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BRIDGED FERROCENES—X[1]

STUDIES IN THE ACETYLATION OF [m]FERROCENOPHAN-1-ONES*

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Abstract—The Friedel–Crafts acetylation of a series of [m]ferrocenophan-1-ones has been carried out and the relative proportions of the isomeric products determined. The results are discussed in relation to the mechanism of electrophilic substitution of ferrocene.

INTRODUCTION

SINCE the original report[2] in 1952 of the aromatic character of ferrocene, a great deal of research endeavour has been devoted to a study of the chemical reactivity of the molecule, particularly with regard to electrophilic substitution reactions. Although the goal of much of this work appears to be restricted to the preparation of new compounds of little intrinsic interest, it is nevertheless surprising that uncertainty still surrounds the question of the mechanism of the reaction of ferrocene with electrophilic reagents.

The early discovery[3] that the metal atom in ferrocene is protonated in strongly acidic media led naturally to the speculation that metal participation might play an important rôle in electrophilic substitution reactions. It was suggested[4] that the first stage in the reaction might involve coordination of a nonbonding pair of metal electrons with the electrophile to give a complex which leads to product through rearrangement to a σ-complex followed by proton loss. This hypothesis, which gained general acceptance,[5] accounted nicely for the observed relationship[6] between the oxidation potentials of ferrocene derivatives and the ease of electrophilic substitution since nonbonding metal electrons are implicated in each process.[7]

More recent work,[8] however, has cast doubt upon the validity of this mechanism and it has been suggested[9] that direct metal participation is unimportant in the electrophilic substitution of ferrocene. From a study of kinetic isotope effects, Traylor has further proposed[9] that, depending upon the electrophilicity of the attacking reagent, direct addition of an electrophile may occur either to the *exo* or the *endo* side of the cyclopentadienyl ring followed by proton loss from an intermediate σ-complex. In the former mode of attack, favoured by reagents more electrophilic than the proton (e.g. RCO^+), the rate-determining step is σ-complex formation whereas for reactions in which weak electrophiles are involved (e.g. $AcOHg^+$), the rate of the reaction is governed by the rate of proton elimination.

Our approach to the problem has centred upon an investigation of the directive effects exerted by substituents in the electrophilic substitution of ferrocene

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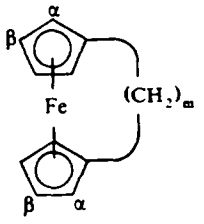

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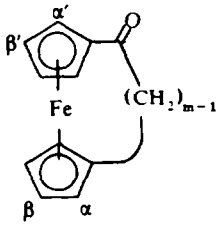

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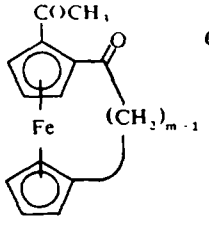
derivatives.[10,11] Recently, we reported[11] the results obtained for the Friedel–Crafts acetylation of a series of [m]ferrocenophanes (1) and we now describe complementary experiments in which the related ketones (2; m = 3, 4, and 5) were used as substrates.‡ These bridged ferrocenes offer a number of advantages in this connection over the non-bridged compounds previously studied[10] since their conformational properties are well understood.[1,13] Since ring–ring torsion is restricted to an extent controlled by the nature of the interannular bridging chain, inter-ring directive influences in the substitution reaction can be investigated. The degree of resonance interaction between the carbonyl group in the ketones (2) and the adjacent cyclopentadienyl ring is also influenced by the bridge length such that the effect of carbonyl conformation upon the substitution pattern can be studied. Finally, comparison of the results obtained[11] for the acetylation of the [m]ferrocenophanes (1) with those for the ketones (2) should, in principle, allow separation of resonance effects from other effects (e.g. steric, inductive) associated with the reaction.

SEPARATION AND CHARACTERISATION OF PRODUCTS

All of the acetylation reactions were carried out under standardized conditions (see Experimental) using CH_2Cl_2 as solvent and a 1:1:2 molar ratio of ferrocenophanone, AcCl, and $AlCl_3$ respectively. After completion of the reaction, the mixture was hydrolyzed and the products isolated by conventional methods. Each experiment was carried out at least twice and reproducible results were obtained. In every case, high overall yields (>90%) of product were isolated. No diacetylation was found.



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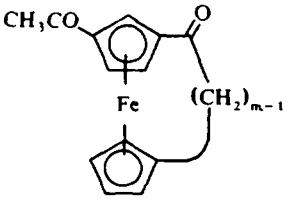

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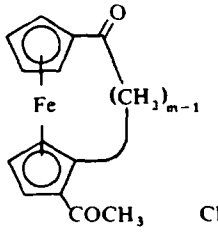

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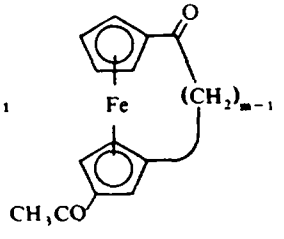

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Separation of isomeric products

In principle, each ketone (2) can afford four monoacetyl isomers corresponding to substitution in the carbonyl-substituted ring [3(α') and 4(β')] and in the alkyl-

‡ Some preliminary results have been published.[12]

substituted ring [5(α) and 6(β)]. For convenience, the positions in the former ring are distinguished by a prime. The product from each reaction was chromatographed on alumina and relatively minor amounts of unchanged starting material were readily separated.

Chromatography of the product from [3]ferrocenophan-1-one (**2**: m = 3) afforded two bands, the first (elution) consisting of a mixture of two isomers and the second a single third isomer. The former was repeatedly chromatographed on alumina of various activities but clean separation of the constituents could not be achieved. Eventually, the two pure compounds were obtained by a procedure of topping and tailing the chromatographic band and by fractional crystallization. The three products formed in the acetylation of [4]ferrocenophan-1-one (**2**; m = 4) were cleanly separated by chromatography. The product from [5]ferrocenophan-1-one (**2**: m = 5) was separated into two bands by chromatography. The first of these afforded a pure compound while pure samples of the two isomers present in the second band were obtained as before by topping and tailing and fractional crystallization. In each case, therefore, three of the four possible acetyl derivatives were formed in the reactions. Analytical data, etc., for these products are collected in Table 1.

TABLE 1. ANALYTICAL DATA

Compound[a]	m.p. (b.p.)	Formulae	Found (%)		Calc. (%)	
			C	H	C	H
3 (m = 3)	157–158°	$C_{15}H_{16}FeO$	64·13	5·27	63·88	5·00
5 (m = 3)	95–97	$C_{15}H_{16}FeO$	63·84	5·09	63·88	5·00
6 (m = 3)	164–165	$C_{15}H_{16}FeO$	63·48	5·01	63·88	5·00
9 (m = 3)	(120/0·05 mm)	$C_{15}H_{18}Fe$	71·15	7·06	70·93	7·14
10 (m = 3)	(151/1·5)	$C_{15}H_{18}Fe$	71·01	7·04	70·93	7·14
3 (m = 4)	95–96	$C_{16}H_{18}FeO$	64·69	5·44	64·92	5·45
5 (m = 4)	78–80	$C_{16}H_{18}FeO$	64·63	5·46	64·92	5·45
6 (m = 4)	140–141	$C_{16}H_{18}FeO$	65·10	5·51	64·92	5·45
9 (m = 4)	(120/0·1)	$C_{16}H_{20}Fe$	71·71	7·47	71·70	7·52
10 (m = 4)	(110/0·025)	$C_{16}H_{20}Fe$	71·81	7·54	71·70	7·52
3 (m = 5)	78–80	$C_{17}H_{20}FeO$	65·94	5·92	65·80	5·85
5 (m = 5)	89–90	$C_{17}H_{20}FeO$	65·94	5·68	65·80	5·85
6 (m = 5)	179–180	$C_{17}H_{20}FeO$	65·94	5·68	65·80	5·85
9 (m = 5)	(120/0·05)	$C_{17}H_{22}Fe$	72·71	8·12	72·40	7·86
10 (m = 5)	(132/0·01)	$C_{17}H_{22}Fe$	72·21	7·86	72·40	7·86

[a] Formulae are given in the text.

Characterization of products

In order to narrow the choice of possible structures for each product, a cross-comparison procedure with the α- and β-acetyl[m]ferrocenophanes (**7** and **8** respectively) was carried out (Fig 1). The structures of these compounds were previously unambiguously established.[11] Each of these six ketones (**7** and **8**; m = 3, 4 and 5) was reduced by mixed hydride ($LAH/AlCl_3$) to the corresponding ethyl-[m]ferrocenophanes (**9** and **10**; m = 3, 4 and 5) and these were compared with the products of mixed-hydride reduction of the products from the acetylation of the

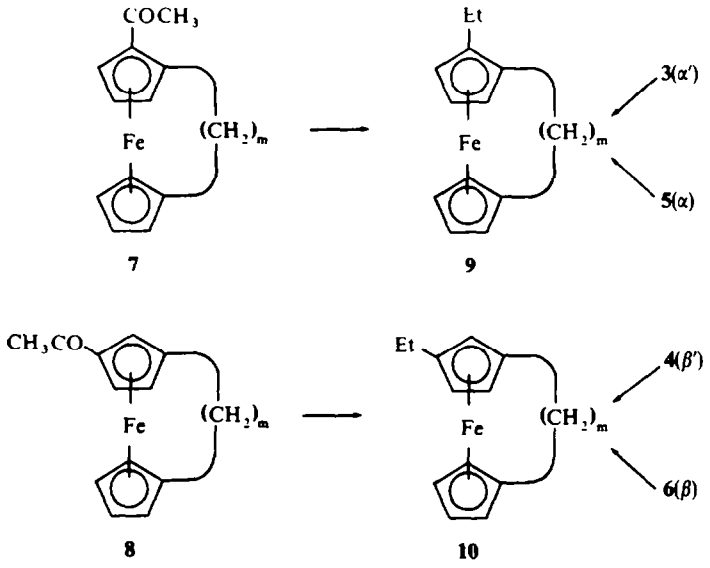


FIG 1. Cross-comparison scheme

ketones (**2**). Since the IR spectra (liquid films) of the α- and β-ethyl derivatives (**9** and **10** respectively) of each ferrocenophane were clearly distinguishable, it was thus possible to establish whether the acetyl group in the diketones was located adjacent to the bridge [i.e. **3** (α') or **5** (α)] or otherwise [i.e. **4** (β') or **6** (β)]. For example, α-ethyl[3]ferrocenophane (**9**; m = 3) is formed upon reduction of α-acetyl[3]ferrocenophane (**7**; m = 3). Consequently, a diketone from the acetylation of [3]ferrocenophan-1-one (**2**; m = 3) which affords the same reduction product must possess either the α' (**3**; m = 3) or α (**5**; m = 3) stereochemistry. By this method, it was established that, in each acetylation reaction, both the α and α' isomers were formed together with an isomer of either the β or β' structure.

Final structural assignments were achieved by analysis of the cyclopentadienyl proton patterns in the NMR spectra of the nine diketone products (summarised in Table 2). In this connection, it is pertinent to consider the spectra of model compounds *viz.* 1,2- and 1,3-diacetylferrocene.§ The proton patterns for the acetylated rings in these compounds are characteristic. The spectrum of the former contains a two-proton doublet at τ 5·06 and a one-proton triplet at τ 5·36 while the corresponding resonances in the spectrum of the 1,3-compound appear as a one-proton triplet at τ 4·55 and a two-proton doublet at τ 4·96 (for $CDCl_3$ solutions). In the latter case, the unique proton flanked by the two carbonyl groups is correspondingly deshielded and resonates at unusually low field, much lower than the resonance of the protons adjacent to a single carbonyl group in the 1,2-compound.

By analogy, one of the diketone products from each acetylation reaction could be clearly assigned the α' structure (**3**) and, since none of the spectra contained a very

§ The authors are indebted to Dr. P. Carty, University of Strathclyde, for provision of a sample of 1,3-diacetylferrocene prepared by oxidation of β-acetylethylferrocene. The 1,2-diacetyl compound was prepared by the reported method.[14]

TABLE 2. NMR SPECTRA[a]

Compound[b]	Cyclopentadienyl protons[c] (τ)		Bridge protons[c] (τ)	Acetyl protons[d] (τ)	Ethyl protons (τ)
3 (m = 3)	5·23 (d) (2H):	5·44 (t) (1H)	6·25–6·76	7·49	—
	5·61 (d) (3H):	5·9–6·1 (1H)	7·1–7·4		
5 (m = 3)	5·1–5·2 (1H):	5·2–5·5 (4H)	6·0–7·3	7·42	—
	5·5–5·7 (2H)				
6 (m = 3)	4·81 (t) (1H):	4·9–5·0 (1H)	7·02 (s)	7·65	—
	5·0–5·2 (2H):	5·2–5·5 (2H)			
	5·6–5·9 (1H)				
9 (m = 3)	5·7–6·6 (7H)		7·4–8·6[e]	—	8·91 (t)
10 (m = 3)	5·7–6·3 (7H)		8·02 (s)	—	7·72 (q)
					8·83 (t)
3 (m = 4)	5·01 (t) (1H):	5·13 (t) (1H)	6·7–8·1	7·53	—
	5·30 (t) (1H):	5·6–5·7 (1H)			
	5·8–5·85 (1H):	5·9–6·0 (2H)			
5 (m = 4)	5·3–5·4 (3H):	5·4–5·6 (3H)	6·6–8·0	7·56	—
	5·75–5·8 (1H)				
6 (m = 4)	5·1–5·4 (5H):	5·5–5·6 (1H)	7·2–8·0	7·63	—
	5·6–5·8 (1H)				
9 (m = 4)	5·6–6·3 (7H)		7·2–8·6[e]	—	8·88 (t)
10 (m = 4)	5·8–6·4 (7H)		7·4–8·4	—	7·73(q)
					8·87(t)
3 (m = 5)	4·9–5·2 (2H):	5·3 (t) (1H)	7·0–8·4	7·47	—
	5·5–5·7 (1H):	5·7–6·0 (3H)			
5 (m = 5)	5·2–5·6 (7H)		6·8–8·4	7·60	—
6 (m = 5)	4·9–5·2 (1H):	5·2–5·4 (4H)	7·2–8·4	7·64	—
	5·4–5·6 (1H):	5·6–5·9 (1H)			
9 (m = 5)	5·7–6·5 (7H)		7·0–8·6[e]	—	8·90 (t)
10 (m = 5)	5·6–6·4 (7H)		7·2–8·6[e]	—	8·86 (t)

[a] For $CDCl_3$ solutions.
[b] Formulae are given in the text.
[c] Multiplets unless indicated otherwise: (s) singlet, (d) doublet, (t) triplet, (q) quartet.
[d] Singlet resonance.
[e] The methylene quartet of the ethyl group is obscured by the resonances of the bridge protons.

low-field one-proton resonance, the β′ structures (**4**) could be excluded. Taken together with the results of the cross-comparison experiments previously described, these conclusions allowed assignment of structure to all of the nine diketones isolated from the acetylation reactions. The NMR spectra of the α- and β-acetyl derivatives (**5** and **6** respectively) were complex but in harmony with the assigned structures. Particularly, the spectra of those compounds assigned the β stereochemistry (**6**) were obviously incompatible with the corresponding β′ structures (**4**).

TABLE 3. ELECTRONIC SPECTRA[a]

Compound[b]	Band I		Band II		Band III		Band IV	
	λ max	ε	λ max	ε	λ max	ε	λ max	ε
3 (m = 3)	229 nm	12,700	256 nm[c]	9390	330 nm 367	1515 1045	440 nm	505
5 (m = 3)	226	11,820	264	8420	324[c] 368	1460 820	450	455
6 (m = 3)	229	13,270	266	8410	336	2460	456	860
3 (m = 4)	226	13,690	263	9415	337[c] 370	1070 1415	442	760
5 (m = 4)	234	13,400	264	11,840	330 364[c]	1580 770	453	595
6 (m = 4)	234	15,010	265	10,450	344	2180	454	545
3 (m = 5)	232[c]	13,520	266	9495	334[c] 376	1120 1560	453	775
5 (m = 5)	228[c]	15,010	266	12,500	329 371	1490 840	458	500
6 (m = 5)	231	16,400	264 281[c]	10,190 8600	343	1940	462	580

[a] For abs EtOH solutions.
[b] Formulae are given in the text.
[c] Shoulder.

Although the electronic spectra of the diketones (Table 3) did not in themselves provide unambiguous support for the structures assigned, the observed absorption characteristics were compatible with those expected from consideration of the spectra of model compounds.[11,15,16] Finally, although partial overlap of the chromatographic bands occurred for two of the three product mixtures, the same order of elution (α′ before α before β) of isomers from alumina was observed in each case.[11,17]

Isomeric product ratios

Since the products from the acetylation of [4]ferrocenophan-1-one could be completely separated by chromatography, isomer ratios were calculated from the

TABLE 4. ISOMERIC PRODUCT RATIOS

Substrate	β/α	α′/α	(α + β)/α
[3]Ferrocenophane	1·57[b]	—	—
[3]Ferrocenophane-1-one	4·2	0·6	9·5
[4]Ferrocenophane	1·65[b]	—	—
[4]Ferrocenophane-1-one	1·2	0·5	4·5
[5]Ferrocenophane	2·19[b]	—	—
[5]Ferrocenophane-1-one	0·8	0·01	170

[a] The ratios given are the average of several experiments.
[b] Values taken from ref. 11.

weights of product isolated. In the other two cases, where partial overlap of two chromatographic bands occurred, the isomer ratios were calculated from NMR spectroscopy.[18] Fortuitously, the chemical shifts of the acetyl singlets in the spectra of the isomers of each series were clearly separated from each other and from the other proton resonances present (Table 2). Since the height to width at half-height ratios of these signals were approximately equal (i.e., the signals were equally sharp), the relative proportions of isomers present in a particular mixture could be obtained simply from a comparison of peak heights. The accuracy of this method was established from analysis of the spectra of various synthetic mixtures of pure isomers in predetermined proportions and good agreement between the actual and calculated ratios was observed. For those mixtures, therefore, which could not be completely separated chromatographically, i.e., α′- and α-acetyl[3]ferrocenophan-1-one and α- and β-acetyl[5]ferrocenophan-1-one, the relative proportions of isomers formed in the acetylation reactions were estimated from the NMR spectrum of the total chromatographic band in which they were contained.

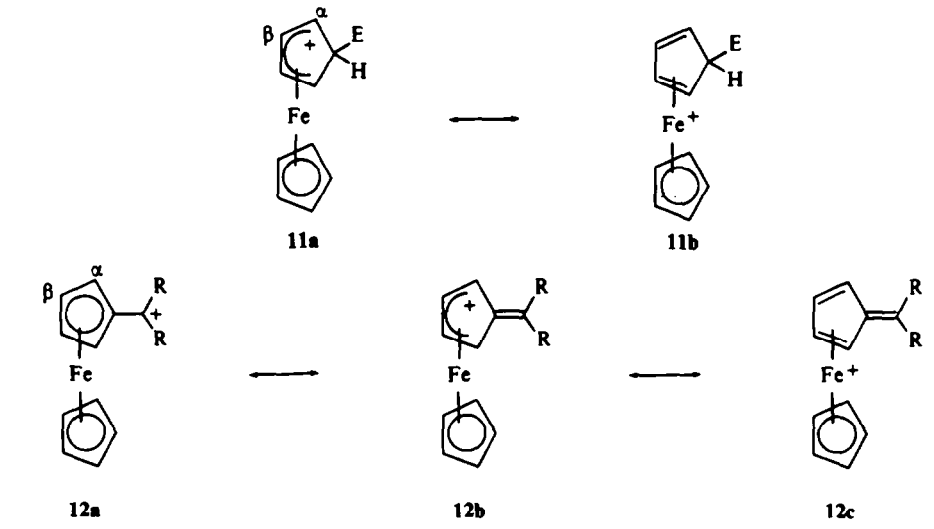
The isomer ratios obtained by these methods are given in Table 4 together with those previously obtained[11] for the acetylation of the corresponding [m]ferrocenophanes (**1**: m = 3, 4, and 5).

DISCUSSION OF RESULTS

Despite painstaking search of the product mixtures from each of the acetylation reactions, no trace of the β′-acetyl compounds (**4**) could be found. While it cannot be categorically stated that β′-substitution does not occur in these reactions, it appears most unlikely that these compounds are formed in significant proportions, particularly since their expected NMR characteristics should facilitate their detection (*vide supra*), even as minor constituents of isomeric mixtures. This result was not unexpected since the absence of 1,3-diacetylferrocene in the products from the acetylation of acetylferrocene has been definitely established.[14, 19]

Although a grossly oversimplified model was used, localized-energy MO calculations[14, 20] predict that, irrespective of the electronic character of the substituent, electrophilic substitution of a substituted ferrocene ring should occur more readily at positions adjacent to the substituent (i.e., α or α′). Experimental support for this conclusion can be drawn from the results of the acetylation of a series of arylferrocenes.[17, 20] The acylation of alkyl-substituted rings, however, occurs preferentially

at the β positions to an extent which increases with increase in the effective steric bulk of the substituent[10,11] or the electrophile.[6] In such reactions, therefore, there exists a delicate balance between steric and electronic effects and this point is further exemplified by the results of a kinetic study of the protodesilylation of a series of alkyl-substituted silylferrocenes.[21]



Considering the distribution of positive charge in the σ-complex (**11**) formed by addition of an electrophile (E^+) to a ring in ferrocene, it is not unreasonable to speculate that there would be an unequal distribution of charge to the ring carbon atoms α and β to the reaction site. In view of the results obtained in this and other studies, we suggest that, in the transition state for the formation of this intermediate, depletion of electron density occurs predominantly at the β positions which accordingly bear a higher proportion of the charge in the resulting cation (**11**) than the corresponding α positions.

Under the experimental conditions employed in this study, the bridge carbonyl group in the substrates (**2**) is complexed with $AlCl_3$ and strongly polarized in consequence (*cf.* **13**). Accepting Traylor's suggestion[9] that the rate-determining step for acetylation is σ-complex formation, addition of an acetylium ion to the α′ positions

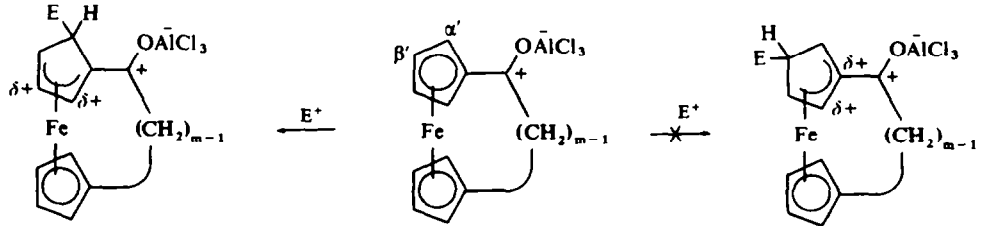


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FIG 2. σ-Complex intermediates in electrophilic addition to the carbonyl-substituted ring

of the acyl-substituted ring of the complex (**13**) would therefore be strongly favoured over β′ substitution despite the steric hindrance to be overcome (Fig 2). The latter pathway would involve unfavourable development of positive charge at a ring carbon atom already bearing a positively charged substituent atom. This mechanism is closely analogous to that advanced to account for the *meta*-directing effect of electron-withdrawing (-R) substituents in the electrophilic substitution of benzene derivatives.[22] Using similar arguments, the preferential β-acetylation of 1,1′-dialkylferrocenes[10] and [m]ferrocenophanes[11] can be accommodated. Substitution at these β positions is also favoured by steric factors as mentioned previously.

It is relevant at this point to compare the electronic structure of the σ-complex intermediate (**11**) with that of the ferrocenylcarbonium ion (**12**). Both species may be regarded as derivatives of the π-cyclopentadiene-π-cyclopentadienyliron cation, particularly if the exocyclic double bond in the latter (*cf.* **12 b, c**) plays an unimportant rôle in bonding the ligand to the metal, as has been suggested.[23] The exceptional thermodynamic stability of ferrocenylcarbonium ions[24] has provoked several interpretations of the bonding arrangement with controversy surrounding the interpretation of the NMR spectra of these species. It has been established[25,26] that the cyclopentadienyl protons located β to the formal positive centre (*cf.* **12a**) resonate at much lower field than the other ring protons and the original explanation for this effect, based upon a "ring-slip" model,[27] has been discredited.[26] In accord with our proposal (*vide supra*) concerning the distribution of positive charge in the related σ-complex (**11**), we suggest that a similar situation may obtain with the cation (**12**), with a greater proportion of the charge located at the β ring carbon atoms than at the corresponding α carbons. The low-field resonance of the β protons is thus readily explained.*

(α + β)/α′ Product ratios

From previous studies,[10] it is clear that the activating or deactivating influence of a substituent in ferrocene is felt to a greater extent by the ring bearing the substituent than by the other ring in the molecule. As evidenced by the (α + β)/α′ product ratios (Table 4), therefore, it is unsurprising that acetylation of the alkyl-substituted ring of the ketones (**2**) is favoured over substitution of the acyl-substituted ring. The extent of this preference, however, was found to vary considerably with the nature of the interannular bridge. The (α + β)/α′ ratio was found to be much higher for the [5]-1-one (**2**; m = 5) than for the [3]- and [4]-homologues (**2**; m = 3 and 4 respectively).

It has earlier been established[13,16] that the carbonyl group in the [5]-ketone may attain coplanarity and thus maximum resonance interaction with the adjacent cyclopentadienyl ring. The conformational constraints imposed upon the bridging chains of the lower homologues, on the other hand, preclude full conjugation of these groups (*cf.* crystal structure[28]). In consequence, the electron-withdrawing (-R) effect of the carbonyl group deactivates (towards electrophilic attack) the acyl-substituted ring of the [5]-ketone to a much more pronounced extent than in the case of the other two ketones, leading to a much higher (α + β)/α′ product ratio.

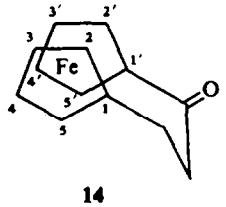
The finding that the (α + β)/α′ ratio for the [3]-ketone is approximately twice that for the [4]-ketone is perplexing. It seems unreasonable to argue that carbonyl-

* However, see Ref. 37.

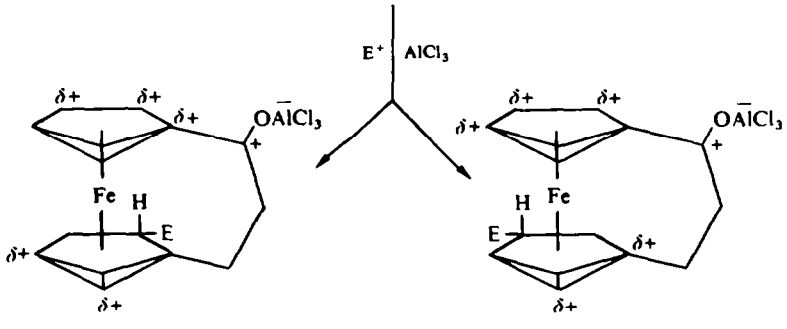
cyclopentadienyl conjugation would be weaker for the latter ketone and steric hindrance to substitution at ring positions adjacent to the bridge should be of a similar magnitude for each ketone [*cf.* β/α ratios for the corresponding ferrocenophanes (**1**; m = 3 and 4); Table 4]. We have previously commented,[16] however, upon the anomalous electronic absorption characteristics of compounds of the [4]ferrocenophane series and it is possible that a greater distortion of the ferrocene nucleus (e.g. by ring-tilting) is occasioned by a 4-carbon bridge than by a 3-carbon bridge. Molecular distortion of this nature would be accompanied by electronic reorganisation of the molecule[29] and the reactivity of the various ring positions to electrophilic attack could be affected unequally. Alternatively, it is perhaps possible that the alkyl-substituted ring in the [4]-ketone is deactivated to a greater extent by the bridge carbonyl group than the corresponding ring in the [3]-ketone. It is hoped that further research[30] will clarify the situation.

β/α *Product ratios*

Although the relative populations of the various conformers would be different, replacement of a methylene group at the terminus of an [m]ferrocenophane bridge by a carbonyl group would be expected to cause little change in the conformational *flexibility* of the molecule. In other words, the extent to which ring–ring torsion is permitted and the magnitude of the steric shielding of the alkyl-substituted rings by the bridges should be similar for the ferrocenophane (**1**) and ferrocenophanone (**2**) possessing the same number of bridging carbon atoms. With this in mind, comparison of the β/α product ratios for the ketones (**2**) with those for the corresponding ferrocenophanes (**1**) permits evaluation of the nature of the interannular directive influence of a carbonyl substituent with respect to electrophilic substitution.



14



15 **16**

FIG 3. σ-Complex intermediates in electrophilic addition to the alkyl-substituted ring

Consider first the [3]ferrocenophane system. The β/α product ratio for the ferrocenophane (**1**; m = 3) itself was found to be *ca.* 1·6 and the preference for β substitution can be attributed to a combination of steric[11] and perhaps electronic (*vide supra*) factors. Introduction of a carbonyl group at the bridge terminus remote from the ring in question, however, produces a marked increase in the β/α ratio (to 4·2). It must be concluded, therefore, that the carbonyl group deactivates the α positions towards electrophilic attack to a greater extent than the β positions. Although the transmission of electronic effects between the rings in ferrocene has long been recognised,[6, 10] the apparent stereospecificity of the effect has not previously been noted.

The molecular structure[28] and conformational characteristics[13] of the ketone (**2**; m = 3) are well documented. The cyclopentadienyl rings are constrained by the bridge to a near prismatic (eclipsed) conformation (**14**) and ring–ring torsion is severely limited.[13] From the previous discussion (*vide supra*), it may be postulated that addition of an electrophile (E^+) to an α position of this molecule would lead to a greater accumulation of positive charge at the carbon atoms of the same ring furthest removed from the reaction site [i.e., positions 4 and 5 in (**14**); see Fig 3]. If a sympathetic polarization of the bonds disposed from the iron atom to the carbon atoms pseudo-*trans* to these electron-deficient centres (i.e., the bonds to positions 1′, 2′, and 3′) is thereby induced, positive charge would be transmitted stereospecifically between the rings. In the corresponding intermediate for β substitution (**16**), similar reasoning leads to the conclusion that positive charge would be transmitted by the iron atom from positions 1 and 5 in one ring to positions 2′, 3′, and 4′ in the other. Comparison of the charge distribution in these σ-complex intermediates (**15** and **16**) shows that β substitution should be favoured as found experimentally. The transition state for α substitution would involve unfavourable development of positive charge at the ring carbon atom already bearing a strongly polarised carbonyl substituent (*cf.* **15**).

The operation of *trans*-effects in the chemistry of transition metal complexes has long been recognised and various theories have been advanced to account for the reaction behaviour observed.[31] However, no attempt has been made to interpret interannular electronic effects in metallocene or other sandwich-type molecules in terms of a *trans*-mechanism. In the majority of the published studies in this area, the substrates used were non-bridged ferrocenes[20] in which essentially free rotation of the cyclopentadienyl rings can occur.† Thus, although stereospecific interannular transmission of electronic effects may operate, observation of the process is masked in these systems. From the results we have obtained, we suggest that positive change may be transmitted stereospecifically by the metal atom from one ring to another in sandwich molecules as indicated (Fig 4) for the prismatic and antiprismatic rotameric conformations of ferrocene.

The β/α product ratios for [4]- and [5]ferrocenophan-1-one (**2**; m = 4 and 5 respectively) are both close to unity and thus significantly lower than the corresponding ratios for the [3]-homologue (**2**; m = 3) and the parent ferrocenophanes (**1**; m = 4 and 5) (Table 4). Since β substitution is favoured by steric factors,[11] this result implies that the bridge carbonyl group in these ketones deactivates the β ring positions to a

† From electron-diffraction studies, the potential barrier to rotation of the rings in gaseous ferrocene has been estimated to be 0·9 ± 0·3 kcal/mole.[32]

FIG 4. Interannular transmission of positive charge in ferrocene by a *trans*-mechanism

greater extent than the α positions such that the combination of steric and electronic factors produces a similar reactivity at these sites towards acetylation. A reversal of the situation found for the [3]-ketone apparently obtains.

Interpretation of this conclusion in terms of the mechanism previously discussed is complicated by the uncertainty concerning the preferred conformation(s) of these molecules in the transition state for acetylation. Previous work[13] has established that these ketones possess much greater torsional freedom of the cyclopentadienyl rings than is possible for the [3]-homologue (*vide supra*) and a greater number of rotameric conformations are possible (e.g. see Fig 5). For these substrates, therefore,

FIG 5. Conformations of [5]ferrocenophan-1-one

the operation of a *trans*-effect in the transition state for acetylation could conceivably deactivate both α and β positions. The experimental results would appear to suggest that the β positions experience the greater deactivation. Implicit in this discussion, of course, is the assumption that electrophilic addition is the rate-determining step in these acetylation reactions. The absence of a kinetic isotope effect for the acetylation of ferrocene itself ($k_H/k_D = 1{\cdot}0^9$), however, eliminates the possibility that the proton-removal step is rate-determining.

Finally, the possibility that the different substitution patterns observed for the ketones (**2**) may arise through the operation of electrostatic or field effects merits consideration. Qualitatively, it is difficult to apply the modern molecular-orbital treatment of this phenomenon[33] to the systems involved in this study. The earlier, less sophisticated theories[34] of Westheimer and others, however, stress that the magnitude of the field effect experienced at a molecular site is strongly dependent upon the relative orientation of the dipole producing the effect. In this study, the geometrical relationship between the orientation of the carbonyl dipole and the reaction sites in the acyl- and alkyl-substituted rings of the ketones (**2**) varies considerably with the nature and conformational properties of the different inter-annular bridging groups. It is conceivable that the different substitution patterns observed could result from a variation in the field effects induced by the carbonyl groups at the reaction sites in question. Further research into this problem is clearly required before a final interpretation can be reached.

EXPERIMENTAL

For general remarks, see Part I.[35] The methods of preparation of the ferrocenophanones have been described previously.[35,36] All of the reactions were carried out under an atmosphere of purified nitrogen and product yields are based upon starting material consumed. Electronic spectra were recorded on an Unicam SP800A recording spectrometer and NMR spectra on Perkin–Elmer R10 and R12 spectrometers operating at 60 MHz and 100 MHz respectively, using TMS as internal standard.

Chromatographies were carried out using Spence Grade H alumina which had been partially deactivated by exposure to the atmosphere for 6 hr.

Acetylation reactions. Only one such reaction is described in detail. The other acetylations were carried out in an exactly similar manner. The acetylation of each ketone was carried out at least twice and reproducible results were obtained. The products isolated from chromatographic bands were dried under reduced pressure using a rotary evaporator until a constant weight was observed.

Acetylation of [3]*ferrocenophan-1-one* (**2**; m = 3). Freshly sublimed and finely ground $AlCl_3$ (2·3 g; 17 mmole) was added to a stirred soln of the ketone (**2**; m = 3) (2·0 g; 8·3 mmole) and freshly distilled AcCl (0·7 g; 8·9 mmole) in CH_2Cl_2 (250 ml). A blood-red colour developed. The mixture was stirred overnight at room temp and then poured into water (500 ml). The organic phase was separated and combined with several CH_2Cl_2 extracts of the aqueous phase. The total extract was washed (H_2O), dried (Na_2SO_4), and evaporated. The residue was dissolved in ether and chromatographed. Ether eluted unchanged starting material (0·068 g; 3·4% recovery). Ether then eluted two well separated bands which afforded 0·557 g (first band; 24·5%) and 1·50 g (second band; 66·1%) of product (total yield 90·6%). The second band was found to be the pure β-acetyl isomer (**6**; m = 3) and the first a mixture of the α′- and α-acetyl isomers (**3** and **5** respectively; m = 3). A sample of this mixture was removed for NMR investigation and the remainder was redissolved in ether and chromatographed on a long thin column. From the first runnings of the band there was obtained after several recrystallizations the pure α′-acetyl isomer (**3**; m = 3). By a similar procedure, the pure α-isomer (**5**; m = 3) was isolated from the tailings of the chromatographic band. From the NMR spectra of the original mixture and of the pure components, it was calculated that the α′/α ratio was 47/90. The original mixture was thus calculated to contain 0·190 g α′ isomer and 0·367 g α-isomer.

Analytical data, etc., for the products from these reactions are collected in Table 1, NMR spectra in Table 2, electronic spectra in Table 3, and product isomer ratios in Table 4.

Mixed-hydride reduction reactions. Mixed-hydride reagent was prepared by careful portionwise addition of LAH to a stirred suspension of pure finely ground $AlCl_3$ in ether. The molar ratio of LAH to $AlCl_3$ was 1 to 2 respectively. In each reaction, a large excess of the reducing agent was used. A typical experiment is described below.

β-*Ethyl*[4]*ferrocenophane* (**10**, m = 4). β-Acetyl[4]ferrocenophane[11] (0·5 g; 1·8 mmole) was added portionwise to a large excess of mixed-hydride reagent, freshly prepared in ether (100 ml). The mixture was stirred overnight and the excess of hydride was destroyed by careful addition of wet ether. The mixture was poured into water (100 ml) and the ether layer was separated and combined with an ether extract of the aqueous layer. The total extract was dried (Na_2SO_4) and evaporated. The residue was dissolved in ligroin (b.p. 40–60°) and chromatographed. Ligroin eluted the sole product, β-ethyl[4]ferrocenophane (0·44 g; 92%), a yellow oil, which was purified by bulb-to-bulb distillation under reduced pressure.

The other ethyl[m]ferrocenophanes were similarly prepared from the corresponding acetyl[m]ferrocenophanes.[11] The IR spectra, determined as liquid films, of the α- and β-ethyl derivatives of each ferrocenophane were similar but clearly distinguishable. Identification of the products from the mixed hydride reduction of the acetyl[m]ferrocenophanones was achieved in this way. Analytical data, etc., for these compounds are given in Table 1 and the NMR spectra are summarized in Table 2.

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