

## Directed Metallation Reactions. A Specific Route to 1,2,3-Trisubstituted and 1,3-Disubstituted Ferrocenes

By D. W. SLOCUM,\* R. L. MARCHAL, and W. E. JONES

(Neckers Laboratory, Southern Illinois University, Carbondale, Illinois 62901)

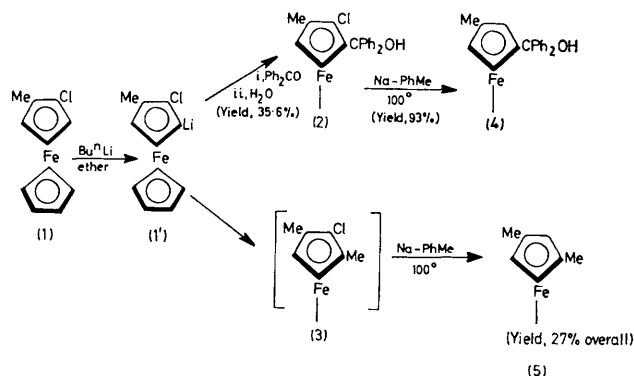
**Summary** Sequential directed metallation of chloroferrocene has led to two 1,2,3-trisubstituted ferrocenes which can be dechlorinated to provide the corresponding 1,3-disubstituted ferrocenes.

THE directed metallation reaction is potentially useful as an alternative to electrophilic substitution and other methods for the synthesis of 1,3-disubstituted aromatics. The technique involves sequential double directed metallation at each of the positions adjacent to the substituent to produce a 1,2,3-trisubstituted aromatic compound. Removal of the directing substituent from position 2 would then produce a 1,3-disubstituted aromatic. We now report the first application of this technique.

Directed metallation with *n*-butyllithium has proved useful for the preparation of 1,2-disubstituted ferrocenes.<sup>1</sup> However, no specific route has been proposed for 1,3-disubstituted ferrocenes.<sup>2</sup> Recent developments in the use of the chloro group as a 2-directing substituent<sup>3</sup> have opened up a specific route to 1,3-di- and 1,2,3-trisubstituted ferrocenes, the reactions depending on the fact that lithiation of a 2-substituted chloroferrocene provides metallation in the remaining position adjacent to the directing group.†

2-Chloro-1-methylferrocene (1) was metallated with *n*-butyllithium in ether for 4–6 h to give the 3-lithio species

(1'). Treatment of this intermediate with (a) benzophenone or (b) methyl iodide gave, respectively, 2-chloro-3-diphenylhydroxymethyl-1-methylferrocene (2), m.p. 175–180° (decomp.), and 2,5-dimethyl-1-chloroferrocene (3).



SCHEME

Dechlorination of (2) and (3) using sodium dispersed in toluene gave 3-diphenylhydroxymethyl-1-methylferrocene (4), m.p. 137–139°, and 1,3-dimethylferrocene (5), (Scheme). Satisfactory elemental analyses were obtained for compounds (2) and (4).

† While this work was in progress, Huffman and Cope<sup>3d</sup> reported the isolation of an unstable carboxylic acid from the metallation and carbonation of (1).

The orientation of substituents proposed for (2) and (4) was supported by physical data. The n.m.r. spectrum of (2) exhibited doublets for the two substituted ring hydrogens with a coupling constant of 3.0 Hz (similar to the coupling previously reported between vicinal protons on the ferrocene ring).<sup>4</sup> In the n.m.r. spectrum of (4) the lack of a significant upfield shift expected for methyl protons adjacent to a diphenylhydroxymethyl substituent<sup>5</sup> ruled out the 1,2-isomer.<sup>6</sup> The only homoannular substitution pattern which remained was that of 1,3-orientation. A mass spectrum exhibited an abundant peak at *m/e* 244 which was assigned to a methyl-6,6-diphenylfulvene structure analogous to the diphenylfulvene fragment arising from diphenylhydroxymethylferrocene.<sup>7</sup>

A similar method was used to prepare 1,3-dimethylferrocene, which has been isolated only after tedious separation procedures have been applied to various mix-

tures.<sup>8</sup> The intermediate (1') was treated with methyl iodide to give a mixture of unreacted (1) and 2,5-dimethyl chloroferrocene (3). This mixture was not separated but was dechlorinated (Na-toluene) to give a mixture of methylferrocene and 1,3-dimethylferrocene (5), easily separable by v.p.c. and identified by its i.r. spectrum.<sup>9</sup>

Using this method the 1,3-disubstituted product is formed exclusively and only separation from unreacted starting material is generally necessary. A disadvantage is that many substituents will not survive removal of the chloro group *via* a sodium dispersion so a search for milder dechlorinating conditions, and other suitable substituents is in progress.

We thank the office of research and projects, Southern Illinois University, for support.

(Received, 13th August 1974; Com. 1049.)

<sup>1</sup> D. W. Slocum, T. R. Engelmann, C. Ernst, C. A. Jennings, W. E. Jones, B. Koonsvitsky, J. Lewis, and P. Shenkin, *J. Chem. Educ.*, 1969, **46**, 144; E. Kaiser and D. W. Slocum in 'Organic Reactive Intermediates,' ed. S. McManus, Academic Press, New York, 1973; D. W. Slocum and D. I. Sugarman in *Advances in Chemistry Series*, number 130, ed. A. Langer, American Chemical Society Washington, 1974.

<sup>2</sup> M. Rosenblum, 'Chemistry of the Iron Group Metallocenes,' Interscience, New York, 1965, chapter 4; G. R. Knox, I. G. Morrison, P. L. Pauson, M. A. Sandhu, W. E. Watts, and J. H. Richards, *J. Org. Chem.*, 1963, **28**, 1549; for a general summary of electronic effects in metallocenes *cf.* D. W. Slocum and C. R. Ernst, *Adv. Organometallic Chem.*, 1972, **10**, 79.

<sup>3</sup> (a) A. N. Nesmeyanov, V. A. Sazonova, and V. N. Drozd, *Doklady Akad. Nauk. S.S.S.R.*, 1959, **126**, 1004; (b) J. N. Huffman, L. H. Keith, and R. L. Asbury, *J. Org. Chem.*, 1965, **30**, 1600; (c) D. W. Slocum, B. P. Koonsvitsky, and C. R. Ernst, *J. Organometallic Chem.*, 1972, **38**, 125; (d) J. N. Huffman and J. F. Cope, *J. Org. Chem.*, 1971, **36**, 4068.

<sup>4</sup> M. J. Levenberg and J. H. Richard, *J. Amer. Chem. Soc.*, 1964, **86**, 2043.

<sup>5</sup> D. W. Slocum and C. A. Jennings, *J.C.S. Chem. Comm.*, 1972, 54.

<sup>6</sup> In 2-diphenylhydroxymethyl methylferrocene, an upfield shift for the methyl group relative to the methyl group of methylferrocene of 18.6 Hz was observed; D. W. Slocum, R. L. Marchal, and W. E. Jones, *J. Organometallic Chem.*, 1974, **72**, 227.

<sup>7</sup> D. W. Slocum, R. Lewis, and G. J. Mains, *Chem. & Ind.*, 1966, 2095.

<sup>8</sup> *Cf.* D. W. Slocum, W. Jones, T. Crimmens, and C. R. Hauser, *J. Org. Chem.*, 1969, **34**, 1973 and references therein.

<sup>9</sup> K. Schlögl and M. Fried, *Monatsh.*, 1964, **95**, 558.