J. Org. Chem. **1999,** *64,* 5315−5317

Ion-Pair Acidity of Some Substituted Ferrocenes in Tetrahydrofuran. Stabilization of a Carbanion by Ferrocene[1]

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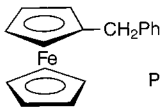
Received April 15, 1999

Introduction

Ferrocene is well-known to be a strong electron-donor in stabilizing carbocations. It is reactive toward electrophilic aromatic substitution (e.g., acylation is 3.3 × 10^6 as fast as benzene),[2] and it stabilizes positive charge in the α-position.[3,4] The ferrocene ring system also exerts an inductive effect that is electron-donating. In the p-position, it increases the pK_a of benzoic acid, phenol, and the anilinium ion;[5] $\sigma_p = -0.17$,[6] which puts it between methyl ($\sigma_p = -0.14$) and methoxy ($\sigma_p = -0.28$). It is remarkable that there have been no quantitative studies of the effect of the ferrocene ring on carbanions, and there are precious few qualitative studies.

From metalation reactions of alkyl-substituted ferrocenes, it has been proposed that there is little or no stabilization of a ferrocenylmethyl anion from the conjugation of the cyclopentadienyl ring.[7] [1,1′]Ferrocenophane (**3**), however, can be deprotonated by *n*-butyllithium as shown by subsequent methylation of the bridge with methyl iodide; the corresponding diferrocenylmethane does not undergo comparable metalation.[8] Neutral ferrocenophane is quite flexible,[9−11] but the anion is rigid.[12,13] The stability of the latter was originally attributed to intramolecular hydrogen bonding between the bridgehead carbons; however, both dynamic NMR and X-ray crystallography of the lithium ion-pair show no such bridging. The metalated carbon is effectively sp^3 in both the crystal and solution state.

To provide a quantitative assessment of the electronic effect of a ferrocene group in a carbanion, we report in this paper the ion-pair acidities of benzylferrocene (**1**), 1,1′-dibenzylferrocene (**2**), and [1,1′]ferrocenophane (**3**) in THF at 25 °C and compare the experimental results with related systems.



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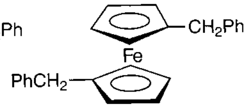

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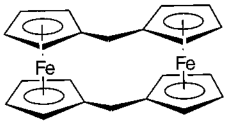

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Results and Discussion

Ion-pair acidity is defined as the transmetalation equilibrium in eq 1 where RH is the carbon acid whose pK is to be measured and InH is an indicator whose pK is on the established acidity scale.[14,15]

$$\mathrm{RH} + \mathrm{In}^- \, \mathrm{M}^+ \overset{K}{\rightleftharpoons} \mathrm{InH} + \mathrm{R}^- \, \mathrm{M}^+ \tag{1}$$

$$-\log K = \mathrm{p}K_{\mathrm{RH}} - \mathrm{p}K_{\mathrm{InH}} \tag{2}$$

For cesium as the counterion ($\mathrm{M}^+ = \mathrm{Cs}^+$), the established acidity scale covers a pK range from about 12 to 39, with fluorene as the standard with an assigned pK_a value in DMSO as 22.9 (per hydrogen).[16]

Benzylferrocene and 1,1′-dibenzylferrocene were synthesized as described previously.[17−19] The cesium salts of the ferrocenes were obtained in THF using cumylcesium as the base[20] and studied using UV−vis spectroscopy at 25.0 ± 0.1 °C under argon. The $\lambda_{\max}$ and molar absorptivities for the neutral substrates are all approximately the same (Table 1). The $\lambda_{\max}$ and extinction coefficients (ϵ) of the cesium salts are independent of the concentrations used from 1×10^{-4} to 1×10^{-5} M. Moreover, for the salts of **1** and **3**, there is no apparent dependence of the absorption shape on the concentration of the anion; hence, the ion-pairs are not aggregated at these concentrations.[21−23] The concentrations used in the pK studies were between 1×10^{-3} and 1×10^{-5} M. Spectra of the cesium salts are shown in Figure 1.

Initial addition of cumylcesium to **2** gave the same spectrum as the cesium salt of **1**, **1-Cs**. With further additions, the spectrum changed gradually with excess cumylcesium to that shown in Figure 1 and is attributed to the dicesium salt, **2-Cs$_2$**. The extinction coefficient was determined for this dianion rather than for the monoan-

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[20] The deprotonation of the ferrocenes at 10 °C gave first-order kinetics with cumylcesium for the initial points (i.e., first 4 min of reaction is pseudo first order in the neutral ferrocene). Afterwards, there are complications apparently from decomposition products of the THF and impurities in the cumylcesium.

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10.1021/jo990635k CCC: $18.00

Table 1. Summary of λ_{max}, Extinction Coefficient (ϵ), and Acidity of the Ferrocenes 1, 2 and 3[a]

compound	λ_{max}	ϵ	pK
1	324, 440	70, 110	
1-Cs	383, 542	17600, 9950	35.7 ± 0.1
2	442	132	
2-Cs			35.3 ± 0.3
2-Cs$_2$	386, 546	26300, 11400	36.6 ± 0.4
3	325, 438	196, 217	
3-Cs	425, 581	4810, 6110	35.1 ± 0.3
diphenylmethane[b]	443	50600	33.25
di-m-xylylmethane[b]	446	36000[c]	36.0
toluene[b]			41.2

[a] All UV−vis studies were carried out in THF at 25 °C. [b] Ref 14. [c] Measured in this work; reference 14 reports 35100.

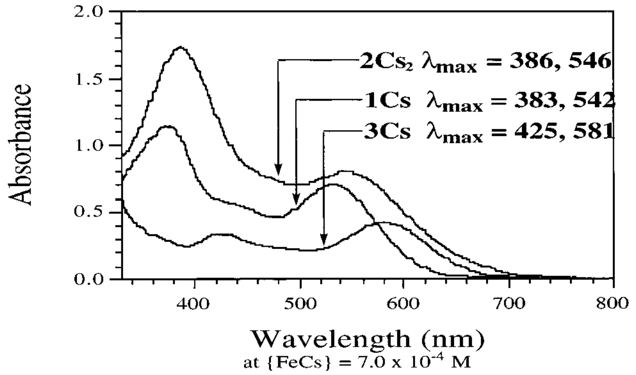


Figure 1. Spectra of the cesium salts of the ferrocenes **1**−**3**.

ion because of the presence of dianion even during the initial deprotonation; i.e. the second pK of **2** is sufficiently low that some dianion is always present when the monoanion is generated.

The cesium ion-pair acidities of the substituted ferrocenes (eq 3) were measured against di-m-xylylmethane (DmXM, pK_{Cs} = 35.96).[14] The separate spectra of the cesium salt of the indicator, CsDmXM, and of the ferrocene salts were used to fit a series of “double indicator” experiments. For **2**, the spectrum of **2-Cs** was taken as that of **1-Cs**; the concentrations of **2-Cs** and **2-Cs$_2$** were determined by deconvoluting the experimental spectra in terms of these spectra for **2-Cs** and **2-Cs$_2$**. The concentrations of the neutral indicator, DmXM, as well as the neutral ferrocene were obtained by difference from the concentration of the corresponding cesium salts. Proton transfers were slow in this pK region and required long equilibration times. Because of decomposition during these long equilibrations, only one point could be taken per experiment.

$$\mathbf{1\text{-}Cs} + \mathrm{DmXM} \rightleftharpoons \mathbf{1} + \mathrm{CsDmXM} \qquad (3)$$

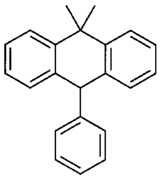
The ion-pair acidity constants for **1**, **2**, and **3** with respect to the indicator, DmXM, were found to be 0.27, 0.52, and 0.51, respectively, from which the ion-pair acidities of these ferrocenes were calculated to have the pK values 35.7 ± 0.1, 35.3 ± 0.3, and 35.1 ± 0.3, respectively (Tables S1−S3, Supporting Information). The acidity experiments of **2** also gave the second pK estimated as 36.6 ± 0.4.

These acidities are statistically corrected to be per hydrogen. For **1**, the correction is log(2) because there are two available hydrogens but only one site for return. For the first deprotonation of **2**, there is a correction of log(4) because of the four available protons but only one site for return. The second deprotonation of **2** needs no correction because there are two possible protons and two possible sites for return. For **3**, however, there is an ambiguity in assigning a corrected pK. If only the exo-hydrogens are considered to be acidic, then the correction is log(2); if both exo- and endo-hydrogens are equivalently reactive, then there would be four acidic hydrogens and two sites for return since the two positions are conformationally distinct and the correction is again log(2). If both hydrogens are acidic but with different pK's, then the situation is more complicated. We have adopted a log(2) correction for simplicity.

Cesium salts are generally contact ion-pairs (CIP) rather than solvent separated ion-pairs (SSIP) in THF,[24] and we assume that these ferrocene salts are also CIP. The ion-pair pK's of cesium salts of delocalized carbanions are generally about the same as the ionic pK_a's in DMSO;[24,25] thus, these ion-pair pK's would probably also apply to the ionic pK_a's in DMSO. The maximum measurable pK_a in DMSO is about 32 because of its leveling effect;[26] thus, it would be impossible to measure the pK_a's of these ferrocenes directly in DMSO (pK_a = 35).[16]

The results summarized in Table 1 show that the ferrocene ring stabilizes a carbanion almost as well as a phenyl group. The second benzene ring in diphenylmethane results in a 7.9 unit lowering of the pK of toluene; the ferrocene ring in **1** lowers the pK of toluene by 5.5 units. Ferrocenophane, **3**, is only 1.8 pK units less acidic than diphenylmethane. The ferrocene ring, just as a phenyl ring, is amphoteric; that is, it stabilizes both positive and negative charges.

At first glance, it may seem rather curious that **3** is as acidic as the benzylferrocenes; since a ferrocene ring is somewhat less stabilizing than a phenyl, one might expect **3** to have a pK perhaps about 2 units higher than that found. This result may well be due to its rigidity. When toluene or diphenylmethane are converted to their anions, the rings are no longer free to rotate, and this entropy effect has an adverse effect on deprotonation.[25] Compound **3** does not suffer such an entropy loss on deprotonation and should, therefore, be more acidic than otherwise expected. Note that 9-phenyl-10,10-dimethyldihydroanthracene **4**, in which two benzene rings are also held rigid, is 3 pK units more acidic than triphenylmethane.[15]



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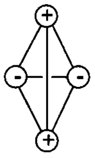

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The next point of interest is that the second ion-pair pK of **2** is hardly larger than the first, whereas **3** does not undergo a second deprotonation. At this point, we take our cue from several hydrocarbons whose second ion-pair pK's are similarly close to or even less than the

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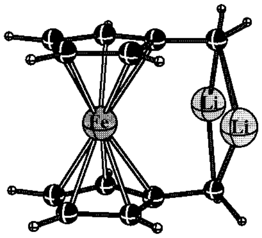

Figure 2. Structure found by ab initio computation of the dilithium salt of 1,1'-dimethylferrocene.[30]

first.[27,28] These results were interpreted in terms of the electrostatic stabilization of a pattern of charges within the triple ion as symbolized by **5**.[29] We suggest correspondingly that the dicesium salt of **2** has a bridged structure with both cesiums coordinated to both carbanion centers. This type of structure was confirmed by an ab initio computation of the dilithium salt of 1,1′-dimethylferrocene that gave the structure shown in Figure 2.[30] A comparable structure for the dicesium salt of **3** is undoubtedly less stable because of steric interactions with the rings.

Conclusion

Previous work had shown that the ferrocene ring strongly stabilizes an adjacent carbocation center. The present work shows that a ferrocene ring stabilizes an adjacent carbanion center almost as well as a phenyl group. Accordingly, the ferrocene ring is an *amphoteric* substituent, as is a phenyl group and stabilizes negative or positive charge as necessary. The nature of this stabilization is the subject of a theoretical study to be published separately.[30]

Experimental Section

General. Ion-pair acidity and spectral studies were carried out in a vacuum/atmosphere glovebox under an argon atmosphere. The UV−vis absorption spectra were obtained on a computer-driven Shimadzu model UV-2101PC spectrophotometer custom fitted with fiber-optic cables. Details of the spectrophotometer and experimental procedure have been published previously.[21] All of the absorption spectra were scanned at a rate of 200 nm/min at 0.5 nm intervals using a 2 nm slit width. Tetrahydrofuran was purified as described previously and stored over Linde 3 Å molecular sieves.

Cumylcesium (CumCs). Stock solutions were prepared by dissolving the appropriate amount of 2,3-dimethyl-2,3-diphenylbutane (bicumyl) in THF and adding a stoichiometric amount of cesium metal. A red color formed immediately on the surface of the metal. Occasional shaking over 2 h yielded a dark red solution, which gave a visible spectrum (λ_{max} = 344 nm) consistent with the literature (λ_{max} = 338 nm for cumylpotassium[31]). The reaction of cumene with cesium hydride gave the same visible spectrum. These solutions decomposed over time to give a yellow solution of unknown composition with λ_{max} = 398.

Synthesis of Materials. The benzyl- and 1,1′-dibenzylferrocenes were synthesized following published procedures for the benzoylation of ferrocene followed by reduction.[17−19] The indicator used in the acidity study, di-*m*-xylylmethane (DmXM), was available from our previous studies. [1.1]Ferrocenophane was a kind gift from Professor Per Ahlberg and his group at the Department of Organic Chemistry, Göteborg University, Göteborg, Sweden.

Benzylferrocene: mp 75.5−76 °C (lit.[18] mp 73.5−74 °C, 75−6 °C); ^{1}H NMR ($CDCl_3$) δ 7.24−7.05 (m, 5H), 4.32 (bs, 9H), 3.62 (bs, 2H); ^{13}C NMR ($CDCl_3$) δ 141.6, 128.4, 128.2, 125.9, 69.0, 67.8, 36.1.

1,1′-Dibenzylferrocene: mp 105−106 °C (lit.[18] mp 105−6 °C); ^{1}H NMR ($CDCl_3$) δ 7.30−7.10 (m, 10H), 4.10 (bs, 8H), 3.70 (bs, 4H). ^{13}C NMR ($CDCl_3$) δ 141.5, 128.3, 128.2, 125.9, 88.4, 69.7, 68.7, 33.8.

UV−vis Studies. The slow reaction of CumCs with the ferrocenes presented a problem for the determination of the p*K* and extinction coefficients of the anions. Therefore, the neutral substrate was treated with a large excess of the base in tetrahydrofuran and left over a period of 8 h for full deprotonation and decomposition of the excess base by reaction with solvent. For the acidity experiments, the indicator was deprotonated first, then the neutral ferrocene was added. The cell was left for a period of 8−16 h depending on the time needed for the equilibration of each ferrocene. Complete equilibration times were determined by the observed increase in absorbance at the λ_{max}. When a decrease was observed for both compounds, the experiment was considered completed. Because of the time constraints, single cell experiments were run for each ferrocene.

Acknowledgment. This work was supported in part by NSF grant CHE 95-28273.

Supporting Information Available: Tables S1−S3. This information is available free of charge via the Internet at http://pubs.acs.org.

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