Efficient Conversion of *O*-Substituted 3-Hydroxy-4-imino-oxazolidin-2-ones into
O-substituted α -Hydroxyamidoximes

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Supporting Information

Melting points (uncorrected) were determined on a Mettler FP 62 apparatus. Elemental analyses were carried out with a Heraeus CHN-O-Rapid instrument. IR spectra were recorded on a Shimadzu FT-IR 8300. ^1H NMR (400 MHz) und ^{13}C NMR (100 MHz) spectra were recorded on a Bruker AMX 400 spectrometer using tetramethylsilane as an internal standard and DMSO- d_6 as solvent. Cyanohydrins (**2**) have been prepared according to established literature procedures and were used after structure conformation by IR and ^1H NMR spectroscopy (Gassman, P. G.; Talley, J. J. *Tetrahedron Lett.* **1978**, 40, 3773.; Kurz, T.; Widyan, K. *Org. Biomol. Chem.* **2004**, 2, 2023).

General procedure for the preparation of 5a-i:

A solution of cyanohydrine (**2**) (6 mmol) in dry CH_2Cl_2 (5 mL) was added dropwise over a period of 10 min to a suspension of 1,1'-carbonyldiimidazole (6.5 mmol) in dry CH_2Cl_2 (6 mL) under ice cooling. After stirring at room temperature for 10 min the appropriate *O*-substituted hydroxylamine (6 mmol) was added and the reaction mixture was stirred at room temperature for 1 h. The solvent was evaporated, the remaining residue dissolved in EtOAc and the organic layer washed with water. The solvent was dried over MgSO_4 , filtered and removed under reduced pressure. Recrystallization of the crude products from diethyl ether-hexane afforded compounds **5a-i** as colorless solids.

5-Benzyl-3-benzyloxy-4-imino-oxazolidin-2-one (5a). colorless solid (90%); mp 84 °C (Et₂O-hexane); IR (KBr) 1800, 1690 cm⁻¹; ¹H NMR (DMSO-*d*₆) δ 3.04-3.31 (m, 2H), 4.71-4.86 (m, 2H), 5.29-5.37 (m, 1H), 7.23-7.46 (m, 10H), 8.84 (s, 1H); ¹³C NMR (DMSO-*d*₆) δ 37.11, 77.46, 78.57, 127.40, 128.65, 128.78, 129.36, 129.84, 130.04, 130.12, 134.90, 156.09; Anal. calcd for C₁₇H₁₆N₂O₃: C, 68.91; H, 5.44; N, 9.45; Found: C, 69.01; H, 5.56; N, 9.37.

5-Benzhydryl-3-benzyloxy-4-imino-oxazolidin-2-one (5b). colorless solid (86%); mp 130 °C (Et₂O-hexane); IR (KBr) 1801, 1690 cm⁻¹; ¹H NMR (DMSO-*d*₆) δ 4.42-4.65 (m, 2H), 4.91 (d, *J* = 4.75 Hz, 1H), 5.88 (d, *J* = 4.58 Hz, 1H), 7.19-7.40 (m, 15H), 8.78 (s, 1H); ¹³C NMR (DMSO-*d*₆) δ 51.49, 77.51, 78.76, 127.32, 127.78, 128.50, 128.69, 128.80, 129.00, 129.41, 129.60, 129.77, 130.06, 137.53, 140.49, 154.70. Anal. calcd for C₂₃H₂₀N₂O₃: C, 74.18; H, 5.41; N, 7.52; Found: C, 74.23; H, 5.38; N, 7.59.

3-Benzyloxy-5-*tert*-butyl-4-imino-oxazolidin-2-one (5c). colorless solid (91%); mp 74 °C (Et₂O-hexane); IR (KBr) 1803, 1690 cm⁻¹; ¹H NMR (DMSO-*d*₆) δ 0.91 (s, 9H), 4.70 (s, 1H), 5.07 (q, *J* = 10.68 Hz, 2H), 7.88-7.55 (m, 5H), 8.11 (s, 1H); ¹³C NMR (DMSO-*d*₆) δ 24.54, 34.75, 78.49, 83.99, 126.85, 129.67, 120.46, 134.05, 153.77; Anal. calcd for C₁₄H₁₈N₂O₃: C, 64.11; H, 6.92; N, 10.68; Found: C, 63.95; H, 7.01; N, 10.73.

3-Benzyloxy-5-cyclopropyl-4-imino-oxazolidin-2-one (5d). colorless solid (90%); mp 87 °C (Et₂O-hexane); IR (KBr) 1801, 1695 cm⁻¹; ¹H NMR (DMSO-*d*₆) δ 0.43-0.69 (m, 4H), 1.20-1.28 (m, 1H), 4.64 (d, *J* = 4.58 Hz, 1H), 5.14 (q, *J* = 10.42 Hz, 2H), 7.40-7.60 (m, 5H), 8.25 (s, 1H); ¹³C NMR (DMSO-*d*₆) δ 1.72, 8.94, 76.89, 79.55, 126.68, 127.45, 127.93, 131.64, 154.62; Anal. calcd for C₁₃H₁₄N₂O₃: C, 63.40; H, 5.73; N, 11.38; Found: C, 63.20; H, 5.61; N, 11.42.

3-*tert*-Butoxy-4-imino-5-*tert*-butyl-oxazolidin-2-one (5e). colorless solid (90%); mp 74 °C (Et₂O-hexane); IR (KBr) 1790, 1697 cm⁻¹; ¹H NMR (DMSO-*d*₆) δ 0.91 (s, 9H), 1.10 (s, 9H), 4.71

(s, 1H), 8.10 (s, 1H); ^{13}C NMR (DMSO- d_6) δ 27.58, 27.94, 36.12, 75.71, 76.57, 153.50. Anal. calcd for $\text{C}_{11}\text{H}_{20}\text{N}_2\text{O}_3$: C, 57.87; H, 8.83; N, 12.27; Found: C, 57.99; H, 8.75; N, 12.19.

5-Benzhydryl-3-*tert*-butoxy-4-imino-oxazolidin-2-one (5f). colorless solid (90%); mp 133 °C (Et₂O-hexane); IR (KBr) 1801, 1695 cm^{-1} ; ^1H NMR (DMSO- d_6) δ 0.94 (s, 9H), 4.66 (d, J = 4.73 Hz, 1H), 5.84 (d, J = 4.58 Hz, 1H), 7.21-7.43 (m, 10H), 8.75(s, 1H); ^{13}C NMR (DMSO- d_6) δ 26.45, 52.55, 79.15, 79.42, 127.23, 127.72, 128.38, 128.77, 128.96, 130.10, 137.79, 140.80; 156.15. Anal. calcd for $\text{C}_{20}\text{H}_{22}\text{N}_2\text{O}_3$: C, 70.99; H, 6.55; N, 8.28; Found: C, 70.75; H, 6.62; N, 8.37.

5-Benzhydryl-3-(3,4-dimethoxy-benzyloxy)-4-imino-oxazolidin-2-one (5g). colorless solid (86%); mp 98 °C (Et₂O-hexane); IR (KBr) 1805, 1690 cm^{-1} ; ^1H NMR (DMSO- d_6) δ 3.74 (s, 3H), 3.76 (s, 3H), 4.50-4.65 (m, 2H), 4.90 (d, J = 4.73 Hz, 1H), 5.90 (d, J = 4.58 Hz, 1H), 6.80-7.00 (m, 3H), 7.23-7.81 (m, 10H), 8.75 (s, 1H); ^{13}C NMR (DMSO- d_6) δ 51.40, 55.80, 55.81, 79.01, 79.63, 111.73, 113.54, 123.03, 125.64, 127.48, 127.87, 128.59, 128.92, 128.94, 129.38, 137.98, 137.56, 148.89, 150.04, 154.75. Anal. calcd for $\text{C}_{25}\text{H}_{24}\text{N}_2\text{O}_5$: C, 69.45; H, 5.59; N, 6.48; Found: C, 69.23; H, 5.42; N, 6.31.

5-Benzhydryl-4-imino-3-methoxy-oxazolidin-2-one (5h). colorless solid (87%); mp 118 °C (Et₂O-hexane); IR (KBr) 1890, 1695 cm^{-1} ; ^1H NMR (DMSO- d_6) δ 3.45(s, 3H), 4.66 (d, J = 4.73 Hz, 1H), 5.84 (d, J = 4.58 Hz, 1H), 7.21-7.43 (m, 10H), 8.75(s, 1H); ^{13}C NMR (DMSO- d_6) δ 54.33, 79.15, 79.42, 127.23, 127.72, 128.38, 128.77, 128.96, 130.10, 137.79, 140.80; 156.15. Anal. calcd for $\text{C}_{17}\text{H}_{16}\text{N}_2\text{O}_3$: C, 68.91; H, 5.44; N, 9.45; Found: C, 69.04; H, 5.50; N, 9.54.

5-Benzhydryl-4-imino-3-phenoxy-oxazolidin-2-one (5i). colorless solid (86%); mp 140 °C (Et₂O-hexane); IR (KBr) 1800, 1695 cm^{-1} ; ^1H NMR (DMSO- d_6) δ 4.82 (d, J = 4.73 Hz, 1H), 6.04 (d, J = 4.58 Hz, 1H), 7.16-7.44 (m, 15H), 8.80 (s, 1H); ^{13}C NMR (DMSO- d_6) δ 52.49, 74.46,

112.61, 113.14, 120.91, 122.62, 126.95, 127.55, 128.82, 129.35, 129.67, 129.88, 130.28, 140.76, 153.98. Anal. calcd for $C_{22}H_{18}N_2O_3$: C, 73.73; H, 5.06; N, 7.82; Found: C, 73.65; H, 5.00; N, 7.92.

General procedure for the preparation of 6a-c:

5a-c were hydrogenated in methanol using catalytic amounts of 10% Pd-C for 3 h. Afterwards the suspension was filtered and the solvent was evaporated. The resulting solids were suspended in diethyl ether and again filtered to give compounds **6a-c** as colorless solids.

5-Benzyl-3-hydroxy-4-imino-oxazolidin-2-one (6a). colorless solid (92%); mp 189 °C (Et₂O-hexane); IR (KBr) 1790, 1695 cm^{-1} ; ¹H NMR (DMSO-*d*₆) δ 3.04-3.32 (m, 2H), 5.37 (q, *J* = 3.81 Hz, 1H), 7.23-7.33 (m, 5H), 8.50 (s, 1H); ¹³C NMR (DMSO-*d*₆) δ 37.06, 76.50, 126.85, 128.19, 129.48, 134.71, 156.09; Anal. calcd for $C_{10}H_{10}N_2O_3$: C, 58.25; H, 4.89; N, 13.59; Found: C, 58.15; H, 5.01; N, 13.70.

5-Benzhydryl-3-hydroxy-4-imino-oxazolidin-2-one (6b). colorless solid (91%); mp 220 °C (Et₂O-hexane); IR (KBr) 1801, 1697 cm^{-1} ; ¹H NMR (DMSO-*d*₆) δ 4.65 (d, *J* = 4.75 Hz, 1H), 5.90 (d, *J* = 4.58 Hz, 1H), 7.00-7.45 (m, 10H), 8.50 (s, 1H); ¹³C NMR (DMSO-*d*₆) δ 51.22, 79.80, 127.04, 127.51, 128.49, 128.67, 129.82, 137.69, 137.97, 140.79, 156.09; Anal. calcd for $C_{16}H_{14}N_2O_3$: C, 68.08; H, 5.00; N, 9.92; Found: C, 68.20; H, 4.90; N, 10.01.

5-tert-Butyl-3-hydroxy-4-imino-oxazolidin-2-one (6c). colorless solid (95%); mp 210 °C (Et₂O-hexane); IR (KBr) 1800, 1690 cm^{-1} ; ¹H NMR (DMSO-*d*₆) δ 0.99 (s, 9H), 4.78 (s, 1H), 8.80 (s, 1H); ¹³C NMR (DMSO-*d*₆) δ 24.63, 34.12, 83.52, 152.90; Anal. calcd for $C_7H_{12}N_2O_3$: C, 48.83; H, 7.02; N, 16.27; Found: C, 48.89; H, 7.24; N, 16.54.

General procedure for the preparation of 7a-i:

To a stirred solution of **5a-i** (1 mmol) in methanol (30 mL) was added sodium methoxide (0.2 mmol) at room temperature. The mixture was refluxed for 1 h and the solvent was removed under reduced pressure. Water (15 mL) was added and the mixture was extracted with EtOAc. The combined extracts were dried over MgSO₄, filtered and the solvent was removed under reduced pressure. Recrystallization of the crude products from diethyl ether-hexane afforded compounds **7a-i** as colorless solids.

N-Benzyloxy-2-hydroxy-3-phenyl-propionamidine (7a). colorless solid (95%); mp 113 °C (Et₂O-hexane); IR (KBr) 1655 cm⁻¹; ¹H NMR (DMSO-*d*₆) δ 2.85 (m, 2H), 3.99-4.03 (m, 1H), 4.83 (s, 2H), 5.27 (d, *J* = 5.59 Hz, 1H), 5.66 (s, 2H), 7.15-7.83 (m, 10H); ¹³C NMR (DMSO-*d*₆) δ 41.52, 70.57, 74.11, 126.27, 127.45, 127.75, 128.29, 128.38, 129.69, 138.96, 139.50, 155.74; Anal. calcd for C₁₆H₁₈N₂O₂: C, 71.09; H, 6.71; N, 10.36; Found: C, 71.15; H, 6.82; N, 10.48.

N-Benzyloxy-2-hydroxy-3-diphenylpropionamidine (7b). colorless solid (92%); mp 130 °C (Et₂O-hexane); IR (KBr) 1660 cm⁻¹; ¹H NMR (DMSO-*d*₆) δ 4.34 (d, *J* = 10.17 Hz, 1H), 4.60-4.64 (m, 1H), 4.72 (s, 2H), 5.36 (d, *J* = 5.85 Hz, 1H), 5.54 (s, 2H), 7.11-7.36 (m, 15H); ¹³C NMR (DMSO-*d*₆) δ 55.05, 71.91, 73.83, 126.16, 126.34, 127.23, 127.39, 128.21, 128.30, 128.37, 128.86, 128.96, 139.67, 142.44, 143.40, 154.72; Anal. calcd for C₂₂H₂₂N₂O₂: C, 76.28; H, 6.40; N, 8.09; Found: C, 76.22; H, 6.46; N, 8.04.

N-Benzyloxy-2-hydroxy-3,3-dimethylbutyramidine (7c). colorless solid (91%); mp 105 °C (Et₂O-hexane); IR (KBr) 1653 cm⁻¹; ¹H NMR (DMSO-*d*₆) δ 0.90 (s, 9H), 3.63 (d, *J* = 5.09 Hz, 1H), 4.97 (s, 2H), 5.22 (d, *J* = 5.59 Hz, 1H), 5.67 (s, 2H), 7.16-7.50 (m, 5H); ¹³C NMR (DMSO-*d*₆) δ 24.46, 25.11, 75.71, 76.57, 125.30, 125.70, 126.16, 137.21, 153.47; Anal. calcd for C₁₃H₂₀N₂O₂: C, 66.07; H, 8.53; N, 11.85; Found: C, 66.17; H, 8.45; N, 11.92.

***N*-Benzyloxy-2-cyclopropyl-2-hydroxy-acetamidine (7d).** colorless solid (92%); mp 90 °C (Et₂O-hexane); IR (KBr) 1655 cm⁻¹; ¹H NMR (DMSO-*d*₆) δ 0.16-0.28 (m, 4H), 0.89-0.98 (m, 1H), 3.05 (q, *J* = 5.08 Hz, 1H), 4.69 (q, *J* = 12.72 Hz, 2H), 5.02 (d, *J* = 5.09 Hz, 1H), 5.30 (s, 2H), 7.08-7.21 (m, 5H); ¹³C NMR (DMSO-*d*₆) δ 1.43, 14.03, 70.53, 71.91, 125.30, 125.70, 126.16, 137.21, 153.89; Anal. calcd for C₁₂H₁₆N₂O₂: C, 65.43; H, 7.32; N, 12.72; Found: C, 65.40; H, 7.28; N, 12.80.

***N*-tert-Butoxy-2-hydroxy-3,3-dimethylbutyramidine (7e).** colorless solid (90%); mp 96 °C (Et₂O-hexane); IR (KBr) 1650 cm⁻¹; ¹H NMR (DMSO-*d*₆) δ 0.89 (s, 9H), 1.18 (s, 9H), 3.63 (d, *J* = 5.09 Hz, 1H), 4.97 (s, 2H), 5.22 (d, *J* = 5.09 Hz, 1H); ¹³C NMR (DMSO-*d*₆) δ 27.58, 27.94, 36.12, 75.71, 76.57, 153.47; Anal. calcd for C₁₀H₂₂N₂O₂: C, 59.37; H, 10.96; N, 13.85; Found: C, 59.05; H, 10.88; N, 13.68.

***N*-tert-Butoxy-2-hydroxy-3,3-diphenylbutyramidine (7f).** colorless solid (91%); mp 160 °C (Et₂O-hexane); IR (KBr) 1653 cm⁻¹; ¹H NMR (DMSO-*d*₆) δ 0.95 (s, 9H), 4.30 (d, *J* = 10.43 Hz, 1H), 4.62-4.66 (m, 1H), 5.22 (s, 2H), 5.29 (d, *J* = 5.60 Hz, 1H), 7.04-7.88 (m, 10H); ¹³C NMR (DMSO-*d*₆) δ 27.73, 55.27, 72.41, 75.77, 126.11, 126.14, 128.36, 128.84, 128.93, 142.60, 143.53, 153.61; Anal. calcd for C₁₉H₂₄N₂O₂: C, 73.05; H, 7.74; N, 8.97; Found: C, 72.95; H, 7.68; N, 9.04.

***N*-(3,4-Dimethoxy-benzyloxy)-2-hydroxy-3,3-diphenyl-propionamidine (7g).** colorless solid (90%); mp 128 °C (Et₂O-hexane); IR (KBr) 1650 cm⁻¹; ¹H NMR (DMSO-*d*₆) δ 3.72 (s, 3H), 3.76 (s, 3H), 4.43 (d, *J* = 10.17 Hz, 1H), 4.51-4.62 (m, 2H), 4.90-5.05 (m, 1H), 5.27 (d, *J* = 5.59 Hz, 1H), 5.54 (s, 2H), 6.80-7.00 (m, 3H), 7.20-7.80 (m, 10H); ¹³C NMR (DMSO-*d*₆) δ 51.45, 55.80, 55.85, 79.05, 79.60, 111.70, 113.50, 123.13, 125.70, 127.48, 127.87, 128.60, 128.90, 128.94,

129.38, 137.56, 137.98, 148.89, 150.04, 155.70. Anal. calcd for $C_{24}H_{26}N_2O_4$: C, 70.92; H, 6.45; N, 6.89; Found: C, 70.70; H, 6.29; N, 6.70.

2-Hydroxy-*N*-methoxy-3,3-diphenylpropionamidine (7h). colorless solid (95%); mp 117 °C (Et₂O-hexane); IR (KBr) 1655 cm⁻¹; ¹H NMR (DMSO-*d*₆) δ 3.40 (s, 3H), 4.32 (d, *J* = 10.43 Hz, 1H), 4.58-4.62 (m, 1H), 5.34 (d, *J* = 5.60 Hz, 1H), 5.45 (s, 2H), 7.04-7.86 (m, 10H); ¹³C NMR (DMSO-*d*₆) δ 54.99, 60.15, 72.81, 126.66, 126.18, 128.31, 128.43, 128.93, 129.38, 142.50, 143.53, 154.52; Anal. calcd for $C_{16}H_{18}N_2O_2$: C, 71.09; H, 6.71; N, 10.36; Found: C, 70.95; H, 6.83; N, 10.52.

2-Hydroxy-*N*-phenoxy-3,3-diphenylpropionamidine (7i). colorless solid (90%); mp 135 °C (Et₂O-hexane); IR (KBr) 1660 cm⁻¹; ¹H NMR (DMSO-*d*₆) δ 4.30 (d, *J* = 10.43 Hz, 1H), 4.60-4.65 (m, 1H), 5.30 (d, *J* = 5.60 Hz, 1H), 5.45 (s, 2H), 7.04-7.86 (m, 15H); ¹³C NMR (DMSO-*d*₆) δ 52.49, 74.46, 112.61, 113.14, 120.91, 122.62, 126.95, 127.55, 128.82, 129.35, 129.67, 129.88, 130.28, 140.76, 153.61; Anal. calcd for $C_{21}H_{20}N_2O_2$: C, 75.88; H, 6.06; N, 8.43; Found: C, 76.01; H, 5.98; N, 8.37.

Procedures for the preparation of 8a-c:

Method A: 7a-c were hydrogenated in methanol using catalytic amounts of 10% Pd-C for 3 h. Afterwards the suspension was filtered and the solvent was evaporated. The remaining solid was suspended in diethyl ether and filtered to afford 8a-c.

Method B: A mixture of 6a (1 mmol) and sodium methoxide (2 mmol) in methanol (30 mL) was refluxed for 1 h and the solvent was removed under reduced pressure. After neutralization with 10% citric acid, the mixture was extracted with EtOAc and the combined extracts were dried over MgSO₄. Filtration and removal of the solvent gave 8a as a solid product, which was suspended in diethyl ether and filtered.

2,*N*-Dihydroxy-3-phenyl-propionamidine (8a). colorless solid (95% method A, 70% method B); mp 150 °C; IR (KBr) 1645 cm⁻¹; ¹H NMR (DMSO-*d*₆) δ 2.79-2.91 (m, 2H), 4.00-4.05 (m, 1H), 5.15 (d, *J* = 5.59 Hz, 1H), 5.23 (s, 2H), 7.16-7.27 (m, 5H), 8.89 (s, 1H); ¹³C NMR (DMSO-*d*₆) δ 41.43, 71.01, 126.21, 128.14, 129.64, 139.27, 156.98; Anal. calcd for C₉H₁₂N₂O₂: C, 59.99, H, 6.71; N, 15.55; Found: C, 59.89; H, 6.60; N, 15.49.

2,*N*-Dihydroxy-3,3-diphenyl-propionamidine (8b). colorless solid (93%); mp 196 °C; IR (KBr) 1650 cm⁻¹; ¹H NMR (DMSO-*d*₆) δ 4.34 (d, *J* = 10.17 Hz, 1H), 4.60 (m, *J* = 4.63 Hz, 1H), 5.20 (s, 2H), 7.08-7.36 (m, 10H), 8.82 (s, 1H); ¹³C NMR (DMSO-*d*₆) δ 54.94, 72.28, 126.10, 126.27, 128.25, 128.35, 128.81, 128.95, 142.77, 143.64, 153.98; Anal. calcd for C₁₅H₁₆N₂O₂: C, 70.29; H, 6.29; N, 10.93; Found: C, 70.15; H, 6.18; N, 11.01.

2,*N*-Dihydroxy-3,3-dimethyl-butyramidine (8c). colorless solid (97%); mp 165 °C; IR (KBr) 1640 cm⁻¹; ¹H NMR (DMSO-*d*₆) δ 0.88 (s, 9H), 3.61 (d, *J* = 5.09 Hz, 1H), 4.93 (s, 2H), 5.16 (d, *J* = 5.08 Hz, 1H), 8.93 (s, 1H); ¹³C NMR (DMSO-*d*₆) δ 26.82, 35.00, 76.74, 154.15; Anal. calcd for C₆H₁₄N₂O₂: C, 49.30; H, 9.65; N, 19.16; Found: C, 49.19; H, 9.80; N, 19.01.