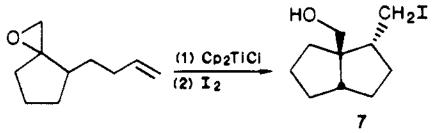
Treatment of the nucleophilic organotitanium derivative in Scheme I with electrophiles other than the proton should provide a route to bifunctional cyclopentane derivatives. To demonstrate this approach we treated two of the product mixtures with iodine. The iodoalcohol **7** was isolated in isomerically pure form (as the *tert*-butyldimethylsilyl ether) in 63% yield. In contrast, the *cis*-organotitanium intermediate in eq 5 cyclized to tetrahydrofuran **8** in 52% isolated yield. In both cases other isomeric products were presumably formed but were not isolated.



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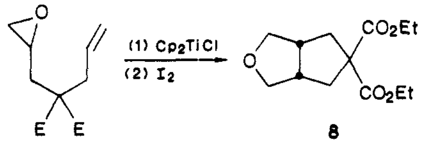
(4)



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(5)

We acticipate that this reaction, while quite useful in its own right, may also be the prototype for other novel transformations based on transition-metal-centered radicals.[12] As a first step in this direction we plan to explore *intermolecular* additions of epoxides to activated olefins.

Supplementary Material Available: Details of isolation and characterization (^{13}C NMR, ^{1}H NMR, HRMS, elemental analysis) of products **1**–**8** (4 pages). Ordering information is given on any current masthead page.

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(11) Other radical routes from carbohydrates to chiral cyclopentanes: Wilcox, C. S.; Gaudino, J. J. *J. Am. Chem. Soc.* **1986**, *108*, 3102–3104. RajanBabu, T. V. *J. Am. Chem. Soc.* **1987**, *109*, 609–611.

(12) Roskamp and Pedersen have reported that another d^1 complex, $NbCl_4(THF)_2$, promotes an unprecedented dimerization of silylimines and nitriles to vicinal diamines. However, they note that 5-hexenenitrile is not cyclized suggesting that there is no long-lived carbon radical associated with the system: Roskamp, E. J.; Pedersen, S. F. *J. Am. Chem. Soc.* **1987**, *109*, 3152–3154.

Electrosynthesis of Porphyrins from *a*,*c*-Biladienes

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One of the most successful syntheses of porphyrins from open-chain tetrapyrroles involves the copper(II)-catalyzed cyclization of 1′,8′-dimethyl-*a*,*c*-biladiene salts **1** to give copper(II) porphyrins **2**. This procedure was discovered in 1961 by Johnson and Kay[1] and has been generalized[2–5] for preparation of completely unsymmetrical porphyrins by way of tripyrrenes and 1′,8′-dimethyl-*a*,*c*-biladienes. The approach does suffer some disadvantages, the most notable being the vigorous conditions required in the final cyclization step [Cu(II) in dimethyl formamide at 140–150 °C], the erratic yields of porphyrin (varying between 20 and 75%), and the fact that the product is a copper(II) porphyrin **2** which must subsequently be demetalated with concentrated sulfuric and trifluoroacetic acids. A room temperature copper(II)-promoted cyclization procedure and other metal salt oxidants have been described[6] but do not offer substantial improvements.

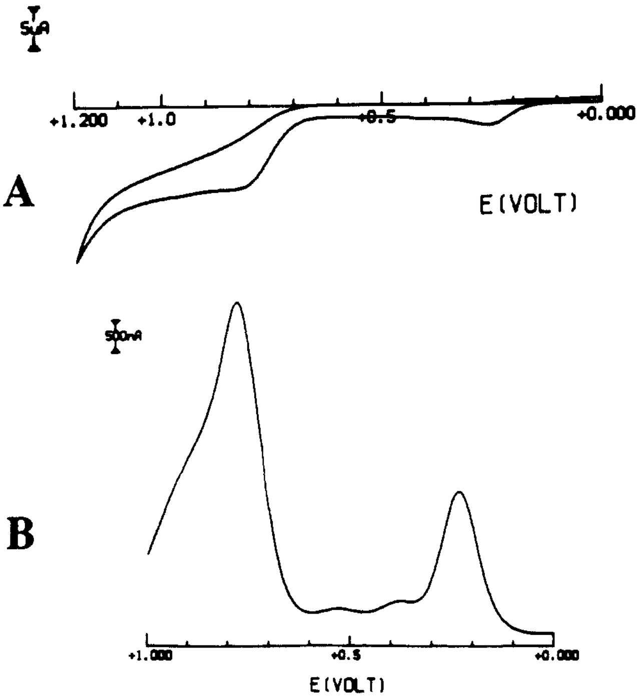
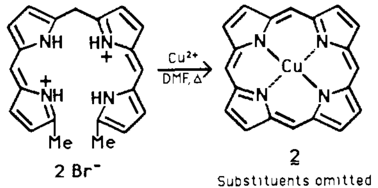
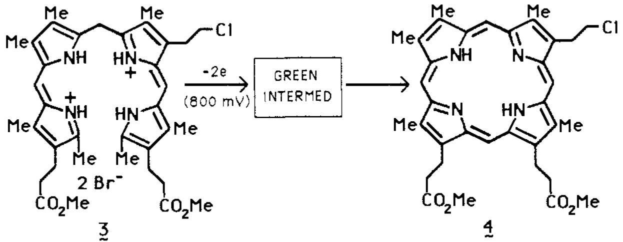


Figure 1. Cyclic voltammogram[11] (A) and square wave voltammogram (B) of chloroethyl-*a*,*c*-biladiene **3**.



2 Br⁻
1

2
Substituents omitted for clarity



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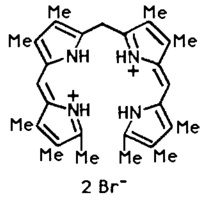

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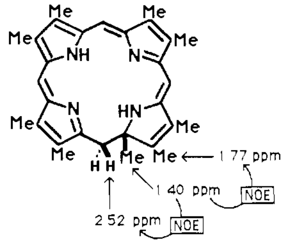

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Using carbon-13 labeling, the mechanism of the *a*,*c*-biladiene cyclization was investigated,[7,8] these studies establishing both the origin of the new meso carbon atom as well as a plausible pathway from 1′,8′-dimethyl-*a*,*c*-biladiene to copper(II) porphyrin.[8,9] No

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(1) Johnson, A. W.; Kay, I. T. *J. Chem. Soc.* **1961**, 2418–2423.

(2) de Almeida, J. A. P. B.; Kenner, G. W.; Rimmer, J.; Smith, K. M. *Tetrahedron* **1976**, *32*, 1793–1799.

(3) Smith, K. M.; Craig, G. W. *J. Org. Chem.* **1983**, *48*, 4302–4306.

(4) Engel, J.; Gossauer, A. *Liebigs Ann. Chem.* **1976**, 1637–1658.

(5) Mironov, A. F.; Rumyantseva, V. D.; Rozynov, B. V.; Evstigneeva, R. P. *Zh. Org. Khim.* **1979**, *7*, 165–168. Mironov, A. F.; Kulish, M. A.; Kobak, V. V.; Rozynov, B. V.; Evstigneeva, R. P. *Zh. Obshch. Khim.* **1974**, *44*, 1407–1410. Kulish, M. A.; Kozhich, D. T.; Mironov, A. F.; Evstigneeva, R. P. *Bioorg. Khim.* **1978**, *4*, 1237–1243.

(6) Smith, K. M.; Minnetian, O. M. *J. Chem. Soc., Perkin Trans. 1* **1986**, 277–280.

(7) Smith, K. M.; Kehres, L. A. *J. Chem. Soc., Perkin Trans. 1* **1983**, 2329–2335.

(8) Smith, K. M.; Minnetian, O. M. *J. Org. Chem.* **1985**, *50*, 2073–2080.

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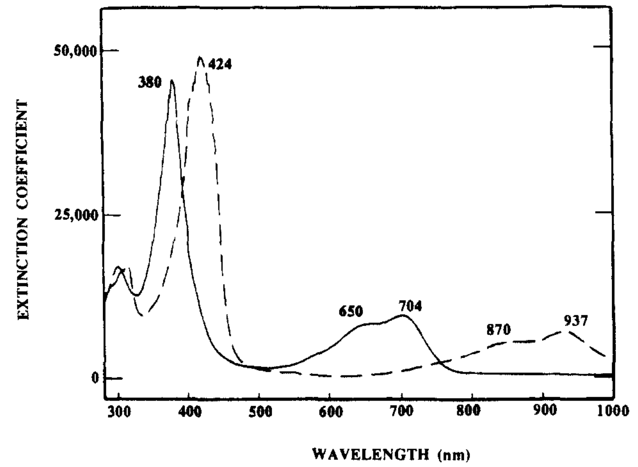


Figure 2. Optical spectra, in dichloromethane, of cyclized intermediate obtained by electrolysis of *a,c*-biladiene **3** (full line) and of the intermediate in the presence of trifluoroacetic acid [broken line; λ_{max} 424 (ϵ 49 650), 870 (inf; 4950), 937 nm (6000)].

intermediates in the proposed pathway have ever been isolated or characterized, and such intermediates bearing an "α-substituent", as for example when a 1′,8′-dimethyl-*a,c*-biladiene is cyclized, have been predicted to be highly unstable.[10] We now show that use of the troublesome copper(II) oxidant can be eliminated by use of electrochemical oxidation and that this milder approach allows isolation of a key, stable, "α-substituted" macrocyclic intermediate.

Cyclic voltammetry[11] indicated (Figure 1) that the unsymmetrical *a,c*-biladiene **3** and the zinc(II) complex (not shown)[12] have irreversible oxidations at 0.84 and 0.68 V and weak waves at 0.27 and 0.03 V, respectively. Room temperature electrolysis of the zinc(II) complex in a conventional "H" cell[13] left the chelate unchanged (spectrophotometry) after 6 h at 0.50 V. Electrolysis at 0.8 V for 6 h followed by an aqueous workup gave 40% of the desired zinc(II) porphyrin. Electrolysis of unsymmetrical *a,c*-biladiene **3** at 0.8 V without zinc(II) gave a considerable quantity of porphyrin after 4 h. Both analytical thin-layer chromatography (TLC) and spectrophotometry (monitoring appearance of the Soret absorption at 406 nm) confirmed that oxidative cyclization of the *a,c*-biladiene to give porphyrin **4** (42% yield) was complete after 8 h. Spectrophotometric control experiments showed no porphyrin is formed even after 25 h under identical conditions but in the absence of an applied potential. This is the first example of porphyrin synthesis from 1′,8′-dimethyl-*a,c*-biladienes in the absence of chemical oxidants.

Attempts to scale the electrolysis of *a,c*-biladiene (to 50 mg) provided an unexpected result. Bulk electrolysis of unsymmetrical *a,c*-biladiene **3** at 0.8 V for 24 h afforded, after workup and alumina chromatography, 9 mg of a blue-green compound, which eluted first and was followed by the desired porphyrin **4** (9%). The optical spectrum of the intermediate [Figure 2; λ_{max} 305 (ϵ 15 000), 380 (45 000), 650 (inf; 7800), 704 nm (9000)] clearly indicated a species, similar to an *a,b,c*-bilatriene, in which four pyrrole subunits are conjugated.[14] However, high field proton NMR (not shown) clearly showed a mixture of two geometrical isomers which precludes the possibility of an open-chain *a,b,c*-bilatriene. Treating the blue-green compound separately with DDQ, bromine, or zinc(II) acetate gave varying amounts of porphyrin; simple heating also gave porphyrin. Electrochemical oxidation of the blue-green compound (800 mV vs Ag/AgCl, in dimethyl formamide containing tetraethylammonium *p*-toluenesulfonate, for 2.5 h) furnished a clean conversion to porphyrin (70% yield) clearly indicating that the blue-green species is an intermediate along the oxidative pathway to porphyrin **4**.

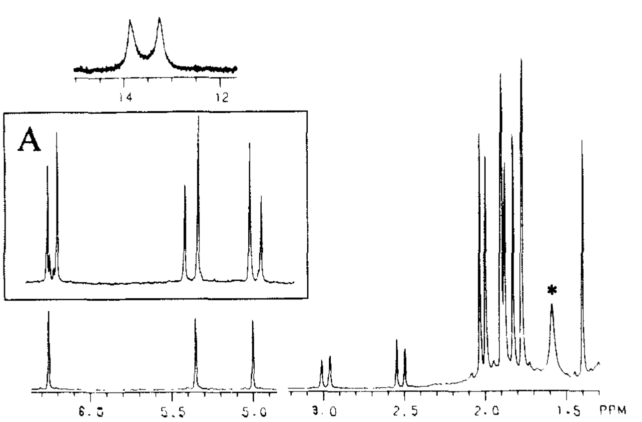
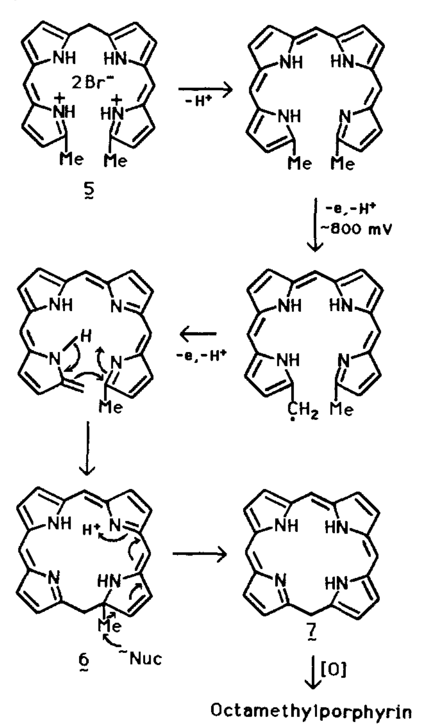


Figure 3. Proton NMR spectrum (in $CDCl_3$; 300 MHz; GE QE300 instrument) of the intermediate **6**. The insert A shows the corresponding spectrum of the methine region from the intermediate obtained by electrocyclization of *a,c*-biladiene **3**. Vertical scales in the insert and for the NH prtons (13–14 ppm) are expanded. * = water.

Scheme I. Proposed Mechanistic Pathway for Electrosynthesis of Porphyrin from 1′,8′-Dimethyl-*a,c*-biladiene Dihydrobromide **5** by Way of the Cyclic Intermediate **6** and Phlorin **7**



To better understand this intermediate the decamethyl-*a,c*-biladiene **5** was synthesized[15] and electrolyzed by using similar

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[9] In an independent study, Clezy et al. have studied the mechanism of the copper(II)-catalyzed *b*-bilene cyclization: Clezy, P. S.; Duncan, M. W.; Ravi, B. N.; Thuc, L. V. *Aust. J. Chem.* **1986**, *39*, 399–417.

[10] Fuhrhop, J.-H. In *Porphyrins and Metalloporphyrins*; Smith, K. M., Ed.; Elsevier: Amsterdam, 1975; p 628.

[11] Cyclic voltammograms were measured in dimethyl formamide with 0.2 M tetraethylammonium *p*-toluenesulfonate as supporting electrolyte with a three-electrode assembly and by using a BAS 100A electrochemical workstation. The working electrode was a platinum button, with a platinum wire counter electrode, and potentials were measured vs the Ag/AgCl electrode.

[12] Prepared by mixing a 1:1 mass ratio of the *a,c*-biladiene and $Zn(OAc)_2$ in DMF electrolyte solution.

[13] The cell was separated by a Celanese potential membrane. Dimethyl formamide was used as solvent with 0.2 M tetraethylammonium *p*-toluenesulfonate as supporting electrolyte. A platinum gauze working electrode and platinum wire counter electrode were used, and potentials were applied with reference to the Ag/AgCl couple.

[14] Bullock et al. (Bullock, E.; Grigg, R.; Johnson, A. W.; Wasley, J. W. F. *J. Chem. Soc.* **1963**, 2326–2335) report λ_{max} 305 (ϵ 19 950), 385 (53 700), 605 (inf; 10 500), 705 nm (12 000).

[15] The *a,c*-biladiene **5** [NMR ($CDCl_3$), 13.25, 13.14 (each br s, 2 H, NH), 7.07 (s, 2 H, 2 × =CH—), 5.15 (s, 2 H, —CH_2—), 2.67, 2.27, 2.20, 1.99, 1.89 (each s, 6 H, Me); VIS (CH_2Cl_2), λ_{max} 450 nm (ϵ 135 000), 526 (70 700)] was synthesized in high yield by using standard methods[2,3] from 3,3′,4,4′-tetramethylpyrromethane-5,5′-dicarboxylic acid and 2-formyl-3,4,5-trimethylpyrrole.

electrochemical methods, to furnish 38–52% yields of a blue-green intermediate **6**. The optical spectrum [λ_{max} 303 (ϵ 15 300), 380 (45 300), 646 (inf; 8000), 704 nm (9300)] was almost identical with that of the previous intermediate; the greatly simplified proton NMR spectrum showed three methine peaks (6.26, 5.35, 5.00 ppm), two NHs (13.84, 13.22 ppm), nine methyl resonances (2.03–1.77, 1.40 ppm), and an AB quartet [2.98, 2.52 ppm (each d, J_{AB} = 15.3 Hz)] (Figure 3). Insert A in Figure 3 shows the methine protons of the intermediate from the unsymmetrical *a,c*-biladiene **3** and demonstrates the presence of unequal amounts of two isomeric structures depending upon which of the two terminal methyls in **3** forms the macrocyclic bridging carbon. Irradiation of the methyl singlet in **6** at 1.40 ppm gave a nuclear Overhauser enhancement at the upfield doublet (2.52 ppm) and also at a methyl resonance (1.77 ppm). On the basis of this evidence, we propose structure **6** for the intermediate, with proton NMR assignments as annotated. High resolution FAB mass spectrometry[16] confirmed the expected molecular weight.

The mechanism shown in Scheme I is proposed for the decamethyl-*a,c*-biladiene **5** electrocyclization; following deprotonation[17] the conjugated tetrapyrrole suffers two-electron oxidation and macrocyclization to give the intermediate **6**. Nucleophilic attack,[18] presumably by the electrolyte, causes formation of the phlorin **7** which undergoes spontaneous oxidation[19] to give porphyrin. Thin-layer spectroelectrochemistry (not shown) indicates that the order of the nucleophilic attack/oxidation steps may be reversed in the electrochemical conversion of 6 into porphyrin.

Acknowledgment. We thank the U.S. Office of Naval Research (N00014-85-C-0317), Aquanautics Corporation, and the National Science Foundation (CHE-86-19034) for support of this research. The mass spectrometer was purchased with funds provided in part by the National Institutes of Health (RR01460-01).

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(16) Mass spectra were measured on a VG Analytical ZAB-HS-2F instrument by using fast atom bombardment and a tetraethylene glycol matrix. Compound **6**, found 438.2787. Calcd for $C_{29}H_{34}N_4$ 438.2784.

(17) The precise order of deprotonation and oxidation steps cannot be defined at this point in time.

(18) Johnson, A. W. In *Porphyrins and Metalloporphyrins*; Smith, K. M., Ed.; Elsevier: Amsterdam, 1975; pp 741–743.

(19) Hopf, F. R.; Whitten, D. G. In *Porphyrins and Metalloporphyrins*; Smith, K. M., Ed.; Elsevier: Amsterdam, 1975; pp 678–680, and references therein.

Para Hydrogen Induced Polarization in Hydrogenation Reactions Catalyzed by Ruthenium–Phosphine Complexes

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Para hydrogen induced polarization (PHIP) leading to enhanced ^{1}H NMR absorptions and emissions has recently been reported for hydrogenation and hydrogen addition reactions.[1,2] The basis of PHIP, which was presented initially by Weitekamp, involves pairwise transfer of para-enriched H_2 to substrate.[1,3] If this happens fast relative to proton relaxation, then the transferred protons will reflect initially the nuclear spin populations of the starting dihydrogen and give rise to polarized or enhanced transitions for the product resonances. The occurrence of PHIP is thus definitive evidence for pairwise hydrogen transfers. In this paper, we describe studies including the observation of PHIP for hydrogenation reactions catalyzed by ruthenium phosphine complexes.

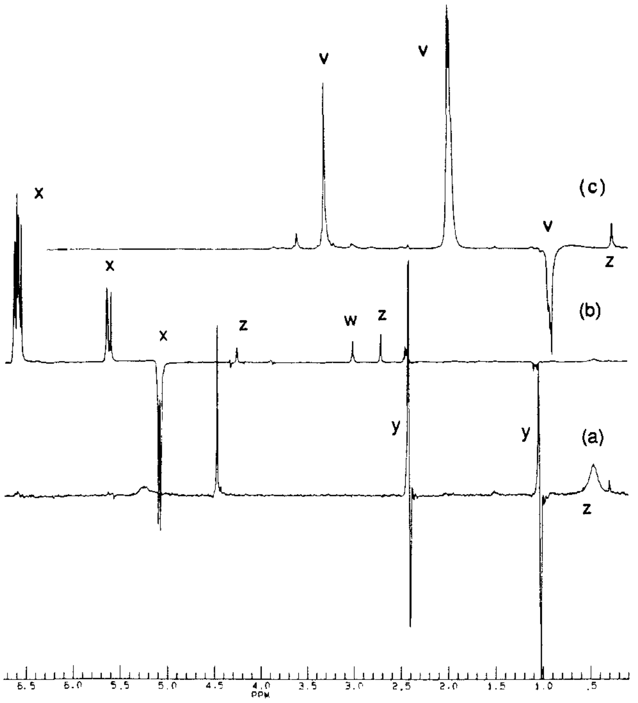

Figure 1. PHIP in the ^{1}H NMR spectra of $RuH_4(PPh_3)_3$-catalyzed hydrogenations in C_6D_6 under ~3 atm para-enriched H_2 at room temperature for (a) styrene-d_8, (b) phenylacetylene, and (c) methyl acrylate: v = $CH_3CH_2COOCH_3$, w = PhC≡CH, x = PhCH=CH_2, y = $C_6D_5CDHCHD_2$, and z = solvent impurities. The resonance at δ 4.45 ppm corresponds to H_2 (while para H_2 is NMR silent, ortho H_2 is not).

The tetrahydride species $RuH_4(PPh_3)_3$ is a known hydrogenation catalyst which readily exchanges H_2 and has recently been shown to be a dihydrogen complex.[4] When $RuH_4(PPh_3)_3$ is used to catalyze hydrogenation of styrene-d_8 in benzene-d_6 under 2–3 atm of para-enriched hydrogen, a strong absorption/emission pattern characteristic of PHIP is seen in the ^{1}H resonances of the $C_6D_5CHDCHD_2$ product as shown in Figure 1a.[5] The polarization is observable for up to 2 min and decays exponentially with a first-order rate constant of ~0.044 s^{-1}. During this period the broad hydride resonance of $RuH_4(PPh_3)_3$ at δ −7.52 ppm is observable and remains unchanged. Hydrogenation of C_2D_4 using $RuH_4(PPh_3)_3$ under these conditions also yields para hydrogen induced polarization in the CHD_2CHD_2 product identical with that reported previously.[2]

When methyl acrylate and the alkynes PhC≡CH, *t*-BuC≡CH, and $MeOCH_2C$≡CH are employed as the substrate in these hydrogenations, the nature of the polarization changes dramatically. This is shown for PhC≡CH and CH_2=CHCOOMe in Figure 1 (parts b and c, respectively), in which the initial product resonances (styrene in part b and methyl propionate in part c

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(1) (a) Bowers, C. R.; Weitekamp, D. P. *J. Am. Chem. Soc.* **1987**, *109*, 5541. (b) Bowers, C. R.; Weitekamp, D. P. *Phys. Rev. Lett.* **1986**, *57*, 2645. (c) Pravica, M. G.; Weitekamp, D. P. *Chem. Phys. Lett.* **1988**, *145*, 255.

(2) Eisenschmid, T. E.; Kirss, R. U.; Deutsch, P. P.; Hommeltoft, S. I.; Eisenbertg, R.; Bargon, J.; Lawler, R. G.; Balch, A. L. *J. Am. Chem. Soc.* **1987**, *109*, 8089.

(3) (a) Weitekamp suggests the acronym PASADENA for "parahydrogen and synthesis allow dynamically enhanced nuclear alignment". We prefer the shorter, less geographically specific PHIP. (b) The term "pairwise" means that both transferred hydrogen atoms originate from the same H_2 molecule. Pairwise transfer need not be concerted or synchronous; for PHIP it must be short relative to loss of spin correlation (relaxation) and requires that the protons maintain coupling throughout the hydrogenation process.

(4) (a) Komiya, A.; Yamamoto, A. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 2553. (b) Cole-Hamilton, D. J.; Wilkinson, G. *Nouv. J. Chim.* **1977**, *1*, 141. (c) Sanchez-Delgado, R. A.; Bradley, J. S.; Wilkinson, G. *J. Chem. Soc., Dalton Trans.* **1976**, 399. (d) Crabtree, R. H.; Hamilton, D. G. *J. Am. Chem. Soc.* **1986**, *108*, 3124. (e) Linn, D. E.; Halpern, J. *J. Am. Chem. Soc.* **1987**, *109*, 2969.

(5) These experiments were carried out in 5-mm NMR tubes equipped with a Teflon valve. Solvents (0.5 mL) and substrates (10 μL) were vacuum transfered to an NMR tube containing ~3 mg of the ruthenium complex. The tubes were stored at −196 °C. Para enriched hydrogen (prepared by storing H_2 over a Fe_2O_3/silica/C catalyst at −196 °C for 3–4 h) was added just prior to thawing the tube and insertion into the magnetic field.

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