

# Cyclization of 1-chloroacetyl-1'-cinnamoylferrocene. I. Base-catalyzed reaction

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Cyclization of 1-chloroacetyl-1'-cinnamoylferrocene, either by potassium hydroxide in ethanol or in the presence of alumina leads to a halogen-not-containing product. The structure of cyclization products thus formed was suggested basing upon the p.m.r. spectral and synthetic evidence.

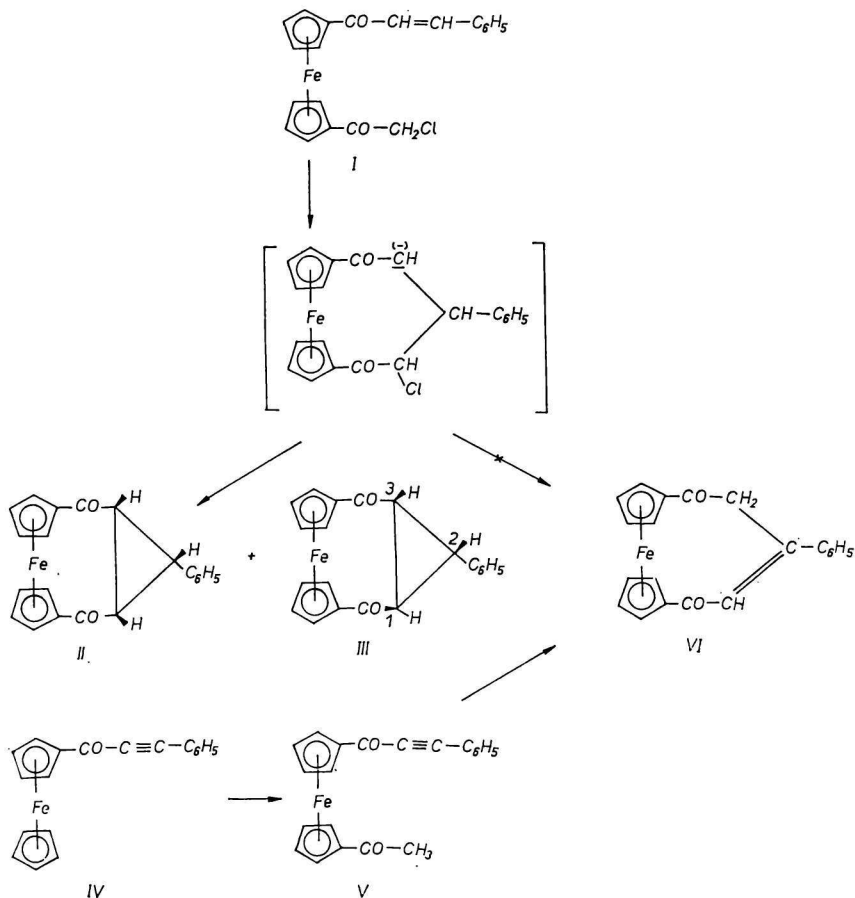
When studying the intramolecular Michael addition leading to *vic*-disubstituted derivatives of [5]ferrocenophane-1,5-dione [1], we attempted to synthesize a derivative with chlorine atom attached to the bridge by cyclization of 1-chloroacetyl-1'-cinnamoylferrocene. We found, however, that products resulting from this reaction do not contain halogen. The aim of this paper is the structure elucidation of those products.

1-Chloroacetyl-1'-cinnamoylferrocene (*I*) gave, when cyclized with potassium hydroxide as catalyst in ethanol, a yellow high melting substance *II* of molecular formula  $C_{21}H_{16}FeO_2$ . It could be anticipated this product to be 3-phenyl[5]ferrocenophan-2-ene-1,5-dione (*VI*) formed by elimination of hydrogen chloride from the product of intramolecular Michael addition (Scheme 1).

Cyclization of *I* by standing on the alumina column afforded two products in approximately 1 : 1 ratio according to the broadness of the chromatographic bands. The less polar has been shown to be identical with *II*; the other (*III*) underwent isomerization to *II* while standing overnight over the alumina column. The pure compound *III* was obtained by crystallization of the product eluted from the second band and also by acylation of cinnamoylferrocene by chloroacetyl chloride followed by a rapid chromatography over alumina. It isomerized in an ethanolic solution of potassium hydroxide to give *II*.

The formation of both isomers could not be rationalized by a dehydrohalogenation of the presumed 2-chloro-3-phenyl[5]ferrocenophane-1,5-dione and the substitution of chlorine by a hydroxyl was precluded on the basis of i.r. and p.m.r. spectral evidence of substances *II* and *III*.

Substance *VI* was prepared independently for comparison purposes according to Scheme 1. Phenylpropionylferrocene (*IV*), synthesized by Friedel-Crafts acylation of ferrocene with phenylpropionyl chloride (what is more advantageous than by a three-step procedure described by Schlögl [3] from ferrocene *via* ferrocenecarbaldehyde and 3-phenyl-1-ferrocenylpropinol) was acetylated to yield 1-acetyl-1'-phenylpropionylferro-



Scheme 1

cene (V). The same product was obtained by Friedel-Crafts acylation of acetylferrocene by phenylpropionyl chloride. Hydrogen chloride should be removed from the reaction mixture by passing it with nitrogen in order not to be added to the triple bond. Substance VI, obtained in high yield from V by cyclization with alcoholic potassium hydroxide, was not identical with any of the cyclization products of I. The attempt to cyclize V over an alumina column failed.

The formation of isomers could be explained by an intramolecular Michael addition in which the carbanion in the transition state was not stabilized by addition of a proton, but by a transannular nucleophilic substitution of chlorine. The structure of products, seen in Scheme 1 was suggested from the i.r. and p.m.r. spectral evidence.

Because of the low solubility of products in CDCl<sub>3</sub> only the p.m.r. spectrum of III was measured (in saturated solution). All the three cyclopropane ring protons reveal signals at various magnetic fields ( $\delta_3 = 2.62, \text{dd}, J_{1,3} \sim 14 \text{ Hz}, J_{2,3} \sim 2.5 \text{ Hz}, \delta_1 = 3.53, \text{dd}, J_{1,2} \sim 2.5 \text{ Hz}, \delta_2 = 5.29, \text{broad multiplet}$ ). Both chemical shifts and coupling constants are in consonance with those reported [4, 5].

Two absorption bands of not equivalent carbonyl groups at 1666 and 1689  $\text{cm}^{-1}$  could be resolved in the i.r. spectrum.

The given data are in agreement with the transoid arrangement of carbonyl groups on the cyclopropane ring. Inspection of Dreiding models showed that the hydrogen at  $\text{C}_2$  and also the carbonyl group at  $\text{C}_1$  could be influenced by  $\pi$ -electrons of the benzene ring at  $\text{C}_2$ . As shown by the model, such a molecule has a substantial tension due to a ring tilting of cyclopentadiene rings so that an easy isomerization of *III* to *II* could occur.

Substance *II* reveals in the carbonyl vibration region a poorly resolved doublet likely associated with the Fermi resonance ( $\nu(\text{C}=\text{O})$  1670 and 1683  $\text{cm}^{-1}$ ). In the C—C stretching vibration and C—H deformation vibration regions substances *II* and *III* are markedly different: *II* — 825 (m), 877 (m), 909 (w), 1036 (m), 1064 (m), 1076 (m), 1087 (m), 1237 (m), 1294  $\text{cm}^{-1}$  (m); *III* — 838 (m), 986 (w), 1044 (w), 1065 (w), 1093 (w), 1218 (m), 1240 (w), 1288  $\text{cm}^{-1}$  (m).

In the structure of *II* we assume the carbonyl groups at the cyclopropane ring to be *cis*-arranged. The more detailed structure, *i.e.* whether all-*cis*, or *exo*, or *endo* (the mutual position of ferrocene and cyclopropane) derivatives are involved, could not be assigned from the data at hand.

The p.m.r. spectra of *II* and *III* in 6D-DMSO were not sufficiently significant since a part of resonance signals is overlapped by signals of the solvent, water, and DMSO impurities [6]. The spectrum is complex also due to the oxidation ability of DMSO to almost all bridged derivatives of ferrocene [7]; paramagnetic particles appearing thus in the sample cause broadening of signals.

An experiment to add hydrogen bromide to *II* was supposed to evidence the product to be a cyclopropane derivative.

## Experimental

The p.m.r. spectra were taken with an 80 MHz Tesla BS 487 A spectrophotometer in  $\text{CDCl}_3$  and 6D-DMSO solutions, tetramethylsilane being the internal reference substance.

Infrared spectra were measured with a UR-20 (Zeiss, Jena) apparatus in nujol mull. Melting points were determined on a Kofler hot-stage apparatus in fused capillary tubes. Chromatographic carriers were  $\text{SiO}_2$  (Kavalier, Votice) and  $\text{Al}_2\text{O}_3$  (Brockmann II, Reanal, Budapest).

1-Chloroacetyl-1'-cinnamoylferrocene (*I*) was prepared according to [2].

### 1,1'-(3-Phenyl-*cis*-1,2-cyclopropanedicarbonyl)ferrocene (*II*)

Substance *I* (0.39 g, 1 mmole), potassium hydroxide (0.3 g, 5 mmoles), and ethanol (60 ml, 96%) were refluxed for 1 hr. Separated yellow crystals were filtered and washed with water to neutral reaction. Yield 0.25 g (64.1%) of *II*. The filtrate was extracted with dichloromethane, the solvent was dried with sodium sulfate and evaporated. The residue chromatographed over silica gel with benzene—ethyl acetate (5%) as eluent gave additional 0.05 g (12.4%) of *II*. Other three bands of low intensity have not been investigated.

The yield of *II* totalled 76.5%, m.p. 298–300°C (dec.). Infrared bands  $\nu(\text{C}=\text{O})$  1670 and 1683  $\text{cm}^{-1}$  (poorly resolved).

For  $\text{C}_{21}\text{H}_{16}\text{FeO}_2$  (356.20) calculated: 70.81% C, 4.52% H, 15.67% Fe; found: 70.37% C, 4.82% H, 15.98% Fe.

*1,1'-(3-Phenyl-trans-1,2-cyclopropanedicarbonyl)ferrocene (III)*

To cinnamoylferrocene (1.6 g, 5 mmoles), anhydrous aluminium chloride and dichloromethane (1.7 g, 0.012 mole and 30 ml, resp.) a solution of chloroacetyl chloride (0.56 g, 5 mmoles) in anhydrous dichloromethane (15 ml) was added during 20 min while cooling with water, stirring, and excluding the air moisture. The reaction mixture was then stirred for 4 hrs and poured on crushed ice. The product was extracted with dichloromethane, the solvent was washed with water, dried over sodium sulfate, and chromatographed over a  $25 \times 2$  cm alumina column with benzene-ethyl acetate (2%). Yield 0.45 g (25.2%) of *III*. M.p. 234–236°C (dec.); p.m.r.  $\delta_1 = 3.53$  (dd, 1H),  $\delta_2 = 5.29$  (m, 1H),  $\delta_3 = 2.62$  (dd, 1H),  $\delta_{C_5H_4} = 4.5-5.0$  (m, 8H),  $\delta_{C_6H_5} = 7.5-7.8$  (m, 5H); i.r.  $\nu(C=O)$  1666 and 1689  $cm^{-1}$ .

For  $C_{21}H_{16}FeO_2$  (356.20) calculated: 70.81% C, 4.52% H, 15.67% Fe; found: 70.52% C, 4.93% H, 15.15% Fe. Recovery of unchanged cinnamoylferrocene 0.55 g (30%).

Substance *III* gave, when heated with potassium hydroxide in 96% ethanol substance *II*.

*Cyclization of 1-chloroacetyl-1'-cinnamoylferrocene (I) over alumina*

Compound *I* (0.35 g) dissolved in benzene-ethyl acetate (2%) was poured onto a  $30 \times 2.5$  cm alumina column and allowed to stand for 12 hrs. Elution with benzene-ethyl acetate (7%) afforded 0.13 g (36.8%) of *II* from the first band. The second band remaining 16 hrs on the column gave 0.15 g of a product, which after crystallization from benzene yielded additional 0.05 g (14%) of *II*. Compound *III* (0.10 g, 28%) was separated from the mother liquor.

*Phenylpropionylferrocene (IV)*

To ferrocene (3.72 g, 0.02 mole) and anhydrous aluminium chloride (2.75 g, 0.021 mole) in dichloromethane (40 ml) a solution of phenylpropionyl chloride (3.3 g, 0.02 mole) in dichloromethane (20 ml) was added under stirring during 20 min at room temperature. A mild stream of purified dry nitrogen was passed through the reaction mixture for 4 hrs. After this period the mixture was poured on ice and the product extracted with dichloromethane. The solvent washed with water and dried with sodium sulfate was evaporated and the residue was chromatographed over silica gel with benzene. The first band consisted of ferrocene, the second one afforded *IV* (0.95 g, 15.1%); its m.p. 103–106°C is in agreement with [3].

Phenylpropionylferrocene (*IV*) reveals the following p.m.r. signals:  $\delta_{C_5H_5} = 4.32$  (s, 5H),  $\delta_B = 4.65$  (t, 2H),  $J \sim 1.5$  Hz,  $\delta_\alpha = 5.03$  (t, 2H),  $\delta_{C_6H_5} = 7.3-7.8$  (m, 5H); i.r.  $\nu(C=O)$  1620  $cm^{-1}$ ,  $\omega(C_5H_5)$  1008 and 1110  $cm^{-1}$ ,  $\nu(C\equiv C)$  2210  $cm^{-1}$  (w).

Further band gave 0.38 g of substance of m.p. 134°C (benzene-light petroleum) which was identified to be cinnamoylferrocene.

*1-Acetyl-1'-phenylpropionylferrocene (V)*

A solution of acetyl chloride (0.47 g, 6 mmoles) in dichloromethane (20 ml) was added to *IV* (1.1 g, 3.4 mmoles), anhydrous aluminium chloride (0.80 g, 6 mmoles) in dichloromethane (40 ml). The reaction mixture was worked up as with *IV*. Upon chromatography over silica gel with benzene-ethyl acetate (3%), 0.35 g (30%) of starting material and 0.7 g (58.8%) of an oily product were obtained. Rechromatography of this product

with benzene—ethyl acetate (5%) gave crystals of m.p. 83–84°C (benzene—light petroleum).

P.m.r.  $\delta_{\text{CH}_3} = 2.39$  (s,3H),  $\delta_{\beta,\beta'} = 4.6$  (m,4H),  $\delta_{\alpha'} = 4.85$  (t,2H),  $J \sim 1.2$  Hz,  $\delta_{\alpha} = 5.0$  (t,2H),  $\delta_{\text{C}_6\text{H}_5} = 7.3\text{--}7.8$  (m,5H); i.r.  $\nu(\text{C}=\text{O})$  1638 and 1671  $\text{cm}^{-1}$ ,  $\nu(\text{C}\equiv\text{C})$  2210  $\text{cm}^{-1}$ .

For  $\text{C}_{21}\text{H}_{16}\text{FeO}_2$  (356.20) calculated: 70.81% C, 4.52% H, 15.67% Fe; found: 70.93% C, 4.39% H, 15.84 Fe.

The same product was obtained by acetylation of acetylferrocene with phenylisopropyl chloride in 20% yield.

### 3-Phenyl[5]ferrocenophan-2-ene-1,5-dione (VI)

Compound V (0.3 g, 2.8 mmoles), potassium hydroxide (0.7 g, 0.12 mole), and ethanol (30 ml, 96%) were refluxed for 30 min. After cooling, the separated crystals were filtered, washed with water to neutral reaction, and dried, yielding thus 0.2 g of VI. The filtrate was extracted with dichloromethane, the organic layer washed with water, dried with sodium sulfate, and evaporated. The residue, upon chromatography over silica gel with benzene, gave additional 0.03 g of VI, so that 0.23 g (76.6%) was obtained. M.p. 215°C (ethanol).

P.m.r.  $\delta_{\text{CH}_2} = 3.78$  (s,2H),  $\delta_{\beta,\beta'} = 4.64$  (m,4H),  $\delta_{\alpha,\alpha'} = 4.83$  (m,4H),  $\delta_{\text{CH}} = 6.46$  (s,1H),  $\delta_{\text{C}_6\text{H}_5} = 7.3\text{--}7.8$  (m,5H); i.r.  $\nu(\text{C}=\text{O})$  1666 and 1678  $\text{cm}^{-1}$ ,  $\nu(\text{C}=\text{C})$  1635  $\text{cm}^{-1}$  (sh).

For  $\text{C}_{21}\text{H}_{16}\text{FeO}_2$  (356.20) calculated: 70.81% C, 4.52% H, 15.67% Fe; found: 71.03% C, 4.76% H, 15.85% Fe.

### Addition of hydrogen bromide to 1,1'-(3-phenyl-cis-1,2-cyclopropanedicarbonyl)ferrocene

Substance II (0.13 g, 0.036 mmole), glacial acetic acid (10 ml), and hydrobromic acid (3 ml, 47%) were allowed to react at room temperature for 60 hrs. After pouring into water the reaction mixture was extracted with dichloromethane, the organic solvent was washed with water, dried with sodium sulfate, and evaporated. The residue was chromatographed over a silica gel column with benzene—ethyl acetate (3%). The first band afforded starting material (0.07 g, 54%), the second one a bromine-containing substance (0.016 g, 10%), which crystallized from acetone—light petroleum. Crystals decomposed without melting even when rapidly heated on a Kofler hot-stage apparatus.

For  $\text{C}_{21}\text{H}_{17}\text{BrFeO}_2$  (437.11) calculated: 12.77% Fe, 18.27% Br; found: 13.23% Fe, 18.97% Br.

The p.m.r. spectrum could not be taken for a low solubility of the product.

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