Conversion of homochiral amines, β-amino alcohols and α-amino acids to their chiral 2-substituted pyrrole derivatives

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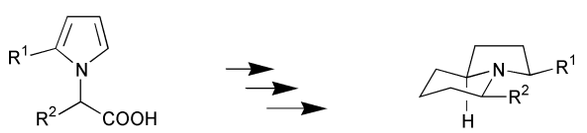
The conversion of the amino group of chiral amines, amino alcohols, amino acids and their esters into chiral 2-substituted pyrrole derivatives with various halogeno enones is described. The conversion works in good yield and without racemization. The synthesis of 2-phenylpyrrole derivatives was possible with amino alcohols but not with amino acids or their esters.

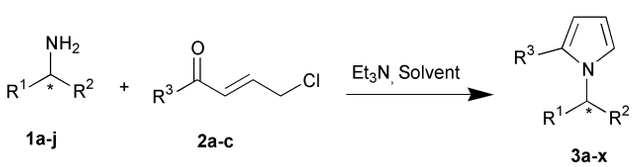
Introduction

Compounds containing a pyrrole ring can be found in many naturally occurring compounds and they have found applications in medicine and agriculture.[1] Chiral pyrrole derivatives of amines and amino acids are important starting materials for the synthesis of many different biologically active compounds. Several useful variants of classical methods can be found in the literature.[2] A stereoselective approach to the synthesis of indolizidine alkaloids based on the reaction of pyrrole derivatives of amino acids has been reported.[3] C-2 substituted pyrrole derivatives also provide access to substituted indolizidine alkaloids as outlined in Scheme 1.



Scheme 1

The Paal–Knorr synthesis, starting from primary amines and 1,4-dicarbonyl compounds[4] and their masked equivalents such as tetrahydro-2,5-dimethoxyfuran, is often used for the construction of pyrrole rings.[3] During the condensation reaction for the formation of the pyrrole ring with amino acids, partial racemization often occurs. Therefore, the development of a flexible and selective method to obtain such compounds is desirable. As we described in a previous paper, we have designed a convenient new route to 2-methyl-substituted pyrrole rings from amines, amino alcohols and amino acids with 5-chloropent-3-en-2-one prepared from acetyl chloride and allyl chlorides in the presence of $AlCl_3$[5] (Scheme 2). As part of our



Scheme 2

continued interest in the chemistry of 2-substituted pyrroles, we have extended this chemistry to the conversion of homochiral amines, β-amino alcohols and α-amino acids to their chiral 2-methyl-, -isopropyl-, -cyclohexyl-, and -phenyl-substituted pyrrole derivatives.

Results and discussion

Halogeno enones are valuable intermediates for the construction of nitrogen heterocycles. Chloro enones **2a**–**c** provide four carbon units with a carbonyl and halide functionality to form pyrrole rings with primary amines. According to Scheme 2, L-alanine methyl ester (*S*)-**1a** is refluxed with chloro enone **2a** in benzene and water for 5 hours and during this time the reaction is monitored by TLC. Purification of the crude product afforded the desired pyrrole derivative (*S*)-**3a** in 80% yield as a colorless oil. The same reaction was also carried out with the isopropyl and cyclohexyl derivatives of the enone (**2b** and **2c**). The reaction afforded the corresponding pyrrole derivatives **3b** (76%) and **3c** (72%). The reaction also works with alanine under similar conditions to obtain the free acid pyrrole derivative (*S*)-**3d** in 52% yield.

Under the same reaction conditions, valine, valine methyl ester, aspartic acid methyl ester, tyrosine ethyl ester and phenylglycine are converted to their 2-methyl-, isopropyl- and cyclohexyl-pyrrole derivatives in 44–82% yields as summarized in Table 1. Most of the products are solids or semisolids and their spectroscopic data are fully in agreement with their structure.

As shown in Table 1, the esters of amino acids give higher yields than their free acids. Comparable yields are obtained with different R^3-groups and this shows that varying the substituents on the chloro enone does not have a large influence on the yield of the products.

Formation of the optically pure pyrrole derivative of L-valinol, (*S*)-**3q**, starting from chloro enone **2a** with optically pure L-valinol and L-valine methyl ester, showed that no racemization occurred during the formation of (*S*)-**3g** (Scheme 3).

The pyrrole derivative of amino acid esters and amino alcohols showed excellent separation properties by chiral HPLC column.[6] Comparison of the optical purity of the products with that of racemic mixtures by chiral HPLC column gave the same result, which is that no racemization occurs by the formation of a pyrrole ring from amino acids and their esters.

By the same method, amino alcohols **1h**,**i** and amine **1j** were also converted to their 2-substituted derivatives in high yields.

Chloro enones **2a**–**c** are synthesized starting from the corresponding acyl chlorides and allyl chloride in the presence of $AlCl_3$. According to the ^1H NMR spectrum of the crude products, the reaction afforded the chloro enones **2a**–**c** as the major products. Isomers **4a**–**c** were formed as minor products.[7] The crude mixtures were used for pyrrole-ring formation without further purification.

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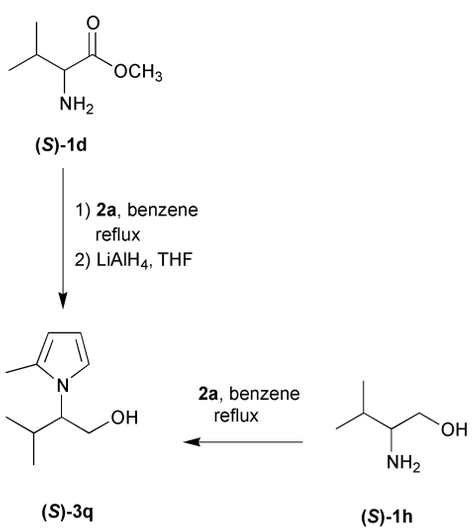
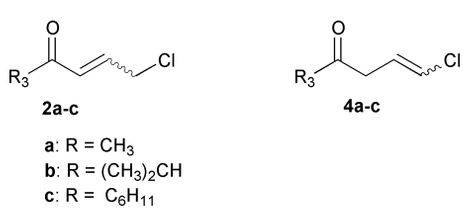
Table 1 Preparation of 2-substituted pyrrole derivatives

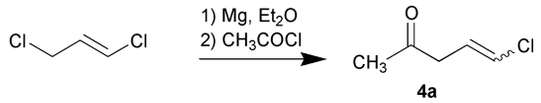
Amine **1**		Product **3**		
R^1	R^2	R^3		Yield (%)
(*S*)-**1a** CH_3	$COOCH_3$	CH_3	(*S*)-**3a**	80
(*S*)-**1a**		$(CH_3)_2CH$	(*S*)-**3b**	76
(*S*)-**1a**		C_6H_{11}	(*S*)-**3c**	72
(*S*)-**1b** CH_3	COOH	$(CH_3)_2CH$	(*S*)-**3d**	52
(*S*)-**1c** $(CH_3)_2CH$	COOH	CH_3	(*S*)-**3e**	48
(*S*)-**1c**		C_6H_{11}	(*S*)-**3f**	56
(*S*)-**1d** $(CH_3)_2CH$	$COOCH_3$	CH_3	(*S*)-**3g**	75
(*S*)-**1d**		$(CH_3)_2CH$	(*S*)-**3h**	78
(*S*)-**1e** CH_2COOCH_3	$COOCH_3$	CH_3	(*S*)-**3i**	80
(*S*)-**1e**		$(CH_3)_2CH$	(*S*)-**3j**	72
(*S*)-**1f** C_6H_5	COOH	CH_3	(*S*)-**3k**	61
(*S*)-**1f**		$(CH_3)_2CH$	(*S*)-**3l**	44
(*S*)-**1f**		C_6H_{11}	(*S*)-**3m**	47
(*S*)-**1g** 4-$HOC_6H_4CH_2$	$COOC_2H_5$	CH_3	(*S*)-**3n**	82
(*S*)-**1g**		$(CH_3)_2CH$	(*S*)-**3o**	77
(*S*)-**1g**		C_6H_{11}	(*S*)-**3p**	75
(*S*)-**1h** $(CH_3)_2CH$	CH_2OH	CH_3	(*S*)-**3q**	75
(*S*)-**1h**		$(CH_3)_2CH$	(*S*)-**3r**	76
(*R*)-**1h**		$(CH_3)_2CH$	(*S*)-**3r**	78
(*S*)-**1h**		C_6H_5	(*S*)-**3s**	85
(*R*,*S*)-**1i** CH_3	CH(OH)Ph	CH_3	(*S*)-**3t**	78
(*S*,*R*)-**1i**		$(CH_3)_2CH$	(*S*)-**3u**	85
(*R*,*S*)-**1i**		$(CH_3)_2CH$	(*S*)-**3u**	88
(*S*,*R*)-**1i**		C_6H_{11}	(*S*)-**3v**	81
(*R*,*S*)-**1i**		C_6H_{11}	(*S*)-**3v**	75
(*S*,*R*)-**1i**		C_6H_5	(*S*)-**3w**	75
(*R*,*S*)-**1i**		C_6H_5	(*S*)-**3w**	76
(*S*)-**1j** C_6H_5	CH_3	CH_3	(*S*)-**3x**	90



Scheme 3



The isolated yields of the pyrrole products indicated that both isomers were reacting in the cyclization. For example, isomer **4a** is synthesized by a Grignard reaction starting from 1,3-dichloropropene (Scheme 4).[7e] The reaction of **4a** with (*S*)-**1a** afforded the pyrrole derivative (*S*)-**3a** in 68% yield. We propose therefore that enone **2a** is an essential starting material for the formation of the pyrrole ring and that chloro enones **4a**–**c** isomerize to **2a**–**c** during the ring formation reaction.



Scheme 4

In the case of 2-phenyl-substituted pyrrole derivatives, problems occurred during the synthesis of the corresponding chloro enone. The reaction of allyl chloride with benzoyl chloride in the presence of $AlCl_3$ afforded the chloro enone in very low yield (4–6%, ^{1}H NMR).

For the synthesis of 2-phenyl derivatives of pyrrole, the use of the dibromo compound **9** was suggested. As shown in Scheme 5, the reaction of **5** with **6** afforded the alcohol **7** in 75% yield according to a literature procedure.[8] The bromination of alcohol **7** and subsequent CrO_3-mediated oxidation of dibromo alcohol **8** afforded the desired dibromo compound **9** in 80% yield.

As illustrated in Scheme 5, the reaction of dibromo compound **9** with valinol, (*S*)-**1h**, afforded two different products after separation of the crude product by column chromatography. The major product was identified as the desired 2-phenylpyrrole derivative (*S*)-**3s** (85%). The minor product was obtained in 10% yield and identified as a cyclopropane derivative **10** using ^{1}H and ^{13}C NMR spectroscopy. The cyclopropane ring is assigned as *trans*. For the formation of **10** we propose the following mechanism: The enone **11** can be formed from **9** with Et_3N. It is possible that this compound yields furan derivative **12**, which can then form **13** with **11** *via* the Michael addition reaction. The intramolecular cyclization reaction of **13** in the presence of Et_3N can form **10**. This reaction, which is outlined in Scheme 5, takes 4–6 hours. With interruption of the reaction after 2 hours it is possible to isolate the products **12** and **13** from the reaction mixture. Both products are identified spectroscopically. The formation of the pyrrole ring from **9** should work *via* the formation of enone **11** in the presence of Et_3N. Using a similar reaction norephedrine **1i** is also converted into 2-phenylpyrrole derivatives in good yield (Table 1). In all reactions, **10** was formed as a minor product. The formation of **10** and the direct formation of a cyclopropane derivative with a structure similar to that of **10** from dibromo ketones are still under investigation.

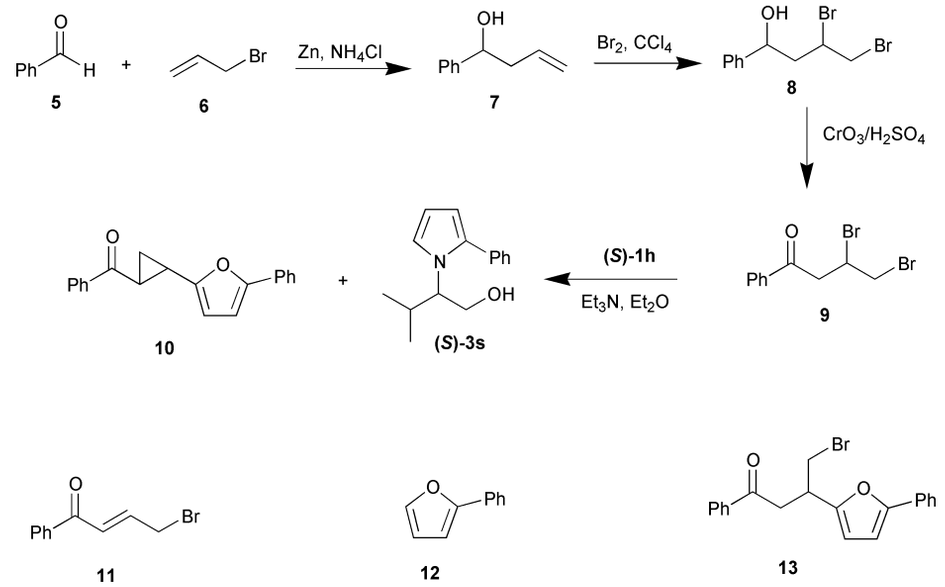
No product formation was observed with **9** with the use of amino acids and their esters. The reactions afforded an undefined mixture of products.

Conclusions

In conclusion, we have developed a new synthetic method for the efficient preparation of 2-substituted pyrroles from halogeno enones and amines, amino alcohols and amino acids. The cyclization works without racemization. It was not possible to synthesize the 2-phenyl-substituted pyrrole derivatives of amino acids and esters by this method. The synthesis of 2-phenylpyrrole derivatives works only with amino alcohols. This reaction also yields a cyclopropane derivative *via* the formation of the phenylfuran, Michael additions, and intramolecular cyclopropanation reaction. Furthermore, this methodology can be extended to the synthesis of polyfunctionalized pyrroles and alkaloids.

Experimental

All reagents were of commercial quality and reagent-quality solvents were used without further purification. Optical rotations were measured on a Bellingham and Stanley P-20 polarimeter; $[\alpha]_D$-values are given in units of 10^{-1} deg cm^2 g^{-1}. IR spectra were determined on a Philips model PU9700 spectrometer. ^{1}H NMR spectra were determined on a Bruker 400 MHz FT spectrometer. GLC analyses were carried out on an HP 5890 gas chromatograph. Mass spectra were obtained on



Scheme 5

a VGTrio2 spectrometer at an ionization energy of 70 eV. Halogeno enones **2a**, **2b**, **2c** and **4a** are synthesized according to the literature.[7]

General procedure for amino acid esters

To a stirred solution of amino acid ester (10 mmol) in 5 ml of water and 10 ml of benzene was added 5 ml of triethylamine at room temperature. Then chloro enone (**2a**, **2b**, or **2c**) (10 mmol) in 5 ml of benzene was added and the mixture was refluxed for 4–6 hours. After cooling to room temperature, it was diluted with water and extracted with dichloromethane (3 × 25 ml). The combined extracts were washed with brine (25 ml), dried over $MgSO_4$, and concentrated under reduced pressure. Further purification was performed by flash column chromatography on silica gel.

(−)-Methyl (2*S*)-2-(2-methyl-1*H*-pyrrol-1-yl)propanoate (*S*)-3a. Obtained according to general procedure, by using 1.03 g of *S*-**1a** and 1.18 g of **2a**, as a viscous oil (1.34 g, 80%); R_f 0.64 (1 : 4 EtOAc–hexane); $[a]_D^{22}$ −48.1 (*c* 2 in CH_3OH) (Found: C, 64.77; H, 7.71; N, 8.18. Calc. for $C_9H_{13}NO_2$: C, 64.65; H, 7.84; N, 8.38%); ν_{max} (neat)/cm^{-1} 2995–2850, 1745, 1420, 1295, 1200, 1085; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.70 (3H, d, *J* 7.2, CH_3), 2.25 (3H, s, CH_3), 3.60 (3H, s, OCH_3), 4.80 (1H, q, *J* 7.0, CHN), 5.95 (1H, m, CH), 6.10 (1H, m, CH), 6.75 (1H, m, CH); δ_C (100 MHz; $CDCl_3$; Me_4Si) 12.5 (q), 18.6 (q), 53.2 (q), 54.3 (d), 108.3 (d), 108.6 (d), 118.0 (d), 129.8 (s), 173.3 (s).

(−)-Methyl (2*S*)-2-(2-isopropyl-1*H*-pyrrol-1-yl)propanoate (*S*)-3b. Obtained according to general procedure, by using 1.03 g of *S*-**1a** and 1.46 g of **2b**, as a viscous oil (1.48 g, 76%); R_f 0.66 (1 : 5 EtOAc–hexane); $[a]_D^{22}$ −15.2 (*c* 0.7 in CH_3OH) (Found: C, 67.51; H, 8.52; N, 6.92. Calc. for $C_{11}H_{17}NO_2$: C, 67.66; H, 8.78; N, 7.17%); ν_{max} (neat)/cm^{-1} 3025–2875, 1750, 1475, 1356, 1340, 1276; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.06 (3H, d, *J* 6.8, CH_3), 1.15 (3H, d, *J* 6.8, CH_3), 1.60 (3H, d, *J* 7.1, CH_3), 2.73 (1H, m, CH), 3.62 (3H, s, OCH_3), 4.74 (1H, q, *J* 7.0, CHN), 5.78 (1H, d, *J* 1.8, CH), 5.99 (1H, d, *J* 3.2, CH), 6.56 (1H, d, *J* 1.8, CH); δ_C (100 MHz; $CDCl_3$; Me_4Si) 18.5 (q), 19.1 (q), 21.3 (q), 23.9 (d), 52.6 (q), 53.1 (d), 103.8 (d), 108.2 (d), 117.5 (d), 130.1 (s), 172.1 (s).

(+)-Methyl (2*S*)-2-(2-cyclohexyl-1*H*-pyrrol-1-yl)propanoate (*S*)-3c. Obtained according to general procedure, by using 1.03 g of *S*-**1a** and 1.86 g of **2c**, as a yellow solid (1.6 g, 72%), mp 118–120 °C; R_f 0.25 (1 : 10 diethyl ether–hexane); $[a]_D^{22}$ 23.5 (*c* 0.5 in CH_3OH) (Found: C, 71.16; H, 8.67; N, 5.73. Calc. for $C_{14}H_{21}NO_2$: C, 71.46; H, 8.99; N, 5.95%); ν_{max} (neat)/cm^{-1} 3050–2860, 1730, 1410, 1340, 1213; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.18–1.32 (10H, m, CH_2), 1.61 (3H, d, *J* 7.2, CH_3), 2.60–2.71 (1H, m, CH), 3.65 (3H, s, OCH_3), 4.72 (1H, q, *J* 7.2, CHN), 5.76 (1H, d, *J* 1.5, CH), 6.00 (1H, t, *J* 3.2, CH), 6.56 (1H, d, *J* 1.8, CH); δ_C (100 MHz; $CDCl_3$; Me_4Si) 19.3 (q), 26.3 (t), 27.2 (t), 30.2 (t), 33.9 (d), 52.9 (q), 53.8 (d), 104.2 (d), 108.3 (d), 117.3 (d), 134.5 (s), 173.0 (s).

(−)-Methyl (2*S*)-3-methyl-2-(2-methyl-1*H*-pyrrol-1-yl)butanoate (*S*)-3g. Obtained according to general procedure, by using 1.31 g of *S*-**1d** and 1.18 g of **2a**, as a colorless oil (1.46 g, 75%), R_f 0.58 (1 : 4 EtOAc–hexane); $[a]_D^{22}$ −50.1 (*c* 4 in CH_3OH) (Found: C, 67.86; H, 8.61; N, 6.98. Calc. for $C_{11}H_{17}NO_2$: C, 67.66; H, 8.78; N, 7.17%); ν_{max} (neat)/cm^{-1} 3050–2850, 1765, 1530, 1470, 1345; δ_H (400 MHz; $CDCl_3$; Me_4Si) 0.78 (3H, d, *J* 6.5, CH_3), 1.07 (3H, d, *J* 6.7, CH_3), 2.28 (3H, s, CH_3), 2.48 (1H, m, CH), 3.75 (3H, s, OCH_3), 4.20 (1H, d, *J* 10.4, CHN), 5.88 (1H, s, CH), 6.12 (1H, m, CH), 6.85 (1H, d, *J* 2.3, CH); δ_C (100 MHz; $CDCl_3$; Me_4Si) 12.7 (q), 19.3 (q), 20.1 (q), 32.4 (d), 52.8 (d), 65.4 (q), 107.6 (d), 108.8 (d), 118.9 (d), 130.1 (s), 172.4 (s).

(−)-Methyl (2*S*)-2-(2-isopropyl-1*H*-pyrrol-1-yl)-3-methylbutanoate (*S*)-3h. Obtained according to general procedure, by using 1.31 g of *S*-**1d** and 1.46 g of **2b**, as a colorless oil (1.74 g, 78%), R_f 0.59 (1 : 4 EtOAc–hexane); $[a]_D^{22}$ −6.6 (*c* 0.3 in $CHCl_3$) (Found: C, 69.78; H, 9.22; N, 6.05. Calc. for $C_{13}H_{21}NO_2$: C, 69.92; H, 9.48; N, 6.27%); ν_{max} (neat)/cm^{-1} 2980–2820, 1745, 1475, 1350, 1295; δ_H (400 MHz; $CDCl_3$; Me_4Si) 0.63 (3H, d, *J* 6.7, CH_3), 0.94 (3H, d, *J* 6.6, CH_3), 1.14 (3H, d, *J* 6.8, CH_3), 1.18 (3H, d, *J* 6.8, CH_3), 2.35 (1H, dqq, *J* 10.8, 6.6, 6.7, CH), 2.78 (1H, m, CH), 3.63 (3H, s, OCH_3), 4.12 (1H, d, *J* 10.8, CHN), 5.75 (1H, dd, *J* 1.6, 0.7, CH), 5.97 (1H, t, *J* 1.6, CH), 6.68 (1H, dd, *J* 1.6, 0.7, CH); δ_C (100 MHz; $CDCl_3$; Me_4Si) 19.2 (q), 20.1 (q), 23.4 (q), 24.1 (q), 25.7 (d), 32.6 (d), 52.4 (q), 64.5 (d), 103.5 (d), 108.2 (d), 117.9 (d), 140.1 (s), 171.2 (s).

(−)-Dimethyl (2*S*)-2-(2-methyl-1*H*-pyrrol-1-yl)butanedioate (*S*)-3i. Obtained according to general procedure, by using 1.61 g of *S*-**1e** and 1.18 g of **2a**, as a viscous oil (1.80 g, 80%), R_f 0.45 (1 : 4 EtOAc–hexane); $[a]_D^{22}$ −48.1 (*c* 2 in CH_3OH) (Found: C, 58.46; H, 6.77; N, 6.43. Calc. for $C_{11}H_{15}NO_4$: C, 58.66; H, 6.71; N, 6.22%); ν_{max} (neat)/cm^{-1} 2990–2850, 1745, 1740, 1570, 1345, 1224; δ_H (400 MHz; $CDCl_3$; Me_4Si) 2.20 (3H, s, CH_3), 2.92 (1H, dd, *J* 15.7, 6.9, diastereotopic proton of CH_2), 3.30 (1H, dd,

J 15.7, 7.9, diastereotopic proton of CH_2), 3.70 (3H, s, OCH_3), 3.74 (3H, s, OCH_3), 5.18 (1H, t, *J* 7.4, CHN), 5.90 (1H, s, CH), 6.11 (1H, t, *J* 3.2, CH), 6.61 (1H, s, CH); δ_C (100 MHz; $CDCl_3$; Me_4Si) 12.4 (q), 37.7 (t), 52.8 (q), 53.5 (q), 54.9 (d), 108.3 (d), 109.6 (d), 118.5 (d), 130.2 (s), 171.6 (s), 171.8 (s).

(−)-Dimethyl(2*S*)-2-(2-isopropyl-1*H*-pyrrol-1-yl)butanedioate (*S*)-3j. Obtained according to general procedure, by using 1.61 g of *S*-**1e** and 1.46 g of **2b**, as a viscous oil (1.82 g, 72%), R_f 0.5 (1 : 3 EtOAc–hexane); $[a]_D^{22}$ −17.66 (*c* 0.1 in $CHCl_3$) (Found: C, 61.28; H, 7.52; N, 5.33. Calc. for $C_{13}H_{19}NO_4$: C, 61.64; H, 7.56; N, 5.53%); ν_{max} (neat)/cm^{-1} 3025–2890, 1740, 1730, 1520, 1346, 1225; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.18 (3H, d, *J* 6.8, CH_3), 1.21 (3H, d, *J* 6.8, CH_3), 2.70–2.76 (1H, m, diastereotopic proton of CH_2), 2.85–2.92 (1H, m, CH), 3.19–3.25 (1H, m, diastereotopic proton of CH_2), 3.63 (3H, s, OCH_3), 3.67 (3H, s, OCH_3), 5.09–5.13 (1H, m, CHN), 5.79 (1H, s, CH), 5.99 (1H, m, CH), 6.44 (1H, s, CH); δ_C (100 MHz; $CDCl_3$; Me_4Si) 16.1 (q), 23.6 (q), 25.6 (d), 37.9 (t), 52.3 (d), 53.1 (q), 53.9 (q), 104.1 (d), 109.1 (d), 117.4 (d), 140.2 (s), 170.5 (s), 170.6 (s).

(−)-Ethyl (2*S*)-3-(4-hydroxyphenyl)-2-(2-methyl-1*H*-pyrrol-1-yl)propanoate (*S*)-3n. Obtained according to general procedure, by using 2.09 g of *S*-**1g** and 1.18 g of **2a**, as a white solid (2.24 g, 82%), mp 128–130 °C; R_f 0.52 (1 : 3 EtOAc–hexane); $[a]_D^{22}$ −37.80 (*c* 0.6 in CH_3OH) (Found: C, 70.11; H, 6.91; N, 5.36. Calc. for $C_{16}H_{19}NO_3$: C, 70.31; H, 7.01; N, 5.12%); ν_{max} (neat)/cm^{-1} 3460, 3040–2850, 1735, 1580, 1550, 1435, 1285; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.13 (3H, t, *J* 3.8, CH_3), 1.86 (3H, s, CH_3), 2.99 (1H, m, diastereotopic proton of CH_2), 3.20 (1H, dd, diastereotopic proton of CH_2), 4.06 (2H, q, *J* 3.8, CH_2), 4.57 (1H, m, CHN), 5.67 (1H, d, *J* 1.7, CH), 5.97 (1H, t, *J* 3.1, CH), 6.53 (2H, d, *J* 8.4, Ar-H), 6.70 (2H, d, *J* 8.3, Ar-H), 6.72 (1H, br s, CH); δ_C (100 MHz; $CDCl_3$; Me_4Si) 14.5 (q), 21.4 (q), 39.0 (t), 60.5 (d), 61.9 (t), 96.6 (d), 108.5 (d), 115.8 (d), 117.8 (d), 128.6 (d), 129.2 (s), 130.5 (s), 155.3 (s), 171.8 (s).

(−)-Ethyl (2*S*)-3-(4-hydroxyphenyl)-2-(2-isopropyl-1*H*-pyrrol-1-yl)propanoate (*S*)-3o. Obtained according to general procedure, by using 2.09 g of *S*-**1g** and 1.46 g of **2b**, as a viscous oil (2.32 g, 77%), R_f 0.41 (1 : 3 EtOAc–hexane); $[a]_D^{22}$ −25.77 (*c* 0.6 in $CHCl_3$); ν_{max} (neat)/cm^{-1} 3550, 3025–2870, 1735, 1590, 1478, 1325, 1272 (Found: C, 71.51; H, 7.51; N, 4.48. Calc. for $C_{18}H_{23}NO_3$: C, 71.73; H, 7.69; N, 4.65%); δ_H (400 MHz; $CDCl_3$; Me_4Si) 0.87 (3H, d, *J* 6.6, CH_3), 1.06 (3H, d, *J* 6.5, CH_3), 1.11 (3H, t, *J* 3.9, CH_3), 2.42–2.48 (1H, m, CH), 3.01–3.06 (1H, m, diastereotopic proton of CH_2), 3.19–3.24 (1H, m, diastereotopic proton of CH_2), 4.06 (2H, q, *J* 4.0, OCH_2), 4.62–4.66 (1H, m, CHN), 5.71 (1H, m, CH), 6.03 (1H, m, CH), 6.53 (2H, d, *J* 8.1, Ar-H), 6.71 (2H, d, *J* 8.2, Ar-H), 6.75 (1H, m, CH); δ_C (100 MHz; $CDCl_3$; Me_4Si) 14.4 (q), 23.2 (q), 23.7 (q), 25.5 (d), 39.3 (t), 59.9 (d), 61.9 (t), 103.5 (d), 108.6 (d), 115.8 (d), 117.7 (d), 128.7 (d), 130.6 (s), 140.6 (s), 155.3 (s), 173.0 (s).

(+)-Ethyl (2*S*)-2-(2-cyclohexyl-1*H*-pyrrol-1-yl)-3-(4-hydroxyphenyl)propanoate (*S*)-3p. Obtained according to general procedure, by using 2.09 g of *S*-**1g** and 1.86 g of **2c**, as a white solid (2.55 g, 75%), mp 145–148 °C; R_f 0.52 (1 : 3 EtOAc–hexane); $[a]_D^{22}$ 34.6 (*c* 0.8 in CH_3OH) (Found: C, 73.61; H, 7.66; N, 4.31. Calc. for $C_{21}H_{27}NO_3$: C, 73.87; H, 7.97; N, 4.10%); ν_{max} (neat)/cm^{-1} 3480, 3030–2860, 1735, 1570, 1470, 1254; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.15 (3H, t, *J* 3.1, CH_3), 1.21–1.34 (10H, m, CH_2), 2.30–2.41 (1H, m, CH), 2.99 (1H, m, diastereotopic proton of CH_2), 3.20 (1H, m, diastereotopic proton of CH_2), 4.06 (2H, q, *J* 3.8, CH_2), 4.57 (1H, t, *J* 8.3, CHN), 5.65 (1H, d, *J* 1.7, CH), 5.98 (1H, t, *J* 3.0, CH), 6.53 (2H, d, *J* 8.4, Ar-H), 6.70 (2H, d, *J* 8.3, Ar-H), 6.72 (1H, d, *J* 3.1, CH); δ_C (100 MHz; $CDCl_3$; Me_4Si) 21.4 (q), 27.3 (t), 28.3 (t), 30.2 (t), 33.9 (d), 39.0 (t), 60.5 (d), 61.9 (t), 96.6 (d), 108.5 (d), 115.8 (d), 117.8 (d), 128.6 (d), 129.2 (s), 130.5 (s), 155.4 (s), 171.8 (s).

General procedure for amino acids

To a stirred solution of amino acid (10 mmol) in 5 ml of water and 10 ml of benzene at room temperature was added 5 ml of triethylamine. Then a chloro enone **(2a, 2b, 2c)** (10 mmol) in 5 ml of benzene was added and the mixture was refluxed for 4–6 hours. After cooling to room temperature, it was diluted with water and extracted with dichloromethane (3 × 25 ml). The combined extracts were washed with brine (25 ml), dried over $MgSO_4$, and concentrated under reduced pressure. Further purification was performed by flash column chromatography on silica gel.

(+)-(2*S*)-2-(2-Isopropyl-1*H*-pyrrol-1-yl)propanoic acid (*S*)-3d. Obtained according to general procedure, by using 0.89 g of *S*-**1b** and 1.46 g of **2b**, as a viscous oil (0.94 g, 52%), R_f 0.38 (1 : 1 : 3 EtOAc–MeOH–hexane); $[a]_D^{22}$ 23.5 (*c* 0.5 in $CHCl_3$) (Found: C, 66.43; H, 8.11; N, 7.89. Calc. for $C_{10}H_{15}NO_2$: C, 66.27; H, 8.34; N, 7.73%); ν_{max} (neat)/cm^{-1} 3335–2860, 1725, 1540, 1285, 1225; δ_H (400 MHz; $CDCl_3$; Me_4Si) 0.91–1.21 (9H, br d, CH_3), 2.85–2.92 (1H, m, CH), 4.33–4.42 (1H, m, CHN), 5.79 (1H, s, CH), 5.99 (1H, m, CH), 6.44 (1H, s, CH); δ_C (100 MHz; $CDCl_3$; Me_4Si) 19.5 (q), 23.2 (q), 23.9 (q), 25.6 (d), 55.1 (d), 102.8 (d), 107.9 (d), 120.2 (d), 140.2 (s), 180.0 (s).

(−)-(2*S*)-3-Methyl-2-(2-methyl-1*H*-pyrrol-1-yl)butanoic acid (*S*)-3e. Obtained according to general procedure, by using 1.17 g of *S*-**1c** and 1.18 g of **2a**, as a viscous oil (0.86 g, 48%), R_f 0.43 (1 : 1 : 1 EtOAc–MeOH–hexane); $[a]_D^{22}$ −22.1 (*c* 0.5 in $CHCl_3$) (Found: C, 66.47; H, 8.52; N, 7.91. Calc. for $C_{10}H_{15}NO_2$: C, 66.27; H, 8.34; N, 7.73%); ν_{max} (neat)/cm^{-1} 3345, 3030–2880, 1730, 1490, 1385, 1220; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.24 (6H, br d, CH_3), 2.05 (3H, s, CH_3), 2.21 (1H, m, CH), 3.96 (1H, m, CHN), 5.72 (1H, s, CH), 5.80 (1H, m, CH), 6.60 (1H, s, CH); δ_C (100 MHz; $CDCl_3$; Me_4Si) 12.2 (q), 18.7 (q), 21.3 (q), 24.6 (d), 59.6 (d), 105.6 (d), 107.4 (d), 117.9 (s), 128.4 (d), 173.0 (s).

(+)-(2*S*)-2-(2-Cyclohexyl-1*H*-pyrrol-1-yl)-3-methylbutanoic acid (*S*)-3f. Obtained according to general procedure, by using 1.17 g of *S*-**1c** and 1.86 g of **2c**, as a colorless solid (1.39 g, 56%), R_f 0.38 (1 : 2 : 1 EtOAc–hexane–MeOH); mp > 250 °C; $[a]_D^{22}$ 23.5 (*c* 0.5 in CH_3OH) (Found: C, 72.46; H, 9.11; N, 5.91. Calc. for $C_{15}H_{23}NO_2$: C, 72.25; H, 9.30; N, 5.62%); ν_{max} (neat)/cm^{-1} 3340, 3025–2870, 1730, 1578, 1345, 1213; δ_H (400 MHz; $CDCl_3$, Me_4Si) 0.68 (3H, d, *J* 6.7, CH_3), 1.03 (3H, d, *J* 6.5, CH_3), 1.16–1.96 (11H, m, CH + CH_2), 2.34–2.39 (1H, m, CH), 4.12 (1H, d, *J* 10.6, CHN), 5.76 (1H, d, *J* 1.9, CH), 6.00 (1H, t, *J* 3.2, CH), 6.66 (1H, d, *J* 1.8, CH); δ_C (100 MHz; $CDCl_3$; Me_4Si) 19.2 (q), 20.1 (q), 25.7 (t), 26.6 (t), 27.1 (t), 27.2 (d), 30.1 (d), 55.1 (d), 104.1 (d), 108.6 (d), 117.6 (d), 139.8 (s), 169.5 (s).

(−)-(2*S*)-2-(2-Methyl-1*H*-pyrrol-1-yl)-2-phenylethanoic acid (*S*)-3k. Obtained according to general procedure, by using 1.51 g of *S*-**1f** and 1.18 g of **2a**, as a semisolid (1.31 g, 61%), R_f 0.45 (1 : 1 : 1 EtOAc–MeOH–hexane); $[a]_D^{22}$ −24.3 (*c* 0.5 in $CHCl_3$) (Found: C, 72.43; H, 6.21; N, 6.72. Calc. for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09; N, 6.51%); ν_{max} (neat)/cm^{-1} 3360, 3025–2855, 1740, 1600, 1425, 1356, 1205; δ_H (400 MHz; $CDCl_3$; Me_4Si) 2.11 (3H, s, CH_3), 4.00 (1H, s, CHN), 5.50 (1H, br s, CH), 5.80 (1H, m, CH), 6.30 (1H, s, CH), 7.00–7.25 (5H, br s, Ar-H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 8.7 (q), 60.4 (d), 104.3 (d), 106.5 (s), 107.4 (d), 118.7 (d), 126.3 (d), 127.9 (d), 128.2 (d), 136.2 (s), 175.8 (s).

(−)-(2S)-2-(2-Isopropyl-1*H*-pyrrol-1-yl)-2-phenylethanoic acid (*S*)-3l. Obtained according to general procedure, by using 1.51 g of *S*-**1f** and 1.46 g of **2b**, as a semisolid (1.06 g, 44%), R_f 0.71 (1 : 1 : 1 EtOAc–MeOH–hexane); $[a]_D^{22}$ −27.5 (*c* 0.5 in $CHCl_3$) (Found: C, 74.21; H, 6.89; N, 5.97. Calc. for $C_{15}H_{17}NO_2$: C, 74.05; H, 7.04; N, 5.76%); ν_{max} (neat)/cm^{-1} 3355,

3030–2870, 1745, 1570, 1490, 1465, 1302, 1223; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.28 (6H, d, *J* 6.8, CH_3), 3.12–3.25 (1H, m, CH), 5.68 (1H, s, CH), 5.85 (1H, s, CHN), 5.98 (1H, m, CH), 6.42 (1H, s, CH), 7.00–7.25 (5H, m, Ar-H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 25.2 (q), 25.4 (q), 25.9 (d), 63.0 (d), 107.9 (d), 108.7 (d), 121.3 (d), 127.3 (d), 128.9 (d), 129.9 (d), 134.2 (s), 135.0 (s), 178.0 (s).

(+)-(2*S*)-2-(2-Cyclohexyl-1*H*-pyrrol-1-yl)-2-phenylethanoic acid (*S*)-3m. Obtained according to general procedure, by using 1.51 g of *S*-**1f** and 1.86 g of **2c**, as a semisolid (1.33 g, 47%), R_f 0.71 (1 : 1 : 1 EtOAc–hexane–MeOH); $[a]_D^{22}$ 25.8 (*c* 0.5 in $CHCl_3$) (Found: C, 76.12; H, 7.53; N, 4.75. Calc. for $C_{18}H_{21}NO_2$: C, 76.29; H, 7.47; N, 4.94%); ν_{max} (neat)/cm^{-1} 3365, 3025–2875, 1745, 1610, 1505, 1478, 1223, 1025; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.11–1.21 (6H, m, CH_2), 1.52–1.54 (4H, m, CH_2), 2.20–2.41 (1H, m, CH), 5.67 (1H, s, CHN), 5.75 (1H, s, CH), 5.98 (1H, m, CH), 6.42 (1H, s, CH), 7.00–7.20 (5H, m, Ar-H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 26.6 (t), 27.4 (t), 36.9 (t), 37.8 (d), 66.8 (d), 105.6 (d), 108.8 (d), 122.4 (d), 129.7 (d), 130.5 (d), 130.7 (d), 139.3 (s), 140.0 (s), 177.5 (s).

General procedure for amino alcohols

12.5 mmol of amino alcohol, 12.5 mmol of chloro enone **(2a, 2b, 2c** or bromo ketone **9**) and 25 mmol of triethylamine were refluxed in 20 ml of diethyl ether for 5–7 hours. The mixture was cooled to room temperature, diluted with water, and extracted with diethyl ether (3 × 20 ml). The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. Further purification was performed by flash column chromatography on silica gel.

(−)-(2*S*)-3-Methyl-2-(2-methyl-1*H*-pyrrol-1-yl)butan-1-ol (*S*)-3q. Obtained according to general procedure, by using 1.03 g of *S*-**1h** and 1.18 g of **2a**, as a colorless oil (1.25 g, 75%), R_f 0.45 (1 : 4 EtOAc–hexane); $[a]_D^{22}$ −13.2 (*c* 3 in CH_3OH) (Found: C, 71.96; H, 10.41; N; 8.51. Calc. for $C_{10}H_{17}NO$: C, 71.81; H, 10.25; N, 8.37%); ν_{max} (neat)/cm^{-1} 3470, 2980–2850, 1403, 1358, 1278, 1125; δ_H (400 MHz; $CDCl_3$; Me_4Si) 0.70 (3H, d, *J* 6.4, CH_3), 1.00 (3H, d, *J* 6.4, CH_3), 1.90 (1H, m, CH), 2.15 (3H, s, CH_3), 3.65 (1H, m, CH), 3.70 (2H, m, OCH_2), 5.80 (1H, m, CH), 6.10 (1H, m, CH), 6.55 (1H, m, CH); δ_C (100 MHz; $CDCl_3$; Me_4Si) 13.0 (q), 19.5 (q), 20.3 (q), 31.8 (d), 64.7 (d), 65.0 (t), 107.0 (d), 108.8 (d), 116.9 (d), 131.1 (s).

(−)-(2*S*)-2-(2-Isopropyl-1*H*-pyrrol-1-yl)-3-methylbutan-1-ol (*S*)-3r and (+)-(2*R*)-2-(2-isopropyl-1*H*-pyrrol-1-yl)-3-methylbutan-1-ol (*R*)-3r. Obtained according to general procedure, by using 1.03 g of *S*-**1h** and *R*-**1h** with 1.46 g of **2b**, as viscous oils (1.48 g, 76%) and (1.52 g, 78%) respectively, R_f 0.49 (1 : 3 EtOAc–hexane); $[\alpha]_D^{22}$ −27.54 (*c* 0.07 in $CHCl_3$) for *S*-**3r**, $[\alpha]_D^{22}$ 27.5 (*c* 0.07 in $CHCl_3$) for *R*-**3r** (Found: C, 73.96; H, 10.68; N, 6.92. Calc. for $C_{12}H_{21}NO$: C, 73.80; H, 10.84; N, 7.17%); ν_{max} (neat)/cm^{-1} 3485, 3015–2880, 1302, 1278, 1025; δ_H (400 MHz; $CDCl_3$; Me_4Si) 0.63 (3H, d, *J* 6.7, CH_3), 0.97 (3H, d, *J* 6.6, CH_3), 1.16 (3H, d, *J* 7.3, CH_3), 1.20 (3H, d, *J* 7.3, CH_3), 1.45–1.54 (1H, m, OH), 1.87–1.94 (1H, m, CH), 2.78–2.85 (1H, m, CH), 3.62–3.66 (2H, m, OCH_2), 3.76–3.80 (1H, m, CH), 5.77 (1H, d, *J* 1.6, CH), 5.99–6.01 (1H, m, CH), 6.47 (1H, s, CH); δ_C (100 MHz; $CDCl_3$; Me_4Si) 12.5 (q), 18.1 (q), 21.4 (q), 22.2 (q), 23.5 (d), 29.5 (d), 61.4 (d), 62.6 (t), 100.9 (d), 106.4 (d), 113.4 (d), 139.6 (s).

(−)-(2*S*)-3-Methyl-2-(2-phenyl-1*H*-pyrrol-1-yl)butan-1-ol (*S*)-3s. Obtained according to general procedure, by using 1.03 g of *S*-**1h** and 3.05 g of **9**, as a viscous oil (1.94 g, 85%), R_f 0.53 (1 : 3 EtOAc–hexane); $[a]_D^{22}$ −49.2 (*c* 0.3 in CH_3OH) (Found: C, 78.36; H, 8.09; N, 6.38. Calc.for $C_{15}H_{19}NO$: C 78.56; H, 8.35; N, 6.11%); ν_{max} (neat)/cm^{-1} 3490, 3025–2880, 1570, 1402, 1356, 1278, 1085; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.17 (3H, d, *J* 7.1, CH_3), 1.21 (3H, d, *J* 7.0, CH_3), 2.30 (1H, m, CH), 3.67 (2H, m, CH_2), 3.97 (1H, m, CH), 6.15 (1H, t, *J* 1.8, CH), 6.21 (1H, t, *J* 3.2, CH), 6.78 (1H, t, *J* 1.7, CH), 7.15–7.42 (5H, m, Ar-H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 22.5 (q), 24.2 (q), 25.8 (d), 54.5 (d), 64.3 (t), 108.5 (d), 108.8 (d), 118.8 (d), 125.8 (s), 127.0 (d), 127.1 (d), 127.5 (d), 128.3 (s).

(+)-(1*R*,2*S*)-2-(2-Methyl-1*H*-pyrrol-1-yl)-1-phenylpropan-1-ol (*R*,*S*)-3t. Obtained according to general procedure, by using 1.51 g of (*R*,*S*)-**1i** and 1.18 g of **2a**, as a white solid (1.67 g, 78%), R_f 0.45 (1 : 3 EtOAc–hexane); mp 55–56 °C; $[a]_D^{22}$ 52.6 (*c* 4 in EtOH) (Found: C, 78,32; H, 7.77; N, 6.34. Calc. for $C_{14}H_{17}NO$: C, 78.10; H, 7.96; N, 6.51%); ν_{max} (neat)/cm^{-1} 3510, 3010–2850, 1560, 1510, 1490, 1325, 1267, 1123; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.37 (3H, d, *J* 6.9, CH_3), 2.06 (3H, s, CH_3), 2.19 (1H, s, OH), 4.28 (1H, m, CH), 4.82 (1H, d, *J* 5.2, CH), 5.83 (1H, s, CH), 6.12 (1H, t, *J* 2.7, CH), 6.80 (1H, s, CH), 7.20–7.40 (5H, m, Ar-H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 12.5 (q), 15.6 (q), 57.6 (d), 77.6 (d), 107.5 (d), 108.2 (d), 117.9 (d), 126.9 (d), 128.9 (d), 129.5 (s), 129.6 (d), 142.5 (s).

(+)-(1*R*,2*S*)-2-(2-Isopropyl-1*H*-pyrrol-1-yl)-1-phenylpropan-1-ol (*R*,*S*)-3u and (−)-(1*S*,2*R*)-2-(2-isopropyl-1*H*-pyrrol-1-yl)-1-phenylpropan-1-ol (*S*,*R*)-3u. Obtained according to general procedure, by using 1.51 g of (*R*,*S*)-**1i** and (*S*,*R*)-**1i** with 1.46 g of **2b**, as crystals (2.13 g, 88%) and (2.06 g, 85%) respectively; mp 64–65 °C; R_f 0.49 (1 : 3 EtOAc–hexane); $[a]_D^{22}$ 21.45 (*c* 0.3 in $CHCl_3$) for (*R*,*S*)-**3u**, $[a]_D^{22}$ −21.15 (*c* 0.3 in $CHCl_3$) for (*S*,*R*)-**3u** (Found: C, 79.16; H, 8.58; N, 5.98. Calc. for $C_{16}H_{21}NO$: C, 78.97; H, 8.70; N, 5.76%); ν_{max} (neat)/cm^{-1} 3505, 3020–2880, 1590, 1458, 1324, 1301, 1278, 1078; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.06 (3H, d, *J* 6.8, CH_3), 1.11 (3H, d, *J* 6.8, CH_3), 1.49 (3H, d, *J* 6.8, CH_3), 2.05 (1H, br s, OH), 2.58–2.64 (1H, m, CH), 4.26–4.33 (1H, m, CHN), 4.82 (1H, d, *J* 5.5, CH), 5.81 (1H, d, *J* 3.1, CH), 6.12 (1H, dd, *J* 3.1, CH), 6.82 (1H, d, *J* 2.3, CH), 7.19–7.36 (5H, m, Ar-H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 15.8 (q), 22.2 (q), 24.6 (q), 25.4 (d), 56.3 (d), 77.6 (d), 102.8 (d), 107.5 (d), 116.6 (d), 125.7 (d), 127.7 (d), 128.3 (d), 139.6 (s), 141.5 (s).

(+)-(1*R*,2*S*)-2-(2-Cyclohexyl-1*H*-pyrrol-1-yl)-1-phenylpropan-1-ol (*R*,*S*)-3v and (−)-(1*S*,2*R*)-2-(2-cyclohexyl-1*H*-pyrrol-1-yl)-1-phenylpropan-1-ol (*S*,*R*)-3v. Obtained according to general procedure, by using 1.51 g of (*R*,*S*)-**1i** and (*S*,*R*)-**1i** with 1.86 g of **2c**, as viscous oils (2.12 g, 75%) and (2.29 g, 81%) respectively; R_f 0.6 (1 : 2 EtOAc–hexane); $[a]_D^{22}$ 15.62 (*c* 1.7 in $CHCl_3$) for (*R*,*S*)-**3v**, $[a]_D^{22}$ −15.83 (*c* 1.7 in $CHCl_3$) for (*S*,*R*)-**3v** (Found: C, 80.71; H, 8.65; N, 5.23. Calc. for $C_{19}H_{25}NO$: C, 80.52; H, 8.89; N, 4.94%); ν_{max} (neat)/cm^{-1} 3495, 3030–2850, 1560, 1523, 1402, 1325, 1208, 1027, 743; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.04–1.75 (10H, m, CH_2), 1.41 (3H, d, *J* 6.9, CH_3), 1.92 (1H, s, OH), 2.30–2.41 (1H, m, CH), 4.30 (1H, m, CH-N), 4.69 (1H, d, *J* 5.5, CH), 5.64 (1H, d, *J* 1.5, CH), 5.98 (1H, t, *J* 3.1, CH), 6.66 (1H, d, *J* 2.5, CH), 7.07–7.21 (5H, m, Ar-H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 16.1 (q), 26.6 (t), 27.3 (t), 27.4 (t), 32.3 (d), 54.5 (d), 80.0 (d), 103.6 (d), 107.9 (d), 116.7 (d), 126.0 (d), 128.0 (d), 128.6 (d), 134.1 (s), 139.3 (s).

(+)-(1*R*,2*S*)-1-Phenyl-2-(2-phenyl-1*H*-pyrrol-1-yl)-propan-1-ol (*R*,*S*)-3w and (−)-(1*S*,2*R*)-1-phenyl-2-(2-phenyl-1*H*-pyrrol-1-yl)propan-1-ol (*S*,*R*)-3w. Obtained according to general procedure, by using 1.51 g of (*R*,*S*)-**1i** and (*S*,*R*)-**1i** with 3.05 g of **9**, as viscous oils (2.10 g, 76%) and (2.07 g, 75%) respectively, R_f 0.57 (1 : 2 EtOAc–hexane); $[a]_D^{22}$ 6.36 (*c* 0.072 in $CHCl_3$) for (*R*,*S*)-**3w**, $[a]_D^{22}$ −5.4 (*c* 0.09 in $CHCl_3$) for (*S*,*R*)-**3w** (Found: C, 82.44; H, 6.72; N, 4.78. Calc. for $C_{19}H_{19}NO$: C, 82.28; H, 6.90; N, 5.05%); ν_{max} (neat)/cm^{-1} 3485, 3020–2860, 1595, 1502, 1489, 1452, 1321, 1208, 749; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.40 (3H, d, *J* 6.8, CH_3), 2.11 (1H, br s, OH), 4.37–4.44 (1H, m, CH), 4.53 (1H, d, *J* 4.7, CH), 5.97 (1H, d, *J* 3.2, CH), 6.11 (1H, t, *J* 1.9, CH), 6.80 (1H, d, *J* 3.4, CH), 7.03–7.30 (10H, m, Ar-H); δ_C (100

MHz; $CDCl_3$; Me_4Si) 15.3 (q), 57.4 (d), 86.7 (d), 108.7 (d), 109.3 (d), 119.1 (d), 126.0 (s), 127.5 (d), 127.9 (d), 128.6 (d), 128.7 (d), 130.1 (s), 134.1 (d), 134.9 (s), 141.7 (d).

(−)-2-Methyl-1[(1*S*)-1-phenylethyl]-1*H*-pyrrole (*S*)-3x. Obtained according to general procedure, by using 1.21 g of *S*-**1j** and 1.18 g of **2a**, as crystals (1.66 g, 90%), R_f 0.45 (1 : 3 EtOAc–hexane); mp 52 °C; $[\alpha]_D^{22}$ −16.7 (*c* 1 in CH_3OH) (Found: C, 84.38; H, 8.33; N, 7.56. Calc. for $C_{13}H_{15}N$: C, 84.28; H, 8.16; N, 7.56%); ν_{max} (neat)/cm^{-1} 3040–2870, 1580, 1425, 1365, 1203, 1102; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.84 (3H, d, *J* 7.1, CH_3), 2.13 (3H, s, CH_3), 5.30 (1H, q, *J* 7.1, CH), 5.96 (1H, br s, CH), 6.17 (1H, m, CH), 6.83 (1H, br s, CH), 7.00–7.05 (2H, m, Ar-H), 7.20–7.35 (3H, m, Ar-H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 12.7 (q), 22.9 (q), 55.7 (d), 107.8 (d), 108.1 (d), 118.1 (d), 126.8 (s), 127.1 (d), 128.3 (d), 133.3 (d), 149.5 (s).

1-Phenylbut-3-en-1-ol 7

To a 100 ml flask charged with Zn (0.12 mol), 25 ml of saturated aq. NH_4Cl and 3 ml of THF, was added a mixture of 14.5 g (0.12 mol) of 3-bromopropene and 10 ml (0.10 mol) of benzaldehyde dropwise. The temperature of the reaction was kept at 30–40 °C for 4 hours. The mixture was stirred for one hour at room temperature. Finally, it was quenched with 10 ml of 7% HCl and 5 ml of saturated NH_4Cl, and the water layer was extracted with diethyl ether (3 × 15 ml). The combined extracts were washed successively with water (2 × 10 ml) and brine (2 × 10 ml), dried over $MgSO_4$, and concentrated under reduced pressure. Further purification of the crude product was achieved by vacuum distillation (bp 81–82 °C, 1 mmHg) (12.52 g, 75%), R_f 0.65 (1 : 4 EtOAc–hexane); δ_H (400 MHz; $CDCl_3$; Me_4Si) 2.45 (2H, t, *J* 6.7, CH_2), 2.77 (1H, s, OH), 4.65 (1H, t, *J* 6.7, CH), 5.04–5.13 (2H, m, CH_2), 5.68–5.81 (1H, m, CH), 7.19–7.26 (5H, m, Ar-H).

3,4-Dibromo-1-phenylbutan-1-ol 8

0.059 Mol of Br_2 in 10 ml of CCl_4 was added dropwise to a solution of 1-phenylbut-3-en-1-ol **7** (0.067 mol) in 25 ml of CCl_4 at 0 °C. After the addition was complete, the mixture was stirred at room temperature for one hour. Then the mixture was evaporated and the product obtained was used in the next step without any further purification (15.43 g, 85%), R_f 0.54 (1 : 4 EtOAc–hexane); δ_H (400 MHz; $CDCl_3$; Me_4Si) 2.23 (2H, m, CH_2), 2.85 (1H, s, OH), 3.83 (2H, m, CH_2), 4.53 (1H, m, CH), 4.86–4.94 (1H, m, CH), 7.24–7.51 (5H, m, Ar-H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 35.8 (t), 46.6 (d), 49.4 (t), 73.4 (d), 128.3 (d), 128.7 (d), 129.2 (s), 129.4 (d).

3,4-Dibromo-1-phenylbutan-1-one 9

3,4-Dibromo-1-phenylbutan-1-ol **8** (0.05 mol) was dissolved in 35 ml of acetone in a 200 ml three-necked flask. CrO_3 (0.17 mol), 6 ml of concentrated H_2SO_4, and 10 ml of distilled water mixture was added dropwise with the temperature kept at 20–25 °C. After the addition was complete, the reaction mixture was stirred for four hours. The layers were separated and the water layer was extracted with diethyl ether (3 × 15 ml). The combined extracts were washed successively with water and brine, dried over $MgSO_4$, and concentrated under reduced pressure. Crystallization of the crude product in diethyl ether–hexane afforded ketone **9** as yellow crystals (mp 38–40 °C) (12.31 g, 80%), R_f 0.48 (1 : 4 EtOAc–hexane); δ_H (400 MHz; $CDCl_3$; Me_4Si) 3.18 (2H, m, CH_2), 4.01–4.04 (2H, m, CH_2), 4.76–4.83 (1H, m, CH), 7.47–7.99 (5H, m, Ar-H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 36.9 (d), 44.9 (t), 45.5 (t), 128.5 (d), 129.9 (d), 134.0 (d), 136.5 (s), 196.1 (s).

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