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(6) A carefully optimized procedure, involving cyclization of **1** with 0.2 M TFA in CH_2Cl_2 at −50 °C, gave, after saponification of the trifluoroacetates, the mixture of diastereomers **2** in 60% yield and the rearranged hydrocarbon **3** in 10% yield. See Ph.D. dissertations of L. A. Bunes (1974) and C. E. Ward (1977), Stanford University.
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(11) The product was chromatographed (a) by preparative column techniques on silica gel or (b) by thin layer techniques on silica gel.
(12) The product was evaporatively distilled (using a Büchi Kugelrohroffen) at temperatures ranging between 150 and 220 °C and pressures of 10-50 μ.
(13) (a) The product was of adequate purity for proceeding to the next step. (b) The NMR and IR spectra were consistent with the assigned structure. (c) Satisfactory C, H analyses were obtained on an appropriately purified specimen.
(14) Except for *o*-chloromethyl-2-phenylethanol,[13a,b] all of the other intermediates between **8** and **10** were fully characterized.[13]
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(17) Compound **4** (0.12 mmol) in 1 mL of dichloromethane was added dropwise to 1.2 mL of 0.1 M stannic chloride in dichloromethane at −25 °C over a period of 3 min. After another 3 min at −25 °C, the reaction was quenched with 0.1 mL of pyridine.
(18) The chromatography of the reaction mixture also afforded a polar fraction (12% yield), consisting of what appeared to be (by NMR) the product of backbone rearrangement, i.e., formula **3** with an *o*-hydroxyethyl substituent on the phenyl group.
(19) Details of the X-ray analyses will be reported elsewhere.
(20) A solution of 0.4 mL of 0.1 M stannic chloride in dichloromethane was added to 0.3 mmol of **5** in 3 mL of dichloromethane at −21 °C over a period of 0.5 min. The reaction was quenched with 1 mL of 33% pyridine in dichloromethane.

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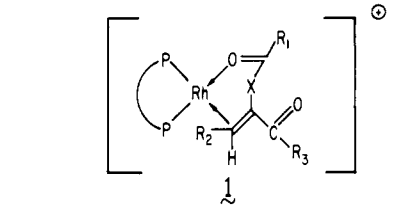
Catalytic Asymmetric Hydrogenation with a Rhodium(I) Chiral Bisphosphine System. A Study of Itaconic Acid and Some of Its Derivatives and Homologues

Sir:

The catalytic asymmetric hydrogenation of prochiral olefins with rhodium(I) chiral bisphosphine complexes is especially successful (i.e., fast rates and high enantiomeric excesses (ee)) when the olefins are (*Z*)-α-acylaminoacrylic acids[1] or (*Z*)-α-acyloxyacrylic esters.[1f,h] This is presumably because of their ability to form chelates of the type **1a** and **1b**.[1f,2] Chelation is important because it generates a low-energy complex in the transition state, which results in a fast rate, and because it produces a rigid complex which maximizes the substrate-ligand interactions and consequently the enantioface discriminating ability of the catalyst. Itaconic acid **2**, which should form a similar type of chelate **1c**, has met with low asymmetric induction when hydrogenated with most catalyst systems.[3a,b] A recent exception affords an 84% ee as the free acid[3c] which is increased to 92% ee as the anion,[3a] an inexplicably high induction considering that this chiral ligand **8** is very similar to the rest.

An explanation for the anomalous behavior of itaconic acid in its asymmetric hydrogenations with rhodium(I) chiral bisphosphines has not been proposed. Such an explanation, however, may be useful in designing both ligands and substrates for asymmetric reduction. In particular (a) why does itaconic acid hydrogenate poorly with most catalyst systems



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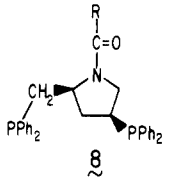
	R_1	R_2	R_3	X
a.	CH_3, Ph	H, alkyl, aryl	OH, OCH_3, NH_2	NH
b.	CH_3	H, Ph	OCH_3	O
c.	OH	H	OH	CH_2



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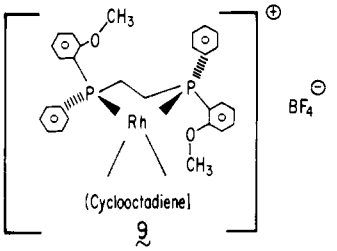

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and (b) why does it hydrogenate efficiently when the ligand is **8**?

In this communication, these questions are addressed by studying the asymmetric hydrogenation behavior of **2** and some of its derivatives **3**–**7** with the [Rh(1,5-COD)(DiPAMP)]$^+$-BF_4^- catalyst precursor **9**. Then, as an additional probe of substrate requirements, the hydrogenation properties of the α-methyleneglutaric acid derivatives **13** and **14** (homologues of itaconic acid derivatives **3** and **4**) are briefly explored with the same catalyst system. The results are summarized in Table I.

All of the data can be explained in terms of the substrates ability to form a bidentate complex in the transition state with the rhodium(I) phosphine system. For itaconic acid and its derivatives, this chelating ability appears to be influenced by the H-bonding properties of the substrate, as explained below.

Itaconic acid **2** hydrogenates slowly with a poor 38% ee at a 0.4 M concentration in alcohol. Interestingly, a very dilute 0.002 M solution of **2** is hydrogenated in a respectable 77% ee, suggesting that intermolecular H-bonding interactions are affecting the transition state and, consequently, the optical discrimination of the catalyst. This result can be explained by supposing that **2** exists exclusively as an intermolecular H-bonded species, either dimeric or polymeric, at the higher concentration. (Itaconic acid has been shown by X-ray analysis to exist as a polymer in the crystal.[4]) This dimeric and/or polymeric species is not a good substrate, presumably because its H-bonded nature prevents the necessary chelate formation, probably because of unavailability of the 4-carbonyl function. In a very dilute solution, **2** is monomeric (with the 4-carbonyl group free in at least one conformation) and can form a chelate of the type **1c** which hydrogenates with good stereoselectivity. Itaconic acid dianion **3** and dimethyl itaconate **4**, in which H-bonded interactions cannot interfere with chelate formation, hydrogenate rapidly with high optical bias, 78 and 88%, respectively.

The half-ester **5** reduces with the same low optical bias (55% ee) and slower rates at both 0.4 and 0.002 M concentrations! A possible explanation is that, at both high and low concentrations, **5** exists entirely as the intramolecular H-bonded

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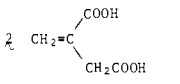
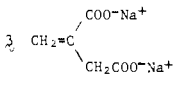
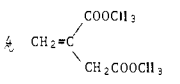
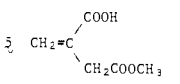
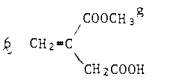
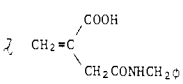
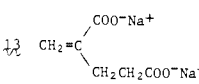
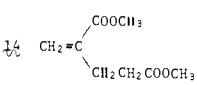
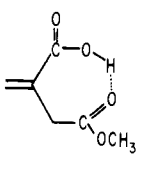
Table I. Hydrogenation of Itaconic and α-Methylene Glutaric Acid Derivatives with the [Rh(1,5-COD)(DiPAMP)]$^+BF_4^-$ Catalyst Precursor[a]

	Substrate	% ee (0.4M)	% ee (0.002M)	Relative Rate[b] (0.4M)
2		38% R[c]	77% R	9
3		78% R[d]		50
4		88% R[e]		100
5		55% R[f]	55% R	2
6		88% R[f]		100
7		90% R[h]		100
13		10%[i]		0.6
14		2.8%[j]		10

[a] All hydrogenations were carried out under 50-psig hydrogen pressure at 50 °C. Substrates **2** and **7** were hydrogenated in ethanol, **4**, **5**, and **6** were hydrogenated in methanol, and **3** was reduced in 50% aqueous ethanol. Additional experimental data may be found in ref 1f. [b] In comparison, the common substrate (*Z*)-α-acetamidocinnamic acid reduces with a relative rate of 59.[1f] [c] $[\alpha]^{20}_D$ +17.01° (*c* 4.41, EtOH): R. Rossi et al., *Gazz. Chim. Ital.*, **98**, 1391 (1968). [d] Converted into the diacid to determine ee. [e] $[\alpha]^{25}_D$ +6.11° (neat): reference in *c*. [f] Converted into the diester to determine ee. [g] Prepared by heating itaconic anhydride with 4-methoxybenzyl alcohol to get the half-ester. This was treated with diazomethane and then heated with trifluoroacetic acid in toluene to give **6**. [h] $[\alpha]^{20}_D$ +15.3° (*c* 1.01, EtOH); determined by repeated crystallization of the 90% ee material from EtOH. [i] Converted into the diacid to determine ee. $[\alpha]^{20}_D$ +21.3° (*c* 2.0, EtOH): E. Berner and R. Leonardsen, *Justus Liebigs Ann. Chem.*, **538**, 1 (1939). [j] $[\alpha]^{20}_D$ +24.46° (neat): reference in *i*.

species **10**.[5] In this conformation, **5** cannot form a chelate with rhodium and thus hydrogenates via a less efficient monodentate complex. Half-ester **6** can assume only the intramolecular H-bonded structure **11** which would still leave the 4-carbonyl oxygen free and properly oriented for chelation. Consequently, **6** is hydrogenated rapidly with a resultant good 88% ee. The proposed preference of the half-esters (**5** and **6**) to H bond intramolecularly in contrast to the intermolecular H bonding for itaconic acid is reasonable considering that (a) intermolecular association results in two H bonds per molecule for itaconic acid, while intramolecular H bonding would result in only one per molecule; (b) the half-esters achieve one H bond per molecule regardless of whether they are intra- or intermolecularly H bonded.



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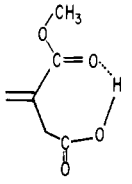

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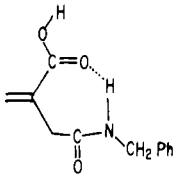

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Finally, for the itaconic acid series, the half-amide **7** reduces rapidly and with a high enantioselectivity of 90%. Since an amide group has a preference for a trans conformation[6] (A), **7** cannot form a dimeric or polymeric species similar to itaconic acid. Consequently, the amide can exist to some extent as an H-bonded species (cf. **12**) leaving the 4-carbonyl function available for chelation.

A

Two α-methyleneglutaric acid derivatives **13** and **14**, chosen because no H-bonding complications can exist, were hydrogenated in order to probe the geometric requirements for chelate formation. Both were found to hydrogenate slowly and with low optical inductions. Apparently a suitable bidentate complex does not form when the ring is seven membered (counting both carbons of the coordinating olefin).

Now, concerning the questions raised at the beginning of this communication, we propose that (a) itaconic acid is a poor substrate with most rhodium(I) bisphosphine catalyst systems because H bonding prevents it from forming a bidentate complex in the transition state (in the absence of such influences it hydrogenates efficiently, being geometrically and electronically suitable); (b) bisphosphine **8** successfully reduces **2** because the amide moiety in the ligand can act to break up H bonding in the coordinated substrate so as to allow chelation. CPK models show that the ligand's amide oxygen can be properly oriented for interaction with the 1-carbonyl hydrogen.[3b]

The basic conclusion seems to be that the major limitation to efficient asymmetric hydrogenation with rhodium(I) chiral bisphosphines is the ability of the substrate to form a bidentate complex in the transition state. This study has contributed to an understanding of the requirements necessary for chelation. The demands for chelation appear to be stringent, as demonstrated by the facts that perturbations as small as an unfavorable H-bonded conformation or chelate ring extention by one CH_2 (i.e., going from itaconic to α-methyleneglutaric acid derivatives) destroys the ring-forming properties. Still, there may well be new rhodium(I)-based chiral ligand-substrate combinations found that give efficient asymmetric reduction. Their design will most likely be facilitated, however, by considering all the known effects, including those presented in this communication.

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Conformational Preference and Structural Similarity of the Lanthanide [2.2.1] Cryptates

Sir:

While ligand conformations preferred by d-transition metal chelates have received careful study,[1] no observations of this phenomenon have heretofore been observed for complex ions of f-transiton elements.[2] We now report a 180-MHz ^{1}H NMR examination of the trivalent lanthanide [2.2.1] cryptates, [Ln(2.2.1)]X_3 ($X = Cl^-, NO_3^-, ClO_4^-$), which reveals that these species either show strong *conformational preference* or are structurally rigid within the time frame of the NMR experiment and are, as well, *isostructural* over the entire series.[3] The low-energy barriers known for conformational motion in five-membered chelate rings render the preference of ligand gauche conformations most likely,[1] but our NMR studies cannot distinguish between rigidity or preference of conformation.[1d,4]

Several representative ^{1}H NMR spectra of the title compounds are shown in Figure 1. Of particular interest is that displayed by a CD_3CN solution of [La(2.2.1)]$(NO_3)_3$ wherein signal assignments have been verified by decoupling methods. Geminal methylene protons α to bridgehead nitrogens on the two dioxygen strands may be seen to exhibit an AM doublet (J_{AM} = 13.5 Hz) which is vicinally coupled to the adjacent β-CH_2 group denoted as protons H_X and H_Y ($J_{AX} = J_{AY}$ = 3.5, J_{MX} = 9.45, J_{MY} = 6.15 Hz). Observation of a single AMXY pattern for all four N-CH_2 dioxygen fragments of the molecule implies either that both strands have the same rigid conformation, or that a single conformation is highly favored thermodynamically.[1d,4] The observed variance in vicinal M(X,Y) coupling constants arises from dihedral angle differences as expected from the Karplus equation.[5] The remaining triplet in the N-CH_2 spectral region is due to the monooxygen strand α-CH_2 coupling to symmetry equivalent β-CH_2 protons with J_{KL} = 5.25 Hz. The O-CH_2 spectral region is complicated by extensive resonance overlaps, but the A and B branches of an AA'BB' pattern due to protons H_E, H_F, $H_{E'}$, and $H_{F'}$ (J_{EF} = 36.5 Hz) may be seen on either side of a complex pattern which is made up of the triplet of the β-CH_2 protons of the monooxygen ligand strands (J_{KL} = 5.25 Hz) and the multiplet from the β-CH_2 protons of the dioxygen strands. The essential spectral features discussed above are also detected for the salts in D_2O, but with less chemical shift separation in the α-CH_2 spectral region.

Evidence for structural identity of lanthanide [2.2.1] cryptates is deduced from ^{1}H NMR spectra of the paramagnetic ion species in D_2O which show eight widely dispersed, equally intense resonances (see Figure 1) which were assigned by considering resonance frequencies and line widths. Lanthanide ion induced chemical shifts obey an equation of the form

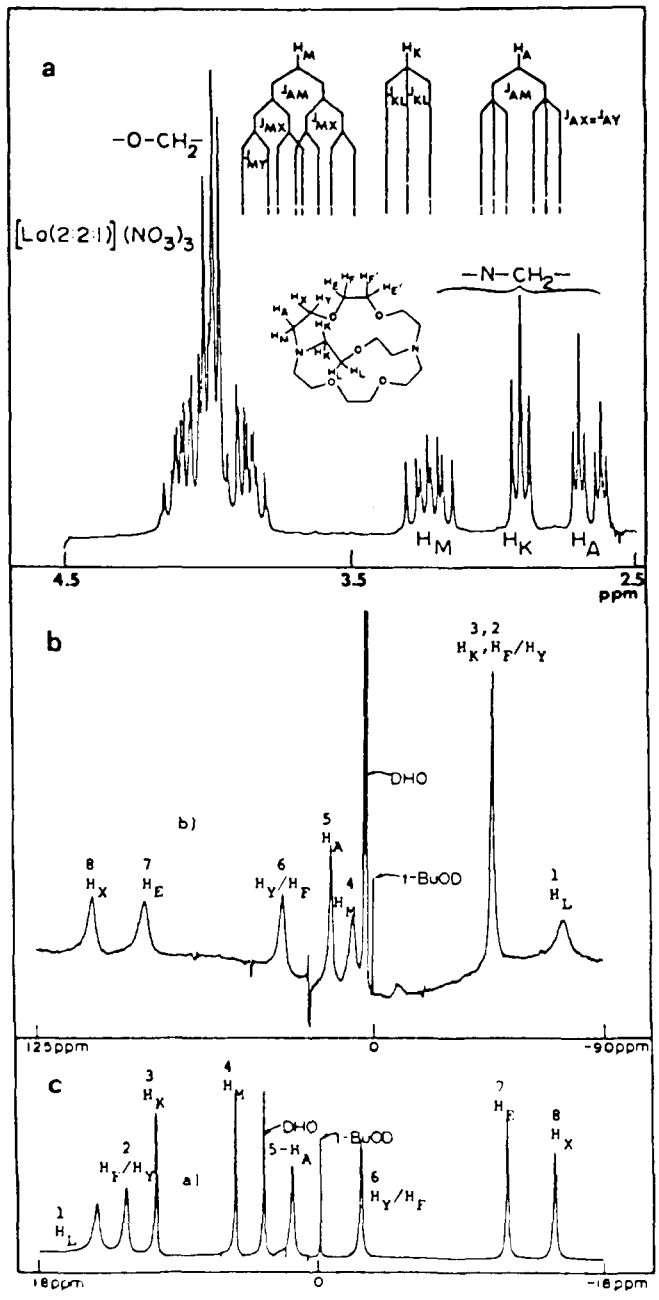

Figure 1. 180-MHz ^{1}H NMR spectra of some lanthanide [2.2.1] cryptates: (a) [La(2.2.1)]$(NO_3)_3$ in CD_3CN solution, Me_4Si reference; (b) [Pr(2.2.1)]$(NO_3)_3$ in D_2O; (c) [Er(2.2.1)]$(NO_3)_3$ in D_2O; *t*-BuOD reference in D_2O.

$$\delta_i = A_i(S_z) + DG_i \qquad (1)$$

where δ_i is the chemical shift of the ith proton measured from the diamagnetic resonance position of the La^{3+} complex, $A_i(S_z)$ is the Fermi contact term, G_i is a geometric factor dependent on the position of the proton relative to the ion, and D is a constant of different value for each lanthanide whose magnitude is determined by temperature and g value anisotropy.[6] Relative proton resonance line widths in lanthanide complexes depend on the radial distance of the proton from the ion[7] as shown in eq 2. By using X-ray structural data, it is therefore possible to calculate metal-proton distances and expected radius and line width ratios.

$$T_2^A/T_2^B = \Delta\nu_{1/2}^B/\Delta\nu_{1/2}^A = r_A^6/r_B^6 \qquad (2)$$

Since no detailed crystal data were available for any lanthanide cryptates, the recently published structure[8] of the

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