Supporting Information

Synthesis, *in vitro* anticancer activity and SAR studies of arylated imidazo[1,2-*a*]pyrazine-coumarin hybrids

Richa Goel, Vijay Luxami and Kamaldeep Paul*

School of Chemistry and Biochemistry, Thapar University, Patiala- 147 001, India

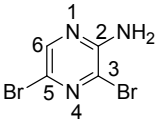
E-mail: kpaul@thapar.edu

Instrumentations and chemicals:

All commercially available compounds (Avra, Spectrochem, Aldrich, Merck etc.) were used without purification. Unless otherwise noted, all reactions were performed in oven-dried glassware. Final reactions were carried out in an oil bath using Microwave Vials (10-15 ml). Melting points were determined in open capillaries and were uncorrected. ^{1}H and ^{13}C NMR spectra were performed on Jeol ECS 400 NMR spectrometer, which was operated at 400 MHz for ^{1}H nuclei and 100 MHz for ^{13}C nuclei, using $CDCl_3$ and trifluoroacetic acid (TFA) as solvents. Chemical shifts are reported in parts per million (ppm) with TMS as internal reference and *J* values are given in hertz. 2D NOE studies were performed on same instrument. Mass Spectra of the synthesized compounds were recorded at Water Micromass-Q-T of Micro. Reactions were monitored by thin layer chromatography (TLC) with silica plate coated with silica gel HF-254 and column chromatography was performed with silica gel 60-120/100-200 mesh. Chloroform/ethyl acetate and chloroform/methanol were adopted solvent systems.

Typical procedure for synthesis of 2-amino-3,5-dibromopyrazine (2)

N-Bromosuccinimide (14.95 g, 83.99 mmol) was added over 50 min to a mixture of 2-aminopyrazine **1** (3.80 g, 40 mmol) in DMSO : H_2O (9:1) below 15 ^oC. Mixture was then stirred for 6 h at room temperature. After completion of reaction, mixture was then extracted with water and ethyl acetate. Ethyl acetate layer was separated, dried over sodium sulphate, filtered and concentrated in vacuum. Crude product was purified by column chromatography using hexane: ethyl acetate (9:1) as eluents.

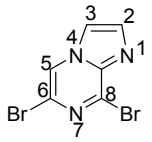


Spectral data 2-amino-3,5-dibromopyrazine (2): White solid; Yield: 90%; mp 115-116 ^oC (lit.[1] mp 117-118 ^oC) ; ^1H NMR ($CDCl_3$, 400 MHz): δ 5.12 (bs, 1H, NH_2), 8.04 (s, 1H, C_6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 123.5, 123.9, 143.1, 151.8.

Typical procedure for synthesis of 6,8-dibromo-imidazo[1,2-*a*]pyrazine (3)

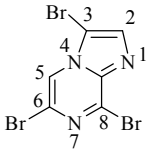
To 2-amino-3,5-dibromopyrazine **2** (5.0 g, 19.8 mmol) in 100 ml of isopropyl alcohol (IPA), 50% aqueous solution of chloroacetaldehyde (99 mmol) was added dropwise. The reaction mixture was refluxed at 110 ^oC for 72 h. After the completion of the reaction, cooled the reaction mixture to room temperature and then extracted with water and chloroform. Chloroform layer was separated, dried over sodium sulphate, filtered and concentrated in vacuum to get the crude product. The product was purified by column chromatography using hexane: ethyl acetate (6:4) as eluents.

Spectral data of 6,8-dibromoimidazo[1,2-*a*]pyrazine (3): White solid; Yield: 80%; mp 163-165



^oC**,** (lit.[2] m p 165-166 ^oC); ^1H NMR ($CDCl_3$, 400 MHz): δ 7.80 (d, J = 0.92 Hz, 1H, C_2H), 7.86 (d, J = 1.36 Hz, 1H, C_3H), 8.29 (s, 1H, C_5H); ^{13}C NMR ($CDCl_3$, 400 MHz): δ 115.9, 119.3, 119.9, 137.0, 137.4, 142.5.

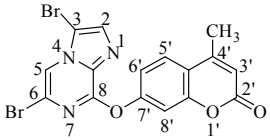
Typical procedure for synthesis of 3,6,8-tribromoimidazo[1,2-*a*]pyrazine (4): N-Bromosuccinimide (6.29 g, 35.34 mmol) was added to 6,8-dibromoimidazo[1,2-*a*]pyrazine **3** (10 g, 36 mmol) in acetonitrile and stirred at room temperature for 2 h. After completion of reaction (indicated by TLC), mixture was then extracted with water and chloroform. Chloroform layer was dried over sodium sulphate and concentrated in vacuum. Crude product was purified by column chromatography using hexane: ethyl acetate (8.5:1.5) as eluents.

Spectral data of 3,6,8-tribromoimidazo[1,2-*a*]pyrazine (4): White solid; Yield: 90%; mp 162-164  °C, (lit.[3] m p 161-165 °C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.84 (s, 1H, C_2H), 8.22 (s, 1H, C_5H); ^{13}C NMR ($CDCl_3$, 400 MHz): δ 116.12, 119.28, 120.97, 137.03, 137.39, 142.54.

Typical procedure for synthesis of imidazo[1,2-*a*]pyrazine-coumarin hybrid (6)

To the solution of 3,6,8-tribromoimidazo[1,2-*a*]pyrazine **4** (10 g, 28.09 mmol) in 50 ml dry DMF, 7-hydroxy-4-methyl coumarin **5** (4.94 g, 28.09 mmol) and K_2CO_3 (3.87 g, 28.09 mmol) were added and allowed to stir at room temperature for 12 h. After completion of reaction, the reaction mixture was poured into crushed ice. The crude solid was filtered through and dried in vacuum. The solid was recrystallized from hot ethanol to obtain pure white solid of compound **6**.

Spectral data of 7'-(3,6-dibromoimidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one

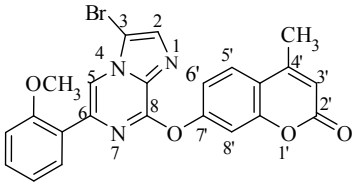


(6): Off white solid; Yield: 85%; mp 280-282 °C; ^{1}H NMR ($CDCl_3$+TFA, 400 MHz): δ 2.48 (d, J = 1.36 Hz, 3H, CH_3), 6.32 (d, J = 0.92 Hz, 1H, C3'H) 7.32 (dd, ^2J = 8.68 Hz, ^3J = 2.74 Hz, 1H, C5'H), 7.43 (d, J = 2.32 Hz, 1H, C8'H), 7.71 (d, J = 8.68 Hz, 1H, C6'H), 7.86 (s, 1H, C2H), 8.08 (s, 1H, C5H); ^{13}C NMR ($CDCl_3$+TFA, 100 MHz): δ 18.7 (CH_3), 100.6, 110.1, 114.0, 114.3, 118.2, 118.3, 122.2, 126.2, 130.2, 131.7, 149.4, 153.5, 153.7, 154.3 (ArC), 162.9 (C=O); MS (EI): m/z 451.9 (M^++1); Anal. Calcd for $C_{16}H_9Br_2N_3O_3$: C, 42.60; H, 2.01; N, 9.32. Found: C, 42.72; H, 2.08; N, 9.12.

Typical procedure for synthesis of monoarylated (7a, 8a) and symmetrical hybrids (7b-19b)

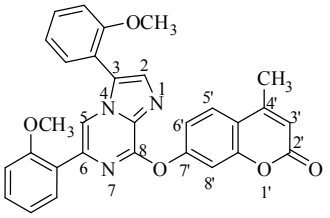
To a solution of 3,6-dibromoimidazo[1,2-*a*]pyrazine-coumarin hybrid **6** (0.46 g, 1.0 mmol) in mixture of 1,2-DME : water (9:1) in a sealed tube, boronic acid (1 eq.) and K_2CO_3 (0.150 g, 1.0 mmol) were added under inert atmosphere. Then, $Pd(PPh_3)_4$ (5mol%) was added with continued nitrogen purging and refluxed the reaction mixture for 8-12 h. Completion of reaction was determined by TLC. The mixture was extracted with chloroform and water. Chloroform layer was dried using sodium sulphate to obtain crude product which was further purified by column chromatography using chloroform: ethylacetate / chloroform: methanol as eluents.

Spectral data of 7'-(3-bromo-6-(2-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-



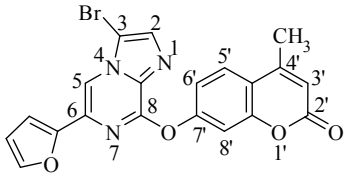
2*H*-chromen-2'-one (7a): White solid; Yield: 61%; mp 239-240 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.49 (s, 3H, CH_3), 3.99 (s, 3H, OCH_3), 6.30 (s, 1H, C3'H), 6.97-7.02 (m, 2H, ArH), 7.31-7.38 (m, 2H, ArH), 7.48 (d, J = 2.32 Hz, 1H, C8'H), 7.68 (d, J = 8.72 Hz, 1H, ArH), 7.76 -7.79 (m, 2H, ArH), 8.74 (s, 1H, C5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.7 (CH_3), 55.6 (OCH_3), 99.1, 110.3, 111.2, 114.1, 114.3, 117.3, 118.1, 121.0, 123.6, 125.2, 129.9, 130.1, 132.6, 133.7, 134.9, 150.8, 152.1, 154.1, 155.0, 156.7 (ArC), 160.7 (C=O); MS (EI): m/z 480.1 (M^{+}+2); Anal. Calcd for $C_{23}H_{16}BrN_3O_4$: C, 57.76; H, 3.37; N, 8.79. Found: C, 57.50; H, 3.22; N, 8.68.

Spectral data of 7'-(3,6-bis(2-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-



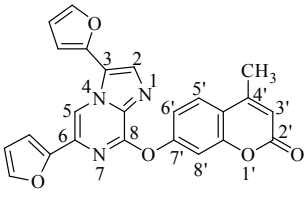
chromen-2'-one (7b): White solid; Yield: 33%; mp 204-205 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.48 (d, J = 0.92 Hz, 3H, CH_3), 3.85 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 6.29 (d, J = 1.40 Hz, 1H, C3'H), 6.93-6.99 (m, 2H, ArH), 7.10-7.16 (m, 2H, ArH), 7.28-7.30 (m, 1H, ArH), 7.42 (dd, ^{2}J = 8.68 Hz, ^{3}J = 2.28 Hz, 1H, C5'H), 7.48-7.52 (m, 2H, ArH), 7.54 (d, J = 2.28 Hz, 1H, C8'H), 7.68 (d, J = 8.72 Hz, 1H, ArH), 7.79 (dd, ^{2}J = 7.76 Hz, ^{3}J = 1.82 Hz, 1H, ArH), 7.82 (s, 1H, C2H), 8.49 (s, 1H, C5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.7 (CH_3), 55.5 (OCH_3), 110.2, 111.1, 111.2, 113.9, 116.0, 116.8, 117.0, 118.1, 120.9, 121.0, 124.4, 125.2, 126.5, 129.4, 130.1, 130.9, 131.4, 132.3, 134.5, 150.9, 152.2, 154.2, 155.5, 156.7, 157.0 (ArC), 160.9 (C=O); MS (EI): m/z 506.2 (M^{+}+1); Anal. Calcd for: $C_{30}H_{23}N_3O_5$: C, 71.28; H, 4.59; N, 8.31. Found: C, 71.41; H, 4.37; N, 8.22.

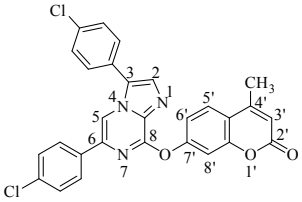
Spectral data of 7'-(3-bromo-6-(furan-2-yl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-

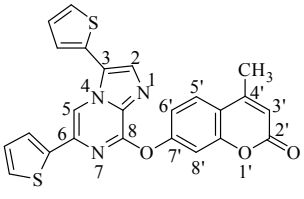


chromen-2'-one (8a): White solid; Yield: 48%; mp 225-226 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.50 (d, J = 1.40 Hz, 3H, CH_3), 6.32 (d, J = 1.36 Hz, 1H, C3'H), 6.45 (q, J = 1.60 Hz, 1H, ArH), 6.69 (d, J = 3.20 Hz, 1H, ArH), 7.37 (dd, ^{2}J = 8.72 Hz, ^{3}J = 2.28 Hz, 1H, C5'H), 7.47 (d, J = 0.92 Hz, 1H, ArH), 7.51 (d, J = 2.28 Hz, 1H, C8'H), 7.69 (d, J = 8.72 Hz, 1H, ArH), 7.75 (s, 1H, C2H), 8.20 (s, 1H, C5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.8 (CH_3), 99.6, 107.9, 109.7, 110.4, 112.0, 114.3, 117.5, 118.1, 125.2, 130.1, 132.6, 135.0, 143.1, 150.2, 151.7, 152.1, 154.1, 154.7 (ArC), 160.7 (C=O); MS (EI): m/z 440.1 (M^{+}+2); Anal. Calcd for $C_{20}H_{12}BrN_3O_4$: C,

54.81; H, 2.76; N, 9.59. Found: C, 54.76; H, 2.69; N, 9.73.

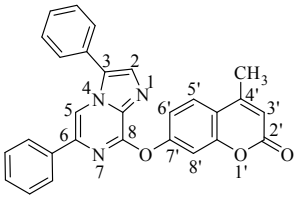
Spectral data of 7'-(3,6-di(furan-2-yl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (8b): 
Off White solid; Yield: 25%; mp 192-194 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.50 (s, 3H, CH_3), 6.31 (s, 1H, C3'H), 6.46 (q, *J* = 1.82 Hz, 1H, ArH), 6.64 (q, *J* = 1.82 Hz, 1H, ArH), 6.69 (d, *J* = 3.20 Hz, 1H, ArH), 6.81 (d, *J* = 3.68 Hz, 1H, ArH), 7.40 (dd, ^{2}J = 8.72 Hz, ^{3}J = 2.28 Hz, 1H, C5'H), 7.46 (s, 1H, ArH), 7.53 (d, *J* = 2.28 Hz, 1H, C8'H), 7.68-7.70 (m, 2H, ArH), 7.96 (s, 1H, C2H), 8.66 (s, 1H, C5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.8 (CH_3), 108.4, 109.3, 109.4, 110.4, 111.7, 111.9, 114.2, 117.4, 118.2, 121.2, 125.2, 129.9, 132.0, 132.9, 142.8, 143.1, 143.2, 150.5, 152.0, 152.1, 154.1, 154.9 (ArC), 160.8 (C=O); MS (EI): m/z 426.2 (M^{+}+1); Anal. Calcd for $C_{24}H_{15}N_3O_5$: C, 67.76; H, 3.55; N, 9.88. Found: C, 67.59; H, 3.63; N, 9.70.

Spectral data of 7'-(3,6-bis(4-chlorophenyl)imidazo[1,2-a]pyrazin-8-yloxy)-4'-methyl-2H-chromen-2'-one (9b): 
White solid; Yield: 42%; mp 245-247 ^{o}C; ^{1}H NMR ($CDCl_3$ + TFA, 400 MHz): δ 2.55 (d, *J* = 0.88 Hz, 3H, CH_3), 6.43 (d, *J* = 0.92 Hz, 1H, C3'H), 7.40-7.43 (m, 3H, ArH), 7.53 (d, *J* = 2.32 Hz, 1H, C8'H), 7.58-7.63 (m, 4H, ArH), 7.69 (d, *J* = 8.72 Hz, 2H, ArH), 7.81 (d, *J* = 8.68 Hz, 1H, ArH), 8.17 (s, 1H, C2H), 8.33 (s, 1H, C5H); ^{13}C NMR ($CDCl_3$ + TFA, 100 MHz): δ 18.8 (CH_3), 108.6, 110.2, 114.4, 118.1, 118.5, 122.2, 124.7, 126.2, 126.9, 127.7, 129.3, 129.5, 130.3, 130.6, 131.6, 136.9, 138.0, 141.3, 149.5, 153.4, 153.6, 153.7 (ArC), 162.1 (C=O); MS (EI): m/z 514.1 (M^{+}+1); Anal. Calcd for $C_{28}H_{17}Cl_2N_3O_3$: C, 65.38; H, 3.33; N, 8.17. Found: C, 65.48; H, 3.50; N, 8.20.

Spectral data of 7'-(3,6-di(thiophen-2-yl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (10b): 
Light green solid; Yield: 66%; mp 191-192 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.50 (d, *J* = 0.88 Hz, 3H, CH_3), 6.32 (d, *J* = 1.36 Hz, 1H, C3'H), 7.03-7.05 (m, 1H, ArH), 7.27-7.31 (m, 2H, ArH), 7.39 (dd, ^{2}J = 3.68 Hz, ^{3}J = 1.36 Hz, 1H, ArH), 7.40-7.44 (m, 2H, ArH),

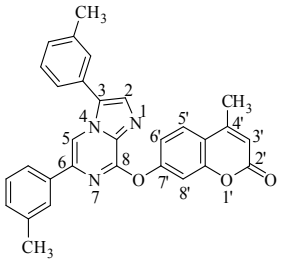
7.55-7.58 (m, 2H, ArH), 7.71 (d, J = 8.72 Hz, 1H, ArH), 7.88 (s, 1H, C2H), 8.40 (s, 1H, C5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.8 (CH_3), 108.0, 110.5, 114.2, 117.4, 118.2, 123.1, 124.0, 125.2, 126.7, 127.1, 127.3, 128.0, 128.2, 132.5, 133.1, 134.6, 140.2, 151.7, 152.1, 154.1, 154.8 (ArC), 160.8 (C=O); MS (EI): m/z 458.1 (M^++1); Anal. Calcd for $C_{24}H_{15}N_3O_3S_2$: C, 63.00; H, 3.30; N, 9.18; S, 14.02. Found: C, 63.28; H, 3.19; N, 9.26; S, 13.93.

Spectral data of 7'-(3,6-diphenylimidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one



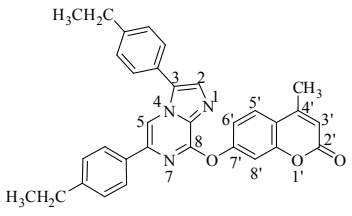
(11b): White solid; Yield: 74%; mp 204-206 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.50 (d, J = 0.68 Hz, 3H, CH_3), 6.32 (d, J = 0.88 Hz, 1H, C3'H), 7.34-7.43 (m, 4H, ArH), 7.51-7.56 (m, 2H, ArH), 7.59-7.66 (m, 4H, ArH), 7.69-7.72 (m, 3H, ArH), 7.86 (s, 1H, C2H), 8.40, (s, 1H, C5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.5 (CH_3), 109.4, 110.5, 114.2, 117.4, 118.3, 125.3, 125.9, 128.0, 128.2, 128.8, 129.2, 129.4, 129.5, 132.6, 133.8, 135.6, 136.9, 152.2, 154.2, 155.1 (ArC), 160.8 (C=O); MS (EI): m/z 446.1 (M^++1); Anal. Calcd for $C_{28}H_{19}N_3O_3$: C, 75.49; H, 4.30; N, 9.43. Found: C, 75.28; H, 4.39; N, 9.58.

Spectral data of 7'-(3,6-di-*m*-tolylimidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one



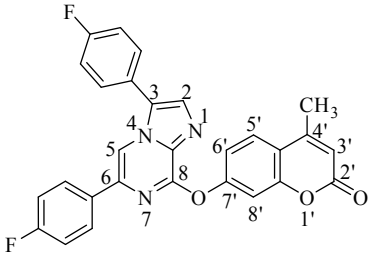
(12b): White solid; Yield: 70%; mp 198-199 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.36 (s, 3H, CH_3), 2.50 (s, 6H, CH_3), 6.31 (d, J = 0.92 Hz, 1H, C3'H), 7.16 (d, J = 7.76 Hz, 1H, ArH), 7.30 (d, J = 2.76 Hz, 1H, ArH), 7.35 (d, J = 7.80 Hz, 1H, ArH), 7.41-7.45 (m, 3H, ArH), 7.49-7.53 (m, 4H, ArH), 7.70 (d, J = 8.72 Hz, 1H, ArH), 7.83 (s, 1H, C2H), 8.37 (s, 1H, C5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.8 (CH_3), 21.5 (CH_3), 109.6, 110.4, 114.1, 117.3, 118.2, 123.3, 125.1, 125.2, 126.5, 127.9, 128.8, 129.0, 129.4, 129.5, 129.6, 130.0, 132.5, 133.8, 135.6, 137.0, 138.4, 139.5, 152.0, 152.2, 154.2, 155.2 (ArC), 160.8 (C=O); MS (EI): m/z 474.2 (M^++1); Anal. Calcd for: $C_{30}H_{23}N_3O_3$: C, 76.09; H, 4.90; N, 8.87. Found: C, 76.42; H, 4.88; N, 8.76.

Spectral data of 7'-(3,6-bis(4-ethylphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-



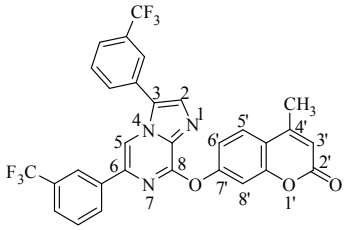
chromen-2'-one (13b): White solid; Yield: 69%; mp 179-181 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.22 (t, *J* = 7.56 Hz, 3H, CH_3), 1.34 (t, *J* = 7.80 Hz, 3H, CH_3), 2.49 (d, *J* = 0.68 Hz, 3H, CH_3), 2.64 (q, *J* = 7.64 Hz, 2H, CH_2), 2.78 (q, *J* = 7.64 Hz, 2H, CH_2), 6.31 (d, *J* = 1.40 Hz, 1H, C3'H), 7.21 (d, *J* = 8.24 Hz, 2H, ArH), 7.40-7.44 (m, 3H, ArH), 7.52 (d, *J* = 1.80 Hz, 1H, C8'H), 7.55 (d, *J* = 8.24 Hz, 2H, ArH), 7.62 (d, *J* = 8.24 Hz, 2H, ArH), 7.70 (d, *J* = 8.72 Hz, 1H, ArH), 7.81 (s, 1H, C2H), 8.36 (s, 1H, C5H); ^{13}C NMR ($CDCl_3$,100 MHz): δ 15.4 (CH_3), 15.5 (CH_3), 18.8 (CH_3), 28.5 (CH_2), 28.7 (CH_2), 109.0, 110.5, 114.1, 117.3, 118.3, 125.2, 125.3, 125.9, 128.1, 128.3, 129.0, 129.3, 132.4, 133.1, 133.5, 136.9, 145.1, 145.5, 152.0, 152.2, 154.2, 155.2 (ArC), 160.8 (C=O); MS (EI): m/z 502.2 (M^++1); Anal. Calcd for C_{33} $H_{27}N_3O_3$: C, 76.63; H, 5.43; N, 8.38. Found: C, 76.82; H, 5.57; N, 8.45.

Spectral data of 7'-(3,6-bis(4-fluorophenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-



chromen-2'-one (14b): White solid; Yield: 72%; mp 240-242 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.51 (d, *J* = 1.40 Hz, 3H, CH_3), 6.32 (d, *J* = 1.36 Hz, 1H, C3'H), 7.04-7.09 (m, 2H, ArH), 7.29-7.34 (m, 2H, ArH), 7.41 (dd, ^2J = 8.72 Hz, ^3J = 2.28 Hz, 1H, C5'H), 7.48 (d, *J* = 2.28 Hz, 1H, C8'H), 7.59-7.62 (m, 2H, ArH), 7.65-7.69 (m, 2H, ArH), 7.72 (d, *J* = 8.72 Hz, 1H, ArH), 7.83 (s, 1H, C2H), 8.24 (s, 1H, C5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.8 (CH_3), 108.8, 110.5, 114.3, 115.7, 115.9, 116.7, 116.9, 117.5, 118.2, 123.9, 125.4, 127.7, 127.8, 128.4, 130.2, 130.3, 131.6, 132.4, 133.8, 136.3, 152.1, 152.2, 154.2, 154.9 (ArC), 160.7 (C=O), 161.9, 162.0, 164.4, 164.5 (ArC); MS (EI): m/z 482.2 (M^++1); Anal. Calcd for $C_{28}H_{17}F_2N_3O_3$: C, 69.85; H, 3.56; N, 8.73. Found: C, 69.56; H, 3.65; N, 8.99.

Spectral data of 7'-(3,6-bis(3-(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl



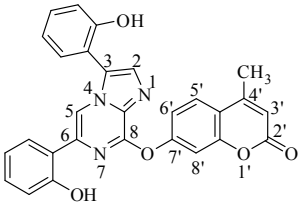
-2*H*-chromen-2'-one (15b): White solid; Yield: 60%; mp 195-196 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.51 (d, *J* = 0.92 Hz, 3H, CH_3), 6.33 (d, *J* = 1.40 Hz, 1H, C3'H), 7.43 (dd, ^2J = 8.24 Hz, ^3J = 2.52 Hz, 1H, C5'H), 7.48 (d, *J* = 2.28 Hz, 1H, C8'H), 7.52 (t, *J* = 7.78 Hz, 1H, ArH), 7.60 (d, *J* = 7.80 Hz, 1H, ArH), 7.73 (d, *J* = 8.72 Hz, 1H, ArH), 7.76-7.82 (m, 2H, ArH), 7.84 (s, 1H, ArH), 7.86-7.87 (m, 1H, ArH), 7.90 (d, *J* = 1.84 Hz, 1H, ArH), 7.92

(s, 1H, ArH), 7.94 (s, 1H, C2H), 8.36 (s, 1H, C5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.8 (CH_3), 109.4, 110.5, 114.4, 117.7, 118.3, 122.2, 122.4, 122.6, 122.7, 125.2, 125.3, 125.4, 125.6, 125.7, 126.1, 128.1, 128.6, 129.1, 129.5, 130.3, 131.1, 131.3, 131.4, 132.1, 132.4, 132.7, 132.9, 134.5, 136.0, 136.1, 152.0, 152.5, 154.2, 154.7 (ArC), 160.6 (C=O); MS (EI): m/z 582.2 (M^++1); Anal. Calcd for: $C_{30}H_{17}F_6N_3O_3$: C, 61.97; H, 2.95; N, 7.23. Found: C, 62.13; H, 2.82; N, 7.03.

Spectral data of 7'-(3,6-bis(4-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (16b): White solid; Yield: 73%; mp 224-226 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.50 (d, J = 0.92 Hz, 3H, CH_3), 3.81 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 6.31 (d, J = 1.36 Hz, 1H, C3'H), 6.90 (d, J = 8.68 Hz, 2H, ArH), 7.12 (d, J = 9.16 Hz, 2H, ArH), 7.42 (dd, ^2J = 8.72 Hz, ^3J = 2.28 Hz, 1H, C5'H), 7.52 (d, J = 2.28 Hz, 1H, C8'H), 7.54 (d, J = 8.72 Hz, 2H, ArH), 7.63 (d, J = 8.72 Hz, 2H, ArH), 7.70 (d, J = 8.72 Hz, 1H, ArH), 7.77 (s, 1H, C2H), 8.25 (s, 1H, C5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.8 (CH_3), 55.3 (OCH_3), 55.4 (OCH_3), 108.2, 110.4, 114.1, 114.2, 114.9, 117.3, 118.3, 120.2, 125.2, 127.2, 128.3, 129.1, 129.7, 132.1, 133.3, 136.6, 151.9, 152.2, 154.2, 155.2, 160.1, 160.2 (ArC), 160.8 (C=O); MS (EI): m/z 506.3 (M^++1); Anal. Calcd for $C_{30}H_{23}N_3O_5$: C, 71.28; H, 4.59; N, 8.31. Found: C, 71.03; H, 4.48; N, 8.18.

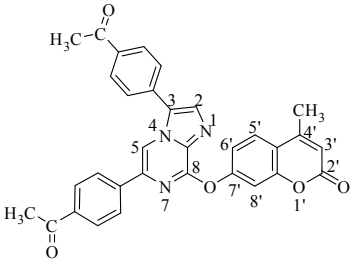
Spectral data of 4,4'-(8-(4'-methyl-2'-oxo-2*H*-chromen-7'-yloxy)imidazo[1,2-*a*]pyrazine-3,6-diyl)dibenzaldehyde (17b): White solid; Yield: 70%; mp >300 °C; ^{1}H NMR ($CDCl_3$ + TFA, 400 MHz): δ 2.56 (s, 3H, CH_3), 6.45 (d, J = 0.92 Hz, 1H, C3'H), 7.46 (dd, ^2J = 8.68 Hz, ^3J = 2.28 Hz, 1H, C5'H), 7.60 (d, J = 2.28 Hz, 1H, C8'H), 7.83 (d, J = 8.68 Hz, 1H, ArH), 7.87-7.90 (m, 4H, ArH), 7.97 (d, J = 8.24 Hz, 2H, ArH), 8.22-8.26 (m, 3H, ArH), 8.52 (s, 1H, C5H), 10.02 (s, 1H, CHO), 10.18 (s, 1H, CHO); ^{13}C NMR ($CDCl_3$ + TFA, 100 MHz): δ 18.9 (CH_3), 109.9, 110.3, 114.4, 118.2, 118.5, 126.2, 127.1, 128.5, 129.4, 130.1, 130.7, 131.3, 136.9, 137.6, 139.2, 140.4, 150.2, 153.6, 153.7, 153.8 (ArC), 162.5 (C=O), 191.6 (CHO), 192.4 (CHO); MS (EI): m/z 501.2 (M^++1); Anal. Calcd for $C_{30}H_{19}N_3O_5$: C, 71.85; H, 3.82; N, 8.38. Found: C, 71.69; H, 3.66; N, 8.19.

Spectral data of 7'-(3,6-bis(2-hydroxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-



chromen-2'-one (18b): White solid; Yield: 68%; mp >300 °C; ^{1}H NMR ($CDCl_3$ + TFA, 400 MHz): δ 2.58 (d, J = 0.92 Hz, 3H, CH_3), 6.52 (d, J = 1.40 Hz, 1H, C3'H), 6.86-6.95 (m, 2H, ArH), 7.14-7.23 (m, 2H, ArH), 7.28-7.32 (m, 1H, ArH), 7.40 (dd, ^2J = 8.72 Hz, ^3J = 2.28 Hz, 1H, ArH), 7.43-7.46 (m, 2H, ArH), 7.53 (dd, ^2J = 8.24 Hz, ^3J = 1.36 Hz, 1H, ArH), 7.56-7.60 (m, 1H, ArH), 7.88 (d, J = 8.68 Hz, 1H, ArH), 8.15 (s, 1H, C2H), 8.37 (s, 1H, C5H); ^{13}C NMR ($CDCl_3$ + TFA, 100 MHz): δ 18.8 (CH_3), 109.8, 110.4, 111.7, 114.4, 116.0, 117.0, 118.6, 119.3, 121.2, 122.0, 124.1, 124.8, 126.7, 127.2, 128.9, 131.6, 132.9, 133.9, 141.1, 148.2, 152.9, 153.7, 154.2, 155.1, 155.7 (ArC), 163.7 (C=O); MS (EI): m/z 478.2 (M^++1); Anal. Calcd for: $C_{28}H_{19}N_3O_5$: C, 70.43; H, 4.01; N, 8.80. Found: C, 70.61; H, 3.89; N, 8.63

Spectral data of 1,1'-(4,4'-(8-(4'-methyl-2'-oxo-2*H*-chromen-7'-yloxy)imidazo[1,2-*a*]pyrazin-3,6-diyl)bis(4,1-phenylene)diethanone (19b): White solid; Yield: 54%; mp >300 °C; ^{1}H NMR ($CDCl_3$ + TFA, 400 MHz): δ 2.55 (d, J = 0.92 Hz, 3H, CH_3), 2.64 (s, 3H, CH_3), 2.75 (s, 3H, CH_3), 6.42 (d, J = 1.40 Hz, 1H, C3'H), 7.44 (dd, ^2J = 8.72 Hz, ^3J = 2.28 Hz, 1H, C5'H), 7.62 (d, J = 2.28 Hz, 1H, C8'H), 7.79 (d, J = 8.24 Hz, 3H, ArH), 7.83 (d, J = 8.72 Hz, 2H, ArH), 8.03 (d, J = 8.72 Hz, 2H, ArH), 8.18 (s, 1H, C2H), 8.27 (d, J = 8.28 Hz, 2H, ArH), 8.49 (s, 1H, C5H); ^{13}C NMR ($CDCl_3$ + TFA, 100 MHz): δ 18.9 (CH_3), 26.6 (CH_3), 26.7 (CH_3), 109.7, 110.2, 114.4, 118.1, 118.4, 126.2, 126.6, 127.5, 128.6, 128.7, 129.0, 129.2, 129.3, 129.4, 130.0, 137.7, 138.1, 138.5, 140.1, 150.2, 153.5, 153.6, 153.7 (ArC), 162.2 (C=O), 198.1 (C=O), 199.0 (C=O); MS (EI): m/z 530.2 (M^++1); Anal. Calcd for $C_{32}H_{23}N_3O_5$: C, 72.58; H, 4.38; N, 7.94. Found: C, 72.71; H, 4.22; N, 7.84.



Typical procedure for synthesis of unsymmetrical hybrids (20-30)

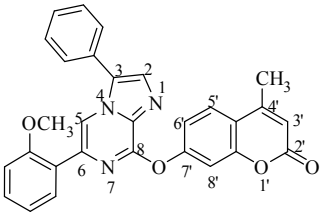
Monoarylated imidazo[1,2-*a*]pyrazine-coumarin hybrid was dissolved in a mixture of 1,2-DME : water (9:1) in a sealed tube. Boronic acid (1 eq.) and K_2CO_3 (1.1 eq.) were added and purged the reaction mixture with nitrogen. Then, $Pd(PPh_3)_4$ (5mol%) was added with continued nitrogen purging, sealed the vial and refluxed for 6-8 h. Completion of reaction was determined by TLC. The mixture was extracted with chloroform and water. Chloroform layer was dried over sodium

sulphate to obtain crude product which was further purified by column chromatography using chloroform: ethylacetate / chloroform: methanol as eluents.

Spectral data of 7'-(6-(2-methoxyphenyl)-3-(thiophen-2-yl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (20): Off White solid; Yield: 64%; mp 221-223 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.49 (d, J = 1.36 Hz, 3H, CH_3), 3.96 (s, 3H, OCH_3), 6.30 (d, J = 0.92 Hz, 1H, C3'H), 6.98-7.01 (m, 2H, ArH), 7.28-7.34 (m, 2H, ArH), 7.41 (dd, ^2J = 8.72 Hz, ^3J = 2.28 Hz, 1H, C5'H), 7.44 (dd, ^2J = 3.64 Hz, ^3J = 0.92 Hz, 1H, ArH), 7.51 (d, J = 2.28 Hz, 1H, C8'H), 7.55 (dd, ^2J = 5.04 Hz, ^3J = 0.92 Hz, 1H, ArH), 7.69 (d, J = 8.72 Hz, 1H, ArH), 7.82 (dd, ^2J = 8.24 Hz, ^3J = 1.60 Hz, 1H, ArH), 7.91 (s, 1H, C2H), 9.12 (s, 1H, C5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.8 (CH_3), 55.7 (OCH_3), 110.3, 111.2, 114.1, 114.7, 117.2, 118.2, 121.1, 123.1, 123.9, 125.2, 126.5, 126.7, 128.0, 128.9, 129.7, 130.1, 132.5, 133.5, 134.2, 151.2, 152.2, 154.2, 155.3, 156.7 (ArC), 160.8 (C=O); MS (EI): m/z 482.1 (M^++1); Anal. Calcd for $C_{27}H_{19}N_3O_4S$: C, 67.35; H, 3.98; N, 8.73; S, 6.66. Found: C, 67.63; H, 4.10; N, 8.61; S, 6.51.

Spectral data of 7'-(3-(furan-2-yl)-6-(2-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (21): Off White solid; Yield: 52%; mp 204-205 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.49 (s, 3H, CH_3), 3.99 (s, 3H, OCH_3), 6.30 (d, J = 1.36 Hz, 1H, C3'H), 6.64 (q, J = 1.62 Hz, 1H, ArH), 6.78 (d, J = 3.68 Hz, 1H, ArH), 6.98-7.02 (m, 2H, ArH), 7.30-7.35 (m, 1H, ArH), 7.41 (dd, ^2J = 8.72 Hz, ^3J = 2.32 Hz, 1H, C5'H), 7.52 (d, J = 2.32 Hz, 1H, C8'H), 7.64 (d, J = 1.84 Hz, 1H, ArH), 7.68 (d, J = 8.68 Hz, 1H, ArH), 7.81 (dd, ^2J = 7.80 Hz, ^3J = 1.84 Hz, 1H, ArH), 7.99 (s, 1H, C2H), 9.19 (s, 1H, C5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.8 (CH_3), 55.7 (OCH_3), 107.7, 110.3, 111.3, 111.7, 114.1, 115.7, 117.2, 118.2, 120.9, 121.1, 124.1, 125.2, 129.7, 130.2, 132.1, 133.0, 133.6, 142.7, 143.6, 151.1, 152.2, 154.2, 155.3, 156.8 (ArC), 160.8 (C=O); MS (EI): m/z 466.1 (M^++1); Anal. Calcd for $C_{27}H_{19}N_3O_5$: C, 69.67; H, 4.11; N, 9.03. Found: C, 69.85; H, 4.01; N, 9.18.

Spectral data of 7'-(6-(2-methoxyphenyl)-3-phenylimidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-



chromen-2'-one (22): White solid; Yield: 69%; mp 194-195 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.49 (d, J = 1.40 Hz, 3H, CH_3), 3.90 (s, 3H, OCH_3), 6.29 (d, J = 0.92 Hz, 1H, C3'H), 6.95-7.00 (m, 2H, ArH), 7.28-7.32 (m, 1H, ArH), 7.42 (dd, ^{2}J = 8.72 Hz, ^{3}J = 2.28 Hz, 1H, C5'H), 7.48-7.50 (m, 1H, ArH), 7.52 (d, J = 2.28 Hz, 1H, C8'H), 7.59 (t, J = 7.58 Hz, 2H, ArH), 7.67-7.70 (m, 3H, ArH), 7.81 (dd, ^{2}J = 7.80 Hz, ^{3}J = 1.82 Hz, 1H, ArH), 7.86 (s, 1H, C2H), 8.99 (s, 1H, C5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.7 (CH_3), 55.6 (OCH_3), 110.3, 111.2, 114.0, 114.3, 117.2, 118.2, 121.1, 124.1, 125.2, 128.0, 128.3, 128.9, 129.2, 129.3, 129.6, 130.1, 132.5, 133.2, 133.6, 151.4, 152.1, 154.3, 155.4, 156.7 (ArC), 160.8 (C=O); MS (EI): m/z 476.2 (M^{+}+1); Anal. Calcd for $C_{29}H_{21}N_3O_4$: C, 73.25; H, 4.45; N, 8.84. Found: C, 73.49; H, 4.62; N, 8.99.

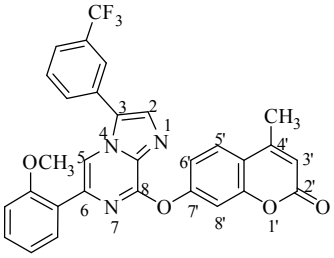
Spectral data of 7'-(6-(2-methoxyphenyl)-3-*m*-tolylimidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (23): White solid; Yield: 72%; mp 202-203 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.49 (d, J = 1.36 Hz, 3H, CH_3), 2.50 (s, 3H, CH_3), 3.92 (s, 3H, OCH_3), 6.30 (d, J = 1.36 Hz, 1H, C3'H), 6.96-7.00 (m, 2H, ArH), 7.28-7.32 (m, 2H, ArH), 7.42 (dd, ^{2}J = 8.72 Hz, ^{3}J = 2.28 Hz, 1H, C5'H), 7.48 (d, J = 5.48 Hz, 2H, ArH), 7.50 (s, 1H, ArH), 7.52 (d, J = 2.28 Hz, 1H, C8'H), 7.69 (d, J = 8.72 Hz, 1H, ArH), 7.81 (dd, ^{2}J = 7.32 Hz, ^{3}J = 1.60 Hz, 1H, ArH), 7.85 (s, 1H, C2H), 9.00 (s, 1H, C5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.8 (CH_3), 21.5 (CH_3), 55.5 (OCH_3), 110.3, 111.1, 114.0, 114.4, 117.2, 118.2, 121.1, 124.1, 125.0, 125.2, 128.2, 128.5, 129.1, 129.3, 129.6, 129.7, 130.1, 132.4, 132.9, 133.6, 139.1, 151.3, 152.2, 154.2, 155.4, 156.6 (ArC), 160.9 (C=O); MS (EI): m/z 490.2 (M^{+}+1); Anal. Calcd for $C_{30}H_{23}N_3O_4$: C, 73.61; H, 4.74; N, 8.58. Found: C, 73.72; H, 4.82; N, 8.33.

Spectral data of 7'-(3-(4-ethylphenyl)-6-(2-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (24): Off White solid; Yield: 55%; mp 179-180 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.33 (t, J = 7.56 Hz, 3H, CH_3), 2.48 (d, J = 0.92 Hz, 3H, CH_3), 2.77 (q, J = 7.56 Hz, 2H, CH_2), 3.91 (s, 3H, OCH_3), 6.29 (d, J = 1.20 Hz, 1H, C3'H), 6.95-7.00 (m, 2H, ArH), 7.27-7.31 (m, 1H, ArH), 7.39-7.42 (m, 3H, ArH), 7.52 (d, J = 2.28 Hz, 1H, C8'H), 7.59 (d, J = 8.24 Hz, 2H, ArH), 7.68 (d, J = 8.72 Hz, 1H, ArH), 7.77-7.82

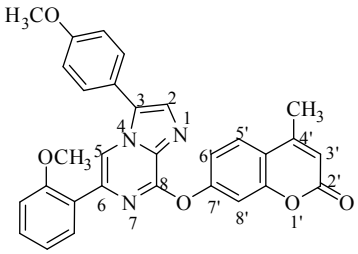
(m, 1H, ArH), 7.83 (s, 1H, C2H), 8.97 (s, 1H, C5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 15.4 (CH_3), 18.8 (CH_3), 28.7 (CH_2), 55.6 (OCH_3), 110.3, 111.1, 114.0, 114.4, 117.2, 118.2, 121.1, 124.5, 125.2, 127.9, 128.7, 130.1, 130.9, 131.4, 132.3, 133.0, 133.4, 134.5, 151.3, 152.2, 154.2, 155.4, 156.7 (ArC), 160.9 (C=O); MS (EI): m/z 504.2 (M^++1); Anal. Calcd for $C_{31}H_{25}N_3O_4$: C, 73.94; H, 5.00; N, 8.34; Found: C, 74.16; H, 4.89; N, 8.17.

Spectral data of 7'-(3-(4-fluorophenyl)-6-(2-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (25): White solid; Yield: 75%; mp 235-237 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.49 (d, J = 1.36 Hz, 3H, CH_3), 3.90 (s, 3H, OCH_3), 6.30 (d, J = 0.92 Hz, 1H, C3'H), 6.96-7.01 (m, 2H, ArH), 7.27-7.33 (m, 3H, ArH), 7.42 (dd, ^2J = 8.72 Hz, ^3J = 2.28 Hz, 1H, C5'H), 7.52 (d, J = 2.32 Hz, 1H, C8'H), 7.63-7.66 (m, 2H, ArH), 7.69 (d, J = 8.72 Hz, 1H, ArH), 7.81 (dd, ^2J = 7.80 Hz, ^3J = 1.84 Hz, 1H, ArH), 7.83 (s, 1H, C2H), 8.89 (s, 1H, C5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.8 (CH_3), 55.6 (OCH_3), 110.3, 111.1, 114.0, 114.1, 116.4, 116.6, 117.2, 118.2, 121.1, 123.9, 124.4, 125.2, 128.1, 129.7, 130.0, 130.1, 132.5, 133.2, 133.6, 151.4, 152.2, 154.2, 155.3, 156.6, 160.8 (C=O), 161.7, 164.1 (ArC); MS (EI): m/z 494.2 (M^++1); Anal. Calcd for $C_{29}H_{20}FN_3O_4$: C, 70.58; H, 4.08; N, 8.51. Found: C, 70.69; H, 3.97; N, 8.32.

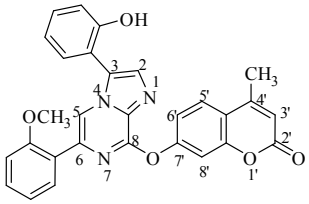
Spectral data of 7'-(3-(4-chlorophenyl)-6-(2-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (26): White solid; Yield: 65%; mp 243-245 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.49 (d, J = 1.36 Hz, 3H, CH_3), 3.92 (s, 3H, OCH_3), 6.30 (d, J = 1.40 Hz, 1H, C3'H), 6.97-7.01 (m, 2H, ArH), 7.29-7.33 (m, 1H, ArH), 7.41 (dd, ^2J = 8.68 Hz, ^3J = 2.28 Hz, 1H, C5'H), 7.51 (d, J = 2.28 Hz, 1H, C8'H), 7.55-7.58 (m, 2H, ArH), 7.60-7.63 (m, 2H, ArH), 7.69 (d, J = 8.72 Hz, 1H, ArH), 7.81 (dd, ^2J = 7.76 Hz, ^3J = 1.82 Hz, 1H, ArH), 7.85 (s, 1H, C2H), 8.92 (s, 1H, C5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.8 (CH_3), 55.7 (OCH_3), 110.3, 111.2, 114.0, 114.1, 117.3, 118.2, 121.2, 123.9, 125.2, 126.8, 128.0, 129.2, 129.6, 129.7, 130.1, 132.6, 133.4, 133.8, 134.9, 151.4, 152.2, 154.2, 155.3, 156.6 (ArC), 160.8 (C=O); MS (EI): m/z 510.1 (M^++1); Anal. Calcd for $C_{29}H_{20}ClN_3O_4$: C, 68.30; H, 3.95; N, 8.24. Found: C, 68.61; H, 4.06; N, 8.16.

Spectral data of 7'-(6-(2-methoxyphenyl)-3-(3-(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (27): 

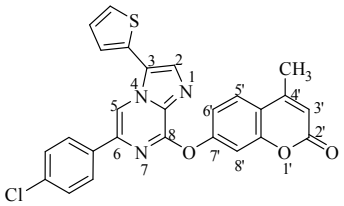
White solid; Yield: 55%; mp 204-206 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.49 (d, J = 0.92 Hz, 3H, CH_3), 3.92 (s, 3H, OCH_3), 6.31 (d, J = 0.68 Hz, 1H, C3'H), 6.97-7.00 (m, 2H, ArH), 7.28-7.33 (m, 1H, ArH), 7.42 (dd, ^{2}J = 8.68 Hz, ^{3}J = 2.30 Hz, 1H, C5'H), 7.50 (d, J = 2.28 Hz, 1H, C8'H), 7.70 (d, J = 8.68 Hz, 1H, ArH), 7.73-7.78 (m, 2H ArH), 7.84 (dd, ^{2}J = 8.24 Hz, ^{3}J = 1.84 Hz, 1H, ArH), 7.86 (d, J = 7.32 Hz, 1H, ArH), 7.92 (s, 1H, ArH), 7.98 (s, 1H, C2H), 9.01 (s, 1H, C5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.8 (CH_3), 55.4 (OCH_3), 110.3, 111.1, 113.9, 114.1, 117.3, 118.2, 121.1, 123.6, 124.1, 124.2, 125.1, 125.3, 125.5, 125.6, 127.6, 129.3, 129.8, 130.0, 131.5, 131.6, 131.9, 132.9, 133.5, 134.2, 151.5, 152.1, 154.2, 155.2, 156.7 (ArC), 160.8 (C=O); MS (EI): m/z 544.2 (M^{+}+1); Anal. Calcd for $C_{30}H_{20}F_3N_3O_4$: C, 66.30; H, 3.71; N, 7.73. Found: C, 66.03; H, 3.60; N, 7.66.

Spectral data of 7'-(6-(2-methoxyphenyl)-3-(4-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (28): 

White solid; Yield: 64%; mp 239-241 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.49 (d, J = 1.40 Hz, 3H, CH_3), 3.90 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 6.30 (d, J = 0.92 Hz, 1H, C3'H), 6.95-7.00 (m, 2H, ArH), 7.11 (d, J = 9.16 Hz, 2H, ArH), 7.28-7.32 (m, 1H, ArH), 7.42 (dd, ^{2}J = 8.72 Hz, ^{3}J = 2.30 Hz, 1H, C5'H), 7.52 (d, J = 2.28 Hz, 1H, C8'H), 7.59 (d, J = 8.68 Hz, 2H, ArH), 7.68 (d, J = 8.72 Hz, 1H, ArH), 7.78-7.80 (m, 2H, ArH, C2H), 8.91 (s, 1H, C5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.7 (CH_3), 55.4 (OCH_3), 55.6 (OCH_3), 110.2, 111.1, 114.0, 114.2, 114.6, 117.1, 118.2, 120.5, 121.1, 124.1, 125.2, 129.0, 129.4, 129.5, 130.0, 132.2, 132.9, 133.1, 151.3, 152.2, 154.2, 155.4, 156.6, 160.0 (ArC), 160.8 (C=O); MS (EI): m/z 506.2 (M^{+}+1); Anal. Calcd for $C_{30}H_{23}N_3O_5$: C, 71.28; H, 4.59; N, 8.31. Found: C, 71.46; H, 4.70; N, 8.18.

Spectral data of 7'-(3-(2-hydroxyphenyl)-6-(2-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (29): 

White solid; Yield: 53%; mp >300 ^{o}C; ^{1}H NMR ($CDCl_3$ + TFA, 400 MHz): δ 2.58 (d, J = 0.92 Hz, 3H, CH_3), 3.85 (s, 3H, OCH_3), 6.51 (s, 1H, C3'H), 6.98-7.01 (m, 2H, ArH), 7.13-7.20 (m, 2H, ArH), 7.37-7.41 (m, 1H, ArH), 7.46 (d, J = 7.76 Hz, 2H, ArH), 7.53--7.58 (m, 2H, ArH), 7.72 (dd, ^{2}J = 8.24 Hz, ^{3}J = 1.60 Hz, 1H, ArH), 7.85 (d, J = 8.72 Hz, 1H, ArH), 8.10 (s, 1H, C2H), 8.86 (s, 1H, C5H); ^{13}C NMR ($CDCl_3$+TFA, 100 MHz): δ 18.9 (CH_3), 55.6 (OCH_3), 111.2, 111.6, 113.6, 115.4, 116.8, 118.4, 118.8, 121.4, 121.7, 123.2, 125.1, 126.5, 128.0, 130.2, 131.2, 131.8, 133.6, 139.1, 147.3, 153.4, 153.9, 154.4, 155.9, 157.1 (ArC), 164.6 (C=O); MS (EI): m/z 492.2 (M^{+}+1); Anal. Calcd for $C_{29}H_{21}N_3O_5$: C, 70.87; H, 4.31; N, 8.55. Found: C, 70.77; H, 4.28; N, 8.70.

Spectral data of 7'-(6-(4-chlorophenyl)-3-(thiophen-2-yl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (30): 

White solid; Yield: 61%; mp 187-189 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.52 (d, J = 0.92 Hz, 3H, CH_3), 6.32 (d, J = 1.40 Hz, 1H, C3'H), 7.28-7.30 (m, 1H, ArH), 7.33-7.40 (m, 3H, ArH), 7.42 (dd, ^{2}J = 3.68 Hz, ^{3}J = 1.38 Hz, 1H, ArH), 7.47 (d, J = 2.28 Hz, 1H, C8'H), 7.57-7.58 (m, 1H, ArH), 7.66 (d, J = 8.72 Hz, 2H, ArH), 7.71 (d, J = 8.72 Hz, 1H, ArH), 7.90 (s, 1H, C2H), 8.47 (s, 1H, C5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.8 (CH_3), 109.7, 110.5, 114.3, 117.5, 118.2, 123.1, 125.3, 127.2, 127.3, 127.3, 128.2, 129.0, 129.4, 129.9, 132.6, 133.9, 134.7, 134.8, 136.1, 152.1, 154.2, 154.9 (ArC), 160.7 (C=O); MS (EI): m/z 486.1 (M^{+}+1); Anal. Calcd for $C_{20}H_{16}ClN_3O_3S$: C, 64.26; H, 3.32; N, 8.65; S, 6.60. Found: C, 64.41; H, 3.24; N, 8.78; S, 6.43.

References

1 B. Jiang, C.-G. Yang, W.-N. Xiong and J. Wang, *Bioorg. Med. Chem.,* 2001, **9**, 1149.

2 H. Zeng, D. B. Belanger, P. J. Curran, G. W. Shipps, H. Miao, J. B. Bracken, M. A. Siddiqui, M. Malkowski and Y. Wang, *Bioorg. Med. Chem. Lett.,* 2011, **21,** 5870.

3 J. Bradac, Z. Furek, D. Janezic, S. Molan, I. Smerkolj, B. Stanovnik, M. Tisler and B. Vercek *J. Org. Chem.,* 1977, **42**, 4197.

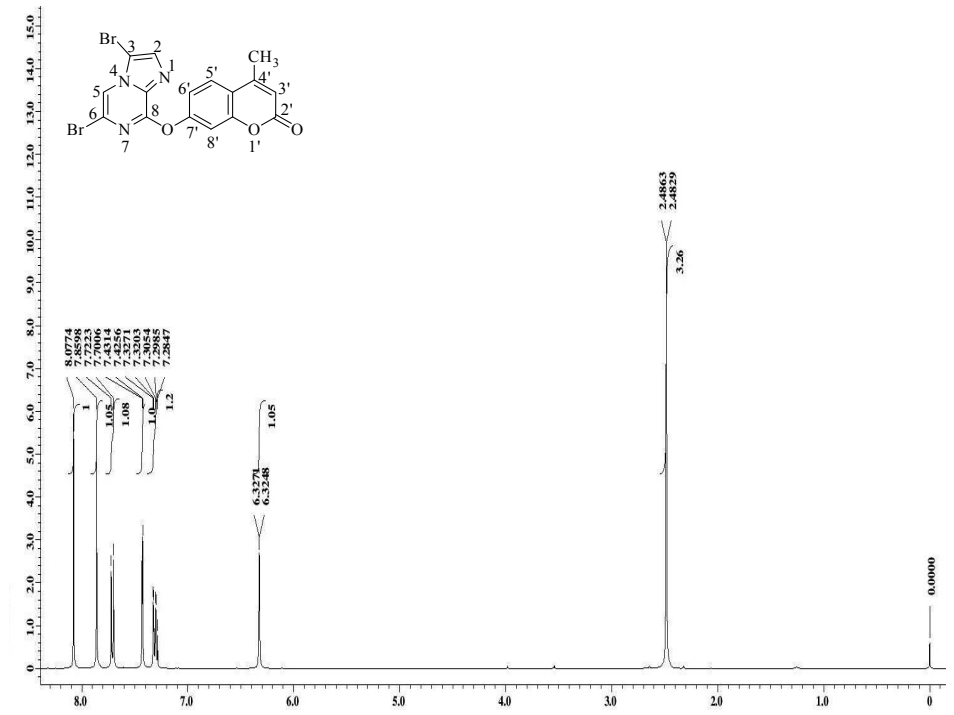


Fig S1: ^{1}H NMR spectrum of 7'-(3,6-dibromoimidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (6)

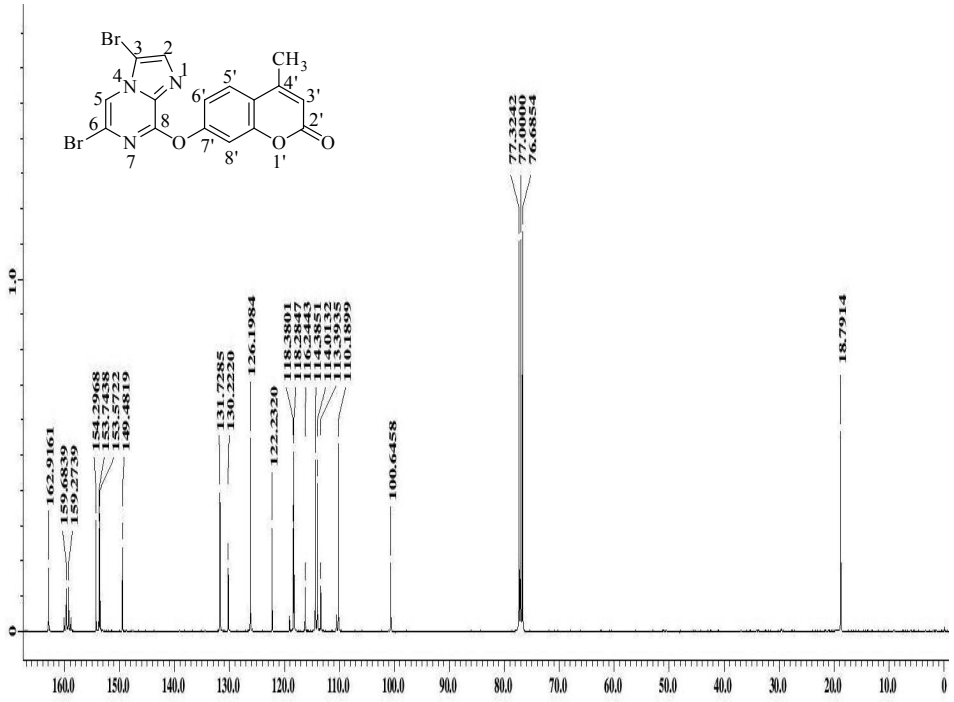


Fig S2: ^{13}C NMR spectrum of 7'-(3,6-dibromoimidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (6)

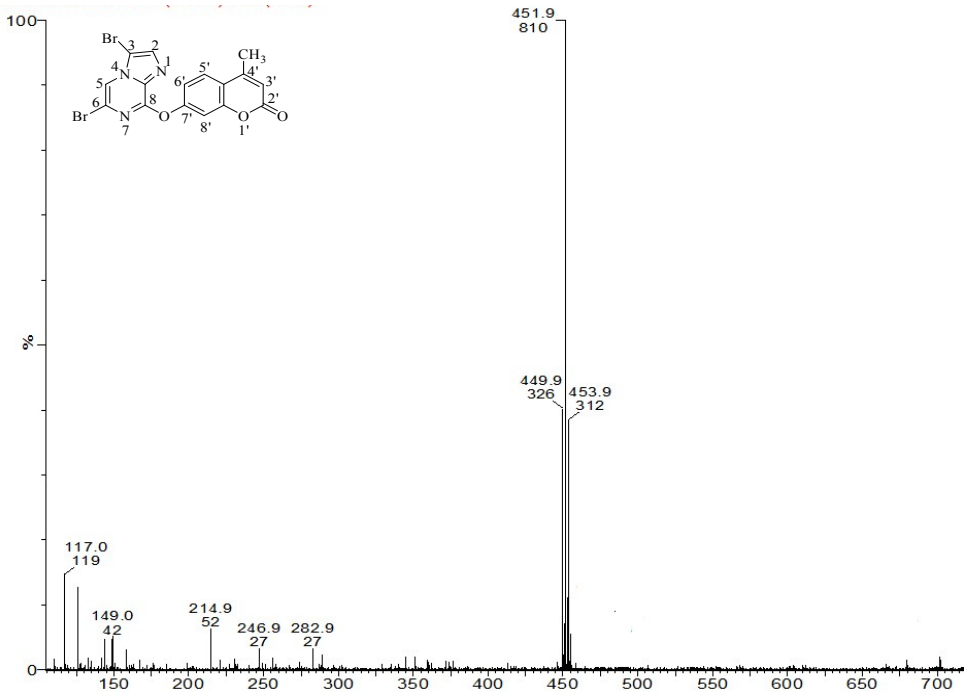


Fig S3: Mass spectrum of 7'-(3,6-dibromoimidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (6)

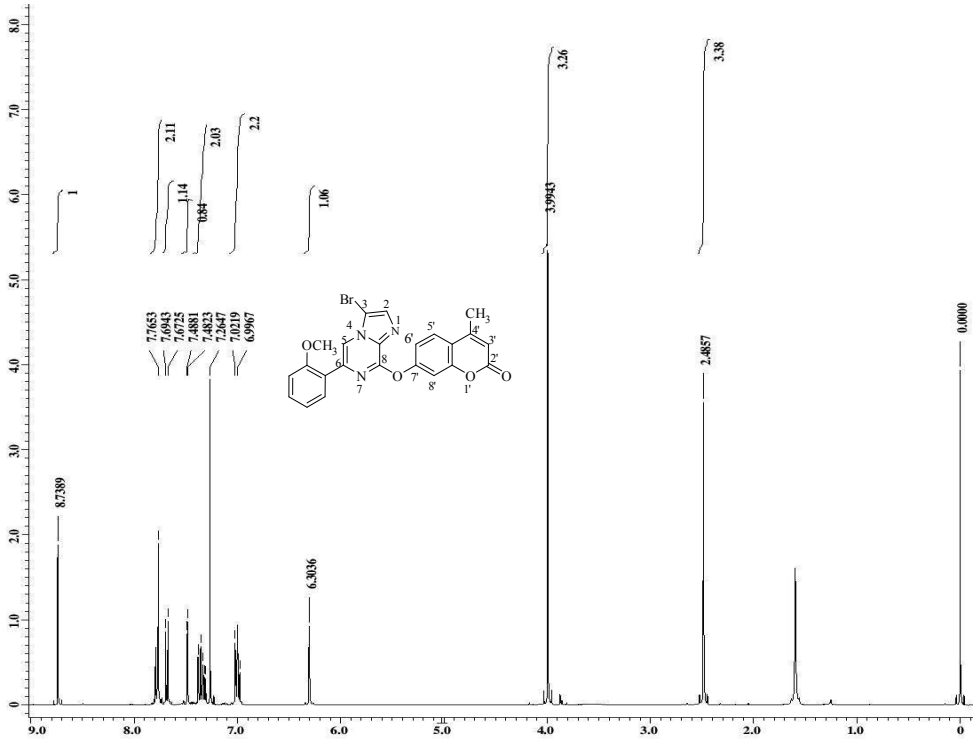


Fig S4: ^{1}H NMR spectrum of 7'-(3-bromo-6-(2-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (7a)

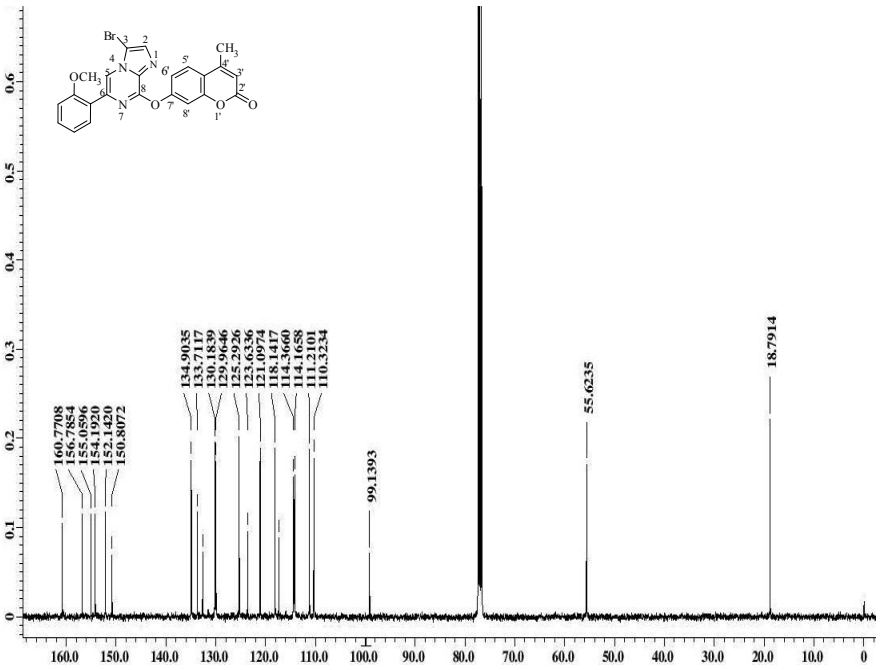


Fig S5: ^{13}C NMR spectrum of 7'-(3-bromo-6-(2-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (7a)

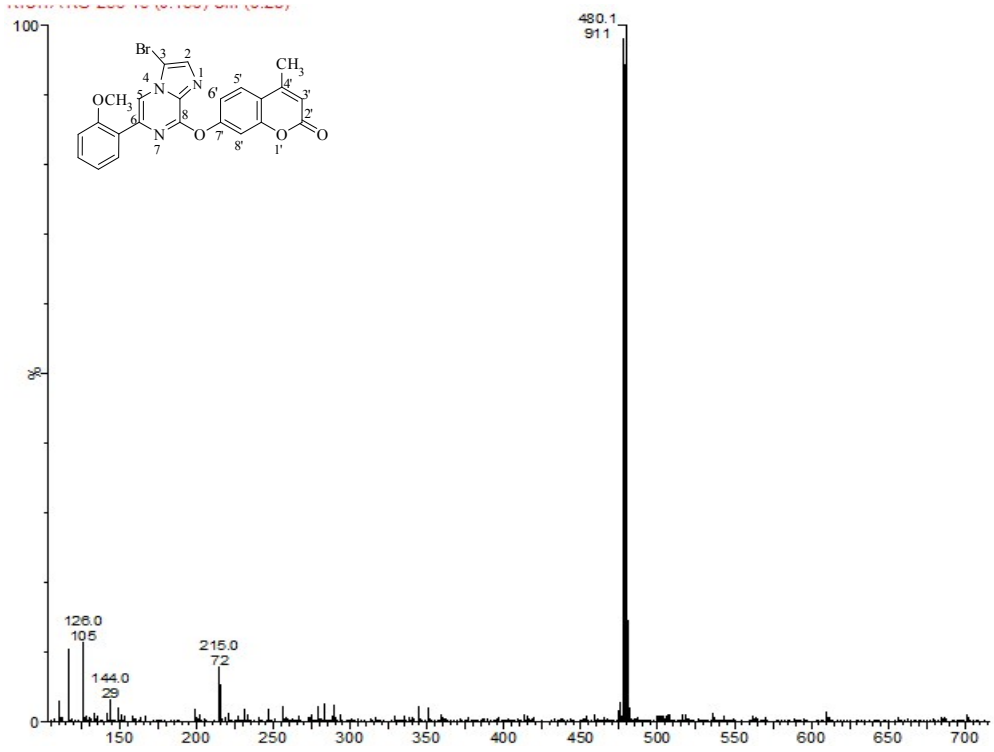


Fig S6: Mass spectrum of 7'-(3-bromo-6-(2-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (7a)

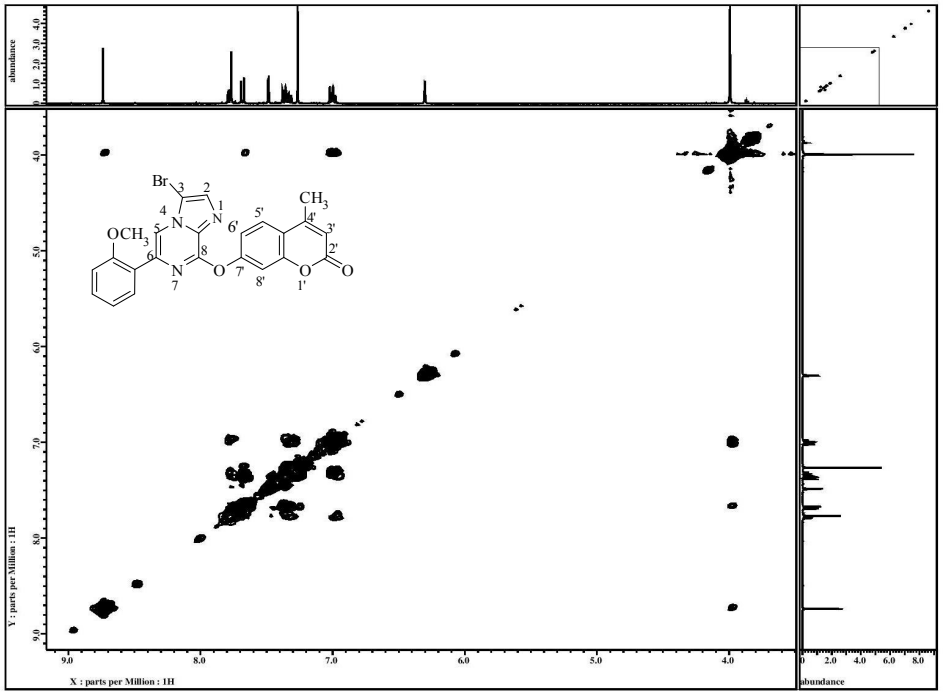


Fig S7: NOE spectrum of 7'-(3-bromo-6-(2-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (7a)

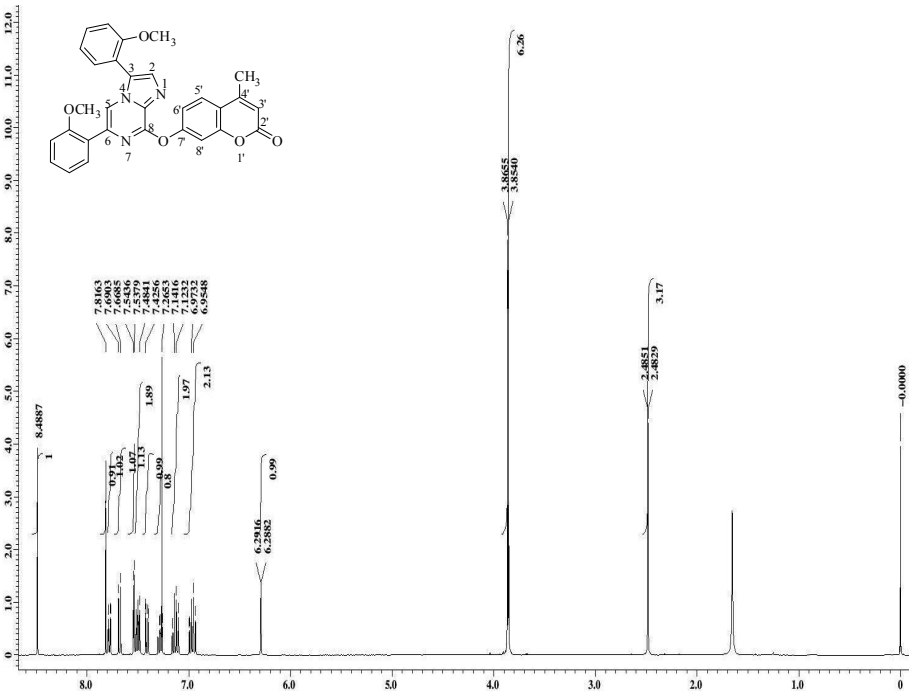


Fig S8: ^{1}H NMR spectrum of 7'-(3,6-bis(2-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (7b)

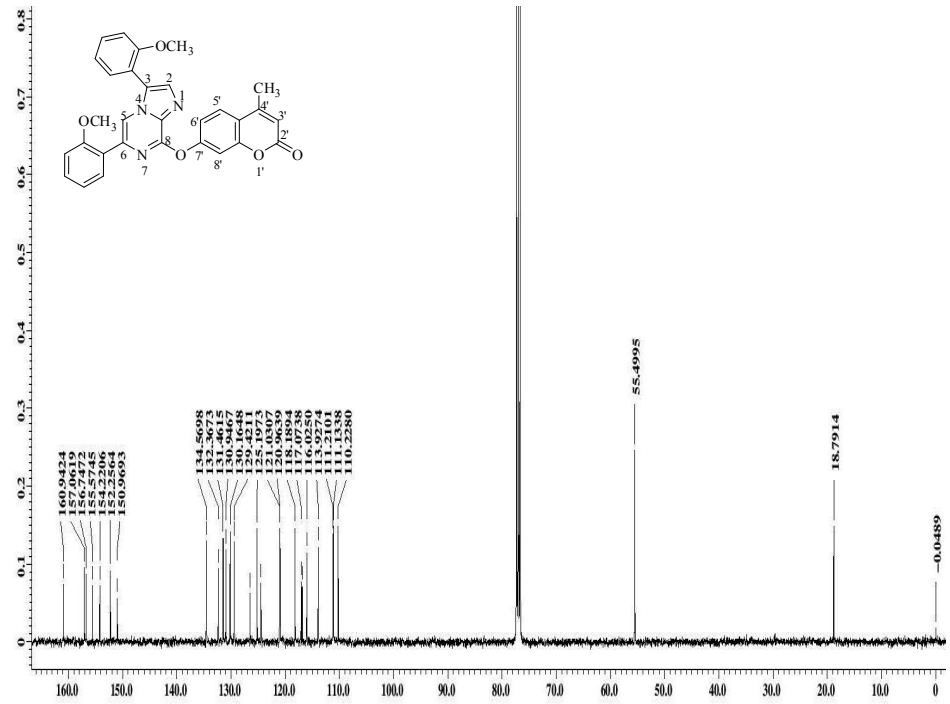


Fig S9: ^{13}C NMR spectrum of 7'-(3,6-bis(2-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (7b)

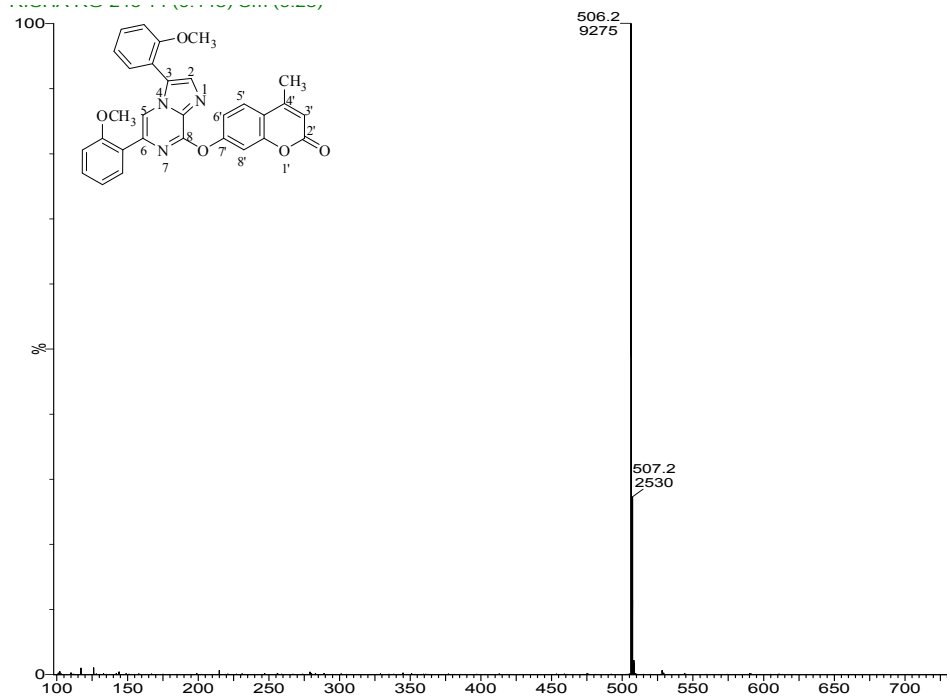


Fig S10: Mass spectrum of 7'-(3,6-bis(2-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (7b)

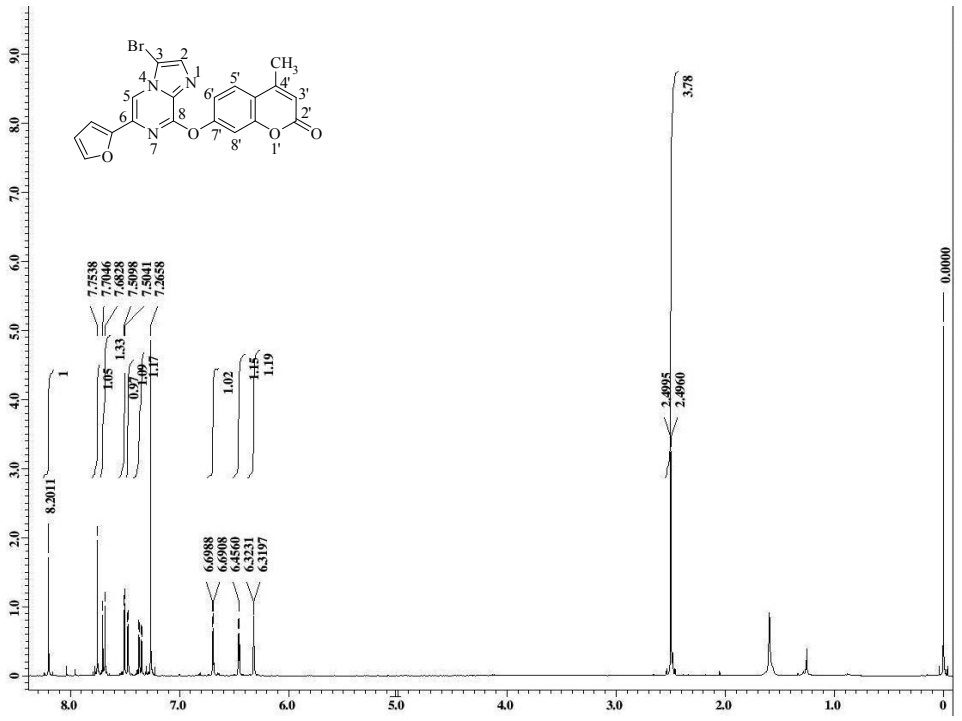


Fig S11: ^{1}H NMR spectrum of 7'-(3-bromo-6-(furan-2-yl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (8a)

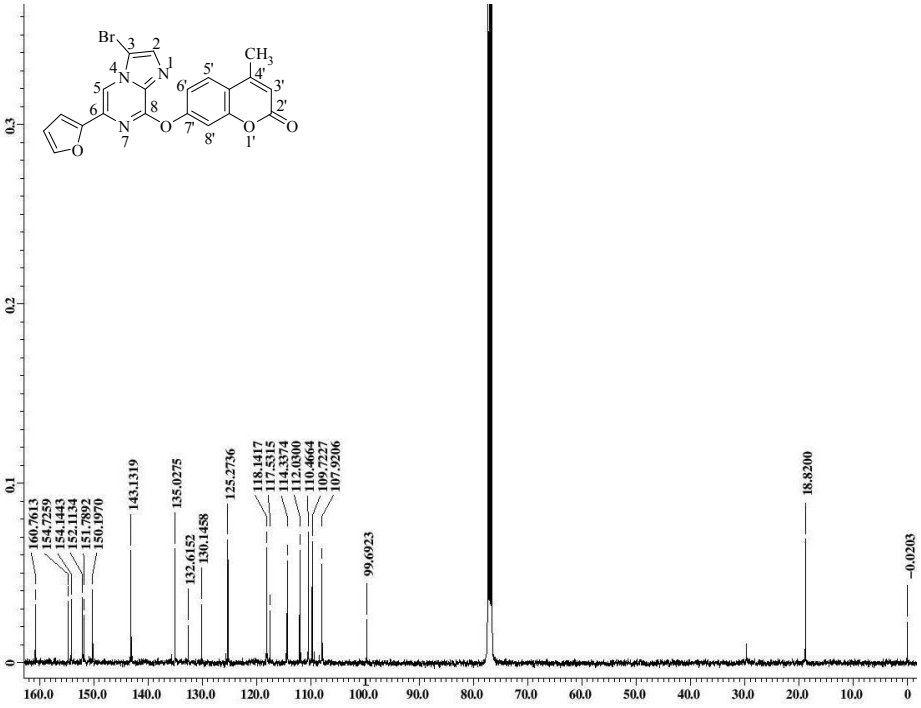


Fig S12: ^{13}C NMR spectrum of 7'-(3-bromo-6-(furan-2-yl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (8a)

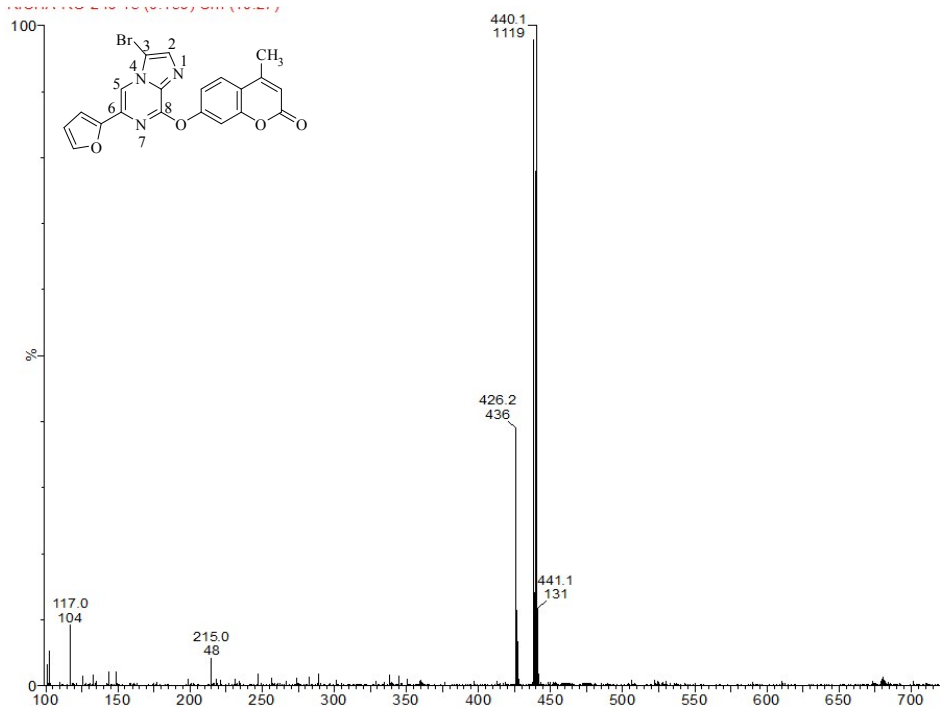


Fig S13: Mass spectrum of 7'-(3-bromo-6-(furan-2-yl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (8a)

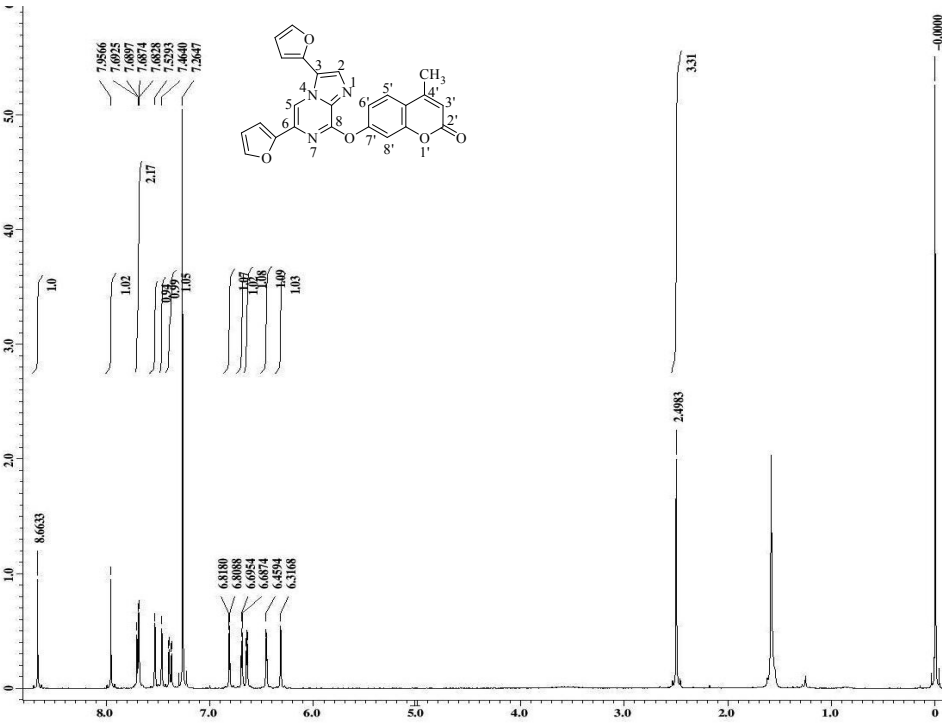


Fig S14: ^{1}H NMR spectrum of 7'-(3,6-di(furan-2-yl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (8b)

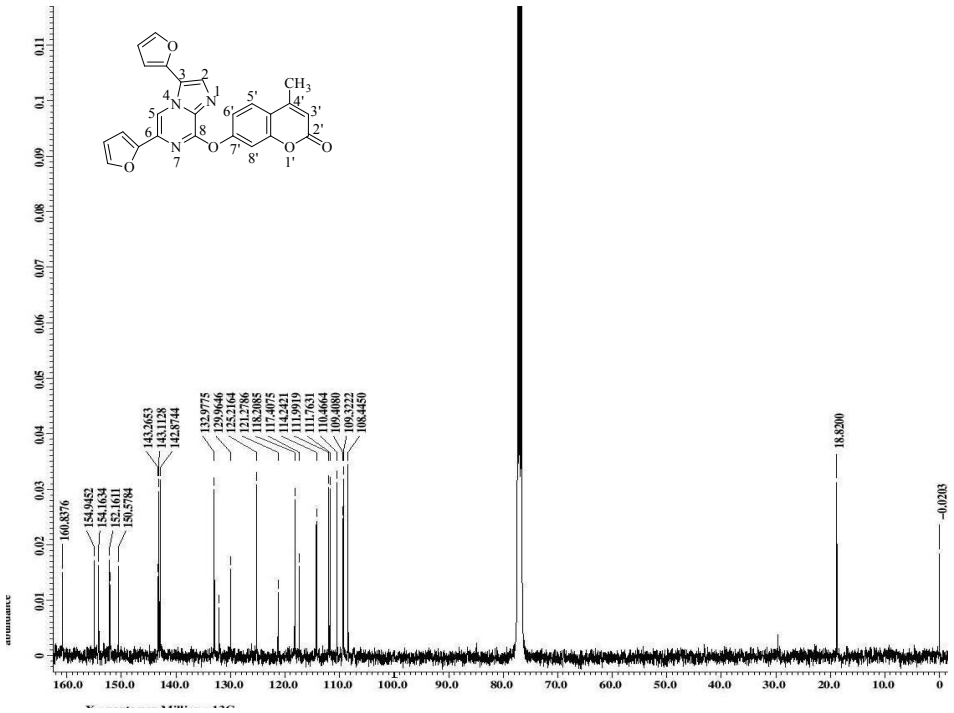


Fig S15: ^{13}C NMR spectrum of 7'-(3,6-di(furan-2-yl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (8b)

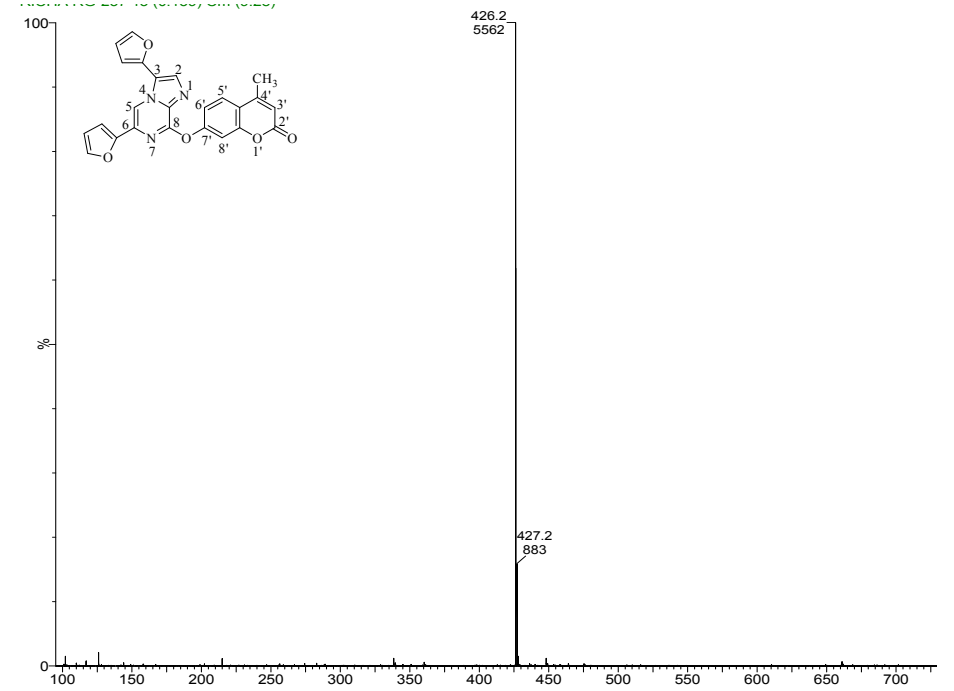


Fig S16: Mass spectrum of 7'-(3,6-di(furan-2-yl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (8b)

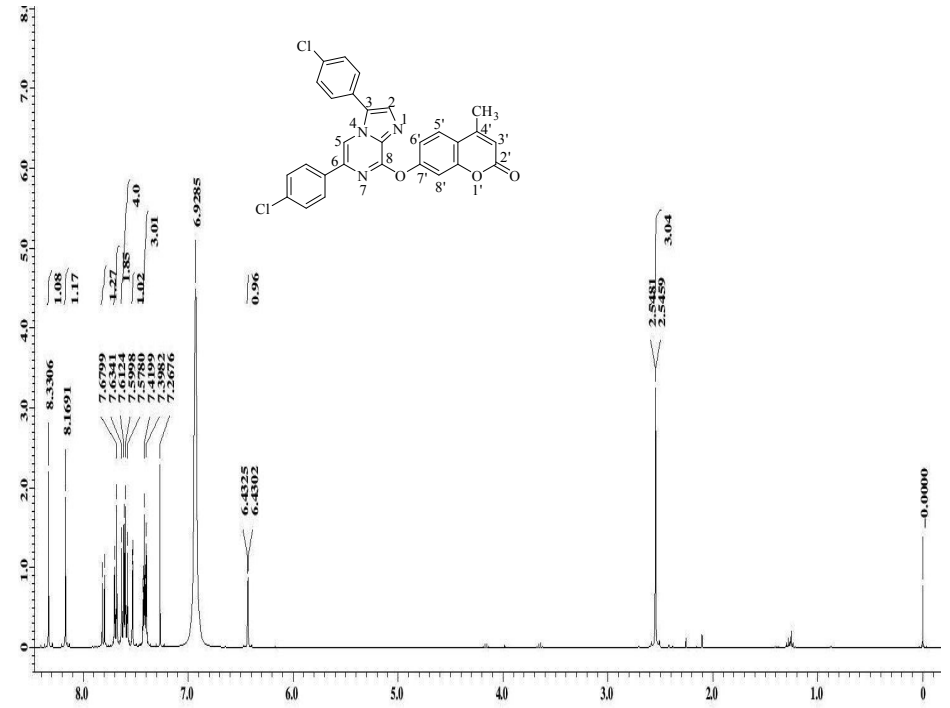


Fig S17: ^{1}H NMR spectrum of 7'-(3,6-bis(4-chlorophenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'methyl-2*H*-chromen-2'-one (9b)

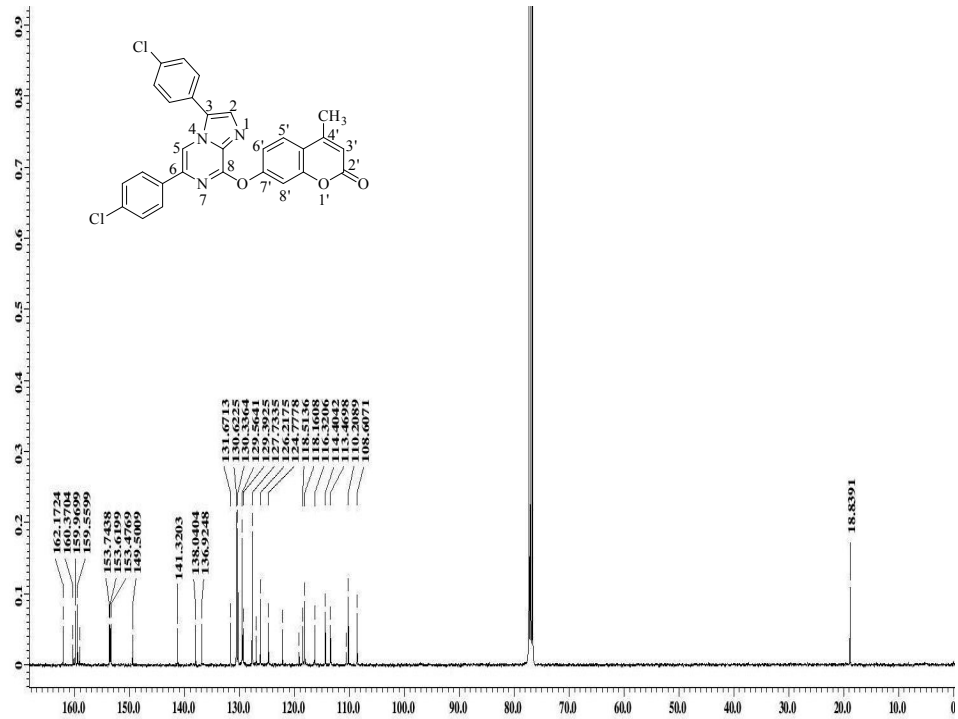


Fig S18: ^{13}C NMR spectrum of 7'-(3,6-bis(4-chlorophenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4-methyl-2*H*-chromen-2-one (9b)

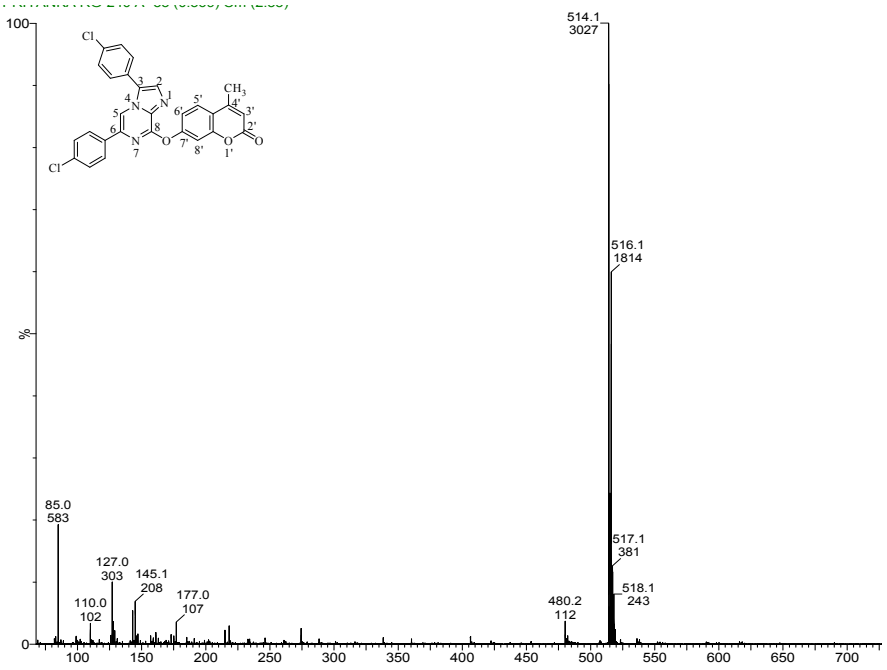


Fig S19: Mass spectrum of 7'-(3,6-bis(4-chlorophenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (9b)

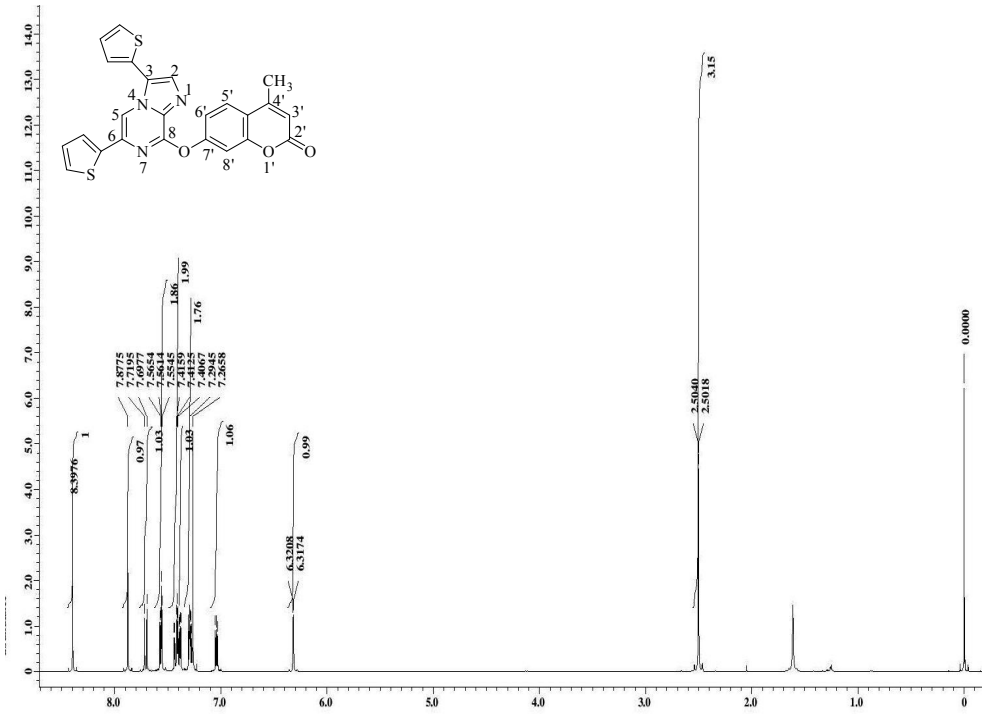


Fig S20: ^{1}H NMR spectrum of 7'-(3,6-di(thiophen-2-yl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (10b)

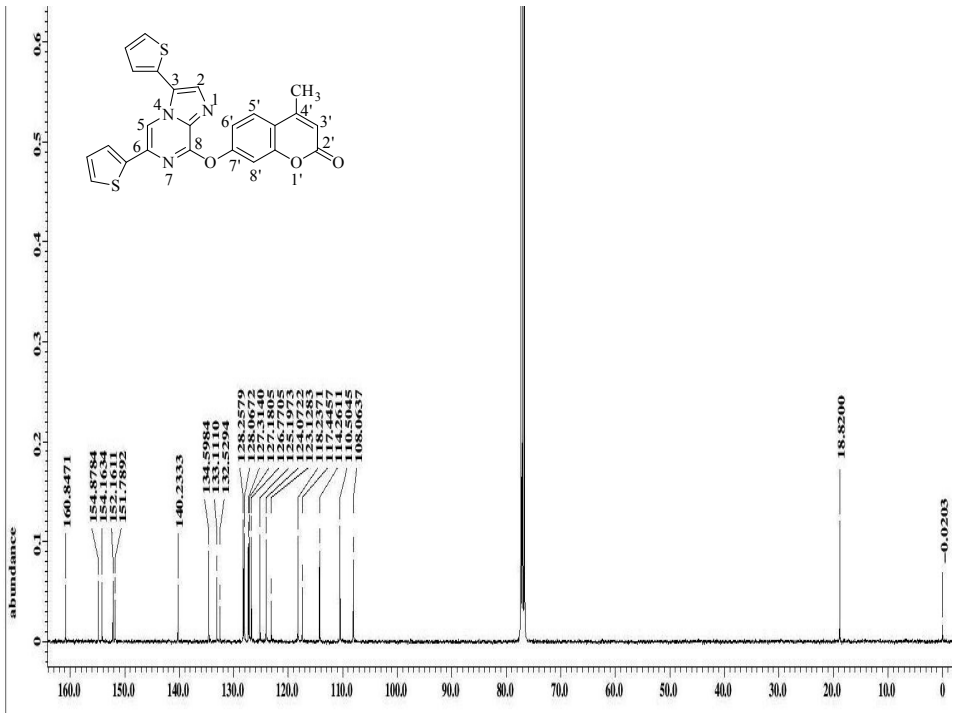


Fig S21: ^{13}C NMR spectrum of 7'-(3,6-di(thiophen-2-yl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (10b)

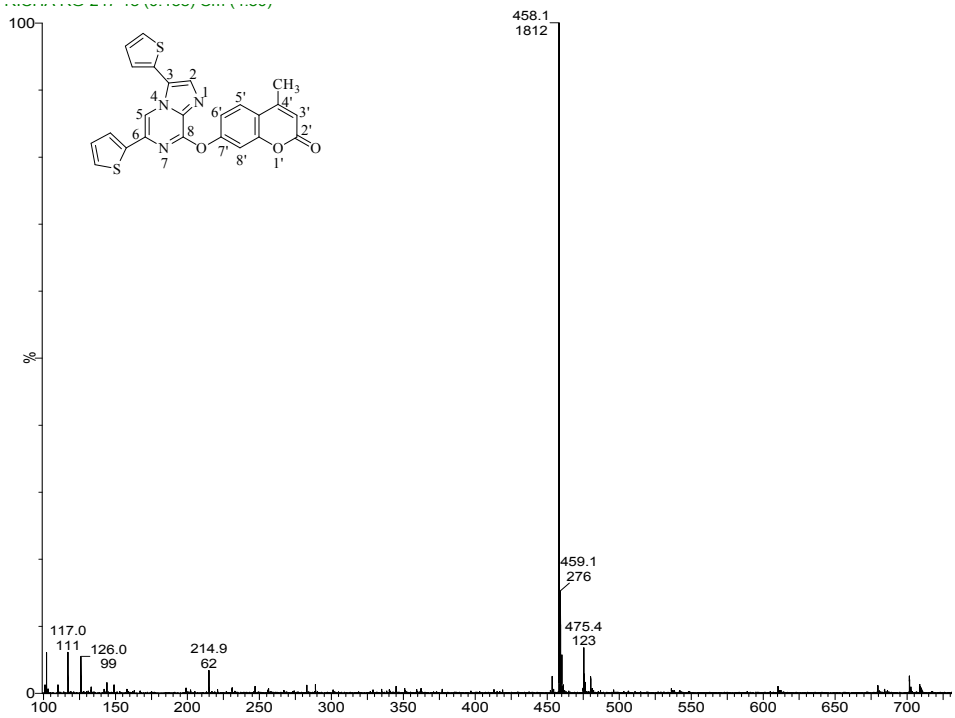


Fig S22: Mass spectrum of 7'-(3,6-di(thiophen-2-yl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (10b)

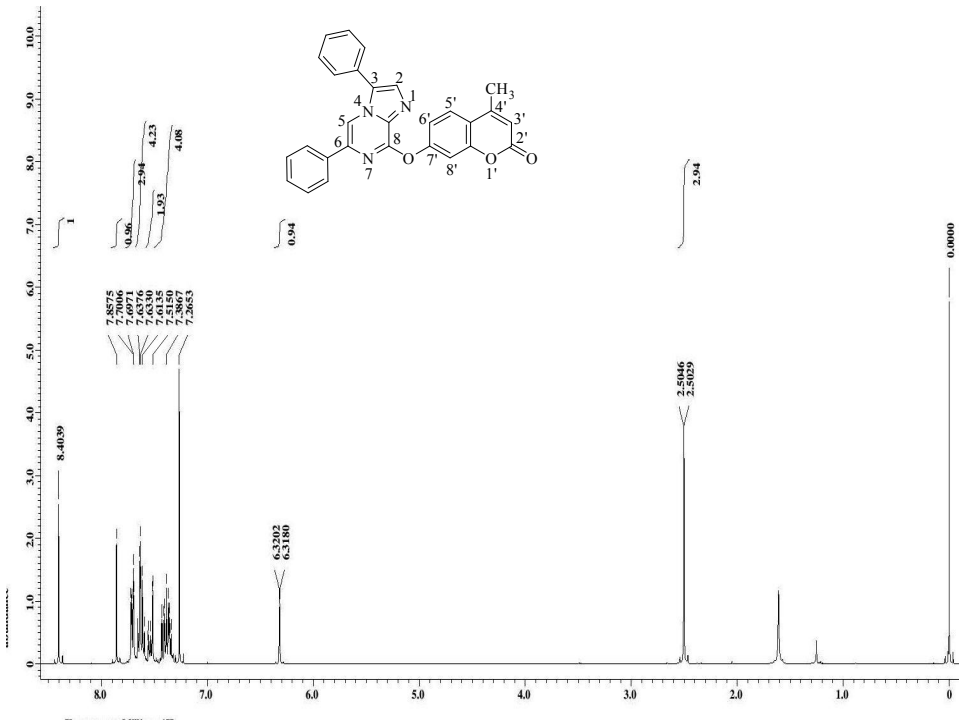


Fig S23: ^{1}H NMR spectrum of 7'-(3,6-diphenylimidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (11b)

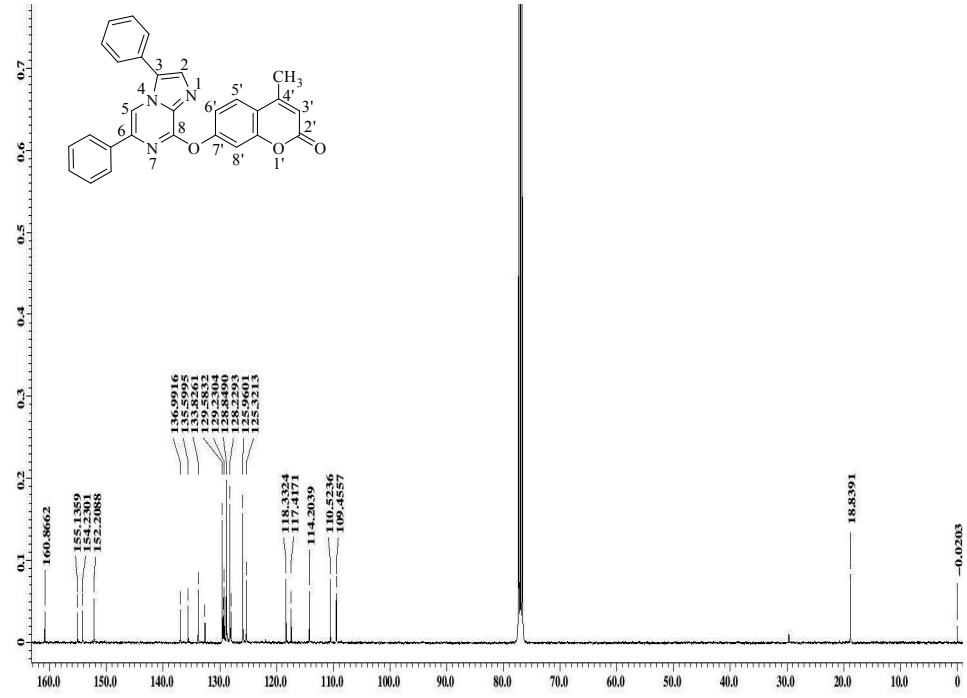


Fig S24: ^{13}C NMR spectrum of 7'-(3,6-diphenylimidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (11b)

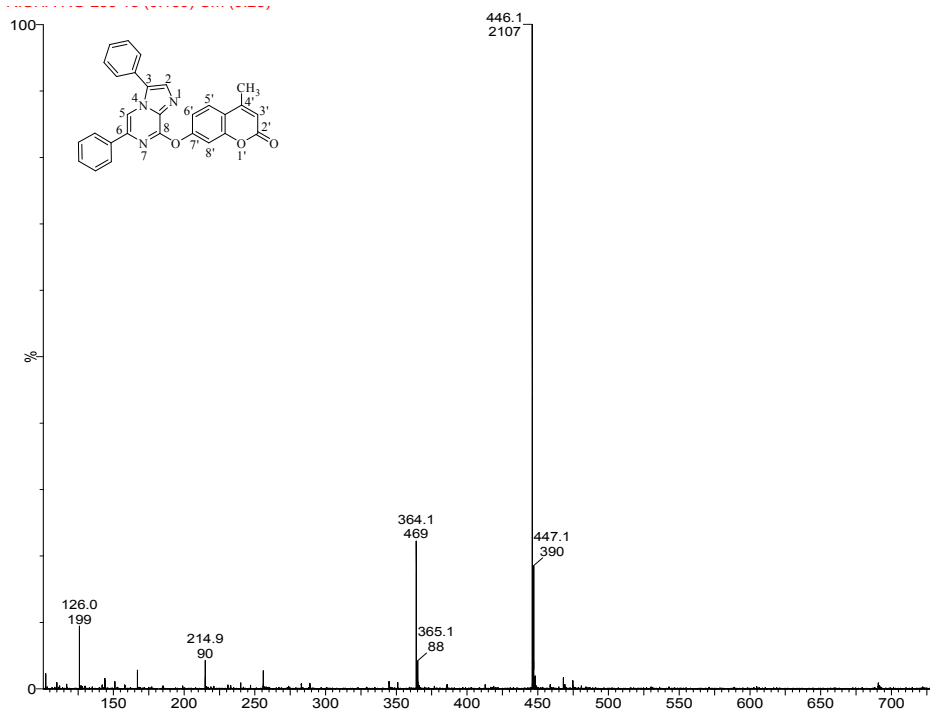


Fig S25: Mass spectrum of 7'-(3,6-diphenylimidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (11b)

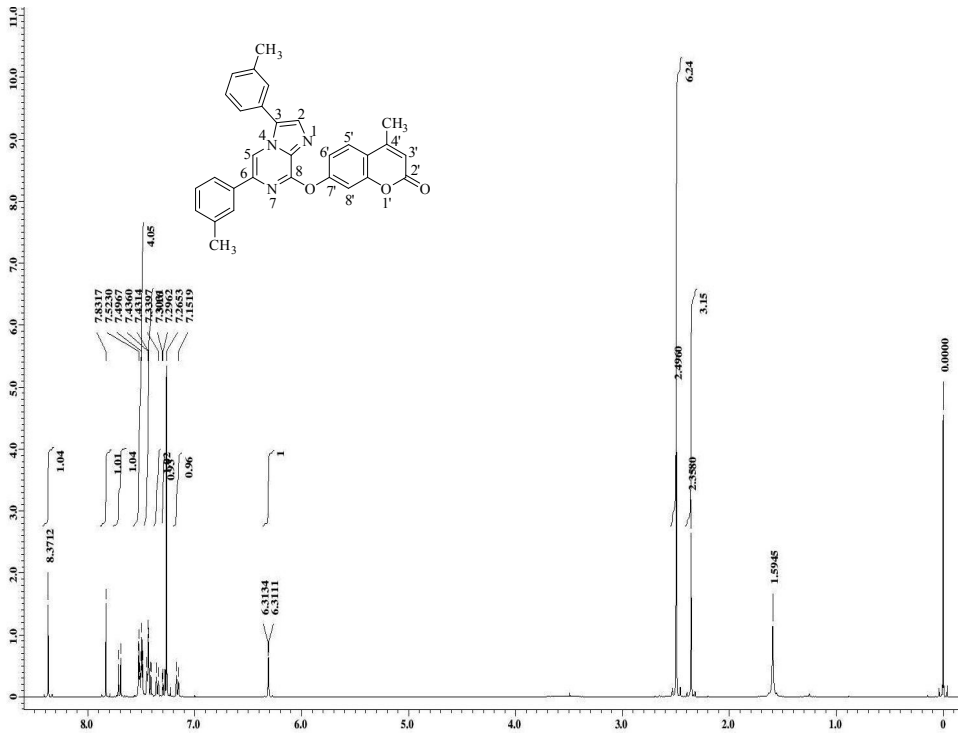


Fig S26: ^{1}H NMR spectrum of 7'-(3,6-di*m*-tolylimidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (12b)

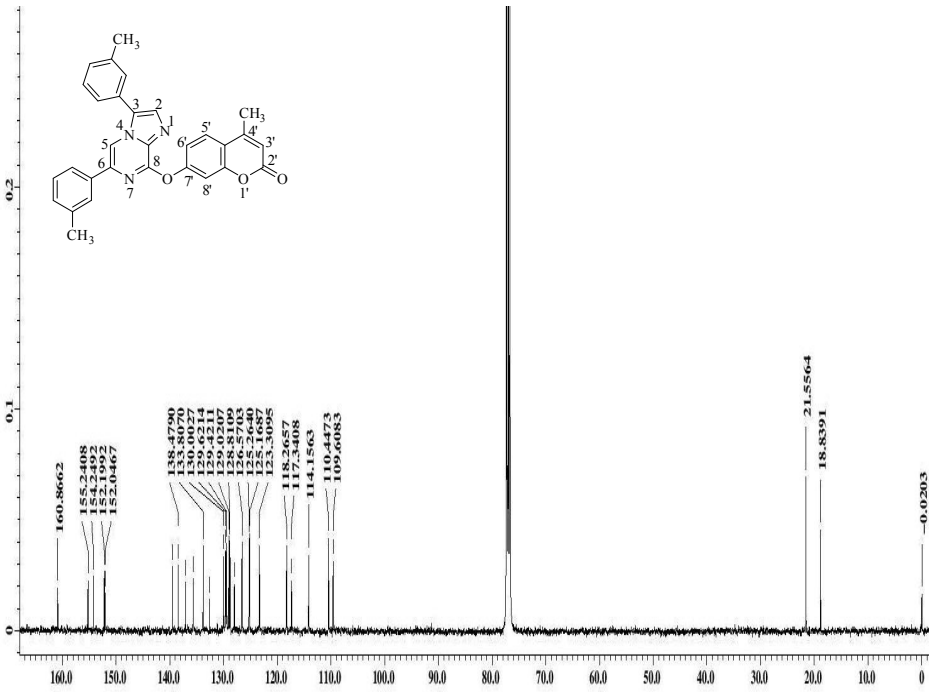


Fig S27: ^{13}C NMR spectrum of 7'-(3,6-di*m*-tolylimidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (12b)

Fig S28: Mass spectrum of 7'-(3,6-di*m*-tolylimidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (12b)

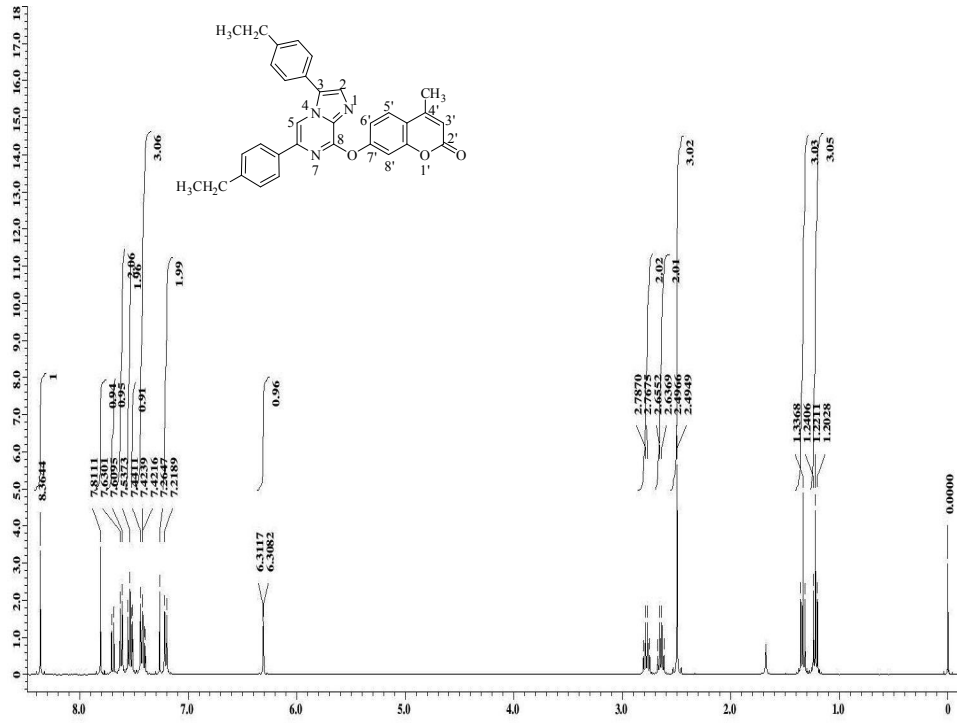


Fig S29: ^{1}H NMR spectrum of 7'-(3,6-bis(4-ethylphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (13b)

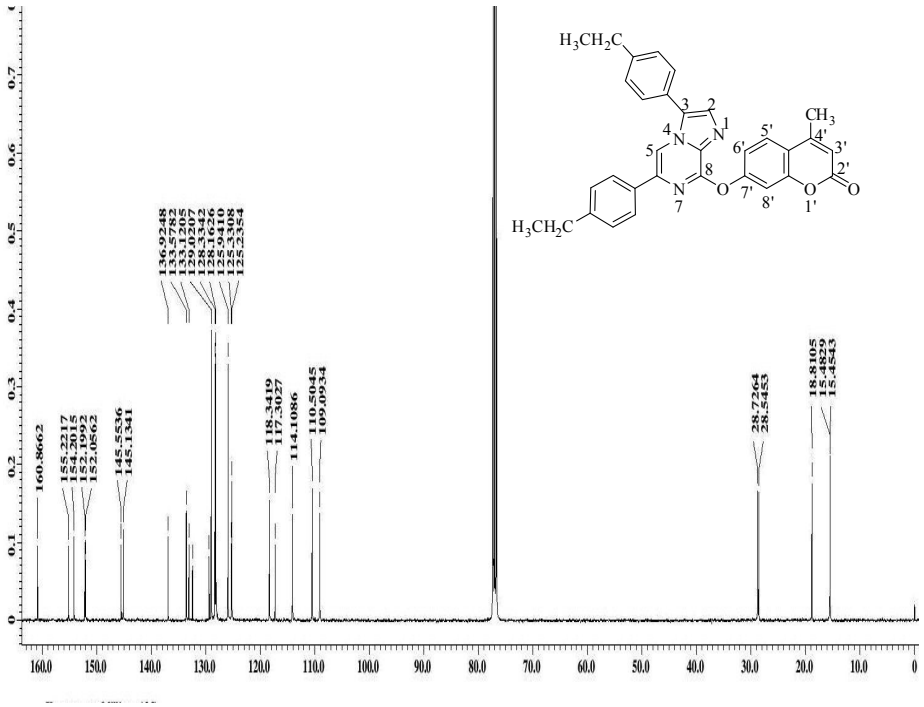


Fig S30: ^{13}C NMR spectrum of 7'-(3,6-bis(4-ethylphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (13b)

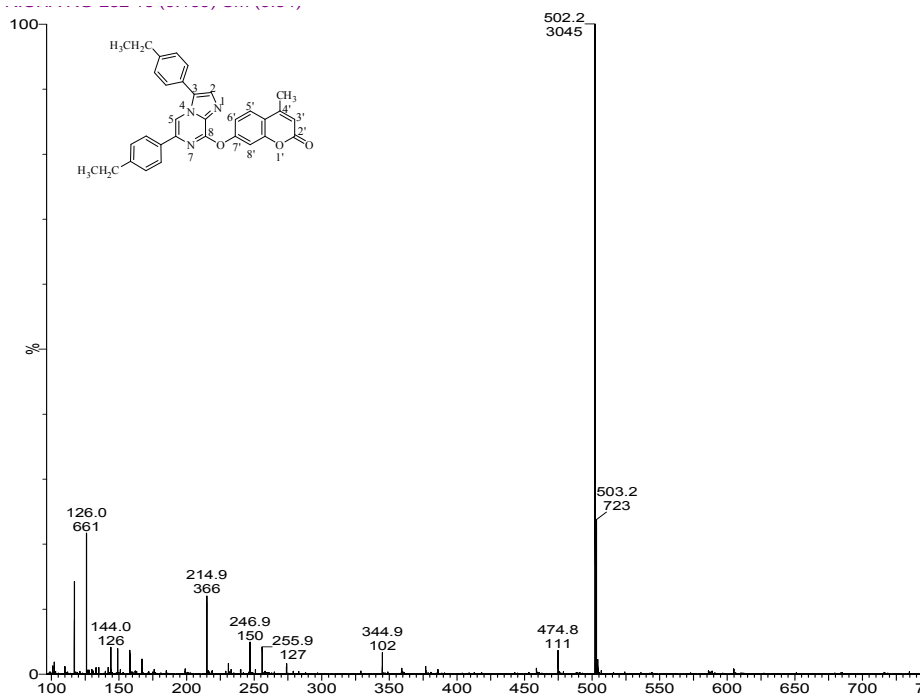


Fig S31: Mass spectrum of 7'-(3,6-bis(4-ethylphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (13b)

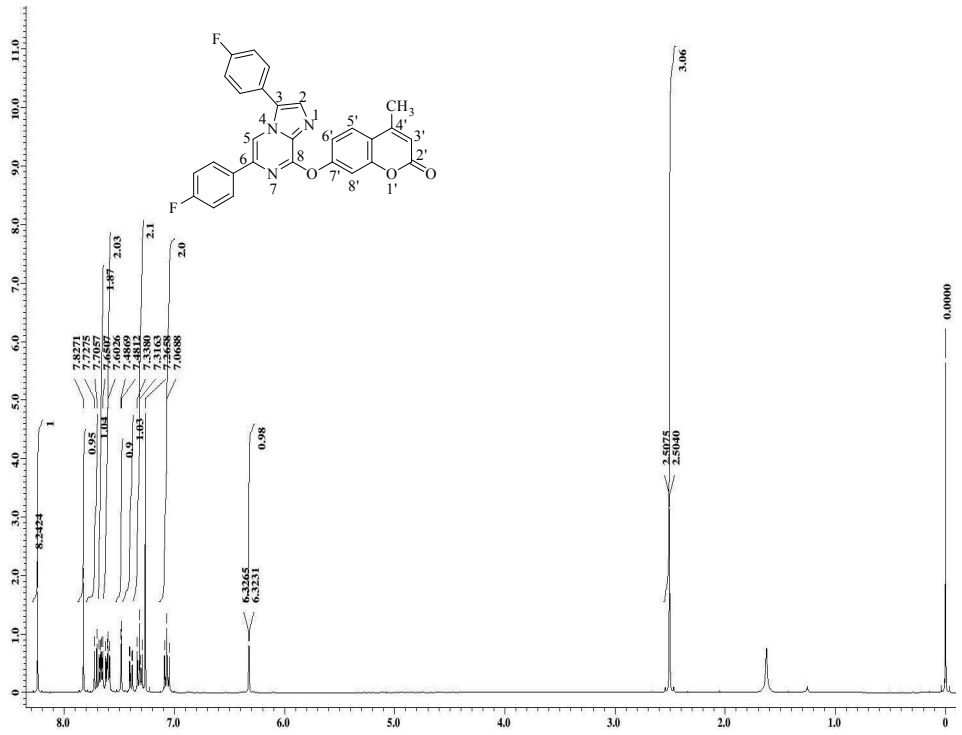


Fig S32: ^{1}H NMR spectrum of 7'-(3,6-bis(4-fluorophenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (14b)

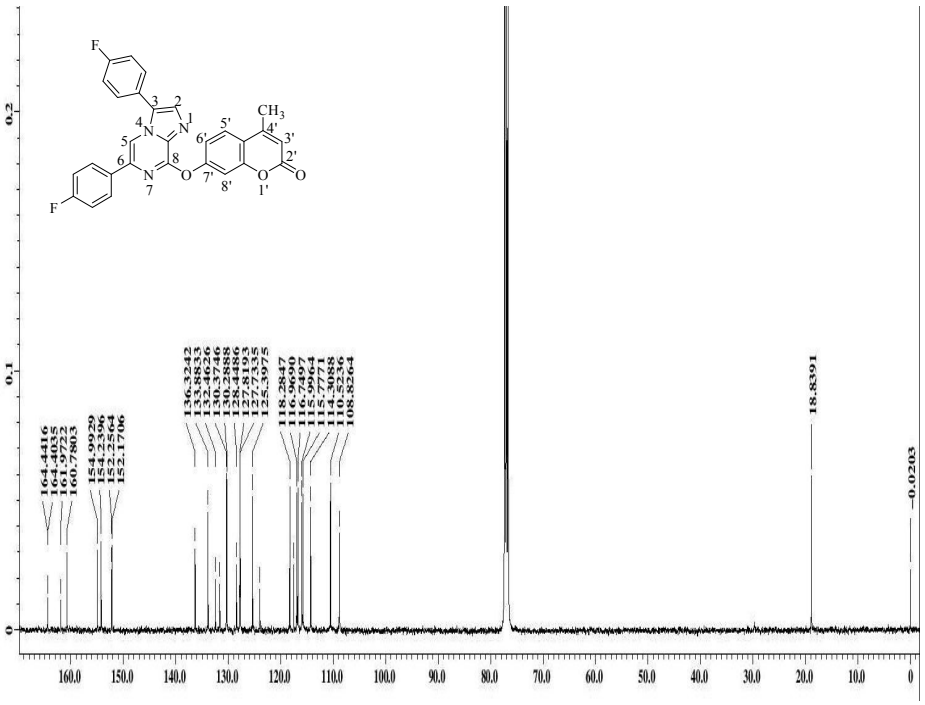


Fig S33: ^{13}C NMR spectrum of 7'-(3,6-bis(4-fluorophenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (14b)

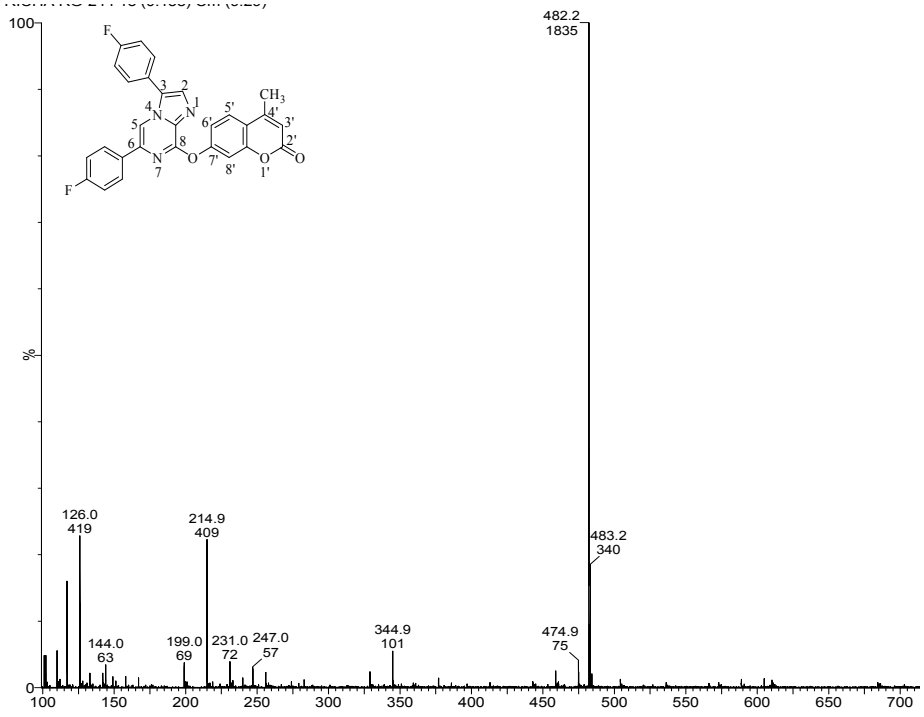


Fig S34: Mass spectrum of 7'-(3,6-bis(4-fluorophenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (14b)

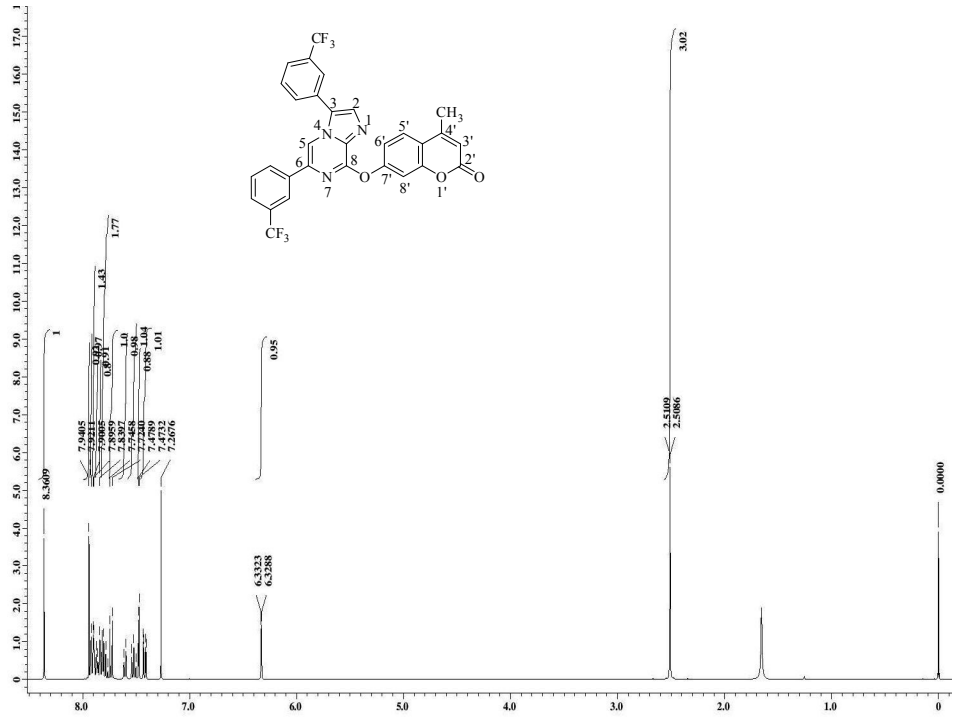


Fig S35: ^{1}H NMR spectrum of 7'-(3,6-bis(3-(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (15b)

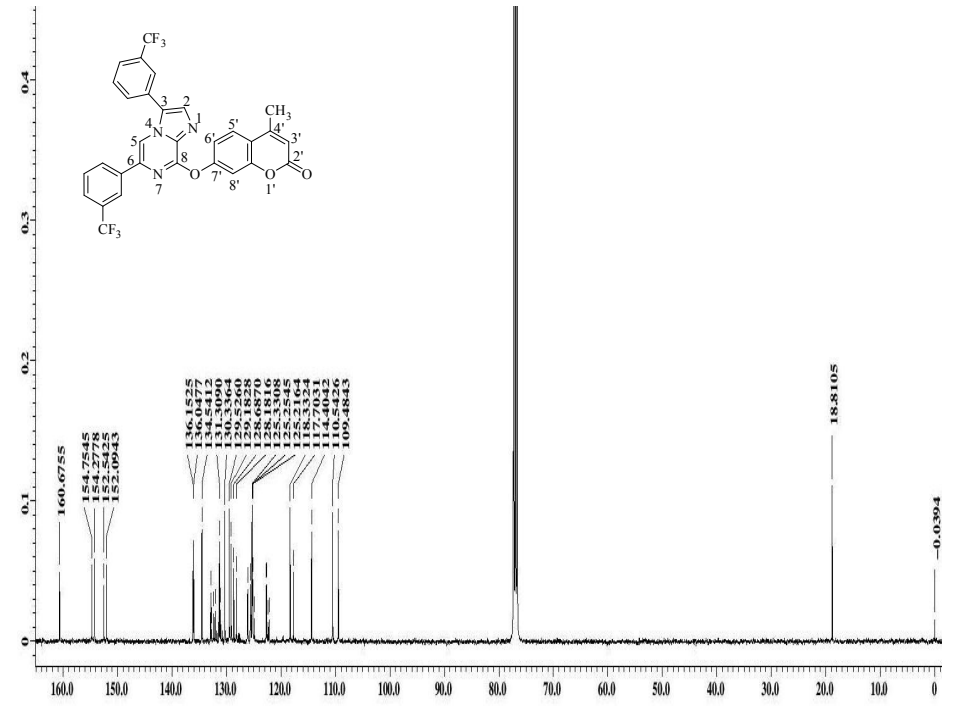


Fig S36: ^{13}C NMR spectrum of 7'-(3,6-bis(3-(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (15b)

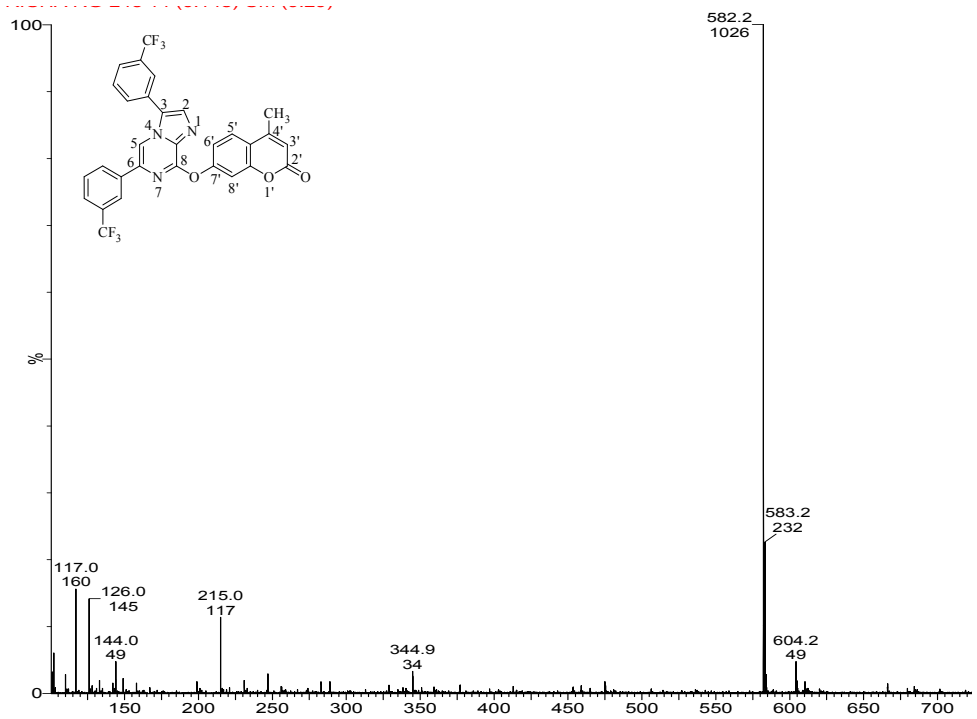


Fig S37: Mass spectrum of 7'-(3,6-bis(3-(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (15b)

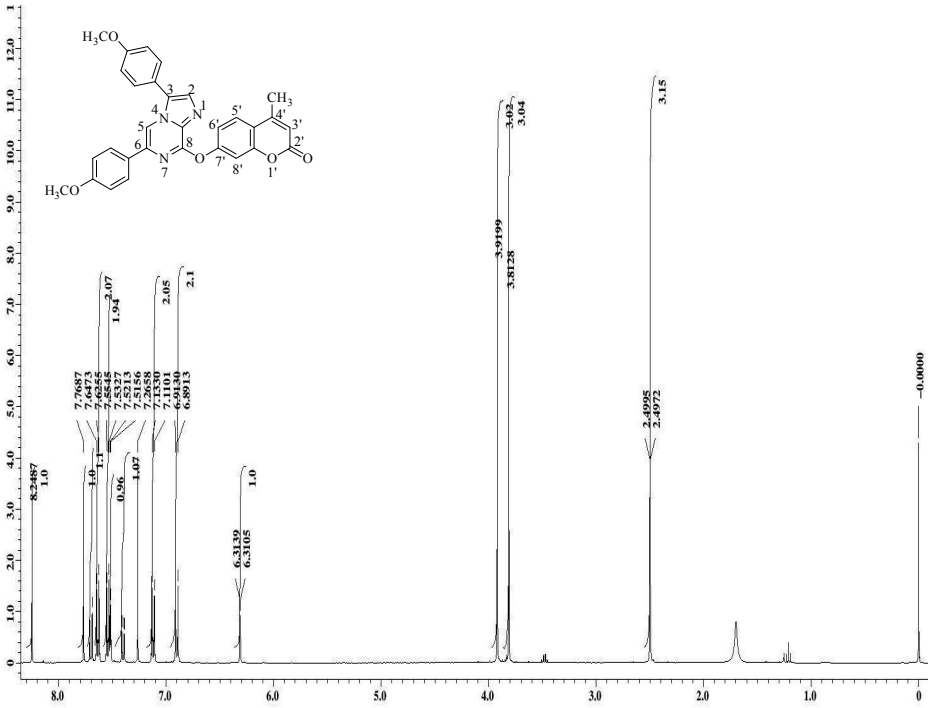


Fig S38: ^{1}H NMR spectrum of 7'-(3,6-bis(4-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (16b)

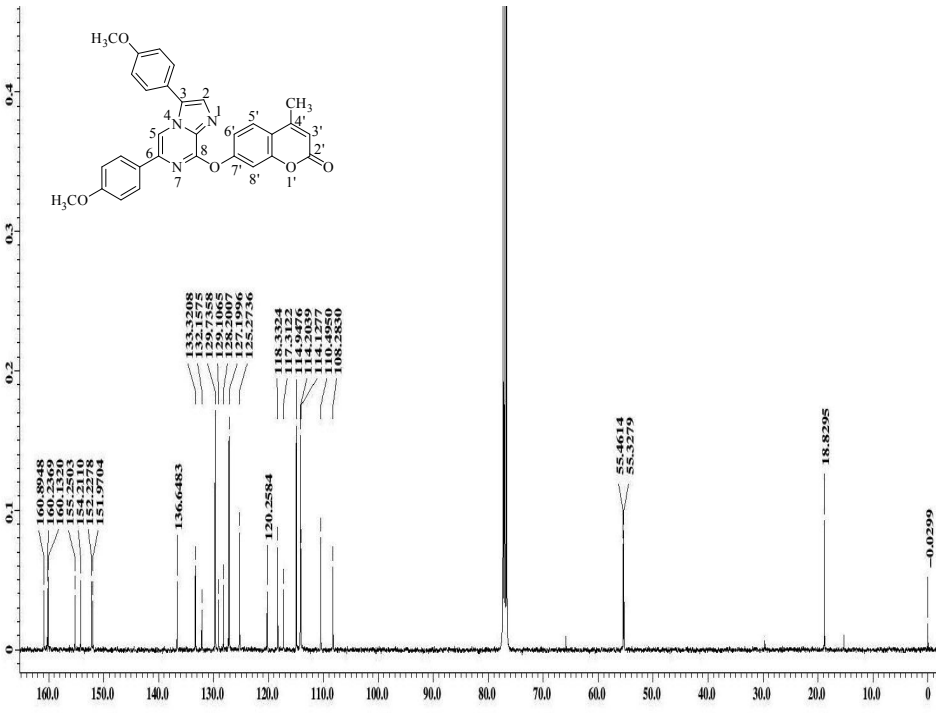


Fig S39: ^{13}C NMR spectrum of 7'-(3,6-bis(4-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (16b)

Fig S40: Mass spectrum of 7'-(3,6-bis(4-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (16b)

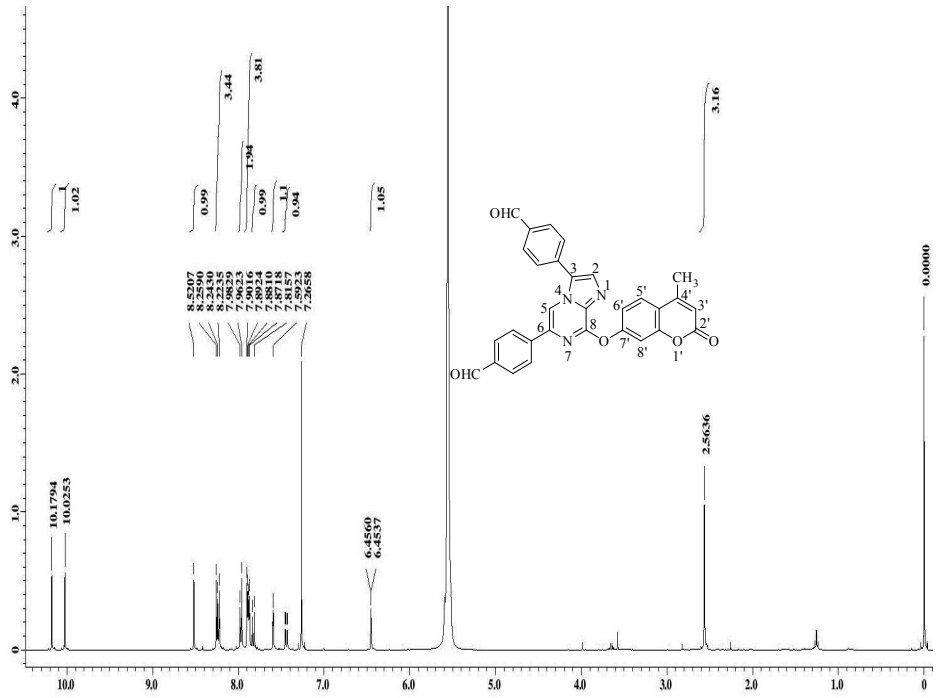


Fig S41: ^{1}H NMR spectrum of 4,4'-(8-(4-methyl-2-oxo-2*H*-chromen-7'-yloxy)imidazo[1,2-*a*]pyrazine-3,6-diyl)dibenzaldehyde (17b)

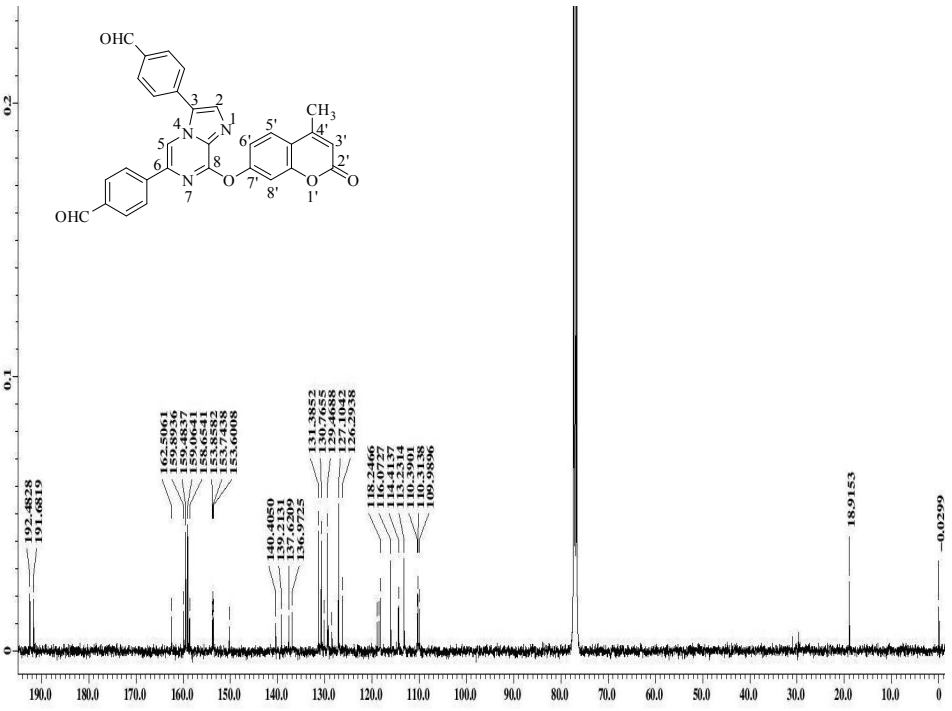


Fig S42: ^{13}C NMR spectrum of 4,4'-(8-(4-methyl-2-oxo-2*H*-chromen-7'-yloxy)imidazo[1,2-*a*]pyrazine-3,6-diyl)dibenzaldehyde (17b)

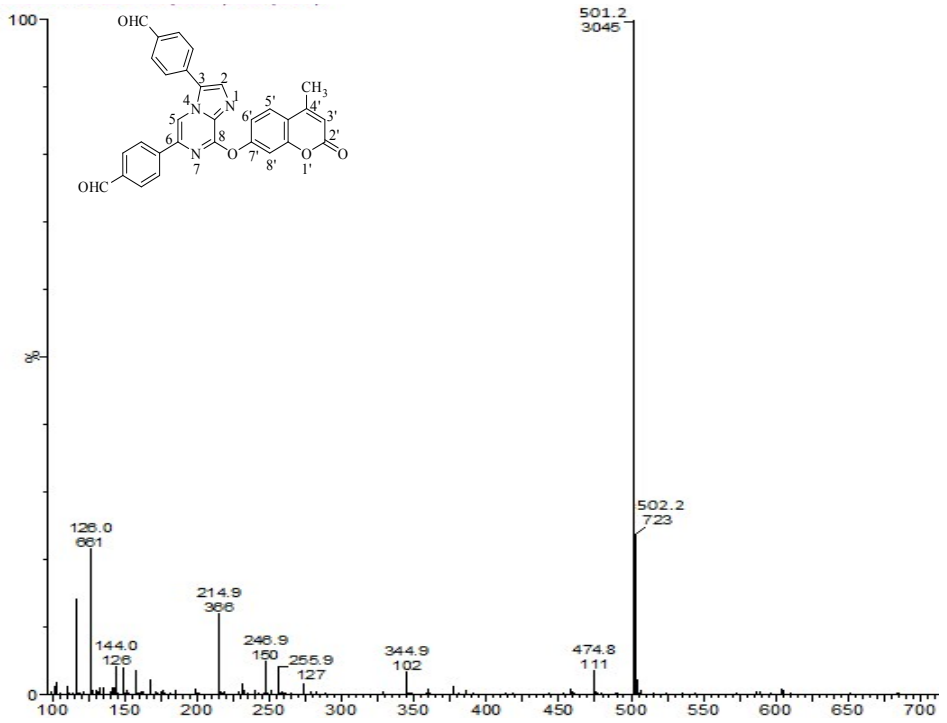


Fig S43: Mass spectrum of 4,4'-(8-(4-methyl-2-oxo-2*H*-chromen-7'-yloxy)imidazo[1,2-*a*]pyrazine-3,6-diyl)dibenzaldehyde (17b)

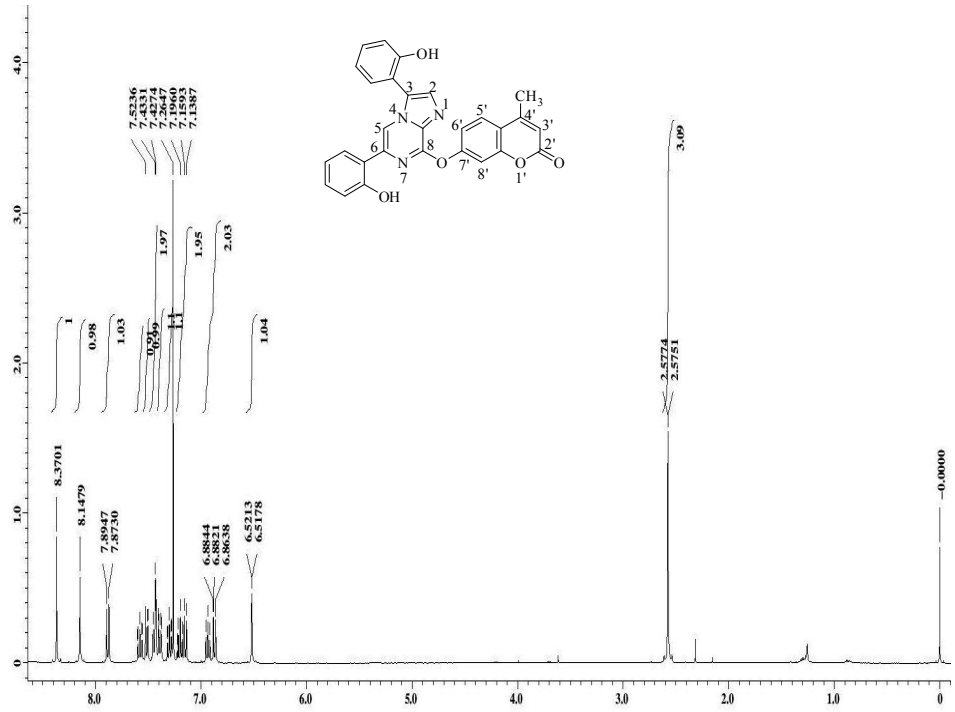


Fig S44: ^{1}H NMR spectrum of 7'-(3,6-bis(2-hydroxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (18b)

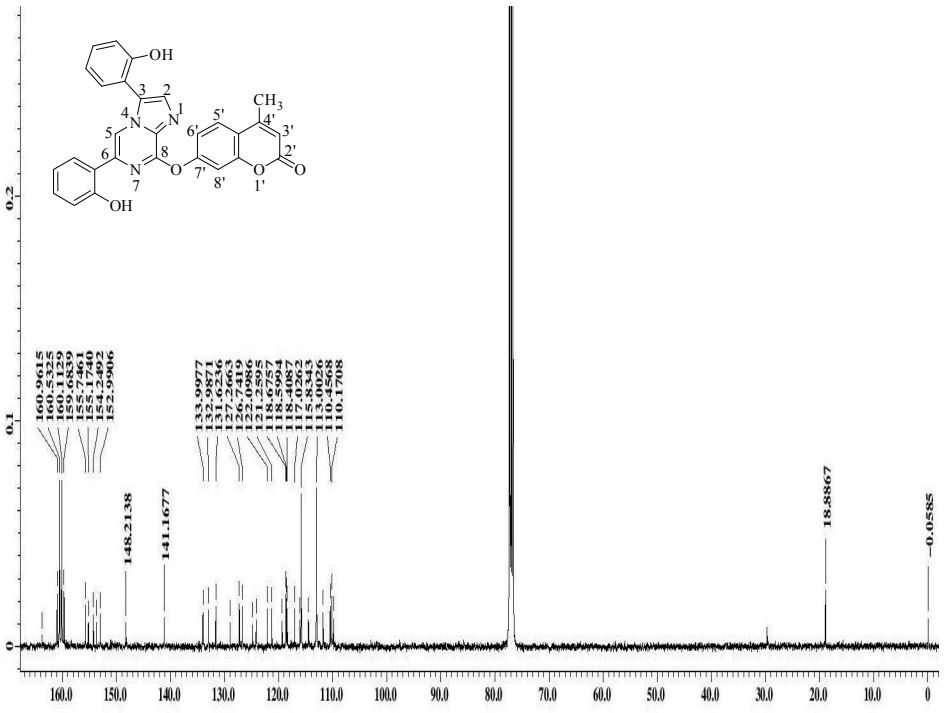


Fig S45: ^{13}C NMR spectrum of 7'-(3,6-bis(2-hydroxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (18b)

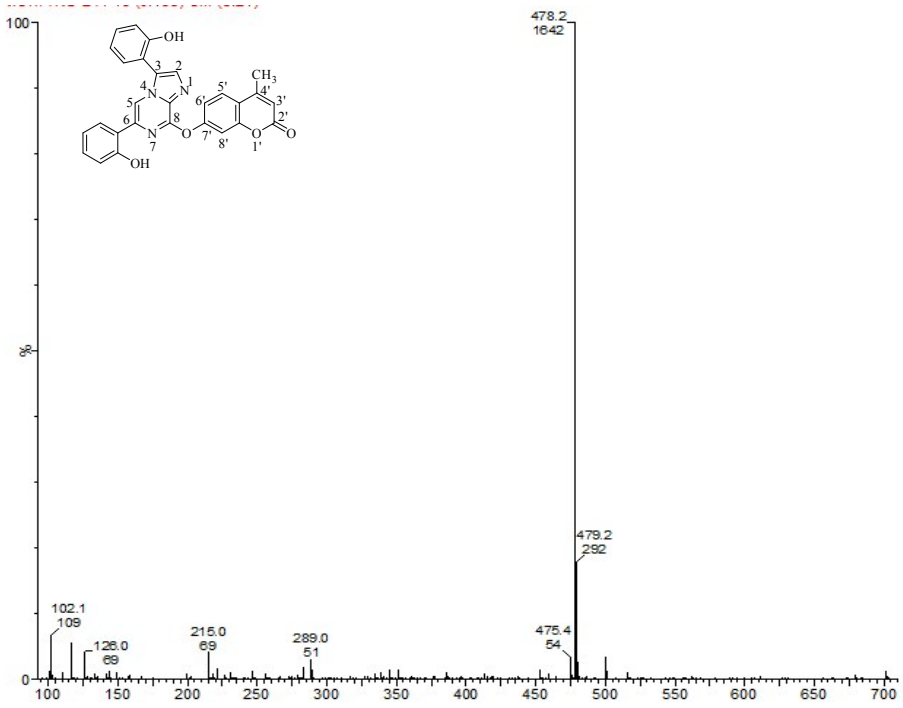


Fig S46: Mass spectrum of 7'-(3,6-bis(2-hydroxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (18b)

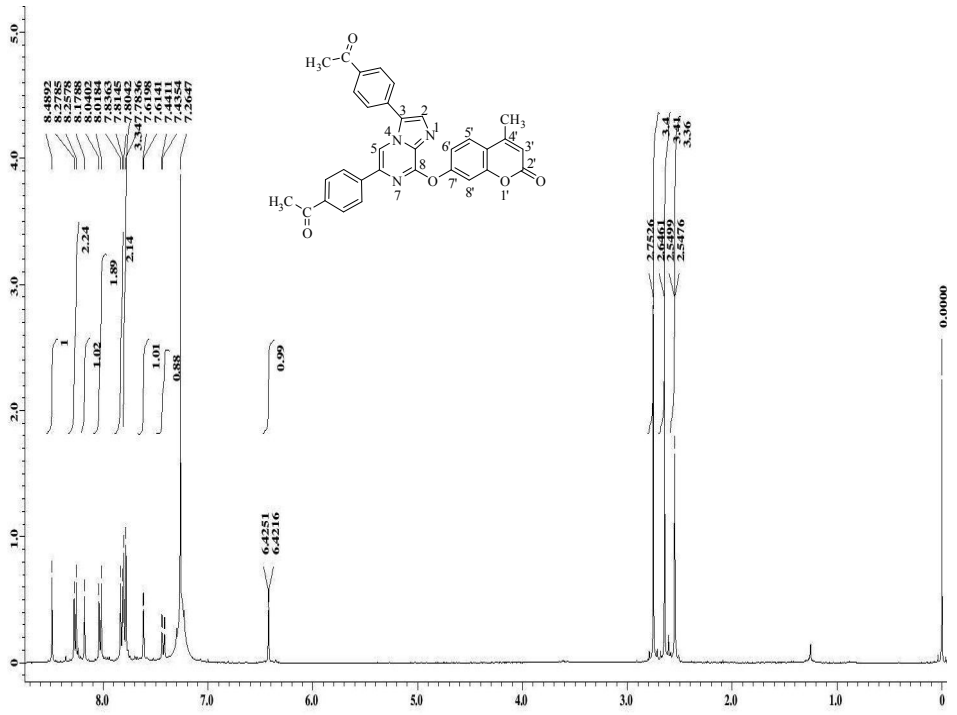


Fig S47: ^{1}H NMR spectrum of 1,1'-(4,4'-(8-(4-methyl-2-oxo-2*H*-chromen-7'-yloxy)imidazo[1,2-*a*]pyrazin-3,6-diyl)bis(4,1-phenylene)diethanone (19b)

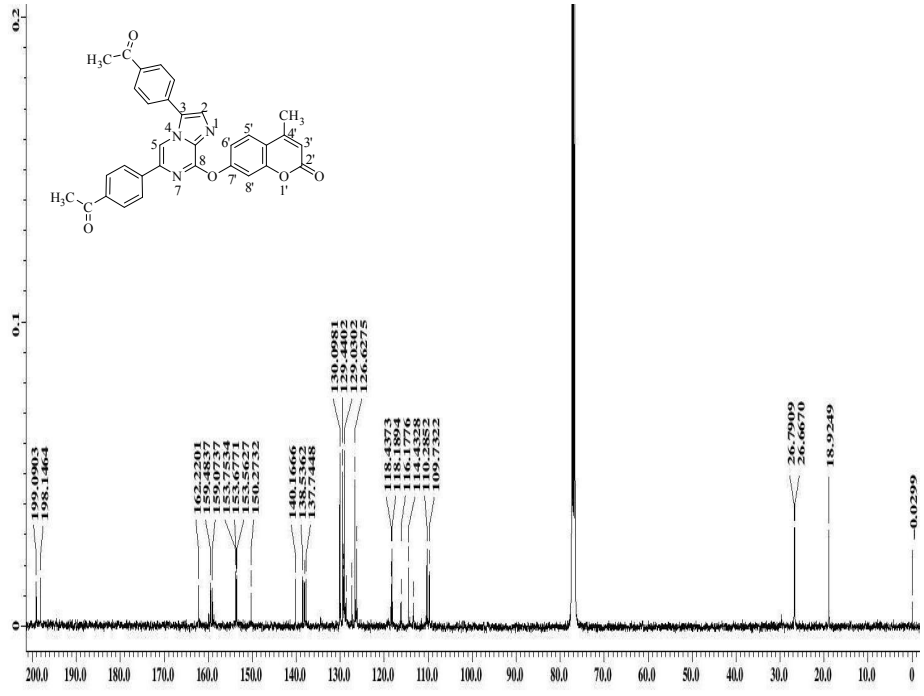


Fig S48: ^{13}C NMR spectrum of 1,1'-(4,4'-(8-(4-methyl-2-oxo-2*H*-chromen-7'-yloxy)imidazo[1,2-*a*]pyrazin-3,6-diyl)bis(4,1-phenylene)diethanone (19b)

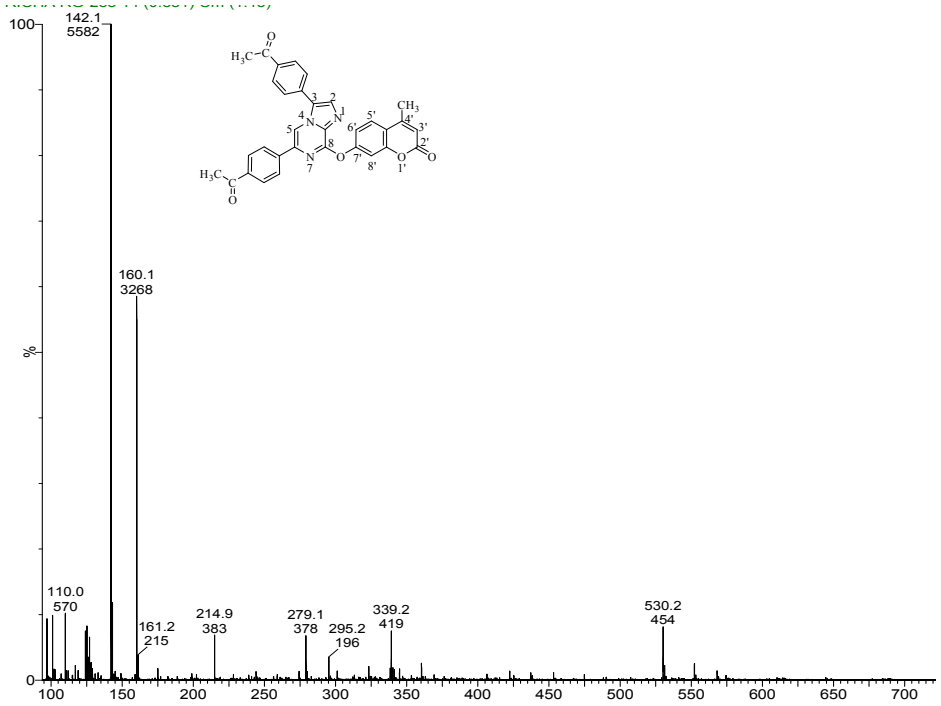


Fig S49: Mass spectrum of 1,1'-(4,4'-(8-(4-methyl-2-oxo-2*H*-chromen-7'-yloxy)imidazo[1,2-*a*]pyrazin-3,6-diyl)bis(4,1-phenylene)diethanone (19b)

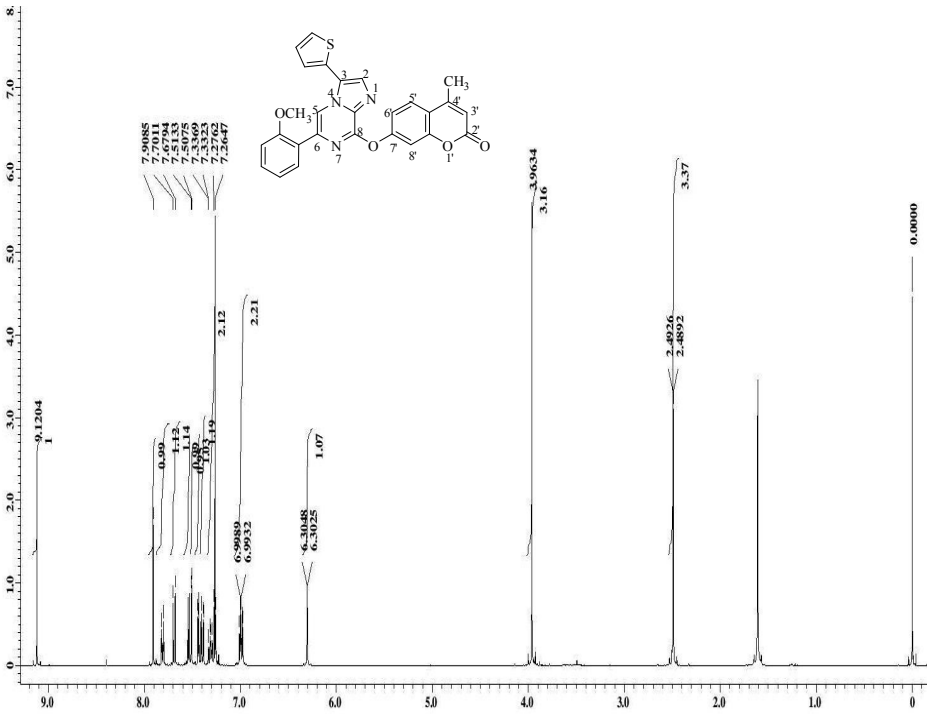


Fig S50: ^{1}H NMR spectrum of 7'-(6-(2-methoxyphenyl)-3-(thiophen-2-yl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (20)

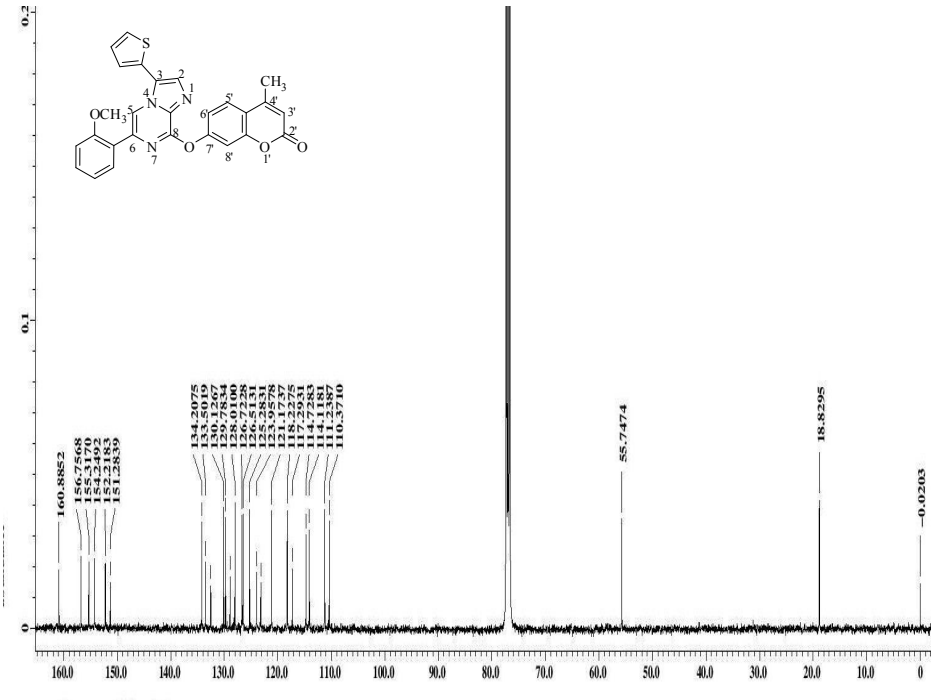


Fig S51: ^{13}C NMR spectrum of 7'-(6-(2-methoxyphenyl)-3-(thiophen-2-yl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (20)

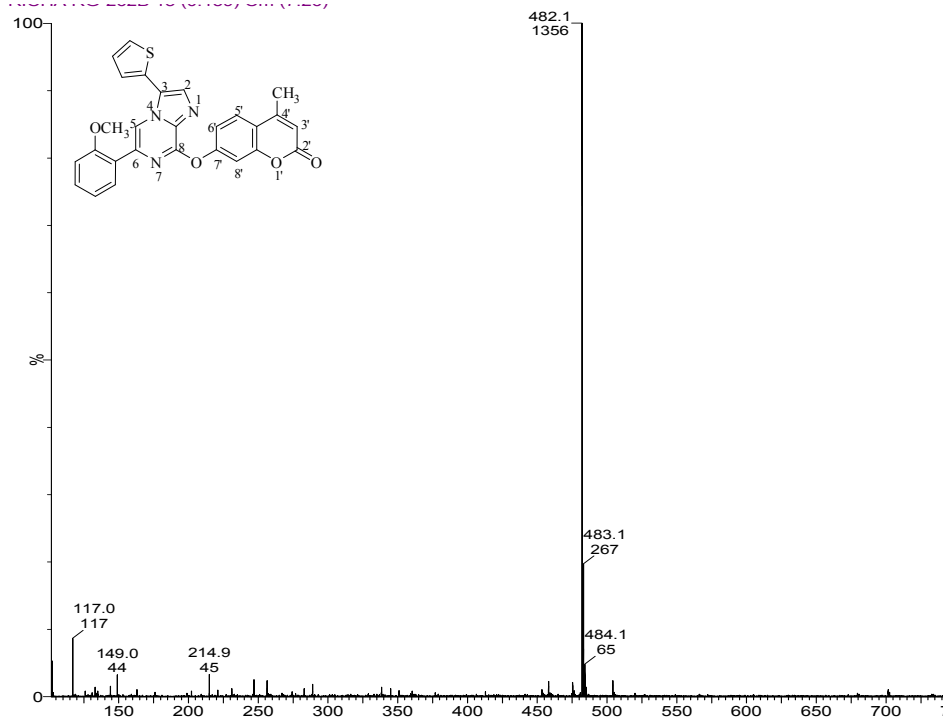


Fig S52: Mass spectrum of 7'-(6-(2-methoxyphenyl)-3-(thiophen-2-yl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (20)

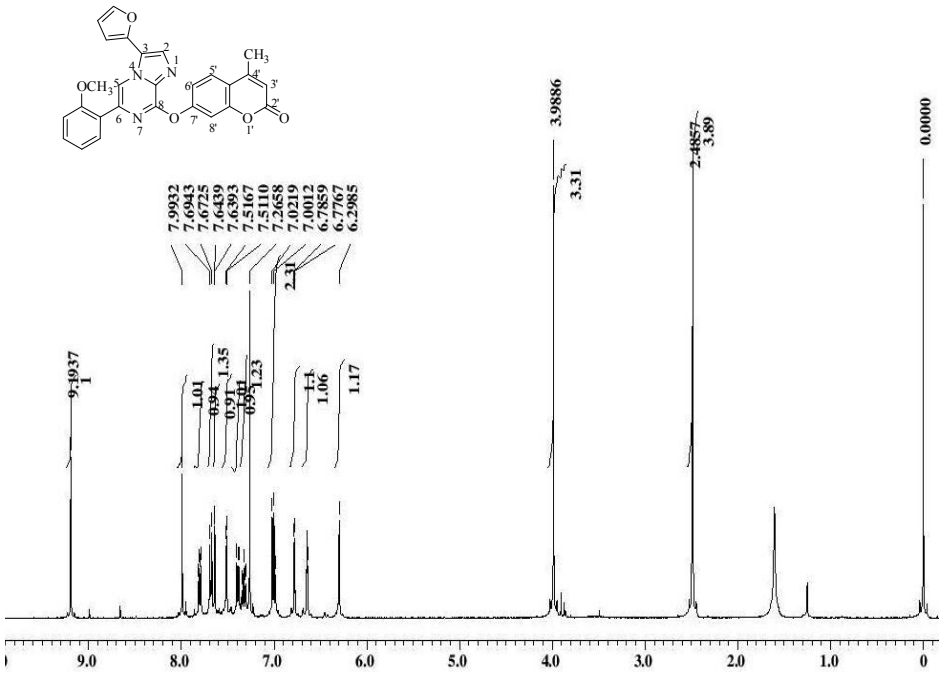


Fig S53: ^{1}H NMR spectrum of 7'-(3-(furan-2-yl)-6-(2-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (21)

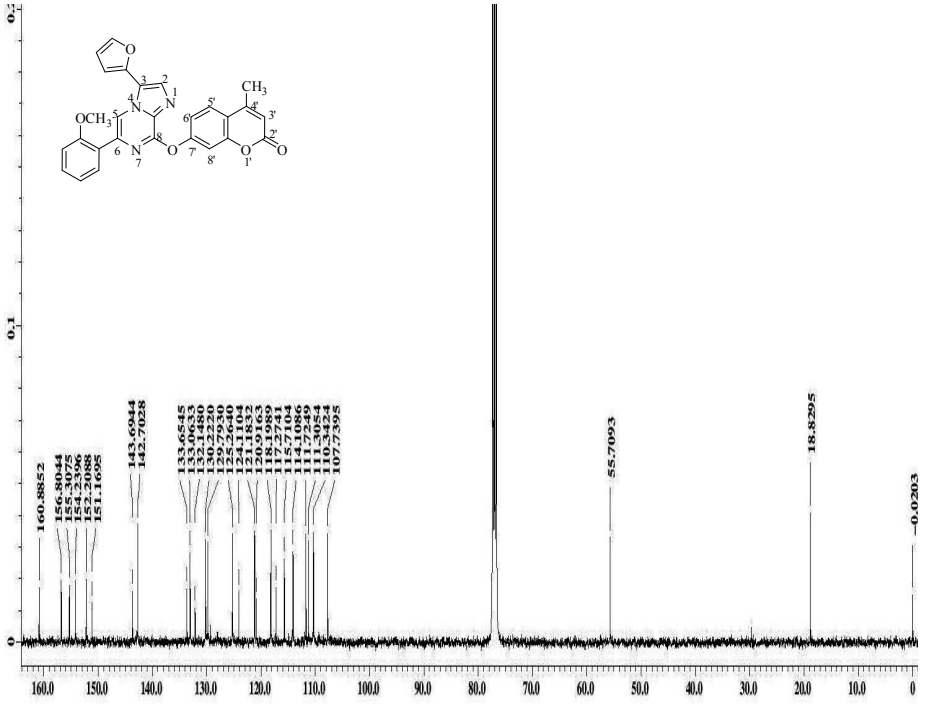


Fig S54: ^{13}C NMR spectrum of 7'-(3-(furan-2-yl)-6-(2-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (21)

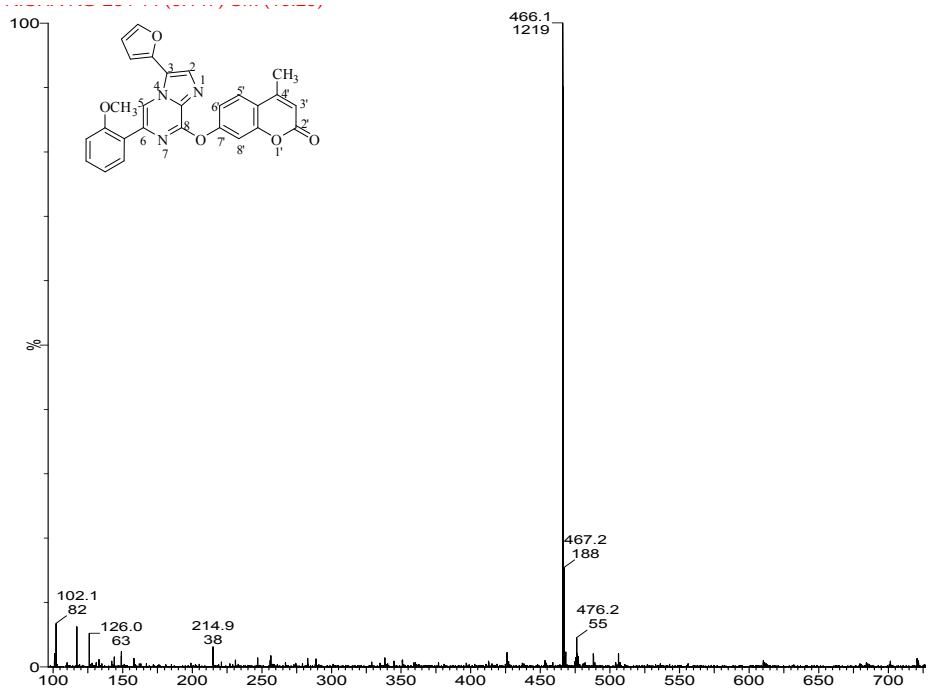


Fig S55: Mass spectrum of 7'-(3-(furan-2-yl)-6-(2-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (21)

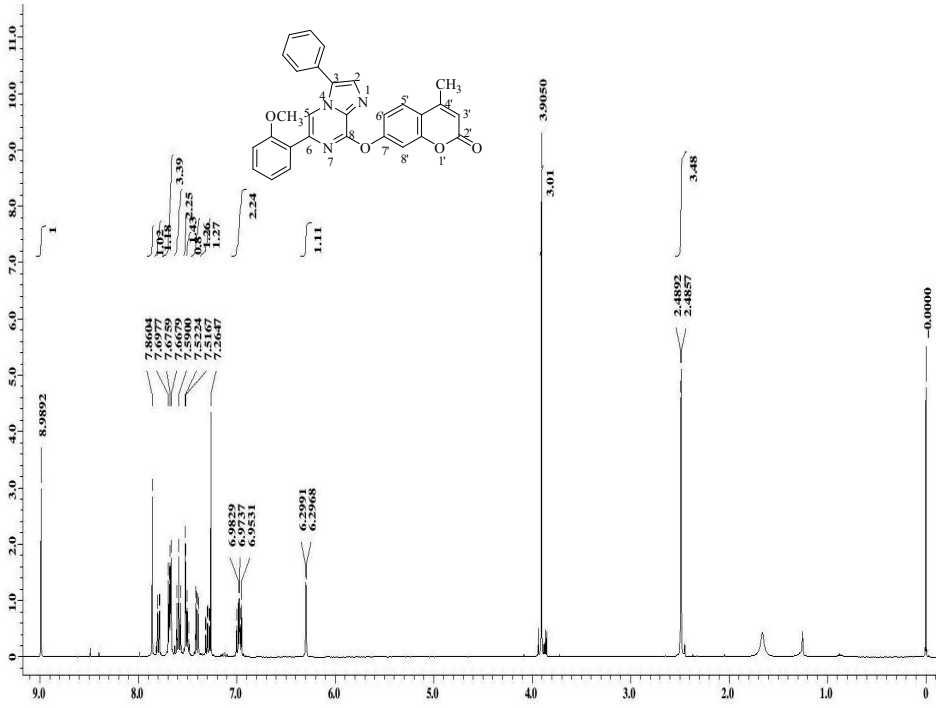


Fig S56: ^{1}H NMR spectrum of 7'-(6-(2-methoxyphenyl)-3-phenylimidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (22)

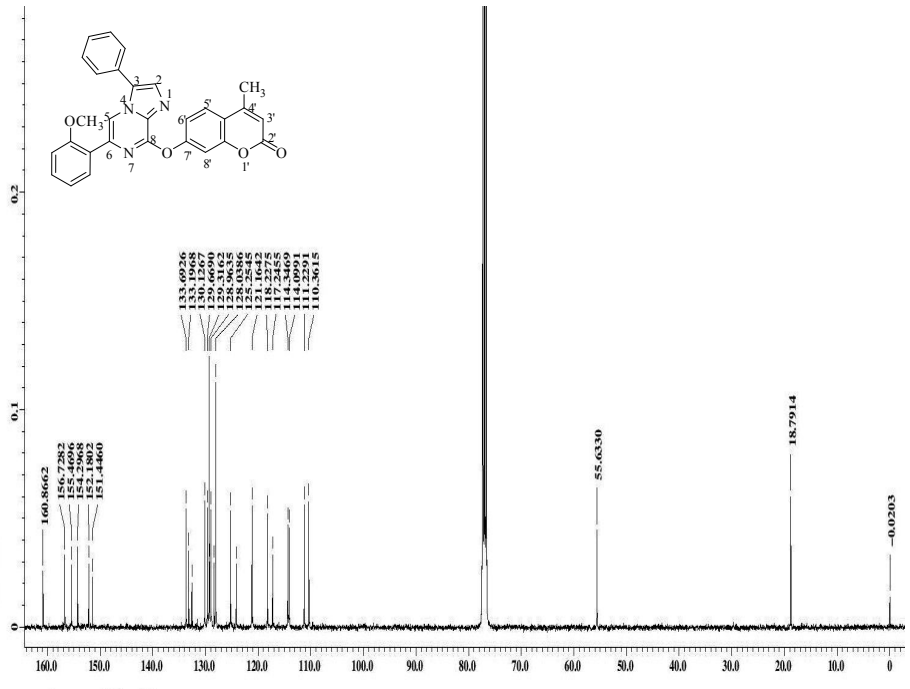


Fig S57: ^{13}C NMR spectrum of 7'-(6-(2-methoxyphenyl)-3-phenylimidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (22)

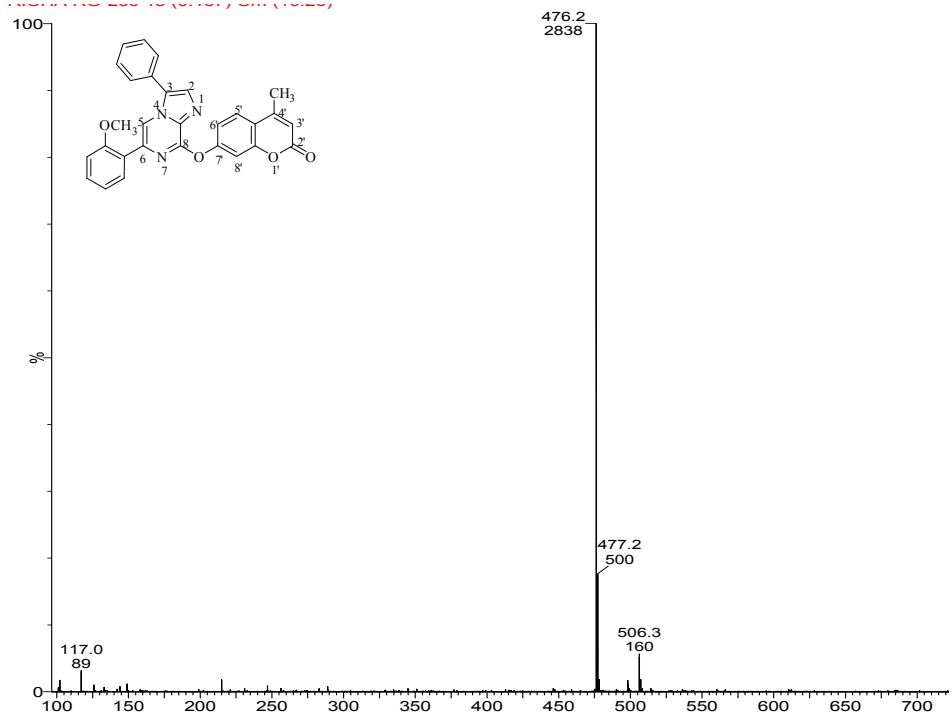


Fig S58: Mass spectrum of 7'-(6-(2-methoxyphenyl)-3-phenylimidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (22)

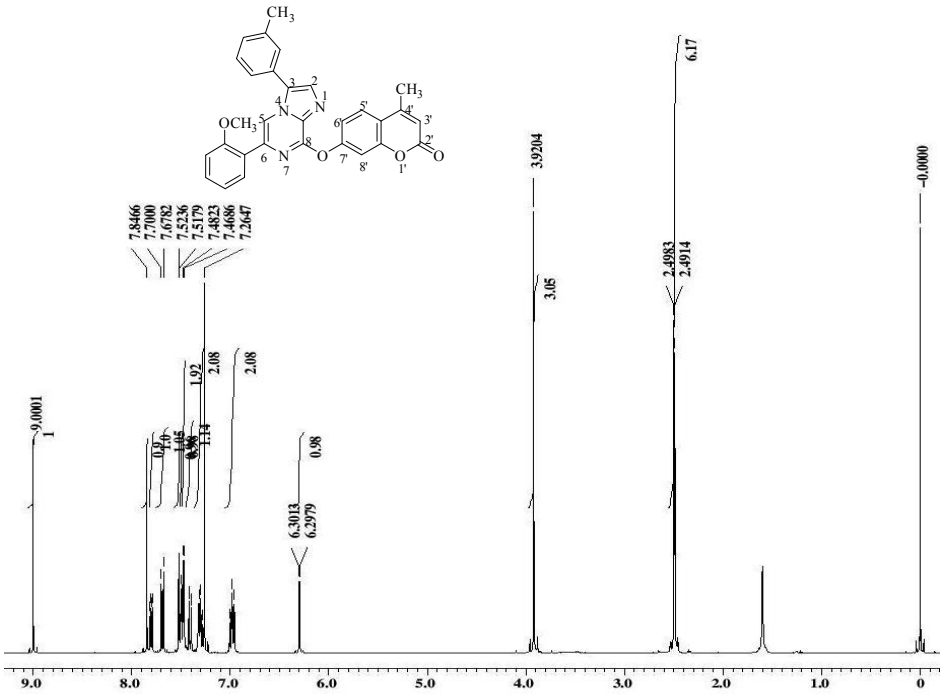


Fig S59: ^{1}H NMR spectrum of 7'-(6-(2-methoxyphenyl)-3-*m*-tolylimidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (23)

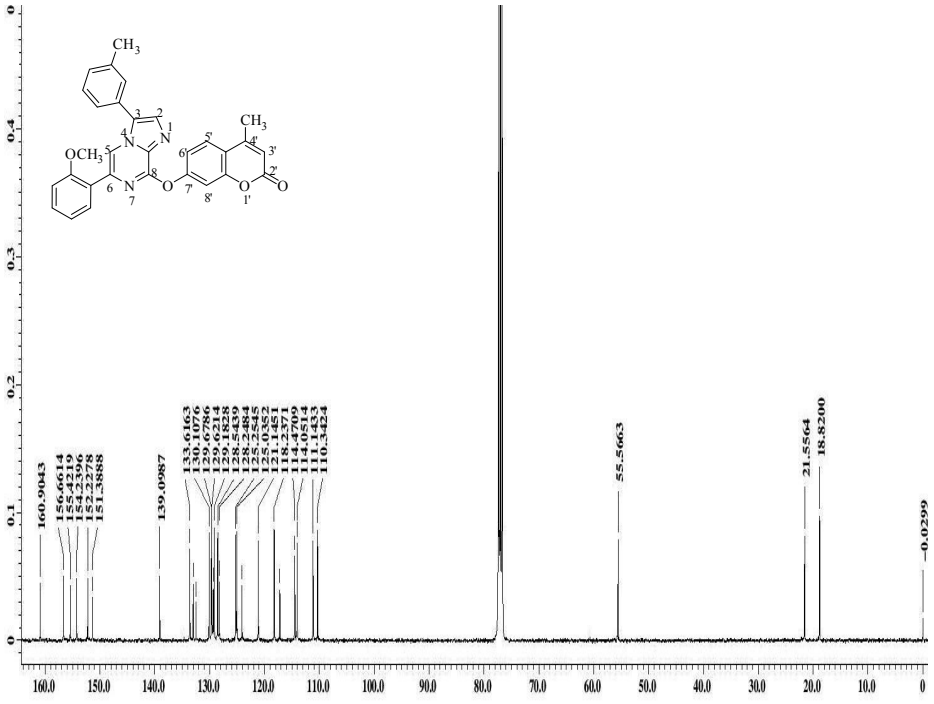


Fig S60: ^{13}C NMR spectrum of 7'-(6-(2-methoxyphenyl)-3-*m*-tolylimidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (23)

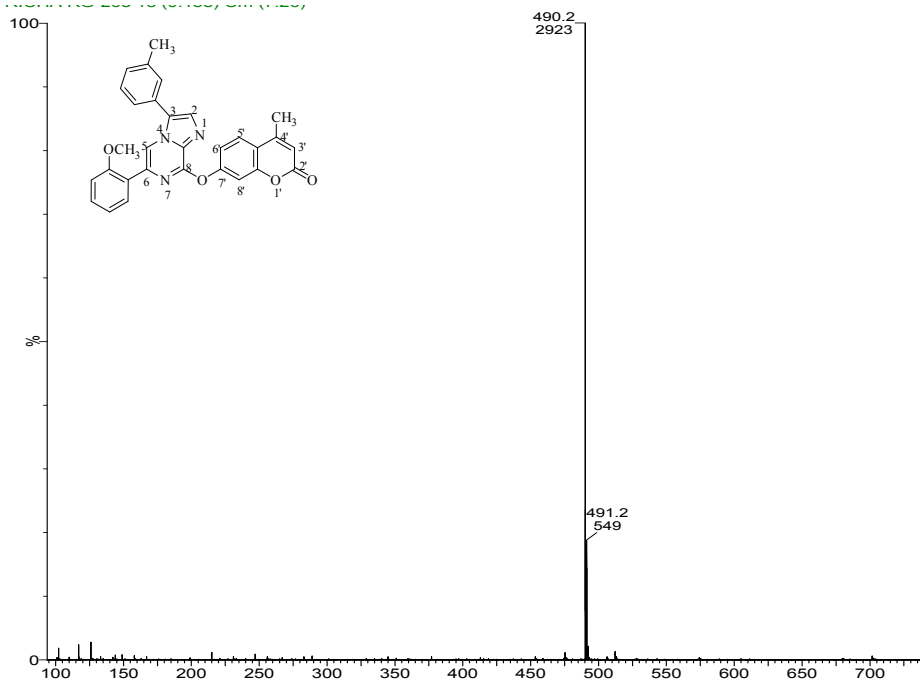


Fig S61: Mass spectrum of 7'-(6-(2-methoxyphenyl)-3-*m*-tolylimidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (23)

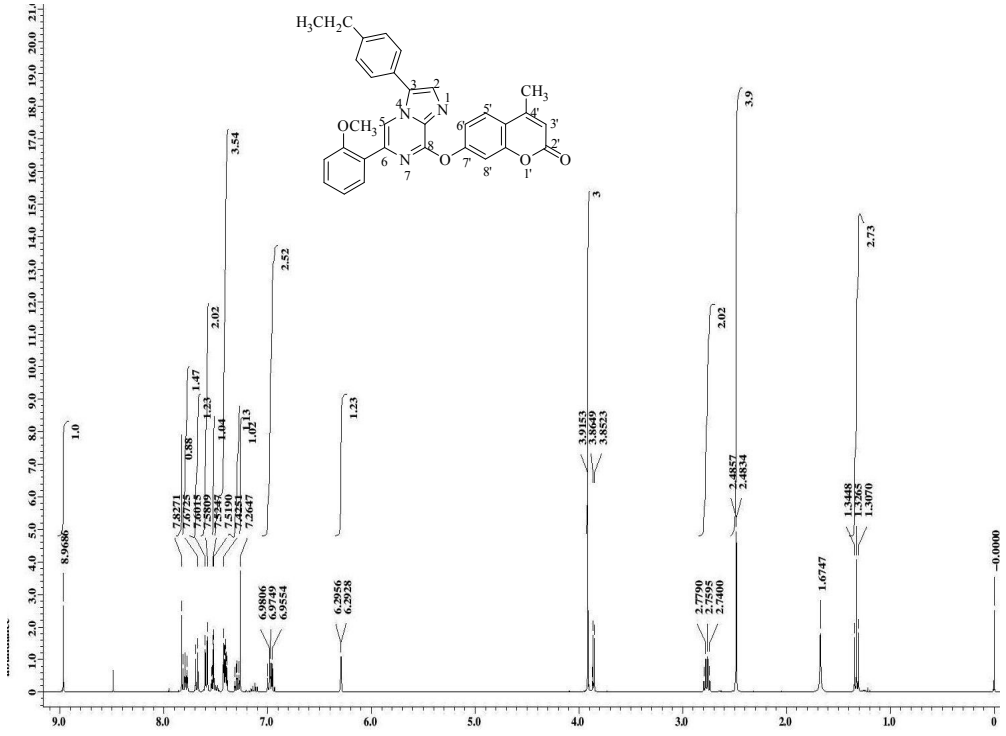


Fig S62: ^{1}H NMR spectrum of 7'-(3-(4-ethylphenyl)-6-(2-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'methyl-2*H*-chromen-2'-one (24)

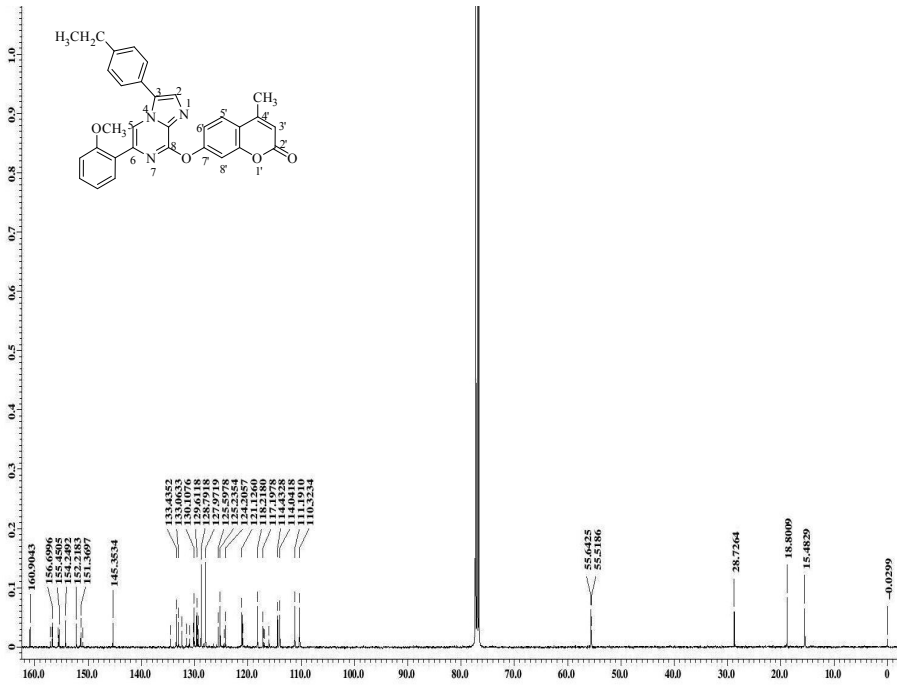


Fig S63: ^{13}C NMR spectrum of 7'-(3-(4-ethylphenyl)-6-(2-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (24)

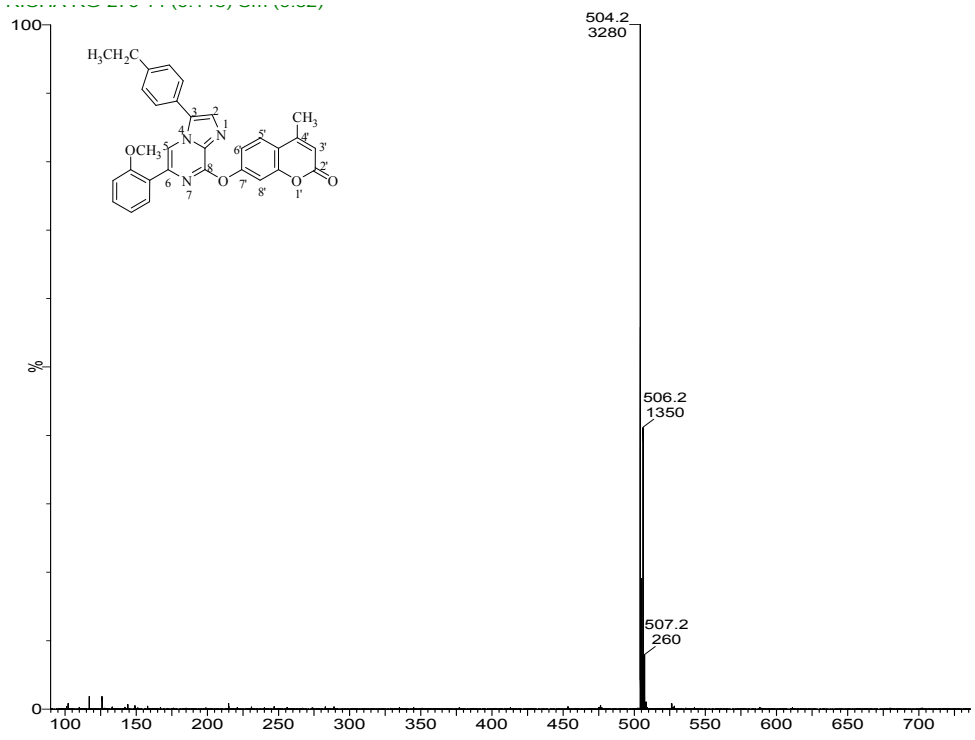


Fig S64: Mass spectrum of 7'-(3-(4-ethylphenyl)-6-(2-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (24)

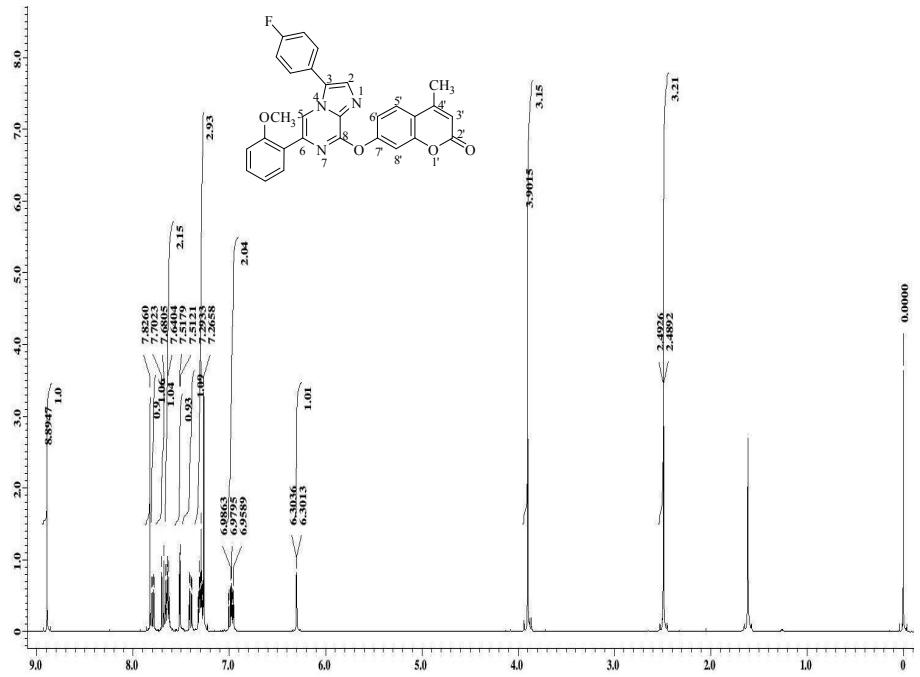


Fig S65: ^{1}H NMR spectrum of 7'-(3-(4-fluorophenyl)-6-(2-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (25)

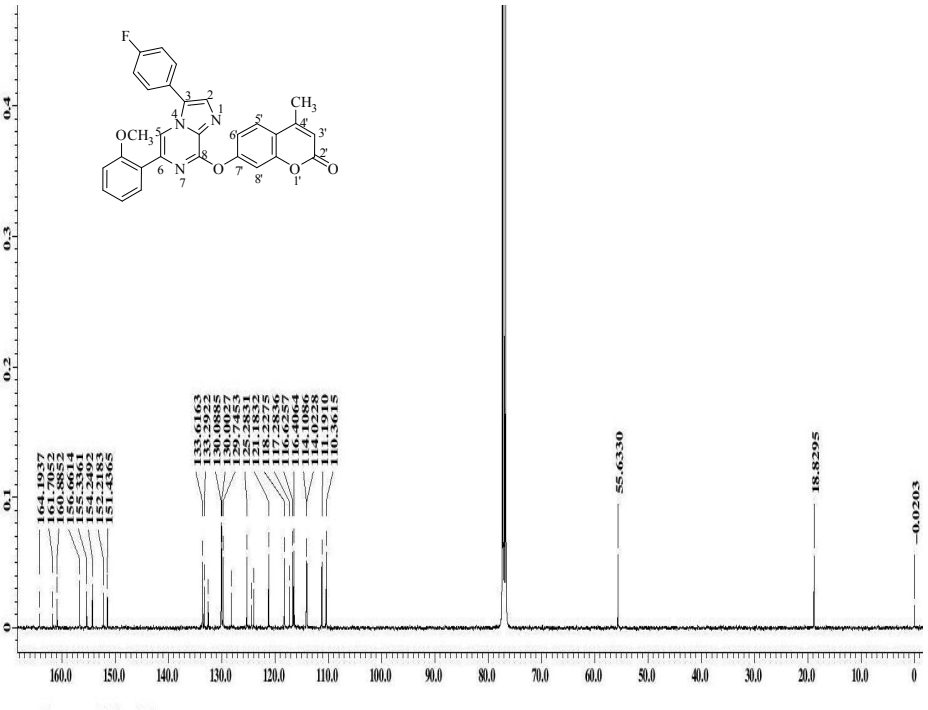


Fig S66: ^{13}C NMR spectrum of 7'-(3-(4-fluorophenyl)-6-(2-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (25)

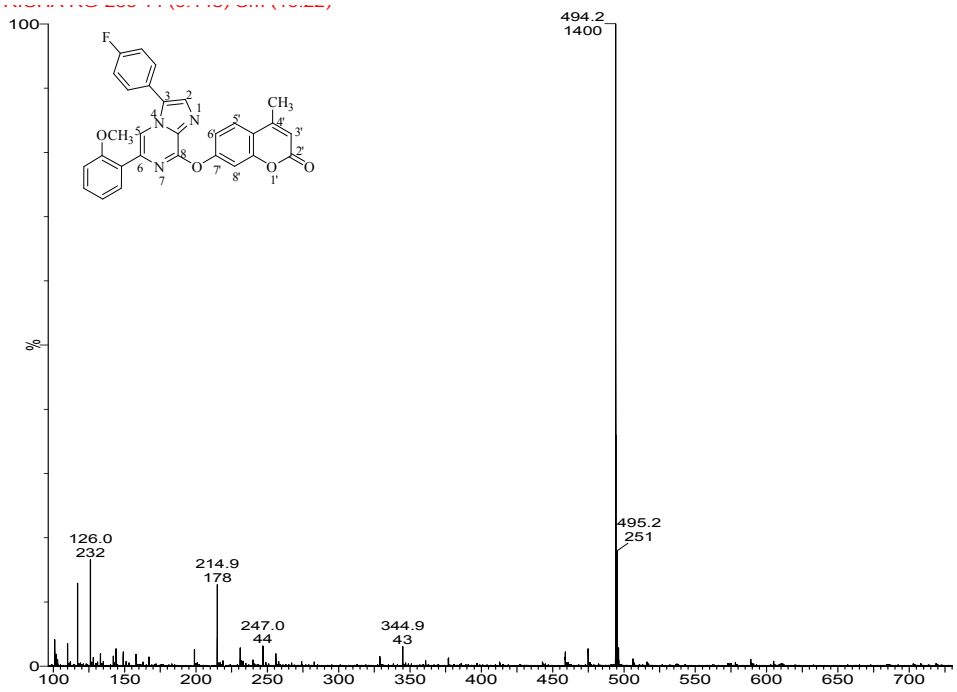


Fig S67: Mass spectrum of 7'-(3-(4-fluorophenyl)-6-(2-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (25)

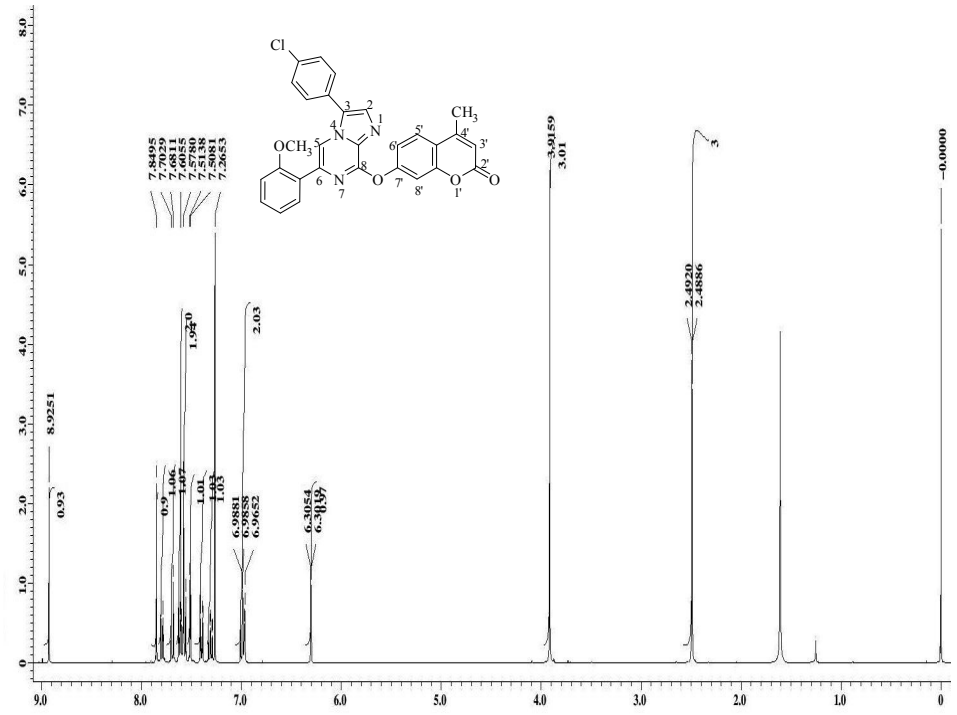


Fig S68: ^{1}H NMR spectrum of 7'-(3-(4-chlorophenyl)-6-(2-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (26)

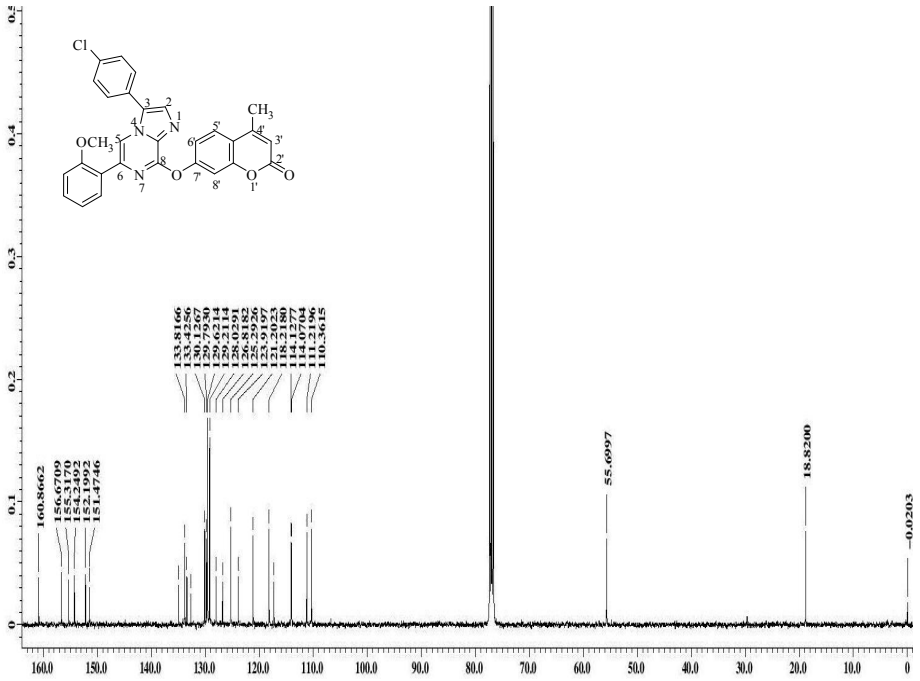


Fig S69: ^{13}C NMR spectrum of 7'-(3-(4-chlorophenyl)-6-(2-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (26)

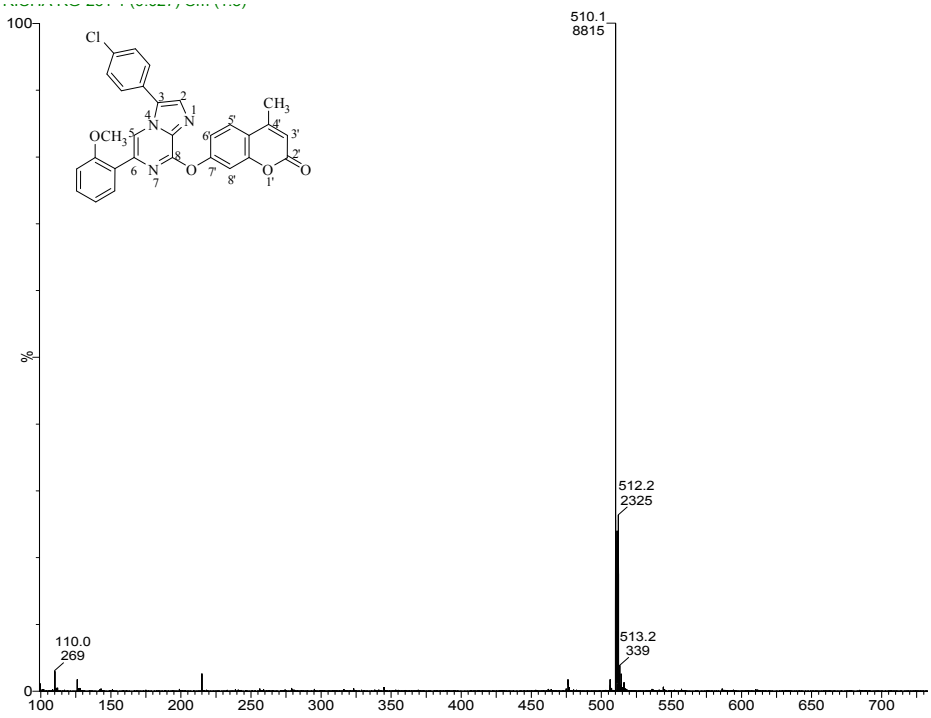


Fig S70: Mass spectrum of 7'-(3-(4-chlorophenyl)-6-(2-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (26)

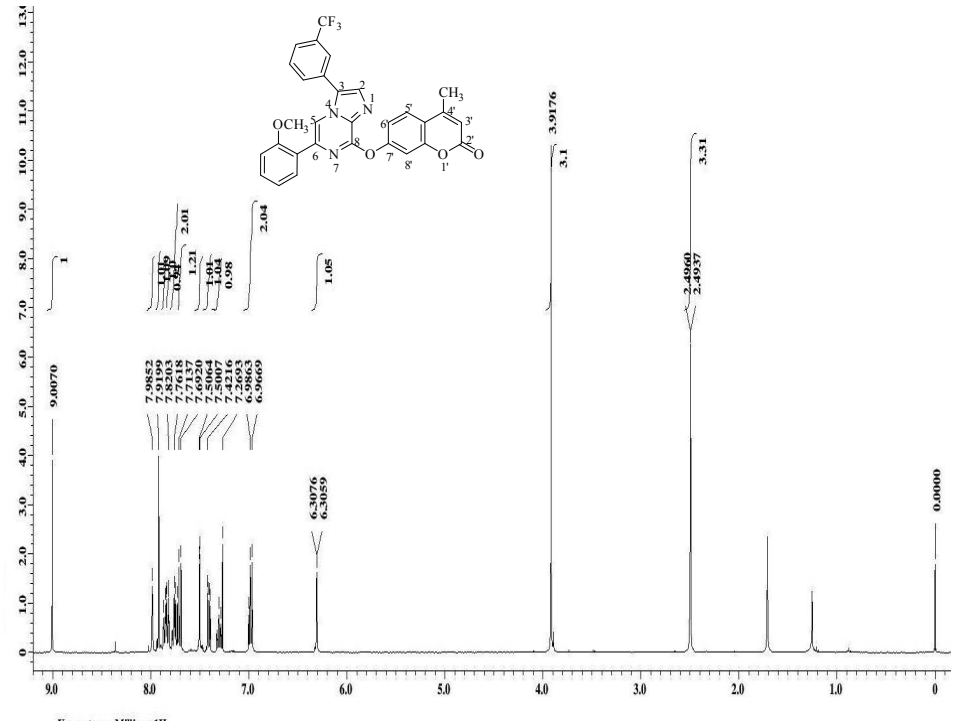


Fig S71: ^{1}H NMR spectrum of 7'-(6-(2-methoxyphenyl)-3-(3 (trifluoromethyl)phenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (27)

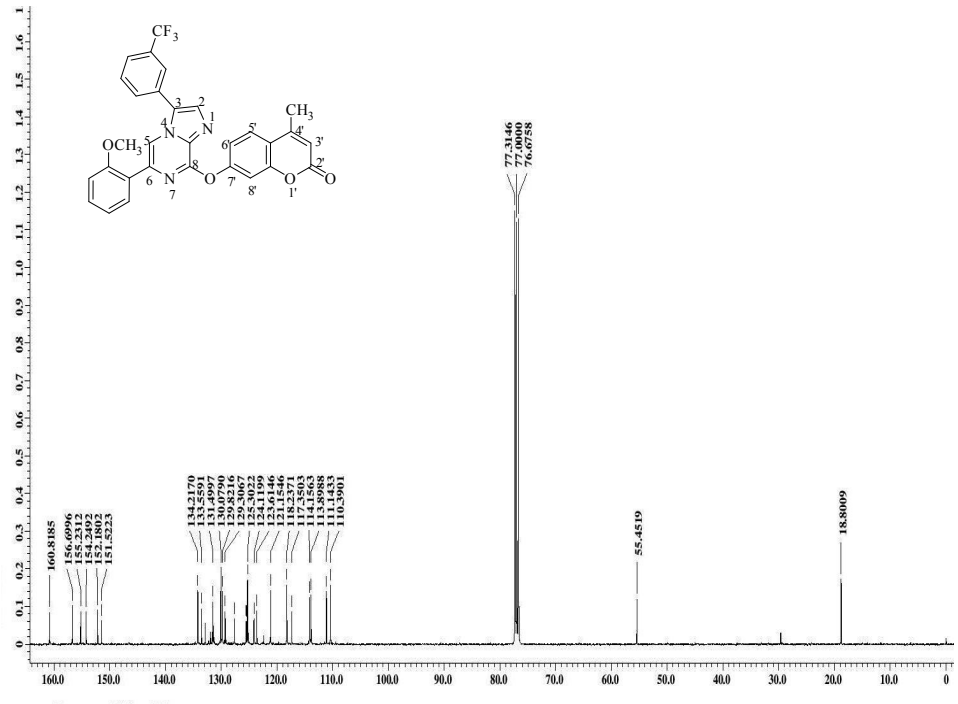


Fig S72: ^{13}C NMR spectrum of 7'-(6-(2-methoxyphenyl)-3-(3 (trifluoromethyl)phenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (27)

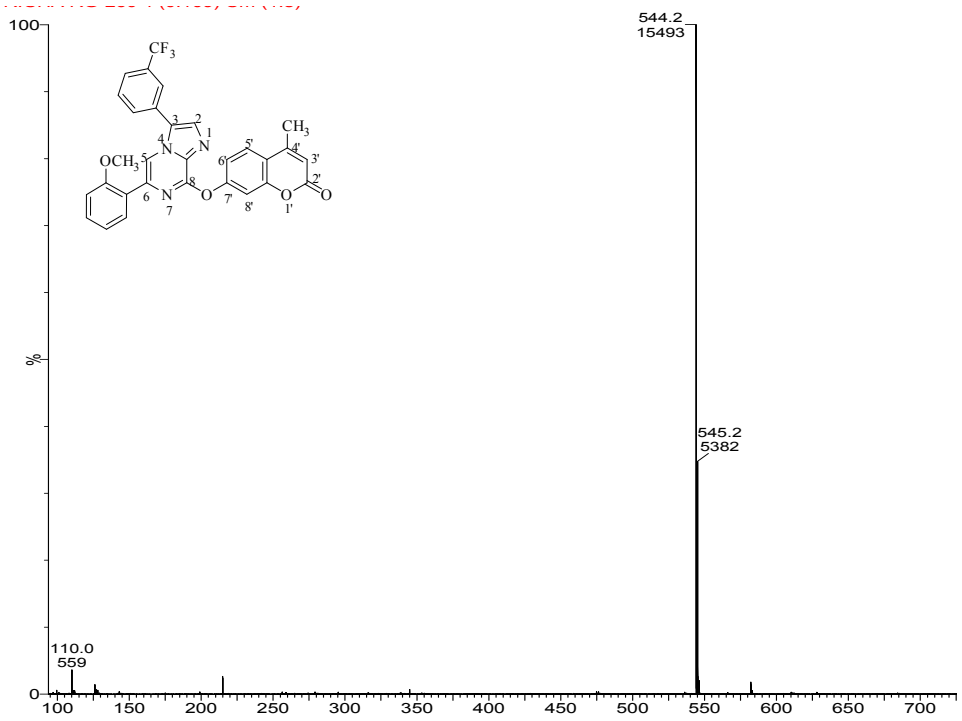


Fig S73: Mass spectrum of 7'-(6-(2-methoxyphenyl)-3-(3 (trifluoromethyl)phenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (27)

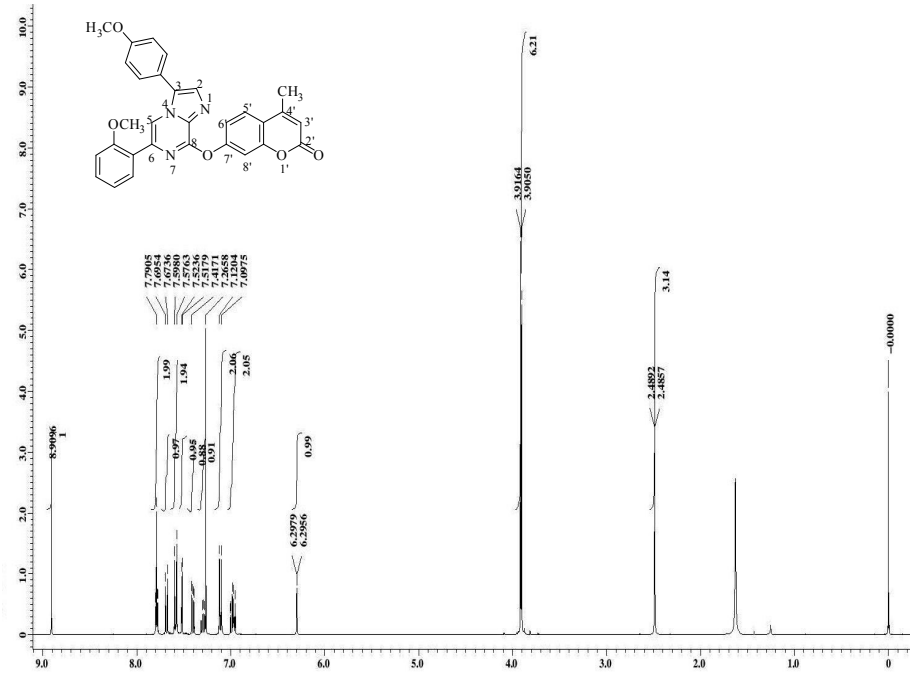


Fig S74: ^{1}H NMR spectrum of 7'-(6-(2-methoxyphenyl)-3-(4-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (28)

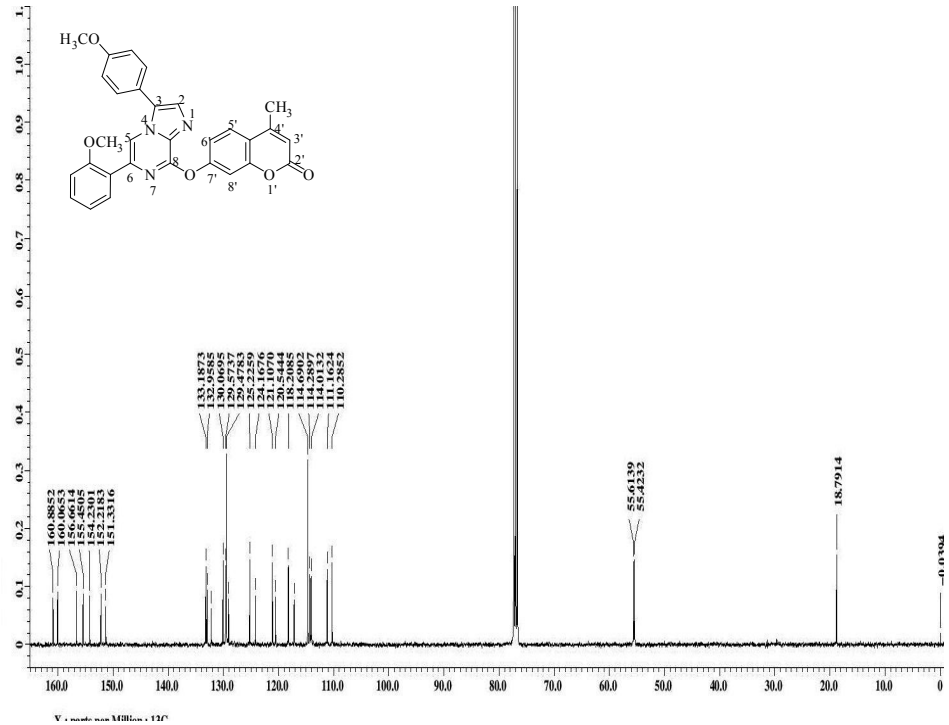


Fig S75: ^{13}C NMR spectrum of 7'-(6-(2-methoxyphenyl)-3-(4-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (28)

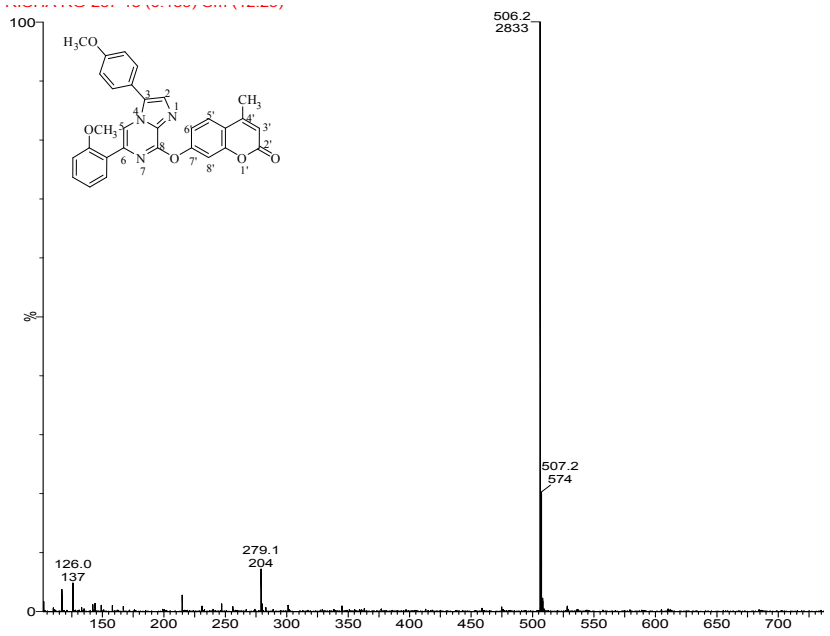


Fig S76: Mass spectrum of 7'-(6-(2-methoxyphenyl)-3-(4-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (28)

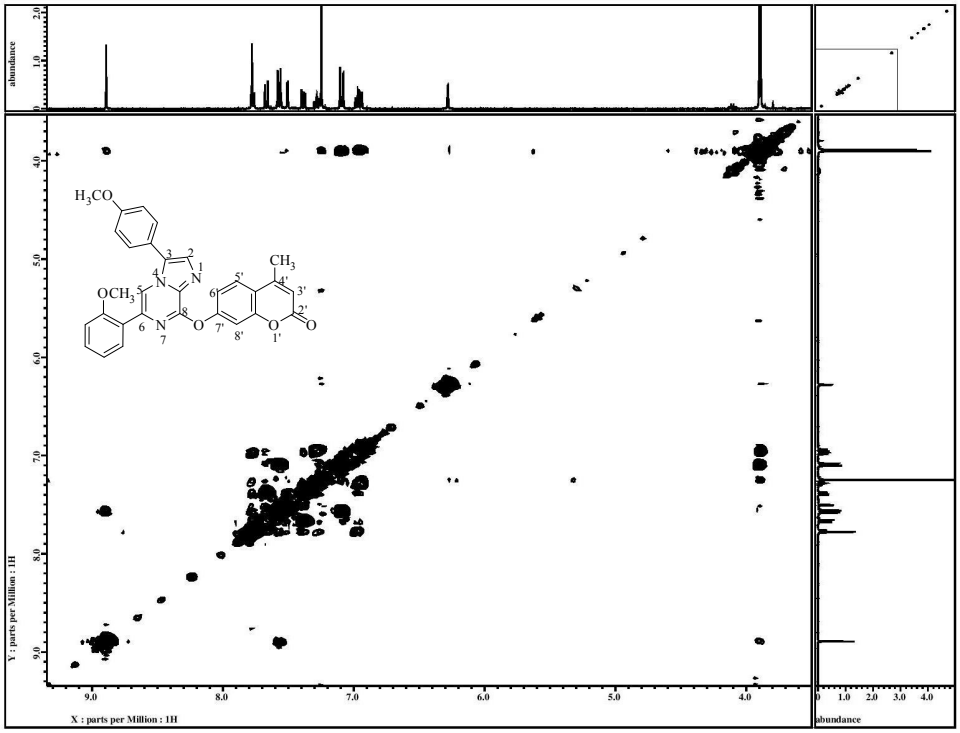


Fig S77: NOE spectrum of 7'-(6-(2-methoxyphenyl)-3-(4-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (28)

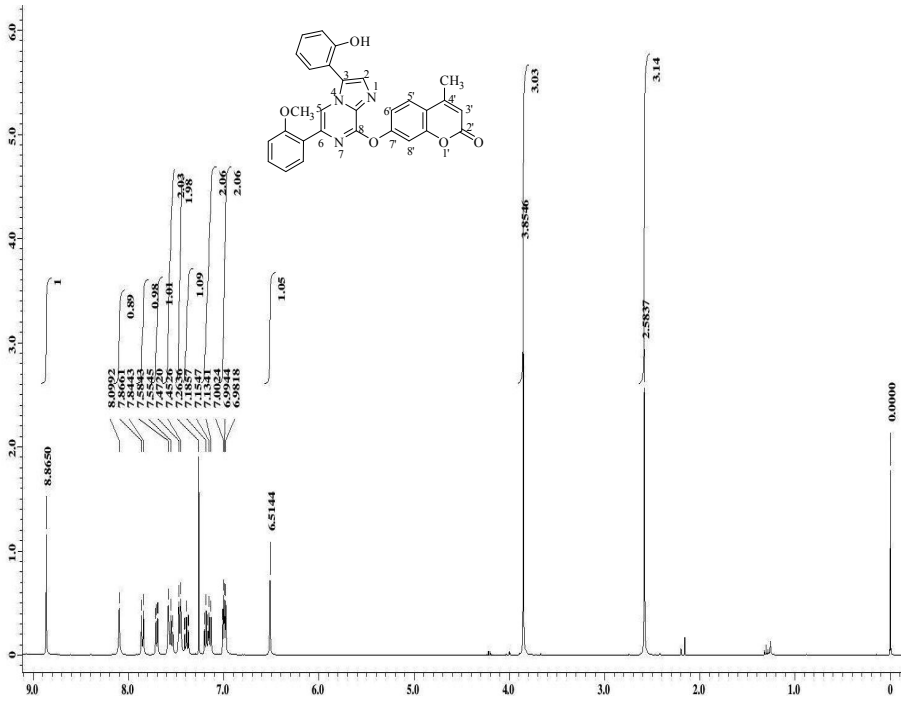


Fig S78: ^{1}H NMR spectrum of 7'-(3-(2-hydroxyphenyl)-6-(2-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (29)

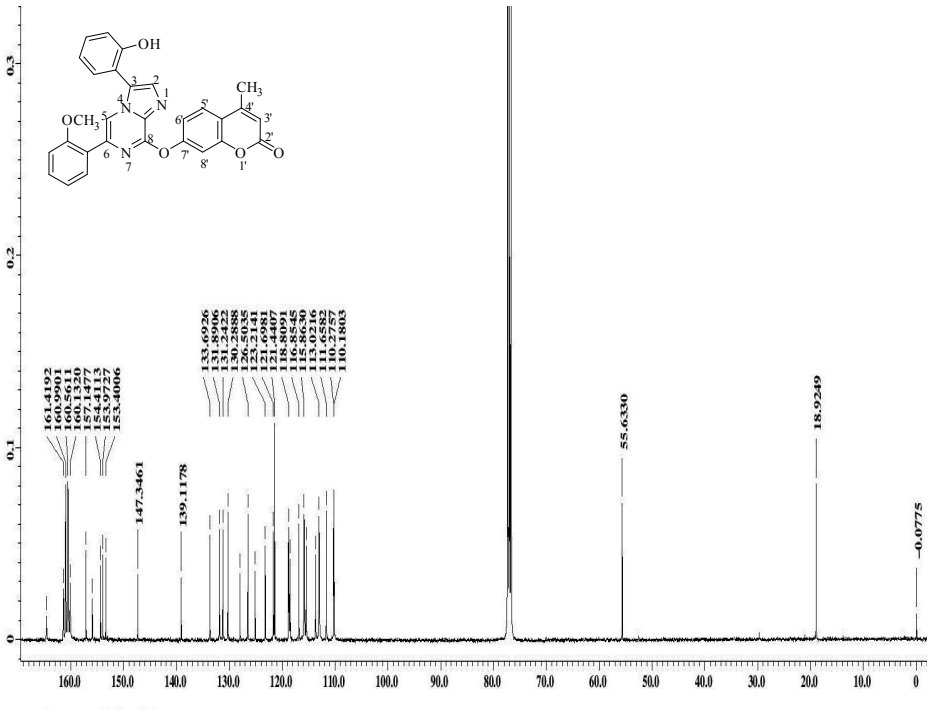


Fig S79: ^{13}C NMR spectrum of 7'-(3-(2-hydroxyphenyl)-6-(2-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (29)

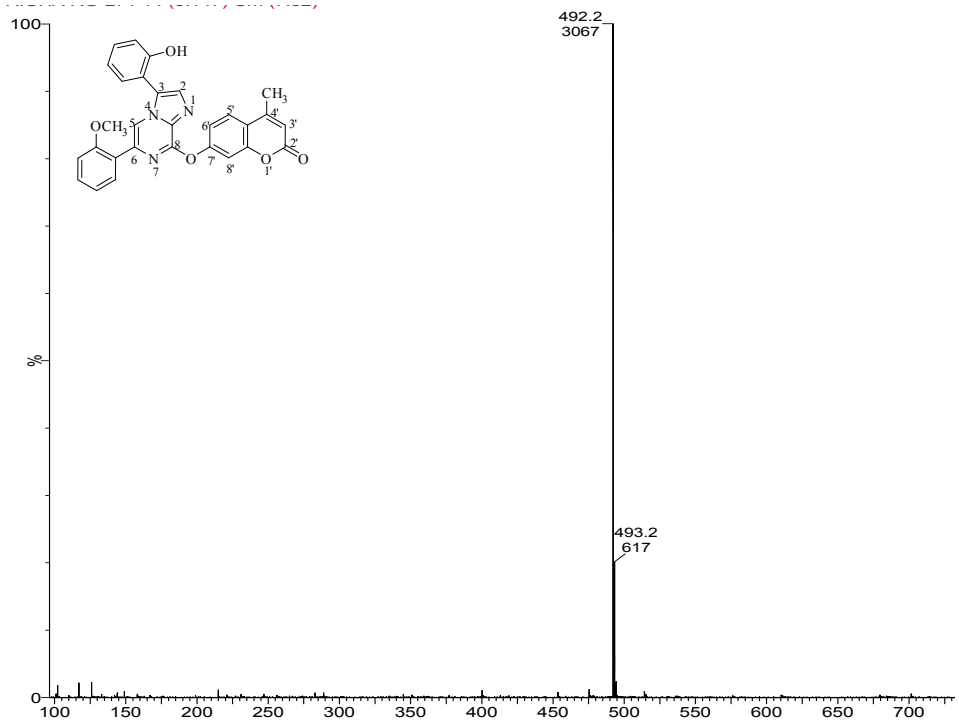


Fig S80: Mass spectrum of 7'-(3-(2-hydroxyphenyl)-6-(2-methoxyphenyl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (29)

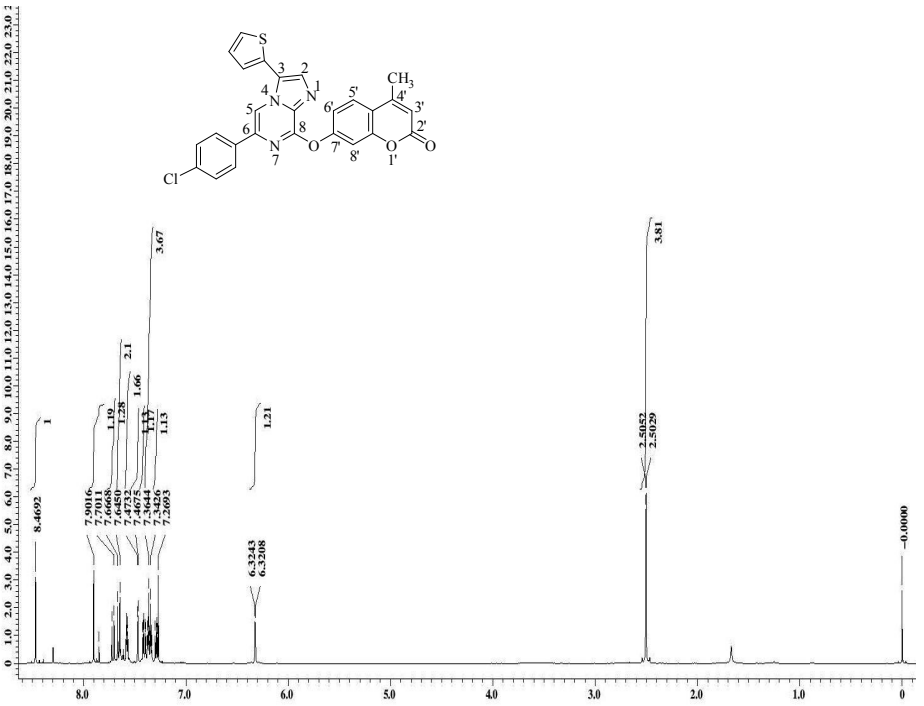


Fig S81: ^{1}H NMR spectrum of 7'-(6-(4-chlorophenyl)-3-(thiophen-2-yl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (30)

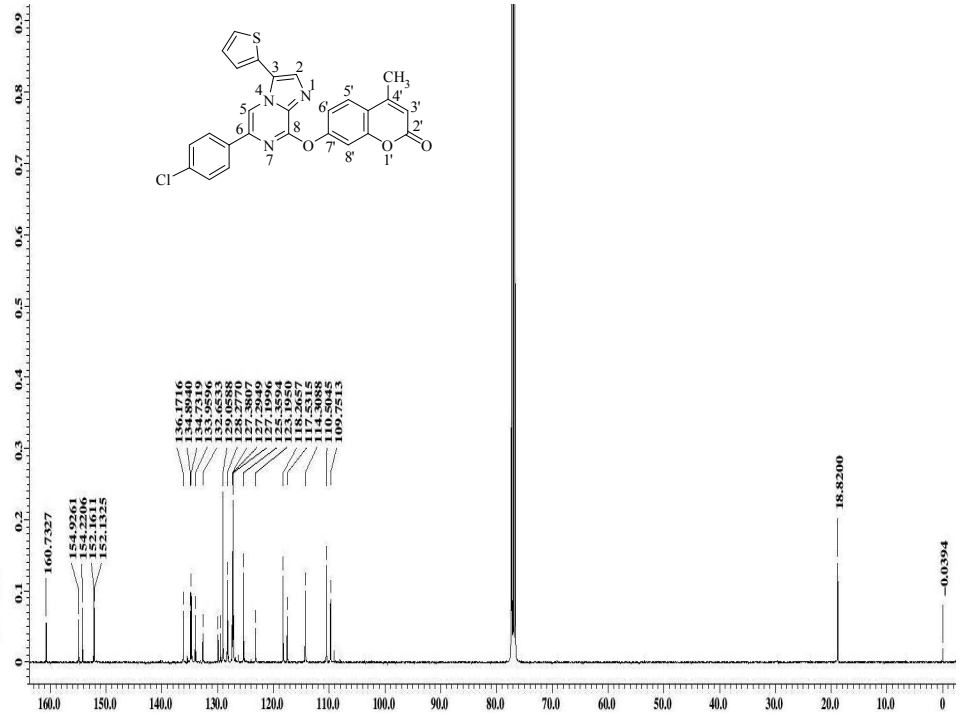


Fig S82: ^{13}C NMR spectrum of 7'-(6-(4-chlorophenyl)-3-(thiophen-2-yl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (30)

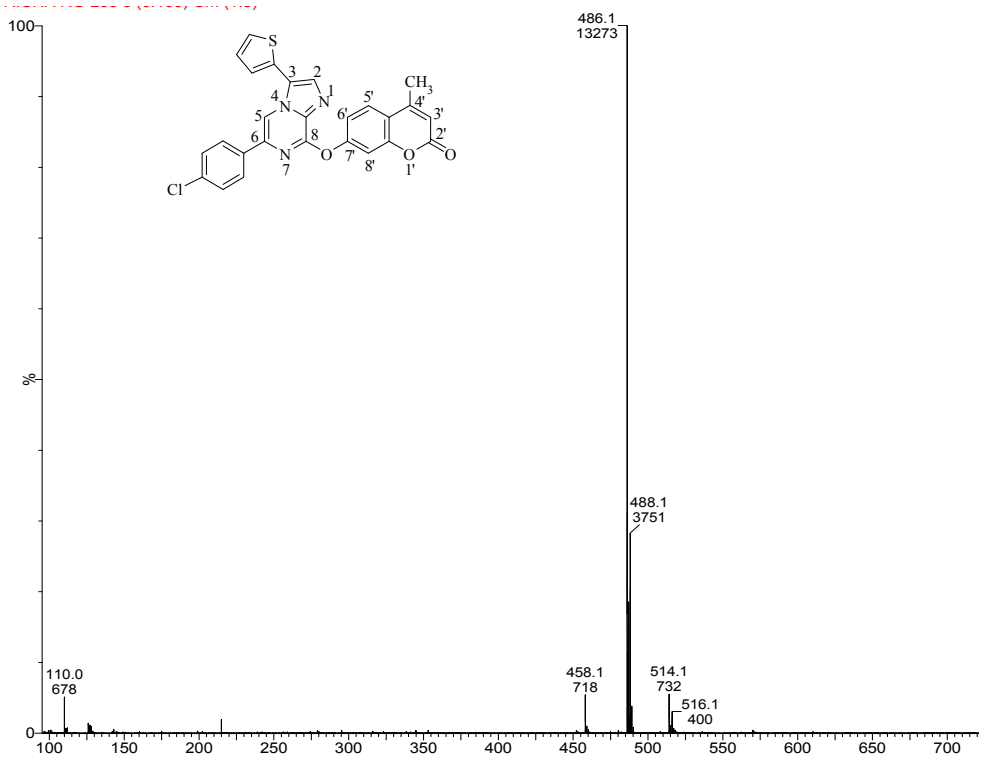


Fig S83: Mass spectrum of 7'-(6-(4-chlorophenyl)-3-(thiophen-2-yl)imidazo[1,2-*a*]pyrazin-8-yloxy)-4'-methyl-2*H*-chromen-2'-one (30)

MTT assay: % Cytotoxicity of compound 16b at different concentrations

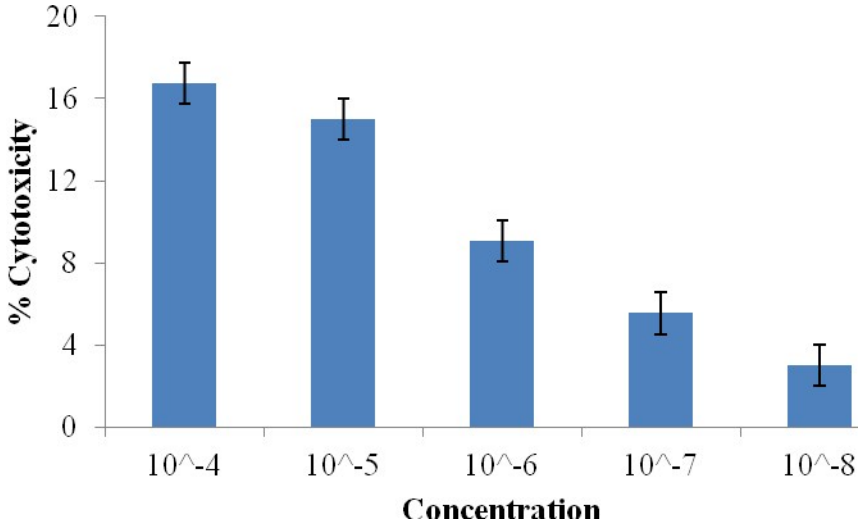


Fig S84: Graph showing cytotoxicity of compound **16b** on Hek293 cells

Shake-flask method: Partition coefficient for the target compounds was determined at room temperature using n-octanol–phosphate buffer (0.15 M, pH = 7.4). The experiments were performed in the system phosphate buffer: n-octanol at different volumes (30: 1, 50: 1). The stock solutions of the entire compounds were prepared in dimethylsulfoxide (spectroscopy grade) at concentration of 5×10^{-4} M. All solutions were pipette into glass vials; phosphate buffer and stock solution (125µL, 250µL) were added with a micropipette. The wavelength chosen according to the λ_{max} of the compounds i.e., 307, 315, 287, 323, 283, 290, 272, and 294 for **6**, **7a**, **9b**, **10b**, **11b**, **16b**, **28** and **30** respectively. Initial absorbance (A_i) of stock solution in the buffer phase was recorded for each compound. Followed this, n-Octanol was added into each vial. The phases were shaken together on a mechanical shaker (METREX, Cat No. MRS-50H) for 45 minutes, centrifuged (REMI R-24) at 2500 rpm for 30 min to afford complete phase separation, and n-octanol phase was removed. Absorbance of the buffer phase was measured spectrophotometrically using a CHAMPION UV-500 spectrophotometer.

P values were calculated from the following equation:-

$$P = \frac{A_i - A_f}{A_f} \times \frac{V_w}{V_o}$$

Where A_i and A_f represent the absorbance of compounds in the aqueous phase before and after partitioning, respectively. V_w and V_o represent the volume of the aqueous and organic phases used in the octanol/buffer system.

Molecular Modelling (Docking): Coordinates from the X-ray crystal structure of (PDB ID: 3OG7) were taken from the RCSB Protein Data Bank. Compounds were constructed with the builder toolkit of the software package ArgusLab 4.0.1 (www.arguslab.com) and energy minimized using the semiempirical quantum mechanical method PM3. The monomeric structure of the enzyme was chosen, and the active site was defined around the ligand. The molecule to be docked in the enzyme active site was inserted into the work space carrying the structure of the enzyme. The docking program implements an efficient grid-based docking algorithm, which approximates an exhaustive search within the free volume of the binding site cavity. The conformational space was surveyed by the geometry optimization of the flexible ligand (rings are treated as rigid) in combination with the incremental construction of the ligand torsions. Thus, docking occurred between the flexible ligand parts of the compound and enzyme. The ligand orientation was determined by a shape scoring function based on A score and the final positions were ranked by lowest interaction energy values. Hydrogen bond and hydrophobic interactions between the compound and enzyme were explored by distance measurements.