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STEREOCHEMICAL CONSEQUENCES OF THE INTRAMOLECULAR HYDROGEN BOND IN 1′-ACETYL-1-α-HYDROXYETHYL- AND 1,1′-BIS(α-HYDROXYETHYL)FERROCENES

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Summary

1′-Acetyl-1-α-hydroxyethyl- and 1,1′-bis(α-hydroxyethyl)ferrocenes and the carbocations derived from them have been characterized by electronic, infrared and NMR spectroscopy. The existence of intramolecular hydrogen bonds between the interannular substituents in the various species examined has been established. The restricted rotation caused by such interaction leads to preferential formation of pairs of enantiomers.

Introduction

During studies of the stability of α-ferrocenyl carbocations, we observed peculiar behavior of 1′-acetyl-1-α-hydroxyethyl- and 1,1′-bis(α-hydroxyethyl)-ferrocenes in the ionization reaction in aqueous sulfuric acid, and we attributed it to the existence of an intramolecular hydrogen bond between the two hetero-annular substituents [1]. A detailed spectral investigation of the two compounds and of the corresponding carbocations is described below. Not only are the hydrogen bond interactions confirmed, but their role in stabilizing certain dissymmetric and conformational states of the molecules is demonstrated.

Results and discussion

The ultraviolet spectrum of 1′-acetyl-1-α-hydroxyethylferrocene in water shows absorption maxima at the following wavelengths (with molar absorptivities in parentheses): 230 (13800), 268 (6800), 342 (1440), 455 (660) nm. The spectrum does not substantially change in ethanol or 1% aqueous H_2SO_4. In the light of the spectral characteristics of ferrocenyl alcohols and ketones [1,2], this spectrum appears to be essentially determined by the presence of the acyl group, since the alcoholic group does not give rise to any electronic absorption in the wavelength range investigated.

When the compound is dissolved in sulfuric acid the observed spectral changes depend on the range of the acid concentration used. At acid concentrations higher than 40%, the expected formation of the carbocations is clearly identified; the spectrum shows a maximum at 260 nm (ϵ 15200) in accordance with the previously described properties of the ferrocenyl carbocations [1,2]. Since the half-ionization of ferrocenyl alcohols occurs in the range 3—26% H_2SO_4 [1], and that of ferrocenyl ketones in the range 36—63% [2], ionization of the alcoholic group is also assumed to be more likely in the bifunctional compound. Surprisingly, in contrast with the situation for ferrocenyl alcohols, at acid concentrations lower than 40% the spectral changes cannot be easily interpreted in terms of carbocation formation. In view of the possibility of complicating hydrogen bond interactions we sought evidence for such interactions by an IR and NMR spectral study.

The infrared spectrum of a dilute solution of 1'-acetyl-1-α-hydroxyethylferrocene in CCl_4 shows absorptions of the O—H and C=O stretching modes as broad bands centered at 3500 and 1660 cm^{-1}, respectively. No peaks due to free secondary hydroxyl groups, such as those given by substituted 2-hydroxybenzophenones [3], were observed. Acetyl- and 1,1'-diacetylferrocene show carbonyl absorption at 1680 cm^{-1} as narrow peaks and 1-ferrocenylethanol shows three signals at 3617 (two superimposed bands) and 3577 cm^{-1}, which have been assigned to the free, π-bonded and metal-bonded hydroxyl absorptions [4]. The interaction of the hydroxyl group both with the cyclopentadienyl ring and with the iron atom makes the intermolecular hydrogen bonding negligible for ferrocenyl alcohols in dilute solutions.

Since the characteristic effects of the H bond on the vibrational spectra include a shift of the absorption of the O—H and C=O stretching modes to lower frequencies and strong broadening of the band width [5,6], the infrared spectra are indeed consistent with the presence of an intramolecular hydrogen bond between the hydroxylic and carbonylic group in 1'-acetyl-1-α-hydroxyethylferrocene. The magnitude of the shift of O—H vibration indicates that the strength of the intramolecular H bond is high [6].

It seemed of interest to compare this compound with 1,1'-bis(α-hydroxyethyl)ferrocene, in which the hydroxyl groups act both as proton donor and proton acceptor within the one molecule. The electronic spectra of 1,1'-bis(α-hydroxyethyl)ferrocene in H_2SO_4 are in good agreement with the formation of the carbocation [1]. The infrared spectrum shows a small peak at 3620 cm^{-1} due to the free OH, and a broad band centered at 3300 cm^{-1} due to the intramolecularly hydrogen bonded hydroxyl groups; the shift of the latter OH vibration to lower frequencies from the free OH absorption is quite marked.

The relevant NMR data for 1'-acetyl-1-α-hydroxyethylferrocene in $CDCl_3$ and in a 1/2 $CDCl_3/CF_3CO_2H$ mixture are shown in Table 1 (see also Fig. 1). Several significant features are found in the spectrum of the un-ionized compound. The presence of two main doublets (τ 8.54 and 8.60 ppm, $\Delta\nu$ 4.5 Hz, J 6 Hz, area ratio nearly 1/1) of the CHOH—CH_3 methyl groups suggests that there are at least two different types of such groups, although only one doublet is found in 1-ferrocenylethanol [1]. Further, the four protons of the acetyl-substituted cyclopentadienyl ring give rise to four distinct signal groups (centered at τ 5.30, 5.35, 5.54 and 5.61 ppm), while in the acetylferrocene spectrum

TABLE 1

NMR DATA FOR 1'-ACETYL-1-α-HYDROXYETHYL AND 1,1'-BIS(α-HYDROXYETHYL)-FERROCENES (τ, ppm)[a]

——— CHOH—CH$_3$ A ring
Fe
——— X B ring

Substituent X	A ring moiety					B ring moiety				
	H$_\alpha$	H$_\beta$	CH	OH	CH$_3$	H$_\alpha$	H$_\beta$	CH	OH	CH$_3$
CH$_3$CO[b]	———		5.85	———	8.54 d 8.60 d	5.2-5.6				7.65 s
CH$_3$CO[c]	5.77		4.15 q		8.37 d	5.22-5.40				7.57 s
CH$_3$CHOH[b]	5.95		5.39 q	4.61	8.651 d 8.631 d 8.613 d 8.580 d					
CH$_3$CHOH[d]	5.04 5.44	3.54 3.77	2.67 q		7.681 d	4.83[e] 4.61[e]		4.20[e]		8.367 d 8.384 d

[a] Relative to internal TMS. [b] In CDCl$_3$. [c] In CF$_3$CO$_2$H/CDCl$_3$ 1/2. [d] In neat CF$_3$CO$_2$H. [e] The assignments between CH, H$_\alpha$ and H$_\beta$ atoms is uncertain.

no such distinction between either α and α' or β and β' protons [2] is found; the CO—CH$_3$ methyl group gives two major signals, with $\Delta\nu$ 1.3 Hz. The spectrum does not vary with temperature up to 120° in 1,1,2,2-tetrachloroethane [3]. All these results are consistent with the presence of an intramolecular hydrogen bond between the OH and CO groups.

The restricted rotation required by the hydrogen bond may give rise to distinct conformers, which are characterized by different spatial orientations of the CHOH—CH$_3$ and CO—CH$_3$ substituents which cause the π carbonyl and ring electrons and the non-bonding electrons of the iron atom to affect the methyl protons in a different way. Each conformer is dissymmetric and can be converted

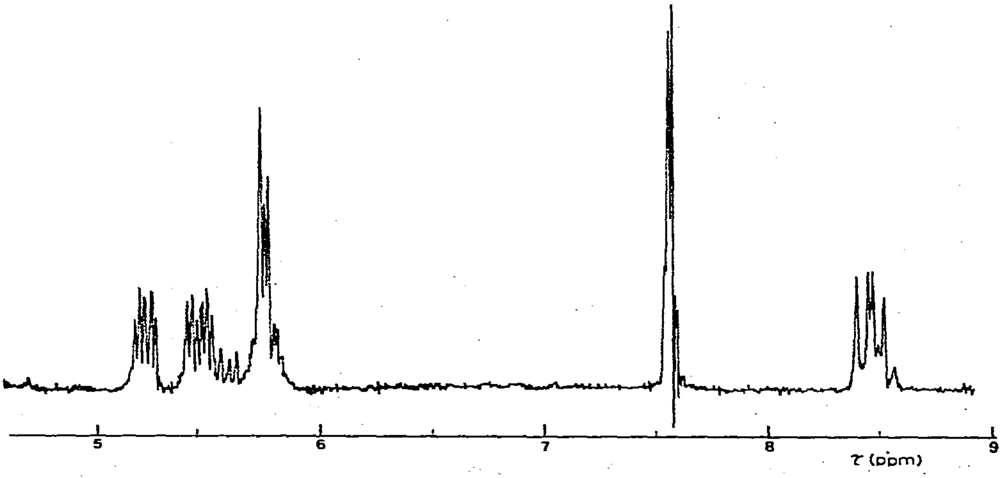

Fig. 1. The NMR spectrum of 1'-acetyl-1-α-hydroxyethylferrocene in CDCl$_3$.

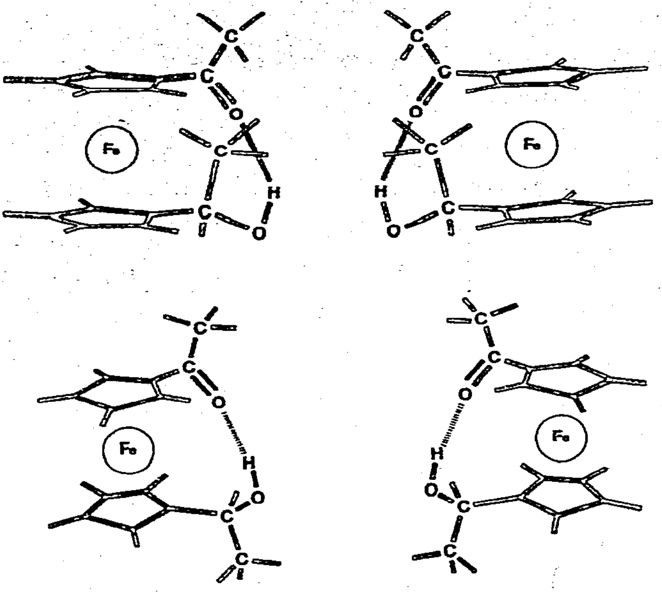

Fig. 2. Conformational and enantiomeric forms of the intramolecularly hydrogen bonded 1′-acetyl-1-α-hydroxyethylferrocene.

into its own enantiomer by restricted rotation without the breaking of the hydrogen bond. An enantiomeric pair is shown in Fig. 2 with the aid of Dreiding-type models.

It is also worth noting that, while in acetylferrocene the reorientation process of the cyclopentadienyl rings around their five-fold axes of symmetry occurs with an activation energy of 4.6 kcal/mole [7], in 1′-acetyl-1-α-hydroxyethylferrocene the hydrogen bond would increase the energy barrier and lead to restricted rotation of the rings with respect to each other.

In the formation of the carbocation in sufficiently concentrated acid solutions, the rigid hydrogen bonded structure is destroyed because of the ionization of the alcoholic group, and the cyclopentadienyl rings may rotate more freely around the common orthogonal axis. The structure of the carbocation is revealed by the NMR spectrum (Table 1), as shown by the presence of a doublet for the $^{+}CH-CH_3$ methyl group (J 6 Hz), and a quartet for the ^{+}CH proton. The deshielding of the carbocation signals compared to those of the non-ionized compound is in agreement with the general trend observed for the α-ferrocenyl carbocations [1].

The NMR spectrum of 1,1′-bis(α-hydroxyethyl)ferrocene in $CDCl_3$ is reported in Fig. 3 and in Table 1. The OH resonance at τ 4.61 ppm is deshielded with respect to the other α-ferrocenyl alcohols, whose OH signal falls in the range τ 7.5—8.5 ppm [1], and exchanges slowly on shaking the D_2O. The observed phenomena are similar to those of furoquinoline alkaloid [8], supporting the hypothesis of an intramolecular hydrogen bond interaction. The methine signals appear as at least a quartet in the region around τ 5.4 ppm (J 6.4 ± 0.2 Hz).

Owing to the existence of two chiral centers in 1,1′-bis(α-hydroxyethyl)-ferrocene, the signal of the methyl groups would be expected to consist of two doublets, corresponding to the methyl groups of the *meso* and *d,l* forms. A detailed analysis of the methyl peak (which is reported in an expanded scale in Fig. 3b) in fact shows eight signals (at τ 8.532, 8.576, 8.596, 8.604, 8.629, 8.650, 8.667, 8.669 ppm), which correspond to at least four doublets centered at τ 8.580, 8.613, 8.631 and 8.651 ppm, with J 6.5, 6.7, 6.4 and 6.3 Hz, respectively.

The presence of a number of different methyl signals higher than expected can also be explained by the existence of the intramolecular hydrogen bond interaction since it gives rise to distinct conformers characterized by different spatial orientations of the methyl groups. This behavior appears to be analogous to that of the cyclohexane diols, in which the possibility of the intramolecular hydrogen bond formation influences the conformations [9]. Moreover, in comparison with 1′-acetyl-1-α-hydroxyethylferrocene, a higher flexibility of the hydrogen bond in 1,1′-bis(α-hydroxyethyl)ferrocene (as shown in Fig. 4) and the participation of either lone pairs of the acceptor oxygen atom increase the number of important conformers. This situation is confirmed by the NMR spectrum (Fig. 3a and b) of the methyl region, which shows the complex structure of the eight signals.

The interpretation of the NMR spectral data for 1,1′-bis(α-hydroxyethyl)ferrocene finds good support in the analysis of the NMR spectrum of the compound in neat CF_3CO_2H (Table 1 and Fig. 3c), since the structure of the carbocation is presumably simpler than that of the un-ionized compound. The structure of the monocarbocation is well established on the basis of the ^+CH quartet

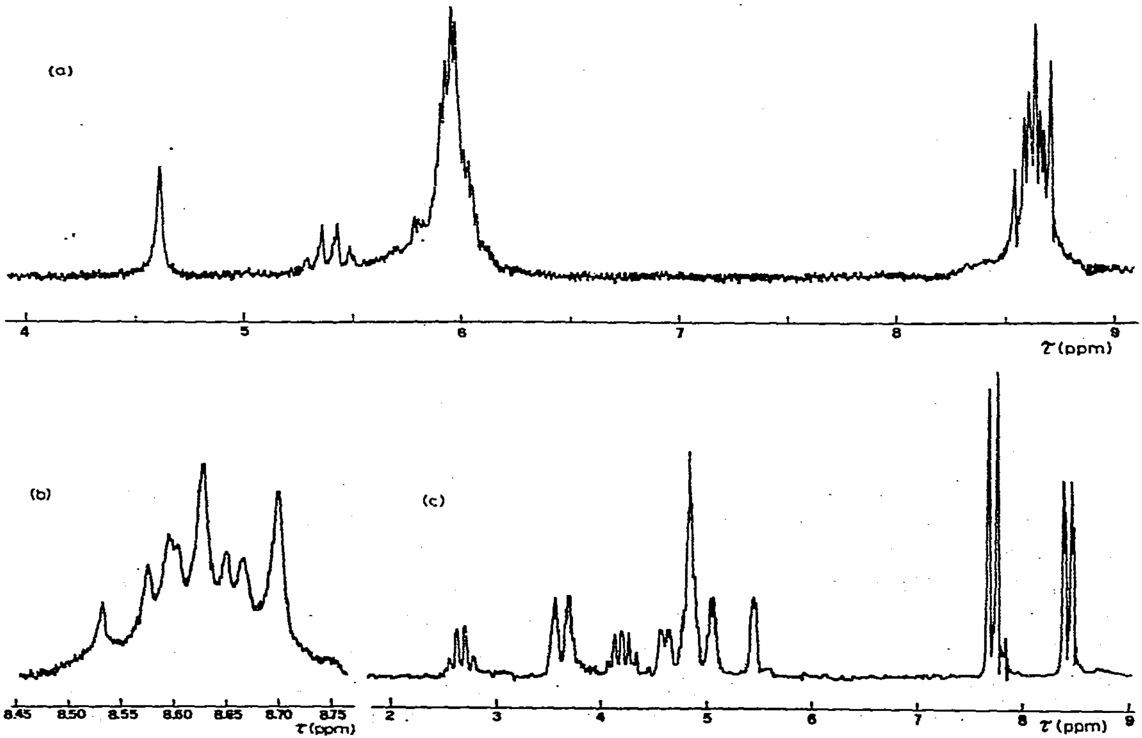

Fig. 3. The NMR spectrum of 1,1′-bis(α-hydroxyethyl)ferrocene: (a) in $CDCl_3$; (b) the methyl region of (a) on an expanded scale; (c) in neat CF_3CO_2H.

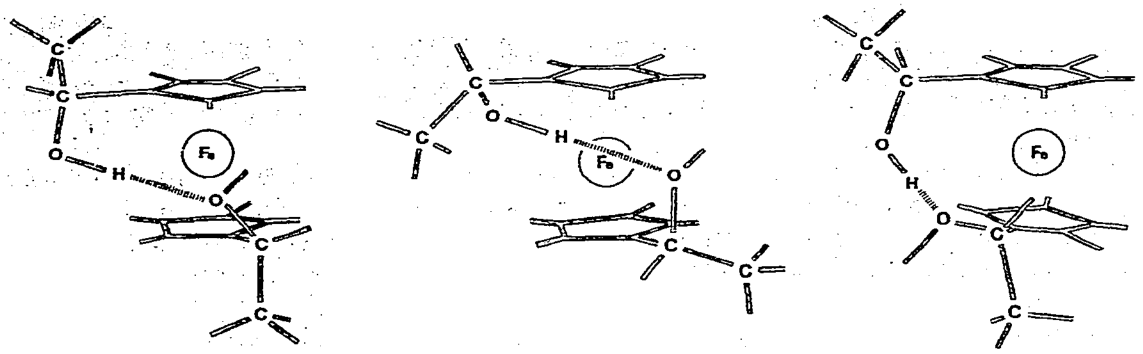

Fig. 4. Some conformational isomers of *meso* 1,1′-bis(α-hydroxyethyl)ferrocene.

centered at τ 2.667 ppm (J 7 Hz) and the existence of a few well separated signals of the two methyl groups. The ionized $^{+}$CH—CH$_3$ methyl group appears as a downfield doublet at τ 7.681 ppm (J 7 Hz) for the deshielding by the positive charge (1-ferrocenylethanol in CF$_3$CO$_2$H shows the same signal at τ 7.73 ppm [1]). The un-ionized CHOH—CH$_3$ methyl group appears as two doublets at τ 8.367 (J 6.5 Hz) and τ 8.384 ppm (J 6.5 Hz), respectively, with $\Delta\nu$ 1.5 Hz (1-ferrocenylethanol in CDCl$_3$ shows a doublet at τ 8.58 ppm [1]).

The resonance of the un-ionized CHOH—CH$_3$ methyl group as two doublets indicates that the monocarbocation may also possess a rigid structure because of the hydrogen bond interaction, the OH group being the acceptor and the $^{+}$CH group the proton-donor. As a consequence, the monocarbocation may exist in two conformational isomers, with two differently oriented methyl groups. Calculation of the bond distances on the basis of the structural parameters of ferrocene [10,11] makes this hypothesis reasonable.

We conclude that both the IR and NMR spectral behavior are consistent with interannular H bonding formation in 1′-acetyl-1-α-hydroxyethylferrocene, in 1,1′-bis(α-hydroxyethyl)ferrocene, and its carbocation, and that, owing to the special geometry of the metallocene system, one or more pairs of enantiomers are preferentially formed.

Experimental

1,1′-Bis(α-hydroxyethyl)ferrocene was prepared by the published method [12].

1′-Acetyl-1-α-hydroxyethylferrocene was prepared as follows. A solution of 9 g (3.33 mmol) of 1,1′-diacetylferrocene in 250 ml of methanol (Erba, Karl Fischer reagent) was treated with 1.26 g (3.33 mmol) of NaBH$_4$. The mixture was stirred at room temperature for 14 h and then added slowly to 250 ml of water containing a small amount of HCl. The solution was extracted several times with diethyl ether, and the collected extracts were dried over Na$_2$SO$_4$ and evaporated. The crude material was chromatographed on a 60 × 5 cm basic alumina column (100 g of neutral I Brockmann Al$_2$O$_3$ treated with 10 ml of a saturated Na$_2$CO$_3$ solution). On elution with benzene, three bands developed: the first was 1,1′-diacetylferrocene, the second 1′-acetyl-1-α-hydroxyethylferrocene, and the third 1,1′-bis(α-hydroxyethyl)ferrocene.

The NMR spectra were recorded on a Bruker HX-90 MHz spectrometer at room temperature with TMS as internal reference. The spectra of the α-ferrocenylcarbonium ions were recorded immediately after dissolution of the compounds in CF_3CO_2H (Merck, Uvasol) and monitored for at least one hour.

The infrared spectra were measured using a Beckmann IR 20 and/or Perkin—Elmer 257 spectrophotometers, in CCl_4 solutions. The ultraviolet and visible spectra were recorded with a Perkin—Elmer 402 self-recording spectrophotometer.

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