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BRIDGED FERROCENES

VII *. SYNTHESIS OF DI- AND TRI-BRIDGED FERROCENES WITH PENTAMETHYLENE CHAINS

MASAO HISATOME

Department of Energy and Environment, Division of Chemical Sciences Brookhaven National Laboratory, Upton, N.Y. 11973 (U.S.A.)
and Faculty of Pharmaceutical Sciences, Science University of Tokyo, Shinjuku-ku, Tokyo 162 (Japan) **

and MANNY HILLMAN

Brookhaven National Laboratory, Upton, N.Y., 11973 (U.S.A.)

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Summary

Double or successive bridge-enlargement reactions were used on appropriate α-ketones followed by reduction to prepare 1,1′-pentamethyleneferrocene, VIII, 1,1′,3,3′-bis(pentamethylene)ferrocene, XX, and 1,1′,2,2′,4,4′-tris(pentamethylene)ferrocene, XXX. The bridge-enlarging reactions are discussed, and the PMR spectral behavior of the polybridged ferrocenes is briefly discussed.

Introduction

Studies on polybridged ferrocenes are of interest because of their unusual chemical and physical properties, possibly due to the strain caused by bridging with polymethylene chains and possibly due to interactions of the iron atom with the bridges. Syntheses, reactions and properties of ferrocenes with tri- and tetramethylene bridges have been reported by several groups [2—15], but there has been no report of ferrocenes with two or more pentamethylene bridges except for that of a bis(pentamethylene)-bridged ferrocene with substituents on one bridge [16]. Since Watts et al. [17,18] suggested that the reactions and the PMR spectra of pentamethylene-bridged ferrocenes, IV and

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** Permanent address of Masao Hisatome.

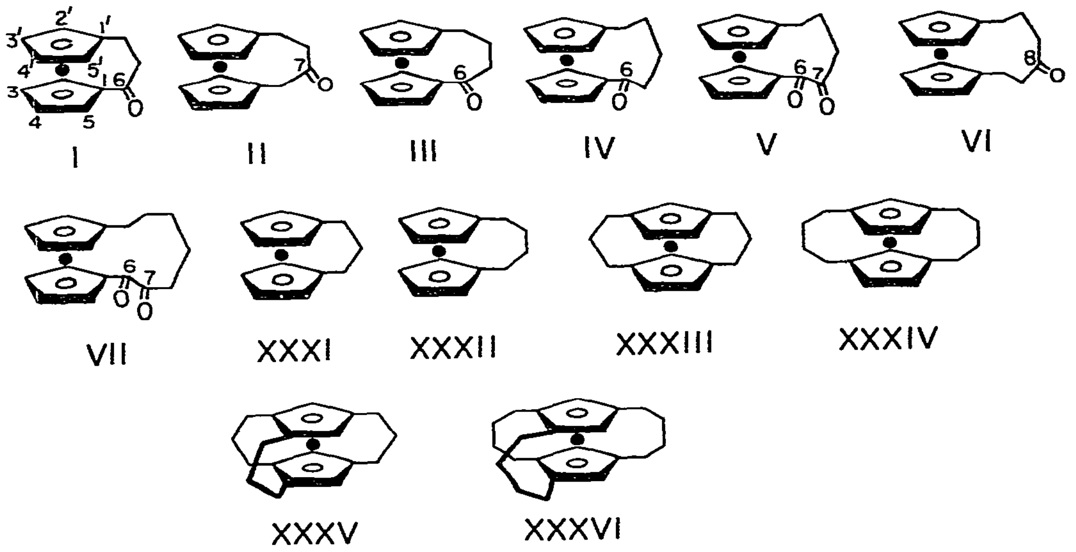

Fig. 1. Compounds and reaction schemes. The dark circles are iron atoms. I: 1,1′-trimethyleneferrocen-6-one, II: 1,1′-tetramethyleneferrocen-7-one, III: 1,1′-tetramethyleneferrocen-6-one, IV: 1,1′-pentamethyleneferrocen-6-one, V: 1,1′-pentamethyleneferrocen-6,7-dione, VI: 1,1′-hexamethyleneferrocen-8-one, VII: 1,1′-heptamethyleneferrocen-6,7-dione, VIII: 1,1′-pentamethyleneferrocene, IX: 2-formyl-1,1′-pentamethyleneferrocene, X: 3-formyl-1,1′-pentamethyleneferrocene, XI: 3-(β-carboxyvinyl)-1,1′-pentamethyleneferrocene, XII: 3-(β-carboxyethyl)-1,1′-pentamethyleneferrocene, XIII: 1,1′-pentamethylene-3,3′-trimethyleneferrocen-11-one, XIV: 1,1′-pentamethylene-3,4′-trimethyleneferrocen-11-one, XV: 1,1′-pentamethylene-3,3′-tetramethyleneferrocen-12-one, XVI: 1,1′-pentamethylene-3,3′-tetramethylene-ferrocen-11-one. XVII: 1,1′,3,3′-bis(pentamethylene)ferrocen-6-one, XVIII: 1,1′-hexamethylene-3,3′-pentamethyleneferrocen-6-one, XIX: 1,1′-pentamethylene-3,3′-tetramethyleneferrocene, XX: 1,1′,3,3′-bis(pentamethylene)ferrocene, XXI: 2-formyl-1,1′,3,3′-bis(pentamethylene)ferrocene, XXII: 4-formyl-1,1′,3,3′-bis(pentamethylene)ferrocene, XXIII: 4-(β-carboxyvinyl)-1,1′,3,3′-bis(pentamethylene)ferrocene, XXIV: 4-(β-carboxyethyl)-1,1′,3,3′-bis(pentamethylene)ferrocene, XXV: 1,1′,3,3′-bis(pentamethylene)-4,5-trimethyleneferrocen-16-one, XXVI: 1,1′,3,3′-bis(pentamethylene)-4.5′-trimethyleneferrocene-16-one, XXVII: 1,1′,3,3′-bis(pentamethylene)-4,4′-trimethyleneferrocene-16-one, XXVIII: 1,1′,3,3′-bis(pentamethylene)-4,4′-tetramethyleneferrocene-16-one, XXIX: 1,1′,2,2′,4,4′-tris(pentamethylene)ferrocen-6-one, XXX: 1,1′,2,2′,4,4′-tris(pentamethylene)ferrocene, XXXI: 1,1′-trimethyleneferrocene, XXXII: 1,1′-tetramethyleneferrocene, XXXIII: 1,1′3,3′-bis(trimethylene)ferrocene, XXXIV: 1,1′,3,3′-bis(tetramethylene)ferrocene, XXXV: 1,1′,2,2′,4,4′-tris(trimethylene)ferrocene, XXXVI: 1,1′,2,2′,4,4′-tris(tetramethylene)ferrocene.

VIII *, differed from those of tri- and tetramethylene-bridged ferrocenes, a more thorough investigation of pentamethylene-bridged ferrocenes appeared to be in order. This paper reports the synthesis and properties of bis- and tris-(pentamethylene)-bridged ferrocenes.

Condensations described by Barr and Watts [17,19,20] and other groups [16,21,22] for the preparation of derivatives of VIII and XX are unfavorable for the stepwise synthesis of XXX, because, in the preparation of the precursor diacylferrocenes, substitution at the desired positions of the cyclopentadienyl rings is not preferred, and separation of the desired diacyl isomers from the others is difficult. We, instead, synthesized pentamethylene-bridged ferrocenes by bridge enlargement of the appropriate, easily prepared α-ketotrimethylene-bridged ferrocenes.

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* All compounds described with Roman numerals are illustrated and named in Fig. 1.

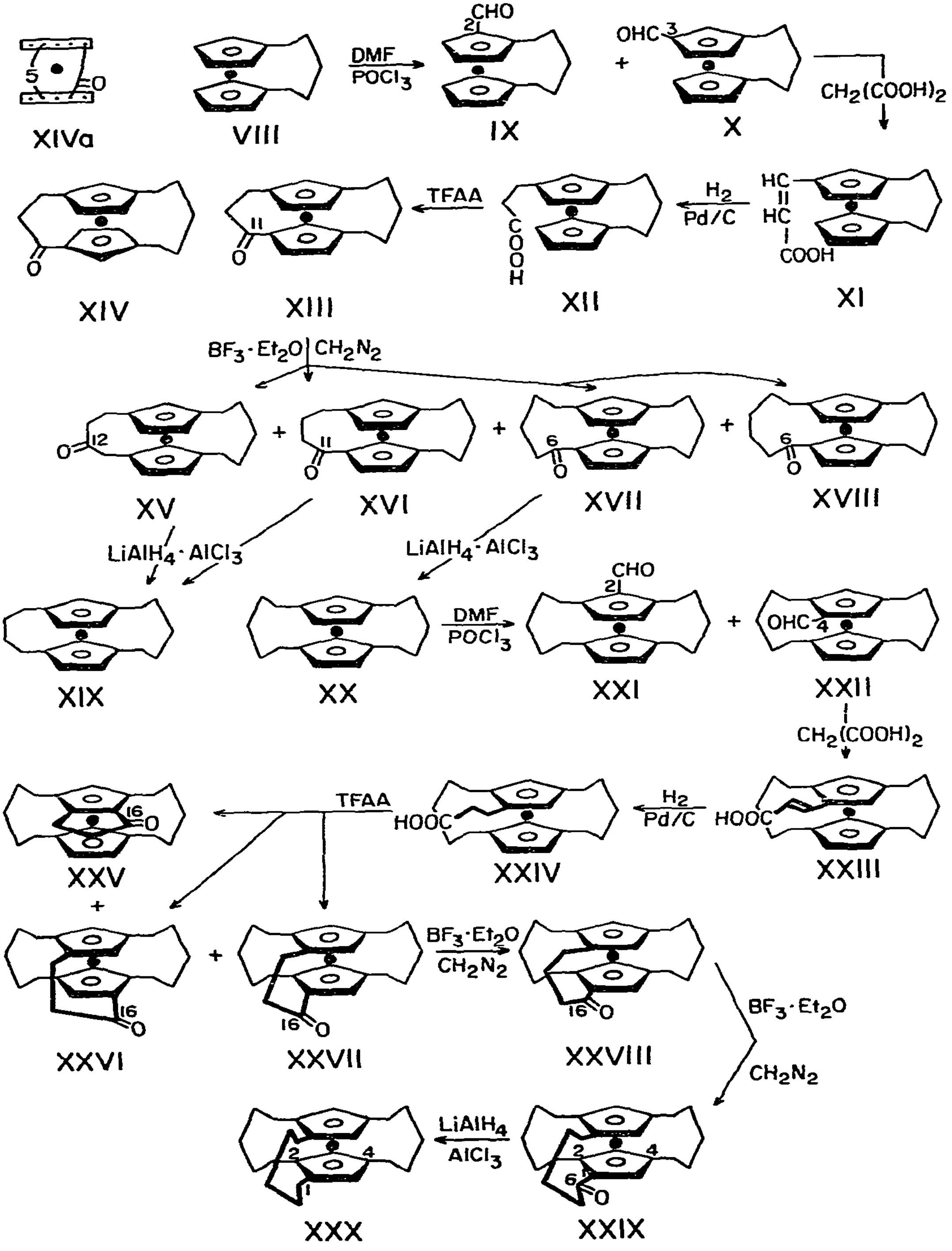

Fig. 1. continued.

TABLE 1

RESULTS OF BRIDGE ENLARGEMENT OF I—III WITH C_2N_2 AND LEWIS ACIDS

SM [b]	Solvent	Catalyst	SM/Cat/CH_2N_2 (mole ratio)	Yields of products [c] (%)						
				I	II	III	IV	V	VI	VII
II [a]	Diglyme	$AlCl_3$	4.0/4.0/17	—	31	—	0	14	4.4	1.6
II	Diglyme	$AlCl_3$	4.0/4.5/22	—	0	—	0	0	23	6.9
I	Benzene	$BF_3 \cdot Et_2O$	5.0/11/22	4.2	29	9.8	28	0	0	0
III	Benzene	$BF_3 \cdot Et_2O$	1.0/2.1/5.4	—	—	22	52	0	0	0

[a] Most of II was recovered under the following conditions: II/$AlCl_3$/CH_2N_2 (4.0/4.5/8.4) in diglyme, II/$BF_3 \cdot Et_2O$/CH_2N_2 (1.2/1.4/7.1) in diglyme, II/$BF_3 \cdot Et_2O$/CH_2N_2 (2.0/4.0/14) in benzene, and II/MeOH/CH_2N_2 (2.0/2.0/24, 1 month) in ether. [b] Starting material. [c] Several other products were formed but could not be isolated because of overlapping in chromatography.

Results

Bridge enlargement of α-ketotrimethyleneferrocene, I, with diazomethane to give II has been reported by Rosenblum et al. [23] and has been applied to the syntheses of tetramethylene-bridged ferrocenes [8,9]. Muller et al. [24] reported the insertion of two methylene units into cyclooctanone with diazomethane and Lewis acids, and $BF_3 \cdot Et_2O$ was reported to be an excellent Lewis acid for this purpose [10,25]. In our experience, on treatment of the β-ketone, II, with diazomethane, most of the starting material was recovered unchanged with or without $BF_3 \cdot Et_2O$ as a Lewis acid, even when using a large excess of diazomethane. Reaction of II with diazomethane and $AlCl_3$ in 2-methoxyethyl ether (diglyme), however, gave several bridge-enlargement products of which three compounds, V-VII, were isolated by chromatography. The pentamethyleneferrocene was obtained in low conversion (Table 1) as the α,β-diketone, V. The α,β-diketones V and VII were possibly formed by oxidation of the corresponding β-ketones during work-up (e.g. during chromatography) by the action of air and/or light *.

On the other hand, the insertion reaction of diazomethane into the α-ketones I or III in the presence of $BF_3 \cdot Et_2O$ gave the desired results. III was apparently formed first from I and then IV was derived by further insertion of diazomethane into III. As will be described later, preferential formation of α-ketones was also found for the bridge-enlargement of the corresponding polybridged ferrocenes.

Elaboration of additional bridges proceeded as in Fig. 1. Formylation of VIII gave two isomers, IX and X. The major product, X, was assigned as the 3-formyl isomer on the basis of a triplet with *meta* coupling (1.5 Hz) in its PMR spectrum, while the spectrum of the 2-formyl isomer, IX, has a triplet with *ortho* coupling (2.6 Hz). Both compounds have two double doublet signals with *ortho* and *meta* coupling. X was converted to the propionic acid, XII,

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* Air oxidation at the α-position of β-ketotetramethylene-bridged ferrocenes has been reported [8,26].

by condensation with malonic acid and subsequent hydrogenation. Cyclization of XII gave only one product, XIII, which agreed in its melting point and PMR spectrum with the compound reported by Brown and Winstead [6]. The possibility of the formation of XIV, a slant * cyclization product, was ruled out since three ketotrimethylene products were formed from XXIV, as described below.

Treatment of XIII with diazomethane in the presence of $BF_3 \cdot Et_2O$ afforded the four bridge-enlargement products XV—XVIII. The properties of compound XV agreed with those described by Brown and Winstead [6]. XVI, which was not described in their paper, was reduced to give XIX, the same reduction product obtained from XV. The mass and IR spectra of XVII indicated the insertion of two methylene units and the presence of an α-keto group. The NMR spectra of XVII also supported the assigned structure; four double doublets and two triplets with *meta* coupling of ring protons and methylene signals corresponding to nine carbons appeared in the PMR and ^{13}C NMR spectra, respectively. The reduction product, XX, of XVII had PMR and ^{13}C NMR spectra with signals of two ring protons with an intensity ratio of 1 : 2 and three kinds of ring carbons with an intensity ratio of 2 : 1 : 2.

Formylation of XX gave the two isomers, XXI and XXII, of which the 2- and 4-substituted structures were confirmed by their PMR spectra. The major product, XXII, was converted to the propionic acid, XXIV. Three cyclization products, XXV—XXVII, were obtained from XXIV. The minor product, XXV, was assigned the homoannular structure on the basis of a singlet peak in the PMR spectrum corresponding to an acylated ring proton. The PMR spectra of the other minor product, XXVI, and of the major product, XXVII, showed two doublet signals arising from acylated cyclopentadienyl rings. These signals established both as heteroannular cyclization products. The structure of XXVII was established by the determination of the structure of XXX as described below. The fact that two heteroannular and one homoannular cyclization products were produced confirms the assigned structure of XIII. Cyclization of a propionic acid derived from XIV would have given at most one heteroannular and one homoannular product.

The ketone, XXVII, was treated with diazomethane to give XXVIII. No XXIX was formed. XXVIII was further treated with diazomethane to afford XXIX. The structural assignement of XXIX was supported by the IR spectrum, the mass spectrum, and two doublets with *meta* coupling corresponding to ring protons on an acylated ring in the PMR. Reduction of XXIX gave XXX, whose structure was confirmed by its mass spectrum and by the presence of one singlet corresponding to ring protons in the PMR spectrum and three ring carbon signals and six methylene carbons in the ^{13}C NMR spectrum. These simple spectra reveal the high symmetry of XXX. Five kinds of ring carbons and nine methylene carbons would be expected from a corresponding slant cyclization product, and even if there were some overlap, a simple spectrum like that of XXX would not be expected. The previous assumption of the structure of XXVII is thus also confirmed.

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* The term "slant" arises from the alternative projection used in illustrating these compounds (e.g. XIVa) in which one of the bridges appears as a slanted arc.

Discussion

Synthesis of XXX was achieved because of the predominant formation of α-ketones in bridge-enlargements with diazomethane and $BF_3 \cdot Et_2O$. If formation of an α-ketone were not preferential, the insertion of a second methylene would be resisted as was found in the experiments with II. The preference of α-ketone formation is interesting in view of the overwhelming predominant production of a β-ketone in the treatment of I with diazomethane in methanol [8,9,23]. An intermediate, XXXVII, as suggested by House et al. [25] for ring enlargement with diazomethane and Lewis acids, is converted to β- or α-ketones by migration of the ferrocenyl (route B) or the methylene (route A), respectively (Fig. 2). XXXVIII and XXXIX are important resonance contributions to the individual transition states. With a strong Lewis acid, XXXIX is at a relatively lower energy than XXXVIII because of the strong electron-donation of the ferrocenyl group, and the migration of the methylene (route A) is preferred over that of the ferrocenyl. The predominance of formation of α-ketones in the presence of Lewis acids had also been observed [10,27] in the synthesis of polybridged ferrocenes with tetramethylene bridges.

While no slant-bridged compounds have been observed in the trimethylene-bridged ferrocene series [3], in the tetramethylene ferrocene series slant-bridged products were formed in relatively large yields [9]. Unexpectedly, slant-bridged compounds were formed in very small amounts, if at all, in the pentamethylene series even though in this series torsional freedom between the two cyclopentadienyl rings may obtain more easily than in the tri- and tetramethylene-bridged ferrocene series.

An unexpected behavior in the pentamethylene-bridged ferrocene series was also found in the chemical shifts of the ring protons. The chemical shifts for the corresponding tri-, tetra-, and pentamethylene-bridged ferrocenes are given in Table 2. The 2-protons of the cyclopentadienyl ring in XX appear at a higher field than the 4,5-protons. This is the same behavior as observed in the corresponding trimethylene-bridged ferrocene, XXXIII, but just the opposite of that observed in the corresponding tetramethylene-bridged ferrocene, XXXIV. Rinehart et al. [3] suggested that the higher field shift of the 2-protons than the 4,5-protons in XXXIII arose from the inductive effects of the two alkyl

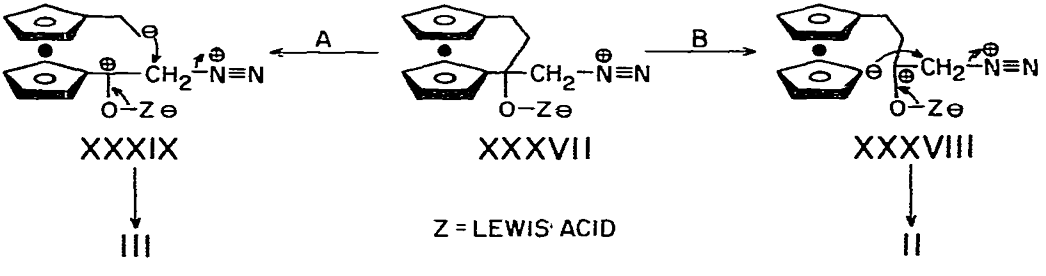

Fig. 2. A possilbe mechanism in bridge enlargement of bridged ferrocenes with diazomethane and Lewis acids.

TABLE 2

CHEMICAL SHIFTS OF RING PROTONS AT 360 MHz [a]

	Ring protons (δ, ppm)			
	2-H	3-H	4-H	5-H
XXXI	3.98	4.02	4.02	3.98
XXXII	4.14	4.10	4.10	4.13
VIII	3.96	4.08	4.08	3.96
XXXIII	3.84	—	3.89	
XXXIV	4.04	—	3.96	
XX	3.76	—	3.86	3.86
XXXV	—	3.76	—	3.76
XXXVI	—	3.94	—	3.94
XXX	—	3.67	—	3.67

[a] All measurements were made in $CDCl_3$.

bridges and from the proximity of the 2-protons to the iron nucleus. Barr and Watts [17] suggested that the split of the ring protons in VIII but not in XXXII * could be explained by steric compression of the 2,5-protons with the β-methylenes. Since significant ring tilting and iron to ring shortening is not expected in VIII, XX, XXX, XXXII, or XXXIV, and was not observed in XXXVI [28], proximity of the proton to the iron cannot be important. If the steric compression occurs, however, the 2-proton of XX would be expected to appear at a lower field than the 4,5-protons and also at a lower field than the 2-protons of XXXIII, but not at the higher fields as observed. Furthermore, the higher field shift of the ring protons in XXX, compared with that in XXXV, can not be explained by these effects. Accordingly, alternative explanations must be sought for both the chemical shifts and the observed chemical behavior. To this end, studies of properties of the pentamethylene-bridged ferrocene series are proceeding in our laboratories.

Experimental

All melting points are uncorrected. High pressure liquid chromatography (HPLC) was carried out with a Waters Co. Prep System 500. IR spectra were measured using a Hitachi-Perkin-Elmer model 225 grating infra-red spectrometer employing KBr disks. All IR spectral data are given in cm^{-1}. The PMR spectra at 360 MHz in Table 3 were obtained with a Bruker WH-360 spectrometer. We are indebted to Dr. A. MacLaughlin and to Mr. D. Lawler for the spectra at 360 MHz. PMR (Table 3) and ^{13}C NMR (Table 4) spectra were measured on a JEOL JNM FX-100 spectrometer at 100 MHz and 25.1 MHz, respectively, in $CDCl_3$ at room temperature relative to tetramethylsilane as an internal standard.

All chemical shifts are in ppm on the δ scale. Coupling constants were obtained from spectra expanded by five times on the chemical shift axis. Mass

(Continued on p. 227)

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* Splitting of the ring protons in XXXII was recently found at 360 MHz (Table 2), but this split is smaller than that in either XXXI or VIII.

TABLE 3

PMR SPECTRAL DATA (δ, ppm) [a]

	Cyclopentadienyl ring protons	Methylene protons
IV	4.10 (4 H, m, 2′-, 3′-, 4′-, 5′-), 4.50, 4.71 (2 H, 2 H, AA′XX′, 2-, 3-, 4-, 5-)	1.84 (2 H, m), 2.22 (2 H, m), 2.40 (2 H, m), 2.62 (2 H, m)
V	4.05, 4.12 (2 H, 2 H, AA′XX′, 2′-, 3′-, 4′-, 5′-), 4.70, 4.88 (2 H, 2 H, AA′XX′, 2-, 3-, 4-, 5-)	2.01 (2 H, m; 9-), 2.46 (2 H, m, 10-), 2.87 (2 H, m, 8-)
VI	3.89 (2 H, m), 3.99 (2 H, m), 4.07 (4 H, m)	2.09 (2 H, m, 10-), 2.41 (2 H, m), 2.70 (4 H, m), 2.96 (2 H, m)
VII	3.96, 4.28 (2 H, 2 H, AA′XX′, 2′-, 3′-, 4′-, 5′-), 4.64, 5.13 (2 H, 2 H, AA′XX′, 2-, 3-, 4-, 5-)	1.62 (4 H, m), 2.12 (4 H, m), 2.74 (2 H, m, 8-)
IX [b]	3.91, 4.12, 4.20 (1 H, 2 H, 1 H, m, 2′-, 3′-, 4′-, 5′-), 4.40 (1 H, dd, 1.4, 2.6 Hz, 5-), 4.56 (1 H, t, 2.6 Hz, 4-), 4.67 (1 H, dd, 1.4, 2.6 Hz, 3-)	1.5—3.0 (10 H, m)
X [c]	3.94, 4.17, 4.26 (1 H, 2 H, 1 H, m, 2′-, 3′-, 4′-, 5′-), 4.41 (1 H, dd, 1.5, 2.4 Hz, 5-), 4.59 (1 H, t, 1.5 Hz, 2′-), 4.70 (1 H, dd, 1.5, 2.4 Hz, 4-)	1.6—2.5 (10 H, m)
XI [d]	3.81, 3.88, 4.18, 4.27 (1 H, 1 H, 1 H, 2 H, m, 2′-, 3′-, 4′-, 5-, 5′-), 4.34 (1 H, t, 1.4 Hz, 2-), 4.44 (1 H, dd, 1.4, 2.4 Hz, 4-)	1.6—2.5 (10 H, m)
XIII	3.86, 4.51 (1 H, 1 H, dd, 1.5, 2.5 Hz, 4′-, 5′-), 4.21 (1 H, dd, 1.5, 2.5 Hz, 5-), 4.44 (1 H, t, 1.5 Hz, 2′-), 4.67 (1 H, t, 1.4 Hz, 2-), 4.77 (1 H, dd, 1.4, 2.5 Hz, 4-)	1.5—2.3 (10 H, m), 2.89 (4 H, AA′BB′, 12-, 13-)
XVI	3.88, 3.96, (2 H, 1 H, ABX, 2′-, 4′-, 5′-), 4.37 (1 H, dd, 1.4, 2.5 Hz, 5-), 4.52 (1 H, t, 1.4 Hz, 2-), 4.58 (1 H, dd, 1.4, 2.5 Hz, 4-)	1.75 (6 H, m), 2.20 (8 H, m), 2.55 (2 H, m)
XVII	3.87, 4.03 (1 H, 1 H, dd, 1.6, 2.3 Hz, 4′-, 5′-), 3.95 (1 H, t, 1.6 Hz, 2′-), 4.31 (1 H, dd, 1.4, 2.5 Hz, 4-), 4.51 (1 H, t, 1.4 Hz, 2-), 4.64 (1 H, dd, 1.4, 2.5 Hz, 5-)	1.6—2.1 (8 H, m), 2.1—2.7 (10 H, m)

XVIII	3.82, 4.10 (1 H, 1 H, dd, 1.4, 2.4 Hz, 4′-, 5′-), 4.01 (1 H, t, 1.4 Hz, 2′-), 4.31 (1 H, dd, 1.4, 2.5 Hz, 4-), 4.56 (1 H, t, 1.4 Hz, 2-), 4.72 (1 H, dd, 1.4, 2.5 Hz, 5-)	1.82 (12 H, m), 2.20 (4 H, m), 2.40 (4 H, m)
XX	3.76 (2 H, t, 1.4 Hz, 2-, 2′-), 3.86 (4 H, d, 1.4 Hz, 4-, 4′-, 5-, 5′-)	1.82 (8 H, m), 2.06 (4 H, m), 2.36 (8 H, m)
XXI[e]	3.91 (3 H, s, 2′-, 4′-, 5′-), 4.41 (2 H, s, 4-, 5-)	1.4—3.1 (20 H, m)
XXII[f]	3.72(1 H, t, 1.5 Hz, 2′-), 3.98, 4.02 (1 H, 1 H, m, 4′-, 5′-), 4.21 (1 H, d, 1.5 Hz, 2-) 4.48 (1 H, d, 1.5 Hz, 5-)	1.4—3.1 (20 H, m)
XXIII[g]	3.58, 3.62, 4.00 (1 H, 1 H, 1 H, m, 2′-, 4′-, 5′-), 4.09 (1 H; d, 1.3 Hz, 2-), 4.33 (1 H, d, 1.3 Hz, 5-)	1.4—2.8 (20 H, m)
XXIV	3.40, 3.72, 3.81, 3.93 (1 H, 2 H, 1 H, 1 H, m)	1.2—2.8 (24 H, m)
XXV	3.36 (1 H, m, 2′-), 3.62 (2 H, m, 4′-, 5′-), 4.11 (1 H, s, 2-)	1.2—3.0 (24 H, m)
XXVI	3.67, 3.84 (1 H, 1 H, d, 1.5 Hz, 2′-, 4′-), 4.11 (1 H, d, 1.5 Hz, 2-), 4.41 (1 H, d, 1.5 Hz, 5-)	1.2—3.5 (24 H, m)
XXVII	3.53, 3.90, 1 H, 1 H, d, 1.4 Hz, 2′-, 5′-), 4.41 (1 H, d, 1.5 Hz, 2-), 4.64 (1 H, d, 1.5 Hz, 5-)	1.2—3.5 (24 H, m)
XXVIII	3.75, 3.81 (1 H, 1 H, d, 1.4 Hz, 2′-, 5′-), 4.11 (1 H, d, 1.4 Hz, 2-), 4.31, (1 H, d, 1.4 Hz, 5-)	1.2—3.0 (26 H, m)
XXIX	3.67, 3.97 (1 H, 1 H, d, 1.4 Hz, 3′-, 5′-), 4.11 (1 H, d, 1.5 Hz, 3-), 4.35 (1 H, d, 1.5 Hz, 5-)	1.2—3.2 (28 H, m)
XXX	3.67 (4 H, s, 3-, 3′-, 5-, 5′-)	1.2—3.0 (30 H, m)

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[a] The data were obtained at 100 MHz. Relative intensities (1 H, 2 H, etc.), multiplets, coupling constants, and position assignments (1-, 1′-, etc.) are in parentheses. Assignments of signals not definitely assigned are not given in the table. [b] CHO protons at 10.09 ppm. [c] CHO proton at 9.86 ppm. [d] Olefin protons at 5.95, 7.64 ppm (AX, 15 Hz). [e] CHO proton at 10.22 ppm. [f] CHO proton at 10.02 ppm. [g] Olefin protons at 5.93, 7.77 ppm (AX, 15 Hz).

TABLE 4

^{13}C NMR SPECTRAL DATA (δ, ppm) [a]

	Unsubstituted ring carbons	Substituted ring carbons	Methylene carbons	C=O carbons
VIII	66.663(4C), 68.172(4C)	88.931(2C)	24.754(2C), 24.900(8-), 25.144(2C)	
XIII	69.219(2C), 69.630 70.217, 72.096, 73.564	72.566(3-), 86.891, 91.879, 95.637	24.306, 24.540(2C), 24.658, 25.480 31.879(13-), 43.739(12-)	212.466
XV	66.577, 67.233, 68.280(2C), 68.574, 68.926	74.973, 84,778(3-, 3'-), 90.061, 90.235(1-, 1'-)	24.716(5C), 25.304, 39.629, 41.038(11-, 13-)	207.009
XVI	68.045, 68.926, 69.806, 69.924, 70.570, 74.503	77.615(3-), 88.065, 92.058, 96.402	23.718, 23.895, 24.129, 24.775, 25.480, 25.891, 28.180, 39.688(12-)	230.777
XVII	67.106, 68.750, 68.926, 69.102, 70.746, 72.859	78.554(1-), 86.774, 89.709, 93.288	22.075, 24.071, 24.423, 24.716, 25.186, 25.421(3C), 41.566(7-)	205.600
XIX	66.468(2C), 67.540(2C), 68.562(2C)	86.545(2C, 3-, 3'-), 89.126(2C, 1-, 1'-)	24.413(2C), 25.096(2C), 25.729(8-), 26.119(2C), 27.825(2C)	
XX	66.858(4C, 4-, 4'-, 5-, 5'-), 68.756(2C, 2-, 2'-)	87.032(4C)	23.829(2C, 8-, 13-), 24.657(4C), 25.973(4C)	
XXV	68.221, 71.744, 73.153 77.145	76.793(4-), 83.251, 86.774, 89.592, 91.292, 100.277(5-)	21.194, 23.131, 23.660, 24.012, 24.247 24.658(2C), 25.304, 25.538(2C), 25.773, 42.036(17-)	209.122
XXVII	68,574, 70.687, 72.624, 73.329	71.098(4-), 83.425, 84.247, 85.656, 92.410, 92.997	21.311, 22.251, 22.662, 24.834(2C), 25.069(2C), 25.714, 26.302(2C), 28.533, 45.324(17-)	213.584
XXVIII	65.286, 70.687, 73.388, 76.089	76.265(4-), 84.190, 84.365, 86.187, 90.705, 94.524	18.552, 21.546(2C), 23.660, 24.188, 24.834, 25.069(3C), 25.480, 25.832(2C), 35.989(17-)	204.425
XXIX	67.458, 70.394, 72.918, 73.975	74.973(1-), 83.721, 84.308, 87.770, 89.297, 92.762	21.077, 21.722, 21.840, 23.895, 24.716(2C), 24.951(2C), 25.597(3C), 25.891, 26.243, 42.623(7-)	207.534
XXX	67.930(4C, 3-, 3'-, 5-, 5'-)	83.083(4C, 1-, 1'-, 2-, 2'-), 88.151(2C, 4-, 4'-)	21.831(2C), 22.659(4C), 24.754(18-), 24.998(2C), 25.973(2C, 26.265(4C)	

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[a] The relaxation time of each signal was taken into consideration for assessment of the relative intensity. The intensities are given as 2C, 3C, etc. for signals corresponding to two or more carbons, but not for one carbon. Only assignments of the signals which have definitely been assigned are given as 1-, 2-, 3-, etc.

spectra were obtained at 70 eV ionizing energy with a Hitachi RMU-7M double focusing mass spectrometer by the direct insertion method. Mass spectral data are shown in *m/e*. High-resolution mass spectra were analyzed on a Hitachi Datalyser System 002.

With the exception of compounds IX, X, XI, XVI, XXI, XXII, XXIII, and XXIV, which were intermediates and side products in the syntheses of the desired compounds, the molecular formulas of the new compounds were confirmed by means of the high resolution mass spectra. The molecular formulas of the exceptions were assumed as stated since 1) they were formed by established reactions from fully characterized compounds, and/or 2) they were converted by established reactions to fully characterized compounds. Moreover, the proton magnetic resonance spectra not only indicated the purity and the isomeric composition of these compounds, but they also provided the expected ratios of the various kinds of protons in the molecules, and low resolution mass spectra provided the expected masses.

Compounds I, II, and III were prepared by literature methods [3,8,23]. Except for the investigations of the reactions of diazomethane with I, II, and III, compound VIII was prepared by the method of Barr and Watts [19].

Treatment of I, II and III with diazomethane

A solution of the ketone in dry solvent was cooled (if in diglyme to 0°C; if in benzene to 10°C) under a N_2 atmosphere. To the stirred solution was slowly added $AlCl_3$ or a solution of $BF_3 \cdot Et_2O$ in diglyme or benzene. An ether solution of alcohol-free diazomethane (ca. 0.2 *M*), which had been prepared from Diazald(TM) obtained from Aldrich Chemical Co. and stored over KOH, was rapidly added to the solution of the complex and stirred for the required time. The reaction mixture in diglyme was poured into water, and the resultant was extracted with ethyl acetate. The reaction mixture in benzene was poured into water and the aqueous phase was removed. The organic solutions were washed with 3 *N* HCl, with saturated Na_2CO_3, and with water several times, then dried over Na_2SO_4 and evaporated to dryness. The resulting residue was chromatographed on open silica gel columns, on the HPLC, or on preparative TLC plates to separate the products. The products were characterized as follows: IV) m.p. 118—119°C (lit. [19] m.p. 123.5—124.5°C). IR spectrum: 1637 (C=O). Mass spectrum: 268.0545 (M^+, calcd. mol. wt. for $C_{15}H_{16}OFe$, 268.0549). V) m.p. 138—139°C. IR spectrum: 1634, 1700 (C=O). Mass spectrum: 282.0339 (M^+, calcd. mol. wt. for $C_{15}H_{14}O_2Fe$, 282.0341). VI) m.p. 98—100°C. IR spectrum: 1692 (C=O). Mass spectrum: 282.0696 (M^+, calcd. mol. wt. for $C_{16}H_{18}OFe$, 282.0705). VII) m.p. 119—121°C. IR spectrum: 1629, 1696 (C=O). Mass spectrum: 310.0643 (M^+, calcd. mol. wt. for $C_{17}H_{18}O_2Fe$, 310.0655). The results of the bridge enlargements are summarized in Table 1. Reduction of IV, which had resulted from the reaction of I and III with diazomethane/$BF_3 \cdot Et_2O$, gave VIII (m.p. 59.5—61°C, lit. [29] 60—61°C).

Formylation of VIII

A solution of VIII (24.7 g, 97 mmol) and dimethylformamide (14.6 g, 200 mmol) in chloroform (90 ml) was stirred at 0°C for 15 min under a N_2 atmosphere. To the cooled mixture a solution of phosphorous oxychloride (30.6 g, 200 mmol) in chloroform (10 ml) was added dropwise over 50 min. The reaction mixture was slowly stirred at room temperature under a N_2 atmosphere for 17 h, and then evaporated to dryness. Water was added to the residue, and powdered Na_2CO_3 was slowly added to the stirred aqueous mixture. The mixture (containing a dark red oily precipitate) was extracted with benzene several times, and the extracts were washed with saturated NaCl, dried over Na_2SO_4, and evaporated. Chromatography of the residue over silica gel using HPLC with benzene as an eluent separated three components. The first band contained starting material (0.19 g, 0.8%). The second band yielded IX (3.70 g, 14%), which was recrystallized from hexane/ether to give deep red granules, m.p. 51—53°C. IR spectrum: 1670 (C=O). Mass spectrum: 282 (M^+).

The third eluted component was X (19.66 g, 72%), which was recrystallized from hexane/ether to give deep red granules, m.p. 40—41°C. IR spectrum: 1667 (C=O). Mass spectrum: 282 (M^+).

Preparation of XIII

A mixture of X (17.2 g, 61 mmol), malonic acid (15.6 g, 150 mmol) and piperidine (13.0 g, 150 mmol) in pyridine (400 ml) was heated at 90—95°C with stirring under a N_2 atmosphere for 4 h and then allowed to stand overnight at room temperature. The reaction mixture was acidified with 3 *N* HCl to precipitate a red powder. The filtrate was extracted with benzene four times, and the extracts were washed with saturated NaCl, dried over Na_2SO_4, and evaporated to dryness. The residue, together with the above powder, weighed 19.86 g. The crude product was recrystallized from acetone/dichloromethane to give XI as orange-red flakes, m.p. 185—186°C. IR spectrum: 1616, 1674 (C=C and C=O). Mass spectrum: 324 (M^+).

The crude XI (18.5 g, 57 mmol) was reduced with H_2 gas and 10% Pd/C (5.0 g) in 1000 ml of acetone for 19 h. The reaction mixture was filtered, and the filtrate was evaporated to dryness. The residue was dissolved in dichloromethane, and the solution was washed with aqueous ascrobic acid and saturated NaCl, dried over Na_2SO_4, and evaporated. The residue, XII, weighed 16.8 g (91% from X). The crude product was recrystallized from ethanol to give yellow plates, m.p. 93—94°C (lit. [6] m.p. 95—96°C).

A solution of XII (14.6 g, 45 mmol) in dichloromethane (300 ml) was added dropwise to a solution of TFAA (24.0 g, 114 mmol) in dichloromethane (300 ml) at 0°C under an N_2 atmosphere. The reaction mixture was stirred at room temperature for 3 h and then poured into ice-water containing ascorbic acid. The mixture was made alkaline with 10% aq. Na_2CO_3, and the phases were separated. The organic layer was washed with saturated NaCl, dried over Na_2SO_4, and evaporated. The residue was column-chromatographed over silica gel with 2% ethyl acetate in benzene as an eluent. A main orange band yielded XIII (13.0 g, 94%), which was recrystallized from hexane/ethyl acetate to give reddish orange needles, m.p. 104—105°C (lit. [6], m.p. 105—106°C).

Bridge enlargement of XIII

According to the procedure used for I, II and III, $BF_3 \cdot Et_2O$ (450 mg, 3.17 mmol) in benzene (2 ml), XIII (460 mg, 1.50 mmol) in benzene (23 ml), diazomethane (33 ml, 6.6 mmol) were allowed to react for 5 min. The product was column-chromatographed over silica gel. After a few bands of unknown compounds, the first band eluted with benzene yielded XV (70 mg, 15%), m.p. 114—115°C (lit. [6], m.p. 114—115.5°C). The second band eluted with 2% ethyl acetate in benzene yielded the starting material (20 mg, 4.3%). The third band eluted with 2% ethyl acetate in benzene yielded XVII (230 mg, 46%), which was recrystallized from hexane/ethyl acetate to give orange flakes, m.p. 111.5—112°C. IR spectrum: 1643 (C=O). Mass spectrum: 336.1146 (M^+, calcd. mol. wt. for $C_{20}H_{24}OFe$, 336.1175). The last band eluted with 2—5% ethyl acetate in benzene yielded XVI (130 mg, 27%), which was recrystallized from hexane/ethyl acetate to give orange-red prisms, m.p. 67—68°C. IR spectrum: 1631 (C=O). Mass spectrum: 322 (M^+). XVI was reduced with $LiAlH_4/AlCl_3$ in ether to give XIX, m.p. 33—34°C (lit. [6] m.p. 34.5—36°C), in accord with the reduction product of XV.

In another experiment, a small amount of XVIII (1.6%) was eluted just before a band containing XVII. XVIII was recrystallized from hexane/ethyl acetate to give red plates, m.p. 108—111°C. IR spectrum: 1642 (C=O). Mass spectrum: 350.1332 (M^+, calcd. mol. wt. for $C_{21}H_{26}OFe$, 350.1332).

Preparation of XX

$LiAlH_4$ (0.32 g, 8.4 mmol) was added to a solution of $AlCl_3$ (1.12 g, 8.4 mmol) in ether (60 ml) under a N_2 atmosphere. A solution of XVII (1.43 g, 4.2 mmol) in ether (40 ml) and benzene (10 ml) was added dropwise to the suspension. After the reaction mixture was refluxed for 3 h, first, ethyl acetate and then a mixture of ether and water was added. The organic layer was washed with water, dried over Na_2SO_4, and evaporated. The residue was column-chromatographed over alumina, and the first band, eluted with 25% benzene in hexane, yielded XX (1.33 g, 98%), which was recrystallized from hexane to give orange plates, m.p. 86—87°C. Mass spectrum: 322.1382 (M^+, calcd. mol. wt. for $C_{20}H_{26}Fe$, 322.1382).

Formylation of XX

The formylation was carried out according to the procedure used with VIII using 3.84 g (11.9 mmol) of XX, 4.38 g (60 mmol) of dimethylformamide, 9.21 g (60 mmol) of phosphorus oxychloride and 60 ml of chloroform. The reaction time was 20 h. The crude products were column-chromatographed over silica gel with benzene. Recovered starting material weighed 25 mg (0.7%). The next band yielded XXI (38 mg, 0.9%), which was recrystallized from hexane/ethyl acetate to give red prisms, m.p. 124—125°C. IR spectrum: 1665 (C=O). Mass spectrum: 350 (M^+).

The third band yielded XXII (3.79 g, 91%), which was recrystallized from hexane/ethyl acetate to give red prisms, m.p. 96—97°C. IR spectrum: 1670 (C=O). Mass spectrum: 350 (M^+).

Preparation of XXVII

Synthesis of XXVII from XXII was carried out according to the procedure used for the preparation of XIII from X. Using 3.27 g (9.3 mmol) of XXII, 2.42 g (23.3 mmol) of malonic acid, 1.98 g (23.3 mmol) of piperidine and 80 ml of pyridine, the condensation gave crude XXIII (2.76 g, 76%), which was recrystallized from acetone/dichloromethane to give red prisms, m.p. 195—196°C. IR spectrum: 1601, 1666(sh), and 1677 (C=C and C=O). Mass spectrum: 392 (M^+).

Hydrogenation of XXIII (2.50 g, 6.38 mmol) with 10% Pd/C (0.73 g) in acetone (200 ml) gave XXIV (2.43 g, 97%), which was recrystallized from hexane/ethyl acetate to give orange-yellow prisms, m.p. 123—125°C. IR spectrum: 1703 (C=O). Mass spectrum: 394 (M^+).

Cyclization of XXIV (1.66 g, 4.21 mmol) with TFAA (2.21 g, 10.5 mmol) in dichloromethane (70 ml) gave three products, which were separated by column chromatography over silica gel. The first band eluted with benzene yielded XXVII (1.24 g, 78%), which was recrystallized from hexane/ethyl acetate to give red prisms, m.p. 125—126°C. IR spectrum: 1666 (C=O). Mass spectrum: 376.1478 (M^+, calcd. mol. wt. for $C_{23}H_{28}OFe$, 376.1487).

The second band eluted with benzene yielded XXVI (0.025 g, 1.6%) which was recrystallized from hexane/ethyl acetate to give orange-red prisms, m.p. 167—169°C. IR spectrum: 1647 (C=O). Mass spectrum: 376.1466 (M^+, calcd. mol. wt. for $C_{23}H_{28}OFe$, 376.1487).

The third band eluted with 2% ethyl acetate in benzene yielded XXV (0.020 g, 1.3%), which was recrystallized from hexane/ethyl acetate to give orange prisms, m.p. 145—147°C. IR spectrum: 1692 (C=O) Mass spectrum: 376.1494 (M^+, calcd. mol. wt. for $C_{23}H_{28}OFe$, 376.1487).

Bridge enlargement of XXVII

The reaction of XXVII (200 mg, 0.53 mmol) with diazomethane (2.5 mmol in 12 ml of ether) and $BF_3 \cdot Et_2O$ (150 mg, 1.06 mmol) in benzene (12 ml) followed by column chromatography over silica gel with benzene gave XXVIII (102 mg, 49%) in the last band. The earlier eluted band yielded a mixture of the starting material and unknown products which could not be separated. Recrystallization of XXVIII from hexane/ethyl acetate gave red-orange prisms, m.p. 143—144°C. IR spectrum: 1650 (C=O). Mass spectrum: 390.1662 (M^+, calcd. wt. for $C_{24}H_{30}OFe$, 390.1664). XXVII (257 mg, 0.66 mmol) was treated with diazomethane (1.7 mmol in 8 ml of ether) and $BF_3 \cdot Et_2O$ (100 mg, 0.70 mmol), and the crude product was column-chromatographed over silica gel with benzene. The first and third bands yielded small amounts of unknown products and the starting material (80 mg, 31%), respectively. The second band was XXIX (170 mg, 64%), which was recrystallized from hexane/ethyl acetate to give orange-yellow granules, m.p. 146—147°C. IR spectrum: 1638 (C=O). Mass spectrum: 404.1798 (M^+, calcd. mol. wt. for $C_{25}H_{32}OFe$, 404.1800).

Preparation of XXX

Reduction of XXIX (286 mg, 0.71 mmol) with $LiAlH_4$ (80 mg, 2.1 mmol) and $AlCl_3$ (280 mg, 2.1 mmol) in ether (25 ml) and benzene (5 ml) according to the same procedure as in the reduction of XVII gave XXX (250 mg, 90%), which was recrystallized from hexane/ethyl acetate to give orange-yellow prisms, m.p. 177—179°C. Mass spectrum: 390.1992 (M^+, calcd. mol. wt. for $C_{25}H_{34}Fe$, 390.2008).

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