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Ferrocene Compounds. VI.* Reactions of Ferrocene with Dicarboxylic Acid Chlorides

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The Friedel-Crafts reactions of ferrocene with dicarboxylic acid chlorides have been reinvestigated under diacylation conditions. In the reaction of ferrocene and succinyl chloride only the previously described compounds 1,4-diferrocenyl-1,4-butanedione (I) and γ-ferocenyl-γ-oxobutyric acid[1] (II) were isolated. By the action of ferrocene with adipoyl chloride in addition to the known polymeric product VIII[2] the mono- and diacylated compounds (VI, VII, XII, and XV) and their transformation products (IX, X, XIV, and XVI) were obtained. The structure of the compounds prepared is confirmed by their IR, UV, ^{1}H-NMR, and mass spectra.

INTRODUCTION

Sugiyama et al.[1] reported the formation of 1,4-diferrocenyl-1,4-butanedione (I), γ-ferrocenyl-γ-oxobutyric acid (II) and γ,γ-diferrocenylbutyrolactone in the Friedel-Crafts acylation of ferrocene with succinyl chloride. Polycondensation reactions of ferrocene with adipoyl chloride have been investigated in the presence or in the absence of acid catalysts. The best yields of the polymere VIII ($n \approx 24$) were obtained when ferrocene was treated with liquid adipoyl chloride in the absence of catalyst and solvent[2].

In an earlier paper[3] we reported the reaction of ferrocene with glutaroyl chloride under diacylation conditions. The reaction of ferrocene, glutaroyl chloride and aluminium chloride in molar ratio 1 : 1.4 : 2.5 gave a mixture of 24% of δ-ferrocenyl-δ-oxovaleric acid and 8% of 1,2-(α,ε-dioxopentamethylene)ferrocene (IIIb). The formation of heteroannularly bridged 1,1'-(α,ε-dioxopentamethylene)ferrocene (IVb) was not observed.

In conection with these studies it was of interest to find out the conditions under which the reactions of ferrocene with succinyl and adipoyl chloride, resp., would lead to the products of bimolecular diacylation IIIa, IIIc, IVa or IVc. The possibility of intramolecular acylation was judged to be feasible upon consideration of molecular models.

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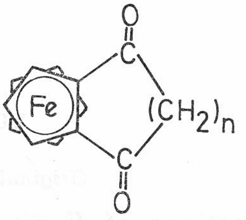
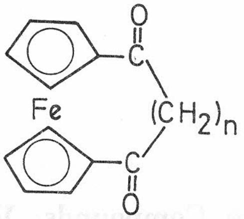
* Part V: M. Lačan and Z. Ibrišagić, *Croat. Chem. Acta* **46** (1974) 107.
Note. — A detailed conformational analysis of α,β-unsaturated ketones obtained in the present work on the basis of IR UV, ^{1}H-NMR, and mass spectra will be described in a subsequent paper.





a, n = 2

III b, n = 3 IV

c, n = 4

Figure 1.

RESULTS AND DISCUSSION

The experiments were performed with mixtures of ferocene : dicarboxylic acid chloride : aluminium chloride in a molar ratio 1 : 1.4 : 2.5 in different solvents (methylene chloride, ethylene chloride or carbon disulfide). We tried to find conditions for the formation of compounds of type III and IV by changing the order of mixing of reactants and also by variations in the experimental conditions.

The reactions of ferrocene and succinyl chloride were performed using methods *A* and *B* (described in Experimental section). In both cases only the previously described[1] compounds I (30—42% yield) and II (10—11% yield) were isolated.

TABLE I

Reactions of Ferrocene with Adipoyl Chlorid[a,b]

Method[c]	Sovent	Yield/%									
		VI	VII	VIII	IX	X	XII	XIV	XV	*E*-XVI	Z-XVI
A	CH_2Cl_2	10	—	13	1.7	d	d	d	d	1	1.5
A	CS_2	9	11	20	—	—	13	—	—	0.5	0.7
B	CH_2Cl_2	8	—	36	4	d	d	d	d	4	2
C	CH_2Cl_2	—	—	20	—	5	—	30	11	—	—
D	CH_2Cl_2	9	—	40	2	—	7	—	—	5	3.5
D	$ClCH_2CH_2Cl$	8	—	30	6	—	8	—	—	3	5

[a] Reactions of ferrocene with succinyl chloride in CH_2Cl_2 gave the following products [Method, No of compound. (% yield) given]: *A*, I (42), II (11); *B*, I (30), II (10).

[b] Structural formulae are given in the Figures 2,3 and in text.

[c] See Experimental.

[d] Acid fraction was not separated into components.

In the Friedel-Crafts reactions of ferrocene and adipoyl chloride methods *A* through *D* (see Experimental) were applied. In all these experiments extremely complex mixtures were formed, which were separated into acidic and neutral fractions. The mixtures of the acids X, XII, XIV, and XV were then esterified with diazomethane or ethanol/hydrochloric acid. The mixtures of esters and previously mentioned neutral fractions were then separated into components by both column and preparative thin layer chromatography (TLC). Chromatography of the mixtures of the esters gave the following compounds: X — dimethyl ester (Xa); XII — ethylester (XIIa); XIV — methylester (XIVa); XIV — ethylester (XIVb); and XV — diethylester (XVa).

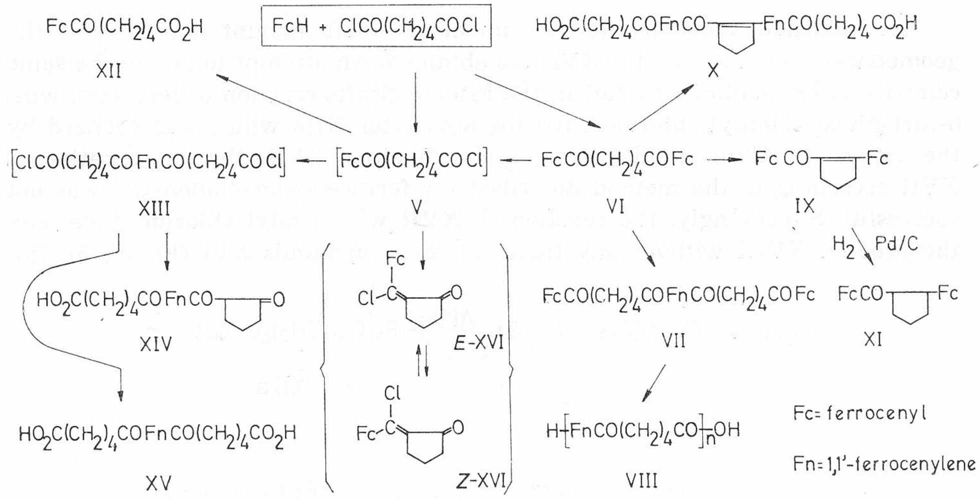


Figure 2.

The proposed course of these reactions is presented in Figure 2. From Table I it is evident that the polymer VIII was the main product (20—40% yield) in all these cases. The yields of the other products depended upon the method employed. Following the course of these reactions by TLC it was noted that at the beginning of the reactions chloride V was predominant. This chloride V was converted to diketone VI, or to keto acid XIV and XV or to a mixture of diastereomeric unsaturated ketones XVI depending upon the reaction conditions used. The appearance and the intensification of spots with lower R_f-values yield) in all these cases. The yields of the other products depended upon the indicating the route presented in the Figure 2. On the other hand compound IX was isolated in a poor yield in almost all operations.

It is known that the analogous compound to IX, 1-benzoyl-2-phenyl-1-cyclopentene, could be prepared by an intramolecular aldol condensation of 1,6-diphenyl-1,6-hexanedione in the presence of a basic catalyst[5]. Our attempts to prepare 1-ferrocenoyl-2-ferrocenyl-1-cyclopentene (IX) by the action of either hydroxyl or *tert*-butoxide ion on 1,6-diferrocenyl-1,6-hexanedione (VI) were unsuccessful. However, the acid catalyzed reaction gave an almost quantitative yield of IX. This fact could be explained in terms of the higher basicity of the carbonyl group in acylferrocenes than in their benzenoid analogue, because of the great electron releasing effect of the ferrocene nucleus[6].

In the reaction of ferrocene : adipoyl chloride : aluminium chloride in a molar ratio 2 : 1 : 2.2 ketone IX was obtained in a good yield, presumably by aluminium chloride induced cyclisation of the initially formed diketone VI. The structure of IX was confirmed through its catalyic hydrogenation to 1-ferrocenoyl-2-ferrocenylcyclopentane (XI).

Among the other products, in the Friedel-Crafts reactions performed by method *C* the keto acid X, which is related to IX, was isolated.

As indicated above in all experiments a small amount (0.7—5%) of the geometrical isomers *E*- and *Z*-XVI was obtained. An attempt to obtain the same compounds by another way failed; the Friedel-Crafts reaction of ferrocene with δ-carbethoxyvaleroyl chloride gave the keto ester XIIa which was cyclized by the action of sodium amide giving cyclic diketone XVII; the halogenation of XVII according to the method described for ferrocenoylacetaldehyde[7] was not successful. Surprisingly, the reaction of XVII with oxalyl chloride gave only the product XVIII without any traces of the compounds XVI (Figure 3). However, the comparison of the spectra of all three of these compounds, was useful for the structure determination of the geometrical isomers *E*- and *Z*-XVI.

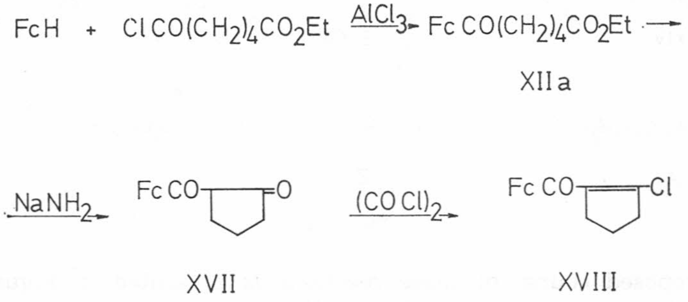


Figure 3.

From the above described work it could be noticed that methods *A* through *C* do not lead to the desired products III or IV.

Also, starting from the acid chloride V which is readily accessible using method *A* (the molar ratio ferrocene : adipoyl chloride : aluminium chloride 1 : 1.3 : 1.4), intramolecular acylation was attemped. However, this route using additional aluminium chloride (1.4 mol) was also unsuccessful (method *D*). After a prolonged reaction, only products VI, VIII, IX, XII, and XVI could be isolated.

On the basis of the results obtained it seems likely that the mechanism presented in Figure 4 is operative in the formation of the compounds IX, XIV, and XVI.

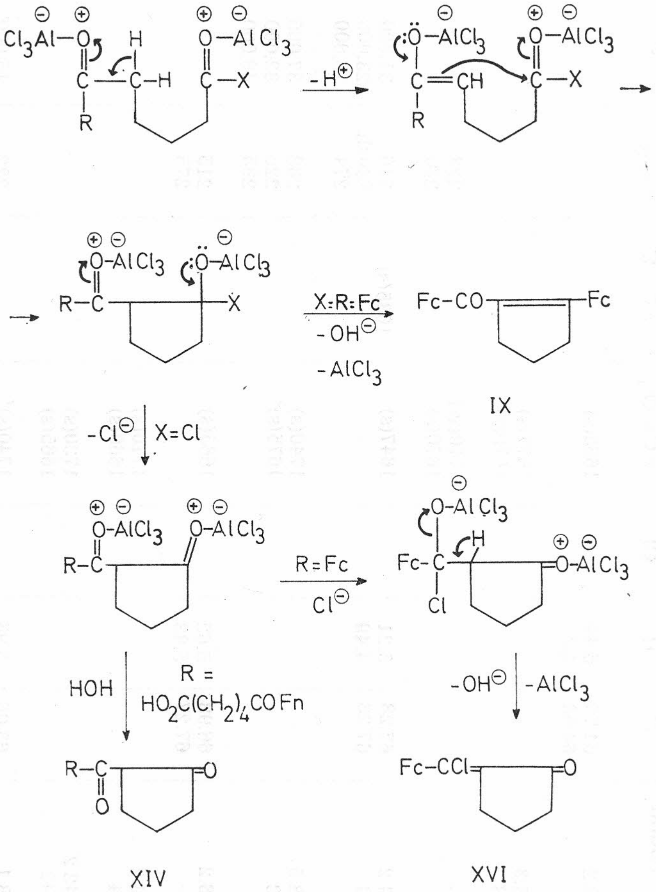


Figure 4.

EXPERIMENTAL

General

The experiments were performed under an argon atmosphere. The course of the reactions was followed by TLC on chromatoplates of silicagel G (Merck) in benzene: :ethanol (v/v) 30:1 and 15:1.

The reaction products were purified by alumina or silicagel (Riedel) column chromatography, and preparative TLC on silicagel G. The solid substances were recrystallized from absolute or aqueous ethanol.

The melting points were determined on a Büchi apparatus and are uncorrected. The IR spectra were recorded as KBr pellets (or CCl_4 solutions) with a Perkin-Elmer Infracord Model 137 and 257 Grating Infrared Spectrophotometer. The UV spectra (in ethanol) were measured on a Varian UV/VIS Model 635 spectrometer. The ^{1}H-NMR spectra (τ values, in $CDCl_3$ solution, if not stated otherwise) were recorded on a Varian A-60 spectrometer with tetramethylsilane as internal standard. The analyses were performed in the analytical Laboratory of the »Ruđer Bošković« Institute. Mass spectra were taken with a Varian MAT CH 7 in Lehrkanzel für Organische Chemie der Universität, Wien.

The yields given on the products of the Friedel-Crafts reactions are based on reacted ferrocene; 10—30% of unreacted ferrocene was isolated in these reactions.

TABLE II[a]

Compd.[b]	M. p./°C	Formula	Mol. weight Calc'd. Found[c]	Anal. Calc'd./% Found/% C	H	Cl	IR/cm^{-1} ν C=O	ν C=C	UV γ_{max} nm	ε
VI	131.5—2	$C_{26}H_{26}Fe_2O_2$	482.2 —	64.76 64.50	5.44 5.43		1665(s)			
VII	110—12	$C_{42}H_{42}Fe_3O_4$	778.3 778				1677(s) 1670(s)			
VIII	—	—	—				1710(w)[d] 1670(s)		223 280	
IX	146—7	$C_{26}H_{24}Fe_2O$	464.2 464	67.28 67.28	5.21 4.49		1647(s)	1635(s)	216 230sh 274	31,000 23,000 13,000
Xa	(oil)	$C_{40}H_{44}Fe_2O_7$	748.5 748				1740(s) 1675(s)[e]		208 226 285	37,000 32,000 48,000
XI	174—6	$C_{26}H_{26}Fe_2O$	466.2 —	66.98 67.27	5.62 5.83		1665(s)		215 275	
XII	80—2[g]	$C_{16}H_{18}FeO_3$	314.2 314				1710(s) 1660(s)			
XIIa	(oil)	$C_{18}H_{22}FeO_3$	342.2 342				1730(s) 1665(s)			
XIVa	94—6	$C_{23}H_{26}FeO_5$	438.1 —	63.06 63.10	5.98 6.22		1740(s)[f] 1672(s)		222 282	15,000 19,000
XIVb	72—3	$C_{24}H_{28}FeO_5$	452.3 452				1735(s)[f,h] 1675(s)			

Table II, contd.

Compd.[b]	M. p./°C	Formula	Mol. weight Calc'd./Found[c]	Anal. Calc'd./%/Found/% C	H	Cl	IR/cm^{-1} ν C=O	ν C=C	UV γ_{max} nm	ε
XVa	(oil)	$C_{26}H_{34}FeO_6$	498.4 498				1733(s)[h] 1670(s)			
E-XVI	(paste)	$C_{16}H_{15}ClFeO$	314.6 314			11.27 10.61	1740(s)[h]	1583(m)	214 267 307	9,100 4,000 6,200
Z-XVI	„	„	„				1723(s)[h]	1585(s)	216 266 307	12,500 6,700 11,000
XVII	84—6	$C_{16}H_{16}FeO_2$	295.9 296				1610(s)[i]		212 225 268 333	14,000 12,000 6,200 8,300
XVIII	82—3	$C_{16}H_{15}ClFeO$	314.6 —			11.27 10.85	1652(s)	1636(s)	211 230 280	13,000 9,600 9,300

[a] See Introduction to Experimental section.

[b] See the footnote[b] of the Table I.

[c] Mass spectrum.

[d] These data are identical with the in spectrum given in reference[2].

[e, f] This broad band probably includes: [e] ν CO of keto group and ν C=C of cyclopentene, [f] ν CO of carbalkoxy group and cyclopentanone ring.

[g] Literature[6] m. p. = 83.4—84.5 °C.

[h] in CCl_4.

[i] The band in the region 1680—1530 cm^{-1} centered at 1610 cm^{-1} indicates a hydrogen bonding in the enolyzed β-diketone XVII.

TABLE III

^{1}H NMR Spectra[a]

Compd.[b]	Ferrocene protons[c]			Side-chain protons			
	Substituted ring		Unsubstituted ring	—CH_2CO—	—CH_2C=C—	—CH_2CO_2R[d]	—CH_2—$(CH_2)_{1-2}$——CH_2—
	2— 5—	3— 4—	1'— …5'—				
I	5.14t (4)	5.50t (4)	5.75s (10)	6.86s (4)	—	—	—
II[e]	5.12t (2)	5.42t (2)	5.73s (5)	6.90m (2)	—	7.22m (2)	—
VI	5.21t (4)	5.52t (2)	5.81s (10)	7.21m (4)	—	—	8.20m (4)
VII	5.21t (8)	5.54t (8)	5.81 (10)	7.25m (8)	—	—	8.22m (8)
IX[b]	5.32m (2)	5.58m (2)	5.82m (10)	—	7.10m (4)	—	7.88m (2)
Xa[f]	5.30m (6)	5.58m (6)	—	g	g	g	8.28m (8)
XIIa	5.22t (2)	5.52t (2)	5.80s (5)	7.28m (2)	—	7.63m (2)	8.28m (4)
XIVa[h]	5.20m (4)	5.50m (4)	—	7.29m (4)	—	7.62m (2)	8.25m (8)
XIVb[b]	5.20m (4)	5.50m (4)	—	7.30m (4)	—	7.65m (2)	8.28m (8)
XVa	5.22t (4)	5.52m (4)	—	7.32m (4)	—	7.65m (4)	3.32m (8)
E-XVI	5.07m (1)	5.58m (2)	5.80m (6)	7.14m (2)	7.62m (2)	—	8.08m (2)
Z-XVI	5.28t (2)	5.57t (2)	5.78s (5)	7.20m (2)	7.64m (2)	—	8.10m (2)
XVII[i]	5.21m (2)	5.55m (2)	5.83s (5)	7.28m (2)	7.63m (2)	—	8.00m (2)
XVIII	5.22m (2)	5.52m (2)	5.82s (5)	—	7.20m (4)	—	7.89m (2)

[a] See Introduction to Experimental section; s = singlet, t = triplet, m = multiplet; numerals in parantheses denote a number of protons.

[b] See the footnote[b] of Table I.

[c] The numerals reffer to positions in substituted (2-through 5-) and unsubstituted ferrocene ring (1'-through 5'-).

[d] II (R=H); Xa, XIVa ($R=CH_3$); XIIa, XIVb, XVa ($R=C_2H_5$).

[e] Taken in deuterated acetic acid.

[f] Chemical shifts of protons in carbonyl substituted ferrocene ring(s) are giwen; the 4 protons in ferrocene ring substituted with cyclopentenyl in the compounds IX and Xa, resp., give signals at τ 5.94s (4) and 5.82m (4) ppm, resp.

[g] A broad unresolved multiplet at about τ 7.10—7.90 ppm have been assigned to these methylenic groups (integral 14 H)

[h] The methyne proton (—CO—*CH*—CO—) gives a multiplet at τ 5.85 ppm.

[i] The signal at τ —4.40 ppm (~1H) indicates an intramolecular hydrogen bonding in the enolic form of the β-diketone XVII.

Reactions of Ferrocene with Dicarboxylic Acid Chlorides (I, II, VI—X, XII, XIV—XVI)

Method A. — 25 mmoles of anhydrous $AlCl_3$ in 40 ml of an appropriate anhydrous solvent was placed in a three-necked flask fitted with a magnetical stirrer, reflux condenser, and a dropping funnel. A solution of 10 mmoles of ferrocene and 14 mmoles of dicarboxylic acid chloride in 120 ml of the same solvent was dropped during 2 to 3 hours. After 20 hours of stirring, or 1 to 3 hours of refluxing, the reaction mixture was hydrolyzed by pouring it onto crushed ice containing some ascorbic acid. The aqueous layer was extracted with ether and the combined organic phases were washed with water and extracted several times with 10% aqueous sodium carbonate (the so obtained *acid fraction* was then esterified with CH_2N_2 or ethanol/HCl and separated into components by preparative TLC). The organic layer was then washed with water until neutral, dried over Na_2SO_4, and evaporated in vacuo until dry; the crude product was separated into components on an alumina column using petroleum ether, benzene, and ether as eluents, and on preparative TLC plates in benzene:ethanol (v/v) 30:1 and 15:1 (see Tables I—III).

Method B. — 26 mmoles of dicarboxylic acid chloride was added to the stirred and cooled solution of 20 mmoles of ferocene in 100 ml of CH_2Cl_2 at 0 to 5 °C. 50 mmoles of $AlCl_3$ was then added in small portions at the same temperature. The reaction mixture was stirred for an additional 1 1/2 hour at 0 to 5 °C, 20 hours at room temperature; then treated as described under *A* (see Tables I—III).

Method C. — To a vigorously stirred suspension of 50 mmoles of $AlCl_3$ in 60 ml of CH_2Cl_2 a solution of 26 mmoles of adipoyl chloride in CH_2Cl_2 was added slowly, dissolving the $AlCl_3$. A solution of 20 mmoles of ferrocene in 100 ml of the same solvent was then added dropwise over a period of 2 to 3 hours. After 20 hours of stirring at room temperature the reaction mixture was treated as described under *A* (see Tables I—III).

Method D. — The procedure was performed in a similar way as described under *A* with reactants — ferrocene : adipoyl chloride : $AlCl_3$ — in molar ratio 1 : 1.3 : : 1.4. After 20 hours of stirring at room temperature or 3 to 4 hours of refluxing* a further 1.4 mmol of $AlCl_3$ was added in small portions. Stirring was continued overnight, and the reaction mixture treated as described under *A* (see Tables I—III).

1,6-Diferrocenyl-1,6-hexanedione (VI) and 1-Ferrocenoyl-2-ferrocenyl--1-cyclopentene (IX)

The Perrier complex (from 22 mmoles of $AlCl_3$ and 10 mmoles of adipoyl chloride) was prepared as described under *method C*. The solution was filtered to remove a small amount of undissolved $AlCl_3$ and then added dropwise to a stirred solution of 20 mmoles of ferrocene in 80 ml of CH_2Cl_2 over 1/2 hour at 0 to 5 °C. After 20 hours of stirring at room temperature it was worked up as described under *A*. The residue was dissolved in CCl_4 and chromatographed on a silicagel column. Elution with benzene afforded 2.2 g of recovered ferrocene. The second band, eluted with 10% ether in benzene, gave 1.2 g (57%) of IX. From the third band (ether) 570 mg (26%) of VI was obtained.

1-Ferrocenoyl-2-ferrocenyl-1-cyclopentene (IX)

A solution of 1,6-diferrocenyl-1,6-hexanedione (VI) in anhydrous CH_2Cl_2 was saturated with dried gaseous HCl and stirred overnight. The reaction mixture was washed with water containing some ascorbic acid and then with water. After evaporating the solvent to dryness 95% of IX was obtained.

1-Ferrocenoyl-2-ferrocenylcyclopentane (XI)

An ethanolic solution of 460 mg (1 mmol) of 1-ferrocenoyl-2-ferrocenyl-1-cyclopentene (IX) containing Pt-C catalyst was stirred under hydrogen pressure of 1 atm**

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* At this point 20% of VI and 22% of XII could be isolated.

** 1 atm = 101 325 Pa

over a period of 6 hours. The catalyst was filtered off and thoroughly washed with acetone. After evaporating the solvents to dryness the residue was chromatographed on preparative TLC plates and recrystallized from absolute ethanol yielding 200 mg (43%) of XI.

2-Ferrocenoyl-1-cyclopentanone (XVII)

A solution of 5.5 g (16 mmoles) of ethyl ε-ferrocenyl-ε-oxocaproate* in absolute benzene was added dropwise during 1/4 hour to a vigorously stirred suspension of 32 mmoles of sodium amide (in the form of a 50% suspension in toluene) in 70 ml of benzene (anhydrous). After refluxing for 2 hours the reaction mixture turned solid; after cooling it was poured onto crushed ice and water and acidified with dilute hydrochloric acid to pH 4. The reaction product was then extracted several times with ether; the combined organic phases were washed with water until neutral, dried with Na_2SO_4 and evaporated in vacuo to dryness; yield 3.9 g (82%) of XVII; m. p. 83—4 °C.

1-Chloro-2-ferrocenoyl-1-cyclopentene (XVIII)

To a stirred and cooled solution of 3 g (10 mmoles) of diketone XVII in 200 ml of anhydrous CCl_4 a solution of 1.5 g (12 mmoles) of oxalyl chloride in the same solvent at 0 to 4 °C was slowly added. The reaction mixture was stirred for 1 hour at room temperature, and the volume was then reduced to a minimum and immediately purified on preparative TLC plates using benzene as eluent; yield 700 mg (22%) of XVIII m. p. 82—3 °C.

Acknowledgment. The authors are indebted to Professor D. E. Sunko, Zagreb, for helpful discussions. Grateful acknowledgement is made to Professor K. Schlögl, Vienna, who enabled the recording of mass spectra in his Laboratory, and to Dr. J. Rolich, Zagreb, for taking IR spectra.

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* Rinehart et al.[9] have described the preparation of the corresponding acid by the acylation of ferrocene with δ-carbethoxyvaleroyl chloride (the intermediate ethyl ε-ferrocenyl-ε-oxocaproate was not isolated, but immediately hydrolyzed with ethanolic KOH).

SAŽETAK

Reakcije ferocena s kloridima dikarboksilnih kiselina

M. Laćan, V. Rapić i A. Brbot-Šaranović

Provedeno je ponovno ispitivanje Friedel-Crafts-ovih reakcija ferocena s kloridima dikarboksilnih kiselina uz uvjete diaciliranja. Međutim u reakciji ferocena sa sukcinoilkloridom dobiveni su samo prije opisani[1] spojevi — 1,4-diferocenil-1,4-butandion (I) i γ-ferocenil-γ-oksomaslačna kiseline (II). Reakcijom ferocena s adipoilkloridom pripravljeni su, osim prije opisanog polimera VIII[2], mono- i diacilirani spojevi (VI, VII, XII i XV) i njihovi transformacijski produkti (IX, X, XIV i XV). Struktura ovih spojeva potvrđena je njihovim IR, UV, ^{1}H-NMR i masenim spektrima.

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