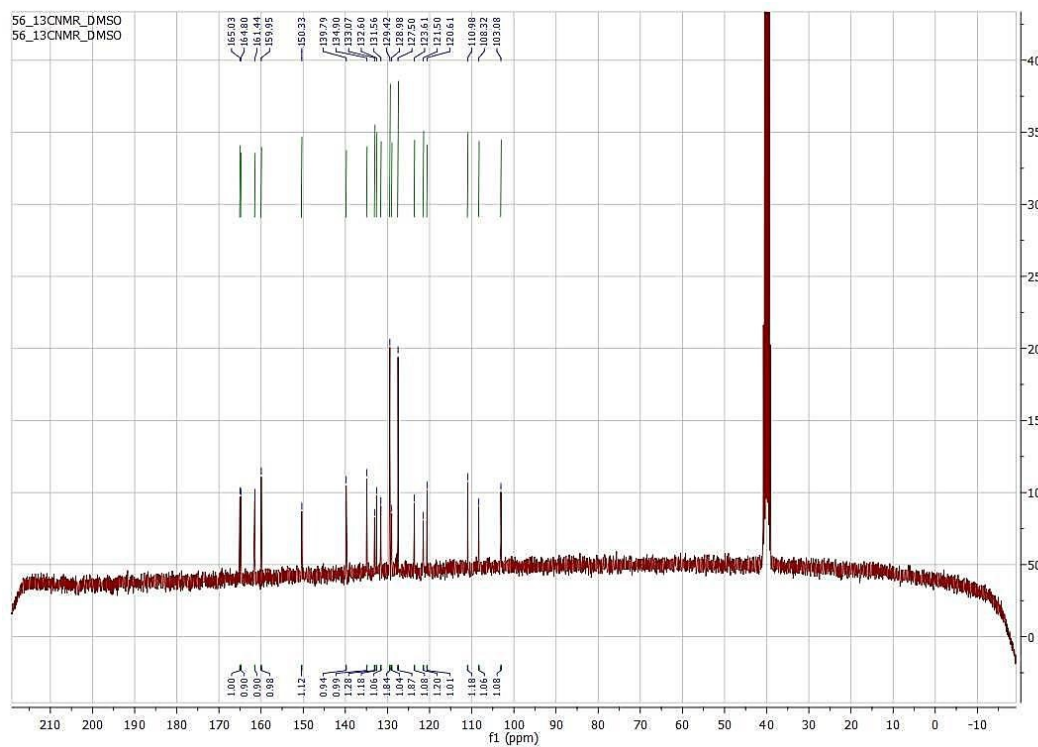
13C NMR Compound 9



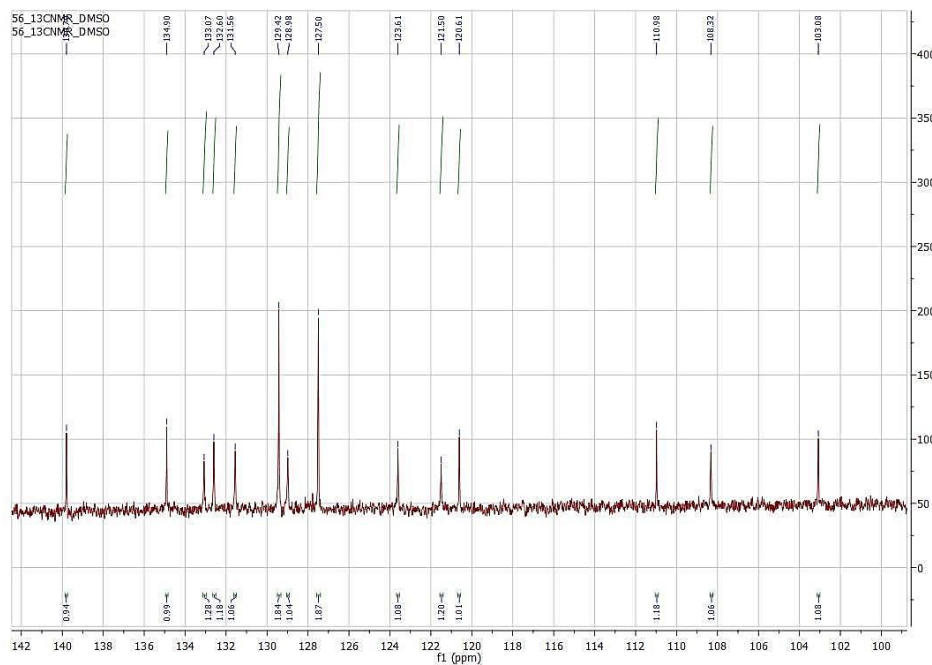
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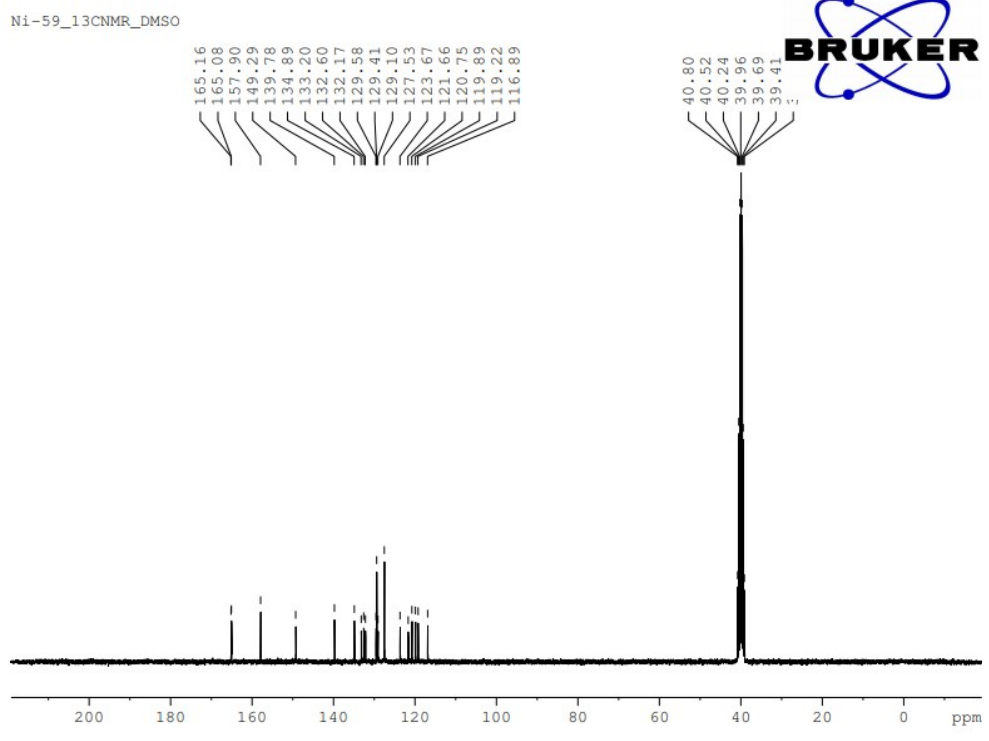
13C NMR Compound 10



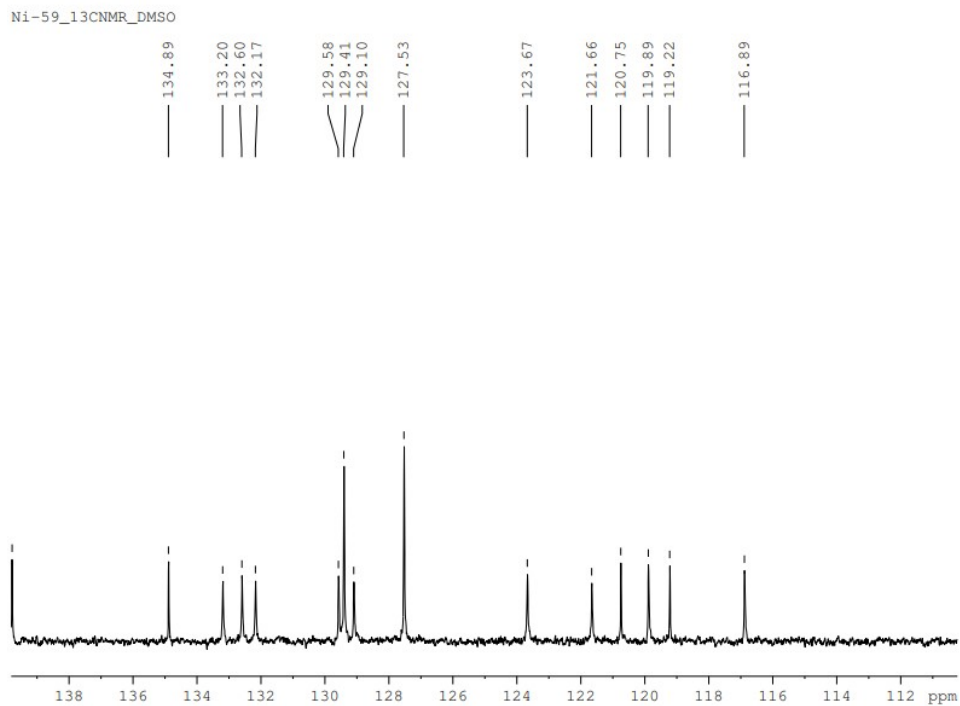
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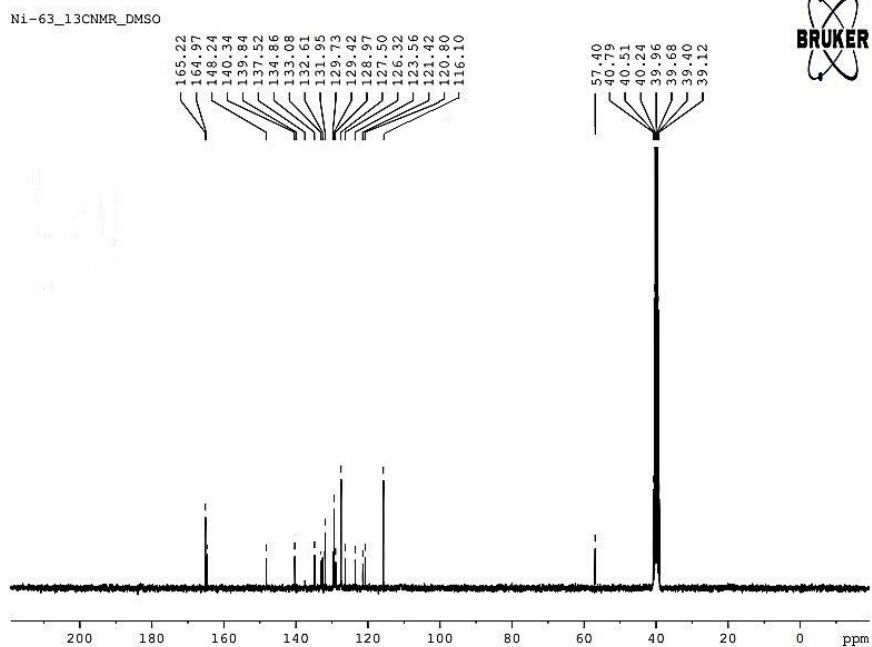
13C NMR Compound 11



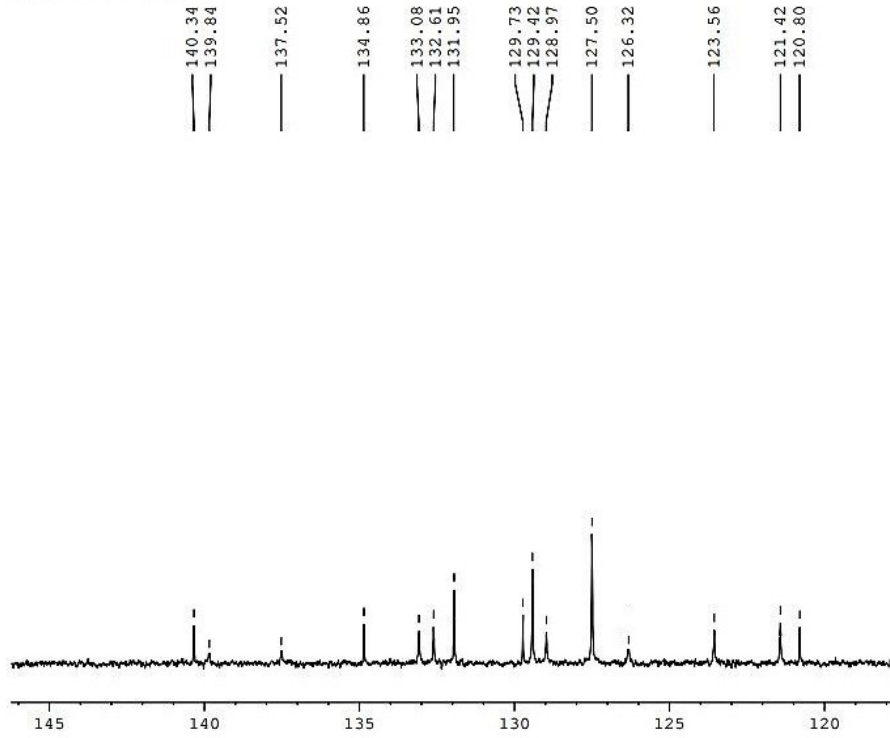
13C NMR Compound 11



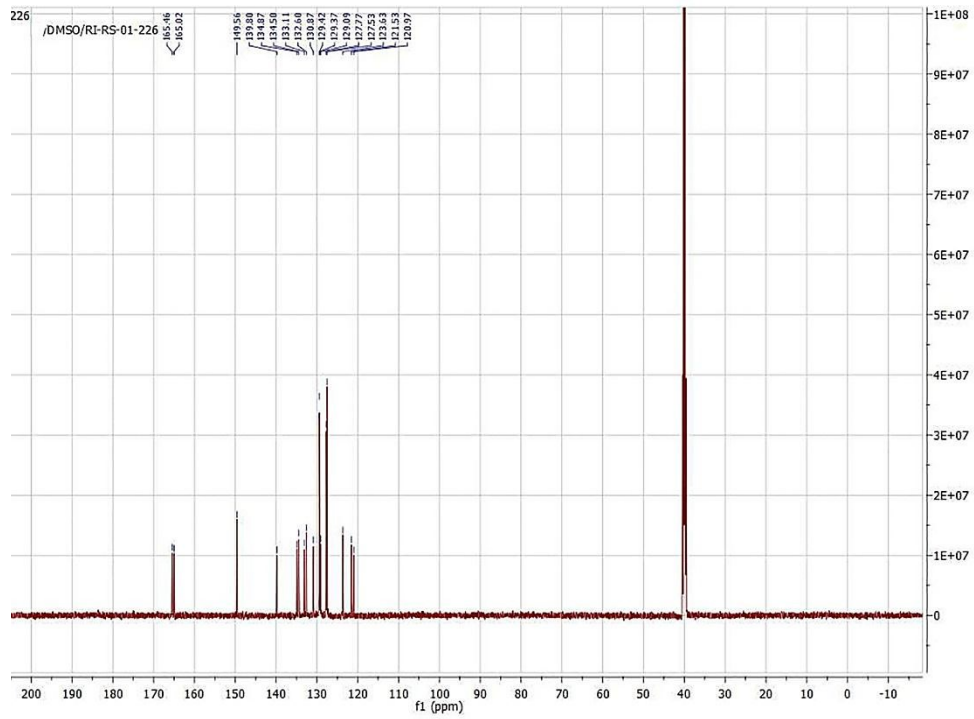
13C NMR Compound 12



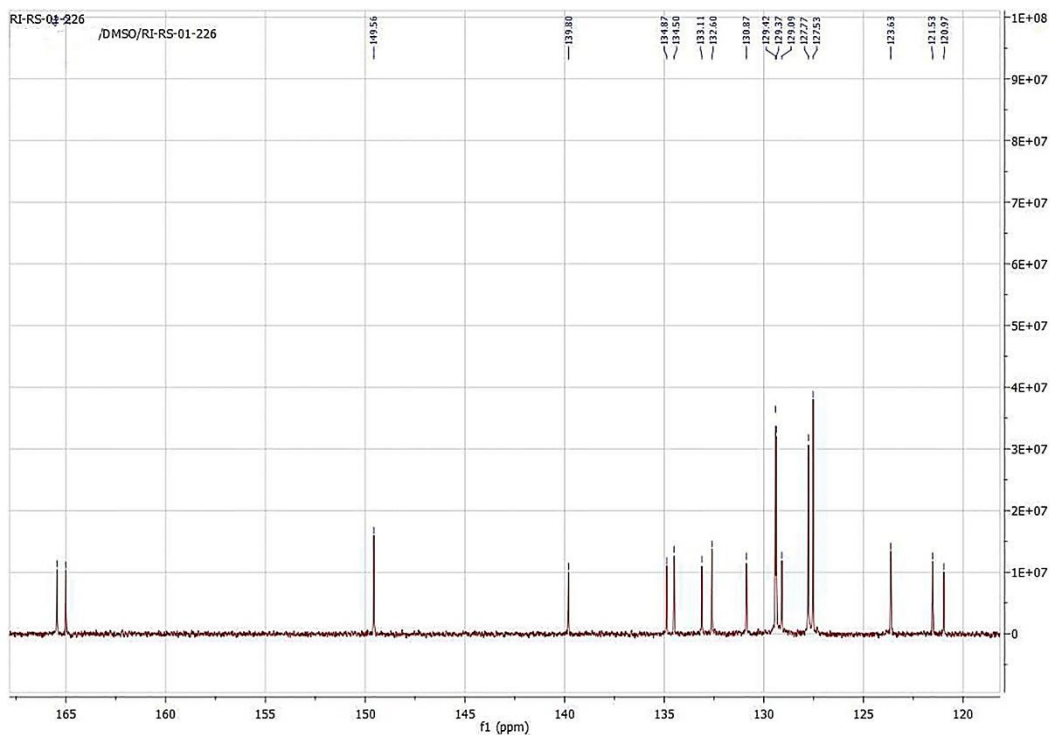
13C NMR Compound 12



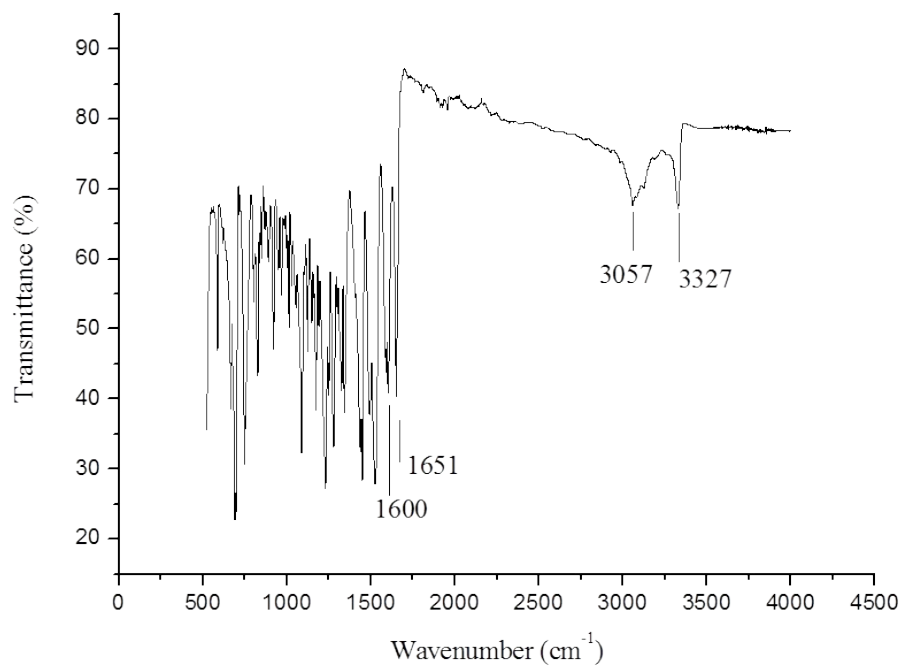
13C NMR Compound 13



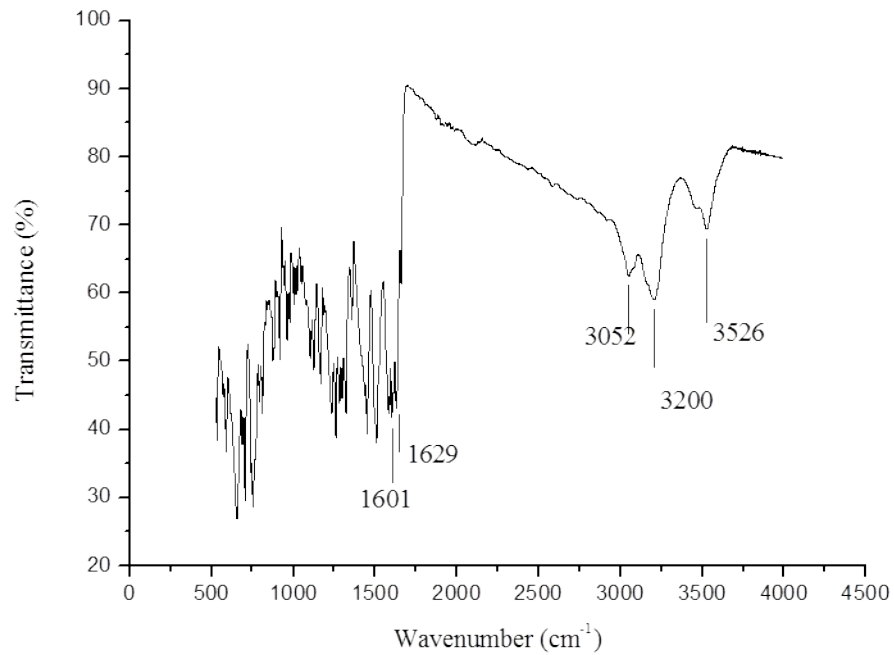
13C NMR Compound 13



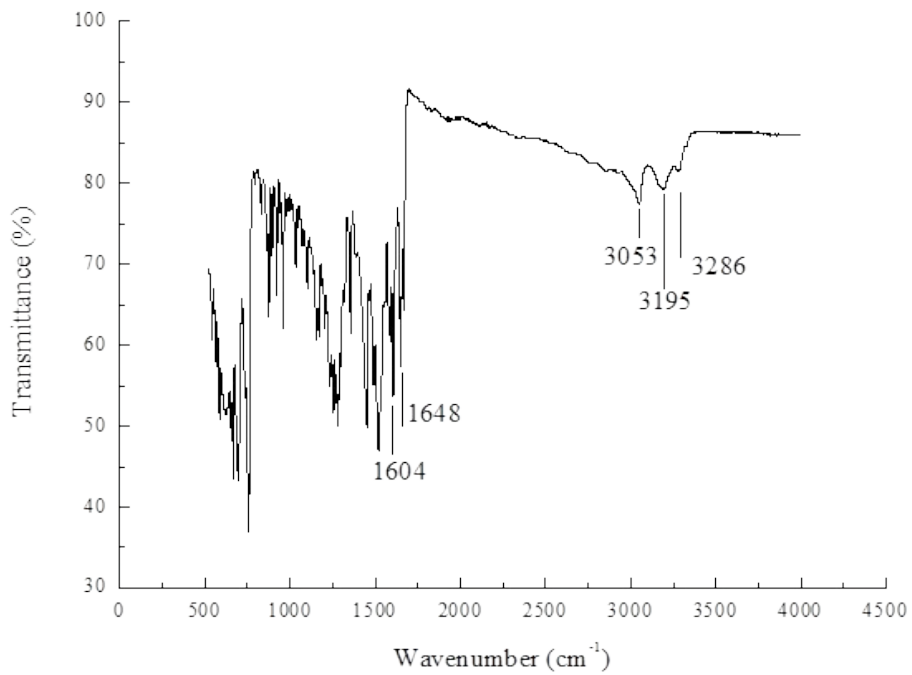
FTIR Compound 5



FTIR Compound 10



FTIR Compound 11



Mass Spectrum Compound 10

Sample 7f -Negative-Mode

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T: ITMS - p ESI Full ms [100.00-800.00]

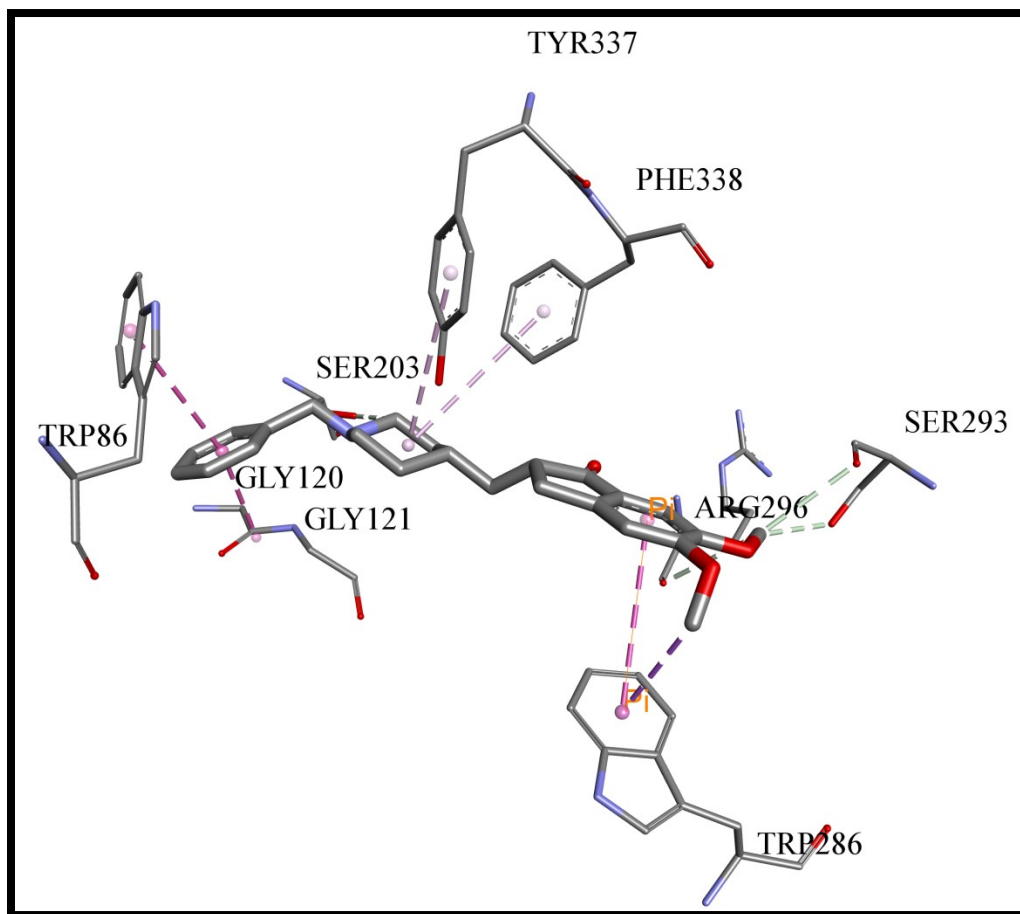
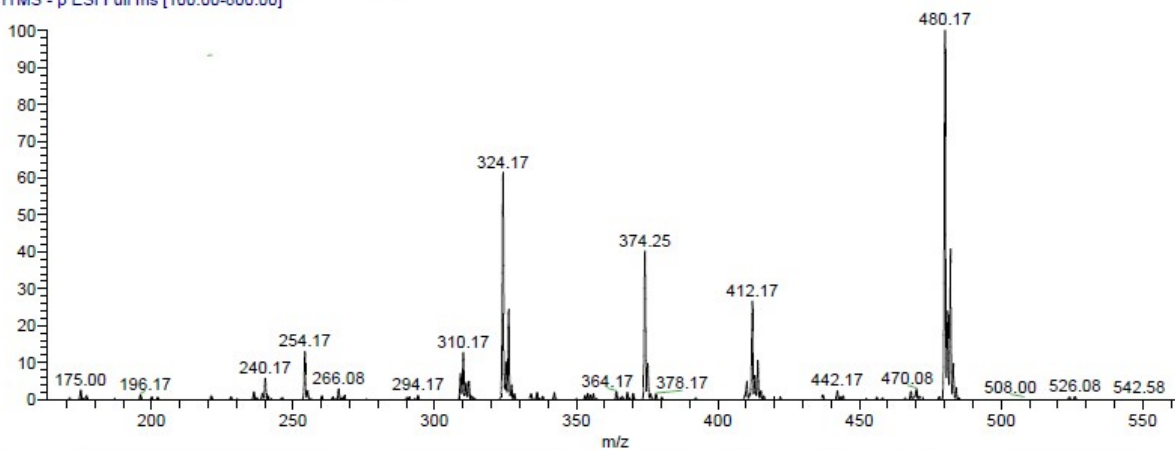


Figure S1: Putative binding approaches of Donepezil inside AChE enzyme