Pergamon

Tetrahedron: *Asymmetry* 9 (1998) 1051–1057

TETRAHEDRON: *ASYMMETRY*

Acylation and *O*-sulfonylation of Quincorine® and Quincoridine®. Efficient intramolecular catalysis

H. M. R. Hoffmann * and Olaf Schrake

Department of Organic Chemistry, University of Hannover, Schneiderberg 1B, D-30167 Hannover, Germany

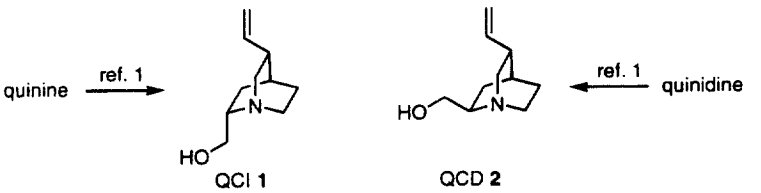
Received 29 January 1998; accepted 12 February 1998

Abstract

A convenient preparation of enantiopure *O*-acyl and *O*-sulfonyl derivatives of Quincorine® and Quincoridine® is described.

1. Introduction

We have recently described the transformation of quinine and quinidine into Quincorine® **1** and Quincoridine® **2**, respectively (Scheme 1).[1–3]



Scheme 1.

These new amino alcohols have four stereodefined centres each, including the bridgehead nitrogen, and they contain the same stereochemistry about the azabicyclic core as encountered in quinine and quinidine.

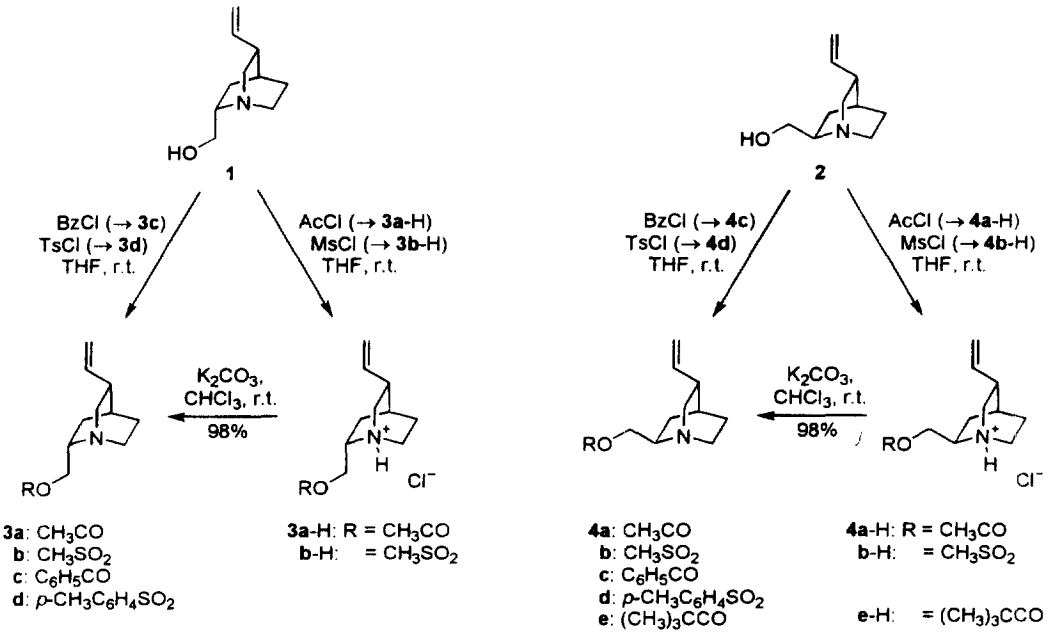
Although further transformations of QCI and QCD may look simple, not all of them are trivial.[4] We herein describe the convenient preparation of a series of bicyclic carboxylic esters and sulfonic esters.

* Corresponding author. E-mail: hoffmann@mbox.uni-hannover.de

0957-4166/98/$19.00
PII: S0957-4166(98)00066-4

2. Results and discussion

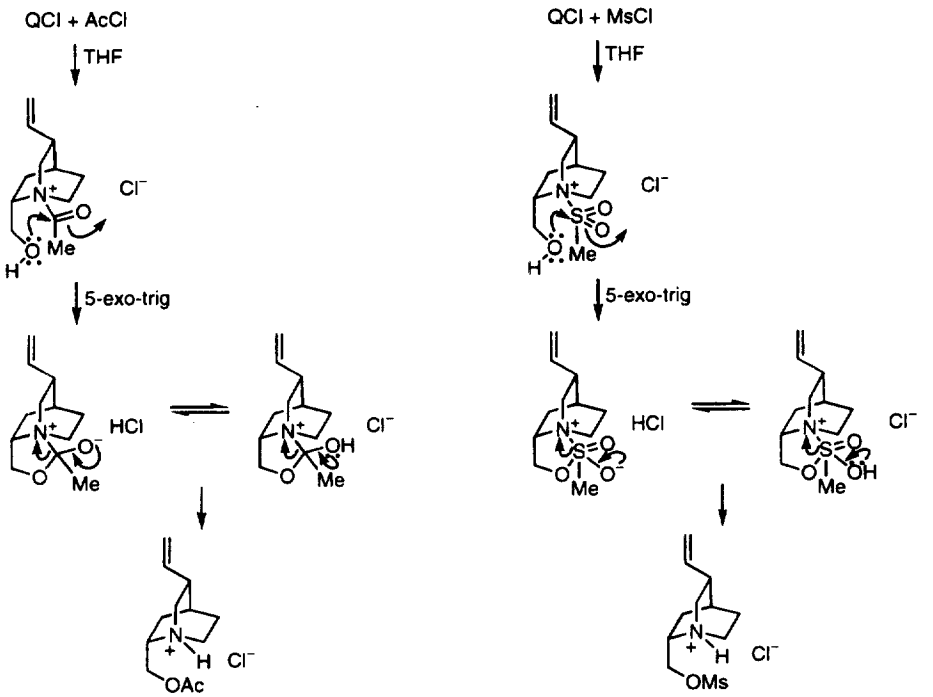
In our work we found that the conformationally constrained β-nitrogen is very reactive towards electrophiles. Thus, preparation of the methyl ether and benzyl ether is not straightforward.[5] However, the stereoisomeric amino alcohols **1** and **2** were easily converted into their corresponding acetates (Scheme 2). Provided that acetyl chloride rather than acetic anhydride was used in THF as the solvent, the acetates **3a** and **4a** were formed in excellent yield (>95%) within 10 min. Addition of a supplementary acylation catalyst such as triethylamine, pyridine or DMAP did not increase the yield further nor did it shorten the reaction time.



Scheme 2.

Simple reaction with acetyl chloride gave a crystalline precipitate, which was filtered and washed with THF, resulting in pure product. Aqueous workup or further purification were unnecessary. On standing, the acetates were found to suffer self-induced deacetylation. For this reason it is advantageous to store these amino esters as their hydrochloride salts, which are easily converted into the free amines on treatment with solid K_2CO_3 in chloroform (5 min). Not only are both acetates **3a** and **4a** accessible following this procedure, but the sterically more demanding pivaloyl chloride and QCD combined to form the corresponding pivalate **4e** (>95%). The parent quinidine reacted rapidly giving the C9-OAc derivative in excellent yield (5 h, 94%).[6,7] Here again, THF is the solvent of choice which dissolves the starting material, but not the product hydrochloride. Similarly, benzoate **3c** was obtained (85% yield). The significantly longer reaction time could be curtailed by heating the mixture. In this case, utilizing dichloromethane as the solvent shortened the reaction time to 6 h. Benzoate **3c** was not isolated as its hydrochloride, but obtained as the free amine by aqueous workup.

Finally, using these general procedures we have prepared the epimeric mesylates **3b** and **4b**, and tosylates **3d** and **4d**. These facile and atom-efficient reactions are proposed to proceed via nucleophilic catalysis of the bridgehead amine (Scheme 3), which takes on the role of pyridine or p-dimethylaminopyridine (DMAP)[8] in conventional esterifications. The final step is *intra*molecular, and ideally, the product hydrochloride is also precipitated.



Scheme 3.

3. Experimental

3.1. General

Melting points were determined on a Büchi apparatus. 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 an internal standard. Mass spectra were recorded on a Finnigan MAT 312 (70 eV) or a VG Autospec spectrometer at r.t. unless otherwise stated. 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 F_{254} plates (E. Merck). THF was distilled over sodium and benzophenone before use. CH_2Cl_2 (DCM) was distilled over CaH_2 before use. $CHCl_3$ was distilled before use.

3.2. General procedure

The amino alcohol was dissolved in a small amount of THF (3 ml/1 mmol amino alcohol) and cooled to 0°C. The respective acid chloride or the sulfonyl chloride (1.3 equiv.) was added dropwise. After 10 min the resulting white precipitate was filtered off and washed with THF. The hydrochloride (**3a**-H, **3b**-H, **4a**-H, **4b**-H, **4e**-H) was dissolved in $CHCl_3$ and 2 equiv. of solid K_2CO_3 was added. After being stirred at r.t. for 5 min the suspension was filtered. The solvent was removed giving the ester in 85–97% yield. For compounds **3c**, **3d**, **4c** and **4d** it was advantagous to use dichloromethane as solvent. In these cases the reaction time was about 6 h and the free amine (78–88%) was obtained after aqueous work-up using sat. $NaHCO_3$ solution. Further work-up and purification were unnecessary.

3.3. (1S,2S,4S,5R)-2-(Acetoxymethyl)-5-ethenyl-1-azabicyclo[2.2.2]octane **3a**

QCI **1** and AcCl were allowed to react according to the general procedure to afford **3a** (89–97%), $[\alpha]_D$=32 (*c* 1.45, CH_2Cl_2). IR ($CHCl_3$) ν 3076, 2936, 2864, 1740, 1636, 1452, 1372, 1320, 1244, 1152, 1108, 1040, 992, 912, 604 cm^{-1}; ^1H NMR (400 MHz) δ 5.88 (ddd, 1H, $^3J_{trans}$=17.6 Hz, $^3J_{cis}$=10.5 Hz, ^2J=7.4 Hz, H-10), 5.08 (ddd, 1H, $^3J_{trans}$=17.6 Hz, ^2J=1.5 Hz, ^4J=1.5 Hz, H-11), 5.07 (ddd, 1H, $^3J_{cis}$=10.3 Hz, ^2J=1.5 Hz, ^4J=1.5 Hz, H-11), 4.11 (dd, 1H, ^3J=9.2 Hz, ^2J=11.8 Hz, H-9), 4.04 (dd, 1H, ^3J=5.2 Hz, ^2J=11.8 Hz, H-9), 3.25 (dd, 1H, ^2J=13.8 Hz, ^3J=10.1 Hz, H-6), 3.2–2.9 (m, 2H, H-7, H-2), 2.82–271 (m, 2H, H-7, H-6), 2.41–2.32 (m, 1H, H-5), 2.09 (s, 3H, CH_3), 1.96–1.87 (m, 1H, H-3), 1.83–1.78 (m, 1H, H-4), 1.64–1.51 (m, 2H, H-8), 1.01–0.94 (m, 1H, H-3); ^{13}C NMR (100 MHz) δ 171.21 (C=O), 141.04 (C-10), 114.85 (C-11), 64.67 (C-9), 54.84 (C-6), 54.39 (C-2), 40.49 (C-7), 39.16 (C-5), 27.25 (C-4), 27.24 (C-8), 24.60 (C-3), 21.00 (CH_3); MS *m/z* 209 (M^+, 9), 197 (1), 168 (7), 167 (3), 150 (17), 137 (12), 136 (100), 129 (6), 114 (7), 108 (6), 95 (6), 81 (12), 72 (23); HRMS calcd for $C_{12}H_{19}NO_2$: 209.1413, found 209.1416.

3.4. (1S,2R,4S,5R)-2-(Acetoxymethyl)-5-ethenyl-1-azabicyclo[2.2.2]octane **4a**

QCD **2** and AcCl were allowed to react according to the general procedure to afford **4a** (88–94%), $[\alpha]_D$=119 (*c* 1.35, CH_2Cl_2). IR ($CHCl_3$) ν 3080, 3008, 2940, 2876, 1736, 1636, 1456, 1420, 1376, 1324, 1248, 1036, 992, 916, 604 cm^{-1}; ^1H NMR (400 MHz) δ 5.85 (ddd, 1H, $^3J_{trans}$=17.3 Hz, $^3J_{cis}$=10.6 Hz, ^2J=7 Hz, H-10), 5.06 (ddd, 1H, $^3J_{cis}$=10.6 Hz, ^2J=1.6 Hz, ^4J=1.6 Hz, H-11), 5.04 (ddd, 1H, $^3J_{trans}$=17.1 Hz, ^2J=1.6 Hz, ^4J=1.6 Hz, H-11), 4.12 (dd, 1H, ^3J=9 Hz, ^2J=11.8 Hz, H-9), 4.02 (dd, 1H, ^3J=4.8 Hz, ^2J=11.8 Hz, H-9), 3.18–2.86 (m, 4H, H-7, H-7, H-6, H-2), 2.75 (ddd, 1H, ^2J=14.3 Hz, *J*=7.7 Hz, *J*=2.4 Hz, H-6), 2.34–2.25 (m, 1H, H-5), 2.08 (s, 3H, CH_3), 1.81–1.76 (m, 1H, H-4), 1.68–1.49 (m, 3H, H-8, H-8, H-3), 1.35–1.27 (m, 1H, H-3); ^{13}C NMR (100 MHz) δ 139.92 (C-10), 114.93 (C-11), 64.28 (C-9), 54.55 (C-2), 48.63 (C-6), 46.87 (C-7), 39.43 (C-5), 27.41 (C-4), 26.38 (C-8), 23.96 (C-3), 21.05 (CH_3); MS *m/z* 209 (M^+, 9), 168 (7), 167 (3), 166 (6), 150 (17), 137 (12), 136 (100), 129 (6), 114 (7), 108 (6), 95 (6), 81 (12), 72 (23); HRMS calcd for $C_{12}H_{19}NO_2$: 209.1413, found 209.1415.

3.5. (1S,2S,4S,5R)-2-(Methylsulfonylmethyl)-5-ethenyl-1-azabicyclo[2.2.2]octane **3b**

QCI **1** and MsCl were allowed to react according to the general procedure to afford **3b** (92–95%), $[\alpha]_D$=−19.5 (*c* 0.99, CH_2Cl_2). IR ($CHCl_3$) ν 3072, 2936, 1724, 1636, 1452, 1416, 1396, 1352, 1224, 1172, 1112, 1052, 984, 964, 920, 828, 748, 668 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 5.94–5.83 (m, 1H, H-10), 5.10–5.04 (m, 2H, H-11, H-11), 4.24 (dd, 1H, ^2J=10.8 Hz, ^3J=9.2 Hz, H-9), 4.11 (dd, 1H, ^2J=10.8 Hz, ^3J=5.2 Hz, H-9), 3.19 (dd, 1H, ^2J=14 Hz, ^3J=10.1, H-6), 3.20–3.12 (m, 1H, H-2), 3.09 (s, 3H, CH_3), 3.04–2.94 (m, 1H, H-7), 2.76–2.68 (m, 2H, H-7, H-6), 2.37–2.29 (m, 1H, H-5), 1.94–1.85 (m, 1H, H-3), 1.82–1.77 (m, 1H, H-4), 1.61–1.47 (m, 2H, H-8, H-8), 0.97–0.89 (m, 1H, H-3); ^{13}C NMR (100 MHz, CD_3OD) δ 141.37 (C-10), 114.72 (C-11), 69.27 (C-9), 55.47 (C-6), 54.83 (C-2), 40.86 (C-7), 39.40 (C-5), 37.86 (C-4), 27.58 (C-8), 27.15 (CH_3), 24.46 (C-3); MS *m/z* 245 (M^+, 9), 218 (1), 204 (5), 190 (1), 166 (7), 150 (21), 137 (11), 136 (100), 122 (2), 108 (5), 96 (7), 79 (14); HRMS calcd for $C_{11}H_{19}NO_3S$: 245.3428, found 245.3426.

3.6. (1S,2R,4S,5R)-2-(Methylsulfonylmethyl)-5-ethenyl-1-azabicyclo[2.2.2]octane **4b**

QCD **2** and MsCl were allowed to react according to the general procedure to afford **4b** (88–95%), $[\alpha]_D$=124.7 (*c* 1.35, CH_2Cl_2). IR ($CHCl_3$) ν 3072, 2964, 2944, 1722, 1636, 1452, 1356, 1231, 1176, 1100, 1036, 968, 920, 832, 740 cm^{-1}; ^1H NMR (400 MHz) δ 5.92 (ddd, 1H, $^3J_{trans}$=17.5 Hz, $^3J_{cis}$=10.5 Hz, ^2J=7.2 Hz, H-10), 5.08 (ddd, 1H, $^3J_{trans}$=17.3 Hz, ^2J=1.5 Hz, ^4J=1.5 Hz, H-11), 5.06 (ddd, 1H, $^3J_{cis}$=10.5 Hz, ^2J=1.5 Hz, ^4J=1.5 Hz, H-11), 4.25 (dd, 1H, ^3J=8.8 Hz, ^2J=10.9 Hz, H-9), 4.12 (dd, 1H, ^3J=5.2 Hz, ^2J=10.9 Hz, H-9), 3.21–2.84 (m, 4H, H-7, H-7, H-6, H-2), 3.11 (s, 3H, CH_3), 2.76 (ddd, 1H, ^2J=14.2 Hz, *J*=7.7 Hz, *J*=2.2 Hz, H-6), 2.39–2.29 (m, 1H, H-5), 1.79–1.75 (m, 1H, H-4), 1.74–1.65 (m, 2H, H-8, H-8), 1.64–1.55 (m, 1H, H-3), 1.43–1.35 (m, 1H, H-3); ^{13}C NMR (100 MHz) δ 141.60 (C-10), 116.07 (C-11), 70.67 (C-9), 56.50 (C-2), 50.12 (C-6), 48.48 (C-7), 41.20 (C-5), 37.75 (C-4), 29.25 (CH_3), 29.25 (C-8), 24.79 (C-3); MS *m/z* 245 (M^+, 12), 226 (3), 204 (8), 190 (1), 166 (7), 150 (31), 136 (100), 129 (2), 120 (4), 107 (8), 95 (17), 85 (2), 79 (19); HRMS calcd for $C_{11}H_{19}NO_3S$: 245.3428, found 245.3431.

3.7. (1S,2S,4S,5R)-2-(Benzoyloxymethyl)-5-ethenyl-1-azabicyclo[2.2.2]octane **3c**

QCI **1** and BzCl were allowed to react according to the general procedure to afford **3c** (82–88%), $[\alpha]_D$=21 (*c* 1.4, CH_2Cl_2). IR ($CHCl_3$) ν 3064 (m), 2944 (s), 2876 (m), 1716 (s), 1636 (m), 1600 (m), 1368 (m), 1340 (m), 1316 (m), 1272 (s), 1176 (m), 1116 (s), 1068 (m), 1024 (m), 992 (m), 916 (m), 824 (m) cm^{-1}; ^1H NMR (400 MHz) δ 8.12–8.05 (m, 2H, H-12, H-12), 7.58–7.46 (m, 1H, H-14), 7.44–7.37 (m, 2 H H-13, H-13), 5.9 (ddd, 1H, $^3J_{trans}$=17.5 Hz, $^3J_{cis}$=10.1 Hz, ^2J=7.4 Hz, H-10), 5.1 (ddd, 1H, $^3J_{trans}$=17.1 Hz, ^2J=1.5 Hz, ^4J=1.5 Hz, H-11), 5.08 (ddd, 1H, $^3J_{cis}$=10.3 Hz, ^2J=1.5 Hz, ^4J=1.5 Hz, H-11), 4.45 (dd, 1H, ^3J=8.5 Hz, ^2J=11.7 Hz, H-9), 4.31 (dd, 1H, ^2J=11.7 Hz, ^3J=5.7 Hz, H-9), 3.33 (dd, 1H, ^2J=13.8 Hz, ^3J=10.1 Hz, H-6), 3.44–3.35 (m, 1H, H-7), 3.23–3.13 (m, 1H, H-3), 2.93–2.81 (m, 2H, H-3, H-7), 2.46–2.37 (m, 1H, H-2), 2.06–1.97 (m, 1H, H-6), 1.88–1.84 (m, 1H, H-4), 1.68–1.62 (m, 2H, H-8, H-8), 1.19–1.12 (m, 1H, H-5); ^{13}C NMR (100 MHz) δ 166.81 (C=O), 141.00 (C-10), 133.09 (C14′), 129.91 (C-13), 128.42 (C-12), 127.84 (C-14) 115.13 (C-11), 65.62 (C-9), 54.59 (C-6), 54.73 (C-2), 41.01 (C-7), 39.12 (C-5), 27.43 (C-4), 27.26 (C-8), 24.82 (C-3); MS *m/z* 271 (M^+, 7), 230 (4), 166 (7), 150 (11), 137 (10), 136 (100), 122 (4), 105 (41), 95 (3), 82 (4), 77 (20), 67 (3); HRMS calcd for $C_{17}H_{21}NO_2$: 271.1573, found 271.1572.

3.8. (1S,2R,4S,5R)-2-(Benzoyloxymethyl)-5-ethenyl-1-azabicyclo[2.2.2]octane **4c**

QCD **2** and BzCl were allowed to react according to the general procedure to afford **4c** (80–85%), $[\alpha]_D$=86.7 (*c* 1.45, CH_2Cl_2). IR ($CHCl_3$) ν 3062 (m), 2942 (s), 2876 (m), 1719 (s), 1636 (m), 1600 (m), 1368 (m), 1342 (m), 1316 (m), 1272 (s), 1176 (m), 1118 (s), 1058 (m), 1020 (m), 992 (m), 916 (m), 824 (m) cm^{-1}; ^1H NMR (400 MHz) δ 8.09–8.04 (m, 2H, H-12, H-12), 7.54–7.48 (m, 1H, H-14), 7.41–7.35 (m, 2H, H-13, H-13), 5.88 (ddddd, 1H, $^3J_{trans}$=16.4 Hz, $^3J_{cis}$=11.4 Hz, ^3J=9.4 Hz, ^4J=1.8 Hz, *J*=6.8 Hz, H-10), 5.10–5.04 (m, 2H, H-11, H-11), 4.46 (dd, 1H, ^3J=8.1 Hz, ^2J=11.7 Hz, H-9), 4.28 (dd, 1H, ^3J=5.5 Hz, ^2J=11.7 Hz, H-9), 3.34–2.93 (m, 4H, H-7, H-7, H-6, H-2), 2.87 (dd, 1H, ^2J=14.16 Hz, *J*=7.9 Hz, *J*=2.4 Hz, H-6), 2.39–2.3 (m, 1H, H-5), 1.86–1.8 (m, 1H, H-4), 1.73–1.6 (m, 3H, H-8, H-8, H-3), 1.51–1.43 (m, 1H, H-3); ^{13}C NMR (100 MHz) δ 166.67 (C=O), 139.72 (C-10), 132.87 (C-14′), 130.03 (C-13), 129.74 (C-12), 127.68 (C-14), 115.05 (C-11), 64.96 (C-9), 54.62 (C-2), 48.57 (C-6), 47.09 (C-7), 39.28 (C-5), 27.37 (C-4), 26.19 (C-8), 24.19 (C-3); MS *m/z* 271 (M^+, 11), 230 (9), 216 (2), 191 (100),

166 (12), 150 (25), 144 (2), 136 (64), 122 (4), 116 (9), 105 (100), 95 (5), 82 (8), 77 (53), 67 (5); HRMS calcd for $C_{17}H_{21}NO_2$: 271.1573, found 271.1574.

3.9. (1S,2S,4S,5R)-2-(p-Methylphenylsulfonylmethyl)-5-ethenyl-1-azabicyclo[2.2.2]octane **3d**

QCI **1** and TsCl were allowed to react according to the general procedure to afford **3d** (78–86%), $[\alpha]_D$=18 (*c* 1.05, CH_2Cl_2). Melting point: 32°C; IR ($CHCl_3$) ν 2948, 2888, 2868, 1636, 1600 (w), 1452, 1356, 1231, 1176, 1100, 1036, 968, 920, 832, 740 cm^{-1}; ^1H NMR (400 MHz) δ 7.81 (d, 2H, ^3J=8.5 Hz, H-12, H-12), 7.35 (d, 2H, ^3J=8.5 Hz, H-13, H-13), 5.82 (ddd, 1H, $^3J_{trans}$=17.6 Hz, $^3J_{cis}$=9.9 Hz, ^2J=7.5 Hz, H-10), 5.02 (ddd, 1H, $^3J_{trans}$=17.6 Hz, ^2J=1.6 Hz, ^4J=1.6 Hz, H-11), 5.01 (ddd, 1H, $^3J_{cis}$=8.6 Hz, ^2J=1.6 Hz, ^4J=1.6 Hz, H-11), 3.99 (dd, 1H, ^3J=10.1 Hz, ^2J=8 Hz, H-9), 3.94 (dd, 1H, ^2J=10.1 Hz, ^3J=6.5 Hz, H-9), 3.11 (dd, 1H, ^2J=14 Hz, ^3J=10.1 Hz, H-6), 3.08–2.73 (m, 2H, H-7, H-2), 2.67–2.57 (m, 2H, H-7, H-6), 2.45 (s, 3H, CH_3), 2.31–2.22 (m, 1H, H-5), 1.87–1.78 (m, 1H, H-3), 1.76–1.71 (m, 1H, H-4), 1.55–1.38 (m, 2H, H-8), 0.97–0.89 (m, 1H, H-3); ^{13}C NMR (100 MHz) δ 144.78 (C-14′), 141.42 (C-10), 133.22 (C-14), 129.83 (C-13), 127.99 (C-12), 114.55 (C-11), 70.83 (C-9), 55.60 (C-6), 54.37 (C-2), 41.20 (C-7), 39.42 (C-5), 27.53 (C-8), 27.14 (C-4), 24.72 (C-3), 21.65 (CH_3); MS *m/z* 321 (M^+, 8), 280 (4), 226 (1), 166 (6), 150 (19), 137 (12), 136 (100), 123 (2), 108 (3), 91 (20), 81 (9); HRMS calcd for $C_{17}H_{23}NO_3S$: 321.1395, found 321.1398.

3.10. (1S,2R,4S,5R)-2-(p-Methylphenylsulfonylmethyl)-5-ethenyl-1-azabicyclo[2.2.2]octane **4d**

QCD **2** and TsCl were allowed to react according to the general procedure to afford **4d** (79–86%), $[\alpha]_D$=198.6 (*c* 1.35, CH_2Cl_2). IR ($CHCl_3$) ν 2944, 2876, 1636, 1600, 1456, 1400, 1364, 1288, 1232, 1176, 1096, 1056, 976, 936, 920 cm^{-1}; ^1H NMR (400 MHz) δ 7.81 (d, 2H, ^3J=8.3 Hz, H-12, H-12), 7.34 (d, 2H, ^3J=8.3 Hz, H-13, H-13), 5.74 (ddd, 1H, $^3J_{trans}$=17.3 Hz, $^3J_{cis}$=10.5 Hz, ^2J=7 Hz, H-10), 4.98 (ddd, 1H, $^3J_{cis}$=10.5 Hz, ^2J=1.5 Hz, ^4J=1.5 Hz, H-11), 4.95 (ddd, 1H, $^3J_{trans}$=17.1 Hz, ^2J=1.5 Hz, ^4J=1.5 Hz, H-11), 3.99 (dd, 1H, ^3J=7.9 Hz, ^2J=10.1 Hz, H-9), 3.92 (dd, 1H, ^3J=6.4 Hz, ^2J=10.1 Hz, H-9), 3.06–2.75 (m, 4H, H-7, H-7, H-6, H-2), 2.52–2.45 (m, 1H, H-6), 2.42 (s, 3H, CH_3) 2.25–2.16 (m, 1H, H-5), 1.75–1.7 (m, 1H, H-4), 1.59–1.53 (m, 2H, H-8, H-8), 1.53–1.44 (m, 1H, H-3), 1.29–1.2 (m, 1H, H-3); ^{13}C NMR (100 MHz) δ 144.75 (C-14′), 140.02 (C-10), 133.21 (C-14), 129.80 (C-13), 128.00 (C-12), 114.70 (C-11), 70.32 (C-9), 54.33 (C-2), 49.00 (C-6), 47.61 (C-7), 39.48 (C-5), 27.22 (C-4), 26.48 (C-8), 23.99 (C-3), 21.64 (CH_3); MS *m/z* 321 (M^+, 35), 280 (14), 266 (3), 226 (4), 211 (2), 191 (2), 179 (1), 166 (32), 150 (71), 136 (100), 123 (3), 109 (10), 91 (43), 80 (22); HRMS calcd for $C_{17}H_{23}NO_3S$: 321.1395, found 321.1397.

3.11. (1S,2R,4S,5R)-2-(Pivaloyloxymethyl)-5-ethenyl-1-azabicyclo[2.2.2]octane **4e**

QCD **2** and PvCl were allowed to react according to the general procedure to afford **4e** (91%), $[\alpha]_D$=121 (*c* 1.315, CH_2Cl_2). IR ($CHCl_3$) ν 2940 (s), 2872 (m), 1720 (s), 1636 (w), 1480 (m), 1456 (m), 1400 (w), 1364 (w), 1324 (w), 1284 (s), 1232 (m), 1156 (s), 1108 (w), 1080 (w), 1056 (w), 1032 (w), 984 (m), 940 (w), 916 (m), 860 (w), 828 (w) cm^{-1}; ^1H NMR (400 MHz) δ 5.89 (ddddd, 1H, $^3J_{trans}$=15.9 Hz, $^3J_{cis}$=11.2 Hz, ^3J=9.4 Hz, ^4J=1.9 Hz, *J*=7 Hz, H-10), 5.09–5.01 (m, 2H, H-11, H-11), 4.13 (dd, 1H, ^3J=76.8 Hz, ^2J=11 Hz, H-9), 4.07 (dd, 1H, ^3J=7 Hz, ^2J=11 Hz, H-9), 3.06–2.83 (m, 4H, H-7, H-7, H-6, H-2), 2.72 (ddd, 1H, ^2J=14 Hz, *J*=7.9 Hz, *J*=2.4 Hz, H-6), 2.33–2.22 (m, 1H, H-5), 1.81–1.74 (m, 1H, H-4), 1.69–1.51 (m, 3H, H-8, H-8, H-3), 1.47–1.37 (m, 1H, H-3), 1.22 (s, 9H, CH_3); ^{13}C NMR (100 MHz) δ 178.60 (C=O), 140.15 (C-10), 114.77 (C-11), 65.50 (C-9), 54.41 (C-2), 48.97 (C-6), 47.94 (C-

7), 39.74 (C-5), 38.77 ($C(CH_3)_3$), 27.49 (C-4), 27.21 (CH_3), 26.49 (C-8), 24.62 (C-3); MS *m/z* 251 (M^+, 25), 236 (8), 224 (2), 21 (19), 196 (3), 166 (19), 150 (35), 137 (100), 122 (4), 108 (8), 96 (6), 83 (12), 67 (7).

Acknowledgements

We thank Buchler GmbH-Chininfabrik Braunschweig for a generous gift of QCI and QCD and the Graduiertenförderung for support (O. S.).

References

1. Hoffmann, H. M. R.; Plessner, T.; von Riesen, C. *Synlett* **1996**, 690.
2. QCI stands for quin-cor(e)-ine, QCD for quin-cor(e)-idine. In German the syllable *cor* stands for '*C* ohne *R*est' (carbon without residual group) analogous to *nor* (*N* ohne *R*est; e.g. adrenaline and *nor*adrenaline).
3. Available from Buchler GmbH, Harxbütteler Str. 3, D-38110 Braunschweig, Germany (fax: +49 (0) 5307-93131) and from Aldrich-Fluka.
4. For studies on the related 2-hydroxymethyl quinuclidine system see: Prelog, V.; Cerkovnikov, E. *Liebigs Annalen* **1940**, *545*, 259–262.
5. Eggert, U.; Hoffmann, H. M. R., unpublished.
6. Standard acetylation of quinidine using acetic anhydride, DMAP and pyridine as a solvent results in 90% product after 4 days. Furthermore aqueous work-up and column chromatography are necessary for purification: von Riesen, C.; Jones, P. G.; Hoffmann, H. M. R. *Chem. Eur. J.* **1996**, *2*, 673.
7. For the regioselective esterification of a quinine derivative containing an additional, primary hydroxy function see: Waddell, T. G.; Rambalakos, T.; Christie, K. R. *J. Org. Chem.* **1990**, *55*, 4765.
8. Höfle, G.; Steglich, W.; Vorbrüggen, H. *Angew. Chem.* **1978**, *90*, 602; *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 569.