Bridged Ferrocenes. Part 14.[1] A Kinetic Study of the Hydrolysis of [*m*]Ferrocenophan-1-yl Acetates †

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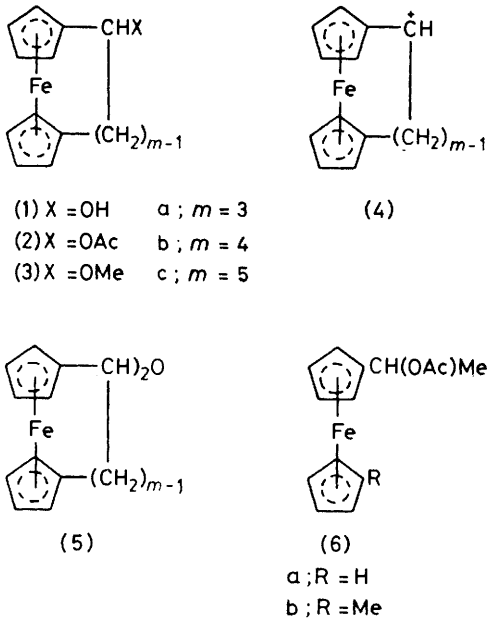
[*m*]Ferrocenophan-1-yl acetates undergo solvolysis in aqueous acetone by an S_N1 mechanism, the rates increasing sharply through the series [3]- < FcCH(OAc)Me < [5]- < [4]-. Under these conditions, or in ethanol, [4]ferrocenophan-2-yl acetate is inert.

KINETIC studies [2-5] have established that ferrocenylalkyl substrates of the type FcCH(X)R (X = Cl, OAc, *etc.*) undergo fast S_N1 solvolysis reactions *via* intermediate carbocations whose stability is manifest in their selectivity of combination with nucleophiles present in solution. These reactions proceed, whenever possible, by preferential *exo*-departure of the leaving-group (X^-) and a similar *exo*-stereoselectivity is associated with the nucleophilic addition step.[6] The reaction rates are sensitive to steric and conformational effects,[2c,5] and to the presence of a substituent in either ring of the ferrocenyl group,[2c,e] with the influence of homoannular substitution the more pronounced.

Introduction of an interannular bridging group into the ferrocene system restricts the torsional freedom of the cyclopentadienyl rings and, depending on the bridge length, may impose ring-tilt distortion.[7] The structural and conformational properties of these [*m*]ferrocenophanes have been thoroughly studied.[8] For S_N1 reactions of substrates of the type (2), the orientation of departure of the leaving-group relative to the ferrocene residue (and hence the reaction rate) would be controlled by the length and conformational flexibility of the bridging chain. Indeed, early work [2a] had shown that the rate of hydrolysis of [3]ferrocenophan-1-yl acetate (2a) is much slower than that of an unbridged analogue under the same conditions. In order to investigate these effects more fully, we have measured the rates of solvolysis in aqueous acetone of the [3]-, [4]-, and [5]-bridged acetates (2a—c). These were prepared conventionally (Ac_2O–pyridine) from the corresponding alcohols (1) which, in turn, were obtained by reduction ($LiAlH_4$) of the known bridged ketones.



Preliminary experiments established that the esters (2) are solvolysed, as expected, by rate-limiting formation of the corresponding secondary carbocations (4). In some preparative-scale reactions in aqueous acetone, the symmetrical ethers (5) were isolated in addition to the alcohol products (1), a further indication of the selectivity of collapse of ferrocenyl-carbocations in nucleophilic media. Under the conditions of the kinetic experiments, when much more dilute solutions were used, the alcohols were the sole products. Solvolysis in methanol led to the quantitative formation of the methyl ethers (3). No trace of alkene products resulting from carbocation deprotonation was detected in any of these experiments.

For each ferrocenophanyl acetate, the rate of solvolysis in '80% aqueous acetone' was measured titrimetrically at several suitable temperatures using an automatic titrator–pH-stat assembly which provided continuous neutralisation of the acetic acid liberated during the reaction (see Experimental section). Good first-order kinetic behaviour was observed for each run and duplicate runs gave acceptable agreement. Rate constants and derived activation energies are in the Table. The rate constants determined for the hydrolysis of the [3]-acetate (2a) and also for 1-ferrocenylethyl acetate (6a), which was used as a reference compound, agreed well with values obtained [2a,b,9] earlier using a conventional aliquot-sampling titrimetric method. Consequently, any depression of the solvolysis rates caused by acetate ion accumulating during the kinetic runs must be insignificant at the salt concentrations involved.

The rate constants for hydrolysis of the three ferrocenophanyl acetates reveal a surprisingly wide disparity in reactivity. Relative to the property of the unbridged reference compound (6a), the [3]-acetate (2a) is much less reactive whereas the [4]- and [5]-homologues (2b and c) are much more reactive (see $k_{rel.}$ values; Table). The diminished reactivity of (2a) is readily

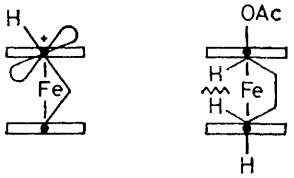
† Abstracted in part from the Ph.D Thesis of J. P., University of Strathclyde, 1971.

Rate constants and activation energies [a]

Substrate	T/K [b]	k/s^{-1}	$k_{rel.}$ [c]	$\Delta H^{\ddagger}$/kJ mol^{-1}	$\Delta S^{\ddagger}$/J mol^{-1} K^{-1}
(2a) [d]	273	(2.86×10^{-8}) [e]	0.0058	98.2	−29.2
	303	2.38×10^{-6}			
	308	4.34×10^{-6}			
	313	8.24×10^{-6}			
	318	1.56×10^{-5}			
(2b)	273	6.07×10^{-4}	122	70.9	−46.4
	278	1.09×10^{-3}			
	283	1.84×10^{-3}			
	288	3.30×10^{-3}			
(2c)	273	1.58×10^{-4}	31.8	92.5	−22.9
	278	3.46×10^{-4}			
	283	6.92×10^{-4}			
(6a) [f]	273	4.97×10^{-6}	1.00		
(6b)	273	(1.03×10^{-5}) [g]	2.07		

[a] For solvolysis in '80% aqueous acetone.' [b] ±0.2° (at 273 K), ±0.1° (at temperatures ⩾278 K). [c] Relative rate constants at 273 K. [d] Lit.[9] rate constants: 2.26×10^{-6} s^{-1} at 303 K, 1.39×10^{-5} s^{-1} at 318 K. [e] Value extrapolated from rate constants at higher temperatures using Arrhenius plot. [f] Lit.[2b] rate constant: 4.90×10^{-6} s^{-1} at 273 K. [g] Value from ref. 2e.

understandable. Evidence has been obtained[5] to suggest that carbocation formation is well advanced in the transition state for generation of a ferrocenyl-carbocation by a heterolytic process. In the case of the [3]ferrocenophanyl system, however, the steric constraints imposed on the bridging chain prevent full $p(d)_{\pi}$–p_{π} conjugation of the ferrocene group and the carbocation centre developing during solvolysis [*cf.* (7) ≡ (4a)]. Stabilisation of the transition state through electron release from the ferrocene residue is correspondingly attenuated compared with that which obtains for sterically unconstrained analogues such as (6a).*

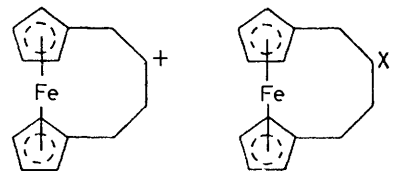


(7) (8)

The greatly enhanced reactivity of the other ferrocenophanes is more difficult to rationalise. Molecular models of the carbocations (4b and c) indicate that, for each structure, almost complete ferrocene–C^{+} conjugation is possible and the ferrocene residue is not subject to ring-tilt deformation.† Although the presence of a 1′-alkyl substituent would be expected to accelerate the rates of solvolysis of (2b and c) relative to that of (6a), this effect alone can neither accommodate the greater reactivity of the [4]- compared with the [5]-acetate, nor satisfactorily account for the magnitudes of the rate accelerations found. Thus, introduction of a 1′-methyl substituent leads [2e] only to a twofold increase in the rate of solvolysis of (6a) in aqueous acetone at 273 K [see k_{rel} values for (6a and b); Table].

* Additionally, the direction of cyclopentadienyl ring-tilting which is likely to obtain for [3]ferrocenophanyl species (*cf.* crystal structure [10] of [3]ferrocenophan-1-one) would reduce the capacity of the metal atom to provide anchimeric assistance to departure of acetate ion from (2a).

A likely cause of the enhanced solvolytic reactivities of the esters (2b and c) is relief of strain (eclipsing and/or non-bonded interaction) in the bridging group associated with ionisation. For example, of the few molecular conformations of the [4]-acetate which provide for anchimerically assisted *exo*-departure of the leaving group, one incorporates a serious non-bonded 1,4-interaction between the *endo*-hydrogen atoms attached to the terminal carbon atoms of the bridge [*cf.* (8) ≡ (2b)]. This compression would be relieved as heterolysis proceeds. The longer bridging chain of the [5]-acetate possesses greater conformational freedom, and strain relief during ionisation would have a correspondingly smaller accelerating effect on the rate of reaction.



(9) (10)

a; X = OAc

b; X = OH

The generation and observation (^{1}H n.m.r.) of the [4]ferrocenophan-2-yl cation (9) in solution in CF_3CO_2H has recently been reported,[12] suggesting that such secondary 2-ferrocenylalkyl cations may be stabilised by direct Fe · · · C^{+} interaction. With this effect in mind, we have attempted the solvolysis of [4]ferrocenophan-2-yl acetate (10a). However, this ester was recovered unchanged after one week in solution either in '80% aqueous acetone' at 318 K or in boiling ethanol, conditions under which the ferrocenophan-1-yl acetates (2) solvolyse readily. There was no indication of metal-assisted heterolysis.

EXPERIMENTAL

For general remarks, see Part 12.[13]

Preparation of Alcohols.—The ferrocenophanols (1a),[14] m.p. 159—160°, (1b),[12] m.p. 107—108°, (1c),[15] m.p. 106—107°, and (10b),[12] m.p. 118—120°, were prepared by reduction of the corresponding ferrocenophanones with $LiAlH_4$ in ether using the literature procedures.

[3]*Ferrocenophan-1-yl Acetate* (2a).—A solution of the alcohol (1a) (0.5 g, 2 mmol) in acetic anhydride (1.5 ml) and dry pyridine (5 ml) was allowed to stand for 72 h at room temperature. The mixture was then poured into ice–water. The title *ester* was filtered off and, after purification by crystallisation from light petroleum, was obtained as a yellow solid (0.45 g, 86%), m.p. 136—137° (Found: C, 65.5; H, 6.6. $C_{15}H_{16}FeO_2$ requires C, 65.4; H, 6.5%); τ(CDCl$_3$) 5.1—5.5 (1 H, m, CH), 5.6—6.2 (8 H, m, ferrocene protons), and 7.2—8.6 (7 H, m + s, remaining protons).

† In the crystal structure [11] of [4]ferrocenophan-1-one, a reasonable model for the carbocation (4b), the carbonyl group is only slightly twisted from the plane of the attached cyclopentadienyl ring and the ferrocene residue shows no significant ring-tilt distortion.

[4]*Ferrocenophan*-1-*yl Acetate* (2b).—This ester was pre-prepared from the alcohol (1b) as described in the previous experiment and was obtained as an orange-yellow solid, m.p. 71—72° (Found: C, 64.7; H, 6.0. $C_{16}H_{18}FeO_2$ requires C, 64.5; H, 6.1%); τ($CDCl_3$) 4.3—4.5 (1 H, m, CH), 5.5—6.1 (8 H, m, ferrocene protons), and 7.3—8.4 (9 H, m + s, remaining protons).

[5]*Ferrocenophan*-1-*yl Acetate* (2c).—This *ester* was prepared from the alcohol (1c) using the procedure described previously and was obtained as an orange solid, m.p. 101—103° (Found: C, 65.5; H, 6.6. $C_{17}H_{20}FeO_2$ requires C, 65.4; H, 6.5%); τ($CDCl_3$) 3.8—4.3 (1 H, m, CH), 5.6—6.1 (8 H, m, ferrocene protons), and 7.4—8.4 (11 H, m + s, remaining protons).

1-*Ferrocenylethyl Acetate* (6a).—This ester was prepared from 1-ferrocenylethanol using the procedure described previously and was obtained as a yellow solid, m.p. 67—68° (lit.,[2b] 70.2—71°).

[4]*Ferrocenophan*-2-*yl Acetate* (10a).—This *ester* was prepared from the alcohol (10b) using the procedure described previously and was obtained as a yellow solid, m.p. 86—87° (Found: C, 64.8; H, 6.2. $C_{16}H_{18}FeO_2$ requires C, 64.5; H, 6.1%); τ($CDCl_3$) 4.7—4.9 (1 H, m, CH), 5.8—6.0 (8 H, m, ferrocene protons), and 7.2—8.1 (9 H, m + s, remaining protons).

Hydrolysis of Acetates.—The following general procedure was used. A solution of the ester (0.1 g) in aqueous acetone (100 ml) was heated under reflux [for (2a)] or allowed to stand at room temperature [for (2b and c)] until hydrolysis was complete. The solution was then diluted with aqueous K_2CO_3 solution, most of the acetone was evaporated, and the residual solution was extracted with ether. The extract was washed (H_2O), dried ($MgSO_4$), and evaporated, and the residue was chromatographed on neutral Al_2O_3 using light petroleum–ether mixtures as eluants.

From the acetate (2a), the sole product was the alcohol (1a), identified by comparison with an authentic sample.

From the acetate (2b), there was obtained the alcohol (1b), identical with an authentic sample, and the *ether* (5b), a yellow solid, m.p. 236—238° (Found: C, 68.1; H, 6.1. $C_{28}H_{30}Fe_2O$ requires C, 68.0; H, 6.2%); τ($CDCl_3$) 5.6—6.1 (8 H, m, ferrocene protons), 6.26 (1 H, d, CH), and 7.4—8.8 (6 H, m, remaining protons).

From the acetate (2c), there was obtained the alcohol (1c), identical with an authentic sample, and the *ether* (5c), a yellow solid, m.p. 240—242° (Found: C, 68.7; H, 6.3. $C_{30}H_{34}Fe_2O$ requires C, 68.8; H, 6.5%); τ($CDCl_3$) 5.5—6.1 (9 H, m, CH + ferrocene protons) and 7.6—8.6 (8 H, m, remaining protons).

Methanolysis of Acetates.—A solution of the ester (0.25 g) in dry methanol (100 ml) was refluxed for several hours. The solution was then diluted with water and extracted with ether. The extract was washed (H_2O), dried ($MgSO_4$), and evaporated, and the residue was chromatographed on neutral Al_2O_3 using light petroleum–ether mixtures as eluants.

From the acetate (2a), the sole product was the *ether* (3a), an orange solid, m.p. 56—57° (Found: C, 65.3; H, 6.1. $C_{14}H_{16}FeO$ requires C, 65.6; H, 6.3%); τ($CDCl_3$) 5.7—6.2 (9 H, m, CH + ferrocene protons), 6.68 (3 H, s, OMe), and 7.4—8.1 (4 H, m, remaining protons).

From the acetate (2c), the sole product was the *ether* (3c), a viscous orange liquid (Found: C, 67.3; H, 7.0. $C_{16}H_{20}FeO$ requires C, 67.6; H, 7.0%); τ($CDCl_3$) 5.6—6.2 (9 H, m, CH + ferrocene protons), 6.86 (3 H, s, OMe), and 7.4—8.6 (8 H, m, remaining protons).

Attempted Solvolysis of the Acetate (10a).—(*a*) A solution of the acetate (10a) in '80% aqueous acetone' was maintained at 318 K for one week. The product was isolated and shown to be identical with the starting material. No trace of the alcohol (10b) was detected.

(*b*) A solution of the acetate (10a) in ethanol was heated under reflux for one week. Only unchanged starting material was recovered.

Kinetic Studies.—The solvent, '80% aqueous acetone' was prepared exactly as described[2b] previously. The automatic titration assembly, supplied by the Radiometer Co., Copenhagen, comprised an autoburette type ABU13, automatic titrator type TTT11, pH meter type pHm26, titrigraph type SBR2c, and titration vessel (capacity *ca.* 25 ml) equipped with thermostat jacket, magnetic stirrer, and electrode. The titration vessel, about two-thirds filled with solvent, was thermostatted at a desired temperature by means of circulating aqueous ethylene glycol (1 : 1 v/v) and the automatic titrator was set to maintain the measured pH of the solvent. The acetate (10—20 mg), dissolved in the minimum of acetone, was then added to the stirred solvent. The rate of delivery of aqueous sodium hydroxide solution (2×10^{-2}M) to the solution to maintain the pre-set pH was recorded and the reaction was followed to completion. Duplicate runs gave good reproducibility. Independent kinetic experiments (using the aliquot-sampling method) established that the small change in the composition of the solvent during the solvolysis had no significant effect on the observed rates. From the titration curves obtained, the first-order rate constants and thermodynamic quantities (for 298 K) were calculated conventionally[16] using least-squares best-fit computer programs. Correlation coefficients better than 0.999 were found in all cases. The results are in the Table. The solvolysis products, recovered after completion of representative kinetic runs, were found to be exclusively the corresponding alcohols.

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