Synthesis of tricyclic N,O-acetals from α-functionalized rubanone. A masked 1,2,3-tricarbonyl system from quinidine

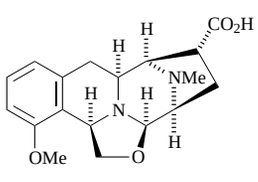
Peter Langer, Jens Frackenpohl and H. M. R. Hoffmann *

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

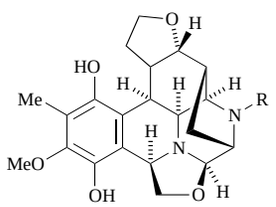
A series of protected 2-bromorubanones derived from quinidine has been prepared diastereoselectively and converted into tricyclic N,O-acetals containing a masked 1,2,3-tricarbonyl functionality. Good yields have been achieved using formyl-, acetyl- and propionyl-protecting groups. The novel one-pot conversion of protected 2-bromorubanones into tricyclic *Cinchona* cage compounds is suggested to include a reduction–oxidation sequence and an intramolecular acyl transfer.

Introduction

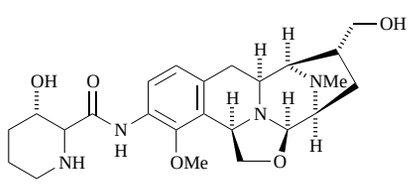
Five-ring N,O-acetals of the tetrahydrooxazole variety have been encountered in quinocarcin, the bioxalomycins and tetrazomine. These heterocycles have been shown to display interesting biological activities in antitumor and antimicrobial assays.[1] Tetrazomine shows good antimicrobial activity against both Gram-negative and Gram-positive organisms and activity against P388 leukemia *in vivo*, whereas quinocarcin, as the citrate salt, displays promising antitumor activity against several lines of solid mammalian carcinomas. Modes of action for quinocarcin, tetrazomine and the bioxalomycins include the oxidative cleavage of DNA *via* redox disproportionation reactions of their five-ring N,O-acetal moieties and subsequent production of superoxide under aerobic conditions.[2] Furthermore, isoxazolidines are of continued interest as intermediates in organic synthesis and in pharmacology.[3,4] We have recently observed tricyclic N,O-acetals as side products from the chloramine T-mediated epoxidation of isoquinidine in low yield.[5] Due to the intrinsic interest of this system we considered a more efficient approach and investigated the possibility of a direct α-functionalization of protected rubanones at carbon C-2 and a suitable intramolecular ring closure.



Quinocarcin



R = H Bioxalomycin α-1
R = Me Bioxalomycin α-2



Tetrazomine

Results and discussion

Unprotected rubanone **1-H** has recently been prepared from quinidine by a reliable five-step sequence.[5] TBDS-Protected rubanone **1a** was prepared under modified standard conditions.[6] Acylated rubanones **1b–f** were obtained from **1-H** by conventional methodology. Formylated derivative **1g** was prepared from **1-H** and mixed acetic formic anhydride (AFA) in 94% yield.[7] We were pleased to find that the α-bromination of a variety of protected rubanones **1a–g** was feasible and proceeded in satisfactory yield and with complete diastereoselectivity. Novel α-bromo ketones **2a–g** were less polar than their precursor ketones **1a–g** and they were isolated and purified by chromatography. In our hands, it was essential to (i) use acetic acid as a solvent, (ii) adjust the concentration of protected rubanone **1b** (*ca.* 0.6 mol l^{-1}), (iii) use *ca.* three equivalents of bromine and (iv) add bromine at room temperature (see Tables 1 and 2). The resulting product was reasonably stable, presumably because loss of bromide with formation of iminium ion is forbidden by the Bredt rule. The configuration at carbon C-2 was established by a strong NOE H2–H9 (11.6%) of the acetate **2b**. Diastereoselectivity is assumed to be controlled on steric grounds. The presence of a strong NOE H9–H5′ (20.2%) and of NOEs H8–H3′ (7.1%) and H2–H5′ (1.2%) suggests that acetylated rubanone **2b** adopts an *anti*-closed conformation in $CDCl_3$ (Fig. 1). This is in agreement with the investigation of Wynberg and his colleagues who showed that the *anti*-closed conformation is characteristic for the parent acylated quinidines.[8]

Treatment of **2b** with K_2CO_3–MeOH resulted in a complex

Table 1 Reaction conditions for α-brominations **1b**→**2b**

1b/mmol	Solvent	Concentration of **1b**/mol l^{-1}	Equiv. Br_2	*T*/°C	Yield (%)
1.1	CH_2Cl_2	0.8	3.0	20	0
1.1	HOAc	0.6	3.0	0	11
1.1	HOAc	0.02	1.2	0	0
1.1	HOAc	0.2	2.0	20	40
1.1	HOAc	0.6	3.0	20	72
5.6	HOAc	0.6	3.0	20	37
5.6	HOAc	0.8	5.0	20	50

Table 2 Diastereoselective synthesis of α-brominated rubanones **2a–g**. Variation of acyl groups.

Compound	R	Yield (%)
2a	TBDS	68
2b	Me	69
2c	Et	66
2d	Pr^i	61
2e	Bu^t	64
2f	Ph	70
2g	H	57

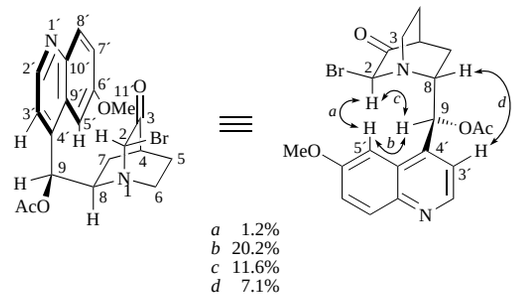
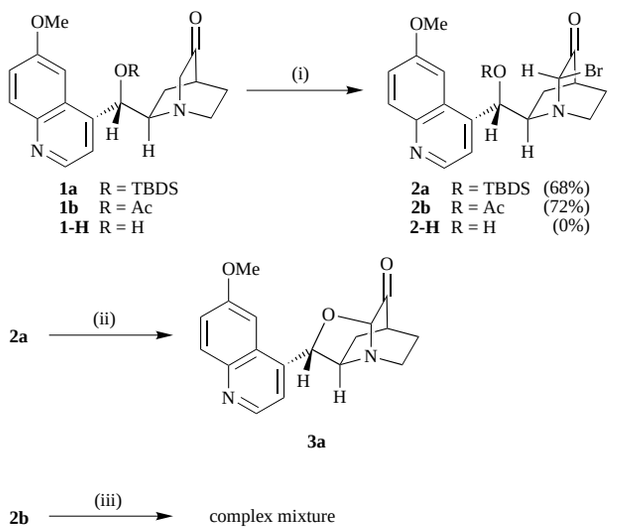


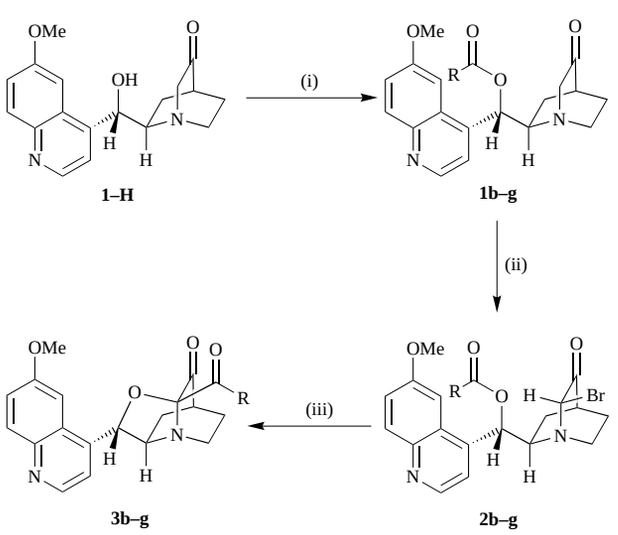
Fig. 1 *anti*-Closed conformation adopted by **2b** (solvent $CHCl_3$)

reaction mixture which suggests that unprotected α-bromorubanone **2-H** is unstable. In addition, parent **2-H** could not be prepared by bromination of **1-H**. However, desilylation of **2a** with TBAF furnished the desired tricyclic cage system **3a** under mild conditions, but in low yield (22%) (Scheme 1). To our



Scheme 1 (i) Br_2 (3.0 equiv.), PBr_3 (1.2 equiv.), HOAc, 20 °C, 80%; (ii) TBAF, THF, 0 to 20 °C, 22%; (iii) K_2CO_3, MeOH

surprise, the reaction of α-bromorubanone **2b** with sodium azide and sodium iodide furnished tricyclic diketone **3b** in good yield (75%) (Scheme 2).



Scheme 2 (i) RCOCl (1.2 equiv.), NEt_3 (1.5 equiv.), THF, 0 °C; (ii) Br_2 (3.0 equiv.), PBr_3 (1.2 equiv.), HOAc, 20 °C; (iii) NaN_3 (excess), NaI (1 equiv.), DMF, 115 °C

FAB-MS of **3b** gave a molecular ion peak. The ^{13}C NMR spectrum showed two carbonyl peaks at δ 204.59 and 210.91 and an acetalic carbon C-2 at δ 93.89. The resonance of carbon

Table 3 Reaction conditions for tricyclization **2b**→**3b** (one equivalent NaI present in all experiments)

Entry	**2b**/mmol	DMF/ml	NaN_3/mmol	*T*/°C	Yield (%)
1	0.3	2	6	115	traces
2	0.3	2	40	20	0
3	0.3	2	40	80	15
4	0.3	2	40	115	75
5	0.3	2	—	115	0
6	0.3	1	20	115	66
7	0.8	5	100	115	74
8	1.6	5	100	115	63

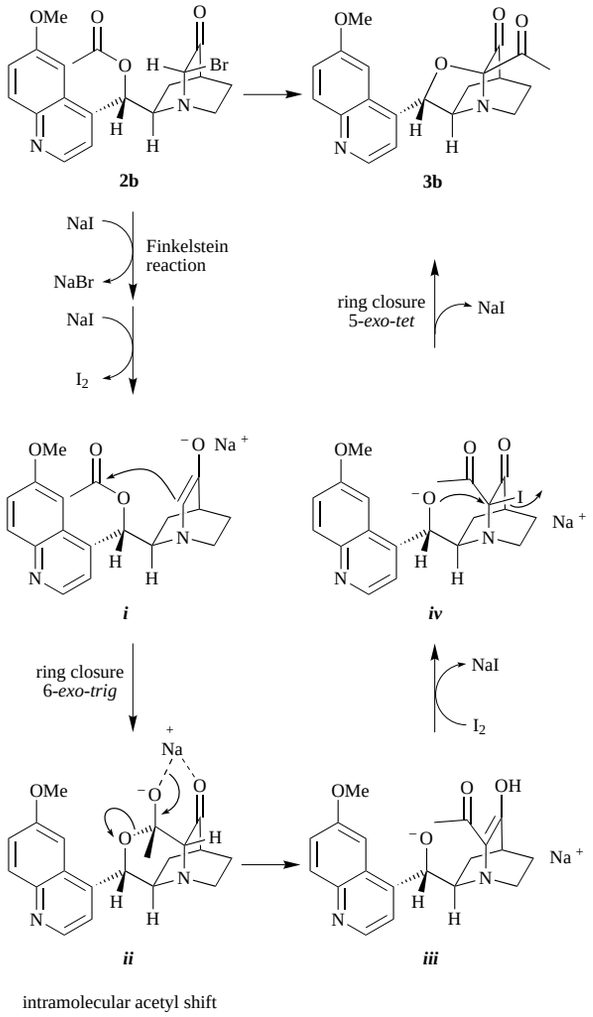
Table 4 Synthesis of tricyclic N,O-acetals **3b**–**g** as a function of acyl groups

Entry	Compound	R	Reaction time *t*/h	Yield (%)
1	**3b**	Me	10	75
2	**3c**	Et	10	73
3	**3d**	Pr^i	10	65
4	**3e**	Bu^t	14	51
5	**3f**	Ph	48	0
6	**3g**	H	10	76

C-9 (δ 79.52) is shifted downfield by *ca*. 6–11 ppm relative to bicyclic precursor **2b**. The C-9 chemical shift (δ 79.52) is characteristic for tricyclic *Cinchona* alkaloid cage structures that we have prepared.[5] The ^1H NMR spectrum showed that the CH_3 carbon next to the carbonyl group in **3b** (δ 2.49) was shifted downfield with respect to the precursor acetate **2b** (δ 2.24). The IR spectrum revealed two carbonyl bands at 1712 and 1748 cm^{-1}. The ^3J H(8),H(9) coupling constant is an indicator of the open–closed conformation equilibrium in *Cinchona* alkaloids.[8] The small ^3J H(8),H(9) = 4 Hz suggested a staggered (open) conformation for **3b**. In contrast, the acetate precursor **2b** showed ^3J = 6 Hz, due to a change in conformation from *anti*-open to *anti*-closed. Note that the *anti*-closed–*anti*-open conformational equilibrium changes on protection of the C-9 hydroxy group. The yield of the tricyclic product **3b** was investigated with respect to temperature and concentration of sodium azide (Table 3). Given an excess of sodium azide and an elevated temperature (115 °C) the desired tricyclic N,O-acetal **3b** was obtained in 74% yield (entry 7). The highest yields of tricyclic derivatives **3b**–**g** were achieved after protection of **1-H** by formyl (R = H), acetyl (R = Me) and propionyl (R = Et) (Table 4).

Reductive removal of the bromine substituent is assumed to proceed by nucleophilic attack of positively polarized bromine by a soft nucleophile (a preceding Finkelstein displacement is, of course, possible and further facilitates formation of the enolate ***i***). The subsequent 6-*exo*-*trig* attack at the ester carbonyl carbon generates a cyclic hemiacetal (***i***→***ii***), which opens to the 1,3-diketone ***iii*** with intramolecular acyl transfer. The resulting 1,3-diketone or its anion are thought to be amenable to oxidation by molecular iodine (or BrI) giving doubly activated iododiketone ***iv***, which undergoes an intramolecular S_N2 displacement to the observed diketo N,O-acetals **3b**–**g**. Sodium azide furnishes soft azide ion, which is assumed to generate comparatively stable BrN_3. In turn, BrN_3 or IN_3 might serve as an alternative to I_2 in the oxidizing step ***iii***→***iv***. A typical temperature range for the transformation of **2b**–**g** into **3b**–**g** is 110–120 °C under our conditions (Scheme 3). The postulated transacylation sequence ***i***→***ii***→***iii*** is thought to be energetically costly and facilitated by an acetyl and formyl group, but precluded by the benzoyl group (entry 5) presumably on electronic grounds. Transfer of the sterically demanding pivaloyl group is feasible because of intramolecularity (entry 4) (Table 4).

In conclusion, we have developed a practical and diastereoselective route to α-brominated rubanones **2a**–**g**. These α-halo-



Scheme 3

genated ketones were converted in a single step into tricyclic *Cinchona* cage compounds **3b**–**g** containing the 1,3-diketo-2-N,O-acetal functionality. The one-pot reaction involves a reduction–oxidation sequence and a transacylation.

Tricyclic N,O-acetals **3b**–**g** are quite interesting as potential catalysts that could complement the better known quinine, quinidine and derivatives thereof. A masked 1,2,3-triketone as in **3b**–**g** is also a segment of macrolide FK-506[9] (Tsukubaenolide), a potent immunosuppressant.

Experimental

General

Melting points were determined on a Büchi apparatus and are uncorrected. 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. Coupling constants are given in Hz. ^{13}C NMR signal assignments for each signal were established by DEPT measurements; 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. 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). DMF was dried over BaO, distilled over calcium hydride under reduced pressure and stored over 4 Å molecular sieves. THF was distilled over sodium and benzophenone before use. Ethyl acetate (EA) and methyl *tert*-butyl ether (MTBE) were distilled before use.

The Chemical Abstracts name of rubanone **1-H** is {1*R*-[1α, 4α, 6β(*S**)]}-6-[hydroxy(6-methoxy-4-quinolinyl)methyl]-1-azabicyclo[2.2.2]octan-3-one. Our numbering of *Cinchona* alkaloids follows the cinchonane convention as indicated in Fig. 1.

Silylated rubanone **1a** and acetylated rubanone **1b** have been described previously.[5,6]

Preparation of acylated rubanones 1c–g

To a solution of rubanone **1-H** (400 mg, 1.28 mmol) in abs. THF (10 ml) was added NEt_3 (0.27 ml, 2.05 mmol) under argon. The reaction mixture was cooled to 0 °C and acid chloride (1.3 equiv.) was added within 20 min. The solution was stirred for 10 h at r.t., diluted with $CHCl_3$ and extracted with H_2O and sat. aq. $NaHCO_3$. The organic layer was dried ($MgSO_4$) and the solvent was removed. Purification by column chromatography afforded the acylated rubanones **1c**–**g**.

(8*R*,9*S*)-9-Propionyloxyruban-3-one 1c. Rubanone **1-H** (800 mg, 2.6 mmol) afforded after chromatography (MTBE–MeOH, 20:1) **1c** (842 mg, 88%) as a colourless solid, mp 180 °C; ν_{max}($CHCl_3$)/cm^{-1} 3008, 2960, 2872, 1736, 1620, 1592, 1508, 1472, 1432, 1364, 1232, 1168 and 1080; δ_H(400 MHz; $CDCl_3$) 1.18 (3 H, t, *J* 8, CH_2CH_3), 1.95, 2.01, 2.22 (4 H, m, H-5, H-7), 2.45 (2 H, q, *J* 8, CH_2CH_3), 2.56 (1 H, m, H-4), 2.87, 2.99 (2 H, m, H-6), 3.14 (1 H, d, *J* 19, H-2$_{exo}$), 3.48 (1 H, m, H-8), 3.66 (1 H, d, *J* 19, H-2$_{endo}$), 3.98 (3 H, s, H-11′), 6.56 (1 H, d, *J* 5, H-9), 7.34 (1 H, d, *J* 1.5, H-5′), 7.29 (1 H, d, *J* 4, H-3′), 7.41 (1 H, dd, *J* 2 and 9, H-7′), 8.05 (1 H, d, *J* 9, H-8′) and 8.74 (1 H, d, *J* 4, H-2′); δ_C(100 MHz; $CDCl_3$) 8.84 (CH_3, CH_2CH_3), 24.58, 27.08, 27.65 (CH_2, C-5, C-7 and CH_2CH_3), 40.31 (CH, C-4), 50.11 (CH_2, C-6), 55.60 (CH_3, C-11′), 57.89 (CH, C-8), 58.52 (CH_2, C-2), 73.37 (CH, C-9), 100.91 (CH, C-5′), 117.79 (CH, C-3′), 121.92 (CH, C-7′), 126.37 (C, C-9′), 131.85 (CH, C-8′), 143.02, 144.48 (C, C-4′, C-10′), 147.25 (CH, C-2′), 158.12 (C, C-6′), 172.91 (C, C-12) and 218.42 (C, C-3).

(8*R*,9*S*)-9-Isobutyryloxyruban-3-one 1d. Rubanone **1-H** (400 mg, 1.28 mmol) afforded after chromatography (EA–MeOH, 6:1) **1d** (415 mg, 85%) as a colourless solid, mp 186 °C; ν_{max}(KBr)/cm^{-1} 2972, 2876, 1736, 1718, 1620, 1592, 1508, 1472, 1432, 1388, 1308, 1228, 1148, 1112, 1080 and 1032; δ_H(400 MHz; $CDCl_3$) 1.20–1.28 (6 H, m, H-14 and H-15), 1.98–2.08 (2 H, m, H-5), 2.25–2.29 (2 H, m, H-7), 2.61 (1 H, m, H-4), 2.73 (1 H, septet, *J* 7, H-13), 2.94 (1 H, m, H-6), 3.06 (1 H, m, H-6), 3.23 (1 H, d, *J* 19, H-2$_{exo}$), 3.55 (1 H, m, H-8), 3.82 (1 H, d, *J* 19, H-2$_{endo}$), 4.02 (3 H, s, H-11′), 6.59 (1 H, d, *J* 5, H-9), 7.33 (1 H, d, *J* 4, H-3′), 7.39 (1 H, d, *J* 2, H-5′), 7.46 (1 H, dd, *J* 2 and 9, H-7′), 8.12 (1 H, d, *J* 9, H-8′) and 8.79 (1 H, d, *J* 4, H-2′); δ_C(100 MHz; $CDCl_3$) 18.75 (CH_3, C-15), 19.05 (CH_3, C-14), 24.50 (CH_2, C-5), 27.00 (CH_2, C-7), 34.16 (CH, C-13), 40.44 (CH, C-4), 50.08 (CH_2, C-6), 55.74 (CH_3, C-11′), 58.04 (CH, C-8), 58.48 (CH_2, C-2), 73.14 (CH, C-9), 100.96 (CH, C-5′), 117.73 (CH, C-3′), 122.25 (CH, C-7′), 126.55 (C, C-9′), 131.65 (CH, C-8′), 143.45 (C, C-4′), 144.37 (C, C-10′), 147.09 (CH, C-2′), 158.33 (C, C-6′), 175.51 (C, C-12) and 217.82 (C, C-3); *m*/*z* (150 °C) (EI) 382.1896 (M^+. $C_{22}H_{26}N_2O_4$ requires 382.1893), 354 (51%), 339 (28), 313 (8), 295 (3), 283 (22), 267 (100), 253 (21), 243 (19), 225 (20), 210 (28), 200 (12), 186 (18), 172 (43), 154 (6), 141 (5), 116 (6) and 96 (24).

(8*R*,9*S*)-9-Pivaloyloxyruban-3-one 1e. Rubanone **1-H** (400 mg, 1.28 mmol) afforded after chromatography (EA–MeOH, 6:1) **1e** (461 mg, 91%) as a colourless solid, mp 182 °C; ν_{max}(KBr)/cm^{-1} 2960, 2872, 1732, 1718, 1620, 1592, 1508, 1472, 1432, 1364, 1304, 1228, 1144, 1080 and 1032; δ_H(400 MHz; $CDCl_3$) 1.27 (9 H, s, H-14, H-15 and H-16), 1.95–2.01 (2 H, m, H-5), 2.13 (1 H, m, H-7), 2.31 (1 H, m, H-7), 2.59 (1 H, m, H-4), 2.90 (1 H, m, H-6), 3.03 (1 H, m, H-6), 3.19 (1 H, d, *J* 18, H-2$_{exo}$), 3.53 (1 H, m, H-8), 3.77 (1 H, d, *J* 18, H-2$_{endo}$), 4.00 (3 H, s, H-11′), 6.51 (1 H, d, *J* 6, H-9), 7.31 (1 H, d, *J* 4, H-3′), 7.38

(1 H, d, *J* 2, H-5′), 7.45 (1 H, dd, *J* 2 and 9, H-7′), 8.09 (1 H, d, *J* 9, H-8′) and 8.78 (1 H, d, *J* 4, H-2′); δ_C(100 MHz; $CDCl_3$) 24.79 (CH_2, C-5), 27.06 (CH_3, C-16), 27.09 (CH_3, C-15), 27.19 (CH_3, C-14), 27.80 (CH_2, C-7), 38.94 (C, C-13), 40.48 (CH, C-4), 50.21 (CH_2, C-6), 55.66 (CH_3, C-11′), 58.40 (CH, C-8), 58.58 (CH_2, C-2), 73.47 (CH, C-9), 100.98 (CH, C-5′), 117.60 (CH, C-3′), 122.03 (CH, C-7′), 126.57 (C, C-9′), 131.99 (CH, C-8′), 143.51 (C, C-4′), 144.73 (C, C-10′), 147.36 (CH, C-2′), 158.16 (C, C-6′), 177.02 (C, C-12) and 218.40 (C, C-3); *m*/*z* (140 °C) (EI) 396.2054 (M^+. $C_{23}H_{28}N_2O_4$ requires 396.2049), 381 (2%), 368 (45), 353 (27), 337 (2), 327 (9), 296 (5), 284 (36), 267 (100), 253 (21), 240 (10), 225 (18), 210 (24), 200 (12), 188 (14), 172 (37), 154 (7), 141 (5), 116 (4) and 96 (23).

(8*R*,9*S*)-9-Benzoyloxyruban-3-one 1f. Rubanone **1-H** (800 mg, 2.6 mmol) afforded after chromatography (MTBE–MeOH, 20 : 1) **1f** (963 mg, 88%) as a colourless solid, mp 175 °C (Found: C, 71.85; H, 6.02; N, 6.30; $C_{25}H_{24}N_2O_4$ requires C, 72.09; H, 5.81; N, 6.73%); ν_{max}(KBr)/cm^{-1} 3068, 2944, 2872, 1728, 1620, 1592, 1508, 1472, 1452, 1312, 1272 and 1108; δ_H(400 MHz; $CDCl_3$) 1.97, 2.08, 2.40 (4 H, m, H-5, H-7), 2.60 (1 H, m, H-4), 2.88, 3.05 (2 H, m, H-6), 3.17 (1 H, d, *J* 18, H-2$_{exo}$), 3.60 (1 H, m, H-8), 3.79 (1 H, d, *J* 18, H-2$_{endo}$), 3.99 (3 H, s, H-11′), 6.80 (1 H, d, *J* 6, H-9), 7.34–7.55 (5 H, m, Ar), 7.64 (1 H, m, Ar), 8.05 (3 H, m, Ar) and 8.71 (1 H, d, *J* 4, H-2′); δ_C(100 MHz; $CDCl_3$) 24.63, 27.16 (CH_2, C-5, C-7), 40.58 (CH, C-4), 50.45 (CH_2, C-6), 55.72 (CH_3, C-11′), 58.17 (CH, C-8), 58.90 (CH_2, C-2), 74.52 (CH, C-9), 101.02 (CH, C-5′), 117.87 (CH, C-3′), 122.04 (CH, C-7′), 126.28 (C, C-9′), 128.78, 129.77, 133.82 (CH, Ph), 129.27 (C, Ph), 132.04 (CH, C-8′), 142.94, 144.80 (C, C-4′, C-10′), 147.45 (CH, C-2′), 158.32 (C, C-6′), 165.28 (C, C-12) and 218.37 (C, C-3); *m*/*z* (EI) 416.0985 (M^+. $C_{25}H_{24}N_2O_4$ requires 416.1008), 388 (34%), 373 (15), 347 (6), 284 (20), 267 (61), 253 (15), 225 (14), 210 (22), 188 (14), 172 (31) and 105 (100).

(8*R*,9*S*)-9-Formyloxyruban-3-one 1g. To a mixture (1 : 1) of formic acid (0.18 ml, 4.8 mmol) and acetic anhydride (0.45 ml, 4.8 mmol) was added pyridine (0.1 ml, cat.). After stirring for 15 min rubanone **1-H** (624 mg, 2.0 mmol) was added in portions. The homogeneous reaction mixture was stirred for 18 h at r.t. and then evaporated. The residue was diluted with $CHCl_3$, extracted with sat. aq. $NaHCO_3$, dried ($MgSO_4$) and evaporated. Purification by column chromatography (EA–MeOH, 6 : 1) yielded **1g** (639 mg, 94%); ν_{max}(KBr)/cm^{-1} 2944, 2872, 1728, 1620, 1592, 1508, 1472, 1432, 1360, 1308, 1256, 1228, 1156, 1080 and 1028; δ_H(400 MHz; $CDCl_3$) 1.62–1.54 (2 H, m, H-5), 1.85–1.94 (2 H, m, H-7), 2.34 (1 H, m, H-4), 2.76 (1 H, m, H-6), 2.87 (1 H, m, H-6), 2.96 (1 H, d, *J* 17, H-2$_{exo}$), 3.39 (1 H, m, H-8), 3.72 (1 H, d, *J* 17, H-2$_{endo}$), 3.99 (3 H, s, H-11′), 6.67 (1 H, d, *J* 7, H-9), 7.37 (1 H, d, *J* 4, H-3′), 7.40 (1 H, d, *J* 2, H-5′), 7.43 (1 H, dd, *J* 2 and 9, H-7′), 8.10 (1 H, d, *J* 9, H-8′), 8.22 (1 H, s, H-12) and 8.78 (1 H, d, *J* 4, H-2′); δ_C(100 MHz; $CDCl_3$) 24.11 (CH_2, C-5), 26.31 (CH_2, C-7), 39.70 (CH, C-4), 49.83 (CH_2, C-6), 55.84 (CH_3, C-11′), 58.96 (CH, C-8), 59.79 (CH_2, C-2), 73.24 (CH, C-9), 101.35 (CH, C-5′), 118.56 (CH, C-3′), 121.87 (CH, C-7′), 126.89 (C, C-9′), 131.86 (CH, C-8′), 143.04 (C, C-4′), 144.73 (C, C-10′), 147.42 (CH, C-2′), 158.00 (C, C-6′), 160.01 (CH, C-12) and 212.34 (C, C-3); *m*/*z* (170 °C) (EI) 340.1424 (M^+. $C_{19}H_{20}N_2O_4$ requires 340.1423), 326 (2%), 312 (63), 297 (31), 283 (10), 267 (100), 253 (23), 237 (9), 225 (28), 210 (48), 200 (14), 184 (15), 172 (73), 154 (11), 140 (10), 117 (11) and 96 (23).

Preparation of α-brominated rubanones 2a–g

To a solution of acylated rubanone (1 mmol) in acetic acid (17 ml) were added bromine (0.16 ml, 3 mmol) (at such a rate that the resulting cloudiness always disappeared) and PBr_3 (0.11 ml, 1.2 mmol) under argon. After stirring for 6 h at r.t. the reaction mixture was treated with $NaHCO_3$ and extracted with $CHCl_3$. The combined organic layer was dried ($MgSO_4$), evaporated and purified by chromatography to furnish the α-brominated rubanones.

(2*S*,8*R*,9*S*)-2-Bromo-9-*tert*-butyldimethylsilyloxyruban-3-one 2a. Rubanone **1a** (468 mg, 1.1 mmol) afforded after chromatography (MTBE–MeOH, 40 : 1) **2a** (377 mg, 68%) as a light yellow, waxy solid; ν_{max}(KBr)/cm^{-1} 3076, 2952, 2928, 2884, 2856, 1744, 1620, 1592, 1508, 1472, 1388, 1256, 1228, 1116, 1072 and 1028; δ_H(400 MHz; $CDCl_3$) −0.22, 0.31 [6 H, s, $Si(CH_3)_2$], 1.02 [9 H, s, $C(CH_3)_3$], 1.43, 1.79, 2.02, 2.45 (4 H, m, H-5, H-7), 2.69 (1 H, m, H-4), 2.99, 3.35 (2 H, m, H-6), 3.45 (1 H, m, H-8), 4.02 (3 H, s, H-11′), 5.98 (1 H, s, H-2), 6.61 (1 H, s, H-9), 7.20 (1 H, d, *J* 1.5, H-5′), 7.55 (d, 1 H, *J* 4, H-3′), 7.48 (dd, 1 H, *J* 2 and 9, H-7′), 8.13 (d, 1 H, *J* 9, H-8′) and 8.81 (d, 1 H, *J* 4, H-2′); δ_C(100 MHz; $CDCl_3$) −0.52, −0.45 [CH_3, $Si(CH_3)_2$], 18.00 [C, $C(CH_3)_3$], 22.65, 25.82 (CH_2, C-5, C-7), 25.80 [CH_3, $C(CH_3)_3$], 40.81 (CH, C-4), 45.04 (CH_2, C-6), 55.89 (CH_3, C-11′), 60.27 (CH, C-8), 70.08 (CH, C-9), 72.60 (CH, C-2), 100.29 (CH, C-5′), 118.70 (CH, C-3′), 121.58 (CH, C-7′), 126.65 (C, C-9′), 132.15 (CH, C-8′), 144.22, 145.61 (C, C-4′, C-10′), 147.26 (CH, C-2′), 158.33 (C, C-6′) and 211.78 (C, C-3); *m*/*z* (150 °C) (EI) 506 (2%), 504.1442 (M^+. $C_{24}H_{33}N_2O_3Si^{79}Br$ requires 504.1444), 477/475 (15), 448/446 (5), 396 (72), 366 (8), 338 (11), 265 (31) and 171 (76).

(2*S*,8*R*,9*S*)-9-Acetoxy-2-bromoruban-3-one 2b. Rubanone **1b** (390 mg, 1.1 mmol) afforded after chromatography (MTBE–MeOH, 40 : 1) **2b** (342 mg, 72%) as a colourless solid, mp 170 °C (decomp.) (Found: C, 54.83; H, 5.04; N, 6.15; $C_{20}H_{21}N_2O_4Br$ requires C, 55.04; H, 4.98; N, 6.37%); ν_{max}(KBr)/cm^{-1} 2952, 2888, 1748, 1620, 1592, 1508, 1472, 1456, 1432, 1372, 1308, 1228, 1148, 1104, 1068 and 1028; δ_H(400 MHz; $CDCl_3$) 1.86–2.01 (2 H, m, H-5), 2.03–2.15 (2 H, m, H-7), 2.24 (3 H, s, H-13), 2.74 (1 H, m, H-4), 2.92 (1 H, m, H-6), 3.45 (1 H, m, H-6), 3.73 (1 H, m, H-8), 4.04 (3 H, s, H-11′), 6.03 (1 H, s, H-2), 6.73 (1 H, d, *J* 6, H-9), 7.39 (1 H, d, *J* 2, H-5′), 7.47 (1 H, d, *J* 4, H-3′), 7.51 (1 H, dd, *J* 2 and 9, H-7′), 8.22 (1 H, d, *J* 9, H-8′) and 8.89 (1 H, d, *J* 4, H-2′); δ_C(100 MHz; $CDCl_3$) 20.91 (CH_3, C-13), 25.61 (CH_2, C-7), 25.99 (CH_2, C-5), 40.27 (CH, C-4), 44.69 (CH_2, C-6), 56.08 (CH_3, C-11′), 59.76 (CH, C-8), 68.10 (CH, C-2), 72.89 (CH, C-9), 100.90 (CH, C-5′), 117.87 (CH, C-3′), 120.81 (CH, C-7′), 126.72 (C, C-9′), 130.49 (CH, C-8′), 143.17 (C, C-4′), 145.62 (C, C-10′), 147.41 (CH, C-2′), 158.89 (C, C-6′), 169.13 (C, C-12) and 210.74 (C, C-3); *m*/*z* (240 °C) (EI) 434 (M^+, 6%), 432.0685 (M^+. $C_{20}H_{21}N_2O_4{}^{79}Br$ requires 432.0685) 407 (24), 405 (22), 390 (7), 345 (12), 325 (77), 311 (5), 283 (30), 265 (100), 254 (10), 224 (11), 212 (20), 198 (18), 184 (14), 172 (24), 159 (9), 141 (7), 116 (9) and 95 (11).

(2*S*,8*R*,9*S*)-2-Bromo-9-propionyloxyruban-3-one 2c. Rubanone **1c** (405 mg, 1.1 mmol) afforded after chromatography (MTBE–MeOH, 40 : 1) **2c** (324 mg, 66%) as a colourless solid, mp 170 °C; δ_H(400 MHz; $CDCl_3$) 1.19 (3 H, t, *J* 8, CH_2CH_3), 1.88, 2.05, 2.27 (4 H, m, H-5, H-7), 2.49 (2 H, q, *J* 8, CH_2CH_3), 2.69 (1 H, m, H-4), 2.87, 3.38 (2 H, m, H-6), 3.63 (1 H, m, H-8), 3.98 (3 H, s, H-11′), 6.03 (1 H, s, H-2), 6.71 (1 H, d, *J* 5, H-9), 7.29 (2 H, m, H-5′, H-3′), 7.43 (1 H, dd, *J* 2 and 9, H-7′), 8.07 (1 H, d, *J* 9, H-8′) and 8.76 (1 H, d, *J* 4, H-2′); δ_C(100 MHz; $CDCl_3$) 9.03 (CH_2CH_3), 25.58, 25.77, 27.74 (CH_2, C-5, C-7, CH_2CH_3), 40.25 (CH, C-4), 44.70 (CH_2, C-6), 55.81 (CH_3, C-11′), 59.59 (CH, C-8), 68.16 (CH, C-9), 72.98 (CH, C-2), 100.17 (CH, C-5′), 117.63 (CH, C-3′), 122.28 (CH, C-7′), 126.17 (C, C-9′), 131.94 (CH, C-8′), 142.60, 144.59 (C, C-4′, C-10′), 147.28 (CH, C-2′), 158.38 (C, C-6′), 172.80 (C, C-12) and 211.00 (C, C-3); *m*/*z* (200 °C) (EI) 448 (M^+, 9%), 446.0841 (M^+. $C_{21}H_{23}N_2O_4{}^{79}Br$ requires 446.0841), 447/445 (11), 421/419 (11), 420/418 (21), 405/403 (9), 373/371 (9), 339 (62) and 265 (100).

(2*S*,8*R*,9*S*)-2-Bromo-9-isobutyryloxyruban-3-one 2d. Rubanone **1d** (382 mg, 1 mmol) afforded after chromatography (EA–MeOH, 20 : 1) **2d** (282 mg, 61%); ν_{max}(KBr)/cm^{-1} 3056, 2968, 2932, 2872, 1744, 1620, 1576, 1508, 1468, 1384, 1372, 1308, 1244, 1188, 1144, 1108, 1068 and 852; δ_H(400 MHz;

$CDCl_3$) 1.18–1.32 (6 H, m, H-14 and H-15), 1.94 (1 H, m, H-5), 2.15 (1 H, m, H-5), 2.20–2.35 (2 H, m, H-7), 2.78 (1 H, m, H-4), 2.88 (1 H, m, H-13), 3.01 (1 H, m, H-6), 3.42 (1 H, m, H-6), 3.72 (1 H, m, H-8), 4.06 (3 H, s, H-11′), 6.07 (1 H, s, H-2), 6.73 (1 H, d, *J* 6, H-9), 7.42 (1 H, d, *J* 2, H-5′), 7.46 (1 H, d, *J* 4, H-3′), 7.56 (1 H, dd, *J* 2 and 9, H-7′), 8.15 (1 H, d, *J* 9, H-8′) and 8.78 (1 H, d, *J* 4, H-2′); δ_C(100 MHz; $CDCl_3$) 18.861 (CH_3, C-15), 18.993 (CH_3, C-14), 24.361 (CH_2, C-5), 25.510 (CH_2, C-7), 34.219 (CH, C-13), 40.756 (CH, C-4), 45.026 (CH_2, C-6), 56.209 (CH_3, C-11′), 59.493 (CH, C-8), 69.335 (CH, C-2), 73.147 (CH, C-9), 100.839 (CH, C-5′), 118.899 (CH, C-3′), 120.915 (CH, C-7′), 125.336 (C, C-9′), 132.265 (CH, C-8′), 143.672 (C, C-4′), 144.059 (C, C-10′), 146.676 (CH, C-2′), 159.152 (C, C-6′), 175.048 (C, C-12) and 211.533 (C, C-3); *m*/*z* (180 °C) (EI) 462 (M^+, 1%), 460.4510 (M^+. $C_{22}H_{25}N_2O_4{}^{79}Br$ requires 460.4505), 280 (6), 267 (5), 259 (9), 245 (8), 201 (5), 189 (11), 172 (21), 158 (20), 149 (24), 121 (24), 115 (7), 106 (8), 96 (23), 94 (25), 82 (95) and 73 (100).

(2*S*,8*R*,9*S*)-2-Bromo-9-pivaloyloxyruban-3-one 2e. Rubanone **1e** (396 mg, 1 mmol) afforded after chromatography (EA–MeOH, 20:1) **2e** (305 mg, 64%); ν_{max}(KBr)/cm^{-1} 3080, 2972, 2876, 1740, 1712, 1620, 1592, 1508, 1476, 1432, 1368, 1276, 1236, 1188, 1136, 1072 and 1032; δ_H(400 MHz; $CDCl_3$) 1.27 (9 H, s, H-14, H-15 and H-16), 2.02 (1 H, m, H-7), 2.06–2.16 (2 H, m, H-5), 2.31 (1 H, m, H-7), 2.75 (1 H, m, H-4), 3.45 (1 H, m, H-6), 2.93 (1 H, m, H-6), 3.71 (1 H, m, H-8), 4.04 (3 H, s, H-11′), 6.09 (1 H, s, H-2), 6.71 (1 H, d, *J* 5, H-9), 7.34 (1 H, d, *J* 4, H-3′), 7.36 (1 H, d, *J* 2, H-5′), 7.49 (1 H, dd, *J* 2 and 9, H-7′), 8.15 (1 H, d, *J* 9, H-8′) and 8.82 (1 H, d, *J* 4, H-2′); δ_C(100 MHz; $CDCl_3$) 25.53 (CH_2, C-5), 25.92 (CH_2, C-7), 27.043 (CH_3, C-16), 27.047 (CH_3, C-15), 27.079 (CH_3, C-14), 38.988 (C, C-13), 40.32 (CH, C-4), 44.56 (CH_2, C-6), 55.78 (CH_3, C-11′), 59.84 (CH, C-8), 68.03 (CH, C-2), 72.89 (CH, C-9), 100.61 (CH, C-5′), 118.33 (CH, C-3′), 122.61 (CH, C-7′), 126.16 (C, C-9′), 131.31 (CH, C-8′), 143.50 (C, C-4′), 143.94 (C, C-10′), 146.68 (CH, C-2′), 158.57 (C, C-6′), 176.72 (C, C-12) and 210.79 (C, C-3); *m*/*z* (150 °C) (EI) 476 (M^+, 2%), 474.1149 (M^+. $C_{23}H_{27}N_2O_4{}^{79}Br$ requires 474.1154), 448 (14), 446 (14), 395 (9), 367 (53), 345 (7), 310 (4), 281 (21), 265 (100), 253 (7), 224 (8), 212 (13), 198 (12), 184 (10), 172 (14), 154 (6), 116 (5), 85 (10) and 75 (21).

(2*S*,8*R*,9*S*)-9-Benzoyloxy-2-bromoruban-3-one 2f. Rubanone **1f** (458 mg, 1.1 mmol) afforded after chromatography (MTBE–MeOH, 40:1) **2f** (380 mg, 70%) as a light pink solid, mp 166 °C; ν_{max}(KBr)/cm^{-1} 2956, 2872, 1732, 1724, 1620, 1600, 1508, 1472, 1312, 1268, 1228 and 1108; δ_H(400 MHz; $CDCl_3$) 1.91, 2.07, 2.42 (4 H, m, H-5, H-7), 2.73 (1 H, m, H-4), 2.90, 3.43 (2 H, m, H-6), 3.79 (1 H, m, H-8), 4.02 (3 H, s, H-11′), 6.07 (1 H, s, H-2), 6.93 (1 H, d, *J* 5, H-9), 7.34–7.55 (5 H, m, Ar), 7.64 (1 H, m, Ar), 8.05 (3 H, m, Ar) and 8.72 (1 H, d, *J* 4, H-2′); δ_C(100 MHz; $CDCl_3$) 25.42, 26.09 (CH_2, C-5, C-7), 40.39 (CH, C-4), 44.64 (CH_2, C-6), 55.79 (CH_3, C-11′), 60.01 (CH, C-8), 67.90 (CH, C-9), 73.71 (CH, C-2), 100.88 (CH, C-5′), 117.92 (CH, C-3′), 122.26 (CH, C-7′), 126.30 (C, C-9′), 128.91, 129.61, 134.01 (CH, Ph), 129.39 (C, Ph), 132.08 (CH, C-8′), 142.51, 144.68 (C, C-4′, C-10′), 147.30 (CH, C-2′), 158.48 (C, C-6′), 164.99 (C, C-12) and 211.04 (C, C-3); *m*/*z* (190 °C) (EI) 496 (M^+, 3%), 494.0835 (M^+. $C_{25}H_{23}N_2O_4{}^{79}Br$ requires 494.0841), 495/493 (3), 468/466 (7), 453/451 (3), 388/386 (8), 387 (24), 265 (43), 182 (4), 105 (100).

(2*S*,8*R*,9*S*)-2-Bromo-9-formyloxyruban-3-one 2g. Rubanone **1g** (340 mg, 1 mmol) afforded after chromatography (EA–MeOH, 20:1) **2g** (239 mg, 57%) as a light yellow solid, mp 163 °C; ν_{max}(KBr)/cm^{-1} 3068, 2952, 2872, 1744, 1620, 1592, 1508, 1456, 1432, 1372, 1308, 1228, 1144, 1068 and 1048; δ_H(400 MHz; $CDCl_3$) 1.75 (1 H, m, H-5), 1.98 (1 H, m, H-5), 2.22 (1 H, m, H-7), 2.36 (1 H, m, H-7), 2.72 (1 H, m, H-4), 3.40 (1 H, m, H-6), 3.04 (1 H, m, H-6), 3.83 (1 H, m, H-8), 4.08 (3 H, s, H-11′), 6.09 (1 H, s, H-2), 6.86 (1 H, d, *J* 6, H-9), 7.43 (1 H, d, *J* 2, H-5′), 7.52 (1 H, d, *J* 4, H-3′), 7.58 (1 H, dd, *J* 2 and 9, H-7′), 8.15 (1 H, d, *J* 9, H-8′), 8.32 (1 H, s, H-12) and 8.78 (1 H, d, *J* 4, H-2′); δ_C(100 MHz; $CDCl_3$) 24.21 (CH_2, C-5), 25.46 (CH_2, C-7), 40.54 (CH, C-4), 45.17 (CH_2, C-6), 56.12 (CH_3, C-11′), 60.42 (CH, C-8), 69.55 (CH, C-2), 73.28 (CH, C-9), 101.26 (CH, C-5′), 118.24 (CH, C-3′), 121.07 (CH, C-7′), 125.21 (C, C-9′), 132.33 (CH, C-8′), 143.77 (C, C-4′), 144.53 (C, C-10′), 146.69 (CH, C-2′), 159.19 (C, C-6′), 159.46 (CH, C-12) and 211.34 (C, C-3); *m*/*z* (150 °C) (EI) 390 (M^+ − HCO, 3%), 375 (2), 311 (5), 283 (3), 266 (6), 251 (3), 224 (2), 210 (3), 199 (3), 184 (3), 173 (5), 159 (5), 149 (5), 121 (8), 96 (28), 82 (100), 81 (46) and 79 (48).

Preparation of N,O-acetals 3b–e and 3g

Pure starting material is essential for the synthesis of N,O-acetals. A mixture of α-brominated ketone (0.3 mmol), NaI (45 mg, 0.3 mmol) and NaN_3 (2.6 g, 40 mmol) in abs. DMF (2 ml) was stirred for 10 h at 110 °C. After cooling the reaction mixture to r.t. $CHCl_3$ was added and the mixture was extracted with water. The organic layer was dried ($MgSO_4$), evaporated and purified by chromatography.

(2*R*,8*R*,9*S*)-2-Acetyl-2,9-epoxyruban-3-one 3b. α-Brominated ketone **2b** (130 mg, 0.3 mmol) afforded after chromatography (MTBE–MeOH, 20:1) **3b** (79 mg, 75%) as a solid, mp 172 °C (Found: C, 67.67; H, 6.28; N, 7.82; $C_{20}H_{20}N_2O_4$ requires C, 67.77; H, 6.26; N, 7.91%); ν_{max}(KBr)/cm^{-1} 2956, 2888, 1748, 1712, 1676, 1620, 1508, 1472, 1356, 1228, 1124 and 1028; δ_H(400 MHz; $CDCl_3$) 1.32, 1.68, 2.00, 2.19 (4 H, m, H-5, H-7), 2.32 (1 H, m, H-4), 2.49 (3 H, s, H-13), 3.18, 3.32 (2 H, m, H-6), 3.97 (3 H, s, H-11′), 4.31 (1 H, m, H-8), 6.05 (1 H, d, *J* 4, H-9), 7.05 (1 H, d, *J* 2.5, H-5′), 7.41 (1 H, dd, *J* 2.5 and 10, H-7′), 7.44 (1 H, d, *J* 4, H-3′), 8.07 (1 H, d, *J* 10, H-8′) and 8.78 (1 H, d, *J* 4, H-2′); δ_C(100 MHz; $CDCl_3$) 22.72, 27.38 (CH_2, C-5, C-7), 26.37 (CH_3, C-13), 36.70 (CH, C-4), 37.46 (CH_2, C-6), 55.69 (CH_3, C-11′), 57.21 (CH, C-8), 79.52 (CH, C-9), 93.89 (C, C-2), 100.83 (CH, C-5′), 119.12 (CH, C-3′), 121.63 (CH, C-7′), 125.93 (C, C-9′), 132.11 (CH, C-8′), 140.27, 144.10 (C, C-4′, C-10′), 148.03 (CH, C-2′), 158.16 (C, C-6′), 204.59 (C, C-12) and 210.91 (C, C-3); *m*/*z* (FAB) (EI) 353 (M^+ + 1, 100%) and 324 (37).

(2*R*,8*R*,9*S*)-2,9-Epoxy-2-propionylruban-3-one 3c. α-Brominated ketone **2c** (134 mg, 0.3 mmol) afforded after chromatography (MTBE–MeOH, 20:1) **3c** (80 mg, 73%) as a colourless solid, mp 180 °C; ν_{max}(KBr)/cm^{-1} 2956, 2876, 1748, 1716, 1672, 1620, 1592, 1508, 1472, 1432, 1356, 1240, 1172, 1144, 1124 and 1052; δ_H(400 MHz; $CDCl_3$) 1.14 (3 H, t, *J* 8, CH_2CH_3), 1.33, 1.67, 2.02, 2.22 (4 H, m, H-5, H-7), 2.33 (1 H, m, H-4), 2.93 (2 H, m, CH_2CH_3), 3.15, 3.35 (2 H, m, H-6), 3.95 (3 H, s, H-11′), 4.29 (1 H, m, H-8), 6.03 (1 H, d, *J* 4, H-9), 7.04 (1 H, d, *J* 2.5, H-5′), 7.42 (1 H, dd, *J* 2.5 and 10, H-7′), 7.44 (1 H, d, *J* 4, H-3′), 8.08 (1 H, d, *J* 10, H-8′) and 8.78 (1 H, d, *J* 4, H-2′); δ_C(100 MHz; $CDCl_3$) 6.79 (CH_2CH_3), 22.78, 27.40 (CH_2, C-5, C-7), 31.91 (CH_2, CH_2CH_3), 36.68 (CH, C-4), 37.60 (CH_2, C-6), 55.59 (CH_3, C-11′), 57.19 (CH, C-8), 79.41 (CH, C-9), 93.89 (C, C-2), 100.68 (CH, C-5′), 119.12 (CH, C-3′), 121.53 (CH, C-7′), 125.82 (C, C-9′), 132.06 (CH, C-8′), 140.28, 143.96 (C, C-4′, C-10′), 148.05 (CH, C-2′), 158.04 (C, C-6′), 207.01 (C, C-12) and 211.11 (C, C-3); *m*/*z* (FAB) (EI) 367 (M^+ + 1, 100%) and 338 (27).

(2*R*,8*R*,9*S*)-2,9-Epoxy-2-isobutyrylruban-3-one 3d. α-Brominated ketone **2d** (139 mg, 0.3 mmol) afforded after chromatography (EA–MeOH, 20:1) **3d** (74 mg, 65%) (Found: C, 69.34; H, 6.26; N, 7.74; $C_{22}H_{24}N_2O_4$ requires C, 69.45; H, 6.35; N, 7.40%); ν_{max}(KBr)/cm^{-1} 2972, 2872, 1732, 1718, 1672, 1640, 1592, 1508, 1468, 1432, 1384, 1368, 1264, 1228, 1144, 1092, 1052 and 1032; δ_H(400 MHz; $CDCl_3$) 1.19–1.34 (6 H, m, H-14 and H-15), 1.65 (1 H, m, H-7), 1.98–2.09 (2 H, m, H-5), 2.23 (1 H, m, H-7), 2.33 (1 H, m, H-4), 2.85 (1 H, m, H-13), 3.44 (1 H, m, H-6), 3.75 (1 H, m, H-6), 3.99 (3 H, s, H-11′), 4.34 (1 H, m, H-8), 6.06 (1 H, d, *J* 4, H-9), 7.08 (1 H, d, *J* 2, H-5′), 7.45 (1 H, dd, *J* 2 and 9, H-7′), 7.48 (1 H, d, *J* 4, H-3′), 8.11

(1 H, d, *J* 9, H-8′) and 8.79 (1 H, d, *J* 4, H-2′); δ_C(100 MHz; $CDCl_3$), 22.66 (CH_2, C-5), 23.46 (CH_3, C-15), 23.57 (CH_3, C-14), 27.39 (CH_2, C-7), 36.14 (CH, C-4), 37.54 (CH_2, C-6), 42.58 (CH, C-13), 55.70 (CH_3, C-11′), 57.25 (CH, C-8), 79.54 (CH, C-9), 94.41 (C, C-2), 100.78 (CH, C-5′), 119.21 (CH, C-3′), 121.64 (CH, C-7′), 125.93 (C, C-9′), 132.10 (CH, C-8′), 140.57 (C, C-4′), 143.93 (C, C-10′), 147.93 (CH, C-2′), 158.14 (C, C-6′), 209.94 (C, C-12) and 211.21 (C, C-3); *m*/*z* (120 °C) (EI) 366 (M^+ − Me, 3%), 353 (1), 283 (9), 267 (10), 265 (100), 253 (2), 237 (3), 224 (7), 211 (2), 168 (2), 147 (1), 102 (2), 83 (2) and 75 (11); *m*/*z* (FAB) (EI) 381 (M^+ + 1, 28%), 149 (30) and 133 (100).

(2*R*,8*R*,9*S*)-2,9-Epoxy-2-pivaloylruban-3-one 3e. α-Brominated ketone **2e** (142 mg, 0.3 mmol) afforded after chromatography (EA–MeOH, 20 : 1) **3e** (60 mg, 51%); $\nu_{max}(CHCl_3)$/cm^{-1} 2960, 2928, 2872, 1732, 1718, 1672, 1620, 1508, 1468, 1428, 1364, 1340, 1264, 1224, 1148, 1100, 1072 and 1032; δ_H(400 MHz; $CDCl_3$) 1.26 (9 H, s, H-14, H-15 and H-16), 1.62 (1 H, m, H-5), 2.10 (1 H, m, H-5), 2.23 (1 H, m, H-7), 2.35 (1 H, m, H-7), 2.60 (1 H, m, H-4), 3.28 (1 H, m, H-6), 3.65 (1 H, m, H-6), 3.91 (3 H, s, H-11′), 4.51 (1 H, m, H-8), 6.21 (1 H, d, *J* 2, H-9), 6.99 (1 H, d, *J* 2, H-5′), 7.37 (1 H, d, *J* 4, H-3′), 7.40 (1 H, dd, *J* 2 and 9, H-7′), 8.08 (1 H, d, *J* 9, H-8′) and 8.89 (1 H, d, *J* 4, H-2′); δ_C(100 MHz; $CDCl_3$) 22.70 (CH_2, C-5), 27.07 (CH_3, C-16), 27.16 (CH_3, C-15), 27.23 (CH_3, C-14), 27.61 (CH_2, C-7), 36.23 (CH, C-4), 40.15 (CH_2, C-6), 47.43 (C, C-13), 55.69 (CH_3, C-11′), 56.43 (CH, C-8), 77.86 (CH, C-9), 95.09 (C, C-2), 100.62 (CH, C-5′), 118.34 (CH, C-3′), 121.98 (CH, C-7′), 127.96 (C, C-9′), 131.78 (CH, C-8′), 143.92 (C, C-4′), 144.03 (C, C-10′), 147.45 (CH, C-2′), 158.58 (C, C-6′), 214.88 (C, C-12) and 216.98 (C, C-3); *m*/*z* (160 °C) (EI) 394.2254 (M^+. $C_{23}H_{26}N_2O_4$ requires 394.2256), 368 (40%), 353 (24), 283 (31), 267 (100), 253 (19), 225 (17), 210 (21), 196 (7), 188 (16), 172 (35), 154 (7) and 96 (18).

(2*R*,8*R*,9*S*)-2,9-Epoxy-2-formylruban-3-one 3g. α-Brominated ketone **2g** (126 mg, 0.3 mmol) afforded after chromatography (EA–MeOH, 20 : 1) **3g** (77 mg, 76%) (Found: C, 67.86; H, 5.53; N, 8.30; $C_{19}H_{18}N_2O_4$ requires C, 67.45; H, 5.35; N, 8.28%); $\nu_{max}(CHCl_3)/cm^{-1}$ 2944, 2872, 1732, 1620, 1592, 1508, 1472, 1428, 1348, 1304, 1260, 1228, 1144, 1120, 1092, 1056 and 1028; δ_H(400 MHz; $CDCl_3$) 1.32 (1 H, m, H-5), 1.64 (1 H, m, H-5), 2.14 (2 H, m, H-7), 2.31 (1 H, m, H-4), 3.28 (1 H, m, H-6), 3.39 (1 H, m, H-6), 3.98 (3 H, s, H-11′), 4.29 (1 H, m, H-8), 5.94 (1 H, d, *J* 4, H-9), 7.09 (1 H, d, *J* 4, H-3′), 7.42 (1 H, d, *J* 2, H-5′), 7.46 (1 H, dd, *J* 2 and 9, H-7′), 8.09 (1 H, d, *J* 9, H-8′), 8.79 (1 H, d, *J* 4, H-2′) and 9.89 (1 H, s, H-12); δ_C(100 MHz; $CDCl_3$) 22.23 (CH_2, C-5), 29.75 (CH_2, C-7), 35.95 (CH, C-4), 37.22 (CH_2, C-6), 55.48 (CH_3, C-11′), 57.39 (CH, C-8), 80.18 (CH, C-9), 91.74 (C, C-2), 100.97 (CH, C-5′), 119.31 (CH, C-3′), 121.45 (CH, C-7′), 126.06 (C, C-9′), 132.11 (CH, C-8′), 141.09 (C, C-4′), 144.10 (C, C-10′), 148.13 (CH, C-2′), 158.03 (C, C-6′), 210.34 (C, C-3) and 213.44 (CH, C-12); *m*/*z* (170 °C) (EI) 309 (M^+ − HCO, 0.4%), 285 (1), 283 (35), 267 (5), 241 (5), 224 (16), 210 (100), 196 (13), 183 (51), 169 (13), 154 (9), 141 (8), 115 (6), 106 (6) and 89 (4).

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