

I. ELECTROPHILIC SUBSTITUTION REACTIONS
OF SOME SUBSTITUTED FERROCENES

II. THE EFFECTS OF HETEROANNULAR SUBSTITUENTS
ON THE RATES OF SOLVOLYSES OF
METHYLFERROCENYLCARBINYL ACETATES; A
COMPARISON WITH SUBSTITUENT EFFECTS IN
OTHER REACTIONS OF FERROCENE

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ABSTRACT

PART I

The directive effects of substituents in ferrocene have been investigated by means of Friedel-Crafts acetylation studies. It was demonstrated that the effect of an alkoxy-carbonylamino group is comparable to that of an alkyl group in the acetylation of 1, 1'-disubstituted ferrocenes. Contrary to expectations, acetylation of acetamido- and alkoxy-carbonylaminoferrocenes gave chiefly the heteroannular isomers. Only small amounts of the 1, 2-isomers were formed; no 1, 3-isomers were isolated.

The iodine in iodoferrocene was replaced by hydrogen under the conditions of the Friedel-Crafts reaction. Bromo- and chloroferrocenes were readily acetylated; only heteroannularly substituted isomers were formed.

PART II

The nature of the transmission of substituent effects from one cyclopentadienyl ring of ferrocene to a reaction center on the other ring was investigated by means of solvolyses studies on heteroannularly substituted methylferrocenylcarbinyl acetates. The evidence indicates that inductive or field effects predominate, and that resonance interactions play at most a minor role.

Substituents possessing unshared pairs of electrons can apparently undergo nucleophilic participation with the central iron atom. This interaction very likely requires that the ring bearing the substituent be shifted or tilted in the transition state so that the substituent can be sufficiently close to the iron atom.

A linear relationship has been shown to exist between substituent effects in all side-chain reactions of ferrocene reported to date and the reversible quarter-wave oxidation potentials of the appropriately substituted ferrocenes.

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I

ELECTROPHILIC SUBSTITUTION REACTIONS OF
SOME SUBSTITUTED FERROCENES

INTRODUCTION

The chemistry of ferrocene has been described in several recent reviews (1, 2, 3). The present discussion will therefore be limited to a summary of the studies which are pertinent to the investigation of the reactivity of ferrocene in electrophilic substitution reactions.

The aromaticity of ferrocene was demonstrated by its failure to react with maleic anhydride or to be reduced with hydrogen over a platinum catalyst, whereas it is readily acetylated under Friedel-Crafts conditions (4). Ferrocene cannot be directly nitrated or halogenated because the reagents themselves cause oxidation of ferrocene to the ferricinium ion (4, 5, 6). Broadhead, Osgerby and Pauson have demonstrated that ferrocene is substantially more reactive than anisole in a competitive acetylation and have estimated that the reactivity of ferrocene is comparable to that of phenol (7). No other direct comparison of the reactivity of ferrocene with the reactivities of other aromatic substrates has been reported. Hill has summarized experiments of a more qualitative nature which provide a further demonstration of the high reactivity of ferrocene in electrophilic substitution reactions (8). Hill's evaluation of these experiments shows that ferrocene is of about the same order of reactivity as thiophene, furan and resorcinol toward electrophilic substitution reagents.

Although ferrocene was demonstrated to be a highly reactive aromatic compound fairly soon after its discovery, very little was known about the effect of substituents upon the reactivity of ferrocene. It was known that an acetyl group on one ring deactivates the second ring towards further acetylation (9). The ring bearing the acetyl group is deactivated to an even more marked degree; the yield of homoannularly diacetylated product, identified as 1,2-diacetylferrocene, is only about 1.2% under conditions in which the heteroannularly disubstituted isomer, 1,1'-diacetylferrocene, is isolated in a yield of approximately 76% (9).

At the time the present research was undertaken only three studies concerned with intraannular directive effects in ferrocene had been published (9, 10, 11). In all three studies alkyl substituted ferrocenes were used as substrates in acetylation reactions. In one study the experimenters failed to isolate one of the isomers (11). The results of the other two studies are given in Table I. The system of nomenclature for designating the positions available for substitution in ferrocene is given in figure 1.

The continuous decrease in the ratio of 2 to 3-acetylalkylferrocene isomers as the size of the alkyl substituent is increased is consistent with the view expressed by the respective authors that steric factors largely determine the course of acetylation of ferrocene substrates of this type.

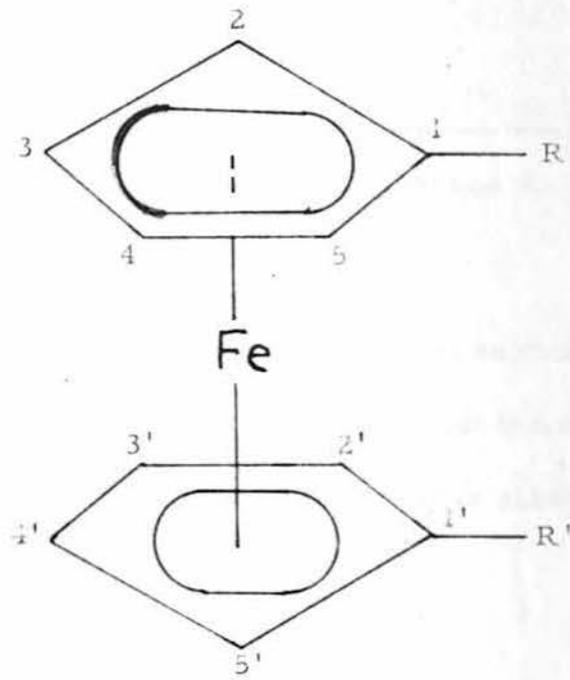


Figure 1

Table I

Ratio of Isomeric Acetylalkylferrocenes Formed During the Friedel-Crafts Acetylation Reaction.

<u>ferrocene compound</u>	<u>ratio of 2:3 acetylalkyl isomers</u>
1, 1'-dimethylferrocene ^a	1:2:3
ethylferrocene ^b	1:3:0
1, 1'-diisopropylferrocene ^a	1:4:3

a. Reference 10.

b. Reference 9.

The research described in the next section of this thesis was conducted in an attempt to learn more about the nature of the directing influence of substituents in the homoannular electrophilic substitution of ferrocene.

Results

In general acylation proceeds under mild conditions with a variety of ferrocene derivatives and affords respectable yields of readily characterizable products. The reaction is essentially irreversible under the experimental conditions employed, thus fulfilling a fundamental prerequisite for these studies (12).

Isomeric products were separated by chromatography on alumina. Structural assignments were made on the basis of comparisons

of the respective infrared, ultraviolet, and in some instances, nuclear magnetic resonance spectra. Isomer yields were calculated on the basis of the weight of materials isolated after removal of solvent from the chromatographic fractions but before any further purification was done. The purity of the materials at this stage of purification was checked by comparing the infrared spectra with spectra determined from samples of analytical purity.

Table II summarizes the results of acetylation reactions on mono- and disubstituted ferrocenes conducted in the course of the present research.

A limited study was made on the formylation (7) of 1,1'-diethylferrocene to see if this reaction would show more selectivity than was observed in the acetylation of this compound. Surprisingly, the 3-substituted isomer only was isolated; the yield was about 40%. Rinehart has subsequently reported that the formylation of 1,1'-trimethyleneferrocene gives only the 3-substituted product (13).

Since the acetamido and urethano substituents apparently deactivated the ring to which they were attached, as evidence by the much greater amount of heteroannular substitution than homoannular substitution, a competitive acetylation was conducted. Acetamidoferrocene and ferrocene were allowed to compete for one half of a molar equivalent of 1:1 acetyl chloride-aluminum chloride. Table III summarizes the results of this experiment.

Table II

Acetylation of Mono- and Disubstituted Ferrocenes.^a

Compound	Starting Material Recovered(%)	Isomer Yields, % Conversion		
		1'-	2-	3-
1, 1'-diethylferrocene	12.3 ^b	---	2.5	6.5
1, 1'-di(ethoxycarbonylamino)ferrocene	21.0 ^c	---	19	46
1, 1'-dibromoferrocene	20 ^{d, e}	a mixture of mono- and di-acetylated products was obtained		
acetamidoferrocene	42 ^f	37.4	0 ^g	0
	39.6 ^b	29.7	0 ^g	0
	17.8 ^c	69.2	3.3	0
	> 50 ^h	10-15	0	0
ethoxycarbonylaminoferrocene	--- ^{f, i}	50 ^j	< 5	0
methoxycarbonylaminoferrocene	--- ^{f, i}	50 ^j	< 5	0
cyanoferrocene	0 ^f	100	0	0
bromoferrocene	0 ^f	75	0	0
chloroferrocene	0 ^f	81	0	0
iodoferrocene	--- ^{f, k}	only acetylferrocene and di-acetylferrocene were isolated		

Table II (continued) - Legend

- a. See figure 1 for the numbering system; R' = H in the case of the monosubstituted ferrocenes.
- b. Silicon tetraacetate and stannic chloride were used.
- c. Acetic anhydride and boron trifluoride were used.
- d. This fraction was assumed to be starting material on the basis of its ease of elution from alumina; it was not characterized in any other way.
- e. The reagents used were a large excess of aluminum chloride and a smaller excess of acetyl chloride.
- f. Preformed 1:1 aluminum chloride-acetyl chloride was used.
- g. This isomer was probably present but was not isolated.
- h. The acetylating reagent was generated from acetic anhydride, acetyl chloride, acetic acid and sodium perchlorate.
- i. The amount of material recovered was not determined.
- j. This is an approximate value.
- k. A mixture of iodoferrocene and ferrocene was recovered.

Table III

Competitive Acetylation of Ferrocene and Acetamidoferrocene
with 1:1 Aluminum Chloride-Acetyl Chloride.

Run	Wt. of A (mg.) ^a	Wt. of B ^b	Wt. of Recovered		Wt. of Acetylated	
			A	B	A	B ^d
1	1130	1480	837	1299	305	135
2	1052	1377	784	1256	317	174(84) ^c

a. A is ferrocene.

b. B is acetamidoferrocene.

c. Weight of first crop after recrystallization; no attempt was made to recover more material from the recrystallization.

d. No 2-substituted isomer was isolated.

The calculated relative rates of acetylation based on the average of the two runs is $k(\text{ferrocene})/k(\text{acetamidoferrocene})$ equal to 2.0 ± 0.2 .

In addition to this competitive rate data the lesser reactivity of acetamidoferrocene compared with ferrocene is also apparent from the reaction of these two compounds with acylium perchlorate generated from a mixture of acetic acid, acetic anhydride, acetyl chloride and sodium perchlorate. Under identical conditions of temperature and reaction time acetylferrocene was formed in a yield of 40 to 50% whereas 1'-acetylacetamidoferrocene was formed in a yield of 10-15%.

Identification of Isomers

Pertinent ultraviolet data are given in Table IV and infrared data are given in Table V.

The two isomeric acetyldiethylferrocenes were assigned structures on the basis of comparisons of their ultraviolet spectra with those reported for other acetylalkylferrocenes (10). From Table IV it can be seen that 2-acetyl-1,1'-dimethyl- and 1,1'-diisopropylferrocenes possess absorption maxima which are not significantly displaced from those of acetylferrocene whereas the 3-acetyl-isomers possess absorption maxima which are shifted by 5-6 $m\mu$ to longer wavelengths from the 226 $m\mu$ absorption of acetylferrocene and by 4-5 $m\mu$ from the 269 $m\mu$ band.

In general it has been found that 1,2-disubstituted ferrocenes are more readily eluted from alumina than are 1,1'- or 1,3-disubstituted isomers (14). The acetyl-1,1'-diethylferrocene isomer eluted from the alumina chromatographic column first possessed ultraviolet maxima compatible with the structural assignment 2-acetyl-1,1'-diethylferrocene. The ultraviolet spectrum of the isomer eluted last was compatible with that to be expected for 3-acetyl-1,1'-diethylferrocene.

The structural assignment for 3-formyl-1,1'-diethylferrocene was similarly based on the generalization that the 3-isomer absorbs at longer wavelengths than either acetylferrocene or the 1,2-disubstituted carbonyl-alkylferrocenes.

Table IV

Ultraviolet Absorption Data for Some Substituted Ferrocenes.

Compound	$\lambda_{\text{max.}}, \text{m}\mu^{\text{a}}$	$\epsilon_{\text{max.}}^{\text{a}}$
acetylferrocene	226 ^{b, c}	16,500 ^{b, c}
	269	6,500
2-acetyl-1, 1'-dimethyl-ferrocene	227 ^{b, c}	18,600 ^{b, c}
	271	6,800
3-acetyl-1, 1'-dimethyl-ferrocene	232 ^{b, c}	15,800 ^{b, c}
	274	6,600
2-acetyl-1, 1'-diisopropyl-ferrocene	226 ^{b, c}	18,200 ^{b, c}
	271	6,700
3-acetyl-1, 1'-diisopropyl-ferrocene	231 ^{b, c}	15,600 ^{b, c}
	273	6,700
2-acetyl-1, 1'-diethyl-ferrocene	226	----
	269	----
3-acetyl-1, 1'-diethyl-ferrocene	232	----
	273	----
ferrocenealdehyde	226 ^e	17,000 ^e
	271	7,600
3-formyl-1, 1'-diethyl-ferrocene	233	----
	274	----
acetamidoferrocene	268	----
1'-acetylacetamido-ferrocene	222	18,300
	262	8,000
2-acetylacetamido-ferrocene	233 ^b	21,250 ^b
	265-270	10,700
	338-339	3,750
	237-238 ^d	19,900 ^d
	269-271	9,400
1'-acetyloxyethylaminoferrrocene	222-223	19,000
	222-223 ^b	20,200 ^b
	220 ^d	23,400 ^d
	280(broad shoulder)	3,000

Table IV (continued)

Compound	$\lambda_{\text{max.}}$, m ^a	$\epsilon_{\text{max.}}$ ^a
2-acetyl-1, 1'-di(ethoxy-carbonylamino)ferrocene	230	22,500
	280(broad shoulder)	7,550
3-acetyl-1, 1'-di(ethoxy-carbonylamino)ferrocene	226-227	22,150
	290(very broad shoulder)	6,100
1'-acetylbromoferrocene	223-224	----
	250-260(inflexion)	----
1'-acetylchloroferrocene	224-225	----
	270	----
1'-acetylcyanoferrocene	221	19,900
	253	10,600
	325(shoulder)	950
	220-222 ^d	----
	254	----
	310	----

- a. In methanol unless otherwise indicated.
- b. In 95% ethanol.
- c. Reference 10.
- d. In cyclohexane.
- e. Reference 7.

Table V

Infrared Absorption Bands of Some Substituted Ferrocenes

Compound	Solvent	Absorption Maxima (cm^{-1})			
acetamidoferrocene	CCl_4	3460	1694-1701	1107	1005
	CHCl_3	3450	1682	1103	1001
	nujol	3265 3220 ^a	1654 1289	1103	1001
2-acetylacetamidoferrocene	CCl_4	3340	1695, 1653	1292	poor resolution in other regions
	CS_2	3360	1700, 1659	1300	1109 1004
	nujol	3345	1686, 1650	1305	1107 1006
1'-acetylacetamidoferrocene	CCl_4	3445 (3320) ^b	1695, 1666	1278	1117
methoxycarbonylaminoferrocene	CHCl_3	3450 (3320) ^b	1686, 1666	1279	1112
2-acetylmethoxycarbonyl- aminoferrocene	CCl_4	3450	1745	1106	1007
1'-acetylmethoxycarbonyl- aminoferrocene	CCl_4	3350 (3450) ^b	1740, 1656	1296	1107 1005
	CCl_4	3450 (3320) ^b	1743, 1673	1278	1115
ethoxycarbonylaminoferrocene	nujol	3245	1715	1106	1001

Table V (continued)

Compound	Solvent	Absorption Maxima (cm ⁻¹)
2-acetyloxyferrocene	CS ₂ ^c	1722, 1645
2-acetyloxyferrocene	CS ₂ ^c	3315 ^b (3415) ^b
1'-acetyloxyferrocene	smear ^d	1730, 1655
1'-acetyloxyferrocene	smear ^d	3350
1'-acetyloxyferrocene	CCl ₄	1277
1'-acetyloxyferrocene	CCl ₄	1295
1'-acetyloxyferrocene	CCl ₄	1105
1'-acetyloxyferrocene	CCl ₄	1003
1'-acetyloxyferrocene	CCl ₄	1738, 1671
1'-acetyloxyferrocene	CCl ₄	3445 ^b (3320) ^b
1'-acetyloxyferrocene	CCl ₄	1277
1'-acetyloxyferrocene	CCl ₄	1115
1'-acetyloxyferrocene	CCl ₄	1282
1'-acetyloxyferrocene	CCl ₄	1115
1'-acetyloxyferrocene	CCl ₄	1305 ^g
1'-acetyloxyferrocene	CCl ₄	1735
1'-acetyloxyferrocene	CCl ₄	3450 ^f (3375) ^f
1'-acetyloxyferrocene	CCl ₄	1296
1'-acetyloxyferrocene	CCl ₄	1735, 1654
1'-acetyloxyferrocene	CCl ₄	3447 ^h 3345 ⁱ
1'-acetyloxyferrocene	CCl ₄	1296
1'-acetyloxyferrocene	CCl ₄	1735, 1654
1'-acetyloxyferrocene	CCl ₄	3358
1'-acetyloxyferrocene	CCl ₄	3248
1'-acetyloxyferrocene	CCl ₄	1301
1'-acetyloxyferrocene	CCl ₄	1113 ^g
1'-acetyloxyferrocene	CCl ₄	1723, 1652 (1675) ^g
1'-acetyloxyferrocene	CCl ₄	1305
1'-acetyloxyferrocene	CCl ₄	1725, 1664
1'-acetyloxyferrocene	CCl ₄	1304
1'-acetyloxyferrocene	CCl ₄	1726, 1640 1702
1'-acetyloxyferrocene	CCl ₄	1682
1'-acetyloxyferrocene	CCl ₄	1276
1'-acetyloxyferrocene	CCl ₄	1114
1'-acetyloxyferrocene	CCl ₄	1107
1'-acetyloxyferrocene	CCl ₄	1005
1'-acetyloxyferrocene	CCl ₄	1108
1'-acetyloxyferrocene	CCl ₄	1005
1'-acetyloxyferrocene	CCl ₄	1107
1'-acetyloxyferrocene	CCl ₄	1003
1'-acetyloxyferrocene	CCl ₄	1107
1'-acetyloxyferrocene	CCl ₄	1003

Table V (continued)

Compound	Solvent	Absorption Maxima (cm^{-1})		
1'-acetylchloroferrocene	CCl_4^c	1690	1281	1118
cyanoferrocene	CCl_4	2232	1109	1012
1'-acetylcyanoferrocene	CCl_4	2234	1685	1277 1117

- a. Shoulder.
- b. Very faint peak, presence is uncertain.
- c. Spectrum appears to be shifted slightly due to improper tracking.
- d. Spectrum of crude material after chromatography but before the material had solidified.
- e. Solution was very concentrated.
- f. May be due to intermolecular hydrogen bonding in the concentrated solution.
- g. Very weak, but definitely present.
- h. Due to the non-hydrogen bonded urethane group in the 1'-position.
- i. Due to the hydrogen bonded urethane group in the 2-position.

The isomeric ketones resulting from the acetylation of 1,1'-di(ethoxycarbonylamino)ferrocene were readily assigned structures on the basis of their infrared spectra. The isomer eluted first from alumina displayed a doublet in the N-H region and a carbonyl peak which was shifted to a lower frequency relative to that observed for acetylferrocene. This is compatible with hydrogen bonding which can occur if the acetyl and ethoxycarbonylamino substituents are on adjacent ring positions (15). The isomer eluted last from alumina displayed only a single absorption band in the N-H region and the carbonyl peak was only slightly shifted relative to that of acetylferrocene.

The correlation between position of substitution and wavelength of maximum absorption in the ultraviolet region found for acetyl-alkylferrocenes does not apply to the acetyl-1,1'-di(ethoxycarbonylamino)ferrocenes. In fact, the relationship between position of substitution and wavelength of maximum absorption is the inverse of that found for the acetyl-alkylferrocenes. In the case of 3-acetyl-1,1'-di(ethoxycarbonylamino)ferrocene, the maxima are not shifted significantly from those of acetylferrocene. However, the maxima of the 2-isomer are shifted by about 4 m μ to longer wavelengths. The absorption intensities are enhanced relative to those found for acetyl-alkylferrocenes (10).

The ketones resulting from the acetylation of acetamido-ferrocene and the urethanoferrocenes also displayed hydrogen bonding

between the amide hydrogen and the carbonyl function for the isomer eluted first from alumina but not for the isomer eluted last. In this instance no 3-substituted isomer was formed. The major isomer was the 1'-acetyl compound.

Rosenblum (16, 17) has shown that ferrocenes possessing an unsubstituted ring have absorptions in the infrared near 9 and 10 μ (1111 and 1000 cm^{-1}). In addition, if a ferrocene ring possesses only a single acetyl substituent and no other substituent there is a further characteristic absorption near 8.95 μ (1115 cm^{-1}) (17).

The three ketones resulting from the acetylation of acetamido-, methoxycarbonylamino- and ethoxycarbonylaminoferrocenes which were assigned the 1,2-disubstituted structure on the basis of hydrogen bonding evidence, also show bands at 9 and 10 μ characteristic of the unsubstituted ring and no band at 8.95 μ characteristic of a ring bearing only an acetyl substituent. The compounds assigned the 1,1'-disubstituted structure on the basis of order of elution from alumina and lack of peaks in the infrared indicative of hydrogen bonding all failed to show the 9 and 10 μ bands but did show the band at 8.95 μ characteristic of the acetyl substituted ring.

The assignment of structures to the two ketones resulting from the acetylation of methoxycarbonylaminoferrocene was substantiated by the nuclear magnetic resonance spectra of the two compounds. The isomer assigned the 1,2- structure on the basis of infrared

evidence showed a single intense absorption line characteristic of an unsubstituted cyclopentadienyl ring in ferrocene; the isomer assigned the 1, 1'- structure did not show the single sharp peak in the n. m. r. spectrum (13, 18).

The single ketone isolated in each instance when chloro-, bromo- or cyanoferrocene was acetylated showed no 9-10 μ absorption in the infrared spectrum but did show the absorption at 8.95 μ . On this basis these ketones were assigned the 1, 1'-disubstituted structure.

Discussion

Richards (19) and Rosenblum (20) have shown that the simple linear-combination-of-atomic orbitals (LCAO) molecular orbital method (21) predicts a higher reactivity towards electrophilic substitution on ferrocene at sites adjacent to carbon atoms bearing both electron donating and electron withdrawing groups than at sites non-adjacent to atoms so substituted. In the treatments of both Richards and Rosenblum the model for the ferrocene ring is a substituted cyclopentadienyl radical. This treatment is in accord with the molecular orbital description given by Moffitt (22) and by Dunitz and Orgel (23) in which primary metal to ring bonding is derived from essentially a single delocalized covalent electron pair bond. The approximations introduced by Roberts and Streitwieser (24), in which substituent types are generalized in terms of an anionic or cationic carbon center, have been employed in

these calculations. In Rosenblum's treatment the non-orthogonality integral, S , between adjacent carbon atoms was taken as 0.25 (21); in Richards' treatment this term was neglected (25). Table VI gives the localization energies for substitution at the 2- and 3-positions.

Table VI

Localization Energies ($-\beta$)

Model	Rosenblum's Treatment		Richards' Treatment	
	2-position	3-position	2-position	3-position
$C_5H_5-\bar{C}H_2$	1.149	1.356	1.748	1.784
$C_5H_5-\overset{+}{C}H_2$	1.685	1.734	2.384	2.386

While both treatments clearly predict a higher reactivity for substitution at the 2-position than at the 3-position for both electron donating and electron withdrawing groups, it must be kept in mind that the system under consideration is a non-alternant hydrocarbon. The simple LCAO method is known to be less reliable for non-alternant hydrocarbons because of the presence of a non-self-consistent field (25). In addition, electronegativity factors have not been considered.

Rosenblum (20) has also pointed out that a descriptive resonance treatment, in which the primary covalent iron to ring bond is formalized in terms of a position variable single bond, predicts a greater electrophilic substitution reactivity at the 2-position than at the 3-position for ferrocenes bearing electron donor groups. However, this

treatment predicts a greater reactivity at the 3- position for ferrocenes bearing electron withdrawing groups.

Studies of electrophilic substitution reactions of alkylferrocenes, including the work described herein, give results which are contrary to those predicted from the molecular orbital calculations. In all instances the 3- position of alkylferrocenes is observed experimentally to be more reactive than the 2- position. This has been attributed to steric factors (10). It is known that an alkyl group does not affect the reactivity of ferrocene to nearly so great an extent as it does the reactivity of benzene. Garwood found that in a competitive acetylation using boron trifluoride and acetic anhydride 1,1'-diethylferrocene is only 1.7 times more reactive than ferrocene (26). He found that under these conditions the 2:3 isomer ratio was 1:2.0.

The small activating effect of an alkyl group in the acetylation of 1,1'-diethylferrocene is very notable when contrasted with the effect of an alkyl group in the acetylation of toluene. Brown reported that toluene is 128 times more reactive than benzene in a competitive acetylation using acetyl chloride and aluminum chloride (27). The difference in the effect of an alkyl group in the two systems is even more marked if one considers that 1,1'-diethylferrocene was acetylated with a more selective reagent (28). If toluene and benzene could be acetylated with acetic anhydride and boron trifluoride, toluene would

presumably be quite a bit more than 128 times more reactive than benzene.

Inasmuch as the course of acetylation of alkyl substituted ferrocenes appeared to be governed mainly by steric factors, it was decided that a ferrocene substituted with a more strongly ortho-para orienting group should be studied. At the time this phase of the research was initiated an acetamido substituted ferrocene appeared to be the most readily accessible compound of the type desired. The acetamido group is known to be ortho-para directing in the electrophilic substitution of benzene compounds (29). It is considerably more activating than a methyl group in mercuration (30) and halogenation (31) reactions.

Initially we had hoped to acetylate 1, 1'-di(acetamido)ferrocene in order to avoid the possibility of having three isomers to isolate and identify. However, numerous attempts to prepare the disubstituted compound by methods which gave the monosubstituted compound in good yield all failed. This difficulty was circumvented by demonstrating that the ethoxycarbonylamino group gave essentially the same results as the acetamido group in the acetylation of the monosubstituted substrates and then preparing 1, 1'-di(ethoxycarbonylamino)ferrocene by a known method (32). The acetylation of 1, 1'-di(ethoxycarbonylamino)ferrocene with boron trifluoride and acetic anhydride gave two to three times more 3-acetyl than 2-acetyl substituted product. This

result is essentially the same as that obtained when 1,1'-dimethylferrocene (10) or 1,1'-diethylferrocene is acetylated (26).

The results of the acetylation of acetamido- and urethano-substituted ferrocenes were rather surprising. The monosubstituted compounds in all instances gave predominately the heteroannularly substituted isomer. Rinehart has subsequently confirmed the observation that acetamidoferrocene gives chiefly 1'-acetylacetamidoferrocene upon acetylation (13). In the present work, some runs gave the 1,2-homoannularly substituted product; in none of the runs was any 1,3-substituted isomer detected. In two experiments the 1,1'-isomer was subjected to repeated chromatography and numerous fractions were taken and studied individually in an attempt to detect small amounts of a different isomer.

The predominance of heteroannular substitution indicates that the ring bearing the acetamido or urethano group is deactivated towards acetylation instead of being activated as had been anticipated. A competitive acetylation study confirmed that acetamidoferrocene is less reactive than ferrocene by about a factor of two.

Brown (30) and Stock (31) have reported data which indicate that the acetamido group is a powerful electron donor in mercuration and bromination reactions on acetanilide. In contrast to this, however, there are several studies of a qualitative nature which indicate that acetanilide is less reactive than benzene in certain nitration (33) and

acetylation (34, 35) reactions. Under the conditions of these reactions, it is likely that the amide group had formed a salt or complex and thus did not activate the benzene nucleus towards electrophilic substitution.

The reason for the deactivating effect of the acetamido and urethano groups in the acetylation of the substituted ferrocenes is less clear. In the case of the competitive acetylation reaction one explanation for the lesser reactivity of acetamidoferrocene as compared with ferrocene may be that acetamidoferrocene is selectively deactivated by protonation. Rosenblum has presented convincing evidence that ferrocene may be effectively removed from the acetylation reaction through formation of a relatively stable, non-acylable complex salt with aluminum chloride and hydrogen chloride (12). Competitive acetylation data for substituted ferrocenes are therefore somewhat ambiguous to the extent that one substrate may form this complex more readily than another.

It must be kept in mind, however, that acetamidoferrocene and the urethanoferrocenes gave, within the limits of experimental error, essentially the same ratios of homoannular to heteroannular substitution in reactions involving large variations in the concentration and composition of the acetylating reagent. This fact supports the hypothesis that the observed predominance of heteroannular over homoannular substitution is due to the nature of the substituent on ferrocene rather than deactivation of the ring bearing the substituent because of the formation

of a complex between the substituent and the electrophile or a Lewis acid. A choice between these two explanations cannot be made on the basis of the data presently available.

The deactivating influence of the acetamido and urethano groups in the acetylation of acetamido- and urethano- substituted ferrocenes is in direct contrast to the activating effect these groups have in the chronopotentiometric oxidation of these substituted ferrocenes.* In the oxidation of ferrocene to the ferricinium ion the acetamido and urethano groups facilitate the reaction to at least the same extent as a methoxy group. Surprisingly, an alkyl group facilitates the oxidation reaction to about the same extent as any of the above mentioned groups.

Recently Morrison and Pauson have reported that in the Friedel-Crafts acetylation of chloro-, methylthio-, and methoxyferrocenes the substituents were replaced by hydrogen (36). They found that when chloroferrocene was acetylated ferrocene was isolated and that when methoxyferrocene was acetylated acetylferrocene was isolated.

In the present research it was found, in accord with the observation of Morrison and Pauson, that a halogen atom may be replaced by hydrogen during the reaction. However, the results of the present study differ from those of Morrison and Pauson in that under the conditions employed herein the halogen atom in iodoferrocene only was replaced; both chloroferrocene and bromoferrocene were acetylated to

*A discussion of the oxidation reaction is given in Part II of this thesis.

give the heteroannularly substituted isomers in good yield. There was no indication that homoannular substitution had occurred. Nesmeyanov has also found that when bromoferrocene is acetylated only the heteroannularly substituted isomer is formed (37).

Two attempts to acetylate iodoferrocene under the same conditions used to acetylate bromo- and chloroferrocenes gave only acetylferrrocene and 1, 1'-diacetylferrrocene; an approximately 1:1 mixture of iodoferrocene and ferrrocene was recovered. No attempt was made to separate possible coupling products or diiodoferrocene from the non-ketonic fractions. If these materials were present in small amounts they would not be readily detected by the spectroscopic methods used to characterize the non-ketonic fraction.

Morrison and Pauson have proposed the mechanism for the loss of chlorine during the acetylation of chloroferrocene outlined in figure 2 (36). The protonated chloroferrocene (II) given in equation 1 is analogous to the protonated ferrrocene-aluminum chloride complex proposed by Rosenblum to account for the anomalous acetylation of ferrrocene (12). Morrison and Pauson state that the cation (III) may then react according to one or both of the schemes given in equations 2 and 3. Since they isolated no dichloroferrocene derivative they suggest that the reaction proceeds according to equation 2, or some related mode of reaction.

When Morrison and Pauson treated methoxy- and methylthioferrrocenes with aluminum chloride, however, not only ferrrocene, but

also mixtures of the isomeric dimethoxy- and di(methylthio)ferrocenes were formed. Thus, in the case of these two compounds, it seems that the course of reaction indicated in equation 3 is followed.

It is interesting to note that the acetylation of 1, 1'-dibromo-ferrocene, using a large excess of aluminum chloride and a somewhat smaller excess of acetyl chloride, apparently gives a mixture of mono- and diacetylated products. That diacetylation should occur is a little surprising since the molecule bears two deactivating groups. Although the elemental analysis is not very satisfactory, it does support the conclusion that the diacetylated compound still contains two bromine atoms. Infrared data, with the possible exception of that obtained for one of the diacetylated isomers, indicates that the acetyl groups are on rings which also bear other substituents (17).

Recent studies by several workers have demonstrated that the 2-position is more reactive than the 3-position towards electrophilic substitution in the case of ferrocene substituted with substituents other than those mentioned in the preceding discussion.

Knox, Pauson and Tiers (38) found for the aminomethylation of 1, 1'-bis-methylthioferrocene a 2:3 isomer ratio of 1.9:1. They also found, judging on the basis of relative yield data, that ferrocene was probably the more reactive of the two compounds. Rosenblum has pointed out that the sulfur atom may facilitate substitution at the 2-position (20).

Rosenblum has demonstrated for a series of phenyl- and p-substituted phenylferrocene derivatives that the 2-position is more reactive than the 3-position towards acetylation using 1:1 aluminum chloride-acetyl chloride (20). His data are summarized in Tables VII and VIII. The data for ethylferrocene are included for comparison.

Table VII

Relative Site Reactivities in Aryl Substituted Ferrocenes.

ferrocene	Site Reactivities			
	p-position	1'-	2-	3-
1, 1'-diphenyl	0.50 ^a	---	1.65	1.00
1, 1'-bis-p-methoxyphenyl	---	---	1.95	1.00
1, 1'-bis-p-bromophenyl	---	---	1.11	1.00
phenyl-	0.23	1.00	0.77	0.47
p-methoxyphenyl-	---	1.00	1.16	0.60
ethyl-	---	1.00	1.4	4.2

a. Value is probably high.

Table VIII

Site Reactivities in Diarylferrocenes Compared with Ferrocene.^a

ferrocene	Site Reactivities		
	p-position	2-position	3-position
1, 1'-diphenyl-	0.22 ^b	0.71	0.43
1, 1'-bis-p-bromophenyl-	---	0.33	0.30

a. Each position in ferrocene is assigned unit reactivity.

b. Calculated value is probably high.

On the basis of the experiments just described, Rosenblum (20) has made the following statement:

For the monoarylferrocenes, the difference in reactivity between those sites in the unsubstituted and those in the substituted ferrocene rings, manifest in phenylferrocene, are diminished in p-methoxyphenylferrocene as a consequence of a reduction in the electronegativity of the aryl substituent and of enhanced resonance stabilization by the methoxyl group of processes involving homoannular substitution.

This evidence for a resonance interaction is to be contrasted with the results of competition experiments on 1, 1'-diethylferrocene (26) and on acetamidoferrocene discussed above. The effect of alkyl and acetamido substituents on the reactivity of ferrocene in the acetylation reaction seems to speak against a resonance interaction. The results for the acetylation of acetamidoferrocene are, of course, not free from the ambiguity of deactivation towards electrophilic substitution because of complex formation between the amide group and the reagents.

The data of Knox, Pauson and Tiers (38) on the aminomethylation of methylthio substituted ferrocenes also is evidence against a resonance interaction. Had they performed a competition experiment instead of judging the relative reactivities of ferrocene and methylthioferrocene from yield data, the evidence against a resonance interaction would have been more conclusive. Brown has shown that the methylthio group is an electron donor of nearly the same order of magnitude as a methoxy group (39).

Clearly, the next step in the investigation of substituent effects in ferrocene should be a series of competition experiments involving the electrophilic substitution of ferrocenes bearing substituents such as methoxy, the halogens, cyano and nitro.

A better test of the molecular orbital predictions would be obtained if the electrophilic substitution reactions of 1, 1'-disubstituted ferrocenes bearing substituents such as methoxy, chloro and cyano groups were studied. It may well be that the order of reactivity at the 2- and 3- positions reverses depending upon factors other than steric.

Summary

It has been shown that in the acetylation of 1, 1'-di(ethoxycarbonylamino)ferrocene with boron trifluoride and acetic anhydride substitution at the 3- position predominates over substitution at the 2-

position by about a factor of three. Acetylation of acetamido- and urethano- ferrocenes gives chiefly the 1'- isomer; the 2- substituted isomers are formed in low yield and apparently no 3- substituted isomers are formed at all. A competitive acetylation between acetamidoferrocene and ferrocene showed that ferrocene was the more reactive compound by about a factor of two. Acetylation of ferrocene bearing bromo, chloro or cyano groups was shown to give only the 1'- substituted isomer. Iodoferrocene lost iodine under Friedel-Crafts acetylation conditions; no acetyliodoferrocene was formed.

EXPERIMENTAL

All melting points are reported uncorrected and were determined on an Eimer and Amend melting point block unless otherwise indicated. Infrared spectra were determined on a Beckman IR-7 recording spectrophotometer and a Perkin-Elmer model 237 spectrophotometer. Ultraviolet spectra were determined on a Cary model 11 M recording spectrophotometer. Nuclear magnetic resonance spectra were determined on a Varian Associates model A-60 spectrometer.

Elemental analyses were performed by Elek Microanalytical Laboratory, Los Angeles, California; Spang Microanalytical Laboratory, Ann Arbor, Michigan; and by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

Reactions were customarily run under a nitrogen atmosphere and in vessels wrapped with aluminum foil to protect the contents from light.

A. Materials

Ferrocene was in part donated by the E. I. duPont de Nemours Company and in part obtained commercially.

Acetylferrocene was prepared by acetylating ferrocene with acetic anhydride and boron trifluoride (40) and with acetic anhydride and phosphoric acid (41).

1, 1'-Diacetylferrocene was prepared by acetylating ferrocene with acetyl chloride and aluminum chloride according to the procedure of Rosenblum (9).

1, 1'-Diethylferrocene was prepared by reducing 1, 1'-diacetylferrocene according to procedure number two of three procedures given by Nystrom and Berger (42) for reduction with a mixture of lithium aluminum hydride with aluminum chloride.

Lithium aluminum hydride (3.8 g., 0.10 mole) in 100 ml. of ether was added over a period of three to five minutes to aluminum chloride (13.3 g., 0.10 mole) in 100 ml. of ether in a 1-l. flask equipped with a reflux condenser, a stirrer and a dropping funnel. 1, 1'-Diacetylferrocene (10.0 g., 0.037 mole) in 150 ml. of tetrahydrofuran was added dropwise over a period of 0.5 hr. The reaction mixture was stirred an additional 0.5 hr. then water (20 ml.) was added cautiously. Sulfuric acid (50 ml.; 6 N) was added and the mixture was filtered and the organic fraction separated. The aqueous fraction was washed with ether and the ether washings were combined with the main organic fraction. The organic solution was washed with water, dried over anhydrous sodium sulfate and filtered. The red oil resulting after the removal of solvent was taken up in n-heptane and chromatographed on alumina. No trace of diacetylferrocene was observed and very little tarry material was present. Nine grams (essentially a quantitative conversion) of 1, 1'-diethylferrocene was isolated.

The infrared spectrum and vapor phase chromatography indicated that the product was free from impurities. Some solid impurity was present after the compound had stood in a closed container for two days. The product was distilled in a 50-ml. Claisen distillation flask; a center cut was taken at 106° and a pressure of 190 μ . The index of refraction of the freshly distilled material is 1.5768 at 27° (lit., n_D^{25} 1.5760 (32); 1.5761 (43).

Ferrocenecarboxylic acid was prepared in part by the oxidation of acetylferrocene with iodine in pyridine according to the procedure reported by Weinmayr (44). This compound was prepared more conveniently by the method of Little and Eisenthal (45). In the latter method, diphenylcarbonylferrocene was prepared by the Friedel-Crafts reaction between N,N-diphenylcarbonyl chloride and ferrocene in the presence of aluminum chloride. The amide was readily hydrolyzed in an alkaline solution of ethanol and water. Ferrocenecarboxylic acid was isolated from the hydrolysis mixture in a yield of about 70%, based on ferrocene.

Ferrocene-1,1'-dicarboxylic acid was prepared in part by the method of Rosenblum wherein 1,1'-diacetylferrocene is oxidized with hypohalite (32). This compound was prepared more conveniently by carbonation of 1,1'-dilithioferrocene, according to the procedure given by Mayo, Shaw and Rausch (46). In the present study, modification six of their general procedure proved to be the most convenient.

In agreement with their report, the overall conversion was about 60%, based on ferrocene; about two times as much ferrocene-1, 1'-dicarboxylic acid as ferrocenecarboxylic acid was isolated. The acids were readily separated on the basis of their greatly different solubilities in ether.

Numerous attempts to oxidize 1, 1'-diacetylferrocene by the iodine-pyridine method failed. In some instances a small amount of 1'-acetylferrocenecarboxylic acid was isolated, but generally, only tarry decomposition products were formed.

Carbazidoferrocene was prepared by a procedure based on modifications of existing procedures which employ the reaction of sodium azide with chlorocarbonylferrocene (47, 48). To ferrocenecarboxylic acid (17.5 g., 0.076 mole) partly dissolved and partly suspended in dry benzene (175 ml.) in a 500-ml. Morton flask equipped with a high-speed stirrer and an apparatus for maintaining a nitrogen atmosphere was added phosphorus pentachloride (17.5 g., 0.084 mole) in 0.5-g. portions over a period of one hour. A small amount of phosphorus pentachloride was filtered from the reaction mixture after it had been stirred for one hour after the addition was completed. Benzene and phosphorus oxychloride, which was formed during the course of the reaction, were distilled under reduced pressure. The product was maintained at 80° under a pressure of 25 mm. for 0.5 hr. to insure that no phosphorus oxychloride remained. Sodium azide (6.5 g., 0.10 mole) in water (20 ml.) was added over a period of 3 to

5 min. to the crude dark-red oily product in acetone (100 ml.) at 0°. The solution was stirred for 15 min. after the addition was completed, then the ice bath was removed and the solution was stirred for 30 min. The mixture was poured into 700 ml. of ice water and agitated vigorously for a few minutes. A large amount of brown solid was filtered and suction dried. A chloroform extract of the aqueous filtrate yielded no organic material. The crude product was dried in a vacuum desiccator and then it was extracted in a Soxhlet apparatus for 6 hrs. with petroleum ether boiling at about 40°. The solvent in the reboiling flask was chilled with dry ice and filtered. Carbazidoferrocene (12.2 g., 63%) was isolated in the form of fine orange crystals melting at 84.5 to 85° (lit. (47, 48) m. p. 74 to 75°; 84 to 86°).

A modification of the above procedure consisted in preparing the acid chloride by treating ferrocenecarboxylic acid with phosphorus trichloride instead of phosphorus pentachloride. This reagent reportedly gives the acid chloride in nearly a quantitative yield (49, 50).

In a single run in the present work carbazidoferrocene was isolated in only a 33% yield using this modification; it is probable that this could be improved very easily.

Carbazidoferrocene was also prepared by treating the mixed anhydride resulting from the reaction of ethylchloroformate with ferrocenecarboxylic acid and triethylamine with sodium azide in water. Weinstock has reported that *cis*-2-phenylcyclopropylamine can be

prepared in 77% yield from *cis*-2-phenylcyclopropanecarboxylic acid by using the mixed anhydride to prepare the intermediate carboxylic acid azide (51).

To ferrocenecarboxylic acid (7.0 g., 0.03 mole) partially dissolved in 15 ml. of water and 75 ml. of acetone in a 200-ml. round bottomed flask equipped with a magnetic stirrer, a dropping funnel with a pressure equalizing side tube, and an apparatus for maintaining a nitrogen atmosphere was added triethylamine (5.7 ml., 0.04 mole) in 75 ml. of acetone. The solution appeared to be homogeneous at this point. Ethyl chloroformate (5.2 ml., 0.05 mole) in 25 ml. of acetone was added dropwise to the solution at room temperature over a period of 30 min. The reaction mixture was stirred an additional 15 min. and then sodium azide (4.3 g., 0.065 mole) in water (15 ml.) was added over a period of 15 min. The mixture was stirred at room temperature for one hour after the addition was completed; it was then poured into one liter of ice water. The yellow solid resulting was filtered; the filtrate was acidified and more yellow solid precipitated. The suspension was extracted with chloroform; a very light yellow green aqueous phase and a yellow chloroform phase containing suspended solid resulted. The organic phase was separated and used to extract the solid (still on the filter pad) collected initially. Only a small amount of yellow solid remained undissolved on the filter pad. The dark cherry-red chloroform solution was washed with a total of 100 ml. of

5% sodium hydroxide solution. Ferrocenecarboxylic acid (weight 3.3 g. after drying in a vacuum desiccator for six days) resulted from working up the basic aqueous phase.* The chloroform solution was washed with water, dried over sodium sulfate and filtered. Distillation of the chloroform gave carbazidoferrocene (4.3 g., 56% conversion, or 111% based on recovered ferrocenecarboxylic acid, which was probably not quite dry) melting at 82.5 to 84.5°.

This procedure is very much faster than previously reported methods and it gives good conversion with little decomposition of starting material.

Carbazidoferrocene was prepared in low yield using the method reported by Rosenblum for the preparation of 1, 1'-dicarbazidoferrocene (32). The method is laborious and is of little value in view of the success achieved with the previously described procedures.

1, 1'-Dicarbazidoferrocene was prepared according to Rosenblum's procedure (32) by the reaction of hydrazine with crude 1, 1'-dicarbomethoxyferrocene (8) in yields of 50 to 60%. Treatment of 1, 1'-dicarbohydrazidoferrocene with sodium nitrite in dilute hydrochloric acid gave the desired di-azide in yields of 70 to 80% (m.p., sealed tube, 115°, dec.; lit (32) m.p., 100°, dec.).

*It was subsequently found that ferrocenecarboxylic acid and ferrocene-1, 1'-dicarboxylic acid require drying at 90 to 100° at a pressure of about 2 mm. for about 2 hrs. to ensure complete removal of water.

One attempt was made to prepare 1,1'-dicarbazidoferrocene by the reaction of 1,1'-chlorocarbonylferrocene (made from ferrocene-1,1'-dicarboxylic acid and phosphorus trichloride) with sodium azide in aqueous acetone. About half the starting amount of ferrocene-1,1'-dicarboxylic acid was recovered; no 1,1'-dicarbazidoferrocene could be isolated. It appeared that the acid chloride may have hydrolyzed when the aqueous solution of sodium azide was added since some white vapor, which could have been hydrochloric acid, evolved at that point. Nesmeyanov has observed that 1,1'-dichlorocarbonylferrocene is hydrolyzed slowly in the presence of 20% sodium carbonate (50).

Acetamidoferrocene was prepared by heating carbazidoferrocene in acetic anhydride and hydrolyzing the resulting diacetylated amine under mild conditions to remove one acetyl function. Several examples of this method for preparing N-acylated aromatic amines from aromatic carboxylic acid azides have been reported in the literature (52). Carbazidoferrocene (5.0 g., 0.02 mole) was added to 200 ml. of acetic anhydride in a 500-ml. Morton flask equipped with a high speed stirrer. Most of the suspended solid dissolved when the mixture was heated to 100°. The mixture was stirred at this temperature vigorously for 4 hrs. and then all but a few ml. of the acetic anhydride was distilled under reduced pressure. Water (300 ml., saturated with nitrogen) was added to the residue and the mixture was stirred for 18 hrs. at room temperature. Filtration gave no solid; most of the product

remained in the reaction flask as a gum. The aqueous filtrate was extracted with chloroform; this extract was combined with a chloroform extract of the material still in the flask and the combined solutions were dried over anhydrous sodium sulfate and filtered. Chloroform was distilled under reduced pressure and the residue was taken up in benzene and chromatographed on alumina. Ethyl ether was required to elute the yellow product band from the column. Yellow platelets of acetamidoferrocene (3.3 g., 73% of theory) melting at 168 to 170° were collected upon removal of solvent from the product cut. Careful recrystallization raised the m.p. to 173 to 173.5° (lit. (47) m.p. 170.5 to 171°).

Anal. Calculated for $C_{12}H_{13}NO_2Fe$: C, 59.29; H, 5.39; N, 5.76.

Found (Elek): C, 59.32; H, 5.44; N, 5.69.

In an attempt to find a milder method for rearranging carazidoferrocene and obtain the N-acetylated amine without isolation of the intermediate isocyanate the following method, based on procedures existing in the literature for similar reactions on other compounds, was devised (53).

Crude ferrocenoyl chloride (prepared from ferrocenecarboxylic acid (0.65 g., 4.4×10^{-3} mole) and phosphorus trichloride) was dissolved in 50 ml. of dry benzene in a 500-ml. Morton flask equipped with a paddle blade stirrer and an apparatus for measuring the volume

of nitrogen evolved. Sodium azide (1.0 g., 0.016 mole) was added as a powder and the mixture was refluxed for 1 hr. Nitrogen evolution ceased after the first 0.5 hr. of refluxing; roughly the theoretical amount of nitrogen was collected. The reaction mixture was cooled to room temperature and filtered. The cherry red filtrate was transferred to a 500-ml. round bottomed flask equipped with a magnetic stirrer, reflux condenser and an apparatus for measuring the amount of carbon dioxide evolved. Ten ml. of 5% acetic anhydride in acetic acid was added and the solution was refluxed for 1 hr. (54). Carbon dioxide ceased to evolve after 15 min. of refluxing; only about one half the theoretical amount of carbon dioxide was collected. Volatile components were distilled from the dark brown mixture under reduced pressure. The orange solid remaining in the reaction vessel was extracted with a total of 150 ml. of hot toluene; the resulting light orange solution was filtered and a small amount of base-insoluble dark solid was collected. The toluene solution was reduced to a volume of 25 ml. and allowed to cool to room temperature slowly. Fine cottony amber needles were filtered, washed with petroleum ether and suction dried. This material proved to be ferrocenecarboxylic acid (m.p. 200 to 210°, dec.; lit. (32) 210 dec.).

1, 1'-Di(acetamido)ferrocene could not be prepared by heating 1, 1'-dicarbazidoferrocene in acetic anhydride. Several runs gave only tars and traces of material displaying a peak in the infrared spectrum

characteristic of the carbazido group in carbazidoferrocene.

Heating 1, 1'-dicarbazidoferrocene in benzene followed by treatment of the resulting diisocyanate with 5% acetic anhydride in acetic acid resulted in decomposition of the material, just as described above in the case of carbazidoferrocene.

Knox has reported the synthesis of 1, 1'-di(methoxycarbonylamino)ferrocene by treating 1, 1'-diaminoferrocene, prepared in situ by reductive cleavage of 1, 1'-diphenylazoferrocene, with methyl chlorocarbonate (55). 1, 1'-Diaminoferrocene is very unstable and has not been isolated to date (32). Treatment of 1, 1'-diaminoferrocene prepared according to the procedure of Knox with standard acetylating reagents appeared to be a good route to 1, 1'-di(acetamido)ferrocene.

Diazocyclopentadiene (56) (5.2 g., 0.06 mole) in ether (40 ml.) was added dropwise during 0.5 hr. to a solution of phenyllithium (from 0.12 mole of bromobenzene and 0.24 mole lithium in 100 ml. of ether at -30° with rapid stirring. A nitrogen atmosphere was maintained during the addition and subsequent reactions. Anhydrous ferrous chloride (10.2 g., 0.085 mole; prepared by drying the tetrahydrate at 300° and 0.5 mm.) was added and the mixture was stirred for 13 hrs. At the end of this time the temperature had risen to 7° . A large amount of brown solid was filtered; the filtrate was washed with water and then dried over anhydrous sodium sulfate. The solid was washed with acetone (total volume 100 ml.) to remove tarry impurities, then it was

placed in a Soxhlet apparatus and extracted for 14 hrs. Fine black crystals weighing 4.8 g. were collected from the reboiling flask. About 0.2 grams of product was isolated when the ether solution filtered initially was worked up. The total yield of 1,1'-diphenylazoferrocene was 5.0 g. (42% of theory based on diazocyclopentadiene), m.p. 175 to 177° (lit. (55) m.p., after six recrystallizations, 183 to 185°).

Three hydrogenation runs on 1,1'-diphenylazoferrocene using platinum oxide in glacial acetic acid proceeded smoothly. Hydrogen uptake was generally slightly over the theoretical amount.

In a typical run 1,1'-diphenylazoferrocene (0.45 g., 1.14×10^{-3} mole) and platinum oxide (0.70 g.) in 15 ml. of glacial acetic acid were placed in the reaction flask and the apparatus was flushed with hydrogen several times before the reaction was started by stirring the catalyst. About 3 to 4 hrs. were required for the reaction to go to completion. Generally a good sharp break in the curve resulting from plotting uptake of hydrogen against time was observed in the vicinity of theoretical hydrogen uptake. The acetic acid solution was filtered and made basic with dilute sodium hydroxide solution. The brown solid that precipitated did not dissolve when the aqueous suspension was washed with ether. The solid was filtered and then dissolved in 20 ml. of dilute hydrochloric acid. The acid solution was washed with chloroform and then chilled and made basic. The brown

solid resulting was filtered, washed with water and then dried in a desiccator under a nitrogen atmosphere.

Several attempts to acetylate the crude product using acetic anhydride and either pyridine or sodium acetate resulted only in tar formation. Sublimation of the crude material at 120° and a pressure of 0.5 mm. gave a small amount of yellow solid which decomposed without melting between 100 and 130°. The infrared spectrum of the sublimed material is compatible with that expected for 1, 1'-diaminoferrocene. Nothing further was done to characterize the compound. An attempt to acetylate the purified material resulted in its decomposition.

Nitriles have been hydrogenated at hydrogen pressures of three to four atmospheres in acetic anhydride using platinum oxide as a catalyst (57). Yields of acetylated amine as high as 85% have been reported for this method.

In the present study 1, 1'-diphenylazoferrocene (0.441 g.) was hydrogenated at one atmosphere pressure of hydrogen using platinum oxide (0.044 g.) in acetic anhydride (10 ml.). The reaction was completed in about 10 hrs.; slightly more than the theoretical amount of hydrogen was absorbed. A fairly large amount of pale green solid was filtered. The solid turned black rapidly when exposed to air but turned green again when it was washed with a few drops of water. When the material was dried in a desiccator it formed a hard resin

which did not melt up to 185°. The material was insoluble in organic solvents. It was not further characterized.

Ethoxycarbonylaminoferrocene was prepared by refluxing carbazidoferrocene (2.0 g., 8.7×10^{-3} mole) in absolute ethanol (100 ml.) for 7 hrs. and then distilling the ethanol under reduced pressure. The crude product was recrystallized from petroleum ether. Yellow platelets of ethoxycarbonylaminoferrocene (1.86 g., 78% of theory) were collected (m.p. 88 to 90°).

1,1'-Di(ethoxycarbonylamino)ferrocene was prepared in a manner similar to that used to prepare ethoxycarbonylaminoferrocene. 1,1'-Dicarbazidoferrocene (2.0 g., 6.1×10^{-3} mole) was refluxed for 6 hrs. in absolute ethanol; the ethanol was distilled under reduced pressure and the crude product was dissolved in benzene and chromatographed on alumina. Roughly 0.5 gram of 1,1'-di(ethoxycarbonylamino)ferrocene was isolated (m.p. 118 to 120°; lit. (32) m.p. 122-123°).

Methoxycarbonylaminoferrocene was prepared by refluxing carbazidoferrocene in methanol and also by first heating carbazidoferrocene in toluene until nitrogen ceased to evolve and then adding methanol and heating for two hours. Neither method gave methoxycarbonylaminoferrocene in as high a yield as was obtained in the case of refluxing carbazidoferrocene in ethanol to get the ethyl urethane. The product melted at 139 to 143° (lit. (48) m.p. 145 to 147°) after chromatography and recrystallization.

1, 1'-Di(methoxycarbonylamino)ferrocene (55) was prepared using both methods described for the preparation of methoxycarbonylaminoferrocene. Again, the yields tended to be rather low. Purification by chromatography gave yellow granules (m.p. 152 to 153°).

Ferrocenylboronic acid and 1, 1'-ferrocenylenediboronic acid were prepared according to the procedure of Schechter and Helling (58). Tributyl borate required for the synthesis was in part prepared (59) and in part purchased from Matheson, Coleman and Bell. In the present work ferrocenylboric acid was generally obtained in about a 25% yield and 1, 1'-ferrocenylenediboronic acid in about a 35% yield. Schechter and Helling reported the synthesis of the monoboronic acid in 44% yield and the diboronic acid in 18% yield. These compounds must be dried over 65% sulfuric acid; stronger desiccants cause anhydrides to form.

Ferrocenylacetate (60) was prepared according to the procedure given by Nesmeyanov by heating an aqueous suspension of ferrocenylboronic acid with cupric acetate. The product was obtained in about half the yield (30%) reported by Nesmeyanov (m.p. 64 to 68°; lit. m.p. 64.5 to 66°). The carbonyl group absorption occurs at 1759 cm^{-1} in the infrared spectrum (CCl_4).

1, 1'-Ferrocenylenediacetate (60) was prepared in a similar manner. The yield in this instance also was about half that reported by Nesmeyanov (m.p., sealed tube, 54 to 55°; lit. m.p. 55 to 55.5°). The carbonyl absorption occurs at 1759 cm^{-1} in the infrared spectrum (CCl_4).

Methoxyferrocene (60) was prepared by treating a solution of ferrocenylacetate and dimethylsulfate in methanol with 50% potassium hydroxide solution. The yield was 37% of yellow crystals melting between 35 and 40° (lit. m.p. 39.5 to 40.5°).

Chloroferrocene (60) was prepared from 1, 1'-ferrocenylene-diboronic acid by first preparing 1'-chloroferrocenylboronic acid and then removing the boronic acid group by treating the compound with aqueous zinc chloride solution. Light yellow platelets (m.p. 56 to 58°; lit. m.p. 58 to 59°) were isolated in a 25% yield. The diboronic acid was used as starting material since there was no ferrocenylboronic acid on hand at the time this synthesis was undertaken.

Bromoferrocene (60) was prepared by heating an aqueous mixture of ferrocenylboronic acid and cupric bromide. Yellow, nearly transparent crystals of bromoferrocene were collected after sublimation of the crude material at 60° and a pressure of 100 to 150 μ . The yield was 25% of theory.

1, 1'-Dibromoferrocene (60) was prepared by heating an aqueous mixture of 1, 1'-ferrocenyldiboronic acid and cupric bromide. The product was isolated in the form of yellow, finely divided crystals (m.p. 50 to 52°; lit. m.p. 50 to 51°) in a 22% yield.

Chloromercuriferrocene was prepared by treating ferrocene with mercuric acetate in 1:1 ether-methanol (61). The resulting mixture of ferrocenylmercuric acetate and 1, 1'-ferrocenylenedi(mercuric

acetate) was decomposed with aqueous potassium chloride to give chloromercuriferrocene and 1, 1'-di(chloromercuri)ferrocene. Chloromercuriferrocene is readily separated on the basis of its solubility in benzene; 1, 1'-di(chloromercuri)ferrocene is insoluble even in boiling benzene.

Iodoferrocene was prepared in 50% yield according to the procedure of Nesmeyanov (62). Chloromercuriferrocene was treated with iodine in hot xylene and the resulting complex was decomposed with aqueous sodium thiosulfate to give iodoferrocene. The product melted at 43.5 to 44.5° (lit. m. p. 44 to 45°) after chromatography on alumina and recrystallization from heptane.

Cyanoferrocene was prepared by refluxing ferrocene, ferric chloride and anhydrous hydrogen cyanide (63) in tetrahydrofuran, according to the procedure of Nesmeyanov (64). Yellow-orange platelets melting at 108.8 to 110.8° (lit. (64) m. p. 107 to 108°) were isolated in a 76% yield. The cyano substituent displays strong absorption at 2232 cm^{-1} in the infrared spectrum (CCl_4).

B. Reactions

Ferrocene was acetylated using a mixture of acetic acid, acetic anhydride, acetyl chloride and sodium perchlorate, according to the procedure of Mathur et al. for the acetylation of phenol ethers (65). Anhydrous sodium perchlorate (G. F. Smith reagent; 3.1 g., 0.025 mole) was dissolved in glacial acetic acid (duPont; 12 g., 0.20 mole) by warming the mixture to 60° in a 125-ml. Erlenmeyer flask with a

standard taper neck. When the solution was cooled to room temperature, about one quarter of the sodium perchlorate precipitated; Mathur et al. reported that the solution was homogeneous at room temperature. Acetyl chloride (Baker and Adamson; 3.0 g., 0.025 mole) was added to the mixture and then the flask was flushed with nitrogen and stoppered. The mixture was stirred vigorously with a magnetic stirrer for several minutes; the stopper was loosened at intervals to permit the escape of any hydrochloric acid which might be liberated. No gas evolution was evident. Ferrocene (1.0 g., 5.4×10^{-3} mole) in benzene (10 ml.) and acetic anhydride (Baker and Adamson reagent; 8.6 g., 0.075 mole) were added. The solution immediately changed to a dark blue-green color and a small amount of hydrochloric acid evolved. The flask was flushed with nitrogen and stoppered; the stopper was loosened at intervals over a period of one hour. No gas evolution was evident. The reaction mixture was stirred at room temperature for 20 hrs. and then it was poured onto 200 ml. of crushed ice. Ascorbic acid (approximately 1 g.) was added to reduce the ferricinium ion. The hydrolysis mixture was washed several times with ether (total volume 300 ml.); the nearly colorless aqueous phase was discarded. The ether solution was washed with dilute sodium hydroxide solution and then with water. The solution was worked up in the usual manner and the residue was chromatographed on alumina. Acetylferrocene and ferrocene were isolated in approximately equal amounts. No diacetylferrocene was formed. The yield was not determined.

In a second run the reactants were stirred for 4 hrs. at 55 to 60° and then worked up in the usual manner. In this run anisole was used as the solvent instead of benzene. Acetylferrocene was isolated in 41% yield, based on recovered ferrocene. No attempt was made to isolate anisole or possible substituted anisoles. It is unlikely that anisole was substituted (7).

An attempt was made to acetylate ferrocene using N-methylacetanilide and phosphorous oxychloride in a manner analogous to the formylation of ferrocene using N-methylformanilide and phosphorous oxychloride (7).

Phosphorous oxychloride (10.0 g., 0.064 mole) and N-methylacetanilide (9.55 g., 0.64 mole) were carefully mixed in a 125-ml. Erlenmeyer flask with a standard taper neck. An exothermic reaction took place when the reagents were mixed. The solution was allowed to stand for two hours and then it was cooled in an ice bath while ferrocene (6.0 g., 0.032 mole) was added as a powder over a period of 15 min. The flask was flushed with nitrogen and stoppered securely. The reactants were allowed to stand at room temperature for three days; the mixture was chilled and 100 ml. of ice water was added. The hydrolysis mixture was left at room temperature for 7 hrs. and then it was extracted with carbon tetrachloride. The aqueous phase was a very deep blue color, indicating that some ferrocene had been oxidized to ferricinium ion. No attempt was made to recover ferrocene from the aqueous phase. The carbon tetrachloride solution was worked up in the

usual manner and the residue was chromatographed on alumina. The only non-tar fraction isolated gave ferrocene (3.5 g.).

A second attempt to acetylate ferrocene by this method using a reaction time of 2 hrs. at 95 to 100° also failed. Only ferrocene was recovered; quite a bit of decomposition had taken place.

1,1'-Diethylferrocene was acetylated using silicon tetraacetate and stannic chloride (11). Stannic chloride (Baker and Adamson; 2.86 g., 1.1×10^{-2} mole) was added to 1,1'-diethylferrocene (2.65 g., 1.1×10^{-2} mole) and silicon tetraacetate (66) (1.6 g., 6.0×10^{-3} mole) in 50 ml. of benzene in an Erlenmeyer flask with a standard taper neck. The flask was flushed with nitrogen before and after the reagents were added. The reaction flask was stoppered securely and allowed to stand at room temperature for 89 hrs. Water (25 ml.) was added and the mixture was stirred for a few minutes. The benzene layer was decanted and the aqueous phase was washed four times with 50-ml. portions of benzene. The benzene solutions were combined and worked up in the usual manner. A red oil (2.14 g.) resulted when solvent was distilled under reduced pressure. The crude product was dissolved in 25 ml. of benzene and chromatographed on alumina (40 g., 4 x 18 cm.). Four bands developed; each band was collected in a single fraction. The first fraction, eluted with benzene, gave 1,1'-diethylferrocene (0.326 g.) after work up. The second fraction, eluted with 1:1 benzene-toluene, gave 2-acetyl-1,1'-diethylferrocene (0.077 g., 2.8% of theory based on recovered starting material). The third fraction, eluted with

ten percent ether in toluene, gave 3-acetyl-1, 1'-diethylferrocene (0.202 g., 7.4% of theory based on recovered starting material). The fourth fraction, presumably containing higher acetylation products, was eluted with 20% ether in toluene. The material in this fraction was not collected.

1, 1'-Diethylferrocene was formylated by a modification of the procedure for the formylation of ferrocene reported by Pauson and co-workers (7). N-Methylformanilide (67) (4.4 g., 3.2×10^{-2} mole) and phosphorus oxychloride (5.0 g., 3.2×10^{-2} mole) were mixed in a 125-ml. Erlenmeyer flask with a standard taper neck and allowed to stand at room temperature for 1 hr. o-Dichlorobenzene (35 ml.) was added as a solvent. 1, 1'-Diethylferrocene (3.9 g., 1.6×10^{-2} mole) in 10 ml. of o-dichlorobenzene was added to the mixture over a period of 15 min. The flask was flushed with nitrogen and stoppered securely. The solution was stirred with a magnetic stirrer for 50 hrs.; a saturated solution of sodium acetate (40 ml.) was added and the mixture was allowed to stand overnight. The mixture was neutralized with dilute base and extracted with benzene. The benzene solution was worked up in the usual manner and the residue was chromatographed on alumina. Only two non-tar bands developed. Starting material (between 1 and 2 ml.) was recovered from a yellow band that was eluted with benzene. A red-orange band was eluted after the yellow band with 1:1 benzene-toluene. Work up of this fraction gave approximately 2 ml.

of red oil. This red oil was chromatographed on alumina a second time; there was no indication that more than a single component was present. The red oil resulting from the second chromatographic purification was distilled at a pressure of 2 mm. The product fraction (1 g.) was collected at 139 to 140°. The ultraviolet spectrum (methanol) displays maxima at 232 m μ ($\epsilon = 23,600$) and 275 m μ ($\epsilon = 8,730$) in the region 210 to 300 m μ . The conversion is 23% of theory. The semicarbazone melts at 133 to 134°.

Anal. Calculated for C₁₆H₂₁N₃OFe: C, 58.73; H, 6.47; N, 12.84.

Found (Elek): C, 59.22; H, 6.50; N, 13.00.

Acetamidoferrocene was acetylated by four methods.

1) The acetylating reagent was made up according to the Perrier modification of the Friedel-Crafts synthesis by mixing acetyl chloride (0.73 g., 9.3×10^{-3} mole) and aluminum chloride (2.0 g., 1.5×10^{-2} mole) in dichloromethane (30 ml.). This mixture was decanted (under nitrogen) through glass wool into a dropping funnel (previously flushed with nitrogen) equipped with a pressure equalizing side tube. The solution was added dropwise over a period of 1 hr. to a solution of acetamidoferrocene (2.2 g., 9×10^{-3} mole) in dichloromethane (150 ml.) at 0°. The solution was stirred an additional 1 hr. with the ice bath removed and then it was poured into ice water (200 ml.). The organic phase was separated; two 50-ml. dichloromethane washings of the aqueous phase were combined with the main organic fractions. The combined solutions were worked up in the usual manner. Distillation

of the solvent gave a red oil which crystallized on standing. Two recrystallizations of this solid gave acetamidoferrocene (0.443 g., m.p. and ultraviolet spectrum identical with those of starting material). Chromatography of the mother liquor on alumina gave an additional 0.480 g. of starting material (eluted with ether) and 1'-acetylacetamidoferrocene (eluted with 1% methanol in benzene). The yield of 1'-acetylacetamidoferrocene (m.p. 115.5 to 116°) was 0.965 g. or 61.5% based on recovered starting material.

Anal. Calculated for $C_{14}H_{15}NO_2Fe$: C, 58.97; H, 5.30; N, 4.91.
Found (Elek): C, 59.00; H, 5.41; N, 4.88.

2) Acetamidoferrocene (0.27 g., 1.1×10^{-3} mole), silicon tetraacetate (66) (0.16 g., 6.0×10^{-4} mole) and stannic chloride (0.29 g., 1.1×10^{-3} mole) were dissolved in benzene (5 ml.) in a 10-ml. Erlenmeyer flask and stirred at room temperature for 28 hrs. The reaction mixture was decomposed with water and then sodium carbonate was added until the solution tested slightly basic. The mixture was washed first with benzene and then with ether. The combined organic washings were worked up in the usual manner and the crude product was chromatographed on alumina. Three non-tar bands developed. A narrow orange band was eluted (benzene) first; a broad yellow band was eluted (benzene) second and a broad orange band was eluted (ether) last. The material in the first fraction was not isolated; on the basis of later experiments the material is probably

2-acetylacetamidoferrocene. The fraction containing material from the yellow band gave acetamidoferrocene (0.107 g., m.p. and infrared spectrum identical with those of starting material). The fraction containing the last band eluted gave a red-orange glass (0.094 g., 50% of theory based on recovered starting material) which was identified as 1'-acetylacetamidoferrocene by its infrared spectrum.

3) Acetamidoferrocene (2.55 g., 0.010 mole) and acetic anhydride (0.97 g., 0.010 mole) were dissolved in dichloromethane (150 ml.) in a 200-ml. three-necked, round bottomed flask equipped with a magnetic stirrer and gas inlet and outlet tubes. The solution was flushed with nitrogen and cooled with an ice bath. Boron trifluoride was bubbled into the solution for three minutes; the solution changed to a deep purple color. The reaction mixture was stirred at 0° for 15 min. and then the ice bath was removed. The mixture was stirred for an additional 2.5 hrs. The solution was decanted into about 250 ml. of saturated sodium acetate solution and stirred for a few minutes. The organic phase was separated and dichloromethane washings of the aqueous phase were added to it. The combined organic solutions were worked up in the usual manner and the residue was chromatographed on alumina. Three bands developed. A leading narrow orange band eluted with ether gave 2-acetylacetamidoferrocene (0.098 g., 4% of theory based on recovered starting material) melting at 109 to 109.5°. A yellow band eluted with ether gave acetamidoferrocene (0.453 g.).

A broad orange band eluted last with 3% methanol in benzene gave 1'-acetylacetamidoferrocene (2.068 g., 85% of theory based on recovered starting material) melting at 115.5 to 116°. This last compound was chromatographed a second time. Three fractions were collected; each fraction yielded only material having a melting point and infrared spectrum identical with those of the sample before chromatography. It should be noted that 1'-acetylacetamidoferrocene sometimes crystallizes in the form of long red-amber needles melting around 50°. These needles will, if heated slowly, undergo transformation at several intermediate temperatures and eventually melt at 115 to 116°. The infrared and ultraviolet spectra of the low melting crystals are identical with those previously observed for the higher melting crystals. Only 2-acetylacetamidoferrocene was analyzed since the other isomer possessed physical properties identical with those of a previously analyzed sample of 1'-acetylacetamidoferrocene.

Anal. Calculated for $C_{14}H_{15}NO_2Fe$: C, 58.97; H, 5.30; N, 4.91.

Found (Elek): C, 57.66, 62.49; H, 5.46, 6.51; N, 4.68, 5.16.

Found (Schwarzkopf): C, 59.04; H, 5.31; N, 4.52.

4) Acetamidoferrocene was acetylated by the acetylium perchlorate method described above for the acetylation of ferrocene. The conditions were identical in every respect. 1'-Acetylacetamidoferrocene was formed in a conversion of only 10 to 15%; there was no indication that other isomers were formed. Well over half of the starting material was recovered.

Methoxycarbonylaminoferrocene was acetylated using acetyl chloride and aluminum chloride according to the procedure described for the acetylation of acetamidoferrocene. 2-Acetylmethoxycarbonylaminoferrocene was isolated as an oil in low yield. 1'-Acetylmethoxycarbonylaminoferrocene (m.p. 135-136°) was isolated in a yield of approximately 50%. Only the 1'-isomer was analyzed.

Anal. Calculated for $C_{14}H_{15}NO_3Fe$: C, 55.84; H, 5.02; N, 4.65.

Found (Spang): C, 56.00; H, 5.10; N, 4.54.

Ethoxycarbonylaminoferrocene was acetylated using boron trifluoride and acetic anhydride according to the procedure used to acetylate acetamidoferrocene with these reagents. 2-Acetylethoxycarbonylaminoferrocene was isolated as an oil in low yield. 1'-Acetylethoxycarbonylaminoferrocene (m.p. 149.5 to 150°) was isolated in a yield of approximately 50%. Only the heteroannularly substituted isomer was analyzed.

Anal. Calculated for $C_{15}H_{17}NO_3Fe$: C, 57.16; H, 5.44; N, 4.44.

Found (Schwarzkopf): C, 56.93; H, 5.50; N, 4.66.

1, 1'-Di(ethoxycarbonylamino)ferrocene was acetylated using boron trifluoride and acetic anhydride. The procedure was the same as that previously described. A solution of 1, 1'-di(ethoxycarbonylamino)ferrocene (0.40 g., 1.1×10^{-3} mole) and acetic anhydride (0.15 g., 1.5×10^{-3} mole) in dichloromethane (30 ml.) was saturated at 0° with boron trifluoride and then stirred at room temperature for

5 hrs. The reaction mixture was worked up in the usual manner and the crude product was chromatographed on alumina. Elution with benzene caused four bands to develop. The first two bands, a leading yellow band and an orange band, were incompletely separated and were eluted together with 10% ether in benzene as fraction one. A broad orange band was eluted next with 20% ether in benzene as fraction two. A very narrow red-orange band remained at the top of the column; this band did not move down the column even upon elution with pure ether. The material (probably less than 5 mg.) in this last band was not isolated. Fraction two gave a red glass (0.206 g.) upon work up. Recrystallization of this material gave 3-acetyl-1,1'-di(ethoxycarbonylamino)ferrocene (0.102 g., m.p. 140.8 to 142°). The material isolated from fraction one was chromatographed a second time. Again a leading yellow band only partially separated from a trailing orange band resulted. Fraction A from this chromatography gave 1,1'-di(ethoxycarbonylamino)ferrocene (0.009 g.; m.p. and mixed m.p. identical with that of starting material). Fraction B gave a red glass (0.148 g.). Recrystallization of the red glass from fraction B gave approximately equal amounts of crystals of starting material and of 2-acetyl-1,1'-di(ethoxycarbonylamino)ferrocene (m.p. 109.5 to 110°); the crystals were separated mechanically and purified further. For the purpose of calculating a yield it was assumed that the red oil from fraction B was a 1:1 mixture of starting material and the 2-acetyl-

isomer. The yield of 3-acetyl-1,1'-di(ethoxycarbonylamino)ferrocene was 46% of theory (58% based on the estimated amount of recovered starting material). The yield of 2-acetyl-1,1'-di(ethoxycarbonylamino)ferrocene was 22% of theory, based on the estimated amount of recovered starting material. Only 3-acetyl-1,1'-di(ethoxycarbonylamino)ferrocene was analyzed since the numerous purifications required gave very pure 2-acetyl-isomer in an amount insufficient for analysis.

Anal. Calculated for $C_{18}H_{22}N_2O_5Fe$: C, 53.75; H, 5.51.

Found: (Schwarzkopf): C, 53.86; H, 5.68.

Cyanoferrocene (3.5 g., 1.66×10^{-2} mole) in 100 ml. of dichloromethane was acetylated using 1:1 aluminum chloride-acetyl chloride (0.06 mole, made up in the previously described manner). The acetylating reagent was added to the cyanoferrocene solution at 0° over a period of 20 min. The ice bath was removed and the mixture was stirred for 5 hrs. The reaction mixture was hydrolyzed and worked up in the usual manner. The crude product was chromatographed on alumina. Exhaustive elution with benzene caused the development of a single large orange band extending over two thirds of the column. There was no evidence of tarry decomposition products. The material in the single large band was collected in several fractions by elution with approximately 1:3 ether-benzene. Work up of these fractions gave 1'-acetylcyanoferrocene (3.98 g., 100% of theory; m.p. 99.8 to 101°) as the sole product.

Anal. Calculated for $C_{13}H_{11}NOFe$: C, 61.94; H, 4.38; N, 5.54.

Found (Elek): C, 61.82; H, 4.48; N, 5.41.

Chloroferrocene (0.585 g., 2.65×10^{-3} mole) was acetylated using 1:1 aluminum chloride-acetyl chloride (9×10^{-3} mole). The acetylating reagent was added to a dichloromethane solution of chloroferrocene at 0° over a period of 45 min. The reaction mixture was stirred for 1.5 hr. at 0° . The ice bath was removed and stirring was continued for 1 hr. The reaction mixture was hydrolyzed and worked up in the usual manner. Chromatography of the crude product gave 1'-acetylchloroferrocene (0.562 g., 81% of theory; m.p., sealed tube, 53 to 55°). A very small orange band was eluted after the main fraction was collected. Work up of this fraction gave a few mg. of brown oil; the material was not characterized.

Bromoferrocene was acetylated by the same procedure as chloroferrocene. The sole product was 1'-acetylbromoferrocene (75% yield; m.p. 56 to 58° ; lit. (37) m.p. 61.5 to 63°).

Anal. Calculated for $C_{12}H_{11}BrOFe$: C, 46.95; H, 3.61; Br, 26.03.

Found (Spang): C, 47.02; H, 3.65; Br, 26.10.

1, 1'-Dibromoferrocene was acetylated using acetyl chloride and excess aluminum chloride. 1, 1'-Dibromoferrocene (0.80 g., 2.7×10^{-3} mole) in dichloromethane (10 ml.) was added over a period of 5 min. to an ice cold mixture of acetyl chloride (0.44 g., 5.5×10^{-3} mole) and aluminum chloride (1.3 g., 1.0×10^{-2} mole) in dichloromethane

(50 ml.). The mixture was stirred at 0° for 45 min.; the ice bath was removed and stirring was continued for 2 hrs. The reaction mixture was hydrolyzed and worked up in the usual manner. Chromatography of the crude product on alumina resulted in the separation of three fractions. The first fraction eluted gave a yellow oil (0.158 g.) which was presumed to be starting material on the basis of the ease with which it was eluted from alumina.

Repeated chromatography of the second fraction resulted in the separation of two more components. Both of these products were oils; it may be that they were still not pure compounds. The first product eluted possesses maxima in the ultraviolet region at 225-240 m μ (small inflection on the end absorption curve) and at 270 m μ (shoulder with horizontal portion centered at the specified wavelength). In the infrared spectrum the carbonyl absorption occurs as a sharp peak at 1683 cm⁻¹ and the aromatic ketone band occurs as a partially resolved doublet at 1279-1273 cm⁻¹. The absence of absorption near 1117 cm⁻¹ indicates that the acetyl group (or groups) is situated on a ring which also bears another substituent. There is also no absorption near 1107 and 1005 cm⁻¹; this indicates that both rings are substituted. The order of elution of this compound from alumina suggests that it is monoacetylated, and further, that the acetyl group is in the 2-position with respect to a bromine atom. The ultraviolet spectrum also suggests that the acetyl group is on a carbon atom adjacent to one bearing a bromine atom; lack of a clearly defined maximum is consistent with

a structure in which the carbonyl group is prevented from achieving coplanarity with the ring (68). The n.m.r. spectrum is also compatible with this structure; two peaks are present in the region associated with the methyl hydrogens of acetylferrocene. Two distinct conformations for the acetyl group would be possible if its rotation was hindered by a bulky substituent such as bromine. Tentatively this compound is assigned the structure 2-acetyl-1,1'-dibromoferrocene.

The second component eluted possesses a well-defined maximum in the ultraviolet region at 222 m μ with a shoulder at 250-260 m μ . The infrared spectrum of this compound possesses peaks at 1681, 1274 and 1113 (weak) cm⁻¹. The compound was not further characterized.

Repeated chromatography of the third fraction from the initial chromatography of the crude reaction product also resulted in the separation of two components. The component first eluted was a red oil which solidified on standing (0.15 g., 15% conversion). The oily solid possesses well-defined maxima in the ultraviolet region at 223 and 267 m μ . The n.m.r. spectrum possesses two peaks in the region associated with the methyl hydrogens of acetylferrocene; the ratio of peak heights is about 3:4. Recrystallization of this material from heptane gave well-formed, orange-yellow crystals melting at 117-118°. The infrared spectrum of these crystals possesses peaks at 1684, 1280-1272 (partially resolved doublet) and 1126 cm⁻¹.

Anal. Calculated for $C_{14}H_{12}Br_2O_2Fe$: C, 39.30; H, 2.81; Br, 37.40.

Calculated for $C_{12}H_{10}Br_2OFe$: C, 37.41; H, 2.62; Br, 41.50.

Found (Elek): C, 39.53; H, 3.15; Br, 39.38.

The carbon-hydrogen analysis indicates that the compound is a diacetylated dibromoferrocene; the bromine analysis is intermediate between the two possibilities.

Work up of the component eluted last gave a red oil (0.089 g.) which possesses maxima at 223 and 262.5 $m\mu$ in the ultraviolet spectrum (methanol). The infrared spectrum was determined (carbon tetrachloride) but the compound was not further characterized.

Two attempts were made to acetylate iodoferrocene using 1:1 acetyl chloride-aluminum chloride according to the procedure used to acetylate chloroferrocene and bromoferrocene. In the first run only acetylferrocene and a mixture of ferrocene and iodoferrocene were obtained. In the second run a sample of iodoferrocene (0.608 g., 1.95×10^{-3} mole) which was known to be free from ferrocene by its nuclear magnetic resonance spectrum gave, after chromatography, a non-ketonic fraction (0.259 g., m.p. 60 to 115°), a trace of acetylferrocene (less than 5 mg.) and 1,1'-diacetylferrocene (0.096 g.; m.p. 121 to 124°; m.p. of an authentic sample was 122 to 125° on the same instrument). Acetylferrocene was identified by its infrared spectrum. 1,1'-Diacetylferrocene was identified by its infrared and its

nuclear magnetic resonance spectra. In the first run the non-ketonic fraction possesses a nuclear magnetic resonance spectrum compatible with that expected for a 1:1 mixture of ferrocene and iodoferrocene. The possibility that a coupling product was present has not been eliminated. The nuclear magnetic resonance spectrum of the non-ketonic fraction from the second run was not taken.

Competitive Acetylation of Ferrocene and Acetamidoferrocene.

A 1:1 mixture of acetyl chloride and aluminum chloride (6.07×10^{-3} mole) was added over a period of 20 min. to ferrocene (1.13 g., 6.07×10^{-3} mole) and acetamidoferrocene (1.48 g., 6.07×10^{-3} mole) in 60 ml. of dichloromethane at 0° . The reaction mixture was stirred for 0.5 hr. at 0° ; the ice bath was removed and the mixture was stirred for an additional one hour. The reaction mixture was hydrolyzed and worked up in the usual manner. Recrystallization of the crude solid resulting gave well-formed platelets of acetamidoferrocene (0.854 g.). Chromatography of the filtrate on alumina gave ferrocene (0.837 g., 74% recovery), acetylferrocene (0.305 g., 22% conversion or 86% of theory based on recovered ferrocene), acetamidoferrocene (0.445 g., total amount recovered is 88%) and 1'-acetylacetamidoferrocene (0.135 g., 7.8% conversion or 65% of theory based on recovered acetamidoferrocene).

In a second run the reaction was carried out at room temperature. Ferrocene (1.052 g., 5.66×10^{-3} mole) and acetamidoferrocene

(1.377 g., 5.66×10^{-3} mole) added initially gave acetylferrocene (0.317 g., 24.5% conversion or 96.5% of theory based on recovered ferrocene) and 1'-acetylacetamidoferrocene (0.174 g., 10.8% conversion or 120% of theory based on recovered acetamidoferrocene). Recrystallization of the 0.174 g. of 1'-acetylacetamidoferrocene isolated after chromatography gave 0.084 g. of well-formed crystals (5.2% conversion or 58% of theory based on recovered acetamidoferrocene). Ferrocene isolated after chromatography of the crude acetylation products weighed 0.784 g. (74.5% recovery); acetamidoferrocene similarly recovered weighed 1.256 g. (91.2% recovery).

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II

THE EFFECTS OF HETEROANNULAR SUBSTITUENTS
ON THE RATES OF SOLVOLYSES OF METHYLFERRO-
CENYLCARBINYL ACETATES; A COMPARISON WITH
SUBSTITUENT EFFECTS IN OTHER REACTIONS
OF FERROCENE

INTRODUCTION

In recent years several studies have been made on heteroannularly substituted ferrocene derivatives in an attempt to learn more about the nature of the transmission of electronic effects from one cyclopentadienyl ring of ferrocene to the other. These studies have dealt with substituent effects on the ionization of ferrocenecarboxylic acids, on the rates of reaction of ferrocenecarboxylic acids with diphenyldiazomethane and on carbonyl stretching frequencies of the acids and their methyl esters.

A. Effect of Heteroannular Substituents on the Ionization of Ferrocenecarboxylic Acids

Nesmeyanov (1,2), Little and Eisenthal (3), and Benkeser and Hall (4) have studied the effects of 1'-substituents on the ionization of ferrocenecarboxylic acids. Table I summarizes the data of Nesmeyanov and Little and Eisenthal. It can be seen that the acid strengths of the substituted ferrocenecarboxylic acids vary in the manner expected according to the electron donating or withdrawing properties of the substituents.

Little and Eisenthal reported that they obtained a satisfactory straight line of slope 0.74 when they plotted their pK_a values against Hammett's σ_p (5). However, this plot was based on only four substituents

Table I

pK_a Values of Heteroannularly Substituted Ferrocenoic Acids^a

R'	pK_a , 50% ethanol, 24°	pK_a , 68% methanol, 20°
-CH ₃	---- ^b	6.52 ^c
-C ₂ H ₅	6.34 ± 0.01	6.43
-C ₄ H ₇	----	6.50
-CH ₂ -CH ₆ H ₅	6.25 ± 0.01	----
-H	6.11 ± 0.01	6.29
-COOCH ₃	----	6.08
-COC ₃ H ₇	----	5.95
-COCH ₃	5.76 ± 0.02	5.91
-COC ₆ H ₅	5.90 ± 0.02	----
-CH(OH)C ₆ H ₅	5.84 ± 0.01	----
-CN	----	5.82

pK_a for benzoic acid in 50% ethanol at 25° is 5.68^d

pK_a for benzoic acid in 68% methanol at 20° is 5.93^c

-
- a. See figure 1 given in Part I, p. 4, for an explanation of the system used for designating the positions for ring substitution in ferrocene.
- b. Taken from reference 3.
- c. Taken from references 1 and 2.
- d. Reference 7.

since the authors could find no acid dissociation constants reported for benzylbenzoic and α -hydroxybenzylbenzoic acids. When they used a value of σ_p derived from the chronopotentiometric studies of Kuwana et al. (6), they found that α -hydroxybenzylferrocenoic acid is a much stronger acid than is predicted from the plot. The authors suggest that this discrepancy may be due to the stabilization of the anion of α -hydroxybenzylferrocenoic acid by hydrogen bonding.

Little and Eisenthal also treated Nesmeyanov's data, which was obtained in 68% methanol, in a similar manner; they state that a straight line with a slope of 0.81 results.

Nesmeyanov's data have been plotted against Hammett's σ_p and σ_m (5) constants in the present study since Little and Eisenthal reported no correlation factors for their treatment. In the least squares treatment, only those substituents were included which possessed sigma values based on the ionization of the appropriately substituted benzoic acid in water at 25°. Brown (5b) has recommended that only sigma constants based on the ionization of the appropriately substituted benzoic acid in water at 25° be used to determine the reaction constant, ρ . Thus, the least squares treatment for the plot of pK_a vs. σ_p is based on five substituents. The value determined for ρ is 0.804 ($r = 0.993$; $s = 0.044$). The correlation is excellent according to Jaffe's arbitrary standards (7).*

*The standard deviation from the regression line and the

against σ_m , based on four substituents, gives a value for ρ of 0.945 ($r = 0.972$; $s = 0.095$). It appears that the data are better correlated with σ_p than with σ_m . Considering the small value of ρ in both cases and the limited number of substituents, one should not try to say that in this ionization reaction the electronic effects of 1'-substituents in ferrocene are transmitted to the reaction center in the other cyclopentadienyl ring in a manner analogous to that for the transmission of effects of para substituents in benzene to the side chain reaction center.

Benkeser and Hall (4) report that the ionization constants of 1'-substituted ferrocenoic acids (in 66% ethanol) are correlated poorly by σ_m , fairly well by σ_p and quite well by Taft's polar sigma, σ^* (8). Hill (9) has estimated ρ values of 1.4 for the σ_m correlation and 0.94 for the σ_p correlation from the plots given by Benkeser and Hall. Hill has pointed out that a comparison of these ρ values with those reported for benzoic acids in 50% ethanol of 1.52 (5b) or 1.46 (10) suggests that electronic effects are transmitted quite readily between the cyclopentadienyl rings of ferrocene. Hill has further pointed out that in the σ^* correlation, points for 1'-carboxy and 1'-carboethoxy were omitted. When these were included, assuming their σ^* values to

correlation coefficient are referred to simply as s and r , respectively. Jaffe has considered $r > 0.99$ to indicate excellent, $r > 0.95$ satisfactory, and $r > 0.90$ fair fit to the Hammett equation. If $r < 0.90$ but > 0.80 while $\rho > 1.0$, and if $r < 0.80$ while $\rho > 0.50$, the data are considered as not being adequately represented by the Hammett equation. Reactions are also considered to violate the Hammett equation if s exceeds certain values for certain ranges of ρ , as follows: $s > 0.40$ for all ρ , $s > 0.30$ for $\rho > 3$, $s > 0.25$ for $\rho > 2.0$, and $s > 0.20$ for $\rho > 1.0$.

be comparable to that known for carbomethoxy, the points deviated badly.

In the present study, it was found that the pK_a data determined by Nesmeyanov cannot be correlated with σ^* .

B. Reaction of Ferrocenecarboxylic Acids with Diphenyldiazomethane

Little and Eisenthal have also studied the reaction of hetero-annularly substituted ferrocenoic acids with diphenyldiazomethane under second-order conditions (11). The reaction of carboxylic acids with diaryldiazomethanes has been thoroughly studied kinetically (10, 12, 13, 14, 15); the second order rate constants for this esterification have been correlated with Hammett's sigma constants in the aromatic series (10, 13). These authors obtained a linear correlation when the logarithms of the second-order rate constants were plotted against the difference in pK_a values between the 1'-substituted acids and ferrocenoic acid. Table II summarizes their data.

Table II shows that the rate constants for esterification of the substituted acids parallel their acid strengths, with the exception of the α -hydroxybenzyl substituted acid, which reacts much faster than one would predict on the basis of its acid constant.

Figure 1 shows a plot of $\log k_2$ vs. $pK^0 - pK$ for the data of Little and Eisenthal. The authors report the linear correlation coefficient, r , is equal to 0.95, indicating a satisfactory fit of the points

Table II

Rate Constants for the Reaction of Heteroannular Substituted
Ferrocenoic Acids with Diphenyldiazomethane in Toluene at 30°

Substituent	k_2 , $\ell \cdot \text{mole}^{-1} \text{min}^{-1}$	pK_a of acid in 50% ethanol
-H	0.1020 ± 0.0028^a	6.11 ^b
-COCH ₃	0.9110 ± 0.0048	5.76
-COC ₆ H ₅	0.7547 ± 0.0013	5.90
-C ₂ H ₅	0.566 ± 0.0010	6.34
-CH ₂ -C ₆ H ₅	0.595 ± 0.0002	6.25
-CH(OH)C ₆ H ₅	10.04 ± 0.14	5.84

a. The data are taken from reference 11.

b. In their publication Little and Eisenthal have inadvertently cited Nesmeyanov's value for ferrocenoic acid in 68% methanol, i. e., $\text{pK}_a = 6.29$. See Table I.

to a straight line (7). The least squares treatment of these data was repeated in the present work, excluding, as did the original authors, the value for the α -hydroxybenzyl substituted compound; the slope of the line was calculated to be 2.4 ($r = 0.97$; $s = 0.17$).

Little and Eisenthal also plotted their $\log k_2$ data against σ_p (fig. 2) and σ_m , and against Taft's polar σ^* (fig. 3).

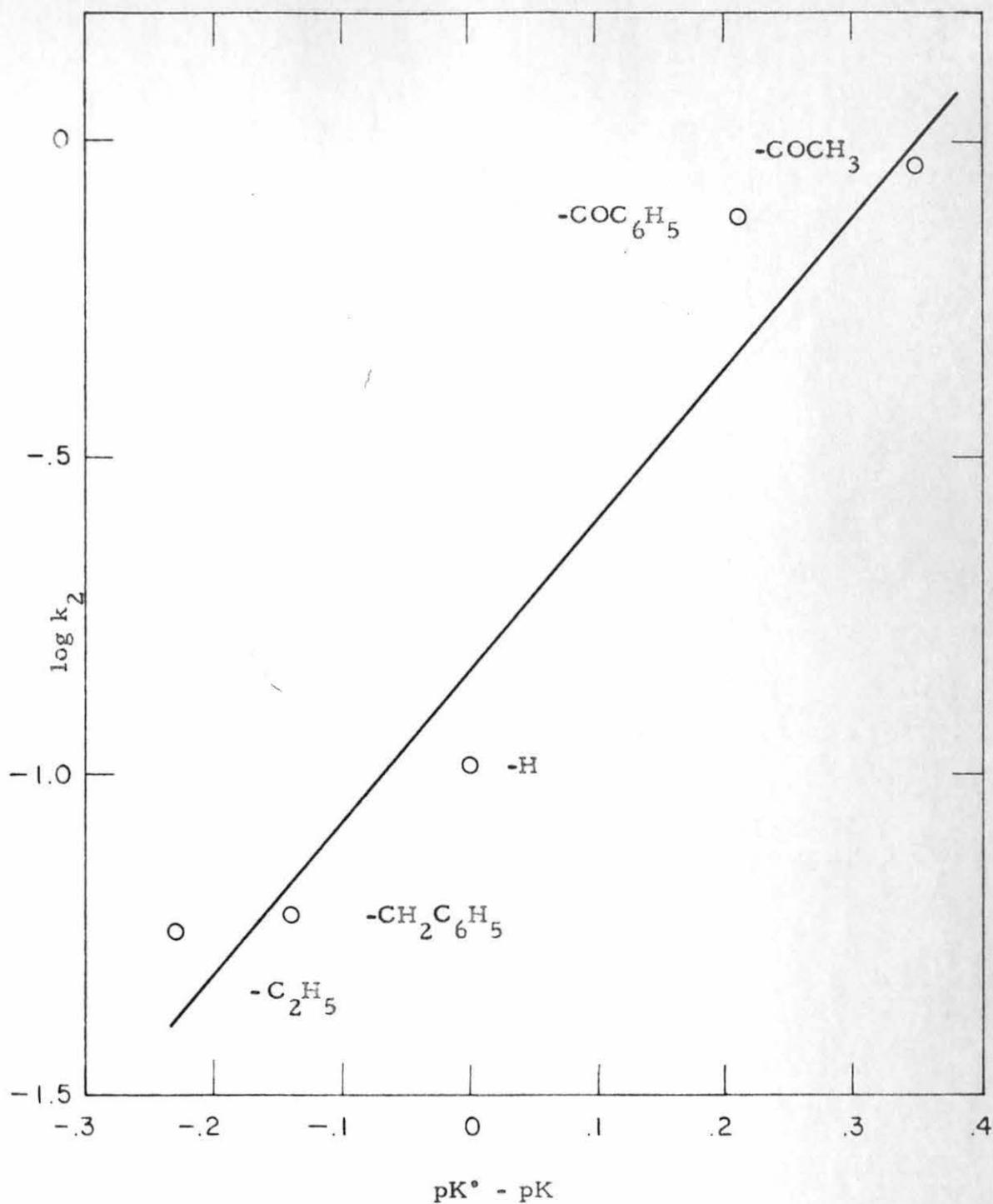


Figure 1.- Plot of $\log k_2$ vs. $pK^\circ - pK$; reported by Little and Eisenthal.

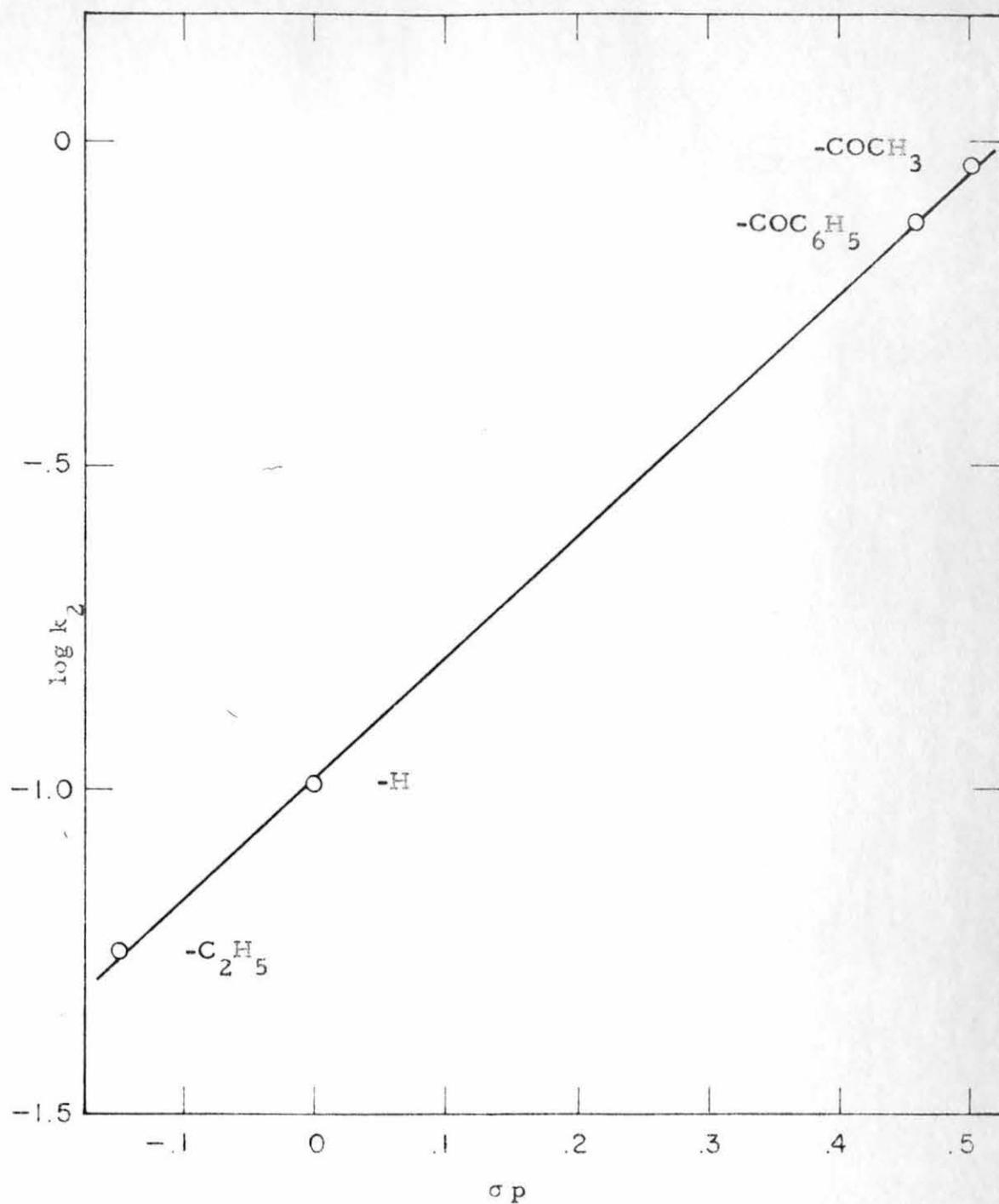


Figure 2.- Plot of $\log k_2$ vs. σ_p ; reported by Little and Eisenthal.

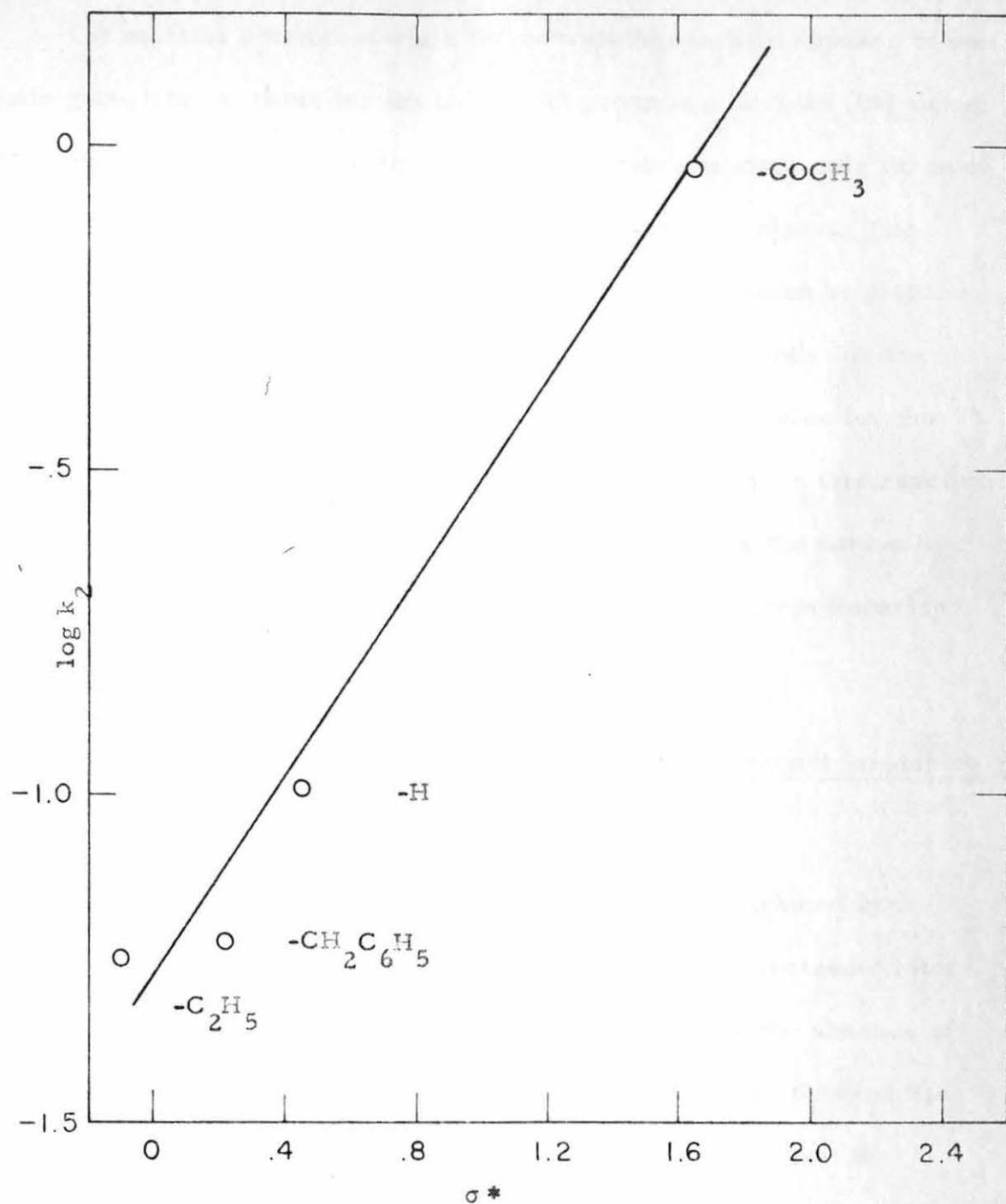


Figure 3. - Plot of $\log k_2$ vs. σ^* ; reported by Little and Eisenthal.

It must be noted that while the correlation with σ_p appears to be quite good, the σ value for the p-benzoyl group is a derived (5b) value; this detracts from the significance of the correlation since only three of the four substituents considered have well-defined σ values. The authors state that a reasonably good correlation is obtained by plotting $\log k_2$ vs. σ_m . However, σ_m constants were available only for the three substituents, hydrogen, ethyl and acetyl; the σ_m value for the ethyl group is a derived value (5b). Thus, it seems that in this reaction also, there is no clear-cut choice between correlating the data with σ_p or with σ_m . Figure 3 shows the greater deviations from linearity for the plot against σ^* .

C. Effects of Heteroannular Substituents on the Carbonyl Stretching Frequencies of Ferrocenecarboxylic Acids and Esters

It has been well established that the aromatic carbonyl band shifts offer a sensitive method for the detection of the electronic interactions of a substituent with the aromatic ring (16). In the absence of any complicating steric, bonding or solvent interactions, these shifts may be directly attributed to the change of electron density at the carbonyl group caused by a combination of resonance and inductive effects engendered by the substituent (17, 18). Insofar as the Hammett sigma constants are also measures of the electron density at the reaction site, one might expect an approximate linear relationship between

the shift in carbonyl stretching frequency and the sigma constant. Deviations from an exact linear relationship may be expected inasmuch as the frequency shifts are influenced only by static factors typical of the molecule in its resting state, while sigma constants are derived from compounds which are subject to the electronic influence of the attacking reagent (19). Such an approximate linear relationship has been demonstrated for benzaldehydes and acetophenones (17, 20, 21).

Nesmeyanov has obtained data on the carbonyl stretching frequencies of 1'-substituted ferrocenoic acids and esters (22). Table III summarizes his data.

It is clear from an inspection of Table III that an increase in the electrophilic nature of the substituent increases the frequency of the C=O bond of the carboxyl (and carbomethoxy) group attached to the other ring of the ferrocene molecule, and, accordingly, the substituents can be arranged in the following order:

- 1) with respect to effect on carboxyl (in increasing order of shift to higher frequency): n-butyl = ethyl, carbomethoxy, acetyl, cyano, sulfonamide = sulfonyl fluoride.
- 2) with respect to effect on carbomethoxy (in increasing order of shift to higher frequency): n-butyl, ethyl, carboxy, carbomethoxy, butyryl = acetyl, sulfonyl chloride, sulfonyl fluoride = methyl sulfonate.

Table III

Carbonyl Stretching Frequencies of 1'-Substituted Ferrocenoic
Acids and Esters^a

<u>1'-substituted esters^b</u>	C=O frequency in solution	
	<u>CCl₄</u>	<u>CHCl₃</u>
-SO ₃ CH ₃	1723	1723
-SO ₂ F	1730	1722
-SO ₂ Cl	1731	1718
-COCH ₃	1678, 1722	1676, 1716
-COC ₃ H ₇	1679, 1718	1676, 1715
-COOCH ₃	1730	1712
-H	1730	1712 (diffuse)
-C ₂ H ₅	1718	1707
-COOH	----	1678, 1696-1708
-C ₄ H ₉	1704 to 1712	1696 to 1704
<u>1'-substituted acids</u>		
-SO ₂ F	----	1704
-SO ₂ NH ₂	----	1704
-CN	----	1692
-COCH ₃	----	1663, shoulder 1682
-COOH	----	1672
-C ₂ H ₅	1682	1672
-C ₄ H ₉	1682	1672
-H	----	1682

Table III (continued)

- a. Taken from reference 22.
- b. In the case of keto acids and keto esters, the lower frequency is assigned to the ketone carbonyl and the higher to the acid or ester carbonyl. In the case of the monoester and the ester-amide of ferrocenedicarboxylic acid the higher frequency was assigned to the ester carbonyl.

These series are in good agreement with each other and with the series based on a comparison of the dissociation constants of ferrocene carboxylic acids. An exception is the position of the absorption bands of unsubstituted acids and esters which are found at 1712 cm^{-1} for the ester and 1682 cm^{-1} for the acid; i. e., hydrogen falls in the series between the acetyl and carbomethoxy groups, while in the series based on acid dissociation constants hydrogen falls between the alkyl and carbomethoxy groups. The authors do not have an explanation for this. An increase in the characteristic frequency of the C=O bond occurs concurrently with an increase in the dissociation constant of the corresponding acid.

There is little point in plotting Nesmeyanov's data against Hammett sigma constants since either too few of the substituents have well-defined values for sigma or else the carbonyl stretching frequency was determined in chloroform, a solvent known to cause shifts in the frequency (23). Thus, in this instance also there is no way to determine

whether or not resonance effects are transmitted across the iron atom.

Summary

From the limited number of studies conducted so far it appears that substituent effects are readily transmitted from one cyclopentadienyl ring of ferrocene to the other. The question of whether interannular resonance or interannular inductive effects predominate is not answerable on the basis of the experiments described above.

RESULTS AND DISCUSSION

A. Solvolyses of Heteroannularly Substituted Methylferrocenyl-carbinyl Acetates

Richards and Hill have shown that the solvolysis of methylferrocenylcarbinyl acetate in 80% acetone proceeds via an uncatalyzed ionization of the neutral ester with cleavage of the alkyl-oxygen bond (24). They have further demonstrated that the remarkable stability of α metallocenylcarbonium ions formed during the solvolysis reaction is most likely largely due to direct metal participation (24, 25).

Hill's correlation of the rates of solvolyses of three 1'-substituted methylferrocenylcarbinyl acetates with σ_m indicates that for this reaction ρ , the reaction constant, is about -4.6 (9). This large value for ρ shows that substituent effects are quite important in determining the rates of solvolyses (7). For this reason the solvolysis reaction appears to be a particularly good one to employ in investigating the nature of the transmission of substituent effects in ferrocene.

In the present study, the rates of solvolyses of methyl-(1'-substituted-ferrocenyl)carbinyl acetates having acetyl, bromo, chloro and cyano groups in the 1'-position were determined in 80% acetone at 45°. Table IV summarizes the results.

Table IV

Solvolyses Rates of 1'-Substituted Methylferrocenylcarbinyl Acetates
in 80% Acetone at 45°^a

1'-substituent	$k \times 10^5$	Rel. k, 45°	Rel. k, 30°	$\Delta\Delta H$ (k cal.)	$\Delta\Delta S$ (e. u.)
-CH ₃ ^b	100.07 ^c	1.29 ^c	1.97 ^c	-0.42 _{-0.38}	0.0
-H ^b	77.63 ^c	1.00 ^c	1.00	0.0 _{+0.57}	0.0
-COOCH ₃ ^b	1.394	0.018	0.014	+2.33 _{+1.13}	+1.5
-COCH ₃	1.242	0.016			
-Cl	3.91	0.050			
-Br	3.13	0.040	0.037 ^d	+0.78 _{+1.5} ^e	-2.15
-CN	0.1814	0.0023			

a. For complete data see Table XXIV, page 144.

b. Reference 9.

c. Extrapolated from other temperatures.

d. Based on a single run at 30°.

e. Assumed the same uncertainty for the single run at 30° as was observed for the runs at 45°; the uncertainty was calculated by using the error equation given in reference 9.

The logarithms of the rate constants at 45° were plotted against the difference in pK_a 's for the ionization of 1'-substituted ferrocenoic acids determined by Nesmeyanov (1,2) (fig. 4). Unfortunately, acid dissociation constants have not yet been published for ferrocenoic acids

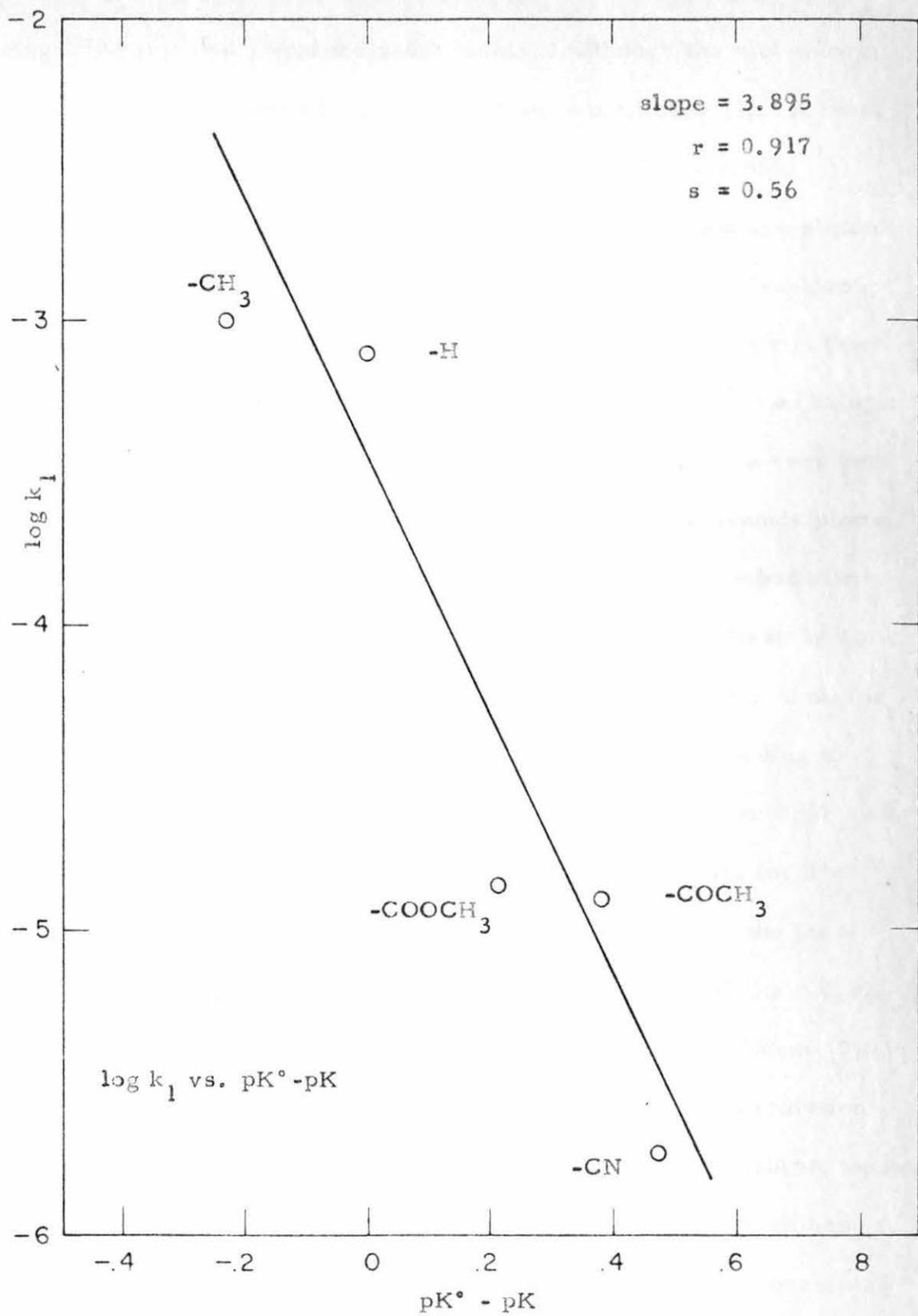


Figure 4.

having 1'-bromo and 1'-chloro substituents. Although the plot shows roughly the trends expected, the correlation is not linear (7). A least squares treatment gave a slope of -3.895 ($r = 0.917$; $s = 0.56$).

A limited correlation is obtained when the rate data are plotted against σ_m (fig. 5). The compounds having 1'-bromo and 1'-chloro substituents solvolyze considerably faster than one would predict from the Hammett plot based on the other five compounds. If the two halogen substituted compounds are not included in the calculations, a very good correlation is obtained for the rates of the other five compounds plotted against σ_m . A least squares treatment based on the four substituents possessing well-defined σ_m values, which appear to be linearly correlated, gives $\rho = -4.49$ ($r = 0.998$; $s = 0.10$). The value for σ_m for the carbomethoxy substituent calculated from this plot according to Jaffe's method (7) is 0.365 ; this agrees well with the value of $0.37 \pm .1$ listed by Brown (5b) for the carboethoxy group. If the data for 1'-bromo and 1'-chloro substituted compounds are included in the least squares calculations, ρ is calculated to be -4.16 ($r = 0.977$; $s = 0.8$). The large value for s indicates that the correlation is not linear (7).

A plot of $\log k_1$ vs. σ_p gives a satisfactory linear correlation for all the compounds studied (fig. 6). A least squares calculation based on the compounds bearing substituents with well-defined σ_p values gives $\rho = -3.345$ ($r = 0.971$; $s = 0.282$). The data cannot be correlated with σ^* or σ' (26).

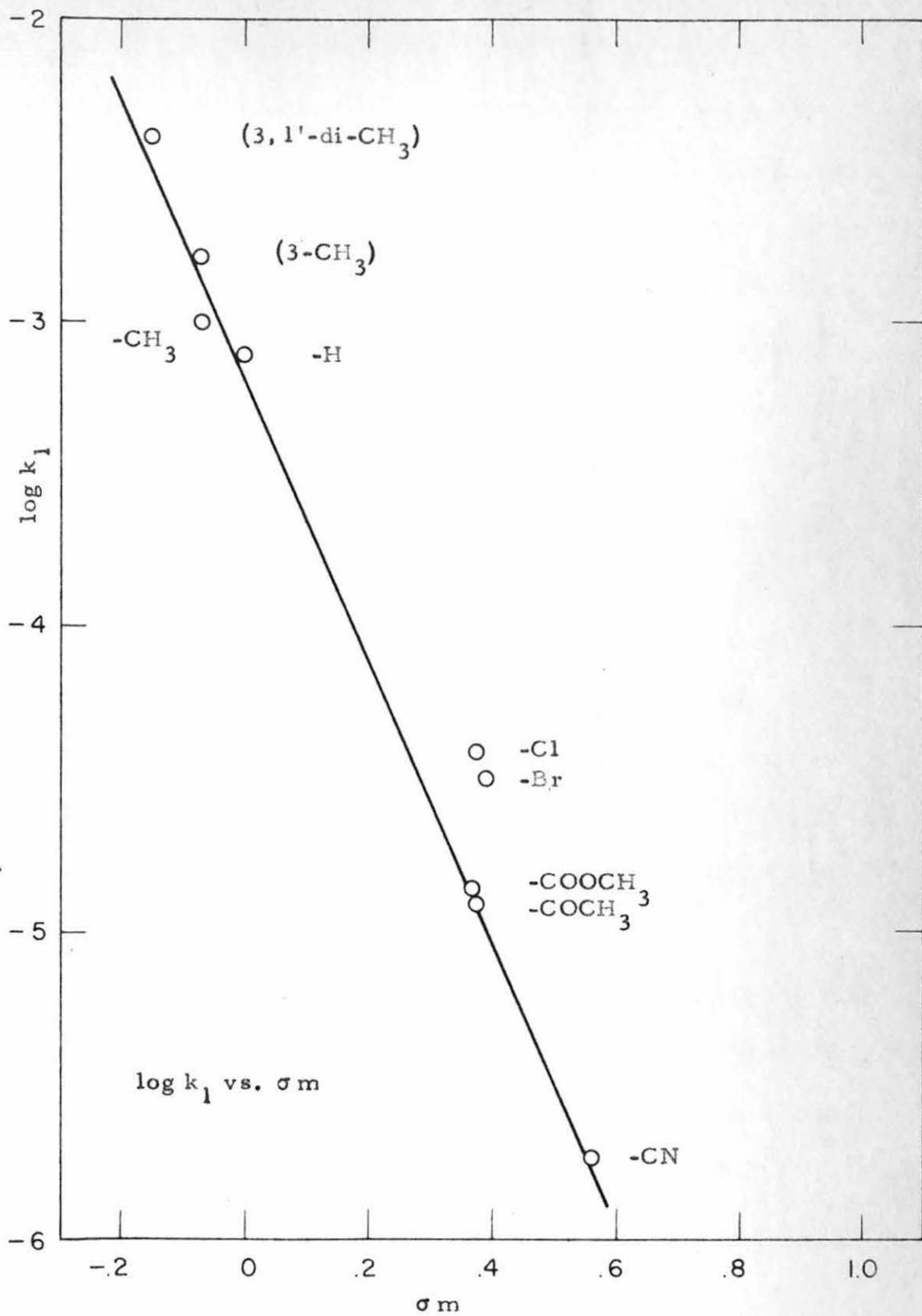


Figure 5.

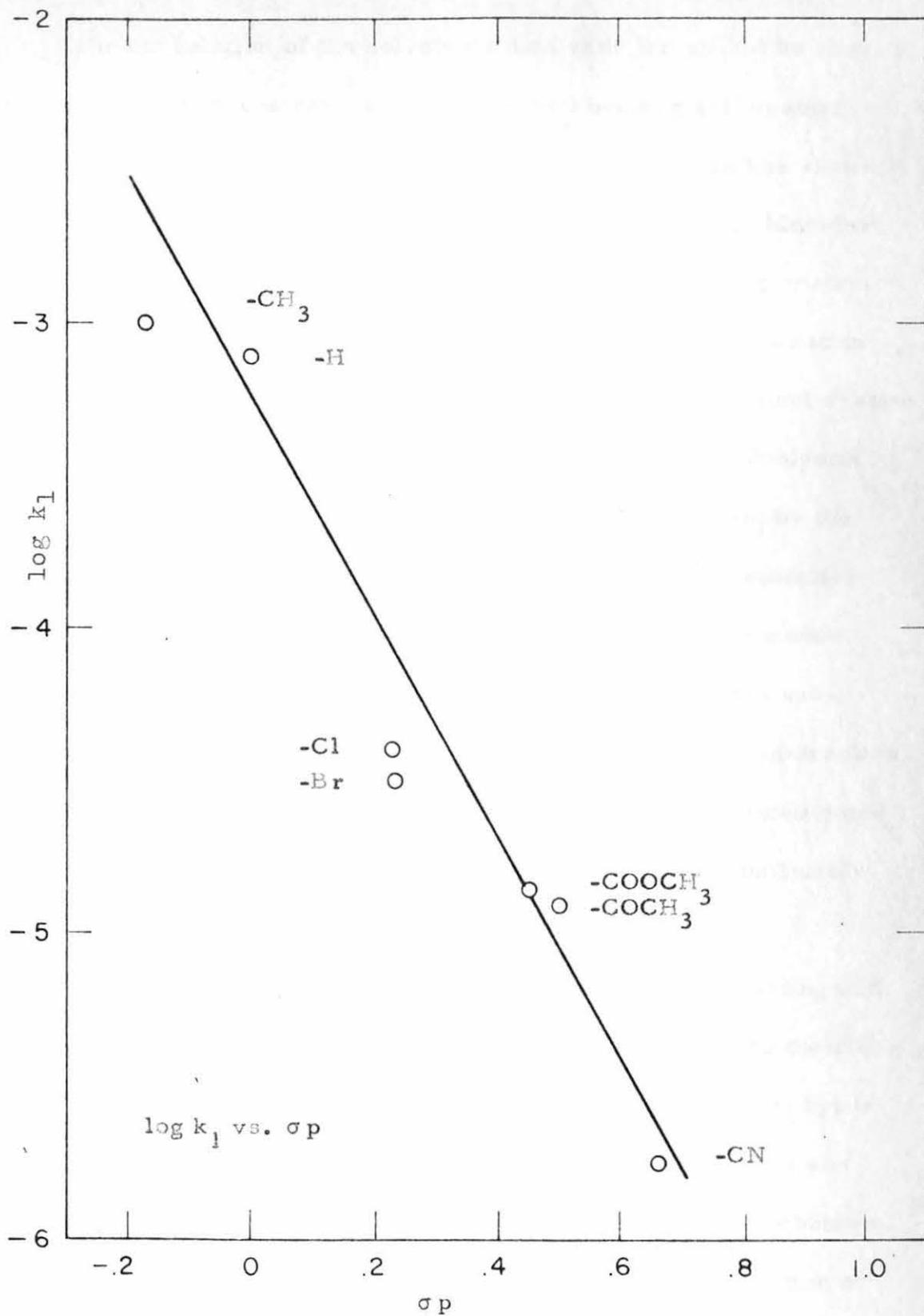


Figure 6.

The correlation of the solvolysis data with σ_p should be viewed with suspicion since the rate for the compound bearing a 1'-methyl substituent also is correlated well in the σ_m plot. Brown has shown that in the solvolyses of substituted phenyldimethylcarbinyl chlorides in 90% acetone there is a large resonance stabilization by a p-methyl group (27). Clearly, there is no appreciable resonance stabilization by a 1'-methyl group when methyl-(1'-methylferrocenyl)carbinyl acetate is solvolyzed. It seems likely that the correlation of the solvolyses data with σ_p is fortuitous. The deviations from the σ_m plot by the 1'-halogen substituted compounds are probably not due to resonance stabilization by these substituents. One cannot invoke a resonance interaction as the reason for the deviations since a 1'-methyl substituent does not stabilize the carbonium ion by a resonance interaction. The anomalously high rates observed for the halogen substituted compounds must be due to some special interaction by these substituents which cannot be undergone by a methyl group.

It seems reasonable that the halogens may be coordinating with the iron atom and thereby transferring electrons indirectly to the electron deficient reaction center. This is an especially attractive hypothesis in view of the work done by Hill and Richards in which it was demonstrated that the metal atom can donate electrons to a carbonium ion adjacent to the ring (24, 25). More evidence for an interaction of the type described here will be presented in the next section. Theoretical considerations will also be discussed.

Summary

The rates of solvolyses of methyl-(1'-substituted-ferrocenyl)-carbinyl acetates in 80% acetone can be correlated with σ_p . Evidence has been presented which indicates that the correlation with σ_p may be fortuitous. A good correlation is obtained when the data are plotted against σ_m , if the results for compounds bearing 1'-halogen substituents are omitted. The anomalously high rates observed for the solvolyses of the halogen substituted compounds are explained in terms of indirect transfer of electrons by these substituents to the electron deficient reaction center via coordination of the substituents with the iron atom.

B. Chronopotentiometric Oxidation of Ferrocene Compounds

Kuwana, Bublitz and Hoh have shown that reversible quarter-wave potentials for some substituted ferrocenes in acetonitrile may be correlated with Taft's σ^* (6). Hoh, McEwen and Kleinberg subsequently reported that the quarter-wave potentials of a number of substituted ferrocenes in acetonitrile can be correlated using σ_p (28). However, both studies were incomplete in the sense that the range of substituent constants covered was too small.

In the present study, which was done in collaboration with Dr. Charles Russell, the number of substituted ferrocenes for which oxidation potential data are available has been significantly increased.

Tables V and VI summarize our results. Previously reported quarter-wave potentials are given in Table VII.

The data of Kuwana, Bublitz and Hoh, measured with respect to a saturated calomel electrode, were converted to our potential scale by subtracting 0.241 volts. A correction of 0.269 volts was subtracted from the data of Hoh, McEwen and Kleinberg, also measured with respect to a saturated calomel electrode. These values were chosen to give the best agreement among quarter-wave potentials measured by different investigators for identical compounds. Russell has stated that the difference between the two correction factors reflects the difference between quarter-wave potentials reported by the two groups for identical compounds and is probably due to differences in the liquid junction potentials for their calomel electrodes (29). Russell chose the silver-silver perchlorate electrode for the present study only after experiencing difficulty with a saturated calomel electrode.

A plot of the reversible quarter-wave potentials vs. $\Sigma \sigma_m$ (7) (fig. 7) reveals a striking similarity between substituent effects in the oxidation reaction and substituent effects in the solvolyses of methyl-(1⁺-substituted-ferrocenyl)carbonyl acetates. A very good correlation is obtained if those compounds having oxygen, nitrogen, chlorine or bromine attached to the ring are omitted. As in the case of the correlation of the solvolyses rate data with σ_m , the alkyl substituted compounds fall very close to the correlation line. This certainly implies that

Table V

Oxidation Potentials for Reversibly Oxidized Ferrocene Derivatives

Substituent	$E_{1/4}$ 0.010 V.
1, 1'-(C ₂ H ₅ CONH) ₂ -	-.076
1, 1'-(CH ₃ CONH) ₂ -	-.074
CH ₃ CONH-	-.007
CH ₃ CONH-	-.005
CH ₃ O-	.005
HO(CH ₂) ₄ -	.039
H ₂ NCH ₂ -	.039 ^a
CH ₃ CHOH-	.062
H-	.063
CH ₃ CH(OCH ₃)-	.081
CH ₃ CH(OCOCH ₃)-	.140
3-CH ₃ CO-1, 1'-(CH ₃) ₂ -	.211
1'-CH ₃ CO-1-CH ₃ CONH-	.220
1'-CH ₃ CO-1-CH ₃ CONH-	.234
2-CH ₃ CO-1-CH ₃ CONH-	.313
1, 1'-Br ₂ -	.380
NC-	.438
1'-CH ₃ CO-1-Br-	.469
1'-CH ₃ CO-1-Cl-	.490
1, 1'-(CH ₃ CO) ₂ -	.551
1'-CH ₃ CO-1-CN-	.661 ^b

a. First of two waves

b. Assumed reversible, but reversibility was not checked.

Table VI

Oxidation Potentials for Irreversibly Oxidized Ferrocene Compounds

Compound	$E_{1/4}$ Volts	i ma/cm ²	$10^3 C$ moles/l
3-acetyl-1,1'-di(ethoxy-carbonylamino)ferrocene	.217	.15	1.6
3-acetyl-1,1'-trimethylene-ferrocene	.263	.26	1.9

Table VII

Oxidized Potentials for Reversibly Oxidized Ferrocene Derivatives

A. Data from Kuwana, Bublitz and Hoh (6)

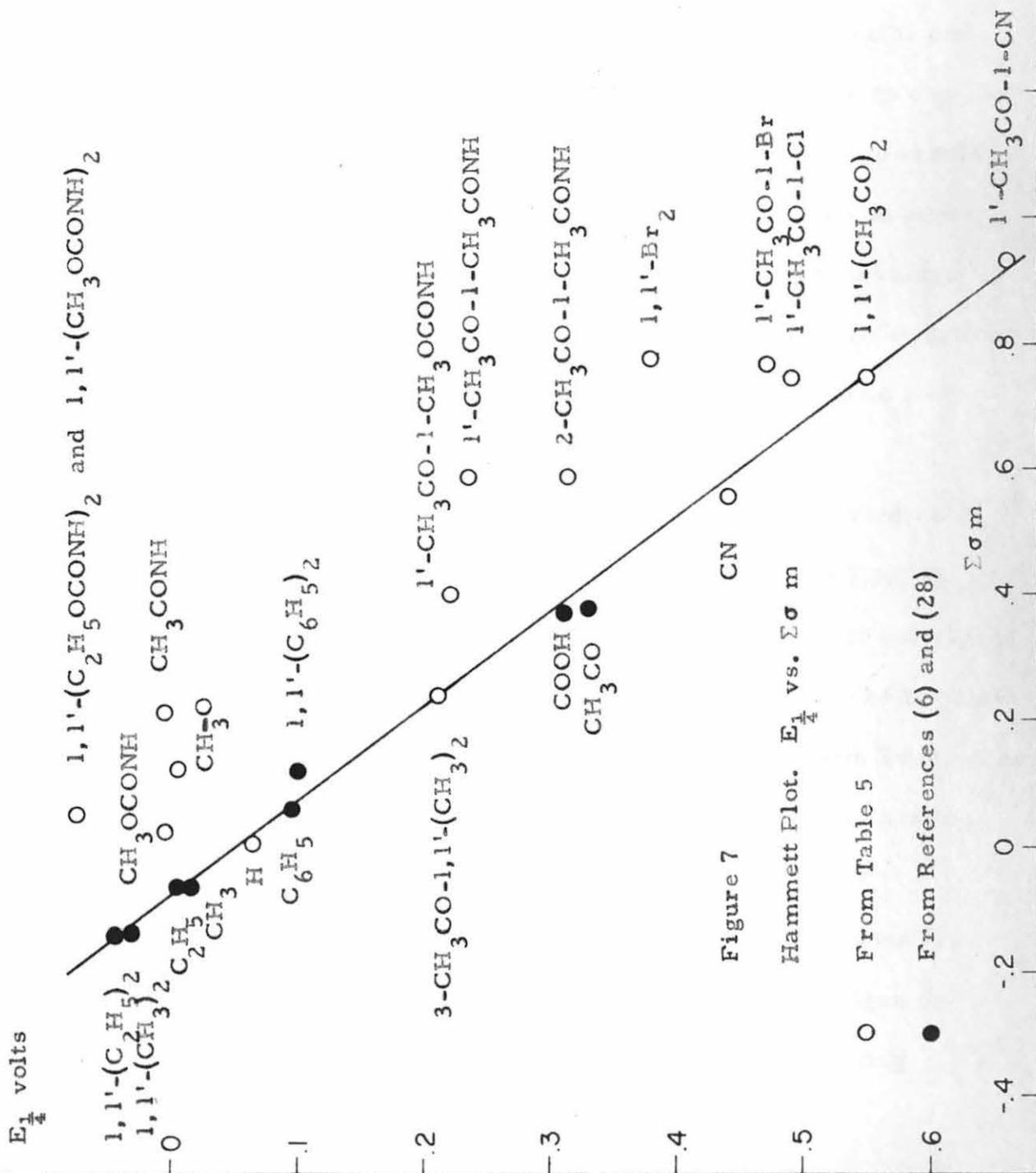
Substituent	$E_{1/4}$
1, 1'-(C ₂ H ₅) ₂ -	-.047
C ₂ H ₅ -	.004
CH ₃ CHOH-	.057
H-	.066
C ₆ H ₅ CHOH-	.077
CH ₂ =CH-	.084
HOOC-	.309
C ₆ H ₅ CO-	.330
CH ₃ CO-	.332
1, 1'-(CH ₃ CO) ₂ -	.555

B. Data from Hoh, McEwen and Kleinberg (28)

Substituent	$E_{1/4}$
(C ₁₀ H ₂₁) ₂ -	-.047
1, 1'-(C ₂ H ₅) ₂ -	-.045
(C ₈ H ₁₇) ₂ -	-.041
1, 1'-(CH ₃) ₂ -	-.028
CH ₃ CHC(CH ₃) ₃ -	-.011
C ₂ H ₅ -	.012
CH ₃ -	.012
n-C ₃ H ₇ -	.015

Table VII (continued)

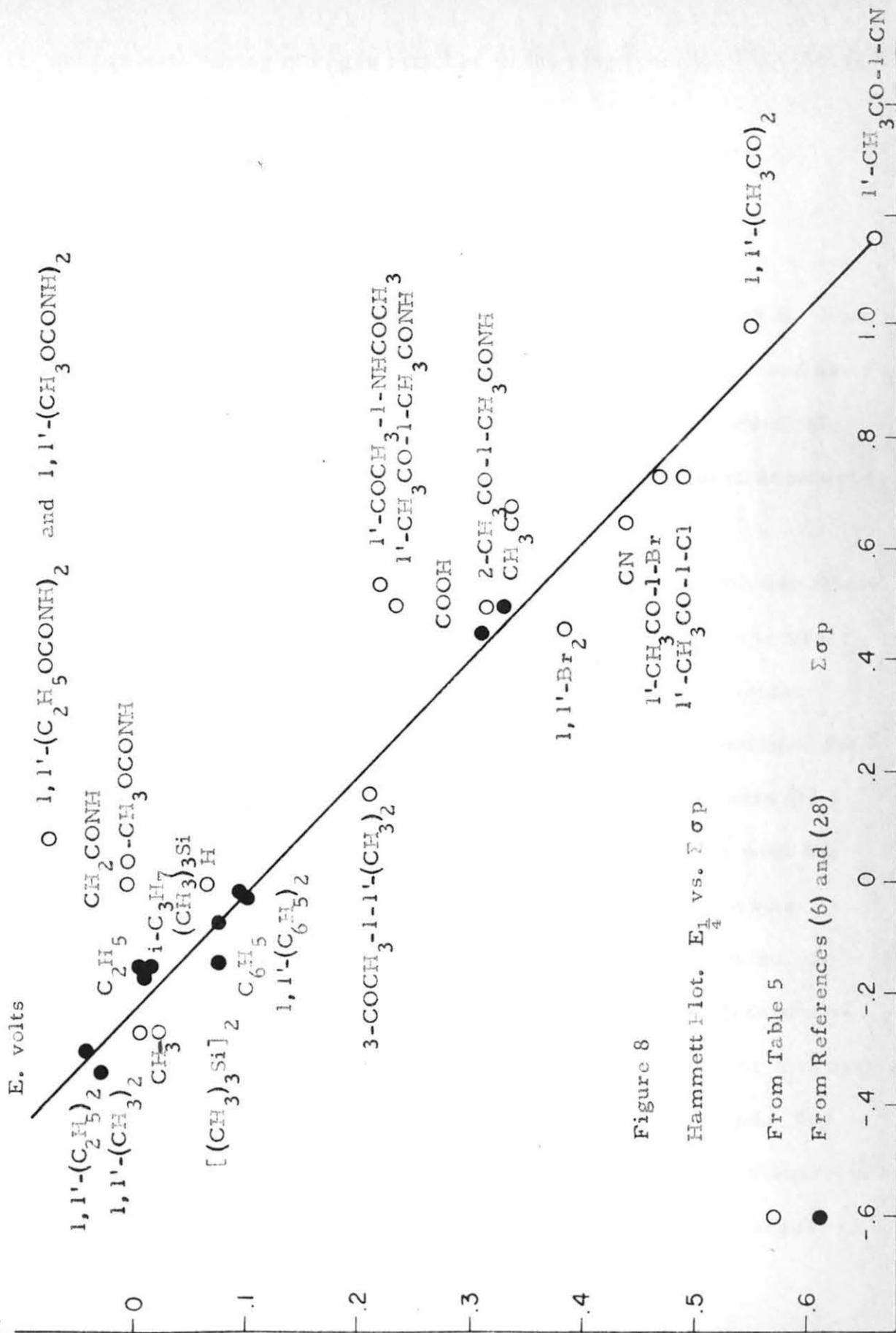
Substituent	$E_{1/4}$
1-C ₃ H ₇ -	.017
sec-C ₄ H ₉ -	.019
1, 1'-(C ₆ H ₅ CH ₂) ₂ -	.027
C ₆ H ₅ (CH ₂) ₂ -	.027
CH ₃ CH ₂ CH(C ₆ H ₅)-	.036
C ₆ H ₅ CH ₂ -	.045
CH ₃ CH(C ₆ H ₅)-	.046
CH ₃ CH=CH-	.047
C ₆ H ₅ CH=CH-	.059
CH ₃ OCH ₂ -	.071
H-	.072
(CH ₃) ₃ Si-	.077
Bis-(CH ₃) ₃ Si-	.077
C ₆ H ₅ -	.097
1, 1'-(C ₆ H ₅) ₂ -	.101
C ₆ H ₃ CO-	.318
C ₆ H ₅ CH=CHCO-	.325
CHO-	.355
p-CH ₃ OC ₆ H ₄ -	.054
p-ClC ₆ H ₄ -	.118
p-BrC ₆ H ₄ -	.127
p-CH ₃ COC ₆ H ₄ -	.157
p-NO ₂ C ₆ H ₄ -	.195



resonance interactions are not very important. The deviations by compounds bearing substituents such as methoxy, acetamido, urethano, chloro or bromo are likely due to coordination of these groups with the positive iron atom. Another argument against resonance stabilization by these groups is the fact that the acetamido and urethano groups stabilize the positive charge on the iron atom at least as much, and possibly more than a methoxy group. A comparison of the σ_p constants for these substituents indicates that the methoxy group should stabilize an electron deficient center more effectively than an acetamido or urethano group. Further, a comparison of the σ_p values for alkyl and methoxy groups indicates that the difference in oxidation potentials for ferrocenes substituted with these groups should be greater than that actually observed.

The quarter-wave potential data can also be correlated, with the exception of acetamido- and urethanoferrocenes, with $\Sigma\sigma_p$ (7) (fig. 8). As was mentioned in the case of the correlation of solvolyses rate data with σ_p , the correlation is probably fortuitous since the alkyl substituted compounds do not deviate in the correlation with $\Sigma\sigma_m$. The acetamido and urethano substituents are far more electron donating than one would predict from the $\Sigma\sigma_p$ correlation.

Russell has calculated equations of the regression lines for the two plots, eliminating substituents having oxygen, nitrogen or halogen attached to the ring from the $\Sigma\sigma_m$ plot and eliminating



substituents having nitrogen attached to the ring from the $\Sigma\sigma_p$ plot (29).

These are:

$$E_{1/4} = 0.663 \Sigma\sigma_m + 0.055$$

$$E_{1/4} = 0.478 \Sigma\sigma_p + 0.110$$

Correlation coefficients calculated by Russell are 0.998 for the $\Sigma\sigma_m$ plot and 0.993 for the $\Sigma\sigma_p$ plot. The substituent constants used are those tabulated by McDaniel and Brown (5b), with the exception of those for the urethanes. Substituent constants for the urethanes were reported by Kaplan (30).

As has already been pointed out by Russell (29), the deviations from the $\Sigma\sigma_m$ plot by compounds having substituents which interact with the iron are additive and independent of other substituents.

If one takes into account deviations due to coordination of the substituent with the central iron atom, the substituent effects are additive for the wide variety of polysubstituted ferrocenes with but one exception. The compound 2-acetylacetamidoferrocene was oxidized at a potential 0.13 volts more positive than predicted. In Part I of this thesis it was pointed out, on the basis of infrared evidence, that a strong hydrogen bond exists between the amide hydrogen and the oxygen of the adjacent acetyl group in this compound. Apparently either the hydrogen bonding prevents the nitrogen atom from donating electrons as effectively to the positive iron atom because of

an unfavorable geometrical constraint, or else the energy of hydrogen bonding is lost when the nitrogen coordinates with the iron atom.

The data for the oxidation of methylferrocenylcarbinol, methylferrocenylcarbiny acetate, methyl(ferrocenylmethyl) ether and ferrocenylcarbiny amine indicate that there is no direct interaction between the iron atom and oxygen or nitrogen atoms separated from the ring by a methylene group. The effects of these substituents are about what one would expect on the basis of inductive effects.

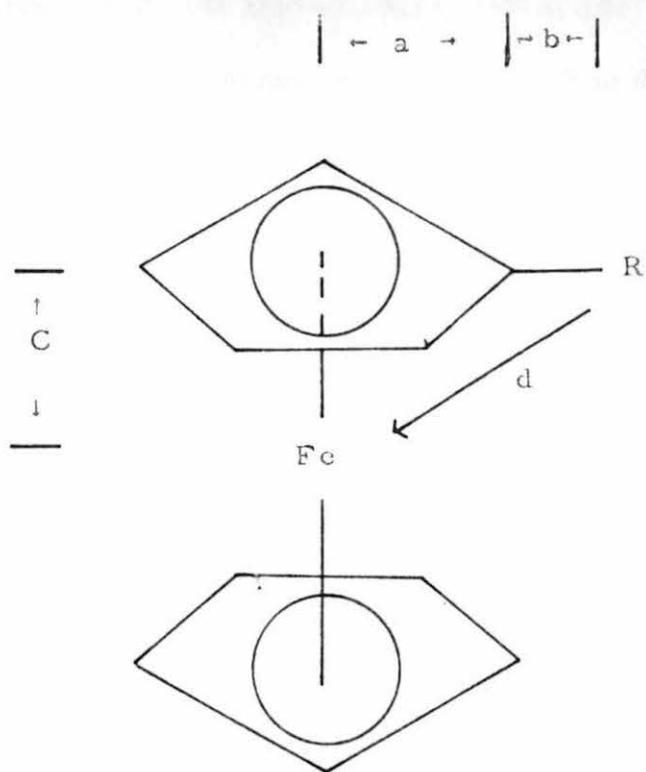
A schematic representation of the interaction of a substituent possessing an unshared pair of electrons with the positive iron atom is given in figure 9.

Table VIII lists distances between a donor atom on the ring and the iron atom. The calculations were made on the basis of the assumption that no distortion takes place on forming the positive ion from the neutral molecule. The further assumption was made that the substituent is coplanar with the ring. Known covalent radii (31) and interatomic distances for ferrocene were used (32).

Table VIII

Iron-Donor Atom Distance

Donor Atom	Distance to iron atom (Å)
N	3.15
O	3.11
Cl	3.40
Br	3.55



$$d = \sqrt{(a + b)^2 + c^2}$$

$$a = 1.216 \text{ \AA}$$

$$b = \text{C-R bond length (31)}$$

$$c = 1.69 \text{ \AA}$$

d, tabulated in Table VIII

Figure 9

For comparison, the iron-halogen distance is 2.48 \AA in ferric chloride (33) and 2.63 \AA in ferric bromide (34). The distances between the donor atoms and the iron atom in ferrocene listed in Table VIII are rather long for a significant interaction to occur. It is probable that the ring bearing the donor atom shifts or tilts in some manner and thereby shortens the distance between the donor atom and the iron atom.

Hill and Richards have presented convincing evidence that the central iron atom stabilizes an α -carbonium ion by nucleophilic participation. This evidence is based upon the effects of simple substituents in the solvolyses of ferrocenylcarbinyl acetates, the effect of joining the rings by a three-carbon bridge, the solvolysis of the acetate vinylogous to methylferrocenylcarbinyl acetate, and finally, upon the stereochemistry of the solvolyses of derivatives with substitution in the 2-position of the ferrocene nucleus (9). They further presented molecular orbital calculations which, at least qualitatively, showed that significant stabilization of the carbonium ion by the iron atom could occur if the ring bearing the reaction center was shifted as little as 0.2 \AA (9, 24).

In view of the work of Hill and Richards, our postulate concerning coordination of a donor atom on a ferrocene ring with the central iron atom, likely necessitating some distortion of the molecule, seems reasonable. In the case of the solvolyses of methylferrocenylcarbinyl acetates bearing donor atoms in the 1'-position, it is likely that both rings are shifted or tilted to some extent.

Russell has suggested that since the deviations due to direct interaction with the iron are additive, it would be possible to define a set of σ constants which would take this interaction into account (29). One limitation to this idea should be mentioned. The interaction is apparently not constant for a given substituent from one reaction to another. For example, in the oxidation reaction the new σ constant for bromine would be $0.50 \sigma_m$ while in the solvolysis reaction it would be $0.70 \sigma_m$. One could probably assume that participation is greatest in the oxidation reaction and at least use this concept for predicting reaction rates within certain limits.

That a linear free energy relationship exists for the reactions of ferrocene compounds is probably best demonstrated by comparing the several reactions studied to date with one another. The reaction selected as a basis for comparison is the oxidation reaction. A wide range of substituents has been studied in this reaction and the experimental errors are probably smaller than those encountered in the other reactions.

A plot of the data for the solvolyses of heteroannularly substituted methylferrocenylcarbonyl acetates vs. the quarter-wave potentials for the oxidation reaction (fig. 10) shows that there is an excellent linear correlation. It also shows that the anomalous interactions of the halogen substituents in the two reactions are similar, but not necessarily of the same magnitude. The slope of the correlation

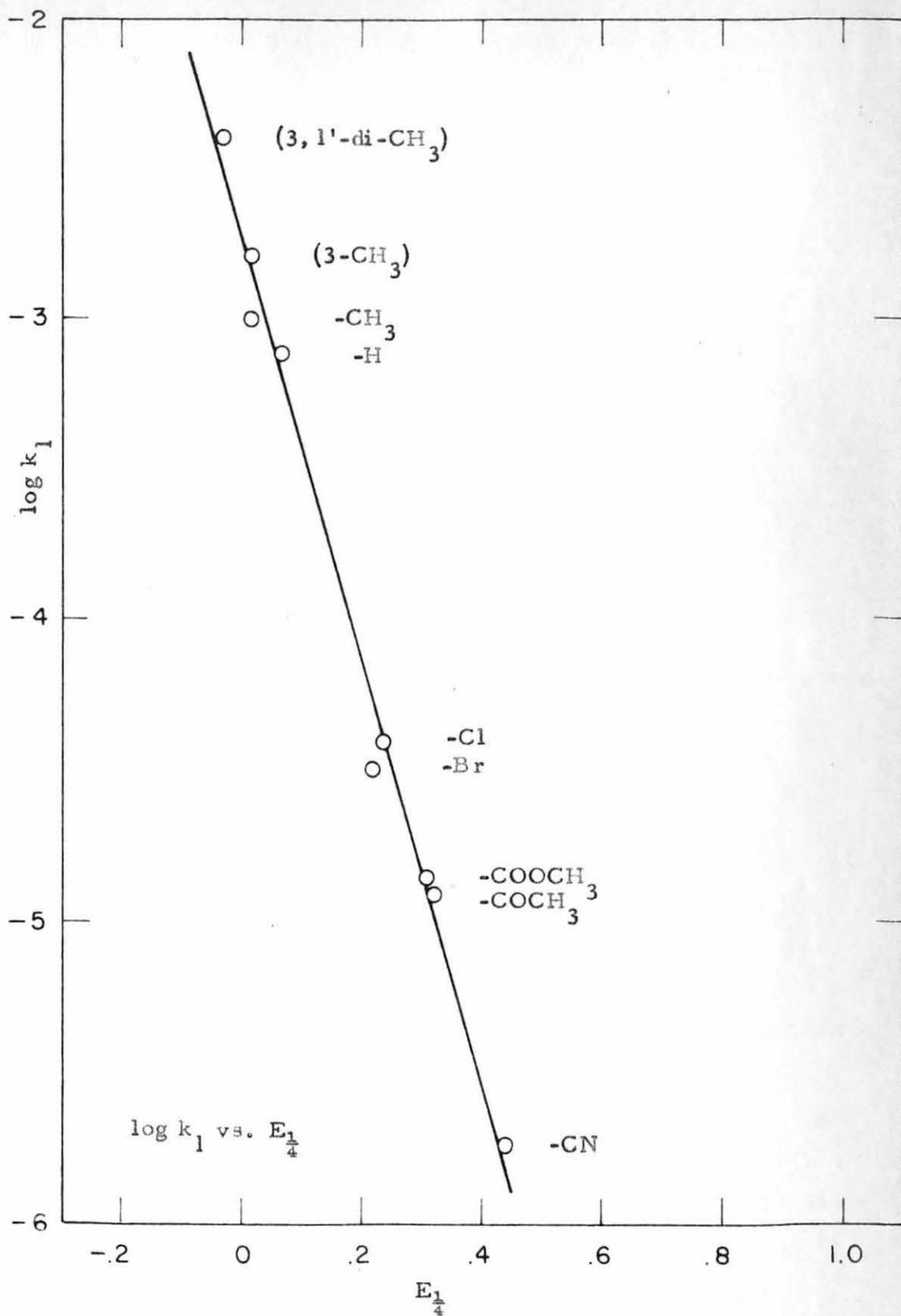


Figure 10.

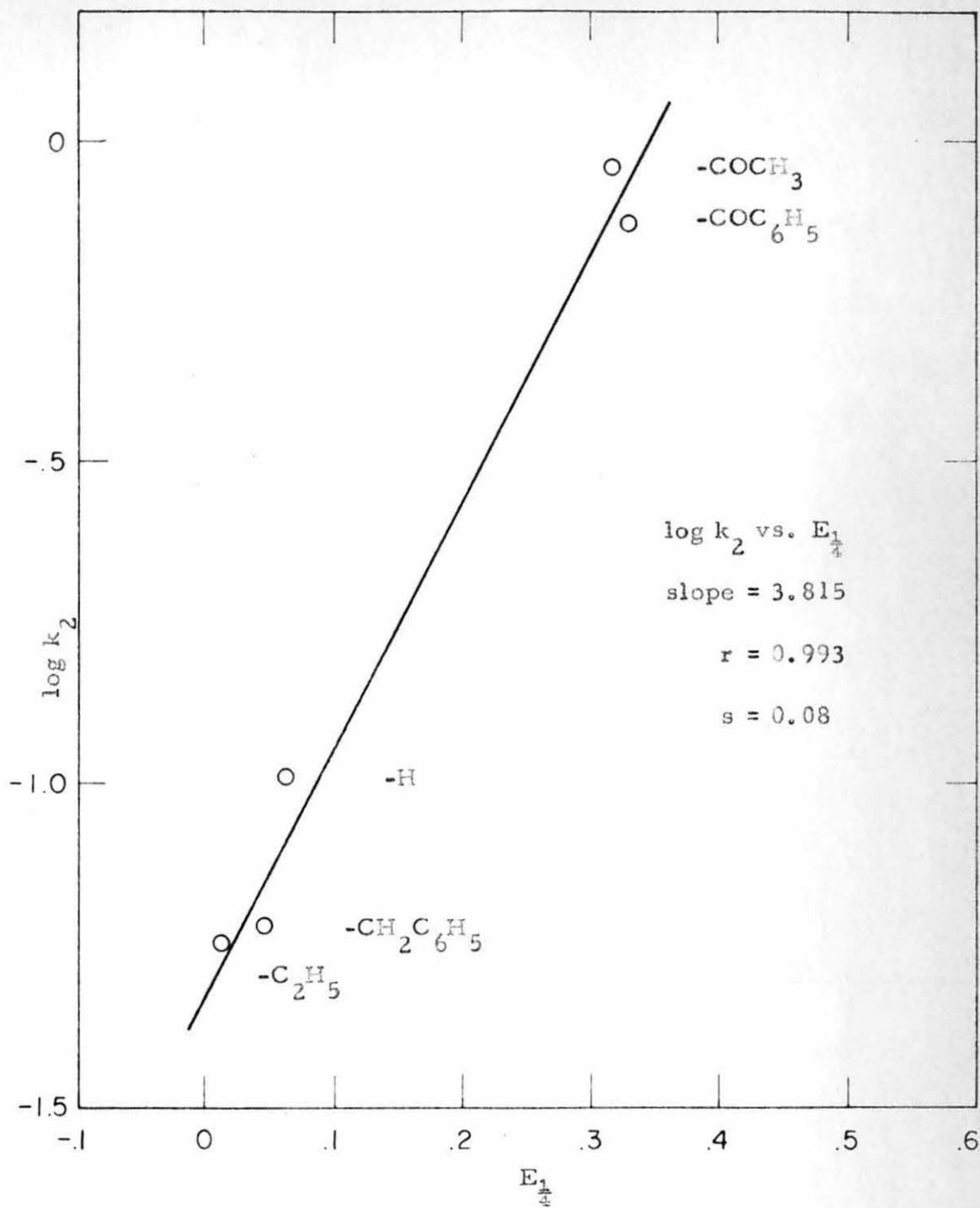


Figure 11.

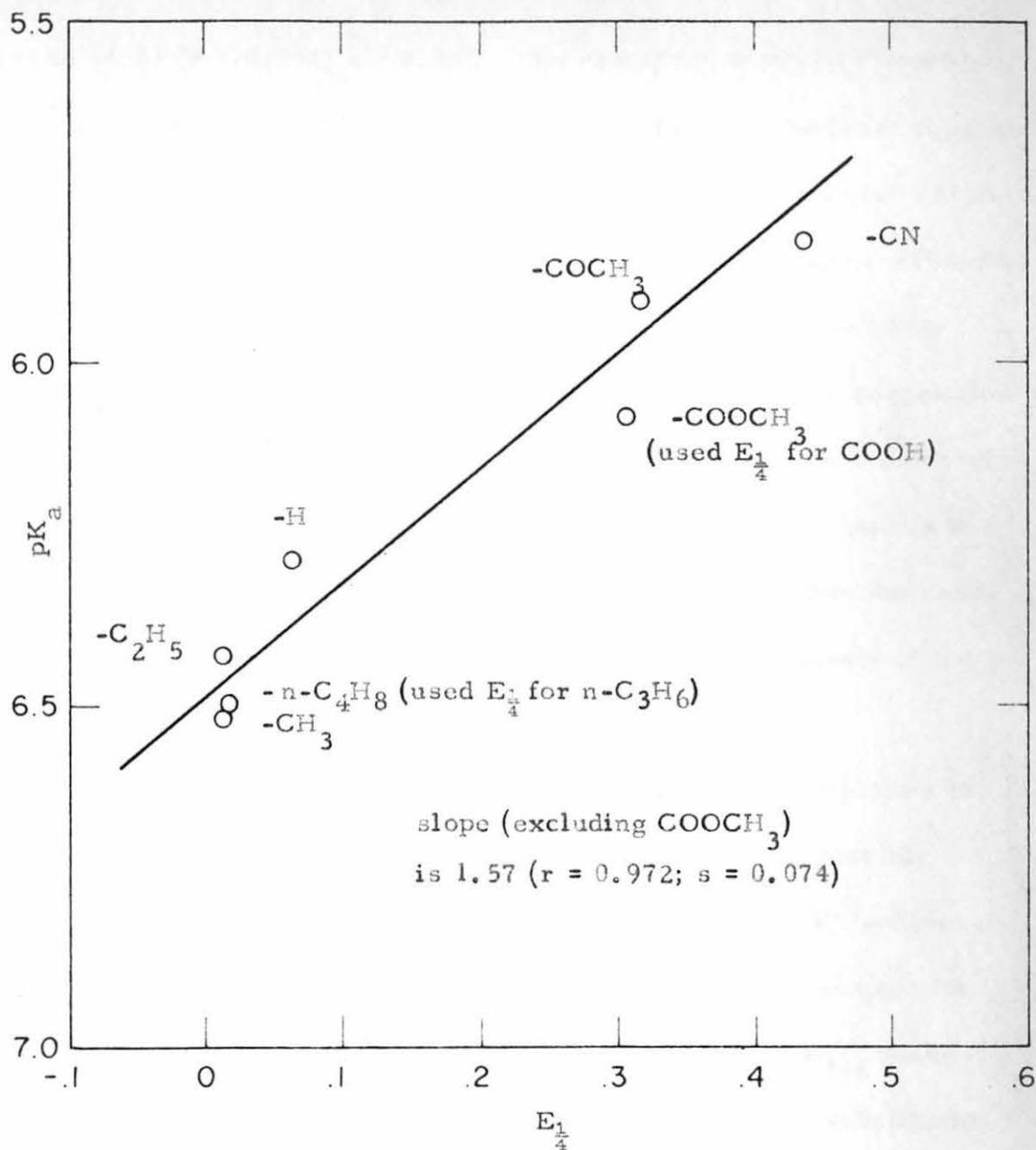


Figure 12.- Plot of Nesmeyanov's pK_a data vs. $E_{\frac{1}{4}}$.

line is -6.65 ($r = 0.994$; $s = 0.13$). The result for methyl-(1'-carbo-methoxyferrocenyl)carbinyl acetate is not included in the least squares treatment since there is no quarter-wave potential reported for carbo-methoxyferrocene. However, if the $E_{1/4}$ value for ferrocenecarboxylic acid is used instead, the point falls very near the correlation line.

The point for the bromo-substituted compound falls off the correlation line, but not so far that it detracts from the significance of the correlation. The deviation by the bromo-substituted compound supports the conclusion, drawn from the plots of the solvolysis and oxidation reactions vs. σ_m , that the interaction by bromine is not precisely of the same magnitude in the two reactions.

The behavior of the chloro-substituted compounds relative to the bromo-substituted compounds in the two reactions is possibly anomalous. The rate constant for the solvolysis of methyl(1'-chloroferrocenyl)carbinyl acetate is 25% greater than the rate constant for the solvolysis of the bromo-substituted compound. The $E_{1/4}$ value for chloroferrocene, calculated by assuming additivity of substituent effects in 1'-acetylchloroferrocene, is about 22 mV greater than the $E_{1/4}$ value calculated for bromoferrocene. The two values for the $E_{1/4}$ for bromoferrocene, calculated from the data for 1,1'-dibromoferrocene and 1'-acetylbromoferrocene, differ by only 3 mV. Thus, the effect of a chloro relative to a bromo substituent in the two reactions varies in opposite directions. Possibly this anomaly is due to a larger error in

the determination of the $E_{1/4}$ for 1'-acetylchloroferrocene than was ordinarily encountered. It would be desirable to determine the quarter-wave potentials for bromo- and chloroferrocenes directly, rather than calculate them from other data. However, the deviations mentioned here are small and do not detract from the argument for a linear free energy relationship.

The rate constants determined by Little and Eisenthal (11) for the reaction of heteroannularly substituted ferrocenoic acids with diphenyldiazomethane also bear a linear relationship to the quarter-wave potentials (fig. 11). The slope of the correlation line is 3.82 ($r = 0.993$; $s = 0.08$). It would be desirable to extend the study of Little and Eisenthal and obtain data for acids bearing substituents such as methoxy, acetamido and the halogens in the 1'-position. A comparison of the reaction rates of these ferrocenoic acids with quarter-wave potentials and with Hammett's sigma constants would be valuable in investigating the nature of the anomalous behavior of compounds substituted with such substituents in the oxidation and solvolysis reactions.

The pK_a values determined by Nesmeyanov (1, 2) for the ionization of heteroannularly substituted ferrocenoic acids in 68% methanol can also be correlated with the quarter-wave potentials (fig. 12). The slope of the correlation line is 1.57 ($r = 0.972$; $s = 0.074$). It is rather peculiar that the pK_a data and the data for the solvolyses of methylferrocenylcarbonyl acetates can be correlated with the quarter-wave

potentials; it was shown above (fig. 4, p. 87) that the solvolyses data cannot be correlated with the pK_a data. Obviously, the range of substituents should be extended in the study of the ionization of ferrocenecarboxylic acids.

One final interesting observation should be recorded at this point. If the rate data reported by Hill (9) for the solvolyses of methyl-(3-methylferrocenyl)carbinyl acetate and methyl-3-(1,1'-dimethylferrocenyl)carbinyl acetate are extrapolated to 45°, these data are correlated well with the quarter-wave potentials (fig. 10) and with σ_m (fig. 5, p. 89). This indicates that intraannular resonance effects are small in the solvolysis reaction. In Part I of this thesis, evidence, unfortunately not free from some ambiguity, was presented which indicates that homoannular resonance effects may not be important in the electrophilic substitution reactions of substituted ferrocenes. Certainly, the investigation of homoannular substituent effects in ferrocene should be carried out in parallel with the investigation of heteroannular substituent effects. At the present time, it seems that there may be unexpected similarities between the effects of homoannular and heteroannular substituents, at least in the case of those reactions in which the iron atom is postulated to play an important role.

Summary

Reversible quarter-wave potentials for substituted ferrocenes in acetonitrile may be correlated with $\Sigma\sigma_m$ with the exception of those

compounds substituted on the ring with atoms capable of nucleophilic participation with the positive iron atom. An apparent correlation of much of the data with $\Sigma\sigma_p$ is fortuitous. Substituent effects in the chronopotentiometric oxidation of substituted ferrocenes have been demonstrated to be analogous to substituent effects in the solvolyses of heteroannularly substituted methylferrocenylcarbinyl acetates. Interaction between a donor atom and the central iron atom very likely requires some distortion of the ferrocene molecule. All of the side-chain reactions of ferrocene reported to date bear a linear relationship to the quarter-wave potentials.

C. Carbonyl Stretching Frequencies

In the Introduction (p. 80) it was pointed out that shifts in the carbonyl stretching frequencies of substituted acetophenones and benzaldehydes are known to be sensitive indicators of the electronic effects of substituents. In the course of the present research a number of substituted acetylferrocenes were prepared. The carbonyl stretching frequency of each of these compounds was carefully determined in dilute carbon tetrachloride solution. Only in the case of the determination for 1'-acetylacetamidoferrocene was the infrared spectrophotometer calibrated against an external standard; most of the other measurements are probably good only to within plus or minus 2 cm^{-1} , and are in fact very likely low by $1\text{-}2\text{ cm}^{-1}$. The data are summarized in Table IX.

Table IX

Carbonyl Stretching Frequencies of Substituted Acetylferrocenes^a

Substituents	ν (cm^{-1})	$\Delta\nu$ (cm^{-1})
1'-NHCOCH ₃	1669; 1695-1701 ^b	-7
1'-NHCOOCH ₃	1673; 1743	-3
1'-NHCOOC ₂ H ₅	1671; 1738	-5
2, 1'-di-CH ₃	1670.5 ^c	-5.5
3, 1'-di-CH ₃	1670.5 ^c	-5.5
1'-CH ₃	1673.5 ^c	-2.5
2-CH ₃	1673 ^{c, d}	-3
H	1676 ^c	0
2-NHCOCH ₃	1653; 1695	-23
2-NHCOOCH ₃	1656; 1740	-20
2-NHCOOC ₂ H ₅	1654; 1731-41	-22
2-1'-di-NHCOOC ₂ H ₅	1653-55; 1735	-22
1'-COOCH ₃	1680.5; 1723	+4.5
1'-Br	1682	+6
1'-CN	1684-1685	+8.5

a. In carbon tetrachloride unless otherwise noted.

b. In every instance the ketone carbonyl is assigned the lower frequency.

c. Taken from reference 9.

d. In carbon disulfide.

Bearing in mind the fact that the accuracy of the infrared measurements is not quite what one would like for a study of this kind, some interesting comparisons can still be made. A plot of the shift in carbonyl stretching frequency vs. the reversible quarter-wave potentials (fig. 13) reveals a reasonably linear correlation between the two. Notable deviations are found in the case of the 2-substituted amide and the 2-substituted urethane. The very large shift to lower frequency observed for these two compounds can certainly be ascribed to the effect of hydrogen bonding (Part I, p. 14). The smaller, but still significant deviation found for 1'-acetylacetamidoferrocene remains at present unexplained. The large deviation for 1'-acetylchloroferrocene is almost certainly due to an error in the determination of the carbonyl stretching frequency for this compound.

When the shifts in carbonyl stretching frequencies of 1'-substituted acetylferrocenes are plotted against σ_m (fig. 14) or σ_p (fig. 15), reasonably good correlations are obtained in both cases. Again, notable deviations occur for the acetamido and urethano substituted compounds. It would be difficult to ascribe the rather large shifts observed to donation of electrons by the acetamido and urethano substituents by a resonance interaction since the frequencies for the carbonyl groups of the substituents are not shifted from those observed

for the parent compounds. Freedman has reported that the shifts for the carbonyl stretching frequencies of substituted acetanilides can be linearly correlated with the Hammett constants of the substituent groups (19).

The slope of the correlation line for the shift in carbonyl stretching frequencies is rather small. When the data are plotted against σ_m , the slope of the correlation line is about 9.5 cm^{-1} per sigma unit. A value of 15 cm^{-1} per sigma unit has been reported for substituted acetophenones (21). The small slope of the correlation line does not permit a choice between correlating the data with σ_m or with σ_p .

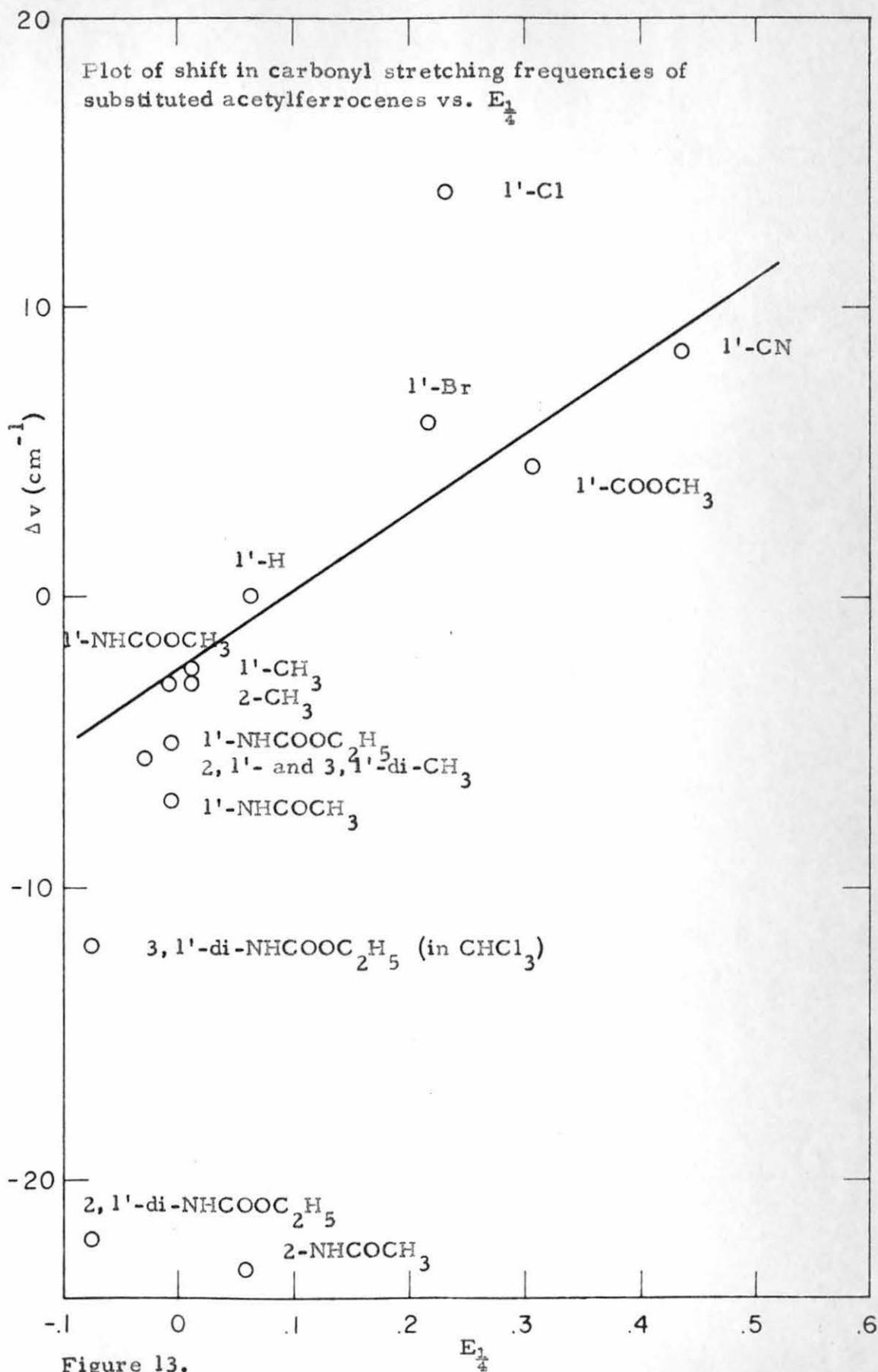


Figure 13.

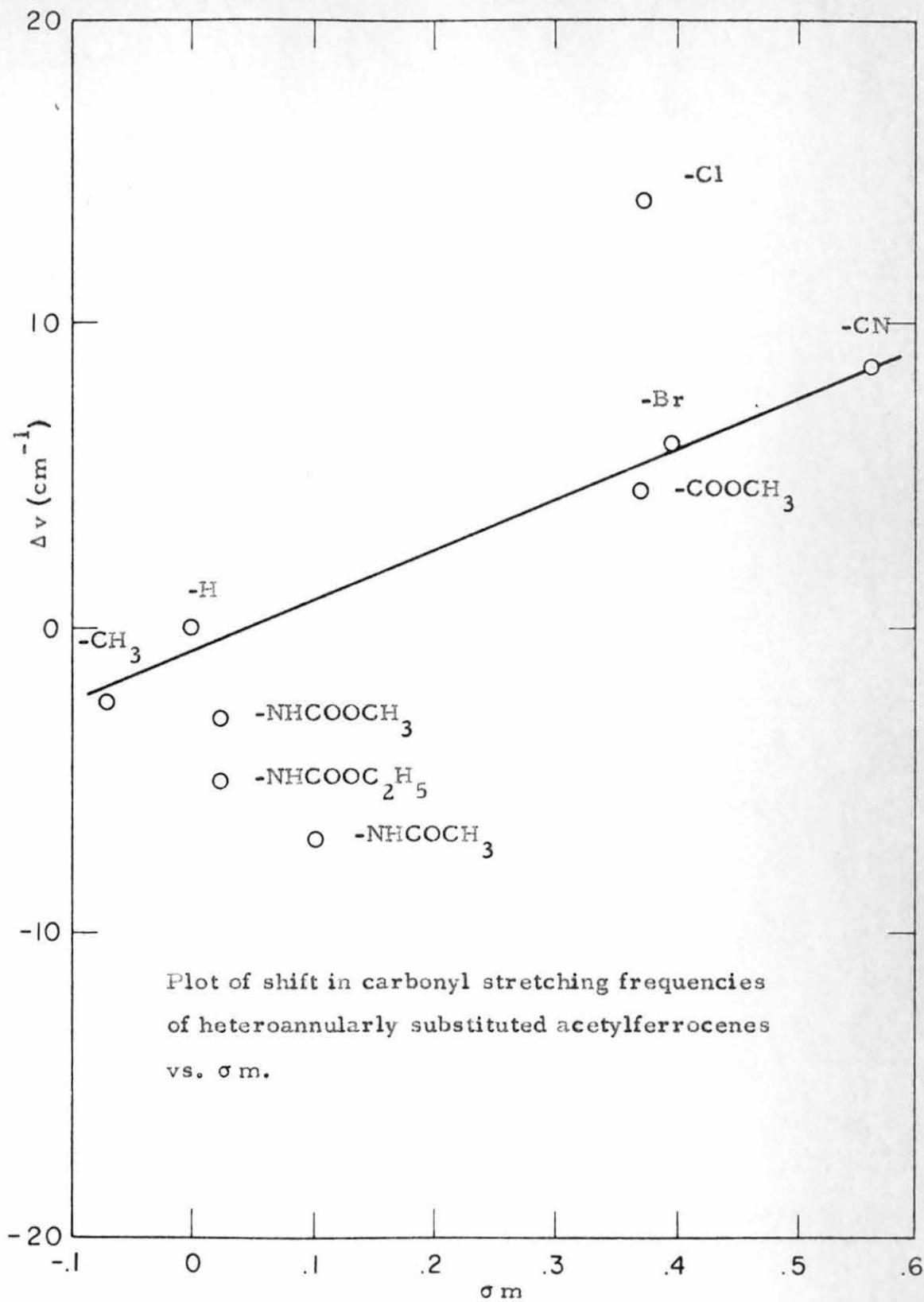


Figure 14.

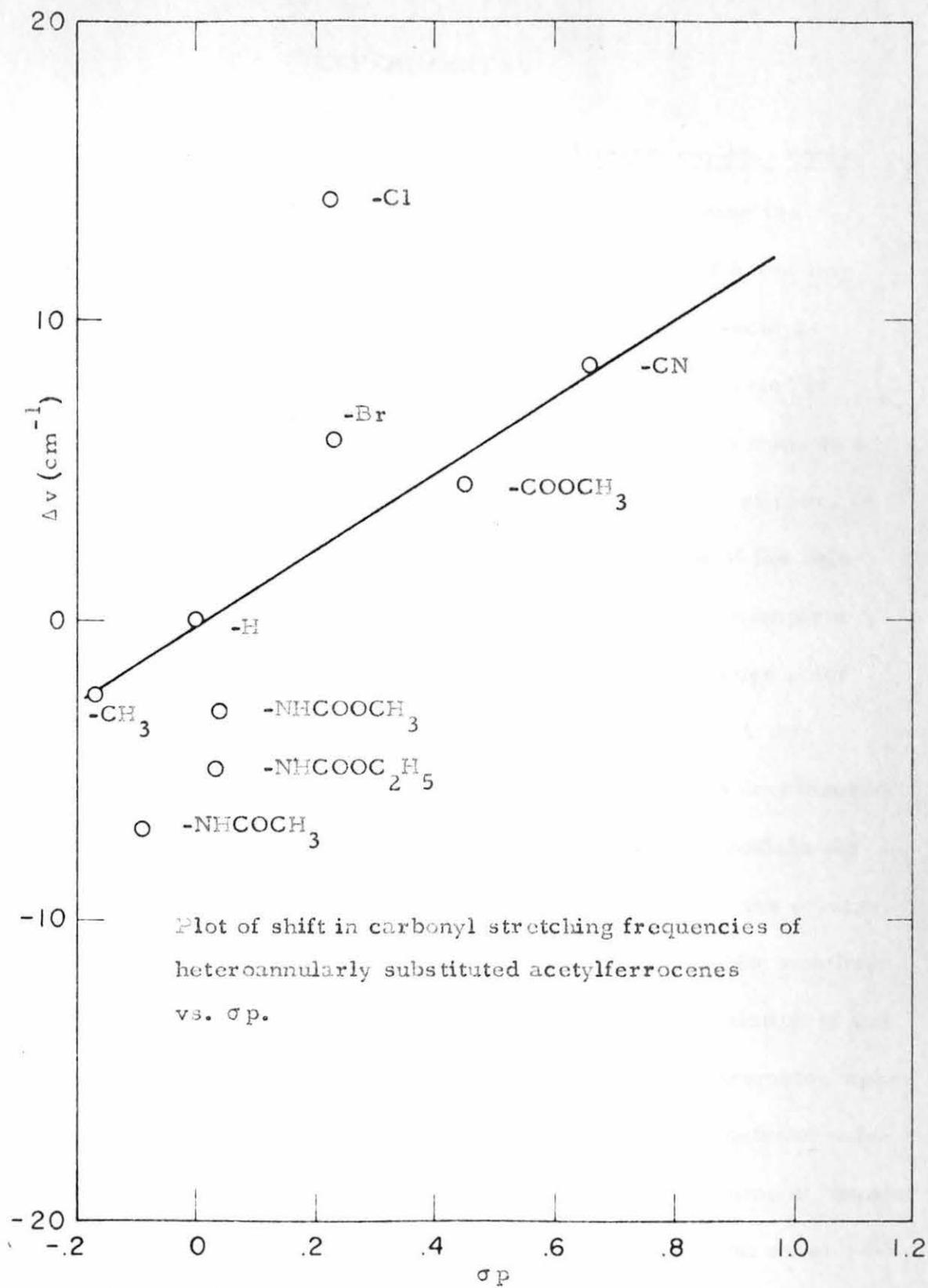


Figure 15.

EXPERIMENTAL

A. Preparation of Methyl-(1'-substituted-ferrocenyl)carbinols

In every case the alcohol was prepared by reducing the appropriate ketone with sodium borohydride in methanol according to the procedure reported by Hill for the reduction of 1'-acetyl-carbomethoxyferrocene (9). The general procedure consisted in adding sodium borohydride powder over a period of 2 to 5 min. to a methanolic solution of the ketone stirred with a magnetic stirrer. A gentle stream of nitrogen was directed onto the surface of the solution during the reaction. The reductions were generally complete in about 0.5 hr. The solutions changed from the red-orange color of the ketones to the straw-yellow color of the alcohols. After approximately one hour, excess sodium borohydride was decomposed with acetone. The reaction mixture was poured into approximately 200 ml. of water and ammonium chloride was added until the solution tested weakly basic. The alcohol was extracted with dichloromethane. Hill (9) has reported that ether formation occurs if the solution of the alcohol is dried over anhydrous magnesium sulfate or chromatographed on acid-washed alumina. For this reason, the dichloromethane solutions were worked up by adding them to an equivalent volume of benzene in a solvent stripping apparatus, and then distilling solvent under reduced pressure. The last traces of solvent were removed either at

room temperature or else on a warm water bath maintained at a temperature no greater than 50°. The crude alcohol was used directly to prepare the acetate or else it was further purified by chromatography on neutral or basic alumina that had been deactivated by the addition of water (roughly 5% by weight). The crude alcohol was used directly to prepare the acetate only when its infrared spectrum indicated that none of the starting ketone remained unreduced. Hill has observed that liquid methylferrocenylcarbinols in general give poor elemental analyses whereas the liquid acetates give satisfactory analyses (9). For this reason only the acetates were analyzed in the present study.

Preparation of Ferrocenylcarbinyl Acetates

The acetates were also prepared by the general procedure reported by Hill (9). About 1 g. of the alcohol was mixed with pyridine (5 ml.) and acetic anhydride (2 ml.) and allowed to stand overnight at room temperature under a nitrogen atmosphere. Pyridine and acetic anhydride were distilled at a pressure of 0.5 mm. and temperatures up to 50°. The crude acetate was dissolved in a small amount of dichloromethane and transferred to a molecular distillation apparatus. The bulk of the dichloromethane was removed by evaporation with a stream of nitrogen. The last traces of solvent were removed by placing a stopper in place of the cold finger of the still, and then maintaining a pressure of 0.5 to 1.0 mm. for about 0.5 hrs.

The molecular still used in the present study for the purification of all acetates except methyl-(1'-acetylferrocenyl)carbinyl acetate has a heating chamber 25 mm. in diameter with a path length between the base and the cold finger of 20 mm. The chamber is fitted with a removable oil bath heating assembly. Since the heating chamber is in contact with a glass sleeve rather than the oil bath itself, the temperature of the material in the heating chamber is probably somewhat less than the temperature of the oil bath. For this reason the temperatures reported below for the distillation of the acetates should be regarded as maximum temperatures to be employed if a conventional molecular still were to be used to purify these acetates.

The purified acetates were transferred either to tared vials and stoppered under a nitrogen atmosphere or else to tarred ampoules and sealed under a nitrogen atmosphere. When the acetate was stored in a tarred vial, it was used within one day after it was collected from the distillation.

Methyl-(1'-acetylferrocenyl)carbinol was prepared by partially reducing crude 1,1'-diacetylferrocene (6.0 g., 22 mmole) with sodium borohydride (1.0 g., 27 mmole) in methanol (375 ml.). The mixture was stirred for 1.25 hrs. at room temperature; it was then worked up in the usual manner. The crude product was chromatographed on a column of basic alumina (3 x 30 cm.) that had been deactivated by

the addition of water (4.6% by weight). Traces of acetylferrocene and methylferrocenylcarbinol were eluted first with benzene. An undetermined amount of diacetylferrocene was eluted next with 10% ether in benzene. Methyl-(1'-acetylferrocenyl)carbinol (1.80 g.; 30% conversion) was eluted just after the diacetylferrocene band; it was collected in seven fractions (total volume 6 l.). An undetermined amount of bis-(1-hydroxyethyl)cyclopentadienyl iron contaminated with an orange oil (probably the ether) was eluted last with 20% ether in benzene. Further purification of the di-alcohol gave yellow needles melting at 70 to 72° (lit. (35, 36) m.p. 69 to 71°; 105 to 106°). The other compounds isolated were identified by infrared spectra and, when applicable, by melting points.

The infrared spectrum (carbon tetrachloride) of methyl-(1'-acetylferrocenyl)carbinol possesses a fairly well-resolved doublet carbonyl absorption at 1667 and 1677 cm^{-1} . A strong aromatic ketone band occurs at 1282 cm^{-1} . Hill (9) observed a doublet carbonyl absorption in the case of methyl-(1'-carbomethoxyferrocenyl)carbinol.

The acetate was prepared from the alcohol by the pyridine procedure. The yield was approximately 90% of theory after molecular distillation (apparatus with a conventional oil bath attached to the heating chamber) at 60° and approximately 5 μ . The product was a clear red-orange oil, n_D^{25} 1.5850. The infrared spectrum was

determined from a liquid smear and in carbon tetrachloride. The ultraviolet spectrum was determined in methanol (maxima at 226 m μ , ϵ = 17,480; 269 m μ , ϵ = 6,220; and 337 m μ , ϵ = 1,222) and in cyclohexane (maxima at 223 m μ , ϵ = 23,200; 269 m μ , ϵ = 5,280; shoulder at 325 m μ , ϵ = 884).

Anal. Calculated for C₁₆H₁₈O₃Fe: C, 61.19; H, 5.74

Found (Elek): C, 61.10; H, 5.84.

Methyl-(1'-cyanoferrocenyl)carbinol was prepared from 1'-acetylcyanoferrocene in the usual way. The alcohol was isolated in nearly a quantitative yield after chromatography on alumina. The infrared spectrum of this material possesses no maxima in the carbonyl region.

The acetate was prepared in the usual manner and molecularly distilled over a period of 8 hrs. at 110° and 5 to 10 μ . The product was a red oil, n_D^{25} 1.5849. The infrared spectrum (carbon tetrachloride) displays a carbonyl absorption at 1740 cm⁻¹ and a nitrile absorption at 2235 cm⁻¹.

Anal. Calculated for C₁₅H₁₅NO₂Fe: C, 60.63; H, 5.09; N, 4.71.

Found (Elek): C, 60.87, 59.96; H, 5.26, 5.46; N, 3.99, 4.53.

Methyl-(1'-bromoferrocenyl)carbinol was prepared by reducing 1'-acetylbromoferrocene (1.37 g., 4.5 mmole). The infrared spectrum of the crude alcohol displays no bands in the carbonyl region.

The acetate was prepared from the crude alcohol in the usual

manner and molecularly distilled at 80° and approximately 5 μ . The product was a red oil (1.2 g., 75% conversion based on 1'-acetyl-bromoferrocene used in the reduction reaction), n_D^{25} 1.5959. The nuclear magnetic resonance spectrum was determined from a neat sample and from a sample diluted with carbon tetrachloride; it is compatible with the assigned structure. The infrared spectrum (liquid smear) displays a carbonyl absorption centered at 1736 cm^{-1} .

Anal. Calculated for $\text{C}_{14}\text{H}_{15}\text{BrO}_2\text{Fe}$: C, 47.90; H, 4.31; Br, 22.77. Found (Elek): C, 48.44; H, 4.37; Br, 23.10.

Methyl-(1'-chloroferrocenyl)carbinol was prepared by reducing 1-acetylchloroferrocene (0.55 g., 2.1 mmole).

The acetate was prepared from the crude alcohol in the usual manner and molecularly distilled over a period of 4 hrs. at 60 to 80° and 5 to 10 μ . The product was a red-orange oil (0.5 g., 86% conversion based on the amount of 1'-acetylchloroferrocene used in the reduction reaction), n_D^{25} 1.5806. The infrared spectrum was determined from a liquid smear and from a carbon tetrachloride solution; the carbonyl absorption occurs at 1735 to 1740 cm^{-1} . Two samples from the same batch of freshly distilled material were sent simultaneously for analysis.

Anal. Calculated for $\text{C}_{14}\text{H}_{15}\text{ClO}_2\text{Fe}$: C, 54.85; H, 4.93; Cl, 11.57; Fe, 18.22.

Found (Elek): C, 54.67; H, 5.52; Fe, 19.08.

Found (Spang): C, 54.79; H, 5.06; Cl, 11.45.

Methyl-(1'-ethoxycarbonylaminoferrocenyl)carbinol was prepared by reducing 1'-acetylethoxycarbonylaminoferrocene in the usual manner. The product, after purification by chromatography, was a yellow oil. The infrared spectrum displays a small band at 3625 cm^{-1} , a larger, broader band at 3500 cm^{-1} and a strong, very sharp band at 3450 cm^{-1} . The urethane carbonyl is present as a partially resolved doublet at 1727 cm^{-1} and 1740 cm^{-1} . Spontaneous ether formation took place during the several weeks before the acetate synthesis was attempted.

B. Preparation of Compounds for Chronopotentiometric Studies

Methyl(ferrocenylmethyl) ether was prepared according to Hill's procedure (9) by refluxing methylferrocenylcarbinol overnight in methanol which contained two drops of glacial acetic acid. The crude product was purified by chromatography on alumina. The infrared spectrum (liquid smear) is compatible with the assigned structure.

Ferrocenylcarbinyl amine (37) was prepared by reducing cyanoferrocene with lithium aluminum hydride in ether solution. The compound was purified by chromatography on basic alumina. The infrared spectrum (CCl_4) is compatible with the assigned structure. A small amount of ferrocenecarboxaldehyde was isolated as a by-product.

This compound was identified by comparing the m.p. and the infrared spectrum with those reported in the literature (38).

C. Kinetic Procedure

The procedure is the same as that given by Hill (9). The solvolyses were performed in 80% acetone; the acetone was reagent grade that had been further purified by the method of Hammond and Kochi. The density of the acetone solution was determined at 25° and compared with the density determined by Hill to ensure that the solvent systems were as nearly alike as possible.

The solvolyses were carried out by equilibrating 99 ml. (pipetted at 30°) of stock solution in a 100-ml. volumetric flask, or more conveniently, in a 125-ml. standard taper Erlenmeyer flask in an oil bath maintained at the temperature for the run. The sample of acetate (carefully weighed on an analytical balance) was dissolved in one ml. of acetone and added to the reaction flask. The flask was stoppered and the contents were mixed for a minute or two by swirling the flask while it was still immersed in the oil bath. The starting time for the reaction was taken as the instant when the sample was added; an uncertainty of even one minute in the starting time is at most 0.3% of one half-life for the most rapidly solvolyzing compound studied in the present work.

At suitable intervals after the sample was added, 5-ml. aliquots were removed and titrated with 0.0308 N. sodium hydroxide solution (standardized against potassium acid phthalate). The aliquots were delivered into quenching solution composed of 85% acetone and 15% boiled distilled water maintained at 0°. The quenching solution was saturated with nitrogen (carbon dioxide free) for at least five minutes before the aliquot was added.

The titration vessels were designed by Carter (40); they consist of flat-bottomed cylindrical flasks of about 50 ml. capacity fitted with two 19/38 necks diametrically opposed. Nitrogen was introduced by means of a glass tube passing through a rubber sleeve on a 19/38 male joint. The nitrogen delivery tube was raised to a level just above the surface of the liquid during the titration. The solution was stirred with a magnetic stirrer. Standard base was delivered with a one-ml. microburet equipped with a reservoir of about 30 ml. capacity. The capillary tip of the buret was placed just under the surface of the solution during the titration. Hill (9) has reported that duplicate titrations could customarily be reproduced within 0.003 ml. or better out of a total volume of 0.700 ml. by this method. This observation has been confirmed by Carter (40) and by the present study.

D. Calculation of rate constants

The reaction rate constant was determined by using the standard

integrated first-order rate equation (41)

$$\log (a-x) = \frac{kt}{2.303} + \log a$$

where a is the infinity titer, x is the titer at time t , and k is the first-order constant. The rate constants were determined graphically by plotting $\log (a-x)$ vs. t and drawing the "best straight line." The half-life was estimated from this line and the rate constant was calculated from the equation (42) $k = \frac{\ln 2}{t_{\frac{1}{2}}} = \frac{0.693}{t_{\frac{1}{2}}}$.

Hill (9) has discussed sources of error in the kinetic procedure in detail. In addition to the errors discussed by Hill there exists another complicating factor in the present work. Two of the compounds solvolyzed possess such long half-lives in 80% acetone that infinity titers could not be determined with any reasonable degree of accuracy. These compounds began to decompose at 45° after about eight half-lives. Attempts to obtain accurate infinity titers by sealing aliquots in tubes and heating them for shorter periods of time at higher temperatures also failed because of decomposition. Theoretical infinity titers were used to calculate the rate constants for these two compounds.

Hill has calculated that the theoretical infinity titer at 45° is 0.986 times the value at 30° (43). In the present work, the temperature correction factor determined experimentally was 0.9919. The

difference may be accounted for by the fact that the aliquot has cooled from 45° to some lower temperature by the time it is delivered. The experimentally determined temperature correction factor was used in the present work to obtain theoretical infinity titers at 45°.

Table X

Run 2: Solvolysis of Methyl-(1'-acetylferrocenyl)carbinyl Acetate

80% Acetone, 45°

Sample: 0.1390 g.

Initial concentration: 4.43×10^{-3} m./l.

Titration	Titer (x ml. of 0.0308 N. NaOH)	Titer of unchanged acetate (0.714 - x) ml.	t (min.)
1	0.000	0.714	4
2	0.000	0.714	15
3	0.004	0.710	32
4	0.039	0.675	82
5	0.093	0.621	186
6	0.099	0.615	200
7	0.169	0.545	370
8	0.170	0.544	385
9	0.262	0.452	614
10	0.269	0.445	634
11	0.278	0.436	649
12	0.427	0.287	1206
13	0.433	0.281	1218
14	0.468	0.246	1381
15	0.461	0.253	1400
16	0.468	0.246	1424

Infinity titers: 0.779; 0.806; 0.800 ml. at 30°

Theoretical infinity titer: 0.720 ml. at 30°; 0.714 ml. at 45°

% Followed to completion: 65.5

Rate constant: $1.260 \times 10^{-5} \text{ sec}^{-1}$ (graphically)

Table XI

Run 3: Solvolysis of Methyl-(1'-acetylferrocenyl)carbinyl Acetate

80% Acetone, 45°

Sample: 0.2152 g. Initial concentration: 6.85×10^{-3} m./l.

Titration	Titer (x ml. of 0.0308 N. NaOH)	Titer of unchanged acetate (1.105 - x) ml.	t (min.)
1	0.020	1.085	32
2	0.096	1.009	123
3	0.159	0.946	204
4	0.206	0.899	269
5	0.337	0.768	486
6	0.336	0.769	486
7	0.489	0.616	788
8	0.712	0.394	1313
9	0.725	0.380	1366
10	0.835	0.270	1744

Infinity titers: 1.172; 1.181 at 45°

Theoretical infinity titer: 1.114 ml. at 30°; 1.105 ml. at 45°

% Followed to completion: 75.5

Rate constant: $1.235 \times 10^{-5} \text{ sec}^{-1}$ (graphically)

Table XII

Run 4: Solvolysis of Methyl-(1'-acetylferrocenyl)carbinyl Acetate

80% Acetone, 45°

Sample: 0.2280 g.

Initial concentration: 7.25×10^{-3} m./l.

Titration	Titer (x ml. of 0.0308 N. NaOH)	Titer of unchanged acetate (1.171 - x) ml.	t (min.)
1	0.019	1.152	31
2	0.124	1.047	158
3	0.136	1.035	172
4	0.205	0.966	263
5	0.355	0.816	490
6	0.490	0.681	745
7	0.494	0.677	745
8	0.715	0.456	1275
9	0.868	0.303	1710

Infinity titer: 1.230 ml. at 45°

Theoretical infinity titer: 1.181 ml. at 30°; 1.171 ml. at 45°

% Followed to completion: 74

Rate constant: $1.230 \times 10^{-5} \text{ sec}^{-1}$ (graphically)

Table XIII

Run 5: Solvolysis of Methyl-(1'-cyanoferrocenyl)carbinyl Acetate

80% Acetone, 45°

Sample: 0.1069 g. Initial concentration: 3.59×10^{-3} m./l.

Titration	Titer (x ml. 0.0308 N. NaOH)	Titer of unchanged acetate (0.580 - x) ml.	t (min.)
1	0.005	0.575	73
2	0.018	0.562	290
3	0.095	0.485	1681
4	0.128	0.452	2397
5	0.145	0.435	2810
6	0.163	0.417	3171
7	0.189	0.391	3886
8	0.251	0.329	5346
9	0.300	0.280	6773
10	0.300	0.280	6793

Infinity titer: none determined, material decomposed

Theoretical infinity titer: 0.585 ml. at 30°; 0.580 ml. at 45°

% Followed to completion: 51.3

Rate constant: $1.783 \times 10^{-6} \text{ sec}^{-1}$ (graphically)

Table XIV

Run 6: Solvolysis of Methyl-(1'-cyanoferrocenyl)carbinyl Acetate

80% Acetone, 45°

Sample: 0.1141 g.

Initial concentration: 3.83×10^{-3} m./l.

Titration	Titer (x ml. 0.0308 N. NaOH)	Titer of unchanged acetate (0.580 - x) ml.	t (min.)
1	0.004	0.615	74
2	0.026	0.593	403
3	0.051	0.568	720
4	0.089	0.530	1440
5	0.170	0.449	2895
6	0.234	0.385	4342
7	0.302	0.317	5879
8	0.297	0.322	5901
9	0.304	0.315	5989

Infinity titer: 0.626 ml. at 30° (sealed tube, slight decomp.)

Theoretical infinity titer: 0.624 ml. at 30°; 0.619 ml. at 45°

% Followed to completion: 48.7

Rate constant: $1.768 \times 10^{-6} \text{ sec}^{-1}$ (graphically)

Table XV

Run 7: Solvolysis of Methyl-(1'-cyanoferrocenyl)carbinyl Acetate

80% Acetone, 45°

Sample: 0.1724 g.

Initial concentration: 5.78×10^{-3} m./l.

Titration	Titer (x ml. of 0.0308 N. NaOH)	Titer of unchanged acetate (0.936 - x) ml.	t (min.)
1	0.004	0.932	89
2	0.045	0.891	417
3	0.048	0.888	439
4	0.078	0.858	730
5	0.133	0.803	1454
6	0.254	0.682	2905
7	0.357	0.579	4351
8	0.371	0.565	4393
9	0.357	0.579	4409
10 ^a	0.453	---	5910
11 ^a	0.462	---	5929
12	0.449	0.487	5946
13	0.448	0.488	5968

a. Nitrogen purifying system failed.

Infinity titer: none determined

Theoretical infinity titer: 0.943 ml. at 30°; 0.936 ml. at 45°

% Followed to completion: 47.5

Rate constant: $1.890 \times 10^{-6} \text{ sec}^{-1}$ (graphically)

Table XVI

Run 9: Solvolysis of Methyl-(1'-cyanoferrocenyl)carbinyl Acetate

80% Acetone, 45°

Sample: 0.1793 g. Initial concentration: 9.55×10^{-3} m./l.

Titration	Titer (x ml. of 0.0308 N. NaOH)	Titer of unchanged acetate (0.973 - x) ml.	t (min.)
1	0.018	0.955	212
2	0.124	0.849	1408
3	0.195	0.778	2062
4	0.245	0.728	2704
5	0.244	0.729	2725
6	0.278	0.695	3118
7	0.362	0.611	4396

Infinity titers: 0.988 at approximately 15°; 1.010 at approximately 25°
(sealed tube, some decomposition evident)

Theoretical infinity titer: 0.981 ml. at 30°; 0.973 ml. at 45°

% Followed to completion: 37.3

Rate constant: $1.67 \times 10^{-6} \text{ sec}^{-1}$ (graphically)

Table XVII

Run 10: Solvolysis of Methyl-(1'-bromoferrocenyl)carbonyl Acetate

80% Acetone, 45°

Sample: 0.1950 g. Initial concentration: 5.56×10^{-3} m./l.

Titration	Titer (x ml. of 0.0308 NaOH)	Titer of unchanged acetate (0.880 - x) ml.	t (min.)
1	0.179	0.701	69
2	0.265	0.615	127
3	0.312	0.568	167
4	0.373	0.507	227
5	0.428	0.452	293
6	0.512	0.368	397
7	0.517	0.363	398
8	0.596	0.284	536
9	0.657	0.223	666
10	0.656	0.224	667

Infinity titers: 0.879; 0.881 ml. at 45° (after 72 hrs.)
 0.886; 0.885 ml. at 30° (after 72 hrs.)
 0.886 ml. at 45° (after 120 hrs.)

Theoretical titer: 0.903 ml. at 30°; 0.896 ml. at 45°

% Followed to completion: 74.5

Rate constant: $3.12 \times 10^{-5} \text{ sec}^{-1}$ (graphically)

Table XVIII

Run 11: Solvolysis of Methyl-(1'-bromoferrocenyl)carbinyl Acetate

80% Acetone, 45°

Sample: 0.2884 g.

Initial Concentration: 8.23×10^{-3} m./l.

Titration	Titer (x ml. of 0.0308 N. NaOH)	Titer of unchanged acetate (1.328 - x) ml.	t (min.)
1	0.254	1.071	91
2	0.338	0.987	138
3	0.404	0.921	177
4	0.523	0.802	262
5	0.707	0.618	421
6	0.710	0.615	422
7	0.828	0.497	508
8	0.827	0.498	509

Infinity titers: 1.340; 1.346; 1.341 ml. at 45° (after 72 hrs.)
 1.427; 1.428 ml. at 45° (after 120 hrs.)
 1.436 ml. at 30° (after 120 hrs.)

Theoretical infinity titer: 1.336 ml. at 30°; 1.328 ml. at 45°

% Followed to completion: 62

Rate constant: $2.82 \times 10^{-5} \text{ sec}^{-1}$ (graphically)

Table XIX

Run 12: Solvolysis of Methyl-(1'-bromoferrocenyl)carbinyl Acetate

80% Acetone, 45°

Sample: 0.2001 g. Initial concentration: 5.70×10^{-3} m./l.

Titration	Titer (x ml. of 0.0308 N. NaOH)	Titer of unchanged acetate (0.889 - x) ml.	t (min.)
1	0.230	0.659	105
2	0.289	0.600	150
3	0.334	0.555	193
4	0.417	0.472	275
5	0.543	0.346	443
6	0.633	0.256	598
7	0.808	0.081	1238
8	0.811	0.078	1239

Infinity titers: 0.888; 0.890 ml. at 45° (after 72 hrs.)
 0.900; 0.898 ml. at 30° (after 72 hrs.)
 0.911 ml. at 45° (after 120 hrs.)

Theoretical infinity titer: 0.927 ml. at 30°

% Followed to completion: 91

Rate constant: $3.14 \times 10^{-5} \text{ sec}^{-1}$ (graphically)

Table XX

Run 13: Solvolysis of Methyl-(1'-chloroferrocenyl)carbinyl Acetate

80% Acetone, 45°

Sample: 0.1417 g. Initial concentration: 4.62×10^{-3} m./l.

Titration	Titer (x ml. of 0.0308 N. NaOH)	Titer of unchanged acetate (0.746 - x) ml.	t (min.)
1	0.025	0.721	10
2	0.144	0.602	94
3	0.312	0.434	234
4	0.369	0.377	299
5	0.393	0.353	319
6	0.413	0.333	338
7	0.443	0.303	378
8	0.592	0.154	702
9	0.596	0.150	716
10	0.686	0.060	1267
11	0.699	0.047	1287

Infinity titers: 0.771; 0.772 ml. at 45° (after 55 hrs.)
0.792; 0.795 ml. at 45° (after 73 hrs.)

Theoretical infinity titer: 0.752 ml. at 30°; 0.746 ml. at 45°

% Followed to completion: 93.8

Rate constant: $3.75 \times 10^{-5} \text{ sec}^{-1}$ (graphically)

Table XXI

Run 14: Solvolysis of Methyl-(1'-chloroferrocenyl)carbinyl Acetate

80% Acetone, 45°

Sample: 0.1240 g.

Initial concentration: 4.05×10^{-3} m./l.

Titration	Titer (x ml. of 0.0308 N. NaOH)	Titer of unchanged acetate (0.653 - x) ml.	t (min.)
1	0.024	0.629	10
2	0.095	0.558	60
3	0.137	0.516	92
4	0.192	0.461	141
5	0.280	0.373	231
6	0.368	0.285	345
7	0.402	0.251	387
8	0.491	0.162	583
9	0.638	0.015	1536

Infinity titers: 0.679; 0.683 ml. at 45° (after 52 hrs.)
 0.696; 0.700 ml. at 45° (after 71 hrs.)

Theoretical infinity titer: 0.658 ml. at 30°; 0.653 ml. at 45°

% Followed to completion: 97

Rate constant: $3.96 \times 10^{-5} \text{ sec}^{-1}$ (graphically)

Table XXII

Run 15: Solvolysis of Methyl-(1'-chloroferrocenyl)carbinyl Acetate

80% Acetone, 45°

Sample: 0.1003 g.

Initial concentration: 3.27×10^{-3} m./l.

Titration	Titer (x ml. of 0.0308 N. NaOH)	Titer of unchanged acetate (0.507 - x) ml.	t (min.)
1	0.025	0.482	21
2	0.060	0.447	49
3	0.107	0.400	100
4	0.147	0.360	145
5	0.186	0.321	190
6	0.277	0.219	334
7	0.308	0.199	386
8	0.315	0.192	402

Infinity titers: 0.570; 0.579 ml. at 45° (from solvolysis flask;
obvious evaporation loss)

0.507 ml. at 40° (from 25 ml. aliquot removed at
0.513 ml. at 30° beginning of run)

Theoretical infinity titer: 0.532 ml. at 30° ; 0.528 ml. at 45°

% Followed to completion: 59

Rate constant: $4.03 \times 10^{-5} \text{ sec}^{-1}$ (graphically)

($3.75 \times 10^{-5} \text{ sec}^{-1}$; graphically, using theoretical
infinity titer at 45°)

Table XXIII

Run 16: Solvolysis of Methyl-(1'-bromoferrocenyl)carbinyl Acetate

80% Acetone, 30°

Sample: 0.1752 g. Initial concentration: 5.0×10^{-3} m./l.

Titration	Titer (x ml. of 0.0308 N. NaOH)	Titer of unchanged acetate (0.751 - x) ml.	t (min.)
1	0.010	0.741	27
2	0.038	0.713	96
3	0.237	0.514	872
4	0.248	0.503	917
5	0.262	0.489	994
6	0.276	0.475	1061
7	0.296	0.455	1192
8	0.301	0.450	1217
9	0.344	0.407	1446
10	0.450	0.301	2311

Infinity titers: 0.745; 0.752; 0.756 ml. at 26 to 28°
(from a 25 ml. aliquot removed at the beginning of
the run and maintained at 45° for 72 hrs.)

Theoretical infinity titer: 0.812 ml. at 30°

% Followed to completion: 60

Rate constant: $6.36 \times 10^{-6} \text{ sec}^{-1}$ (graphically)
($7.0 \times 10^{-6} \text{ sec}^{-1}$; graphically, based on theoretical
infinity titer)

Table XXIV

Rate Constants for Solvolyses

Compound	T°C.	Run	Conc. x 10 ³ mole/liter	% Followed	k x 10 ⁵ ^a	k x 10 ⁵ av.
Methyl-(1'-acetyl-ferrocenyl)carbonyl Acetate	45	2	4.43	65.5	1.260	1.242+0.012
		3	6.85	75.5	1.235	
		4	7.25	74	1.230	
Methyl-(1'-cyano-ferrocenyl)carbonyl Acetate	45	5	3.59	51.3	0.1783	0.1814+0.0051
		6	3.83	48.7	0.1768	
		7	5.78	47.5	0.1890	
		9	9.55	37.3	(0.167) ^c	
Methyl-(1'-bromo-ferrocenyl)carbonyl Acetate	45	10	5.56	74.5	3.12 ^b	3.13+0.01
		11	8.23	62	(2.82)	
		12	5.70	91	3.14 ^b	
		16	5.0	60	0.636 ^b	
					(0.70) ^c	
Methyl-(1'-chloro-ferrocenyl)carbonyl Acetate	45	13	4.62	93.8	3.75	3.91+0.11
		14	4.05	97	3.96	
		15	3.27	59	4.03 ^b	
					(3.75) ^c	

a. Theoretical infinity titer was used unless otherwise noted.

b. The experimental infinity titer was used.

c. Rates in parentheses were not used for further calculations.

APPENDIX A*

Electrolysis cell. The electrolysis cell is illustrated in figure 16. Working and auxiliary electrode compartments were separated by a fine porosity sintered-glass disk. The shape of the working electrode compartment was designed to promote linear diffusion and current flow perpendicular to the electrode surface and consequently a uniform current density over the surface (44). The underside of the working electrode was sealed over with glass and connection was made by a spot-welded platinum lead wire passing through the glass. The lead wire was insulated by a length of Teflon spaghetti sealed to the glass with epoxy resin. The reference electrode was connected with the working electrode compartment in a manner which minimized ohmic drop. The electrode area was calculated as 0.529 cm^2 from the transition time for the reduction of $0.004 \text{ M K}_3\text{Fe}(\text{CN})_6$, 1.00 M KCl in water (6). The potentiostatically determined value of $7.63 \times 10^{-6} \text{ cm}^2/\text{sec}$ for the diffusion coefficient of ferricyanide ion which von Stackelberg, Pilgram, and Toome (45) reported for solutions of this composition was used in the calculation.

Reference electrodes. Two reference electrodes were used, both of which are illustrated in figure 16. The $\text{Ag}/0.01 \text{ M AgNO}_3$,

*The material in this appendix is excerpted directly from reference 29.

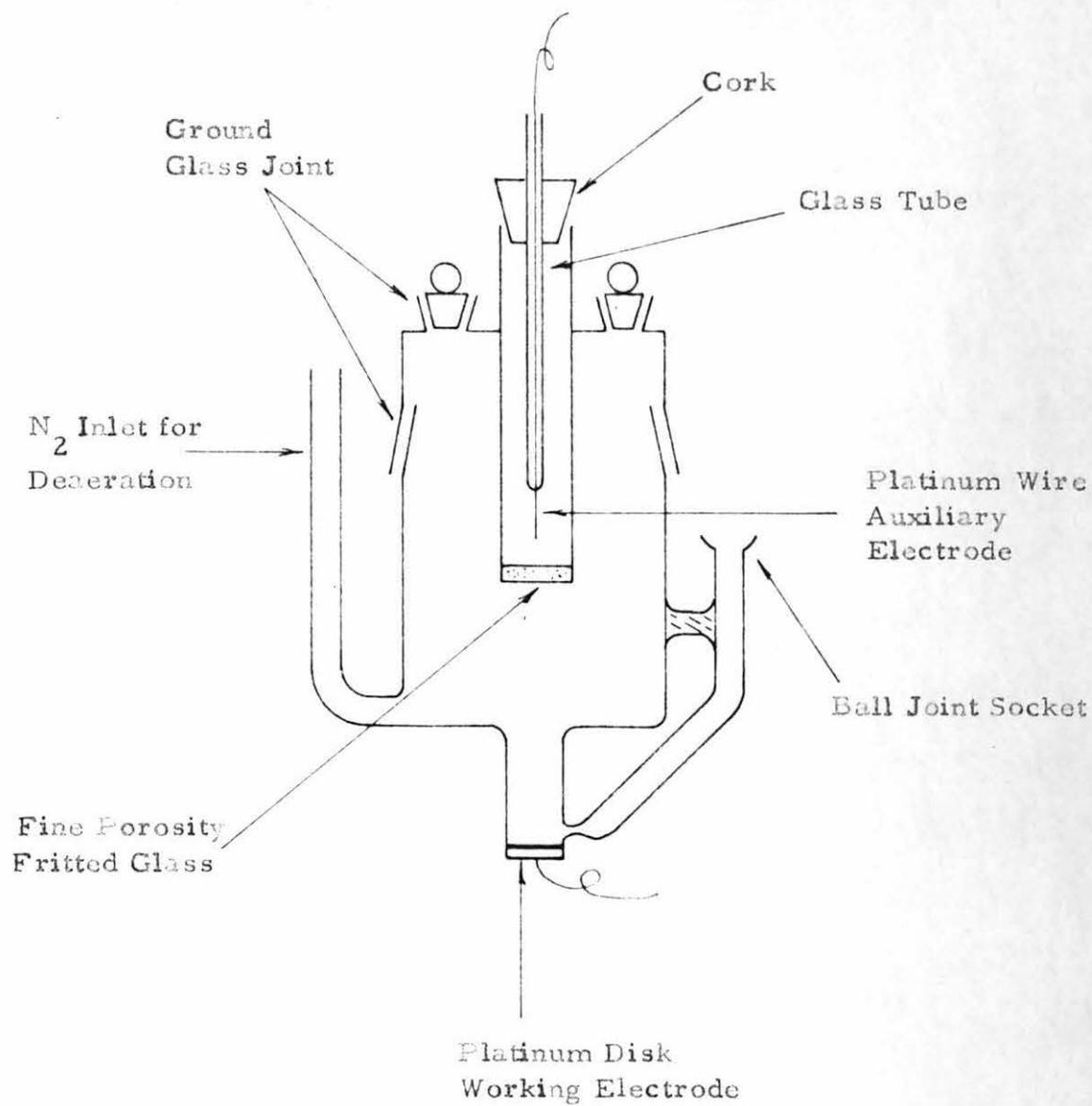
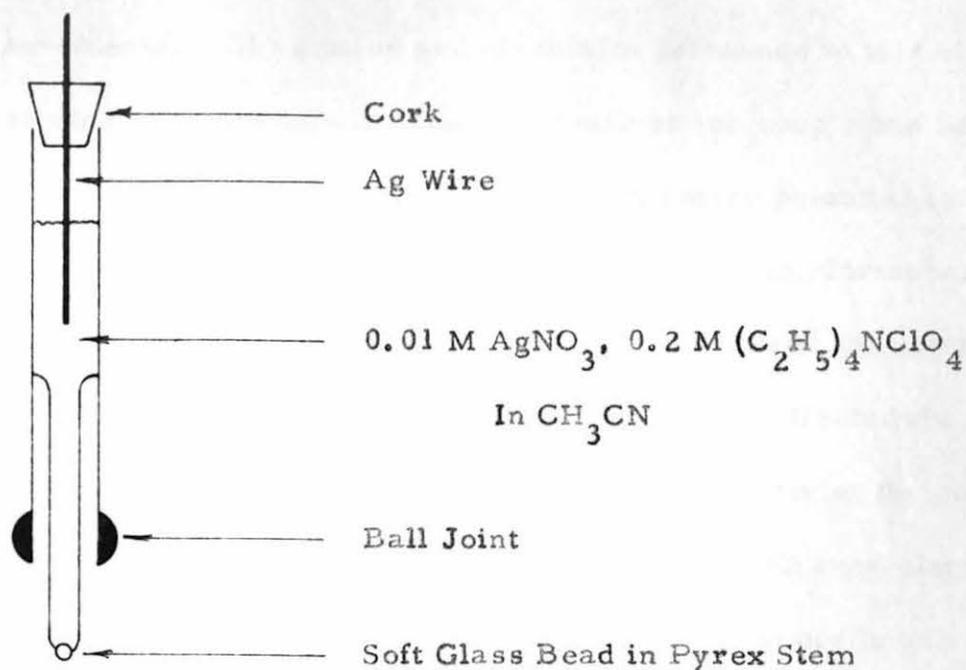


Figure 16. Chronopotentiometric Cell

REFERENCE ELECTRODES



SILVER NITRATE REFERENCE ELECTRODE

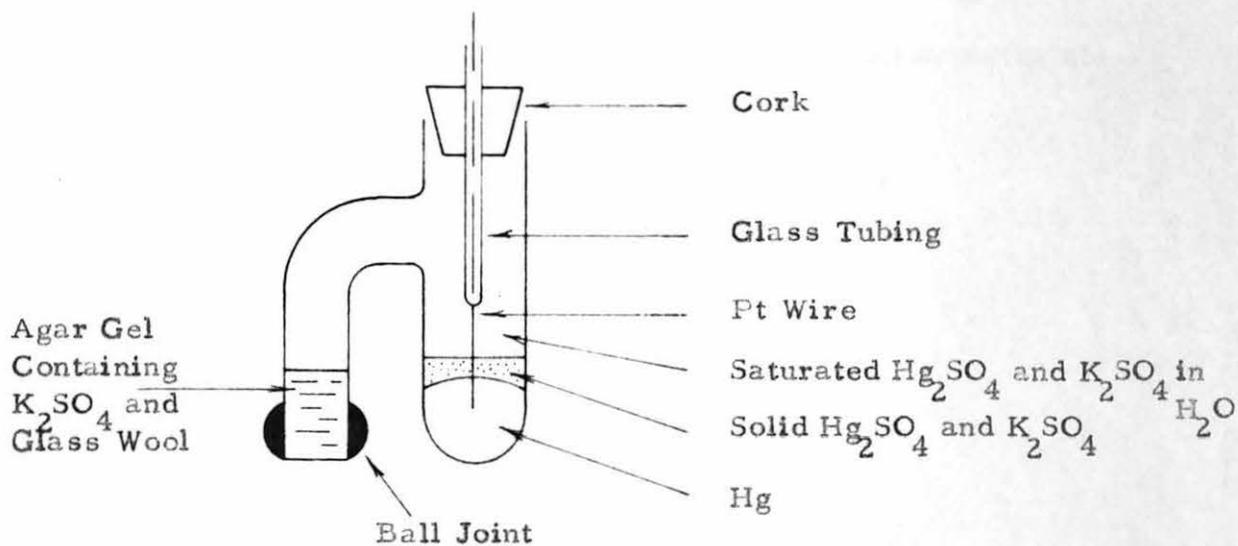


Figure 17.

0.2 M $(\text{C}_2\text{H}_5)_4\text{NClO}_4$ in CH_3CN reference electrode was used for most measurements. All voltages are given with reference to this electrode unless otherwise specified. The silver-silver ion couple has been recommended by a number of authors as a primary potential reference in acetonitrile (46, 47, 48). Tetraethylammonium perchlorate was added to eliminate the liquid-junction potential between the reference electrode and the solution in the cell; this will have affected the electrode potential somewhat but it ensured reproducibility of the potential measurements. Leakage from the silver nitrate reference electrode was very low, amounting to no more than a half drop per hour. It was cleaned, dried and refilled with fresh silver nitrate solution each day.

The $\text{Hg}/\text{Hg}_2\text{SO}_4, \text{K}_2\text{SO}_4$ (sat. aq.) electrode did not function as well in acetonitrile solutions, its potential drifting about ± 0.02 V. It was used to compare potentials for oxide film formation on the electrode surface in water and in acetonitrile.

APPENDIX B*

Solutions of approximately 2 mM concentration in the ferrocene compound and 0.20 M in reagent grade anhydrous NaClO_4 (G. F. Smith Chemical Company) were prepared using spectral grade acetonitrile (Matheson, Coleman and Bell Company). The electrolysis cell was described in Appendix A. The cracked-bead reference electrode described in Appendix A was used, except that 0.0100 M AgClO_4 , 0.20 M NaClO_4 was used in place of silver nitrate solution. The current source was a Wenking potentiostat (Elektronische Werkstätten, Göttingen, Germany) which controlled the voltage across a standard resistor in series with the cell and hence the current through the cell. Chronopotentiograms were recorded on a Moseley X-Y-time recorder connected to the anode and to the reference electrode through two follower amplifiers of the DeFord type (49) constructed with George A. Philbrick Company plug-in amplifiers. The ohmic drop between anode and reference electrode was measured using a method described by Anson (50) and found to be only a few millivolts; due correction was made to the measured potentials. All measurements were performed at 25.0° C.

*This discussion is excerpted directly from reference 29.

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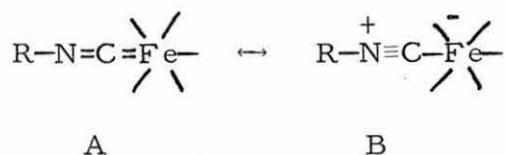
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PROPOSITIONS

I

Heldt has investigated the electrophilic substitution of cyanopentabenzylisonitrileiron (II) hydrogen sulfate and dicyanotetrabenzylisonitrileiron (II) (1). He found that nitration, sulfonation, alkylation, and bromination of these compounds gave almost exclusively products in which the electrophilic group entered the para position. Competitive nitration experiments revealed that cyanopentabenzylisonitrileiron (II) hydrogen sulfate nitrates in the first string about 350 times faster than benzene and about 180 times faster than toluene. The competitive nitration studies were carried out at 10° in concentrated sulfuric acid medium.

The two resonance structures for the isonitrile complex may be written as



Cotton (2) has shown that B is the more important resonance form in complexes of divalent metals. However, there is also evidence that some double bond character exists in the complex since the iron-carbon bond is shorter than expected for a single bond (3).

As Heldt has pointed out in his paper, it is very surprising

that the isonitrile substituent activates the para position if the immonium form B is indeed the more important resonance structure. Even if structure A were the more important, the reactivity of the compound would be expected to fall between the reactivities of benzene and toluene rather than exceed the reactivity of toluene by a factor of 180.

To account for the high reactivity of this coordination compound, Heldt has postulated that a powerful anchimeric, rate-accelerating effect must operate in the transition state of the electrophilic substitution which exceeds the electron withdrawing effect of the immonium form B in the monopositive cation.

In his paper Heldt has formulated this transition state poorly; he draws resonance arrows in one instance where an equilibrium should have been indicated. Further, the electrophilic reagent is not even considered. Heldt's formulation implies that the isonitrile complex should be in equilibrium with a cyclic immonium form (fig. 1).

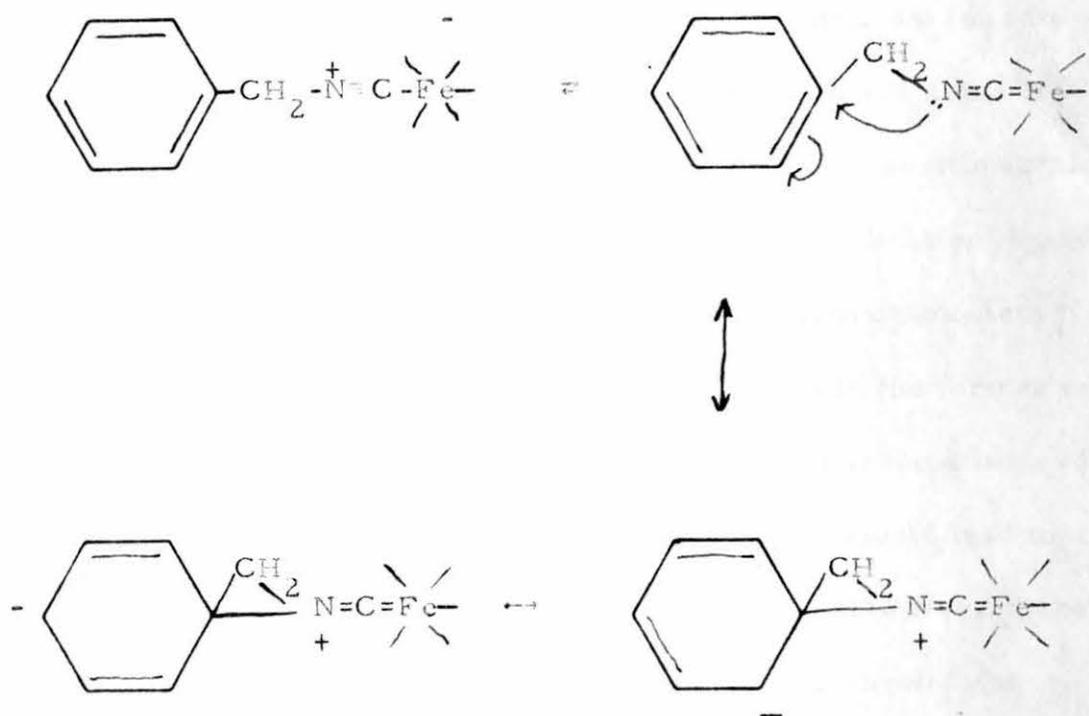


Figure 1

Clearly this cyclic species is not going to exist in the ground state. Such a cyclic transition state, at least when properly formulated, does seem to be the best explanation for Heldt's observations concerning substitution only at the para position and the enhanced reactivity relative to benzene and toluene. Ethyleneimmonium ion intermediates have been demonstrated to occur in certain reactions of tertiary amines (4, 5). It would seem that the cyclic transition state postulated in the electrophilic substitution of the coordination ligands would be less stable than intermediates of the ethyleneimmonium type postulated in the reactions of tertiary amines since in the former compounds the nitrogen is doubly bonded (at least) to a carbon atom rather than substituted by two alkyl groups. This situation should lead to greater steric strain in the three-membered ring. However, there seems to be nothing reported in the literature which invalidates Heldt's postulated transition state.

There does seem to be one anomaly in Heldt's results which he does not comment on. He finds that his coordination ligand compounds do not react with acetyl chloride and aluminum chloride; he attributes this to addition of the Lewis acid to the slightly basic nitrogen atom. It is pointed out in another proposition that a similar situation probably exists in the Friedel-Crafts acetylation of acetanilide. However, in the case of reactions on acetanilide, the acetamido group is converted to a meta director by protonation, as for

example in nitration (6). It would seem that in the case under discussion, if the nitrogen atom is complexed with aluminum chloride and therefore does not react, it should also be protonated in the concentrated sulfuric acid medium used in the nitration reactions. If all the acylation reactions Heldt ran are comparable to the two described in his paper, the failure to obtain any acylated products may be due to the use of insufficiently stringent conditions, rather than complexing of the nitrogen atom with aluminum chloride.

A. It is proposed that more quantitative studies be done on the rates of electrophilic substitution reactions of cyanopentabenzylisonitrileiron (II) hydrogen sulfate in order to establish conclusively that the rates of these reactions are greatly enhanced relative to similar reactions of benzene and toluene. Mercuration and bromination reactions would be especially well suited for such studies since a great deal of quantitative data is available for benzene under experimental conditions that would be easily adaptable to the compounds presently under discussion (7, 8).

B. It is proposed that model compounds be studied in detail to determine if anchimeric assistance in the electrophilic substitution of benzene derivatives is a general phenomenon. One such model compound is N-benzylacetamide. A mercuration study on this compound gave ortho- and para- substituted isomers in good yield; the ratio of ortho- to para- substitution was 1:1:3 (9). No rate studies have been done on this compound.

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II

Friedel-Crafts acylation of ruthenocene (bis-cyclopentadienyl-ruthenium) has been demonstrated to proceed smoothly (1, 2). Exhaustive studies on bis-indenylruthenium have shown that this compound cannot be readily acetylated (3). In no instance has an acetyl derivative of this compound been isolated; it is possible of course that small amounts of acetylated derivatives have been formed but gone undetected in the work up. Reagents employed in the studies include acetic anhydride and boron trifluoride; acetic anhydride and phosphoric acid; silicon tetraacetate and stannic chloride; and acetyl chloride and aluminum chloride. Generally, a large portion of the starting material decomposed under the conditions of the reactions.

A further example of the instability of the bis-indenylruthenium is found in the behavior of this compound in the presence of rubeanic acid (dithiooxamide), a common spot test reagent for ruthenium (4). Bis-indenylruthenium was observed to give the blue color characteristic of ruthenium salts within five seconds after being introduced into hot test solution (5). * At room temperature the first noticeable blue precipitate was evident after five minutes. The complex with ruthenium salts is reported to be soluble (4). Ruthenocene, acetyl-ruthenocene, and methylruthenocenylcarbinol failed to give a positive

*The reactions between rubeanic acid and the several ruthenium compounds listed were studied by the author in the course of working up this proposition.

test even after the test solution was refluxed for two to three minutes.

Apparently decomposition of the bis-indenylruthenium prior to the attack of rubeanic acid is not necessary; it was observed that bis-indenylruthenium was not decomposed when an acetic acid solution of the compound was refluxed for five minutes. The reaction of bis-indenylruthenium with rubeanic acid probably does not involve an oxidation step since the reaction proceeds smoothly in the presence of ascorbic acid. Ascorbic acid is known to reduce bis-indenylruthenium (IV) to bis-indenylruthenium (II).

Webb has shown from X-ray diffraction studies that the structure of bis-indenylruthenium is quite analogous to that of ruthenocene (5). There is nothing in Webb's data which would explain the marked instability of bis-indenylruthenium towards the reagents listed above.

Chronopotentiometric oxidation studies performed by Russell show that, within the rather wide limits inherent in measurements on irreversible systems, bis-indenylruthenium is oxidized only slightly more readily than ruthenocene (6).

It is proposed that acetylation, mercuration and lithiation reactions be studied on a series of compounds related to bis-indenylruthenium, and on bis-indenylruthenium itself in the case of the mercuration and lithiation reactions.

Steric effects could be evaluated by studying the reactions on bis-tetrahydroindenylruthenium (7). The effect of the fused benzene

ring could be evaluated by studying cyclopentadienyl (indenyl)ruthenium; complications due to steric interactions should not be serious. The iron and osmium analogs of these compounds should also be studied.

It is further proposed that the products resulting from the reaction of rubeanic acid and any of the above ruthenium compounds be analyzed in order to investigate the possibility that the metal-rubeanic acid complex still has the organic residues attached to the metal.

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III

Ingold has compiled a list of substituents in order of their relative ortho- and para-orienting influence in the electrophilic substitution reactions of substituted benzenes (1, 2, 3). The ordering of substituents in the compilation was arrived at on the basis of nitration studies on ortho-disubstituted benzenes. If the nitro group enters para chiefly to one substituent, this substituent is considered to be the more powerfully ortho-para orienting of the two substituents. Table I summarizes Ingold's data.

Table I

Competitive orientation by N, O, and F in the nitration^a of ortho-disubstituted benzenes.

<u>Substituents</u>	Nitration ortho and para	
	to:	
	<u>X(%)</u>	<u>Y(%)</u>
X = MeO- Y = CH ₃ CONH-	13	76
X = MeO- Y = CH ₃ CON(CH ₃)-	4	69
X = CH ₃ COO- Y = CH ₃ CONH-	0 ^b	71
X = MeO- Y = F-	97	3

-
- a. The nitrations were carried out using nitric acid in acetic anhydride.
- b. Fieser lists the acetoxy group as a more powerful electron donor than the methyl group (4). This is probably incorrect; see reference 5.

Chuchani has compiled a similar list based on the condensation of the triphenylmethylcarbonium ion with ortho disubstituted benzenes (6). He arrived at the following order of substituent effects, listed according to decreasing ortho-para activating power:

$\text{OH} \rightarrow \text{NH}_2 \rightarrow \text{CH}_3\text{CONH} \rightarrow \text{CH}_3\text{O} \rightarrow \text{CH}_3$ -. The triphenylmethylcarbonium ion was generated from trityl chloride and also from triphenylmethanol and acid.

In a subsequent paper Chuchani demonstrated by direct competition experiments that aniline was more reactive than phenol (7). He suggests that the anomalous results for the study on the ortho disubstituted benzene must be due to hydrogen bonding between the hydroxyl hydrogen and the amino nitrogen.

Examination of the lists compiled by Ingold and Chuchani reveals a striking anomaly. In both the nitration and tritylation reactions, the acetamido group controls orientation in competition with a methoxy group. Since ortho-para activation by substituents of this type involves electron release to the reaction site by a resonance interaction, it is difficult to account for the fact that the site para to the acetamido group is activated more strongly than the site para to the methoxy group. There is qualitative evidence, and some quantitative evidence, which indicates that the methoxy group is more potent as a donor of electrons by conjugative electron release than is the acetamido group.

For example, several workers report that more vigorous conditions are required to acetylate acetanilide than are required to acetylate benzene. Kunckell found with excess aluminum chloride and carbon disulfide solvent that the acyl halide should have a boiling point in excess of 90° or that it should be halogenated if the acylation were to succeed (8). Sacha and Patel established that para-acetylacetanilide is obtained in good yield when 1:1:3 parts by weight respectively of acetanilide, acetyl chloride and aluminum chloride are used (9). The reaction was carried out at 100° in the absence of solvent. The study of Sacha and Patel was repeated by Russian workers with the same result (10). Brown has acetylated benzene and alkyl benzenes under much less vigorous conditions than those reported above for the acetylation of acetanilide (11). The facile acetylation of anisole has been reported by Noller and Adams (12) and by Brown (13).

Unfortunately there is no direct comparison of the relative reactivities of anisole and acetanilide in the acetylation reaction, either from rate data or from competition experiments, published to date. There are also no studies reported in the literature which are concerned with a direct comparison of the reactivities of anisole and acetanilide in the nitration reaction. Ingold and Shaw reported that in a competition experiment between benzene and anisole only anisole was nitrated (14). In a similar experiment only benzene was nitrated in competition with acetanilide; however, the reaction media was more

acidic than in the experiment using anisole and benzene. On the basis of other experiments reported by Ingold and Shaw it is likely that the competition experiment between benzene and acetanilide is not valid because of protonation of the amide group.

The only really quantitative comparison of the reactivities of acetanilide and anisole has been provided recently by Brown (15) and Stock (16). Table II summarizes data for two reactions.

Table II

Relative reactivities of Anisole, acetanilide, toluene and benzene.

<u>substituent</u>	<u>relative rate</u>	<u>reaction</u>
methoxy	448.0	mercuration at 25° ^a
acetamido	46.1	
methyl	6.54	
hydrogen	1.00	
methoxy	1.8×10^9	bromination in acetic acid at 25° ^b
acetamido	2.1×10^8	
methyl	6.0×10^2	
hydrogen	1.00	

a. Reference 15.

b. Reference 16.

The data of Brown and Stock show that the acetamido group is strongly activating; however, it is still only about one tenth as potent as a methoxy group.

Clearly, the results of the nitration and tritylation of ortho-acetanilide, in which the acetamido group controls orientation, are incompatible with the available evidence concerning the relative reactivities of anisole and acetanilide. Also, the low reactivity of acetanilide in the acetylation and nitration reactions is anomalous in view of the work of Brown and Stock on mercuration and halogenation.

The low reactivity of acetanilide in the Friedel-Crafts acylation reaction may be due to complex formation between the catalyst and the amide group, or possibly to reversible acylation of the carbonyl oxygen.

Fuson, in his advanced organic textbook, states that "in anilides the nitrogen atom is practically neutral and has lost most of its power to coordinate with the catalyst" (17). A check on Fuson's literature references revealed that this statement was based solely on the report made by Kunckell in 1900 (8). As has been mentioned in more detail above, Kunckell found that very drastic conditions were required to acylate acetanilide. Apparently Fuson overlooked the conditions employed and based his judgment on the fact that the para-acylated isomer was the only product formed.

The lower reactivity of acetanilide in certain nitration reactions is probably due to salt formation in highly acidic media. Japanese workers have reported that ortho-nitroacetanilide is obtained in over

50% yield when acetanilide in acetic anhydride is warmed to 50° in the presence of copper nitrate for three hours (18). This reaction demonstrates the facile nitration of acetanilide in neutral media.

Summary

It has been pointed out in this proposition that the results of nitration and tritylation experiments on ortho-acetanilide, in which the acetamido group controls the orientation of the entering group, are incompatible with the results of several other experiments in which the higher reactivity of anisole as compared with acetanilide was demonstrated.

Proposed Research

It is proposed that the rate of protonolysis of phenyltrimethylsilane substituted in the para position with an acetamido group be determined. Eaborn has studied a number of such compounds, including the methoxy substituted compound (19). His data can be correlated using the electrophilic substitution constants, $\sigma +$ (20). This experiment will give a quantitative measurement of the capacity of the acetamido group to stabilize a positive charge on a benzene ring. This rate data will be free from the possible ambiguity caused by interaction of an electrophile or catalyst with the amide group. Although the mercuration and bromination studies show that the methoxy

group is about ten times more powerfully electron donating than the acetamido group, spectroscopic studies indicate that there is very little difference in the electron donating powers of the two groups (5). In one study, in which empirical spectroscopic substituent constants were determined by studying K band shifts in para substituted nitrobenzenes, the acetamido group proved to be measurably more electron donating than the methoxy group (21).

It would also be interesting to do a competitive tritylation study on acetanilide and anisole and see if the relative reactivities of the two compounds follow the order of the relative orienting powers of the methoxy and acetamido groups in ortho-acetanisidide.

Should the experiments proposed above demonstrate conclusively that the methoxy group is a more powerful electron donor than the acetamido group, then experiments should be performed to determine why the acetamido group controls orientation in the nitration and tritylation of ortho-acetanisidide. For example, one could study para-acetanisidide to evaluate the importance of steric interactions between the two groups in ortho-acetanisidide. Molecular models indicate that both the methoxy group and the acetamido group can be coplanar with the benzene ring at the same time. However, subtle solvation requirements of these groups in the transition state could complicate the situation. It might be profitable to determine the rates of several reactions on ortho-acetanisidide and compare these with

rate studies on para-acetanilide and also with the results that would be expected from additivity of substituent constants (22).

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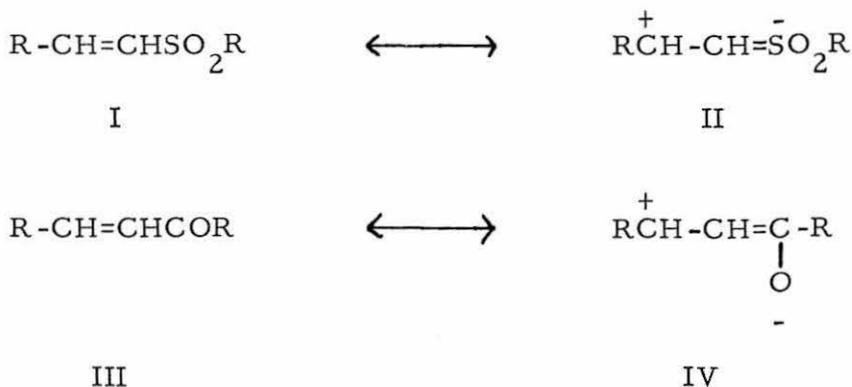
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IV

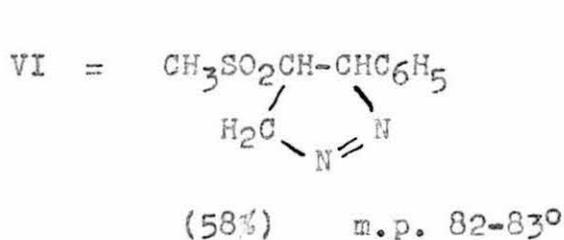
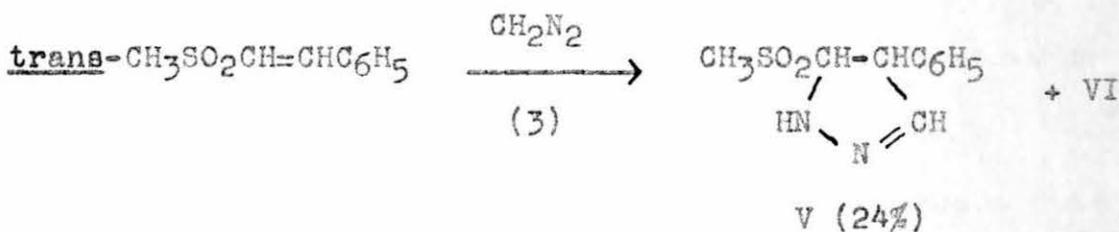
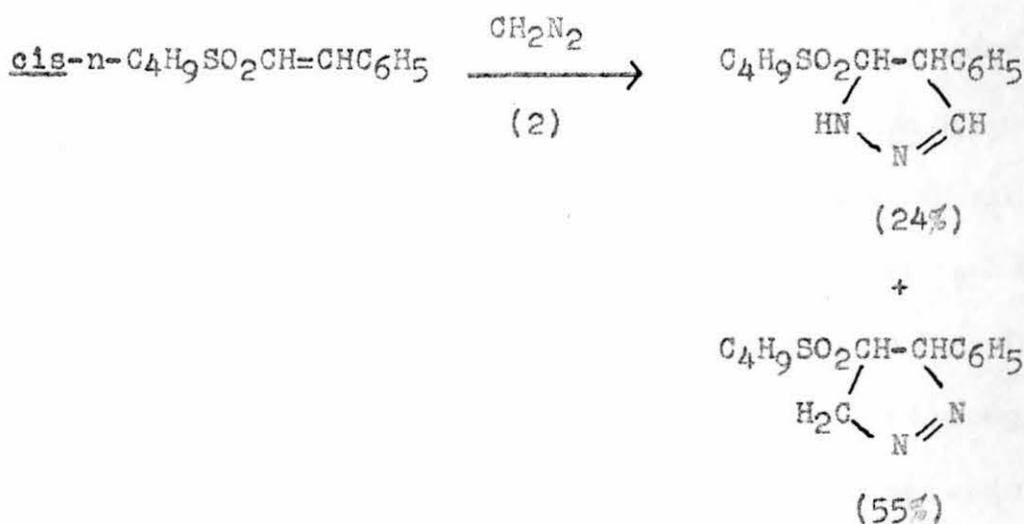
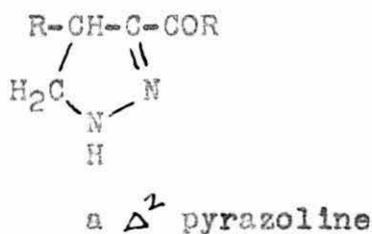
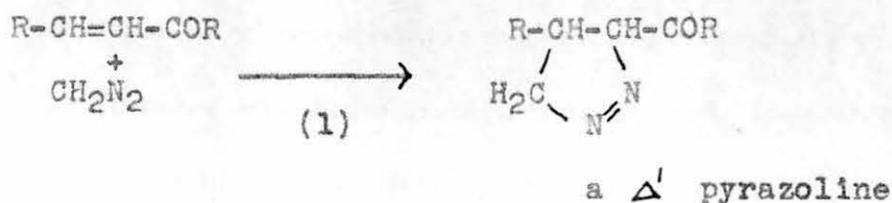
The reaction of diazomethane with conjugated olefins to give pyrazolines has been studied fairly extensively over the past 70 years (1). The reaction is generalized in equation 1. Equation 1 is not intended to be representative of a mechanism; it merely indicates the stereochemistry involved.

Parham has reported that the addition of diazomethane to α, β -unsaturated sulfones gives a mixture of pyrazolines resulting from both α and β addition (2). For example, cis-n-butyl β styryl sulfone gives, by "normal," or β addition, 4-phenyl-5-butylsulfonylpyrazoline in 24% yield and by "abnormal," or α addition, 3-phenyl-4-butylsulfonylpyrazoline in a yield of 55% (equation 2).

Parham states that α -addition occurs in the α, β -unsaturated sulfones because resonance form II is not as favorable as resonance form IV because of less favorable d-orbital interaction of sulfur (3).



Parham has assumed that the stereochemistry of the olefins was maintained during formation of the pyrazolines. However, he



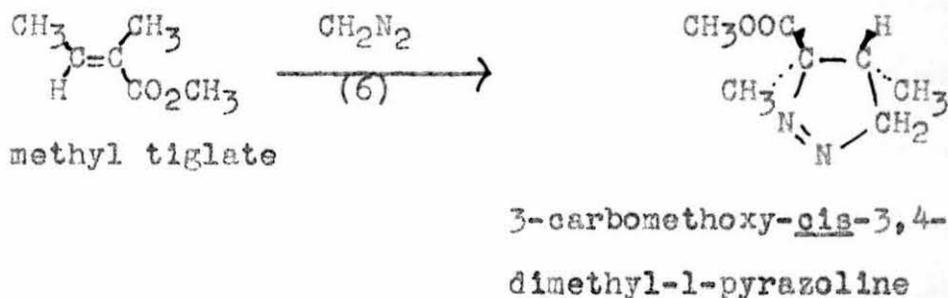
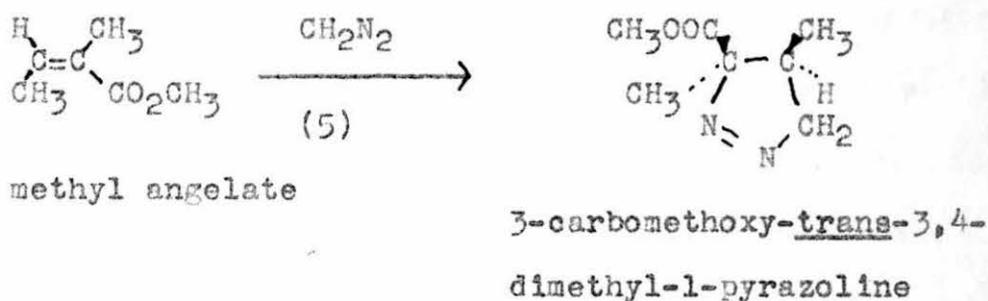
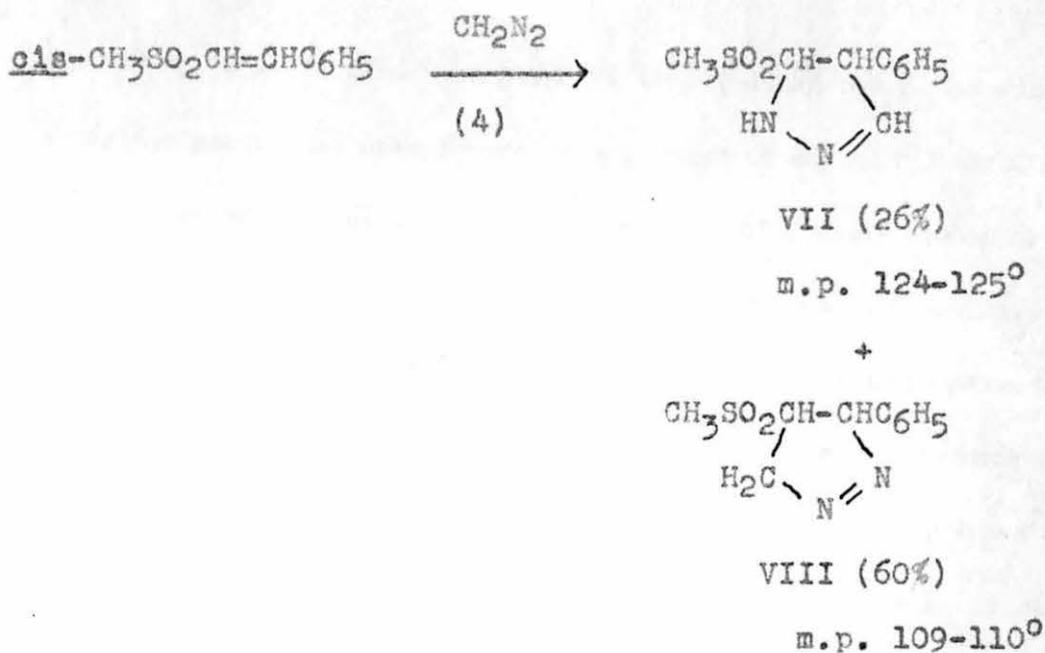
m.p. $72-73^\circ$;
 $124-125^\circ$

was unable to establish the exact stereochemistry of the pyrazolines since there was some ambiguity in the only experiment in which additions to olefins differing only in the geometry about the double bond were studied.

In this experiment, trans-methyl β styryl sulfone gave the products indicated in equation 3. cis-Methyl β styryl sulfone gave the products indicated in equation 4. However, the "normal" addition product, V, upon recrystallization from ethanol, gave a compound having a m. p. and mixed m. p. identical with that of compound VII. Parham states that cis-trans isomerization of the pyrazoline V is responsible for the change in m. p. noted after recrystallization.

Parham assigned Δ^1 or Δ^2 structures to the pyrazolines on the basis of the presence or absence of absorptions in the infrared spectra characteristic for the NH group or for the N=N group. He states that the "normal" pyrazolines are Δ^2 pyrazolines and that the "abnormal" pyrazolines are Δ^1 pyrazolines. Parham places the double bond in the Δ^2 pyrazolines in a position non-conjugated with the sulfone group; he gives no justification for this.

The structures of the pyrazolines were established by their conversion to pyrazoles. They were readily converted by treatment with potassium hydroxide in cold methanol. This procedure, of course, gives no information concerning the geometry of the original pyrazoline; it merely distinguishes between pyrazolines resulting from α addition and those resulting from β addition.



This method for the proof of structure of the pyrazolines does not permit an unequivocal assignment of structure for the pyrazoline which results from the addition of diazomethane to phenyl vinyl sulfone; the products from both α addition and β addition would give pyrazole upon treatment with alcoholic potassium hydroxide.

Rinehart (4) reported, subsequent to the appearance of Parham's paper and to the original formulation of this proposition, that the addition of diazomethane to methyl angelate and to methyl tiglate proceeds with a stereospecificity of at least 98% (equations 5 and 6). Rinehart's study constitutes the first really rigorous proof that the addition of diazomethane to double bonds activated by electron withdrawing groups proceeds by cis-addition. Rinehart assigned structures to the pyrazolines on the basis of infrared and n. m. r. spectra, and also by identification of the cyclopropanes resulting from the stereospecific photolysis of the Δ^1 pyrazolines (4).

A. It is proposed that both the starting α, β -unsaturated sulfones and the pyrazolines resulting from their reaction with diazomethane be subjected to n. m. r. analysis. The starting sulfones should also be subjected to gas chromatographic analysis to ensure that isomeric impurities are not present; Parham depended solely upon infrared analyses as a basis for presuming the absence of such impurities. These studies would fix with more certainty the geometry of the materials used. The technique of n. m. r. analysis reported by

Rinehart (4) can be applied directly to the pyrazolines presently under discussion. This would permit an unambiguous assignment of the stereochemistry of these pyrazolines. This analysis would be especially valuable in the case of the pyrazoline resulting from the addition of diazomethane to phenyl vinyl sulfone; the possibility of α -addition occurring in this instance could then be proved or disproved.

B. Parham's assignment of the position of the double bond in the Δ^2 pyrazolines he prepared is almost certainly incorrect. It is reasonably certain, at least in the case of the reaction of diazomethane with α, β -unsaturated esters which have an α -hydrogen atom, that initially Δ^1 pyrazolines are formed and that these spontaneously rearrange to the more stable Δ^2 form with the double bond conjugated with the ester group (5). The Δ^2 pyrazoline is formed spontaneously usually only if a conjugated system results; otherwise, Δ^1 -pyrazolines can be isolated and subsequently converted to Δ^2 -pyrazolines with acid (6). In a few instances, the Δ^1 -pyrazolines can be isolated even when the Δ^2 compounds contain conjugated systems; the rearrangement to the Δ^2 -isomer occurs on recrystallization or brief heating (7).

Parham isolated only Δ^2 -pyrazolines as the "normal" addition products; this certainly implies that the Δ^1 -pyrazolines, which were almost certainly formed initially, isomerized spontaneously to the Δ^2 -isomers with the double bond conjugated with the sulfone group. The proposed n. m. r. study would settle the question concerning the

position of this double bond; Parham probably should have been able to assign the position from his infrared data.

C. It is proposed that the reaction of diazomethane with cis- and trans-methyl β styryl sulfones be reinvestigated (equations 3 and 4) since this study is important in investigating the effect of the stereochemistry of the vinyl sulfone upon the orientation of addition. Parham has stated that the "normal" addition product, V, from trans-methyl β styryl sulfone undergoes cis-trans isomerization upon recrystallization from ethanol to give the same pyrazoline, VII, that results from the "normal" addition to cis-methyl β styryl sulfone. It seems very unlikely that this is the correct explanation. Rinehart has shown that the pyrazolines resulting from the reaction of diazomethane with methyl angelate and methyl tiglate do not isomerize even under conditions vigorous enough to promote pyrolysis (4).

It is likely that Parham has assigned the wrong structure to one of the compounds in this series and that the compound in question is merely undergoing an isomerization from a Δ^1 -pyrazoline to a Δ^2 -pyrazoline. The infrared and n. m. r. spectra of the lower melting form of compound V would clear up this point.

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PART I

Evidence has been presented that substituent effects in the chronopotentiometric oxidation of substituted ferrocenes and in the solvolyses of methyl-(1'-substituted-ferrocenyl)carbonyl acetates can be correlated with Hammett's σ_m (1). It was observed, however, that compounds substituted directly on the ring with atoms possessing unshared pairs of electrons deviated from the σ_m correlation. These discrepancies have been attributed to an interaction by such substituents with the positive iron atom. In the case of the solvolysis reaction, it is known that the iron atom stabilizes a carbonium ion adjacent to the ring by nucleophilic participation (2); in this instance, therefore, the iron atom is postulated to be interacting with an electron rich substituent on one ring and an electron deficient center on the other ring.

Calculations made on the basis of the assumption that no distortion takes place on forming the positive ion from the neutral molecule in the case of the oxidation reaction show that the distance from the donor atom to the iron atom is probably too great for a significant interaction to occur (1). If the postulated interaction is occurring, then the ring bearing the substituent must be displaced

from the central axis of the molecule to some extent so that the donor atom may be sufficiently close to the iron atom.

It is proposed that direct evidence can be obtained to support the hypothesis that a direct interaction occurs by determining the bromine-iron distance in the bromoferricinium ion by an X-ray diffraction study. The study will also show the positions of the rings relative to one another and to the iron atom. Thus, the relative amounts of shifting of the rings to tilting of the rings can also be found.

PART II

Evidence has been put forth by Hill and Richards (2) to demonstrate that the iron atom interacts with an α -carbonium ion and thereby greatly stabilizes the positively charged species. Such an interaction very likely requires that the ring bearing the reaction center be displaced to some extent so that close approach by the iron atom is permitted. In the case of the solvolyses of methyl-(1'-substituted-ferrocenyl)carbinyl acetates, both rings would have to be displaced from the central axis of the molecule for the interactions discussed here to occur.

It is proposed that a study be made of the solvolyses of methyl-(3-substituted-ferrocenyl)carbinyl acetates. In this series, an atom with an unshared pair of electrons would not be able to

interact with the iron atom at the same time the iron atom is interacting with the α -carbonium ion.

In addition to providing a further test of the hypothesis that a donor atom may stabilize an incipient positive charge on the iron atom by a direct interaction, this study will also provide information about the transmission of homoannular substituent effects. It would be useful to compare such effects with those already found in the solvolyses of the heteroannularly substituted compounds.

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