

SUPPLEMENTARY MATERIAL TO  
**Microwave-assisted synthesis of a series of 4,5-dihydro-1H-  
-pyrazoles endowed with selective COX-1 inhibitory potency**

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*1-(4-Cyanophenyl)-5-(3,4-methylenedioxyphenyl)-3-(2-thienyl)-4,5-dihydro-1H-pyrazole (2a)*<sup>28</sup>

Beige powder. M.P.: 156-158 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3103, 3076, 2976, 2899, 2208, 1600, 1521, 1510, 1481, 1440, 1396, 1325, 1311, 1242, 1193, 1174, 1151, 1132, 1118, 1095, 1056, 1035, 993, 958, 933, 900, 860, 840, 821, 802, 734, 727, 665. <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  / ppm: 3.26 (dd,  $J_{AB} = 17.64$  Hz,  $J_{AX} = 4.95$  Hz, 1H, C<sub>4</sub>-H<sub>A</sub> pyrazoline), 4.00 (dd,  $J_{BA} = 17.70$  Hz,  $J_{BX} = 11.97$  Hz, 1H, C<sub>4</sub>-H<sub>B</sub> pyrazoline), 5.63 (dd,  $J_{BX} = 11.85$  Hz,  $J_{AX} = 4.95$  Hz, 1H, C<sub>5</sub>-H<sub>X</sub> pyrazoline), 6.04 (d,  $J = 2.40$  Hz, 2H), 6.78-6.81 (m, 2H), 6.93 (d,  $J = 7.92$  Hz, 1H), 7.07 (d,  $J = 8.82$  Hz, 2H), 7.18-7.21 (m, 1H), 7.42 (d,  $J = 3.57$  Hz, 1H), 7.63 (d,  $J = 8.85$  Hz, 2H), 7.74-7.76 (m, 1H). <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  / ppm: 44.3 (CH<sub>2</sub>), 62.5 (CH), 99.5 (C), 101.6 (CH<sub>2</sub>), 106.4 (CH), 109.2 (CH), 113.2 (2CH), 119.4 (CH), 120.4 (C), 128.5 (CH), 129.2 (CH), 129.5 (CH), 133.8 (2CH), 135.4 (d,  $J = 17.26$  Hz, 2C), 146.8 (C), 147.2 (C), 147.5 (C), 148.3 (C). HRMS (*m/z*): [M+H]<sup>+</sup> calcd. for C<sub>21</sub>H<sub>15</sub>N<sub>3</sub>O<sub>2</sub>S: 374.0958. Found: 374.0964.

*1-(4-Fluorophenyl)-5-(3,4-methylenedioxyphenyl)-3-(2-thienyl)-4,5-dihydro-1H-pyrazole (2b)*<sup>28</sup>

Brown powder. M.P.: 138-139 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3082, 2960, 2885, 1604, 1504, 1496, 1481, 1442, 1373, 1361, 1315, 1288, 1247, 1224, 1180, 1153, 1109, 1078, 1033, 993, 927, 910, 866, 813, 802, 746, 707, 661. <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  / ppm: 3.17 (dd,  $J_{AB} = 17.31$  Hz,  $J_{AX} = 6.81$  Hz, 1H, C<sub>4</sub>-H<sub>A</sub> pyrazoline), 3.93 (dd,  $J_{BA} = 17.31$  Hz,  $J_{BX} = 11.94$  Hz, 1H, C<sub>4</sub>-H<sub>B</sub> pyrazoline), 5.42 (dd,  $J_{BX} = 11.94$  Hz,  $J_{AX} = 6.81$  Hz, 1H, C<sub>5</sub>-H<sub>X</sub> pyrazoline), 6.04 (s, 2H), 6.83-6.86 (m, 2H), 6.94-6.97 (m, 1H), 6.98-7.00 (m, 2H), 7.05-7.11 (m, 2H), 7.14-7.17 (m, 1H), 7.31 (d,  $J = 3.48$  Hz, 1H), 7.66 (d,  $J = 4.98$  Hz, 1H). <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  / ppm: 44.4 (CH<sub>2</sub>), 64.1 (CH), 101.6 (CH<sub>2</sub>), 106.6 (CH), 109.1 (CH), 114.7 (d,  $J = 7.49$  Hz, 2CH), 115.9 (d,  $J = 22.18$  Hz, 2CH), 119.7 (CH), 123.2 (C), 128.1 (d,  $J = 22.19$  Hz, 2CH), 136.2 (d,  $J = 20.52$  Hz, CH), 141.5 (C), 144.5 (C), 147.1 (C), 148.2 (C), 154.9 (C), 157.9 (C). HRMS (*m/z*): [M+H]<sup>+</sup> calcd. for C<sub>20</sub>H<sub>15</sub>FN<sub>2</sub>O<sub>2</sub>S: 367.0911. Found: 367.0917.

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*1-(4-Bromophenyl)-5-(3,4-methylenedioxyphenyl)-3-(2-thienyl)-4,5-dihydro-1H-pyrazole (2c)*<sup>28</sup>

Dark beige powder. M.P.: 107-108 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3105, 3070, 2962, 2899, 1589, 1481, 1442, 1381, 1319, 1240, 1193, 1128, 1118, 1107, 1093, 1072, 1035, 997, 958, 937, 898, 854, 813, 802, 748, 721, 705, 690. <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  / ppm: 3.18 (dd,  $J_{AB}$  = 17.43 Hz,  $J_{AX}$  = 6.21 Hz, 1H, C<sub>4</sub>-H<sub>A</sub> pyrazoline), 3.94 (dd,  $J_{BA}$  = 17.25 Hz,  $J_{BX}$  = 12.03 Hz, 1H, C<sub>4</sub>-H<sub>B</sub> pyrazoline), 5.47 (dd,  $J_{BX}$  = 12.06 Hz,  $J_{AX}$  = 5.91 Hz, 1H, C<sub>5</sub>-H<sub>X</sub> pyrazoline), 6.03 (s, 2H), 6.82-6.85 (m, 2H), 6.91-6.96 (m, 2H), 7.01 (d,  $J$  = 8.70 Hz, 1H), 7.15-7.21 (m, 2H), 7.32-7.38 (m, 2H), 7.68 (d,  $J$  = 5.04 Hz, 1H). <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  / ppm: 44.3 (CH<sub>2</sub>), 63.3 (CH), 101.6 (CH<sub>2</sub>), 106.5 (CH), 109.1 (CH), 110.3 (C), 113.5 (CH), 115.3 (2CH), 119.4 (d,  $J$  = 30.54 Hz, CH), 128.1 (d,  $J$  = 28.02 Hz, CH), 129.4 (CH), 131.9 (2CH), 136.3 (d,  $J$  = 43.55 Hz, 2C), 143.6 (C), 145.1 (C), 147.1 (C), 148.2 (C). HRMS ( $m/z$ ): [M+H]<sup>+</sup> calcd. for C<sub>20</sub>H<sub>15</sub>BrN<sub>2</sub>O<sub>2</sub>S: 427.0110. Found: 427.0111.

*1-(4-Methylphenyl)-5-(3,4-methylenedioxyphenyl)-3-(2-thienyl)-4,5-dihydro-1H-pyrazole (2d)*<sup>28</sup>

Dark brown powder. M.P.: 152-154 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3107, 3070, 2916, 2860, 1606, 1556, 1514, 1504, 1483, 1442, 1377, 1321, 1311, 1240, 1193, 1130, 1114, 1099, 1037, 995, 939, 898, 854, 817, 804, 721, 702, 665. <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  / ppm: 2.16 (s, 3H), 3.08 (dd,  $J_{AB}$  = 17.28 Hz,  $J_{AX}$  = 6.54 Hz, 1H, C<sub>4</sub>-H<sub>A</sub> pyrazoline), 3.84 (dd,  $J_{BA}$  = 17.28 Hz,  $J_{BX}$  = 12.06 Hz, 1H, C<sub>4</sub>-H<sub>B</sub> pyrazoline), 5.36 (dd,  $J_{BX}$  = 11.97 Hz,  $J_{AX}$  = 6.54 Hz, 1H, C<sub>5</sub>-H<sub>X</sub> pyrazoline), 5.97 (s, 2H), 6.77 (s, 2H), 6.85 (d,  $J$  = 8.37 Hz, 2H), 6.95-6.98 (m, 3H), 7.07-7.10 (m, 1H), 7.21-7.22 (m, 1H), 7.58 (d,  $J$  = 4.86 Hz, 1H). <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  / ppm: 20.6 (CH<sub>3</sub>), 44.1 (CH<sub>2</sub>), 63.8 (CH), 101.5 (CH<sub>2</sub>), 106.6 (CH), 109.0 (CH), 113.7 (2CH), 119.6 (CH), 123.1 (C), 125.6 (CH), 127.8 (d,  $J$  = 19.81 Hz, CH), 128.2 (CH), 129.9 (d,  $J$  = 16.17 Hz, 2CH), 136.6 (2C), 142.4 (C), 143.7 (C), 146.9 (C), 148.1 (C). HRMS ( $m/z$ ): [M+H]<sup>+</sup> calcd. for C<sub>21</sub>H<sub>18</sub>N<sub>2</sub>O<sub>2</sub>S: 363.1162. Found: 363.1167.

*1-(4-Methylsulfonylphenyl)-5-(3,4-methylenedioxyphenyl)-3-(2-thienyl)-4,5-dihydro-1H-pyrazole (2e)*<sup>28</sup>

Yellow powder. M.P.: 170-171 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3099, 3001, 2924, 2823, 1589, 1502, 1483, 1442, 1419, 1388, 1315, 1298, 1246, 1139, 1089, 1029, 948, 921, 900, 821, 769, 717. <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  / ppm: 3.07 (s, 3H), 3.19 (dd,  $J_{AB}$  = 17.58 Hz,  $J_{AX}$  = 5.01 Hz, 1H, C<sub>4</sub>-H<sub>A</sub> pyrazoline), 3.96 (dd,  $J_{BA}$  = 17.61 Hz,  $J_{BX}$  = 11.91 Hz, 1H, C<sub>4</sub>-H<sub>B</sub> pyrazoline), 5.58 (dd,  $J_{BX}$  = 11.88 Hz,  $J_{AX}$  = 5.01 Hz, 1H, C<sub>5</sub>-H<sub>X</sub> pyrazoline), 5.99 (d,  $J$  = 1.74 Hz, 2H), 6.74-6.79 (m, 2H), 6.88 (d,  $J$  = 7.92 Hz, 1H), 7.07 (d,  $J$  = 8.88 Hz, 2H), 7.14 (dd,  $J$  = 4.98 Hz,  $J$  = 3.69 Hz, 1H), 7.36 (d,  $J$  = 3.51 Hz, 1H), 7.65-7.69 (m, 3H). <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  / ppm: 44.3 (CH<sub>3</sub>), 44.6 (CH<sub>2</sub>), 62.6 (CH), 101.6 (CH<sub>2</sub>), 106.4 (CH), 109.2 (CH), 112.6 (2CH), 119.4 (CH), 128.5 (CH), 129.1 (2CH), 129.4 (CH), 129.6 (CH), 135.3 (C), 135.6 (2C), 147.3 (3C), 148.3 (C). HRMS ( $m/z$ ): [M+H]<sup>+</sup> calcd. for C<sub>21</sub>H<sub>18</sub>N<sub>2</sub>O<sub>4</sub>S<sub>2</sub>: 427.0781. Found: 427.0781.

*1-(3-Nitrophenyl)-5-(3,4-methylenedioxyphenyl)-3-(2-thienyl)-4,5-dihydro-1H-pyrazole (2f)*

Orange powder. M.P.: 179-181 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3113, 2914, 2887, 1612, 1570, 1519, 1498, 1481, 1438, 1379, 1344, 1319, 1242, 1205, 1186, 1111, 1099, 1033, 1008, 966, 929, 887, 856, 848, 827, 804, 786, 734, 709, 663. <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  / ppm: 3.22

(dd,  $J_{AB}$  = 17.58 Hz,  $J_{AX}$  = 5.58 Hz, 1H, C<sub>4</sub>-H<sub>A</sub> pyrazoline), 3.96 (dd,  $J_{BA}$  = 17.55 Hz,  $J_{BX}$  = 11.94 Hz, 1H, C<sub>4</sub>-H<sub>B</sub> pyrazoline), 5.56 (dd,  $J_{BX}$  = 11.88 Hz,  $J_{AX}$  = 5.70 Hz, 1H, C<sub>5</sub>-H<sub>X</sub> pyrazoline), 5.99 (d,  $J$  = 2.46 Hz, 2H), 6.78-6.83 (m, 2H), 6.89 (d,  $J$  = 7.83 Hz, 1H), 7.14 (dd,  $J$  = 3.63 Hz,  $J$  = 5.01 Hz, 1H), 7.25 (dd,  $J$  = 8.22 Hz and  $J$  = 2.31 Hz, 1H), 7.35 (d,  $J$  = 3.60 Hz, 1H), 7.43 (t,  $J$  = 8.16 Hz, 8.10 Hz, 16.26 Hz, 1H), 7.54 (dd,  $J$  = 8.04 Hz,  $J$  = 2.22 Hz, 1H), 7.68 (d,  $J$  = 5.04 Hz, 1H), 7.76-7.78 (m, 1H). <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  / ppm: 44.4 (CH<sub>2</sub>), 63.2 (CH), 101.6 (CH<sub>2</sub>), 106.5 (CH), 107.1 (CH), 109.2 (CH), 113.1 (CH), 119.1 (CH), 119.7 (CH), 128.4 (CH), 128.9 (CH), 129.1 (CH), 130.8 (CH), 135.5 (2C), 145.0 (C), 146.6 (C), 147.3 (C), 148.4 (C), 149.0 (C). HRMS (*m/z*): [M+H]<sup>+</sup> calcd. for C<sub>20</sub>H<sub>15</sub>N<sub>3</sub>O<sub>4</sub>S: 394.0856. Found: 394.0862.

*1-(3-Fluorophenyl)-5-(3,4-methylenedioxyphenyl)-3-(2-thienyl)-4,5-dihydro-1H-pyrazole (2g)*

Yellow powder. M.P.: 130-131 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3105, 3072, 2904, 1604, 1571, 1490, 1483, 1442, 1382, 1323, 1269, 1242, 1230, 1186, 1155, 1130, 1112, 1037, 1006, 960, 939, 891, 840, 819, 802, 761, 719, 680, 669. <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  / ppm: 3.14 (dd,  $J_{AB}$  = 17.46 Hz,  $J_{AX}$  = 5.91 Hz, 1H, C<sub>4</sub>-H<sub>A</sub> pyrazoline), 3.90 (dd,  $J_{BA}$  = 17.46 Hz,  $J_{BX}$  = 12.00 Hz, 1H, C<sub>4</sub>-H<sub>B</sub> pyrazoline), 5.44 (dd,  $J_{BX}$  = 11.94 Hz,  $J_{AX}$  = 5.88 Hz, 1H, C<sub>5</sub>-H<sub>X</sub> pyrazoline), 5.98 (s, 2H), 6.47-6.54 (m, 1H), 6.69-6.79 (m, 4H), 6.88 (d,  $J$  = 7.68 Hz, 1H), 7.10-7.13 (m, 1H), 7.17 (d,  $J$  = 7.23 Hz, 1H), 7.29 (d,  $J$  = 3.57 Hz, 1H), 7.63 (d,  $J$  = 5.04 Hz, 1H). <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  / ppm: 44.3 (CH<sub>2</sub>), 63.3 (CH), 99.9 (CH), 100.3 (CH), 101.6 (CH<sub>2</sub>), 105.1 (CH), 105.4 (CH), 106.5 (CH), 109.2 (d,  $J$  = 17.66 Hz, 2CH), 119.6 (CH), 128.4 (d,  $J$  = 14.67 Hz, 2CH), 131.1 (C), 135.7 (C), 136.1 (C), 145.4 (C), 147.1 (C), 148.3 (C), 161.8 and 164.9 (C). HRMS (*m/z*): [M+H]<sup>+</sup> calcd. for C<sub>20</sub>H<sub>15</sub>FN<sub>2</sub>O<sub>2</sub>S: 367.0911. Found: 367.0911.

*1-(3-Bromophenyl)-5-(3,4-methylenedioxyphenyl)-3-(2-thienyl)-4,5-dihydro-1H-pyrazole (2h)*

Beige powder. M.P.: 125-126 °C. IR  $\nu_{\max}$  (cm<sup>-1</sup>): 3107, 3070, 2914, 2872, 1589, 1579, 1556, 1500, 1475, 1444, 1373, 1346, 1317, 1238, 1203, 1184, 1118, 1099, 1078, 1035, 1001, 985, 933, 910, 858, 837, 817, 758, 715, 705, 675. <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  / ppm: 3.14 (dd,  $J_{AB}$  = 17.49 Hz,  $J_{AX}$  = 5.82 Hz, 1H, C<sub>4</sub>-H<sub>A</sub> pyrazoline), 3.89 (dd,  $J_{BA}$  = 17.52 Hz,  $J_{BX}$  = 12.03 Hz, 1H, C<sub>4</sub>-H<sub>B</sub> pyrazoline), 5.45 (dd,  $J_{BX}$  = 11.94 Hz,  $J_{AX}$  = 5.82 Hz, 1H, C<sub>5</sub>-H<sub>X</sub> pyrazoline), 5.98 (s, 2H), 6.75-6.78 (m, 2H), 6.83-6.89 (m, 3H), 7.07-7.15 (m, 3H), 7.30 (dd,  $J$  = 3.57 Hz,  $J$  = 0.93 Hz, 1H), 7.64 (dd,  $J$  = 5.04 Hz,  $J$  = 0.93 Hz, 1H). <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  / ppm: 44.3 (CH<sub>2</sub>), 63.1 (CH), 101.6 (CH<sub>2</sub>), 106.5 (CH), 109.1 (CH), 112.2 (CH), 115.6 (CH), 119.6 (CH), 121.4 (CH), 122.7 (C), 128.4 (d,  $J$  = 7.41 Hz, 2CH), 128.6 (CH), 131.3 (CH), 135.8 (d,  $J$  = 22.81 Hz, 2C), 145.7 (d,  $J$  = 5.97 Hz, 2C), 147.1 (C), 148.3 (C). HRMS (*m/z*): [M+H]<sup>+</sup> calcd. for C<sub>20</sub>H<sub>15</sub>BrN<sub>2</sub>O<sub>2</sub>S: 427.0110. Found: 427.0119.







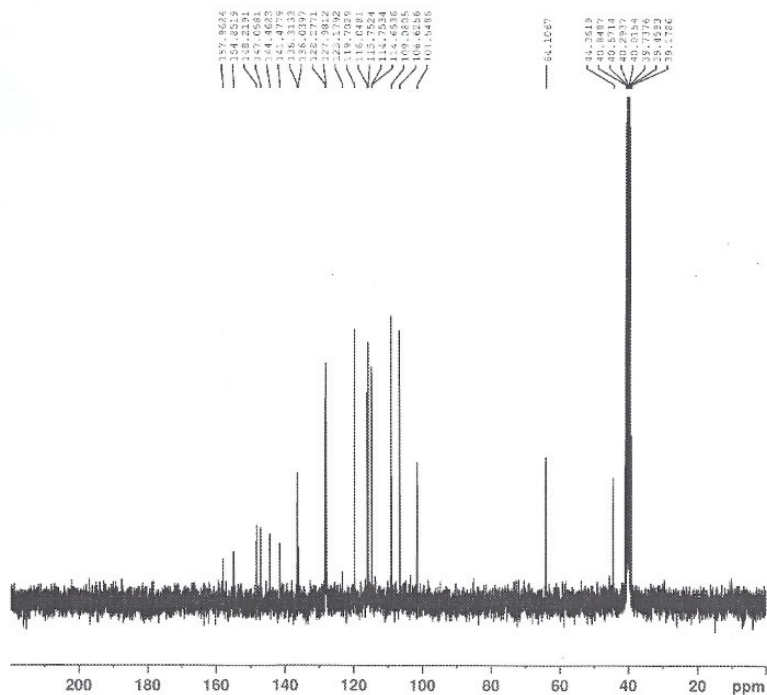


Figure S-7.  $^{13}\text{C}$  NMR spectrum of compound **2b**

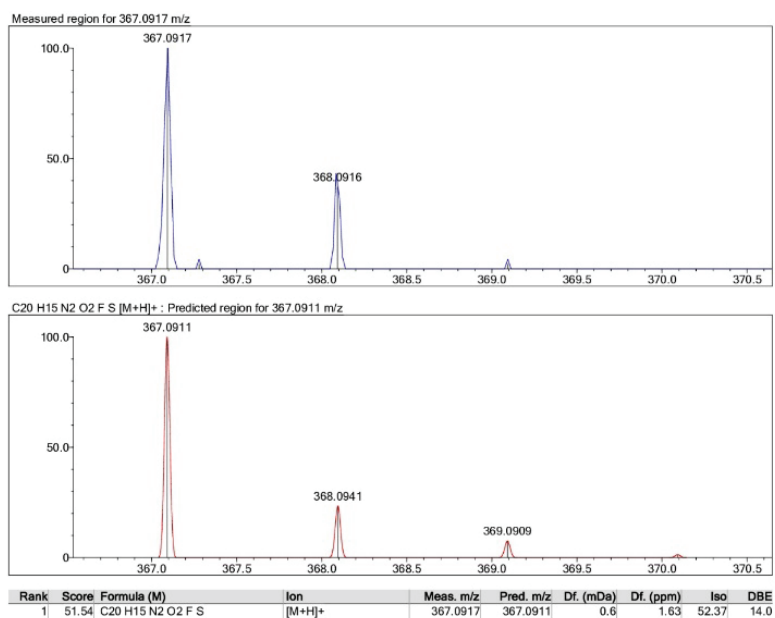


Figure S-8. HRMS spectrum of compound **2b**





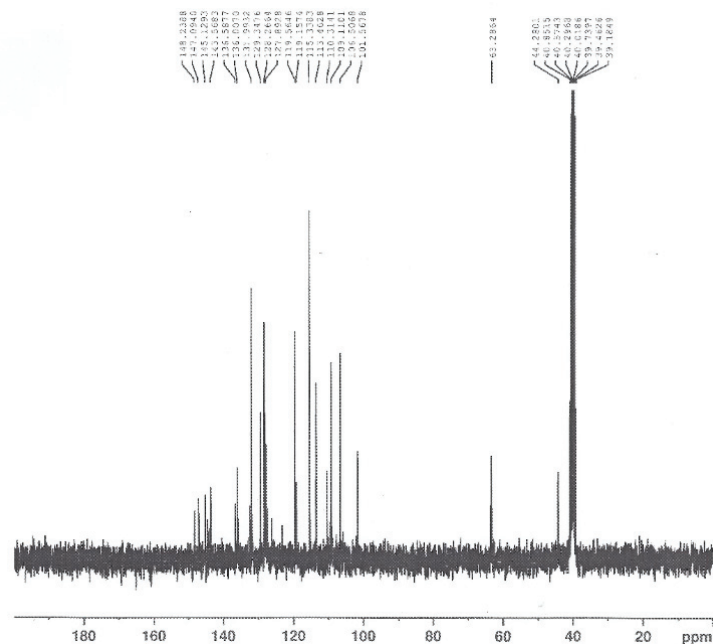


Figure S-11.  $^{13}\text{C}$  NMR spectrum of compound **2c**

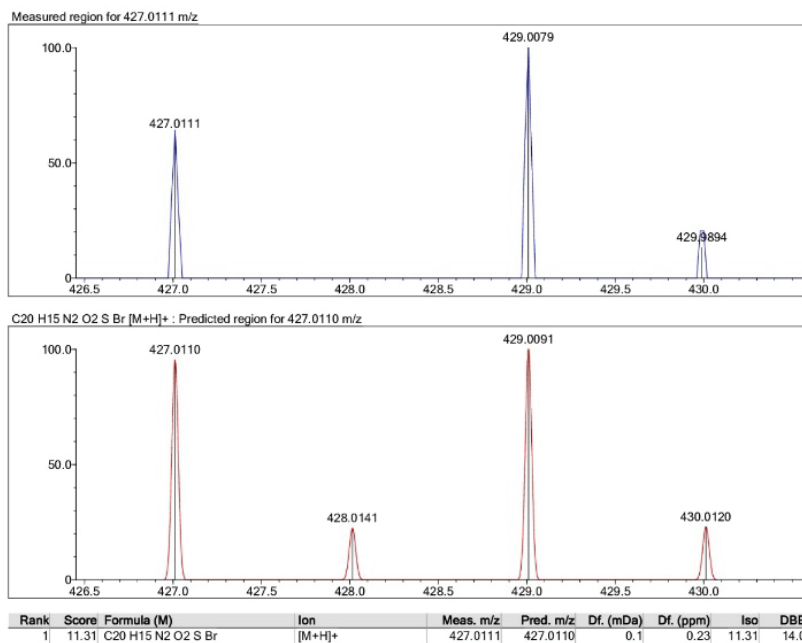


Figure S-12. HRMS spectrum of compound **2c**

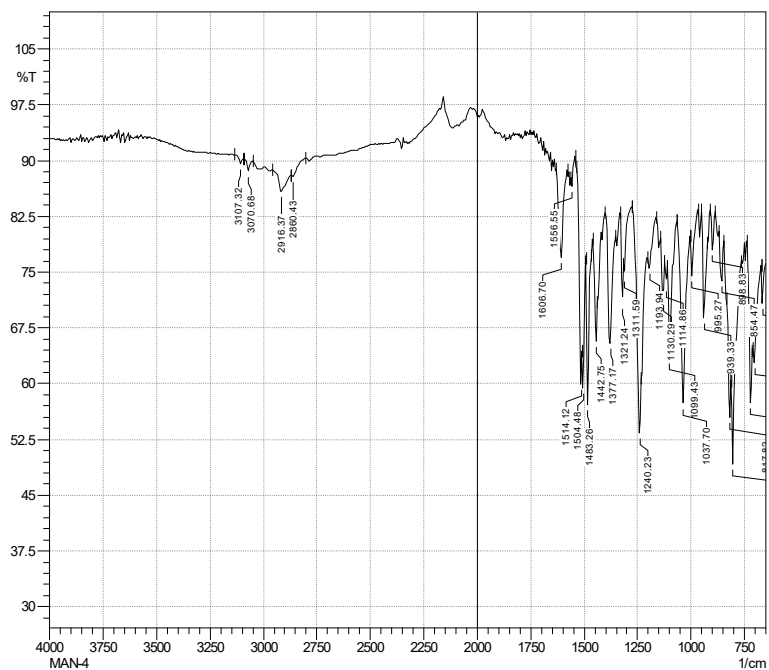
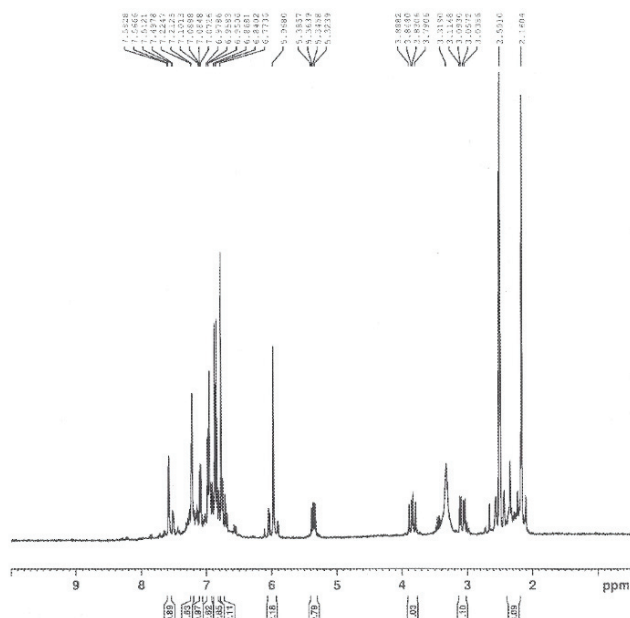


Figure S-13. IR spectrum of compound 2d







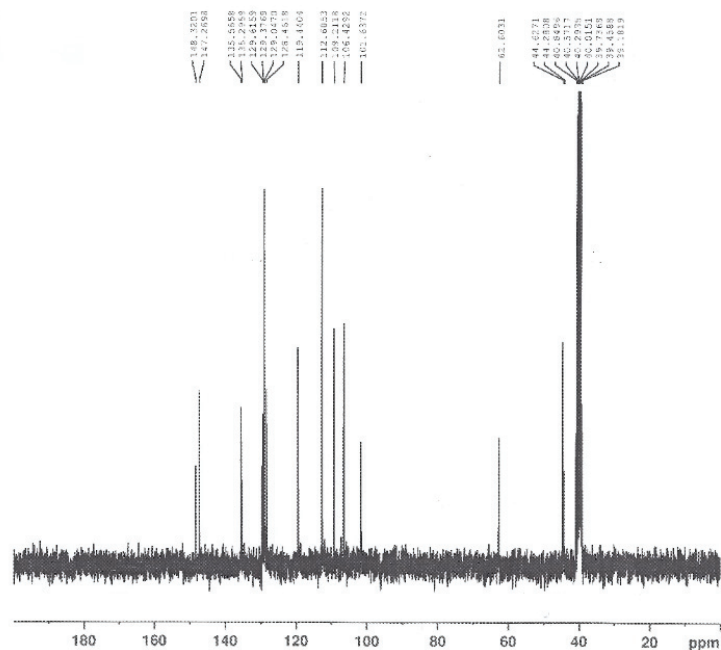


Figure S-19. <sup>13</sup>C NMR spectrum of compound **2e**

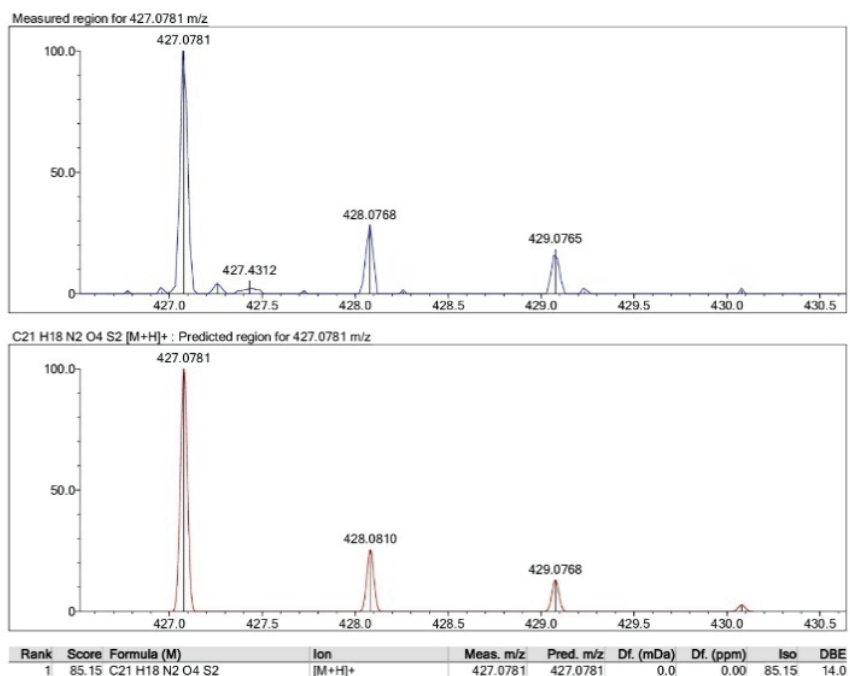


Figure S-20. HRMS spectrum of compound **2e**



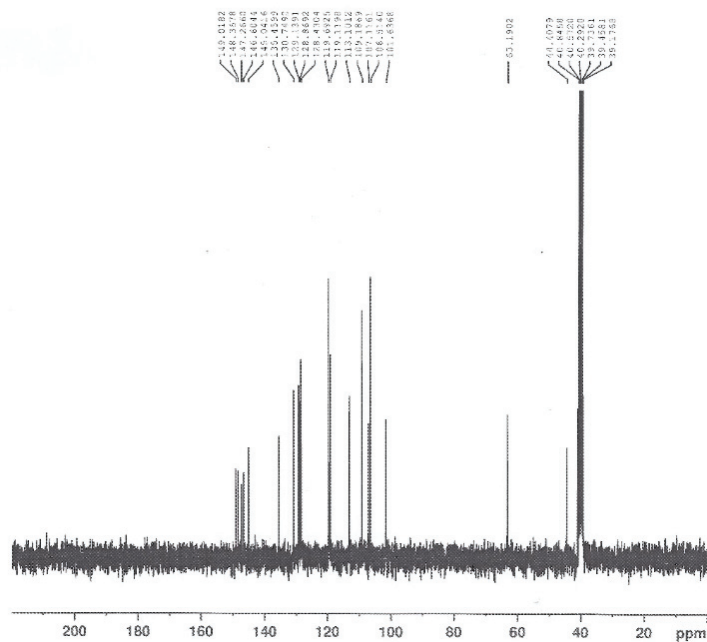


Figure S-23. <sup>13</sup>C NMR spectrum of compound **2f**

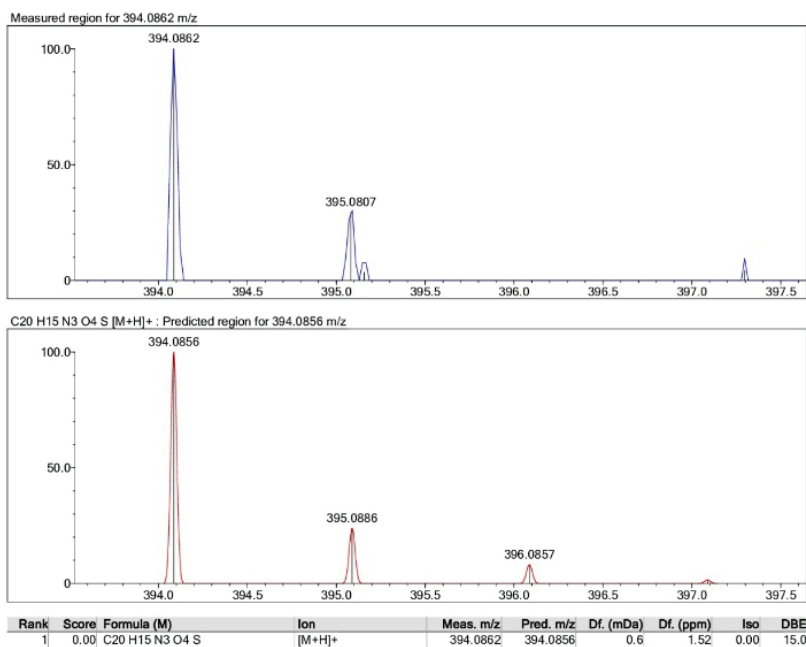


Figure S-24. HRMS spectrum of compound **2f**





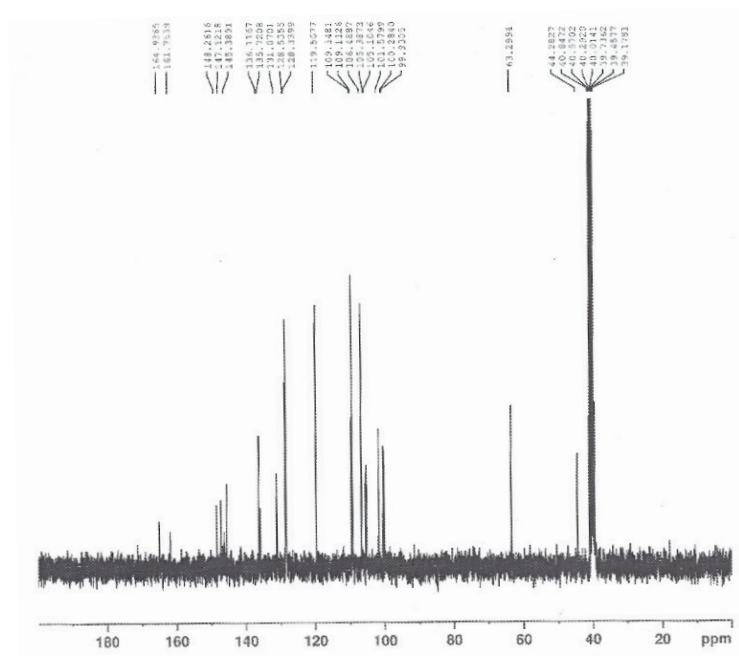


Figure S-27. <sup>13</sup>C NMR spectrum of compound **2g**

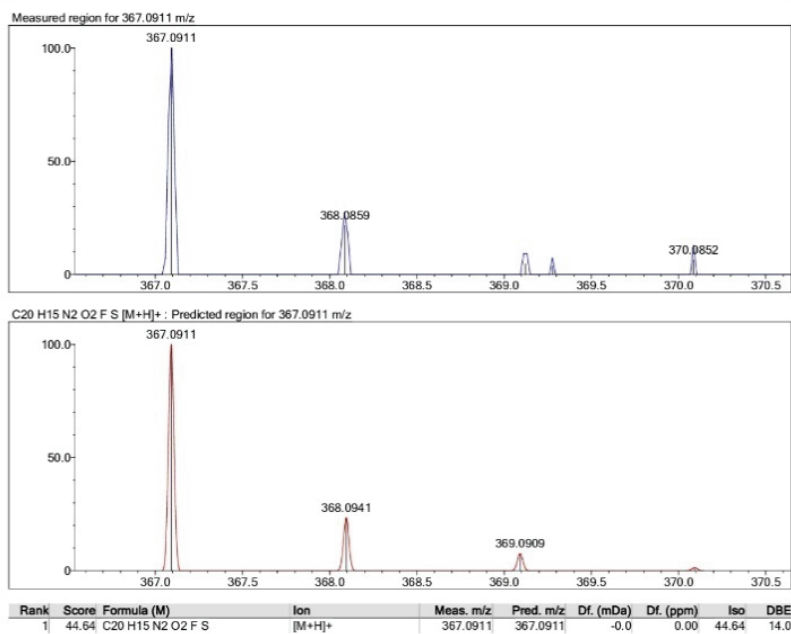


Figure S-28. HRMS spectrum of compound **2g**



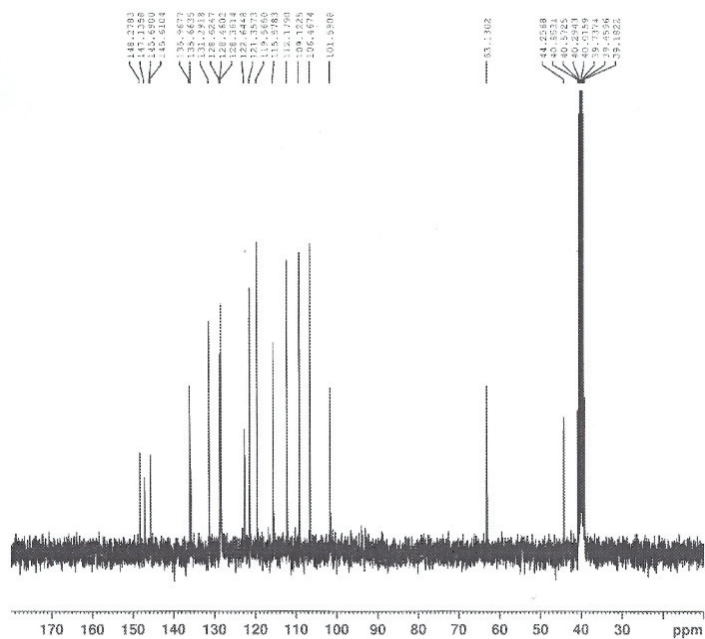


Figure S-31.  $^{13}\text{C}$  NMR spectrum of compound **2h**

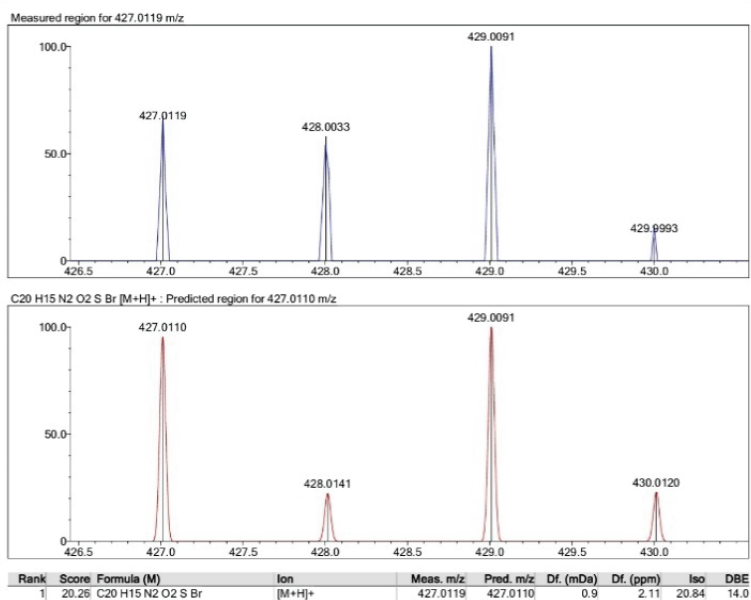


Figure S-32. HRMS spectrum of compound **2h**.