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Conformational Studies by Dynamic NMR. 72.[1] Stereolabile Enantiomers of Acyl and Thioacyl Ferrocenes

Bianca F. Bonini, Mariafrancesca Fochi,
Lodovico Lunazzi, and Andrea Mazzanti*

Department of Organic Chemistry "A. Mangini", University of Bologna, Risorgimento, 4 Bologna 40136, Italy

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Even when substituted by an acyl group, ferrocenes still maintain a time-averaged plane of symmetry, owing to the rapid rotation about the cyclopentadienyl−carbonyl (Cp−CO) bond. However, when such a rotation is rendered sufficiently slow at low temperature, a chiral conformer is created, since the cyclopentadienyl ring and the acyl substituent are essentially coplanar, so that no plane of symmetry is left to the molecule as a whole. In other words the Cp−CO bond can be regarded as a stereolabile chirality axis. Actually Sandström and Seita[2] observed anisochronous signals at low temperature for the pairs of atoms in positions 2,5 and 3,4 in a number of 1-acyl ferrocenes, Fc−C(O)R.

An interesting consequence of this observation is that in ferrocenes where each ring bears the same acyl substituent, as for instance 1,1′-diacetylferrocene, **1**, there are two such chirality axes, so that two conformational diastereoisomers of different stability should be, in principle, observable.

These are shown in Scheme 1, where the conformer with carbonyl groups in a *syn* relationship (**1a**) corresponds to a meso form, having retained a plane of symmetry, whereas the conformer with carbonyl groups in an *anti* relationship (**1b**) corresponds to a racemic form, since the absence of a plane (or center) of symmetry gives rise to a pair of stereolabile enantiomers.

Although the rapid ring's rotation about the Cp−Fe−Cp axis allows the *syn* conformer to visit situations lacking a plane of symmetry, the continuous passage through the symmetric form **1a** leads in any case to a time-averaged plane of symmetry, which justifies the meso attribution. On the contrary this does not hold for the same type of motion occurring in **1b**, where a symmetric situation is never visited.

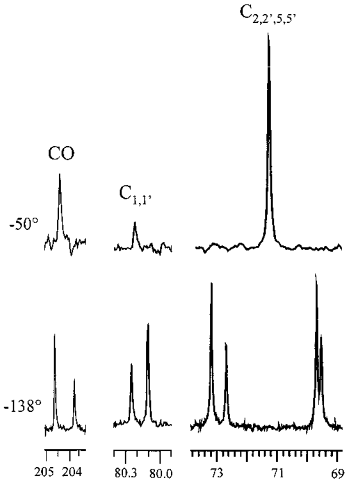
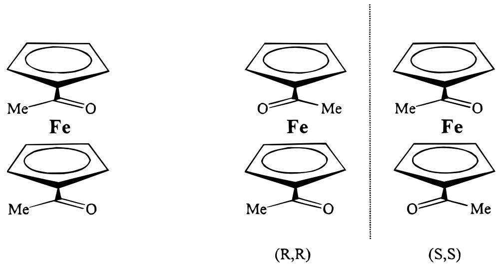


Figure 1. 75.5 MHz signals of the CO, $C_{1,1'}$, and $C_{2,2',5,5'}$ carbons of **1** as a function of temperature.

Scheme 1. Schematic View of the *Syn* (1a) and *Anti* (1a) Conformers of 1,1′-Diacetylferrocene



1a *syn* (meso) **1b** *anti* (racemic)

Two such conformational diastereoisomers in a 2:1 proportion were indeed observed in the ^{13}C spectrum of **1** at −138 °C.[3] In Figure 1 it is shown how the single line of the quaternary and carbonyl carbons each splits into pairs of 2:1 lines on lowering the temperature. On the other hand, the single signal of carbons 2,5 and 2′,5′ splits into four lines, i.e., a 1:1 doublet twice as intense as a second 1:1 doublet. This is because carbon 2 differs from 5 (and 2′ from 5′) in each of the two unequally populated conformers. A line shape analysis yielded a barrier ($\Delta G^{\ddagger}$), for interconverting the more into the less stable conformer, which is equal to 7.5 ± 0.15 kcal mol^{-1}. This corresponds to the rotation barrier of a single MeCO group which, in so doing, transforms the major into the minor conformer. For this reason a transmission coefficient of $^{1}/_{2}$ was used in the Eyring equation to obtain the free energy of activation, in that each MeCO group has the same probability to rotate.[4,5] Since in the racemic conformer **1b** the interconversion of one enantiomer into the other requires the rotation of both the acetyl groups, the process must occur through the meso form **1a**, so that the free energy of activation of 7.5 kcal mol^{-1} also corresponds to the enantiomerization barrier. The enthalpy difference between the meso and the racemic form is likely to be very small, but the latter has twice the probability to occur, so that the observed 2:1 ratio essentially derives from a statistical distribution (entropic factor).

A X-ray diffraction determination of **1**[6] did show that in the single crystal only the conformer having the two MeCO groups in an *anti* relationship (i.e., the racemic **1b**) is populated.[7] It thus seems conceivable to assign this

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[1] For Part 71 see: Anderson, J. E.; Casarini, D.; Lunazzi, L.; Mazzanti, A. *J. Org. Chem.* **2000**, *65*, 1729−1737.

[2] Sandström, J.; Seita, J. *J. Organometallic Chem.* **1976**, *108*, 371.

[3] The detection of two conformers in **1** was not reported in ref 2. The largest shift separation between the corresponding 2:1 lines (displayed by the ^{13}C carbonyl signals at −138 °C) is 50.8 Hz at 75.45 MHz: probably these lines could not be resolved by the 15.1 MHz spectrometer used in that work, since the separation was reduced there by a factor of 5 (i.e., to about 10 Hz).

[4] The use of an unitary coefficient would lead to a $\Delta G^{\ddagger}$ value of 7.75 kcal mol^{-1}.

[5] Casarini, D.; Lunazzi, L.; Foresti, E.; Macciantelli, D. *J. Org. Chem.* **1994**, *59*, 4637. Casarini, D.; Lunazzi, L.; Mazzanti, A. *J. Org. Chem.* **1997**, *62*, 7592.

[6] Palenk, G. J. *Inorg. Chem.* **1970**, *9*, 2424.

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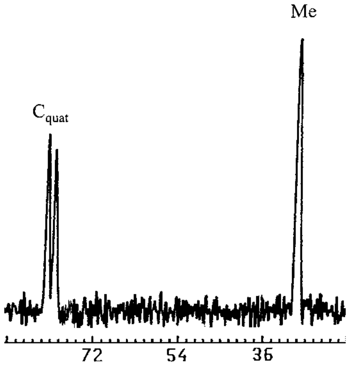

Figure 2. High-field region of the ^{13}C solid state (CP-MAS, 75.5 MHz) spectrum of **1** at −50 °C in the NQS mode, showing the signals for the methyl and for the quaternary ethylenic carbons.

structure to the more stable of the two conformers observed in solution. A solid-state CP-MAS ^{13}C NMR spectrum of **1** confirms that a single conformer is present not only in the single crystal but also in the whole solid bulk. For the rotation barriers in the solid state are much higher than in the liquid so that, if both conformers had been populated in the crystal, they should have been detected at much higher temperature than in solution, possibly even at ambient temperature, as observed in the X-ray diffraction. In Figure 2 the high field portion of the solid-state spectrum of **1**, taken at −50 °C by the nonquaternary suppression (NQS) pulse sequence, is reported.[8] In these conditions the CH carbon signals are canceled, and only the quaternary and residual methyl signals are visible.

The quaternary carbons bearing the acetyl substituents display two ^{13}C signals in a 1:1 ratio (shift separation of 1.3 ppm) because in the *anti* structure they are not related by a plane (or center) of symmetry. Whereas in solution these carbons are enantiotopic, thus yielding an isochronous signal in both the *anti* and *syn* conformers (as shown in Figure 1), they are diastereotopic in the solid. The crystal lattice provides in fact a reference frame, with regard to which they experience different environments (hence the observed diastereotopicity). Such a reference frame is absent in solution, due to the rapid molecular tumbling, so that these carbons appear to be equivalent (enantiotopic).[9] For the same reason also the CO carbons are diastereotopic in the solid state (their lines, not reported in Figure 2, are separated by 0.6 ppm) whereas the analogous separation expected for the methyl signals is smaller than the line width, thus preventing their resolution. The doubling of the NMR signals in the solids is an inherent property of the molecular asymmetry of racemic **1** and should occur either if the rotation of the rings about the Cp−Fe−Cp axis is still fast (as in solution) or if it has become slow (as it appears in the X-ray diffraction measurement[6]).

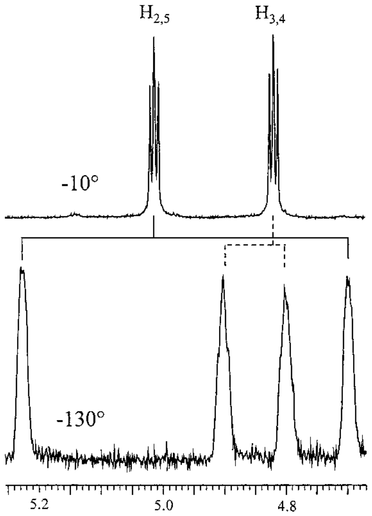

Figure 3. 300 MHz signals of $H_{2,5}$ and $H_{3,4}$ of **2** as function of temperature.

Table 1. Free Energies of Activation ($\Delta G^{\ddagger}$ in kcal mol^{-1}) for the Enantiomerization in 1−5

compd	1	2	3	4	5
$\Delta G^{\ddagger}$	7.5	8.8	8.3	8.25	7.75

We wished to extend this investigation to thiocarbonyl derivatives of ferrocenes, that should also yield stereolabile enantiomers, whose existence might be likewise inferred by changes in the signal multiplicity of the NMR solution spectra at low temperature. For this purpose the thiocarbonyl derivatives **2** and **3** were prepared and their sterodynamic behavior compared with that of the corresponding carbonyl derivatives **4** and **5**:

$$\mathrm{Fc{-}C(S){-}SiMe_2Ph},\ \mathbf{2};\quad \mathrm{Fc{-}C(S){-}SiMe_3},\ \mathbf{3};$$
$$\mathrm{Fc{-}C(O){-}SiMe_2Ph},\ \mathbf{4};\quad \mathrm{Fc{-}C(O){-}SiMe_3},\ \mathbf{5}$$

In Figure 3 are displayed the ^{1}H signals of the cyclopentadienyl hydrogens of **2** that yield an AA′BB′ type spectrum at −10 °C. At −130 °C the signal due to H_3,H_4 is split into a pair of equally intense signals separated by 0.1 ppm and, likewise, is split the signal due to H_2,H_5, the separation being 0.51 ppm at the same temperature.

Computer line shape analysis yields rate constants from which a $\Delta G^{\ddagger}$ value of 8.8 kcal mol^{-1} is obtained (Table 1) for the enantiomerization process brought about by the Cp−C(S) rotation. The existence of a chiral conformation is made also evident by the splitting observed at low temperature (both at the ^{1}H and ^{13}C frequencies) for the methyl signals of **2**. For even in the presence of a fast Si−C(S) rotation, the methyl groups are expected to become diastereotopic if the Cp−C(S) rotation is slow. This is because the whole molecule has a plane of symmetry coincident with the local plane of symmetry of the Me_2Si moiety when the Cp−C(S) rotation is rapid (thus yielding isochronous Me signals). Such a coincidence is however destroyed, leading to anisochronous Me signals, when the slow Cp−C(S) rotation process creates a chiral conformer which, obviously, does not have any molecular plane of symmetry. Accordingly, the barrier determined by monitoring the line shape of the ^{1}H methyl signals (reported in Figure 4) must yield the same barrier as that derived when monitoring the cyclopentadienyl signals. This was indeed the case, in that the same $\Delta G^{\ddagger}$ value of 8.8 kcal mol^{-1} was obtained from the spectra of Figure 4.

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(7) In the crystalline state, where the ring's rotation process about the Cp−Fe−Cp is slow with respect to the time-scale of the X-ray experiment, the *anti* structure displays one of the acetyl groups in position 1, the other in position 3′ (anticlinal).[6]

(8) The solid-state spectrum, acquired in the normal mode, showed a number of poorly resolved, intense lines for the CH carbons (74−76 ppm) that obscured in part the quaternary signals with lower intensity. For this reason the NQS spectrum was more informative.

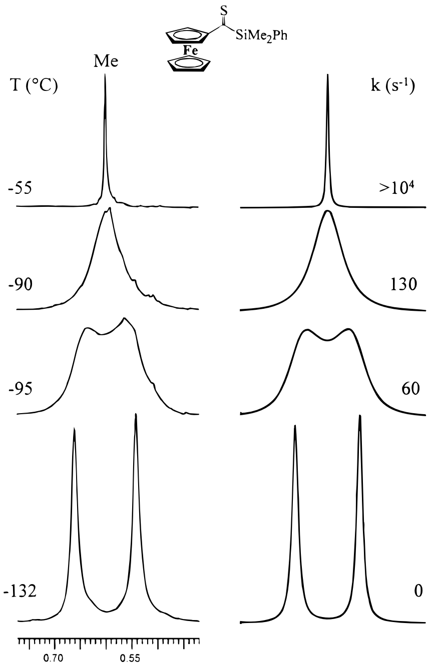

Figure 4. Left: experimental methyl signals of **2** as function of temperature. Right: computer-simulated traces with the rate constants (k in s^{-1}) indicated.

Compound **3** displays an enantiomerization barrier lower than that of **2** (Table 1), and the same difference (0.5 kcal mol^{-1}) is also observed between the barriers of the corresponding carbonyl compounds **4** and **5** (Table 1). This is a consequence of the difference in the steric hindrance exerted by the silicon bonded groups upon the ground state, where the cyclopentadienyl ring is coplanar with the C=S (or C=O) substituent. For, the planar ground state will be destabilized in the case of **3** and **5** with respect to **2** and **4** since the $SiMe_3$ group has larger steric effects than the $SiMe_2Ph$ group. In the latter, in fact, the planar phenyl ring can adopt a position which minimizes its steric interactions, as shown in the X-ray structure of the carbonyl derivative **4**.[10] In the transition state, where the C=S (or C=O) moieties are orthogonal to the cyclopentadienyl ring, the differences of the steric effects are obviously much less important. Accordingly, the energy separation between the ground and transition state is lower in **3** and **5** with respect to **2** and **4**, and this accounts for the larger barriers measured in the latter compounds.

The enantiomerization barriers of derivatives **2** and **3** are larger (by 0.55 kcal mol^{-1}) than those of the corresponding carbonyl derivatives **4** and **5** (Table 1). This agrees with the trend observed in other cases, where the barriers to rotation involving the C=S group were also found higher than those of the corresponding C=O group.[11,12] Such a feature had been explained as a consequence of the greater stabilization of the ground state in thiocarbonyl derivatives, due to the LUMO being located at a lower energy level than in the corresponding carbonyl derivatives.[11]

Experimental Section

Material. 1,1′-Diacetylferrocene was commercially available and was purified by chromatography (eluent Et_2O). Derivatives **2**−**5** were synthesized according to the literature.[13]

NMR Measurements. The samples for the low temperature determinations were prepared by connecting to a vacuum line the NMR tubes containing the desired compounds dissolved in CD_2Cl_2 and condensing therein the gaseous CHF_2Cl (solvent ratio 1:2 v/v). The tubes were subsequently sealed *in vacuo* and introduced into the precooled probe of the spectrometer (Varian, Gemini 300) operating at 300 MHz for ^{1}H and at 75.45 MHz for ^{13}C. The temperatures were calibrated by substituting the sample with a precision Cu/Ni thermocouple before the measurements. Line shape simulations were obtained with a PC computer program based upon the DNMR 6 routines.[14] The high-resolution ^{13}C NMR solid-state CP-MAS spectra (Bruker, CXP 300) were obtained at 75.5 MHz. The sample was packed in a 7 mm zirconia rotor spun at the magic angle with a speed of about 3000 Hz. The chemical shifts were measured, by replacement, with respect to the lower frequency signal of the adamantane (29.4 ppm). The cooling was achieved by means of a flow of dry nitrogen, precooled in a heat exchanger immersed in liquid nitrogen.

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(9) In a chiral solution, however, they should become diastereotopic when the rotation about the two Cp−CO bonds is locked at low temperature.

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