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I: ferrocene derivative with COOH and Y substituents in different rings

Figure 1: I: ferrocene derivative with COOH and Y substituents in different rings

Abstract

Full Text

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THE INFLUENCE OF SUBSTITUENTS ON THE STRENGTH OF FERROCENECARBOXYLIC ACIDS

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As is known, in substitution reactions ferrocene exhibits the properties of an aromatic compound ([1–8]). In the present work we consider the related question of the transmission of the mutual influence of substituents through the ferrocene nucleus.

We have obtained ferrocenecarboxylic acids of the general formula I ($Y = -C_2H_5,\ -C_4H_9,\ -H,\ -COOCH_3,\ -COC_3H_7,\ -COCH_3$) and measured their dissociation constants.

Acetylferrocenecarboxylic acid was obtained by the Friedel-Crafts reaction from the methyl ester of ferrocenecarboxylic acid, followed by saponification of the product formed. The position of the substituents in this compound was proved by oxidizing it to the ferrocenedicarboxylic acid described by Woodward, whose carboxyl groups are located in different rings; this had been established by various methods ([4,9,10]). Ethylferrocenecarboxylic acid was obtained by Clemmensen reduction of acetylferrocenecarboxylic acid and, consequently, has the same arrangement of substituent groups. Butyrylferrocenecarboxylic acid was obtained by the Friedel-Crafts reaction, and its reduction gave butylferrocenecarboxylic acid*. The infrared spectrum of the methyl ester of the first of these acids (the frequencies 1000 and 1107 cm^{-1}, characteristic of an unsubstituted ring, are absent), as well as the method of preparation itself (similar to that for diacetylferrocene and for acetylferrocenecarboxylic acid), indicate that the substituents are located in different rings.

I

The monomethyl ester of ferrocenedicarboxylic acid was obtained from the dimethyl ester of this acid by incomplete hydrolysis.

The dissociation constants of the acids obtained by us, as well as of ferrocenecarboxylic, butyric, and benzoic acids, are given in Table 1.

Comparison of the dissociation constants of ferrocenecarboxylic acids shows that introduction of an alkyl group into the unsubstituted ring of ferrocenecarboxylic acid lowers the dissociation constant, while introduction of a negative substituent raises it. Thus, acetylferrocenecarboxylic acid is 2.4 times stronger than ferrocenecarboxylic acid and 3.3 times stronger than ethylferrocenecarboxylic acid.

In the benzene series, *n*-acetylbenzoic acid is 4.2 times stronger than benzoic acid ([11]), and *n*-carbomethoxybenzoic acid is 3.8 times stronger than the latter (in 50% ethanol by volume) ([12]). Thus, the influence of substituents on the dissociation constant of ferrocenecarboxylic acid from the other ring of the molecule is quite comparable with the influence of the same substituents on the dissociation constant of benzoic acid from the *n*-position.

* The syntheses of butyryl- and butylferrocenecarboxylic acids, as well as the determination of their dissociation constants, were carried out jointly with G. N. Lapshina.

The fact that the influence of substituents from one ferrocene ring is transmitted to its other ring is also confirmed by the sulfonation of ferrocene carried out by us in the presence of an equimolar amount of ferrocenecarboxylic acid (competitive sulfonation). In this case the ferrocenecarboxylic acid is not changed, while ferrocene is almost completely sulfonated. Under more severe conditions ferrocenecarboxylic acid was sulfonated by us. Thus the carboxyl group exerts a passivating action on the unsubstituted ring of the molecule.

It should be noted that all systems well studied up to the present, which effectively transmit mutual influence, have a continuous chain of carbon atoms. The ferrocene molecule differs fundamentally in that one of the links of the conducting system in it is an iron atom.

Preparation of acetylferrocenecarboxylic acid. To a mixture of 5.0 g (0.037 mole) of aluminum chloride, 2.35 g (0.030 mole) of acetyl chloride, and 30 ml of CCl_4, cooled to +10°, was added over the course of

Table 1

Acid	$K_D \cdot 10^6$	pK_D
	68% CH_3OH, 20°	68% CH_3OH, 20°
$CH_3CH_2CH_2COOH$	0.30	6.52
$C_4H_7–C_5H_4–Fe–C_5H_4–COOH$	0.31	6.50
$C_2H_5–C_5H_4–Fe–C_5H_4–COOH$	0.37	6.43
$H–C_5H_4–Fe–C_5H_4–COOH$	0.51	6.29
$CH_3OOC–C_5H_4–Fe–C_5H_4–COOH$	0.83	6.08
$C_3H_7OC–C_5H_4–Fe–C_5H_4–COOH$	1.13	5.95
$CH_3OC–C_5H_4–Fe–C_5H_4–COOH$	1.25	5.91

Acid	$K_D \cdot 10^6$	pK_D
C_6H_5–COOH	1.17	5.93

15 min a solution of 5 g (0.0205 mole) of the methyl ester of ferrocenecarboxylic acid. After standing for one hour with periodic stirring, the mixture was treated with ice water. The substance obtained after removal of the solvent was recrystallized from methanol; yield 3.2 g (58% of theory). The methyl ester of acetylferrocenecarboxylic acid, after two recrystallizations from ligroin, melts at 92.5–94.5°.

Found, %:	C 58.78; 58.69;	H 5.05; 5.02;	Fe 19.46; 19.43
$C_{14}H_{14}FeO_3$. Calculated, %:	C 58.77;	H 4.94;	Fe 19.52

The methyl ester of acetylferrocenecarboxylic acid was saponified by heating with 20% NaOH. Acetylferrocenecarboxylic acid, after two recrystallizations from benzene, has m.p. 153–155°.

Found, %:	C 57.74; 57.58;	H 4.47; 4.33;	Fe 20.34; 20.15
$C_{13}H_{12}FeO_3$. Calculated, %:	C 57.38;	H 4.45;	Fe 20.52

Preparation of ethylferrocenecarboxylic acid. A suspension of 7 g of acetylferrocenecarboxylic acid in 50 ml of acetic acid was poured onto amalgamated zinc (prepared from 20 g of powdered zinc and 1.5 g of mercuric chloride). To the mixture was added, with stirring, 20 ml of hydrochloric acid, and after an hour and a half the same amount again. The mixture was heated at 70° for one hour, diluted with a double volume of water; the precipitated solid was filtered off, extracted repeatedly with hot chloroform; the solvent was removed in vacuo. Yield 4.9 g (70% of theory). After recrystallization from ligroin and ethanol, m.p. 75.5–77.5°.

Found, %:	C 60.58; 60.44;	H 5.27; 5.48;	Fe 21.89; 21.77
$C_{13}H_{14}FeO_2$. Calculated, %:	C 60.50;	H 5.47;	Fe 21.64

Preparation of butyrylferrocenecarboxylic acid. The methyl ester of butyrylferrocenecarboxylic acid was obtained by the same method as the methyl ester of diacetylferrocenecarboxylic acid, in 45% yield; m.p. 54.5–55.5°.

Found, %:	C 61.86; 61.75;	H 5.90; 5.89;	Fe 17.63; 17.51
$C_{16}H_{18}FeO_3$. Calculated, %:	C 61.21;	H 5.81;	Fe 17.89

Saponification of this ester gave butyrylferrocenecarboxylic acid. After recrystallization from CCl_4 and methanol, m.p. 114–115°.

Found, %:	C 60.36; 60.14;	H 5.52; 5.38;	Fe 17.71; 17.50
$C_{15}H_{16}FeO_3$. Calculated, %:	C 60.01;	H 5.37;	Fe 17.61

Preparation of butylferrocenecarboxylic acid. Butylferrocenecarboxylic acid was obtained by the same method as ethylferrocenecarboxylic acid. Recrystallized from ligroin and methanol. Yield 74%; m.p. 73–74.5°.

Found, %:	C 63.16; 63.05;	H 6.59; 6.45;	Fe 19.41; 19.34
$C_{15}H_{18}FeO_2$. Calculated, %:	C 62.96;	H 6.34;	Fe 19.52

Oxidation of acetylferrocenecarboxylic acid. A mixture of 0.7 g (0.0026 mole) of acetylferrocenecarboxylic acid and 0.9 g (0.0036 mole) of iodine was heated in 1 ml of pyridine at 100° for two hours, after which 10 ml of 15% NaOH was added, and the mixture was heated on a boiling water bath for another two hours. The reaction mass was then diluted with 20 ml of hot water and filtered. From the filtrate, hydrochloric acid precipitated a mixture of ferrocenedicarboxylic acid and the starting acid; the latter was extracted with hot benzene. The residue was recrystallized from acetic acid, giving 0.1 g of ferrocenedicarboxylic acid, which was methylated with diazomethane. After recrystallization from methanol, 0.06 g of the dimethyl ester of ferrocenedicarboxylic acid was obtained, m.p. 114–115°; no depression of the melting point with an authentic sample was observed (literature m.p. 114–115° (4)).

Preparation of the monomethyl ester of ferrocenedicarboxylic acid. The monomethyl ester of ferrocenedicarboxylic acid was obtained by heating 4.5 g (0.015 mole) of the dimethyl ester of ferrocenedicarboxylic acid with 0.6 g (0.015 mole) of NaOH, 2 ml of water, and 60 ml of methanol for 50 minutes; m.p. 147.5–149.5°. Yield 1.05 g (24.5% of theory).

Found, %:	C 54.75; 54.73;	H 4.50; 4.43;	Fe 19.42; 19.27
$C_{13}H_{12}FeO_3$. Calculated, %:	C 54.30;	H 4.20;	Fe 19.38

Sulfonation of the methyl ester of ferrocenecarboxylic acid. To a solution, cooled to +5°, of 1.9 g (0.0078 mole) of the methyl ester of ferrocenecarboxylic acid in 20 ml of dry dichloroethane was added, in portions, a previously prepared solution of 1.2 g (0.015 mole) of sulfur trioxide and 3.0 g (0.034 mole) of dioxane in 20 ml of dichloroethane. The mixture was left in a closed vessel at 0° and, after 24 hours, was gradually poured, with stirring, into an ice-cooled ethereal solution of diazomethane (threefold excess of diazomethane). After

standing for one hour, the solution was filtered, washed with water, and the solvent was removed in vacuo. The dimethyl ester of ferrocenesulfocarboxylic acid was recrystallized from ligroin and methanol; m.p. 93-95°; yield 0.9 g (34% of theory)*.

Found, %:	C 45.95; 46.08; H 4.09; 4.25
$C_{13}H_{14}FeO_5S$. Calculated, %:	C 46.16; H 4.17

Competitive sulfonation. 2.30 g (0.01 mole) of ferrocenecarboxylic acid and 1.86 g (0.01 mole) of ferrocene were dissolved in 250 ml of dichloroethane, the solution was cooled to +5°, and to it was added dropwise a pre–

* Ferrocenecarboxylic acid can also be sulfonated by the same method.

a freshly prepared solution of 0.85 g (0.0105 mole) of sulfuric anhydride and 4 g (0.045 mole) of dioxane in 15 ml of dichloroethane over the course of 45 min. After standing for one hour at 5° and for 16 hours at 15-20°, the solvent was distilled off in vacuo and the residue was treated with 25 ml of 5% NaOH. The solution was filtered; 0.18 g of ferrocene (10%) remained on the filter. From the filtrate, 2.0 g (90%) of ferrocenecarboxylic acid was precipitated with hydrochloric acid; a further 0.10 g (4%) of this acid was extracted from the filtrate with ether. From the remaining solution the solvent was removed in a stream of air with moderate heating; the sodium salt of ferrocenesulfonic acid was recrystallized from water, giving 1.2 g of substance. The benzylthiuronium salt of ferrocenesulfonic acid, after recrystallization, melts at 219-221° (literature value 220-222°) ([3]).

Determination of the dissociation constants. The dissociation constants were determined by the potentiometric method in aqueous 68% methanol by weight at 20°. The calculations were made according to the formulas:

$$K_d = [\mathrm{H}^+]\frac{[\mathrm{NaOH}] + [\mathrm{H}^+]}{M - \{[\mathrm{NaOH}] + [\mathrm{H}^+]\}}; \quad \mathrm{p}K_d = \mathrm{pH} + \lg\frac{M - \{[\mathrm{NaOH}] + [\mathrm{H}^+]\}}{[\mathrm{NaOH}] + [\mathrm{H}^+]}, \tag{13}$$

where M is the molar concentration of the acid in solution, which was always equal to $5.0000 \cdot 10^{-3}$ M. The pH values were measured for each acid at three different degrees of neutralization; thus the NaOH concentration in these buffer solutions was: 1) $1.4145 \cdot 10^{-3}$ M, 2) $2.3575 \cdot 10^{-3}$ M, 3) $3.3005 \cdot 10^{-3}$ M.

The pH measurements were made on an LP-4 type potentiometer; the potentiometer scale was set with a buffer of pH 7.09. The differences between the individual $\mathrm{p}K_d$ values calculated according to the above formula did not exceed 0.03 $\mathrm{p}K_d$ unit for each acid.

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Note: Figure translations are in progress. See original paper for figures.