

Facile Synthesis of Tricyclic 1,2,4-Oxadiazolines-Fused Tetrahydro-Isoquinolines from Oxime Chlorides with 3,4-Dihydroisoquinoline Imines

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Supporting Information

Table of Contents

1. General methods

2. General procedure for synthesis of 1,2,4-oxadiazolo[5,4-*a*]isoquinoline compounds

3. Crystal data and structural refinement for 3j

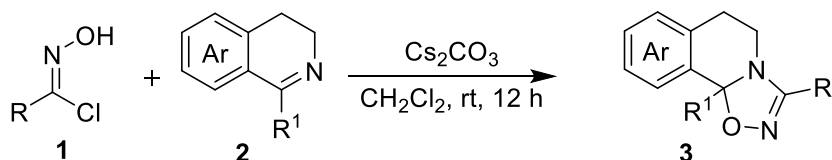
4. NMR spectra

1. General methods

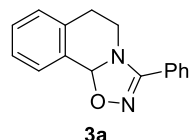
The hydroximoyl chloride **1** [1–3] and isolable 2,4,6-trimethylbenzonitrile oxide **1a'** [4,5] were prepared according to the literature procedures. The cyclic imines **2** were prepared according to the literature procedures [6–8].

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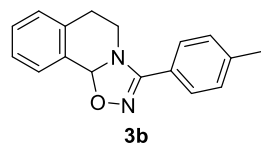
2. General procedure for synthesis of 1,2,4-oxadiazolo[5,4-*a*]isoquinoline compounds



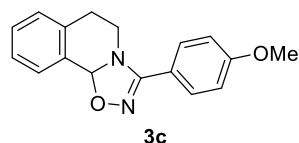
Cs₂CO₃ (0.22 mmol) was added to a solution of oxime chlorides **1** (0.22 mmol), cyclic imines **2** (0.2 mmol) in CH₂Cl₂ (1 mL). The solution was stirred at rt for 12 h. After completion, product **3** was obtained by flash chromatography on silica gel (petroleum ether/ethyl acetate = 15:1 to 10:1).



3-Phenyl-6,10b-dihydro-5H-[1,2,4]oxadiazolo[5,4-*a*]isoquinoline 3a, 47.5 mg, 95% yield, white solid; ¹H NMR (400 MHz, CDCl₃) δ 7.70 (d, *J* = 7.6 Hz, 2H), 7.50–7.43 (m, 4H), 7.32–7.24 (m, 2H), 7.12 (d, *J* = 5.6 Hz, 1H), 6.51 (s, 1H), 3.48 (dt, *J* = 12.8, 4.4 Hz, 1H), 3.37–3.31 (m, 1H), 2.78 (ddd, *J* = 15.2, 10.0, 4.4 Hz, 1H), 2.63 (dt, *J* = 15.6, 3.6 Hz, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃) δ 159.6, 135.8, 131.7, 130.9, 128.9, 128.4, 128.3, 128.2, 127.2, 125.7, 92.0, 43.4, 28.2 ppm. ESI-HRMS: C₁₆H₁₄N₂O+H⁺ 251.1179, found 251.1176.

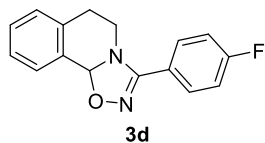


3-(*p*-Tolyl)-6,10b-dihydro-5H-[1,2,4]oxadiazolo[5,4-*a*]isoquinoline 3b, 48.0 mg, 91% yield, white solid; ¹H NMR (400 MHz, CDCl₃) δ 7.59 (d, *J* = 8.0 Hz, 2H), 7.45 (d, *J* = 5.6 Hz, 1H), 7.34–7.31 (m, 2H), 7.27 (d, *J* = 8.4 Hz, 2H), 7.13 (d, *J* = 5.6 Hz, 1H), 6.51 (s, 1H), 3.49 (dt, *J* = 12.8, 4.4 Hz, 1H), 3.37–3.30 (m, 1H), 2.78 (ddd, *J* = 15.2, 10.4, 4.4 Hz, 1H), 2.63 (d, *J* = 15.6 Hz, 1H), 2.41 (s, 3H) ppm. ¹³C NMR (100 MHz, CDCl₃) δ 159.6, 141.2, 135.9, 131.8, 129.6, 128.9, 128.4, 128.3, 128.2, 127.2, 122.7, 91.8, 43.4, 28.3, 21.5 ppm. ESI-HRMS: C₁₇H₁₆N₂O+H⁺ 265.1335, found 265.1332.

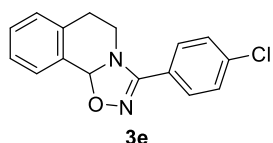


3-(4-Methoxyphenyl)-6,10b-dihydro-5H-[1,2,4]oxadiazolo[5,4-*a*]isoquinoline 3c, 50.4 mg, 90% yield, white solid; ¹H NMR (400 MHz, CDCl₃) δ 7.65 (d, *J* = 8.4 Hz, 2H), 7.46–7.44 (m, 1H), 7.34–7.26 (m, 2H), 7.14–7.12 (m, 1H), 6.97 (d, *J* = 8.4 Hz, 2H), 6.46 (s, 1H),

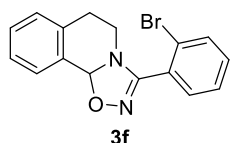
3.85 (s, 3H), 3.46 (dt, $J = 12.8, 4.4$ Hz, 1H), 3.36–3.29 (m, 1H), 2.83–2.75 (m, 1H), 2.65 (dt, $J = 15.6, 3.6$ Hz, 1H) ppm. ^{13}C NMR (100 MHz, CDCl_3) δ 161.7, 159.5, 136.0, 131.7, 129.9, 128.9, 128.34, 128.32, 127.1, 117.9, 114.4, 91.7, 55.4, 43.6, 28.4 ppm. ESI-HRMS: $\text{C}_{17}\text{H}_{16}\text{N}_2\text{O}_2 + \text{H}^+$ 281.1285, found 281.1281.



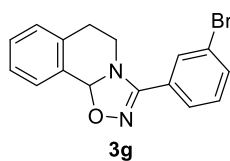
3-(4-Fluorophenyl)-6,10b-dihydro-5H-[1,2,4]oxadiazolo[5,4-a]isoquinoline 3d, 50.9 mg, 95% yield, white solid; ^1H NMR (400 MHz, CDCl_3) δ 7.73–7.69 (m, 2H), 7.45 (d, $J = 4.4$ Hz, 1H), 7.34–7.32 (m, 2H), 7.18–7.14 (m, 3H), 6.50 (s, 1H), 3.47–3.30 (m, 2H), 2.82–2.64 (m, 2H) ppm. ^{13}C NMR (100 MHz, CDCl_3) δ 164.2 (d, $J = 250.0$ Hz), 158.9, 135.8, 131.4, 130.36 (d, $J = 8.6$ Hz), 129.0, 128.4, 128.3, 127.2, 121.8 (d, $J = 3.3$ Hz), 116.2 (d, $J = 21.8$ Hz), 92.0, 43.5, 28.3 ppm. ESI-HRMS: $\text{C}_{16}\text{H}_{13}\text{FN}_2\text{O} + \text{H}^+$ 269.1085, found 269.1083.



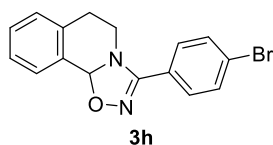
3-(4-Chlorophenyl)-6,10b-dihydro-5H-[1,2,4]oxadiazolo[5,4-a]isoquinoline 3e, 53.4 mg, 94% yield, white solid; ^1H NMR (400 MHz, CDCl_3) δ 7.66 (d, $J = 8.4$ Hz, 2H), 7.44 (d, $J = 7.6$ Hz, 3H), 7.35–7.30 (m, 2H), 7.15 (d, $J = 4.8$ Hz, 1H), 6.50 (s, 1H), 3.43 (dt, $J = 12.8, 4.4$ Hz, 1H), 3.37–3.30 (m, 1H), 2.79 (ddd, $J = 15.2, 10.0, 4.4$ Hz, 1H), 2.66 (dt, $J = 15.6, 3.6$ Hz, 1H) ppm. ^{13}C NMR (100 MHz, CDCl_3) δ 158.9, 137.0, 135.8, 131.3, 129.5, 129.3, 129.0, 128.4, 128.3, 127.2, 124.2, 92.1, 43.5, 28.3 ppm. ESI-HRMS: $\text{C}_{16}\text{H}_{13}\text{ClN}_2\text{O} + \text{H}^+$ 285.0789, found 285.0786.



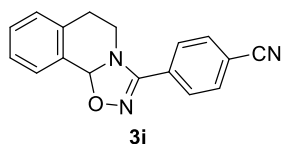
3-(2-Bromophenyl)-6,10b-dihydro-5H-[1,2,4]oxadiazolo[5,4-a]isoquinoline 3f, 60.4 mg, 92% yield, white solid; ^1H NMR (400 MHz, CDCl_3) δ 7.69 (d, $J = 8.0$ Hz, 1H), 7.50 (dd, $J = 7.6, 1.6$ Hz, 1H), 7.45 (d, $J = 6.8$ Hz, 1H), 7.42–7.45 (m, 2H), 7.33–7.28 (m, 2H), 7.10 (d, $J = 6.8$ Hz, 1H), 6.72 (s, 1H), 3.40–3.28 (m, 2H), 2.90–2.81 (m, 1H), 2.58 (d, $J = 16.0$ Hz, 1H) ppm. ^{13}C NMR (100 MHz, CDCl_3) δ 157.4, 134.9, 133.8, 133.0, 131.97, 131.91, 128.7, 128.6, 127.6, 127.3, 126.8, 122.9, 91.6, 41.8, 27.9 ppm. ESI-HRMS: $\text{C}_{16}\text{H}_{13}\text{BrN}_2\text{O} + \text{H}^+$ 329.0284 (^{79}Br) and 331.0264 (^{81}Br), found 329.0283 and 331.0261.



3-(3-Bromophenyl)-6,10b-dihydro-5H-[1,2,4]oxadiazolo[5,4-a]isoquinoline 3g, 61.7 mg, 94% yield, white solid; ^1H NMR (400 MHz, CDCl_3) δ 7.87 (s, 1H), 7.66–7.61 (m, 2H), 7.46–7.44 (m, 1H), 7.36–7.31 (m, 3H), 7.16–7.14 (m, 1H), 6.51 (s, 1H), 3.45 (dt, $J = 12.8, 4.4$ Hz, 1H), 3.38–3.31 (m, 1H), 2.80 (ddd, $J = 15.2, 10.0, 4.4$ Hz, 1H), 2.67 (dt, $J = 16.0, 3.6$ Hz, 1H) ppm. ^{13}C NMR (100 MHz, CDCl_3) δ 158.5, 135.7, 133.9, 131.2, 131.1, 130.5, 129.1, 128.4, 128.3, 127.7, 127.3, 126.8, 122.9, 92.2, 43.6, 28.3 ppm. ESI-HRMS: $\text{C}_{16}\text{H}_{13}\text{BrN}_2\text{O} + \text{H}^+$ 329.0284 (^{79}Br) and 331.0264 (^{81}Br), found 329.0282 and 331.0260.



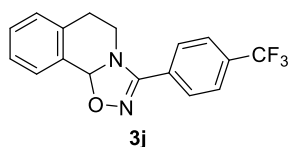
3-(4-Bromophenyl)-6,10b-dihydro-5H-[1,2,4]oxadiazolo[5,4-a]isoquinoline 3h, 62.3mg, 95% yield, white solid; ^1H NMR (400 MHz, CDCl_3) δ 7.61–7.57 (m, 4H), 7.44 (d, $J = 4.4$ Hz, 1H), 7.32 (dd, $J = 4.4, 2.8$ Hz, 2H), 7.14 (d, $J = 4.4$ Hz, 1H), 6.49 (s, 1H), 3.45–3.39 (m, 1H), 3.36–3.30 (m, 1H), 2.82–2.74 (m, 1H), 2.66 (d, $J = 16.0$ Hz, 1H) ppm. ^{13}C NMR (100 MHz, CDCl_3) δ 158.9, 135.7, 132.2, 131.3, 129.7, 129.1, 128.4, 128.3, 127.2, 125.3, 124.7, 92.2, 43.6, 28.3 ppm. ESI-HRMS: $\text{C}_{16}\text{H}_{13}\text{BrN}_2\text{O} + \text{H}^+$ 329.0284 (^{79}Br) and 331.0264 (^{81}Br), found 329.0281 and 331.0260.



4-(6,10b-Dihydro-5H-[1,2,4]oxadiazolo[5,4-a]isoquinolin-3-yl)benzonitrile 3i, 52.8 mg,

96% yield, white solid; ^1H NMR (400 MHz, CDCl_3) δ 7.85 (d, J = 8.0 Hz, 2H), 7.77 (d, J = 8.4 Hz, 2H), 7.47–7.45 (m, 1H), 7.35 (dd, J = 5.6, 3.6 Hz, 2H), 7.18–7.15 (m, 1H), 6.53 (s, 1H), 3.43–3.33 (m, 2H), 2.84–2.67 (m, 2H) ppm. ^{13}C NMR (100 MHz, CDCl_3) δ 158.5,

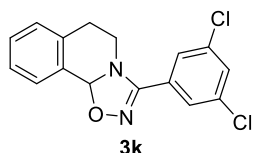
135.6, 132.7, 130.8, 130.2, 129.3, 128.7, 128.4, 128.3, 127.4, 118.1, 114.4, 92.7, 43.7, 28.3 ppm. ESI-HRMS: $\text{C}_{17}\text{H}_{13}\text{N}_3\text{O}+\text{H}^+$ 276.1131, found 276.1130.



3-(4-(Trifluoromethyl)phenyl)-6,10b-dihydro-5H-[1,2,4]oxadiazolo[5,4-a]isoquinoline 3j, 61.1 mg, 96% yield, white solid; ^1H NMR (400 MHz, CDCl_3) δ 7.85 (d, J = 8.4 Hz, 2H),

7.73 (d, J = 8.0 Hz, 2H), 7.47–7.45 (m, 1H), 7.36–7.31 (m, 2H), 7.16–7.14 (m, 1H), 6.54 (s, 1H), 3.46–3.33 (m, 2H), 2.79 (ddd, J = 15.2, 9.6, 4.4 Hz, 1H), 2.68 (dt, J = 16.0, 4.0 Hz, 1H) ppm. ^{13}C NMR (100

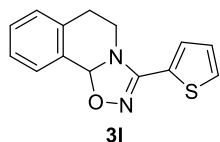
MHz, CDCl_3) δ 158.7, 135.7, 132.7 (q, J = 32.5 Hz), 131.2, 129.4, 129.2, 128.6, 128.4, 128.3, 127.3, 125.9 (q, J = 3.7 Hz), 123.7 (q, J = 268.8 Hz), 92.5, 43.6, 28.3 ppm. ESI-HRMS: $\text{C}_{17}\text{H}_{13}\text{F}_3\text{N}_2\text{O}+\text{H}^+$ 319.1053, found 319.1051.



3-(3,5-Dichlorophenyl)-6,10b-dihydro-5H-[1,2,4]oxadiazolo[5,4-a]isoquinoline 3k, 59.8

mg, 94% yield, white solid; ^1H NMR (400 MHz, CDCl_3) δ 7.61 (s, 2H), 7.48 (s, 1H), 7.44 (d, J = 4.4 Hz, 1H), 7.33 (dd, J = 7.2, 4.0 Hz, 2H), 7.16 (d, J = 3.6 Hz, 1H), 6.49 (s, 1H), 3.43–3.31 (m, 2H), 2.84–2.77 (m, 1H), 2.74–2.69 (m, 1H) ppm. ^{13}C NMR (100 MHz, CDCl_3) δ 157.9,

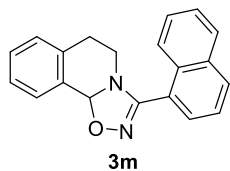
135.73, 135.67, 130.84, 130.82, 129.2, 128.7, 128.4, 128.3, 127.3, 126.5, 92.6, 43.7, 28.3 ppm. ESI-HRMS: $\text{C}_{16}\text{H}_{12}\text{Cl}_2\text{N}_2\text{O}+\text{H}^+$ 319.0399, found 319.0397.



3-(Thiophen-2-yl)-6,10b-dihydro-5H-[1,2,4]oxadiazolo[5,4-a]isoquinoline 3l, 46.1 mg, 90%

yield, white solid; ^1H NMR (400 MHz, CDCl_3) δ 7.45–7.43 (m, 1H), 7.33 (dd, J = 8.4, 4.0 Hz, 2H), 7.26 (d, J = 4.4 Hz, 2H), 7.17–7.15 (m, 1H), 6.96 (d, J = 3.6 Hz, 1H), 6.42 (s, 1H), 3.60–

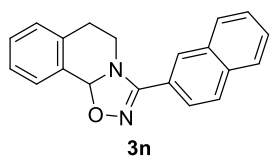
3.55 (m, 1H), 3.42–3.35 (m, 1H), 2.90–2.83 (m, 1H), 2.76–2.70 (m, 1H) ppm. ^{13}C NMR (100 MHz, CDCl_3) δ 154.5, 135.8, 133.9, 130.8, 129.2, 128.7, 128.3, 127.2, 126.9, 125.6, 92.2, 44.1, 28.4 ppm. ESI-HRMS: $\text{C}_{14}\text{H}_{12}\text{N}_2\text{OS}+\text{H}^+$ 257.0743, found 257.0738.



3-(Naphthalen-1-yl)-6,10b-dihydro-5H-[1,2,4]oxadiazolo[5,4-a]isoquinoline 3m, 54.6 mg,

91% yield, white solid; ^1H NMR (400 MHz, CDCl_3) δ 8.39 (d, J = 8.8 Hz, 1H), 7.98 (d, J = 8.0 Hz, 1H), 7.91–7.89 (m, 1H), 7.73 (d, J = 6.8 Hz, 1H), 7.56–7.52 (m, 4H), 7.37–7.29 (m, 2H), 7.07 (d, J = 7.2 Hz, 1H), 6.79 (s, 1H), 3.32–3.28 (m, 2H), 2.78–2.70 (m, 1H), 2.49 (d, J = 16.0

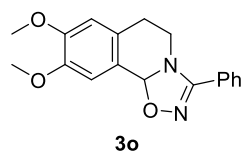
Hz, 1H) ppm. ^{13}C NMR (100 MHz, CDCl_3) δ 158.0, 135.1, 133.6, 133.1, 131.24, 131.19, 128.7, 128.6, 128.53, 128.46, 127.8, 127.34, 127.32, 126.5, 125.2, 122.5, 91.6, 42.3, 28.0 ppm. ESI-HRMS: $\text{C}_{20}\text{H}_{16}\text{N}_2\text{O}+\text{H}^+$ 301.1335, found 301.1332.



3-(Naphthalen-2-yl)-6,10b-dihydro-5H-[1,2,4]oxadiazolo[5,4-a]isoquinoline 3n, 54.0 mg,

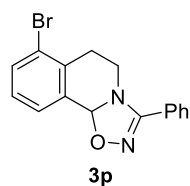
90% yield, white solid; ^1H NMR (400 MHz, CDCl_3) δ 8.21 (s, 1H), 7.93–7.87 (m, 3H), 7.79 (d, J = 8.4 Hz, 1H), 7.58–7.52 (m, 3H), 7.36–7.30 (m, 2H), 7.14 (d, J = 6.4 Hz, 1H), 6.56 (s,

1H), 3.55 (dt, $J = 12.8, 4.4$ Hz, 1H), 3.44–3.38 (m, 1H), 2.85–2.78 (m, 1H), 2.66 (d, $J = 15.6$ Hz, 1H) ppm. ^{13}C NMR (100 MHz, CDCl_3) δ 159.8, 135.9, 134.4, 132.9, 131.5, 129.0, 128.8, 128.54, 128.46, 128.4, 128.3, 127.8, 127.5, 127.2, 126.8, 124.8, 123.0, 92.1, 43.7, 28.3 ppm. ESI-HRMS: $\text{C}_{20}\text{H}_{16}\text{N}_2\text{O}+\text{H}^+$ 301.1335, found 301.1334.



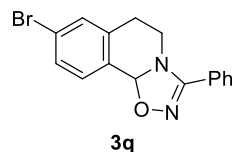
8,9-Dimethoxy-3-phenyl-6,10b-dihydro-5H-[1,2,4]oxadiazolo[5,4-a]isoquinoline 3o, 58.9

mg, 95% yield, white solid; ^1H NMR (400 MHz, CDCl_3) δ 7.67 (d, $J = 6.4$ Hz, 2H), 7.46 (d, $J = 6.8$ Hz, 3H), 6.92 (s, 1H), 6.59 (s, 1H), 6.50 (s, 1H), 3.92 (s, 3H), 3.86 (s, 3H), 3.51 (d, $J = 13.2$ Hz, 1H), 3.34 (t, $J = 8.8$ Hz, 1H), 2.73–2.66 (m, 1H), 2.53 (d, $J = 15.6$ Hz, 1H) ppm. ^{13}C NMR (100 MHz, CDCl_3) δ 159.4, 149.3, 148.2, 130.8, 128.9, 128.2, 128.0, 125.6, 123.9, 111.0, 110.3, 91.9, 56.0, 55.9, 43.2, 27.6 ppm. ESI-HRMS: $\text{C}_{18}\text{H}_{18}\text{N}_2\text{O}_3+\text{H}^+$ 311.1390, found 311.1386.



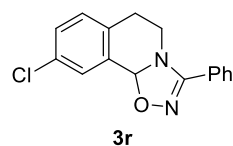
7-Bromo-3-phenyl-6,10b-dihydro-5H-[1,2,4]oxadiazolo[5,4-a]isoquinoline 3p, 59.0 mg, 90%

yield, white solid; ^1H NMR (400 MHz, CDCl_3) δ 7.66 (d, $J = 7.2$ Hz, 2H), 7.57 (d, $J = 7.6$ Hz, 1H), 7.52–7.45 (m, 3H), 7.42 (d, $J = 7.6$ Hz, 1H), 7.21 (t, $J = 8.0$ Hz, 1H), 6.52 (s, 1H), 3.59 (dt, $J = 13.6, 4.4$ Hz, 1H), 3.39–3.33 (m, 1H), 2.80 (d, $J = 16.8$ Hz, 1H), 2.67–2.59 (m, 1H) ppm. ^{13}C NMR (100 MHz, CDCl_3) δ 159.1, 135.2, 134.9, 132.8, 131.0, 129.0, 128.4, 128.2, 127.2, 125.2, 124.4, 91.6, 42.5, 27.9 ppm. ESI-HRMS: $\text{C}_{16}\text{H}_{13}\text{BrN}_2\text{O}+\text{H}^+$ 329.0284 (^{79}Br) and 331.0264 (^{81}Br), found 329.0281 and 331.0260.



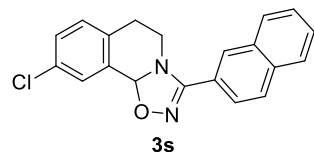
8-Bromo-3-phenyl-6,10b-dihydro-5H-[1,2,4]oxadiazolo[5,4-a]isoquinoline 3q, 59.7 mg, 91%

yield, white solid; ^1H NMR (400 MHz, CDCl_3) δ 7.69–7.67 (m, 2H), 7.53–7.45 (m, 4H), 7.33–7.30 (m, 2H), 6.48 (s, 1H), 3.49 (dt, $J = 13.2, 4.4$ Hz, 1H), 3.37–3.30 (m, 1H), 2.75 (ddd, $J = 15.6, 10.4, 4.4$ Hz, 1H), 2.60 (dt, $J = 15.6, 3.6$ Hz, 1H) ppm. ^{13}C NMR (100 MHz, CDCl_3) δ 159.5, 138.0, 131.3, 131.0, 130.9, 130.4, 129.8, 129.0, 128.2, 125.3, 123.0, 91.4, 43.0, 27.9 ppm. ESI-HRMS: $\text{C}_{16}\text{H}_{13}\text{BrN}_2\text{O}+\text{H}^+$ 329.0284 (^{79}Br) and 331.0264 (^{81}Br), found 329.0280 and 331.0258.



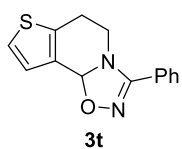
9-Chloro-3-phenyl-6,10b-dihydro-5H-[1,2,4]oxadiazolo[5,4-a]isoquinoline 3r, 50.0 mg, 88%

yield, white solid; ^1H NMR (400 MHz, CDCl_3) δ 7.68 (d, $J = 7.6$ Hz, 2H), 7.52–7.45 (m, 4H), 7.29–7.26 (m, 1H), 7.06 (d, $J = 8.0$ Hz, 1H), 6.48 (s, 1H), 3.51 (dt, $J = 13.2, 4.4$ Hz, 1H), 3.39–3.32 (m, 1H), 2.72 (ddd, $J = 15.2, 10.0, 4.4$ Hz, 1H), 2.60 (dt, $J = 15.2, 3.6$ Hz, 1H) ppm. ^{13}C NMR (100 MHz, CDCl_3) δ 159.4, 134.0, 133.8, 132.9, 131.0, 129.8, 129.03, 129.0, 128.3, 128.1, 125.4, 91.3, 43.1, 27.6 ppm. ESI-HRMS: $\text{C}_{16}\text{H}_{13}\text{ClN}_2\text{O}+\text{H}^+$ 285.0789, found 285.0786.

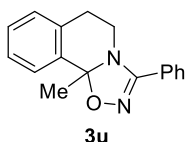


9-Chloro-3-(naphthalen-2-yl)-6,10b-dihydro-5H-[1,2,4]oxadiazolo[5,4-a]isoquinoline 3s, 60.8 mg, 91% yield, white solid; ^1H NMR (400 MHz, CDCl_3) δ 8.18 (s, 1H), 7.93–

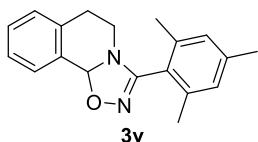
7.87 (m, 3H), 7.75 (d, $J = 8.4$ Hz, 1H), 7.59–7.53 (m, 2H), 7.47 (s, 1H), 7.28 (d, $J = 8.4$ Hz, 1H), 7.06 (d, $J = 8.0$ Hz, 1H), 6.51 (s, 1H), 3.56 (dt, $J = 12.8, 4.4$ Hz, 1H), 3.44–3.37 (m, 1H), 2.74 (ddd, $J = 15.2, 10.0, 4.4$ Hz, 1H), 2.64–2.59 (m, 1H) ppm. ^{13}C NMR (100 MHz, CDCl_3) δ 159.6, 134.4, 134.1, 133.6, 132.9, 132.8, 129.8, 129.1, 128.9, 128.53, 128.47, 128.1, 127.9, 127.6, 126.9, 124.7, 122.7, 91.5, 43.3, 27.6 ppm. ESI-HRMS: $\text{C}_{20}\text{H}_{15}\text{ClN}_2\text{O}+\text{H}^+$ 335.0946, found 335.0941.



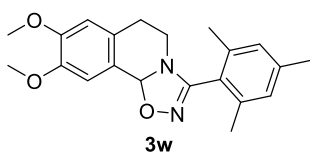
3-Phenyl-6,9b-dihydro-5H-[1,2,4]oxadiazolo[4,5-a]thieno[3,2-c]pyridine 3t, 47.6 mg, 93% yield, white solid; ^1H NMR (400 MHz, CDCl_3) δ 7.61 (d, J = 7.2 Hz, 2H), 7.51–7.44 (m, 3H), 7.19 (d, J = 5.2 Hz, 1H), 7.07 (d, J = 5.2 Hz, 1H), 6.63 (s, 1H), 3.69 (dt, J = 13.6, 3.6 Hz, 1H), 3.47–3.40 (m, 1H), 2.75–2.63 (m, 2H) ppm. ^{13}C NMR (100 MHz, CDCl_3) δ 158.7, 137.1, 132.2, 130.8, 128.9, 128.2, 125.5, 125.4, 124.1, 90.2, 42.6, 24.0 ppm. ESI-HRMS: $\text{C}_{14}\text{H}_{12}\text{N}_2\text{OS}+\text{H}^+$ 257.0743, found 257.0740.



10b-Methyl-3-phenyl-6,10b-dihydro-5H-[1,2,4]oxadiazolo[5,4-a]isoquinoline 3u, 50.7 mg, 96% yield, white solid; ^1H NMR (400 MHz, CDCl_3) δ 7.62 (d, J = 7.2 Hz, 2H), 7.51 (d, J = 7.6 Hz, 1H), 7.46–7.41 (m, 3H), 7.30 (t, J = 7.2 Hz, 1H), 7.25–7.21 (m, 1H), 7.03 (d, J = 7.6 Hz, 1H), 3.49–3.40 (m, 2H), 2.73–2.56 (m, 2H), 1.89 (s, 3H) ppm. ^{13}C NMR (100 MHz, CDCl_3) δ 158.4, 137.3, 133.6, 130.6, 128.8, 128.2, 128.1, 127.2, 126.4, 126.0, 97.2, 42.2, 27.95, 27.88 ppm. ESI-HRMS: $\text{C}_{17}\text{H}_{16}\text{N}_2\text{O}+\text{H}^+$ 265.1335, found 265.1333.

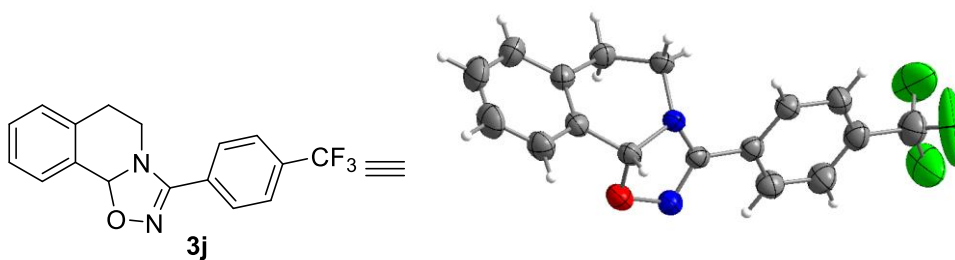


3-Mesityl-6,10b-dihydro-5H-[1,2,4]oxadiazolo[5,4-a]isoquinoline 3v, 54.3 mg, 93% yield, white solid; ^1H NMR (400 MHz, CDCl_3) δ 7.50–7.48 (m, 1H), 7.35–7.27 (m, 2H), 7.10 (d, J = 7.2 Hz, 1H), 6.93 (s, 2H), 6.65 (s, 1H), 3.30 (ddd, J = 13.6, 11.2, 4.4 Hz, 1H), 3.17 (ddd, J = 12.8, 5.6, 2.8 Hz, 1H), 2.78 (ddd, J = 16.0, 10.8, 5.6 Hz, 1H), 2.60 (dt, J = 16.0, 3.6 Hz, 1H), 2.37 (s, 3H), 2.31 (s, 3H), 2.21 (s, 3H) ppm. ^{13}C NMR (100 MHz, CDCl_3) δ 156.3, 139.9, 138.5, 138.1, 134.4, 134.2, 128.8, 128.61, 128.59, 127.3, 127.2, 121.1, 90.1, 40.6, 28.0, 21.2, 20.3, 19.7 ppm. ESI-HRMS: $\text{C}_{19}\text{H}_{20}\text{N}_2\text{O}+\text{H}^+$ 293.1648, found 293.1647.



3-Mesityl-8,9-dimethoxy-6,10b-dihydro-5H-[1,2,4]oxadiazolo[5,4-a]isoquinoline 3w, 66.9 mg, 95% yield, white solid; ^1H NMR (400 MHz, CDCl_3) δ 6.95 (s, 1H), 6.92 (s, 2H), 6.61 (s, 1H), 6.54 (s, 1H), 3.92 (s, 3H), 3.86 (s, 3H), 3.29 (ddd, J = 13.6, 11.2, 4.4 Hz, 1H), 3.18 (ddd, J = 16.0, 5.6, 2.4 Hz, 1H), 2.69 (ddd, J = 16.4, 11.6, 6.0 Hz, 1H), 2.47 (dd, J = 12.8, 3.2 Hz, 1H), 2.35 (s, 3H), 2.30 (s, 3H), 2.22 (s, 3H) ppm. ^{13}C NMR (100 MHz, CDCl_3) δ 156.2, 149.2, 148.3, 139.8, 138.5, 138.0, 128.9, 128.7, 126.5, 126.3, 121.0, 111.0, 109.4, 90.1, 56.0, 55.9, 40.5, 27.3, 21.2, 20.3, 19.6 ppm. ESI-HRMS: $\text{C}_{21}\text{H}_{24}\text{N}_2\text{O}_3+\text{H}^+$ 353.1860, found 353.1858.

3. Crystal data and structural refinement for 3j



CCDC 2160406

Identification code	3j
Empirical formula	C ₁₇ H ₁₃ F ₃ N ₂ O
Formula weight	318.29
Temperature/K	296
Crystal system	monoclinic
Space group	P 21/c
a/Å	15.121(3)
b/Å	8.7521(18)
c/Å	11.671(2)
α/°	90
β/°	110.785(3)
γ/°	90
Volume/Å ³	1444.0(5)
Z	4
ρ _{calc} /cm ³	1.464
μ/mm ⁻¹	0.119
F(000)	656.0
Crystal size/mm ³	0.26 × 0.25 × 0.2
Radiation	MoKα (λ = 0.71073)
2θ range for data collection/°	2.737 to 24.998
Index ranges	-17 ≤ h ≤ 17, -8 ≤ k ≤ 10, -13 ≤ l ≤ 13
Reflections collected	7110
Independent reflections	1918 [R _{int} = 0.0240]
Data/restraints/parameters	2535 / 3 / 237
Goodness-of-fit on F ²	0.992
Final R indexes [I ≥ 2σ (I)]	R ₁ = 0.0377, wR ₂ = 0.1075
R indices (all data)	R ₁ = 0.0511, wR ₂ = 0.1160
Largest diff. peak and hole/ 1-sigma level	0.155 / -0.133/0.031

S7

