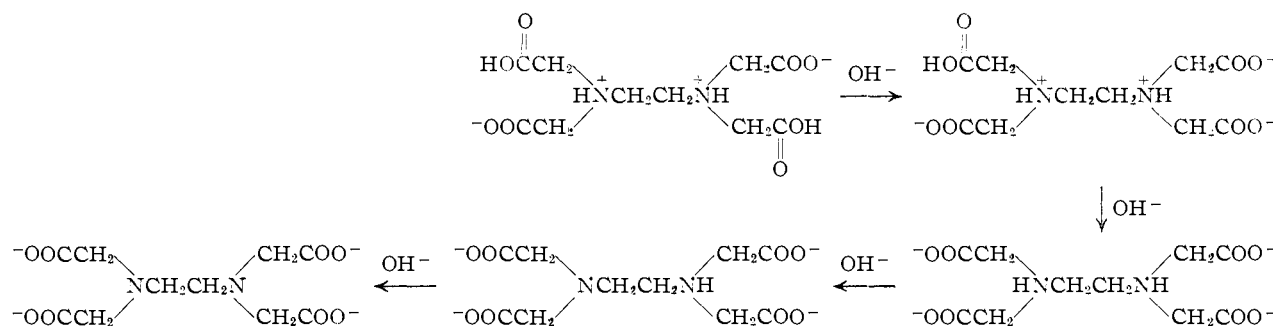


1620 cm^{-1} would be expected if one COOH group plus three COO^- groups attached to the protonated nitrogen atoms is the proper structure. Curve A of Fig. 1 is for such conditions and indicates that such a structure is correct.

A conclusion that the 1620 cm^{-1} band is due to a COO^- group in the presence of a protonated nitrogen atom appears to be totally justified, especially in view of the massive amount of information for amino acids and their infrared spectra.¹⁰ For such systems which are quite similar to EDTA, the acidic proton is definitely on the nitrogen atom; and the frequency for the COO^- group is approximately 1600 cm^{-1} and increases with substitution on the nitrogen atom.^{10,11} Although efforts to observe the presence of a proton on the nitrogen atom by infrared and n.m.r. studies have yielded negative results, these are not the anticipated rapid exchange rate would hinder n.m.r. studies of this type of nitrogen-proton bond. Assuming the double "zwitterion" structure, the dissociation steps and the associated structures for the protonated forms of EDTA in solution can be written as



which are similar to the structures proposed by Schwarzenbach and Ackermann² and Olson and Margerum.⁷ However, the structure for HY^{\equiv} proposed here is different from that proposed by these two groups and indicates that the proton is located on only one nitrogen atom. If it were bridged between the two nitrogen atoms, only a single peak would be observed rather than a double peak (curve C, Fig. 1). The spectra in Fig. 1

are qualitatively and quantitatively compatible with these structures. Thus, if $\text{H}_3\text{Y}^{\equiv}$ were soluble in water, an absorption band at 1700 cm^{-1} and another at 1620 cm^{-1} would be observed. The species $\text{H}_3\text{Y}^{\equiv}$, as expected, gives two peaks at 1700 and 1620 cm^{-1} , while $\text{H}_2\text{Y}^{\equiv}$ gives only a single band at 1620 cm^{-1} because all four COO^- groups are identical. Previous work^{1,4} has noted two peaks for $\text{Na}_2\text{H}_2\text{Y}$ in the solid phase, one at 1675 and one at 1630 cm^{-1} . Apparently there is some difference in the arrangement of the protons when in the solid phase rather than in the solution phase. For HY^{\equiv} two equal area peaks are observed, one at 1620 cm^{-1} due to two COO^- groups which are attached to a protonated nitrogen atom and the other at 1585 cm^{-1} due to two free COO^- groups.

It seems highly unlikely that the 1620 cm^{-1} peak is due to a hydrogen bridge between two carboxylate groups; if it were the structures proposed by Chapman⁴ would be consistent with the data presented here. However, this would be in conflict with the data observed for similar half-neutralized dicarboxylic acids. In any case the data of Fig. 1 are not consistent with

the carboxylate-nitrogen-proton bridge structure proposed by Charles.⁶

Acknowledgment.—We wish to thank the United States Atomic Energy Commission for support of this work under Contract No. AT(11-1)-34, Project No. 45. Preliminary infrared measurements were made by Miss J. M. McKinnie and by Mr. L. V. Interrante.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF BRANDEIS UNIVERSITY, WALTHAM 54, MASS.]

The Structure and Chemistry of Ferrocene. VII. Bridged Ferrocenes¹

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The synthesis of several new bridged ferrocenes is described. Among these are β,β -dimethyl-1,1'-trimethyleneferrocene and transformation products of α -keto-1,1'-trimethyleneferrocene, in which a double bond is included in the bridging elements. Certain aspects of the structure of these substances, in particular ring tilting and conformational mobility within the bridge, are discussed in terms of their n.m.r., infrared and ultraviolet spectra.

Introduction

Ferrocenes having elements bridging the aromatic rings were among the first derivatives of the parent substance to be prepared. Of the several general methods available for the synthesis of such substances, the internal Friedel-Crafts acylation of a suitably chosen ferrocenylalkanecarboxylic acid was initially employed by Woodward and Csendes³ and subsequently by Rinehart,

Curby and Sokol⁴ for the preparation of α -keto-1,1'-trimethyleneferrocene (III) from β -ferrocenylpropionic acid (II). The method appears to be confined to the synthesis of derivatives bridged by a three carbon unit,⁵ since γ -ferrocenylbutyric acid and δ -ferrocenylvaleric acid have been reported to give products of homoannular cyclization.⁴ Schlogl and Seiler⁶ as well as Rinehart, Bublitz and Gustafson⁷ have recently reported

(1) This research was supported by a grant (RG-5978) from the National Institutes of Health, Public Health Service, and by the U. S. Army Research Office (Durham) under contract DA-18-020-ORD-4757.

(2) National Science Foundation Undergraduate Research Participant under Grant G11914.

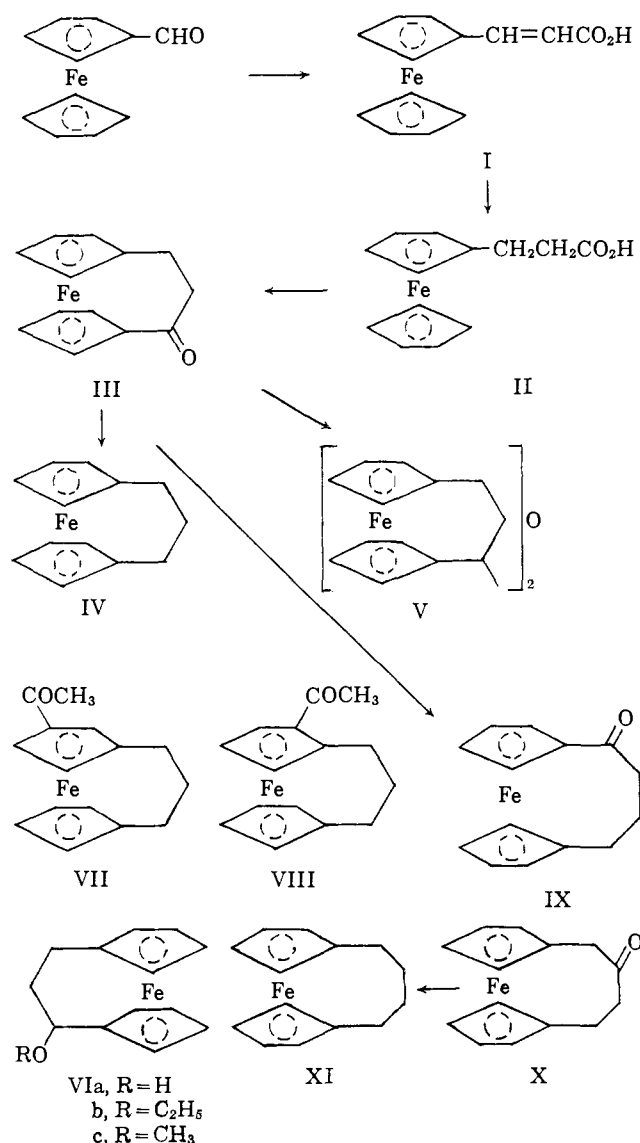
(3) R. B. Woodward and E. Csendes, private communication, 1953; M. Rosenblum, thesis, Harvard University, 1953.

(4) K. L. Rinehart, R. J. Curby and P. E. Sokol, *J. Am. Chem. Soc.*, **79**, 3420 (1957).

(5) This statement may be true only for unbranched alkyl carboxylic acids.

(6) K. Schlogl and H. Seiler, *Tetrahedron Letters*, **7**, 4 (1960).

(7) K. L. Rinehart, D. E. Bublitz and D. H. Gustafson, Abstracts of Papers of the 141st Meeting of the American Chemical Society, Washington, D. C., March, 1962, p. 19-O.



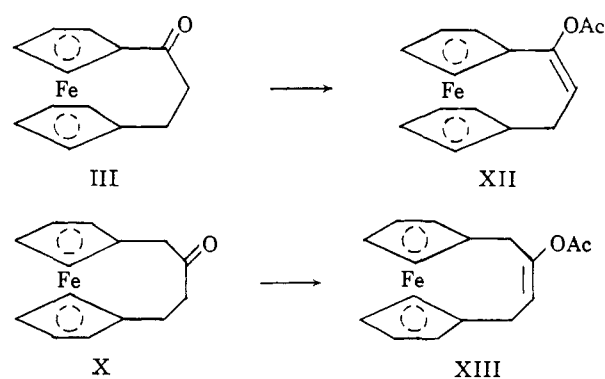
elaborations of this procedure by which the first doubly and triply bridged ferrocenes have been prepared, and it is probable that with suitable modification the method may be further extended to the preparation of a fully articulated derivative.

The present paper is concerned with the synthesis and chemistry of several new bridged ferrocenes and with some fundamental aspects of their molecular structure.

Results

The simplest of these bridged derivatives, α -keto-1,1'-trimethyleneferrocene (III), was prepared by treatment of β -ferrocenylpropionic acid (II) in methylene chloride solution with trifluoroacetic anhydride, following the method of Csendes³ and of Rinehart⁴ (Fig. 1). The acid is in turn most advantageously obtained from ferrocene aldehyde⁵ by condensation with malonic acid and subsequent reduction of the resulting β -ferrocenylacrylic acid (I).^{5c} Its cyclization under the above conditions affords little if any of the homocyclic isomer and the entire sequence of reactions may be accomplished in over-all yield of 50% from ferrocene. Conversion of the ketone to 1,1'-trimethyleneferrocene (IV) can be effected by either Clemmensen, Wolff-

(8) (a) M. Rosenblum, *Chemistry & Industry*, 72 (1957); (b) P. J. Graham, *et al.*, *J. Am. Chem. Soc.*, **79**, 3416 (1957); (c) G. D. Broadhead, J. M. Osgerby and P. L. Pauson, *J. Chem. Soc.*, 650 (1958).



Kishner or catalytic reduction.⁹ The latter procedure was found to be somewhat variable, giving rise in some experiments to considerable quantities of the symmetric ether V and smaller amounts of the alcohol VIa.

The bridged compound was readily acetylated in the presence of acetyl chloride and aluminum chloride affording the isomeric ketones 3-acetyl-1,1'-trimethyleneferrocene (VII) and 2-acetyl-1,1'-trimethyleneferrocene (VIII) in a ratio of 1.75:1.00. These isomers, recently reported by Hill and Richards,¹⁰ were conveniently separated by elution chromatography on alumina, and their structures assigned on the basis of their relative adsorbabilities and their infrared spectral pattern in the region of 11μ .¹¹

The ketone III reacted smoothly with diazomethane, yielding the two isomeric homologous ketones IX and X. Of these, the unconjugated ketone X, identified by its infrared and ultraviolet spectra, was formed preponderantly. Reduction of this isomer under Wolff-Kishner conditions yielded 1,1'-tetramethyleneferrocene (XI) in 80% yield. This substance has previously been reported by Luttringhaus and Kullick¹² who prepared it in very low yield from 1,4-biscyclopentadienylbutane.

The strain attending the introduction of double bond in IV is manifest in the failure of the ketone III to undergo appreciable deuterium exchange on treatment at room temperature with deuterium oxide and base for a period of 22 hours. By contrast, the ring-enlarged ketone X, the enol forms of which are less strained, was observed to undergo considerable deuterium exchange under similar reaction conditions. In accord with these results, III is recovered unchanged on treatment with potassium *t*-butoxide and methyl iodide, and numerous attempts to convert the alcohol VIa, prepared by lithium aluminum hydride reduction of III, to an olefin met with uniform failure. Thus, distillation of the alcohol from potassium acid sulfate led to the formation of the ether V as the only detectable product. Similarly, pyrolysis of the *p*-nitrobenzoate, xanthate and ethyl and methyl carbonates of VIa failed to afford the expected olefin. The latter two reactions gave instead good yields of the ethyl and methyl ethers VIb and VIc, respectively, as well as smaller amounts of the symmetrical ether V and of alcohol VIa. The formation of ethers VIb and VIc, which is very likely the consequence of the stability of the α -metallocenyl radical or carbonium ion and of the strain inherent in an olefinic bridge, has its analogy in the formation of trityl ether on pyrolysis of trityl carbonate.¹³

(9) Reduction may also be accomplished conveniently with lithium aluminum hydride in the presence of aluminum chloride (private communication from K. L. Rinehart).

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

(11) M. Rosenblum and W. Glenn Howells, *ibid.*, **84**, 1167 (1962); M. Rosenblum, *Chemistry & Industry*, 953 (1958).

(12) A. Luttringhaus and W. Kullick, *Angew. Chem.*, **70**, 438 (1958).

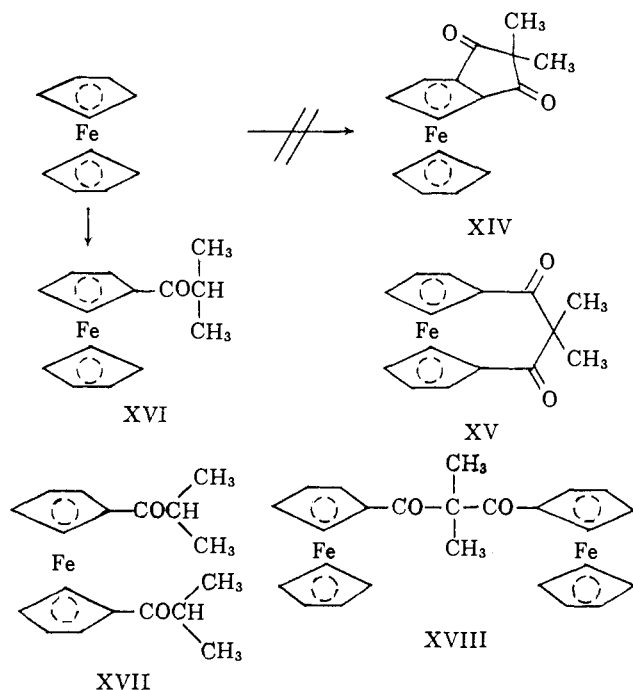


Fig. 3.

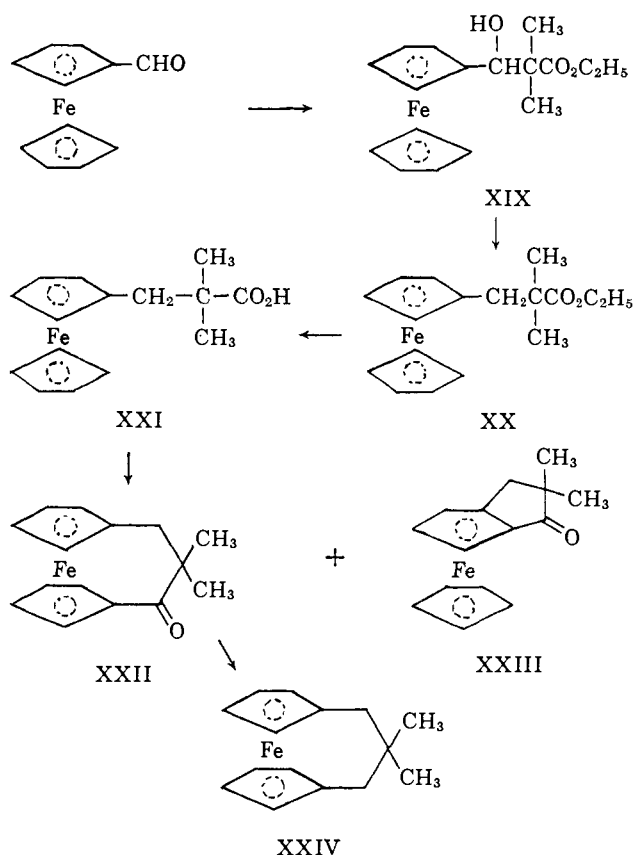


Fig. 4.

The unsymmetrical ethers are readily prepared from VI by treatment with the requisite alcohol in the presence of a trace of acid. The relative ease with which the ethers are formed under these reaction conditions illustrates the remarkable stabilization of α -metalloenyl carbonium ions even in those circumstances in which the stereochemistry of the vacant p -orbital is not entirely favorable for its stabilization by overlap with either ring or metal orbitals.¹⁴

(13) M. Gomberg, *J. Am. Chem. Soc.*, **35**, 200 (1913).

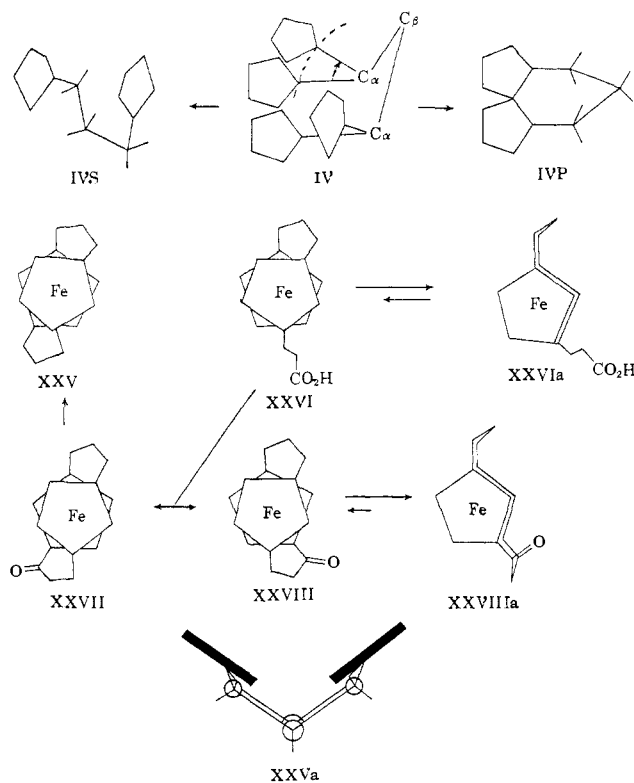


Fig. 5.

Introduction of a double bond into a three-carbon bridged ferrocene was ultimately achieved by conversion of III to its enol acetate XII. The strain inherent in the olefin is reflected in the relatively low yield of XII contrasted with the more facile formation of XIII from the homologous ketone X under similar reaction conditions. The position of the double bond in XIII is assigned unambiguously on the basis of its n.m.r. spectrum (*vide infra*).

As noted above, initial attempts to introduce substituents at a bridging β -carbon atom by alkylation of III were unsuccessful. We therefore turned our attention to the synthesis of such a substance by the Friedel-Crafts reaction of ferrocene with dimethylmalonyl chloride. This diacid chloride has been reported to give dimethylindanediones and related intramolecular acylation products with a variety of reactive aromatics such as naphthalene, anthracene and phenanthrene.¹⁵ With ferrocene, however, neither the product of homoannular acylation (XIV) nor of heteroannular acylation (XV) was observed. The products were instead the mono- and dinuclear ferrocenes XVI, XVII and XVIII (Fig. 3).

The failure of the reaction to follow its anticipated course is very likely the consequence of unfavorable angle deformations and steric factors which allow intermolecular reactions to compete effectively with internal cyclization. Thus, the formation of a 5-5 fused ring system as in XIV is attended by larger angle deformations than are cyclizations which lead to a 6-5 system. Such factors may account for the exclusive formation of α -isobutyrylthiophene and 2,2-bis-(α -thiophenoylpropane) when thiophene is treated with dimethylmalonyl chloride.¹⁵ Heteroannular cyclization may similarly be retarded by steric interactions involving the *gem*-dimethyl group and the metal atom.

(14) J. H. Richards and E. A. Hill, *ibid.*, **81**, 3484 (1959). The facile formation of ethers from ferrocenylcarbinol has also been reported by H. N. Nesmeyanov, E. G. Perevalova and Yu A. Ustynuk, *Doklady Akad. Nauk S.S.S.R.*, **133**, 1105 (1960).

(15) M. Freund and K. Fleischer, *Ann.*, **399**, 197 (1913).

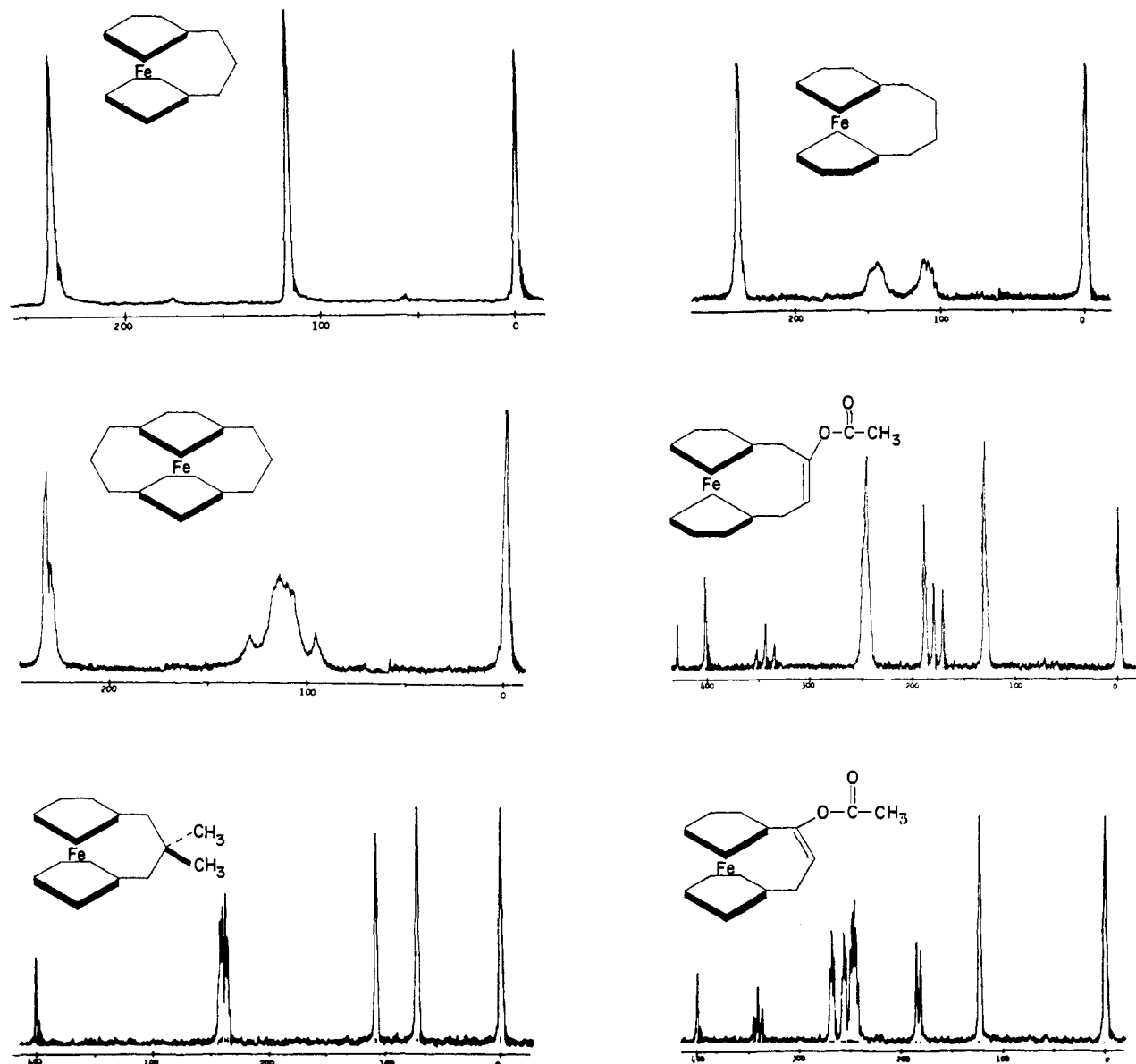


Fig. 6.—N.m.r. spectra of bridged ferrocenes.²⁰ The scale is in c.p.s. from tetramethylsilane as internal standard.

The synthesis of a trimethylene bridged ferrocene having substituents at the β -carbon atom was accomplished by the procedures outlined in Fig. 4. The hydroxy ester XIX was obtained from ferrocene aldehyde by treatment with ethyl α -bromoisobutyrate and amalgamated magnesium. Catalytic reduction and saponification of the ester gave the acid XXI, which on treatment with trifluoroacetic anhydride in refluxing methylene chloride afforded the heterocyclic and homocyclic ketones XXII and XXIII in approximately equal amounts. The lower reactivity of XXI compared with II, as evidenced by the more vigorous conditions required to effect its cyclization, is very likely due to steric interference from the *gem*-dimethyl group. The formation of products derived from both homoannular and heteroannular cyclization contrasts sharply with the exclusive formation of the bridged ketone III from the unsubstituted propionic acid II, and illustrates the very fine energy balance which must subsist between these alternate modes of reaction. Conversion of XXII to XXIV proceeded poorly in the Wolff-Kishner reaction, but was effected in good yield by catalytic hydrogenation over platinum.

Discussion

Conformation of Bridged Ferrocenes. General Aspects.¹⁶—By contrast with ferrocene in which the preferred relative orientation of the rings is of the staggered or antiprismatic form, models suggest that 1,1'-trimethyleneferrocene the rings are forced to adopt a more nearly prismatic configuration. Moreover, an unmodified half cyclohexane conformation for the three-carbon bridge in this substance is precluded by a consideration of the distance separating the terminal carbon atoms of such a conformation (2.52 Å.) and the normal distance between ferrocene rings (3.32 Å.).¹⁷ Appreciable compression of the metal-ring bond to accommodate the bridge is unlikely, especially in view of the proximity of heteroannular carbon atoms in ferrocene itself, and of the expected further decrease in carbon atom separation in the bridged substance. These geometrical requirements are readily accommodated by rotation of C_α valences about the C_α - C_β bond axis or by

(16) This subject was treated briefly in a previous note; M. Rosenblum, A. K. Banerjee, N. Danieli and L. K. Herrick, *Tetrahedron Letters*, **10**, 423 (1962).

(17) J. D. Dunitz and L. E. Orgel, *Nature*, **171**, 121 (1953).

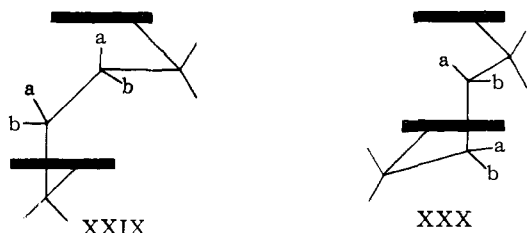


Fig. 7.

a combination of such transformations and valence angle deformation at C_β (Fig. 5). In the former circumstance, in which no angle strain is introduced in the bridge, a rotation of $23^\circ 55'$ suffices to accommodate the normal distance separating the rings and results in a tilting of each of the rings by an angle of $15^\circ 3'$ from their otherwise parallel orientation. This calculated angle is undoubtedly a maximum figure since it does not take into account out of plane exocyclic valence deformations, in addition to angle distortion at C_β . Metal-ring bond distortions of this magnitude are probably not attended by a large increase in potential energy in bridged ferrocenes,¹⁸ although the lower stability of these substances is evident in their slow decomposition on storage.

N.m.r. Spectra. Derivatives of Trimethyleneferrocene.—Although ring protons in $\alpha,\alpha,\alpha',\alpha'$ -tetramethyl-1,1'-dimethyleneferrocene are reported to exhibit a difference in chemical shift of 0.74 p.p.m., due to ring tilting,¹⁹ the degree of tilting in IV is apparently insufficient to introduce any detectable magnetic inequivalence in its ring protons. These give rise to a sharp singlet absorption at 6.05 τ . (The spectrum of this substance and of the other bridged ferrocenes discussed below are shown in Fig. 6.)²⁰

The apparent magnetic equivalence of methylene protons in IV, evidenced by singlet absorption at 8.05 τ , is admissible only in terms of a rapid inversion of the chain which effectively averages the spatial orientations of the protons and their distance from the metal atom and furthermore requires that the resulting average chemical shifts of α - and β -protons be very nearly identical. It is unlikely that such inversion involves the simple planar transition state IVP for the bridge since, in the absence of appreciable strain in IV, the activation energy associated with the planar transition state, estimated to be 20 to 30 kcal./mole, would be expected to impose greater conformational rigidity than is observed. Chain inversion is best accounted for in terms of transition states such as IVS which involve ring-metal bending modes with considerably diminished valence angle distortions and non-bonded repulsions in the chain.

The importance of ring bending modes for chain inversion is manifest in the spectrum of the doubly bridged derivative XXV wherein ring-metal deformations are largely precluded by the greatly increased rigidity of the molecule. This substance was prepared by cyclization of the acid XXVI with trifluoroacetic anhydride and Wolff-Kishner reduction of the ketonic product, following the general path employed by Schlogl and Seiler.⁶ Although, in principle, two geometrically isomeric ketones having 1,3-dispositions of the bridge termini on each ring may exist, the cyclization of XXVI yielded only one such ketonic product. This result is best accounted for in terms of the pris-

matic conformation XXVIa imposed by the three-carbon bridge, and requires that the ketonic product possess structure XXVIII \rightleftharpoons XXVIIIa, rather than structure XXVII proposed earlier.⁶ Resonance absorption for the methylene protons in XXV which appears as a broad band centered at 8.10 τ (width at half-height, 14 c.p.s.) with two smaller, broad satellite bands approximately 17 cycles to either side of this peak suggests an intermediate rate of chain inversion. The small spin splitting observed for ring proton resonance in this substance (major peak 6.13 τ) is also attributable to the rigid ring tilted conformation of this molecule, which brings one proton on each of the rings considerably closer to the metal atom than the other two as shown in projection structure XXVa.

The magnetic inequivalence of ring protons in XXIV, evidenced by the closely spaced pair of triplets at 5.97 and 6.06 τ ($J = 2$ c.p.s.), is very likely the consequence of an increase in the angle of ring tilt in this substance brought about in part by a contraction of the internal valence angle at C_β due to the *gem*-dimethyl group. The appearance of sharp singlet absorption for both methyl and methylene protons indicates rapid inversion of the bridge in this compound as in IV and rules out long range spin-spin coupling as the cause of the observed ring proton splitting.

Derivatives of Tetramethyleneferrocene.—The rate of conformation exchange must be considerably diminished in 1,1'-tetramethyleneferrocene (XI) since the α - and β -bridge proton resonances appear as two broad, well separated, structureless peaks centered at 7.58 and 8.17 τ . Models suggest that the larger barrier to effective conformational equilibration of α - and β -methylene protons on the bridge derives from the circumstance that such equilibration requires passage of each of the β -methylene groups through the inside of the bridge. Such transition states must involve considerable repulsion between the metal atom and the chain, as well as distortion in the chain and in the ring-metal bond. The situation is best illustrated in terms of the β -methylene protons shown in projection structures XXIX and XXX. Considering the four-carbon atoms of the chain as well as the two to which the bridge termini are bonded, these conformations are related as twisted boat and chair conformations of cyclohexane. In these, the rings attain the more stable antiprismatic configuration, and rapid interconversion of each to its mirror image form by rotation of the rings about an axis passing through their centers serves to equilibrate all pairs of non-equivalent a and b type protons. As in cyclohexane, the interconversion of a and b type protons requires establishment of an equilibrium between XXX and XXIX, but here such a transformation can only be achieved by rotation of a β -methylene group through the inside of the bridge.

Derivatives Possessing an Olefinic Bridge.—The n.m.r. spectrum of the enol acetate of X, in particular the presence of triplet absorption at 4.28 τ ($J = 9$ c.p.s.) for a single ethylenic proton and of doublet absorption at 7.07 τ ($J = 9$ c.p.s.) for two methylenic protons, establishes its structure as XIII. The absence of appreciable ring tilting in this substance is indicated by singlet absorption at 5.93 τ for ring protons in both rings. Models confirm that the rings may be readily bridged without appreciable distortion of metal-ring bonds or of C-C valence angles in the bridge, and the appearance of a typical first-order A_2X pattern for the ethylenic proton and the adjacent methylene protons requires that the chain possess considerable conformational flexibility.

Multiplet absorption for the ring protons on each of the rings in the enol acetate derived from III reflects the

(18) C. J. Ballhausen and J. P. Dahl, *Acta Chem. Scand.*, **15**, 1333 (1961); E. R. Lippincott and R. D. Nelson, *Spectrochim. Acta*, **10**, 307 (1958).

(19) K. L. Rinehart, *et al.*, *J. Am. Chem. Soc.*, **82**, 4111 (1960).

(20) N.m.r. spectra were determined in $CDCl_3$ solution at a concentration of approximately 60 mg./cc. and recorded at 60 Mc. with a Varian Model V-4300 spectrometer. Peak positions, given in values of τ , were calibrated against tetramethylsilane as internal standard by sidebanding.

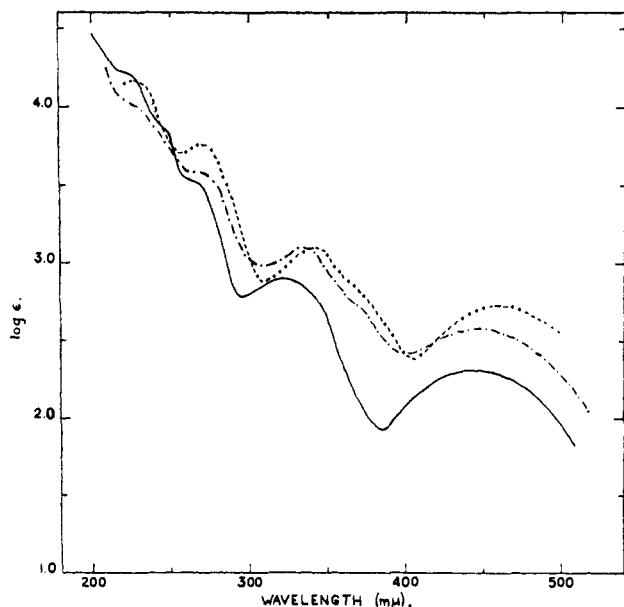


Fig. 8.—Ultraviolet absorption spectra: ---, 1-acetyl-1'-ethylferrocene, taken in 95% ethanol; - · - · - ·, α -keto-1,1'-trimethyleneferrocene (III), taken in 95% ethanol; —, α -keto- β,β -dimethyl-1,1'-trimethyleneferrocene (XXII), taken in isoöctane.

somewhat greater distortion of metal-ring bond angles in this substance (calculated to be $20\text{--}25^\circ$). The high field pair of triplets at 5.83 and 5.92τ are assigned to the α - and β -protons of the methylene substituted ring, while those at lower field at 5.51 and 5.72τ are attributable to the α - and β -protons of the second ring, by comparison with the spectrum of the enol acetate of acetylferrocene (unsubstituted ring, 5.83τ ; substituted ring, $5.63, 5.75\tau$). The lower coupling constant for the A_2X system of XII compared with XIII may be due to the increased rigidity of the chain which fixes the dihedral angle between the spin coupled protons near 60° in XII.

Ultraviolet Spectra.—The ultraviolet spectra of bridged acylferrocenes provide a sensitive measure of the extent to which coplanarity of the carbonyl group with the ring is achieved in these substances. In particular, the intensity of the absorption band near $270\text{ m}\mu$, associated with transitions involving ring localized orbitals, is particularly diagnostic.²¹ As illustrated in Fig. 8, the intensity of this band is significantly lower in the spectrum of III and XXII than in that of its open chain analog, 1-acetyl-1'-ethylferrocene.²² By contrast, the spectrum of α -keto-1,1'-tetramethyleneferrocene (IX) (shown in Fig. 9) is essentially identical with that of the open-chain model since the four-carbon bridge permits the carbonyl group to assume a conformation in which it is effectively conjugated with the ring. As expected, the spectrum of the isomeric ketone X, shown in Fig. 10, fails to exhibit any pronounced absorption peak in the region below $300\text{ m}\mu$. The enhancement in extinction coefficient of the peak at $320\text{ m}\mu$, which like that at $430\text{ m}\mu$ is probably associated with a forbidden d-d transition,²³ may be attributable to a decrease in molecular symmetry, or to direct interaction between metal and carbonyl orbitals in the excited state.

The orthogonality of olefinic and ring π -orbitals in the enol acetate XII, which precludes their interaction,

(21) For related studies of the degree of conjugation of carbonyl groups with benzenoid nuclei, cf. H. Rapoport and G. Smolinsky, *J. Am. Chem. Soc.*, **82**, 1171 (1960); R. Huisgen, *et al.*, *Ann.*, **586**, 1, 52 (1954); and K. C. Dewhirst and D. J. Cram, *J. Am. Chem. Soc.*, **80**, 3115 (1958).

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

(23) D. R. Scott and R. S. Becker, *J. Chem. Phys.*, **35**, 516 (1961).

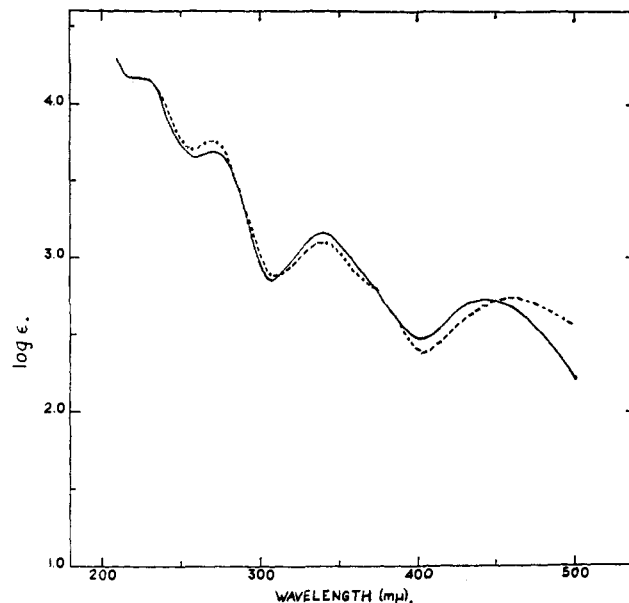


Fig. 9.—Ultraviolet absorption spectra, taken in 95% ethanol: ---, 1-acetyl-1'-ethylferrocene; —, α -keto-1,1'-tetramethyleneferrocene (IX).

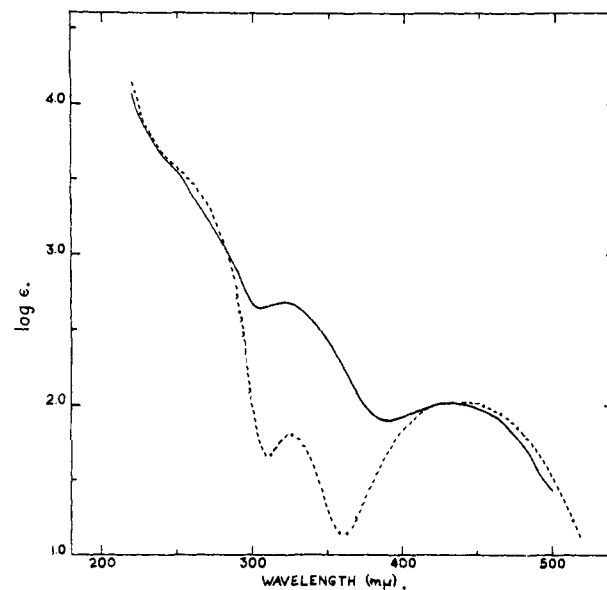


Fig. 10.—Ultraviolet absorption spectra, taken in 95% ethanol: ---, 1,1'-diethylferrocene; —, β -keto-1,1'-tetramethyleneferrocene (X).

is very strikingly illustrated in the close correspondence of its spectrum with that of 1,1'-trimethyleneferrocene (Fig. 11). Similarly, the π -orbitals associated with the olefinic band in the enol acetate XIII exhibit no interaction with the ferrocene nucleus, as is demonstrated by the near identity of its spectrum with that of IV.

Infrared Spectra.—Notwithstanding diminished conjugation of the carbonyl function in III with the rings, its position of absorption at $5.95\text{ }\mu$ is quite close to that of its open-chain analog 1-acetyl-1'-ethylferrocene ($5.99\text{ }\mu$) and probably is a consequence of valence angle spreading in the bridge.²⁴ The apparent sensitivity of this absorption to such deformations is further illustrated in a comparison of the spectrum of III with that of the more highly distorted ketone XXII which exhibits carbonyl absorption at $6.01\text{ }\mu$, notwithstanding a further decrease in conjugation of functional group

(24) For a discussion of the effects of valence angle distortion on the position of carbonyl absorption cf. J. O. Halford, *ibid.*, **24**, 830 (1956).

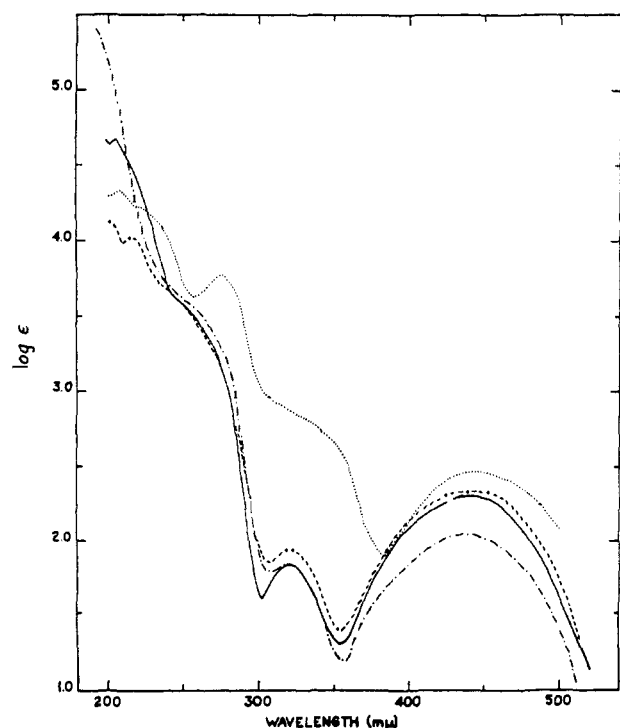


Fig. 11.—Ultraviolet absorption spectra, taken in isoöctane: , acetylferrocene enol acetate; - - - - , α -keto-1,1'-trimethylene ferrocene enol acetate (XII); - · - · - , β -keto-1,1'-tetramethyleneferrocene enol acetate (XIII); ———, 1,1'-trimethyleneferrocene (IV).

with the ring. These deformations must also be responsible for the bathochromic shifts observed in the position of carbonyl absorption for the isomeric ketones IX (6.07 μ) and X (5.86 μ).

Acknowledgment.—We are indebted to Mr. L. K. Herrick for determination of several of the n.m.r. spectra.

Experimental

All melting points were determined using a Fisher-Johns melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer double beam recording spectrophotometer, Model 21; ultraviolet spectra on a Cary Model 14, recording spectrophotometer. Analyses were performed at the Schwarzkopf Microanalytical Laboratory, New York, N. Y., at the Alfred Berhardt Microanalytical Laboratory, Mulheim Germany, and by Dr. C. Fritz, Needham, Mass.

Formylferrocene.—Ferrocene (11.16 g., 0.06 mole) was added in small portions over a period of 15 minutes to a vigorously stirred solution prepared from 21.6 g. (0.16 mole) of N-methylformanilide and 15.3 g. (0.10 mole) of phosphorus oxychloride. The purple viscous mixture was stirred for 1 hour at room temperature and then at 65–70° for 2 hours in a nitrogen atmosphere. The mixture was then cooled to 0° and 50 g. of sodium acetate dissolved in 400 ml. of water was added and the solution stirred overnight. The reaction mixture was extracted twice with 400 ml. of ether and the ether extracts were combined and washed successively with 1 N HCl, water, saturated sodium bicarbonate solution and finally water, all saturated with sodium chloride. The ether extract was concentrated to a volume of 50 ml. and shaken with a cold solution prepared by dissolving 40 g. of sodium bisulfite in 100 ml. of water. The bisulfite addition compound was collected, washed with cold saturated sodium bisulfite and then ether and was finally dried (yield 15.40 g.).

The bisulfite addition compound was taken up in 200 ml. of 2 N sodium hydroxide and the liberated aldehyde extracted into ether. The combined ether extract was washed with saturated sodium chloride solution and then dried over magnesium sulfate. Removal of solvent left 10.2 g. of dark purple crystals of the aldehyde (80%).

β -Ferrocenylpropionic Acid (II).— β -Ferrocenylacrylic acid was prepared according to the method of Broadhead, Osgerby and Pauson²⁵ in a yield of 78% by treatment of the aldehyde with malonic acid in pyridine solution containing a small amount of piperidine. Hydrogenation of 11 g. of this acid in absolute ethanol over platinum oxide catalyst gave 10.3 g. of β -ferrocenylpropionic acid, m.p. 119–120° (lit.^{4,25} 117–118°, 115–116°).

α -Keto-1,1'-trimethyleneferrocene (III).— β -Ferrocenylpropionic acid (5.0 g., 0.019 mole) in 100 ml. of dry methylene chloride was added slowly to a magnetically stirred, ice-cooled solution of 7.5 g. of trifluoroacetic anhydride in 100 ml. of the same solvent. The reaction was allowed to proceed at 0° for 5 hours in a nitrogen atmosphere. The solution was then poured into sodium bicarbonate solution and the organic layer separated. The aqueous layer was washed with ether and the combined organic solution was washed to neutrality and dried over magnesium sulfate. The crude product obtained on removal of solvent was recrystallized from petroleum ether to give 4.1 g. (88%) of ketone, m.p. 148–150° (lit.^{3,25} 144–145°, 141–142°).

1,1'-Trimethyleneferrocene (IV). **Clemmensen Reduction.**— α -Keto-1,1'-trimethyleneferrocene (450 mg.) was treated with amalgamated zinc in 20 ml. of an ethanol, benzene and concentrated hydrochloric acid mixture. Reaction was carried out at reflux temperature in an atmosphere of nitrogen for 4 hours. Work-up gave 400 mg. of impure product, m.p. 95–105°, which was purified either by sublimation at reduced pressures or by chromatography on alumina.

Catalytic Reduction.—The ketone, dissolved in ethanol containing a small amount of hydrochloric acid, was hydrogenated over platinum oxide in a Parr apparatus. In several runs the highest yield of crude product melting in the range of 95–105° was 89%, but the yield in many experiments was considerably below this and the product was contaminated with variable amounts of the symmetric ether V and the alcohol VIa. Thus in one experiment, reduction of 8.3 g. of ketone gave after chromatography on alumina, 0.9 g. of V, m.p. 229–230° (recrystallized from methylene chloride-petroleum ether).

Anal. Calcd. for $C_{26}H_{26}OFe_2$: C, 66.98; H, 5.62. Found: C, 67.24; H, 5.68.

The last fraction, eluted with chloroform, contained 1.6 g. of the alcohol VIa, m.p. 160–162°. Recrystallization from ether yielded an analytical sample, m.p. 162–163°, as fine yellow needles.

Anal. Calcd. for $C_{13}H_{14}OFe$: C, 64.49; H, 5.82. Found: C, 64.18; H, 5.70.

Wolff-Kishner Reduction.—The ketone (2 g., 8.3 mmoles) was taken up in 50 ml. of diethylene glycol containing 5.5 g. of sodium hydroxide and 0.364 g. (13 mmoles) of hydrazine. The solution was refluxed in a nitrogen atmosphere for 5 hours, then cooled, poured into water, and extracted with ether. The combined ether extract was washed to neutrality, dried over magnesium sulfate and solvent removed. The crude product, purified by sublimation *in vacuo*, gave 1.4 g. of 1,1'-trimethyleneferrocene, m.p. 108–109° (lit.³ 104.5–105.0°).

Acetylation of 1,1'-Trimethyleneferrocene.—Acetyl chloride (0.47 g., 6.0 mmoles) in 50 ml. of dry methylene chloride was added dropwise over a period of 1 hour to a mixture of 1.36 g. (6.0 mmoles) of trimethyleneferrocene and 0.80 g. (6.0 mmoles) of aluminum chloride in the same solvent. The reaction was allowed to proceed at 0° in a nitrogen atmosphere for 2 hours following addition and was then quenched by pouring into ice-water. The oily residue obtained on work-up weighed 1.30 g. and was chromatographed on 200 g. of grade 2 Merck alumina employing mixtures of petroleum ether (b.p. 30–60°) and benzene as eluent. Three bands developed, the first yielding 200 mg. of starting material. The second band gave, after recrystallization from low boiling petroleum ether, 370 mg. of 2-acetyl-1,1'-trimethyleneferrocene (VIII), m.p. 77.5–78.5° (lit.¹⁰ m.p. 77.5–78.5°).

Anal. Calcd. for $C_{15}H_{16}OFe$: C, 67.18; H, 6.01. Found: C, 67.06; H, 5.73.

The third band gave, after recrystallization from low boiling petroleum ether, 610 mg. of 3-acetyl-1,1'-trimethyleneferrocene (VII), m.p. 103–104° (lit.¹⁰ m.p. 100–101°).

Anal. Calcd. for $C_{15}H_{16}OFe$: C, 67.18; H, 6.01. Found: C, 67.49; H, 6.03.

α -Hydroxyl-1,1'-trimethyleneferrocene (VIa).—A solution of 5 g. of α -keto-1,1'-trimethyleneferrocene in 100 ml. of anhydrous ether was added dropwise to a solution of 5 g. of lithium aluminum hydride in 100 ml. of the same solvent. The mixture was stirred at reflux for 5 hours and then decomposed by addition of 2 ml. of water, 2 ml. of 15% sodium hydroxide and finally 6 ml. of water. The organic solution was dried over magnesium sulfate and solvent was removed. Recrystallization of the product from ether gave 4.65 g. of the pure alcohol, m.p. 163–164°, as fine yellow needles (lit.³ 154–155°).

Ethyl Carbonate Derivative.—Ethyl chlorocarbonate (10 ml.) was added dropwise to a magnetically stirred solution of 2.5 g. of the alcohol VIa in 25 ml. of pyridine maintained at 0°. The solution was stirred at 0° for 6 hours then at room temperature overnight. It was then poured into 100 ml. of ice-water and the aqueous solution was extracted several times with ether.

(25) J. M. Osgerby and P. L. Pauson, *J. Chem. Soc.*, 656 (1958).

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

Isolation of the product and recrystallization from methylene chloride-petroleum ether gave 2.35 g. of the carbonate, m.p. 120–121°, as fine yellow plates. A second crop yielded an additional 300 mg. of carbonate, m.p. 117–119°.

Anal. Calcd. for $C_{15}H_{18}O_3Fe$: C, 61.17; H, 5.77. Found: C, 60.89; H, 5.72.

Pyrolysis of the Ethyl Carbonate Derivative.—A solution prepared from 1 g. of the carbonate in 10 ml. of dry xylene was dropped slowly in a slow stream of nitrogen, through a tube packed with aluminum chips and heated to 283°. The pyrolysis tube was allowed to cool and was then washed through with ether until the washings were colorless. After removal of the ether, the remaining xylene solution was placed on a chromatographic column prepared from 200 g. of neutral Woelm alumina (5% water added). On elution with petroleum ether (b.p. 30–60°) three bands developed. The first yielded 410 mg. of yellow oil, which crystallized on cooling. After further purification by rechromatographing on alumina followed by sublimation *in vacuo* this substance gave 300 mg. of α -ethoxy-1,1'-trimethyleneferrocene (VIb), m.p. 46–47°, as fine yellow needles. The material is identical by mixed m.p. with the product obtained by treatment of the alcohol VIa with ethanol in the presence of mineral acid.

Anal. Calcd. for $C_{15}H_{18}OFe$: C, 66.68; H, 6.72. Found: C, 66.30; H, 6.75.

The second band yielded 122 mg. of the symmetric ether V, m.p. 226–228°.

The third band gave 46 mg. of the alcohol VIa, m.p. 161–163°. **α -Ethoxy-1,1'-trimethyleneferrocene (VIb).**—A solution of 250 mg. of the alcohol VIa in 20 ml. of ethanol, to which 5 drops of 70% perchloric acid had been added, was stirred at room temperature for 6 hours in a nitrogen atmosphere.

Chromatographic purification of the crude product on 100 g. of alumina gave 294 mg. of ether, m.p. 45–46°. The compound is also formed by heating VIa in aqueous ethanol solution in the presence of a trace of acetic acid.

The methyl carbonate derivative was prepared in 66% yield following the procedure given for the synthesis of the ethyl carbonate. The compound crystallized from ether-petroleum ether solutions as yellow blocks, m.p. 143–144°.

Anal. Calcd. for $C_{15}H_{18}O_3Fe$: C, 60.02; H, 5.37. Found: C, 60.36; H, 5.50.

Pyrolysis of the Methyl Carbonate Derivative.—The reaction was carried out on 500 mg. of substance in a manner essentially identical with that described for the pyrolysis of the ethyl carbonate. After purification of the crude product by chromatography on alumina, the following compounds were isolated: 281 mg. of the methyl ether VIc, m.p. 57.5–58.5°, identical by mixed m.p. with the product obtained directly from VIa and methanol; 32 mg. of the symmetric ether V; and 11 mg. of the alcohol VIa.

α -Methoxy-1,1'-trimethyleneferrocene (VIc).—A solution prepared from 250 mg. of alcohol VIa in 10 ml. of methanol and 0.1 ml. of acetic acid was heated at reflux in a nitrogen atmosphere for 2 hours. Isolation procedures similar to those employed for the preparation of the ethyl ether VIb gave 242 mg. of product, m.p. 57–58°, as yellow-orange blocks from petroleum ether.

Anal. Calcd. for $C_{15}H_{18}OFe$: C, 65.65; H, 6.30; Fe, 21.81. Found: C, 65.84; H, 6.53; Fe, 21.96.

Bridge Enlargement in α -Keto-1,1'-trimethylferrocene.—Four grams (0.016 mole) of the ketone III dissolved in 150 ml. of absolute methanol was added to 125 ml. of an ethereal solution containing 0.018 mole of diazomethane. The solution was kept at 0° in the dark for 72 hours, at the end of which time acetic acid was kept at 0° in the dark for 72 hours, at the end of which time acetic acid was added to destroy unreacted diazomethane. Solvent was removed leaving 3.8 g. of partially crystalline material. This was taken up in 10 ml. of anhydrous ether and chromatographed on 800 g. of Merck alumina employing petroleum ether (b.p. 30–60°) as initial eluent. Three bands developed, the first (yellow), eluted with petroleum ether-ether (95:5), gave, after recrystallization from petroleum ether, 2.25 g. of β -keto-1,1'-tetramethyleneferrocene, m.p. 113.5–114.5°.

Anal. Calcd. for $C_{14}H_{14}OFe$: C, 66.17; H, 5.55. Found: C, 66.23; H, 5.64.

A second orange band, eluted with petroleum ether-ether (9:1), afforded 1.3 g. of unreacted ketone III, while a third orange band gave a small amount of α -keto-1,1'-tetramethyleneferrocene (VII), m.p. 101–102°.

Reduction of β -Keto-1,1'-tetramethyleneferrocene.—The ketone (800 mg.) was dissolved in 50 ml. of freshly distilled diethylene glycol and to this was added 5 g. of potassium hydroxide and 400 mg. of hydrazine hydrate. The solution was heated in a nitrogen atmosphere at 220° for 1 hour and then at reflux for 6 hours. The solution was then cooled, poured into 15 ml. of ice-water and neutralized with dilute sulfuric acid. The aqueous solution was extracted several times with ether and the combined organic solution was washed with water and dried over

magnesium sulfate. Removal of drying reagent and solvent left 620 mg. of yellow oil which was taken up in 10 ml. of petroleum ether (b.p. 30–60°) and chromatographed on 400 g. of alumina employing the same solvent as eluent. The major fraction which was eluted rapidly gave 600 mg. of 1,1'-tetramethyleneferrocene, m.p. 63–64° (lit.¹² 61–62°).

Enol Acetate of β -Keto-1,1'-tetramethyleneferrocene (XIII).—A mixture of 193.4 mg. (0.76 mmole) of β -keto-1,1'-tetramethyleneferrocene, 38.7 mg. (0.20 mmole) of *p*-toluenesulfonic acid and 30 ml. of freshly distilled isopropenyl acetate was refluxed in a nitrogen atmosphere for 48 hours. The excess isopropenyl acetate was distilled off under reduced pressure, leaving an orange-brown residue, which was dissolved in 200 ml. of diethyl ether. The ether solution was washed 3 times with 25-ml. portions of 1% sodium bicarbonate and 6 times with 50-ml. portions of water. After drying the yellow ether solution over anhydrous magnesium sulfate, solvent and isopropenyl acetate were removed *in vacuo*. The brown residue was dissolved in a few milliliters of Skellysolve B and chromatographed on Florosil. Two bands developed and separated cleanly with ether-petroleum ether (1:9) solution. The first band was eluted readily yielding 45.5 mg. (21%) of enol acetate as little yellow needles, m.p. 123–124°.

Anal. Calcd. for $C_{15}H_{18}O_2Fe$: C, 64.89; H, 5.44. Found: C, 64.76; H, 5.43.

A second, orange band, eluted with ether-petroleum solution (1:1), yielded 147.3 mg. of starting material.

Enol Acetate of α -Keto-1,1'-trimethyleneferrocene (XII).—This substance was obtained as orange, granular crystals, m.p. 129–130°, in yields of 7–10% on refluxing III in isopropenyl acetate solution in the presence of *p*-toluenesulfonic acid for 50 hours.

Anal. Calcd. for $C_{15}H_{14}O_2Fe$: C, 63.85; H, 5.00. Found: C, 64.30; H, 5.10.

Enol Acetate of Acetylferrocene.—Treatment of acetylferrocene under conditions identical with those employed for the preparation of XII gave this substance as orange, flat needles, m.p. 50.5–51.0°, in a yield of 25%.

Anal. Calcd. for $C_{14}H_{14}O_2Fe$: C, 62.25; H, 5.22. Found: C, 62.58; H, 5.18.

Reaction of Ferrocene with Dimethylmalonyl Chloride.—Ferrocene (5 g., 0.027 mole), dissolved in 300 ml. of methylene chloride, was added over a period of 6 hours to a stirred solution of freshly distilled dimethylmalonyl chloride (5 g., 0.030 mole) in methylene chloride maintained at 0°. The reaction was allowed to proceed overnight at 0°, after which time ice water was added to the violet solution. The organic layer was separated, washed separately with sodium carbonate solution, then with water to neutrality and finally dried over magnesium sulfate. After filtering off drying reagent and removal of solvent, the crude product was taken up in Skellysolve B and placed on a chromatographic column prepared from 500 g. of Merck alumina (2% water added). Elution with benzene-Skellysolve B mixture led to the isolation of three ketonic products. Isobutyrylferrocene was eluted first as a yellow oil. This substance was not analyzed, but its structure is assigned on the basis of the essential identity of its infrared spectrum with that of 1,1'-disobutyrylferrocene. This latter substance was isolated as yellow-orange plates, m.p. 50–51°.

Anal. Calcd. for $C_{18}H_{22}O_2Fe$: C, 66.24; H, 6.74. Found: C, 66.20; H, 6.94.

The final band yielded dimethyldiferrocenyloimethane, m.p. 141–142°, as orange needles from petroleum ether.

Anal. Calcd. for $C_{26}H_{24}O_2Fe_2$: C, 64.10; H, 5.13. Found: C, 64.57; H, 5.28.

The same products were isolated when the reaction was carried out at reflux temperature in methylene chloride under conditions of high dilution.

Ethyl α,α -Dimethyl- β -hydroxy- β -ferrocenylpropionate (XIX).—A solution of freshly sublimed formylferrocene (15 g., 0.07 mole) and 38 g. (0.20 mole) of distilled ethyl α -bromoisobutyrate in 250 ml. of anhydrous ether was added to a stirred suspension of magnesium amalgam in 200 ml. of dry ether at such a rate that gentle refluxing of the solvent was maintained. After addition was complete, the reaction mixture was warmed on the steam-bath for 20 minutes, then cooled and decomposed with ice and 200 ml. of cold 10% sulfuric acid solution. The organic phase was withdrawn and the aqueous solution extracted with ether until the extracts were colorless. The combined organic solution was washed to neutrality and dried over magnesium sulfate. Drying reagent was filtered off, solvent removed and the remaining oil was vacuum distilled at 70° (2 mm.) to remove unreacted bromoester. The crude hydroxyester, which remained as a viscous yellow oil, weighed 22.5 g.

Ethyl α,α -Dimethyl- β -ferrocenylpropionate (XX).—The ester obtained above was taken up in 150 ml. of glacial acetic acid

containing 1.5 ml. of 70% perchloric acid and 900 mg. of platinum oxide catalyst, and hydrogenated at atmospheric pressure. At the end of 3 days uptake was essentially complete and the reaction mixture was poured into 1000 ml. of water containing sodium bisulfite, and extracted repeatedly with ether. The combined ether extract was washed with saturated sodium carbonate solution and finally with saturated sodium chloride solution to neutrality, and then dried over magnesium sulfate. Drying reagent was filtered off and solvent removed leaving 19.5 g. of ester as a yellow oil.

α,α -Dimethyl- β -ferrocenylpropionic Acid (XXI).—Five grams of the above ester were dissolved in 200 ml. of methanol containing 10 g. of potassium hydroxide. The solution was heated at reflux in a nitrogen atmosphere for 4 hours, cooled and poured into water. Workup gave 2.94 g. of the acid, m.p. 143–147°. An analytical sample was obtained by recrystallization of the product from ether–petroleum ether.

Anal. Calcd. for $C_{15}H_{18}O_2Fe$: C, 62.93; H, 6.29. Found: C, 62.80; H, 6.35.

Cyclization of α,α -Dimethyl- β -ferrocenylpropionic Acid.—The acid (3.0 g., 0.01 mole), dissolved in 40 ml. of dry methylene chloride, was added, in a nitrogen atmosphere, to a refluxing solution of 5.5 g. of trifluoroacetic anhydride (0.03 mole) in 30 ml. of the same solvent. At the end of 24 hours, the solution was cooled and poured into 100 ml. of a 1% aqueous sodium hydroxide solution. After workup, the product was chromatographed on 600 g. of Merck alumina, eluting with petroleum ether–ether mixtures. Two bands developed; the first, light orange in color, gave 1.2 g. of crystalline ketone XXII which after one recrystallization from ether–petroleum ether had m.p. 134–135°.

Anal. Calcd. for $C_{15}H_{16}OFe$: C, 67.16; H, 5.97. Found: C, 67.00; H, 6.37.

The deeper orange band which followed this afforded 1.1 g. of the isomeric ketone as an orange oil.

Reduction of α -Keto- β,β -dimethyl-1,1'-trimethyleneferrocene.—The bridged ketone (1.8 g.) was taken up in 200 ml. of glacial acetic acid containing 2 ml. of 70% perchloric acid and hydrogenated in the presence of 200 mg. of platinum oxide catalyst at a pressure of 27 lb. After 24 hours, uptake was essentially complete and the reaction mixture was worked up in the normal manner. The crude product was taken up in a small volume of ether–petroleum ether (b.p. 30–60) and chromatographed on 200 g. of Merck alumina (2% water added) employing petroleum ether as eluent. In this manner 1.4 g. of product was obtained, m.p. 98–101°. Recrystallization from petroleum ether gave an analytical sample, m.p. 101–103°.

Anal. Calcd. for $C_{15}H_{18}Fe$: C, 70.86; H, 7.08. Found: C, 70.59; H, 7.22.

Deuterium Exchange Reactions.— β -Keto-1,1'-tetramethyleneferrocene (50.8 mg.), dissolved in 25 ml. of tetrahydrofuran freshly distilled from lithium aluminum hydride, was treated with 5 ml. of deuterium oxide and 54 mg. of sodium methoxide. After stirring the reaction mixture in a nitrogen atmosphere at room temperature for 16 hours, workup gave 44 mg. of ketone, m.p. 113–114°, whose infrared spectrum exhibited two new bands at 4.5 and 4.54 μ as well as deep seated alteration in peak positions between 7 and 12 μ .

Similar treatment of α -keto-1,1'-trimethyleneferrocene for a period of 22 hr. gave a product whose infrared spectrum was identical with that of the starting material.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, STANFORD UNIVERSITY, STANFORD, CALIF.]

Optical Rotatory Dispersion Studies. LXXIX.¹ The Location of the $n-\pi^*$ Absorption Band of α -Iodo Ketones and its Relation to Circular Dichroism and Optical Rotatory Dispersion²

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The ultraviolet absorption, circular dichroism and optical rotatory dispersion curves have been measured of six optically active α -iodo ketones, in which the iodine atom either possessed the axial or equatorial orientation, or was attached to a methyl ketone grouping. In all but one instance, the ultraviolet absorption spectrum was nearly or totally useless in locating the $n-\pi^*$ absorption band in the 300 $m\mu$ region. It could, however, be recognized very readily by means of circular dichroism or optical rotatory dispersion measurements. The location of this band, as well as that of the iodine absorption in the 260 $m\mu$ region, can be related to the orientation (axial *vs.* equatorial) of the iodine atom in the same manner as has been done earlier with α -bromo- and α -chloro-ketones. Attention is called to the observation that, in the two steroidal α -iodo methyl ketones available for study, both optical rotatory dispersion and circular dichroism indicated the presence or even preponderance of that rotomer in which the I—C—C=O geometry approaches that of an axial α -iodocyclohexanone. For comparison purposes, ultraviolet absorption, circular dichroism and optical rotatory dispersion curves are also recorded for the analogous α -bromo ketones, where the $n-\pi^*$ absorption can be readily recognized by all three methods.

The ultraviolet absorption spectra of α -bromo- and α -chlorocyclohexanones (notably in the steroid series) have been studied in detail by Cookson,³ who has noted characteristic shifts of the $n-\pi^*$ absorption band depending upon the axial or equatorial orientation of the halogen atom. The identical shifts were noted^{4,5} in the optical rotatory dispersion curves and this physical tool is at times preferable for configurational assignments—especially among equatorially substituted α -halo ketones—where the ultraviolet absorption maxima are often ill defined.

In contrast to the wealth of published information on the close correlation of ultraviolet absorption and optical rotatory dispersion among α -bromo- and α -chlorocyclohexanones, very little is known about the corresponding situation among α -iodo ketones. The

two measurements which have been recorded⁶ indicate that while a hypsochromic shift is noted in the ultraviolet absorption maximum—when compared with that of the halogen-free parent ketone—the rotatory dispersion extrema suffer a bathochromic shift. The following explanation was offered⁷ for this apparent major discrepancy: “The absorption band at 258 $m\mu$ is due to the iodine atom and apparently is not optically active, whereas the Cotton effect is associated with a second ultraviolet absorption maximum in the 290 $m\mu$ region—of sufficiently low intensity as to be masked by the iodine absorption and not detectable under the experimental condition employed—which is optically active and which corresponds to the carbonyl group. Circular dichroism studies would be very instructive with such α -iodo ketones, since they would settle this point unambiguously.” The present paper is concerned with such measurements, which confirm completely the correctness of our earlier views.⁷ Furthermore, we wish to call attention to some observations on the relative preference of axial *vs.* equatorial orientation in α -iodo ketones.

Just as in our earlier¹ communication on the relation of ultraviolet absorption, circular dichroism and optical

(1) Paper LXXXVIII, C. Djerassi, H. Wolf and E. Bunnenberg, *J. Am. Chem. Soc.*, **84**, 4552 (1962).

(2) Supported by the National Science Foundation (grant No. G 19905) and the National Cancer Institute (grant No. CRTY-5061) of the National Institutes of Health, U. S. Public Health Service.

(3) R. C. Cookson, *J. Chem. Soc.*, 282 (1954); R. C. Cookson and S. H. Dandegaonker, *ibid.*, 352 (1955).

(4) C. Djerassi, J. Osiecki, R. Riniker and B. Riniker, *J. Am. Chem. Soc.*, **80**, 1216 (1958).

(5) C. Djerassi, “Optical Rotatory Dispersion: Applications to Organic Chemistry,” McGraw-Hill Book Co., Inc., New York, N. Y., 1960, Chapter 9.

(6) C. Djerassi, I. Fornaguera and O. Mancera, *J. Am. Chem. Soc.*, **81**, 2383 (1959).

(7) Reference 5, p. 118.