spectrum, m/z 258.1 (MH^+).

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Supplementary Material Available: ^1H and ^{13}C NMR spectral data recorded for $(CD_3)_2SO$ solutions (3 pages). Ordering information is given on any current masthead page.

Mechanism of the Asymmetric Isomerization of Allylamines to Enamines Catalyzed by 2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl-Rhodium Complexes

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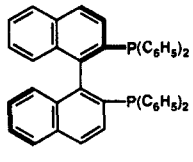
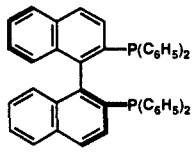
Abstract: Cationic Rh complexes containing the 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (BINAP) ligand catalyze a highly enantioselective isomerization of diethylgeranylamine or -nerylamine to give (*R*)- or (*S*)-citronellal (*E*)-diethylenamine in >95% ee. A new, nitrogen-triggered mechanism is postulated for the double-bond-migration reaction on the basis of ^1H and ^{31}P NMR studies, kinetic measurements, and deuterium-labeling experiments. The initial nitrogen-coordinated allylamine–Rh^+ complex causes a four-centered hydride elimination from C(1) via dissociative mechanism to generate a transient iminium–RhH complex. Delivery of the hydrogen from Rh to C(3) gives the enamine η^3-complex. The latter, having an aza-allyl structure, serves as the chain carrier in the catalytic cycle. The BINAP–Rh^+ complexes differentiate efficiently the enantiotopic C(1) hydrogens of the allylamines through interaction with the adjacent nitrogen atoms. The overall 1,3-hydrogen shift occurs in a suprafacial manner from an s-trans-type conformer of the flexible substrates. The origin of the chiral recognition has been interpreted in terms of the chiral environments of the BINAP-based Rh^+ complexes.

The successful design of the 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (BINAP) ligand (**1**),[1] characterized by C_2 chirality, a fully arylated structure, and molecular pliancy, has allowed innovative asymmetric catalyses with transition-metal complexes.[2] The cationic Rh complexes possessing this unique diphosphine ligand cause asymmetric isomerization of diethylgeranylamine (**2**) or -nerylamine to give citronellal (*E*)-diethylenamine (**3**) in >95% ee.[3] This highly enantioselective



(*R*)-1

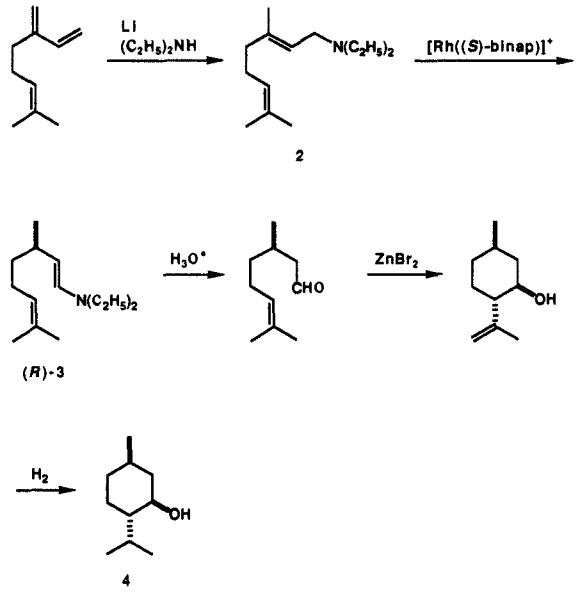


(*S*)-1

reaction now serves as a key step in the industrial production of (−)-menthol (**4**)[4] (Scheme I), providing an example of the most effective applications of transition-metal-catalyzed asymmetric reactions in homogeneous phase which have been developed during the past two decades.[5]

We describe herein the mechanism and steric course of the isomerization, elucidated by using ^1H and ^{31}P NMR techniques, kinetic study, and deuterium-labeled experiments. For transition-metal-catalyzed double bond migration, two mechanisms have been recognized.[6] One is the metal hydride addition–elimination mechanism (eq 1)[7] and the other is the π-allyl mechanism resulting

Scheme I



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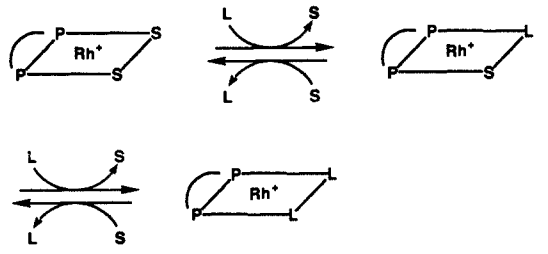
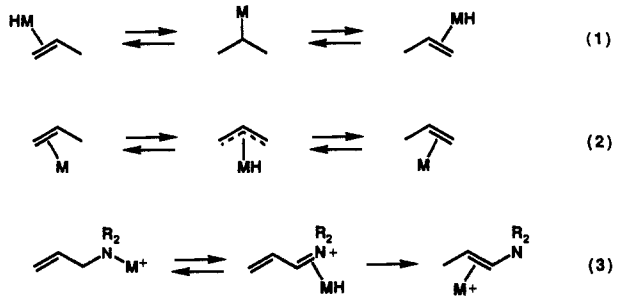
Scheme II



in an intramolecular 1,3-hydrogen shift (eq 2).[8] However, many lines of evidence indicate that the Rh-catalyzed isomerization of allylamines proceeds via a new, nitrogen-triggered mechanism (eq 3).



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(4) The catalytic process is working on up to a 7-ton scale at Takasago International Co. Ltd., Japan.

(5) To our best knowledge, the first example was given in 1966: Nozaki, H.; Moriuti, S.; Takaya, H.; Noyori, R. *Tetrahedron Lett.* **1966**, 5239. For a pertinent review, see: Kagan, H. B. *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon Press: Oxford, 1982; Vol. 8, p 463. *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press, Inc.: Orlando, FL, 1985; Vol. 5. Noyori, R.; Kitamura, M. *Modern Synthetic Methods*; Scheffold, R., Ed.; Springer Verlag: Berlin, 1989; p 115.

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Results and Discussion

Behavior of the BINAP–Rh$^+$ Complexes in the Presence of Donor Molecules. As outlined in Scheme II, the square-planar d^8 Rh$^+$ complexes of type $[Rh(binap)S_2]^+$ (S = solvent or other coordinative molecule) undergo ligand exchange reaction with other donor ligands (L). The reaction proceeds with retention of configuration via an associative mechanism probably involving transient trigonal-bipyramidal intermediates.[9] Occurrence of such ligand exchange was conveniently monitored by ^{31}P NMR spectroscopy (162 MHz, 85% H_3PO_4 as external standard).[10] The complexes of type $[Rh(binap)S_2]^+$ or $[Rh(binap)L_2]^+$ have two homotopic phosphorus atoms, exhibiting a doublet split by Rh–P coupling. The phosphorus nuclei of the mixed-ligand complex, $[Rh(binap)SL]^+$, however, are diastereotopic and hence the mutual coupling gives two sets of doublets of doublets (eight-line signals). Thus when $[Rh((S)\text{-binap})(CH_3OH)_2]ClO_4$ was dissolved in acetone-d_6 at −80 °C and the temperature was raised to 0 °C, the ^{31}P NMR spectrum showed only one doublet centered at δ 53.52 (J_{Rh-P} = 199.6 Hz) due to $[Rh((S)\text{-binap})(\text{acetone-}d_6)_2]ClO_4$. Addition of 5 equiv of triethylamine, an inactive analogue of **2**, to this solution at −40 °C produced $[Rh((S)\text{-binap})(\text{acetone-}d_6)(\text{triethylamine})]ClO_4$ exhibiting two doublets of doublets at δ 43.53 (J_{Rh-P} = 191.8 Hz, J_{P-P} = 47.0 Hz) and 53.90 (J_{Rh-P} = 217.1 Hz), and then $[Rh((S)\text{-binap})(\text{triethylamine})_2]ClO_4$ which showed a single doublet at δ 51.60 (J_{Rh-P} = 195.7 Hz). The ligand-exchange reaction with the tertiary amine took place only above −60 °C. At −80 °C, no change was observed in the ^{31}P NMR spectrum. The ^1H NMR spectrum showed line broadening and a ~0.1 ppm downfield shift of the methylene signal of triethylamine, ascribable to rapid, reversible formation of a donor–acceptor complex between $[Rh((S)\text{-binap})(\text{acetone-}d_6)_2]^+$ and triethylamine. No signals due to intermediary pentacoordinated complexes were detected at −80 °C. Addition of 10 equiv of 2-methyl-2-butene (a trisubstituted olefin related to **2**) did not cause any spectral change in the temperature range −80–25 °C.[10]

The bis-BINAP complex, $[Rh((S)\text{-binap})_2]ClO_4$ is rather inert to the ligand exchange, but a ^{31}P NMR study confirmed that ligand displacement between this complex (^{31}P doublet at δ 27.24) and triethylamine (20 equiv) could occur at 90° C, giving some free BINAP (δ −13.97) and $[Rh((S)\text{-binap})(\text{triethylamine})_2]ClO_4$.

Mechanism of the Rh-Catalyzed Isomerization of Allylamines. The simplest mechanism of the BINAP–Rh complex-promoted isomerization of diethylgeranylamine (**2**) and other related allylic amines is outlined in Scheme III, where structures of the allylic amines are simplified. The reaction starts from the simple nitrogen-coordinated Rh$^+$ complex **6** generated by ligand exchange between the bis-solvent complex **5** and the substrate **2**. The square planar complex **6** undergoes β-elimination via liberation of the solvent molecule[11] to form a transient iminium–RhH π complex **7**.[12,13] This complex is converted to the η^3 enamine complex **8** by delivery of the hydrogen atom from Rh to C(3). The aza-allyl type structure **8** acts as catalyst in the real catalytic cycle involving **9** in place of **6**. Liberation of the enamine product from the mixed

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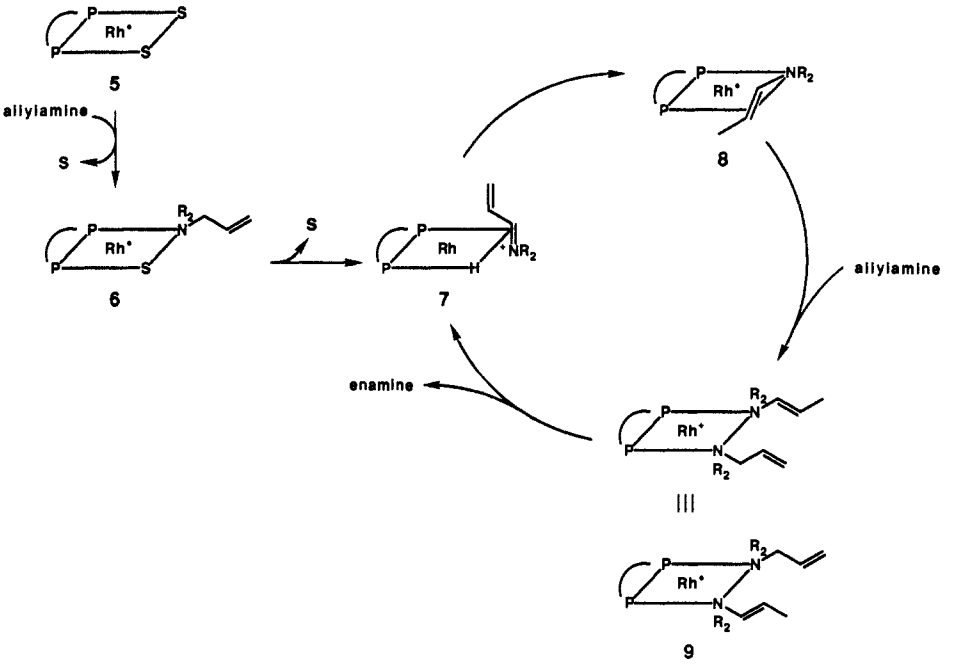
(10) Chemical shift of ^{31}P signals of BINAP–Rh$^+$ complexes is highly dependent on the nature of the trans ligands. Phosphorus atoms trans to oxygen or nitrogen ligands give signals at low field, 40–54 ppm, while signals due to the nuclei trans to olefinic ligands (norbornadiene, 1,5-cyclooctadiene, etc.) appear at rather high field, 25–26 ppm. See also ref 1b.

(11) The reaction has been conceived to occur directly from 16-electron complex **6** or **9**.[2m] We deeply appreciate a referee pointing out the significance of the dissociative mechanism. See: Thorn, D. L.; Hoffmann, R. *J. Am. Chem. Soc.* **1978**, *100*, 2079. For stable 14-electron, T-shaped tricoordinate Rh(I) complexes, see: Yoshida, T.; Okano, T.; Thorn, D. L.; Tulip, T. H.; Otsuka, S.; Ibers, J. A. *J. Organomet. Chem.* **1979**, *181*, 183.

(12) Murahashi, S.; Watanabe, T. *J. Am. Chem. Soc.* **1979**, *101*, 7429. Shvo, Y.; Laine, R. M. *J. Chem. Soc., Chem. Commun.* **1980**, 753. Laine, R. M.; Thomas, D. W.; Cary, L. W.; Buttrill, S. E. *J. Am. Chem. Soc.* **1978**, *100*, 6527. Shvo, Y.; Thomas, D. W.; Laine, R. M. *Ibid.* **1981**, *103*, 2461. Gamage, N. S.; Morris, R. H.; Rettig, S. J.; Thackray, D. C.; Thorburn, I. S.; James, B. R. *J. Chem. Soc., Chem. Commun.* **1987**, 894.

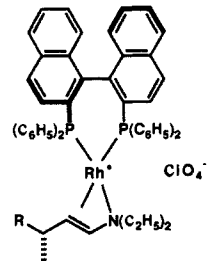
(13) For η^2-iminium–metal complexes, see: Fong, C. W.; Wilkinson, G. *J. Chem. Soc., Dalton Trans.* **1975**, 1100.

Scheme III

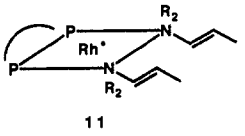


ligand complex **9**, giving a 14-electron species, is followed by immediate hydride elimination to form **7**, which goes back to **8**. Thus the catalytic cycle is completed.

To test the validity of this mechanism, reactions of geranylamine **2** and BINAP-Rh^+ complexes were examined by NMR at temperatures ranging from −80 °C to room temperature, and the presence of several species given in this scheme was proven. As has been observed with triethylamine model, the substrate **2** has only a weak interaction with [Rh((*S*)-binap)(acetone-d_6)$_2$]$^+$ at −80 °C; the ^{1}H NMR spectrum of the equimolar mixture of **2** and [Rh((*S*)-binap)(acetone-d_6)$_2$]ClO_4 in acetone-d_6 (each 0.01 M) displayed merely line broadening and slight downfield shift of the NCH_2CH_3 signal. The ^{31}P NMR spectrum showed a single doublet at δ 53.25 and no signal change was observed, suggesting maintenance of the original tetracoordinate Rh structure. However, when the mixture was warmed up to −60 °C, the intensity of the doublet decreased with concomitant appearance of a pair of four-line signal, centered at δ 30.42 (J_{Rh-P} = 193.7 Hz, J_{P-P} = 58.7 Hz) and 49.87 (J_{Rh-P} = 193.7 Hz). The signal pattern indicates the presence of two diastereotopic phosphorus nuclei and we assigned this complex to the η^3-enamine complex **8** possessing an aza-allyl structure. These new signals developed substantially at −40 °C, but still a considerable amount of the starting bis-acetone–Rh complex remained unchanged. Above 0 °C, this same reaction proceeded smoothly, and toward the end of the reaction a new doublet emerged at δ 50.99 (J_{Rh-P} = 199.5 Hz), assignable to the nitrogen-coordinated bis-enamine–Rh–BINAP complex of type **11**. The η^1 ligand in **11** dissolved in $CDCl_3$ was not affected by addition of acetone or THF. These mono- and bis-enamine complexes, **8** and **11**, respectively, were also formed by addition of (*R*)-enamine **3** to [Rh((*S*)-binap)(acetone-d_6)$_2$]ClO_4 in acetone-d_6 at −40 °C.[14]



8, R = $(CH_3)_2C{=}CHCH_2CH_2$
10, R = CH_3



The enamine complex **8** was isolated as deep-red powder by evaporation of solvent followed by washing with cold pentane. This compound (>95% pure), giving consistent NMR spectra in CD_2Cl_2 (see Experimental Section), was extremely air-sensitive and thermally unstable, and decomposed easily above −30 °C in the solid state. The instability and difficulty in purification were somewhat mitigated by using a simple model substrate. Thus reaction of [Rh((*S*)-binap)(acetone)$_2$]ClO_4 and diethyl(3-methyl-2-butenyl)amine in acetone at −80 °C for 7 days afforded **10**, which showed eight-line ^{31}P NMR signals centered at δ 29.4 and 49.8 in CD_2Cl_2. The ^{1}H NMR spectrum in CD_2Cl_2 was fully consistent: δ 0.03 (m, $CH(CH_3)_2$), 0.21 (d, J = 6.4 Hz, $CH(CH_3)_2$), 0.45 (t, J = 7.0 Hz, NCH_2CH_3), 0.67 (d, J = 6.4 Hz, $CH(CH_3)_2$), 0.73 (t, J = 6.7 Hz, NCH_2CH_3), 1.50–1.52 and 1.90–2.05 (two multiplets coupled with protons at δ 0.45, NCH_2CH_3), 3.10–3.23 and 3.23–3.35 (two multiplets coupled with protons at δ 0.73, NCH_2CH_3), 4.92 (broad t-like, $J_{C(1)H-C(2)H}$ = 14.0 Hz, $J_{C(2)H-C(3)H}$ = 7.3 Hz, C(2)H), and 5.06 (broad d, C(1)H). The enantiotopic isopropyl methyls and *N*-ethyls of the enamine become diastereotopic in the Rh complex **10**. In addition, on going from the free enamine to the Rh-bound enamine, line broadening of the olefinic proton signals is seen owing to the coupling with Rh,[15] and the C(1) proton causes upfield shift (Δ 0.81 ppm), while C(2) proton exhibits downfield shift (Δ 0.83 ppm). Integration of the signals established the 1:1 stoichiometry of BINAP and the enamine and no incorporation of acetone molecules. No substantial solvent effect (acetone-d_6 vs CD_2Cl_2) was observed on the NMR spectra.

Similar changes in the ^{31}P NMR signal patterns of the BINAP–Rh complexes were observed with a higher (8:1) substrate/complex ratio. Other short-lived complexes could not be detected by the present NMR techniques. Although spectroscopic evidence for the formation of the key mixed-ligand complex **6**, has not been obtained, judging from the model exchange reaction using **5** and triethylamine, it must form during the isomerization reaction.

The induction process, **5** to **8**, has thus been substantiated by *stoichiometric* reaction of the Rh complex **5** and substrate **2**. In the actual *catalytic* reaction, the aza-allyl Rh complex **8** is the only detectable intermediate and is acting as the chain-carrying species. Isolated **8** indeed catalyzed the isomerization of **2**. In this overall scheme, conversion of **8** to **9** by the interaction with the substrate would be the rate-determining step. Reaction of **8** and enamine product **3**, giving **11**, terminates or retards the catalytic reaction.

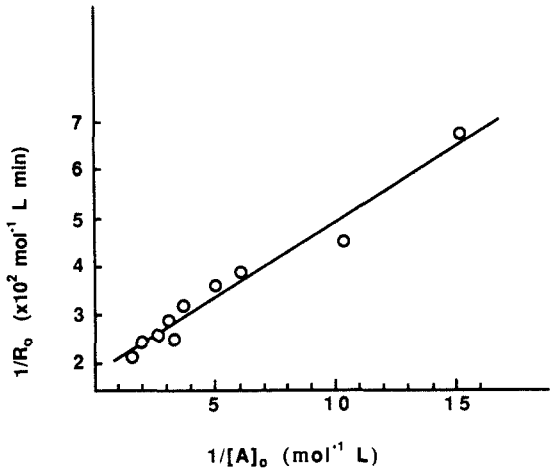


Figure 1. Plots of the reciprocal of the initial rate of the isomerization versus the reciprocal of the initial substrate concentration for the isomerization of diethylgeranylamine (**2**) with $[Rh((S)\text{-binap})(CH_3OH)_2]ClO_4$ in acetone-d_6 at 15 °C.

The bis-BINAP complex, $[Rh(binap)_2]ClO_4$, also serves as excellent catalyst precursor for the enantioselective isomerization. Although a rather high temperature (80–100 °C) is required to gain a reasonable reaction rate,[3c] a distinct practical advantage is secured by its high stability and crystallinity. Since triethylamine is capable of displacing the BINAP ligand at 90 °C, even in this case, the dissociated mono-BINAP–Rh complexes are considered to effect the isomerization. Indeed, addition of free BINAP ligand to the reaction system caused a marked retardation of the isomerization. Further, when the reaction of **2** with 10 mol % of the bis-BINAP complex in acetone at 90 °C was monitored by ^{31}P NMR, a very small singlet (<1%) due to free BINAP appeared at δ −13.96 together with an intense doublet at δ 27.25 of unchanged bis-BINAP–Rh complex. These results, coupled with the information from the ^{31}P NMR monitoring of the reactions of Scheme II and III, suggest that the aza-allyl complex **8** is much more reactive than $[Rh(binap)_2]^+$, $[Rh(binap)(diene)]^+$, or even $[Rh(binap)S_2]^+$.

It should be noted that, among various Rh catalysts so far examined, currently the BINAP-coordinated complexes exhibit the highest reactivity and selectivity.[3] The fully arylated BINAP ligand, unlike other tertiary diphosphines,[3b] confers Lewis acidity on the metal center, thereby facilitating the coordination of the amine substrates and also the hydride movement from the coordinated substrate to Rh. It is known that certain transition metals or their complexes cause hydride abstraction from tertiary amines.[12] This process is reversible and endothermic in nature. In the present case, however, the higher stability of the enamine relative to the allylamine[16] drives the reaction to forward direction, making the catalytic process possible.

Kinetics of the Catalyzed 1,3-Hydrogen Shift. Kinetic measurements using $[Rh((S)\text{-binap})(CH_3OH)_2]ClO_4$ and **2** at 15 °C with catalyst and substrate concentrations ranging 3–6 mM and 50–800 mM, respectively, gave results consistent with the arguments above. The rates of isomerization of **2** were easily determined by monitoring ^1H NMR signals of the substrate and product because the reaction proceeds very cleanly and affords **3** as the sole detectable product. The kinetic data displayed the following features: (a) Time-conversion curves for several runs showed that the initial phase of the reaction obeys the first-order rate law, but as the initial substrate concentration ($[A]_0$) is increased, the rate starts to deviate from the first-order plots at a relatively early stage of the reaction, implying a product inhibition. (b) The dependence of the initial rate R_0 on the initial catalyst concentration $[C]_0$ was first-order, ranging from 100 to 1200 mM. (c) A plot of log R_0 versus log $[A]_0$ indicates that the initial rates show a first-order dependence on $[A]_0$, but approach zeroth order upon increase of $[A]_0$. These findings indicate that the catalytic cycle proceeds by a mechanism similar to that of Michaelis–Menten type reactions and can be represented, to a first approximation, as described in eq 4, where C is catalyst, A is substrate, P is product, and CA is the catalyst–substrate complex, respectively. Proceeding as usual for a steady-state derivation, the rate of the reaction (R) determined by the method of initial rates is given by eq 5, in which [A], [C], and [P] are concentrations of substrate, catalyst, and product, respectively. The parameters α and β are

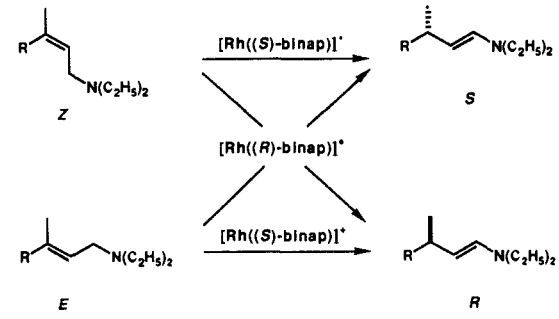
$$C + A \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} CA \xrightarrow{k_2} P + C \qquad (4)$$

$$R = \alpha[C]_0/(1 + \beta/[A]) \qquad (5)$$

as follows: $\alpha = k_2$, $\beta = (k_{-1} + k_2)/k_1$. Thus, a plot of $1/R_0$ versus $1/[A]_0$ (a Lineweaver–Burk plot) should be a straight line. As shown in Figure 1, a plot of the reciprocal of initial rate versus reciprocal of initial substrate concentration gave a straight line. Thus, our kinetic data indicate that the reaction obeys Michaelis–Menten type kinetics and are compatible with the proposed mechanism.

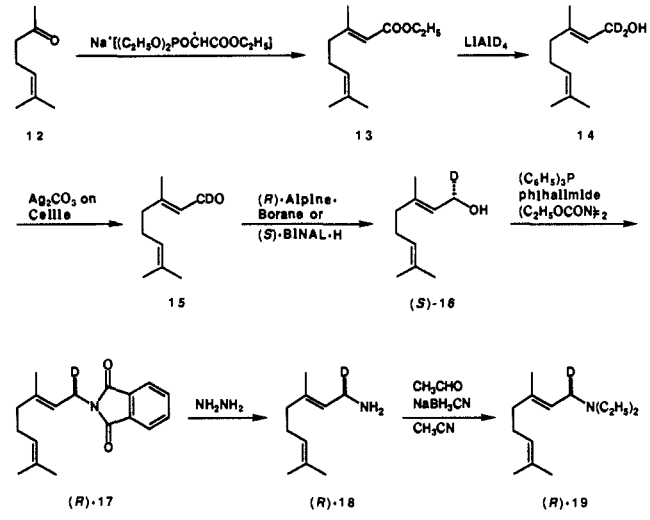
Steric Course of the Isomerization. The stereochemical outcome of the present 1,3-hydrogen migration is summarized in Scheme IV. The relationship between the substrate geometry, BINAP chirality, and the configuration of the products is distinct. The Z- and E-geometrical isomers afford similarly high enantioselectivities but deliver opposite chirality, indicating that the chiral Rh complexes recognize enantiotopicity of the C(1) hydrogens

Scheme IV



R = $(CH_3)_2C{=}CHCH_2CH_2$, simple alkyl, C_6H_5, *etc.*

Scheme V



(14) Since (R)-citronellal enamine has two diastereofaces with respect to C(1)–C(2), the η^3 mono-enamine complex thus formed may be a mixture of diastereomers, which are indistinguishable by ^{31}P NMR. When racemic citronellal enamine was added to $[Rh((S)\text{-binap})(acetone)_2]ClO_4$, the ^{31}P NMR distinguishable diastereomeric complexes were formed (^{31}P evidence).

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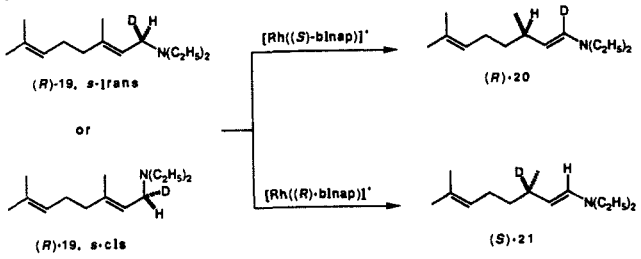
(16) Doering, W. von E.; Birladeanu, L.; Andrews, D. W.; Pagnotta, M. *J. Am. Chem. Soc.* **1985**, *107*, 428.

Scheme VI



or C(2) faces of allylamines, determining the absolute stereochemistry of the enamine products.[17] The substitution pattern at C(3) is unimportant in the chiral recognition. Stereochemical problems remain to be answered are (1) which enantiotopic hydrogen (*pro-R* or *pro-S*) migrates from C(1) to C(3), and (2) how is the chiral recognition achieved by the BINAP-Rh^+ complexes?

In order to determine the migrating hydrogen, a deuterium-labeled substrate, (*R*)-diethylgeranylamine-*1-d* [(*R*)-**19**] was prepared from prenylacetone (**12**) in seven steps by the sequence outlined in Scheme V. The recently developed chiral reducing agents, (*S*)-binaphthol-modified lithium aluminum hydride (BINAL-H)[18] or (*R*)-Alpine-borane,[19] allowed the highly enantioselective (>90%) reduction of geranial-*1-d* (**15**) to (*S*)-geraniol-*1-d* [(*S*)-**16**]. The Mitsunobu amination[20] of (*S*)-**16** with phthalimide as nucleophile occurred with clean inversion of configuration, and hydrazinolysis of crystalline (*R*)-**17** afforded (*R*)-geranylamine-*1-d* [(*R*)-**18**] in 93% ee (98.6% deuterium content). The enantiomeric excess was determined by 400-MHz ^1H NMR analysis of the (*R*)-MTPA amide[21] by using a triple resonance technique. Synthesis of the desired tertiary amine substrate, (*R*)-**19**, was completed by reductive condensation with acetaldehyde.[22]

When (*R*)-**19** was treated with 2.5–5 mol % of the chiral catalyst precursor, $[Rh((S)\text{-binap})(CH_3OH)_2]ClO_4$, in THF at 40 °C for 24 h, a clean intramolecular migration of C(1) protium took place to give (*R,E*)-enamine, (*R*)-**20**. Exposure of (*R*)-**19** to the corresponding (*R*)-BINAP-Rh^+ catalyst caused a 1,3-deuterium shift, affording (*S,E*)-enamine, (*S*)-**21**. The enantiomeric purity, determined by 400-MHz ^1H and 61-MHz ^2H NMR analyses, was greater than 97%. No isotope effect on the selectivity was observed. Scheme VI illustrates the formal stereorelationship of the geranylamine substrate **19** (drawn by hypothetical *canonical* conformations) and the enamine **20** or **21** possessing *E* configuration. If one assumes an s-trans-type conformation for the geranylamine (with respect to the C(2)–C(3) double bond and the diethylamino function), the 1,3-hydrogen shift is seen to be occurring in a suprafacial manner.[23] Alternatively, the stereochemical outcome may be envisaged as antarafacial shift from the s-cis conformer which involves bond rotation around C(2)–C(3) at some stage of the multistep conversion.

Mechanism and Origin of the Chiral Recognition. Now with the stereochemical outcome in hand, we would hope to analyze how the two enantiotopic hydrogens at C(1) are discriminated by the action of the BINAP-based Rh catalysts. Any postulated mechanisms should be reasonable from the viewpoints of both organic and coordination chemistry.

In Scheme III, a nitrogen-triggered pathway has been described for the 1,3-hydrogen migration. The stereo-determining step, we postulate, is the hydride abstraction in the tricoordinate species, [Rh(binap)(allylamine)]$^+$, formed from **6** or **9**. Scheme VII illustrates the steric course of the (*S*)-BINAP–Rh-promoted isomerization of geranylamine **22** to give *R,E* enamine **27**. Overall, the enantioselection is a result of kinetic differentiation of the enantiomeric conformers of the allylic amines. Among various rotamers possible for the free geranylamine substrate **22**, the most stable are **22A** and **22B**.[24] In these enantiomeric conformers (H/D difference neglected), being populated in 1:1 ratio, one of the C(1) hydrogens, *pro-R* or *pro-S* [H_R(deuterium) and H_S(protium), respectively], is in the molecular plane, while the other hydrogen and the bulky diethylamino moiety are out of the plane. It would not be unreasonable to assume that, even in the Rh complexes of type **23**, the allylamine has similar conformations, because metal coordination to the nitrogen atom increases the bulkiness of the amino group and also its electronegativity (which enhances the π/σ^* orbital interaction). With the introduction of the (*S*)-BINAP ligand, **23A** and **23B** become diastereomeric. Both **23A** and **23B** can be formed but, for the reason described below, an eminent kinetic preference is provided on the diastereomer **23A**. Here only the noneclipsed out-of-plane hydrogen is accessible to the metal hydride elimination, which results in the excellent enantioselection displayed. Thus dissociation of S from **23A** generates reactive 14-electron species **24**, which undergoes a four-centered elimination of H_S(protium) to give the iminium complex **25**. This process requires up to 60°-rotation about the C(1)–N axis (see the Newman projection formula of **24**). Then hydrogen delivery occurs from Rh to the *si* face of C(3) within the coordination sphere, forming the η^3-enamine complex **26** which ultimately gives free **27**. H_R (deuterium) remains untouched during the reaction. Thus, as a whole, the 1,3-hydrogen migration in this flexible molecule is viewed to occur in a suprafacial fashion by way of the s-trans-type, chiral conformer **22A**. The (*S*)-BINAP–Rh catalyst carries the *pro-S* hydrogen from C(1) leading to the 3*R* product, and the (*R*)-BINAP complex promotes the shift of the *pro-R* hydrogen forming the 3*S* enantiomer.

Why does (*S*)-BINAP offer eminent kinetic selectivity to **23A** rather than **23B**? The intermediate **23A** and the corresponding tricoordinate complex **24** are not isolable, but inspection of molecular models for the hypothetical tetracoordinate Rh species **28** (a box representing a coordination site) provides an insight into factors controlling this stereochemistry. Figure 2 illustrates schematically the square-planar coordination sphere having a seven-membered chelate ring; the naphthalene rings are omitted for the sake of clarity. The structures, created on the basis of single-crystal X-ray analysis of $[Rh(binap)(norbornadiene)]ClO_4$,[25] indicate that the whole environment approximates C_2 chirality and that the Rh chelate ring has a highly skewed, δ conformation. The phenyl groups bonded to the phosphorus atoms have a chiral array and, particularly, the equatorially oriented groups play a major role in determining the stabilities of such complexes and of transition states through which reactions take place. The hydrogen abstraction occurs from a T-shaped tricoordinate complex **29** formed from **23**. When **29** possesses a simple achiral phosphine ligand, the P–Rh–P plane is coplanar with the N–C(1)–C(2) linkage and bisects the Et–N–Et and D–C(1)–H angles,[26] where H and D are enantiotopic. Some other conformers may be possible, but the *pro-S* and *pro-R* hydrogens at C(1) are not distinguishable. However, the ligation of (*S*)-BINAP in **29** causes some clockwise rotation about the Rh–N bond to minimize the nonbonded repulsion between the equatorially disposed phenyl ring and the *N*-ethyl groups. Such distortion induces incidental rotation about the N–C(1) axis (see arrows in **29**), reducing the tortional strain. As a consequence, the C(1) enantiotopic hydrogens are clearly differentiated to facilitate H_S (protium) abstraction from conformer **23A** via transition state **30**. The ste-

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(20) Mitsunobu, O.; Wada, M.; Sano, T. *J. Am. Chem. Soc.* **1972**, *94*, 679.
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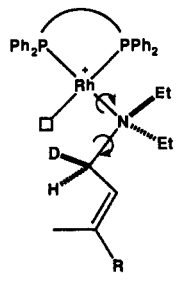
(22) For related procedure, see: Borch, R. F.; Hassid, A. I. *J. Org. Chem.* **1972**, *37*, 1673.
(23) Cowherd, F. G.; von Rosemberg, J. L. *J. Am. Chem. Soc.* **1969**, *91*, 2157.
(24) Kao, J.; Seeman, J. I. *J. Computational Chem.* **1984**, *5*, 200.
(25) Toriumi, K.; Ito, T.; Takaya, H.; Souchi, T.; Noyori, R. *Acta Crystallogr.* **1982**, *B 38*, 807.
(26) Preliminary ab initio MO calculations on $[Rh(PH_3)_2(CH_3NH_2)]^+$ support this view. M. Yamakawa (Kinjo Gakuin University, Nagoya, Japan), unpublished results.



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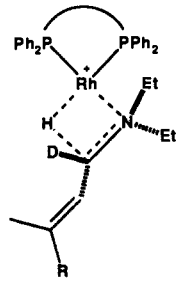

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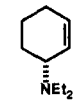
R = $(CH_3)_2C{=}CHCH_2CH_2$

reochemical correlation given in Scheme IV can be consistently explained in a like manner.

Additional Information Relevant to the Mechanism. The nitrogen-triggered mechanism is consistent not only with behavior of the acyclic, flexible substrates but also accounts for equal reactivities of certain sterically constrained systems. For instance, 3-(diethylamino)cyclohexene (**31**) undergoes facile isomerization through transition state **32** by the action of the BINAP–Rh catalyst.[3b] The atomic arrangement having a fixed s-trans structure is ideal for this mechanism. On the other hand, *trans*-3-(diethylamino)-4-isopropyl-1-methylcyclohexene (**33**) is inert to the catalytic conditions, because substantial I strain develops in the transition state.[3b,27] On the basis of the reactivity of **31**, any other mechanism starting from N,π-chelate complexes with s-trans[28] or s-cis conformation[29,30] of type **34** and **35** (for antarafacial 1,3-shift), respectively, should be dismissed.[31] The pathway involving the simple π complexes of type **36** is also highly unlikely, because (1) no NMR evidence was obtained for interaction of $[Rh(binap)S_2]^+$ and the olefinic bond in **2** or simple olefins, (2) the isomerization of allylic amines was markedly retarded by addition of triethylamine, but the rate was not affected by the presence of a large excess of 2-methyl-2-butene, and (3) $[Rh(binap)S_2]^+$ forms stable complexes with triethylamine but not with allylamine substrates. The allylamine complexes, once formed, undergo immediate isomerization.

Conclusion

The BINAP–Rh^+ complexes differentiate efficiently between the enantiotopic C(1) hydrogens of diethylgeranyl- and diethylnerylamines through interaction with the adjacent nitrogen atoms. The overall 1,3-hydrogen shift occurs in a suprafacial manner from the s-trans-type chiral conformers, leading to (*R*,*E*)- or (*S*,*E*)-citronellal diethylenamine. Salient features of the chiral metal complexes include (1) the degeneracy caused by C_2 chirality of the BINAP ligand which minimizes the numbers of the reactive intermediates and transition states, (2) full aromatic substitution in BINAP exerting electronic influence to provide high Lewis acidity to the central metal, (3) the flexible atropisomeric skeletal backbone of BINAP which produces a conformationally unambiguous, highly skewed chiral seven-membered ring, and (4) phenyl rings attached to the phosphorus atoms which modulate stabilities



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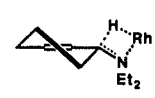

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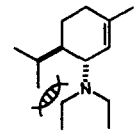

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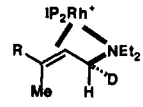

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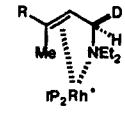

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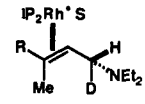


36

of the intermediary diastereomer complexes and transition states. These factors cooperate in the realization of highly efficient asymmetric catalysis in a homogeneous phase.

Experimental Section

Apparatus. All melting points were recorded on a Yanagimoto micro melting point apparatus and are uncorrected. Infrared spectra (IR) were determined with a JASCO IRA-1 spectrophotometer. ^1H NMR spectra were determined with a JEOL FX-90QE, JNM-FX100, or JNM-GX400 spectrometer. The chemical shifts were recorded with use of tetramethylsilane as internal standard unless otherwise mentioned. Singlet, doublet, triplet, quartet, and multiplet are abbreviated to s, d, t, q, and m, respectively. Long-range coupling constants are not described. The chemical shifts of the proton resonances of sealed samples for mechanistic studies were referenced to the residual proton resonances of THF-d_8 or acetone-d_6. ^{31}P NMR spectra were measured on a JNM-GX400 spectrometer (162 MHz), and chemical shifts are given relative to external 85% phosphoric acid. Low-resolution mass spectra (LRMS) were recorded on a Hitachi RMU-6 or JEOL JMS-D300 spectrometer at an ionization voltage of 20–70 eV and only molecular ions are described. High-resolution mass spectra (HRMS) were taken on a JEOL JMS-D300. Optical rotations were measured on a JASCO DIP-181 digital polarimeter. Short-path distillations were conducted with a Büchi Kugelrohr apparatus. The oven temperature is recorded as boiling point.

Chemicals. Tetrahydrofuran (THF) was first distilled from sodium benzophenone ketyl under argon. For catalytic reactions it was redistilled from Na/K alloy under argon. Pyridine, benzene, and pentane were distilled from finely powdered calcium hydride. Acetonitrile was distilled from P_2O_5. Methanol was distilled from magnesium chips. Geraniol and nerol were supplied by Takasago International Co. Ltd. and distilled from sodium borohydride before use. Tetrahydrofuran-d_8 (CEA, 99%) and acetone-d_6 (CEA, >99.8%) were dried over freshly baked molecular sieves (3 Å), vacuum distilled, and stored over molecular sieves (3 Å) in a calibrated Schlenk tube equipped with a J. Young Teflon screwcock. For NMR measurements these solvents were vacuum-transferred into the NMR tubes prior to sealing. Active manganese oxide, silver carbonate on Celite,[32] and (*R*)-(+)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride (MTPACl) were prepared according to published procedures.[21] Other commercial solvents and chemicals were used without further purification. All air-sensitive compounds were handled in an argon atmosphere by standard Schlenk techniques.

Chromatography. Thin-layer chromatography (TLC) were carried out with Kieselgel 60 F_{254} (E. Merck, Art. 5715, 0.25 mm thick) and spots were recorded by R_f values. For column chromatography Kieselgel 60 (E. Merck, Art. 7734, 70–230 mesh) was used. High-performance liquid chromatography (HPLC) was done on a Waters 6000A instrument equipped with JASCO UVIDEC-100 (254 nm). For analytical purpose a YMC Si100 (3 μm, 4.6 × 300 mm) column was used, while for isolation and purification of the samples a YMC Si70 (15 μm, 22 × 300 mm) column was used. Peak positions were described by retention volumes (V_R). Gas chromatography (GLC) was performed on a Hitachi 163 instrument equipped with flame-ionization detector using nitrogen as carrier gas. A stainless steel column (3 × 3000 mm) packed with 5% Carbowax 20M on Chromosorb WAW was used unless otherwise stated.

(27) Johnson, F.; Whitehead, A. *Tetrahedron Lett.* **1964**, 3825. Malhotra, S. K.; Johnson, F. *Ibid.* **1965**, 4027. Johnson, F. *Chem. Rev.* **1968**, *68*, 375.

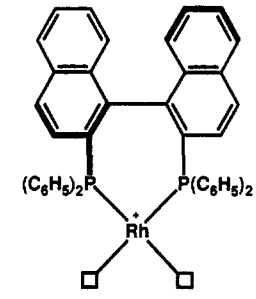
(28) Otsuka, S. *Fundamental Research in Homogeneous Catalysis*, Graziani, M., Giongo, M., Eds.; Plenum Press: New York, 1984; Vol. 4, p 145. Otsuka, S.; Tani, K. *Asymmetric Synthesis*; Morrison, J. D., Ed., Academic Press: New York, 1985; Vol. V, Chapter 6.

(29) Such type of intermediate has been postulated for isomerization of allylphenylamine catalyzed by $[RhCl(C_2H_4)_2]_2$, a neutral Rh(I) complex without chelating diphosphine ligand: Aresta, M.; Quaranta, E.; Ibers, J. A. *Organometallics* **1988**, *7*, 577. In the present reactions, however, such kind of complexes have neither been isolated nor detected by NMR spectroscopy.

(30) Allylamines do not form chelate complexes with Pt(II) but tend to act as bridging ligands to form dimeric and polymeric complexes, see: Denning, R. G.; Venanzi, L. M. *J. Chem. Soc.* **1963**, 3241.

(31) This does not necessarily mean that s-cis-type allylic amines are unable to undergo suprafacial 1,3-hydrogen shift. The earlier description should be revised as given here: Tani, K. *Pure Appl. Chem.* **1985**, *57*, 1845.

(32) Fetizon, M.; Golfier, M. *C. R. Acad. Sci. C* **1968**, *267*, 900.



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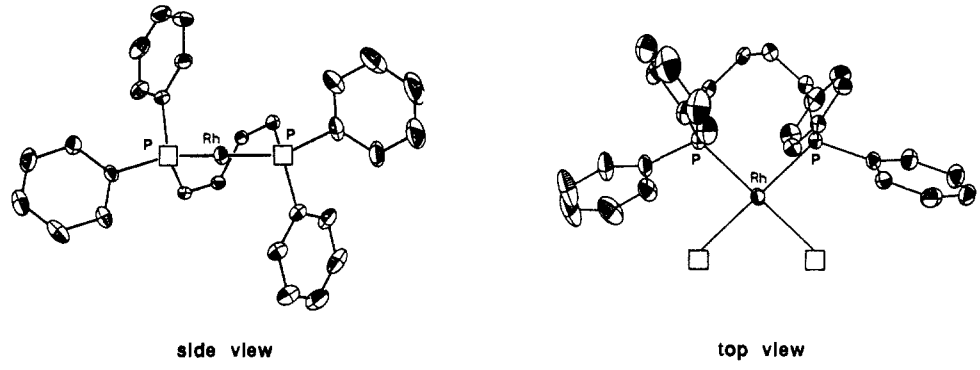


side view top view

Figure 2. Side and top views of the square planar structure of (*S*)-BINAP–Rh^+ complex **28**.

^1H and ^{31}P NMR Studies on the (*S*)-BINAP–Rh^+-Catalyzed Asymmetric Isomerization of Diethylgeranylamine (2) in Acetone-d_6. In a 10-mm diameter NMR tube was placed [Rh((*S*)-binap)$(CH_3OH)_2$]ClO_4 (28.0 mg, 0.0314 mmol) under argon and to this was added dry and degassed acetone-d_6 (2 mL) by trap-to-trap distillation. The mixture was placed in an ice–water mixture and allowed to stand for 30 min with occasional shaking. The resulting orange-red solution was cooled to −90 °C, and into this was transferred carefully a cooled, degassed solution of diethylgeranylamine (6.6 mg, 0.0314 mmol) in 1 mL of acetone-d_6 via Teflon tubing by use of a slight positive pressure of argon. The mixture was frozen under vacuum, and the tube was sealed. This sample was stored in a cold bath, keeping the temperature below −90 °C. The sample thus prepared was quickly loaded in an NMR probe which had been kept at −80 °C. ^1H and ^{31}P NMR were recorded alternatively at specified temperature and time intervals.

Synthesis of Geranial. The following series of syntheses were done to obtain authentic samples of (±)-**16**–(±)-**19**. A mixture of geraniol (7.70 g, 50 mmol), active manganese oxide (60 g), and pentane (300 mL) was stirred at 25 °C for 4 h under argon. Solid material was removed by filtration and the filtrate was concentrated to give geranial (5.41 g, 77%) as a pale yellow liquid. GLC analysis (180 °C) indicated that this product was a mixture of 90% geranial (t_R 4.69 min) and 10% neral (4.09 min). ^1H NMR spectrum and GLC retention times were identical with those of authentic samples.

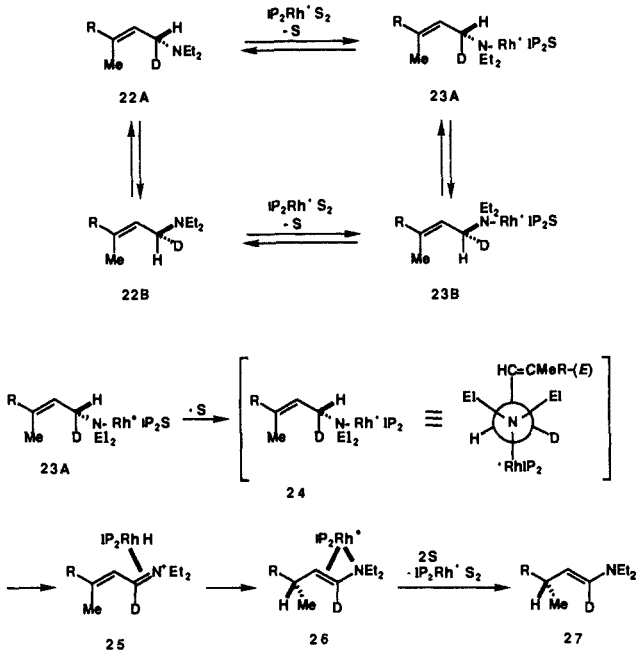
Synthesis of (±)-Geraniol-*1-d*. To a stirred suspension of $LiAlD_4$ (935 mg, 22.2 mmol) in THF (40 mL) was added dropwise a solution of geranial (6.77 g, 44.5 mmol) in the same solvent (15 mL) at 0 °C under argon. The mixture was stirred at 0 °C for 30 min and added ether (60 mL) followed by 1 N NaOH (3 mL). Insoluble material was removed by filtration, and the filtrate was concentrated to give (±)-geraniol-*1-d* (6.06 g, 88%) as a colorless oil: IR (neat) 3320 cm^{-1} (OH); ^1H NMR ($CDCl_3$) δ 1.26 (broad s, OH), 1.61 (s, CH_3), 1.68 (s, $2CH_3$), 2.05 (broad s, $2CH_2$), 4.13 (d, J = 7.0 Hz, CHD), 5.10 (m, =CH), 5.41 (d, J = 7.0 Hz, =CH); LRMS m/z 155 (M^+). The deuterium content was calculated to be 98.3% by ^1H NMR. This sample was used for further reaction without purification.

Synthesis of *N*-(Geranyl-*1-d*)phthalimide [(±)-17]. A solution of (±)-geraniol-*1-d* (6.0 g, 38.7 mmol) in THF (50 mL) was added dropwise to a mixture of triphenylphosphine (15.2 g, 58.1 mmol), diethyl azodicarboxylate (10.1 g, 58.1 mmol), and phthalimide (8.54 g, 58.1 mmol) in THF (250 mL) at 0 °C. The mixture was stirred at the same temperature for 30 min, at 25 °C for 12 h, and then concentrated. The residue was dissolved in CH_2Cl_2 (200 mL) and the solution was washed with two 50-mL portions of 1 N NaOH, then twice with each 50 mL of saturated brine, and dried over Na_2SO_4. Evaporation of the solvent afforded a yellow solid which was purified by column chromatography on silica gel (10% ethyl acetate in hexane) to give *N*-(geranyl-*1-d*)-phthalimide [(±)-**17**] (9.78 g, 89%, E/Z = 90:10). Recrystallization from hexane at 0 °C afforded a sample with 98% purity contaminated with 2% of *N*-(neryl-*1-d*)phthalimide. (±)-**17**: V_R = 12.8 mL (10% ether in hexane); mp 51–52 °C; IR ($CHCl_3$) 1775, 1724, 1715 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.44 (s, CH_3), 1.51 (s, CH_3), 1.70 (s, CH_3), 1.89 (broad s, $2CH_2$), 4.13 (d, J = 7.5 Hz, CHD), 4.92 (m, =CH), 5.15 (d, J = 7.5 Hz, =CH), 7.65 (m, aromatic protons); LRMS m/z 284 (M^+); HRMS calcd for $C_{18}H_{20}NO_2D$ 284.1634, found 284.1634. *N*-(neryl-*1-d*)phthalimide: V_R = 11.9 mL (10% ether in hexane); mp 56–57 °C (from hexane at −20 °C); IR ($CHCl_3$) 1775, 1715 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.64 (s, CH_3), 1.70 (s, $2CH_3$), 2.22 (m, $2CH_2$), 4.25 (d, J = 6.4 Hz, CHD), 5.17 (m, =CH), 5.28 (d, J = 6.4 Hz, =CH); LRMS m/z 284 (M^+); HRMS calcd for $C_{18}H_{20}NO_2D$ 284.1635, found 284.1635.

Synthesis of (±)-Geranylamine-*1-d* [(±)-18]. A mixture of *N*-((±)-geranyl-*1-d*)phthalimide (10.0 g, 35.2 mmol) and hydrazine hydrate (2.56 mL, 52.8 mmol) in methanol (300 mL) was heated at reflux for 1 h and then concentrated in vacuo. The residue was dissolved in 1 N HCl (120 mL) and insoluble compounds were removed by filtration. The filtrate was made basic with 5 N NaOH and extracted with three 150-mL portions of ether. The combined ether layer was washed twice with 50 mL of saturated brine and dried over K_2CO_3. Evaporation of the solvent afforded (±)-geranylamine-*1-d* [(±)-**18**] (4.25 g, 79%) as pale yellow liquid. An analytical sample was obtained by short-path distillation, bp 90–140 °C (4 mm): IR ($CHCl_3$) 3360, 3200 cm^{-1} (NH_2); ^1H NMR ($CDCl_3$) δ 1.20 (s, NH_2), 1.62 (s, $2CH_3$), 1.68 (s, CH_3), 2.02 (broad s, $2CH_2$), 3.25 (d, J = 6.8 Hz, CHD), 5.10 (m, =CH), 5.25 (d, J = 6.8 Hz, =CH); LRMS m/z 154 (M^+); HRMS calcd for $C_{10}H_{18}ND$ 154.1580, found 154.1573.

Synthesis of (±)-Diethylgeranylamine-*1-d* [(±)-19]. To a mixture of (±)-geranylamine-*1-d* [(±)-**18**] (9.89 g, 64.2 mmol) and acetaldehyde (17.9 mL, 321 mmol) in acetonitrile (200 mL) was added sodium cyanoborohydride (6.45 g, 103 mmol) at 0 °C. The mixture was stirred at 25 °C for 15 min and then neutralized with acetic acid. This mixture was further stirred for 2 h in which period the pH of the mixture was occasionally examined and neutralized by addition of acetic acid. The solvent was removed under reduced pressure and the residue was taken up into 2 N NaOH (150 mL). The solution was extracted with three 150-mL portions of ether. The combined ether layer was extracted three times with 50 mL of 1 N HCl and the aqueous layer was made basic with 5 N NaOH. The liberated (±)-diethylgeranylamine-*1-d* [(±)-**19**] was extracted with three 150-mL portions of ether and the combined ether layer was washed with saturated brine. After being dried over K_2CO_3, the solution was concentrated to give a yellow oil. Distillation in vacuo gave 8.79 g (66%) of (±)-**19** as a colorless liquid, bp 86–88 °C (2 mm). GLC (130 °C) analysis showed that this sample was contaminated with 2% of the Z isomer. (±)-**19**: IR ($CHCl_3$) absorptions due to NH_2 group were not observed; ^1H NMR ($CDCl_3$) δ 1.03 (t, J = 7.03 Hz, $2CH_3$), 1.59 (s, CH_3), 1.63 (s, CH_3), 1.67 (s, CH_3), 2.04 (broad s, $2CH_2$), 2.50

Scheme VII



(q, J = 7.03 Hz, $2CH_2$), 3.03 (d, J = 6.4 Hz, CHD), 5.09 (m, =CH), 5.25 (d, J = 6.4 Hz, =CH); LRMS m/z 210 (M^+); HRMS calcd for $C_{14}H_{26}ND$ 210.2205, found 210.2204.

Synthesis of Ethyl Geranate (13). In a 500-mL three-necked flask equipped with a dropping funnel, magnetic stirring bar, and thermometer was placed sodium hydride (60% mineral oil dispersion, 1.56 g, 39.0 mmol) and the contents were washed three times with hexane. To this was added dry THF (30 mL) and the flask was surrounded by an ice–salt mixture. Then a solution of triethyl phosphonoacetate (8.73 g, 39.0 mmol) in THF (50 mL) was added with stirring at 0 °C, and the mixture was further stirred at this temperature for 30 min. To this was added dropwise a solution of 6-methyl-5-hepten-2-one (3.70 g, 30.0 mmol) in THF (20 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 1 h, then at 25 °C for 12 h, and then poured into a mixture of ether (200 mL) and saturated aqueous ammonium chloride (50 mL). The ether layer was separated, and the aqueous layer was extracted with ether (100 mL). The combined organic layer was dried over $MgSO_4$, and evaporation of the solvent gave a yellow oil. GLC analysis (5% PEG-HT on Uniport HP, 3 × 3000 mm) indicated that (*E*)-**13** (t_R 14.0 min) and (*Z*)-**13** (t_R 10.6 min) were formed in 78:22 ratio. This crude product was purified on column chromatography with silica gel (2% ether in hexane) to give 5.29 g (90% yield) of a mixture of (*E*)-**13** and (*Z*)-**13**. Effective separation of (*E*)-**13** and (*Z*)-**13** was attained by spinning-band distillation under reduced pressure (1 mm). (*E*)-**13**: IR ($CHCl_3$) 1715 (C=O), 1643 cm^{-1} (C=C); ^1H NMR ($CDCl_3$) δ 1.20 (t, J = 7.0 Hz, CH_2CH_3), 1.53 (s, CH_3), 1.61 (s, CH_3), 2.07 (s, CH_3), 2.09 (s, $2CH_2$), 4.07 (q, CH_2CH_3), 5.00 (m, =CH), 5.59 (s, =CH); LRMS m/z 196 (M^+); HRMS calcd for $C_{12}H_{20}O_2$ 196.1463, found 196.1461. (*Z*)-**13**: IR ($CHCl_3$) 1715 (C=O), 1642 cm^{-1} (C=C); ^1H NMR ($CDCl_3$) δ 1.27 (t, J = 7.0 Hz, CH_2CH_3), 1.62 (s, CH_3), 1.68 (s, CH_3), 1.88 (d-like, J = 1.3 Hz, CH_3), 2.18 (m, CH_2), 2.64 (t-like, J = 7.5 Hz, CH_2), 4.14 (q, CH_2CH_3), 5.15 (m, =CH), 5.65 (m, =CH); LRMS m/z 196 (M^+); HRMS calcd for $C_{12}H_{20}O_2$ 196.1463, found 196.1470.

Synthesis of Geraniol-1,1-d_2 (14). To a stirred suspension of $LiAlD_4$ (1.0 g, 23.8 mmol) in benzene (70 mL) was added dropwise a solution of (*E*)-**13** (contaminated with 2% of (*Z*)-**13**, 4.67 g, 23.8 mmol) in benzene (30 mL) at 0 °C. The mixture was stirred at 26 °C for 5 h and then diluted with ether (100 mL). To this was added carefully 1 N NaOH (5 mL), and the resulting solid material was removed by filtration. Evaporation of the solvent gave **14** (3.90 g, 100%) which was used for further reaction without purification. The analytical sample of **14** (*E*/*Z* = 98:2) was obtained by short-path distillation, bp 100–150 °C (4 mm): IR ($CHCl_3$) 3610, 3440 cm^{-1} (OH); ^1H NMR ($CDCl_3$) δ 1.18 (broad s, OH), 1.61 (s, CH_3), 1.67 (s, CH_3), 1.69 (s, CH_3), 2.05 (broad s, $2CH_2$), 5.10 (m, =CH), 5.41 (broad s, =CH); LRMS m/z 156 (M^+); HRMS calcd for $C_{10}H_{16}OD_2$ 156.1483, found 156.1477.

Synthesis of Geranial-1-d (15). A mixture of **14** (1.56 g, 10.0 mmol), silver carbonate on Celite (22.8 g, 40.0 mmol), and benzene (300 mL) was stirred and gently heated. When refluxing started, about 100 mL of benzene was removed by distillation from the reaction mixture. Heating was continued for 1 h, and then the mixture was cooled to room temperature. Solid material was removed by filtration, and the filtrate was concentrated to give **15** (1.62 g, 100%) as a pale yellow oil. This product was subjected to further reaction without purification. The structure of **15** was established by comparison of its ^1H NMR spectrum with that of authentic sample.[16] The (*E*)-**15** (t_R 14.2 min) to (*Z*)-**15** (t_R 11.5 min) ratio determined by GLC (130 °C) was 98:2.

Synthesis of (*S*)-(+)-Geraniol-1-d [(*S*)-16]. To a stirred solution of **15** (12.3 g, 80.0 mmol) in dry THF (80 mL) was dropwise added a solution of (*R*)-Alpine-borane (0.5 M in THF, 192 mL, 96 mmol) at 0 °C. The reaction mixture was stirred at 27 °C for 5 h and cooled to 0 °C. To this was added acetaldehyde (2.2 mL, 40 mmol), and stirring was continued for 15 min at room temperature. The mixture was concentrated under reduced pressure (0.04 mm), and the residue was diluted with ether (300 mL). 2-Aminoethanol (5.79 mL, 96 mmol) was added carefully at 0 °C, and the precipitated material was removed by filtration. The filtrate was washed with saturated brine and dried over $MgSO_4$. Evaporation of the solvent afforded a yellow oil, which was subjected to purification on column chromatography (10% ethyl acetate in hexane) to give **16** (10.6 g, 85%) as a colorless oil. Analytical sample was obtained by short-path distillation, bp 90–150 °C (4 mm). The structure of **16** was supported by comparison of its chromatographic properties (TLC and GLC) and ^1H NMR spectrum with those of nondeuterated authentic sample, $[\alpha]^{26}_D$ +0.44° (*c* 1.23, cyclopentane) (lit.[18] $[\alpha]^{24}_D$ +1.51° (*c* 1.06, cyclopentane). The deuterium content was calculated to be 97.7% by comparison of its ^1H NMR spectrum with that of authentic sample obtained by the (*S*)-BINAL-H reduction.[18] The absolute configuration of **16** was assigned to be *S* by ^1H NMR taken in the presence of $Eu(hfbc)_3$.

Synthesis of *N*-[(*R*)-(−)-Geranyl-1-d]phthalimide [(*R*)-17]. To a stirred mixture of triphenylphosphine (23.7 g, 90.6 mmol), phthalimide (13.3 g, 90.6 mmol), and diethyl azodicarboxylate (15.8 g, 90.6 mmol) in THF (200 mL) was added dropwise a solution of (*S*)-**16** (9.30 g, 60.4 mmol) in THF (50 mL) at 0 °C. The reaction mixture was stirred at 25 °C for 12 h and then concentrated under reduced pressure. The residue was purified on silica gel column chromatography (10% ethyl acetate in hexane) to give 10.8 g (63%, *E*/*Z* = 98:2) of crude (*R*)-**17**. Recrystallization of this product from hexane at 0 °C afforded almost pure sample (*E*/*Z* = 99.7:0.3) of (*R*)-**17**: mp 60–61 °C; $[\alpha]^{26}_D$ −0.244° (*c* 1.34, $CHCl_3$). The structure of (*R*)-**17** was confirmed by comparison of t_R and V_R values and ^1H NMR spectrum with those of nondeuterated authentic samples derived from geraniol and phthalimide. *N*-[(*R*)-Neryl-1-*d*]phthalimide was obtained by concentration of the mother liquor followed by purification on HPLC (5% ether in hexane): mp 56–57 °C (from hexane); $[\alpha]^{26}_D$ +0.874° (*c* 1.17, $CHCl_3$).

Synthesis of (*R*)-(−)-Geranylamine-1-d [(*R*)-18]. A mixture of (*R*)-**17** (10.5 g, 37.0 mmol) and hydrazine hydrate (2.78 mL, 55.6 mmol) in methanol (300 mL) was heated at reflux with stirring. The mixture was cooled to room temperature and concentrated. The residue was dissolved in 1 N HCl (130 mL) and insoluble material was removed by filtration. The filtrate was made basic with 5 N NaOH and extracted with three 150-mL portions of ether. The combined organic layer was washed twice with saturated brine (50 mL), dried over K_2CO_3, and concentrated to give (*R*)-**18** (4.45 g, 78%) as a pale yellow oil. This compound was used for further reaction without purification. An analytical sample was prepared by short-path distillation: bp 100–150 °C (3 mm); $[\alpha]^{26}_D$ −0.816° (*c* 1.13, cyclopentane). The structure of (*R*)-**18** was assigned by comparison of ^1H NMR spectrum with that of the nondeuterated geranylamine.

Synthesis of (*R*)-(+)-Diethylgeranylamine-1-d [(*R*)-19]. To a stirred mixture of the amine (*R*)-**18** (2.31 g, 15 mmol), acetaldehyde (4.2 mL, 75 mmol), and acetonitrile (100 mL) was added sodium cyanoborohydride (1.51 g, 24 mmol) at 30 °C. After stirring of the mixture for 15 min, the mixture was neutralized with acetic acid. Stirring was continued for 1 h, and the solvent was removed under vacuum. To the residue was added 2 N NaOH (70 mL), and the mixture was extracted with three 50-mL portions of ether. The combined ether layer was extracted three times with each 50 mL of 1 N HCl. The aqueous layer combined was made basic with 5 N NaOH and extracted three times with 100-mL portion of ether. The combined ether layer was washed three times with saturated brine and dried over K_2CO_3. Evaporation of the solvent left a yellow oil which was subjected to short-path distillation to give (*R*)-**19** (1.72 g, 55%): bp 140 °C (3 mm); $[\alpha]^{26}_D$ +2.06° (*c* 1.47, cyclopentane). This product contained 0.3% of the *Z* isomer. Comparison of the gas chromatographic properties (GLC) and ^1H NMR of (*R*)-**19** with those of nondeuterated diethylgeranylamine established its structure. For Rh(I)-catalyzed reactions this product was distilled in the

presence of Vitride [sodium dihydridobis(2-methoxyethoxy)aluminate] in toluene before use.

Preparation of MTPA Ester of (±)-Geraniol-*1-d* and (*S*)-(+)-Geraniol-*1-d* [(*S*)-16]. A mixture of (±)-geraniol-*1-d* (21.4 mg, 0.138 mmol), pyridine (0.15 mL), and (*R*)-(+)-MTPACl (150 μL) in CH_2Cl_2 (1 mL) was stirred at 0 °C for 30 min. Ether (30 mL) was added, and the mixture was washed two times with 5-mL portion of 1 N HCl and then with saturated brine. The organic layer was dried over $MgSO_4$ and concentrated in vacuo to give an oil which was purified by column chromatography on silica gel (5% ethyl acetate in hexane) to give (*R*)-(+)-MTPA ester of (±)-geraniol-*1-d* (34 mg, 66%): R_f 0.32 (5% ethyl acetate in hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.59 (s, CH_3), 1.66 (s, CH_3), 1.71 (s, CH_3), 2.06 (m, $2CH_2$), 3.55 (s, OCH_3), 4.78 (d, J = 7.33 Hz, 0.5 H, CHD), 4.83 (d, J = 7.02 Hz, 0.5 H, CHD), 5.06 (m, =CH), 5.38 (d, J = 6.4 Hz, =CH), 7.39 and 7.51 (m, C_6H_5). When the signal at δ 5.38 was irradiated, doublets at δ 4.78 and 4.83 collapsed to singlets at δ 4.76 and 4.81, respectively.

Similarly, (*R*)-(+)-MTPA ester of (*S*)-(+)-geraniol-*1-d* was prepared. The optical purity of (*S*)-**16** was determined to be 91.2% ee by cut-and-weigh method based on the ^{1}H NMR signals at δ 4.66 and 4.81.

Preparation of (*R*)-(+)-MTPA Amide of (±)-Geranylamine-*1-d* [(±)-18] and (*R*)-(−)-Geranylamine-*1-d* [(*R*)-18]. To a stirred mixture of (±)-geranylamine-*1-d* (25.2 mg) and pyridine (0.15 mL) in CH_2Cl_2 (1 mL) was added (*R*)-(+)-MTPACl (50 μL) at 0 °C. The mixture was stirred at 0 °C for 1 h, diluted with ether (30 mL), and then washed successively twice with 1 N HCl (5 mL) and with saturated brine. The organic layer was dried over $MgSO_4$ and concentrated to give an oily product which was purified by column chromatography on silica gel (10% ethyl acetate in hexane). The amide (33 mg) was obtained as colorless oil: R_f 0.18 (5% ethyl acetate in hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.60 (s, CH_3), 1.67 (s, $2CH_3$), 2.04 (m, CH_2), 2.06 (m, CH_3), 3.41 (s, OCH_3), 3.93 (m, CHD), 5.07 (m, =CH), 5.19 (d, J = 6.1 Hz, =CH), 6.66 (broad s, NH), 7.40 and 7.53 (m, C_6H_5). When signals at δ 5.19 and 6.66 were irradiated at the same time, the multiplet at δ 3.93 changed into two singlets at δ 3.89 and 3.92 with equal intensity. (*R*)-(+)-MTPA amide of (*R*)-(−)-geranylamine-*1-d* [(*R*)-**18**] was prepared by similar procedure. Optical purity of (*R*)-**18** was determined to be 92.6% ee by ^{1}H NMR with use of a triple resonance technique integrating the signals at δ 3.89 and 3.92.

(*S*)-BINAP-Rh$^+$-Catalyzed Asymmetric Isomerization of (*R*)-(+)-Diethylgeranylamine-*1-d* [(*R*)-19] to (*R*,*E*)-*N*,*N*-Diethyl-3,7-dimethyl-1,6-octadienylamine-*1-d* [(*R*)-20]. Because the catalytic isomerization of **2** to **3** has been shown to proceed in very high selectivity, studies on the stereochemistry of the isomerization were carried out by the direct analysis of the reaction mixture by ^{1}H and ^{2}H NMR. A 10-mm diameter NMR tube was connected to a vacuum line and filled with argon. To this was added a solution of [Rh((*S*)-(−)-binap)(cod)]ClO_4 (20.0 mg, 0.02 mmol) in THF (3.5 mL) and agitated for 1 h under 1 atm of hydrogen at room temperature. After 15–20 min, orange-red precipitates appeared. To this catalyst mixture was added a solution of (*R*)-**19** (97.1 mg, 0.464 mmol) in THF (1.0 mL), and the tube was sealed off. The reaction mixture was kept at 40 °C for 40 h, and the product was directly analyzed by ^{2}H NMR (61 MHz). An intense singlet due to vinylic C(1)-D was observed at δ 5.86, while a very weak singlet due to C(3)-D was observed at δ 2.00, indicating that the hydrogen atom at C(1) of (*R*)-**19** was specifically transferred to C(3) position to give (*R*)-**20**. Integration of these signals showed that the enantiospecificity of the 1,3-hydrogen transfer reaction was 97.2%. When (*R*)-BINAP-Rh$^+$ complex was used as catalyst, (*S*)-**21** was produced in which deuterium atom at C(1) of (*R*)-**19** was shown to shift to C(3) position. On the basis of the integrated peak areas of ^{2}H NMR signals the enantiospecificity was calculated to be 97.2%. In a similar manner, reactions of (*R*)-**19** catalyzed by the (*R*)- or (*S*)-BINAP-Rh$^+$ complex in THF-d_8 were carried out in 5-mm diameter NMR tubes, and ^{1}H NMR spectra were recorded. The results were quite compatible with those obtained in THF. ^{1}H and ^{2}H NMR spectral data of the enamine products are as follows. (*R*,*E*)-*N*,*N*-diethyl-3,7-dimethyl-1,6-octadienylamine ((*R*)-citronellal (*E*)-enamine) [(*R*)-**3**]: ^{1}H NMR (acetone-d_6) δ 0.97 (d, J = 6.84 Hz, CH_3CHCH=), 1.04 (t, J = 7.08 Hz, NCH_2CH_3), 1.18–1.37 (m, =$CHCH_2CH_2$), 1.60 (s, *trans*-CH_3C=CH), 1.67 (s, *cis*-CH_3C=CH), 1.90–2.40 (m, CH_3CHCH= and =$CHCH_2$), 2.96 (q, NCH_2), 3.96 (dd, J = 8.30 and 13.67 Hz, CH=CHN), 5.12 (t with fine splitting, =$CHCH_2$), 5.84 (d, J = 13.67 Hz, CH=CHN). (*R*,*E*)-*N*,*N*-Diethyl-3,7-dimethyl-1,6-octadienylamine-*1-d*(0.5)-*3-d*(0.5): ^{1}H NMR (THF-d_8) δ 0.97 (d, J = 6.72 Hz, CH_3CHCH=), 1.04 (t, J = 7.02 Hz, NCH_2CH_3), 1.20–1.35 (m, =$CHCH_2CH_2$), 1.59 (s, *trans*-CH_3C=CH), 1.68 (s, *cis*-CH_3C=CH), 1.90–2.04 (m, CH_3CHCH= and =$CHCH_2$), 2.93 (q, NCH_2), 4.03 (dd, J = 7.93 and 13.89 Hz, CH=CHN), 5.80 (d, J = 13.89 Hz, CH=CHN); ^{2}H NMR (THF) δ 1.96 (s, CH_3CDCH=), 5.81 (s, =CDN). (*R*)-**20**: ^{1}H NMR (THF-d_8) δ 0.95 (d, J = 6.71 Hz, CH_3CHCH=), 1.02 (t, J = 7.02 Hz, NCH_2CH_3), 1.15–1.35 (m, =$CHCH_2CH_2$), 1.60 (s, *trans*-CH_3C=CH), 1.66 (s, *cis*-CH_3C=CH), 1.90–2.08 (m, CH_3CHCH= and =$CHCH_2$), 2.92 (q, NCH_2), 3.92 (d, J = 8.24 Hz, CH=CDN), 5.10 (t with fine splitting, =$CHCH_2$), 5.79 (d, very weak, J = 13.73 Hz, CH=CHN); ^{2}H NMR (THF) δ 1.99 (s, relative intensity 3.7, CH_3CDCH=), 5.86 (s, 96.3, =CDN). (*S*)-**21**: ^{1}H NMR (THF-d_8) δ 0.95 (s, CH_3CDCH=), 1.02 (t, J = 7.02 Hz, NCH_2CH_3), 1.18–1.34 (m, =$CHCH_2CH_2$), 1.58 (s, *trans*-CH_3C=CH), 1.66 (s, *cis*-CH_3C=CH), 1.90–2.05 (m, =$CHCH_2$), 2.93 (q, NCH_2), 3.93 (d, J = 13.89 Hz, CH=CHN), 5.10 (t with fine splitting, =$CHCH_2$), 5.79 (d, CH=CHN); ^{2}H NMR (THF) δ 1.95 (s, relative intensity 96.3, CH_3CDCH=), 5.82 (s, 3.7, =CDN).

Isolation of the Complex 8. To a solution of [Rh((*S*)-binap)$(CH_3OH)_2$]ClO_4 (11.6 mg, 0.013 mmol) in acetone-d_6 (2 mL) placed in an NMR sample tube (10-mm diameter) was added quickly a solution of **2** (23.3 mg, 0.111 mmol) in the same solvent (1 mL) below −70 °C by use of a cannula under argon. The tube was sealed and kept at −85 °C for 7 days. The formation of the complex **8** was confirmed by ^{31}P NMR spectroscopy. The reaction mixture was transferred to a 20-mL Schlenk tube and concentrated under reduced pressure below −45 °C. Pentane (10 mL) was slowly added to the residue at −70 °C, and an oily substance obtained after removal of pentane layer by use of a cannula was dissolved in dichloromethane (1 mL) at −80 °C. This mixture was transferred into a vigorously stirred pentane (20 mL) at −80 °C. The liquid layer was removed by use of a cannula to give yellow-orange solid which was washed twice with 10-mL portions of cooled pentane. The product was dried at −30 °C under reduced pressure to afford **8** as deep red powder. This complex gradually decomposes above −30 °C even in solid state. **8**: ^{1}H NMR (CD_2Cl_2, −60 °C) δ 0.33 (d, J = 6.4 Hz, CH_3CHCH=), 0.64 (t, J = 7.3 Hz, $N(CH_2CH_3)_2$), 0.90 (t, J = 7.0 Hz, $N(CH_2CH_3)_2$), 4.83 and 5.13 (two ill-resolved signals assignable to CH=CHN and CH=CHN, respectively); ^{31}P NMR (CD_2Cl_2, −60 °C) δ 49.07 (dd, J_{Rh-P} = 193.7 Hz, J_{P-P} = 56.7 Hz) and 29.19 (dd, J_{Rh-P} = 193.7 Hz, J_{P-P} = 56.7 Hz).

Isolation of the Complex 10. To a solution of [Rh((*S*)-binap)$(CH_3OH)_2$]ClO_4 (27.9 mg, 0.031 mmol) in acetone-d_6 (1.5 mL) placed in an NMR sample tube (10-mm diameter) was added a cooled solution of diethyl(3-methyl-2-butenyl)amine (34.9 mg, 0.25 mmol) in the same solvent (1.5 mL) below −80 °C by use of a cannula under argon. The reaction mixture was allowed to stand at −80 °C for 7 days with occasional shaking. After the completion of the reaction had been confirmed by ^{1}H and ^{31}P NMR spectroscopy, the product was isolated according to the procedure described for the preparation of **8** to give **10** as brown powder. The ^{1}H and ^{31}P NMR spectral data of **10** are given in the text.

Kinetic Studies on the Isomerization of Diethylgeranylamine (2) Catalyzed by the (*S*)-BINAP-Rh$^+$-Complex in Acetone-d_6. A solution of [Rh((*S*)-binap)$(CH_3OH)_2$]ClO_4 (47.5 mg, 5.33×10^{-2} mmol) in acetone-d_6 (6.00 mL) was prepared and allowed to stand at room temperature for ca. 5 h. Then, 300 μL of the solution was transferred into a Schlenk tube by using a gas-tight syringe and cooled to −80 °C. An appropriate amount of **2** was weighed in an NMR tube and the volume of the liquid was adjusted to 400 μL by the addition of dry acetone-d_6. This solution was also cooled to −80 °C. The catalyst solution was then transferred into a solution of the substrate in an NMR tube by use of cannula at −80 °C, and the tube was sealed with a gas flame. The mixture was shaken for a few minutes to get a homogeneous solution of the catalyst and the substrate at this temperature and then introduced rapidly to a ^{1}H NMR probe kept at −75 °C. After optimizing the resolution of the machine, the temperature of the probe was set at 15 °C, taking ca. 4 min to raise the probe temperature from −75 to 15 °C, immediately after which data were collected at 5-min intervals for about 30 min. The concentration of the catalyst was 3.8 mM, while substrate concentrations were 50–800 mM with a substrate to catalyst ratio of 15–250. The consumption of the starting allylamine **2** and the formation of the product enamine **3** were determined on the basis of signal intensities at δ 2.51 and 2.96 due to the methylene protons of *N*-ethyl group of **2** and those of *N*-ethyl groups of the product **3**, respectively. The conversions of the allylamine to the enamine were 10–45%. When the initial reaction rates were plotted against the initial concentration of the substrates, a parabola was obtained. A plot of the reciprocal of initial rate versus reciprocal of initial substrate concentration gave a straight line (Figure 1), which suggests that the reaction obeys a mechanism similar to those of Michaelis–Menten-type reactions. The maximum rate (R_{max}) and the Michaelis constant (K_m) determined are 1.9×10^2 mol L^{-1} min and 0.16 mol L^{-1}, respectively.

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