

Competitive intermolecular additions in the chemistry of ferrocene. II.

Synthesis and cyclization of 1-(ω -benzoylalkanyl)-1'-cinnamoyl ferrocenes

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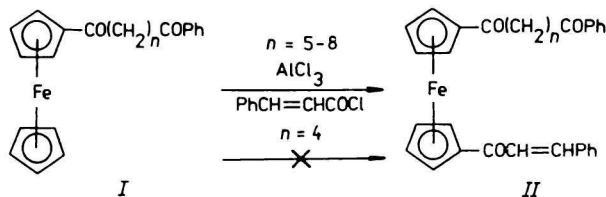
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ω -Benzoylalkanyl ferrocenes (*I*, $n = 4-8$) were acylated with cinnamoyl chloride and the prepared 1-(ω -benzoylalkanyl)-1'-cinnamoyl ferrocenes (*II*, $n = 5-8$) were submitted to base-catalyzed cyclization. In all cases, derivatives of [5]ferrocenophanes were the sole products.

Было осуществлено ацилирование ω -бензоилалканойлферроценов (*I*, $n = 4-8$) с хлористым циннамоилом. Приготовленные 1-(ω -бензоилалканойл)-1'-циннамоилферроцены (*II*, $n = 5-8$) были подвергнуты циклизации при щелочном катализе. Во всех случаях образовались только производные [5]ферроцефана.

We have previously studied [1] competitive intermolecular Michael addition reactions with ferrocene derivatives containing one activated methylene group and two activated double bonds. The aim of the present work was to study competitive intermolecular Michael additions with derivatives containing two nonequivalent activated methylene groups and one activated double bond.

Friedel—Crafts acylations of diketones *I* ($n = 5-8$) with cinnamoyl chloride were smooth reactions and expected 1-(ω -benzoylalkanyl)-1'-cinnamoyl ferrocenes (*II*, Scheme 1) were isolated as the main products. On the other hand, acylation of

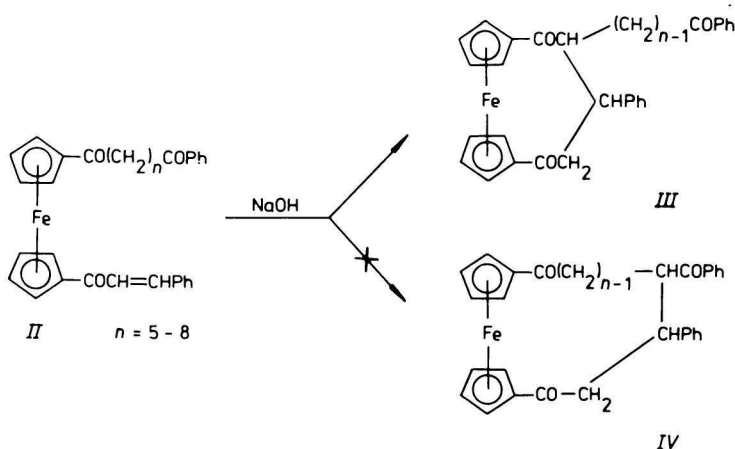


Scheme 1

the diketone *I* ($n = 4$) with the same reagent did not occur and the only substance which could be isolated from the complicated reaction mixture was 1-benzoyl-2-ferrocenylcycloheptene [2], the product of cyclization of the starting diketone. In addition to *II*, acylation of diketones *I* ($n = 5, 7$) afforded also small amounts of cyclization products *III*.

Cyclizations of 1-(ω -benzoylalkanyl)-1'-cinnamoyl ferrocenes with sodium hydroxide as a catalyst in ethanol at room temperature proceeded smoothly and the cyclization products were isolated in 66–80% yields.

Owing to the nonequivalent, activated methylene groups (FcCOCH₂– and –CH₂COC₆H₅; Fc — ferrocenyl) present in the starting material, the intermolecular Michael addition of 1-(ω -benzoylalkyl)-1'-cinnamoyl ferrocenes can proceed in two ways (Scheme 2).



Scheme 2

Signals corresponding to the two methylene groups present in the starting material can be easily distinguished by ¹H-n.m.r. spectroscopy (δ 2.65 and 2.95, respectively). The chemical shifts for FcCOCH₂– and –CH₂COPh protons could be unambiguously assigned by comparing with the spectra of symmetrical FcCO(CH₂)_nCOFc ketones. It follows from the above-mentioned chemical shifts that the hydrogen atoms of the methylene group in the vicinity of the benzoyl residue are more acidic, since they resonate at a lower field.

Compared with the ¹H-n.m.r. spectra of the starting materials, the spectra of the products of Michael addition do not show the triplet of the FcCOCH₂– group, and only slight upfield shift is observed for the –CH₂COPh triplet.

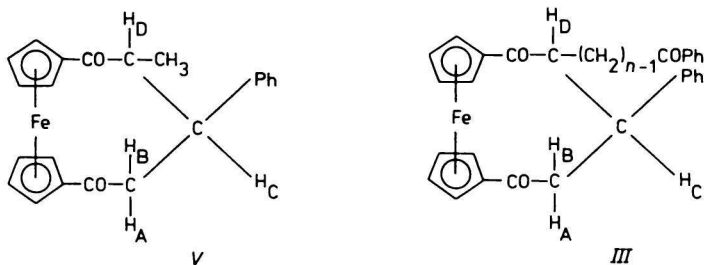
The fact that the reaction yields [5]ferrocenophanes was ascertained by detailed comparison of the spectra of our substances with those of 3-phenyl-2-methyl-[5]ferrocenophane-1,5-diones (*V*) prepared by *Elečko* [3, 4].

The ^1H -n.m.r. spectra of [5]ferrocenophanes *III* show signals for aromatic protons at δ 7.9 (m, 2H), corresponding to *ortho* protons of the benzoyl group, and another multiplet at δ 7.4 of the other 8 phenyl protons. Three multiplets (δ 5.0, 4.75, and 4.6 for 2H, 1H, and 5H, respectively) are present in the region characteristic of ferrocene protons. The multiplet at δ 4.08, integrating for 1H, was assigned to H_C . Also, the spectra show a two-proton multiplet and a one-proton doublet of doublets. We proved by applying the INDOR technique that the multiplet at δ 3.25 (2H) corresponds to one of the methylene protons (H_A) and to H_D proton. The doublet of doublets at δ 2.41 (1H) was then assigned to the other methylene proton (H_B). The coupling constants indicate a *threo* configuration of the $-\text{CH}_C\text{Ph}-\text{CH}_D-(\text{CH}_2)$ groups.

^1H -n.m.r. data for the two types of cyclizates are as follows:

Type *III*: H_A 3.28 δ ; H_B 2.41 δ ; H_C 4.08 δ ; H_D 3.20 δ ; J_{AB} 14.0 Hz; J_{AC} 12.8 Hz; J_{BC} 3.8 Hz; J_{DC} 5.1 Hz.

Type *V*: H_A 3.26 δ ; H_B 2.57 δ ; H_C 4.31 δ ; H_D 3.19 δ ; J_{AB} 13.6 Hz; J_{AC} 12.3 Hz; J_{BC} 3.9 Hz; J_{DC} 5.2 Hz.



It follows that the Michael addition of 1-(ω -benzoylalkanoyl)-1'-cinnamoyl-1-ferrocenes is a thermodynamically governed reaction. If it were a reaction controlled kinetically, it would occur predominantly at the "more acidic" methylene group, the one bearing the benzoyl residue. As a result, ferrocenophanes of the type *IV*, having the number of carbon atoms in the bridge larger than 5, would be formed.

One cyclization reaction at elevated temperature has also been attempted. A mixture of products was formed from which a product analogous to that described above was isolated by chromatography. In addition, a small amount of higher-melting material was also obtained and we assume, in analogy with the observation by *Elečko* [3, 4], that it is the *erythro* derivative of the corresponding [5]ferrocenophane. Its ^1H -n.m.r. spectrum shows an unaltered triplet of the methylene group bearing the benzoyl residue.

In the case of compound *II* ($n=8$) an attempt was made at a kinetically controlled reaction. The cyclization was conducted in anhydrous ether in the presence of less than an equimolar amount of sodium methoxide. The obtained product was identical to the material obtained from the sodium hydroxide-ca-

talyzed reaction. Attempted isomerization of *II* ($n = 8$) carried out in ethanol at reflux temperature in the presence of a catalytic amount of sodium hydroxide afforded a higher-melting substance (m.p. 173—176°C *vs.* 134—136°C). The $^1\text{H-n.m.r.}$ spectrum of this isomer shows two multiplets integrating each for four protons, belonging to the ferrocene moiety. The doublet of triplets for the H_C proton shows $J_{AC} \sim J_{DC} \sim 12$ Hz and $J_{BC} \sim 2$ Hz. Since the lower-melting isomer shows $J_{DC} = 5.2$ Hz, whereas in this case $J_{DC} = 12$ Hz is observed, H_C and H_D must be in a *trans* arrangement (*erythro* configuration [3, 4]). The H_A and H_D signals are overlapped by the triplet of the CH_2CO group. The signal for H_B appears as a doublet of doublets ($J_{AB} \sim 12$ Hz, $J_{BC} \sim 2$ Hz).

It follows from the given data, since a substance containing a longer than 5-membered bridge could not be isolated in either case, that the formation of a 5-membered bridge is strongly preferred in these reactions.

Experimental

The $^1\text{H-n.m.r.}$ spectra for 10% solutions in chloroform (99.5% of D) were measured at 24°C using Tesla BS 487 A, 80 MHz spectrometer (internal standard tetramethylsilane). Chemical shifts are given with the accuracy of ± 0.01 p.p.m.

Column chromatography on silica gel (Kavalier, Votice) was performed by applying gradient elution technique, with benzene—ethyl acetate mixtures (19:1 \rightarrow 3:1). Melting points were determined on a Kofler hot-stage. Acylations were conducted in a nitrogen atmosphere. The starting ω -benzoylalkanoyl ferrocenes were prepared as described [2].

1-(ω -Benzoylalkanoyl)-1'-cinnamoyl ferrocenes (type II compounds)

Aluminium chloride (0.03 mol) was added portionwise at 0—5°C to a solution of cinnamoyl chloride (0.015 mol) in anhydrous dichloromethane (50 ml), followed by slow

Table I
Characteristic data for compounds of type I

<i>n</i>	Formula	<i>M</i>	Calculated/found			Yield %	M.p., °C Solvent
			% C	% H	% Fe		
5	$\text{C}_{32}\text{H}_{30}\text{FeO}_3$	518.44	74.13	6.83	10.77	25	98—101 Benzene—petroleum ether
			74.79	6.02	10.23		
6	$\text{C}_{33}\text{H}_{32}\text{FeO}_3$	532.47	74.43	6.06	10.48	66	127—130 Benzene—petroleum ether
			74.04	6.21	10.08		
7	$\text{C}_{34}\text{H}_{34}\text{FeO}_3$	546.49	74.72	6.27	10.21	78	95—97 Benzene—petroleum ether
			75.04	6.18	10.15		
8	$\text{C}_{35}\text{H}_{36}\text{FeO}_3$	560.52	74.99	6.47	9.96	64	112—114 Benzene—petroleum ether
			75.01	6.74	9.87		

Table 2

Characteristic data for compounds of type II

n	Formula	M	Calculated/found			Yield %	M.p., °C Solvent
			% C	% H	% Fe		
5	C ₃₂ H ₃₀ FeO ₃	518.44	74.13	5.83	10.77	80.2	198—200
			74.59	6.16	10.88		Benzene—petroleum ether
6	C ₃₃ H ₃₂ FeO ₃	532.47	74.43	6.06	10.48	75.7	135—138
			73.95	6.16	10.40		Benzene—petroleum ether
7	C ₃₄ H ₃₄ FeO ₃	546.49	74.72	6.27	10.21	71.5	93—95
			74.99	6.41	10.30		Benzene—petroleum ether
8	C ₃₅ H ₃₅ FeO ₃	560.52	74.99	6.47	9.96	66.6	132—134
			74.78	6.60	9.91		Benzene—petroleum ether

addition (30 min, with stirring) of a solution of ω -benzoylalkanoyl ferrocene (0.005 mol) in dichloromethane (25 ml). The stirring was continued at ambient temperature for 2 h and then at 35°C for 1—2 h. When the reaction was complete (t.l.c.) the mixture was poured into water and the product was extracted with dichloromethane. The extract was washed with water, dried with anhydrous sodium sulfate, concentrated and the residue was chromatographed. Small amount of material eluted first (less than 20 mg) was discarded and later fractions yielded starting material (10—20%), and the expected product of the type II (Tables 1 and 3). In the case of $n = 5, 7$ a small amount of cyclizate, identical to that isolated from products of cyclization under alkaline conditions, was also obtained.

Cyclization of 1-(ω -benzoylalkanoyl)-1'-cinnamoyl ferrocenes and isolation of compounds of the type III

1-(ω -Benzoylalkanoyl)-1'-cinnamoyl ferrocene (0.5 mmol) was dissolved in warm ethanol (65°C, 96%, 70 ml) and a solution of sodium hydroxide (0.3 g; 7.5 mmol) in water (3 ml) was added at 35°C. The mixture was shaken occasionally and, after 2 h at room temperature, poured into water. The mixture was neutralized with dilute hydrochloric acid and extracted with dichloromethane. The organic phase was washed with water, dried with anhydrous sodium sulfate, concentrated, and the residue was chromatographed.

Cyclizate of the type III ([5]ferrocenophane, 70—80%, Tables 2 and 4) was eluted first, followed by a small amount of starting material.

Attempted sodium methoxide-catalyzed cyclization of II (n = 8) in ether

A mixture of 1-(ω -benzoylnonanoyl)-1'-cinnamoyl ferrocene (0.28 g; 5 mmol) in anhydrous ether (60 ml) was refluxed for 30 min with stirring. Methanolic 1% sodium methoxide (0.5 mmol) was added and after 2 h, at which time all starting material had

Table 3

¹H-NMR chemical shifts (δ) for compounds of type I

<i>n</i>	-CH ₂ -	-CH ₂ COC ₅ H ₄	-CH ₂ COC ₆ H ₅	H _{β}	H _{β'}	H _{α}	H _{α'}	C ₆ H ₅ + -CH=CH-
5	1.0—2.0 m, 6H	2.65 t, 2H	2.95 t, 2H	4.50 t, 2H	4.57 t, 2H	4.78 t, 2H	4.90 t, 2H	6.8—8.1 m, 12H
6	1.0—2.0 m, 8H	2.65 t, 2H	2.96 t, 2H	4.50 t, 2H	4.58 t, 2H	4.80 t, 2H	4.92 t, 2H	6.9—9.1 m, 12H
7	1.0—2.0 m, 10H	2.63 t, 2H	2.95 t, 2H	4.50 t, 2H	4.57 t, 2H	4.78 t, 2H	4.90 t, 2H	6.9—8.1 m, 12H
8	1.0—1.9 m, 12H	2.63 t, 2H	2.93 t, 2H	4.48 t, 2H	4.56 t, 2H	4.78 t, 2H	4.88 t, 2H	6.9—8.0 m, 12H

Table 4

¹H-NMR chemical shifts (δ) for compounds of type II*

<i>n</i>	-CH ₂ -	H _B	-CH ₂ COC ₆ H ₅	H _D	H _A	H _C	C ₃ H ₄	C ₆ H ₅
5	1.0—1.8 m, 6H	2.43 dd, 1H	2.75 t, 2H	3.21 m, 1H	3.28 t, 1H	4.05 m, 1H	4.63 m, 5H	4.77 m, 1H 5.00 m, 2H 7.1—8.0 m, 10H
6	1.0—1.8 m, 8H	2.40 dd, 1H	2.79 t, 2H	3.20 m, 1H	3.28 t, 1H	4.05 m, 1H	4.61 m, 1H 4.75 m, 1H 5.00 m, 2H 7.1—8.0 m, 10H	
7	1.0—1.8 m, 10H	2.39 dd, 1H	2.81 t, 2H	3.18 m, 1H	3.26 t, 1H	4.05 m, 1H	4.60 m, 5H 4.74 m, 1H 4.98 m, 2H 7.1—8.0 m, 10H	
8	0.8—1.9 m, 12H	2.39 dd, 1H	2.85 t, 2H	3.18 m, 1H	3.26 t, 1H	4.05 m, 1H	4.61 m, 5H 4.75 m, 2H 4.98 m, 2H 7.0—8.0 m, 10H	

*Chemical shifts for H_{A—D} are given as data observed for centra of multiplets; $J_{AB} \sim 13.5$ Hz, $J_{AC} \sim 12$ Hz, $J_{BC} \sim 3.8$ Hz.

dissolved, t.l.c. showed that the reaction was complete. The ethereal solution was washed with water, dried, concentrated, and the residue was chromatographed to give traces of starting material, and *III* ($n = 8$, 0.24 g, 85%), identical with the material obtained from the sodium hydroxide-catalyzed reaction (see above).

*Attempted sodium hydroxide-catalyzed isomerization of II (n = 8)
in boiling ethanol*

A solution of sodium hydroxide (0.2 g) in water (2 ml) was added to a solution of *II* ($n = 8$, 0.2 g) in ethanol (30 ml) and, after 3 h at refluxing temperature, the mixture was poured into water. The product was extracted with ether, the ethereal solution was concentrated, and the residue was recrystallized from benzene to afford 0.16 g (80%) of material melting at 173—175°C.

For $C_{35}H_{35}FeO_3$ (560.5) calculated: 74.99% C, 6.47% H, 9.96% Fe; found: 74.93% C, 6.51% H, 10.02% Fe.

1H -N.m.r. data (δ): 0.8—1.8 (m, 12H, CH_2); 2.38 (dd, 1H, H_B , $J_{AB} \sim 12$ Hz, $J_{BC} 2$ Hz); 2.7—3.2 (m, 4H, $CH_2CO + H_A + H_D$); 3.96 (dt, 1H, H_C , $J_{AC} \sim J_{DC} \sim 12$ Hz, $J_{BC} \sim 2$ Hz); 4.6 (m, 4H, H_p); 4.9 (m, 4H, H_a); 7—8 (m, 10H, C_6H_5).

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