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TETRAHEDRON: *ASYMMETRY*

Asymmetric routes towards polyfunctionalized pyrrolidines: application to the synthesis of alkaloid analogues

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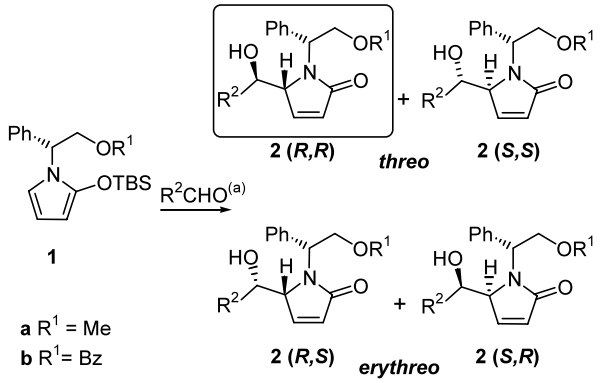
Abstract—The Mukaiyama aldol type condensation of *t*-butyldimethylsilyloxypyrrole **1b** with methyl 2-formylbenzoate furnished the aldol adduct **9** with high yield and complete stereoselectivity. An *erythro* (*anti*) configuration was established (X-ray) in sharp contrast with the reaction of **1b** with aliphatic aldehydes. Simple chemical transformations were used to transform **9** into original phthalidopyrrolidine compound analogous of bicuculline alkaloids.

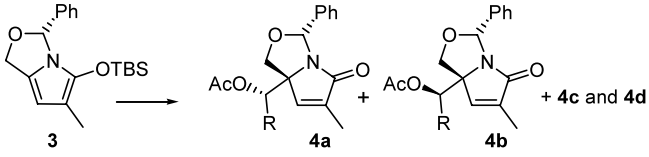
1. Introduction

In previous papers, we reported on the Mukaiyama–aldol type condensation[1] between chiral non-racemic silyloxypyrroles **1** and various aliphatic aldehydes (Scheme 1).[2–4] The reactions occurred in high yield and good diastereoselectivity. Further studies showed improved yields and selectivities by the use of benzoylated silyloxypyrrole **1b**.[4] In the latter case, only *threo* (*syn*) derivatives **2b** were observed. The diastereofacial selectivity of the reaction was generally good (*RR*:*SS* >75:25) allowing the synthesis of pyrrolidine derivatives.[3,4]

In our previous studies, aromatic aldehydes were not extensively examined since the only example we reported on was the condensation of **1a** with benzaldehyde which exhibited apparent good diastereoselectivity but in rather low yield (only 25%).[2] We were particularly interested to investigate further the condensation with aromatic aldehydes in order to improve the diversity of R^2 substituents. Moreover the possibility to obtain *erythro* (*anti*) derivatives instead of *threo* could be expected. In fact, it was reported by Baldwin and Uno that a reverse relative configuration was observed when aromatic or aliphatic aldehydes were condensed with silyloxypyrrolooxazole **3** (Scheme 2).[5–7] This difference of selectivity was rationalised by those authors



Scheme 1. *Reaction conditions*: (a) $BF_3{\cdot}OEt_2$, CH_2Cl_2, –70°C.



Scheme 2.

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with transition states implying aromatic π–π interactions.[7]

Herein we present recent results on the condensation of silyloxypyrrole **1b** with some aromatic aldehydes. We show that good reverse diastereoselectvity can be observed with one particular aromatic aldehyde. Applications of this reaction to the efficient asymmetric synthesis of alkaloid analogues is described. These molecules have potential activities on the nervous central system by analogy to phthalidoisoquinoline such as bicuculline (Fig. 1) and congeners (strong antagonists of Gaba receptors).[8–12]

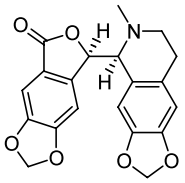


Figure 1.

2. Results and discussion

2.1. Aldol condensation

The condensation of **1b** with some aromatic aldehydes was conducted using standard conditions: CH_2Cl_2, −70°C, $BF_3{\cdot}OEt_2$ (Scheme 1). The results of this aldolisation reaction are summarized in Table 1.

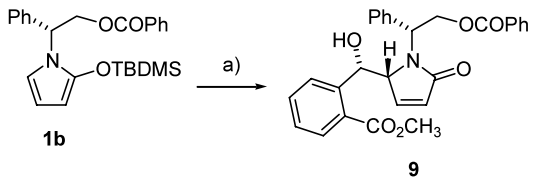
Table 1. Aldol condensation of silyloxypyrrole **1b** with various aromatic aldehydes

R^2		Yield (%)[a]	Isomeric ratio[b]
C_6H_5	**5**	94	40/40/20
p-$NO_2C_6H_4$	**6**	99	40/38/18/4
1-Naphthyl	**7**	80	40/35/25
2-Naphthyl	**8**	80	50/25/25

[a] Isolated yield after purification by flash chromatography on silica gel.

[b] Determined by ^1H and ^{13}C NMR of the crude reaction mixture.

In every case, very good yields for aldol products **2b** were obtained, but most of them were isolated as a mixture of stereoisomers without any selectivity. In some instances, one epimer could be separated from the mixture but not many attempts were made in order to determine its relative configuration. At this point, we thought to try heteroaromatic aldehydes. The presence of a supplementary chelating center could help to rigidify the transition state and then improve the diastereoselectivity. Unfortunately, reaction with pyridine-, furane-, *N*-methylpyrrole-, free and *N*-protected indole-carboxaldehyde failed to give aldol adducts under the above conditions. The thiophene-2-carboxaldehyde is the only heteroaromatic carboxaldehyde which could be condensed but in poor yield and with almost no stereoselectivity. Then, we decided to consider the introduction of a chelating goup on the phenyl ring. By constrast we were delighted to observe that reaction of **1b** with methyl-2-formylbenzoate gave aldol adduct **9** with both excellent yield and selectivity (Scheme 3). In this case, only one diastereoisomer was isolated. Careful analysis of ^1H NMR spectra of **9** showed a very small coupling constant ($J \sim 1$ Hz) between the two protons borne at the stereogenic carbons. This coupling constant value contrasts with previous observations made with aliphatic derivatives ($J \sim 6$ Hz) and could suggest a stereochemical change as was indicated above. Proof of the *erythro* (*anti*) configuration was assigned by single crystal X-ray analysis on a further derivative as shown below (Scheme 5, Fig. 3).



Scheme 3. *Reagents and conditions*: (a) *o*-$MeO_2CC_6H_4CHO$, $BF_3{\cdot}OEt_2$, CH_2Cl_2, −70°C, 95%.

The difference of selectivity could be explained, because of steric influences, by a [4+2] *exo* transition state $\mathbf{T_A}$ for aliphatic aldehydes where the Lewis acid is *s-trans* relative to the R^2 substituent (Fig. 2). In contrast, with the methyl 2-formylbenzoate, a synclinal approach $\mathbf{T_B}$ can be suggested. In the latter case, the boron atom adopts an *s-cis* conformation relative to the substituent by linking the ester group and, therefore, π–π interactions between the aromatic ring and the pyrrole moiety become the controlling factor.

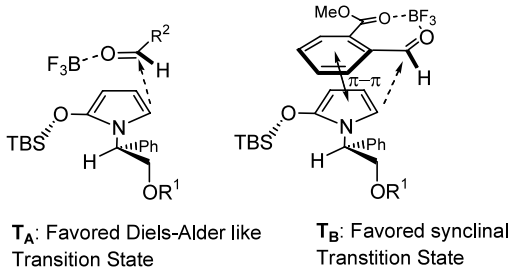
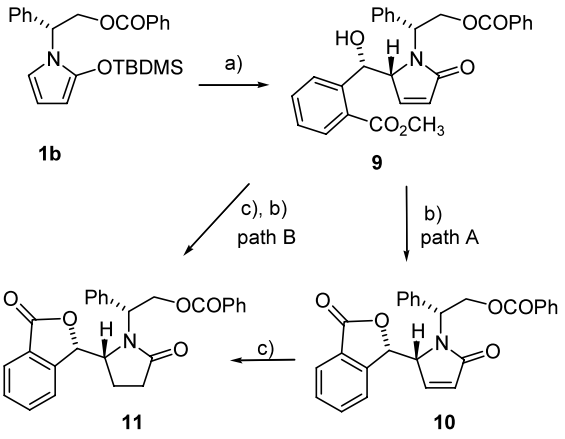


Figure 2.

2.2. Synthesis of alkaloid analogues

The presence of the ester group induces a new relative configuration during the aldolisation reaction and also allows access to the phthalidopyrrolidine moiety with a relative *erythro* (*anti*) configuration in agreement with the natural bicuculline to be considered. In fact, after purification on silica gel, it appears that the major aldol product **9** was contaminated by small amount of cyclized product **10** (Scheme 4). Aldol adduct **9** was then cleanly and completely cyclised to **10** in an excellent yield (90–98%) in the presence of silica gel in



Scheme 4. *Reagents and conditions*: (a) *o*-$MeO_2CC_6H_4CHO$, $BF_3{\cdot}OEt_2$, CH_2Cl_2, −70°C, 95%. Path A: (b) SiO_2, CH_2Cl_2, 90–98%; (c) H_2, Pd/C, CH_3OH, 90%. Path B: (a), (c), (b) 79% overall.

dichloromethane at room temperature, or with a catalytic amount of titanium tetraisopropoxide in refluxing chloroform (95%).[13]

The reduction of the double bond of **10** was easily achieved by simple palladium catalysed hydrogenation to give **11** as a single stereomer after flash chromatography. After optimisation, it was found more convenient to first reduce the double bond of adduct **9** and then perform the cyclization by simple stirring in CH_2Cl_2 in the presence of some silica gel (Scheme 4, path B). Compound **11** was then isolated in 79% overall yield from silyloxypyrrole **1b** with only one final silica gel purification. The synthesis was followed by the selective reduction of the lactam function of **11**. This was obtained by the use of $BH_3{\cdot}THF$ which allowed the preparation of the pyrrolidine phthalide **12** in 81% yield after purification (Scheme 5). At this stage, it was possible to determine the absolute configuration of the two stereogenic centers generated through the aldol condensation as discussed above. Pyrrolidine phthalide **12** furnished crystals which were found suitable for single crystal X-ray analysis (the ORTEP representation is given in Fig. 3).

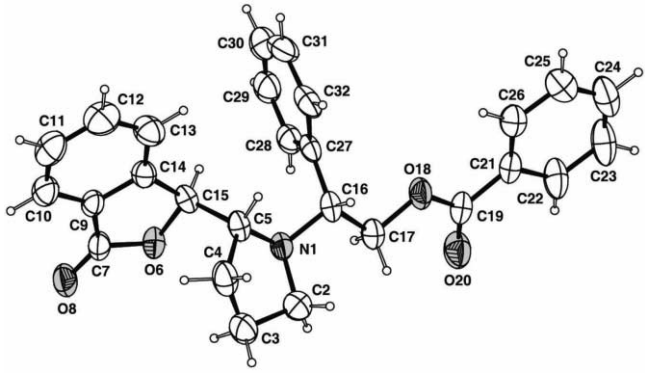
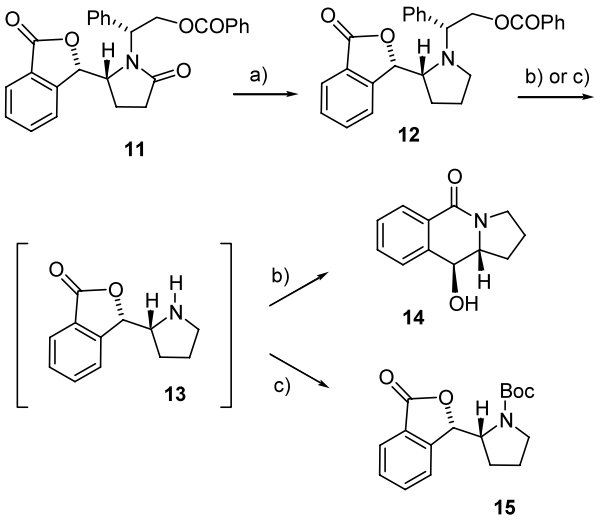


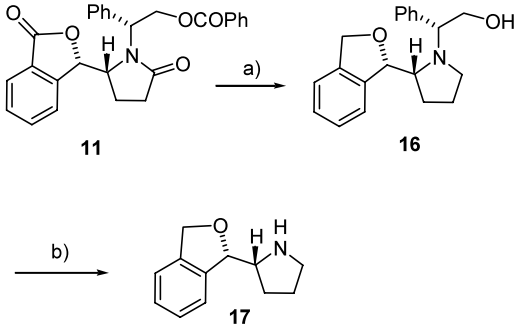
Figure 3. ORTEP drawing of **12**. Displacement ellipsoids are shown at the 30% probability level.



Scheme 5. *Reagents and conditions*: (a) $BH_3{\cdot}THF$, 81%; (b) H_2, $Pd(OH)_2/C$, AcONa, CH_3OH, 54%; (c) H_2, Pd/C, Boc_2O, proton sponge, CH_3OH, 95%.

Cleavage of the chiral auxiliary of pyrrolidine phthalide **12** occurred in the presence of Pd/C at atmospheric pressure of hydrogen to give the pyrrolidine **13**. Unfortunately, the latter was not stable and upon purification was transformed into the hydroxy-lactam **14** which could be isolated in 54% yield. An *N*-Boc derivative **15** was eventually prepared and obtained in 95% yield when the hydrogenolysis was performed in the presence of Boc_2O providing a stable *N*-protected derivative of the target molecule (Scheme 5).

A totally reduced compound **16** was obtained from **11** in a quantitative yield by reaction with $LiAlH_4$ in refluxing THF. Deprotection of the chiral auxiliary by hydrogenolysis led to the dihydroisobenzofuranpyrrolidine **17** (Scheme 6).



Scheme 6. *Reagents and conditions*: (a) $LiAlH_4$, THF, reflux, 99%; (b) H_2, Pd/C, CH_3OH, 59%.

In conclusion, we have shown that condensation of **1b** with benzaldehyde *ortho*-substituted by an ester group furnished the aldol product in high yield and completely stereoselectively. X-Ray crystallographic analysis showed that this reaction occurred with an opposite relative configuration as that usually observed with

aliphatic aldehydes. This process allowed us to synthesise enantiomerically pure pyrrolidines bearing lactone or dihydrobenzofuran moieties in only five steps (from **1b**) with excellent overall yields of 61 and 46%, respectively.

3. Experimental

3.1. General

All solvents were purified by standard methods. Melting points were determinated on a Büchi BS-540 melting point microscope and are uncorrected. IR spectra were obtained using a Nicolet 205-FT infrared spectrophotometer. Only noteworthy IR absorptions are listed (cm^{-1}). ^1H and ^{13}C NMR spectra (δ (ppm), J (hertz), solvent $CDCl_3$) were recorded with a Bruker AC-300 (300 and 75.5 MHz) instrument. Elementary analyses were performed at the Institut de Chimie des Substances Naturelles, in Gif sur Yvette, France. Mass spectra were recorded with a AEI MS-9 instrument. Optical rotations were measured with a Perkin–Elmer 241 polarimeter. Analytical TLC were carried out using aluminium-backed plates coated with 0.2 mm silica gel 60 F_{254} Merck. Preparative flash chromatography was carried out using SDS silica gel 60 (35–70 μm).

3.2. Benzoic acid 2-[2-oxo-(5*R*)-5-[(1*S*)-3-oxo-1,3-dihydroisobenzofuran-1-yl]-2,5-dihydropyrrolidin-1-yl]-(2*R*)-2-phenylethyl ester 10

To a solution of 500 mg of silyloxypyrrole **1b**[4] (1.19 mmol) in 5 mL of dichloromethane at −78°C under argon, were added 275 mg of methyl 2-formylbenzoate (1.677 mmol) and 0.16 mL of boron trifluoride diethyl etherate (1.73 mmol). The reaction mixture was stirred at −78°C for 2 h and the temperature was allowed to warm to 0°C. The reaction was quenched by addition of water and the aqueous layer was extracted twice with CH_2Cl_2. The organic layers were joined, dried over Na_2SO_4. Drying agent was removed by filtration and silica gel was added to the CH_2Cl_2 solution (about 20 mL) in order to obtain a thick. After stirring for 2 h at room temperature, the silica gel was filtered off and rinsed with a mixture of CH_2Cl_2–CH_3OH (95–5). The filtrate was evaporated and the product was purified by flash chromatography on SiO_2 using heptane–AcOEt (1–1) as eluent, to afford 497 mg (95%) of pure **10**. Amorphous white solid. $[\alpha]_D^{20}=+175$ (c 0.5, $CHCl_3$); ^1H NMR δ 4.75 (s, 1H), 4.85 (dd, $J=6.4$, 11, 1H), 5.10 (t, $J=11$, 1H), 5.35 (t, $J=6.4$, 1H), 5.70 (s, 1H), 6.35 (d, $J=5.4$, 1H), 6.75 (d, $J=5.4$, 2H), 7.20 (s, 5H), 7.4 (m, 4 H), 7.5 (m, 3H), 7.95 (d, $J=7.2$, 2H); ^{13}C NMR δ 58.3, 63.7, 67.0, 78.6, 121.4, 126.1, 126.3, 127.4, 127.8, 128.3, 128.6, 128.9, 129.5, 129.7, 129.8, 131.9, 133.1, 133.9, 135.8, 141.7, 144.4, 165.9, 168.8, 172.2.

3.3. Benzoic acid 2-[2-oxo-(5*R*)-5-[(1*S*)-3-oxo-1,3-dihydroisobenzofuran-1-yl]pyrrolidin-1-yl]-(2*R*)-2-phenylethyl ester 11

To a solution of 20 g of silyloxypyrrole **1b**[4] (47.5 mmol) in 100 mL of dichloromethane at −78°C under argon, were added 11 g of methyl 2-formylbenzoate (71.3 mmol) and 8.8 mL of boron trifluoride diethyl etherate (71.3 mmol). The reaction mixture was stirred at −78°C for 2 h and the temperature was allowed to warm to 0°C. The reaction was quenched by addition of water (50 mL) and the aqueous layer was extracted twice with CH_2Cl_2. The organic layers were dried over Na_2SO_4 and concentrated to dryness. The resulted oil was dissolved in methanol (200 mL), 2 g of Pd/C were added and the reaction mixture was stirred under hydrogen (1 atm) for 4 h. The catalyst was removed by filtration and the filtrate was evaporated to dryness. The residue was dissolved in 100 mL of CH_2Cl_2 and silica gel was added in order to obtain a thick suspension. After stirring for 2 h at room temperature, the silica gel was filtered off and rinsed with a mixture of CH_2Cl_2–CH_3OH (95–5). The filtrate was evaporated and the product was purified by flash chromatography on SiO_2 using heptane–AcOEt (1–1) as eluent, to afford 16.6 g (79%) of pure **11**. Amorphous white solid. $[\alpha]_D^{20}=+56$ (c 0.7, $CHCl_3$); ^1H NMR δ 1.25 (m, 1H), 1.7 (m, 1H), 2.3 (ddd, $J=2.8$, 10, 16.6, 1H), 2.65 (m, 1H), 3.9 (d, $J=3.9$, 1H), 5.05 (m, 2H), 5.6 (m, 2H), 7.05 (d, $J=7.4$, 1H), 7.4–7.7 (m, 10 H), 7.9 (d, $J=7.0$, 1H), 8.05 (d, $J=7.4$, 1H); ^{13}C NMR δ 17.9, 30.3, 56.1, 60.9, 63.1, 80.3, 121.1, 125.1, 127.3, 128, 128.7, 129.2, 129.5, 129.6, 132.8, 134, 135.3, 145.1, 165.9, 168.8, 172.2; IR (neat) 1769, 1719, 1688; Anal. calcd for $C_{27}H_{23}NO_5$: C, 73.46; H, 5.25; N, 3.17. Found: C, 73.14; H, 5.81; N, 3.16; m/z (CI) 442 $(M+H)^+$, 351 (M−OCOPh).

3.4. Benzoic acid 2-[(2*R*)-2-[(1*S*)-3-oxo-1,3-dihydroisobenzofuran-1-yl]pyrrolidin-1-yl]-(2*R*)-2-phenylethyl ester 12

To a THF solution of **11** (10 mL, 1.6 g, 36.2 mmol) at 0°C under argon, were added 10.8 mL of BH_3·THF (10.9 mmol). The reaction mixture was stirred at room temperature for 4 h then the reaction was quenched with methanol. The solvents were evaporated and the residue was dissolved in a mixture of CH_2Cl_2–water (10 mL, 1–1) and the biphasic mixture was stirred at room temperature for 2 h. The organic layer was then separated, washed with water, dried over Na_2SO_4 and evaporated to dryness. After recrystallisation from methanol, 1.55 g of pure **12** was obtained (81%). Colourless crystals; mp 107°C (CH_3OH), $[\alpha]_D^{20}=+34$ (c 1.6, $CHCl_3$); ^1H NMR δ 1.15 (m, 1H), 1.5 (m, 1H), 1.65 (m, 1H), 1.9 (m, 1H), 2.8 (m, 1H), 3.25 (m, 1H), 3.5 (td, $J=2.8$, 9.2, 1H), 4.15 (t, $J=6.4$, 1H), 4.65 (dd, $J=6.8$, 11.2, 1H), 4.85 (dd, $J=6.0$, 11.2, 1H), 5.1 (d, $J=2.2$, 1H), 7.0 (d, $J=7.8$, 1H), 7.2–7.5 (m, 10H), 7.8 (d, $J=2.6$, 1H), 7.9 (d, $J=6.0$, 2H); ^{13}C NMR δ 25.0, 52.0, 65.5, 66.5, 66.6, 83.5, 122.0, 125.7, 126.7, 127.6, 128.1, 128.5, 128.6, 128.7, 129.1, 129.6, 133.4, 140.5, 166.4, 171.0; IR (neat) 1762, 1717, 1688; Anal. calcd for $C_{27}H_{25}NO_4$: C, 75.86; H, 5.89; N, 3.28. Found: C, 75.51; H, 6.21; N, 3.17; m/z (CI) 428 $(M+H)^+$, 306 (M−OCOPh).

3.4.1. X-Ray structure analysis of compound 12. Data were obtained from a colorless small crystal of 0.38×0.45×0.62 mm. The compound: $C_{27}H_{25}NO_4$, M_w = 427.48, crystallizes in the monoclinic system, space group $P2_1$. There are two molecules ($Z=2$) in the unit-cell of parameters: $a=9.318(9)$, $b=10.476(12)$, $c=12.259(12)$ Å, $\beta=108.30(5)°$, $V=1136$ Å^3, $D_{calcd}=1.250$ g cm^{-3}, $F(000)=452$, λ (Mo Kα) = 0.71073 Å, $\mu=0.20$ mm^{-1}; 6062 intensity data were measured in phi scans, up to $q=29.7°$, with a Nonius Kappa-CCD area-detector diffractometer.

The structure was solved with program SHELXS-8622 and refined with SHELXL-9323.[14,15] All the H atoms were located on difference maps and fitted at theoretical positions. Refinement converged to $R_1(F)=0.0488$ for the 2723 observed reflections having $F_o \geq 4\sigma(F_o)$ and $wR_2(F_2)=0.1145$ for all the 3399 unique data, goodness-of-fit $S=1.104$. The residual electron density was found between −0.25 and 0.15 e Å^{-3}. In the crystal, only van der Waals contacts are observed.

Crystallographic data for the structure in this paper have been deposited at the Cambridge Crystallographic Data Centre (CIF file), as supplementary publication number CCDC 198 123. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].

3.5. 10-Hydroxy-(10*S*,10a*R*)-2,3,10,10a-tetrahydro-1*H*-pyrrolo[1,2-*b*]isoquinolin-5-one 14

Compound **12** (500 mg, 1.18 mmol) was dissolved in 100 mL of methanol. 200 mg of $Pd(OH)_2$ and 97 mg (1.18 mmol) of sodium acetate were added and the reaction mixture was stirred under hydrogen (1 atm) for 3 days. The reaction mixture was filtered through a Celite pad, the filtrate was evaporated to dryness and the product was purified by flash chromatography on SiO_2 using CH_2Cl_2–CH_3OH (95–5), to afford 129 mg (54%) of pure **14**. Amorphous white solid; mp 168°C; $[\alpha]_D^{20}=-172$ (*c* 0.5, $CHCl_3$); ^{1}H NMR δ 1.85 (m, 2H), 2.1 (m, 1H), 2.45 (m, 1H), 3.65 (m, 2H), 3.75 (ddd, $J=2.6$, 8.2, 10.8, 1H), 4.75 (d, $J=11.0$, 1H), 7.35 (td, $J=1.6$, 8.0, 1H), 7.6 (m, 10H), 8.0 (d, $J=8.0$, 1H), 8.05 (d, $J=7.4$, 2H); ^{13}C NMR δ 23.1, 32.1, 45.5, 62.9, 72.6, 123.5, 127.5, 127.8, 132.2, 135.3, 141.6, 163.2; IR (neat) 3290, 1630; Anal. calcd for $C_{12}H_{13}NO_2$: C, 70.89; H, 6.42; N, 6.71. Found: C, 70.92; H, 6.45; N, 6.89; HRMS calcd for $C_{12}H_{14}NO_2$ (MH^+) 204.1025, found 204.1026.

3.6. (2*R*)-2-[(1*S*)-3-Oxo-1,3-dihydroisobenzofuran-1-yl]-pyrrolodone-1-carboxylic acid *tert*-butyl ester 15

Compound **12** (61 mg, 0.14 mmol) was dissolved in 3 mL of methanol. 30 mg of Pd/C, 156 μl of di-*t*-butyldicarbonate (0.68 mmol) and 36 mg of *N*,*N*,*N*′,*N*′-tetramethyl-1,8-naphtalenediamine (0.17 mmol) were added. The reaction mixture was stirred under hydrogen (1 atm) for 3 days then filtered over Celite and the filtrate was evaporated to dryness. The compound was purified by flash chromatography on SiO_2 using cyclohexane–AcOEt (60–40) to afford 41 mg (95%) of pure **15**. Colourless oil; $[\alpha]_D^{20}=+51$ (*c* 0.7, $CHCl_3$); NMR of the major conformer ^{1}H NMR δ 1.5 (s, 9H), 1.5–1.85 (m, 3H), 2.0 (m, 1H), 3.5 (m, 2H), 4.4 (m, 1H), 6.2 (bs, 1H), 7.55 (t, $J=7.0$, 2H), 7.7 (t, $J=7.0$, 1H), 7.95 (d, $J=7.0$, 1H); ^{13}C NMR δ 24.1, 24.6, 28.6, 47.0, 59.9, 81.2, 122.2, 125.8, 129.4, 134.3, 147.7; IR (neat) 1756, 1687; Anal. calcd for $C_{17}H_{21}NO_4 \cdot 0.5H_2O$: C, 65.35; H, 7.1; N, 4.49. Found: C, 65.22; H, 7.09; N, 4.62; HRMS calcd for $C_{17}H_{22}NO_4$ (MH^+) 304.1549, found 304.1547.

3.7. (2*R*)-2-[2-[(1*S*)-1,3-Dihydroisobenzofuran-1-yl]-pyrrolidin-1-yl]-(2*R*)-2-phenylethanol 16

To a THF solution of **15** (15 mL, 206 mg, 0.48 mmol) at room temperature under argon, lithium aluminium hydride (73 mg, 1.9 mmol) was added by small portions. The reaction mixture was stirred under reflux for 3 h then allowed to cool to room temperature. Excess $LiAlH_4$ was destroyed by addition of ethyl acetate followed by addition of saturated aqueous solution of Na_2SO_4. The aqueous layer was extracted three times with CH_2Cl_2 and the organic layers were washed with water and dried over Na_2SO_4. The solvents were evaporated to dryness to lead to 180 mg of crude **16** engaged without further purification in the next step. ^{1}H NMR δ 1.3 (m, 1H), 1.55 (m, 2H), 1.8 (m, 1H), 2.7 (m, 1H), 2.95 (m, 1H), 3.2 (m, 1H), 3.55 (m, 3H), 4.15 (d, $J=4.3$, 1H), 4.35 (d, $J=12.9$, 1H), 4.5 (d, $J=5.9$, 1H), 6.95 (m, 2H), 7.15 (m, 7H), 7.35 (m, 1H); ^{13}C NMR 24.5, 26.5, 52.1, 62.7, 63.2, 66.5, 68.5, 70.4, 126.9, 127.5, 127.9, 128.3, 128.6, 128.7, 129.3, 129.7, 138.0, 139.3, 140.9; *m*/*z* (CI) 310 $(M+H)^+$, 328 $(M+NH_4)^+$.

3.8. (2*R*)-2-[(1*S*)-1,3-Dihydroisobenzofuran-1-yl]-pyrrolidine 17

Crude **16** (180 mg) was dissolved in 20 mL of methanol. 60 mg of Pd/C were added and the reaction mixture was stirred overnight under hydrogen (1 atm). The catalyst was removed by filtration and the filtrate was evaporated to dryness. The compound was purified by flash chromatography on SiO_2 using CH_2Cl_2–CH_3OH–NEt_3 (95–4.5–0.5) to afford 53 mg (59%) of pure **17**. White solid; mp 164°C; $[\alpha]_D^{20}=+24$ (*c* 0.45, CH_3OH); ^{1}H NMR δ 1.6–2.1 (m, 4H), 2.8 (m, 2H), 3.25 (m, 1H), 4.45 (d, $J=11.8$, 1H), 4.75 (m, 2H), 7.1–7.6 (m, 4H); ^{13}C NMR δ 25.5, 28.9, 45.8, 61.9, 63.8, 72.1, 126.3, 127.2, 128.2, 129.0; IR (neat) 3284; HRMS calcd for $C_{12}H_{16}NO$ (MH^+) 190.1232, found 190.1229. Addition of HCl/CH_3OH solution followed by evaporation to dryness, furnished the HCl salt as an amorphous solid. Anal. calcd for $C_{12}H_{15}NO \cdot HCl \cdot 2H_2O$: C, 55.15; H, 7.72; N, 5.36. Found: C, 55.57; H, 7.27; N, 5.40.

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