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ELECTROCHEMICAL SUBSTITUTION OF HYDROGEN IN FERROCENE

S.P. GUBIN, L.I. DENISOVICH *, N.V. ZAKURIN and M.G. PETERLEITNER
Institute of Organo-Element Compounds, Academy of Sciences of the U.S.S.R., Moscow (U.S.S.R.)

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Summary

Interaction of radicals $R^\cdot$ formed in anode decarboxylation of carboxylate anions with the ferricinium cation generated at the same electrode leads to alkylferrocene derivatives. A similar reaction of the ferricinium cation with radicals formed from dibasic acids or their semiesters yields esters of ferrocenyl-containing carboxylic acids. Monosubstituted ferrocene, particularly those containing electron donor substituents, undergo further substitution to give di- and polysubstituted products. The procedures are described that lead to predominant isolation of either mono- or poly-substituted products.

The results of qualitative and quantitative analyses of the polymethylation products show that orienting effects by the substituents are the same for radical substitution in the ferricinium cation and for electrophilic substitution in ferrocene.

Anode displacement of hydrogen in aromatic compounds has been studied in detail [1]. Depending on the substituting reagent Z^-, the process may lead to acyloxylation, methoxylation, cyanation, halogenation, etc. Such reactions mostly proceed by the nucleophilic substitution mechanism, via the formation of cation radicals (EC_NEC_B).

$$HArR \xrightarrow[E]{-e} [HArR]^{+\cdot} \xrightarrow[C_N]{Z^-} [ZHArR]^{\cdot} \xrightarrow[E]{-e} [ZHArR]^{+} \xrightarrow[C_B]{-H^+} ZArR$$

The reaction with the nucleophile Z^- is believed [1] to occur at the step of the formation of a cation radical. Because the presence of aromatic compounds hinders oxidation of Z^-, radical alkylation of aromatic compounds only occurs as a by-process in anode carboxylation ($Z = RCOO^-$) [2].

Ferrocene and other metallocenes are known [3] to undergo oxidation to the cation more readily than aromatic compounds. These organometallic compounds as a rule add nucleophiles to give metallicinium salts rather than products of substitution in π-bonded rings. The process is sometimes accom-

TABLE 1

ELECTROLYSIS CONDITIONS AND ANALYSIS OF THE COMPOSITION OF ALKYLATION PRODUCTS (PROCEDURE I)

Experiment No.	Initial amount of ferrocene (g)	Amount of alkylation products (g)	Flow rate (ml/min)	Mass spectrometric and GLC data						
				Values of n in molecular ions Alk_nFc	Composition of reaction mixture (%)					
					Fc	MeFc	Me_2Fc	Me_3Fc	Me_4Fc	Pr
1	1,82	1,60	6	0–4	44,7	26,8	18,7	9,7		
2	1,85	1,88	2		24,5	13,8	21,4	26,3	13,8	
3	3,95	4,10	7	0–4	81,0	16,0	3,0			
4	2,32[a]	2,10	8	0–6	69,0	21,4	9,6			
5	1,27[a]	1,12	8	0–6	34,7	33,7	23,5	8,2		
6	0,85[a]	0,29	0	0–7	0,5	18,3	49,3	31,9		
7	1,92[b]	2,03	7	0–4	83,1					16,9
8	2,0[c]	1,30	8	0–2						

[a] The products obtained in experiments 3, 4, and 5 were used as starting materials in experiments 4, 5, and 6, respectively. [b] The reaction was carried out with butyric acid. [c] The reaction was carried out with myristinic acid.

panied by redox reactions leading to partial or complete destruction of the ferrocene nucleus [4]. One may therefore expect that the above scheme cannot be realized with ferrocene as aromatic substrate. On the contrary, the paramagnetic ferricinium cation bearing 17 electrons is known [illegible] react with radicals R$^{\cdot}$ generated by chemical methods to give substitution products [5,6]. We have suggested that simultaneous generation of ferricinium cations and radicals R$^{\cdot}$ as well as their interaction may be accomplished by electrochemical methods in co-electrolysis of ferrocene and carboxylate anions, $RCOO^-$, despite the difference in their oxidation potentials (for ferrocene, $E_{1/2} = +0.01$ V, and for $RCOO^-$, $E_{1/2} = +1.80$ V). We have found that, in agreement with this expectation, Pt-anode decarboxylation of carboxylate anions in methanol (the conditions of the Kolbe reaction) in the presence of ferrocene leads to alkylation of ferrocene *. Various alkylferrocenes may be synthesized depending on the carboxylate reagent. Thus, electrolysis of a mixture of CH_3COOK, CH_3COOH, and ferrocene leads to methylated ferrocene along with the usual Kolbe reaction product, ethane. Likewise, electrolysis in the presence of partially neutralized propionic, butyric, or myristinic acids gives ethyl-, propyl-, and cetyl- ferrocenes, respectively.

The electrochemical alkylation reactions do not terminate with the formation of monosubstituted species. The resulting reaction mixtures contain products with one to seven alkyl groups per molecule depending on the conditions. Di- and polyalkylferrocenes occurs as isomer mixtures. The formation of acyloxyferrocene is not observed. Separation of ferrocene from alkylferrocenes and division of alkylferrocene mixtures poses a difficult problem not fully solved as yet (see, e.g. [8]). So we did not attempt separation of the product mixtures. Variation of the reaction conditions and of the conditions of product isolation, however, allowed us to direct the process mainly to poly- or di- and mono-alkylferrocenes (Tables 1—3).

Preferred formation of mono-derivatives occurs when the products are rapidly removed from the reaction zone (flow electrolysis, procedure I). Reaction mixtures from flow electrolysis mainly contain unreacted ferrocene and monomethylferrocene and small amounts of di- and tri- methylferrocenes. Repeated electrolysis of the products thus obtained leads to an increase in the proportion of methyl- and dimethylferrocenes (Table 1, experiments 3—6). Decrease of the flow rate favours the formation of polyalkylferrocenes (cf. experiments 1 and 2, Table 1).

Electrolysis without passage of the solution through the cell mainly yields polyalkylferrocenes (procedure II). The product composition depends markedly on the quantity of electricity passed through the reaction mixture. The analytical data given in Tables 2 and 3 show that the proportion of polyalkylferrocenes increases with that quantity. It is worthwhile mentioning that after passing 0.22 F, no unreacted ferrocene occurs in the mixture, and almost quantitative yield of different methylferrocenes is observed. Similar results have been obtained in electrochemical ethylation of ferrocene. The process, however, gives no fully substituted product, and decamethylferrocene is not observed even after the passage of 1.45 F of electricity. Substitution appears to terminate at hexa-

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* Preliminary results were published in a short communication [7].

TABLE 2

ELECTROLYSIS CONDITIONS AND ANALYSIS OF THE COMPOSITION OF METHYLATION PRODUCTS (PROCEDURE II)

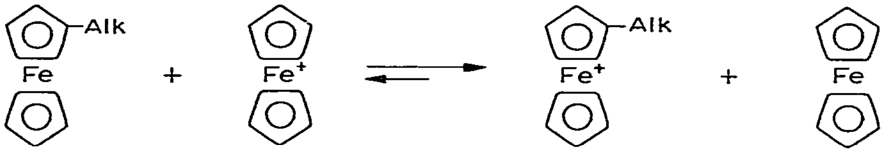
Experiment No.	Quantity of electricity (F)	Initial amount of ferrocene (g)	Amount of alkylation products (fractions I and II) (g)	Mass spectrometric and GLC data							
				Values of *n* in molecular ions Me_nFc	Composition of reaction mixture (%)						
					Fc	MeFc	Me_2Fc	Me_3Fc	Me_4Fc	Me_5Fc	Me_6Fc
9	0,1	1,0	I 0,95	0—5	21,0	6,7	19,9	40,5	11,0		
			II 0,21	2—6				10,7	50,9	38,4	
10	0,2	1,0	I 0,88	0—5	1,9	14,4	52,6	31,1			
			II 0,26	3—6					49,0	51,0	
11	0,4	1,5	I 1,42	0—6	0,6	4,7	15,7	35,8	7,4		
			II 0,37	2—7					35,0	65,0	
12	1,0	1,5	I 1,9	3—7				4,6	50,1	45,2	
13	1,4	1,5	I 1,92						15,5	74,6	9,7
			II 0,56							44,2	55,9

TABLE 3

ELECTROLYSIS CONDITIONS AND ANALYSIS OF THE COMPOSITION OF ETHYLATION PRODUCTS (PROCEDURE II)

Experiment No.	Quantity of electricity (F)	Initial amount of ferrocene (g)	Amount of alkylation products (fractions I and II) (g)	Relative intensities of molecular ions (%)							
				Et_2Fc	Et_3Fc	Et_4Fc	Et_5Fc	Et_6Fc	Et_7Fc	n_D^{20}	$E_{1/2}$ (V)
14	0,2	1,0	I 0,88	2,4	36,8	100,0	53,7	4,9		1,5413	0,20
			II 0,35		4,2	65,5	100,0	22,6	1,1	1,5473	0,16
15 ·	1,0	1,5	I 1,60	2,4	39,0	100,0	68,2	12,9	1,2		
			II 0,33		5,4	34,5	100,0	85,0	13,7		

substituted species, as is clearly seen from voltammetric measurements. Fig. 1 represents the anode-cathode wave of the solution, $E_{1/2}$, as a function of time. $E_{1/2}$ shifts to less positive potentials with accumulation of alkyl derivatives in the solution, in full agreement with the well known fact that alkyl substituents facilitate oxidation of ferrocene. However, the observed decrease is not linear: $E_{1/2}$ approaches its limiting value corresponding to $E_{1/2}$ of a mixture of penta- and hexamethylferrocenes. Heptamethylferrocenes could only be detected mass-spectrometrically. Voltammetric measurements also show (Fig. 2) that ca. 80% of the reaction products occurs in the reduced forms, and only some 20% are in the oxidized forms. Polyalkyl derivatives, which are much easier to oxidize than ferrocene, may be expected to occur in the oxidized forms. Increase in the number of alkyl substituents should shift the equilibrium to the



right. Treatment of solutions after electrolysis confirm this suggestion. At first alkylferrocenes in reduced form were separated using extraction (fraction I, See experimental section). Then the solution was reduced and fraction II mainly containing penta- and hexamethyl (or ethyl) ferrocenes was obtained. Thus, mixtures containing the components expected may be obtained depending on the electrolysis conditions and on the conditions of isolation of the products.

Application of a similar technique to a solution containing ferrocene and anions of dibasic acids (electrolysis with Pt electrodes) leads to esters of ferrocenylcarboxylic acids. Coelectrolysis of oxalic acid and ferrocene produced methyl esters of ferrocenecarboxylic and ferrocenedicarboxylic acids formed in the interaction of the ferricinium cation with the $HOOC^{\cdot}$ radical followed by esterification of the resulting acids. We have also isolated mono-, di-, and tri(γ-carbomethoxypropyl)ferrocene from the products of electrolysis of ferrocene in the presence of the partially neutralized semiester of glutaric acid. In order to reduce the yield of the Kolbe dimer, $CH_3OOC(CH_2)_6COOCH_3$,

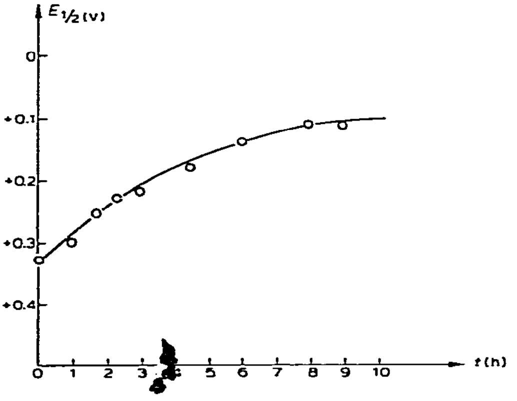


Fig. 1. Anode wave $E_{1/2}$ of the reaction mixture as a function of time of electrolysis.

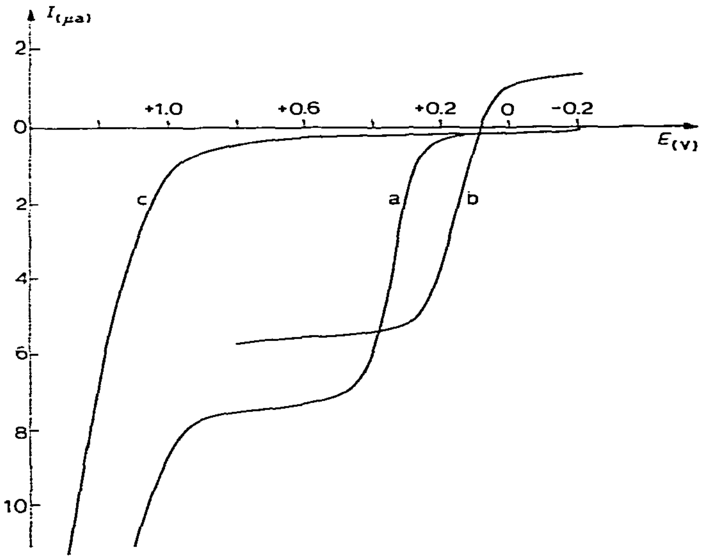


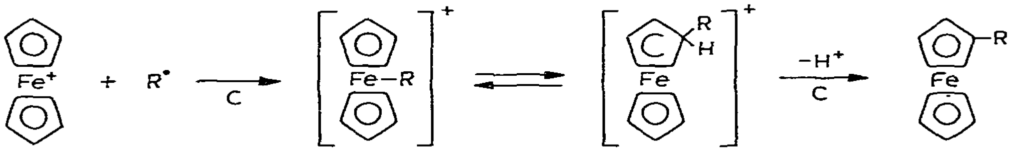
Fig. 2. Voltammetric data on the reaction mixture: (a) Prior to electrolysis; (b) Near the completion of electrolysis; (c) For a solution of CH_3COOH and CH_3COONa in CH_3OH.

which makes the separation of the products difficult, we used lower current densities in this reaction than in ferrocene alkylation.

The following step-wise scheme may be suggested for the alkylation of ferrocene:

$$RCOO^- \xrightarrow[E']{-e} RCOO^\bullet \xrightarrow[C']{-CO_2} R^\bullet \qquad (R = CH_3,\ C_2H_5,\ C_{13}H_{27},\ HOOC,\ H_3COOC(CH_2)_3)$$

$$(C_5H_5)_2Fe \xrightarrow[E]{-e} (C_5H_5)_2Fe^+$$



The reaction of the ferricinium cation with the radical R˙ should occur at the electrode surface because strongly adsorbed short-living radicals R˙ cannot exist in the solution [1]. This process provides the first example of the E(E′C′)CC-type reactions with ferrocene as substrate.

Monoalkylferrocene which is easier to oxidize than ferrocene may undergo further alkylation (see Scheme). The second methyl group may appear in the already substituted as well as unsubstituted π-cyclopentadienyl rings. Chromatography patterns of the reaction mixture (Fig. 3) contain peaks corresponding to three possible isomeric dimethylferrocenes. Further alkylation of dimethylferrocene leads to isomeric trimethylferrocenes etc. We found that the ratio of isomeric forms remains constant for alkylferrocenes containing a certain number of methyl substituents irrespective of the reaction conditions. This may be due to orienting effects by the substituents present in the molecule. The products

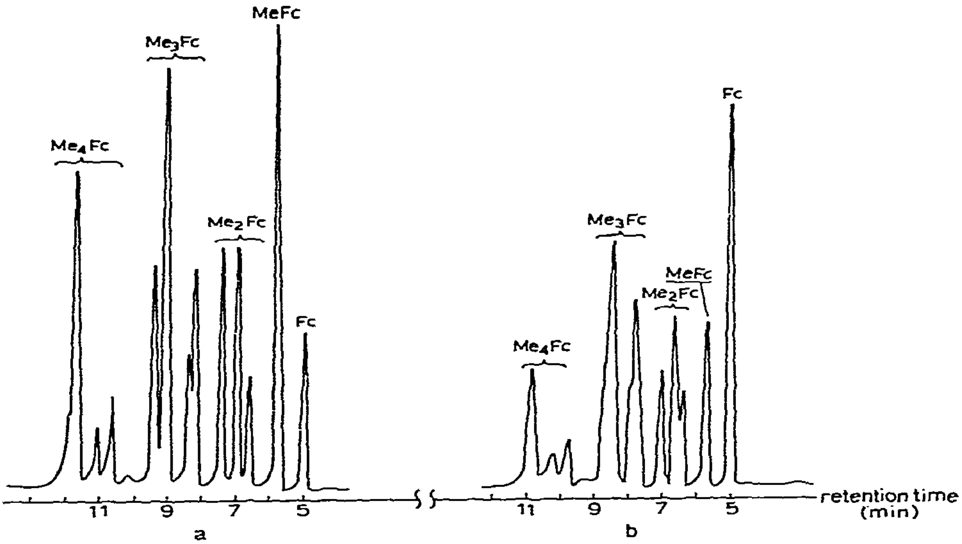
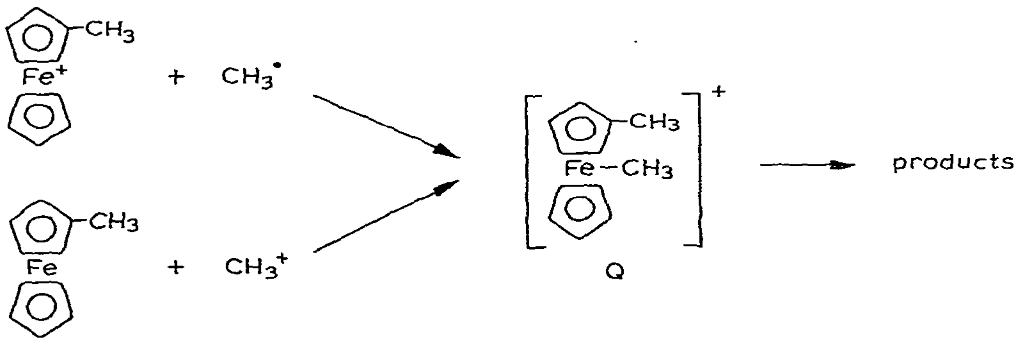


Fig. 3. Chromatography patterns: (a) Of a reaction mixture of electrophilic methylation of methylferrocene; (b) Of a reaction mixture of electrochemical methylation of methylferricinium.

of methylation of monomethylferrocene, isomeric dimethylferrocenes, provide an example of such an orienting effect. Table 4 gives percentages of 1,1′, 1,2, and 1,3-dimethylferrocenes in the reaction mixture as obtained from GLC data * and relative site reactivity for positions 1′, 2, and 3 of the monomethylferricinium cation toward the methyl radical. As seen from Table 4, the electron releasing methyl group activates positions 2 and 3 of the substituted ring to a greater extent than position 1′, in agreement with what is usually observed for electrophilic substitution. The data obtained (Table 4) are in good agreement with relative site reactivity for methylferrocene in acylation and electrophilic methylation reactions. Moreover, comparison of the GLC data for the reaction mixture obtained at the first steps of electrophilic methylation [10] and anode methylation (Fig. 3) shows them to be almost identical in the type, number, and relative quantities of the components. These observations indicate that the same transition state Q is involved in both anode alkylation and electrophilic substitution of methylferrocenes:



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* Assignment of peaks at the chromatographic pattern established according to the data of [9].

TABLE 4

RELATIVE AMOUNTS OF 1,2-, 1,3- AND 1,1'-ISOMERS OF DIMETHYLFERROCENE (%) AND RELATIVE SITE REACTIVITY [a] FOR POSITIONS 1, 2, AND 3 IN METHYLFERROCENE

Reaction	Isomers					
	1,1'		1,2		1,3	
	%	*f*	%	*f*	%	*f*
Radical alkylation of methylferricinium cation	49.8	1.0	27.1	1.36	22.8	1.14
Electrophilic acylation of methylferrocene [11]	47.7	1.0	21.9	1.15	30.4	1.59
Electrophilic methylation of methylferrocene [a]	40.4	1.0	41.5	2.56	18.0	1.11
Electrophilic methylation of methylferrocene [b]	45.4	1.0	22.7	1.25	31.8	1.75

[a] Calculated from the data cited in ref. 10. [b] Calculated from the data cited in ref. 9.

This is the necessary condition for the directing effect by a given substituent to be identical in ferrocene and the ferricinium cation.

We have found that the dimethyl ester of ferrocenedicarboxylic acid obtained by electrolysis of ferrocene in the presence of oxalic acid is the 1,1'-isomer. This follows from the absence of 1000 and 1100 cm^{-1} absorption bands in the IR spectrum and of the signal from the unsubstituted cyclopentadienyl ring in the proton NMR spectrum (Table 5). Hence the electron withdrawing CH_3OOC substituent in ferricinium orients further radical substitution into the unsubstituted ring. This is again similar to what occurs in electrophilic substitution of ferrocene containing electron withdrawing substituents [5]. The results obtained provide yet another piece of evidence for the attack on the metal in reactions of both ferrocene and ferricinium cation.

Anode alkylation may be applied to other transition metal π-complexes that can be oxidized to cation radicals. Preliminary experiments show that anode oxidation of the acetate anion in the presence of cyclopentadienylmanganese-tricarbonyl (CTM) yields methylated CTM. It is also possible that for π-complexes other electrochemical substitution reactions may be observed. Studies in this field are under way in this laboratory.

Experimental

Apparatus

Electrolysis was performed in a glass cylindrical vessel (up to 350 cm^3) without a membrane. In the alkylation processes, Pt screen electrodes (cathode and anode) were placed perpendicularly to the vessel axis at 10 mm spacing. Each electrode was of 16 cm^2 surface area. In the carboxylation reactions, the anode was a 26 cm^2 Pt screen, and the cathode was Pt foil. Spacing between electrodes (4 mm) was fixed with a Teflon ring.

Electrolysis was carried out without anode potential control.

Reagents

CH_3OH was purified as recommended in [12]. CH_3COOK was dried over P_2O_5 at 120°C in vacuo. Ferrocene was recrystallized from heptane. Acetonitrile for voltammetric measurements was purified according to [13]. Bu_4NBF_4 was prepared and purified as described in [14].

Analysis of reaction products

Alkylation products were analyzed by GLC using mixtures of known compositions as reference samples (Apiezon L, capillary column 30 m × 2.5 mm), and also by the methods of mass and chromatomass spectroscopy. The chromatography and mass spectrum data of a mixture of alkylferrocenes are shown in Fig. 4. Alkylation product yields were determined from the GLC data. The GLC quantitative data obtained by peak area measurements were accurate to within 3—3.5% [15].

Electrochemical alkylation

Two electrolysis procedures were used: in a series of experiments the solution was passed through the electrolyzer (procedure I), and in other experiments, the solution was placed in the electrolytic cell until the completion of the reaction (procedure II).

Procedure I

A weighed amount of ferrocene contained in a special holder was placed in the electrolytic cell in close proximity to the anode (the upper Pt screen). Stock solution of a carboxylic acid, CH_3COOH or C_3H_7COOH (60 cm^3), in methanol (1000 cm^3) neutralized by 3% was passed through the vessel at the rate given in Table 1. Operating conditions were: current densities 5 to 7 × 10^{-2} A/cm^2, voltage 30—40 V. On heating of the mixture there was evolution, a bluish-green ferrocinium colouration appeared, and the formation of gaseous products was observed during the reaction. The product mixture was reduced with $SnCl_2$

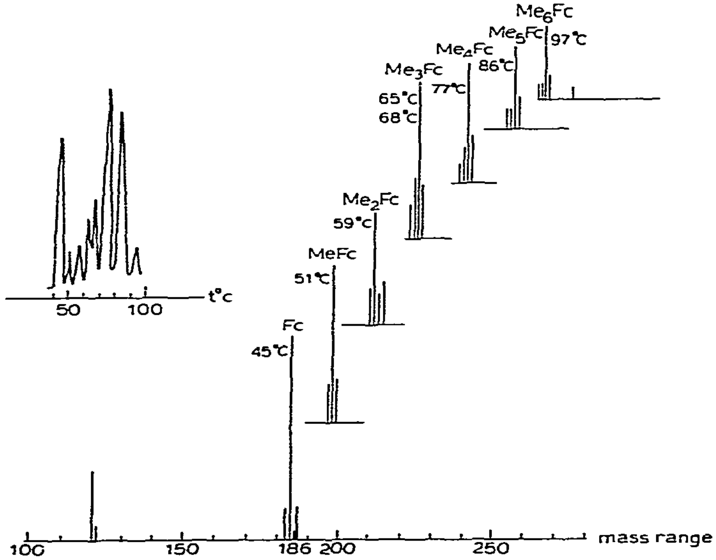

Fig. 4. Chromato-mass spectrometric pattern for the products of electrochemical methylation of ferrocene.

TABLE 5

ANALYSIS OF DATA FOR ESTERS OF FERROCENYL-CONTAINING CARBOXYLIC ACIDS

Physico-chemical parameters	Esters of ferrocenyl-containing carboxylic acids				
	Methyl ester of ferrocene-carboxylic acid, mol. wt. 241	Dimethyl ester of ferrocene dicarboxylic acid, mol. wt. 302	(γ-Carbomethoxypropyl)ferrocene, mol. wt. 286	Di(γ-carbomethoxypropyl)ferrocene, mol. wt. 386	Tri(γ-carbomethoxypropyl)ferrocene, mol. wt. 486
m/e M^+	244	302	286	386	486
IR frequencies (cm^{-1})	1000, 1100, 1450, 1750	1450, 1750	1000, 1100, 1450, 1750	1450, 1750	1450, 1750
Proton NMR spectra (in CCl_4, ppm)		two triplets, 4.76 and 4.31 singlet, 3.80			

(HCl) and extracted with petroleum ether. After washing the organic layer with Na_2CO_3 solution and drying, the solvent was removed under vacuum. The electrolysis conditions and the analysis of the composition of the alkylation products are given in Table 1.

Electrolysis of ferrocene in the presence of partially neutralized myristinic acid was performed in the same manner. The alkylation products were separated from unreacted ferrocene as described in [16]. The formation of $C_{13}H_{27}Fc$ and $(C_{13}H_{27})_2Fc$ was suggested on the basis of the mass spectrum of the product mixture (the ions *m/e* 368 and 550).

Electrolysis of CTM in the presence of partially neutralized acetic acid was carried out likewise. The mass spectrum of the product mixture contained the ions *m/e* 218, 232, and 246 indicative of the presence of MeCTM, Me_2CTM, and Me_3CTM.

Procedure II

A solution of ferrocene containing CH_3COOH or C_2H_5COOH (35 cm^3, neutralized by 3%) was subjected to electrolysis at a 12×10^3 A/m^3 current density and 50 V voltage potential. CO_2 and C_2H_6 evolved during electrolysis were detected by gas chromatography. After electrolysis, the solution was extracted with petroleum ether, reduced by $SnCl_2$ or $Na_2S_2O_3$ and extracted with petroleum ether once more. Ether layers (I and II) were washed with Na_2CO_3 solution and water and dried. The solvent was then distilled off under vacuum. The electrolysis conditions and the analysis of the composition of alkylation products are given in Tables 2 and 3.

The alkylation product yields based on reacted ferrocene were 85 to 90%.

Electrochemical synthesis of esters of ferrocenecarboxylic acids

(1) Preparation of methyl esters of ferrocenecarboxylic acids. A solution of ferrocene (9.5 g) and oxalic acid (25 g) in dry methanol (280 cm^3) was subjected to electrolysis at a current density of 3.8×10^{-2} A/cm^2 and voltage potential of 25 V (15°C). After passing 0.4 F of electricity, the solution was reduced with $Na_2S_2O_3$ and extracted with benzene. The benzene layer was washed with Na_2CO_3 solution and water and dried over $MgSO_4$. After the removal of benzene, the residue (8.1 g) was subjected to thin layer chromatography with petroleum ether as eluent to give unreacted ferrocene (6.8 g, 65%), methyl ester of ferrocenecarboxylic acid (0.85 g, 20% *) and dimethyl ester of 1,1-ferrocenedicarboxylic acid.

(2) Preparation of γ-carbomethoxypropylferrocene. Ferrocene (9.5 g) and monomethylglutarate (50 g neutralized by 40% with KOH) dissolved in 280 cm^3 of dry CH_3OH were subjected to electrolysis at current density of 2.3×10^{-2} A/cm^2 and voltage potential of 3 V (20°C). After passing 0.3 F of electricity, reduction, extraction and chromatographic separation on SiO_2, the reaction mixture gave unreacted ferrocene (2.5 g, 26%, eluent petroleum ether) and carbomethoxypropylferrocenes (2.6 g, eluent benzene). The product mixture was further separated by thin layer chromatography on SiO_2. Three fractions of a total weight of 2.33 g were isolated. According to the IR and mass spec-

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* Here and below, the yields based on reacted ferrocene are given.

troscopic evidence (Table 5), fraction 1 mainly contained γ-carbomethoxypropylferrocene (0.7 g, 7%), fraction 2 was di(γ-carbomethoxypropyl)ferrocene (0.23 g, 1.6%), and fraction 3 was tri(γ-carbomethoxypropyl)ferrocene (1.4 g, 8%). However, the components could not have been fully separated because of similarity in the R_f values.

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