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Ferrocene Compounds. IV*. Reactions of Ferrocene with Glutaryl Chloride

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The reactions of ferrocene with glutaryl chloride, in the presence of aluminium chloride, were investigated. Depending upon the reaction conditions and the molar ratios of reactants, δ-ferrocenyl-δ-oxovaleric acid (I), 1,5-diferrocenyl-1,5-pentanedione (III) (the product of intermolecular acylation), and homoannularly cyclized 1,2-(α,ε-dioxopentamethylene)ferrocene (V) were obtained. These reactions proceeded via δ-ferrocenyl-δ-oxovaleric acid chloride (Ia).

INTRODUCTION

The Friedel-Crafts acylation of ferrocene with dicarboxylic acid anhydrides or halfester halides for preparation of ω-ferrocenyl-ω-oxoaliphatic acids, and their subsequent reduction to appropriate ω-ferrocenilaliphatic acids, have been reported in several papers[1-3].

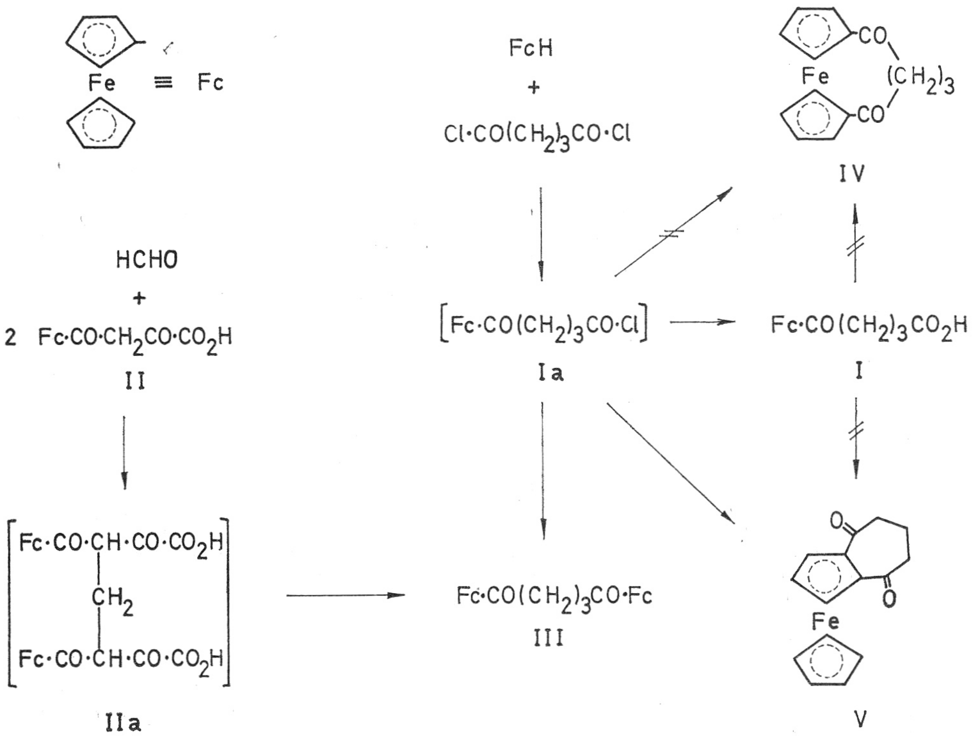
By the action of either trifluoroacetic acid anhydride or polyphosphoric acid, it was shown that these ferrocenylaliphatic acids gave products with either a heteroannular or a homoannular ring closure or polymers, depending on the aliphatic chain length[4-6]. In the literature there is no example of a successful cyclization of ω-ferrocenyl-ω-oxoaliphatic acids. Nesmeyanov et al.[3] assumed that such reactions are inhibited because of the deactivating influence of the carbonyl group on the ferrocene nucleus.

The Japanese authors[7] have showed that the reaction of ferrocene with succinyl chloride gives γ-ferrocenyl-γ-oxobutyric acid, γ,γ-diferrocenylbutyrolactone, and 1,4-diferrocenyl-1,4-butanedione, but they have not isolated the products of intramolecular cyclization.

RESULTS AND DISCUSSION

We should like to report the reactions of ferrocene with glutaryl chloride in order to find out the possibility of the formation of the intramolecularly cyclized specimens IV or V.

Refluxing ferrocene, glutaryl chloride, and aluminium chloride in the molar ratio 2 : 1 : 2 in methylene chloride, 1,5-diferrocenyl-1,5-pentanedione (III), (42%) and a small amount of δ-ferrocenyl-δ-oxovaleric acid (I) were obtained. The identical compound (III) can be prepared in a good yield by the base-catalyzed condensation of γ-ferrocenyl-α,γ-dioxobutyric acid (II)[8]



with 35% aqueous formaldehyde, and subsequent treatment of the reaction mixture with concentrated aqueous sodium hydroxyde. This reaction probably proceeds via intermediate IIa, which is cleaved by the action of aqueous sodium hydroxyde to III. The diketone III was characterized by its dioxime (IIIa) and mono(2,4-dinitrophenylhydrazone) (IIIb).

In order to increase the possibility of the intramolecular cyclization of ferrocene with glutaryl chloride, we worked under the conditions of diacylation[9]. The reaction of ferrocene, glutaryl chloride and aluminium chloride in molar ratio 1 : 1.4 : 2.5 in methylene chloride gave the mixture od 24.4% of the keto acid I and 8.4% of 1,2-(α,ε-dioxopentamethylene)ferrocene (V). The presence of heteroannularly bridged 1,1′-(α,ε-dioxopentamethylene)ferrocene (IV) (which can be prepared by base-catalyzed condensation of 1,1′-diacetylferrocene with formaldehyde[10]) was not observed.

The structure of diketone V was supported from its dioxime derivative (Va), molecular weight measurement, and from spectral data. The ir. spectrum of V is related to the spectrum of known 1,2-(α-oxopentamethylene)ferrocene (VI)[5]: the two absorption bands characteristic for carbonyl group (at about 1660 and 1290 cm^{-1}) as well as the bands indicating the homoannular substitution[11] (at about 1100 and 1000 cm^{-1}) are present in both spectra. The absorption maximum at 225 nm in the uv. spectrum of diketone V is near to the maximum of the related ketone VI ($\lambda_{max} = 227$ nm). The methylene proton signals in the NMR spectra of compound V and 1,5-diferrocenyl-1,5-pentanedione (III) have similar chemical shifts which appear at standard positions (τ): multiplets at about 7.00—7.30 (both methylenes next to carbonyl groups) and at about 7.70—8.20 (the third aliphatic methylene) ppm. In the spectrum of diketone V the five protons belonging to the unsubstituted ferrocene ring give a singlet at 5.82 ppm. The three protons of the other symmetrically 1,2-diacylated ferrocene ring give signals as two lines at $\tau = 5.27$ (2 H) and three lines at $\tau = 5.60$ (1 H). As compared to the A_2B_2 system of monoacyl substituted ferrocene ring[12] the present pattern indicates an A_2B spin system with $J_{AB} (\nu_A - \nu_B) = 0.05$[13].

In conclusion it can be stated that the reactions of ferrocene with glutaryl chloride gave, depending on reaction conditions and molar ratios of reactants, δ-ferrocenyl-δ-oxovaleric acid (I), 1,5-diferrocenyl-1,5-pentanedione (III), and 1,2-(α,ε-dioxopentamethylene)ferrocene (V). Following the course of these reactions by thin layer chromatography[14], and analysing the ir. spectra of intermediate (I), it was concluded that they proceeded via unisolated δ-ferrocenyl-δ-oxovaleric acid chloride (Ia).

Attempts to cyclize δ-ferrocenyl-δ-oxovaleric acid (I) to IV or V, by the action of either trifluoroacetic acid anhydride or polyphosphoric acid, were unsuccessful.

EXPERIMENTAL

The melting points were determined on a Kofler heating microscope and are uncorrected. The ir. spectra were recorded as KBr pellets with a Perkin-Elmer Infracord Model 137 spectrometer. The uv. spectrum of compound V (in ethanol) was measured on a Perkin-Elmer UV/VIS Model 124 spectrophotometer. The NMR spectra (in deuteriochloroform solution) were recorded on a Varian A-60 spectrometer with tetramethylsilane as internal standard. The molecular weight of V (in chloroform) was recorded on a Perkin-Elmer Model 115 Molecular weight apparatus by vapor pressure method. Thin-layer chromatography (TLC) was done on chromatoplates of silicagel G (Merck) in benzene — ethanol (30 : 1 and 15 : 1)[14].

γ-Ferrocenyl-α,γ-dioxobutyric acid (II) was prepared from acetylferrocene and diethyl oxalates according to the procedure described in Part I[8] of this series.

Reaction of ferrocene with glutaryl chloride in the molar ratio 2 : 1

To a vigorously stirred solution of 2.2 g (12 mmol) of ferrocene in 20 ml of methylene chloride 1.6 g (12 mmol) of aluminium chloride was added under an atmosphere of nitrogen. Then, 1.0 g (6 mmol) of glutaryl chloride, dissolved in 10 ml of the same solvent, was dropped in under the same conditions during 1/2 hour. The course of the reaction was followed by pouring aliquots of the reaction mixture from time to time into cold water, and extracting with ether. TLC of ether extracts in the beginning of the reaction indicated δ-ferrocenyl-δ-oxovaleric acid (I) as the main product (by comparison with the R_f-value of authentic specimen I[2]). The ether extracts were evaporated and separated from unreacted ferrocene by dissolving residues in sodium carbonate solution, followed by neutralization with diluted hydrochloric acid. The ir. spectra of the samples obtained in this manner were identical with those of the authentic specimen I[2].

This strongly indicates the presence of the keto acid chloride (Ia) in the reaction mixture during the initial period of reaction. After refluxing for 2 hours, the reaction mixture was cooled and poured onto crushed ice and water. On removal of the aqueous layer, the methylene chloride solution was washed with water and separated into a neutral and an acidic fraction by extraction with 25 ml of 25% aqueous sodium carbonate. The acid fraction, on neutralization with diluted hydrochloric acid, gave 0.2 g (5.7%) of δ-ferrocenyl-δ-oxovaleric acid (I); m. p. 134—136 °C (lit.[2] 136—137 °C); the ir. spectrum shows bands as quoted in the reference[2] (3060 m, 1706 s, 1667 s, 1108 w, 1006 w, 824 s cm^{-1}).

The neutral fraction was washed with water, and dried over sodium sulfate; after evaporation of the solvent in *vacuo* until dry, 1.2 g (42.0%) of 1,5-diferrocenyl-

-1,5-pentanedione (III) was isolated; yellow-brownish glittering crystals (from 75% aqueous ethanol); m. p. 130—132 °C; ir. spectrum: 1655 s (ketone CO) cm^{-1}.

Anal. $C_{25}H_{24}Fe_2O_2$ (468.1) calc'd.: C 64.14; H 5.17%
found: C 64.36; H 5.47%

1,5-Diferrocenyl-1,5-pentanedione (III)

To a solution of 1.2 g (4 mmol) of γ-ferrocenyl-α,γ-dioxobutyric acid (II) in 10 ml of 96% ethanol, 0.16 g (2 mmol) of 35% aqueous formaldehyde and several drops of aqueous diethylamine were added. The reaction mixture was left to stand at room temperature for 2 days. Then, it was treated with concentrated aqueous sodium hydroxide to precipitate a yellow-brownish flocculated substance, which was filtered off and washed with water until neutral; yield 0.6 g (64.5%) of diketone III. The substance is identical to the main product (III) of the preparation described above [mixed melting points, ir. spectra, and R_f values (TLC)].

1,5-Diferrocenyl-1,5-pentanedione dioxime (IIIa)

To prepare dioxime (IIIa), 0.5 g of hydroxylamine hydrochloride dissolved in 3 ml of water, and 2 ml of 10% aqueous sodium hydroxide were added to a solution of 0.2 g of diketone III in 10 ml of 96% ethanol. The reaction mixture was refluxed for 2 hours, and evaporated *in vacuo* to a small volume. After recrystallization from ethanol, the yellow crystalline dioxime (m. p. 181.5—182 °C) was obtained; ir. spectrum: 3250 s (oximine OH), 1625 w (oximine C=N), 945 s (oximine NO) cm^{-1}.

Anal. $C_{25}H_{27}Fe_2N_2O_2$ (499.2) calc'd.: C 60.16; H 5.45; N 5.61%
found: C 60.14; H 5.52; N 5.38%

1,5-Diferrocenyl-1,5-pentanedione mono(2,4-dinitrophenylhydrazone) (IIIb)

Compound IIIb was prepared by the action of excess of 2,4-dinitrophenylhydrazine reagent[15] on an ethanolic solution of the diketone III; red-brownish crystalline substance (from benzene), m. p. 187—188 °C; ir. spectrum: 3460 w (hydrazine NH), 1675 m (ketone CO), 1515 s and 1340 s (nitrophenyl NO) cm^{-1}.

Anal. $C_{31}H_{28}Fe_2N_4O_5$ (648.3) calc'd.: C 57.43; H 4.36; N 8.67%
found: C 57.27; H 4.36; N 8.78%

Reaction of ferrocene with glutaryl chloride in molar ratio 1 : 1.4

To a suspension of 40 g (0.30 mol) of aluminium chloride in 120 ml of methylene chloride a solution of 29 g (0.17 mol) of glutaryl chloride was added slowly, dissolving the aluminium chloride. A nitrogen atmosphere and stirring were maintained throughout the reaction. A solution of 22 g (0.12 mol) of ferrocene in 140 ml of the same solvent was added dropwise over a period of 2.5 hours. After 20 hours of stirring the reaction mixture was hydrolyzed by pouring it onto crushed ice. On removal of the aqueous layer the organic phase was washed with water and extracted several times with 10% aqueous sodium carbonate. The acidic fraction after neutralization with dilute hydrochloric acid gave 6.5 g (24.4%) of keto acid I, m. p. 134.5—136 °C (see the above acylation of ferrocene).

The organic phase was then washed with water until neutral, dried over sodium sulfate and evaporated *in vacuo* until dry; the residual resinous substance was dissolved in benzene and chromatographed over alumina (Merck, basic) and eluted as follows: (1) benzene gave 5.5 g of unchanged ferrocene and (2) chloroform gave 2.1 g (8.4%) of 1,2-(α,ε-dioxopentamethylene)ferrocene (V), m. p. 99—100 °C; repeated column chromatography of this material gave red crystalline product melting at 100—101 °C; ir. spectrum: 1660 s and 1293 m (ketone CO) cm^{-1}; measured molecular weight 277 ± 2%.

Anal. $C_{15}H_{14}FeO_2$ (282.1) calc'd.: C 63.86; H 5.00%
found.: C 63.56; H 5.19%

1,2-(α,ε-Dioxopentamethylene)ferrocene dioxime (Va)

Dioxime (Va) was prepared by mixing an aqueous solution of 0.7 g of hydroxylamine hydrochloride with an ethanolic solution of the diketone V. The reaction mixture was adjusted to pH 6—7 by the addition of aqueous sodium hydroxide, and left to stand at room temperature for 24 hours. Then it was concentrated under reduced pressure and diluted with water to precipitate a yellow amorphous substance, m. p. 184—185 °C (recrystallized from ethanol); ir. spectrum: 3240 s (oximine OH), 1630 w (oximine C=N) and 956 m (oximine NO) cm^{-1}.

Anal. $C_{15}H_{16}FeN_2O_2$ (310.1) calc'd.: C 58.09; H 5.20; N 9.03%
found: C 58.17; H 5.00; N 9.04%

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SAŽETAK

Reakcija ferocena s glutaroil-kloridom

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Istraživane su reakcije ferocena s glutaroil-kloridom u prisutnosti aluminijeva klorida. U ovisnosti o reakcijskim uvjetima i molarnim omjerima reaktanata pripravljeni su δ-ferocenil-δ-oksovalerijanska kiselina (I), 1,5-diferocenil-1,5-pentandion (III) (produkt intermolekularnog aciliranja) i homoanularno ciklizirani 1,2-(α,ε-dioksopentametilen)ferocen (V). U ovim reakcijama kao intermedijer nastaje klorid δ-ferocenil-δ-oksovalerijanske kiseline (Ia).

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