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BRIDGED FERROCENES

XV *. CONFORMATIONAL PROPERTIES OF [1.1]FERROCENOPHANE AND SOME OF ITS BRIDGE- AND RING-SUBSTITUTED DERIVATIVES

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Summary

Friedel-Crafts acetylation of [1.1]ferrocenophane has afforded the α- and β-acetyl derivatives, which have been separated and converted into the corresponding ethyl derivatives. The effects of ring and bridge substituents upon the conformational mobility of [1.1]ferrocenophane are discussed in the light of the NMR spectra.

Introduction

Although [1.1]ferrocenophane (**1a**) and bridge-substituted derivatives were first prepared in 1966 [2], exploration of the chemistry of the system has been hindered by the inconvenience of the early synthetic methods which gave poor and erratic yields of desired products [3–5]. Recently, however, an efficient two-stage synthesis has been developed [6], starting from the readily accessible 1,1′-dilithioferrocene and 6-(dimethylamino)pentafulvene, which makes available the parent compound (**1a**) in amounts sufficient to allow investigation of its properties. In this paper, we describe the preparation of ring-substituted derivatives and discuss the unusual conformational properties of the [1.1]ferrocenophane system.

Results and discussion

Interest in the conformational behaviour of [1.1]ferrocenophanes stems from the early observation [2b] that the ^{1}H NMR spectrum of the parent compound (**1a**)

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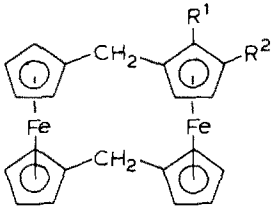
consists simply of two triplets (A_2B_2 pattern) for the cyclopentadienyl ring protons and a sharp singlet for the bridging methylene protons. Since any static conformation locates each of the four protons of a ring and the two protons of a bridge in a different molecular environment, and in view of the pronounced magnetic anisotropy associated with the ferrocene system [7], the molecule must undergo a fast conformational exchange process which renders equivalent on time-average the sets of eight α-ring protons, eight β-ring protons, and four methylene protons, producing the observed triplet-triplet-singlet spectrum. Such an exchange process would also accord with the ^{13}C NMR spectrum [8] of **1a** which shows only three kinds of ring carbon atoms, viz. α, β, and tertiary.

Information bearing on the mechanism of conformational exchange in this system can be gained from analysis of the ^1H NMR spectra of bridge- and ring-substituted derivatives. Several compounds of the former type have already been prepared but the synthesis of examples of the latter type was required.



(1)

(a $R^1 = R^2 = H$;
b R^1 = COMe, $R^2 = H$;
c $R^1 = H$, R^2 = COMe;
d R^1 = Et, $R^2 = H$;
e $R^1 = H$, R^2 = Et)

Synthetic methods

Reaction of [1.1]ferrocenophane (**1a**) in CH_2Cl_2 with the Perrier complex $MeCOCl \cdot AlCl_3$ gave the α- and β-acetyl derivatives **1b** and **1c**, respectively, which could be separated cleanly by chromatography on Al_2O_3, the α-isomers eluting first as found in earlier related studies [9]. The lower polarity of α-acylalkylferrocenes, as compared with that of β-isomers, is a consequence of steric repulsion between the vicinal ring substituents which causes diminished $p\pi$–$p(d)\pi$ conjugation of the carbonyl group and the cyclopentadienyl ring. Only one α-acetyl and one β-acetyl product was isolated. Thus, although the two α-positions and the two β-positions of each ring are non-equivalent in any static [1.1]ferrocenophane structure, conformational site exchange excludes the possibility of separation of individual structural (but not optical!) isomers. In order to avoid any possible complication of carbonyl anisotropy effects in the interpretation of the ^1H NMR spectra, the α- and β-ketones were each reduced with mixed-hydride reagent ($LiAlH_4/AlCl_3$), giving the corresponding α- and β-ethyl derivatives **1d** and **1e**, respectively.

Structural assignments were confirmed by the ^1H NMR spectra (Table 1). As in previous studies [9], the ketones were readily differentiated by the appearance of the proton-resonance patterns for the acylated ring; e.g. the spectrum of the α-ketone **1b** contains a well-separated one-proton multiplet at lowest field for the unique ring proton adjacent to the carbonyl group. The ethyl derivatives also give distinctive ring-proton resonances; e.g. the spectrum of the conformationally flexible derivative **1e** contains two finely split multiplets in the intensity ratio 7 (higher field)/8(lower field). The ethyl substituent must therefore occupy a β-position because it is known that the lower-field triplet in the spectrum of the parent compound **1a** is due to the

TABLE 1

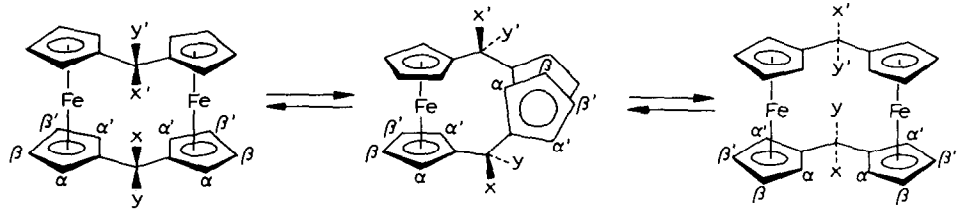
^{1}H NMR SPECTRA OF RING-SUBSTITUTED [1.1]FERROCENOPHANES [a]

Compound	Cyclopentadienyl protons	Bridge protons	Substituent protons
1a	4.18(t,8H), 4.39(t,8H)	3.55(s)	
1b	3.95, 4.66, 5.18 (each 1H) 4.15–4.35(7H) 4.45–4.60(5H)	3.32, 3.63(2d) [b] 3.55, 4.37(2d) [b]	2.45(s)
1c	4.05, 4.70, 4.78, 5.06 (each 1H) 4.15–4.50(11H)	3.52, 3.64(2s)	2.45(s)
1d	4.48, 4.58, 4.74 (each 1H) 4.00–4.25(12H)	3.20–3.80 [c]	1.20(t) 2.44(q)
1e	4.15–4.25(7H) 4.30–4.45(8H)	3.54, 3.56(2s)	1.25(t) 2.40(q)

[a] For $CDCl_3$ solutions, with TMS as internal reference (δ values); multiplets unless indicated otherwise; (s) singlet, (d) doublet, (t) triplet, (q) quartet. [b] AB quartet; J(AB) ca. 18 Hz. [c] Two closely overlapping AB quartets; J(AB) ca. 18 Hz.

resonance of the α-ring protons which are selectively deshielded by the adjacent ferrocene residue [2a].

The β/α product ratio for acetylation of **1a** was substantially higher (4.5) than those found previously for dialkylferrocenes of the type $(\eta\text{-}C_5H_4CH_2R)_2Fe$; cf. β/α ratios in the range 1.6–2.9 have been reported [9,10] for Friedel-Crafts acetylation of 1,1′-diethylferrocene and [m]ferrocenophanes ($m = 3$–5) under the same reaction conditions. The preference for β-substitution of an alkylferrocene ring is due principally to steric shielding of the α-ring sites. In the case of **1a**, fast conformational exchange (see later) brings each α-site in turn into an environment where it is effectively screened by the other ferrocene residue from attack of the electrophile, whereas access to the β-sites remains unimpeded.



(4) (5) (6)

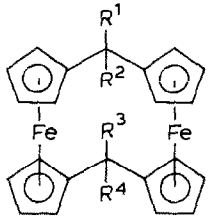
SCHEME 1. Conformational exchange in [1.1]ferrocenophane. For clarity, the ring sites of one ligand only are labelled, but the stereochemical consequences for the other ligand are identical. Twist of one ferrocene residue relative to the other can occur in the opposite direction to that shown, with the same stereochemical consequences, the intermediate conformation being the mirror image of **5**.

(2) (3)

Conformational behaviour

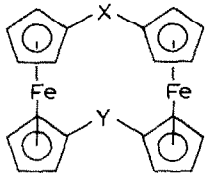
Crystallographic studies [8,11] and chemical correlations [3] have established that [1.1]ferrocenophanes adopt a *syn* structure (**2**), which molecular models show to be extremely flexible, in preference to the alternative *anti* arrangement (**3**) which is relatively inflexible and incorporates severe non-bonded interaction between the pair of inner α-hydrogen atoms of each ligand. In the *syn* structure, this interaction can be easily relieved by twisting. The flexibility of the structure allows reorientation of the ferrocene residues from a relationship in which the ring-metal-ring axes of each are parallel (**4**), to one in which they are mutually perpendicular (**5**), and thence to another parallel arrangement (**6**) which is structurally identical with the starting conformation **4**. As shown in Scheme 1, interconversion of the conformers **4** and **6** brings about exchange of the α- and α'-ring sites, the β- and β'-ring sites, and the protons (or groups) attached *exo* and *endo* to the bridging carbon atoms.

The height of the energy barrier to interconversion of the conformers **4** and **6** of [1.1]ferrocenophane is unexpectedly low. Variable-temperature ^{1}H NMR spectroscopic studies [6] have shown that, at temperatures as low as -100°C, the rate of exchange is still sufficiently fast to render equivalent on time-average the *exo*- and *endo*-protons of the bridging groups for which a clear chemical-shift separation would have otherwise been expected [7,12].



(**7**)

(a $R^1 = R^4 = Me$, $R^2 = R^3 = H$;
b $R^1 = R^4 = Ph$, $R^2 = R^3 = H$;
c $R^1 = R^3 = Me$, $R^2 = R^4 = H$)



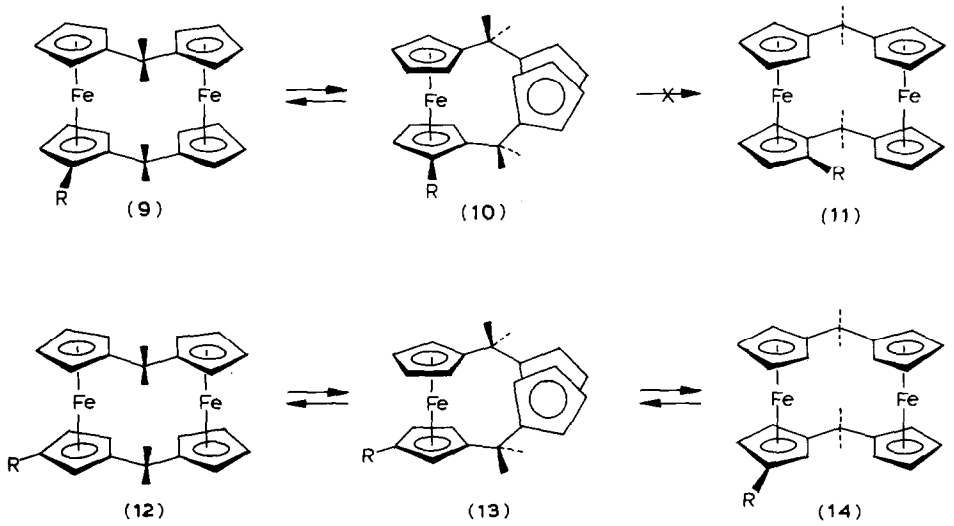
(**8**)

(a X = CO, Y = CH_2 ;
b X = Y = CO ;
c X = $\overset{+}{C}H$, Y = CH_2 ;
b XY = $(CH\cdots H\cdots CH)^-$)

The validity of the conformational exchange process depicted in Scheme 1 can be tested by investigation of the effect of substituents attached to various sites in the parent molecule **1a**. For example, the *exo,exo*-Me_2 derivative **7a** ≡ (**4**; $x = x' = H$, $y = y' = Me$) [2a], whose crystal structure has been determined [11], is prevented from rotation into the corresponding *endo,endo*-conformation **6** because this would involve severe steric overcrowding of the methyl groups. The conformational mobility of this compound is thus limited to an oscillation between structures **4** and **5**, as evidenced by the ^{1}H NMR spectrum [3] which shows substantial chemical-shift separation (ca. 0.4 ppm) of the resonances of the α- and α'-ring protons. A similar situation obtains for the *exo,exo*-Ph_2 derivative **7b** [3], but the *exo,endo*-Me_2 deriva-

tive **7c** ≡ (**4**; $x = y' = Me$, $x' = y = H$) can complete the exchange **4** ⇄ **6** and its ^1H NMR spectrum [6] shows equivalence of the α- and α′-protons and of the β- and β′-protons.

The spectra of the monoketone **8a** [3] and the diketone **8b** [5] likewise show that degenerate conformational exchange must occur. The carbocation **8c**, on the other hand, is conformationally inflexible; cf. the CH_2 resonance in the ^1H NMR spectrum appears as an AB quartet, and twelve distinct carbon resonances are present in the ^{13}C NMR spectrum [8]. Although the energy barriers to rotation around the Fc–$\overset{+}{C}$ bonds in ferrocenylcarbenium ions may be substantial (e.g. for Fc$\overset{+}{C}$HMe, E_a 84 kJ mol^{-1} [13]), the evident rigidity of the cation **8c** is surprising because the ^1H and ^{13}C NMR spectra of the non-cyclic analogue $Fc_2\overset{+}{C}H$ indicate conformational mobility [8,14]. The carbanion **8d** also appears to be conformationally frozen, rotation from an eclipsed structure being prevented by the presence of an unprecedented intramolecular hydrogen bond between the bridging carbon atoms [15].



SCHEME 2. Conformational exchange in α- and β-substituted [1.1]ferrocenophanes.

Introduction of a ring substituent into [1.1]ferrocenophane may also affect the conformational mobility of the system. Models show that the exchange process suggested for the parent compound (Scheme 1) involves close approach of four α-sites, one in each ring, during rotation from one eclipsed conformation to the other. While the barrier to this process can be surmounted by the parent molecule, exchange would be prohibited for an α-substituted derivative. As shown in Scheme 2, the eclipsed conformer **9** can twist in one direction only, and the resulting conformer **10** cannot rotate to complete the exchange as this would bring the ring substituent unacceptably close to an α-site in the adjacent cyclopentadienyl ring **11**. Motion in α-substituted compounds is therefore limited to an oscillation between conformations **9** and **10**. With a β-substituted derivative, on the other hand, there is no steric impediment to interconversion of the eclipsed conformers **12** and **14** through intermediate **13** or its mirror image.

These observations lead to the conclusion that conformational motion in a β-substituted [1.1]ferrocenophane should result in *exo* ⇄ *endo* site exchange of the protons of the CH_2 bridges, whereas such site exchange of the bridge protons of an α-substituted derivative would be prevented. It should be noted that interconversion of eclipsed conformations of a ring-substituted [1.1]ferrocenophane does not produce structural equivalence of the protons of the individual bridges, as with the parent compound; e.g. the *exo*-protons of the same bridge in conformations **12** and **14** have different stereochemical relationships to the ring substituent. However, the dominant influence which discriminates between the NMR chemical shifts of these bridge protons is their relationship, whether *exo* or *endo*, to the ferrocene residues [7].

The ^1H NMR spectra of the ring-substituted derivatives (**1b**–**1e**) fully support these interpretations. The bridge-proton resonances of the β-acetyl **1c** and β-ethyl **1e** derivatives appear as two singlets separated by 0.12 and 0.02 ppm, respectively, in accord with *exo* ⇄ *endo* site exchange. The larger bridge-signal separation for the ketone is unsurprising because the electron-withdrawing effect of the carbonyl group would be felt more strongly by the CH_2 bridge of the acetylated ligand than by that of the other ligand. The bridge-proton resonances of the α-acetyl **1b** and α-ethyl **1d** derivatives are much more complex and appear as overlapping AB quartets, showing that *exo* ⇄ *endo* site exchange does not occur. The spectrum of the α-ketone **1b** is particularly interesting in that the *exo/endo* chemical shift difference for one of the CH_2 bridges is much larger (0.82 ppm) than that for the other (0.31 ppm). Because the conformational mobility of this compound is restricted, this is presumably a result of differential shielding by the carbonyl group of the protons of the neighbouring bridge, additional to the discriminatory *exo/endo* shielding effect of the ferrocene residues.

Conclusions

The effects of bridge and ring substituents upon the conformational flexibility of [1.1]ferrocenophane, as revealed by ^1H NMR spectroscopy, are in accord with the operation of the unusual degenerate exchange process depicted in Scheme 1.

Experimental

All reactions were conducted under an atmosphere of dry N_2. Solvents were thoroughly dried and redistilled before use. Petrol refers to the fraction of b.p. 40–60°C. Column chromatographies were carried out using neutral Spence Grade H alumina which had been partially deactivated by exposure to the atmosphere for 6 h. M.p.'s are uncorrected. ^1H NMR spectra (Table 1) were obtained using a Perkin–Elmer R32 spectrometer operating at 90 MHz.

Acetylation of [1.1]ferrocenophane

A solution of freshly distilled acetyl chloride (115 mg; 1.5 mmol) in CH_2Cl_2 (30 ml) was stirred for 0.5 h with a large excess of finely ground aluminium chloride. The mixture was then filtered and the solid residue was washed with CH_2Cl_2 (20 ml). The filtrate was added dropwise over 0.5 h to a stirred solution of [1.1]ferrocenophane [6] (475 mg; 1.2 mmol) in CH_2Cl_2 (30 ml) at 0–5°C. The resulting blue-violet solution was stirred for 2 h at room temperature, then washed several

times with water, dried ($MgSO_4$), and evaporated to low bulk. The residual solution was chromatographed on Al_2O_3. Petroleum/ether (2/3 v/v) eluted the α-ketone **1b** (40 mg, 8%), which crystallised from hexane as an orange solid, m.p. 130–132°C; (Found: C, 66.0; H, 5.2. $C_{24}H_{22}Fe_2O$ calcd.: C, 65.8; H, 5.1%). The same solvent eluted the β-ketone **1c** (180 mg, 34%), which crystallised from petroleum/ether as an orange-red solid, m.p. 148–150°C; (Found: C, 66.1; H, 5.3. $C_{24}H_{22}Fe_2O$ calcd.: C, 65.8; H, 5.1%). More polar material, probably either diketonic or polymeric, was also formed in the reaction but was not separated. Similar yields of the two ketones were obtained when the reaction was repeated.

Mixed-hydride reduction of the ketones

The following general procedure was used. A solution of the ketone (100 mg; 0.2 mmol) in ether (10 ml) was added dropwise over 0.25 h to a stirred suspension of $LiAlH_4$ (25 mg; 0.6 mmol) and finely ground Al_2Cl_6 (100 mg; 0.4 mmol) in ether (40 ml) at 0–5°C. The mixture was stirred for 0.75 h, then poured into ice-cold water. The organic layer was separated and combined with ether extracts of the aqueous layer. The total extract was washed with water, dried over anhydrous Na_2CO_3, and evaporated to dryness, leaving a quantitative yield of the ethyl[1.1]ferrocenophane which was crystallised from petrol.

The α-ethyl derivative **1d** was obtained from **1b** as a waxy low-melting yellow solid; (Found: C, 68.4; H, 6.0. $C_{24}H_{24}Fe_2$ calcd.: C, 68.0; H, 5.7%).

The β-ethyl derivative **1e** was obtained from **1c** as a yellow solid, m.p. 116–118°C; (Found: C, 68.2; H, 5.8. $C_{24}H_{24}Fe_2$ calcd.: C, 68.0; H, 5.7%).

Acknowledgements

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