Structural Features of Lithio[3]ferrocenophane Systems Bearing Stabilizing Dimethylamino Substituents

Chao Chen, Roland Fröhlich,[#] Gerald Kehr, and Gerhard Erker*

Organisch-Chemisches Institut der Universität Münster, Corrensstrasse 40, 48149 Münster, Germany

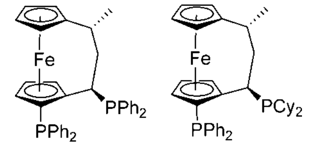
Received February 28, 2008

Treatment of the α-dimethylamino[3]ferrocenophane derivative **3** with *n*-butyllithium results in a directed *o*-metalation at the adjacent Cp ring of the ferrocene unit to selectively yield the (*R**,*R**,*p*-*S**) diastereomer **4**. Similarly, lithiation of *rac*-**12** gives (*R**,*p*-*S**)-**13**. Both these compounds form *meso*-type dimers in the crystal that feature a central C_2Li_2 four-membered-ring moiety. Compound **13** crystallizes with excess *n*-butyllithium to form a (**13**·*n*-BuLi) dimer that was also characterized by X-ray diffraction. Directed lithiation of the nonbridged ferrocene derivative 1-(dimethylaminobenzyl)ferrocene (**16**) with *tert*-butyllithium resulted in an opposite stereoselectivity to yield (*R**,*p*-*R**)-**17**, which forms a chiral dimeric structure in the solid state, as was revealed by its X-ray crystal structure analysis.

Introduction

Ferrocene-based ligand systems have played an increasingly important role in homogeneous catalysis, especially in the asymmetric formation of organic target molecules.[1] Chelate ligands such as Josiphos, Walphos, Ferriphos, and many more[2] have consequently been used extensively in asymmetry catalysis, especially in asymmetric catalytic hydrogenation and related processes. We[3] and others[4] have contributed to this field by the design and synthesis of various chiral [3]ferrocenophane-derived chelate ligand systems. So far, the P,P-chelate ligands **1** and **2** (see Scheme 1) have shown an interesting performance as components in palladium-catalyzed alternating CO/ethene[5] or asymmetric alternating CO/propene copolymerization,[6] respectively.

Scheme 1



rac-**1** (*R*, *R*, *p*-*R*)-**2**

The synthesis of most of the ligands mentioned above and many of their congeners at one stage involves a stereoselective-directed lithiation step at the ferrocene nucleus. Analogous to the corresponding arene lithiation chemistry[7] this is usually achieved in ferrocene chemistry by treatment of a precursor, which features a suitably positioned pendant −OR or $-NR_2$ substituent, with, for example, butyllithium. Li^+ coordination during the reaction then often very efficiently leads to highly regioselective arene or ferrocene metalation.[3,5,6] Quenching of the resulting ferrocenyl lithium derivative with a suitable electrophile (e.g., halogen, organic carbonyl, chlorophosphine derivatives) then leads to the respective functionalized product. Scheme 2 shows a typical example.

The respective ferrocenyl-Li systems, e.g., **4**, and their structural and chemical features, play a decisive role in this chemistry. Since there were surprisingly few structural studies

---

* Corresponding author. E-mail: erker@uni-muenster.de.

[#] X-ray crystal structure analyses.

(1) Togni, A.; Hayashi, T., Eds. *Ferrocenes: Homogenous Catalysis, Organic Synthesis, Materials Science*; VCH: Weinheim, 1995. Togni, A.; Dorta, R.; Kollner, C.; Pioda, G. *Pure Appl. Chem.* **1998**, *70*, 1477–1485. Ojima, I., Ed. *Catalytic Asymmetric Synthesis*; Wiley-VCH: New York, 2000. Barbaro, P.; Bianchini, C.; Giambastiani, G.; Parisel, S. L. *Coord. Chem. Rev.* **2004**, *248*, 2131–2150. Arrayás, R. G.; Adrio, J.; Carretero, J. C. *Angew. Chem.* **2006**, *118*, 7836–7878; *Angew. Chem., Int. Ed.* **2006**, *45*, 7674−7715.

(2) Togni, A.; Breutel, C.; Schnyder, A.; Spindler, F.; Landert, H.; Tijani, A. *J. Am. Chem. Soc.* **1994**, *116*, 4062–4066. Ireland, T.; Grossheimann, G.; Wieser-Jeunesse, C.; Knochel, P. *Angew. Chem.* **1999**, *111*, 3397–3400; *Angew. Chem., Int. Ed.* **1999**, *38*, 3212−3215. Perea, J. J. A.; Lotz, M.; Knochel, P. *Tetrahedron: Asymmetry* **1999**, *10*, 375–384. Sturm, T.; Weissensteiner, W.; Spindler, F. *Adv. Synth. Catal.* **2003**, *345*, 160–164. Lopez, F.; Harutyunyan, S. R.; Minnaard, A. J.; Feringa, B. L. *J. Am. Chem. Soc.* **2004**, *126*, 12784–12785. Chen, W.; Mbafor, W.; Roberts, S. M.; Whittall, J. *J. Am. Chem. Soc.* **2006**, *128*, 3922–3923. Chen, W.; McCormack, P. J.; Mohammed, K.; Mbafor, W.; Roberts, S. M.; Whittall, J. *Angew. Chem.* **2007**, *119*, 4219–4222; *Angew. Chem., Int. Ed.* **2007**, *46*, 4141−4144. For some recent use of the Josiphos ligand see e.g.: Bercot, E. A.; Rovis, T. *J. Am. Chem. Soc.* **2004**, *126*, 10248–10249. Hsiao, Y.; Rivera, N. R.; Rosner, T.; Krska, S. W.; Njolito, E.; Wang, F.; Sun, Y.; Armstrong, J. D., III; Grabowski, E. J. J.; Tillyer, R. D.; Spindler, F.; Malan, C. *J. Am. Chem. Soc.* **2004**, *126*, 9918–9919. Lipshutz, B. H.; Servesko, J. M.; Taft, B. R. *J. Am. Chem. Soc.* **2004**, *126*, 8352–8353. Walphos: Moran, W. J.; Morken, J. P. *Org. Lett.* **2006**, *8*, 2413–2415. Ferriphos: Cho, Y.-h.; Zunic, V.; Senboku, H.; Olsen, M.; Lautens, M. *J. Am. Chem. Soc.* **2006**, *128*, 6837–6846.

(3) Liptau, P.; Knüppel, S.; Kehr, G.; Kataeva, O.; Fröhlich, R.; Erker, G. *J. Organomet. Chem.* **2001**, *637*, 621–630. Liptau, P.; Tebben, L.; Kehr, G.; Wibbeling, B.; Fröhlich, R.; Erker, G. *Eur. J. Inorg. Chem.* **2003**, *3590−3600*, 4261. Tebben, L.; Kehr, G.; Fröhlich, R.; Erker, G. *Synthesis* **2004**, 1971–1976. Tebben, L.; Neumann, M.; Kehr, G.; Fröhlich, R.; Erker, G.; Losi, S.; Zanello, P. *Dalton Trans.* **2006**, 1715–1720. Nilewski, C.; Neumann, M.; Tebben, L.; Fröhlich, R.; Kehr, G.; Erker, G. *Synthesis* **2006**, 2191–2200.

(4) Sturm, T.; Weissensteiner, W. *Organometallics* **2002**, *21*, 1766–1774. Cayuela, E.; Jalón, F. A.; Manzano, B. R.; Espino, G.; Weissensteiner, W.; Mereiter, K. *J. Am. Chem. Soc.* **2004**, *126*, 7049–7062.

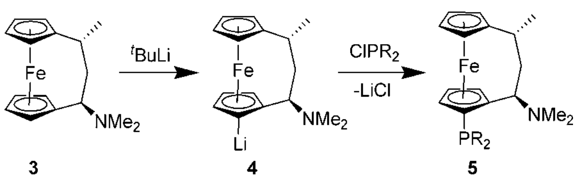
(5) Liptau, P.; Seki, T.; Kehr, G.; Abele, A.; Fröhlich, R.; Erker, G.; Grimme, S. *Organometallics* **2003**, *22*, 2226–2232.

(6) Liptau, P.; Tebben, L.; Kehr, G.; Fröhlich, R.; Erker, G.; Hollmann, F.; Rieger, B. *Eur. J. Org. Chem.* **2005**, 1909–1918.

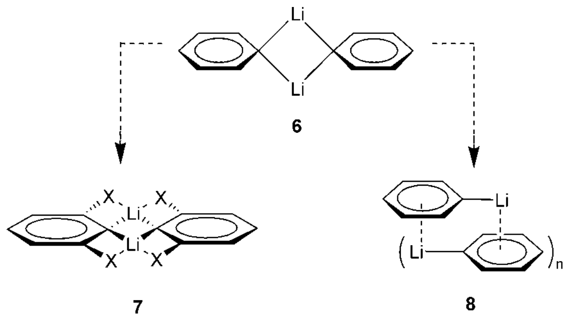
(7) Jastrzebski, J. T. B. H.; van Koten, G.; Konijn, M.; Stam, C. H. *J. Am. Chem. Soc.* **1982**, *104*, 5490–5491. Reich, H. J.; Gudmundsson, B. *J. Am. Chem. Soc.* **1996**, *118*, 6074–6075. Reich, H. J.; Goldenberg, W. S.; Gudmundsson, B.; Sanders, A. W.; Kulicke, K. J.; Simon, K.; Guzei, I. A. *J. Am. Chem. Soc.* **2001**, *123*, 8067–8079. Kronenburg, C. M. P.; Rijnberg, E.; Jastrzebski, J. T. B. H.; Kooijman, H.; Spek, A. L.; van Koten, G. *Eur. J. Org. Chem.* **2004**, 153–159. Arink, A. M.; Kronenburg, C. M. P.; Jastrzebski, J. T. B. H.; Lutz, M.; Spek, A. L.; Gossage, R. A.; van Koten, G. *J. Am. Chem. Soc.* **2004**, *126*, 16249–16258. Kronenburg, C. M. P.; Rijnberg, E.; Jastrzebski, J. T. B. H.; Kooijman, H.; Lutz, M.; Spek, A. L.; Gossage, R. A.; van Koten, G. *Chem.−Eur. J.* **2005**, *11*, 253–261.

10.1021/om8001894 CCC: $40.75

Scheme 2



Scheme 3



of lithioferrocene-containing systems reported in the literature,[8–10] we decided to investigate the structural properties of the $-NMe_2$-substituted lithio[3]ferrocenophane system (**4**) and some related complexes.

Such systems might be compared with the preferred structural arrangements of the underlying metal-free carbocyclic lithioarene compounds, which often exhibit dimeric or higher aggregated structures in the solid state. Ligand-free phenyllithium (**6**) features an orthogonal dimeric structure in the crystal[11] (see Scheme 3). Several donor ligand-stabilized analogues feature similar structures,[12] but such systems show a tendency toward two major structural distortions. The attachment of donor substituents in the *ortho*-positions often leads to bending of the $C_{ipso}Li_2C_{ipso}$ plane[13] toward a nearly planar tetracoordinate carbon environment[14–16] such as **7** in Scheme 3. Alternatively, an unsymmetrical shifting of the Li-positions may occur that ultimately leads to structures of the type **8**, which have been found in some higher or mixed aggregates (see Scheme 3).[17]

Combinations of these distortions may in some cases occur.[18] We will see how the α-NMe_2-substituted lithio[3]ferrocenophane systems structurally behave in comparison to these ArLi reference systems.

Results and Discussion

Syntheses. The lithio[3]ferrocenophane system **4** (see Scheme 2) was obtained from a synthetic sequence previously reported by us. 1,1′-Diacetylferrocene **9**[19] was subjected to an intramolecular Mannich condensation reaction to yield the unsaturated [3]ferrocenophane derivative **10**[20] (see Scheme 4). This was then catalytically hydrogenated (Pd/C, H_2) to give a *trans*/*cis* mixture of the saturated amino[3]ferrocenophane derivative **3**. Recrystallization followed by treatment with *n*-butyllithium eventually gave pure **4** (*R**,*R**,*p*-*S** diastereomer) after crystallization from ether (70%).

---

(8) Lai, C.-K.; Naiini, A. A.; Brubaker, C. H., Jr *Inorg. Chim. Acta* **1989**, *164*, 205–210. Ahlberg, P.; Davidsson, O.; Hilmersson, G.; Löwendahl, M.; Håkasson, M. *J. Chem. Soc., Chem. Commun.* **1994**, 1573–1574. Voigt, F.; Fischer, A.; Pietzsch, C.; Jacob, K. *Z. Anorg. Allg. Chem.* **2001**, *627*, 2337–2343.

(9) Jacob, K.; Schäfer, M.; Steiner, A.; Sheldrick, G. M.; Edelmann, F. T. *J. Organomet. Chem.* **1995**, *487*, C18–C20. Jacob, K.; Scholz, J.; Pietzsch, C.; Edelmann, F. T. *J. Organomet. Chem.* **1995**, *501*, 71–77. Bucaille, A.; Le Borgne, T.; Ephritikhine, M.; Daran, J.-C. *Organometallics* **2000**, *19*, 4912–4914.

(10) Seidel, N.; Jacob, K.; Fischer, A. K.; Pietzsch, C.; Zanello, P.; Fontani, M. *Eur. J. Inorg. Chem.* **2001**, 145–151. Henderson, K. W.; Kennedy, A. R.; Mulvey, R. E.; O'Hara, C. T.; Rowlings, R. B. *Chem. Commun.* **2001**, 1678–1679.

(11) Thoennis, D.; Weiss, E. *Chem. Ber.* **1978**, *111*, 3157–3161. Dinnebier, R. E.; Behrens, U.; Obricht, F. *J. Am. Chem. Soc.* **1998**, *120*, 1430–1433. Actually, $[PhLi]_n$ is a polymer of dimers in the crystal, which shows both structural motifs, namely, σ-coordination to the single "carbanionic" aryl *ipso*-carbon atom to form the central Li_2C_2 four-membered ring and coordination to the π-system of the next adjacent aryl group. Although $[(Et_2O)LiPh]_4$ is a tetramer (see: Hope, H.; Power, P.P. *J. Am. Chem. Soc.* **1983**, *105*, 5320−5324), the dimer like in $[(TMEDA)LiPh]_2$ is a leading structural motif in aryl lithiums, like the structures presented in this paper. See e.g.: Stey, T.; Stalke, D. Lead structures in lithium organic chemistry. In *The Chemistry of Organolithium Compounds*; Rappoport, Z., Marek, I., Eds.; John Wiley & Sons: Chichester, 2004; pp 47−120. See also for a comparison: Dinnebier, R. E.; Behrens, U.; Obricht, F. *Organometallics* **1997**, *16*, 3855–3858.

(12) See also: Goldstein, M. J.; Wenzel, T. T. *Helv. Chim. Acta* **1984**, *67*, 2029–2036. Olmstead, M. M.; Power, P. P. *J. Am. Chem. Soc.* **1990**, *112*, 8008–8014. Markies, P. R.; Schat, G.; Akkerman, O. S.; Bickelhaupt, F.; Smeets, W. J. J.; van der Sluis, P.; Spek, A. L. *J. Organomet. Chem.* **1990**, *393*, 315–331. Lenders, B.; Grove, D. M.; Smeets, W. J. J.; von der Sluis, P.; Spek, A. L.; van Koten, G. *Organometallics* **1991**, *10*, 786–791.

(13) van Koten, G.; Noltes, J. G. *J. Am. Chem. Soc.* **1979**, *101*, 6593–6599. Harder, S.; Boersma, J.; Brandsma, L.; Kanters, J. A.; Duisenberg, A. J. M.; van Lenthe, J. H. *Organometallics* **1991**, *10*, 1623–1627. Harder, S.; Brandsma, L.; Kanters, J. A.; Duisenberg, A.; van Lenthe, J. H. *J. Organomet. Chem.* **1991**, *420*, 143–154. Harder, S.; Ekhart, P. F.; Brandsma, L.; Kanters, J. A.; Duisenberg, A. J. M.; von Ragué Schleyer, P. *Organometallics* **1992**, *11*, 2623–2627. Pepels, A.; Günther, H.; Amoureux, J.-P.; Fernandéz, C. *J. Am. Chem. Soc.* **2000**, *122*, 9858–9859. Gossage, R. A.; Jastrzebski, J. T. B. H.; van Koten, G. *Angew. Chem.* **2005**, *117*, 1472–1478; *Angew. Chem., Int. Ed.* **2005**, *44*, 1448−1452.

(14) Chandrasekhar, J.; von Ragué Schleyer, P. *J. Chem. Soc., Chem. Commun.* **1981**, 260–261. Harder, S.; Boersma, J.; Brandsma, L.; van Heteren, A.; Kanters, J. A.; Bauer, W.; von Ragué Schleyer, P. *J. Am. Chem. Soc.* **1988**, *110*, 7802–7806. Markies, P. R.; Schat, G.; Villena, A.; Akkerman, O. S.; Bickelhaupt, F.; Smeets, W. J. J.; Spek, A. L. *J. Organomet. Chem.* **1991**, *411*, 291–302. Sorger, K.; Schleyer, P. v. R.; Stalke, D. *J. Chem. Soc., Chem. Commun.* **1995**, 2279–2280. Sorger, K.; Schleyer, P. v. R.; Fleischer, R.; Stalke, D. *J. Am. Chem. Soc.* **1996**, *118*, 6924–6933. Jantzi, K. L.; Guzei, I. A.; Reich, H. J. *Organometallics* **2006**, *25*, 5390–5395.

(15) Hoffmann, R.; Alder, R. W.; Wilcox, C. F., Jr *J. Am. Chem. Soc.* **1970**, *92*, 4992–4993. Röttger, D.; Erker, G. *Angew. Chem.* **1997**, *109*, 840–856; *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 812−827. Erker, G. *Chem. Soc. Rev.* **1999**, *28*, 307–314. Erker, G.; Venne-Dunker, S.; Kehr, G.; Kleigrewe, N.; Fröhlich, R.; Mueck-Lichtenfeld, C.; Grimme, S. *Organometallics* **2004**, *23*, 4391–4395.

(16) Frenking, G. *Chem. Phys. Lett.* **1984**, *111*, 529–532. Buchwald, S. L.; Lucas, E. A.; Davis, W. M. *J. Am. Chem. Soc.* **1989**, *111*, 397–398. Bosold, F.; Zulauf, P.; Marsch, M.; Harms, K.; Lohrenz, J.; Boche, G. *Angew. Chem.* **1991**, *103*, 1497–1499; *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1455−1457. Poumbga, C. N.; Bénard, M.; Hyla-Kryspin, I. *J. Am. Chem. Soc.* **1994**, *116*, 8259–8265.

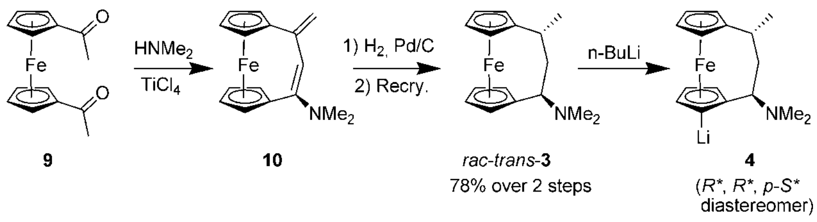
(17) Markies, P. R.; Schat, G.; Akkerman, O. S.; Bickelhaupt, F.; Smeets, W. J. J.; Spek, A. L. *Organometallics* **1990**, *9*, 2243–2247. Waggoner, K. M.; Power, P. P. *Organometallics* **1992**, *11*, 3209–3214. Ruhlandt-Senge, K.; Ellison, J. J.; Wehmschulte, R. J.; Pauer, F.; Power, P. P. *J. Am. Chem. Soc.* **1993**, *115*, 11353–11357.

(18) Arvidsson, P. I.; Ahlberg, P.; Hilmersson, G. *Chem.−Eur. J.* **1999**, *5*, 1348–1354. Goldfuss, B.; Khan, S. I.; Houk, K. N. *Organometallics* **1999**, *18*, 2927–2929.

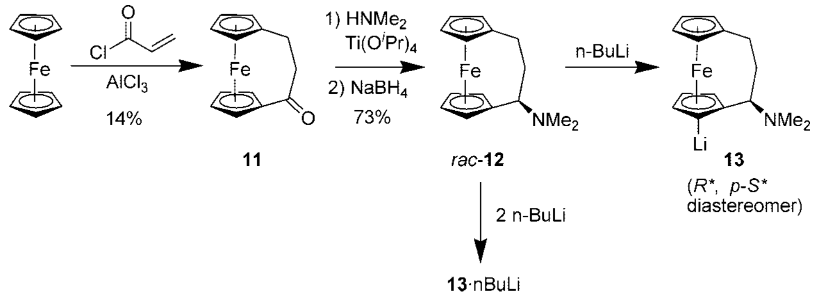
(19) Woodward, R. B.; Rosenblum, M.; Whiting, M. C. *J. Am. Chem. Soc.* **1952**, *74*, 3458–3459. Schwink, L.; Knochel, P. *Chem.−Eur. J.* **1998**, *4*, 950–968.

(20) Knüppel, S.; Fröhlich, R.; Erker, G. *J. Organomet. Chem.* **1999**, *586*, 218–222. Knüppel, S.; Fröhlich, R.; Erker, G. *J. Organomet. Chem.* **2000**, *595*, 308–312. See also: Knüppel, S.; Erker, G.; Fröhlich, R. *Angew. Chem.* **1999**, *111*, 2048–2051; *Angew. Chem., Int. Ed.* **1999**, *38*, 1923−1926. Bai, S.-D.; Wei, X.-H.; Guo, J.-P.; Liu, D.-S.; Zhou, Z.-Y. *Angew. Chem.* **1999**, *111*, 2051–2054; **1999**, *38*, 1926−1928. Knüppel, S.; Wang, C.; Kehr, G.; Fröhlich, R.; Erker, G. *J. Organomet. Chem.* **2005**, *690*, 14–32.

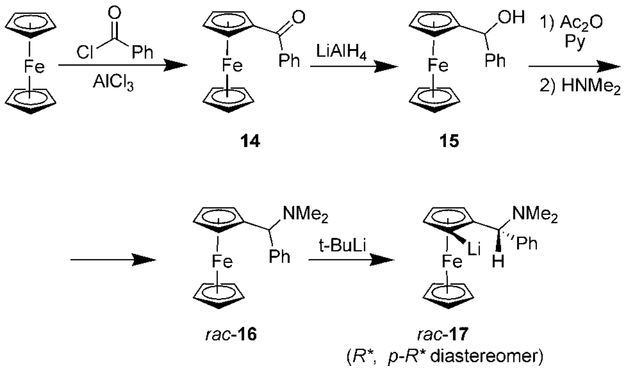
Scheme 4



Scheme 5



Scheme 6



For a comparison we prepared the related α-dimethylamino[3]-ferrocenophane (**13**). The sequence[21] started with a Friedel–Crafts reaction of ferrocene with acryloyl chloride to give **11**. Reductive amination (dimethylamine/Ti(O^{i}Pr)$_4$; NaBH$_4$) then gave the product (**12**). Its lithiation with 1 molar equiv of *n*-butyllithium in ether followed by crystallization gave **13** in >70% yield (see Scheme 5). Treatment of **12** with 2 molar equiv of *n*-BuLi under similar conditions eventually gave large crystals of **13**·*n*-BuLi in 60% yield.

Also for the purpose of structural comparison we prepared the related unbridged (α-dimethylamino)lithioferrocene derivative (**17**). The corresponding starting material (**16**) was synthesized according to a literature procedure[22] (see Scheme 6). The final lithiation step (*t*-BuLi in ether/pentane) furnished the product (**17**), which crystallized with coordination of a molecule of ether in the solid state.

Descriptions of Crystal Structures of the Lithiated Ferrocenophane Compounds. The chirality centers in *trans*-**3** are not independent of each other. Consequently, selective directed lithiation at the proximal position of the ferrocene C_5H_3 ring adjacent to the α-NMe$_2$ substituent must lead to the diastereomer of **4** with the relative configuration (*R**,*R**,*p*-*S**). In the crystal isolated dimers of **4** were found. Of the two possible combinations we find only the *meso*-dimer (see Figure 1). It contains a pair of monomeric units of opposite relative stereochemistry bridged by two lithium atoms. The lithium atoms and their adjacent ferrocene *ipso*-carbon centers form a central C_2Li_2 four-membered substructure. The dimeric structure of *meso*-**4** is constrained in the solid state by a crystallographic center of symmetry.

The side view of the structure (see Figure 1, bottom) shows that the central C_2Li_2 unit features a marked rhombohedral distortion. One lithium atom is almost coplanar with its adjacent C_5H_4 ring (Li1–C14: 2.144(3) Å; angle centroid Cp–C14–Li: 147.4°). The other lithium atom (Li1*–C14: 2.103(3) Å) features a slightly shorter Li–C distance and is displaced out of the C10–C14 plane (angle centroid Cp–C14–Li*: 135.2°) toward the iron center [Li1 is 0.426 Å below the C10–C14 plane; Li1* is 1.407 Å above]. The Li1···Li1* distance is 2.391(5) Å. The Li1*···Fe1 separation amounts to 2.853(2) Å.

The adjacent amine nitrogen atom is coordinated to Li1 (Li1–N1: 2.067(3) Å). The resulting five-membered heterocycle features an envelope-shaped conformation with the atoms Li1, C14, C10, and C9 being oriented in one plane and N1 (the "tip of the envelope") out of the plane away from the central Fe atom (angle C9–N1–Li1: 98.3(1)°; deviation of N1 from the adjacent plane: 0.774 Å).

In the structure of the *meso*-**4** dimer the two ferrocene units are offset to each other by half a ferrocene unit, which is determined by the specific combination of the positions of the connecting lithium atoms. In the dimer the central C_2Li_2 plane deviates markedly from the mean Cp planes of their adjacent ferrocene units (angle between the C14, Li1, C14*, Li1* vs the C10–C14 plane: 55.4°).

Complex **13** features a very similar dimeric structure in the crystal (*meso*-**13** dimer). It is composed at two chiral monomeric subunits of opposite stereochemistry (i.e., *R*,*p*-*S*/*S*,*p*-*R*). Again, the *meso*-dimer contains a rhombohedrally shaped central C_2Li_2 ring system that is rotated by ca. 55.7° from an orthogonal arrangement with the adjacent Cp planes. The characteristic individual bond lengths amount to 2.150(4) Å (Li1–C14) and

---

[21] Rosenblum, M.; Banerjee, A. K.; Danieli, N.; Fish, R. W.; Schlatter, V. *J. Am. Chem. Soc.* **1963**, *85*, 316–324. Dixneuf, P.; Dabard, R. *Bull. Soc. Chim. Fr.* **1972**, *7*, 2838–47. Dixneuf, P.; Dabard, R. *Bull. Soc. Chim. Fr.* **1972**, *7*, 2847–54. Turbitt, T. D.; Watts, W. E. *J. Organomet. Chem.* **1972**, *46*, 109–348. Cayuela, E. M.; Xiao, L.; Sturm, T.; Manzano, B. R.; Jalon, F. A.; Weissensteiner, W. *Tetrahedron: Asymmetry* **2000**, *11*, 861–869. Faux, N.; Razafimahefa, D.; Picart-Goetgheluck, S.; Brocard, J. *Tetrahedron: Asymmetry* **2005**, *16*, 1189–1197.

[22] Fukuzawa, S.-i.; Fujimoto, K.; Komuro, Y.; Matsuzawa, H. *Org. Lett.* **2002**, *4*, 707–709. Tappe, K.; Knochel, P. *Tetrahedron: Asymmetry* **2004**, *15*, 91–102.

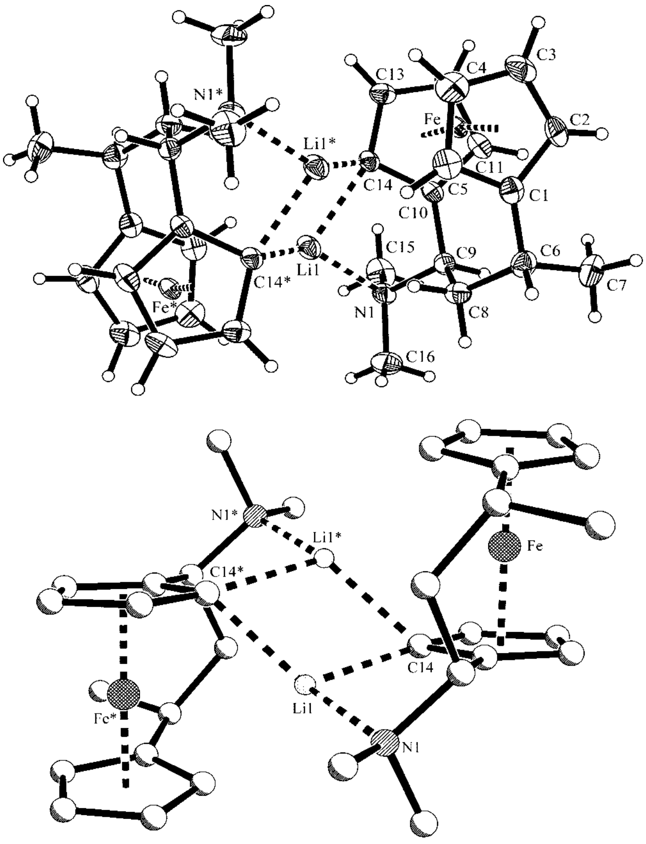


Figure 1. Two views of the molecular structure of the *meso*-**4** dimer in the crystal (thermal ellipsoids at the 50% level). Selected bond lengths (Å) and angles (deg): $\mathrm{Fe-C_{Cp}}$ 2.006(1)−2.106(1), Fe−Li1* 2.853(2), C5−Li1* 2.638(3), C1−C6 1.508(2). C6−C7 1.529 (2). C6−C8 1.543(2), C8−C9 1.549(2), C9−C10 1.519(2), C9−N1 1.501(2), C9−Li1 2.725(3), C10−Li1 2.739(3), C14−Li1 2.144(3), C14−Li1* 2.103(3), N1−Li1 2.067(3); C1−C6−C7 112.1(1), C1−C6−C8 112.8(1), C7−C6−C8 111.8(1), C6−C8−C9 116.3(1), C8−C9−C10 114.1(1), C8−C9−N1 109.7(1), C10−C9−N1 107.0(1), C9−N1−Li1 98.3(1), N1−Li1−C14 89.2(1), N1−Li1−C14* 137.0(1), C14−Li1−C14*111.5(1).

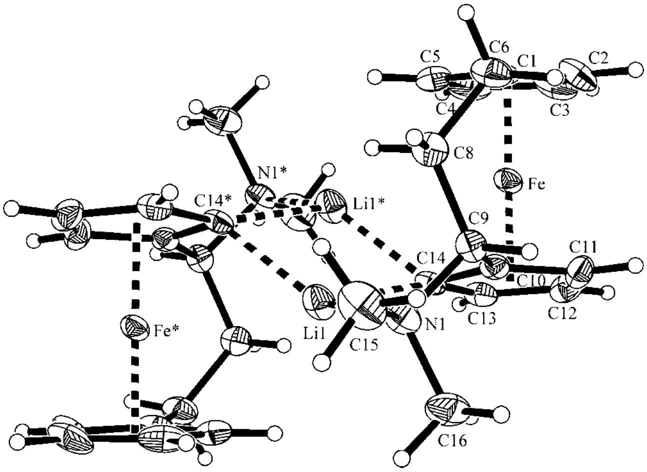


Figure 2. Projection of the structure of the *meso*-**13** dimer (thermal ellipsoids at the 50% level). Selected bond lengths (Å) and angles (deg: $\mathrm{Fe-C_{Cp}}$ 2.001(2)−2.104(2), Fe−Li1* 2.882(3), C5−Li1* 2.647(4), C1−C6 1.503(3). C6−C8 1.534(3), C8−C9 1.544(3), C9−C10 1.518(2), C9−N1 1.499(2), C9−Li1 2.717(4), C10−Li1 2.738(4), C14−Li1 2.150(4), C14−Li1* 2.105(4), N1−Li1 2.073(4); C1−C6−C8 114.7(2), C6−C8−C9 115.3(2), C8−C9−C10 114.2(2), C8−C9−N1 110.2(2), C10−C9−N1 106.7(2), C9−N1−Li1 97.7(1), N1−Li1−C14 89.1(2), N1−Li1−C14* 136.9(2), C14−Li1−C14*111.7(2).

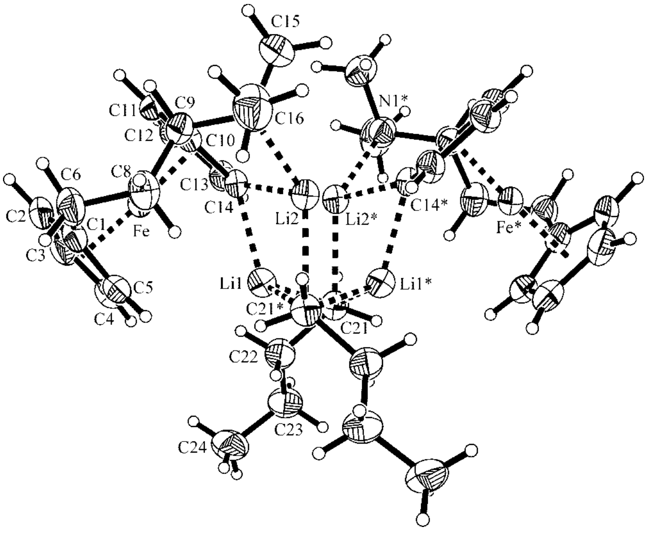


Figure 3. View of the molecular structure of the **13**•*n*-BuLi dimer (thermal ellipsoids at the 50% level). Selected bond lengths (Å) and angles (deg): $\mathrm{Fe-C_{Cp}}$ 2.002(2)−2.094(2), C1−C6 1.495(3). C6−C8 1.537(3), C8−C9 1.540(3), C9−C10 1.518(3), C9−N1 1.502(2), C9−Li2 2.781(4), C14−Li2 2.252(4), C14−Li2* 2.226(3), N1−Li2 2.088(4), C14−Li1 2.136(4), C21−Li1 2.212(4), C21−Li1* 2.219(4), C21−Li2* 2.316(4); C1−C6−C8 114.0(2), C6−C8−C9 114.2(2), C8−C9−C10 114.5(2), C8−C9−N1 110.0(2), C10−C9−N1 107.5(1), C9−N1−Li2 100.3(1), N1−Li2−C14 88.4(2), N1−Li2−C14* 122.4(2), C14−Li2−C14* 107.0(1).

2.073(4) Å (Li1−N1). The internal chelate ring features bond angles of 89.1(2)° (C14−Li1−N1), 97.7(1)° (Li1−N1−C9), 106.7(1)° (N1−C9−C10), 123.1(2)° (C9−C10−C14), and 96.9(2)° (C10−C14−Li1). The Li1 ••• Li1* distance in the *meso*-**13** dimer amounts to 2.388(7) Å.

The molecular structure of the *n*-butyllithium adduct [**13**•*n*-BuLi dimer] is markedly different. It contains molecular entities that are comprised of two lithioferrocene (**13**) and two *n*-butyllithium subunits. In this case the pair of [3]ferrocenophane entities is of the same chirality [i.e., *R**,*p*-*S**,*R**,*p*-*S**]. In the overall C_2-symmetrical structure two lithium atoms (Li2, Li2*) are bridging the ferrocene units such that they are both oriented close to the adjacent C_5H_3 plane (C14−Li2: 2.252(4) Å, angle Li2−C14−Li2*: 70.9(1)°). The angle between the Li1−C14−Li2 and C10−C14 planes amounts to 49.4°. Consequently, we note a weak N1−Li2 (2.088(4) Å) interaction in this subunit. The additional pair of lithium atoms brought in by the formal addition of two *n*-butyllithium building blocks are oriented such that the total of four alkali metal atoms form a tetrahedral Li_4 cluster in the center of this molecular arrangement. It is characterized by bond distances Li1−Li2 2.457(5) Å, Li1−Li1* 2.443(7) Å, Li2−Li2* 2.597(6) Å, and Li1−Li2* 2.547(5) Å. The pair of *n*-butyl substituents is C_2-symmetrically oriented toward the outside. Their α-CH_2 groups are bridging between pairs of lithium atoms [Li1−C21*: 2.219(4) Å, Li2−C21*: 2.316(4) Å, angle Li1−C21*−Li2: 65.6(2)°].

The X-ray crystal structure analysis of *rac*-**17** has revealed that the directed lithiation of the open aminomethylferrocene precursor **16** has resulted in a different stereochemical result as compared to the bridged α-amino[3]ferrocenophane systems (**3**). The latter consistently led to the formation of lithioferrocenophanes with *R**,*p*-*S** configuration [e.g., (*R**,*R**,*p*-*S**)-**4** or (*R**,*p*-*S**)-**13**], whereas

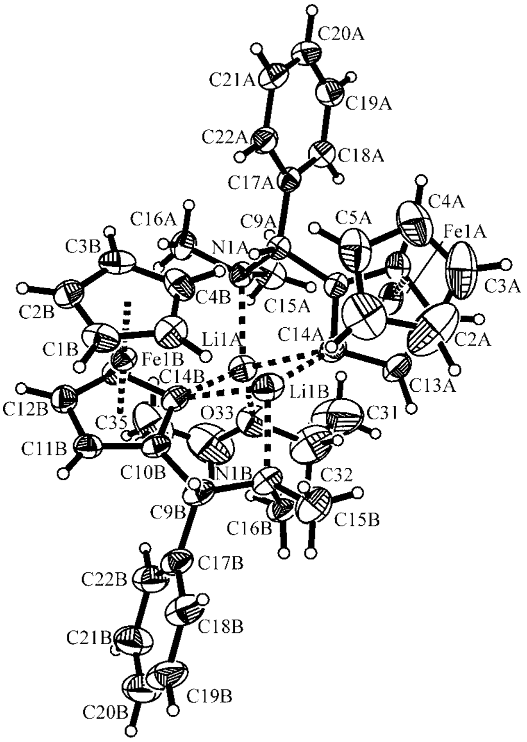


Figure 4. View of the molecular geometry of the **17**$\cdot$0.5Et$_2$O dimer (thermal ellipsoids at the 50% level). Selected bond lengths (Å) and angles (deg): Fe−C$_{Cp}$ 2.025(3)−2.111(2) [2.033(2)−2.119(2)], C9−C10 1.515(2) [1.522(3)], C9−N1 1.500(2) [1.495(3)], C14−Li1A 2.234(4) [2.231(4)], C14−Li1B 2.119(4) [2.128(4)], N1−Li1 2.198(4) [2.059(4)], O33−Li1A 1.983(3); C10−C9−N1 108.6(1) [110.1(2)], C9−N1−Li1 98.1(1) [103.7(2)], N1−Li1−C14 87.0(1) [88.8(2)], N1−Li1−C14* 117.6(2) [124.3(2)], C14−Li1−C14* 108.8(1) [117.5(2)], N1A−Li1A−O33 112.0(2).

directed lithiation of **16** resulted in the formation of product **17** with a "like" configuration, i.e., (*R**,*p*-*R**)-**17**.

In the crystal we find isolated dimeric molecular entities of **17**. Each dimer is composed of a pair of monomeric lithiocene derivatives of the same chirality [i.e., *R**,*p*-*R**,*R**,*p*-*R**]. There is an additional ether molecule present in each dimer. The ferrocene moieties are connected by a pair of lithium atoms. The bridging is unsymmetrical (bond lengths C14A−Li1A: 2.234(4) Å, C14A−Li1B: 2.119(4) Å, C14B−Li1B: 2.128(4) Å, C14B−Li1A: 2.231(4) Å). The bond angles inside the central C$_2$Li$_2$ four-membered ring amount to C14A−Li1A−C14B 108.8(1)°, C14B−Li1B−C14A 117.5(2)°, Li1A−C14B−Li1B 66.5(1)°, Li1A−C14A−Li1B 66.6(1)°. The angle between the Li1A−C14A−Li1B plane and the adjacent C10A−C14A Cp plane is 90.6°; the corresponding angle between the C10B−C14B and Li1A−C14B−Li1B planes amounts to 38.4°. This places the structure of the **17** dimer somewhere between the extremes of **6** and **7** (see Scheme 3 and Figure 4).

We note that lithium atom Li1A carries a coordinated diethyl ether ligand (Li1A−O33: 1.983(3) Å). It is also weakly bonded to the nitrogen center of the adjacent −NMe$_2$ group (Li1A−N1A: 2.198(4) Å, angles Li1A−N1A−C9A: 98.1(1)°, N1A−Li1A−O33: 112.0(2)°). Lithium atom Li1B is coordinated only to its neighboring dimethylamino nitrogen center (Li1B−N1B: 2.059(4) Å).

Some Conclusions

The stereochemistry of the directed lithiation of the α-dimethylamino[3]ferrocenophane systems **3** and **12** is determined by the rigid orientation of the −NMe$_2$ substituent at the C$_3$-bridge. This relatively large group in all cases adopts a pseudoequatorial position. It directs the attack of the organolithium base selectively into the ferrocene ring position, which leads to the formation of a single diastereoisomeric lithio[3]ferrocenophane derivative with (*R**,*R**,*p*-*S**) configuration. This was for the first time directly observed in this study, by characterizing the molecular structures of the respective products **4** and **13**. Quenching of the lithio[3]ferrocenophane (*R**,*R**,*p*-*S**)-**4** with ClPR$_2$ reagents had previously resulted in the formation of the corresponding (*R**,*R**,*p*-*R**)-**5** derivatives: the change of *p*-*S** to *p*-*R** results from a formal Cahn, Ingold, Prelog priority reversal. In contrast, the nonbridged system (**16**) leads to a different stereochemical result, again to the best of our knowledge for the first time observed here directly. Here a specific conformational control of the pendent −CHPh(NMe$_2$) substituent leads to the specific formation of the (*R**,*p*-*R**)-**17** diastereomer at the ferrocenyllithium stage.

The results of our X-ray diffraction analyses of these lithium-bridged dimers reveal some interesting structural arrangements. The structures of the lithiated [3]ferrocenophanes (**4**, **13**) feature both a rotation of the central Li$_2$C$_2$ plane relative to the adjacent Cp planes and a shifting of the lithium atoms. This can be described as a combination of both the **6** → **7** and **6** → **8** distortions as they were schematically depicted in Scheme 3. However, in both cases the overall structure is still reminiscent of a regular (i.e., perpendicular) aryl lithium dimer structure.

The same is true for the **13**$\cdot$*n*-BuLi dimer. In this case this distorted bonding arrangement seems to be strongly stabilized by the presence of the pair of added *n*-butyllithium units, which gives rise to the formation of a central Li$_4$ cluster inside the supramolecular architecture.[23]

The structure of the **17**$\cdot$0.5Et$_2$O dimer represents an interesting borderline case between the structural extremes **6** and **7** sketched in Scheme 3. Here the open architecture has apparently induced a marked rotation of the Li−Li vector from an orthogonal arrangement (reminiscent of **6**) toward a more coplanar orientation. It seems that a more flexible system may conformationally favor this rather unusual planarized geometry, especially if that is stabilized by the coordination of an additional ligand.

Experimental Section

General Procedures. All experiments were carried out under a dry argon atmosphere using standard Schlenk techniques or in a glovebox. Solvents (including deuterated solvents used for NMR) were dried and distilled prior to use. ^{1}H and ^{13}C spectra were recorded on a Bruker AV300 or a Varian 600 Unity Plus spectrometer. ^{1}H and ^{13}C data were determined by 1D- (APT, TOCSY, NOE) and 2D-NMR experiments (^{13}C,^{1}H GHSQC, ^{13}C,^{1}H GHMBC, and ^{1}H,^{1}H COSY). Elemental analysis was performed on a Foss-Heraeus CHNO-Rapid. The starting materials *rac*-*trans*-**3**,[3] *rac*-**12**,[21] and *rac*-**16**[22] were prepared according to the reported procedures.

X-ray Crystal Structure Analyses. Data sets were collected with a Nonius KappaCCD diffractometer, equipped with a rotating anode generator. Programs used: data collection COLLECT (Nonius B.V., 1998), data reduction Denzo-SMN (Otwinowski, Z.; Minor, W. *Methods Enzymol.* **1997**, *276*, 307−326), absorption correction SORTAV (Blessing, R. H. *Acta Crystallogr.* **1995**, *A51*, 33−37; Blessing, R. H. *J. Appl. Crystallogr.* **1997**, *30*, 421−426) and Denzo

---

[23] See for a comparison: Marsch, M.; Harms, K.; Lochmann, L.; Boche, G. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 308–309; *Angew. Chem.* **1990**, *102*, 334−336 [(*n*-BuLi)$_4$(LiO-*t*-Bu)$_4$]Davies, R. P.; Raithby, P. R.; Snaith, R. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1215–1217; *Angew. Chem.* **1997**, *109*, 1261−1263 [(Et$_2$O)$_4$(*n*-BuLi)$_2${Ph(C$_6$H$_4$Li)NLi}$_2$(LiNPh$_2$)]

(Otwinowski, Z.; Borek, D.; Majewski, W.; Minor, W. *Acta Crystallogr.* **2003**, *A59*, 228−234), structure solution SHELXS-97 (Sheldrick, G. M. *Acta Crystallogr.* **1990**, *A46*, 467−473), structure refinement SHELXL-97 (Sheldrick, G. M. Universität Göttingen, 1997; Sheldrick, G. M. *Acta Crystallogr.* **2008**, *A64*, 112−122), graphics XP (BrukerAXS, 2000) and SCHAKAL (Keller, E. Universität Freiburg, 1997).

Preparation of Lithio[3]ferrocenophane 4. A solution of *rac-trans*-**3** (420 mg, 1.5 mmol) in diethyl ether (10 mL) was cooled with an ice−salt bath (ca. −20 °C). After *n*-BuLi (1.6 mL, 1.6 M in hexane, 3.2 mmol) was added, the cooling bath was removed and the solution was kept without any agitation for 48 h. Big crystals of **4** (300 mg, 70%) were isolated by decanting the solvent in a glovebox. Anal. Calcd for $C_{16}H_{20}FeLiN$: C 66.47, H 6.97, N 4.84. Found: C 65.49, H 7.08, N 4.51. ^1H NMR (300 MHz, d_8-THF, 298 K): δ 1.23 (d, $^3J = 7.4$ Hz, 3H, 7-H), 2.06 (ddd, $^2J = 12.8$ Hz, $^3J = 3.6$, 2.1 Hz, 1H, 8-H), 2.22 (s, 6H, NMe_2), 2.67 (dd, $^3J = 11.7$, 2.1 Hz, 1H, 9-H), 2.76 (qt, $^3J = 7.4$, 3.6 Hz, 1H, 6-H), 3.28 (ddd, $^2J = 12.8$, $^3J = 11.9$, 3.6 Hz, 1H, 8-H′), 3.74, 3.94, 3.95, 4.43 (each m, each 1H, 2,3,4,5-H), 3.90, 4.15 (each m, each 1H, 11,13-H), 3.98 (m, 1H, 12-H). $^{13}C\{^1H\}$ NMR (75 MHz, d_8-THF, 298 K): δ 17.5 (C7), 29.4 (C6), 45.8 (NMe_2), 45.8 (C8), 64.6 (C9), 65.8, 67.1, 69.4, 72.2 (C2,3,4,5), 69.7 (C12), 74.4, 81.0 (C11,13), 90.1 (C10), 92.4 (C1), n.o. (C14).

X-ray crystal structure analysis for 4: formula $C_{16}H_{20}FeLiN$, $M = 289.12$, orange crystal 0.55 × 0.25 × 0.25 mm, $a = 7.5675(1)$ Å, $b = 9.2846(2)$ Å, $c = 10.4913(2)$ Å, $\alpha = 106.946(1)$, $\beta = 98.020(1)°$, $\gamma = 102.853(2)°$, $V = 670.75(2)$ Å^3, $\rho_{calc} = 1.432$ g cm^{-3}, $\mu = 1.106$ mm^{-1}, empirical absorption correction ($0.582 \le T \le 0.770$), $Z = 2$, triclinic, space group $P\bar{1}$ (No. 2), $\lambda = 0.71073$ Å, $T = 198$ K, ω and φ scans, 6967 reflections collected ($\pm h$, $\pm k$, $\pm l$), $[(\sin \theta)/\lambda] = 0.67$ Å^{-1}, 3227 independent ($R_{int} = 0.034$) and 3069 observed reflections [$I \ge 2\sigma(I)$], 175 refined parameters, $R = 0.026$, $wR^2 = 0.070$, max. residual electron density 0.36 (−0.45) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

Preparation of Lithio[3]ferrocenophane 13. A solution of *rac*-**12** (270 mg, 1.0 mmol) in ether (5 mL) was cooled with an ice−salt bath (ca. −20 °C). After *n*-BuLi (0.6 mL, 1.6 M in hexane, 0.96 mmol) was added, the bath was removed and the solution was kept without any agitation for 48 h. Big crystals of **13** were isolated by decanting the solvent in a glovebox (198 mg, 72%). Anal. Calcd for $C_{15}H_{18}FeLiN$: C 65.49, H 6.60, N 5.09. Found: C 64.61, H 6.65, N 4.87. ^1H NMR (300 MHz, d_8-THF, 298): δ 1.88 (td, $^2J = 14.0$, $^3J = 14.0$, 2.3 Hz, 1H, 6-H), 2.13 (br m, 1H, H-8), 2.23 (s, 6H, NMe_2), 2.45 (dd, $^3J = 11.0$, 1.5 Hz, 1H, 9-H), 2.51 (dt, $^2J = 14.0$, $^3J = 3.4$ Hz, 1H, 6-H′), 3.10 (br m, 1H, 8-H′), 3.71, 3.87, 3.95, 4.40 (each br, each 1H, 2,3,4,5-H), 3.93, 3.99, 4.16 (each br, each 1H, 11,12,13-H). $^{13}C\{^1H\}$ NMR (75.0 MHz, d_8-THF, 298 K): δ 27.6 (C6), 38.8 (C8), 45.7(NMe_2), 65.9, 69.7, 70.4, 71.6 (C2,3,4,5), 70.0, 74.8, 80.9 (C11,12,13), 72.2 (C9), 87.6 (C1), 89.8 (C10), n.o. (C14).

X-ray crystal structure analysis for 13: formula $C_{15}H_{18}FeLiN$, $M = 275.10$, orange crystal 0.30 × 0.15 × 0.10 mm, $a = 7.4443(1)$ Å, $b = 9.2993(2)$ Å, $c = 9.9602(3)$ Å, $\alpha = 95.318(1)°$, $\beta = 108.510(1)°$, $\gamma = 102.226(2)°$, $V = 629.43(2)$ Å^3, $\rho_{calc} = 1.451$ g cm^{-3}, $\mu = 1.174$ mm^{-1}, empirical absorption correction ($0.720 \le T \le 0.892$), $Z = 2$, triclinic, space group $P\bar{1}$ (No. 2), $\lambda = 0.71073$ Å, $T = 198$ K, ω and φ scans, 5795 reflections collected ($\pm h$, $\pm k$, $\pm l$), $[(\sin \theta)/\lambda] = 0.67$ Å^{-1}, 3013 independent ($R_{int} = 0.039$) and 2587 observed reflections [$I \ge 2\sigma(I)$], 165 refined parameters, $R = 0.034$, $wR^2 = 0.080$, max. residual electron density 0.46 (−0.41) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

Preparation of Lithio[3]ferrocenophane 13·*n*-BuLi. A solution of *rac*-**12** (270 mg, 1.0 mmol) in ether (5 mL) was cooled with an ice−salt bath (ca. −20 °C). After *n*-BuLi (1.3 mL, 1.6 M in hexane, 2.08 mmol) was added, the bath was removed and the solution was kept without any agitation for 48 h at room temperature. Again the solution was cooled to −32 °C for crystallization. Crystalline **13**·*n*-BuLi was isolated by decanting the solvent in a glovebox (203 mg, 60%). A satisfactory result of element analysis for this compound was not obtained due to its high sensitivity. ^1H NMR (600 MHz, d_8-toluene, 298 K): δ −0.41(m)/−0.44 (br) (Σ 2H), 1.15 (pt, 3H), 1.72/1.92 (each m, each 1H), 1.76 (m, 2H) (Bu), 1.47 (s, 3H, NMe), 1.51/2.29 (each m, each 1H, 6-H), 1.93 (m, 1H, 9-H), 1.94/1.98 (each m, each 1H, 8-H), 2.02 (s, 3H, NMe), 3.82, 3.97, 4.25 (each m, each 1H, 11,12,13-H), 3.95, 3.96, 3.97, 4.00 (each m, each 1H, 2,3,4,5-H). $^{13}C\{^1H\}$ NMR (125 MHz, d_8-toluene, 298 K): δ 14.3, 32.7, 33.4, n.o. (Bu), 25.2 (C6), 39.5 (C8), 43.1 (NMe), 45.9 (NMe), 64.4, 67.5, 68.9, 71.8 (C2,3,4,5), 68.1 (C9), 71.4, 74.9, 78.1 (C11,12,13), 86.1 (C1), 98.2 (C10), n.o. (C14).

X-ray crystal structure analysis for 13·*n*-BuLi: formula $[C_{15}H_{18}FeLiN \cdot LiC_4H_9]_2$, $M = 678.29$, orange crystal 0.45 × 0.25 × 0.20 mm, $a = 21.6614(3)$ Å, $b = 10.6671(2)$ Å, $c = 19.0435(3)$ Å, $\beta = 124.613(1)°$, $V = 3621.46(10)$ Å^3, $\rho_{calc} = 1.244$ g cm^{-3}, $\mu = 0.828$ mm^{-1}, empirical absorption correction ($0.707 \le T \le 0.852$), $Z = 4$, monoclinic, space group $C2/c$ (No. 15), $\lambda = 0.71073$ Å, $T = 198$ K, ω and φ scans, 13 024 reflections collected ($\pm h$, $\pm k$, $\pm l$), $[(\sin \theta)/\lambda] = 0.66$ Å^{-1}, 4263 independent ($R_{int} = 0.048$) and 3394 observed reflections [$I \ge 2\sigma(I)$], 240 refined parameters, $R = 0.037$, $wR^2 = 0.102$, max. residual electron density 0.41 (−0.44) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

Preparation of 17. A solution of **16** (320 mg, 1.0 mmol) in ether (5 mL) was cooled with an ice−salt bath (ca. −20 °C). After *t*-BuLi (0.6 mL, 1.5 M in pentane, 0.9 mmol) was added, the bath was removed and the solution was kept without any agitation for 24 h. Big crystals of **17** (232 mg, 64%) were isolated by decanting the solvent in a glovebox. NMR data were obtained by dissolving the crystals at −78 °C and directly measured at −75 °C. At −5 °C the detected compound rearranged to a complex mixture (see the Supporting Information). Anal. Calcd for $(C_{19}H_{20}FeLiN)_2 \cdot Et_2O$: C 69.63, H 6.96, N 3.87. Found: C 69.39, H 6.91, N 3.86. ^1H NMR (600 MHz, d_8-THF, 198 K): δ 1.92 (br, 6H, NMe_2), 3.34 (br, 5H, Cp), 3.76, 3.93. 3.95 (each br, each 1H, 11,12,13-H), 4.02 (br, 1H, 9-H), 7.17 (pt, 1H, p-Ph), 7.31 (pt, 2H, m-Ph), 7.58 (pd, 2H, o-Ph). ^{13}C NMR (125 MHz, d_8-THF, 198 K): δ 45.5 (br, NMe_2), 67.7, 70.2, 76.5 (C11,12,13), 68.8 (Cp), 73.4 (C9), 99.0 (C10), 126.3 (p-Ph), 128.0 (m-Ph), 129.0 (o-Ph), 148.3 (i-Ph), n.o. (C14).

X-ray crystal structure analysis for 17·0.5Et$_2$O: formula $(C_{19}H_{20}FeLiN)_2{*}C_4H_{10}O$, $M = 724.42$, orange crystal 0.30 × 0.25 × 0.20 mm, $a = 10.9229(1)$ Å, $b = 12.9582(2)$ Å, $c = 13.9885(2)$ Å, $\alpha = 75.410(1)°$, $\beta = 84.683(1)°$, $\gamma = 83.606(1)°$, $V = 1899.88(4)$ Å^3, $\rho_{calc} = 1.266$ g cm^{-3}, $\mu = 0.797$ mm^{-1}, empirical absorption correction ($0.796 \le T \le 0.857$), $Z = 2$, triclinic, space group $P\bar{1}$ (No. 2), $\lambda = 0.71073$ Å, $T = 198$ K, ω and φ scans, 20 005 reflections collected ($\pm h$, $\pm k$, $\pm l$), $[(\sin \theta)/\lambda] = 0.66$ Å^{-1}, 8977 independent ($R_{int} = 0.054$) and 7248 observed reflections [$I \ge 2\sigma(I)$], 448 refined parameters, $R = 0.040$, $wR^2 = 0.104$, max. residual electron density 0.42 (−0.59) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

Acknowledgment. Financial support from the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and the Alexander von Humboldt-Stiftung (Forschungsstipendium to C.C.) is gratefully acknowledged. We thank the reviewers for helpful and interesting comments.

Supporting Information Available: Details of the X-ray crystal structure analyses and additional experimental and spectroscopic data. This material is available free of charge via the Internet at http://pubs.acs.org.

OM8001894