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SHORT COMMUNICATIONS

Pincers Ligands Based on α-Amino Acids: II.* Synthesis of Polydentate Ligands Based on 1,1'-Diformylferrocene

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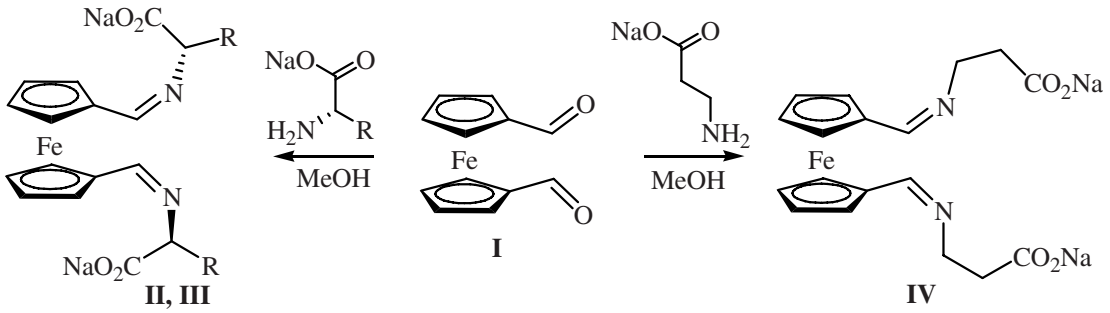
Polydentate ligands based on natural amino acids and their complexes attract much attention as models of the active sites of enzymes [2] and also of centers of chiral induction in asymmetrical catalysis [3–5]. Another interesting aspect of amino acids complexes is their capability to perform chiral recognition of optically active substrates. Artificial receptors for stereoselective recognition of substrates are compexes with polypeptides [6], cyclodextrines derivatives [7], and also chiral cyclic amides [8]. Schiff's bases containing natural amino acids possess good stereoinducing qualities, and therefore they can be used to prepare enantiomeric nonnatural amino acids [3, 6]. Azomethine receptors formed from dicarbonyl compounds and optically active amino acids are potentially capable of chiral recognition of optically active substrates: amino acids and even peptides. The introduction of a ferrocene moiety into the receptor molecule permits designing efficient electrochemical sensors [9].

Published examples exist of Schiff's bases syntheses from amino acids and their esters with 1-formyl ferrocene [10] in a solid phase [11] or by the classical reaction in alcohols [12]. However symmetrical pincers ligands based on dicarbonyl ferrocene derivatives are yet unknown. We used the classical condensation of 1,1'-diformylferrocene with a series of amino acids (β-alanine, L-histidine, and L-methionine) in ethanol for it was known that in the solid-phase synthesis histidine derivatives were capable to form tautomeric products resulting from intramolecular closure of imidazolo[3,4-*c*]pyrimidine ring [11]; the process did not occur in the synteses in solution [12].

In the course of our investigation of symmetrical pincers ligands we synthesized new azomethines based on 1,1'-diformylferrocene (**I**). In reaction of sodium salts of L-methionine, L-histidine, and β-alanine with1,1'-diformylferrocene in anhydrous ethanol in the presence of

Scheme 1.



R = $CH_3SCH_2CH_2$ (**II**), 2-imidazolylmethyl (**III**).

* For Communication I, see [1].

molecular sieves 3A azomethines **II–IV** formed in high yield (60–70%) (Scheme 1).

Schiff's bases salts **II–IV** are dark-brown amorphous substances soluble in polar organic solvents, easily hydrolyzed with water and air moisture. The reduction of azomethines **II–IV** with sodium tetrahydroborate at molar reagents ratio 1:3 in methanol was carried out at –30°C and provided the corresponding aminomethyl ferrocene derivatives **V–VII** (Schemes 2 and 3).

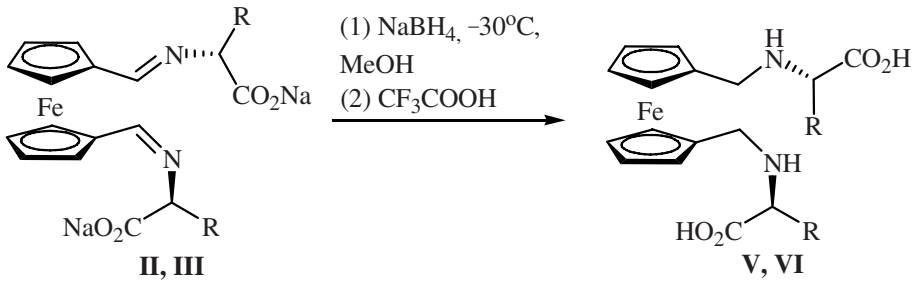
Compound **V** was too poorly soluble to register ^{1}H NMR spectrum, therefore by treating with sodium methylate it was converted into disodium salt $Fe[C_5H_4CH_2NHCH(CH_2CH_2SCH_3)COONa]_2$ (**VIII**).

(*S*,*S*)-1,1'-Bis[(1-carboxy-3-methylsulfanylpropyl)iminomethyl]ferrocene disodium salt (II). To a solution of 0.23 g (10 mmol) of sodium in 100 ml of anhydrous ethanol was added at room temperature 1.49 g (10 mmol) of L-ethionine, and the mixture was stirred for 1 h. To the solution obtained was added 1.21 g (5 mmol) of dialdehyde **I** and 4 g of molecular sieves 3A, the reaction mixture was stirred for 10 h and filtered. The filtrate was evaporated in a vacuum. The precipitate separated at cooling to –30°C was filtered off, washed with ether, and dried in a vacuum. Yield 1.78 g (65%), brown powder, mp 216–218°C (decomp.). IR spectrum (KBr), ν, cm^{-1}: 1590 (C=O), 1637 (C=N). ^{1}H NMR spectrum (MeOH-d_4), δ, ppm: 2.10 s (6H, $2CH_3$), 2.12–2.70 m (8H, $4CH_2$), 3.85 t (2H, 2CH, *J* 6.4 Hz), 4.50 br.s (4H, $2C_5H_4$), 4.79 br.s (4H, $2C_5H_4$), 8.16 s (2H, 2CH=N). Found, %: C 48.33; H 4.91; N 4.90. $C_{22}H_{26}FeN_2Na_2O_4S_2$. Calculated, %: C 48.18; H 4.78; N 5.11.

***S*,*S*)-1,1'-Bis{[1-carboxy-2-(2-imidazolyl)ethyl]iminomethyl}ferrocene disodium salt (III)** was prepared similarly from 1.55 g (10 mmol) of L-histidine and 1.21 g (5 mmol) of dialdehyde **I**. Yield 1.68 g (60%), brown powder, mp 155–157°C (decomp.). IR spectrum (KBr), ν, cm^{-1}: 1593 (C=O), 1635 (C=N). ^{1}H NMR spectrum (MeOH-d_4), δ, ppm: 3.20 d (4H, $2CH_2$, *J* 6.1 Hz), 3.92 t (2H, 2CH, *J* 6.7 Hz), 4.43 br.s (4H, $2C_5H_4$), 4.62 br.s (4H, $2C_5H_4$), 6.83 s (2H, 2CH), 7.56 s (2H, 2CH), 7.92 s (2H, 2CH=N). Found, %: C 51.63; H 4.18; N 14.81. $C_{24}H_{22}FeN_6Na_2O_4$. Calculated, %: C 51.45; H 3.96; N 15.00.

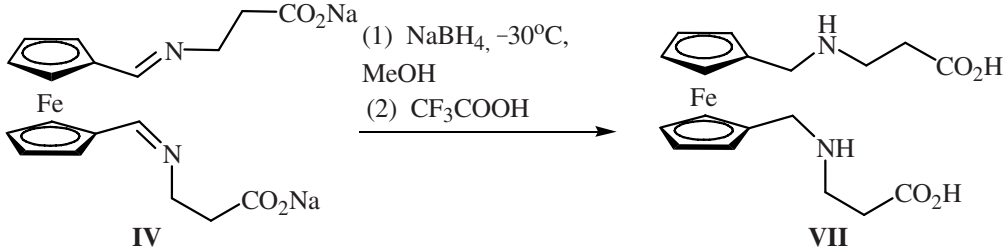
1,1'-Bis(2-carboxyethyliminomethyl)ferrocene disodium salt (IV) was prepared similarly from 0.89 g (10 mmol) of β-alanine and 1.21 g (5 mmol) of dialdehyde **I**. Yield 1.50 g (70%), brown powder, decomposed without melting. IR spectrum (KBr), ν, cm^{-1}: 1563 (C=O), 1644 (C=N). ^{1}H NMR spectrum NMR spectrum (MeOH-d_4), δ, ppm: 2.49 t (4H, $2CH_2$, *J* 7.0 Hz), 3.69 t (4H, $2CH_2$, *J* 7.1 Hz), 4.45 t (4H, $2C_5H_4$, *J* 1.8 Hz), 4.70 t (4H, $2C_5H_4$, *J* 1.8 Hz), 8.18 C (2H, 2CH=N). Found, %: C 50.67; H 4.48; N 6.27. $C_{18}H_{18}FeN_2Na_2O_4$. Calculated, %: C 50.49; H 4.24; N 6.54.

Scheme 1.



II, III **V, VI**

Scheme 2.



IV **VII**

R = $CH_3SCH_2CH_2$ (**V**), 2-imidazolylmethyl (**VI**).

(*S*,*S*)-1,1'-Bis[(1-carboxy-3-methylsulfanylpropyl)aminomethyl]ferrocene (V). To a solution of 1.37 g (2.5 mmol) of azomethine **II** in 75 ml of anhydrous methanol cooled to –30°C was added at vigorous stirring 0.285 g (7.5 mmol) of $NaBH_4$. The reaction mixture was stirred at –30°C for 1 h, and the temperature was raised to ambient. To the filtrate was added dropwise 1.425 g (12.5 mmol) of trifluoroacetic acid. The separated precipitate was filtered off, washed with methanol, with ether, and dried in a vacuum. Yield 1.02 g (80%), light-brown powder, mp 198–200°C (decomp.). Found, %: C 52.14; H 6.51; N 5.39. $C_{22}H_{32}FeN_2O_4S_2$. Calculated, %: C 51.97; H 6.34; N 5.51.

(*S*,*S*)-1,1'-Bis{[1-carboxy-2-(2-imidazolyl)ethyl]aminomethyl}ferrocene (VI) was similarly obtained from 1.4 g (2.5 mmol) of azomethine **III** and 0.285 g (7.5 mmol) of $NaBH_4$. The reaction product was precipitated by acetone. Yield 0.74 g (57%), light-brown powder, mp 170–173°C. ^{1}H NMR spectrum (D_2O), δ, ppm: 3.17 d (4H, $2CH_2$, *J* 6.2 Hz), 3.83 t (2H, 2CH, *J* 6.7 Hz), 4.05 s (4H, $2CH_2$), 4.39 br.s (8H, $2C_5H_4$), 7.03 s (2H, 2CH), 7.76 s (2H, 2CH). Found, %: C 55.59; H 5.71; N 16.00. $C_{24}H_{28}FeN_6O_4$. Calculated, %: C 55.40; H 5.42; N 16.15.

1,1'-Bis[(2-carboxyethyl)aminomethyl]ferrocene (VII) was similarly obtained from 1.07 g (2.5 mmol) of azomethine **IV** and 0.285 g (7.5 mmol) of $NaBH_4$. Yield 0.58 g (60%), light-brown powder, mp 225–227°C (decomp.). ^{1}H NMR spectrum (D_2O), δ, ppm: 2.57 t (4H, $2CH_2$, *J* 6.6 Hz), 3.22 t (4H, $2CH_2$, *J* 6.5 Hz), 4.15 s (4H, $2CH_2$), 4.45 br.s (4H, $2C_5H_4$), 4.51 br.s (4H, $2C_5H_4$). Found, %: C 55.83; H 6.17; N 6.98. $C_{18}H_{24}FeN_2O_4$. Calculated, %: C 55.69; H 6.23; N 7.22.

1,1'-Bis[(1-carboxy-3-methylsulfanylpropyl)aminomethyl]ferrocene disodium salt (VIII). To a solution of 0.046 g (2 mmol) of sodium in 50 ml of methanol was added 0.51 g (1 mmol) of amine **V**. The reaction mixture was stirred for 2 h and filtered. The filtrate was concentrated in a vacuum. The separated precipitate was filtered off, washed with acetone, and dried in a vacuum. Yield 0.47 g (85%), light-brown powder, decomposed without melting. ^{1}H NMR spectrum (D_2O), δ, ppm: 1.68–2.06 m (4H, $2CH_2$), 2.17 C (6H, $2CH_3$), 2.56 t (4H, $2CH_2$, *J* 7.8 Hz), 3.24 t (2H, 2CH, *J* 7.1 Hz), 3.53 d (4H, $2CH_2$, *J* 6.1 Hz), 4.29 br.s (4H, $2C_5H_4$), 4.33 br.s (4H, $2C_5H_4$). Found, %: C 48.06; H 5.70; N 5.16. $C_{22}H_{30}FeN_2Na_2O_4S_2$. Calculated, %: C 47.83; H 5.47; N 5.07.

IR spectra of compounds were recorded on an IR Fourier spectrophotometer Protege-460. ^{1}H NMR spectra were registered on spectrometers Bruker Avance-400 and Tesla BS-567A. The synthesis of 1,1'-diformylferrocene was carried out by procedure [13]. All syntheses were performed in anhydrous solvents under an argon atmosphere.

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