

## Supporting Information

# Design and Optimization of a Series of 1-Sulfonyl-pyrazolo[4,3-*b*]pyridines as Selective c-Met Inhibitors

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*spectral data of compound 9 (Scheme 1)*

The compound **9** was prepared as described for the synthesis of compound **7**.

6-(1-Methyl-1*H*-pyrazol-4-yl)-1-((2-nitrophenyl)sulfonyl)-1*H*-pyrazolo[4,3-*b*]pyridine(**9**).74% yield; LC-MS *m/z* (ESI) found 385 (M + H)<sup>+</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.90 (d, *J* = 1.9 Hz, 1H), 8.45–8.42 (m, 1H), 8.41 (d, *J* = 0.9 Hz, 1H), 8.38 (dd, *J* = 1.9, 0.9 Hz, 1H), 7.95 (d, *J* = 0.8 Hz, 1H), 7.89–7.87 (m, 1H), 7.86–7.82 (m, 2H), 7.78–7.74 (m, 1H), 4.03 (s, 3H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 147.30, 146.56, 141.89, 140.28, 136.87, 135.27, 134.60, 132.33, 132.10, 130.04, 128.62, 127.82, 124.32, 118.83, 116.52, 38.89. HRMS *m/z* (ESI) found 385.0730 (M + H)<sup>+</sup>, C<sub>16</sub>H<sub>13</sub>N<sub>6</sub>O<sub>4</sub>S<sup>+</sup> calcd for 385.0719; retention time 2.99 min., >98% pure.

*spectral data of compounds 65 and 66 (General Procedure A)*

The compounds **65** and **66** were prepared as described for the synthesis of compound **64** according to the General Procedure A.

6-Bromoimidazo[1,2-*a*]pyridine-3-sulfonyl Chloride (**65**). 34% yield; MS *m/z* (EI) found 296 (M)<sup>+</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.97 (m, 1H), 8.47 (s, 1H), 7.89 (d, *J* = 9.6 Hz, 1H), 7.83 (dd, *J* = 9.6, 1.7 Hz, 1H).

6-Nitroimidazo[1,2-*a*]pyridine-3-sulfonyl Chloride (**66**). 49% yield; MS *m/z* (EI) found 261 (M)<sup>+</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.43–9.30 (m, 1H), 8.48 (d, *J* = 0.8 Hz, 1H), 8.21 (dd, *J* = 10.1, 2.2 Hz, 1H), 7.90 (dt, *J* = 10.0, 0.8 Hz, 1H).

*spectral data of compounds 11-26 and 69 (General Procedure B and Scheme 3)*

Compounds **11-26** and **69** were prepared as described for the synthesis of compound **10** according to the General Procedure B.

1-((3-Fluorophenyl)sulfonyl)-6-(1-methyl-1*H*-pyrazol-4-yl)-1*H*-pyrazolo[4,3-*b*]pyridine (**11**). 54% yield; LC-MS *m/z* (ESI) found 358 (M + H)<sup>+</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.86 (s, 1H), 8.46 (s, 1H), 8.40 (s, 1H), 7.94 (s, 1H), 7.91–7.78 (m, 2H), 7.72 (d, *J* = 7.4 Hz, 1H), 7.54–7.41 (m, 1H), 7.32 (s, 1H), 4.03 (s, 3H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 162.33 (d, *J* = 253.3 Hz), 147.06, 142.58, 141.68, 138.96 (d, *J* = 7.1 Hz), 137.40, 134.55, 131.43 (d, *J* = 7.8 Hz), 129.18, 128.21, 123.69 (d, *J* = 3.5 Hz), 122.11 (d, *J* = 21.2 Hz), 119.28, 116.01, 115.29 (d, *J* = 25.1 Hz), 39.52. HRMS *m/z* (ESI) found 358.0765 (M + H)<sup>+</sup>, C<sub>16</sub>H<sub>13</sub>N<sub>5</sub>O<sub>2</sub>FS<sup>+</sup> calcd for 358.0774; retention time

3.02 min., >98% pure.

1-((4-Fluorophenyl)sulfonyl)-6-(1-methyl-1*H*-pyrazol-4-yl)-1*H*-pyrazolo[4,3-*b*]pyridine (12).

56% yield; LC-MS *m/z* (ESI) found 358 (M + H)<sup>+</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.85 (d, *J* = 1.9 Hz, 1H), 8.47 (dd, *J* = 1.9, 0.9 Hz, 1H), 8.38 (d, *J* = 0.9 Hz, 1H), 8.09–8.01 (m, 2H), 7.94 (d, *J* = 0.8 Hz, 1H), 7.85 (s, 1H), 7.23–7.14 (m, 2H), 4.03 (s, 3H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 166.22 (d, *J* = 258.5 Hz), 146.84, 142.22, 141.53, 137.29, 134.36, 133.10, 133.07, 130.77 (d, *J* = 9.9 Hz), 128.95, 128.05, 119.22, 116.98, 116.79, 115.93, 39.39. HRMS *m/z* (ESI) found 358.0774 (M + H)<sup>+</sup>, C<sub>16</sub>H<sub>13</sub>N<sub>5</sub>O<sub>2</sub>F<sup>+</sup> calcd for 358.0774; retention time 3.00 min, >98% pure.

6-(1-Methyl-1*H*-pyrazol-4-yl)-1-((2-(trifluoromethyl)phenyl)sulfonyl)-1*H*-pyrazolo[4,3-*b*]pyridine (13).

71% yield; LC-MS *m/z* (ESI) found 408 (M + H)<sup>+</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.87 (d, *J* = 1.9 Hz, 1H), 8.50–8.46 (m, 2H), 8.36 (d, *J* = 0.8 Hz, 1H), 7.94 (s, 1H), 7.91–7.87 (m, 1H), 7.86–7.80 (m, 3H), 4.03 (s, 3H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 146.81, 141.75, 140.77, 137.30, 136.02, 134.85, 134.70, 133.64, 132.75, 128.93, 128.51, 128.49 (q, *J* = 6.8 Hz), 128.17, 128.12, 119.30, 116.60, 39.37. HRMS *m/z* (ESI) found 408.0736 (M + H)<sup>+</sup>, C<sub>17</sub>H<sub>13</sub>N<sub>5</sub>O<sub>2</sub>F<sub>3</sub>S<sup>+</sup> calcd for 408.0742; retention time 3.17 min, >98% pure.

6-(1-Methyl-1*H*-pyrazol-4-yl)-1-((4-(trifluoromethyl)phenyl)sulfonyl)-1*H*-pyrazolo[4,3-*b*]pyridine (14).

74% yield; LC-MS *m/z* (ESI) found 408 (M + H)<sup>+</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.86 (d, *J* = 1.9 Hz, 1H), 8.47 (d, *J* = 1.0 Hz, 1H), 8.40 (d, *J* = 0.8 Hz, 1H), 8.15 (d, *J* = 8.2 Hz, 2H), 7.94 (s, 1H), 7.86 (s, 1H), 7.77 (d, *J* = 8.3 Hz, 2H), 4.03 (s, 3H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 147.05, 142.75, 141.57, 140.43, 137.29, 136.22, 135.95, 134.48, 129.17, 128.36, 128.11, 126.62 (q, *J* = 3.6 Hz), 123.88, 121.71, 119.09, 115.83, 39.42. HRMS *m/z* (ESI) found 408.0743 (M + H)<sup>+</sup>, C<sub>17</sub>H<sub>13</sub>N<sub>5</sub>O<sub>2</sub>F<sub>3</sub>S<sup>+</sup> calcd for 408.0742; retention time 3.32 min, >98% pure.

6-(1-Methyl-1*H*-pyrazol-4-yl)-1-((3-(trifluoromethyl)phenyl)sulfonyl)-1*H*-pyrazolo[4,3-*b*]pyridine (15).

72% yield; LC-MS *m/z* (ESI) found 408 (M + H)<sup>+</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.87 (s, 1H), 8.47 (s, 1H), 8.41 (s, 1H), 8.31 (s, 1H), 8.22 (d, *J* = 8.2 Hz, 1H), 7.95 (s, 1H), 7.93–7.83 (m, 2H), 7.68 (t, *J* = 8.0 Hz, 1H), 4.03 (s, 3H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 146.56, 142.21, 141.05, 137.81, 136.83, 131.84, 131.57, 130.81, 130.78, 130.57, 129.85, 128.71, 127.65, 124.42 (q, *J* = 4.2 Hz), 118.65, 115.38, 38.93. HRMS *m/z* (ESI) found 408.0730 (M + H)<sup>+</sup>, C<sub>17</sub>H<sub>13</sub>N<sub>5</sub>O<sub>2</sub>F<sub>3</sub>S<sup>+</sup> calcd for 408.0742; retention time 3.28 min, >98% pure.

2-(((6-(1-Methyl-1*H*-pyrazol-4-yl)-1*H*-pyrazolo[4,3-*b*]pyridin-1-yl)sulfonyl)benzotrile (16). 79%

yield; LC-MS  $m/z$  (ESI) found 365 (M + H)<sup>+</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.89 (d,  $J$  = 1.9 Hz, 1H), 8.71 (dd,  $J$  = 1.9, 0.9 Hz, 1H), 8.42 (dd,  $J$  = 8.3, 1.1 Hz, 1H), 8.39 (d,  $J$  = 0.9 Hz, 1H), 7.96 (d,  $J$  = 0.7 Hz, 1H), 7.89 (s, 1H), 7.81 (m, 3H), 4.01 (s, 3H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 147.18, 142.98, 141.20, 138.97, 137.29, 135.84, 135.05, 134.50, 133.44, 131.43, 129.23, 128.48, 119.23, 117.42, 115.36, 111.01, 39.37. HRMS  $m/z$  (ESI) found 365.0817 (M + H)<sup>+</sup>, C<sub>17</sub>H<sub>13</sub>N<sub>6</sub>O<sub>2</sub>S<sup>+</sup> calcd for 365.0821; retention time 2.88 min, >98% pure.

1-((3,4-Dimethoxyphenyl)sulfonyl)-6-(1-methyl-1*H*-pyrazol-4-yl)-1*H*-pyrazolo[4,3-*b*]pyridine (**17**). 46% yield; LC-MS  $m/z$  (ESI) found 400 (M + H)<sup>+</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.84 (d,  $J$  = 1.9 Hz, 1H), 8.48 (dd,  $J$  = 1.9, 0.9 Hz, 1H), 8.37 (d,  $J$  = 0.9 Hz, 1H), 7.94 (d,  $J$  = 0.8 Hz, 1H), 7.86 (s, 1H), 7.63 (dd,  $J$  = 8.6, 2.2 Hz, 1H), 7.46 (d,  $J$  = 2.2 Hz, 1H), 6.89 (d,  $J$  = 8.7 Hz, 1H), 4.03 (s, 3H), 3.90 (s, 3H), 3.89 (s, 3H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 153.77, 148.81, 146.15, 141.21, 141.07, 136.80, 133.76, 128.22, 127.94, 127.55, 121.66, 118.88, 115.54, 110.19, 109.53, 55.90, 55.82, 38.93. HRMS  $m/z$  (ESI) found 400.1071 (M + H)<sup>+</sup>, C<sub>18</sub>H<sub>18</sub>N<sub>5</sub>O<sub>4</sub>S<sup>+</sup> calcd for 400.1079; retention time 2.88 min, >98% pure.

1-(4-((6-(1-Methyl-1*H*-pyrazol-4-yl)-1*H*-pyrazolo[4,3-*b*]pyridin-1-yl)sulfonyl)phenyl)ethanone (**18**). 75% yield; LC-MS  $m/z$  (ESI) found 382 (M + H)<sup>+</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.86 (d,  $J$  = 1.9 Hz, 1H), 8.48 (dd,  $J$  = 1.9, 0.9 Hz, 1H), 8.39 (d,  $J$  = 0.8 Hz, 1H), 8.14–8.09 (m, 2H), 8.06–8.02 (m, 2H), 7.95 (s, 1H), 7.86 (s, 1H), 4.03 (s, 3H), 2.61 (s, 3H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 196.23, 146.98, 142.57, 141.59, 141.36, 140.58, 137.30, 134.48, 129.09×2, 128.12×2, 128.09×2, 119.15, 115.90, 39.41, 26.87. HRMS  $m/z$  (ESI) found 382.0963 (M + H)<sup>+</sup>, C<sub>18</sub>H<sub>16</sub>N<sub>5</sub>O<sub>3</sub>S<sup>+</sup> calcd for 382.0963; retention time 2.90 min, >98% pure.

3,5-Dimethyl-4-((6-(1-methyl-1*H*-pyrazol-4-yl)-1*H*-pyrazolo[4,3-*b*]pyridin-1-yl)sulfonyl)isoxazole (**19**). 69% yield; LC-MS  $m/z$  (ESI) found 359 (M + H)<sup>+</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.88 (d,  $J$  = 1.9 Hz, 1H), 8.43 (dd,  $J$  = 1.9, 0.9 Hz, 1H), 8.40 (d,  $J$  = 0.9 Hz, 1H), 7.92 (s, 1H), 7.84 (s, 1H), 4.03 (s, 3H), 2.78 (s, 3H), 2.39 (s, 3H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 176.24, 157.79, 146.99, 142.15, 141.33, 137.25, 134.20, 129.04, 128.00, 119.15, 115.73, 114.61, 39.41, 13.26, 11.07. HRMS  $m/z$  (ESI) found 359.0932 (M + H)<sup>+</sup>, C<sub>15</sub>H<sub>15</sub>N<sub>6</sub>O<sub>3</sub>S<sup>+</sup> calcd for 359.0926; retention time 2.98 min, >98% pure.

6-Chloro-5-((6-(1-methyl-1*H*-pyrazol-4-yl)-1*H*-pyrazolo[4,3-*b*]pyridin-1-yl)sulfonyl)imidazo[2,1-*b*]thiazole (**20**). 64% yield; LC-MS  $m/z$  (ESI) found 420 (M + H)<sup>+</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ

8.88 (d,  $J = 1.8$  Hz, 1H), 8.54 (s, 1H), 8.35 (s, 1H), 8.21 (d,  $J = 4.6$  Hz, 1H), 7.93 (s, 1H), 7.84 (s, 1H), 7.17 (d,  $J = 4.5$  Hz, 1H), 4.03 (s, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  151.78, 147.08, 142.45, 141.49, 140.84, 137.30, 134.38, 129.09, 128.07, 121.12, 119.20, 116.39, 116.32, 115.13, 39.41. HRMS  $m/z$  (ESI) found 420.0093 ( $\text{M} + \text{H}$ ) $^+$ ,  $\text{C}_{15}\text{H}_{11}\text{N}_7\text{O}_2\text{S}_2\text{Cl}^+$  calcd for 420.0104; retention time 3.00 min, >98% pure.

4-((6-(1-Methyl-1*H*-pyrazol-4-yl)-1*H*-pyrazolo[4,3-*b*]pyridin-1-yl)sulfonyl)benzo[*c*][1,2,5]oxadiazole (**21**). 69% yield; LC-MS  $m/z$  (ESI) found 382 ( $\text{M} + \text{H}$ ) $^+$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.89 (d,  $J = 1.9$  Hz, 1H), 8.74 (dd,  $J = 1.9, 0.8$  Hz, 1H), 8.45 (dd,  $J = 6.9, 0.7$  Hz, 1H), 8.35 (d,  $J = 0.8$  Hz, 1H), 8.18 (dd,  $J = 9.0, 0.7$  Hz, 1H), 8.00 (s, 1H), 7.93 (s, 1H), 7.65 (dd,  $J = 9.1, 6.9$  Hz, 1H), 4.05 (s, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  148.79, 146.70, 143.56, 142.45, 140.71, 136.92, 135.72, 134.64, 129.64, 128.65, 127.79, 125.92, 123.25, 118.84, 116.82, 38.94. HRMS  $m/z$  (ESI) found 382.0726 ( $\text{M} + \text{H}$ ) $^+$ ,  $\text{C}_{16}\text{H}_{12}\text{N}_7\text{O}_3\text{S}^+$  calcd for 382.0722; retention time 2.91 min, >95% pure.

1-(Imidazo[1,2-*a*]pyridin-3-ylsulfonyl)-6-(1-methyl-1*H*-pyrazol-4-yl)-1*H*-pyrazolo[4,3-*b*]pyridine (**22**). 81% yield; LC-MS  $m/z$  (ESI) found 380 ( $\text{M} + \text{H}$ ) $^+$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.13 (d,  $J = 6.9$  Hz, 1H), 8.85 (d,  $J = 1.5$  Hz, 1H), 8.46 (s, 1H), 8.32 (d,  $J = 3.4$  Hz, 2H), 7.94 (s, 1H), 7.86 (s, 1H), 7.74 (d,  $J = 9.2$  Hz, 1H), 7.61–7.46 (m, 1H), 7.17 (t,  $J = 6.9$  Hz, 1H), 4.03 (s, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  148.67, 146.47, 141.42, 141.38, 141.15, 136.83, 133.22, 128.92, 128.59, 127.63, 126.95, 118.70, 117.86, 117.64, 115.37, 114.82, 38.92. HRMS  $m/z$  (ESI) found 380.0940 ( $\text{M} + \text{H}$ ) $^+$ ,  $\text{C}_{17}\text{H}_{14}\text{N}_7\text{O}_2\text{S}^+$  calcd for 380.0930; retention time 2.76 min, >95% pure.

1-(Imidazo[1,2-*b*]pyridazin-3-ylsulfonyl)-6-(1-methyl-1*H*-pyrazol-4-yl)-1*H*-pyrazolo[4,3-*b*]pyridine (**23**). 79% yield; LC-MS  $m/z$  (ESI) found 381 ( $\text{M} + \text{H}$ ) $^+$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.87 (d,  $J = 1.9$  Hz, 1H), 8.64 (dd,  $J = 1.9, 0.9$  Hz, 1H), 8.58 (s, 1H), 8.35 (d,  $J = 0.9$  Hz, 1H), 8.30 (dd,  $J = 4.6, 1.6$  Hz, 1H), 8.07 (dd,  $J = 9.3, 1.6$  Hz, 1H), 7.98 (d,  $J = 0.8$  Hz, 1H), 7.94–7.87 (m, 1H), 7.26–7.22 (m, 1H), 4.04 (s, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{DMSO-}d_6$ )  $\delta$  146.58, 146.08, 142.87, 142.14, 141.13, 140.46, 136.89, 134.52, 129.44, 128.66, 126.90, 122.26, 121.22, 118.12, 115.41, 38.81. HRMS  $m/z$  (ESI) found 381.0874 ( $\text{M} + \text{H}$ ) $^+$ ,  $\text{C}_{16}\text{H}_{13}\text{N}_8\text{O}_2\text{S}^+$  calcd for 381.0882; retention time 2.60 min, >98% pure.

6-(1-Methyl-1*H*-pyrazol-4-yl)-1-(pyrazolo[1,5-*a*]pyrimidin-3-ylsulfonyl)-1*H*-pyrazolo[4,3-*b*]pyridine (**24**). 77% yield; LC-MS  $m/z$  (ESI) found 381 ( $\text{M} + \text{H}$ ) $^+$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.83 (d,  $J = 1.8$  Hz, 1H), 8.76 (dd,  $J = 7.0, 1.7$  Hz, 1H), 8.71 (d,  $J = 4.1$  Hz, 2H), 8.66 (s, 1H), 8.35 (s,

1H), 7.97 (s, 1H), 7.88 (s, 1H), 7.11 (dd,  $J = 6.9, 4.3$  Hz, 1H), 4.03 (s, 3H).  $^{13}\text{C}$  NMR (126 MHz, DMSO- $d_6$ )  $\delta$  155.14, 146.36, 146.16, 145.60, 141.25, 140.73, 138.19, 136.83, 133.71, 129.34, 128.34, 118.21, 115.37, 112.00, 105.05, 38.81. HRMS  $m/z$  (ESI) found 381.0873 ( $\text{M} + \text{H}$ ) $^+$ ,  $\text{C}_{16}\text{H}_{13}\text{N}_8\text{O}_2\text{S}^+$  calcd for 381.0882; retention time 2.55 min, >98% pure.

1-((6-Bromoimidazo[1,2-*a*]pyridin-3-yl)sulfonyl)-6-(1-methyl-1*H*-pyrazol-4-yl)-1*H*-pyrazolo[4,3-*b*]pyridine (**25**). 67% yield; LC-MS  $m/z$  (ESI) found 458, 460 ( $\text{M} + \text{H}$ ) $^+$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.28 (dd,  $J = 1.7, 1.0$  Hz, 1H), 8.86 (d,  $J = 1.9$  Hz, 1H), 8.44 (dd,  $J = 1.8, 0.8$  Hz, 1H), 8.37 (d,  $J = 0.8$  Hz, 1H), 8.26 (s, 1H), 7.95 (d,  $J = 0.7$  Hz, 1H), 7.86 (s, 1H), 7.63 (dd,  $J = 9.5, 0.9$  Hz, 1H), 7.59 (dd,  $J = 9.5, 1.7$  Hz, 1H), 4.03 (s, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  147.07, 142.32, 141.75, 141.62, 137.33 $\times 2$ , 133.77, 133.01, 129.21, 128.13, 127.51, 119.11, 118.82, 118.66, 115.82, 110.36, 39.44. HRMS  $m/z$  (EI) found 456.9956 ( $\text{M}$ ) $^+$ ,  $\text{C}_{17}\text{H}_{12}\text{N}_7\text{O}_2\text{SBr}^+$  calcd for 456.9955; retention time 3.10 min, >98% pure.

1-((6-Methoxyimidazo[1,2-*a*]pyridin-3-yl)sulfonyl)-6-(1-methyl-1*H*-pyrazol-4-yl)-1*H*-pyrazolo[4,3-*b*]pyridine (**26**). 51% yield; LC-MS  $m/z$  (ESI) found 410 ( $\text{M} + \text{H}$ ) $^+$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.85 (d,  $J = 1.9$  Hz, 1H), 8.67–8.62 (m, 1H), 8.44 (dd,  $J = 1.9, 0.9$  Hz, 1H), 8.33 (d,  $J = 0.9$  Hz, 1H), 8.23 (s, 1H), 7.93 (d,  $J = 0.9$  Hz, 1H), 7.85 (s, 1H), 7.59 (dd,  $J = 9.8, 0.8$  Hz, 1H), 7.27 (s, 1H), 4.03 (s, 3H), 3.95 (s, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  150.87, 146.93, 145.87, 141.73, 141.66, 141.20, 137.28, 133.64, 129.04, 128.07, 124.26, 119.17, 118.50, 118.18, 115.82, 109.33, 56.52, 39.40. HRMS  $m/z$  (ESI) found 410.1039 ( $\text{M} + \text{H}$ ) $^+$ ,  $\text{C}_{18}\text{H}_{16}\text{N}_7\text{O}_3\text{S}^+$  calcd for 410.1035; retention time 2.88 min, >98% pure.

6-(1-Methyl-1*H*-pyrazol-4-yl)-1-((6-nitroimidazo[1,2-*a*]pyridin-3-yl)sulfonyl)-1*H*-pyrazolo[4,3-*b*]pyridine (**69**). 68% yield; LC-MS  $m/z$  (ESI) found 425 ( $\text{M} + \text{H}$ ) $^+$ ;  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )  $\delta$  9.88–9.80 (m, 1H), 9.10 (s, 1H), 8.92 (d,  $J = 2.0$  Hz, 1H), 8.87 (d,  $J = 0.9$  Hz, 1H), 8.72–8.65 (m, 1H), 8.18 (s, 1H), 8.09 (dd,  $J = 10.1, 2.3$  Hz, 1H), 8.00 (s, 1H), 7.79 (d,  $J = 10.1$  Hz, 1H), 3.97 (s, 3H).

### *spectral data of compounds 28 and 29 (Scheme 3)*

Compounds **28** and **29** were prepared as described for the synthesis of compound **27**.

3-((6-(1-Methyl-1*H*-pyrazol-4-yl)-1*H*-pyrazolo[4,3-*b*]pyridin-1-yl)sulfonyl)imidazo[1,2-*a*]pyridin-6-yl furan-2-carboxylate (**28**). 94% yield; LC-MS  $m/z$  (ESI) found 490 ( $\text{M} + \text{H}$ ) $^+$ ;  $^1\text{H}$  NMR (400

MHz, CDCl<sub>3</sub>) δ 9.31–9.20 (m, 1H), 8.94–8.83 (m, 1H), 8.52–8.45 (m, 1H), 8.41 (d, *J* = 0.9 Hz, 1H), 8.39–8.35 (m, 1H), 7.97 (d, *J* = 6.0 Hz, 1H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.82 (d, *J* = 9.8 Hz, 1H), 7.78 (dt, *J* = 1.7, 0.9 Hz, 1H), 7.66 – 7.63 (m, 1H), 7.56–7.50 (m, 2H), 4.06 (d, *J* = 0.9 Hz, 3H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 156.06, 148.11, 146.94, 146.69, 142.23, 142.04, 141.02, 137.31, 133.83, 129.19, 128.28, 128.20, 126.36, 121.04, 120.71, 119.13, 118.86, 118.11, 116.01, 112.64, 112.05, 39.37. HRMS *m/z* (ESI) found 512.0742 (M + Na)<sup>+</sup>, C<sub>22</sub>H<sub>15</sub>N<sub>7</sub>O<sub>5</sub>SNa<sup>+</sup> calcd for 512.0748; retention time 2.87min, >95% pure.

*N*-(3-((6-(1-methyl-1*H*-pyrazol-4-yl)-1*H*-pyrazolo[4,3-*b*]pyridin-1-yl)sulfonyl)imidazo[1,2-*a*]pyridin-6-yl)acetamide (**29**). 92% yield; LC–MS *m/z* (ESI) found 437 (M + H)<sup>+</sup>; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 10.24 (s, 1H), 9.34 (d, *J* = 1.9 Hz, 1H), 9.06 (d, *J* = 1.9 Hz, 1H), 9.03 (s, 1H), 8.71 (s, 1H), 8.54 (s, 1H), 8.48 (d, *J* = 1.4 Hz, 1H), 8.17 (s, 1H), 7.55 (d, *J* = 9.8 Hz, 1H), 7.28 (dd, *J* = 9.9, 2.0 Hz, 1H), 3.93 (s, 3H), 2.08 (s, 3H). <sup>13</sup>C NMR (126 MHz, DMSO-*d*<sub>6</sub>) δ 169.28, 147.13, 143.01, 142.59, 141.37, 139.55, 137.40, 134.79, 129.97, 129.25, 128.69, 124.60, 119.30, 118.55, 118.41, 116.57, 115.41, 39.31, 24.15. HRMS *m/z* (ESI) found 437.1156 (M + H)<sup>+</sup>, C<sub>19</sub>H<sub>17</sub>N<sub>8</sub>O<sub>3</sub>S<sup>+</sup> calcd for 437.1144; retention time 2.55 min, >93% pure.

### *spectral data of compounds 32-43 (Scheme 3)*

Compounds **32-43** were prepared as described for the synthesis of compound **31**.

6-(1-Methyl-1*H*-pyrazol-4-yl)-1-((6-(thiophen-3-yl)imidazo[1,2-*a*]pyridin-3-yl)sulfonyl)-1*H*-pyrazolo[4,3-*b*]pyridine (**32**). 64% yield; LC–MS *m/z* (ESI) found 462 (M + H)<sup>+</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.30 (s, 1H), 8.86 (d, *J* = 1.8 Hz, 1H), 8.48 (dd, *J* = 1.8, 0.8 Hz, 1H), 8.34 (d, *J* = 0.7 Hz, 1H), 8.32 (s, 1H), 7.95 (d, *J* = 0.6 Hz, 1H), 7.86 (s, 1H), 7.76 (d, *J* = 1.6 Hz, 2H), 7.57 (dd, *J* = 2.9, 1.4 Hz, 1H), 7.50 (dd, *J* = 5.0, 2.9 Hz, 1H), 7.43 (dd, *J* = 5.0, 1.4 Hz, 1H), 4.04 (s, 3H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 148.17, 146.97, 141.99×2, 141.64, 137.31, 136.77, 133.74, 129.31, 129.08, 128.13, 127.68, 125.79, 124.79, 123.78, 122.32, 119.15, 118.40, 118.14, 115.84, 39.43. HRMS *m/z* (ESI) found 462.0797 (M + H)<sup>+</sup>, C<sub>21</sub>H<sub>16</sub>N<sub>7</sub>O<sub>2</sub>S<sub>2</sub><sup>+</sup> calcd for 462.0807; retention time 3.29 min., >98% pure.

6-(1-Methyl-1*H*-pyrazol-4-yl)-1-((6-(1-methyl-1*H*-pyrazol-4-yl)imidazo[1,2-*a*]pyridin-3-yl)sulfonyl)-1*H*-pyrazolo[4,3-*b*]pyridine (**33**). 78% yield; LC–MS *m/z* (ESI) found 460 (M + H)<sup>+</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.17 (dd, *J* = 1.5, 0.9 Hz, 1H), 8.85 (d, *J* = 1.9 Hz, 1H), 8.46 (dd, *J* = 1.8, 0.8



Hz, 1H), 8.33 (d,  $J = 0.8$  Hz, 1H), 8.28 (s, 1H), 7.95 (d,  $J = 0.4$  Hz, 1H), 7.86 (s, 1H), 7.82 (d,  $J = 0.6$  Hz, 1H), 7.74 (s, 1H), 7.72 (dd,  $J = 9.3, 0.8$  Hz, 1H), 7.63 (dd,  $J = 9.3, 1.7$  Hz, 1H), 4.04 (s, 3H), 4.00 (s, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  147.95, 146.93, 141.88, 141.73, 141.62, 137.26, 136.89, 135.85, 133.65, 129.03, 128.88, 128.07, 127.47, 122.36, 121.77, 119.12, 118.21, 118.07, 115.78, 39.38, 39.31. HRMS  $m/z$  (EI) found 459.1211 ( $\text{M}$ )<sup>+</sup>,  $\text{C}_{21}\text{H}_{17}\text{N}_9\text{O}_2\text{S}^+$  calcd for 459.1206; retention time 3.17 min, >98% pure.

1-((6-(6-Fluoropyridin-3-yl)imidazo[1,2-*a*]pyridin-3-yl)sulfonyl)-6-(1-methyl-1H-pyrazol-4-yl)-1H-pyrazolo[4,3-*b*]pyridine (**34**). 55% yield; LC-MS  $m/z$  (ESI) found 475 ( $\text{M} + \text{H}$ )<sup>+</sup>;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.34 (s, 1H), 8.89 (d,  $J = 1.8$  Hz, 1H), 8.53 (d,  $J = 2.6$  Hz, 1H), 8.48 (d,  $J = 1.0$  Hz, 1H), 8.36 (s, 2H), 8.08 (m, 1H), 7.97 (s, 1H), 7.87 (m, 2H), 7.72 (dd,  $J = 9.3, 1.8$  Hz, 1H), 7.15 (dd,  $J = 8.7, 3.0$  Hz, 1H), 4.06 (s, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  163.36 (d,  $J = 242.2$  Hz), 147.77, 146.63, 145.75 (d,  $J = 15.2$  Hz), 141.67 (d,  $J = 4.7$  Hz), 141.13, 139.50, 139.43, 136.83, 133.27, 129.60, 128.76, 128.58, 127.66, 124.98, 124.39, 118.61, 118.27, 115.32, 110.02, 109.72, 38.94. HRMS  $m/z$  (ESI) found 475.1093 ( $\text{M} + \text{H}$ )<sup>+</sup>,  $\text{C}_{22}\text{H}_{16}\text{N}_8\text{O}_2\text{SF}^+$  calcd for 475.1101; retention time 3.29 min, >98% pure.

1-((6-(Benzo[*d*][1,3]dioxol-5-yl)imidazo[1,2-*a*]pyridin-3-yl)sulfonyl)-6-(1-methyl-1H-pyrazol-4-yl)-1H-pyrazolo[4,3-*b*]pyridine (**35**). 54% yield; LC-MS  $m/z$  (ESI) found 500 ( $\text{M} + \text{H}$ )<sup>+</sup>;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.18 (dd,  $J = 1.6, 1.0$  Hz, 1H), 8.86 (d,  $J = 1.9$  Hz, 1H), 8.47 (dd,  $J = 1.8, 0.8$  Hz, 1H), 8.35 (d,  $J = 0.7$  Hz, 1H), 8.32 (s, 1H), 7.94 (d,  $J = 0.6$  Hz, 1H), 7.85 (m, 1H), 7.75 (dd,  $J = 9.3, 0.9$  Hz, 1H), 7.69 (dd,  $J = 9.4, 1.9$  Hz, 1H), 7.07 (m, 2H), 6.93 (d,  $J = 8.5$  Hz, 1H), 6.07 (s, 2H), 4.04 (s, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  148.71, 148.33, 148.20, 146.97, 142.04, 141.97, 141.65, 137.32, 133.76, 129.98, 129.85, 129.68, 129.09, 128.10, 124.06, 121.12, 119.18, 118.31, 117.99, 115.86, 109.11, 107.58, 101.62, 39.40. HRMS  $m/z$  (ESI) found 500.1130 ( $\text{M} + \text{H}$ )<sup>+</sup>,  $\text{C}_{24}\text{H}_{18}\text{N}_7\text{O}_4\text{S}^+$  calcd for 500.1135; retention time 3.35 min, >95% pure.

1-((6-(4-Methoxyphenyl)imidazo[1,2-*a*]pyridin-3-yl)sulfonyl)-6-(1-methyl-1H-pyrazol-4-yl)-1H-pyrazolo[4,3-*b*]pyridine (**36**). 42% yield; LC-MS  $m/z$  (ESI) found 486 ( $\text{M} + \text{H}$ )<sup>+</sup>;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.20 (t,  $J = 1.3$  Hz, 1H), 8.86 (d,  $J = 1.9$  Hz, 1H), 8.48 (m, 1H), 8.35 (s, 1H), 8.32 (s, 1H), 7.95 (s, 1H), 7.85 (s, 1H), 7.75 (m, 2H), 7.54 (d,  $J = 8.8$  Hz, 2H), 7.02 (d,  $J = 8.8$  Hz, 2H), 4.04 (s, 3H), 3.89 (s, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  159.75, 147.71, 146.47, 141.58, 141.48, 141.20, 136.86, 133.31, 129.35, 129.11, 128.59, 127.90 $\times$ 2, 127.76, 127.66, 123.31, 118.73, 117.74,

117.50, 115.41, 114.39×2, 55.01, 38.95. HRMS  $m/z$  (ESI) found 486.1338 (M + H)<sup>+</sup>, C<sub>24</sub>H<sub>20</sub>N<sub>7</sub>O<sub>3</sub>S<sup>+</sup> calcd for 486.1348; retention time 3.37 min, >98% pure.

1-((6-(3,4-Dimethoxyphenyl)imidazo[1,2-*a*]pyridin-3-yl)sulfonyl)-6-(1-methyl-1*H*-pyrazol-4-yl)-1*H*-pyrazolo[4,3-*b*]pyridine (**37**). 38% yield; LC-MS  $m/z$  (ESI) found 516 (M + H)<sup>+</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.23 (t, *J* = 1.2 Hz, 1H), 8.86 (d, *J* = 1.9 Hz, 1H), 8.47 (dd, *J* = 1.8, 0.6 Hz, 1H), 8.33 (s, 2H), 7.94 (s, 1H), 7.85 (s, 1H), 7.75 (m, 2H), 7.16 (dd, *J* = 8.3, 2.1 Hz, 1H), 7.10 (d, *J* = 2.1 Hz, 1H), 6.98 (d, *J* = 8.4 Hz, 1H), 4.03 (s, 3H), 3.99 (s, 3H), 3.97 (s, 3H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 149.30, 149.18, 147.73, 146.48, 141.57, 141.38, 141.16, 136.84, 133.27, 129.44, 129.32, 128.61, 128.20, 127.66, 123.54, 119.38, 118.70, 117.77, 117.46, 115.37, 111.37, 109.83, 55.62×2, 38.94. HRMS  $m/z$  (ESI) found 516.1467 (M + H)<sup>+</sup>, C<sub>25</sub>H<sub>22</sub>N<sub>7</sub>O<sub>4</sub>S<sup>+</sup> calcd for 516.1454; retention time 3.22 min, >98% pure.

3-(3-((6-(1-Methyl-1*H*-pyrazol-4-yl)-1*H*-pyrazolo[4,3-*b*]pyridin-1-yl)sulfonyl)imidazo[1,2-*a*]pyridin-6-yl)benzotrile (**38**). 64% yield; LC-MS  $m/z$  (ESI) found 481 (M + H)<sup>+</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.33 (s, 1H), 8.87 (d, *J* = 1.8 Hz, 1H), 8.47 (dd, *J* = 1.8, 0.8 Hz, 1H), 8.35 (m, 2H), 7.95 (d, *J* = 2.9 Hz, 1H), 7.87 (m, 4H), 7.78 (m, 1H), 7.72 (dd, *J* = 9.4, 1.8 Hz, 1H), 7.67 (m, 1H), 4.04 (s, 3H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 148.31, 147.11, 142.20×2, 141.60, 137.43, 137.31, 133.77, 132.18, 131.57, 130.74, 130.37, 129.24, 129.07, 128.14, 127.60, 125.10, 119.09, 118.94, 118.69, 118.18, 115.79, 113.83, 39.43. HRMS  $m/z$  (ESI) found 481.1206 (M + H)<sup>+</sup>, C<sub>24</sub>H<sub>17</sub>N<sub>8</sub>O<sub>2</sub>S<sup>+</sup> calcd for 481.1195; retention time 3.22 min, >98% pure.

1-((6-(4-Isopropoxyphenyl)imidazo[1,2-*a*]pyridin-3-yl)sulfonyl)-6-(1-methyl-1*H*-pyrazol-4-yl)-1*H*-pyrazolo[4,3-*b*]pyridine (**39**). 45% yield; LC-MS  $m/z$  (ESI) found 514 (M + H)<sup>+</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.27 (m, 1H), 8.85 (d, *J* = 1.9 Hz, 1H), 8.47 (dd, *J* = 1.8, 0.8 Hz, 1H), 8.34 (m, 2H), 7.94 (d, *J* = 0.6 Hz, 1H), 7.85 (s, 1H), 7.76 (m, 2H), 7.39 (t, *J* = 7.9 Hz, 1H), 7.14 (t, *J* = 4.9 Hz, 2H), 6.98 (dd, *J* = 8.0, 2.1 Hz, 1H), 4.66 (m, 1H), 4.03 (s, 3H), 1.41 (d, *J* = 6.1 Hz, 6H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 158.17, 147.93, 146.50, 141.65, 141.47, 141.19, 136.92, 136.85, 133.29, 130.01, 129.49, 129.34, 128.62, 127.66, 124.12, 118.84, 118.72, 117.92, 117.53, 115.41, 115.07, 114.72, 69.68, 38.95, 21.61×2. HRMS  $m/z$  (ESI) found 514.1650 (M + H)<sup>+</sup>, C<sub>26</sub>H<sub>24</sub>N<sub>7</sub>O<sub>3</sub>S<sup>+</sup> calcd for 514.1661; retention time 3.71 min, >98% pure.

1-((6-(2,4-Difluorophenyl)imidazo[1,2-*a*]pyridin-3-yl)sulfonyl)-6-(1-methyl-1*H*-pyrazol-4-yl)-1*H*-pyrazolo[4,3-*b*]pyridine (**40**). 60% yield; LC-MS  $m/z$  (ESI) found 492 (M + H)<sup>+</sup>; <sup>1</sup>H NMR (400

MHz, CDCl<sub>3</sub>) δ 9.24 (s, 1H), 8.86 (d, *J* = 1.8 Hz, 1H), 8.46 (dd, *J* = 1.8, 0.8 Hz, 1H), 8.35 (d, *J* = 0.8 Hz, 2H), 7.94 (d, *J* = 0.5 Hz, 1H), 7.86 (s, 1H), 7.79 (dd, *J* = 9.3, 0.8 Hz, 1H), 7.67 (dt, *J* = 9.3, 1.6 Hz, 1H), 7.48 (td, *J* = 8.6, 6.2 Hz, 1H), 7.02 (m, 2H), 4.04 (s, 3H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 163.23 (dd, *J* = 252.0, 11.9 Hz), 159.97 (dd, *J* = 251.8, 12.0 Hz), 148.16, 146.99, 142.21, 142.08, 141.67, 137.30, 133.76, 131.34 (dd, *J* = 9.8, 4.2 Hz), 130.84 (d, *J* = 3.1 Hz), 129.11, 128.09, 126.35 (d, *J* = 3.6 Hz), 123.55, 120.14 (dd, *J* = 13.4, 3.9 Hz), 119.15, 118.58, 117.93, 115.83, 112.43 (dd, *J* = 21.6, 3.8 Hz), 105.03 (t, *J* = 25.8 Hz), 39.40. HRMS *m/z* (ESI) found 492.1060 (M + H)<sup>+</sup>, C<sub>23</sub>H<sub>16</sub>N<sub>7</sub>O<sub>2</sub>F<sub>2</sub>S<sup>+</sup> calcd for 492.1054; retention time 3.41 min, >98% pure.

6-(1-Methyl-1*H*-pyrazol-4-yl)-1-((6-(3-(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyridin-3-yl)sulfonyl)-1*H*-pyrazolo[4,3-*b*]pyridine (**41**). 74% yield; LC-MS *m/z* (ESI) found 524 (M + H)<sup>+</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.35 (s, 1H), 8.87 (d, *J* = 1.9 Hz, 1H), 8.47 (d, *J* = 1.0 Hz, 1H), 8.36 (s, 2H), 7.94 (s, 1H), 7.84 (m, 4H), 7.76 (m, 2H), 7.67 (t, *J* = 7.8 Hz, 1H), 4.04 (s, 3H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 147.84, 146.57, 141.66, 141.59, 141.14, 136.84, 136.43, 133.29, 131.31, 130.11, 129.60, 129.06, 128.73, 128.02, 127.67, 125.07 (q, *J* = 4.2 Hz), 124.56, 123.68, 123.65, 118.65, 118.33, 117.99, 115.35, 38.94. HRMS *m/z* (ESI) found 524.1122 (M + H)<sup>+</sup>, C<sub>24</sub>H<sub>17</sub>N<sub>7</sub>O<sub>2</sub>F<sub>3</sub>S<sup>+</sup> calcd for 524.1117; retention time 3.65 min, >97% pure.

*N,N*-dimethyl-4-(3-((6-(1-methyl-1*H*-pyrazol-4-yl)-1*H*-pyrazolo[4,3-*b*]pyridin-1-yl)sulfonyl)imidazo[1,2-*a*]pyridin-6-yl)aniline (**42**). 69% yield; LC-MS *m/z* (ESI) found 499 (M + H)<sup>+</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.14 (t, *J* = 1.3 Hz, 1H), 8.86 (d, *J* = 1.9 Hz, 1H), 8.49 (dd, *J* = 1.9, 0.8 Hz, 1H), 8.35 (d, *J* = 0.8 Hz, 1H), 8.31 (s, 1H), 7.96 (d, *J* = 0.6 Hz, 1H), 7.86 (s, 1H), 7.73 (dd, *J* = 3.5, 2.0 Hz, 2H), 7.46 (d, *J* = 8.9 Hz, 2H), 6.78 (d, *J* = 8.9 Hz, 2H), 4.03 (s, 3H), 3.03 (s, 6H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 150.24, 147.58, 146.40, 141.51, 141.38, 141.21, 136.87, 133.33, 129.60, 129.22, 128.51, 127.68, 127.33×2, 122.60, 122.37, 118.78, 117.44, 117.31, 115.42, 112.31×2, 39.90×2, 38.94. HRMS *m/z* (ESI) found 499.1671 (M + H)<sup>+</sup>, C<sub>25</sub>H<sub>23</sub>N<sub>8</sub>O<sub>2</sub>S<sup>+</sup> calcd for 499.1665; retention time 2.82 min, >95% pure.

6-(1-Methyl-1*H*-pyrazol-4-yl)-1-((6-(1-(piperidin-4-yl)-1*H*-pyrazol-4-yl)imidazo[1,2-*a*]pyridin-3-yl)sulfonyl)-1*H*-pyrazolo[4,3-*b*]pyridine (**43**). 37% yield; LC-MS *m/z* (ESI) found 529 (M + H)<sup>+</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.05 (d, *J* = 1.8 Hz, 1H), 8.96 (s, 1H), 8.75 (s, 1H), 8.65 (s, 1H), 8.60 (s, 2H), 8.36 (s, 1H), 8.27 (s, 1H), 7.96 (d, *J* = 13.6 Hz, 2H), 7.90 (d, *J* = 8.9 Hz, 1H), 3.95 (s, 3H), 3.74–3.57 (m, 3H), 3.33–3.17 (m, 2H), 2.51–2.45 (m, 2H), 2.06–2.02 (m, 2H),

NH on piperidine is missing.  $^{13}\text{C}$  NMR (126 MHz,  $\text{DMSO-}d_6$ )  $\delta$  148.04, 147.31, 143.01, 142.96, 141.55, 137.67, 136.92, 133.92, 130.22, 129.77, 129.59, 127.14, 122.13, 121.18, 118.82, 118.48, 117.48, 117.23, 114.95, 55.92, 55.38 $\times$ 2, 42.63, 29.28, 29.02. HRMS  $m/z$  (ESI) found 529.1878 ( $\text{M} + \text{H}$ ) $^+$ ,  $\text{C}_{25}\text{H}_{25}\text{N}_{10}\text{O}_2\text{S}^+$  calcd for 529.1883; retention time 2.53 min, >95% pure.

*spectral data of compounds 45-53 (Scheme 4)*

Compounds **45-53** were prepared as described for the synthesis of compound **44**.

1-((6-(1-Methyl-1*H*-pyrazol-4-yl)imidazo[1,2-*a*]pyridin-3-yl)sulfonyl)-6-(1-(piperidin-4-yl)-1*H*-pyrazol-4-yl)-1*H*-pyrazolo[4,3-*b*]pyridine (**45**). 41% yield; LC-MS  $m/z$  (ESI) found 529 ( $\text{M} + \text{H}$ ) $^+$ ;  $^1\text{H}$ -NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  9.05 (d,  $J = 1.8$  Hz, 1H), 8.96 (s, 1H), 8.75 (s, 1H), 8.65 (s, 1H), 8.60 (s, 2H), 8.36 (s, 1H), 8.27 (s, 1H), 7.96 (d,  $J = 13.6$  Hz, 2H), 7.90 (d,  $J = 8.9$  Hz, 1H), 4.01 (s, 3H), 3.75–3.58 (m, 3H), 3.33–3.18 (m, 2H), 2.50–2.45 (m, 2H), 2.08–2.03 (m, 2H), NH on piperidine is missing.  $^{13}\text{C}$  NMR (126 MHz,  $\text{DMSO-}d_6$ )  $\delta$  149.50, 147.98, 147.10, 144.16, 143.47, 142.97, 142.77, 142.14, 137.20, 136.66, 136.09, 133.58, 129.73, 129.10, 122.29, 121.02, 118.81, 118.21, 117.38, 55.91, 55.38 $\times$ 2, 42.62, 29.29, 29.01. HRMS  $m/z$  (ESI) found 529.1876 ( $\text{M} + \text{H}$ ) $^+$ ,  $\text{C}_{25}\text{H}_{25}\text{N}_{10}\text{O}_2\text{S}^+$  calcd for 529.1877; retention time 2.52 min, >95% pure.

6-(1-(1-Isopropylpiperidin-4-yl)-1*H*-pyrazol-4-yl)-1-((6-(1-methyl-1*H*-pyrazol-4-yl)imidazo[1,2-*a*]pyridin-3-yl)sulfonyl)-1*H*-pyrazolo[4,3-*b*]pyridine (**46**). 61% yield; LC-MS  $m/z$  (ESI) found 571 ( $\text{M} + \text{H}$ ) $^+$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.16 (s, 1H), 8.85 (s, 1H), 8.46 (s, 1H), 8.33 (s, 1H), 8.29 (s, 1H), 7.94 (d,  $J = 6.8$  Hz, 2H), 7.81 (s, 1H), 7.74 (s, 1H), 7.72 (d,  $J = 9.3$  Hz, 1H), 7.63 (d,  $J = 9.4$  Hz, 1H), 4.27 (td,  $J = 10.9, 5.4$  Hz, 1H), 4.00 (s, 3H), 3.12 (dd,  $J = 9.7, 6.1$  Hz, 2H), 2.91 (p,  $J = 6.6$  Hz, 1H), 2.46 (t,  $J = 11.5$  Hz, 2H), 2.40–2.28 (m, 2H), 2.23–2.01 (m, 2H), 1.14 (d,  $J = 6.5$  Hz, 6H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  147.97, 146.99, 141.93, 141.76, 141.61, 136.92, 136.78, 133.70, 129.22, 128.92, 127.54, 124.75, 122.38, 121.81, 118.72 $\times$ 2, 118.23, 118.09, 115.79, 59.83, 54.82, 47.48 $\times$ 2, 39.36 $\times$ 2, 32.57, 18.29 $\times$ 2. HRMS  $m/z$  (ESI) found 571.2353 ( $\text{M} + \text{H}$ ) $^+$ ,  $\text{C}_{28}\text{H}_{31}\text{N}_{10}\text{O}_2\text{S}^+$  calcd for 571.2347; retention time 2.67 min, >98% pure.

6-(1-(1-Cyclopentylpiperidin-4-yl)-1*H*-pyrazol-4-yl)-1-((6-(1-methyl-1*H*-pyrazol-4-yl)imidazo[1,2-*a*]pyridin-3-yl)sulfonyl)-1*H*-pyrazolo[4,3-*b*]pyridine (**47**). 59% yield; LC-MS  $m/z$  (ESI) found 597 ( $\text{M} + \text{H}$ ) $^+$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.16 (s, 1H), 8.85 (d,  $J = 1.8$  Hz, 1H), 8.50–8.44 (m, 1H), 8.34 (s, 1H), 8.30 (s, 1H), 8.00 (s, 1H), 7.94 (s, 1H), 7.80 (s, 1H), 7.76 (s, 1H), 7.72 (d,  $J =$

9.2 Hz, 1H), 7.63 (dd,  $J = 9.3, 1.7$  Hz, 1H), 4.59–4.46 (m, 1H), 4.01 (s, 3H), 3.55 (q,  $J = 10.0$  Hz, 2H), 3.14 (dd,  $J = 21.5, 6.8$  Hz, 1H), 2.53–2.42 (m, 2H), 2.06 (dt,  $J = 13.3, 7.1$  Hz, 3H), 2.00–1.81 (m, 6H), 1.64 (dd,  $J = 12.8, 4.8$  Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  147.99, 146.96, 141.90, 141.80, 137.19, 136.90 $\times 2$ , 133.60, 128.98, 128.77, 127.59, 122.38, 121.85, 119.22, 118.24 $\times 2$ , 118.09, 118.05, 116.02, 67.98, 39.38 $\times 2$ , 29.72, 29.95, 29.14, 29.10, 29.02, 28.94, 23.89 $\times 2$ . HRMS  $m/z$  (ESI) found 597.2502 ( $\text{M} + \text{H}$ ) $^+$ ,  $\text{C}_{30}\text{H}_{33}\text{N}_{10}\text{O}_2\text{S}^+$  calcd for 597.2509; retention time 2.70 min, >98% pure.

1-((6-(1-Methyl-1*H*-pyrazol-4-yl)imidazo[1,2-*a*]pyridin-3-yl)sulfonyl)-6-phenyl-1*H*-pyrazolo[4,3-*b*]pyridine (**48**). 73% yield; LC–MS  $m/z$  (ESI) found 456 ( $\text{M} + \text{H}$ ) $^+$ ;  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  9.18 (s, 1H), 8.95 (d,  $J = 1.9$  Hz, 1H), 8.67–8.58 (m, 1H), 8.40 (s, 1H), 8.29 (s, 1H), 7.82 (s, 1H), 7.74–7.67 (m, 4H), 7.63 (dd,  $J = 9.2, 1.7$  Hz, 1H), 7.57 (t,  $J = 7.4$  Hz, 2H), 7.54–7.48 (m, 1H), 4.00 (s, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  148.42, 142.46, 141.85 $\times 2$ , 137.18, 137.04, 136.96 $\times 2$ , 133.49, 129.42 $\times 2$ , 129.00, 128.96, 127.94 $\times 2$ , 127.52, 122.35, 121.86, 118.48, 118.28, 118.10, 118.07, 39.38. HRMS  $m/z$  (ESI) found 456.1240 ( $\text{M} + \text{H}$ ) $^+$ ,  $\text{C}_{23}\text{H}_{18}\text{N}_7\text{O}_2\text{S}^+$  calcd for 456.1243; retention time 2.63 min, >98% pure.

4-(4-(1-((6-(1-Methyl-1*H*-pyrazol-4-yl)imidazo[1,2-*a*]pyridin-3-yl)sulfonyl)-1*H*-pyrazolo[4,3-*b*]pyridin-6-yl)benzyl)morpholine (**49**). 62% yield; LC–MS  $m/z$  (ESI) found 555 ( $\text{M} + \text{H}$ ) $^+$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.18 (s, 1H), 8.94 (s, 1H), 8.60 (s, 1H), 8.40 (s, 1H), 8.29 (s, 1H), 7.82 (s, 1H), 7.75 (s, 1H), 7.72 (d,  $J = 9.3$  Hz, 1H), 7.65 (d,  $J = 7.5$  Hz, 3H), 7.53 (d,  $J = 7.9$  Hz, 2H), 4.01 (s, 3H), 3.76 (t,  $J = 4.6$  Hz, 4H), 3.60 (s, 2H), 2.59–2.44 (m, 4H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  148.35, 148.00, 142.41, 141.83, 141.80, 139.06, 136.94 $\times 2$ , 135.89, 133.48, 130.14 $\times 2$ , 128.97, 127.84 $\times 2$ , 127.55, 122.36, 121.86, 118.31, 118.26, 118.10, 118.07, 67.04 $\times 2$ , 62.96, 53.68 $\times 2$ , 39.38. HRMS  $m/z$  (ESI) found 555.1921 ( $\text{M} + \text{H}$ ) $^+$ ,  $\text{C}_{28}\text{H}_{27}\text{N}_8\text{O}_3\text{S}^+$  calcd for 555.1927; retention time 2.62 min, >98% pure.

(4-(1-((6-(1-Methyl-1*H*-pyrazol-4-yl)imidazo[1,2-*a*]pyridin-3-yl)sulfonyl)-1*H*-pyrazolo[4,3-*b*]pyridin-6-yl)phenyl)(4-methylpiperazin-1-yl)methanone (**50**). 74% yield; LC–MS  $m/z$  (ESI) found 582 ( $\text{M} + \text{H}$ ) $^+$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.19 (s, 1H), 8.94 (d,  $J = 1.8$  Hz, 1H), 8.65–8.59 (m, 1H), 8.41 (s, 1H), 8.29 (s, 1H), 7.83 (s, 1H), 7.77–7.70 (m, 4H), 7.67–7.58 (m, 3H), 4.01 (s, 3H), 3.94–3.80 (m, 2H), 3.61–3.45 (m, 2H), 2.62–2.50 (m, 2H), 2.48–2.39 (m, 2H), 2.36 (s, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  169.52, 148.14, 148.05, 142.75, 141.86, 141.76, 138.44, 136.93, 136.17,

136.15, 133.30, 129.05, 128.21×2, 128.11×2, 127.57, 122.36, 121.94, 118.63, 118.28, 118.07, 117.98, 55.25, 54.70, 46.01, 45.92, 41.93, 39.41. HRMS  $m/z$  (ESI) found 582.2036 (M + H)<sup>+</sup>, C<sub>29</sub>H<sub>28</sub>N<sub>9</sub>O<sub>3</sub>S<sup>+</sup> calcd for 582.2030; retention time 2.60 min, >98% pure.

1-((6-(1-Methyl-1*H*-pyrazol-4-yl)imidazo[1,2-*a*]pyridin-3-yl)sulfonyl)-6-(1,2,3,6-tetrahydropyridin-4-yl)-1*H*-pyrazolo[4,3-*b*]pyridine (**51**). 31% yield; LC-MS  $m/z$  (ESI) found 461 (M + H)<sup>+</sup>; <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 9.15 (s, 1H), 8.81–8.76 (m, 1H), 8.36 (d, *J* = 1.8 Hz, 1H), 8.33 (s, 1H), 8.27 (s, 1H), 7.81 (s, 1H), 7.76 (s, 1H), 7.71 (d, *J* = 9.2 Hz, 1H), 7.66–7.58 (m, 1H), 6.39 (m, 1H), 4.02 (s, 3H), 3.65 (m, 2H), 3.21 (t, *J* = 5.6 Hz, 2H), 2.59 (m, 2H), NH on 1,2,3,6-tetrahydropyridine is missing. <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 147.96, 146.88, 142.22, 141.82, 141.73, 137.24, 136.91, 133.49, 132.55, 128.92, 128.27, 127.58, 122.35, 122.26, 121.81, 118.25, 118.11, 116.07, 45.54, 42.95, 39.39, 27.77. HRMS  $m/z$  (ESI) found 461.1517 (M + H)<sup>+</sup>, C<sub>22</sub>H<sub>21</sub>N<sub>8</sub>O<sub>2</sub>S<sup>+</sup> calcd for 461.1508; retention time 2.42 min, >95% pure.

6-(1-Isopropyl-1,2,3,6-tetrahydropyridin-4-yl)-1-((6-(1-methyl-1*H*-pyrazol-4-yl)imidazo[1,2-*a*]pyridin-3-yl)sulfonyl)-1*H*-pyrazolo[4,3-*b*]pyridine (**52**). 34% yield; LC-MS  $m/z$  (ESI) found 503 (M + H)<sup>+</sup>; <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 9.14 (dd, *J* = 1.9, 1.0 Hz, 1H), 8.77 (d, *J* = 1.9 Hz, 1H), 8.42–8.38 (m, 1H), 8.35 (d, *J* = 0.9 Hz, 1H), 8.30 (s, 1H), 7.80 (d, *J* = 0.9 Hz, 1H), 7.77 (s, 1H), 7.72 (dd, *J* = 9.3, 1.0 Hz, 1H), 7.63 (dd, *J* = 9.3, 1.8 Hz, 1H), 6.30 (m, 1H), 4.02 (s, 3H), 3.72 (m, 2H), 3.46–3.36 (m, 1H), 3.25 (m, 2H), 3.02 (m, 2H), 1.41 (d, *J* = 6.6 Hz, 6H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 148.01, 146.56, 142.74, 142.01, 141.69, 136.89×2, 133.37, 133.12, 129.03, 127.67, 122.32, 121.91, 118.28×2, 118.06, 117.89, 116.74, 56.52, 46.49, 45.56, 39.42, 26.23, 17.30×2. HRMS  $m/z$  (ESI) found 503.1975 (M + H)<sup>+</sup>, C<sub>25</sub>H<sub>27</sub>N<sub>8</sub>O<sub>2</sub>S<sup>+</sup> calcd for 503.1978; retention time 2.54 min, >95% pure.

6-(1-Cyclopentyl-1,2,3,6-tetrahydropyridin-4-yl)-1-((6-(1-methyl-1*H*-pyrazol-4-yl)imidazo[1,2-*a*]pyridin-3-yl)sulfonyl)-1*H*-pyrazolo[4,3-*b*]pyridine (**53**). 36% yield; LC-MS  $m/z$  (ESI) found 529 (M + H)<sup>+</sup>; <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 9.14 (d, *J* = 1.7 Hz, 1H), 8.78 (d, *J* = 1.9 Hz, 1H), 8.41–8.37 (m, 1H), 8.34 (s, 1H), 8.28 (s, 1H), 7.81 (s, 1H), 7.77 (s, 1H), 7.72 (d, *J* = 9.2 Hz, 1H), 7.63 (dd, *J* = 9.3, 1.7 Hz, 1H), 6.30 (m, 1H), 4.03 (s, 3H), 3.67 (m, 2H), 3.21 (m, 2H), 3.12 (m, 1H), 2.95 (m, 2H), 2.08 (m, 2H), 1.99–1.84 (m, 4H), 1.65 (m, 2H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 147.98, 146.62, 142.56, 141.86, 141.71, 136.89×2, 133.21, 132.88, 129.02, 127.63, 122.32, 121.89, 118.26×2, 118.06, 117.95, 116.52, 67.04, 50.88, 48.22, 39.41×2, 29.38, 26.31, 23.93×2.

HRMS  $m/z$  (ESI) found 529.2120 ( $M + H$ )<sup>+</sup>,  $C_{27}H_{29}N_8O_2S^+$  calcd for 529.2134; retention time 2.63 min, >98% pure.