At pH 9, where the enzyme is most active, ferric lipoxygenase exhibits an EPR spectrum with components similar to those seen at pH 7, although the ratios of intensities differ and the lines are considerably broader.[12] Addition of ethanol results in a single major component with apparent g values of 6.2, 5.8, and 2. Small line broadenings were observed in the presence of $H_2{}^{17}O$ before and after addition of ethanol, but quantitation was frustrated by the 120 G line widths.

This report presents evidence for at least one coordinated water (or hydroxide) at the iron site in ferric soybean lipoxygenase-1. This water is not displaced by ethanol or HCN, both of which affect the electronic structure of the iron. However, there is no significant line-broadening from $H_2{}^{17}O$ in spectra of the nitrosyl complex of ferrous soybean lipoxygenase-1;[4] either no water is coordinated to the iron in that complex, or the bound ^{17}O nucleus is only weakly coupled to the electron spin. Coordination of NO may displace water, or the water may be a ligand only in the oxidized enzyme. That point, the quantitation of the number of waters bound, and the extension to enzyme–inhibitor and enzyme–product complexes are being pursued currently by electron nuclear double resonance spectroscopy.

Water usually is assumed to be a readily displaceable ligand. The observation of water coordinated to the iron leaves open the question of whether the substrate or any intermediate of the reaction does bind to the iron and encourages the effort to design lipoxygenase inhibitors based on iron coordination chemistry.

Inclusion Tuning of Nonlinear Optical Materials: Switching the SHG of *p*-Nitroaniline and 2-Methyl-*p*-nitroaniline with Molecular Sieve Hosts

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Inclusion of a guest species into a host framework can be used in a combinatorial or synergistic mode to create nonlinear optic properties which are dramatically different from those of either host or guest independently. Molecular dipolar alignment has been observed in organic and organometallic host–guest chemistry where, for example, *p*-nitroaniline (NA, SHG = 0 due to its centrosymmetric crystal structure) in β-cyclodextrin has an SHG = 64 x quartz.[1] Inclusion chemistry can also be used to modify wave mixing and wave guide characteristics as illustrated by the use of ion exchange in the potassium titanyl phosphate (KTP) family.[2]

These observations and the fact that nonlinear optical properties are particularly sensitive to structural variations[3,4] suggest that inclusion chemistry can be used as a means for achieving fine control, through careful synthetic choices, of a variety of nonlinear optical effects. This paper gives the first report of the use of inorganic hosts and organic guests to form nonlinear optic materials. An SHG signal ten times larger than that of any previously reported organic or organometallic inclusion complex is observed.

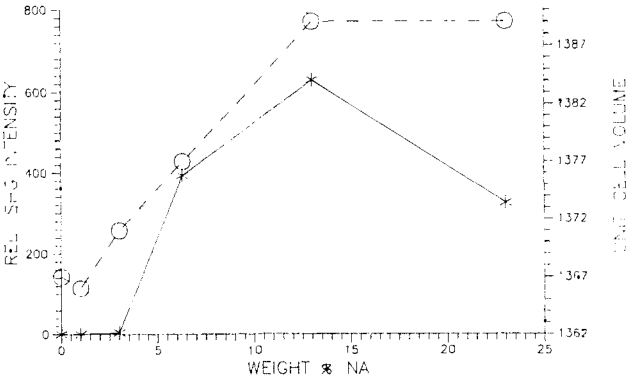

Figure 1. *p*-Nitroaniline in ALPO-5. Loading level (weight % NA) versus SHG intensity relative to quartz (solid line, *) and unit cell volume in Å^3 (dashed line, O).

Second harmonic generation (SHG) requires noncentrosymmetric structural features[3,5] which can be imposed on a sorbate by an acentric host or created by sorbate–host interactions. Many zeolites have ideal pore dimensions for the ordering or alignment of aromatic sorbates such as NA, and some have acentric structures. NA and 2-methyl-*p*-nitroaniline (MNA, SHG = 375[6]), which have similar second order molecular hyperpolarizabilities,[7,8] were introduced into a variety of acentric and centrosymmetric zeolite hosts by a vapor-phase loading method.[9] Loading levels are easily varied by this method up to a maximum at which pore-filling occurs. The guest molecules are strongly adsorbed. Heating to 100 °C under dynamic vacuum does not result in appreciable weight loss below the pore-filling level specific to each host–guest pair. The samples have a uniform bright yellow or yellow-orange color which pales slightly as the loading is lowered. Exposure to ambient air does not cause displacement of adsorbed organic from the molecular sieve pores according to X-ray powder diffraction pattern, which shows peaks due to the organic only when the pore capacity of the zeolite is exceeded.

NA in zeolites Y, Omega, and Mordenite[10] shows no SHG.[11] These are all centrosymmetric molecular sieves.[12] Figure 1 on the left-hand axis shows the SHG results for NA in ALPO-5,[10] an acentric (space group *P6cc*) molecular sieve with a neutral framework composed of alternating AlO_4 and PO_4 tetrahedra linked by oxygen bridges forming an array of one-dimensional 12-ring channels.[13] The SHG is near zero up to 3 wt % loading and then rapidly increases to a maximum of 630 at 13 wt % NA. This maximum is ten times larger than for any NA–organic host complex. SHG intensity tapers off at higher loadings due to dilution with external NA. Changes in unit cell volume with

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(1) Tomaru, S.; Zembutsu, S.; Kawachi, M.; Kobayashi, M. *J. Chem. Soc., Chem. Commun.* **1984**, 1207–1208. (b) Tomaru, S.; Zembutsu, S.; Kawachi, M.; Kobayashi, M. *J. Incl. Phenom.* **1984**, *2*, 885–890. (c) Wang, Y.; Eaton, D. F. *Chem. Phys. Lett.* **1985**, *120*, 441–444. (d) Eaton, D. F.; Anderson, A. G.; Tam, W.; Wang, Y. *J. Am. Chem. Soc.* **1987**, *109*, 1886–1888.

(2) Bierlein, J. D.; Gier, T. E. U.S. Patent No. 3 949 323, 1976. (b) Gier, T. E. U.S. Patent No. 4 231 838, 1980. (c) Gier, T. E. U.S. Patent No. 4 305 778, 1981. (d) Bierlein, J. D.; Ferretti, A.; Brixner, L. H.; Hsu, W. H. *Appl. Phys. Lett.* **1987**, *50*, 1216–1218. (e) Eddy, M. M.; Gier, T. E.; Keder, N. L.; Cox, D. E.; Bierlein, J. D.; Jones, G.; Stucky, G. D. *Inorg. Chem.* **1988**, submitted for publication.

(3) (a) Zyss, Z.; Oudar, J. L. *Phys. Rev.* **1982**, *A26*, 2016–2027. (b) Oudar, J. L.; Zyss, Z. *Ibid.* **1982**, *A26*, 2028–2048.

(4) Panunto, T. W.; Urbanczyk-Lipkowdka, Z.; Johnson, R.; Etter, M. C., private communication to be published. (b) Etter, M. C. *Isr. J. Chem.* **1985**, *25*, 312–319. (c) Etter, M. C. *J. Am. Chem. Soc.* **1982**, *104*, 1095–1096.

(5) Williams, D. J. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 690–703.

(6) Powder intensity reported in ref 5. Matching of coherence length and particle size can give a much larger SHG intensity (>5000).

(7) (a) Levine, B. F. *Chem. Phys. Lett.* **1976**, *37*, 516–520. (b) Oudar, J. L.; Chemla, D. S. *J. Chem. Phys.* **1977**, *66*, 2664–2668.

(8) (a) Levine, B. F.; Bethea, C. G.; Thurmond, C. D.; Lynch, R. T.; Bernstein, J. L. *J. Appl. Phys.* **1979**, *50*, 2523–2527. (b) Lipscomb, G. F.; Garito, A. F.; Narang, R. S. *J. Chem. Phys.* **1981**, *75*, 1509–1516.

(9) The desired portions of predried molecular sieve and NA or MNA (purified by vacuum sublimation followed by recrystallization from 95% ethanol) are placed in an ampoule connected to a vacuum stopcock. This step is done in a dry atmosphere. The ampoule is evacuated, closed off, and heated to 100 °C for 16 h.

(10) Sample kindly provided by Union Carbide Corporation.

(11) SHG measurements were made as described by Dougherty and Kurtz (Dougherty, J. P.; Kurtz, S. K. *J. Appl. Cryst.* **1976**, *9*, 145–158). The values quoted are in reference to quartz samples.

(12) Breck, D. W. *Zeolite Molecular Sieves*; J. Wiley & Sons: New York, 1974; pp 163, 167, 177.

(13) Bennet, J. M.; Cohen, J. P.; Flanigen, E. M.; Pluth, J. J.; Smith, J. V. In *Intrazeolite Chemistry*; Stucky, G. D., Dwyer, F. G., Eds.; ACS Symposium Series 218; American Chemical Society: Washington, DC, 1983; pp 109–118.

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loading, determined from indexed X-ray powder patterns, are shown on the right-hand axis of Figure 1. There is a steady increase in unit cell volume up to the loading level where maximum SHG is observed followed by a flattening off thereafter. This shows that the NA is within the pores and that the maximum SHG signal occurs when the pores are full.

In contrast, MNA in ALPO-5 shows nearly complete loss of SHG on inclusion. A 13 wt % MNA sample shows SHG of 0.66. Only at higher loadings, when MNA is outside the pores of the zeolite as shown by X-ray powder diffraction, does the SHG increase. In all other respects (color, stability, unit cell volume increase with loading) the NA and MNA samples are very similar.

ALPO-5 thus switches NA on and MNA off. This is a dramatic demonstration of how inclusion can influence nonlinear optical properties. It is clear that subtle size, shape, and symmetry effects are at play. The extra size of the methyl group in MNA must restrict its orientation in the ALPO-5 channels in ways which prohibit the required bulk dipolar alignment. These restrictions must be missing for NA. The acentric structure of ALPO-5 is an important factor in switching on the SHG of NA since the centrosymmetric hosts did not have the same effect.

A more thorough look at loading levels, other sorbate-host combinations including other acentric hosts, and further structural characterization is underway.

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Direct α-Phosphoryloxylation of Ketones and Phosphoryloxylactonization of Pentenoic Acids with [Hydroxy((bis(phenyloxy)phosphoryl)oxy)iodo]benzene

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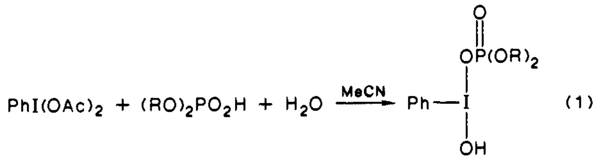
The ability of [hydroxy(tosyloxy)iodo]benzene (**1**) to introduce the tosylate ligand into ketones, alkenes, and alkenoic acids to give α-tosyloxy ketones,[1] *vic*-ditosyloxyalkanes,[2] and tosyloxy lactones[3] prompted us to investigate the synthesis of reagents analogous to **1** with iodine(III)-bound phosphate ligands[4] and to

$$\underset{\mathbf{1}}{\mathrm{PhI(OH)OTs}} \qquad \underset{\mathbf{2}}{\mathrm{RC{\equiv}COP(O)(OEt)_2}}$$

$$\underset{\mathbf{3}}{\mathrm{RC{\equiv}C{-}I^{+}{-}Ph,\ {}^{-}O_2P(OEt)_2}}$$

explore their efficacy for the preparation of phosphate esters. Precedent for the phosphoryloxylation of carbon via hypervalent iodine species has recently been provided by Stang and his coworkers who described the synthesis of the first alkynyl phosphates **2** from alkynyl(phenyl)iodonium phosphates **3**.[5] We now report the preparation of [hydroxy((bis(phenyloxy)phosphoryl)oxy)iodo]benzene (**4a**) and a preliminary study of its reactions with ketones and alkenoic acids.

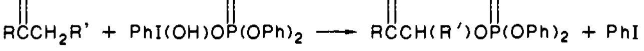
[Hydroxy((bis(phenyloxy)phosphoryl)oxy)iodo]benzene was made from (diacetoxyiodo)benzene and diphenyl phosphate in acetonitrile spiked with water (eq 1) and appropriately characterized.[6] In one preparation, a mixture of $PhI(OAc)_2$ (60 mmol), $(PhO)_2PO_2H$ (61 mmol), and H_2O (120 mmol) in MeCN (150 mL), after ca. 4 h at room temperature and refrigeration, gave a 90% yield of **4a**.



$$\mathrm{PhI(OAc)_2 + (RO)_2PO_2H + H_2O \xrightarrow{MeCN} Ph{-}\overset{\overset{\displaystyle OP(O)(OR)_2}{|}}{\underset{\underset{\displaystyle OH}{|}}{I}}} \qquad (1)$$

4a: R = Ph
b: R = $PhCH_2$

Various ketones were converted directly by **4a** into ketol phosphates **5**, compounds of interest as sugar analogues[7] (eq 2).



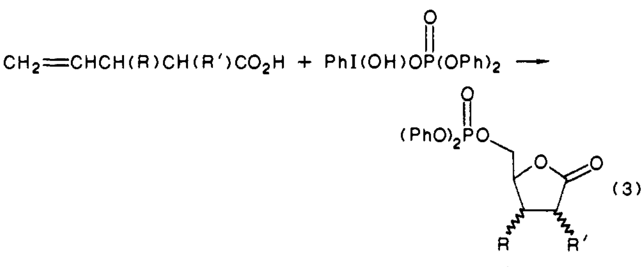
$$\mathrm{R\overset{\overset{\displaystyle O}{\|}}{C}CH_2R' + PhI(OH)O\overset{\overset{\displaystyle O}{\|}}{P}(OPh)_2 \longrightarrow R\overset{\overset{\displaystyle O}{\|}}{C}CH(R')O\overset{\overset{\displaystyle O}{\|}}{P}(OPh)_2 + PhI} \qquad (2)$$

5a: R = Ph, R′ = H
b: R = Me, R′ = H
c: R = cyclopropyl, R′ = H
d: R, R′ = $-(CH_2)_4-$
e: R = Ph, R′ = PhCO (2)

For example, a mixture of **4a** and acetophenone in MeCN was heated and concentrated. Treatment of the residual oil (in CH_2Cl_2) with H_2O and 5% $NaHCO_3$ and removal of volatile impurities (e.g., PhI, PhCOMe) gave α-((bis(phenyloxy)phosphoryl)oxy)acetophenone (**5a**) in 59% yield. Similar reactions of acetone, cyclopropyl methyl ketone, cyclohexanone, and dibenzoylmethane with **4a** gave the ketol phosphates **5b–e**; conditions and yields are summarized in Table I.

In addition to characteristic C=O and P=O absorptions in the infrared, the α-carbon–phosphate linkage produces NMR resonances which are particularly diagnostic of the ketol phosphate structures; i.e., the α-hydrogens are deshielded, and both the α-hydrogens and α-carbon are coupled with phosphorus. Selected spectral data for **5a–e** are given in Table II.

4-Pentenoic acids react with **4a** to give 5-(bis(phenyloxy)-phosphoryl)oxy-4-pentanolactones **6** (eq 3.) For example, a solution of 4-pentenoic acid and **4a** in CH_2Cl_2 was stirred at room temperature (2 h, 40 min), diluted with CH_2Cl_2, washed (H_2O, 5% $NaHCO_3$), dried, and concentrated. Crystallization of the residual oil gave crude **6a** in 55% yield. Similar treatment of 2-methyl-4-pentenoic acid with **4a** gave **6b** as a mixture (ca. 1.2 to 1.4:1) of diastereomers (NMR analysis).



6a: R = R′ = H
b: R = H, R′ = Me
c: R = OH, R′ = H

The structural relationship of **6a** and **6b** to the pentofuranose-5-phosphates suggested a study of the action of **4a** on 3-hydroxy-4-pentenoic acid.[8] 3-Hydroxy-4-pentanolactone **6c**

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[1] Koser, G. F.; Relenyi, A. G.; Kalos, A. N.; Rebrovic, L.; Wettach, R. H. *J. Org. Chem.* **1982**, *47*, 2487.

[2] Rebrovic, L.; Koser, G. F. *J. Org. Chem.* **1984**, *49*, 2462.

[3] Shah, M.; Taschner, M. J.; Koser, G. F.; Rach, N. L. *Tetrahedron Lett.* **1986**, *27*, 4557.

[4] "*o*-Iodosophenylphosphoric acid" and its methyl ester, heterocyclic iodine(III) phosphates, have been reported, but their chemistry has been little explored, see: Leffler, J. E.; Jaffe, H. *J. Org. Chem.* **1973**, *38*, 2719.

[5] Stang, P. J.; Boeshar, M.; Lin, J. *J. Am. Chem. Soc.* **1986**, *108*, 7832.

[6] White solid; needles from MeCN [mp (uncorrected) 102–105 °C]; IR (CH_2Cl_2) 3399 cm^{-1} br, OH); ^1H NMR (300 MHz, $CDCl_3$) δ 6.95–7.14 (m, 6 H), 7.14–7.34 (m, 6 H), 7.35–7.43 (apparent t with fine structure, 1 H), 7.75–7.95 (d, 2 H), OH not observed; ^{13}C NMR ($CDCl_3$) δ 120.2 (d, J_{CP} = 5.1 Hz), 124.0 (s), 124.1 (s), 129.4 (s), 130.8 (s), 131.3 (d, J_{CP} = 6.5 Hz), 132.3 (s), 151.8 (d, J_{CP} = 7.3 Hz); ^{31}P NMR ($CDCl_3$) δ −12.4 (s); Anal. Calcd for $C_{18}H_{16}O_5IP$: C, 45.98; H, 3.43; P, 6.59. Found: C, 45.84; H, 3.52; P, 7.08; 6.53 (second sample); molecular weight, calcd 470.2, found (iodometric titration) 473.6.