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Electrofugality of Some Ferrocenylphenylmethyl Cations

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THIS PAPER IS DEDICATED TO PROF. KATA MLINARIĆ-MAJERSKI ON THE OCCASION OF HER 70TH BIRTHDAY

Abstract: The electrofugality scale has been extended with new substituted ferrocenylphenylmethyl cations **1–4**. E_f values were determined by applying the linear free energy relationship (LFER): $\log k = s_f (E_f + N_f)$. Due to ability of the ferrocene moiety to efficiently stabilize the positive charge, ferrocenylphenylmethyl cations constitute a group of very powerful electrofuges ($E_f > 1$). Impact of the phenyl group in ferrocenylphenylmethyl derivatives on stabilization of the positive charge is considerably leveled by the ferrocenyl group, so the rate effect of the alkyl substituents (methyl, ethyl and *tert*-butyl) on the phenyl ring is suppressed, causing narrow range of E_f parameters. Lack of breakdown of Hammett-Brown plot if the rates for the complete set of substrates **1–5** have been correlated, indicates that the ferrocenyl group in α -position diminishes the stabilizing effects of electron-donating substituents as well.

Keywords: electrofugality, nucleofugality, ferrocenylphenylmethyl cation, solvolysis, substituent effect.

INTRODUCTION

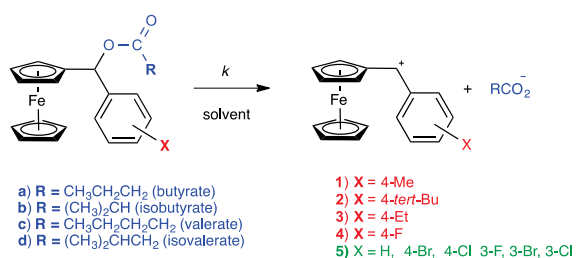
THE first step in solvolytic S_N1 reactions involves the heterolytic cleavage of the carbon—leaving group bond and formation of the carbocation intermediate (electrofuge) and the free leaving group (nucleofuge).^[1] The reactivity of a substrate is determined with both abilities the leaving group and the carbocation to depart from the substrate, i.e., with their electrofugality and nucleofugality. A comprehensive electrofugality and nucleofugality scales have been constructed based on solvolytic reactivity of benzhydryl derivatives in various solvents. Accordingly, the heterolysis rate constant of any substrate in a given solvent can be predicted by using the following three-parameter LFER (Equation 1):^[2,3]

$$\log k = s_f (N_f + E_f) \quad (1)$$

in which k is first-order rate constant at 25 °C, s_f is the nucleofuge-specific slope parameter, N_f is the nucleofugality in a given solvent, and E_f is the independent variable referring to electrofugality. According to above

equation, the nucleofuge specific parameters can be derived from $\log k$ vs. E_f plots,^[4] while the electrofugalities can be derived from $\log k/s_f$ vs. N_f plots, taking the known s_f and N_f parameters. The E_f values obtained are justified if the linear plots obtained have a slopes of unity.^[5]

In our previous work we determined the electrofugality of some ferrocenylphenylmethyl cations, mostly those with electron-accepting groups on the phenyl ring (**5** in Scheme 1).^[6] In this work we chose to extend the spectrum of E_f parameters for ferrocenylphenylmethyl substrates by investigating some more reactive ferrocenylphenylmethyl electrofuges (**1–4**, Scheme 1). The aim was to (a) collect additional E_f parameters that can be used for estimation of the absolute first-order heterolysis rates in a given solvent for variety of substrates that are combination of ferrocenylphenylmethyl moiety and any nucleofuge of known s_f and N_f parameters, by applying Equation (1), (b) to determine if the stabilizing effect of the ferrocenyl group is similar to that in less reactive substrates, and (c) to make feasible comparison of reactivities of the series of ferrocenylphenylmethyl cations with numerous electrofuges with known E_f values.



Scheme 1. The heterolytic step in the solvolysis of some X-substituted ferrocenylphenylmethyl carboxylates.

To enable measurements using conventional kinetic methods available for us, such a reactive electrofuges should be combined with poor nucleofuges. Up to now the least reactive nucleofuge on the scale is acetate anion (N_f from -3.55 to -4.8 in various solvents).^[6,7] It turned out that acetates of ferrocenylphenylmethyl cations **1–4** solvolyze too fast, so electrofuges **1–4** should be combined with less reactive nucleofuges. Having in mind that according a qualitative rule of thumb, the abilities of leaving groups are arranged in the same order as the acidities of their conjugate Brønsted acids, we assumed that carboxylates with longer alkyl chain, as are butyrate, isobutyrate, valerate, and isovalerate (**a–d**, Scheme 1), would be appropriate. Hence, the first step was determining their nucleofugalities.

To get N_f and s_f values, according to well established procedure, the series of benzhydryl butyrate, isobutyrate, valerate, and isovalerate should have been subjected to kinetic measurement in a given solvent, and the corresponding nucleofuge-specific parameters would have been derived from $\log k$ vs. E_f plots (Equation 1). However, except dianysylmethyl isobutyrate, the synthesis of other substrates failed. Therefore, instead using reactive benzhydryl substrates ($E_f > 0$) to get the nucleofugality parameters from $\log k$ vs. E_f plots, we used ferrocenylphenylmethyl derivatives whose E_f values have already been determined.^[6]

RESULTS AND DISCUSSION

A series of X-substituted ferrocenylphenylmethyl butyrates, isobutyrate, valerate, and isovalerate (**5a–5d**) which were prepared according to the procedure presented in the Supporting Information, were subjected to solvolysis in various solvents. The solvolysis rates were measured titrimetrically (details are given in Kinetic Methods in the Experimental) at 25 °C or at least three different temperatures and the rate constants were extrapolated to 25 °C by using Eyring plot. The first-order rate constants at 25 °C (measured and extrapolated) are presented in Table S1 (Supporting Information).

The trends observed from the kinetic data can be summarized as follows. Carboxylates with straight side chains are slightly more reactive than the corresponding carboxylates with branched side chains (Tables S1). Also, the solvolytic reactivities of substrates with non-branched carboxylates (butyrates and valerates) are similar (Figure S1a), whereas those with branched chain somewhat differ, i.e., isovalerate is slightly more reactive than isobutyrate (Figure S1b).

To extract the nucleofugality parameters (N_f and s_f) for carboxylates **a–d**, the logarithms of the first-order solvolysis rate constants in the given solvents were plotted against published E_f values of ferrocenylphenylmethyl cations **5**.^[6] The correlation lines are presented in Figure S1a and S1b in the Supporting Information. The nucleofuge-specific parameters (N_f and s_f) are presented in Table 1.

Once the nucleofuge specific parameters for the four carboxylates **a–d** in various solvents have been determined, the electrofugality of ferrocenylphenylmethyl cations **1–4** could be assessed. The substrates prepared were the combination of electrofuges **1–4** and the carboxylates **a–d** (preparation is presented in Experimental). Solvolysis rates were measured in various aqueous solvents (Table 2).

To extract the electrofugalities, $\log k/s_f$ vs. N_f were plotted for the series of ferrocenylphenylmethyl

Table 1. Nucleofugality parameters N_f and s_f for butyrate, isobutyrate, valerate and isovalerate in various solvents

Solvent ^(a)	Butyrate		Isobutyrate		Valerate		Isovalerate	
	N_f	s_f	N_f	s_f	N_f	s_f	N_f	s_f
100M	-4.61	0.99	-4.80	1.00	-4.71	0.95	-4.78	0.93
90M10W	-4.23	0.94	-4.55	0.89	-4.31	0.92	-4.60	0.81
90E10W	-4.58	1.03	-4.70	1.03	-4.61	0.97	-4.68	0.93
80AN20W	-5.15	1.01	-5.24	1.04	-5.28	0.97	-5.38	0.95
80A20W	-5.33	1.14	-5.67	1.11	-5.88	0.94	–	–

^(a) Binary solvents are given as v/v; A = acetone, AN = acetonitrile, E = ethanol, M = methanol, and W = water.

Table 2. Solvolysis rate constants of some **1–4** ferrocenylphenylmethyl butyrates (**a**), isobutyrate (**b**), valerate (**c**), and isovalerate (**d**) in various solvents at 25 °C

Substrate	Electrofuge ^(a)	LG ^(b)	Solvent ^(c)	k/s^{-1} ^(d)
1a	4-MeC ₆ H ₅ FcCH ⁺	But	80AN20W	4.23×10^{-3} (e,f)
1b		Isobut	90E10W	1.09×10^{-2} (e,g)
			80AN20W	$3.02 \pm 0.03 \times 10^{-3}$
1c		Val	80AN20W	3.97×10^{-3} (e,h)
1d		Isoval	80AN20W	$(3.66 \pm 0.06) \times 10^{-3}$
2a	4-tButC ₆ H ₅ FcCH ⁺	But	80AN20W	$(3.62 \pm 0.04) \times 10^{-3}$
2b		Isobut	90E10W	1.06×10^{-2} (e,i)
2c		Val	80AN20W	$(3.46 \pm 0.02) \times 10^{-3}$
2d		Isoval	80AN20W	$(3.21 \pm 0.06) \times 10^{-4}$
3a	4-EtC ₆ H ₅ FcCH ⁺	But	80AN20W	$(3.73 \pm 0.05) \times 10^{-3}$
3b		Isobut	90E10W	8.47×10^{-3} (e,j)
			80AN20W	$(2.31 \pm 0.03) \times 10^{-3}$
3c		Val	80AN20W	$(2.91 \pm 0.01) \times 10^{-3}$
4a		But	90E10W	4.75×10^{-3} (e,k)
			80AN20W	$(1.45 \pm 0.03) \times 10^{-3}$
4b		Isobut	90E10W	$(3.65 \pm 0.03) \times 10^{-3}$
			80AN20W	$(1.05 \pm 0.01) \times 10^{-3}$
4c		Val	80AN20W	$(1.22 \pm 0.07) \times 10^{-3}$
		Isoval	80AN20W	$(1.32 \pm 0.01) \times 10^{-3}$

^(a) Fc = ferrocene.

^(b) But = CH₃CH₂CH₂COO⁻, Isobut = (CH₃)₂CHCOO⁻, Val = CH₃CH₂CH₂CH₂COO⁻, and Isoval = (CH₃)₂CHCH₂COO⁻.

^(c) Binary solvents are given as v/v at 25 °C; AN = acetonitrile, E = ethanol, W = water.

^(d) Average rate constants from at least three runs performed at 25 °C. Errors are SD.

^(e) Extrapolated from data at different temperatures by use of the Eyring equation; errors for activation parameters shown are standard errors.

^(f) $\Delta H^\ddagger = 66.0 \pm 0.9$ kJmol⁻¹, $\Delta S^\ddagger = -68.9 \pm 3.0$ JK⁻¹mol⁻¹.

^(g) $\Delta H^\ddagger = 71.3 \pm 0.1$ kJmol⁻¹, $\Delta S^\ddagger = -43.3 \pm 0.5$ JK⁻¹mol⁻¹.

^(h) $\Delta H^\ddagger = 69.5 \pm 0.8$ kJmol⁻¹, $\Delta S^\ddagger = -58.0 \pm 2.9$ JK⁻¹mol⁻¹.

⁽ⁱ⁾ $\Delta H^\ddagger = 73.3 \pm 1.1$ kJmol⁻¹, $\Delta S^\ddagger = -36.9 \pm 3.8$ JK⁻¹mol⁻¹.

^(j) $\Delta H^\ddagger = 61.9 \pm 3.2$ kJmol⁻¹, $\Delta S^\ddagger = -76.8 \pm 11.6$ JK⁻¹mol⁻¹.

^(k) $\Delta H^\ddagger = 51.3 \pm 1.5$ kJmol⁻¹, $\Delta S^\ddagger = -117.4 \pm 5.1$ JK⁻¹mol⁻¹.

carboxylates **1–4** (Figure 1). The weighted average of the slopes of correlation lines in Figure 1 is 0.9969 ± 0.004 . The electrofugalities obtained from the correlations are shown in Table 3 in which, for sake of comparison, the electrofugality of some less reactive ferrocenylphenylmethyl cations as well as benzhydryl cations are presented.

By comparing the E_f values of ferrocenylphenylmethyl cations and benzhydryl cations it is obvious that the effect of the substituent on the phenyl ring is much more pronounced in benzhydryl derivatives. Thus, switching from 4-methyl to 3-chloro substituent in benzhydryl substrates cause decrease of E_f values for about three units, which roughly corresponds to difference in reactivity of three orders of magnitude. On the other hand, the difference of E_f parameters between 3-chloroferrocenylphenylmethyl cation and 4-methylferrocenylphenylmethyl cation is about one unit, i.e., 4-methyl derivative is only about ten times more reactive than 3-chloro derivative.

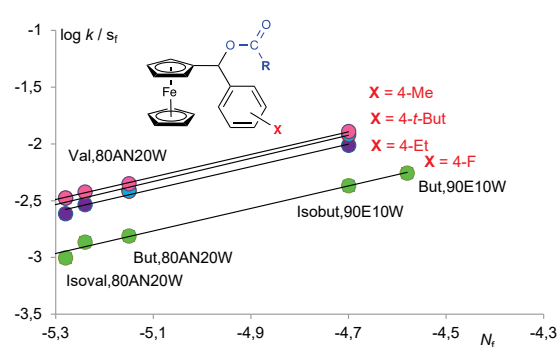


Figure 1. Plots $\log k/s_f$ against N_f for the solvolysis of substituted ferrocenylphenylmethyl butyrates, isobutyrate, valerate, and isovalerate **1–4** in various solvents. But = CH₃CH₂CH₂COO⁻, Isobut = (CH₃)₂CHCOO⁻, Val = CH₃CH₂CH₂CH₂COO⁻, Isoval = (CH₃)₂CHCH₂COO⁻. Binary solvents are given as v/v. AN = acetonitrile, E = ethanol, and W = water.

Table 3. Electrofugality parameters of some substituted ferrocenylphenylmethyl cations and the corresponding benzhydryl cations.

Substituent X	E_f	
	Ferrocenyl-X-phenylmethyl cation	X-Benzhydryl cation ^(b)
4-Me (1)	2.80	-4.63
4-tBut (2)	2.83	
4-Et (3)	2.68	
H	2.40 ^(a)	-6.03
4-F (4)	2.31	-5.72
4-Br	2.15 ^(a)	-6.62
3-F	1.77 ^(a)	-7.53
3-Cl	1.67 ^(a)	-7.69

^(a) E_f parameters for ferrocenyl-X-phenylmethyl cations (X = H, 4-Br, 3-F, 3-Cl) are taken from Ref. [6].

^(b) E_f parameters for benzhydryl cations are taken from Ref. [3a].

Kinetic results obtained earlier with the series of ferrocenylphenylmethyl derivatives **5** as well as quantum chemical calculations showed that the effect of the substituents on the phenyl ring is suppressed due to very strong electron donating ability of the α -ferrocenyl group, i.e., leveling occurs.^[6] The question arose if this applied to all X substituents (**1–5**), or electron-donating substituents on the phenyl in substrates **1–3** had somewhat more pronounced effect than in **5**. This assumption was tested with Hammett-Brown correlation. If the effects of electron-donating substituents in **1–3** were stronger than those in the series of **5** examined earlier, breakdown of the σ^+ , ρ^+ correlation line would occur. However, as presented in Figure 2, linear correlation has been obtained if all data for substrates **1–5** are included. In the limits of experimental error, essentially the same slope has been obtained in e.g. 90 % aq. ethanol for the complete set of ferrocenylphenylmethyl isobutyrylates **1–5** ($\rho^+ = -1.60$) and that for the series of **5** determined earlier ($\rho^+ = -1.46$), due to very strong electron-donating ability of the ferrocenyl group (Figure 2).

EXPERIMENTAL

Substrate Preparation: The ferrocenyl phenyl ketones were prepared by standard acylation.^[8] using the corresponding benzoyl chloride and ferrocene in dichloromethane with $AlCl_3$ as catalyst at low (0 °C) or ambient temperature. Reduction of ferrocenyl phenyl ketones with $LiAlH_4$ in diethyl ether according to published procedure^[9] gave 4-fluorophenylferrocenemethanol (69 %), 4-methylphenylferrocenemethanol (86 %), 4-ethylphenylferrocenemethanol (77 %), and 4-*tert*-butylphenylferrocenemethanol (66 %), respectively.

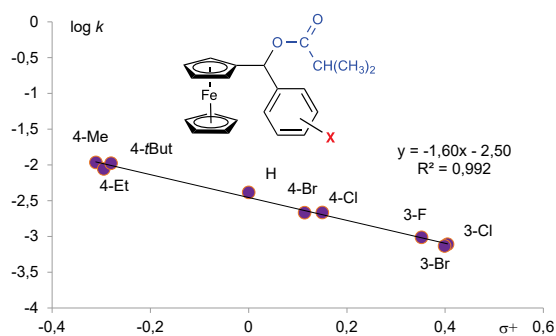


Figure 2. Hammett–Brown plot for the solvolysis of X-substituted ferrocenylphenylmethyl isobutyrylates in 90 % aq. ethanol at 25 °C.

General Procedure for the Synthesis of Ferrocenylphenylmethyl Butyrates, Isobutyrylates, Valerates, and Isovalerates: A solution of butyryl, isobutyryl, valeroyl, and isovaleryl chloride (≈ 2 eq) in anhydrous benzene (10 mL) was added dropwise to a previously prepared stirred solution of the appropriate phenylferrocenemethanol (1 eq) and pyridine (0.5 g, 6.32 mmol) in anhydrous benzene (10 mL). The reaction mixture was stirred under argon at ambient temperature for from 1–2 h to overnight. Precipitated pyridinium chloride was removed by filtration, and excess of pyridine was removed with hydrochloric acid (15 mL, 5 %). The benzene layer was separated and washed with concentrated solution of sodium hydroxide and water. After drying over anhydrous sodium sulfate, benzene was evaporated in vacuum. Butyrates, isobutyrylates, valerates, and isovalerates were obtained as dark red crystals or oils (yield 44.2–85.9 %).

4-Methylphenylferrocenylmethyl Butyrate (1a): This compound was obtained from 4-methylphenylferrocenemethanol (0.5 g, 1.63 mmol), pyridine (0.5 g, 6.32 mmol), and butyryl chloride (0.35 g, 3.28 mol); yield 0.46 g, 74.8 %. 1H NMR (400 MHz, $CDCl_3$, 25 °C): δ /ppm = 0.93 (t, $J = 7.4$ Hz, 3H; $CH_3CH_2CH_2COOR$), 1.64–1.70 (m, 5H; $CH_3CH_2CH_2COOR + CH_3Ar$), 2.34 (t, $J = 7.4$ Hz, 2H; $CH_3CH_2CH_2COOR$), 4.0–4.30 (m, 4H; C_5H_4), 4.09 (s, 5H; C_5H_5), 6.72 (s, 1H; ArCHFc), 7.13 (d, $J = 7.9$ Hz, 2H; Ar), 7.29 (d, $J = 8.0$ Hz, 2H; Ar). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ /ppm = 13.8 ($CH_3CH_2CH_2COOR$), 18.6 ($CH_3CH_2CH_2COOR$), 21.3 (CH_3Ar), 36.6 ($CH_3CH_2CH_2COOR$), 67.5, 67.7, 68.2, 68.3 (C_5H_4), 69.0 (C_5H_5), 74.0 (ArCHFc), 88.4 (Fc), 127.2, 129.0, 137.5, 137.7 (Ar), 172.7 (COOR).

4-*tert*-Butylphenylferrocenylmethyl Butyrate (2a): This compound was obtained from 4-*tert*-butylphenylferrocenemethanol (0.5 g, 1.44 mmol), pyridine (0.5 g, 6.32 mmol), and butyryl chloride (0.30 g, 2.82 mol); yield 0.42 g, 69.4 %. 1H NMR (400 MHz, $CDCl_3$, 25 °C): δ /ppm = 0.95 (t, $J = 7.3$ Hz, 3H; $CH_3CH_2CH_2COOR$), 1.31 (s, 9H, $(CH_3)_3CAR$), 1.67–1.72 (m, 2H; $CH_3CH_2CH_2COOR$), 2.35 (t, $J = 7.3$ Hz, 2H;

CH₃CH₂CH₂COOR), 4.04–4.31 (m, 4H; C₅H₄), 4.10 (s, 5H; C₅H₅), 6.74 (s, 1H; ArCHFc), 7.29–7.39 (m, 4H; Ar). ¹³C NMR (100 MHz, CDCl₃, 25 °C): δ/ppm = 13.8 (CH₃CH₂CH₂COOR), 18.5 (CH₃CH₂CH₂COOR), 31.6 ((CH₃)₃CAr), 34.6 ((CH₃)₃CAr), 36.6 (CH₃CH₂CH₂COOR), 67.5, 67.5, 68.0, 68.1 (C₅H₄), 68.8 (C₅H₅), 73.7 (ArCHFc), 88.4 (Fc), 125.1, 126.8, 137.4, 150.7 (Ar), 172.7 (COOR).

4-Ethylphenylferrocenylmethyl Butyrate (3a): This compound was obtained from 4-ethylphenylferrocenemethanol (0.5 g, 1.56 mmol), pyridine (0.5 g, 6.32 mmol), and butyryl chloride (0.30 g, 2.82 mol); yield 0.46 g, 75.6 %. ¹H NMR (400 MHz, CDCl₃, 25 °C): δ/ppm = 0.94 (t, *J* = 7.4 Hz, 3H; CH₃CH₂CH₂COOR), 1.23 (t, *J* = 7.6 Hz, 3H; CH₃CH₂Ar), 1.65–1.71 (m, 2H; CH₃CH₂CH₂COOR), 2.34 (t, *J* = 7.4 Hz, 2H; CH₃CH₂CH₂COOR), 2.64 (q, *J* = 7.6 Hz, 2H; CH₃CH₂Ar), 4.02–4.31 (m, 4H; C₅H₄), 4.10 (s, 5H; C₅H₅), 6.73 (s, 1H; ArCHFc), 7.16 (d, *J* = 7.9 Hz, 2H; Ar). 7.31 (d, *J* = 8.1 Hz, 2H; Ar). ¹³C NMR (100 MHz, CDCl₃, 25 °C): δ/ppm = 13.9 (CH₃CH₂CH₂COOR), 15.6 (CH₃CH₂Ar), 18.6 (CH₃CH₂CH₂COOR), 28.7 (CH₃CH₂Ar), 36.7 (CH₃CH₂CH₂COOR), 67.6, 67.7, 68.2, 68.3 (C₅H₄), 69.0 (C₅H₅), 74.0 (ArCHFc), 88.5 (Fc), 127.3, 127.8, 137.7, 144.0 (Ar), 172.8 (COOR).

4-Fluorophenylferrocenylmethyl Butyrate (4a): This compound was obtained from 4-fluorophenylferrocenemethanol (0.5 g, 1.61 mmol), pyridine (0.5 g, 6.32 mmol), and butyryl chloride (0.27 g, 2.53 mmol); yield 0.38 g, 62.1 %. ¹H NMR (400 MHz, CDCl₃, 25 °C) δ/ppm = 0.93 (t, *J* = 7.4 Hz, 3H; CH₃CH₂CH₂COOR), 1.65–1.71 (m, 2H; CH₃CH₂CH₂COOR), 2.34 (t, *J* = 7.5 Hz, 2H; CH₃CH₂CH₂COOR), 3.98–4.30 (m, 4H; C₅H₄), 4.10 (s, 5H; C₅H₅), 6.73 (s, 1H; ArCHFc), 7.00–7.40 (m, 4H; Ar). ¹⁹F NMR (376 MHz, CDCl₃, 25 °C): δ/ppm = –114.06 (m). ¹³C NMR (100 MHz, CDCl₃, 25 °C): δ/ppm = 13.8 (CH₃CH₂CH₂COOR), 18.6 (CH₃CH₂CH₂COOR), 36.6 (CH₃CH₂CH₂COOR), 67.4, 67.6, 68.3, 68.4 (C₅H₄), 69.0 (C₅H₅), 73.5 (ArCHFc), 88.0 (Fc), 115.2 (d, *J* = 21.5 Hz; Ar–F), 129.1 (d, *J* = 8.1 Hz; Ar–F), 136.4 (d, *J* = 3.3 Hz; Ar–F), 162.4 (d, *J* = 246.5 Hz; Ar–F), 172.7 (COOR).

4-Methylphenylferrocenylmethyl Isobutyrate (1b): This compound was obtained from 4-methylphenylferrocenemethanol (0.5 g, 1.63 mmol), pyridine (0.5 g, 6.32 mmol), and isobutyryl chloride (0.35 g, 3.28 mol); yield 0.42 g, 68.7 %. ¹H NMR (400 MHz, CDCl₃, 25 °C): δ/ppm = 1.18–1.22 (d+d, *J* = 7.0 Hz + *J* = 7.0 Hz, 3H+3H; (CH₃)₂CHCOOR), 2.33 (s, 3H; CH₃Ar), 2.57–2.64 (m, 1H; (CH₃)₂CHCOOR), 4.00–4.29 (m, 4H; C₅H₄), 4.11 (s, 5H; C₅H₅), 6.70 (s, 1H; ArCHFc), 7.13 (d, *J* = 8.0 Hz, 2H; Ar), 7.27 (d, *J* = 8.0 Hz, 2H; Ar). ¹³C NMR (100 MHz, CDCl₃, 25 °C): δ/ppm = 19.0 + 19.0 ((CH₃)₂CHCOOR), 21.2 (CH₃Ar), 34.2 ((CH₃)₂CHCOOR), 67.3, 67.3, 68.0, 68.1 (C₅H₄), 68.8 (C₅H₅), 73.9 (ArCHFc), 88.5 (Fc), 127.0, 129.0, 137.6, 137.6 (Ar), 176.0 (COOR).

4-tert-butylphenylferrocenylmethyl Isobutyrate (2b): This compound was obtained from 4-tert-butylphenylferrocenemethanol (0.5 g, 1.44 mmol), pyridine (0.5 g, 6.32 mmol), and isobutyryl chloride (0.21 g, 1.97 mol); yield 0.43 g, 71.5 %. ¹H NMR (400 MHz, CDCl₃, 25 °C): δ/ppm = 1.21–1.25 (d+d, *J* = 7.0 Hz + *J* = 7.0 Hz, 3H+3H; (CH₃)₂CHCOOR), 1.31 (s, 9H; (CH₃)₃CAr), 2.60–2.67 (m, 1H; (CH₃)₂CHCOOR), 4.04–4.31 (m, 4H; C₅H₄), 4.12 (s, 5H; C₅H₅), 6.73 (s, 1H; ArCHFc), 7.29–7.36 (m, 4H; Ar). ¹³C NMR (100 MHz, CDCl₃, 25 °C): δ/ppm = 19.1 + 19.2 ((CH₃)₂CHCOOR), 31.5 ((CH₃)₃CAr), 34.4 ((CH₃)₂CHCOOR), 34.6 ((CH₃)₃CAr), 67.3, 67.4, 68.1, 68.1 (C₅H₄), 69.0 (C₅H₅), 73.8 (ArCHFc), 88.8 (Fc), 125.2, 126.8, 137.7, 150.8 (Ar), 176.1 (COOR).

4-Ethylphenylferrocenylmethyl Isobutyrate (3b): This compound was obtained from 4-ethylphenylferrocenemethanol (0.5 g, 1.56 mmol), pyridine (0.5 g, 6.32 mmol), and butyryl chloride (0.27 g, 2.53 mol); yield 0.42 g, 69.2 %. ¹H NMR (400 MHz, CDCl₃, 25 °C): δ/ppm = 1.18–1.24 (m, 9H; (CH₃)₂CHCOOR + CH₃CH₂Ar), 2.60–2.66 (m, 3H; (CH₃)₂CHCOOR + CH₃CH₂Ar), 4.01–4.29 (m, 4H; C₅H₄), 4.11 (s, 5H; C₅H₅), 6.71 (s, 1H; ArCHFc), 7.16 (d, *J* = 7.9 Hz, 2H; Ar), 7.30 (d, *J* = 8.0 Hz, 2H; Ar). ¹³C NMR (100 MHz, CDCl₃, 25 °C): δ/ppm = 15.6 (CH₃CH₂Ar), 19.1 + 19.2 ((CH₃)₂CHCOOR), 28.7 (CH₃CH₂Ar), 34.4 ((CH₃)₂CHCOOR), 67.4, 67.4, 68.1, 68.2 (C₅H₄), 69.0 (C₅H₅), 73.9 (ArCHFc), 88.7 (Fc), 127.1, 127.8, 137.3, 144.0 (Ar), 176.1 (COOR).

4-Fluorophenylferrocenylmethyl Isobutyrate (4b): This compound was obtained from 4-fluorophenylferrocenemethanol (0.5 g, 1.61 mmol), pyridine (0.5 g, 6.32 mmol), and butyryl chloride (0.21 g, 1.97 mmol); yield 0.43 g, 70.2 %. ¹H NMR (400 MHz, CDCl₃, 25 °C): δ/ppm = 1.18–1.22 (d+d, *J* = 7.0 Hz + *J* = 7.0 Hz, 3H+3H; (CH₃)₂CHCOOR), 2.58–2.65 (m, 1H; (CH₃)₂CHCOOR), 3.98–4.29 (m, 4H; C₅H₄), 4.11 (s, 5H; C₅H₅), 6.71 (s, 1H; ArCHFc), 7.00–7.38 (m, 4H; Ar). ¹⁹F NMR (376 MHz, CDCl₃, 25 °C): δ/ppm = –114.1 (m). ¹³C NMR (100 MHz, CDCl₃, 25 °C): δ/ppm = 19.1 + 19.1 ((CH₃)₂CHCOOR), 34.3 ((CH₃)₂CHCOOR), 67.3, 67.34, 68.3, 68.3 (C₅H₄), 69.0 (C₅H₅), 73.4 (ArCHFc), 88.2 (Fc), 115.3 (d, *J* = 21.5 Hz; Ar–F), 128.9 (d, *J* = 8.1 Hz; Ar–F), 136.5 (d, *J* = 3.2 Hz; Ar–F), 162.4 (d, *J* = 246.3 Hz; Ar–F), 176.0 (COOR).

4-Methylphenylferrocenylmethyl Valerate (1c): This compound was obtained from 4-methylphenylferrocenemethanol (0.5 g, 1.63 mmol), pyridine (0.5 g, 6.32 mmol), and valeroyl chloride (0.39 g, 3.23 mol); yield 0.37 g, 58.3 %. ¹H NMR (400 MHz, CDCl₃, 25 °C): δ/ppm = 0.90 (t, *J* = 7.3 Hz, 3H; CH₃CH₂CH₂CH₂COOR), 1.32–1.36 (m, 2H; CH₃CH₂CH₂CH₂COOR), 1.61–1.65 (m, 2H; CH₃CH₂CH₂CH₂COOR), 2.33–2.38 (m, 5H; CH₃CH₂CH₂CH₂COOR + CH₃Ar), 4.00–4.30 (m, 4H; C₅H₄), 4.09 (s, 5H; C₅H₅), 6.71 (s, 1H; ArCHFc), 7.14 (d, *J* = 8.0 Hz, 2H; Ar), 7.29 (d, *J* = 8.0 Hz, 2H; Ar). ¹³C NMR (100 MHz,

CDCl₃, 25 °C): δ /ppm = 13.9 (CH₃CH₂CH₂CH₂COOR), 21.3 (CH₃Ar), 22.4 (CH₃CH₂CH₂CH₂COOR), 27.2 (CH₃CH₂CH₂CH₂COOR), 34.5 (CH₃CH₂CH₂CH₂COOR), 67.6, 67.7, 68.2, 68.3 (C₅H₄), 69.0 (C₅H₅), 74.0 (ArCHFc), 88.4 (Fc), 127.2, 129.0, 137.5, 137.7 (Ar), 172.9 (COOR).

4-*tert*-butylphenylferrocenylmethyl Valerate (2c): This compound was obtained from 4-*tert*-butylphenylferrocenemethanol (0.5 g, 1.44 mmol), pyridine (0.5 g, 6.32 mmol), and valeroyl chloride (0.35 g, 2.90 mol); yield 0.40 g, 73.6 %. ¹H NMR (400 MHz, CDCl₃, 25 °C): δ /ppm = 0.91 (t, *J* = 7.3 Hz, 3H; CH₃CH₂CH₂CH₂COOR), 1.31–1.38 (m, 11H; CH₃CH₂CH₂CH₂COOR + (CH₃)₃CAr), 1.61–1.67 (m, 2H; CH₃CH₂CH₂CH₂COOR), 2.38 (t, *J* = 7.4 Hz, 2H; CH₃CH₂CH₂CH₂COOR), 4.04–4.32 (m, 4H; C₅H₄), 4.10 (s, 5H; C₅H₅), 6.74 (s, 1H; ArCHFc), 7.31–7.36 (m, 4H; Ar). ¹³C NMR (100 MHz, CDCl₃, 25 °C): δ /ppm = 13.9 (CH₃CH₂CH₂CH₂COOR), 22.4 (CH₃CH₂CH₂CH₂COOR), 27.2 (CH₃CH₂CH₂CH₂COOR), 31.5 ((CH₃)₃CAr), 34.5 (CH₃CH₂CH₂CH₂COOR), 34.7 ((CH₃)₃CAr), 67.6, 67.6, 68.2, 68.2 (C₅H₄), 69.0 (C₅H₅), 73.9 (ArCHFc), 88.6 (Fc), 125.2, 127.0, 137.5, 150.9 (Ar), 173.0 (COOR).

4-Ethylphenylferrocenylmethyl Valerate (3c): This compound was obtained from 4-ethylphenylferrocenemethanol (0.5 g, 1.56 mmol), pyridine (0.5 g, 6.32 mmol), and valeroyl chloride (0.37 g, 3.07 mol); yield 0.48 g, 76.3 %. ¹H NMR (400 MHz, CDCl₃, 25 °C): δ /ppm = 0.92 (t, *J* = 7.3 Hz, 3H; CH₃CH₂CH₂CH₂COOR), 1.24 (t, *J* = 7.6 Hz, 3H; CH₃CH₂Ar), 1.32–1.38 (m, 2H; CH₃CH₂CH₂CH₂COOR), 1.61–1.67 (m, 2H; CH₃CH₂CH₂CH₂COOR), 2.37 (t, *J* = 7.3 Hz, 2H; CH₃CH₂CH₂CH₂COOR), 2.65 (q, *J* = 7.6 Hz, 2H; CH₃CH₂Ar), 4.03–4.32 (m, 4H; C₅H₄), 4.11 (s, 5H; C₅H₅), 6.74 (s, 1H; ArCHFc), 7.18 (d, *J* = 8.0 Hz, 2H; Ar), 7.33 (d, *J* = 8.1 Hz, 2H; Ar). ¹³C NMR (100 MHz, CDCl₃, 25 °C): δ /ppm = 13.8 (CH₃CH₂CH₂CH₂COOR), 15.5 (CH₃CH₂Ar), 22.3 (CH₃CH₂CH₂CH₂COOR), 27.1 (CH₃CH₂CH₂CH₂COOR), 28.6 (CH₃CH₂Ar), 34.4 (CH₃CH₂CH₂CH₂COOR), 67.5, 67.6, 68.1, 68.2 (C₅H₄), 68.8 (C₅H₅), 73.9 (ArCHFc), 88.4 (Fc), 127.2, 127.7, 137.6, 143.9 (Ar), 172.8 (COOR).

4-Fluorophenylferrocenylmethyl Valerate (4c): This compound was obtained from 4-fluorophenylferrocenemethanol (0.5 g, 1.61 mmol), pyridine (0.5 g, 6.32 mmol), and valeroyl chloride (0.40 g, 3.32 mmol); yield 0.40 g, 62.7 %. ¹H NMR (400 MHz, CDCl₃, 25 °C): δ /ppm = 0.90 (t, *J* = 7.3 Hz, 3H; CH₃CH₂CH₂CH₂COOR), 1.30–1.36 (m, 2H; CH₃CH₂CH₂CH₂COOR), 1.61–1.64 (m, 2H; CH₃CH₂CH₂CH₂COOR), 2.36 (t, *J* = 7.5 Hz, 2H; CH₃CH₂CH₂CH₂COOR), 3.98–4.30 (m, 4H; C₅H₄), 4.10 (s, 5H; C₅H₅), 6.72 (s, 1H; ArCHFc), 7.00–7.39 (m, 4H; Ar). ¹⁹F NMR (376 MHz, CDCl₃, 25 °C): δ /ppm = –114.1 (m). ¹³C NMR (100 MHz, CDCl₃, 25 °C): δ /ppm = 13.86 (CH₃CH₂CH₂CH₂COOR), 22.4 (CH₃CH₂CH₂CH₂COOR), 27.2 (CH₃CH₂CH₂CH₂COOR), 34.4 (CH₃CH₂CH₂CH₂COOR), 67.4, 67.6, 68.3, 68.5 (C₅H₄), 69.0 (C₅H₅), 73.5 (ArCHFc), 88.0 (Fc),

115.2 (d, *J* = 21.5 Hz; Ar–F), 129.1 (d, *J* = 8.1 Hz; Ar–F), 136.4 (d, *J* = 3.0 Hz; Ar–F), 162.4 (d, *J* = 246.3 Hz; Ar–F), 172.9 (COOR).

4-Methylphenylferrocenylmethyl Isovalerate (1d): This compound was obtained from 4-methylphenylferrocenemethanol (0.5 g, 1.63 mmol), pyridine (0.5 g, 6.32 mmol), and isovaleryl chloride (0.39 g, 3.23 mol); yield 0.37 g, 58.3 %. ¹H NMR (400 MHz, CDCl₃, 25 °C): δ /ppm = 0.92–0.94 (d+d, *J* = 3.1 Hz + *J* = 3.0 Hz, 3H+3H; (CH₃)₂CHCH₂COOR), 2.09–2.16 (m, 1H; (CH₃)₂CHCH₂COOR), 2.23 (d, *J* = 7.1 Hz, 2H; (CH₃)₂CHCH₂COOR), 2.34 (s, 3H; CH₃Ar), 3.99–4.30 (m, 4H; C₅H₄), 4.09 (s, 5H; C₅H₅), 6.71 (s, 1H; ArCHFc), 7.15 (d, *J* = 8.0 Hz, 2H; Ar), 7.30 (d, *J* = 7.9 Hz, 2H; Ar). ¹³C NMR (100 MHz, CDCl₃, 25 °C): δ /ppm = 21.3 (CH₃Ar), 22.6 + 22.6 ((CH₃)₂CHCH₂COOR), 25.9 ((CH₃)₂CHCH₂COOR), 43.8 ((CH₃)₂CHCH₂COOR), 67.6, 67.9, 68.2, 68.3 (C₅H₄), 69.0 (C₅H₅), 74.1 (ArCHFc), 88.4 (Fc), 127.3, 129.0, 137.4, 137.8 (Ar), 172.3 (COOR).

4-*tert*-butylphenylferrocenylmethyl Isovalerate (2d): This compound was obtained from 4-*tert*-butylphenylferrocenemethanol (0.5 g, 1.44 mmol), pyridine (0.5 g, 6.32 mmol), and isovaleryl chloride (0.26 g, 2.16 mol); yield 0.37 g, 58.3 %. ¹H NMR (400 MHz, CDCl₃, 25 °C): δ /ppm = 0.93–0.95 (d+d, *J* = 3.0 Hz + *J* = 3.0 Hz, 3H+3H; (CH₃)₂CHCH₂COOR), 1.30 (s, 9H; (CH₃)₃CAr), 2.10–2.17 (m, 1H; (CH₃)₂CHCH₂COOR), 2.24 (d, *J* = 7.0 Hz, 2H; (CH₃)₂CHCH₂COOR), 4.02–4.31 (m, 4H; C₅H₄), 4.10 (s, 5H; C₅H₅), 6.74 (s, 1H; ArCHFc), 7.31–7.36 (m, 4H; Ar). ¹³C NMR (100 MHz, CDCl₃, 25 °C): δ /ppm = 22.6 + 22.6 ((CH₃)₂CHCH₂COOR), 25.8 ((CH₃)₂CHCH₂COOR), 31.5 (CH₃)₃CAr), 34.7 (CH₃)₃CAr), 43.8 ((CH₃)₂CHCH₂COOR), 67.6, 67.7, 68.2, 68.2 (C₅H₄), 69.0 (C₅H₅), 73.9 (ArCHFc), 88.5 (Fc), 125.2, 127.0, 137.4, 150.8 (Ar), 172.3 (COOR).

4-Ethylphenylferrocenylmethyl Isovalerate (3d): This compound was obtained from 4-ethylphenylferrocenemethanol (0.5 g, 1.56 mmol), pyridine (0.5 g, 6.32 mmol), and isovaleryl chloride (0.28 g, 2.32 mol); yield 0.28 g, 44.2 %. ¹H NMR (400 MHz, CDCl₃, 25 °C): δ /ppm = 0.93–0.94 (d+d, *J* = 3.1 Hz + *J* = 3.1 Hz, 3H+3H; (CH₃)₂CHCH₂COOR), 1.23 (t, *J* = 7.6 Hz, 3H; CH₃CH₂Ar), 2.09–2.16 (m, 1H; (CH₃)₂CHCH₂COOR), 2.24 (d, *J* = 7.1 Hz, 2H; (CH₃)₂CHCH₂COOR), 2.64 (q, *J* = 7.6 Hz, 2H; CH₃CH₂Ar), 4.00–4.31 (m, 4H; C₅H₄), 4.10 (s, 5H; C₅H₅), 6.67 (s, 1H; ArCHFc), 7.17 (d, 2H, *J* = 8.1 Hz; Ar), 7.32 (d, 2H, *J* = 8.0 Hz; Ar). ¹³C NMR (100 MHz, CDCl₃, 25 °C): δ /ppm = 15.6 (CH₃CH₂Ar), 22.6 + 22.6 ((CH₃)₂CHCH₂COOR), 25.8 ((CH₃)₂CHCH₂COOR), 28.7 (CH₃CH₂Ar), 43.8 ((CH₃)₂CHCH₂COOR), 67.6, 67.8, 68.2, 68.3 (C₅H₄), 69.0 (C₅H₅), 74.1 (ArCHFc), 88.4 (Fc), 127.3, 127.8, 137.7, 144.0 (Ar), 172.3 (COOR).

4-Fluorophenylferrocenylmethyl Isovalerate (4d): This compound was obtained from 4-fluorophenylferrocene-methanol (0.5 g, 1.61 mmol), pyridine (0.5 g, 6.32 mmol), and isovaleryl chloride (0.29 g, 2.41 mmol); yield 0.37 g, 58.4 %. ¹H NMR (400 MHz, CDCl₃, 25 °C): δ/ppm = 0.92–0.94 (d+d, J = 3.0 Hz + J = 2.8 Hz, 3H+3H; (CH₃)₂CHCH₂COOR), 2.10–2.15 (m, 1H; (CH₃)₂CHCH₂COOR), 2.24 (d, J = 7.1 Hz, 2H; (CH₃)₂CHCH₂COOR), 3.97–4.30 (m, 4H; C₅H₄), 4.10 (s, 5H; C₅H₅), 6.72 (s, 1H; ArCHFc), 7.01–7.40 (m, 4H; Ar). ¹⁹F NMR (376 MHz, CDCl₃, 25 °C): δ/ppm = –114.1 (m). ¹³C NMR (100 MHz, CDCl₃, 25 °C): δ/ppm = 22.5 + 22.6 ((CH₃)₂CHCH₂COOR), 25.9 ((CH₃)₂CHCH₂COOR), 43.7 ((CH₃)₂CHCH₂COOR), 67.4, 67.8, 68.4, 68.5 (C₅H₄), 69.0 (C₅H₅), 73.5 (ArCHFc), 88.0 (Fc), 115.2 (d, J = 21.5 Hz; Ar–F), 129.1 (d, J = 8.1 Hz; Ar–F), 136.3 (d, J = 3.3 Hz; Ar–F), 162.4 (d, J = 246.4 Hz; Ar–F), 172.2 (COOR).

Kinetic Methods: Solvolysis rate constants were measured titrimetrically by means of TIM 856 titration manager (Radiometer Analytical SAS Villeurbanne Cedex, France), using a Red Rod Ag/AgCl combined pH electrode. Typically, 20–50 mg of the carboxylates were dissolved in 0.10–0.20 mL of dichloromethane, and injected into the solvent that was thermostated at the required temperature (± 0.01 °C). The liberated acid was continuously titrated at pH = 7.00–7.80 by using a 0.016 M or 0.032 M solution of sodium hydroxide in appropriate solvent. Individual rate constants were obtained by the least-squares fitting of data to the first-order kinetic equation for three to four half-lives. The rate constants were averaged from at least three measurements.

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Supplementary Information. Supporting information to the paper is attached to the electronic version of the article at: <https://doi.org/10.5562/cca3553>.

PDF files with attached documents are best viewed with Adobe Acrobat Reader which is free and can be downloaded from [Adobe's web site](https://www.adobe.com/acrobat).

REFERENCES

- [1] [a] M. B. Smith, J. March, *March's Advanced Organic Chemistry: Reactions, Mechanisms and Structure*, 6th ed., A John Wiley & Sons, Inc.; Hoboken, New Jersey, **2007**. [b] T. H. Lowry, K. S. Richardson, *Mechanism and Theory in Organic Chemistry*, 3rd ed., Harper & Row, New York, **1987**.
- [2] [a] B. Denegri, A. Streiter, S. Jurić, A. R. Ofial, O. Kronja, H. Mayr, *Chem.-Eur. J.* **2006**, *12*, 1648–1656. <https://doi.org/10.1002/chem.200500845> [b] Correction: B. Denegri, A. Streiter, S. Jurić, A. R. Ofial, O. Kronja, H. Mayr, *Chem.-Eur. J.* **2006**, *12*, 5415–5415. <https://doi.org/10.1002/chem.200690066> [c] B. Denegri, A. R. Ofial, S. Jurić, A. Streiter, O. Kronja, H. Mayr, *Chem.-Eur. J.* **2006**, *12*, 1657–1666. <https://doi.org/10.1002/chem.200500847>
- [3] [a] N. Streidl, B. Denegri, O. Kronja, H. Mayr, *Acc. Chem. Res.* **2010**, *43*, 1537–1549. <https://doi.org/10.1021/ar100091m> [b] B. Denegri, M. Matic, O. Kronja, *Synthesis* **2017**, *49*, 3422–3432. <https://doi.org/10.1055/s-0036-1590792>
- [4] for some selected examples see: [a] S. Jurić, B. Denegri, O. Kronja, *J. Org. Chem.* **2010**, *75*, 3851–3854. <https://doi.org/10.1021/jo100327c> [b] S. Jurić, B. Denegri, O. Kronja, *J. Phys. Org. Chem.* **2012**, *25*, 147–152. <https://doi.org/10.1002/poc.1886> [c] S. Jurić, O. Kronja, *J. Phys. Org. Chem.* **2015**, *28*, 314–319. <https://doi.org/10.1002/poc.3412> [d] S. Jurić, T. Portolan, O. Kronja, *Croat. Chem. Acta* **2016**, *89*, 65–70. <https://doi.org/10.5562/cca2822> [e] M. Matic, B. Denegri, S. Jurić, O. Kronja, *Croat. Chem. Acta* **2017**, *90*, 571–581. <https://doi.org/10.5562/cca3283>
- [5] M. Horn, C. Metz, H. Mayr, *Eur. J. Org. Chem.* **2011**, 6476–6485. <https://doi.org/10.1002/ejoc.201100912>
- [6] M. Marijan, S. Jurić, Z. Mihalić, O. Kronja, *Eur. J. Org. Chem.* **2019**, 537–546. <https://doi.org/10.1002/ejoc.201801133>
- [7] [a] M. Matic, B. Denegri, O. Kronja, *Eur. J. Org. Chem.* **2014**, 1477–1486. <https://doi.org/10.1002/ejoc.201301574> [b] B. Denegri, O. Kronja, *Croat. Chem. Acta* **2010**, *83*, 223–226.
- [8] [a] M. Rousch, M. Vogel, H. Rosenberg, *J. Org. Chem.* **1957**, *22*, 903–906. <https://doi.org/10.1021/jo01359a012> [b] R. L. Schaaf, *J. Org. Chem.* **1962**, *27*, 107–111. <https://doi.org/10.1021/jo01048a027>
- [9] K. Schlögl, *Monatsh. Chem.* **1957**, *88*, 601–621. <https://doi.org/10.1007/BF00901345>