

Acylation of anisole with ω -ferrocenylalkanoyl chlorides

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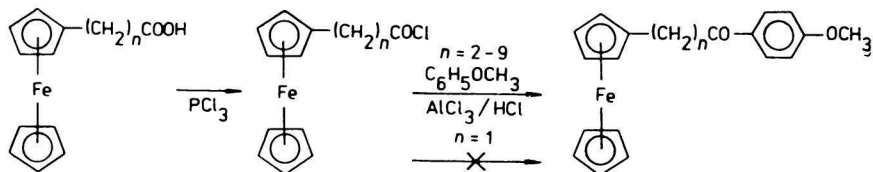
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Anisole (AnH) was acylated with acyl chlorides of general formula $\text{Fc}(\text{CH}_2)_n\text{COCl}$. Yields of ketones $\text{Fc}(\text{CH}_2)_n\text{COAn}$ varied within 50–70% providing $n = 4$ –9. Were $n = 2$ –4, also products of intramolecular acylation of ferrocene were isolated; when $n = 2$ additional products formed by a consecutive reaction with anisole were obtained. Attempts to acylate anisole with ferrocenylacetyl chloride resulted in decomposition of the ferrocene derivative and isolation of trimethoxyterphenyl. The oxidation of ferrocenylacetonitrile is discussed.

Было осуществлено ацилирование анизола (AnH) хлоридами кислот $\text{Fc}(\text{CH}_2)_n\text{COCl}$. Выходы кетонов $\text{Fc}(\text{CH}_2)_n\text{COAn}$ были 50–70% для $n = 4$ –9. В случае $n = 2$ –4 были изолированы также продукты внутримолекулярного ацилирования ферроцена и при $n = 2$ также продукты их последующей реакции с анизолом. При попытках ацилирования анизола ферроценилацетилхлоридом производное ферроцена разложилось и был выделен триметокситерфенил. Обсуждается проблема окисления ферроценилацетонитрила.

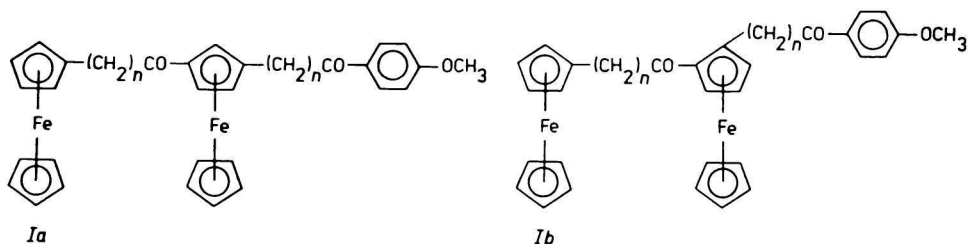
A method of preparation of aryl ω -ferrocenylalkyl ketones was elaborated in connection with the synthesis of [m]ferrocenophanes from 1-(ω -aroylalkyl)-1'-cinnamoylferrocenes, *i.e.* compounds having the active methylene group separated from ferrocene by several methylene groups. So far, no general method of preparation of those substances has been reported; nevertheless ferrocenylacetaldehyde [1], ferrocenylacetone [2, 3], phenacylferrocene [4], and 4-ferrocenyl-2-butanone [5] were described. The first three of them are unstable, so that their reactions could not be studied, the latter served as a synthon for the preparation of [7]ferrocenophane [6].

Friedel—Crafts' acylation is a direct method for the synthesis of acyl derivatives of aromatic compounds. The synthesis of aryl ω -ferrocenylalkyl ketones requires an acylation of aromatic compounds with ω -ferrocenylalkanoyl chlorides. Due to a high reactivity of ferrocene towards electrophilic reagents possibly resulting in intra- and intermolecular acylations of ferrocene, the substrate had to be very reactive. Anisole, which has been chosen, is less reactive than ferrocene [7] and therefore, the unwanted reactions at ferrocene should be suppressed by an excess of the substrate. Preliminary attempts showed that neither a 10-fold molar excess of anisole suppressed the concurrent reactions. Thin-layer chromatography of the reaction mixtures revealed the presence of about 10 ferrocene-containing compounds. Further experiments were done in anisole as a solvent and the reactivity of ferrocene was lowered by its protonization at the iron atom similarly, as has already been reported [8]. These conditions enabled this reaction to proceed in good, *i.e.* 40—70% yields (Scheme 1). Neither this arrangement completely avoided the



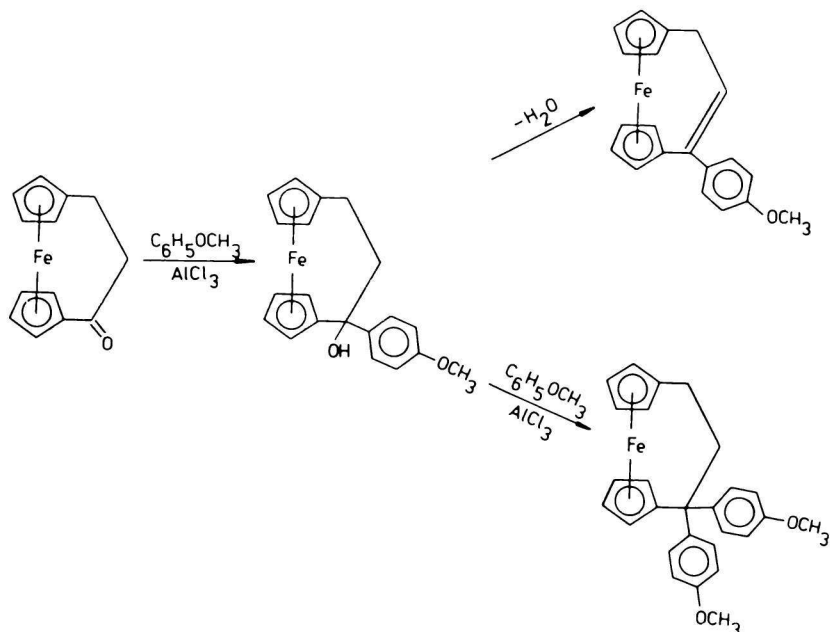
Scheme 1

formation of by-products. Were $n=4-9$ a small amount of products of a consecutive acylation was formed, in other words compounds *Ia* and *Ib* were obtained.



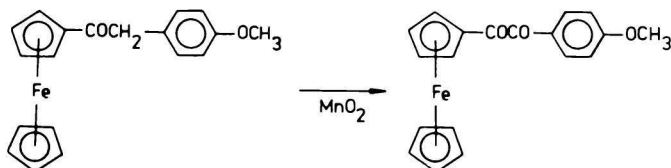
At $n=2-4$ products of intramolecular acylation of ferrocene were isolated: 2,3-ferroceno-2-cyclohexen-1-one from $n=3$ and 2,3-ferroceno-2-cyclohepten-1-one from $n=4$ were obtained in 35 and 21% yields, respectively.

Acylation with β -ferrocenylpropionyl chloride afforded β -anisolyethylferrocene in only 17% yield. The principal product of this reaction was [3]ferrocenophan-1-one and compounds formed by consecutive reactions of the latter with anisole (Scheme 2).



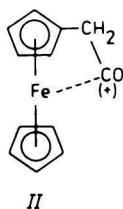
Scheme 2

Attempts to prepare *p*-methoxyphenacylferrocene by acylation of anisole with ferrocenylacetyl chloride resulted in failure. Thin-layer chromatography displayed the presence of a greater amount of compounds not containing ferrocene, and 1H -n.m.r. showed products containing ferrocene but in a minimum ratio with regard to anisole. Fully identified was only trimethoxyterphenyl, which could be formed by dehydroarylation of anisole under catalysis of $FeCl_2$ generated by decomposition of some derivative of ferrocene. Dehydrodimerization of benzene catalyzed by $CuCl_2/AlCl_3$ was several times described [9, 10]. (Dimethoxybiphenyl was obtained as a by-product when acetylating anisole with acetyl chloride under catalysis of $AlCl_3$ [11].) In addition $FcCOCO(C_6H_4OCH_3)_6$ (Fc = ferrocenyl) was identified on the basis of 1H -n.m.r. and i.r. evidences; it was formed during the work-up of the reaction mixture and chromatography from $FcCH_2CO(C_6H_4OCH_3)_6$.



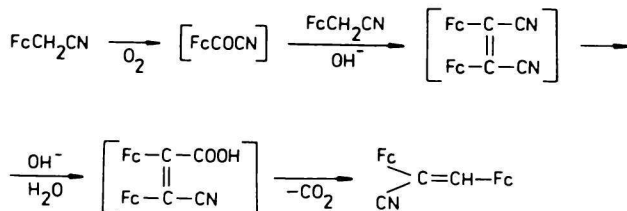
Scheme 3

To clear whether the ferrocenylacetyl chloride or the product of oxidation of the anticipated *p*-methoxyphenacetylferrocene (*i.e.* *p*-methoxyphenylglyoxalylferrocene) were decomposed in the presence of AlCl_3 , the latter was synthesized (Scheme 3) and subjected to conditions of acetylation. It has been shown [2] that compounds $\text{FcCH}_2\text{—Z}$, where *Z* stands for electron-accepting groups, readily undergo oxidation. As found, *p*-methoxyphenylglyoxalyl is relatively stable, whereas ferrocenylacetyl chloride underwent an immediate decomposition with AlCl_3 in dichloromethane. A like finding on acylation of ferrocene with this chloride, leading to about 25% recovery of ferrocene and traces of unidentified compounds was reported [12]. It is dubious whether intermediates *II*



or $\text{Fc}\overset{\cdot}{\text{C}}\text{H—Z}$ or $\text{Fc—}\overset{(+)}{\text{C}}\text{H—Z}$, formed from ferrocenylacetonitrile by the action of FeCl_3 in methanol [13], were involved in the decomposition.

An attempt to prepare ferrocenylacetic acid from an older ferrocenylacetonitrile [14] resulted in isolation of 1,2-diferrocenyl-1-cyanoethylene. The latter was probably formed *via* a series of reactions shown in Scheme 4. The suggested



Scheme 4

intermediate was the oxidation product of acetonitrile, this being in accordance with the easy oxidation of compounds containing between ferrocene and an electron-accepting group a methylene link [2].

Experimental

The ^1H -n.m.r. spectra of 10% deuteriochloroform (99.5% CDCl_3) solutions were measured with a Tesla BS 487 A spectrometer operating at 80 MHz and 24°C with tetramethylsilane as an internal reference substance. Chemical shifts (δ , p.p.m.) are accurate to ± 0.01 p.p.m. IR spectra (in CHCl_3), measured with a Perkin—Elmer 567 apparatus, corresponded to a 75—80% absorption. The solvent system for column chromatography (Al_2O_3 , according to Brockmann, activity grade II, Reanal, Budapest) was benzene—ethyl acetate (9.7:0.3—9.5:0.5). The products are presented in their elution sequence. Melting points were determined on a Kofler micro hot-stage. All reactions were carried out under nitrogen. The ω -ferrocenylalkane acids were obtained by reduction of the respective ω -ferrocenylalkane acids synthesized from ferrocene with ester chlorides of suitable dicarboxylic acids [15].

ω -Anisolyalkylferrocenes

Phosphorous chloride (7 ml) was added to a solution of ω -ferrocenylalkane acid of general formula $\text{Fc}(\text{CH}_2)_n\text{COOH}$ (3 mmol) in anhydrous benzene (100 ml). This mixture was kept between 60 — 70°C for 3 h, cooled, benzene was decanted and phosphorous acid sticking to the walls of the flask was washed once more with benzene. Benzene layers were collected and the solvent removed under diminished pressure. Aluminium chloride (7.5 mmol) was stepwise added at room temperature to a stirred solution of ω -ferrocenylalkanoyl chloride, remaining after removal of benzene, dissolved in anhydrous anisole (80 ml) saturated for 2 h prior to reaction with gaseous HCl . Stirring was continued for 1—2 h during which the reaction course was monitored by thin-layer chromatography. When the reaction was over, the mixture was poured into water and the ferricinium salts were reduced with NaHSO_3 . Organic material was extracted with ether, washed with water, dried with Na_2SO_4 and the solvent removed. The residue was chromatographed on an Al_2O_3 column. The characteristic data of ω -anisolyalkylferrocenes crystallizing from benzene—light petroleum are given in Tables 1 and 2. When n of the starting acid was 4—9, small amounts of further products were isolated. Their structure was fully proved in two cases only (when $n = 5$ and 7), the remaining structures were elucidated on the basis of comparison of their ^1H -n.m.r. spectra.

Compound *Ia*, $n = 5$ (yellow oil), for $\text{C}_{39}\text{H}_{44}\text{Fe}_2\text{O}_3$ (672.48) calculated: 69.65% C, 6.69% H, 16.61% Fe; found: 69.75% C, 6.84% H, 16.42% Fe. ^1H -NMR: 1.00—1.90 (m, 12H, CH_2), 2.27 (m, 4H, CH_2Fc), 2.66 (t, 2H, CH_2COFc), 2.88 (t, 2H, CH_2COAn), 3.84 (s, 3H, OCH_3), 4.08 (m, 12H, $\text{C}_5\text{H}_5 + \text{H}_\beta$), 4.40 (m, 3H, $\text{H}_{\alpha,\beta}$), 4.66 (m, 2H, H_α), 6.90 (d, 2H, C_6H_4), 7.92 (d, 2H, AB q, $J_{\text{AB}} = 9$ Hz).

Compound *Ib*, $n = 7$ (yellow oil), for $\text{C}_{43}\text{H}_{52}\text{Fe}_2\text{O}_3$ (728.56) calculated: 70.88% C, 7.19% H, 15.33% Fe; found: 69.95% C, 7.3% H, 14.76% Fe. ^1H -NMR: 1.15—1.95 (m, 20H, CH_2), 2.15—2.78 (m, 6H, $\text{CH}_2\text{Fc} + \text{CH}_2\text{COFc}$), 2.88 (t, 2H, CH_2COAn), 3.85 (s, 3H, OCH_3), 4.07 (m, 14H, $\text{C}_5\text{H}_5 + \text{C}_6\text{H}_4$), 4.30 (m, 1H, H_β), 4.37 (m, 1H, H_β), 4.57 (m, 1H, H_α), 6.90 (d, 2H, C_6H_4), 7.92 (d, 2H, AB q, $J_{\text{AB}} = 9$ Hz).

As evidenced by ^1H -n.m.r. spectroscopy, the attempt to acylate anisole with ferrocenylacetyl chloride led to isolation of a greater amount of compounds not containing

Table 1

Characterization of the synthesized compounds

<i>n</i>	Formula	<i>M</i>	Calculated/found			M. p., °C	Yield %
			% C	% H	% Fe		
2	C ₂₀ H ₂₀ FeO ₂	348.23	68.98	5.87	16.03	80—85	17
			69.25	5.87	15.57		
3	C ₂₁ H ₂₂ FeO ₂	362.26	69.62	6.12	15.41	83—85	32
			69.75	6.18	15.47		
4	C ₂₂ H ₂₄ FeO ₂	376.28	70.22	6.42	14.84	69—75	49
			70.19	6.38	14.70		
5	C ₂₃ H ₂₆ FeO ₂	390.31	70.77	6.71	14.31	62—63	58
			70.97	6.83	14.36		
6	C ₂₄ H ₂₈ FeO ₂	404.34	71.29	6.98	13.81	75—77	50
			71.21	6.99	13.98		
7	C ₂₅ H ₃₀ FeO ₂	418.36	71.77	7.23	13.35	76—79	57
			71.67	7.36	13.47		
8	C ₂₆ H ₃₂ FeO ₂	432.39	72.22	7.45	12.91	62—65	68
			72.17	7.38	12.87		
9	C ₂₇ H ₃₄ FeO ₂	446.42	72.64	7.67	12.51	52—54	52
			72.62	7.72	12.54		

ferrocene, or containing it but only in a minimum amount. Among them we succeeded to isolate trimethoxyterphenyl (1 g), m.p. 180—185°C (benzene).

For C₂₁H₂₀O₃ (320.16) calculated: 78.73% C, 6.29% H; found: 78.66% C, 6.40% H. ¹H-NMR: 7.80—8.00 (m, 3H, H_{ar}) and 6.72—7.1 (m, 8H), 3.75 (s, 3H, OCH₃), and 3.83 (s, 6H); EIMS, *m/z* (relative intensity): 320 (100), 289 (70), 213 (40), 185 (90), 135 (85), 77 (80).

Further product was probably ferrocenylglyoxalylhexamethoxysexiphenyl[®] (violet product). ¹H-NMR: 3.75 (s, 6H, OCH₃) and 3.83 (s, 12H), 4.50 (s, 5H, C₅H₅), 4.56 (t, 2H, H_β), 4.81 (t, 2H, H_α), 6.70—7.10 (m, 17H, H_{ar}) and 7.8—8.1 (m, 6H). IR: 1640 and 1660 cm⁻¹ (ν(CO)).

Acylation with β-ferrocenylpropionyl chloride afforded:

1-(4-Methoxyphenyl)[3]ferrocenophan-1-ene, orange-yellow crystals, m.p. 129—132°C in a 25% yield.

For C₂₈H₁₈FeO (M⁺, *m/z* 330) calculated: 72.74% C, 5.49% H, 16.91% Fe; found: 72.35% C, 5.76% H, 17.02% Fe. ¹H-NMR: 3.07 (d, 2H, CH₂), 3.75 (s, 3H, OCH₃), 4.15 (m, 8H, C₅H₄), 6.39 (t, 1H, CH=), 6.78 (d, 2H, C₆H₄), 7.32 (d, 2H, AB q, J_{AB} = 9 Hz). EIMS, *m/z* (relative intensity): 330 (100), 331 (22.3), 242 (28), 201 (5.3), 165 (4.3), 104 (16.2), 96 (7.3).

1,1-Bis(4-methoxyphenyl)[3]ferrocenophane, orange-yellow crystals, m.p. 152—155°C (yield 7%).

Table 2

¹H-NMR chemical shifts (p.p.m. δ scale) of the synthesized compounds

<i>n</i>	—CH ₂ —	—CH ₂ C ₆ H ₄	—CH ₂ CO—	—OCH ₃	C ₅ H ₅ +C ₅ H ₄	C ₆ H ₄	C ₆ H ₄	<i>J</i> _{AB} /Hz
2	—	2.73 t, 2H	3.10 t, 2H	3.83 s, 3H	3.9—4.2 m, 9H	6.89 d, 2H	7.90 d, 2H	8.9
3	1.9 k, 2H	2.41 t, 2H	2.90 t, 2H	3.83 s, 3H	3.9—4.2 m, 9H	6.88 d, 2H	7.88 d, 2H	8.9
4	1.3—2.0 m, 4H	2.36 t, 2H	2.90 t, 2H	3.85 s, 3H	3.9—4.2 m, 9H	6.91 d, 2H	7.92 d, 2H	8.9
5	1.3—2.0 m, 6H	2.36 t, 2H	2.92 t, 2H	3.87 s, 3H	4.0—4.2 m, 9H	6.94 d, 2H	7.94 d, 2H	9.0
6	1.2—1.9 m, 8H	2.30 t, 2H	2.88 t, 2H	3.83 s, 3H	3.9—4.2 m, 9H	6.88 d, 2H	7.89 d, 2H	8.9
8	1.1—2.0 m, 12H	2.35 t, 2H	2.89 t, 2H	3.85 s, 3H	3.9—4.2 m, 9H	6.90 d, 2H	7.91 d, 2H	9.0
9	1.1—1.9 m, 14H	2.31 t, 2H	2.89 t, 2H	3.85 s, 3H	3.9—4.2 m, 9H	6.90 d, 2H	7.90 d, 2H	8.7

For $C_{27}H_{26}FeO_2$ (M^+ , m/z 438) calculated: 73.98% C, 5.98% H, 12.74% Fe; found: 74.42% C, 6.58% H, 13.05% Fe. 1H -NMR: 2.37 (m, 2H, CH_2), 2.85 (m, 2H, CH_2), 3.75 (s, 6H, OCH_3), 4.07 (m, 9H, $C_5H_5 + C_5H_4$), 6.73 (d, 4H, C_6H_4), 7.31 (d, 4H, AB q, $J_{AB} = 9$ Hz). EIMS, m/z (relative intensity): 438 (100), 439 (38.5), 331 (2.5), 288 (6.7).

β -Anisolyethylferrocene — see Tables 1 and 2.

[3]Ferrocenophan-1-one [15] (21% yield).

Acylation with γ -ferrocenylbutyryl chloride gave 2,3-ferroceno-2-cyclohexan-1-one [16] in a 35% yield as a by-product.

The by-product of acylation with δ -ferrocenylvaleroyl chloride was 2,3-ferroceno-2-cyclohepten-1-one [16] obtained in a 21% yield.

p-Methoxyphenylacetylferrocene

A solution of *p*-methoxyphenylacetyl chloride (3.9 g; 20 mmol) and anhydrous aluminium chloride (2.76 g; 20 mmol) in dichloromethane (40 ml) was added to a stirred solution of ferrocene (3.87 g; 20 mmol) and anhydrous aluminium chloride (2.76 g; 20 mmol) in dichloromethane at room temperature. The mixture was after 3 h of stirring poured into ice-cold water, $NaHSO_3$ was added and organic compounds were extracted with dichloromethane. The extract was washed with water, dried and the residue, remaining after evaporation of the solvent, was chromatographed over silica gel. Yield 1.3 g (34%) of the unreacted ferrocene and 3.86 g (57%) of *p*-methoxyphenylacetylferrocene, m.p. 91–92°C (benzene—petroleum ether).

For $C_{19}H_{18}FeO_2$ (334.20) calculated: 68.28% C, 5.43% H, 16.71% Fe; found: 68.27% C, 5.52% H, 16.78% Fe. 1H -NMR: 3.75 (s, 3H, OCH_3), 3.90 (s, 2H, $COCH_2$), 4.01 (s, 5H, C_5H_5), 4.47 (t, 2H, H_β), 4.80 (t, 2H, H_α), 6.84 (d, 2H, C_6H_4), and 7.25 (d, 2H, AB q, $J_{AB} = 9.6$ Hz).

p-Methoxyphenylglyoxalylferrocene

Manganese(IV) oxide (8 g) was added [17] to a solution of *p*-methoxyphenylacetylferrocene (1 g; 0.3 mol) in anhydrous benzene (60 ml), the mixture was refluxed and the reaction course was monitored by thin-layer chromatography. Manganese(IV) oxide was after 4 h filtered off, the filtrate concentrated and chromatographed. Yield 0.7 g (72%) of the title product, m.p. 83–84°C (benzene—light petroleum).

For $C_{19}H_{16}FeO_3$ (348.18) calculated: 65.54% C, 4.63% H, 16.04% Fe; found: 65.62% C, 4.61% H, 16.03% Fe. 1H -NMR: 3.87 (s, 3H, OCH_3), 4.27 (s, 5H, C_5H_5), 4.65 (t, 2H, H_β), 4.87 (t, 2H, H_α), 6.96 (d, 2H, C_6H_4) and 8.04 (d, 2H, AB q, $J_{AB} = 9.2$ Hz). IR: 1650 and 1666 cm^{-1} ($\nu(CO)$).

Decomposition of p-methoxyphenylglyoxalylferrocene in anisole

Anhydrous aluminium chloride (1.3 g; 10 mmol) was added to a stirred solution of *p*-methoxyphenylglyoxalylferrocene (0.5 g; 1.5 mmol) in anisole (80 ml) at room temperature. Stirring was continued for 4 1/2 h, the mixture was poured into water and worked up in a usual manner. Chromatography on silica gel evidenced the presence of the starting

material (0.1 g, 28%) in addition to several, ferrocene not containing products analogous to those isolated upon acylation of anisole with ferrocenylacetyl chloride.

Reaction of ferrocenylacetyl chloride with aluminium chloride

Anhydrous aluminium chloride (0.8 g; 6 mmol) was added at room temperature to a stirred solution of ferrocenylacetyl chloride prepared from ferrocenylacetic acid (1.4 g; 6 mmol) in dichloromethane (40 ml). The separation of a precipitate on the flask wall followed after this exothermic reaction. The mixture was after 8 h of stirring poured into water, NaHSO₃ was added and the aqueous layer extracted with dichloromethane; the solution was dried, the solvent removed.

The residue was a highly polar polymeric material from which the starting acid could not be isolated even by extraction with 10% NaOH.

Isolation of the auto-oxidation product of ferrocenylacetonitrile

Ferrocenylacetonitrile (2.6 g; 22 mmol) prepared according to [14] was left to stand at room temperature for 1 month and then hydrolyzed with NaOH. The alkaline solution was extracted with dichloromethane, the solvent distilled off and the oily residue (0.56 g) was chromatographed on a silica gel column. 1,2-Diferrocenyl-1-cyanoethylene isolated in a 57% yield (0.32 g) had after crystallization from benzene—light petroleum m.p. 173—175°C.

For C₂₃H₁₉Fe₂N (421.1) calculated: 65.60% C, 4.54% H, 26.52% Fe, 3.32% N; found: 66.28% C, 4.87% H, 25.96% Fe, 3.26% N. ¹H-NMR: 4.21 (s, 10H, C₃H₅), 4.32 (t, 2H, H_β), 4.87 (t, 2H, H_α), 4.46 (t, 2H, H_β), 4.53 (t, 2H, H_α), 6.9 (s, 1H, CH). IR: 2215 cm⁻¹ (ν(CN)), 1615 cm⁻¹ (ν(C=C)). EIMS, *m/z* (relative intensity): M²⁺ 210.5 (66.4), M⁺ 299 (5.7), 235 (21.6), 186 (100).

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