

## Preparation of Enantiopure 1-Azabicyclo[3.2.2]nonanes Functionalized at Carbon C3, from Cinchonine and Cinchonidine. Stereoselective Solvolysis and an Easily Enolizable Ketone

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### General:

The atom numbering follows the *Cinchona* alkaloid convention. The new ring expanded *Cinchona* alkaloids are numbered according to the Beilstein AutoNom.

Infrared spectra were recorded on a Perkin-Elmer 1710 infrared spectrometer. <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra were recorded on Bruker AVS 400 and Bruker AVM 500 spectrometer in deuterated chloroform unless otherwise stated, with tetramethylsilane as internal standard. Mass spectra were recorded on a Finnigan MAT 312 (70 eV) or a VG Autospec spectrometer. Microanalyses were performed in the Department of Organic Chemistry of the University of Hannover. Preparative column chromatography was performed on J. T. Baker silica gel (particle size 30 - 60 µm). Analytical TLC was carried out on aluminum-backed 0.2-mm silica gel 60 F254 plates (E. Merck). Petrol ether (PE) and methyl *t*-butyl ether (MTBE) were distilled before use. Methanol was dried over calcium hydride and citric acid and distilled over magnesium before use.

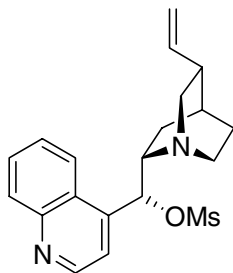
### General procedure for preparation of mesylates 1-OMs and 2-OMs

Cinchonine was dissolved in abs. THF (6 mL/mmol). NEt<sub>3</sub> (2 equiv.) and MsCl (1.8 equiv.) were added parallel. The reaction stirred for 2-4h at room temperature. Sat. aq. NaHCO<sub>3</sub> was added and the aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined organic layer was dried (Na<sub>2</sub>SO<sub>4</sub>) and the solvent was removed in vacuo. The crude product was purified by column chromatography (MTBE) to furnish **2-OMs**.

Methanesulfonic acid quinolin-4-yl-(5-vinyl-1-aza-bicyclo[2.2.2]oct-2-yl)-methyl ester **1-OMs**

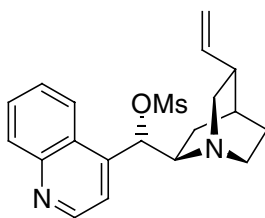
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$^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.99 (d,  $J = 4.3$  Hz, H-2'); 8.17 (m, H-5', H-8'); 7.81-7.72 (m, H-7'); 7.67-7.60 (m, H-6'); 7.57-7.43 (bs, H-3'); 6.58-6.01 (bs, H-9); 5.82 (ddd,  $J = 7.4, 9.9, 13.6$  Hz, H-10); 5.07-4.96 (m, H-11, H-11); 3.58-3.31 (bs, H-8); 3.18-3.02 (m, H-6); 3.0-2.91 (m, H-2); 2.68-2.47 (m, H-2, H-6, H-12, OMs); 2.31-2.22 (m, H-3); 2.15-1.89 (m, H-4, H-7); 1.81-1.71 (m, H-5); 1.70-1.59 (m, H-7); 1.60-1.50 (m, H-5).  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  149.99 (CH, C-2'); 148.76 (C, C-10'); 141.49 (CH, C-10); 130.79 (CH, C-8'); 129.55 (CH, C-7'); 127.38 (CH, C-6'); 125.42 (C, C-9'); 122.86 (CH, C-5'); 112.86 ( $\text{CH}_2$ , C-11); 60.20 (CH, C-8); 56.51 ( $\text{CH}_2$ , C-2); 42.09 ( $\text{CH}_2$ , C-6); 39.51 (CH, C-3); 39.10 ( $\text{CH}_3$ , C-12, OMs); 27.61 ( $\text{CH}_2$ , C-7); 27.31 (CH, C-4); 25.03 ( $\text{CH}_2$ , C-5). Because of Coaleszenz signals for C4', C3' and C9 are missing. IR (Golden Gate ATR)  $\nu$  2937 w, 1593 w, 1509 w, 1422 w, 1345 s, 1172 vs, 944 m, 922 vs, 869 m, 854 m, 832 m, 781 m. Ms-MAT (130  $^\circ\text{C}$ ):  $m/z$  373 ( $\text{M}^+ + 1$ , 21.77); 372 ( $\text{M}^+$ , 87.42); 306 (8.52); 294 (12.94); 277 (99.85); 262 (40.96); 235 (6.18); 223 (8.39); 209 (5.43); 195 (8.30); 183 (18.69); 167 (18.93); 158 (28.88); 142 (10.26); 163 (100); 108 (10.63); 91 (12.12); 81 (21.33); 71 (8.80). HRMS ( $\text{C}_{20}\text{H}_{24}\text{N}_2\text{O}_3\text{S}$ ): calcd.: 372.1507; found: 372.1508.

Methanesulfonic acid quinolin-4-yl-(5-vinyl-1-aza-bicyclo[2.2.2]oct-2-yl)-methyl ester **2-OMs**



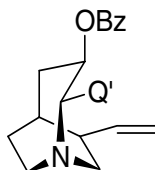
$^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.95 (d,  $J = 4.4$  Hz, H-2'); 8.21-8.11 (m, H-5', H-8'); 7.79-7.73 (m, H-7'); 7.67-7.62 (m, H-6'); 7.56-7.46 (bs, H-3'); 6.37-6.11 (bs, H-9); 6.04 (ddd,  $J = 7.4, 10.4, 17.3$  Hz, H-10); 5.17-5.09 (m, H-11, H-11); 3.47-3.30 (bs, H-8); 2.92-2.82 (m, H-2, H-6); 2.74-2.55 (m, H-6, H-3,  $\text{CH}_3$ , OMs); 2.31-2.23 (m, H-3); 2.0-1.91 (m, H-7); 1.90-1.83 (m, H-4); 1.78-1.66 (m, H-5); 1.60-1.50 (m, H-7, H-5).  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  149.94 (CH, C-2'); 148.64 (C, C-10'); 143.37 (C, C-4'); 139.85 (CH, C-10); 130.69 (CH, C-8'); 129.50 (CH, C-7'); 127.32 (CH, C-6'); 125.43 (C, C-9'); 122.81 (CH, C-5'); ( $\text{CH}_2$ , C-); 115.07 ( $\text{CH}_2$ , C-11); 60.17 (CH, C-8); 49.70 ( $\text{CH}_2$ , C-2); 48.76 ( $\text{CH}_2$ , C-6); 39.66 ( $\text{CH}_3$ , C-12, OMs); 37.26 (CH, C-3); 27.65

(CH, C-4); 26.20 (CH<sub>2</sub>, C-7); 25.76 (CH<sub>2</sub>, C-5). Because of Coaleszenz signals for C3' and C9' are missing. IR (Golden Gate ATR)  $\nu$  2935 w, 2871 w, 1635 w, 1592 w, 1569 w, 1510 w, 1455 w, 1353 m, 1173 s, 1057 w, 1027 w, 973 w, 922 s, 861 m, 823 w, 757 m, 663. Ms-MAT (90 °C): m/z 372 (M<sup>+</sup>, 2.86); 293 (2.95); 278 (7.07); 221 (4.21); 207 (3.75); 196 (3.83); 181 (5.65); 167 (10.44); 154 (5.11); 143 (7.27); 136 (100); 108 (3.76); 95 (5.78); 81 (9.16); 79 (6.73). LC-MS (ESI, calcd. for M<sup>+</sup>+1, C<sub>20</sub>H<sub>24</sub>N<sub>2</sub>O<sub>3</sub>S): 373.1586; found: 373.1571.

### General procedure for preparation of -amino ether and -amino benzoate:

Sodium benzoate (2 equiv) was added to a solution of *O*-mesylated cinchonine **2-OMs** in abs. methanol (5 mL/mmol) and the mixture was refluxed for 3 d. Sat. aq. NaHCO<sub>3</sub> was added and the aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined organic layer was dried (Na<sub>2</sub>SO<sub>4</sub>) and the solvent was removed in vacuo. The crude product was purified by column chromatography (MTBE) to furnish -amino ether **4-OMe** and -amino benzoate **4-OBz**.

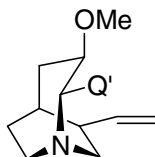
Benzoic acid 2-quinolin-4-yl-6-vinyl-1-azabicyclo[3.2.2]non-3-yl-ester **3-OBz**:



<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 8.80 (d, *J* = 4.6 Hz, H-2'); 8.19-8.07 (m, H-5', H8'); 7.76-7.66 (m, H-7', H-Ar, H-Ar); 7.65-7.59 (m, H-6'); 7.46-7.41 (m, H-16); 7.38 (d, *J* = 4.6 Hz, H-3'); 7.30-7.22 (m, H-H-Ar, H-Ar); 6.22 (ddd, *J* = 17.2, 10.3, 7.2 Hz, H-10); 6.10-5.98 (m, H-3); 5.28-5.15 (m, H-11, H-11); 4.84 (d, *J* = 10.8 Hz, H-2); 3.58-3.45 (m, H-8); 3.23-3.10 (m, H-8); 3.03-2.93 (m, H-7, H-7); 2.92-2.81 (m, H-4); 2.57-2.46 (m, H-6); 2.25-2.16 (m, H-5); 2.11-1.92 (m, H-9, H-9); 1.85-1.75 (m, H-4); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): 165.70 (C, C-12); 150.18 (CH, C-2'); 148.96 (C, C-10'); 146.84 (C, C-4'); 139.95 (CH, C-10); 132.90 (CH, C-16); 130.47 (CH, C-8'); 129.70 (C, C-13); 129.4 (CH, C-Ar, C-Ar); 128.81 (CH, C-7'); 128.12 (CH, C-Ar, C-Ar); 127.50 (CH, C-9'); 126.57 (CH, C-6'); 123.68 (CH, C-5'); 116.40 (CH, C-3'); 115.43 (CH<sub>2</sub>, C-11); 69.45 (CH, C-3); 64.47 (CH, C-2); 49.06 (CH<sub>2</sub>, C-8); 47.53 (CH<sub>2</sub>, C-7); 41.18 (CH, C-6); 36.86 (CH<sub>2</sub>, C-4); 31.24 (CH<sub>2</sub>, C-9); 30.12 (CH, C-5); IR (Golden Gate ATR): 3066 w, 2929 m, 2865 w, 1709 s, 1591 m, 1508 w, 1451 w, 1268 s, 1108 s, 1068 m, 1025 m, 974 m, 912 w, 810 m, 749 m, 710 s; MS-MAT (130 °C): m/z 399 (M<sup>+</sup>+1, 32.13); 398 (M<sup>+</sup>, 100.0); 295 (10.42); 293 (46.12); 277 (20.60); 249 (10.73); 221 (7.05); 194 (13.28); 183 (13.90); 182 (12.73); 167

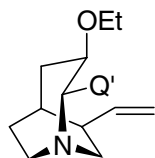
(16.72); 149 (21.29); 128 (2.49); 121 (21.14); 105 (28.33); 77 (15.82); HRMS  $C_{26}H_{26}N_2O_2$ : calcd.: 398.1994; found.: 398.1994.

3-Methoxy-2-quinolin-4-yl-6-vinyl-1-aza-bicyclo[3.2.2]nonane **3-OMe**:



$^1H$ -NMR (400 MHz,  $CDCl_3$ ): 9.91 (d,  $J = 4.6$  Hz, H-2'); 8.13-8.04 (m, H-5', H-8'); 7.71-7.66 (m, H-7'); 7.58-7.52 (m, H-6'); 7.36 (d,  $J = 4.6$  Hz, H-3'); 6.01 (ddd,  $J = 6.7, 10.8, 16.2$  Hz, H-10); 5.18-5.11 (m, H-11, H-11); 4.47 (d,  $J = 10.3$  Hz, H-2); 4.11-4.01 (m, H-3); 3.44-3.35 (m, H-8); 3.23 (s, H-12, OCH<sub>3</sub>); 3.11-3.02 (m, H-7); 2.95-2.79 (m, H-8, H-7, H-4); 2.51-2.40 (m, H-6); 2.22-2.04 (m, H-5); 2.05-1.83 (m, H-9, H-9); 1.69-1.59 (m, H-4);  $^{13}C$ -NMR (100 MHz,  $CDCl_3$ ): 149.88 (CH, C-2'); 149.06 (C, C-10'); 148.57 (C, C-4'); 140.51 (CH, C-10); 130.30 (CH, C-8'); 128.74 (CH, C-7'); 127.89 (C, C-9'); 126.38 (CH, C-6'); 123.87 (CH, C-5'); 116.42 (CH, C-3'); 114.73 (CH<sub>2</sub>, C-11); 76.43 (CH, C2); 65.27 (CH, C-3); 56.89 (CH<sub>3</sub>, C12, OCH<sub>3</sub>); 49.00 (CH<sub>2</sub>, C-8); 47.68 (CH<sub>2</sub>, C-7); 40.85 (CH, C-6); 36.13 (CH<sub>2</sub>, C-4); 31.24 (CH<sub>2</sub>, C-9); 29.67 (CH, C-5); IR (Golden Gate ATR): 3392 w, 2926 m, 2863 m, 1634 w, 1590 m, 1507 m, 1454 m, 1237 w, 1099 vs, 972 m, 908 m, 768 m, 748 s; MS-MAT (80 °C):  $m/z$  309 ( $M^+ + 1$ , 2.09); 308 ( $M^+$ , 2.65); 293 (2.79); 277 (3.20); 263 (3.94); 220 (3.20); 191 (5.39); 169 (3.08); 149 (2.39); 138 (1.74); 121 (9.17); 119 (6.86); 105 (5.16); 97 (2.82); 88 (19.0); 84 (100); 73 (4.74); HRMS  $C_{20}H_{24}N_2O$ : calcd.: 308.1888; found: 308.1887.

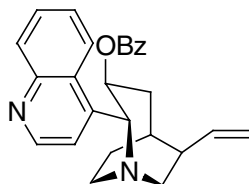
3-Ethoxy-2-quinolin-4-yl-6-vinyl-1-aza-bicyclo[3.2.2]nonane **3-OEt**:



$^1H$ -NMR (400 MHz,  $CDCl_3$ ): 8.89 (d,  $J = 4.6$  Hz, H-2'); 8.13-8.16 (m, H-5', H-8'); 7.71-7.62 (m, H-6'); 7.58-7.51 (m, H-7'); 7.38 (d,  $J = 4.6$  Hz, H-3'); 6.05-5.93 (m, H-10); 5.19-5.09 (m, H-11, H-11); 4.49 (d,  $J = 10.4$  Hz, H-2); 4.25-4.04 (m, H-3); 3.52 (dq,  $J = 9.0$  Hz,  $J = 7.0$  Hz, H-12); 3.42-3.32 (m, H-8); 3.18 (dq,  $J = 9.0$  Hz,  $J = 7.0$  Hz, H-12); 3.09-3.02 (m, H-8); 3.01-2.95

(m, H-7); 2.94-2.86 (m, H-7); 2.82-2.73 (m, H-4); 2.49-2.40 (m, H-6); 2.19-2.11 (m, H-5); 2.09-1.85 (m, H-9, H-9); 1.73-1.68 (m, H-4); 0.87 (t,  $J = 7.0$  Hz, 3x H-13);  $^{13}\text{C}$ -NMR (100 MHz,  $\text{CDCl}_3$ ): 149.80 (CH, C-2'); 149.04 (C, C-10'); 148.92 (C, C-4'); 140.51 (CH, C-10); 130.14 (CH, C-8'); 128.66 (CH, C-7'); 127.95 (C, C-9'); 126.14 (CH, C-6'); 124.22 (CH, C-5'); 116.66 (CH, C-3'); 114.64 ( $\text{CH}_2$ , C-11); 75.34 (CH, C-3); 65.29 (CH, C-2); 64.97 (CH, C-12); 49.02 ( $\text{CH}_2$ , C-8); 47.95 ( $\text{CH}_2$ , C-7); 40.86 (CH, C-6); 37.22 ( $\text{CH}_2$ , C-4); 31.21 ( $\text{CH}_2$ , C-9); 29.82 (CH, C-5); 15.38 ( $\text{CH}_3$ , C-13); IR (Golden Gate ATR): 3076 w, 2971 w, 2925 m, 2863 m, 2324 w, 2110 w, 1982 w, 1917 w, 1635 w, 1590 m, 1571 w, 1507 m, 1481 w, 1453 m, 1421 w, 1373 w, 1358 w, 1322 w, 1267 w, 1238 w, 1202 w, 1161 w, 1139 w, 1089 s, 1026 m, 990 w, 957 w, 909 m, 872 w, 846 w, 811 m, 768 m, 748 s, 698 w, 666 m; MS-MAT (80 °C):  $m/z$  323 ( $\text{M}^+ + 1$ , 23.25); 322 ( $\text{M}^+$ , 71.25); 294 (39.95); 293 (79.94); 279 (71.30); 277 (66.71); 276 (48.57); 263 (12.30); 249 (25.57); 235 (13.64); 223 (15.97); 221 (20.94); 209 (14.16); 207 (14.81); 195 (20.54); 183 (43.87); 169 (48.87); 168 (54.99); 154 (17.11); 143 (27.59); 142 (29.20); 136 (44.08); 115 (19.25); 91 (8.28); 73 (100.0); HRMS  $\text{C}_{21}\text{H}_{26}\text{N}_2\text{O}$ : calcd.: 322.2045; found.: 322.2044.

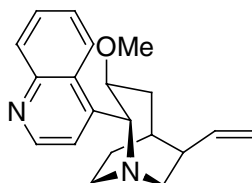
Benzoic acid 2-quinolin-4-yl-6-vinyl-1-aza-bicyclo[3.2.2]non-3-yl-ester **4-OBz**:



$^1\text{H}$ -NMR (400 MHz,  $\text{CDCl}_3$ ): 8.79 (d,  $J = 4.5$  Hz, H-2'); 8.20-8.08 (m, H-5', H8'); 7.81-7.76 (m, H-Ar, H-Ar); 7.72-7.65 (m, H-7'); 7.65-7.60 (m, H-6'); 7.45-7.40 (m, H-Ar); 7.36 (d,  $J = 4.5$  Hz, H-3'); 7.31-7.27 (m, H-Ar, H-Ar); 6.18-6.08 (m, H-3); 6.01 (d,  $J = 6.6, 10.9, 16.8$  Hz, H-10); 5.22-5.14 (m, H-11, H-11); 4.76 (d,  $J = 9.7$  Hz, H-2); 3.74-3.65 (m, H-7); 3.36-3.28 (m, H-7); 2.91-2.81 (m, H-8); 2.64-2.54 (m, H-8); 2.49-2.39 (m, H-6, H-4); 2.27-2.20 (m, H-5); 2.20-2.05 (m, H-4, H-9); 1.76-1.65 (m, H-9);  $^{13}\text{C}$ -NMR (100 MHz,  $\text{CDCl}_3$ ): 165.72 (C, C-12); 149.81 (CH, C-2'); 149.02 (C, C-10'); 145.34 (C, C-4'); 140.49 (CH, C-10); 132.98 (CH, C-Ar); 130.34 (CH, C-8'); 129.81 (C, C-13); 129.47/129.45 (CH, C-Ar, C-Ar); 128.81 (CH, C-7'); 128.21 (CH, C-Ar, C-Ar); 127.83 (C, C-9'); 126.61 (CH, C-6'); 124.11 (CH, C-5'); 117.07 (CH, C-3'); 115.24 ( $\text{CH}_2$ , C-11); 70.07 (CH, C-3); 68.64 (CH, C-2); 56.78 ( $\text{CH}_2$ , C-7); 42.81 (CH, C-6); 39.50 ( $\text{CH}_2$ , C-8); 30.63 ( $\text{CH}_2$ , C-4); 29.86 (CH, C-5); 27.87 (CH, C-9); IR (Golden Gate ATR): 3071 w, 2926 s, 2855 m, 2163 w, 2112 w, 2051 w, 1981 w, 1709 s, 1639 w, 1598 w, 1454 m, 1305 m, 1271 s, 1112 vs, 1208 m, 999 m, 971 m, 708 s, 701 s; MS-MAT (130 °C):  $m/z$  399 ( $\text{M}^+ + 1$ ,

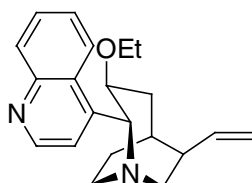
31.05); 398 ( $M^+$ , 79.69); 349 (9.28); 336 (11.35); 333 (33.63); 322 (29.26); 321 (24.87); 312 (13.64); 293 (100); 277 (50.94); 250 (13.27); 249 (17.93); 221 (14.52); 207 (10.80); 195 (14.80); 186 (31.55); 183 (32.94); 173 (28.89); 168 (39.91); 154 (16.03); 142 (22.21); 136 (5.75); 121 (10.77); 115 (14.10); 107 (8.41); 105 (23.22); 95 (10.83); 81 (13.28); 77 (17.41); 73 (53.56); 67 (18.12); HRMS  $C_{26}H_{26}N_2O_2$ : calcd.: 398.1990; found: 398.1994.

3-Methoxy-2-quinolin-4-yl-6-vinyl-1-aza-bicyclo[3.2.2]nonane **4-OMe**:



$^1H$ -NMR (400 MHz,  $CDCl_3$ ): 8.90 (d,  $J = 4.5$  Hz, H-2'); 8.12-8.07 (m, H-8', H-5'); 7.65 (ddd,  $J = 1.3, 6.8, 8.3$  Hz, H-7'); 7.56 (ddd,  $J = 1.4, 6.9, 8.4$  Hz, H-6'); 7.30 (d,  $J = 4.5$  Hz, H-3'); 5.99 (ddd,  $J = 7.0, 10.7, 17.4$  Hz, H-10); 5.17-5.11 (m, H-11, H-11); 4.39 (d,  $J = 10.1$  Hz, H-2); 4.21-4.12 (m, H-3); 3.59 (dd,  $J = 9.4, 14.2$  Hz, H-7); 3.33 (s,  $OCH_3$ , H-12); 3.25-3.17 (m, H-7); 2.86-2.74 (m, H-8); 2.68-2.48 (m, H-8); 2.47-2.35 (m, H-4, H-6); 2.21-2.15 (m, H-4); 1.91-1.79 (m, H-9, H-5); 1.68-1.57 (m, H-9);  $^{13}C$ -NMR (100 MHz,  $CDCl_3$ ): 149.47 (CH, C-2'); 149.15 (C, C-10'); 146.80 (C, C-4'); 140.69 (CH, C-10); 130.20 (CH, C-8'); 128.70 (CH, C-7'); 128.19 (C, C-9'); 126.46 (CH, C-6'); 124.14 (CH, C-5); 117.01 (CH, C-3'); 115.03 ( $CH_2$ , C-11); 77.25 (CH, C-3); 69.68 (CH, C-2); 56.72 ( $CH_3$ , OMe); 56.70 ( $CH_2$ , C-7); 43.05 (CH, C-6); 39.56 ( $CH_2$ , C-8); 29.66 (CH, C-4); 29.05 ( $CH_2$ , C-5); 27.91 ( $CH_2$ , C-9); IR (Golden Gate ATR): 3079 w, 2928 m, 2905 m, 2857 m, 1715 w, 1595 m, 1508 m, 1448 m, 1328 w, 1244 w, 1113 m, 1092 vs, 1034 m, 974 m, 928 s, 813 m, 769 s, 754 s, 745 s, 656 m; MS-MAT (70  $^{\circ}C$ ):  $m/z$  309 ( $M^+ + 1$ , 3.06); 308 ( $M^+$ , 5.53); 293 (4.60); 277 (3.85); 236 (2.58); 191 (4.48); 169 (3.32); 149 (6.33); 136 (3.01); 121 (10.55); 119 (11.86); 106 (3.38); 88 (21.93); 86 (93.71); 84 (100); 73 (23.38); 71 (20.42).; HRMS  $C_{20}H_{24}N_2O$ : calcd.: 308.1888; found: 308.1889.

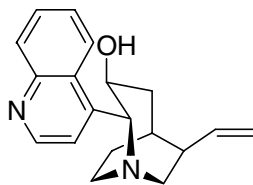
3-Ethoxy-2-quinolin-4-yl-6-vinyl-1-aza-bicyclo[3.2.2]nonane **4-OEt**:



$^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ): 8.90 (d,  $J = 4.5$  Hz, H-2'); 8.13-8.08 (m, H-8', H-5'); 7.71-7.64 (m, H-7'); 7.60-7.53 (m, H-6'); 7.32 (d,  $J = 4.5$  Hz, H-3'); 5.98 (d,  $J = 7.5, 10.6, 17.6$  Hz, H-10); 5.17-5.10 (m, H-11, H-11); 4.42 (d,  $J = 10.2$  Hz, H-2); 4.31-4.26 (m, H-3); 3.72-3.65 (m, H-12); 3.60 (d,  $J = 9.4, 14.2$  Hz, H-7); 3.45-3.37 (m, H-12); 3.25-3.17 (m, H-7); 2.83-2.72 (m, H-8); 2.58-2.48 (m, H-8); 2.45-2.33 (m, H-4, H-6, H-4); 2.21-1.95 (m, H-5); 1.91-1.81 (m, H-9, H-9); 1.01 (t,  $J = 7.0$  Hz,  $\text{CH}_3$ , H-13);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ): 149.42 (CH, C-2'); 149.11 (C, C-10'); 147.11 (C, C-4'); 140.79 (CH, C-10); 130.15 (CH, C-8'); 128.71 (CH, C-7'); 128.23 (C, C-9'); 126.41 (C, C-6'); 124.38 (CH, C-5'); 117.16 (CH, C-3'); 115.03 ( $\text{CH}_2$ , C-11); 75.94 (CH, C-3); 69.75 (CH, C-2); 64.78 ( $\text{CH}_2$ , C-12); 56.74 ( $\text{CH}_2$ , C-7); 43.19 (CH, C-6); 39.63 ( $\text{CH}_2$ , C-8); 30.08 ( $\text{CH}_2$ , C-4); 29.85 (CH, C-5); 28.02 ( $\text{CH}_2$ , C-9); 15.62 ( $\text{CH}_3$ , C-13); MS-MAT (70 °C):  $m/z$  324 ( $\text{M}^+ + 1$ , 3.02); 323 ( $\text{M}^+$ , 272); 293 (10.63); 276 (12.63); 261 (3.83); 247 (2.27); 223 (6.00); 222 (3.32); 209 (4.31); 205 (4.34); 195 (4.06); 191 (4.36); 182 (3.38); 169 (5.75); 154 (3.17); 149 (46.72); 136 (4.93); 121 (14.37); 119 (17.16); 105 (14.88); 97 (5.48); 91 (18.45); 84 (100); 73 (12.88); 69 (6.48); IR (Golden Gate ATR): 3077 w, 2925 m, 2864 m, 1713 w, 1636 w, 1591 m, 1572 m, 1451 m, 1343 w, 1314 m, 1268 m, 1091 s, 1023 m, 911 m, 812 m, 768 s, 753 s. MS-MAT (70 °C):  $m/z$  323 ( $\text{M}^+ + 1$ , 2.72), 322 ( $\text{M}^+$ , 5.67); 306 (1.38); 293 (10.63); 276 (12.63); 269 (2.50); 261 (3.83); 235 (2.61); 223 (6.00); 209 (4.31); 195 (4.06); 190 (4.19); 182 (3.38); 169 (5.75); 149 (46.72); 139 (3.19); 121 (14.37); 119 (17.16); 105 (14.88); 97 (5.48); 88 (32.53); 84 (100); 71 (13.52); 67 (4.15); HRMS  $\text{C}_{21}\text{H}_{26}\text{N}_2\text{O}$ : calcd.: 322.2045; found: 322.2047.

Illustrative preparation of  $\alpha$ -amino alcohol **4-OH**: To a solution of **4-OBz** (160 mg, 0.40 mmol) in MeOH/ $\text{H}_2\text{O}$  (5:1) was added  $\text{Ba}(\text{OH})_2 \cdot 8\text{H}_2\text{O}$  (258 mg, 0.82 mmol). The reaction was stirred for 16 h. After work up with  $\text{H}_2\text{O}$  and extraction with  $\text{CH}_2\text{Cl}_2$  the crude product was purified by column chromatography (MTBE) to furnish **4-OH** (96 mg, 82%).

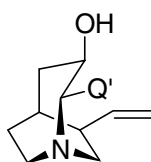
2-Quinolin-4-yl-6-vinyl-1-aza-bicyclo[3.2.2]nonan-3-ol **4-OH**



$^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ): 8.84 (d,  $J = 4.5$  Hz, H-2'); 8.10-8.05 (m, H-8', H-5'); 7.69-7.63 (m, H-7'); 7.60-7.54 (m, H-6'); 7.42 (d,  $J = 4.5$  Hz, H-3'); 6.01 (ddd,  $J = 7.1, 9.5, 17.3$  Hz, H-10); 5.18-5.09 (m, H-11, H-11); 4.75-4.65 (m, H-3); 4.33 (d,  $J = 10.1$  Hz, H-2); 3.59 (dd,  $J = 9.5, 15.1$  Hz, H-7); 3.29-3.18 (m, H-8); 2.88-2.78 (m, H-8); 2.61-2.51 (m, H-7); 2.44-2.35 (m, H-6); 2.29-2.21 (m, H-4); 2.20-2.13 (m, H-5); 2.08-2.00 (m, H-4); 1.92-1.83 (m, H-9) 1.71-1.59 (m, H-9);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ): 149.51 (CH, C-2'); 148.88 (C, C-10'); 146.56 (C, C-4'); 140.77 (CH, C-10); 130.06 (CH, C-8'); 128.89 (CH, C-7'); 128.19 (C, C-9'); 126.65 (CH, C-6');

124.07 (CH, C-5'); 117.25 (CH, C-3'); 115.05 (CH<sub>2</sub>, C-11); 71.04 (CH, C-3); 67.95 (CH, C-2); 56.94 (CH<sub>2</sub>, C-7); 42.85 (CH, C-6); 39.76 (CH, C-5); 39.76 (CH<sub>2</sub>, C-8); 34.27 (CH<sub>2</sub>, C-4); 30.00 (CH, C-5); 28.14 (CH<sub>2</sub>, C-9) IR (Golden Gate ATR): 3261 b; 2929 m, 2862 m, 1591 w, 1509 m, 1449 w, 1327 w, 1240 w, 1139 w, 1050 s, 1028 s, 908 m, 817 s, 770 s, 750 s, 654 m, 630 m. Ms-MAT (150 °C): m/z 295 (M<sup>+</sup>+1, 60.27); 294 (M<sup>+</sup>, 100); 278 (9.66); 277 (36.85); 267 (9.64); 251 (10.79); 249 (41.35); 235 (22.63); 221 (26.13); 209 (20); 195 (29.84); 183 (71.13); 169 (78.17); 168 (65.52); 155 (23.77); 142 (25.61); 115 (20.07); 108 (4.47); 95 (11.74); 81 (16.01); 71 (11.19); HRMS calcd.: 294.1732; found: 294.1731.

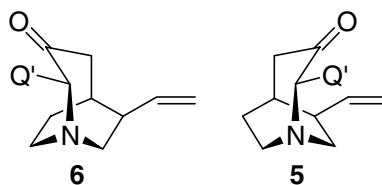
### 2-Quinolin-4-yl-6-vinyl-1-aza-bicyclo[3.2.2]nonan-3-ol **3-OH**



<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 8.82 (d, *J* = 4.5 Hz, H-2'); 8.11 (m, H-5', H-8'); 7.66-7.60 (m, H-7'); 7.58-7.51 (m, H-6'); 7.46(d, *J* = 4.6 Hz, H-3'); 6.01 (ddd, *J* = 6.8, 11.1, 16.4 Hz, H-10); 5.17-5.11 (m, H-11, H-11); 4.62-4.52 (m, H-3); 4.42 (d, *J* = 10.3 Hz, H-2); 3.44-3.32 (m, H-8); 3.11-2.89 (m, H-7, H-7, H-8); 2.76-2.64 (m, H-4); 2.53-2.43 (m, H-6); 2.20-2.12 (m, H-5); 2.10-1.88 (m, H-9, H-9); 1.82-1.74 (m, H-4); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): 149.74 (CH, C-2'); 148.70 (C, C-10'); 148.42 (C, C-4'); 140.28 (CH, C-10); 129.88 (CH, C-8'); 128.87 (CH, C-7'); 127.72 (C, C-9'); 126.49 (CH, C-6'); 123.79 (CH, C-5'); 116.79 (CH, C-3'); 114.83 (CH<sub>2</sub>, C-11); 67.78 (CH, C-3); 66.22 (CH, C-2); 49.25 (CH<sub>2</sub>, C-8); 48.25 (CH<sub>2</sub>, C-7); 40.84 (CH, C-6); 40.74 (CH<sub>2</sub>, C-4); 31.07 (CH<sub>2</sub>, C-9); 30.03 (CH, C-5); IR (Golden Gate ATR): 3236 b, 2930 m, 2859 m, 1635 w, 1590 w, 1509 m, 1455 w, 1240 w, 1140 w, 1047 s, 989 m, 908 m, 818 m, 774 m, 749 s, 666 m; Ms-MAT (100 °C): m/z 295 (M<sup>+</sup>+1, 27.18); 294 (M<sup>+</sup>, 100); 277 (16.61); 276 (11.61); 261 (5.21); 249 (25.13); 235 (14.77); 221 (15.90); 209 (11.26); 195 (17.21); 184 (26.56); 183 (46.13); 169 (47.49); 154 (13.44); 142 (20.29); 115 (15.72); 108 (6.07); 95 (7.06); 81 (10.40); 73 (19.73); HRMS calcd.: 294.1732; found: 294.1730.

### 2-Quinolin-4-yl-6-vinyl-1-azabicyclo[3.2.2]nonan-3-one **5** and **6**

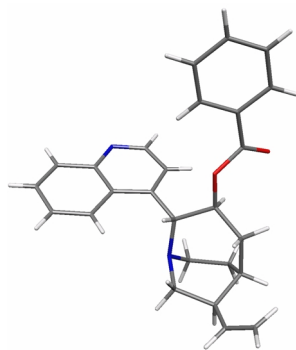




Oxalyl chloride (1.70 mmol, 0.15 mL) in dry  $\text{CH}_2\text{Cl}_2$  (3 mL) was cooled to  $-78\text{ }^\circ\text{C}$ , and DMSO (1.70 mmol, 0.12 mL) was added slowly. After 30 min the alcohol (250 mg, 0.85 mmol) in  $\text{CH}_2\text{Cl}_2$  was added dropwise. The mixture was stirred for additional 30 min at  $-78\text{ }^\circ\text{C}$  and then treated with triethylamine (4.25 mmol, 0.59 mL). The reaction was allowed to warm up to room temperature and stirred for an additional hour. The reaction mixture was treated with sat. aq.  $\text{NaHCO}_3$  and extracted with  $\text{CH}_2\text{Cl}_2$ . The combined organic layer was dried over  $\text{Na}_2\text{SO}_4$ , evaporated and purified by column chromatography (PE:MTBE 1:1) to furnish ketone **5** and **6** as an epimeric mixture (224 mg, 90%).

$^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ): 8.88 (d,  $J = 4.5\text{ Hz}$ , H-2'<sub>5</sub>); 8.85 (d,  $J = 4.6\text{ Hz}$ , H-2'<sub>6</sub>); 8.15-8.09 (m, H-8'<sub>5</sub>, H-8'<sub>6</sub>); 7.81-7.76 (m, H-5'<sub>5</sub>); 8.05-8.01 (m, H-5'<sub>6</sub>); 7.72-7.64 (m, H-7'<sub>5</sub>, H-7'<sub>6</sub>); 7.75-7.46 (m, H-6'<sub>5</sub>, H-6'<sub>6</sub>); 7.26 (d,  $J = 4.5\text{ Hz}$ , H-3'<sub>5</sub>); 7.16 (d,  $J = 4.5\text{ Hz}$ , H-3'<sub>6</sub>); 5.92 (ddd,  $J = 6.9, 10.5, 16.8\text{ Hz}$ , H-10<sub>6</sub>); 5.73 (ddd,  $J = 7.2, 10.5, 17.4\text{ Hz}$ , H-10<sub>5</sub>); 5.27-5.24 (bs, H-2<sub>6</sub>); 5.23-5.21 (bs, H-2<sub>5</sub>); 5.20-5.12 (m, H-11<sub>6</sub>, H-11<sub>5</sub>); 5.07-4.96 (m, H-11<sub>5</sub>, H-11<sub>6</sub>); 3.65 (dd,  $J = 9.2, 14.4\text{ Hz}$ , H-7<sub>6</sub>); 3.34-3.04 (m, H-8<sub>5</sub>, H-8<sub>6</sub>, H-7<sub>5</sub>, H-7<sub>6</sub>); 3.03-2.96 (m, H-4<sub>5</sub>); 2.84-2.74 (m, H-7<sub>5</sub>, H-8<sub>6</sub>, H-8<sub>5</sub>, H-4<sub>6</sub>); 2.73-2.56 (m, H-6<sub>5</sub>, H-6<sub>6</sub>, H-4<sub>6</sub>); 2.27-2.19 (m, H-5<sub>5</sub>, H-5<sub>6</sub>); 2.13-2.05 (m, H-9<sub>5</sub>, H-9<sub>6</sub>); 1.88-1.80 (m, H-9<sub>6</sub>, H-9<sub>5</sub>);  $^{13}\text{C-NMR}$  ( $\text{CD}_2\text{Cl}_2$ ): 215.49 (C, C-3<sub>6</sub>); 212.19 (C, C-3<sub>5</sub>); 150.44 (CH, C-2'<sub>5</sub>); 150.17 (CH, C-2'<sub>6</sub>); 148.99 (C, C-10'<sub>6</sub>); 148.63 (C, C-10'<sub>5</sub>); 145.27 (C, C-4'<sub>5</sub>); 143.99 (C, C-4'<sub>6</sub>); 140.63 (CH, C-10<sub>6</sub>); 139.70 (CH, C-10<sub>5</sub>); 130.46 (CH, C-8'<sub>5</sub>); 129.39 (CH, C-8'<sub>6</sub>); 129.16 (CH, C-7'<sub>5,6</sub>); 127.82 (C, C-9'<sub>5</sub>); 127.74 (C, C-9'<sub>6</sub>); 126.82 (CH, C-6'<sub>6</sub>); 126.57 (CH, C-6'<sub>5</sub>); 124.58 (CH, C-5'<sub>6</sub>); 124.28 (CH, C-5'<sub>5</sub>); 120.44 (CH, C-3'<sub>6</sub>); 119.90 (CH, C-3'<sub>5</sub>); 115.72 ( $\text{CH}_2$ , C-11<sub>6</sub>); 115.68 ( $\text{CH}_2$ , C-11<sub>5</sub>); 76.15 (CH, C-2<sub>6</sub>); 74.16 (CH, C-2<sub>5</sub>); 54.28 ( $\text{CH}_2$ , C-7<sub>6</sub>); 50.06 ( $\text{CH}_2$ , C-8<sub>5</sub>); 48.38 ( $\text{CH}_2$ , C-7<sub>5</sub>); 48.02 ( $\text{CH}_2$ , C-4<sub>5</sub>); 47.41 ( $\text{CH}_2$ , C-8<sub>6</sub>); 41.73 ( $\text{CH}_2$ , C-4<sub>6</sub>); 41.45 (CH, C-6<sub>6</sub>); 41.38 (CH, C-6<sub>5</sub>); 30.98 (CH, C-5<sub>5</sub>); 30.72 (CH, C-5<sub>6</sub>); 28.78 ( $\text{CH}_2$ , C-9<sub>5</sub>); 28.06 ( $\text{CH}_2$ , C-9<sub>6</sub>); IR (Golden Gate ATR): 2920 m, 2852 m, 1714 m, 1628 s, 1509 w, 1464 m, 1445 m, 1257 m, 1170 m, 998 m, 766 m; LC-MS (ESI)  $\text{C}_{19}\text{H}_{21}\text{N}_2\text{O}$  ( $\text{M}^++1$ ): calcd.: 293.1654; found: 293.1652.

Benzoic acid 2-quinolin-4-yl-6-vinyl-1-aza-bicyclo[3.2.2]non-3-yl-ester **4-OBz**<sup>†</sup>:



Crystal structure analysis of **4-OBz**:  $C_{26}H_{26}N_2O_2$ ,  $M_r = 398.49$ , orthorhombic, space group  $P2_12_12_1$ (No. 19),  $a = 8.241$  (2),  $b = 13.333$  (3),  $c = 19.522$  (4) Å,  $\alpha = 90$ ,  $\beta = 90$ ,  $\gamma = 90^\circ$ ,  $V = 21445(8)$  Å<sup>3</sup>,  $Z = 4$ ,  $\rho_{\text{calcd}} = 1.234$  g cm<sup>-3</sup>,  $F(000) = 848$ , crystal size 1.55 x 0.61 x 0.56 mm,  $T = 300$  K. Data collection: diffractometer Stoe IPDS (Imaging Plate), graphite-monochromated  $MoK\alpha$  radiation fine-focus sealed tube,  $\lambda = 0.71073$  Å,  $2\Theta_{\text{max}} = 52.07^\circ$ , set h,k,l -10:10; -16:16; -24:24, total data 30834, unique data 4191, observed data 2667 with  $I > 2\sigma(I)$ ,  $R_{\text{int}} = 0.0853$ . Structure solution by SHELXS-86 and refinement by SHELXL-93, hydrogen atoms in geometrically calculated positions, max./min. residual electron density 0.16/-0.12 e Å<sup>-3</sup>,  $R(F^1) = 0.0344$  based on 2667 reflections with  $F_o > 4\sigma(F_o)$ ,  $wR2 = 0.0724$ ,  $wR2$  based on  $F^2$  of 4191 reflections, Flack parameter 0.4932.

<sup>i</sup> X-ray structure was plotted by Molekel 4.1; Flükiger, H. P.; Lüthi, H. P.; Portmann, S.; Weber, J. *Swiss Center for Scientific Computing*, Manno (Switzerland) **2000-2001**.