Formation of functionalized [3]ferrocenophane derivatives by an enamine condensation reaction[☆]

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Abstract

Treatment of 1,1′-diacetylferrocene (**10**) with excess piperidine and a stoichiometric amount of TiCl₄ in pentane leads to CC-coupling of the two functional groups at the ferrocene framework. This enamine condensation reaction leads to the formation of the 1,3-connected dienamine-bridged [3]ferrocenophane system **13a**. Complex **13a** was characterised by X-ray crystal structure analysis. The analogous TiCl₄-mediated coupling and condensation reactions of **10** with morpholine, pyrrolidine or methyl-iso-propylamine yield the corresponding substituted [3]ferrocenophane systems **13b–d**. © 2000 Elsevier Science S.A. All rights reserved.

Keywords: Enamine condensation reaction; Dienamine formation; [3]Ferrocenophane synthesis; Ferrocene

1. Introduction

Functionalized [3]ferrocenophanes can be synthesised by means of a variety of classical organic CC-coupling reactions. Typical examples include the formation of **1** by Friedel–Crafts acylation via ferrocenyl-propionic acid derivatives, or the synthesis of **2** by means of an intramolecular Claisen condensation reaction of 1-acetyl-ferrocene-1′-alkylcarboxylates [1,2]. Surprisingly, there is little known about the simple aldol condensation reaction of e.g. 1,1′-diacetylferrocene, that would lead to the interesting unsaturated [3]ferrocenophane derivative **3** (see Scheme 1) [3]. Such systems, or derivatives thereof, seem not to be readily available, mostly due to preferred intermolecular reaction courses that give rise to dimeric or oligomeric condensation products under typical aldol reaction conditions [4–6].

We have recently described a related, i.e. Mannich-type, condensation reaction at Group 4 metallocene frameworks that leads to a similarly structured unsaturated C₃-bridged ansa-metallocene situation [7]. In that case bis(1-aminoalkenyl-Cp)MCl₂ complexes (M = Ti, Zr, Hf) were prepared by the reaction sequence depicted in Scheme 2, and subsequently coupled (to yield **6**). Condensation occurred with the loss of one amine equivalent by treatment with a catalytic amount of a suitable Lewis acid (e.g. TiCl₄, ZrCl₄ or HfCl₄) or a Brønsted acid catalyst (e.g. HNMe₂Ph⁺BAr₄⁻). The corresponding 1,3-dienamino-bridged systems **9** were obtained in good yield. For practical purposes we have developed a one-pot synthesis of the ansa-metallocenes, where treatment of the (1-aminoalkenyl-Cp)Li reagents (**5**) with a slight excess of the respective MX₄ starting material, which served as both the necessary stoichiometric metal halide reagent and the Lewis acid catalyst for the condensation step, resulted in the direct synthesis of **9** in good yield. Examples of the products **9** were derived from various aminofulvenes **4**. Some were characterised by X-ray crystal structure analysis [7].

Scheme 1.

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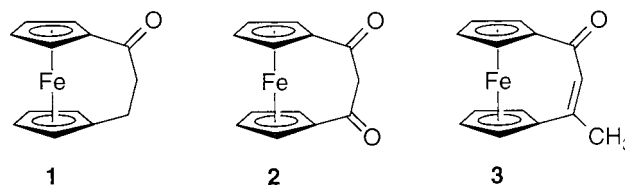
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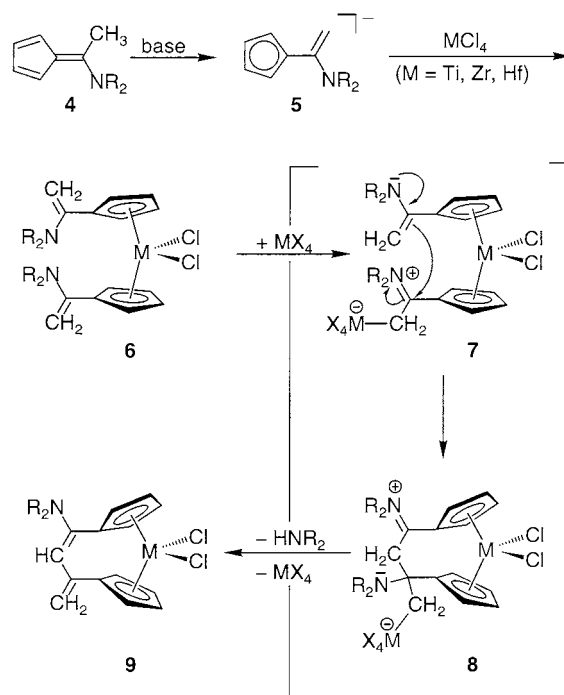[1] X-ray crystal structure analysis.

We have now adapted this condensation reaction from Group 4 metallocene chemistry and made it suitable for the preparation of the related [3]ferrocenophanes containing the unsaturated 1,3-attached dienamino-bridge.

2. Results and discussion

For the preparation of the unsaturated [3]ferrocenophanes **13** we chose 1,1′-diacetylferrocene (**12**) as a starting material. This was employed in the Lewis acid-catalysed enamine synthesis as described by White and Weingarten [8]. As a typical example, a solution of TiCl$_4$ in pentane was added slowly to a mixture of 1,1′-diacetylferrocene and excess (ca. 15–20 fold) piperidine in pentane at 0°C (Ti:Fe ratio, ca. 1.2) and then warmed to room temperature (r.t.). We assume that transformation of an acetyl group to the corresponding enamine takes place. We consider it likely that TiCl$_4$ activation of the second acetyl substituent opens a very favourable pathway for intramolecular attack by the adjacent enamine nucleophile with carbon–carbon coupling (see Scheme 3). However, none of the alleged intermediates of the rapidly proceeding reaction sequence could be isolated or observed, since Ti-supported HO-elimination provides a favourable irreversible pathway under the applied reaction conditions to directly yield the [3]ferrocenophane condensation product **13a**. Complex **13a** was isolated in close to 80% yield from the reaction mixture after conventional workup.

The dienamino-bridged [3]ferrocenophane **13a** was characterised by elemental analysis, spectroscopically and by X-ray diffraction. In solution complex **13a** shows NMR spectra consistent with a conformationally equilibrated C_s-symmetric structure. The forming of the C$_3$-bridge has made the two monosubstituted Cp rings chemically inequivalent. This situation gives rise to the observation of two *ipso*-C(Cp) ^{13}C-NMR signals at δ 89.7 and 84.1 ppm (C1, C1′, see Scheme 3) and a total of two pairs of C$_5$H$_4$ methine carbon signals (δ 71.4, 70.0, 69.8, 69.7, C2/2′, C3/3′). The newly formed bridging ligand of the [3]ferrocenophane **13a** shows very typical ^{1}H-NMR signals at δ 5.96 (5H), 5.24 and 5.04 (7H/H′, in benzene-d_6) and ^{13}C-NMR signals at δ 147.1, 142.7 (C4, C6), 111.4 and 110.6 (C5, C7), in addition to the signals attributed to the piperidino substituent attached at carbon atom C4 (see Scheme 3).

Fig. 1 shows a view of the molecular structure of **13a** in the solid state (with unsystematical atom numbering scheme). It exhibits an almost unstrained ferrocene framework [9]. The attachment of the unsaturated C$_3$-bridge has resulted in only a marginal tilting of the Cp ligands at iron (angle between the Cp-planes in **13a**: $\alpha = 12.8°$; in **2**: $\alpha = 13.6°$ [2]). The Cp(cen-

troid)–Fe–Cp(centroid) angle in **13a** is 172°. The individual metal–carbon bond lengths of the (C1–C5)Cp ligand amount to 2.055(2) (both Fe–C2, Fe–C3); the Fe–C1 distance is 2.022(2), the Fe–C4 bond length 2.031(2) Å. The Fe–C5 (i.e. –C(ipso)) bond is still slightly shorter at 1.990(2) Å. A similar pattern is observed at the other mono-substituted C$_5$H$_4$ ligand.
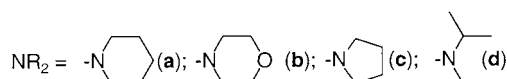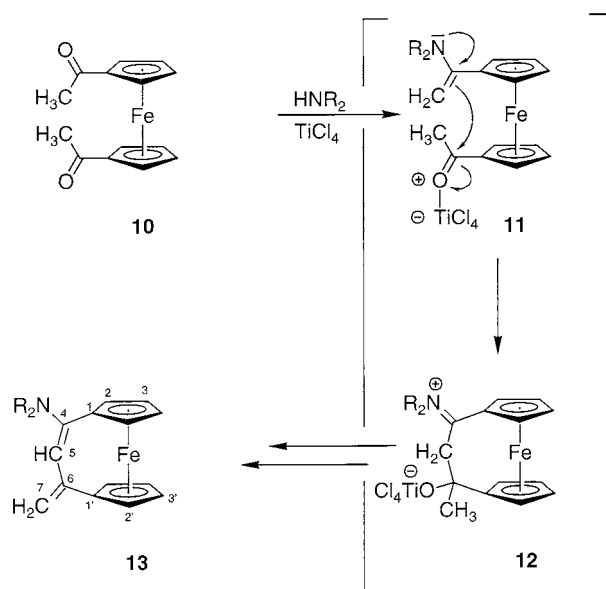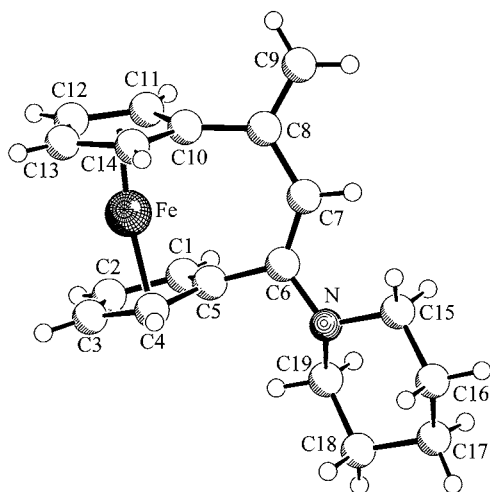

Scheme 2.

Scheme 3.

Fig. 1. A view of the molecular structure of complex **13a** (with unsystematical atom numbering scheme). Selected bond lengths (Å) and angles (°): C1–C2 1.430(3), C2–C3 1.419(3), C3–C4 1.425(2), C4–C5 1.429(3), C1–C5 1.430(2), C5–C6 1.493(2), C6–N 1.409(2), C10–C11 1.431(2), C10–C14 1.426(3), C11–C12 1.422(3), C12–C13 1.427(3), C13–C14 1.425(3), C8–C10 1.482(3), N–C15 1.463(2), C15–C16 1.522(3), C16–C17 1.519(3), C17–C18 1.521(3), C18–C19 1.520(3), N–C19 1.471(2), C5–C6–C7 123.84(15), C5–C6–N 113.44(13), N–C6–C7 122.65(14), C9–C8–C10 118.37(17), C7–C8–C9 119.73(17), C7–C8–C10 121.91(15); for additional data see the text.

Again the bonds of iron to the distal pair of Cp ligands are rather long (Fe–C12, 2.060(2); Fe–C13, 2.047(2) Å). The adjacent Fe–C11 (2.039(2) Å) and Fe–C14 (2.010(2) Å) connections are slightly shorter, and the Fe–C10 bond is further decreased in length at 2.001(2) Å. The Cp rings are attached in 1,3-positions (i.e. at the carbon atoms marked as C6 and C8 in Fig. 1) at the 1-amino-1,3-butadiene framework, that was formed by the condensation reaction. The dienamine moiety exhibits the typical bond alternation (C6–C7, 1.354(2); C7–C8, 1.467(3); C8–C9, 1.340(3) Å). The adjacent connecting bonds to the Cp rings are in the expected range of $C(sp^2)$–$C(sp^2)$ single bonds (see Fig. 1). The bond angles around the carbon atoms C6, C7 and C8 are in the typical range of a $C(sp^2)$-containing framework (the largest deviation is observed at C7: 129.6(2)°, (C6–C7–C8); see Fig. 1). These features indicate that complex **13a** contains a rather unstrained bridged metallocene framework, which is in accord with its straightforward formation in the applied enamine condensation reaction.

Other secondary amines can be used as well to achieve the coupling of the two functional groups of the 1,1′-diacetylferrocene starting material **10** under the influence of $TiCl_4$ to yield the condensation products **13**. The corresponding 1,3-annelated dienamino-[3]ferrocenophanes **13b**–**d** were readily obtained under similar conditions from **10**/$TiCl_4$ and the amines morpholine (**b**), pyrrolidine (**c**) or methyl-isopropylamine (**d**). The respective compounds **13b**–**d** were obtained in

moderate to good yields. They show very similar spectroscopic features of the unsaturated core [3]ferrocenophane moiety as described for **13a** (for details see Section 3). This series of reactions and the preceding ansa-zirconocene coupling reactions (see above) [7] show that intramolecular condensation involving enamine chemistry is very useful in constructing and functionalizing organometallic frameworks. Adapting organic functional group chemistry for extending the scope of organometallic synthetic methodology is actively pursued in our laboratory.

3. Experimental

Reactions were carried out under argon using Schlenk-type glassware or in a glovebox. NMR spectra were measured on a Bruker AC 200 P FT NMR spectrometer (^{1}H, 200.13; ^{13}C, 50.32 MHz; atom numbering as given in Scheme 3); melting points given were obtained by DSC. 1,1′-Diacetylferrocene (**10**) was prepared according to a standard literature procedure [10].

3.1. Preparation of 13a

A solution of $TiCl_4$ (0.98 ml, 1.68 g, 8.88 mmol) in 40 ml of pentane was added dropwise with stirring at 0°C for 20 min, to a suspension of 2.0 g (7.4 mmol) of 1,1′-diacetylferrocene (**10**) and 11.9 ml (10.22 g, 120 mmol) of piperidine in 80 ml of pentane. The mixture was allowed to warm to r.t. and stirred for an additional 5 h. A precipitate was then removed by filtration and the solvent removed from the clear yellow filtrate to yield 1.84 g (78%) of **13a**. Recrystallization from ether gave single crystals that were suited for the X-ray crystal structure analysis, m.p. 75°C (dec. 164°C, DSC). ^{1}H-NMR (benzene-d_6): $\delta = 5.96$ (s, 1H, 5-H), 5.24 (s, 1H, 7-H), 5.04 (s, 1H, 7-H′), 4.32 (m, 2H, Cp–H), 4.22 (m, 2H, Cp–H), 4.04 (m, 4H, Cp–H), 2.86 (m, 4H), and 1.27–1.10 (bm, 6H, piperidino–CH_2) ppm. ^{13}C-NMR (benzene-d_6): $\delta = 147.1$, 142.7 (C-4/C-6), 111.4, 110.6 (C-5/C-7), 71.7, 70.5, 70.2, 70.1 (C2, C3/C2′, C3′), 49.6, 25.9, 24.6 (piperidino–CH_2). IR (KBr): $\tilde{\nu} = 3083$ (m), 2927 (s), 2919 (s), 2914 (m), 1593 (s), 1228 (s), 1114 (s), 1092 (s), 1023 (s), 866 (s), 823 (s), 805 (s), 790 (s) cm^{-1}. Anal. Calc. for $C_{19}H_{21}NFe$ (319.22): C, 71.49; H, 6.63; N, 4.39. Found: C, 70.99; H, 6.27; N, 4.17%. HRMS Calc.: 319.1023. Found: 319.1020.

3.1.1. X-ray crystal structure analysis of 13a

Formula $C_{19}H_{21}NFe$, $M = 319.22$, yellow crystal, $0.35 \times 0.20 \times 0.20$ mm, $a = 16.892(1)$, $b = 10.913(1)$, $c = 9.227(1)$ Å, $\beta = 118.76(1)°$, $V = 1491.1(2)$ Å^3, $D_{calc} = 1.422$ g cm^{-3}, $F(000) = 672$ e, $\mu = 10.04$ cm^{-1}, absorption correction via SORTAV ($0.720 \leq T \leq 0.825$), $Z = 4$, monoclinic, space group Cc (no. 9), $\lambda = 0.71073$

Å, $T = 198$ K, ω and φ scans, 5389 reflections collected ($\pm h$, $\pm k$, $\pm l$), $[(\sin\theta)/\lambda] = 0.71$ Å^{-1}, 3078 independent and 3023 observed reflections $[I \geq 2\sigma(I)]$, 190 refined parameters, $R = 0.022$, $wR_2 = 0.055$, max. residual electron density 0.24 (-0.27) e Å^{-3}, Flack parameter $-0.01(1)$, hydrogens calculated and refined as riding atoms. Data set was collected with an Nonius Kappa CCD diffractometer on a rotating anode generator. Programs used: data acquisition COLLECT, data reduction Denzo-SMN, absorption correction SORTAV, structure solution SHELXS-97, structure refinement SHELXL-97, graphics SCHAKAL-92.

3.2. Preparation of 13b

1,1′-Diacetylferrocene (2.0 g, 7.4 mmol), morpholine (5.16 g, 60 mmol) and TiCl$_4$ (1.68 g, 8.88 mmol) were reacted analogously as described above in pentane to yield 808 mg (34%) of 13b, m.p. 70°C. ^{1}H-NMR (benzene-d_6): $\delta = 5.65$ (s, 1H, 5-H), 5.26 (d, 1H, 7-H, $^2J = 1$ Hz), 5.06 (d, 1H, 7-H′, $^2J = 1$ Hz), 4.29 (m, 2H, Cp–H), 4.15 (m, 2H, Cp–H), 4.04 (m, 4H, Cp–H), 3.42–3.37 (m, 4H), 2.72–2.67 (morpholino–CH$_2$) ppm. IR (KBr): $\tilde{v} = 3089$ (w), 3978 (w), 2957 (m), 2949 (m), 1598 (s), 1442 (s), 1264 (vs), 1118 (vs), 1106 (vs), 1096 (vs), 1036 (vs), 1014 (vs), 870 (s), 862 (s), 818 (s), 800 (s) cm^{-1}. Anal. Calc. for C$_{18}$H$_{19}$NOFe (321.20): C, 67.31; H, 5.96; N, 4.36. Found: C, 68.01; H, 6.35; N 4.52%. HRMS Calc.: 321.0816. Found: 321.0814.

3.3. Preparation of 13c

Analogously as described above 2.0 g (7.4 mmol) of 10 were treated with 10.0 ml (8.52 g, 120 mmol) of pyrrolidine and 1.68 g (8.88 mmol) of TiCl$_4$ in pentane to yield 1.25 g (55%) of 13c as an orange–yellow solid, m.p. 75°C. ^{1}H-NMR (benzene-d_6): $\delta = 5.59$ (s, 1H, 5-H), 5.31 (d, 1H, 7-H, $^2J = 1$ Hz), 5.00 (d, 1H, 7-H′, $^2J = 1$ Hz), 4.34 (m, 2H, Cp–H), 4.13 (m, 2H, Cp–H), 4.06 (m, 4H, Cp–H), 2.95–2.89 (m, 4H), 1.44–1.37 (pyrrolidino–CH$_2$) ppm. ^{13}C-NMR (benzene-d_6): $\delta = 142.8$, 142.4 (C-4/C-6), 109.0, 108.0 (C-5/C-7), 90.3, 84.7 (C-1/C-1′), 71.3, 70.5, 69.9, 69.8 (C-2, C-2′, C-3, C-3′), 48.7, 25.4 (pyrrolidino–CH$_2$) ppm. IR (KBr): $\tilde{v} = 2965$ (m), 2958 (m), 2938 (m), 1586 (s), 1459 (s), 1262 (s), 1098 (s), 1079 (s), 1032 (s), 1021 (vs), 851 (s), 817 (s), 806 (s), 798 (s) cm^{-1}. HRMS Calc. for C$_{18}$H$_{19}$NFe (305.20): 305.0867. Found: 305.0878.

3.4. Preparation of 13d

The reaction of 1.94 g (7.16 mmol) of 10 with 8.96 ml (6.29 g, 86 mmol) of methyl-isopropylamine and 0.94 ml (1.60 g, 8.52 mmol) of TiCl$_4$ in pentane analogously as described above gave 906 mg (41%) of 13d, m.p. 54°C. ^{1}H-NMR (benzene-d_6): $\delta = 5.66$ (s, 1H, 5-H),

5.24 (d, 1H, 7-H, $^2J = 2$ Hz), 5.01 (d, 1H, 7-H′, $^2J = 2$ Hz), 4.34 (m, 2H, Cp–H), 4.18 (m, 2H, Cp–H), 4.12 (m, 2H, Cp–H), 4.05 (m, 2H, Cp–H), 3.83 (sept, 1H, CHMe$_2$, $^3J = 7$ Hz), 2.41 (s, 3H, CH$_3$), 0.76 (d, 6H, CH(CH$_3$)$_2$, $^3J = 7$ Hz) ppm. ^{13}C-NMR (benzene-d_6): $\delta = 145.8$, 142.3 (C-4/C-6), 108.8, 108.0 (C-5/C-7), 89.9, 84.0 (C-1/C-1′), 71.1, 70.4, 69.9, 69.6 (C-2, C-2′, C-3, C-3′), 49.2 (CHMe$_2$), 30.6 ([N]CH$_3$), 19.6 (CH(CH$_3$)$_2$) ppm. IR (KBr): $\tilde{v} = 3080$ (w), 2965 (m), 2945 (m), 1589 (m), 1259 (s), 1089 (s), 1020 (s), 1017 (s), 859 (m), 799 (s) cm^{-1}. Anal. Calc. for C$_{18}$H$_{21}$NFe (307.22): C, 70.37; H, 6.89; N, 4.56. Found: C, 68.92; H, 6.71; N, 4.49%. HRMS Calc.: 307.1023. Found: 307.1031.

4. Supplementary material

Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication No. CCDC-116695. Copies of the data can be obtained free of charge on application to The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-1223-336033, e-mail: deposit@ccdc.cam.ac.uk).

References

[1] (a) A. Eisenstadt, M. Cais, Isr. J. Chem. 5 (1967) 37p. (b) T.D. Turbitt, W.E. Watts, J. Organomet. Chem. 46 (1972) 109. (c) P. Dodey, B. Gautheron, C.R. Hebd. Seance Acad. Sci. Ser. C (1975) 1113. (d) W. Crawford, T.D. Turbitt, W.E. Watts, J. Organomet. Chem. 105 (1976) 341.

[2] (a) M. Sališová, Š. Toma, E. Solčániová, J. Organomet. Chem. 132 (1977) 419. (b) E. Gyepes, T. Glowiak, Š. Toma, J. Soldánová, J. Organomet. Chem. 276 (1984) 209. (c) E. Gyepes, T. Glowiak, Š. Toma, J. Organomet. Chem. 316 (1986) 163.

[3] For two formally related aldol examples see: (a) M. Sališova, Š. Toma, E. Solčániová, Coll. Czech. Chem. Commun. 45 (1980) 1290. (b) Y. Omote, R. Kobayashi, Y. Nakada, N. Sugiyama, Bull. Chem. Soc. Jpn. 46 (1973) 3315. For indications of a reversible intramolecular aldol coupling of 10 see: (c) C.R. Hauser, C.E. Cain, J. Org. Chem. 23 (1958) 1142. (d) C.E. Cain, T.A. Mashburn, C.R. Hauser, J. Org. Chem. 26 (1961) 1030. (e) C.R. Hauser, T.A. Mashburn, J. Org. Chem. 26 (1961) 1795.

[4] (a) I.M. Paushkin, L.S. Polak, T.P. Vishnyakova, I.I. Patalakh, F.F. Macchus, T.A. Sokolinskaya, J. Polym. Sci. C 4 (1963) 1481. (b) H. Kono, M. Shiga, I. Motoyama, K. Hata, Bull. Chem. Soc. Jpn. 42 (1969) 3267. (c) A. Kasahara, T. Izumi, I. Shimizu, Chem. Lett. (1979) 1317. (d) S. Kamiyama, A. Kasa-

hara, T. Izumi, I. Shimizu, H. Watabe, Bull. Chem. Soc. Jpn. 54 (1981) 2079. (e) J. Mirek, S. Rachwał, T. Górecki, B. Kawałek, P. Milart, E. Szneler, J. Organomet. Chem. 344 (1988) 363. (f) J.J.C. Erasmus, G.J. Lamprecht, J.C. Swarts, A. Roodt, A. Oskarsson, Acta Crystallogr. C 52 (1996) 3000.

[5] In contrast, Michael additions are frequently used to prepare [5]ferrocenophanes or larger ring systems. For examples see: (a) T.A. Mashburn, C.E. Cain, C.R. Hauser, J. Org. Chem. 25 (1960) 1982. (b) M. Furdik, Š. Toma, J. Suchy, P. Elecko, Chem. Zvesti, 15 (1961) 45. (c) Š. Toma, A. Gaplovsky, Coll. Czech. Chem. Commun. 47 (1983) 1988. (d) R. Dabard, H. Patin, Bull. Soc. Chim. Fr. (1973) 2158. (e) I.H. Barr, W.E. Watts, Tetrahedron 24 (1968) 3219.

[6] Reviews: (a) Fe organic compounds, Gmelin Handbook of Inorganic Chemistry, 8th ed., vol. A8, Springer, Berlin, 1986. (b) B.W. Rockett, G. Marr, J. Organomet. Chem. 416 (1991) 327 and preceding annual reviews by these authors.

[7] (a) S. Knüppel, G. Erker, R. Fröhlich, Angew. Chem. (1999), in press. See also: (b) S.-D. Bai, X.-H. Wei, J.-P. Guo, D.-S. Liu, Z.-Y. Zhou, Angew. Chem. (1999), in press.

[8] W.A. White, H. Weingarten, J. Org. Chem. 32 (1967) 213.

[9] J.C. Green, Chem. Soc. Rev. 27 (1998) 263.

[10] (a) M. Rosenblum, R.B. Woodward, J. Am. Chem. Soc. 80 (1958) 5443. See also: (b) A.N. Nesmeyanov, E.V. Leonova, N.S. Kochetkova, A.I. Malkova, J. Organomet. Chem. 96 (1975) 271.