Supplementary information

Synthesis of carboxyimidamide-substituted benzo[c][1,2,5]oxadiazoles and their analogs, and evaluation of biological activity against *Leishmania donovani*

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General procedure for the reaction of oximes with isocyanates. **Method A:** A mixture of 5 (89.0 mg, 0.500 mmol) and isocyanate (0.550 mmol, 1.1 equiv) in anhydrous THF (5 mL) was stirred under an Ar atmosphere at rt for 3-21 h. The solvent was evaporated.

**Method B:** A mixture of an appropriate oxime (1.0 mmol) and isocyanate (1.2-1.5 mmol, 1.2-1.5 equiv) in 1,4-dioxane (5 mL) was stirred under an Ar atmosphere at rt for 2-5 h. The resulting mixture was quenched with water, filtered, washed with water and dried.

*N*-[(Phenylcarbamoyl)oxy]benzo[c][1,2,5]oxadiazole-5-carboximidamide (6). A mixture of 5 (0.15 g, 0.84 mmol) and phenyl isocyanate (0.14 mL, 1.26 mmol, 1.5 equiv) in CHCl$_3$ was stirred at rt for 4 days. After evaporation the crude product was purified by flash SiO$_2$ column chromatography (EtOAc/n-hexane 1:1) and recrystallized from EtOAc/n-hexane to yield 6 (0.14 g, 56%) as a white powder. Mp: 184-185 °C. $^1$H NMR (300 MHz, DMSO-$d_6$) δ 9.40 (s, 1H), 8.57-8.56 (m, 1H), 8.17-8.08 (m, 2H), 7.57-7.54 (m, 2H), 7.37-7.31 (m, 2H), 7.10-7.05 (m, 3H). $^{13}$C NMR (75 MHz, DMSO-$d_6$) δ 153.2, 152.2, 148.9, 148.8, 138.3, 135.0, 131.3, 128.7 (2C), 123.2, 119.5 (2C), 116.0, 114.4. LC-MS: [M+H]$^+$ 298.2 m/z ($t_r$ = 6.1 min). FT-IR (ATR, cm$^{-1}$): 3350, 1713, 1644, 1506, 1202. HRMS (ESI): m/z calcd for C$_{14}$H$_{12}$N$_5$O$_3$ [M+Na]$^+$ 320.0760, found 320.0762.

*N*-[(o-Tolylcarbamoyl)oxy]benzo[c][1,2,5]oxadiazole-5-carboximidamide (7). Method A. The crude product was purified by flash SiO$_2$ column chromatography (EtOAc/n-hexane 1:2 to 1:1) and recrystallized from EtOAc/n-hexane to give 7 (85 mg, 55%) as light yellow crystals. Mp: 190 °C. $^1$H NMR (300 MHz, DMSO-$d_6$) δ 8.99 (s, 1H), 8.59 (t, $J$ = 1.2 Hz, 1H), 8.20 (dd, $J$ = 9.5, 1.4 Hz, 1H), 8.10 (dd, $J$ = 9.5, 0.9 Hz, 1H), 7.55-7.52 (m, 2H), 7.27-7.19 (m, 4H), 7.11 (td, $J$ = 7.4, 1.3 Hz, 1H), 2.28 (s, 3H). $^{13}$C NMR (75 MHz, DMSO-$d_6$) δ 152.7, 152.5, 148.9, 148.8, 136.0, 135.0, 131.3, 130.3, 126.2, 125.0, 124.0, 116.0, 114.4, 17.5. LC-MS: [M+H]$^+$ 312.2 m/z ($t_r$ = 6.5 min). FT-IR (ATR, cm$^{-1}$): 3461, 3348, 1726, 1513. HRMS (ESI): m/z calcd for C$_{15}$H$_{13}$N$_3$O$_3$ [M+H]$^+$ 312.1097, found 312.1099.
**N^\text{3}-(m-Tolylcarbamoyl)oxy|benzo[c][1,2,5]oxadiazole-5-carboximidamide (8).** Method A. The crude product was purified by flash SiO\textsubscript{2} column chromatography (EtOAc/n-hexane 1:2 to 1:1) to yield 8 (0.11 g, 70%) as a light yellow solid. \(^1\)H NMR (300 MHz, DMSO-\textit{d}\textsubscript{6}) \(\delta\) 9.37 (br s, 1H), 8.57 (t, \(J = 1.2\) Hz, 1H), 8.17 (dd, \(J = 9.5, 1.2\) Hz, 1H), 8.11 (dd, \(J = 9.5, 1.2\) Hz, 1H), 7.37-7.35 (m, 2H), 7.22 (t, \(J = 5.6\) Hz, 1H), 7.14 (br s, 2H), 6.90 (d, \(J = 5.6\) Hz, 1H), 2.30 (s, 3H). \(^{13}\)C NMR (75 MHz, DMSO-\textit{d}\textsubscript{6}) \(\delta\) 153.1, 152.1, 148.9, 148.8, 138.2, 137.9, 135.0, 131.4, 128.5, 123.9, 120.0, 116.7, 115.9, 114.4, 21.1. LC-MS: [M+H]\(^+\) 312.2 \textit{m/z} (\(t_r = 6.6\) min). FT-IR (ATR, cm\(^{-1}\)): 3478, 3438, 3351, 3288, 1712, 1518, 1204. HRMS (ESI): \textit{m/z} calcd for C\textsubscript{15}H\textsubscript{14}N\textsubscript{5}O\textsubscript{3} [M+H]\(^+\) 312.1096, found 312.1100.

**N^\text{3}-(p-Tolylcarbamoyl)oxy|benzo[c][1,2,5]oxadiazole-5-carboximidamide (9).** Method A. The crude product was purified by flash SiO\textsubscript{2} column chromatography (EtOAc/n-hexane 1:2 to 4:1) and recrystallized from EtOAc/n-hexane to yield 9 (77 mg, 49%) as yellow crystals. Mp: 188-189 °C. \(^1\)H NMR (300 MHz, DMSO-\textit{d}\textsubscript{6}) \(\delta\) 9.36 (br s, 1H), 8.57 (t, \(J = 1.2\) Hz, 1H), 8.17 (dd, \(J = 9.5, 1.2\) Hz, 1H), 8.11 (dd, \(J = 9.5, 1.2\) Hz, 1H), 7.46-7.41 (m, 2H), 7.16-7.13 (m, 4H), 2.27 (s, 3H). \(^{13}\)C NMR (75 MHz, DMSO-\textit{d}\textsubscript{6}) \(\delta\) 153.1, 152.2, 148.9, 148.8, 135.7, 135.0, 132.1, 131.4, 129.1, 119.6, 115.9, 114.4, 20.3. LC-MS: [M+H]\(^+\) 312.2 \textit{m/z} (\(t_r = 6.6\) min). FT-IR (ATR, cm\(^{-1}\)): 3468, 3342, 1724, 1517, 1181, 1006, 920. HRMS (ESI): 	extit{m/z} calcd for C\textsubscript{15}H\textsubscript{14}N\textsubscript{5}O\textsubscript{3} [M+H]\(^+\) 312.1096, found 312.1099.

**N^\text{3}-(2-Methoxyphenyl)carbamoyl|oxy|benzo[c][1,2,5]oxadiazole-5-carboximidamide (10).** Method A. The crude product was purified by flash SiO\textsubscript{2} column chromatography (EtOAc/n-hexane 1:2 to 4:1) and recrystallized from MeCN/H\textsubscript{2}O to yield 10 (57 mg, 36%) as a light yellow solid. Mp: 203 °C. \(^1\)H NMR (300 MHz, DMSO-\textit{d}\textsubscript{6}) \(\delta\) 9.09 (s, 1H), 8.54 (m, 1H), 8.20-8.16 (m, 1H), 8.03-7.99 (m, 1H), 7.95 (d, \(J = 8.1\) Hz, 1H), 7.36 (s, 2H), 7.09-7.07 (m, 2H), 7.01-6.92 (m, 1H), 3.90 (s, 3H). \(^{13}\)C NMR (75 MHz, DMSO-\textit{d}\textsubscript{6}) \(\delta\) 152.7, 151.7, 148.9, 148.8, 148.7, 134.8, 130.7, 126.7, 123.7, 120.6, 118.9, 116.4, 114.6, 111.1, 56.0. LC-MS: [M+H]\(^+\) 328.2 \textit{m/z} (\(t_r = 6.7\) min). FT-IR (ATR, cm\(^{-1}\)): 3434, 3334, 1730, 1536. HRMS (ESI): 	extit{m/z} calcd for C\textsubscript{15}H\textsubscript{13}N\textsubscript{5}O\textsubscript{4} [M+H]\(^+\) 328.1046, found 328.1048.

**N^\text{3}-(3-Methoxyphenyl)carbamoyl|oxy|benzo[c][1,2,5]oxadiazole-5-carboximidamide (11).** Method A. The crude product was purified by flash SiO\textsubscript{2} column chromatography (EtOAc/n-hexane 1:2 to 1:1) and recrystallized from EtOAc/n-hexane to give 11 (62 mg, 38%) as white crystals. Mp: 186-187 °C. \(^1\)H NMR (300 MHz, DMSO-\textit{d}\textsubscript{6}) \(\delta\) 9.43 (s, 1H), 8.56 (t, \(J = 1.3\) Hz, 1H), 8.15 (dd, \(J = 9.8, 1.3\) Hz, 1H), 8.11 (dd, \(J = 9.8, 1.3\) Hz, 1H), 7.27-7.20 (m, 2H), 7.14-1.13 (m, 1H), 7.12 (s, 2H), 6.65 (ddd, \(J = 8.1, 2.5, 0.8\) Hz, 1H), 3.75 (s, 3H). \(^{13}\)C NMR (75 MHz, DMSO-\textit{d}\textsubscript{6}) \(\delta\) 159.6, 153.3, 152.0, 148.9, 148.8, 139.5, 135.0, 131.3, 129.5, 116.0, 114.4, 111.6, 108.5, 105.2, 55.0. LC-MS: [M+H]\(^+\) 328.1 \textit{m/z} (\(t_r = 6.1\) min). FT-
IR (ATR, cm⁻¹): 3470, 3362, 3063, 1733, 1500, 1179, 1041. HRMS (ESI): m/z calcd for C_{15}H_{14}N_5O_4 [M+H]^+ 328.1046, found 328.1045.

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\text{N'-[[(4-Methoxyphenyl)carbamoyl]oxy]benzo[c][1,2,5]oxadiazole-5-carboximidamide (12). Method A. The crude product was purified by flash SiO}_2 \text{ column chromatography (EtOAc/n-hexane 1:2 to 2:3) and recrystallized from MeCN to yield 12 (70 mg, 43%) as yellow crystals. Mp: 196-197 °C. 1H NMR (300 MHz, DMSO-d_6) δ 9.30 (br s, 1H), 8.57 (t, J = 1.2 Hz, 1H), 8.19 (dd, J = 9.6, 1.2 Hz, 1H), 8.11 (dd, J = 9.6, 1.2 Hz, 1H), 7.47-7.42 (m, 2H), 7.13 (br s, 2H), 6.95-6.89 (m, 2H), 3.74 (s, 3H). 13C NMR (75 MHz, DMSO-d_6) δ 155.4, 152.8, 152.6, 148.9, 135.0, 131.5, 131.2, 121.6, 115.9, 114.3, 113.9, 55.2. LC-MS: [M+H]^+ 328.1 m/z (t_r = 5.9 min). FT-IR (ATR, cm⁻¹): 3482, 3465, 3358, 3290, 1703, 1511, 1200. HRMS (ESI): m/z calcd for C_{15}H_{14}N_5O_4 [M+H]^+ 328.1049, found 328.1046.}

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\text{N'-[[(2-Chlorophenyl)carbamoyl]oxy]benzo[c][1,2,5]oxadiazole-5-carboximidamide (13). Method A. The crude product was recrystallized from THF to yield 13 (0.11 g, 65%) as a white fluffy solid. Mp: 217-218 °C. 1H NMR (300 MHz, DMSO-d_6) δ 9.29 (br s, 1H), 8.58 (t, J = 1.2 Hz, 1H), 8.16 (dd, J = 9.5, 1.2 Hz, 1H), 8.09 (dd, J = 9.5, 1.2 Hz, 1H), 7.95 (dd, J = 8.1, 1.6 Hz, 1H), 7.55 (dd, J = 8.1, 1.5 Hz, 1H), 7.42-7.37 (m, 3H), 7.20 (td, J = 7.6, 1.6 Hz, 1H). 13C NMR (75 MHz, DMSO-d_6) δ 152.9, 152.0, 148.9, 148.8, 134.8, 134.5, 130.9, 129.4, 127.8, 125.6, 124.9, 123.1, 116.3, 114.7. LC-MS: [M+H]^+ 332.1 m/z (t_r = 7.2 min). FT-IR (ATR, cm⁻¹): 3446, 3355, 3329, 1736, 1522, 1191, 1007. HRMS (ESI): m/z calcd for C_{14}H_{11}N_5O_3Cl [M+H]^+ 332.0551, found 332.0552.}

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\text{N'-[[(4-Chlorophenyl)carbamoyl]oxy]benzo[c][1,2,5]oxadiazole-5-carboximidamide (15). Method A. The crude product was purified by flash SiO}_2 \text{ column chromatography (EtOAc/n-hexane 1:2 to 1:1) and recrystallized from MeCN to yield 15 (45 mg, 27%) as light yellow crystals. Mp: 198-202 °C. 1H NMR (300 MHz, DMSO-d_6) δ 9.62 (br s, 1H), 8.57 (t, J = 1.2 Hz, 1H), 8.12 (dd, J = 9.5, 1.2 Hz, 1H), 8.05 (dd, J = 9.5, 1.2 Hz, 1H), 7.62-7.57 (m, 2H), 7.42-7.37 (m, 2H), 7.16 (br s, 2H). 13C NMR (75 MHz, DMSO-d_6) δ 153.4, 152.1, 148.9, 148.8, 137.4, 134.9, 131.3, 128.6, 126.8, 121.0, 116.0, 114.5. LC-MS: [M+H]^+ 332.1 m/z (t_r = 6.8 min). FT-IR (ATR, cm⁻¹): 3467, 3341, 1721, 1515, 1183, 1005, 806. HRMS (ESI): m/z calcd for C_{14}H_{11}N_5O_3Cl [M+H]^+ 332.0551, found 332.0554.}

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\text{N'-[[2-(Trifluoromethyl)phenyl]carbamoyl]oxy]benzo[c][1,2,5]oxadiazole-5-carboximidamide (16). Method A. The crude product was purified by flash SiO}_2 \text{ column chromatography (EtOAc/n-hexane 1:2 to 1:1) and recrystallized from EtOAc/n-hexane to yield 16 (60 mg, 33%) as an off-white powder. 1H NMR (300 MHz, DMSO-d_6) δ 9.29 (s, 1H), 8.58 (t, J = 1.1 Hz, 1H), 8.15 (dd, J = 9.5, 1.0 Hz, 1H), 8.06 (dd, J = 9.5, 1.3 Hz, 1H), 7.90 (d, J = 8.2 Hz, 1H), 7.70-7.71 (m, 2H), 7.44 (t, J = 7.6 Hz, 1H), 7.38 (s, 1H). 13C NMR}

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corresponding acyl chloride (0.77 mmol, 1.1 equiv) were added, and the resulting mixture was heated to 70 °C. After heating the mixture for 2-4 h, the mixture was let cool to rt and evaporated to dryness. The residue was dissolved in EtOAc and washed with H₂O.

7.86 (d, J = 8.3 Hz, 1H), 7.58 (t, J = 8.0 Hz, 1H), 7.42-7.39 (m, 1H), 7.20 (s, 2H). 13C NMR (75 MHz, DMSO-d₆) δ 153.6, 152.3, 148.9, 148.8, 139.3, 134.9, 131.4, 129.9, 129.5 (q, JCF = 32 Hz) 129.1, 124.4 (q, JCF = 270 Hz), 119.0 (2C), 116.1, 114.6. LC-MS: [M+H]^+ 366.1 m/z (t_r = 7.2 min). FT-IR (ATR, cm⁻¹): 3473, 1716, 1507, 1318.

General procedure for the reaction of oximes with acyl chlorides. Method C. The amidoxime 5 (125 mg, 0.70 mmol) was dissolved in anhydrous THF (5 mL) under an Ar atmosphere. To this mixture distilled Et₃N (195 µL, 1.40 mmol, 2.0 equiv) and the corresponding acyl chloride (0.77 mmol, 1.1 equiv) were added, and the resulting mixture was heated to 70 °C. After heating the mixture for 2-4 h, the mixture was let cool to rt and evaporated to dryness. The residue was dissolved in EtOAc and washed with H₂O, the organic phase was dried with anhydrous Na₂SO₄, evaporated, and dried in vacuo. The crude product was purified by flash SiO₂ column chromatography (EtOAc/n-hexane 1:2 to 1:1) and recrystallized from MeCN to yield 17 (87 mg, 48%) as light yellow crystals. Mp: 198 °C. 1H NMR (300 MHz, DMSO-d₆) δ 9.88 (s, 1H), 8.12 (m, 2H), 7.79 (d, J = 8.7 Hz, 2H), 7.70 (d, J = 8.8 Hz, 2H), 7.18 (s, 2H). 13C NMR (75 MHz, DMSO-d₆) δ 153.8, 152.0, 148.9, 148.8, 139.3, 134.9, 131.4, 129.9, 129.5 (q, JCF = 32 Hz) 129.1, 124.4 (q, JCF = 270 Hz), 119.0 (2C), 116.1, 114.6. LC-MS: [M+H]^+ 366.1 m/z (t_r = 7.2 min). FT-IR (ATR, cm⁻¹): 3473, 1716, 1507, 1318. HRMS (ESI): m/z calcd for C₁₅H₁₀F₃N₅O₃ [M+H]^+ 366.0815, found 366.0815.

N'-(4-(Trifluoromethyl)phenyl)carbamoyl][oxbenzo[c][1,2,5]oxadiazole-5-carboximidamide (18). Method A. The crude product was purified by flash SiO₂ column chromatography (EtOAc/n-hexane 1:2 to 1:1) and recrystallized from MeCN to yield 18 (87 mg, 48%) as light yellow crystals. Mp: 198 °C. 1H NMR (300 MHz, DMSO-d₆) δ 9.88 (s, 1H), 8.12 (m, 2H), 7.79 (d, J = 8.7 Hz, 2H), 7.70 (d, J = 8.8 Hz, 2H), 7.18 (s, 2H). 13C NMR (75 MHz, DMSO-d₆) δ 153.8, 152.0, 148.9, 148.8, 139.3, 134.9, 131.4, 129.9, 129.5 (q, JCF = 32 Hz) 129.1, 124.4 (q, JCF = 270 Hz), 119.0 (2C), 116.1, 114.6. LC-MS: [M+H]^+ 366.1 m/z (t_r = 7.2 min). FT-IR (ATR, cm⁻¹): 3473, 1716, 1507, 1318. HRMS (ESI): m/z calcd for C₁₅H₁₀F₃N₅O₃ [M+H]^+ 366.0815, found 366.0815.

N'-(3-(Trifluoromethyl)phenyl)carbamoyl][oxbenzo[c][1,2,5]oxadiazole-5-carboximidamide (17). Method A. The product was purified by flash SiO₂ column chromatography (EtOAc/n-hexane 1:2) to yield 17 (0.14 g, 78%) as an off-white powder. 1H NMR (300 MHz, DMSO-d₆) δ 9.83 (s, 1H), 8.58 (s, 1H), 8.15-8.13 (m, 2H), 8.00 (s, 1H), 7.86 (d, J = 8.3 Hz, 1H), 7.58 (t, J = 8.0 Hz, 1H), 7.42-7.39 (m, 1H), 7.20 (s, 2H). 13C NMR (75 MHz, DMSO-d₆) δ 153.6, 152.3, 148.9, 148.8, 139.3, 134.9, 131.4, 129.9, 129.5 (q, JCF = 32 Hz) 129.1, 124.1 (q, JCF = 4 Hz), 119.5 (q, JCF = 4 Hz), 116.0, 114.6. LC-MS: [M+H]^+ 366.1 m/z (t_r = 7.2 min). FT-IR (ATR, cm⁻¹): 3473, 3347, 1731, 1528. HRMS (ESI): m/z calcd for C₁₅H₁₀F₃N₅O₃ [M+H]^+ 366.0815, found 366.0815.

N'-[[4-(Trifluoromethyl)phenyl]carbamoyl][oxbenzo[c][1,2,5]oxadiazole-5-carboximidamide (21). The reaction was carried out according to the Method C to yield 21 (73 mg, 36%) as a light yellow solid. 1H NMR (300 MHz, DMSO-d₆) δ 8.56 (t, J = 1.2 Hz, 1H), 8.25-8.21 (m, 2H), 8.14 (dd, J = 9.5, 1.2 Hz, 1H), 8.02 (dd, J = 9.5, 1.2 Hz, 1H), 7.72-7.67 (m, 1H), 7.60-7.54 (m, 2H), 7.27 (br s, 2H). 13C NMR (75 MHz, DMSO-d₆) δ 163.3, 154.7, 148.9, 148.8, 135.4, 133.3, 131.3, 129.6, 129.0, 128.6, 116.2, 114.7. LC-MS: [M+H]^+ 366.1 m/z (t_r = 5.7 min). FT-IR (ATR, cm⁻¹): 3503, 3402, 1727, 1606, 1258, 1090, 705 HRMS (ESI): m/z calcd for C₁₄H₁₁N₄O₃ [M+H]^+ 283.0831, found 283.0836.
**N’-(Phenoxy carbonyl)oxy]benzo[c][1,2,5]oxadiazole-5-carboximidamide (22).** The reaction was carried out according to the Method C to yield 22 (0.11 g, 63%) as a light yellow solid. \(^1\)H NMR (300 MHz, DMSO-\(d_6\)) \(\delta\) 8.52 (t, \(J = 1.1\) Hz, 1H), 8.13 (dd, \(J = 9.5, 1.1\) Hz, 1H), 7.93 (dd, \(J = 9.5, 1.1\) Hz, 1H), 7.52-7.45 (m, 2H), 7.52-7.45 (m, 2H), 7.38-7.29 (m, 5H). 13\(^{\text{C}}\) NMR (75 MHz, DMSO-\(d_6\)) \(\delta\) 155.1, 151.8, 150.7, 148.9, 148.7, 134.9, 131.0, 129.7, 126.2, 121.3, 116.3, 115.0. LC-MS: [M+H]\(^+\) 299.1 m/z (\(t_r = 5.1\) min). FT-IR (ATR, cm\(^{-1}\)): 3484, 3385, 1776, 1642, 1240, 1199, 932. HRMS (ESI): m/z calcd for C\(_{14}\)H\(_{11}\)N\(_4\)O\(_4\) [M+H]\(^+\) 299.0780, found 299.0780.

**N’-(2-Phenylacetoxy)benzo[c][1,2,5]oxadiazole-5-carboximidamide (23).** The reaction was carried out according to the Method C. The crude product was recrystallized from EtOAc/n-hexane to yield 23 (29 mg, 14%) as white crystals. Mp. 153-155 °C. \(^1\)H NMR (300 MHz, DMSO-\(d_6\)) \(\delta\) 8.49 (t, \(J = 1.2\) Hz, 1H), 8.11 (dd, \(J = 9.5, 1.2\) Hz, 1H), 7.94 (dd, \(J = 9.5, 1.2\) Hz, 1H), 7.38-7.26 (m, 5H), 7.20 (br s, 2H), 3.87 (s, 2H). 13\(^{\text{C}}\) NMR (75 MHz, DMSO-\(d_6\)) \(\delta\) 168.7, 154.6, 148.9, 148.8, 135.2, 134.4, 131.1, 129.4, 128.4, 126.8, 116.2, 114.6. LC-MS: [M+H]\(^+\) 297.2 m/z (\(t_r = 5.9\) min). FT-IR (ATR, cm\(^{-1}\)): 3472, 3365, 1741, 1634, 1142, 882, 708. HRMS (ESI): m/z calcd for C\(_{15}\)H\(_{13}\)N\(_4\)O\(_3\) [M+H]\(^+\) 297.0988, found 297.0991.

**N’-[(Cyclohexylcarbamoyl)oxy]benzo[c][1,2,5]oxadiazole-5-carboximidamide (24).** A mixture of 5 (95 mg, 0.53 mmol) and cyclohexyl isocyanate (136 µL, 1.06 mmol, 2.0 equiv) in CHCl\(_3\) was stirred at rt for 5 days. The reaction mixture was evaporated in vacuo, and the residue was purified by flash SiO\(_2\) column chromatography (EtOAc) and recrystallization (MeOH) to give 24 (0.10 g, 64%) as a light yellow solid. Mp: 200 °C. \(^1\)H NMR (300 MHz, DMSO-\(d_6\)) \(\delta\) 8.53 (t, \(J = 1.0\) Hz, 1H), 8.14 (dd, \(J = 9.6, 1.1\) Hz, 1H), 7.94 (dd, \(J = 9.5, 1.2\) Hz, 1H), 7.38-7.26 (m, 5H), 7.20 (br s, 2H), 3.87 (s, 2H). 13\(^{\text{C}}\) NMR (75 MHz, DMSO-\(d_6\)) \(\delta\) 168.7, 154.6, 148.9, 148.8, 135.2, 134.4, 131.1, 129.4, 128.4, 126.8, 116.2, 114.6. LC-MS: [M+H]\(^+\) 304.2 m/z (\(t_r = 6.5\) min). FT-IR (ATR, cm\(^{-1}\)): 3357, 2930, 1702, 1641, 1510, 1208. HRMS (ESI): m/z calcd for C\(_{14}\)H\(_{18}\)N\(_5\)O\(_3\) [M+H]\(^+\) 304.1410, found 304.1409.

**1H-Benimidazole-5-carbonitrile (25).** A mixture of 2,4-diaminobenzonitrile (0.40 g, 3.00 mmol) and formic acid (10 mL) was refluxed for 1 h. The reaction mixture was evaporated to dryness, and a saturated solution of NaHCO\(_3\) was added to the residue. The resulting mixture was extracted with EtOAc, and the combined organic phases were washed with brine, dried over anhydrous Na\(_2\)SO\(_4\) and evaporated to give 25 (0.35 g, 81%) as a light brown powder. \(^1\)H NMR (300 MHz, DMSO-\(d_6\)) \(\delta\) 12.96 (s, 1H), 8.47 (s, 1H), 8.16 (m, 1H), 7.76 (d, \(J = 8.4\) Hz, 1H), 7.59 (dd, \(J = 8.4, 1.5\) Hz, 1H). Spectral data is consistent with those reported earlier.\(^1\)
N'-Hydroxybenzimidamide (26). A mixture of benzonitrile (1.00 mL, 9.70 mmol), H$_2$NOH·HCl (1.01 g, 14.6 mmol, 1.5 equiv) and Et$_3$N (2.02 mL, 14.6 mmol, 1.5 equiv) in EtOH (20 mL) was stirred at rt for 20 h. After evaporation and extraction of the residue with EtOAc, the organic phase was washed with water and brine, dried over anhydrous Na$_2$SO$_4$. The filtrate was evaporated in vacuo to give the crude 26 (1.12 g, 98%).$^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 9.59 (s, 1H), 7.67-7.65 (m, 2H), 7.39-7.35 (m, 3H), 5.77 (s, 2H). Spectral data is consistent with those reported earlier.$^2$

N'-Hydroxy-2-naphthimidamide (27). To solution of 2-naphthonitrile (0.50 g, 3.26 mmol) in EtOH (10 mL) a solution of H$_2$NOH·HCl (0.56 g, 8.15 mmol, 2.5 equiv) and Na$_2$CO$_3$ (0.56 g, 5.20 mmol, 1.6 equiv) in H$_2$O (10 mL) was added at rt. The resulting mixture was heated at 100 °C for 19 h. After evaporation of the reaction mixture to dryness and dissolving the residue with EtOAc, the combined organic phases were washed with brine, and dried over anhydrous Na$_2$SO$_4$. The filtrate was evaporated to give the crude 27 (0.52 g, 86%) as off-white crystals.$^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 9.75 (s, 1H), 8.21 (s, 1H), 7.93-7.60 (m, 4H), 7.54-7.51 (m, 2H), 5.90 (s, 2H).

N'-Hydroxy-1H-benzimidazole-5-carboximidamide (28). To solution of 24 (0.29 g, 2.00 mmol) in EtOH (2 mL), a solution of H$_2$NOH·HCl (0.35 g, 5.00 mmol, 2.5 equiv) and Na$_2$CO$_3$ (0.34 g, 3.20 mmol, 1.6 equiv) in H$_2$O (2 mL) was added rt. The resulting mixture was heated at 100 °C for 3.5 h. After evaporation of the reaction mixture to dryness and dissolving the residue with EtOAc, the combined organic phases were washed with brine, dried over anhydrous Na$_2$SO$_4$. The filtrate was evaporated to give the crude 28 (0.25 g, 71%) as light brown powder. $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 12.52 (s, 1H), 9.52 (s, 1H), 8.23 (s, 1H), 7.90 (s, 1H), 7.54 (m, 2H), 5.79 (s, 2H). Spectral data is consistent with those reported earlier.$^2$

General procedure for the reaction of nitriles with H$_2$NOH·HCl. Method D. To a solution of the corresponding nitrile (5.0 mmol) in EtOH (10 mL), a solution of H$_2$NOH·HCl (0.87 g, 12.5 mmol, 2.5 equiv) and Na$_2$CO$_3$ (0.85 g, 8.00 mmol, 1.6 equiv) in H$_2$O (10 mL) was added at rt. The resulting solution was heated at 100 °C for 3.5 h. After evaporation of the reaction mixture to dryness and dissolving the residue with EtOAc, the combined organic phases were washed with brine, dried over anhydrous Na$_2$SO$_4$. The filtrate was evaporated to give the crude product.

N'-Hydroxybenzothiophene-5-carboximidamide (29). Method D. The crude product was purified by flash SiO$_2$ column chromatography (EtOAc/$n$-hexane 1:2 to 1:1) to give 29 (0.36 g, 38%) as a white powder. $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 9.68 (s, 1H), 8.20 (d, $J$ = 1.3
N'-Hydroxybenzofuran-5-carboximidamide (30). Method D. The crude product was purified by flash SiO₂ column chromatography (EtOAc/n-hexane 1:2 to 1:1) to yield 30 (0.43 g, 49%) as a white powder. ¹H NMR (300 MHz, DMSO-d₆) δ 9.55 (s, 1H), 8.00 (d, J = 2.2 Hz, 1H), 7.96 (d, J = 1.7 Hz, 1H), 7.66 (dd, J = 8.7, 1.8 Hz, 1H), 7.57 (d, J = 8.4 Hz, 1H), 6.98 (d, J = 2.2 Hz, 1H), 5.81 (s, 2H). ¹³C NMR (75 MHz, DMSO-d₆) δ 154.6, 151.2, 146.5, 128.6, 126.9, 122.2, 118.5, 110.8, 101.5.

N'-Hydroxy-1H-indole-5-carboximidamide (31). A solution of 5-cyanoindole (0.71 g, 5.00 mmol), H₂NOH·HCl (0.52 g, 7.5 mmol, 1.5 equiv), and Et₃N (1.04 mL, 7.50 mmol, 1.5 equiv) in EtOH (30 mL) was stirred at rt for 24 h. Then another portions of H₂NOH·HCl (0.52 g, 7.50 mmol) and Et₃N (1.04 mL, 7.50 mmol) were added to the reaction mixture, and it was stirred at rt for additional 24 h and at reflux temperature for 6 h. The solution was evaporated in vacuo and EtOAc was added to the residue, washed twice with brine, dried over anhydrous Na₂SO₄ and evaporated. The crude product was purified by flash SiO₂ column chromatography (EtOAc/n-hexane 1:1 to 1:0) to yield 31 (0.36 g, 40%) as a light brown powder. ¹H NMR (300 MHz, DMSO-d₆) δ 11.12 (s, 1H), 9.33 (s, 1H), 7.85 (d, J = 1.3 Hz, 1H), 7.46 (dd, J = 8.6, 1.6 Hz, 1H), 7.36-7.34 (m, 2H), 6.45 (d, J = 2.9 Hz, 1H), 5.66 (s, 2H). ¹³C NMR (75 MHz, DMSO-d₆) δ 152.1, 136.2, 127.1, 125.8, 124.3, 119.0, 117.3, 110.8, 101.5.

N'-Hydroxybenzo[1,3]dioxole-5-carboximidamide (32). A solution of piperonylnitrile (0.74 g, 5.00 mmol), H₂NOH·HCl (0.52 g, 7.50 mmol, 1.5 equiv), and Et₃N (1.04 mL, 7.50 mmol, 1.5 equiv) in EtOH (30 mL) was stirred at rt for 24 h. Then another portions of H₂NOH·HCl (0.52 g, 7.50 mmol) and Et₃N (1.04 mL, 7.50 mmol) were added to the reaction mixture, and it was stirred at rt for additional 24 h. The solution was evaporated in vacuo and EtOAc was added to the residue, washed twice with brine, dried over anhydrous Na₂SO₄ and evaporated to give the crude 32 (0.80 g, 89%) as a white powder. ¹H NMR (300 MHz, DMSO) δ 9.50 (s, 1H), 7.21-7.18 (m, 2H), 6.91-6.88 (m, 1H), 6.03 (s, 2H), 5.71 (s, 2H). ¹³C NMR (75 MHz, DMSO) δ 150.5, 147.8, 147.1, 127.4, 119.3, 107.8, 105.7, 101.1. Spectral data is consistent with those reported earlier.³

N'-(Phenylcarbamoyl)oxy]benzimidamide (33). Method A (1.00 mmol of starting material). The crude product was purified by flash SiO₂ column chromatography (EtOAc/n-hexane 1:4 to 1:1) to give 33 (0.22 g, 85%) as a white powder. ¹H NMR (300 MHz, DMSO-d₆) δ 9.29 (s, 1H), 7.83-7.80 (m, 2H), 7.56-7.44 (m, 5H), 7.32 (t, J = 7.7 Hz, 2H), 7.05 (t, J = 7.3 Hz, 1H), 6.76 (s, 2H). ¹³C NMR (75 MHz, DMSO-d₆) δ 154.6, 152.9, 137.4, 131.4, 131.0,
129.2 (2C), 129.1 (2C), 126.7 (2C), 124.2, 119.9 (2C). LC-MS: [M+H]+ 256.3 m/z (t<sub>r</sub> = 5.8 min). FT-IR (ATR, cm<sup>-1</sup>): 3354, 1727, 1207. HRMS (ESI): m/z calcd for C<sub>14</sub>H<sub>14</sub>N<sub>3</sub>O<sub>2</sub> [M+H]+ 256.1086, found 256.1090.

![Chemical structure](image)

**N'-[(Phenylcarbamoyl)oxy]-2-naphthimidamide (34).** Method A (1.00 mmol of starting material). The crude product was purified by flash SiO<sub>2</sub> column chromatography (EtOAc/n-hexane 1:2 to 1:1) and recrystallization (EtOAc/n-hexane) to yield 34 (95 mg, 30%) as a white powder. Mp: 179 °C. ¹H NMR (300 MHz, DMSO-d<sub>6</sub>) δ 9.42 (s, 1H), 8.43 (s, 1H), 8.04 (m, 4H), 7.62-7.52 (m, 4H), 7.34 (t, J = 7.8 Hz, 2H), 7.06 (t, J = 7.4 Hz, 1H), 6.96 (s, 2H).

**N'-[(Phenylcarbamoyl)oxy]-1H-benzoimidazo-5-carboximidamide (35).** Method A (1.99 mmol of starting material, reaction time 48 h). The crude product was purified by flash SiO<sub>2</sub> column chromatography (EtOAc/MeOH 5%→10%) to give 35 (0.15 g, 51%) as a white powder. ¹H NMR (300 MHz, DMSO-d<sub>6</sub>) δ 12.56 (br s, 1H), 9.36 (s, 1H), 8.32 (s, 1H), 8.08 (s, 1H), 7.71 (dd, J = 8.5, 1.5 Hz, 1H), 7.64 (d, J = 8.5 Hz, 1H), 7.57-7.54 (m, 2H), 7.07-7.08 (m, 1H), 6.81 (s, 2H).

**N'-[(Phenylcarbamoyl)oxy]benzothiophene-5-carboximidamide (36).** Method B. The crude product was purified by flash SiO<sub>2</sub> column chromatography (EtOAc/n-hexane 1:2 to 1:1) to yield 36 (0.14 g, 44%) as a white powder. ¹H NMR (300 MHz, DMSO-d<sub>6</sub>) δ 9.36 (s, 1H), 8.36 (d, J = 1.5 Hz, 1H), 8.09 (d, J = 8.4 Hz, 1H), 7.87-7.80 (m, 2H), 7.58-7.54 (m, 3H), 7.39-7.30 (m, 2H), 7.08-7.03 (m, 1H), 6.88 (s, 2H).

**N'-[(Phenylcarbamoyl)oxy]benzofuran-5-carboximidamide (37).** Method B. The crude product was purified by flash SiO<sub>2</sub> column chromatography (EtOAc/n-hexane 1:2 to 1:1) to give 37 (0.24 g, 79%) as a white powder. ¹H NMR (300 MHz, DMSO-d<sub>6</sub>) δ 154.4, 151.5, 137.5, 132.8, 131.3, 127.7 (2C), 127.4, 126.8, 126.6, 126.2, 125.6, 125.5, 123.0, 121.9, 118.1 (2C). LC-MS: [M+H]+ 306.2 m/z (t<sub>r</sub> = 7.0 min). FT-IR (ATR, cm<sup>-1</sup>): 3290, 1709, 1219. HRMS (ESI): m/z calcd for C<sub>18</sub>H<sub>16</sub>N<sub>2</sub>O<sub>2</sub> [M+H]+ 306.1243, found 306.1241.
123.4, 122.9, 120.2, 119.1 (2C), 111.1, 107.0. LC-MS: \([M+Na]^+\) 318.2 \(m/z\) (\(t_r = 6.3\) min). FT-IR (ATR, \(\text{cm}^{-1}\)): 3467, 3357, 2930, 2852, 1703, 1641, 1510, 1208. HRMS (ESI): \(m/z\) calcd for C_{16}H_{14}N_{3}O_{3} \([M+H]^+\) 296.1035, found 296.1035.

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\text{N'-[(Phenylcarbamoyl)oxy]-1H-indole-5-carboximidamide (38). Method B. The crude product was purified by flash SiO}_2 column chromatography (EtOAc/n-hexane 1:1 to 2:1) and recrystallization (MeCN/H}_2O) to give 38 (80 mg, 28%) as an off-white solid. Mp: 156 °C. \(^1\)H NMR (300 MHz, DMSO-\(d_6\)) \(\delta\) 11.25 (s, 1H), 9.30 (s, 1H), 8.03 (s, 1H), 7.58-7.55 (m, 3H), 7.44-7.39 (m, 2H), 7.33-7.28 (m, 2H), 7.05-7.00 (m, 1H), 6.66 (s, 1H), 6.51 (s, 1H). \(^{13}\)C NMR (75 MHz, DMSO-\(d_6\)) \(\delta\) 156.8, 152.7, 138.6, 137.0, 128.7 (2C), 127.1, 126.4, 122.8, 121.9, 119.9, 119.1, 119.0, 111.1, 101.8. LC-MS: \([M+Na]^+\) 317.1 \(m/z\) (\(t_r = 5.4\) min). FT-IR (ATR, \(\text{cm}^{-1}\)): 3511, 3387, 3196, 1750, 1517, 1193. HRMS (ESI): \(m/z\) calcd for C_{16}H_{15}N_{4}O_{2} \([M+H]^+\) 295.1195, found, 295.1197.

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\text{N'-[(Phenylcarbamoyl)oxy]benzo[\text{d}][\text{1,3}]dioxole-5-carboximidamide (39). A solution of 35 (0.18 g, 1.00 mmol) and phenyl isocyanate (0.14 mL, 1.5 mmol 1.5 equiv) was stirred in ethanol-free CHCl}_3 for 3 days. The reaction mixture was evaporated in vacuo, and the residue was purified by flash SiO}_2 column chromatography (EtOAc/n-hexane 1:2 to 1:1) and recrystallization (EtOAc) to yield 39 (17 mg, 6%) as a white powder. Mp: 140-141 °C. \(^1\)H NMR (300 MHz, DMSO-\(d_6\)) \(\delta\) 9.34 (s, 1H), 7.57-7.28 (m, 2H), 7.43 (d, \(J = 1.7\) Hz, 1H), 7.38 (dd, \(J = 8.1, 1.8\) Hz, 1H), 7.35-7.28 (m, 2H), 7.08-7.02 (m, 1H), 7.0 (d, \(J = 8.2\) Hz, 1H), 6.77 (s, 2H), 6.09 (s, 2H). \(^{13}\)C NMR (75 MHz, DMSO-\(d_6\)) \(\delta\) 155.0, 152.6, 149.1, 147.3, 138.5, 128.7 (2C), 125.0, 123.0, 121.1, 119.4 (2C), 108.1, 107.1, 101.6. LC-MS: \([M+Na]^+\) 322.1 \(m/z\) (\(t_r = 5.7\) min). FT-IR (ATR, \(\text{cm}^{-1}\)): 3303, 1720, 1525, 1206. HRMS (ESI): \(m/z\) calcd for C_{15}H_{14}N_{3}O_{4} \([M+H]^+\) 300.0984, found, 300.0984.

References
