

# Simple reduction of ferrocenyl aldehydes and ketones by sodium boranuide in trifluoroacetic acid: new, efficient, general preparation of alkylferrocenes

Sukanta Bhattacharyya\*

Department of Chemistry, Vijoygarh College, Calcutta 700032, India

Alkylferrocenes are obtained in excellent yields by ionic hydrogenation of ferrocenyl aldehydes and ketones using sodium boranuide and trifluoroacetic acid.

## Introduction

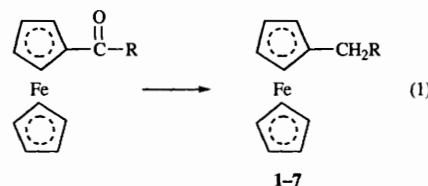
Owing to their interesting optical, thermal and redox properties, ferrocene derivatives have emerged as strong candidates for materials and catalysts.<sup>1</sup> The design and synthesis of ferrocene derivatives possessing functionalized tethers continue to attract considerable attention due to their potential applications<sup>2</sup> in molecular recognition, in the construction of dendrimers, in multi-electron redox catalysis, in molecular electronics, as agents used chemically to modify electrode surfaces, and as electrochemical and spectroscopic probes of surfaces and interfaces, among other applications.

## Results and discussion

The most direct approach for the preparation of alkylferrocenes is, in principle, the Friedel–Crafts alkylations of ferrocene. However, these reactions<sup>3</sup> proceed in poor yields and invariably produce intractable mixtures of mono- and poly-alkylated derivatives. The Friedel–Crafts acylations<sup>4</sup> of ferrocene, on the other hand, furnish good yields of mono- and di-acylated ferrocenes with a remarkable degree of regioselectivity. Consequently, alkylferrocenes are normally prepared<sup>5</sup> *via* reduction of acylferrocenes. The classical protocols for this transformation include catalytic hydrogenolysis,<sup>6</sup> Clemmensen reduction,<sup>7</sup> and reductive deoxygenation employing lithium aluminium hydride<sup>8</sup> in the presence of anhydrous aluminium chloride. However, the possibility of having other functionality in the molecule is limited under these reaction conditions.

As part of our efforts towards the development of new applications of boranuide-based reducing systems<sup>9</sup> in selective transformations, we chose to explore the use of sodium boranuide in acidic media<sup>10</sup> for the reductive deoxygenation of ferrocenyl aldehydes and ketones. Here, we report on the results of the novel application of the sodium boranuide–trifluoroacetic acid (TFA) system in the ionic hydrogenation of acylferrocenes at room temperature, an effective, rapid method for the preparation of alkylferrocenes [equations (1) and (2)].

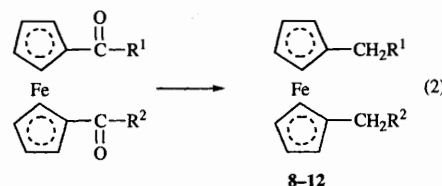
Treatment of acylferrocenes with sodium boranuide and TFA in dichloromethane for 1 h led to the formation of alkylferrocenes in excellent yields. In a typical experiment, sodium boranuide (20 mmol) was added to a stirred solution of benzoylferrocene (5 mmol) in TFA (10 cm<sup>3</sup>)–dichloromethane (10 cm<sup>3</sup>). The resulting mixture was further stirred for 1 h, diluted with dichloromethane (30 cm<sup>3</sup>), and quenched with aq. sodium hydroxide (2 mol dm<sup>-3</sup>). Separation of the organic layer, drying of this layer over Na<sub>2</sub>SO<sub>4</sub>, removal of solvent,



Reagents and conditions: TFA, NaBH<sub>4</sub>, CH<sub>2</sub>Cl<sub>2</sub>, 25 °C

Products:

- |                             |  |
|-----------------------------|--|
| 1 R = H (88%)               | 5 R = [CH <sub>2</sub> ] <sub>2</sub> CO <sub>2</sub> H (90%)  |
| 2 R = CH <sub>3</sub> (90%) | 6 R = [CH <sub>2</sub> ] <sub>2</sub> CO <sub>2</sub> Me (88%) |
| 3 R = Pr <sup>i</sup> (92%) | 7 R = [CH <sub>2</sub> ] <sub>4</sub> Cl (94%)                 |
| 4 R = Ph (92%)              |  |



Reagents and conditions: TFA, NaBH<sub>4</sub>, CH<sub>2</sub>Cl<sub>2</sub>, 25 °C

Products:

- |   |   |
|---|---|
| 8 R <sup>1</sup> = R <sup>2</sup> = H (90%)               | 11 R <sup>1</sup> = R <sup>2</sup> = [CH <sub>2</sub> ] <sub>2</sub> CO <sub>2</sub> Me (86%) |
| 9 R <sup>1</sup> = R <sup>2</sup> = CH <sub>3</sub> (92%) | 12 R <sup>1</sup> = R <sup>2</sup> = [CH <sub>2</sub> ] <sub>2</sub> (92%)                    |
| 10 R <sup>1</sup> = R <sup>2</sup> = Ph (94%)             |   |

and flash chromatography of the residue over silica gel with diethyl ether–hexanes (1:9) as the eluent afforded pure benzylferrocene in 92% yield. The reactions proceed at room temperature, the procedure is easy to perform, and no special handling technique is required. The scope of the method proved to be quite general for a variety of ferrocenyl aldehydes and ketones. It seems likely that the reaction proceeds through the formation of the corresponding  $\alpha$ -ferrocenyl alcohol as the intermediate, which is then reduced *via* the simple formation of remarkably stable  $\alpha$ -ferrocenylalkyl carbocation<sup>11</sup> in the presence of TFA. The conversion of ferrocenylmethanol and  $\alpha$ -ferrocenylethanol into the corresponding alkylferrocenes, following the same procedure, further supports the intermediacy of  $\alpha$ -ferrocenyl alcohols in these reactions. The method is equally efficient for the deoxygenation of diacylated ferrocenes [equation (2)]; the bridged ferrocenyl diketone (entry 12)<sup>12</sup> can be converted into the corresponding ferrocenophane in high yield. The present method allows synthesis of alkylferrocenes bearing terminally functionalized pendant chains, *e.g.* (3-carboxypropyl)ferrocene (entry 5), (3-methoxycarbonylpropyl)ferrocene (entry 6), (5-chloropentyl)ferrocene (entry 7) and 1,1'-bis[3-methoxycarbonylpropyl]ferrocene (entry 11) were obtained in high yields from the corresponding acylferrocenes. It is noteworthy that attempts<sup>13</sup> to perform Wolff–Kishner or Clemmensen reduction on similar acylferrocenes were unsuccessful. The simplicity of this procedure, coupled with the

\* Current address: Department of Chemistry, University of Mississippi, University, MS 38677, USA.

high yields of the pure products, should make it the method of choice for the preparation of alkylferrocenes, particularly for those bearing functionalized pendant chains.

In conclusion, the present procedure provides a fast, high yielding, practical method for the reductive deoxygenation of acylferrocenes, suitable for the preparation of alkylferrocenes possessing functionalized tethers.

## Experimental

All mps were measured on a Thomas-Hoover capillary melting point apparatus and are uncorrected.  $^1\text{H}$  NMR spectra were recorded at 60 MHz on an EM 360 spectrometer (Varian Associates) and at 300 MHz on a Bruker AM 300 spectrometer for samples in  $\text{CDCl}_3$  solution with  $\text{SiMe}_4$  as an internal standard ( $J$  values in Hz). IR spectra were recorded on a Perkin-Elmer 298 spectrometer for samples in  $\text{CHCl}_3$  solution. TLC was done on precoated silica gel plates. The commercially available acylferrocenes (entries 1, 2, 4 and 9) were used as received from their respective suppliers. The bridged diketone (entry 12) was prepared from commercially available 1,1'-diacetylferrocene following a known procedure.<sup>12</sup> The remaining substrates were prepared<sup>4</sup> by Friedel-Crafts acylations of ferrocene.

### General procedure for the preparation of alkylferrocenes from acylferrocenes

Sodium boranuide (0.76 g, 20 mmol) was added portionwise over a period of 15 min to a magnetically stirred solution of the acylferrocene (5 mmol) in TFA (10  $\text{cm}^3$ )-dichloromethane (10  $\text{cm}^3$ ). The contents were further stirred at room temperature for 45 min. The reaction mixture was then diluted with dichloromethane (30  $\text{cm}^3$ ), and aq. sodium hydroxide (2 mol  $\text{dm}^{-3}$ ) was added dropwise till the aqueous phase was alkaline (pH 10 by Hydrion pH test paper). The organic layer was separated, dried over  $\text{Na}_2\text{SO}_4$  and concentrated. Flash chromatography of the residue over silica gel with hexanes-diethyl ether (9:1) as eluent afforded the pure alkylferrocenes in 86–94% yield.

For the preparations of carboxyalkylferrocenes, the reaction was quenched by the addition of water instead of aq. sodium hydroxide and the organic phase was washed with portions (20  $\text{cm}^3$ ) of water until the aqueous part was neutral (pH 7 by Hydrion pH test paper).

In the case of diacylated ferrocenes the same general procedure was followed except that double the amounts of TFA and sodium boranuide were used.

Data below correspond to the entries in equations (1) and (2).

Entry 1. Mp 36 °C (lit.,<sup>6d,7c</sup> 35.5–36.5 °C);  $\nu_{\text{max}}/\text{cm}^{-1}$  3054, 2976, 1416, 1100 and 1057;  $\delta$  1.98 (3 H, s), 4.03–4.07 (4 H, m) and 4.09 (5 H, s).

Entry 2. Bp 102–105 °C (4 mmHg) [lit.,<sup>6d</sup> 121–123 °C (10 mmHg)];  $\nu_{\text{max}}/\text{cm}^{-1}$  3103, 2962, 2933, 2876, 1451, 1430, 1104, 1061, 1040 and 820;  $\delta$  1.17 (3 H, t,  $J$  7.5), 2.34 (2 H, q,  $J$  7.5), 4.03–4.07 (4 H, m) and 4.10 (5 H, s).

Entry 3. Bp 112–115 °C (0.5 mmHg) [lit.,<sup>14</sup> 118–122 °C (0.5 mmHg)];  $\nu_{\text{max}}/\text{cm}^{-1}$  3096, 2962, 2947, 2926, 1465, 1104, 1040, 997, 919 and 820;  $\delta$  0.84 (6 H, d,  $J$  6.6), 1.57 (1 H, heptet,  $J$  6.6), 2.23 (2 H, d,  $J$  6.6), 4.03 (4 H, s) and 4.08 (5 H, s).

Entry 4. Mp 75–76 °C (lit.,<sup>15</sup> 74.5–75.5 °C);  $\nu_{\text{max}}/\text{cm}^{-1}$  3089, 3061, 3025, 2926, 1600, 1494, 1430, 1104, 1026, 912 and 820;  $\delta$  3.68 (2 H, s), 4.06–4.10 (9 H, m) and 7.16–7.3 (5 H, m).

Entry 5. Mp 118–119 °C (lit.,<sup>6b</sup> 117–118 °C);  $\nu_{\text{max}}/\text{cm}^{-1}$  3522br, 3089, 2947, 2862, 1700, 1409, 1267, 1097, 1040, 1005 and 820;  $\delta$  1.90 (2 H, quin,  $J$  7), 2.43 (4 H, t,  $J$  7), 4.07 (4 H, br s) and 4.12 (5 H, s).

Entry 6. Bp 155–158 °C (2 mmHg) [lit.,<sup>16</sup> 168–170 °C (4 mmHg)];  $\nu_{\text{max}}/\text{cm}^{-1}$  3096, 2954, 2855, 1721, 1437, 1260, 1210, 1175, 1040 and 813;  $\delta$  1.84 (2 H, quin,  $J$  7.5), 2.34 and 2.37 (4 H, 2 t,  $J$  7.5), 3.68 (3 H, s), 4.05 (4 H, br s) and 4.10 (5 H, s).

Entry 7. Bp 135–140 °C (0.5 mmHg);  $\nu_{\text{max}}/\text{cm}^{-1}$  3096, 2962,

2933, 2855, 1451, 1437, 1267, 1168, 1104, 1033, 997, 884 and 820;  $\delta$  1.42–1.55 (4 H, m), 1.73–1.82 (2 H, m), 2.22–2.32 (2 H, m), 3.53 (2 H, t,  $J$  6.6) and 4.1–4.25 (9 H, m) (Found: C, 61.85; H, 6.7.  $\text{C}_{15}\text{H}_{19}\text{ClFe}$  requires C, 61.97; H, 6.59%).

Entry 8. Mp 40 °C (lit.,<sup>17</sup> 39–40.5 °C);  $\nu_{\text{max}}/\text{cm}^{-1}$  3090, 2976, 2926, 1458, 1040, 1012 and 820;  $\delta$  1.97 (6 H, s) and 3.96 (8 H, s).

Entry 9. Mp 36 °C (lit.,<sup>8b</sup> 35 °C);  $\nu_{\text{max}}/\text{cm}^{-1}$  3089, 2977, 2962, 2954, 2924, 1473, 1458, 1267, 1040, 1010, 823 and 763;  $\delta$  1.16 (6 H, t,  $J$  7.5), 2.35 (4 H, q,  $J$  7.5) and 4.00 (8 H, s).

Entry 10. Mp 104–105.5 °C (lit.,<sup>6a,15b</sup> 103–105 °C);  $\nu_{\text{max}}/\text{cm}^{-1}$  3082, 3025, 2919, 1600, 1487, 1451, 1033, 919, 877 and 763;  $\delta$  3.67 (4 H, s), 4.06 (8 H, s) and 7.12–7.32 (10 H, m).

Entry 11. Bp 182–185 °C (0.1 mmHg) [lit.,<sup>18</sup> 200–210 °C (0.2 mmHg)];  $\nu_{\text{max}}/\text{cm}^{-1}$  3090, 2954, 1728, 1437, 1246, 1203 and 905;  $\delta$  1.80 (4 H, quin,  $J$  7.4), 2.31 and 2.34 (8 H, 2 t,  $J$  7.4), 3.66 (6 H, s) and 3.95–4.01 (8 H, m).

Entry 12. Mp 62–63 °C (lit.,<sup>7c</sup> 63–64 °C);  $\nu_{\text{max}}/\text{cm}^{-1}$  3089, 2969, 2926, 2905, 2855, 1473, 1444, 1040, 1019 and 912;  $\delta$  1.80–1.90 (4 H, m), 2.38–2.48 (4 H, m) and 3.97–4.1 (8 H, m).

## References

- 1 See, for example: A. M. Giroud-Godquin and P. M. Maitlis, *Angew. Chem., Int. Ed. Engl.*, 1991, **30**, 375; A. Ulman, *An Introduction to Ultrathin Organic Films from Langmuir-Blodgett to Self-Assembly*, Academic Press, Boston, MA, 1991; *Ferrocenes: Homogeneous Catalysis, Organic Synthesis, Materials Science*, ed. A. Togni and T. Hayashi, VCH Verlagsgesellschaft, Weinheim, 1995.
- 2 For some of the leading references, see: Y. Degani and A. Heller, *J. Phys. Chem.*, 1987, **91**, 1285; H. A. U. Hill, D. J. Page and N. J. Walton, *J. Electroanal. Chem. Interfacial Electrochem.*, 1987, **217**, 141; K. Uosaki, Y. Sato and H. Kita, *Langmuir*, 1991, **7**, 1510; P. D. Beer, Z. Chen, M. G. B. Drew, J. Kingston, M. Ogden and P. Spencer, *J. Chem. Soc., Chem. Commun.*, 1993, 1046; C. D. Hall, J. H. R. Tucker, S. Y. F. Chu, A. W. Parkins and S. C. Nyburg, *J. Chem. Soc., Chem. Commun.*, 1993, 1505; J. L. Fillaut, J. Linares and D. Astruc, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 2460; G. K. Rowe and S. E. Creager, *Langmuir*, 1994, **10**, 1186; R. Deschenaux and J. Santiago, *Tetrahedron Lett.*, 1994, **35**, 2169; J. T. Yli-Kauhalauma, J. A. Ashley, C. H. Lo, L. Tucker, M. M. Wolfe and K. D. Janda, *J. Am. Chem. Soc.*, 1995, **117**, 7041; T. J. Gardner, C. D. Frisbie and M. S. Wrighton, *J. Am. Chem. Soc.*, 1995, **117**, 6927 and references therein; A. Riklin, E. Katz, I. Willner, A. Stocker and A. F. Bueckmann, *Nature*, 1995, **376**, 672.
- 3 M. Vogel, M. D. Rausch and H. Rosenberg, *J. Org. Chem.*, 1957, **22**, 1016; A. N. Nesmeyanov and N. S. Kochetkova, *Dokl. Akad. Nauk SSSR*, 1956, **109**, 543 (*Chem. Abstr.*, 1957, **51**, 5057); 1957, **114**, 800 (*Chem. Abstr.*, 1958, **52**, 3794); *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 1958, 242 (*Chem. Abstr.*, 1958, **52**, 12 852); E. W. Neuse and D. S. Trifan, *J. Am. Chem. Soc.*, 1962, **84**, 1850; D. E. Bublitz, *Can. J. Chem.*, 1964, **42**, 2381.
- 4 M. Rosenblum, *Chemistry of the Iron Group Metalloenes: ferrocene, ruthenocene, osmocene*, Wiley, New York, 1965, Pt. 1, pp. 62–119 and references therein; D. E. Bublitz and K. L. Rinehart, Jr., *Org. React.*, 1969, **17**, 24.
- 5 M. Rosenblum, *Chemistry of the Iron Group Metalloenes: ferrocene, ruthenocene, osmocene*, Wiley, New York, 1965, Pt. 1, p. 146; D. E. Bublitz and K. L. Rinehart, Jr., *Org. React.*, 1969, **17**, 28.
- 6 (a) M. D. Rausch, M. Vogel and H. Rosenberg, *J. Org. Chem.*, 1957, **22**, 903; (b) K. L. Rinehart, R. J. Curby and P. E. Sokol, *J. Am. Chem. Soc.*, 1957, **79**, 3420; (c) M. Rosenblum and R. B. Woodward, *J. Am. Chem. Soc.*, 1958, **80**, 5443; (d) K. Schloegl and A. Mohar, *Monatsh. Chem.*, 1961, **92**, 219.
- 7 (a) N. Weliky and E. S. Gould, *J. Am. Chem. Soc.*, 1957, **79**, 2742; (b) E. L. DeYoung, *J. Org. Chem.*, 1961, **26**, 1312; (c) J. M. Osgerby and P. L. Pauson, *J. Chem. Soc.*, 1961, 4604; (d) M. Rosenblum, A. K. Banerjee, N. Danieli, R. W. Fish and V. Schlatter, *J. Am. Chem. Soc.*, 1963, **85**, 316; (e) P. L. Pauson and W. E. Watts, *J. Chem. Soc.*, 1962, 3880.
- 8 (a) K. L. Rinehart, A. F. Ellis, C. J. Micejda and P. A. Kittle, *J. Am. Chem. Soc.*, 1960, **82**, 4112; (b) K. Schloegl, A. Mohar and M. Peterlik, *Monatsh. Chem.*, 1961, **92**, 921; (c) K. Schloegl and A. Mohar, *Monatsh. Chem.*, 1962, **93**, 861.
- 9 S. Bhattacharyya, A. Chatterjee and S. K. Duttachowdhury, *J. Chem. Soc., Perkin Trans. 1*, 1994, 1; S. Bhattacharyya, *Tetrahedron Lett.*, 1994, **35**, 2401; *Synlett*, 1994, 1029; *J. Org. Chem.*, 1995, **60**, 4928; *J. Chem. Soc., Perkin Trans. 1*, 1995, 1845; *Synlett*, 1995, 971.

- 10 For a review, see: G. W. Gribble and C. F. Nutaitis, *Org. Prep. Proced. Int.*, 1985, **17**, 317.
- 11 M. Cais, *Organomet. Chem. Rev.*, 1966, **1**, 435; J. Feinberg and M. Rosenblum, *J. Am. Chem. Soc.*, 1969, **91**, 4324; T. D. Turbitt and W. E. Watts, *J. Chem. Soc., Chem. Commun.*, 1973, 182.
- 12 Y. Ito, T. Konoike, T. Harada and T. Saegusa, *J. Am. Chem. Soc.*, 1977, **99**, 1487.
- 13 P. J. Graham, R. V. Lindsey, G. W. Parshall, M. L. Peterson and G. M. Whitman, *J. Am. Chem. Soc.*, 1957, **79**, 3416.
- 14 L. A. Day, *Br. Pat.* 864 198, 1961 (*Chem. Abstr.*, 1961, **55**, 17 647).
- 15 (a) A. L. J. Beckwith and R. J. Leydon, *Tetrahedron Lett.*, 1963, 385; (b) B. F. Hallam and P. L. Pauson, *J. Chem. Soc.*, 1956, 3030.
- 16 J. B. Thompson, *Chem. Ind. (London)*, 1959, 1122.
- 17 E. A. Hill and J. H. Richards, *J. Am. Chem. Soc.*, 1961, **83**, 4216.
- 18 K. Schoegl and H. Seiler, *Monatsh. Chem.*, 1960, **91**, 79; *Angew. Chem.*, 1960, **72**, 38.

Paper 5/07842C

Received 1st December 1995

Accepted 21st December 1995