Supporting Information

Novel Bridged Bicyclic α-Amino Acid Esters and Key Derivatives from Quincorine® and Quincoridine®

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General Information. Reactions which involved dry solvents were carried out in flame-dried glassware unter an atmosphere of argon or nitrogen with magnetic stirring unless otherwise stated. Dichloromethane and triethylamine was destilled from calcium hydride under an atmosphere of argon. Reagents and solvents were purified using standard means[1].

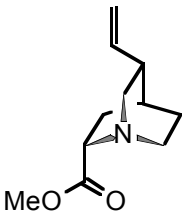
Infrared spectra were recorded on a Perkin-Elmer 1710 infrared spectrometer. – ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AM-400 spectrometer in deuterated chloroform unless otherwise stated with tetramethylsilane as internal standard. – Data are reported as follows: chemical shifts in ppm from tetramethylsilane on the δ scale, multiplicitsy (b = broard, s = singulet, d = dublet, t = triplet, q = quartet and m = multiplet), integration, coupling constant (Hz) and assignment. ^{13}C NMR signal assignments for each signal were established by DEPT measurements; chemical shifts are reported in ppm from tetramethylsilane on the δ scale, multiplicities are indicated by CH_3 (primary), CH_2 (secondary), CH (tertiary) or C (quaternary). – Mass spectra were recorded on a Finnigan MAT 312 (70 eV) or a VG Autospec spectrometer. – 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 F_{254} plates (E. Merck).

General Procedure for the synthesis of C9 esters.

A solution of Quincorine® **1** or Quincoridine® **5** (1 eq) in acetone was cooled to 0°C and treated dropwise with Jones reagent (2.67 M solution, 3.6 eq). The mixture was refluxed for 3 d, followed by addition of *iso*-propanol at r.t. and stirred for 30 min. The solvent was removed under reduced pressure and the residue was dried for 3 d *in vacuo*. The solid was dissolved in abs. MeOH under argon at r.t., catalytic amounts of hydrochloric acid (conc.) were added and the reaction mixture was refluxed for 3 d. 2/3 of the solvent was removed. The solution was cooled to 0°C and the pH was adjusted to 7-8 by adding $NaHCO_3$ (sat. aq.), Ethylenediamine was added dropwise within 15 min. Thereafter Et_2O was added for liquid-liquid extraction over 2 d. The organic layer was dried ($MgSO_4$), the solvent evaporated *in vacuo* and the crude product purified by column chromatography (EtOAc/MeOH 10:1) to provide the desired esters as pale yellow oils.

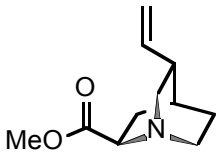
(1) Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals*, Oxford, **1988**.

(1S,2S,4S,5R)-5-Vinyl-1-azabicyclo[2.2.2]octane-2-carboxylic acid methyl ester **2**



Quincorine® **1** (840 mg, 5.00 mmol, 1.0 eq) was allowed to react according to the general procedure to yield C9 ester **2** (60 %, 586 mg, 3.00 mmol). IR ($CHCl_3$) ν 2952, 2870, 1734, 1637, 1456, 1437, 1372, 1264, 1230, 1081, 1036, 993, 909, 834 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.89 (ddd, 1H, *J* = 17.8, 10.5 and 7.3 Hz, H-10), 5.10-5.04 (m, 2H, C-11), 3.76 (s, 3H, OMe), 3.56-3.49 (m, 1H, H-2), 3.19 (dd, 1H, *J* = 14.4 and 10.0 Hz, C-6), 2.95-2.85 (m, 1H, H-7), 2.83-2.70 (m, 2H, H-6, H-7), 2.35-2.26 (m, 1H, H-5), 2.01-1.92 (m, 1H, H-4), 1.86-1.78 (m, 2H, H-8), 1.66-1.46 (m, 2H, H-3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.36 (C, C-9), 141.36 (CH, C-10), 114.63 (CH_2, C-11), 58.72 (CH_3, OMe), 55.00 (CH_2, C-6), 52.23 (CH, C-2), 43.09 (CH_2, C-7), 39.30 (CH, C-5), 27.23 (CH_2, C-8), 27.10 (CH, C-4), 23.77 (CH_2, C-3); MS *m/z* 195 (M^+, 15.02), 180 (4.77), 154 (2.92), 137 (11.98), 136 (100.00), 122 (2.57), 108 (5.47), 100 (5.86), 95 (4.59), 81 (12.45), 77 (3.28), 67 (5.01); HRMS for $C_{11}H_{17}N_1O_2$: 195.1259, found 195.1259.

(1S,2R,4S,5R)-5-Vinyl-1-azabicyclo[2.2.2]octane-2-carboxylic acid methyl ester **6**



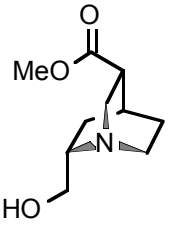
Quincoridine® **1** (104 mg, 0,53 mmol, 1.0 eq) was allowed to react according to the general procedure to yield C9 ester **6** (60 %, 61 mg, 0,32 mmol). IR (CHCl3) ν 2948, 2868, 1734, 1632, 1453, 1436, 1366, 1296, 1262, 1228, 1086, 1032, 992, 916, 816 cm−1; ^1H NMR (400 MHz, $CDCl_3$): δ 5.88 (ddd, 1 H, *J* = 17.3, 10 and 7.5 Hz, H-10), 5.03 (ddd, 1 H, *J* = 11.3, 1.6 Hz and 1.1 Hz, H-11), 5.02 (ddd, 1 H, *J* = 17.3, 1.3 Hz and 1.1 Hz, H-11), 3.75 (s, 3 H, OMe), 3.53-3.45 (m, 1 H, H-2), 3.05-2.95 (m, 2 H, H-7, H-6), 2.93-2.84 (m, 1 H, H-7), 2.64 (ddd, 1 H, *J* = 14, 7.8 and 2.4 Hz, H-6), 2.31-2.22 (m, 1 H, H-5), 2.13-2.05 (m, 1 H, H-3), 1.82-1.77 (m, 1 H, H-4), 1.70-1.65 (m, 1 H, H-3), 1.64-1.57 (m, 2 H, 2 H-8, H-8); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.47 (C=O), 140.14 (CH, C-10), 114.74 (CH, C-11), 58.50 (CH, CH3), 52.14 (CH, C-2), 49.59 (CH, C-6), 48.37 (CH, C-7), 39.71 (CH, C-5), 27.10 (CH, C-4), 26.57 (CH, C-8), 23.67 (CH, C-3); MS m/z 195 (29.38), 180 (6.66), 173 (3.93), 168 (3.54), 154 (6.06), 141 (1.15), 136 (100), 127 (1.21), 122 (2.70), 108 (10.50), 100 (8.78), 86 (5.94), 81 (12.00), 77 (3.27), 66 (4.91); HRMS for C11H17N1O2: 195.1259, found 195.1259.

General procedure for the synthesis of C10 esters including C9, C10 diesters.

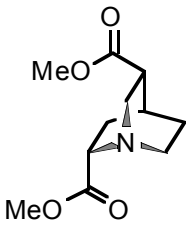
A solution of $KMnO_4$ (2.05 eq) in H_2O was slowly added to a vigorously stirred solution of the corresponding 1,2-amino alcohol sulfate (1.0 eq) in 2N H_2SO_4 at 0°C under argon. After beeing stirred at r.t. for 5 h the reaction mixture was concentrated and dried under reduced pressure. The residue was dissolved in abs. MeOH, conc. HCl (catal.) was added and the reaction mixture was stirred at r.t. for 5 d. After neutralization with sat. aq. $NaHCO_3$, the aqueous layer was extracted (CH_2Cl_2). The organic layer was dried, the solvent evaporated and the crude product purified by column chromatography (EtOAc / MeOH 6:1) to afford the C10 ester and the corresponding C9, C10 diester as a side product.

(1S,2S,4S,5R)-2-(Hydroxymethyl)-1-azabicyclo[2.2.2]octane-5-carboxylic acid methyl ester **3** (1S,2S,4S,5R)-1-azabicyclo[2.2.2]octane-2,5-dicarboxylic acid dimethyl ester **4**

Quincorine sulfate (7.93 g , 30.0 mmol, 1.0 eq) was allowed to react according to the general procedure to yield C10 ester **3** (53 %, 3.16 g, 15.9 mmol) as main product and C9, C10 diester **4** (16 %, 1.087 g, 4.79 mmol) as a side product.



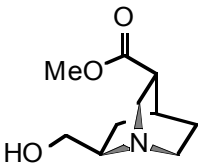
Data for **3**. IR ($CHCl_3$) ν 3434, 2999, 2952, 2878, 1728, 1456, 1437, 1371, 1333, 1236, 1198, 1178, 1138, 1100, 1050, 1017, 983 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.72-3.68 (m, 1H, H-9), 3.69 (s, 3H, OMe), 3.62 (dd, 1H, *J* = 11.5 and 10.4 Hz, H-9), 3.44-3.36 (m, 2H, H-2, H-6), 3.02-2.92 (m, 2H, H-7, H-7), 2.88 (dd, 1H, *J* = 13.3 and 8.9 Hz, H-6), 2.57-2.51 (m, 1H, H-5), 2.23-2.19 (m, 1H, H-4), 1.70-1.64 (m, 2H, H-3, H-8), 1.57-1.49 (m, 1H, H-8), 1.10-1.03 (m, 1H, H-3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.54 (C, C-10), 62.02 (CH_2, C-9), 57.47 (CH, C-2), 51.93 (CH_3, C-11), 48.76 (CH_2, C-6), 42.94 (CH_2, C-7), 41.20 (CH, C-5), 25.89 (CH_2, C-3), 25.18 (CH, C-4), 24.64 (CH_2, C-8); MS *m/z* 199 (M^+, 71.00), 197 (22.27), 182 (36.77), 168 (100.00), 158 (64.92), 140 (75.08), 126 (18.40), 112 (25.66), 96 (17.63), 82 (65.44); HRMS for $C_{10}H_{17}NO_3$: 199.1208, found: 199.1208.



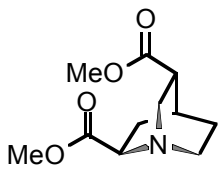
Data for **4**. IR ($CHCl_3$) ν 3434, 2951, 2878, 1776, 1731, 1462, 1410, 1372, 1292, 1230, 1151, 1136, 1119, 1086, 1027, 996, 834 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.77 (s, 3H, OMe), 3.69 (s, 3H, OMe), 3.53-3.45 (m, 1H, H-2), 3.26 (ddd, 1H, *J* = 14.5, 7.5 and 2.4 Hz, H-6), 3.05-2.97 (m, 2H, H-7, H-7), 2.91-2.82 (m, 1H, H-6), 2.54-2.48 (m, 1H, H-5), 2.30-2.26 (m, 1H, H-4), 2.02-1.96 (m, 1H, H-3), 1.79-1.71 (m, 1H, H-8), 1.65-1.59 (m, 2H, H-8, H-3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.44 (C, C-10), 173.03 (C, C-9), 58.08 (CH, C-2), 52.24 (CH_3, C-11), 51.81 (CH_3, C-12), 48.34 (CH_2, C-6), 46.01 (CH_2, C-7), 40.86 (CH, C-5), 25.82 (CH_2, C-3), 25.02 (CH, C-4), 24.94 (CH_2, C-8); MS *m/z* 227 (M^+, 44.95), 212 (22.55), 196 (16.75), 186 (2.84), 168 (100.00), 155 (10.13), 140 (53.19), 126 (3.99), 113 (13.81), 100 (14.87), 82 (47.16); HRMS for $C_{11}H_{17}NO_4$: 227.1157, found: 227.1157.

(1S,2R,4S,5R)-2-(Hydroxymethyl)-1-azabicyclo[2.2.2]octane-5-carboxylic acid methyl ester **7** (1S,2R,4S,5R)-1-azabicyclo[2.2.2]octane-2,5-dicarboxylic acid dimethyl ester **8**

Quincoridine sulfate (6.35 g , 23.95 mmol, 1.0 eq) was allowed to react according to the general procedure to yield C10 ester **7** (57 %, 2.72 g, 13,65 mmol) as main product and C9, C10 diester **4** (11 %, 598 mg, 2.63 mmol) as a side product.



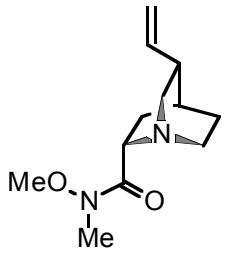
Data for **7**. IR ($CHCl_3$) ν 3435, 2953, 2879, 1732, 1458, 1437, 1366, 1290, 1234, 1198, 1181, 1080, 1034, 987, 839; ^1H NMR (400 MHz, $CDCl_3$) δ 4,23 (dd, 1H, *J* = 8.92 and 5.04 Hz, H-9), 4.01 (d, 1H, *J* = 8.88 Hz, H-9), 3.71 (s, 3H, H_3CO_2CR), 3.17 (d, 1H, *J* = 11.8 Hz, H-6), 2.73-2.62 (m, 2H, H-6, H-2), 2.50-2.43 (m, 2H, H-7, H-7), 2.28-2.26 (m, 1H, H-5), 2.23-2.18 (m, 1H, H-4), 1.93-1.81 (m, 3H, H-3, H-8, H-8), 1.65-1.55 (m, 1H, H-3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.29 (C, C-10), 71.21 (CH_2, C-9), 53.25 (CH, C-2), 52.19 (CH_3, C-11), 46.39 (CH_2, C-6), 45.17 (CH_2, C-7), 40.05 (CH, C-5), 27.14 (CH_2, C-3), 25.04 (CH, C-4), 24.78 (CH_2, C-8); MS *m/z* 199 (M^+, 1.46), 197 (7.71), 182 (3.84), 168 (9.91), 155 (57.76), 140 (8.52), 127 (32.51), 114 (100.00), 96 (39.19), 83 (36.40); HRMS calcd for $C_{10}H_{17}NO_3$: 199.1208, found: 199.1200.



Data for **8**. IR ($CHCl_3$) ν 3434, 2953, 2879, 1776, 1732, 1665, 1457, 1437, 1372, 1291, 1230, 1152, 1136, 1120, 1081, 1027, 991, 838; ^1H NMR (400 MHz, $CDCl_3$) δ 3.76 (s, 3H, H_3CO_2CR), 3.69 (s, 3H, H_3CO_2CR), 3.52-3.44 (m, 1H, H-2), 3.28 (ddd, 1H, *J* = 14.3, 7.4 and 2.6 Hz, H-6), 3.22-3.15 (m, 1H, H-6), 3.04-2.96 (m, 2H, H-7,

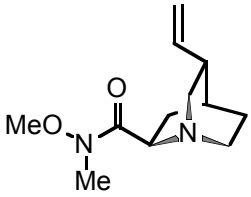
H-7), 2.72-2.61 (m, 1H, H-5), 2.54-2.41 (m, 1H, H-4), 2.01-1.88 (m, 1H, H-3), 1.79-1.70 (m, 1H, H-8), 1.65-1.58 (m, 2H, H-8, H-3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.42 (C, C-10), 172.99 (C, C-9), 58.07 (CH, C-2), 52.21 (CH_3, C-11), 51.81 (CH_3, C-12), 48.32 (CH_2, C-6), 45.97 (CH_2, C-7), 40.89 (CH, C-5), 25.83 (CH_2, C-3), 25.83 (CH, C-4), 25.04 (CH_2, C-8); MS *m/z* 227 (M^+, 44.95), 212 (22.55), 196 (16.75), 186 (2.84), 168 (100.00), 155 (10.13), 140 (53.19), 126 (3.99), 113 (13.81), 100 (14.87), 82 (47.16); HRMS calcd for $C_{11}H_{17}NO_4$: 227.1157, found: 227.1157.

(1S,2S,4S,5R)-5-Vinyl-1-azabicyclo[2.2.2]octane-2-carboxylic-acid-N-methoxy-N-methyl amide **9**



Ester 2 (50 mg, 0.29 mmol, 1 eq) was allowed to react according to the literature procedure[2] to afford C9 amide **9** (87 %, 58 mg, 0.26 mmol). IR ($CHCl_3$) ν 3080, 2999, 2941, 2868, 2461, 1728, 1658, 1456, 1391, 1327, 1264, 1239, 1179, 1122, 1022, 983, 950, 910, 878 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.91 (ddd, 1H, *J* = 17.4, 10.4 and 7.4 Hz, H-10), 5.12-5.04 (m, 2H, H-11), 3.75 (s, 3H, OMe), 3.77-3.70 (m, 1H, H-2), 3.22 (s, 3H, NMe), 3.19-3.11 (m, 2H, H-6), 2.85-2.76 (m, 1H, H-7), 2.70-2.61 (m, 1H, H-7), 2.36-2.28 (m, 1H, H-5), 2.00-1.88 (m, 1H, H-4), 1.86-1.82 (m, 1H, H-3), 1.80-1.68 (m, 2H, H-8), 1.52-1.42 (m, 1H, H-3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.39 (C, C-9), 141.95 (CH, C-10), 114.33 (CH_2, C-11), 61.36 (CH_3, OMe), 55.42 (CH_2, C-6), 52.22 (CH, C-2), 42.70 (CH_2, C-7), 40.99 (CH_3, NMe), 39.29 (CH, C-5), 27.24 (CH_2, C-8), 27.10 (CH, C-4), 23.77 (C-3); MS *m/z* 224 (M^+, 4.27), 193 (2.20), 163 (3.25), 137 (11.04), 136 (100.00), 109 (3.12), 95 (4.64), 94 (2.39), 82 (6.23), 81 (11.53), 80 (3.19), 79 (5.13), 77 (2.09), 75 (10.69), 67 (3.04). HRMS calcd for $C_{12}H_{20}N_2O_2$: 224.1525, found: 224.1524.

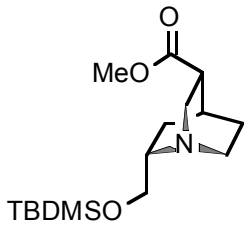
(1S,2R,4S,5R)-5-Vinyl-1-azabicyclo[2.2.2]octane-2-carboxylic-acid-N-methoxy-N-methyl amide **12**



Ester **2** (224 mg, 1.0 mmol, 1 eq) was allowed to react according to the literature procedure[2] to afford C9 amide **12** (59 %, 132 mg, 0.59 mmol). IR ($CHCl_3$) ν 3000 , 2936, 2872 , 1732, 1656, 1456 , 1424 , 1388 , 1328 , 1260, 1228 , 1176 , 1120, 1048, 1024 , 980 , 916 , 876 , 832 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.03 (ddd, 1 H, *J* = 17.3 Hz, 10.2 and 7.8 Hz, H-10), 5.03 (ddd, 1 H, *J* = 17.3, 1.9 and 1 Hz, H-11), 5.01 (ddd, 1 H, *J* = 10.2, 1.1 and 1 Hz, H-11), 3.75-3.73 (m, 2 H, H-2, H-6), 3.74 (s, 3 H, OMe), 3.21 (s, 3 H, NMe), 3.04-2.90 (m, 1 H, H-7), 2.89-2.77 (m, 2 H, H-7, H-6), 2.27-2.16 (m, 2 H, H-3, H-5), 1.81-1.75 (m, 1 H, H-4), 1.66-1.58 (m, 2 H, H-8, H-8), 1.48-1.38 (m, 1 H, H-3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.26 (C=O), 140.73 (CH, C-10), 114.44 (CH, C-11), 61.33 (OMe), 55.24 (CH, C-2), 48.97 (CH, C-6), 48.64 (CH, C-7), 40.35 (CH, C-5), 32.74 (NMe), 29.70 (CH, C-8), 27.71 (CH, C-4), 26.67 (CH, C-3); MS *m/z* 224 (14.42), 204 (1.62), 193 (40.25), 164 (21.54), 152 (4.08), 136 (100), 122 (6.68), 108 (15.55), 95 (14.31), 86 (1.77), 81 (27.05), 74 (37.00), 67 (9.06); HRMS calcd for $C_{12}H_{20}N_2O_2$: 224.1525, found 224.1526.

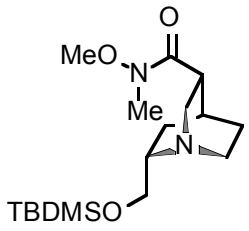
(2) a) Nahm, S. Weinreb, S. M. *Tetrahedron Lett.* **1981**, *22*, 3815. b) Shimizu, T.; Osako, K.; Nakata, T. *Tetrahedron Lett.* **1997**, *38*, 2685. c) Mentzel, M.; Hoffmann, H. M. R. *J. prakt. Chem* **1997**, *339*, 517.

(1S,2S,4S,5R)-2-(*tert*-Butyldimethylsilyloxy)-1-azabicyclo[2.2.2]octane-5-carboxylic acid methyl ester **TBDMS-3**



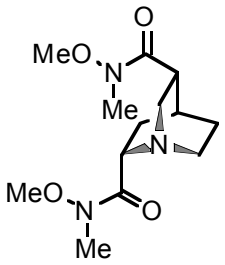
Triethylamine (0.45 ml, 3.27 mmol, 1.3 eq) was added to a solution of unprotected ester **3** (500 mg, 2.51 mmol, 1 eq) in abs. CH_2Cl_2 (10 ml) at r.t. After stirring under argon for 15 min DMAP (31 mg, 0.25 mmol, 0.1 eq) and *tert.*-butyldimethylsilyl chloride (415 mg, 2.77 mmol, 1.1 eq) were added at 0 °C. The homogeneous reaction mixture was stirred for 16 h at r.t., followed by extraction with sat. aq. $NaHCO_3$ and CH_2Cl_2. The combined organic layer was dried ($MgSO_4$), evaporated and purified by chromatography (EtOAc/MeOH 20:1) to afford silylated C-10 ester **TBDMS-3** (64 %, 503 mg, 1.61 mmol). IR ($CHCl_3$) ν 2952, 2881, 2858, 1726, 1462, 1437, 1362, 1323, 1256, 1198, 1178, 1117, 1083, 1057, 1027, 1006, 837; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.73 (dd, 1H, *J* = 10.2 and 6.0 Hz, H-9), 3.70 (s, 3H, OMe), 3.63 (dd, 1H, *J* = 10.1 and 7.2 Hz, H-9), 3.40 (ddd, 1H, *J* = 14.3, 7.4 and 2.4 Hz, H-6), 3.00-2.77 (m, 4H, H-2, H-6, H-7, H-7), 2.50-2.45 (m, 1H, H-5), 2.23-2.20 (m, 1H, H-4), 1.63-1.51 (m, 3H, H-3, H-8, H-8), 1.39-1.33 (m, 1H, H-3), 0.90 (s, 9H, t-Bu), 0.07 (s, 3H, SiMe), 0.06 (s, 3H, SiMe); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.90 (C, C-10), 65.35 (CH_2, C-9), 57.18 (CH, C-2), 51.69 (CH_3, C-11), 49.33 (CH_2, C-6), 44.81 (CH_2, C-7), 41.41 (CH, C-5), 26.06 (CH_3, t-Bu), 26.01 (CH_2, C-3), 25.87 (CH_2, C-8), 25.38 (CH, C-4), 18.43 (C, t-Bu), -5.28 (CH_3, SiMe), -5.31 (CH_3, SiMe); MS *m/z* 314 (M^++1, 6.48), 299 (7.04), 283 (2.86), 273 (6.78), 257 (100.00), 243 (2.10), 227 (1.40), 212 (3.37), 184 (4.47), 168 (5.97), 141 (6.79), 105 (3.04), 89 (6.16); HRMS calcd for $C_{16}H_{31}NO_3Si$: 313.2073, found: 313.2065.

(1S,2S,4S,5R)-2-(*tert*-Butyldimethylsilyloxy)-1-azabicyclo[2.2.2]octane-5-carboxylic acid-N-methyloxy-N-methylamide **10**



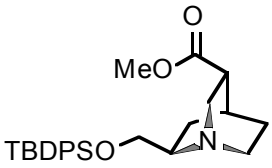
TBDMS-3 (300 mg, 0.96 mmol, 1 eq) was allowed to react according to the literature procedure[2] to afford silylated C-10 Weinreb amide **10** (69 %, 226 mg, 0.66 mmol). IR ($CHCl_3$) ν 2999, 2953, 2931, 2882, 2858, 1633, 1463, 1390, 1362, 1322, 1256, 1192, 1119, 1085, 1053, 1007, 939, 837; ^{1}H NMR (400 MHz, $CDCl_3$) ? 3.83-3.78 (m, 1H, H-9), 3.67 (dd, 1H, *J* = 10.5 and 6.5 Hz, H-9), 3.68 (s, 3H, OMe), 3.48-3.39 (m, 1H, H-6), 3.21 (s, 3H, NMe) 3.09-2.74 (m, 4H, H-2, H-6, H-7, H-7), 2.73-2.58 (m, 1H, H-5), 2.26-2.20 (m, 1H, H-4), 1.75-1.48 (m, 4H, H-3, H-8, H-8, H-3), 0.88 (s, 9H, t-Bu), 0.07 (s, 3H, SiCH_3), 0.06 (s, 3H, SiCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.16 (C, C-10), 68.50 (CH_3, OMe), 64.02 (CH_2, C-9), 57.81 (CH, C-2), 49.07 (CH_2, C-6), 44.37 (CH_2, C-7), 37.69 (CH_3, NMe), 35.74 (CH, C-5), 31.46 (CH, C-4), 26.03 (CH_3, t-Bu), 25.65 (CH_2, C-3), 24.80 (CH_2, C-8), 18.42 (C, t-Bu), -5.25 (CH_3, SiMe), -5.36 (CH_3, SiMe); MS *m/z* 341 (M^+-1, 1.58), 313 (9.13), 300 (5.80), 283 (11.97), 271 (100.00), 255 (19.64), 240 (3.51), 226 (5.13), 197 (3.44), 183 (33.14), 168 (5.16), 150 (3.63), 123 (3.63), 96 (6.17), 82 (12.18), 73 (20.66); HRMS calcd for $C_{17}H_{34}N_2O_3Si$: 342.2338, found: 342.2327.

(1S,2S,4S,5R)-1-azabicyclo[2.2.2]octane-2,5-dicarboxylic acid N-methyloxy-N-methylamide **11**



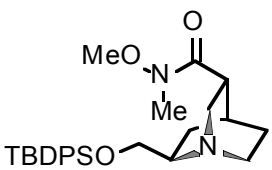
Diester **4** (114 mg, 0.50 mmol, 1 eq)) was allowed to react according to the literature procedure[2] to afford Weinreb amide **11** (72 %, 103 mg, 0.36 mmol). IR ($CHCl_3$) ν 2999, 2941, 2874, 1729, 1658, 1458, 1390, 1331, 1231, 1177, 1119, 1022, 983; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.78-3.67 (m, 2H, H-6, H-2), 3.70 (s, 3H, OMe), 3.67 (s, 3H, OMe), 3.24-3.11 (m, 3H, H-6, H-7, H-7), 3.17 (s, 3H, NMe), 3.15 (s, 3H, NMe), 3.07-2.95 (m, 1H, H-5), 2.31-2.20 (m, 1H, H-4), 1.73-1.54 (m, 4H, H-3, H-8, H-8, H-3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.39 (C, C-10), 173.54 (C, C-9), 61.32 (CH_3, OMe), 61.19 (CH_3, OMe), 51.75 (CH, C-2), 48.61 (CH_2, C-6), 46.30 (CH_2, C-7), 41.02 (CH_3, NMe), 40.91 (CH_3, NMe), 38.56 (CH, C-5), 26.49 (CH_2, C-3), 25.99 (CH_2, C-8), 24.64 (CH, C-4); MS *m/z* 285 (M^+, 3.85), 271 (81.88), 254 (12.62), 225 (100.00), 196 (45.94), 184 (11.50), 168 (76.33), 153 (32.52), 141 (31.14), 136 (30.28), 108 (90.09), 96 (14.38), 82 (62.77), 74 (82.63); HRMS calcd for $C_{13}H_{23}N_3O_4$: 285.1688, found: 285.1675.

(1S,2R,4S,5R)-2-(*tert*-Butyldiphenylsilyloxy)-1-azabicyclo[2.2.2]octane-5-carboxylic acid methyl ester **TBDPS-7**



Triethylamine (0.31 ml, 2.21 mmol, 2.0 eq) was added to a solution of unprotected ester **3** (220 mg, 1.11 mmol, 1 eq) in abs. CH_2Cl_2 (5 ml) at r.t. After stirring under argon for 15 min DMAP (14 mg, 0.11 mmol, 0.1 eq) and *tert.*-butyldiphenylsilyl chloride (0.37 ml, 1.44 mmol, 1.3 eq) were added at 0 °C. The homogeneous reaction mixture was stirred for 14 h at r.t., followed by extraction with sat. aq. $NaHCO_3$ and CH_2Cl_2. The combined organic layer was dried ($MgSO_4$), evaporated and purified by chromatography (EtOAc/MeOH 20:1) to afford TBDPS-protected C-10 ester **TBDPS-7** (91 %, 439 mg, 1.01 mmol). IR ($CHCl_3$) ν 3052 , 2999 , 2951, 2860, 1727, 1602, 1589, 1461 , 1428, 1363 , 1323 , 1247 , 1198, 1179, 1113, 1083, 1027 , 1007, 999 , 823 ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69-7.62 (m, 4H, Ar-H), 7.43-7.34 (m, 6H, Ar-H), 3.77 (dd, 1H, *J* = 10.0 and 5.8 Hz, H-9), 3.70 (dd, 1H, *J* = 10.1 and 7.3 Hz, H-9), 3.65 (s, 3H, OMe), 3.25 (ddd, 1H, *J* = 14.3, 7.4 and 2.2 Hz, H-6), 2.96-2.71 (m, 4H, H-2, H-6, H-7, H-7), 2.47-2.41 (m, 1H, H-5), 2.23-2.19 (m, 1H, H-4), 1.64-1.55 (m, 3H, H-3, H-8, H-8), 1.51-1.43 (m, 1H, H-3), 1.05 (s, 9H, t-Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.75 (C, C-10), 135.66 (CH, Ar-H), 133.81 (C, Ar-Si), 129.54 (CH, Ar-H), 127.61 (CH, Ar-H), 66.11 (CH_2, C-9), 57.05 (CH, C-2), 51.65 (CH_3, C-11), 49.25 (CH_2, C-6), 44.99 (CH_2, C-7), 41.37 (CH, C-5), 26.89 (CH_3, t-Bu), 26.85 (CH_2, C-3), 26.05 (CH_2, C-8), 25.29 (CH, C-4), 19.27 (C, t-Bu).

(1S,2R,4S,5R)-2-(*tert*-Butyldimethylsilyloxy)-1-azabicyclo[2.2.2]octane-5-carboxylic acid-N-methyloxy-N-methylamide **13**



TBDPS-7 (437 mg, 1.00 mmol, 1 eq) was allowed to react according to the literature procedure[2] to afford Weinreb amide **13** (65 %, 303 mg, 0.65 mmol). IR ($CHCl_3$) ν 3054, 2999, 2951, 2892, 1631, 1602, 1589, 1467, 1391, 1363, 1316, 1248, 1189, 1117, 1090, 1047, 1007, 989, 823; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68-7.61 (m, 4H, Ar-H), 7.45-7.36 (m, 6H, Ar-H), 3.77-3.72 (m, 1H, H-9), 3.69 (s, 3H, OMe), 3.61 (dd, 1H, *J* = 10.2 and 6.3 Hz, H-9), 3.44-3.34 (m, 1H, H-6), 3.18 (s, 3H, NMe) 3.10-2.72 (m, 4H, H-2, H-6, H-7, H-7), 2.61-2.53 (m, 1H, H-5), 2.24-2.18 (m, 1H, H-4), 1.69-1.38 (m, 4H, H-3, H-8, H-8, H-3), 1.03 (s, 9H, t-Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.58 (C, C-10), 135.58 (CH, Ar-H), 133.64 (C, Ar-Si), 129.37 (CH, Ar-H), 127.62 (CH, Ar-H), 68.32 (CH_3, OMe), 65.70

(CH_2, C-9), 57.89 (CH, C-2), 49.14 (CH_2, C-6), 48.62 (CH_2, C-7), 39.56 (CH, C-5), 37.05 (CH_3, NMe), 26.71 (CH, C-4), 26.08 (CH_3, t-Bu), 25.83 (CH_2, C-3), 24.96 (CH_2, C-8), 19.03 (C, t-Bu).