optical yield (see Table I for results). The best ratio of 1/BNPPA is 20/1), with 10/1 giving inferior results. Similarly, naproxen was obtained in good yield and in up to 91% optical yield.

Let us compare this new asymmetric hydrocarboxylation reaction with several recent, metal-catalyzed approaches to optically active ibuprofen or naproxen. A higher degree of optical purity of (*S*)-(+)-naproxen was attained by BINAP–ruthenium(II)-catalyzed hydrogenation of 2-(6-methoxynaphthyl)-2-propenoic acid.[14] Unfortunately, a high pressure of hydrogen (135 atm) is required, and the acrylic acid derivative has to be synthesized via several steps. In 1987, Parrinello and Stille[15] described the use of a Pt(II) complex of (2*S*,4*S*)-*N*-(*tert*-butoxycarbonyl)-4-(diphenylphosphino)-2-[(diphenylphosphino)methyl]pyrrolidine [(-)-BPPM], with $SnCl_2$, for the hydroformylation of **1**, **2**, and other olefins. While the percent enantiomeric excess of the formed aldehyde approaches 80%, the regioselectivity was poor, with an unfavorable branched/linear ratio (~0.5). Consequently, the chemical yields of the desired aldehydes were modest. Furthermore, hydroformylation of **1** and **2** required drastic conditions (2400 psi) and a subsequent oxidation step to produce the acids.

In summary, the hydrocarboxylation of olefins with BNPPA occurs under exceptionally mild conditions (room temperature, 1 atm), is completely regiospecific (linear acids were not formed), and affords acid in both high chemical and high optical yields.

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Registry No. **1**, 63444-56-4; **2**, 63444-51-9; (*S*)-BNPPA, 124756-11-2; (*R*)-BNPPA, 124756-12-3; *p*-bromostyrene, 2039-82-9; *tert*-butylmagnesium bromide, 5674-02-2; 2-bromo-6-methoxynaphthalene, 5111-65-9; vinylmagnesium bromide, 1826-67-1; (*S*)-(+)-ibuprofen, 51146-56-6; (*R*)-(-)-ibuprofen, 51146-57-7; (*S*)-naproxen, 22204-53-1; (*R*)-naproxen, 23979-41-1.

(14) Ohta, T.; Takaya, H.; Kitamura, M.; Nagai, K.; Noyori, R. *J. Org. Chem.* **1987**, *52*, 3176.
(15) Parrinello, G.; Stille, J. K. *J. Am. Chem. Soc.* **1987**, *109*, 7122.

^{57}Fe Nuclear Magnetic Resonance Chemical Shifts of Hindered Iron Porphyrins. Ruffling as a Possible Mechanism for d-Orbital Energy Level Inversion

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The discrimination of binding between carbon monoxide and oxygen in heme proteins has inspired the syntheses of porphyrins with one side hindered by, e.g., a "cap",[1] a "pocket",[2] a "strap",[3] a "basket handle",[4] or some other device for the purpose of obstructing the binding of ligands to one side of the porphyrin, but the properties of these model hemes have not led to a straightforward explanation of the natural regulatory mechanism. So far, there is only one demonstrated example of a model compound that exhibits a tilt of the CO relative to the heme normal in the solid state, the "pocket" porphyrin.[5] In the series of hybrid "basket-handle" porphyrins, for example, the effect of a decrease in the length of the aliphatic chain spanning one side of the porphyrin is not to increase the degree of tilt of the bound carbonyl but rather to increase the degree of ruffling[6] of the porphyrin core.[7] Among the heme proteins, myoglobin-CO exhibits a tilted CO and an almost flat porphyrin,[8] but in human carbonyl hemoglobin,[9] the tilt is very small and the porphyrin is clearly ruffled. Thus, the intriguing question of CO regulation still inspires investigations of heme proteins and heme models.

Table I. ^{57}Fe Nuclear Magnetic Resonance Chemical Shifts of Some Carbonyl Iron(II) Porphyrin Complexes in Toluene-d_8 at 25 °C

compd	δ, ppm	Δδ[a]
FePF(BuIm)(CO)	8110	+14
FeBH12(BuIm)(CO)	8036	+19
FeBH10(BuIm)(CO)	7728	-11
FeBH9(BuIm)(CO)	7500	-12
Fe(PPIX)(py-d_5)(CO)[b]	8205	
Fe(meso-PIX)(py-d_5)(CO)[b]	8188	
FePF(BuIm)(CO)[c]	8131	

[a] Effect on chemical shift of replacing axial BuIm with py. [b] Solvent is D_2O. [c] Solvent is DMF:H_2O, 90:10. PF is picket fence; BH is basket handle; 12, 10, and 9 indicate number of carbon atoms in superstructure; PPIX is protoporphyrin IX; meso-PIX is mesoporphyrin IX.

It follows that spectroscopic tools for the investigation of structure in these systems are of considerable interest. NMR techniques are often the natural first choice in such a case but the ^{1}H and ^{13}C NMR spectra are practically uninformative, with regard to the subtle details of porphyrin conformation, and the coupling constant $^1J_{Fe-C}$ does not vary significantly between the known complexes. The resonance Raman frequencies and the IR CO stretching frequency do vary[10] but not in an easily interpretable way, and the observed frequency shifts are very small. The UV/vis spectra do not provide any detailed structural information. In particular, the weak d–d transitions are not observable under the intense $\pi-\pi^*$ transitions.[11]

In this communication, we report that the ^{57}Fe NMR chemical shifts are extremely sensitive to deformation of the porphyrin geometry and that novel information about the electronic levels may be extracted from investigations of substituent effects on the chemical shift within the simple framework of the Ramsey equation. In the hybrid "basket-handle" porphyrins, the ruffling leads to large changes in the iron d-orbital energies that may be important in understanding ligand binding in heme proteins and models.

The ^{57}Fe NMR experiments were carried out on a Varian VXR 400 NMR instrument operating at 13.05 MHz, using 15-mm nonspinning sample tubes and a solenoid coil probe, with a 90° pulse width of 90 μs. The syntheses of "basket-handle" porphyrins were carried out according to the literature.[4] After reduction to the ferrous state, no paramagnetic material could be detected in the ^{1}H NMR spectra, the ^{57}Fe NMR chemical shift measurements were reproducible, and at the concentration of ferrous porphyrin used, 5 mM, the rate of electron transfer from trace amounts of ferric material would be too slow to affect the chemical shift measurements.

The factors affecting the ^{57}Fe NMR chemical shift (Table I) in iron porphyrins can be derived from a simple ligand-field argument.[12] A more electron releasing group on the porphyrin

(1) Hashimoto, T.; Dyer, R. L.; Crossley, M. J.; Baldwin, J. E.; Basolo, F. *J. Am. Chem. Soc.* **1982**, *104*, 2101.
(2) Collman, J. P.; Brauman, J. I.; Collins, T. J.; Iverson, B. L.; Lang, G.; Pettman, R. B.; Sessler, J. L.; Walters, M. A. *J. Am. Chem. Soc.* **1983**, *105*, 3038.
(3) Ward, B.; Wang, C.-B.; Chang, C.-K. *J. Am. Chem. Soc.* **1981**, *103*, 5236.
(4) Momenteau, M.; Loock, B.; Tetreau, C.; Lavalette, D.; Croisy, A.; Schaeffer, C.; Huel, C.; Lhoste, J.-M. *J. Chem. Soc., Perkin Trans. 2* **1987**, 249.
(5) Kim, K.; Fettinger, J.; Sessler, J. L.; Cyr, M.; Hugdahl, J.; Collman, J. P.; Ibers, J. A. *J. Am. Chem. Soc.* **1989**, *111*, 403.
(6) Li, X.-Y.; Czernuszewicz, S.; Kincaid, J. R.; Spiro, T. G. *J. Am. Chem. Soc.* **1989**, *111*, 7012.
(7) Michel Momenteau, personal communication.
(8) Kuriyan, J.; Wilz, S.; Karplus, M.; Petsko, G. A. *J. Mol. Biol.* **1986**, *192*, 133.
(9) Derewenda, Z.; Dodson, G.; Emsley, P.; Harris, D.; Nagai, K.; Perutz, M. F.; Reneaud, J.-P. *J. Mol. Biol.* In press.
(10) Desbois, A.; Momenteau, M.; Lutz, M. *Inorg. Chem.* **1989**, *28*, 825. Li, Y.-X.; Spiro, T. G. *J. Am. Chem. Soc.* **1988**, *110*, 6024.
(11) Makinen, M. W.; Churg, A. K. *Iron Porphyrins Part One*; Addison-Wesley: Reading, MA, 1989; p 141.

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periphery will give a shift to higher field, in analogy with ^{59}Co chemical shifts.[12] An increase in basicity of the axial base will give roughly a 10 ppm shift to higher field[13] per pK_a unit. A change in solvent polarity from that of DMF-H_2O, 90:10, to toluene gives rise to a 20 ppm upfield shift for FePF(BuIm)(CO), Table I. The effect of tilting the carbonyl relative to the heme normal can then be estimated from the chemical shifts of MbCO, 8234 ppm,[14] and Fe(PPIX)(1-MeIm)(CO), 8151 ppm.[13] In MbCO, the porphyrin is flat and the CO is tilted by about 15°.[8] In Fe(PPIX)(1-MeIm)(CO), the plane is nearly flat and the CO is linear.[15] The chemical shift difference must be due to a difference in coordination of the imidazole residues, a medium effect, and the effect of forcing the carbonyl off axis. The effect of restricted vinyl rotation can be estimated from a comparison between Fe(PPIX)(py-d_5)(CO) and Fe(meso-PIX)(py-d_5)(CO) and should introduce a small upfield shift. A nonideal coordination from histidine to iron in MbCO would suggest a downfield shift by 20-50 ppm.[13] The medium effect on going from aqueous solution to the nonpolar interior of the heme pocket would roughly cancel that, leaving a downfield shift of 50-80 ppm as the effect of tilting the carbonyl.

The magnitudes of all of these shifts are substantially smaller than the ones encountered as an effect of perturbations of the porphyrin core. In Table 1, the chemical shifts are given for the picket-fence porphyrin and a series of sterically hindered iron porphyrins, derivatives of the hybrid "basket-handle" porphyrins by Momenteau and co-workers.[4] From the crystal structures of some of these, it is clear that the carbonyl lies along the heme normal and that the porphyrin is clearly ruffled; the shorter the aliphatic chain, the more it is ruffled.[7] The chemical shift varies by more than 600 ppm between the two extremes and in a seemingly regular fashion, giving a high-field shift with increased ruffling. The magnitude of the shifts is such that they can be interpreted. An upfield shift of more than 100 ppm relative to some reference compound can only be caused by perturbations of the porphyrin residue. Considering the large number of heme proteins and protein mutants under study, this should be a very helpful tool for the investigation of detailed structure. Also, we conclude from the difference in magnitude of the chemical shifts that the perturbation of the d-orbital energies are much larger than what is observed upon changing the ligands in a strictly octahedral complex.

Further information can be extracted from the substituent effects on the chemical shifts when the axial base is varied in the series of carbonyl complexes. As reported previously,[13] the ^{57}Fe NMR resonance is shifted to higher field as the electron-donating ability of the axial base is increased, in a series of Fe(PPIX)(B)(CO) complexes, completely in accordance with prediction. This is true also for the picket-fence and the "largest" basket-handle complex, but for the more tightly packed superstructures, the reverse is true, Table I. Within the framework of the Ramsey equation,[12] the high-field shift of FePF(BuIm)(CO) and FeBH12(BuIm)(CO) can be viewed as originating from an increased repulsion of the d_{z^2} orbital giving rise to an increase in ΔE and a decrease in the chemical shift. With FeBH10(BuIm)(CO) and FeBH9(BuIm)(CO), the data suggest that an increase in the electron-donating ability of the axial base causes a repulsion of the same orbital but that this leads to a decrease in ΔE. This is deduced from the fact that the chemical shift is downfield. This is only possible if the d_{z^2} orbital is no longer unoccupied and one of the previously occupied orbitals has increased its energy so much as to become unoccupied; in other words, there has been an energy level crossover. This requires, of course, that the Ramsay equation is valid under these conditions. An unequivocal proof of an energy level crossover would be to observe a paramagnetic iron(II) porphyrin complex for a certain amount of superstructure tightness, and a reversal of substituent effects for a more pronounced tightness. We were not able to observe a paramagnetic state, but in a similar class of compounds, such an observation has been made. Ellis et al.[16] reported several years ago that they observed paramagnetism in a "capped" porphyrin. They attributed this paramagnetism to nonlinear coordination of one of the axial bases. An alternative explanation is that the porphyrin core is ruffled. In the present case, it is clear that both axial ligands bind in a linear way.

The relevance of this observation is obvious when one considers the importance of spin state for ligand binding in heme proteins. Since the ruffled porphyrins are clearly biologically significant, this should be of considerable interest.

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Registry No. Fe(PPIX)(py-d_5)(CO), 125592-90-7; ^{57}Fe, 14762-69-7.

(12) Bramley, R.; Brorson, M.; Sargeson, A. M.; Schäffer, C. E. *J. Am. Chem. Soc.* **1985**, *107*, 2780.
(13) Baltzer, L.; Landergren, M. *J. Chem. Soc., Chem. Commun.* **1987**, 32.
(14) Baltzer, L.; Becker, E. D.; Tschudin, R. G.; Gansow, O. A. *J. Chem. Soc., Chem. Commun.* **1985**, 1040.
(15) Peng, S. M.; Ibers, J. A. *J. Am. Chem. Soc.* **1976**, *98*, 8032.
(16) Ellis, P. E., Jr.; Linard, J. E.; Szymanski, T.; Jones, R. D.; Budge, J. R.; Basolo, F. *J. Am. Chem. Soc.* **1980**, *102*, 1889.

Flash Photolytic Generation and Study of α-(Trimethylsilyl)vinyl Alcohol: The Effect of α-Silyl Substitution on Enol Chemistry

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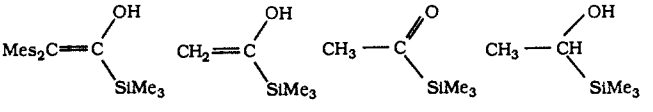
Recent interest in the chemistry of simple enols[1] has led to the prediction that α-silyl substitution should stabilize enols relative to their keto isomers markedly, and that has produced the synthesis of the first stable α-silyl enol, β,β-dimesityl-α-(trimethylsilyl)vinyl alcohol (**1**) (Mes = mesityl = 2,4,6-trimethylphenyl).[2] This enol



1 **2** **3** **4**

could not be converted to its keto isomer under conditions much more drastic than required for ketonization of silicon-free analogues; it therefore certainly does possess unusual kinetic stability. However, because equilibration with the keto isomer could not be achieved, its thermodynamic stability could not be assessed and the effect of silyl substitution on keto-enol equilibria could not be determined. We report that we have now generated another α-silyl enol, the prototype substance α-(trimethylsilyl)vinyl alcohol (**2**), under conditions where this enol is converted to its keto isomer, acetyltrimethylsilane (**3**);[3] this has enabled us to evaluate the keto-enol equilibrium constant for this system as well as acidity constants of the keto and enol forms.

We produced this enol by photooxidation[4] of the corresponding alcohol, α-(trimethylsilyl)ethanol (**4**),[5] using acetone as the oxidant. The two ketyl radicals formed in this reaction, eq 1, may dis-

(1) For reviews, see: (a) Kresge, A. J. *CHEMTECH* **1986**, *16*, 250-254; *Acc. Chem. Res.* **1990**, *23*, 43. (b) Capon, B.; Guo, B.; Kwok, F. C.; Siddhanta, A.; Zucco, C. *Acc. Chem. Res.* **1988**, *21*, 135-140. (c) Rappoport, Z.; Biali, S. *Acc. Chem. Res.* **1988**, *21*, 442-449.
(2) Nadler, E. B.; Rappoport, Z.; Arad, D.; Apeloig, Y. *J. Am. Chem. Soc.* **1987**, *109*, 7873-7875.
(3) Cunico, R. F.; Kuan, C. P. *J. Org. Chem.* **1985**, *50*, 5410-5413.
(4) Keeffe, J. R.; Kresge, A. J.; Schepp, N. P. *J. Am. Chem. Soc.* **1988**, *110*, 1993-1995.
(5) Lim, T. F. O.; Myers, J. K.; Rogers, G. T.; Jones, P. R. *J. Organomet. Chem.* **1977**, *135*, 249-259.

0002-7863/90/1512-2805$02.50/0