Supplementary file

Quinoline and Isoindoline Integrated Polycyclic Compounds as Antioxidant, and Antidiabetic Agents Targeting Dual Inhibition of α-glycosidase and α-amylase enzymes

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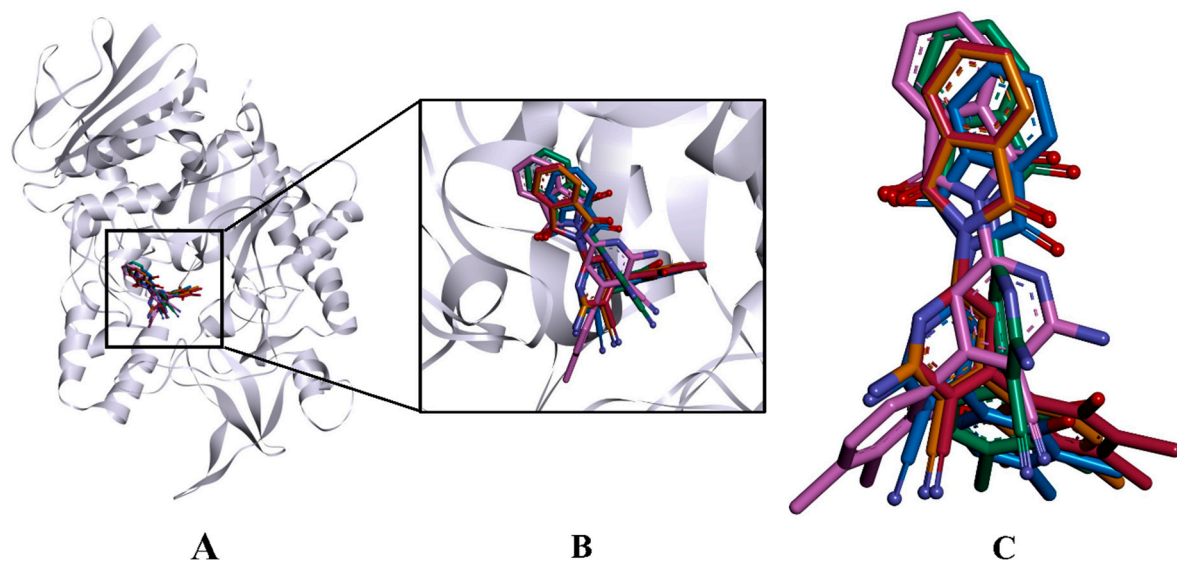
Figure S1: Snapshots from the MD simulation of compound **7d** with α-glucosidase at different time intervals. A) ligand 7d bound conformations inside the inhibitor binding site; B) Arrangement of the binding conformations; and C) ligand-only conformations of 7d. Red: 20 ns, Orange: 40 ns, Blue: 60 ns, Magenta: 80 ns, and Green: 100 ns.
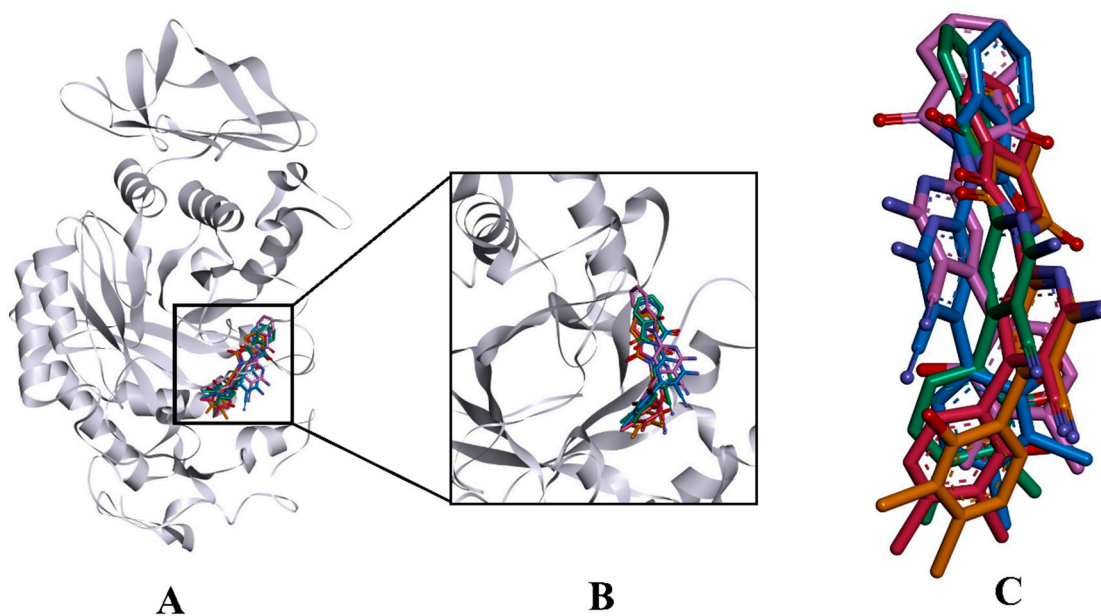

Figure S2: Snapshots from the MD simulation of compound **7d** with α-amylase at different time intervals. A) ligand 7d bound conformations inside the inhibitor binding site; B) Arrangement of

the binding conformations; and C) ligand-only conformations of 7d. Red: 20 ns, Orange: 40 ns, Blue: 60 ns, Magenta: 80 ns, and Green: 100 ns.
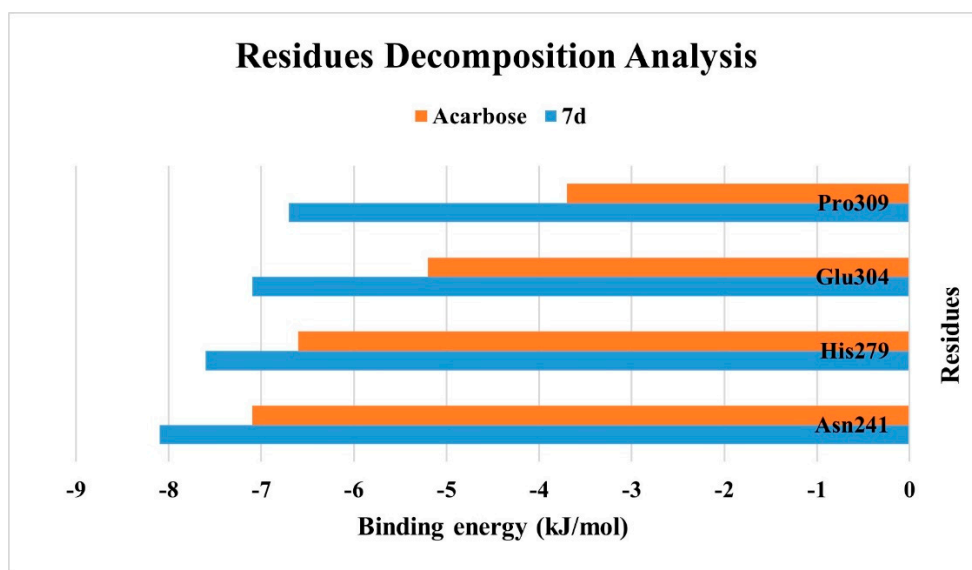

Figure S3: The interactive amino acid residues decomposition analysis of α-glucosidase with compound 7d and acarbose. The binding energy (kJ/mol) contribution of Pro309, Glu304, His279, and Asn24 in α-glucosidase-compound 7d complex estimated from 5000 frames (50 ns) of MD simulation.
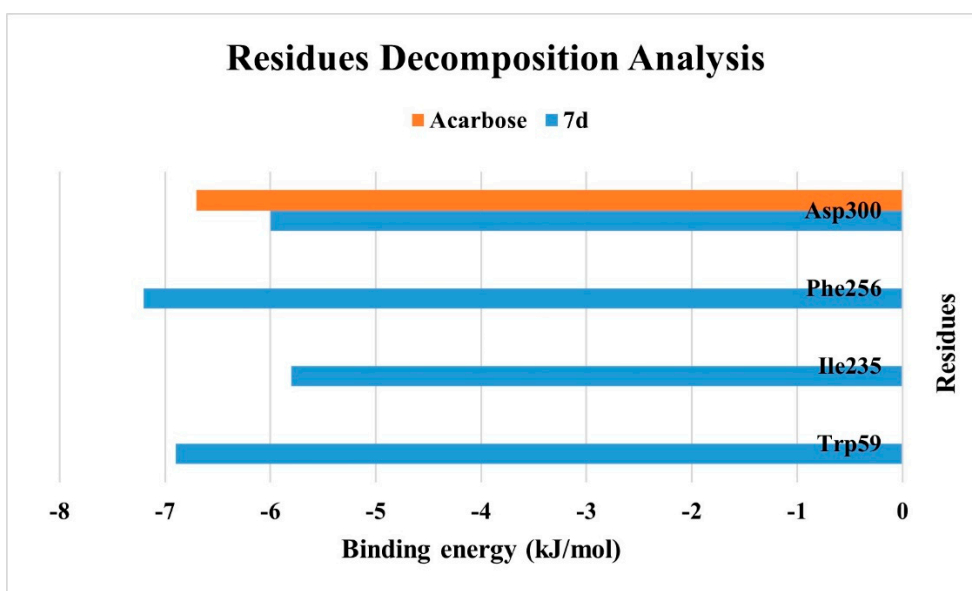
**Figure S4:** The interactive amino acid residues decomposition analysis of α-amylase with compound 7d and acarbose. The binding energy (kJ/mol) contribution of Asp300, Phe256, Ile235, and Trp59 in α-amylase-compound 7d complex estimated from 5000 frames (50 ns) of MD simulation.

¹H NMR of *N′*-(1-(4-(1,3-dioxoisoindolin-2-yl)phenyl)ethylidene)-2-(quinolin-8-yloxy)acetohydrazide 3.
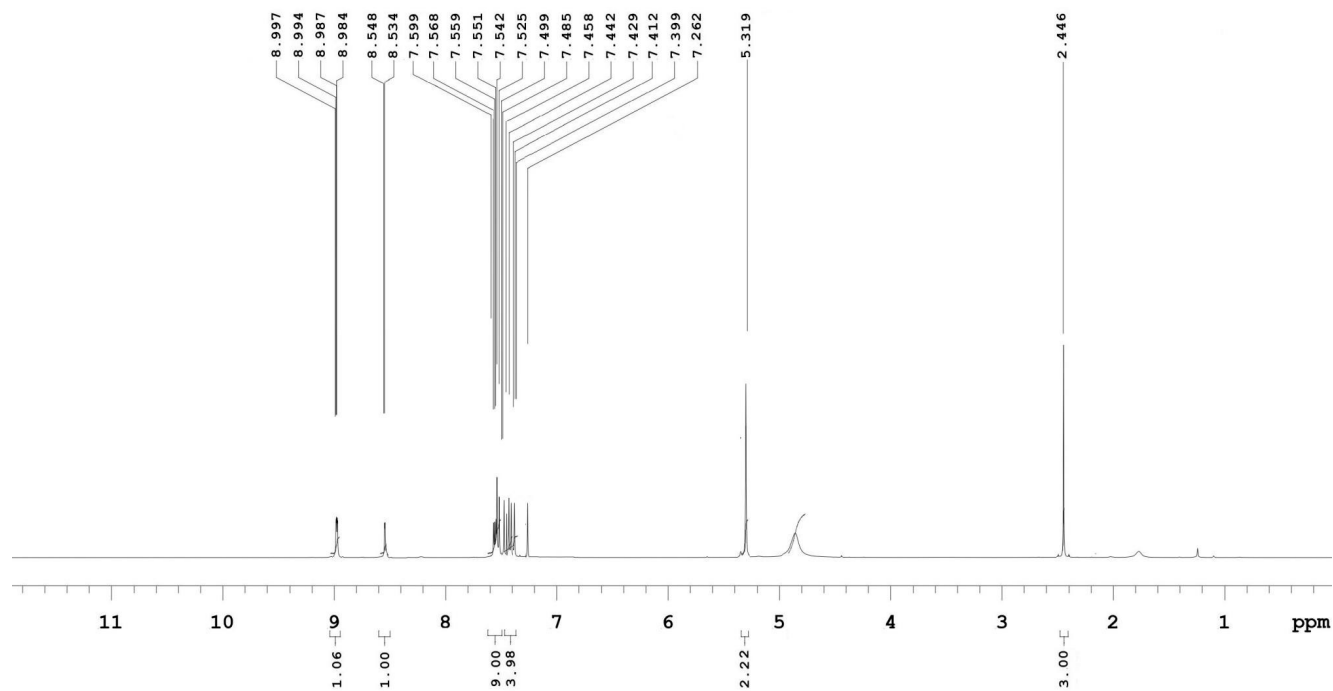
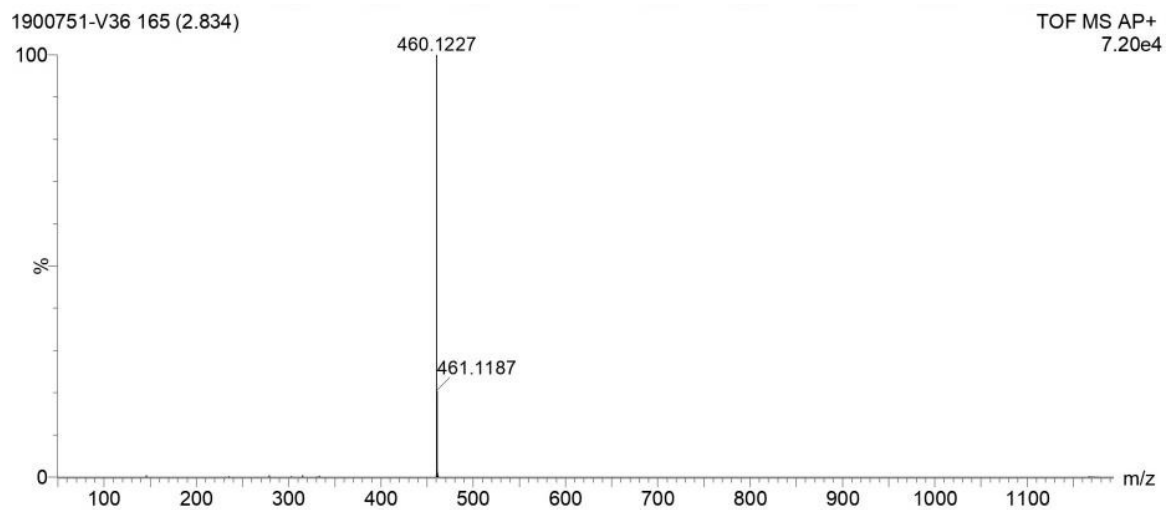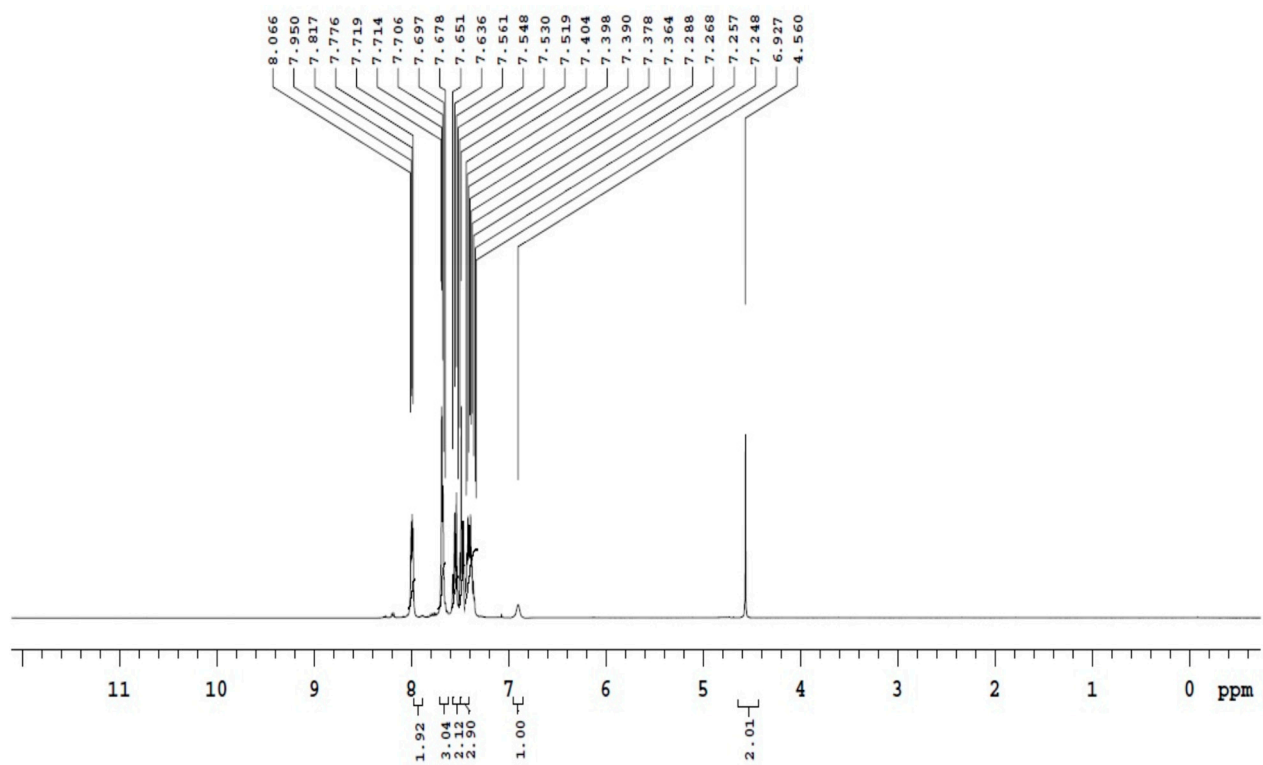**¹³C NMR of *N'*-(1-(4-(1,3-dioxoisoindolin-2-yl)phenyl)ethylidene)-2-(quinolin-8-yloxy)acetohydrazide 3.**
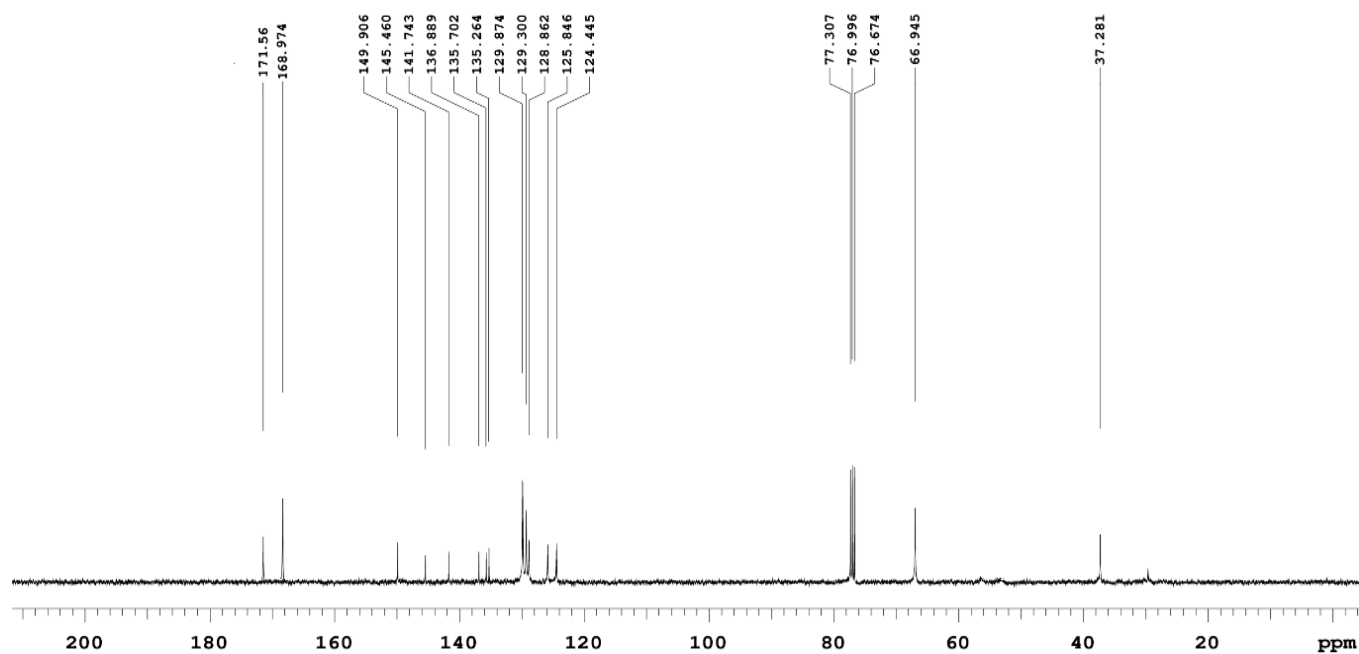
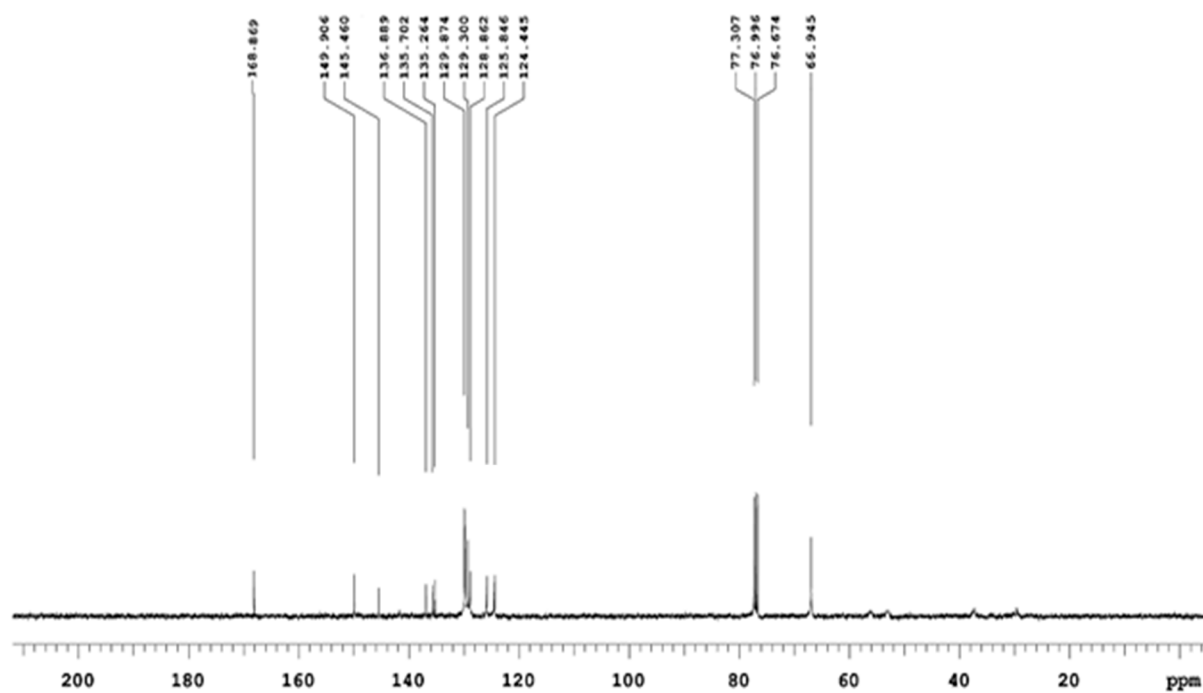**Mass spectrum of *N'*-(1-(4-(1,3-dioxoisoindolin-2-yl)phenyl)ethylidene)-2-(quinolin-8-yloxy)acetohydrazide 3.**

1900751-V36 165 (2.834)   TOF MS AP+
                                                                             7.20e4

460.1227

461.1187

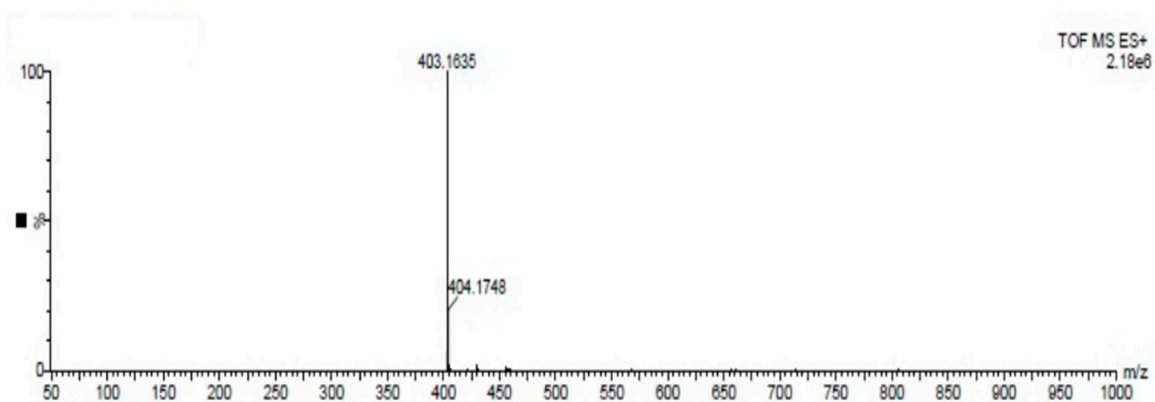**¹H NMR of 5-Amino-3-(4-chlorophenyl)-1-(2-(quinolin-8-yloxy)acetyl)-1*H*-pyrazole-4-carbonitrile 4b.**

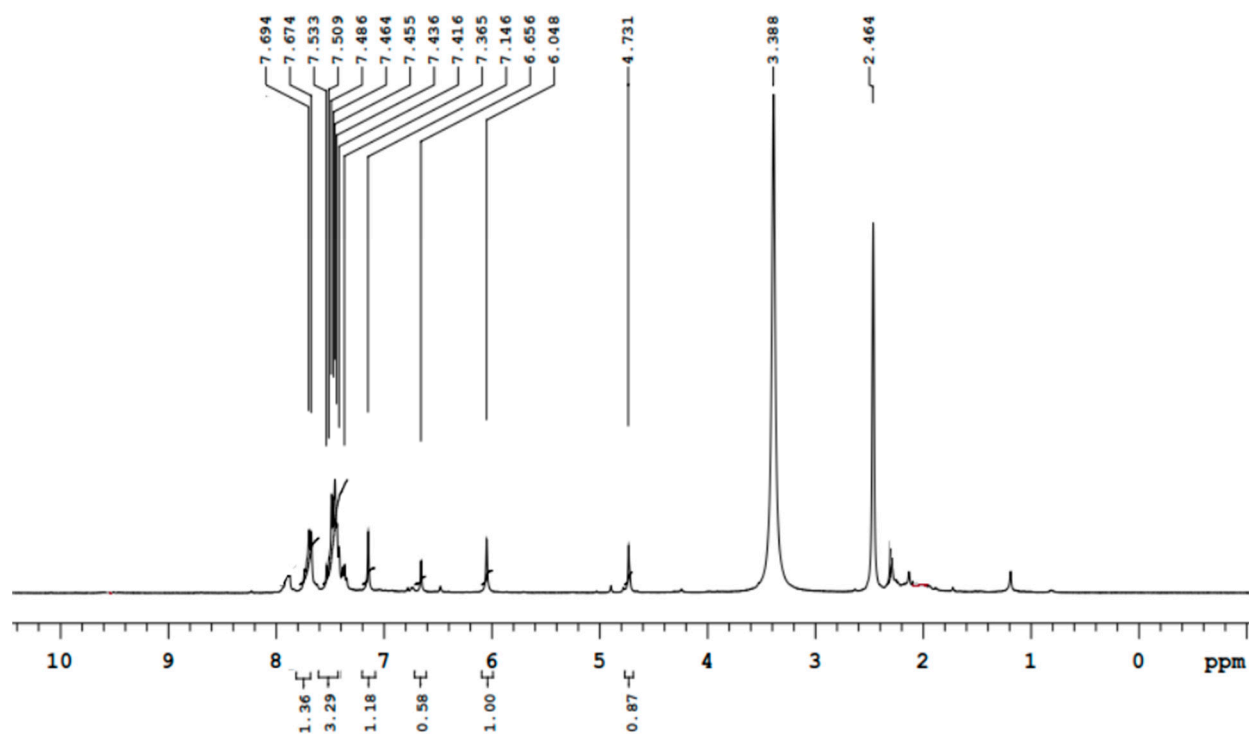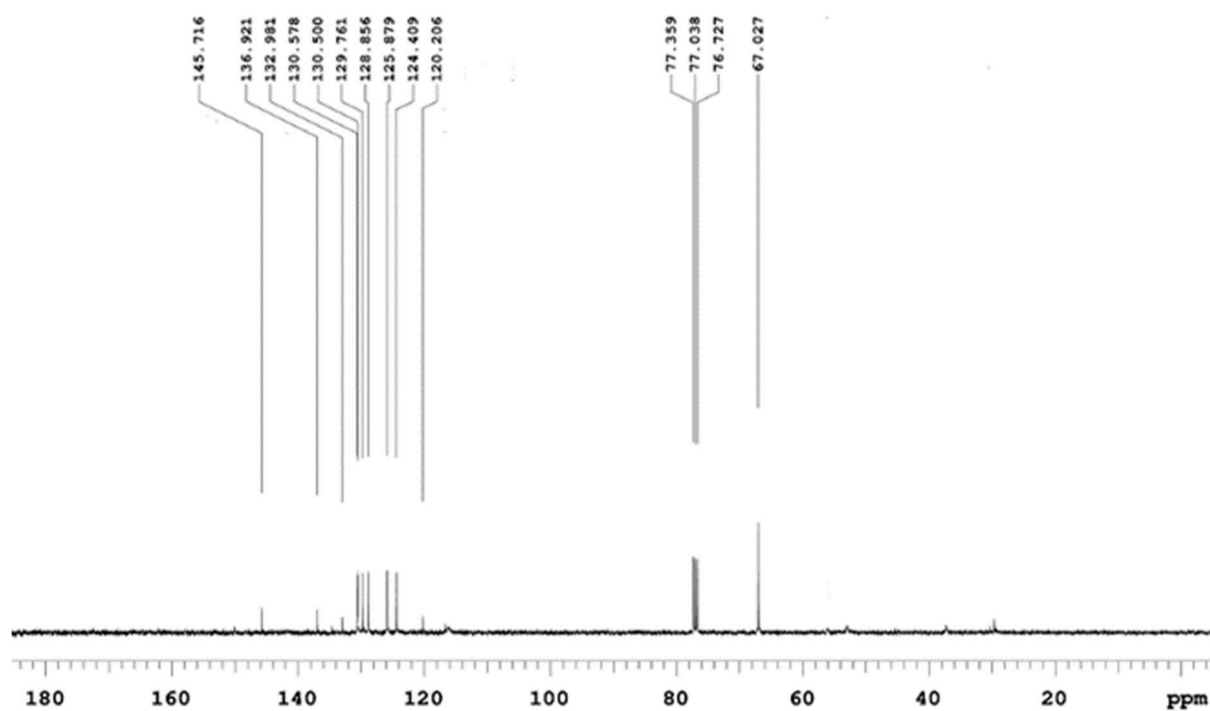**13C NMR of 5-Amino-3-(4-chlorophenyl)-1-(2-(quinolin-8-yloxy)acetyl)-1*H*-pyrazole-4-carbonitrile 4b.**

Mass spectrum of 5-Amino-3-(4-chlorophenyl)-1-(2-(quinolin-8-yloxy)acetyl)-1*H*-pyrazole-4-carbonitrile 4b.
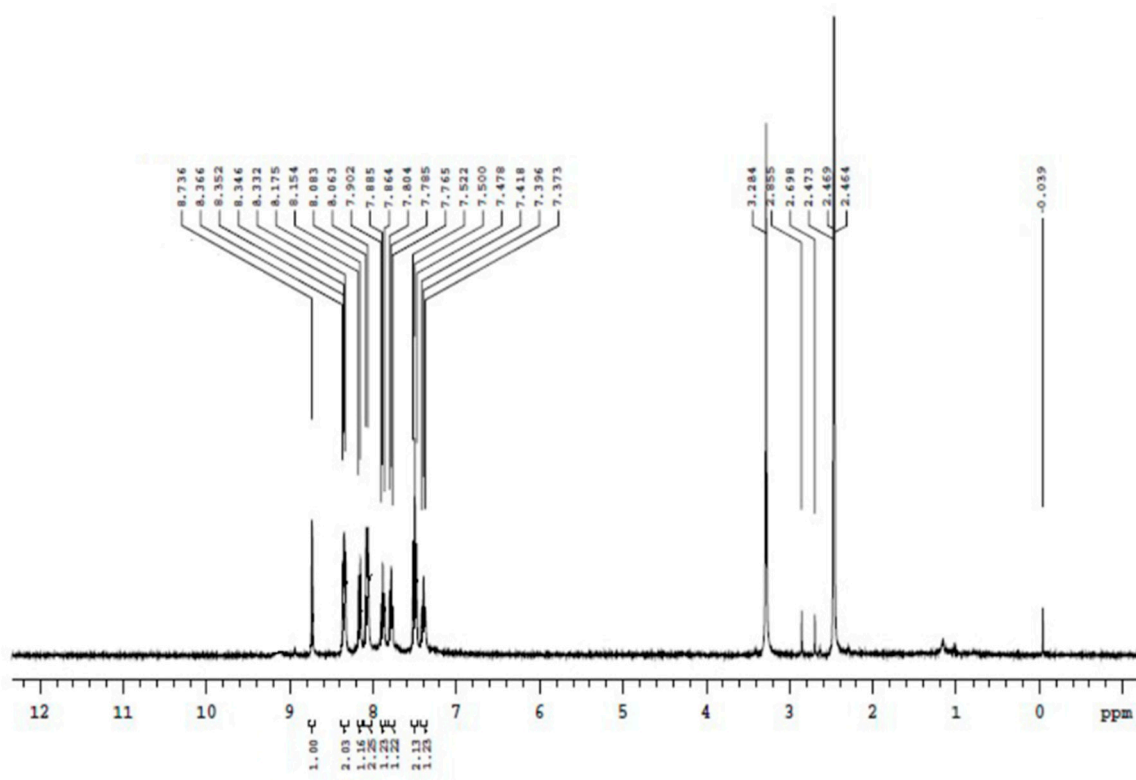
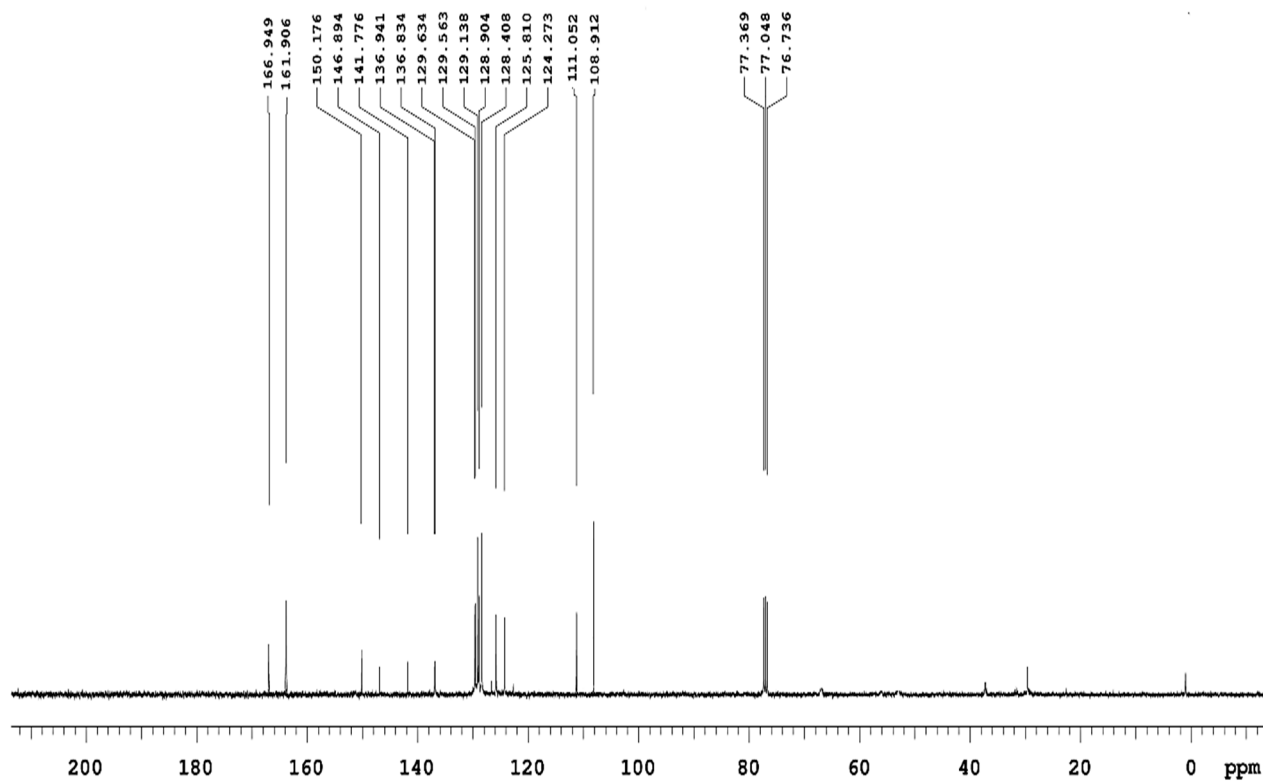**¹H NMR of 5-((quinolin-8-yloxy)methyl)-3*H*-1,2,4-triazole-3-thione 6.**

**13C NMR of 5-((quinolin-8-yloxy)methyl)-3*H*-1,2,4-triazole-3-thione 6.**

145.716, 136.921, 132.981, 130.578, 130.500, 129.761, 128.856, 125.879, 124.409, 120.206, 77.359, 77.038, 76.727, 67.027

¹H NMR of 2-amino-6-(1,3-dioxoisoindolin-2-yl)-4-phenylnicotinonitrile 7a.
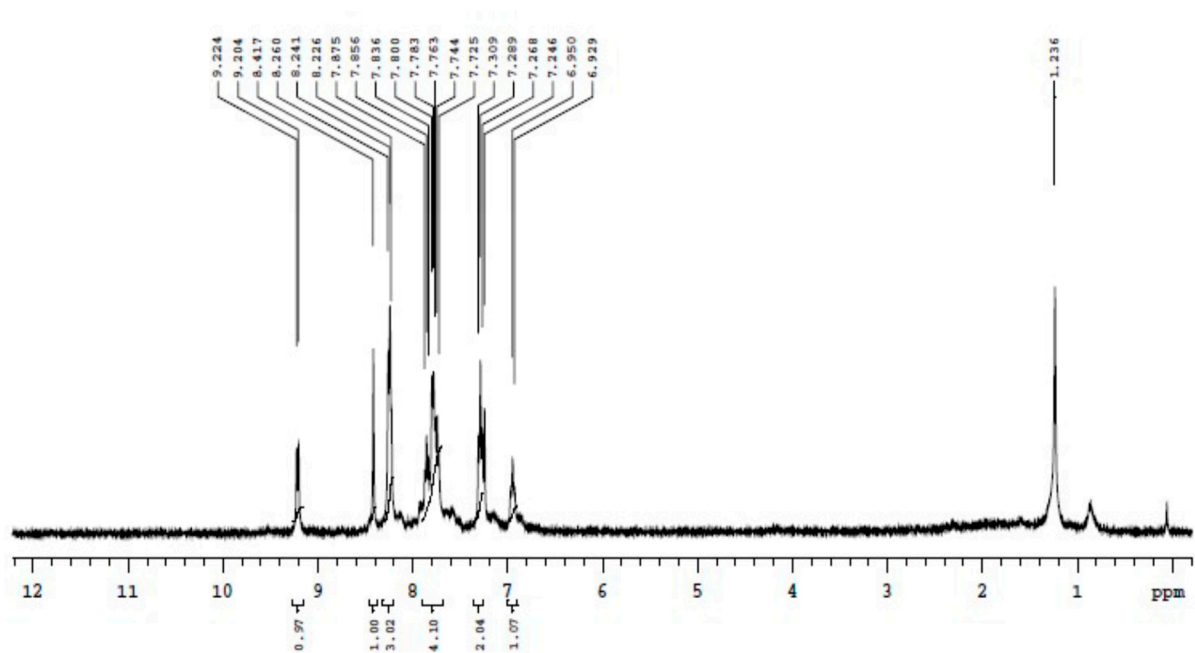
^{13}C NMR of 2-amino-6-(1,3-dioxoisoindolin-2-yl)-4-phenylnicotinonitrile 7a.
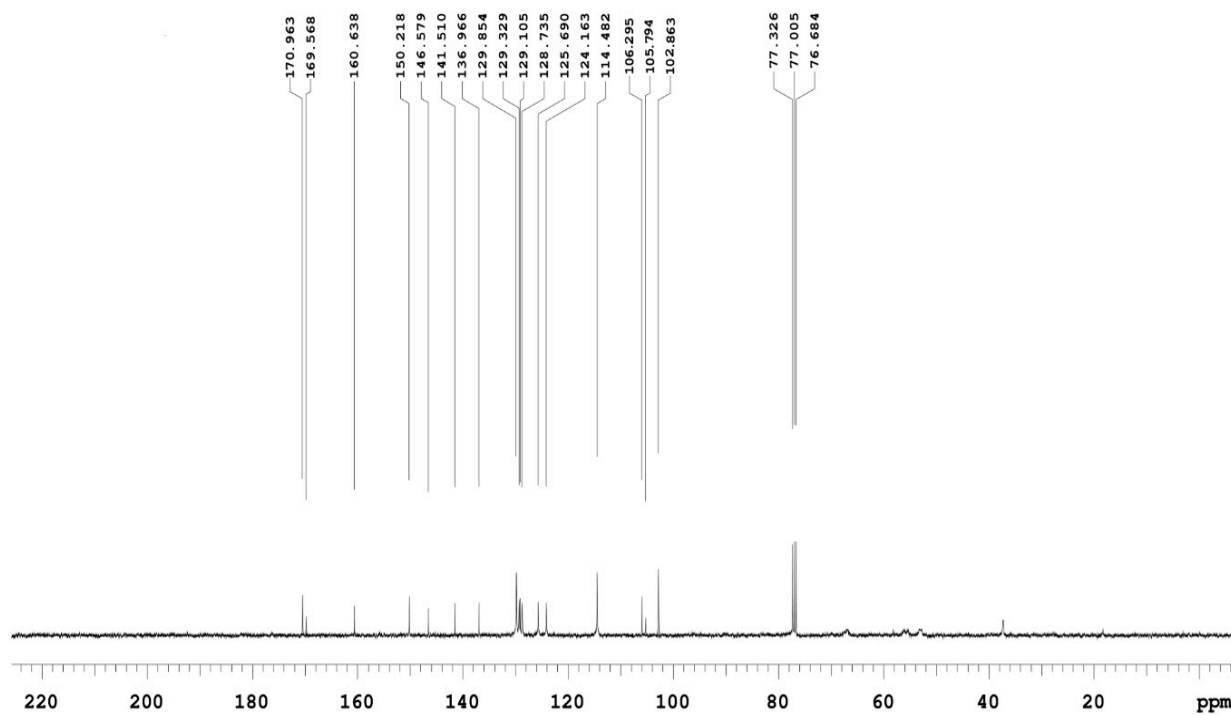
Mass spectrum of 2-amino-6-(1,3-dioxoisoindolin-2-yl)-4-phenylnicotinonitrile 7a.
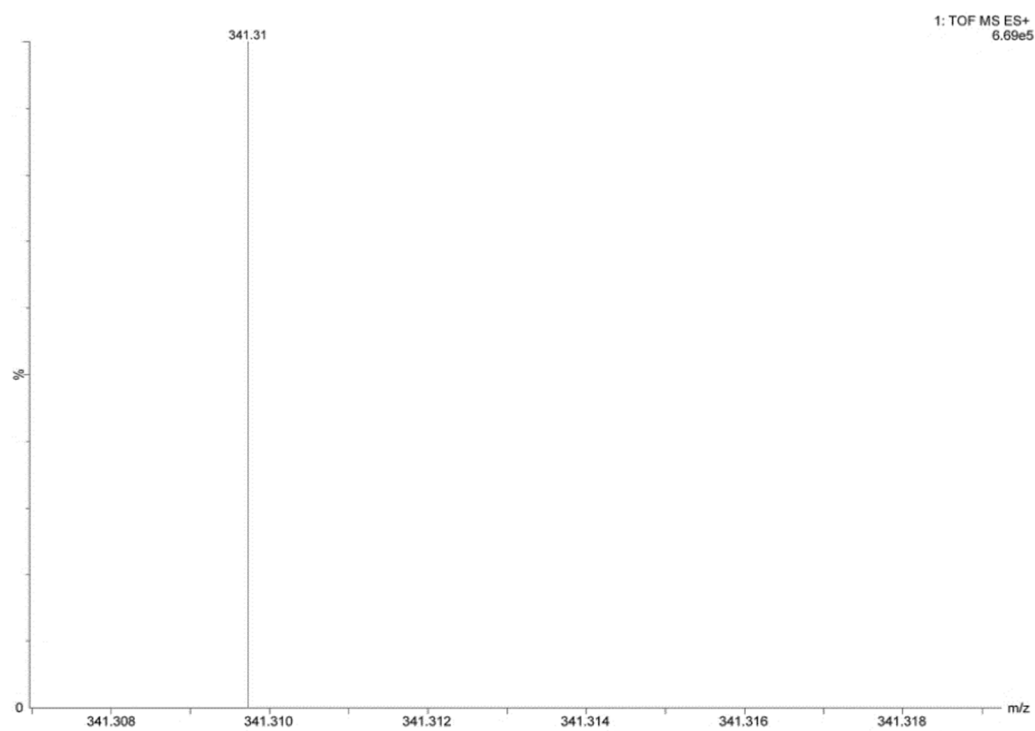
¹H NMR of 6-(1,3-dioxoisoindolin-2-yl)-2-oxo-4-phenyl-1,2-dihydropyridine-3-carbonitrile 8a.
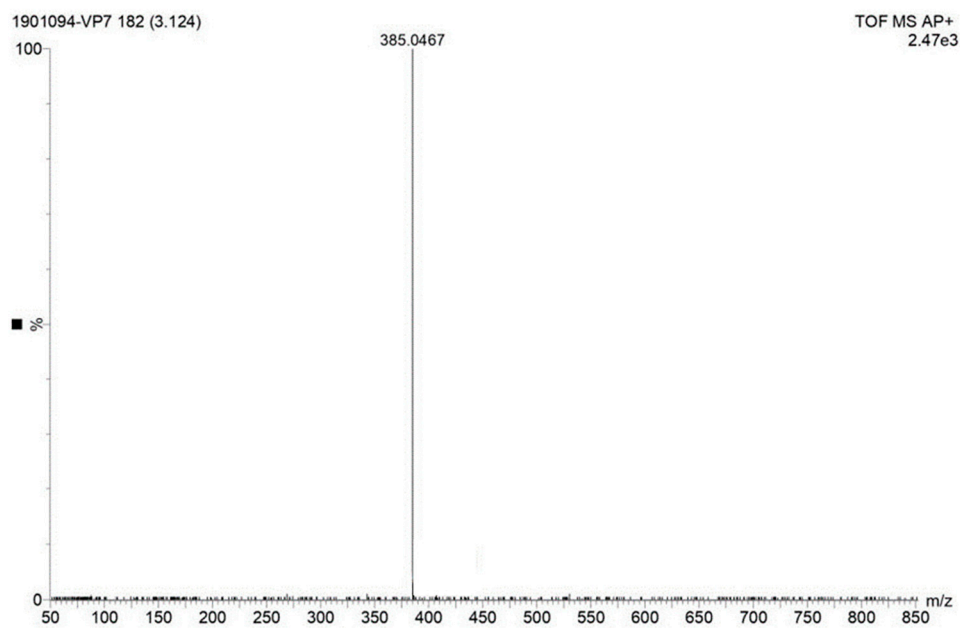
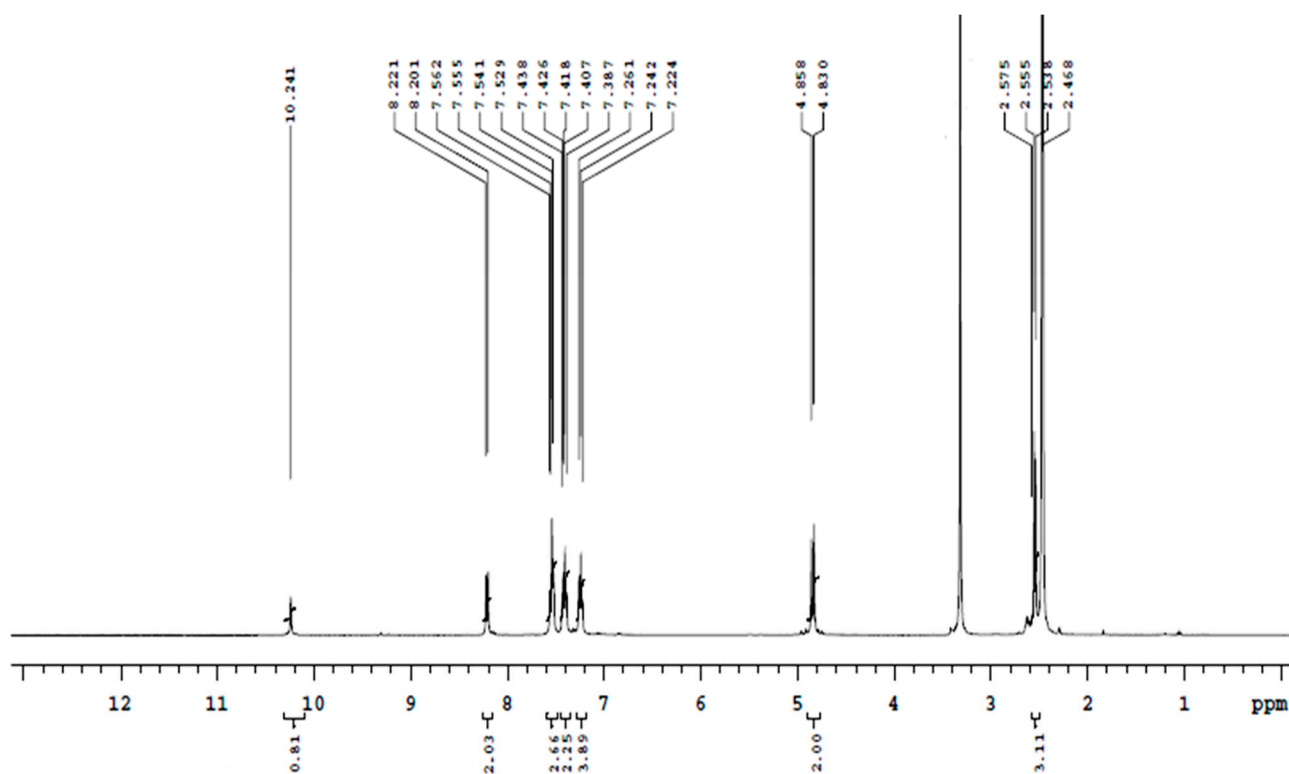**^{13}C NMR of 6-(1,3-dioxoisoindolin-2-yl)-2-oxo-4-phenyl-1,2-dihydropyridine-3-carbonitrile 8a.**

Mass spectrum of 6-(1,3-dioxoisoindolin-2-yl)-2-oxo-4-phenyl-1,2-dihydropyridine-3-carbonitrile 8a.

1901094-VP7 182 (3.124)

TOF MS AP+
2.47e3

385.0467

¹H NMR of 8-(2-((2-(1-(4-(1H-Tetrazol-1-yl)phenyl)ethylidene)hydrazinyl)oxy)-2-oxoethoxy)quinoline 2

¹H NMR of 5-Amino-3-(4-nitrophenyl)-1-(2-(quinolin-8-yloxy)acetyl)-1H-pyrazole-4-carbonitrile 4a
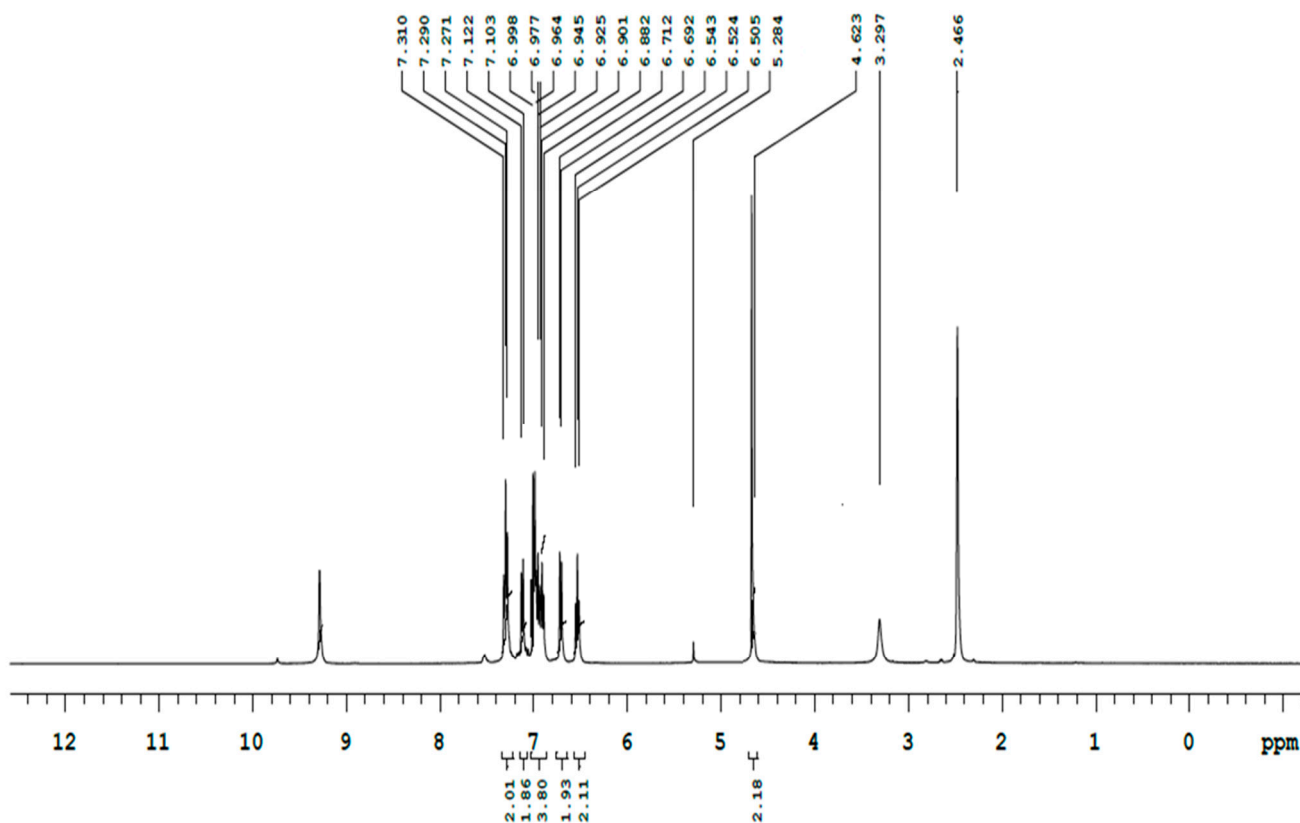
¹H NMR for 6-(1,3-Dioxoisoindolin-2-yl)-4-(4-nitrophenyl)-2-oxo-1,2-dihydropyridine-3-carbonitrile 8b