Preparation and Reactions of Decachloroferrocene and Decachlororuthenocene

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Abstract: The first perhalo and oxidatively stable metallocene, decachloroferrocene, and a number of polychlorinated ferrocenes were prepared from 1,1′-dichloroferrocene by a series of repetitive metalation exchange–halogenation reactions. Structures of the polychlorinated intermediates were established unequivocally by nmr and high-resolution mass spectral analysis. Ruthenocene was converted analogously to decachlororuthenocene by a similar synthetic route. A number of substituted perchlorometallocenes were obtained from the parent perhalometallocenes by metalation exchange or nucleophilic substitution reactions.

A preliminary report of the preparation and properties of decachloroferrocene (Ie), the first metallocene completely substituted with electron-withdrawing groups, and its polychlorinated precursors, Ia–d, together with a thorough mass spectral analysis of Ie and its related polychlorinated ferrocenes Ia–d and IIa–e, has recently appeared.[1–4] The present paper describes in detail the synthesis, reactions, and physical properties of these unique series of compounds as well as that of the second perhalogenated metallocene, decachlororuthenocene (IIIa).

The preparation of decachloroferrocene (Ie) was carried out in a four-step synthesis as shown in Scheme I, starting with 1,1′-dichloroferrocene (Ia) which is readily available by a recently developed procedure.[5] The key to successive addition of chlorine to the ferrocene ring is the fact that chloroferrocene undergoes an α-proton abstraction upon reaction with *n*-butyllithium, in contrast to bromo- and iodoferrocene which undergo a metal–halogen exchange reaction with *n*-butyllithium.[6] Heteroannular dilithiation of Ia was accomplished most conveniently with *n*-butyllithium as its *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) complex in hexane, and occurred, as anticipated, in the 2 and 2′ positions to give If. Inverse addition of If to hexachloroethane[7] afforded 1,1′,2,2′-tetrachloroferrocene (Ib) in good yield. Subsequent lithiation steps were carried out with *n*-butyllithium in tetrahydrofuran (THF) due to the low solubility of compounds Ib–e in hexane. Thus, by dilithiation, followed by exchange chlorination, Ib was converted to 1,1′,2,2′,3,3′-hexachloroferrocene (Ic). Ic was converted to 1,1′,2,2′,3,3′,4,4′-octachloroferrocene (Id) and Id was converted to 1,1′,2,2′,3,3′,4,4′,5,5′-decachloroferrocene (Ie).

The yields of Ic and Id decreased sharply as a result of the formation of by-products in each step which were exceedingly difficult to remove from the main product. Although these by-products were not isolated and definitively identified, their glc behavior indicated that they were probably starting material, monochlorinated starting material, and higher chlorinated starting material. The yield of these by-products was increased markedly by direct addition of the hexachloroethane to the lithiated intermediate. Increase of the reaction time did not noticeably decrease the amount of monochlorinated starting material, but led only to lower overall yields. From this evidence, it appears that both the monochlorinated and original starting material are secondary reaction products, formed as shown in Scheme II, rather than being the result of lower reactivity of the chlorinated metallocene toward lithiation and chlorination.

When a chlorine atom on a metallocene ring is flanked by one or more additional chlorine atoms, it becomes activated sufficiently so that metal–halogen exchange becomes competitive with hydrogen abstraction. A competition of this type has previously been reported for 1,2,3-trichlorobenzene and 1,2,3,4-tetrachlorobenzene in reactions with *n*-butyllithium.[8] The small amounts of more highly chlorinated by-products are undoubtedly due to abstraction of more than two protons from the starting material. The similarity of all of these by-products to the desired product probably accounts for their resistance to removal by recrystallization.

As a result of the low yields obtained in the synthesis of Ic and Id, the overall yield of decachloroferrocene was only 7%. On the assumption that the by-products removed from the intermediates at each step of the synthesis were themselves chlorinated ferrocenes, Ia was also converted to Ie without purifying the intermediates. Five lithiation–chlorination reactions afforded a 42% overall yield of Ie, making this procedure the preferred route to Ie.

A modification of the above direct route from Ia to Ie was also found applicable to the synthesis of decachlororuthenocene (IIIa) from ruthenocene. A total of seven successive lithiation–chlorination reactions were used, with complex mixtures of products resulting in each of the early reactions. The degree of

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(1) F. L. Hedberg and H. Rosenberg, Abstracts of Papers, 159th National Meeting of the American Chemical Society, Houston, Texas, Feb 1970.

(2) F. L. Hedberg and H. Rosenberg, *J. Amer. Chem. Soc.*, **92**, 3239 (1970).

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(4) L. D. Smithson, A. K. Bhattacharya, and F. L. Hedberg, *Org. Mass Spectrom.*, **4**, 383 (1970).

(5) R. F. Kovar, M. D. Rausch, and H. Rosenberg, *Organometal. Chem. Syn.*, **1**, 173 (1971).

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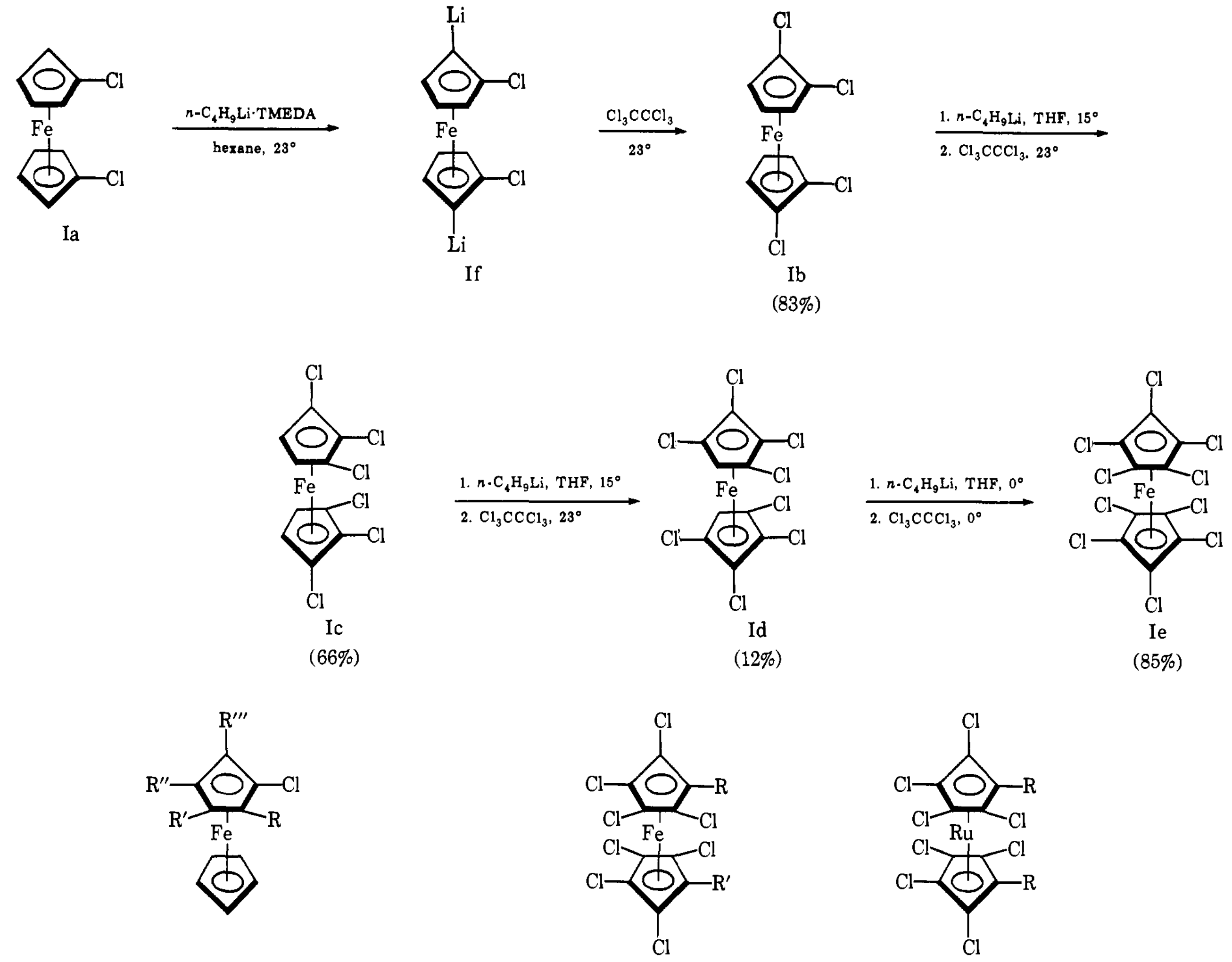
(7) R. L. Gay, T. F. Crimmins, and C. R. Hauser, *Chem. Ind.* (*London*), 1635 (1966).

(8) I. Haiduc and H. Gilman, *J. Organometal. Chem.*, **13**, P4 (1968).

Scheme I



IIa, R, R′, R″, R‴ = H
b, R = Cl; R′, R″, R‴ = H
c, R, R′ = Cl; R″, R‴ = H
d, R, R′, R″ = Cl; R‴ = H
e, R, R′, R″, R‴ = Cl

Ig, R, R′ = Li
h, R, R′ = I
i, R, R′ = COOH
j, R = OCH_3; R′ = Cl
k, R, R′ = OCH_3
l, R = OC_2H_5; R′ = Cl
m, R, R′ = OC_2H_5

IIIa, R = Cl
b, R = Li
c, R = I

polylithiation and metal-halogen exchange occurring during the lithiation half of these reactions predictably appeared to be much greater than that observed with the ferrocene system. This suggests that the only convenient way of isolating the intermediate chlorinated ruthenocenes would be by means of preparative glc. The yield of IIIa (based on ruthenocene) was 14%. In considering alternate syntheses for perchlorometallocenes it would appear that the most desirable route to either Ie to IIIa would be *via* a one-step "sandwiching" of a polychlorinated cyclopentadienide. Two previous attempts to form Ie by reacting ferrous chloride with either pentachlorocyclopentadienyllithium or the corresponding Grignard[9] have been reported. The failure of these attempts is probably due to the low reactivity of the pentachlorocyclopentadienyl anion. We were equally unsuccessful in trying to react pentachlorocyclopentadienyllithium with either ferrous iodide or ferrous acetylacetonate, as well as in attempting to react pentachlorocyclopentadiene with diethylamine and ferrous acetylacetonate. In a study of reactions of the perchlorometallocenes it was found that both Ie and IIIa underwent heteroannular dilithiation upon reaction with *n*-butyllithium to give Ig and IIIb, respectively. These versatile intermediates, in turn, provide synthetic routes to a variety of substituted perchloroferrocenes and perchlororuthenocenes. As examples, Ig was hydrolyzed to give Id, was reacted with iodine to give 1,1′-diiodooctachloroferrocene (Ih), and was carbonated to give octachloroferrocene-1,1′-dicarboxylic acid (Ii). IIIb was similarly reacted with iodine to give 1,1′-diiodooctachlororuthenocene (IIIc).

Direct nucleophilic substitution of Ie was also carried out. Reaction of Ie with sodium methoxide afforded both methoxynonachloroferrocene (Ij) and 1,1′-dimethoxyoctachloroferrocene (Ik), with the relative amounts of each dependent upon reaction time. Sodium ethoxide reacted with Ie to form not only ethoxynonachloroferrocene (Il) and 1,1′-diethoxyoctachloroferrocene (Im) but also a mixture of isomers containing three and four ethoxy groups. Glc indi-

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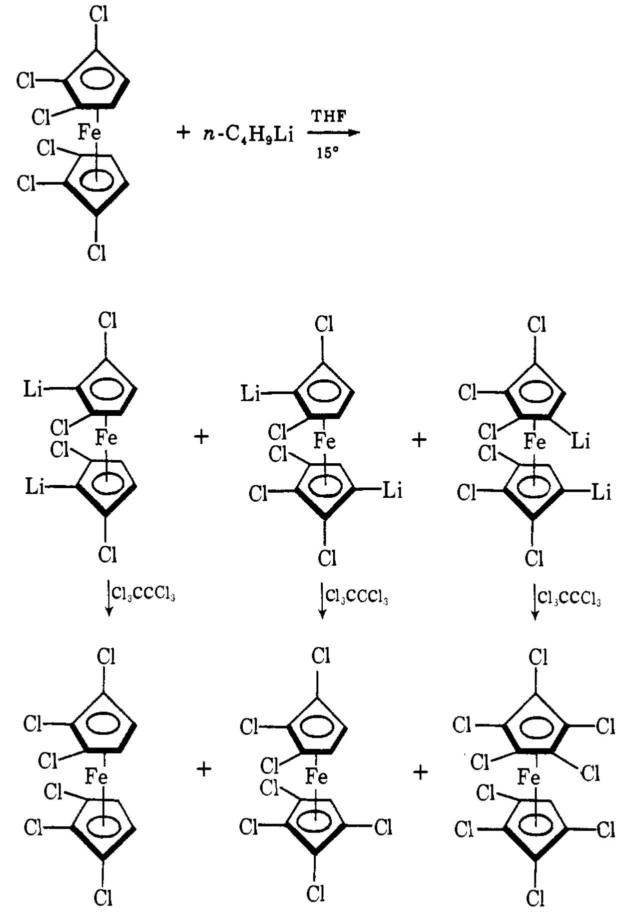
(9) R. L. Schaaf, P. T. Kan, and K. L. Rinehart, Jr., Wright Air Development Center Technical Report 58-187, Part II, May 1960, AD 243 566L.

Scheme II



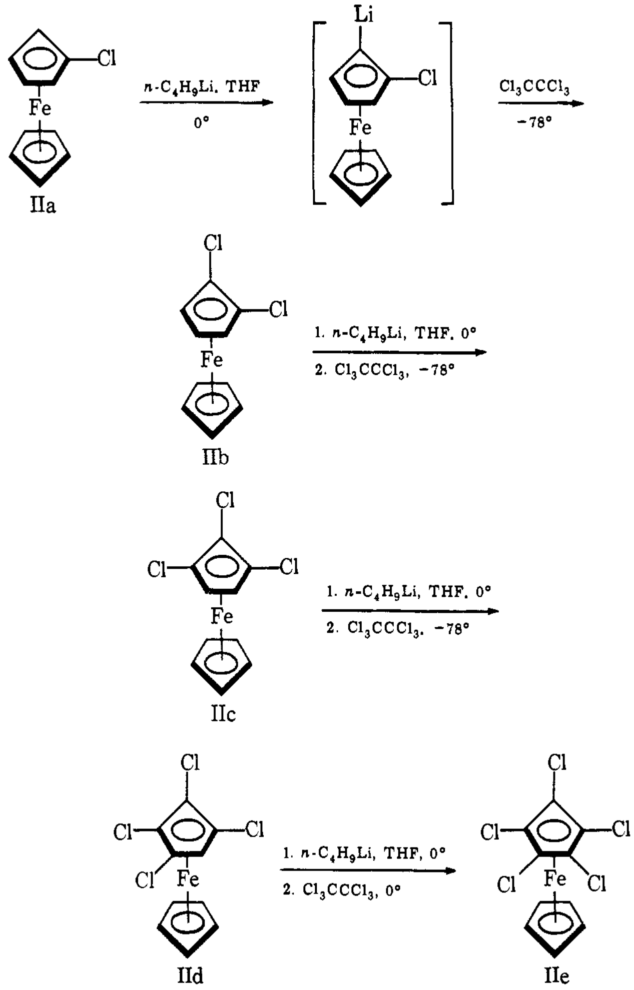
cated the presence of two triethoxy isomers and three tetraethoxy isomers.

In contrast to Ie, the methoxy and ethoxy derivatives were very soluble in all common solvents, making their purification very difficult. Only Im was obtained in sufficient purity to afford a satisfactory elemental analysis. However, the mass spectra of all of these compounds afforded molecular ion peaks with the calculated isotopic distributions. The expected metal–ring fragmentation was also present for each compound. The location of the second ethoxy or methoxy group in the 1′ position in compounds Ik and Im was shown by the absence of a $[M - C_5Cl_5]^+$ peak. Similarly, a distribution of two ethoxy groups per ring in the mixture of tetraethoxy isomers was indicated by the absence of either $[M - C_5Cl_5]^+$ or $[M - C_5Cl_4OC_2H_5]^+$ peaks, and a distribution of two ethoxy groups in one ring and one in the other in the mixture of triethoxy isomers was indicated by the absence of either $[M - C_5Cl_5]^+$ or $[M - C_5Cl_2(OC_2H_5)_3]^+$ peaks. We may thus conclude that the three tetraethoxy isomers are the 1,1′,2,2′, the 1,1′,2,3′, and the 1,1′,3,3′ isomers, while the triethoxy isomers must be the 1,1′,2 and 1,1′,3 isomers.

Attempts to prepare decafluoroferrocene or decafluororuthenocene by an exchange reaction involving treatment of Ie or IIIa with cesium fluoride were unsuccessful. Efforts to react cesium fluoride with either Ih or IIIc were equally unfruitful.

The synthesis of the homoannularly polychlorinated derivatives, IIb–e, was carried out by a procedure analogous to that used for the preparation of Ib–e, as outlined in Scheme III. No attempt was made to optimize yields in any of the four cases.

Scheme III



The primary evidence for the structures proposed for the two series of polychlorinated ferrocenes, Ib–e and IIb–e, was obtained from satisfactory elemental analyses, glc analyses, mass spectral analyses, and the nmr spectra of the compounds. Glc (on SE-30 silicone rubber columns) showed an approximate incremental increase in retention time with increasing chlorine content for the compounds of each series. A thorough analysis of the mass spectra of these compounds has been given in a separate publication[4] and will not be presented in detail here. The molecular ion peaks, isotopic distributions, and fragmentation patterns were all in accord with the proposed structures. The most interesting fragmentation pathway was *via* the elimination of $FeCl_2$, suggesting a possible intramolecular fulvalene formation.

While the mass spectral fragmentation patterns show the distribution of the chlorine atoms between the rings, the distribution of the chlorine atoms within the rings cannot be ascertained. This latter information, however, can be obtained from the nmr spectra of the compounds. The nmr absorbance peaks for compounds Ia–e, IIa–e, and ferrocene are given in Table I. These figures substantiate the prediction that lithiation will occur in a position α to a chlorine atom. For compounds Id and IId it can be seen that there is a marked downfield shift in the absorbance of the lone proton in the substituted ring or rings. This proton must neces-

Table I Nmr Absorbance Peaks[a]

Compd	Unsubstd ring	α protons	β protons
Ia		263, 265, 267	246, 248, 250
Ib		264, 267	245, 248, 251
Ic		265	
Id		275	
Ie			
IIa	250	260, 261.5, 263	238, 240, 242
IIb	255	260, 263	235, 238, 241
IIc	257	259	
IId	262	284	
IIe	263		
Ferrocene	246		

[a] Values are given in cps from TMS as internal standard in $CDCl_3$.

sarily be flanked by a chlorine atom on each side in these two compounds. This observation, coupled with the fact that the center of α-proton absorbance does not vary for compounds Ia–c and IIa–c, is firm evidence that each of the substituted ring protons in Ib, Ic, IIb, and IIc is flanked by a single chlorine atom. Such a situation can only exist if the chlorine atoms are all located adjacent to one another. The integration ratio and multiplicity of each proton absorbance are also in accord with the proposed structures in every case.

Also of interest in the nmr spectra is the lack of significant variance in the position of the β-proton absorbance in Ia–b and IIa–b. These findings suggest that protons α to a chlorine atom are influenced only by electron-withdrawing inductive effects to a degree dependent upon the number of α-chlorine atoms. On the other hand, no negative inductive influence, but only a positive resonance effect, is exerted upon protons β to a chlorine atom. This resonance effect is completely superseded by the inductive effect of an α-chlorine atom, and only shows up in the absence of α-chlorine atoms.

Experimental Section

General. All reactions were carried out under an atmosphere of high-purity nitrogen (99.99%). *n*-Butyllithium in hexane was obtained from Foote Mineral Co., and was found by titration to be 1.5 *M*. Chloroferrocene was prepared by a reported procedure[10] from ferroceneboronic acid, and was purified by preparative glc. Ruthenocene was prepared[11] by a reported procedure and purified by recrystallization from methanol. Glc analyses were performed on either an F & M Model 500 gas chromatograph, using 2 ft × 0.25 in. o.d. columns packed with 10% SE-30 silicone rubber on Chromosorb P, or an F & M Model 402 gas chromatograph, using 4 ft × $^1/_8$ in. o.d. glass columns packed with5% SE-30 gum rubber on Chromosorb P. Molecular weight determinations were carried out on all compounds except Ii with a CEC Model 21-1108 mass spectrometer. Chlorine isotope distributions obtained for the ferrocene derivatives and chlorine–ruthenium isotope distributions obtained for the ruthenocene derivatives were all in agreement with the calculated isotopic patterns. For those compounds for which an exact mass determination was not made, the correct nominal mass was obtained for all peaks in the molecular ion cluster. All melting points reported, except those of compounds Ib–c, were obtained with a Mel-Temp. In the case of compounds Ib–e, the Mel-Temp data were verified by precise values obtained from differential scanning calorimetry at a heating rate of 5°/min. The figures reported for Ib and Id represent the transition points between isotropic liquids and the intermediate liquid crystalline states found for these two compounds.[12]

1,1′,2,2′-Tetrachloroferrocene (Ib). A solution of 1,1′-dichloroferrocene[6] (15.7 g, 0.0616 mol) in hexane (900 ml) was stirred at 23° while a solution of *n*-butyllithium in hexane (100 ml, 0.15 mol) was added, followed by the addition of TMEDA (18.6 g, 0.16 mol). The reaction mixture was stirred at 23° for 50 min and then added over a 35-min period to a stirred solution of hexachloroethane (47 g, 0.20 mol) in hexane (300 ml). After addition was complete, stirring was continued for 5 min and the reaction mixture was filtered through a bed of alumina. The filtrate was concentrated to dryness and the residue was fractionally sublimed. After removal of hexachloroethane at 45° (0.25 mm), the product was sublimed at 120–125° (0.25). The sublimate weighed 16.55 g and consisted (by glc analysis) of trichloroferrocene (2%) and 1,1′,2,2′-tetrachloroferrocene (98%). The latter represents an 83% yield of Ib. Recrystallization from hexane afforded 1,1′,2,2′-tetrachloroferrocene of mp 147°. *Anal.* Calcd for $C_{10}H_6Cl_4Fe$: C, 37.09; H, 1.87; Cl, 43.80; Fe, 17.25; mol wt ($^{35}Cl_3{}^{37}Cl$ isotopes), 323.8543. Found: C, 37.10, 36.87; H, 1.74, 1.91; Cl, 43.86, 43.71; Fe, 17.46, 17.21; mol wt, 323.8519.

1,1′,2,2′,3,3′-Hexachloroferrocene (Ic). A solution of 1,1′,2,2′-tetrachloroferrocene (7.73 g, 0.0238 mol) in dry THF (700 ml) was stirred at 15° while a solution of *n*-butyllithium in hexane (100 ml, 0.15 mol) was added. The reaction mixture was stirred for 2.5 hr at 15° and then added over a 20-min period to a solution of hexachloroethane (48 g, 0.20 mol) in hexane (400 ml). After addition was complete, stirring was continued for 5 min and the reaction mixture was filtered through a bed of alumina. The filtrate was concentrated to dryness and the residue was fractionally sublimed. The product weighed 8.83 g and consisted (by glc analysis) of pentachloroferrocene (7%), 1,1′,2,2′,3,3′-hexachloroferrocene (92.5%), and heptachloroferrocene (0.5%). Recrystallization from hexane afforded 6.17 g (66%) of 1,1′,2,2′,3,3′-hexachloroferrocene of mp 191°. *Anal.* Calcd for $C_{10}H_4Cl_6Fe$: C, 30.58; H, 1.03; Cl, 54.17; Fe, 14.22; mol wt ($^{35}Cl_5{}^{37}Cl$ isotopes), 391.7764. Found: C, 31.03, 30.97; H, 1.03, 1.03; Cl, 53.65, 53.78; Fe, 14.87, 14.92; mol wt, 391.7755.

1,1′,2,2′,3,3′,4,4′-Octachloroferrocene (Id). The experimental procedure used was the same as described above for 1,1′,2,2′,3,3′-hexachloroferrocene, except that lithiation was carried out for only 1.5 hr. From 1.40 g of 1,1′,2,2′,3,3′-hexachloroferrocene there was obtained 1.28 g of material which consisted (by glc analysis) of hexachloroferrocene (1.5%), heptachloroferrocene (15%), 1,1′,2,2′,3,3′,4,4′-octachloroferrocene (79%), nonachloroferrocene (3%), and decachloroferrocene (1.5%). Recrystallization from hexane afforded 0.19 g (12%) of 1,1′,2,2′,3,3′,4,4′-octachloroferrocene of mp 212°. *Anal.* Calcd for $C_{10}H_2Cl_8Fe$: C, 26.02; H, 0.44; Cl, 61.45; Fe, 12.10; mol wt ($^{35}Cl_6{}^{37}Cl_2$ isotopes), 461.6955. Found: C, 26.23, 26.09; H, 0.57, 0.52; Cl, 16.90; 61.84; Fe, 11.91, 11.92; mol wt 461.6933.

Decachloroferrocene (Ie). (a) From Octachloroferrocene. A solution of 1,1′,2,2′,3,3′,4,4′-octachloroferrocene (0.584 g, 0.00126 mol) in dry THF (130 ml) was stirred at 0° while a solution of *n*-butyllithium in hexane (2.5 ml, 0.0037 mol) was added. The reaction mixture was stirred at 0° for 1 hr and then hexachloroethane (2.37 g, 0.010 mol) was added. Stirring was continued for 15 min and the reaction mixture was then filtered through a bed of alumina. The filtrate was concentrated to dryness and dry-column chromatography of the residue (hexane as eluent) afforded 0.623 g of material which consisted (by glc analysis) of octachloroferrocene (1%), nonachloroferrocene (8%), and decachloroferrocene (91%). This mixture was dissolved in carbon tetrachloride and stirred with concentrated nitric acid for 29 hr. The carbon tetrachloride layer was then passed through a column of alumina to give 0.565 g of decachloroferrocene (85%) of mp 245–246° (dec). *Anal.* Calcd for $C_{10}Cl_{10}Fe$: C, 22.64; Cl, 66.83; Fe, 10.53; mol wt ($^{35}Cl_8{}^{37}Cl_2$ isotopes), 529.6175. Found: C, 22.82, 22.85; Cl, 66.31, 66.32; Fe, 9.75, 9.72; mol wt, 529.6120.

(b) From 1,1′-Dichloroferrocene—Direct Method. 1,1′-Dichloroferrocene[6] (17.47 g, 0.0686 mol) in hexane (1500 ml) was stirred at 23° while a solution of *n*-butyllithium in hexane (133 ml, 0.20 mol), followed by TMEDA (23 g, 0.20 mol), was added. The reaction mixture was stirred at 23° for 1 hr and then cooled to −70°.

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(10) V. A. Sazonova and V. N. Drozd, *Dokl. Akad. Nauk SSSR*, **126**, 1004 (1959); *Chem. Ber.*, **93**, 2717 (1960).

(11) D. E. Bublitz, W. E. McEwen, and J. Kleinberg, *Org. Syn.*, **41**, 96 (1961).

(12) Full details of this thermal analysis study will appear in a forthcoming paper on the thermal and oxidative stability of polychlorinated metallocenes.

Hexachloroethane (71 g, 0.30 mol) was added, and the temperature was allowed to rise to 10° over a 1-hr period. The reaction mixture was then extracted with water, and the hexane layer separated and concentrated to dryness. The hexachloroethane was removed by sublimation and the crude residue was reacted with *n*-butyllithium (200 ml, 0.30 mol) in dry THF (1:1) at 0° for 3 hr. The reaction mixture was cooled to −70°, and hexachloroethane (95 g, 0.40 mol) was added. The temperature was allowed to rise to 5° over a 1-hr period, and the reaction mixture was then passed through a column of alumina (THF as eluent). The solvent was distilled from the eluate at 23° *in vacuo* and the hexachloroethane removed by sublimation. The residue was subjected to the above described (lithiation–halogenation) reaction in THF and the accompanying work-up procedures three more times, the sole modification being a decrease in the lithiation time to 2.5 hr, 60 and 30 min for the final three runs. The crude product from the last reaction, after removal of hexachloroethane by sublimation, was recrystallized from hexane to give 13.0 g of Ie of 98% purity by glc. The residue from the mother liquor was stirred with a mixture of carbon tetrachloride–concentrated nitric acid for 5 hr and chromatographed on alumina to give an additional 2.2 g of Ie of 98% purity (by glc). The total amount (15.2 g) thus obtained represents a 42% yield of Ie.

Decachlororuthenocene (IIIa). A solution of ruthenocene (11.55 g, 0.0500 mol) in hexane (1000 ml) was stirred and heated at reflux while a solution of *n*-butyllithium in hexane (115 ml, 0.15 mol) was added. Heating was discontinued and TMEDA (22 ml, 0.15 mol) added at a rate which maintained reflux. The reaction mixture was refluxed for 1 hr and then cooled to −20°. Hexachloroethane (47.4 g, 0.20 mol) was added and the temperature was allowed to rise to 10° over a 30-min period. After removal of the solids present by filtration, the hexane filtrate was passed through a column packed with alumina. Hexachloroethane was eluted with petroleum ether, and the mixture of chlorinated ruthenocenes eluted with carbon tetrachloride. The crude mixture, after removal of solvent, was subjected to the same reaction as described above, except that lithiation was carried out at 23° instead of at reflux temperature. The crude product obtained was dissolved in THF (500 ml) and stirred at −70° while a solution of *n*-butyllithium in hexane (200 ml, 0.30 mol) was added. The reaction mixture was warmed to 0° over a 30-min period, stirred at 0° for 2 hr, and cooled to −70°. Hexachloroethane (95 g, 0.40 mol) was added, and the temperature was allowed to rise to 10° over a 1-hr period. The entire reaction mixture was then absorbed on alumina, and the THF removed by evaporation. Dry-column chromatography was carried out on the dried alumina to remove hexachloroethane upon elution with petroleum ether and to afford a crude mixture of chlorinated ruthenocenes upon elution with carbon tetrachloride. This mixture was subjected to the above-described reaction in THF four more times with the following lithiation temperatures/lithiation times: 0°/1 hr; 0°/1 hr; −70°/30 min; −70°/30 min. The product from the final reaction was recrystallized from heptane to give 4.2 g (14%) of IIIa of 99% purity (by glc). The material showed some evidence of sublimation above 300° and decomposed at 360–365°. *Anal.* Calcd for $C_{10}Cl_{10}Ru$: C, 20.86; Cl, 61.58. Found: C, 20.88, 20.76; Cl, 61.80, 61.77. The molecular ion cluster was a unique and complex pattern from 566 to 586 mass units, which was identical with the pattern calculated for the compound.

Attempted "Sandwiching" Preparations of Ie. A solution of pentachlorocyclopentadienyllithium[9] prepared from hexachlorocyclopentadiene (13.6 g, 0.050 mol) and *n*-butyllithium (33 ml, 0.050 mol) was reacted with ferrous iodide (3.1 g, 0.010 mol) at −70°. The reaction mixture was warmed to 5° over a 45-min period, and passed through a bed of alumina (with methylene chloride as eluent). The solvent was removed, and the residue extracted with hot heptane. Chromatography on an alumina of the heptane extracts yielded none of the desired metallocene but only pentachlorocyclopentadiene together with its dimer. Similar results were obtained when the pyridine complex of ferrous acetylacetonate[13] was used in place of the ferrous iodide. When a mixture of pentachlorocyclopentadiene,[14] diethylamine, and ferrous acetylacetonate was refluxed in pyridine, followed by the same work-up described above, again no trace of the desired metallocene was observed.

Lithiation and Hydrolysis of Decachloroferrocene. A solution of decachloroferrocene (0.411 g, 0.000774 mol) in dry THF (75 ml) was cooled with liquid nitrogen until frozen. A solution of *n*-butyllithium in hexane (2.0 ml, 0.0030 mol) was added, and the reaction mixture was allowed to warm, with stirring, over a 15-min period to −40°. Distilled water (2 ml, 0.09 mol) was added, giving a voluminous white precipitate, and stirring was continued for 10 min while the mixture was allowed to warm to 0°. The mixture was then filtered and the filtrate concentrated to dryness. Dry-column chromatography of the residue on alumina afforded 0.359 g (100%) of material which consisted (by glc analysis) of pure 1,1′,2,2′,3,3′,4,4′-octachloroferrocene (glc retention time, mp, and infrared spectrum identical with those of an authentic sample).

1,1′-Diiodooctachloroferrocene (Ih). A suspension of decachloroferrocene (1.00 g, 0.00190 mol) in dry diethyl ether (175 ml) was stirred at −70° while a solution of *n*-butyllithium in hexane (3.8 ml, 0.0057 mol) was added. After 30 min at −70°, an orange solution was present. Continued stirring for 30 min more afforded a voluminous precipitate. Iodine (2.54 g, 0.010 mol) was added, and the reaction mixture was warmed to 5° over a 40-min period. Passage through a bed of alumina (methylene chloride as eluent) followed by removal of solvent afforded 1.35 g (99%) of Ih, 98% purity by glc. Recrystallization from hexane gave mp 240° (dec with evolution of I_2). *Anal.* Calcd for $C_{10}Cl_8I_2Fe$: C, 16.83; Cl, 39.75; I, 35.57; Fe, 7.82. Found: C, 16.83, 16.74; Cl, 39.54, 39.63; I, 35.27, 35.41; Fe, 8.01, 7.96.

Octachloroferrocene-1,1′-dicarboxylic Acid (Ii). A solution of decachloroferrocene (0.80 g, 0.00151 mol) in dry THF (125 ml) was stirred at −70° while a solution of *n*-butyllithium in hexane (3.0 ml, 0.0045 mol) was added. The resultant deep orange solution was stirred at −70° for 10 min and then excess Dry Ice was added. The reaction mixture was stirred for 20 min while warming to 0°, and then poured into 500 ml of water and extracted 3 × 200 ml with hexane. The aqueous layer was acidified with 10% HCl, affording a voluminous precipitate which was collected, washed with water, and dried to give 0.81 g (97%) of Ii, mp 245 (dec) after recrystallization from THF–benzene. *Anal.* Calcd for $C_{12}H_2O_4Cl_8Fe$: C, 26.22; H, 0.36; Cl, 51.60; Fe, 10.16. Found: C, 26.12, 26.37; H, 0.31, 0.34; Cl, 51.39; 51.36; Fe, 10.48, 10.43. The ir spectrum (KBr) showed an intense C=O band at 1680–1695 cm^{-1}.

1,1′-Diiodooctachlororuthenocene (IIIb). A solution of decachlororuthenocene (0.70 g, 0.0012 mol) in dry THF (125 ml) was stirred at −70° while a solution of *n*-butyllithium in hexane (2.4 ml, 0.0036 mol) was added. After stirring at −70° for 15 min, iodine (2.0 g, 0.0080 mol) was added and the reaction mixture was warmed to 10° over a 40-min period. Passage through a bed of alumina followed by removal of solvent left 0.89 g (98%) of IIIb. After recrystallization from hexane, the material showed sublimation above 300°, darkening above 325°, and iodine elimination above 350°. *Anal.* Calcd for $C_{10}Cl_8I_2Ru$: C, 15.70; I, 33.19; Ru, 13.21. Found: C, 16.06, 15.83; I, 32.72, 32.71; Ru, 12.71, 12.73. The mass spectrum of the compound, analogous to that of IIIa, afforded a "fingerprint" pattern identical with the calculated pattern.

Reaction of Decachloroferrocene with Sodium Methoxide. A mixture of decachloroferrocene (0.21 g, 0.00040 mol) and sodium methoxide (0.5 g, 0.01 mol) in methanol (125 ml) was stirred and refluxed for 18 hr. Repeated analysis of the reaction mixture during this period was carried out by thin layer chromatography (tlc) on silica gel with CCl_4 as developer. A steady decrease in the intensity of the starting material (R_f 0.85) was noted, accompanied by the formation of two new compounds of R_f 0.62 and 0.40, respectively. The formation of the latter compound appeared to be much slower than that of the former at first, but the ratio of intensities of the latter to the former compound increased with time. After 18 hr, the reaction mixture was cooled, absorbed on alumina, and chromatographed on alumina. Two bands were eluted with CCl_4, but separation was poor. Subsequent rechromatography on silica gel afforded good separation of the two bands. The material from the first band weighed 0.15 g (72%) and was determined by mass spectrometry to be methoxynonachloroferrocene (Ij). The material from the second band weighed 0.06 g (28%) and was determined by mass spectrometry to be 1,1′-dimethoxyoctachloroferrocene (Ik). Both methoxy derivatives were very soluble in all common solvents, but we were unable to effect complete purification for elemental analysis.

Reaction of Decachloroferrocene with Sodium Ethoxide. To a solution formed by dissolving sodium metal (0.80 g, 0.035 mol) in absolute ethanol (175 ml) was added decachloroferrocene (1.00 g, 0.00190 mol), and the resultant mixture was stirred and refluxed

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for 59 days. At intervals during the reaction, samples were withdrawn and analyzed by tlc, glc, and mass spectrometry. The following times and percentages (determined by glc) of starting material, monoethoxy, diethoxy, triethoxy, and tetraethoxy derivatives, were obtained: 1 hr, 2, 95, 3, 0, 0; 4 hr, 0, 50, 50, 0, 0; 6 hr, 0, 25, 75, 0, 0; 43 hr, 0, 0, 65, 30, 5; 117 hr, 0, 0, 23, 60, 17; 208 hr, 0, 0, 4, 73, 23; 384 hr, 0, 0, 0, 76, 24. After 59 days (1416 hr) the reaction mixture was cooled, absorbed on silica gel, and chromatographed. CCl_4 eluted two bands from which were obtained 0.192 g (28%) of triethoxyheptachloroferrocene as an oil and 0.480 g (72%) of tetraethoxyhexachloroferrocene as an oily solid. Glc of the triethoxy derivative showed two isomers of which the relative percentages in order of increasing retention time were 83 and 17%. Glc of the tetraethoxy derivative showed three isomers of which the relative percentages in order of increasing retention time were 59, 36, and 5%.

A second reaction was carried out under the same conditions as described above, using 0.10 mol of sodium ethoxide. The reaction mixture was worked up after 6 hr to give 0.81 g (67%) of 1,1′-diethoxyoctachloroferrocene (Im) and 0.27 g (22%) of triethoxyheptachloroferrocene. The Im was recrystallized from a small volume of hexane to give mp 107–108°. *Anal.* Calcd for $C_{14}H_{10}O_2Cl_8Fe$: C, 30.69; H, 1.83; Cl, 51.59; Fe, 10.16. Found: C, 30.60, 30.46; H, 2.21, 2.29; Cl, 51.30; Fe, 10.13.

Attempted Preparations of Decafluoroferrocene. Decachloroferrocene was heated with excess (~50:1) cesium fluoride in sulfolane at 100° for 24 hr to give no reaction. When the temperature was raised to 145°, gradual decomposition took place. At 190°, decomposition was very rapid.

1,1′-Diiodooctachloroferrocene was heated with excess cesium fluoride in sulfolane at 155–160° for 20 min. Extensive decomposition occurred, and only a small amount of material was obtained from column chromatography. Mass spectrometric analysis indicated the eluate to consist of octachloroferrocene, iodooctachloroferrocene, and butyliodooctachloroferrocene, the last named possibly being formed by breakdown of the sulfolane.

Attempted Preparation of Decafluororuthenocene. Decachlororuthenocene and excess cesium fluoride were heated in sulfolane at 240° for 1 hr to give a 50% recovery of the starting material after column chromatography. Gradual decomposition also occurred upon heating 1,1′-diiodooctachlororuthenocene and excess cesium fluoride in sulfolane at 190°.

1,2-Dichloroferrocene (IIb). A solution of chloroferrocene (4.42 g, 0.0200 mol) in dry THF (125 ml) was stirred at 0° while a solution of *n*-butyllithium in hexane (30 ml, 0.045 mol) was added. The reaction mixture was stirred at 0° for 1.5 hr and then cooled at −78°. A solution of hexachloroethane (14.2 g, 0.060 mol) in hexane (50 ml) was added, and the reaction mixture was then allowed to warm to 0° over a 30-min period. Subsequent work-up consisted of dry-column chromatography on alumina with hexane as eluent. The excess hexachloroethane eluted first, followed by a yellow band from which, after solvent removal, there was obtained 3.48 g of material consisting (by glc analysis) of 1,2-dichloroferrocene (81%) and a material (19%) determined (by mass spectral analysis) to be a trichloroferrocene. Recrystallization from methanol afforded 1,2-dichloroferrocene of mp 88–90° (lit.[1] mp 88.5–90°). *Anal.* Calcd for $C_{10}H_8Cl_2Fe$: C, 47.11; H, 3.16; mol wt 253.9351. Found: C, 47.39, 47.22, H, 3.14, 3.05; mol wt 253.9355.

1,2,3-Trichloroferrocene (IIc). The experimental procedure used was the same as described above for 1,2-dichloroferrocene. From 4.50 g of 1,2-dichloroferrocene, there was obtained 5.12 g of material which consisted (by glc analysis) of 1,2-dichloroferrocene (3%), 1,2,3-trichloroferrocene (86%), and tetrachloroferrocene (11%). Recrystallization from methanol afforded 1,2,3-trichloroferrocene of mp 103.5–104.5°. *Anal.* Calcd for $C_{10}H_7Cl_3Fe$: C, 41.51; H, 2.44; mol wt 287.8961. Found: C, 41.57, 41.46, H, 2.47, 2.42; mol wt 287.8982.

1,2,3,4-Tetrachloroferrocene (IId). The experimental procedure used was the same as described above for 1,2-dichloroferrocene. From 0.70 g of 1,2,3-trichloroferrocene, there was obtained 0.62 g of material which consisted (by glc analysis) of 1,2,3-trichloroferrocene (10%), 1,2,3,4-tetrachloroferrocene (80%) and pentachloroferrocene (10%). Preparative glc afforded 1,2,3,4-tetrachloroferrocene of mp 81–82°. *Anal.* Calcd for $C_{10}H_6Cl_4Fe$: C, 37.09; H, 1.87; mol wt ($^{35}Cl_3{}^{37}Cl$ isotopes), 323.8543. Found: C, 37.38, 37.12; H, 1.86, 1.98; mol wt, 323.8559.

1,2,3,4,5-Pentachloroferrocene (IIe). A mixture of 1,2-dichloroferrocene (25%) and 1,2,3-trichloroferrocene (75%) was subjected to the reaction procedure described above for 1,2-dichloroferrocene to give a material consisting of 1,2,3-trichloroferrocene (42%), 1,2,3,4-tetrachloroferrocene (29%), and pentachloroferrocene (29%). Repetition of the reaction with this mixture afforded a material consisting of 1,2,3,4-tetrachloroferrocene (42%) and 1,2,3,4,5-pentachloroferrocene (58%) together with a small amount of hexachloroferrocene. This mixture was reacted in dry ether with excess *n*-butyllithium–hexane solution, followed by addition of hexachloroethane at 0°. Dry-column chromatography afforded a mixture of tetrachloroferrocene (20%), 1,2,3,4,5-pentachloroferrocene (70%), and hexachloroferrocene (10%). Recrystallization from methanol afforded 1,2,3,4,5-pentachloroferrocene of mp 143–144°. *Anal.* Calcd for $C_{10}H_5Cl_5Fe$: C, 33.52; H, 1.41; mol wt ($^{35}Cl_4{}^{37}Cl$ isotopes) 357.8154. Found: C, 33.25, 33.53; H, 1.41, 1.45; mol wt 357.8144.

Total Synthesis of a Monocyclic Peptide Lactone Antibiotic, Etamycin

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Abstract: The antibiotic etamycin **1** has been synthesized by joining two peptide fragments, 3-benzyloxypicolinyl-L-threonyl-D-leucine *tert*-butyl ester (**2**) and *tert*-butoxycarbonyl-(*O*-*tert*-butyl)-D-allohydroxyprolylsarcosyl-L-*N*,β-dimethylleucyl-L-alanyl-L-phenylsarcosine (**3**), through an ester linkage, **6**. Deblocking, cyclization, and hydrogenation gave etamycin. A new synthesis of threo-L-*N*,β-dimethylleucine is also reported.

The antibiotic etamycin **1** has been shown to be a macrocyclic peptide lactone. Of the natural peptide lactones, actinomycin C[1] and actinomycin D[1–3] have been synthesized, both of which have double lactone structures. Two analogs of monocyclic peptide lactones, 6-proline-staphylomycin S[4] and 6-(4-hydroxy-

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