

**Supporting Information**  
**for**  
**Combined experimental and theoretical studies of regio-  
and stereoselectivity in reactions of  $\beta$ -isoxazolyl- and  $\beta$ -  
imidazolyl enamines with nitrile oxides**

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## Experimental part

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### General procedure for the preparation of 4-azolyl isoxazoles 4d–g,i–p.

To a solution of the corresponding enamine **1** (1.1 mmol) in 1,4-dioxane (5 mL) an appropriate hydroxamoyl chloride **2** (1 mmol) was added. The reaction mixture was stirred at room temperature for 12–32 h. The solvent was removed under reduced pressure and then 10 mL of a C<sub>2</sub>H<sub>5</sub>OH/H<sub>2</sub>O (1:1) mixture was added to the oily precipitate. The formed precipitate was filtered off, washed with EtOH and purified by silica gel (60–120) column chromatography (EtOAc/hexane, CHCl<sub>3</sub>/EtOH, CH<sub>2</sub>Cl<sub>2</sub>) or crystallization from EtOH to afford the desired isoxazole **4**.

#### **3-(2-Chloro-6-fluorophenyl)-4-(1-methyl-5-nitro-1*H*-imidazol-4-yl)isoxazole (4d).**

Red powder, yield 86%, mp 170–172 °C (column, CHCl<sub>3</sub>/EtOH 20:1). IR (v/cm<sup>-1</sup>): 3154, 3113, 1610, 1497, 1354, 1125. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 3.96 (s, 3 H, CH<sub>3</sub>), 7.07 (m, 1 H, CH<sub>Ar</sub>), 7.20–7.30 (m, 1 H, CH<sub>Ar</sub>), 7.31–7.43 (m, 2 H, CH<sub>Ar</sub> + CH<sub>imidaz.</sub>), 9.38 (s, 1 H, C<sup>5</sup>-H). <sup>13</sup>C NMR (CDCl<sub>3</sub>): 36.0, 112.9, 114.1, 118.1, 125.16, 131.3, 133.8, 135.0, 135.2, 140.5, 155.0, 160.2, 160.9 (*J* 250 Hz). MS-EI, (*m/z*): 322 [M]<sup>+</sup>. Found: C, 48.74; H, 2.19; N, 17.57. C<sub>13</sub>H<sub>8</sub>ClFN<sub>4</sub>O<sub>3</sub> requires: C, 48.39; H, 2.50; N, 17.36%.

#### **3-Cyclohexyl-4-(1-methyl-5-nitro-1*H*-imidazol-4-yl)isoxazole (4e).**

Pink powder, yield 47%, mp 82–84 °C (column, CH<sub>2</sub>Cl<sub>2</sub>). IR (v/cm<sup>-1</sup>): 3111, 2931, 2854, 1613, 1486, 1357. <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): δ 1.11–1.34 (m, 3 H, CH<sub>cyclohex.</sub>), 1.34–1.54 (m, 2 H, CH<sub>cyclohex.</sub>), 1.57–1.81 (m, 3 H, CH<sub>cyclohex.</sub>), 1.89 (d, *J* 12.3 Hz, 2 H, CH<sub>cyclohex.</sub>), 3.03–3.21 (m, 1 H, CH<sub>cyclohex.</sub>), 3.95 (s, 3 H, CH<sub>3</sub>), 8.16 (s, 1 H, CH<sub>cyclohex.</sub>), 9.22 (s, 1 H, H-5). <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): 25.5, 25.7, 31.1, 34.8, 35.6, 110.5, 133.0, 135.4, 141.9, 159.8, 165.5. MS-EI (*m/z*): 276 [M]<sup>+</sup>. Found: C, 56.59; H, 5.75; N, 20.22. C<sub>13</sub>H<sub>16</sub>N<sub>4</sub>O<sub>3</sub> requires: C, 56.51; H, 5.84; N, 20.28%.

#### **4-[4-(1-Methyl-4-nitro-1*H*-imidazol-5-yl)isoxazol-3-yl]benzotrile (4f).**

Pink powder, yield 45%, mp 221–223 °C (column, CHCl<sub>3</sub>/EtOH 50:1). IR (v/cm<sup>-1</sup>): 3125, 2225, 1536, 1494, 1331. <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): δ 3.61 (s, 3 H, CH<sub>3</sub>), 7.59 (d, *J* 8.5 Hz, 2 H, H<sub>Ar</sub>), 7.90 (d, *J* 8.5 Hz, 2 H, H<sub>Ar</sub>), 8.09 (s, 1 H, CH<sub>imidaz.</sub>), 9.52 (s, 1 H, C<sup>5</sup>-H). <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): δ 32.9, 105.8, 112.9, 118.1, 120.6, 127.8, 132.2, 133.0, 138.5, 144.8, 159.4, 162.0. MS-EI (*m/z*): 295 [M]<sup>+</sup>. Found: C, 56.89; H, 3.12; N, 23.81. C<sub>14</sub>H<sub>9</sub>N<sub>5</sub>O<sub>3</sub> requires: C, 56.95; H, 3.07; N, 23.72%.

**3-(2-Chloro-6-fluorophenyl)-4-(1-methyl-4-nitro-1*H*-imidazol-5-yl)isoxazole (4g).**

Colorless powder, yield 83%, mp 210–213 °C (column, CHCl<sub>3</sub>/EtOH 20:1). IR (v/cm<sup>-1</sup>): 3121, 3097, 1607, 1572, 1330, 1120. <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): δ 3.64 (s, 3 H, CH<sub>3</sub>), 7.30–7.45 (m, 2 H, CH<sub>Ar</sub>), 7.56 (m, 1 H, CH<sub>Ar</sub>), 8.01 (s, 1 H, CH<sub>imidaz.</sub>), 9.66 (s, 1 H, C<sup>5</sup>-H). <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): δ 32.7, 108.0, 115.1, 115.3, 120.4, 125.9, 133.1, 133.2, 138.3, 144.5, 154.6, 159.8, 161.2. MS-EI (*m/z*): 287 [M-Cl]<sup>+</sup>. Found: C, 48.72; H, 2.19; N, 17.57. C<sub>13</sub>H<sub>8</sub>ClFN<sub>4</sub>O<sub>3</sub> requires: C, 48.39; H, 2.50; N, 17.36.

**Methyl 3-(4-methoxyphenyl)-3'-phenyl-4,5'-bi-isoxazole-4'-carboxylate (4i).**

Colorless powder, yield 73%, mp 115–116 °C (column, EtOAc/hexane 1:2). IR (v/cm<sup>-1</sup>): 3124, 1720, 1609, 1524, 1254, 1120. <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): δ 3.48 (s, 3 H, OCH<sub>3</sub>), 3.80 (s, 3 H, OCH<sub>3</sub>), 7.02–7.07 (m, 2 H, H<sub>Ar</sub>), 7.42–7.60 (m, 5 H, H<sub>Ar</sub>), 7.63–7.68 (m, 2 H, H<sub>Ar</sub>), 9.70 (s, 1 H, C<sup>5</sup>-H). <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): δ 52.4, 55.8, 106.9, 110.6, 115.0, 119.8, 127.8, 128.8, 129.5, 129.8, 130.7, 159.8, 161.1, 161.3, 162.8, 163.4, 164.5. MS-EI (*m/z*): 376 [M]<sup>+</sup>. Found: C, 67.13; H, 4.44; N, 7.32. C<sub>21</sub>H<sub>16</sub>N<sub>2</sub>O<sub>5</sub> requires: C, 67.02; H, 4.28; N, 7.44%.

**Methyl 3-(4-cyanophenyl)-3'-phenyl-4,5'-bi-isoxazole-4'-carboxylate (4j).**

Colorless powder, yield 65%, mp 174–175 °C (column, EtOAc/hexane 1:2). IR (v/cm<sup>-1</sup>): 3116, 2227, 1715, 1633, 1125. <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): δ 3.55 (s, 3 H, OCH<sub>3</sub>), 7.44–7.56 (m, 3 H, H<sub>Ar</sub>), 7.60–7.65 (m, 2 H, H<sub>Ar</sub>), 7.74 (d, *J* 8.5 Hz, 2 H, H<sub>Ar</sub>), 7.89 (d, *J* 8.5 Hz, 2 H, H<sub>Ar</sub>), 9.72 (s, 1 H, C<sup>5</sup>-H). <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): δ 52.4, 107.4, 110.5, 113.6, 118.7, 127.7, 128.8, 129.4, 129.6, 130.7, 132.4, 133.4, 159.2, 161.0, 162.9, 163.7, 164.0. MS-EI (*m/z*): 371 [M]<sup>+</sup>. Found: C, 67.98; H, 3.47; N, 11.38. C<sub>21</sub>H<sub>13</sub>N<sub>3</sub>O<sub>4</sub> requires: C, 67.92; H, 3.53; N, 11.32%.

**Methyl 3-(4-chlorophenyl)-3'-phenyl-4,5'-bi-isoxazole-4'-carboxylate (4k).**

Colorless powder, yield 80%, mp 135–136 °C (column, EtOAc/hexane 1:2). IR (v/cm<sup>-1</sup>): 3134, 1706, 1620, 1556, 1142. <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): δ 3.55 (s, 3 H, OCH<sub>3</sub>), 7.43–7.58 (m, 7 H, H<sub>Ar</sub>), 7.60–7.66 (m, 2 H, H<sub>Ar</sub>), 9.62 (s, 1 H, C<sup>5</sup>-H). <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): δ 52.4, 107.2, 110.5, 126.6, 127.7, 128.8, 129.5, 129.6, 130.3, 130.7, 135.8, 159.4, 161.1, 162.8, 163.7, 164.0. MS-EI (*m/z*): 380 [M]<sup>+</sup>. Found: C, 63.02; H, 3.37; N, 7.51. C<sub>20</sub>H<sub>13</sub>ClN<sub>2</sub>O<sub>4</sub> requires: C, 63.08; H, 3.44; N, 7.36%.

**Methyl 3-(2-chloro-6-fluorophenyl)-3'-phenyl-4,5'-bi-isoxazole-4'-carboxylate (4l).**

Colorless powder, yield 90%, mp 101–102 °C (column, EtOAc/hexane 1:1). IR ( $\nu/\text{cm}^{-1}$ ): 3150, 2923, 1707, 1610, 1567, 1130.  $^1\text{H}$  NMR (DMSO- $d_6$ ):  $\delta$  3.66 (s, 3 H, OCH<sub>3</sub>), 7.43–7.63 (m, 8 H, H<sub>Ar</sub>), 7.70–7.73 (m, 1 H, H<sub>Ar</sub>), 10.04 (s, 1 H, C<sup>5</sup>-H).  $^{13}\text{C}$  NMR (DMSO- $d_6$ ):  $\delta$  52.7, 109.0, 109.4, 115.6, 116.0, 126.5, 127.7, 128.8, 129.5, 130.7, 134.0, 134.3, 153.5, 159.4, 161.3, 161.9, 162.8, 163.4. MS-EI ( $m/z$ ): 398 [M]<sup>+</sup>. Found: C, 60.13; H, 3.15; N, 7.11. C<sub>20</sub>H<sub>12</sub>ClFN<sub>2</sub>O<sub>4</sub> requires: C, 60.24; H, 3.03; N, 7.02%.

**Methyl 3-cyclohexyl-3'-phenyl-4,5'-bi-isoxazole-4'-carboxylate (4m).**

Colorless powder, yield 54%, mp 65–67 °C (column, EtOAc/hexane 1:1). IR ( $\nu/\text{cm}^{-1}$ ): 2936, 2857, 1721, 1327, 1121.  $^1\text{H}$  NMR (DMSO- $d_6$ ):  $\delta$  1.22–1.50 (m, 4 H, CH<sub>cyclohex.</sub>), 1.52–1.63 (m, 2 H, CH<sub>cyclohex.</sub>), 1.74–1.77 (m, 1 H, CH<sub>cyclohex.</sub>), 1.81–1.94 (m, 1 H, CH<sub>cyclohex.</sub>), 2.01 (m, 2 H, CH<sub>cyclohex.</sub>), 3.04–3.15 (m, 1 H, CH<sub>cyclohex.</sub>), 3.72 (s, 3H, OCH<sub>3</sub>), 7.43–7.54 (m, 3 H, H<sub>Ar</sub>), 7.60 (m, 2 H, H<sub>Ar</sub>), 9.51 (s, 1 H, C<sup>5</sup>-H).  $^{13}\text{C}$  NMR (DMSO- $d_6$ ):  $\delta$  25.4, 25.6, 31.2, 35.4, 52.1, 106.3, 109.1, 127.5, 128.3, 129.0, 130.1, 161.0, 162.2, 162.3, 164.3, 164.5. MS-EI ( $m/z$ ): 352 [M]<sup>+</sup>. Found: C, 68.25; H, 5.79; N, 7.85. C<sub>20</sub>H<sub>20</sub>N<sub>2</sub>O<sub>4</sub> requires: C, 68.17; H, 5.72; N, 7.95%.

**Methyl 3'-(2-chlorophenyl)-3-(4-chlorophenyl)-4,5'-bi-isoxazole-4'-carboxylate (4n).**

Colorless powder, yield 80%, mp 101–102 °C (column, EtOAc/hexane 1:1).  $^1\text{H}$  NMR (DMSO- $d_6$ ):  $\delta$  3.43 (s, 3 H, OCH<sub>3</sub>), 7.43–7.72 (m, 8 H, H<sub>Ar</sub>), 9.85 (s, 1 H, C<sup>5</sup>-H).  $^{13}\text{C}$  NMR (DMSO- $d_6$ ):  $\delta$  52.4, 106.9, 111.6, 126.7, 127.5, 127.8, 129.6, 129.9, 130.3, 131.8, 132.3, 133.2, 135.8, 159.5, 160.6, 161.4, 163.6, 163.9. MS-EI ( $m/z$ ): 414 [M]<sup>+</sup>. Found: C, 57.79; H, 2.81; N, 6.89. C<sub>20</sub>H<sub>12</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>4</sub> requires: C, 57.85; H, 2.91; N, 6.75%.

**Methyl 3'-phenyl-3-(pyridin-2-yl)-4,5'-bi-isoxazole-4'-carboxylate (4o).**

Colorless powder, yield 50%, mp 147–149 °C (column, EtOAc/hexane 1:1). IR ( $\nu/\text{cm}^{-1}$ ): 3128, 1716, 1647, 1447, 1384, 1126.  $^1\text{H}$  NMR (DMSO- $d_6$ ):  $\delta$  3.24 (s, 3 H, OCH<sub>3</sub>), 7.50–7.56 (m, 4 H, H<sub>Ar</sub>), 7.67–7.69 (m, 2 H, H<sub>Ar</sub>), 8.00–8.05 (m, 2 H, H<sub>Ar</sub>), 8.51–8.52 (m, 1 H, H<sub>Ar</sub>), 9.81 (s, 1 H, C<sup>5</sup>-H).  $^{13}\text{C}$  NMR (DMSO- $d_6$ ):  $\delta$  51.3, 107.3, 110.2, 122.6, 125.2, 127.4, 128.4, 129.0, 130.2, 137.7, 147.0, 149.7, 159.0, 160.8, 162.1, 163.0, 164.5. MS-EI ( $m/z$ ): 347 [M]<sup>+</sup>. Found: C, 66.07; H, 4.11; N, 12.31. C<sub>19</sub>H<sub>13</sub>N<sub>3</sub>O<sub>4</sub> requires: C, 65.70; H, 3.77; N, 12.10%.

**Ethyl 3,3'-diphenyl-4,5'-bi-isoxazole-4'-carboxylate (4p).** Colorless powder, yield 60%, mp 104–105 °C (column, EtOAc/hexane 1:1). IR ( $\nu/\text{cm}^{-1}$ ): 3134, 1715, 1643, 1444, 1122.  $^1\text{H}$  NMR ( $\text{DMSO-}d_6$ ):  $\delta$  1.02 (t,  $J$  7.1 Hz, 3 H,  $\text{OCH}_2\text{CH}_3$ ), 3.96 (q,  $J$  7.1 Hz, 2 H,  $\text{OCH}_2\text{CH}_3$ ), 7.43–7.56 (m, 8 H,  $\text{H}_{\text{Ar}}$ ), 7.62–7.64 (m, 2 H,  $\text{H}_{\text{Ar}}$ ), 9.62 (s, 1 H,  $\text{C}^5\text{-H}$ ).  $^{13}\text{C}$  NMR ( $\text{DMSO-}d_6$ ):  $\delta$  13.8, 61.4, 107.0, 111.0, 127.7, 127.8, 128.3, 128.7, 129.5, 129.6, 130.7, 130.9, 160.2, 160.6, 162.8, 163.6, 164.3. MS-EI ( $m/z$ ): 360  $[\text{M}]^+$ . Found: C, 69.81; H, 4.63; N, 7.65.  $\text{C}_{21}\text{H}_{16}\text{N}_2\text{O}_4$  requires: C, 69.99; H, 4.48; N, 7.77%.

### Preparation of isoxazolines 3c.

Isoxazoline **3c** was synthesized in the same manner as isoxazoles **4a,b,d-g,i-p** (See general procedure). The reaction time is 48 h.

### 3-Cyclohexyl-*N,N*-dimethyl-4-(1-methyl-4-nitro-1*H*-imidazol-5-yl)-4,5-

**dihydroisoxazol-5-amine (3c).** Yellow powder, yield 21%, mp 169–171 °C (column,  $\text{CHCl}_3/\text{EtOH}$  1:1). IR ( $\nu/\text{cm}^{-1}$ ): 2929, 2852, 1555, 1504, 1334.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  1.03–1.82 (m, 10 H,  $\text{CH}_{\text{cyclohex.}}$ ), 2.20–2.78 (m, 1 H, CH), 2.36 (s, 6 H,  $\text{NMe}_2$ ), 3.60 (s, 3 H,  $\text{CH}_3$ ), 5.18 (d,  $J$  4.0 Hz, 1 H, CH), 5.71 (d,  $J$  4.0 Hz, 1 H, CH), 7.37 (s, 1 H,  $\text{CH}_{\text{imidaz.}}$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  25.6, 25.6, 25.8, 29.9, 30.9, 32.5, 37.1, 39.0, 46.2, 70.6, 100.9, 127.8, 137.1, 145.3, 159.0. MS-EI ( $m/z$ ): 321. Found: 56.44; H, 7.52; N, 21.53.  $\text{C}_{15}\text{H}_{23}\text{N}_5\text{O}_3$  requires: C, 56.06; H, 7.21; N, 21.79%.

### Transformation of isoxazolines 3b,c to isoxazoles 4c,h.

A solution isoxazoline **3c** (1 mmol) in a mixture of  $\text{H}_2\text{O}:\text{HOAc}$  (1:1) (2 mL) was stirred at room temperature overnight. The formed precipitate was filtered off, washed with  $\text{H}_2\text{O}$  and dried in a desiccator over  $\text{P}_2\text{O}_5$  and purified by flash column chromatography ( $\text{CH}_2\text{Cl}_2$ ).

**3-Cyclohexyl-4-(1-methyl-4-nitro-1*H*-imidazol-5-yl)isoxazole (4h).** Colorless powder, yield 72%, mp 123–125 °C (column,  $\text{CH}_2\text{Cl}_2$ ). IR ( $\nu/\text{cm}^{-1}$ ): 3133, 2930, 2855, 1496, 1331.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  1.16–1.75 (m, 10 H,  $\text{CH}_2$ ), 2.48–2.54 (m, 1 H, CH), 3.55 (s, 3 H,  $\text{CH}_3$ ), 7.59 (s, 1 H,  $\text{C}^5\text{-H}$ ), 8.47 (s, 1 H,  $\text{CH}_{\text{imidaz.}}$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  25.7, 26.0, 33.0, 35.9, 105.6, 121.0, 136.8, 146.4, 158.3, 166.4. MS-EI ( $m/z$ ): 276  $[\text{M}]^+$ . Found: C, 56.88; H, 6.07; N, 19.97.  $\text{C}_{13}\text{H}_{16}\text{N}_4\text{O}_3$  requires: C, 56.51; H, 5.84; N, 20.28%.