

A CONVENIENT METHOD FOR THE PREPARATION OF MONOLITHIOFERROCENE

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Abstract: Monolithioferrocene has been prepared in 70% yield from the reaction of ferrocene with *t*-BuLi in THF, and some examples of its almost quantitative reactions are described.

Ferrocene is a starting material for the preparation of numerous derivatives used in many areas of chemistry (inorganic chemistry, material science, chiral ligands in catalysis...) ¹. It is transformed into its derivatives mostly by electrophilic substitution or by reactions involving metallation as a first step ^{2,3}. Monolithioferrocene is thus a key reagent for the preparation of many substituted ferrocenes; it is usually prepared by one of the three following procedures ⁴ :

i) Lithiation of ferrocene by excess of *n*-butyllithium in diethyl ether at room temperature. Monolithioferrocene is reported to be formed in 25% yield, the remaining material being unreacted ferrocene ^{2,5}.

ii) Metal-halogen exchange reaction between bromoferrocene and *n*-butyllithium in diethyl ether. Monolithioferrocene is obtained in excellent yields ⁶.

iii) Transmetallation between chloromercuriferrocene and *n*-butyllithium in diethyl ether. The yield of monolithioferrocene is about 65% ^{7,8}.

Dilithioferrocene is obtained in good yields by direct metallation of ferrocene with *n*-butyllithium/TMEDA ⁹ in hexane or with *tert*-butyllithium in diethyl ether at room temperature ⁴. By contrast the monolithiation of ferrocene (direct route i)) is not efficient and has to be replaced by indirect routes ii) and iii). We wish to report here a method which significantly improves the monolithiation of ferrocene and is very convenient for the preparation of many ferrocene derivatives.

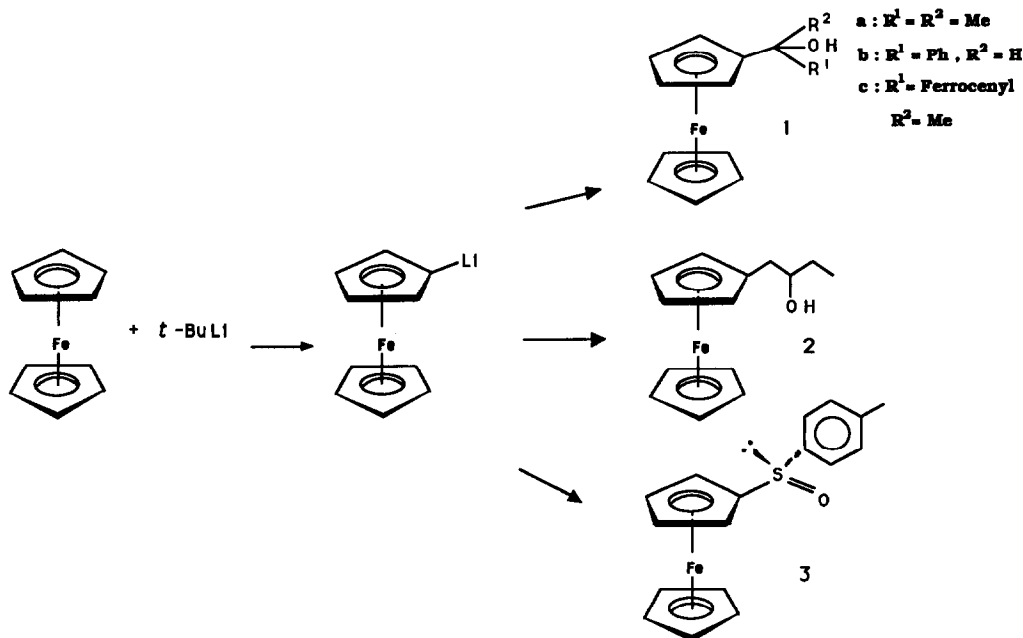
Preparation of monolithioferrocene

Ferrocene (12 mmol, 2.2 g) is dissolved at 0°C in a Schlenk tube in 10 mL THF (distilled on sodium benzophenone). *Tert*-butyllithium (10 mmol, 5.9 mL of 1.7 M hexane solution, Aldrich) is slowly added at 0°C. After standing 15 min at 0°C, the solution is warmed up to room temperature. The yield in monolithioferrocene is about 70% (based on *t*-BuLi), as measured by reaction with electrophiles (see below).

Some reactions of monolithioferrocene

The usefulness of the above lithiation procedure can be illustrated by a few selected reactions such as with acetone, benzaldehyde, 1,2-epoxybutane or (+)-menthyl *p*-tolylsulfinate. The results are listed in Table 1.

Excellent yields (with respect to substrate) are obtained by using a solution of monolithioferrocene in excess (1.3 equiv based on *t*-BuLi). The product is easily separated from residual ferrocene by flash-chromatography. Quenching of the reaction in entry 6 (Table 1) by D₂O does not lead to incorporation of deuterium in ferrocenyl rings of **1a**. This is a confirmation that our procedure selectively gives the monolithiation of ferrocene¹³.



In conclusion, the simple method developed here allows one to introduce almost quantitatively a ferrocenyl group in many substrates, by using ferrocene itself as a starting material.

TABLE 1

Some reactions with monolithioferrocene

	Electrophiles ^a	Products	Isolated yield ^b
1	Acetone	1a	85%
2	Benzaldehyde	1b	98%
3	1,2-epoxybutane	2	85%
4	(+)-(R) _S (1S)-menthyl <i>p</i> -tolyl sulfinate	3	98%
5	Ethyl acetate	1c	70% ^c
6	Acetone	1a	70%
7	Benzaldehyde	1b	70%
8	1,2-epoxybutane	2	70%

a) Entries 1 to 4 : Ferrocene / *t*-BuLi / Electrophile = 1.5 / 1.3 / 1.

Entries 5 to 8 : Ferrocene / *t*-BuLi / Electrophile = 1.2 / 1 / 1.

Monolithioferrocene is prepared as described in the text. Reactions are performed at r.t. The standard procedure is exemplified by the preparation of sulfoxide **3**. A solution of monolithioferrocene is prepared from 4.5 mmol of *t*-BuLi (2.7 mL of pentane 1.7 M solution) and 5.4 mmol ferrocene (in 8 mL THF). This solution is maintained at 0°C and 3 mmol of (+) (R)_S (1S)-menthyl *p*-tolylsulfinate (Fluka) in 5 mL THF are added rapidly. After 10 min at 0°C the reaction is quenched with 10 mL of water. The crude product (mixed with ferrocene and with menthol) is recovered by ether extraction. A flash-chromatography on silica (elution by cyclohexane-AcOEt = 2:1) gives 950 mg of pure (R)-**3**. Yield 95% (with respect to (+) (R)_S (1S)-menthyl *p*-tolylsulfinate)¹⁰.

b) Entries 1 to 4 : yields are expressed with respect to electrophiles.

Entries 5 to 8 : yields are expressed with respect to *t*-BuLi.

c) Yield measured by ¹H nmr. Isolation by flash-chromatography destroyed the compound.

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- (10) (R) configuration at sulfur was assigned to sulfoxide **3**, because of the inversion occurring in the Andersen method^{11,12}.
 (R)-**3** : mp=127-128°C, $[\alpha]_D^{25} = -4^\circ \pm 1^\circ$ (C= 0.9, CHCl₃), ¹H nmr (CDCl₃) ppm: 2.35 (s, Me), 4.3 (1 H in ferrocenyl), 4.35 (7 H in ferrocenyl), 4.6 (1 H in ferrocenyl), 7.15-7.5 (4 H, tolyl). Anal. C₁₇H₁₆SOFe Calc. C=62.98, H=4.97, S=9.89, Found : 62.93; 5.07; 9.93.
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- (13) A change in the ratio between ferrocene and *t*-BuLi (eg 1:1 or 1:2) did not allow to increase the amount of monolithioferrocene above 70% (with respect to *t*-BuLi).

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