Reductive Deoxygenation of α-Ferrocenyl Carbonyls and Alcohols to Alkylferrocenes by Borane−Dimethyl Sulfide

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Summary: The reductive deoxygenation of α-ferrocenyl aldehydes, ketones, alcohols, and carboxylic acid into the corresponding alkylferrocenes is accomplished solely by borane−dimethyl sulfide (BMS) in the absence of any Lewis acid catalyst. This is the first example of such reactivity of BMS. The present method allows the synthesis of alkylferrocenes including those bearing terminally functionalized pendant chains.

Introduction

Reductive deoxygenation of aldehyde, ketone, carboxylic acid, or alcohol leading to the formation of corresponding alkane is a useful synthetic route and can be achieved in various ways.[1−3] A wide variety of substrates with aliphatic or aromatic functionalities are susceptible to such transformation. Bhattacharyya has further demonstrated in a series of papers that α-ferrocenyl ketones, alcohols, and aldehydes undergo readily reductive deoxygenation using the hydride/Lewis acid system such as $Et_3SiH/TiCl_4$, $Zn(BH_4)_2/ZnCl_2$, and $NaBH_4/CF_3COOH$.[4] These findings are of particular interest in that terminally functionalized alkylferrocenes draw special attention owing to their potential utilities in materials science.[5] Although the Friedel−Crafts alkylation can, in principle, provide the most direct route to the synthesis of alkylferrocenes, this reaction is known to proceed in poor yields and invariably produces intractable mixtures of mono- and polyalkylated derivatives.[6] In contrast, however, the Friedel−Crafts acylation of ferrocenes affords 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 reactions in the preparation of alkylferrocenes.[7]

In our continuing effort on the design and synthesis of new ferrocene-based chiral ligands for use in asymmetric catalysis,[8] we have discovered serentipitously that direct reductive deoxygenation rather than hydrogenolysis takes place to give alkylferrocenes from the reactions of α-ferrocenyl aldehydes, ketones, alcohols, or carboxylic acid with borane−dimethyl sulfide (BMS) in the absence of any Lewis acid catalyst. We now put a new entry into a mild, efficient system for the reductive deoxygenation.

Results and Discussion

Stirring a 1:1 (or 1:2 for 1,1′-disubstituted ferrocenes and a diketone) mixture of BMS and α-ferrocenyl aldehyde, ketone, alcohol, or carboxylic acid in CH_2Cl_2 (or THF) at room temperature provides the corresponding alkylferrocene in a nearly quantitative yield. Table 1 shows that most reactions go to completion within a few hours under very mild conditions and that the reaction is general for a variety of α-ferrocenyl derivatives.

The conversion rate seems to decrease with increasing steric hindrance from the carbonyl α-chain, thus revealing the following order: aldehyde, primary alcohol (entries 1, 2, and 7) > acetylferrocene, secondary alcohol, carboxylic acid, benzoylferrocene (entries 3, 4, 8, 9, 10,

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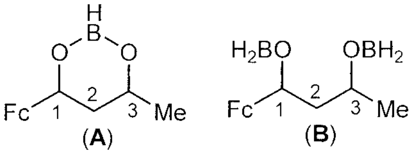
Table 1. Reductive Deoxygenation of α-Ferrocenyl Derivatives by BH$_3$·SMe$_2$

entry	substrate[a]	time (h)	product[b]	yield (%)[c]
1	Fc−CHO	3	Fc−CH$_3$	95
2	1,1′-Fc(CHO)$_2$	3	1,1′-Fc(CH$_3$)$_2$	95
3	Fc−COCH$_3$	3.5	Fc−CH$_2$CH$_3$	95
4	Fc−COPh	6	Fc−CH$_2$Ph	93
5	Fc−COCH$_2$Cl	30	Fc−(CH$_2$)$_2$Cl	92
6	Fc−COCH$_2$COCH$_3$	30	Fc(CH$_2$)$_2$CH(OH)CH$_3$	31
			Fc(CH$_2$)$_3$CH$_3$	20
			FcCH(OH)(CH$_2$)$_2$CH$_3$	17
7	1,1′-Fc(CH$_2$OH)$_2$	3	1,1′-Fc(CH$_3$)$_2$	95
8	Fc−CH(OH)CH$_3$	3.5	Fc−CH$_2$CH$_3$	95
9	Fc−CH(OH)CH$_2$Cl	8	Fc−CH$_2$CH$_2$Cl	92
10	Fc−CH(OH)CH$_2$OH	3.5	Fc−CH$_2$CH$_2$OH	95
11	1,1′-Fc(COOH)$_2$	6	1,1′-Fc(CH$_3$)$_2$	83

[a] Fc = ferrocenyl. [b] Spectroscopic and analytical data for all products were in complete agreement with the literature (or expected) values (see the Experimental Section). [c] Yields are isolated ones.

Chart 1



and 11) > α-substituted acetylferrocene (entries 5 and 6). There seems to be, however, little difference in the total reaction time between mono- and disubstitution (compare entries 1 and 2, for instance).

It seems likely that the reactions of ferrocenyl carbonyls proceed through the formation of corresponding α-ferrocenyl alcohols, which are in turn reduced further to alkylferrocenes via the facile formation of a remarkably stable α-ferrocenylalkyl carbocation. It is now well-established that the extraordinary stability of the α-ferrocenylalkyl carbocation stems from direct participation of the iron atom in charge delocaliztion.[9]

The reaction of a diketone (entry 6) is intriguing. The TLC analysis of the reaction mixture 30 min after mixing shows a complex pattern, which changes over time (∼30 h) to give eventually only three spots. These are identified, after usual workup including column chromatography, to be 3-hydroxybutylferrocene (31%), butylferrocene (20%), and 1-hydroxybutylferrocene (17%). Although the formation of 3-hydroxybutylferrocene may be as expected on the basis of the results obtained with 1,2-dihydroxyethylferrocene (entry 10), the formation of butylferrocene and 4-hydroxybutylferrocene is rather unusual and inconsistent with other results listed in the table. Unusual observations with the latter two products are that even the aliphatic ketone would undergo complete reduction under the present conditions so as to give the deoxygenated alkyl ferrocenes.

Although an unambiguous mechanism in accord with these observations is hard to imagine at the present moment, a ferrocenyl borate of the type **A** or **B** in Chart 1 may be suggested as an initial intermediate that slowly undergoes further transformations involving carbon 1 and/or carbon 3.

In conclusion, unlike the exisiting systems, the present method requires no additional agents (or catalysts) but BMS, and in this respect can be an excellent substitute for the exisitng procedures for the reductive deoxygenation of α-ferrocenyl aldehydes, ketones, alcohols, and carboxylic acids into corresponding alkylferrocenes. Work is under way to investigate the scope of this reaction to other organometallics capable of generating a stable carbocation.

Experimental Section

General Data. All manipulations were carried out under an argon atmosphere using Schlenk techniques. Solvents were freshly distilled from sodium/benzophenone prior to use. Ferrocene, ferrocenecarboxaldehyde, ferrocene-1,1′-dicarboxylic acid, and borane−dimethyl sulfide (1 M in CH$_2$Cl$_2$) were purchased from Aldrich. Acetylferrocene,[7] ferrocene-1,1′-dicarboxaldehyde,[10] chloroacetylferrocene,[11] benzoylferrocene (entry 5),[12] 1-ferrocenyl-1,3-butadione (entry 6),[13] and 1-[(1,2-dihydroxy)ethyl]ferrocene (entry 10)[14] were prepared according to the literature methods. 1,1′-Bis(hydroxymethyl)ferrocene, 1-(2-hydroxyethyl)ferrocene, and 1-(2-chloro-1-hydroxyethyl)-ferrocene were obtained by NaBH$_4$ reduction of ferrocene-1,1′-dicarboxaldehyde, acetylferrocene, and chloroacetylferrocene, respectively.

General Procedure for the Reaction. To a solution of acetylferrocene (0.18 g, 0.78 mmol) in CH$_2$Cl$_2$ (3 mL) in a Schlenk tube was added a solution of BMS (0.78 mL, 0.78 mmol) in CH$_2$Cl$_2$. The reaction mixture was stirred at room temperature for 3−30 h, after which time the mixture was quenched with aqueous NH$_4$Cl (20 mL). The organic layer was separated, and the aqueous layer was extracted with CH$_2$Cl$_2$ (15 mL). The combined organic extracts were dried over anhydrous MgSO$_4$, and the solvent was removed under reduced pressure. The residue was chromatographed on silica gel (eluent: hexane/diethyl ether, 9:1) to afford the pure ethylferrocene (0.16 g, 95%).

In the case of 1,1′-disubstituted ferrocenes and 1-ferrocenylbutane-1,3-dione (entry 6), the same general procedure was followed except that the amount of BMS was doubled.

Methylferrocene. Yellow crystals; ^{1}H NMR (400 MHz, CDCl$_3$): δ 1.91 (s, 3H, CH$_3$), 3.95 (s) and 4.00 (s) (4H, C$_5$H$_4$), 4.02 (s, 5H, C$_5$H$_5$). Anal. Calcd for C$_{11}$H$_{12}$: C, 66.04; H, 6.05. Found: C, 66.28; H, 6.15.

1,1′-Dimethylferrocene. Red crystals; ^{1}H NMR (400 MHz, CDCl$_3$): δ 1.94 (s, 6H, CH$_3$), 4.02 (s, 8H, C$_5$H$_4$). Anal. Calcd for C$_{12}$H$_{14}$: C, 67.32; H, 6.59. Found: C, 66.76; H, 6.59.

Ethylferrocene. Orange oil; ^{1}H NMR (400 MHz, CDCl$_3$): δ 1.17 (t, J = 7.5 Hz, 3H, CH$_3$), 2.33 (q, J = 7.5 Hz, 2H, CH$_2$), 4.04 (s) and 4.06 (s) (4H, C$_5$H$_4$), 4.10 (s, 5H, C$_5$H$_5$). EIMS m/z (rel. intensity): 214 (M$^+$, 100).

2-Chloroethylferrocene. Orange crystals; ^{1}H NMR (400 MHz, CDCl$_3$): δ 2.75 (t, J = 7.0 Hz, 2H, FcCH$_2$), 3.58 (t, J = 7.0 Hz, 2H, CH$_2$Cl), 4.19 (s, 9H, C$_5$H$_5$FeC$_5$H$_4$). Anal. Calcd for C$_{12}$H$_{13}$Cl: C, 57.99; H, 5.27. Found: C, 57.76; H, 5.35.

Benzylferrocene. Yellow crystals; ^{1}H NMR (400 MHz, CDCl$_3$): δ 3.62 (s, 2H, CH$_2$), 4.01(s) and 4.04 (s) (9H, C$_5$H$_5$-FeC$_5$H$_4$), 7.10−7.19 (m, 5H, C$_6$H$_5$). Anal. Calcd for C$_{17}$H$_{16}$: C, 73.94; H, 5.84. Found: C, 74.44; H, 5.99.

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2-Hydroxyethylferrocene. Red oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.61 (t, $J = 6.3$ Hz, 1H, OH), 2.59 (t, $J = 6.4$ Hz, 2H, Fc-CH_2), 3.72 (m, 2H, CH_2OH). Anal. Calcd for $C_{12}H_{14}O$: C, 62.64; H, 6.13. Found: C, 62.73; H, 6.32. EIMS *m*/*z* (rel. intensity): 230 (M^+, 100).

3-Hydroxybutylferrocene. Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.21 (d, $J = 6.1$ Hz, 3H, CH_3), 1.37 (s, 1H, OH), 1.62−1.69 (m, 2H, CH_2), 2.32−2.47 (m, 2H, $FcCH_2$), 3.82 (m, 1H, CH), 4.08 and 4.16 (AB, 4H, C_5H_4), 4.13 (s, 5H, C_5H_5). HRMS (EI, *m*/*z*): Calcd for $C_{14}H_{18}FeO$: 258.0707 (M^+). Found: 258.0712.

Butylferrocene. Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.91 (t, $J = 7.2$ Hz, 3H, CH_3), 1.31−1.39 (m, 2H, CH_2Me), 1.44−1.51 (m, 2H, CCH_2C), 2.29 (t, $J = 7.7$ Hz, 2H, $FcCH_2$), 4.08 and 4.10 (AB, 4H, C_5H_4), 4.13 (s, 5H, C_5H_5). HRMS (EI, *m*/*z*): Calcd for $C_{14}H_{18}Fe$: 242.0758 (M^+). Found: 242.0757.

1-Hydroxybutylferrocene. Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.95 (t, $J = 7.2$ Hz, 3H, CH_3), 1.43−1.50 (m, 2H, CH_2Me), 1.81 (s, 1H, OH), 2.37−2.58 (m, 2H, CCH_2C), 3.52 (m, 1H, CH), 4.05 and 4.13 (AB, 4H, C_5H_4), 4.13 (s, 5H, C_5H_5). HRMS (EI, *m*/*z*): Calcd for $C_{14}H_{18}FeO$: 258.0707 (M^+). Found: 258.0708.

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