Supplementary document

The synthesis and investigation of novel 3-benzoylbenzofurans and pyrazole derivatives for anti-HIV activity

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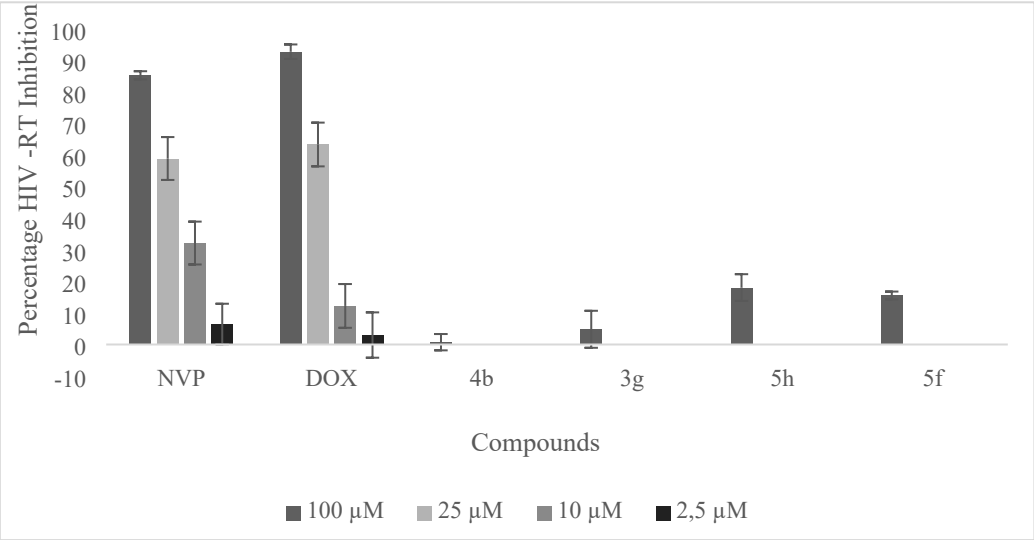


Fig. S1: Inhibition of HIV-1 RT by active compounds. Doxorubicin (DOX) and nevirapine (NVP) were used as controls in four decreasing concentrations to test the validity of the kit. The bars represent the mean ± SEM obtained from three independent experiments.

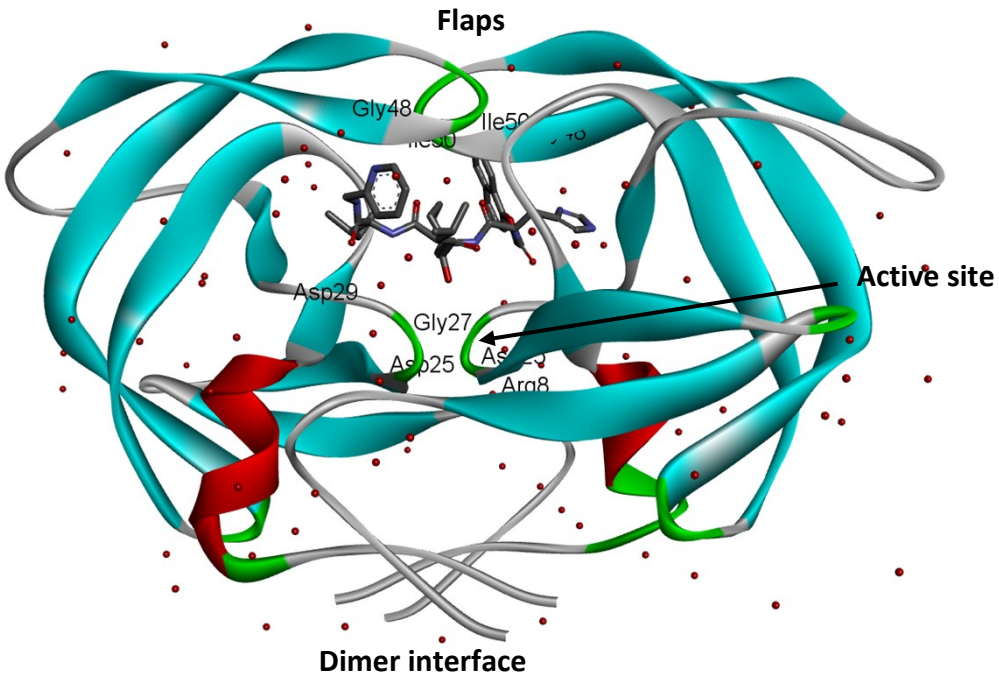


Fig. S2: Crystal structure of HIV-1 PR with an inhibitor. The catalytic site of HIV-1 protease showing a ligand and the amino acid residues that makes up the active site. Created using Discovery Studio 2024.

Table S1: Analysis of drug-likeness of 3-benzoylbenzofurans and pyrazole derivatives according to the Lipinski and Pfizer rule.

Compound	MW (g/mol)	MLogP	nHA	nHD	TPSA Å²	Lipinski rule	Pfizer rule	PAINS alerts
4b	340.37	1.75	5	0	57.90	Yes	No	0
5b	354.40	1.78	5	2	76.60	Yes	Yes	0
4d	411.25	2.94	4	0	48.67	Yes	No	0
5d	425.28	2.96	4	2	67.37	Yes	No	0
3f	286.25	1.76	5	1	59.67	Yes	No	0
5f	300.28	1.78	5	3	78.37	Yes	Yes	0
3g	328.32	0.74	6	1	78.13	Yes	Yes	0
5g	342.35	0.79	6	3	96.83	Yes	Yes	0
3h	298.29	1.05	5	1	68.90	Yes	No	0
5h	312.32	1.08	5	3	87.60	Yes	Yes	0
Saquenavir	670.84	1.40	7	5	166.75	No	Yes	0
Lenacapavir	968.30	4.86	12	2	174.70	No	Yes	0

Molecular weight; MW; g/mol, Lipophilicity; MlogP, Number of hydrogen bond acceptors; nHA, Number of hydrogen bond donors; nHD.

1.2 Spectra and analysis of chromatograms

1.2.1 NMR Spectra

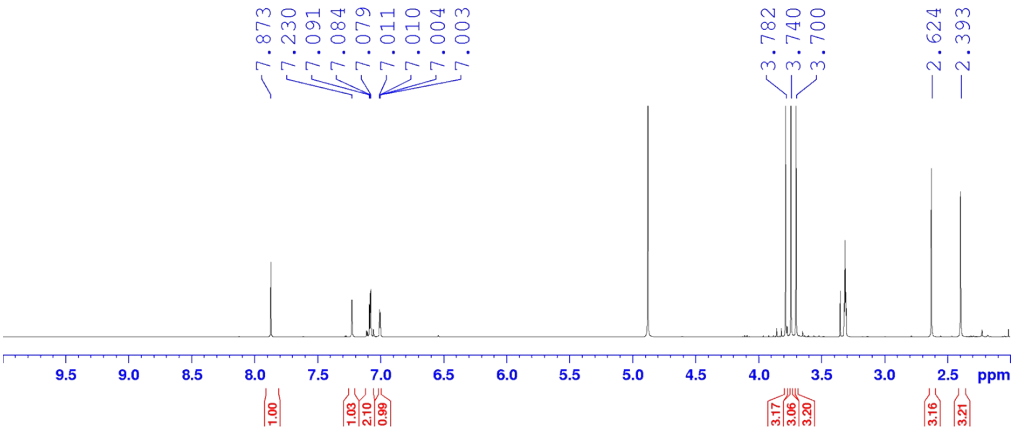


Plate 1a: The ^{1}H NMR (400 MHz, Methanol-d_4) spectrum for (2,5-dimethoxyphenyl)(5-methoxy-4,7-dimethyl-1-benzofuran-3-yl)methanone (4a).

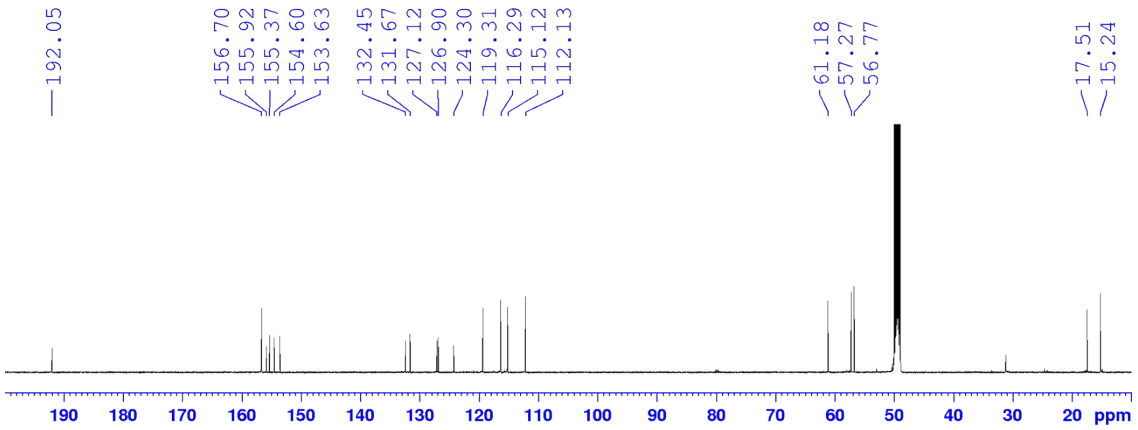


Plate 1b: The ^{13}C NMR (125 MHz, Methanol-d_4) spectrum for (2,5-dimethoxyphenyl)(5-methoxy-4,7-dimethyl-1-benzofuran-3-yl)methanone (4a).

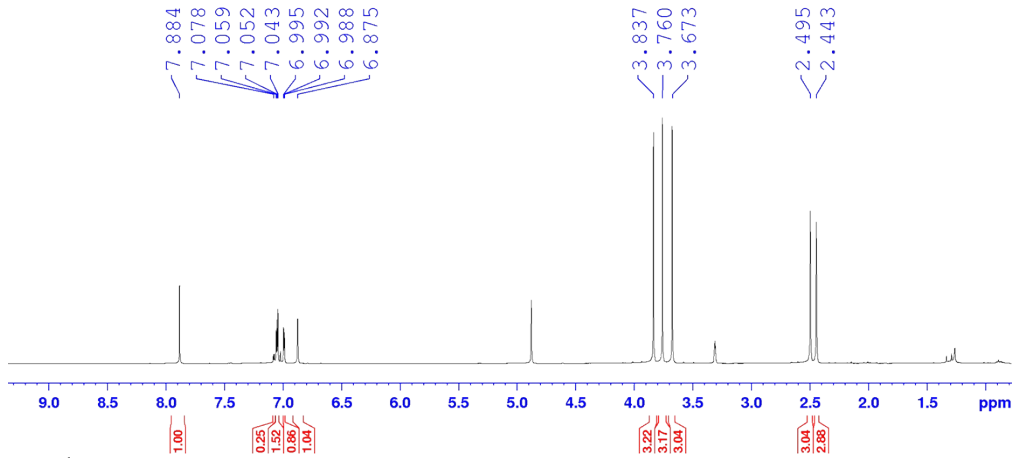


Plate 2a: The ^{1}H NMR (400 MHz, Methanol-d_4) spectrum of (2,5-dimethoxyphenyl)(5-methoxy-4,6-dimethyl-1-benzofuran-3-yl)methanone (4b).

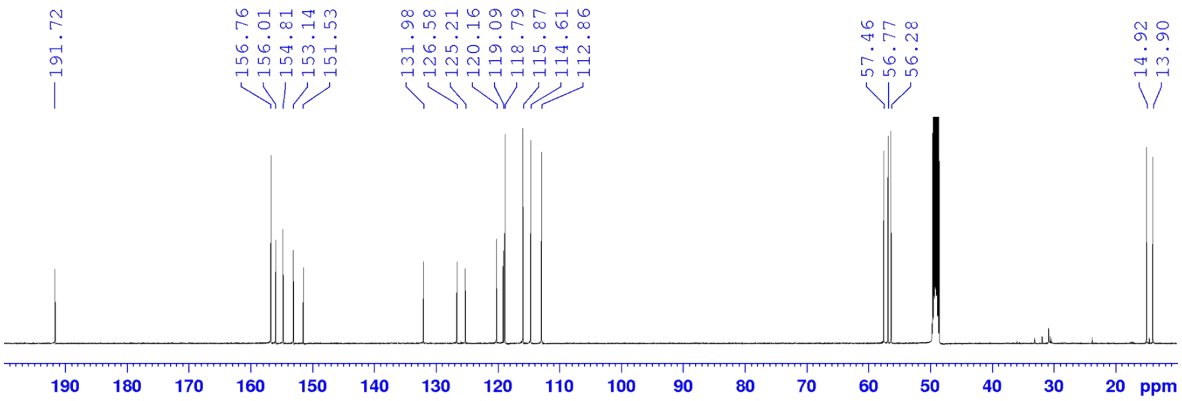


Plate 2b: The ^{13}C NMR (125 MHz, Methanol-d_4) spectrum of (2,5-dimethoxyphenyl)(5-methoxy-4,6-dimethyl-1-benzofuran-3-yl)methanone (4b).

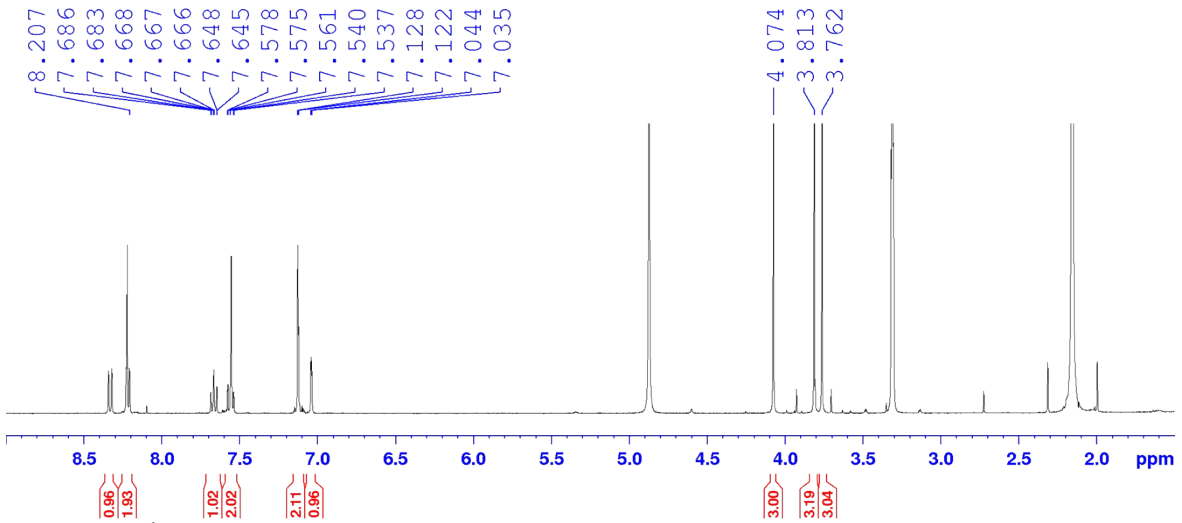


Plate 3a: The ^{1}H NMR (400 MHz, Methanol-d_4) spectrum of (2,5-dimethoxyphenyl)(5-methoxynaphtho[1,2-*b*]furan-3-yl)methanone (4c).

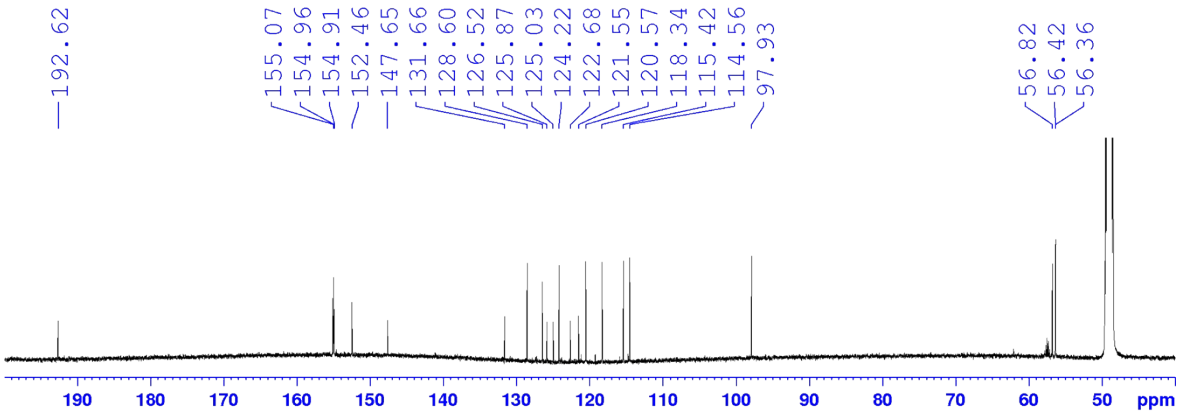


Plate 3b: The ^{13}C NMR (125 MHz, Methanol-d_4) spectrum of (2,5-dimethoxyphenyl)(5-methoxynaphtho[1,2-*b*]furan-3-yl)methanone (4c).

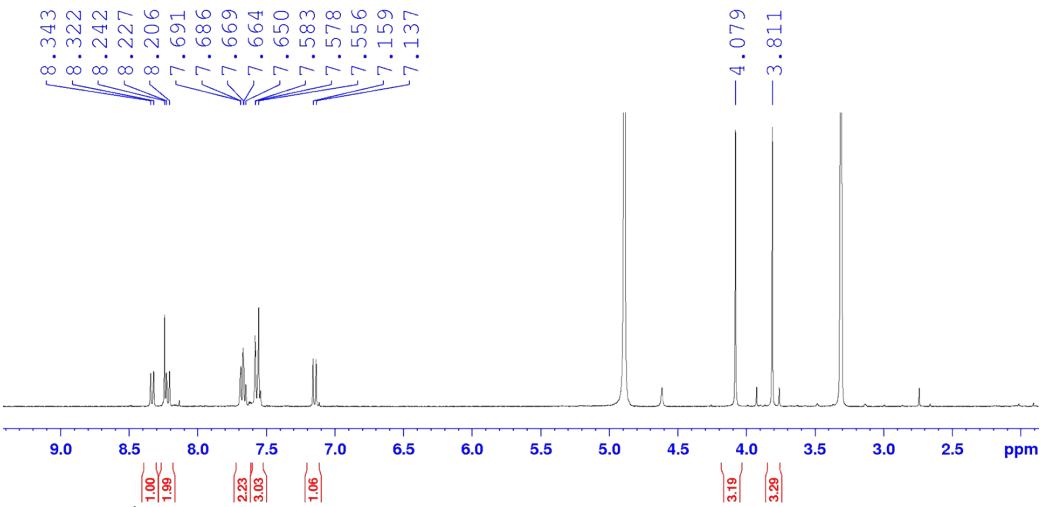


Plate 4a: The ^{1}H NMR (400 MHz, Methanol-d_4) spectrum for (5-bromo-2-methoxyphenyl)(5-methoxynaphtho[1,2-*b*]furan-3-yl)methanone (4d).

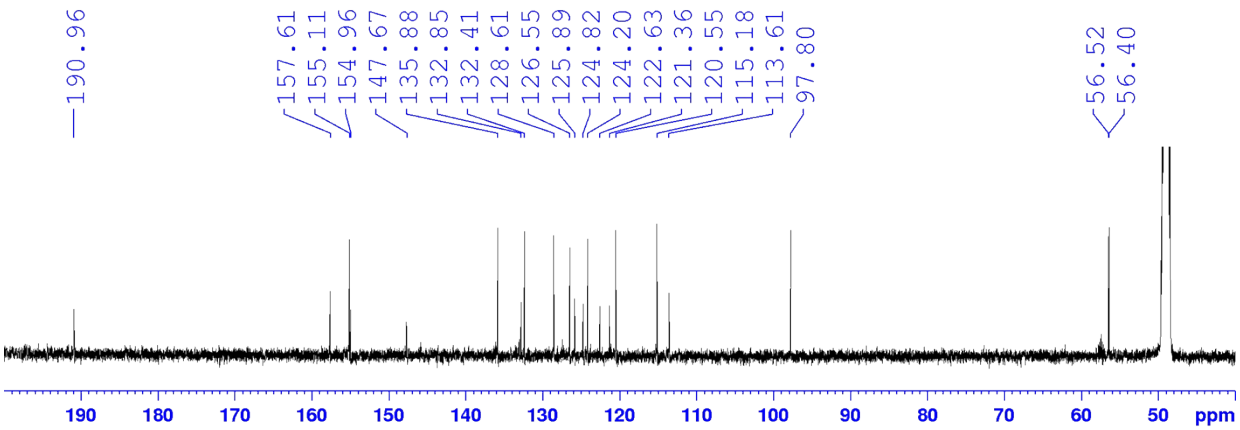


Plate 4b: The ^{13}C NMR (125 MHz, Methanol-d_4) spectrum for (5-bromo-2-methoxyphenyl)(5-methoxynaphtho[1,2-*b*]furan-3-yl)methanone (4d).

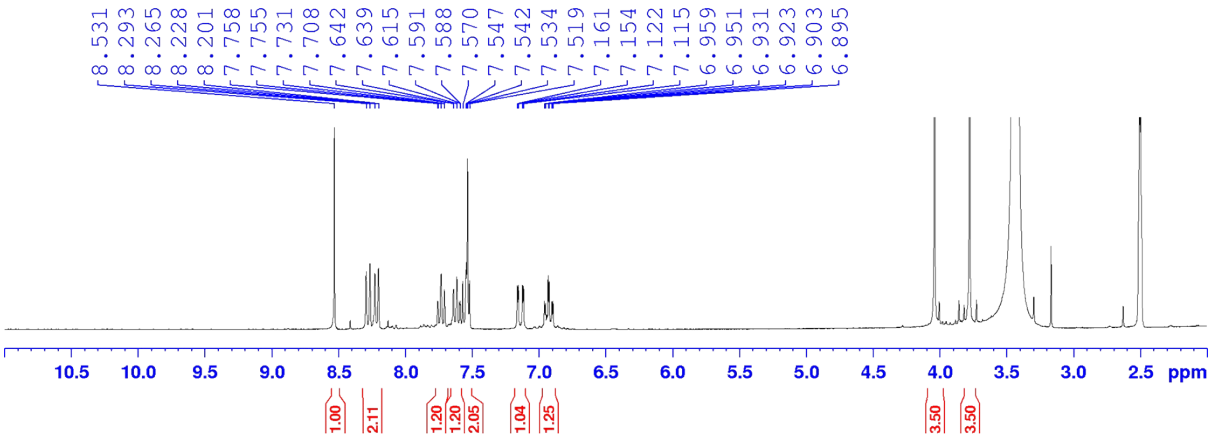


Plate 5a: The ^{1}H NMR (300 MHz, Methanol-d_4) spectrum for (4-fluoro-2-methoxyphenyl)(5-methoxynaphtho[1,2-*b*]furan-3-yl)methanone (4e).

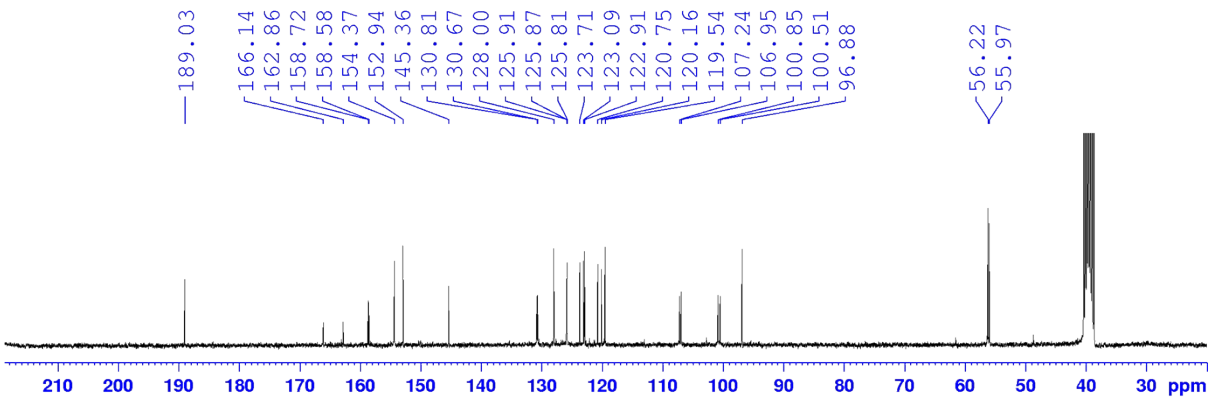


Plate 5b: The ^{13}C NMR (75 MHz, Methanol-d_4) spectrum for (4-fluoro-2-methoxyphenyl)(5-methoxynaphtho[1,2-b]furan-3-yl)methanone (4e).

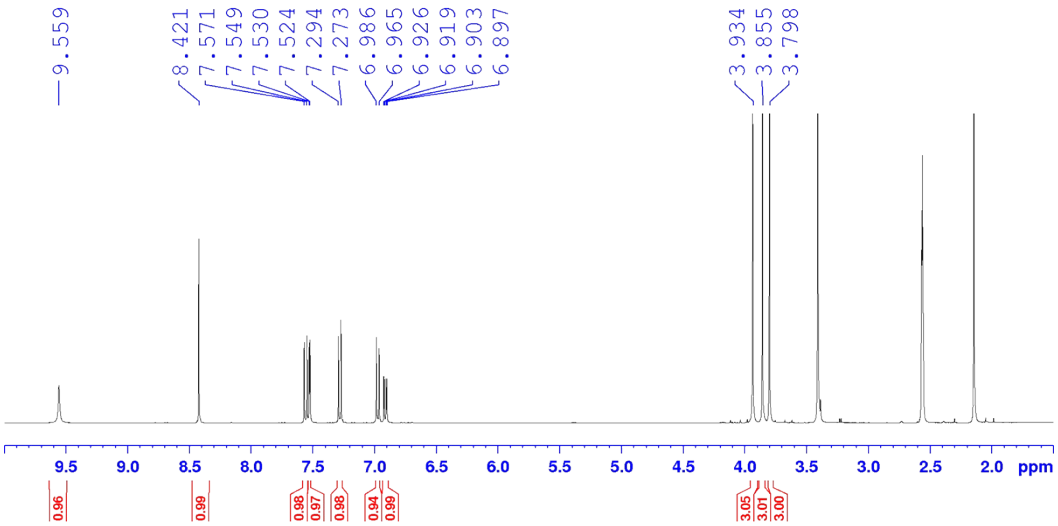


Plate 6a: The ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of (5-hydroxy-1-benzofuran-3-yl)(2,3,4-trimethoxyphenyl)methanone (3g).

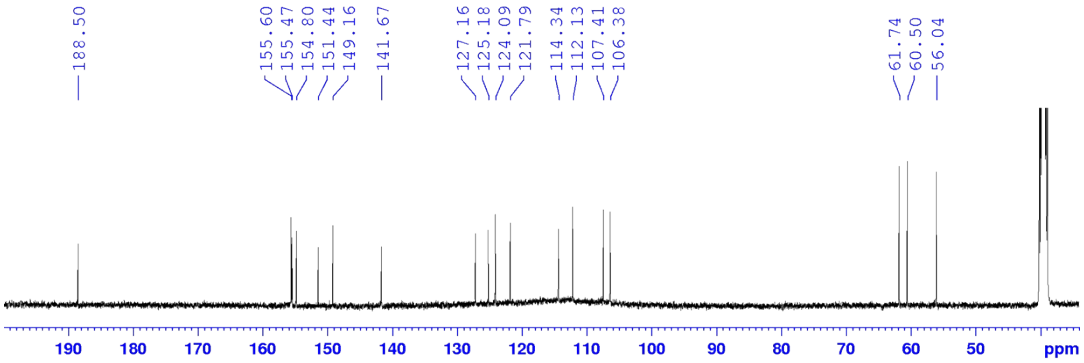


Plate 6b: The ^{13}C NMR (100 MHz, DMSO-d_6) spectrum of (5-hydroxy-1-benzofuran-3-yl)(2,3,4-trimethoxyphenyl)methanone (3g).

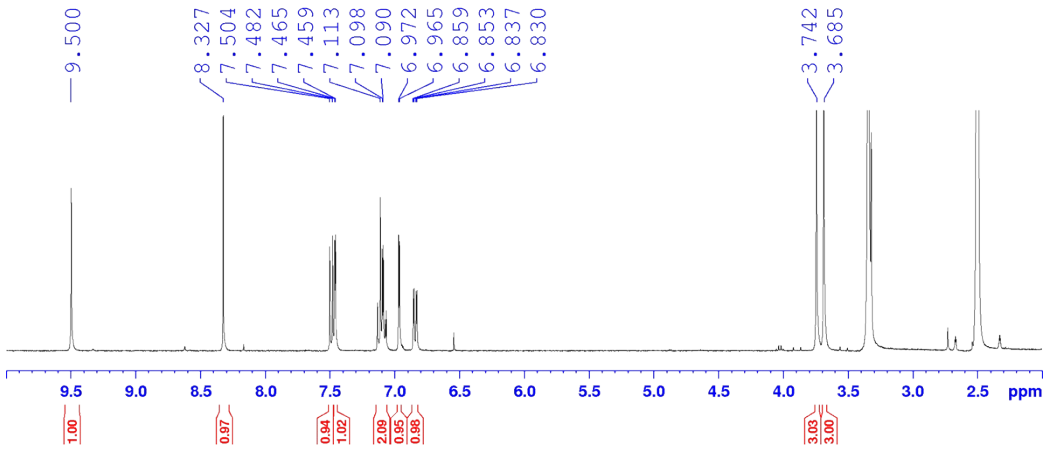


Plate 7a: The ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of (2,5-dimethoxyphenyl)(5-hydroxy-1-benzofuran-3-yl)methanone (3h).

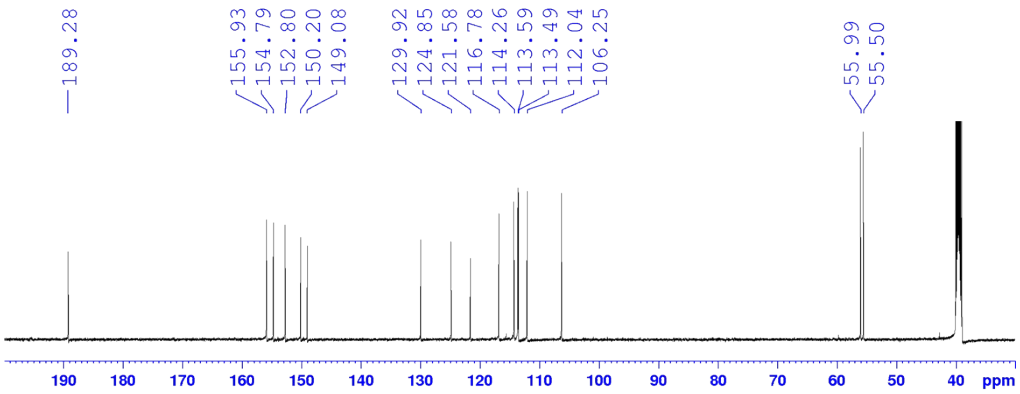


Plate 7b: The ^{13}C NMR (125 MHz, DMSO-d_6) spectrum of (2,5-dimethoxyphenyl)(5-hydroxy-1-benzofuran-3-yl)methanone (3h).

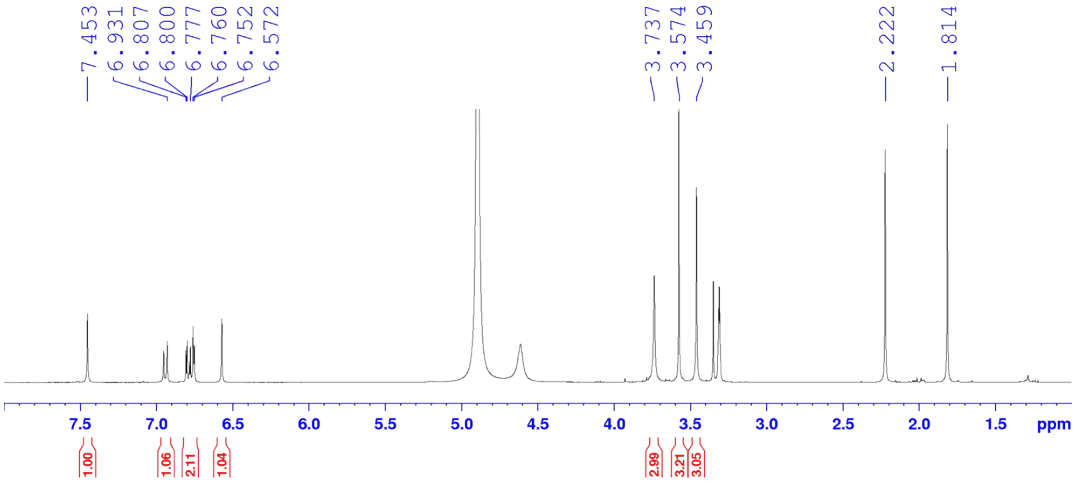


Plate 8a: The ^{1}H NMR (400 MHz, Methanol-d_4) spectrum of 2-[3-(2,5-dimethoxyphenyl)-1*H*-pyrazol-4-yl]-4-methoxy-3,6-dimethylphenol (5a).

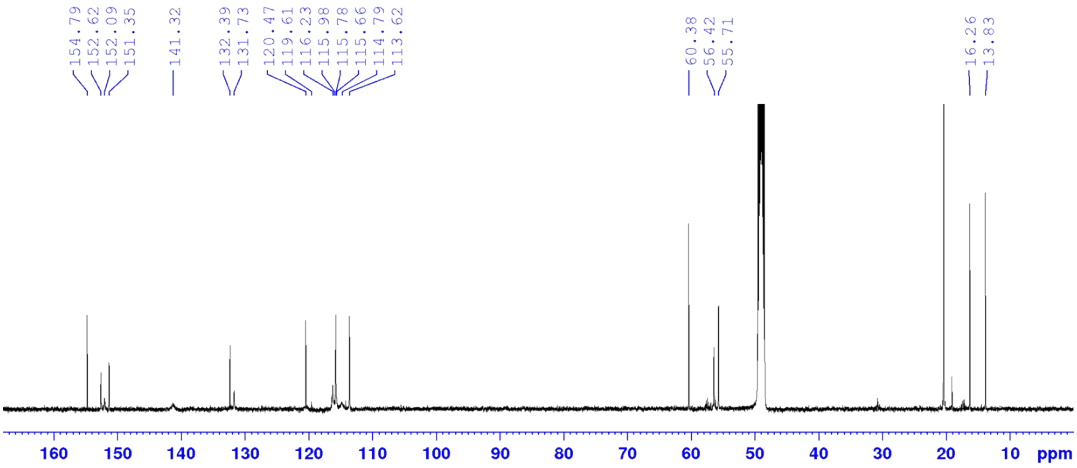


Plate 8b: The ^{13}C NMR (125 MHz, Methanol-d_4) spectrum of 2-[3-(2,5-dimethoxyphenyl)-1*H*-pyrazol-4-yl]-4-methoxy-3,6-dimethylphenol (5a).

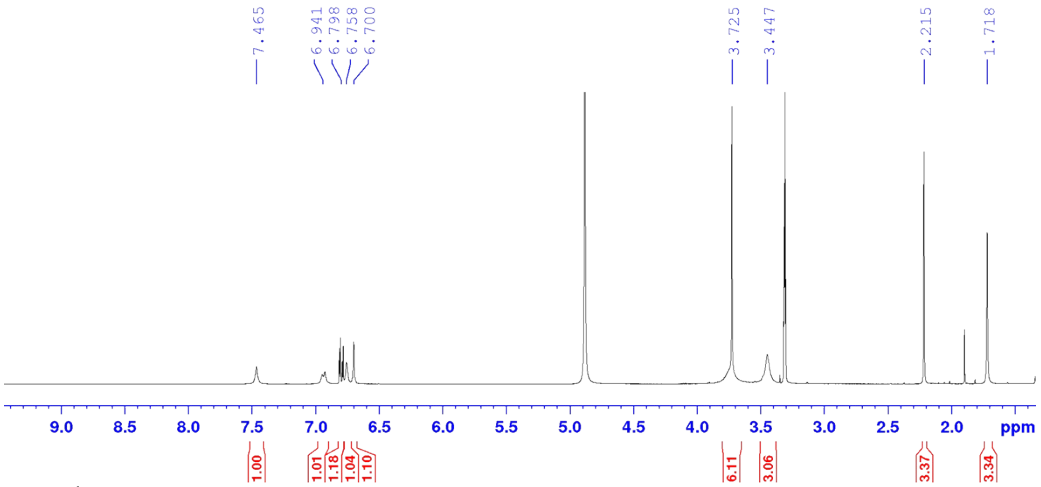


Plate 9a: The ^{1}H NMR (400 MHz, Methanol-d_4) spectrum for 2-[3-(2,5-dimethoxyphenyl)-1H-pyrazol-4-yl]-4-methoxy-3,5-dimethylphenol (5b).

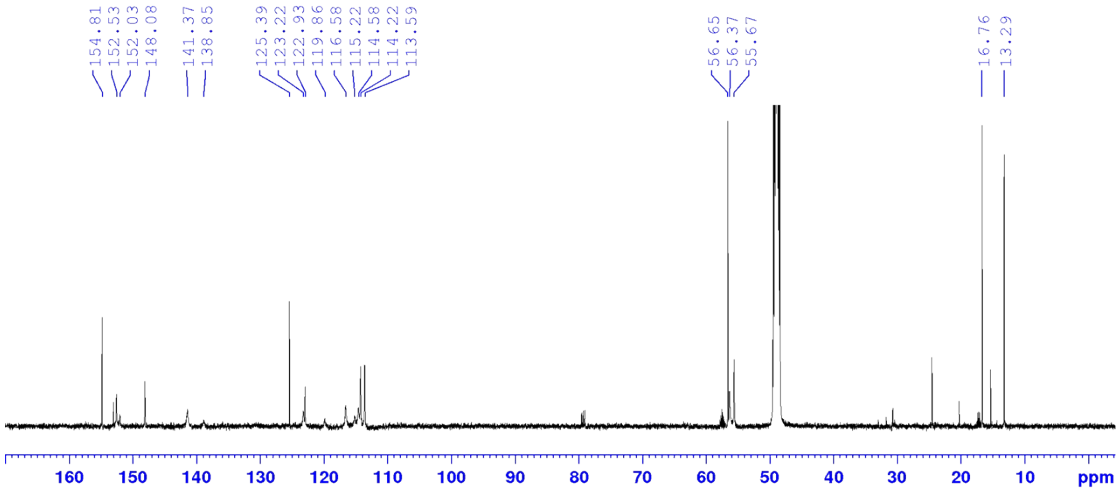


Plate 9b: The ^{13}C NMR (125 MHz, Methanol-d_4) spectrum of 2-[3-(2,5-dimethoxyphenyl)-1H-pyrazol-4-yl]-4-methoxy-3,5-dimethylphenol (5b).

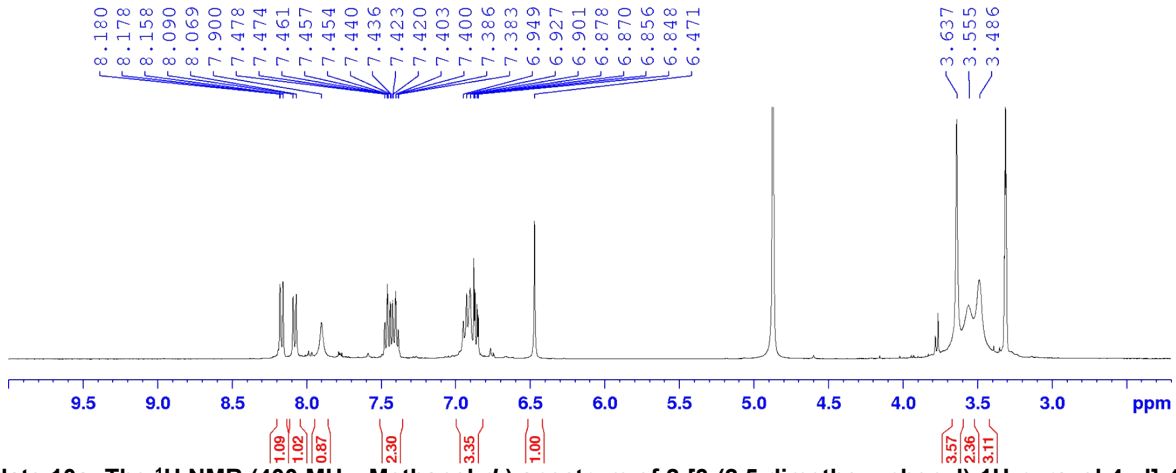


Plate 10a: The ^{1}H NMR (400 MHz, Methanol-d_4) spectrum of 2-[3-(2,5-dimethoxyphenyl)-1H-pyrazol-4-yl]-4-methoxynaphthalen-1-ol (5c).

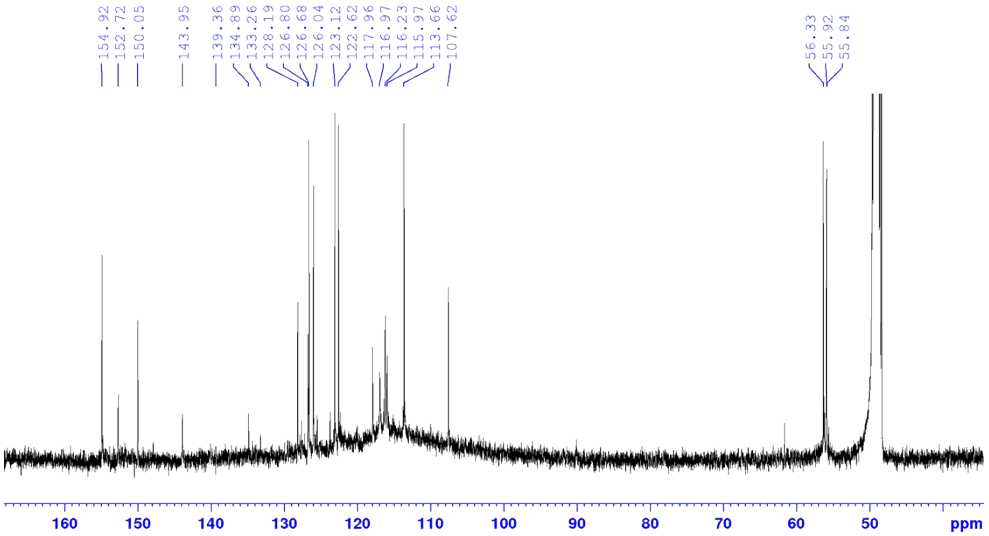


Plate 10b: The ^{13}C NMR (100 MHz, Methanol-d_4) spectrum for 2-[3-(2,5-dimethoxyphenyl)-1H-pyrazol-4-yl]-4-methoxynaphthalen-1-ol (5c).

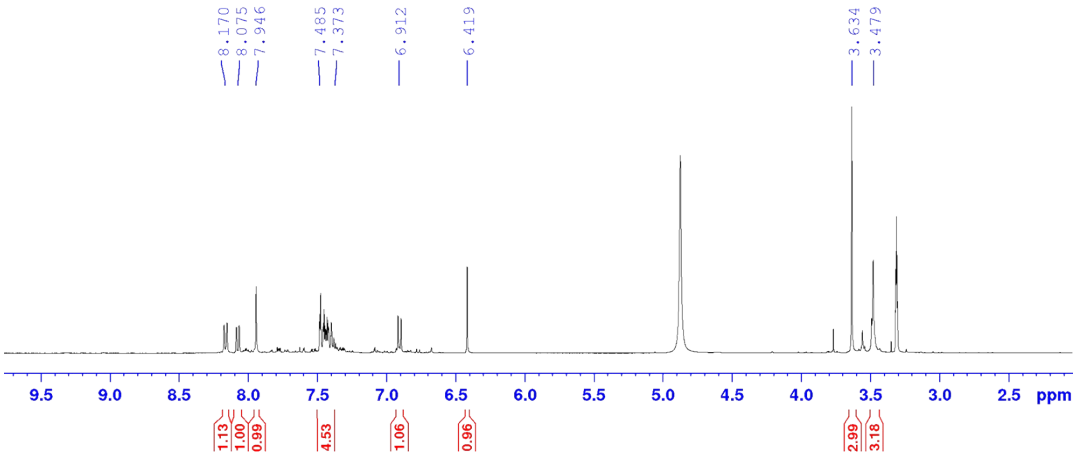


Plate 11a: The ^{1}H NMR (400 MHz, Methanol-d_4) spectrum of 2-[3-(5-bromo-2-methoxyphenyl)-1*H*-pyrazol-4-yl]-4-methoxynaphthalen-1-ol (5d).

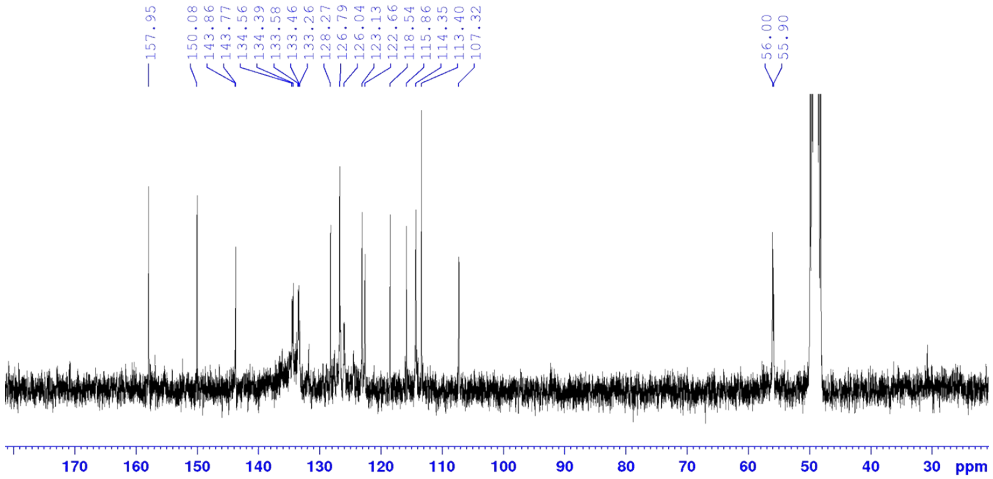


Plate 11b: The ^{13}C NMR (75 MHz, Methanol-d_4) spectrum of 2-[3-(5-bromo-2-methoxyphenyl)-1*H*-pyrazol-4-yl]-4-methoxynaphthalen-1-ol (5d).

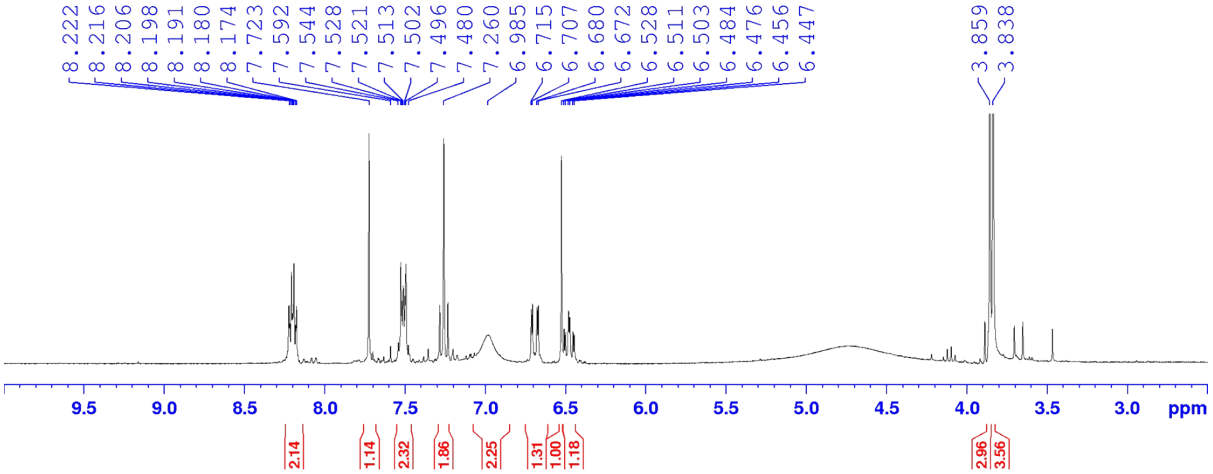


Plate 12a: The ^{1}H NMR (300 MHz, Chloroform-d_1) spectrum of 2-[3-(4-fluoro-2-methoxyphenyl)-1*H*-pyrazol-4-yl]-4-methoxynaphthalen-1-ol (5e).

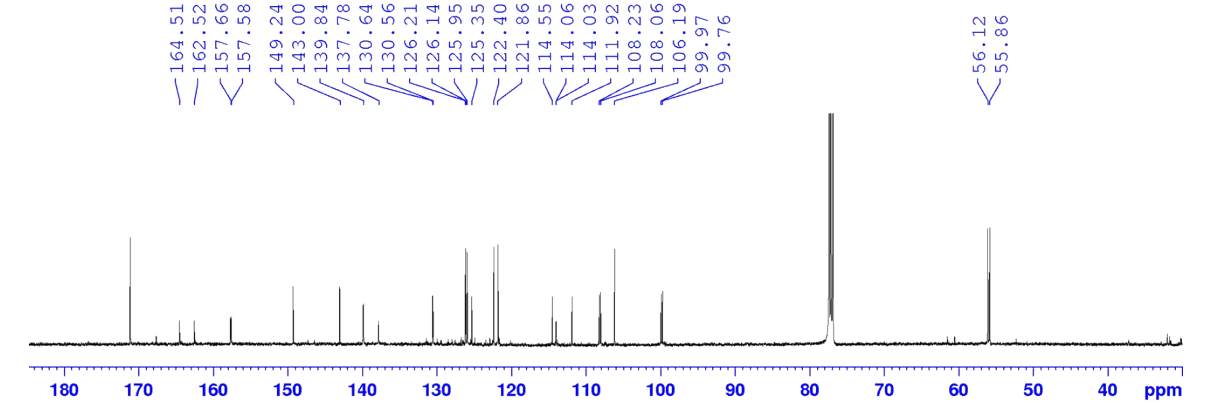


Plate 12b: The ^{13}C NMR (125 MHz, Chloroform-d_1) spectrum of 2-[3-(4-fluoro-2-methoxyphenyl)-1*H*-pyrazol-4-yl]-4-methoxynaphthalen-1-ol (5e).

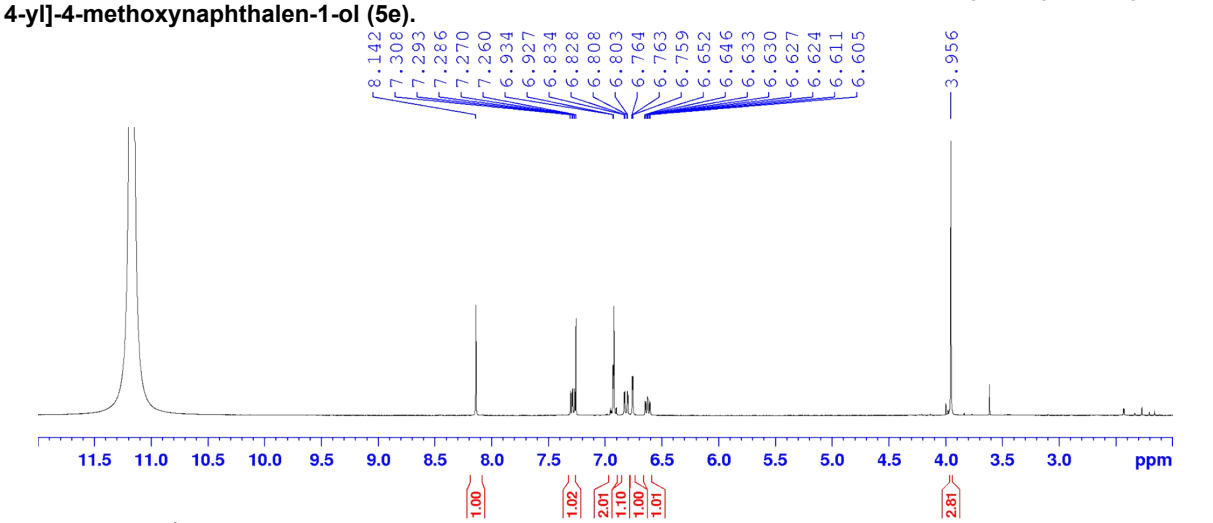


Plate 13a: The ^{1}H NMR (400 MHz, Chloroform-d_1) spectrum for 2-[3-(4-fluoro-2-methoxyphenyl)-1H-pyrazol-4-yl]benzene-1,4-diol (5f).

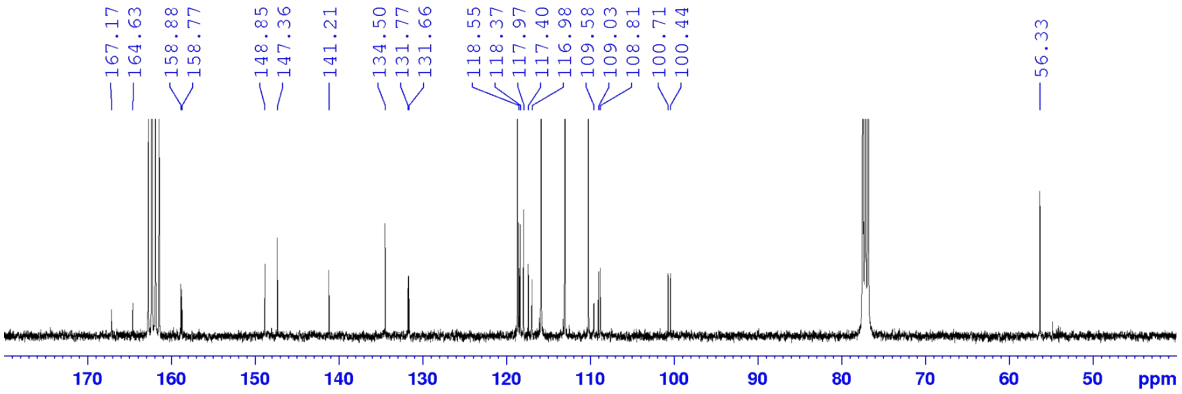


Plate 13b: The ^{13}C NMR (100 MHz, Chloroform-d_1) spectrum for 2-[3-(4-fluoro-2-methoxyphenyl)-1H-pyrazol-4-yl]benzene-1,4-diol (5f).

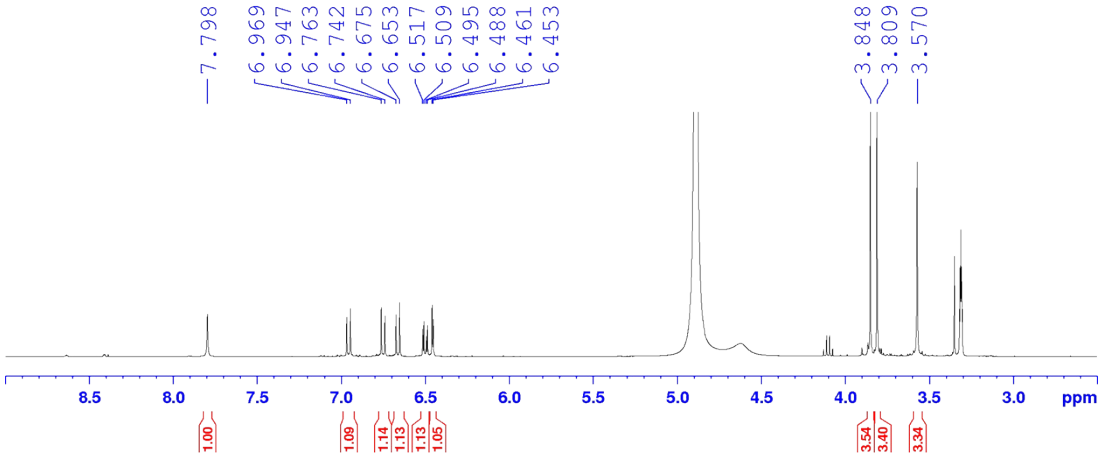


Plate 14a: The ^{1}H NMR (400 MHz, Methanol-d_4) spectrum for 2-[3-(2,3,4-trimethoxyphenyl)-1H-pyrazol-4-yl]benzene-1,4-diol (5g).

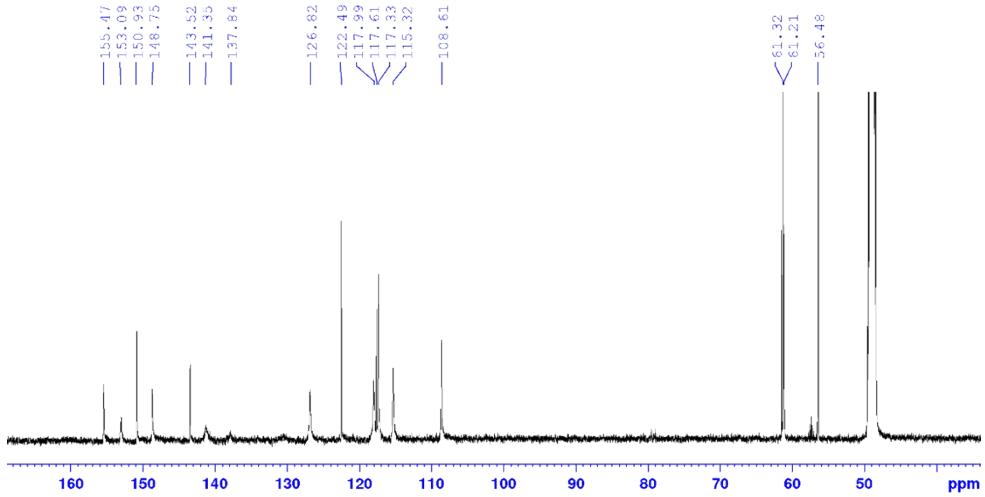


Plate 14b: The ^{13}C NMR (100 MHz, Methanol-d_4) spectrum for 2-[3-(2,3,4-trimethoxyphenyl)-1H-pyrazol-4-yl]benzene-1,4-diol (5g).

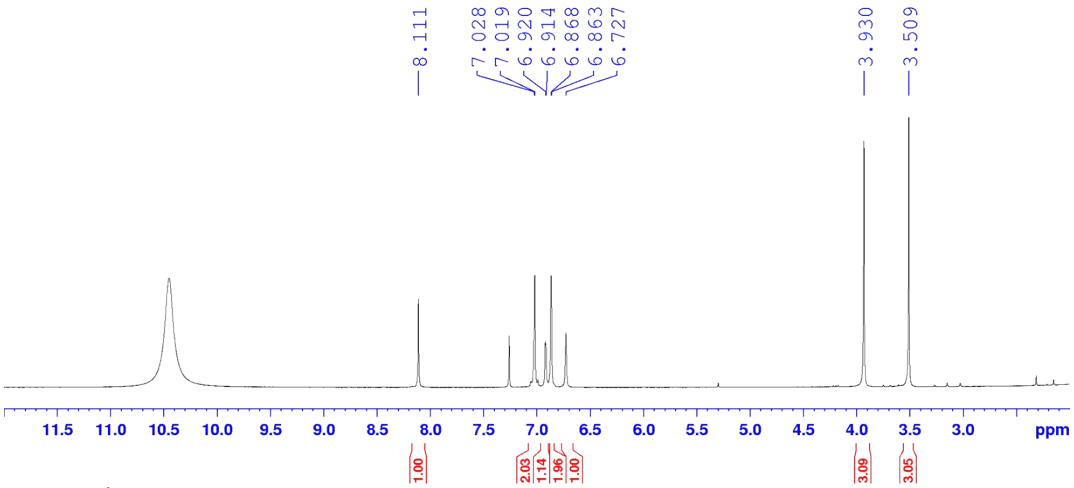


Plate 15a: The ^{1}H NMR (300 MHz, Chloroform-d_1) spectrum for 2-[3-(2,5-dimethoxyphenyl)-1H-pyrazol-4-yl]benzene-1,4-diol (5h).

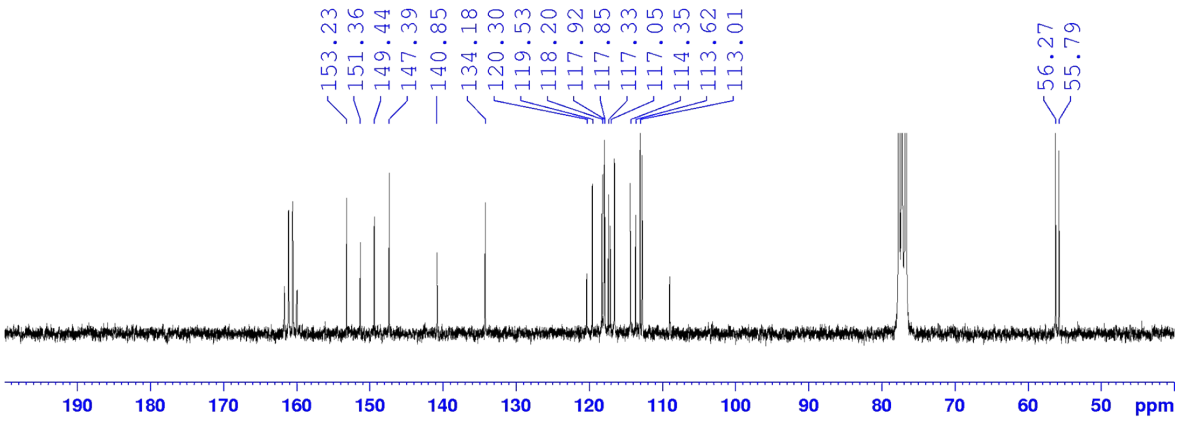
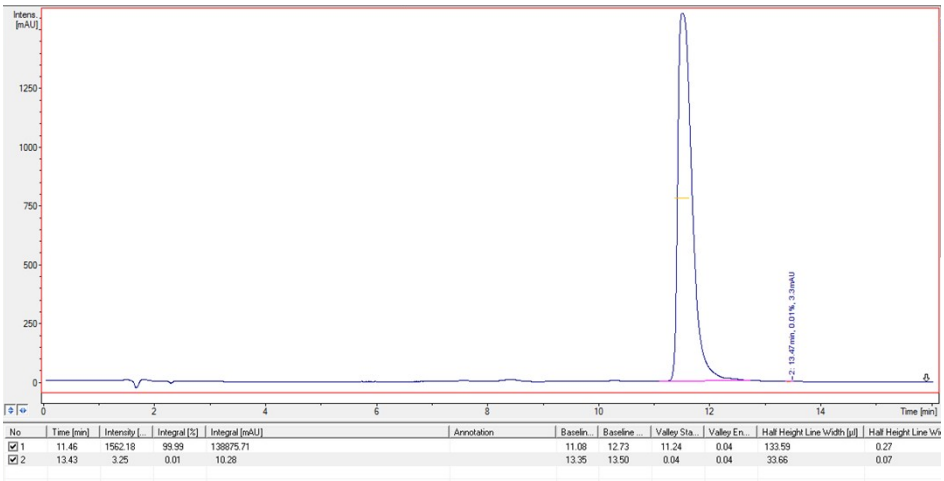


Plate 15b: The ^{13}C NMR (75 MHz, Chloroform-d_1) spectrum for 2-[3-(2,5-dimethoxyphenyl)-1H-pyrazol-4-yl]benzene-1,4-diol (5h).

1.2.2 Chromatograms



No	Time [min]	Intensity [...	Integral [%]	Integral [mAU]	Annotation	Baselin...	Baseline ...	Valley Sta...	Valley En...	Half Height Line Width [µl]	Half Height Line Wi
1	11.46	1562.18	99.99	138875.71		11.08	12.73	11.24	0.04	133.59	0.27
2	13.43	3.25	0.01	10.28		13.35	13.50	0.04	0.04	33.66	0.07

Plate 1c: UV chromatogram of (2,5-dimethoxyphenyl)(5-methoxy-4,7-dimethyl-1-benzofuran-3-yl)methanone (4a) measured at 280 nm.

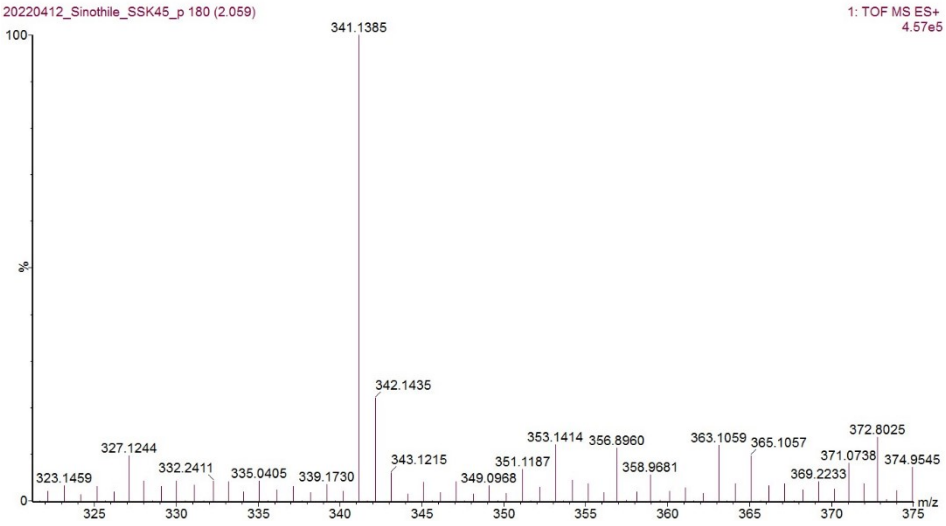


Plate 1d: HR-MS spectrum of (2,5-dimethoxyphenyl)(5-methoxy-4,7-dimethyl-1-benzofuran-3-yl)methanone (4a).

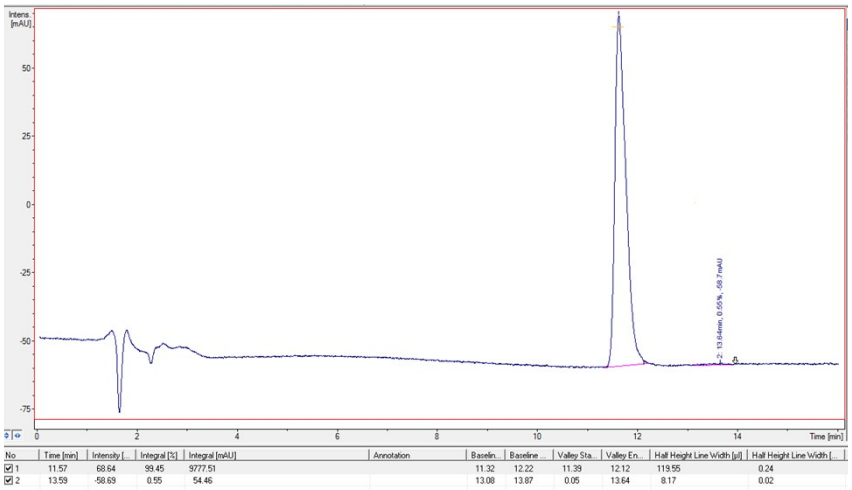


Plate 2c: UV chromatogram of (2,5-dimethoxyphenyl)(5-methoxy-4,6-dimethyl-1-benzofuran-3-yl)methanone (4b) measured at 280 nm.

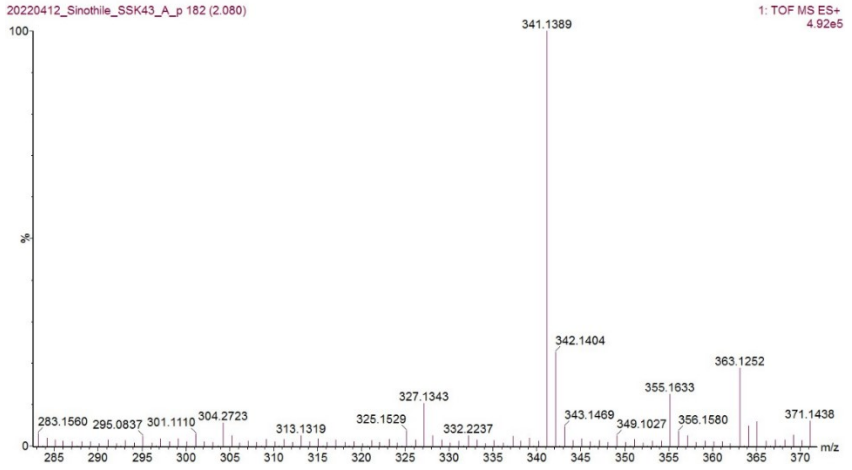


Plate 2d: HR-MS spectrum of (2,5-dimethoxyphenyl)(5-methoxy-4,6-dimethyl-1-benzofuran-3-yl)methanone (4b).

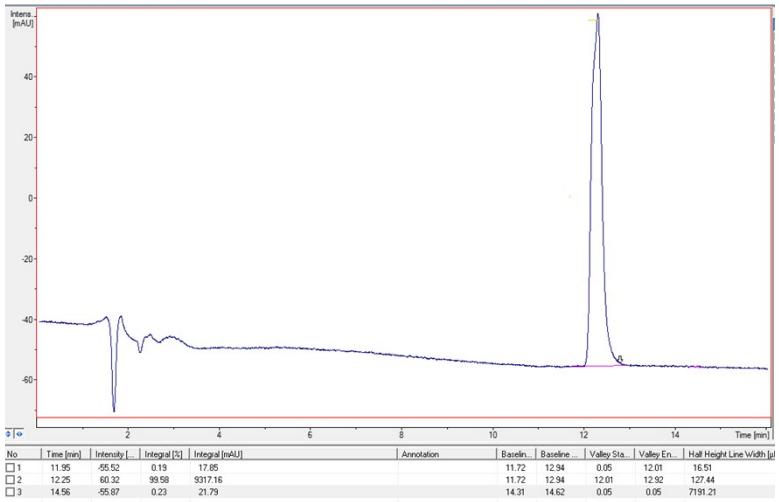


Plate 3c: UV chromatogram of (2,5-dimethoxyphenyl)(5-methoxynaphtho[1,2-*b*]furan-3-yl)methanone (4c).

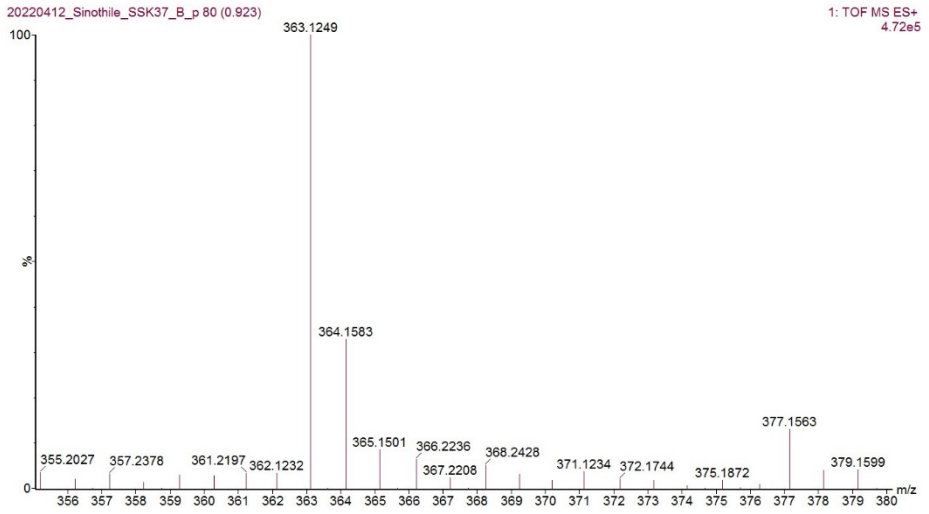


Plate 3d: HR-MS spectrum of (2,5-dimethoxyphenyl)(5-methoxynaphtho[1,2-*b*]furan-3-yl)methanone (4c).

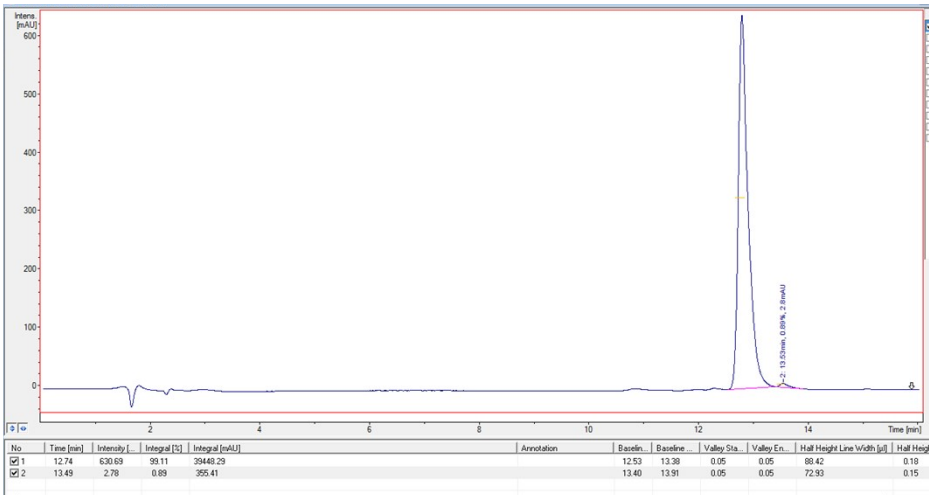


Plate 4c: UV chromatogram of (5-bromo-2-methoxyphenyl)(5-methoxynaphtho[1,2-*b*]furan-3-yl)methanone (4d) measured at 280 nm.

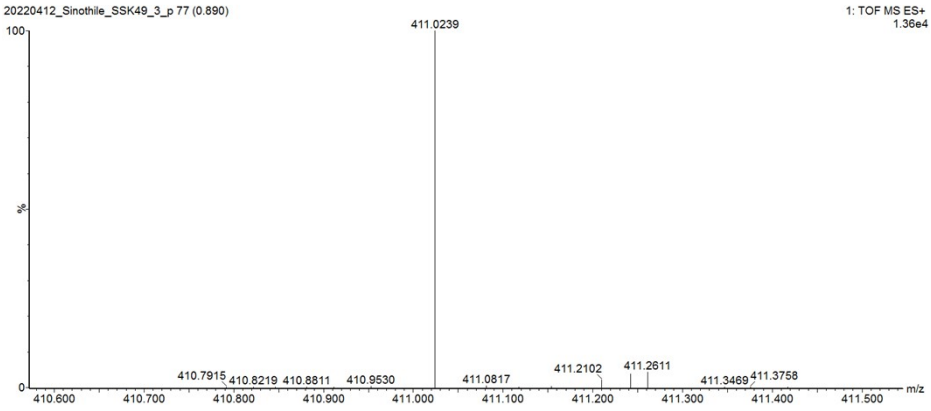


Plate 4d: HR-MS spectrum of (5-bromo-2-methoxyphenyl)(5-methoxynaphtho[1,2-*b*]furan-3-yl)methanone (4d).

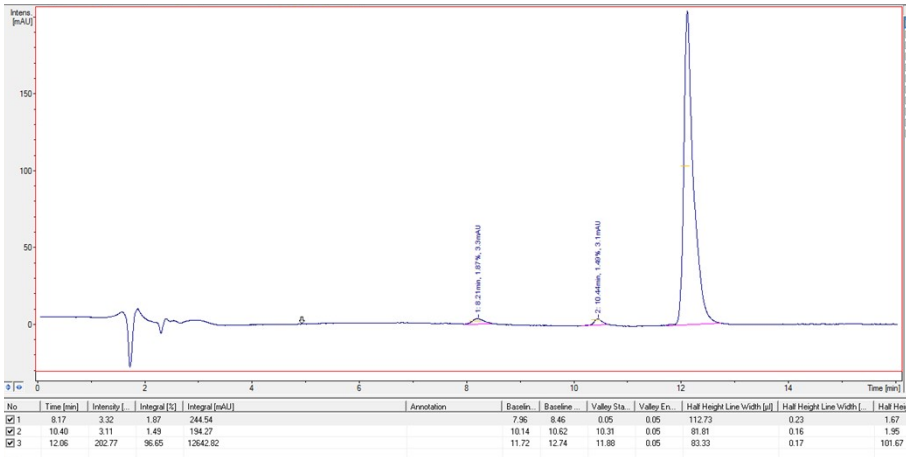


Plate 5c: UV chromatogram of (4-fluoro-2-methoxyphenyl)(5-methoxynaphtho[1,2-b]furan-3-yl)methanone (4e) measured at 280 nm.

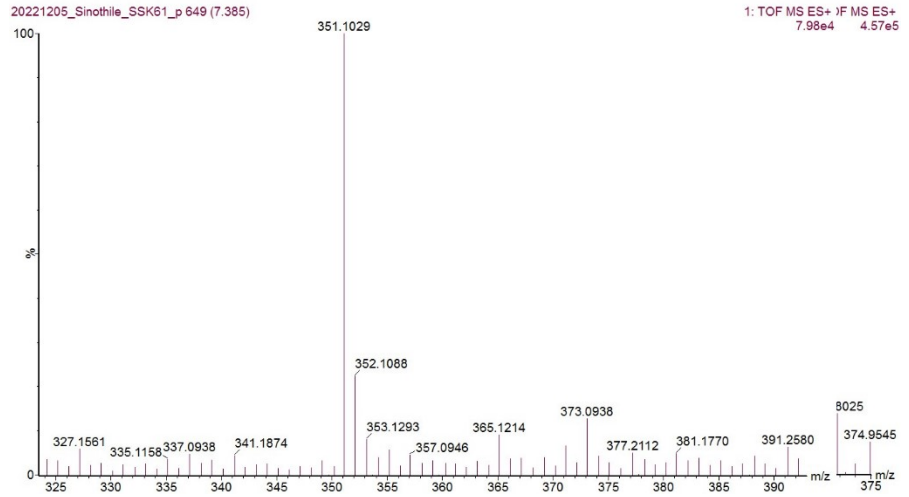


Plate 5d: HR-MS spectrum of (4-fluoro-2-methoxyphenyl)(5-methoxynaphtho[1,2-b]furan-3-yl)methanone (4e).

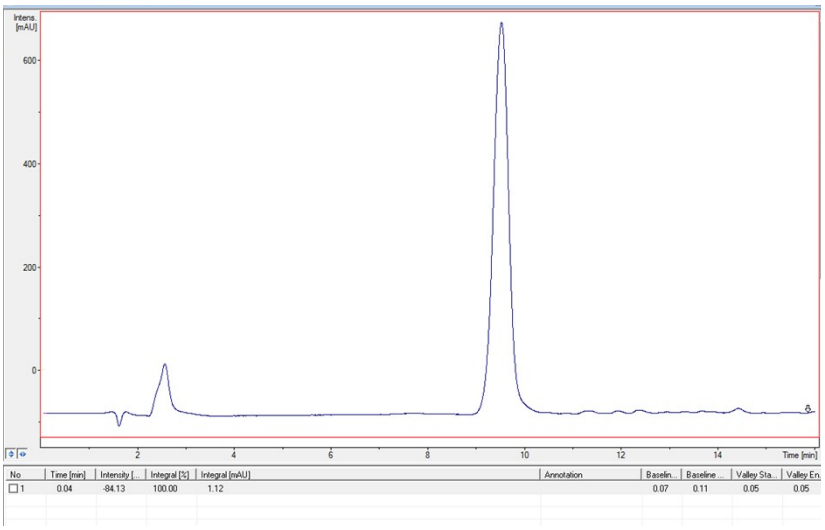


Plate 6c: UV chromatogram of (5-hydroxy-1-benzofuran-3-yl)(2,3,4-trimethoxyphenyl)methanone (3g) measured at 280 nm.

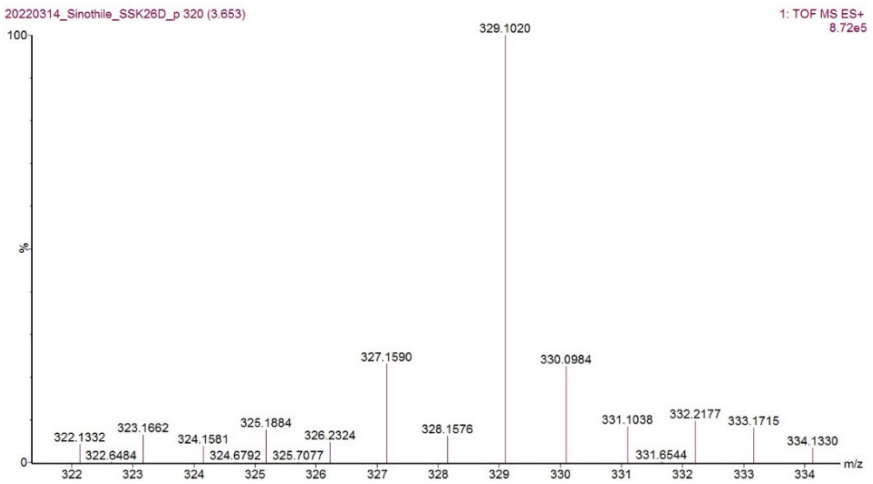


Plate 6d: HR-MS spectrum of (5-hydroxy-1-benzofuran-3-yl)(2,3,4-trimethoxyphenyl)methanone (3g).

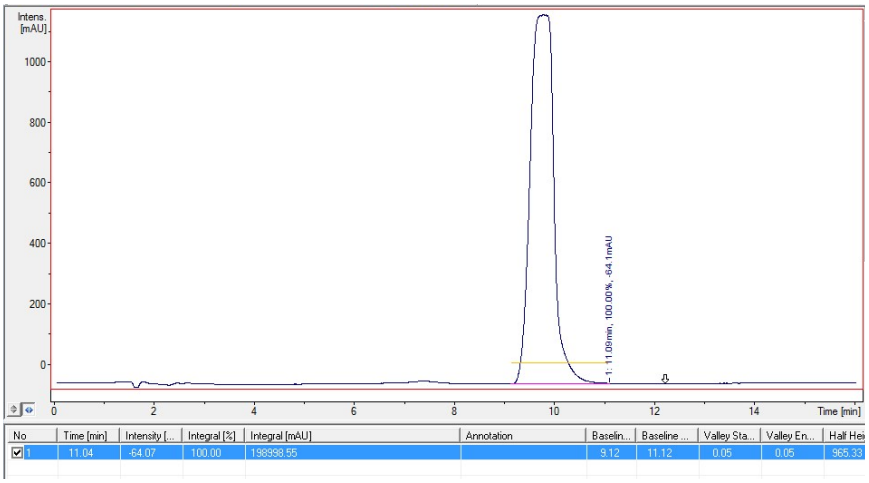


Plate 7c: UV chromatogram of (2,5-dimethoxyphenyl)(5-hydroxy-1-benzofuran-3-yl)methanone (3h) measured at 280 nm.

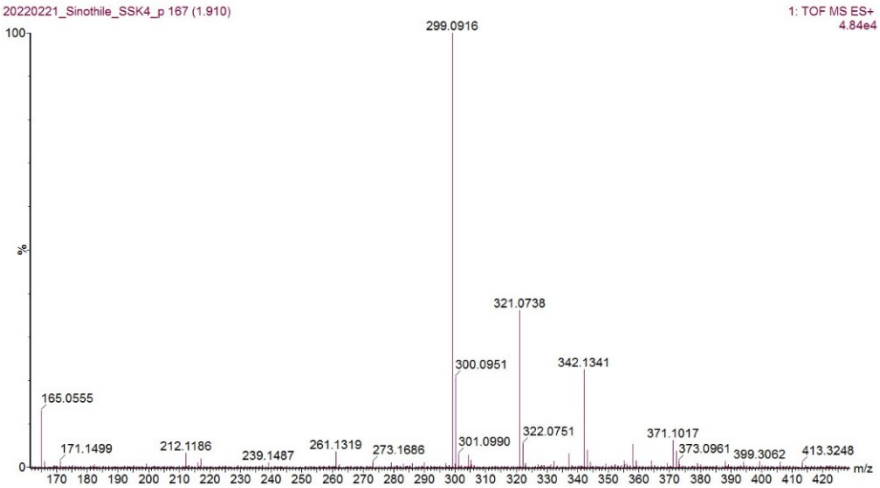


Plate 7d: HR-MS spectrum of (2,5-dimethoxyphenyl)(5-hydroxy-1-benzofuran-3-yl)methanone (3h).

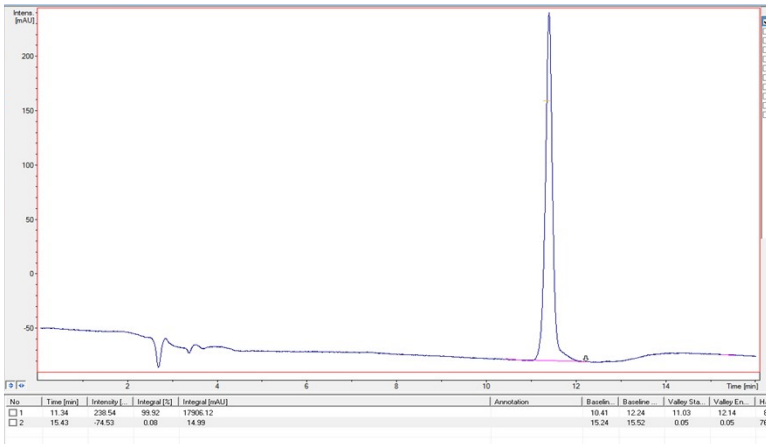


Plate 8c: UV chromatogram of 2-[3-(2,5-dimethoxyphenyl)-1*H*-pyrazol-4-yl]-4-methoxy-3,6-dimethylphenol (5a) measured at 280 nm.

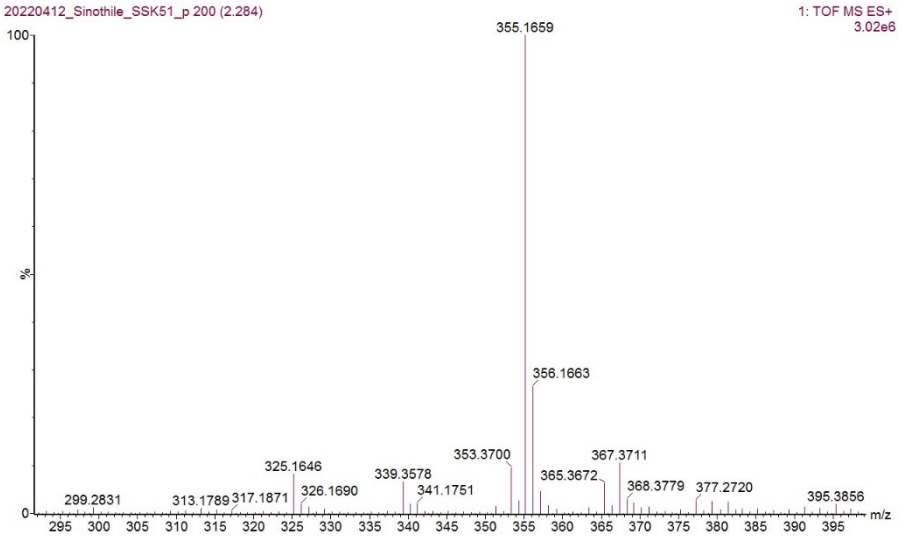


Plate 8d: HR-MS spectrum of 2-[3-(2,5-dimethoxyphenyl)-1*H*-pyrazol-4-yl]-4-methoxy-3,6-dimethylphenol (5a).

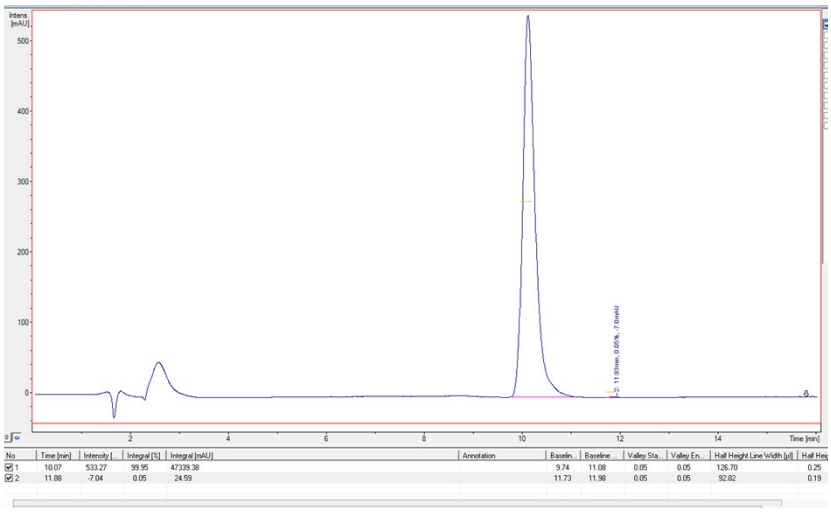


Plate 9c: UV chromatogram of 2-[3-(2,5-dimethoxyphenyl)-1H-pyrazol-4-yl]-4-methoxy-3,5-dimethylphenol (5b) measured at 280 nm.

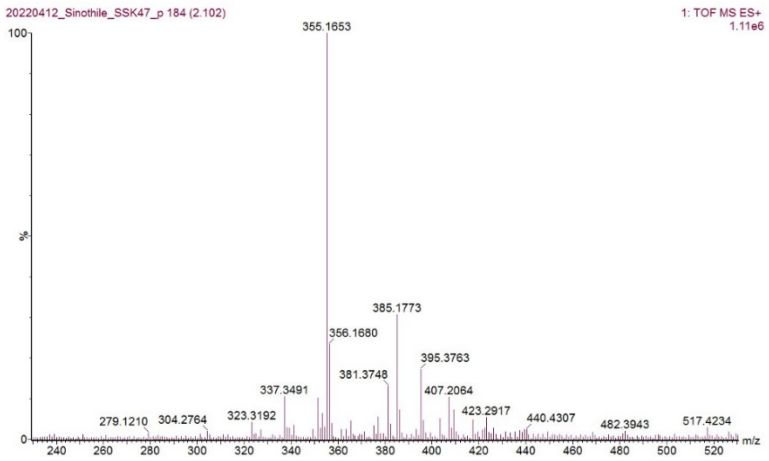


Plate 9d: HR-MS spectrum for 2-[3-(2,5-dimethoxyphenyl)-1H-pyrazol-4-yl]-4-methoxy-3,5 dimethylphenol (5b).

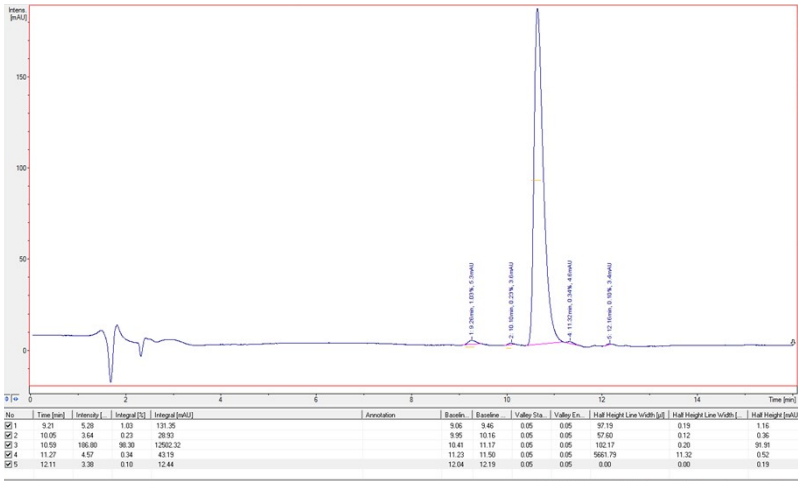


Plate 10c: UV chromatogram of 2-[3-(2,5-dimethoxyphenyl)-1H-pyrazol-4-yl]-4-methoxynaphthalen-1-ol (5c) measured at 260 nm.

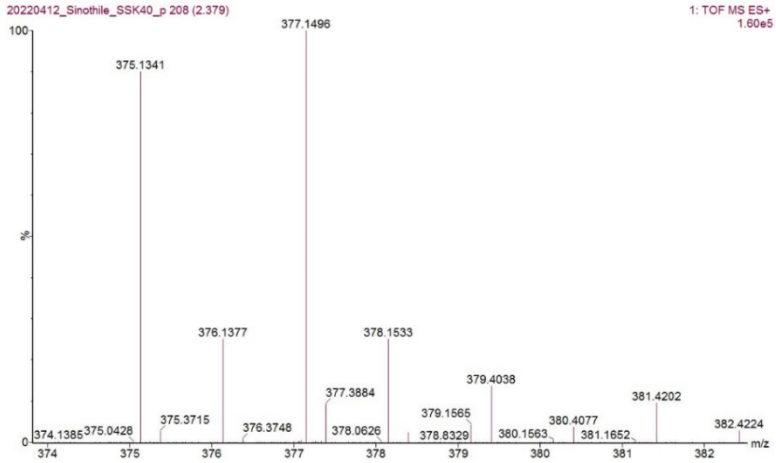


Plate 10d: HR-MS spectrum for 2-[3-(2,5-dimethoxyphenyl)-1H-pyrazol-4-yl]-4-methoxynaphthalen-1-ol (5c).

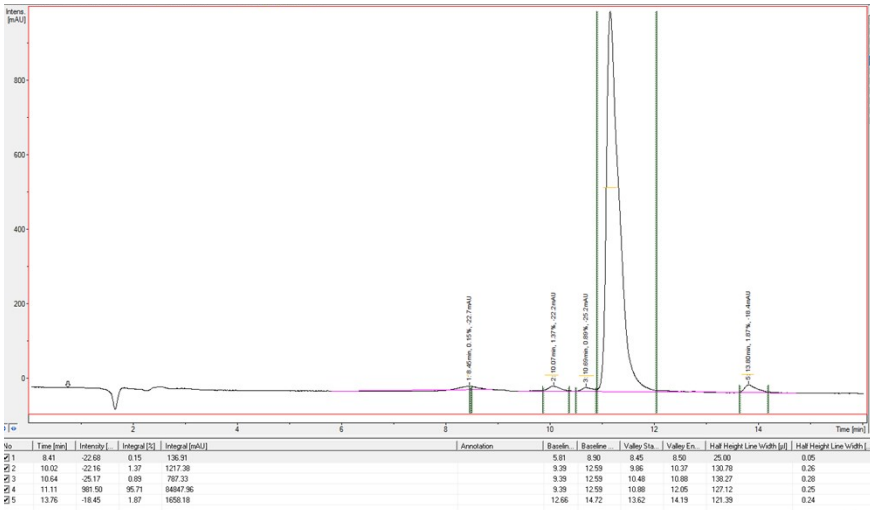


Plate 11c: UV chromatogram of 2-[3-(5-bromo-2-methoxyphenyl)-1*H*-pyrazol-4-yl]-4-methoxynaphthalen-1-ol (5d) measured at 260 nm.

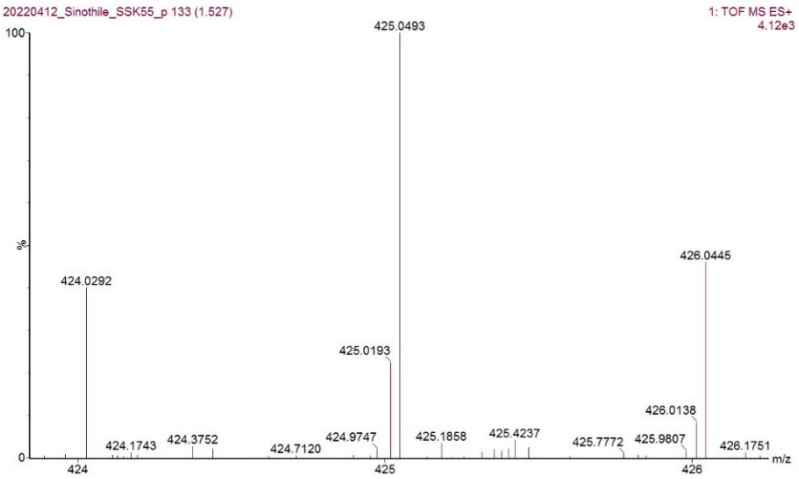


Plate 11d: HR-MS spectrum of 2-[3-(5-bromo-2-methoxyphenyl)-1*H*-pyrazol-4-yl]-4-methoxynaphthalen-1-ol (5d).

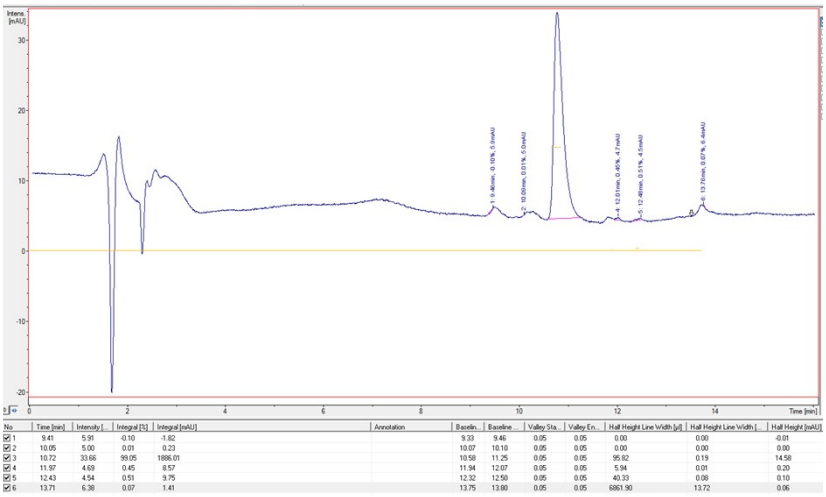


Plate 12c: UV chromatogram of 2-[3-(4-fluoro-2-methoxyphenyl)-1H-pyrazol-4-yl]-4-methoxynaphthalen-1-ol (5e).

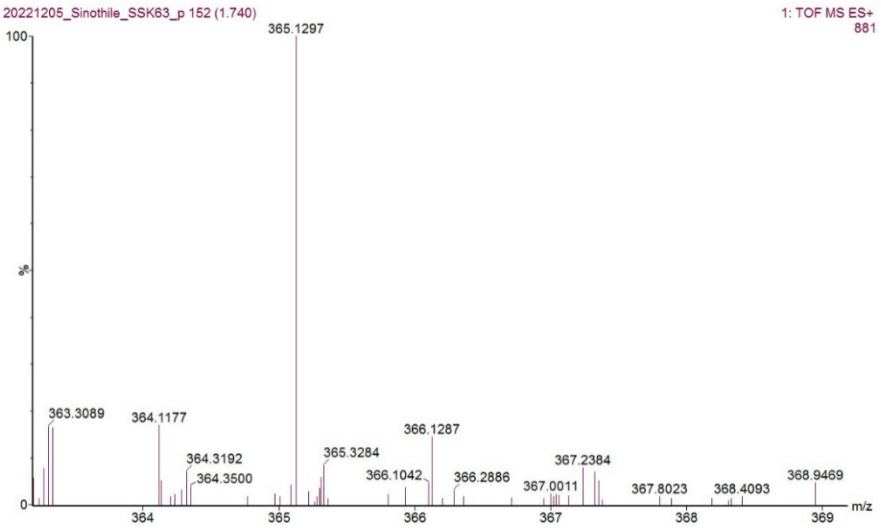


Plate 12d: HR-MS spectrum of 2-[3-(4-fluoro-2-methoxyphenyl)-1*H*-pyrazol-4-yl]-4-methoxynaphthalen-1-ol (5e).

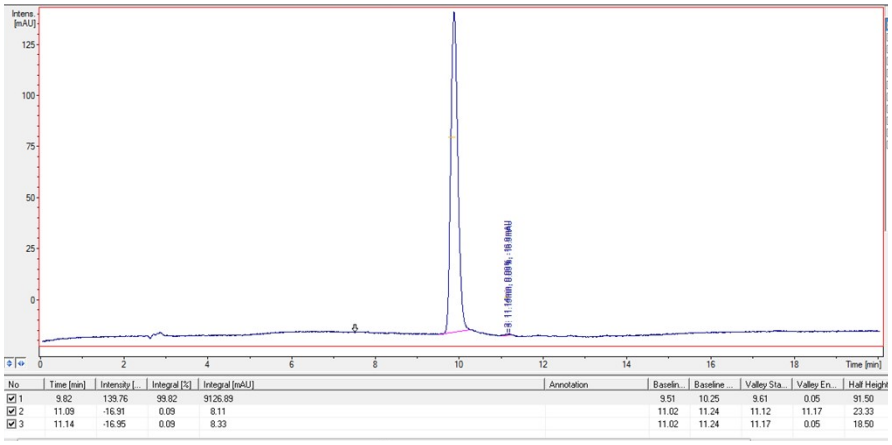


Plate 13c: UV chromatogram of 2-[3-(4-fluoro-2-methoxyphenyl)-1H-pyrazol-4-yl]benzene-1,4-diol (5f) measured at 280 nm.

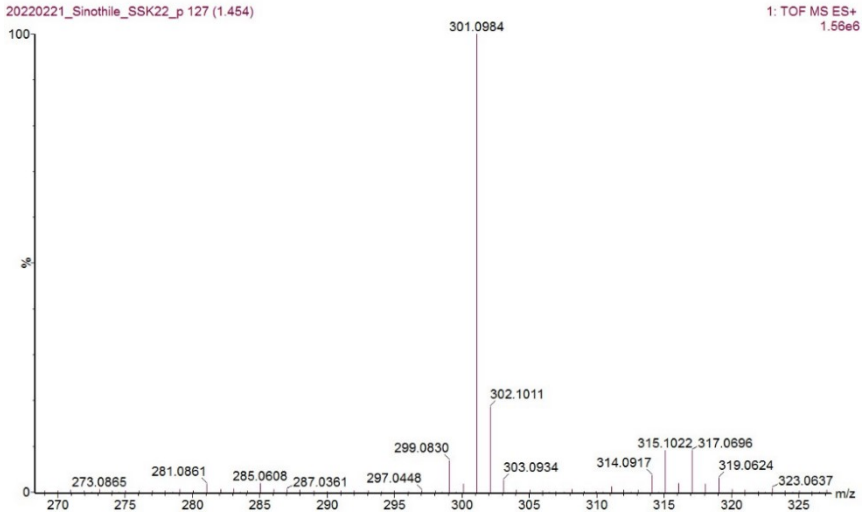


Plate 13d: HR-MS spectrum of 2-[3-(4-fluoro-2-methoxyphenyl)-1H-pyrazol-4-yl]benzene-1,4-diol (5f).

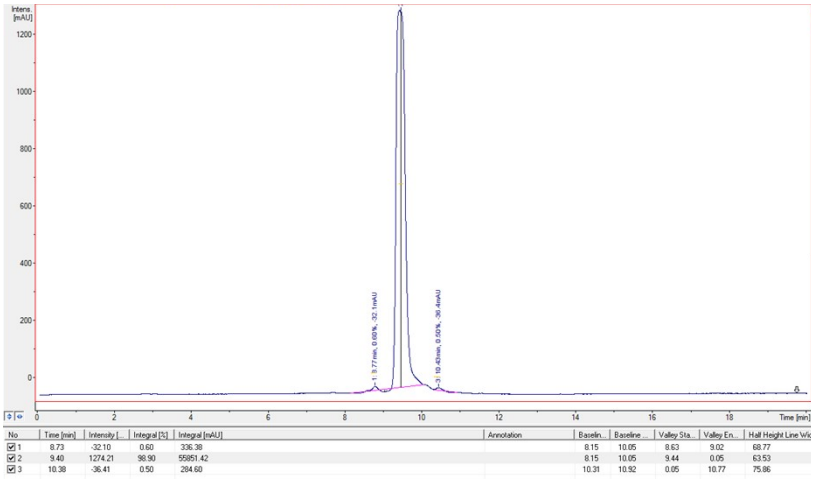


Plate 14c: UV chromatogram of 2-[3-(2,3,4-trimethoxyphenyl)-1H-pyrazol-4-yl]benzene-1,4-diol (5g) at 280 nm.

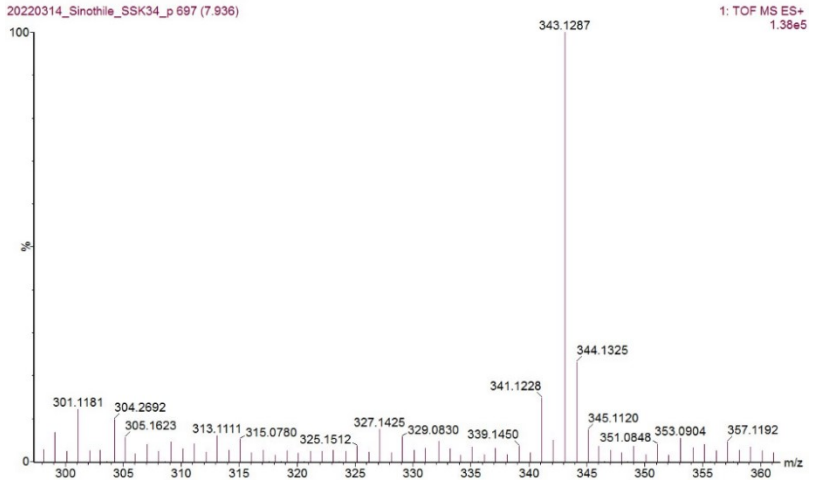


Plate 14d: HR-MS spectrum of 2-[3-(2,3,4-trimethoxyphenyl)-1H-pyrazol-4-yl]benzene-1,4-diol (5g).

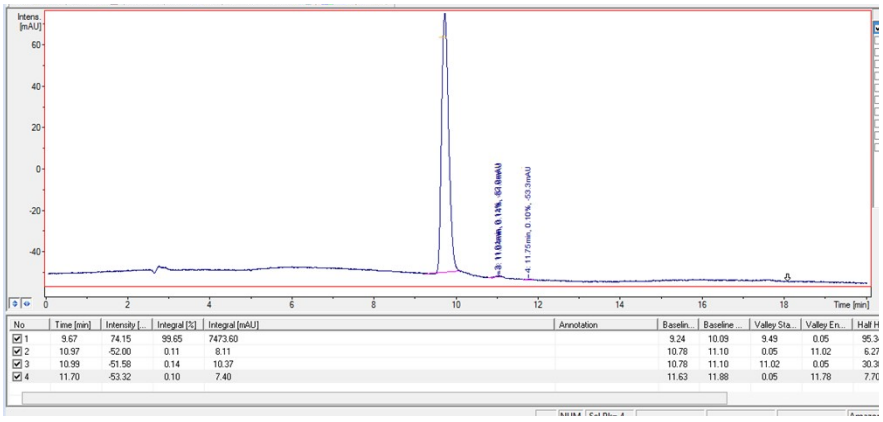


Plate 15c: UV chromatogram for 2-[3-(2,5-dimethoxyphenyl)-1H-pyrazol-4-yl]benzene-1,4-diol (5h) measured at 280 nm.

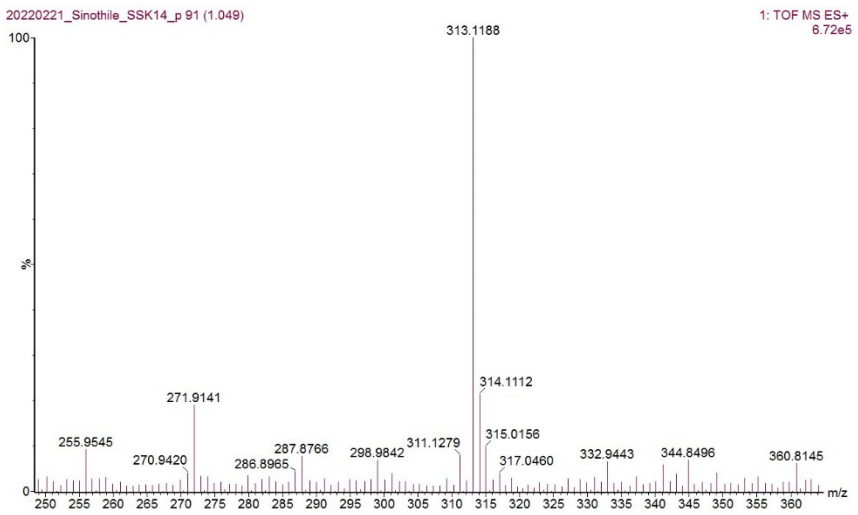


Plate 15d: HR-MS spectrum for 2-[3-(2,5-dimethoxyphenyl)-1H-pyrazol-4-yl]benzene-1,4-diol (5h) measured at 280 nm.