troduced by the protein in the neighborhood of the chromophore. It was suggested previously that nonconjugated charges exist in the binding site of bacteriorhodopsin, influencing its absorption maximum.[3d,e,4,15] However, a significant effect on the emission spectrum of chromophore **1** by a nonconjugated charge should be accompanied by a considerable effect on the absorption maxima. This conclusion is borne out from studies of chromophores **2** and **3**, bearing nonconjugated positive charges in the vicinity of the chromophore. As outlined in Table II, both the absorption and the fluorescence spectra are shifted by similar magnitudes, due to the presence of the charge. The direction of the shift is determined by the charge location (blue in **2** and red in **3**, due to destabilization or stabilization of the excited state, respectively). Since the significant blue-shifted emission spectrum of the complex chromophore **1**-bacterioopsin (relative to the emission in water) is not accompanied by a similar magnitude of shift of the absorption, we conclude that the complex emission spectrum is not affected significantly by nonconjugated charges and that the blue-shifted fluorescence spectrum observed for the complex (centered at 23 529 cm^{-1}, relative to 18 867 cm^{-1} of the chromophore in water) points to the resultant field of the peptide bonds reaching a low value at the probe site.

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Enantioselective Hydrogenation of Allylic and Homoallylic Alcohols

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Homogeneous asymmetric hydrogenation of olefins with transition-metal-complex catalysts[2] offers an attractive tool for stereoselective organic synthesis. Recently much attention has been given to directing effects of hydroxyl functionality on the stereochemical course. Some cationic Rh and Ir phosphine complexes are known to catalyze diastereoselective hydrogenation of *chiral* allylic and homoallylic alcohols,[3] where the preexisting chirality of the sp^3-hybridized carbons induces new asymmetry on the neighboring olefinic diastereofaces through coordination of the hydroxyl group to the transition metals.[4] However, highly enantioselective hydrogenation of the *prochiral* substrates is still elusive.[5] This process is based on catalyst/substrate *intermolecular* asymmetric induction, holding potential for chemical multiplication of chirality. We disclose here that the new Ru(II) dicarboxylate complexes containing BINAP ligands,[6] **1**,[7] as catalysts exhibit high reactivity and excellent selectivity, thereby solving this important and difficult problem.

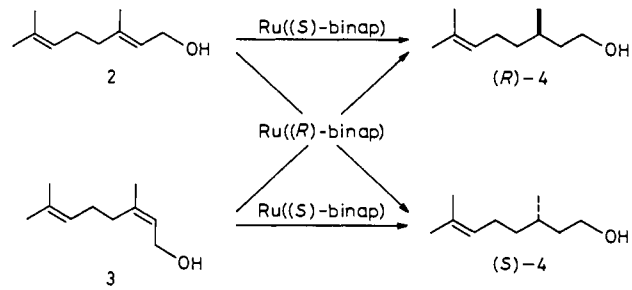
We selected stereochemically pure geraniol (**2**) and nerol (**3**) as substrates. Here the requirements for achieving a practically valuable asymmetric synthesis are (1) high chemical and optical yields of the citronellol product,[8] (2) regioselective reaction

Table I. Asymmetric Hydrogenation of Geraniol (**2**) and Nerol (**3**) Catalyzed by BINAP-Ru(II) Complexes[a]

substrate	catalyst	S/C	citronellol (**4**) optical purity[b]	% ee[c]	configuration
2	(*S*)-**1a**	530	98	96	*R*
2	(*S*)-**1b**	500		98	*R*
2[d]	(*S*)-**1c**	10 000	99	96	*R*
2[d]	Ru((*S*)-binap)$(OCOCF_3)_2$[e]	50 000	96		*R*
2[d]	Ru((*S*)-tolbinap)$(OCOCF_3)_2$[e]	50 000	97		*R*
3	(*R*)-**1a**	540		98	*R*
3	(*S*)-**1c**	570		98	*S*

[a] The reaction was carried out with stirring in a stainless steel autoclave at 18-20 °C with a 0.35-0.61 M solution of the substrate in methanol with exclusion of air. After removal of the Ru complex by precipitation by adding pentane followed by filtration through Celite 545, the whole mixture was concentrated and distilled to give **4** in 97-100% yields. [b] Authentic sample of (*R*)-**4** in 98% ee exhibits $[\alpha]^{25}_D$ +5.12° (*c* 21.0, $CHCl_3$). [c] Determined by HPLC analysis (Chemco Nucleosil 100-3, 4.6 × 300 mm, 3:7 ether-hexane) of the diastereomeric amides prepared by condensation of citronellic acid, obtained by the Jones oxidation, and (*R*)-1-(1-naphthyl)-ethylamine.[10] [d] Reaction using 5.8 M solution of **2** in methanol at initial hydrogen pressure of 30 atm for 12-14 h. [e] These complexes (tentative structures) were prepared from **1a** and **1c**, respectively, by ligand replacement by addition of excess trifluoroacetic acid.

Scheme I



† Institute for Molecular Science.
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§ Nagoya University.

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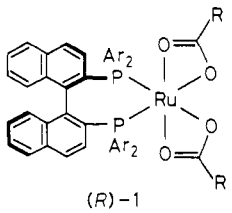
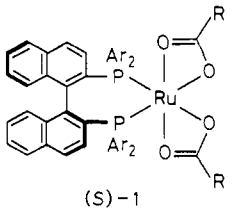
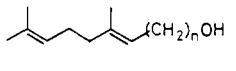




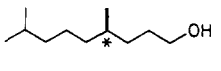
a. Ar = C_6H_5; R = CH_3 c. Ar = p-$CH_3C_6H_4$; R = CH_3
b. Ar = C_6H_5; R = $C(CH_3)_3$

avoiding hydrogenation of the C(6)=C(7) bond, (3) lack of double-bond migration[3] or E/Z isomerization, (4) high substrate/catalyst (S/C) mole ratio, and (5) easy recovery or reusability of the catalysts.

BINAP-based Ru(II) dicarboxylate complexes (**1**) were found to serve as efficient catalyst precursors, meeting all the above described criteria. Some representative results obtained under varying reaction conditions are summarized in Table I. (*R*)- or (*S*)-Citronellol, **4**, was obtained in nearly quantitative yield and with 96–99% enantioselectivity. The allylic and nonallylic double bonds in **2** and **3** can be clearly differentiated; the product was accompanied by less than 0.5% of, if any, dihydrocitronellol.[11] Initial hydrogen pressure higher than 30 atm afforded satisfactory enantioselectivities. The S/C mole ratio is extremely high and, in certain cases, the efficiency of the chiral multiplication, defined as [major stereoisomer − minor stereoisomer (in mol)]/chiral source in mol, approaches 48 500! The catalyst can be recovered, if one desires, by simple distillation of the product under reduced pressure (35 °C/1.5 × 10^{-5} mmHg); the air-sensitive BINAP-Ru complex residue acts as a catalyst for further runs without substantial loss of activity and selectivity. The stereochemical outcome outlined in Scheme I implies that the BINAP-Ru species differentiates the C(2) enantiofaces at a certain stage of the catalysis. Thus, both *R* and *S* enantiomers are accessible by either variation of allylic olefin geometry or choice of handedness of the catalysts. The relative position of the hydroxyl group and olefinic bond strongly affects the reactivity and selectivity. Hydrogenation of homogeraniol (**5**) aided by (*S*)-**1a** (S/C = 200, CH_3OH, 30 °C, 3 h, 100 atm) occurred regioselectively to produce (*R*)-**7** in 96% yield and in 92% ee.[10] Sense of the asymmetric induction was identical with that of the reaction of **2**. However, the higher homologue **6** was inert to the comparable hydrogenation conditions.



5, n = 2
6, n = 3



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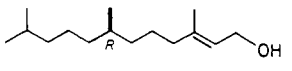

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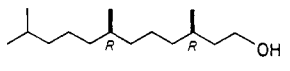

9

High levels (>90%) of enantioselective hydrogenations have been attained only with α-acylaminoacrylic acids or esters[2] and related substrates.[7] The present result marks the first example of the high enantioselection with simple prochiral unsaturated alcohols, providing a new, powerful means in the synthesis of optically active terpenes and related compounds. Indeed, this procedure has been successfully applied to the asymmetric synthesis of (3*R*,7*R*)-3,7,11-trimethyldodecanol (**9**),[13] a versatile intermediate for convergent synthesis of α-tocopherol (vitamin E). When the pure *R*,*E* allylic alcohol **8**, derived from homochiral isopulegol,[14] was hydrogenated in the presence of (*S*)-**1a** (S/C = 520, CH_3OH, 20 °C, 3.5 h, 100 atm), the desired saturated alcohol **9** was obtained in 99% yield. The diastereomeric purity of the 3*R*,7*R* alcohol, $[\alpha]^{25}_D$ +3.19° (*c* 3.76, $CHCl_3$), was determined to be 99% by HPLC analysis of the amide,[13c] derived from the oxidized 3,7,11-trimethyldodecanoic acid and (*R*)-1-(1-naphthyl)ethylamine.[10,15] Since the requisite **8** now becomes obtainable in 98% ee in a practical manner starting from (*R*)-citronellal, synthesized by the BINAP–Rh^+-catalyzed asymmetric isomerization of diethylgeranylamine (1,3-hydrogen shift) followed by hydrolysis,[6c] combination of the chiral C_{15} building block, **9**, and readily accessible (*S*)-chroman-2-carboxylic acid[16] opens a promising, straightforward way to α-tocopherol.[17]

(8) (*S*)-(−)-Citronellol of optical purity up to 92% can be obtained in a limited quantity from rose oil. (*R*)-(+)-Citronellol has been obtained by hydrogenation of naturally occurring citronellal of <85% optical purity. Enantiomerically pure (*R*)-(+)-citronellol has been obtained by a microbiological reduction of geraniol.[9]

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Enantioselective Total Synthesis of Aphidicolin

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The diterpene tetraol aphidicolin (**1**), isolated from *Cephalosporium aphidicolia* petch,[2] has been found to reduce the mitotic rate of mouse L cells and to inhibit the growth of *Herpes simplex* Type I.[3] The strong in vitro activity of aphidicolin against herpes virus is presumed to arise through inhibition of virus DNA synthesis.[4] Its structure was first elucidated by chemical and spectroscopic means, and the structure and absolute configuration were confirmed by X-ray crystal analysis.[2a]

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