Experimental

Materials.[12]—(+)-*trans*-α,γ-Dimethylallyl-*p*-nitrobenzoate carbonyl-^{18}O, 3.70% [18]O,[12] m.p. 46.2–47.4°, [α][25]D 41.6° (CHCl₃) (lit.[3] m.p. 45.7–46.7°, [α][25]D 42.5°) was prepared as described earlier[3] from (+)-*trans*-α,γ-dimethylallyl acid phthalate, m.p. 80.5–82.8°, [α][25]D 38.0° (*l* 4, *c* 1.25, CHCl₃).

(+)-*trans*-α,γ-Dimethylallyl *p*-nitrobenzoate-ether-^{18}O, 2.51% [18]O, m.p. 45.0–46.0°, [α][25]D 41.9° (CHCl₃) was prepared as follows. Crotonaldehyde-carbonyl-^{18}O, 2.90% [18]O, b.p. 98–102°, n^{25}D 1.4337, was obtained by equilibration of freshly distilled crotonaldehyde with ^{18}O-water, *ca.* 5% [18]O, according to a general procedure.[20] This was converted[4] to *trans*-α,γ-dimethylallyl alcohol-^{18}O which in turn was converted to the acid phthalate derivative, 2.89% [18]O, m.p. 88.0–89.5°. Resolution[4] gave optically pure *trans*-α,γ-dimethylallyl acid phthalate-ether-^{18}O, 2.82% [18]O, m.p. 76.6–78.1°, [α][25]D 38.0°. This was converted to ^{18}O-labeled (+)-*trans*-α,γ-dimethylallyl alcohol by reduction with lithium aluminum hydride.[3] Reaction of the alcohol with *p*-nitrobenzoyl chloride gave ether-[18]O-(+)-I. That this material was discretely labeled in the ether oxygen position was shown as follows. A small portion of the labeled ester, 2.51% [18]O, was reduced[3] to *trans*-α,γ-dimethylallyl alcohol which was reconverted to the *p*-nitrobenzoate I and acid phthalate derivatives. The *p*-nitrobenzoate derivative I contained 2.52% [18]O; the acid phthalate contained 2.49% [18]O. These experiments prove that the *p*-nitrobenzoate derivative is labeled exclusively in the ether position and that the transformations used to determine the ^{18}O-distribution in the unsolvolyzed *p*-nitrobenzoate do not lead to loss or scrambling of the ^{18}O-label.

The aqueous acetone[10] was prepared from purified[21] acetone and conductivity water.

(20) H. L. Goering and R. E. Dilgren, *J. Am. Chem. Soc.*, **82**, 5744 (1960).

(21) J. K. Kochi and G. S. Hammond, *ibid.*, **75**, 3445 (1953).

Kinetic Experiments.—All concentration are given for 25°. The polarimetric and titrimetric rates were determined by methods described earlier.[3,4] In the polarimetric experiments the total change in rotation was over 2° and individual measurements were reproducible to within 0.01°. For the titrimetric experiments reactions were followed by titrating 5-ml. aliquots with 0.0485 *N* aqueous sodium hydroxide to the brom thymol blue end-point. The change in titer for a typical experiment was about 5 ml. and titrations were reproducible to within 0.005 ml.

Determination of ^{18}O-Equilibration and Scrambling.—All ^{18}O-contents were determined[3] in triplicate and the average deviation from the mean was less than 1%. Samples used for ^{18}O-determinations were shown to be pure by their physical properties including infrared spectra.

The rate of ^{18}O-equilibration (eq. 2) was determined by the method described earlier.[6] The data are summarized in Table II.

Rates of ^{18}O-scrambling in the enantiomers (eq. 3) were also determined by a method described earlier.[3] Pertinent data are given in Tables III and IV.

Determination of Optical Purity of (+)-*trans*-α,γ-**Dimethylallyl Acid Phthalate.**—The optical purity was established by a modification of an isotope dilution method described earlier.[8,22] Equal weights of (+)-*trans*-α,γ-dimethylallyl acid phthalate, [α][25]D 38.0° (*l* 4, *c* 1.25, CHCl₃), and *dl*-*trans*-α,γ-dimethylallyl acid phthalate, 5.90 ± 0.01% [18]O, were mixed and the resulting mixture resolved[4] to a constant rotation of [α][25]D 38.0° (*l* 4, *c* 1.25, CHCl₃). The latter had an ^{18}O-content of 1.98 ± 0.02%. From these data it can be shown[6] that acid phthalate, [α][25]D 38.0°, is 100 ± 5% optically pure.

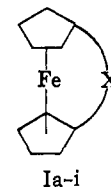(22) J. S. Berson and D. A. Ben-Efraim, *ibid.*, **81**, 4083 (1959).

Organic Chemistry of Ferrocene. VI.[1] Acetylation of Mono-, Di- and Tri-bridged Ferrocenes[2]

By Kenneth L. Rinehart, Jr.,[3] Donald E. Bublitz and David H. Gustafson

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Synthesis of the isomeric bis- and tris-(trimethylene)-ferrocenes has been achieved. These compounds and the mono-bridged analog have been acetylated and the ratios of the isomeric acetyl products have been determined. Cyclization of certain bridged ferrocene-propionic acids has been shown to give homoannular ketonic products, as well as the expected heteroannular compounds. Nuclear magnetic resonance spectra of the compounds prepared are discussed.

Since the original reports[4,5] of the preparation of a bridged ferrocene, 1,1'-(α-ketotrimethylene)-ferrocene (Ia), considerable interest has been displayed in compounds of this type and a number of other mono-bridged compounds have been prepared, as Ib,[1] Ic,[1,6–8] Id,[6] Ie,[9] If,[10] Ig,[7] Ih,[10] Ii.[11,12] Recently, too, the di-bridged ferrocene XI and its α-keto derivative X have been reported by Schlögl and Seiler.[13] The ketone X was prepared by them by cyclization of 1,1'-trimethyleneferrocene-3-propionic acid (IX),[14] which

(1) Paper V, K. L. Rinehart, Jr., R. J. Curby, Jr., D. H. Gustafson, K. G. Harbison, R. E. Bozak and D. E. Bublitz, *J. Am. Chem. Soc.*, **84**, 3263 (1962).

(2) Presented in part at the 141st National A.C.S. Meeting, Washington, D. C., March 20–29, 1962; *cf.* Abstracts, p. 19-O.

(3) Alfred P. Sloan Foundation Fellow.

(4) K. L. Rinehart, Jr., and R. J. Curby, Jr., *J. Am. Chem. Soc.*, **79**, 3290 (1957).

(5) In the Ph.D. Thesis of M. Rosenblum (Harvard University, August, 1953) it is noted that R. B. Woodward and E. Csendes obtained compound Ia, a m.p. is given, and a tentative structure is assigned.

(6) A. Lüttringhaus and W. Kullick, *Angew. Chem.*, **70**, 438 (1958).

(7) K. Schlögl and H. Seiler, *Monatsh.*, **91**, 79 (1960).

(8) E. A. Hill and J. H. Richards, *J. Am. Chem. Soc.*, **83**, 4216 (1961).

(9) R. L. Schaaf, P. T. Kan and C. T. Lenk, *J. Org. Chem.*, **26**, 1790 (1961).

(10) K. L. Rinehart, Jr., A. K. Frerichs, P. A. Kittle, L. F. Westman, D. H. Gustafson, R. L. Pruett and J. E. McMahon, *J. Am. Chem. Soc.*, **82**, 4111 (1960).

(11) T. A. Mashburn, Jr., and C. R. Hauser, *J. Org. Chem.*, **26**, 1671 (1961).

(12) E. C. Winslow and E. W. Brewster, *ibid.*, **26**, 2982 (1961).

(13) K. Schlögl and H. Seiler, *Tetrahedron Letters*, No. 7, 4 (1960).

Ia–i

Ia, X = –CH₂CH₂CO–
b, X = –CH₂CH₂CHOH–
c, X = –(CH₂)₃–
d, X = –(CH₂)$_n$–; n = 4,5
e, X = –Si(CH₃)₂–O–Si(CH₃)₂–
f, X = –CH₂–O–CH₂–
g, X = –(CH₂)$_n$COCHOH(CH₂)$_m$–; $n = m$ = 1,2,3,4; n = 3, m = 4
h, X = –C(CH₃)₂C(CH₃)₂–
i, X = –CH(CH₃)–O–CH(CH₃)–

in turn had been obtained by three routes: (1) formylation of 1,1'-trimethyleneferrocene (Ic) to an aldehyde (presumably 1,1'-trimethyleneferrocene-3-carboxaldehyde), which was converted *via* condensation with malonic acid in the Doebner reaction and subsequent hydrogenation to IX; (2) cyclization in trifluoroacetic anhydride of 1,1'-ferrocenedipropionic acid XII and

(14) Nomenclature employed throughout the present paper accords pre-eminence to the ring positions substituted by the hydrocarbon bridges; other groups are considered substituents of these basic skeletons. This system has the considerable advantage of consistency and is somewhat similar to that employed for bicyclic hydrocarbons.

hydrogenolysis of the product to IX; (3) cyclization of 1,3-ferrocenedipropionic acid (the product of formylation, Doebner condensation and reduction of methyl β-ferrocenylpropionate) and hydrogenolysis of the product to IX. The formylation and cyclization products were assumed to be the β-isomers from the previously observed predominant β-acylation of alkylferrocenes,[15,16] and β-substitution was also assigned from the presence of infrared bands at 905 and 930 cm.$^{-1}$ in the spectrum of X, and at 911 and 936 cm.$^{-1}$ in that of XI, regions in which known 1,3-acylalkyl and dialkyl ferrocenes are known to show absorption.[15–17]
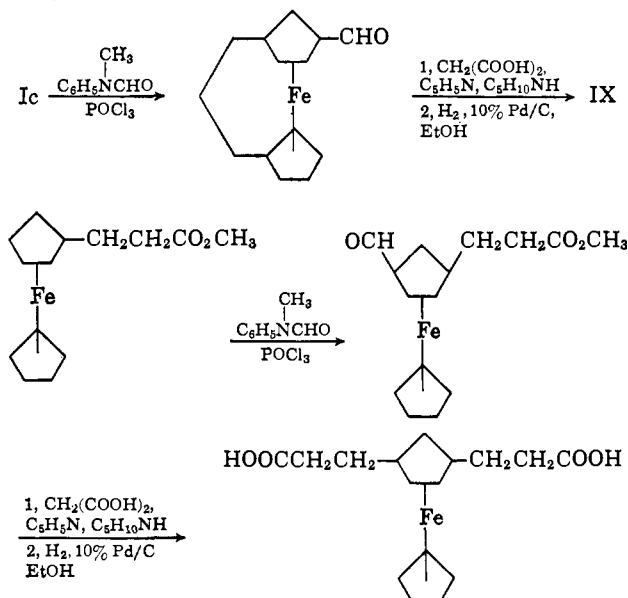
In the present paper are described our own results on the synthesis and properties of di- and tri-bridged ferrocenes.

Synthesis.—The general route employed in the present study for the introduction of trimethylene bridges was that described earlier[1] for the preparation of Ic: carbethoxylation of the acetyl compound with diethyl carbonate, employing a dispersion of sodium hydride in hydrocarbon solvent, hydrogenolysis of the resulting β-keto ester over platinum oxide in acetic acid; saponification of the propionate ester; cyclization of the propionic acid with trifluoroacetic anhydride in carbon tetrachloride; reduction of the bridged ketone to the hydrocarbon with lithium aluminum hydride–aluminum chloride.
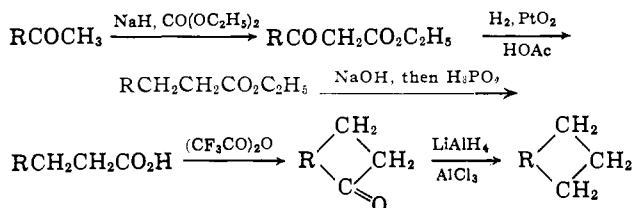
The di-bridged 1,1′;2,2′- and 1,1′;3,3′-bis-(trimethylene)-ferrocenes, VIII and XI, respectively, were obtained from two synthetic sequences (Fig. 1). That which most clearly assigns their structures proceeds from the isomeric 2-acetyl- and 3-acetyl-1,1′-trimethyleneferrocenes (II and III, respectively). These two compounds (together with 3,4′-diacetyl-1,1′-trimethyleneferrocene (IV) whose structure is discussed below) were obtained by Friedel–Crafts acylation of Ic with

(15) K. L. Rinehart, Jr., K. L. Motz and S. Moon, *J. Am. Chem. Soc.*, **79**, 2749 (1957).

(16) M. Rosenblum and R. B. Woodward, *ibid.*, **80**, 5443 (1958).

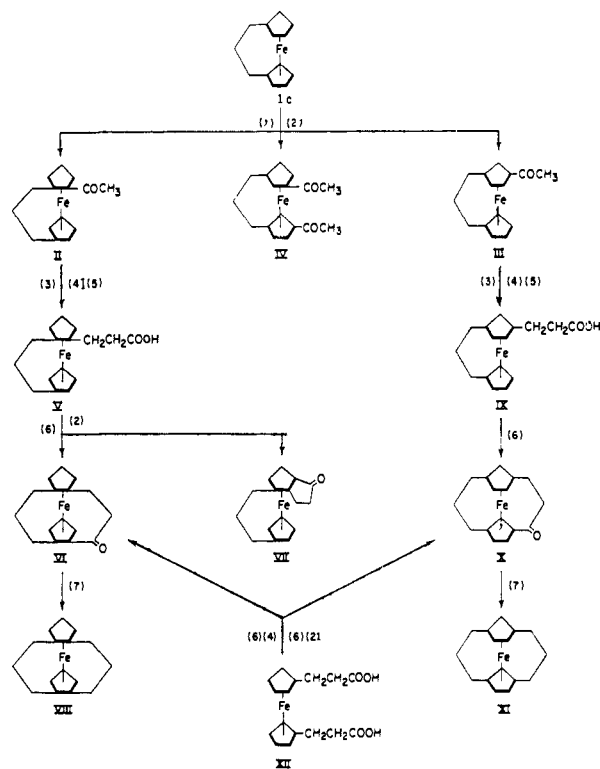(17) (a) M. Rosenblum, *Chem. Ind.* (London), 953 (1958); (b) *J. Am. Chem. Soc.*, **81**, 4530 (1959).

acetic anhydride–aluminum chloride (cf. Table I). Their structures may be assigned definitively from their infrared spectra (Table III), since the 2-acetyl isomer (like other 2-acetyl-1,1′-dialkylferrocenes)[15] contains a strong band at 1260 cm.$^{-1}$ and the 3-acetyl isomer[15] contains a strong band at 1290 cm.$^{-1}$. Confirmation of this assignment is found in the prior elution of the 2-acetyl isomer from alumina,[15,16] in the shorter wave length but higher extinction coefficient of the 2-acetyl isomer's ultraviolet maximum near 230 mμ (Table IV),[15] and in the n.m.r. spectra of the two isomers, discussed below. The over-all yield of VIII from II was 19%, while the yield of XI from III was 46%. Cyclization of 1,1′-trimethyleneferrocene-2-propionic acid (V), the intermediate en route to VI, gave, in addition to 19% (over-all from II) of VI, 5% of the homoannularly cyclized ketone VII. This observed homoannular cyclization is undoubtedly the result of steric hindrance by the trimethylene bridge at the 2′-position of the second ring, since homoannular cyclization was not observed in the cyclization of the unsubstituted ferrocenepropionic acid[1] or of the bridged 3-propionic acid (IX).

An alternative route to VI and X in the present study was that employed earlier by Schlögl and Seiler[13] and described above, from 1,1′-ferrocenedipropionic acid (XII) obtained here in 50% yield from 1,1′-diacetylferrocene. Although the earlier authors reported only one isomer (X) from this reaction sequence, we have isolated both VI and X, identical with the compounds obtained from the 2-acetyl- and 3-acetyl-1,1′-trimethyleneferrocenes, II and III, respectively. The failure of Schlögl and Seiler to observe both isomers could lie in some purification step, since in the present work no attempt was made to purify the intermediates between the dipropionic acid XII and the keto-dibridged compounds VI and X. In contrast to the results of the route from II, no homoannularly cyclized

Fig. 1.—Synthetic routes to 1,1′;2,2′- and 1,1′;3,3′-bis-(trimethylene)-ferrocene (VIII and XI): numbered steps: (1) (CH$_3$CO)$_2$O, AlCl$_3$; (2) chromatographic separation; (3) NaH, CO(OC$_2$H$_5$)$_2$; (4) H$_2$, PtO$_2$, CH$_3$COOH; (5) NaOH then H$_3$PO$_4$; (6) (CF$_3$CO)$_2$O; (7) LiAlH$_4$–AlCl$_3$.

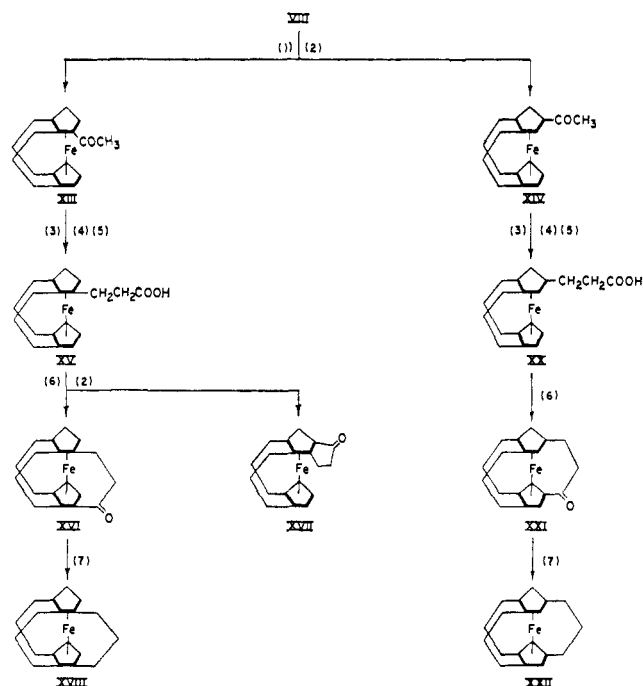Fig. 2.—Products from 1,1′;2,2′-bis-(trimethylene)-ferrocene (VIII); numbered steps same as in Fig. 1.

Fig. 3.—Products from 1,1′;3,3′-bis-(trimethylene)-ferrocene (XI); numbered steps same as in Fig. 1.

product (VIII) was isolated in the route from XII. This is not surprising since only a small amount of VI (1% vs. 32% of X) was found and the amount of VII would be only about one-fourth that of VI.

From the α-di-bridged VIII it was possible to prepare both isomeric tri-bridged compounds 1,1′;2,2′;3,3′- and 1,1′;2,2′;4,4′-tris-(trimethylene)-ferrocenes, XVIII and XXII, respectively, employing the general procedures described above (Fig. 2). Here again, the first step involved acetylation (cf. Table I), this time to give 3-acetyl- and 4-acetyl-1,1′;2,2′-bis-(trimethylene)-ferrocenes (XIII and XIV, respectively). The infrared spectra of the isomers were of less direct help in establishing their structures in this case, since trisubstituted ferrocenyl rings have not previously been investigated. Other evidence for the structures were the longer wave length but lower extinction coefficient of the 4-acetyl isomer maximum near 225 mμ (cf. Table IV), the prior elution from alumina of the 3-acetyl isomer and, conclusively, the n.m.r. spectra of the two compounds which are discussed below. The over-all yield of XVIII from XIII was 8%, that of XXII from XIV was 47%. Here again, in the isomeric pair of propionic acids XV and XX, the less hindered propionic acid XX gave only heteroannular cyclization, while the more hindered XV gave a mixture of heteroannularly and homoannularly cyclized ketones, XVI and XVII, respectively. In this case, homoannular cyclization predominated (9% yield of XVI from XIII, 19% yield of XVII). The structures of the two cyclization products were established by their n.m.r. and their ultraviolet spectra (Table IV), either of which were definitive (cf. below).

From the β-di-bridged XI it was only possible to prepare the 1,2,4-tri-bridged XXII (Fig. 3) as attempts to cyclize the propionic acid XXV with trifluoroacetic anhydride gave only a compound tentatively identified as the trifluoromethyl ketone XXVI, and unchanged acid. Trifluoromethyl ketone formation was observed earlier as a side reaction in the preparation of 1,1′-α-ketotrimethyleneferrocene (I) from β-ferrocenylpropionic acid[1]; here, probably due to steric resistance to closure between the two trimethylene bridges, it is the
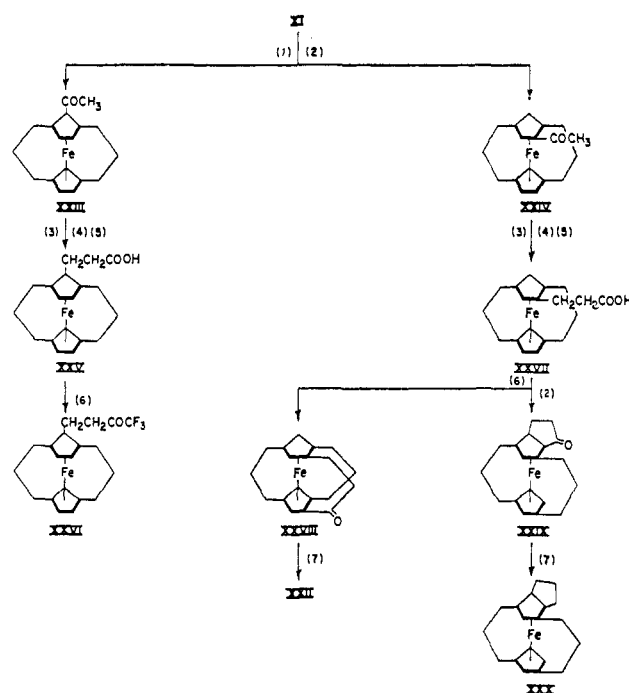
sole reaction. An attempt to cyclize the propionic acid XXV in polyphosphoric acid gave tar and the Friedel–Crafts reaction of its acid chloride gave only recovered starting material. By contrast, the preparation of the 1,1′;2,2′;4,4′-tris-(trimethylene)-ferrocene proceeded quite smoothly, in 28% over-all yield from 4-acetyl-1,1′;3,3′-bis-(trimethylene)-ferrocene (XXIV). The latter compound, together with its 2-acetyl isomer XXIII, was obtained by acetylation (Table I) of the β-dibridged compound XI. The structures of the acetyl isomers followed directly from their n.m.r. spectra, discussed below, but were also inferred from their relative yields (4-acetyl > 2-acetyl), from their order of elution from alumina (2-acetyl before 4-acetyl) and from the relative extinction coefficients of their ultraviolet maxima near 225 mμ (4-acetyl > 2-acetyl; cf. Table IV). As in the other sterically hindered cyclization discussed above, treatment of the intermediate 4-propionic acid XXVII with trifluoroacetic anhydride led to a mixture of heteroannularly and homoannularly cyclized ketones (XXVIII and XXIX, respectively); the latter was favored some 1.4 to 1. The structure of the former was demonstrated most conclusively by its conversion to the known XXII, identical with that obtained from XXI. The homoannular ketone XXIX was identified conclusively by its n.m.r. spectrum and the acetylation products of the reduced compound XXX (cf. below). It displayed the same characteristics as the other homoannular ketones VII and XVII in that, relative to their heteroannular isomers, all of these compounds show higher extinction coefficients near 225 mμ (Table IV) and are eluted later from alumina columns.

Discussion of the third product from acetylation of 1,1′-trimethyleneferrocene (Ic), the disubstituted 3,4′-diacetyl-1,1′-trimethyleneferrocene (IV), has been deferred until now. Its very late elution from alumina and its microanalytical values indicated that it was a diacetyl derivative of Ic, while the presence of a strong band at 1290 cm.$^{-1}$ and absence of absorption at 1260 cm.$^{-1}$ in its infrared spectrum showed it to be a β,β′-diacetyl derivative.[15,18] Barring the exceedingly un-

likely introduction of two acetyl groups on the same ring,[19] it must have been either IV or 3,3'-diacetyl-1,1'-trimethyleneferrocene. In the latter compound the two acetyl groups would be directly under one another if, as now seems clear from n.m.r. spectral considerations (cf. below), trimethylene-bridged ferrocenes are found predominantly in the eclipsed conformation. That the diacetyl compound is not the 3,3'-isomer is seen from the double ring closure of the dipropionic acid XXXI derived from IV, when subjected to the same series of reactions as that employed above for ferrocenedipropionic acid. The products of this reaction sequence were the same heteroannular and homoannular ketones (XXVIII and XXIX, respectively) obtained from cyclization of XXVII; thus the structure of IV is established. The 3,4'-diacetyl isomer might well have been predicted (and not the 3,3'-isomer) from the known steric requirements of the Friedel–Crafts reagent.

$$IV \rightarrow$$

XXXI

$$\rightarrow XXVII \rightarrow XXVIII + XXIX$$
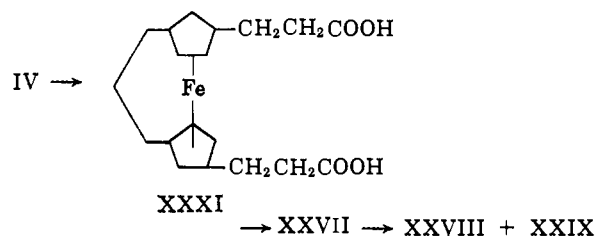
Although the n.m.r. spectra of XXII and XXX are conclusive in establishing their structures, additional evidence in distinguishing between them is provided by their acetylation products. The tri-bridged compound XXII is quite symmetrical and would be expected to give only one monoacetylation product, which it does (in 82% yield). On the other hand, compound XXX should give three isomeric monoacetylation products. Acetylation of XXX did, indeed, give a mixture of monoacetyl derivatives and evidence was obtained for the presence of at least three of these. One derivative, 4'-acetyl-1,1';2,2';4,5-tris-(trimethyl-

$$XXII \rightarrow$$

XXXII

$$XXX \rightarrow$$

XXXIII   +

XXXV

+

XXXIV

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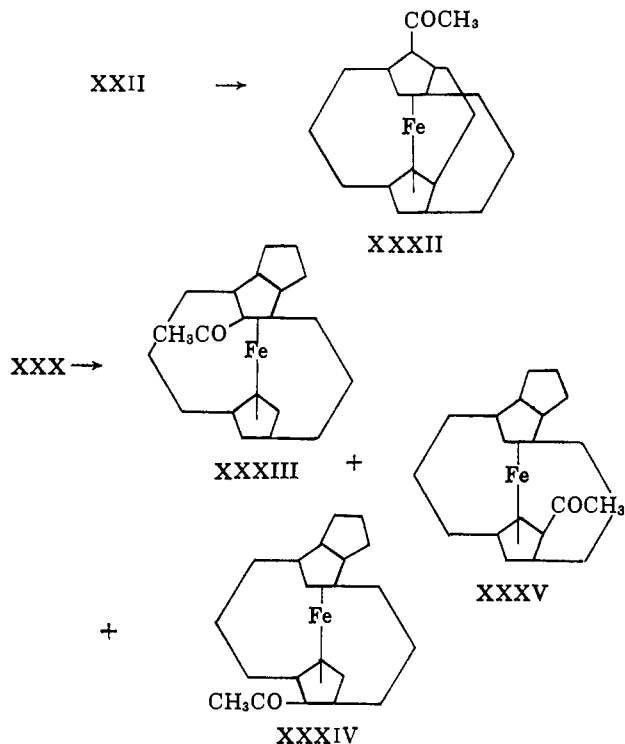
(18) K. L. Rinehart, Jr., and K. L. Motz, *Chem. Ind.* (London), 1150 (1957).

(19) J. H. Richards and T. J. Curphey, *ibid.*, 1456 (1956).

ene)-ferrocene (XXXV), was obtained in pure form, but the other two isomers could not be separated on alumina. However, the n.m.r. spectrum of the mixture establishes the presence of the two isomers (XXXIII and XXXIV).

Acetylation Ratios.—The directive influence of substituent groups on the position of further substitution of the ferrocene nucleus has been of interest in ferrocene chemistry from the outset with the early observation that acetylation of acetylferrocene gives predominantly the heteroannular · product, 1,1'-diacetylferrocene.[19-21] Other studies of acetylations have centered on the mono- and diarylferrocenes,[22,23] and acetamidoferrocene recently has been shown to give almost exclusively 1'-acetyl-1-acetamidoferrocene.[24] Other reactions for which selectivity has been studied include aminomethylation of mono- and 1,1'-di-(methylthio)-ferrocenes,[25] and lithiation of 1,1'-dimethylferrocene (treatment with n-butyllithium and subsequent carboxylation),[26] which gave a 1:2 ratio of 2-carboxylic acid to 3-carboxylic acid with little or none of the acetic acid (which would arise from methyl group lithiation).

Of greatest pertinence to the present investigation, whose results are presented in Table I, are the carbon-

TABLE I
ACETYLATION OF ALKYL FERROCENES

Ferrocene	Conversion[a] (and yield[b]),%	Acetyl products, relative amounts			Isomeric activity coefficients[c]
		2-	3-	4-	
1,1'-Dimethyl-[d]	72	1.0	2.3	..	2.3
Ethyl-[e]		1.0	3.0[g]	..	3.0
1,1'-Diisopropyl-[d]	45(76)	1.0	4.3	..	4.5
Ic[f]	74(81)	1.0	1.60	..	1.60
VIII[f]	71(91)	..	1.45	1.00	1.38
XI[f]	81(96)	1.0	..	2.73	1.37
XXII[f]	82(95)	..	..	..	..

[a] Total of all acetyl products. [b] Based on recovered bridged ferrocene. [c] Ratio of amounts of homoannularly isomeric products, statistically corrected for number of available positions; expressed as less hindered isomer/more hindered isomer, e.g., 3-acetyl/2-acetyl for Ic. [d] Ref. 15 in text. [e] Ref. 16 in text. [f] Structures in text. [g] Plus 1.8 parts 1'-acetyl isomer.

ylation (Vilsmeier reaction) of 1,1'-trimethyleneferrocene (Ic), from which only the 3-carboxaldehyde was reported,[13] and the acetylation of other alkylferrocenes (Table I).[15,16] Earlier acetylations of alkylferrocenes have showed rather low stereoselectivity. As expected, the alkyl group exerts an activating effect on the ring bearing it[16] and the ratio of 2-isomer to 3-isomer decreases with alkyl bulk (cf. Table I).[15] However, in the dimethyl compound steric and electronic factors are rather well balanced and the reactivities of the two positions are not greatly dissimilar; even in the diisopropyl compound 18% of the acetyl product consists of the 2-isomer.

In the present acetylation studies good conversions to acetyl products have been obtained (and better yields), but even less stereoselectivity has been observed (Table I). In the mono-bridged Ic the propor-

(20) R. B. Woodward, M. Rosenblum and M. C. Whiting, *J. Am. Chem. Soc.*, **74**, 3458 (1952).

(21) A. N. Nesmeyanov, E. G. Perevalova, R. V. Golovnya, T. V. Nikitina and N. A. Simukova, *Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk*, 739 (1956).

(22) M. Rosenblum, *J. Am. Chem. Soc.*, **81**, 4530 (1959).

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

(24) K. L. Rinehart, Jr., R. E. Bozak, P. A. Kittle, H. Grubert and L. F. Westman, paper in preparation.

(25) G. R. Knox, P. L. Pauson and G. V. D. Tiers, *Chem. Ind.* (London), 1046 (1959).

(26) K. L. Rinehart, Jr., J. T. Marvel, L. F. Westman and F. B. Miles, paper in preparation. Dimethylferrocene earlier was reported to be unreactive to butyllithium [A. N. Nesmeyanov, E. G. Perevalova, Z. A. Beinoravichute and I. L. Malygina, *Doklady Akad. Nauk S.S.S.R.*, **120**, 1263 (1958)], but yields as high as 44% have been obtained.

tion of 2-isomer formed is still higher (1:1.60) than with 1,1'-dimethylferrocene.[15] It is rather difficult to ascribe this result to electronic factors. Inductive effects should not be greatly different in bridged and non-bridged alkyl-substituted systems and, while possible hyperconjugative effects might be different due to some preferred conformation required for hyperconjugative electron release, the relative effect of this requirement should be about equal on the two positions. The most plausible explanation appears to employ steric effects, for the effective bulk of the trimethylene bridge is undoubtedly less than that of a rotating alkyl group, even methyl, in the region above the ferrocene nucleus, but probably greater in the region between the cyclopentadienyl rings. While the present results are not definitive, their lack of stereoselectivity does not support here a Friedel–Crafts acetylation mechanism involving initial attack of the ferrocene nucleus from a lateral direction to form a bridged complex between the rings, as has been suggested elsewhere.[23,26a]

Acetylation ratios of the di-bridged compounds VIII and XI do not differ greatly from that of the mono-bridged Ic. Although the *more* hindered 3-acetyl isomer is actually formed in greater yield from VIII, and the less hindered 4-acetyl isomer is strongly favored from XI, these are largely statistical effects and the relative activity coefficients (Table I) of the two positions are in each case about 1.4. While the less hindered positions are still favored, the striking result is that this is even less so in VIII and XI than with the mono-bridged Ic. The small difference between the activity coefficients 1.6 and 1.4 is probably not of much significance and one is reluctant to seek a principal cause among the tangle of overlapping influences. What is evident is that here, again, steric effects are surprisingly small and that, especially in the 1,3-di-bridged compound XI, an intermediate Friedel–Crafts complex formed by initial attack between the cyclopentadienyl rings seems unlikely.

Table II presents the ratios of isomers resulting from trifluoroacetic anhydride cyclization of the intermediate propionic acids V, IX, XII, XV, XX, XXV, XXVII and XXXI. In contrast to the Friedel–Crafts acetylations discussed above, these cyclic acylations are exceedingly susceptible to steric influence. In reactions where heteroannular cyclization would occur at a position beta to the nearest bridge, only the bridged ketone is formed (from IX, XII and XX). However, where it is required that the heteroannular cyclization occur at an α-position, adjacent to an existing bridge, two isomers are invariably isolated (from V, XV and XXVII)—the bridged and the homoannularly cyclized ketones; from XV and XXVII the homoannular ketones are the favored products. Products isolated from the dipropionic acids XII and XXXI are those expected from results with the mono-acids.

Formation of the strained fused 5–5 ring system (a substituted dihydropentalene) seems especially strong indication of the difficulty of heteroannular cyclization adjacent to a bridge. Indeed, when cyclization was attempted between two bridges (with XXV), no heteroannular ketone was formed at all and the only product isolated was the trifluoromethyl ketone XXVI. Since in these cyclization reactions the attacking group (a form of the acylium ion or its trifluoroacetoxy derivative) must approach the second ring from the region between the two rings, and it is subject to the considerable steric hindrance from the trimethylene bridge, the observation that Friedel–

(26) J. H. Richards, 135th National American Chemical Society Meeting, Boston, Mass., April, 1959; cf. Abstracts, p. 86-O.

Crafts acetylation of the same compounds is not subject to this steric hindrance may be taken as additional evidence that attack in their Friedel–Crafts reaction is from a direction other than from the region between the rings.

TABLE II
PROPIONIC ACID CYCLIZATIONS

	Conversion to ketones,[a] %			Conversion to ketones,[a] %	
Acid	Homo-annular	Hetero-annular	Acid	Homo-annular	Hetero-annular
V	5	19	XX	..	47
IX	..	60	XXV	..	..[c]
XII	..	44[b]	XXVII	37	30
XV	19	9	XXXI	13	14

[a] In trifluoroacetic anhydride. [b] 1,3-Di-bridge, 43%; 1,2-di-bridge, 1%. [c] Only trifluoromethyl ketone was isolated.

Infrared Spectra.—Infrared spectra of the acylferrocenes prepared contain the usual aromatic carbonyl stretching band between 1686 and 1640 cm.$^{-1}$ (*cf.* Table III) and, in most cases, the previously noted[15]

TABLE III
INFRARED BANDS OF ACYLFERROCENES

Acylferrocene	Phase[a]	Bands, cm.$^{-1}$	
Acetylferrocenes		1662[g]	..
Acetyl-[b]	N	1661	1285
2-Acetyl-1,1'-dimethyl-[b]	S	1667	1275
3-Acetyl-1,1'-dimethyl-[b]	N	1666	1299
II[c]	CCl₄	1667	1284
III[c]	CCl₄	1664	1290
XIII[c]	KBr	1657	1296
XIV[x]	KBr	1659	..
XXIII[c]	KBr	1668	1289
XXIV[c]	KBr	1644	1290
XXXII[c]	KBr	1640	1294
XXXIII[c]	CCl₄	1668	..
XXXIV[c]	CCl₄	1668	..
XXXV[c]	KBr	1659	1295
1,1'-Diacetyl-	CCl₄	1670	..
2,2'-Diacetyl-1,1'-dimethyl-[d]	CS₂	1673	1274
3,3'-Diacetyl-1,1'-dimethyl-[d]	CS₂	1676	1298
IV[c]	N	1662	1293
Acetophenone[b]	S	1683	1269
Bridged ketones		1671[h]	
1,1'-α-Ketotrimethylene-[e]	N	1682	1266
VI[c]	KBr	1680	1285
X[c]	KBr	1665	1284
XVI[c]	KBr	1673	..
XXI[c]	KBr	1656	1285
XXVIII[c]	KBr	1670	1290
Homoannular ketones		1685[i]	
VII[c]	KBr	1686	1298
XVII[c]	KBr	1685	..
XXIX[c]	KBr	1683	1295
1,2-α-Ketotetramethylene-[e]	N	1679	1281
1,2-α-Ketopentamethylene-[e]	N	1655	1290
Indanone[f]	KBr	1706	1277

[a] KBr = potassium bromide pellet; N = Nujol mull; S = liquid smear; CS₂ = carbon disulfide solution; CCl₄ = carbon tetrachloride solution. [b] Ref. 15 in text. [c] Formulas in text. [d] Ref. 29 in text. Band positions of *cis* and *trans* isomers are the same. [e] Ref. 4 in text. [f] Sadtler Standard Spectra no. 4890. [g] Average value of acetylferrocenes in Table. [h] Average value of bridged ketones in table. [i] Average value of ferrocyclopentenones in table.

strong second band near 1290 cm.$^{-1}$. There is considerable individual variation of the carbonyl stretching frequency among the compounds studied, but there is general correlation with ketonic type—acetyl, bridged ketone or ferrocyclopentenone—and the stretching frequency increases in the order named. Thus, this band appears in the acetylferrocenes of Table III be-

tween 1640 and 1668 cm.$^{-1}$, at an average value of 1660 cm.$^{-1}$, some 24 cm.$^{-1}$ more "aromatic" than the band of acetophenone. The carbonyl stretching frequencies of the bridged ketones are generally higher (1656–1680 cm.$^{-1}$, average 1671 cm.$^{-1}$) than those of the acetyl derivatives. This may be attributed to their decreased "aromatic" character since the axis of the carbonyl group of the bridge is, of necessity, inclined to the plane of the cyclopentadienyl ring; the decrease in aromaticity is, however, more manifest in the ultraviolet spectra of the bridged ketones, discussed below.[27] A still stronger effect, due to the 5-membered ring, is exhibited in the stretching frequencies (near 1685 cm.$^{-1}$) of the homoannularly cyclic ketones VII, XVII and XXIX, which are considerably higher than those of the acetyl compounds although their ultraviolet maxima are similar in position and magnitude (*cf.* below). The same small-ring effect is manifest in a comparison of the infrared bands of acetophenone and indanone.[28] As expected, the corresponding ferroçocyclohexenone and -cycloheptenone display more normal acylferrocene carbonyl stretching frequencies.

It was noted earlier[15,16] that 2-acetyl-1,1'-dialkylferrocenes contain a second band near 1270 cm.$^{-1}$, at a lower frequency than the 3-acetyl isomers (band near 1290 cm.$^{-1}$) and this correlation held for the diacetyldimethylferrocene isomers.[29] In the present compounds the simplest series—containing the mono- and diacetyl derivatives II, III and IV of the mono-bridged Ic—follows the same pattern; II contains a band at 1284 cm.$^{-1}$, III at 1290 cm.$^{-1}$ and IV at 1293 cm.$^{-1}$. However, in the more complex pairs of isomers the correlation fails and it is apparently not applicable to multi-substituted cyclopentadienyl rings; the band in question is at the same position in the spectra of XXIII and XXIV and is missing from the spectrum of XIV, though found at 1296 cm.$^{-1}$ in the spectrum of XIII. The correlation, suggested by Rosenblum,[23] of bands in the 10.9–11.3 μ region, does not appear to hold here.

Ultraviolet Spectra.—Ultraviolet spectra of the ketones prepared are summarized in Table IV. As was noted earlier for the acetyldialkylferrocenes,[15] acylferrocenes give strong ultraviolet maxima near 230 and 265 mμ. This is confirmed in the present series of compounds (Table IV) and it is noted that most of them also contain a less intense maximum near 340 mμ. In the earlier study[15] it was noted that the "230 mμ" maximum of the 2-acetyl isomer is more intense, but appears at shorter wave length, than that of the 3-acetyl isomer (*cf.* 2-acetyl- and 3-acetyl-1,1'-dimethylferrocenes in Table IV) and this correlation holds for the mono-bridged system here, too (*cf.* II and III), but is not applicable to the more complex systems (*cf.* XIII and XIV, XXIII and XXIV).

Of special interest are the compounds with an acetyl group between two bridges (XXIII, XXXII, XXXIII and XXXIV). Since the carbonyl groups are sterically hindered from achieving coplanarity with the cyclopentadienyl ring, the extinction coefficients are considerably lower than in other acetylferrocenes. Another compound (XXXV), in which an acetyl group is fixed directly under an alkyl residue on the other cyclopentadienyl ring, is also unusual in that its "230 mμ" band is at longer wave length than usual (though of

(27) Ring strain is here of little importance and should, if anything, lower the stretching frequency due to slight spreading of the valence angles required for formation of the 3-carbon bridge.

(28) L. J. Bellamy, "Infrared Spectra of Complex Organic Molecules," 2nd ed., John Wiley and Sons, New York, N. Y., 1958, p. 148.

(29) K. L. Rinehart. Jr., and K. L. Motz, *Chem. Ind.* (London), 1150 (1957).

TABLE IV

ULTRAVIOLET MAXIMA OF ACYLFERROCENES

Acylferrocenes	λmax, mμ (εmax)[a]		
Acetylferrocenes	228(15,000)[g]		
Acetyl-[b]	226(16,500)	269(6500)	
2-Acetyl-1,1'-dimethyl-[b]	227(18,600)	271(6800)	
3-Acetyl-1,1'-dimethyl-[b]	232(15,800)	274(6600)	
II[c]	222(15,300)	264(7140)	
III[c]	228(13,780)	263(6490)	338(1574)
XIII[c]	230(16,420)[j]	268(4810)	332(968)
XIV[c]	231(14,200)	264(8790)	343(2540)
XXIII[c]	227(11,520)	256(5450)	
XXIV[c]	222(14,100)	254(9150)	336(1965)
XXXII[c]	230(9,260)	261(5960)	312(1927)
XXXV[c]	237(12,350)	245(2921)	
1,1'-Diacetyl-	224(8,030)	262(5950)	
2,2'-Diacetyl-1,1'-dimethyl-[d]	226(17,300)[k]	(15,800)[l]	
3,3'-Diacetyl-1,1'-dimethyl-[d]	231(18,100)[k]	(16,700)[l]	
IV[c]	220(13,670)	263(11,820)	320(1850)
Acetophenone[b]	242(12,000)		
Bridged ketones	228(6600)[h]		
1,1'-α-Ketotrimethylene-[e]	227(8030)	265(2350)	335(648)
VI[c]	224(7320)	264(2400)	340(513)
X[c]	228(4380)	262(1778)	332(643)
XVI[c]	228(6880)	267(2200)	340(440)
XXI[c]	230(3890)	260(2140)	330(815)
XXVIII[c]	230(9500)		333(1332)
Homoannular ketones	226(15,800)[i]		
VII[c]	226(13,400)	266(5025)	330(1015)
XVII[c]	228(17,450)	263(8820)	335(1642)
XXIX[c]	225(16,300)	257(7140)	327(1292)
1,2-α-Ketotetramethylene-[e]	226(17,600)	270(7500)	
1,2-α-Ketopentamethylene-[e]	227(15,500)	269(7400)	
Indanone	243(9,320)	288(2065)	

[a] Determined on solutions in 95% ethanol. [b–i] Same as Table III. [j] Estimated. [k] *cis*-Isomer. [l] *trans*-Isomer.

somewhat lower intensity), but its "265 mμ" band is shifted hypsochromically all the way to 245 mμ and is of very low intensity. If these compounds (XXIII, XXXII, XXXIII, XXXIV and XXXV) are omitted, the average extinction coefficient of the "230 mμ" band of the monoacetylferrocenes in Table IV is 15,600. This is not greatly different for the corresponding "230 mμ" band of the diacetylferrocenes shown. However, the "265 mμ" band is about twice as intense in the diacetyl compounds, suggesting that this band is due to an electronic transition involving a carbonyl group and one ring only. The same effect may be noted in comparing the ultraviolet spectra of 1,2-α-ketotetramethyleneferrocene and 1,2;1',2'-bis-(α-ketotetramethylene)-ferrocene.[1]

Ultraviolet maxima of the homoannular ketones are very similar, both in position and intensity, to those of the acetylferrocenes. By contrast, the bridged ketones are quite abnormal in that all three maxima—"230 mμ," "265 mμ," "340 mμ"—are of much lower intensity than those of the acetylferrocenes and homoannular ketones. This is especially true of the "230 mμ" band which appears as only a shoulder in some spectra. The low intensity of these bridged ketone spectra is undoubtedly due to the geometry of the 3-carbon bridge, which requires that the carbonyl group be oriented skew to the ring, with its π-electrons nearly perpendicular to the π-electron system of the ring.
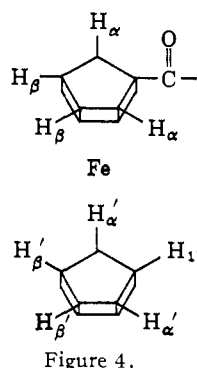
Figure 4.

Since the electronic transitions involved require overlap of the carbonyl and ring π-electrons, their lack of coplanarity reduces the transition probability (hence the ϵ_{max}).

Nuclear magnetic resonance spectra of the compounds prepared in the present study, summarized in Table V, demonstrate a number of interesting effects and regularities. Simplest to interpret[30] are the spectra of the alkyl and alkyl-bridged ferrocenes. Ring proton signals of an alkylferrocene are shifted to ca. 0.1 p.p.m. higher field (compared to ferrocene; cf. values of ethylferrocene and 1,1'-dimethylferrocene in Table V), as expected from alkylbenzene results,[31] and, while this effect is most apparent on the alkyl-substituted ring, it can be slightly manifest on an unsubstituted ring (cf. 1'-proton of methylferrocene vs. protons of ferrocene). There is, however, very little distinction between the 2- and 3-protons of a freely rotating monoalkyl substituted ring.

The same upfield shift on alkyl substitution is seen in the ring proton spectra of all the bridged ferrocenes of Table V. Here, however, there is a differential shift of the protons of the ring; this differentiation is observed even in the spectrum of Ic[32] and is pronounced in the di-bridged VIII and XI. The chemical shift difference between the 2- and 3-protons was originally ascribed to tilting of the cyclopentadienyl rings[10] and is most pronounced in Ih, with a 2-carbon bridge. In that note[10] the protons at higher field were assigned to the 2-position and it was suggested that this is due to their proximity to the iron nucleus.

(30) Only the chemical shifts of the cyclopentadienyl ring protons are discussed here. In general, the side-chain protons appear at normal positions, e.g., acetyl methyl near τ 7.90, so long as they are in open chains. Ring formation gives rise to very complicated spectra in the alkyl region, though occasionally fortuitous simplification occurs due to coincidence of chemical shifts, as in the three methylene groups of Ic, which all occur at τ 8.22, and the two methylene groups of Ia, which both occur at τ 7.13. The alkyl regions of some of these spectra will be discussed in a subsequent paper [K. L. Rinehart, Jr., K. L. Motz, C. D. Mitchell, S. Moon and D. E. Bublitz, in preparation]. It may be assumed throughout the present discussion of ring protons that peak areas and splitting patterns correspond to those expected; indeed, they were employed in making the assignments given. Coupling constants between adjacent ("ortho") protons in the simpler systems are approximately 2.5 c.p.s. and those between "meta" protons are about 1.5 c.p.s. These results parallel those in substituted benzenes, where ortho coupling constants are larger than meta.[31]

(31) L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, New York, N. Y., 1959, p. 63.

(32) Differentiation between the 2- and 3-protons is observed in benzene solution, as originally noted by Richards and Hill (139th National A.C.S. Meeting, St. Louis, Mo., March 21–30, 1961; cf. Abstracts, p. 11-O), and this solvent has been employed in the present study. The 2- and 3-protons of Ic occur at the same position in the less diamagnetically anisotropic chloroform.[10] Solvent effects on the n.m.r. spectra of aromatic compounds have been discussed by Diehl [Helv. Chim. Acta, **45**, 568 (1962)], who noted that there is frequently a differential solvent effect at the different positions of substituted benzenes. This is also true in the present study and, indeed, the differential between the chemical shifts of different ferrocene protons is not always greater in benzene solution (cf. VI in chloroform and benzene); this was also noted for substituted benzenes by Diehl. In the present study the recorded chemical shifts are usually lower (0.1 to 0.4 p.p.m.) in chloroform than in benzene solution.

In the present study the assignment of the higher field protons as those nearer the iron atom has been confirmed by the area ratios of VIII and XI. Of particular interest are the 2-protons of XI, which occur at very high field (τ 6.43). This is felt to be due to the combined inductive effects of the two alkyl bridges, plus the enhanced proximity of the 2-proton to the iron nucleus, a result of the fulcrum nature of the two trimethylene bridges. For comparison, the six ring protons of 3,3'-diethyl-1,1'-dimethylferrocene appear as a singlet at τ 6.26.[30] Spanning the 2- and 2'-positions with a third trimethylene bridge (as in XVIII) leaves the 4- and 5-protons still relatively removed from the iron nucleus, but the introduction of a third bridge in the 4,4'-position (as in XXII) pulls the two rings together and, though two of the protons (the former H-2 and H-2') are now slightly further from the iron atom and occur at somewhat lower field (τ 6.37 vs. 6.44), the two others (the former H-5 and H-5') are considerably closer and occur at higher field (τ 6.37 vs. 6.14). Another interesting effect is shown in the positions of the 4'- and 5'-protons of XXX which occur at τ 6.44 (as do H-2 and H-2' of XXX). This upfield shift of 0.30 p.p.m. from the corresponding protons of XI probably is due to shielding by the homoannular trimethylene cycle of the 4'- and 5'-protons from the field of the other cyclopentadienyl ring.

The ring proton spectra of those compounds of Table V containing keto groups are considerably more complex than the spectra of those with only alkyl substituents. The deshielding or shielding effect of a carbonyl group depends not only on its position in the molecule, but also on its conformation. As pointed out by Jackman[33] and by Pople,[34] the diamagnetic anisotropy of the carbonyl group leads to regions of shielding in cones above and below the plane of the carbonyl group and to regions of deshielding elsewhere about the group, if the principal magnetic susceptibility (X_1) is perpendicular to this plane. As discussed elsewhere,[35] a positive (or shielding) region has indeed been observed above the π-electrons of the olefinic bond and also above the benzene ring, while the more common deshielding effects in other (negative) regions about olefins, aromatic nuclei and carbonyl groups are well recognized.[36]

Many of the ketones prepared in the present study are good models for a study of the anisotropy of the carbonyl group since they provide a rigid matrix, with the symmetrical ferrocene nucleus locked by its trimethylene bridges, and with many of the carbonyl groups forced into known geometry, either by the requirements of ring formation or by steric compression of adjacent groups.

It is perhaps clearest to deal with the compounds in groups according to the ketone type. In each of the bridged ketones the plane of a carbonyl group, adjacent to one ring, is essentially perpendicular to the cyclopentadienyl rings, a conformation confirmed by their ultraviolet spectra (cf. above). Some of these bridged ketones are highly symmetrical and the spectra of all of them are interpretable on comparison to the corresponding alkyl-bridged compounds. For purposes of discussion it is useful to classify the effects of the carbonyl group according to the protons on which they are exerted. Thus, in a rigid ferrocene system (Fig. 4), there may be protons *alpha* and *beta* to the substituent (at position 1) on the same ring and corresponding protons on the second ring (i.e., α'-, β'-

(33) Reference 31, pp. 122–124.

(34) J. A. Pople. Proc. Roy. Soc. (London), **A239**, 541, 550 (1957).

(35) For a review, cf. ref. 31, pp. 125–130.

(36) Reference 31, Chapt. 4.

TABLE V

N.M.R. PEAKS OF FERROCENE RING PROTONS[a]

	2-	3-	4-	5-	1'-	2'-	3'-	4'-	5'-	Coupling, c.p.s.
				Chemical shifts at ring positions, τ and multiplicity[b]						
Alkyl and alkyl-bridged ferrocenes										
Ferrocene	6.00s	6.00	6.00	6.00	6.00	6.00	6.00	6.00	6.00	
Ferrocene[d]	5.85s	5.85	5.85	5.85	5.85	5.85	5.85	5.85	5.85	
Methyl[c]	6.07s	6.07	6.07	6.07	6.03	6.03	6.03	6.03	6.03	
Dimethyl[c]	6.11sb	6.11	6.11	6.11	..	6.11	6.11	6.11	6.11	
Ic	6.14t	5.99t	5.99	6.14	..	6.14	5.99	5.99	6.14	
Ic[d]	6.04s	6.04	6.04	6.04	..	6.04	6.04	6.04	6.04	
Ih	6.01t	5.46t	5.46	6.01	..	6.01	5.46	5.46	6.01	
Ih[d]	6.04t	5.37t	5.37	6.04	..	6.04	5.37	5.37	6.04	
VIII	..	6.20d	5.89t	6.20	..	..	6.20	5.89	6.20	$J_{34} = 2.5$
XI	6.43t	..	6.14d	6.14	..	6.43	..	6.14	6.14	$J_{24} = 1.5$
XVIII	..	..	6.04s	6.04	..	..	..	6.04	6.04	
XXII	..	6.37s	..	6.37	..	..	6.37	..	6.37	
XXX	6.44sb	..	..	..	..	6.44	..	6.44	6.44	
Bridged ketones										
Ia	5.38m	5.95m	5.95	5.38	..	5.78m	6.23m	6.23	5.78	
Ia[d]	5.25sb	5.68sb	5.68	5.25	..	5.45sb	6.04sb	6.04	5.45	
VI	..	5.67t (u)	6.11m[e]	6.11	..	..	5.85t (u)	6.11	6.46t (u)	
VI[d]	..	5.30t (u)	5.86m[e]	5.86	..	..	5.47t (u)	5.86	6.19t (u)	
X	5.54t	..	5.38q	6.06q	..	5.86t	..	5.77t	6.42t	$J_{24} = 1.5$ $J_{25} = 1.5$ $J_{45} = 2.4$
XVI	..	..	5.52d	6.14d	..	..	..	5.74d	6.25d	$J_{45} = J_{4'5'} = 2.5$
XXI	..	5.67s	..	5.67	..	..	5.97s	..	5.97	
XXVIII	6.30d	..	..	5.66d	..	6.62d	..	..	5.88d	$J_{25} = J_{2'5'} = 1.5$
Acetylferrocenes										
Acetyl[c]	5.40t	5.94t	5.94	5.40	6.18s	6.18	6.18	6.18	6.18	
Acetyl[d]	5.28t	5.54t	5.54	5.28	5.80s	5.80	5.80	5.80	5.80	
II[d]	..	5.46t	5.76m[h]	6.34m[i]	..	5.76	5.76	6.14	6.33m[j]	
III[d]	5.47m	..	5.47	5.86m	..	6.17sb	5.86	5.86	6.17	
XIII	..	..	5.65d	6.15d	..	..	6.40m[f]	5.95t	6.40	$J_{45} = 2.8$
XIV	..	5.83s	..	5.80	..	..	6.20m[g]	6.20	6.20	
XXIII	..	..	6.06s	6.06	..	6.18t (u)	..	6.26d (u)	6.26	
XXIV	6.28m	..	..	5.83d	..	6.62t (u)	..	6.28	6.10q (u)	$J_{25} = 1.7$
XXXII	..	..	..	6.31s	..	..	6.26d	..	6.54d	$J_{3'6'} = 1.35$
XXXIII	..	..	..	..	..	6.25sb	..	6.62d (u)	6.62	$J_{2'4'} = 1.4$
XXXIV	6.25s	..	..	..	..	..	..	6.38s	6.38	
XXXV	6.69s	..	..	..	..	6.22d	..	..	6.15d	$J_{2'5'} = 1.7$
Diacetyl[c]	5.55t	6.07t	6.07	5.55	..	5.55	6.07	6.07	5.55	
IV	5.65m	..	5.65	6.02q	..	6.02	5.65	..	5.65	$J_{25} = 1.59$ $J_{45} = 2.40$
Homoannular ketones										
XVII	..	..	..	5.70s	..	..	6.10q	6.77q	5.99t	
XXIX	6.25m	..	..	..	..	6.70t (u)	..	6.70	6.25	
Tetra[c]	..	5.91d	5.91	5.13t	6.12s	6.12	6.12	6.12	6.12	

[a] Determined on ca. 10% solutions, in benzene except as noted. [b] s = singlet, d = doublet, t = triplet, q = quadruplet, m = multiplet, sb = singlet, broad, (u) = unresolved. [c] Dimethyl = 1,1'-dimethylferrocene, methyl = methylferrocene, acetyl = acetylferrocene, diacetyl = 1,1'-diacetylferrocene, tetra = 1,2-(α-ketotetramethylene)-ferrocene. [d] Deuteriochloroform solution. [e–i] Centers of broad unresolved multiplets, approximate widths: [e] 12 c.p.s., [f] 7 c.p.s., [g] 6 c.p.s., [h] 9 c.p.s., [i] 10 c.p.s., [j] 5 c.p.s.

and 1'-protons), and the effects may be called α-, β-, α'-, β'- and 1'-effects. For example, the α- and α'- protons of XXII (which occur as a singlet at τ 6.37) are lowered to singlets at τ 5.67 and 5.97, respectively, in the spectrum of XXI. Thus, the skew carbonyl group deshields ring protons (α- and α'-) adjacent to its bridge, but the effect is greater on the protons (α) of the ring bearing the carbonyl group. A similar effect is found in the spectrum of XXVIII (compared to XXII), where the 5-proton (α) occurs at τ 5.66 and the 5'-proton (α') at τ 5.88. The spectrum of XXVIII also demonstrates two other generalities: (a) protons on the β'-position of the ring away from the carbonyl (i.e., H-2' in XXVIII) are shifted to higher field (positive β'-effect) by the carbonyl group; and (b) protons in the β-position of the ring bearing the carbonyl group (i.e., H-2 in XXVIII) are little affected by the carbonyl (small β-effect). For the six bridged ketones of Table V these rules hold well. Thus, the α-effect is always strongly negative (−0.42 to −0.89) and the α'-effect also negative but somewhat smaller (−0.34 to −0.69). The β-effect

is variable (−0.33 to +0.22) and the β′-effect always positive (+0.05 to +0.28). (If one omits the first member of the series (Ia), which is probably more flexible and whose carbonyl group is doubtless more nearly coplanar with the cyclopentadienyl ring, the values are still more consistent: α, −0.42 to −0.89; α′, −0.24 to −0.57; β, −0.08 to +0.22; β′, +0.21 to +0.28.) The α- and α′-protons are thus in the deshielding (negative) region about the carbonyl group, whose effect is greater on the nearer α-proton. The consistent shift of the β′-proton to higher field is rather unexpected, but appears to be due to no particular orientation of the carbonyl group since the same positive β′-effect is shown in the acetyl bridged ferrocenes discussed next. It seems more likely due to a reduction in the electron density of the unacylated ring by the carbonyl group, with a consequent reduction in its ring current and in its deshielding. Such transannular electron withdrawal has been demonstrated by the pK_a's of acyl-substituted ferrocenoic acids.[37]

The spectra of the acetylferrocenes are still more complex than those of the bridged ketones, partly because the acetyl groups can assume different orientations to the rings. However, self-consistent assignments can be made to all from consideration of the chemical shifts of the ring protons of the more symmetrical members of the group, XIV, XXIII and XXXII, compared to those of the corresponding unacetylated compounds VIII, XI and XXII, respectively. As is well known from benzene studies,[33,36] an acetyl group greatly deshields ring protons adjacent to it. This is also observed in the spectra of acetylferrocene itself, of XIV, and of all the other acetylferrocenes of Table V. This deshielding (α-effect) varies from −0.24 to −0.67 p.p.m. Two other generalities are apparent from the spectrum of XIV: (a) The acetyl group has little effect on ring protons (α′-protons) adjacent to the position directly under it: in XIV this α′-effect amounts to +0.01 p.p.m.; in other acetyl compounds of Table V it varies from −0.13 to +0.04 p.p.m. (b) In XIV, where the acetyl group is unhindered by adjacent substituents, it probably assumes a preferred conformation nearly coplanar with the cyclopentadienyl ring (cf. ultraviolet spectra above). In this conformation it shields the proton directly beneath it which lies in the positive cone of the carbonyl group. In the spectrum of XIV this positive 1′-effect is +0.31 p.p.m.

However, in certain other acetylferrocenes of Table V the acetyl group is forced to assume a preferred conformation with its plane perpendicular to that of the cyclopentadienyl ring. Here, as demonstrated in the spectra of XXIII and XXXII, the proton directly below the carbonyl group lies in the negative region about it and is deshielded (negative 1′-effect), by −0.25 and −0.11 p.p.m., respectively. Thus, the acetyl group may either shield or deshield a proton directly beneath it on the ferrocene nucleus, in substantiation of the suggested geometry of carbonyl diamagnetic anisotropy.[33,34] In other compounds of Table V, the acetyl groups (e.g., where adjacent to only one bridge) appear to assume a variety of conformations to the ring, and values of the 1′-effect are between the −0.25 p.p.m. of XXIII and +0.31 p.p.m. of XIV. In the spectra of XXIII and XXXII it is also clear that protons beta to the acetyl group (on the same ring) are deshielded, but less so than those alpha to the acetyl group (in other compounds). This negative β-effect varies from −0.06 to −0.28 p.p.m. Finally, β′-protons, of the unacetylated ring,

are shifted to higher field by the acetyl group, regardless of its conformation; this β′-effect varies from +0.15 to +0.21 p.p.m., a range similar to that of the β′-effect of the bridged ketones discussed above.

Conformationally purer than the acetylferrocenes are the homoannular ketones VII, XVII and XXIX. In these compounds the carbonyl group is rigidly fixed coplanar with the cyclopentadienyl ring and, as predicted from the above considerations, the ring proton directly beneath the carbonyl group (1′-proton) is shifted to considerably higher values (positive 1′-effect). In XXIX the 4′-proton, directly beneath the carbonyl, appears at 0.56 p.p.m. higher field than in XI, and in XVII this upfield shift (from VIII) amounts to 0.88 p.p.m.! Other effects parallel those of the acetylferrocenes: a rather large positive β′-effect (+0.26 p.p.m. in XXIX) and smaller β- and α′-effects (both −0.19 in XXIX).

In the discussion above, only the spectra in benzene solution have been treated, as these in general showed maximum separation of chemical shifts. As may be seen from the few chloroform spectra of Table V, differential solvent effects may be important for these compounds and the conclusions drawn are considered applicable only to benzene solutions. A case in point is the behavior of acetylferrocene itself. In benzene solution, as expected, the ring α-protons are greatly deshielded and the β-protons somewhat so, appearing at −0.60 p.p.m. and −0.06 p.p.m., respectively, relative to the signal of ferrocene; the protons of the unsubstituted ring appear at 0.18 p.p.m. higher field than those of ferrocene, i.e., they are shielded by the acetyl group. This is especially clear in the n.m.r. spectrum of a benzene solution containing equimolar quantities of acetylferrocene and ferrocene, where the unsubstituted ring protons of acetylferrocene appear as a singlet of half the area of the ferrocene singlet and at somewhat higher field than the latter. In deuteriochloroform solution the α- and β-ring protons are still shifted to lower field (−0.57 and −0.31 p.p.m., respectively, relative to ferrocene in deuteriochloroform), but the protons of the unsubstituted ring also appear at lower field (−0.05 p.p.m.) relative to ferrocene in this solvent.[38] A more general assignment of substituent effects must thus await more detailed investigations in a range of solvents.

Experimental[39]

Acetylation of 1,1′-Trimethyleneferrocene (Ic).—A solution of 0.90 g. (8.84 mmoles) of acetic anhydride in 100 ml. of methylene chloride was added dropwise under a nitrogen atmosphere to 2.00 g. (8.85 mmoles) of 1,1′-trimethyleneferrocene and 2.59 g. (19.5 mmoles) of aluminum chloride (fresh bottle) in 100 ml. of methylene chloride. The mixture was maintained at reflux during addition and for 14–18 hours longer, then was cooled and poured over ice. Ascorbic acid was added to reduce any ferricinium ions present, the layers were separated and the aqueous layer was extracted repeatedly with methylene chloride. The combined organic phases were washed with water, saturated sodium bicarbonate, and water, then dried over sodium sulfate. Methylene chloride was removed on a rotary evaporator and the

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

(38) It has been pointed out by the referee (and subsequently confirmed in this laboratory) that in carbon tetrachloride solution, too, the ring protons of the unsubstituted ring of acetylferrocene appear at lower field than those of ferrocene itself; our values for acetylferrocene are τ 5.33t (α-protons), 5.63t (β-protons), 5.87s (1′-protons) and for ferrocene τ 5.94.

(39) Melting points, uncorrected, were determined either in a Hershberg melting point apparatus or on a Kofler micro-hot-stage. Microanalyses were obtained by the University of Illinois Microanalytical Laboratory, under Mr. J. Nemeth; ultraviolet spectra on a Cary recording ultraviolet spectrophotometer, model 14, by Miss C. Juan and Mr. P. K. Hon; infrared spectra on a Perkin-Elmer spectrophotometer, model 21, and nuclear magnetic resonance spectra on a Varian n.m.r. spectrometer, model V4300b at 60 Mc. in benzene solution employing an internal tetramethylsilane standard, by Messrs. O. W. Norton and D. H. Johnson. Values are expressed in terms of the τ scale.[40] Molecular weights were determined by means of a vapor pressure osmometer, model 301-A, obtained from Mechrolab, Inc.

(40) G. V. D. Tiers, J. Phys. Chem., 62, 1151 (1958).

oily residue, in Skelly B solvent, was placed on a column of basic alumina (Merck, activity III,[41] 2.5 × 43 cm.). Elution with Skelly B developed four bands. The first band from the column yielded 0.285 g. (14%) of recovered starting material.

The second band, eluted from the column with 5% ether in Skelly B, gave (after crystallization from hexane) 0.748 g. (26%) of 2-acetyl-1,1'-trimethyleneferrocene (II), m.p. 78.0–78.5° (reported[8,42] 77.5–78.5°). Infrared, ultraviolet and n.m.r. spectral properties are reported in Tables III, IV and V, respectively.

Anal. Calcd. for $C_{15}H_{16}FeO$: C, 67.20; H, 6.00. Found: C, 67.59; H, 6.19.

The third fraction, eluted with 25% ether in Skelly B, yielded, after crystallization from hexane, 1.245 g. (44%) of 3-acetyl-1,1'-trimethyleneferrocene (III), m.p. 99–100° (reported[8,42] 100–101°). Spectral properties are summarized in Tables III, IV and V.

Anal. Found: C, 67.28; H, 6.15.

The last fraction was eluted with ether and yielded, after crystallization from hexane, 0.119 g. (4%) of 3,4'-diacetyl-1,1'-trimethyleneferrocene (IV), m.p. 131–132°. Spectral properties are summarized in Tables III, IV and V.

Anal. Calcd. for $C_{17}H_{18}FeO_2$: C, 65.80; H, 5.81. Found: C, 65.91; H, 6.01.

In the above experiment the ratio of α-isomer to β-isomer is 1 : 1.84 (including the diacetyl compound). In a series of four small-scale acetylations the ratio of α- to β-isomer was found by chromatography to be 1 : 1.60 ± 0.05, with only trace amounts of diacetylation products. In this series the molar ratio of reactants was 1.00 trimethyleneferrocene : 1.07 acetic anhydride : 2.20 aluminum chloride.

Conversion of 2-acetyl-1,1'-trimethyleneferrocene (II) to 1,1';2,2'-bis-(trimethylene)-ferrocene (VIII) was effected *via* the method employed earlier[1] for the conversion of acetylferrocene to 1,1'-trimethyleneferrocene. A solution of 1.0 g. (3.25 mmoles) of II in 150 ml. of xylene was added dropwise, under nitrogen, to a stirred mixture of 0.32 g. (6.6 mmoles) of a mineral oil dispersion of sodium hydride (50%) and 0.78 g. (6.6 mmoles) of diethyl carbonate in 225 ml. of xylene. Reflux was maintained during addition and for 12 hours thereafter, when the mixture was cooled to room temperature and hydrolyzed with ice–water containing 10 mmoles of hydrochloric acid. After separation from the aqueous phase, the organic layer was dried over magnesium sulfate. Evaporation of the solvent left the β-keto ester as a viscous red oil.

The crude β-keto ester was dissolved in 40 ml. of acetic acid and hydrogenolyzed over 1.0 g. of platinum oxide at 40 p.s.i. for 46 hours, at which time hydrogen uptake had ceased. The solution was filtered and acetic acid was removed on a rotary evaporator. A solution of the residual ester (crude, 1.1 g., 90%), in 50 ml. of ethanol and 4.0 ml. of 2 N sodium hydroxide was heated for 2 hours at reflux. The basic solution was diluted with water and washed repeatedly with ether, then acidified with phosphoric acid, and extracted again with ether. The acidic ether extract was dried over magnesium sulfate and evaporated to dryness to give 0.9 g. (crude, 89%) of the propionic acid V.

A solution of the propionic acid in 200 ml. of carbon tetrachloride, which had been previously bubbled with nitrogen, and 4.0 g. of trifluoroacetic anhydride was stirred for 4 hours in a dark, stoppered flask, then poured into an excess of sodium bicarbonate solution. The aqueous layer was extracted with methylene chloride and the organic extract was dried over magnesium sulfate, then evaporated to dryness. The residue, in a minimal amount of benzene, was placed on an alumina column (Alcoa F-20, activity III, 1.8 cm. × 60 cm.). Elution with 2% ether in Skelly B gave 0.206 g. (19% from II) of 2,2'-(α-keto-trimethylene)-1,1'-trimethyleneferrocene (VI), whose structure was assigned from its spectral properties (*cf.* Tables III, IV and V). Recrystallization from Skelly B gave 0.16 g. of red-brown crystals which underwent a form modification at 199–201° and decomposed above 220°.

Anal. Calcd. for $C_{16}H_{16}FeO$: C, 68.59; H, 5.76; Fe, 19.95; mol. wt., 280. Found: C, 68.75; H, 5.82; Fe, 19.76; mol. wt. (osmometer), 296.

Elution of the same column with 20% ether in Skelly B gave 0.053 g. (5%) of the homoannular ketone 3,2-(α-ketotrimethylene)-1,1'-trimethyleneferrocene (VII), m.p. 132.0–133.0°, also identified by its spectral properties (Tables III and IV).

Anal. Found: C, 68.25; H, 5.73; Fe, 19.77; mol. wt. (osmometer), 269.

A solution of 0.053 g. (1.9 mmoles) of the above 2,2'-(α-ketotrimethylene)-1,1'-trimethyleneferrocene (VI) in 100 ml. of ether was added dropwise to a stirred mixture of 0.30 g. (2.3 mmoles) of aluminum chloride and 0.087 g. (2.3 mmoles) of lithium aluminum hydride in 100 ml. of ether. Reflux was maintained during addition and for 30 minutes thereafter. The reaction was cooled in an ice-bath and carefully decomposed with wet ether. Water was added, the layers were separated and the organic layer was dried over magnesium sulfate, filtered, and evaporated to 0.462 g. (91%) of 1,1'; 2,2'-bis-(trimethylene)-ferrocene (VIII). Recrystallization from hexane gave 0.45 g. of yellow crystals, m.p. 216–218°, after a crystal modification at 191–192°. The material sublimed at 120° (0.05 mm.). The nuclear magnetic resonance spectrum is presented in Table V.

Anal. Calcd. for $C_{16}H_{18}Fe$: C, 72.20; H, 6.82; Fe, 20.99. Found: C, 73.14; H, 7.51; Fe, 19.03.

Conversion of 3-acetyl-1,1'-trimethyleneferrocene (III) to 1,1';-3,3'-bis-(trimethylene)-ferrocene (XI) followed precisely the procedure described above for the 2-acetyl isomer. From 10.0 g. (37 mmoles) of 3-acetyl-1,1'-trimethyleneferrocene, 3.5 g. (73 mmoles) of a mineral oil dispersion of sodium hydride (50%) and 8.8 g. (75 mmoles) of diethyl carbonate in a total of 75 ml. of benzene was obtained 12.2 g. (96%) of crude β-keto ester. From this β-keto ester was obtained, after hydrogenolysis (over 1.0 g. of platinum oxide at 40 p.s.i.) and saponification, 6.7 g. (61%) of crude propionic acid IX. From the propionic acid (6.7 g., 22 mmoles) and 25 ml. of trifluoroacetic anhydride in 200 ml. of carbon tetrachloride was obtained, after work-up and chromatography (10% ether in Skelly B eluent), 6.3 g. (60% from III) of 3,3'-(α-ketotrimethylene)-1,1'-trimethyleneferrocene (X), m.p. 107–110° (lit.[13] 110–113°), whose spectral properties are summarized in Tables III, IV and V. No isomeric ketone was obtained from the chromatography.

Anal. Calcd. for $C_{16}H_{16}FeO$: C, 68.59; H, 5.76; Fe, 19.95; mol. wt., 280. Found: C, 69.01; H, 5.83; Fe, 19.52; mol. wt. (osmometer), 280.

As in the preceding section, the ketone X, (0.73 g., 2.6 mmoles) was converted by lithium aluminum hydride (0.99 g., 26 mmoles)–aluminum chloride (5.2 g., 39 mmoles) reduction to the hydrocarbon bridged compound, 1,1';3,3'-bis-(trimethylene)-ferrocene (XI, 0.69 g. quantitative), which melted at 89.0–91.5° (lit.[13] 88–91°) after recrystallization from hexane. Nuclear magnetic resonance spectral data are presented in Table V.

Preparation of 1,1'-ferrocenedipropionic acid (XII) was effected by the procedure described earlier[1] for the preparation of the monopropionic acid. A solution of 5.60 g. (20.4 mmoles) of 1,1'-diacetylferrocene (prepared by the procedure of Rosenblum and Woodward,[16] utilizing acetyl chloride and aluminum chloride)[43] in 250 ml. of dry benzene was added dropwise during 1 hour to a stirred mixture of 3.94 g. (81.6 mmoles) of sodium hydride–mineral oil dispersion (50%) and 9.64 g. (81.6 mmoles) of diethyl carbonate (freshly distilled from calcium hydride) in 250 ml. of benzene. The mixture was stirred for 5 hours at room temperature, then at reflux for 5 additional hours. The reaction mixture was cooled, then treated with absolute ethanol, finally with ice and hydrochloric acid. The organic phase was dried, filtered and concentrated. Residual diethyl carbonate was decanted from the remaining viscous red oil, which weighed 5.9 g. (70%).

The crude bis-β-keto ester was dissolved in acetic acid and hydrogenolyzed at room temperature and 10–15 atm. over platinum oxide; hydrogen uptake ceased after 24–48 hours. The mixture was filtered, poured into water and partially neutralized with sodium hydroxide. The ester was extracted into an ether layer, which was washed with bicarbonate solution and water, then dried, filtered and concentrated. The crude ester weighed 5.5 g. (94%).

The ester was hydrolyzed at reflux with a slight excess of 1 N sodium hydroxide in ethanol–water. Phosphoric acid acidification of the cold basic solution gave 3.1 g. (50% from diacetylferrocene) of 1,1'-ferrocenedipropionic acid (XII), m.p. 135–137° (lit.[7] 142–145°). In other runs the yields of β-keto ester, reduced ester and dipropionic acid were 74%, 87% and 75%, respectively.

Cyclization Products from 1,1'-Ferrocenedipropionic Acid (XII).—A mixture of 4.8 g. (1.54 mmoles) of 1,1'-ferrocenedipropionic acid, 250 ml. of deoxygenated carbon tetrachloride and 24 g. (11 mmoles) of trifluoroacetic anhydride was stirred for 4 hours under nitrogen in the dark at room temperature, then poured into excess sodium bicarbonate solution. The aqueous layer was extracted with methylene chloride and the combined organic layers were washed with water, dried and concentrated to a viscous red-brown oil, the crude keto-bridged propionic acid mixture (4.5 g., 98%). This material, in acetic

(41) H. Brockmann and H. Schodder, *Ber.*, **74**, 73 (1941).

(42) Some confusion exists in the nomenclature accorded these compounds noted in ref. 8 (which in their nomenclature should be 2,1'-trimethylene-acetoferrocene and 3,1'-trimethyleneacetoferrocene in order of elution), but from their order of elution and melting point there is no doubt of their identities with the present compounds.

(43) The method of Hauser and Lindsay, *J. Org. Chem.*, **22**, 482 (1957), gave only 1,1'-diacetylferrocene when employed on a small scale; however, in a large scale reaction a mixture of mono- and diacetylferrocenes was obtained.

acid, was hydrogenolyzed for 24 hours over 1.0 g. of platinum oxide at room temperature and 40 p.s.i. The mixture was filtered and poured into water, and the resulting suspension was extracted with ether. The ether extract was washed to neutrality with water, then dried and concentrated to a yellow-brown oil, the crude mixed propionic acids V and IX (3.9 g., 86%).

The mixture was cyclized under the precise conditions employed in the preceding paragraph for the cyclization of the dipropionic acid XII. The neutral product from the cyclization was chromatographed over alumina (Alcoa F-20, activity III, 1.8 cm. × 50 cm.). Elution with 2% ether in Skelly B removed 0.10 g. (1%) of 2,2'-(α-ketotrimethylene)-1,1'-trimethyleneferrocene (VI) whose spectral properties and melting behavior were identical with those of the same compound obtained from II. After the compound had been recrystallized from Skelly B it underwent a crystal modification at 198–199° and decomposed above 225°.

Anal. Found: C, 68.73; H, 5.82; Fe, 19.50; mol. wt. (osmometer), 262.

Elution with 20% ether in Skelly B removed 0.99 g. (43%) of 3,3'-(α-ketotrimethylene)-1,1'-trimethyleneferrocene (X), m.p. 111.0–112.3° (lit.[13] 110–113°), whose infrared spectrum was identical with that of the compound above from III. In other runs the yields of mixed keto-bridged propionic acids, hydrocarbon bridged propionic acids and di-bridged products were 98%, 56% and 33%, respectively.

Acetylation of 1,1';2,2'-Bis-(trimethylene)-ferrocene (VIII).— A mixture of 0.40 g. (3.0 mmoles) of aluminum chloride and 0.32 g. (3.1 mmoles) of acetic anhydride in 25 ml. of methylene chloride was added dropwise under nitrogen to a stirred, refluxing solution of 0.75 g. (2.7 mmoles) of 1,1';2,2'-bis-(trimethylene)-ferrocene in 25 ml. of methylene chloride. The solution was heated for 8 hours under reflux, then worked up in the usual manner and the reaction product was chromatographed over alumina. Elution with Skelly B gave 0.162 g. (22%) of unchanged 1,1';2,2'-bis-(trimethylene)-ferrocene, while elution with 5% ether in Skelly B gave 0.339 g. (41%) of 3-acetyl-1,1';2,2'-bis-(trimethylene)-ferrocene, (XIII), identified by its infrared, ultraviolet and n.m.r. spectra (Tables III, IV, V). Recrystallization from Skelly B gave 0.34 g. of red needles, m.p. 162.0–163.5°.

Anal. Calcd. for C₁₈H₂₀FeO: C, 70.14; H, 6.54. Found: C, 69.99; H, 6.66.

Elution with 20% ether in Skelly B removed 0.24 g. (30%) of 4-acetyl-1,1';2,2'-bis-(trimethylene)-ferrocene (XIV) also identified by its spectral properties (Tables III, IV and V). The compound was recrystallized from hexane and had m.p. 126.0–127.5°.

Anal. Found: C, 69.83; H, 6.57.

In another reaction 38% of the 3-acetyl isomer XIII, 25% of the 4-acetyl isomer XIV and 25% of unchanged hydrocarbon were obtained. Thus, the ratio of 3-acetyl to 4-acetyl isomer in the two runs was 1.45 ± 0.08 to 1.00.

Conversion of 3-acetyl-1,1';2,2'-bis-(trimethylene)-ferrocene (XIII) to 1,1';2,2';3,3'-tris-(trimethylene)-ferrocene (XVIII) followed the conversion of II to VIII. The mixture of 0.52 g. (1.7 mmoles) of XIII, 3.8 mmoles of sodium hydride and 0.48 g. (3.2 mmoles) of diethyl carbonate in 60 ml. of xylene was heated at reflux for 16 hours after addition, then worked up as usual to give the β-keto ester. The latter was hydrogenolyzed over 0.5 g. of platinum oxide at 40 p.s.i. Isolation of the reduced ester and saponification in refluxing ethanolic sodium hydroxide then followed to give, after acidification, the crude propionic acid XV.

A solution of the crude acid, 50 ml. of carbon tetrachloride and 2 ml. of trifluoroacetic anhydride was stirred in the dark for 4 hours, then worked up in the usual manner. Chromatography of the neutral material over alumina (activity grade III) with 2% ether in Skelly B as eluent removed 0.045 g. (9% from acetyl compound) of 3,3'-(α-ketotrimethylene)-1,1';2,2'-bis-(trimethylene)-ferrocene (XVI), identified by its infrared, ultraviolet and nuclear magnetic resonance spectra (Tables III, IV, and V). Recrystallization from Skelly B gave 0.04 g. of yellow crystals, m.p. 190–193°, after a crystalline modification at 183–187°.

Continued elution with 20% ether in Skelly B removed 0.102 g. (19% from acetyl starting material) of 4,3-(α-ketotrimethylene)-1,1';2,2'-bis-(trimethylene)-ferrocene (XVII), identified by its nuclear magnetic resonance, infrared, and ultraviolet spectra (Tables III, IV and V). Recrystallization from hexane–benzene gave red-brown crystals, m.p. 160–163°.

Anal. Calcd. for C₁₉H₂₀FeO: C, 71.31; H, 6.30; Fe, 17.45. Found: C, 70.85; H, 6.22; Fe, 17.64.

Reduction of 30 mg. of the ketone XVI with a 10-fold excess of lithium aluminum hydride–aluminum chloride gave 28.6 mg. (92%) of 1,1';2,2';3,3'-tris-(trimethylene)-ferrocene (XVIII), whose nuclear resonance spectrum is summarized in Table V.

Sublimation at 130° (0.08 mm.) gave a yellow solid, m.p. 178–181°, after a crystalline modification at 138–148°.

Anal. Calcd. for C₁₉H₂₂Fe: C, 74.52; H, 7.24; Fe, 18.24. Found: C, 74.05; H, 7.27; Fe, 17.77.

Conversion of 4-acetyl-1,1';2,2'-bis-(trimethylene)-ferrocene (XIV) to 1,1';2,2';4,4'-tris-(trimethylene)-ferrocene (XXII) followed the conversion of II to VIII. The mixture of 0.356 g. (1.14 mmoles) of XIV, 2.20 mmoles of sodium hydride and 0.28 g. (2.37 mmoles) of diethyl carbonate in 40 ml. of xylene was heated at reflux for 18 hours after addition, then worked up in the usual manner. The crude β-keto ester was hydrogenolyzed over 0.5 g. of platinum oxide at 40 p.s.i., and the reduced ester then saponified to give 0.50 g. of the crude propionic acid XX.

A mixture of the acid, 20 ml. of carbon tetrachloride and 2 ml. of trifluoroacetic anhydride was stirred in the dark for 4 hours, then worked up as usual. Chromatography of the neutral product over alumina (activity grade III), employing 5% ether in Skelly B as eluent, gave 0.177 g. (47%) of 4,4'-(α-ketotrimethylene)-1,1';2,2'-bis-(trimethylene)-ferrocene (XXI), identified by its infrared, ultraviolet and nuclear magnetic resonance spectra (Tables III, IV and V). Recrystallization from hexane gave yellow crystals, m.p. 170–172°.

Anal. Calcd. for C₁₉H₂₀FeO: C, 71.31; H, 6.30; Fe, 17.45. Found: C, 71.07; H, 6.45; Fe, 17.49.

A portion of the ketone (50 mg.) was reduced with an excess of lithium aluminum hydride–aluminum chloride, as described in previous sections. The product, 1,1';2,2';4,4'-tris-(trimethylene)-ferrocene (XXII), obtained in quantitative yield, melted at 145–151°; n.m.r. spectral properties are found in Table V.

Anal. Calcd. for C₁₉H₂₂Fe: C, 74.52; H, 7.25; Fe, 18.24. Found: C, 74.59; H, 7.34; Fe, 18.43.

Acetylation of 1,1';3,3'-bis-(trimethylene)-ferrocene (XI) was performed as in the acetylation of VIII. The resulting mixture of 1.75 g. (12.9 mmoles) of aluminum chloride, 1.32 g. (12.9 mmoles) of acetic anhydride and 2.29 g. (8.6 mmoles) of XI in 200 ml. of methylene chloride was stirred for 18 hours at room temperature, then was hydrolyzed and worked up in the usual manner. The crude product was transferred to an alumina column (Alcoa F-20, activity III, 1.8 cm. × 60 cm.), which was eluted with Skelly B to remove 0.37 g. (16%) of unchanged starting material, then with 2% ether in Skelly B to give 0.57 g. (21%) of 2-acetyl-1,1';3,3'-bis-(trimethylene)-ferrocene (XXIII). Recrystallization from hexane gave 0.5 g. of orange rods, m.p. 101.0–102.5°. Spectral properties are reported in Tables III, IV and V.

Anal. Calcd. for C₁₈H₂₀FeO: C, 70.14; H, 6.54; Fe, 18.12. Found: C, 68.87; H, 6.75; Fe, 17.97.

When the elutant was then changed to 10% ether in Skelly B, 1.59 g. (60%) of 4-acetyl-1,1';3,3'-bis-(trimethylene)-ferrocene (XXIV) was obtained. Recrystallization from hexane gave 1.3 g. of light orange needles, m.p. 148.5–149.8°. Spectral properties are reported in Tables III, IV and V.

Anal. Found: C, 70.21; H, 6.29; Fe, 17.59.

In five acetylations the total yields of acetyl products varied from 82% to 93% and the product ratio of 4-acetyl to 2-acetyl isomers was 2.73 ± 0.06 to 1.

Attempted conversion of 2-acetyl-1,1';3,3'-bis-(trimethylene)-ferrocene (XXIII) to 1,1';2,2';3,3'-tris-(trimethylene)-ferrocene followed methods described in detail above for other acetyl compounds (e.g. II to VII). Starting material was 0.85 g. (2.75 mmoles) of the 2-acetyl isomer XXIII, 0.26 g. (5.4 mmoles) of the sodium hydride–mineral oil dispersion (50%) and 0.65 g. (5.5 mmoles) of diethyl carbonate. Intermediates from the carbethoxylation, hydrogenolysis and saponification had properties similar to those of the compounds described above. However, when an attempt was made to cyclize the propionic acid intermediate XXV (0.72 g.) with 4.0 ml. of trifluoroacetic anhydride in 20 ml. of carbon tetrachloride the only products obtained were unchanged acid and a compound tentatively identified as β-[1,1';3,3'-bis-(trimethylene)-ferrocenyl]-ethyl trifluoromethyl ketone (XXVI). This was shown by its infrared spectrum and by its etching of glass on pyrolysis.

When attempts to cyclize the acid (0.5 g.) with polyphosphoric acid (7 ml.) were made for 2 hours at various temperatures from 0–65° no reaction was observed to take place. As reaction time progressed at 85°, increasing amounts of tar with correspondingly decreasing amounts of acid were observed, no neutral material being detected. The crude propionic acid XXV also was converted to its acid chloride by treatment with phosphorus pentachloride, then the acid chloride was treated with aluminum chloride in methylene chloride. The mixture was heated for 3 hours at reflux, then worked up. The only product obtained was recovered XXV.

Conversion of 4-acetyl-1,1';3,3'-bis-(trimethylene)-ferrocene (XXIV) to 1,1';2,2';4,4'-tris-(trimethylene)-ferrocene (XXII) followed that of II to VIII. A mixture of 1.635 g. (5.3 mmoles) of XXIV, 8.4 mmoles of sodium hydride and 1.20 g. (10 mmoles)

of diethyl carbonate in 120 ml. of xylene was stirred under nitrogen for 21 hours at reflux, then worked up as above. The crude β-keto ester (1.81 g., 89%), a dark red viscous oil, was hydrogenolyzed over 1.0 g. of platinum oxide at 40 p.s.i. Normal work-up gave 1.7 g. (85%) of the reduced ester as a light yellow oil, which was saponified to the crude propionic acid XXVII, a viscous yellow oil (1.2 g., 80%).

Reaction of 1.266 g. of the propionic acid, 40 ml. of carbon tetrachloride and 10.0 g. of trifluoroacetic anhydride gave 1.10 g. of crude product, which was transferred to a column of activity III alumina. Elution with 2% ether in Skelly B removed 0.36 g. (30% from the acetyl starting material) of 4,4'-α-ketotrimethylene-1,1';3,3'-bis-(trimethylene)-ferrocene (XXVIII) identified by its n.m.r., ultraviolet and infrared spectra (cf. Tables III, IV and V). After sublimation at 140° (0.08 mm.), it had m.p. 184–186°.

Anal. Calcd. for $C_{19}H_{20}FeO$: C, 71.31; H, 6.30; Fe, 17.45. Found: C, 71.36; H, 6.43; Fe, 17.43.

Elution with 5% ether in Skelly B removed 0.44 g. (37%) of 4,5-(α-ketotrimethylene)-1,1';3,3'-bis-(trimethylene)-ferrocene (XXIX), also identified by its spectral properties (Tables III, IV and V). After sublimation at 140° (0.08 mm.), it had m.p. 165.5–167.0°.

Anal. Found: C, 71.51; H, 6.49; Fe, 17.29.

A mixture of 0.132 g. of the hetero-bridged ketone XXVIII, 0.83 g. of aluminum chloride and 0.15 g. of lithium aluminum hydride in 60 ml. of ether was stirred for 1 hour at room temperature, then worked up in the usual manner. Elution with Skelly B of the crude materal from an alumina column gave 0.118 g. (94%) of 1,1';2,2';4,4'-tris-(trimethylene)-ferrocene (XXII), identical with a sample of XXII obtained from XIV. Further purification by sublimation at 115° (0.07 mm.) gave light yellow crystals, m.p. 144–150°. Recrystallization from hexane gave beautiful pale yellow needles, but did not alter the melting point. The n.m.r. spectrum is summarized in Table V.

Lithium alumunum hydride–aluminum chloride reduction of 4,5-(α-ketotrimethylene)-1,1';3,3'-bis-(trimethylene)-ferrocene (XXIX), the favored homoannular ketone by-product above, in a manner identical with that of the preceding paragraph, gave a quantitative yield of 1,1';3,3';4,5-tris-(trimethylene)-ferrocene (XXX). Purification by sublimation or by recrystallization from hexane gave light yellow needles, m.p. 160.0–162.5°. The n.m.r. spectrum is summarized in Table V.

Anal. Found: C, 74.52; H, 7.20; Fe, 18.19.

Preparation of 1,1'-Trimethyleneferrocene-3,4'-dipropionic Acid (XXXI).—A mixture of 0.400 g. (1.29 mmoles) of 3,4'-diacetyl-1,1'-trimethyleneferrocene (IV), 5.16 mmoles of sodium hydride and 0.608 g. (5.16 mmoles) of diethyl carbonate in 250 ml. of sodium-dried benzene was heated for 75 hours at reflux under nitrogen, then cooled, treated with absolute ethanol, and finally with ice and hydrochloric acid. The aqueous layer was extracted with ether and the combined organic phase was washed with water, bicarbonate solution and water, then dried. Removal of solvent on a rotary evaporator yielded 0.83 g. of a wine-red oil, the very crude (0.59 g. theoretical) di-β-keto ester contaminated with diethyl carbonate. This oil was hydrogenolyzed in glacial acetic acid over 1.0 g. of platinum oxide at 39 p.s.i.; work-up yielded 0.48 g. (87% over-all) of crude reduced diester as a yellow oil, which was saponified at reflux with 0.1 N sodium hydroxide in ethanol–water (3:2); work-up gave 0.30 g. (72% from diacetyl starting material) of 1,1'-trimethyleneferrocene-3,4'-dipropionic acid (XXXI), m.p. 152–156° dec., whose infrared spectrum contained carbonyl absorption at 1730 cm.⁻¹.

Anal. Calcd. for $C_{19}H_{22}FeO_4$: C, 61.65; H, 5.95. Found: C, 61.07; H, 6.15.

Cyclization Products from 1,1'-Trimethyleneferrocene-3,4'-dipropionic Acid (XXXI).—A mixture of 90 mg. (0.24 mmole) of the dipropionic acid XXI, 75 ml. of carbon tetrachloride and 1.0 g. of trifluoroacetic anhydride was stirred for 4 hours at room temperature in a tightly stoppered flask, then poured into excess bicarbonate solution. The organic phase was extracted repeatedly with bicarbonate solution, then the combined bicarbonate layers were acidified to pH 4 with hydrochloric acid and extracted with ether. The ether extract was washed with water to pH 5, dried and concentrated to 60 mg. (71%) of a yellow oil, the crude bridged ketone, with infrared carbonyl absorption at 1680, 1720 cm.⁻¹. The keto acid was hydrogenated over 50 mg. of platinum oxide at 40 p.s.i. to yield 57.8 mg. (99%) of the crude yellow oily di-bridged propionic acid XXVII, whose infrared spectrum had broad carbonyl absorption at 1715 cm.⁻¹. A mixture of this oil, 50 ml. of carbon tetrachloride and 578 mg. of trifluoroacetic anhydride was stirred for 4 hours at room temperature, then poured into excess bicarbonate solution. The aqueous layer was extracted with methylene chloride and the combined organic phases were washed with 1 N potassium

hydroxide, with bicarbonate solution and with water to neutrality, then dried and concentrated to 42.1 mg. of an orange oil.

The oil was chromatographed over an acid-washed alumina column, 2.2 × 18 cm. The first fraction was eluted with benzene and yielded 11.3 mg. of a light yellow solid, m.p. 157–161°, whose infrared spectrum was similar to that of 4,4'-α-ketotrimethylene - 1,1';3,3' - bis - (trimethylene) - ferrocene (XXVIII), and which was presumably the impure hetero-bridged ketone. The remaining fraction on the column was obtained by extrusion of adsorbent and extraction with chloroform. Removal of chloroform and crystallization from pentane yielded 10 mg. of 4,5-α-keto trimethylene-1,1';3,3'bis-(trimethyl-ferrocene (XXIX), m.p. 163–165°, whose infrared spectrum was identical with that of the authentic sample obtained above from XXIV.

Acetylation of 1,1';2,2';4,4'-tris-(trimethylene)-ferrocene (XXII) followed the procedure employed for acetylation of VIII. The mixture of 0.166 g. (1.63 mmoles) of acetic anhydride, 0.228 g. (1.63 mmoles) of aluminum chloride and 0.250 g. (0.817 mmole) of the tri-bridged compound XXII in 25 ml. of dry methylene chloride was stirred overnight under nitrogen, hydrolyzed with ice-water and worked up as usual to give a yellow-brown product, which was chromatographed over alumina (activity III); elution with Skelly B removed 8.1 mg. (3%) of starting material; elution with 1% ether in Skelly B gave 0.234 g. (82%) of 3-acetyl-1,1';2,2';4,4'-tris-(trimethylene)-ferrocene (XXXII), whose spectral properties are shown in Tables III, IV and V. Recrystallization from hexane gave yellow-brown crystals, m.p. 119.0–120.0°.

Anal. Calcd. for $C_{21}H_{24}FeO$: C, 72.42; H, 6.95; Fe, 16.04. Found: C, 72.54; H, 7.22; Fe, 16.12.

Elution with 20% ether in Skelly B gave 3% of a material of melting point 176–183° and having the composition of a diacetyl-tris-(trimethylene)-ferrocene. Its n.m.r. spectrum indicates it to be 3,3'- or 3,5-diacetyl-1,1';2,2';4,4'-tris-(trimethylene)-ferrocene.

Anal. Calcd. for $C_{23}H_{26}FeO_2$: C, 70.78; H, 6.70; Fe, 14.31. Found: C, 70.23; H, 6.71; Fe, 14.63.

Acetylation of 1,1';3,3';4,5-tris-(trimethylene)-ferrocene (XXX) (0.361 g.) was carried out exactly as described above for the acetylations of VIII, XI and XIII; in the present reaction 0.24 g. of acetic anhydride and 0.31 g. of aluminum chloride were employed. Chromatography of the product over alumina (activity III) gave 31.3 mg. (9%) of starting material, eluted with Skelly B. Elution with 1% ether in Skelly B gave 0.177 g. (43%) of a mixture of 2-acetyl- and 2'-acetyl-1,1';3,3';4,5-tris-(trimethylene)-ferrocenes accompanied by a small amount of 3-acetyl-1,1';2,2';4,4'-tris-(trimethylene)-ferrocene, arising either from a small amount of the tris-(trimethylene)-ferrocene in the starting material or, more likely, from isomerization of the strained fused 5-carbon ring under Friedel–Crafts conditions. Rechromatography over alumina separated the latter compound from the former two; it was eluted more slowly from Activity II alumina and was identified by its m.p., 108–112°, and its n.m.r. spectrum, identical with that of an authentic sample. The 2- and 2'-acetyl-1,1';2,2';4,5-tris-(trimethylene)-ferrocene isomers could not be separated on alumina, however, and they were obtained together as an oil. The n.m.r. spectrum of the oil indicated clearly the presence of two isomers since it would have been uninterpretable for either XXXIII or XXXIV alone. From area ratios of the peaks at 6.62 and 6.34 τ (4:3) it could be shown that the 2-acetyl isomer XXXIII was formed in somewhat greater amount. Microanalyses of the mixture were in agreement with the structures.

Anal. Calcd. for $C_{21}H_{24}FeO$: C, 72.43; H, 6.95; Fe, 16.04. Found: C, 72.02, 72.51; H, 7.06, 6.93; Fe, 15.93, 16.28.

Elution with 2% ether in Skelly B removed 0.1626 g. (40%) of 4'-acetyl-1,1';3,3';4,5-tris-(trimethylene)-ferrocene (XXXV), identified by its spectral properties (Tables III, IV and V). Recrystallization from hexane gave 0.14 g. of yellow-brown crystals, m.p. 139.5–142.0°.

Anal. Found: C, 72.36; H, 6.84; Fe, 16.25.

Continued elution with 5% ether in Skelly B removed another fraction, 25.0 mg. (5%), identified as a diacetyl derivative, probably 2,2'-diacetyl- or 2,4'-diacetyl-1,1';3,3';4,5-tris-(trimethylene)-ferrocene, m.p. 124–140° after recrystallization from hexane.

Anal. Calcd. for $C_{23}H_{26}FeO_2$: C, 70.77; H, 6.71; Fe, 13.98. Found: C, 70.64; H, 6.76; Fe, 14.57.

The Carbonylation of Organoboranes. II. The Carbonylation of Trialkylboranes in the Presence of Glycols[1,2]

BY M. E. D. HILLMAN[3]

The carbonylation of trialkylboranes in the presence of glycols gave cyclic esters of trialkylcarbinylboronic acids having 5–7 atoms in the ring. The use of 1,5- or 1,6-diols gave rise to polymeric materials. The compounds prepared had unusual hydrolytic and oxidative stability.

Results and Discussion

When the lower trialkylboranes (I) were carbonylated in the presence of water, readily distillable trialkylcarbinylboronic anhydrides (boroximes) (III) were obtained in good yields.[4] However, with larger alkyl groups, the trimeric, high molecular weight products
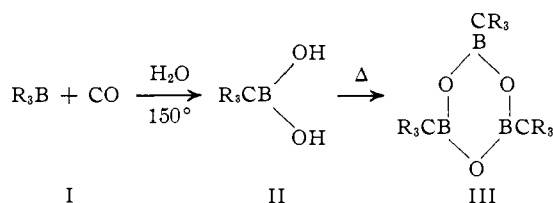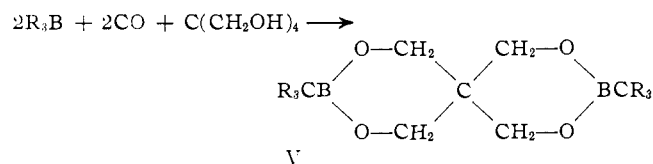

could not be vacuum distilled. Attempts to find monomeric derivatives of the boronic acids (II) led to the present discovery. For example, 2-trialkylcarbinyl-2-bora-1,3-dioxolanes (IV) were prepared in excellent yield by running the carbonylation reaction
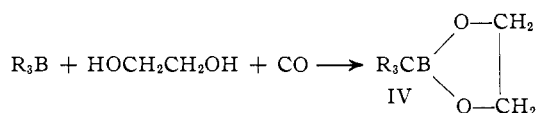
in the presence of excess ethylene glycol. This product was also prepared by esterifying the boronic anhydride (III) with ethylene glycol. Corresponding products were obtained by running the carbonylation reaction in 1,3-propanediol, 1,4-butanediol, 2,3-butanediol, 1,3-butanediol or 1,5-pentanediol. The product from the latter reaction partially polymerized on distillation. The product from the reaction of 1,6-hexanediol had the appearance and properties of a low molecular weight polymer. The cyclic boronic ester from pinacol was obtained by the esterification procedure.

A novel spiro compound (V) was prepared by running the carbonylation of triethylboron in the presence of pentaerythritol.

$$2R_3B + 2CO + C(CH_2OH)_4 \longrightarrow$$

All of the cyclic boronic esters were stable to air and water and were soluble in all common organic solvents including hydrocarbons but were insoluble in water. The lower members were distilled at atmospheric pressure without detectable decomposition or air oxidation. The product from triethylborane and ethylene glycol (IV, $R = C_2H_5$) was steam distilled with no indication of hydrolysis. Oxidation of the cyclic esters with basic peroxide gave the corresponding trialkylcarbinols in good yields.

When the carbonylation of triethylboron was carried out in the presence of polyvinylalcohol, approximately 85% of the hydroxyl groups was esterified, resulting in a water-insoluble, hydrolytically stable polymer (VI) which was soluble in common organic solvents.

VI
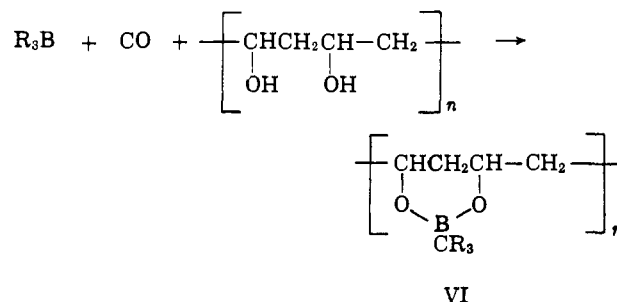
The polymer could be cast into transparent colorless films and drawn into fibers.

Table I contains a summary of the reaction conditions, yields and analyses of some of the carbonylation reactions carried out during this investigation. The reactions were all run for about 1 hour at 25–50° then at 150° for 2 hours. Some representative examples are described in detail in the Experimental section.

Mechanism.—The mechanism of the carbonylation in water and non-hydroxylic solvents has already been discussed in detail.[1] The first part of the reaction path may be identical with the reaction when carried out in water.

(1) Paper I, M. E. D. Hillman, *J. Am. Chem. Soc.*, **84**, 4715 (1962).

(2) Presented at the Pacific Southwest Regional Meeting of the American Chemical Society, Claremont, Calif., December 1, 1962.

(3) Exploratory Chemicals Section, California Research Corporation, Richmond, Calif.

(4) M. E. D. Hillman, Abstracts of the 142nd National Meeting of the American Chemical Society, Atlantic City, N. J., September, 1962; Abstracts, p. 9-Q.