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Polyhydroxylated pyrrolizidines. Part 5: Stereoselective synthesis of 1,2-dihydroxypyrrolizidines as a model for the preparation of densely polyhydroxylated pyrrolizidines☆

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Abstract—The reaction of *N*-benzyloxycarbonyl-L-prolinal **5** with (methoxycarbonylmethylene)triphenylphosphorane in CH_2Cl_2 afforded methyl (*E*)-3-[(2′*S*)-*N*-benzyloxycarbonylpyrrolidin-2′-yl]propenoate **7**. When the reaction was performed in MeOH, an appreciable amount of the (*Z*)-isomer **6** was obtained. Compounds **7** and **6** were dihydroxylated to the corresponding 2,3-dihydroxy esters **8**–**9** and **20**–**21**, respectively. The stereochemistry of the latter compounds could be determined after their transformations into the corresponding 1,2-dihydroxypyrrolizidin-3-ones **11**–**16** and **23**–**25**, respectively. Finally, lactams **11**, **16**, and **25** were reduced to the related pyrrolizidines **14**, **19**, and **27**.

1. Introduction

Continuing with our efforts on the synthesis of polyhydroxylated pyrrolizidinic alkaloids (PHPAs), we were interested in exploring the possibility of preparing those with the highest degree of hydroxylation found in nature so far, such as casuarine **1**[2] and hyacinthacine C_1 **2**.[3]

According to Figure 1, construction of the target PHPAs **1** and **2** can be accomplished as follows: ring **A** comes from a suitably protected polyhydroxypyrrolizidine[4] (DGDP, DMDP, etc.), which transfers its inherent chirality to the final compound, whereas the **B** ring, with the appropriate stereochemistry, can be built up following a synthetic route similar to that

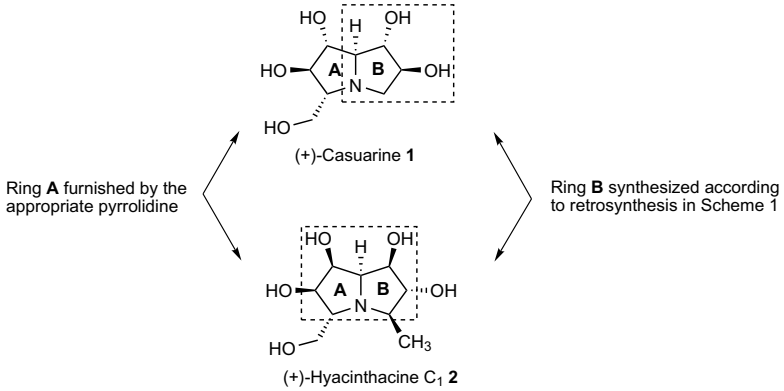

Figure 1. (+)-Casuarine **1** and (+)-hyacinthacine C_1 **2**.

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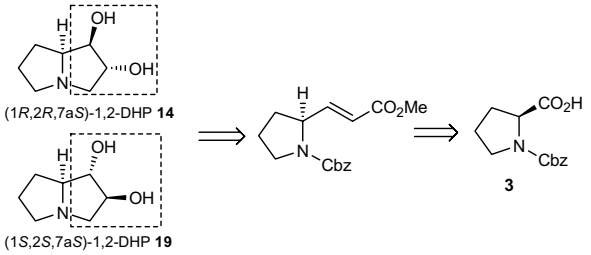
outlined in Scheme 1, where the retrosynthesis for less elaborated 1,2-dihydroxypyrrolizidines[5] with chiralities matching those in the target molecules is displayed, consisting of a carbon-chain lengthening and subsequent dihydroxylation under the absence and presence of chiral ligands. Accordingly, the commercial *N*-benzyloxycarbonyl-L-proline **3** would be an excellent starting material for these purposes in order to investigate not only the suitability of the synthetic proposal, but also the possibility of controlling its stereochemical outcomes and hence apply these results in the preparation of **1** and **2**.

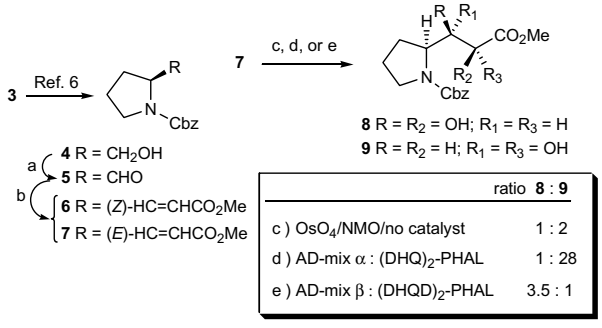


Scheme 1. Retrosynthesis of (1*R*,2*R*,7a*S*)-**14** and (1*S*,2*S*,7a*S*)-1,2-dihydroxypyrrolizidine **19** from *N*-Cbz-L-proline **3**.

2. Results and discussion

With the above objective in mind, compound **3** was reduced[6] to alcohol **4** and subsequently transformed into the related derivative of L-prolinal **5**[7] by oxidation with PCC. Reaction of **5** with (methoxycarbonylmethylene)triphenyl phosphorane gave methyl (*E*)-3-[(2′*S*)-*N*-benzyloxycarbonylpyrrolidin-2′-yl]propenoate **7** in a highly stereoselective manner,[8] which was shown to be a mixture of rotamers (^{1}H and ^{13}C NMR evidence).[9] Analytical and spectroscopic data for **7** are in accordance with those previously reported for *rac*-**7**.[10]

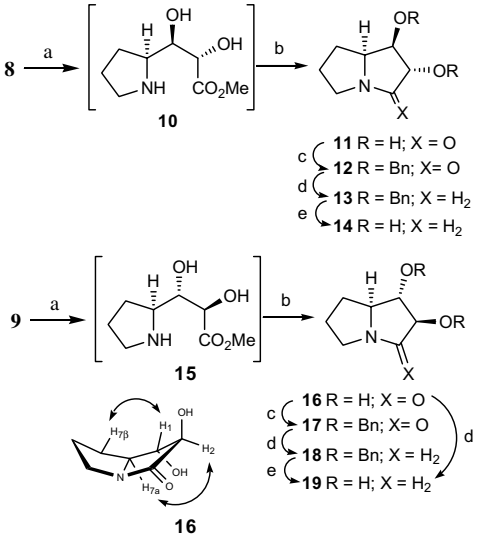
Following Scheme 2, dihydroxylation (DH) of α-β-unsaturated ester **7** gave a resolvable mixture of the methyl (2*S*,3*R*)-**8** and (2*R*,3*S*)-2,3-dihydroxy-3-[(2′*S*)-*N*-benzyloxycarbonylpyrrolidin-2′-yl]propanoate **9**, in a moderate 1:2 diastereomeric excess [GLC analysis (B) of TMS derivatives[11]]. When the reaction was performed under Sharpless conditions (ADH),[12] a notable increase in the diastereomeric ratio (1:28) in the presence of an AD-mix α® catalyst was observed, whereas a reverse stereoselectivity (3.5:1) was obtained when the AD-mix β® catalyst was used. These results agree with the empirical rule outlined for ADH,[13] and with those recently reported by Robina and co-workers,[14] where a similar behavior for an analogue of **7** was observed.



Scheme 2. Reagents and conditions: (a) PCC/4 Å MS/CH_2Cl_2; (b) $Ph_3P{=}CHCO_2Me$/either CH_2Cl_2 or MeOH/rt.

The absolute configurations of the new stereogenic centers in **8** and **9** could be determined after their transformations into the related γ-lactams **11** and **16**. This involved *N*-deprotection to **10** and **15**, respectively, followed by the corresponding cyclization promoted by basic medium (MeONa/MeOH). Compound **16** had spectroscopic data, which closely matched those previously reported,[5b] although some discrepancy occurred with the optical data. Nevertheless, ^{1}H–^{1}H and ^{1}H–^{13}C COSY, and extensive NOE experiments confirmed the proposed structure for **16** and allowed the assignment of its ^{1}H and ^{13}C NMR signals.

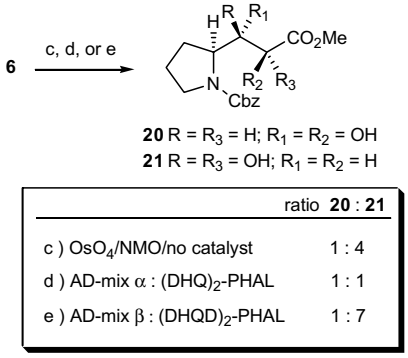
From the above results it was concluded that the configurations for **8**–**11** must be those shown in Scheme 3.



Scheme 3. Reagents and conditions: (a) H_2/10% Pd–C/MeOH; (b) MeONa (cat.)/MeOH/Δ; (c) $NaCH_2SOMe$/DMSO/BnBr; (d) LAH/Et_2O; (e) H_2/10% Pd–C/HCl/MeOH then Amberlite IRA-400 (OH^- form). NOE interactions in **16**.

Reduction of **16** with LAH to pyrrolizidine **19** went to completion (TLC analysis) but resulted in an unsatisfactory recovery of the final compound. For this reason, both **11** and **16** were transformed into the 1,2-di-*O*-benzyl derivatives **12** and **17** prior to their respective reductions affording in this case, pyrrolizidines **13** and **18** in good yields, which were finally, *O*-debenzylated to the required **14** and **19**. The latter has the same spectroscopy data to those reported for itself,[5b] but a discrepancy in the optical data was found again, although ^{1}H–^{1}H and ^{1}H–^{13}C COSY, and NOE experiments confirmed the proposed structure for **19** and hence that of **14**.

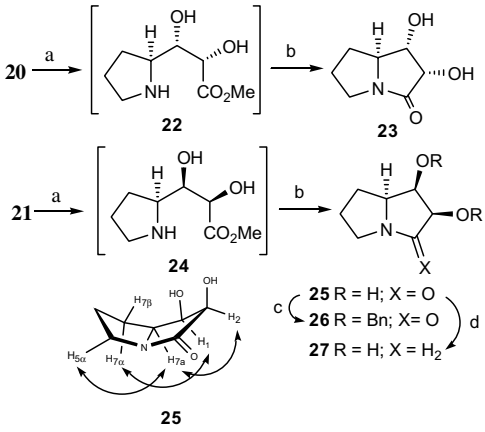
In a similar manner, the DH reaction on methyl (*Z*)-3-[(2′*S*)-*N*-benzyloxycarbonylpyrrolidin-2′-yl]propenoate **6** afforded methyl (2*S*,3*S*)-**20** and (2*R*,3*R*)-2,3-dihydroxy-3-[(2′*S*)-*N*-benzyloxycarbonylpyrrolidin-2′-yl]propanoate **21** in the ratios shown in Scheme 4 (GLC analysis, B), depending on the reaction conditions.



	ratio **20** : **21**
c) OsO_4/NMO/no catalyst	1 : 4
d) AD-mix α : $(DHQ)_2$-PHAL	1 : 1
e) AD-mix β : $(DHQD)_2$-PHAL	1 : 7

Scheme 4. Dihydroxylations of **6**.

The stereochemistry of dihydroxyesters **20** and **21**, were established after their transformation into the related-lactams **23** and **25** as above. Thus, NOE experiments on dihydroxylactam **25** (Scheme 5) were consistent with a (1*R*,2*R*)-configuration, lately confirmed by reduction to the well known pyrrolizidine **27**.[5a] On the basis of these results the absolute configurations for **23**, and hence that for **20**, must be those above mentioned.



Scheme 5. Reagents and conditions: (a) H_2/10% Pd–C/MeOH; (b) MeONa (cat.)/MeOH/Δ; (c) NaH/DMSO/BnBr; (d) H_3B–SMe_2/THF, rt. NOE interactions in **25**.

From all the above results, it can be concluded that the synthetic methodology reported herein, is very appropriate for preparing highly hydroxylated pyrrolizidines in a stereocontrolled manner.

3. Experimental

Solutions were dried over $MgSO_4$ before concentration under reduced pressure. The ^1H and ^{13}C NMR spectra were recorded with Bruker AMX-300, AM-300, and ARX-400 spectrometers for solutions in $CDCl_3$ (internal Me_4Si). IR spectra were recorded with a Perkin–Elmer 782 instrument and mass spectra with a Hewlett–Packard HP-5988-A and Fisons mod. Platform II and VG Autospec-Q mass spectrometers. Optical rotations were measured for solutions in $CHCl_3$ (1 dm tube) with a Jasco DIP-370 polarimeter. GLC was performed on a Hewlett–Packard 6890 gas chromatograph equipped with a split/splitless injector, a flame-ionization detector, and a capillary HP-5 column (30 m × 0.25 mm i.d. × 0.25 μm film thickness) at: (A) 10 min at 230 °C, program to 250 °C, 20 °C/min; the He flow rate was 0.7 mL/min; the injection port and the zone-detector temperatures were 250 °C; (B) 3 min at 110 °C program to 250 °C, 20 °C/min, the He flow rate was 1.1 mL/min, the injection port and the zone-detector temperatures were 285 °C. TLC was performed on precoated silica gel 60 F_{254} aluminum sheets and detection by charring with H_2SO_4. Column chromatography was performed on silica gel (Merck, 7734). The noncrystalline compounds were shown to be homogeneous by chromatographic methods and characterized by NMR, MS, and HRMS.

3.1. *N*-Benzyloxycarbonyl-L-prolinal 5

To a stirred solution of *N*-benzyloxycarbonyl-L-prolinol[6] **4** (2 g, 8.5 mmol) in dry CH_2Cl_2 (30 mL) were added pyridinium chlorochromate (3 g, 13.8 mmol) and 4 Å molecular sieves (3 g). Stirring was continued for 2 h at room temperature. GLC (A) showed that **4** (t_R 5.66 min) had disappeared and that a new compound (t_R 5.02 min) was present. Et_2O (30 mL) was added and after 15 min, the mixture was filtered through a Silica Gel G pad and concentrated to a residue that was percolated (Et_2O) to afford pure **5** (1.8 g, 90%), which had physical and spectroscopic data in accordance with those previously reported.[7a]

3.2. Methyl (*Z*)-6 and (*E*)-3-[(2′*S*)-*N*-benzyloxycarbonylpyrrolidin-2′-yl]propenoate 7

3.2.1. Reaction in CH_2Cl_2. To a solution of **5** (1.4 g, 6 mmol) in CH_2Cl_2 (20 mL) (methoxycarbonylmethylenetriphenyl)phosphorane (3 g, 9 mmol) was added, and the mixture left at rt. After 6 h, GLC (A) showed a new compound (t_R 9.65 min) and no aldehyde. The reaction mixture was supported on silica gel and submitted to chromatography (Et_2O–hexane, 2:1) to afford pure **7** (1.5 g, 86%) as a colorless thick syrup, which had $[\alpha]_D^{26} = -67$ (*c* 1.1). IR (KBr): 3032 (aromatic), 1716, 1708, and 1699 (C=O and C=C), and 696 cm^{-1} (aromatic). NMR data (400 MHz): ^1H, δ 7.35–7.28 (m, 5H, Ph), 6.84 and 6.80 (2dd, 1H, $J_{2',3}$ 5.6 Hz, H-3), 5.86 and 5.76 (2d, 1H, $J_{2,3}$ 15.6 Hz, H-2), 5.14 and 5.07 (2d, *J* 12.5 Hz, CH_2Ph) and 5.08 (s, CH_2Ph), 4.54 and 4.47 (2m, 1H, H-2′), 3.76–3.62 and 3.50–3.39 (2m, 2H, H-5′a,5′b), 3.70 (s, 3H, OMe), 2.12–2.01 and 1.90–1.75 (2m, 4H, H-3′a,3′b,4′a,4′b); ^{13}C (100 MHz, inter alia): δ 166.83 (C-1), 154.81 (C=O, Cbz), 148.29 and 147.83 (C-3), 120.53 (C-2), 66.95 and 66.75 (*C*H_2Ph), 58.12 and 57.75 (C-2′), 51.64 (OMe), 46.85 and 46.48 (C-5′),

31.71 and 30.83 (C-4′), 23.63 and 22.82 (C-3′). Mass spectrum (LSIMS): *m/z*: 312.1215 [M^++Na] for $C_{16}H_{19}NO_4Na$ 312.1212 (deviation − 1.1 ppm).

3.2.2. Reaction in MeOH. To a solution of **5** (1.64 g, 7 mmol) in dry MeOH (50 mL), (methoxycarbonylmethylenetriphenyl)phosphorane (3.5 g, 10.6 mmol) was added, and the mixture left at rt for 3 h. GLC (A) showed no aldehyde, and the presence of **7** together with new compound **6** (t_R 8.40 min) in a 1.3:1 ratio, respectively. The reaction mixture was supported on silica gel and submitted to chromatography (Et_2O–hexane, 1:4) to first afford pure **6** (414 mg) as a colorless syrup, which had $[\alpha]_D^{24} = +32$ (*c* 1); t_R 8.40 min. IR (KBr): 3033 (aromatic), 1704, 1700, and 1648 (C=O and C=C), 698 cm^{-1} (aromatic). NMR data (400 MHz): ^1H, δ 7.35–7.27 (m, 5H, Ph), 6.23 and 6.13 (2dd, 1H, $J_{2',3}$ 8.2 Hz, H-3), 5.78 and 5.70 (2d, 1H, $J_{2,3}$ 11.5 Hz, H-2), 5.35 (m, 1H, H-2′), 5.10 (m, 2H, CH_2Ph) 3.76 and 3.67 (m, 2H, H-5′a,5′b), 3.69 and 3.68 (2s, 3H, OMe), 2.36–2.28, 1.90–1.80, and 1.75–1.60 (3m, 4H, H-3′a,3′b,4′a,4′b); ^{13}C (100 MHz, inter alia): δ 166.31 and 164.60 (C-1), 155.07 (C=O, Cbz), 152.26 and 152.01 (C-3), 118.76 and 118.35 (C-2), 66.81 and 66.69 (CH_2Ph), 56.48 and 55.52 (C-2′), 51.27 (OMe), 47.25 and 46.89 (C-5′), 33.14 and 32.49 (C-4′), 24.77 and 24.08 (C-3′). Mass spectrum (LSIMS): *m/z*: 312.1214 [M^++Na] for $C_{16}H_{19}NO_4Na$ 312.1212 (deviation − 0.6 ppm).

Eluted second was a mixture of **6** and **7** (370 mg) and finally pure **7** (1.15 g). Total yield 95%.

3.3. Methyl (2*S*,3*R*)-8 and (2*R*,3*S*)-2,3-dihydroxy-3-[(2′S)-*N*-benzyloxycarbonylpyrrolidin-2′-yl]propanoate (9)

3.3.1. Dihydroxylation of 7 without a chiral catalyst. To a stirred solution of **7** (2.6 g, 9 mmol) in acetone–water 8:1 v/v (36 mL), was added *N*-oxide-*N*-methylmorpholine (2 g, 18 mmol) and aqueous 1% OsO_4 (4 mL). The mixture was left at room temperature overnight. GLC[11] (B) then revealed the presence of two new products (t_R 17.73 and 18.02 min) in a 1:2 ratio. The mixture was concentrated to a residue that was submitted to chromatography (Et_2O–hexane, 4:1). Eluted first was pure **8** (780 mg, 27%) as a colorless syrup; t_R 17.73 min; $[\alpha]_D^{27} = -51$ (*c* 1). IR (neat): 3415 (OH), 3064 (aromatic), 1747 and 1669 (C=O), and 697 cm^{-1} (aromatic). NMR data (400 MHz): ^1H, δ 7.33 (m, 5H, Ph), 5.14 and 5.10 (2d, 2H, *J* 12.5 Hz, CH_2Ph), 4.18 (dt, 1H, *J* 5.5, *J* 8.2 Hz, H-2′), 4.14 (s, 1H, H-2), 3.83 (d, 1H, $J_{2',3}$ 8.7 Hz, H-3), 3.79 (s, 3H, OMe), 3.61 and 3.36 (2dt, 2H, *J* 6.8, *J* 10.8 Hz, H-5′a,5′b), 2.16–2.07 (m, 1H, H-3′a), 1.96–1.78 (2m, 2H, H-4′a,4′b), and 1.76–1.68 (m, 1H, H-3′b); ^{13}C (100 MHz): δ 173.34 (C-1), 158.54 (Cbz), 136.21, 128.62, 128.29, 128.12 (Ph), 76.96 (C-3), 72.11 (C-2), 67.83 (CH_2Ph), 60.42 (C-2′), 52.73 (OMe), 47.39 (C-5′), 28.70 (C-3′), and 24.21 (C-4′). Mass spectrum (LSIMS): *m/z*: 346.1261 [M^++Na] for $C_{16}H_{21}NO_6Na$ 346.1267 (deviation + 1.7 ppm).

Eluted second was pure **9** (1.44 g, 50%); t_R 18.02 min, as white crystals, mp 100–102 °C (from Et_2O–hexane); $[\alpha]_D^{26} = -55$ (*c* 1, MeOH). IR (KBr): 3300 (OH), 3010 (aromatic), 1752 (C=O, ester), 1691 (C=O, Cbz), and 700 cm^{-1} (aromatic). NMR data (400 MHz): ^1H, δ 7.33 (m, 5H, Ph), 5.12 (s, 2H, CH_2Ph), 4.83 (d, 1H, $J_{2,OH}$ 4.7 Hz, HO-2), 4.27 (d, 1H, H-2), 3.90 (br t, 1H, H-2′), 3.77 (s, 3H, OMe), 3.65 (br d, 1H, $J_{2',3}$ 8.8 Hz, H-3), 3.42 (br t, 2H, *J* 5.5 Hz, H-5′a,5′b), 2.74 (br s, 1H, HO-3), 2.15 (m, 1H, H-4′a), 1.92 (m, 3H, H-3′a,3′b,4′b); ^{13}C (100 MHz): δ 172.23 (C-1), 157.54 (Cbz), 136.19, 128.66, 128.33, 128.00 (Ph), 73.64 (C-3), 70.88 (C-2), 67.72 (CH_2Ph), 59.74 (C-2′), 52.50 (OMe), 47.24 (C-5′), 27.71 (C-4′), and 23.24 (C-3′). Mass spectrum (LSIMS): *m/z*: 346.1261 [M^++Na] for $C_{16}H_{21}NO_6Na$ 346.1267 (deviation + 1.6 ppm). Anal. Calcd for $C_{16}H_{21}NO_6$: C, 59.43; H, 6.55; N, 4.33. Found: C, 59.57; H, 6.48; N, 3.97.

A mixture of **8** and **9** (160 mg, 5.5%) was also obtained.

3.3.2. Dihydroxylation of 7 with chiral catalyst. Potassium ferricyanide (III) (170 mg, 0.52 mmol), K_2CO_3 (67 mg, 0.68 mmol) and either hydroquinine-1,4-phthalazinediyldiether [$(DHQ)_2PHAL$] (1.4 mg, 1.8 μmol) or hydroquinidine-1,4-phthalazinediyldiether [$(DHQD)_2PHAL$] were stirred in 2-propanol–water (1:1, 7 mL) after which 0.071 M OsO_4 in water (5 μL) was added. The mixture was stirred at rt for 15 min. To this was added methanesulfonamide (18 mg, 190 μmol) and the mixture ice-water cooled. Compound **7** (50 mg, 170 μmol) in 2-propanol–water (1:1, 3 mL) was added and the mixture stirred for 2 h and then allowed to reach rt overnight. TLC (Et_2O) revealed the absence of **7** and the presence of **8** and **9**. The reaction was quenched by the addition of Na_2SO_3 (270 mg) followed by stirring at rt for another 30 min. The mixture was subsequently extracted with EtOAc (4 × 5 mL). The combined organic extracts were concentrated and the residue analyzed[11] by GLC (B) to give **8** and **9** in 1:28 and 3.5:1 ratios, respectively.

3.4. (1*R*,2*S*,7a*S*)-1,2-Dihydroxypyrrolizidin-3-one 11

A solution of **8** (730 mg, 2.26 mmol) in MeOH (20 mL) was stirred at rt with 10% Pd–C (90 mg) in an H_2 atmosphere for 3 h. TLC (Et_2O) showed the presence of a non-mobile compound, presumably the *N*-deprotected pyrrolidine **10**. The catalyst was filtered off, washed with MeOH and the combined filtrate and washings (50 mL) treated with 2 M MeONa (2 mL) and refluxed for 6 h. TLC (Et_2O–MeOH, 1:1) revealed the presence of a faster-running product. The mixture was neutralized with aqueous 10% HCl, supported on silica gel and submitted to chromatography (Et_2O–MeOH, 20:1) to afford **11** (220 mg, 61%) as white crystals, mp 143–144 °C (from EtOAc); $[\alpha]_D^{23} = +6.3$ (*c* 1, MeOH). IR (KBr): 3397 (OH), and 1671 cm^{-1} (C=O, lactam). NMR data (400 MHz, MeOH-d_4): ^1H, δ 4.47 (d, 1H, $J_{1,2}$ 4.0 Hz, H-2), 4.30 (t, 1H, $J_{1,7a}$ 4.0 Hz, H-1), 3.81 (dt, 1H, $J_{7,7a} = J_{7',7a} = 7.2$ Hz, H-7a), 3.49–3.42 (m, 1H, H-5), 3.06–2.99 (m, 1H, H-5′), 2.02–1.92 (m, 3H, H-6,6′,7), and 1.82–1.74 (m, 1H, H-7′); ^{13}C (100 MHz,

MeOH-d_4): δ 175.53 (C-3), 76.28 (C-2), 72.40 (C-1), 63.12 (C-7a), 42.90 (C-5), 26.55 (C-6), and 24.11 (C-7). Anal. Calcd for $C_7H_{11}NO_3$: C, 53.49; H, 7.05; N, 8.91. Found: C, 53.57; H, 7.29; N, 8.98.

3.5. (1*R*,2*S*,7a*S*)-1,2-Dibenzyloxypyrrolizidin-3-one 12

A stirred solution of NaH (60% oil dispersion, 90 mg, 2.1 mmol)) in anhydrous DMSO (6 mL) was heated at 60 °C for 15 min, then cooled at rt, and a solution of **11** (110 mg, 0.7 mmol) in the same solvent (4 mL) added and the mixture heated again at 60 °C for an additional 15 min, under argon. After cooling at rt, BnBr (330 μL, 2.8 mmol) was added, and the reaction mixture stirred for 3 h. TLC (Et_2O) then revealed a faster-running compound. The mixture was then partitioned into water (10 mL) and Et_2O (40 mL), the organic phase was separated, then concentrated. Column chromatography (Et_2O–hexane, 3:1) of the residue afforded pure **12** (180 mg, 76%) as white crystals, mp 72–73 °C; $[\alpha]_D^{21} = +31$ (*c* 1). IR (KBr): 3036 (aromatic), and 1695 cm^{-1} (C=O, lactam). NMR data (400 MHz): ^1H, δ 7.40–7.23 (m, 10H, $2CH_2Ph$), 5.01 and 4.78 (2d, 2H, *J* 12.3 Hz, CH_2Ph), 4.78 and 4.58 (2d, 2H, *J* 12.1 Hz, CH_2Ph), 4.28 (d, 1H, $J_{1,2}$ 3.9 Hz, H-2), 4.14 (t, 1H, $J_{1,7a}$ 3.7 Hz, H-1), 3.67 (dt, 1H, $J_{7,7a}$ 3.7, $J_{7',7a}$ 7.1 Hz, H-7a), 3.60 (dt, 1H, $J_{5,6} = J_{5,6'} = 7.3$, $J_{5,5'}$ 11.3 Hz, H-5), 3.01 (ddd, 1H, $J_{5',6}$ 4.7, $J_{5',6'}$ 8.4 Hz, H-5′), 2.07–1.95 (m, 2H, H-6,7), 1.93–1.84 (m, 1H, H-6′), and 1.78–1.72 (m, 1H, H-7′); ^{13}C (100 MHz): δ 171.86 (C-3), 138.26, 137.92, 128.45, 128.36, 127.92, 127.82, 127.79, and 127.69 (CH_2Ph), 80.92 (C-2), 77.30 (C-1), 73.33 and 72.59 (CH_2 Ph), 61.03 (C-7a), 42.08 (C-5), 25.80 (C-6), and 24.16 (C-7). Anal. Calcd for $C_{21}H_{23}NO_3$: C, 74.75; H, 6.87; N, 4.15. Found: C, 74.57; H, 7.10; N, 4.08. Mass spectrum (LSIMS): *m*/*z*: 360.1572 [M^++Na] for $C_{21}H_{23}NO_3Na$ 360.1576 (deviation + 0.9).

3.6. (1*R*,2*R*,7a*S*)-1,2-Dibenzyloxypyrrolizidine 13

To a stirred solution of **12** (137 mg, 0.4 mmol) in anhydrous THF (6 mL) was added $LiAlH_4$ (35 mg, 0.92 mmol), and the mixture refluxed overnight. TLC (Et_2O) then revealed that the starting material was not present. Aqueous 0.5 M NaOH (2 mL) was cautiously added and the mixture partitioned into EtAcO (5 mL) and water (5 mL). The organic phase was separated and the aqueous extracted with EtAcO (3 × 5 mL). The combined extracts were concentrated and the residue submitted to column chromatography (Et_2O–MeOH, 20:1) to afford pure **13** (90 mg, 70%) as a white syrup; $[\alpha]_D^{25} = -15$ (*c* 0.9). IR (neat): 3031 cm^{-1} (aromatic). NMR data (400 MHz, MeOH-d_4): ^1H, δ 7.32 (m, 10H, $2CH_2Ph$), 4.75 and 4.57 (2d, 2H, *J* 11.7 Hz, CH_2Ph), 4.59 and 4.54 (2d, 2H, *J* 11.1 Hz, CH_2Ph), 4.07 (m, 1H, H-2), 3.97 (br s, 1H, H-1), 3.52 (br q, 1H, *J* 6.5 Hz, H-7a), 3.15 (dd, 1H, $J_{2,3}$ 5.8, $J_{3,3'}$ 9.6 Hz, H-3), 3.00 (m, 1H, H-5), 2.74 (t, 1H, $J_{2,3'}$ 9.2 Hz, H-3′), 2.61 (m, 1H, H-5′), 2.20–2.07 (m, 1H, H-7), 2.00–1.88 (m, 1H, H-6), and 1.75–1.65 (m, 2H, H-6′,7′); ^{13}C (100 MHz, inter alia): δ 82.59 (C-2), 78.99 (C-1), 74.40 and 73.31 (CH_2Ph), 66.92 (C-7a), 57.07 (C-5), 56.27 (C-3), 27.87 (C-6), and 26.12 (C-7). Mass spectrum (LSIMS): *m*/*z*: 323.1885 [M^+] for $C_{21}H_{25}NO_2$ 323.1885 (deviation 0.0 ppm).

3.7. (1*R*,2*R*,7a*S*)-1,2-Dihydroxypyrrolizidine 14

A solution of **13** (90 mg, 0.28 mmol) in MeOH (10 mL) was acidified with concd HCl and stirred at rt with 10% Pd–C (50 mg) in an H_2 atmosphere overnight. TLC (Et_2O–MeOH–Et_3N, 2:1:0.1) then showed that **13** had disappeared. The catalyst filtered off, and washed with MeOH. The mixture was neutralized with Amberlite IRA-400, the resin was filtered off washed with MeOH and the filtrate and washings concentrated to afford **14** (22 mg, 56%) as a colorless thick syrup; $[\alpha]_D^{22} = -16$ (*c* 1, MeOH). NMR data (400 MHz, MeOH-d_4): ^1H, δ 4.19 (ddd, 1H, H-2), 3.88 (t, 1H, $J_{1,2} = J_{1,7a} = 4.0$ Hz, H-1), 3.55 (m, 1H, H-7a), 3.19 (dd, 1H, $J_{2,3}$ 6.5, $J_{3,3'}$ 9.9 Hz, H-3), 3.04 (dt, 1H, $J_{5,6} = J_{5,6'} = 5.5$, $J_{5,5'}$ 10.1 Hz, H-5), 2.62 (m, 1H, H-5′), 2.58 (t, 1H, $J_{2,3'}$ 9.6 Hz, H-3′), 2.12 (m, 1H, H-7), 1.97 (m, 1H, H-6), and 1.82–1.68 (m, 2H, H-6′,7′); ^{13}C (100 MHz): δ 75.34 (C-2), 72.60 (C-1), 67.73 (C-7a), 58.03 (C-3), 56.84 (C-5), 27.89 (C-6), and 25.25 (C-7). Mass spectrum (LSIMS): *m*/*z*: 143.0945 [M^+] for $C_7H_{13}NO_2$ 143.0946 (deviation + 0.9).

3.8. (1*S*,2*R*,7a*S*)-1,2-Dihydroxypyrrolizidin-3-one 16

A solution of **9** (1.33 g, 4.1 mmol) in MeOH (30 mL) was stirred at rt with 10% Pd–C (200 mg) in an H_2 atmosphere for 3 h. TLC (Et_2O) showed the presence of a non mobile compound, presumably the *N*-deprotected pyrrolidine **15**. The catalyst was filtered off, washed with MeOH and the combined filtrate and washings (50 mL) treated with 2 M MeONa (4 mL) and refluxed for 6 h. TLC (Et_2O–MeOH, 1:1) then revealed the presence of a faster-running product. The mixture was neutralized with aqueous 10% HCl, supported on silica gel and submitted to chromatography (Et_2O–MeOH, 20:1) to afford **16** (470 mg, 72%) as white crystals, mp 168–170 °C (from EtOAc); $[\alpha]_D^{22} = +17$ (*c* 1, MeOH). {Lit.[5b] mp 165–166 °C; $[\alpha]_D^{22} = +2.4$ (*c* 1.06, MeOH)}. IR (KBr): 3364 (OH), and 1669 cm^{-1} (C=O, lactam). NMR data (400 MHz, MeOH-d_4): ^1H, δ 4.33 (d, 1H, $J_{1,2}$ 8.7 Hz, H-2), 3.75 (dd, 1H, $J_{1,7a}$ 7.3 Hz, H-1), 3.52 (m, 1H, H-5), 3.49 (m, 1H, H-7a), 3.05 (m, 1H, H-5′), 2.20 (ddt, 1H, $J_{6,7}$ 4.3, $J_{6',7} = J_{7,7a} = 6.4$, $J_{7,7'}$ 12.3 Hz, H-7), 2.04–1.98 (m, 2H, H-6,6′), and 1.52 (dq, 1H, $J_{6,7'} = J_{6',7'} = J_{7',7a} = 8.8$ Hz, H-7′). ^{13}C (100 MHz, MeOH-d_4): δ 173.79 (C-3), 83.17 (C-1), 80.15 (C-2), 64.33 (C-7a), 42.91 (C-5), 31.00 (C-7), and 26.67 (C-6). Anal. Calcd for $C_7H_{11}NO_3$: C, 53.49; H, 7.05; N, 8.91. Found: C, 53.76; H, 6.98; N, 8.72.

3.9. (1*S*,2*R*,7a*S*)-1,2-Dibenzyloxypyrrolizidin-3-one 17

A stirred solution of NaH (60% oil dispersion, 150 mg, 3.8 mmol) in anhydrous DMSO (8 mL) was heated at 60 °C for 15 min, then cooled at rt, and a solution of **16** (200 mg, 1.27 mmol) in the same solvent (4 mL) added and the mixture heated again at 60 °C for an additional 15 min under argon. After cooling at rt, BnBr (600 μL,

5.1 mmol) was added, and the reaction mixture stirred for 3 h. TLC (Et_2O) then revealed a faster-running compound. The mixture was then partitioned into water (10 mL) and Et_2O (40 mL). The organic phase was separated and then concentrated. Column chromatography (Et_2O–hexane, 3:1) of the residue afforded pure **17** (420 mg, 95%) as a colorless syrupy oil; $[\alpha]_D^{22} = +44$ (*c* 1). IR (neat): 3032 (aromatic), and 1707 cm^{-1} (C=O, lactam). NMR data (400 MHz): ^1H, 7.40–7.27 (m, 10H, $2CH_2Ph$), 5.10 and 4.79 (2d, 2H, *J* 11.6 Hz, CH_2Ph), 4.62 and 4.56 (2d, 2H, *J* 11.8 Hz, CH_2Ph), 4.48 (d, 1H, $J_{1,2}$ 8.0 Hz, H-2), 3.89 (dd, 1H, $J_{1,7a}$ 6.5 Hz, H-1), 3.61–3.54 (m, 2H, H-5,7a), 3.04 (m, 1H, H-5′), 2.10–1.86 (m, 3H, H-6,6′,7), and 1.42 (dq, 1H, $J_{6,7'} = J_{6',7'} = J_{7',7a} = 8.6$, $J_{7,7'}$ 12.1 Hz, H-7′); ^{13}C (100 MHz): δ 170.8 (C-3), 137.80, 137.60, 128.52, 128.40, 128.26, 127.99, 127.81, and 127.78 (CH_2Ph), 86.82 (C-1), 84.14 (C-2), 72.70 and 72.44 (CH_2Ph), 62.03 (C-7a), 41.55 (C-5), 31.02 (C-7), and 25.82 (C-6). Mass spectrum (LSIMS): *m/z*: 360.1578 [M^++Na] for $C_{21}H_{23}NO_3Na$ 360.1576 (deviation − 0.7).

3.10. (1*S*,2*S*,7a*S*)-1,2-Dibenzyloxypyrrolizidine 18

To a stirred solution of **17** (250 mg, 0.74 mmol) in anhydrous THF (6 mL) was added $LiAlH_4$ (56 mg, 1.4 mmol), and the mixture refluxed overnight. TLC (Et_2O) then revealed that no starting material was present. Aqueous 0.5 M NaOH (2 mL) was cautiously added and the mixture partitioned into EtAcO (5 mL) and water (5 mL). The organic phase was separated and the aqueous extracted with EtAcO (3 × 5 mL). The combined extracts were concentrated and the residue submitted to column chromatography (Et_2O–MeOH, 20:1) to afford pure **18** (180 mg, 75%) as a colorless syrup; $[\alpha]_D^{26} = -4$ (*c* 1). IR (neat): 3029 cm^{-1} (aromatic). NMR data (300 MHz): ^1H, δ 7.34 (m, 10H, $2CH_2Ph$), 4.60 and 4.57 (2d, 2H, *J* 11.8 Hz, CH_2Ph), 4.63 (s, 2H, CH_2Ph), 4.21 (q, 1H, $J_{1,2} = J_{2,3} = J_{2,3'} = 5.7$ Hz, H-2), 3.80 (t, 1H, $J_{1,7a}$ 5 Hz, H-1), 3.47 (br q, 1H, *J* 5.0 Hz, H-7a), 3.37 (dd, 1H, $J_{3,3'}$ 10.2 Hz, H-3), 3.04 (m, 1H, H-5), 2.76–2.69 (m, 2H, H-3′,5′), 2.05–1.95 (m, 1H, H-7), 1.94–1.85 (m, 1H, H-6), and 1.83–1.64 (m, 2H, H-6′,7′); ^{13}C (75 MHz, inter alia): δ 88.46 (C-1), 84.99 (C-2), 72.11 and 71.83 (CH_2Ph), 68.52 (C-7a), 57.13 (C-3), 55.45 (C-5), 31.18 (C-7), and 25.88 (C-6). Mass spectrum (LSIMS): *m/z*: 324.1958 [M^++1] for $C_{21}H_{26}NO_2$ 324.1964 (deviation + 1.8 ppm).

3.11. (1*S*,2*S*,7a*S*)-1,2-Dihydroxypyrrolizidine 19

A solution of **18** (275 mg, 0.85 mmol) in MeOH (10 mL) was acidified with concd HCl and stirred at rt with 10% Pd–C (75 mg) in an H_2 atmosphere overnight. TLC (Et_2O–MeOH–Et_3N, 2:1:0.1) then showed that **18** had disappeared. The catalyst was filtered off and washed with MeOH. The mixture was neutralized with Amberlite IRA-400, the resin filtered off, washed with MeOH and the filtrate and washings concentrated to afford **19** (107 mg, 88%) as white crystals, mp 164–165 °C (from Et_2O–MeOH); $[\alpha]_D^{23} = +11$ (*c* 0.5, MeOH). Lit.[5b] $[\alpha]_D^{24} = -3.4$ (*c* 0.5, MeOH). NMR data (400 MHz, MeOH-d_4): ^1H, δ 4.03 (q, 1H, $J_{2,3\alpha} = J_{2,3\beta} = 5.8$ Hz, H-2), 3.63 (t, 1H, $J_{1,2} = J_{1,7a} = 5.8$ Hz, H-1), 3.22 (dd, 1H, H-3α), 3.20 (q, 1H, H-7a), 2.91 (dt, 1H, $J_{5\alpha,6\alpha} = J_{5\alpha,6\beta} = 6$, $J_{5\alpha,5\beta}$ 10.4 Hz, H-5α), 2.72 (dt, 1H, $J_{5\beta,6\alpha} = J_{5\beta,6\beta} = 6.5$ Hz, H-5β), 2.53 (dd, 1H, $J_{3\alpha,3\beta}$ 10.5 Hz, H-3β), 1.96 (dq, 1H, $J_{6\alpha,7\alpha} = J_{6\beta,7\alpha} = J_{7\alpha,7a} = 6.3$, $J_{7\alpha,7\beta}$ 13.6 Hz, H-7α),1.88 (dquin, 1H, $J_{5\alpha,6\beta} = J_{5\beta,6\beta} = J_{6\beta,7\beta} = 5.7$, $J_{6\alpha,6\beta}$ 12.0 Hz, H-6β), 1.78 (dq, 1H, $J_{7\ a,7\beta} = J_{6\alpha,7\beta} = 6.5$ Hz, H-7β), and 1.70 (dquin, 1H, H-6α). ^{13}C (100 MHz), δ 82.93 (C-1), 78.63 (C-2), 70.74 (C-7a), 59.62 (C-3), 56.64 (C-5), 31.43 (C-7), and 26.23 (C-6). Anal. Calcd for $C_7H_{13}NO_2$: C, 58.72; H, 9.15; N, 9.78. Found: C, 58.45; H, 9.31; N, 10.00.

3.12. Methyl (2*S*,3*S*)-20 and (2*R*,3*R*)-2,3-dihydroxy-3-[(2′*S*)-*N*-benzyloxycarbonylpyrrolidin-2′-yl]propanoate 21

3.12.1. Dihydroxylation of 6 without chiral catalyst. Compound **6** (1.4 g, 4.84 mmol) was hydroxylated as for **7** in acetone–water 8:1 v/v (18 mL), with *N*-oxide-*N*-methylmorpholine (1.13 g, 9.64 mmol) and aqueous 1% OsO_4 (4 mL). The mixture was left at room temperature overnight. GLC[11] (B) then revealed the presence of two new products (t_R 17.33 and 17.67 min) in a 1:4 ratio. The mixture was concentrated to a residue that was submitted to chromatography (Et_2O–hexane, 2:1). Eluted first was pure **20** (160 mg, 10%) as a colorless syrup; t_R 17.33 min; $[\alpha]_D^{25} = -51$ (*c* 1.25). IR (neat): 3402 (OH), 3032 (aromatic), 1746 and 1669 (C=O), and 699 cm^{-1} (aromatic). NMR data (400 MHz): ^1H, δ 7.34 (m, 5H, Ph), 5.13 (s, 2H, CH_2Ph), 4.96 (br d, 1H, *J* 6.5 Hz, HO), 4.23 (dt, 1H, *J* 3.8, *J* 7.8 Hz, H-2′), 4.10 (m, 2H, H-2, OH), 3.80 (br s, 4H, OMe, H-3), 3.59 (dt, 1H, $J_{4'a,5'a} = J_{4'b,5'a} = 7.4$, $J_{5'a,5'b}$ 10.7 Hz, H-5′a), 3.39 (ddd, 1H, $J_{4'a,5'b}$ 5.3, $J_{4'b,5'b}$ 7.3 Hz, H-5′b), 2.11–2.00, 1.92–1.86, and 1.84–1.75 (3m, 4H, H-3′a,3′b,4′a,4′b); ^{13}C (100 MHz), δ 173.48 (C-1), 158.07 (Cbz), 136.21, 128.61, 128.26, 127.99 (Ph), 77.12 (C-3), 72.47 (C-2), 67.76 (CH_2Ph), 58.48 (C-2′), 52.58 (OMe), 47.83 (C-5′), 29.07 and 24.37 (C-3′,4′). Mass spectrum (LSIMS): *m/z*: 346.1263 [M^++Na] for $C_{16}H_{21}NO_6Na$ 346.1267 (deviation + 0.9 ppm).

Eluted second was pure **21** (1.1 g, 70%) as a colorless syrup; t_R 17.67 min; $[\alpha]_D^{24} = -48$ (*c* 1). IR (neat): 3393 (OH), 3033 (aromatic), 1742 (C=O, ester), 1674 (C=O, Cbz), and 699 cm^{-1} (aromatic). NMR data (400 MHz): ^1H, δ 7.34 (m, 5H, Ph), 5.15 and 5.08 (2d, 2H, *J* 12.3 Hz, CH_2Ph), 4.27 (br s, 1H, H-2), 3.99 (br s, 2H, H-3,2′), 3.63 (s, 3H, OMe), 3.39 (m, 1H, H-5′a), 3.16 (m, 1H, H-5′b), 2.08 and 1.90 (2m, 4H, H-3′a,3′b,4′a,4′b); ^{13}C (100 MHz): δ 172.44 (C-1), 156.96 (Cbz), 136.13, 128.59, 128.27, 128.13 (Ph), 73.75 (C-3), 73.66 (C-2), 67.80 (CH_2Ph), 59.75 (C-2′), 52.25 (OMe), 46.67 (C-5′), 27.73 and 23.39 (C-3′,4′). Mass spectrum (LSIMS): *m/z*: 346.1267 [M^++Na] for $C_{16}H_{21}NO_6Na$ 346.1267 (deviation 0.0 ppm).

3.12.2. Dihydroxylation of 6 with chiral catalyst. Compound **6** (50 mg, 170 μmol) was dihydroxylated under the same conditions as **7** (see above) to yield mixtures of **20**

and **21**, which were analyzed[11] by GLC (B) resulting in a 1:1 (AD-mix α) and 1:7 (AD-mix β) ratios, respectively.

3.13. (1*S*,2*S*,7a*S*)-1,2-Dihydroxypyrrolizidin-3-one 23

Compound **20** (160 mg, 0.49 mmol) was transformed into **23**, following the same protocol used for **9** (37 mg, 48%) as white crystals, mp 130–132 °C (from EtOAc); $[\alpha]_D^{24} = +7$, $[\alpha]_{405}^{24} = +17$ (*c* 0.6, MeOH). IR (KBr): 3305 (OH), and 1685 cm^{-1} (C=O, lactam). NMR data (400 MHz, MeOH-d_4): ^{1}H, δ 4.49 (d, 1H, $J_{1,2}$ 4.0 Hz, H-2), 4.31 (t, 1H, $J_{1,7a}$ 3.7 Hz, H-1), 3.83 (dt, 1H, $J_{7,7a} = J_{7',7a} = 7.2$ Hz, H-7a), 3.48 (dt, 1H, $J_{5,6} = J_{5,6'} = 7.5$, $J_{5,5'}$ 11.6 Hz, H-5), 3.05 (dt, 1H, $J_{5',6} = J_{5',6'} = 6.0$ Hz, H-5′), 2.04–1.96 (m, 3H, H-6,6′,7), and 1.84–1.76 (m, 1H, H-7′); ^{13}C (100 MHz): δ 175.57 (C-3), 76.31 (C-2), 72.42 (C-1), 63.16 (C-7a), 42.92 (C-5), 26.56 (C-6), and 24.13 (C-7). Anal. Calcd for $C_7H_{11}NO_3$: C, 53.49; H, 7.05; N, 8.91. Found: C, 53.23; H, 7.40; N, 9.11.

3.14. (1*R*,2*R*,7a*S*)-1,2-Dihydroxypyrrolizidin-3-one 25

Compound **21** (700 mg, 2.16 mmol) was transformed into **25**, following the same procedure used for **20** (230 mg, 68%) as white crystals, mp 157–159 °C; $[\alpha]_D^{23} = +11.8$ (*c* 1, MeOH). IR (KBr): 3359 (OH), and 1672 cm^{-1} (C=O, lactam). NMR data (400 MHz, MeOH-d_4): ^{1}H, δ 4.32 (d, 1H, $J_{1,2}$ 8.7 Hz, H-2), 3.74 (dd, 1H, $J_{1,7a}$ 7.1 Hz, H-1), 3.54–3.47 (m, 2H, H-7a,5), 3.05 (m, 1H, H-5′), 2.19 (ddt, 1H, $J_{7,7a} = J_{6,7} = 6.4$, $J_{6',7}$ 4.1, $J_{7,7'}$ 12.5 Hz, H-7), 2.04–1.95 (m, 2H, H-6,6′), and 1.52 (dq, 1H, $J_{6,7'} = J_{6',7'} = J_{7',7a} = 8.7$ Hz, H-7′). ^{13}C (100 MHz): δ 173.82 (C-3), 83.22 (C-1), 80.20 (C-2), 64.36 (C-7a), 42.93 (C-5), 31.01 (C-7), and 26.66 (C-6). Anal. Calcd for $C_7H_{11}NO_3$: C, 53.49; H, 7.05; N, 8.91. Found: C, 53.31; H, 7.50; N, 8.57.

3.15. (1*R*,2*R*,7a*S*)-1,2-Dibenzyloxypyrrolizidin-3-one 26

A stirred solution of NaH (60% oil dispersion, 90 mg, 2.1 mmol) in anhydrous DMSO (6 mL) was heated at 60 °C for 15 min, then cooled at rt, and a solution of **25** (110 mg, 0.7 mmol) in the same solvent (4 mL) added and the mixture heated again at 60 °C for an additional 15 min, under argon. After cooling at rt, BnBr (330 μL, 2.8 mmol) was added, and the reaction mixture stirred for 3 h. TLC (Et_2O) then revealed a faster-running compound. The mixture was then partitioned into water (10 mL) and Et_2O (40 mL) and the organic phase separated and then concentrated. Column chromatography (Et_2O–hexane, 3:1) of the residue afforded pure **26** (210 mg, 90%) as a colorless syrup; $[\alpha]_D^{23} = +41.6$ (*c* 1). IR (neat): 3031 (aromatic), and 1707 cm^{-1} (C=O, lactam). NMR data (400 MHz): ^{1}H, δ 7.40–7.29 (m, 10H, 2CH_2Ph), 5.11 and 4.79 (2d, 2H, *J* 11.7 Hz, CH_2Ph), 4.62 and 4.56 (2d, 2H, *J* 11.8 Hz, CH_2Ph), 4.47 (d, 1H, $J_{1,2}$ 8.0 Hz, H-2), 3.89 (dd, 1H, $J_{1,7a}$ 6.6 Hz, H-1), 3.61–3.54 (m, 2H, H-5,7a), 3.04 (m, 1H, H-5′), 2.10–2.03 (m, 1H, H-7), 2.01–1.86 (m, 2H, H-6,6′), and 1.42 (dq, 1H, $J_{6,7'} = J_{6',7'} = J_{7',7a} = 9.0$, $J_{7,7'}$ 12.1 Hz, H-7′); ^{13}C NMR (100 MHz): δ 170.51 (C-3), 137.82, 137.62, 128.53, 128.42, 128.28, 128.00, 127.83, and 127.80 (CH_2 *Ph*), 86.84 (C-1), 84.16 (C-2), 72.72 and 72.47 (*C*H_2Ph), 62.05 (C-7a), 41.57 (C-5), 31.04 (C-7), and 25.83 (C-6). Mass spectrum (LSIMS): *m*/*z*: 360.1581 [M^++Na] for $C_{21}H_{23}NO_3Na$ 360.1576 (deviation − 1.5).

3.16. (1*R*,2*S*,7a*S*)-1,2-Hydroxypyrrolizidine 27

To a stirred solution of **25** (180 mg, 1.14 mmol) in anhydrous THF (6 mL) added a H_3B–SMe_2 complex solution in the same solvent (10 M, 1.14 mL) under argon, and the mixture left at rt overnight. TLC (Et_2O–MeOH, 1:1) then revealed the absence of **25**. MeOH (2 mL) was cautiously added and the reaction mixture was concentrated to a residue that was dissolved in MeOH (20 mL) and refluxed for 6 h, then concentrated. The residue was supported on silica gel and chromatographed (Et_2O → Et_2O–MeOH–Et_3N, 1:1:1) to give **27** (106 mg, 65%) as pale yellow crystals, mp 137–138 °C; $[\alpha]_D^{24} = +3$, $[\alpha]_{405}^{24} = +13$, (*c* 1, MeOH). Lit.[5a] $[\alpha]_D^{24} = +7.46$ (*c* 0.67, MeOH). IR (KBr): 3269 cm^{-1} (HO). NMR data (300 MHz, MeOH-d_4): ^{1}H, δ 4.09 (q, 1H, $J_{1,2} = J_{2,3} = J_{2,3'} = 5.2$ Hz, H-2), 3.73 (t, 1H, $J_{1,7a}$ 5.2 Hz, H-1), 3.33 (m, 1H, H-7a), 3.32 (dd, 1H, H-3), 3.05 (dt, 1H, $J_{5,6} = J_{5,6'} = 5.7$, $J_{5,5'}$ 10.5 Hz, H-5), 2.83 (dt, 1H, $J_{5',6} = J_{5',6'} = 6.0$ Hz, H-5′), 2.66 (dd, 1H, $J_{3,3'}$ 10.9 Hz, H-3′), 2.10–1.72 (m, 4H, H-7,6,7′,6′); ^{13}C (75 MHz): δ 82.61 (C-1), 78.72 (C-2), 71.56 (C-7a), 59.69 (C-3), 56.85 (C-5), 31.23 (C-7), and 26.30 (C-6). Anal. Calcd for $C_7H_{13}NO_2$: C, 58.72; H, 9.15; N, 9.78. Found: C, 58.41; H, 9.46; N, 9.91.

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