Synthesis and Structure of an Enantiomerically Pure C_2 Symmetric Ferrocenyl Carbene

by **Diego Broggini** and **Antonio Togni***

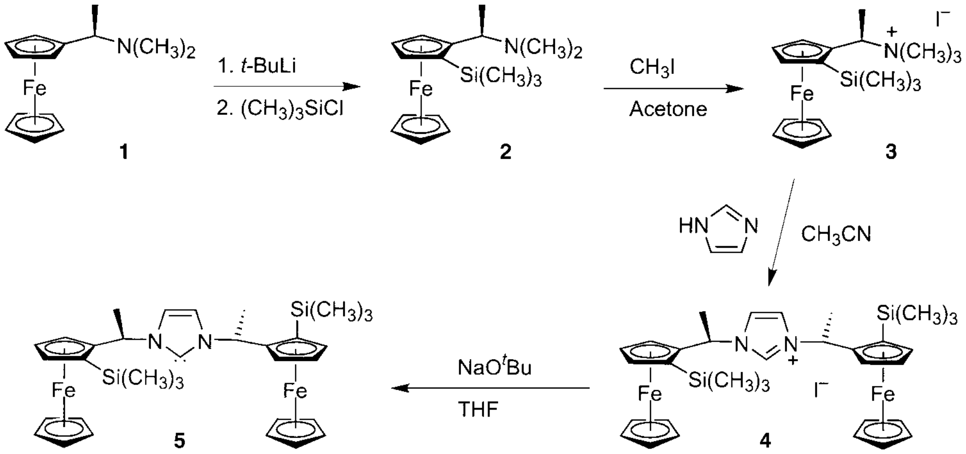
Department of Chemistry, Swiss Federal Institute of Technology, ETH-Hönggerberg,
CH-8093 Zürich (Tel.: 01 632 2236; e-mail: togni@inorg.chem.ethz.ch)

The straightforward, high-yield synthesis and X-ray structural analysis of the air-stable planar-chiral bis(ferrocenyl)carbene 1,3-bis-{(1*R*)-1-[(1*R*)-1-(trimethylsilyl)ferrocen-2-yl]ethyl}imidazol-2-ylidene (**5**) is reported. Compound **5** is obtained in four steps from the amine [(1*R*)-1-(dimethylamino)ethyl]ferrocene (**1**) upon diastereoselective silylation, methylation, nucleophilic substitution by imidazole, and deprotonation. The X-ray crystal structure of the free carbene shows the typical conformational features of the 1,2-disubstituted ferrocenyl units, as found in other ferrocenyl ligands derived from **1**.

1. Introduction. – Stable N-heterocyclic carbenes (NHCs) [1][2], mostly bearing bulky substituents at the N-atoms, are becoming ubiquitous ligands in organometallic chemistry [3] and homogeneous catalysis [4–11] as phosphine substitutes [12]. However, chiral enantiomerically pure derivatives are still quite rare, and only a very limited number of applications have been reported [13–17]. Furthermore, chiral ferrocenyl derivatives have proven very successful in asymmetric catalysis, as ligands often displaying both central and planar chirality, because of their great synthetic versatility [18]. These two observations prompted us to develop a simple synthesis of a ferrocene-based carbene for use as a monodentate ligand in asymmetric catalysis. We reasoned that such a preparation should start from a readily available chiral ferrocene derivative that would also be set up for a modular construction of possibly a range of related compounds. Most sensibly, this starting material should be the amine **1** ([(1*R*)-1-(dimethylamino)ethyl]ferrocene, *Scheme*) because of both its typical diastereoselective *ortho*-lithiation chemistry and the ease of nucleophilic replacement of the amino group by a variety of nucleophiles. Very recently, *Bolm et al.* reported a more elaborate preparation of a monoferrocenyl carbene starting from a chiral ferrocenyl sulfoxide [19].

2. Results and Discussion. – For a more straightforward preparation of a chiral ferrocenyl carbene, we thus chose to work with the known compound **2**, which is obtained in high yield after lithiation of **1** with *t*-BuLi and addition of Me_3SiCl, as shown in the *Scheme*. Subsequent methylation in acetone in the presence of 4.5 equiv. MeI led to the ammonium salt **3** in 90% yield. This compound is sensitive to moisture and is best stored under Ar at $-20°$, as it readily undergoes an elimination reaction to give the corresponding vinyl ferrocene. The 2D $^{14}N,^{1}H$ HMQC NMR spectrum of **3** shows a signal at δ 39.2 ppm that displays coupling only with the Me H-atoms at the stereogenic center (*Me*CH, $^{3}J(H,N) = 7$ Hz). Reacting 2.3 equiv. of **3** with imidazole in MeCN afforded, after double substitution, the imidazolium salt **4** in 70% yield as a pale

Scheme. *Four-Step Synthesis of the Stable Carbene* **5** *from the Commercially Available Amine* **1** *in 57% Overall Yield*



yellow powder. This material is air-stable and shows typical ^{1}H-NMR signals for the imidazolium H-atoms at δ 10.26 ppm (NC*H*N) and 6.87 ppm (*H*C=C*H*), and for the C-atoms at δ 134.4 and 120.0 ppm in the ^{13}C-NMR spectrum.

Compound **4** could be quantitatively converted to the target carbene **5** by deprotonation with 1.5 equiv. *t*-BuONa in THF, the course of the reaction being monitored by ^{1}H-NMR. After evaporation of the solvent, carbene **5** was dissolved in a pentane/toluene mixture, filtered, and crystallized at $-78°$. The carbene is clearly identified in the ^{13}C-NMR spectrum by the signal at δ 212.6 ppm. Further evidence is provided by the high-field shift of the signals of two olefinic H-atoms at δ 6.24 ppm, though this could also derive from the anisotropic shielding of the two ferrocene units, depending on the conformation.

Crystals suitable for an X-ray-diffraction study were obtained by cooling a saturated solution of **5** in toluene/pentane. Carbene **5** crystallizes in the monoclinic space group $P2_1$, but the molecule present in the asymmetric unit does not reside on the twofold symmetry axis. An ORTEP view of **5** is depicted in the *Figure*. The structure displays a typically small N(1)–C(8)–N(2) angle of 102° at the carbene center C(8) compared to the values for imidazolium salts of 107.6°–109.7° [1][20–22]. The bond lengths N(1/2)–C(9/10) and C(8)–N(1/2) are larger than the expected values for an imidazolium salt [1][20–22], and confirm the carbene nature of **5**. The overall conformation of the molecule is approximately C_2-symmetric such that the two Me_3Si groups are placed above and below the plane of the heterocycle. Relative to the same plane, the two ferrocene moieties assume a pseudo-equatorial orientation, however, protruding towards the region where a metal center should interact with the carbene center. It is, therefore, reasonable to assume that they will be 'sterically active' in complexes of **5**. The conformation of the ferrocene side-chain reflects the one typically observed also in *Josiphos*-type ligands, with the heteroatom substituent in a pseudo-axial position with respect to each of the ferrocenyl units [18].

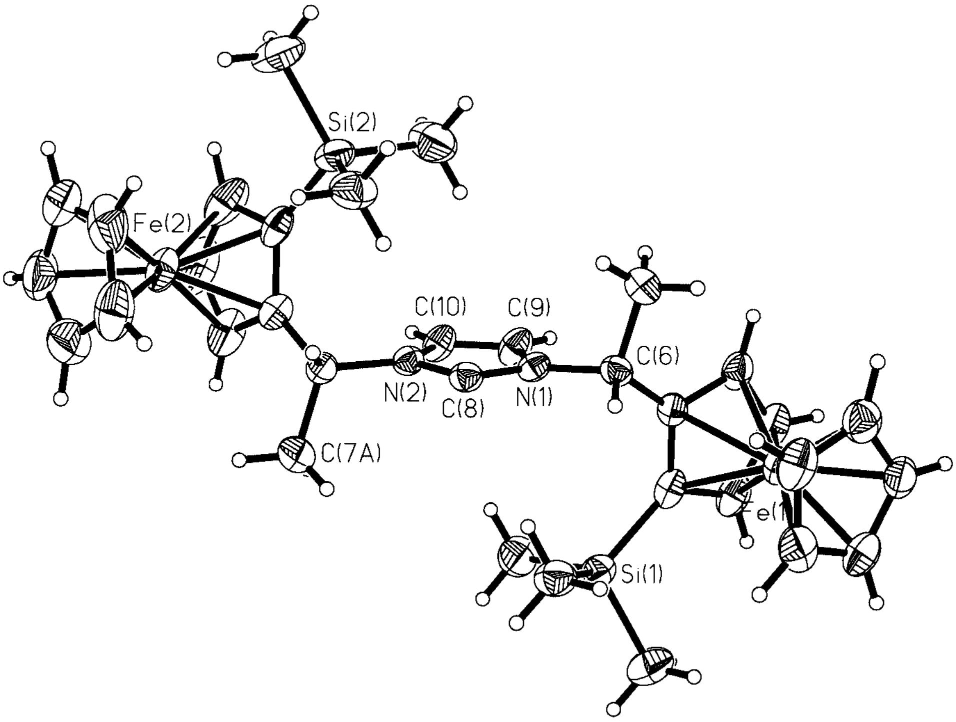


Figure. *ORTEP View* (30% probability ellipsoids) *of carbene* **5** *with H-atoms at calculated positions.* Selected bond lengths [Å] and angles [deg]: N(1)–C(8) 1.364(6), N(1)–C(9) 1.380(6), N(1)–C(6) 1.471(6), N(2)–C(8) 1.357(6), N(2)–C(10) 1.376(6), N(2)–C(6A) 1.478(6), C(9)–C(10) 1.328(6), C(8)–N(1)–C(9) 111.9(4), C(8)–N(1)–C(6) 121.9(4), C(9)–N(1)–C(6) 125.9(4), C(8)–N(2)–C(10) 113.0(4), C(8)–N(2)–C(6A) 120.2(4), N(2)–C(8)–N(1) 102.0(4).

3. Conclusions. – The simple synthesis reported here opens up a short route to a variety of stable C_2-symmetric chiral carbenes bearing two ferrocenyl groups. We are currently exploring the coordination chemistry of **5**, as well as potential applications in asymmetric catalysis.

We are grateful to *Heinz Rüegger* for assistance with 2D-NMR experiments and to the ETH for a Ph.D grant to *D.B.*

Experimental Part

*General. [(1*R*)-1-(Dimethylamino)ethyl]ferrocene* (**1**) was generously provided by *Solvias AG* (Basel). All commercially available reagents were used without further purification. MeCN and CH_2Cl_2 were freshly distilled from CaH_2, acetone from $CaSO_4$, Et_2O from NaK, and THF from Na. All reactions were performed under an inert atmosphere and air-sensitive substances were handled in a glove box. NMR Spectra: *Bruker DPX-250* and *-300*; δ in ppm, referenced to Me_4Si (= 0 ppm; ^1H, ^{28}Si) or solvent signal (^{13}C; δ ($CDCl_3$) 77.0; δ ((D_8)toluene) 137.5), J in Hz. MS: *Finnigan TSQ-7000* for electrospray ionisation (ESI), and *VG-TRIBRID* for electron impact (EI, 70 eV); *m/z* (rel. intensity in %).

*(1*R*)-2-[(1*R*)-1-(Dimethylamino)ethyl]-1-(trimethylsilyl)ferrocene* (**2**). A soln. of *t*-BuLi in pentane (41.2 ml; 1.65M, 77.8 mmol) was added at –78° to a soln. of 20.0 g (77.8 mmol) of **1** in 200 ml of Et_2O. After stirring for 30 min, the soln. was warmed to r.t. and stirred for 1 h. The mixture was then cooled to –78°, and

10.8 ml (85.4 mmol) of Me_3SiCl were added. After warming to r.t. overnight, the soln. was treated with 50 ml of H_2O. The org. layer was washed with H_2O (3 × 50 ml) and brine (2 × 50 ml), and dried ($MgSO_4$). Evaporation of the solvent yielded a crude product that was purified by flash chromatography (hexane/Et_2O containing 2% Et_3N): 24.2 g (94.5%) of **2**. Red oil. ^{1}H-NMR (250 MHz, $CDCl_3$): 0.25 (*s*, Me_3Si); 1.22 (*d*, $J = 6.6$, *Me*CH); 2.04 (*s*, Me_2N); 3.81 (*q*, $J = 6.6$, MeC*H*); 4.05 (*m*, 1 H, CH(cp)); 4.06 (*s*, 5 H, cp); 4.23 (*t*, $J = 2.4$, 1 H, CH(cp)); 4.28 (*m*, 1 H, CH(cp)).

*Trimethyl{(1*R*)-1-[(1*R*)-1-(trimethylsilyl)ferrocen-2-yl]ethyl}ammonium Iodide* (**3**). MeI (20 ml, 330 mmol) was added dropwise to a soln. of 24.2 g (73.4 mmol) of **2** in 200 ml of acetone at 0°. After 2 h at 0°, the soln. solidified. Et_2O was then added, the suspension was filtered, and the residue was washed with Et_2O (2 × 50 ml) and a mixture Et_2O/acetone (5 : 1, 2 × 50 ml). The powdery material thus obtained was dried and stored at −20° under Ar: 31.0 g (90%) of **3**. ^{1}H-NMR (250 MHz, $CDCl_3$): 0.37 (*s*, Me_3Si); 2.09 (*dt*, $J = 6.9$, 1.6, *Me*CH); 3.22 (*s*, Me_3N); 4.17 (*q*, $J = 6.9$, MeC*H*); 4.20 (*s*, 5 H, cp); 4.25 (*dd*, $J = 2.6$, 1.3, 1 H, CH(cp)); 4.64 (*m*, 2 H, CH(cp)). ^{14}N-NMR (18.059 MHz, $CDCl_3$): 39.2.

*1,3-Bis{(1*R*)-1-[(1*R*)-1-(trimethylsilyl)ferrocen-2-yl]ethyl}-1*H*-imidazolium Iodide* (**4**). A soln. of 5 g (10.6 mmol) of **3** and 0.314 g (4.6 mmol) 1*H*-imidazole in 40 ml of MeCN was stirred at r.t. for 72 h, whereby a white precipitate formed. CH_2Cl_2 (100 ml) and *t*-BuOMe (100 ml) were added, and the org. layer was washed with H_2O (6 × 100 ml) and brine (3 × 100 ml), and dried ($MgSO_4$). After filtration and evaporation, the raw product was crystallized from CH_2Cl_2/Et_2O, washed with Et_2O, and dried: 2.45 g (70%) of **4**. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.11 (*s*, 2 Me_3Si); 2.00 (*d*, $J = 6.8$, 2, *Me*CH); 4.17 (*dd*, $J = 2.4$, 1.1, 2 H, CH(cp)); 4.22 (*s*, 10 H, cp); 4.47 (*t*, $J = 2.4$, 2 H, CH(cp)); 4.57 (*dd*, $J = 2.4$, 1.1, 2 H, CH(cp)); 5.77 (*q*, $J = 6.8$, 2 H, MeC*H*); 6.86 (*d*, $J = 1.6$, 2 H, NC*H*=C*H*N); 10.26 (*t*, $J = 1.6$, 1 H, N=CHN). ^{13}C-NMR (75.432 MHz, $CDCl_3$): 0.84; 23.55; 57.54; 69.83; 69.94; 71.77; 72.44; 76.46; 88.75; 119.99; 134,39. ^{15}N-NMR (50.664 MHz, $CDCl_3$, ref NH_3): 201. ESI-MS (CH_2Cl_2, T(cap.) = 150°, 20 V) 636.9. Anal. calc. for $C_{33}H_{45}Fe_2IN_2Si_2$ (764.50): C 51.85, H 5.93 N 3.66; found: C 51.96, H 5.93, N, 3.62.

*1,3-Bis{(1*R*)-1-[(1*R*)-1-(trimethylsilyl)ferrocen-2-yl]ethyl}-1*H*-imidazol-2-ylidene* (**5**). To a soln. of 1 g (1.31 mmol) of **4** in 20 ml of THF were added 198 mg (1.76 mmol) *t*-BuONa. After 3 h, ^{1}H-NMR monitoring showed complete conversion. The solvent was removed, and the product was extracted with toluene. The material thus obtained was recrystallized from a mixture of pentane/toluene (3 : 1) at −78°: 792 mg (95%) of **5**. ^{1}H-NMR (300 MHz, (D_8)toluene): 0.30 (*s*, 2 Me_3Si); 1.67 (*d*, $J = 6.6$, 2 *Me*CH); 3.98 (*dd*, $J = 1.3$, 2.3, 2 H, cp); 4.00 (s, 10 H, cp); 4.15 (t, $J = 2.3$, 2 H, cp); 4.27 (*dd*, $J = 1.3$, 2.3, 2 H, cp); 5.74 (*q*, $J = 6.6$, 2 H, MeC*H*); 6.24 (*s*, NCH=CHN). ^{13}C-NMR (75.432 MHz, (D_8)toluene): δ 0.17; 23.16; 55.54; 69.29; 69.71; 70.09; 72.3; 75.51; 93.67; 115.58; 212.63. ^{15}N-NMR (50.664 MHz, (D_8)toluene, ref. NH_3): 209. ^{28}Si-NMR (59.595 MHz, (D_8)toluene): −3.7. EI-MS (70 eV): 636.2 (0.15, M^+), 400.1 (2), 352 (84), 284 (100) . Anal. calc. for $C_{33}H_{44}Fe_2N_2Si_2$ (636.59): C 62.26, H 6.97, N 4.40; found: C 61.53, H 6.85, N 4.23.

Selected Crystal Data for Carbene **5**. Orange crystals (0.36 × 0.22 × 0.08 mm) $M_R = 636.58$, monoclinic, space group $P2_1$ (No. 4), $a = 9.8226(14)$, $b = 12.4192(18)$, $c = 13.829(2)$ Å, $\beta = 99.156(3)°$, $V = 1665.4(4)$ Å^3, $Z = 2$, $D_c = 1.269$ g cm^{-3}, $\lambda = 0.71073$ Å, 9923 reflections measured, 5283 unique, 352 parameters, agreement factors $R = 0.0495$, $R_w = 0.0853$. Crystallographic data (excluding structure factors) for this structure have been deposited with the *Cambridge Crystallographic Data Centre* as supplementary publication No. 180816. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223 336-033; e-mail: deposit@ccdc.cam.ac.uk).

REFERENCES

[1] A. J. Arduengo, R. L. Harlow, M. Kline, *J. Am. Chem. Soc.* **1991**, *113*, 361.

[2] D. Bourissou, O. Guerret, F. P. Gabbai, G. Bertrand, *Chem. Rev.* **2000**, *100*, 39.

[3] W. A. Herrmann, F. J. Kohl, J. Schwarz, in 'Synthetic Methods of Organometallic and Inorganic Chemistry, Transition Metals', Part 3, Vol. 9, Ed. W. A. Herrmann, Thieme, New York, 2000, pp. 84–112.

[4] L. Jafarpour, A. C. Hillier, S. P. Nolan, *Organometallics* **2002**, *21*, 442.

[5] J. P. Morgan, C. Morrill, R. H. Grubbs, *Org. Lett.* **2002**, *4*, 67.

[6] A. Fürstner, L. Ackermann, B. Gabor, R. Goddard, C. W. Lehmann, R. Mynott, F. Stelzer, O. R. Thiel, *Chem.–Eur. J.* **2001**, *7*, 3236.

[7] S. R. Stauffer, S. W. Lee, J. P. Stambuli, S. I. Hauck, J. F. Hartwig, *Org. Lett.* **2000**, *2*, 1423.

[8] A. C. Hillier, H. M. Lee, E. D. Stevens, S. P. Nolan, *Organometallics* **2001**, *20*, 4246.

[9] C. L. Yang, H. M. Lee, S. P. Nolan, *Org. Lett.* **2001**, *3*, 1511.

[10] D. S. McGuinness, K. J. Cavell, *Organometallics* **2000**, *19*, 741.
[11] V. P. W. Bohm, C. W. K. Gstottmayr, T. Weskamp, W. A. Herrmann, *J. Organomet. Chem.* **2000**, *595*, 186.
[12] L. Jafarpour, S. P. Nolan, *Adv. Organomet. Chem.* **2001**, *46*, 181.
[13] T. J. Seiders, D. W. Ward, R. H. Grubbs, *Org. Lett.* **2001**, *3*, 3225.
[14] D. S. Clyne, J. Jin, E. Genest, J. C. Gallucci, T. V. Rajanbabu, *Org. Lett.* **2000**, *2*, 1125.
[15] W. A. Herrmann, L. J. Goossen, M. Spiegler, *Organometallics* **1998**, *17*, 2162.
[16] S. Lee, J. F. Hartwig, *J. Org. Chem.* **2001**, *66*, 3402.
[17] D. Enders, H. Gielen, *J. Organomet. Chem.* **2001**, *617–618*, 70.
[18] A. Togni, in 'Metallocenes: Synthesis, Reactivity, Applications', Vol. 2, Eds. A. Togni, R. Halterman, Wiley-VCH, Weinheim, 1998, pp. 685–721.
[19] C. Bolm, M. Kesselgruber, G. Raabe, *Organometallics* **2002**, *21*, 707.
[20] A. J. Arduengo, R. Krafczyk, R. Schmutzler, H. A. Craig, J. R. Goerlich, W. J. Marshall, M. Unverzagt, *Tetrahedron* **1999**, *55*, 14523.
[21] A. J. Arduengo, S. F. Gamper, M. Tamm, J. C. Calabrese, F. Davidson, H. A. Craig, *J. Am. Chem. Soc.* **1995**, *117*, 572.
[22] B. Bildstein, M. Malaun, H. Kopacka, K. H. Ongania, K. Wurst, *J. Organomet. Chem.* **1999**, *572*, 177.

Received May 30, 2002