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Ferrocene Compounds. II.* 1,1'-Diacetylferrocene and Diethyl Oxalate Condensation Products and their Derivatives

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By the reaction of 1,1′-diacetylferrocene with diethyl oxalate, γ,γ′-(1,1′-ferrocenylene)-bis(α,γ-dioxobutyric acid) (I) and its diethyl ester II were prepared in yields of 52 and 54% respectively. The polyoxo compounds I and II were converted by the action of suitable reagents into 1,1′-bis[3(5)-carboxyhydrazido-5(3)-pyrazolyl]ferrocene (III), 1,1′-bis[3(5)-carbethoxy-5(3)-pyrazolyl]-ferrocene (IV), 1,1′-bis[2-oxo-3-piperazinylideneacetyl]ferrocene (V), 1,1′-bis[3(5)-carbethoxy-1-phenyl-5(3)-pyrazolyl]ferrocene (VI) and 1,1′-bis[3(5)-carbethoxy-5(3)-isoxazolyl]ferrocene (VII).

As a part of a research program on polyoxo compounds in the chemistry of ferrocene, the condensation of 1,1′-diacetylferrocene[1] with diethyl oxalate has been studied. γ,γ′-(1,1′-Ferrocenylene)-bis(α,γ-dioxobutyric acid) (I) and its diethyl ester II were obtained in yields of 52 and 54% respectively.

By the reaction of hydrazine with I and II, heterocyclic systems containing ferrocene residues have been prepared as 1,1′-bis[3(5)-carboxyhydrazido-5(3)-pyrazolyl]ferrocene (III) and 1,1′-bis[3(5)-carbethoxy-5(3)-pyrazolyl]ferrocene (IV). 1,1′-Bis[3(5)-carbethoxy-1-phenyl-5(3)-pyrazolyl]ferrocene (V), 1,1′-bis[2-oxo-3-piperazinylideneacetyl]ferrocene (VI) and 1,1′-bis[3(5)-carbethoxy-5(3)-isoxazolyl]ferrocene (VII) have been prepared by cyclization of II with phenylhydrazine hydrochloride, ethylenediamine[2] and hydroxylamine hydrochloride, respectively.

The general method available for the synthesis of polyoxo compounds, initially employed by Brömme and Claisen[3] for the condensation of acetophenone with diethyl oxalate, has been applied for the preparation of I and II.

In accordance with examples in the literature[4] it has been found that both methyl ketone groups of diacetylferrocene are converted to the corresponding bis β-diketones I and II with diethyl oxalate. The support for structures of I and II is their conversion to the corresponding heterocyclic compounds III—VII, IR and NMR data.

The ethoxy group of the ester II is identified by the typical four-three pattern of resonance lines at τ 5.6 and 8.6. The presence of the enol form of compound II is shown by the small band at τ — 3.8 for the hydrogen bonded hydroxyl proton and by a band at τ 3.5 for the α-proton.

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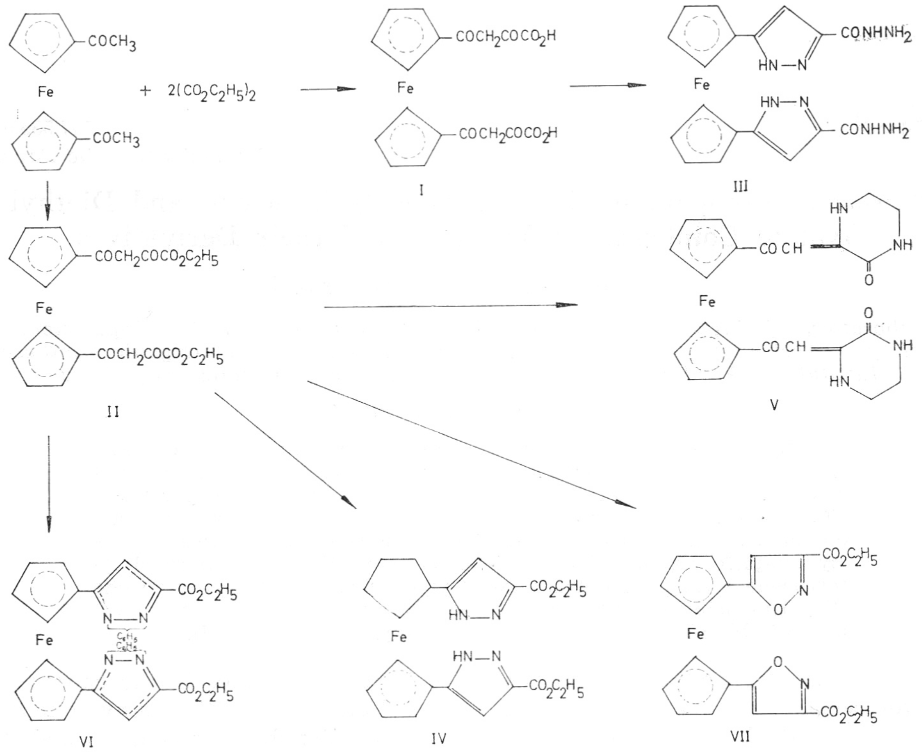
* The paper cited under 9. should be referred to as part I of this series.



The sample I was only partly soluble in suitable solvents and its chemical shifts could not be measured.

Spectroscopic evidence supports the structure of V. The IR spectrum shows the following bands, characteristic for oxo derivatives of piperazine[5]: 3250, 1690, 1450, 1350, 964 and 828 cm^{-1}. The UV spectrum * [λ_{max} 250 mμ (ε 13 000), λ_{max} 366 mμ (ε 26 900)] corresponds to the spectrum of 3-benzoylmethylene-2-piperazinone [λ_{max} 258 mμ (ε 6400), λ_{max} 370 mμ (ε 17 000)][2].

NMR data** indicate the protons of both ferrocenic and piperazinic rings with side chain. The chemical shifts of eight protons belonging to cyclopentadienyl rings of the compound V are the same as those of 1,1′-diacetylferrocene.[6]

	Chemical shifts at ring positions, τ	
1,1′-Diacetylferrocene	5.23 (t)	5.49 (t)
Compound V	5.27 (t)	5.58 (t)

The side chain protons and the piperazinic ring protons appear at standard positions (τ): 6.59 (ring CH$_2$)[7], 3.94 (CH), 1.21 and 1.6 (enol OH, hydrogen on a lactam nitrogen).

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* The UV spectrum (in dioxane) was recorded with a Perkin-Elmer UV/VIS Model 137 spectrometer.

** NMR spectra were performed on a Varian A-60*A* instrument using deuteriochloroform as a solvent for compound II, deuteriodimethylsulfoxide as a solvent for compound V and tetramethylsilane as an internal standard.

EXPERIMENTAL

The melting points are uncorrected. All IR spectra were recorded as KBr pellets with a Perkin-Elmer Infracord Model 137 spectrometer.

γ,γ'-(1,1'-Ferrocenylene)-bis(α,γ-dioxobutyric acid) (I)

To a boiling solution of sodium ethoxide in ethanol [from 3.68 g. (0.16 mole) sodium and 50 ml. of abs. ethanol] in a round bottom flask equipped with a reflux condenser, a solution of 10.8 g. (0.04 mole) of 1,1'-diacetylferrocene[8] in 100 ml. of abs. ethanol was added, followed by 10.8 ml. (0.08 mole) of diethyl oxalate which was added dropwise through the condenser during half an hour. The reaction mixture was refluxed during a subsequent hour under shaking and allowed to stand at room temperature overnight and then evaporated to dryness *in vacuo*. The residue was pulverized and suspended in 5 litres of ice-cold water, and the insoluble material filtered from the solution. The by-products were precipitated by acidification with diluted acetic acid under vigorous mixing and cooling with ice and separated by filtration. The addition of 20% hydrochloric acid to the filtrate precipitated 8.5 g., 52% of crude acid I. By recrystallization from abs. ethanol, a violet substance with m. p. 150—153° was obtained. IR spectrum: 3100—2500 w (dimeric carboxyl CO), 1740 s (carboxyl CO), 1620 s (enol CO), 930 w (carboxyl and enol OH) cm^{-1}.

Anal. $C_{18}H_{14}FeO_8$ (414.14) calc'd.: C 52.00; H 3.41%
found: C 51.76; H 3.41%

Diethyl γ,γ'-(1,1'-ferrocenylene)-bis(α,γ-dioxobutyrate) (II)

To an ethanol solution of sodium ethoxide [from 1.37 g. (59.4 Mmole) of sodium and 30 ml. of abs. ethanol] in a round bottom flask externally cooled with ice, a suspension of 8.0 g. (29.7 Mmole) of 1,1'-diacetylferrocene in 100 ml. abs. ethanol is added, followed by 8.2 ml. (59.4 Mmole) of diethyl oxalate, added dropwise through the condenser during half an hour under vigorous shaking which was continued during a subsequent hour. The reaction mixture was allowed to stand for two days at room temperature with occasional shaking and then evaporated *in vacuo* without heating. The pulverized raw material was suspended in 5—6 litres of ice-cold water and the insoluble material filtered from the solution. Under cooling with ice and vigorous shaking the filtrate was acidified to *p*H 4 with diluted acetic acid and left to stand overnight; 7.5 g. (54%) of the ester was filtered off and recrystallized from abs. ethanol.

Deep-violet substance m. p. 111—115° (> 95° with carbonization) was obtained. IR spectrum: 1740 s (carboxyl CO), 1610 s (enol CO), 940 w (enol OH) cm^{-1}.

Anal. $C_{22}H_{22}FeO_8$ (470.25) calc'd.: C 56.18; H 4.72%
found: C 56.43; H 4.48%

1,1'-Bis[3(5)-carboxyhydrazido-5(3)-pyrazolyl]ferrocene (III)

To a boiling solution of 0.5 g. (1.21 Mmole) of II in 150 ml. abs. ethanol, 0.15 g. (48.4 Mmole) of 95% hydrazine mixed with 2 ml. abs. ethanol and a drop of glacial acetic acid were added. The reaction mixture was refluxed for 10 minutes, cooled down to the room temperature and allowed to stand overnight. A yellow orange crystalline substance was filtered off (0.4 g., 76.5%).

By recrystallization from *N,N*-dimethyl formamide a yellow crystalline substance m. p. > 300° (with carbonization) was obtained. IR spectrum: 3250 b (with a shoulder at 3380), 1660 s (amide I), 1550 m (amide II), 1630 m (pyrazolic C = N), 1460 w (unassigned pyrazolic band) cm^{-1}.

Anal. $C_{18}H_{18}FeN_8O_2$ (434.24) calc'd.: C 49.79; H 4.21; N 25.80%
found: C 49.82; H 4.52; N 25.70%

1,1'-Bis[3(5)-carbethoxy-5(3)-pyrazolyl]ferrocene (IV)

To a boling solution of 2.0 g. (4.22 Mmole) of the ester II in 300 ml. abs. ethanol, a solution of 0.27 g. (8.44 Mmole) 96% hydrazine in 8 ml. abs. ethanol and a drop of glacial acetic acid were added. The reaction mixture was refluxed for half an hour, filtered, slowly cooled down to room temperature and allowed to stand overnight in a refrigerator; the crude product (1.1 g., 56%) was filtered off. By recrystallization from dioxane, a yellow substance, m. p. > 270° (with carbonization) was obtained.

IR spectrum: 1720 s (carbethoxyl CO), 1250 s (C—O ester), 1620 w (pyrazolic C=N), 1540 (pyrazolic C=C), 1420 (unassigned pyrazolic band) cm^{-1}.

Anal. $C_{22}H_{22}FeN_4O_4$ (462.30) calc'd.: C 57.17; H 4.80; N 12.13%
found: C 57.01; H 5.12; N 12.59%

1,1'-Bis[2-oxo-3-piperazinylideneacetyl]ferrocene (V)

Into a boiling solution of 1.0 g. (2.12 Mmole) of the ester II in 100 ml. abs. ethanol, a solution of 0.36 g. (6.0 Mmole) of ethylenediamine in 3 ml. abs. ethanol was added. The reaction mixture was refluxed for 2 hours and the solvent evaporated *in vacuo* until dry. The residue was treated with 2*N* hydrochloric acid, filtered off and washed with water until neutral (0.7 g., 71%). By recrystallization from dioxane, a red substance m. p. 270° (with carbonization) was obtained. The spectral data are presented in the theoretical part of this paper.

Anal. $C_{22}H_{22}FeN_4O_4$ (462.28) calc'd.: C 57.17; H 4.80; N 12.13%
found: C 57.64; H 5.07; N 12.52%

1,1'-Bis[3(5)-carbethoxy-1-phenyl-5(3)-pyrazolyl]ferrocene (VI)

Into a boiling solution of 4.0 g. (8.5 Mmole) of the ester II in 400 ml. abs. ethanol, 4.91 g. (34.0 Mmole) of phenylhydrazine hydrochloride in 100 ml. boiling abs. ethanol was added. The reaction mixture was refluxed for an hour, slowly cooled down to room temperature and allowed to stand overnight in a refrigerator. The crude yellow crystalline substance was filtered off (2.7 g., 52%). From the filtrate an additional quantity of yellow-brownish substance (total yield 81%) was precipitated on addition of water. By recrystallization from dioxane, a yellow crystalline substance, m. p. 205—208°, was obtained. IR spectrum: 1710 s (carbethoxyl CO), 1250 s (C—O ester), 1620 w (pyrazolic C=N), 1570 w (pyrazolic C=C), 1450 w (unassigned pyrazolic band) cm^{-1}.

Anal. $C_{34}H_{30}FeN_4O_4$ (614.46) calc'd.: C 66.45; H 4.92; N 9.12%
found: C 66.05; H 5.17; N 9.18%

1,1'-Bis[3(5)-carbethoxy-5(3)-isoxazolyl]ferrocene (VII)

To a boiling solution of 1.5 g. (3.19 Mmole) of the ester II in 100 ml. abs. ethanol, 0.442 g. (6.4 Mmole) of hydroxylamine hydrochloride in 5 drops of water was added. The reaction mixture was refluxed for 5 hours. After cooling to room temperature and standing in a refrigerator overnight, red needle-shaped crystals were filtered off (1.0 g., 67%). By recrystallization from abs. ethanol, a red crystalline substance, m. p. 227—229°, was obtained.

IR spectrum: 1750 s (carbethoxyl CO), 1250 s (C—O ester), 1620 m, 1500 m, 1400 w (ring stretching band for isoxazole) cm^{-1}.

Anal. $C_{22}H_{18}FeN_2O_6$ (462.23) calc'd.: C 57.16; H 3.92; N 6.06%
found: C 56.90; H 4.35; N 6.18%

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IZVOD

Kondenzacioni produkti 1,1'-diacetilferocena i dietiloksalata i njihovi derivati

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Kondenzacijom 1,1'-diacetilferocena i dietiloksalata pripravljeni su γ,γ'-(1,1'-ferocenilen)-bis(α,γ-dioksomaslačna kiselina) (I) i njen dietilni ester (II). Ovi poliokso-spojevi prevedeni su djelovanjem pogodnih reagensa u 1,1'-bis[3(5)-karboksihidrazido-5(3)-pirazolil]ferocen (III), 1,1'-bis[3(5)-karbetoksi-5(3)-pirazolil]ferocen (IV), 1,1'-bis[(2-okso-3-piperazinilidenacetil)]ferocen (V), 1,1'-bis[3(5)-karbetoksi-1-fenil-5(3)-pirazolil]ferocen (VI) i 1,1'-bis[3(5)-karbetoksi-5(3)-izoksazolil]ferocen (VII).

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