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Ferrocene Compounds. XIV*. Synthesis and Reactions of 3-Aryl-5-ferrocenyl-5-oxovaleric Acids

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The Michael condensation of 3-aryl-1-ferrocenyl-2-propene--1-ones with diethyl malonate gave diethyl (1-aryl-3-ferrocenyl--3-oxopropyl)malonates. The alkaline hydrolysis of these products gave the corresponding dicarboxylic acids which were decarboxylated to the title compounds. 3-Aryl-5-ferrocenyl-5-oxovaleric acids were cyclized by trifluoroacetic anhydride to 4-aryl-6-ferrocenyl-3,4-dihydro-2-pyrones.

In several previous papers[1] we have studied the syntheses and intramolecular cyclizations of some ferrocenecarboxylic acids.

In the continuation of our work we planned to prepare new types of ferrocenecarboxylic acids — 3-aryl-5-ferrocenyl-5-oxovaleric acids and 3-aryl--5-ferrocenylvaleric acids — in order to examine the possibilities of their intramolecular cyclizations with respect to ferrocene and benzene rings.

Preparation of these acids started from the Michael condensation products of the described chalcone analogues I a-c[2] with ethyl cyanoacetate or diethyl malonate. The condensation of I a with ethyl cyanoacetate gave ethyl 2-cyano--5-ferrocenyl-5-oxo-3-phenylvalerate[3], which was hydrolized to a mixture of III a, 2-cyano-5-ferrocenyl-5-oxo-3-phenylvaleric acid and ethyl hydrogen (3-ferrocenyl-3-oxo-1-phenylpropyl)malonate. The condensation products of chalcones I a-c with diethyl malonate (II a-c) were hydrolized with 43—66% yield to the desired dicarboxylic acids III a-c. Decarboxylation of these acids gave a good yield in monocarboxylic acids IV a-c, which were characterized as methyl esters V a-c. Attempts to reduce the keto group of IV a-c to methylene were unsuccessful. Clemmensen reduction, catalytic hydrogenation (Pd/C), and Wolff-Kishner reduction furnished only unreacted and decomposed material. This fact could be rationalized in terms of blocking carbonyl by the bulky ferrocene and phenyl groups. Literature data[4] reveal that the reduction of the analogous, but sterically less hindered 3,5-diphenyl-5-oxovaleric acid gave 3,5-diphenylvaleric acid only in poor yields.

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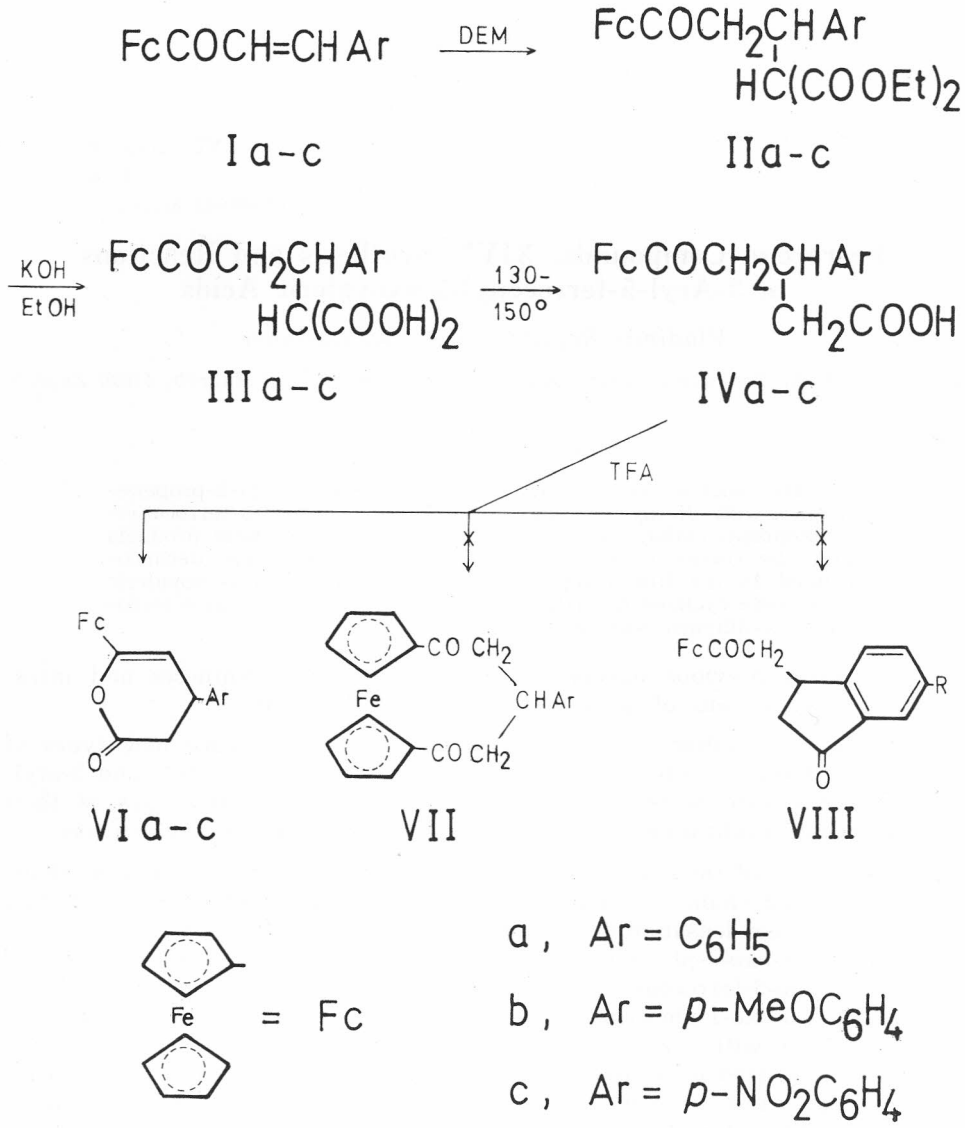

= Fc

a, Ar = C_6H_5

b, Ar = *p*-$MeOC_6H_4$

c, Ar = *p*-$NO_2C_6H_4$

The intramolecular cyclizations of the acids IV a-c were performed by the action of trifluoroacetic anhydride (TFA) in 1,2-dichloroethane. These reactions gave high yields in single products — unsaturated δ-lactones VI a-c, which quickly hydrolized to the starting acids IV a-c in methanolic sodium hydroxide. The energetically unfavoured formation of the isomeric cyclization products VII and VIII (R = H, OMe, or NO_2) was not observed. The intramolecular cyclization of IV a-c in the sense of formation of VII and the cor-

responding homoannularly disubstituted product is inhibited by deactivating effect of carbonyl group.

EXPERIMENTAL

The m. p.'s were determined on a Büchi apparatus and are uncorrected. The IR spectra were recorded as KBr pellets with a Perkin-Elmer 257 Grating Infrared Spectrophotometer. The ^{1}H NMR spectra (δ values, in $CDCl_3$ solution) were recorded using a Varian EM 360 spectrometer with tetramethylsilane as internal standard.

The experiments were performed under an argone atmosphere. The m. p.'s and the IR spectra of the prepared chalcone analogues I a-c corresponded to those described in literature[2]. The samples were purified by preparative TLC on silicagel G in benzene/ethanol (v/v) 30/1 and 15/1, and/or by recrystallization from (aqueous) ethanol.

Diethyl (1-Aryl-3-ferrocenyl-3-oxopropyl)malonates (II a-c)

To a solution of 6 mmol of I a-c in a mixture of ethanol abs. and ether anhyd. 1.0 g (6.3 mmol) of freshly destilled diethyl malonte (DEM) and 1.2 cm^3 of 10% ethanolic sodium ethylate were added. After resting for 14 days the precipitated crystals were filtered off; an additional quantity of the product precipitated from the filtrate after acidification with diluted hydrochloric acid.

IIa (52%); m. p. 117—118° (m. p.[2] 118—120°); IR spectrum: 3120 (w) (ν C—H Fc), 1720 (vs) (ν C= O COOEt), 1660 (s) (ν C=O FcCO), and 1600 cm^{-1} (w) (ν C=C); ^{1}H NMR spectrum: 1.01, 1.27, (2t, 6H, OCH_2CH_3); 3.16 (J = 1.2 Hz), 3.22 (J = 3 Hz), (2d, 2H, CH_2CO); 3.80—4.00 (m, 2H, CH); 3.93 (s, 5H, H_1, —H_5, Fc); 3.94, 4.21, (2q, 4H OCH_2CH_3); 4.43 (t, 2H, H_3 and H_4 Fc); 4.71 (t, 2H, H_2 and H_5 Fc); 7.32 (m, 5H, C_6H_5).

IIb (48%); yellow crystals; m. p. 135—136°; IR spectrum: 3110 (w) (ν C—H Fc), 2820 (w) (ν C—H OMe), 1722 (s) (ν C=O COOEt), 1652 (s) (ν C=O FcCO), and 1606 cm^{-1} (m) (ν C=C); ^{1}H NMR spectrum: 1.04, 1.27 (2t, 6H, OCH_2CH_3); 3.13 (s), 3.19 (d) (J = 1.8 H_2) (2H, CH_2CO); 3.90—4.00 (m, 2H, CH); 3.72 (s, 3H, OCH_3); 3.96, 4.21 (2q, 4H, OCH_2CH_3); 3.97 (s, 5H, H_1, -H_5, Fc); 4.43 (t, 2H, H_3 and H_4 Fc); 4.71 (t, 2H, H_2 and H_5 Fc); 6.80, 7.26 (2d, 4H, C_6H_4, J = 6 Hz).

Anal. $C_{27}H_{30}FeO_6$ (506.4) calc'd.: C 64.04; H 5.97%
found: C 64.03; H 6.23%

IIc (81%); m. p. 163—164°; IR spectrum: 3120 (w) (ν C—H Fc), 1725 (vs) (ν C=O COOEt), 1652 (s) (ν C=O FcCO), 1595 (w) (ν C=C), and 1336 cm^{-1} (s) (ν N$\overset{\cdot\cdot}{\underset{\cdot\cdot}{}}$O NO_2); ^{1}H NMR spectrum: 1.07, 1.28 (2t, 6H, OCH_2CH_3), 3.24 (d, J = 1.2 Hz), 3.32 (s, 2H, CH_2CO); 3.80—3.40 (m, 2H, CH); 3.92, 4.24 (2q, 4H, OCH_2CH_3); 4.03 (s, 5H, H_1 -H_5 Fc); 4.48 (t, 2H, H_3 and H_4 Fc); 4.72 (t, 2H, H_2 and H_5 Fc); 7.54, 8.15 (2d, 4H, C_6H_4, J = 6.0 Hz).

Anal. $C_{26}H_{27}FeNO_7$ (521.3) calc'd.: C 59.90; H 5.22; N 2.69%
found: C 59.88; H 4.93; N 2.77%

(1-Aryl-3-ferrocenyl-3-oxopropyl)malonic Acids (III a-c)

To a solution of 10 mmol of II a-c in 100 cm^3 of 96% ethanol a solution of 3 g potassium hydroxide in 10 cm^3 of water was added. The reaction mixture was heated on a water-bath at 60—80° under occasional shaking for 3—5 hrs, and then evaporated to dryness; water was added to the crude residue and some undissolved material was filtered off. The filtrate was carefully acidified with 6 mol/dm^3 hydrochloric acid to precipitate dicarboxylic acid III a-c, which was filtered off, washed with water, and dried.

IIIa (66%); orange crystals; m. p. 153—154°; IR spectrum: 3120 (w) (ν C—H Fc), 1735 (s), 1710 (s) (ν C=O COOH), 1660 (s) (ν C=O FcCO), and 1605 cm^{-1} (m) (ν C=C).

IIIb (54%); brown-yellow crystals; m. p. 108—110°; IR spectrum: 3100 w (ν C—H Fc), 2830 (w) (ν C—H OMe), 1740 (s), 1713 (s) (ν C=O COOH), 1640 (s) (ν C=O FcCO), and 1606 cm^{-1} (m) (ν C=C).

IIIc (43%); brownish material; m. p. 113—115°; IR spectrum: 3110 (w) (ν C—H Fc), 1732 (s), 1715 (s) (ν C=O COOH), 1642 (m) (ν C=O FcCO), 1602 (m) (ν C=C), 1338 cm^{-1} (vs) (ν N⋯O $ArNO_2$).

3-Aryl-5-ferrocenyl-5-oxovaleric Acids (IV a-c)

2 mmol of raw product III a-c was heated in a flask immersed in an oil bath at 130—150° for 20—30 min. (until frothing ceased). The resulting residue was pulverized and dissolved in 1 mol/dm^3 sodium hydroxide and the solution boiled with decolorizing carbon. After filtering, the solution was cooled and acidified with 6 mol/dm^3 hydrochloric acid to precipitate monocarboxylic acid IV a-c.

IVa (75%); pale-yellow crystals; m. p. 172.5—173°; IR spectrum: 3080 (w) (ν C—H Fc), 1700 (s) (ν C=O COOH), 1647 cm^{-1} (s) (ν C=O FcCO); ^1H NMR spectrum: 3.10 (m, 2H, CH_2COO); 3.36 (m, 2H, CH_2CO); 3.65 (m, 1H, CH); 4.01 (s, 5H, H_1, -H_5, Fc); 4.51 (m, 2H, H_3 and H_4 Fc); 4.71 (m, 2H, H_2 and H_5 Fc).

Anal. $C_{21}H_{20}FeO_3$ (376.2) calc'd.: C 67.04; H 5.36%
found: C 67.21; H 5.58%

IVb (83%); yellow-orange crystals; m. p. 162—163°; IR spectrum: 3100 (w) (ν C—H Fc), 2820 (w) (ν C—H OMe), 1695 (s) (ν C=O COOH), 1640 (s) (ν C=O FcCO), 1602 cm^{-1} (w) (ν C=C);

Anal. $C_{22}H_{22}FeO_4$ (406.3) calc'd.: C 65.04; H 5.46%
found: C 65.33; H 5.28%

IVc (58%); orange crystals; m. p. 165—167°; IR spectrum: 3105 (w) (ν C—H Fc), 1703 (s) (ν C=O COOH), 1652 (s) (ν C=O FcCO), 1599 (m) (ν C=C), and 1336 cm^{-1} (ν N⋯O NO_2).

Anal. $C_{21}H_{19}FeNO_5$ (421.2) calc'd.: C 59.88; H 4.55; N 3.33%
found: C 60.00; H 4.71; N 3.68%

Methyl 3-Aryl-5-ferrocenyl-5-oxovalerates (V a-c)

A methanolic solution of 1 mmol of acid IV a-c was esterified with diazomethane/ether; after filtering through a short alumina column the obtained ester was purified by preparative TL chromatography.

Va (93%); light-yellow prismatic crystals; m. p. 99—101°; IR spectrum: 3100 (w) (ν C—H Fc), 1723 (s) (ν C=O COOMe), 1635 (s) (ν C=O FcCO), and 1595 cm^{-1} (w) (ν C=C); ^1H NMR spectrum: 2.71 (J = 1.2 Hz), 2.80 (J = 1.8 Hz) (2d, 2H, CH_2COO); 3.03 (J = 1.2 Hz), 3.11 (J = 0.6 Hz) (2d, 2H, CH_2CO); 3.58 (s, 3H, CH_3O) 3.80—4.00 (m, 1H, CH); 4.00 (s, 5H, H_1, -H_5, Fc); 4.44 (t, 2H, H_3, H_4 Fc); 4.71 (m, 2H, H_2, H_5 Fc); 7.29 (m, 5H, C_6H_6).

Anal. $C_{22}H_{22}FeO_3$ (390.3) calc'd.: C 67.70; H 5.68%
found: C 67.61; H 5.78%

Vb (97%); yellow needless crystals; m. p. 110—111°; IR spectrum: 3100 (w) (ν C—H Fc), 1724 (s) (ν C=O COOMe), 2820 (w), (ν C—H OMe), 1645 (s) (ν C=O FcCO), and 1603 cm^{-1} (w) (ν C=C); ^1H NMR spectrum: 2.68 (d, J = 2.4 Hz), 2.76 (d, J = 1.8 Hz) (2H, CH_2COO); 2.99, 3.07 (2s, 2H, CH_2CO); 3.58, 3.74 (2s, 6H, $COOCH_3$, $ArOCH_3$); 3.82—4.02 (m, 1H, CH); 4.02 (s, 5H H_1, -H_5, Fc); 4.44 (t, 2H, H_3 and H_4 Fc); 4.71 (m, 2H, H_2 and H_5 Fc); 6.84, 7.22 (2d, 4H, C_6H_4, J = 4.8 Hz).

Anal. $C_{23}H_{24}FeO_4$ (420.3) calc'd.: C 65.73; H 5.76%
found: C 65.52; H 5.82%

Vc (94%); yellow-orange crystals; m. p. 143—145°; IR spectrum: 3115 (w) (ν C—H Fc), 1724 (s) (ν C=O COOMe), 1652 (s) (ν C=O FcCO), 1590 (w) (ν C=C), and 1337 cm^{-1} (s) (ν N⋯⋯ NO_2); ^1H NMR spectrum: 2.75 (d, J = 3 Hz), 2.83 (d, J = 1.8 Hz) (2H, CH_2COO); 3.09, 3.17 (2s, 2H, CH_2CO); 3.61 (s, 3H, OCH_3); 3.89—4.06 (m, 1H, CH); 4.06 (s, 5H, H_1, -H_5, Fc); 4.49 (t, 2H, H_3 and H_4 Fc); 4.43 (t, 2H, H_2 and H_5 Fc); 7.50, 8.18 (2d, 4H, C_6H_4, J = 6.0 Hz).

Anal. $C_{22}H_{21}FeNO_5$ (435.3) calc'd.: C 60.71; H 4.86; N 3.22%
found: C 60.93; H 4.95; N 3.38%

4-Aryl-6-ferrocenyl-3,4-dihydro-2-pyrones (VI a-c)

To a stirred mixture of 3 cm^3 of TFA in 20 cm^3 of 1,2-dichloroethane a solution of 1 mmol of IV a-c in the same solvent was added dropwise at room temperature. The reaction mixture was refluxed for 3 hours dripping an additional amount of 2 cm^3 of TFA. After cooling it was poured onto ice and water containing some ascorbic acid, and extracted with ether. The organic phase was washed successively with 10% sodium hydrogencarbonate and water, dried over magnesium sulphate and evaporated to dryness in vacuo. The dark-violet oily product solidified after standing.

VIa (98%); dark-violet material; m. p. 49—50°; IR spectrum: 3080 (w) (ν C—H Fc), 1781 (s) (ν C=O lactone), 1605 (w) (ν C=C), and 1154 cm^{-1} (s) (ν C—O lactone); ^1H NMR spectrum: 3.03 (s), 3.08 (d, J = 1.2 Hz) (2H, CH_2); 3.72 (m, 1H, CH); 4.22—4.28 (m, 2H, H_3 and H_4 Fc); 4.24 (s, 5H, H_1, -H_5, Fc), 4.54 (m, 2H, H_2 and H_5 Fc); 4.72 (m, 1H, C=CH); 7.30 (m, 5H, C_6H_5).

Anal. $C_{21}H_{18}FeO_2$ (358.2) calc'd.: C 70.41; H 5.06%
found: C 70.78; H 4.72%

VIb (97%); dark-violet; m. p. 56—58°; IR spectrum: 3090 (w) (ν C—H Fc), 2815 (w) (ν C—H OCH_3), 1777 (s) (ν C=O lactone), 1604 (w) (ν C=C), and 1155 cm^{-1} (s) (ν C—O lactone); ^1H NMR spectrum: 2.99 (s), 3.04 (d, J = 1.2 Hz), (2H, CH_2); 3.71 (m, 1H, CH); 3.77 (s, 3H, OCH_3); 4.19—4.26 (m, 2H, H_3 and H_4 Fc); 4.24 (s, 5H, H_1, -H_5, Fc); 4.53 (m, 2H, H_2 and H_5 Fc); 4.70 (m, 1H, C=CH); 6.85, 7.13 (2d, 4H, C_6H_4, J = 6 Hz).

Anal. $C_{22}H_{20}FeO_3$ (388.2) calc'd.: C 68.06; H 5.19%
found: C 68.42; H 5.46%

VIc (92%); dark-violet material; m. p. 63—65°; IR spectrum: 3100 (w) (ν C—H Fc), 1780 (s) (ν C=O lactone), 1600 (w) (ν C=C); 1355 (ν N—O NO_2); and 1151 cm^{-1} (s) (ν C—O lactone); ^1H NMR spectrum: 3.00 (s), 3.07 (d, J = 1.2) (2H, CH_2); 3.73 (m, 1H, CH); 4.20—4.28 (m, 2H, H_3 and H_4 Fc); 4.23 (s, 5H, H_1, -H_5, Fc); 4.34 (m, 2H, H_2 and H_5 Fc); 4.70 (m, 1H, C=CH); 7.51, 8.16 (2d, 4H, C_6H_4, J = 6 Hz).

Anal. $C_{21}H_{17}FeNO_4$ (403.2) calc'd.: C 62.55; H 4.25%
found: C 62.13; H 4.36%

Lactones VIa-c were hydrolized by 1 mol/dm^3 methanolic potassium hydroxide at room temperature. The dark-violet colour of the solution changed thereby instantaneously to a brown-yellowish hue. The reaction mixture was evaporated to dryness, dissolved in water, and acidified with diluted hydrochloric acid, giving the starting acids IVa-c. The IR spectra, m. p.'s and R_F values of these acids and the previously prepared samples IVa-c were identical.

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SAŽETAK

Priprava i reakcije 3-aril-5-ferocenil-5-oksovalerijanskih kiselina

V. Rapić i J. Lasinger

Michaelovom kondenzacijom 3-aril-1-ferocenil-2-propen-1-ona s dietil-malonatom pripravljeni su dietil-(1-aril-3-ferocenil-3-oksopropil)malonati. Alkalnom hidrolizom ti spojevi su prevedeni u odgovarajuće dikarboksilne kiseline koje su dekarboksilirane u 3-aril-5-ferocenil-5-oksovalerijanske kiseline. Te kiseline djelovanjem anhidrida trifluoroctene kiseline cikliziraju u 4-aril-6-ferocenil-3,4-dihidropirone.