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Amination/annulation of chlorobutenones with chiral amine compounds: synthesis of 1,2,4-trisubstituted pyrroles

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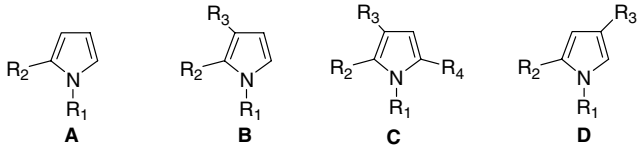
Abstract—A series of 1,2,4-trisubstituted pyrroles have been synthesized in 83–96% yields on treatment of chiral primary amines, amino alcohols and esters of α-amino acids with different chlorobutenones in benzene-triethylamine. The conversions proceed without racemization.

1. Introduction

Pyrrole derivatives represent a class of compounds that are of great importance in heterocyclic chemistry primarily due to the fact that many pyrroles are subunits of natural products, pharmaceutical agents and polymers.[1] The valuable and diverse biological properties of pyrroles lead to the development of efficient methods for the preparation of these compounds, which have a defined substitution pattern, the focus of considerable synthetic effort.

A stereoselective approach to the synthesis of indolizidine alkaloids, based on the reaction of pyrrole derivatives of amino acids, has been reported. The Paal–Knorr synthesis, starting from primary amines and 1,4-dicarbonyl compounds and their masked equivalents such as tetrahydro-2,5-dimethoxyfuran, is often used for the construction of pyrrole rings. During the condensation reaction for the formation of the pyrrole ring with amino acids, partial racemization often occurs.[2] Pyrrole-amino acid *N*-conjugates are effective $^1O_2$ quenchers. Their quenching ability towards $^1O_2$ compares favourably with that of natural antioxidants such as vitamins E and C.[3] Recently, it was shown that 1,2,4-substituted pyrroles are a new class of synthetic hystone deacetylase inhibitors.[4] Although there are quite a number of methods already available for the synthesis of pyrroles,[5] most of them involve multi-step synthetic operations, which lower the overall yield while there are limited reports on the preparation of enantiomers of pyrrole derivatives having **1-N** directly linked to the stereogenic centre.[2] The development of a flexible and selective method for obtaining pyrroles with a variety of substituents is desirable. Herein, we report a convenient route to 1,2-**A**, 1,2,3-**B** and 1,2,3,5-**C** substituted pyrrole rings from amines, amino alcohols and amino acids with simple accessible haloenones.[6] As part of our continued interest in the chemistry of homochiral pyrrole derivatives, we have extended this chemistry to the synthesis of 1,2,4-trisubstituted pyrrole derivatives **D**.



2. Results and discussion

Haloenones are valuable intermediates for the construction of nitrogen heterocycles. Chlorobutenones **2a**–**d** provide a four carbon unit with a carbonyl and halide functionality to form pyrrole rings with primary amines. Chlorobutenones **2a**–**d** were synthesized starting from the corresponding acyl chlorides and 3-chloro-2-methylprop-1-ene in the presence of $AlCl_3$.[7] According to the ^1H NMR spectrum of the crude products, the reaction furnished the chlorobutenones **2a**–**d** as the major products. Isomers **2a′**–**d′** were formed as minor products. The use of silver tetrafluoroborate as a Lewis

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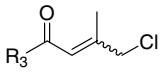
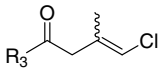
acid[7a] furnished **2a′–d′** as a major product. In both cases, the crude mixtures were used for pyrrole ring formation without further purification.



2a-d



2a'-d'

According to Scheme 1, L-alanine methyl ester (*S*)-**1a** was refluxed with chlorobutenone **2a** in benzene and the reaction monitored by TLC. Purification of the crude product furnished the desired pyrrole derivative (*S*)-**3a** in 83% yield as an oil.

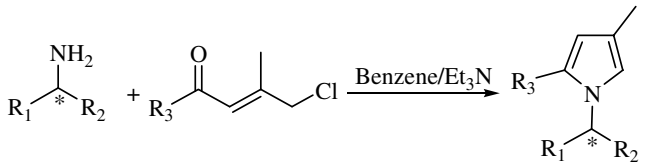
Using the same reaction conditions, different chiral amine compounds were converted to their substituted pyrrole derivatives in 83–96% yields as summarized in Table 1. The products are viscose oil and their spectroscopic data are in full agreement with their structure.

The isolated yields of the pyrrole products indicated that both isomers of chlorobutenones **2a–d** and **2a′–d′** were reacting in the cyclization. We propose therefore that enones **2a–d** are vital starting materials for the formation of the pyrrole ring and that chlorobutenones **2a′–d′** isomerize to **2a–d** during the ring formation reaction.[6b]

As shown in Table 1, comparable yields were obtained with different R^1-, R^2- and R^3-groups, which shows that varying the substituents on nitrogen and chloroenone does not have a large influence on the yield of the products.

The pyrrole derivative of amino acid esters and amino alcohols showed excellent separation properties by chiral HPLC column. Therefore, pyrroles (*S*)-, (*R*)- and *rac*-**3a**, synthesized starting from the corresponding (*S*)-, (*R*)- and *rac*-alanine methyl ester, were analyzed by HPLC using chiral column. The results showed that because of the formation of a pyrrole ring from amino acid esters, no racemization occurs.[8]

The suggested mechanism for the formation of pyrroles **3** is outlined in Scheme 2. It seems reasonable to suggest that the amine reacts initially with the chlorobutenone to form **4** and the cyclization onto the ketone occurs as the ring closing step, followed by elimination of water giving the product **3**.



1a-e **2a-d** **3a-m**

Scheme 1.

3. Conclusion

In conclusion, we have developed a new synthetic method for the efficient preparation of 1,2,4-substituted pyrroles from chlorobutenones and amines, amino alcohols and esters of amino acids. The cyclization works without racemization. Furthermore, this methodology can be extended to the synthesis of polyfunctionalized pyrroles and alkaloids.

4. Experimental

All reagents were of commercial quality and reagent quality solvents were used without further purification. IR spectra were determined on a Philips model PU9700 spectrometer. NMR spectra were recorded on a Bruker DPX 400. Chemical shifts δ are reported in parts per million relative to $CHCl_3$ (^1H: $\delta = 7.27$), $CDCl_3$ (^{13}C: $\delta = 77.0$) and CCl_4 (^{13}C: $\delta = 96.4$) as internal standards. Column chromatography was conducted on silica gel 60 (40–63 μm). TLC was carried out on aluminium sheets precoated with silica gel $60F_{254}$ (Merck), and the spots were visualized with UV light ($\lambda = 254$ nm). Enantiomeric excesses were determined by HPLC analysis using a Thermo Finnigan Surveyor equipped with an appropriate chiral phase column. MS: ThermoQuest Finnigan multi Mass (EI, 70 eV). Optical rotations were measured with a Krüss P3002RS automatic polarimeter. Chlorobutenones **2a–d** are synthesized according to the literature.[7]

4.1. General procedure for pyrrole formation

To a stirred solution of amine or amino acid ester (5 mmol) in 15 ml of benzene was added 3.5 ml of triethylamine at room temperature. Then, chlorobutenone **2a**, **2b**, **2c** or **2d** (5 mmol) was added and the mixture refluxed for 4–6 h. After cooling to room temperature, it was diluted with water and extracted with dichloromethane (3 × 25 ml). 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 neutral aluminium oxide.

4.1.1. (*S*)-2-(2,4-Dimethyl-pyrrol-1-yl)-propionic acid methyl ester (*S*)-3a. Yellow oil (0.75 g, 83%). $[\alpha]_D^{25} = +3.75$ (*c* 0.8, CH_2Cl_2); IR(neat): 2890, 1780, 1470 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 6.39$ (s, 1H), 5.66 (s, 1H), 4.62 (q, $J = 7.3$ Hz, 1H), 3.64 (s, 3H), 2.08 (s, 3H), 1.98 (s, 3H), 1.58 (d, $J = 7.3$ Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$): $\delta = 172.0$, 128.5, 118.2, 115.2, 108.8, 53.3, 52.5, 18.0, 11.93, 11.90. Anal. Calcd for $C_{10}H_{15}NO_2$ (181.23): C, 66.27; H, 8.34; N, 7.73. Found C, 66.54; H, 8.52.

4.1.2. (*R*)-2-(2,4-Dimethyl-pyrrol-1-yl)-propionic acid methyl ester (*R*)-3a. Yellow oil (0.78 g, 86%). $[\alpha]_D^{25} = -3.8$ (*c* 0.8, CH_2Cl_2).

4.1.3. (*R*)-2,4-Dimethyl-1-(1-phenyl-ethyl)-1*H*-pyrrole (*R*)-3b. Yellow oil (0.93 g, 93%). $[\alpha]_D^{25} = -4.2$ (*c* 1.1,

Table 1. The synthesis of 1,2,4-trisubstituted pyrroles

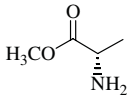
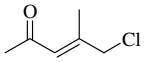
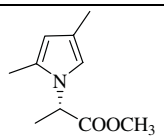
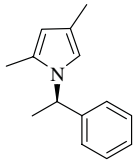
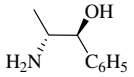
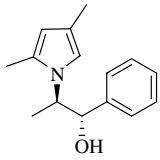
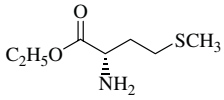
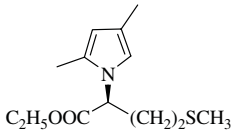
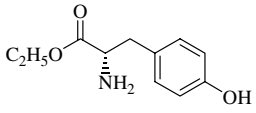
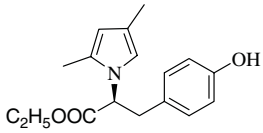
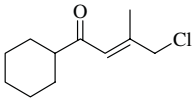
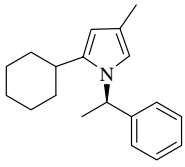
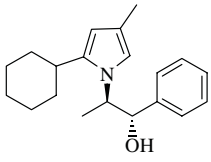
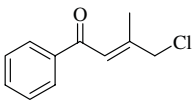
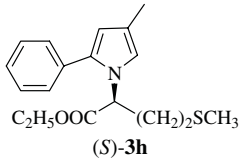
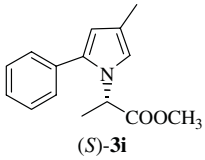
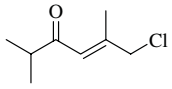
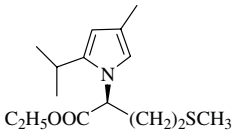
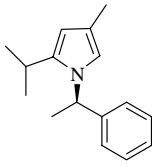
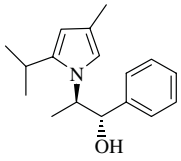
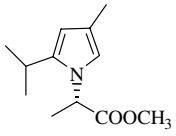
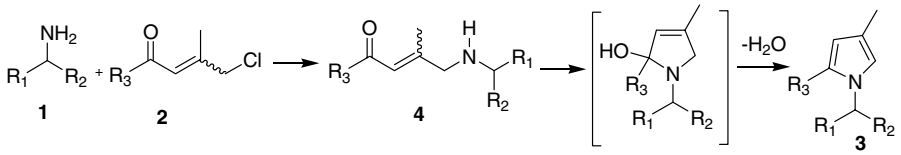
Amine compound **1**	Chlorobutenone **2**	Yield (%)	Pyrrole **3**
 (*S*)-**1a**	 **2a**	83	 (*S*)-**3a**
(*R*)-**1a**	**2a**	86	(*R*)-**3a**
 (*R*)-**1b**	**2a**	93	 (*R*)-**3b**
 (*S*,*R*)-**1c**	**2a**	89	 (*S*,*R*)-**3c**
 (*S*)-**1d**	**2a**	86	 (*S*)-**3d**
 (*S*)-**1e**	**2a**	89	 (*S*)-**3e**
(*R*)-**1b**	 **2b**	90	 (*R*)-**3f**
(*S*,*R*)-**1c**	**2b**	87	 (*S*,*R*)-**3g**
(*S*)-**1d**	 **2c**	86	 (*S*)-**3h**
(*S*)-**1a**	**2c**	87	 (*S*)-**3i**

Table 1 (*continued*)

Amine compound **1**	Chlorobutenone **2**	Yield (%)	Pyrrole **3**
(*S*)-**1d**	 **2d**	91	 (*S*)-**3j**
(*R*)-**1b**	**2d**	95	 (*R*)-**3k**
(*S*,*R*)-**1c**	**2d**	96	 (*S*,*R*)-**3l**
(*S*)-**1a**	**2d**	87	 (*S*)-**3m**



Scheme 2.

$CHCl_3$); IR(neat): 2840, 1540 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 6.39$ (s, 1H), 5.60 (s, 1H), 4.58 (q, $J = 7.2$ Hz, 1H), 3.64 (s, 3H), 2.08 (s, 3H), 1.96 (s, 3H), 1.58 (d, $J = 7.3$ Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$): $\delta = 171.6$, 128.1, 118.1, 114.8, 109.0, 53.2, 52.3, 18.0, 12.0, 11.9. Anal. Calcd for $C_{14}H_{17}N$ (199.2): C, 84.37; H, 8.60; N, 7.03. Found C, 84.12; H, 8.46.

4.1.4. (*S*,*R*)-2-(2,4-Dimethyl-pyrrole-1-yl)-1-phenyl-propan-1-ol (*S*,*R*)-3c. Yellow oil (1.02 g, 89%). $[\alpha]_D^{25} = -3.8$ (*c* 0.6, $CHCl_3$); IR(neat): 3600, 1560, 1210 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.11$ (m, 5H), 6.35 (s, 1H), 5.45 (s, 1H), 4.56 (d, $J = 5.1$ Hz, 1H), 3.99 (m, 1H), 2.32 (br s, 1H), 1.91 (s, 3H), 1.83 (s, 3H), 1.27 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$): $\delta = 141.6$, 128.2 (2C), 128.0, 127.7, 127.6, 125.8, 117.5, 114.5, 108.3, 56.7, 15.0, 12.1, 12.0. Anal. Calcd for $C_{15}H_{19}NO$ (229.3): C, 78.56; H, 8.35; N, 6.11. Found C, 78.77; H, 8.58.

4.1.5. (*S*)-2-(2,4-Dimethyl-pyrrol-1-yl)-4-methylsulfanyl-butyric acid ethyl ester (*S*)-3d. Yellow oil (1.10 g, 86%). $[\alpha]_D^{25} = -3.4$ (*c* 1.3, $CHCl_3$); IR(neat): 2890, 1776, 1470 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 6.27$ (s, 1H), 5.56 (s, 1H), 4.66 (m, 1H), 4.10 (m, 2H), 2.35 (m, 1H), 2.22–2.11 (m, 3H), 2.10 (s, 3H), 1.98 (s, 3H), 1.94 (s, 3H), 1.17 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$): $\delta = 170.5$, 128.8, 118.5, 114.8, 108.9, 61.2, 56.0, 31.2, 30.2, 15.2, 14.1, 12.1, 12.0. Anal. Calcd for $C_{13}H_{21}NO_2S$ (255.3): C, 61.14; H, 8.29; N, 5.48. Found C, 61.32; H, 8.48.

4.1.6. (*S*)-2-(2,4-Dimethyl-pyrrol-1-yl)-3-(4-hydroxy-phenyl)-propionic acid ethyl ester (*S*)-3e. Yellow oil (1.28 g, 89%). $[\alpha]_D^{25} = -4.4$ (c 1, $CHCl_3$); IR(neat): 3735, 1740, 1680, 1530 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 6.69$ (d, $J = 8.4$ Hz, 2H), 6.51 (d, $J = 8.5$ Hz, 2H), 6.46 (s, 1H), 5.49 (s, 1H), 4.0 (m, 1H), 3.99 (m, 2H), 3.15 (dd, $J_1 = 13.8$, $J_2 = 6.5$ Hz, 1H), 2.96 (dd, $J_1 = 13.8$ $J_2 = 8.6$ Hz, 1H), 1.93 (s, 3H), 1.80 (s, 3H), 1.06 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$): $\delta = 170.5$, 154.8, 129.9, 128.6, 127.7, 118.0, 115.2, 114.7, 108.2, 61.2, 59.6, 44.8, 38.0, 21.0, 13.6, 11.7, 11.4. Anal. Calcd for $C_{17}H_{21}NO_3$ (287.3): C, 71.06; H, 7.37; N, 4.87. Found C, 71.33; H, 7.55.

4.1.7. (*R*)-2-Cyclohexyl-4-methyl-1-(1-phenyl-ethyl)-1*H*-pyrrole (*R*)-3f. Yellow oil (1.20 g, 90%). $[\alpha]_D^{25} = -2.8$ (*c* 0.9, $CHCl_3$); IR(neat): 2860, 1540 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.23$ (m, 3H), 7.0 (d, $J = 7.0$ Hz, 2H), 6.43 (s, 1H), 5.77 (s, 1H), 5.27 (q, $J = 7.1$ Hz, 1H), 2.36 (m, 1H), 2.09 (s, 3H), 1.88 (m, 1H), 1.75 (d, $J = 7.0$ Hz, 3H), 1.65–1.51 (m, 3H), 1.41–1.11 (m, 6H); ^{13}C NMR (400 MHz, $CDCl_3$): $\delta = 144.4$, 139.6, 129.1, 128.6, 128.4, 127.1, 125.8, 117.5, 114.6, 105.3, 53.8, 35.8, 34.9, 33.8, 27.0, 26.9, 26.3, 22.6, 12.3. Anal. Calcd for $C_{19}H_{25}N$ (267.4): C, 85.34; H, 9.42; N, 5.24. Found C, 85.11; H, 9.71.

4.1.8. (*S*,*R*)-2-(2-Cyclohexyl-4-methyl-pyrrol-1-yl)-1-phenyl-propan-1-ol (*S*,*R*)-3g. Yellow oil (1.29 g, 87%). $[\alpha]_D^{25} = +2.5$ (*c* 0.5, $CHCl_3$); IR(neat): 3600, 1560, 1210 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.21$ (m, 5H), 6.41 (s, 1H), 5.47 (s, 1H), 4.67 (d, $J = 5.5$ Hz, 1H), 4.13 (m, 1H), 2.31 (br s, 1H), 1.97 (s, 3H), 1.34 (d, $J = 6.9$ Hz, 3H), 1.78–1.51 (m, 5H), 1.42–1.11 (m, 6H); ^{13}C NMR (400 MHz, $CDCl_3$): $\delta = 176.5$, 141.7, 138.8, 128.4, 127.9, 126.3, 125.6, 114.1, 104.8, 56.1, 50.7, 35.6, 32.7, 29.7, 29.5, 26.8, 26.2, 25.7, 15.4, 12.2. Anal. Calcd for $C_{20}H_{27}NO$ (297.4): C, 80.76; H, 9.15; N, 4.71. Found C, 80.51; H, 9.33.

4.1.9. (*S*)-2-(4-Methyl-2-phenyl-pyrrol-1-yl)-4-methylsulfanyl-butyric acid ethyl ester (*S*)-3h. Yellow oil (1.36 g, 86%). $[\alpha]_D^{25} = -9.6$ (*c* 1.3, $CHCl_3$); IR(neat): 2885, 1780, 1465 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.85$ (m, 1H), 7.29 (m, 4H), 6.53 (s, 1H), 5.90 (s, 1H), 4.79 (q, $J = 5.1$ Hz, 1H), 4.13 (q, $J = 7.2$ Hz, 2H), 2.17 (m, 4H), 2.05 (s, 3H), 1.87 (s, 3H), 1.21 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$): $\delta = 170.0$, 132.6, 135.0, 128.8, 128.1, 127.9, 127.8, 126.6, 122.5, 119.5, 116.4, 60.9, 56.4, 32.1, 29.5, 14.8, 13.7, 11.6. Anal. Calcd for $C_{18}H_{23}NO_2S$ (317.4): C, 68.10; H, 7.30; N, 4.41. Found C, 68.36; H, 4.66.

4.1.10. (*S*)-2-(4-Methyl-2-phenyl-pyrrol-1-yl)-propionic acid methyl ester (*S*)-3i. Yellow oil (1.06 g, 87%). $[\alpha]_D^{25} = +4.2$ (*c* 0.5, $CHCl_3$); IR(neat): 2890, 1770, 1470 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.85$ (m, 1H), 7.24 (m, 4H), 6.53 (s, 1H), 5.90 (s, 1H), 4.79 (q, $J = 7.2$ Hz, 1H), 3.63 (s, 3H), 2.05 (s, 3H), 1.53 (d, $J = 7.3$ Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$): $\delta =$ 171.8, 134.7, 133.2, 129.1, 128.6, 128.4, 128.3, 127.1, 119.4, 110.5, 53.4, 52.3, 18.9, 17.5, 12.0. Anal. Calcd for $C_{15}H_{17}NO_2$ (243.3): C, 74.05; H, 7.04; N, 5.76. Found C, 74.36; H, 7.22.

4.1.11. (*S*)-2-(2-Isopropyl-4-methyl-pyrrol-1-yl)-4-methylsulfanyl-butyric acid ethyl ester (*S*)-3j. Yellow oil (1.29 g, 91%). $[\alpha]_D^{25} = -15.6$ (*c* 3, $CHCl_3$); IR(neat): 2890, 1776, 1470 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 6.29$ (s, 1H), 5.63 (s, 1H), 4.76 (m, 1H), 4.14 (m, 2H), 2.85 (m, 1H), 2.37 (m, 1H), 2.20 (m, 6H), 2.02 (s, 3H), 2.00 (s, 3H), 1.21 (t, $J = 8.2$ Hz, 3H), 1.12 (d, $J = 6.8$ Hz, 2H); ^{13}C NMR (400 MHz, $CDCl_3$): $\delta =$ 170.7, 140.3, 118.5, 114.7, 105.0, 61.3, 55.6, 31.8, 30.3, 25.2, 23.6, 23.1, 15.3, 14.1, 12.1. Anal. Calcd for $C_{15}H_{25}NO_2S$ (283.4): C, 63.56; H, 8.89; N, 4.94. Found C, 63.38; H, 8.67.

4.1.12. (*R*)-2-Isopropyl-4-methyl-1-(1-phenylethyl)-1*H*-pyrrole (*R*)-3k. Yellow oil (1.08 g, 95%). $[\alpha]_D^{25} = +31.6$ (*c* 3.3, $CHCl_3$); IR(neat): 2850, 1550 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.18$ (m, 3H), 6.89 (d, $J = 7.6$ Hz, 2H), 6.35 (s, 1H), 5.68 (s, 1H), 5.20 (q, $J = 7.1$ Hz, 1H), 2.67 (q, $J = 6.8$ Hz, 1H), 2.01 (s, 3H), 1.69 (d, $J = 7.1$ Hz, 3H), 1.14 (d, $J = 6.8$ Hz, 3H), 0.96 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$): $\delta = 144.3$, 140.0, 128.5 (2C), 126.9, 125.7 (2C), 117.3, 114.6, 105.0, 53.8, 25.4, 24.1, 23.1, 22.6, 12.2. Anal. Calcd for $C_{16}H_{21}N$ (227.3): C, 84.53; H, 9.31; N, 6.16. Found C, 84.78; H, 9.57.

4.1.13. (*S*,*R*)-2-(2-Isopropyl-4-methyl-pyrrol-1-yl)-1-phenyl-propan-1-ol (*S*,*R*)-3l. Yellow oil (1.24 g, 96%). $[\alpha]_D^{25} = -5.14$ (*c* 1.3, $CHCl_3$); IR(neat): 3580, 2860, 1550, 1210 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.19$ (m, 5H), 6.50 (s, 1H), 5.59 (s, 1H), 4.73 (d, $J = 5.2$ Hz, 1H), 4.17 (m, 1H), 2.50 (m, 1H), 2.07 (br s, 1H), 2.03 (s, 3H), 1.39 (d, $J = 6.9$ Hz, 3H), 1.08 (d, $J = 6.7$ Hz, 3H), 1.03 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$): $\delta = 141.5$, 139.6, 128.2, 128.0, 127.5, 125.7 (2C), 117.6, 114.4, 104.4, 77.4, 56.1, 25.3, 24.5, 22.2, 15.3, 12.1. Anal. Calcd for $C_{17}H_{23}NO$ (257.3): C, 79.33; H, 9.01; N, 5.44. Found C, 79.52; H, 9.24.

4.1.14. (*S*)-2-(2-Isopropyl-4-methyl-pyrrol-1-yl)-propionic acid methyl ester (*S*)-3m. Yellow oil (0.91 g, 87%). $[\alpha]_D^{25} = +3.6$ (*c* 1.2, $CHCl_3$); IR(neat): 2885, 1776, 1470 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 6.34$ (s, 1H), 5.64 (s, 1H), 4.68 (q, $J = 7.2$ Hz, 1H), 3.64 (s, 3H) 2.73 (m, 1H), 1.96 (s, 3H), 1.58 (d, $J = 7.2$ Hz, 3H), 1.15 (dd, $J_1 = 6.7$, $J_2 = 5.0$ Hz, 6H); ^{13}C NMR (400 MHz, $CDCl_3$): $\delta = 171.3$, 138.9, 117.6, 114.3, 104.6, 52.1, 51.8, 24.8, 23.1, 22.4, 18.2, 11.6. Anal. Calcd for $C_{12}H_{19}NO_2$ (209.2): C, 68.87; H, 9.15; N, 6.69. Found C, 68.61; H, 9.31.

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8. Chiralcel OD, UV detection at 254 nm, 90:10 hexane/2-propanol, flow 0.8 ml/min. t_R (R) = 8.6 min; t_R (S) = 10.2 min.