

## ELECTRONIC SUPPLEMENTARY INFORMATION

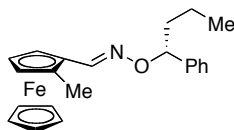
**Competition between planar and central chiral control elements in nucleophilic addition to ferrocenyl imine derivatives**

Kévin M. Joly, Claire Wilson, Alexander J. Blake, James H. R. Tucker, and Christopher J.

Moody

**PREPARATION OF FERROCENYL OXIME ETHERS**

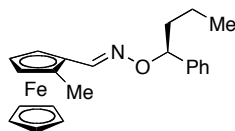
**(*E*)-(*R,R*<sub>p</sub>)-(+)-*O*-(1-Phenylbutyl)-2-methylferrocene-1-carboxaldoxime 5**



A suspension of (*R*)-(-)-*N*-(1-phenylbutoxy)phthalimide (0.680 g, 2.30 mmol) in ethanol (12 mL) was heated at 55 °C until the phthalimide dissolved. Hydrazine hydrate (0.123 mL, 2.53 mmol) was added at this temperature and the reaction mixture was heated at reflux for a further 1 h. The mixture was then allowed to cool to room temperature, (*R*)-2-methylferrocene-1-carboxaldehyde (0.625 g, 2.77 mmol) was added and the reaction mixture stirred overnight. Removal of the solvents under reduced pressure and purification by column chromatography on silica gel, eluting with ether – light petroleum (1 : 17) afforded the *title compound* (0.665 g, 77%) as an orange oil; (Found: C, 70.5; H, 6.8; N, 3.7. C<sub>22</sub>H<sub>25</sub>FeNO requires C, 70.4; H, 6.7; N, 3.7%); (Found: MH<sup>+</sup>, 376.1345. C<sub>22</sub>H<sub>25</sub>FeNO + H requires 376.1358); [ $\alpha$ ]<sub>D</sub><sup>28</sup> +74.1 (*c* 0.95, acetone);  $\nu_{\max}$ (neat)/cm<sup>-1</sup> 3095, 2958, 2872, 1607, 1495, 1454, 1411, 1379, 1362, 1309, 1244, 1204, 1166, 1106, 1060, 1025, 1001, 964, 933, 837, 809, 754;

$\delta_{\text{H}}$ (400 MHz;  $\text{CDCl}_3$ ) 8.04 (1H, s,  $\text{FcCH}=\text{N}$ ), 7.22 – 7.39 (5H, m, ArH), 5.10 (1H, t,  $J$  6.9,  $\text{OCHCH}_2$ ), 4.41 (1H, brs, FcH), 4.20 (1H, brs, FcH), 4.14 (1H, brs, FcH), 4.02 (5H, s, FcH), 1.95 – 2.07 (4H, m), 1.73 – 1.85 (1H, m), 1.33 – 1.52 (2H, m), 0.96 (3H, t,  $J$  7.3,  $\text{MeCH}_2$ );  $\delta_{\text{C}}$ (100 MHz;  $\text{CDCl}_3$ ) 148.6 (CH), 142.8 (C), 128.1 (CH), 127.2 (CH), 126.9 (CH), 84.7 (C), 84.1 (C), 71.7 (CH), 69.8 (CH), 67.9 (CH), 67.1 (CH), 38.1 ( $\text{CH}_2$ ), 18.9 ( $\text{CH}_2$ ), 14.1 (Me), 13.9 (Me);  $m/z$  (ES) 376 ( $[\text{M}+\text{H}]^+$ , 100%).

**(*E*)-(S,*R*<sub>p</sub>)-(+)-O-(1-Phenylbutyl)-2-methylferrocene-1-carboxaldoxime 8**

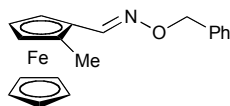


A suspension of (*S*)-(-)-*N*-(1-phenylbutoxy)phthalimide (0.534 g, 1.81 mmol) in ethanol (8 mL) was heated at 55 °C until the phthalimide dissolved. Hydrazine hydrate (0.101 mL, 2.08 mmol) was added at this temperature and the reaction mixture was heated at reflux for a further 1 h. The mixture was allowed to cool to room temperature, a solution of (*R*)-2-methylferrocene-1-carboxaldehyde (0.613 g, 2.71 mmol) in ethanol (5 mL) was added and the reaction mixture stirred overnight. Removal of the solvents under reduced pressure and purification by column chromatography on silica gel, eluting with ether – light petroleum (1 : 17) afforded the *title compound* (0.355 g, 52%) as an orange oil; (Found:  $\text{MH}^+$ , 376.1356.

$\text{C}_{22}\text{H}_{25}\text{FeNO} + \text{H}$  requires 376.1358);  $[\alpha]_{\text{D}}^{29} +436.4$  ( $c$  0.83, acetone);  $\nu_{\text{max}}$ (neat)/ $\text{cm}^{-1}$  2958, 2870, 1606, 1494, 1453, 1379, 1308, 1204, 1106, 1059, 1026, 1001, 934, 854, 813, 787, 757, 736;  $\delta_{\text{H}}$ (400 MHz; acetone-*d*) 8.12 (1H, s,  $\text{FcCH}=\text{N}$ ), 7.22-7.42 (5H, m, ArH), 5.10 (1H, m,  $\text{OCHCH}_2$ ), 4.37-4.43 (1H, m, FcH), 4.24 (1H, brs, FcH), 4.14-4.19 (1H, m, FcH), 3.99 (5H, s, FcH), 2.09 (3H, s,  $\text{FcMe}$ ), 1.89-2.00 (1H, m), 1.69-1.83 (1H, m), 1.32-1.54 (2H, m), 0.94 (3H, t,  $J$  7.4,  $\text{MeCH}_2$ );  $\delta_{\text{C}}$ (100 MHz; acetone-*d*) 149.9 (CH), 145.2 (C), 129.9 (CH), 128.9 (CH),

128.6 (CH), 86.2 (C), 85.8 (C), 73.2 (CH), 71.5 (CH), 69.6 (CH), 68.1 (CH), 40.1 (CH<sub>2</sub>), 20.6 (CH<sub>2</sub>), 15.3 (Me), 14.7 (Me);  $m/z$  (ES) 376 ([M+H]<sup>+</sup>, 100%).

**(E)-(R<sub>p</sub>)-(+)-O-(Benzyl)- $\alpha$ -methylferrocene-1-carboxaldoxime 10**



*O*-Benzylhydroxylamine hydrochloride salt (408 mg, 2.56 mmol) was added to a stirred solution of (*R*)-2-methylferrocene-1-carboxaldehyde (445 mg, 1.97 mmol) in pyridine (14 mL), and the reaction mixture was stirred at room temperature for 16 h. The solvents were removed under reduced pressure, the resulting material was taken back in ethyl acetate (15 mL) and washed with aqueous copper sulfate solution (2 × 15 mL), then water (15 mL) and brine (15 mL). The organic extract was dried (MgSO<sub>4</sub>), filtered and evaporated. The residue was purified by column chromatography on silica gel, eluting with ethyl acetate – light petroleum (1 : 19) to give, in order of elution: the *title compound* (0.377 g, 57%) as a red oil; (Found: M+Na<sup>+</sup>, 356.0700. C<sub>19</sub>H<sub>19</sub>FeNO + Na requires 356.0708); [ $\alpha$ ]<sub>D</sub><sup>23</sup> +297.7 (*c* 1.06, acetone);  $\nu_{\max}$ (neat)/cm<sup>-1</sup> 3092, 2924, 1606, 1496, 1454, 1411, 1365, 1276, 1207, 1106, 1018, 1002, 933, 913, 835, 816, 781, 734, 712;  $\delta_{\text{H}}$ (400 MHz; acetone-*d*) 8.11 (1H, s, FcCH=N), 7.28-7.44 (5H, m, ArH), 5.09 (2H, s, OCH<sub>2</sub>Ph), 4.46 (1H, dd, *J* 2.5, 1.5, FcH), 4.27-4.29 (1H, m, FcH), 4.20 (1H, t, *J* 2.5, FcH), 4.07 (5H, s, FcH), 2.10 (3H, s, FcMe);  $\delta_{\text{C}}$ (100 MHz, acetone-*d*) 150.4 (CH), 140.5 (C), 130.0 (CH), 129.4 (CH), 85.8 (C), 77.2 (C), 77.1 (CH<sub>2</sub>), 73.4 (CH), 71.5 (CH), 69.7 (CH), 68.4 (CH), 14.9 (Me);  $m/z$  (ES) 356 ([M+Na]<sup>+</sup>, 48%), 334 (100, [M+H]<sup>+</sup>).

And then the second (*Z*)-isomer (0.119 g, 18%) as a red oil; (Found: M+H<sup>+</sup>, 334.0892.

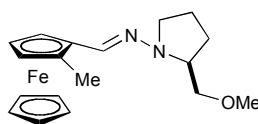
C<sub>19</sub>H<sub>19</sub>FeNO + H requires 334.0889); [ $\alpha$ ]<sub>D</sub><sup>23</sup> +1657.5 (*c* 0.83, acetone);  $\nu_{\max}$ (neat)/cm<sup>-1</sup> 1619, 1495, 1453, 1416, 1368, 1306, 1273, 1207, 1106, 1042, 1020, 1002, 910, 845, 819, 792, 733;

$\delta_{\text{H}}$ (400 MHz; acetone-*d*) 7.30-7.51 (6H, m, ArH, FcCH=N), 5.19 (2H, s, OCH<sub>2</sub>Ph), 5.06-5.12 (1H, m, FcH), 4.23-4.30 (2H, m, FcH), 4.06 (5H, s, FcH), 2.12 (3H, s, FcMe);  $\delta_{\text{C}}$ (100 MHz, acetone-*d*) 146.9 (CH), 140.7 (C), 130.1 (CH), 129.8 (CH), 129.4 (CH), 86.6 (C), 77.8 (CH<sub>2</sub>), 73.6 (CH), 73.0 (CH), 71.6 (CH), 70.2 (CH), 14.3 (Me); *m/z* (ES) 356 ([M+Na]<sup>+</sup>, 30%), 334 (100, [M+H]<sup>+</sup>).

## PREPARATION OF FERROCENYL HYDRAZONES

### (*E*)-(*S,R<sub>p</sub>*)-(+)-*N*-[2-(Methoxymethyl)pyrrolidin-1-yl]- $\alpha$ -methylferrocene-1-methanimine

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(*S*)-(-)-1-Amino-2-(methoxymethyl)pyrrolidine (0.242 mL, 1.80 mmol) was added to a stirred mixture of (*R*)-2-methylferrocene-1-carboxaldehyde (326 mg, 1.44 mmol) and molecular sieves 4 Å (326 mg) in ether (7 mL), at 0 °C. The reaction mixture was stirred at room temperature for 18 h, then diluted with ether (15 mL), dried (MgSO<sub>4</sub>) and filtered.

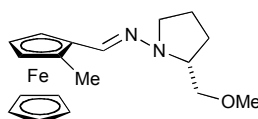
Evaporation of the solvents gave a red oil, which was purified by column chromatography on silica gel, eluting with ethyl acetate – light petroleum (1 : 12) to give the *title compound*

(0.408 g, 83%) as a red oil; (Found: M+Na<sup>+</sup>, 363.1124. C<sub>18</sub>H<sub>24</sub>FeN<sub>2</sub>O + Na requires 363.1130);  $[\alpha]_{\text{D}}^{22}$  +269.0 (*c* 1.00, acetone);  $\nu_{\text{max}}$ (CHCl<sub>3</sub>)/cm<sup>-1</sup> 3097, 3011, 2979, 2928, 2882, 2831, 1670, 1582, 1459, 1438, 1382, 1340, 1304, 1280, 1193, 1105, 1033, 1001, 970, 903, 821;  $\delta_{\text{H}}$ (400 MHz; acetone-*d*) 7.18 (1H, s, FcCH=N), 4.42-4.44 (1H, m, FcH), 4.14 (1H, s, FcH), 4.05 (1H, t, *J* 2.5, FcH), 4.02 (5H, s, FcH), 3.64 (1H, dd, *J* 8.4, 2.8, NCHCH<sub>2</sub>), 3.36-3.48 (3H, m, NCHH, CH<sub>2</sub>OMe), 3.34 (3H, s, OMe), 2.90 (1H, dd, *J* 16.4, 7.8, NCHH), 2.12 (3H, s, FcMe), 1.89-2.02 (3H, m, CH<sub>2</sub>CHH), 1.75-1.84 (1H, m, CH<sub>2</sub>CHH);  $\delta_{\text{C}}$ (100 MHz,

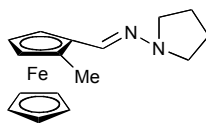
acetone-*d*) 133.5 (CH), 84.0 (C), 83.8 (C), 76.6 (CH<sub>2</sub>), 72.1 (CH), 71.3 (CH), 68.0 (CH), 67.3 (CH), 66.1 (CH), 60.2 (Me), 50.8 (CH<sub>2</sub>), 28.6 (CH<sub>2</sub>), 23.6 (CH<sub>2</sub>), 15.1 (Me); *m/z* (ES) 363 ([M+Na]<sup>+</sup>, 100%), 340 (30, M<sup>+</sup>).

**(*E*)-(*R,R<sub>p</sub>*)-(+)-*N*-[2-(Methoxymethyl)pyrrolidin-1-yl]- $\alpha$ -methylferrocene-1-methanimine**

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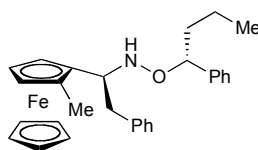
(*R*)-(-)-1-Amino-2-(methoxymethyl)pyrrolidine (0.120 mL, 0.892 mmol) was added to a stirred mixture of (*R*)-2-methylferrocene-1-carboxaldehyde (161 mg, 0.713 mmol) and molecular sieves 4 Å (161 mg) in ether (4 mL), at 0 °C. The reaction mixture was stirred at room temperature for 17 h, then diluted with ether (10 mL), dried (MgSO<sub>4</sub>) and filtered. Evaporation of the solvents gave a red oil, which was purified by column chromatography on silica gel, eluting with ethyl acetate – light petroleum (1 : 12) to give the *title compound* (0.209 g, 86%) as a red oil; (Found: M+Na<sup>+</sup>, 363.1135. C<sub>18</sub>H<sub>24</sub>FeN<sub>2</sub>O + Na requires 363.1130); [ $\alpha$ ]<sub>D</sub><sup>24</sup> +408.9 (*c* 1.08, acetone);  $\nu_{\max}$ (CHCl<sub>3</sub>)/cm<sup>-1</sup> 3097, 3011, 2979, 2928, 2882, 2831, 1728, 1670, 1602, 1460, 1438, 1412, 1382, 1340, 1304, 1280, 1193, 1105, 1034, 1001, 970, 904, 821;  $\delta_{\text{H}}$ (400 MHz; acetone-*d*) 7.19 (1H, s, FcCH=N), 4.40-4.42 (1H, m, FcH), 4.12-4.16 (1H, m, FcH), 4.05 (1H, t, *J* 2.4, FcH), 4.01 (5H, s, FcH), 3.61 (1H, dd, *J* 9.0, 3.5, NCHCH<sub>2</sub>), 3.35-3.48 (3H, m, NCHH, CH<sub>2</sub>OMe), 3.32 (3H, s, OMe), 2.93 (1H, dd, *J* 16.6, 8.2, NCHH), 2.13 (3H, s, FcMe), 1.89-2.01 (3H, m, CH<sub>2</sub>CHH), 1.73-1.83 (1H, m, CH<sub>2</sub>CHH);  $\delta_{\text{C}}$ (100 MHz, acetone-*d*) 133.7 (CH), 84.0 (C), 83.8 (C), 76.7 (CH<sub>2</sub>), 72.1 (CH), 71.3 (CH), 68.0 (CH), 67.3 (CH), 65.0 (CH), 60.1 (Me), 50.9 (CH<sub>2</sub>), 28.6 (CH<sub>2</sub>), 23.6 (CH<sub>2</sub>), 15.2 (Me); *m/z* (ES) 363 ([M+Na]<sup>+</sup>, 100%), 341 (15, [M+H]<sup>+</sup>).

**(E)-(R<sub>p</sub>)-(+)-N-(Pyrrolidin-1-yl)- $\alpha$ -methylferrocene-1-methanimine 17**

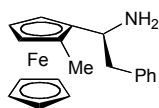
A solution of *N*-nitrosopyrrolidine (0.434 mL, 4.70 mmol) in ether (5 mL) was added dropwise to a stirred suspension of LiAlH<sub>4</sub> (357 mg, 9.40 mmol) in ether (15 mL), over 10 min. The resulting mixture was stirred at room temperature for a further 1 h, then ether (10 mL) was added, and the mixture cooled to 0 °C. Water (0.35 mL), aqueous sodium hydroxide solution (2 M; 0.50 mL) and water (0.35 mL) were successively added, and the resulting mixture was stirred at room temperature for 16 h.

Molecular sieves 4 Å (425 mg) were added, the mixture was then cooled to 0 °C and then a solution of (*R*)-2-methylferrocene-1-carboxaldehyde (425 mg, 1.88 mmol) in ether (5 mL) was added. The reaction mixture was stirred at room temperature for 20 h, then diluted with ether (30 mL), dried (MgSO<sub>4</sub>) and filtered. Evaporation of the solvents gave a red oil, which was purified by column chromatography on silica gel, eluting with ethyl acetate – light petroleum (1 : 11) to give the *title compound* (0.368 g, 66%) as a red oil; (Found: M+H<sup>+</sup>, 297.1038. C<sub>16</sub>H<sub>20</sub>FeN<sub>2</sub> + H requires 297.1049); [ $\alpha$ ]<sub>D</sub><sup>25</sup> +517.2 (*c* 1.07, CHCl<sub>3</sub>);  $\nu_{\max}$ (CHCl<sub>3</sub>)/cm<sup>-1</sup> 3097, 3010, 2974, 2879, 1580, 1485, 1459, 1437, 1411, 1382, 1339, 1240, 1142, 1105, 1091, 1034, 1001, 877, 821;  $\delta_{\text{H}}$ (400 MHz; acetone-*d*) 7.14 (1H, s, FcCH=N), 4.42 (1H, dd, *J* 2.3, 1.6, FcH), 4.12-4.16 (1H, m, FcH), 4.04-4.06 (1H, m, FcH), 4.01 (5H, s, FcH), 3.13-3.22 (4H, m, CH<sub>2</sub>NCH<sub>2</sub>), 2.10 (3H, s, FcMe), 1.86-1.92 (4H, m, NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>);  $\delta_{\text{C}}$ (100 MHz, acetone-*d*) 133.6 (CH), 84.0 (C), 83.8 (C), 72.0 (CH), 71.3 (CH), 68.0 (CH), 66.9 (CH), 52.8 (CH<sub>2</sub>), 24.7 (CH<sub>2</sub>), 15.0 (Me); *m/z* (ES) 297 ([M+H]<sup>+</sup>, 100%).

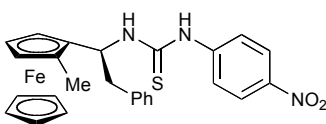
**ADDITION OF ORGANOMETALLIC REAGENTS WITH ISOLATION OF INTERMEDIATE HYDROXYLAMINE**

**(1*S*,1'*R*,*R*<sub>p</sub>)-(+)-1-[ $\alpha$ -(Methyl)ferrocenyl]-2-phenyl-*N*-(1-phenylbutoxy)-1-ethylamine 6a**

Oxime ether **5** (0.350 g, 0.933 mmol) was dissolved in toluene (5 mL) under nitrogen and cooled to  $-78\text{ }^{\circ}\text{C}$ . Boron trifluoride diethyl etherate (0.473 mL, 3.73 mmol) was added and the mixture stirred for 30 min. Benzylmagnesium chloride (3.73 mL of a 1 M solution in ether, 3.73 mmol) was then added dropwise over 10 min, and the mixture stirred at  $-78\text{ }^{\circ}\text{C}$  for 5 h. The reaction mixture was then quenched at this temperature with aqueous ammonium chloride solution (3 mL), and allowed to warm to room temperature. The product was extracted with ether (3  $\times$  15 mL), the extracts combined, dried ( $\text{MgSO}_4$ ), filtered and evaporated. The crude product was purified by column chromatography on silica gel, eluting with ether – light petroleum (1 : 16) to give the *title compound* (0.249 g, 57%) as an orange oil; (Found:  $\text{M-H}^+$ , 466.1837.  $\text{C}_{29}\text{H}_{33}\text{FeNO} - \text{H}$  requires 466.1828);  $[\alpha]_D^{23} +76.1$  (*c* 1.40, acetone);  $\nu_{\text{max}}(\text{neat})/\text{cm}^{-1}$  3028, 2956, 2932, 2879, 1494, 1454, 1408, 1379, 1103, 1068, 1030, 1000, 973, 939, 903, 856, 820, 765;  $\delta_{\text{H}}(400\text{ MHz}; \text{CDCl}_3)$  7.28 – 7.50 (5H, m, ArH), 7.10 – 7.18 (3H, m, ArH), 6.85 – 6.92 (2H, m, ArH), 5.94 (1H, s, NH), 4.79 (1H, t, *J* 6.7, OCH), 3.82 – 4.10 (9H, m,  $\text{FcH}$ ,  $\text{FcCHNH}$ ), 3.25 (1H, dd, *J* 12.8, 4.4,  $\text{ArCHHCH}$ ), 2.62 (1H, dd, *J* 12.8, 8.8,  $\text{ArCHHCH}$ ), 1.95 – 2.05 (1H, m), 1.70 – 1.82 (1H, m), 1.36 – 1.63 (2H, m), 1.26 (3H, s,  $\text{FcMe}$ ), 1.01 (3H, t, *J* 7.4,  $\text{MeCH}_2$ );  $\delta_{\text{C}}(100\text{ MHz}; \text{CDCl}_3)$  142.4 (C), 138.8 (C), 129.8 (CH), 128.5 (CH), 127.8 (CH), 127.7 (CH), 127.0 (CH), 125.8 (CH), 88.7 (C), 84.3 (CH), 83.5 (C), 68.9 (CH), 68.7 (CH), 65.7 (CH), 65.6 (CH), 58.7 (CH), 41.4 ( $\text{CH}_2$ ), 38.3 ( $\text{CH}_2$ ), 19.3 ( $\text{CH}_2$ ), 14.2 (Me), 12.8 (Me); *m/z* (ES) 467 ( $[\text{M}]^+$ , 18%), 466 (43,  $[\text{M-H}]^+$ ), 303 (100,  $[\text{M-NHOCH}(\text{Ph})\text{CH}_2\text{CH}_2\text{Me}]^+$ ).

**(*S,R<sub>p</sub>*)-(-)-*N*-[1-(1- $\alpha$ -(Methyl)ferrocenyl-2-phenyl)ethyl]-*N'*-4-nitrophenylthiourea **7a****

(a) Zinc dust (1.26 g, 19.2 mmol) was added to a solution of hydroxylamine **6a** (0.225 g, 0.481 mmol) in acetic acid : water : THF (14 mL, 3 : 2 : 0.3). The mixture was placed into a sonic bath, at 40 °C, for 4 h. The zinc was then filtered, washing with ether and water. The filtrate was extracted with ether (2  $\times$  50 mL), and the aqueous layer was basified to pH12 with aqueous sodium hydroxide solution (4 M), then saturated ammonium chloride solution was added to disperse any emulsion formed. Ethyl acetate (100 mL) was added and the layers were separated. The aqueous layer was extracted with ethyl acetate (60 mL), and the combined organic extracts were dried (MgSO<sub>4</sub>). The drying agent was removed by filtration and the filtrate concentrated under reduced pressure to provide (*S,R<sub>p</sub>*)-(-)-1-[ $\alpha$ -(methyl)ferrocenyl]-2-phenyl-1-ethylamine (0.116 g, 75%) as an orange powder, which was used without any further purification.



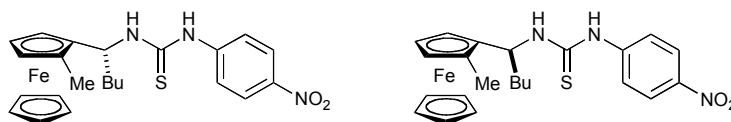
(b) A solution of 4-nitrophenyl isothiocyanate (50 mg, 0.277 mmol) in dichloromethane (4 mL) was slowly added, over 2 min, to a solution of primary amine (68 mg, 0.213 mmol) in dichloromethane (10 mL), at 0 °C. The resulting mixture was stirred at room temperature for 5 h. Evaporation of the solvents under reduced pressure left a brown oil, which was purified by column chromatography on silica gel, eluting with ethyl acetate – light petroleum (1 : 4) to give the *title compound* (93 mg, 88%) as an orange powder; mp 144 – 146 °C; (Found: C, 62.9; H, 5.3; N, 8.1. C<sub>26</sub>H<sub>25</sub>FeN<sub>3</sub>O<sub>2</sub>S requires C, 62.5; H, 5.1; N, 8.4%); (Found: M<sup>+</sup>,



499.0987.  $C_{26}H_{25}FeN_3O_2S$  requires 499.1011);  $[\alpha]_D^{30}$  -70.7 ( $c$  1.00, acetone);  $\nu_{\max}(\text{neat})/\text{cm}^{-1}$  3336 (NH), 2922, 1607, 1594, 1536, 1507, 1342, 1300, 1247, 1189, 1107, 1033, 1001, 833, 806, 754;  $\delta_H$ (400 MHz; acetone- $d$ ) 9.61 (1H, s,  $NHAr$ ), 8.21 – 8.29 (2H, m, ArH), 8.00 – 8.11 (2H, m, ArH), 7.88 (1H, d,  $J$  8.2,  $CHNH$ ), 7.13 – 7.20 (3H, m, ArH), 6.95 – 7.04 (2H, m, ArH), 5.67 – 5.79 (1H, m,  $CHNH$ ), 4.06 (5H, s, FcH), 4.00 – 4.04 (3H, m, FcH), 3.24 (1H, dd,  $J$  12.6, 4.7,  $ArCHH$ ), 2.78 (1H, dd,  $J$  12.6, 8.6,  $ArCHH$ ), 1.51 (3H, s, FcMe);  $\delta_C$ (100 MHz; acetone- $d$ ) 181.1 (C), 148.0 (C), 144.9 (C), 139.4 (C), 131.7(CH), 129.7 (CH), 128.0 (CH), 126.2 (CH), 123.3 (CH), 90.2 (C), 85.2 (C), 70.9 (CH), 70.6 (CH), 67.6 (CH), 65.8 (CH), 55.4 (CH), 45.3 ( $CH_2$ ), 14.2 (Me);  $m/z$  (ES) 522 ( $[M+Na]^+$ , 34%), 500 (64,  $[M+H]^+$ ), 499 (100,  $M^+$ ), 303 (88,  $[M-NHC(O)NHPhNO_2]^+$ ).

## ADDITION OF ORGANOMETALLIC REAGENTS WITHOUT ISOLATION OF INTERMEDIATE HYDROXYLAMINES OR HYDRAZINES

General procedure for the synthesis of (*S,R<sub>p</sub>*)-(-)-*N*-[1-(1- $\alpha$ -(methyl)ferrocenyl)pentyl]-*N'*-4-nitrophenylthiourea **7b** and (*R,R<sub>p</sub>*)-(-)-*N*-[1-(1- $\alpha$ -(methyl)ferrocenyl)pentyl]-*N'*-4-nitrophenylthiourea **14**



### (a) From oximes

The desired oxime ether **5/8/10** (0.533 mmol) was dissolved in toluene (5 mL) under nitrogen and cooled to -78 °C. Boron trifluoride diethyl etherate (0.236 mL, 1.87 mmol) was added and the mixture stirred for 30 min. Butyllithium (0.848 mL of a 2.2 M solution in hexane, 1.87 mmol) was then added dropwise over 6 min, and the mixture stirred at -78 °C for 2 h. The reaction mixture was then quenched at this temperature with aqueous ammonium

chloride solution (3 mL), and allowed to warm to room temperature. The product was extracted with ethyl acetate (3 × 20 mL), the extracts combined, dried (MgSO<sub>4</sub>), filtered and evaporated to afford the crude hydroxylamine as a dark-orange oil.

Zinc dust (1.39 g, 21.3 mmol) was added to a solution of crude hydroxylamine **6b/9b/11b** in acetic acid : water : THF (16 mL, 3 : 2 : 0.3). The mixture was placed into a sonic bath, at 40 °C, for 4 h. The zinc was then filtered, washing with ether and water. The filtrate was extracted with ether (2 × 60 mL), and the aqueous layer was basified to pH12 with aqueous sodium hydroxide solution (4 M), then saturated ammonium chloride solution was added to disperse any emulsion formed. Ethyl acetate (110 mL) was added and the layers were separated. The aqueous layer was extracted with ethyl acetate (80 mL), and the combined organic extracts were dried (MgSO<sub>4</sub>), filtered and evaporated to give the crude amine as an orange oil, which was used without any further purification.

The crude amine was dissolved in dichloromethane (16 mL) and cooled to 0 °C. A solution of 4-nitrophenyl isothiocyanate in dichloromethane (9 mL) was added over 2 min and the resulting reaction mixture was stirred at room temperature for 17 h. The solvents were removed under reduced pressure, and then ethyl acetate (25 mL) and water (25 mL) were added. The layers were separated and the aqueous layer was extracted with ethyl acetate (15 mL). The combined organic extracts were washed with brine (20 mL), dried (MgSO<sub>4</sub>), filtered and evaporated. The residue was analysed by <sup>1</sup>H NMR spectroscopy, and the diastereomeric ratio (dr) was determined from the ratio of the signals for ArNH at δ9.48 for **7b** (and δ9.21 for **14**). The crude thiourea was purified by column chromatography on silica gel, eluting with ethyl acetate – light petroleum (1 : 4) to give the *title compound* **7b**.

**(b) From hydrazones**

The hydrazone **12/15/17** (0.567 mmol) was dissolved in ether (6 mL) and cooled to  $-100\text{ }^{\circ}\text{C}$ . Butyllithium (0.774 mL of a 2.2 M solution in hexane, 1.70 mmol) was then added dropwise over 7 min, and the mixture stirred for 17 h, while slowly warming to room temperature. The reaction mixture was then cooled to  $0\text{ }^{\circ}\text{C}$  and quenched with water (1.1 mL). Ether (15 mL) and brine (15 mL) were added, and the layers separated. The organic layer was washed with brine (15 mL), dried ( $\text{MgSO}_4$ ), filtered and evaporated to afford the crude hydrazine **13/16/18** as an orange oil.

The crude hydrazine was dissolved in THF (11 mL),  $\text{BH}_3\cdot\text{THF}$  complex (5.67 mL of a 1 M solution in THF, 5.67 mmol) was added and the resulting reaction mixture was heated at reflux for 5 h. The mixture was cooled to  $-5\text{ }^{\circ}\text{C}$ , quenched by addition of aqueous hydrochloric acid solution (4 M), stirred at  $-5\text{ }^{\circ}\text{C}$  for a further 30 min, then at room temperature for 1 h. The THF was evaporated under reduced pressure; the aqueous solution was basified with solid sodium hydroxide and stirred for 30 min. The resulting amine was extracted with ether/dichloromethane (3:1,  $3 \times 20\text{ mL}$ ), dried ( $\text{MgSO}_4$ ), filtered and evaporated to give a dark-orange oil.

The crude amine was dissolved in dichloromethane (17 mL) and cooled to  $0\text{ }^{\circ}\text{C}$ . A solution of 4-nitrophenyl isothiocyanate in dichloromethane (8 mL) was added over 3 min and the resulting reaction mixture was stirred at room temperature for 14 h. The solvents were removed under reduced pressure, and then ethyl acetate (20 mL) and water (20 mL) were added. The layers were separated and the aqueous layer was extracted with ethyl acetate (15 mL). The combined organic extracts were washed with brine (20 mL), dried ( $\text{MgSO}_4$ ), filtered and evaporated. The residue was analysed by  $^1\text{H}$  NMR spectroscopy, and the diastereomeric ratio (dr) was determined from the ratio of the signals for  $\text{ArNH}$  at  $\delta 9.48$  for **7b** (and  $\delta 9.21$  for **14**). The crude thiourea was purified by column chromatography on silica gel, eluting with ethyl acetate – light petroleum (1 : 4) to give, in order of elution;

The *title compound 14* as an orange powder; mp 123 – 125 °C; (Found: C, 59.3; H, 5.9; N, 9.1. C<sub>23</sub>H<sub>27</sub>FeN<sub>3</sub>O<sub>2</sub>S requires C, 59.4; H, 5.9; N, 9.0%); (Found: M+Na<sup>+</sup>, 488.1050.

C<sub>23</sub>H<sub>27</sub>FeN<sub>3</sub>O<sub>2</sub>S + Na requires 488.1066); [ $\alpha$ ]<sub>D</sub><sup>26</sup> -234.0 (*c* 0.96, CHCl<sub>3</sub>);  $\nu_{\max}$ (CHCl<sub>3</sub>)/cm<sup>-1</sup> 3385, 3098, 3011, 2961, 2933, 2861, 1702, 1632, 1597, 1581, 1501, 1441, 1425, 1344, 1301, 1240, 1178, 1138, 1113, 1032, 1001, 854, 824;  $\delta_{\text{H}}$ (400 MHz; acetone-*d*) 9.21 (1H, s, ArNH), 8.15 (2H, d, *J* 9.0, ArH), 7.90 (2H, d, *J* 9.0, ArH), 7.44 (1H, d, *J* 8.2, FcCHNH), 5.79 (1H, s, FcCHNH), 3.99-4.16 (8H, m, FcH), 2.20-2.32 (1H, m, FcCHCHH), 2.06 (3H, s, FcMe), 1.82-1.94 (1H, m, FcCHCHH), 1.35-1.72 (4H, m, CH<sub>2</sub>CH<sub>2</sub>Me), 0.97 (3H, t, *J* 7.0, CH<sub>2</sub>Me);  $\delta_{\text{C}}$ (100 MHz, acetone-*d*) 181.3 (C), 148.3 (C), 126.1 (CH), 122.6 (CH), 90.2 (C), 85.1 (C), 71.7 (CH), 71.1 (CH), 67.6 (CH), 67.3 (CH), 53.6 (CH), 36.2 (CH<sub>2</sub>), 30.0 (CH<sub>2</sub>), 24.6 (CH<sub>2</sub>), 15.51 (Me), 15.45 (Me); *m/z* (ES) 488 ([M+Na]<sup>+</sup>, 100%), 465 (65, M<sup>+</sup>).

And the *title compound 7b* as an orange powder; mp 148 – 150 °C; (Found: C, 59.3; H, 5.9; N, 8.9. C<sub>23</sub>H<sub>27</sub>FeN<sub>3</sub>O<sub>2</sub>S requires C, 59.4; H, 5.9; N, 9.0%); (Found: M+Na<sup>+</sup>, 488.1061.

C<sub>23</sub>H<sub>27</sub>FeN<sub>3</sub>O<sub>2</sub>S + Na requires 488.1066); [ $\alpha$ ]<sub>D</sub><sup>26</sup> +6.2 (*c* 0.96, CHCl<sub>3</sub>);  $\nu_{\max}$ (CHCl<sub>3</sub>)/cm<sup>-1</sup> 3396, 3083, 3011, 2961, 2932, 2861, 1707, 1597, 1527, 1501, 1345, 1301, 1240, 1178, 1113, 1001, 857, 824;  $\delta_{\text{H}}$ (400 MHz; acetone-*d*) 9.48 (1H, s, ArNH), 8.23 (2H, d, *J* 8.7, ArH), 8.05 (2H, d, *J* 8.7, ArH), 7.83-7.95 (1H, m, FcCHNH), 5.66 (1H, s, FcCHNH), 4.00-4.20 (8H, m, FcH), 2.03 (3H, s, FcMe), 1.57-1.79 (2H, m, FcCHCH<sub>2</sub>), 1.21-1.41 (4H, m, CH<sub>2</sub>CH<sub>2</sub>Me), 0.84 (3H, t, *J* 6.9, CH<sub>2</sub>Me);  $\delta_{\text{C}}$ (100 MHz, acetone-*d*) 181.4 (C), 148.2 (C), 144.8 (C), 126.2 (CH), 123.2 (CH), 92.5 (C), 84.3 (C), 71.2 (CH), 70.9 (CH), 67.6 (CH), 65.9 (CH), 53.4 (CH), 39.4 (CH<sub>2</sub>), 29.5 (CH<sub>2</sub>), 24.3 (CH<sub>2</sub>), 15.3 (Me), 14.7 (Me); *m/z* (ES) 488 ([M+Na]<sup>+</sup>, 71%), 465 (100, M<sup>+</sup>), 396 (57).