**Supporting Information**

# New Ligands with Affinity for the $\alpha_4\beta_2$ Subtype of Nicotinic Acetylcholine Receptors. Synthesis, Receptor Binding and 3D-QSAR Modelling.

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Table 1. Elemental Analysis Results.

| | | Calcd. | | | Found | | |
|---|---|---|---|---|---|---|---|
| Compd. | | C | H | N | C | H | N |
| **1** | $C_{10}H_{15}N_3O\times0.5C_4H_4O_4\times H_2O$ | 53.52 | 7.11 | 15.60 | 53.49 | 6.65 | 15.68 |
| **2** | $C_{11}H_{15}N_3O\times1.2C_4H_4O_4$ | 55.08 | 5.79 | 12.20 | 55.21 | 5.80 | 12.45 |
| **3** | $C_{10}H_{14}N_3OBr\times1.2C_4H_4O_4\times0.5H_2O$ | 42.28 | 4.75 | 9.99 | 42.37 | 4.37 | 9.80 |
| **4** | $C_9H_{11}N_3BrCl\times1.2C_4H_4O_4$ | 39.85 | 3.82 | 10.10 | 39.83 | 3.73 | 10.46 |
| **5** | $C_{10}H_{14}N_3Cl\times1.4C_4H_4O_4\times0.5H_2O$ | 48.90 | 5.42 | 10.97 | 49.00 | 5.12 | 10.63 |
| **6** | $C_{11}H_{13}N_3\times1.2C_4H_4O_4$ | 58.12 | 5.49 | 12.87 | 58.41 | 5.52 | 13.12 |
| **9** | $C_{13}H_{19}N_3O\times C_4H_4O_4$ | 58.44 | 6.63 | 10.69 | 58.09 | 6.61 | 12.03 |
| **10** | $C_{10}H_{13}N_3BrCl\times C_4H_4O_4$ | 41.35 | 4.21 | 10.33 | 41.48 | 4.08 | 10.06 |
| **11** | $C_{10}H_{13}N_3ClBr\times1.2C_4H_4O_4\times0.1H_2O$ | 41.18 | 4.20 | 9.73 | 40.87 | 4.03 | 9.93 |
| **12** | $C_{10}H_{14}N_3OI\times2HCL\times0.3H_2O$ | 30.30 | 3.97 | 10.60 | 30.00 | 4.09 | 10.32 |
| **13** | $C_{13}H_{19}N_3\times1.5C_4H_4O_4$ | 58.30 | 6.44 | 10.74 | 58.03 | 6.41 | 10.70 |
| **30** | $C_{15}H_{21}N_3O\times1.3\ C_4H_4O_4\times2H_2O$ | 54.37 | 6.82 | 9.42 | 54.68 | 6.34 | 9.72 |
| **31** | $C_{14}H_{21}N_3O\times1.5\ C_4H_4O_4\times0.5H_2O$ | 55.81 | 6.56 | 9.76 | 56.22 | 6.36 | 9.80 |
| **32** | $C_{15}H_{21}N_3O\times1.1\ C_4H_4O_4$ | 60.20 | 6.61 | 10.86 | 60.24 | 6.60 | 10.93 |
| **33** | $C_{13}H_{19}N_3O\times1.2\ C_4H_4O_4$ | 57.38 | 6.44 | 11.28 | 57.44 | 6.44 | 11.53 |
| **34** | $C_{14}H_{21}N_3O\times2\ C_4H_4O_4$ | 55.11 | 6.10 | 8.76 | 55.43 | 6.41 | 8.94 |
| **35** | $C_{13}H_{18}ClN_3\times1.2\ C_4H_4O_4$ | 54.67 | 5.88 | 10.75 | 54.89 | 5.89 | 10.96 |
| **36** | $C_{10}H_{13}ClN_2O\times\ C_4H_4O_4$ | 51.15 | 5.21 | 8.52 | 51.24 | 5.14 | 8.39 |
| **38** | $C_{12}H_{19}N_3O\times1.5\ C_4H_4O_4$ | 54.68 | 6.37 | 10.63 | 54.51 | 6.33 | 10.54 |
| **39** | $C_{15}H_{25}N_3O\times1.5C_4H_4O_4$ | 57.65 | 7.14 | 9.60 | 57.71 | 7.17 | 9.60 |
| **40** | $C_{11}H_{17}N_3\times2C_4H_4O_4\times0.3H_2O$ | 53.22 | 6.02 | 9.80 | 53.02 | 5.91 | 9.42 |
| **41** | $C_{11}H_{16}N_3Br\times1.5C_4O_4H_4$ | 45.96 | 4.99 | 9.46 | 45.96 | 4.99 | 9.46 |
| **42** | $C_{11}H_{16}ClN_3\times1.6C_4H_4O_4$ | 50.79 | 5.49 | 10.21 | 50.68 | 5.58 | 10.61 |
| **43** | $C_{13}H_{18}N_3OBr\times C_4H_4O_4\times H_2O$ | 45.75 | 5.42 | 9.42 | 45.65 | 5.15 | 9.38 |
| **48** | $C_{11}H_{16}N_3Br\times0.7\ C_4H_4O_4\times0.8H_2O$ | 45.31 | 5.62 | 11.49 | 45.55 | 5.55 | 11.57 |
| **49** | $C_{12}H_{16}N_3BrO\times1.2\ C_4H_4O_4$ | 46.13 | 4.79 | 9.61 | 46.09 | 4.78 | 9.99 |
| **50** | $C_9H_{12}N_3Br\times0.8\ C_4H_4O_4\times0.5H_2O$ | 42.60 | 4.75 | 12.22 | 42.81 | 4.51 | 12.60 |

## Experimental Details

**Chemistry.** Solvents and reagents were purchased from commercial sources and used without further purification unless otherwise stated. $^1$H NMR spectra were recorded on a Bruker AM 500-MHz spectrometer. Splitting patterns are described as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m) and broad (b). The chemical shifts are recorded in parts per million (δ) referenced to TMS. The fumarate protons are generally seen at 6.48 ppm. The uncorrected melting points were determined on a Griffin melting point apparatus. After extraction, the organic mixtures were dried with $MgSO_4$, filtered and evaporated. Column chromatography (CC) was performed on silica gel (Merck, 0.040-0.063 mm). All moisture-sensitive reactions were performed under nitrogen using oven-dried glassware. A-85380 (**56**) was synthesized as previously described[28]. Elemental analysis were performed by the University of Copenhagen.

## Spectroscopic Data

**3-Bromo-5-methoxypyridine (1a).** $^1$H NMR ($CDCl_3$): $\delta$8.45 (1H, s), 8.40 (1H, s), 7.54 (1H, s), 4.01 (3H, m).

**4-(5-Methoxypyridin-3-yl)-piperazine-1-carboxylic acid *tert*-butyl ester (1c).** $^1$H NMR ($CDCl_3$): $\delta$7.97 (1H, s), 7.84 (1H, s), 6.71 (1H, s), 3.81 (3H, m), 3.56 (4H, m), 3.13 (4H, m), 1.45 (9H, m).

**1-(5-Methoxypyridin-3-yl)-piperazine fumaric acid salt (1).** $^1$H NMR (DMSO-*d6*): $\delta$ 7.90 (1H, s), 7.70 (1H, s), 6.43 (1H, s), 3.78 (3H, m), 3.20 (4H, m), 2.90 (4H, m).

**2-(5-Chloropyridin-3-yloxy)-ethanol (2c).** $^1$H NMR ($CDCl_3$): $\delta$8.29 (2H, m), 7.29 (1H, m), 4.20 (2H, m), 4.05 (2H, m).

**3-Chloro-5-vinyloxypyridine (2d).** $^1$H NMR (DMSO-*d6*): $\delta$8.10 (2H, m), 7.19 (1H, m), 6.51 (1H, m), 4.81 (1H, m), 4.53 (1H, m).

**1-(5-Vinyloxypyridin-3-yl)-piperazine fumaric acid salt (2).** $^1$H NMR (DMSO-*d6*): $\delta$ 8.09 (1H, s), 7.80 (1H, s), 7.01 (1H, s), 6.96 (1H, m), 4.79 (1H, m), 4.50 (1H, m), 3.30 (4H, m), 3.01 (4H, m).

**4-*tert*-Butoxycarbonyl-1-(6-bromo-5-methoxypyridin-3-yl)-piperazine (3a).** $^1$H NMR ($CDCl_3$): $\delta$7.71 (1H, s), 6.90 (1H, s), 3.92 (3H, s), 3.65 (4H, s), 3.22 (4H, s), 1.51 (9H, m).

**1-(6-Bromo-5-methoxypyridin-3-yl)-piperazine fumaric acid salt (3).** $^1$H NMR (DMSO-*d6*): $\delta$7.64 (1H, s), 7.01 (1H, s), 3.85 (3H, s), 3.37 (4H, m), 3.18 (4H, m).

**1-(5-Bromopyridin-3-yl)-piperazine (4b).** $^1$H NMR (DMSO-*d6*): $\delta$8.32 (1H, s), 8.09 (1H, s), 7.59 (1H, s), 3.39 (4H, m), 3.09 (4H, m).

**1-(5-Bromopyridin-3-yl)-piperazine-1-carboxylic acid *tert*-butyl ester (4c).** $^1$H NMR ($CDCl_3$): $\delta$8.18 (1H, s), 8.11 (1H, s), 7.23 (1H, s), 3.56 (4H, m), 3.18 (4H, m), 1.46 (9H, m).

**1-(5,6-Dibromopyridin-3-yl)-piperazine-1-carboxylic acid *tert*-butyl ester (4d).** $^1$H NMR ($CDCl_3$): $\delta$8.00 (1H, s), 7.42 (1H, s), 3.62 (4H, m), 3.20 (4H, m), 1.51 (9H, s).

**1-(5,6-Dibromopyridin-3-yl)-piperazine (4e).** $^1$H NMR (DMSO-*d6*): $\delta$8.03 (1H, s), 7.64 (1H, s), 4.10 (1H, m), 3.11 (4H, m), 2.79 (4H, m).

**1-(5-Bromo-6-chloropyridin-3-yl)-piperazine fumaric acid salt (4).** $^1$H NMR (DMSO-*d6*): $\delta$8.13 (1H, m), 7.80 (1H, m), 3.21 (4H, m), 2.87 (4H, m).

**1-(5-Chloropyridin-3-yl)-4-*tert*-butoxycarbonylpiperazine (5b).** $^1$H NMR ($CDCl_3$): $\delta$ 8.15 (1H, s), 8.08 (1H, s), 7.20 (1H, s), 3.52 (4H, m), 3.12 (4H, m), 1.45 (9H, m).
**1-(6-Bromo-5-chloropyridin-3-yl)-4-*tert*-butoxycarbonylpiperazine (5c).** $^1$H NMR ($CDCl_3$): $\delta$7.98 (1H, m), 7.24 (1H, m), 3.61 (4H, m), 3.20 (4H, m), 1.50 (9H, m).
**1-(5-Chloro-6-methylpyridin-3-yl)-piperazine fumaric acid salt (5).** $^1$H NMR (DMSO-*d6*): $\delta$8.28 (1H, m), 7.56 (1H, m), 3.51 (4H, m), 3.20 (4H, m), 2.59 (3H, m).
**1-(5-Ethynylpyridin-3-yl)-4-*tert*-butoxycarbonyl-piperazine (6a).** $^1$H NMR ($CDCl_3$): $\delta$ 8.30 (1H, s), 8.12 (1H, s), 7.28 (1H, s), 3.61 (4H, m), 3.21 (5H, m), 1.51 (9H, m).
**1-(5-Ethynyl-pyridin-3-yl)-piperazine fumaric acid salt (6).** $^1$H NMR (DMSO-*d6*): $\delta$ 8.31 (1H, m), 8.09 (1H, s), 7.40 (1H, s), 4.46 (1H, m), 3.30 (4H, m), 3.01 (4H, m).
**(*Z*)-3-bromo-5-(prop-1-enyloxy)pyridine (9b)**. $^1$H NMR ($CDCl_3$): $\delta$8.50 (1H, s), 8.22 (1H, s), 7.32 (1H, s), 6.21 (1H, m), 4.94 (1H, m), 1.61 (3H, m).
**cis-1-(5-Propen-1-yloxypyridin-3-yl)-[1,4]diazepane fumaric acid salt (9).** $^1$H NMR (DMSO-*d6*): $\delta$7.90 (1H, s), 7.68 (1H, s), 6.78 (1H, s), 6.67 (1H, d, *J*= 7.3 Hz), 4.90 (1H, m), 3.69 (2H, t, *J*= 5.6 Hz ), 3.54 (2H, t, *J*= 5.6 Hz), 3.14 (2H, t, *J*= 6.5 Hz), 3.01 (2H, t, *J*= 6.5 Hz), 2.01 (2H, m), 1.65 (3H, m).
**1-(5-Chloropyridin-3-yl)-[1,4]diazepane (10a).** $^1$H NMR ($CDCl_3$): $\delta$ 8.06 (1H, s), 7.95 (1H, s), 7.06 (1H, s), 3.56 (4H, m), 3.08 (2H, m), 2.87 (2H, m), 1.95 (2H, m).
**4-(5-Chloropyridin-3-yl)-[1,4]diazepane-1-carboxylic acid *tert*-butyl ester (10b).** $^1$H NMR ($CDCl_3$): $\delta$ 7.99 (1H, s), 7.87 (1H, s), 6.91 (1H, m), 3.55 (4H, m), 3.33 (1H, m), 3.22 (1H, m), 1.96 (2H, m), 1.64 (2H, m), 1.40 (9H, m).
**4-(6-Bromo-5-chloropyridin-3-yl)-[1,4]diazepane-1-carboxylic acid *tert*-butyl ester (10c).** $^1$H NMR ($CDCl_3$): $\delta$ 7.80 (1H, s), 7.09 (1H, s), 3.60 (6H, m), 3.41 (1H, t, *J* = 3.6 Hz), 3.30 (1H, t, *J* = 3.6 Hz), 1.99 (2H, m), 1.48 (9H, m).
**1-(6-Bromo-5-chloropyridin-3-yl)-[1,4]diazepane fumaric acid salt (10).** $^1$H NMR (DMSO-*d6*): $\delta$ 7.72 (1H, d, *J* = 2.6 Hz), 7.20 (1H, d, *J* = 2.6 Hz), 3.41 (2H, t, *J* = 4.5 Hz), 3.34 (2H, t, *J* = 4.5 Hz), 2.69 (2H, t, *J* = 5.4 Hz), 2.39 (2H, t, *J* = 5.4 Hz), 1.60 (2H, t, *J* = 5.4 Hz).
**4-(5-Bromopyridin-3-yl)-[1,4]diazepane (11a).** $^1$H NMR ($CDCl_3$): $\delta$8.08 (1H, s), 7.99 (1H, s), 7.10 (1H, s), 3.61 (4H, m), 3.11 (2H, m), 2.90 (2H, m), 1.98 (2H, m).
**4-(5-Bromopyridin-3-yl)-[1,4]diazepane-1-carboxylic acid *tert*-butyl ester (11b).** $^1$H NMR ($CDCl_3$): $\delta$8.01 (1H, s), 7.95 (1H, s), 7.11 (1H, m), 3.58 (4H, m), 3.34 (1H, m), 3.22 (1H, m), 1.93 (2H, m), 1.62 (1H, m), 1.39 (9H, m), 1.23 (1H, m).
**4-(5-Bromo-6-chloropyridin-3-yl)-[1,4]diazepane-1-carboxylic acid *tert*-butyl ester (11c).** $^1$H NMR ($CDCl_3$): $\delta$8.09 (1H, s), 7.51 (1H, s), 3.62 (2H, s), 3.58 (2H, s), 3.26 (4H, m), 2.05 (2H, m), 1.49 (9H, m).
**4-(5-Bromo-6-chloropyridin-3-yl)-[1,4]diazepane fumaric acid salt (11).** $^1$H NMR (DMSO-*d6*): $\delta$7.93 (1H, d, *J*= 2.6 Hz), 7.54 (1H, d, *J*= 2.6 Hz), 6.48 (4H, s), 3.65 (2H, t, *J*= 5.6 Hz), 3.52 (2H, t, *J*= 5.6 Hz), 3.07 (2H, t, *J*= 5.0 Hz), 2.94 (2H, t, *J*= 5.0 Hz), 1.93 (2H, m).
**3-Chloro-5-methoxymethoxypyridine (12b).** $^1$H NMR ($CDCl_3$): $\delta$8.21 (1H, s), 8.14 (1H, s), 7.16 (1H, s), 5.11 (2H, s), 3.40 (3H, s).
**4-(5-Methoxymethoxypyridin-3-yl)-[1,4]diazepane (12c).** $^1$H NMR ($CDCl_3$): $\delta$7.67 (1H, s), 7.59 (1H, s), 6.49 (1H, s), 5.01 (2H, s), 3.42 (3H, m), 3.34 (3H, m), 2.92 (2H, m), 2.73 (2H, m ), 2.19 (2H, s), 1.79 (2H, m).

**4-(5-Methoxymethoxypyridin-3-yl)-[1,4]diazepane-1-carboxylic acid *tert*-butyl ester (12d).** $^1$H NMR ($CDCl_3$): $\delta$7.82 (1H, s), 7.79 (1H, s), 6.69 (1H, s), 5.18 (2H, s), 3.59 (6H, m), 3.49 (3H, m), 3.31 (1H, m), 3.22 (1H, m ), 1.98 (2H, m), 1.40 (9H, m).
**4-(6-Iodo-5-methoxymethoxypyridin-3-yl)-[1,4]diazepane-1-carboxylic acid *tert*-butyl ester (12e).** $^1$H NMR ($CDCl_3$): $\delta$7.65 (1H, s), 6.70 (1H, s), 5.23 (2H, s), 3.59 (6H, m), 3.51 (3H, m), 3.33 (1H, m), 3.23 (1H, m ), 1.98 (2H, m), 1.40 (9H, m).
**5-[1,4]Diazepan-1-yl-2-iodo-pyridin-3-ol hydrochloric acid salt (12).** $^1$H NMR (DMSO-*d6*): $\delta$10.69 (1H, s), 9.09 (1H, s), 7.58 (1H, s), 6.65 (1H, s), 3.69 (2H, m), 3.44 (2H, m), 3.19 (2H, m), 3.10 (2H, m ), 2.0 (2H, m).
**4-(5-Cyclopropylpyridin-3-yl)-[1,4]diazepane-1-carboxylic acid *tert*-butyl ester (13a).** $^1$H NMR ($CDCl_3$): $\delta$7.93 (1H, s), 7.78 (1H, m), 6.67 (1H, s), 4.12 (2H, m), 3.59 (2H, m), 3.37 (2H, m), 3.22 (2H, m), 2.08 (2H, m), 1.98 (1H, m), 1.39 (9H, m), 1.00 (2H, m), 0.72 (2H, m).
**1-(5-Cyclopropylpyridin-3-yl)-[1,4]diazepane fumaric acid salt (13).** $^1$H NMR (DMSO-*d6*): $\delta$7.91 (1H, s), 7.67 (1H, m), 6.70 (1H, s), 3.70 (2H, m), 3.51 (2H, m), 3.18 (2H, m), 3.02 (2H, m ), 2.02 (2H, m), 1.89 (1H, m), 0.92 (2H, m), 0.73 (2H, m).
**(+/-)-9-Methyl-3,9-diazabicyclo[4.2.1]nonan-4-one (30b).** $^1$H NMR ($CDCl_3$): $\delta$6.29 (1H, s), 3.59 (1H, m), 3.23 (1H, m), 3.18 (1H, m), 2.82 (2H, m), 2.41 (4H, m), 2.10 (2H, m), 1.82 (1H, m), 1.70 (1H, m).
**(+/-)-9-Methyl-3,9-diazabicyclo[4.2.1]nonane (30c).** $^1$H NMR ($CDCl_3$): $\delta$3.28 (1H, m), 3.17 (1H, m), 2.90 (3H, m), 2.69 (1H, m), 2.42 (3H, m), 2.19 (2H, m), 1.88 (1H, m), 1.59 (2H, m), 1.48 (1H, m).
**3-Chloro-5-propen-cis-yloxypyridine (30d).** $^1$H NMR ($CDCl_3$): $\delta$8.51 (1H, s), 8.23 (1H, s), 7.22 (1H, s), 6.38 (1H, d, *J*= 7.5 Hz), 5.09 (1H, m), 1.76 (3H, m).
**(+/-)-cis-9-Methyl-3-(5-propen-1-yl-oxypyridin-3-yl)-3,9-diazabicyclo [4.2.1]nonane (30e).** $^1$H NMR ($CDCl_3$): $\delta$7.89 (1H, s), 7.60 (1H, s), 6.59 (1H, m), 6.34 (1H, d, *J*= 7.5 Hz), 4.89 (1H, m), 3.69 (2H, m), 3.54 (2H, m), 3.29 (3H, m), 2.31 (3H, s), 2.19 (1H, m), 2.02 (2H, m), 1.79 (1H, m), 1.70 (3H, m), 1.40 (1H, m).
**(+/-)-cis-3-(5-Propen-1-yloxypyridin-3-yl)-3,9-diazabicyclo[4.2.1]nonane fumaric acid salt (30**). $^1$H NMR (DMSO-*d6*): $\delta$7.98 (1H, s), 7.61 (1H, s), 6.87 (1H, m), 6.67 (1H, d, *J*= 7.5 Hz), 4.88 (1H, m), 4.06 (2H, m), 3.97 (2H, m), 3.72 (1H, m), 3.54 (1H, m), 3.30 (1H, m), 2.04 (1H, m), 1.94 (2H, m), 1.85 (1H, m), 1.62 (3H, m), 1.38 (1H, m).
**3-Chloro-5-ethoxypyridine (31a).** $^1$H NMR ($CDCl_3$): $\delta$8.21 (2H, m), 7.22 (1H, m), 4.11 (2H, m), 1.49 (3H, m).
**(+/-)-3-(5-Ethoxypyridin-3-yl)-9-methyl-3,9-diazabicyclo[4.2.1]nonane (31b).** $^1$H NMR ($CDCl_3$): $\delta$7.79 (1H, s), 7.58 (1H, s), 6.49 (1H, s), 4.02 (3H, m), 3.68 (1H, m), 3.50 (2H, m), 3.29 (2H, m), 3.20 (1H, m), 2.71 (1H, s), 2.45 (2H, s), 2.19 (1H, m), 2.02 (1H, m), 1.93 (1H, m), 1.74 (1H, m), 1.50 (1H, m), 1.40 (3H, m).
**(+/-)-3-(5-Ethoxypyridin-3-yl)-3,9-diazabicyclo[4.2.1]nonane fumaric acid salt (31).** $^1$H NMR (DMSO-*d6*): $\delta$7.58 (1H, s), 6.80 (1H, s), 6.52 (3H, s), 4.59 (1H, s), 4.07 (3H, m), 3.94 (1H, m), 3.71 (1H, m), 3.52 (1H, m), 3.26 (1H, m), 2.05 (1H, m), 1.91 (2H, m), 1.81 (1H, m), 1.62 (1H, m), 1.31 (2H, m), 1.12 (3H, m).
**(+/-)-9-Benzyl-3,9-diazabicyclo[4.2.1]nonane-4-one (32b).** $^1$H NMR ($CDCl_3$): $\delta$ 7.35 (2H, m), 7.30 (2H, m), 7.26 (1H, m), 6.12 (1H, s), 3.72 (2H, m), 3.59 (1H, m), 3.32 (1H, s), 3.21 (1H, s), 2.88 (2H, m), 2.49 (1H, m), 2.11 (2H, m), 1.86 (1H, m), 1.74 (1H, m).

**(+/-)-9-Benzyl-3,9-diazabicyclo[4.2.1]nonane (32c).** $^1$H NMR ($CDCl_3$): $\delta$ 7.27 (2H, m), 7.18 (2H, m), 7.10 (1H, m), 3.59 (2H, m), 3.18 (1H, m), 3.08 (1H, m), 2.90 (1H, m), 2.71 (2H, m), 2.50 (1H, m), 2.03 (2H, m), 1.68 (2H, m), 1.38 (1H, m), 1.09 (1H, m).
**(+/-)-9-Benzyl-3,9-diazabicyclo[4.2.1]nonane 3-carboxylic acid *tert*-butyl ester (32d).** $^1$H NMR ($CDCl_3$): $\delta$7.39 (2H, m), 7.29 (2H, m), 7.21 (1H, m), 3.80 (1H, m), 3.73 (1H, m), 3.67 (2H, m), 3.28 (2H, m), 2.24 (1H, m), 2.00 (1H, m), 1.77 (1H, m), 1.64 (1H, m), 1.52 (1H, m), 1.41 (9H, s), 1.26 (3H, m).
**(+/-)-3,9-Diaza-bicyclo[4.2.1]nonane-3-carboxylic acid *tert*-butyl ester (32e).** $^1$H NMR ($CDCl_3$): $\delta$3.87 (2H, m), 3.69 (2H, m), 3.50 (1H, m), 3.11 (1H, m), 2.89 (1H, m), 2.02 (1H, m), 1.78 (4H, m), 1.46 (9H, m).
**(+/-)-cis-9-(5-Propen-1-yloxy-pyridin-3-yl)-3,9-diaza-bicyclo[4.2.1]nonane-3-carboxylic acid *tert*-butyl ester (32f).** $^1$H NMR ($CDCl_3$): $\delta$ 7.79 (1H, s), 7.69 (1H, s), 6.52 (1H, m), 6.38 (1H, d, *J*= 7.4 Hz), 4.92 (1H, m), 4.29 (1H, m), 4.08 (1H, m), 3.71 (1H, m), 3.31 (1H, m), 2.58 (1H, m), 2.39 (1H, m), 2.24 (2H, m), 2.02 (2H, m), 1.70 (3H, m), 1.41 (9H, m) 1.23 (1H, m).
**(+/-)-cis-9-(5-Propen-1-yloxypyridin-3-yl)-3,9-diazabicyclo[4.2.1]nonane fumaric acid salt (32).** $^1$H NMR (DMSO-*d6*): $\delta$ 7.80 (1H, s), 7.59 (1H, s), 6.69 (1H, s), 6.68 (1H, d, *J*= 7.4 Hz), 4.87 (1H, m), 4.43 (1H, m), 4.36 (1H, m), 3.12 (1H, m), 2.94 (1H, m), 2.82 (1H, m), 2.24 (1H, m), 2.26 (1H, m), 2.11 (2H, m), 1.87 (2H, m), 1.64 (3H, m) 1.61 (1H, s).
**3-Chloro-5-methoxypyridine (33a).** $^1$H NMR ($CDCl_3$): $\delta$8.26 (2H, m), 7.28 (1H, s), 3.91 (3H, m).
**(+/-)-1-(9-Benzyl-3,9-diazabicyclo-[4.2.1]non-3-yl)-ethanone (33b).** $^1$H NMR ($CDCl_3$): $\delta$7.38 (2H, m), 7.27 (2H, m), 7.18 (1H, m), 4.27 (1H, d, *J*= 9.6 Hz), 3.89 (1H, m), 3.71 (2H, m), 3.59 (2H, m), 3.32 (4H, m), 2.82 (1H, d, *J*= 9.6 Hz), 2.07 (3H, m), 1.65 (3H, m).
**(+/-)-1-(3,9-Diazabicyclo-[4.2.1]non-3-yl)-ethanone (33c).** $^1$H NMR ($CDCl_3$): $\delta$4.30 (1H, bd), 3.92 (1H, m), 3.59 (2H, m), 3.30 (4H, m), 2.79 (1H, bd), 2.09 (3H, m), 1.67 (3H, m).
**(+/-)-9-(5-Methoxypyridin-3-yl)-3,9-diazabicyclo[4.2.1]non-3-yl-ethanone (33d).** $^1$H NMR ($CDCl_3$): $\delta$7.84 (1H, m), 7.67 (2H, m), 4.28 (1H, m), 3.94 (1H, m), 3.65 (2H, m), 3.26 (4H, m), 2.79 (1H, m), 2.12 (3H, m), 2.08 (3H, m), 1.72 (3H, m).
**(+/-)-9-(5-Methoxypyridin-3-yl)-3,9-diazabicyclo[4.2.1]nonane fumaric acid salt (33).** $^1$H NMR (DMSO-*d6*): $\delta$7.67 (2H, m), 7.50 (1H, s), 4.35 (2H, m), 3.77 (3H, s), 3.07 (1H, m), 2.88 (1H, m), 2.76 (2H, m ), 2.26 (2H, m), 2.17 (1H, m), 2.04 (1H, m), 1.88 (2H, m), 1.56 (1H, m).
**(+/-)-9-(5-Ethoxypyridin-3-yl)-3,9-diazabicyclo[4.2.1]nonane-3-carboxylic acid *tert*-butyl ester (34a).** $^1$H NMR ($CDCl_3$): $\delta$7.61 (1H, s), 7.55 (1H, s), 6.80 (1H, m), 4.29 (1H, m), 4.22 (1H, m), 4.10 (2H, m), 3.84 (1H, m), 3.30 (1H, m), 2.55 (1H, m), 2.26 (2H, m), 2.11 (1H, m), 2.04 (1H, m), 1.80 (2H, m), 1.58 (1H, m), 1.44 (9H, m), 1.28 (3H, m).
**(+/-)-9-(5-Ethoxypyridin-3-yl)-3,9-diazabicyclo[4.2.1]nonane fumaric acid salt (34).** $^1$H NMR (DMSO-*d6*): $\delta$7.67 (1H, s), 7.50 (1H, s), 6.51 (1H, s), 4.39 (1H, d, *J* = 5.2 Hz), 4.33 (1H, t, *J* = 5.2 Hz), 4.05 (2H, q, *J* = 5.2 Hz), 3.08 (1H, m), 2.91 (1H, m), 2.76 (1H, m), 2.28 (2H, m), 2.16 (1H, m), 2.05 (1H, m), 1.86 (2H, m), 1.58 (1H, m), 1.31 (3H, m).
**9-Benzyl-9-azabicyclo[3.3.1]nonan-3-one (35b).** $^1$H NMR ($CDCl_3$): $\delta$7.29 (5H, m), 3.82 (2H, m), 3.26 (2H, m), 2.68 (2H, m), 2.19 (2H, m), 1.90 (2H, m), 1.50 (4H, m).

**(+)-10-Benzyl-3,10-diazabicyclo[4.3.1]decan-4-one (35c).** $^1$H NMR (DMSO-*d6*): $\delta$7.32 (2H, m), 7.28 (2H, m), 7.20 (1H, m), 3.89 (2H, m), 3.61 (1H, m), 3.31 (1H, m), 2.90 (2H, m), 2.81 (1H, m), 2.73 (1H, m), 2.18 (1H, m), 2.07 (1H, m), 1.87 (2H, m), 1.46 (2H, m).
**(+)-10-Benzyl-3,10-diazabicyclo[4.3.1]decane (35d).** $^1$H NMR ($CDCl_3$): $\delta$7.36 (2H, m), 7.22 (2H, m), 7.18 (1H, m), 3.93 (2H, m), 3.09 (3H, m), 3.00 (1H, m), 2.81 (2H, m), 2.02 (2H, m), 1.88 (2H, m), 1.67 (1H, m), 1.52 (1H, m), 1.39 (1H, m), 1.22 (1H, m).
**(+)-10-Benzyl-3,10-diazabicyclo[4.3.1]decane-3-carboxylic acid *tert*-butyl ester (35e).** $^1$H NMR ($CDCl_3$): $\delta$7.40 (2H, m), 7.32 (2H, m), 7.28 (1H, m), 4.48 (1H, m), 4.18 (1H, m), 3.94 (2H, m), 3.71 (1H, m), 3.39 (1H, m), 3.12 (1H, m), 2.91 (1H, m), 2.08 (1H, m), 1.88 (3H, m), 1.70 (2H, m), 1.50 (9H, m), 1.43 (1H, m), 1.31 (1H, m).
**(+/-)-3,10-Diazabicyclo[4.3.1]decane-3-carboxylic acid *tert*-butyl ester (35f).** $^1$H NMR ($CDCl_3$): $\delta$3.83 (1H, m), 3.72 (1H, m), 3.47 (1H, m), 3.32 (1H, m), 3.24 (1H, m), 3.18 (1H, m), 1.99 (1H, m), 1.81 (3H, m), 1.68 (2H, m), 1.59 (1H, m), 1.50 (9H, m).
(+/-)-**10-(5-Chloropyridin-3-yl)-3,10-diazabicyclo[4.3.1]decane-3-carboxylic acid *tert*-butyl ester (35g).** $^1$H NMR ($CDCl_3$): $\delta$8.11 (1H, s), 7.79 (1H, m), 7.26 (1H, m), 4.19 (2H, m), 3.00 (1H, m), 2.92 (2H, m), 2.32 (1H, m), 2.26 (1H, m), 2.18 (1H, m), 1.79 (2H, m), 1.69 (2H, m), 1.54 (1H, s), 1.51 (9H, m), 1.39 (1H, m).
**(+/-)-10-(5-Chloro-pyridin-3-yl)-3,10-diaza-bicyclo[4.3.1]decane fumaric acid salt (35).** $^1$H NMR (DMSO-*d6*): $\delta$8.19 (1H, s), 7.80 (1H, s), 7.30 (1H, m), 4.23 (2H, m), 3.02 (1H, m), 2.94 (2H, m), 2.39 (1H, m), 2.30 (1H, m), 2.22 (1H, m), 1.80 (2H, m), 1.69 (2H, m), 1.53 (1H, m), 1.46 (1H, m).
**(+/-)-3-Hydroxypiperidine-1-carboxylic acid *tert*-butyl ester (36b).** $^1$H NMR ($CDCl_3$): $\delta$3.72 (2H, m), 3.54 (1H, m), 3.10 (2H, m), 1.90 (1H, m), 1.79 (2H, m), 1.47 (9H, m).
**(+/-)-3-Chloro-5-(piperidin-3-yloxy)-pyridine-1-carboxylic acid *tert*-butyl ester (36c).** $^1$H NMR ($CDCl_3$): $\delta$7.70 (1H, m), 7.50 (1H, m), 7.26 (1H, m), 4.31 (1H, m), 3.59 (4H, m), 2.06 (1H, m), 1.90 (1H, m), 1.69 (1H, m), 1.59 (1H, m), 1.41 (9H, m).
**(+/-)-3-Chloro-5-(piperidin-3-yloxy)-pyridine fumaric acid salt (36).** $^1$H NMR (DMSO-*d6*): $\delta$8.32 (1H, d, *J*= 7.1 Hz), 8.23 (1H, d, *J*= 7.1 Hz), 7.70 (1H, m), 4.80 (1H, m), 3.27 (1H, m), 3.14 (1H, m), 3.01 (2H, t, *J*= 6.5 Hz), 1.92 (1H, m), 1.85 (1H, m), 1.79 (1H, m), 1.64 (1H, m).
**[1,5]Diazocane-1-carboxylic acid *tert*-butyl ester (38b).** $^1$H NMR ($CDCl_3$): $\delta$3.38 (4H, m), 2.90 (4H, m), 1.84 (4H, m), 1.47 (9H, m).
**5-(5-Methoxypyridin-3-yl)-[1,5]diazocane-1-carboxylic acid *tert*-butyl ester (38c).** $^1$H NMR ($CDCl_3$): $\delta$7.59 (2H, m), 6.79 (1H, s), 3.83 (3H, m), 3.53 (4H, m), 3.36 (4H, m), 1.89 (4H, m), 1.22 (9H, m).
**1-(5-Methoxypyridin-3-yl)-[1,5]diazocane fumaric acid salt (38).** $^1$H NMR (DMSO-*d6*): $\delta$7.70 (1H, s), 7.60 (1H, s), 6.51 (1H, s), 3.79 (3H, m), 3.52 (4H, t, *J* = 5.6 Hz), 3.00 (4H, t, *J* = 5.6 Hz), 1.90 (4H, m).
**3-n-Butoxy-5-chloropyridine (39a).** $^1$H NMR ($CDCl_3$): $\delta$8.25 (1H, s), 8.21 (1H, s), 7.26 (1H, s), 4.08 (2H, m), 1.87 (2H, m), 1.56 (2H, m), 1.04 (3H, m).
**[1,5]Diazocane (39b).** $^1$H NMR ($CDCl_3$): $\delta$3.49 (4H, m), 3.32 (4H, m), 1.87 (4H, m).
**5-[(5-(1-Butoxy)-pyridin-3-yl]-[1,5]diazocane fumaric acid salt (39).** $^1$H NMR (DMSO-*d6*): $\delta$7.71 (1H, s), 7.61 (1H, s), 6.51 (1H, s), 4.01 (2H, t, *J* = 5.6 Hz), 3.54 (4H, m), 3.06 (4H, m), 1.96 (4H, m), 1.69 (2H, t, *J* = 6.2 Hz), 1.43 (2H, q, *J* = 6.2 Hz), 0.93 (3H, t ,*J* = 5.6 Hz).

**1-Pyridin-3-yl-[1,5]diazocane fumaric acid salt (40).** $^1$H NMR (DMSO-*d6*): $\delta$8.09 (1H, s), 7.86 (1H, s), 7.19 (1H, m), 7.07 (1H, m), 3.57 (4H, m), 3.02 (4H, m), 1.91 (4H, m).

**4-(Pyridin-3-yl)-[1,5]diazocane acid *tert*-butyl ester (41a).** $^1$H NMR ($CDCl_3$): $\delta$8.11 (1H, s), 7.98 (1H, m), 7.19 (1H, s), 7.00 (1H, s), 3.63 (4H, m), 3.49 (2H, m), 3.35 (2H, m), 1.97 (4H, m), 1.32 (9H, m).

**5-(6-Bromopyridin-3-yl)-[1,5]diazocane-1-carboxylic acid *tert*-butyl ester (41b).** $^1$H NMR ($CDCl_3$): $\delta$7.92 (1H, s), 7.17 (1H, s), 7.01 (1H, s), 3.58 (4H, m), 3.26 (4H, s), 1.82 (4H, s).

**1-(6-Bromopyridin-3-yl)-[1,5]diazocane fumaric acid salt (41).** $^1$H NMR (DMSO-*d6*): $\delta$7.80 (1H, s), 7.31 (1H, m), 7.06 (1H, m), 3.51 (4H, m), 3.05 (4H, s), 1.89 (4H, s).

**1-(5-Chloropyridin-3-yl)-[1,5]diazocane fumaric acid salt (42).** $^1$H NMR (DMSO-*d6*): $\delta$8.05 (1H, m), 7.84 (1H, m), 7.11 (1H, m), 3.58 (4H, m), 3.00 (4H, s), 1.87 (4H, m).

**5-(5-Vinyloxypyridin-3-yl)-[1,5]diazocane-1-carboxylic acid *tert*-butyl ester (43a).** $^1$H NMR ($CDCl_3$): $\delta$7.51 (2H, s), 7.13 (1H, m), 7.09 (1H, m), 4.17 (1H, m), 4.08 (1H, m), 3.69 (4H, m), 3.54 (2H, m), 3.40 (2H, m), 2.02 (4H, m).

**5-(6-Bromo-5-vinyloxypyridin-3-yl)-[1,5]diazocane-1-carboxylic acid *tert*-butyl ester (43b).** $^1$H NMR ($CDCl_3$): $\delta$7.70 (1H, s), 6.72 (1H, s), 6.57 (1H, m), 4.94 (1H, d, $J$ = 9.6 Hz), 4.71 (1H, m), 3.64 (2H, m), 3.57 (2H, m), 3.50 (2H, s), 3.40 (2H, s), 1.98 (4H, m), 1.34 (9H, m).

**1-(6-Bromo-5-vinyloxypyridin-3-yl)-[1,5]diazocane fumaric acid salt (43).** $^1$H NMR (DMSO-*d6*): $\delta$7.63 (1H, s), 6.91 (1H, m), 6.80 (1H, s), 4.78 (1H, d, $J$ = 9.6 Hz), 4.59 (1H, s), 3.56 (4H, s), 3.05 (4H, s), 1.91 (4H, s).

**1-(5-Bromopyridin-3-yl)-[1,5]diazocane fumaric acid salt (48).** $^1$H NMR (DMSO-*d6*): $\delta$ 8.05 (1H, s), 7.88 (1H, s), 7.19 (1H, s), 6.46 (4H, s), 3.52 (4H, m), 2.91 (4H, m), 1.79 (4H, m).

**1-(5-Vinylpyridin-3-yl)-[1,4]diazepane-1-carboxylic acid *tert*-butyl ester (49a).** $^1$H NMR ($CDCl_3$): $\delta$7.90 (1H, s), 7.76 (1H, s), 6.60 (1H, s), 4.81 (1H, d $J$= 9.6 Hz), 4.49 (1H, m), 3.58 (6H, m), 3.38 (1H, m), 3.28 (1H, m), 2.00 (2H, m), 1.46 (9H, m), 1.30 (1H, m).

**1-(6-Bromo-5-vinylpyridin-3-yl)-[1,4]diazepane-1-carboxylic acid *tert*-butyl ester (49b).** $^1$H NMR ($CDCl_3$): $\delta$7.55 (1H, s), 6.55 (1H, s), 4.71 (1H, d $J$= 9.6 Hz), 4.50 (1H, m), 3.49 (6H, m), 3.28 (1H, m), 3.19 (1H, m), 1.89 (2H, m), 1.32 (9H, m), 1.19 (1H, m).

**1-(6-Bromo-5-vinylpyridin-3-yl)-[1,4]diazepane fumaric acid salt (49).** $^1$H NMR (DMSO-*d6*): $\delta$7.69 (1H, s), 6.92 (1H, m), 6.88 (1H, s), 4.77 (1H, m), 4.75 (1H, m), 3.62 (2H, m), 3.51 (2H, m), 3.07 (2H, m), 2.90 (2H, m), 1.91 (2H, m).

**4-(Pyridin-3-yl)-piperazine-1-carboxylic acid *tert*-butyl ester (50b).** $^1$H NMR (DMSO-*d6*): $\delta$8.40 (1H, s), 8.19 (1H, s), 7.24 (2H, s), 3.68 (4H, m), 3.25 (4H, m), 1.58 (9H, m).

**4-(6-Bromopyridin-3-yl)-piperazine-1-carboxylic acid *tert*-butyl ester (50c).** $^1$H NMR (DMSO-*d6*): $\delta$8.08 (1H, m), 7.29 (1H, m), 7.14 (1H, m), 3.66 (3H, m), 3.01 (1H, m), 1.52 (9H, m).

**1-(6-Bromopyridin-3-yl)-piperazine fumaric acid salt (50).** $^1$H NMR (DMSO-*d6*): $\delta$ 8.09 (1H, s), 7.40 (1H, m), 7.34 (1H, m), 3.20 (4H, m), 2.97 (4H, m).