ganometallic molecules studied to date.[4] The γ values are also increased compared to related organic species, particularly for $Cp_2Ti(C{\equiv}C\phi)_2$ ($\phi = C_6H_5$). A trend of the γ value with respect to the metal atom exists: as one goes down the periodic chart, γ decreases.

One mechanism for increasing the γ values of the metallocene–phenylacetylide complexes over $HC{\equiv}C\phi$ is for the Cp_2M moiety to act as an electron-accepting group for the phenylacetylene ligand. Acceptor-substituted organic compounds have increased third-order susceptibilities over their unsubstituted analogs. Nitro substitution of styrene leads to a 2-fold increase in γ (β-nitrostyrene, $\gamma = 29 \times 10^{-36}$ esu;[14] styrene, $\gamma = 17 \times 10^{-36}$ esu[4a]). The increase in γ seen for the group 4 metallocenes is greater than that seen in related organic compounds. Assuming that the Cp_2TiCl fragment contributes $<5 \times 10^{-36}$ esu to γ, substitution of $HC{\equiv}C\phi$ with the metallocene $[Cp_2Ti(Cl)C{\equiv}C\phi]$ leads to an increase in γ by greater than a factor of 4.

If the Cp_2M unit is acting only as an electron-accepting group, the γ value for $Cp_2Ti(Cl)C{\equiv}C\phi$ should be at least half of that observed for $Cp_2Ti(C{\equiv}C\phi)_2$. The measured γ of $Cp_2Tl(Cl)$-$C{\equiv}C\phi$ is approximately one-third that of $Cp_2Ti(C{\equiv}C\phi)_2$, demonstrating that another electronic process is contributing to the third-order properties as well. The most likely candidate for the contributing process is the linking of the acetylide units via interaction of the metal d and acetylide π orbitals to form an extended π system. The decreasing trend in γ values (Ti > Zr $\gtrsim$ Hf) is rationalized by assuming that the Ti d orbitals are closer in energy to the alkynyl π orbitals than to the Zr or Hf d orbitals, which leads to more significant mixing between these orbitals for the Ti complexes as compared to the Zr of Hf complexes. The closer energy match also makes Ti a better acceptor for the alkyne π system, enforcing the observed trend. This smaller energy gap between the metal and organic ligand orbitals is seen in the absorption spectra (Ti is red shifted relative to Zr and Hf). The π symmetry orbitals of the cyclopentadienyl ligands may also be involved in the electronic structure leading to the observed NLO properties. Theoretical calculations suggest that, for group 4 bent metallocene complexes with unsaturated hydrocarbon ligands (i.e., carbene or acetylide), significant mixing occurs between the cyclopentadienyl and hydrocarbon π orbitals.[15] This mixing leads to molecular orbitals which extend over the entire molecule.

In conclusion, we have determined the third-order properties of a series of group 4 transition metal complexes. The third-order nonlinear optical properties of the metallocene–phenylacetylide complexes are tuned by the choice of metal atom, with Ti giving a larger optical nonlinearity than either Zr of Hf. We are continuing this study by exploring group 4 complexes (with and without Cp ligands) to obtain a better understanding of the origin and magnitude of the third-order nonlinearities in these materials.

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Registry No. Cp'_2TiF_2, 38498-31-6; Cp'_2TiCl_2, 1282-40-2; Cp'_2Br_2, 72622-32-3; Cp_2ZrCl_2, 1291-32-3; $Cp_2Ti(C{\equiv}C\phi)_2$, 12303-93-4; $Cp_2Zr(C{\equiv}C\phi)_2$, 72982-57-1; $Cp_2Hf(C{\equiv}C\phi)_2$, 84879-48-1; $\phi C{\equiv}CC{\equiv}C\phi$, 886-66-8; $HC{\equiv}C\phi$, 536-74-3; $Cp_2Ti(C{\equiv}C\phi)Cl$, 142867-28-5; $(C_5H_4$-n-$Bu)_2Fe$, 1274-08-4.

Supplementary Material Available: Description of the data analysis procedures for the third harmonic generation measurements and a representative set of THG data ($Cp_2Hf(C{\equiv}C\phi)_2$) (9 pages). Ordering information is given on any current masthead page.

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Cryptic Stereospecificity of Methane Monooxygenase

N. D. Priestley,† H. G. Floss,*,† W. A. Froland,‡ J. D. Lipscomb,*,‡ P. G. Williams,§ and H. Morimoto§

Department of Chemistry BG-10 University of Washington, Seattle, Washington 98195 Department of Biochemistry, Medical School University of Minnesota Minneapolis, Minnesota 55455 National Tritium Labeling Facility Lawrence Berkeley Laboratory, 1 Cyclotron Road Berkeley, California 94720

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Methane monooxygenase (MMO, EC 1.14.13.25) catalyzes the NAD(P)H- and O_2-dependent hydroxylation of methane to methanol.[1-4] Soluble MMO from the methanotrophic bacterium, *Methylosinus trichosporium* OB3b, consists of a 245 kDa hydroxylase component containing a μ-(R/H)-oxo bridged binuclear iron cluster, a 40 kDa NAD(P)H-dependent oxidoreductase component, and a 15.8 kDa protein, component B, which has no associated cofactors.[4,5] The hydroxylase component alone can carry out the same oxidations as the reconstituted three-component system when H_2O_2 is used as the source of oxygen and reducing equivalents.[6,7]

Several mechanisms have been proposed for MMO-catalyzed alkane oxidation; these invoke an intermediate substrate radical,[4,8,10-12] an additional substrate carbocation intermediate,[13] or a concerted oxygen insertion into a substrate carbon–iron bond.[14] Recent studies support the formation of a substrate intermediate not bound to the iron;[10,11,13,15] however, they utilized diagnostic substrates that may not be representative of the natural substrate, methane. The experiments described here address this question more directly by determining the steric course of the oxidation of (*S*)- or (*R*)-[1-$^2H_1$,1-$^3H_1$]ethane to ethanol catalyzed by MMO.

† University of Washington.
‡ University of Minnesota.
§ Lawrence Berkeley Laboratory.

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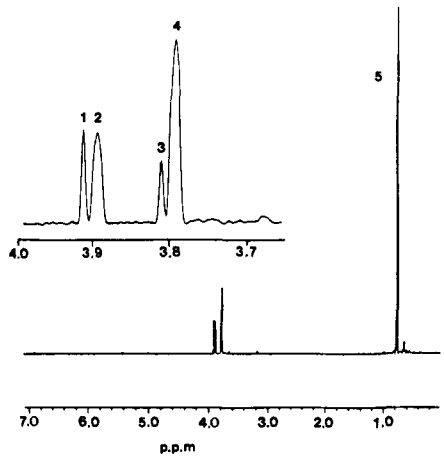

Figure 1. ^3H NMR spectrum (320 MHz, ^1H decoupled) of the (2*R*)-2-acetoxy-2-phenylethanoate derivative of ethanol recovered from the incubation of (*R*)-[1-$^2H_1$,1-$^3H_1$]ethane with MMO: (1) (*R*)-[1-$^3H_1$]-ethanol; (2) (*R*)-[1-$^2H_1$,1-$^3H_1$]ethanol; (3) (*S*)-[1-$^3H_1$]ethanol; (4) (*S*)-[1-$^2H_1$,1-$^3H_1$]ethanol; and (5) [2-$^2H_1$,2-$^3H_1$]ethanol. NMR signal assignments were made according to the method of Parker.[20]

The ethane samples were synthesized by reaction of carrier-free $LiEt_3B^3H$ (5.7 Ci per synthesis)[16] with the known (*R*)- or (*S*)-[1-$^2H_1$]ethyl tosylate (>98 atom % ^2H, 88 and 96% ee, respectively) and incubated with the purified and reconstituted MMO system (hydroxylase specific activity = 870 nmol/min/mg under standard assay conditions[4]). ^3H NMR analysis of the resulting ethanol samples gave an intramolecular primary kinetic isotope effect for hydrogen abstraction from the labeled methyl group of $k_H/k_D = 4.2 \pm 0.2$.[17] The (2*R*)-2-acetoxy-2-phenylethanoate derivatives[20] of the ethanol samples showed well-resolved resonances corresponding to all four possible species carrying ^3H in the methylene group (Figure 1, Table I). (*R*)-[1-$^2H_1$,1-$^3H_1$]Ethane gave predominantly (*S*)-[1-$^2H_1$,1-$^3H_1$]- and (*R*)-[1-$^3H_1$]ethanol, and conversely, (*S*)-[1-$^2H_1$,1-$^3H_1$]ethane afforded predominantly (*R*)-[1-$^2H_1$,1-$^3H_1$]- and (*S*)-[1-$^3H_1$]ethanol. The results show that the hydroxylation of ethane proceeds with predominant retention of configuration, consistent with the mechanistic similarity[4,6] to P450-catalyzed reactions.[18,21] Almost identical results were obtained for the reaction catalyzed by the MMO hydroxylase component alone in the presence of H_2O_2 (data not shown).

The overall retention of configuration of the MMO-catalyzed reaction is accompanied by approximately 35% inversion (Table I). On the basis of the amount of H^3HO observed in the ^3H NMR spectra of the products recovered from the individual incubations (about 10% of the total ^3H), this does not represent racemization due to an exchange process. The relatively high degree of inversion observed thus must be due to "flipping" of a free substrate intermediate that has a sufficiently long lifetime to undergo configurational inversion with appreciable frequency. This intermediate is likely to be an ethyl radical, because an ethyl cation has an exceptionally high energetic barrier to direct formation[22] and is markedly unstable. These results thus support a radical-based mechanism as proposed by Fox et al.[4,11] and argue against mechanisms not involving a free substrate intermediate in the enzyme active site.[14] They do not, however, give any information on the proposed[13] *additional* involvement of a carbocation intermediate.

Table I. Percentage Distribution of ^3H Label in the Methylene Group of the (2*R*)-2-Acetoxy-2-phenylethanoate Derivatives of the Samples Generated by MMO[a]

SUBSTRATE \ PRODUCT	^3H % in methylene group: 4#	1#	2#	3#
(R)	53	12	26	9
	retention = 68 %		inversion* = 32 %	
(S)	27	7	52	14
	inversion* = 36 %		retention = 64 %	

[a] Inversion/retention data have been corrected for the enantiomeric purity of the substrates. * indicates configurational inversion is due to flipping of the intermediate radical. # indicates that the numbering scheme here corresponds with that in Figure 1.

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Asymmetric Titanocene-Catalyzed Hydrogenation of Imines

Christopher A. Willoughby and Stephen L. Buchwald*

Department of Chemistry
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139

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Significant progress has been made in the asymmetric reduction of ketones to alcohols.[1,2] The solutions for the analogous production of enantiopure amines from ketimines,[3] while noteworthy, have been less successful. Herein we report our initial results on the use of a chiral titanium catalyst for the hydrogenation[4] of ketimines to enantioenriched amines.

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