

# Multicatalytic Tandem Reaction of *N'*-(2-Alkynylbenzylidene)hydrazide with Indole

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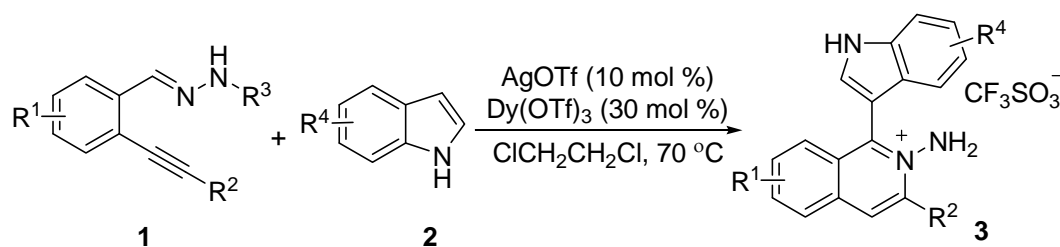
## Supporting Information

1. General experimental method (S2)
2. General Experimental procedure (S2)
3. Characterization data of compound **3** (S3-S8)
4. <sup>1</sup>H and <sup>13</sup>C NMR spectra of compound **3** (S9-S36)
5. X-ray ORTEP illustration of compound **3j**·CF<sub>3</sub>SO<sub>3</sub> (S37)

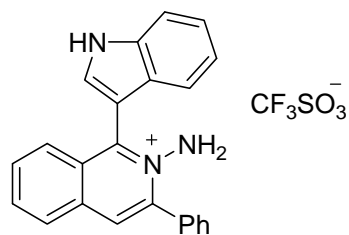
**General experimental method:**

All reactions were performed in test tubes under nitrogen atmosphere at 70 °C. Flash column chromatography was performed using silica gel (60-Å pore size, 32–63 µm, standard grade). Analytical thin-layer chromatography was performed using glass plates pre-coated with 0.25 mm 230–400 mesh silica gel impregnated with a fluorescent indicator (254 nm). Thin layer chromatography plates were visualized by exposure to ultraviolet light. Organic solutions were concentrated at ~20 Torr (house vacuum) at 25–35 °C. Solvents were re-distilled prior to use in the reactions. Other commercial reagents were used as received.

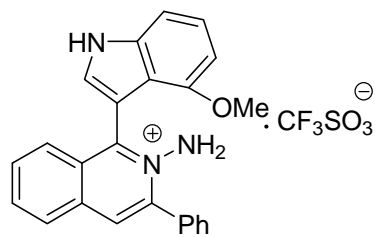
**General experimental procedure for the AgOTf and Dy(OTf)<sub>3</sub> co-catalyzed tandem reaction of *N'*-(2-alkynylbenzylidene)hydrazide **1** with indole **2**:**



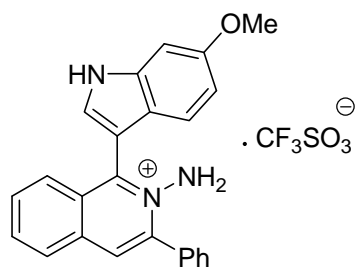
A mixture of *N'*-(2-alkynylbenzylidene)hydrazide **1** (0.3 mmol), indole **2** (0.6 mmol, 2.0 equiv), AgOTf (10 mol %) and Dy(OTf)<sub>3</sub> (30 mol %) in 1,2-dichloroethane (1.0 mL) was stirred at 70 °C. After completion of reaction as indicated by TLC, the mixture was allowed to cool to room temperature, diluted with ethyl acetate (5 mL), filtered through a thin pad of silica gel (eluting with ethyl acetate), and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (eluting with PE/EA = 1/1 to 1/10) to provide the desired product **3**.



$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ): 6.42(s, 2H), 7.12 (t,  $J = 7.8$  Hz, 1H), 7.19-7.23 (m, 2H), 7.56-7.57 (m, 3H), 7.60-7.66 (m, 2H), 7.75-7.77 (m, 2H), 7.89-8.00 (m, 5H), 11.17 (s, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  101.1, 113.5, 120.4 (q,  $^1J_{\text{CF}} = 318$  Hz), 119.4, 121.9, 123.7, 125.3, 125.7, 127.4, 128.2, 129.3, 130.0, 130.3, 130.8, 131.0, 131.4, 134.6, 135.2, 136.6, 142.8, 148.9; IR (KBr,  $\text{cm}^{-1}$ ): 3464, 1636, 1456;  $m/z$  (ESI): 336 ( $\text{M}^+\text{+H}$ ); HRMS calcd for  $\text{C}_{23}\text{H}_{18}\text{N}_3$  ( $\text{M}^+\text{+H}$ ): 336.1501, found: 336.1518.

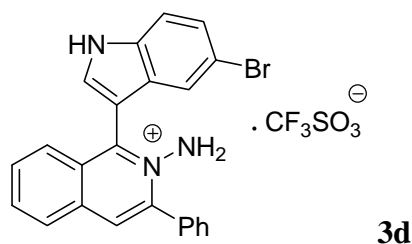


$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ): 3.59 (s, 3H), 6.05 (s, 2H), 6.48 (d,  $J = 7.9$  Hz, 1H), 7.07 (t,  $J = 7.9$  Hz, 1H), 7.17 (d,  $J = 9.7$  Hz, 1H), 7.46-7.47 (m, 3H), 7.57-7.58 (m, 4H), 7.81-7.93 (m, 4H), 11.05 (s, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  55.5, 100.0, 101.6, 106.8, 115.7, 120.4 (q,  $^1J_{\text{CF}} = 318$  Hz), 124.7, 125.3, 127.0, 128.6, 129.1, 129.5, 129.7, 130.4, 130.5, 130.6, 131.3, 134.7, 135.4, 138.2, 143.6, 152.0, 152.1; IR (KBr,  $\text{cm}^{-1}$ ): 3447, 1636, 1457;  $m/z$  (ESI): 366 ( $\text{M}^+\text{+H}$ ); HRMS calcd for  $\text{C}_{24}\text{H}_{20}\text{N}_3\text{O}$  ( $\text{M}^+\text{+H}$ ): 366.1606, found: 366.1626.

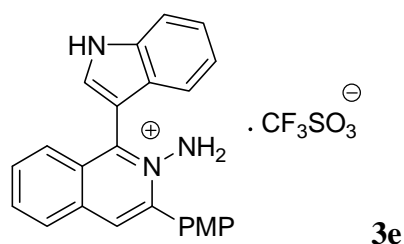


$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ): 3.76 (s, 3H), 6.45 (s, 2H), 6.77 (d,  $J = 8.5$  Hz, 1H), 7.09-7.13 (m, 2H), 7.55-7.56 (m, 3H), 7.64 (t,  $J = 7.3$  Hz, 1H), 7.74-7.75 (m, 3H),

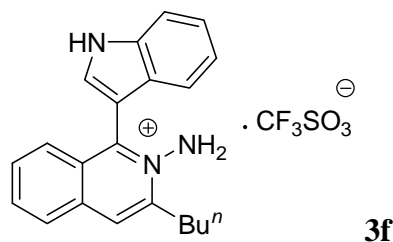
7.87-7.98 (m, 4H), 11.08 (s, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  55.4, 95.7, 100.9, 112.6, 119.2, 119.9, 120.4 (q,  $^1J_{\text{CF}} = 318$  Hz), 125.3, 127.1, 128.1, 129.2, 129.8, 130.1, 130.3, 130.6, 130.7, 130.9, 134.4, 135.0, 137.6, 142.6, 148.8, 157.2; IR (KBr,  $\text{cm}^{-1}$ ): 3465, 1636, 1455;  $m/z$  (ESI): 366 ( $\text{M}^+\text{H}$ ); HRMS calcd for  $\text{C}_{24}\text{H}_{20}\text{N}_3\text{O}$  ( $\text{M}^+\text{H}$ ): 366.1606, found: 366.1622.



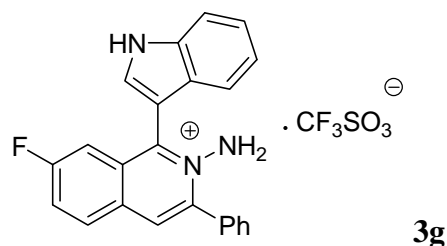
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ): 6.44 (s, 2H), 7.23-7.25 (m, 1H), 7.32-7.33 (m, 1H), 7.48 (d,  $J = 8.8$  Hz, 1H), 7.56-7.58 (m, 3H), 7.66 (t,  $J = 8.3$  Hz, 1H), 7.74-7.76 (m, 2H), 7.84 (d,  $J = 8.8$  Hz, 1H), 7.90-7.92 (m, 2H), 7.98-8.01 (m, 2H), 11.45 (s, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  100.7, 115.0, 115.1, 120.4 (q,  $^1J_{\text{CF}} = 318$  Hz), 121.8, 126.0, 126.5, 127.1, 127.5, 128.3, 129.4, 130.0, 130.6, 131.0, 131.2, 132.3, 134.8, 135.2, 135.4, 143.0, 148.3; IR (KBr,  $\text{cm}^{-1}$ ): 3445, 1636, 1452;  $m/z$  (ESI): 414 ( $\text{M}^+\text{H}$ ); HRMS calcd for  $\text{C}_{23}\text{H}_{17}\text{BrN}_3$  ( $\text{M}^+\text{H}$ ): 414.0606, found: 414.0624.



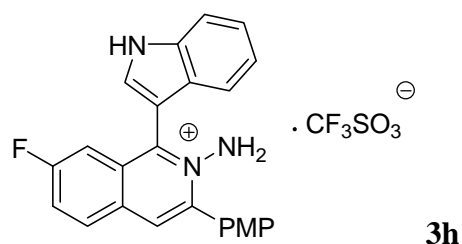
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ): 3.86 (s, 3H), 6.41 (s, 2H), 7.06-7.14 (m, 3H), 7.18-7.23 (m, 2H), 7.59-7.62 (m, 2H), 7.68-7.71 (m, 2H), 7.86-7.89 (m, 3H), 7.93 (s, 1H), 7.97 (d,  $J = 8.3$  Hz, 1H), 11.05 (s, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  55.6, 101.2, 113.6, 114.8, 119.4, 120.4 (q,  $^1J_{\text{CF}} = 318$  Hz), 121.8, 122.6, 123.6, 125.3, 125.5, 127.2, 128.1, 130.4, 130.6, 131.4, 131.6, 134.4, 135.2, 136.6, 142.8, 148.6, 161.6; IR (KBr,  $\text{cm}^{-1}$ ): 3449, 1636, 1450;  $m/z$  (ESI): 366 ( $\text{M}^+\text{H}$ ); HRMS calcd for  $\text{C}_{24}\text{H}_{20}\text{N}_3\text{O}$  ( $\text{M}^+\text{H}$ ): 366.1606, found: 366.1622.



$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ): 1.02 (t,  $J = 7.3$  Hz, 3H), 1.54-1.56 (m, 2H), 1.89-1.91 (m, 2H), 3.24-3.28 (m, 2H), 6.80 (s, 2H), 7.12-7.20 (m, 3H), 7.55 (t,  $J = 7.3$  Hz, 1H), 7.64 (d,  $J = 8.3$  Hz, 1H), 7.76-7.77 (m, 2H), 7.86 (t,  $J = 7.3$  Hz, 1H), 7.95 (t,  $J = 8.3$  Hz, 2H), 11.08 (s, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  13.7, 22.2, 28.8, 31.5, 100.8, 113.5, 118.6, 120.4 (q,  $^1J_{\text{CF}} = 318$  Hz), 121.9, 122.8, 123.7, 125.3, 126.6, 127.6, 129.9, 134.3, 135.4, 136.6, 146.3, 149.5; IR (KBr,  $\text{cm}^{-1}$ ): 3446, 1636, 1452;  $m/z$  (ESI): 316 ( $\text{M}^+\text{+H}$ ); HRMS calcd for  $\text{C}_{21}\text{H}_{22}\text{N}_3$  ( $\text{M}^+\text{+H}$ ): 316.1814, found: 316.1817.

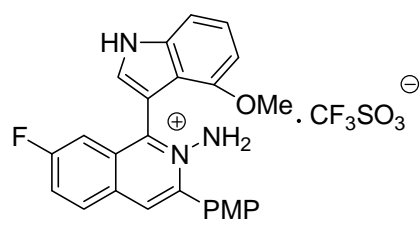


$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ): 6.37 (s, 2H), 7.11 (t,  $J = 7.3$  Hz, 1H), 7.18 (t,  $J = 7.3$  Hz, 1H), 7.23 (d,  $J = 7.8$  Hz, 1H), 7.48-7.53 (m, 4H), 7.57-7.62 (m, 2H), 7.71-7.74 (m, 2H), 7.85-7.86 (m, 1H), 7.97 (s, 1H), 8.01-8.05 (m, 1H), 11.12 (s, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  100.8, 113.4, 113.9 (d,  $^2J_{\text{CF}} = 24$  Hz), 119.2, 120.4 (q,  $^1J_{\text{CF}} = 318$  Hz), 121.9, 123.6, 124.9, 125.0 (d,  $^2J_{\text{CF}} = 25$  Hz), 125.4, 129.2, 129.7 (d,  $^3J_{\text{CF}} = 10$  Hz), 129.9, 130.3, 130.4, 131.0, 132.2, 136.5, 142.2, 147.6, 147.7, 162.7 (d,  $^1J_{\text{CF}} = 254$  Hz); IR (KBr,  $\text{cm}^{-1}$ ): 3445, 1636, 1450;  $m/z$  (ESI): 354 ( $\text{M}^+\text{+H}$ ); HRMS calcd for  $\text{C}_{23}\text{H}_{17}\text{FN}_3$  ( $\text{M}^+\text{+H}$ ): 354.1407, found: 354.1415.

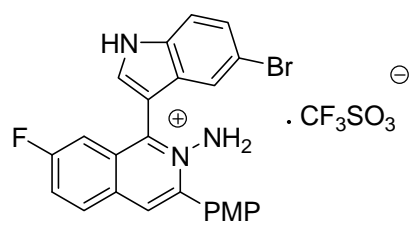


$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ): 3.82 (s, 3H), 6.48 (s, 2H), 7.03 (d,  $J = 7.3$  Hz, 2H), 7.11

(t,  $J = 7.3$  Hz, 1H), 7.18 (t,  $J = 6.8$  Hz, 1H), 7.23 (d,  $J = 7.8$  Hz, 1H), 7.48 (d,  $J = 9.2$  Hz, 1H), 7.57-7.63 (m, 2H), 7.69 (d,  $J = 8.3$  Hz, 2H), 7.87 (s, 1H), 7.97 (s, 1H), 8.01-8.04 (m, 1H), 11.16 (s, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  55.4, 100.9, 113.4, 113.8 (d,  $^2J_{\text{CF}} = 25$  Hz), 114.7, 119.2, 120.4 (q,  $^1J_{\text{CF}} = 318$  Hz), 121.8, 122.2, 123.6, 124.6, 124.9, 125.3, 129.5, 130.3, 131.0, 131.5, 132.2, 136.5, 142.2, 147.4, 161.5, 162.6 (d,  $^1J_{\text{CF}} = 254$  Hz); IR (KBr,  $\text{cm}^{-1}$ ): 3463, 1636, 1455;  $m/z$  (ESI): 384 ( $\text{M}^+\text{H}$ ); HRMS calcd for  $\text{C}_{24}\text{H}_{19}\text{FN}_3\text{O}$  ( $\text{M}^+\text{H}$ ): 384.1512, found: 384.1526.

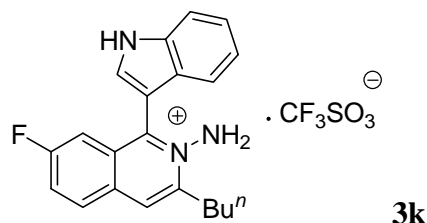


$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ): 3.64 (s, 3H), 3.81 (s, 3H), 6.27 (s, 2H), 6.53 (d,  $J = 8.0$  Hz, 1H), 7.03 (d,  $J = 8.8$  Hz, 2H), 7.11 (t,  $J = 8.0$  Hz, 1H), 7.20 (d,  $J = 8.4$  Hz, 1H), 7.47 (dd,  $J = 9.6, 2.4$  Hz, 1H), 7.59-7.64 (m, 4H), 8.00 (s, 1H), 8.03-8.07 (m, 1H), 11.03 (s, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  55.5, 55.6, 100.0, 101.7, 106.8, 113.8 (d,  $^2J_{\text{CF}} = 25$  Hz), 114.8, 115.7, 120.4 (q,  $^1J_{\text{CF}} = 318$  Hz), 122.9, 124.9, 125.1, 125.4, 128.9, 130.1 (d,  $^3J_{\text{CF}} = 10$  Hz), 130.4 (d,  $^3J_{\text{CF}} = 9$  Hz), 131.4, 132.6, 138.3, 142.8, 150.0, 152.3, 161.5, 162.7 (d,  $^1J_{\text{CF}} = 253$  Hz); IR (KBr,  $\text{cm}^{-1}$ ): 3446, 1618, 1514, 1464;  $m/z$  (ESI): 414 ( $\text{M}^+\text{H}$ ); HRMS calcd for  $\text{C}_{25}\text{H}_{21}\text{FN}_3\text{O}_2$  ( $\text{M}^+\text{H}$ ): 414.1618, found: 414.1636.

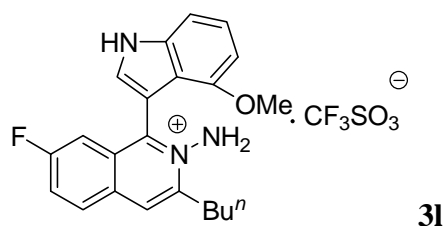


$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ): 3.78 (s, 3H), 6.50 (s, 2H), 7.00 (d,  $J = 8.8$  Hz, 2H), 7.22 (d,  $J = 8.8$  Hz, 1H), 7.37-7.39 (m, 2H), 7.45 (d,  $J = 8.8$  Hz, 1H), 7.59-7.67 (m, 3H), 7.85 (s, 1H), 8.03 (s, 1H), 8.05-8.09 (m, 1H), 11.31 (s, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  55.3, 100.3, 113.0 (d,  $^2J_{\text{CF}} = 24$  Hz), 114.6, 114.8, 114.9, 120.4 (d,  $^1J_{\text{CF}} =$

318 Hz), 121.7, 124.9 (d,  $^2J_{CF} = 25$  Hz), 125.7, 126.3, 129.4 (d,  $^3J_{CF} = 9$  Hz), 130.5, 131.3, 131.6, 132.2, 135.1, 142.0, 146.1, 146.2, 161.4, 162.6 (d,  $^1J_{CF} = 254$  Hz); IR (KBr,  $\text{cm}^{-1}$ ): 3447, 1628, 1456;  $m/z$  (ESI): 462 ( $M^+ + H$ ); HRMS calcd for  $C_{24}H_{18}BrFN_3O$  ( $M^+ + H$ ): 462.0617, found: 462.0630.

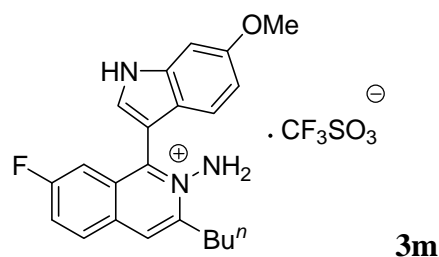


$^1H$  NMR (400 MHz,  $CDCl_3$ ): 1.00 (t,  $J = 7.2$  Hz, 3H), 1.47-1.57 (m, 2H), 1.85-1.92 (m, 2H), 3.16-3.30 (m, 2H), 6.86 (s, 2H), 7.10-7.22 (m, 3H), 7.37 (dd,  $J = 9.2, 2.0$  Hz, 1H), 7.58-7.64 (m, 2H), 7.78 (d,  $J = 2.4$  Hz, 1H), 7.96 (s, 1H), 7.99-8.03 (m, 1H), 11.09 (s, 1H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  12.8, 22.1, 28.8, 31.4, 101.4, 112.4, 112.6, 118.8, 120.4 (q,  $^1J_{CF} = 318$  Hz), 121.6, 123.4, 123.5, 124.6 (d,  $^2J_{CF} = 25$  Hz), 125.4, 129.2 (d,  $^3J_{CF} = 10$  Hz), 129.9, 130.5 (d,  $^3J_{CF} = 9$  Hz), 133.1, 136.9, 145.9, 148.7, 162.5 (d,  $^1J_{CF} = 251$  Hz); IR (KBr,  $\text{cm}^{-1}$ ): 3446, 1638, 1536, 1450;  $m/z$  (ESI): 334 ( $M^+ + H$ ); HRMS calcd for  $C_{21}H_{21}FN_3$  ( $M^+ + H$ ): 334.1720, found: 334.1730.

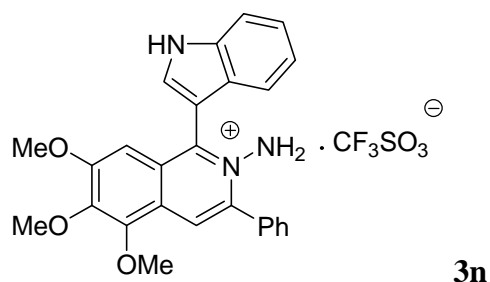


$^1H$  NMR (400 MHz,  $CDCl_3$ ): 0.98 (t,  $J = 6.9$  Hz, 3H), 1.44-1.52 (m, 2H), 1.82-1.89 (m, 2H), 3.11-3.18 (m, 1H), 3.31-3.37 (m, 1H), 3.58 (s, 3H), 6.53 (s, 1H), 6.55 (s, 2H), 7.12 (t,  $J = 8.3$  Hz, 1H), 7.23 (d,  $J = 8.3$  Hz, 1H), 7.39 (d,  $J = 7.8$  Hz, 1H), 7.56-7.63 (m, 2H), 8.00 (s, 1H), 8.03-8.07 (m, 1H), 11.15 (s, 1H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  13.8, 22.3, 29.5, 32.0, 55.5, 99.9, 101.7, 106.7, 113.6 (d,  $^2J_{CF} = 24$  Hz), 115.6, 120.4 (q,  $^1J_{CF} = 318$  Hz), 123.3, 125.0, 125.2 (d,  $^2J_{CF} = 25$  Hz), 128.5, 129.6 (d,  $^3J_{CF} = 11$  Hz), 129.9, 133.1, 138.4, 146.6, 151.8, 152.2, 162.3 (d,  $^1J_{CF} = 253$  Hz); IR (KBr,  $\text{cm}^{-1}$ ): 3446, 1638, 1507, 1456;  $m/z$  (ESI): 364 ( $M^+ + H$ ); HRMS calcd for  $C_{22}H_{23}FN_3O$

(M<sup>+</sup>+H): 364.1825, found: 364.1839.



<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 0.99 (t, *J* = 7.2 Hz, 3H), 1.46-1.53 (m, 2H), 1.81-1.87 (m, 2H), 3.13-3.26 (m, 2H), 3.75 (s, 3H), 6.77 (d, *J* = 8.4 Hz, 1H), 6.87 (s, 2H), 7.00 (d, *J* = 8.8 Hz, 1H), 7.14 (s, 1H), 7.39 (d, *J* = 8.8 Hz, 1H), 7.58 (t, *J* = 8.4 Hz, 1H), 7.63 (s, 1H), 7.87 (s, 1H), 7.93-7.97 (m, 1H), 10.94 (s, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 13.8, 22.3, 28.8, 31.5, 55.6, 95.9, 100.7, 113.0, 113.4 (d, <sup>2</sup>*J*<sub>CF</sub> = 25 Hz), 119.1, 119.4, 120.4 (q, <sup>1</sup>*J*<sub>CF</sub> = 318 Hz), 122.7, 125.0 (d, <sup>2</sup>*J*<sub>CF</sub> = 26 Hz), 128.6, 129.0 (d, <sup>3</sup>*J*<sub>CF</sub> = 11 Hz), 129.9 (d, <sup>3</sup>*J*<sub>CF</sub> = 9 Hz), 132.6, 137.9, 145.8, 148.4, 157.6, 162.4 (d, <sup>1</sup>*J*<sub>CF</sub> = 253 Hz); IR (KBr, cm<sup>-1</sup>): 3446, 1638, 1473, 1456; *m/z* (ESI): 364 (M<sup>+</sup>+H); HRMS calcd for C<sub>22</sub>H<sub>23</sub>FN<sub>3</sub>O (M<sup>+</sup>+H): 364.1825, found: 364.1843.



<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 3.66 (s, 3H), 4.07 (s, 3H), 4.08 (s, 3H), 6.31 (s, 2H), 7.00 (s, 1H), 7.13 (t, *J* = 7.3 Hz, 1H), 7.20-7.26 (m, 2H), 7.56-7.57 (m, 3H), 7.63 (d, *J* = 8.3 Hz, 1H), 7.73-7.74 (m, 2H), 8.02 (d, *J* = 3.0 Hz, 1H), 8.12 (s, 1H), 11.19 (s, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 56.3, 61.4, 61.8, 101.1, 104.2, 113.5, 119.2, 119.5, 120.4 (q, <sup>1</sup>*J*<sub>CF</sub> = 318 Hz), 121.4, 123.4, 125.0, 125.4, 127.4, 129.1, 129.9, 130.6, 130.8, 131.3, 136.6, 141.0, 146.2, 146.3, 147.0, 156.4; IR (KBr, cm<sup>-1</sup>): 3445, 1636, 1540, 1456; *m/z* (ESI): 426 (M<sup>+</sup>+H); HRMS calcd for C<sub>26</sub>H<sub>24</sub>N<sub>3</sub>O<sub>3</sub> (M<sup>+</sup>+H): 426.1818, found: 426.1837.



