Metalation of Toluene with *n*-Butylpotassium. Molten potassium metal (3.9 g, 0.1 g-atom) was subjected to high-speed stirring in 150 ml of octane for 3 min. To the cooled mixture was added *n*-butyl chloride (4.6 g, 0.05 mole) in 25 ml of octane, dropwise, over a 15-min interval. The temperature was maintained between −10 and −5° and the reaction mixture allowed to stir for 30 min after completion of addition while warming to room temperature. Toluene (46 g, 0.5 mole) was added rapidly and stirring was continued for 30 min. Carbonation was effected by pouring over a large excess of solid carbon dioxide. All operations were conducted under an argon atmosphere. The usual work-up[1e] provided a crude acid product (2.65 g) which was esterified using methanol and a catalytic amount of sulfuric acid. Analysis by glpc gave two peaks with relative areas of 11.5 and 88.5. These two peaks accounted for a minumum of 99% of the total area recorded on the chromatogram. The minor component had a retention time identical with that of methyl valerate and a sample of this compound, collected by glpc, had an infrared spectrum superimposable on that obtained from an authentic sample of methyl valerate. The major peak was identical with methyl phenylacetate by glpc.

The Problem of Metal Atom Participation in Electrophilic Substitution Reactions of the Iron Group Metallocenes

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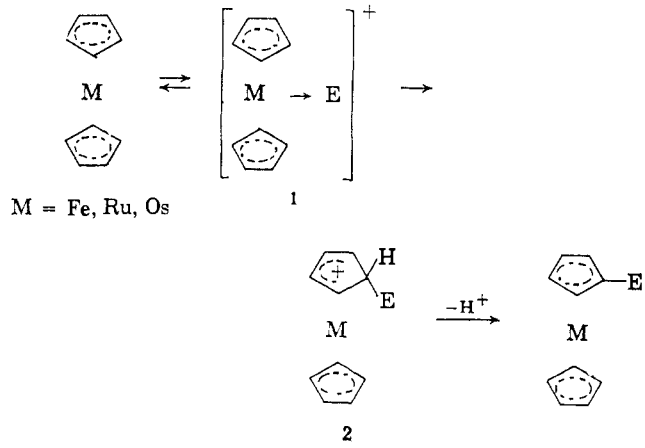
Contribution from the Department of Chemistry, Brandeis University, Waltham, Massachusetts 02154. *Received March 30, 1966*

Abstract: In order to examine the question of metal atom participation in the electrophilic substitution reactions of ferrocene, intramolecular ring acylation by the epimeric pair of acids **13** and **14**, which are constrained by their stereochemistry to either exo- or endocyclic electrophilic attack, has been studied. The synthesis and proof of structure of these acids are described. Each of these acids cyclized in the presence of trifluoroacetic acid to a homocyclic ketone, the rate of cyclization of the *exo* acid being somewhat more rapid than that of the *endo* acid. These results demonstrate that the metal atom is not an essential participant in the acylation of ferrocene, and suggest furthermore that it does not provide any particular energetic advantage in these processes.

Participation by the nonbonding metal 3d-orbital electrons in the reactions of the iron group metallocenes has been a subject of continued interest since the major outlines of the chemistry and electronic structure of these substances became apparent. Aside from oxidation of the metallocenes in which one or more of these electrons are undoubtedly involved, the metal atom has been suggested as the site of protonation[2] and of hydrogen bonding,[3] and has been invoked as a neighboring group in internal electron-transfer reactions of α-metallocenyl carbonium ions[4] and in solvolyses of α-metallocenylcarbinyl acetates.[3b,5] The latter attribution has recently been questioned by Ware and Traylor.[6]

Recently we suggested that the metal atom might play a critical role in electrophilic substitution reactions of the metallocenes by functioning as the primary site of electrophilic attack.[7] Ring substitution was proposed to occur through rate-limiting rearrangement of this cation **1** to a σ complex **2** followed by the loss of a proton.



Although many features of this mechanism seemed attractive, the evidence supporting it was indirect and largely inferential. Moreover, certain other observations[8] appeared to be at variance with it, and, accordingly, a more rigorous examination of these proposals was undertaken. The present paper provides some preliminary results of this investigation.

Results

Since an essential aspect of the proposed mechanism is the endocyclic mode by which ring substitution is assumed to take place, we chose to examine the intramolecular acylation reactions of an epimeric pair of ferrocenecarboxylic acids which would be constrained by their stereochemistry to either exocyclic or endocyclic electrophilic attack.

(1) Taken in part from a dissertation submitted by F. W. Abbate in partial fulfillment of the requirements for the Ph.D. degree.

(2) M. Rosenblum and J. O. Santer, *J. Am. Chem. Soc.*, **81**, 5517 (1959); T. J. Curphey, J. O. Santer, M. Rosenblum, and J. H. Richards, *ibid.*, **82**, 5249 (1960).

(3) (a) D. S. Trifan, J. L. Weinmann, and L. P. Kuhn, *ibid.*, **79**, 6566 (1957); D. S. Trifan and R. Bacskai, *ibid.*, **82**, 5010 (1960); (b) E. A. Hill and J. H. Richards, *ibid.*, **83**, 4216 (1961); (c) M. Rosenblum, "Chemistry of the Iron Group Metallocenes," Interscience Publishers, Inc., New York, N. Y., 1965, p 136.

(4) K. L. Rinehart, C. J. Michejda, and P. A. Kittle, *J. Am. Chem. Soc.*, **81**, 3162 (1959).

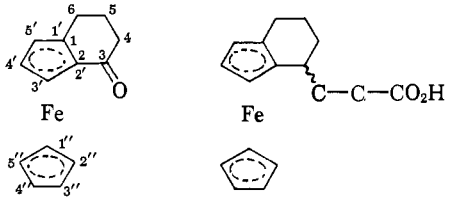
(5) (a) E. A. Hill and J. H. Richards, *ibid.*, **83**, 3840 (1961); J. H. Richards and E. A. Hill, *ibid.*, **81**, 3484 (1959); (b) D. S. Trifan and R. Bacskai, *Tetrahedron Letters*, 1 (1960).

(6) J. C. Ware and T. G. Traylor, *ibid.*, 1295 (1965).

(7) M. Rosenblum, J. O. Santer, and W. G. Howells, *J. Am. Chem. Soc.*, **85**, 1450 (1963). That the metal atom might play some role in these reactions was an idea first advanced by J. H. Richards, Abstracts, 135th National Meeting of the American Chemical Society, Boston, Mass., April 1959, p 86-O.

(8) (a) K. L. Rinehart, D. E. Bublitz, and D. H. Gustafson, *ibid.*, **85**, 970 (1963); (b) R. A. Benkeser, Y. Nagai, and J. Hooz, *ibid.*, **86**, 3742 (1964).

The fused ring derivative (**3**)[9] seemed well suited as a starting material for the synthesis of such epimers since the α-keto group provided a site for the introduction of a carboxylic acid chain adjacent to the ferrocene nucleus, while the fused cyclohexenyl ring would be expected to impose the required stereochemical orientation on this substituent. Furthermore, it is evident that we required a pair of acids the endocyclic epimer of which would cyclize predominantly if not exclusively to a homoannular ketone. As will be evident in the sequel, a three-carbon acid chain as in **4** was found to meet these requirements. It may be remarked in passing that homoannular cyclization of γ-ferrocenylbutyric acids, of which **4** is a representative, is apparently a rather general phenomenon.[9,10]



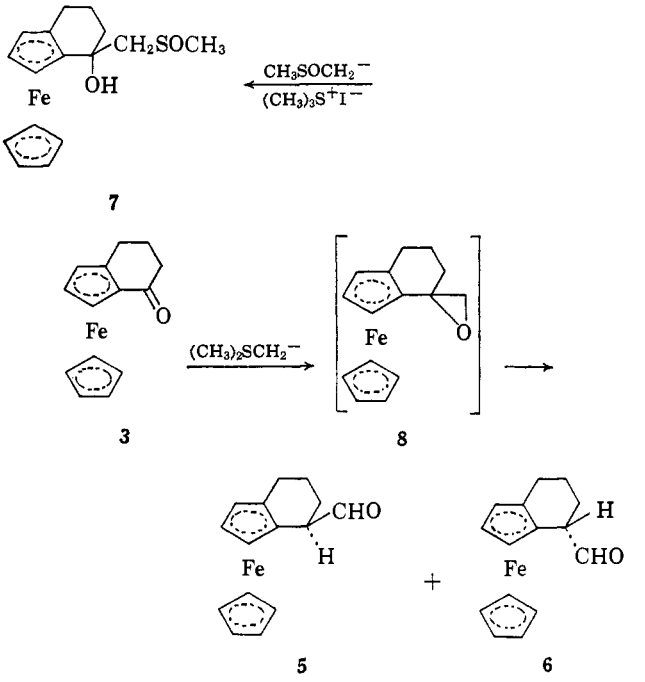
3 **4**

Initial attempts to effect the conversion of the ketone function in **3** to an aldehyde group with methoxymethylphosphorane[11] were without success, due apparently to the comparatively low reactivity of the carbonyl group in **3**.[12]

Dimethyloxosulfonium methylide, a reagent introduced recently by Corey and Chaykovsky[13] as a methylene transfer reagent, similarly failed to condense with **3**. However the more reactive ylide, dimethylsulfonium methylide, condensed readily, affording a mixture of *exo* and *endo* aldehydes (**5** and **6**), after acid work-up of the reaction mixture. The manner in which the reagents are brought into reaction is, however, critical to the outcome. When a mixture of the ketone **3** and trimethylsulfonium iodide were added to a solution of methylsulfinyl carbanion in dimethyl sulfoxide–tetrahydrofuran at $-5°$, the only product formed was the β-hydroxy sulfoxide (**7**). Methylsulfinyl carbanion does not by itself condense with **3** as was shown in a separate experiment. It is possible that these results are due to rapid but reversible addition of the methylsulfinyl carbanion to **3**, the equilibrium of which is unfavorable in the absence of a proton source such as the sulfonium salt.

When, however, the ketone **3** was added to a preformed solution of dimethylsulfonium methylide in dimethyl sulfoxide–tetrahydrofuran at $-5°$, the aldehydes **5** and **6** were isolated in moderate yield. The epoxide **8** is undoubtedly an intermediate in this reaction, but the very great ease with which α-ferrocenyl carbonium ions are generated must make it relatively labile toward ring opening and consequent isomerization to the aldehyde.

The crude mixture of aldehydes was conveniently purified by chromatography on alumina, although separation of the epimers could not be achieved by this procedure. Some care must be exercised in the use of neutralized and deactivated alumina, since with commercially available acid or basic alumina the aldehydes were largely destroyed, in part being converted to the starting ketone.



The aldehydes were readily separated by fractional crystallization, the preponderant, lower melting, *exo* aldehyde being considerably more soluble in ether–Skellysolve B than its *endo* isomer. The epimeric nature of these substances was confirmed by the conversion of each in base to a mixture of the two in which, as might be anticipated, the *exo* isomer predominated.

The nmr spectra of the aldehydes, which are reproduced in Figure 1, confirm their structural assignments, as well

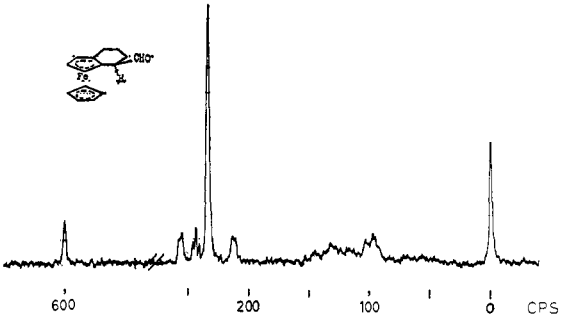


Figure 1a. Nmr spectrum of 1,2-ferroceno-1-cyclohexene-*exo*-3-carboxaldehyde (**5**), determined at 60 Mc in $CDCl_3$.

as the pseudo-equatorial conformation of the aldehyde group in each of the epimers, as shown in structures **9** and **10**. As would be expected from these structures, the chemical shifts of the aldehydic proton in the two

(9) (a) K. L. Rinehart *et al.*, *J. Am. Chem. Soc.*, **84**, 3263 (1962); (b) A. N. Nesmeyanov, N. A. Vol'kenau, and V. D. Vil'chevskaya, *Dokl. Akad. Nauk SSSR*, **118**, 512 (1958).

(10) J. Tirouflet, R. Dabard, and B. Gautheron, *Bull. Soc. Chim. France*, 96 (1965); J. Tirouflet and G. Tainturier, *Tetrahedron Letters*, 4177 (1965); H. Falk and K. Schlogl, *Monatsh.*, **96**, 1065 (1965); A. N. Nesmeyanov, N. A. Vol'kenau, and V. D. Vil'chevskaya, *Dokl. Akad. Nauk SSSR*, 111, 362 (1956).

(11) S. G. Levine, *J. Am. Chem. Soc.*, **80**, 6150 (1958); G. Wittig, W. Böll, and K. H. Kruck, *Ber.*, **95**, 2514 (1962).

(12) For other examples of this behavior see ref 3c, p 81.

(13) E. J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, **87**, 1353 (1965).

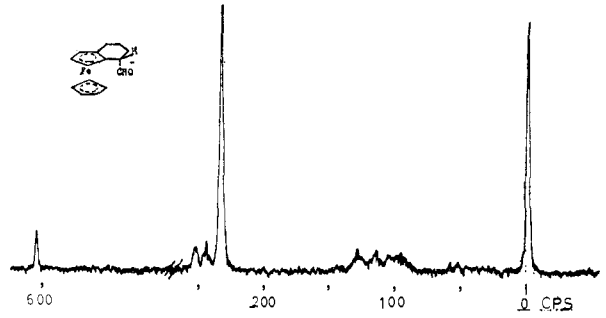
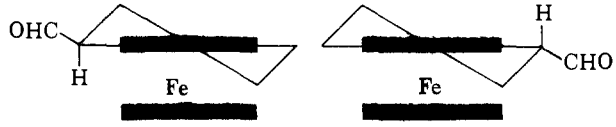


Figure 1b. Nmr spectrum of 1,2-ferroceno-1-cyclohexene-*endo*-3-carboxaldehyde (**6**), taken at 60 Mc in $CDCl_3$.

epimers do not differ significantly, since their average spatial dispositions are not widely different. By contrast, the chemical shifts of the tertiary protons (H_3) do, as required by their pseudo-axial conformation, differ widely. This resonance peak in the *endo* aldehyde lies under the complex band envelope due to aliphatic protons, between τ 7.5 and 8,8, while in the *exo* aldehyde in which this proton is held in the strongly deshielding region between the rings,[14] the resonance is shifted downfield to τ 6.43.



9 **10**

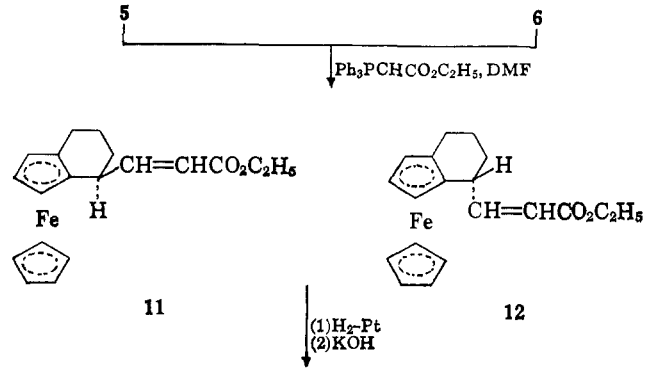
Both aldehydes, when condensed with carbethoxymethylenetriphenylphosphorane in dimethylformamide–tetrahydrofuran at 125°, were transformed to the same mixture of unsaturated esters (**11** and **12**). These were, in turn, hydrogenated over platinum oxide and saponified by ethanolic potassium hydroxide to a mixture of *exo*- and *endo*-propionic acids (**13** and **14**), which could be separated by fractional crystallization.

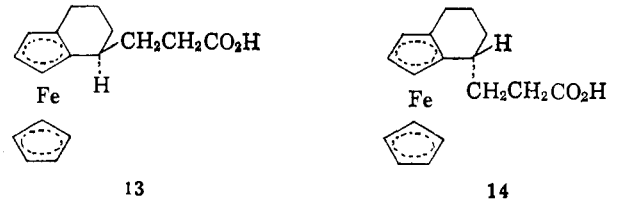
The structures of these acids were established by the following sequence of reactions. Condensation of the ketone **3** with ethyl bromoacetate under forcing conditions of the Reformatsky reaction[15] gave the hydroxy ester **15**, which was readily dehydrated to the unsaturated ester **16**. This latter substance could be obtained in good yield directly from the Reformatsky reaction under acid work-up conditions. The position of the double bond is confirmed by the presence of carbonyl absorption at 5.90 μ and by the small splitting (J = 1.6 cps) of the doublet vinyl proton resonance at τ 4.05. Catalytic hydrogenation of this substance gave the saturated ester **17**, which on saponification afforded the acid **18**.

The assignment of an *endo* configuration to the side chain in these latter two compounds follows from the mode of formation of the ester **17**, and is further supported by cyclization of the acid, in the presence of trifluoroacetic acid, to the bridged ketone **19**. That this latter substance is a bridged ferrocene is attested by the absence both of absorption at 9 and 10 μ in its infrared spectrum and of a singlet five-proton peak in its nmr

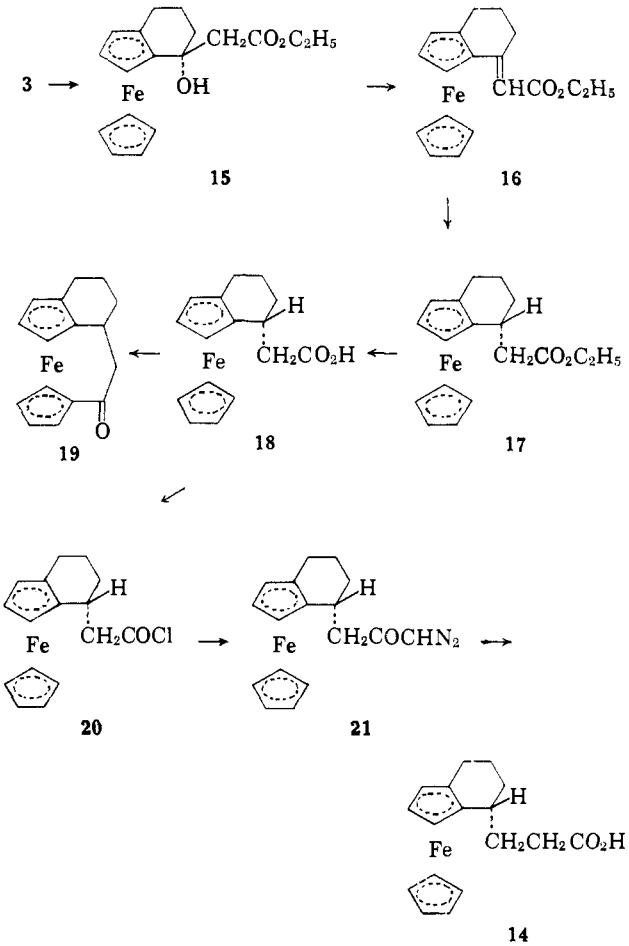
(14) L. N. Mulay and A. Attalla, *J. Chem. Phys.*, **38**, 760 (1963); see ref 3c, p 217.

(15) W. E. Bachman, W. Cole, and A. L. Wilds, *J. Am. Chem. Soc.*, **62**, 834 (1940).





spectrum. The heteroannular mode of cyclization of this acid is in keeping with the general behavior of β-ferrocenylpropionic acids to which this acid is structurally related.[16]

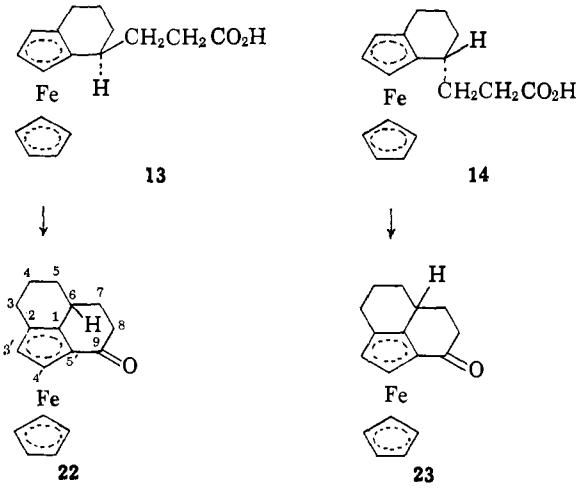


This acid (**18**) was converted to the corresponding acid chloride **20** with phosphorous trichloride and then to the diazo ketone **21**. Wolff rearrangement of this

(16) See ref 8a and M. Rosenblum, A. K. Banerjee, N. Danielli, R. W. Fish, and V. Schlatter, *ibid.*, **85**, 316 (1963). These references also illustrate some exceptions to this behavior.

substance in collidine–benzyl alcohol solution and saponification of the resulting ester gave an acid identical in all respects with the higher melting acid obtained from the Wittig reaction sequence. The *endo* configuration **14** for this acid is therefore established.

On treatment with trifluoroacetic anhydride in methylene chloride, both the *exo* and *endo* acids (**13** and **14**) cyclized to the corresponding homocyclic ketones (**22** and **23**). Molecular weight determinations established the monomeric nature of each of these substances, while the presence of bands at 9 and 10 μ in their infrared spectra and of a five-proton singlet absorption in their nmr spectra (Figure 2) confirm their homoannular character.



The relative cyclization rates of the epimeric acids were determined in a series of competitive reactions carried out in the presence of trifluoroacetic anhydride. Product analysis was readily achieved by gas chromatography employing a 6% QF-1 column on Chromosorb W at a temperature of 220°. The results of these experiments are given in Table I, in which the value of the rate ratio K is derived from the expression

$$K = \log (A/A_0)_{exo}/\log (A/A_0)_{endo}$$

where A and A_0 are the final and initial moles of acids.

Table I. Cyclization of *exo*- and *endo*-3-(β-Carboxyethyl)-1,2-ferroceno-1-cyclohexene

Run	Temp, °C	Reaction time, min	Log A/A_0 *endo*	Log A/A_0 *exo*	$K_{exo/endo}$
1	0	30	0.044	0.250	5.9
2	0	30	0.036	0.268	7.4
3	0	60	0.070	0.281	4.0
4[a]	0	20	0.043	0.174	4.0

[a] Reaction run in the presence of a large initial excess of trifluoroacetic acid.

Discussion

The data of Table I show a significant decrease in the value of K when the reaction time is prolonged from 30 to 60 min. Although the precision measure of the figures derived from the first two runs is undoubtedly lower than that of run 3, owing to the smaller amount of *endo*-carboxylic acid **14** consumed in these runs, the difference in K between the average of runs 1 and 2 and

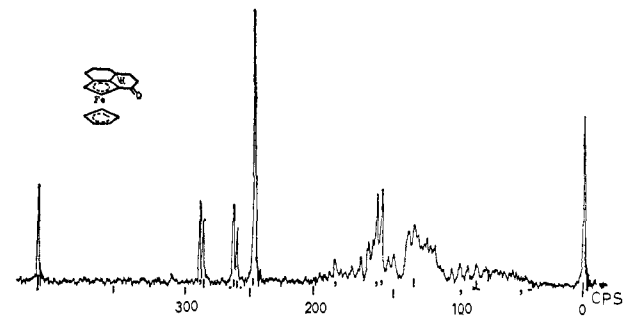


Figure 2a. Nmr spectrum of *exo*-6,5′-propano-1,2-ferroceno-1-cyclohexen-9-one (**22**), determined at 60 Mc in $CDCl_3$.

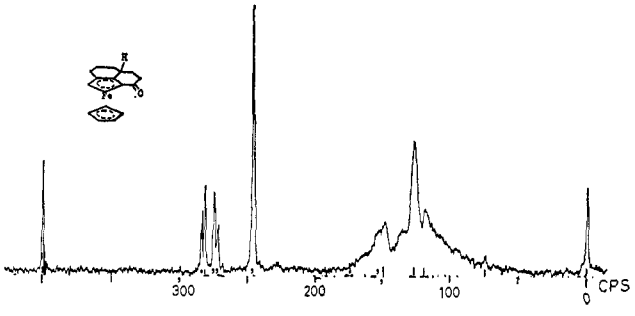


Figure 2b. Nmr spectrum of *endo*-6,5′-propano-1,2-ferroceno-1-cyclohexen-9-one (**23**), determined at 60 Mc in $CDCl_3$.

run 3 is probably real. The decrease in the magnitude of K is most reasonably attributed to more effective catalysis of *endo*-carboxylic acid cyclization by the trifluoroacetic acid generated in the course of the reaction. A more cogent demonstration of the effect of catalysis by trifluoroacetic acid is provided by the results of run 4 in which a large excess of this acid was added initially to the reaction. The effect of trifluoroacetic acid, not only in catalyzing acylation reactions involving acyl trifluoroacetates but in oftimes altering the course of these reactions, has been commented upon by others,[17] and has been attributed to promotion of the ionization of the mixed anhydride.[18]

While the data of Table I must, from a quantitative point of view, be considered as preliminary, the relative rates of cyclization of the epimeric acids (**13** and **14**) reflect no particular energetic advantage for endocyclic ring substitution. In fact, quite the opposite appears to be true, and unless acid catalysis of the competing reactions differs very significantly or the equilibrium concentrations of the epimeric mixed anhydrides are widely disparate,[19] the rate ratios observed must approximate the relative activation energies for ring substitution by these acids. These latter points remain to be examined. In comparing the relative reactivities of the epimeric acids, the greater steric retardation expected for reaction of the *endo* acid cannot be neglected. However, this is a factor which in general is likely to operate to a similar degree in these acylation reactions whether the substitution is intra- or inter-

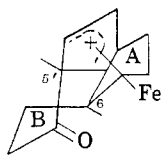
(17) E. J. Bourne, M. Stacey, J. C. Tatlow, and R. Worrall, *J. Chem. Soc.*, 2006 (1954).

(18) J. M. Tedder, *Chem. Rev.*, **55**, 787 (1955).

(19) At least for simple carboxylic acids and trifluoroacetic anhydride, infrared spectral measurements indicate that at equilibrium acyltrifluoroacetates are formed almost quantitatively: W. D. Emmons, K. S. McCallum, and A. F. Ferris, *J. Am. Chem. Soc.*, **75**, 6047 (1953), and ref 18.

molecular. It seems probable therefore that, within the limits of the uncertainties indicated above, there do not appear to be strong energetic factors favoring endocyclic substitution of the cyclopentadienyl rings.

The possibility that both the *exo* as well as the *endo* epimers effect ring substitution by an endocyclic mode must be considered. Since the carboxylic acid side chain in each of the epimeric acids (**13** and **14**) is most likely pseudo-equatorial as in the related aldehydes (**5** and **6**), the spatial orientation of these are not widely different with respect to the cyclopentadienyl ring plane, and models indicate that the acid function of the *exo* isomer may, without apparent difficulty, approach the general vicinity of the metal atom between the cyclopentadienyl rings. However, the energies of the isomeric σ complexes resulting from *cis* or *trans* addition by either of the epimeric acids to the cyclopentadienyl ring would be expected to differ significantly and to favor *cis* addition. Thus, in the σ-complex intermediate **24** which would result from endocyclic addition of an acylium ion derived from the exocyclic acid (**13**), ring B is forced to adopt a rigid boat conformation because of the *trans* fusion at C_6 and $C_{5'}$. The isomeric intermediate **25** which results from *cis* addition is free of these difficulties.



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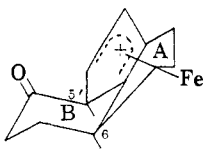

25

In conclusion, the present results demonstrate that the metal atom is not an *essential* participant in electrophilic substitution of ferrocene. Whether or not its participation in these processes provides some energetic advantage may yet be considered unresolved. Certainly it cannot do so for the simple process of acid-catalyzed hydrogen exchange,[20] and the present findings, although preliminary in nature, provide no support for the view that it does so for ring acylation.

Experimental Section[21]

Preparation of 1,2-Ferroceno-1-cyclohexen-3-one (3). To a solution of 25 g of trifluoroacetic anhydride in 100 ml of dry methylene chloride, cooled to 0°, was added a solution (16.5 g, 0.061 mole) of 4-ferrocenylbutyric acid[9] in 150 ml of the same solvent. Stirring was continued for 1.0 hr at 0°, and at room temperature for an additional 1.5 hr. The dark red solution was poured into a mixture of ice, water, and ascorbic acid. The layers were separated, and the aqueous phase was extracted with ether until both phases were colorless. The combined organic phase was then washed with water, 1 *N* sodium hydroxide, and saturated salt solution, and then dried over magnesium sulfate. Evaporation of the solvent and chromatography of the residue on 200 g of Merck acid alumina with ether gave one dark red band which yielded on slow evaporation 14.5 g (94%) of dark red crystals, mp 85.5–86.5° (lit.[9a] 87.5–88.5°).

Addition of Methylsulfinyl Carbanion to 1,2-Ferroceno-1-cyclohexen-3-one in the Presence of Trimethylsulfonium Iodide. A solution of methylsulfinyl carbanion was made from 8.0 mmoles of sodium hydride and 10 ml of dimethyl sulfoxide, freshly distilled from calcium hydride. The solution was diluted with 10 ml of tetrahydrofuran, also freshly distilled from calcium hydride. The mixture was then cooled to −5° in an ice–brine bath. A finely ground solid mixture of 1.00 g (3.94 mmoles) of the ketone **3** and 1.65 g (8.0 mmoles) of trimethylsulfonium iodide was mixed with stirring. The reaction was allowed to run for 0.5 hr at −5° and at room temperature for an additional 0.5 hr. It was then diluted with a large excess of saturated salt solution and extracted with ether until the water phase was colorless. The combined ethereal extract was washed with saturated salt solution and then dried over magnesium sulfate. Evaporation of the solvent and chromatography of the residue on 150 g of Merck acid-washed alumina (3% water added) gave, on elution with ether, 0.222 g of the starting ketone. Chloroform–ether mixtures eluted small amounts of materials, while elution with 100% chloroform yielded *exo*-3-methylsulfoxymethyl-1,2-ferroceno-1-cyclohexen-3-ol (**7**), 0.482 g, as a yellow solid, mp 95°. Recrystallization from ether gave yellow crystals, mp 107.5–109.5°.

Anal. Calcd for $C_{16}H_{20}O_2SFe$: C, 57.84; H, 6.07; S, 9.65; Fe, 16.81. Found: C, 57.85, 57.50; H, 5.87, 6.18; S, 9.26; Fe, 16.00.

Conversion of 1,2-Ferroceno-1-cyclohexen-3-one (3) to 1,2-Ferroceno-1-cyclohexene-*exo*- and -*endo*-3-carboxaldehyde (5 and 6). A 50% mineral oil dispersion of sodium hydride (0.576 g, 12.0 moles) was placed in a round-bottomed flask equipped with a syringe cap, a gas inlet connected to a vacuum system, and a nitrogen source. The flask was repeatedly evacuated and filled with nitrogen. Then 120 ml of dimethyl sulfoxide, freshly distilled from calcium hydride, was added *via* a syringe. The mixture was heated for 1 hr at 65–70°. After this time, all the hydride had dissolved, and the solution was nearly colorless. The solution was cooled to room temperature and diluted by syringe addition with 140 ml of tetrahydrofuran, freshly distilled from calcium hydride. The solution was cooled to −5° in ice and brine for 10 min. Trimethylsulfonium iodide (2.56 g, 12.3 moles) was added as a solid to this solution. When, after 10–15 min, all the iodide was dissolved, the ketone **3** (2.50 g, 1.00 mole), in tetrahydrofuran, was also added *via* a syringe. The reaction mixture was allowed to stir for 0.5 hr at −5°, and for 1 hr at room temperature.

The mixture was filtered into 200 ml of rapidly stirred 10% hydrochloric acid which had been previously deaerated by bubbling through a stream of nitrogen. After 0.5 hr at room temperature, the reaction mixture was extracted with ether until both phases were colorless. The combined ethereal solution was washed successively with water, 1 *N* sodium hydroxide, and saturated salt solution until the washings were neutral, and then dried quickly over magnesium sulfate. The solution was concentrated at room temperature under vacuum to a small volume, and chromatographed on 250 g of Fisher neutralized alumina. Elution with 25% ether–Skellysolve B removed one yellow band, care being taken to collect only the band and not any of the forerun which contains an odiferous substance detrimental to the stability of the aldehydes. Partial evaporation of the solvent from this solution yielded 0.229 g of the highly insoluble 1,2-ferroceno-1-cyclohexene-*endo*-3-carboxaldehyde (**6**) in two crystalline forms: small orange cubes, mp 181–184°, and fluffy yellow needles, mp 190.5–191.0°. Concentration of the solvent to a small volume yielded 0.447 g of 1,2-ferroceno-1-cyclohexene-*exo*-3-carboxaldehyde (**5**), as dense, red-orange crystals, mp 164.5–165.0°. Further elution with ether yielded 0.55 g of the starting ketone. The total yield of *exo* and *endo* aldehyde, based on recovered ketone, was 33%. Over many reactions, the largest yield was 52%. The average ratio of *exo*/*endo* aldehydes was 2/1.

Anal. Calcd for $C_{15}H_{16}OFe$: C, 67.19; H, 6.02; Fe, 20.83. Found (*exo*): C, 67.33; H, 5.92; Fe, 20.85. Found (*endo*): C, 67.23; H, 5.67; Fe, 20.86.

Epimerization of 1,2-Ferroceno-1-cyclohexene-*endo*- and -*exo*-3-carboxaldehydes. The *exo* or *endo* aldehydes (**5** and **6**), respectively, dissolved in tetrahydrofuran, were added to a solution of 25 ml of tetrahydrofuran and 0.25 ml of water in which a sliver of sodium metal had been dissolved. The mixture was refluxed for the allotted time, cooled to room temperature, diluted with water, and extracted with ether; the combined ethereal extract was washed to neutrality with water and then dried over magnesium sulfate.

(20) Since the intermediate σ complexes derived *via* either the exocyclic or the endocyclic reaction paths must be identical for proton exchange.

(21) All melting points were determined using a Fisher–Johns melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Infracord, Model 137. Nuclear magnetic resonance spectra were determined in 5% deuteriochloroform solutions, and recorded at 60 Mc with a Varian Model V-4300 spectrometer. Peak positions were calibrated against tetramethylsilane as internal standard by sidebanding. Analyses were performed by the Alfred Bernhardt Microanalytical Laboratory, Mulheim, Germany; by Dr. S. J. Nagy, Microanalytical Laboratory, Massachusetts Institute of Technology; and by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

After filtration of the drying reagent, the solvent was concentrated to a small volume, Skellysolve B was added, and the aldehydes were allowed to crystallize. The fractions were collected in small amounts and weighed and the melting points were taken. The results are tabulated below.

Table II

Starting aldehyde	Reaction time, hr	*exo*/*endo*
endo	2.0	0.2
	12.0	1.0
	24.0	2.5
exo	8.0	5.0
	36.0	4.4

Conversion of 1,2-Ferroceno-1-cyclohexene-*exo*- and -*endo*-3-carboxaldehyde to *exo*- and -*endo*-3-(β-Carboxyethyl)-1,2-ferroceno-1-cyclohexene (13 and 14). The *endo* aldehyde **6** (0.360 g, 1.40 mmoles) was placed in an extraction thimble, suspended under a reflux condenser, and attached to a round-bottomed flask, with a syringe cap and a nitrogen inlet, containing a solution of 40 ml of N,N-dimethylformamide, freshly distilled from calcium hydride, and 0.70 g (2.01 mmoles) of carbethoxymethylenetriphenylphosphorane. Enough tetrahydrofuran was then added *via* a syringe to maintain a reflux temperature of 125–130°. After 1 hr, all the aldehyde had been extracted into the reaction medium, and the resulting deep red solution was then poured into 250 ml of saturated salt solution. The aqueous phase was extracted with ether, and the combined ether extract was washed with saturated salt solution and then dried over magnesium sulfate.

Evaporation of the solvent and chromatography of the residue on Fisher neutralized alumina with 15% ether–Slellysolve B as eluent removed one yellow band. The solvent was allowed to evaporate and the residue was triturated with ether to allow crystallization of unreacted aldehyde, which was removed by filtration. A mixture of *exo*- and *endo*-3-(β-carbethoxyvinyl)-1,2-ferroceno-1-cyclohexene remained as a red oil.

The unsaturated esters were dissolved in 25 ml of absolute ethanol and hydrogenated at atmospheric pressure and room temperature using 16 mg of platinum oxide as catalyst. Reaction was complete within 1 hr when uptake of hydrogen had ceased. The reaction mixture was diluted with water, after filtration through Celite, to remove the catalyst. The aqueous phase was extracted with ether, and the combined organic extract was washed with water and then dried over magnesium sulfate. After evaporation of the solvent, chromatography on 30 g of Merck acid alumina with 15% ether–Skellysolve B afforded one yellow band which, on evaporation of the solvent, left 0.215 g of the mixture of *exo*- and *endo*-3-(β-carbethoxyethyl)-1,2-ferroceno-1-cyclohexene (**5** and **6**) as a yellow oil.

The ester mixture was saponified by heating in 50 ml of 10% ethanolic potassium hydroxide for 4 hr. Crystallization from ether, after work-up, gave 66 mg of the *endo*-propionic acid (**14**), mp 130–138°. Several crystallizations of this substance from ether afforded an analytical sample, mp 140–141°.

Anal. Calcd for $C_{17}H_{20}O_2Fe$: C, 65.40; H, 6.46; Fe, 17.89. Found: C, 65.53; H, 6.41; Fe, 17.77.

Repeated fractional crystallizations from ether–petroleum ether (bp 30–60°) removed remaining small amounts of the *endo* acid. The *exo* acid (**13**) finally crystallized from the mother liquors as yellow plates, mp 85.5–87.5°, or as fine yellow needles, mp 88–90°. The ratio of *exo*/*endo* was approximately 4/1.

Anal. Calcd for $C_{17}H_{20}O_2Fe$: C, 65.40; H, 6.46; Fe, 17.89. Found: C, 65.47; 64.87; H, 6.87, 6.40; Fe, 17.74.

Using the same sequence, starting with 0.758 g (2.82 mmoles) of the *exo* aldehyde (**5**), 0.442 g (50%) of the saturated propionic ester was obtained, which on saponification in ethanolic potassium hydroxide afforded the mixture of acids in 97% yield. These were also separated by fractional crystallization into a small amount of *endo* acid (**14**), the main fraction being the *exo* acid (**13**), which was again approximately 80% of the acid yield.

Conversion of 1,2-Ferroceno-1-cyclohexen-3-one (3) to *exo*-3-Carbethoxymethyl-1,2-ferroceno-1-cyclohexen-3-ol (15). 1,2-Ferroceno-1-cyclohexen-3-one (**3**) (5.23 g, 0.0206 mole) was dissolved in 100 ml each of sodium-dried benzene and sodium-dried ether. The mixture was brought to reflux temperature, and zinc dust (3.0 g), previously washed with 2% hydrochloric acid, water, acetone, and ether, and dried at 110°, was added along with 3.0 ml of ethyl bromoacetate. Four subsequent additions of 2.0 g of zinc dust and 2.0 ml of ethyl bromoacetate were made at 45-min intervals. Refluxing was continued for 1 hr after the last addition. The straw-colored mixture was cooled to room temperature and 100 ml of 10% acetic acid in methanol was added. The zinc was filtered off and washed with ether. The organic phase was washed with water, 1 *N* sodium hydroxide, and saturated salt solution, and then dried over magnesium sulfate. Evaporation of the solvent and chromatography of the residue on 250 g of Fisher basic alumina yielded two bands on development with Skellysolve B. The first, a dark red band, was eluted with 25% ether–Skellysolve B, and on evaporation of the solvent yielded 50 mg of 3-carbethoxymethylene-1,2-ferroceno-1-cyclohexene (**16**) as a deep red oil. Further elution with ether removed a yellow band containing *exo*-3-carbethoxymethyl-1,2-ferroceno-1-cyclohexen-3-ol (**15**), 6.01 g (86%), which solidified on standing at 0°. Purification of the alcohol by chromatography on a Fisher basic alumina column with ether yielded, on slow evaporation and cooling, yellow crystals, mp 42.5–43.5°.

Anal. Calcd for $C_{18}H_{22}O_3Fe$: C, 63.17; H, 6.48. Found: C, 63.29; H, 6.54.

Conversion of *exo*-3-Carbethoxymethyl-1,2-ferroceno-1-cyclohexen-3-ol (15) to 3-Carbethoxymethylene-1,2-ferroceno-1-cyclohexene (16). The hydroxy ester (**15**), 6.01 g in 150 ml of tetrahydrofuran, 50 ml of water, and 1.5 ml of concentrated hydrochloric acid, was refluxed for 3.0 hr. The resulting deep red solution was diluted with water, the layers were separated, and the aqueous phase was extracted with ether until the ether layer was colorless. The combined organic phase was washed with water, sodium bicarbonate solution, and saturated salt solution, and then dried over magnesium sulfate. The solvent was removed and the residue chromatographed on 75 g of Fisher basic alumina. Elution with 25% ether–Skellysolve B removed the one red band present. Evaporation of the solvent yielded 5.76 g (98%) of the unsaturated acetate ester (**16**).

Direct Preparation of 3-Carbethoxymethylene-1,2-ferroceno-1-cyclohexene (16) from the Reformatsky Reaction. 1,2-Ferroceno-1-cyclohexen-3-one (**3**), 4.98 g, was treated with ethyl bromoacetate and zinc dust. When the reaction had cooled to room temperature, dilute hydrochloric acid was used to decompose any zinc complex present. The solution became deep dark red. The zinc was filtered off and washed with ether. The organic phase, after separation from the water, was washed successively with water, 10% sodium carbonate solution, and saturated salt solution, and then dried over magnesium sulfate. The solvent was evaporated, and the residue chromatographed on 250 g of Fisher basic alumina. Elution with 25% ether–Skellysolve B afforded 4.90 g (77%) of the unsaturated ester (**16**). Elution with ether yielded 0.637 g (10%) of the hydroxy ester (**15**).

Reduction of 3-Carbethoxymethylene-1,2-ferroceno-1-cyclohexene (16). The unsaturated acetate ester (**16**), 5.60 g, in 50 ml of absolute ethanol was hydrogenated at atmospheric pressure and room temperature using 0.540 g of 10% palladium on powdered charcoal as a catalyst. The reaction was complete in 2 hr, when there was no more uptake of hydrogen. The solution was filtered through Celite into a large excess of water and then extracted with ether. The combined ethereal solution was washed with water and dried over magnesium sulfate. Evaporation of the solvent and chromatography of the product over 75 g of Fisher basic alumina, employing a 10% ether–Skellysolve B as eluent, yielded *endo*-3-carbethoxymethyl-1,2-ferroceno-1-cyclohexene (**17**), 5.47 g (98%), as a yellow-orange oil.

Preparation of *endo*-3-Carboxymethyl-1,2-ferroceno-1-cyclohexene (18). The *endo*-ethyl ester (**17**), 5.27 g, dissolved in 150 ml of 10% ethanolic potassium hydroxide solution was refluxed overnight. Work-up yielded 4.67 g (97%) of a yellow powder, mp 110–112°. Crystallization from ether–hexane gave the acid **18** as yellow crystals, mp 115–116°. *Anal.* Calcd for $C_{16}H_{18}O_2Fe$: C, 64.45; H, 6.08. Found: C, 64.35; H, 6.11.

Arndt–Eistert Synthesis of *endo*-3-(β-Carboxyethyl)-1,2-ferroceno-1-cyclohexene (14). To 10 ml of phosphorus trichloride cooled to 0° was added 1.00 g (3.36 mmoles) of the *endo*-acetic acid (**18**). The mixture was allowed to come to room temperature, and was then left standing overnight. The phosphorus trichloride was removed under vacuum at room temperature leaving the acid chloride (**20**) as a red oil. This was taken up in dry methylene chloride and added dropwise, at 0°, to a dried solution of diazomethane in ether, prepared from 8.0 g (37 mmoles) of "Diazald." The ice bath was allowed to come to room temperature. After 6 hr, the solvent was removed on a rotary evaporator without the use of additional heat. The residue was taken up in ether and

filtered. Evaporation of solvent at room temperature left the crude diazo ketone (**21**) as a yellow solid, mp 58–67°.

To the crude diazo ketone was added 9 ml each of benzyl alcohol and collidine. The solution was plunged into an oil bath at 180° for 5 min. The resulting dark red mixture, after cooling to room temperature, was diluted with ether, and then washed successively with water, 10% hydrochloric acid, sodium bicarbonate solution, and saturated salt solution to neutrality. After drying over magnesium sulfate, the residue, upon concentration to a small volume, was chromatographed on 80 g of Merck acid-washed alumina with mixtures of ether–Skellysolve B until all the color was removed. The solvent was evaporated and the residue saponified by refluxing in 50 ml of 10% ethanolic potassium hydroxide for 4 hr. After the usual work-up, 0.42 g (52%) of *endo*-3-(β-carboxyethyl)-1,2-ferroceno-1-cyclohexene (**14**) was obtained as yellow plates, mp 135–138°, identical in all respects with the acid obtained from the aldehydes **5** and **6**.

Cyclization of *endo*-3-Carboxymethyl-1,2-ferroceno-1-cyclohexene (18) to 3,1′′-Ethano-1,2-ferroceno-1-cyclohexen-8-one (19). Trifluoroacetic anhydride, 5.0 ml, was added with stirring to a solution of 0.502 g (1.69 mmoles) of the *endo*-acetic acid (**14**) in 50 ml of dry methylene chloride at 0°. After 1 hr at 0°, the ice bath was removed, and the reaction was allowed to continue at room temperature for an additional 1.5 hr. The reaction was quenched by pouring the solution into a mixture of ice and water. Ether was added, and the layers were separated. The aqueous layer was washed once with ether, and the combined organic phase was washed with water, 1 *N* sodium hydroxide, and saturated salt solution to neutrality, and then dried over magnesium sulfate. Evaporation of the solvent and chromatography of the residue on 60 g of Merck acid alumina yielded, on elution with ether, 0.457 g (95%) of 3,1′′-ethano-1,2-ferroceno-1-cyclohexen-8-one (**19**) as a red solid, mp 112–117°. Recrystallization from ether afforded red crystals, mp 120–121.5°.

Anal. Calcd for $C_{16}H_{16}OFe$: C, 68.59; H, 5.76. Found: C, 68.35; H, 5.71.

Analysis of the neutral ether extract and the mother liquors from recrystallization by vpc failed to show any isomeric substances.

Cyclization of *endo*-3-(β-Carboxyethyl)-1,2-ferroceno-1-cyclohexene (14) to *endo*-6,5′-Propano-1,2-ferroceno-1-cyclohexen-9-one (23). Trifluoroacetic anhydride (3.0 ml) was added at 0° to a stirred solution of 0.301 g (0.965 mmole) of the *endo*-propionic acid (**14**) in 50 ml of dry methylene chloride. The ice bath was removed, and the solution was stirred at room temperature for 4 hr. The reaction was quenched by pouring the solution into ice and water. Ether was added and the layers were separated. The water layer was washed once with ether. The combined ethereal extract was washed with water, 1 *N* sodium hydroxide, and saturated salt solution to neutrality, and then dried over magnesium sulfate. Removal of the solvent and chromatography of the residue on 40 g of Merck acid alumina with ether yielded 0.106 g (36%) of *endo*-6,5′-propano-1,2-ferroceno-1-cyclohexen-9-one (**23**) as a red solid, mp 110–118°. Recrystallization from ether afforded red crystals, mp 116–118°. Only 28 mg of unreacted acid was recovered.

Anal. Calcd for $C_{17}H_{18}OFe$: C, 69.41; H, 6.17; Fe, 18.99; mol wt, 294. Found: C, 69.16; H, 5.85; Fe, 18.85; mol wt, 287.

Cyclization of *exo*-3-(β-Carboxyethyl)-1,2-ferroceno-1-cyclohexene (13) to *exo*-6,5′-Propano-1,2-ferroceno-1-cyclohexen-9-one (22). Trifluoroacetic anhydride (3.0 ml) was added with stirring to a solution of 0.300 g (0.962 mmole) of *exo*-propionic acid (**13**) in 50 ml of dry methylene chloride at 0°. The ice bath was removed and stirring was continued at room temperature for 4 hr. After work-up, the crude product was chromatographed on 40 g of Merck acid alumina using ether as eluent. A rose-colored band was removed which, on evaporation and cooling at 0°, yielded 0.137 g (48%) of *exo*-6,5′-propano-1,2-ferroceno-1-cyclohexen-9-one (**22**) as a dark red solid, mp 61–65°. Recrystallization from ether–hexane afforded dark red crystals, mp 74–76°.

Anal. Calcd for $C_{17}H_{18}OFe$: C, 69.41; H, 6.17; Fe, 18.99; mol wt, 294. Found: C, 69.42; H, 6.08; Fe, 19.20; mol wt, 306.

Competitive Rates of Cyclization in Trifluoroacetic Anhydride of *exo*- and -*endo*-3-(β-Carboxyethyl)-1,2-ferroceno-1-cyclohexene. Trifluoroacetic anhydride (2.0 ml) was added at the required temperature, with stirring, to a solution of the two acids in 25 ml of dry methylene chloride. After a specified amount of time, the reaction was quenched by pouring the solution into ice and water. The aqueous layer generally had a faint blue tinge which was removed by the addition of ascorbic acid. Ether was added and the layers were separated. The aqueous phase was extracted once with ether, and the combined organic fraction was washed with water, 1 *N* sodium hydroxide, and saturated salt solution, and then dried over magnesium sulfate. The solvent was evaporated, and the residue was diluted to 1.0 ml with benzene and analyzed by vpc employing an Aerograph Model A90-P chromatograph with a 6 ft × 0.25 in. aluminum column filled with 6% QF-1 on 60–80 mesh Chromosorb W and heated at 220°. The retention times for the ketones, with a flow rate of helium of 220 ml/min, were: *exo*-ketone **22**, 3.6 min; *endo*-ketone **23**, 10.4 min. Peaks were recorded using a Sargent Model SR recorder equipped with a disk integrator. Peak areas were calibrated against concentration for each of the ketones separately. Experimental data are recorded in Table III.

Table III

Run	Initial moles × 10^{-6} *endo* acid	Initial moles × 10^{-6} *exo* acid	Moles reacted × 10^{-6} *endo* acid	Moles reacted × 10^{-6} *exo* acid
1	146	147	14	66
2	152	80.8	12	36
3	183.8	99.2	27	47
4[a]	160	75.2	15	25

[a] 0.9 ml of trifluoroacetic acid was added initially to the reaction.

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