In summary, we have developed a novel enantioselective synthesis of α-amino acids in either (*S*) or (*R*) (unnatural) form (depending on the use of catalyst **1** or its enantiomer), which is broad in scope, simple in application, and advantageous for many α-amino acids of interest in chemistry, biology, and medicine.[9]

Supplementary Material Available: Experimental procedures, spectral data, and ^{1}H NMR spectra for trichloromethyl alcohols, α-azido acids, and α-amino acids (25 pages). Ordering information is given on any current masthead page.

(9) This research was assisted financially by generous grants from the National Institutes of Health and the National Science Foundation.

Rates of Catalytic Hydrogenation Estimated Spectroscopically through Enhanced Resonances

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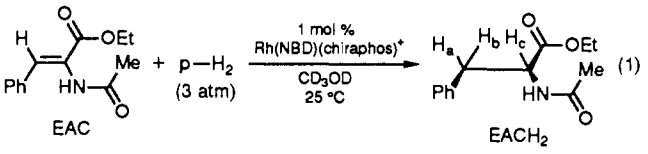
Received August 8, 1991

Parahydrogen-induced polarization (PHIP) can arise when H_2 enriched in the para state is added to substrate while maintaining spin correlation between the added protons, leading to unusual intensities in product NMR spectra.[1-7] Qualitative understanding of PHIP has led to its use as a mechanistic probe of whether hydrogenation proceeds by pairwise transfer of the component atoms of H_2. In this report, we describe a quantitative analysis of polarization behavior and its utility in determining *r*ates *o*f *c*atalytic *h*ydrogenation *e*stimated *s*pectroscopically *t*hrough *e*nhanced *r*esonances (ROCHESTER).

The system chosen for analysis is the asymmetric hydrogenation of ethyl (*Z*)-α-acetamidocinnamate (EAC) using [Rh(NBD)(chiraphos)]BF_4 (**1**) as the catalyst. The choice of this system was based on the following facts: (a) it is well understood mechanistically, and (b) in hydrogenations utilizing RhP_2^+ catalysts (P_2 = diphos or dipamp), no para to ortho H_2 conversion occurs while substrate is present.[8] The latter fact precludes simple H_2 oxidative addition and reductive elimination for converting para-enriched H_2 to normal H_2 when excess EAC is present. In a typical experiment, a 210 mM solution of EAC was hydrogenated under ca. 3 atm of para-enriched H_2 (eq 1).[9] Prior to reaction the sample was stored at 77 K. Rapid thawing in a 25 °C water bath and shaking of the sample followed by insertion into the probe led to data acquisition within 60 s of initiating the reaction.



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(9) Parahydrogen was enriched to ca. 50 mol % by immersing a 1-L flask containing iron(III) oxide on silica in liquid N_2 up to its neck. H_2 was added while 730 mm ambient hydrogen pressure was maintained. In this manner, 3-4 atm of para-enriched hydrogen could be produced.

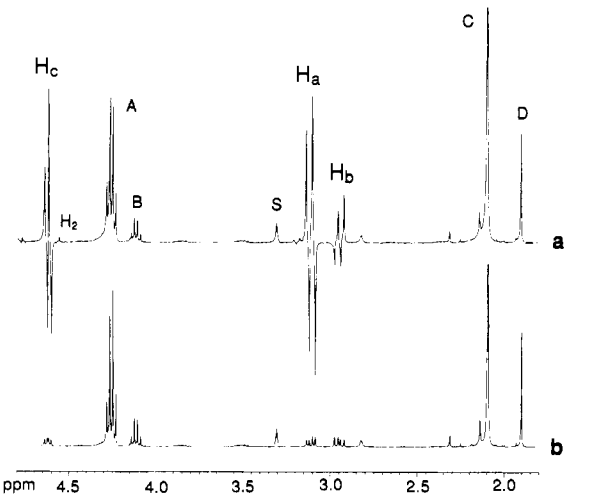

Figure 1. PHIP in the hydrogenation of EAC with Rh(chiraphos)$^+$ 60 s after shaking and insertion into the probe (a). Resonances H_a, H_b, and H_c are assigned in the text. Resonances A and B are ethyl resonances of EAC and $EACH_2$, C and D are methyl acyl resonances of EAC and $EACH_2$, and S is from CHD_2OD in CD_3OD solvent. (b) Same sample ca. 450 s later.

Table I. Kinetic Data for the Hydrogenation of EAC by [Rh(NBD)(chiraphos)]BF_4[a,b]

$[Rh]_T$ (× 10^3 M)	k_{obsd}(PHIP) (× 10^3 s^{-1})	k_2'(PROD) (× 10^3 s^{-1})
2.1	1.23 (1)	4.3 (2)
8.8	6.6 (2)	6.1 (4)
17	15 (1)	15 (2)

[a] k_{obsd} values were determined from PHIP runs; corresponding k_2' values were obtained from product integrals vs time (PROD). Reported values are the average of two or more runs. [b] Uncertainties are averaged standard deviations from curve fitting analysis.

The ^{1}H NMR spectrum upon initial exposure of the sample to para-enriched H_2 displayed large net effect polarization[2,10] in the vinyl and aliphatic regions of 1-norbornene.[6] This polarization decayed within ca. 60-90 s, consistent with rapid hydrogenation of chelated norbornadiene producing catalytically active Rh(chiraphos)(EAC)$^+$ (**2**). Little polarization was realized during this run in the hydrogenated EAC substrate. Depletion of H_2 from NBD hydrogenation was evident as little NMR-active ortho H_2 was observed in solution. The ^{1}H NMR spectrum, after the sample was removed from the probe, reshaken to reestablish dissolved H_2, and reinserted into the probe, revealed multiplet effect polarization[1] in the methine and diastereotopic benzyl protons of the hydrogenation product, *N*-acetyl-(*R*)-phenylalanine ethyl ester ($EACH_2$) (Figure 1). The resonances at δ 4.61 and 3.10 ppm correspond respectively to the methine proton H_c and a benzyl proton H_a, which exhibit absorption/emission/absorption/emission (a/e/a/e) patterns of similar intensity. Benzyl proton H_b at δ 2.94 ppm shows a weaker pattern of opposite phase (e/a/e/a). The similar polarization of the first two resonances indicates that these protons originate from the same para H_2 molecule, while the weaker polarization and opposite phase of the third resonance arise via cross-relaxation from H_a to H_b as seen previously.[1] The specific occurrence of polarization in Figure 1 thus allows a definitive assignment of diastereotopic proton resonances consistent with the established cis addition of H_2 to the EAC substrate.[11]

The decay of polarization intensity in protons H_a and H_b was followed by ^{1}H NMR spectroscopy at 400 MHz; resonance H_c at δ 4.61 ppm was often obscured by a large solvent resonance,[12]

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0002-7863/92/1514-1908$03.00/0

obviating accurate quantitation of this polarized proton. For each FID, eight scans were collected within 12 s using a 30° observe pulse; a 20-s delay was incorporated between each FID. The integral area[13] in the polarized resonances was quantified every 32 s for 448–480 s. Polarization measured after the sample was removed, reshaken, and reinserted into the spectrometer showed reproducible decay of the polarization intensity. Samples containing 2.1 mM **1** exhibited exponential decay of polarization intensity during the time of NMR observation. Concomitant disappearance of the NMR-active ortho H_2[14] resonance was also noted. Polarization curves from samples containing higher catalyst concentrations exhibited more rapid decay of polarized signal. The rate constants of polarization decay (k_{obsd}) were determined by fitting the polarization intensity curves to a decaying exponential function. A plot of k_{obsd} vs total catalyst concentration produced a straight-line graph with slope of 0.87 M^{-1} s^{-1} and intercept at the origin. This number compares favorably with Halpern's reported value of 1.6 M^{-1} s^{-1}.[11]

A striking feature of our study was that the time dependence of polarization agreed with the rate of hydrogenation, as measured by integrating the unpolarized acyl methyl resonance of $EACH_2$ versus time (shown in Table I under k_2'(PROD)). In the regime of these experiments where EAC is present in excess, H_2 is the limiting reagent. Thus the rate equation for EAC hydrogenation

$$\text{rate} = \frac{k_2K[\text{Rh}]_T[\text{EAC}][\text{H}_2]}{(1 + K[\text{EAC}])} \simeq k_2'[\text{H}_2] \qquad (2)$$

(eq 2),[15] where $[Rh]_T$ is the total catalyst concentration, K is the equilibrium constant between Rh(chiraphos)$^+$ + free EAC and **2**, and k_2 is the rate constant for the hydrogenation of **2**, simplifies to a first-order rate expression in $[H_2]$ with $k_2' = k_2[Rh]_T$.

A simple analysis of the time dependence of PHIP reveals its relationship to the rate of hydrogenation. For PHIP to occur, H_2 enriched in the para spin state is required. The factors influencing the time dependence of polarization in PHIP include the following: (1) proton spin-lattice relaxation, (2) cross-relaxation, (3) the rate of chemical reaction to produce polarized product, (4) promotion of para H_2–ortho H_2 interconversion, and (5) para-enriched H_2 diffusion from the gas phase into solution within the NMR tube. Point 2 is removed from consideration by combining the integrals of H_a and H_b in our data analysis. It is clear from T_1 values for H_a and H_b determined by the inversion–recovery method as 1.7 s ($1/T_1 = k_1 = 0.57$ s^{-1}) that polarization lasts far longer than would be predicted on the basis of spin-lattice relaxation alone. This means that newly polarized product is formed in the probe as "older" product undergoes rapid relaxation, eq 3, leading to eqs 4 and 5 for the time dependence of the concentration of polarized product where $A_0 = \{k_2'/(k_1 - k_2')\}[\text{para } H_2]_0$. When $k_1 \gg k_2'$, contribution from the second

$$\text{EAC} + \text{para } H_2 \xrightarrow[k_2]{\text{Rh(chiraphos)}^+} {}^*\text{EACH}_2 \xrightarrow[k_1 = 1/T_1]{} \text{EACH}_2 \qquad (3)$$

$$\frac{d[{}^*\text{EACH}_2]}{dt} = k_2'[\text{para } H_2] - k_1[{}^*\text{EACH}_2] \qquad (4)$$

$$[{}^*\text{EACH}_2] = A_0 \exp(-k_2't) - (A_0 - [{}^*\text{EACH}_2]_0) \exp(-k_1t) \approx A_0 \exp(-k_2't) \qquad (5)$$

term of the time dependence of polarized product rapidly approaches zero, and beyond this initial period, $[{}^*EACH_2]$ behaves as a simple exponential with rate constant k_2'. Thus $[{}^*EACH_2]$, which depends on the amount of para-enriched H_2 in solution, reflects the rate of reaction.

The catalytic aspect of eq 1 ensures that significant amounts of polarized product are generated during the time period of observation. The time dependence of polarization thus serves as an accurate monitor of the synthesis of newly polarized product even in light of rapid spin-lattice relaxation. This implies that the ROCHESTER technique can be applied to a wide range of hydrogenations that display PHIP to yield kinetic information from quantitation of enhanced resonances.

Acknowledgment. Financial support of this work from the National Science Foundation (Grant No. CHE 89-06090) and a generous loan of rhodium chloride from the Johnson-Matthey Co. are gratefully recognized. We also wish to thank Prof. Clark Landis for insightful comments.

(12) CD_3OH occurs at 4.78 ppm at 25 °C relative to CD_2HOD (3.30 ppm).

(13) For NMR signals that exhibited emission and absorption, the square root of the power spectrum of these integrals was used as a measure of signal intensity.

(14) Para H_2 has no magnetic moment and is therefore silent in NMR spectroscopy.

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Opening of Metal Carbonyl Cluster Complexes by Ligand Addition. Synthesis and Structural Characterization of $Os_3(CO)_{11}(\mu\text{-}CNCF_3)_2$, a Stabilized Derivative of the Hypothetical Complex $Os_3(CO)_{13}$

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Received November 4, 1991

The mechanisms of ligand addition and substitution are fundamental to understanding the reactivity of metal carbonyl cluster complexes.[1] The trinuclear metal carbonyl cluster complexes of the iron subgroup $M_3(CO)_{12}$ (M = Fe, Ru, Os) are the starting points for the study of a wide range of today's transition metal clusters complexes.[1] Investigations of ligand substitution and cluster fragmentation reactions of these complexes have revealed two-term rate expressions that have been interpreted in terms of dissociative and associative mechanisms, respectively.[2] A variety of structures having a cleaved metal–metal bond have been proposed to explain the intermediates anticipated by the addition of a ligand to these complexes.[2,3] In an attempt to prepare the complex $Os_3(CO)_{11}(CNCF_3)$, we accidentally obtained the addition product $Os_3(CO)_{11}(\mu\text{-}CNCF_3)_2$ (**1**), a stabilized derivative of the unknown complex $Os_3(CO)_{13}$ and a possible structural model for the ligand addition products of other reactions with the $M_3(CO)_{12}$ cluster complexes.

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