[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF PURDUE UNIVERSITY, WEST LAFAYETTE, IND.]

Electronic and Steric Effects in Monosubstituted Ferrocenes as Determined by Relative Site Reactivities and Desilylation[1]

BY ROBERT A. BENKESER, YOICHIRO NAGAI, AND JOHN HOOZ

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Site reactivities relative to both the 1'-position and to a position in ferrocene itself were determined for the monoacylation of methyl-, ethyl-, isopropyl-, and *t*-butylferrocene. The detriethylsilylation rates for 1'-methyl-, 1'-isopropyl-, and 1'-*t*-butyltriethylsilylferrocenes were also measured. An unusual steric effect was detected in the detriethylsilylation of 1'-*t*-butyltriethylsilylferrocene. The results indicate that the 3-position in an alkylferrocene is activated with respect both to the 1'-position as well as to a position in unsubstituted ferrocene. This activation is in the inductive order, *t*-Bu > *i*-Pr > Et > Me. One can also conclude with assurance that the presence of an alkyl group does activate a 1'-position relative to a position in unsubstituted ferrocene. While these "interannular" effects are in the order indicative of resonance interactions (Me > Et > *i*-Pr > *t*-Bu) one is not justified in drawing this conclusion from the data since the desilylation results indicate that there could exist hitherto unrecognized steric factors operating between the ferrocene rings during electrophilic substitution.

Considerable effort[2] has been expended in the past few years to elucidate the type of electronic transmission which occurs both within and across the rings of ferrocene. The mode of attack on this problem has involved a variety of approaches. Thus Hoh[3] and coworkers studied substituent effects in chronopotentiometric oxidation of a wide variety of mono- and disubstituted ferrocenes. They obtained a satisfactory correlation between the quarter-wave potentials and σ_p. Nesmeyanov and Reutov[4] studied the effect of structure on the ionization constants of various heteroannularly substituted ferrocenecarboxylic acids. Little and Eisenthal,[5] in a similar type study, found a linear relationship between pK_a values of five substituted ferrocenecarboxylic acids with the Hammett *para*-σ-constants. A similar linear relationship[6] was found to exist for the rates of esterification of heteroannularly substituted ferrocenecarboxylic acids with diphenyldiazomethane. These results were interpreted in terms of a resonance contribution of the substituents across the ferrocene ring systems. Some semiquantitative data involving the relative rates of acetylation[7] of ferrocene and acetylferrocene seemingly support this same conclusion. Each position in ferrocene is almost four orders of magnitude more reactive than comparable sites in acetylferrocene. Mildly disturbing are the results of absorption spectra studies[7,8] indicating that aryl substituents in 1,1'-disubstituted ferrocenes show an absence of conjugation. This apparent discrepancy was explained recently[7] by the postulation of a three-step mechanism for electrophilic substitution into the ferrocene nucleus. The first step is envisioned as the formation of a d-orbital complex between the electrophile and the metal atom; the second step (rate determining) involves endocyclic σ-complex formation; and step three, proton loss.

Much of the earlier work in ferrocene chemistry was hampered by the lack of convenient analytical methods for product separation and identification. Heavy reliance was necessarily placed on column chromatography for purifications, which, while satisfactory in some cases, often proved laborious.[9] Likewise, infrared and ultraviolet spectra were the principal means of identifying position isomers. Often the spectral differences between closely related structures were uncomfortably small.

The demonstration that vapor phase chromatography[10,11] and n.m.r. spectroscopy[10-12] constitute useful tools in ferrocene chemistry should simplify considerably some of the structural problems inherent in this class of compounds. Our successful applications[10,11] of n.m.r. to substituted ferrocenes have thus far been contingent on the presence of an alkyl group and a substituent which greatly deshields adjacent protons, such as acetyl or carbomethoxy.

For example, previous site reactivity studies on the acetylation of alkyl- or aryl-substituted ferrocenes have been restricted almost exclusively to the simpler cases involving symmetrical 1,1'-dialkyl[13] and diaryl types.[14,15] In this way, the mixtures[16] resulting from monosubstitution are more amenable to column chromatographic separation. The site reactivities of only three monosubstituted ferrocenes[15] have been studied, only one of which involved a monoalkyl substituent (ethyl).[17]

By means of gas chromatographic separations, we

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(2) See M. Rosenblum, J. O. Santer, and W. G. Howells, *J. Am. Chem. Soc.*, **85**, 1450 (1963), for a comprehensive bibliography which covers much of this earlier work.

(3) G. L. K. Hoh, W. E. McEwen, and J. Kleinberg, *ibid.*, **83**, 3949 (1961).

(4) A. N. Nesmeyanov and O. A. Reutov, *Proc. Acad. Sci. U.S.S.R., Chem. Sect., English Trans.*, **115**, 763 (1957).

(5) W. F. Little and R. Eisenthal, *J. Org. Chem.*, **26**, 3609 (1961).

(6) W. F. Little and R. Eisenthal, *J. Am. Chem. Soc.*, **83**, 4936 (1961).

(7) M. Rosenblum, J. O. Santer, and W. G. Howells, *ibid.*, **85**, 1450 (1963).

(8) R. T. Lundquist and M. Cais, *J. Org. Chem.*, **27**, 1167 (1962).

(9) An extreme example, perhaps, is the separation of 3- and 1'-phenylacetylferrocene on alumina which required continuous elution for approximately 4 months to achieve partial resolution; see M. Rosenblum, *J. Am. Chem. Soc.*, **81**, 4530 (1959).

(10) (a) R. A. Benkeser, Y. Nagai, and J. Hooz, *Bull. Chem. Soc. Japan*, **36**, 482 (1963); (b) Y. Nagai, J. Hooz, and R. A. Benkeser, *ibid.*, **37**, 53 (1964).

(11) R. A. Benkeser and J. L. Bach, *J. Am. Chem. Soc.*, **86**, 890 (1964).

(12) This technique has been used only in isolated instances to distinguish between homoannularly substituted isomers. G. R. Knox, P. L. Pauson, and G. V. D. Tiers, *Chem. Ind.* (London), 1046 (1959), employed n.m.r. to distinguish between 1,1'-di(methylthio)-3- and 1,1'-di(methylthio)-2-dimethylaminomethylferrocene on the basis of the nonequivalence of the methylene protons in the latter due to hindered rotation. Likewise, K. L. Rinehart, D. E. Bublitz, and J. H. Gustafson, *J. Am. Chem. Soc.*, **85**, 970 (1963), effectively employed n.m.r. in a study of the acetylation of a variety of alkyl-bridged ferrocenes.

(13) K. L. Rinehart, Jr., K. L. Motz, and S. Moon, *ibid.*, **79**, 2749 (1957).

(14) M. Rosenblum, *ibid.*, **81**, 4530 (1959).

(15) M. Rosenblum and W. G. Howells, *ibid.*, **84**, 1167 (1962).

(16) Friedel–Crafts acylations have been most commonly studied thus far.

(17) M. Rosenblum and R. B. Woodward, *J. Am. Chem. Soc.*, **80**, 5443 (1958).

have been able to study quite conveniently relative site reactivities for acetylation in methyl-, ethyl-, isopropyl-, and *t*-butylferrocene. These values were obtained both in noncompetitive reactions (using the 1′-position as the standard with an assigned rate of unity) and in competitive reactions with ferrocene itself (where each position of ferrocene was assigned a rate of unity). Acetic anhydride and boron trifluoride etherate were employed as the acylating combination. Likewise, we have studied the rates of acid-catalyzed cleavage of the triethylsilyl group from various 1′-alkyltriethylsilylferrocenes. In previous work[18] we have demonstrated the utility of such desilylations in elucidating electronic and steric influences of substituent groups in substituted benzenes.

Viewed as a composite, our results tend to define rather precisely the electronic and steric factors operative both within one ring and across the ring system of substituted ferrocenes.

Results

The noncompetitive site reactivities (Table I) were obtained by v.p.c. analysis of the mixture resulting from the acetylation of the respective alkylferrocene. The site reactivities for the acetylation of methyl-, ethyl-, and isopropylferrocene could be calculated directly from the observed peak area (determined by a planimeter) for the respective isomers. The areas so obtained were then corrected for the statistical effect of five 1′-, two 2-, and two 3-positions. Thus, the observed peak area for the 1′-position was divided by "5," and for the 2- and 3-sites, the respective areas were divided by "2." The resulting numbers are listed in the column titled "corrected area" in the sample calculation shown for methylferrocene in the Experimental. Site reactivities were then calculated by normalizing the "corrected area" values. Unit reactivity was assigned to the 1′-position (see methylferrocene example in Experimental).

TABLE I

RELATIVE SITE REACTIVITIES[a] FOR THE ACETYLATION OF ALKYLFERROCENES (NONCOMPETITIVE)

Substituent	2-Position	3-Position
Me	1.2	1.6
Et	0.85	1 9
i-Pr	.58	2.4
t-Bu	.26	3.3

[a] The values listed are relative to the 1′-position which has been assigned a rate of 1.00.

Poor v.p.c. resolution of the *t*-butylacetylferrocene isomers prevented a direct calculation of site reactivities as described above. Instead, these values were obtained by making use of the data from the competitive acetylation experiments.

In Table II are listed the relative site reactivities for the competitive acetylation of methyl-, ethyl-, isopropyl-, and *t*-butylferrocene in the presence of ferrocene itself. In these cases, one of the ten available positions of unsubstituted ferrocene has been assigned a rate of unity. In these experiments, the vapor phase chromatograms indicated only poor resolution between acetylferrocene and the isomeric acetylalkylferrocenes. Consequently, each competitive run was first reduced with lithium aluminum hydride–aluminum chloride to give a mixture of ethylferrocene and the isomeric ethylalkylferrocenes.[19] The latter mixtures were amenable to v.p.c. separation.

(18) (a) R. A. Benkeser and H. Krysiak, *J. Am. Chem. Soc.*, **76**, 6353 (1954); (b) R. A. Benkeser, W. Schroeder, and O. H. Thomas, *ibid.*, **80**, 2283 (1958); (c) R. A. Benkeser, R. A. Hickner, D. I. Hoke, and O. H. Thomas, *ibid.*, **80**, 5289 (1958); (d) R. A. Benkeser and F. S. Clark, *ibid.*, **82**, 4881 (1960).

TABLE II

RELATIVE SITE REACTIVITIES[a] FOR THE ACETYLATION OF ALKYLFERROCENES (COMPETITIVE)

Substituent	1′-Position	2-Position	3-Position
Me	2.2	2.5	3.4
Et	2.0	1.7	3.8
i-Pr	1.9	1.1	4.7
t-Bu	1.7	0.44	5.5

[a] The values listed are relative to *one* of the ten available positions of ferrocene; the latter has been assigned a rate of 1.00.

A test of the relative thermal conductivities of ethylferrocene compared with various ethylalkylferrocenes indicated that no appreciable correction factor needed to be applied.

The data listed in Table II were calculated as follows. In the competitive acetylation of methylferrocene in the presence of ferrocene, v.p.c. analysis of the product (after reduction with lithium aluminum hydride–aluminum chloride) gave peak areas of 722 for the total ethylmethylferrocenes formed and 315 for the ethylferrocene. Hence, the rate of acylation of methylferrocene compared to ferrocene is 722/315. Relative to only one of the ten available positions of ferrocene, this becomes 722/315 × 10 or 22.9. The acylation product from methylferrocene consists of 47.7% 1′-isomer and there are five available positions which can lead to this isomer. Hence, the relative rate of acylation of *one* of the 1′-positions of methylferrocene compared to *one* position of unsubstituted ferrocene becomes 22.9 × (0.477/5) = 2.2.

Conclusions.—The data in Tables I and II clearly permit the conclusion that the 3-position in an alkylferrocene is activated both with respect to a 1′-position and to a position in unsubstituted ferrocene. This activation is in an inductive order (*t*-Bu > *i*-Pr > Et > Me).[20] One is tempted from the data of Table II to conclude that alkyl groups in the 3-position exert a greater activating effect than those in the 2-position. However, it is clear from the data in both tables that a steric effect is operative in the 2-position which makes this conclusion hazardous. This steric effect would obviously be at a minimum in the case of methylferrocene and the data for this compound in both tables would indicate position 3 to be slightly more activated than position 2. However, the rate differences are very small, and, even in this case, one cannot be sure that the value for the 2-position does not reflect some steric interference.

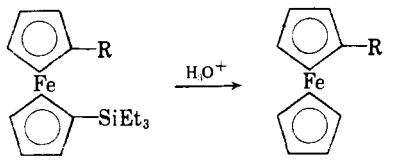
A rigorous comparison of our results with those of previous investigators is precluded in view of the differences in the acetylation media employed. Previously, ethylferrocene[17] was treated with acetyl chloride and aluminum chloride and the monoacetyl isomers were isolated quantitatively by column chromatog-

(19) We demonstrated in a previous publication (ref. 12) that such reductions are virtually quantitative.

(20) There seems to be little gain in comparing our results with alkylferrocenes to the corresponding results obtained with alkylbenzenes [see H. C. Brown and G. Marino, *J. Am. Chem. Soc.*, **81**, 5611 (1959)]. It becomes apparent immediately that the two systems are quite different. About the only similarity is that the *meta* positions of alkylbenzenes are activated in an inductive order toward acylation as are the 3-positions of alkylferrocenes. The *ortho* positions of alkylbenzenes seem to be affected much more by steric factors than are the 2-positions of alkylferrocenes.

raphy. From the isomer distribution thus obtained the partial rate factors for acylation at positions 2 and 3 of the alkylated ring were calculated as 1.4 and 4.2, respectively (the unsubstituted ring positions were assigned a value of 1). In a similar study,[13] 1,1′-dimethyl- and 1,1′-diisopropylferrocene were acylated with acetic anhydride and aluminum chloride. The isomer ratio (obtained by a combination of product isolation by column chromatography and by quantitative ultraviolet analysis) of 2:3 acetylalkyl product was 1:2.3 for 1,1′-dimethylferrocene and 1:4.3 for 1,1′-diisopropylferrocene. Thus, in both of these earlier studies, there was a preference for substitution at the 3- rather than 2-position. This finding is in complete accord with the present results (*cf.* Tables I and II).

It can be concluded with assurance from the present data that the presence of an alkyl group does activate a 1′-position relative to a position in unsubstituted ferrocene (Table II). One might again be tempted from the data in Table II to suggest that this "interannular" effect is dictated by resonance interactions (Me > Et > *i*-Pr > *t*-Bu). It was in an attempt to check this conclusion that we turned our attention to the rates of desilylation of certain alkyltriethylsilylferrocenes. There is ample evidence[21] to show that desilylation in the benzene series follow well-



charted paths typical of electrophilic substitution reactions. In fact, excellent correlations have been found between desilylations and σ^+-values.[22] One would predict, therefore, that, if the same "interannular" electronic effects are operative as depicted possibly in Table II, a "resonance order" for the alkyl groups should be observed (Me > Et > *i*-Pr > *t*-Bu.)

Table IV lists the desilylation rate data obtained for 1′-methyl-, 1′-isopropyl-, and 1′-*t*-butyltriethylsilylferrocene. The rate for the cleavage of triethylsilylferrocene is taken as unity. The most startling thing about these data is the obvious steric effect that is noted in the cleavage of 1′-*t*-butyltriethylsilylferrocene. To our knowledge this is the first fully substantiated case of a steric effect resulting from the presence of a bulky group in one ring of ferrocene affecting the rate of a reaction in the other ring.

TABLE III

RATE DATA FOR THE CLEAVAGE OF 1′-METHYLTRIETHYSILYLFERROCENE[a]

Time, min.	A_2/A_1[b,c]	Cor. areas[d]	$(a-x)$,[e] mole/l.	$\frac{a}{a-x}$	$2.303 \log \frac{a}{a-x}$
20	0.7901	1.0002	0.002270	1 160	0.1483
40	.6773	0.8574	.001946	1.353	.3023
60	.5629	.7126	.001617	1.628	.4875
90	.4491	.5685	.001290	2.042	.7141
120	.3666	.4641	.001053	2.501	.9168

$k_1 = 7.77 \times 10^{-3}$ min.$^{-1}$

[a] The initial concentration (a) of the 1′-methyltriethylsilylferrocene was 0.002634 mole/l. [b] A_1 refers to the v.p.c. peak area for the internal standard, octadecane. The initial concentration of this standard was 0.002270 mole/l. [c] A_2 refers to the v.p.c. peak area of unreacted 1′-methyltriethylsilylferrocene. [d] The values in this column were determined by multiplying the A_2/A_1 values by the area factor of 1.267. The latter number was obtained by v.p.c. analysis of a synthetic mixture of octadecane and 1′-methyltriethylsilylferrocene in a 1:0.7574 molar ratio, respectively. Four separate injections were made of this mixture and the average peak area ratio obtained was 1:0.5977. Hence, the area factor becomes 1.267. [e] This column represents the concentration of unreacted 1′-methyltriethylsilylferrocene at time "*t*." These values were obtained by multiplying the concentration of the internal standard (0.002270 mole/l.) by the corrected area value in the preceding column.

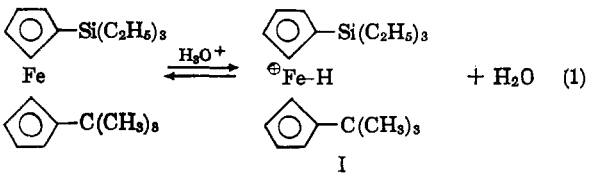
TABLE IV

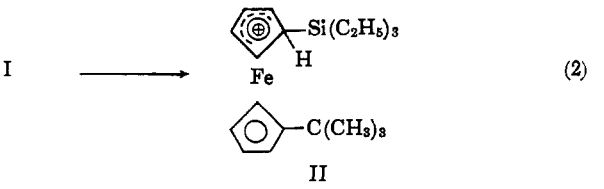
FIRST-ORDER RATE CONSTANT FOR THE ACID-CATALYZED CLEAVAGE OF ALKYL-1-TRIETHYLSILYLFERROCENES IN GLACIAL ACETIC ACID SOLUTION[a] AT 25°

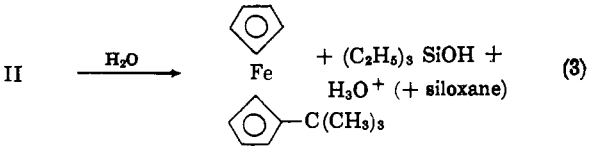
1-Triethylsilylferrocenes (substituent)	$k_1 \times 10^3$, min.	Average	Rel. rate
1′-Me	7.40, 7.77, 7.16	7.44	2.65
1′-*i*-Pr	4.64, 4.39	4.51	1.60
H	2.64, 2.82, 2.96	2.81	1.00
1′-*t*-Bu	1.99, 2.13	2.06	0.73

[a] This solution was 0.00256 *M* in hydrogen chloride and 0.323 *M* in water.

It is interesting to speculate on the origin of the steric effect exhibited in the desilylation of 1′-*t*-butyltriethylsilylferrocene. If one accepts the attractive three-step mechanism that has been suggested[7] for electrophilic substitution reactions of ferrocene, the only logical explanation would lie in the equilibrium depicted in step 1 which results in d-metal complex formation.







The formation of the endocyclic complex II should occur with steric acceleration[23] if any steric factors were manifest at all. Certainly the bulky triethylsilyl group would prefer being "pushed away" from the *t*-butyl group. Furthermore it is difficult to see how attack of the water molecule on the silicon atom in step 3 would be sterically influenced by an alkyl group in the opposite ring. It does seem reasonable, however, that attack of hydronium ions on the iron atom (step 1)

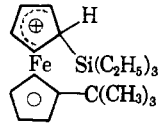
(21) See R. Baker, C. Eaborn, and J. A. Sperry, *J. Chem. Soc.*, 2382 (1962), and previous papers in this series.

(22) F. B. Deans and C. Eaborn, *ibid.*, 2299 (1959).

(23) For example, the highly hindered 2-trimethylsilyl-*m*-xylene undergoes rapid detrimethylsilylation in acid because cleavage results in a relief of steric strain; see ref. 18a.

would be influenced by the presence of two such bulky groups like the *t*-butyl and triethylsilyl. Hence, the over-all rate might well be slower as the alkyl group is increased in size from methyl to isopropyl to *t*-butyl.

It should be noted that the steric effect is equally well explained by a simple two-step mechanism involving the formation of an exocyclic σ-complex (III) in step 1.



III

The bulky triethylsilyl group would resist being pushed in the direction of the *t*-butyl group and hence the cleavage rate would be diminished.

The observation of this unexpected steric effect indicates the extreme caution which must be employed in the interpretation of only limited rate data. It would be tempting to explain the fall-off of desilylation rates (Table IV) in the case of the 1′-methyl-, 1′-isopropyl-, and triethylsilylferrocene in terms of an "interannular" resonance effect. However, the *t*-butyl rate falling below that of triethylsilylferrocene indicates a steric effect in operation *in at least this case*. Hence, it is possible that the general fall-off of rates observed in Table IV is simply a reflection of an increasing steric factor as the alkyl group is increased in size.

Experimental

Alkylferrocenes.—Methyl-, isopropyl-, and *t*-butylferrocene were prepared as described in a previous paper.[12]

Triethylcholorosilane[24] was prepared by treating 1 equivalent of ethylmagnesium bromide with 1 equivalent of diethyldichlorosilane. A 51% yield of triethylchlorosilane was obtained boiling at 137–148°. Redistillation through a Widmer column gave a product boiling at 143.5–146.5°, n^{20}D 1.4312 (lit.[25] b.p. 145°, n^{20}D 1.4311).

Metalation of Ferrocene and Treatment with Triethylchlorosilane.—To an *n*-amylsodium suspension prepared from 14 g. (0.61 g.-atom) of sodium in 80 ml. of decane and 29.8 g. (0.28 mole) of *n*-amyl chloride was added 42.8 g. (0.23 mole) of ferrocene at −10°. Stirring was continued for 24 hr. at room temperature, whereupon addition of 31.8 g. (0.21 mole) of triethylchlorosilane was made dropwise at −10°. After stirring for 48 hr. at room temperature, the mixture was decomposed with 15 ml. of ethanol followed by 100 ml. of water. The products were chromatographed on Merck alumina. There was obtained 28.3 g. (66%) of recovered ferrocene, 5.7 g. (8%) of triethylsilylferrocene, 11.4 g. (12%) bistriethylsilylferrocene, and 2.4 g. (2%) of tristriethylsilylferrocene.

The triethylsilylferrocene was distilled at 155° (0.9 mm) as an amber liquid, n^{20}D 1.5695. This material showed one peak on a 4-ft. silicone rubber column (v.p.c.) at 230°.

Anal. Calcd. for $C_{16}H_{24}FeSi$: C, 63.99; H, 8.06; Fe, 18.59. Found: C, 64.20; H, 8.22; Fe, 18.40.

Analysis of the bistriethylsilylferrocene obtained as described above by v.p.c. disclosed that it was slightly contaminated with other structural isomers. The latter were recovered by repeating the column chromatography process with Merck alumina. The purified product (single peak on a 4-ft. silicone rubber column at 230°, retention time 12 min.) was an amber liquid, b.p. 208° (1 mm.), n^{20}D 1.5477.

Anal. Calcd. for $C_{22}H_{38}FeSi_2$: C, 63.74; H, 9.24; Fe, 13.47. Found: C, 64.03; H, 9.36; Fe, 13.78.

The tristriethylsilylferrocene described above gave a single peak on a 4-ft. silicone rubber column at 230° (retention time, 40 min.). It was an amber liquid with a boiling point of 215° at 0.8 mm., n^{20}D 1.5380.

Anal. Calcd. for $C_{28}H_{52}FeSi_3$: C, 63.59; H, 9.91; Fe, 10.56. Found: C, 63.78; H, 9.72; Fe, 10.31.

Preparation of Methyl-, Isopropyl-, and *t*-Butyltriethylsilylferrocene.—The method of preparing and purifying these three alkyl-substituted triethylsilylferrocenes was similar in all cases. Each compound was prepared by metalating the alkylferrocene with *n*-amylsodium followed by treatment with triethylchlorosilane. The crude product was then either chromatographed on Merck alumina or fractionated to remove starting material and polytriethylsilylated alkylferrocenes. The isomeric mixture of triethylsilylalkylferrocenes thus obtained was purified by v.p.c. The preparation of 1-triethylsilyl-1′-isopropylferrocene is given below in detail as typical of the method.

An *n*-amylsodium suspension was made under nitrogen from 14 g. (0.61 g. atom) of sodium and 37 g. (0.35 mole) of *n*-amyl chloride in 100 ml. of octane. To this suspension was added 40 g. (0.156 mole) of isopropylferrocene at −10°. The mixture was stirred for 27 hr. at room temperature, whereupon 26.4 g. (0.175 mole) of triethylchlorosilane was added at −10°. After the mixture had stirred for 43 hr. at r.t., it was decomposed with water and then extracted with petroleum ether (35–37°). This was chromatographed on Merck alumina to give 20 g. (50% of recovered isopropylferrocene), 8 g. (16%) of crude triethylsilylisopropylferrocene, and a mixture of polytriethylsilylated isopropylferrocenes.

The crude triethylsilylisopropylferrocene was purified by v.p.c. (Apiezon L, 16 ft. × 0.25 in. column, 280°, flow rate He 60 ml./min.). One gram of an amber liquid (b.p. 140° (0.8 mm.)) was collected, n^{20}D 1.5535. The absence of a 9- and 10-μ band in the infrared spectrum of this compound, together with its elemental analysis, identified it as 1-triethylsilyl-1′-isopropylferrocene.

Anal. Calcd. for $C_{19}H_{30}FeSi$: C, 66.65; H, 8.83; Fe, 16.31. Found: C, 67.06; H, 8.88; Fe, 16.17.

In a similar fashion, 1-methyl-1′-triethylsilylferrocene was obtained (Apiezon L column, 16 ft. × 0.25 in., 290°).

Anal. Calcd. for $C_{17}H_{26}FeSi$: C, 64.96; H, 8.34; Fe, 17.77. Found: C, 65.18; H, 8.18; Fe, 17.57.

Likewise, 1′-*t*-butyl-1-triethylsilylferrocene was obtained with b.p. 145° (0.3 mm.), n^{20}D 1.5506 (Apiezon L column, 16 ft. × 0.25 in., 290°).

Anal. Calcd. for $C_{20}H_{32}FeSi$: C, 67.40; H, 9.05; Fe, 15.67. Found: C, 67.68; H, 9.31; Fe, 15.91.

Acetyl-1′-methyl-, -ethyl-, -isopropyl-, and -*t*-butylferrocenes.—The preparation, purification, and characterization of these four acetylalkylferrocenes has been described in detail in a previous paper.[11]

A detailed description of the preparation of methyl-, ethyl-, isopropyl-, and *t*-butylferrocene has also been given before.[12]

Noncompetitive Acetylation of Alkylferrocenes.—A charge of 1.000 g. (5.00 mmoles) of methylferrocene was weighed directly into a 25-ml. volumetric flask. Acetic anhydride (0.81 g., 8.0 mmoles) and approximately 20 ml. of methylene chloride were added, and the flask was immersed in an ice bath. Freshly distilled boron trifluoride etherate (12 mmoles) was added and the volume was quickly brought up to 25 ml. with methylene chloride. The reaction was continued for 30 min. with occasional shaking at 0°, then placed in a constant temperature bath for an additional 30 min. at 25°. The purple reaction mixture was quenched in ice–water, and the organic layer separated. The aqueous layer was extracted exhaustively with methylene chloride and the combined organic extracts were washed several times with water. The organic layer was dried, concentrated, and subjected to v.p.c. analysis directly (DEGS, 15-ft. column, 215°).

The results listed in Table V which were obtained for the acetylation of methylferrocene are typical of all the data collected.

TABLE V

Isomer	Peak areas—Obsd.	Peak areas—Cor.	Isomer distribution, %	Site reactivity
1′	421	84.2	47.7	1.00
2	192	96.5	21.9	1.15
3	269	135	30.4	1.59

In a very similar fashion, the relative site reactivities were obtained for the acetylation of ethyl- and isopropylferrocene.

Unfortunately only poor resolution (by v.p.c.) was realized in the case of the acetyl-*t*-butylferrocenes, in that the 1′- and 3-isomers were difficult to separate. Accordingly, the 1′- and 3-values which were obtained in the case of the competitive acetyla-

(24) J. W. Jenkins and H. W. Post, *J. Org. Chem.*, **15**, 556 (1950).

(25) L. H. Sommer, E. W. Pietrusza, and F. C. Whitmore, *J. Am. Chem. Soc.*, **68**, 2282 (1946).

tions of *t*-butylferrocene and ferrocene (see below) were used in the calculations for the noncompetitive case. Obviously this approach assumes that the proportions of 1′- and 3-acetyl-*t*-butylferrocenes formed in the competition experiment were identical with isomer distributions in the noncompetitive runs.

The results for the site reactivities obtained in all of the noncompetitive runs are listed in Table I.

Competitive Acetylations of Alkylferrocenes.—A mixture of 5.00 mmoles of the alkylferrocene and 5.00 mmoles of ferrocene was acetylated competitively. The general procedure was identical with that described for the noncompetitive experiments.

Analysis of the products by v.p.c. revealed the presence of unreacted ferrocene and alkylferrocene in every instance. There were no products indicative of diacylation. However, the v.p.c. chromatograms indicated only poor resolution between acetylferrocene and the isomeric acetylalkylferrocenes. Hence, each competitive run was reduced quantitatively with a lithium aluminum hydride–aluminum chloride combination. This resulted in a mixture of ethylferrocene and the isomeric ethylalkylferrocenes which could be resolved by v.p.c. (Apiezon L, 16-ft. column, 230°).

In the case of the competitive experiment between methylferrocene and ferrocene, for example, the peak area of ethylferrocene was measured as 315, while the total ethylmethylferrocene peak area was 722. Table II lists the relative site reactivities obtained in these competitive experiments.

Thermal Conductivity Correction Factors.—The thermal conductivities of ethylferrocene *vs.* 1′-methylethylferrocene, 1,2-diethylferrocene, 1′-isopropylethylferrocene, and 1-*t*-butyl-3-ethylferrocene were checked. In every case, the peak areas per mole of sample injected were so close that no correction factor for differences in thermal conductivity was deemed necessary.

Kinetic Experiments.—The glacial acetic acid used was Baker and Adamson reagent grade. This was distilled and a fraction boiling at 117–118° was collected. This cut was further purified by refluxing it with 7.8 ml. of acetic anhydride per 100 ml. of acid. A middle cut of this material was collected by distillation through a 2-ft. column packed with glass helices (b.p. 117–118°). This was stored under dry nitrogen.

The hydrochloric acid (Baker and Adamson, C.P. product) was used without further purification. The concentration of hydrogen chloride was determined with a potentiometric titrimeter.

General Kinetic Procedure.—The cleaving media were prepared at desired concentrations by mixing appropriate amounts of glacial acetic acid, hydrochloric acid, and, if necessary, deionized water. Carefully weighed samples of the silane (about 100 mg.) and an internal standard (about 80 mg. of octadecane, Matheson Coleman and Bell, reagent grade, m.p. 27–28.5°) were placed in a 50-ml. volumetric flask containing about 20 ml. of glacial acetic acid and immersed in a constant-temperature both held at 25 ± 0.02°. At zero time, the cleaving medium was added to the volumetric flask, which was then shaken vigorously, and the liquid volume brought quickly to 50 ml. with additional acetic acid. Aliquots were withdrawn periodically and poured into a sodium hydroxide solution to quench the reaction. The products were extracted twice with petroleum ether (b.p. 35–37°) and the solvent was then removed by evaporation. The residual liquid was analyzed by v.p.c.

Table III lists the data collected for the cleavage of 1′-methyltriethylsilylferrocene and is indicative of the calculations made. Since the reactions were pseudo-first order (carried out in a large excess of water) the following rate equation was used: $2.303 \log a - 2.303 \log (a - x) = k_1 t$. A plot of t *vs.* $\log (a - x)$ gave very satisfactory straight lines in all cases. The rate constants (k_1) were calculated by a least square treatment of the line slopes in each case. Duplicate and triplicate runs were made in all cases. A summary of the rate results are listed in Table IV.

[CONTRIBUTION FROM SHIONOGI RESEARCH LABORATORY, SHIONOGI & CO., LTD., FUKUSHIMA-KU, OSAKA, JAPAN]

Steric Effect on Deshielding of the Aromatic C_4-Proton by a C_5-Proton in an Octahydrophenanthrene Series[1]

BY WATARU NAGATA, TADAO TERASAWA, AND KAZUO TORI

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An n.m.r. study of an A-ring-aromatic octahydrophenanthrene series revealed strong deshielding of the aromatic C_4-proton owing to the steric effect of an equatorial C_5-proton. The degree of this deshielding, which is represented by the difference in the chemical shifts between the C_1- and C_4-protons, is elucidated to be correlated to the van der Waals compression between the C_4- and C_5-hydrogens, which is represented by the interatomic distance between them. Dreiding models show that the distance is closely related to both B/C ring juncture and conformation. A large number of compounds of this series are exemplified to explain this correlation, which is believed to be very useful for estimation of the spatial structure of an analogous compound.

In nuclear magnetic resonance (n.m.r.) studies of steroids, there is considerable evidence that a proton is deshielded by steric effects of other proximate hydrogen atoms.[2,3] Earlier studies on n.m.r. spectra of phenanthrene and 7,8-dihydrophenanthrene suggested that the steric effect may play a role in marked deshielding of the C_4- and C_5-protons besides the ring-current effect.[4,5] In A-ring-aromatic octahydrophenanthrenes, a similar deshielding of the C_4-proton can be anticipated to be caused likewise by the steric effect of the C_5-equatorial proton, at least when the B/C juncture is *trans*. However, no study has been hitherto reported on this point. In the course of a totally synthetic study of steroids we have examined the n.m.r. spectra of a number of derivatives of 2-methoxy- or 2-hydroxy-4b,5,6,7,8,8a,9,10-octahydrophenanthrene (I),[6] and found that remarkable deshielding ascribable to the steric effect actually exists and the degree of this deshielding is closely related to the distance between the C_4- and C_5-protons.

Inspection of molecular models (Dreiding) of various octahydrophenanthrene derivatives of formula I shows

(1) Studies on Total Syntheses of Steroids. XV; part XIV: W. Nagata, T. Terasawa, and T. Aoki, *Tetrahedron Letters*, **No. 14**, 869 (1963).

(2) (a) The signal shift due to deshielding of the 19-methyl group in steroids by a 6β-methyl group was found to be about 0.10 p.p.m. [G. Slomp and B. R. McGarvey, *J. Am. Chem. Soc.*, **81**, 2200 (1959)]. (b) Signal shifts to lower fields of the 18- and 19-methyl groups owing to introduction of an 8β-methyl group were observed to be about 0.06 and 0.10 p.p.m., respectively [K. Tori, T. Tomita, H. Itazaki, M. Narisada, and W. Nagata, *Chem. Pharm. Bull.* (Tokyo), **11**, 956 (1963)]. (c) In spectra of estra-1,3,5(10)-triene derivatives, a 1-methyl signal appears at about 7.6 τ because of a probable interaction with the 11-methylene, whereas a 4-methyl signal appears at about 7.8 τ in the absence of the interaction [E. Caspi, Th. A. Wittstruck, and P. K. Grover, *Chem. Ind.* (London), 1716 (1962)]. (d) A downfield shift of 0.27 p.p.m. was observed in the C_1-proton signal due to introduction of an 11α-methyl group into a $\Delta^{1,4}$-3-keto steroid [K. Tori, unpublished result].

(3) R. J. Abraham and J. S. E. Holker, *J. Chem. Soc.*, 806 (1963).

(4) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High-resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, p. 253.

(5) C. Reid, *J. Mol. Spectry.*, **1**, 18 (1957).

(6) The spatial structures of the new hydrophenanthrene derivatives examined in this study have been elucidated in our laboratory (see W. Nagata, T. Terasawa, and T. Aoki to be published; I. Kikkawa, K. Kawata and W. Nagata, to be published).