Ionic Hydrogenation of Acylferrocenes Using Zinc Borohydride: An Efficient, Mild Method for the Preparation of Alkylferrocenes

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Summary: An effective mild procedure for the reductive deoxygenation of α-ferrocenyl aldehydes, ketones, and alcohols into the corresponding alkylferrocenes is described using a combination of zinc borohydride and zinc chloride. This is the first example of such reactivity of zinc borohydride. The present method allows the synthesis of alkylferrocenes bearing terminally functionalized pendant chains.

In recent years ferrocene derivatives have emerged as the most versatile reagent for materials and catalysts[1] because of their unique optical, thermal, and redox properties. The design and synthesis of ferrocene derivatives possessing terminally functionalized alkane chains are of particular interest in view of their potential utilizations[2] as electrode surface modifiers, in the constructions of dendrimers, in molecular recognition, and in multielectron redox catalysis, among other applications.

The Friedel−Crafts alkylation[3] of ferrocene, which is, in principle, the most direct route for the preparation of alkylferrocenes, however, proceeds in poor yields and invariably produces intractable mixtures of mono- and polyalkylated derivatives. In contrast, the Friedel−Crafts acylation reactions[4] of ferrocene afford excellent yields of mono- and diacylated ferrocenes with a remarkable degree of regioselectivity. Accordingly, the transformation of acylferrocenes into the corresponding alkylferrocenes constitutes the most frequently encountered reaction[5] in the preparation of both simple alkylferrocenes and those bearing terminally functionalized pendant alkane chains. The prominent protocols for this transformation include catalytic hydrogenolysis,[6] Clemensen reduction,[7] and reductive deoxygenation employing lithium aluminum hydride[8] in the presence of anhydrous aluminum chloride. However, the presence of other functionalities is limited under these reaction conditions.

As part of our efforts in the development of mild borohydride-based reagent systems[9] for selective transformations, we have recently utilized[10] a combination of zinc chloride and zinc borohydride in the reductive methylation of amines. In a continuing study, this paper reports on the results for the novel application of this reagent system in the ionic hydrogenation of acylferrocenes at room temperature, an effective mild method for the preparation of alkylferrocenes (Scheme 1). The use of zinc borohydride, prepared from sodium borohydride and zinc chloride, as a uniquely mild reducing agent has been amply demonstrated in the literature.[11]

Stirring a mixture of acetylferrocene, 2 mol equiv of zinc chloride, and 2 mol equiv of zinc borohydride in anhydrous THF at room temperature for 8 h provided ethylferrocene in 92% yield after quenching of the reaction with aqueous ammonia, extraction with diethyl ether, and concentration. The reaction proceeds under mild conditions, the procedure is easy to perform, and no special handling technique is needed. The method is general for a variety of α-ferrocenyl aldehydes, ketones, and alcohols. All reactions were carried out

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Scheme 1

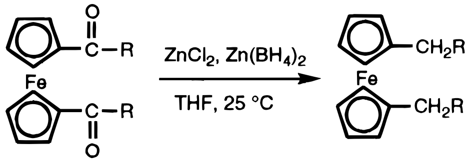
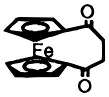
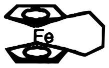
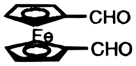
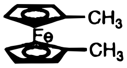
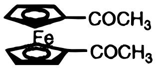
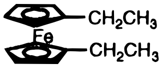
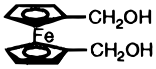
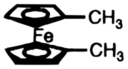


Table 1. Ionic Hydrogenation of Acylferrocenes and α-Ferrocenyl Alcohols Using Zinc Borohydride and Zinc Chloride

Entry	Substrate [a] (Fer = Ferrocenyl)	Time(h)	Product[b]	Yield(%)[c]
1	FerCHO	8	$FerCH_3$	92
2	$FerCOCH_3$	8	$FerCH_2CH_3$	90
3	$FerCOC_6H_5$	8	$FerCH_2C_6H_5$	88
4	$FerCOCH(CH_3)_2$	9	$FerCH_2CH(CH_3)_2$	90
5	$FerCO(CH_2)_2CO_2Me$	9	$Fer(CH_2)_3CO_2Me$	90
6	$FerCO(CH_2)_2CO_2H$	9	$Fer(CH_2)_3CO_2H$	92
7		10		88
8		10		88
9		10		90
10	$FerCH_2OH$	8	$FerCH_3$	90
11		8		92

[a] The ratios starting compound:zinc chloride:zinc borohydride are as follows: entries 1–6, 1:2:2; entries 7–9, 1:4:4; entry 10, 1:1:1; entry 11, 1:2:2. [b] Spectroscopic and physical constant data for all compounds were in complete agreement with the literature data. [c] Yields are of isolated and purified products.

at room temperature, and THF was the solvent of choice. The molar ratio of the reactants and the results obtained for a representative group of compounds are shown in Table 1. It seems likely that the reaction proceeds through the formation of the corresponding α-ferrocenyl alcohol as the intermediate, which is then reduced via the facile formation of a remarkably stable α-ferrocenylalkyl carbocation[12] in the presence of zinc chloride. The conversion of the α-ferrocenyl alcohols (entries 10 and 11) into the corresponding alkylferrocenes following the same procedure further corroborates the intermediacy of α-ferrocenyl alcohols in these reactions. As shown in Table 1, the method is equally efficient for the deoxygenation of diacylated ferrocenes (entries 7–9). The bridged ferrocenyl diketone[13] (entry 7) can be converted into the corresponding ferrocenophane in high yield. Unlike the existing procedures, the mild reaction conditions employed in this method allow syntheses of alkylferrocenes bearing terminally functionalized pendant chains; e.g., ((3-carbomethoxy)propyl)ferrocene (entry 5) and (3-carboxypropyl)ferrocene (entry 6) are obtained in high yields from the corresponding acylferrocenes. It is noteworthy that attempts[14] to perform Wolff–Kishner or Clemmensen reductions on similar acylferrocenes were unsuccessful.

Because of the neutral reaction conditions, easy workup, high yields of pure products, and compatibility[10,11] of zinc borohydride with a variety of normally reducible functional groups, this procedure promises to be the method of choice for the preparation of alkylferrocenes, particularly for those containing functionalized alkane chains.

In conclusion, alkylferrocenes are prepared in high yields by ionic hydrogenation of ferrocenyl aldehydes, ketones, and alcohols using zinc chloride and zinc borohydride. Further utilization of this reagent system in reductive deoxygenation of other types of ketones is currently being explored.

Experimental Section

The commercially available starting ferrocenes (entries 1–3 and 9–11)) were used as received from their respective suppliers. The bridged diketone (entry 7) was prepared from commercially available 1,1′-diacetylferrocene by following a known procedure.[13] The remaining substrates were prepared[4] by Friedel–Crafts acylation of ferrocene. THF was freshly distilled from LAH before use. A stock solution of zinc borohydride in dry THF prepared from sodium borohydride and zinc chloride according to the reported[11a] procedure can be stored in a sealed container at 0–5 °C for 3–4 weeks.

General Procedure for the Preparation of Alkylferrocenes from Acylferrocenes. To a magnetically stirred mixture of the acylferrocene (5 mmol) and zinc chloride (10 mmol) in anhydrous THF (15 mL) was added a solution of zinc borohydride (10 mmol) in THF dropwise over 15 min. The contents were further stirred at room temperature for 8–10 h. The reaction mixture was then diluted with diethyl ether (50 mL) and quenched with aqueous ammonia (30 mL, 2 N). The organic layer was separated, and the aqueous part was extracted with diethyl ether (2 × 20 mL). Drying of the combined organic extracts over Na_2SO_4, solvent removal, and flash chromatography of the residue over silica gel using hexanes-diethyl ether (9:1) as the eluent afforded the pure alkylferrocenes.

In the case of diacylated ferrocenes the same general procedure was followed, except that double the amounts of zinc chloride and zinc borohydride were used.

Supporting Information Available: Figures giving ^1H NMR spectra of all the products (9 pages). Ordering information is given on any current masthead page.

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