Ferrocene Derivatives. Part 22.[1] Friedel-Crafts Arylations with Chloroferrocenes. A New Route to Arylferrocenes.

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In the presence of anhydrous aluminium chloride and aluminium, chloro- and 1,1'-dichloro-ferrocenes act as moderately efficient reagents for the Friedel-Crafts arylation (*i.e.* 'ferrocenylation') of simple arenes. Extensive reductive dechlorination also occurs.

The ability of benzene to react with ferrocene in the presence of aluminium chloride and (preferably, but not necessarily) a reducing metal (*e.g.* aluminium) leading by replacement of a cyclopentadienyl ring to the benzenecyclopentadienyliron salts (1; R = H), was first described by Nesmeyanov and co-workers.[2] Extensions of this reaction have been widely studied and utilised by the same group[3,4] as well as many others including Lee, Sutherland *et al.*,[5] Astruc, Dabard *et al.*,[6] and one of us.[7] The French group[6] have paid particular attention to by-products and mechanistic features of the reaction.

Requiring the benzene(chlorocyclopentadienyl)iron salt (1; R = Cl) for a substitution reaction, we attempted to repeat its preparation[3] from 1,1'-dichloroferrocene, but obtained at best 20% yield as the hexafluorophosphate when using dry reagents. We subsequently applied Astruc's observation[6] that the addition of one mole of water per mole of ferrocene derivative benefits the ring replacement reaction. This raised the yield of the salt (1; R = Cl; X = PF_6) to 60—70%. In the meantime, however, we had identified phenyl- and diphenyl-ferrocenes as products of the reaction under anhydrous conditions, as we now report.

1-Phenylnaphthalene is formed[8] in 40% yield by Friedel-Crafts arylation of benzene with 1-chloronaphthalene under mild conditions. However, few related reactions have been described and monocyclic aryl chlorides and bromides are generally held to be unreactive.[9] Chloroferrocene appears comparable to chlorobenzene in its general lack of reactivity towards nucleophiles[3] and its ability to function as an electrophile towards benzene was therefore unexpected.

Lewis acids facilitate the oxidation of ferrocene, and the use of aluminium in Nesmeyanov's reaction[2–4] probably serves chiefly to avoid side reactions involving such oxidation, but can lead to reductive loss of halogen atoms.[7] In our reaction of 1,1'-dichloroferrocene with benzene, phenylferrocene (2; R = H) was the principal product so that clearly, reductive removal of one chlorine atom had occurred. Moreover, the yield of this product was substantially reduced when aluminium metal was omitted from the reaction mixture, although the ratio of phenyl-(2; R = H) to 1,1'-diphenyl-ferrocene (3; R = H) was effectively unchanged. Since the reductive dehalogenations observed in such systems may well involve radical intermediates, the possibility that substitution of benzene was occurring by a homolytic process had to be excluded.

An attempt to detect radicals was first made using cumene in place of benzene. Although (isopropylphenyl)ferrocenes were formed in modest yield and no bicumyl could be detected, the reaction was complicated by the ease with which cumene reacts with aluminium chloride to give redistribution products (chiefly di-isopropylbenzene). Complete separation of the products was therefore not attempted. Convincing evidence for the electrophilic nature of the substitution was readily obtained,
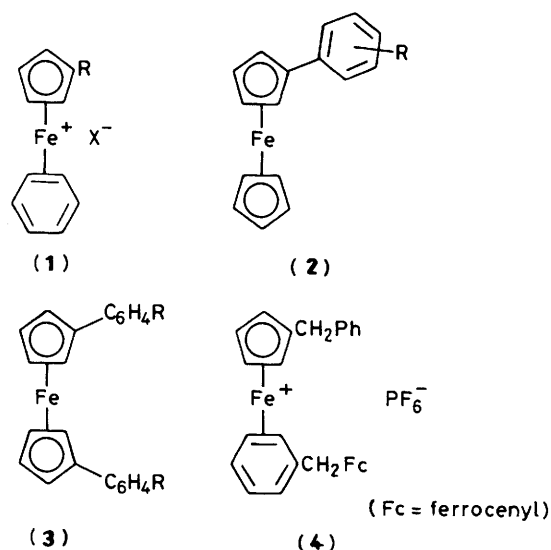

(1)   (2)

(3)   (4)

(Fc = ferrocenyl)

however, from the reaction of toluene with chloroferrocene. This gave *o*- and *p*-tolylferrocenes and neither the *meta* isomer nor bibenzyl could be found in the product mixture. Similarly chlorobenzene yielded chiefly *p*-chlorophenylferrocene together with the *ortho* but little or no *meta* isomer. We conclude that the reaction is indeed a Friedel-Crafts ferrocenylation of the aromatic substrate.

An attempt to use ferric chloride as catalyst for this reaction led only to extensive oxidation; there was no reaction with benzene and after reductive aqueous work-up, 90% of the dichloroferrocene was recovered.

The extensive reductive dechlorination occurring in these reactions is not caused by aluminium metal alone, but requires aluminium chloride. This is evident from experiment No. 8 (Table 1) with anisole: no arylation occurred, presumably because the aluminium chloride was completely tied up, initially in complexing with, and subsequently causing demethylation of, anisole. The dichloroferrocene was recovered substantially unchanged although aluminium metal was available throughout the reaction. More surprisingly, reduction, though significantly diminished in the absence of the metal, is still quite extensive as mentioned above (*e.g.* experiment 2). The recovered ferrocenes from this reaction are a mixture of chloro- and dichloro-ferrocene (in very approximately 1:2 ratio) together with a little ferrocene, whereas the benzene(chlorocyclopentadienyl)iron salt escapes obvious dechlorination. Since the last compound is the expected product from reactions of both chloro- and 1,1'-dichloro-ferrocene, the results may be regarded as self-

Table 1. Reactions of arenes with 1,1'-dichloroferrocene (experiments 1—9) and chloroferrocene (experiments 10,11) (Fc = ferrocenyl)

Expt. No.	Arene	AlCl₃ equiv.	'Recovery' %	FcAr %	FcAr₂ %	[XC₅H₄FeC₆H₆]PF₆ %
1	C₆H₆	2	11[b]	38	9	20; X = H
2	C₆H₆	2[a]	41[c]	17	4	20; X = Cl
3	C₆H₆	3	8[b]	28	17	d
4	C₆H₆[e]	3	46[f]	13	1	d
5	C₆H₆[g]	3[a]	16[c]	<1	0	60—70; X = Cl
6	1,3,5-C₆H₃Me₃	2	6[b]	20	4[h]	d
7	C₆H₅Pr[i]	2[a]	20[c]	16[h]	4[h]	d
8	C₆H₅OMe	2	90[j]	0	0	d
9	C₆H₅Cl	2	16[b]	18[k]	4	d
10	C₆H₆	2	19[b]	38	3	d
11	C₆H₅Me	2	16[b]	42[l]	3	d

[a] Without aluminium metal; [b] As ferrocene. [c] Ratio : dichloroferrocene 60—50%, chloroferrocene 30—40%, ferrocene 3—5%. [d] Not examined; [e] Diluted with heptane (100 ml). [f] Approx. ratio : dichloroferrocene 75%, chloroferrocene 5%, ferrocene, 20%. [g] Water (2 mmol) was also added. [h] Not isolated pure. [j] Almost pure dichloroferrocene. [k] Approx. ratio of o:p 2:3. [l] Approx. ratio of o:p 1:1.

consistent if chloroferrocene is more reactive than the dichloro compound in both the Friedel-Crafts and the ring replacement reactions as well as in reductive dechlorination (see Table 2). 1'-Chloro-1-phenylferrocene was never found although it must be intermediate in the formation of the diphenyl derivative. Perhaps its reductive dechlorination is even easier than that of the chloroferrocenes; in the presence of an increased excess of aluminium chloride however, its faster reaction with benzene leads to an increased proportion of diphenylferrocene in the product as shown by comparison of experiments 1 and 3 (Table 1). The reactions conducted with aluminium metal yield 'recovered' material in which ferrocene is the major component along with the chloroferrocenes. The recovery of much dichloroferrocene in reaction 4 is attributable to the low solubility of aluminium chloride in heptane.

The formation of diaryl ferrocenes even from monochloroferrocene must be accounted for by the disproportionation of the initially formed arylferrocene. Bublitz showed[10] that alkylferrocenes react with aluminium chloride by disproportionation involving redistribution of the cyclopentadienyl groups. Astruc and Dabard,[11] while studying the conversion of benzylferrocene into the salt (4) with aluminium and aluminium chloride, noted the formation of appreciable amounts of ferrocene and dibenzylferrocene; a footnote (p. 284) in their paper implies that disproportionation was similarly observed, but not quantified, in other cases including phenylferrocene. This is confirmed by our results as summarised in Table 2. They show that the extent of disproportionation of phenylferrocene under our reaction conditions is sufficient to account for the yield of diphenylferrocene from chloroferrocene (Table 1, experiment 10). The apparent lack of synproportionation of the mixture of ferrocene and diphenylferrocene is consistent with the wide variation in the ease of such dis- and synproportionation reactions observed by Bublitz.[10] The results also show that the disproportionation does not occur to any marked extent at the chloroferrocene stage. This compound only yielded 1% of dichloroferrocene and the fairly extensive formation of ferrocene must occur by the facile reductive dechlorination noted above. With the mixture of ferrocene and dichloroferrocene, this occurred only after hydrogen chloride was also added, but still accounts better than synproportionation for the observed product ratio.

Experimental

1,1-Dichloroferrocene was obtained in 70—80% yield by treating 1,1'-dilithioferrocene with hexachloroethane;[12] after

Table 2. Disproportionation reactions 2FcX ⇌ FcX₂ + FcH

X	Initial weight ratio (%)			Ratio after 5 h reactions (%)		
	FcH	FcX	FcX₂	FcH	FcX	FcX₂
Cl	42	0	58[a]	42	0	58
Cl[b]	42	0	58	52	5	43
Cl	0	100	0	40	59	1
C₆H₅	35	0	65[a]	35	0	65
C₆H₅	0	100	0	5	86	9

[a] Equimolar. [b] Dry HCl was passed through the mixture continuously.

column chromatography[12] the product contained ferrocene (up to 15%) and a smaller amount of chloroferrocene. The former was conveniently removed by dissolving the mixture (10 g) in dichloromethane (200 ml) and adding excess (ca. 2 mol equiv. based on the amount of ferrocene) of anhydrous iron(III) chloride. After stirring for 1.5 h under nitrogen, water was added and the organic layer was separated, dried (MgSO₄), and evaporated. The residue was recrystallised twice from light petroleum (b.p. 40—60 °C) to give 1,1'-dichloroferrocene, m.p. 78—80 °C (lit.,[12] 79—81 °C) which is of >98% purity according to v.p.c. Chloroferrocene was prepared from chloromercuriferrocene with copper(II) chloride[13] and was recrystallised from methanol. Analytical v.p.c. was performed on Apiezon L on a 200 cm column at 140—160 °C for chloroferrocenes [approx. retention times: C₁₀H₁₀Fe, 4—5 min, C₁₀H₉ClFe 8—10 min, and (C₅H₄Cl)₂Fe 16—20 min] or at 220 °C for separation of substituted phenylferrocene isomers using nitrogen as a carrier gas.

Aromatic hydrocarbons were distilled from sodium hydride under nitrogen, directly into the reaction flask. Heptane refers to the light petroleum fraction distilling at 90—95 °C after washing successively with concentrated sulphuric acid, water and sodium hydrogen carbonate solution, drying (CaCl₂), and distillation from sodium hydride under nitrogen. Sublimed aluminium chloride was powdered under nitrogen prior to use.

General Procedure[3,4,7] *for Reactions of Arenes with Chloroferrocenes.*—1,1'-Dichloroferrocene (510 mg, 2 mmol), aluminium chloride (0.53 or 0.8 g, 4 or 6 mmol calculated as AlCl₃) and aluminium powder (54 mg, 2 mg-atom if used) in the arene (10 ml) were heated to 100 °C (bath temperature) and stirred under nitrogen for 5 h, after which the mixture was cooled and added with stirring to ice-cold water (20 ml). When aluminium

Table 3. Melting points and ^{1}H n.m.r. spectra for compounds $C_5H_5FeC_5H_4C_6H_4X$

X	M.P. °C This work	M.P. °C Lit.	δ (p.p.m.)[a] C_5H_5 s	3,4-C_5H_4 t	2,5-C_5H_4 t	C_6H_4 m	CH_3 s
H	111—12	110—11 [14]	4.02	4.29	4.62	7.15—7.55	
1,3,5-Me$_3$[b]	127—29		4.17	4.35	4.35	6.90[a]	2.58 o
							2.28 p
o-Me	50—52	51—52 [15]	4.12	4.27	4.45	7.05—7.25	2.38
						7.60—7.80	
p-Me	136—38	140—42 [16]	4.02	4.27	4.59	6.90—7.45	2.31
o-Cl		55—56 [16]	4.12	4.31	4.73	7.00—7.30	
						7.55—7.75	
p-Cl	117—19	122 [14]	4.02	4.30	4.59	7.10—7.50	

[a] 90 MHz, CDCl$_3$, TMS. [b] Found: C, 74.3, 74.8; H, 6.6, 6.8; $C_{19}H_{20}Fe$ requires C, 75.0; H, 6.6%.

metal was not used, sufficient sodium thiosulphate solution was added at this stage to discharge the blue-green colour due to ferrocenium salts. The layers were then separated, the aqueous layer was washed thoroughly with ether and the combined organic layers washed with water. Addition of excess of saturated aqueous ammonium hexafluorophosphate precipitated the salts (1; R = H or Cl; X = PF_6). These were collected, dried, and purified, either by reprecipitation from acetone solution by addition of ether, or by column chromatography on neutral alumina using acetone–dichloromethane (1:1) as solvent. Further purification was achieved by crystallisation from methanol. The organic solution was dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed on alumina using light petroleum (b.p. 30—40 °C)–dichloromethane (9:1) as eluant. In general this separated three coloured bands: the first contained ferrocene and chloroferrocenes, the second arylferrocene, and the third diarylferrocene. These fractions were further purified by rechromatography on 'flash' silica and crystallisation from methanol or light petroleum.

The two experiments (numbers 10 and 11 of Table 1) with chloroferrocene (440 mg, 2 mmol) were performed in the same manner. The results are summarised in Table 1 and properties of the products in Table 3.

Disproportionation Reactions.—Mixtures of aluminium chloride (2 mol equiv.) and of monosubstituted ferrocenes or of ferrocene plus disubstituted ferrocene (in equimolar proportions) were heated as above, but in heptane instead of an arene. In the cases of the chloroferrocenes an 0.5 molar scale was used and after complete reaction the washed and dried heptane solutions were examined by v.p.c. only. Pure samples were used to determine the retention times of all the ferrocene derivatives. In the case of the phenyl- and diphenyl-ferrocene experiments a 2 mmol scale was used and product identification was confirmed by isolation.

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