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OXIDATION OF FERROCENYLACETONITRILE

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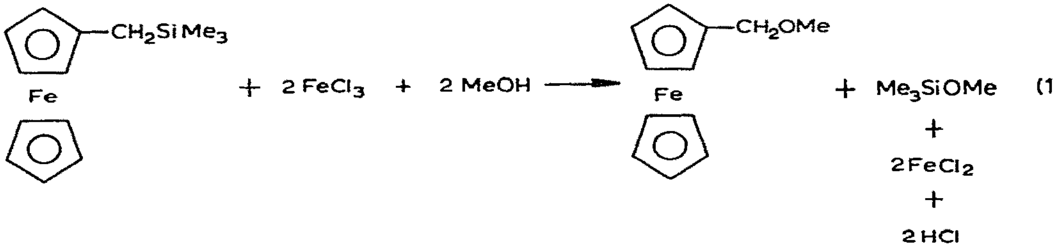
SUMMARY

Ferrocenylacetonitrile reacts with methanol, ethanol, or water in the presence of anhydrous ferric chloride to give α-methoxy-, α-ethoxy-, or α-hydroxyferrocenylacetonitrile, respectively. A possible mechanism for this type of reaction is discussed in terms of stepwise electron transfer processes involving substituted ferricenium ion intermediates.

INTRODUCTION

There are ample examples of side-chain oxidation of substituted ferrocenes with two-electron oxidants, which may be divided into two types of reaction, *viz.*, (*a*) oxidation of alkylferrocenes with manganese dioxide[1] (or by autoxidation[2]) to give acylferrocenes, and (*b*) oxidation of acylferrocenes with hypohalites to give ferrocenecarboxylic acids (haloform reaction)[3]. In these reactions, the iron atom of the ferrocene moiety does not seem to be affected by such two-electron oxidants and no evidence for the formation of the ferricenium ions has been shown in the course of the reaction.

In recent papers[4-6], we reported that the $R_3M{-}MR_2$ and $R_3M{-}CH_2$ bonds (M = Si or Ge) adjacent to the ferrocenyl group undergo anomalously facile cleavage with alcohols when these ferrocene derivatives are oxidized with one-equivalent oxidants, *e.g.* ferric chloride. For example, treatment of [(trimethylsilyl)methyl]ferrocene with anhydrous ferric chloride in methanol gives ferrocenylmethyl methyl ether and methoxytrimethylsilane as shown in eqn. (1). For this reaction, we proposed

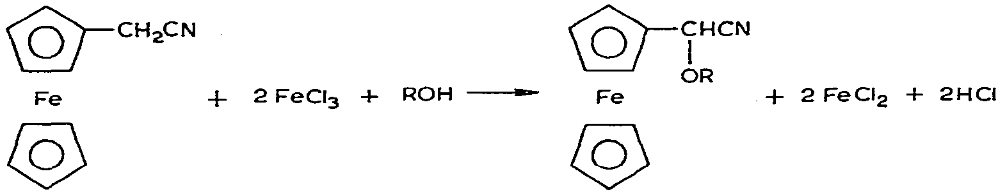


(1)

a possible mechanism involving one-electron transfer to form substituted ferricenium ion intermediates. As part of a continuing program to investigate reactions at the carbon α to the ferrocenyl group, we report here the oxidation of ferrocenylacetonitrile with anhydrous ferric chloride in protic solvents.

RESULTS AND DISCUSSION

When ferrocenylacetonitrile (I) was treated with two equivalents of ferric chloride per equivalent of substrate in methanol at room temperature, (ferrocenyl)(methoxy)acetonitrile (II) was obtained as a major product, along with a trace of methyl ferrocenecarboxylate. Similarly, reaction of (I) in ethanol or water gave (ferrocenyl)(ethoxy)acetonitrile (III) or (ferrocenyl)(hydroxy)acetonitrile (IV), respectively [eqn. (2)].

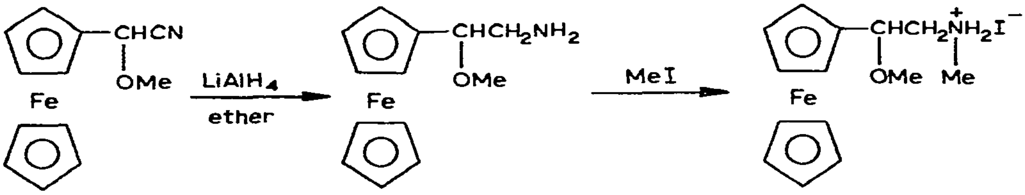


(2)

(I)

R = Me (II)
Et (III)
H (IV)

Elemental analyses, NMR and mass spectra of compounds (II), (III), and (IV) were in accordance with the assigned structures, although the IR spectra showed vanishingly weak absorptions[7] in the region of 2300–2200 cm^{-1}, whereas the spectrum of compound (I) had a sharp absorption at 2250 cm^{-1} characteristic of the C≡N group. To confirm the presence of the C≡N group, compound (II) was converted into the quaternary ammonium salt, (2-ferrocenyl-2-methoxyethyl) methylammonium iodide (V) by reaction with lithium aluminum hydride followed by treatment with methyl iodide [eqn. (3)].

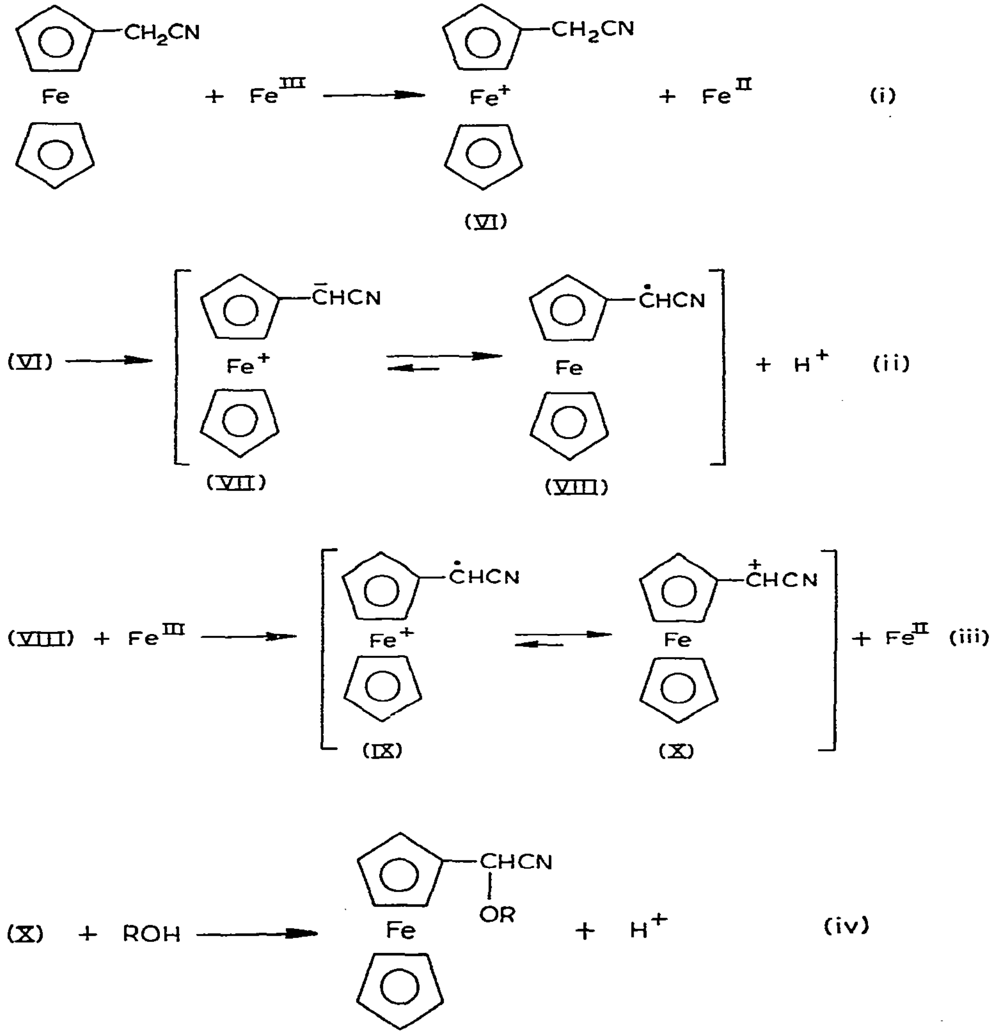


(3)

(V)

For the formation of FcCH(OR)CN (R = Me, Et, or H; Fc = ferrocenyl), we propose a mechanism depicted by Scheme 1, by analogy with the mechanism postulated for the reaction of ferrocenylmethyl derivatives of silicon and germanium with ferric chloride in methanol[5,6]. The mechanism involves formation of a substituted ferricenium ion (VI) by a rapid one-electron oxidation of the iron atom of the substrate with ferric chloride [step (*i*)][8]. The substituted ferricenium ion (VI) thus formed would easily lose an α-proton to give (VII), which in turn would be converted into the ferrocenylcyanomethyl radical (VIII) by a concomitant intramolecular redox process

SCHEME 1



[step (*ii*)]. Both the strongly electron-withdrawing ferricenyl[9] and cyano groups seem to facilitate such proton loss, and its readiness is reasonably related to the known stability of the ferrocenylcyanomethyl carbanion[10]. The ferrocenylcyanomethyl radical (VIII) would then be rapidly oxidized by a second molecule of ferric chloride directly or through another intramolecular redox process[11–13] to ferrocenylcyanomethyl carbonium ion (X) which would react with solvent alcohol to give the corresponding (ferrocenyl)(alkoxy)acetonitrile [step (*iii*) and (*iv*)].

Although this electron transfer mechanism is similar to that suggested for the oxidation of alkylbenzenes by manganic and cobaltic acetates[14–16], the reaction reported here shows that oxidation at the metal atom of the complex selectively causes oxidation of the ligand and hence provides one of the most striking examples of the effect of a change in the oxidation state of the central metal atom on the reactivity of the ligand. The reaction is certainly a new type of side-chain oxidation for substituted ferrocenes. Attempts to extend this reaction to other ferrocene derivatives have been unsuccessful.

It should be noted that although the pathway by which methyl (or ethyl) ferrocenecarboxylate is formed as a by-product of the reaction has not been elucidated, further reaction of part of the primary product, (ferrocenyl)(alkoxy)acetonitrile, with ferric chloride seems to lead finally to such an ester. It has been confirmed that the yield of the ester is scarcely increased when a 4-fold excess of ferric chloride per mole of substrate was employed and that (ferrocenyl)(alkoxy)acetonitriles were almost inert to ferric chloride in alcohols.

EXPERIMENTAL

All reactions were carried out in an atmosphere of nitrogen. Ferrocenylacetonitrile was prepared as reported[17]. IR spectra were recorded on a Hitachi EPI-G3 grating spectrophotometer. NMR spectra were obtained on a Varian T60 spectrometer in carbon tetrachloride solution with TMS as an internal standard and the data are given in τ-values. Molecular weights were obtained from mass spectra recorded on a Hitachi RMS-4 mass spectrometer. A Varian Aerograph Model 90P, equipped with a 20 ft. column packed with Apiezon-L (20% on Celite) was used for isolation and purification.

Reaction of ferrocenylacetonitrile (I) with ferric chloride

(*a*). *In methanol.* Ferrocenylacetonitrile (I) (6.0 g, 26.6 mmoles) and 10.0 g (61.7 mmoles) of anhydrous ferric chloride were dissolved in 300 ml of dry methanol. The solution immediately turned green, indicative of the formation of ferricenium ions[18], and eventually to brown during ca. one day. After stirring at room temperature for 70 h, the reaction mixture was hydrolyzed and extracted with ether. Ether was removed by evaporation and the resulting residue was fractionally distilled to give two fractions: (1) 1.0 g, b.p. 141–147°/2 mmHg and (2) 3.0 g, b.p. 147–150°/2 mmHg. A major product in fraction (1) was isolated by preparative GLC. The crystals thus obtained were recrystallized from methanol and identified as methyl ferrocenecarboxylate, m.p. 66–69° (lit. [19]m.p. 70–71°). Fraction (2) was homogeneous by GLC and solidified at room temperature to give brown crystals which were identified as (ferrocenyl)(methoxy)acetonitrile (44.2% yield), m.p. 37–38.5°. (Found: C, 61.46; H, 5.14; N, 5.54. $C_{13}H_{13}FeNO$ calcd.: C, 61.21; H,5.14; N, 5.49%.) The mass spectrum had a parent peak at *m/e* 255 ($C_{13}H_{13}FeNO$ calcd.: 255.10). The IR spectrum indicated the unsubstituted cyclopentadienyl ring (1110 and 1005 cm^{-1}) and the presence of ether bonding (1083 cm^{-1}). The ^1H NMR spectrum exhibited resonances at 6.62 (s, OCH_3), 5.78 (bs, ring protons), and 5.02 [s, $C\underline{H}$] ppm.

(*b*). *In ethanol.* In a similar way a mixture of (I) (5.0 g, 22.2 mmoles) and $FeCl_3$ (7.2 g, 44.0 mmoles) in 100 ml of ethanol was stirred at room temperature for 216 h. After work-up as described above, distillation gave two fractions: (1) 0.6 g, b.p. 140–145°/2.5 mmHg and (2) 2.6 g, b.p. 145–147°/2.5 mmHg. Isolation by preparative GLC of a major product in fraction (1) yielded brown crystals which were identified as ethyl ferrocenecarboxylate, m.p. 59–61° (lit.[20] m.p. 61–62°). Fraction (2) was pure (ferrocenyl)(ethoxy)acetonitrile (III) (43.5% yield), n_D^{20} 1.5828. (Found: C, 63.18; H, 5.75; N, 5.17. $C_{14}H_{15}FeNO$ calcd.: C, 62.48; H, 5.62; N, 5.20%.) Mass spectrum: m/e 269 ($C_{14}H_{15}FeNO$ calcd.: 269.13). IR: 2220 (C≡N, very weak), 1110 and 1005 (unsubstituted cyclopentadienyl ring), and 1080 cm^{-1} [ether bonding, ν(C–O)]. NMR: 8.78 (t, $C\underline{H}_3$), 6.37 (dq, $OC\underline{H}_2$), 5.84 (bs, ring protons), and 5.04 (s, $C\underline{H}$) ppm.

(*c*) *In water*. Similarly, a mixture of (I) (2.0 g, 8.90 mmoles) and $FeCl_3$ (3.2 g, 19.6 mmoles) in 200 ml of water/THF (3/1) was allowed to react for 48 h. After work-up as above, recrystallization from benzene gave 0.775 g (36.1% yield) of deep-red crystals of (ferrocenyl)(hydroxy)acetonitrile (IV), m.p. 95–100° (decomp.) [lit.[21] m.p. 104–125° (decomp.)]. Its IR spectrum had a band at 3400 cm^{-1} characteristic of ν(OH).

Reduction of (ferrocenyl)(methoxy)acetonitrile (II) with lithium aluminum hydride followed by treatment with methyl iodide

A mixture of 0.365 g (1.45 mmoles) of (II) and 1.39 g (14.3 mmoles) of lithium aluminum hydride in 100 ml of ether was stirred at room temperature for $1\frac{1}{2}$ h. The reaction mixture was then hydrolyzed, the resulting organic layer was separated, and the aqueous phase was extracted with ether. The combined organic layer was dried over anhydrous sodium sulfate and concentrated. To the concentrate was added 5 ml of methyl iodide and the mixture was allowed to stand at room temperature for 37 h. Yellow crystals (158 mg, 27.6% yield) of (2-ferrocenyl-2-methoxyethyl) methylammonium iodide (V) were obtained by filtration, m.p. 154–156°. (Found: C, 42.95; H, 5.18; I, 31.38; N, 3.59. $C_{14}H_{20}FeINO$ calcd.: C, 42.93; H, 5.03; I, 31.64; N, 3.49%.) The IR spectrum showed the presence of the NH_2^+ group (3100–2500 and 1565 cm^{-1}), the unsubstituted cyclopentadienyl ring (1107 and 1000 cm^{-1}), and ether bonding (1080 cm^{-1}).

Attempted reaction of (ferrocenyl)(alkoxy)acetonitrile with anhydrous ferric chloride

(*a*) *(Ferrocenyl)(methoxy)acetonitrile (II)*. A mixture of (II) (274 mg, 1.07 mmoles) and $FeCl_3$ (350 mg, 2.16 mmoles) in 10 ml of absolute methanol in a degassed sealed glass tube was allowed to stand at room temperature for 216 h. Hydrolysis of the mixture was followed by extraction with petroleum ether. After evaporation of the solvent, the residue was chromatographed on alumina using benzene as an eluant to give 168 mg (61.3% yield) of unchanged (II). None of the other ferrocene derivatives was detected.

(*b*) *(Ferrocenyl)(ethoxy)acetonitrile (III)*. Similarly, a mixture of (III) (221 mg, 0.822 mmoles) and $FeCl_3$ (269 mg, 1.66 mmoles) in 10 ml of ethanol was allowed to react at room temperature for 216 h. After work-up, 150 mg (67.9% yield) of unchanged (III) was recovered.

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