A Novel Method to Synthesize Unsymmetrical Disubstituted Ferrocenes

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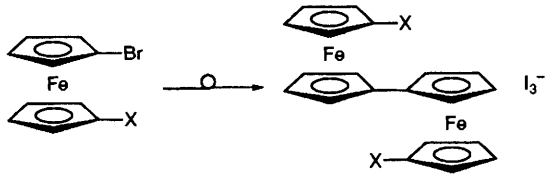
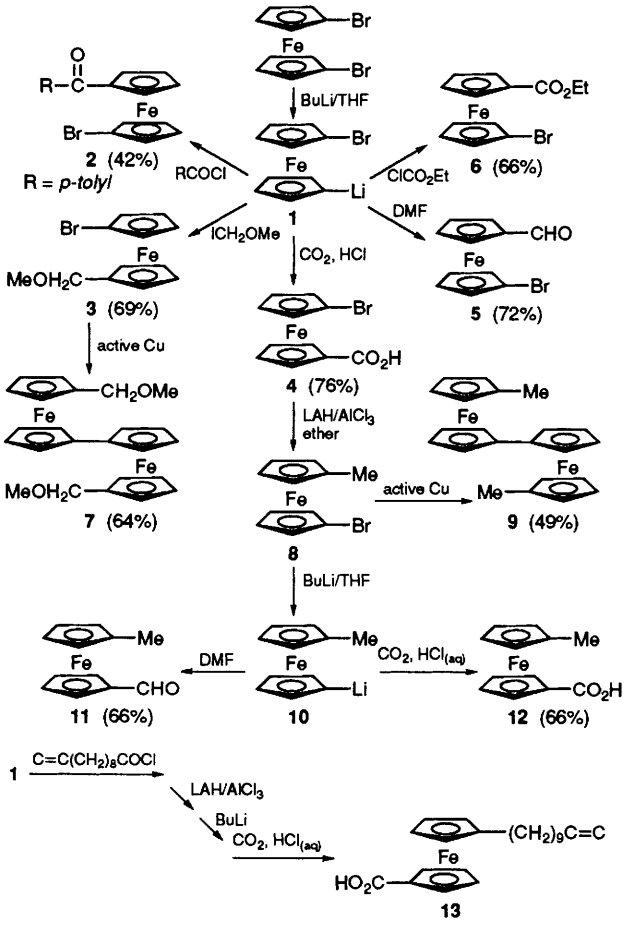
A convenient new method for the preparation of 1′-substituted-1-bromoferrocenes and 1′,1‴-disubstituted-biferrocenes has been developed, which can also be applied to the preparation of unsymmetrical disubstituted ferrocenes, which are potentially useful materials possessing nonlinear optical and liquid crystalline properties.

In continuation of our studies on the electron-transfer rate in mixed-valence biferrocenium salts, the key step in the reaction sequence involved the preparation of 1′-substituted-1-bromoferrocene. However, owing to the methodological limitation in the preparation of 1′-substituted-1-bromoferrocene, *i.e.* acylation of bromoferrocene in the presence of $AlCl_3$ followed by reduction, none of biferrocenium triiodide salts containing heteroatoms have been prepared.[1–7] This, to some extent, limits its generality on understanding the fundamental nature of electron-transfer rate in mixed-valence biferrocenium compounds. Our interest in 1′-substituted-1-bromoferrocene is connected with our studies of mixed-valence biferrocenium salts. Therefore, we have examined the use of the readily accessible 1,1′-dibromoferrocene as a potential precursor for these substances. The purpose of the present communication is to set forth a general procedure to accomplish this aim and to provide an attractive alternative method for the preparation of unsymmetrically disubstituted nonlinear optical and liquid crystalline ferrocene molecules (Scheme 1).



Scheme 1



Lithioferrocene can be obtained by the reaction of ferrocene with butyllithium.[8,9] However, the preparation often has disadvantages, in that mixtures of mono- and di-metalloferrocenes are formed and excess metal alkyl is required. We find that the monolithioferrocene can be prepared easily and conveniently by adding stoichiometric amounts of *n*-butyllithium to a THF solution of 1,1′-dibromoferrocene.† Crude monolithoferrocene obtained in this way can be used in further electrophilic substitution reactions. Our method not only replaces the traditional Friedel–Crafts reaction for preparing bromoferrocene derivatives, but can also successfully produce bromoferrocenes consisting of various functional groups, such as the ester,[10] acid and alkyl groups. Using the traditional method these derivatives were either difficult or impossible to synthesise. It is noteworthy that bromoferrocene is tedious to prepare and cannot be synthesized by the direct bromination of ferrocene. Therefore, it has been obtained through the reaction of chloromercuriferrocene with bromine[11,12] and *N*-bromosuccinimide[13] or through the reaction of ferroceneboronic acid with $CuBr_2$.[14,15] On the other hand, 1,1′-dibromoferrocene is easily obtained in a high yield by the treatment of 1,1′-dilithioferrocene with toluene-*p*-sulfonyl bromide or polybrominated alkanes.[16] Furthermore, the preparation of dibromoferrocene in our laboratory has been carried out on a 0.25 mol scale, and the yield was maintained at 60% after normal work-up and recrystallization.

As the various 1′-substituted-1-bromoferrocenes can be prepared easily, various biferrocene derivatives are obtained efficiently. In our laboratory, biferrocenes **7** and **9** are synthesized by using the traditional coupling method. These biferrocenes will be oxidized by iodine and the corresponding biferrocenium salts will be studied carefully to elucidate the fundamental nature controlling the electron transfer rate.

A sample of 1-methyl-1′-bromoferrocene was also treated with butyllithium, followed by DMF or CO_2 and then aqueous HCl, and the corresponding aldehyde **11** or acid **12** was obtained in good yield. This provides an alternative and efficient method for preparing unsymmetrically disubstituted ferrocenes as novel materials with potential non-linear optical or liquid crystalline properties. For example, compound **13**, which could be an important precursor of liquid crystalline molecules with ester linkages,[17] was prepared by this method in 10% overall yield from dibromoferrocene.

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Footnote

† *General procedure*: Dibromoferrocene or 1'-methyl-1-bromoferrocene (5 mmol) is placed in a three-necked flask and vacuumed under 2 mm Hg at 30 °C for 4 h to remove trace of solvents. Dry THF (20 ml) and *n*-butyllithium (6.3 ml; 1.6 mol dm^{-3} in hexane) is added under nitrogen, and the resulting solution or mixture is maintained at −25 °C for 25 min. The resulting monolithioferrocene **1** or **10** can be directly used in further electrophilic substitution reactions. Various electrophilic reagents (5 mmol) are then added, and the resulting solution or mixture is stirred under nitrogen at −25 °C for 25 min, then at room temp. for 30 min. After general work-up, the desired products are obtained in 42–76% yield. All compounds gave satisfactory spectroscopic and analytical data. *Selected physical data*: **2**, M^+ at *m/z* 382, 384; ^1H NMR (300 MHz, $CDCl_3$) δ 2.43 (s, 3H, CH_3), 4.12 (t, 2H, Cp), 4.41 (t, 2H, Cp), 4.58 (t, 2H, Cp), 4.94 (t, 2H, Cp), 7.27 (d, 2H, phenyl), and 7.84 (d, 2H, phenyl). **3**, M^+ at *m/z* 308, 310; ^1H NMR (300 MHz, $CDCl_3$) δ 3.30 (s, 3H, CH_3), 4.04 (t, 2H, Cp), 4.10 (s, 2H, CH_2), 4.19 (s, 4H, Cp), and 4.34 (t, 2H, Cp). **4**, M^+ at *m/z* 308, 310; ^1H NMR (300 MHz, $CDCl_3$) δ 4.21 (t, 2H, Cp), 4.48–4.51 (m, 4H, Cp), and 4.91 (t, 2H, Cp). **5**, M^+ at *m/z* 292, 294; ^1H NMR (300 MHz, $CDCl_3$) δ 4.21 (t, 2H, Cp), 4.51 (t, 2H, Cp), 4.62 (t, 2H, Cp), 4.82 (t, 2H, Cp), and 9.98 (s, 1H, COH). **6**, M^+ at *m/z* 338, 340; ^1H NMR (300 MHz, $CDCl_3$) δ 1.35 (s, 3H, CH_3), 4.12 (t, 2H, Cp), 4.28 (q, 2H, CH_2), 4.41 (m, 4H, Cp), 4.82 (t, 2H, Cp). **7**, M^+ at *m/z* 458; ^1H NMR (300 MHz, $CDCl_3$) δ 3.21 (t, 6H, CH_3), 3.96 (s, 4H, CH_2), 3.98 (d, 4H, Cp), 4.01 (d, 4H, Cp), 4.17 (t, 4H, Cp), 4.30 (d, 4H, Cp). **8**, M^+ at *m/z* 278, 280; ^1H NMR (300 MHz, $CDCl_3$) δ 1.99 (s, 3H, CH_3), 4.02 (t, 2H, Cp), 4.04 (t, 2H, Cp), 4.09 (t, 2H, Cp), 4.28 (t, 2H, Cp). **9** M^+ at *m/z* 398; ^1H NMR (300 MHz, $CDCl_3$) δ 1.75 (s, 6H, CH_3), 3.85 (s, 4H, Cp), 3.88 (s, 4H, Cp), 4.13 (d, 4H, Cp), 4.26 (d, 4H, Cp). **11**, M^+ at *m/z* 228; ^1H NMR (300 MHz, $CDCl_3$) δ 1.91 (s, 3H, CH_3), 4.14 (s, 2H, Cp), 4.16 (s, 2H, Cp), 4.54 (s, 2H, Cp), 4.70 (s, 2H, Cp). **12**, M^+ at *m/z* 244; ^1H NMR (300 MHz, $CDCl_3$) δ 1.94 (s, 3H, CH_3), 4.11 (s, 4H, Cp), 4.41 (s, 2H, Cp), 4.78 (s, 2H, Cp). **13**, M^+ at *m/z* 382; ^1H NMR (300 MHz, $CDCl_3$) δ 1.26 (s, b, 14H, CH_2), 2.01 (quint, 2H, CH_2), 2.28 (t, 2H, CH_2), 4.12 (s, 4H, Cp), 4.41 (s, 2H, Cp), 4.77 (s, 2H, Cp), 4.90–5.04 (m, 2H, $=CH_2$), 5.71–5.88 (m, 1H, –CH=).

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