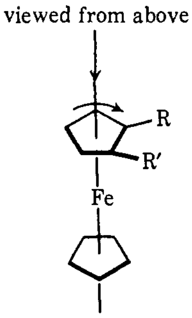
Correlation of Central and Planar Chirality in Ferrocene Derivatives[1]

**Dieter Marquarding,[2a] Hans Klusacek,[2a] George Gokel,[2c]
Peter Hoffmann,[2b] and Ivar Ugi**

Contribution from the Department of Chemistry, the University of Southern California, Los Angeles, California 90007, and the Wissenschaftliches Hauptlaboratorium, Farbenfabriken Bayer A.G., 509, Leverkusen, Germany.
Received November 29, 1969

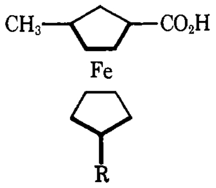
Abstract: 1-Ferrocenylethyldimethylamine (**7**) is readily obtained from 1-ferrocenylethanol by treatment with phosgene and then dimethylamine. The resolution of **7** with (*R*)-(+)-tartaric acid is particularly easy and both antipodes are obtained in high yield. Qualitatively the steric course of the lithiation **7** → **8** is predictable and proceeds with high stereoselectivity (96:4). Subsequent reactions of **8** with trimethylchlorosilane, formaldehyde, or benzophenone produce **9a–c**. The quaternization of **9** in the presence of nucleophiles leads to substitution of the dimethylamino group in **9** with complete configurational retention, which is confirmed by nmr and the cycle {**9a, 10, 14, 13**}. The retention is due to the ease of formation of **11** and its configurational stability under suitable conditions. The reactions presented here provide a basis for convenient, predesignated stereoselective syntheses and configurational assignments of ferrocene derivatives with planar and central elements of chirality.

Optically active ferrocene derivatives[3,4] with planar or both planar and central elements of chirality, *e.g.*, **1** or **9**, respectively, are particularly suitable chiral reference systems for asymmetrically induced syntheses.[8]



1

To our knowledge, there are no methods available for the reliable preparation of optically pure ferrocene derivatives of type **1**, and there is no basis for unambiguous configurational assignments for this class of compounds. In fact, it could be shown by more recent methods that some of the optically active ferrocene derivatives, *e.g.*, **1a** (**1**, R = $CH_2{=}CH-$, R' = CH_3-) and **1b** (**1**, R = $CH_2{=}CH-$, R' = CH_3-), which were obtained *via* resolution of compounds of type **1**,[3] were only 86% optically pure,[9] and not 100% optically pure as was previously assumed. The only optically active ferrocene derivative containing a plane of chirality whose absolute configuration has been determined by X-ray crystallography[10] is **2b**.



2a, R = H
b, R = CH_3

The configurations of **1a** (**1**, R = CH_3, R' = CO_2H) and **2a** were correlated by a series of chemical transformations.[11] An unequivocal correlation of **2a** and **2b**, *e.g.*, by methylation of the unsubstituted cyclopentadienyl moiety of **2a**, would confirm the proposed configurations not only of **1a** but of the whole set of configurationally related ferrocene derivatives of type **1**.[3] At this point, the correlation of **2a** with **2b** is based only upon optical rotation data which do not seem to provide a generally reliable basis for the configurational assignment[1,12,13] of ferrocene derivatives. The comparison of the optical rotations of **2a** and **2b** is particularly dubious because **2b**, in contrast to **2a**,

---

(1) Stereoselective Syntheses. VI. Preceding report: D. Marquarding, P. Hoffmann, H. Heitzer, and I. Ugi, *J. Amer. Chem. Soc.*, **92**, 1969 (1970).

(2) Research Associates in the Department of Chemistry of the University of Southern California in (a) 1969–1970, (b) 1968–1969; (c) NASA Predoctoral Fellow, 1969–present.

(3) K. Schlögl, *Top. Stereochem.*, **1**, 39 (1967).

(4) Metallocenes with more than two different substituents in one ring belong to chirality class b[5,6] and are not subject to the (*R*,*S*) nomenclature. The following modification of the (*R*,*S*) nomenclature[3,7] is suggested for chiral metallocenes which belong to chirality class a,[5] and will be used in this and subsequent papers by the present authors. The observer looks along the principal axis of the parent metallocene, *e.g.*, along the C_5 axis of ferrocene, with the disubstituted ring directed toward him. The configuration of metallocenes, *e.g.*, **1**, with a plane of chirality is termed an "*R*" if the ligands R and R' descend in priority[7] in the shortest possible clockwise arc. Likewise if the priorities ascend in a clockwise direction, the planar element of chirality is "*S*."

For compounds which contain elements of chirality of different types, the (*R*,*S*) symbols will refer to those various elements of chirality in the order: *central* > *axial* > *planar*. *E.g.*, in **9** (*R*,*R*) the first (*R*) refers to the configuration of the *central chirality* in the α-dimethylaminoethyl group, and the second (*R*) refers to the *planar chirality* due to the arrangement of the substituents on the ferrocene nucleus.

(5) E. Ruch, *Theor. Chim. Acta*, **11**, 183 (1968).

(6) I. Ugi, *Z. Naturforsch. B*, **20**, 405 (1965); E. Ruch and I. Ugi, *Theor. Chim. Acta*, **4**, 287 (1966); *Top. Stereochem.*, **4**, 99 (1969).

(7) R. S. Cahn, C. K. Ingold, and V. Prelog, *Angew. Chem.*, **78**, 413 (1966); *Angew. Chem., Int. Ed. Engl.*, **5**, 385 (1966).

(8) I. Ugi, *Rec. Chem. Progr.*, **30**, 289 (1969).

(9) H. Klusacek, D. Marquarding, and I. Ugi, manuscript in preparation.

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

(11) G. Haller and K. Schlögl, *Monatsh. Chem.*, **98**, 2044 (1967).

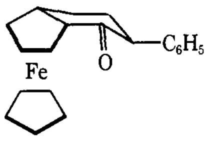
(12) G. Gokel, P. Hoffmann, H. Kleimann, H. Klusacek, D. Marquarding, and I. Ugi, *Tetrahedron Lett.*, 1771 (1970).

(13) H. Falk, C. Krasa, and K. Schlögl, *Monatsh. Chem.*, **100**, 254 (1969).

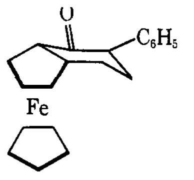
not only contains a plane of chirality, but, because of the additional methyl group, also an axis of chirality, which vanishes only if the internal rotation of the cyclopentadienyl rings of **2b** is unrestricted by potential barriers.[14] The correlation of the configuration of ferrocene derivatives **1** with planar chirality and the known configurations of compounds with central chirality has been attempted[15,16] by chemical means; however, no unambiguous configurational correlations have yet been reported.

The determination of the configurations of the *endo*- and *exo*-2,3-ferroceno-Δ^2-cyclohexenols (**1**, $R,R' = -(CH_2)_3CHOH-$)[15a] by Horeau's method[17] cannot be considered as reliable because stereoselective acylations of the type applied here[18] are not pairs of corresponding reactions.[6] Furthermore Horeau's very elegant method is an empirical correlation of configurations and therefore only applicable within its experimentally established range of validity.

The synthesis of **3**-(*S*,*S*) from (*S*)-α-phenyl-γ-ferrocenylbutyric acid[15b] is the only reported reaction which has some features of a *stereorelating synthesis* (see below) of a ferrocene derivative of type **1**. Yet there is no basis to assert that the transition states which lead to **3**-(*S*,*S*) and **3**-(*S*,*R*), respectively, are rigid *cis–trans* isomers with considerably different steric interactions of the bulky groups of the systems. In fact, for the diastereomers of **3** one can expect only a slight difference in the interactions of the relatively distant ferrocenyl and the preferentially equatorial[19a] phenyl moieties of **3**. This is in accordance with the observation that the diastereomer ratio of **3** depends considerably upon the reaction conditions under which the (*S*)-α-phenyl-γ-ferrocenylbutyric acid is cyclized.[15b]

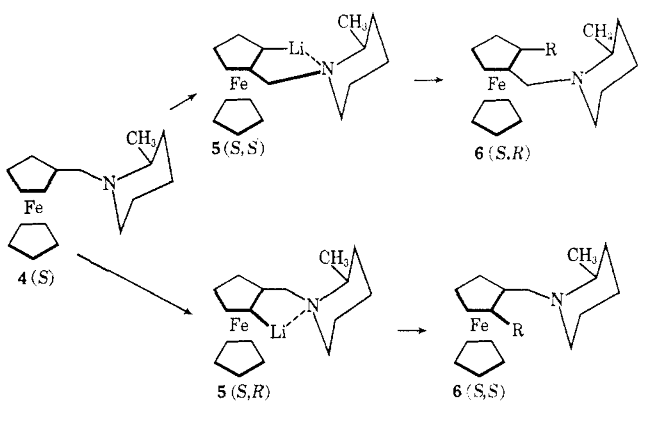


3 (S,S)



3 (S,*R*)

Scheme I[16]



$R = CO_2H, Si(CH_3)_3$

Scheme I was investigated[16] in order to correlate the configurations of **1** with the known configurations of central chiroids. The (*S*,*R*) diastereomers of **6** were reported to be the only products formed by Scheme I, with no detectable amounts of the (*S*,*S*) isomers. Recently, however, it was shown[12] that Scheme I is far less stereoselective than previously claimed. Scheme I is not a stereorelating synthesis by the above criteria, because the asymmetrically inducing center of chirality of **4**-(*S*) is far from the site of the reaction and conformationally flexible transition states determine the steric course of the reaction. The arbitrary assumption that the transition state of **4**-(*S*) → **5**-(*S*,*S*) is energetically favored over the transition state of **4**-(*S*) → **5**-(*S*,*R*) has to be introduced in order to interpret the stereoselectivity. Furthermore, conformations of the transition states with *axial* methyl groups cannot be excluded with certainty.

For similar reasons our earlier attempts[20] to base a synthesis of **1** upon the metallation of (*S*)-4-ferrocenylmethyl-3-phenylmorpholine (this is readily obtained from (*S*)-phenylglycine *via* (*S*)-2-phenyl-N-chloroacetyl-2-aminoethanol) were given up, and the present method[21] was developed. No general *stereorelating synthesis* of any optically active ferrocene derivative of type **1** or **9** from a compound with central chirality and known configuration has yet been reported.

We introduce the term *stereorelating synthesis* to describe stereoselective synthesis for which the steric course of the reaction provides a reliable correlation of the configurations of the products and the starting materials. As a rule, this criterion is met only by reactions which occur by stereospecific mechanisms, *e.g.*, the electrocyclic reactions,[22] and by pairs of corresponding reactions for which the product ratio is determined unequivocally by the stereochemistry of two rigid, *cis–trans* isomeric species.[23]

Results

α-Ferrocenylethyldimethylamine (**7**) is easily prepared from α-ferrocenylethanol by phosgenation and subsequent treatment with dimethylamine, or from ferrocenyldimethylaminoacetonitrile.[24] The resolution of **7** with (*R*)-(+)-tartaric acid is one of the rare cases in which both antipodes are obtained in high yield. The (*R*)-tartrate of **7**-(*S*) crystallizes from methanol, and the (*R*)-tartrate of **7**-(*R*) is obtained by evaporating the mother liquor and recrystallizing from aqueous acetone.

---

(14) M. Rosenblum and R. B. Woodward, *J. Amer. Chem. Soc.*, **80**, 5443 (1958); M. Rosenblum, "Chemistry of the Iron Group Metallocenes," Wiley, New York, N. Y., 1965, p 45.

(15) (a) H. Falk and K. Schlögl, *Monatsh. Chem.*, **96**, 266 (1965); (b) *ibid.*, 96, 1065 (1965).

(16) T. Aratani, T. Gonda, and H. Nozaki, *Tetrahedron Lett.*, 2265 (1969).

(17) A. Horeau, *ibid.*, 506 (1961); 965 (1962); *Bull. Soc. Chim. Fr.*, 2673 (1964); A. Horeau and H. B. Kagan, *Tetrahedron*, **20**, 2431 (1964); O. Červinka and L. Hub, *Chem. Commun.*, 761 (1966); O. Červinka, *Collect. Czech. Chem. Commun.*, **31**, 1371 (1966).

(18) H. Herlinger, H. Kleimann, and I. Ugi, *Ann. Chem.*, **706**, 37 (1967).

(19) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill, New York, N. Y., 1962, (a) p 240; (b) p 151.

(20) P. Hoffmann, unpublished results, 1968.

(21) These investigations of the asymmetrically induced synthesis of **8a** *via* 7 were completed before ref 16 was published. *Cf.* G. Gokel, P. Hoffmann, H. Klusacek, D. Marquarding, E. Ruch, and I. Ugi, *Angew. Chem.*, **82**, 77 (1970).

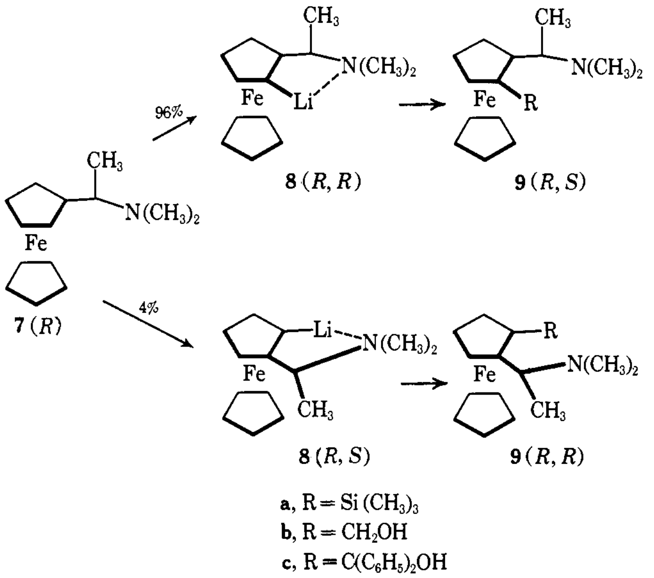
(22) R. B. Woodward and R. Hoffmann, *J. Amer. Chem. Soc.*, **87**, 295 (1965); *Angew. Chem.*, **81**, 797 (1969); R. Hoffmann and R. B. Woodward, *J. Amer. Chem. Soc.*, **87**, 2046 (1965); *Accounts Chem. Res.*, **1**, 17 (1968); *Science*, **165**, 825 (1970).

(23) See, *e.g.*, H. S. Mosher and E. La Combe, *J. Amer. Chem. Soc.*, **72**, 3994, 4991 (1950); W. v. E. Doering and R. W. Young, *ibid.*, **72**, 631 (1950); A. Streitwieser, *ibid.*, **75**, 5014 (1953).

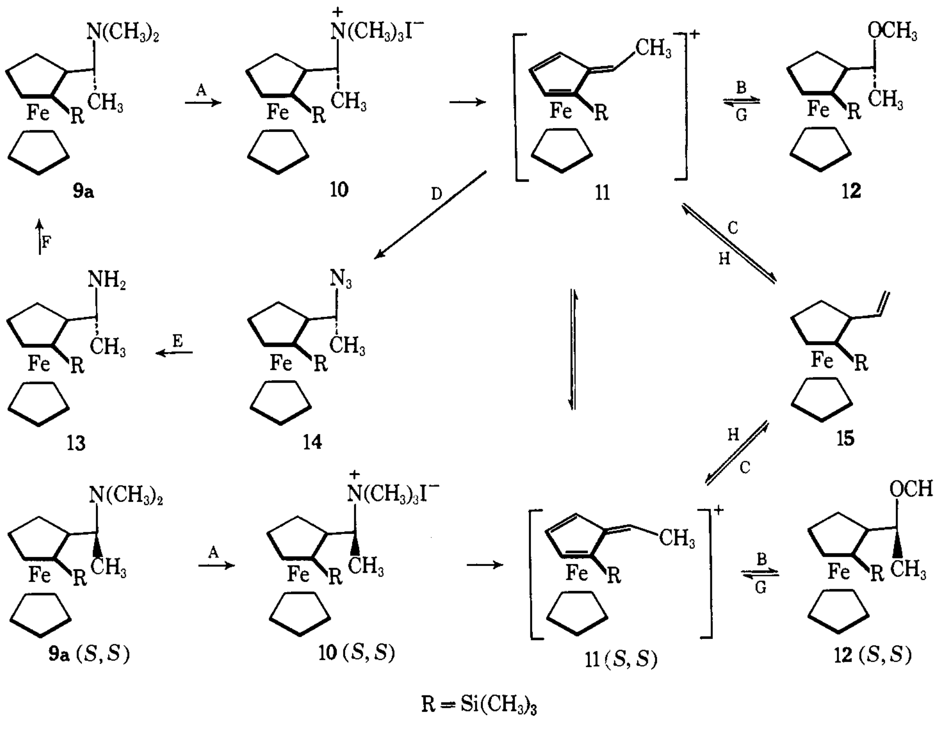
(24) C. R. Hauser and J. K. Lindsey, *J. Org. Chem.*, **22**, 906 (1957).

Metalation of 7-(*R*) with *n*-butyllithium and subsequent treatment with trimethylchlorosilane (or gaseous formaldehyde or benzophenone, respectively) (see Scheme II) produces a 96:4 mixture of **9a**-(*R*,*S*) and **9a**-(*R*,*R*) (or a corresponding mixture of the (*R*,*S*) and (*R*,*R*) isomers of **9b** and **9c**, respectively). The (*R*,*S*)-methiodides **10** cannot be isolated upon treating the (*R*,*S*)-amines **9a** or **9c**, respectively, with methyl iodide in acetone in the absence of nucleophiles (see Scheme III); the corresponding (*S*)-vinyl compounds (**15a** and **c**) are formed. Under the same conditions **10**-(*R*) (R = H) is formed from **7** in good yield.[21] Stoichiometric amounts of methyl iodide and sodium methoxide in methanol transform **9a**-(*R*,*S*) stereospecifically into **12**-(*R*,*S*) and analogously **9a**-(*S*,*S*) into **12**-(*S*,*S*). In the absence of sodium methoxide the treatment with methyl iodide of **9a**-(*R*,*S*) results in the formation of a mixture of the (*R*,*S*) and (*S*,*S*) isomers of **12** in which the (*R*,*S*) diastereomer prevails ($\approx$2:1). A similar mixture of the (*R*,*S*) + (*S*,*S*) isomers of **12** is obtained when **12**-(*R*,*S*) or **15**-(*S*), respectively, are treated with trimethylammonium iodide in methanol. The methylation of **9a**-(*R*,*S*) with methyl iodide in the presence of excess sodium azide in aqueous glyme leads to **14**-(*R*,*S*). The latter is reduced to **13**-(*R*,*S*) by potassium stannite in aqueous glyme, and methylation of this primary amine with excess formaldehyde and sodium borohydride leads back to **9a**-(*R*,*S*).

Scheme II



Scheme III[25]



Discussion

α-Ferrocenyl tertiary amines are lithiated in the 2 position of the ferrocene[16,26,27] because the nitrogen atom of the amino group interacts with the attacking metal. Lithiation occurs through a cyclic mechanism and leads to a chelated organometallic ferrocene derivative. If the starting material is optically active this reaction proceeds with asymmetric induction. The stereoselectivity is determined by reaction conditions, by the ligands at the center of chirality, by the distance from the center of chirality to the reaction site, and by the rigidity of the rate-determining transition states.

---

(25) (a) Scheme III and Table I (the nmr data) refer to the (*R*,*S*) diastereomers, unless otherwise specified. (b) The reagents and reaction conditions are: A = methyl iodide; B = sodium methoxide in methanol at 20°; C = reflux in acetone; D = sodium azide in aqueous glyme at 60°; E = potassium stannite in aqueous glyme at 25°; F = formaldehyde and sodium borohydride in methanol at 0°; G = trimethylammonium iodide in methanol; H = hydrogen bromide in methanol at 20°.

(26) D. W. Slocum, B. W. Rockett, and C. R. Hauser, *J. Amer. Chem. Soc.*, **87**, 1241 (1965); D. W. Slocum, T. R. Englemann, C. Ernst, C. A. Jennings, W. Jones, B. Koonsvitsky, J. Lewis, and P. Shenkin, *J. Chem. Educ.*, **46**, 144 (1969).

(27) J. Tirouflet and C. Moise, *C. R. Acad. Sci., Ser. C*, **262**, 1889 (1966); **267**, 414 (1968); B. J. Booth and B. W. Rockett, *J. Chem. Soc., C*, 656 (1968).

Table I. Nmr Spectra of **9a–c** and **12–14**[a]

Proton compd[b]	$C_5\mathit{H}_5FeC_5\mathit{H}_3C\mathit{H}$	$CH(C\mathit{H}_3)$	R = $Si(C\mathit{H}_3)_3$ or $HC\mathit{H}OH$ or $C(C_6\mathit{H}_5)_2OH$	X = $N(C\mathit{H}_3)_2$ or $OC\mathit{H}_3$ or $N\mathit{H}_2$
9a	~5.75; 5.95; 6.16 (9 H) m, s, q 6.8	8.78 (3 H) d 6.8	9.76 (9 H) s	7.96 (6 H) s
9a-(*R*,*R*)	~5.7; 5.88; ~5.95; 6.67 (9 H) m, s, m, q 7.0	8.82 (3 H) d 7.0	9.71 (9 H) s	7.67 (6 H) s
9b	~5.85; 5.97 (10 H) m, s (includes *H*CHOH)	8.75 (3 H) d 6.9	5.21 (1 H) d J_{gem} = 12.0 Hz	7.87 (6 H) s
9c	~5.8; ~6.1; 6.15 (9 H) m, m, s	8.82 (3 H) d 6.8	~2.3; ~2.8 (10 H) m, m	8.16 (6 H) s
12	~5.65; 5.92 (9 H) m, s	8.48 (3 H) d 6.5	9.72 (9 H) s	6.85 (3 H) s
12-(*S*,*S*)	~5.8; 5.85 (9 H) m, s	8.70 (3 H) d 6.2	9.74 (9 H) s	6.49 (3 H) s
13	~5.7; 5.92; 6.10 (9 H) m, s, q 6.8	8.52 (3 H) d 6.8	9.71 (9 H) s	8.47 (2 H) s
14	~6.0; 6.13 (9 H) m, s	8.63 (3 H) d 6.9	9.72 (9 H) s	

[a] τ (relative area), multiplicity, and *J* (hertz) are listed; Varian A-60; internal TMS; $CDCl_3$. [b] Reference 25a.

The lithiation of **7**-(*R*) leads preferentially to *exo*-**8**-(*R*,*R*), because in the corresponding cyclic transition state the C-methyl group can stay above the plane of the upper ring of the ferrocene system and not interfere with it, whereas in the cyclic transition state of *endo*-**8**-(*R*,*S*) a strong repulsive interaction of the C-methyl and the ferrocene system prevails.

The overall yield of the reactions **7** → **9a–c** is 60%, and the diastereomer product ratio of 96:4 is the same for all of these. This diastereomer ratio of **9a–c** corresponds to the ratio of the rates of the pair of corresponding metallation reactions **7**-(*R*) → **8**-(*R*,*R*) + -(*R*,*S*). There is no rapid interconversion **8**-(*R*,*R*) ⇄ **8**-(*R*,*S*), and the alkylation of **8** or the reaction of **8** with the carbonyl compound is not the stereoselectivity determining process for **7** → **9** in the sense of the *Curtin–Hammett principle*.[19b] It can therefore be concluded that the major products of **7**-(*R*) → **9a–c** are the (*R*,*S*) diastereomers.[28]

The organometallic function of **8** can be used for introducing a wide variety of groups, *R*, and the α-dimethylaminoethyl group of the products of **7** can be transformed into other substituents of the ferrocene, *e.g.*, *via* **15**. Therefore, the highly stereoselective lithiation of 7-(*R*) or -(*S*) or analogous optically active α-ferrocenylalkylamines provides a basis for a generally applicable, convenient synthesis of optically active ferrocene derivatives of type **1** of known configuration.

The cycle {**9a**, **10**, **14**, **13**} of Scheme III, the common features of the nmr spectra[1] of (*R*,*S*) isomers *vs.* the (*R*,*R*) and (*S*,*S*) isomers of **9a** and **12** (see Table I), and the optical rotations of these compounds (see Experimental Section) imply complete configurational retention during the nucleophilic substitutions of Scheme II. This is in accordance with earlier observations[21] on analogous reactions.

The steric course of Scheme III and the fact that **12**-(*S*,*S*) is also formed from **9a**-(*S*,*S*) without diastereomerization are interpreted by assuming that the intermediate carbonium ion **11** or a corresponding ion pair is formed from the indicated conformation of **10** and that bond formation with the nucleophile occurs without stereoisomerization of **11**. The carbonium ion **11** diastereomerizes only under conditions that favor a long lifetime of **11** or equilibrium of **11** with **15** (as in the processes **10** → **12**, **15** → **12**, and the acid-catalyzed diastereomerization of **12**). The fact that **12** diastereomerizes in methanol in the presence of trimethylammonium iodide, in combination with the observation that the latter does not catalyze the formation of **12** from **15**, indicates that **11** is capable of diastereomerization.

Experimental Section

α-Ferrocenylethyldimethylamine (7).[21-24] At −20° the solution of 23.0 g of 1-ferrocenylethanol[29] in 150 ml of toluene is added dropwise to a stirred solution of 12.5 g of phosgene in 100 ml of toluene. One-half hour after the addition is complete the reaction mixture is allowed to warm up to 20° and, without isolation of the chloride,[30] added to a −20° solution of 22.5 g of dimethylamine in 200 ml of isopropyl alcohol. The temperature is allowed to rise to +20°. The reaction mixture is filtered and evaporated to dryness. The residue is taken up in benzene, extracted with 8.5% phosphoric acid, washed with benzene, neutralized with Na_2CO_3, extracted with benzene, dried, and evaporated; crude yield: 24.4 g (95%); yield after distillation (bp 110° (0.45 mm)), with some decomposition[24]): 17.5 g (68%). The undistilled product is sufficiently pure for the resolution of the antipodes of **7**.

Resolution of 7. The solution of 51.4 g of racemic **7** and 30.0 g of (*R*)-(+)-tartaric acid, each in 100 ml of methanol, is mixed at 55° while being stirred. Seeding crystals are added. The temperature is lowered at a rate of 2°/hr. After 24 hr 30.0 g (75% of one antipode) of **7**-tartrate is collected and 19.0 g of partially optically active **7** is set free ($[\alpha]^{25}D$ −11.0° (*c* 1.5, ethanol)). The solutions of this (−)-**7** and 11.1 g of (*R*)-(+)-tartaric acid, each in 50 ml of methanol, are mixed at 55° and seeded. After slow cooling 27.5 g of (−)-**7**-tartrate is obtained; this is converted into 17.0 g (66% overall yield) of **7**-(*S*) (bp 120–121° (0.7 mm); $[\alpha]^{25}D$ −14.1° (*c* 1.6, ethanol)). The mother liquor of the first crystallization is concentrated to 1/4 of its original volume. Diethyl ether is added until no further precipitate is formed. After standing at 0° overnight 48.6 g of **7**-tartrate is collected ($[\alpha]^{25}D$ 7 +8.0° (*c* 1.5, ethanol)) and recrystallized from 800 ml of acetone–water (10:1) to yield 34.5 g (85%); $[\alpha]^{25}D$ +12.0° (*c* 1, ethanol). By a second recrystallization from 500 ml of aqueous acetone one obtains 28.0 g (69%); $[\alpha]^{25}D$ +14.0°. By working up the mother liquors an overall yield of 80–90% of both antipodes can easily be obtained.

(*R*,*R*)- and (*R*,*S*)-α-[2-Trimethylsilylferrocenyl]ethyldimethylamine (9a). (a) At 27° 62 ml of 2.18 *M* *n*-butyllithium in *n*-hexane is added to the stirred solution of 30.0 g of **7**-(*R*) in 180 ml of anhy-

---

[28] The absolute configuration of **9c**-(*R*,*S*) is being confirmed by X-ray crystallography.

[29] F. S. Arimoto and A. C. Haven, *J. Amer. Chem. Soc.*, 77, 6295 (1955).

[30] R. Benkeser and W. P. Fitzgerald, *J. Org. Chem.*, **26**, 4179 (1961).

drous ether. After 1 hr 19.1 g of trimethylchlorosilane in 80 ml of ether is added at reflux temperature. After 3 hr reflux and standing overnight under N_2, water is added at 5°. The organic phase is separated and extracted three times with 8.5% aqueous phosphoric acid. The aqueous solution is separated, made alkaline with 10% aqueous soda, and extracted with chloroform. After drying with anhydrous sodium sulfate the solution is evaporated *in vacuo*.

The residue is separated by column chromatography [activated alumina MC & B; 80–325 mesh, elution by benzene, or silica gel modified by 2% concentrated aqueous ammonia, elution by ligroin (60–80°)–isopropyl alcohol (20:1)]; yield: (1) 22.0 g of **9a**-(*R*,*S*); $R_f = 0.55$ (ligroin (60–80°)–isopropyl alcohol (20:1)); bp 103° (0.04 mm); $[\alpha]^{20}_{546}$ +35.3°; $[\alpha]^{20}_{578}$ +18.5°; $[\alpha]^{20}_{D}$ +15.5° (*c* 1.5, ethanol) (*Anal.* Calcd for $C_{17}H_{27}FeNSi$: C, 62.0; H, 8.2; N, 4.3. Found: C, 62.0; H, 8.4; N, 4.4); (2) 1.0 g of **9a**-(*R*,*R*); $R_f = 0.30$ (ligroin (60–80°)–isopropyl alcohol (20:1)); $[\alpha]^{20}_{546}$ +55.9°; $[\alpha]^{20}_{578}$ +45.1°; $[\alpha]^{20}_{D}$ +42.2° (*c* 0.6, ethanol). *Anal.* Calcd: see above. Found: C, 62.0; H, 8.3; N, 4.2.

(**b**) At 20° 1 g of sodium borohydride is added to a solution of 0.50 g of **13**-(*R*,*S*) and 5.0 ml of 40% aqueous formaldehyde in 25 ml of methanol. After 1 hr at 30–40° the reaction mixture is diluted with 200 ml of water, and extracted with benzene. The product was extracted into 8.5% phosphoric acid and returned to benzene solution by neutralization with 2 *N* aqueous soda. There was obtained 0.41 g (90%) of **9a**-(*R*,*S*) (identified by ir and nmr).

(*R*)-α-[(*S*)-2-Hydroxymethylferrocenyl]ethyldimethylamine (9b). At 27° 10.0 g of **7**-(*R*) is lithiated as described above. Gaseous formaldehyde (generated by heating 30 g of anhydrous paraformaldehyde) is introduced into the refluxing solution and the product, **9b**-(*R*,*S*), is isolated like **9**a: yield 4.51 g (58%); mp 109–110° (from cyclohexane); $[\alpha]^{20}_{546}$ +156.2°; $[\alpha]^{20}_{578}$ 127.9°; $[\alpha]^{20}_{D}$ +121.5° (*c* 1.4, chloroform). *Anal.* Calcd for $C_{15}H_{21}FeNO$: C, 62.7; H, 7.3; N, 4.9. Found: C, 62.6; H, 7.4; N, 4.9.

(*S*)-α-[(*R*)-2-Diphenylhydroxymethylferrocenyl]ethyldimethylamine (9c). The solution of 66.8 g of benzophenone in 120 ml of anhydrous ether is added over 45 min to the refluxing solution of 23.6 g of **7**-(*S*) which has been lithiated according to the preceding procedures. After 4-hr reflux and standing overnight at 20° the product, **9c**-(*S*,*R*), is isolated like **9b** and recrystallized twice from methanol: yield 20.9 g (52%); mp 118–119°; $[\alpha]^{20}_{365}$ +207.0°; $[\alpha]^{20}_{548}$ +274.6°; $[\alpha]^{20}_{578}$ +206.4°; $[\alpha]^{20}_{D}$ +191.6° (*c* 0.5, ethanol). *Anal.* Calcd for $C_{24}H_{29}FeNO$: C, 73.7; H, 6.6; N, 3.2. Found: C, 73.9; H, 6.6; N, 3.3.

(*S*)-2-Trimethylsilyl-1-vinylferrocene (15a). **9a**-(*R*,*S*) (1.00 g) and 10.0 g of methyl iodide in 15 ml of acetone are refluxed for 10 min; then the solution is diluted with 30 ml of ether, washed with 8.5% aqueous phosphoric acid and 10% soda, dried over sodium sulfate, and evaporated. The residue is purified by column chromatography (silica gel; ligroin (60–80°)–benzene, 10:1); bp 78° (0.04 mm); yield 0.64 g (75%); $[\alpha]^{20}_{578}$ +996°; $[\alpha]^{20}_{D}$ +885° (*c* 1.1, acetone); nmr ($CDCl_3$) τ 3.39 ($-CH{=}CH_2$, 1 H, $J_{trans} = 17.5$ Hz, $J_{cis} = 10.5$ Hz), 4.67 ($-CH{=}CH_2$, 2 H, $J_{trans} = 17.5$ Hz, $J_{gem} = 1.8$ Hz), 4.97 ($J_{cis} = 10.5$ Hz, $J_{gem} = 1.8$ Hz), ~5.4 (m), ~5.65 (m), 5.93 (s, $C_5H_5FeC_5H_3$, 8 H), 9.72 ($Si(CH_3)_3$, 9 H, s). *Anal.* Calcd for $C_{15}H_{20}FeSi$: C, 63.3; H, 7.0. Found: C, 63.5; H, 7.1.

(*R*)-2-Diphenylhydroxymethylvinylferrocene (15c). The solution of 5.5 g of **9c**-(*S*,*R*) and 40.0 g of methyl iodide in 50 ml of acetone is refluxed for 10 min. After adding 200 ml of ether, washing with 8.5% phosphoric acid, drying over sodium sulfate, evaporating *in vacuo*, and recrystallizing from methanol, 1.03 g (22%) of **15c** is obtained: mp 125–126°; $[\alpha]^{20}_{546}$ −1075°; $[\alpha]^{20}_{578}$ −757°; $[\alpha]^{20}_{D}$ −668° (*c* 1.1, acetone); nmr ($CDCl_3$) τ ~2.7 ($C(C_6H_5)_2$, 10 H, m), 3.50 ($-CH{=}CH_2$, 1 H, $J_{trans} = 17.8$ Hz, $J_{cis} = 11.0$ Hz), 4.77 ($-CH{=}CH_2$, 2 H, $J_{trans} = 17.8$ Hz, $J_{gem} = 2.0$ Hz), 5.14 ($J_{cis} = 11.0$ Hz, $J_{gem} = 2.0$ Hz), 5.35 (m), 5.81 (s), 6.38 (m, $C_5H_5FeC_5H_3$, 8 H). *Anal.* Calcd for $C_{25}H_{22}FeO$: C, 76.2; H, 5.6. Found: C, 76.1; H, 5.5.

(*R*,*S*)- and (*R*,*R*)-α-[2-Trimethylsilylferrocenyl]methoxyethane (12). (**a**) At 20° 1.00 g of **9a**-(*R*,*S*) in 5 ml of methanol is added to 0.17 g of sodium methoxide and 10.0 g of methyl iodide in 20 ml of anhydrous methanol. After 75 min 100 ml of water and 25 ml of benzene are added. The benzene layer is separated, dried over sodium sulfate, and evaporated *in vacuo*. The residue is purified by column chromatography (silica gel; cyclohexane–ethyl acetate 20:1): yield 0.80 g (95%) of **12**-(*R*,*S*); bp 100° (0.06 mm); $[\alpha]^{20}_{546}$ +5.3°; $[\alpha]^{20}_{578}$ −1.1°; $[\alpha]^{20}_{D}$ −1.7° (*c* 1.2, acetone). *Anal.* Calcd for $C_{16}H_{24}FeOSi$: C, 60.8; H, 7.6. Found: C, 61.0; H, 7.7.

(**b**) An analogous treatment of **9a**-(*R*,*R*) results in 95% **12**-(*R*,*R*); bp 90° (0.06 mm); $[\alpha]^{20}_{546}$ −10.8°; $[\alpha]^{20}_{578}$ +2.4°; $[\alpha]^{20}_{D}$ +4.5° (*c* 1.3, acetone). *Anal.* Calcd: see above. Found: C, 60.8; H, 7.5.

(**c**) **9a**-(*R*,*S*) (1.50 g) is dissolved in a mixture of 5 ml of methanol and 5 ml of methyl iodide. After 70 hr the solvent is evaporated *in vacuo*, and **12**-(*R*,*S*), the major product ($R_f = 0.6$), is separated from the minor product, **12**-(*S*,*S*) ($R_f = 0.8$), by column chromatography (silica gel, ligroin (60–80°)–ethyl acetate 10:1). The diastereomers of **12** are identified by ir, nmr, and optical rotation.

(**d**) The solution of 0.30 g of **12**-(*R*,*S*) and 0.20 g of trimethylammonium iodide in 5 ml of methanol is allowed to stand at 20°. After 2 hr the (*S*,*S*) diastereomer of the starting material can be detected by tlc.

(**e**) The solution of 50 ml of **15a**-(*S*) and 50 mg of hydrogen bromide in 20 ml of methanol is allowed to stand at 20°. After 1 hr tlc shows the formation of the (*R*,*S*) (predominantly) and (*S*,*S*) diastereomers of **12**. In the absence of acids, methanol does not react with **15a**.

(*R*)-α-[(*S*)-Trimethylsilylferrocenyl]ethyl Azide (14). At 60° 14 g of methyl iodide is added slowly to a solution of 8.0 g of **9**a-(*R*,*S*) and 8.0 g of sodium azide in 200 ml of 60% aqueous glyme. After 1 hr the reaction mixture is diluted with 500 ml of water. The product is extracted with benzene and purified by distillation: yield 6.4 g (80%); bp 120° (0.04 mm); ir 2095 cm^{-1} (N_3); $[\alpha]^{20}_{546}$ +96.2°; $[\alpha]^{20}_{578}$ +45.6°; $[\alpha]^{20}_{D}$ +36.5° (*c* 1.4, benzene). *Anal.* Calcd for $C_{15}H_{21}FeN_3Si$: N, 12.8. Found: N, 12.8.

(*R*)-α-[(*S*)-2-Trimethylsilylferrocenyl]ethylamine (13). At 25° a solution of 8.30 g of stannous chloride dihydrate in 42 ml of water and 42 ml of 50% potassium hydroxide is added to 6.33 g of **14**-(*R*,*S*) in 180 ml of glyme. After the evolution of nitrogen has ceased the reaction mixture is diluted with 1000 ml of water and extracted with benzene. The residue of the extract is distilled *in vacuo*: bp 105° (0.03 mm); yield 5.54 g (95%) of **13**-(*R*,*S*); $[\alpha]^{20}_{546}$ +70.8°; $[\alpha]^{20}_{578}$ +40.4°; $[\alpha]^{20}_{D}$ +34.5° (*c* 1.3, benzene). *Anal.* Calcd for $C_{15}H_{23}FeNSi$: N, 4.6. Found: N, 4.7.