Efficient stereoselective nucleophilic addition of pyrroles to chiral nitrones†

Christophe Berini, Frédéric Minassian,* Nadia Pelloux-Léon,* Jean-Noël Denis, Yannick Vallée and Christian Philouze

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Regioselective additions of pyrroles to a variety of optically active nitrones under smooth acidic conditions lead to chiral pyrrolic *N*-hydroxylamines in good to excellent yields. Depending on the position of the chirality on the nitrone partner, the addition products have been isolated with high diastereoselectivity levels. Reaction of glyoxylate based chiral nitrones either at the C-2 or at the C-3 position of the pyrrole nucleus afforded *N*-hydroxyamino esters in high yields as single diastereoisomers. These adducts allow access to enantio-enriched non proteinogenic 2′- and 3′-pyrrolylglycines (**13** and **19** respectively).

Introduction

The chemistry of pyrrole and its derivatives is of great interest due to their abundance in many natural and biologically active compounds.[1,2] Whereas stereoselective alkylation of many aromatic and heteroaromatic compounds is well documented either using organometallic species or under acidic conditions,[3] the use of the pyrrole nucleus as the nucleophile is not common.[4,5] This is probably due to the fact that pyrrolic organometallic species are not easy to handle and because of the relative instability of the pyrrole nucleus in acidic media.

Nucleophilic addition to the carbon–nitrogen double bond of nitrones leads to *N*-hydroxylamines. When chiral nitrones are used, stereocontrolled additions occur and provide chiral *N*-hydroxylamines that are key intermediates for the synthesis of bio-active compounds.[6] A broad range of organometallic species has been tested in this reaction,[7] but the addition of electron-rich aromatic compounds under acidic conditions has scarcely been described.[8]

In a previous report, we showed that pyrroles react with simple *N*-benzylaldonitrones in the presence of hydrogen chloride (Table 1, entries 1 and 4).[9] In each case, the single isolated product came from the addition at the C-2 position of the pyrrole nucleus. It was shown that this method could selectively lead to the corresponding *N*-benzylhydroxylamines or to the 2,2′-bispyrrolylalkanes *via* a second addition step. In the present studies, we extend the scope of this reaction to some functionalized nitrones, with the control of its stereochemical outcome and we apply the same concepts to the C-3 regioselective addition. Such an approach would lead to valuable synthetic precursors of chiral pyrrolidines, pyrrolidinones and enantio-enriched non-proteinogenic α-amino acids.

Département de Chimie Moléculaire (SERCO) UMR-5250, ICMG FR-2607, Université Joseph Fourier, CNRS, BP-53, 38041, Grenoble Cedex 9, France. E-mail: Frederic.Minassian@ujf-grenoble.fr, Nadia.Pelloux-Leon@ujf-grenoble.fr; Fax: +33-4-7663-5983; Tel: +33-4-7651-4908

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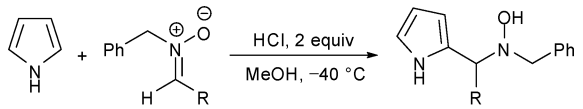
Table 1 Addition of pyrrole **1** to *N*-benzylaldonitrones **2a–d**



1 **2a-d** **3a-d**

Entry	Compound	R	Yield[a](%)
1	**3a**	Et	95
2	**3b**	CH_2NHBoc	94
3	**3c**	CO_2Et	99
4	**3d**	Ph	73

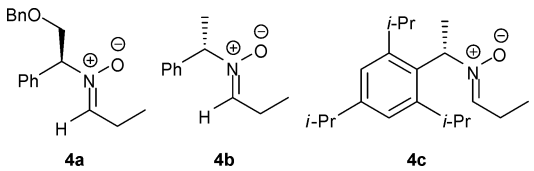
[a] Isolated yields.

Results and discussion

Four examples of this reaction involving non chiral starting materials are reported in Table 1. The use of two equivalents of HCl together with two equivalents of pyrrole **1** was found to be optimal at −40 °C.[10] Under this set of experimental conditions, the polymerisation of pyrrole **1** was minimal and *N*-benzylhydroxylamines **3a–d** were obtained in good to excellent yields. For example, the reaction with the ethyl glyoxylate based nitrone **2c**[11] produced the corresponding *N*-benzylhydroxyamino ester **3c** in a nearly quantitative isolated yield (Table 1, entry 3).

As these encouraging results proved that the method tolerates functionalized nitrones, we then turned our attention to a chiral version of this reaction. We planned to induce diastereoselectivity by using three classes of chiral nitrones: (i) nitrones including a chiral auxiliary on the nitrogen atom, (ii) nitrones bearing a chiral lateral chain, and (iii) glyoxylate based chiral nitrones.

In a first series of experiments, diastereoselective additions of the pyrrole ring to chiral nitrones derived from propionaldehyde and chiral *N*-hydroxylamines were studied. Condensations of *N*-((*S*)-2-benzyloxy-1-phenylethyl)-hydroxylamine,[12] *N*-((*S*)-1-phenylethyl)-hydroxylamine,[13] and *N*-((*S*)-1-(2,4,6-triisopropylphenyl)ethyl)-hydroxylamine,[14] together with propionaldehyde in CH_2Cl_2 in the presence of anhydrous magnesium sulfate afforded nitrones **4a–c** (Scheme 1).[15]



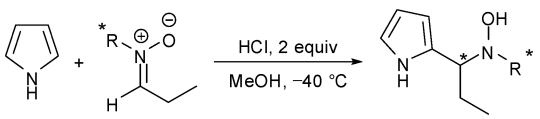
Scheme 1 *N*-Chiral aldonitrones **4a–c**.

In the presence of two equivalents of anhydrous HCl, when pyrrole **1** was added to nitrones **4a–c**, C-2 substituted pyrrolic *N*-hydroxylamines **5a–c** were formed in good to excellent isolated yields (73–98%). Similar nitrones are known to give moderate to good diastereoselectivities in the presence of organometallic nucleophiles.[12–14] The acidic conditions used in our case led to modest asymmetric inductions (65 : 35 diastereomeric ratios) (Table 2, entries 1–3). However, it has to be noted that in each case, both diastereoisomers were isolated separately with high degrees of purity by silica gel chromatography.

In order to improve the stereoselectivity we decided to shift the stereogenic center to the α-carbon atom of the nitrone. We then chose α-chiral aldehydes derived from natural sources, *e.g.* α-amino acids and mannitol, as starting materials. Nitrones **6** were prepared according to the literature by condensation between the suitable aldehydes and *N*-benzylhydroxylamine in the presence of anhydrous magnesium sulfate.[15,16]

Exposure of these nitrones to pyrrole **1** in the presence of two equivalents of HCl afforded the corresponding C-2 pyrrolic *N*-hydroxy adducts **7** with good to excellent yields and diastereoselectivities (Table 3). The relative stereochemistry was determined by X-ray analysis on the major stereoisomers for compounds **7a** and **7b** (Table 3, entries 1 and 2) and revealed an *anti* selectivity (Fig. 1).[17] This result could be rationalized using a cyclic Cram model (Fig. 2).[8b,18] In the case of L-serine and L-proline based nitrones **6c–d** (Table 3, entries 3 and 4), the *syn* and *anti* diastereoisomers were separated by simple column chromatography. With L-proline based nitrone **6d**, the *anti* selectivity was determined using ^{1}H NMR. Indeed, at −40 °C, the coupling constants between $H_{1'}$ and H_2 were respectively 1.6 Hz for the major isomer (*anti*) and 10.5 Hz for the minor isomer (*syn*).[19] In this case, no β-chelation could occur. As the major isomer is *anti*, the Houk open-chain model[20] invoked in some previous studies is not satisfactory.[16b] A Felkin–Anh model is therefore proposed in order to rationalize this selectivity (Fig. 2). These results showed that the addition of pyrrole **1** to α-chiral aldonitrones under acidic conditions allows an efficient and highly diastereoselective access to chiral pyrrolic *N*-hydroxylamines.

Table 2 Additions of pyrrole **1** onto aldonitrones bearing a chiral auxiliary on the nitrogen atom **4a–c**



Entry	Compound	Time/h	Yield[a](%)	dr[b,c,d]
1	**5a**	24	98	65 : 35
2	**5b**	24	91	65 : 35
3	**5c**	5	73	65 : 35

[a] Isolated yields. [b] Ratios determined by ^{1}H NMR analysis of the crude reaction mixtures. [c] Separated by silica gel chromatography. [d] The absolute sense of the chiral transfer was not determined.

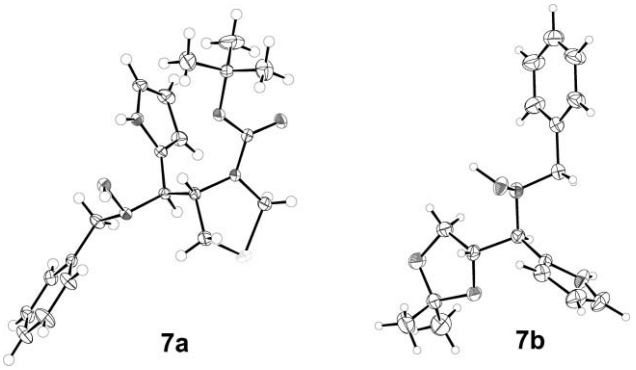


Fig. 1 ORTEP plots of compounds **7a** and **7b**. Ellipsoids are drawn respectively at the 25% and 50% levels.

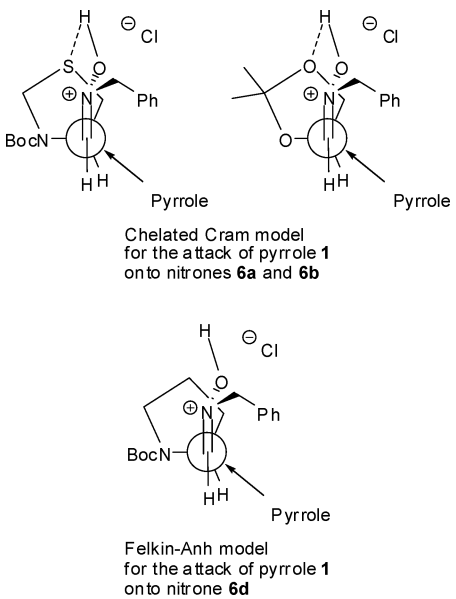
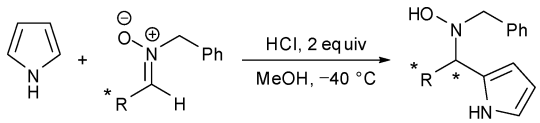


Fig. 2 Proposed models for the addition of pyrrole **1** onto nitrones **6a**, **6b** and **6d**.

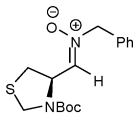
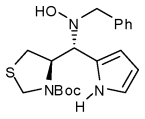
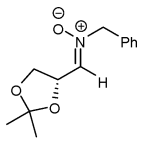
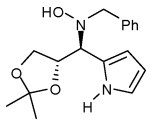
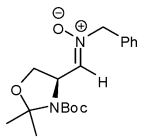
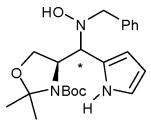
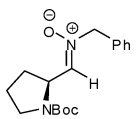
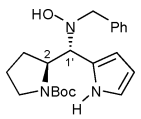
To further extend this methodology, and in order to elaborate enantio-enriched non proteinogenic α-amino acids, we studied the reaction of pyrrole **1** with glyoxylate based chiral nitrones. The initial racemic version of this reaction was indeed highly efficient (Table 1, entry 3). In a first experiment, pyrrole **1** was added to nitrone **8a** prepared from L-menthyl glyoxylate (Scheme 2).[21,22] When HCl was used as a promoter, the reaction proceeded to give the corresponding hydroxylamine **9** in 73% isolated yield. The diastereoisomeric ratio was 65 : 35 (determined by ^{1}H NMR of the crude mixture), the two diastereoisomers being unseparable by column chromatography.

This modest result could presumably be explained by the distance separating the chiral auxiliary and the reacting centers during the reaction pathway. We thought that the incorporation of the chiral source into a rigid cyclic nitrone would seriously increase the degree of stereodifferentiation during the addition of pyrrole **1**.[23]

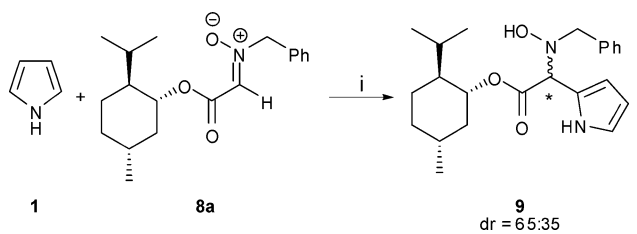
Table 3 Additions of pyrrole **1** onto aldonitrones with a chiral lateral chain **6a–d**



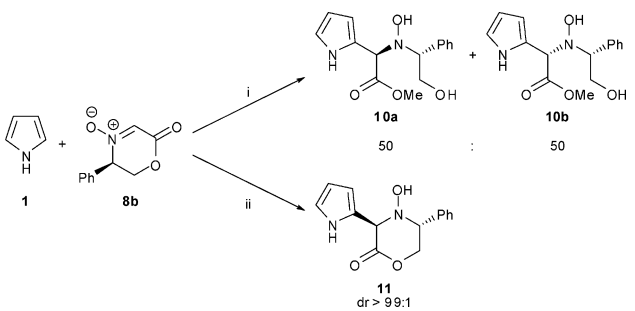
1 **6a-d** **7a-d**

Entry	Nitrone	Product[a]	Yield[b](%)	dr[c,d]
1	 **6a**	 **7a**	94	> 98 : 2 (*anti* : *syn*)[e]
2	 **6b**	 **7b**	95	> 98 : 2 (*anti* : *syn*)[e]
3	 **6c**	 **7c**	98	85 : 15[f]
4	 **6d**	 **7d**	74	90 : 10[g] (*anti* : *syn*)[f]

[a] Single or major isomer depicted. [b] Isolated yields. [c] Ratios determined by ^{1}H NMR analysis of the crude reaction mixtures. [d] Each diastereoisomer could be isolated with dr > 98 : 2 after silica gel chromatography. [e] *Anti* selectivity determined by X-ray analysis.[17] [f] Selectivity was not determined. [g] *Anti* selectivity determined by ^{1}H NMR analysis (see ref. 19*b*).



Scheme 2 *Reagents and conditions*: (i) HCl (2 equiv.), MeOH, −40 °C, 24 h, 73%.



Scheme 3 *Reagents and conditions*: (i) HCl (2 equiv.), MeOH, −40 °C, 24 h, 56%; (ii) HCl (2 equiv.), CH_2Cl_2, −80 °C to −40 °C, 2 h, 76%.

The cyclic chiral nitrone **8b**, which is already known to give access to enantiopure hydroxylamines, was then chosen. Compound **8b** was obtained by a three-step sequence from (*R*)-phenylglycinol.[24] When methanol was used as the solvent for the addition step, the reaction was not diastereoselective, presumably because of the initial ring opening of **8b** by transesterification followed by the addition on an open-chain nitrone, which lead to a mixture of **10a**,**b**. When the reaction was performed in dichloromethane, the expected cyclic hydroxylamine **11** was obtained as a single diastereoisomer in 76% isolated yield (Scheme 3).[25] As compound **8b** was synthesized from enantiopure (*R*)-phenylglycinol, the X-ray analysis of compound **11** (Fig. 3) allowed the attribution of a (3*R*,5*R*) absolute configuration.

This compound is a key intermediate for the preparation of the optically active pyrrolic α-amino acid **13** (Scheme 4). To the best of our knowledge, only one derivative of compound **13** has been previously synthesized in racemic form and moderate yield.[26] Hydroxylamine **11** was subsequently converted into **10a** in acidic methanol (89%). Upon treatment with H_2 (1 atm) in the presence of black palladium in a MeOH–HCOOH mixture

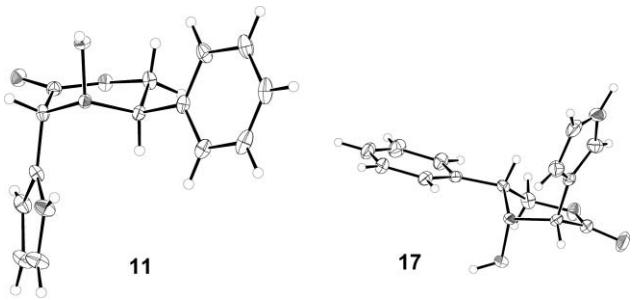
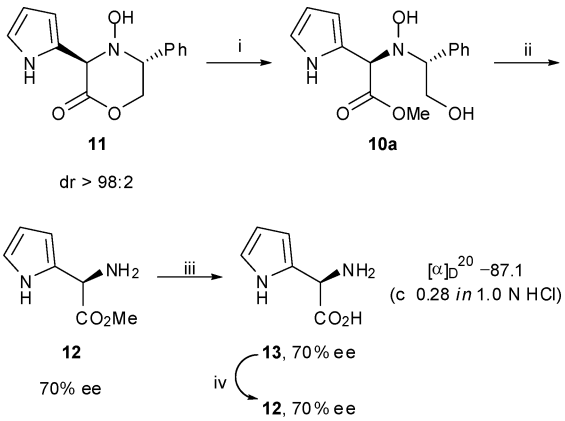


Fig. 3 ORTEP plots of compounds **11** and **17**. Ellipsoids are drawn at the 25% level.

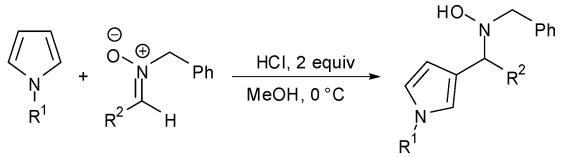


Scheme 4 *Reagents and conditions*: (i) HCl, MeOH, −20 °C, 24 h, 89%; (ii) H_2, Pd black, MeOH–HCOOH (9 : 1), rt, 1 h, 40%; (iii) LiOH, THF–H_2O (3 : 1), 0 °C, 2 h, 80%; (iv) CH_3COCl, MeOH, reflux, 12 h, 65%.

(9 : 1), concomitant reduction of the *N*-hydroxylamine moiety and deprotection of the benzyl group were observed in 40% yield. At this stage, a 70% ee was measured by examination of the ^{1}H NMR spectrum of α-amino methyl ester **12** in the presence of a Eu(III) based chiral shift reagent. Such an eroded ee could be presumably explained by the acidity of the α-amino acid proton in compound **12**. Jørgensen and co-workers also observed that the copper(I) catalyzed asymmetric aza-Friedel–Crafts reaction of *N*-methylpyrrole with a *N*-Moc protected α-imino ester led to the corresponding adduct with only 59% ee.[5] A slightly higher ee is obtained in our case, in the absence of any substituent or protecting group on the pyrrolic nitrogen atom. In a final step, alkaline hydrolysis of the methyl ester was carried out with LiOH in a THF–H_2O mixture (3 : 1). The resulting crude mixture was purified by Dowex 50W-X8 ion exchange resin (H^+ form). Lyophilization afforded α-amino acid **13** in 80% yield. The optical rotation was $[a]_D^{20}$ −87.1 (*c* 0.28 in 1 N HCl). In order to check the final enantiomeric ratio, α-amino acid **13** was re-converted into α-amino methyl ester **12**.[27] A ^{1}H NMR spectrum was then recorded in the presence of the chiral europium salt, showing again an 85 : 15 enantiomeric ratio. Our synthetic approach to amino acid **13** is still more efficient than other methods considering the overall yield and final enantiomeric purity.

Finally, it was decided to explore the reactivity at the C-3 position of the pyrrole nucleus. So far, the reactivity of this position towards nitrones was not studied and it would be interesting to introduce an alkylhydroxylamino group on this less reactive site.

Table 4 Reactivity of pyrroles **14a–b** towards aldonitrones **2a–d**



Entry	Pyrrole[a]	Compound	R^2	Yield[b](%)
1	**14b**	**15a**	Et	59
2	**14b**	**15b**	CH_2NHBoc	62
3	**14b**	**15c**	CO_2Et	77

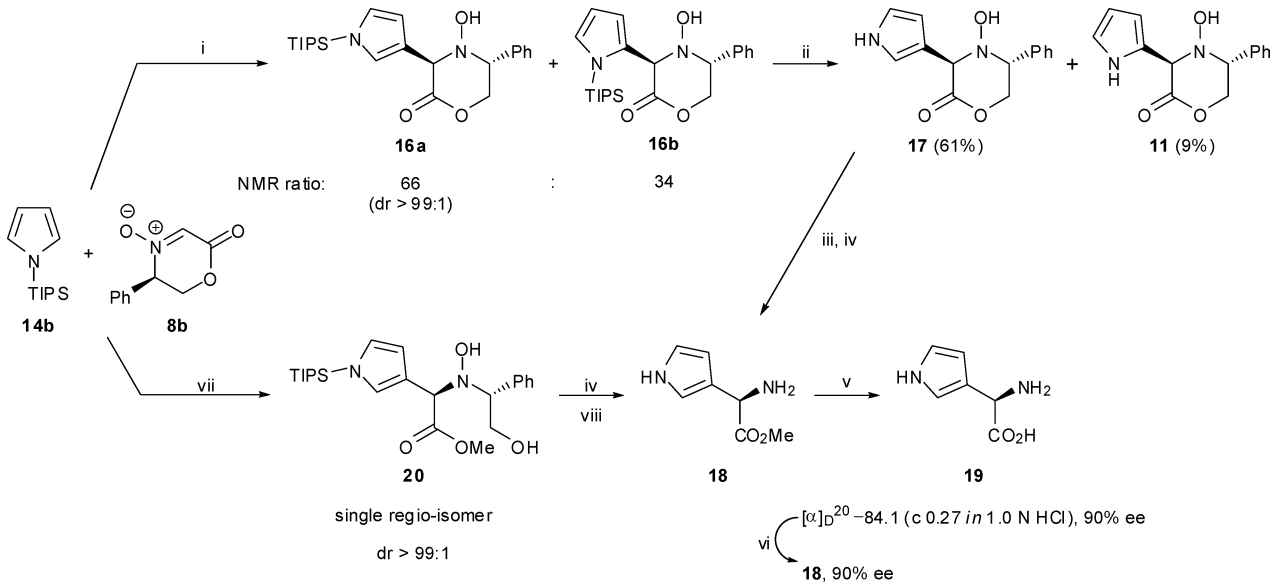
[a] When pyrrole **14a** was put in reaction with nitrones **2a**, **2c** and **2d** (R^2 = Et, CO_2Et, Ph), starting materials were fully recovered. [b] Isolated yields.

With this purpose in mind, we chose to deactivate the C-2 position of the pyrrole nucleus by protection of the nitrogen atom with an electron-withdrawing benzenesulfonyl group.[28] Unfortunately, *N*-benzenesulfonylpyrrole **14a** was not sufficiently reactive towards nitrones **2a–d** (Table 4). *N*-Triisopropylsilylpyrrole **14b** was then used as the starting material because it is known that the large steric bulk of the triisopropylsilyl group has a C-3 directing effect in electrophilic substitutions.[29] The addition of the TIPS-substituted pyrrole **14b** to aldonitrones **2a–c** needed higher temperatures than those using pyrrole **1** (Table 4, entries 1–3). The reactions were found to be totally regioselective.

Encouraged by these results, we then decided to explore the diastereoselectivity of the addition of *N*-TIPS pyrrole **14b** to the cyclic chiral nitrone **8b**. When the reaction was performed at 0 °C using 2 equivalents of HCl in dichloromethane, a mixture of regioisomers was obtained (overall yield: 57%, ratio: 66 : 34, major isomer **16a**) (Scheme 5). The C-3 and C-2 regioisomers were not separable at this stage.

Cleavage of the *N*-triisopropylsilyl group was performed under classical conditions to give the two regio-isomeric *N*-hydroxylamines **17** and **11**, which were separated by column chromatography. Once more, as enantiopure (*R*)-phenylglycinol was used as the starting material, a (3*R*,5*R*) configuration was indirectly deduced from an X-ray analysis of the major isomer (**17**) (Fig. 3).[30] The synthesis of optically active 3′-pyrrolyl glycine **19** was then completed within a three-step sequence. Transesterification was carried out in acidic methanol at 0 °C, followed by reductive hydrogenolysis using H_2/cat $Pd(OH)_2$ to give α-amino methyl ester **18** in 73% yield over two steps. The chiral shift reagent, $Eu(hfc)_3$, was used to measure the enantiomeric ratio (95 : 5). Finally, compound **18** was converted to the desired α-amino acid **19** in 95% yield. Its optical rotation was $[a]_D^{20}$ −84.1 (*c* 0.27 in 1 N HCl) and its enantiomeric ratio was 95 : 5.[27]

The regioselectivity of the initial addition was improved by lowering the reaction temperature to −20 °C. Furthermore, we found that the transesterification step could be performed in the same pot, leading finally to the open-chain hydroxylamine **20** as a single diastereoisomer (Scheme 5). Reductive hydrogenolysis and removal of the silyl group gave α-amino methyl ester **18** in 80% yield over two steps. Finally, compound **18** was converted to 3′-pyrrolyl glycine **19** in 95% yield (Scheme 5). Once again, a 95 : 5 enantiomeric ratio was measured for this new synthetic α-amino



Scheme 5 *Reagents and conditions*: (i) HCl (2 equiv.), CH_2Cl_2, 0 °C, 12 h, 57%; (ii) TBAF, CH_3COOH, THF, rt, 15 min, 70%; (iii) HCl, MeOH, 0 °C, 12 h; (iv) H_2, cat. $Pd(OH)_2$, MeOH–CH_3COOH (9 : 1), rt, 12 h, 73% (over two steps); (v) LiOH, THF–H_2O (3 : 1), 0 °C, 2 h, 95%; (vi) CH_3COCl, MeOH, reflux, 12 h, 99%; (vii) HCl (2 equiv.), CH_2Cl_2, −20 °C, 12 h then MeOH, 0 °C, 24 h, 63%; (viii) TBAF, THF, rt, 5 min, 80% (over two steps).

acid. These results show that the optical purity of α-amino acid **19** is higher than the one measured on α-amino acid **13**. This could be explained by a higher acidity of the α-amino acid proton in the case of the C-2 regioisomer because of the greater resonance stabilization of its conjugated base.

In conclusion, this study shows that high levels of diastereoselectivities can be observed when α-chiral aldonitrones are chosen as starting materials. When the cyclic chiral nitrone **8b** was used, a total diastereoselection was observed and allowed the first and unprecedented efficient syntheses of enantio-enriched pyrrolic α-amino acids **13** and **19**. We are now applying this new methodology to the synthesis of natural products.

Experimental

General experimental

All reactions were carried out using oven-dried glassware under an argon atmosphere. Solvents were purified prior to use by conventional methods. All other reagent-grade chemicals were used as supplied (analytical or HPLC grade) without prior purification. Thin layer chromatography was performed on aluminium plates coated with 60 PF254 silica. Plates were visualised using UV light (254 nm), followed by heating after treatment with an appropriate revelatory ($KMnO_4$, TTC, phosphomolybdic acid, ninhydrine). Flash column chromatography was performed on Kieselgel 60 silica (40–60 mesh).

Elemental analyses were recorded by the microanalysis service of the Département de Chimie Moléculaire, Grenoble, France. Melting points were recorded on a Büchi B35 apparatus and are uncorrected. Optical rotations were recorded on a Perkin-Elmer 341 polarimeter with a water-jacketed 10 cm cell. Specific rotations are reported in 10^{-1} deg cm^2 g^{-1} and concentrations in g per 100 mL. IR spectra were recorded on a Nicolet Impact-400 Fourier transform infrared spectrometer (FTIR) as either thin films on NaCl plates (thin film) or a KBr disc (KBr disc), as stated. Selected characteristic bands are reported in cm^{-1}. NMR spectra were recorded either on a Bruker Advance300 or on an Advance400 spectrometer in deuterated solvent as stated. The field was locked by external referencing to the relevant deuteron resonance. Low resolution mass spectra (LRMS) were recorded on a Bruker Esquire 3000 plus (ESI) or a ThermoFinnigan PolarisQ ion-trap spectrometer, using DCI (ammonia–isobutane 63 : 37). Accurate mass measurements were run in the "Structure et Fonction de Molécules Bioactives" laboratory, Paris, France.

General procedure for the preparation of aldonitrones 4

The appropriate *N*-alkylhydroxylamine (1.0 mmol) was dissolved in anhydrous dichloromethane (8 mL). Anhydrous magnesium sulfate (241 mg, 2.0 mmol) was added, followed by freshly distilled propanal (58 mg, 1.0 mmol). The solution was stirred until complete disappearance of the starting material (followed by TLC). The mixture was filtered over celite and concentrated. The crude product was purified by flash chromatography on silica gel.

(1*S*)-(*Z*)-2-Benzyloxy-*N*-propylidene-1-phenylethylamine *N*-oxide 4a

Prepared according to the above general procedure from 500 mg (2.06 mmol) of *N*-((*S*)-2-benzyloxy-1-phenylethyl)-hydroxylamine[12] in 16 mL of CH_2Cl_2, 495 mg (2.12 mmol) of anhydrous $MgSO_4$ and 116 mg (2.06 mmol) of propanal. The mixture was stirred for 4 hours. Purification (eluent: pentane–EtOAc, 1 : 1 to 0 : 1) afforded nitrone **4a** (429 mg, 73%) as a colourless oil; $[\alpha]_D^{20}$ +6.7 (*c* 1.00 in $CHCl_3$); ν_{max}/cm^{-1} (thin film) 1588 (CN); δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.09 (3H, t, $J = 7.7$ Hz, C(3′)H_3), 2.40–2.65 (2H, m, C(2′)H_2), 3.76 (1H, dd, $J = 10.2$ and

3.8 Hz, C(2)H_2), 4.48 (1H, dd, J = 10.2 and 9.2 Hz, C(2)H_2), 4.61 (2H, AB_q, J_{AB} = 12.0 Hz, δ_A–δ_B = 29.7 Hz, CH_2Ph), 4.93 (1H, dd, J = 9.1 and 3.8 Hz, C(1)H), 6.80 (1H, t, J = 5.8 Hz, CH=N), 7.28–7.50 (10H, m, ArH); δ_C (75 MHz; $CDCl_3$; Me_4Si) 9.9 (C(3′)H_3), 20.2 (C(2′)H_2), 69.7 (C(2)H_2), 73.3 (CH$_2$Ph), 77.8 (C(1)H), 127.7 (ArCH), 127.9 (ArCH), 128.4 (ArCH), 128.6 (ArCH), 128.9 (ArCH), 134.9 (ArC), 138.0 (ArC), 140.6 (CH=N); m/z (DCI, NH_3–isobutane) 284 ([M + H]$^+$, 100%), 268, 193, 146, 106; Elemental analysis, calcd (%) for $C_{18}H_{21}NO_2$: C, 76.30; H, 7.47; N, 4.95. Found: C, 76.58; H, 7.60; N, 4.89.

(1*S*)-(*Z*)-*N*-Propylidene-1-phenylethylamine *N*-oxide 4b

Prepared according to the above general procedure from 300 mg (2.19 mmol) of *N*-((*S*)-1-phenylethyl)-hydroxylamine[13] in 16 mL of CH_2Cl_2, 530 mg (4.40 mmol) of anhydrous $MgSO_4$ and 127 mg (2.19 mmol) of propanal. The mixture was stirred for 4 hours. Purification (eluent: pentane–EtOAc, 1 : 1 to 0 : 1) afforded nitrone **4b** (333 mg, 86%) as a white solid; mp 75–76 °C; $[\alpha]_D^{20}$ −95.7 (*c* 1.04 in $CHCl_3$); ν_{max}/cm^{-1} (KBr disc) 1587 (CN); δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.07 (3H, t, J = 7.7 Hz, C(3′)H_3), 1.80 (3H, d, J = 6.9 Hz, C(2)H_3), 2.43–2.54 (2H, m, C(2′)H_2), 4.98 (1H, q, J = 6.9 Hz, C(1)H), 6.69 (1H, t, J = 5.7 Hz, CH=N), 7.33–7.47 (5H, m, ArH); δ_C (75 MHz; $CDCl_3$; Me_4Si) 10.0 (C(3′)H_3), 19.2 (C(2)H_3), 20.1 (C(2′)H_2), 73.3 (C(1)H), 127.3 (ArCH), 128.6 (ArCH), 128.7 (ArCH), 138.5 (ArC), 138.8 (CH=N); m/z (DCI, NH_3–isobutane) 178 ([M + H]$^+$, 100%), 162, 105; Elemental analysis, calcd (%) for $C_{11}H_{15}NO$: C, 74.55; H, 8.53; N, 7.91. Found: C, 74.93; H, 8.56; N, 7.82.

Nitrone 4c was prepared following the procedure previously described.[14]

General procedure for the preparation of C-2 substituted pyrrolic *N*-hydroxylamines 3a–d, 5a–c, 7a–d, 9 and 10a–b

Freshly distilled acetyl chloride (157 mg, 2.0 mmol, 142 μL) was added dropwise at 0 °C to anhydrous methanol (5 mL) and the mixture was stirred for 15 min. The appropriate nitrone (1.0 mmol) was added and the mixture was cooled to −78 °C before the addition of freshly distilled pyrrole (134 mg, 2.0 mmol). It was then slowly warmed to −40 °C, and stirred at this temperature until complete disappearance of the starting material (followed by TLC) at this temperature. The mixture was then treated with saturated aqueous $NaHCO_3$ solution and then allowed to warm to room temperature. The pH value was then 8–9. The aqueous layer was extracted three times with CH_2Cl_2. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$ and concentrated. The obtained *N*-hydroxylamine was purified by flash chromatography on silica gel.

N-Benzyl-*N*-[(1*H*-pyrrol-2-yl)propyl]hydroxylamine 3a

Prepared according to the above general procedure from 135 mg (0.83 mmol) of nitrone **2a** in 4.1 mL of MeOH, 111 mg (1.66 mmol) of pyrrole and 130 mg (1.66 mmol) of acetyl chloride. The mixture was stirred for 24 hours. Purification (eluent: CH_2Cl_2–EtOAc, 8 : 2) afforded *N*-hydroxylamine **3a** (182 mg, 95%) as a colourless oil; ν_{max}/cm^{-1} (thin film) 3453 (broad, OH); δ_H (300 MHz; $CDCl_3$; Me_4Si) 0.88 (3H, t, J = 7.4 Hz, C(3)H_3), 1.70–2.00 (2H, m, C(2)H_2), 3.48–3.68 (3H, m, C(1)H, CH_2Ph), 5.89 (1H, br s, OH), 6.04 (1H, s, pyrr$H$), 6.16 (1H, dd, J = 5.7 and 2.8 Hz, pyrr$H$), 6.78 (1H, dd, J = 4.0 and 2.5 Hz, pyrr$H$), 7.23–7.33 (5H, m, ArH), 8.66 (1H, br s, NH); δ_C (75 MHz; $CDCl_3$; Me_4Si) 11.4 (C(3)H_3), 25.3 (C(2)H_2), 60.1 (CH$_2$Ph), 65.5 (C(1)H), 107.2 (pyrr$C$H), 108.3 (pyrr$C$H), 117.6 (pyrr$C$H), 127.3 (ArCH), 128.2 (ArCH), 129.7 (pyrr$C$), 129.8 (ArCH), 137.9 (ArC); m/z (ESI$^+$) 231 ([M + H]$^+$), 124 (100%), 108; Elemental analysis, calcd (%) for $C_{14}H_{18}N_2O$: C, 73.01; H, 7.88; N, 12.16. Found: C, 72.63; H, 7.93; N, 11.98.

[2-(*N*-Benzyl-*N*-hydroxy-amino)-2-(1*H*-pyrrol-2-yl)ethyl]carbamic acid *tert*-butyl ester 3b

Prepared according to the above general procedure from 24 mg (0.09 mmol) of nitrone **2b** in 500 μL of MeOH, 12 mg (0.18 mmol) of pyrrole and 14 mg (0.18 mmol) of acetyl chloride. The mixture was stirred for 24 hours. Purification (eluent: CH_2Cl_2) afforded *N*-hydroxylamine **3b** (28 mg, 94%) as a white solid; mp 131–132 °C; ν_{max}/cm^{-1} (KBr disc) 3430–3360 (broad, OH, NH), 1688 (CO); δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.49 (9H, m, C(CH_3)$_3$), 3.15–3.22 (1H, m, C(1)H), 3.61–3.86 (4H, m, C(1)H, C(2)H, CH_2Ph), 4.82 (1H, br s, NHBoc), 6.04 (1H, s, pyrr$H$), 6.16 (1H, dd, J = 5.1 and 2.8 Hz, pyrr$H$), 6.78–6.79 (1H, m, pyrr$H$), 6.88 (1H, br s, OH), 7.27–7.29 (5H, m, ArH), 9.08 (1H, br s, NH); δ_C (75 MHz; $CDCl_3$; Me_4Si) 28.4 (C(CH$_3$)$_3$), 43.4 (C(1)H$_2$), 60.3 (CH$_2$Ph), 63.8 (C(2)H), 80.0 (C(CH$_3$)$_3$), 107.4 (pyrr$C$H), 108.5 (pyrr$C$H), 118.3 (pyrr$C$H), 126.9 (ArCH), 128.1 (ArCH), 128.4 (pyrr$C$), 128.6 (ArCH), 138.4 (ArC), 157.9 (C=O); m/z (DCI, NH_3–isobutane) 332 ([M + H]$^+$), 209, 153 (100%); Elemental analysis, calcd (%) for $C_{18}H_{25}N_3O_3$: C, 65.24; H, 7.61; N, 12.68. Found: C, 65.50; H, 7.72; N, 12.76.

(*N*-Benzyl-*N*-hydroxy-amino)-(1*H*-pyrrol-2-yl)acetic acid ethyl ester 3c

Prepared according to the above general procedure from 104 mg (0.50 mmol) of nitrone **2c** in 2.5 mL of MeOH, 67 mg (1.00 mmol) of pyrrole and 79 mg (1.00 mmol) of acetyl chloride. The mixture was stirred for 24 hours. Purification (eluent: pentane–EtOAc, 8 : 2) afforded *N*-hydroxylamine **3c** (136 mg, 99%) as a yellow oil; ν_{max}/cm^{-1} (thin film) 3423 (broad, OH), 1734 (CO); δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.20 (3H, t, J = 7.1 Hz, C(2′)H_3), 3.69 (2H, AB_q, J_{AB} = 13.4 Hz, δ_A–δ_B = 87.4 Hz, CH_2Ph), 4.01–4.19 (2H, m, C(1′)H_2), 4.54 (1H, s, C(2)H), 6.13 (1H, dd, J = 5.7 and 2.9 Hz, pyrr$H$), 6.20 (1H, s, pyrr$H$), 6.38 (1H, br s, OH), 6.75 (1H, dd, J = 4.1 and 2.6 Hz, pyrr$H$), 7.25–7.28 (5H, m, ArH), 9.04 (1H, br s, NH); δ_C (75 MHz; $CDCl_3$; Me_4Si) 13.9 (C(2′)H_3), 60.5 (C(1′)H_2), 61.3 (CH$_2$Ph), 67.8 (C(2)H), 107.9 (pyrr$C$H), 110.0 (pyrr$C$H), 119.3 (pyrr$C$H), 123.7 (pyrr$C$), 127.3 (ArCH), 128.1 (ArCH), 129.7 (ArCH), 136.9 (ArC), 170.8 (C=O); m/z (DCI, NH_3–isobutane) 275 ([M + H]$^+$), 257, 152 (100%); Elemental analysis, calcd (%) for $C_{15}H_{18}N_2O_3$: C, 65.68; H, 6.62; N, 10.22. Found: C, 65.77; H, 6.77; N, 10.09.

N-Benzyl-*N*-[phenyl-(1*H*-pyrrol-2-yl)methyl]hydroxylamine 3d

Prepared according to the above general procedure from 157 mg (0.74 mmol) of nitrone **2d** in 3.7 mL of MeOH, 99 mg (1.48 mmol) of pyrrole and 116 mg (1.48 mmol) of acetyl chloride. The mixture was stirred for 24 hours. Purification (eluent: CH_2Cl_2) afforded *N*-hydroxylamine **3d** (150 mg, 73%) as a colourless oil; ν_{max}/cm^{-1}

(thin film) 3438 (broad OH); δ_H (300 MHz; $CDCl_3$; Me_4Si) 3.79 (2H, s, CH_2Ph), 4.93–4.99 (2H, m, C(1)*H*, O*H*), 6.09 (1H, s, pyrr*H*), 6.17–6.18 (1H, m, pyrr*H*), 6.80 (1H, s, pyrr*H*), 7.24–7.39 (10H, m, Ar*H*), 8.72 (1H, br s, N*H*); δ_C (75 MHz; $CDCl_3$; Me_4Si) 61.5 (*C*H_2Ph), 67.9 (*C*(1)H), 107.7 (pyrr*C*H), 109.4 (pyrr*C*H), 118.0 (pyrr*C*H), 127.2 (Ar*C*H), 127.3 (Ar*C*H), 128.2 (Ar*C*H), 128.3 (Ar*C*H), 128.5 (Ar*C*H), 129.3 (Ar*C*H), 129.5 (pyrr*C*), 138.0 (Ar*C*), 140.6 (Ar*C*); *m/z* (ESI$^-$) 277 ([M − H]$^-$, 100%), 259; Elemental analysis, calcd (%) for $C_{18}H_{18}N_2O$: C, 77.67; H, 6.52; N, 10.06. Found: C, 77.37; H, 6.71; N, 9.83.

N-((*S*)-2-Benzyloxy-1-phenyl-ethyl)-*N*-[1-(1*H*-pyrrol-2-yl)propyl]hydroxylamine 5a

Prepared according to the above general procedure from 147 mg (0.52 mmol) of nitrone **4a** in 2.5 mL of MeOH, 70 mg (1.04 mmol) of pyrrole and 82 mg (1.04 mmol) of acetyl chloride. The mixture was stirred for 24 hours. Purification (eluent: pentane–EtOAc, 8 : 2 to 1 : 1) afforded *N*-hydroxylamine **5a** (180 mg, 98%, dr = 65 : 35) as a brown oil; compound **5a** (major isomer): $[\alpha]_D^{20}$ +5.2 (*c* 1.02 in $CHCl_3$); ν_{max}/cm^{-1} (thin film) 3450–3300 (broad, OH, NH); δ_H (300 MHz; $CDCl_3$; Me_4Si) 0.91 (3H, t, *J* = 7.4 Hz, C(3)H_3), 1.74–1.88 (1H, m, C(2)H_2), 1.98–2.12 (1H, m, C(2)H_2), 3.60–3.66 (1H, m, C(2′)H_2), 3.80–3.87 (2H, m, C(1′)*H*, C(2′)H_2), 4.05 (1H, t, *J* = 7.3 Hz, C(1)*H*), 4.24 (1H, br s, O*H*), 4.50 (2H, s, CH_2Ph), 6.02–6.04 (1H, m, pyrr*H*), 6.14 (1H, dd, *J* = 5.8 and 2.8 Hz, pyrr*H*), 6.68 (1H, dd, *J* = 4.1 and 2.6 Hz, pyrr*H*), 7.21–7.38 (10H, m, Ar*H*), 9.00 (1H, br s, N*H*); δ_C (75 MHz; $CDCl_3$; Me_4Si) 11.6 (*C*(3)H_3), 25.5 (*C*(2)H_2), 62.4 (*C*(1)H), 68.8 (*C*(1′)H), 73.2 (*C*(2′)H_2), 73.6 (*C*H_2Ph), 107.6 (pyrr*C*H), 108.2 (pyrr*C*H), 117.2 (pyrr*C*H), 127.3 (Ar*C*H), 127.9 (Ar*C*H), 128.0 (Ar*C*H), 128.4 (Ar*C*H), 128.6 (Ar*C*H), 129.0 (pyrr*C*), 137.4 (Ar*C*), 141.0 (Ar*C*); *m/z* (DCI, NH_3–isobutane) 351 ([M + H]$^+$), 333, 284, 244 (100%), 228, 193; HRMS (ESI$^-$) $C_{22}H_{25}N_2O_2$ ([M − H]$^-$) requires 349.19105 found 349.19153; compound **5a** (minor isomer): $[\alpha]_D^{20}$ +50.3 (*c* 1.00 in $CHCl_3$); δ_H (300 MHz; $CDCl_3$; Me_4Si) 0.76 (3H, t, *J* = 7.4 Hz, C(3)H_3), 1.64–1.78 (1H, m, C(2)H_2), 1.90–2.04 (m, 1H, C(2)H_2), 3.42–3.49 (1H, m, C(2′)H_2), 3.71–3.76 (2H, m, C(1)*H*, C(2′)H_2), 3.83–3.90 (1H, m, C(1′)*H*), 4.43 (2H, AB_q, J_{AB} = 12.0 Hz, δ_A–δ_B = 17.6 Hz, CH_2Ph), 5.19 (1H, s, O*H*), 5.76–5.78 (1H, m, pyrr*H*), 6.10 (1H, dd, *J* = 5.8 and 2.7 Hz, pyrr*H*), 6.74 (1H, dd, *J* = 4.1 and 2.6 Hz, pyrr*H*), 7.17–7.33 (10H, m, Ar*H*), 8.60 (1H, br s, N*H*); δ_C (75 MHz; $CDCl_3$; Me_4Si) 11.1 (*C*(3)H_3), 26.7 (*C*(2)H_2), 62.2 (*C*(1)H), 68.3 (*C*(1′)H), 73.2 (*C*H_2Ph), 73.6 (*C*(2′)H_2), 107.0 (pyrr*C*H), 109.0 (pyrr*C*H), 117.4 (pyrr*C*H), 127.6 (Ar*C*H), 127.7 (Ar*C*H), 128.2 (Ar*C*H), 128.3 (Ar*C*H), 129.0 (Ar*C*H), 129.6 (pyrr*C*), 138.1 (Ar*C*), 138.9 (Ar*C*); *m/z* (DCI, NH_3–isobutane) 351 ([M + H]$^+$), 284, 244, 108 (100%).

N-((*S*)-1-Phenyl-ethyl)-*N*-[1-(1*H*-pyrrol-2-yl)propyl]hydroxylamine 5b

Prepared according to the above general procedure from 89 mg (0.50 mmol) of nitrone **4b** in 2.5 mL of MeOH, 67 mg (1.0 mmol) of pyrrole and 79 mg (1.0 mmol) of acetyl chloride. The mixture was stirred for 24 hours. Purification (eluent: pentane–EtOAc, 8 : 2) afforded *N*-hydroxylamine **5b** (111 mg, 91%, dr = 65 : 35) as a brown oil; compound **5b** (major isomer): $[\alpha]_D^{20}$ −91.9 (*c* 1.05 in $CHCl_3$); ν_{max}/cm^{-1} (thin film) 3550–3400 (broad, OH, NH); δ_H (300 MHz; $CDCl_3$; Me_4Si) 0.79 (3H, t, *J* = 7.4 Hz, C(3)H_3), 1.39 (3H, d, *J* = 6.5 Hz, C(2′)H_3), 1.64–1.78 (1H, m, C(2)H_2), 1.87–2.01 (1H, m, C(2)H_2), 3.46 (1H, t, *J* = 7.5 Hz, C(1)*H*), 3.60 (1H, q, *J* = 6.5 Hz, C(1′)*H*), 4.66 (1H, br s, O*H*), 5.80–5.83 (1H, m, pyrr*H*), 6.12 (1H, dd, *J* = 5.8 and 2.7 Hz, pyrr*H*), 6.75 (1H, dd, *J* = 4.1 and 2.5 Hz, pyrr*H*), 7.23–7.34 (5H, m, Ar*H*), 8.61 (1H, br s, N*H*); δ_C (75 MHz; $CDCl_3$; Me_4Si) 11.2 (*C*(3)H_3), 22.2 (*C*(2′)H_3), 26.9 (*C*(2)H_2), 61.9 (*C*(1′)H), 64.3 (*C*(1)H), 107.0 (pyrr*C*H), 108.8 (pyrr*C*H), 117.3 (pyrr*C*H), 127.2 (Ar*C*H), 127.7 (Ar*C*H), 128.4 (Ar*C*H), 130.0 (pyrr*C*), 143.7 (Ar*C*); *m/z* (DCI, NH_3–isobutane) 245 ([M + H]$^+$, 100%), 227, 199, 178; HRMS (ESI$^+$) $C_{15}H_{20}N_2ONa$: ([M + Na]$^+$) requires 267.14678 found 267.14731; compound **5b** (minor isomer): $[\alpha]_D^{20}$ −47.6 (*c* 1.00 in $CHCl_3$); δ_H (300 MHz; $CDCl_3$; Me_4Si) 0.91 (3H, t, *J* = 7.4 Hz, C(3)H_3), 1.27 (3H, d, *J* = 6.6 Hz, C(2′)H_3), 1.73–1.88 (1H, m, C(2)H_2), 1.94–2.08 (1H, m, C(2)H_2), 3.59 (1H, q, *J* = 6.6 Hz, C(1)*H*), 3.89 (1H, dd, *J* = 8.2 and 6.5 Hz, C(1′)*H*), 4.46 (1H, br s, O*H*), 6.04–6.07 (1H, m, pyrr*H*), 6.14 (1H, dd, *J* = 5.8 and 2.4 Hz, pyrr*H*), 6.75 (1H, dd, *J* = 4.1 and 2.6 Hz, pyrr*H*), 7.19–7.31 (5H, m, Ar*H*), 8.73 (1H, br s, N*H*); δ_C (75 MHz; $CDCl_3$; Me_4Si) 11.4 (*C*(3)H_3), 20.4 (*C*(2)H_2), 26.8 (*C*(2′)H_3), 61.6 (*C*(1′)H), 64.2 (*C*(1)H), 106.8 (pyrr*C*H), 108.2 (pyrr*C*H), 117.6 (pyrr*C*H), 126.9 (Ar*C*H), 127.2 (Ar*C*H), 128.4 (Ar*C*H), 130.4 (pyrr*C*), 145.1 (Ar*C*); *m/z* (DCI, NH_3–isobutane) 245 ([M + H]$^+$), 227, 199 (100%), 178, 162.

N-[1-(1*H*-Pyrrol-2-yl)propyl]-*N*-[((*S*)-2,4,6-triisopropylphenyl)ethyl]hydroxylamine 5c

Prepared according to the above general procedure from 150 mg (0.49 mmol) of nitrone **4c** in 2.5 mL of MeOH, 67 mg (1.0 mmol) of pyrrole and 79 mg (1.0 mmol) of acetyl chloride. The mixture was stirred for 5 hours. Purification (eluent: pentane–EtOAc, 9 : 1 to 7 : 3) afforded *N*-hydroxylamine **5c** (132 mg, 73%, dr = 65 : 35) as a white foam; compound **5c** (major isomer): $[\alpha]_D^{20}$ +63.4 (*c* 1.05 in $CHCl_3$); ν_{max}/cm^{-1} (KBr disc) 3584 and 3475 (OH, NH); δ_H (300 MHz; $CDCl_3$; Me_4Si) 0.98 (3H, t, *J* = 7.4 Hz, C(3′)H_3), 1.04–1.08 (6H, m, CH(CH_3)$_2$), 1.23 (12H, m, CH(CH_3)$_2$), 1.36 (3H, d, *J* = 6.9 Hz, C(2)H_3), 1.74–1.88 (1H, m, C(2′)H_2), 1.96–2.11 (1H, m, C(2′)H_2), 2.77–2.97 (2H, m, C*H*(CH$_3$)$_2$), 3.95 (1H, t, *J* = 7.5 Hz, C(1′)*H*), 4.12 (1H, s, O*H*), 4.20 (1H, m, C*H*(CH$_3$)$_2$), 4.29 (1H, q, *J* = 6.9 Hz, C(1)*H*), 6.06–6.09 (1H, m, pyrr*H*), 6.14 (1H, dd, *J* = 5.7 and 2.8 Hz, pyrr*H*), 6.74 (1H, dd, *J* = 4.0 and 2.5 Hz, pyrr*H*), 6.89 (1H, d, *J* = 1.3 Hz, Ar*H*), 7.02 (1H, s, Ar*H*), 8.81 (1H, br s, N*H*); δ_C (75 MHz; $CDCl_3$; Me_4Si) 11.6 (*C*(3′)H$_3$), 19.4 (*C*(2)H$_3$), 23.7 (CH(*C*H$_3$)$_2$), 23.9 (CH(*C*H$_3$)$_2$), 24.9 (CH(*C*H$_3$)$_2$), 25.5 (CH(*C*H$_3$)$_2$), 27.3 (*C*(2′)H$_2$), 28.3 (*C*H(CH$_3$)$_2$), 29.2 (*C*H(CH$_3$)$_2$), 33.9 (*C*H(CH$_3$)$_2$), 58.2 (*C*(1′)H), 61.4 (*C*(1)H), 106.8 (pyrr*C*H), 108.2 (pyrr*C*H), 117.4 (pyrr*C*H), 120.8 (Ar*C*H), 123.0 (Ar*C*H), 130.7 (pyrr*C*), 134.6 (Ar*C*), 146.5 (Ar*C*), 146.6 (Ar*C*), 148.2 (Ar*C*); *m/z* (DCI, NH_3–isobutane) 371 ([M + H]$^+$), 246, 231 (100%); HRMS (ESI$^+$) $C_{24}H_{38}N_2ONa$ ([M + Na]$^+$) requires 393.28764 found 393.28851; compound **5c** (minor isomer): $[\alpha]_D^{20}$ +95.6 (*c* 1.05 in $CHCl_3$); δ_H (300 MHz; $CDCl_3$; Me_4Si) 0.70 (3H, t, *J* = 7.5 Hz, C(3′)H_3), 0.89 (3H, d, *J* = 6.9 Hz, C(2)H_3), 1.12 (3H, d, *J* = 6.6 Hz, CH(CH_3)$_2$), 1.19–1.26 (12H, m, CH(CH_3)$_2$), 1.48 (3H, d, *J* = 6.6 Hz, CH(CH_3)$_2$), 1.81–1.92 (2H, m, C(2′)H_2), 2.81–2.91 (2H, m, C*H*(CH$_3$)$_2$), 3.49 (1H, dd, *J* = 8.6 and 6.3 Hz, C(1)*H*), 4.10–4.19 (1H, m, C*H*(CH$_3$)$_2$), 4.25 (1H, q, *J* = 6.6 Hz, C(1′)*H*), 4.88 (1H, br s, O*H*), 5.60 (1H, m,

pyrr*H*), 6.03 (1H, dd, $J = 5.8$ and 2.8 Hz, pyrr*H*), 6.71 (1H, dd, $J = 4.1$ and 2.6 Hz, pyrr*H*), 6.91 (1H, d, $J = 1.8$ Hz, Ar*H*), 7.00 (1H, s, Ar*H*), 8.70 (1H, br s, N*H*); δ_C (75 MHz; $CDCl_3$; Me_4Si) 11.2 (*C*(3′)H_3), 21.0 (*C*(2)H_3), 22.8 (CH(*C*H_3)$_2$), 23.9 (CH(*C*H_3)$_2$), 24.0 (CH(*C*H_3)$_2$), 24.4 (CH(*C*H_3)$_2$), 25.1 (*C*(2′)H_2), 25.4 (CH(*C*H_3)$_2$), 25.7 (CH(*C*H_3)$_2$), 28.6 (C*H*(CH$_3$)$_2$), 28.8 (C*H*(CH$_3$)$_2$), 33.8 (C*H*(CH$_3$)$_2$), 59.3 (*C*(1′)H), 62.2 (*C*(1)H), 107.0 (pyrr*C*H), 109.0 (pyrr*C*H), 117.0 (pyrr*C*H), 120.8 (Ar*C*H), 122.8 (Ar*C*H), 130.3 (pyrr*C*), 133.9 (Ar*C*), 146.5 (Ar*C*), 146.9 (Ar*C*), 148.2 (Ar*C*); *m*/*z* (DCI, NH_3–isobutane) 371 ([M + H]$^+$), 246, 231 (100%).

(*R*)-4-[(*S*)-(*N*-Benzyl-*N*-hydroxy-amino)-(1*H*-pyrrol-2-yl)methyl]thiazolidine-3-carboxylic acid *tert*-butyl ester 7a

Prepared according to the above general procedure from 30 mg (0.09 mmol) of nitrone **6a** in 0.5 mL of MeOH, 12 mg (0.18 mmol) of pyrrole and 14 mg (0.18 mmol) of acetyl chloride. The mixture was stirred for 24 hours. Purification (eluent: CH_2Cl_2) afforded *N*-hydroxylamine **7a** (34 mg, 94%, dr > 98 : 2) as a white solid. Its absolute configuration was determined by X-ray analysis and revealed a (4*R*,1′*S*) configuration;‡ mp 110–111 °C; $[\alpha]_D^{20}$ −52.3 (*c* 0.85 in $CHCl_3$); ν_{max}/cm^{-1} (KBr disc) 3450–3300 (broad, OH, NH), 1675 (CO); δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.36 (9H, s, C(CH_3)$_3$), 3.08–3.24 (2H, m, C(5)H_2), 3.64–3.79 (3H, m, C(2)H_2, CH_2Ph), 3.91 (1H, d, $J = 7.8$ Hz, C(1′)*H*), 4.60–4.62 (1H, m, C(2)H_2), 5.19 (1H, br s, C(4)*H*), 6.06–6.12 (2H, m, pyrr*H*), 6.74 (1H, br s, pyrr*H*), 7.22–7.30 (5H, m, Ar*H*), 8.95 (1H, br s, N*H*); δ_C (75 MHz; $CDCl_3$; Me_4Si) 28.2 (*C*H_3), 33.5 (*C*(5)H_2), 47.5 (*C*(2)H_2), 60.1 (*C*(4)H), 61.7 (*C*H_2Ph), 65.9 (*C*(1′)H), 81.1 (*C*(CH$_3$)$_3$), 107.1 (pyrr*C*H), 110.4 (pyrr*C*H), 118.4 (pyrr*C*H), 125.2 (pyrr*C*), 127.1 (Ar*C*H), 128.2 (Ar*C*H), 128.9 (Ar*C*H), 138.0 (Ar*C*), 154.6 (C=O); *m*/*z* (DCI, NH_3–isobutane) 390 ([M + H]$^+$), 267, 211 (100%); Elemental analysis, calcd (%) for $C_{20}H_{27}N_3O_3S$: C, 61.68; H, 6.99; N, 10.79. Found: C, 61.58; H, 7.08; N, 10.57.

N-Benzyl-*N*-[(*S*)-((*S*)-2,2-dimethyl-1,3-dioxolan-4-yl)-(1*H*-pyrrol-2-yl)methyl]-*N*-hydroxylamine 7b

Prepared according to the above general procedure from 118 mg (0.50 mmol) of nitrone **6b** in 2.5 mL of MeOH, 67 mg (1.0 mmol) of pyrrole and 79 mg (1.0 mmol) of acetyl chloride. The mixture was stirred for 5 hours. Purification (eluent: CH_2Cl_2–MeOH, 100 : 0 to 95 : 5) afforded *N*-hydroxylamine **7b** (143 mg, 95%, dr > 98 : 2) as a white solid. Its absolute configuration was determined by X-ray analysis and revealed a (4*S*,1′*S*) configuration;‡ mp 72–73 °C; $[\alpha]_D^{20}$ −3.1 (*c* 1.04 in $CHCl_3$); ν_{max}/cm^{-1} (KBr disc) 3500–3300 (broad, OH, NH); δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.25 (3H, s, C(CH_3)$_2$), 1.35 (3H, s, C(CH_3)$_2$), 3.55–3.80 (4H, m, C(1′)*H*, C(5)H_2, CH_2Ph), 4.07 (1H, dd, $J = 8.2$ and 6.4 Hz, C(5)H_2), 4.70 (1H, dd, $J = 11,7$ and 6.7 Hz, C(4)*H*), 5.10 (1H, s, O*H*), 6.11–6.13 (1H, m, pyrr*H*), 6.18 (1H, dd, $J = 5.7$ and 2.9 Hz, pyrr*H*), 6.81 (dd, $J = 4.0$ and 2.5 Hz, 1H, pyrr*H*), 7.25–7.34 (5H, m, Ar*H*), 8.89 (1H, br s, N*H*); δ_C (75 MHz; $CDCl_3$; Me_4Si) 25.7 (*C*H_3), 26.2 (*C*H_3), 61.9 (*C*H_2Ph), 65.5 (*C*(1′)H), 67.6 (*C*(5)H_2), 76.8 (*C*(4)H), 107.4 (pyrr*C*H), 109.8 (*C*(CH$_3$)$_2$), 110.3 (pyrr*C*H), 118.2 (pyrr*C*H), 125.6 (pyrr*C*), 127.3 (Ar*C*H), 128.3 (Ar*C*H), 129.5 (Ar*C*H), 137.6 (Ar*C*); *m*/*z* (DCI, NH_3–isobutane) 303 ([M + H]$^+$), 285, 180 (100%), 122; HRMS (ESI$^+$) $C_{17}H_{22}N_2O_3Na$ ([M + Na]$^+$) requires 325.15226 found 325.15234.

‡ CCDC reference numbers 679400–679403. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b802997k

(*R*)-4-[(*N*-Benzyl-*N*-hydroxy-amino)-(1*H*-pyrrol-2-yl)methyl]-2,2-dimethyl-oxazolidine-3-carboxylic acid *tert*-butyl ester 7c

Prepared according to the above general procedure from 134 mg (0.40 mmol) of nitrone **6c** in 2 mL of MeOH, 54 mg (0.80 mmol) of pyrrole and 63 mg (0.80 mmol) of acetyl chloride. The mixture was stirred for 28 hours. Purification (eluent: CH_2Cl_2–pentane, 6 : 4 to 10 : 0) afforded *N*-hydroxylamine **7c** (157 mg, 98%, dr = 85 : 15) as a white solid; mp 44–45 °C; $[\alpha]_D^{20}$ +7.0 (*c* 1.03 in $CHCl_3$); ν_{max}/cm^{-1} (KBr disc) 3500–3300 (broad, OH, NH), 1662 (CO); δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.43–1.57 (15H, m, C(CH_3)$_2$, C(CH_3)$_3$), 3.60–3.87 (5H, m, C(1′)*H*, C(5)H_2, CH_2Ph), 4.31 (1H, dd, $J = 10.8$ and 4.0 Hz, C(4)*H*), 6.10–6.13 (1H, m, pyrr*H*), 6.17 (1H, dd, $J = 5.8$ and 2.8 Hz, pyrr*H*), 6.80 (1H, dd, $J = 4.1$ and 2.6 Hz, pyrr*H*), 7.19–7.27 (5H, m, Ar*H*), 8.03 (1H, s, O*H*), 9.39 (1H, br s, N*H*); δ_C (75 MHz; $CDCl_3$; Me_4Si) 24.6 (*C*H_3), 27.4 (*C*H_3), 28.5 (*C*H_3), 58.9 (*C*(4)H), 60.4 (*C*H_2Ph), 64.2 (*C*(1′)H), 65.7 (*C*(5)H_2), 81.2 (*C*(CH$_3$)$_3$), 94.1 (*C*(CH$_3$)$_2$), 107.3 (pyrr*C*H), 110.7 (pyrr*C*H), 118.4 (pyrr*C*H), 126.7 (Ar*C*H), 128.0 (Ar*C*H), 128.1 (pyrr*C*), 128.7 (Ar*C*H), 138.3 (Ar*C*), 153.0 (C=O); *m*/*z* (DCI, NH_3–isobutane) 402 ([M + H]$^+$), 386, 279 (100%), 223; Elemental analysis, calcd (%) for $C_{22}H_{31}N_3O_4$: C, 65.85; H, 7.79; N, 10.47. Found: C, 66.11; H, 8.13; N, 10.33.

(*S*)-2-[(*S*)-(*N*-Benzyl-*N*-hydroxy-amino)-(1*H*-pyrrol-2-yl)methyl]pyrrolidine-1-carboxylic acid *tert*-butyl ester 7d

Prepared according to the above general procedure from 80 mg (0.26 mmol) of nitrone **6d** in 1.3 mL of MeOH, 35 mg (0.52 mmol) of pyrrole and 41 mg (0.52 mmol) of acetyl chloride. The mixture was stirred for 30 hours. Purification (eluent: pentane–EtOAc, 9 : 1) afforded *N*-hydroxylamine **7d** (77 mg, 74%, dr = 90 : 10) as a colourless oil. Its absolute configuration was determined by ^{1}H NMR analysis.[19b] At −40 °C, the coupling constant between $H_{1'}$ and H_2 was 1.6 Hz for the major isomer. This value is in good agreement with the *anti* isomer; compound **7d** (major isomer): $[\alpha]_D^{20}$ −64.8 (*c* 1.00 in $CHCl_3$); ν_{max}/cm^{-1} (thin film) 3500–3200 (broad, OH, NH), 1667 (CO); δ_H (400 MHz; $CDCl_3$; Me_4Si) 0.58 (1H, br s, C(4)H_2), 1.42–1.53 (10H, m, C(4)H_2, C(CH_3)$_3$), 1.67–1.72 (1H, m, C(3)H_2), 1.89–2.00 (1H, m, C(3)H_2), 2.89–2.95 (1H, m, C(5)H_2), 3.27 (1H, app q, $J = 18.5$ and 9.1 Hz, C(5)H_2), 3.65 (1H, d, $J = 2.5$ Hz, C(1′)*H*), 3.66 (2H, AB_q, $J_{AB} = 14.6$ Hz, δ_A–δ_B = 69.9 Hz, CH_2Ph), 4.72 (1H, d, $J = 8.4$ Hz, C(2)*H*), 6.06–6.07 (1H, m, pyrr*H*), 6.12 (1H, dd, $J = 5.8$ and 2.8 Hz, pyrr*H*), 6.74–6.76 (1H, m, pyrr*H*), 7.17–7.32 (m, 5H, Ar*H*), 8.37 (2H, br s, N*H*, O*H*); δ_C (100 MHz; $CDCl_3$; Me_4Si) 22.6 (*C*(4)H_2), 28.5 (*C*H_3), 28.6 (*C*(3)H_2), 48.3 (*C*(5)H_2), 57.8 (*C*(2)H), 59.8 (*C*H_2Ph), 69.8 (*C*(1′)H), 80.4 (*C*(CH$_3$)$_3$), 107.8 (pyrr*C*H), 108.9 (pyrr*C*H), 118.1 (pyrr*C*H), 126.4 (Ar*C*H), 127.4 (pyrr*C*), 127.9 (Ar*C*H), 128.2 (Ar*C*H), 139.3 (Ar*C*), 157.6 (C=O); *m*/*z* (DCI, NH_3–isobutane) 372 ([M + H]$^+$), 249 (100%), 193; HRMS (ESI$^+$) $C_{21}H_{29}N_3O_3Na$ ([M + Na]$^+$) requires 394.21011 found 394.21099; compound **7d** (minor isomer): $[\alpha]_D^{20}$ +34.3 (*c* 1.02 in $CHCl_3$); δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.55 (9H, s, C(CH_3)$_3$), 1.68–1.88 (4H, m, C(3)H_2, C(4)H_2), 3.31–3.49 (3H, m, C(1′)*H*, C(5)H_2), 3.69 (2H, AB_q, $J_{AB} = 14.1$ Hz, δ_A–δ_B = 28.5 Hz, CH_2Ph), 4.30–4.36 (1H, m, C(2)*H*), 6.00–6.02

(1H, m, pyrr*H*), 6.15 (1H, dd, J = 5.8 and 2.7 Hz, pyrr*H*), 6.79 (1H, dd, J = 4.1 and 2.6 Hz, pyrr*H*), 7.16–7.25 (5H, m, Ar*H*), 8.26 (1H, s, O*H*), 9.33 (1H, br s, N*H*); δ_C (100 MHz; $CDCl_3$; Me_4Si) 22.8 (*C*(3)H_2), 27.9 (*C*(4)H_2), 28.5 (*C*H_3), 46.2 (*C*(5)H_2), 57.5 (*C*(2)H), 60.1 (*C*H_2Ph), 65.3 (*C*(1′)H), 80.0 (*C*$(CH_3)_3$), 106.9 (pyrr*C*H), 110.0 (pyrr*C*H), 118.3 (pyrr*C*H), 126.6 (Ar*C*H), 127.9 (Ar*C*H), 128.1 (Ar*C*H), 128.7 (pyrr*C*), 139.0 (Ar*C*), 157.0 (C=O); m/z (ESI$^+$) 410 ([M + K]$^+$), 394 ([M + Na]$^+$), 372 ([M + H]$^+$), 249 (100%).

(Benzyl-hydroxy-amino)-(1*H*-pyrrol-2-yl)-acetic acid (1*R*,2*S*,5*R*)-2-isopropyl-5-menthyl-cyclohexyl ester 9

Prepared according to the above general procedure from 320 mg (1.01 mmol) of nitrone **8a** in 5 mL of MeOH, 135 mg (2.02 mmol) of pyrrole and 158 mg (2.02 mmol) of acetyl chloride. The mixture was stirred for 24 hours. Purification (eluent: CH_2Cl_2) afforded *N*-hydroxylamine **9** as a mixture of diastereoisomers (283 mg, 73%, dr = 65 : 35) as a white solid; ν_{max}/cm^{-1} (KBr disc) 3600–3300 (broad, OH, NH), 1727 (CO); δ_H (300 MHz; $CDCl_3$; Me_4Si) 0.52–2.04 (18H, m, menthol *H*), 3.73 (1.3H, AB_q, J_{AB} = 13.5 Hz, δ_A–δ_B = 80.0 Hz, CH_2Ph$_{major}$), 3.75 (0.7H, AB_q, J_{AB} = 13.5 Hz, δ_A–δ_B = 85.8 Hz, CH_2Ph$_{minor}$), 4.53 (0.35H, s, C(2′)H_{minor}), 4.54 (0.65H, s, C(2′)H_{major}), 4.63–4.80 (1H, m, C(1)*H*), 5.43 (0.65H, s, OH_{major}), 5.62 (0.35H, s, OH_{minor}), 6.13–6.16 (1H, m, pyrr*H*), 6.20–6.23 (1H, m, pyrr*H*), 6.76–6.81 (1H, m, pyrr*H*), 7.27–7.31 (5H, m, Ar*H*), 8.82–8.87 (1H, 2 br s, N*H*); δ_C (75 MHz; $CDCl_3$; Me_4Si) 16.0 and 16.2 (*C*H_3), 20.6 and 20.7 (*C*H_3), 21.9 and 22.0 (*C*H_3), 23.3 (*C*(3)H_2), 25.8 and 26.1 (*C*H$(CH_3)_2$), 31.3 and 31.4 (*C*(5)H), 34.2 (*C*(4)H_2), 40.4 and 40.8 (*C*(6)H_2), 46.9 and 47.2 (*C*(2)H), 60.5 and 60.7 (*C*H_2Ph), 68.4 (*C*(2′)H), 75.4 and 75.5 (*C*(1)H), 108.1 (pyrr*C*H), 109.7 and 110.1 (pyrr*C*H), 118.9 and 119.0 (pyrr*C*H), 124.0 (pyrr*C*), 127.4 (Ar*C*H), 128.2 (Ar*C*H), 129.3 (Ar*C*H), 129.5 (Ar*C*H), 137.3 (Ar*C*), 170.3 (C=O); m/z (ESI$^+$) 423 ([M + K]$^+$), 407 ([M + Na]$^+$), 385 ([M + H]$^+$), 367, 262 (100%); HRMS (ESI$^+$) $C_{23}H_{32}N_2O_3Na$ ([M + Na]$^+$) requires 407.23051 found 407.23071.

(*R*)-[*N*-Hydroxy-((*R*)-2-hydroxy-1-phenylethyl)-amino]-(1*H*-pyrrol-2-yl)acetic acid methyl ester 10a and (*S*)-[*N*-hydroxy-((*R*)-2-hydroxy-1-phenylethyl)-amino]-(1*H*-pyrrol-2-yl)acetic acid methyl ester 10b

Prepared according to the above general procedure from 137 mg (0.72 mmol) of nitrone **8b** in 3.6 mL of MeOH, 96 mg (1.43 mmol) of pyrrole and 112 mg (1.43 mmol) of acetyl chloride. The mixture was stirred for 24 hours. Purification (eluent: pentane–AcOEt, 7 : 3 to 0 : 1) afforded *N*-hydroxylamines **10a** (59 mg, 28%) as a pale pink solid and **10b** (57 mg, 28%) as a colourless oil; compound **10a**: mp 79–80 °C; $[a]_D^{20}$ −132.5 (*c* 0.25 in $CHCl_3$); ν_{max}/cm^{-1} (KBr disc) 3550–3200 (broad, OH × 2, NH), 1740 (CO); δ_H (300 MHz; $CDCl_3$; Me_4Si) 3.65 (3H, s, O*C*H_3), 3.69 (1H, br s, O*H*), 3.81 (1H, dd, J = 10.4 and 4.1 Hz, C(1′)*H*), 4.42 (1H, app. t, J = 10.8 Hz, C(2′)H_2), 4.49 (1H, s, C(2)*H*), 4.53 (1H, br s, C(2′)H_2), 6.07–6.10 (1H, m, pyrr*H*), 6.17 (1H, dd, J = 5.7 and 2.6 Hz, pyrr*H*), 6.87 (1H, dd, J = 4.1 and 2.6 Hz, pyrr*H*), 7.30–7.35 (5H, m, Ar*H*), 7.46 (1H, s, O*H*), 10.10 (1H, br s, N*H*); δ_C (75 MHz; $CDCl_3$; Me_4Si) 52.7 (O*C*H_3), 62.7 (*C*(2′)H_2), 66.2 (*C*(2)H), 67.1 (*C*(1′)H), 108.0 (pyrr*C*H), 110.8 (pyrr*C*H), 120.1 (pyrr*C*H), 122.1 (pyrr*C*), 128.1 (Ar*C*H), 128.3 (Ar*C*H), 130.4 (Ar*C*H), 134.3 (Ar*C*), 173.1 (C=O); m/z (DCI, NH_3–isobutane) 291 ([M + H]$^+$), 273, 241 (100%); Elemental analysis, calcd (%) for $C_{15}H_{18}N_2O_4$: C, 62.06; H, 6.25; N, 9.65. Found: C, 62.41; H, 6.57; N, 9.51; compound **10b**: $[a]_D^{20}$ −15.2 (*c* 1.00 in $CHCl_3$); δ_H (400 MHz; $CDCl_3$; Me_4Si) 3.18 (1H, br s, O*H*), 3.71 (3H, s, O*C*H_3), 3.82 (1H, dd, J = 10.2 and 3.8 Hz, C(2′)H_2), 4.03–4.12 (2H, m, C(1′)*H*, C(2′)H_2), 4.68 (1H, s, C(2)*H*), 6.07–6.09 (2H, m, pyrr*H*), 6.51 (1H, br s, O*H*), 6.68 (1H, dd, J = 4.3 and 2.5 Hz, pyrr*H*), 7.25–7.34 (5H, m, Ar*H*), 9.14 (1H, br s, N*H*); δ_C (75 MHz; $CDCl_3$; Me_4Si) 52.3 (O*C*H_3), 64.6 (*C*(2′)H_2), 64.5 (*C*(2)H), 69.6 (*C*(1′)H), 108.1 (pyrr*C*H), 109.4 (pyrr*C*H), 118.9 (pyrr*C*H), 122.6 (pyrr*C*), 128.1 (Ar*C*H), 128.5 (Ar*C*H), 128.8 (Ar*C*H), 137.0 (Ar*C*), 171.2 (C=O); m/z (ESI$^+$) 329 ([M + K]$^+$), 313 ([M + Na]$^+$, 100%).

Compound **10a** could also be prepared as a single diastereoisomer, following the procedure below: to a stirred solution of hydroxylamine **11** (419 mg, 1.62 mmol) in anhydrous MeOH (8.0 mL) at −40 °C was added HCl (1.6 mL, 2.0 N in Et_2O, 3.24 mmol). It was slowly warmed to −20 °C and stirred at this temperature for 12 hours. The mixture was then treated with a saturated aqueous $NaHCO_3$ solution until pH 8–9. The aqueous layer was extracted three times with CH_2Cl_2. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$ and concentrated. The crude product was purified by flash chromatography on silica gel (eluent: pentane–EtOAc, 9 : 1 to 1 : 9) to afford *N*-hydroxylamine **10a** (419 mg, 89%) as a pale pink solid. Physical and spectral data were found to be identical to those described above.

(3*R*,5*R*)-4-Hydroxy-5-phenyl-3-(1*H*-pyrrol-2-yl)morpholin-2-one 11

To a stirred solution of nitrone **8b** (1,18 g, 6.19 mmol) in anhydrous CH_2Cl_2 (31 mL) at −78 °C was added HCl (6.20 mL, 2.0 N in Et_2O, 12.38 mmol) and the mixture was stirred for 10 minutes. Freshly distilled pyrrole (831 mg, 12.38 mmol, 0.86 mL) was added and the mixture was then slowly warmed to −40 °C within two hours whereupon water was added. The mixture was stirred for 15 minutes at room temperature and the aqueous layer was extracted three times with CH_2Cl_2. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated. The crude product was purified by flash chromatography on silica gel (eluent: pentane–EtOAc, 9 : 1 to 1 : 1) to afford *N*-hydroxylamine **11** as a single diastereoisomer (1.22 g, 76%) as a yellow solid. Its absolute configuration was determined by X-ray analysis and revealed a (3*R*,5*R*) configuration;‡ mp 48–49 °C; $[a]_D^{20}$ −48.9 (*c* 0.51 in $CHCl_3$); ν_{max}/cm^{-1} (KBr disc) 3500–3200 (broad, OH, NH), 1745 (CO); δ_H (300 MHz; $CDCl_3$; Me_4Si) 4.44 (1H, dd, J = 10.6 and 4.8 Hz, C(5)*H*), 4.56 (1H, dd, J = 11.3 and 4.8 Hz, C(6)H_2), 4.97 (1H, t, J = 10.9 Hz, C(6)H_2), 5.11 (1H, s, C(3)*H*), 5.50 (1H, s, O*H*), 6.18–6.21 (1H, m, pyrr*H*), 6.23–6.25 (1H, m, pyrr*H*), 6.77–6.79 (1H, m, pyrr*H*), 7.33–7.48 (5H, m, Ar*H*), 8.72 (1H, br s, N*H*); δ_C (75 MHz; $CDCl_3$; Me_4Si) 58.9 (*C*(5)H), 65.2 (*C*(3)H), 68.0 (*C*(6)H_2), 108.4 (pyrr*C*H), 108.6 (pyrr*C*H), 119.0 (pyrr*C*H), 123.3 (pyrr*C*), 128.0 (Ar*C*H), 128.7 (Ar*C*H), 128.9 (Ar*C*H), 135.3 (Ar*C*), 168.0 (C=O); m/z (DCI, NH_3–isobutane) 259 ([M + H]$^+$), 241 (100%);

HRMS (ESI$^+$) $C_{14}H_{14}N_2O_3K$ ([M + K]$^+$) requires 297.06360 found 297.06398.

(*R*)-Amino-(1*H*-pyrrol-2-yl)acetic acid methyl ester 12

To a stirred solution of hydroxylamine **10a** (29 mg, 0.10 mmol) in anhydrous MeOH (3.0 mL) and formic acid (0.3 mL) was added black palladium (60 mg, 0.56 mmol). The resulting mixture was stirred for 1 hour. It was then filtered on celite and methanol was removed under vacuum. Then CH_2Cl_2 and $NaHCO_3$ were added, filtrated and concentrated. The crude product was purified by flash chromatography on silica gel (eluent: pentane–EtOAc, 3 : 7 to 0 : 1) to afford unstable α-amino methyl ester **12** (6 mg, 40%) as a brown oil. The enantiomeric ratio was determined by ^{1}H NMR spectrum in the presence of the chiral shift reagent, europium(III) tris-(3-heptafluoropropylhydroxymethylene)-(+)-camphorate, and was 85 : 15; ν_{max}/cm^{-1} (thin film) 3400–3200 (broad, NH, NH_2), 1723 (CO); δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.89 (2H, br s, NH_2), 3.77 (3H, s, OCH_3), 4.72 (1H, s, C(2)H), 6.14–6.16 (2H, m, pyrr$H$), 6.74–6.75 (1H, m, pyrr$H$), 8.70 (1H, br s, NH); δ_C (75 MHz; $CDCl_3$; Me_4Si) 52.5 (OCH$_3$), 52.6 (*C*(2)H), 105.9 (pyrr*C*H), 108.7 (pyrr*C*H), 117.8 (pyrr*C*H), 129.1 (pyrr*C*), 173.6 (C=O); *m*/*z* (ESI$^+$) 138 ([M + H − NH_3]$^+$, 100%).

(*R*)-Amino-(1*H*-pyrrol-2-yl)acetic acid 13

To a stirred solution of freshly prepared α-amino methyl ester **12** (48 mg, 0.31 mmol) in THF (12 mL) and water (4 mL) at 0 °C was added lithium hydroxide monohydrate (260 mg, 0.62 mmol) and the resulting mixture was stirred for 2 hours at this temperature. It was then acidified with aqueous 0.2 N HCl to pH 3. After removal of the solvent, the residue was passed through a column of Dowex 50W-X8 ion exchange resin (H^+ form), eluting with water and then aqueous ammonia (1.0 N). Lyophilization afforded amino acid **13** (35 mg, 80%) as a white solid; mp 165–166 °C (dec.); $[\alpha]_D^{20}$ −87.1 (*c* 0.28 in 1.0 N HCl); ν_{max}/cm^{-1} (KBr disc) 3333 (NH), 3200–2900 (NH_3^+), 1639 (CO); δ_H (300 MHz, D_2O) 4.95 (1H, s, C(2)H), 6.28 (1H, t, J = 3.1 Hz, pyrr$H$), 6.34 (1H, dd, J = 3.4 and 1.4 Hz, pyrr$H$), 6.97 (1H, dd, J = 2.7 and 1.5 Hz, pyrr$H$); δ_C (75 MHz, D_2O) 52.1 (*C*(2)H), 108.4 (pyrr*C*H), 108.5 (pyrr*C*), 120.1 (pyrr*C*H), 123.8 (pyrr*C*H), 172.3 (C=O); *m*/*z* (DCI, NH_3–isobutane) 139 ([M − H]$^-$, 100%); HRMS (ESI$^-$) $C_6H_8N_2O_2$ ([M − H]$^-$) requires 139.05130 found 139.05142.

General procedure for the preparation of C-3 substituted pyrrolic *N*-hydroxylamines 15a–c

Freshly distilled acetyl chloride (157 mg, 2.0 mmol, 142 μL) was added dropwise at 0 °C to anhydrous methanol (5 mL) and the mixture was stirred for 15 min. The appropriate nitrone **2** (1.0 mmol) was added and the mixture was cooled to −40 °C before the addition of *N*-triisopropylsilylpyrrole **14b** (*N*-TIPS-pyrrole) (246 mg, 1.1 mmol). The mixture was slowly warmed to 0 °C, and stirred at this temperature until complete disappearance of starting material (followed by TLC). The mixture was then treated with saturated aqueous $NaHCO_3$ solution until pH 8–9. The aqueous layer was extracted three times with CH_2Cl_2. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$ and concentrated. The obtained *N*-hydroxylamine was purified by flash chromatography on silica gel.

N-Benzyl-*N*-[1-(1-triisopropylsilanyl-1*H*-pyrrol-3-yl)propyl]hydroxylamine 15a

Prepared according to the above general procedure from 163 mg (1.00 mmol) of nitrone **2a** in 5.0 mL of MeOH, 241 mg (1.08 mmol) of *N*-TIPS-pyrrole **14b** and 157 mg (2.00 mmol) of acetyl chloride. The mixture was stirred for 24 hours. Purification (eluent: pentane–EtOAc, 9 : 1) afforded *N*-hydroxylamine **15a** (227 mg, 59%) as a beige solid; mp 76–77 °C; ν_{max}/cm^{-1} (KBr disc) 3300–3150 (broad, OH); δ_H (300 MHz; $CDCl_3$; Me_4Si) 0.84 (3H, t, J = 7.4 Hz, C(3)H_3), 1.10–1.12 (18H, m, ((CH_3)$_2$CH)$_3$Si), 1.38–1.53 (3H, m, ((CH_3)$_2$CH)$_3$Si), 1.68–1.83 (1H, m, C(2)H_2), 2.03–2.17 (1H, m, C(2)H_2), 3.63 (1H, dd, J = 9.0 and 5.3 Hz, C(1)H), 3.69 (2H, AB_q, J_{AB} = 13.3 Hz, δ_A–δ_B = 93.1 Hz, CH_2Ph), 6.29 (1H, dd, J = 2.6 and 1.4 Hz, pyrr$H$), 6.67–6.70 (1H, m, pyrr$H$), 6.78 (1H, t, J = 2.4 Hz, pyrr$H$), 7.19–7.35 (5H, m, ArH); δ_C (75 MHz; $CDCl_3$; Me_4Si) 11.2 (((CH_3)$_2$*C*H)$_3$Si), 11.7 (*C*(3)H$_3$), 17.8 (((CH_3)$_2$CH)$_3$Si), 26.4 (*C*(2)H$_2$), 61.3 (*C*H$_2$Ph), 66.6 (*C*(1)H), 110.8 (pyrr*C*H), 123.5 (pyrr*C*H), 124.4 (pyrr*C*H), 127.0 (Ar*C*H), 128.2 (Ar*C*H), 129.4 (Ar*C*H), 135.7 (pyrr*C*), 138.4 (Ar*C*); *m*/*z* (ESI$^+$) 425 ([M + K]$^+$), 409 ([M + Na]$^+$), 387 ([M + H]$^+$, 100%); Elemental analysis, calcd (%) for $C_{23}H_{38}N_2OSi$: C, 71.45; H, 9.91; N, 7.25. Found: C, 71.51; H, 9.92; N, 7.13.

[2-(*N*-Benzyl-*N*-hydroxy-amino)-2-(1-triisopropylsilanyl-1*H*-pyrrol-3-yl)ethyl]carbamic acid *tert*-butyl ester 15b

Prepared according to the above general procedure from 82 mg (0.31 mmol) of nitrone **2b** in 1.6 mL of MeOH, 76 mg (0.34 mmol) of *N*-TIPS-pyrrole **14b** and 49 mg (0.62 mmol) of acetyl chloride. The mixture was stirred for 30 hours. Purification (eluent: pentane–EtOAc, 9 : 1 to 7 : 3) to afford *N*-hydroxylamine **15b** (93 mg, 62%) as a white solid; mp 99–100 °C; ν_{max}/cm^{-1} (KBr disc) 3450–3300 (broad, OH, NH), 1706 (CO); δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.08–1.11 (18H, m, ((CH_3)$_2$CH)$_3$Si), 1.36–1.47 (12H, m, ((CH_3)$_2$CH)$_3$Si, C(CH_3)$_3$), 3.37–3.58 (2H, m, C(1)H_2), 3.71 (1H, dd, J = 6.5 and 4.5 Hz, C(2)H), 3.75 (2H, AB_q, J_{AB} = 13.9 Hz, δ_A–δ_B = 91.0 Hz, CH_2Ph), 4.88–4.92 (1H, m, NH), 6.02 (1H, br s, OH), 6.28 (1H, dd, J = 2.6 and 1.4 Hz, pyrr$H$), 6.71–6.73 (1H, m, pyrr$H$), 6.75 (1H, t, J = 2.3 Hz, pyrr$H$), 7.17–7.33 (5H, m, ArH); δ_C (75 MHz; $CDCl_3$; Me_4Si) 11.7 (((CH_3)$_2$*C*H)$_3$Si), 17.8 (((CH_3)$_2$CH)$_3$Si), 28.4 (C(*C*H$_3$)$_3$), 43.4 (*C*(1)H$_2$), 60.5 (*C*H$_2$Ph), 64.5 (*C*(2)H), 79.3 (*C*(CH$_3$)$_3$), 110.7 (pyrr*C*H), 121.2 (pyrr*C*), 123.0 (pyrr*C*H), 124.3 (pyrr*C*H), 126.6 (Ar*C*H), 128.0 (Ar*C*H), 128.7 (Ar*C*H), 139.2 (Ar*C*), 154.5 (C=O); *m*/*z* (DCI, NH_3–isobutane) 488 ([M + H]$^+$), 472, 365, 390 (100%); Elemental analysis, calcd (%) for $C_{27}H_{45}N_3O_3Si$: C, 66.49; H, 9.30; N, 8.62. Found: C, 66.43; H, 9.44; N, 8.39.

(*N*-Benzyl-*N*-hydroxy-amino)-(1-triisopropylsilanyl-1*H*-pyrrol-3-yl)acetic acid ethyl ester 15c

Prepared according to the above general procedure from 290 mg (1.35 mmol) of nitrone **2c** in 6.8 mL of MeOH, 332 mg (1.49 mmol) of *N*-TIPS-pyrrole **14b** and 211 mg (2.70 mmol) of acetyl chloride. The mixture was stirred for 12 hours. Purification (eluent: pentane–EtOAc, 9 : 1 to 7 : 3) afforded *N*-hydroxylamine **15c** (447 mg, 77%) as a white solid; mp 99–100 °C; ν_{max}/cm^{-1} (KBr disc) 3500–3350 (broad, OH), 1752 (CO); δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.09 (18H, d, J = 7.5 Hz, ((CH_3)$_2$CH)$_3$Si), 1.20 (3H, t,

J = 7.1 Hz, C(2′)H_3), 1.35–1.52 (3H, m, ((CH_3)$_2$CH)$_3$Si), 3.77 (2H, AB_q, J_{AB} = 13.6 Hz, δ_A–δ_B = 136.8 Hz, CH_2Ph), 4.17 (2H, q, J = 7.1 Hz, C(1′)H_2), 4.48 (1H, s, C(2)H), 5.35 (1H, br s, OH), 6.39 (1H, dd, J = 2.7 and 1.4 Hz, pyrr$H$), 6.72–6.74 (1H, m, pyrr$H$), 6.73 (1H, t, J = 2.4 Hz, pyrr$H$), 7.21–7.35 (5H, m, ArH); δ_C (75 MHz; $CDCl_3$; Me_4Si) 11.6 (((CH_3)$_2$$C$H)$_3$Si), 14.1 ($C$(2′)H$_3$), 17.8 ((($CH_3$)$_2$CH)$_3$Si), 60.1 ($CH_2$Ph), 60.7 ($C$(1′)H$_2$), 69.3 ($C$(2)H), 110.8 (pyrr$C$H), 119.3 (pyrr$C$), 123.9 (pyrr$C$H), 124.6 (pyrr$C$H), 127.1 (Ar$C$H), 128.1 (Ar$C$H), 129.6 (Ar$C$H), 137.8 (Ar$C$), 171.8 (C=O); m/z (DCI, NH_3–isobutane) 431 ([M + H]$^+$), 415, 308 (100%); Elemental analysis, calcd (%) for $C_{24}H_{38}N_2O_3Si$: C, 66.94; H, 8.90; N, 6.51. Found: C, 67.18; H, 9.03; N, 6.40.

(3*R*,5*R*)-4-Hydroxy-5-phenyl-3-(1-triisopropylsilanyl-1*H*-pyrrol-3-yl)morpholin-2-one 16a and (3*R*,5*R*)-4-hydroxy-5-phenyl-3-(1-triisopropylsilanyl-1*H*-pyrrol-2-yl)morpholin-2-one 16b

To a stirred solution of nitrone **8b** (102 mg, 0.53 mmol) in anhydrous CH_2Cl_2 (2,5 mL) at 0 °C was added HCl (530 µL, 2.0 N in Et_2O, 1.06 mmol) and *N*-TIPS-pyrrole **14b** (119 mg, 0.53 mmol) and the mixture was stirred 0 °C for 12 hours. The mixture was then treated with saturated aqueous $NaHCO_3$ solution until pH 8–9. The aqueous layer was extracted three times with CH_2Cl_2. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$ and concentrated. The crude product was purified by flash chromatography on silica gel (eluent: pentane–EtOAc, 9 : 1 to 7 : 3) to afford a mixture of two regioisomers **16a**,**b**, **16a** being the major isomer (124 mg, 57%, regio-isomeric ratio before purification 66 : 34) as a beige solid; ν_{max}/cm^{-1} (KBr disc) 3600–3300 (broad, OH), 1748 (CO); δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.07–1.16 (18H, 3d, J = 7.3, 7.4 and 7.5 Hz, ((CH_3)$_2$CH)$_3$Si), 1.38–1.48 (3H, m, ((CH_3)$_2$CH)$_3$Si), 4.46 (1.56H, m, C(5)H, C(6)H_2), 4.77–4.81 (0.44H, m, C(5)H, C(6)H_2), 5.02–5.08 (1.56H, m, C(3)H, C(6)H_2), 5.15–5.23 (0.44H, m, C(3)H, C(6)H_2), 5.67–5.73 (0.78H, m, OH), 6.25 (0.22H, app. t, J = 3.1 Hz, pyrr$H$), 6.31 (0.78H, app. t, J = 3.1 Hz, pyrr$H$), 6.35 (0.22H, dd, J = 3.3 and 1.3 Hz, pyrr$H$), 6.75–6.76 (1.56H, m, pyrr$H$), 6.87 (0.22H, dd, J = 2.7 and 1.4 Hz, pyrr$H$), 7.25–7.39 (5H, m, ArH); δ_C (75 MHz; $CDCl_3$; Me_4Si) 11.6 (((CH_3)$_2$$C$H)$_3Si_{major}$), 13.2 ((($CH_3$)$_2$$C$H)$_3Si_{minor}$), 13.7 ((($CH_3$)$_2$CH)$_3Si_{major}$), 18.3 ((($CH_3$)$_2$CH)$_3Si_{minor}$), 57.0 ($C$(5)H$_{major}$), 59.1 ($C$(5)H$_{minor}$), 66.1 ($C$(3)H$_{major}$), 67.1 ($C$(6)H$_{2minor}$), 67.7 ($C$(6)H$_{2major}$), 110.0 (pyrr$CH_{minor}$), 110.6 (pyrr$CH_{major}$), 114.4 (pyrr$CH_{minor}$), 118.3 (pyrr$C_{major}$), 123.5 (pyrr$CH_{major}$), 124.9 (pyrr$CH_{major}$), 127.2 (pyrr$CH_{minor}$), 127.9–128.8 (Ar$C$H), 130.4 (pyrr$C_{minor}$), 135.8 (Ar$C_{minor}$), 135.9 (Ar$C_{major}$), 168.4 (C=O$_{minor}$), 169.0 (C=O$_{major}$); m/z (ESI$^+$) 453 ([M + K]$^+$), 437 ([M + Na]$^+$, 100%), 415 ([M + H]$^+$); Elemental analysis, calcd (%) for $C_{23}H_{34}N_2O_3Si$: C, 66.63; H, 8.27; N, 6.76. Found: C, 66.71; H, 8.29; N, 6.82.

(*R*)-[Hydroxy-((*R*)-2-hydroxy-1-phenylethyl)amino]-(1-triisopropylsilanyl-1*H*-pyrrol-3-yl)acetic acid methyl ester 20

To a stirred solution of nitrone **8b** (0.96 g, 5.02 mmol) in anhydrous CH_2Cl_2 (25 mL) at −40 °C was added HCl (5.0 mL, 2.0 N in Et_2O, 10.00 mmol) and *N*-TIPS-pyrrole **14b** (1.23 g, 5.51 mmol). It was slowly warmed to −20 °C and then stirred at this temperature for 12 hours whereupon anhydrous MeOH (25 mL) was added. It was then allowed to run at 0 °C for 24 hours. The mixture was then treated with a saturated aqueous $NaHCO_3$ solution until pH 8–9. The aqueous layer was extracted three times with CH_2Cl_2. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$ and concentrated. The crude product was purified by flash chromatography on silica gel (eluent: pentane–EtOAc, 9 : 1 to 7 : 3) to afford pure *N*-hydroxylamine **20** (1.48 g, 66%) as a pale pink solid; mp 50–51 °C; $[\alpha]_D^{20}$ −113.0 (c 1.00 in $CHCl_3$); ν_{max}/cm^{-1} (KBr disc) 3550–3350 (broad, OH × 2), 1752 (CO); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.09–1.13 (18H, m, ((CH_3)$_2$CH)$_3$Si), 1.38–1.50 (3H, m, ((CH_3)$_2$CH)$_3$Si), 3.54–3.58 (1H, m, C(2′)H_2), 3.63 (3H, s, OCH_3), 4.00 (1H, dd, J = 9.7 and 3.8 Hz, C(1′)H), 4.23 (1H, br s, OH), 4.33–4.38 (1H, m, C(2′)H_2), 4.39 (1H, s, C(2)H), 6.42 (1H, dd, J = 2.4 and 1.2 Hz, pyrr$H$), 6.57 (1H, s, OH), 6.70 (1H, s, pyrr$H$), 6.76 (1H, t, J = 2.4 Hz, pyrr$H$), 7.30–7.32 (5H, m, ArH); δ_C (75 MHz; $CDCl_3$; Me_4Si) 11.7 (((CH_3)$_2$$C$H)$_3$Si), 17.8 ((($CH_3$)$_2$CH)$_3$Si), 52.2 (O$CH_3$), 63.4 ($C$(2′)H$_2$), 66.6 ($C$(2)H), 67.6 ($C$(1′)H), 110.5 (pyrr$C$H), 117.8 (pyrr$C$), 124.5 (pyrr$C$H), 124.9 (pyrr$C$H), 127.8 (Ar$C$H), 127.9 (Ar$C$H), 130.2 (Ar$C$H), 140.2 (Ar$C$), 174.0 (C=O); m/z (DCI, NH_3–isobutane) 447 ([M + H]$^+$), 431, 399, 294 (100%); Elemental analysis, calcd (%) for $C_{24}H_{38}N_2O_4Si$: C, 64.54; H, 8.58; N, 6.28. Found: C, 64.36; H, 8.73; N, 6.38.

Synthesis of (*R*)-amino-(1*H*-pyrrol-3-yl)acetic methyl ester 18

First strategy (from 16a,b)

(3*R*,5*R*)-4-Hydroxy-5-phenyl-3-(1*H*-pyrrol-3-yl)morpholin-2-one 17

To a stirred solution of hydroxylamines **16a**,**b** (464 mg, 1.12 mmol) in anhydrous THF (11.2 mL) was added acetic acid (385 µL, 6.72 mmol). TBAF (2.24 mL, 1.0 M solution in THF, 2.24 mmol) was then added dropwise and the mixture was stirred for 15 minutes. The mixture was treated with a saturated aqueous solution of ammonium chloride. The aqueous layer was extracted three times with CH_2Cl_2. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$ and concentrated. The crude product was purified by flash chromatography on silica gel (eluent: pentane–EtOAc, 7 : 3) to afford *N*-hydroxylamine **17** (177 mg, 61%) as a beige solid and *N*-hydroxylamine **11** (26 mg, 9%) as a yellow solid. The absolute configuration of compound **17** was determined by X-ray analysis and revealed a (3*R*,5*R*) configuration;‡ characterization data for **17**: mp 69–70 °C; $[\alpha]_D^{20}$ +25.4 (c 0.54 in $CHCl_3$); ν_{max}/cm^{-1} (KBr disc) 3600–3200 (broad, OH, NH), 1745 (CO); δ_H (300 MHz; $CDCl_3$; Me_4Si) 4.49–4.59 (2H, m, C(5)H, C(6)H_2), 4.99–5.06 (1H, m, C(6)H_2), 5.09 (1H, s, C(3)H), 5.18 (1H, s, OH), 6.32 (1H, dd, J = 4.2 and 2.6 Hz, pyrr$H$), 6.81 (1H, dd, J = 5.0 and 2.6 Hz, pyrr$H$), 6.85–6.86 (1H, m, pyrr$H$), 7.36–7.38 (5H, m, ArH), 8.31 (1H, br s, NH); δ_C (75 MHz; $CDCl_3$; Me_4Si) 57.4 (C(5)H), 65.7 (C(3)H), 67.9 (C(6)H$_2$), 108.5 (pyrr$C$H), 116.3 (pyrr$C$), 117.8 (pyrr$C$H), 118.7 (pyrr$C$H), 128.1 (ArCH), 128.4 (ArCH), 128.7 (ArCH), 135.7 (ArC), 169.2 (C=O); m/z (ESI$^+$) 297 ([M + K]$^+$), 281 ([M + Na]$^+$), 259 ([M + H]$^+$, 100%); HRMS (ESI$^+$) $C_{14}H_{14}N_2O_3Na$ ([M + Na]$^+$) requires 281.08966 found 281.08904.

(*R*)-Amino-(1*H*-pyrrol-3-yl)acetic acid methyl ester 18

To a stirred solution of hydroxylamine **17** (123 mg, 0.48 mmol) in anhydrous MeOH (2.4 mL) at −20 °C was added HCl (480 µL,

2.0 N in Et_2O, 0.96 mmol) and the mixture was slowly warmed to 0 °C and stirred at this temperature for 12 hours. The mixture was then treated with a saturated aqueous $NaHCO_3$ solution until pH 8–9. The aqueous layer was extracted three times with CH_2Cl_2. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$ and concentrated. The crude product was purified by flash chromatography on silica gel (eluent: pentane–EtOAc, 9 : 1 to 3 : 7) to afford pure *N*-hydroxylamine (127 mg, 92%) as a pale purple solid. This hydroxylamine (100 mg, 0.34 mmol) was dissolved in anhydrous MeOH (1.6 mL) and acetic acid (170 μL) and Pearlman's catalyst ($Pd(OH)_2$) was added (48 mg, 20% in weight, 0.07 mmol). The resulting mixture was stirred under a hydrogen atmosphere at room temperature for 12 hours. It was then filtered on celite, methanol was removed under vacuum, and acetic acid was removed azeotropically with toluene. The crude product was purified by flash chromatography on silica gel (eluent: pentane–EtOAc, 1 : 1 to 0 : 1) to afford α-amino methyl ester **18** (0.42 g, 80%) as a yellow oil; $[\alpha]_D^{20}$ −92.2 (*c* 0.50 in $CHCl_3$); ν_{max}/cm^{-1} (thin film) 3600–3100 (broad, NH, NH_2), 1736 (CO); δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.92 (2H, s, N*H*$_2$), 3.72 (3H, s, OC*H*$_3$), 4.60 (1H, s, C(2)*H*), 6.20 (1H, dd, *J* = 4.2 and 2.6 Hz, pyrr*H*), 6.70 (1H, dd, *J* = 4.8 and 2.5 Hz, pyrr*H*), 6.74–6.75 (1H, m, pyrr*H*), 8.78 (1H, br s, N*H*); δ_C (75 MHz; $CDCl_3$; Me_4Si) 52.1 (O*C*H$_3$), 52.5 (*C*(2)H), 106.6 (pyrr*C*H), 115.5 (pyrr*C*H), 118.4 (pyrr*C*H), 122.8 (pyrr*C*), 175.3 (C=O); *m*/*z* (DCI, NH_3–isobutane) 155 ([M + H]$^+$), 138 (100%); HRMS (ESI$^+$) $C_7H_{11}N_2O_2$ ([M + H]$^+$) requires 155.08150 found 155.08147.

Second strategy (from 20)

To a stirred solution of hydroxylamine **20** (1.32 g, 2.96 mmol) in anhydrous MeOH (14.3 mL) and acetic acid (1.6 mL) was added Pearlman's catalyst ($Pd(OH)_2$) (415 mg, 20% in weight, 0.59 mmol). The resulting mixture was stirred under a hydrogen atmosphere at room temperature for 12 hours. It was then filtered through celite, methanol was removed under vacuum, and acetic acid was removed by azeotropic distillation with toluene. The crude product was purified by flash chromatography on silica gel (eluent: pentane–EtOAc, 1 : 1 to 0 : 1) to afford α-amino methyl ester (0.92 g, quant.) as a yellow oil. The α-amino methyl ester (249 mg, 0.80 mmol) was dissolved in anhydrous THF (5.3 mL) and TBAF was added dropwise (0.88 mL, 1.0 M solution in THF, 0.88 mmol). The resulting mixture was stirred at room temperature for 5 minutes, then the reaction mixture was concentrated and the crude product was purified by flash chromatography on silica gel (eluent: pentane–EtOAc, 1 : 1 to 0 : 1) to afford α-amino methyl ester **18** (99 mg, 80%) as a yellow oil. The enantiomeric ratio was determined by ^{1}H NMR in the presence of the chiral shift reagent, europium(III) tris-(3-heptafluoropropylhydroxymethylene)-(+)-camphorate, and was 95 : 5; $[\alpha]_D^{20}$ −91.1 (*c* 0.50 in $CHCl_3$).

(*R*)-Amino-(1*H*-pyrrol-3-yl)acetic acid 19

To a stirred solution of amino-ester **18** (18 mg, 0.12 mmol) in THF (4.5 mL) and water (1.5 mL) at 0 °C was added lithium hydroxide monohydrate (10 mg, 0.24 mmol) and the resulting mixture was stirred for 2 hours. It was then acidified with aqueous 0.2 N HCl to pH 3. After removal of the solvent *in vacuo*, the residue was passed through a column of Dowex 50W-X8 ion exchange resin (H^+ form), eluting with water and then aqueous ammonia (1.0 N). Lyophilization afforded amino acid **19** (16 mg, 95%) as a pale brown solid; mp 166–167 °C (dec.); $[\alpha]_D^{20}$ −84.1 (*c* 0.27 in 1.0 N HCl); ν_{max}/cm^{-1} (KBr disc) 3600–2800 (broad, NH, NH_3^+), 1623 (CO); δ_H (300 MHz, D_2O) 4.84 (1H, s, C(2)*H*), 6.29 (1H, dd, *J* = 2.8 and 1.7 Hz, pyrr*H*), 6.93 (1H, dd, *J* = 2.7 and 2.2 Hz, pyrr*H*), 7.03 (1H, t, *J* = 1.8 Hz, pyrr*H*); δ_C (75 MHz, D_2O) 52.5 (*C*(2)H), 106.4 (pyrr*C*H), 116.0 (pyrr*C*), 118.3 (pyrr*C*H), 119.4 (pyrr*C*H), 174.5 (C=O); *m*/*z* (ESI$^+$) 141 ([M + H]$^+$), 124 (100%); HRMS (ESI$^-$) $C_6H_8N_2O_2$ ([M − H]$^-$) requires 139.05130 found 139.05125.

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