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FERROCENE COMPOUNDS

XI *. SYNTHESIS AND CYCLIZATION OF SOME FERROCENECARBOXYLIC ACIDS

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Summary

The ferrocenecarboxylic acids $FcCH{=}C(CO_2H)(CH_2)_{1\text{-}2}CO_2H$ (Fc = ferrocenyl) were converted in good yields, under the conditions of the Clemmensen reduction, to the saturated products $FcCH_2CH(CO_2H)(CH_2)_{1\text{-}2}CO_2H$. The possible course of these reactions, via the corresponding δ- or γ-lactones, is discussed.

By the action of trifluoroacetic anhydride (or acetic anhydride) these ferrocenecarboxylic acids were converted into the corresponding cyclic anhydrides. The intramolecular Friedel–Crafts reaction of α-ferrocenylmethylglutaric anhydride gave the heteroannularly cyclized product 1,1′-[β-(2-carboxyethyl)-α-oxotrimethylene]ferrocene, and under the same conditions α-ferrocenylmethylsuccinic anhydride was converted into the homoannularly cyclized cyclopentadienyl(4,5,6,7-tetrahydro-5-carboxy-7-oxoindenyl)iron.

Introduction

It is well known that, depending on the chain length, unbranched ω-ferrocenylaliphatic acids undergo hetero- and homo-annular ring closure and polymer formation [1]. In several papers the intramolecular reaction of some other types of ferrocenecarboxylic acids are described; in the compounds $FcCH_2CHRCO_2H$ and $FcCH_2CR_2CO_2H$ (Fc = ferrocenyl, R = alkyl) concurrent homo- and hetero-annular cyclization occurs [2] and in acids $FcCH(CH_2CO_2H)(CH_2)_nCO_2H$ ($n = 2, 3$) the shorter chain reacts preferently giving heteroannular ring closure [3].

In this connection and in continuation of our work in the field of ferrocenecarboxylic acids [4,5] we found it interesting to study the intramolecular cyclizations of ferrocenedicarboxylic acids of the type $FcCH_2CH(CO_2H)(CH_2)_{1\text{-}2}CO_2H$.

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* For Part X see ref. 11.

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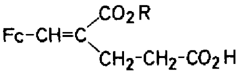
Results and discussion

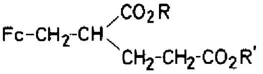
Preparation of the acids $FcCH_2CH(CO_2H)(CH_2)_{1-2}CO_2H$ was planned to start with the Stobbe condensation products of ferrocenecarbaldehyde and succinic and glutaric esters, i.e. $FcCH{=}C(CO_2R)(CH_2)_{1-2}CO_2H$ (R = H, ethyl), described in our previous papers [4,5].

The catalytic hydrogenation of these compounds using Pd/C catalyst in ethanol or acetic acid, under a pressure of 101325–420296 Pa (1–4.41 atm), and at 20–60°C was unsuccessful, probably because of the presence of the bulky ferrocenyl and carboxyl or ethoxycarbonyl groups.



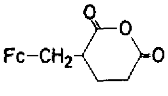
$Fc{-}CH{=}C(CO_2R){-}CH_2{-}CH_2{-}CO_2H$

I, R = C_2H_5
II, R = H



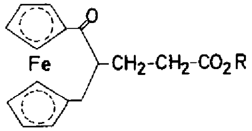
$Fc{-}CH_2{-}CH(CO_2R){-}CH_2{-}CH_2{-}CO_2R'$

III, R = C_2H_5, R' = H
IV, R = R' = H
VI, R = R' = CH_3



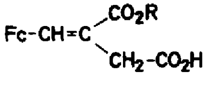
VIII

Fc = ferrocenyl



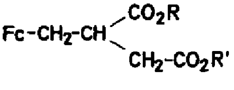
IX, R = H
X, R = CH_3

Surprisingly, reduction of the double bond in compounds I, II, XI, and XII can be achieved in good yield under the conditions of the Clemmensen reduction. Thus, refluxing I and zinc amalgam in glacial acetic acid and hydrochloric acid for 8 h gave 83% of III (and a small amount of IV), which was hydrolyzed to IV. Under similar conditions, II gave a mixture of the acids IV and V, which were separated by preparative TLC after conversion into the corresponding esters (25% of VI and 31% of $Fc(CH_2)_3CO_2CH_3$ (VII)). By the Clemmensen reduction, XI was converted into a mixture of 55% of XIII and 34% of XIV, and XII was converted into 90% of XIV.



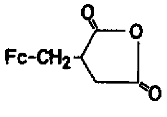
$Fc{-}CH{=}C(CO_2R){-}CH_2{-}CO_2H$

XI, R = C_2H_5
XII, R = H

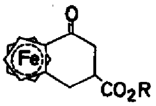


$Fc{-}CH_2{-}CH(CO_2R){-}CH_2{-}CO_2R'$

XIII, R = C_2H_5, R' = H
XIV, R = R' = H
XV, R = C_2H_5, R' = CH_3
XVI, R = R' = CH_3



XVII

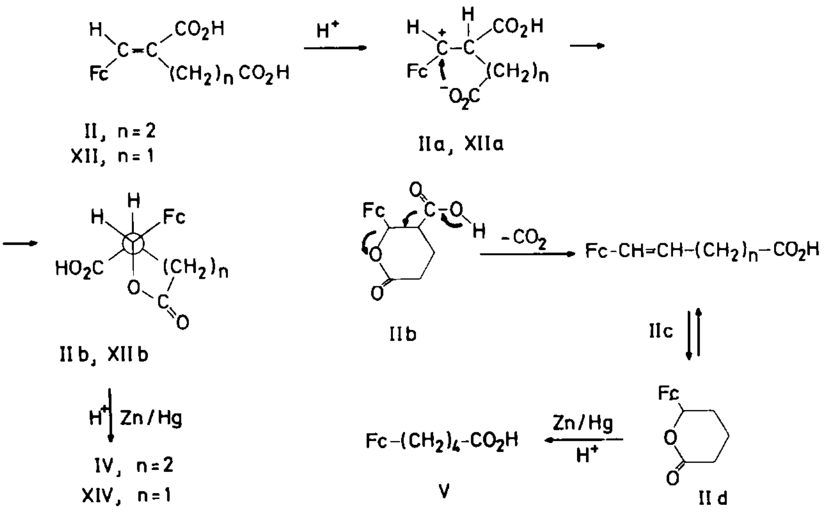


XVIII, R = H
XIX, R = CH_3

As far as we know there are no reported examples of the Clemmensen reduction of the structure $CH{=}CHCO_2R$ ($R = H$ or alkyl); on the other hand, reduction of γ-lactones (which are tautomers of β,γ-unsaturated acids [6]) with zinc amalgam, giving the corresponding saturated acids in good yield, is described in several works [7,8]. It can therefore be assumed that reduction of compounds I, II, XI, and XII takes place via the corresponding γ- or δ-lactones. The formation of these lactones is sterically possible, in spite of the presence of the bulky ferrocenyl and CO_2R groups, for the compounds I and XI have been prepared by the Stobbe condensation, which involves the same lactone intermediates!

In the first step of these reductions the double bond in the molecules II and XII is protonated, giving the resonance stabilized α-ferrocenylcarbonium ion (IIa or XIIa), which is then converted, by the internal nucleophilic attack of the carboxylate ion, to a lactone (IIb or XIIa) (Scheme 1). The lactone is then reduced to the desired dicarboxylic acid, IV or XIV, but in the reduction of II, formation of the decarboxylation product V is also observed. It is highly possible that the loss of carbon dioxide occurred from the lactonic acid IIb, as in the mineral acid-catalyzed decarboxylation of some Stobbe condensation products [6]. The lactone group serves in the decarboxylation reaction as an electron-acceptor; decarboxylation could also be assisted by a proton transfer from the carboxylic to the lactone group (by a cyclic mechanism) because of their convenient spacial arrangement (see the Newman projection of IIb).

SCHEME 1



The experiments on the intramolecular cyclizations of the dicarboxylic acids IV and XIV were done by the action of boiling acetic anhydride or trifluoroacetic anhydride (TFA) in methylene chloride. The reaction of IV with acetic anhydride was unsuccessful, and the treatment with TFA gave a unique product which after isolation rapidly decomposes to the starting material, so that the spectra could not be taken. It can be assumed that this material is the anhydride VIII, because, by the action of aluminium chloride it gave the heteroannularly bridged acid IX and some starting material, IV. In the reaction of XIV with acetic anhydride or TFA the anhydride XVII was obtained in yields of 80 and 88%, respectively. By the action of aluminium chloride, compound XVII gave 93% of the homoannularly cyclized product XVIII. Acids IX and XVIII were converted by the action of diazomethane into their methyl esters, X and XIX, respectively.

The structure of the compounds X and XIX was unambiguously assigned from their molecular weights (monomers) and their IR and ^{1}H NMR spectra. The IR spectrum of XIX contained the bands at 1105 and 1000 cm^{-1} which are characteristic of an unsubstituted ring [9] and which were absent from the spectrum of heteroannularly cyclized product X.

The ketone carbonyl stretching frequency of X (at 1674 cm^{-1}) is higher than that of XIX (at 1666 cm^{-1}) indicating an inclination of the axis of the carbonyl group in X to the plane of the cyclopentadienyl ring as the consequence of its geometry. As expected, compound XIX, in which the ketone carbonyl and cyclopentadienyl ring are coplanar, displays a carbonyl frequency close to that of acetylferrocene (1661 cm^{-1}) [10].

It can be concluded that: (a) the action of cyclizing reagents on the acids IV and XIV gave their anhydrides, but no hetero- and homo-annularly cyclized products IX and XVIII, as in the case of the similar acids described by the French authors [3]; (b) anhydride VIII was converted in an intramolecular Friedel–Crafts reaction to the heteroannularly cyclized product IX, and anhydride XVII gave, in a similar way, the homoannularly cyclized acid XVIII, according to the "rules" for cyclization of ω-ferrocenylcarboxylic acids [1].

Experimental

General

The same techniques and apparatus were used as described previously [4].

The IR spectra were recorded of liquid films. The ^{1}H NMR spectra (δ values) were taken in $CDCl_3$ solution.

The samples were purified by preparative TLC on silicagel G in benzene/ethanol (v/v) 30/1 and 15/1, or by recrystallization from aqueous ethanol.

The elemental analyses of new compounds are shown in Table 1.

1-Ethyl hydrogen 2-ferrocenylmethylglutarate (III)

(a) A suspension of 10% Pd/C in 15 cm^3 of ethanol or acetic acid was mechanically stirred and hydrogenated under atmospheric pressure for 1 h; 0.3 g (8 mmol) of 1-ethyl hydrogen 2-ferrocenylmethyleneglutarate (I) [4] was then added and stirred under a hydrogen atmosphere at room temperature or refluxed for 4 h. The work up of the reaction mixture gave the starting material only.

(b) Hydrogenation of the half-ester I in a Paar apparatus in the presence of 10% Pd/C under a pressure of 420296 Pa (4.41 atm) during 24 h was also unsuccessful.

(c) A mixture of 1.5 g (42 mmol) of I and zinc amalgam (from 3 g of zinc dust, 0.3 g of mercuric chloride, 0.2 cm^3 of concentrated hydrochloric acid, and 4 cm^3 of water) in 5 cm ^{3} of glacial acetic acid was refluxed for 8 h. During this time 4 cm^3 of concentrated hydrochloric acid was added succesively. The reaction mixture was diluted with water containing some ascorbic acid and extracted with diethyl ether; the ethereal extracts were washed with a saturated aqueous solution of sodium chloride, dried ($MgSO_4$) and evaporated to leave 1.25 g (83%) of III (and a small

TABLE 1

ELEMENTAL ANALYSIS OF NEW COMPOUNDS

Compound	Formula	Mol. wt.	Analysis (Found (calcd.) (%))	
			C	H
III	$C_{18}H_{22}FeO_4$	358.2	60.35 (60.51)	6.19 (6.10)
IV	$C_{16}H_{18}FeO_4$	330.2	58.20 (58.29)	5.49 (5.31)
VI	$C_{18}H_{22}FeO_4$	358.2	60.35 (60.60)	6.19 (6.21)
X	$C_{17}H_{18}FeO_3$	326.2	62.60 (62.49)	5.56 (5.53)
XIII	$C_{17}H_{20}FeO_4$	344.2	59.32 (59.51)	5.86 (5.99)
XIV	$C_{15}H_{16}FeO_4$	316.1	56.99 (57.15)	5.10 (5.10)
XVI	$C_{17}H_{20}FeO_4$	344.2	59.32 (59.19)	5.86 (5.91)
XVII	$C_{15}H_{14}FeO_3$	298.1	60.43 (59.92)	4.73 (5.01)
XVIII	$C_{15}H_{14}FeO_3$	298.1	60.43 (60.28)	4.73 (4.83)
XIX	$C_{16}H_{16}FeO_3$	312.1	61.56 (61.75)	5.17 (5.30)

amount of diacid IV). III: $C_{18}H_{22}FeO_4$ (358.2); IR: 2920(m), 2830(m), 1725(sh) (ν(C=O) $CO_2C_2H_5$), 1705 (s) (ν(C=O) CO_2H), 1105(w), and 999(w) cm^{-1}.

2-Ferrocenylmethylglutaric acid (IV) and 5-ferrocenylvaleric acid (V)

(a) Hydrogenation of acid II [4] according to the procedures (a) and (b) for the hydrogenation of I was unsuccessful.

(b) The Clemmensen reduction of 2.5 g (7.6 mmol) of II was performed under similar conditions to those described above, giving, after refluxing for 3 h, 1.7 g of yellow material consisting of a mixture of acid IV and 5-ferrocenylvaleric acid (V). The raw product was esterified by ethereal diazomethane (see below for the procedure) and the resulting mixture of esters VI and VII separated by preparative TLC into components, which gave after hydrolysis in a boiling methanolic solution of potassium hydroxide 650 mg (26%) of IV, and 630 mg (29%) of V [1].

IV: $C_{16}H_{18}FeO_4$ (330.2); IR: 3090(w), 2960(m), 2850(m), 1708(sh) and 1692(s) (ν(C=O)), 1103(m), and 997(w) cm^{-1}. V: $C_{15}H_{18}FeO_2$ (286.2), $M^+ = 286$; IR: 2920(s), 2850(m), 1700(s) (ν(C=O)), 1100(m), and 995(w) cm^{-1}; ^1H NMR spectrum: 11.25 (broad, 1H, CO_2H), 4.9(s), 4.04(m) (9H, ferrocene), 2.36(t), (4H, $FcCH_2$, CH_2CO_2) and 1.57–1.64(m) (4H, CH_2–CH_2–CH_2–CH_2) ppm.

(c) 170 mg (0.5 mmol) of raw product III was refluxed for 2 h in a methanolic solution of potassium hydroxide containing some water. The reaction mixture was evaporated to dryness and worked up as usual giving 140 mg (90%) of IV. The IR spectra of samples IV obtained in both experiments are superimposable.

Dimethyl 2-ferrocenylmehylglutarate (VI) and methyl 5-ferrocenylvalerate (VII)

A methanolic solution of 200 mg (0.9 mmol) of the raw product obtained in the above procedure (b) (preparation of IV/V) was esterified with ethereal diazomethane for 2 h. By preparative TLC 80 mg (25%) of VI, and 83 mg (31%), of VII were obtained. VI: $C_{18}H_{22}FeO_4$ (358.2); IR: 3095(m), 2960(s), 2853(m), 1740(s) and 1730(s) (ν(C=O)), 1103(m), and 997(w) cm^{-1}; ^1H NMR spectrum: 4.09(s), 4.04(m) (9H, ferrocene), 3.64(m), 3.62(m), (6H, OCH_3), 2.11–2.78(m) (5H, CH_2–CH–CH_2–CH_2) and 1.74–1.97(m) ppm (2H, CH_2–CH–CH_2–CH_2). VII: $C_{16}H_{20}FeO_2$ (299.2); IR: 3095(m), 2933(s), 2855(s), 1737(s) (ν(C=O)), 1103(m) and 997(m) cm^{-1}; ^1H NMR spectrum: 4.08(s), 4.03(m) (9H, ferrocene), 3.65(s), (3H, OCH_3), 2.32 (t, 4H, $FeCH_2$, CH_2–CO_2), and 4.40–1.86(m) (4H, CH_2–CH_2–CH_2–CH_2) ppm.

α-Ferrocenylmethylglutaric anhydride (VIII)

To a stirred mixture of 4 cm^3 of trifluoroacetic anhydride (TFA) and 25 cm^3 of methylene chloride, a solution of 180 mg (0.6 mmol) of the acid IV in the same solvent was added dropwise. The reaction mixture was stirred for an additional h and poured onto crushed ice and water containing some ascorbic acid, and extracted with ether; the ethereal extracts were washed successively with 5% sodium hydrogen carbonate and water, dried ($MgSO_4$) and used for the next preparation without isolation of product VIII (evaporation of the ethereal extracts gave 120 mg (70%) of VIII, which rapidly decomposed); $C_{16}H_{16}FeO_3$ (312.1).

1,1′-[β-(2-Methoxycarbonylethyl)-α-oxotrimethylene]ferrocene (X)

Aluminium chloride (140 mg, 1.3 mmol) was added in several portions over a period of 1/2 h to a stirred methylene chloride solution of VIII (from the previous preparation using 0.6 mmol of IV) at 0–3°C. After 2 h of stirring at room temperature the reaction mixture was hydrolyzed by pouring it onto crushed ice and water, and extracted with ether; the ethereal extracts were dried ($MgSO_4$) and esterified with ethereal diazomethane giving, after separation by TLC, 120 mg (67%) of X and 50 mg of VI.

X: $C_{17}H_{18}FeO_3$ (326.2), $M^+ = 326$; IR: 3095(w), 2955(m), 2922(m), 2855(w), 1738 (ν(C=O) CO_2CH_3), and 1674 cm^{-1} (ν(C=O) ketone); ^1H NMR spectrum: 4.73 (2H, H(2) and H(5)), 4.43 (2H, H(2′) and H(5′)), 4.35 (2H, H(3) and H(4)), 3.95 (2H, H(3′) and H(4′)) (all ferrocene protons), 3.90(s) (3H, OCH_3), 2.75(t) (2H, CH_2CO_2), and 1.70–2.21 (CH_2–CH–CH_2–CH_2–CO_2) ppm.

1-Ethyl hydrogen 2-ferrocenylmethylsuccinate (XIII) and 2-ferrocenylmethylsuccinic acid (XIV)

(a) Hydrogenation of the half-ester XI [5] and the acid XII, under the conditions described in the procedures (a) and (b) for the hydrogenation of I, gave compounds XIII and XIV in traces.

(b) The Clemmensen reduction of 2 g (5.8 mmol) of the half-ester XI, under similar conditions to those described above, gave 1.5 g of a mixture of XIII and XIV. The mixture was then separated into its components by preparative TLC to give 1.1 g (55%) of XIII and 620 mg (34%) of XIV. XIII: $C_{17}H_{20}FeO_4$ (344.2); IR: 3095(w), 2940(m), 2870(m), 1743(s) (ν(C=O) $CO_2C_2H_5$), 1710(s) (ν(C=O) CO_2H), 1104(w), and 1020(w) cm^{-1}. XIV: $C_{15}H_{16}FeO_4$ (316.1); $M^+ = 316$; IR: 3100(w), 2970(w), 2929(w), 2855(w), 1710(s) (ν(C=O)), 1105(s), and 995(s) cm^{-1}.

(c) By the Clemmensen reduction of 1 g (3 mmol) of the acid XII, 900 mg (90%) of the acid XIV was obtained.

1-Ethyl 5-methyl 2-ferrocenylmethylsuccinate (XV) and dimethyl 2-ferrocenylmethylsuccinate (XVI)

Esterification of the half-ester XIII and the diacid XIV with diazomethane gave 89% of the ester XV and 68% of ester XVI. XV: $C_{18}H_{22}FeO_4$ (358.2); IR: 3100(w), 2990(s), 2960(s), 1740(sh), and 1728(s) (ν(C=O) CO_2CH_3 and $CO_2C_2H_5$), 1003(s), and 997(s) cm^{-1}; ^{1}H NMR spectrum: 4.10(s), 4.23–4.05(m) (11H, ferrocene and OCH_2CH_3), 3.63(s) (3H, OCH_3), 2.32–3.0(m), (5H, CH_2–CH–CH_2), and 1.22(t) (3H, OCH_2CH_3) ppm. XVI: $C_{17}H_{20}FeO_4$ (344.2); IR: 3095(w), 2968(m), 2928(m), 2850(w), 1740(s) and 1730(s) (ν(C=O)), 1103(m), and 1037(w) cm^{-1}; ^{1}H NMR spectrum: 4.10(s), 4.03(m) (9H, ferrocene), 3.68(s), 3.60(s) (6H, OCH_3), and 2.40–3.00(m) (5H, CH_2–CH–CH_2) ppm.

α-Ferrocenylmethylsuccinic anhydride (XVII)

(a) A similar procedure to that described for a preparation of VIII, but starting from 200 mg (0.6 mmol) of acid XIV, gave 167 mg (88%) of XVII.

$C_{15}H_{14}FeO_3$ (298.1), $M^+ = 298$; ^{1}H NMR spectrum: 4.13(s), 4.11(m) (9H, ferrocene), 2.61–3.08(m) (3H, succinic anhydride), and 2.20(d) (2H, Fc-CH_2) ppm.

(b) A mechanically stirred solution of 200 mg (0.6 mmol) of acid XIV in 3 cm^3 of acetic anhydride was heated at 40°C for 4 h. After cooling, the reaction mixture was poured onto crushed ice and worked up as described for the preparation of VIII, giving 152 mg (80%) of XVII.

Cyclopentadienyl(4,5,6,7-tetrahydro-7-oxo-5-oxycarbonylindenyl)iron (XVIII)

In a similar way to that described for the preparation of X, but starting from 150 mg (0.5 mmol) of the anhydride XVII and 1.4 mmol of aluminium chloride, 140 mg (93%) of XVIII was obtained. $C_{15}H_{14}FeO_3$ (298.1), $M^+ = 299$.

Cyclopentadienyl(4,5,6,7-tetrahydro-7-oxo-5-methoxycarbonylindenyl)iron (XIX)

A methanolic solution of 150 mg (0.5 mmol) of acid XVIII was esterified with ethereal diazomethane, giving 137 mg (88%) of XIX. $C_{16}H_{16}FeO_3$ (312.1), $M^+ = 312$; IR: 3100(m), 2960(s), 2930(s), 1733(s) (ν(C=O) CO_2CH_3), 1666(s) (ν(C=O) ketone), 1105(m), and 1000(m) cm^{-1}; ^{1}H NMR spectrum: 4.87(m) (1H, H(1) indene), 4.53 (m) (2H, H(2) and H(3) indene), 4.22(s) (5H, cyclopentadiene), 3.77(s), (3H, OCH_3), and 2.22–3.06(m) (5H, H(4), H(5) and H(6) indene) ppm.

Acknowledgements

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