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Titanium(IV) Chloride−Triethylsilane: An Efficient, Mild System for the Reduction of Acylferrocenes to Alkylferrocenes

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In recent years, ferrocene derivatives have been identified as strong candidates for materials and catalysts[1,2] because of their unique optical, thermal, and redox behavior. Ferrocenes are a peerless class of one-electron donors with well-established voltammetric signatures and have been extensively used[2] as redox markers in the studies of self-assembled monolayers on modified electrode surfaces. In this respect, the mixed-ligand FeCpCp′ compounds are particularly valuable because they display a tunable ferrocene−ferricenium oxidation potential[3] with the variation of substituents on the Cp rings, thereby offering a unique possibility to influence their applications. The design and synthesis of alkyl derivatives of ferrocene with reagent-sensitive chromophores are of more current interest.

Alkylferrocenes are generally obtained by a two-step protocol[4] involving the Friedel−Crafts acylation of ferrocene followed by reduction of the acylated ferrocene. This is mainly due to the following factors: (i) the Friedel−Crafts acylation reactions[4] of ferrocene proceed with a high degree of regioselectivity to afford mono- and 1,1′-diacylated ferrocenes in good yields, and (ii) the Friedel−Crafts alkylations[4] of ferrocene produce intractable mixtures of mono- and polyalkylated derivatives in low yields. As a consequence, a number of methods have been developed for carrying out reductive deoxygenation of acylated ferrocenes. However, the presence of additional functionality in the molecule is severely limited under these reported[4,5] reaction conditions.

As a part of our efforts in the development of mild borohydride-based reagent systems[6] for selective transformations, we have recently described[7] a combination of titanium(IV) chloride and sodium cyanoborohydride for the reductive deoxygenation of acylated ferrocenes. However, sodium cyanoborohydride is a highly toxic[8] and expensive reagent that raises the risk of cyanide contamination[9] in the product as well as in the waste stream. In an attempt to develop an alternative, benign, and mild method, we now report a novel procedure for the ionic hydrogenation of α-ferrocenyl aldehydes, ketones, and alcohols using a composite of triethylsilane and titanium(IV) chloride in dichloromethane. Notable advantages of the present method include (i) the simplicity of the procedure requiring no special equipment, (ii) the ability to perform the reactions in nonprotic solvents at room temperature, (iii) the compatibility of the reagent system with a variety of otherwise reducible functional groups, (iv) the use of safe and inexpensive reagents, and (v) high yields of pure products. The use of triethylsilane as a reducing agent in strong acidic media has been amply demonstrated in the literature.[10]

The scope of the method proved to be quite general for a variety of α-ferrocenyl aldehydes, ketones, and alcohols. The molar ratios of the reactants and the experimental results are summarized in Tables 1, 2, and 3. It seems likely that the reactions with acylated ferrocenes proceed in two steps. They are first reduced to the corresponding α-ferrocenyl alcohols, which are then further reduced to the alkylferrocenes via the formation of a remarkably stable α-ferrocenylalkyl carbocation[11] in the presence of titanium(IV) chloride. In a typical procedure, a mixture

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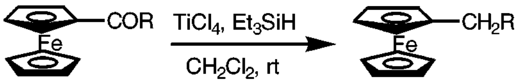
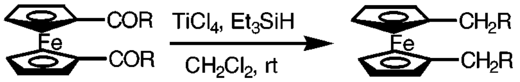
Table 1. Preparation of 1-Alkylferrocence



entry[a]	R	yield (%)
1	H	88
2	Me	88
3	^{i}Pr	85
4	Ph	92
5	CH_2CH_2COOH	84
6	CH_2CH_2COOMe	82
7	$(CH_2)_4Cl$	84
8	$(CH_2)_7Br$	80

[a] The ratio of acylferrocene:Et_3SiH:$TiCl_4$ is 1:4:1.

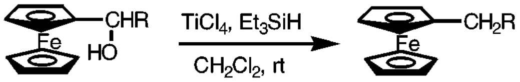
Table 2. Preparation of 1,1′-Dialkylferrocene



entry[a]	R	yield (%)
1	H	85
2	Me	82
3	Ph	90
4	CH_2CH_2COOMe	80
5	$(CH_2)_4Cl$	82
6	$(CH_2)_7Br$	82
7	$(CH_2)_{10}Br$	84
8	$-CH_2CH_2-$	80

[a] The ratio of diacylferrocene:Et_3SiH:$TiCl_4$ is 1:8:2.

Table 3. Reduction of 1-Ferrocenylcarbinols



entry[a]	R	yield (%)
1	H	90
2	Me	93
3	^{i}Pr	89
4	Ph	92

[a] The ratio of ferrocenylcarbinol:Et_3SiH:$TiCl_4$ is 1:2:1.

of benzoylferrocene, titanium(IV) chloride (1 molar equiv), and triethylsilane (4 molar equiv) in anhydrous dichloromethane was stirred at room temperature for 8 h. The reaction was then quenched with aqueous sodium carbonate, and the organic layer was separated and concentrated after drying. Flash chromatography of the residue over silica gel using hexanes as the eluent afforded benzylferrocene in almost quantitative yield. As shown in Table 2, the method is equally efficient for the deoxygenation of diacylated ferrocenes. The same general procedure was followed with the exception that double the amounts of titanium(IV) chloride and triethylsilane were used. The bridged ferrocenyl diketone[12] (Table 2, entry 8) can be converted into the corresponding ferrocenophane in high yield. The α-ferrocenyl carbinols (Table 3) afforded the corresponding alkylferrocenes in high yields. The method is particularly suitable for the synthesis of alkylferrocenes bearing otherwise reducible chromophores such as carboxy, carbalkoxy, bromo, and chloro analogs (Table 1, entries 5−8 and Table 2, entries 4−7).

In conclusion, alkylferrocenes are prepared in high yields by the reduction of α-ferrocenyl aldehydes, ketones, and alcohols using titanium(IV) chloride and triethylsilane. The present method allows the preparation of alkylferrocenes with reagent-sensitive motifs and is adaptable to multigram preparations. Further utilization of this method in the preparation of other metallocenes is currently being explored.

Experimental Section

The commercially available starting ferrocenes (Table 1, entries 1, 2, and 4; Table 2, entry, 2; and Table 3, entry 1) and triethylsilane were used as received from their respective suppliers. The bridged diketone (Table 2, entry 8) was prepared from commercially available 1,1′-diacetylferrocene following a known procedure.[12] The remaining substrates mentioned in Tables 1 and 2 were prepared[4] by Friedel−Crafts acylation of ferrocene. α-Ferrocenyl alcohols (Table 3, entries 2−4) were obtained by $NaBH_4$ reduction of the corresponding acylated ferrocenes in ethanol. Dichloromethane was freshly distilled from CaH_2 before use. Proton NMR spectra were recorded at 300 MHz on a Bruker AM 300 spectrometer in $CDCl_3$ solutions with $SiMe_4$ as an internal standard. Yields reported in Tables 1, 2, and 3 are of isolated and purified products. All products were characterized by their ^1H NMR and IR spectra and comparison with the literature data.

General Procedure for the Preparation of Alkylferrocenes. To a magnetically stirred solution of the acylated ferrocene (5 mmol) in dry dichloromethane (30 mL) was added dropwise a solution of titanium(IV) chloride (0.60 mL, 5 mmol) in dry dichloromethane (10 mL) under an atmosphere of nitrogen. Triethylsilane (3.30 mL, 20 mmol) was then added to the reaction mixture, and the contents were further stirred at room temperature for 8−10 h. The reaction mixture was then quenched with aqueous sodium carbonate (20 mL, 5% w/v), and the resulting inorganic precipitate was filtered. The organic layer was separated and dried over Na_2SO_4, and the solvent was removed. 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, with the exception that double the amounts of titanium(IV) chloride and triethylsilane were used.

Supporting Information Available: ^1H NMR spectra of some of the alkylferrocenes prepared (15 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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