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Synthesis of enantiopure 1,2-dihydroxyhexahydropyrroloisoquinolines as potential tools for asymmetric catalysis

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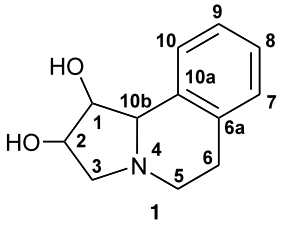
Abstract—The stereocontrolled synthesis of enantiopure 1,2-dihydroxyhexahydropyrroloisoquinolines **2**–**4** and a formal synthesis of *ent*-**2**–**4** starting from D-mannose and L-tartaric acid is reported. The strong tertiary amine bases **2**–**4** containing hydroxyl groups, able to activate electrophiles through hydrogen bonding, are potentially useful as a catalysts in base-catalyzed processes as well as new ligands in metal-based catalysis.

1. Introduction

One of the most rapidly developing areas within synthetic organic chemistry is asymmetric homogeneous catalysis.[1] The critical importance for the continuous growth of this area is the availability of new 'custom-designed' compounds, which can play the role of ligands in metal based catalysis[2] or catalysts in organocatalysis.[3] Chiral amino alcohols, both natural and synthetic, are employed in a wide range of enantioselective syntheses, i.e. organozinc additions to the carbonyl compounds,[4] Baylis–Hillman reaction,[5] Michael additions,[6] transfer hydrogenation of ketones,[7] reduction of ketones with $THF{\cdot}BH_3$[8] and phase-transfer alkylation.[9] In our studies on the new stereoselective reactions we focused our attention on the 1,2-dihydroxyhexahydropyrroloisoqinolines of general structure **1**.



1,2-Dihydroxy-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]-isoquinoline **1**

Strong tertiary amine bases, such as **1**, are able to activate electrophiles through hydrogen bonding. This property makes them promising candidates as catalysts in base-catalyzed processes.[10] Judicious structural modification of **1** should have an influence on the phase differentiation, which is critical to the outcome of asymmetric transformations. 1,2-dihydroxyhexahydropyrroloisoqinolines are especially attractive in this respect, because of the ready preparation of the analogues, substituted at C-5, C-6, C-10b and at the aromatic carbon atoms.

2. Results and discussion

The numerous syntheses of compounds with the pyrroloisoquinoline skeleton, reported to-date, were aimed either at the synthesis of natural alkaloids of interesting bioactivity[11–13] or at the preparation of new antidepressant drugs.[14]

The most effective method for the construction of such compounds, with excellent stereocontrol, usually proceeds via cyclization of the *N*-acyliminium ion.[11–14] Herein, we describe the stereocontrolled syntheses of the 1,2-dihydroxypyrroloisoquinolines **2**–**4** and a formal synthesis of *ent*-**2**–**4** starting from the D-ribose and L-tartaric acid via cyclization of the *N*-acyliminium ion. The lactone **5**, readily available from D-ribose,[15] was subjected to condensation with phenethylamine using a procedure analogous to that reported by Kotsuki et al.[16] (Scheme 1).

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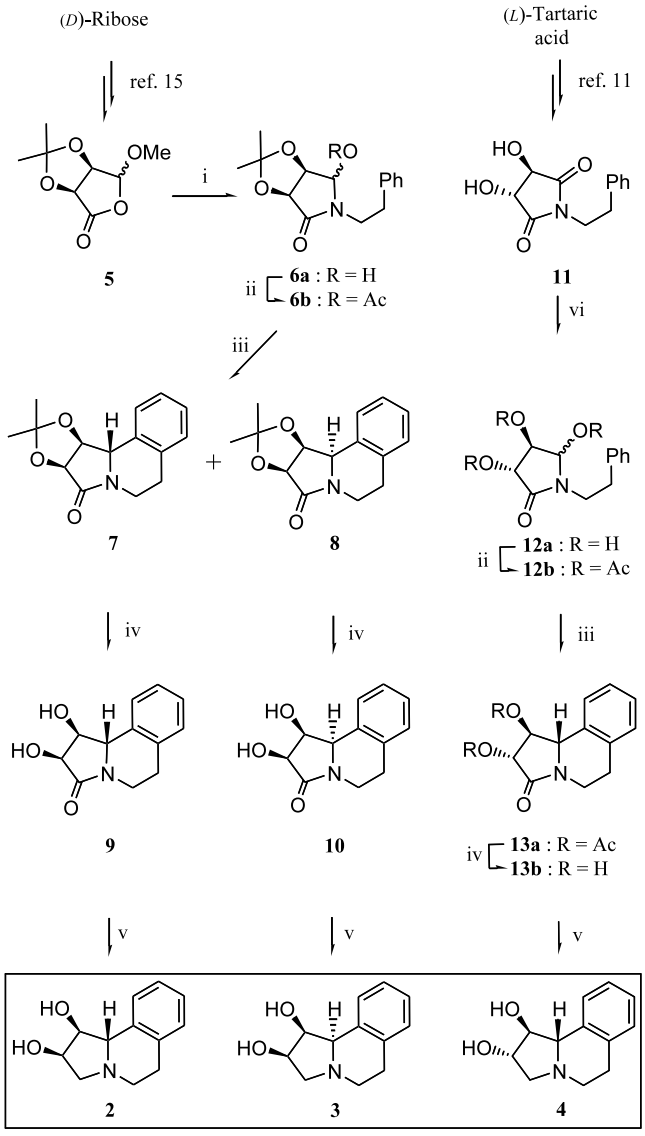


Scheme 1. *Reagents and conditions*: (i) $FnNH_2$, EtOH, 1 h at 0°C, then overnight at rt; (ii) Ac_2O, pyridine, cat. DMAP; (iii) $BF_3{\cdot}Et_2O$, CH_2Cl_2, 0°C, then 3 h at rt; (iv) HCl/MeOH, rt; (v) $LiAlH_4$, THF, reflux; (vi) $NaBH_4$, MeOH, −10°C, 2 h.

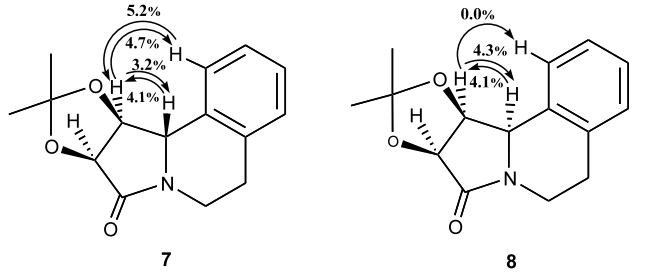


Figure 1.

The hydroxypyrrolidone **6a** was purified on silica gel, acetylated and purified by chromatography again to give **6b** in a 61% overall yield. Alternatively, the crude **6a** was first acetylated and then purified, furnishing **6b** in 76% yield. The acetoxypyrrolidone **6b**, when treated with $BF_3{\cdot}Et_2O$ in CH_2Cl_2 at room temperature, undergoes intramolecular cyclization to the pyrroloisoquinolines **7** and **8** in a 2.9:1 ratio.[†] The yield and the rate of cyclization depends on the amount of Lewis acid present during the reaction. With more than 1 equiv. of $BF_3{\cdot}Et_2O$, reaction proceeded rapidly and efficiently, otherwise the process was very sluggish. The best yield of **7** and **8** (67 and 23%, respectively) was obtained using 3 equiv. of $BF_3{\cdot}Et_2O$. NOESY experiments, performed on the epimers **7** and **8**, showed in both cases interaction between hydrogen atoms at C-1 and C-10b (Fig. 1). Interestingly, the hydrogen atom at C-1 of isomer **7** showed a strong positive NOE effect with the aromatic proton at C-10. Such a spin interaction in the case of compound **8** was not observed, what indicates that the pyrroloisochinoliones **7** and **8** possess **10b***S* and **10b***R* configuration, respectively. Our predictions were confirmed by single X-ray crystallography, which provided unequivocal proof of the absolute configuration of both epimers (Fig. 2).

Removal of the isopropylidene protecting group of compounds **7** and **8** using hydrogen chloride in anhydrous methanol led to the 1,2-dihydroxypyrroloisoquinolinones **9** and **10**. The isoquinolines **9** and **10** were subsequently reduced with $LiAlH_4$ in refluxing THF to amines **2** and **3** in 58 and 49% yields, respectively. Increasing the time of the reduction reaction resulted in diminished yields of the desired amine, most likely due to the formation of by-products. Spectroscopic data were identical to those of 5,6-dihydropyrrolo[2,1-*a*]-isoquinoline.[17]

For the preparation of *trans*-1,2-dihydroxypyrroloisoquinoline we applied the modified procedure proposed by Lee et al.[11] Thus, pyrrolidinone **11**, readily prepared from L-tartaric acid, was subjected to the $NaBH_4$ reduction in anhydrous methanol to give **12a**. The reduction product with free hydroxy-groups was found to undergo cyclization in low yield only. It appears that an acetoxy residue at C-5 should be a better leaving group than the ethoxy group.[11] For these reasons, the crude **12a** was acetylated and isolated as the triacetate **12b** in 81% overall yield. The Lewis acid ($BF_3{\cdot}Et_2O$)-promoted cyclization of **12b** followed by aqueous sodium bicarbonate work-up and crystallization gave the pyrroloisoquinolinone **13a** as the sole product in 92% yield. Reduction of **13a** with $LiAlH_4$ provided *trans*-1,2-dihydroxypyrroloisoqinoline **4** in 78% yield. Employing the same overall sequence, *ent*-**4** can be easily obtained from the inexpensive D-tartaric acid. Although it certainly appears possible, the synthesis of *ent*-**2** and *ent*-**3** starting from L-mannose may not be attractive due to the high cost of the starting material. Hence, we decided to elaborate the methodology of preparation of *cis*-1,2-dihydroxypyrroloisoqinolines

[†] Recently, Kotsuki et al.[16] have demonstrated the highly stereoselective intermolecular nucleophilic substitution at pyrrolidinone that differs from our compound **6b** only in the substituent at the nitrogen atom. Rationalization of the unexpectedly low stereoselectivity in the cyclization to form **7** and **8** is presently under examination and the results will be published in due course.

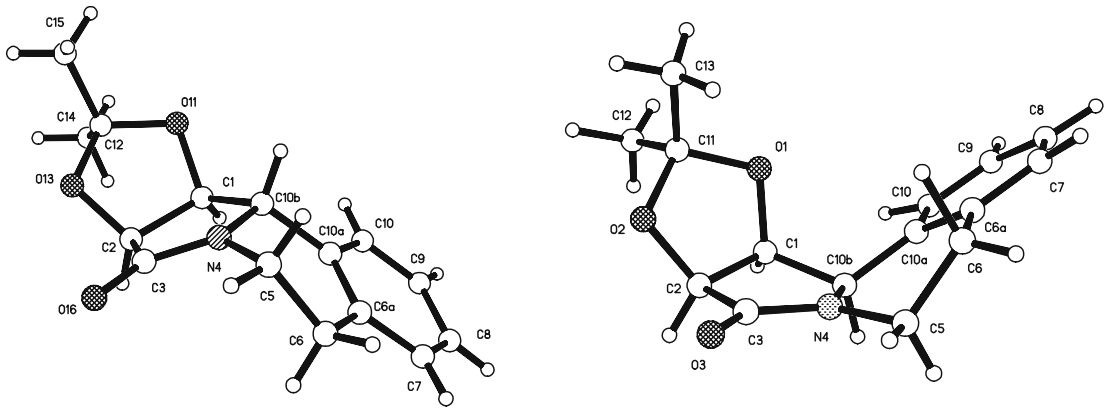
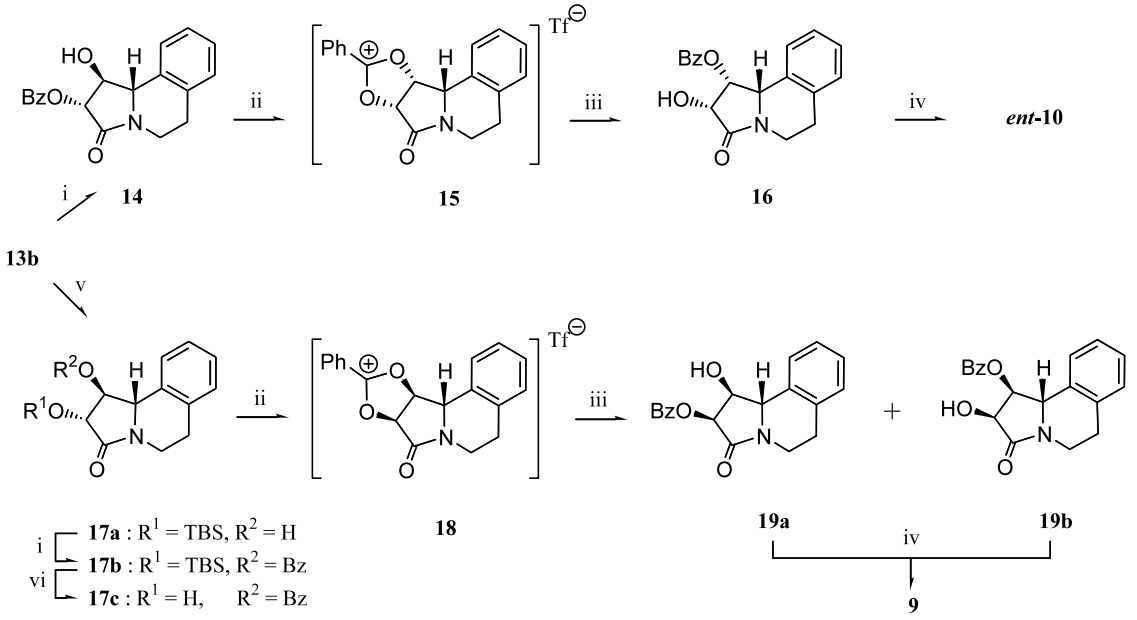


Figure 2.

starting from **13b** by the selective inversion of configuration at C-1 and C-2. The classical methods for the inversion of configuration of alcohols, widely utilized in hydroxypyrrolizidine chemistry, such as, for example, mesylation–nucleophilic substitution by carboxylate ion,[18] oxidation–reduction[19] and Mitsunobu inversion,[20] all failed in the case of mono-protected **13b**. Successful inversion was achieved by the intramolecular S_N2 displacement of triflate by the adjacent benzoate group (Scheme 2).[20]

The monoprotected **14** was obtained by the selective benzoylation of **13b**. Attempts to prepare the triflate of **14** under the standard conditions (Tf_2O/pyridine) gave instantly the benzoxonium ion **15** which, on hydrolysis, afforded monobenzoate **16** in 75% yield. The treatment of **16** with NaOMe in anhydrous methanol yielded *ent*-**10**. The spectroscopic properties of *ent*-**10** were identical to those of compound **10** and its specific rotation had the similar absolute value but the opposite sign to that of **10**. The substrate (*ent*-**13b**) suitable for the synthesis of *ent*-**2** via inversion at C-2 should be derived from D-tartaric acid. For reasons of simplicity, as a proof of the synthetic potential of the discussed methodology, we used the **13b** as a starting material. In the first step **13b** was protected by selective silylation to form **17a**. Benzoylation of **17a** and subsequent deprotection of silyl ether at C-2 gave the respective monoester **17c**. The inversion of configuration at C-2 of **17c** proceeded via cation **18**, which on treatment with water afforded the corresponding *cis*-diol as a 1:9 mixture of monobenzoate **19a** and **19b**. The treatment of benzoate **19a** and **19b** with the NaOMe in anhydrous methanol yielded pyrroloisoquinolinone **9**. The spectro-



Scheme 2. *Reagents and conditions*: (i) BzCl, pyridine, −30°C, 1 h then overnight at 0°C; (ii) Tf_2O, pyridine, CH_2Cl_2, −30°C gradually to rt, 2 h, then 1 h at rt; (iii) H_2O, overnight, rt; (iv) MeONa, MeOH; (v) TBS-Cl, imidazole, DMF, rt, 2 days; (vi) $Bu_4NF{\cdot}xH_2O$, AcOH, THF, rt, 3 days.

scopic properties of **9** prepared from D-mannose and that derived from L-tartaric acid were identical and in both cases the specific rotation had the same sign and similar value.

3. Conclusion

In summary, we have successfully developed the five-step synthesis of enantiopure *cis*-1,2-dihydroxyhexahydropyrroloisoquinolines **2** and **3** starting from lactone **5**, derived from D-mannose. Due to the high cost of the unnatural L-mannose, we have also elaborated an alternative methodology for the preparation of *ent*-**2** and *ent*-**3**, starting from the *trans*-1,2-dihydroxyamide **13b**. The latter is readily available in both the L- and D-enantiomeric forms, starting from the inexpensive L- or D-tartaric acid, respectively. The methodology presented employs the selective inversion of configuration at C-1 or C-2 via intramolecular S_N2 displacement of triflate with the adjacent benzoate group. The obtained amino alcohols **2**, **3**, and **4** as well as their readily available respective enantiomers appear to have a significant potential as a catalysts in base-catalyzed processes and as ligands in metal-based catalysis.

4. Experimental

The melting points are uncorrected. Optical rotations were measured using a JASCO Dip-360 digital polarimeter. IR spectra were obtained using an FT-IR-1600 Perkin–Elmer spectrophotometer. ^{1}H NMR spectra were recorded using a Bruker AM 500 spectrometer with TMS as the internal standard. The resonances for aromatic protons (phenyls) were not characteristic and, therefore, they were not included in the reported spectral data. Mass spectra were recorded using an AMD 604 mass spectrometer. Column chromatography was performed using Merck Kiesel gel (230–400 mesh). All reactions were carried out under an argon atmosphere using anhydrous solvents. Most reagents were obtained from commercial suppliers and were used without further purification, unless noted. THF was distilled from Na and benzophenone, methylene chloride and toluene were distilled from CaH_2.

4.1. General procedures for the preparation of pyrrolones 6a–b from tetrahydrofuranone 5

To the stirred solution of **5** (4.7 g, 25 mmol) in ethanol (50 mL) at 0°C the phenethylamine (27.5 mmol) in 40 mL of ethanol was added dropwise over a 1 h period. Stirring was continued at 0°C for 3 h, and then the reaction mixture was left overnight at rt. The solvent was evaporated in vacuum, crude hydroxypyrrol-4-one was purified by flash column chromatography (*t*-BuOMe:CH_2Cl_2, 1:1) and finally acetylated (acetic anhydride, pyridine, cat. DMAP), Method A, or acetylated and then purified, Method B.

4.1.1. (1*R*,3*S*,6*S*)- and (1*R*,3*S*,6*R*)-6-Hydroxy-2,2-dimethyl-5-phenethyltetrahydro[1,3]dioxolo[4,5-*c*]pyrrol-4-one, 6a. White solid, yield 65%; IR (CH_2Cl_2): 3595, 3385, 2993, 2941, 1713 cm^{-1}. Selected data for the mixture of epimers **6a***S*:**6a***R* = 6.5:1. **6a***S* epimer: ^{1}H NMR ($CDCl_3$): 4.92 (d, 1H, J = 6.7 Hz), 4.75 (d, 1H, J = 5.8 Hz), 4.42 (d, 1H, J = 5.8 Hz), 3.72 (m, 1H), 3.49 (m, 1H), 2.92 (m, 2H), 2.68 (d, 1H, OH, J = 6.7), 1.36 and 1.34 (two s, 6H); ^{13}C NMR ($CDCl_3$): 171.69, 128.76, 128.68, 126.70, 113.19, 85.39, 79.61, 76.67, 42.05, 33.44, 26.90, 25.66. **6a***R* epimer: ^{1}H NMR ($CDCl_3$): 4.87 (d, 1H, J = 4.8 Hz), 4.83 (d, 1H, J = 4.8 Hz), 1.47 and 1.42 (two s, 6H); ^{13}C NMR ($CDCl_3$): 128.58, 126.61, 113.92, 79.96, 77.33, 72.94, 41.48, 25.94; MS (EI, HR) m/z: (M^+) calcd for $C_{15}H_{19}NO_4$: 277.13017. Found: 277.13141. Anal. calcd for $C_{15}H_{19}NO_4$: C, 64.97; H, 6.91; N, 5.05. Found: C, 65.06; H, 6.84; N, 5.09%.

4.1.2. (1*R*,3*S*,6*S*)- and (1*R*,3*S*,6*R*)-6-Acetoxy-2,2-dimethyl-5-phenethyltetrahydro[1,3]dioxolo[4,5-*c*]pyrrol-4-one, 6b. **Method A**: To a solution of **6a** (2.77 g, 10 mmol) and 4-dimethylaminopyridine (61 mg, 0.5 mmol) in pyridine (10 mL) cooled to 0°C was added acetic anhydride (1.41 mL, 15 mmol). The reaction mixture was stirred at 0°C for 15 min, followed by additional 2 h at rt. The solution was poured into an ice–water mixture (50 mL) and extracted with ethyl acetate (2×30 mL). Combined extracts were washed with water (3×50 mL), saturated solution of sodium bicarbonate (50 mL), dried ($MgSO_4$) and evaporated. The crude product was purified by flash column chromatography (hexane:*t*-BuOMe, 1:1) to give **6b** (3.01 g, 94% yield) as an oil.

Method B: Crude **6a** was obtained according to Section 4.1, and then acetylated and purified as described for Method A. Oil, yield 76% calculated for two steps. IR (CH_2Cl_2): 2989, 2941, 1745 1723 cm^{-1}. Selected data for the mixture of epimers **6***S*:**6***R* (12:1). **6b***S* epimer: ^{1}H NMR ($CDCl_3$): 6.02 (s, 1H), 4.76 (d, 1H, J = 5.7 Hz), 4.48 (d, 1H, J = 5.7 Hz), 3.83 (m, 1H), 3.25 (m, 1H), 2.94 (m, 1H), 2.83 (m, 1H), 1.35 and 1.34 (two s, 6H); ^{13}C NMR ($CDCl_3$): 171.92, 169.93, 137.73, 128.69, 128.49, 126.54, 113.54, 84.83, 77.31, 76.20, 42.25, 33.24, 26.78, 25.65, 20.77. **6b***R* epimer: ^{1}H NMR ($CDCl_3$): 5.79 (d, 1H, J = 5.3 Hz), 4.78 (dd, 1H, J = 6.7, 5.3 Hz), 4.59 (d, 1H, J = 6.7), 2.12 (s, 3H), 1.45 (s, 3H), 1.38 (s, 3H); ^{13}C NMR ($CDCl_3$): 169.73, 169.56, 139.15, 128.55, 128.53, 125.64, 114.76, 82.52, 76.51, 72.36, 42.42, 33.41, 26.20, 25.82, 20.67; MS (LSIMS(+), HR) m/z: ($M+Na^+$) calcd for $C_{17}H_{21}O_5NNa$: 342.13174. Found: 342.13002. Anal. calcd for $C_{17}H_{21}NO_5$: C, 63.94; H, 6.63; N, 4.39. Found: C, 63.28; H, 6.69; N, 4.46%.

4.2. General procedures for the preparation of pyrroloisoquinolinones 7, 8, 13a from 6b and 12b

To a solution of pyrrolones **6b** or **12b** (8 mmol) in CH_2Cl_2 (40 mL) cooled to 0°C, $BF_3{\cdot}Et_2O$ (3.04 mL, 24 mmol) was added. The reaction mixture was warmed to rt and stirred until the disappearance of starting mate-

rial (TLC control) ~3 h. The solution was diluted with CH_2Cl_2 (60 mL), cooled to 0°C and treated with saturated solution of sodium bicarbonate (50 mL) while vigorously stirring. Stirring was continued for 5 min, the organic phase was separated, washed with water (2×50 mL), dried ($MgSO_4$) and evaporated.

4.2.1. (7a*S*,10a*S*,10b*S*)- and (7a*S*,10a*S*,10b*R*)-9,9-Dimethyl-5,7a,10a,10b-tetrahydro-6*H*-8,10-dioxa-6a-azapentaleno[1,2-*a*]naphtalen-7-one, 7 and 8. Flash column chromatography (step gradient from hexane:ethyl acetate 1:1 to 0:1) of crude mixture of **7** and **8** (ratio of 2.9:1, ^{1}H NMR) gave the following compounds.

Compound **7**: colourless crystals, yield 66.7% (less polar), mp 88–90°C (hexane/*t*-BuOMe); IR (CH_2Cl_2): 3055, 2992, 1703 cm^{-1}; $[\alpha]_D$ = +133.8 (*c* 1, CH_2Cl_2); ^{1}H NMR ($CDCl_3$): 4.79 (m, 2H), 4.65 (d, 1H, *J* = 7.2 Hz), 4.39 (ddd, 1H, *J* = 13.0, 6.5, 1.7 Hz), 3.13 (dt, *J* = 13.0, 4.7 Hz), 2.99 (m, 1H), 2.74 (m, 1H), 1.57 and 1.44 (two s, 6H); ^{13}C NMR ($CDCl_3$): 168.54, 134.09, 133.87, 129.55, 127.60, 127.00, 125.20, 113.68, 79.93, 78.30, 63.31, 37.60, 27.92, 26.78, 25.34; MS (EI, HR) *m*/*z*: (M^+) calcd for $C_{15}H_{17}O_3N$: 259.12084. Found: 259.12208. Anal. calcd for $C_{15}H_{17}O_3N$: C, 69.48; H, 6.61; N, 5.40. Found: C, 69.25; H, 6.69; N, 5.33%

Compound **8**: colourless crystals, yield 23.4%, mp 202–204°C (hexane/ethyl acetate); IR (CH_2Cl_2): 2991, 2940, 1704 cm^{-1}; $[\alpha]_D$ = −241.6 (*c* 1, CH_2Cl_2); ^{1}H NMR ($CDCl_3$): 5.03 (t, 1H, *J* = 4.7 Hz), 4.95 (bd, 1H, *J* = 4.7 Hz), 4.87 (dd, 1H, *J* = 4.7, 1.2 Hz), 4.38 (ddd, 1H, *J* = 12.8, 5.7, 2.1 Hz), 3.04 (ddd, 1H, *J* = 12.8, 3.9, 1.3 Hz), 2.90 (m, 1H), 2.75 (m, 1H), 1.34 and 1.26 (two s, 6H); ^{13}C NMR ($CDCl_3$): 170.37, 134.63, 131.13, 129.30, 127.10, 126.71, 125.98, 112.70, 78.82, 75.97, 58.16, 37.21, 28.30, 27.44, 26.44; MS (EI, HR) *m*/*z*: (M^+) calcd for $C_{15}H_{17}O_3N$: 259.12084. Found: 259.1211. Anal. calcd for $C_{15}H_{17}O_3N$: C, 69.48; H, 6.61; N, 5.40. Found: C, 69.49; H, 6.79; N, 5.25%.

4.2.2. (1*S*,2*R*,10b*S*)-1,2-Diacetoxy-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinolin-3-one, 13a. Crystallization of crude reaction mixture (hexane/ethyl acetate) gave **13a** as colourless crystals, yield 92%, mp 185–6°C; IR (CH_2Cl_2): 3060, 2938, 1754, 1720 cm^{-1}; $[\alpha]_D$ = +90 (*c* 1, CH_2Cl_2); ^{1}H NMR ($CDCl_3$): 5.66 (dd, 1H, *J* = 7.1, 1.1 Hz), 5.42 (t, 1H, *J* = 7.1 Hz), 4.82 (d, 1H, *J* = 7.1 Hz), 3.34 (ddd, 1H, *J* = 12.7, 5.8, 2.8 Hz), 3.12 (m, 1H), 3.00 (m, 1H), 2.79 (m, 1H), 2.21 and 2.13 (two s, 6H); ^{13}C NMR ($CDCl_3$): 170.29, 169.92, 165.39, 133.53, 133.32, 129.42, 127.82, 127.28, 124.50, 78.40, 75.35, 56.53, 37.13, 28.16, 20.90, 20.63; MS (LSIMS(+), HR) *m*/*z*: ($M+Na^+$) calcd for $C_{16}H_{17}O_5NNa$: 326.1004. Found: 326.1009. Anal. calcd for $C_{16}H_{17}O_5N$: C, 63.36; H, 5.65; N, 4.62. Found: C, 63.48; H, 5.75; N, 4.75%.

4.3. General procedure for the preparation of 1,2-dihydroxypyrroloisoquinolinones 9, 10, and 13b from 7, 8, and 13a

The acetyl chloride (10 mL) was added dropwise to the anhydrous methanol (100 mL), while stirring at 0°C. To the resulted solution the pyrroloisoquinolinone **7**, **8** or **13a** (15 mmol) dissolved in methanol (50 mL) was added. The reaction mixture was allowed to warm to rt and stirred for 3 h. The solvent was evaporated in vacuum and the residue was co-evaporated with additional methanol (2×20 mL). The crude product was filtered through silica gel and recrystallized from a methanol–ethyl acetate mixture.

4.3.1. (1*S*,2*S*,10b*S*)-1,2-Dihydroxy-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinolin-3-one, 9. Colourless crystals, yield 88%, mp 186–187°C; IR (KBr): 3336, 3265, 2941, 2879, 1679, 1 cm^{-1}; $[\alpha]_D$ = +94 (*c* 1.1, DMSO); ^{1}H NMR (DMSO-d_6): 5.73 (d, 1H, *J* = 5.0 Hz), 5.41 (d, 1H, *J* = 7.4 Hz), 4.54 (d, 1H, *J* = 6.3 Hz), 4.03 (m, 1H), 3.81 (m, 2H), 2.99 (m, 1H), 2.75 (m 2H); ^{13}C NMR (DMSO-d_6): 170.19, 135.68, 133.45, 128.74, 126.52, 126.31, 125.23, 73.79, 70.67, 59.65, 35.68, 28.08; MS (EI, HR) *m*/*z*: (M^+) calcd for $C_{12}H_{13}O_3N$: 219.0895. Found: 219.0907. Anal. calcd for $C_{12}H_{13}O_3N$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.76; H, 6.08; N, 6.56%.

4.3.2. (1*S*,2*S*,10b*R*)-1,2-Dihydroxy-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinolin-3-one, 10. Colourless crystals, yield 94%, mp 225–228°C (MeOH); IR (KBr): 3333, 3305, 2842, 1682 cm^{-1}; $[\alpha]_D$ = −316 (*c* 1.0, DMSO); ^{1}H NMR (DMSO-d_6): 5.33 (bs, 1H), 4.73 (d, 1H, *J* = 3.2 Hz), 4.59 (bs, 1H), 4.48 (dd, 1H, *J* = 3.6, 3.2 Hz), 4.31 (d, 1H, *J* = 3.6 Hz), 4.07 (m, 1H), 2.89 (m, 1H), 2.68 (m, 2H); ^{13}C NMR (DMSO-d_6): 171.39, 135.03, 132.51, 128.64, 126.23, 126.02, 125.98, 72.61, 70.92, 57.67, 35.85, 28.04; MS (EI, HR) *m*/*z*: (M^+) calcd for $C_{12}H_{13}O_3N$: 219.0895. Found: 219.0887. Anal. calcd for $C_{12}H_{13}O_3N$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.83; H, 6.16; N, 6.20%.

4.3.3. (1*S*,2*R*,10b*S*)-1,2-Dihydroxy-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinolin-3-one, 13b. Colourless crystals, yield 90%. Mp 160–162°C (MeOH). Lit.[11] mp 161–163°C.

4.4. General procedures for the preparation of 1,2-dihydroxypyrroloisoquinolines 2, 3 and 4

To a stirred suspension of $LiAlH_4$ (0.19 g, 5 mmol) in THF (10 mL) was added the pyrroloisoquinolinone **9**, **10** or **13a** (1 mmol) and the resulting mixture was heated under reflux for 4–6 h (TLC control). The solution was cooled to rt and was quenched with vigorous stirring by the successive addition of water (0.2 mL), 20% aqueous sodium hydroxide solution (0.2 mL) and ammonium hydroxide 25% (0.4 mL). The mixture was filtered through a pad of Celite, and the white precipitate washed several times with THF containing ~1% of concentrated ammonium hydroxide. The combined filtrates were concentrated and purified by flash column chromatography on silica gel (CH_2Cl_2:MeOH:NH_4OH/H_2O (25%), 9:1:0.1).

4.4.1. (1*S*,2*R*,10b*S*)-1,2-Dihydroxy-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline, 2. Foam, yield 58%; IR (CH_2Cl_2): 3605, 3355, 3050, 2928 cm^{-1}; $[\alpha]_D = +13$ (*c* 0.8, CH_2Cl_2); ^1H NMR ($CDCl_3$+D_2O): 4.33 (m, 1H), 4.1 (t, 1H, $J = 6.7$ Hz), 3.64 (d, 1H, $J = 6.7$ Hz), 3.34 (dd, 1H, $J = 10.4$, 5.6 Hz), 3.05 (m, 1H), 2.98 (m, 1H), 2.80 (m, 1H), 2.71 (m, 2H); ^{13}C NMR ($CDCl_3$): 136.56, 134.21, 128.52, 126.48, 126.26, 125.59, 77.20, 69.18, 66.36, 59.00, 47.95, 26.91; MS (EI, HR) *m*/*z*: (M^+) calcd for $C_{12}H_{15}O_2N$: 205.1103. Found: 205.1095.

4.4.2. (1*S*,2*R*,10b*R*)-1,2-Dihydroxy-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline, 3. Oil, yield 49%; IR (CH_2Cl_2): 3601, 3361, 3052, 2927 cm^{-1}; $[\alpha]_D = -206$ (*c* 1.3, CH_2Cl_2); ^1H NMR ($CDCl_3$+D_2O): 4.45 (dd, 1H, $J = 5.4$, 3.6 Hz), 4.38 (m, 1H), 3.54 (bd, 1H, $J = 3.3$ Hz), 3.18 (ddd, 1H, $J = 11.0$, 6.3, 1.9 Hz), 3.08 (m, 1H), 3.03 (dd, 1H, $J = 11.0$, 2.8 Hz), 2.73 (m, 2H), 2.53 (m, 1H); ^{13}C NMR ($CDCl_3$): 135.65, 131.90, 128.94, 126.94, 126.25, 126.23, 71.74, 70.40, 66.94, 60.40, 48.88, 28.17; MS (EI, HR) *m*/*z*: (M^+) calcd for $C_{12}H_{15}O_2N$: 205.1103. Found: 205.1098.

4.4.3. (1*S*,2*S*,10b*S*)-1,2-Dihydroxy-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline, 4. Colourless crystals, yield 78%, mp 123–125°C (hexane/CH_2Cl_2); IR (CH_2Cl_2): 3603, 3351, 3052, 2930, 2808 cm^{-1}; $[\alpha]_D = +55$ (*c* 1, CH_2Cl_2); ^1H NMR ($CDCl_3$+D_2O): 4.12 (m, 1H), 3.96 (dd, 1H, $J = 7.5$, 3.3 Hz), 3.37 (d, 1H, $J = 7.5$ Hz), 3.08 (m, 2H), 2.88 (dd, 1H, $J = 10.3$, 3.0 Hz), 2.80 (dd, 1H, $J = 10.3$, 6.3 Hz), 2.71 (m, 1H), 2.60 (m, 1H); ^{13}C NMR ($CDCl_3$): 136.35, 133.99, 128.49, 126.62, 126.14, 125.00, 84.48, 78.21, 67.75, 59.04, 48.63, 27.37; MS (EI, HR) *m*/*z*: (M^+) calcd for $C_{12}H_{15}O_2N$: 205.1103. Found: 205.1096. Anal. calcd for $C_{12}H_{15}O_2N$: C, 70.22; H, 7.37; N, 6.82. Found: C, 70.06; H, 7.31; N, 6.83%.

4.5. (3*R*,4*R*,5*S*)- and (3*R*,4*R*,5*R*)-1-Phenethyl-3,4,5-triacetoxypyrrolidin-2-one, 12b

To a stirred solution of imide **11** (4.7 g, 20 mmol) in anhydrous methanol (60 mL), the $NaBH_4$ (0.84 g, 22 mmol) was added at −10°C. Stirring was continued at −10°C for 2 h (TLC control). Subsequently, the saturated solution of $NaHCO_3$ (20 mL) was added, and mixture was vigorously stirred for 20 min. The precipitate was filtered off and the filtrate was evaporated under reduced pressure. The oily residue was dissolved in pyridine (30 mL), DMAP (0.1 g) and Ac_2O (15 mL) were added and left in the refrigerator overnight. The solution was poured into ice–water mixture (150 mL) and extracted with ethyl acetate (2×50 mL). The combined extracts were washed with water (3×50 mL), saturated solution of sodium bicarbonate (50 mL), dried ($MgSO_4$) and evaporated. The crude product was purified by flash column chromatography (hexane: *t*-BuOMe, 1:3) to give **12b** (5.88 g, 81% yield calculated for two steps); oil; IR (CH_2Cl_2): 3064, 3031, 2947, 1755, 1736 cm^{-1}. Selected data for the mixture of epimers **5***S*:**5***R* (1:1); ^1H NMR ($CDCl_3$): 5.99 (d, 1H, $J = 1.9$ Hz), 5.69 (d, 1H, $J = 8.2$ Hz), 5.24 (m, 2H), 5.13 (dd, 1H, $J = 3.8$, 1.9 Hz), 3.83 (m, 2H), 3.36 (m, 1H), 3.22 (m, 1H), 2.95 (m, 2H), 2.83 (m, 2H); ^{13}C NMR ($CDCl_3$): 170.19, 169.95, 169.83, 169.69, 169.56, 169.48, 167.82, 167.68, 137.66, 137.65, 128.76, 128.72, 128.70, 128.64, 126.85, 126.75, 83.79, 79.22, 75.92, 75.90, 70.91, 70.76, 43.52, 42.17, 33.84, 33.49, 20.77, 20.66, 20.62, 20.55, 20.51, 20.36; MS (EI, HR) *m*/*z*: (M^+) calcd for $C_{18}H_{21}O_7N$: 363.1318. Found: 363.1304.

4.6. (1*S*,2*R*,10b*S*)-2-Benzoyloxy-1-hydroxy-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinolin-3-one, 14

To a stirred solution of **13b** (0.219 g, 1 mmol) in pyridine (3.8 mL), cooled to −30°C, the benzoyl chloride (0.156 g, 1.1 mmol) was added dropwise. The mixture was stirred for 1 h at −30°C and was allowed to warm very slowly (over 3 h) to 0°C and left in refrigerator overnight. Ethyl acetate was added (15 mL) and the mixture was washed with 2N HCl. The organic layer was washed additionally with brine, dried over $MgSO_4$ and evaporated under reduced pressure. The residue was purified by flash column chromatography (CH_2Cl_2:MeOH:NH_3/aq., 20:1:0.1) to give benzoate **14** (0.259 g, 80% yield); colourless crystals, mp 153–155°C (hexane/ethyl acetate); IR (CH_2Cl_2): 3364, 3062, 2934, 1731, 1696 cm^{-1}; $[\alpha]_D = +87$ (*c* 1.7, CH_2Cl_2); ^1H NMR ($CDCl_3$+D_2O): 5.52 (dd, 1H, $J = 7.0$, 1.3 Hz), 4.71 (bd, 1H, $J = 7.0$ Hz), 4.34 (ddd, 1H, $J = 12.9$, 6.0, 2.8 Hz), 4.28 (t, 1H, $J = 7.0$ Hz), 3.15 (m, 1H), 2.99 (m, 1H), 2.81 (m, 1H); ^{13}C NMR ($CDCl_3$): 168.04, 165.29, 134.45, 133.89, 132.98, 130.22, 129.03, 128.53, 128.49, 127.48, 127.16, 125.43, 80.90, 79.67, 58.86, 36.95, 28.11; MS (LSIMS(+), HR) *m*/*z*: ($M+H^+$) calcd for $C_{19}H_{18}O_4N$: 324.1236. Found: 324.1237. Anal. calcd for $C_{19}H_{17}O_4N$: C, 70.58; H, 5.30; N, 4.33. Found: C, 70.41; H, 5.31; N, 4.17%.

4.7. (1*R*,2*R*,10b*S*)-1-Benzoyloxy-2-hydroxy-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinolin-3-one, 16

A vigorously stirred solution of compound **14** (0.646 g, 2 mmol) and pyridine (0.32 g, 0.32 mL, 4 mmol) in CH_2Cl_2 (10 mL) was cooled to −30°C. To this solution triflic anhydride (0.9 g, 0.53 mL, 3.2 mmol) was added dropwise and the mixture was allowed to reach rt very slowly (2 h). The mixture was stirred at rt for additional 1 h (TLC monitoring), then water (1.5 mL) was added and the reaction mixture was left overnight with stirring at rt. The mixture was poured into water, extracted with CH_2Cl_2, extracts washed with water, saturated solution of $NaHCO_3$, dried over $MgSO_4$ and evaporated under reduced pressure. The residue was purified by flash column chromatography (hexane:ethyl acetate, 1:4) to give benzoate **16** (0.486 g, 75% yield); foam; IR (CH_2Cl_2): 3550, 3063, 2942, 1713 cm^{-1}; $[\alpha]_D = +239$ (*c* 0.5, CH_2Cl_2); ^1H NMR ($CDCl_3$+D_2O): 6.23 (m, 1H), 5.12 (bd, 1H, $J = 3.6$ Hz), 4.73 (dd, 1H, $J = 4.5$, 1.2 Hz), 4.45 (ddd, 1H, $J = 12.1$, 5.4, 2.3 Hz), 3.09 (ddd, 1H, $J = 12.1$, 3.0, 1.2 Hz), 3.01 (m, 1H), 2.82 (m, 1H); ^{13}C NMR ($CDCl_3$): 171.16, 165.57, 134.70, 133.07, 129.60, 129.38, 129.24, 129.13, 128.16, 127.43, 127.00, 125.89, 72.93, 71.98, 57.46, 37.17, 28.74; MS (LSIMS(+), HR) *m*/*z*: ($M+Na^+$) calcd for $C_{19}H_{17}O_4NNa$: 346.1055. Found: 346.1044.

4.8. (1*R*,2*R*,10b*S*)-1,2-Dihydroxy-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinolin-3-one, *ent*-10

Compound **16** (0.322 g, 1 mmol) was dissolved in an anhydrous methanol (5 mL) at rt. While the solution was stirring, the MeONa (0.006 g, 0.1 mmol) was added. Stirring was continued for 3 h (TLC control), then reaction was quenched by the addition of a small piece of dry ice, precipitate was filtered off, and the filtrate was evaporated under reduced pressure. The crude product was recrystallized from methanol to give *ent*-**10** (0.18 g, 83%), mp 223–225°C (MeOH); $[\alpha]_D = +309$ (*c* 0.8, DMSO).

4.9. (1*S*,2*R*,10b*S*)-2-(*tert*-Butyldimethylsilanyloxy)-1-hydroxy-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinolin-3-one, 17a

To the stirred solution of **13b** (0.876 g, 4 mmol) and imidazole (0.6 g, 8.8 mmol) in DMF (9 mL) was added *tert*-butyldimethylchlorosilane (0.72 g, 4.4 mmol) and the mixture was stirred for 2 days at rt. The mixture was poured into the water, extracted with ethyl acetate, washed with water, brine, dried over $MgSO_4$, and evaporated under reduced pressure. The residue was purified by flash column chromatography (CH_2Cl_2:*t*-BuOMe:acetone, 98:1:1) to give **17a** (0.99 g, 75% yield); colourless crystals, mp 147–150°C (hexane/ether); IR (CH_2Cl_2): 3377, 2930, 1692 cm^{-1}; $[\alpha]_D = +194$ (*c* 1.0, CH_2Cl_2); ^1H NMR ($CDCl_3$): 4.51 (bd, 1H, $J = 7.8$ Hz), 4.44 (dd, 1H, $J = 7.8$, 1.0 Hz), 4.29 (m, 1H), 4.02 (t, 1H, $J = 7.8$ Hz), 2.95 (m, 2H), 2.74 (m, 1H), 0.94 (s, 9H), 0.23 and 0.19 (two s, 6H); ^{13}C NMR ($CDCl_3$): 169.21, 134.49, 133.41, 129.26, 127.25, 126.89, 125.30, 81.81, 78.24, 57.32, 36.23, 28.50, 25.79, 18.37, –4.23, –5.00; MS (LSIMS(+), HR) *m*/*z*: ($M+H^+$) calcd for $C_{18}H_{28}O_3NSi$: 334.1838. Found: 334.1822. Anal. calcd for $C_{18}H_{27}O_3NSi$: C, 63.83; H, 8.16; N, 4.20. Found: C, 64.89; H, 7.93; N, 4.25%.

4.10. (1*S*,2*R*,10b*S*)-1-Benzoyloxy-2-(*tert*-butyldimethylsilanyloxy)-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinolin-3-one, 17b

A mixture of **17a** (0.8 g, 2.4 mmol), benzoic anhydride (0.81 g, 3.6 mmol) and DMAP (catalytic amount) in pyridine (8 mL) was stirred overnight at rt. The solution was poured into the water, extracted with ethyl acetate, washed with water, brine, dried over $MgSO_4$, and evaporated under reduced pressure. The residue was purified by flash column chromatography (CH_2Cl_2:*t*-BuOMe:acetone, 98:1:1) to give **17b** (0.65 g, 62% yield); colourless crystals, mp 145–146°C (hexane); IR (CH_2Cl_2): 2930, 1722, 1694 cm^{-1}; $[\alpha]_D = +104$ (*c* 1.0, CH_2Cl_2); ^1H NMR ($CDCl_3$): 5.67 (t, 1H, $J = 7.0$ Hz), 4.84 (bd, 1H, $J = 7.0$ Hz), 4.68 (dd, 1H, $J = 7.0$, 1.1 Hz), 4.31 (ddd, 1H, $J = 12.6$, 5.7, 3.1 Hz), 3.08 (m, 1H), 3.00 (m, 1H), 2.76 (m, 1H), 0.81 (s, 9H), 0.13 and 0.04 (two s, 6H); ^{13}C NMR ($CDCl_3$): 168.85, 165.14, 133.72, 133.54, 133.52, 129.82, 129.54, 129.32, 128.63, 127.54, 127.16, 124.89, 80.88, 76.32, 56.64, 36.85, 28.36, 25.49, 18.19, –4.54, –5.31; MS (LSIMS(+), HR) *m*/*z*: ($M+H^+$) calcd for $C_{25}H_{32}O_4NSi$: 438.2101. Found: 438.2096. Anal. calcd for $C_{25}H_{31}O_4NSi$: C, 68.62; H, 7.14; N, 3.20. Found: C, 68.63; H, 7.20; N, 3.24%.

4.11. (1*S*,2*R*,10b*S*)-1-Benzoyloxy-2-hydroxy-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinolin-3-one, 17c

To a stirred solution of compound **17b** (0.75 g, 1.7 mmol) in THF (5 mL), the tetrabutylammonium fluoride trihydrate (0.7 g, 2.26 mmol) and acetic acid (0.135 g, 0.13 mL, 2.26 mmol) were added. The mixture was stirred for 3 days at rt. The solution was poured into the water, extracted with ethyl acetate, washed with water, brine, dried over $MgSO_4$, and evaporated under reduced pressure. The residue was purified by flash column chromatography (hexane:ethyl acetate, 2:3, gradually changing to 1:4) to give **17c** (0.38 g, 69% yield); colourless crystals, mp 203–204°C (benzene); IR (CH_2Cl_2): 3686, 3526, 2929, 1716, cm^{-1}; $[\alpha]_D = -43$ (*c* 1.1, CH_2Cl_2); ^1H NMR ($CDCl_3$+D_2O): 5.35 (t, 1H, $J = 7.1$ Hz), 4.98 (bd, 1H, $J = 7.1$ Hz), 4.69 (dd, 1H, $J = 7.1$, 1.2 Hz), 4.37 (ddd, 1H, $J = 12.8$, 5.8, 2.8 Hz), 3.15 (m, 1H), 3.01 (m, 1H), 2.82 (m, 1H); ^{13}C NMR ($CDCl_3$): 168.48, 166.70, 133.95, 133.58, 133.48, 130.00, 129.46, 128.91, 128.75, 127.80, 127.34, 124.80, 83.26, 75.67, 56.53, 37.01, 28.30; MS (LSIMS(+), HR) *m*/*z*: ($M+H^+$) calcd for $C_{19}H_{18}O_4N$: 324.1236. Found: 324.1226. Anal. calcd for $C_{19}H_{17}O_4N$: C, 70.58; H, 5.30; N, 4.33. Found: C, 70.37; H, 5.34; N, 4.35%.

4.12. (1*S*,2*S*,10b*S*)-2-Benzoyloxy-1-hydroxy-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinolin-3-one, 19a and (1*S*,2*S*,10b*S*)-1-benzoyloxy-2-hydroxy-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinolin-3-one, 19b

Benzoate **17c** (0.646 g, 2 mmol) was treated with Tf_2O/Py in the same way as described for **14** to give mixture of **19a** and **19b** (1:9). The residue was purified by flash column chromatography (hexane:ethyl acetate, 2:3).

Compound **19a**: colourless crystals, yield 0.042 g (6.5%), mp 179–182°C (hexane/ethyl acetate); IR (CH_2Cl_2): 3583, 3058, 2929, 1710, cm^{-1}; $[\alpha]_D = +42$ (*c* 1.0, CH_2Cl_2); ^1H NMR ($CDCl_3$+D_2O): 5.45 (d, 1H, $J = 6.2$ Hz), 4.80 (bd, 1H, $J = 6.4$ Hz), 4.41 (m, 2H), 3.19 (m, 1H), 2.96 (m, 1H), 2.83 (m 1H); ^{13}C NMR ($CDCl_3$): 166.97, 166.49, 134.23, 133.73, 133.19, 130.17, 129.17, 128.83, 128.50, 127.53, 127.14, 125.59, 73.57, 73.13, 61.00, 37.13, 28.45; MS (LSIMS(+), HR) *m*/*z*: ($M+H^+$) calcd for $C_{19}H_{18}O_4N$: 324.1236. Found: 324.1245. Anal. calcd for $C_{19}H_{17}O_4N$: C, 70.58; H, 5.30; N, 4.33. Found: C, 70.40; H, 5.29; N, 4.06%.

Compound **19b**: semisolid, yield 0.378 g (59%); IR (CH_2Cl_2): 3585, 3323, 3057, 1711, 1689 cm^{-1}; $[\alpha]_D = -93$ (*c* 1.1, CH_2Cl_2); ^1H NMR ($CDCl_3$+D_2O): 5.36 (dd, 1H, $J = 6.2$, 5.2 Hz), 5.10 (bd, 1H, $J = 5.1$ Hz), 4.58 (d, 1H, $J = 6.2$ Hz), 4.35 (ddd, 1H, $J = 12.7$, 6.3, 2.4 Hz), 3.19 (m, 1H), 2.99 (m, 1H), 2.80 (m, 1H); ^{13}C NMR ($CDCl_3$): 170.47, 165.91, 133.63, 133.60, 133.48, 129.98, 129.47, 129.22, 128.59, 127.75, 127.19, 125.24, 74.74,

69.77, 59.37, 37.44, 28.22; MS (LSIMS(+), HR) m/z: ($M+H^+$) calcd for $C_{19}H_{18}O_4N$: 324.1236. Found: 324.1234.

4.13. Preparation of (1*S*,2*S*,10b*S*)-1,2-dihydroxy-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinolin-3-one 9 from 19a and 19b

Benzoates **19a** and **19b** were separately treated with NaOMe/MeOH in the same way as described for *ent*-**10**, giving in both cases **9** (~80% yield after crystallization from MeOH/EtOAc), colourless crystals, mp 184–186°C; $[\alpha]_D = +92$ (*c* 0.8, DMSO).

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References

1. Jacobsen, E. N.; Pfatz, A.; Yamamoto, H., Eds. *Comprehensive Asymmetric Catalysis*; Springer: New York, 1999.
2. Seyden-Penne, J. *Chiral Auxiliaries and Ligands in Asymmetric Synthesis*; J. Wiley: New York, 1995.
3. Dalko, P. I.; Moisan, L. *Angew. Chem., Int. Ed.* **2001**, *40*, 3726–3748.
4. Pu, L.; Yu, H.-B. *Chem. Rev.* **2001**, *101*, 757–824.
5. Basavaiah, D.; Rao, P. D.; Hyma, R. S. *Tetrahedron* **1996**, *52*, 8001–8062.
6. Manickam, G.; Sundararjan, G. *Tetrahedron* **1999**, *55*, 2721–2736.
7. Nordin, S. J. M.; Roth, P.; Tarnaj, T.; Alonso, D. A.; Brandt, P.; Andresson, P. G. *Chem. Eur. J.* **2001**, *7*, 1431–1436.
8. Corey, E. J.; Bakshi, R. K.; Shibata, S. *J. Am. Chem. Soc.* **1987**, *109*, 5551–5553.
9. Corey, E. J.; Xu, F.; Noe, M. C. *J. Am. Chem. Soc.* **1997**, *119*, 12414–12415.
10. Ostendorf, M.; van der Neut, S.; Rutjes, F. P. J.; Himestra, H. *Eur. J. Org. Chem.* **2000**, 105–113.
11. Lee, Y. S.; Kang, D. W.; Lee, S. J.; Park, H. *Synth. Commun.* **1995**, *25*, 1947–1956.
12. Lee, Y. S.; Kang, D. W.; Lee, S. J.; Park, H. *J. Org. Chem.* **1995**, *60*, 7149–7152.
13. Lee, Y. S.; Lee, Y. J.; Park, H. *Synth. Commun.* **1997**, *27*, 2799–2812.
14. Maryanoff, B. E.; McComsey, D. F.; Gadocki, J. F.; Shank, R. P.; Costanzo, M. J.; Nortey, S. O.; Schneider, C. R.; Setler, P. E. *J. Med. Chem.* **1987**, *30*, 1433–1454.
15. Ali, S. M.; Ramesh, K.; Borchardt, R. T. *Tetrahedron Lett.* **1990**, *31*, 1509–1512.
16. Kotsuki, H.; Iwasaki, M.; Ochi, M. *Heterocycles* **1994**, *38*, 17–20.
17. Grigg, R.; Myers, P.; Somasunderam, A.; Sridharan, V. *Tetrahedron* **1992**, *48*, 9735–9744.
18. Casiraghi, G.; Spanu, P.; Rassu, G.; Pinna, L.; Ulgheri, F. *J. Org. Chem.* **1994**, *59*, 2906–2909.
19. Carpenter, N. M.; Fleet, W. J.; Bello, I. C.; Winchester, B.; Fellows, L. E.; Nash, R. J. *Tetrahedron Lett.* **1989**, *30*, 7261–7264.
20. Almeida, J. F.; Grande, M.; Moran, J. R.; Anaya, J.; Mussons, M. L.; Caballero, M. C. *Tetrahedron: Asymmetry* **1993**, *4*, 2483–2494.