Supplementary Material

Efficient synthesis of novel 1-hydroxy-2,4,5-trisubstituted imidazole derivatives *via* a one-pot, four-component reaction between hydroxylamine, benzonitriles, arylglyoxals and 1,3-dicarbonyl compounds

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Experimental Section

General. All chemicals were purchased from Aldrich and Merck with high-grade quality, and used without any purification. All melting points were obtained by Barnstead Electrothermal 9200 apparatus and are uncorrected. The reactions were monitored by TLC and all yields refer to isolated products. NMR spectra were obtained on a Varian 500 MHz spectrometer (^{1}H NMR at 500 MHz, ^{13}C NMR at 125 MHz) in DMSO using TMS as an internal standard. Infrared spectra were recorded on a Bruker FT-IR Equinax-55 spectrophotometer in KBr with absorption in cm^{-1}. Elemental analyses were performed using a Carlo Erba EA 1108 instrument. All products were characterized by their spectral and physical data.

General procedure for the synthesis of 1-hydroxy-2,4,5-trisubstituted imidazole derivatives.
A mixture of hydroxylamine (**1**) (2.0 mmol) and benzonitrile (**2**) (1.0 mmol) was stirred in 10 mL of ethanol at reflux for 3 hr to give amidoxime. Then, 1,3-dicarbonyl compound (**3**) (1.0 mmol) and arylglyoxal (**4**) (1.0 mmol) was added, and obtain mixture was stirred at reflux for 1 hr. After completion of the reaction, determined by TLC, the solvent was removed under reduced pressure, and the resulting crude product was purified by recrystallization from ethanol to give the pure compounds **5a–l** (65–87%).

5-(5-(4-Chlorophenyl)-1-hydroxy-2-phenyl-1*H*-imidazol-4-yl)-6-hydroxy-2,2-dimethyl-4*H*-1,3-dioxin-4-one (5a). mp 213-215 °C. IR υ/cm^{-1} (KBr): 3424, 2991, 1639. ^{1}H NMR (500 MHz, DMSO): δ 1.64 (s, 6H, 2CH$_3$), 2.06 (s, 1H, OH), 7.51 (d, *J* 10.0 Hz, 2H, ArH), 7.55 (s, 2H, ArH), 7.56 (d, *J* 5.0 Hz, 2H, ArH), 7.63 (s, 1H, ArH), 8.04 (m, 2H, ArH), 14.10 (s, 1H, OH) ppm. ^{13}C NMR (125 MHz, DMSO): δ 26.2, 102.23, 122.3, 125.4, 126.5, 128.5, 129.1, 129.3, 129.8, 131.5, 131.5, 131.8, 135.9, 161.8, 165.3, 196.5 ppm. Anal. Calcd for $C_{21}H_{17}ClN_2O_5$ (412.83): C, 61.10; H, 4.15; N, 6.79. Found: C, 61.24; H, 4.17; N, 6.75%.
5-(2-Benzyl-1-hydroxy-5-(p-tolyl)-1*H*-imidazol-4-yl)-6-hydroxy-2,2-dimethyl-4*H*-1,3-dioxin-4-one (5b). mp 208-211 °C. IR υ/cm^{-1} (KBr): 3432, 2998, 1667; ^{1}H NMR (500 MHz, DMSO): δ 1.22 (s, 6H, 2CH$_3$), 1.58 (s, 3H, CH$_3$), 2.07 (s, 1H, OH), 3.76 (s, 2H, CH$_2$), 6.67 (d, *J* 10.0 Hz, 2H, ArH), 6.78 (d, *J* 10.0 Hz, 1H, ArH), 6.82 (s, 2H, ArH), 6.84 (d, *J* 7.9 Hz, 2H, ArH), 6.92 (d, 2H, *J* 7.9 Hz, ArH), 13.31 (s, 1H, OH) ppm. ^{13}C NMR (125 MHz, DMSO): δ 20.8, 25.6, 28.9, 62.6, 101.7, 123.2, 123.7, 125.8, 126.1, 127.1, 128.3, 128.5, 128.6, 133.6, 136.1, 137.6, 165.1, 191.2 ppm. Anal. Calcd for $C_{23}H_{22}N_2O_5$ (406.44): C, 67.97; H, 5.46; N, 6.89. Found: C, 67.19; H, 5.50; N, 6.91%.
5-(2-(2-Chlorophenyl)-5-(4-chlorophenyl)-1-hydroxy-1*H*-imidazol-4-yl)-6-hydroxy-2,2-dimethyl-4*H*-1,3-dioxin-4-one (5c). mp 204-206 °C. IR υ/cm^{-1} (KBr): 3420, 2987, 1609; ^{1}H NMR (500 MHz, DMSO): δ 1.05 (s, 1H, OH), 1.65 (s, 6H, 2CH$_3$), 7.55 (d, *J* 5.0 Hz, 2H, ArH), 7.64 (d, *J* 5.0 Hz, 2H, ArH), 7.71 (t, 2H, ArH), 7.78 (d, *J* 6.9 Hz, 1H, ArH), 7.87 (d, *J* 7.7 Hz, 1H, ArH), 13.85 (s, 1H, OH) ppm. ^{13}C NMR (125 MHz, DMSO): δ 26.3, 69.2, 102.0, 111.8, 115.6, 122.4, 128.1, 128.4, 128.8, 129.0, 130.5, 133.6, 134.0, 134.7, 135.1, 144.2, 164.8, 214.0 ppm. Anal. Calcd for $C_{21}H_{16}Cl_2N_2O_5$ (447.27): C, 56.39; H, 3.61; N, 6.26%.
5-(5-(4-Chlorophenyl)-1-hydroxy-2-(4-methoxyphenyl)-1*H*-imidazol-4-yl)-6-hydroxy-2,2-dimethyl-4*H*-1,3-dioxin-4-one (5d). mp 203-205 °C. IR υ/cm^{-1} (KBr): 3422, 2938, 1610. ^{1}H NMR (500 MHz, DMSO): δ 1.61 (s, 6H, 2CH$_3$), 2.08 (s, 1H, OH), 3.86 (s, 3H, CH$_3$), 7.20 (d, *J* 9.0 Hz, 2H, ArH), 7.54 (d, *J* 8.6 Hz, 2H, ArH), 7.69 (d, *J* 8.6 Hz, 2H, ArH), 8.04 (d, *J* 9.0 Hz, 2H, ArH), 13.51(s, 1H, OH) ppm. ^{13}C NMR (125 MHz, DMSO): δ 26.3, 56.0, 68.1, 101.7, 111.3, 115.0, 126.6, 128.4, 128.6, 128.8, 129.2, 130.4, 133.2, 136.9, 141.1, 164.9, 217.0 ppm. Anal. Calcd for $C_{22}H_{19}ClN_2O_6$ (442.85): C, 59.67; H, 4.32; N, 6.33. Found: C, 59.79; H, 4.33; N, 6.28%.

5-(5-(4-Bromophenyl)-1-hydroxy-2-phenyl-1*H*-imidazol-4-yl)-6-hydroxy-2,2-dimethyl-4*H*-1,3-dioxin-4-one (5e). mp 218-220 °C. IR υ/cm^{-1} (KBr): 3426, 2986, 1639. ^{1}H NMR (500 MHz, DMSO): δ 1.63 (s, 6H, 2CH$_3$), 2.08 (s, 1H, OH), 7.55 (d, *J* 5.0 Hz, 2H, ArH), 7.64 (d, *J* 5.0 Hz, 2H, ArH), 7.68 (s, 1H, ArH), 7.70 (d, *J* 10.0 Hz, 2H, ArH), 8.07 (d, *J* 10.0 Hz, 2H, ArH), 13.75 (s, 1H, OH) ppm. ^{13}C NMR (125 MHz, DMSO): δ 26.3, 78.7, 101.8, 127.4, 128.7, 128.9, 129.3, 129.5, 131.4, 131.7, 132.8, 133.9, 136.7, 140.7, 164.9, 187.4 ppm. Anal. Calcd for $C_{21}H_{17}BrN_2O_5$ (457.28): C, 55.16; H, 3.75; N, 6.13. Found: C, 55.24; H, 3.77; N, 6.08%.

2-(5-(4-Chlorophenyl)-1-hydroxy-2-phenyl-1*H*-imidazol-4-yl-)-3-hydroxy-5,5-dimethylcyclohex-2-en-1-one (5f). mp 205-207 °C. IR υ/cm^{-1} (KBr): 3449، 2954, 1694. ^{1}H NMR (500 MHz, DMSO): δ 1.09 (s, 6H, 2CH$_3$), 2.59 (s, 1H, OH), 3.17 (s, 2H, CH$_2$), 3.32 (d, 2H, CH$_2$), 7.55 (d, *J* 5.0 Hz, 2H, ArH), 7.57 (s, 1H, ArH), 7.61 (d, *J* 10.0 Hz, 2H, ArH), 7.81 (d, *J* 5.0 Hz, 2H, ArH), 8.43 (d, *J* 10.0 Hz, 2H, ArH), 14.01 (s, 1H, OH) ppm. ^{13}C NMR (125 MHz, DMSO): δ 28.1, 32.9, 45.7, 51.4, 120.7, 129.2, 129.4, 129.6, 131.3, 132.9, 133.5, 136.0, 139.5, 164.4, 165.5, 173.5, 192.2, 196.7 ppm. Anal. Calcd for $C_{23}H_{21}ClN_2O_3$ (408.88): C, 67.56; H, 5.18; N, 6.58. Found: C, 67.72; H, 5.23; N, 6.56%.

3-Hydroxy-2-(1-hydroxy-2,5-diphenyl-1*H*-imidazol-4-yl)-5,5-dimethylcyclohex-2-en-1-one (5g). mp 188-190 °C. IR υ/cm^{-1} (KBr): 3362, 2952, 1690. ^{1}H NMR (500 MHz, DMSO): δ 1.09 (s, 6H, 2CH$_3$), 2.49 (s, 1H, OH), 2.59 (s, 2H, CH$_2$), 3.18 (s, 2H, CH$_2$), 7.53 (d, *J* 10.0 Hz, 2H, ArH), 7.54 (d, *J* 10.0 Hz, 2H, ArH), 7.59 (m, 1H, ArH), 7.67 (m, 1H, ArH), 7.78 (d, *J* 5.0 Hz, 2H, ArH), 8.41 (d, *J* 10.0 Hz, 2H, ArH), 14.10 (s, 1H, OH) ppm. ^{13}C NMR (125 MHz, DMSO): δ 28.1, 32.8, 45.7, 51.5, 120.7, 129.1, 129.2, 129.4, 129.5, 132.8, 134.5, 134.8, 136.1, 164.9, 165.5, 173.4, 193.2, 196.6 ppm. Anal. Calcd for $C_{23}H_{22}N_2O_3$ (374.44): C, 73.78; H, 5.92; N, 7.48. Found: C, 73.66; H, 5.91; N, 7.44%.

3-Hydroxy-2-(1-hydroxy-2-phenyl-5-(p-tolyl)-1*H*-imidazol-4-yl)-5,5-dimethylcyclohex-2-en-1-one (5h). mp 150-153 °C. IR υ/cm^{-1} (KBr): 3450, 2958, 1682. ^{1}H NMR (500 MHz, DMSO): δ 1.17 (s, 6H, 2CH$_3$), 2.05 (s, 1H, OH), 2.42 (s, 3H, CH$_3$), 2.55 (s, 2H, CH$_2$), 3.14 (s, 2H, CH$_2$), 7.26 (s, 2H, ArH), 7.50 (m, 2H, ArH), 7.52 (d, *J* 8.3 Hz, 1H, ArH), 7.72 (d, *J* 7.0 Hz, 2H, ArH), 8.56 (d, *J* 7.0 Hz, 2H, ArH), 13.81 (s, 1H, OH) ppm. ^{13}C NMR (125 MHz, DMSO): δ 21.8, 28.3, 32.7, 46.3, 52.0, 117.2, 120.4, 128.6, 129.4, 129.4, 132.1, 136.1, 138.9, 144.7, 148.5, 165.6, 172.0, 195.5, 197.5 ppm. Anal. Calcd for $C_{24}H_{24}N_2O_3$ (388.47): C, 74.21; H, 6.23; N, 7.21. Found: C, 74.37; H, 6.29; N, 7.18%.

2-(2-(4-Bromophenyl)-5-(4-chlorophenyl)-1-hydroxy-1*H*-imidazol-4-yl)-3-hydroxy-5,5-dimethylcyclohex-2-en-1-one (5i). mp 192-194 °C. IR υ/cm^{-1} (KBr): 3425, 2956, 1654. ^{1}H NMR (500 MHz, DMSO): δ 0.79 (s, 3H, CH$_3$), 0.81 (s, 3H, CH$_3$), 2.11(s, 2H, CH$_2$), 2.31 (s, 2H, CH$_2$), 2.66 (s, 1H, OH), 7.03 (d, *J* 8.7 Hz, 2H, ArH), 7.11 (d, *J* 8.6 Hz, 2H, ArH), 7.42 (d, *J* 8.7 Hz, 2H, ArH), 7.59 (d, *J* 8.6 Hz, 2H, ArH), 13.05 (s, 1H, OH) ppm. ^{13}C NMR (125 MHz, DMSO): δ 27.9, 28.0, 30.3, 51.7, 51.9, 104.0, 109.6, 125.1, 126.0, 127.7, 128.3, 129.2, 132.2, 134.1, 136.7, 156.3, 179.0, 199.2, 199.9 ppm.

2-(2-(4-Bromophenyl)-1-hydroxy-5-(p-tolyl)-1*H*-imidazol-4-yl)-3-hydroxy-5,5- dimethylcyclohex-2-en-1-one (5j). mp 193-195 °C. IR υ/cm^{-1} (KBr): 3432, 2954, 1654. ^{1}H NMR (500 MHz, DMSO): δ 0.84 (s, 3H, CH$_3$), 0.87 (s, 3H, CH$_3$), 2.12 (s, 3H, CH$_3$), 2.15 (s, 2H, CH$_2$), 2.37 (s, 2H, CH$_2$), 2.54 (s, 1H, OH), 6.92 (d, *J* 8.0 Hz, 2H, ArH), 7.10 (d, *J* 8.4 Hz, 2H, ArH), 7.48 (d, *J* 8.0 Hz, 2H, ArH), 7.66 (d, *J* 8.4 Hz, 2H, ArH), 13.15 (s, 1H, OH) ppm. ^{13}C NMR (125 MHz, DMSO): δ 21.0, 28.0, 28.1, 30.3, 51.8, 51.9, 104.6, 109.7, 124.3, 125.4, 127.5, 128.9, 129.1, 132.2, 134.9, 138.3, 155.8, 180.1, 199.1, 200.0 ppm. Anal. Calcd for $C_{24}H_{23}BrN_2O_3$ (467.36): C, 61.68; H, 4.96; N, 5.99. Found: C, 61.70; H, 4.99; N, 6.04%.

2-(2-(4-Bromophenyl)-1-hydroxy-5-phenyl-1*H*-imidazol-4-yl)-3-hydroxy-5,5-dimethylcyclohex-2-en-1-one (5k). mp 197-199 °C. IR υ/cm^{-1} (KBr): 3433, 2924, 1655. ^{1}H NMR (500 MHz, DMSO): δ 0.86 (s, 3H, CH$_3$), 0.90 (s, 3H, CH$_3$), 2.18 (s, 2H, CH$_2$), 2.40 (s, 1H, OH), 2.50 (s, 2H, CH$_2$), 7.15 (d, *J* 5.0 Hz, 2H, ArH), 7.25 (s, 2H, ArH), 7.52

(d, *J* 5.0 Hz, 2H, ArH), 7.55 (s, 1H, ArH), 7.69 (d, *J* 7.1 Hz, 2H, ArH), 13.18 (s, 1H, OH) ppm. ^{13}C NMR (125 MHz, DMSO): δ 28.0, 28.0, 30.4, 51.8, 51.9, 104.7, 117.0, 124.4, 127.7, 128.2, 128.5, 129.2, 130.7, 132.2, 132.2, 138.7, 156.0, 180.0, 199.1 ppm.

2-(2-(4-Bromophenyl)-1-hydroxy-5-(4-nitrophenyl)-1*H*-imidazol-4-yl)-3-hydroxy-5,5-dimethyl cyclohex-2-en-1-one (5l). mp 196-198 ºC. IR υ/cm^{-1} (KBr): 3424, 2957, 1660. ^{1}H NMR (500 MHz, DMSO): δ 1.04 (s, 3H, CH_3), 1.07 (s, 3H, CH_3), 1.18 (s, 1H, OH), 2.35 (s, 2H, CH_2), 2.58 (s, 2H, CH_2), 7.61 (m, 2H, ArH), 7.68 (d, *J* 8.1 Hz, 2H, ArH), 7.83 (d, *J* 8.1 Hz, 2H, ArH), 8.18 (d, *J* 8.3 Hz, 2H, ArH), 13.32 (s, 1H, OH) ppm. ^{13}C NMR (125 MHz, DMSO): δ 28.1, 28.3, 30.6, 51.9, 52.1, 104.0, 109.8, 123.7, 124.9, 125.7, 128.4, 129.3, 132.5, 145.1, 148.0, 157.3, 178.5, 199.5, 200.4 ppm. Anal. Calcd for $C_{23}H_{20}BrN_3O_5$ (498.33): C, 55.44; H, 4.05; N, 8.43. Found: C, 55.27; H, 4.01; N, 8.37%.