Table II. ^{19}F Chemical Shifts for $CF_3{}^A CF_2{}^B CF_2{}^C CF_2{}^D SO_2OR$

R	$-\theta^*_A$	$-\theta^*_B$	$-\theta^*_C$	$-\theta^*_D$
Cl	81.4	126.6	121.3	106.4
Br	82.1	126.9	121.8	108.8
CF_2CH_2Cl	81.5	126.3	121.3	110.0
CCl_2CF_2Cl	81.4	126.4	121.0	108.5
$CFClCF_2Cl$	81.4	126.3	121.0	108.3
CF_2CF_2Cl	81.4	126.3	121.0	108.3
CHFCHFCl	81.4	126.3	121.1	110.0
CF_3	81.4	126.2	121.0	108.2
CH_3	81.5	126.4	121.8	111.1
SiF_3	81.4	126.2	121.1	109.6
$SiMe_3$	81.5	126.5	121.7	112.9
SF_5	81.4	126.3	121.0	107.6
POF_2	81.3	126.1	120.8	106.9
CF_2CH_2Br	81.4	126.3	121.1	110.1
CCl_2CF_2Br	81.4	126.4	121.0	108.5
$CFClCF_2Br$	81.4	126.4	121.0	108.5
CHFCHFBr	81.4	126.3	121.1	109.9

nificant variation depending on R. Homonuclear decoupling was used to establish the pattern of chemical shifts for fluorines A–D, although this technique does not allow evaluation of all couplings between fluorines A–D. The spectra of fluorines B and C show second-order effects which are presumed to be due to restricted internal rotation. In the C_4F_9 group, the $^3J_{FF}$ couplings are all near zero which may be due to an averaging of coupling constants of opposite sign in various rotomers. The significant couplings in terms of the observed spectra are then $^4J_{AC}$, $^5J_{AD}$, $^4J_{BD}$, and $^5J_{DF}$, where F is a fluorine in R. A similar $^5J_{DH}$ coupling was too small to be observed. The relevant values are given in the Experimental Section, and a summary of the chemical shifts of fluorines A–D are given in Table II. Two of the new compounds, $C_4F_9SO_2OC_4F_9$ and $C_4F_9SO_2OSO_2OC_4F_9$, are not listed in Table II since it was impossible to assign the observed resonances to the different C_4F_9 groups. On the other hand, eight different resonances in the appropriate areas were observed in each case, confirming the presence of the two different C_4F_9 groups. One additional important observation is the magnitude of $^1J_{PF}$ in $C_4F_9SO_2OP(O)F_2$. This value of 1090 Hz provides a measure of the group electronegativity of $C_4F_9SO_2O$. Within the experimental error, it is identical with CF_3SO_2O, where the same $^1J_{PF}$ value was 1089.2 Hz.[11]

In conclusion, the hypohalites $C_4F_9SO_2OX$ (X = Cl, Br) provide additional examples of the pronounced electrophilic character of the halogen in R_fSO_2OX. In addition, evidence has been found to support identical reaction mechanisms for the addition of R_fSO_2OX (R_f = CF_3, *n*-C_4F_9) to olefin and for the SED reaction with covalent halides. Finally, many new $C_4F_9SO_2O$ esters have been prepared, establishing the utility of $C_4F_9SO_2OX$ in synthesis.

Acknowledgment. Support of this research by the National Science Foundation is gratefully acknowledged. Acknowledgment is also made to the donors of the Petroleum Research Foundation, administered by the American Chemical Society, for partial support of this work.

Registry No. $C_4F_9SO_2OCl$, 79410-50-7; $C_4F_9SO_2OBr$, 79410-51-8; $C_4F_9SO_3H$, 375-73-5; ClF, 7790-89-8; Br_2, 7726-95-6; C_2F_4, 116-14-3; C_2F_3Cl, 79-38-9; CF_2CCl_2, 79-35-6; CF_2CH_2, 75-38-7; *cis*-CHFCHF, 1630-77-9; CF_3Br, 75-63-8; C_4F_9Br, 375-48-4; SiF_3Br, 14049-39-9; Me_3SiCl, 75-77-4; SF_5Br, 15607-89-3; POF_2Br, 14014-18-7; CH_3Cl, 74-87-3; $C_4F_9SO_2OCF_2CF_2Cl$, 79410-52-9; $C_4F_9SO_2OCFClCF_2Cl$, 79410-53-0; $C_4F_9SO_2OCCl_2CF_2Cl$, 79410-54-1; $C_4F_9SO_2OCF_2CH_2Cl$, 79410-55-2; *erythro*-$C_4F_9SO_2OCHFCHFCl$, 79410-56-3; $C_4F_9SO_2OCF_3$, 79410-57-4; $C_4F_9SO_2OC_4F_9$, 77945-21-2; $C_4F_9SO_2OSiF_3$, 79410-58-5; $C_4F_9SO_2OSF_5$, 79410-59-6; $C_4F_9SO_2OSiMe_3$, 68734-62-3; $C_4F_9SO_2OPOF_2$, 79410-60-9; $C_4F_9SO_2OCH_3$, 6401-03-2; *erythro*-$C_4F_9SO_2OCHFCHFBr$, 79410-61-0; $C_4F_9SO_2OCF_2CH_2Br$, 79410-62-1; $C_4F_9SO_2OCFClCF_2Br$, 79410-63-2; $C_4F_9SO_2OCCl_2CF_2Br$, 79420-97-6.

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Catalytic Asymmetric Hydrogenation of Methyl (*E*)- and (*Z*)-2-Acetamido-3-alkylacrylates†

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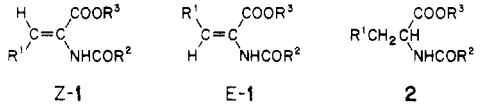
Received August 18, 1981

Rhodium–chiral phosphine complex catalyzed homogeneous hydrogenations of methyl (*Z*)- and (*E*)-2-acetamido-4-methoxybut-2-enoates ((*Z*,*E*)-**10**), methyl (*Z*)- and (*E*)-2-acetamidohex-2-enoates ((*Z*,*E*)-**16A**) and methyl (*Z*)- and (*E*)-2-acetamido-4-methylpent-2-enoates ((*Z*,*E*)-**16B**) are reported. With phosphines in which two achiral phosphorus atoms are connected by a chiral four-carbon unit, higher product enantiomeric excesses (ee's) are obtained from *E* than from *Z* substrates. With phosphines in which a two-carbon chiral unit separates two achiral phosphorus atoms, *Z* substrates are preferred. With dipamp (**28**), both *Z* and *E* substrates (particularly (*Z*,*E*)-**16A**) are reduced with high enantioselectivity. The additional oxygen atom in substrates (*Z*,*E*)-**10** has little effect on product ee with most phosphines.

Rhodium-chiral phosphine complex catalyzed enantioselective hydrogenations of 2-amido-3-arylacrylates **1** (R^1 = aryl) to give the corresponding chiral 2-amido-3-arylpropionates **2** (R^1 = aryl) have been widely studied.[2-4] Hydrogenations of (*Z*)-**1** (R^1 = aryl) are generally both fast and highly enantioselective and are useful synthetically since the pure *Z* isomers are readily prepared. The cor-



Z-1 E-1 2

† Dedicated to the memory of Dr. Willy Leimgruber, deceased July 8, 1981.

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(2) Valentine, D., Jr.; Scott, J. W. *Synthesis* **1978**, 329–356.
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0022-3263/81/1946-5086$01.25/0

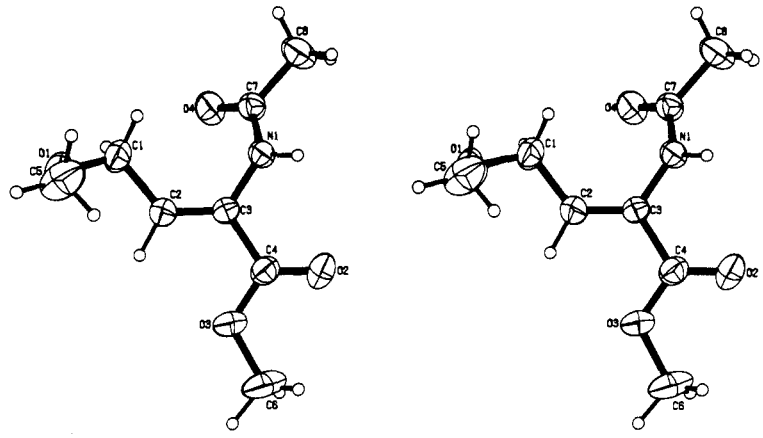
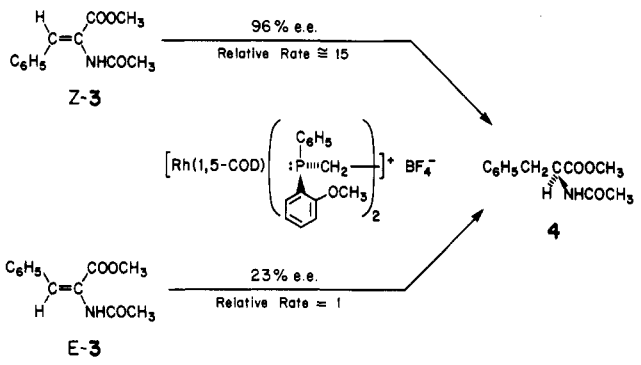


Figure 1. Stereodrawing of (*Z*)-**10** showing the conformation in the solid state. The thermal ellipsoids are scaled to the 50% probability level. The hydrogen atoms are shown as spheres of a fixed arbitrary size.

responding *E* isomers, (*E*)-**1** (R^1 = aryl), are harder to make and are hydrogenated more slowly and with lower enantioselectivities. The synthesis[5] of the protected (*S*)-phenylalanine **4** is a typical example.

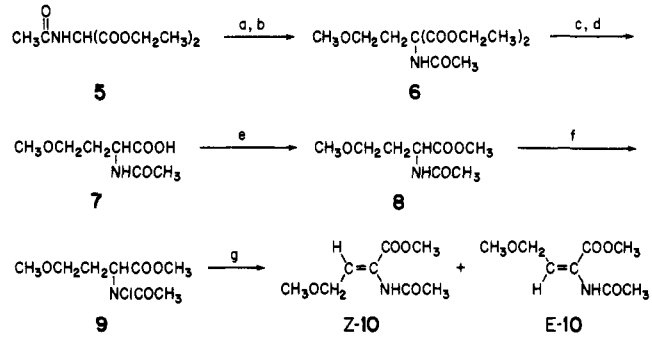


When R^1 = alkyl, (*Z*)-**1** is a good hydrogenation substrate for many[5-9] but not all[10,11] rhodium–chiral phosphine complex catalysts. Hydrogenations of (*Z*)-**1** (R^1 = alkyl) are not of synthetic interest, however, because in general the *Z* isomers are not easily obtained in pure form. The corresponding (*E*)-**1** compounds are even less readily available and to our knowledge had not been studied as substrates for enantioselective hydrogenations prior to this work. This paper describes a systematic study of the rhodium–chiral phosphine complex catalyzed hydrogenations of (*Z*)-**1** (R^1 = alkyl) and (*E*)-**1** (R^1 = alkyl). It will be seen that the results obtained with these substrates are fundamentally similar to those obtained in hydrogenations of **1** (R^1 = aryl).

Results

(i) Substrate Synthesis. As part of another project,[12] we had the occasion to prepare relatively large amounts of the (*Z*)-(methoxymethyl)acrylic acid ester (*Z*)-**10**[13]

Scheme I[a]



[a] (a) EtONa/EtOH/20 °C; (b) $CH_3OCH_2CH_2Br$/↑↓; (c) 2 N NaOH/20 °C → ↑↓; (d) pH 3/↑↓; (e) CH_3I/K_2CO_3/acetone/↑↓; (f) $(CH_3)_3COCl/CCl_4$/20 °C; (g) Dabco/3 → 20 °C.

(Scheme I). Thus, alkylation of diethyl acetamidomalonate (**5**) with 2-methoxyethyl bromide gave diester **6**, which was saponified and decarboxylated to acid **7**. Esterification of **7** with methyl iodide and potassium carbonate gave **8** in 56% yield (from **5**). Chlorination of **8** on nitrogen with *tert*-butyl hypochlorite, followed by dehydrochlorination and double bond migration induced by 1,4-diazabicyclo[2.2.2]octane (Dabco), gave a 60% yield of crystalline product (*Z*)-**10**, mp 62–64.5 °C. By careful HPLC of the crystallization mother liquors, a small amount of (*E*)-**10** was obtained as an oil which solidified upon standing; mp 33–36 °C. The structure of (*Z*)-**10** was determined by single-crystal X-ray analysis (see Figure 1). The ^1H NMR of the vinyl proton in (*Z*)-**10** (δ 6.70) was at higher field than that for (*E*)-**10** (δ 7.30), in agreement with expectation.[14]

We studied asymmetric hydrogenations of (*Z*)-**10** and (*E*)-**10** because we felt the ethereal oxygen could possibly serve as an additional rhodium ligand and alter the course of the reaction. When effects consistent with this hypothesis were observed (vide infra), the preparation of the aliphatic analogues (*Z*)-**16A** and (*E*)-**16A** was undertaken (Scheme II). Of the available syntheses[15] of this type of compound, we chose the method of Shin et al.,[16] who had

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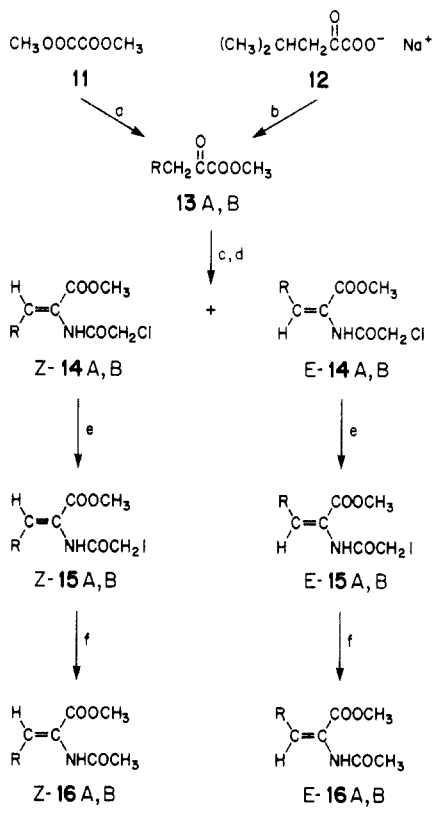
Scheme II[a,b]



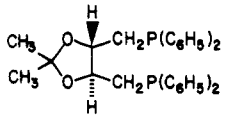
[a] A, R = $CH_2CH_2CH_3$; B, R = $CH(CH_3)_2$. [b] (a) $(CH_3CH_2CH_2CH_2)_3Al/CH_2Cl_2/-25$ °C; (b) CH_2N_2/ether/3 °C; (c) $ClCH_2CONH_2/POCl_3$/toluene/↑↓; (d) HPLC; (e) KI/acetone/↑↓; (f) Zn/CH_3OH/20 °C.

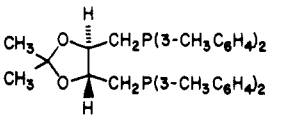
prepared the ethyl esters corresponding to (*Z*)-**16A** and (*E*)-**16A**. The key step in this sequence is the phosphorus oxychloride mediated condensation of chloroacetamide with the δ-keto ester **13A**. This yields approximately equal amounts of the chloro enamides (*Z*)-**14A** and (*E*)-**14A**, which are readily separated by preparative HPLC. The remainder of the sequence is straightforward, involving Finkelstein exchange of iodide for chloride and reduction by zinc in methanol. We thus obtained the desired (*Z*)-**16A** and (*E*)-**16A** and, in an entirely similar manner, the known[16] isopropyl analogues (*Z*)-**16B** and (*E*)-**16B**, which are leucine precursors. The double bond configurations of compounds **14–16** were assigned by ^1H NMR. In each pair, the compound exhibiting the higher field vinyl proton resonance was presumed to be the *Z* isomer.

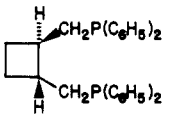
To employ the Shin[16] synthesis, a route to the α-keto esters **13A,B** was needed. The acid salt **12** is commercially available.[17] Its reaction with diazomethane gave **13B**.[18] A convenient method for preparing **13A**[19] was the reaction of dimethyl oxalate (**11**) with tri-*n*-butylaluminum at −25 °C. This method,[20] although not widely used, appears to be one of the most convenient for the preparation of unhindered α-keto esters. Perhaps not surprisingly, triisobutylaluminum did not react with **11** except under more forcing conditions, and **13B** could not be obtained in this manner.

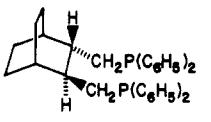
The seventh and eighth hydrogenation substrates employed in our studies were the known unsubstituted ala-

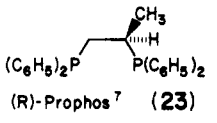
Chart I. Chiral Chelating Bis(phosphines) Used as Ligands in Asymmetric Hydrogenations

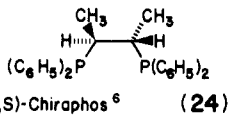

(S,S)-Diop[10] (**19**)

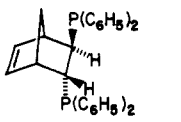

(R,R)-3-CH_3Diop[23] (**20**)

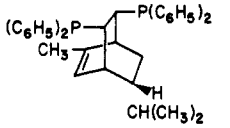

(R,R)-C4Diop[24] (**21**)

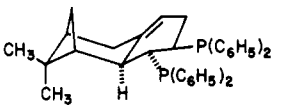

(S,S)-Bcop[23] (**22**)

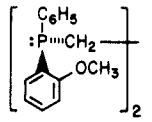

(R)-Prophos[7] (**23**)

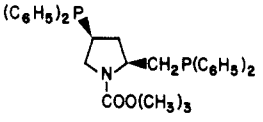

(S,S)-Chiraphos[6] (**24**)


(R,R)-Norphos[25] (**25**)

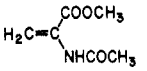

(S,S)-Phellanphos[26,27] (**26**)

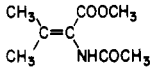

(R,R)-Nopaphos[27] (**27**)


(R,R)-Dipamp[28] (**28**)


(S,S)-Bppm[29] (**29**)

nine precursor **17**[21] and the tetrasubstituted enamide **18**,[22] the reduction of which yields *N*-acetylvaline methyl ester.


17


18

(iia) Hydrogenation Conditions and Methods. The phosphines employed for our hydrogenation studies are shown in Chart I. We chose these bidentate chelating bis(phosphines) since it is well established[2-4] that these

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phosphines give, in general, the best results in phenylalanine syntheses. The results of our hydrogenation experiments are given in Table I, along with reported values for similar hydrogenations of (*Z*)-**3**. To obtain valid comparative data, all our substrates were methyl esters and acetamides. The reactions were run in methanol at ambient temperature and initial hydrogen overpressures of about 50 psi. The substrate to catalyst weight ratio varied from 25:1 to 100:1.[32] Each *Z*,*E* substrate pair was run with each phosphine in side-by-side experiments to obtain relative hydrogenation rates. The enantiomeric excess (ee) values of the hydrogenation products were determined by two methods. In the first of these we used Eu(tfc)$_3$-perturbed[33] ^{1}H NMR spectroscopy, estimating the relative peak heights of the ester and acetyl methyl singlets, both of which were resolved by this technique. A more precise[34] method used gas chromatography with lauroyl-(*S*)-valine *tert*-butyl amide (SP-300[35]) as stationary phase. Values reported in Table I were obtained by this technique. The absolute configuration of the major enantiomer from hydrogenation of substrates **16B**, **17**, and **18** was determined by optical rotation, on the basis of the known rotations of *N*-acetyl-(*S*)-leucine,[36] alanine,[37] and valine[38] methyl esters. Since these materials all have negative rotations, it is assumed that the negatively rotating products of hydrogenation of **10** and **16A** also have the *S* configuration. Support for this assignment comes from the observation that each negatively rotating product gave a gas chromatogram in which the major enantiomer was slower eluting.

(iib) Hydrogenation Results. All of the chiral bis(phosphine) ligands used in this study form rhodium complex hydrogenation catalysts which give highly enantioselective hydrogenations of (*Z*)-amidocinnamic acids.[2-4] With the substrates employed in this work, however, there is a significant dependence of product ee on the nature of the phosphine used and also on the *E*/*Z* isomer ratio of the substrate. Each of the phosphines used forms a rhodium catalyst which converts both the *E* and *Z* isomers of each of the substrates used to the same enantiomer of the product. The substrate isomer which gives the better hydrogenation results depends upon the individual phosphine. In the case of some substrate–phosphine pairs, the *E* isomer gave a higher product ee than the *Z* isomer; in other cases, the *Z* isomer gave better results. Rate data have been omitted from Table I because in our experience the rates of hydrogenations carried out with such high catalyst loadings are notoriously difficult to measure precisely and reproducibly. We have made the qualitative observation, however, that (*Z*)-**10** was in all cases hydrogenated faster than (*E*)-**10**. On the other hand, (*Z*)-**16A**,**B** are hydrogenated more rapidly than (*E*)-**16A**,**B** with phosphines **19**–**22**, **28**, and **29**, while a reverse rate behavior is observed with phosphines **23**–**27**.[39]

Table I. Enantiomeric Excesses from Hydrogenations of Methyl (*E*)- and (*Z*)-2-Acetamido-3-alkylacrylates

	% ee (enantiomer)									
bis(phosphine)	Z-**10**	E-**10**	Z-**16A**	E-**16A**	Z-**16B**	E-**16B**	**17**	**18**	Z-**3**
(*S*,*S*)-diop (**19**)	29 (*S*)	67 (*S*)	30 (*S*)	49 (*S*)	18 (*S*)	54 (*S*)	56 (*S*)[a]		49 (*S*)[c]
(*R*,*R*)-3-CH$_3$diop (**20**)	36 (*R*)	72 (*R*)	40 (*R*)	68 (*R*)	*b*	*f*	58 (*R*)		
(*R*,*R*)-C4diop (**21**)	12 (*R*)	86 (*R*)	15 (*R*)	78 (*R*)	15 (*R*)	43 (*R*)	52 (*R*)		
(*S*,*S*)-bcop (**22**)	30 (*S*)	78 (*S*)	17 (*S*)	55 (*S*)	8 (*S*)	24 (*S*)	45 (*S*)		
(*R*)-prophos (**23**)	74 (*S*)	60 (*S*)	88 (*S*)	53 (*S*)	81 (*S*)	67 (*S*)	80 (*S*)		
(*S*,*S*)-chiraphos (**24**)	87 (*R*)	36 (*R*)	82 (*R*)	22 (*R*)	71 (*R*)	24 (*R*)	79 (*R*)		
(*R*,*R*)-norphos (**25**)			79 (*R*)	0					
(*S*,*S*)-phellanphos (**26**)			*f*	42 (*S*)					
(*R*,*R*)-nopaphos (**27**)			*f*	18 (*R*)					
(*R*,*R*)-dipamp (**28**)	86 (*S*)	94 (*S*)	96 (*S*)	95 (*S*)	65 (*S*)	78 (*S*)	95 (*S*)	55 (*S*)	96 (*S*)[d]
(*S*,*S*)-bppm (**29**)	37 (*R*)	82 (*R*)	80 (*R*)	75 (*R*)	57 (*R*)	72 (*R*)	82 (*R*)	0	95 (*R*)[e]

[a] Reference 30; 60% ee in benzene. [b] No hydrogenation at a substrate/catalyst ratio of 25. [c] Reference 30; hydrogenation in ethanol. [d] Reference 5. [e] Reference 31; hydrogenation in ethanol. [f] No reaction.

(32) In the range of substrate/catalyst ratios used, we found variations in product ee to be <2%.

(33) Goering, H. L.; Eikenberry, J. N.; Koermer, G. S. *J. Am. Chem. Soc.* **1971**, *93*, 5913–5914.

(34) The reduction product of (*Z*)-**16A** over the achiral catalyst RhCl[(C$_6$H$_5$)$_3$P]$_3$ was base-line resolved on this column. The computer-generated relative area measurements (50.30% R, 49.70% S; 0.60% ee R) give, we believe, an indication of the accuracy of the method.

(35) Supelco, Inc.

(36) Smart, N. A.; Young, G. T.; Williams, M. W. *J. Chem. Soc.* **1960**, 3902–3912.

(37) Wolf, J. P., III; Niemann, C. *Biochemistry* **1963**, *2*, 493–497.

(38) Applewhite, T. H.; Waite, H.; Niemann, C. *J. Am. Chem. Soc.* **1958**, *80*, 1465–1469.

(39) To our knowledge there has been only one other reported[40] example of ee and/or rate reversal. In ethanol, (*Z*)-α-benzamidocinnamic acid is reduced over dipamp ca. 20 times faster than the *E* isomer to give 94% ee (vs. 30% ee). In benzene, however, the rates are "similar", and the *Z* isomer gave only 16% ee vs. 84% ee from the *E* isomer.

The enantiomeric excess data given in Table I may be correlated with the bis(phosphine) structures as follows. Phosphines **19–22** are characterized by two achiral phosphorus centers connected by a chiral four carbon bridge having C_2 symmetry. All of these give a higher product ee in hydrogenations of (*E*)-**1** (R^1 = alkyl) compared to those of (*Z*)-**1** (R^1 = alkyl). Phosphines **23–27** are characterized by two achiral phosphorus centers connected by a chiral C_2 bridge. All of these give a higher product ee in hydrogenations of (*Z*)-**1** (R^1 = alkyl) compared to those of (*E*)-**1** (R^1 = alkyl). Phosphine **28**, "dipamp", contains two chiral phosphorus centers connected by an achiral two-carbon bridge. This unique phosphine gives excellent results with both (*E*)- and (*Z*)-**10**, **16A**, and **16B** *under identical conditions*. There is a slight preference for the *E* isomer of the substrate. Another unique phosphine is **29** in which two achiral phosphorus centers are connected by a chiral four-carbon bridge which has no symmetry elements. Again, marginally better results are obtained with *E* isomers of the substrate.

A few substrate comparisons are worthwhile. The substrate pair (*Z*)-**10** and (*E*)-**10** was studied first. The finding of a more enantioselective hydrogenation of an (*E*)-**1** derivative than of the corresponding *Z* isomer was at first attributed to coordination of ethereal oxygen to rhodium. The very similar hydrogenations obtained with **10** and **16A** make the suggestion of special coordination of oxygen to rhodium in the former unlikely. Comparison of **16A** and **16B** is also useful. The latter substrate was prepared in the expectation that the larger alkyl substituent (i.e., isopropyl vs. *n*-propyl) would interfere more with coordination to rhodium, resulting in lower enantioselectivities in hydrogenations. The P–C_4–P-type phosphines **19–22** did in fact give only modest enantioselectivities in **16B** hydrogenations, but results obtained by using P–C_2–P phosphines **23** and **24** to form catalysts for **16A** and **16B** hydrogenations were substantially identical. Substrate **16B** did give a lower ee of product than **16A** in hydrogenations catalyzed by Rh–**28**.

(iic) Deuteriations. In hydrogenations of the type described in this paper, it is not obvious a priori if the product ee's result from the apparent reaction or from *Z,E* substrate isomerization which occurs before or during hydrogenation. It has been shown[40,41] that isomerization can indeed occur during hydrogenation of (*E*)-α-amidocinnamic acids. It was also of interest to learn whether double bond migration, particularly of substrates (*Z*)-**10** and (*E*)-**10**,[42] was occurring prior to hydrogenation. To check these points, we subjected (*Z*)-**10** and (*E*)-**10** to deuteriation[40,41] catalyzed by Rh–dipamp in methanol. If neither double bond isomerization or migration takes place, (*Z*)-**10** will be reduced to (2*S*,3*S*)-**30** while (*E*)-**10** will yield

Z-**10** 2S,3S-**30**

E-**10** 2S,3R-**31**

(2*S*,3*R*)-**31**. The C_3 protons of **30** and **31** are diastereotopic and thus should be distinguishable by ^{1}H NMR. In fact, there were some differences in the ^{1}H NMR spectra of the hydrogenation products from (*Z*)-**10** and (*E*)-**10**, but the crucial C_3-proton signal was partially obscured by the acetyl methyl signal. The addition, however, of an equimolar amount of the achiral shift reagent Eu(fod)$_3$[43] caused the C_{3S} proton of **30** to shift from $\delta \sim 2.0$ to 2.85 while the C_{3R} proton of **31** shifted to δ 3.45. By means of this analysis, it was found that the hydrogenation of (*Z*)-**10** gave product containing ≤5% (estimated limit of detection) of **31** while (*E*)-**10** similarly gave material containing ≤5% of **30**. *E,Z* double bond isomerization was thus limited to this value.

The possibility of double bond migration was ruled out by failure to observe a C_2-proton signal in the spectra of the deuteriation products of (*Z*)- or (*E*)-**10**. Similarly, in each spectrum, the C_4 protons appeared as a clean doublet integrating for two protons.

Discussion

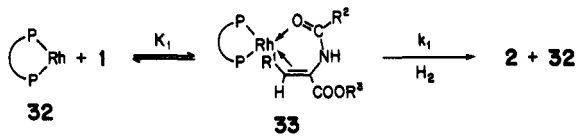
The results presented in this paper indicate that enantioselective hydrogenation of 2-amido-3-alkylacrylates affords a potentially practical synthetic method, subject to availability of the acrylates. In these hydrogenations it is possible to find conditions in many cases where good enantioselectivities are obtained with either pure isomer of the substrate. In at least some instances both *E* and *Z* isomers are converted to high ee's of the same product enantiomer such that in a synthetic sequence it would be unnecessary to separate geometric isomers of the substrate. We did not study the rates of these reactions in detail. Our essentially qualitative data suggest, however, that at least some phosphine–substrate combinations may give hydrogenation reactions which are fast enough to allow optimization for low catalyst loadings.

There are some unusual features of our results on hydrogenations of 2-amido-3-alkylacrylates. Perhaps the most unusual observation is that with phosphines **19–22**, hydrogenations of (*E*)-**10**, (*E*)-**16A**, and (*E*)-**16B** are both slower and more enantioselective than hydrogenations of the corresponding *Z* isomers. The hydrogenations of (*Z*)-**1** (R^1 = aryl) are, conversely, more rapid and more highly enantioselective than hydrogenations of the corresponding *E* isomers under comparable conditions. When phosphines **23–27** are used, the (*Z*)-**1** (R^1 = alkyl) isomers are hydrogenated more enantioselectively and, with the exception of (*Z*)-**10**, more slowly than the *E* isomers. To the best of our knowledge, comparative hydrogenations of (*Z*)- and (*E*)-**1** (R^1 = aryl) with these phosphines have not yet been reported. A striking observation is that (*E*)-**1** (R^1 = alkyl) compounds appear to be generally superior substrates compared to (*E*)-**1** (R^1 = aryl) compounds. This is illustrated clearly by the results with Rh–dipamp catalysts.

Our observations on hydrogenations of 2-amido-3-alkylacrylates vs. 2-amido-3-arylacrylates appear to be consistent with the present understanding of enantioselective hydrogenations catalyzed by rhodium–chiral phosphine complexes.[44] It is now generally believed that in these hydrogenations the rate-limiting and hence enantioselec-

(40) Koenig, K. E.; Knowles, W. S. *J. Am. Chem. Soc.* **1978**, *100*, 7561–7564.
(41) Detellier, C.; Gelbard, G.; Kagan, H. B. *J. Am. Chem. Soc.* **1978**, *100*, 7556–7561.
(42) Triethylamine–pyridine-induced migration of the double bond in very closely related compounds is known; cf. ref 13.
(43) Eisentraut, K. J.; Sievers, R. E. *J. Am. Chem. Soc.* **1965**, *87*, 5254–5256.
(44) See ref 31, 40, 41 and the following: (a) Brown, J. M.; Chaloner, P. A.; Glaser, R.; Geresh, S. *Tetrahedron* **1980**, *36*, 815–825. (b) Brown, J. M.; Chaloner, P. A. *J. Chem. Soc., Chem. Comm.* **1980**, 344–346. (c) Chan, A. S. C.; Halpern, J. *J. Am. Chem. Soc.* **1980**, *102*, 838–840. (d) Chan, A. S. C.; Pluth, J. J.; Halpern, J. *Ibid.* **1980**, *102*, 5952–5954. (e) Koenig, K. E.; Bachman, G. L.; Vineyard, B. D. *J. Org. Chem.* **1980**, *45*, 2362–2365.

tivity-determining process is addition of dihydrogen to a Rh(I) substrate complex, **33**, in which the substrate acts



32 **33**

as a bidentate ligand with the coordination geometry indicated. In considering possible consequences of the above mechanism, it is useful to remember that the simplest substrate, i.e., **17**, which is **1** (R^1 = H), and the corresponding free acid (2-acetamidoacrylic acid) can be hydrogenated with fast rates and high enantioselectivities. Some R^1 = aryl substituents do give (*Z*)-**1** derivatives which are better substrates than **17** (generally faster rates and a wider range of rhodium–phosphine catalysts which give good rates and enantioselectivities). The (*E*)-**1** isomers containing the same R^1 = aryl substituents are generally poor substrates as measured both by rates and enantioselectivities in hydrogenations. This has been ascribed[45] to steric hinderance of the *E* R^1-group-to-olefin coordination. Our new results with (*Z*)-**1** and (*E*)-**1** containing R^1 = alkyl substituents tend to support this conclusion. The more flexible R^1 = alkyl vs. R^1 = aryl group would be expected to interfere less with coordination when in the less favorable (*E*)-**1** geometry. It should be noted, though, that in hydrogenations of **1** (R^1 = alkyl) faster rates do not always correlate with higher enantioselectivities as would be expected if R^1 exerted strong steric hindrance to coordination.

Experimental Section

General Methods. Melting points were taken on a Thomas-Hoover capillary melting point apparatus and are not corrected.

A Waters Associates Prep LC/System 500 with a PrePak-500 compression chamber and PrePak-500/silica cartridges was used for preparative high-pressure liquid chromatography (HPLC).

Gas chromatographic analyses for enantiomeric excess (ee) were obtained on a Hewlett-Packard HP-5710A gas chromatograph equipped with a hydrogen flame ionization detector and operated isothermally at 125 °C. A 1 m × 4 mm column of 5% SP-300 on 100/120-mesh Supelcoport[35] was used with a nitrogen carrier gas flow rate of 30 mL/min.

Methyl 2-Acetamido-4-methoxybutanoate (8). Sodium ethoxide solution was prepared in the usual manner under nitrogen from 168.8 g (7.34 mol) of sodium and 4.84 L of absolute ethanol. The solution was cooled to 20 °C, and 1.60 kg (7.37 mol) of diethyl acetamidomalonate was added in one portion. The mixture was stirred for 5 min, treated in one portion with 1.208 kg (8.69 mol) of 2-methoxyethyl bromide, and heated under reflux overnight. The cooled suspension was stripped of solvent at 70 mm to a thick pasty mass which was slurried with methylene chloride and filtered. The filtrate (pH 7) was washed with brine, saturated $NaHCO_3$ solution, and brine. The aqueous washes were extracted in turn with methylene chloride, and the combined organic solutions were dried (Na_2SO_4) and stripped of solvent to give crude diethyl acetamido(2-methoxyethyl)malonate (**6**) as 1.973 kg of orange-brown oil. An analytical sample was prepared by subjecting a portion of a similarly prepared lot to chromatography on preparative layer silica gel plates with 10:10:0.4 ethyl acetate–methylene chloride–ethanol as eluant. The desired material (R_f ~0.5) was extracted with chloroform, the extract concentrated in vacuo, and the residue distilled in a Kugelrohr apparatus: colorless oil, bp 140–145 °C; IR ($CHCl_3$) 3400, 1735, 1675, 1490, 1370, 1300 cm^{-1}; NMR ($CDCl_3$) δ 1.25 (t, 6 *J* = 6 Hz, 2-OCH_2CH_3), 2.03 (s, 3, $COCH_3$), 2.60 (t, 2, *J* = 6 Hz, CH_2CH_2O), 3.19 (s, 3, OCH_3), 3.37 (t, 2 *J* = 6 Hz, CH_2OCH_3), 4.20 (q, 4, *J* = 6 Hz, 2 OCH_2CH_3), 6.91 (br, 1 NH); mass spectrum, *m/e* 275 (M^+), 244, 230, 216, 202. Anal. $C_{12}H_{21}NO_6$.

A mixture of the crude diester **6** and 9.6 L of 2 N sodium hydroxide solution was stirred for 1 h at ambient temperature and then for 1 h under reflux. The mixture was cooled to 20 °C and brought to pH 3 by the addition of ca. 2.80 L of 4 N hydrochloride acid. The solution was heated under reflux for 3 h and cooled. A large paddled, heavy-duty stirrer was put in the flask, and the solvent was removed by distillation at ca. 1 mm and 50–60 °C until stirring of the viscous residue (acid **7** and salts) could no longer be maintained. To this residue was added 7.6 L of acetone, 981.25 mL (2.236 kg, 15.75 mol) of methyl iodide, and 2.198 kg (15.90 mol) of potassium carbonate. The heterogeneous mixture was stirred rapidly, heated under reflux overnight, cooled, and filtered. The filtrate was stripped of solvent, and the residue was taken up in methylene chloride, washed with brine, and treated with Norite A charcoal and sodium sulfate. Filtration through Celite and solvent removal gave 941 g of crude **8** as a clear yellow oil. Crystallization of this material from 4.95 L of ether, finally at −20 °C, gave 779 g (56%) of the desired product **8** as a granular white solid, mp 62.5–64.5 °C. An analytical sample was prepared by crystallization of similarly prepared material from ether/petroleum ether (bp 30–60 °C): mp 61–63 °C; IR ($CHCl_3$) 3430, 1745, 1675, 1510 cm^{-1}; NMR ($CDCl_3$) δ 1.99 (s, 3, $COCH_3$), 2.04 (m, 2, CH_2CH_2O), 3.27 (s, 3, CH_2OCH_3), 3.42 (t, 2, *J* = 6 Hz, CH_2OCH_3), 3.70 (s, 3, $COOCH_3$), 4.64 (m, 1, CH_2CH_2CH), 6.53 (br, 1, NH); mass spectrum, *m/e* 189 (M^+), 131, 130, 99, 88. Anal. $C_8H_{15}NO_4$.

Methyl (Z)-2-Acetamido-4-methoxybut-2-enoate ((Z)-10). In a foil-wrapped flask was stirred a mixture of 949.5 g (5.02 mol) of methyl 2-acetamido-4-methoxybutanoate (**8**) and 4.75 L of carbon tetrachloride for 15 min and then treated, over 15 min, with 656.5 mL (597.5 g, 5.50 mol) of *tert*-butyl hypochlorite. The mixture was stirred overnight to complete formation of the *N*-chloro compound **9**. Solvent removal from a similar preparation gave a colorless oil: NMR ($CDCl_3$) δ 2.2 (m, 2 CH_2CH_2O), 2.3 (s, 3, $COCH_3$), 3.33 (s, 3, CH_2OCH_3), 3.4 (m, 2, CH_2OCH_3), 3.76 (s, 3, $COOCH_3$), 5.33 (m, 1, CH_2CH_2CH). The solution of **9** was cooled to 0 °C and treated with 678 g (6.04 mol) of 1,4-diazabicyclo[2.2.2]octane in small portions over 50 min as the temperature rose to 15 °C. The mixture was stirred overnight without cooling and filtered. The cloudy filtrate was poured onto 1.9 kg of E. Merck 70–230-mesh silica gel and eluted with 19.0 L of ethyl acetate. Solvent removal gave 881 g of a mixture of (*Z*)-**10** and (*E*)-**10**. This mixture was taken up in 1.5 L of ether at reflux. The solution was seeded with (*Z*)-**10**, cooled to −20 °C, and diluted with 750 mL of petroleum ether (bp 30–60 °C). The solid was collected by filtration and dried to give 600 g of material, mp 58–64 °C. This material was taken up in 3.5 L of ether at reflux. The slightly turbid solution was filtered through Celite and concentrated by distillation until crystallization began. The suspension was cooled to −20 °C and filtered, and the solid was dried to give 561 g (60%) of product (*Z*)-**10** as white granules, mp 62–64.5 °C. Crystallization of similarly prepared material from ether/petroleum ether (bp 30–60 °C) yielded the analytical sample: mp 60–61 °C; UV max (2-PrOH) 226 nm (ε 7500); IR ($CHCl_3$) 3410, 1720 (sh), 1695, 1500 cm^{-1}; NMR ($CDCl_3$) δ 2.14 (s, 3, $COCH_3$), 3.36 (s, 3, CH_2OCH_3), 3.8 (s, 3, $COOCH_3$), 4.1 (d, 2, *J* = 5.5 Hz, $CHCH_2OCH_3$), 6.70 (t, 1, *J* = 5.5 Hz, $=CHCH_2OCH_3$), 7.5 (br, 1, NH); mass spectrum, *m/e* 187 (M^+), 155, 144, 142, 130, 114, 110, 84. Anal. $C_8H_{13}NO_4$.

The crystal data for (*Z*)-**10** are given in Table II. The intensity data were measured on a Hilger-Watts diffractometer by a θ–2θ scan technique. A crystal approximately 0.05 × 0.35 × 0.45 mm in size was used for data collection. Of the 1967 accessible reflections with θ < 76°, 1641 had intensities which were significantly greater than background [$I > 2.5\sigma(I)$]. The structure was solved

Table II. Crystal Data for (*Z*)-10

formula	$C_8H_{13}NO_4$	*a*	13.566 (6) Å
fw	187.20	*b*	8.236 (6) Å
space group	$P2_1/c$	*c*	9.358 (6) Å
d_{calcd}	1.261 g cm^{-3}	β	109.46 (3)°
μ (Cu Kα)	8.7 cm^{-1}	*Z*	4

(45) Koenig, K. E.; Sabacky, M. J.; Bachman, G. L.; Christopfel, W. C.; Barnstorff, H. D.; Friedman, R. B.; Knowles, W. S.; Stults, B. R.; Vineyard, B. D.; Weinkauff, D. J. *Ann. N.Y. Acad. Sci.* **1980**, *333*, 16–22.

by a multiple-solution procedure[46] and was refined by full-matrix least-squares methods. All hydrogens were found on a difference Fourier map calculated after preliminary refinement of the heavier atoms. In the final refinement, anisotropic thermal parameters were used for all the atoms except the hydrogens. The hydrogen atoms were included in the structure factor calculations, but their parameters were not refined. The final discrepancy index was $R = 0.057$ for the 1641 observed reflections.

Methyl (*E*)-2-Acetamido-4-methoxybut-2-enoate ((*E*)-10). The mother liquors from the initial crystallization of (*Z*)-**10** were stripped of solvent and purified by HPLC. An initial pass in 50-g lots with 2:1 ethyl acetate–hexane removed materials other than (*Z*)-**10** and (*E*)-**10**. Separation of these compounds was effected in 10-g batches with the same solvent pair by using two recycles. A clean peak separation was not observed; the more polar fractions, which were shown by NMR to contain only the desired *E* isomer, (*E*)-**10**, were combined [1.5–2 g of (*E*)-**10**/10-g run]. A total of 19.0 g of material was thus isolated. This product crystallized upon being allowed to stand at −20 °C. It was triturated with petroleum ether (bp 30–60 °C), filtered, and dried to give 17.2 g of (*E*)-**10** as a glassy, white solid, mp 33–36 °C. The material had a tendency to decompose and was thus stored under N_2 at −20 °C. The analytical sample was similarly isolated by HPLC but was not crystallized: UV max (C_2H_5OH) 236 nm (ε 6280); IR ($CHCl_3$) 3450, 3410, 1710 (sh), 1690, 1650, 1517 cm^{-1}; NMR ($CDCl_3$) δ 2.13 (s, 3, $COCH_3$), 3.39 (s, 3, $=CHCH_2OCH_3$), 3.87 (s, 3, $COOCH_3$), 4.44 (d, 2, J = 6 Hz, $=CHCH_2OCH_3$), 7.30 (t, 1, J = 6 Hz, $=CHCH_2OCH_3$), 7.46 (br, 1, NH); mass spectrum, m/e 187 (M^+), 155, 144, 142, 130, 114, 110, 84. Anal. $C_8H_{13}NO_4$.

Methyl 2-Oxohexanoate (13A). A solution of 200 g (1.69 mol) of dimethyl oxalate in 2.3 L of methylene chloride was cooled to −25 °C. Tri-*n*-butylaluminum (2.26 L, 24.6% solution in heptane, Texas Alkyls) was added over 1 h at a rate such that the temperature remained at −20 to −25 °C. The orange-yellow reaction mixture was stirred at −25 °C for 1 h, cooled to −30 °C, and hydrolyzed by the addition of 400 mL of 20% H_2SO_4 at a rate such that the temperature remained ≤−20 °C. The aqueous layer was separated and extracted with methylene chloride. The combined organic solutions were dried over $MgSO_4$, stripped of solvent, and distilled through a 10-cm Vireux column to give 163.0 g (67%) of keto ester **13A** as a light yellow oil, bp 75–80 °C (12 mm) (lit.[19] bp 48–52 °C (12 mm)). Although this material was a ca. 4:1 mixture with dimethyl oxalate, as determined by GC, it was entirely suitable for the subsequent reaction.

Methyl (*Z*)-2-(Chloroacetamido)hex-2-enoate ((*Z*)-14A) and Methyl (*E*)-2-(Chloroacetamido)hex-2-enoate ((*E*)-14A). A mixture of 163.0 g (1.13 mol) of keto ester **13A** (containing ca. 20% dimethyl oxalate), 158.0 g (1.69 mol) of 2-chloroacetamide, 58.4 mL (0.68 mol) of phosphorus oxychloride, and 2.0 L of toluene was heated at reflux under N_2, with azeotropic removal of H_2O, for 16 h. The dark brown reaction mixture was washed with H_2O (4 × 250 mL) and 100 mL of saturated $NaHCO_3$. The combined aqueous washes were saturated with NaCl and extracted with 250 mL of toluene. The combined organic solutions were dried over $MgSO_4$ and stripped of solvent to give 198.4 g of orange-brown oil. This mixture was separated by HPLC with 9:1 hexane–ethyl acetate to give, in order of elution, 35.9 g (22%) of recovered keto ester **13A**, 46.9 g (19%) of *E* amide (*E*)-**14A** as a yellow oil and 51.3 g (21%) of *Z* amide (*Z*)-**14A** as a white solid, mp 59–61 °C.

A similarly prepared sample of *Z* amide (*Z*)-**14A** was crystallized from ether–hexane to give the analytical sample: white solid; mp 60–61 °C; IR ($CHCl_3$) 3400, 1720, 1693, 1660, 1510 cm^{-1}; NMR ($CDCl_3$) δ 0.94 (t, 3, CH_2CH_3), 1.51 (m, 2, CH_2CH_3), 2.15 (q, 2, CH_2CH_2), 3.79 (s, 3, $COOCH_3$), 4.14 (s, 2, CH_2Cl), 6.79 (t, 1, J = 7 Hz, =CH), 7.78 (s, 1, NH); mass spectrum, m/e 219 (M^+), 187, 159, 152. This compound is a skin irritant. Anal. $C_9H_{14}ClNO_3$.

A similarly prepared sample of *E* amide (*E*)-**14A** was distilled in a Kugelrohr apparatus to give the analytical sample: colorless liquid; bp 80–90 °C (0.5 mm); IR ($CHCl_3$) 3405, 3365, 1734, 1705, 1680, 1530 cm^{-1}; NMR ($CDCl_3$) δ 0.94 (t, 3, CH_2CH_3), 1.49 (m, 2, CH_2CH_3), 2.57 (q, 2, CH_2CH_2), 3.84 (s, 3, $COOCH_3$), 4.09 (s, 2, CH_2Cl), 7.11 (t, 1, J = 8 Hz, =CH), 8.49 (s, 1, NH); mass spectrum, m/e 219 (M^+), 187, 159, 152. This compound is a skin irritant and is unstable at 20 °C.

Methyl (*Z*)-2-(Iodoacetamido)hex-2-enoate ((*Z*)-15A). A mixture of 30.3 g (0.139 mol) of *Z* chloro amide (*Z*)-**14A**, 45.8 g of KI, and 2.0 L of acetone was heated at reflux under N_2 for 3 h, cooled, filtered, and stripped of solvent. The residual brown oil was triturated with 200 mL of ether and filtered. The filtrate was washed with 1% $Na_2S_2O_3$ and dried over $MgSO_4$. The solvent was removed, and the residue was crystallized from ether–hexane to give 33.5 g (78%) of the desired iodoamide (*Z*)-**15A** as a light white-yellow solid, mp 69–71 °C. The analytical sample was similarly prepared: light yellow solid; mp 64–66 °C; IR ($CHCl_3$) 3420, 1718, 1695, 1660, 1503 cm^{-1}; NMR ($CDCl_3$) δ 0.93 (s, 3, CH_2CH_3), 1.50 (m, 2, CH_2CH_3), 2.17 (q, 2, CH_2CH_2), 3.78 (s, 3, $COOCH_3$), 3.80 (s, 2, CH_2I), 6.76 (t, 1, J = 7 Hz, =CH), 7.36 (s, 1, NH); mass spectrum, m/e 280, 169, 142, 141. This compound is a skin irritant. Anal. $C_9H_{14}INO_3$.

Methyl (*E*)-2-(Iodoacetamido)hex-2-enoate ((*E*)-15A). In the manner described above the *E* chloro amide (*E*)-**14A** was converted to *E* iodo amide (*E*)-**15A**. This compound is quite unstable and is a skin irritant, so the crude material, obtained in 92% yield, was used without purification. An analytical sample was prepared by filtration of a small amount of this material through silica gel with ether: light yellow oil; IR ($CHCl_3$) 3395, 1777, 1738, 1708, 1683 cm^{-1}; NMR ($CDCl_3$) δ 0.94 (s, 3, CH_2CH_3), 1.49 (m, 2, CH_2CH_3), 2.54 (q, 2, CH_2CH_2), 3.79 (s, 2, CH_2I), 3.84 (s, 3, $COOCH_3$), 7.01 (t, 1, J = 8 Hz, =CH), 8.03 (s, 1, NH); mass spectrum, m/e 280, 184, 169. Anal. $C_9H_{14}INO_3$.

Methyl (*Z*)-2-Acetamidohex-2-enoate ((*Z*)-16A). A mixture of 75.4 g (0.242 mol) of *Z* iodo amide (*Z*)-**15A**, 158.4 g (2.42 mol) of zinc dust, and 1.5 L of methanol was stirred at 20 °C overnight and filtered through Celite. The filtrate was stripped of solvent, and the residual glass was taken up in ethyl acetate, washed with 1 N HCl and 1% $Na_2S_2O_3$, and dried over $MgSO_4$. The solution was treated with Norite A charcoal, filtered through Celite, and stripped to give 28.7 g of yellow oil. Crystallization from ether–hexane gave 26.5 g (60%) of (*Z*)-**16A** as a white solid, mp 52–53 °C. The analytical sample was similarly prepared: white solid; mp 55–56 °C; IR ($CHCl_3$) 3420, 1715, 1695, 1660 cm^{-1}; NMR ($CDCl_3$) δ 0.92 (t, 3, CH_2CH_3), 1.48 (m, 2, CH_2CH_3), 2.10 (s, 3, $COCH_3$), 2.14 (q, 2, CH_2CH_2), 3.76 (s, 3, $COOCH_3$), 6.69 (t, 1, J = 8 Hz, =CH), 7.15 (s, 1, NH); mass spectrum, m/e 185 (M^+), 167, 153, 142, 114, 82. Anal. $C_9H_{15}NO_3$.

Methyl (*E*)-2-Acetamidohex-2-enoate ((*E*)-16A). In the manner described above, 61.3 g of *E* iodo amide (*E*)-**15A** was reduced to 25.2 g of yellow oil. This material was purified by HPLC (1:1 ethyl acetate–hexane as eluant) to give 21.7 g of pale yellow oil. Distillation in a Kugelrohr apparatus gave 18.8 g (56%) of colorless oil, bp 80–90 °C (0.5 mm). The analytical sample was similarly prepared: colorless oil; bp 85 °C (0.5 mm); IR ($CHCl_3$) 3445, 3410, 1730, 1703, 1682 cm^{-1}; NMR ($CDCl_3$) δ 0.92 (t, 3, CH_2CH_3), 1.48 (m, 2, CH_2CH_3), 2.06 (s, 3, $COCH_3$), 2.50 (q, 2, CH_2CH_2), 3.81 (s, 3, $COOCH_3$), 6.88 (t, 1, J = 8 Hz, =CH), 7.62 (s, 1, NH); mass spectrum, m/e 185 (M^+), 153, 142, 114. This compound is unstable at 20 °C. Anal. $C_9H_{15}NO_3$.

Methyl (*Z*)-2-Acetamido-4-methylpent-2-enoate ((*Z*)-16B) and Methyl (*E*)-2-Acetamido-4-methylpent-2-enoate ((*E*)-16B). These known[16] compounds were prepared from keto ester **13B**[18] by the methods described above for (*Z*)-**16A** and (*E*)-**16A**.

Methyl (*Z*)-2-(Chloroacetamido)-4-methylpent-2-enoate ((*Z*)-14B): white solid; bp 75 °C (0.5 mm); mp 67–68 °C; NMR ($CDCl_3$) δ 6.61 (=CH) [lit.[16] mp 68.5–69 °C; NMR ($CDCl_3$) δ 6.62]. Anal. $C_9H_{14}ClNO_3$.

Methyl (*E*)-2-(Chloroacetamido)-4-methylpent-2-enoate ((*E*)-14B): oil, bp 75 °C (0.5 mm); NMR ($CDCl_3$) δ 6.92 (=CH) [lit.[16] bp 133–135 °C (1 mm); NMR ($CDCl_3$) δ 6.94]. Anal. $C_9H_{14}ClNO_3$.

Methyl (*Z*)-2-(Iodoacetamido)-4-methylpent-2-enoate ((*Z*)-15B): unstable oil; NMR ($CDCl_3$) δ 6.58 (=CH) [lit.[16] mp 70–71 °C; NMR ($CDCl_3$) δ 6.55].

Methyl (*E*)-2-(Iodoacetamido)-4-methylpent-2-enoate ((*E*)-15B): unstable oil; NMR ($CDCl_3$) δ 6.87 (=CH) [lit.[16] mp 64–65 °C; NMR ($CDCl_3$) δ 6.81].

Methyl (*Z*)-2-Acetamido-4-methylpent-2-enoate ((*Z*)-16B): white solid; mp 73–74 °C; NMR ($CDCl_3$) δ 6.51 (=CH) [lit.[16] syrup; NMR ($CDCl_3$) δ 6.52]. Anal. $C_9H_{15}NO_3$.

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Methyl (*E*)-2-Acetamido-4-methylpent-2-enoate ((*E*)-16B): white solid, bp 80 °C (0.5 mm); mp 40–41 °C; NMR ($CDCl_3$) δ 6.82 (=CH) [lit.[16] syrup; NMR ($CDCl_3$) δ 6.66]. Anal. $C_9H_{15}NO_3$.

Asymmetric Hydrogenations. (4*S*,5*S*)-*trans*-4,5-Bis[(diphenylphosphino)methyl)]-2,2-dimethyl-1,3-dioxolane[10] [(*S*,*S*)-diop, **19**] was purchased from Strem Chemical Co. (4*R*,5*R*)-*trans*-4,5-Bis[[bis(3-methylphenyl)phosphino]methyl]-2,2-dimethyl-1,3-dioxolane[23] [(*R*,*R*)-3-CH_3diop, **20**], (2*S*,3*S*)-*trans*-2,3-bis[(diphenylphosphino)methyl]bicyclo[2.2.2]octane[23] [(*S*,*S*)-bcop, **22**], (1*R*,2*R*)-*trans*-1,2-bis[(diphenylphosphino)methyl]cyclobutane[24] [(*R*,*R*)-C4diop, **21**] and (2*S*,4*S*)-*N*-[(*tert*-butyloxy)carbonyl]-2-[(diphenylphosphino)methyl]-4-(diphenylphosphino)pyrrolidine[29] [(*S*,*S*)-bppm, **29**] were prepared by the literature methods cited. (2*R*,3*R*)-*trans*-2,3-Bis[(diphenylphosphino)methyl]bicyclo[2.2.1]hept-5-ene[25] [(*R*,*R*)-norphos, **25**] was a gift from Professor H. Brunner (Regensburg University). For these six ligands (bicyclo[2.2.1]hepta-2,5-diene)chlororhodium(I) dimer[47] and (cycloocta-1,5-diene)chlororhodium(I) dimer[48] were used interchangeably as rhodium sources. (*R*,*R*)-Dipamp[28] (**28**) was obtained as a gift of (cycloocta-1,5-diene)-[(*R*,*R*)-1,2-ethanediylbis[(*o*-methoxyphenyl)phenylphosphine]]-rhodium tetrafluoroborate from Dr. W. S. Knowles (Monsanto Chemical Co.). (*R*)-1,2-Bis(diphenylphosphino)propane[7] [(*R*)-prophos, **23**] and (2*S*,3*S*)-bis(diphenylphosphino)butane[6] [(*S*,*S*)-chiraphos, **24**] were purchased from Reaction Design Corp. and converted into their rhodium norbornadiene perchlorate complexes by the method of Schrock and Osborn.[49] (*S*,*S*)-Phellanphos[26,27] (**26**) and (*R*,*R*)-nopaphos[27] (**27**) were obtained as gifts of their rhodium cyclooctadiene pentafluorophosphate complexes from Professor H. Kagan (University of Paris, South). Methanol was purified by stirring with Raney nickel under 40 psi of H_2 at 23 °C for 8 h followed by filtration under argon through a fine-porosity filter.

In a typical hydrogenation, a 3-oz. glass aerosol compatibility vessel (Fischer and Porter Co.) was charged under argon with 1.0 g of enamide (*Z*)-**16A** and 2.5 mL of catalyst solution prepared separately from 12 mg of [(norbornadiene)rhodium chloride]$_2$ and 28 mg of bppm (**29**) in 10 mL of methanol. This gave a substrate/catalyst weight ratio of 100/1. The vessel was then thoroughly flushed with H_2 and charged with H_2 to a pressure of 49 psi as determined by using a 0–80 psi pressure gauge. The bright yellow solution was stirred at room temperature until hydrogen uptake, as measured by the pressure drop, ceased (uptake = 15.5 psi of H_2 over 9 min). The vessel was vented, and the solvent was removed on a rotary evaporator. The residue was distilled in a Kugelrohr apparatus at 90–100 °C (0.1 mm) to give 1.0 g of colorless solid: $[\alpha]_D^{25}$ +24.6° (*c* 1.0, CH_3OH); 80% ee (GC).

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Registry No. 5, 1068-90-2; **6**, 75647-46-0; **7**, 57906-57-7; **8**, 75647-47-1; **9**, 75647-48-2; (*Z*)-**10**, 75647-42-6; (*E*)-**10**, 75647-43-7; **11**, 553-90-2; **13A**, 6395-83-1; **13B**, 3682-43-7; (*Z*)-**14A**, 79357-40-7; (*E*)-**14A**, 79357-41-8; (*Z*)-**14B**, 63861-79-0; (*E*)-**14B**, 63822-73-1; (*Z*)-**15A**, 79357-42-9; (*E*)-**15A**, 79357-43-0; (*Z*)-**15B**, 66299-18-1; (*E*)-**15B**, 66299-17-0; (*Z*)-**16A**, 79357-44-1; (*E*)-**16A**, 79357-45-2; (*Z*)-**16B**, 66299-28-3; (*E*)-**16B**, 66299-27-2; **17**, 35356-70-8; **18**, 39239-88-8; **19**, 37002-48-5; **20**, 57221-95-1; **21**, 55629-68-0; **22**, 79390-69-5; **23**, 67884-32-6; **24**, 64896-28-2; **25**, 71042-54-1; **26**, 72021-47-7; **27**, 79357-46-3; **28**, 55739-58-7; **29**, 61478-28-2; *N*-acetyl-*O*-methyl-L-homoserine, methyl ester, 79357-47-4; *N*-acetyl-*O*-methyl-D-homoserine, methyl ester, 79357-48-5; *N*-acetyl-L-norleucine, methyl ester, 3618-99-3; *N*-acetyl-D-norleucine, methyl ester, 79357-49-6; *N*-acetyl-L-leucine, methyl ester, 1492-11-1; *N*-acetyl-D-leucine, methyl ester, 35799-87-2; *N*-acetyl-L-alanine, methyl ester, 3619-02-1; *N*-acetyl-D-alanine, methyl ester, 19914-36-4; *N*-acetyl-L-valine, methyl ester, 1492-15-5; Rh, 7440-16-6.

Supplementary Material Available: Tables of final atomic and anisotropic thermal parameters, bond lengths, and bond angles for (*Z*)-**10** (3 pages). Ordering information is given on any current masthead page.

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