A Tricyclic Dehydrorubanone and New Isomers of the Major Quinidine Metabolite

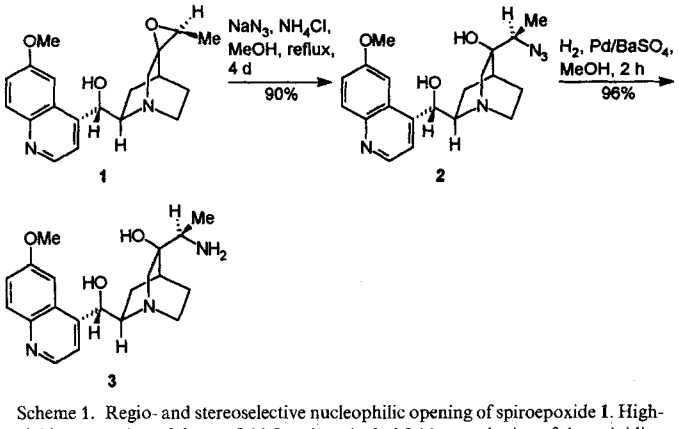
Cornelius von Riesen and H. M. R. Hoffmann*

Abstract: Spiroepoxide **1** was prepared from quinidine and converted into β-amino alcohol **3** (86% over two steps). Dihydroxylation of enantiopure oxazatricylic olefin (*E*)-**4** provided diastereomeric diols **5a** and **5b**. Stereospecific conversion of 1,2-secondary,tertiary diol **5b** into tetracyclic spiroepoxide **6** was accomplished in high yield by a one-pot tosylation–cyclization procedure. 1,2-Diol cleavage with $NaIO_4$ in 80% acetic acid afforded the new tricyclic dehydrorubanone **7**, containing the 4-oxa-7-azatricyclo[4.3.1.$0^{3,7}$]-decan-2-one core structure. Similarly, acetylated rubanone **9** was prepared on a 20 g scale. Reduction with $NaBH_4$ in the presence of $CeCl_3$ provided rubanols **10a** and **10b** (1:1.1). Horner–Wittig reaction of **9** with diethyl cyanomethylphosphonate was (*Z*)-selective, furnishing unsaturated nitrile (*Z*)-**13**. Conversion into the α,β-unsaturated aldehyde (*Z*)-**14** and reduction afforded enantiopure allylic alcohol (*Z*)-**12**, which is a new isomer of the key quinidine metabolite **15**.

Keywords
amino alcohols · asymmetric syntheses · dihydroxylations · diol cleavage
Horner–Wittig reaction

Epoxides are invaluable starting materials for organic synthesis, and enantiopure epoxides have found widespread use as chiral building blocks. In the preceding paper, we have shown that all four possible C(3)C(10) diastereomeric spiroepoxides, derived from quinidine, are readily accessible.[1]

The utility of crystalline spiroepoxide **1**[1] is exemplified by stereospecific conversion into β-amino alcohol **3** (Scheme 1). After the first stage, that is, the regio- and stereoselective nucleophilic opening of epoxide **1**, the resulting azido alcohol **2** was isolated (90%) and stored without decomposition. The azide group serves as a masked amino group. Hydrogenative cleavage of the azide (**2** → **3**) was very clean and allowed us to isolate highly polar bis(amino)diol **3** by simple filtration through a short column. 1,2-Aminodiols are of pharmacological relevance[2] and also as chiral ligands in asymmetric synthesis.[3]



Scheme 1. Regio- and stereoselective nucleophilic opening of spiroepoxide **1**. High-yield preparation of the twofold β-amino alcohol **3** (the numbering of the quinidine skeleton follows cinchona alkaloid convention).

Following previous experience we dihydroxylated crystalline allylic *N,O*-acetal (*E*)-**4**[1] by two methods (Scheme 2). Treatment of configurationally pure olefin (*E*)-**4** according to variant A provided the two diols (**5a**:**5b** = 1:1.9), which were isolated as single diastereomers. Diastereomerically pure 1,2-secondary,tertiary diol **5b** was transformed efficiently (92%) into diastereomerically pure spiroepoxide **6** by a KO*t*Bu-activated monotosylation–cyclization procedure.[1] The absolute configuration of tetracyclic epoxide **6** was derived from the absolute configuration of the 1,2-diol precursor **5b** (NOE on **5a**). Note that the (*E*)-configurated methyl group in the starting olefin (*E*)-**4** is inverted in spiroepoxide **6**; this corresponds to *one* inversion of configuration in the transformation **5b** → **6** (cf. Scheme 7, preceding paper).

In the preparation of dehydrorubanone **7** the configuration of the double bond in the trisubstituted olefinic precursor **4** is necessarily lost. This ketone **7** is prepared conveniently by diol cleavage from a mixture of (*E*)-**4** and (*Z*)-**4**, obtained according to variant B (76% yield vs. 56% by variant A).

Tricyclic dehydrorubanone **7** contains five chiral centres including the bridgehead nitrogen and is a single diastereomer, which is, of course, also enantiomerically pure. It serves as a convenient precursor for further elaboration of this intricate oxazatricyclic framework.

Cleavage of the vicinal diol **8**, which is obtained in four simple stages from quinidine,[1] was expected to yield acetylated rubanone **9**.[4] Treatment of **8** with aqueous $NaIO_4$/ether (1:1) provided the desired ketone **9** and some 6-methoxyquinoline-4-

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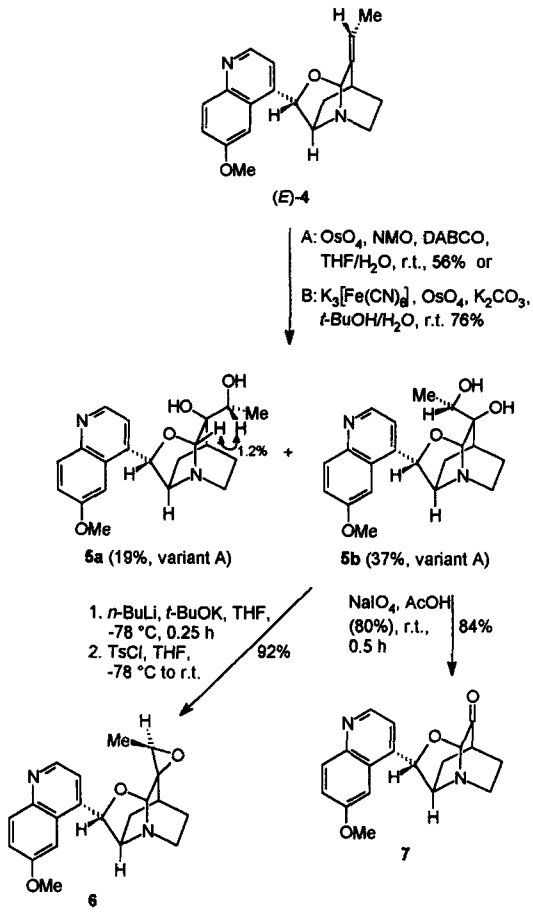
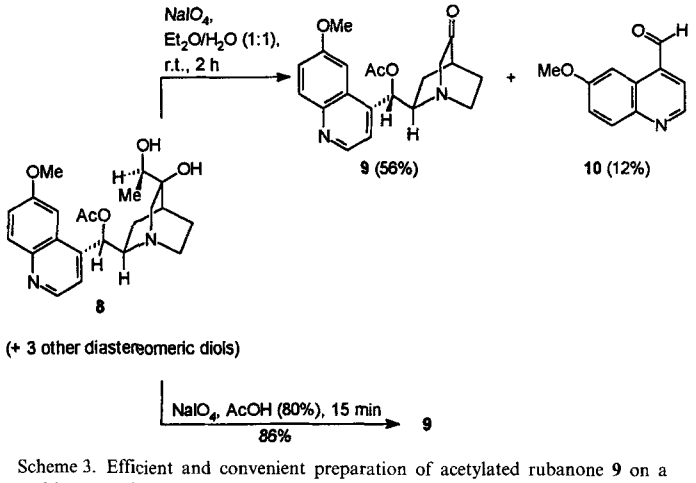


Scheme 2. Four highly functionalized derivatives of oxazatricyclic olefin (*E*)-**4** (DABCO: 1,4-diazabicyclo[2.2.2]octane; NMO: 4-methylmorpholine *N*-oxide).

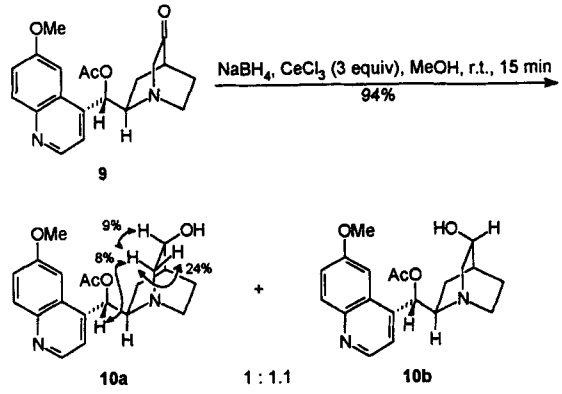
carbaldehyde (**10**) as a by-product. We assume that the acetyl group was partially taken off under the weakly alkaline conditions, furnishing an intermediate β-amino alcohol, which suffered bond cleavage. 1,2-Diol **8** and its three diastereomers were soluble in 80% acetic acid, and acetylated rubanone **9** was prepared in 86% isolated yield on a 20 g scale in this solvent (Scheme 3).

In the context of the DABCO-catalysed reaction of aldehydes with Michael acceptors,[5] we were interested in preparing β-amino alcohols and derivatives of quinidinols, which might be



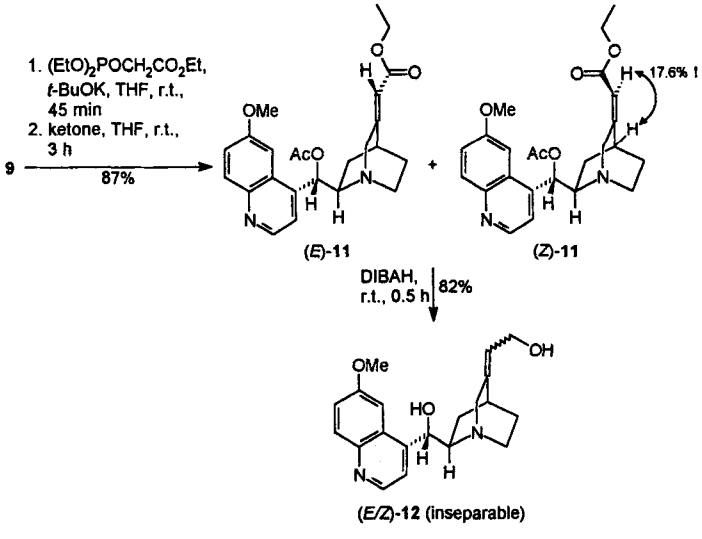
Scheme 3. Efficient and convenient preparation of acetylated rubanone **9** on a multigram scale.

used in an asymmetric variant of the coupling procedure. Reduction of rubanone **9** with $NaBH_4$ was effective, provided that $CeCl_3$ was added. In this way the acetoxy group remained intact, and the diastereomeric rubanols **10a** and **10b** were formed in excellent chemical yield (Scheme 4). Less polar diastereomer **10a** was assigned by NOE as well as CH-COSY and HH-COSY.



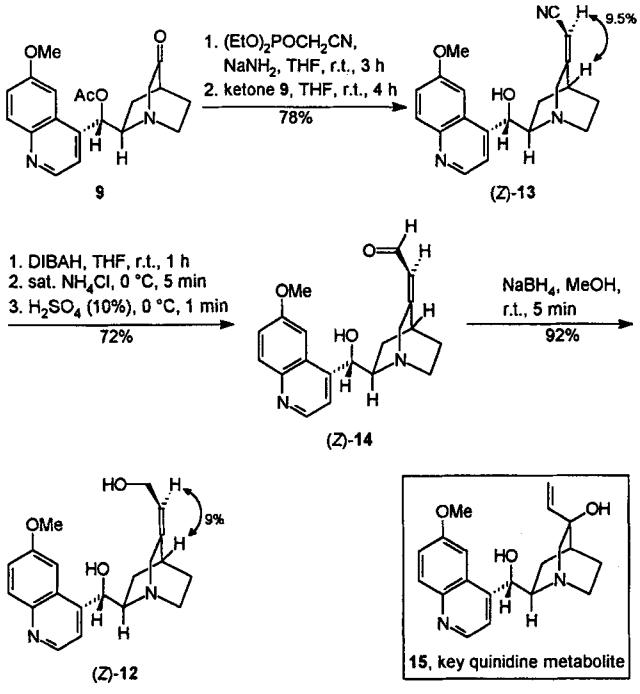
Scheme 4. Diastereomeric rubanols **10a** and **10b** from **9**.

In order to prepare various quinidine metabolites we studied olefination reactions of rubanone (**9**). The Horner reaction afforded the expected olefin **11** as a mixture of (*E*/*Z*) isomers, which were separated on an analytical scale, but were difficult to separate on a preparative scale. Nonetheless, the olefinic configuration was clearly established by NOE. Reduction of the (*E*/*Z*)-**11** mixture with DIBAH gave the allylic alcohols (*E*/*Z*)-**12** in good yield, but again inseparable by chromatography (Scheme 5).



Scheme 5. Horner–Wittig reactions of acetylated rubanone **9** (DIBAH: diisobutylaluminium hydride).

A change of Horner reagent to cyanomethyl diethoxyphosphonate provided a *stereoselective* olefination, giving (*Z*)-configurated cyanomethylidene rubane (*Z*)-**13**. Chemoselective reduction with DIBAH required a large excess of reagent (8 equiv). Standard acidic workup afforded the α,β-unsaturated aldehyde (*Z*)-**14**, which was reduced to the (*Z*)-configurated allylic alcohol (*Z*)-**12**. α,β-Unsaturated nitrile (*Z*)-**13** and unsat-



Scheme 6. (*Z*)-Selective Horner–Wittig reaction of **9**. Synthesis of (*Z*)-configurated allylic alcohol (*Z*)-**12**, isomer of the key quinidine metabolite **15**.

urated aldehyde (*Z*)-**14** were therefore configurationally stable under our conditions. Allylic alcohol (*Z*)-**12** is a double-bond isomer of tertiary allylic alcohol **15**, which is the major quinidine metabolite.[6]

Conclusions

In this and the preceding paper we have harnessed some of the potential of cinchona alkaloids for chemo- and stereoselective transformations. Starting from quinidine, all four diastereomeric 1,2-diols (Scheme 3) of ethylidene rubane have been cleaved to give ketone **9**. Thus, not even a single diastereomeric separation is necessary during this efficient five-step sequence to rubanone **9**. Thanks to a (*Z*)-selective Horner–Wittig reaction, no diastereomeric separation is required in the preparation of (*Z*)-configurated allylic alcohol (*Z*)-**12**, and its unsaturated precursors (*Z*)-**13** and (*Z*)-**14**, which are also Michael acceptors. A range of functionalized tricyclic rubanones, containing the 4-oxa-7-azatricyclo[4.3.1.$0^{3,7}$]decan-2-one framework, have been synthesized for the first time. The five-membered *N,O*-acetal structure occurs also in quinocarcin, an antitumor antibiotic.[6] The various compounds prepared are of interest in their own right and serve as intermediates for further elaboration. Allylic alcohol **12**, like spiroepoxide **1**, is a structural isomer of the important, pharmacologically active metabolite **15** of quinidine.[7]

Experimental Procedure

General Remarks: The numbering of the quinidine skeleton follows the cinchonane/rubane convention for cinchona alkaloids. Melting points: Büchi apparatus, not corrected. Infrared spectra: Perkin–Elmer 1710 spectrometer. ^{1}H NMR spectra: Bruker WH 90, WP 200 SY or AM 300 spectrometer. Chemical shifts are reported in δ values relative to tetramethylsilane (TMS) as internal standard. ^{13}C NMR spectra: Bruker WP 200 SY or a Bruker AM 300. Chemical shifts are reported in δ values relative to TMS. APT (attached proton test): spin echo-based selection of multiplicities of ^{13}C signals. Quaternary C and CH_2 carbon atoms give positive signals (+), while CH and CH_3 give negative signals (−). Low- and high-resolution electron-impact mass spectra: Finnigan MAT 312 spectrometer with an ionization potential of 70 eV at room temperature, unless stated otherwise. 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 aluminium-backed 0.2 mm silica gel 60 F_{254} plates (E. Merck). E (ethyl ether). MTBE (methyl *t*-butyl ether). The preparation of **1**, (*E*)-**4** and **8** was described in the preceding paper.

(3*R*,8*R*,9*S*,10*R*)-10-Azido-10,11-dihydro-3-hydroxy-6′-methoxycinchonan-9-ol (2): A solution of **1** (340 mg, 1 mmol), NaN_3 (163 mg, 2.5 mmol) and NH_4Cl (96 mg, 1.8 mmol) in MeOH (4 mL) was heated to reflux for 4 d. The solvent was removed and the crude product purified by chromatography (MTBE/MeOH) to give **2**, 345 mg (90%), m.p. (decomp.). $[\alpha]_D^{20} = +37.1°$ (c = 1.12 in MeOH). IR (KBr): $\tilde{\nu}$ = 1244, 1471, 1511, 1591, 1622, 2112, 2942, 3418 cm^{-1}. ^{1}H NMR (200 MHz, CD_3OD): δ = 1.13–1.30 (m, 1H), 1.52 (m, 2H), 2.38 (m, 1H), 1.35 (d, J = 6 Hz, 3H; H-11), 1.90 (m, 1H; H-4), 2.74 (m, 2H; H-6), 2.92 (d, J = 15 Hz, 1H; H-2_{exo}), 3.13 (m, 1H; H-8), 3.47 (q, J = 6 Hz, 1H; H-10), 3.51 (d, J = 15 Hz, 1H; H-2_{endo}), 3.98 (s, 3H; H-11′), 5.68 (d, J = 4 Hz, 1H; H-9), 7.31 (dd, J = 2, 9 Hz, 1H; H-7′), 7.43 (d, J = 2 Hz, 1H; H-5′), 7.69 (d, J = 4 Hz, 1H; H-3′), 7.95 (d, J = 9 Hz, 1H, H-8′), 8.67 (d, J = 4 Hz, 1H; H-2′). ^{13}C NMR (50 MHz, APT, CD_3OD): δ = 12.73 (−, C-11), 22.08, 22.63 (+, C-7, C-5), 32.07 (−, C-4), 50.48, 58.45 (+, C-2, C-6), 56.44 (−, C-11′), 59.99 (−, C-8), 63.48 (−, C-10), 72.35 (−, C-9), 74.07 (+, C-3), 102.38 (−, C-5′), 119.94 (−, C-3′), 123.38 (−, C-7′), 128.07 (+, C-9′), 131.34 (−, C-8′), 144.73, 149.93 (+, C-4′, C-10′), 148.12 (−, C-2′), 159.63 (+, C-6′). MS-MAT (170 °C): m/z (%): 383 (8) [M^+], 355 (2), 341 (100), 323 (22), 312 (9), 284 (35), 269 (17), 243 (12), 213 (17), 202 (22), 186 (24), 172 (95), 152 (49). HRMS calcd for $C_{20}H_{25}N_5O_3$: 383.1957, found 383.1951.

(3*R*,8*R*,9*S*,10*R*)-10-Amino-10,11-dihydro-3-hydroxy-6′-methoxycinchonan-9-ol (3): A suspension of **2** (130 mg, 0.34 mmol) and catalyst (Pd/$BaSO_4$, 5%, 10 mg) in MeOH (3 mL) was hydrogenated for 2 h at normal pressure. The extremely polar product was filtered through a very short column (MeOH) to remove the catalyst. Compound **3** was isolated in nearly quantitative yield as a white solid. Yield: 116 mg (96%), m.p. 130 °C. $[\alpha]_D^{20} = +117.1$ (c = 1.05 in MeOH). IR (KBr): $\tilde{\nu}$ = 1029, 1229, 1242, 1434, 1472, 1510, 1592, 1622, 2520, 2877, 2942, 3388 cm^{-1}. ^{1}H NMR (200 MHz, CD_3OD): δ = 1.17 (m, 1H), 1.53 (m, 2H), 2.36 (1H), 1.13 (d, J = 6 Hz, 3H, H-11), 1.92 (m, 1H; H-4), 2.70–3.2 (m, 3H, H-6, H-8), 2.97 (d, J = 15 Hz, 1H, H-2_{exo}), 3.08 (q, J = Hz, 1H; H-10), 3.54 (d, J = 15 Hz, 1H; H-2_{endo}), 3.98 (s, 3H; H-11′), 5.72 (d, J = 3 Hz, 1H; H-9), 7.36 (dd, J = 2, 9 Hz, 1H; H-7′), 7.39 (d, J = 2 Hz, 1H; H-5′), 7.71 (d, J = 4 Hz, 1H; H-3′), 7.93 (d, J = 9 Hz, 1H; H-8′), 8.68 (d, J = 4 Hz, 1H; H-2′). ^{13}C NMR (50 MHz, APT, CD_3OD): δ = 17.30 (−, C-11), 21.78, 22.50 (+, C-7, C-5), 31.96 (−, C-4), 50.63, 58.66 (+, C-6, C-2), 53.87 (−, C-10), 56.49 (−, C-11′), 59.75 (−, C-8), 72.35 (−, C-9), 72.55 (+, C-3), 102.32 (−, C-5′), 119.82 (−, C-3′), 123.40 (−, C-7′), 127.97 (+, C-9′), 131.37 (−, C-8′), 144.71, 149.89 (+, C-4′, C-10′), 148.12 (−, C-2′), 159.695 (+, C-6′). MS-MAT (80 °C): m/z (%): 357 (2) [M^+], 339 (4), 313 (4), 296 (5), 286 (31), 270 (32), 254 (2), 238 (3), 213 (4), 199 (5), 189 (18), 169 (68), 152 (25), 127 (20), 109 (12), 96 (100). HRMS calcd for $C_{20}H_{27}N_3O_3$: 357.2052, found 357.2058.

(2*R*,3*S*,8*R*,9*S*,10*R*)-10,11-Dihydro-3,10-dihydroxy-2,9-epoxy-6′-methoxycinchonane (5a) and (2*R*,3*R*,8*R*, 9*S*,10*S*)-10,11-Dihydro-3,10-dihydroxy-2,9-epoxy-6′-methoxycinchonane (5b): **Variant A**: To a solution of (*E*)-**4** (527 mg, 1.64 mmol), DABCO (551 mg, 4.92 mmol) and an aqueous solution of NMO (1.6 mL, 8.2 mmol, 60%) in THF/H_2O (4:1, 25 mL) was added OsO_4 (0.5 mL, 0.05 mmol, 0.1 M solution in *t*BuOH). After having been stirred for 7 d at RT, the mixture was diluted with $CHCl_3$ and extracted with sat. aq. $NaHSO_3$/NaCl (1:1). The organic layer was dried ($MgSO_4$), the solvent evaporated and the crude product purified by column chromatography (MTBE/MeOH, 15:1, increasing polarity during separation) to afford **5b** (190 mg, 37%), followed by **5a** (140 mg, 19%, contaminated with ≈20% **5b**), (**5a**: **5b** = 1:1.9, isolated yield).

Variant B: To a two-phase sytem of K_2CO_3 (1.17 g, 8.47 mmol), $K_3[Fe(CN)_6]$ (2.67 g, 8.11 mmol) and (*E*/*Z*)-**4** (1.15 g, 3.57mmol) in *t*BuOH/H_2O (1:1) (40 mL) was added OsO_4 (0.36 mL, 0.036 mmol, 0.1 M solution in *t*BuOH). The mixture was stirred for 7 d at RT, a further portion of catalyst (0.72 mL, 0.072 mmol) added and the mixture stirred for further 3 d. Workup as described for variant A afforded a mixture of four diols, 965 mg (76%).

Data for **5a**: IR (KBr): $\tilde{\nu}$ = 1230, 1243, 1265, 1511, 1594, 1622, 2878, 2940, 3430 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3/CD_3OD$): δ = 1.07–1.7 (m, 4H; H-5, H-7), 1.29 (d, J = 6 Hz, 3H; H-11), 1.65 (m, 1H; H-4), 2.98–3.34 (m, 2H; H-6), 3.75 (q, J = 6 Hz, 1H; H-10), 3.96 (m, 1H; H-8), 3.98 (s, 3H; H-11′), 5.03 (s, 1H; H-2), 5.72 (d, J = 4 Hz, 1H; H-9), 7.17 (d, J = 4 Hz, 1H; H-5′), 7.43 (dd, J = 2, 9 Hz, 1H; H-7′), 7.88 (d, J = 4 Hz, 1H; H-3′), 8.05 (d, J = 9 Hz, 1H; H-8′), 8.74 (d, J = 4 Hz, 1H; H-2′). NOE: H-2 with H-10 (1.20). ^{13}C NMR (50 MHz, APT, $CDCl_3/CD_3OD$): δ = 17.46 (−, C-11), 22.59 (+, C-7), 23.27 (+, C-5), 28.12 (−, C-4), 38.15 (+, C-6), 55.08, 55.44 (−, C-11′, C-8), 68.77 (−, C-10), 74.27 (+, C-3), 79.86 (−, C-9), 89.27 (−, C-2), 101.13 (−, C-5′), 119.18 (−, C-3′), 121.56 (−, C-7′), 126.17 (+, C-9′), 130.69 (−, C-8′), 141.63, 143.19 (+, C-4′, C-10′), 147.05

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(–, C-2'), 157.87 (+, C-6'). MS-MAT: *m/z* (%): 356 (13) [M^+], 339 (11), 310 (7), 283 (9), 267 (1), 246 (7), 228 (3), 198 (8), 184 (11), 173 (23), 160 (3), 140 (13). HRMS calcd for $C_{20}H_{24}N_2O_4$: 356.1736, found 356.1731.

Data for **5b**: m.p. 183 °C (decomp.). $[\alpha]_D^{20} = +246.3$ ($c = 0.415$ in $CHCl_3$/MeOH, 9:1). IR (KBr): $\tilde{\nu}$ = 1230, 1511, 1595, 1621, 2872, 2938, 3430 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3/CD_3OD$): δ = 0.92 (m, 1H), 1.13–1.30 (m, 2H), 2.0 (m, 1H), 1.19 (d, J = 6 Hz, 3H; H-11), 1.68 (m, 1H; H-4), 3.22 (m, 2H; H-6), 3.98 (s, 3H; H-11'), 4.47 (q, J = 6 Hz, 1H; H-10), 4.78 (d, J = 1 Hz, 1H; H-2), 5.62 (d, J = 4 Hz, 1H; H-9), 7.17 (d, J = 2 Hz, 1H; H-5'), 7.43 (dd, J = 2, 9 Hz, 1H; H-7'), 7.67 (d, J = 4 Hz, 1H; H-3'), 8.03 (d, J = 9 Hz, 1H; H-8'), 8.75 (d, J = 4 Hz, 1H; H-2'). ^{13}C NMR (50 MHz, APT, $CDCl_3/CD_3OD$): δ = 16.08 (–, C-11), 22.38 (+, C-7), 23.02 (+, C-5), 26.40 (–, C-4), 38.94 (+, C-6), 54.86 (–) 55.79 (–, C-11', C-8), 67.16 (–, C-10), 76.42 (+, C-3), 79.96 (–, C-9), 94.55 (–, C-2), 101.66 (–, C-5'), 119.25 (–, C-3'), 122.03 (–, C-7'), 126.46 (+, C-9'), 131.14 (–, C-8'), 142.17, 143.50 (+, C-4', C-10'), 147.35 (–, C-2'), 158.28 (+, C-6'). MS-MAT (190 °C): *m/z* (%): 356 (12) [M^+], 338 (14), 310 (2), 279 (7), 197 (11), 184 (17), 167 (35), 149 (100), 140 (22). HRMS calcd for $C_{20}H_{24}N_2O_4$: 356.1736, found 356.1730. $C_{20}H_{24}N_2O_4$: C 67.38, H 6.79, N 7.86; found C 67.39, H 6.78, N 7.84.

(2*R*,3*R*,8*R*,9*S*,10*R*)-10,11-Dihydro-2,9-epoxy-3,10-epoxy-6'-methoxycinchonane (6): To a solution of **5b** (120 mg, 0.337 mmol) and *t*BuOK (75.6 mg, 0.674 mmol) in anhydrous THF (8 mL) was added *n*BuLi (0.42 mL, 0.674 mmol, 1.6 M solution in hexane) at –78 °C, followed by tosyl chloride (128.5 mg, 0.674 mmol) in anhydrous THF (2 mL) after 15 min. The mixture was warmed up slowly to RT and then quenched with H_2O. The aqueous layer was extracted with $CHCl_3$ and the organic layer dried ($MgSO_4$) and evaporated. The crude product was purified by column chromatography (MTBE/MeOH) to yield **6**, 105 mg (92%), m.p. 55 °C. $[\alpha]_D^{20} = +279.2$ (c = 0.47, CH_2Cl_2). IR ($CHCl_3$): $\tilde{\nu}$ = 1224, 1472, 1508, 1620, 1672, 2836, 2876, 2944, 3008 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.22–1.48 (m, 3H), 1.94 (m, 1H), 1.28 (m, 1H; H-4), 1.67 (d, J = 6 Hz, 3H; H-11), 3.15 (q, J = 6 Hz, 1H; H-10), 3.23 (m, 2H; H-6), 3.97 (s, 3H; H-11), 4.07 (m, 1H; H-8), 4.80 (s, 1H; H-2), 5.78 (d, J = 4 Hz, 1H; H-9), 7.13 (d, J = 2 Hz, 1H; H-5'), 7.41 (dd, J = 2, 9 Hz, 1H; H-7'), 7.55 (d, J = 4 Hz, 1H; H-3'), 8.08 (d, J = 9 Hz, 1H; H-8'), 8.83 (d, J = 4 Hz, 1H; H-2'). ^{13}C NMR (50 MHz, APT, $CDCl_3$): δ = 16.02 (–, C-11), 23.37 (+, C-7), 23.46 (+, C-5), 27.05 (–, C-4), 38.37 (+, C-6), 55.12, 55.73 (–, C-11', C-8), 60.27 (–, C-10), 65.60 (+, C-3), 79.62 (–, C-9), 92.29 (–, C-2), 100.89 (–, C-5'), 119.30 (–, C-3'), 121.76 (–, C-7'), 126.33 (+, C-9'), 131.75 (–, C-8'), 142.06, 143.91 (+, C-4'C10'), 147.55 (–, C-2'), 157.98 (+, C-6'). MS (GC-MS): *m/z* (%): 338 (12) [M^+], 281 (8), 266 (12), 253 (12), 236 (11), 210 (14), 200 (12), 196 (10), 184 (21), 183 (12), 172 (100), 166 (16). HRMS calcd for $C_{20}H_{22}N_2O_3$: 338.1630, found 338.1639.

(2*R*,8*R*,9*S*)-2,9-Epoxy-6'-methoxyruban-3-one (7): To a solution of **5a,b** (550 mg, 1.5 mmol) in acetic acid (15 mL, 80%) was added $NaIO_4$ (396 mg, 1.85 mmol). The mixture was stirred for 0.5 h at RT, and most of the solvent was removed. The residue was diluted with H_2O, neutralized with $NaHCO_3$ and extracted with $CHCl_3$. After drying ($MgSO_4$) and purification by chromatography (MTBE/MeOH, 30:1) **7** was obtained. Yield: 403 mg (84%), m.p. 190 °C (decomp.). $[\alpha]_D^{20} = +220.3$ (c = 0.65 in CH_2Cl_2). IR (KBr): 1020, 1057, 1080, 1094, 1121, 1148, 1230, 1264, 1433, 1472, 1510, 1621, 1743, 2943 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.25 (m, 1H), 1.59 (ddd, J = 1.5, 8, 14 Hz, 1H), 2.07 (m, 2H), 2.28 (m, 1H), 3.27 (m, 2H; H-6), 3.96 (s, 3H; H-11'), 4.27 (m, 1H; H-8), 4.73 (s, 1H; H-2), 5.91 (d, J = 4 Hz, 1H; H-9), 7.07 (d, J = 2 Hz, 1H; H-5'), 7.39 (dd, J = 2, 9 Hz, 1H; H-7'), 7.43 (d, J = 4 Hz, 1H; H-3'), 8.07 (d, J = 9 Hz, 1H; H-8'), 8.77 (d, J = 4 Hz, 1H; H-2'). ^{13}C NMR (50 MHz, APT, $CDCl_3$): δ = 22.14 (+, C-7), 29.62 (+, C-5), 35.88 (–, C-4), 37.13 (+, C-6), 55.37, 55.65 (–, C-11', C-8), 80.09 (–, C-9), 89.71 (–, C-2), 100.87 (–, C-5'), 119.21 (–, C-3'), 121.47 (–, C-7'), 125.99 (+, C-9'), 131.89 (–, C-8'), 141.13, 143.91 (–, C-4', C-10'), 147.94 (–, C-2'), 157.97 (+, C-6'), 213.39 (+, C-3). MS-MAT (140 °C): *m/z* (%): 282 (100), 267 (4), 241 (6), 224 (17), 210 (100), 196 (13), 184 (47), 183 (53), 169 (10), 141 (6). FAB-MS: *m/z* (%): 311 (57) [$M^+ + 1$], 282 (23), 243 (100), 210 (13). HRMS calcd for $C_{18}H_{18}N_2O_3$: 310.1317, found 310.1317.

(8*R*,9*S*)-9-Acetoxy-6'-methoxyruban-3-one (9) and 6-Methoxychinolin-4-carbaldehyde (10): **Variant A**: To a solution of **8** (15.4 g, 38.5 mmol) in acetic acid (250 mL, 80%) was added $NaIO_4$ (9.88 g, 46.2 mmol). The mixture was stirred for 15 min at RT, the solvent removed and the residue diluted with H_2O. After neutralization ($NaHCO_3$) the aqueous phase was extracted with $CHCl_3$. The organic layer was dried ($MgSO_4$), evaporated and chromatographed (MTBE/MeOH, 30:1) to afford **9**, 11.7 g (86%).

Variant B. To a solution of **8** (312 mg, 0.78 mmol) in Et_2O/H_2O (1:1) (10 mL) was added $NaIO_4$ (250 mg, 1.17 mmol) in portions. The mixture was stirred for 2 h at RT and then extracted with $CHCl_3$. The organic layer was dried ($MgSO_4$) and, after removal of the solvent, purified by column chromatography (MTBE → MTBE/MeOH) to give aldehyde **10** (17.5 mg, 12%) followed by **9** (155 mg, 56%).

Data for **9**: m.p. 167 °C. $[\alpha]_D^{20} = +57.7$ (c = 1.005 in $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 1232, 1308, 1372, 1432, 1456, 1472, 1508, 1592, 1620, 1736, 2884, 2960 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.90–2.29 (m, 4H; H-5, H-7), 2.17 (s, 3H; H-11), 2.56 (m, 1H; H-4), 3.78–3.07 (m, 2H; H-6), 3.15 (d, J = 21 Hz, 1H; H-2_{exo}), 3.48 (m, 1H; H-8), 3.67 (d, J = 21 Hz, 1H; H-2_{endo}), 3.98 (s, 3H; H-11'), 6.56 (d, J = 6 Hz, 1H; H-9), 7.29 (d, J = 4 Hz, 1H; H-3'), 7.32 (d, J = 2 Hz, 1H; H-5'), 7.41 (dd, J = 2, 9 Hz, 1H; H-7'), 8.05 (d, J = 9 Hz, 1H; H-8'), 8.74 (d, J = 4 Hz, 1H; H-2'). ^{13}C NMR (50 MHz, APT, $CDCl_3$): δ = 20.98 (–, C-11), 24.59, 26.94 (+, C-7, C-5), 40.39 (–, C-4), 50.12 (+, C-6), 55.64(–, C-11'), 57.91 (–, C-8), 58.52 (+, C-2), 73.60 (–, C-9), 101.04 (–, C-5'), 117.92 (–, C-3'), 121.96 (–, C-7'), 126.46 (+, C-9'), 131.82 (–, C-8'), 143.03, 144.53 (+, C-4', C-10'), 147.30 (–, C-2'), 158.41 (+, C-6'), 169.62 (+, C-10), 218.42 (+, C-3). MS-MAT (120 °C): *m/z* (%): 354 (53) [M^+], 326 (91), 310 (43), 283 (24), 267 (100), 253 (31), 243 (27), 227 (21), 210 (16), 200 (26), 186 (21), 172 (89), 154 (13). HRMS calcd for $C_{20}H_{22}N_2O_4$: 354.1580, found 354.1576. $C_{20}H_{22}N_2O_4$: C 67.77, H 6.26, N 7.91; found C 67.76, H 6.30, N 7.90.

Data for **10**: IR ($CHCl_3$): $\tilde{\nu}$ = 1076, 1132, 1172, 1240, 1264, 1296, 1352, 1432, 1476, 1504, 1584, 1620, 1700, 2748, 2852, 2932, 2964, 3216 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 4.01 (s, 3H; OMe), 7.47 (dd, J = 2, 9 Hz, 1H; H-7), 7.77 (d, J = 4 Hz, 1H; H-3), 8.11 (d, J = 9 Hz, 1H; H-8), 8.48 (d, J = 2 Hz, H-5), 9.04 (d, J = 4 Hz, 1H; H-2), 10.43 (s, 1H; H-11). ^{13}C NMR (50 MHz, BB, $CDCl_3$): δ = 55.78 (OMe), 102.51 (C-5'), 123.16 (C-7), 125.32 (C-9), 127.18 (C-3), 131.39 (C-8), 135.34 (C-4), 145.89 (C-10), 147.47 (C-2), 160.61 (C-6), 193.46 (C-11). MS-MAT: *m/z* (%): 187 (100) [M^+], 172 (3), 167 (1), 159 (58), 158 (20), 149 (6), 144 (16), 129 (30), 116 (59), 101 (12), 89 (33).

(3*S*,8*R*,9*S*)-9-Acetoxy-3-hydroxy-6'-methoxyrubane (10a, 10b): To a solution of ketone **9** (500 mg, 1.4 mmol) in anhydrous MeOH (12 mL) was added $CeCl_3 \cdot 7H_2O$ (1.56 g, 4.2 mmol) followed by $NaBH_4$ (106 mg, 2.8 mmol) at RT. After 15 min the mixture was carefully treated with H_2O (≈10 mL) and extracted with $CHCl_3$. The organic layer was dried ($MgSO_4$). Chromatography (MTBE/MeOH) afforded pure, unpolar **10a**, whereas polar **10b** is contaminated with diastereomer **10a** (**10a**/**10b** = 1:1.1, ^1H NMR). Yield: **10a,b**, 472 mg (94%).

Data for **10a**: m.p. 88 °C. $[\alpha]_D^{20} = +42.4$ (c = 1.005 in CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 987, 1033, 1083, 1231, 1306, 1371, 1434, 1475, 1510, 1593, 1622, 1746, 2937, 3426 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.25 (m, 1H; H-5), 1.51 (m, 1H; H-7), 1.65 (m, 1H; H-7), 1.88 (m, 2H; H-4, H-5), 2.09 (s, 3H; H-11), 2.53 (d, J = 15 Hz, 1H H-2_{exo}), 2.74 (m, 1H; H-6), 2.88 (m, 1H; H-6), 3.27 (m, 1H; H-8), 3.39 (dd, J = 7.5, 15 Hz, 1H; H-2_{endo}), 3.90 (d, J = 7.5 Hz, 1H; H-3), 3.91 (s, 3H; H-11'), 4.90 (brs, 1H; OH), 6.43 (d, J = 6 Hz, 1H; H-9), 7.28 (d, J = 4 Hz, 1H; H-3'), 7.30 (dd, J = 2, 9 Hz, 1H; H-7'), 7.38 (d, J = 2 Hz, 1H; H-5'), 7.98 (d, J = 9 Hz, 1H; H-8'), 8.67 (d, J = 4 Hz, 1H; H-2'). NOE: H-2_{endo} with H-2_{exo} (24.44), 1H; H-3 (9.20), 1H; H-9 (8.33). ^{13}C NMR (75 MHz, DEPT, $CDCl_3$): δ = 17.89 (2°, C-5), 20.94 (1°, C-11), 26.49 (2°, C-7), 28.94 (3°, C-4), 50.21 (2°, C-6), 53.83 (2°, C-2), 55.65 (1°, C-11'), 57.40 (3°, C-8), 67.24 (3°, C-3), 73.47 (3°, C-9), 101.30 (3°, C-5'), 118.30 (3°, C-3'), 121.98 (3°, C-7'), 126.73 (4°, C-9'), 131.33 (3°, C-8'), 143.52, 144.32 (4°, C-4', C-10'), 146.99 (3°, C-2'), 158.02 (4°, C-6'), 169.72 (4°, C-10). MS-MAT: *m/z* (%): 356 (38) [M^+], 341 (12), 312 (16), 297 (33), 281 (11), 269 (12), 267 (13), 253 (14), 231 (16), 211 (15), 198 (17), 189 (55), 160 (46), 141 (18), 126 (56). HRMS calcd for $C_{20}H_{24}N_2O_4$: 356.1736, found 356.1738.

(8*R*,9*S*)-9-Acetoxy-(*Z*)-3-ethoxycarbonylmethylidene-6'-methoxy-rubane [(*Z*)-11] and (8*R*,9*S*)-9-Acetoxy-(*E*)-3-ethoxycarbonylmethylidene-6'-methoxyrubane [(*E*)-11]: To a solution of KO*t*Bu (712 mg, 6.3 mmol) in anhydrous THF (15 mL) was added triethylphosphonoacetate (1.27 mL, 6.3 mmol) dropwise under N_2. The mixture was stirred for 45 min at RT, and then a solution of **9** (1.5 g, 4.2 mmol) in anhydrous THF (15 mL) was added. The resulting mixture was stirred for further 3 h at RT. After addition of H_2O the aqueous phase was extracted with $CHCl_3$, and the orgnanic layer was dried ($MgSO_4$) and evaporated. Purification by chromatography (E/MeOH, 30:1) afforded pure, unpolar (*Z*)-**11**, whereas polar (*E*)-**11** is contaminated (*Z*)-olefin, [(*Z*)-**11**/(*E*)-**11** = 1.3:1, ^1H NMR]. Yield: (*E*/*Z*)-**11**, 1.56 g (87%).

Data for (*Z*)-**11**: m.p. 66 °C. $[\alpha]_D^{20} = +16.7$ (c = 0.985 in CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 1229, 1374, 1510, 1704, 1746, 2939 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.30 (t, J = 7.5 Hz, 3H; H-13), 1.66–1.96 (m, 4H; H-5, H-7), 2.11 (s, 3H; H-15), 2.58 (m, 1H; H-4), 2.68–2.93 (m, 2H; H-6), 3.47 (m, 1H; H-8), 3.80 (d, J = 20 Hz, 1H; H-2_{exo}), 3.99 (s, 3H; H-11), 4.17 (q, J = 7.5 Hz, 2H; H-12), 4.25 (d, J = 20 Hz, 1H; H-2_{endo}), 5.73 (t, J = 1 Hz, 1H; H-10), 6.48 (d, J = 6 Hz, 1H; H-9), 7.32–7.43 (m, 3H; H-5', H-7', H-3'), 8.03 (d, J = 9 Hz, 1H; H-8'), 8.73 (d, J = 4 Hz, 1H; H-2'). NOE: H-4 with H-5, H-7 (11.15), H-10 (17.60). ^{13}C NMR (75 MHz, APT, $CDCl_3$): δ = 14.37 (–, C-13), 20.92 (–, C-15), 26.08 (+, C-7), 29.36 (+, C-5), 34.41 (–, C-4), 50.42, 52.02 (+, C-2, C-6), 55.64 (–, C-11), 58.69 (–, C-8), 59.75 (+, C-12), 73.72 (–, C-9), 101.16 (–, C-5'), 112.25 (–, C-10), 118.41 (–, C-3'), 121.99 (–, C-7'), 126.83 (+, C-9'), 131.81 (–, C-8'), 143.50, 144.68 (+, C-4', C-10'), 147.36 (–, C-2'), 158.03 (+, C-6'), 166.48, 168.18, 169.80 (+, C-3, C-11, C-14). MS-MAT (150 °C): *m/z* (%): 424 (16) [M^+], 409 (14), 379 (13), 365 (100), 335 (18), 319 (10), 291 (52), 258 (17), 231 (30), 188 (67), 173 (30). HRMS calcd for $C_{24}H_{28}N_2O_5$: 424.1998, found 424.2002. $C_{24}H_{28}N_2O_5$: C 67.89, H 6.65, N 6.60; found C 67.60, H 6.81, N 6.42.

Data for (*E*)-**11**: ^1H NMR (200 MHz, $CDCl_3$): δ = 1.28 (t, J = 7.5 Hz, 3H; H-13), 1.63–1.92 (m, 4H; H-5, H-7), 2.12 (s, 3H; H-15), 2.62–2.98 (m, 3H; H-6, H-4), 3.28 (d, J = 20 Hz, 1H; H-2_{exo}), 3.43 (m, 1H; H-8), 3.97 (s, 3H; H-11'), 4.03 (d, J = 20 Hz, 1H; H-2_{endo}), 4.18 (q, J = 7.5 Hz, 2H; H-12), 5.68 ("t", J = 1 Hz, 1H;

H-10), 6.47 (d, $J = 6$ Hz, 1H; H-9), 7.3–7.42 (m, 3H; H-5′, H-7′, H-3′), 8.02 (d, $J = 9$ Hz, 1H; H-8′), 8.73 (d, $J = 4$ Hz, 1H; H-2′). ^{13}C NMR (50 MHz, APT, $CDCl_3$): $\delta = 14.31$ (−, C-13), 21.04 (−, C-15), 25.68 (+, C-7), 27.21 (−, C-4), 27.60 (+, C-5), 50.53, 52.09 (+, C-2, C-6), 55.67 (−, C-11′), 58.57 (−, C-8), 59.78 (+ C12), 73.69 (−, C-9), 101.30 (−, C-5′), 110.94 (−, C-10), 118.57 (−, C-3′), 121.91 (−, C-7′), 126.82 (+, C-9′), 131.80 (−, C-8′), 143.37, 144.63 (+, C-4′, C-10′), 147.36 (−, C-2′), 158.07 (+, C-6′), 165.95, 166.27, 169.88 (+, C-3, C-11, C-14).

(8*R*,9*S*)-(*Z*)-3-Cyanomethylidene-6′-methoxyruban-9-ol [(*Z*)-**13**]: To a solution of $NaNH_2$ (525 mg, 13.5 mmol) in anhydrous THF (15 mL) was added diethylcyanomethylphosphonate (2.2 mL, 13.5 mmol) in anhydrous THF (15 mL) under N_2, and the mixture was stirred for 3 h at RT. A solution of **9** (1.2 g, 3.37 mmol) in anhydrous THF (15 mL) was added and stirring continued for 4 h. H_2O was added, and the aqueous phase was extracted with $CHCl_3$. The organic layer was dried ($MgSO_4$), freed from solvent and purified by chromatography through a short column (MTBE/MeOH, ≈30:1) to give (*Z*)-**13**, 938 mg (78%), m.p. 165 °C (decomp.). $[\alpha]_D^{20} = +210.3$ ($c = 0.505$ in $CHCl_3$/MeOH, 5:1). IR (KBr): $\tilde{\nu} = 1030$, 1081, 1181, 1178, 1228, 1242, 1366, 1433, 1471, 1511, 1592, 1622, 2214, 2941, 3300 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$/CD_3OD): $\delta = 1.35$ (m, 1H), 1.70 (m, 2H), 2.11 (m, 1H), 2.68 (m, 1H; H-4), 2.75–3.10 (m, 2H; H-6), 3.18 (m, 1H; H-8), 3.63 (d, $J = 18$ Hz, 1H; H-2$_{exo}$), 3.96 (s, 3H; H-11′), 4.70 (d, $J = 18$ Hz, 1H; H-2$_{endo}$), 5.27 (t, $J = 1.75$ Hz, 1H; H-10), 5.68 (d, $J = 1$Hz, 1H; H-9), 7.21 (d, $J = 2$ Hz, 1H; H-5′), 7.36 (dd, $J = 2$, 9 Hz, 1H; H-7′), 7.61 (d, $J = 4$ Hz, 1H; H-3′), 7.95 (d, $J = 9$ Hz, 1H; H-8′), 8.62 (d, $J = 4$ Hz, 1H; H-2′). NOE: H-10 with H-4 (9.50). ^{13}C NMR (50 MHz, APT, $CDCl_3$/CD_3OD): $\delta = 24.91$, 25.99 (+, C-5, C-7), 34.33 (−, C-4), 50.76, 52.07 (+, C-2, C-6), 55.92 (−, C-11′), 58.92 (−, C-8), 70.85 (−, C-9), 89.19 (−, C-10), 101.16 (−, C-5′), 116.25 (+, C-11), 118.71 (−, C-3′), 122.47 (−, C-7′), 126.67 (+, C-9′), 130.87 (−, C-8′), 143.68, 148.62 (+, C-4′, C-10′), 147.24 (−, C-2′), 158.54 (+, C-6′), 173.68 (+, C-3). MS-MAT (190 °C): *m/z* (%): 335 (68) [M^+], 320 (10), 306 (4), 288 (3), 214 (9), 201 (9), 189 (100), 188 (85), 172 (16), 159 (16), 147 (54), 129 (4), 117 (13). HRMS calcd for $C_{20}H_{21}N_3O_2$: 335.1634, found 335.1635.

(8*R*,9*S*)-(*Z*)-3-Formylmethylidene-6′-methoxyruban-9-ol [(*Z*)-**14**]: To a suspension of (*Z*)-**13** (490 mg, 1.46 mmol) in anhydrous THF (25 mL) was added DIBAH (11.7 mL, 11.7 mmol, 1.0 M solution in hexane) under N_2 at RT, and the mixture was stirred for 45 min. The reaction mixture was cooled to 0 °C and sat. aq. NH_4Cl (8 mL) was added, followed by H_2SO_4 (10%) (4 mL). The aqueous phase was neutralized ($NaHCO_3$) and extracted with $CHCl_3$. Precipitated $Al(OH)_3$ was removed by suction filtration and washed with $CHCl_3$. The combined organic layer was dried ($MgSO_4$), freed from solvent and purified by column filtration (E/MeOH, 10:1) to give (*Z*)-**14**, 336 mg (72%), m.p. 170 °C (decomp.). $[\alpha]_D^{20} = +246.0$ ($c = 0.6$ in $CHCl_3$/MeOH, 5:1). IR (KBr): $\tilde{\nu} = 1079$, 1112, 1178, 1242, 1337, 1366, 1433, 1471, 1511, 1621, 1671, 2931, 3399 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$/CD_3OD): $\delta = 1.47$ (m, 1H), 1.78 (m, 2H), 2.19 (m, 1H), 2.63 (m, 1H; H-4), 2.80–3.30 (m, 3H; H-6, H-8), 3.91 (s, 3H; H-11′), 3.99 (d, $J = 19$ Hz, 1H; H-2$_{exo}$), 5.0 (d, $J = 19$ Hz, 1H; H-2$_{endo}$), 5.70 (br s, 1H; H-9), 5.95 (m, 1H; H-10), 7.22 (d, $J = 2$ Hz, 1H; H-5′), 7.32 (dd, $J = 2$, 9 Hz, 1H; H-7′), 7.63 (d, $J = 4$ Hz, 1H; H-3′), 7.92 (d, $J = 9$ Hz, 1H; H-8′), 8.61 (d, $J = 4$ Hz, 1H; H-2′), 9.87 (d, $J = 7$ Hz, 1H; H-11). ^{13}C NMR (50 MHz, APT, $CDCl_3$/CD_3OD): $\delta = 25.09$, 26.05 (+, C-5, C-7), 35.05 (−, C-4), 50.82, 51.58 (+, C-6, C-2), 55.84 (−, C-11′), 58.96 (−, C-8), 70.83 (−, C-9), 101.09 (−, C-5′), 118.70 (−, C-3′), 120.80 (−) 122.36 (−, C-7′, C-10), 126.59 (+, C-9′), 130.79 (−, C-8′), 143.60, 148.53 (+, C-4′, C-10′), 147.17 (−, C-2′), 158.43 (+, C-6′), 172.80 (+, C-3), 191.17 (−, C-11). MS-MAT (60 °C): *m/z* (%): 338 (6) [M^+], 309 (2), 291 (2), 214 (2), 200 (2), 189 (5), 159 (3), 84 (100). HRMS calcd for $C_{20}H_{22}N_2O_3$: 338.1630, found 338.1629.

(8*R*,9*S*)-(*Z*)-3-Hydroxymethylmethylidene-6′-methoxyruban-9-ol [(*Z*)-**12**]: To a solution of (*Z*)-**14** (120 mg, 0.355 mmol) in anhydrous MeOH (3 mL) was added $NaBH_4$ (27 mg, 0.7 mmol) under a weak stream of N_2, and the mixture was stirred for 5 min at RT. The crude product was absorbed on silica gel and purified by column chromatography (E/MeOH, 5:1) to afford (*Z*)-**12**, 111 mg (92%), m.p. 142 °C. $[\alpha]_D^{20} = +173.1$ ($c = 0.965$ in MeOH). IR (Kbr): $\tilde{\nu} = 1080$, 1117, 1229, 1242, 1365, 1433, 1473, 1510, 1592, 1622, 2934, 3370 cm^{-1}. ^{1}H NMR (200 MHz, CD_3OD): $\delta = 1.45$ (m, 1H), 1.76 (m, 2H), 2.22 (m, 1H), 2.49 (m, 1H; H-4), 3.00 (m, 1H; H-6), 3.22 (m, 1H; H-6), 3.48 (m, 1H; H-8), 3.77 (d, $J = 17$ Hz, 1H; H-2$_{exo}$), 3.99 (s, 3H; H-11′), 4.07 (dd, $J = 8$, 15 Hz, 2H; H-11), 4.69 (d, $J = 17$ Hz, 1H; H-2$_{endo}$), 5.48 (m, 1H; H-10), 5.99 (d, $J = 1$ Hz, 1H; H-9), 7.38 (dd, $J = 2$, 9Hz, 1H; H-7′), 7.43 (d, $J = 2$ Hz, 1H; H-5′), 7.68 (d, $J = 4$ Hz, 1H; H-3′), 7.93 (d, $J = 9$ Hz, 1H; H-8′), 8.67 (d, $J = 4$ Hz, 1H; H-2′). NOE: H-10 with H-4 (9.04), H-11 (8.43). ^{13}C NMR (50 MHz, APT, CD_3OD): $\delta = 26.15$, 26.18 (+, C-5, C-7), 33.95 (−, C-4), 50.74, 51.64 (+, C-2, C-6), 56.85 (−, C-11′), 58.54 (+, C-11), 60.70 (−, C-8), 70.30 (−, C-9), 102.21 (−, C-5′), 120.10 (−, C-3′), 121.53 (−, C-7′), 123.57 (−, C-10), 127.74 (+, C-9′), 131.37 (−, C-8′), 140.18 (+, C-3), 144.64, 148.86 (+, C-4′, C-10′), 148.05 (−, C-2′), 159.82 (+, C-6′). MS-MAT (90 °C): *m/z* (%): 340 (5) [M^+], 262 (5), 219 (5), 206 (5), 189 (5), 177 (6), 135 (5), 127 (10), 84 (100). HRMS calcd for $C_{20}H_{24}N_2O_3$: 340.1787, found 340.1783.

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[1] C. von Riesen, P. G. Jones, H. M. R. Hoffmann, *Chem. Eur. J.* **1996**, *2*, 673.
[2] R. B. Silverman, *The Organic Chemistry of Drug Design and Drug Action*, Academic Press, San Diego, **1992**.
[3] H. Brunner, W. Zettlmaier, *Handbook of Enantioselective Catalysis with Transition Metal Compounds*, Vol. 1 and 2, VCH, Weinheim, **1993**; I. Ojima, *Catalytic Asymmetric Synthesis*, VCH, Weinheim, **1993**.
[4] a) F. I. Carroll, P. Abraham, K. Gaetano, S. W. Mascarella, R. A. Wohl, J. Lind, K. Petzoldt, *J. Chem. Soc. Perkin Trans I* **1991**, 3017. b) T. A. Henry, W. Solomon, E. M. Gibbs, *J. Chem. Soc.* **1935**, 966.
[5] For example: A. Weichert, H. M. R. Hoffmann, *J. Org. Chem.* **1991**, *56*, 4098; H. M. R. Hoffmann, J. Rabe, *ibid.* **1985**, *50*, 3849; J. Rabe, H. M. R. Hoffmann, *Angew. Chem.* **1983**, *95*, 796; *Angew. Chem. Int. Ed. Engl.* **1983**, *22*, 796.
[6] M. E. Flanagan, R. M. Wilson, *J. Org. Chem.* **1995**, *60*, 6791; T. Fukuyama, J. J. Nunes, *J. Am. Chem. Soc.* **1988**, *110*, 5196.
[7] For example: a) R. Azerad, *Chimia* **1993**, *47*, 93. b) V. M. Fautrez, M. M. Adamantidis, J. F. Caron, C. C. Libersa, B. A. Dupuis, *Journal of Cardiovascular Pharmacology* **1992**, *19*, 308. c) B. Lecocq, P. Jaillon, V. Lecocq, A. Ferry, M. E. Gardin, C. Jarreau, R. Leroyer, M. Pays, F. X. Jarreau, *Journal of Cardiovascular Pharmacology* **1988**, *12*, 445. d) P. Jaillon, J. M. Poirier, B. Lecocq, C. Jarreau, M. Pays, M. O. Richard, G. Cheymol, *European Journal of Drug Metabolism and Pharmacokinetics* **1986**, *11*, 233.