Supporting Information 3

for

Addressing the Most Neglected Diseases through an Open Research Model: the Discovery of Fenarimols as Novel Drug Candidates for Eumycetoma

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**General Methods for Chemical Synthesis**

**Method A, Lithiation**

*n*-Butyllithium (1.5 equiv, 1.6 M solution in hexanes) was added dropwise to a solution of 3-bromopyridine (1.5 equiv) in dried diethyl ether at –78°C. After stirring for 30 min at –78°C, a solution of the 4-bromobenzaldehyde (1 equiv) in dried tetrahydrofuran was added. After stirring for 1 h at –78°C, the reaction was allowed to warm to –40°C, was quenched with a saturated solution of ammonium chloride and extracted with ethyl acetate. The organic phases were combined, dried (MgSO4) and concentrated under reduced pressure.

**Method B, Lithiation**

*n*-Butyllithium (2 equiv, 1.6 M solution in hexanes) was added dropwise to a solution of 4-bromobenzotrifluoride (2 equiv) in dried diethyl ether at –78°C. The reaction mixture was stirred for 2 h. A solution of diarylmethanone (1 equiv) in dried tetrahydrofuran was added dropwise at –78°C. The reaction was allowed to warm to rt overnight, was quenched with water and extracted with ethyl acetate. The organic phases were combined, dried (MgSO4) and concentrated under reduced pressure.

**Method C, Diarylalcohol Oxidation**

Activated manganese dioxide (3–7 equiv) was added to a solution of diarylalcohol (1 equiv) in dichloromethane. After being heated at reflux for 4 h, the reaction mixture was cooled and filtered through Celite. The filter cake was washed with dichloromethane. The filtrate was concentrated under reduced pressure.

**Method D, Cyanation**

A mixture of bromo-substituted fenarimol (1 equiv), potassium hexacyanoferrate(II) trihydrate (2 equiv), palladium(II) acetate (0.2 equiv), anhydrous sodium carbonate (2 equiv) and anhydrous *N*,*N*-dimethylacetamide was heated under nitrogen at 130°C overnight. After cooling, the reaction mixture was quenched with water. The aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with water, followed by brine, dried (MgSO4) and concentrated under reduced pressure.

**(4-Bromo-2-fluorophenyl)(pyridin-3-yl)methanol, S1**

Prepared according to Method A, using4-bromo-2-fluorobenzaldehyde (5.6 g, 0.027 mol) in tetrahydrofuran (20 mL) to give *the title compound* as a reddish brown waxy solid (7.3 g, 96%), used without further purification.**1H NMR** (500 MHz, Acetone-*d*6) δ 8.62 (d, *J* = 2.4 Hz, 1H), 8.46 (dd, *J* = 4.8, 1.7 Hz, 1H), 7.74 (ddd, *J* = 7.9, 2.5, 1.3 Hz, 1H), 7.65 (t, *J* = 8.1 Hz, 1H), 7.44 (dd, *J* = 8.4, 1.9 Hz, 1H), 7.37 – 7.24 (m, 2H), 6.13 (s, 1H). **19F NMR** (471 MHz, Acetone-*d*6) δ –116.62. **LRMS** *m/z* (ESI) 340 (87%), 338 (100%), 284 ([M+H]+, 20%), 282 ([M+H]+, 18%). **HRMS** (ESI) calcd. for C12H1081BrFNO+ 283.99093 and C12H1079BrFNO+ 281.99298 ([M+H]+), found 283.99035, 281.99242. **IR** (film): *ν*max 3123 (br), 2923, 2853, 1603, 1574, 1479, 1425, 1398 cm–1. Spectroscopic data matched those in the literature.[1](#_ENREF_1) However, literature characterisation was incomplete.

**(4-Bromo-2-fluorophenyl)(pyridin-3-yl)methanone, S2**

Prepared according to Method C, using activated manganese dioxide (5.8 g, 0.025 mol) and a solution of **S1** (6.7 g, 0.076 mol) in dichloromethane (55 mL). The crude mixture was purified by column chromatography to give *the title compound* as a cream solid (0.83 g, 12%) and recovered **S1** as a reddish brown waxy solid (3.4 g, 50%). **m.p.** 55.7 – 58.3°C, no lit. m.p. **1H NMR** (500 MHz, Acetone-*d*6) δ 8.98 – 8.93 (m, 1H), 8.84 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.21 – 8.16 (m, 1H), 7.66 – 7.61 (m, 3H), 7.59 (ddd, *J* = 7.9, 4.9, 0.9 Hz, 1H). **13C NMR** (126 MHz, Acetone-*d*6) δ 190.6, 160.0 (d, *J* = 255.7 Hz), 153.8, 150.4 (d, *J* = 1.7 Hz), 136.5, 132.8, 132.3 (d, *J* = 3.3 Hz), 128.3 (d, *J* = 3.7 Hz), 126.4 (d, *J* = 9.6 Hz), 125.3 (d, *J* = 14.5 Hz), 123.7, 120.0 (d, *J* = 25.2 Hz). **19F NMR** (471 MHz, Acetone-*d*6) δ –109.99. **LRMS** *m/z* (ESI) 340 (87%), 338 (100%), 304 ([M+Na]+, 27%), 302 ([M+Na]+, 21%), 282 ([M+H]+, 27%), 280 ([M+H]+, 23%). **HRMS** (ESI) calcd. for C12H881BrFNO+ 281.97528 and C12H879BrFNO+ 279.97733 ([M+H]+), found 281.97476, 279.97677. **IR** (film): *ν*max 3007, 1654 (s), 1584, 1417, 1395 cm–1. **Anal.** cald. for C12H7BrFNO: C 51.46, H 2.52, N 5.00 %, found C 51.35, H 2.11, N 4.89 %. Spectroscopic data matched those in the literature.[1](#_ENREF_1) However, literature characterisation was incomplete.

**(4-Bromo-2-fluorophenyl)(pyridin-3-yl)(4-(trifluoromethyl)phenyl)methanol, S3**

Prepared according to Method B, using 4-bromobenzotrifluoride (0.90 mL, 0.0054 mol) in diethyl ether (45 mL), *n*-butyllithium (3.8 mL, 1.6 M solution in hexanes, 0.0053 mol) and a solution of **S2** (0.74 g, 0.0027 mol) in tetrahydrofuran (30 mL). The crude mixture was purified by column chromatography (ethyl acetate/hexane) to give *the title compound* as an orange solid (0.40 g, 35%).**m.p.** 167.1–169.0°C, no lit. m.p. **1H NMR** (500 MHz, Acetone-*d*6) δ 8.55 (s, 1H), 8.50 (d, *J* = 4.8 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 3H), 7.62 (d, *J* = 8.2 Hz, 2H), 7.46 (d, *J* = 4.5 Hz, 1H), 7.41 – 7.29 (m, 2H), 6.09 (s, 1H). **13C NMR** (126 MHz, Acetone-*d*6) δ 160.6 (d, *J* = 252.7 Hz), 150.3, 149.7 (d, *J* = 2.2 Hz), 149.5, 141.4, 135.7 (d, *J* = 1.9 Hz), 133.6 (d, *J* = 11.4 Hz), 131.5 (d, *J* = 3.8 Hz), 130.0 (q, *J* = 32.1 Hz), 129.0 (d, *J* = 1.9 Hz), 128.4 (d, *J* = 3.3 Hz), 125.9 (q, *J* = 3.8 Hz), 125.3 (q, *J* = 271.3 Hz), 123.8, 123.0 (d, *J* = 9.5 Hz), 120.6 (d, *J* = 26.2 Hz), 78.7. **LRMS** *m/z* (ESI) 428 ([M+H]+, 91%), 426 ([M+H]+, 100%), 348 (22%), 340 (27%), 338 (32%), 333 (17%), 332 (24%). **HRMS** (ESI) calcd. for C19H1381BrF4NO+ 428.00962 and C19H1379BrF4NO+ 426.01166 ([M+H]+), found 428.00934, 426.01138. **IR** (film): *ν*max 3096 (br), 1601, 1567, 1477, 1419, 1324 cm–1. Spectroscopic data matched those in the literature.[1](#_ENREF_1) However, literature characterisation was incomplete.

**3-Fluoro-4-(hydroxy(pyridin-3-yl)(4-(trifluoromethyl)phenyl)methyl)benzonitrile, S4, EPL-BS0800**

Prepared according to Method D, using **S3** (0.20 g, 0.45 mmol), potassium hexacyanoferrate(II) trihydrate (0.42 g, 0.95 mmol), palladium acetate (0.031 g, 0.062 mmol), anhydrous sodium carbonate (0.057 g, 0.93 mmol) and anhydrous *N*,*N*-dimethylacetamide (2.3 mL). The crude product was purified with column chromatography (hexane/ethyl acetate) to obtain *the title compound* as a pale straw-coloured fine solid (55 mg, 32%). **m.p.** 129.5–132.1°C, no lit. m.p.  **1H NMR** (500 MHz, Acetone-*d*6) δ 8.57 (d, *J* = 2.5 Hz, 1H), 8.53 (dd, *J* = 4.8, 1.6 Hz, 1H), 7.82 (t, *J* = 8.0 Hz, 1H), 7.77 – 7.69 (m, 4H), 7.66 – 7.58 (m, 3H), 7.38 (ddd, *J* = 8.1, 4.7, 0.8 Hz, 1H), 6.22 (s, 1H). **13C NMR** (126 MHz, Acetone-*d*6) δ 160.2 (d, *J* = 251.0 Hz), 149.8, 149.7 (d, *J* = 2.3 Hz), 140.8, 139.5 (d, *J* = 11.4 Hz), 135.7 (d, *J* = 2.1 Hz), 131.1 (d, *J* = 3.8 Hz), 130.4 (q, *J* = 32.2 Hz), 129.5 (d, *J* = 3.7 Hz), 129.0 (d, *J* = 1.9 Hz), 126.0 (q, *J* = 3.8 Hz), 125.2 (q, *J* = 271.2 Hz), 123.9, 121.0 (d, *J* = 26.8 Hz), 117.9 (d, *J* = 2.7 Hz), 114.6 (d, *J* = 10.0 Hz), 78.9 (1 obscured signal). **19F NMR** (471 MHz, Acetone-*d*6) δ –63.07, –104.20. **HRMS** (ESI) calcd. for C20H13F4N2O+ 373.09640 ([M+H]+), found 373.09610. **IR** (film): *ν*max 3077 (br), 2241, 1617, 1562, 1490, 1411, 1325 cm–1. Spectroscopic data matched those in the literature.[1](#_ENREF_1) However, literature characterisation was incomplete.

**(4-Bromophenyl)(pyridin-3-yl)methanol, S5**

Prepared according to Method A, using 4-bromobenzaldehyde (10 g, 0.054 mol) to give *the title compound* as an orange solid (13 g, 95%), used without further purification. **1H NMR** (500 MHz, Acetone-*d*6) δ 8.63 (d, *J* = 2.3 Hz, 1H), 8.44 (dd, *J* = 4.7, 1.7 Hz, 1H), 7.77 – 7.69 (m, 1H), 7.55 – 7.47 (m, 2H), 7.44 – 7.36 (m, 2H), 7.30 (ddd, *J* = 7.8, 4.8, 0.9 Hz, 1H), 5.92 (s, 1H). **13C NMR** (126 MHz, Acetone-*d*6) δ 148.5, 148.3, 144.2, 140.2, 133.7, 131.3, 128.4, 123.2, 120.5, 72.5. **LRMS** *m/z* (ESI) 322 (100%), 320 (95%), 266 ([M+H]+, 28%), 264 ([M+H]+, 27%). **HRMS** (ESI) calcd. for C12H1081BrNONa+ 287.98230, C12H1079BrNONa+ 285.98435 ([M+Na]+), found 287.98208, 285.98414. **IR** (film): *ν*max 3149 (br), 2856, 1588, 1578, 1486, 1474, 1424, 1396 cm–1. No spectroscopic data available for comparison.

**(4-Bromophenyl)(pyridin-3-yl)methanone, S6**

Prepared according to Method C, using activated manganese dioxide (21 g, 0.24 mol) and a solution of **S5** (12 g, 0.045 mol) in dichloromethane (75 mL). The crude mixture was purified by column chromatography to give *the title compound* as a cream solid (7.8 g, 69 %) and recovered **S5** as an orange solid (1.4 g, 12%). **m.p.** 123.3–125.3°C, no lit. m.p. **1H NMR** (500 MHz, Acetone-*d*6) δ 8.94 (dd, *J* = 2.3, 0.9 Hz, 1H), 8.83 (dd, *J* = 4.9, 1.7 Hz, 1H), 8.15 (dt, *J* = 7.9, 2.0 Hz, 1H), 7.86 – 7.69 (m, 4H), 7.58 (ddd, *J* = 7.9, 4.8, 0.9 Hz, 1H). **13C NMR** (126 MHz, Acetone-*d*6) δ 193.5, 153.0, 150.4, 136.8, 136.0, 132.8, 131.9, 131.6, 127.4, 123.4. **LRMS** *m/z* (ESI) 286 ([M+Na]+, 100%), 284 ([M+Na]+, 79%), 264 ([M+H]+, 45%), 262 ([M+H]+, 44%). **HRMS** (ESI) calcd. for C12H881BrNONa+ 285.96665 and C12H879BrNONa+ 283.96870 ([M+Na]+), found 285.96649, 283.96851. **IR** (film): *ν*max 1650 (s), 1581, 1479, 1414, 1393, 1337 cm–1. **Anal.** cald. for C12H8BrNO: C 54.99, H 3.08, N 5.34 %, found C 54.98, H 2.84, N 5.26 %. No spectroscopic data available for comparison.



**(4-Bromophenyl)(pyridin-3-yl)(4-(trifluoromethyl)phenyl)methanol, S7**

Prepared according to Method B, using 4-bromobenzotrifluoride (1.5 mL, 0.011 mol) in diethyl ether (145 mL), *N*-butyllithium (6.6 mL, 1.6 M solution in hexanes, 0.011 mol) and a solution of **S6** (1.5 g, 0.0053 mol) in tetrahydrofuran (90 mL). The crude mix was purified by column chromatography (ethyl acetate/hexane) to give *the title compound* as a straw coloured solid (0.14 g, 5.8%) and recovered **S6** as a cream solid (0.18 g, 12%). **1H NMR** (500 MHz, Acetone-*d*6) δ 8.52 (dd, *J* = 2.5, 0.8 Hz, 1H), 8.50 (dd, *J* = 4.7, 1.6 Hz, 1H), 7.81 – 7.75 (m, 1H), 7.69 (tdd, *J* = 8.7, 2.6, 1.6 Hz, 2H), 7.63 – 7.48 (m, 4H), 7.36 (ddd, *J* = 8.0, 4.8, 0.9 Hz, 1H), 7.32 – 7.19 (m, 2H). **13C NMR** (126 MHz, Acetone-*d*6) δ 150.1, 149.5, 148.7 (d, *J* = 3.5 Hz), 146.5 (d, *J* = 3.9 Hz), 142.7 (d, *J* = 3.6 Hz), 136.0, 132.7, 132.0, 130.8, 130.7 (q, *J* = 31.9 Hz), 129.9, 125.3 (q, *J* = 271.6 Hz), 125.1 (q, *J* = 3.9 Hz), 124.9 (q, *J* = 4.0 Hz), 123.8, 122.1, 80.4 (d, *J* = 10.3 Hz). **19F NMR** (471 MHz, Acetone-*d*6) δ -63.04. **LRMS** *m/z* (ESI) 410 ([M+H]+, 94%), 408 ([M+H]+, 100%). **HRMS** (ESI) calcd. for C19H1481BrF3NO+ 410.01904 and C19H1479BrF3NO+ 408.02109 ([M+H]+), found 410.01868, 408.02072. **IR** (film): *ν*max 3066 (br), 2782, 1589, 1486, 1420, 1394, 1326 cm–1. **Anal.** cald. C 67.80, H 3.70, N 7.84 %, found C 67.50, H 3.03, N 7.82 %. All data support isolation of a pure product, but the %H value is slightly outside tolerance limits that is not easily accounted for by typical solvent or water inclusion. No spectroscopic data available for comparison.

**4-(Hydroxy(pyridin-3-yl)(4-(trifluoromethyl)phenyl)methyl)benzonitrile, S8**

Prepared according to the cyanation general reaction, using **S7** (150 mg, 0.42 mmol), potassium hexacyanoferrate(II) trihydrate (0.35 g, 0.79 mmol), palladium acetate (0.031 g, 0.062 mmol), anhydrous sodium carbonate (63 mg, 1.0 mmol) and anhydrous *N*,*N*-dimethylacetamide (1.8 mL). The crude product was purified with column chromatography (hexane/ethyl acetate) to obtain *the title compound* as a pale straw coloured fine solid (69 mg, 53%). **1H NMR** (500 MHz, Acetone-*d*6) δ 8.55 – 8.47 (m, 2H), 7.89 – 7.75 (m, 3H), 7.70 (ddd, *J* = 8.2, 4.2, 2.1 Hz, 2H), 7.66 – 7.47 (m, 4H), 7.37 (dd, *J* = 8.0, 4.8 Hz, 1H). **13C NMR** (126 MHz, Acetone-*d*6) δ 152.1 (d, *J* = 5.0 Hz), 150.1, 149.7, 148.1 (d, *J* = 5.1 Hz), 142.3 (d, *J* = 5.2 Hz), 136.1, 132.9, 132.7, 130.9 (q, *J* = 32.0 Hz), 130.0, 129.6, 125.3 (q, *J* = 3.8 Hz), 125.2 (q, *J* = 271.7 Hz), 124.9 (q, *J* = 3.9 Hz), 123.9, 119.1, 112.3, 80.5 (d, *J* = 10.8 Hz). **LRMS** *m/z* (ESI) 707 ([2M–H]–, 88%), 353 ([M–H]–, 100%). **HRMS** (ESI) calcd. for C20H14F3N2O+ 355.10582, found 355.10543 ([M+H]+). **IR** (film): *ν*max 3055 (br), 2230 (w), 1606, 1592, 1578, 1501, 1476, 1420, 1327 cm–1. No spectroscopic data available for comparison.

**(4-Chloro-2-fluorophenyl)(pyridin-3-yl)methanol, S9**

Prepared according to Method A, using 4-chloro-2-fluorobenzaldehyde (4.4 g, 0.027 mol) to give *the title compound* as a reddish orange waxy solid (5.6 g, 88%), used without further purification. **1H NMR** (500 MHz, Acetone-*d*6) δ 8.62 (d, *J* = 2.4 Hz, 1H), 8.46 (dd, *J* = 4.7, 1.7 Hz, 1H), 7.92 – 7.57 (m, 2H), 7.51 – 7.26 (m, 2H), 7.20 (m, 1H), 6.14 (s, 1H). **13C NMR** (126 MHz, Acetone-*d*6) δ 160.3 (d, *J* = 248.7 Hz), 149.6, 149.2 (d, *J* = 1.6 Hz), 139.9, 134.6, 134.3 (d, *J* = 10.5 Hz), 131.7 (d, *J* = 13.7 Hz), 129.9 (d, *J* = 5.2 Hz), 125.7 (d, *J* = 3.6 Hz), 124.2, 116.6 (d, *J* = 25.4 Hz), 67.6. **19F NMR** (471 MHz, Acetone-*d*6) δ –116.82. **LRMS** *m/z* (ESI) 296 (27%), 294 (100%), 240 ([M+H]+, 2%), 238 ([M+H]+, 8%). **HRMS** (ESI) calcd. for C12H1037ClFNO+ 240.04054 and C12H1035ClFNO+ 238.04350 ([M+H]+), found 240.04000, 238.04295. **IR** (film): *ν*max 3113 (br), 2929, 1609, 1578, 1482, 1426, 1402 cm–1. No spectroscopic data available for comparison.

***tert*-Butyl 4-((4-chloro-2-fluorophenyl)(pyridin-3-yl)methyl)piperazine-1-carboxylate, S10**

Thionyl chloride (3.6 mL, 0.047 mol) was added to a solution of **S9** (5.0 g, 0.023 mol) in dichloromethane (100 mL) at 0°C. The reaction mixture was allowed to warm to room temperature over 2 h, quenched with a saturated solution of sodium carbonate (100 mL) and extracted with dichloromethane (3 × 100 mL). The organic phases were combined, washed with brine (2 × 75 mL), dried (MgSO4) and concentrated under reduced pressure to give the aryl chloride intermediate **S9a** as a crude light brown oil (3.3 g, 66%), used without further purification.

Anhydrous triethylamine (3.6 mL, 0.026 mol) and dried potassium iodide (1 small spatula tip) were added to a solution of **S9a** (3.0 g) and *tert*-butyl piperazine-1-carboxylate (3.6 g, 0.019 mol) in anhydrous acetonitrile (25 mL). After being heated at 80°C for 48 h, the reaction mixture was cooled and concentrated under reduced pressure. The concentrated residue was partitioned between dichloromethane (100 mL) and a saturated solution of sodium carbonate (100 mL). The aqueous layer was extracted with dichloromethane (2 × 50 mL). The organic phases were combined, dried (MgSO4) and concentrated under reduced pressure to give a crude orange oil. The crude oil was purified with column chromatography to give *the title compound* as an amber resin (3.5 g, 75%). **1H NMR** (200 MHz, Chloroform-*d*) δ 8.59 (d, *J* = 2.2 Hz, 1H), 8.41 (dd, *J* = 4.8, 1.6 Hz, 1H), 7.64 (dt, *J* = 7.9, 2.0 Hz, 1H), 7.46 (t, *J* = 8.0 Hz, 1H), 7.16 (ddd, *J* = 7.9, 4.8, 0.9 Hz, 1H), 7.12 – 6.99 (m, 1H), 6.96 (dd, *J* = 9.9, 2.1 Hz, 1H), 4.64 (s, 1H), 3.38 (t, *J* = 5.1 Hz, 4H), 2.69 – 2.18 (m, 4H), 1.38 (s, 9H). **13C NMR** (75 MHz, Chloroform-*d*) δ 160.3 (d, *J* = 250.1 Hz), 154.6, 149.6, 148.9, 136.3, 135.4, 133.8 (d, *J* = 10.5 Hz), 129.5 (d, *J* = 4.7 Hz), 126.8 (d, *J* = 12.7 Hz), 125.1 (d, *J* = 3.4 Hz), 123.6, 116.5 (d, *J* = 26.1 Hz), 79.6, 64.3, 51.4, 28.4 (1 obscured signal). **LRMS** 430 ([M+Na]+, 35%), 428 ([M+Na]+, 100%), 408 ([M+H]+, 7%), 406 ([M+H]+, 19%). **HRMS** (ESI) calcd. for C21H2537ClFN3O2Na+ 430.14875 and C21H2535ClFN3O2Na+ 428.15170 ([M+Na]+), found 430.14882, 428.15181. **IR** (film): *ν*max 2974, 2814, 1688 (s), 1608, 1578, 1480, 1420, 1365 cm–1. No spectroscopic data available for comparison.

**Ethyl 4-((4-chloro-2-fluorophenyl)(pyridin-3-yl)methyl)piperazine-1-carboxylate, S11, EPL-BS0495**

Trifluoroacetic acid (6 mL, 0.080 mol) was added to a solution of **S10** (3.2 g, 0.0078 mol) and methanol (11 drops) in dichloromethane (35 mL) at 0°C. After stirring at 0°C for 1 h, the reaction mixture was allowed to warm to room temperature overnight, concentrated under reduced pressure to give the crude trifluoroacetic acid salt intermediate **S10a** (6.4 g), used without further purification.

Anhydrous triethylamine (25 mL, 0.18 mol) and ethyl chloroformate (0.75 mL 0.0075 mol) were added to a solution of **S10a** (6.4 g) in dichloromethane (50 mL) at 0°C. The reaction mixture was allowed to warm to rt overnight, quenched with a saturated solution of ammonium chloride (30 mL) and extracted with dichloromethane (3 × 30 mL). The organic phases were combined, dried (MgSO4) and concentrated under reduced pressure. The crude product was purified with column chromatography (ethyl acetate/hexane) to give *the title compound* as an amber resin (2.0 g, 65%). **1H NMR** (500 MHz, Chloroform-*d*) δ 8.63 (d, *J* = 2.2 Hz, 1H), 8.47 (dd, *J* = 4.8, 1.6 Hz, 1H), 7.68 (dt, *J* = 7.9, 2.0 Hz, 1H), 7.50 (t, *J* = 8.0 Hz, 1H), 7.22 (ddd, *J* = 7.9, 4.7, 0.8 Hz, 1H), 7.13 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.03 (dd, *J* = 9.9, 2.1 Hz, 1H), 4.69 (s, 1H), 4.10 (q, *J* = 7.1 Hz, 2H), 3.47 (t, *J* = 5.1 Hz, 4H), 2.55 – 2.07 (m, 4H), 1.22 (t, *J* = 7.1 Hz, 3H). **13C NMR** (126 MHz, Chloroform-*d*) δ 160.4 (d, *J* = 250.0 Hz), 155.5, 149.8, 149.1, 136.4, 135.5, 134.0 (d, *J* = 10.6 Hz), 129.6 (d, *J* = 4.7 Hz), 126.8 (d, *J* = 12.8 Hz), 125.2 (d, *J* = 3.5 Hz), 123.8, 116.7 (d, *J* = 26.0 Hz), 64.4 (d, *J* = 1.7 Hz), 61.5, 51.5, 43.8, 14.8. **LRMS** *m/z* (ESI) 402 ([M+Na]+, 37%), 400 ([M+Na]+, 100%). **HRMS** (ESI) calcd. for C19H2137ClFN3O2Na+ 402.11745 and C19H2135ClFN3O2Na+ 400.12040 ([M+Na]+), found 402.11709 and 400.12007. **IR** (film): *ν*max 2923, 2853, 1603, 1574, 1479, 1425, 1398 cm–1. No spectroscopic data available for comparison.

**Cetirizine hydrochloride, S12**

Purchased from Sigma Aldrich. **1H NMR** (500 MHz, Deuterium Oxide) δ 7.63 – 7.59 (m, 2H), 7.58 – 7.44 (m, 5H), 7.45 – 7.37 (m, 2H), 5.38 (s, 1H), 4.24 (s, 2H), 4.07 – 3.83 (m, 2H), 3.72 (s, 4H), 3.58 – 3.52 (m, 2H), 3.49 (s, 4H). **13C NMR** (126 MHz, Deuterium Oxide) δ 174.5, 135.1, 133.7, 132.6, 129.9, 129.8, 129.5, 127.9, 74.7, 67.5, 63.9, 55.9, 49.1, 48.3 (1 obscured signal). **LRMS** *m/z* (ESI) 413 ([M+Na]+, 38%), 411 ([M+Na]+, 100%), 391 ([M+H]+, 28%), 389 ([M+H]+, 76%), 203 ([M–(C8H15N2O3)–]+, 15%), 201 ([M–(C8H15N2O3)–]+, 40%). **HRMS** (ESI) calcd. for C21H2637ClN2O3+ 391.16025 and C21H2635ClN2O3+ 389.16320 ([M+H]+), found 391.15987, 389.16286. Spectroscopic data matched those in the literature.[2-3](#_ENREF_2)



**References**

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