

Stereochemical Studies. XV. Ferrocene Studies. XXII.  
Planar Elements of Stereochemistry

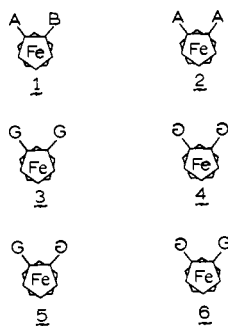
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**Abstract:** Homoannular disubstitution in ferrocene generates stereochemical situations of interest which have been experimentally explored during the present study. Thus, when the two substituents are constitutionally identical and not diastereomeric, three distinct stereochemical situations are realized: one (a single achiral isomer) in which achiral substituents are enantiotopically related and the other (a pair of enantiomers) in which chiral and configurationally identical substituents are diastereotopically related. Finally, if the two substituents are constitutionally identical, chiral and configurationally opposite, then these conditions produce two achiral diastereomers, in each of which the substituents are enantiotopically related. The latter two compounds may be considered as pseudoasymmetric isomers. Examples of each of these categories were synthesized, and their physical, chiroptical, and spectral properties were carefully determined. The configurations of the pseudoasymmetric isomers were unequivocally assigned. This was accomplished by establishing a direct configurational correlation between the planar stereogenic element of pseudoasymmetry of one of the pseudoasymmetric isomers and the planar stereogenic element of chirality of a ferrocene whose absolute configuration was previously established by the X-ray method.

Homoannular disubstitution of metallocenes such as ferrocenes generates various stereochemical situations in which some rarely encountered planar stereogenic elements may be characterized. This is particularly true when the substituents are constitutionally<sup>2</sup> identical. When the substituents are constitutionally distinct, a chiral molecule (1) results, and the stereogenic element is a chiral plane. Many such molecules have been studied in recent years,<sup>4</sup> but the present study was undertaken to examine some of the situations (2–6) which arise when the two homoannular substituents are constitutionally identical.<sup>5</sup> A summary of these situations follows. For this purpose (Scheme I), con-

Scheme I



stitutionally identical substituents are represented by the same letter; achiral substituents are indicated by the

(1) (a) Taken in part from the dissertation submitted by W. D. Bailey to the Graduate School, University of South Carolina, Oct 1970, in partial fulfillment of the requirements for the Ph.D. degree; (b) address to which inquiries should be directed; (c) a member of the Louisiana State University System; formerly known as the Louisiana State University in New Orleans.

(2) The term constitution refers to the sequence of bonded atoms in a molecule or group without any considerations of spatial arrangements. When different molecules or groups possess the same atomic composition and the same constitution, they are necessarily stereoisomers.<sup>3</sup>

(3) K. Mislow, "Introduction to Stereochemistry," W. A. Benjamin, New York, N. Y., 1965, p 50.

(4) See, for example, K. Schlögl, *Top. Stereochem.*, 1, 39 (1967).

(5) Early results of this work were published in preliminary form: (a) S. I. Goldberg and W. D. Bailey, *J. Amer. Chem. Soc.*, 93, 1046 (1971); (b) *Tetrahedron Lett.*, 4087 (1971).

achiral letters, A and B, while the chiral letter, G, and its enantiomer,  $\bar{D}$ , represent constitutionally identical, chiral substituents.<sup>6</sup>

The simplest situation is represented by 2, where the substituents (A) are constitutionally identical and possess no configurational significance. Such molecules are, of course, achiral, although they do possess a planar stereogenic element<sup>7</sup> which is prochiral.<sup>9</sup> The substituents, however, are nonequivalent since they cannot be exchanged by rotation about a simple axis. They are, however, exchanged by a reflection operation; hence, they are enantiotopic.<sup>10</sup>

The planar stereogenic element in 3 is also prochiral. A molecule of this type may be distinguished from that represented by 2 in that the former is chiral (4 is its enantiomer) and by the fact that the constitutionally and configurationally identical substituents possess a higher level of nonequivalence to one another. Because there is no symmetry operation which may be carried out on the molecule to exchange the two substituents, they are diastereotopic.<sup>10</sup>

The representations, 5 and 6, are particularly interesting. They are achiral diastereomers; and while the substituents in each are constitutionally identical and configurationally opposite, they still bear the enantiotopic relationship to one another since they may be exchanged by simple reflection. Isomers represented by 5 and 6 may be called pseudoasymmetric isomers.<sup>11,12a</sup> The principal stereogenic element in each is then a

(6) The letter G is chiral only in two dimensions. It is, therefore, necessary to avoid an out-of-plane rotation which converts it to its enantiomer,  $\bar{D}$ .

(7) While any one of a number of molecular planes in these examples may serve as the stereogenic plane, it is convenient to follow the convention of the Cahn-Ingold-Prelog system<sup>8</sup> and use the plane defined by the substituted cyclopentadienyl ring.

(8) R. S. Cahn, C. Ingold, and V. Prelog, *Angew. Chem., Int. Ed. Engl.*, 5, 511 (1966).

(9) K. R. Hanson, *J. Amer. Chem. Soc.*, 88, 2731 (1966); H. Hirschmann and K. R. Hanson, *J. Org. Chem.*, 36, 3293 (1971); H. Hirschmann and K. R. Hanson, *Eur. J. Biochem.*, 22, 301 (1971).

(10) K. Mislow and M. Raban, *Top. Stereochem.*, 1, 1 (1967).

(11) V. Prelog and G. Helmchen, *Helv. Chim. Acta*, 55, 2581 (1972).

(12) (a) G. Helmchen and V. Prelog, *Helv. Chim. Acta*, 55, 2612 (1972); (b) C. Moise and Y. Mugnier, *Tetrahedron Lett.*, 1848 (1972).

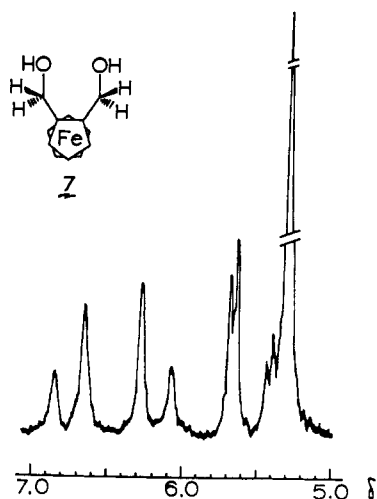


Figure 1. Partial nmr spectrum (60 MHz) of **7** ( $\text{CDCl}_3$ ) in the presence of shift reagent.

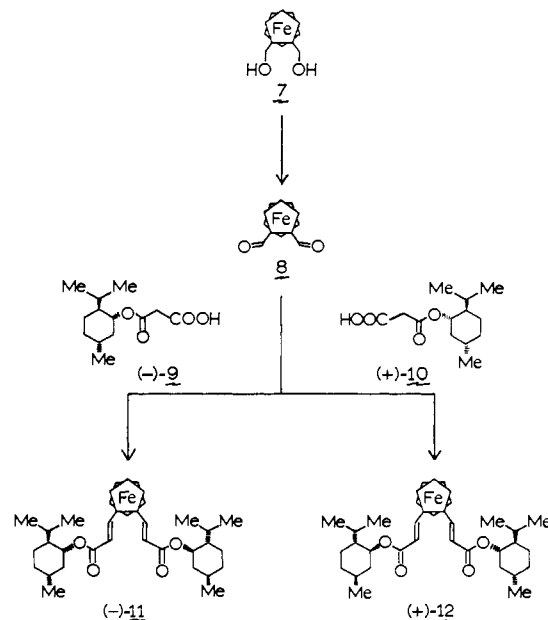
pseudoasymmetric plane. The examples provided by Helmchen and Prelog<sup>12a</sup> and by Moïse and Mugnier<sup>12b</sup> along with those of the present work appear to be the only known cases of this interesting stereocategory. Molecules possessing a pseudoasymmetric axis are also rare; only those of Helmchen and Prelog<sup>13</sup> and of Kost and Raban<sup>14</sup> appear to be known. In contrast, many molecules containing a pseudoasymmetric center are known; indeed, van't Hoff himself commented<sup>15</sup> on the special features of the general arrangement,  $\text{C}(\text{R}_1\text{R}_2\text{R}_3)\text{-C}(\text{R}_4\text{R}_5)\text{C}(\text{R}_1\text{R}_2\text{R}_3)$ . Werner<sup>16</sup> appears to have been the first to use the term pseudoasymmetry in order to make the distinction between cases represented by the van't Hoff formulation above and those possessing asymmetric atoms. Hirschmann and Hanson,<sup>9</sup> however, have traced the development of a history of imprecision and ambiguity in the uses of these two terms. The description of pseudoasymmetry as given by Prelog and Helmchen<sup>11</sup> is precise and is the one used in this paper.<sup>17</sup>

## Results and Discussion

1,2-Bis(hydroxymethyl)ferrocene (**7**) was the starting material in the syntheses (Scheme II) of the compounds represented by **3** and **4**. This compound may also serve as an example of a prochiral compound represented by **2**. The enantiotopic relationship of the two hydroxymethyl substituents is implied in the nmr spectrum determined<sup>19</sup> from **7** (Figure 1) since the signal due to the methylene protons (centered at  $\delta$  6.45, shift reagent) is no more complicated than the AB pattern expected from the diastereotopic geminal hydrogens.

The diol **7** was oxidized to the dialdehyde **8**, which was allowed to condense in turn with 2 equiv of (–)-carbomethoxyacetic acid (**9**) and (+)-carbomethoxy-

## Scheme II



acetic acid (**10**) in separate procedures to give the individual enantiomers, (–)-**11** and (+)-**12**, respectively. These compounds, which are examples of the generalized representations, **3** and **4**, gave rise to identical spectra and melting points; they also show equal chiroptical rotatory magnitude but in opposite directions. The nmr spectra determined from these compounds were identical, but they also showed the diastereotopic relationship between the constitutionally and configurationally identical substituents. This is particularly clear in the spectra determined from the hydrogenated compounds (Figure 3) discussed below.

Preparation of the achiral diastereomers **18** and **19** (the pseudoasymmetric isomers corresponding to the generalized representations **5** and **6**) was somewhat more involved (Scheme III). Partial oxidation of **7** gave the enantiomeric formyl alcohols (**13**), which were condensed with (–)-carbomethoxyacetic acid (**9**) to produce a mixture of the chiral diastereomers, **14** and **15**. The mixture of optically active compounds was converted to the corresponding formyl derivatives, **16** and **17**, through mild oxidation with activated manganese dioxide. The mixture of the achiral diastereomers of interest, **18** and **19**, was obtained after condensation of **16** and **17** with (+)-carbomethoxyacetic acid (**10**).

Although it was not possible to detect the presence of the pseudoasymmetric isomers through the use of otherwise sensitive thin-layer chromatography systems, separation of **18** and **19** was, however, readily achieved through fractional recrystallizations from pentane. Each compound was recrystallized to constant-melting material, and it was rather surprising to find a fairly large difference in the melting points (146.0–148.0 and 173.5–174.5°). Each melting point was depressed significantly upon admixture melting of the compounds. The diastereomeric relationships between **18** and **19** was further substantiated by differences in the solid phase (but not solution) infrared spectra and by slight differences in the proton magnetic resonance spectra determined from the compounds. The achirality of **18** and **19** was strongly implied by the inability to detect optical

(13) G. Helmchen and V. Prelog, *Helv. Chim. Acta*, **55**, 2599 (1972).

(14) D. Kost and M. Raban, *J. Amer. Chem. Soc.*, **94**, 2533 (1972).

(15) J. H. van't Hoff, "The Arrangement of Atoms in Space," 2nd ed, translated by A. Eiloart, Longmans, Green and Co., London, 1898.

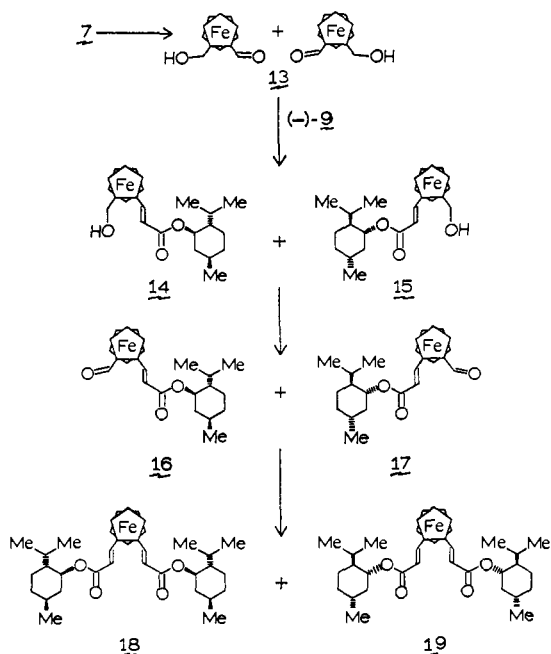
(16) A. Werner, "Lehrbuch der Stereochemie," G. Fischer, Jena, 1904, p 28.

(17) In a preliminary account<sup>6a</sup> of a portion of the present work, we used the term pseudochirality. We now, however, agree with Professor Prelog<sup>18</sup> that the introduction of a new term would serve no useful purpose.

(18) V. Prelog, personal communication.

(19) We are grateful to T. H. Siddall, III, and J. W. Bell for this spectrum.

Scheme III



activity in either compound, even though they were directly obtained from the optically active diastereomers, **16** and **17**.

There are two points of experimental evidence which would strongly reject the possibility that the isomerism among the set of compounds, **11**, **12**, **18**, and **19**, could be attributed to various combinations of configurations of the olefinic linkages. First, the nmr signals due to the vinylic hydrogens in each compound appear as only simple four-line patterns with the magnitude of the indicated coupling constant in each case consistent with that of the *E* configuration. Secondly, hydrogenation of each isomer produces a set of saturated compounds,  $(-)-20$ ,  $(+)-21$ , **22**, and **23** (Scheme IV), which exhibited properties consistent with the stereorelationships discussed for the corresponding set of unsaturated isomers.

The enantiotopic relationships between the two constitutionally identical but configurationally opposite substituents in the pseudoasymmetric compounds and the diastereotopic relationship between the constitutionally and configurationally identical substituents in the optically active compounds are most revealingly seen in their 100-MHz proton magnetic spectra<sup>20</sup> (Figures 2 and 3). The enantiotopic relationship between the two complex substituents attached to the ferrocene nucleus in **22** (and in **23**) means that in its nmr spectrum different chemical shifts due to only three (a, b, and c) of the total six methyl groups should appear, and that each of these should be a doublet. The six-line array is observed (Figure 2), while in contrast a much more complex presentation is present in that region of the spectrum obtained<sup>20</sup> from  $(-)-20$  (Figure 3). In the latter, the diastereotopic relationship with the otherwise identical substituents means that each of the six methyl groups should give rise to distinct chemical shifts. While all of the 12 lines are not resolved (Figure 3), the obvious

(20) We are grateful to Dr. L. H. Keith of the Southeast Water Laboratory, Athens, Ga., for the 100-MHz spectra cited here.

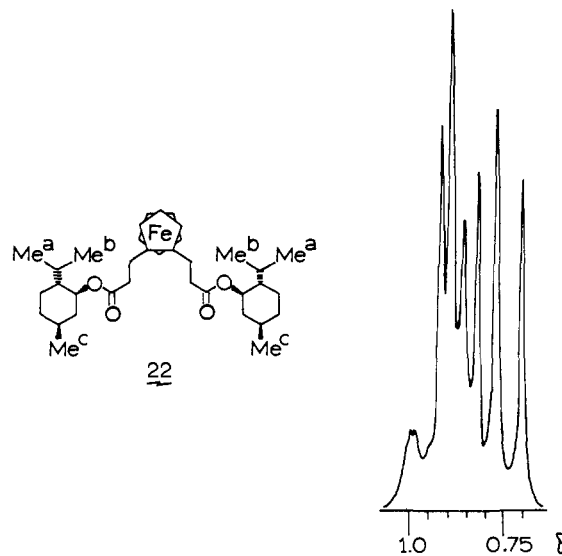
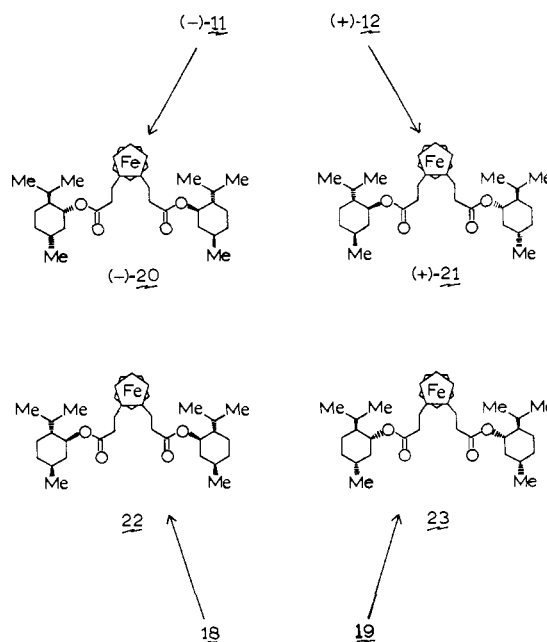


Figure 2. Partial nmr spectrum (100 MHz) of **22** ( $CDCl_3$ ).

Scheme IV



difference in complexity between the two spectra adequately makes the point.

Questions of configurations of the optically active isomers (enantiomers),  $(-)-11$ ,  $(+)-12$ ,  $(-)-20$ , and  $(+)-21$ , were trivial because all assignments followed directly from the known absolute configurations of the initially used  $(-)$ - and  $(+)$ -menthols. This information, however, was insufficient to assign configurations to the pseudoasymmetric isomers, for in those compounds the planar stereogenic elements are of obvious configurational significance. The problem was undertaken and solved (Scheme V) by establishing a direct configurational correlation between the planar stereogenic element of pseudoasymmetry in the lower melting, achiral diastereomer (which turned out to be **18**) and a planar stereogenic element of known absolute chirality.

Lithiation of  $(+)-(-S)-N$ -ferrocenylmethyl-2-methylpiperidine (**24**) with *n*-butyllithium takes place stereo-

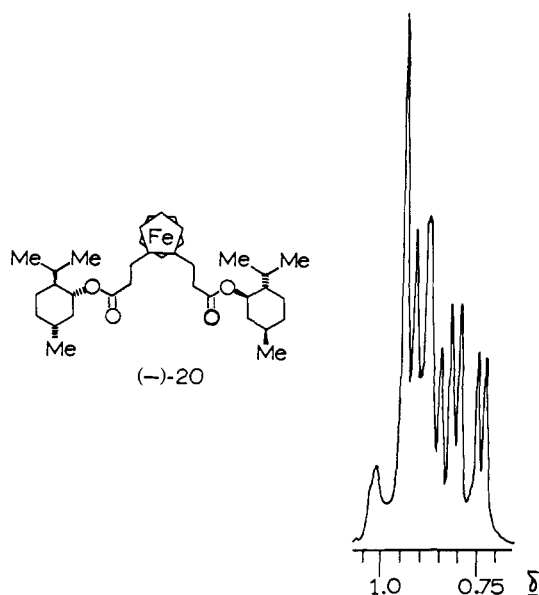
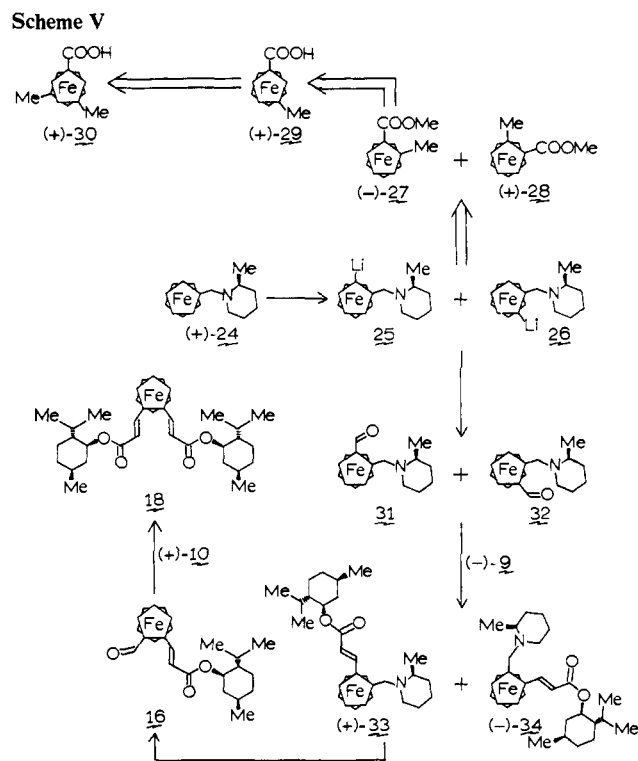


Figure 3. Partial nmr spectrum (100 MHz) of (-)-20 (CDCl<sub>3</sub>).



selectively<sup>21,22</sup> to give the diastereomeric lithio compounds, **25** and **26**, with the former predominating by a factor of 4.<sup>23</sup> Also, the predominant diastereomer is known to be **25** and not **26**. This assignment of absolute chirality results from chemical correlation of the predominant diastereomer with a standard whose absolute configuration was established by X-ray crystallography.

(21) T. Arantani, T. Gonda, and H. Nozaki, *Tetrahedron Lett.*, 2265 (1969).

(22) G. Gokel, P. Hoffmann, H. Kleiman, H. Klusacek, D. Marquarding, and I. Ugi, *Tetrahedron Lett.*, 1771 (1970).

(23) The original report<sup>21</sup> placed the level of stereoselectivity too high. The present work confirms through direct measurements the previous observation<sup>22</sup> that the lithiation proceeded with a lower than quantitative level of stereoselectivity.

Arantani, *et al.*,<sup>21</sup> converted the mixture of diastereomeric lithio compounds (**25** and **26**) to a nonracemic sample of the enantiomeric esters, **27** and **28**, which was levorotatory. Earlier,<sup>24</sup> the relative configuration of the levorotatory ester was equated to that of the dextrorotatory 1,3-methylferrocenecarboxylic acid (**29**), which in turn was shown recently<sup>25</sup> to possess the same configuration as the dextrorotatory acid, **30**. Since the latter is the enantiomer of the acid whose absolute configuration was determined by X-ray technique,<sup>26</sup> all of these configurations are in fact absolute configurations, including that of the predominant lithio amine (**25**, not **26**). Assignments of configuration to the pseudoasymmetric compounds of the present investigation were built upon this solid foundation.

Conversion of the mixture of diastereomeric lithio amines (**25** and **26**) to the corresponding formyl amines (**31** and **32**) was accomplished in 92% yield by treatment of the former with *N,N*-dimethylformamide. Modified Knoevenagel condensation of **31** and **32** with (-)-carbomethoxyacetic acid [(-)-**9**] gave the mixture of optically active, diastereomeric amino esters, **33** and **34**, in 90% yield. Nmr analysis, chromatographic separation, and the previously established absolute configurational correlations allowed for complete description of the mixture: (+)-(*R*)-**33**, the predominant diastereomer, constituted 79% of the mixture, while (-)-(*S*)-**34** was found to make up 21%.<sup>23,27</sup> The separated and characterized predominant diastereomer [(+)-(*R*)-**33**] was oxidized with activated manganese dioxide to (*R*)-**16**, previously prepared and characterized in the presence of its diastereomer (*S*)-**17**. Condensation of (*R*)-**16** with (+)-carbomethoxyacetic acid [(+)-**10**] gave the pseudoasymmetric compound possessing the lower melting point (146–148°), so that compound could be assigned the structure (*s*)-**18**, and assignments to each of the other pseudoasymmetric compounds followed directly from the work already described.

## Experimental Section

**General.** Temperatures were uncorrected. Melting points were determined in open capillary tubes unless noted otherwise. Column (elution) chromatography was with Merck acid-washed alumina except where noted. Mixtures to be chromatographed were dissolved in the minimum volume of solvent (benzene or hexane) and added uniformly to the tops of the alumina columns which were previously prepared by the wet technique with hexane. Thin-layer chromatography (tlc) plates were prepared by coating (0.25 mm) glass plates with Silica Gel G (Brinkmann Instruments Co.). The plates were activated at 110° for 4 hr and stored in a desiccator prior to use. The solvent system used is noted in each case along with the other chromatographic data. Infrared spectra (ir) were determined with a Perkin-Elmer Model 257 spectrophotometer. Except where noted, a Varian A-60 nuclear magnetic resonance (nmr) spectrometer was used to record <sup>1</sup>H nmr spectra from solutions containing tetramethylsilane (TMS) as internal standard. Chemical shifts are reported in ppm under the δ convention relative to the TMS signal (0 ppm). Ultraviolet (uv) spectra were determined with a Perkin-Elmer Model 202 spectrophotometer. An Hitachi Perkin-Elmer, Model RMU-6, spectrometer was used to record mass spectra. Chiroptical measurements at 546 and 589 nm

(24) H. Falk and K. Schlögl, *Monatsh. Chem.*, **98**, 2044 (1967).

(25) H. Falk and K. Schlögl, *Monatsh. Chem.*, **102**, 33 (1971).

(26) O. L. Carter, A. T. McPhail, and G. A. Sim, *J. Chem. Soc. A*, 365 (1967).

(27) Although the stereogenic element in these compounds is the chiral plane, Cahn, Ingold and Prelog<sup>3</sup> recommend that the stereochemical descriptor be determined by considering the appropriate atom as a chiral center (ref 9, p 394). On the other hand, if the stereogenic element is a pseudoasymmetric plane, the system is not treated as a center (ref 9, p 402).

were carried out with Rudolph and Sons, Inc., high-precision polarimeters. Combustion analyses were done by the Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

***N,N*-Dimethylaminoferrrocene.** Following the dropwise addition of *N,N,N,N*-tetramethyldiaminomethane (46 g, 0.46 mol) to a stirred solution of ferrocene (50 g, 0.27 mol), phosphoric acid (46 g), and acetic acid (430 ml), the whole was heated under reflux for 5 hr under nitrogen. Water (500 ml) was added after the mixture was stirred at room temperature overnight, and the whole was extracted with ether (3 × 200 ml). The acidic aqueous residue was cooled in an ice bath before sodium hydroxide (250 g) was carefully added. The dark oil thus freed was extracted into ether (3 × 300 ml). Evaporation of the ether gave crude *N,N*-dimethylaminoferrrocene which was dried by heating it at 140° for 1 hr under reduced pressure (5 mm): 52 g (80% yield). The amine was characterized through its methiodide; light yellow powder, mp 195–200° (lit.<sup>28</sup> mp 200° dec).

**(±)-1-Hydroxymethyl-2-(dimethylaminomethyl)ferrrocene.** To a stirred solution of *N,N*-dimethylaminomethylferrrocene (10 g, 0.041 mol) in ether (40 ml) was added dropwise (15 min) *n*-butyllithium (0.045 mol in hexane). After the solution was stirred at room temperature for 1 hr, paraformaldehyde (1.5 g, 0.048 mol), dissolved in anhydrous ether (50 ml), was added dropwise. The whole was stirred for 1.5 hr at room temperature before it was poured into water (200 ml) and extracted with ether (2 × 50 ml). The combined extracts were washed with water and dried (magnesium sulfate) before they were evaporated to a red oil which was chromatographed on alumina. Elution with ether gave unreacted amine (3.5 g), while a solution of 5% methanol in ether eluted (±)-1-hydroxymethyl-2-(dimethylaminomethyl)ferrrocene: 5.1 g (46% yield), mp 44–46° (lit.<sup>29</sup> mp 45–46°). The methiodide was prepared by dropwise addition of methyl iodide (4.2 g, 0.029 mol) to a stirred solution of the hydroxy amine (4.1 g, 0.015 mol) in acetonitrile (20 ml). Addition of dry ether caused crystallization of the light yellow methiodide: 5.85 g (94% yield), mp dec above 200° (lit.<sup>29</sup> mp dec above 203°).

**1,2-Bis(hydroxymethyl)ferrrocene (7).** The hydroxy amine methiodide (4.1 g, 0.011 mol) was added to 1 *M* aqueous sodium hydroxide (100 ml) and heated in a nitrogen atmosphere under reflux for 2 hr. Tlc analysis (ether) showed the presence of only one component, which was different from the starting material. The mixture was extracted with ether (2 × 100 ml). Evaporation of the combined and dried (magnesium sulfate) extracts gave 1,2-bis(hydroxymethyl)ferrrocene (7) as brilliant yellow plates: 1.95 g (81% yield), mp 117–118° (lit.<sup>29</sup> mp 117–118°).

**1,2-Diformylferrrocene (8).** Activated manganese dioxide<sup>30</sup> (10 g) was added to a solution of 1,2-bis(hydroxymethyl)ferrrocene (7) (1 g, 0.004 mol) in dry chloroform (50 ml). While the mixture was stirred at room temperature, it was monitored by tlc (ether). Only after 22 hr did one spot (*R*<sub>f</sub> 0.6) corresponding to the desired dialdehyde remain. After the mixture was passed through a filter and the filtrate evaporated, the residual red oil was taken up in pentane to allow crystallization (red needles) of 1,2-diformylferrrocene (8): 0.85 g (86% yield), mp 170–172° (lit.<sup>29</sup> mp 170°).

**(±)-1-Formyl-2-hydroxymethylferrrocene (13).** Activated manganese dioxide<sup>30</sup> (5 g) was added to a stirred solution of 1,2-bis(hydroxymethyl)ferrrocene (7) (1 g, 0.004 mol) in dry chloroform (50 ml). Progress of the oxidation was followed by tlc (ether), which showed that after 1.5 hr the mixture consisted of the alcohol aldehyde (*R*<sub>f</sub> 0.4) and a trace of the dialdehyde (*R*<sub>f</sub> 0.6). The mixture was passed through a filter, and the filtrate was evaporated to a red oil. This residue was taken up in pentane to allow crystallization of (±)-1-formyl-2-hydroxymethylferrrocene (13) as orange-red crystals: 0.86 g (87% yield), mp 86–88° (lit.<sup>29</sup> mp 87–88°).

**(-)- and (+)-Carbomethoxyacetic Acid (9 and 10).** To a stirred solution of malonyl dichloride (14 g, 0.077 mol), in dry chloroform (50 ml) at 0°, was added over a 4-hr period a solution of (-)-menthol (15.6 g, 0.10 mol) in chloroform (100 ml). After the addition was complete and the mixture was stirred overnight at room temperature, it was cooled to 10° and made basic with 1.5 *M* aqueous sodium hydroxide solution (200 ml). The aqueous layer was separated, acidified, and extracted with ether. Evaporation of the combined and dried ether extracts left a pale yellow, viscous oil which solidified on standing. Recrystallization of this material from pentane gave (-)-carbomethoxyacetic acid (9) as

colorless needles: 14 g (75% yield), mp 57–58° (lit.<sup>31</sup> mp 57–58°), [ $\alpha$ ]<sub>D</sub><sup>20</sup> -69.6 ± 0.8° (c 2.50, ethanol), lit.<sup>31</sup> [ $\alpha$ ]<sub>D</sub><sup>20,546</sup> -76° (c 5, benzene).

**(+)-Carbomethoxyacetic acid (10)** was prepared by means of the same procedure, using (+)-menthol which was obtained from resolution<sup>32</sup> of (±)-menthol: 67% yield, mp 56–58°, [ $\alpha$ ]<sub>D</sub><sup>20</sup> +68.5 ± 1.0° (c 2.50, ethanol). Spectral data (ir and nmr) determined from each enantiomer were identical: ir (neat)  $\nu$  3150 (broad, carboxyl O-H), 2945, 2920, 2860 (aliphatic C-H), 1740 (broad, ester and carboxyl carbonyl), and 1150 cm<sup>-1</sup> (ester); nmr (CDCl<sub>3</sub>)  $\delta$  0.71, 0.82, 0.95 (9 H, menthyl methyl groups), 1.0–2.0 (9 H, complex, menthyl ring and isopropyl carbinyl protons), 3.35 (2 H, s,  $\alpha$ -CH<sub>2</sub>), 4.7 (1 H, complex, O-CH), and 10.9 (1 H, s, acid proton).

**(+)- and (-)-1-Hydroxymethyl-2-[2-carbo-(1*R*,3*R*,4*S*)-menthoxy-(*E*)-ethenyl]ferrrocene (14 and 15).** A solution of pyridine (20 ml), (-)-carbomethoxyacetic acid (2.5 g, 0.010 mol), (±)-1-formyl-2-hydroxymethylferrrocene (0.80 g, 0.0032 mol), and piperidine (0.5 ml) was heated to 100° under nitrogen and monitored with tlc [2:3 (v/v) ether-hexane]. After 1 hr all of the starting material was consumed, and only one spot (*R*<sub>f</sub> 0.20) which corresponded to the desired material was observed. The reaction mixture was cooled and poured into ether (100 ml). The ether layer was separated, washed with dilute hydrochloric acid and water, and dried (anhydrous magnesium sulfate) before it was evaporated to a residue which was chromatographed on alumina. Elution with 2% methanol in ether gave the mixture of diastereomers, (+)- and (-)-1-hydroxymethyl-2-[2-carbo-(1*R*,3*R*,4*S*)-menthoxy-(*E*)-ethenyl]ferrrocene (14 and 15): 0.89 g (59% yield); ir (neat)  $\nu$  3420 (broad, hydroxyl), 3095, 1100, 1000 (ferrocenyl), 2960, 2930, 2880, 1450 (aliphatic C-H), 1700, 1270 (conjugated ester), and 1630 cm<sup>-1</sup> (C=C); nmr (CDCl<sub>3</sub>)  $\delta$  0.75, 0.86, 0.96 (9 H, menthyl methyl groups), 1.0–2.0 (9 H, complex, menthyl ring and isopropyl carbinyl protons), 3.42 (1 H, hydroxyl), 4.10 (5 H, s, unsubstituted ferrocenyl ring), 4.45 (5 H, complex, substituted ferrocenyl ring and carbinol protons), 6.03 (1 H, d,  $\alpha$  proton<sup>33</sup> of *E* double bond, *J* = 16 Hz), and 7.60 (1 H, d of d,  $\beta$  proton<sup>33</sup> of *E* double bond).

*Anal.* Calcd for C<sub>24</sub>H<sub>32</sub>FeO<sub>3</sub>: C, 68.10; H, 7.63; mol wt, 424. Found: C, 67.78; H, 7.62; mol wt, 424 (mass spectrum).

**(+)- and (-)-1-Formyl-2-[2-carbo-(1*R*,3*R*,4*S*)-menthoxy-(*E*)-ethenyl]ferrrocenes (16 and 17).** Activated manganese dioxide<sup>30</sup> (5 g) was added to a solution of the diastereomeric hydroxy esters (14 and 15) (0.80 g, 0.0019 mol) dissolved in dry chloroform (40 ml), and the suspension was stirred at room temperature. After 0.5 hr, a tlc analysis [2:3 (v/v) ether-hexane] showed the absence of starting material and the presence of only the desired aldehyde ester (*R*<sub>f</sub> 0.37). The reaction mixture was passed through a filter, and the filtrate was evaporated to an unstable red oil, showed to be a mixture of the diastereomers, (+)- and (-)-1-formyl-2-[2-carbo-(1*R*,3*R*,4*S*)-menthoxy-(*E*)-ethenyl]ferrrocenes (16 and 17): 0.68 g (86% yield); ir (neat)  $\nu$  3100, 1100, 995 (ferrocenyl), 2960, 2930, 2875, 1450 (aliphatic C-H), 2725, 1670 (conjugated aldehyde), 1705, 1270 (conjugated ester), and 1630 cm<sup>-1</sup> (C=C); nmr (CDCl<sub>3</sub>)  $\delta$  0.75, 0.87, 0.98 (9 H, menthyl methyl groups), 4.22 (5 H, s, unsubstituted ferrocenyl ring), 4.75 and 4.92 (3 H, t and d, substituted ferrocenyl ring), 6.26 (1 H, d,  $\alpha$  proton<sup>33</sup> of *E* double bond, *J* = 16 Hz), 7.93 (1 H, d of d,  $\beta$  proton<sup>33</sup> of *E* double bond, *J* = 16 Hz), and 10.5 (1 H, s, formyl proton).

*Anal.* Calcd for C<sub>24</sub>H<sub>30</sub>FeO<sub>3</sub>: mol wt, 422. Found: mol wt, 422 (mass spectrum). The instability of the material precluded combustion analysis.

**(*r*)-1-[2-Carbo-(1*S*,3*S*,4*R*)-menthoxy-(*E*)-ethenyl]-2-[2-carbo-(1*R*,3*R*,4*S*)-menthoxy-(*E*)-ethenyl]ferrrocene (19) and (*s*)-1-[2-carbo-(1*R*,3*R*,4*S*)-menthoxy-(*E*)-ethenyl]-2-[2-carbo-(1*S*,3*S*,4*R*)-menthoxy-(*E*)-ethenyl]ferrrocene (18).** A mixture of pyridine (20 ml), (+)-carbomethoxyacetic acid (10) (0.75 g, 0.0031 mol), piperidine (0.5 ml), and the diastereomers, (+)- and (-)-1-formyl-2-[2-carbo-(1*R*,3*R*,4*S*)-menthoxy-(*E*)-ethenyl]ferrrocenes (16 and 17) (0.68 g, 0.0016 mol) was heated to 100° under nitrogen and monitored by tlc analysis [2:3 (v/v) ether-hexane]. After 1 hr only one spot (*R*<sub>f</sub> 0.81), different from that of starting material, was observed. The reaction mixture was cooled to room temperature and poured into ether (100 ml). The ethereal solution was washed with dilute hydrochloric acid and water, before it was dried and evaporated to a red oil which was chromatographed on alumina. Elution with

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1:3 (v/v) ether-hexane gave a red oil (0.65 g) which was shown subsequently to consist of the pseudoasymmetric esters **18** and **19**.

A major portion (0.60 g) of the mixture was dissolved in boiling pentane (50 ml), from which a portion (0.3 g) crystallized, mp 169–172°. This material was redissolved in boiling pentane (25 ml). The fluffy orange crystals obtained (0.15 g) had mp 173.5–174.5°, which did not change upon recrystallization. It was subsequently shown to be (*r*)-1-[2-carbo-(1*S*,3*S*,4*R*)-menthoxy-(*E*)-ethenyl]-2-[2-carbo-(1*R*,3*R*,4*S*)-menthoxy-(*E*)-ethenyl]ferrocene (**19**):  $[\alpha]^{20}_D$  0° (*c* 0.25, ethanol); ir (CHCl<sub>3</sub>)  $\nu$  3100, 1100, 1000 (ferrocenyl), 2960, 2930, 2870, 1450 (aliphatic C–H), 1695, 1280 (conjugated ester), and 1635 cm<sup>-1</sup> (C=C); nmr (100 MHz)<sup>20</sup> (CDCl<sub>3</sub>)  $\delta$  0.80, 0.87, 0.91, 0.92, 0.99 (18 H, menthyl methyls), 1.0–2.2 (18 H, complex, menthyl ring and isopropyl carbinyl protons), 4.14 (5 H, s, unsubstituted ferrocenyl ring), 4.62 and 4.75 (5 H, complex, substituted ferrocenyl ring and menthyl carbinol protons), 6.12 (2 H, d,  $\alpha$  protons<sup>33</sup> of *E* double bonds, *J* = 16 Hz), and 7.75 (2 H,  $\beta$  protons<sup>33</sup> of *E* double bonds, *J* = 16 Hz); uv (EtOH)  $\lambda_{max}$  ( $\epsilon$ ) 210 nm (19,000), 284 (26,000), 367 (3200), and 477 (2300).

*Anal.* Calcd for C<sub>36</sub>H<sub>50</sub>FeO<sub>4</sub>: C, 71.75; H, 8.36; mol wt, 602. Found: C, 71.70; H, 8.46; mol wt, 602 (mass spectrum).

The pentane supernatant of the initial crystallization was reduced in volume to 20 ml, and the crop (0.2 g) of crystalline material obtained had mp 143–146°. This material was recrystallized from pentane to give 0.16 g of constant-melting (146–148°), red plates, subsequently shown to be (*s*)-1-[2-carbo-(1*R*,3*R*,4*S*)-menthoxy-(*E*)-ethenyl]-2-[2-carbo-(1*S*,3*S*,4*R*)-menthoxy-(*E*)-ethenyl]ferrocene (**18**):  $[\alpha]^{20}_D$  0° (*c* 0.25, ethanol); ir (CHCl<sub>3</sub>)  $\nu$  3100, 1100, 1000 (ferrocenyl), 2960, 2930, 2870, 1450 (aliphatic C–H), 1695, 1280 (conjugated ester), and 1635 cm<sup>-1</sup> (C=C); nmr (100 MHz)<sup>20</sup> (CDCl<sub>3</sub>)  $\delta$  0.81, 0.88, 0.93, 1.0 (18 H, menthyl methyls), 1.0–2.2 (18 H, complex, menthyl ring and isopropyl carbinyl protons), 4.15 (5 H, s, unsubstituted ferrocenyl ring), 4.62 and 4.75 (5 H, complex, substituted ferrocenyl ring and menthyl carbinol protons), 6.11 (2 H, d,  $\alpha$  protons<sup>33</sup> of *E* double bonds, *J* = 16 Hz), and 7.74 (2 H, d,  $\beta$  protons<sup>33</sup> of *E* double bonds, *J* = 16 Hz); uv (EtOH)  $\lambda_{max}$  ( $\epsilon$ ) 209 nm (21,000), 283 (24,000), 358 (5000), and 475 (1900).

*Anal.* Calcd for C<sub>36</sub>H<sub>50</sub>FeO<sub>4</sub>: C, 71.75; H, 8.36; mol wt, 602. Found: C, 72.02; H, 8.30; mol wt, 602 (mass spectrum).

(–)-1,2-Bis[2-carbo-(1*R*,3*R*,4*S*)-menthoxy-(*E*)-ethenyl]ferrocene (**11**). A mixture of (–)-carbomenthoxyacetic acid (**9**) (1.5 g, 0.0062 mol), 1,2-diformylferrocene (0.5 g, 0.002 mol), pyridine (10 ml), and piperidine was heated at 100° for 2 hr under nitrogen. After it had cooled to room temperature, the reaction was poured into ether (100 ml). The ethereal solution was washed with dilute hydrochloric acid and water before it was dried (anhydrous magnesium sulfate) and evaporated to a glassy residue. The residue was dissolved in boiling pentane (50 ml) and allowed to crystallize overnight at room temperature. The crystals (0.50 g), which had mp 144–146°, were constant melting. An additional quantity (0.10 g) was obtained from alumina chromatography of the residual material in the supernatant. The total amount of (–)-1,2-bis[2-carbo-(1*R*,3*R*,4*S*)-menthoxy-(*E*)-ethenyl]ferrocene (**11**) was 0.60 g (48% yield): mp 144–146° (depressed when melted in admixture with each achiral isomer, **18** and **19**);  $[\alpha]^{20}_D$  –72.3 ± 2.0° (*c* 0.25, ethanol); ir (CHCl<sub>3</sub>)  $\nu$  3095, 1100, 1000 (ferrocenyl), 2960, 2925, 2870, 1455 (aliphatic C–H), 1695, 1270 (conjugated ester), and 1630 cm<sup>-1</sup> (C=C); nmr (100 MHz)<sup>7</sup> (CDCl<sub>3</sub>)  $\delta$  0.80, 0.87, 0.92, 0.99 (18 H, menthyl methyls), 1.0–2.2 (18 H, complex, menthyl ring and isopropyl carbinyl protons), 4.14 (5 H, s, unsubstituted ferrocenyl ring), 4.62 and 4.76 (5 H, complex, substituted ferrocenyl ring and menthyl carbinol proton), 6.12 (2 H, d,  $\alpha$  protons<sup>33</sup> of *E* double bonds, *J* = 16 Hz), and 7.44 (2 H, d of d,  $\beta$  protons<sup>33</sup> of *E* double bonds, *J* = 16 Hz); uv (EtOH)  $\lambda$  ( $\epsilon$ ) 209 nm (19,000), 285 (24,000), 360 (3300), and 477 (2000).

*Anal.* Calcd for C<sub>36</sub>H<sub>50</sub>FeO<sub>4</sub>: C, 71.75; H, 8.36; mol wt, 602. Found: C, 72.02; H, 8.46; mol wt, 602 (mass spectrum).

(+)-1,2-Bis[2-carbo-(1*S*,3*S*,4*R*)-menthoxy-(*E*)-ethenyl]ferrocene (**12**). Preparation of this compound followed exactly that of its enantiomer (**11**), except that the enantiomeric (+)-carbomenthoxyacetic acid was used. The pure dextrorotatory compound was obtained in 40% yield: mp 144–146° (depressed when melted in admixture with each achiral isomer, **18** and **19**, but undepressed when melted in admixture with the levorotatory isomer, **11**).  $[\alpha]^{20}_D$  +70.0 ± 1.2° (*c* 0.25, ethanol). Ir (CHCl<sub>3</sub>), nmr (CDCl<sub>3</sub>), and uv (EtOH) spectra were superimposable upon the corresponding spectra determined from the levorotatory isomer, **11**.

**Catalytic Hydrogenation of Each Stereoisomeric Diester to the Corresponding Saturated Diester.** Each of the stereomeric, unsaturated diesters was hydrogenated in stirred ethanol solution

over platinum oxide at room temperature and atmospheric pressure. Completeness of each hydrogenation was signaled by the color change, from orange-red to yellow, which took less than 2 hr. After removal of the solid catalyst, each solution was evaporated under reduced pressure to a residue which was chromatographed on alumina. A mixture of ether and pentane (1:3) was used to elute the saturated diester in each case, and a summary of the characterization data of each compound follows.

(*r*)-1-[2-Carbo-(1*S*,3*S*,4*R*)-menthoxyethyl]-2-[2-carbo-(1*R*,3*R*,4*S*)-menthoxyethyl]ferrocene (**23**): yellow crystals, mp 116–118°;  $[\alpha]^{20}_D$  0° (*c* 0.5, ethanol); ir (CHCl<sub>3</sub>)  $\nu$  3095, 1100, 1000 (ferrocenyl), 2965, 2935, 2875, 1455 (aliphatic C–H), and 1725 cm<sup>-1</sup> (ester); nmr (100 MHz)<sup>20</sup> (CDCl<sub>3</sub>)  $\delta$  0.75, 0.82, 0.88, 0.95 (18 H, complex, menthyl methyls), 1.0–2.1 (18 H, complex, menthyl ring and isopropyl carbinyl protons), 2.55 (8 H, complex, ethylene protons), 3.95 (3 H, apparent t, substituted ferrocenyl ring), 4.04 (5 H, s, unsubstituted ferrocenyl ring), and 4.97 (2 H, apparent sextet, menthyl carbinol proton); uv (EtOH)  $\lambda$  ( $\epsilon$ ) 210 nm (21,000), 320 sh (90), and 440 (80).

*Anal.* Calcd for C<sub>36</sub>H<sub>54</sub>FeO<sub>4</sub>: C, 71.27; H, 8.97; mol wt, 606. Found: C, 71.00; H, 8.84; mol wt, 606 (mass spectrum).

(*s*)-1-[2-Carbo-(1*R*,3*R*,4*S*)-menthoxyethyl]-2-[2-carbo-(1*S*,3*S*,4*R*)-menthoxyethyl]ferrocene (**22**): viscous yellow oil;  $[\alpha]^{20}_D$  0° (*c* 0.5, ethanol); ir (CHCl<sub>3</sub>)  $\nu$  3095, 1100, 1000 (ferrocenyl), 2965, 2935, 2875, 1455 (aliphatic C–H), and 1725 cm<sup>-1</sup> (ester); nmr (100 MHz)<sup>20</sup> (CDCl<sub>3</sub>)  $\delta$  0.73, 0.79, 0.84, 0.88, 0.92, 0.94 (18 H, menthyl methyls), 1.0–2.1 (18 H, complex, menthyl ring and isopropyl carbinyl protons), 2.55 (8 H, complex, ethylene protons), 3.95 (3 H, distorted d, substituted ferrocenyl ring), 4.04 (5 H, s, unsubstituted ferrocenyl ring), and 4.97 (2 H, sextet, menthyl carbinol proton); uv (EtOH)  $\lambda$  ( $\epsilon$ ) 211 nm (24,000), 322 sh (80), and 410 (80).

*Anal.* Calcd for C<sub>36</sub>H<sub>54</sub>FeO<sub>4</sub>: C, 71.27; H, 8.97; mol wt, 606. Found: C, 71.40; H, 9.23; mol wt, 606 (mass spectrum).

(–)-1,2-Bis[2-carbo-(1*R*,3*R*,4*S*)-menthoxyethyl]ferrocene (**20**): viscous yellow oil;  $[\alpha]^{20}_D$  –54.2 ± 0.9° and  $[\alpha]^{22}_{46}$  –61.9 ± 0.7° (*c* 0.50, ethanol); ir (CHCl<sub>3</sub>)  $\nu$  3095, 1100, 1000 (ferrocenyl), 2965, 2935, 2875, 1455 (aliphatic C–H), and 1725 cm<sup>-1</sup> (ester); nmr (100 MHz)<sup>20</sup> (CDCl<sub>3</sub>)  $\delta$  0.73, 0.75, 0.79, 0.82, 0.85, 0.88, 0.90, 0.92, 0.95 (18 H, menthyl methyls), 1.0–2.1 (18 H, complex, menthyl ring and isopropyl carbinyl protons), 2.55 (8 H, complex, ethylene protons), 3.97 (3 H, distorted d, substituted ferrocenyl ring), 4.04 (5 H, s, unsubstituted ferrocenyl ring), and 4.72 (2 H, sextet, menthyl carbinol proton); uv (EtOH)  $\lambda$  ( $\epsilon$ ) 211 nm (26,000), 230 sh (110), and 422 (100).

*Anal.* Calcd for C<sub>36</sub>H<sub>54</sub>FeO<sub>4</sub>: C, 71.27; H, 8.97; mol wt, 606. Found: C, 71.26; H, 9.07; mol wt, 606 (mass spectrum).

(+)-1,2-Bis[2-carbo-(1*S*,3*S*,4*R*)-menthoxyethyl]ferrocene (**21**): viscous yellow oil;  $[\alpha]^{20}_D$  +56.3 ± 1.0° and  $[\alpha]^{22}_{46}$  +61.8 ± 1.3° (*c* 0.45, ethanol); ir (CHCl<sub>3</sub>), nmr (100 MHz)<sup>20</sup> (CDCl<sub>3</sub>), and uv (EtOH) spectra were superimposable upon the corresponding spectra determined from the enantiomeric diester, **20**.

(*S*)- and (*R*)-1-Formyl-2-[(2*S*)-methylpiperidinomethyl]ferrocenes (**31** and **32**). A mixture of *N,N*-dimethylaminomethylferrocene methiodide (6.0 g, 0.015 mol), water (90 ml), and freshly resolved<sup>34</sup> (+)-(2*S*)-methylpiperidine (3 g, 0.03 mol) was stirred and heated (reflux) in a nitrogen atmosphere during 5 hr. After the mixture had cooled to room temperature, it was extracted with ether (2 × 100 ml). Evaporation of the dried extracts, followed by column chromatography of the residue on alumina, gave (+)-*N*-ferrocenylmethyl-(2*S*)-methylpiperidine (**24**) as a yellow solid: 4.1 g (92% yield); mp 43–44°;  $[\alpha]^{20}_D$  +148 ± 0.5° (*c* 2, ethanol) [lit.<sup>31</sup> mp 38–39°;  $[\alpha]^{20}_D$  +70°].

*n*-Butyllithium (0.014 mol in hexane) was added dropwise over 30 min to a solution of the amine (3.7 g, 0.13 mol) in ether (20 ml). After the mixture was stirred for 12 hr at room temperature, it was cooled to 0°, and a solution of dimethylformamide (1.8 g, 0.025 mol) in ether (5 ml) was added dropwise. The mixture was stirred for an additional hour at room temperature, before it was poured into water (50 ml) and extracted with ether (2 × 75 ml). The residue obtained after removal of the ether was chromatographed on alumina. Elution with hexane-ether (1:1) gave the recovered amine (**24**), 1.6 g or 43% of the original amount. Ether eluted the mixture of diastereomers, (*S*)- and (*R*)-1-formyl-2-[(2*S*)-methylpiperidinomethyl]ferrocenes (**31** and **32**): red oil; 2.1 g (53% yield);  $[\alpha]^{20}_D$  +308 ± 2° (*c* 0.500, ethanol); ir (neat)  $\nu$  3095, 1105, 1000 (ferrocenyl), 2940, 2860, 1445 (aliphatic C–H), 2790 (methylene

(34)  $[\alpha]^{20}_D$  +35 ± 0.5° (neat, *d*<sup>15</sup>, 0.845); lit.<sup>35</sup>  $[\alpha]^{15}_D$  +36° (neat, *d*<sup>15</sup>, 0.845).

(35) W. Leithe, *Chem. Ber.*, **65**, 929 (1932).

attached to nitrogen), and 1680  $\text{cm}^{-1}$  (amide aldehyde); nmr ( $\text{CDCl}_3$ )  $\delta$  1.1 and 1.2 (3 H, set of doublets, methyl protons), 1.25–1.75 (8 H, complex, ring methylenes), 2.71 (1 H, complex, methine proton adjacent in nitrogen), 3.5 (2 H, apparent d, methylene attached to nitrogen), 4.18 (5 H, s, unsubstituted ferrocenyl ring), 4.50 and 4.75 (3 H, complex, substituted ferrocenyl ring), and 10.5 (1 H, s, formyl proton).

*Anal.* Calcd for  $\text{C}_{18}\text{H}_{23}\text{FeNO}$ : C, 66.48; H, 7.14; mol wt, 325. Found: C, 66.48; H, 7.36; mol wt, 325 (mass spectrum).

(+)-(R)- and (-)-(S)-1-[2-Carbo-(1R,3R,4S)-menthoxy-(E)-ethenyl]-2-[(2S)-methylpiperidinomethyl]ferrocenes (**33** and **34**). To a mixture of (-)-carbomethoxyacetic acid (**9**) (2.5 g, 0.10 mol), (S)- and (R)-1-formyl-2-[(2S)-methylpiperidinomethyl]ferrocenes (**31** and **32**) (1.5 g, 0.046 mol), and pyridine (25 ml) was added dropwise piperidine (1 ml). After the whole was stirred under nitrogen and heated at 100° for 2 hr, it was examined *via* tlc (ether). Only a trace of the starting amino aldehyde ( $R_f$  0.2) remained, while the presence of two new products ( $R_f$  0.5 and 0.7) was indicated. The reaction mixture (room temperature) was poured into ether (150 ml), washed with water, dried, and evaporated to a residue which was chromatographed on alumina. Elution with ether-hexane (1:3) gave the mixture of diastereomeric esters (**33** and **34**):  $R_f$  0.5 and 0.7, respectively; 2.1 g (90% yield). The nmr spectrum determined from the mixture displayed the  $\alpha$  protons of the *E* double bonds ( $\delta$  6.08 and 6.01) with chemical shifts sufficiently separated to allow good integral determinations. Thus, the ratio of the two diastereomeric esters (average of 12 integrations) was determined to be 79:21. This ratio, which represents the level of stereoselectivity during the lithiation of (+)-(2S)-methylpiperidinomethylferrocene (**24**), was confirmed by subsequent separation of the diastereomeric esters.

The mixture was carefully chromatographed on alumina using a high ratio (100:1) of alumina to sample. Elution with ether-hexane (1:1) gave the predominant ester, known<sup>36</sup> to be (+)-(R)-1-[2-carbo-(1R,3R,4S)-menthoxy-(E)-ethenyl]-2-[(2S)-methylpiperidinomethyl]ferrocene (**33**), as a red oil: 0.9 g;  $[\alpha]^{19\text{D}} +770 \pm 8^\circ$  (*c* 0.500, ethanol); ir (neat)  $\nu$  3095, 1105, 1100 (ferrocenyl), 2960, 2930, 2870, 1450 (aliphatic C-H), 2780 (methylene attached to nitrogen), 1705, 1270 (conjugated ester), and 1630  $\text{cm}^{-1}$  (double bond); nmr ( $\text{CDCl}_3$ )  $\delta$  0.75, 0.84, 0.88, 0.97 (9 H, menthyl methyls), 1.20 (3 H, d,  $J = 7$  Hz, piperidyl methyl), 1.0–2.4 (17 H, complex, menthyl and piperidyl protons), 2.6 (1 H, complex, methine proton adjacent to nitrogen), 3.19 and 3.42 (2 H, apparent d, methylene protons adjacent to ferrocenyl), 4.05 (5 H, s, unsubstituted ferrocenyl ring), 4.32, 4.50 (3 H, apparent d and t, respectively, substituted ferrocenyl ring), 4.8 (1 H, complex, methine proton adjacent to oxygen), 6.08 (1 H, d,  $J = 16$  Hz,  $\alpha$  proton<sup>33</sup> of *E* double bond), and 7.66 (1 H, d,  $J = 16$  Hz,  $\beta$  proton<sup>33</sup> of *E* double bond).

*Anal.* Calcd for  $\text{C}_{30}\text{H}_{43}\text{FeNO}_2$ : C, 71.35; H, 8.58; mol wt, 505. Found: C, 71.16; H, 8.38; mol wt, 505 (mass spectrum).

Continued elution did not provide a separated sample of the minor ester (**34**) but rather gave a mixture (1.1 g) of the two esters enriched in the minor diastereomer. Separation, however, was

(36) See text for discussion of configurational correlations upon which this assignment is based.

accomplished by preparative tlc (ether) on "Chrom AR Sheet 1000."<sup>37</sup> The relative amounts of the diastereomers present in the mixture, considered together with the amount of the major isomer already isolated, corroborated the previously determined (nmr) 79:21 ratio of major to minor isomers. The minor isomer, known<sup>36</sup> to be (-)-(S)-1-[2-carbo-(1R,3R,4S)-menthoxy-(E)-ethenyl]-2-[(2S)-methylpiperidinomethyl]ferrocene (**34**), was characterized as follows: red oil;  $[\alpha]^{19\text{D}} -643 \pm 24^\circ$  (*c* 0.330, ethanol); ir (neat)  $\nu$  3090, 1100, 995 (ferrocenyl), 2960, 2930, 2870, 1450 (aliphatic C-H), 2780 (methylene adjacent to nitrogen), 1701, 1270 (conjugated ester), and 1630  $\text{cm}^{-1}$  (double bond); nmr ( $\text{CDCl}_3$ )  $\delta$  0.74, 0.86, 0.96 (9 H, menthyl methyls), 1.23 (3 H, d,  $J = 6$  Hz, piperidyl methyl), 1.32–2.50 (17 H, complex, menthyl and piperidyl protons), 2.60 (1 H, complex, methine proton adjacent to nitrogen), 3.25 (2 H, apparent d, methylene protons adjacent to ferrocenyl), 4.05 (5 H, s, unsubstituted ferrocenyl ring), 4.38, 4.55 (3 H, apparent d and t, respectively, substituted ferrocenyl ring), 6.01 (1 H, d,  $J = 16$  Hz,  $\alpha$  proton<sup>33</sup> of *E* double bond), and 7.65 (1 H, d,  $J = 16$  Hz,  $\beta$  proton<sup>33</sup> of *E* double bond).

*Anal.* Calcd for  $\text{C}_{30}\text{H}_{43}\text{FeNO}_2$ : C, 71.35; H, 8.58; mol wt, 505. Found: C, 70.87; H, 8.16; mol wt, 505 (mass spectrum).

(s)-1-[2-Carbo-(1R,3R,4S)-menthoxy-(E)-ethenyl]-2-[2-carbo-(1S,3S,4R)-menthoxy-(E)-ethenyl]ferrocene (**18**). A mixture of activated manganese dioxide<sup>30</sup> (5 g), (+)-(R)-1-[2-carbo-(1R,3R,4S)-menthoxy-(E)-ethenyl]-2-[(2S)-methylpiperidinomethyl]ferrocene (**33**) (0.80 g, 0.0016 mol), and dry chloroform (30 ml) was stirred at room temperature and monitored by tlc. After 30 hr, the mixture was filtered and the filtrate evaporated to a red oil (0.7 g). This material was shown (tlc) to consist of starting material and the desired ester aldehyde, (R)-1-[2-carbo-(1R,3R,4S)-menthoxy-(E)-ethenyl]-2-formylferrocene (**16**). Because of its instability on alumina, no attempt was made to separate and characterize the ester aldehyde. Rather, the mixture (0.7 g) was added to pyridine (10 ml), (+)-carbomethoxyacetic acid (0.25 g, 0.0010 mol), and piperidine (0.25 ml), and the whole was stirred and heated under nitrogen for 1.5 hr at 100°. Tlc analysis [ether-hexane (1:1.5)] showed the presence of only two compounds:  $R_f$  0.15, the original amino ester (**33**), and  $R_f$  0.75, the desired diester (**18**). The reaction mixture was poured into ether (75 ml), washed with water, dried, and evaporated to a red oil (0.7 g) which was chromatographed on silica gel. Elution with ether-hexane (1:4) gave (s)-1-[2-carbo-(1R,3R,4S)-menthoxy-(E)-ethenyl]-2-[2-carbo-(1S,3S,4R)-menthoxy-(E)-ethenyl]ferrocene (**18**): orange-red crystals (pentane); 40 mg (26% yield based on unrecovered starting material);<sup>38</sup> mp 147–149°;  $[\alpha]^{20\text{D}} 0^\circ$  (*c* 0.25, ethanol). Ir and nmr spectra were superimposable upon those determined from the lower melting diester previously prepared. Admixture melting with the lower melting diester gave no depression, while admixture melting with each of the other isomeric diesters gave significant depression. Thus, based on previous configurational correlations, as discussed in the text of this paper, it was possible to assign the configuration to each of the achiral diastereomeric diesters.

(37) Mallinckrodt Chemical Works, Saint Louis, Mo.

(38) The starting amino ester (**33**) (0.59 g) was eluted with ether-hexane (1:1).