Supporting Information

Structural Modifications on Tetrahydropyridine-3-Carboxylate Esters en route to the Discovery of M_5 Preferring Muscarinic Receptor Orthosteric Antagonists

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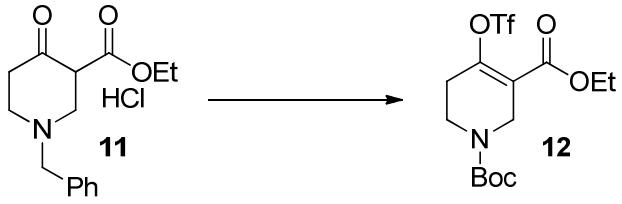
Synthetic Procedures and Tabulated Data

General Methods. All purchased reagents and solvents were used without further purification unless otherwise noted. All reaction sensitive to air and/or moisture were carried out under Argon atmosphere in oven-dried glassware. Flash column chromatography was carried out using 32-63 μm, 60 Å (230-400 mesh) silica gel. Analytical thin layer chromatography was carried out on glass plates precoated with 250 μm silica gel 60 F254. NMR spectra were recorded in $CDCl_3$ on a Varian 300 MHz or 500 MHz spectrometer and chemical shifts are reported in ppm relative to tetramethylsilane as internal standard. Coupling constants are reported in hertz (Hz). Mass spectra were recorded on a JEOL JMS-700T MStation. GC-Mass spectra were recorded on an Agilent 6890 GC incorporating an Agilent 7683 autosampler and an Agilent 5973 MSD. Elemental analyses were carried out on a COSTECH elemental combustion system and are within ±0.4% of theory. All final compounds for biological testing were prepared as salts in ≥ 95% purity, in accord with results from combustion analysis.

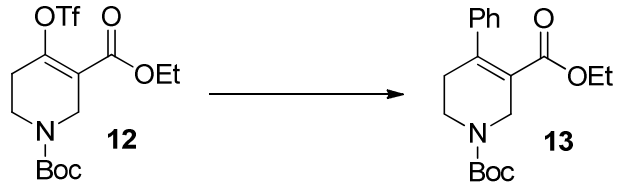
1-*tert*-Butyl 3-ethyl 4-triflate-5,6-dihydropyridine-1,3(*2H*)-dicarboxylate 12.



To a solution of ethyl 1-benzyl-4-oxopiperidine-3-carboxylate hydrochloride (**11**, 100 g, 0.336 mol) in EtOH (1 L) was carefully added Pd/C (10%, 5 g). The mixture was degassed with H_2 and stirred under a hydrogen balloon for 24 h. The catalyst was removed by filtration through a Celite pad. The filter cake was rinsed with EtOH, and the combined organic portions were concentrated under reduced pressure. The resulting residue was recrystallized from EtOH/Et_2O to afford ethyl 4-oxopiperidine-3-carboxylate hydrochloride as an off-white crystal (65 g, 93%

yield). A solution of $(Boc)_2O$ (52 g, 240 mmol) in CH_2Cl_2 (100 mL) was added dropwise to a stirred mixture of above product (41.50 g, 200 mmol), Et_3N (41.8 mL, 300 mmol) and CH_2Cl_2 (150 mL). The resulting mixture was stirred at room temperature overnight and washed with 1.0 N HCl (200 mL × 2) and brine (200 mL × 2), dried over Na_2SO_4, filtered and concentrated to dryness to afford a white solid (quantitative yield), which was used in the next step without further purification. To a cooled (- 78 °C) solution of the above *N*-Boc product (39 g, 144 mmol) in CH_2Cl_2 (400 mL) was added iPr$_2$NH (61 mL, 431 mmol). After stirring for 30 min at the same temperature, Tf_2O was added slowly and continued to stir for 1 h. Half saturated aqueous NH_4Cl (300 mL) was added to quench the reaction. The aqueous phase was extracted with CH_2Cl_2 (100 mL × 2). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated under vacuum. The residue was purified by silica gel column chromatography (10:1 hexanes:EtOAc) to afford **12** (50 g, 86% yield for two steps) as a colorless oil. ^{1}H NMR (300 MHz): δ 4.16-4.37 (m, 4H), 3.63 (t, J = 5.7 Hz, 2H), 2.51 (m, 2H), 1.22-1.60 (m, 12H) ppm; EI-MS *m/z* 388 $(M-15)^+$.

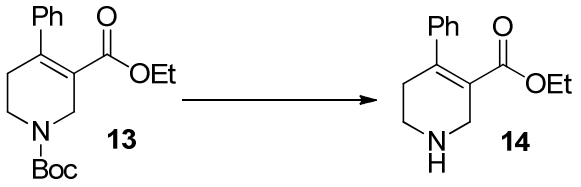
1-*tert*-Butyl 3-ethyl 4-phenyl-5,6-dihydropyridine-1,3(*2H*)-dicarboxylate 13.



A mixture of compound **12** (11.76 g, 29.15 mmol), phenylboronic acid (4.27 g, 34.98 mmol), Na_2CO_3 (2.0 M, 45 mL), and THF (200 mL) was degassed by purging N_2. $Pd(PPh_3)_4$ (101 mg, 0.087 mmol) was added and the mixture was heated at 65 °C for 4 h. Standard Suzuki coupling workup followed by silica gel column purification (20:1 hexanes:EtOAc) to afford **13** (8.91 g, 92% yield) as a white solid. ^{1}H NMR (300 MHz): δ 7.23-7.27 (m, 3H), 7.13 (dd, J = 7.2, 2.4 Hz,

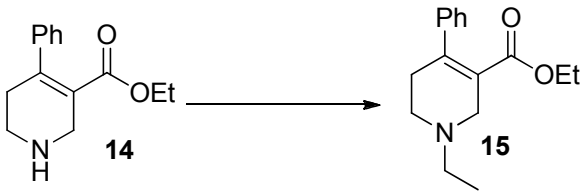
2H), 4.26 (s, 2H), 3.93 (q, J = 7.2 Hz, 2H), 3.61 (t, J = 5.7 Hz, 2H), 2.50 (m, 2H), 1.40-1.57 (m, 9H), 0.90 (t, J = 7.2 Hz, 3H) ppm; EI-MS *m/z* 331 (M^+).

Ethyl 4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 14.



To a cooled (ice bath) solution of compound **13** (3.96 g, 11.95 mmol) in CH_2Cl_2 (15 mL) was added TFA (15 mL). The resulting mixture was brought back to room temperature and stirred for 30 min. Standard workup followed by silica gel column purification (10:1 CH_2Cl_2:MeOH) to afford **14** (1.83 g, 66% yield) as a white solid. ^{1}H NMR (300 MHz): δ 9.96 (br, 1H), 7.30-7.40 (m, 3H), 7.12 (dd, J = 5.4, 1.5 Hz, 2H), 4.04 (s, 1H), 3.92 (q, J = 7.2 Hz, 2H), 3.41 (br, 2H), 2.77 (br, 2H), 0.87 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (75 MHz): δ 165.0, 147.4, 140.4, 128.3, 128.2, 126.7, 120.4, 61.1, 42.3, 40.6, 29.9, 13.7 ppm; EI-MS *m/z* 231 (M^+).

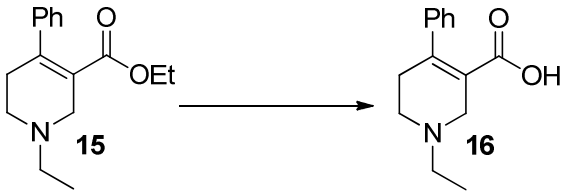
Ethyl 1-ethyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 15.



A mixture of **14** (2.68 g, 11.59 mmol), EtI (2.71 g, 17.38 mmol), and K_2CO_3 (3.20 g, 23.18 mmol) in EtOH (60 mL) was stirred at room temperature for 24 h. Solvent was removed under vacuum. The residue was dissolved in water (30 mL) and extracted with CH_2Cl_2 (30 mL × 3). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated under vacuum. The residue was purified by silica gel column chromatography (2:1 hexanes:EtOAc) to afford **15** (2.55 g, 85% yield) as a light yellow oil. ^{1}H NMR (300 MHz): δ 7.22-7.35 (m, 3H), 7.14 (dd, J =

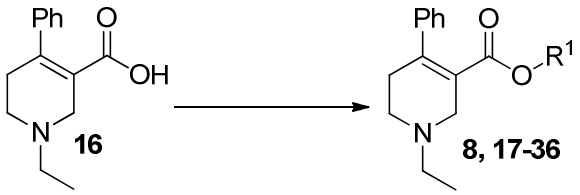
7.8, 1.8 Hz, 2H), 3.88 (q, *J* = 7.2 Hz, 2H), 3.35 (t, *J* = 2.4 Hz, 2H), 2.67 (t, *J* = 5.1 Hz, 2H), 2.50-2.62 (m, 4H), 1.19 (t, *J* = 7.5 Hz, 3H), 0.85 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (75 MHz): δ 167.4, 146.3, 142.4, 140.2, 128.0, 127.2, 126.9, 125.7, 60.2, 53.1, 52.1, 49.6, 34.1, 13.8, 12.5 60.3, 60.2, 53.3, 50.1, 34.11, 33.99, 13.8 ppm; EI-MS *m/z* 259 (M^+).

1-Ethyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylic acid 16.



To a solution of **15** (3.30 g, 12.72 mmol) in EtOH (40 mL) was slowly added aqueous KOH (10%, 40 mL). The mixture was stirred at room temperature overnight. The solution was extracted with Et_2O (40 mL × 3) and then CH_2Cl_2 (40 mL × 2). The pH of the aqueous phase was adjusted to 6.0 using 2.0 N HCl. Water was removed under vacuum. MeOH (20 mL) was added to the residue and stirred for 2 h, filtered, and rinsed with MeOH. Combined MeOH solution was concentrated to dryness under vacuum. The residue was co-evaporated with CH_2Cl_2 (three times) to remove trace amount of MeOH and the resulting white solid was dried under vacuum for 24 h. 3.22 g of **16** was obtained and used for the next step without further purification.

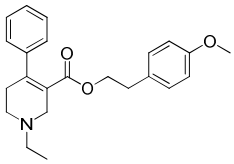
General procedure for synthesis of 8, 17-36.



To a suspension of **16** (1 eq) in CH_2Cl_2 (5 mL per 1 mmol of acid) was added EDCI (1.5 eq), DMAP (0.2 eq), and then alcohol (1.2 eq). The resulting mixture was stirred at room temperature overnight. CH_2Cl_2 (two volume) was added and the mixture was washed subsequently with

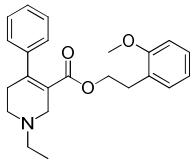
saturated $NaHCO_3$, water, and brine. The organic layer was dried over Na_2SO_4, filtered and concentrated under vacuum. The crude product **8**, **17-36** was purified by silica gel column chromatography (2:1 hexanes:EtOAc then CH_2Cl_2:MeOH 20:1). All of the final compounds were converted to their hydrochloride salts with 1.0 N HCl in Et_2O, and then stirred in dry Et_2O until white solids were obtained. The solids were filtered under a N_2 flow, rinsed with Et_2O, and dried under vacuum in a desiccator for 24 h.

4-Methoxyphenethyl 1-ethyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 8.



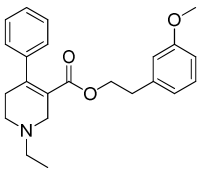
This product was obtained as a colorless oil (135 mg, 55% yield from **15**). ^{1}H NMR (500 MHz): δ 7.23-7.32 (m, 3H), 7.13 (dd, *J* = 8.0, 1.5 Hz, 2H), 6.93 (d, *J* = 9.0 Hz, 2H), 6.76 (d, *J* = 8.5 Hz, 2H), 4.02 (t, *J* = 7.5 Hz, 2H), 3.74 (s, 3H), 3.31 (t, *J* = 1.5 Hz, 2H), 2.66 (t, *J* = 5.5 Hz, 2H), 2.53-2.60 (m, 4H), 2.46 (t, *J* = 7.5 Hz, 2H), 1.17 (t, *J* = 7.0 Hz, 3H) ppm; 13C NMR (125 MHz): δ 167.2, 158.3, 146.6, 142.3, 129.9, 129.8, 128.0, 127.3, 126.9, 125.4, 113.9, 65.0, 55.2, 52.8, 51.8, 49.4, 33.8, 33.7, 12.2 ppm; EI-MS *m/z* 365 (M^+); Anal. ($C_{23}H_{27}NO_3$·HCl·0.5H_2O) C, H, N.

2-Methoxyphenethyl 1-ethyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 17.



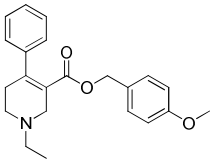
This product was obtained as a light yellow oil (125 mg, 58% yield from **15**). ^{1}H NMR (500 MHz): δ 7.23-7.32 (m, 3H), 7.12-7.20 (m, 3H), 6.91 (d, *J* = 7.5 Hz, 1H), 6.75-6.83 (m, 2H), 4.05 (t, *J* = 7.0 Hz, 2H), 3.74 (s, 3H), 3.30 (t, *J* = 2.5 Hz, 2H), 2.64 (t, *J* = 5.5 Hz, 2H), 2.50-2.70 (m, 6H), 1.17 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz): δ 167.2, 157.6, 146.4, 142.4, 130.7, 128.0, 127.8, 127.2, 127.0, 126.0, 125.6, 120.3, 110.2, 63.6, 55.2, 52.9, 51.9, 49.5, 33.9, 29.5, 12.3 ppm; EI-MS *m/z* 365 (M^+); Anal. ($C_{23}H_{27}NO_3$·HCl·1.2H_2O) C, H, N.

3-Methoxyphenethyl 1-ethyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 18.



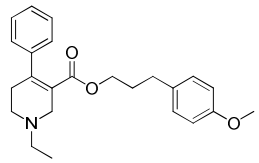
This product was obtained as a colorless oil (138 mg, 64% yield from **15**). ^{1}H NMR (500 MHz): δ 7.23-7.34 (m, 3H), 7.12-7.17 (m, 3H), 6.72 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.61 (dd, *J* = 7.5, 0.5 Hz, 1H), 6.60 (d, *J* = 1.5 Hz, 1H), 4.06 (t, *J* = 7.0 Hz, 2H), 3.75 (s, 3H), 3.31 (t, *J* = 2.5 Hz, 2H), 2.65 (t, *J* = 5.5 Hz, 2H), 2.54-2.60 (m, 4H), 2.50 (t, *J* = 7.0 Hz, 2H), 1.17 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz): δ 167.2, 159.7, 146.8, 142.4, 139.4, 129.4, 128.1, 127.3, 127.0, 125.5, 121.3, 114.7, 111.8, 64.7, 55.2, 52.9, 52.0, 49.5, 34.7, 34.0, 12.3 ppm; EI-MS *m/z* 365 (M^{+}); Anal. ($C_{23}H_{27}NO_3$·HCl·0.2H_2O) C, H, N.

4-Methoxybenzyl 1-ethyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 19.



This product was obtained as a light yellow oil (185 mg, 64% yield from **15**). ^{1}H NMR (500 MHz): δ 7.22-7.28 (m, 3H), 7.11 (dd, *J* = 7.5, 2.0 Hz, 2H), 6.83 (d, *J* = 8.5 Hz, 2H), 6.73 (d, *J* = 8.5 Hz, 2H), 4.82 (s, 2H), 3.75 (s, 3H), 3.35 (t, *J* = 2.5 Hz, 2H), 2.64 (t, *J* = 6.0 Hz, 2H), 2.52-2.60 (m, 4H), 1.17 (t, *J* = 7.5 Hz, 3H) ppm; ^{13}C NMR (125 MHz): δ 167.7, 159.4, 146.4, 142.2, 129.9, 128.2, 127.8, 127.3, 127.0, 125.6, 113.7, 66.0, 55.3, 53.0, 51.9, 49.5, 33.9, 12.4 ppm; EI-MS *m/z* 350 $(M-1)^{+}$; Anal. ($C_{22}H_{25}NO_3$·HCl) C, H, N.

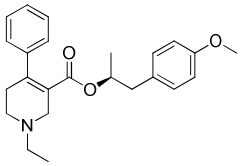
3-(4-Methoxyphenyl)propyl 1-ethyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 20.



This product was obtained as a colorless oil (133 mg, 59% yield from **15**). ^{1}H NMR (500 MHz): δ 7.25-7.32 (m, 3H), 7.16 (dd, *J* = 7.0, 1.5 Hz, 2H), 6.93 (dd, *J* = 7.0, 2.0 Hz, 2H), 6.78 (dd, *J* = 7.0, 2.0 Hz, 2H), 3.86 (t, *J* = 6.5 Hz, 2H), 3.76 (s, 3H), 3.36 (t, *J* = 2.5 Hz, 2H), 2.67 (d, *J* = 5.5 Hz, 2H), 2.56-2.61 (m, 4H), 2.21 (t, *J* = 7.5 Hz, 2H), 1.51 (m, 2H), 1.19 (t, *J* = 7.5 Hz, 3H) ppm; ^{13}C NMR (125 MHz): δ 167.6, 157.9, 146.4, 142.6, 133.5, 129.3, 128.2, 127.4, 127.0, 125.6, 113.9, 63.7, 55.4, 53.1, 52.0,

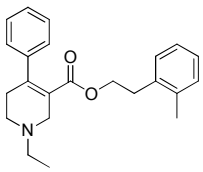
49.5, 34.1, 31.1, 30.1, 12.4 ppm; EI-MS *m/z* 379 (M^+); Anal. ($C_{24}H_{29}NO_3 \cdot HCl \cdot 0.13H_2O$) C, H, N.

(*S*)-1-(4-Methoxyphenyl)propan-2-yl 1-ethyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 21.



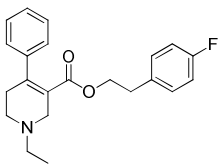
This product was obtained as a colorless oil (98 mg, 38% yield from **15**). ^{1}H NMR (500 MHz): δ 7.23-7.31 (m, 3H), 7.12 (dd, *J* = 7.5, 1.5 Hz, 2H), 6.96 (d, *J* = 9.0 Hz, 2H), 6.77 (d, *J* = 9.0 Hz, 2H), 4.88 (m, 1H), 3.76 (s, 3H), 3.36 (A of ABX2, *J* = 11.5, 2.5 Hz, 1H), 3.30 (B of ABX2, *J* = 11.5, 2.5 Hz, 2H), 2.72 (t, *J* = 6.0 Hz, 2H), 2.63 (q, *J* = 9.0 Hz, 2H), 2.51-2.59 (m, 3H), 2.33 (B of ABX, *J* =13.5, 7.0 Hz, 1H), 1.19 (t, *J* = 7.0 Hz, 3H), 0.86 (d, *J* = 6.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz): δ 166.7, 158.3, 146.0, 142.3, 130.4, 129.7, 128.1, 127.3, 127.1, 125.4, 113.8, 71.8, 55.3, 52.4, 51.6, 49.2, 41.0, 33.4, 18.8, 11.9 ppm; EI-MS *m/z* 379 (M^+); Anal. ($C_{24}H_{29}NO_3 \cdot HCl$) C, H, N.

2-Methylphenethyl 1-ethyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 22.



This product was obtained as a colorless oil (133 mg, 64% yield from **15**). ^{1}H NMR (500 MHz): δ 7.25-7.32 (m, 3H), 7.14 (dd, *J* = 8.0, 1.5 Hz, 2H), 7.05-7.12 (m, 4H), 4.01 (t, *J* = 7.5 Hz, 2H), 3.33 (t, *J* = 2.5 Hz, 2H), 2.66 (d, *J* = 5.5 Hz, 2H), 2.55-2.61 (m, 4H), 2.50 (t, *J* = 7.5 Hz, 2H), 2.20 (s, 3H), 1.18 (t, *J* = 7.5 Hz, 3H) ppm; ^{13}C NMR (125 MHz): δ 167.4, 146.7, 142.4, 136.4, 135.8, 130.3, 129.4, 128.4, 127.4, 127.0, 126.7, 126.1, 125.6, 63.7, 53.0, 52.0, 49.6, 34.0, 31.9, 19.4, 12.4 ppm; EI-MS *m/z* 349 (M^+); Anal. ($C_{23}H_{27}NO_2 \cdot HCl \cdot 0.05H_2O$) C, H, N.

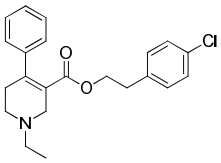
4-Fluorophenethyl 1-ethyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 23.



This product was obtained as a light yellow oil (143 mg, 68% yield from **15**). ^{1}H NMR (500 MHz): δ 7.24-7.33 (m, 3H), 7.13 (t, *J* = 7.0, 1.5 Hz, 2H), 6.88-

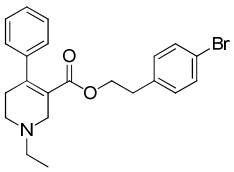
6.98 (m, 4H), 4.03 (t, *J* = 7.0 Hz, 2H), 3.30 (t, *J* = 2.5 Hz, 2H), 2.66 (t, *J* = 5.5 Hz, 2H), 2.53-2.59 (m, 4H), 2.50 (t, *J* = 7.0 Hz, 2H), 1.18 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz): δ 167.3, 162.7, 160.7, 146.8, 142.4, 133.64, 133.61, 130.4, 130.3, 128.1, 127.4, 127.0, 125.4, 115.3, 115.2, 64.7, 53.0, 52.0, 49.5, 34.0, 33.9, 12.4 ppm; EI-MS *m/z* 353 (M^+); Anal. ($C_{22}H_{24}FNO_2$·HCl) C, H, N.

4-Chlorophenethyl 1-ethyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 24.



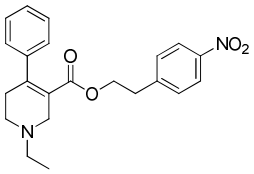
This product was obtained as a colorless oil (141 mg, 57% yield from **15**). ^{1}H NMR (500 MHz): δ 7.22-7.30 (m, 3H), 7.17 (d, *J* = 8.5 Hz, 2H), 7.12 (dd, *J* = 6.5, 1.5 Hz, 2H), 6.91 (d, *J* = 8.5 Hz, 2H), 4.03 (t, *J* = 7.0 Hz, 2H), 3.30 (t, *J* = 1.5 Hz, 2H), 2.65 (t, *J* = 5.5 Hz, 2H), 2.53-2.60 (m, 4H), 2.49 (t, *J* = 7.0 Hz, 2H), 1.17 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz): δ 167.1, 146.7, 142.2, 136.4, 132.2, 130.1, 128.4, 128.0, 127.3, 126.9, 125.2, 64.3, 52.8, 51.8, 49.3, 33.9, 12.2 ppm; EI-MS *m/z* 369/371 (M^+); Anal. ($C_{22}H_{24}ClNO_2$·HCl) C, H, N.

4-Bromophenethyl 1-ethyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 25.



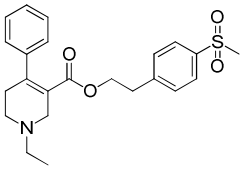
This product was obtained as a colorless oil (170 mg, 74% yield from **15**). ^{1}H NMR (500 MHz): δ 7.23-7.37 (m, 5H), 7.12 (t, *J* = 8.0, 1.5 Hz, 2H), 6.85 (d, *J* = 8.5 Hz, 2H), 4.03 (t, *J* = 7.0 Hz, 2H), 3.29 (t, *J* = 2.5 Hz, 2H), 2.65 (t, *J* = 5.5 Hz, 2H), 2.52-2.59 (m, 4H), 2.47 (t, *J* = 7.0 Hz, 2H), 1.17 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz): δ 167.1, 146.8, 142.3, 136.9, 131.4, 130.6, 128.0, 127.3, 126.9, 125.3, 120.3, 64.2, 52.9, 51.9, 49.4, 34.0, 33.9, 12.3 ppm; EI-MS *m/z* 413/415 (M^+); Anal. ($C_{22}H_{24}BrNO_2$·HCl) C, H, N.

4-Nitrophenethyl 1-ethyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 26.



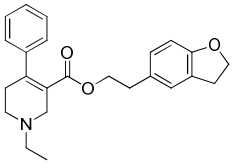
This product was obtained as a light yellow oil (158 mg, 61% yield from **15**). ^{1}H NMR (500 MHz): δ 8.08 (d, *J* = 9.0 Hz, 2H), 7.25-7.32 (m, 3H), 7.10-7.14 (m, 4H), 4.12 (t, *J* = 6.5 Hz, 2H), 3.31 (t, *J* = 2.5 Hz, 2H), 2.69 (t, *J* = 5.5 Hz, 2H), 2.64 (t, *J* = 6.5 Hz, 2H), 2.57-2.61 (m, 4H), 1.18 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz): δ 167.2, 147.3, 145.9, 142.3, 129.8, 129.7, 128.2, 127.5, 127.0, 125.0, 123.7, 63.8, 52.8, 51.9, 49.4, 34.5, 33.9, 12.2 ppm; EI-MS *m/z* 380 (M^+); Anal. ($C_{22}H_{24}N_2O_4$·HCl) C, H, N.

4-(Methylsulfonyl)phenethyl 1-ethyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 27.



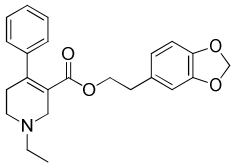
This product was obtained as a light yellow oil (125 mg, 63% yield from **15**). ^{1}H NMR (300 MHz): δ 7.80 (dd, *J* = 8.4, 1.8 Hz, 2H), 7.10-7.38 (m, 7H), 4.10 (t, *J* = 6.6 Hz, 2H), 3.36 (s, 2H), 3.03 (s, 3H), 2.55-2.75 (m, 8H), 1.21 (t, *J* = 7.2 Hz, 3H) ppm; EI-MS *m/z* 412 $(M-1)^+$; Anal. ($C_{23}H_{27}NO_4S$·HCl·0.3H_2O) C, H, N.

2-(2,3-Dihydrobenzofuran-5-yl)ethyl 1-ethyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 28.



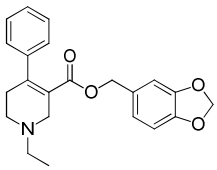
This product was obtained as a colorless oil (98 mg, 54% yield from **15**). ^{1}H NMR (500 MHz): δ 7.25-7.33 (m, 3H), 7.14 (dd, *J* = 7.5, 1.5 Hz, 2H), 6.86 (s, 1H), 6.75 (d, *J* = 8.0 Hz, 1H), 6.64 (d, *J* = 8.0 Hz, 1H), 4.53 (t, *J* = 9.0 Hz, 2H), 4.01 (t, *J* = 7.5 Hz, 2H), 3.32 (t, *J* = 2.5 Hz, 2H), 3.15 (t, *J* = 9.0 Hz, 2H), 2.67 (t, *J* = 6.0 Hz, 2H), 2.55-2.60 (m, 4H), 2.45 (t, *J* = 7.5 Hz, 2H), 1.18 (t, *J* = 7.5 Hz, 3H) ppm; ^{13}C NMR (125 MHz): δ 167.4, 158.9, 146.8, 142.5, 129.9, 128.6, 128.2, 127.5, 127.2, 127.1, 125.7, 125.5, 109.2, 71.4, 65.4, 53.1, 52.1, 49.7, 34.2, 34.1, 30.0, 12.4 ppm; EI-MS *m/z* 377 (M^+); Anal. ($C_{24}H_{27}NO_3$·HCl) C, H, N.

2-(Benzo[*d*][1,3]dioxol-5-yl)ethyl 1-ethyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 29.



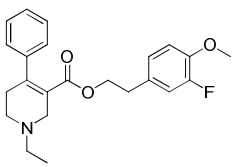
This product was obtained as a colorless oil (115 mg, 56% yield from **15**). ^{1}H NMR (500 MHz): δ 7.25-7.32 (m, 3H), 7.14 (dd, *J* = 6.5, 1.5 Hz, 2H), 6.67 (d, *J* = 8.0 Hz, 1H), 6.49 (d, *J* = 1.5 Hz, 1H), 6.46 (dd, *J* = 8.0, 1.5 Hz, 1H), 5.89 (s, 2H), 4.01 (t, *J* = 7.5 Hz, 2H), 3.35 (t, *J* = 2.5 Hz, 2H), 2.71 (t, *J* = 6.0 Hz, 2H), 2.62 (q, *J* = 7.5 Hz, 2H), 2.59 (m, 2H), 2.44 (t, *J* = 7.5 Hz, 2H), 1.19 (t, *J* = 7.5 Hz, 3H) ppm; ^{13}C NMR (125 MHz): δ 167.2, 147.7, 146.9, 146.3, 142.3, 131.7, 128.2, 127.5, 125.1, 121.9, 109.5, 108.3, 101.0, 65.1, 52.5, 51.7, 49.3, 34.5, 34.4, 33.6, 12.0 ppm; EI-MS *m/z* 379 (M^{+}); Anal. ($C_{23}H_{25}NO_4$·HCl) C, H, N.

Benzo[*d*][1,3]dioxol-5-ylmethyl 1-ethyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 30.



This product was obtained as a colorless oil (180 mg, 70% yield from **15**). ^{1}H NMR (500 MHz): δ 7.22-7.30 (m, 3H), 7.12 (dd, *J* = 7.0, 1.0 Hz, 2H), 6.62 (d, *J* = 8.0 Hz, 1H), 6.42 (d, *J* = 8.0 Hz, 1H), 6.27 (s, 1H), 5.88 (s, 2H), 4.77 (s, 2H), 3.36 (s, 2H), 2.66 (t, *J* = 5.5 Hz, 2H), 2.52-2.60 (m, 4H), 1.17 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz): δ 167.3, 147.5, 147.4, 146.5, 142.2, 129.3, 128.1, 127.3, 126.9, 125.4, 122.0, 108.9, 107.9, 101.0, 66.1, 52.9, 51.8, 49.4, 33.8, 12.3 ppm; EI-MS *m/z* 364 $(M-1)^{+}$; Anal. ($C_{22}H_{23}NO_4$·HCl) C, H, N.

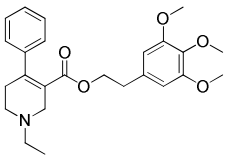
3-Fluoro-4-methoxyphenethyl 1-ethyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 31.



This product was obtained as a colorless oil (115 mg, 63% yield from **15**). ^{1}H NMR (300 MHz): δ 7.25-7.38 (m, 3H), 7.14 (dd, *J* = 7.8, 1.8 Hz, 2H), 6.68-

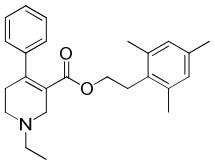
6.88 (m, 3H), 4.02 (t, *J* = 6.9 Hz, 2H), 3.85 (s, 3H), 3.36 (s, 2H), 2.33-2.75 (m, 8H), 1.21 (t, *J* = 7.2 Hz, 3H) ppm; EI-MS *m/z* 383 (M^+); Anal. ($C_{23}H_{26}FNO_3 \cdot HCl \cdot 0.5H_2O$) C, H, N.

3,4,5-Trimethoxyphenethyl 1-ethyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 32.



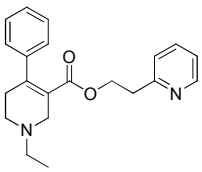
This product was obtained as a light yellow oil (88 mg, 43% yield from **15**). ^{1}H NMR (300 MHz): δ 7.26-7.36 (m, 3H), 7.14 (dd, *J* = 7.5, 1.8 Hz, 2H), 6.27 (s, 2H), 4.07 (t, *J* = 7.2 Hz, 2H), 3.82 (s, 6H), 3.81 (s, 3H), 3.38 (s, 2H), 2.73 (m, 2H), 2.57-2.69 (m, 4H), 2.48 (t, *J* = 7.2 Hz, 2H), 1.21 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (75 MHz): δ 166.9, 153.1, 147.1, 142.1, 136.6, 133.4, 128.1, 127.4, 126.9, 126.3, 105.8, 64.9, 61.0, 56.3, 52.8, 52.1, 49.5, 35.2, 33.9, 12.3 ppm; EI-MS *m/z* 425 (M^+); Anal. ($C_{25}H_{31}NO_5 \cdot HCl \cdot 1.1H_2O$) C, H, N.

2,4,6-Trimethylphenethyl 1-ethyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 33.



This product was obtained as a light yellow oil (120 mg, 54% yield from **15**). ^{1}H NMR (500 MHz): δ 7.22-7.33 (m, 3H), 7.16 (dd, *J* = 8.0, 1.5 Hz, 2H), 6.78 (s, 2H), 3.84 (t, *J* = 8.7 Hz, 2H), 3.35 (t, *J* = 2.5 Hz, 2H), 2.69 (d, *J* = 5.5 Hz, 2H), 2.58-2.62 (m, 4H), 2.49 (t, *J* = 8.0 Hz, 2H), 2.46 (s, 3H), 2.20 (s, 6H), 1.19 (t, *J* = 7.5 Hz, 3H) ppm; ^{13}C NMR (125 MHz): δ 167.7, 146.4, 142.5, 136.9, 136.0, 130.7, 129.1, 128.2, 127.4, 127.1, 125.9, 62.6, 53.0, 52.1, 49.7, 33.9, 28.2, 19.9, 19.8, 12.4 ppm; EI-MS *m/z* 377 (M^+); Anal. ($C_{25}H_{31}NO_2 \cdot HCl$) C, H, N.

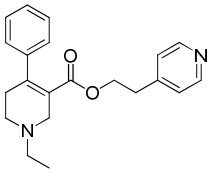
2-(Pyridin-2-yl)ethyl 1-ethyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 34.



This product was obtained as a light yellow oil (105 mg, 46% yield from **15**). ^{1}H NMR (500 MHz): δ 8.47 (d, *J* = 4.0 Hz, 1H), 7.53 (dt, *J* = 8.0, 2.0 Hz, 1H), 7.22-7.32 (m, 3H), 7.07-7.15 (m, 3H), 6.92 (dd, *J* = 8.5 Hz, 1H), 4.25 (t, *J* = 7.0 Hz, 2H), 3.33 (t, *J* = 2.0 Hz, 2H), 2.68-2.75 (m, 4H), 2.60 (q, *J* = 7.5 Hz, 2H), 2.58 (m, 2H), 1.18

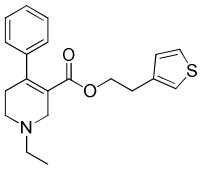
(t, *J* = 7.5 Hz, 3H) ppm; ^{13}C NMR (125 MHz): δ 167.0, 158.0, 149.3, 146.8, 142.2, 136.4, 128.1, 127.4, 126.9, 124.9, 123.4, 121.6, 63.4, 52.5, 51.7, 49.2, 36.8, 33.6, 12.0 ppm; EI-MS *m/z* 336 (M^+); Anal. ($C_{21}H_{24}N_2O_2 \cdot 2HCl \cdot 0.5H_2O$) C, H, N.

2-(Pyridin-4-yl)ethyl 1-ethyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 35.



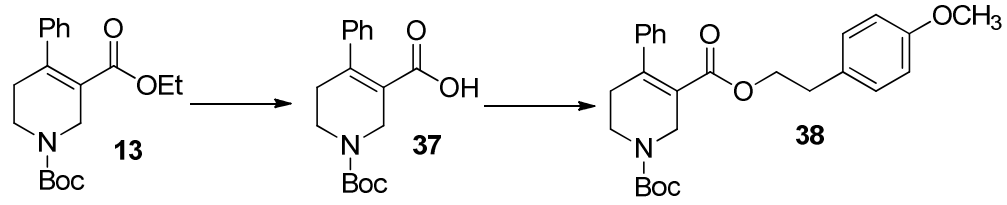
This product was obtained as a yellow oil (88 mg, 44% yield from **15**). ^{1}H NMR (500 MHz): δ 8.45 (br, 2H), 7.27 (dd, *J* = 4.0 Hz, 2H), 7.20-7.27 (m, 3H), 6.99 (d, *J* = 6.0 Hz, 2H), 4.22 (m, 2H), 3.29 (s, 2H), 3.07 (m, 2H), 2.75 (m, 2H), 2.53 (m, 2H), 2.46 (q, *J* = 7.0 Hz, 2H), 1.09 (t, *J* = 7.0 Hz, 3H) ppm; EI-MS *m/z* 336 (M^+); Anal. ($C_{21}H_{24}N_2O_2 \cdot 2HCl \cdot 1.2H_2O$) C, H, N.

2-(Thiophen-3-yl)ethyl 1-ethyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 36.



This product was obtained as a light yellow oil (93 mg, 46% yield from **15**). ^{1}H NMR (500 MHz): δ 7.24-7.33 (m, 3H), 7.18 (d, *J* = 4.0 Hz, 1H), 7.14 (dd, *J* = 7.5, 1.5 Hz, 2H), 6.78 (s, 1H), 6.77 (d, *J* = 4.0 Hz, 1H), 4.06 (t, *J* = 7.0 Hz, 2H), 3.32 (t, *J* = 2.5 Hz, 2H), 2.66 (t, *J* = 6.0 Hz, 2H), 2.52-2.60 (m, 6H), 1.18 (t, *J* = 7.5 Hz, 3H) ppm; ^{13}C NMR (125 MHz): δ 167.3, 146.7, 142.4, 138.1, 128.3, 128.1, 127.4, 127.0, 125.5, 121.5, 64.1, 53.0, 52.0, 49.5, 34.0, 29.1, 12.4 ppm; EI-MS *m/z* 341 (M^+); Anal. ($C_{20}H_{23}NO_2S \cdot HCl$) C, H, N.

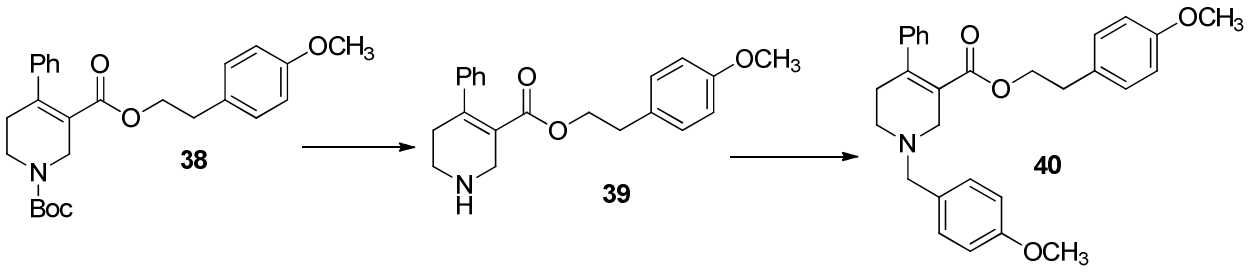
1-*tert*-Butyl 3-(4-methoxyphenethyl) 4-phenyl-5,6-dihydropyridine-1,3(*2H*)-dicarboxylate 38.



To a solution of **13** (3.45 g, 10.41 mmol) in EtOH (70 mL) was slowly added aqueous KOH (10%, 40 mL). The mixture was stirred at room temperature overnight and extracted with Et_2O (40 mL × 3). The aqueous phase was adjusted to pH 4.0 using 2.0 N HCl and extracted with CH_2Cl_2 (40 mL × 3). The combined CH_2Cl_2 extracts were dried over Na_2SO_4, filtered and evaporated to dryness under vacuum. The resulting white solid was dried under vacuum for 24 h. 2.67 g of **37** was obtained and used for the next step without further purification.

To a solution of **37** (579 mg, 1.91 mmol) in CH_2Cl_2 (20 mL) was added EDCI (853 mg, 2.87 mmol), DMAP (29 mg, 0.38 mmol), and 4-methoxyphenethanol (348 mg, 2.29 mmol). The mixture was stirred at room temperature overnight. Workup as described in the general synthesis of **8** and **17-36**. The crude product was purified by silica gel column chromatography (20:1 hexanes:EtOAc) to afford **38** (450 mg, 54% yield based on **37**) as a white solid. ^{1}H NMR (500 MHz): δ 7.26-7.35 (m, 3H), 7.12 (dd, *J* = 8.0, 1.5 Hz, 2H), 6.95 (d, *J* = 8.3 Hz, 2H), 6.78 (dd, *J* = 6.5, 2.0 Hz, 2H), 4.23 (br s, 2H), 4.06 (t, *J* = 7.0 Hz, 2H), 3.78 (t, *J* = 5.5 Hz, 2H), 3.77 (s, 3H), 3.60 (t, *J* = 5.5 Hz, 2H), 2.51 (br, 2H), 1.51 (s, 6H), 1.47 (s, 3H) ppm; EI-MS *m/z* 437 (M^+).

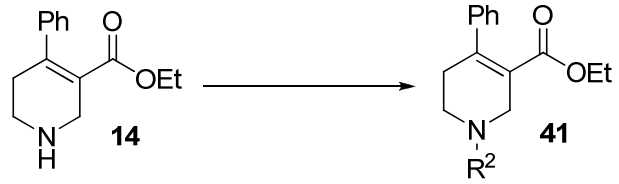
4-Methoxyphenethyl 1-(4-methoxybenzyl)-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxyl-ate 40.



Compound **39** was obtained by treating **38** with TFA/CH_2Cl_2 as described in the reaction from **13** to **14** and was partially purified by PTLC. To a solution of **39** (140 mg, 0.42 mmol) in THF (10 mL) was added subsequently $NaBH(OAc)_3$ (134 mg, 0.63 mmol), anisaldehyde (57 mg, 0.42

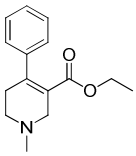
mmol), and HOAc (50 mg, 0.84 mmol). The resulting mixture was stirred at room temperature for 4 h, followed by standard aqueous workup. The crude product was purified by silica gel column chromatography (20:1 to 2:1 hexanes:EtOAc) to afford **40** (110 mg, 23% yield based on **38**) as a colorless oil. ^{1}H NMR (300 M): δ 7.22-7.35 (m, 5H), 7.13 (dd, *J* = 7.8, 1.8 Hz, 2H), 6.85-6.95 (m, 4H), 6.72-6.80 (m, 2H), 4.00 (t, *J* = 7.2 Hz, 2H), 3.80 (s, 3H), 3.76 (s, 3H), 3.62 (s, 2H), 3.33 (t, *J* = 2.7 Hz, 2H), 2.64 (t, *J* = 5.7 Hz, 2H), 2.52 (m, 2H), 2.45 (t, *J* = 7.2 Hz, 2H) ppm; ^{13}C NMR (75 M): δ 167.3, 158.9, 158.2, 146.5, 142.4, 130.5, 129.89, 129.86, 129.8, 128.1, 127.4, 127.0, 125.6, 113.9, 113.8, 65.2, 61.9, 55.5, 53.4, 49.2, 33.94, 33.91 ppm; EI-MS *m/z* 457 (M^+); Anal. ($C_{29}H_{31}NO_4$·HCl·0.2H_2O) C, H, N.

Ethyl 1-alkyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 41.



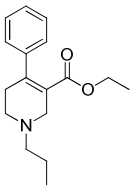
A mixture of **14** (2 g, 8.65 mmol), $NaCNBH_3$ (1.63 g, 25.95 mmol), aldehyde (paraformaldehyde, propionaldehyde, or butyraldehyde), and EtOH (20 mL) was stirred at room temperature overnight followed by standard aqueous workup. The crude product was purified by silica gel column chromatography (2:1 hexanes:EtOAc) to afford **41**.

Ethyl 1-methyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 41a.



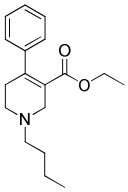
Colorless oil, 1.59 g, 75% yield. ^{1}H NMR (300 MHz): δ 7.26-7.38 (m, 3H), 7.14 (dd, *J* = 7.5, 1.5 Hz, 2H), 3.89 (q, *J* = 7.2 Hz, 2H), 3.33 (t, *J* = 2.7 Hz, 2H), 2.66 (m, 2H), 2.59 (m, 2H), 2.47 (s, 3H), 0.86 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (75 MHz): δ 167.1, 146.4, 142.3, 128.1, 127.3, 126.9, 125.3, 60.3, 55.3, 51.9, 45.6, 34.1, 13.8 ppm; EI-MS *m/z* 245 (M^+).

Ethyl 1-n-propyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 41b.



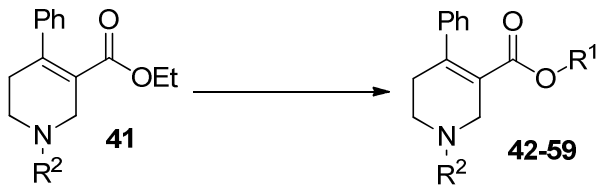
Colorless oil, 1.45 g, 61% yield. ^{1}H NMR (300 MHz): δ 7.23-7.36 (m, 3H), 7.13 (dd, *J* = 7.5, 1.8 Hz, 2H), 3.89 (q, *J* = 7.2 Hz, 2H), 3.37 (t, *J* = 2.7 Hz, 2H), 2.71 (t, *J* = 5.4 Hz, 2H), 2.50-2.62 (m, 4H), 1.83 (m, 2H), 0.96 (t, *J* = 7.5 Hz, 3H), 0.86 (t, *J* = 7.2 Hz, 3H) ppm; EI-MS *m/z* 273 (M^+).

Ethyl 1-n-butyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 41c.



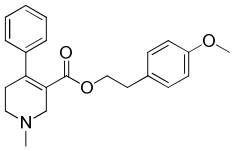
Colorless oil, 1.59 g, 75% yield. ^{1}H NMR (300 MHz): δ 7.23-7.36 (m, 3H), 7.14 (dd, J = 7.5, 1.8 Hz, 2H), 3.90 (q, *J* = 7.2 Hz, 2H), 3.37 (t, *J* = 2.7 Hz, 2H), 2.71 (t, *J* = 5.4 Hz, 2H), 2.50-2.62 (m, 4H), 1.78 (m, 2H), 1.39 (m, 2H), 0.97 (t, *J* = 7.5 Hz, 3H), 0.88 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (75 MHz): δ 167.5, 146.4, 142.1, 128.1, 127.4, 126.9, 120.6, 60.9, 58.0, 53.2, 49.8, 37.5, 29.1, 21.1, 13.8, 13.7 ppm; EI-MS *m/z* 287 (M^+).

General procedure for synthesis of 42-59.



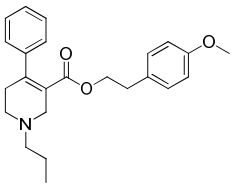
The synthetic procedure from **41** to **42-59** is similar to that from **15** to **8**, **17-36**.

4-Methoxyphenethyl 1-methyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 42.



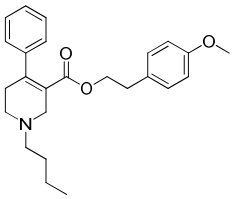
This product was obtained as a colorless oil (108 mg, 53% yield from **41a**). ^{1}H NMR (300 MHz): δ 7.21-7.36 (m, 3H), 7.14 (dd, *J* = 7.5, 1.8 Hz, 2H), 6.94 (dd, *J* = 6.6, 1.8 Hz, 2H), 6.78 (dd, *J* = 6.6, 1.8 Hz, 2H), 4.02 (t, *J* = 7.2 Hz, 2H), 3.77 (s, 3H), 3.27 (t, *J* = 2.4 Hz, 2H), 2.53-2.67 (m, 4H), 2.47 (d, *J* = 7.2 Hz, 2H), 2.45 (s, 3H) ppm; ^{13}C NMR (75 MHz): δ 167.0, 158.2, 146.7, 142.3, 129.9, 128.1, 127.4, 127.0, 125.4, 113.9, 65.2, 55.5, 55.2, 51.9, 45.8, 34.3, 33.9 ppm; EI-MS *m/z* 351 (M^+); Anal. ($C_{22}H_{25}NO_3$·HCl) C, H, N.

4-Methoxyphenethyl 1-*n*-propyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 43.



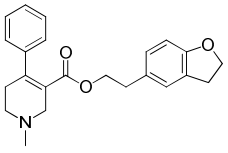
This product was obtained as a light yellow oil (170 mg, 42% yield from **41b**). ^{1}H NMR (300 MHz): δ 7.22-7.36 (m, 3H), 7.15 (dd, *J* = 7.2, 1.8 Hz, 2H), 6.94 (dd, *J* = 6.6, 1.8 Hz, 2H), 6.78 (dd, *J* = 6.6, 1.8 Hz, 2H), 4.02 (t, *J* = 7.5 Hz, 2H), 3.76 (s, 3H), 3.30 (t, *J* = 2.4 Hz, 2H), 2.71 (t, *J* = 5.1 Hz, 2H), 2.33-2.65 (m, 6H), 1.63 (m, 2H), 0.96 (t, *J* = 7.5 Hz, 3H) ppm; ^{13}C NMR (75 MHz): δ 167.3, 158.3, 146.7, 142.2, 129.9, 129.7, 128.1, 127.5, 127.0, 125.5, 113.7, 65.3, 59.9, 53.2, 50.0, 45.8, 34.4, 33.6, 20.8, 12.0 ppm; EI-MS *m/z* 351 (M^+); Anal. ($C_{24}H_{29}NO_3$·HCl·0.8H_2O) C, H, N.

4-Methoxyphenethyl 1-*n*-butyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 44.



This product was obtained as a light yellow oil (130 mg, 28% yield from **41c**). ^{1}H NMR (300 MHz): δ 7.22-7.36 (m, 3H), 7.15 (dd, *J* = 7.5, 1.8 Hz, 2H), 6.94 (dd, *J* = 6.6, 1.8 Hz, 2H), 6.78 (dd, *J* = 6.6, 1.8 Hz, 2H), 4.00 (t, *J* = 7.5 Hz, 2H), 3.75 (s, 3H), 3.30 (t, *J* = 2.7 Hz, 2H), 2.71 (t, *J* = 5.4 Hz, 2H), 2.36-2.65 (m, 6H), 1.59 (m, 2H), 1.34 (m, 2H), 0.95 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (75 MHz): δ 167.2, 158.3, 146.6, 142.3, 130.0, 129.5, 128.6, 127.9, 127.3, 125.7, 113.4, 64.5, 58.6, 53.4, 50.1, 45.7, 34.4, 33.6, 30.7, 21.2, 13.6 ppm; EI-MS *m/z* 351 (M^+); Anal. ($C_{25}H_{31}NO_3$·HCl·1.2H_2O) C, H, N.

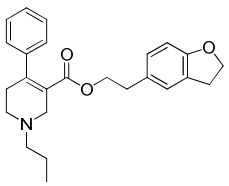
2-(2,3-Dihydrobenzofuran-5-yl)ethyl 1-methyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 45.



This product was obtained as a light yellow oil (109 mg, 44% yield from **41a**). ^{1}H NMR (300 M): δ 7.22-7.38 (m, 3H), 7.14 (dd, *J* = 7.8, 1.8 Hz, 2H), 6.86 (s, 1H), 6.75 (d, *J* = 7.8, 2H), 6.64 (d, *J* = 7.8 Hz, 2H), 4.52 (t, *J* = 8.7 Hz, 2H), 4.01 (t, *J* = 7.2 Hz, 2H), 3.28 (t, *J* = 2.4 Hz, 2H), 3.14 (t, *J* = 8.7 Hz, 2H), 2.52-2.68 (m, 4H), 2.45 (s, 3H), 2.35-2.50 (m, 2H) ppm; ^{13}C NMR (75 M): δ 167.0, 158.7, 146.6, 142.3, 129.6,

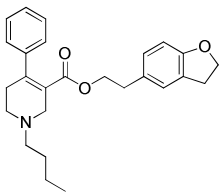
128.4, 128.1, 127.3, 127.1, 126.9, 125.4, 125.3, 109.1, 71.3, 65.4, 55.1, 51.9, 45.7, 34.3, 34.2, 29.9 ppm; EI-MS *m/z* 363 (M^+); Anal. ($C_{23}H_{25}NO_3 \cdot HCl \cdot 1/3H_2O$) C, H, N.

2-(2,3-Dihydrobenzofuran-5-yl)ethyl 1-n-propyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 46.



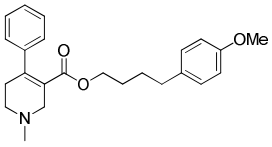
This product was obtained as a light yellow oil (168 mg, 40% yield from **41b**). ^{1}H NMR (300 MHz): δ 7.23-7.36 (m, 3H), 7.16 (dd, *J* = 5.7, 1.8 Hz, 2H), 6.86 (s, 1H), 6.74 (d, *J* = 7.8 Hz, 1H), 6.64 (d, *J* = 7.8 Hz, 1H), 4.53 (q, *J* = 8.7 Hz, 2H), 4.01 (t, *J* = 7.5 Hz, 2H), 3.37 (s, 2H), 3.15 (t, *J* = 8.7 Hz, 2H), 2.72 (t, *J* = 5.1 Hz, 2H), 2.35-2.62 (m, 6H), 1.64 (m, 2H), 0.96 (t, *J* = 7.5 Hz, 3H) ppm; ^{13}C NMR (75 MHz): δ 167.4, 158.7, 146.8, 142.1, 129.6, 128.4, 128.1, 128.0, 127.4, 127.2, 127.1, 125.4, 109.6, 71.3, 65.4, 60.1, 53.1, 49.8, 34.2, 29.9, 20.3, 12.2 ppm; EI-MS *m/z* 391 (M^+); Anal. ($C_{25}H_{29}NO_3 \cdot HCl \cdot 0.5H_2O$) C, H, N.

2-(2,3-Dihydrobenzofuran-5-yl)ethyl 1-n-butyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 47.



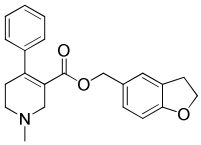
This product was obtained as a light yellow oil (145 mg, 28% yield from **41c**). ^{1}H NMR (300 MHz): δ 7.23-7.36 (m, 3H), 7.16 (dd, *J* = 7.2, 1.2 Hz, 2H), 6.85 (s, 1H), 6.74 (d, *J* = 8.1 Hz, 1H), 6.64 (d, *J* = 8.1 Hz, 1H), 4.54 (q, *J* = 8.7 Hz, 2H), 4.00 (t, *J* = 7.2 Hz, 2H), 3.31 (t, *J* = 2.1 Hz, 2H), 3.16 (t, *J* = 8.7 Hz, 2H), 2.65 (t, *J* = 5.7 Hz, 2H), 2.40-2.58 (m, 6H), 1.57 (m, 2H), 1.36 (m, 2H), 0.95 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (75 MHz): δ 167.2, 158.6, 146.6, 142.2, 130.4, 129.6, 128.4, 128.3, 128.0, 127.3, 126.9, 125.5, 109.1, 71.3, 64.0, 58.1, 53.4, 49.9, 38.7, 33.8, 29.91, 29.85, 21.0, 14.3 ppm; EI-MS *m/z* 405 (M^+); Anal. ($C_{26}H_{31}NO_3 \cdot HCl \cdot 0.8H_2O$) C, H, N.

4-(4-Methoxyphenyl)butyl 1-methyl-1,2,5,6-tetrahydropyridine-3-carboxylate 48.



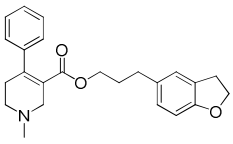
This product was obtained as a light yellow oil (72 mg, 35% yield from **41a**). ^{1}H NMR (300 MHz): δ 7.18-7.35 (m, 3H), 7.08-7.16 (m, 2H), 7.01 (dd, *J* = 6.6, 2.4 Hz, 2H), 6.81 (dd, *J* = 6.6, 2.4 Hz, 2H), 3.85 (t, *J* = 6.0 Hz, 2H), 3.79 (s, 3H), 3.30 (t, *J* = 2.4 Hz, 2H), 2.63 (m, 2H), 2.57 (m, 2H), 2.45 (s, 3H), 2.39 (t, *J* = 7.5 Hz, 2H), 1.20-1.33 (m, 4H) ppm; ^{13}C NMR (75 MHz): δ 167.3, 157.7, 146.4, 142.4, 134.2, 129.3, 128.1, 127.3, 126.9, 125.4, 113.7, 64.4, 55.5, 55.1, 51.9, 45.7, 34.7, 34.3, 27.9 ppm; EI-MS *m/z* 379 (M^+); Anal. ($C_{24}H_{29}NO_3$·HCl) C, H, N.

(2,3-Dihydrobenzofuran-5-yl)methyl 1-methyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 49.



This product was obtained as a light yellow oil (68 mg, 46% yield from **41a**). ^{1}H NMR (300 MHz): δ 7.20-7.38 (m, 4H), 7.12 (m, 1H), 6.68 (s, 1H), 6.58-6.80 (m, 2H), 4.80 (s, 2H), 4.54 (t, *J* = 8.7 Hz, 2H), 3.33 (t, *J* = 2.4 Hz, 2H), 3.12 (t, *J* = 8.7 Hz, 2H), 2.62 (m, 2H), 2.56 (m, 2H), 2.45 (s, 3H) ppm; ^{13}C NMR (75 MHz): δ 166.7, 146.3, 142.1, 129.3, 128.7, 128.1, 128.0, 127.3, 127.0, 126.9, 126.2, 125.4, 108.9, 71.5, 66.5, 55.1, 51.8, 45.6, 34.1, 29.7 ppm; EI-MS *m/z* 348 $(M-1)^+$; Anal. ($C_{22}H_{23}NO_3$·HCl·1.5H_2O) C, H, N.

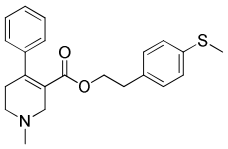
3-(2,3-Dihydrobenzofuran-5-yl)propyl 1-methyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 50.



This product was obtained as a light yellow oil (105 mg, 44% yield from **41a**). ^{1}H NMR (300 MHz): δ 7.20-7.38 (m, 4H), 7.15 (m, 1H), 6.85 (s, 1H), 6.74 (d, *J* = 8.1 Hz, 1H), 6.65 (d, *J* = 8.1 Hz, 1H), 4.51 (t, *J* = 8.7 Hz, 2H), 3.86 (t, *J* = 6.3 Hz, 2H), 3.32 (t, *J* = 2.4 Hz, 2H), 3.14 (t, *J* = 8.7 Hz, 2H), 2.64 (m, 2H), 2.58 (m, 2H), 2.46 (s, 3H), 2.21 (t, *J* = 7.5 Hz, 2H), 1.51 (m, 2H) ppm; ^{13}C NMR (75 MHz): δ 167.1,

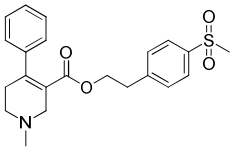
158.2, 146.4, 142.4, 133.2, 128.2, 128.1, 127.7, 127.3, 126.9, 126.8, 124.8, 108.9, 71.2, 63.8, 55.1, 51.8, 45.6, 34.3, 31.5, 30.4, 30.0 ppm; EI-MS *m/z* 377 (M^+); Anal. ($C_{24}H_{27}NO_3$·HCl·0.2H_2O) C, H, N.

4-(Methylthio)phenethyl 1-methyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 51.



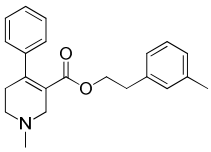
This product was obtained as a light yellow oil (102 mg, 48% yield from **41a**). ^{1}H NMR (300 MHz): δ 7.20-7.36 (m, 3H), 7.03-7.18 (m, 4H), 6.94 (dd, *J* = 6.6, 2.1 Hz, 2H), 4.04 (t, *J* = 7.2 Hz, 2H), 3.28 (t, *J* = 2.7 Hz, 2H), 2.63 (m, 2H), 2.58 (m, 2H), 2.49 (m, 2H), 2.46 (s, 3H), 2.45 (s, 3H) ppm; ^{13}C NMR (75 MHz): δ 166.8, 146.8, 142.2, 136.2, 134.8, 129.4, 128.1, 127.4, 126.92, 126.87, 125.1, 64.8, 55.0, 51.8, 45.6, 34.2, 16.4 ppm; EI-MS *m/z* 367 (M^+); Anal. ($C_{22}H_{25}NO_2S$·HCl) C, H, N.

4-(Methylsulfonyl)phenethyl 1-methyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 52.



This product was obtained as a light yellow oil (115 mg, 52% yield from **41a**). ^{1}H NMR (300 MHz): δ 7.80 (dd, *J* = 8.4, 1.8 Hz, 2H), 7.08-7.38 (m, 7H), 4.11 (t, *J* = 6.6 Hz, 2H), 3.34 (s, 2H), 3.04 (s, 3H), 3.02 (m, 2H), 2.55-2.75 (m, 4H), 2.51 (s, 3H) ppm; EI-MS *m/z* 399 (M^+); Anal. ($C_{22}H_{25}NO_4S$·HCl·0.1H_2O·0.2Et_2O) C, H, N.

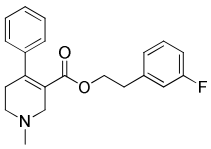
3-Methylphenethyl 1-methyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 53.



This product was obtained as a colorless oil (120 mg, 52% yield from **41a**). ^{1}H NMR (300 MHz): δ 7.22-7.38 (m, 3H), 7.07-7.18 (m, 3H), 6.99 (d, *J* = 7.8 Hz, 1H), 6.86 (s, 1H), 6.83 (dd, *J* = 7.8, 0.6 Hz, 1H), 4.05 (t, *J* = 7.2 Hz, 2H), 3.28 (t, *J* = 2.4 Hz, 2H), 2.54-2.67 (m, 4H), 2.49 (t, *J* = 7.2 Hz, 2H), 2.45 (s, 3H), 2.30 (s, 3H) ppm; ^{13}C NMR (75 MHz): δ 166.8, 146.7, 142.2, 137.9, 137.6, 129.7, 128.3, 128.1, 127.3, 127.2,

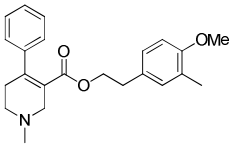
126.9, 125.9, 125.2, 65.0, 55.0, 51.8, 45.6, 34.7, 34.2, 21.6 ppm; EI-MS *m/z* 335 (M^+); Anal. ($C_{22}H_{25}NO_2$·HCl) C, H, N.

3-Fluorophenethyl 1-methyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 54.



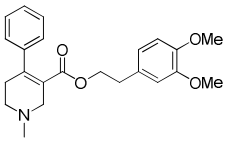
This product was obtained as a colorless oil (125 mg, 53% yield from **41a**). ^{1}H NMR (300 MHz): δ 7.10-7.38 (m, 6H), 6.88 (m, 1H), 6.79 (dd, *J* = 7.5, 0.6 Hz, 1H), 6.71 (dt, *J* = 9.3, 1.8 Hz, 1H), 4.06 (t, *J* = 7.2 Hz, 2H), 3.30 (t, *J* = 2.4 Hz, 2H), 2.65 (m, 2H), 2.60 (m, 2H), 2.52 (t, *J* = 7.2 Hz, 2H), 2.47 (s, 3H) ppm; ^{13}C NMR (75 MHz): δ 166.8, 147.1, 142.2, 129.9, 129.8, 128.4, 128.1, 127.4, 126.9, 126.6, 124.9, 64.5, 54.9, 51.8, 45.6, 34.5, 34.2 ppm; EI-MS *m/z* 339 (M^+); Anal. ($C_{21}H_{22}FNO_2$·HCl·0.6H_2O) C, H, N.

3-Methyl-4-methoxyphenethyl 1-methyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 55.



This product was obtained as a light yellow oil (105 mg, 40% yield from **41a**). ^{1}H NMR (300 MHz): δ 7.18-7.20 (m, 3H), 7.03-7.09 (m, 2H), 6.60-6.78 (m, 3H), 3.94 (t, *J* = 7.2 Hz, 2H), 3.72 (s, 3H), 3.21 (t, *J* = 2.4 Hz, 2H), 2.47-2.60 (m, 4H), 2.38 (s, 3H), 2,37 (t, *J* = 7.2 Hz, 2H), 2.10 (s, 3H) ppm; ^{13}C NMR (75 MHz): δ 167.0, 156.4, 146.7, 142.4, 131.3, 129.4, 128.1, 127.4, 127.0, 126.96, 126.5, 125.4, 109.9, 65.3, 55.6, 55.2, 51.9, 45.8, 34.3, 34.0, 16.5 ppm; EI-MS *m/z* 365 (M^+); Anal. ($C_{23}H_{27}NO_3$·HCl) C, H, N.

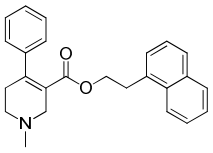
3,4-Dimethoxyphenethyl 1-methyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 56.



This product was obtained as a light yellow oil (100 mg, 35% yield from **41a**). ^{1}H NMR (300 MHz): δ 7.22-7.38 (m, 4H), 7.13 (dd, *J* = 7.8, 1.8 Hz, 1H), 6.74 (d, *J* = 8.7 Hz, 1H), 6.56-6.64 (m, 2H), 4.05 (t, *J* = 7.2 Hz, 2H), 3.85 (s, 3H), 3.84 (s, 3H), 3.30 (t, *J* = 2.4 Hz, 2H), 2.55-2.68 (m, 4H), 2.50 (t, *J* = 7.2 Hz, 2H),

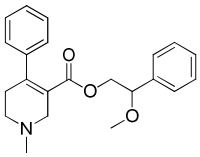
2.46 (s, 3H) ppm; ^{13}C NMR (75 MHz): δ 166.8, 148.8, 147.5, 146.8, 142.1, 130.2, 128.1, 128.0, 127.3, 126.8, 120.8, 112.0, 111.2, 6.7, 142.2, 137.9, 137.6, 129.7, 128.3, 128.1, 127.3, 127.2, 126.9, 125.9, 125.2, 65.0, 55.0, 51.8, 45.6, 34.7, 34.2, 21.6 ppm; EI-MS *m/z* 381 (M^+); Anal. ($C_{23}H_{27}NO_4 \cdot HCl \cdot 1.2H_2O$) C, H, N.

2-(Naphthalene-1-yl)ethyl 1-methyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 57.



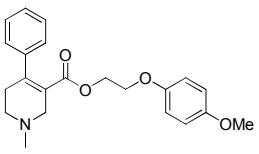
This product was obtained as a light yellow oil (130 mg, 47% yield from **41a**). ^{1}H NMR (300 MHz): δ 7.80-7.90 (m, 2H), 7.70 (d, *J* = 8.1 Hz, 1H), 7.42-7.53 (m, 2H), 7.23-7.40 (m = 5H), 7.10-7.20 (m, 2H), 4.19 (t, *J* = 7.5 Hz, 2H), 3.27 (t, *J* = 2.4 Hz, 2H), 3.00 (t, *J* = 7.5 Hz, 2H), 2.54-2.66 (m, 4H), 2.44 (s, 3H) ppm; ^{13}C NMR (75 MHz): δ 167.0, 146.8, 142.3, 133.8, 133.6, 132.0, 128.8, 128.2, 128.1, 127.4, 126.9, 126.8, 126.1, 125.6, 125.5, 125.2, 123.6, 64.3, 55.0, 51.8, 45.6, 34.2, 31.8 ppm; EI-MS *m/z* 371 (M^+); Anal. ($C_{25}H_{25}NO_2 \cdot HCl$) C, H, N.

2-Methoxy-2-phenethyl 1-methyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 58.



This product was obtained as a light yellow oil (80 mg, 38% yield from **41a**). ^{1}H NMR (300 MHz): δ 7.10-7.42 (m, 10H), 4.01 (d, J = 8.1 Hz, 1H), 3.93 (d, *J* = 3.6 Hz, 1H), 3.85 (dd, *J* = 8.1, 3.6 Hz, 1H), 3.31 (ABq, JAB = 16.2 Hz, 2H), 3.11 (s, 3H), 2.56-2.75 (m, 4H), 2.47 (s, 3H) ppm; ^{13}C NMR (75 MHz): δ 166.7, 147.1, 142.3, 138.0, 128.5, 128.4, 128.3, 128.1, 127.4, 127.0, 126.9, 81.3, 68.0, 57.1, 54.9, 51.8, 45.6, 34.2 ppm; EI-MS *m/z* (M^+); Anal. ($C_{22}H_{25}NO_3 \cdot HCl \cdot 0.2H_2O$) C, H, N.

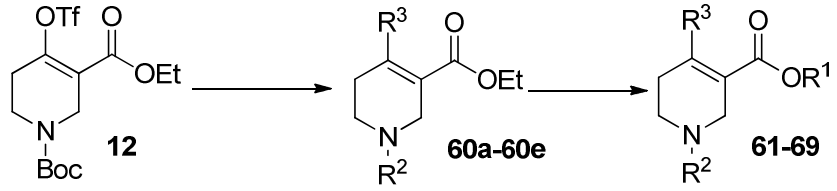
2-(4-Methoxyphenoxy)ethyl 1-methyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 59.



This product was obtained as a light yellow oil (85 mg, 35% yield from **41a**). ^{1}H NMR (300 MHz): δ 7.18-7.25 (m, 3H), 7.08-7.15 (m, 2H), 6.81

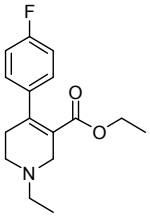
(d, *J* = 9.3 Hz, 2H), 6.71 (d, *J* = 9.3 Hz, 2H), 4.17 (t, *J* = 4.8 Hz, 2H), 3.77 (s, 3H), 3.66 (t, *J* = 4.8 Hz, 2H), 3.31 (t, *J* = 2.4 Hz, 2H), 2.61 (m, 2H), 2.58 (m, 2H), 2.45 (s, 3H) ppm; ^{13}C NMR (75 MHz): δ 166.8, 154.0, 152.6, 147.5, 142.3, 128.0, 127.2, 126.8, 125.0, 115.6, 114.6, 66.2, 62.7, 55.9, 55.0, 51.8, 45.7, 34.5 ppm; EI-MS *m/z* 366 (M^+); Anal. ($C_{22}H_{25}NO_4$·HCl·0.5H_2O) C, H, N.

General procedure for synthesis of 61-69.



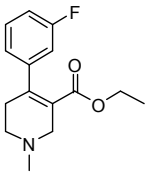
The synthetic procedure from **12** to **61**-**69** is similar to that from **12** to **8**, **17**-**36**.

Ethyl 1-ethyl-4-(4-fluorophenyl)-1,2,5,6-tetrahydropyridine-3-carboxylate 60a.



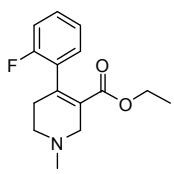
^{1}H NMR (300 MHz): δ 7.38 (d, *J* = 9.0 Hz, 2H), 7.20 (d, *J* = 9.0 Hz, 2H), 4.02 (q, *J* = 7.2 Hz, 2H), 3.37 (t, *J* = 2.7 Hz, 2H), 2.69 (t, *J* = 6.0 Hz, 2H), 2.54-2.67 (m, 4H), 1.18 (t, *J* = 6.0 Hz, 3H), 0.95 (t, *J* = 7.2 Hz, 3H) ppm; EI-MS *m/z* 277 (M^+).

Ethyl 1-methyl-4-(3-fluorophenyl)-1,2,5,6-tetrahydropyridine-3-carboxylate 60b.



^{1}H NMR (300 MHz): δ 7.32 (m, 1H), 7.01 (m, 1H), 6.92 (m, 1H), 6.86 (dd, *J* = 9.9, 1.2 Hz, 1H), 3.95 (dq, *J* = 7.2, 0.6 Hz, 2H), 3.70 (s, 2H), 3.06 (t, *J* = 6.0 Hz, 2H), 2.74 (s, 3H), 2.72 (t, *J* = 6.0 Hz, 2H), 0.93 (dt, *J* = 7.2, 0.6 Hz, 3H) ppm; ^{13}C NMR (75 MHz): δ 165.3, 164.1, 160.9, 145.7, 143.1, 143.0, 130.0, 129.8, 122.9, 122.60, 122.56, 114.8, 114.5, 114.1, 113.8, 61.0, 53.1, 50.6, 43.9, 32.0, 13.8 ppm; EI-MS *m/z* 263 (M^+).

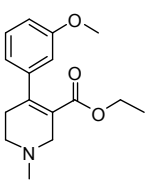
Ethyl 1-methyl-4-(2-fluorophenyl)-1,2,5,6-tetrahydropyridine-3-carboxylate 60c.



^{1}H NMR (300 MHz): δ 7.25 (m, 1H), 6.97-7.12 (m, 3H), 3.93 (q, *J* = 7.2 Hz, 2H), 3.34 (t, *J* = 2.4 Hz, 2H), 2.65 (t, *J* = 8.4 Hz, 2H), 2.57 (m, 2H), 2.47 (s, 3H), 0.90

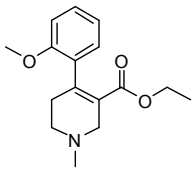
(dt, *J* = 7.2 Hz, 3H) ppm; 13C NMR (75 MHz): δ 166.0, 160.4, 157.1, 141.3, 130.1, 129.8, 128.94, 128.91, 128.8, 127.1, 123.83, 123.79, 115.44, 115.15, 60.3, 54.8, 51.6, 45.7, 33.7, 13.8 ppm; EI-MS *m/z* 263 (M^+).

Ethyl 1-methyl-4-(3-methoxyphenyl)-1,2,5,6-tetrahydropyridine-3-carboxylate 60d.



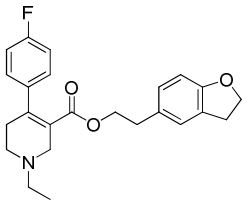
^{1}H NMR (300 MHz): δ 7.23 (t, *J* = 7.8 Hz, 1H), 6.82 (ddd, *J* = 8.4, 2.7, 1.2 Hz, 1H), 6.73 (dt, *J* = 7.8, 1.2 Hz, 1H), 6.69 (dd, *J* = 2.7, 1.2 Hz, 1H), 3.89 (q, *J* = 7.2, 2H), 3.78 (s, 3H), 3.30 (t, *J* = 2.7 Hz, 2H), 2.64 (t, *J* = 2.1 Hz, 2H), 2.57 (m, 2H), 2.46 (s, 3H), 0.90 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (75 MHz): δ 167.1, 159.3, 146.0, 143.7, 129.1, 125.5, 119.4, 112.9, 112.5, 60.3, 55.4, 55.0, 51.9, 45.7, 34.0, 13.9 ppm; EI-MS *m/z* 275 (M^+).

Ethyl 1-methyl-4-(2-methoxyphenyl)-1,2,5,6-tetrahydropyridine-3-carboxylate 60e.



^{1}H NMR (300 MHz): δ 7.24 (ddt, *J* = 7.2, 1.8, 0.6 Hz, 1H), 6.98 (dd, *J* = 7.5, 1.8 Hz, 1H), 6.84-6.93 (m, 2H), 3.87 (q, *J* = 7.2, 2H), 3.78 (s, 3H), 3.33 (br s, 2H), 2.49-2.67 (m, 4H), 2.46 (s, 3H), 0.84 (dt, *J* = 7.2, 0.6 Hz, 3H) ppm; ^{13}C NMR (75 MHz): δ 166.6, 155.7, 144.8, 131.5, 128.4, 128.2, 125.7, 120.4, 110.6, 60.0, 55.7, 54.9, 51.8, 45.8, 33.2, 13.8 ppm; EI-MS *m/z* 275 (M^+).

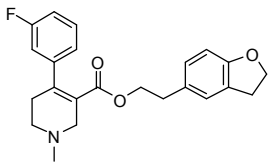
2-(2,3-Dihydrobenzofuran-5-yl)ethyl 1-ethyl-4-(4-fluorophenyl)-1,2,5,6-tetrahydropyridine-3-carboxylate 61.



This product was obtained as a colorless oil (70 mg, 52% yield from **60a**). ^{1}H NMR (300 MHz): δ 7.30 (d, *J* = 9.0 Hz, 2H), 7.02 (d, *J* = 9.0 Hz, 2H), 6.83 (s, 1H), 6.73 (d, *J* = 8.1 Hz, 1H), 6.61 (d, *J* = 8.1 Hz, 1H), 4.49 (t, *J* = 8.7 Hz, 2H), 3.98 (t, *J* = 7.2 Hz, 2H), 3.23 (s, 2H), 3.10 (t, *J* = 8.7 Hz, 2H), 2.60 (t, *J* = 7.5 Hz, 3H), 2.57 (t, *J* = 5.4 Hz, 2H), 2.49 (t, *J* = 5.1, 2.4 Hz, 2H), 2.45 (t, *J* = 7.2 Hz, 2H), 1.18 (t, *J* =

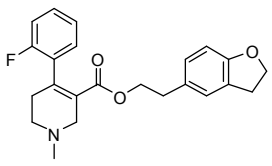
7.5 Hz, 3H) ppm; ^{13}C NMR (75 MHz): δ 166.2, 163.3, 158.8, 144.3, 159.9, 139.2, 139.1, 129.9, 129.1, 129.0, 128.0, 126.6, 125.9, 122.5, 115.4, 115.1, 109.3, 71.3, 65.4, 54.8, 52.0, 49.8, 34.4, 34.3, 30.1, 12.6 ppm; EI-MS *m/z* 395 (M^+); Anal. ($C_{24}H_{26}FNO_3$·HCl) C, H, N.

2-(2,3-Dihydrobenzofuran-5-yl)ethyl 1-methyl-4-(3-fluorophenyl)-1,2,5,6-tetrahydropyridine-3-carboxylate 62.



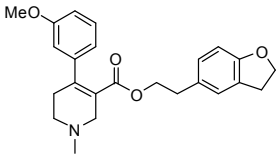
This product was obtained as a colorless oil (125 mg, 43% yield from **60b**). ^{1}H NMR (300 MHz): δ 7.19 (m, 1H), 6.70-6.94 (m, 4H), 6.70 (d, *J* = 8.1 Hz, 1H), 6.59 (d, *J* = 8.1 Hz, 1H), 4.47 (t, *J* = 8.7 Hz, 2H), 3.97 (t, *J* = 7.2 Hz, 2H), 3.21 (s, 2H), 3.08 (t, *J* = 8.7 Hz, 2H), 2.56 (t, *J* = 5.4 Hz, 2H), 2.49 (t, *J* = 5.1, 2.4 Hz, 2H), 2.43 (t, *J* = 7.2 Hz, 2H), 2.39 (s, 3H) ppm; ^{13}C NMR (75 MHz): δ 166.5, 164.2, 160.9, 158.8, 145.3, 144.5, 129,7, 129.6, 129.5, 128.4, 127.2, 126.0, 125.4, 122.8, 122.7, 114.3, 114.2, 114.1, 114.0, 109.1, 71.4, 65.5, 55.0, 51.8, 45.7, 34.3, 34.2, 30.0 ppm; EI-MS *m/z* 381 (M^+); Anal. ($C_{23}H_{24}FNO_3$·HCl) C, H, N.

2-(2,3-Dihydrobenzofuran-5-yl)ethyl 1-methyl-4-(2-fluorophenyl)-1,2,5,6-tetrahydropyridine-3-carboxylate 63.



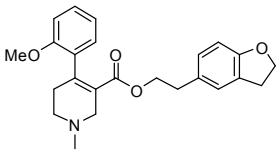
This product was obtained as a light yellow oil (98 mg, 45% yield from **60c**). ^{1}H NMR (300 MHz): δ 7.19 (m, 1H), 6.85-7.05 (m, 3H), 6.81 (s, 1H), 6.70 (dd, *J* = 7.8, 1.5 Hz, 1H), 6.59 (d, *J* = 7.8 Hz, 1H), 4.46 (t, *J* = 8.7 Hz, 2H), 3.97 (t, *J* = 7.2 Hz, 2H), 3.23 (t, *J* = 2.4 Hz, 2H), 3.08 (t, *J* = 8.7 Hz, 2H), 2.57 (t, *J* = 5.4 Hz, 2H), 2.48 (dd, *J* = 5.1, 2.4 Hz, 2H), 2.42 (t, *J* = 7.2 Hz, 2H), 2.38 (s, 3H) ppm; ^{13}C NMR (75 MHz): δ 165.8, 159.2, 158.7, 157.0, 141.6, 129,5, 129.0, 128.9, 128.3, 127.1, 127.0, 125.4, 123.9, 123.8, 115.5, 115.2, 109.1, 71.3, 65.4, 54.9, 51.5, 45.7, 34.2, 34.1, 29.9 ppm; EI-MS *m/z* 381 (M^+); Anal. ($C_{23}H_{24}FNO_3$·HCl·0.3H_2O) C, H, N.

2-(2,3-Dihydrobenzofuran-5-yl)ethyl 1-methyl-4-(3-methoxyphenyl)-1,2,5,6-tetrahydropyridine-3-carboxylate 64.



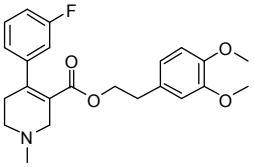
This product was obtained as a light yellow oil (120 mg, 42% yield from **60d**). ^{1}H NMR (300 MHz): δ 7.16 (m, 1H), 6.57-6.87 (m, 6H), 4.46 (t, *J* = 8.7 Hz, 2H), 3.96 (t, *J* = 7.2 Hz, 2H), 3.70 (s, 3H), 3.20 (t, *J* = 2.4 Hz, 2H), 3.08 (t, *J* = 8.7 Hz, 2H), 2.38-2.60 (m, 6H), 2.38 (s, 3H) ppm; ^{13}C NMR (75 MHz): δ 167.0, 159.3, 158.7, 146.2, 143.7, 129.7, 129.2, 128.4, 127.1, 125.4, 119.5, 112.8, 112.6, 109.1, 71.4, 65.4, 55.4, 55.1, 51.9, 45.7, 34.24, 34.17, 30.0 ppm; EI-MS *m/z* 393 (M^{+}); Anal. ($C_{24}H_{27}NO_4$·HCl·0.2H_2O) C, H, N.

2-(2,3-Dihydrobenzofuran-5-yl)ethyl 1-methyl-4-(2-methoxyphenyl)-1,2,5,6-tetrahydropyridine-3-carboxylate 65.



This product was obtained as a colorless oil (103 mg, 38% yield from **60e**). ^{1}H NMR (300 MHz): δ 7.26 (m, 1H), 6.74-7.00 (m, 5H), 6.65 (d, *J* = 8.4 Hz, 1H), 4.53 (t, *J* = 8.7 Hz, 2H), 3.99 (t, *J* = 7.5 Hz, 2H), 3.77 (s, 3H), 3.33 (br s, 2H), 3.15 (t, *J* = 8.7 Hz, 2H), 2.40-2.70 (m, 6H), 2.46 (s, 3H) ppm; ^{13}C NMR (75 MHz): δ 166.4, 158.7, 155.7, 145.2, 131.4, 129.8, 128.6, 128.4, 128.3, 127.1, 125.4, 125.3, 120.5, 110.7, 109.1, 71.4, 65.2, 55.7, 54.6, 51.5, 45.5, 34.2, 32.9, 30.0 ppm; EI-MS *m/z* 393 (M^{+}); Anal. ($C_{24}H_{27}NO_4$·HCl·0.1H_2O) C, H, N.

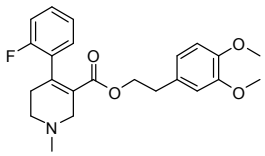
3,4-Dimethoxyphenethyl 1-methyl-4-(3-fluorophenyl)-1,2,5,6-tetrahydropyridine-3-carboxylate 66.



This product was obtained as a colorless oil (128 mg, 43% yield from **60c**). ^{1}H NMR (300 MHz): δ 6.48-7.20 (m, 7H), 4.00 (t, *J* = 7.2 Hz, 2H), 3.78 (s, 3H), 3.77 (s, 3H), 3.19 (t, *J* = 2.1 Hz, 2H), 2.35-2.58 (m, 6H), 2.37 (s, 3H)

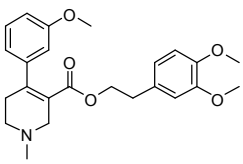
ppm; ^{13}C NMR (75 MHz): δ 166.5, 164.1, 160.8, 148.84, 148.75, 147.6, 145.4, 145.3, 144.5, 144.4, 130.1, 129.6, 129.5, 125.9, 122.7, 122.6, 120.8, 114.2, 114.1, 114.0, 113.8, 112.0, 111.2, 65.1, 56.0, 55.9, 55.0, 51.7, 45.6, 34.4, 34.1 ppm; EI-MS *m/z* 399 (M^+); Anal. ($C_{23}H_{26}FNO_4 \cdot HCl \cdot 0.4H_2O$) C, H, N.

3,4-Dimethoxyphenethyl 1-methyl-4-(2-fluorophenyl)-1,2,5,6-tetrahydropyridine-3-carboxylate 67.



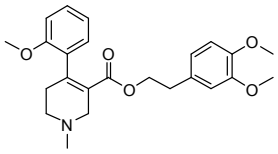
This product was obtained as colorless oil (95 mg, 41% yield from **60b**). ^{1}H NMR (300 MHz): δ 7.18 (m, 1H), 6.95-7.04 (m, 3H), 6.67 (dd, *J* = 8.7, 1.2 Hz, 1H), 6.54 (m, 2H), 4.00 (dt, *J* = 7.2, 1.2 Hz, 2H), 3.77 (s, 3H), 3.76 (s, 3H), 3.23 (s, 2H), 2.38-2.58 (m, 6H), 2.38 (s, 3H) ppm; ^{13}C NMR (75 MHz): δ 165.8, 160.4, 157.1, 148.8, 147.6, 141.7, 130.2, 129.0, 128.92, 128.87, 126.9, 123.9, 123.8, 120.8, 115.5, 115.2, 112.0, 111.2, 65.1, 56.1, 56.0, 54.8, 51.6, 45.7, 34.4, 33.7 ppm; EI-MS *m/z* 381 (M^+); Anal. ($C_{23}H_{26}FNO_4 \cdot HCl$) C, H, N.

3,4-Dimethoxyphenethyl 1-methyl-4-(3-methoxyphenyl)-1,2,5,6-tetrahydropyridine-3-carboxylate 68.



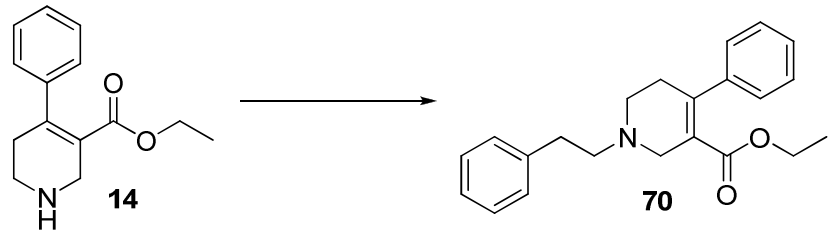
This product was obtained as a light yellow oil (121 mg, 40% yield from **60d**). ^{1}H NMR (300 MHz): δ 7.15 (t, *J* = 7.8 Hz, 1H), 6.74 (ddd, *J* = 8.1, 2.4, 0.9 Hz, 1H), 6.60-6.70 (m, 3H), 6.48-6.54 (m, 2H), 3.99 (t, *J* = 7.2 Hz, 2H), 3.77 (s, 3H), 3.76 (s, 3H), 3.69 (s, 3H), 3.20 (t, *J* = 2.4 Hz, 2H), 2.47-2.60 (m, 4H), 2.44 (t, *J* = 7.2 Hz, 2H), 2.37 (s, 3H) ppm; ^{13}C NMR (75 MHz): δ 166.8, 159.2, 148.7, 147.5, 146.3, 143.6, 130.2, 129.1, 125.2, 120.8, 119.3, 112.7, 112.5, 112.0, 111.2, 65.1, 56.0, 55.9, 55.3, 54.9, 51.7, 45.5, 34.3, 34.0 ppm; EI-MS *m/z* 411 (M^+); Anal. ($C_{24}H_{29}NO_5 \cdot HCl \cdot 1.0H_2O$) C, H, N.

3,4-Dimethoxyphenethyl 1-methyl-4-(2-methoxyphenyl)-1,2,5,6-tetrahydropyridine-3-carboxylate 69.



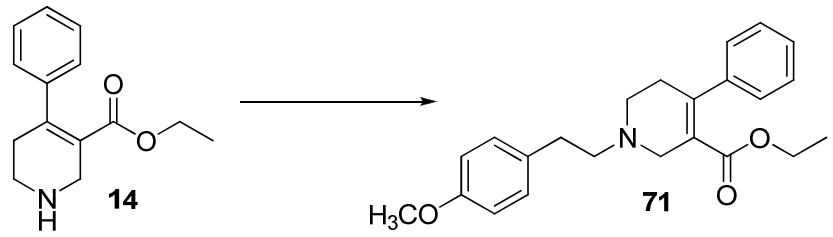
This product was obtained as a light yellow oil (127 mg, 45% yield from **60e**). ^{1}H NMR (300 MHz): δ 7.17 (m, 1H), 6.92 (dd, *J* = 7.5, 2.1 Hz, 1H), 6.84 (dt, *J* = 7.5, 0.9 Hz, 1H), 6.79 (d, *J* = 8.1 Hz, 1H), 6.68 (m, 1H), 6.48-6.55 (m, 2H), 3.96 (t, *J* = 7.2 Hz, 2H), 3.77 (s, 6H), 3.69 (s, 3H), 3.24 (s, 2H), 2.40-2.60 (m, 6H), 2.38 (s, 3H) ppm; ^{13}C NMR (75 MHz): δ 166.3, 155.6, 148.8, 147.6, 145.3, 131.4, 130.4, 128.5, 128.2, 125.5, 120.9, 120.4, 112.1, 111.2, 110.7, 64.8, 56.1, 56.0, 55.7, 54.9, 51.8, 45.8, 34.4, 33.3 ppm; EI-MS *m/z* 411 (M^+); Anal. ($C_{24}H_{29}NO_5 \cdot HCl \cdot 1.3H_2O$) C, H, N.

Ethyl 1-phenethyl-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 70.



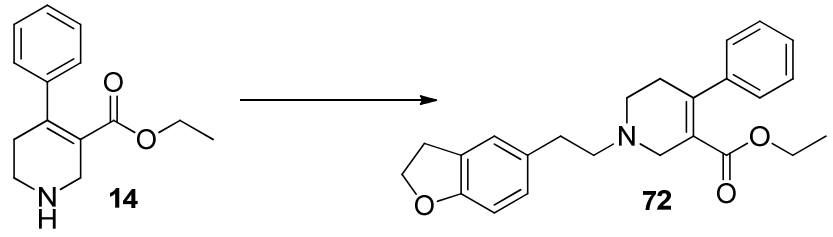
A mixture of **14** (100 mg, 0.43 mmol), phenethyl iodide (200 mg, 0.86 mmol), K_2CO_3 (120 mg, 0.86 mmol), and EtOH (5 mL) was heated at 65 ºC for 24 h. After cooling to room temperature, EtOAc (20 mL) was added and washed with water (10 mL) and saline (10 mL). The organic phase was dried over Na_2SO_4, filtered and concentrated under vacuum. The residue was purified by silica gel column chromatography (2:1 hexanes:EtOAc) to afford **70** (89 mg, 61% yield) as a colorless oil. ^{1}H NMR (300 MHz): δ 7.12-7.37 (m, 10H), 3.89 (q, *J* = 7.2 Hz, 2H), 3.45 (t, *J* = 2.7 Hz, 2H), 2.92 (m, 2H), 2.70-2.82 (m, 4H), 2.59 (m, 2H), 0.85 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (75 MHz): δ 167.4, 146.3, 142.3, 140.2, 128.8, 128.0, 127.3, 126.9, 126.2, 125.6, 60.3, 60.2, 53.3, 50.1, 34.11, 33.99, 13.8 ppm; EI-MS *m/z* 335 (M^+); Anal. ($C_{22}H_{25}NO_2 \cdot HCl$) C, H, N.

Ethyl 1-(4-methoxyphenethyl)-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 71.



A mixture of **14** (150 mg, 0.65 mmol), 4-methoxyphenethyl bromide (180 mg, 0.84 mmol), DIPEA (181 mg, 1.40 mmol), and acetone (5 mL) was refluxed for 24 h. After cooling to room temperature, solvent was removed under vacuum. CH_2Cl_2 (20 mL) was added and washed with water (10 mL) and saline (10 mL). The organic phase was dried over Na_2SO_4, filtered and concentrated under vacuum. The residue was purified by silica gel column chromatography (50:1 CH_2Cl_2:MeOH) to afford **71** (95 mg, 37% yield) as a colorless oil. ^{1}H NMR (300 MHz): δ 7.20-7.35 (m, 3H), 7.10-7.18 (m, 4H), 6.83 (dd, *J* = 8.7, 1.8 Hz, 2H), 3.88 (q, *J* = 7.2 Hz, 2H), 3.77 (s, 3H), 3.42 (t, *J* = 2.7 Hz, 2H), 2.83 (m, 2H), 2.67-2.78 (m, 4H), 2.57 (m, 2H), 0.84 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (75 MHz): δ 167.4, 158.0, 146.3, 142.3, 132.3, 129.7, 128.0, 127.3, 126.9, 125.7, 114.0, 60.4, 60.3, 55.5, 53.4, 50.1, 34.0, 33.2, 13.8 ppm; EI-MS *m/z* 365 (M^+); Anal. ($C_{23}H_{27}NO_3 \cdot C_4H_4O_4 \cdot 1/3H_2O$) C, H, N.

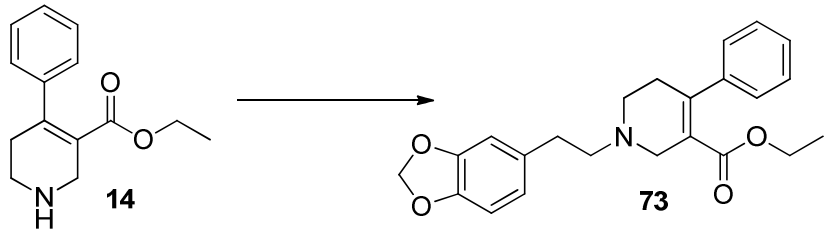
Ethyl 1-(2-(2,3-dihydrobenzofuran-5-yl)-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 72.



A mixture of **14** (150 mg, 0.65 mmol), 5-(2-bromoethyl)-2,3-dihydrobenzofuran (295 mg, 1.30 mmol), K_2CO_3 (179 mg, 1.30 mmol), and acetonitrile (5 mL) was refluxed overnight. After

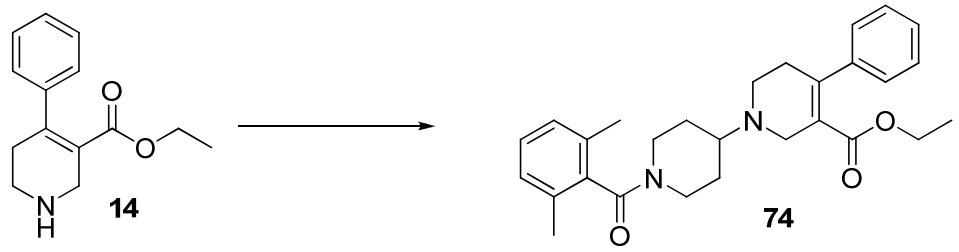
cooling to room temperature, solvent was removed under vacuum. CH_2Cl_2 (20 mL) was added and washed with water (10 mL) and saline (10 mL). The organic phase was dried over Na_2SO_4, filtered and concentrated under vacuum. The residue was purified by silica gel column chromatography (50:1 CH_2Cl_2:MeOH) to afford **72** (128 mg, 52% yield) as a colorless oil. ^{1}H NMR (500 MHz): δ 7.23-7.35 (m, 3H), 7.14 (dd, *J* = 7.0, 1.5 Hz, 2H), 6.78 (s, 1H), 6.67 (d, *J* = 7.5 Hz, 1H), 6.59 (d, *J* = 7.5 Hz, 1H), 4.50 (t, *J* = 9.0 Hz, 2H), 3.90 (q, *J* = 7.5 Hz, 2H), 3.40 (t, *J* = 2.5 Hz, 2H), 3.13 (t, *J* = 9.0 Hz, 2H), 2.87 (m, 2H), 2.66-2.83 (m, 4H), 2.58 (m, 2H), 0.85 (t, *J* = 7.5 Hz, 3H) ppm; EI-MS *m/z* 377 (M^+); Anal. ($C_{23}H_{25}NO_3$·HCl) C, H, N.

Ethyl 1-(2-(2-(benzo[*d*][1,3]dioxol-5-yl)ethyl)-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 73.



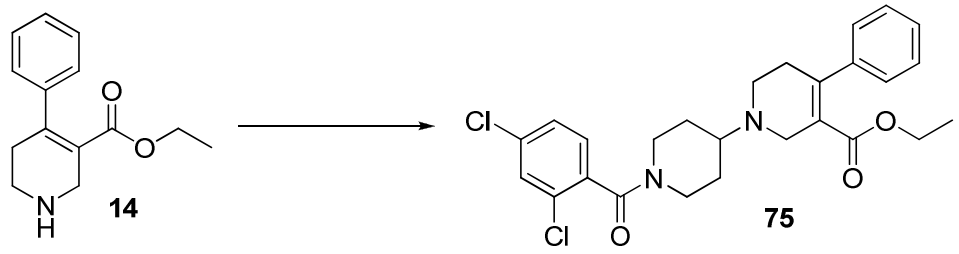
This product was synthesized by utilizing a similar method described for compound **72** from **14** (colorless oil, 102 mg, 57% yield). ^{1}H NMR (300 MHz): δ 7.22-7.35 (m, 3H), 7.15 (dd, *J* = 7.8, 1.8 Hz, 2H), 6.62-6.75 (m, 3H), 5.90 (s, 2H), 3.89 (q, *J* = 7.2 Hz, 2H), 3.42 (t, *J* = 2.7 Hz, 2H), 2.87 (m, 2H), 2.65-2.85 (m, 4H), 2.58 (m, 2H), 0.85 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (75 MHz): δ 167.3, 147.5, 146.2, 145.8, 142.2, 133.8, 127.9, 127.2, 126.8, 121.8, 121.5, 109.2, 108.2, 100.8, 63.7, 60.2, 53.2, 49.9, 39.1, 33.6, 13.7 ppm; EI-MS *m/z* 379 (M^+); Anal. ($C_{23}H_{25}NO_4$·HCl·0.2H_2O) C, H, N.

Ethyl 1-(1-(2,6-dimethylbenzoyl)piperidin-4-yl)-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 74.



To a solution of **14** (120 mg, 0.52 mmol), 1-(2,6-dimethylbenzoyl)piperidine-4-one (120 mg, 0.52 mmol), and HOAc (54 mg, 1.04 mmol) in THF (5 mL) was added carefully $NaBH(OAc)_3$ (143 mg, 0.78 mmol). The mixture was heated at 65 ºC for 8 h and cooled to room temperature. Water (5 mL) was added and the pH of the resulting mixture was adjusted to ~10 by using 2 N NaOH. Extracted with CH_2Cl_2 (10 mL × 3) and the combined organic extracts were dried over Na_2SO_4, filtered and concentrated under vacuum. The residue was purified by silica gel column chromatography (30:1 CH_2Cl_2:MeOH) to afford **74** (93 mg, 44% yield) as a light yellow oil. ^{1}H NMR (300 MHz): δ 7.23-7.40 (m, 5H), 7.08-7.16 (m, 3H), 3.88 (q, *J* = 6.9 Hz, 2H), 3.34-3.50 (m, 6H), 3.09 (m, 1H), 2.65-2.82 (m, 4H), 2.52 (s, 6H), 1.80-1.93 (m, 2H), 1.52-1.70 (m, 2H), 0.86 (2 t, *J* = 6.9 Hz, 3H) ppm; EI-MS *m/z* 446 (M^+); Anal. ($C_{28}H_{34}N_2O_3$·HCl) C, H, N.

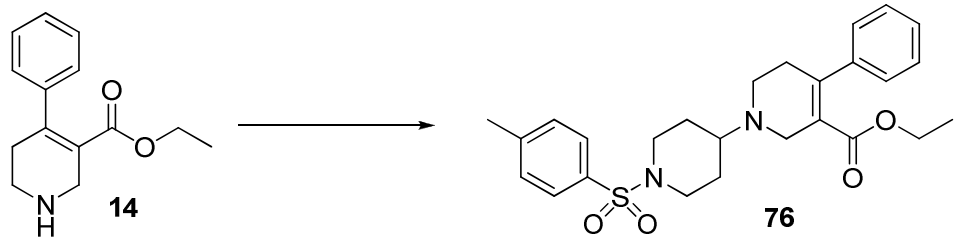
Ethyl 1-(1-(2,4-dichlorobenzoyl)piperidin-4-yl)-4-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylate 75.



To a solution of **14** (105 mg, 0.45 mmol), 1-(2,4-dichlorobenzoyl)piperidine-4-one (124 mg, 0.45 mmol), and HOAc (54 mg, 0.90 mmol) in THF (4 mL) was added carefully $NaBH(OAc)_3$ (143 mg, 0.68 mmol). The mixture was stirred for 6 h at room temperature. Water (4 mL) was added and the pH of the resulting mixture was adjusted to ~10 by using 2 N NaOH. Extracted

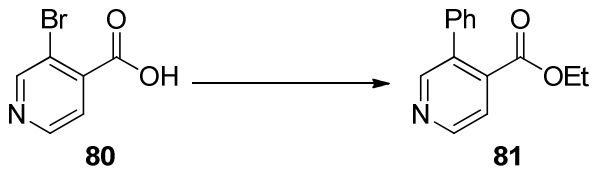
with CH_2Cl_2 (10 mL × 3) and the combined organic extracts were dried over Na_2SO_4, filtered and concentrated under vacuum. The residue was purified by silica gel column chromatography (30:1 CH_2Cl_2:MeOH) to afford **75** (105 g, 48% yield) as a light yellow oil. ^{1}H NMR (300 MHz): δ 7.42 (s, 1H), 7.20-7.38 (m, 5H), 7.14 (d, *J* = 7.8 Hz, 2H), 3.88 (q, *J* = 6.9 Hz, 2H), 3.36-3.55 (m, 6H), 3.07 (m, 1H), 2.62-2.80 (m, 4H), 1.80-1.95 (m, 2H), 1.50-1.70 (m, 2H), 0.84 (2 t, *J* = 6.9 Hz, 3H) ppm; ^{13}C NMR (75 MHz): δ 167.3, 165.8, 146.2, 142.0, 135.3, 131.2, 131.2, 129.6, 128.5, 127.9, 127.6, 127.3, 126.8, 125.6, 65.6, 60.3, 60.2, 46.0, 43.4, 33.3, 27.6, 21.7, 13.6 ppm; EI-MS *m/z* 486/488/490 (M^+); Anal. ($C_{26}H_{28}Cl_2N_2O_3$·HCl) C, H, N.

Ethyl 1-(1-tosylpiperidin-4-yl)-4-phenyl--1,2,5,6-tetrahydropyridine-3-carboxylate 76.



This product was synthesized by utilizing a similar method described for compound **75** from **14** (light yellow oil, 123 mg, 56% yield). ^{1}H NMR (300 MHz): δ 7.63 (2 d, *J* = 8.1 Hz, 2H), 7.22-7.38 (m, 5H), 7.10 (dd, *J* = 7.2, 1.8 Hz, 2H), 3.87 (2 q, *J* = 7.2 Hz, 2H), 3.68 (m, 1H), 3.41 (s, 2H), 3.30 (m, 2H), 2.67-2.82 (m, 4H), 2.43 (s, 3H), 2.30 (m, 2H), 1.80-2.00 (m, 2H), 1.57-1.74 (m, 2H), 0.83 (2 t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (75 MHz): δ 167.3, 146.2, 143.6, 143.5, 141.9, 133.0, 132.8, 129.6, 127.9, 127.6, 127.55, 127.2, 126.7, 125.5, 65.6, 60.3, 60.2, 46.0, 43.4, 33.3, 27.6, 21.7, 13.6 ppm; EI-MS *m/z* 468 (M^+); Anal. ($C_{26}H_{32}N_2O_4S$·HCl) C, H, N.

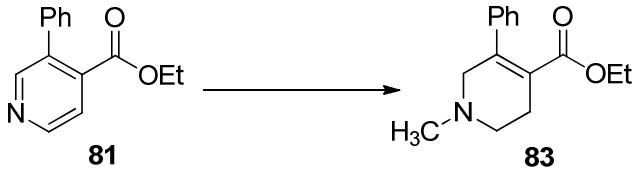
Ethyl 3-phenylisonicotinate 81.



Compound **80** (4.54 g, 22.47 mmol) in EtOH (100 mL) was treated with concentrated H_2SO_4 (1.37 mL, 24.72 mmol). The mixture was refluxed overnight. Majority of the solvent was removed under vacuum. Water (50 mL) was added and the resulting aqueous solution was neutralized with 2 N NaOH to pH 10. Extracted with CH_2Cl_2 (50 mL × 2) and the combined organic extracts were dried over Na_2SO_4, filtered and concentrated under vacuum to afford 4.05 g brown oil (78% yield) which was used for next step without further purification.

The ethyl ester of compound **80** (1.49 g, 7.00 mmol) was undergone Suzuki coupling with phenylboronic acid (1.02 g, 8.40 mmol) by using a similar procedure as described for compound **12**. **81** was purified by silica gel column purification (8:1 hexanes:EtOAc) as a colorless oil (1.49 g, 94% yield). ^{1}H NMR (300 MHz): δ 8.71 (d, J = 4.8 Hz, 1H), 8.69 (s, 1H), 7.63 (d, J = 4.8 Hz, 1H), 7.28-7.44 (m, 5H), 4.15 (q, J = 7.2 Hz, 2H), 1.03 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (75 MHz): δ 167.1, 151.4, 149.0, 138.3, 137.5, 136.1, 128.7, 128.4, 128.1, 122.6, 61.9, 13.9 ppm; EI-MS *m/z* 227 (M^+).

Ethyl 1-metyl-3-phenyl-1,2,5,6-tetrahydropyridine-4-carboxylate 83.



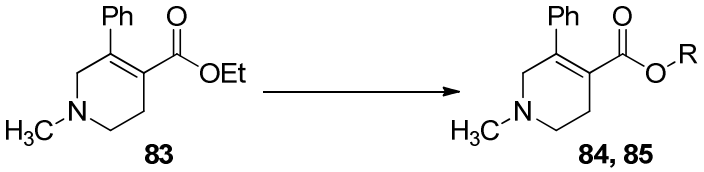
81 **83**

Compound **81** (1.49 g, 6.56 mmol) in acetone (20 mL) was treated with MeI (4.66 g, 32.80 mmol). The mixture was stirred at room temperature overnight. Solvent was removed under vacuum. The residue was washed with Et_2O and filtered to afford 2.41g (quantitative yield) yellow powder.

The above quaternary pyridinium product (1.50 g, 4.06 mmol) in EtOH (20 mL) was treated with $NaBH_4$ (614 mg, 16.24 mmol) at room temperature for 1 h. Reaction was quenched by adding acetone. Solvents were removed under vacuum and the residue was suspended in water (30 mL).

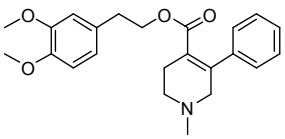
Extracted with CH_2Cl_2 (20 mL × 3) and the combined organic extracts were dried over Na_2SO_4, filtered and concentrated under vacuum. The residue was purified by silica gel column chromatography (10:1 CH_2Cl_2:MeOH) to afford **83** (867 mg, 87% yield) as a colorless oil. ^{1}H NMR (300 MHz): δ 7.20-7.37 (m, 3H), 7.10-7.18 (m, 2H), 3.88 (q, *J* = 7.2 Hz, 2H), 3.20 (s, 2H), 2.52-2.64 (m, 4H), 2.41 (s, 3H), 0.84 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (75 MHz): δ 168.3, 145.2, 140.7, 128.0, 127.4, 127.3, 125.3, 60.7, 60.3, 51.7, 45.5, 27.4, 13.8 ppm; EI-MS *m/z* 345 (M^+).

Synthesis of compound 84 and 85.



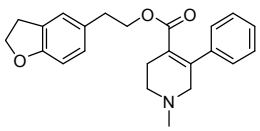
The procedure for the synthesis of **84** and **85** from **83** were similar to the one described for **8**, **17-36** from **15**.

3,4-Dimethoxyphenethyl 1-methyl-3-phenyl-1,2,5,6-tetrahydropyridine-4-carboxylate 84.



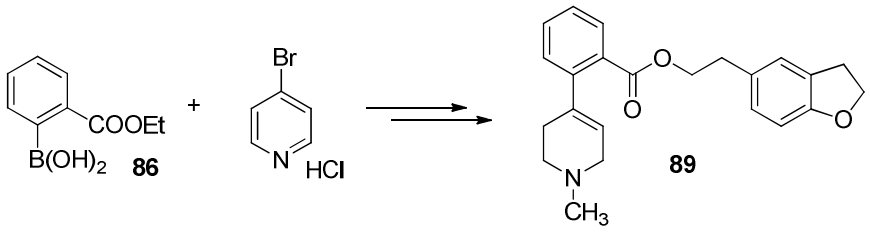
This product was obtained as a light yellow oil (80 mg, 33% yield from **83**). ^{1}H NMR (500 MHz): δ 7.33 (d, *J* = 5, 1.5 Hz, 2H), 7.21-7.27 (m, 3H), 6.74 (d, *J* = 9.0 Hz, 1H), 7.57 (s, 1H), 6.56 (d, *J* = 9.0 Hz, 1H), 4.05 (t, *J* = 7.5 Hz, 2H), 3.80-3.95 (m, 2H), 3.84 (s, 3H), 3.83 (s, 3H), 3.25 (br, 2H), 2.91 (br, 2H), 2.88 (s, 3H), 2.46 (t, *J* = 7.5 Hz, 2H) ppm; ^{13}C NMR (125 MHz): δ 166.7, 149.0, 147.9, 140.6, 138.0, 133.3, 131.3, 130.0, 127.8, 125.2, 121.0, 112.1, 111.4, 65.6, 56.1, 56.0, 55.9, 49.8, 42.7, 42.6, 34.2 ppm; EI-MS *m/z* 381 (M^+); Anal. ($C_{23}H_{27}NO_4 \cdot C_4H_4O_4 \cdot 0.5H_2O$) C, H, N.

2-(2,3-Dihydrobenzofuran-5-yl)ethyl 1-methyl-3-phenyl-1,2,5,6-tetrahydropyridine-4-carboxylate 85.



This product was obtained as a light yellow oil (79 mg, 34% yield from **83**). ^{1}H NMR (300 MHz): δ 7.20-7.38 (m, 3H), 7.12-7.20 (m, 2H), 6.85 (s, 1H), 6.75 (dd, *J* = 8.1, 1.5 Hz, 1H), 6.64 (d, *J* = 8.4 Hz, 1H), 4.53 (t, *J* = 9.0 Hz, 2H), 4.00 (t, *J* = 7.2 Hz, 2H), 3.36 (s, 2H), 3.14 (t, *J* = 9.0 Hz, 2H), 2.70-2.83 (m, 2H), 2.58-2.70 (m, 2H), 2.52 (s, 2H), 2.42 (t, *J* = 7.2 Hz, 2H) ppm; ^{13}C NMR (75 MHz): δ 167.8, 158.7, 140.0, 129.6, 128.4, 128.2, 127.7, 127.6, 127.4, 127.1, 125.4, 125.2, 109.1, 71.4, 65.5, 59.6, 51.2, 44.8, 34.2, 30.0, 26.6 ppm; EI-MS *m/z* 363 (M^+); Anal. ($C_{23}H_{25}NO_3 \cdot 0.95C_4H_4O_4$) C, H, N.

2-(2,3-Dihydrobenzofuran-5-yl)ethyl 2-(1-methyl-1,2,5,6-tetrahydropyridine-4-yl)benzoate 89.



The procedure for the synthesis of **89** from **86** and 4-bromopyridine were similar to the one described for **84** from **80** and phenylboronic acid. **89** was obtained as a colorless oil. ^{1}H NMR (300 MHz): δ 7.82 (d, *J* = 7.5 Hz, 1H), 7.47 (dt, *J* = 7.5, 0.9 Hz, 1H), 7.33 (t, *J* = 7.5 Hz, 1H), 7.24 (d, *J* = 7.8 Hz, 1H), 7.09 (s, 1H), 6.99 (d, *J* = 7.8 Hz, 1H), 6.72 (d, *J* = 8.4 Hz, 1H), 5.47 (s, 1H), 4.56 (t, *J* = 8.7 Hz, 2H), 4.42 (t, *J* = 7.2 Hz, 2H), 3.32 (d, *J* = 2.4 Hz, 2H), 3.18 (t, *J* = 8.7 Hz, 2H), 2.85-3.00 (m, 4H), 2.60 (s, 3H), 2.52 (br s, 2H) ppm; ^{13}C NMR (75 MHz): δ 167.2, 158.9, 143.6, 138.3, 132.1, 130.2, 130.0, 129.6, 129.2, 128.5, 127.43, 127.36, 125.6, 119.4, 109.3, 71.4, 66.1, 53.4, 51.5, 44.3, 34.9, 30.0, 29.4 ppm; EI-MS *m/z* 363 (M^+); Anal. ($C_{23}H_{25}NO_3 \cdot HCl$) C, H, N.