Supporting Information
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Supporting Information

One-Pot Synthesis of 2,4,5-Trisubstituted Oxazoles via a Tandem Passerini 3CC/Staudinger/aza-Wittig/Isomerization Reaction

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General Methods:
All reactions were performed in round-bottom flasks under an atmosphere of air. Unless otherwise noted, materials were purchased from commercial suppliers and used without further purification. Toluene was distilled from Na, and stored over 4Å molecular sieves. Column chromatography purifications were performed under “flash” conditions using 400-630 mesh silica gel. Analytical thin-layer chromatography (TLC) was carried out on silica gel 60 F254 plates, which were visualized by exposure to ultraviolet light. Melting points were uncorrected. MS were measured on Finnigan Trace MS spectrometer or determined using API 2000 liquid chromatography-tandem mass spectrometer. 1H NMR were recorded in CDCl3 on a Varian Mercury 400 or 600 spectrometer and resonances relative to TMS. Data are reported as follows: chemical shift, multiplicity (s = single, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz) and integration. 13C NMR spectra were recorded on Varian Mercury 400/600 (100/150 MHz) with complete proton decoupling spectrophotometers (CDCl3: 77.0 ppm). Elementary analyses were taken on a Vario EL III elementary analysis instrument.

General Procedure for the Synthesis of 2,4,5-Trisubstituted Oxazoles 5
A mixture of α-azidocinnamaldehyde 1 (0.17 g, 1 mmol), isocyanide (1 mmol), and acid (1 mmol) was stirred in dichloromethane (5 mL) at room temperature or 40-50 °C for 24-48 h. Then PPh3 (0.26 g, 1 mmol) in dichloromethane (5 mL) was added dropwise to the reaction system and the reaction mixture was stirred at room temperature for 2 h. The solvent was evaporated under reduced pressure, and toluene (10 mL) was added. After the resulted solution was refluxed for 8-10 h, solid potassium carbonate (0.014 g, 0.1 mmol) was added to the reaction system and the solution was refluxed for further 1-2 h. The solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel (ether/petroleum ether = 1:6, V/V) to give oxazoles 5. The prepared new compounds are as follows:

4-benzyl-N-(tert-butyl)-2-phenyloxazole-5-carboxamide (5a)
White solid, mp 145-146 °C; 1H NMR (CDCl3, 600 MHz) δ (ppm) 8.03 (d, J = 7.2 Hz, 2H, ArH), 7.45-7.18 (m, 7H, ArH), 6.08 (s, 1H, NH), 4.34 (s, 2H, CH2), 1.50 (s, 9H, 3CH3); 13C NMR (CDCl3, 150 MHz) δ (ppm) 159.8, 157.6, 145.4, 139.4, 138.6, 131.1, 129.0, 128.7, 128.3, 126.8, 126.5, 126.3, 51.7, 32.8, 29.0; MS (EI, 70 eV): m/z (%) = 334 (M+, 87), 278 (86), 261 (33), 131 (100), 103 (39). Anal. Calcd for C21H22N2O2: C, 75.42; H, 6.63; N, 8.38. Found: C, 75.56; H, 6.73; N, 8.59.

4-benzyl-N-(tert-butyl)-2-(p-tolyl)oxazole-5-carboxamide (5b)
White solid, mp 169-171 °C; 1H NMR (CDCl3, 600 MHz) δ (ppm) 7.91 (d, J = 7.8 Hz, 2H, ArH), 7.45 (d, J = 7.8 Hz, 2H, ArH), 7.29-7.18 (m, 5H, ArH), 6.07 (s, 1H, NH), 4.33 (s, 2H, CH2), 2.40 (s, 3H, CH3), 1.50 (s, 9H, 3CH3); 13C NMR (CDCl3, 150 MHz) δ (ppm) 160.1, 157.7, 145.4, 141.6, 139.2, 138.7, 129.4, 129.0, 128.3, 126.8, 126.2, 123.8, 51.7, 32.8, 29.0, 21.6; MS (EI, 70 eV): m/z (%) = 348 (M+, 66), 292 (53), 275 (18), 131 (100). Anal. Calcd for C22H24N2O2: C, 75.83; H, 6.64; N, 8.04. Found: C, 75.98; H, 6.93; N, 8.31.

4-benzyl-N-(tert-butyl)-2-(o-tolyl)oxazole-5-carboxamide (5c)
White solid, mp 110-111 °C; 1H NMR (CDCl3, 600 MHz) δ (ppm) 7.92 (d, J = 7.2 Hz, 1H, ArH), 7.48 (d, J = 7.8 Hz, 2H, ArH), 7.37-7.18 (m, 6H, ArH), 6.06 (s, 1H, NH), 4.34 (s, 2H, CH2), 2.65 (s, 3H, CH3), 1.49 (s, 9H, 3CH3); 13C NMR (CDCl3, 150 MHz) δ (ppm) 160.1, 157.7, 145.0, 138.9, 138.8, 138.0, 131.7, 130.6, 129.1, 129.0, 128.3, 126.2, 125.9, 125.6, 51.7, 32.8, 29.0, 21.9; MS (EI, 70 eV): m/z (%) = 348 (M+, 51), 292 (39), 275 (23), 131 (100). Anal. Calcd for C22H24N2O2: C, 75.83; H, 6.94; N, 8.04. Found: C, 76.04; H, 6.77; N, 8.41.
4-benzyl-N-(tert-butyl)-2-(2-chlorophenyl)oxazole-5-carboxamide (5d)

White solid, mp 123-125 °C; $^1$H NMR (CDCl$_3$, 600 MHz) $\delta$ (ppm) 8.04 (d, $J = 7.8$ Hz, 1H, ArH), 7.50-7.19 (m, 8H, ArH), 6.18 (s, 1H, NH), 4.35 (s, 2H, CH$_2$), 1.48 (s, 9H, 3CH$_3$); $^{13}$C NMR (CDCl$_3$, 150 MHz) $\delta$ (ppm) 157.8, 157.4, 144.8, 139.8, 138.5, 132.4, 131.7, 131.5, 129.0, 128.3, 126.9, 126.3, 125.3, 51.6, 32.6, 28.8; MS (EI, 70 eV): m/z (%) = 368 (M$^+$, 41), 312 (36), 295 (10), 201 (9), 131 (100). Anal. Calcd for C$_{21}$H$_{21}$ClN$_2$O$_2$: C, 68.38; H, 5.74; N, 7.59. Found: C, 68.41; H, 5.62; N, 7.76.

4-benzyl-N-(tert-butyl)oxazole-5-carboxamide (5e)

Light yellow solid, mp 47-50 °C; $^1$H NMR (CDCl$_3$, 600 MHz) $\delta$ (ppm) 7.71 (s, 1H, ArH), 7.38 (d, $J = 7.2$ Hz, 2H, ArH), 7.30-7.19 (m, 3H, ArH), 6.07 (s, 1H, NH), 4.30 (s, 2H, CH$_2$), 1.47 (s, 9H, 3CH$_3$); $^{13}$C NMR (CDCl$_3$, 150 MHz) $\delta$ (ppm) 157.2, 149.1, 143.4, 139.5, 138.2, 128.9, 128.3, 126.5, 48.0, 33.2, 32.9, 25.4, 24.9; MS (EI, 70 eV): m/z (%) = 258 (M$^+$, 59), 202 (47), 185 (100), 131 (38), 103 (17). Anal. Calcd for C$_{15}$H$_{18}$N$_2$O$_2$: C, 69.74; H, 7.02; N, 10.84. Found: C, 69.94; H, 6.91; N, 10.89.

4-benzyl-N-cyclohexyl-2-phenyloxazole-5-carboxamide (5f)

White solid, mp 154-156 °C; $^1$H NMR (CDCl$_3$, 600 MHz) $\delta$ (ppm) 8.04 (d, $J = 7.2$ Hz, 2H, ArH), 7.48-7.20 (m, 8H, ArH), 6.13 (d, $J = 7.8$ Hz, 1H, NH), 4.34 (s, 2H, CH$_2$), 4.01-3.96 (m, 1H, NCH), 2.05-1.21 (m, 10H, 5CH$_2$); $^{13}$C NMR (CDCl$_3$, 150 MHz) $\delta$ (ppm) 160.1, 157.3, 146.1, 139.0, 138.6, 131.2, 129.1, 128.7, 128.3, 126.9, 126.5, 126.3, 48.0, 33.2, 32.9, 25.4, 24.9; MS (EI, 70 eV): m/z (%) = 360 (M$^+$, 84), 278 (33), 261 (39), 131 (100). Anal. Calcd for C$_{23}$H$_{24}$N$_2$O$_2$: C, 76.64; H, 6.71; N, 7.77. Found: C, 76.59; H, 6.89; N, 7.71.

4-benzyl-N-cyclohexyl-2-(p-tolyl)oxazole-5-carboxamide (5g)

White solid, mp 165-167 °C; $^1$H NMR (CDCl$_3$, 600 MHz) $\delta$ (ppm) 7.93 (d, $J = 8.4$ Hz, 2H, ArH), 7.46 (d, $J = 7.8$ Hz, 2H, ArH), 6.13 (d, $J = 8.4$ Hz, 1H, NH), 4.34 (s, 2H, CH$_2$), 4.01-3.96 (m, 1H, NCH), 2.40 (s, 3H, CH$_3$), 2.05-1.21 (m, 10H, 5CH$_2$); $^{13}$C NMR (CDCl$_3$, 150 MHz) $\delta$ (ppm) 160.4, 157.4, 146.0, 141.7, 138.7, 138.6, 129.5, 129.1, 128.3, 126.9, 126.3, 123.8, 48.0, 33.3, 32.9, 25.5, 25.0, 21.6; MS (EI, 70 eV): m/z (%) = 374 (M$^+$, 81), 292 (47), 275 (47), 131 (100). Anal. Calcd for C$_{24}$H$_{26}$N$_2$O$_2$: C, 76.98; H, 7.00; N, 7.48. Found: C, 77.15; H, 7.24; N, 7.76.

4-benzyl-2-(2-chlorophenyl)-N-cyclohexyloxazole-5-carboxamide (5h)

White solid, mp 108-111 °C; $^1$H NMR (CDCl$_3$, 600 MHz) $\delta$ (ppm) 7.93 (d, $J = 8.4$ Hz, 2H, ArH), 7.46 (d, $J = 7.8$ Hz, 2H, ArH), 6.12 (d, $J = 8.4$ Hz, 1H, NH), 4.33 (s, 2H, CH$_2$), 4.01-3.96 (m, 1H, NCH), 2.02-1.22 (m, 10H, 5CH$_2$); $^{13}$C NMR (CDCl$_3$, 150 MHz) $\delta$ (ppm) 158.1, 157.1, 145.4, 139.5, 138.5, 132.5, 131.7, 131.6, 131.2, 129.1, 128.4, 126.9, 126.3, 125.5, 47.9, 33.1, 32.7, 25.4, 24.7; MS (EI, 70 eV): m/z (%) = 394 (M$^+$, 44), 312 (17), 295 (11), 240 (9), 131 (100). Anal. Calcd for C$_{23}$H$_{23}$ClN$_2$O$_2$: C, 69.95; H, 5.87; N, 7.09. Found: C, 70.05; H, 5.96; N, 7.34.
4-benzyl-N-(tert-butyl)-2-methyloxazole-5-carboxamide (5i)

White solid, mp 121-124 °C; ¹H NMR (CDCl₃, 600 MHz) δ (ppm) 7.38 (d, J = 6.6 Hz, 2H, ArH), 7.27 (d, J = 7.2 Hz, 2H, ArH), 7.20 (t, J = 7.2 Hz, 1H, ArH), 6.00 (s, 1H, NH), 4.23 (s, 2H, CH₂), 2.43 (s, 3H, CH₃), 1.47 (s, 9H, 3CH₃); ¹³C NMR (CDCl₃, 150 MHz) δ (ppm) 160.2, 157.5, 144.2, 139.4, 138.6, 129.0, 128.3, 126.3, 51.6, 32.6, 28.9, 14.1; MS (EI, 70 eV): m/z (%) = 272 (M⁺, 54), 216 (46), 199 (29), 131 (100). Anal. Calcd for C₁₆H₂₀N₂O₂: C, 70.56; H, 7.40; N, 10.29. Found: C, 70.71; H, 7.28; N, 10.51.

4-benzyl-N-butyl-2-phenyloxazole-5-carboxamide (5j)

White solid, mp 67-69 °C; ¹H NMR (CDCl₃, 600 MHz) δ (ppm) 8.04 (d, J = 7.2 Hz, 2H, ArH), 7.47-7.18 (m, 8H, ArH), 6.27 (s, 1H, NH), 4.35 (s, 2H, CH₂), 3.48-3.45 (m, 2H, NCH₂), 1.64-1.60 (m, 2H, CH₂), 1.45-1.42 (m, 2H, CH₂), 0.98 (t, J = 7.2 Hz, 3H, CH₃); ¹³C NMR (CDCl₃, 150 MHz) δ (ppm) 160.1, 158.1, 145.9, 139.0, 138.5, 131.1, 129.0, 128.6, 128.3, 126.8, 126.4, 38.8, 32.8, 31.7, 20.0, 13.7; MS (EI, 70 eV): m/z (%) = 334 (M⁺, 67), 262 (33), 131 (100). Anal. Calcd for C₂₁H₂₂N₂O₂: C, 75.42; H, 6.63; N, 8.38. Found: C, 75.68; H, 6.68; N, 8.61.

N-tert-butyl-4-ethyl-2-phenyloxazole-5-carboxamide (5k)

White solid, mp 160-161 °C; ¹H NMR (CDCl₃, 600 MHz) δ (ppm) 8.06-7.49 (m, 5H, ArH), 6.08 (s, 1H, NH), 2.99 (q, J = 7.2 Hz, 2H, CH₂), 1.50 (s, 9H, 3CH₃), 1.31 (t, J = 7.2 Hz, CH₃); ¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 159.5, 157.7, 148.5, 138.6, 130.9, 128.7, 126.7, 126.5, 51.5, 28.9, 20.2, 12.9; MS (EI, 70 eV): m/z (%) = 272 (M⁺, 100), 257 (13), 216 (61), 200 (75), 144 (45), 104 (83). Anal. Calcd for C₁₆H₂₀N₂O₂: C, 70.56; H, 7.40; N, 10.29. Found: C, 70.36; H, 7.35; N, 10.47.

N-tert-butyl-4-ethyl-2-p-tolyloxazole-5-carboxamide (5l)

White solid, mp 141-143 °C; ¹H NMR (CDCl₃, 600 MHz) δ (ppm) 7.94 (d, J = 7.2 Hz, 2H, ArH), 7.28 (d, J = 7.8 Hz, 2H, ArH), 6.07 (s, 1H, NH), 2.98 (q, J = 7.2 Hz, 2H, CH₂), 2.42 (s, 3H, CH₃), 1.50 (s, 9H, 3CH₃), 1.31 (t, J = 7.2 Hz, CH₃); ¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 159.9, 157.9, 148.6, 141.5, 138.4, 129.5, 126.7, 123.9, 51.6, 29.0, 21.6, 20.3, 13.0; MS (EI, 70 eV): m/z (%) = 286 (M⁺, 100), 271 (8), 230 (69), 214 (50), 157 (38), 118 (49). Anal. Calcd for C₁₇H₂₂N₂O₂: C, 71.30; H, 7.74; N, 9.78. Found: C, 71.38; H, 7.93; N, 9.53.
$^1$H NMR and $^{13}$C NMR Spectrums for Compounds 5

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