Synthesis of Substituted (R_p)-2-Aminomethyl-1-[(*S*)-4-isopropyloxazolin-2-yl]-ferrocenes

Radovan Šebesta,*[a] Štefan Toma,[a] and Marta Sališová[a]

Keywords: Metallocenes / Oxygen heterocycles / Amines / Nucleophilic substitution / Planar chirality

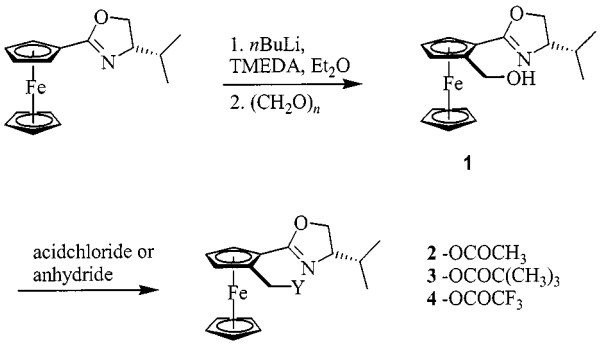
The synthesis of novel *N*-substituted (R_p)-2-aminomethyl-1-[(*S*)-4-isopropyloxazolin-2-yl]ferrocenes is described. The usual synthesis by nucleophilic displacement of an acetoxy group with amine in methanol does not work in the case of the corresponding oxazolinylferrocene. This problem was solved by changing the leaving group to a pivaloyloxy group. Addition of water to the reaction media increases the yields and shortens the reaction times. We have also developed a new methodology for the direct conversion of the hydroxy group to an amine via an intermediate iodide.

Introduction

Chiral oxazoline derivatives, such as bisoxazolines[1,2] or phospinooxazolines[3] have proved to be very useful and versatile ligands in a number of stereoselective reactions. Ferrocenyl oxazolines[4−6] were first reported in 1995 by three independent groups, and these compounds have since attracted much attention for their ability to act as a ligand in many metal-catalyzed reactions or as a chiral auxiliary in the synthesis of other chiral ferrocene derivatives. The oxazolinyl function is a potent chirality mediator and on the ferrocene is able to direct lithiation[7,8] at the *ortho* position in a highly diastereoselective manner, thus enabling the preparation of 2-substituted planar chiral derivatives with high diastereomeric excess. Several useful P,N-, P,S-, P,Se- and N,O ligands have been prepared, such as (S_p)-2-diphenylphosphanyl-1-[(*S*)-4-isopropyloxazolin-2-yl]ferrocene,[7] (S_p)-2-phenylsulfanyl-[9] and (S_p)-2-phenylselenyl-1-[(*S*)-4-isopropyloxazolin-2-yl]ferrocene[10] and (R_p)-2-hydroxydiphenylmethyl-1-[(*S*)-4-isopropyloxazolin-2-yl]ferrocene,[11] and all have been successfully applied in stereoselective synthesis. Until now no example of an N,N-ligand of this type is known. In this work we would like to present the synthesis and characterization of a series of new chiral N,N-ligands, namely N-substituted (R_p)-2-aminomethyl-1-[(*S*)-isopropyloxazolin-2-yl]ferrocene derivatives.

Results and Discussion

The first synthetic plan was to prepare N-substituted 2-aminomethyloxazolinylferrocene derivatives by nucleophilic substitution of the acetoxy group that is easily introduced into the α-position of ferrocene. This methodology is quite common in ferrocene chemistry.[12] The synthesis started by lithiation of isopropyloxazolinylferrocene with *n*BuLi in diethyl ether in the presence of TMEDA.[8] Paraformaldehyde was then added as an electrophile to quench the lithiated derivative. (R_p)-2-Hydroxymethyl-1-[(*S*)-isopropyloxazolin-2-yl]ferrocene (**1**) was isolated in high yield, and was subsequently transformed into the acetoxy derivative by reaction with acetic anhydride (Scheme 1).



Scheme 1. Synthesis of intermediate esters **2**−**4**

Our attempts to prepare the N-substituted (R_p)-2-dimethylaminomethyl-1-[(*S*)-isopropyloxazolin-2-yl]ferrocene were initially unsuccessful. Nucleophilic substitution of acetoxy group with an aqueous solution of dimethylamine in methanol gave only compound **1** after hydrolysis. We assumed that the reaction conditions were not harsh enough and therefore we performed the reaction with piperidine as the nucleophile in refluxing methanol, but again only **1** was isolated. Even when the reaction with piperidine was carried out in an aprotic solvent such as acetonitrile only the starting material **1** was obtained (Table 1, entries 1−3). From these results we concluded that the nucleophile attacks preferentially the carbonyl carbon instead of the desired α-carbon. To test this hypothesis we decided to use the pivaloyloxy

[a] Department of Organic Chemistry, Faculty of Natural Sciences, Comenius University,
Mlynska dolina 842 15, Bratislava, Slovakia
Fax: (internat.) +421-2/6029-6690
E-mail: sebesta@fns.uniba.sk

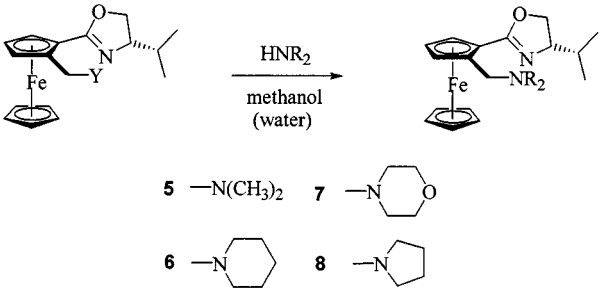
  1434−193X/02/0204−0692 $ 17.50+.50/0 *Eur. J. Org. Chem.* **2002**, 692−695

Table 1. Synthesis of amines **5**−**8** from the intermediate esters

Entry	Y/Solvent	Amine	Yield of amine [%]	Yield of **1** [%]	Recov. start. material [%]	Time [h]
1	$OCOCH_3$ CH_3OH	$HN(CH_3)_2$	–	88	–	24
2	$OCOCH_3$ CH_3OH	Piperidine	–	85	–	24
3	$OCOCH_3$ CH_3CN	Piperidine	–	–	98	20
4	$OCOC(CH_3)_3$ CH_3OH, H_2O	$HN(CH_3)_2$	73	–	–	18
5	$OCOC(CH_3)_3$ CH_3OH	Piperidine	35	31	21	72
6	$OCOC(CH_3)_3$ CH_3OH, H_2O	Piperidine	65	–	–	24
7	$OCOC(CH_3)_3$ CH_3OH	Morpholine	–	63	32	48
8	$OCOC(CH_3)_3$ CH_3OH, H_2O	Morpholine	64	–	–	24
9	$OCOC(CH_3)_3$ CH_3OH	Pyrrolidine	19	25	27	72
10	$OCOC(CH_3)_3$ CH_3OH, H_2O	Pyrrolidine	53	–	–	24
11	$OCOCF_3$ CH_3OH, H_2O	$HN(CH_3)_2$	–	73	–	18
12	$OCOCF_3$ CH_2Cl_2	Piperidine	–	93	–	18

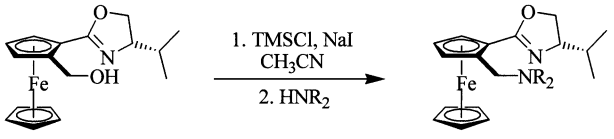
group as the leaving group. This approach gave the desired products, except with morpholine (Table 1, entries 4,5,7,9).

Surprisingly, we obtained much higher yields with an aqueous solution of dimethylamine than with the anhydrous amine (Table 1). We therefore decided to carry out the experiments with other amines in aqueous methanol. An appropriate amount of water was added to the methanol to reach approximately the percentage of water in the aqueous solution of dimethylamine. This arrangement improved the yields of the desired product to 65% (Table 1, entries 6, 8, 10). This observation can be explained by the fact that water is an excellent acceptor in hydrogen bond formation, and this should facilitate the $C_\alpha-OCOCMe_3$ bond dissociation (Scheme 2).



Scheme 2. Synthesis of amines **5**−**8** through the esters

We also decided to examine other common leaving groups such as tosyl, trifluoroacetyl, mesyl and iodide. Our attempts to prepare the tosyl derivative by common procedures such as reaction in pyridine and also in triethylamine were unsuccessful. The synthesis of the trifluoroacetyl derivative was successful, although its reaction with an aqueous solution of amine led only to the hydrolysis of the starting trifluoroacetoxy derivative, producing compound **1**; a one-pot reaction without isolation of the ester did not give the desired product (Table 1, entries 11, 12).



Scheme 3. Synthesis of amines **5**−**8** directly from alcohol **1**

Table 2. Synthesis of amines **5**−**8** directly from alcohol **1**

Entry	Amine	Yield of amine [%]	Time [h]
1	Piperidine	70	18
2	Morpholine	79	18
3	Pyrrolidine	69	18
4	$HN(CH_3)_2/H_2O$	87	18

Preparation of the trifluoromethanesulfonyl derivative failed because trifluromethanesulfonyl anhydride opens the oxazoline ring, as was recently described by Richards.[13]

For the preparation of the iodide derivative a trimethylsilyl chloride/NaI methodology[14] was chosen. The usual procedure was modified slightly by adding the appropriate amine directly to the reaction mixture (Scheme 3). This procedure led directly to the desired amine derivatives **5**−**8** in a straightforward manner and in good yields (Table 2).

Conclusion

We have synthesized the new N-substituted (R_p)-2-aminomethyl-1-[(*S*)-4-isopropyloxazolin-2-yl]ferrocenes **5**−**8**.

Nucleophilic substitution of the acetoxy group with an amine in methanol did not work for the corresponding ferrocenyl oxazoline. Replacing the leaving group with a pivaloyloxy moiety (to give compound **3**) gave the desired products. Addition of water to the media increases the yields and shortens the reaction times. We have also developed a new methodology for the direct conversion of the hydroxy group in **1** to an amine via an intermediate iodide.

Experimental Section

General Remarks: All reactions were carried out under an inert atmosphere. NMR spectra were measured on Varian Gemini 2000 spectrometer operating at 300 MHz for ^{1}H NMR and 75 MHz for ^{13}C NMR spectra; tetramethylsilane was used as an internal standard. IR spectra were measured on a Perkin−Elmer 781 infrared spectrometer. Melting points were measured on a Kofler apparatus. Optical rotations were measured on a Perkin−Elmer 241 polarimeter instrument. HRMS were measured on a Finnigan MAT HSQ-30 apparatus. [(*S*)-4-isopropyloxazolin-2-yl]ferrocene was synthesized according to Richards procedure.[8]

Synthesis of (R_p)-2-Hydroxymethyl-1-[(*S*)-4-isopropyloxazolin-2-yl]-ferrocene (1): A solution of [(*S*)-4-isopropyloxazolin-2-yl]ferrocene (300 mg, 1.01 mmol) and TMEDA (152 mg, 1.31 mmol, 0.20 mL) in anhydrous diethyl ether (8 mL) was cooled to −78 °C. Then, *n*BuLi (0.53 mL, 2.5 M soln. in hexane, 1.31 mmol) was added with a syringe. The solution was stirred at this temperature for 3 h and then for 10 min at 0 °C to complete the lithiation. Para-formaldehyde (40 mg, 1.31 mmol) was suspended in diethyl ether (5 mL) and then added to the reaction mixture and stirred for 18 h, during which time the reaction temperature reached 20 °C. Water (3 mL) was then added, the layers separated, and the water phase extracted with diethyl ether (2 × 5 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and the solvent was evaporated in vacuo. The crude product was purified by column chromatography on Al_2O_3 (50% Et_2O/hexane) to give (R_p)-2-hydroxymethyl-1-[(*S*)-4-isopropyloxazolin-2-yl]ferrocene (**1**) (229 mg, 69%) as orange needles. M.p. 100−102 °C. $[\alpha]_D^{20} = -320.6$ ($CHCl_3$, $c = 0.35$). IR (CCl_4): $\tilde{\nu} = 3340$ cm^{-1} (w, OH), 1995 (m), 1920 (s), 1670 (s, C=N), 1575 (m), 1280 (m), 1230 (m), 1040 (m). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.02 (d, ^3J = 6.6 Hz, 3 H, CH_3), 1.05 (d, ^3J = 6.7 Hz, 3 H, CH_3), 1.82 [m, 1 H, C*H*(CH_3)$_2$], 3.95−4.02 (m, 1 H, NCH), 4.20 (s, 5 H, C_5H_5), 4.13−4.21 (m, 2 H, OCH, C_5H_3), 4.23 (t, ^3J = 2.8 Hz, 1 H, C_5H_3), 4.30−4.41 (m, 2 H, FcC*H*HOH, OCH), 4.60 (dd, ^3J = 2.4, ^4J = 1.4 Hz, 1 H, C_5H_3), 4.65 (d, ^2J = 12.6 Hz, 1 H, FcCH*H*OH), 6.45 (br. s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.5, 18.7 (CH_3), 32.7 [*C*H(CH_3)$_2$], 59.7 (N−CH), 68.1 (O−CH_2), 69.0 (C_5H_3), 70.0 (C_5H_5), 70.2, 70.4, 71.7 (C_5H_3), 72.0 (Fc−*C*H_2), 89.6 (C_5H_3), 167.6 (O−C=N). $C_{17}H_{21}FeNO_2$ (327.2): calcd. C 62.40, H 6.47, N 4.28; found C 62.11, H 6.62, N 4.07.

Synthesis of (R_p)-2-Acetoxymethyl-1-[(*S*)-4-isopropyloxazolin-2-yl]-ferrocene (2): (R_p)-2-Hydroxymethyl-1-[(*S*)-4-isopropyloxazolin-2-yl]ferrocene (**1**) (100 mg, 0.30 mmol) was dissolved in pyridine (3 mL). Acetic acid anhydride (1.5 mL) was then added dropwise and the solution was stirred for 18 h at 20 °C. Diethyl ether (8 mL) and water (16 mL) were added, the layers were separated and the water phase was extracted with diethyl ether (2 × 5 mL). The combined organic layers were dried over anhydrous Na_2SO_4. The solution was then filtered through a plug of silica to remove decomposed material and the solvent was evaporated in vacuo yielding the product as an orange oil (92 mg, 82%). $[\alpha]_D^{22} = -69.1$ ($CHCl_3$, $c = 0.34$). IR (CCl_4): $\tilde{\nu} = 1760$ cm^{-1} (s, C=O), 1670 (s, C=N), 1590 (s), 1390 (m), 1250 (s), 1040 (m), 1025 (m). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.89 (d, ^3J 6.7 Hz, 3 H, CH_3), 1.01 (d, ^3J = 6.8 Hz, 3 H, CH_3), 1.82 [m, 1 H, C*H*(CH_3)$_2$], 2.07 (s, 3 H, $COCH_3$), 3.97−4.08 (m, 2 H, N−CH, O−C*H*$_2$), 4.18 (s, 5 H, C_5H_5), 4.25 (dd, ^2J = 17.3, ^3J = 8.0 Hz, 1 H, O−C*H*H), 4.32 (t, ^3J = 2.5 Hz, 1 H, C_5H_3), 4.46 (dd, ^3J = 2.6, ^4J = 1.3 Hz, 1 H, C_5H_3), 4.73 (dd, ^3J = 2.7, ^4J = 1.4 Hz, 1 H, C_5H_3), 5.24 (AB, ^2J = 11.8 Hz, 1 H, C*H*HOAc), 5.38 (AB, ^2J = 11.8 Hz, 1 H, CH*H*OAc). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.3, 19.0 [CH(*C*H_3)$_2$], 21.3 (CH_3), 32.7 [*C*H(CH_3)$_2$], 62.1 (N−CH), 69.6 (O−CH_2), 69.72, 69.74 (C_5H_3), 70.4 (C_5H_5), 70.6, 71.6 (Fc−*C*H_2), 72.6, 82.5 (C_5H_3), 165.1 (CO), 171.2 (O−C=N). HR-MS ($C_{19}H_{23}FeNO_3$): calcd. 369.1027; found 369.1021.

Synthesis of 1-[(*S*)-4-Isopropyloxazolin-2-yl]-(R_p)-2-pivaloyloxymethylferrocene (3): Compound **1** (125 mg, 0.382 mmol) was dissolved in pyridine (3 mL) and the solution was cooled in an ice bath. Pivaloyl chloride (93 mg, 0.765 mmol, 95 μL) was then added dropwise and the reaction mixture stirred for 18 h at 20 °C. Diethyl ether (10 mL) and water (20 mL) were then added and layers were separated. The water phase was extracted with diethyl ether (2 × 5 mL) and the combined organic layers were dried over anhydrous Na_2SO_4. This solution was filtered through a plug of silica to remove decomposed material and the solvent was evaporated in vacuo yielding the product as an orange oil (130 mg, 83%). $[\alpha]_D^{22} = +11.4$ ($CHCl_3$, $c = 0.29$). IR (CCl_4): $\tilde{\nu} = 1910$ cm^{-1} (m), 1735 (s, C=O), 1660 (s, C=N), 1555 (s), 1290 (m), 1260 (m), 1160 (s). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.93 (d, ^3J = 6.5 Hz, 3 H, CH_3), 1.01 (d, ^3J = 6.7 Hz, 3 H, CH_3), 1.23 [s, 9 H, CH_3(piv.)], 1.80 [m, 1 H, C*H*(CH_3)$_2$], 4.04 (dd, ^2J = 15.1, ^3J = 7.4 Hz, 1 H, O-C*H*H), 3.94−4.06 (m, 2 H, N−CH), 4.17 (s, 5 H, C_5H_5), 4.25−4.31 (m, 1 H, O−CH*H*), 4.30 (t, ^3J = 2.5 Hz, 1 H, C_5H_3), 4.41 (dd, ^3J = 2.8, ^4J = 1.7 Hz, 1 H, C_5H_3), 4.73 (d, ^3J = 2.5, ^4J = 1.4 Hz 1 H, C_5H_3), 5.24 (AB, ^2J = 12.6 Hz, 1 H, Fc−CHH−O), 5.26 (AB, ^2J = 12.6 Hz, 1 H, Fc−CHH−O). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.2, 18.9 [CH(*C*H_3)$_2$], 27.3 [C(*C*H_3)$_3$], 32.6 [*C*H(CH_3)$_2$], 38.8 [*C*(CH_3)$_3$], 47.9 (N−CH), 62.0 (O−CH_2), 69.4, 70.1, 70.2 (C_5H_5), 70.9, 71.6, 72.4, 83.4 (C_5H_3), 164.1 (C=O), 178.2 (O−C=N). HR-MS ($C_{22}H_{29}FeNO_3$): calcd. 441.1497; found 441.1488.

Synthesis of 1-[(*S*)-4-Isopropyloxazolin-2-yl]-(R_p)-2-trifluroacetoxymethylferrocene (4): Compound **1** (60 mg, 0.184 mmol) was dissolved in dichloromethane (1 mL) and trifluoroacetic acid anhydride (77 mg, 51 μL, 0.367 mmol) was added dropwise. The reaction mixture was stirred for 10 min at 20 °C, then all volatiles were removed under vacuum. The resulting dark red oil (**4**) (99%) was not purified further because of its instability. $[\alpha]_D^{22} = +90.5$ ($CHCl_3$, $c = 0.19$). IR (CCl_4): $\tilde{\nu} = 1775$ cm^{-1} (s, C=O), 1635 (s, C=N), 1205 (s), 1160 (s), 995 (m), 970 (m). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.97 (d, ^3J = 6.8 Hz, 3 H, CH_3), 1.02 (d, ^3J = 6.8 Hz, 3 H, CH_3), 2.03 [m, 1 H, C*H*(CH_3)$_2$], 4.39 (s, 5 H, C_5H_5), 4.49 (m, 2 H, C_5H_3, O−CH*H*), 4.62 (m, 1 H, N−CH), 4.86−4.95 (m, 2 H, C_5H_3 + OC*H*H), 5.34 (AB, ^2J = 12.2 Hz, 1 H, CHH−OCOCF$_3$), 5.40 (AB, ^2J = 12.1 Hz, 1 H, CHH−OCOCF$_3$), 5.61 (br. s, 1 H, C_5H_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.1, 17.5 (CH_3), 31.5 [*C*H(CH_3)$_2$], 63.8 (N−CH), 64.6 (O−CH_2), 72.0, 72.2 (C_5H_5), 73.6, 75.1, 75.3, 77.5, 82.0 (C_5H_3), 114.6 (q, $^2J_{C,F}$ = 284.0 Hz, CF_3), 178.0, (q, $^3J_{C,F}$ = 42.2 Hz, CO). HR-MS ($C_{19}H_{20}F_3FeNO_3$): calcd. 423.0745; found 423.0740.

General Procedure for the Preparation of Amines (5−8) in a Methanol/Water Media: 1-[(*S*)-4-Isopropyloxazolin-2-yl]-(R_p)-2-pivaloy-

loxymethylferrocene (**3**) (45 mg, 0.110 mmol) and the amine (10 mmol) were dissolved in methanol (2 mL) and then water (1.2 mL) was added. The reaction mixture was heated to 70 °C for 24 h. Water (10 mL) and diethyl ether (5 mL) were then added to the mixture and the layers were separated. The water layer was extracted with diethyl ether (2 × 3 mL) and the combined organic layers were dried over anhydrous Na_2SO_4. After filtration the solvent was evaporated and the crude product was purified by column chromatography on Al_2O_3 (50% Et_2O/hexane).

Note: When the acetoxy (**2**) and trifluoroacetoxy (**4**) derivative were used as starting material, the reaction mixture was heated to reflux in methanol or acetonitrile with the corresponding amine. The results are summarized in Table 1.

General Procedure for the Preparation of Amines (5−8) Directly from the Alcohol: (R_p)-2-Hydroxymethyl-1-[(*S*)-4-isopropyloxazolin-2-yl]-ferrocene (**1**) (50 mg, 0.153 mmol) and NaI (46 mg, 0.307 mmol) were dissolved in anhydrous acetonitrile (2 mL) at 20 °C. Chlorotrimethylsilane (46 μL, 0.382 mmol) was added dropwise to the reaction mixture, which immediately turned red. After 5 min the appropriate amine (0.612 mmol) was added and mixture was stirred for 18 h at 20 °C. Dichloromethane (5 mL) was then added and the solution was extracted with water (3 × 5 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered and the solvents evaporated. The crude product was purified by flash chromatography on Al_2O_3 (50% Et_2O/hexane). Yields of the products are given in Table 2. Characterizations of compounds (**5−8**) are given below.

(R_p)-2-Dimethylaminomethyl-1-[(*S*)-4-isopropyloxazolin-2-yl]ferrocene (5): Orange oil. $[\alpha]_D^{20} = -63.5$ ($CHCl_3$, $c = 0.34$). IR (CCl_4): $\tilde{\nu} = 1910\ cm^{-1}$ (m), 1660 (s, C=N), 1560 (m), 1475 (m), 1110 (m), 1075 (m), 1005 (s). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.95 (d, ^3J = 6.6 Hz, 3 H, CH_3), 1.03 (d, ^3J = 6.6 Hz, 3 H, CH_3), 1.79 [m, 1 H, C*H*(CH_3)$_2$], 3.24 (d, ^2J = 12.7 Hz, 1 H, FcCH*H*), 3.96−4.10 (m, 2 H, N−CH, O−CH*H*), 4.12 (s, 5 H, C_5H_5), 4.12 (d, ^2J = 12.7 Hz, 1 H, FcC*H*H), 4.22−4.30 (m, 2 H, O−C*H*H, Fc), 4.37 (dd, ^3J = 2.2, ^4J = 1.7 Hz, 1 H, C_5H_3), 4.68 (dd, ^3J = 2.5, ^4J = 1.4 Hz, 1 H, C_5H_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.5, 18.9 [CH(*C*H_3)$_2$], 32.8 [*C*H(CH_3)$_2$], 45.0 [N(CH_3)$_2$], 57.1 (CH_2−N), 68.7 (C_5H_3), 69.2 (O−CH_2), 70.0 (C_5H_5), 70.5 (C_5H_3), 71.2 (N−CH), 72.6, 72.9, 85.0 (C_5H_3), 165.0 (O−C=N). HR-MS ($C_{19}H_{26}FeN_2O$): calcd. 354.1395; found 354.1398.

1-[(*S*)-4-Isopropyloxazolin-2-yl]-(R_p)-2-piperidinomethylferrocene (6): Orange oil. $[\alpha]_D^{20} = +53.6$ ($CHCl_3$, $c = 0.33$). IR (CCl_4): $\tilde{\nu} = 1910\ cm^{-1}$ (m), 1660 (s, C=N), 1560 (s), 1260 (m), 1115 (m), 1080 (m), 1005 (s). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.92 (d, ^3J = 6.9 Hz, 3 H, CH_3), 1.01 (d, ^3J = 7.0 Hz, 3 H, CH_3), 1.37−1.31 [m, 2 H, CH_2(CH_2)$_2$], 1.55−1.49 (m, 4 H, CH_2−CH2-CH_2), 1.81 [m, 1 H, C*H*(CH_3)$_2$], 2.47−2.29 (m, 4 H, CH_2−N−CH_2), 3.43 (d, ^2J = 13.2 Hz, 1 H, FcCH*H*), 4.11−3.95 (m, 2 H, N−CH, O−CH*H*), 4.12 (s, 5 H, Cp), 4.13 (d, ^2J = 13.2 Hz, 1 H, FcC*H*H), 4.26 (t, ^3J = 2.6 Hz, 1 H, C_5H_3), 4.33−4.25 (m, 1 H, O−C*H*H), 4.35 (dd, ^3J = 2.4, ^4J = 1.8 Hz, 1 H, C_5H_3), 4.68 (dd, ^3J = 2.6, ^4J = 1.7 Hz, 1 H, C_5H_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.3, 19.1 (CH_3), 24.4, 26.2 (Pip), 32.8 [*C*H(CH_3)$_2$], 53.8 [N−(CH_2)$_2$], 56.7 (N−CH), 68.9 (C_5H_3), 69.8 (O−CH_2), 69.3 (C_5H_3), 70.2 (C_5H_5), 71.0 (Fc−*C*H_2), 72.6, 73.1, 84.8 (Fc), 165.8 (O−C=N). HR-MS ($C_{22}H_{30}FeN_2O$): calcd. 394.1708; found 394.1703.

1-[(*S*)-4-Isopropyloxazolin-2-yl]-(R_p)-2-morpholinomethylferrocene (7): Orange solid; M.p. 61−62 °C. $[\alpha]_D^{20} = -10.6$ ($CHCl_3$, $c = 0.34$). IR (CCl_4): $\tilde{\nu} = 1915\ cm^{-1}$ (m), 1665 (s, C=N), 1570 (m), 1465 (m), 1295 (m), 1270 (m), 1215 (m), 1130 (s), 1110 (s). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.94 (d, ^3J = 6.6 Hz, 3 H, CH_3), 1.01 (d, ^3J = 6.9 Hz, 3 H, CH_3), 1.79 [m, 1 H, C*H*(CH_3)$_3$], 2.38−2.57 (m, 4 H, CH_2−N−CH_2), 3.39 (d, ^2J = 12.9 Hz, 1 H, FcCH*H*), 3.65 (m, 4 H, CH_2−O−CH_2), 3.95−4.04 (m, 2 H, N−CH, O−CH*H*), 4.13 (s, 5 H, C_5H_5), 4.17 (d, ^2J = 13.1 Hz, 1 H, FcC*H*H), 4.26−4.29 (m, 2 H, O−C*H*H, Fc), 4.27 (t, ^3J = 2.5 Hz, 1 H, C_5H_3), 4.36 (dd, ^3J = 2.5, ^4J = 1.4 Hz, 1 H, C_5H_3), 4.69 (dd, ^3J = 2.5, ^4J = 1.4 Hz, 1 H, C_5H_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.4, 19.1 (CH_3), 32.8 [$CH(CH_3)_2$], 53.2 [N(CH_2)$_2$], 56.6 [O(CH_2)$_2$], 67.2 (O−CH_2), 69.2 (N−CH), 69.3 (Fc−CH_2), 70.1 (C_5H_3), 70.3 (C_5H_5), 70.9, 72.6, 73.1, 84.1 (C_5H_3), 165.5 (O−C=N). HR-MS ($C_{21}H_{28}FeN_2O_2$): calcd. 396.1500; found 396.1496.

1-[(*S*)-4-Isopropyloxazolin-2-yl]-(R_p)-2-pyrrolidinomethylferrocene (8): Orange oil. $[\alpha]_D^{20} = +9.6$ ($CHCl_3$, $c = 0.24$). IR (CCl_4): $\tilde{\nu} = 1910\ cm^{-1}$ (m), 1665 (s, C=N), 1560 (m), 1235 (s), 1120 (m), 1080 (m), 1010 (s). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.94 (d, 3 H, *J* 6.6 Hz, CH_3), 1.02 (d, ^3J = 6.6 Hz, 3 H, CH_3), 1.70−1.74 (m, 4 H, CH_2CH_2), 1.80 [m, 1 H, C*H*(CH_3)$_2$], 2.49−2.58 (m, 4 H, CH_2−N−CH_2), 3.49 (d, ^3J = 13.1 Hz, 1 H, FcCH*H*), 4.00 (dd, ^2J = 13.4, ^3J = 7.4 Hz, 1 H, O-CH*H*), 3.90−4.01 (m, 2 H, N−CH), 4.12 (s, 5 H, C_5H_5), 4.23−4.28 (m, 3 H, O−C*H*H, FcC*H*H), 4.25 (t, ^3J = 2.6 Hz, 1 H, C_5H_3), 4.39 (dd, ^3J = 2.6, ^4J = 1.5 Hz, 1 H, C_5H_3), 4.67 (dd, ^3J = 2.6, ^4J = 1.5 Hz, 1 H, C_5H_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.5, 19.2 (CH_3), 23.6 (CH_2CH_2), 32.9 [*C*H(CH_3)$_2$], 53.3 (N−CH), 53.7 [N(CH_2)$_2$], 68.9 (O−CH_2), 69.3, 69.9, 70.2 (C_5H_5), 70.4, 72.7, 72.8, 86.0 (C_5H_3), 165.6 (O−C=N). HR-MS ($C_{21}H_{28}FeN_2O$): calcd. 380.1551; found 380.1551.

Acknowledgments

We thank Prof. Hans Günter Schmalz (University of Cologne) and Dr. Battsengel Gotov for their valuable suggestions and for measuring the HR-MS spectra. This work was supported by the Slovak Grant Agency for Science, grant no. 1/7013/20.

[1] A. Pfaltz, *Acc. Chem. Res.* **1993**, *26*, 339−345.
[2] A. K. Ghosh, P. Mathivanan, J. Cappiello, *Tetrahedron: Asymmetry* **1998**, *9*, 1−45.
[3] For a review see: G. Helmchen, A. Pfaltz, *Acc. Chem. Res.* **2000**, *33*, 336−345.
[4] T. Sammakia, H. A. Latham, D. R. Schaad, *J. Org. Chem.* **1995**, *60*, 10−11.
[5] C. J. Richards, T. Damalidis, D. E. Hibbs, M. B. Hursthouse, *Synlett* **1995**, 74−76.
[6] Y. Nishibayashi, S. Uemura, *Synlett* **1995**, 79−81.
[7] T. Sammakia, H. A. Latham, *J. Org. Chem.* **1995**, *60*, 6002−6003.
[8] C. J. Richards, A. W. Mulvaney, *Tetrahedron: Asymmetry* **1996**, *7*, 1419−1430.
[9] S.-L. You, Y.-G. Zhou, X.-L. Hou, L.-X. Dai, *Chem. Commun.* **1998**, 2765−2766.
[10] S.-L. You, X.-L. Hou, L.-X. Dai, *Tetrahedron: Asymmetry* **2000**, *11*, 1495−1500.
[11] C. Bolm, K. Muniz-Fernandez, A. Seger, G. Raabe, K. Gunther, *J. Org. Chem.* **1998**, *63*, 7860−7868.
[12] For example: M. Woltersdorf, R. Kranich, H.-G. Schmalz, *Tetrahedron* **1997**, *53*, 7219−7230.
[13] A. J. Locke, T. E. Pickett, C. J. Richards, *Synlett* **2001**, 141−143.
[14] G. Solladie, P. Hugele, R. Bartch, *J. Org. Chem.* **1998**, *63*, 3895−3898.

Received September 18, 2001
[O01448]