

Acid-catalyzed cyclization of 1-chloroacetyl-1'-cinnamoylferrocene and acid-catalyzed condensation of 1-acetyl-1'-chloroacetylferrocene

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Received 7 October 1974

It has been found that the main product of an acid-catalyzed cyclization of 1-chloroacetyl-1'-cinnamoylferrocene is 2-chloro-3-phenyl[5]ferrocenophane-1,5-dione. The acid-catalyzed reaction of 1-acetyl-1'-chloroacetylferrocene with benzaldehyde gives, in addition to 2-chloro-3-phenyl[5]ferrocenophane-1,5-dione, also its acetylation product. Reactions of other 1-acetyl-1'-acylferrocenes with benzaldehyde give also similar acetyl derivatives.

Нашли что основным продуктом кислого катализированной циклизации 1-хлорацетил-1'-цинамоилферроцена является 2-хлор-3-фенил[5]ферроценофан-1,5-дион. При реакции 1-ацетил-1'-хлорацетилферроцена с бензальдегидом, которая катализируется кислотой, кроме 2-хлор-3-фенил[5]ферроценофан-1,5-диона, получается также продукт его ацетилирования. Таким же образом при реакции и других 1-ацетил-1'-ацилферроценов с бензальдегидом были выделены производные, ацетилированные на мостике.

As stated previously [1], by a base-catalyzed cyclization of 1-chloroacetyl-1'-cinnamoylferrocene a cyclopropane derivative is formed. In a subsequent paper [2] it has been showed that the acid-catalyzed cyclization of 1-propionyl-1'-cinnamoylferrocene and 1-acetyl-1'-(α -methylcinnamoyl)ferrocene gives exclusively 2-methyl-3-phenyl[5]ferrocenophane-1,5-diones.

The aim of the present work was to examine whether the cyclization of 1-chloroacetyl-1'-cinnamoylferrocene also results in the formation of cyclopropane derivatives. It was also interesting to find out the nature of the products of acid-catalyzed condensation of 1-acetyl-1'-chloroacetylferrocene with benzaldehyde.

Experimental

The p.m.r. spectra for saturated solutions in deuteriochloroform at 80 MHz and 23°C were obtained with a Tesla BS 487 A spectrometer. Tetramethylsilane was used as an internal standard. Table I contains chemical shifts read with an accuracy of ± 0.1 p.p.m.

Table 1

Chemical shifts and coupling constants found for the substituted [5]ferrocenophane-1,5-diones^a

Com- pound	Alkyl	COCH ₃	H _A	H _B	H _C	H _D	Ferrocene	Phenyl
			<i>J</i> _{AB} , Hz	<i>J</i> _{BC} , Hz	<i>J</i> _{AC} , Hz	<i>J</i> _{DC} , Hz		
<i>II</i>	—	—	3.54 (dd, 1H) 13	2.61 (dd, 1H) 3	4.30 (m, 1H) 12	.29 (d, 1H) 3	4.73 (m, 3H)	7.42 (m, 5H)
<i>III</i>	—	—	2.95 (dd, 2H) 13	2.48 (dd, 2H) 4	4.35 (m, 1H) 11	—	4.60 (m, 4H) 4.90 (t, 4H)	7.35 (m, 5H)
<i>V</i>	1.38 (d, 3H) <i>J</i> _{CH₃H_D} = 7.1 Hz	2.11 (s, 3H) 2.28 (s, 3H)	—	—	6.14 (d, 1H)	3.40 (m, 1H) 9	4.00 (m, 3H) 4.50 (m, 5H)	7.3–7.6 (m, 5H)
<i>VI</i>	0.98 (d, 3H) <i>J</i> _{CH₃H_D} = 7.3 Hz	2.0 (s, 3H) 2.44 (s, 3H)	—	—	5.99 (d, 1H)	3.47 (m, 1H) 10.3	4.59 (m, 4H) 4.73 (m, 1H) 4.80 (m, 1H) 4.94 (m, 2H)	7.40 (m, 5H)
<i>VIII</i>	1.00 (t, 3H) 1.75 (m, 2H)	2.07 (s, 3H) 2.25 (s, 3H)	—	—	6.21 (d, 1H)	3.43 (m, 1H) 8	3.95 (m, 3H) 4.50 (m, 5H)	7.3–7.6 (m, 5H)
<i>IX</i>	0.76 (t, 3H) 1.48 (m, 2H)	2.01 (s, 3H) 2.45 (s, 3H)	— —	— —	6.11 (d, 1H) —	3.44 (m, 1H) 9.7	4.57 (m, 2H) 4.64 (m, 2H) 4.75 (m, 1H) 4.81 (m, 1H) 4.95 (m, 2H)	7.4 (m, 5H)
<i>X</i>	—	2.16 (s, 3H) 2.28 (s, 3H)	— —	— —	— 6.39 (d, 1H)	— 4.92 (d, 1H) 9.4	3.28 (m, 2H) 4.23 (m, 1H) 4.53 (m, 3H) 4.69 (m, 2H)	7.3–7.6 (m, 5H)

^a) Spectral data for *IV* and *VII* (previously published [2]) are not given.
Peak multiplicities: s – singlet; d – doublet; t – triplet; m – multiplet.

Melting points were determined using a Kofler hot stage. Column chromatography on silica gel (Kavalier, Votice) was performed using benzene–ethyl acetate (3–8%) mixtures as the mobile phase.

The starting ferrocene derivatives were prepared as described before [3–5].

Acid-catalyzed cyclization of 1-chloroacetyl-1'-cinnamoylferrocene

A mixture of glacial acetic acid (20 ml) and concentrated sulfuric acid (5 ml) was added during 30 min into a stirred solution of 1-acetyl-1'-cinnamoylferrocene (1.95 g; 0.06 mole) in glacial acetic acid (100 ml). After 24 hrs of continuous stirring the mixture was poured onto crushed ice and extracted with dichloromethane. The extract was thoroughly washed with water, dried with anhydrous sodium sulfate, concentrated, and chromatographed using benzene–ethyl acetate (20 : 1).

Eluted first was 1,1'-(3-phenyl-1,2-cyclopropanedicarbonyl)ferrocene (*I*, 0.1 g; 5.6%) with the m.p. 234–236°C (decomp.) which is in agreement with the value reported previously [1].

Next eluted was *threo*-2-chloro-3-phenyl[5]ferrocenophane-1,5-dione (*II*, 1.65 g; 84.6%), m.p. 206–208°C (from benzene–heptane).

For $C_{21}H_{17}ClFeO_2$ (392.7) calculated: 9.03% Cl, 14.21% Fe; found: 9.04% Cl, 14.16% Fe.

Acid-catalyzed reaction of 1-acetyl-1'-acylferrocenes with benzaldehyde

A mixture of glacial acetic acid (20 ml) and concentrated sulfuric acid (5 ml) was added during 30 min to a stirred solution of 1-acetyl-1'-acylferrocene (0.007 mole; acyl = acetyl, chloroacetyl, propionyl, *n*-butyryl) and benzaldehyde (0.007 mole) in glacial acetic acid (60 ml) while the reaction mixture was cooled with water. The mixture was stirred for 24 hrs, worked up in the usual manner described above, and chromatographed using benzene–ethyl acetate (50 : 1).

Chromatography of the reaction mixture of 1,1'-diacetylferrocene gave 0.54 g (20%) of 3-phenyl[5]ferrocenophane-1,5-dione, identical with the previously described substance [6] (*III*, m.p. 295–296°C, from chloroform), and 0.9 g (47%) of the starting material.

From 1-acetyl-1'-propionylferrocene 0.25 g (10%) of *threo*-2-methyl-3-phenyl[5]ferrocenophane-1,5-dione, identical with the previously described substance [6] (*IV*, m.p. 220–221°C, from ethanol), 1.03 g (52.5%) of the starting material, 0.22 g (6.9%) of 2,2-diacetyl-*erythro*-4-methyl-3-phenyl[5]ferrocenophane-1,5-dione (*V*, m.p. 145–147°C, from acetone–petroleum ether) and 0.33 g (10.4%) of 2,2-diacetyl-*threo*-4-methyl-3-phenyl[5]ferrocenophane-1,5-dione (*VI*, m.p. 164–165°C, from acetone–petroleum ether) was obtained.

For $C_{26}H_{24}FeO_4$ (456.32) calculated: 12.23% Fe; found: for *V* 12.54% Fe, for *VI* 12.69% Fe.

The reaction of 1-acetyl-1'-butyrylferrocene gave 0.15 g (5.72%) of *threo*-2-ethyl-3-phenyl[5]ferrocenophane-1,5-dione (*VII*, m.p. 206–208°C, from ethanol, in agreement with the previously reported data [7]), 1.4 g (68.9%) of the starting material, 0.1 g (3.1%) of 2,2-diacetyl-*erythro*-4-ethyl-3-phenyl[5]ferrocenophane-1,5-dione (*VIII*), and 0.15 g (4.6%) of 2,2-diacetyl-*threo*-4-ethyl-3-phenyl[5]ferrocenophane-1,5-dione (*IX*).

The reaction of 1-acetyl-1'-chloroacetylferrocene gave 1.75 g (79.5%) of the starting material, 0.8 g (29.3%) of *II*, and 0.2 g (5.9%) of 2,2-diacetyl-*erythro*-4-chloro-3-phenyl[5]ferrocenophane-1,5-dione (*IX*, m.p. 170–172°C, from benzene–heptane).

For $C_{25}H_{21}ClFeO_4$ (476.74) calculated: 7.43% Cl, 11.71% Fe; found: 7.63% Cl, 12.23% Fe.

Results and discussion

It can be seen from the data presented (see Experimental), that the acid-catalyzed cyclization of 1-chloroacetyl-1'-cinnamoylferrocene is a smooth reaction giving the expected *threo*-2-chloro-3-phenyl[5]ferrocenophane-1,5-dione (*II*) as the main product. We assume that the halogen-free by-product *I* is a cyclopropane derivative. Its melting point and p.m.r. spectrum differ clearly from those reported previously [1] for 3-phenyl[5]ferrocenophane-2-ene-1,5-dione. The p.m.r. spectrum of *I* differs also from that of 3-phenyl[5]ferrocenophane-1,5-dione (*III*), which may have been formed by cyclization of 1-acetyl-1'-cinnamoylferrocene possibly contaminating the starting 1-chloroacetyl-1'-cinnamoylferrocene. Due to the low solubility of the substance the complete structure determination was not undertaken.

The p.m.r. data (δ): 3.38 (H_A , dd, $J_{AD} \sim 13$ Hz, $J_{AC} \sim 13$ Hz); 2.58 (H_D , dd, $J_{DC} \sim 4$ Hz); 4.28 (H_C , m); 4.65 (Fe, m, 3H); 4.90 (m, 3H); 5.11 (m, 1H); 5.31 (m, 1H); 7.4 (m, 5H, aromatic).

The acid-catalyzed condensation of 1-acetyl-1'-chloroacetylferrocene with benzaldehyde is not such a clearly defined reaction. In addition to the unreacted starting material and *II*, compound *X* was also isolated from this reaction mixture. The p.m.r. spectrum of *X* indicated the presence of two acetyl groups in the molecule. The spectrum shows two singlets (δ 2.16 and 2.28) of the protons of the two acetyl groups and two doublets of H_A and H_C (J_{AC} 9.4 Hz). The H_C proton is considerably deshielded due to the deshielding effect of the carbonyl and phenyl group. Since from J_{AC} alone it was impossible to determine whether the isomer is *threo* or *erythro*

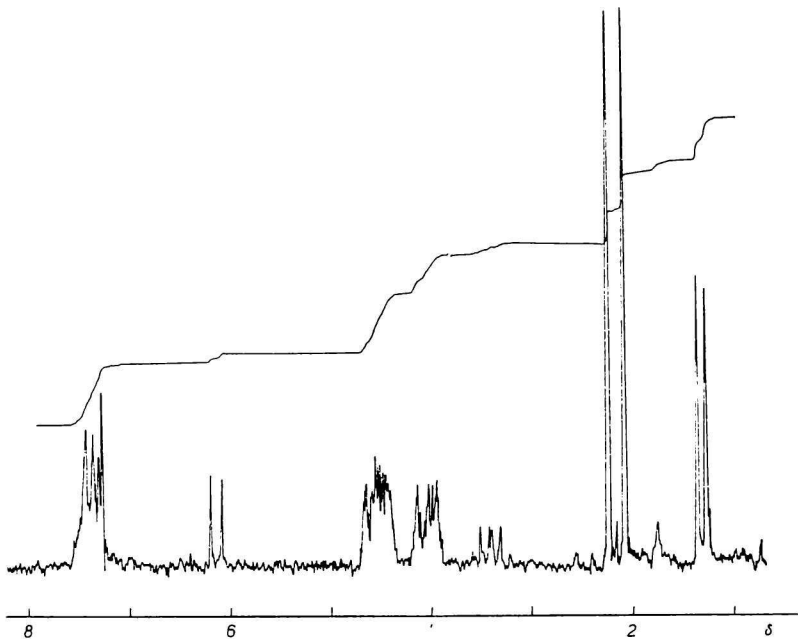


Fig. 1. The p.m.r. spectrum of 2,2-diacetyl-*erythro*-4-methyl-3-phenyl[5]ferrocenophane-1,5-dione (*V*).

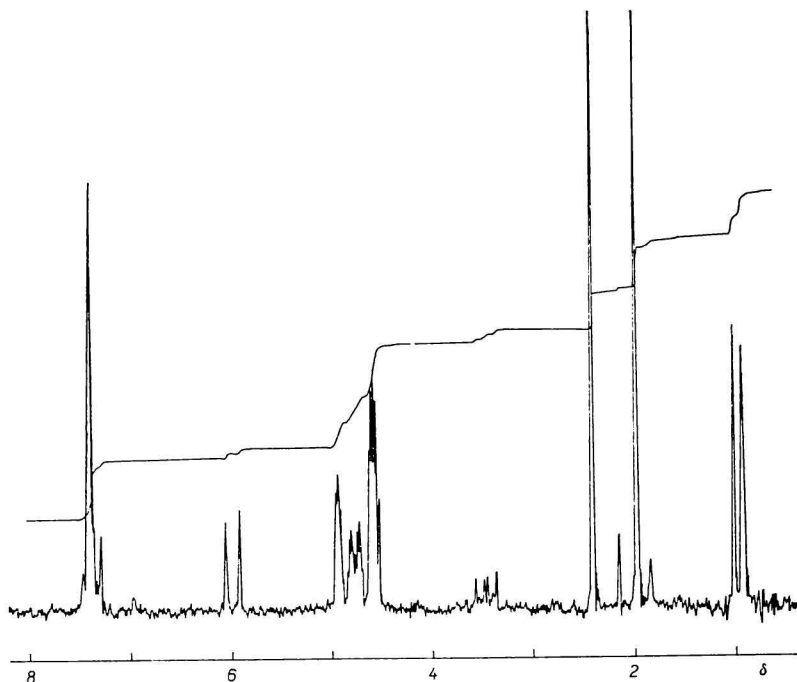


Fig. The p.m.r. spectrum of 2,2-diacetyl-*threo*-4-methyl-3-phenyl[5]ferrocenophane-1,5-dione (VI).

(the coupling constants read from the spectra are very close), the assignments were based on the shape of the resonance signals of the ferrocene and phenyl protons. We have previously observed [2] that in the case of 2-methyl-3-phenyl[5]ferrocenophane-1,5-dione the lower melting isomer has the *threo* configuration. The p.m.r. spectra of all *threo* isomers exhibit the signal of the ferrocene protons in a narrow range of δ 4.5–5.0. In most cases separated multiplets integrating for 4 ($2 \times 1,2$) protons can be observed. In the aromatic region a broad singlet of 5 protons is observed. On the other hand, p.m.r. spectra of the *erythro* isomers exhibit two well separated multiplets of ferrocene protons centered at δ 4 and 4.5 integrating for 3 and 5 protons, respectively. In the aromatic region a multiplet at δ 7.3–7.6 is observed. The structure of 2,2-diacetyl-*erythro*-4-chloro-3-phenyl[5]ferrocenophane-1,5-dione has been assigned to compound X on the basis of its p.m.r. spectrum.

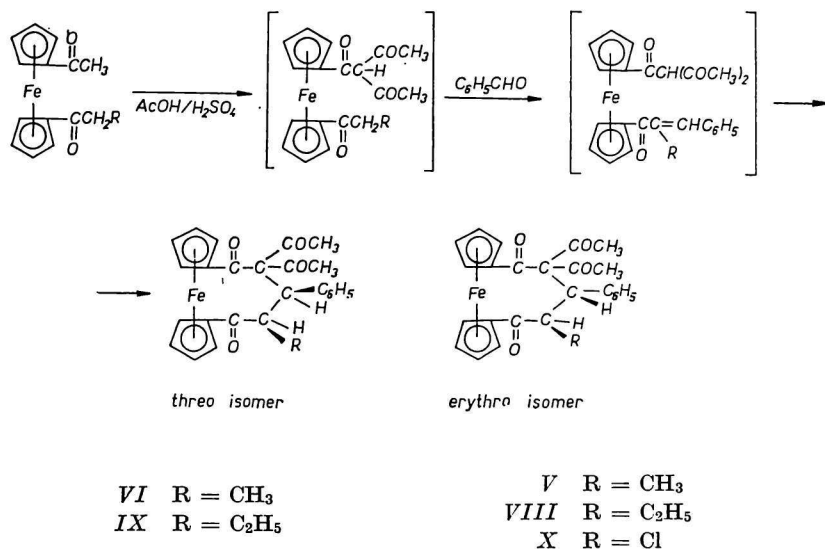
Experiments with the aim to induce base-catalyzed condensation of 1-acetyl-1'-chloroacetylferrocene with benzaldehyde at room and elevated temperature under previously described conditions [7] were also performed. However, the attempts to isolate either the starting material or any cyclization product were unsuccessful. This is rather surprising since condensation of derivatives of bromoacetylbenzene has been described earlier [8]. The product of this reaction was found to be stable under the reaction conditions, and base-catalyzed condensation of 1-acetyl-1'-acylferrocenes [7] did not rise any problems.

The acid-catalyzed condensation of 1-acetyl-1'-acylferrocenes with benzaldehyde proceeds in a manner analogous to the similar condensation of 1-acetyl-1'-chloroacetylferrocene. Most suitable for this type of reaction is 1-acetyl-1'-propionylferrocene which gives, in addition to *threo*-2-methyl-3-phenyl[5]ferrocenophane-1,5-dione (IV), also two diacetyl derivatives. The p.m.r. spectra of these substances clearly differ in the appearance of the resonance signals of the methyl and acetyl protons as well as in the shape and the location of the ferrocene and phenyl protons (Figs. 1 and 2). It seems reasonable to assume that these are acetyl derivatives of *threo*- and *erythro*-2-methyl-3-phenyl[5]ferrocenophane-1,5-diones. The fact that these are true acetyl derivatives and not enol acetates was proved by attempted acid hydrolysis, which left the starting material intact. It may be noted that the isolation of both isomers is a complicated procedure requiring repeated chromatography and fractional crystallization.

1-Acetyl-1'-butyrylferrocene reacted with benzaldehyde in a similar manner giving, however, less of the diacetyl derivatives which are even more difficult to separate than in the previous case. Their presence was proved only by p.m.r. spectroscopy.

From the reaction mixture of the reaction of 1,1'-diacetylferrocene with benzaldehyde only the starting material and 3-phenyl[5]ferrocenophane-1,5-dione (III) were isolated.

In the attempts on cyclization of 1-propionyl-1'-cinnamoylferrocene and 1-acetyl-1'-(α -methylcinnamoyl)ferrocene the formation of diacetyl derivatives was not observed [2]. In the attempted acid-catalyzed isomerization of *threo*-2-methyl-3-phenyl[5]ferrocenophane-1,5-dione the formation of acetylated derivatives was not observed either. Thus acetylated is assumed to be the starting material before the main reaction takes place which can be expressed by the Scheme 1.



Scheme 1

In an appearing contradiction to this mechanism is the fact that in a blank experiment run on 1,1'-diacetylferrocene, 1-acetyl-1'-propionylferrocene or 1-acetyl-1'-butylferrocene in the absence of the aldehyde the presence of the intermediate was not proved. It could probably be explained by the easy decomposition of this type of compound in the reaction medium. The explanation is supported by the fact that the presence of COR groups was found to facilitate the decomposition of ferrocene [9]. The ring resulting from the cyclization probably increases the stability of the formed derivative.

Acknowledgements. The authors wish to express their gratitude to Dr E. Greiplová (Institute of Chemistry, Komenský University) for the elemental analysis.

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Translated by P. Kováč