Prototropic acetylene-allene isomerization in planarly chiral ferrocenes. Intramolecular acymmetric induction in the course of the formation of chiral axis

*L. L. Troitskaya,** *L. A. Bulygina, and V. I. Sokolov*

A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences,
28 ul. Vavilova, 117818 Moscow, Russian Federation.
Fax: +7 (095) 135 5085

Racemic 2-trimethylsilyl- and 2-trimethylstannyl-1-(3-phenyl-2-propynyl)ferrocene (*rac*-**1a**,**b**) as well as the dextrorotatory specimen of the latter, (+)-**1b**, were synthesized in two steps from racemic 1-formyl-2-trimethylsilyl- and 1-formyl-2-trimethylstannylferrocenes (**2a**,**b**) or from the levorotatory specimen of the latter, (−)-**2b**, respectively. On the contact with strongly alkaline alumina compounds **1a**,**b** and (+)-**1b** undergo diastereoselective prototropic acetylene—allene rearrangement to give predominantly one of the two possible stereoisomers of 2-trimethylsilyl- or 2-trimethylstannyl-1-(3-phenyl-1,2-propadienyl)ferrocenes, *rac*-**4a**,**b** or (+)-**4b**, depending on the starting material (d. e. 30—40 %). The extent of intramolecular asymmetric induction in the formation of the axially chiral fragment during the transformation of (+)-**1b** to (+)-**4b** is estimated at 38 %.

Key words: 2-trimethylstannyl(silyl)-1-(3-phenyl-2-propynyl)ferrocenes, synthesis; prototropic acetylene—allene rearrangement, diastereoselectivity; intramolecular asymmetric induction; 2-trimethylstannyl(silyl)-1-(3-phenyl-1,2-propadienyl)ferrocenes.

The double bonds in allenes are located in mutually perpendicular planes. This accounts for the appearance of a chiral axis and possible enantiomery in the allene molecule, when at least three different substituents (asymmetric allenes) or two equal pairs of substituents at the terminal carbon atoms (disymmetric allenes) are present in the molecule.

The described methods of synthesizing optically active allenes traditionally involve the resolution of racemates through diastereomeric derivatives, asymmetric synthesis, and stereospecific synthesis from optically active precursors. To obtain optically active allenes, stereospecific reagents that are capable of converting central chirality to axial chirality, are mainly used. In this case, an asymmetric carbon atom changes from sp^3-hybridization to sp^2-hybridization and becomes a part of the allenic system.[1] Reactions of this type usually proceed through a cyclic transition state to yield enantiotropic allenes.

There is only one example of diastereoselective synthesis of allenes (not organometallic), from compounds with a chiral carbon center where the principle of intramolecular induction[2] is used.

Since we had at our disposal planarly chiral ferrocenes of high enantiomeric purity, we considered that it would be interesting to study the effectiveness of using a chiral plane as an inductor for the creation of chiral axis in the course of formation of α-ferrocenylallenes.

Synthesis of 1-ferrocenylallenes (even racemic ones) is not an easy problem. Only one optically active allene of this series is known, namely, 1,3-diphenyl-1,3-ferrocenylallene; it was obtained by partial separation of the racemate on triacetylcellulose,[3] but in amounts sufficient only for recording its CD spectra. The observed values of its optical rotation appeared to be within the bounds of the experimental error.

There is a plethora of methods for the synthesis of allenes, but only a few of them are appropriate for ferrocene. These are the thermal dehydration of α-ferrocenylallylcarbinols, dehydrohalogenation with simultaneous ring opening of 1-ferrocenyl-2,2-dihalocyclopropanes, and prototropic propargyl rearrangement, which proceeds *via* an intermediate carbanion. The propargyl rearrangement *via* an α-ferrocenylcarbenium ion does not afford allenes due to the high stability of this ion. Therefore, propargylic α-ferrocenylcarbinols, which, in principle, can be obtained in the optically active form, cannot be used for the synthesis of enantiomeric α-ferrocenylallenes.

In the first two methods, the starting compounds contain a chiral center, which is affected during the reaction, and their planarly chiral analogs are already diastereomers and cannot be used as models for the study of induction by chiral plane. Therefore, only prototropic rearrangement is consistent with the purpose of this study.

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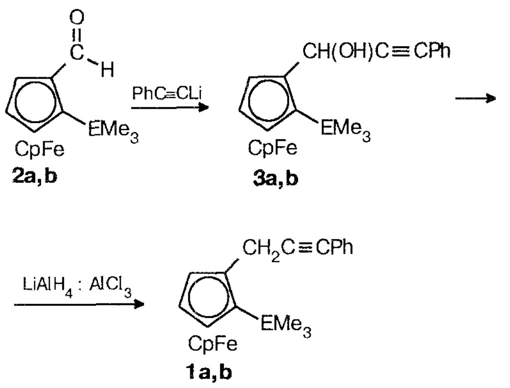
1-Trimethylsilyl- and 1-trimethylstannylsubstituted 2-alkynylferrocenes (**1a**,**b**) synthesized according to Scheme 1 from aldehydes **2a**,**b** *via* carbinols **3a**,**b** were selected as starting compounds. It should be noted that the addition of lithium phenylacetylenide to **2a**,**b** creates a new chiral center at the α-position to the cyclopentadienyl ring with a high order of stereoselectivity. In the ^{1}H NMR spectrum of secondary carbinols **3a**,**b** (obtained in a high yield), only the signals of one diastereomer were observed, and not even traces of the second one could be detected.

Unfortunately, as was mentioned above, it is impossible to convert **3a**,**b** into allenes.

Reduction of **3a**,**b** with $LiAlH_4$—$AlCl_3$ leads to the disappearance of the chiral center and the formation of derivatives **1a**,**b**, which possess a single chiral element, *viz.*, a plane, in a yield up to 92 %.

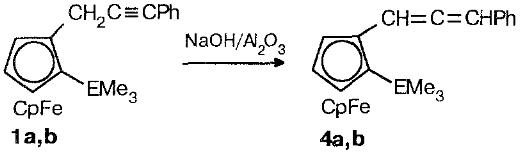
Scheme 1



E = Si (**a**), Sn (**b**)

All of the compounds were characterized by mass spectrometry, and NMR and IR spectroscopy, as well as by $[\alpha]_D$ values.

Literature data show that, of the different methods for carrying out the prototropic rearrangement, the one that gives the best yields of α-ferrocenylallenes involves passing the corresponding acetylenic hydrocarbon through a column with strongly alkaline alumina[4] prepared in a special way. This method appeared to be appropriate for planarly chiral derivatives **1a**,**b**.



The allenes, which formed in 92 % yield, were identified by mass spectrometry and NMR and IR spectroscopy. According to the ^{1}H NMR spectral data, the reaction gives rise to a mixture of diastereomers with a predominance of one of them. The diastereomeric excess was determined by the ratio between the integral intensities of the signals of the C_5H_5 ligand, the $SiMe_3$-group (in the case of **4b**, the signals of the diastereomers are poorly separated), and one of the allenyl protons (see Table 1).

Table 1. Diastereoselectivity of the prototropic acetylene-allene isomerization **1** → **4**

Starting acetylene (%)	Allene	Yield of allene (%)	Diastereomeric excess in allene
rac-**1a**	*rac*-**4a**	—	30±3
rac-**1b**	*rac*-**4b**	84	39±1
(+)-**1b***	(+)-**4b****	91.7	40±5

* $[\alpha]_D$+77.7°. ** $[\alpha]_D$+310—345°.

Taking into consideration the high yield of allenes, the conclusion can be made that these data reflect the diastereoselectivity of the rearrangement, but do not result from the enrichment of the mixture by one of the diastereomers at the expense of the other one (which would have been the case if the latter had been decomposing in the course of the reaction).

The experiments with racemic **1a**,**b** showed that some increase in diastereoselectivity of the reaction takes place, *i.e.*, from 30 % in the case of *rac*-**4a** to 38 % for *rac*-**4b**. Accordingly, only the derivatives with the Me_3Sn-group were used in the optically active series.

In addition, diastereomers **4b** showed a tendency to decompose during chromatography. As a result, the head portion of the allenic fraction appears to be to some extent enriched with the predominant diastereomer, and the excess of the latter increases to 45 %. However, this excess is not enough to determine the absolute configuration of the chiral axis that is predominantly formed by X-ray diffraction analysis.

The observed moderate diastereoselectivity could, nevertheless, be considered as rather high for reactions of this type. Only two cases of the prototropic base-induced isomerization of acetylenes to allenes with established stereochemistry are known. In the first case, allenes are formed from acetylenic diethers t-$BuOCH_2C{\equiv}CCHR^1OR^2$ by treatment with t-BuOK in DMSO.[5] Although intramolecular induction by the neighbouring chiral center is possible here, it was not observed; the reaction was completely non-diastereoselective. In the second case, prototropic isomerization of 1,3-diphenyl- and 1-(*p*-biphenyl)-3-phenyl-1-propynes on alumina impregnated with brucine is an example of asymmetric catalysis.[4] The enantiomeric yield was only 2—3 %, which is significantly lower than the result obtained for (+)-**4b**. It is probably of primary significance that a generally more effective method for intramolecular induction was used in the present work, *viz.*, the isomerization of a chiral substrate on an achiral phase, while earlier[4] external induction was observed, *i.e.*, a conformationally flexible achiral substrate was treated with a chiral phase.

Unfortunately, all attempts to transform diastereomeric allenes to enantiomeric allenes by the elimination of planar chirality were unsuccessful. The known methods[6,7] of replacing SnMe$_3$ with hydrogen lead to the complete destruction of the allene group and formation of a number of unidentified products.

Apparently, preliminary protection of the allenic moiety is necessary, and its deprotection must not provoke isomerization to acetylene. The application of the (η^5-C_5H_4Me)Mn(CO)$_2$ group for the protection of carbonyl-containing allenes has been reported[8]. However, this group was introduced into the starting acetylene and, although it was conserved in the course of the isomerization of acetylene to allene (also over basic Al_2O_3), it appeared to be coordinated to only one of the double bonds of allene.[8] It is the latter fact that makes it problematic to use protective group in the present work. First, there arises the question of which of the double bonds is coordinated with the metal. On the other hand, the second double bond remains unprotected, which excludes the use of destannylation reagents that are reactive towards olefins.

The determination of the absolute configuration of the chiral axis in the predominant diastereomer entail great difficulties. The problems connected with the synthesis of allenes in the ferrocene series, as well as with their reactivity, are a serious obstacle when solving this task by the method of chemical correlation. As was mentioned above, pure stereoisomers are required for X-ray diffraction analysis.

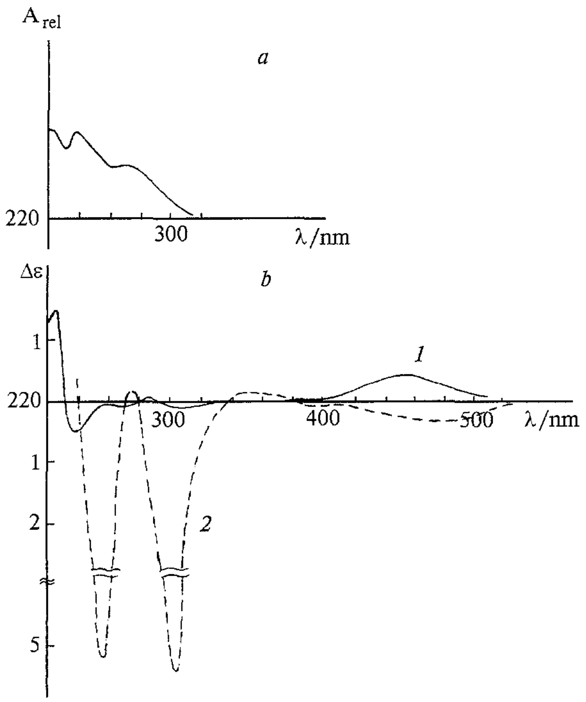
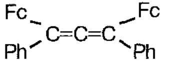
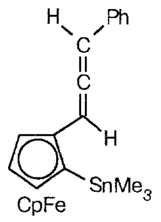


Fig. 1. *a*, UV spectrum Fc'—CH=C=CHPh (Fc' = $C_5H_5FeC_5H_3(SnMe_3)$—); *b*, CD spectra: *1* — Fc'—CH=C=CHPh, *2* —  $\mathrm{(Fc)(Ph)C{=}C{=}C(Fc)(Ph)}$.

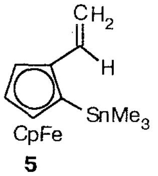
Spectral methods, in particular circular dichroism, can be regarded as the most appropriate. However, in this case, the data for structurally similar compounds with known absolute configurations must be available. It has already been mentioned that only one optically active ferrocenic allene, *viz.*, 1,3-diphenyl-1,3-diferrocenylallene, has been hitherto reported, but its absolute configuration was not established. The CD spectrum of the latter is shown in Fig. 1 together with its UV spectrum and the CD spectrum of allene **4b**. The latter is the sum of the CD spectra of two diastereomers, one of which markedly predominates.

It is known that the allene group itself has a weak π—π*-transition at 225 nm. Therefore the signs and intensities of the Cotton effects are functions of its stereochemical environment, as well as of the nature and configuration of the substituents. The distortion transitions of the aromatic ring and, probably, of ferrocene lie approximately in the same range. Therefore, no differentiation of the Cotton effects in the short-wave region by chromophores or, especially, by electron transitions is possible. The observed long-wave Cotton effect is undoubtedly connected with the d—d*-transition in the ferrocene chromophore.

According to the additivity rule, each dichroic band, whether homogeneous or non-homogeneous, is a result of configurational, vicinal, and conformational contributions of allene fragments with substituents and the planar chirality of ferrocene. Since the substituents at the ends of the allenic system are far apart from each other, it can be assumed that their conformations do not undergo significant changes on passing from one isomer to another, so that both the five-membered ring and the phenyl group remain more or less coplanar with the neighbouring double bonds and the double bond conjugated to ferrocene and, therefore, the whole allenic system is turned with respect to the SnMe$_3$-group, just as in the case of 1-vinyl-2-methylferrocene[9] (**5**).



4b



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In practice this postulate means that there is no shift of the dichroic maxima for the two diastereomers. Consequently, in the CD spectrum of mixture **4b**, only the vicinal contributions of the chiral plane of the same sign are summed; the other contributions characterize the opposite configurations relative to the chiral axis of the allenic fragment and should, therefore, be subtracted. It is impossible to reliably evaluate the relative value of the above-mentioned contributions, but it can be presumed that, in the case of the optically active transitions of the aromatic chromophore not connected to ferrocene, the configurational contribution of allene would be the major one.

The positive Cotton effect in the long-wave reagion corresponding to the d—d*-transition of ferrocene is probably determined by the configuration of the chiral plane, because its sign coincides with that of the effect found for (*R*)-1-vinyl-2-methylferrocene, if the analogous predominant conformation of the planarly chiral ferrocene fragment[9] is accepted for allenes **4b**.

Although it does not seem possible to assign a configuration to the allenic fragment, we should like to note that, in the vicinity of 300 and 250 nm in the CD spectrum of **4b**, negative Cotton effects of low intensity, but of the same sign as strong EC of the (−)-enantiomer of 1,3-diphenyl-1,3-diferrocenylallene, are observed.

As for the Cotton effects of the opposite signs in the long-wave area, the dichroic band for the distorted d—d*-transition of ferrocene in the spectrum of **4b** is presumably a result of overlapping of the configurational effects of the allenic radical and the chiral plane of the ferrocenyl fragment. The second effect apparently predominates, which is in accord with the previous assumption.

Thus prototropic acetylene-allene rearrangement in planarly chiral ferrocene is diastereoselective. The extent of asymmetric induction in the formation of the chiral axis is 38 %. The studied diastereoselective reaction appears to be promising as a new approach to the synthesis of optically active allenes of the ferrocene series on a preparative scale. An increase in diastereoselectivity of this reaction can be achieved by increasing the number of substituents in the allene moiety or by using functionally substituted substituents, because this should be accompanied by an increase in the stability of allenes and, possibly, by greater differences in the adsorption ability of the diastereomers.

Experimental

(+)-1-(2-Trimethylstannylferrocenyl)-3-phenylpropin-1-ol, (+)-3b. 0.7 g (1.6 mmol) of compound **2b** ($[\alpha]_D$−664.2 °, EtOH, *c* = 0.96) obtained by the known procedure[10] in 30 ml of abs. ether was added (under an argon atmosphere at room temperature) to lithium phenylacetylenide obtained from 0.48 g (4.7 mmol) of phenylacetylene in 15 mL of abs. ether and 4 ml of a 1.5 *M* BuLi solution in hexane (6.0 mmol). The reaction mixture was refluxed for 3 h. After cooling, 10 % aqueous NH_4Cl was carefully added at 0 °C. The product was extracted with ether and dried over K_2CO_3. After chromatography on neutral alumina with Et_2O as the eluent, **3b** was obtained in 97 % yield, $[\alpha]_D$+151.4° (C_6H_6, *c* = 1.7). Mass spectrum, *m/z*: 478 [M^+]. ^1H NMR (C_6D_6), δ: 0.35 (s, 9 H, Me_3Sn); 2.05 (d, 1 H, OH); 4.05, 4.2, 4.66 (m, 3 H, C_5H_3); 4.18 (s, 5 H, C_5H_5); 5.3 (d, 1 H, Fc—C$\underline{H}$); 6.95—7.5 (m, 5 H, Ph).

1-(2-Trimethylsilylferrocenyl)-3-phenyl-1-propynol racemic, *rac*-3a. In the same manner as above, 1.35 g (83.3 %) of **3a** was obtained from 1.2 g (4.2 mmol) of **2a**. Mass spectrum, *m/z*: 373 [M^+−Me]. ^1H NMR (C_6D_6), δ: 0.43 (s, 9 H, Me_3Si); 2.33 (d, 1 H, OH); 4.1, 4.21, 4.8 (m, 3 H, C_5H_3); 4.15 (s, 5 H, C_5H_5); 5.6 (d, 1 H, Fc—C$\underline{H}$); 7.02—7.51 (m, 5 H, Ph).

(+)-2-Trimethylstannyl-1-(3-phenyl-2-propynyl)-ferrocene, (+)-1b. 0.25 g (1.9 mmol) of $AlCl_3$ and 0.87 g (1.8 mmol) of **3b** were added to 0.07 g (1.2 mmol) of $LiAlH_4$ in absolute ether at 0 °C under an argon atmosphere. The cooling was removed and the reaction mixture was stirred for 40 min at room temperature. Then the reaction mixture was carefully decomposed with water at 0 °C, and the product was extracted with ether. After drying with K_2CO_3 and evaporation of the solvent, pure **1b** was obtained (yield 94 %), $[\alpha]_D$+77.7 ° (C_6D_6, *c* = 2.3). Mass spectrum, *m/z*: 462 [M^+]. IR (CCl_4), ν/cm^{-1}: 2257 (C=CPh). ^1H NMR (C_6D_6), δ,: 0.33 (s, 9 H, Me_3Sn); 3.4 (d, 2 H, $FcCH_2$—); 4.1 (s, 5 H, C_5H_5); 3.95, 4.2, 4.49 (m, 3 H, C_5H_3); 7.0—7.5 (m, 5 H, Ph).

2-Trimethylsilyl-1-(3-phenyl-prop-2-ynyl)-ferrocene racemic, *rac*-1a. Similarly to **1b**, 0.43 g (93 %) of **1a** was obtained from 0.45 g (1.16 mmol) of **3a**. Mass spectrum, *m/z*: 372 [M^+], 357 [M^+−Me]. Spectrum ^1H NMR (C_6D_6), δ: 0.39 (s, 9 H, Me_3Si); 3.51 (d, 2 H, $FcCH_2$—); 4.14 (s, 5 H, C_5H_5); 4.05, 4.21, 4.57 (m, 3 H, C_5H_3); 7.0—7.51 (m, 5 H, Ph).

(+)-2-Trimethylstannyl-1-(3-phenyl-1,2-propadienyl)ferrocene, (+)-4b. 1b was chromatographed on a strongly basic alumina prepared according to the known procedure[4] using hexane as the eluent. **4b** was obtained in 97 % yield, $[\alpha]_D$+333 ° (C_6H_6, *c* = 0.96). Mass spectrum, *m/z*: 462 [M^+]. IR (CCl_4), ν/cm^{-1}: 1940 (C=C=C). ^1H NMR (C_6D_6), δ: I diastereomer: 0.38 (s, 9 H, Me_3Sn); 4.16 (s, 3 H, C_5H_3); 4.13, 4.33, 4.53 (m, 3 H, C_5H_3); 6.342, 6.432 (d, 2 H, allenic protons, AB-system, *J*= 6.4 Hz); 7.0—7.45 (m, 5 H, Ph); II diastereomer: 0.376 (s, 9 H, Me_3Sn); 4.164 (s, 5 H, C_5H_5); 4.13, 4.33, 4.53 (m, 3 H, C_5H_3); 6.37, 6.45 (d, 2 H, allenic protons, AB-system, *J* = 6.5 Hz); 7.0—7.45 (m, 5 H, Ph).

(+)-2-Trimethylsilyl-1-(3-phenyl-1,2-propadienyl)ferrocene, *rac*-4a. was synthesized similarly to **4b**.

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