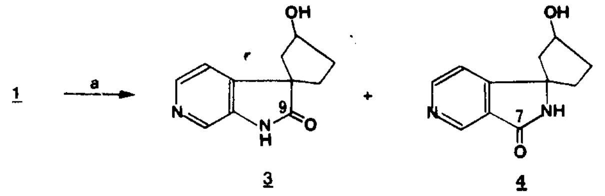
Scheme III



^{a}NaClO, NaOH.

nicotinic acid was shown to reside entirely at the expected position[4] (C-5) by the degradation outlined in Scheme II. These findings demonstrate that nicotinic acid is biosynthesized from tryptophan in *Sesbania* and that nicotinic acid is a specific precursor of sesbanine. The observed formation of nicotinic acid from tryptophan is of interest, since the current evidence for the operation of this pathway in higher plants is equivocal.[5,6]

The origin of ring A and C-7 of sesbanine having been established, efforts were focused on elucidation of the origin of the cyclopentane moiety of the alkaloid. The six carbon atoms (C-9 to C-14) were postulated to be derived from an aromatic ring by a ring-contraction process that might be similar to that observed in the *Cephalotaxus* alkaloids.[7] Accordingly, tyrosine, phenylalanine, and shikimic acid were evaluated as precursors (Table I, experiments 3–5). Tyrosine and phenylalanine gave poor incorporations, while shikimate appeared more promising. Degradation (Scheme I) of the sesbanine derived from [G-^{14}C]shikimate disclosed that the pyridine dicarboxylic ester **2** carried 17% of the total radioactivity (theory = 17%). Further proof that shikimic acid is a specific precursor of sesbanine was obtained by administration of [7-^{14}C]shikimate[8] to *Sesbania*. Degradation of the labeled sesbanine obtained in this experiment (Table I, experiment 6) by the route shown in Scheme III revealed that 90% of the radioactivity was present in the oxindole **3**, while the phthalimidine **4** was inactive. Shikimate therefore appears to be a specific precursor of the cyclopentanoid moiety of sesbanine. Additional information on the mode of incorporation of shikimate was provided by evaluation of *p*-hydroxybenzoic acid, which is known to be derived from chorismic acid in bacteria.[9] Administration of [U-^{14}C]-*p*-hydroxybenzoate to *Sesbania* gave the highest incorporation figure yet observed for a sesbanine precursor (Table I, experiment 7), and degradations proved the incorporation to be specific. Degradation of the sesbanine according to Scheme I yielded diester hydrochloride **2** that carried 18% of the total activity (theory = 17%), while degradation according to Scheme III yielded oxindole **3** bearing 97% of the radioactivity (theory = 100%) and phthalimidine **4** bearing 79% of the radioactivity (theory = 83%).

In summary, our investigations show that sesbanine is biosynthesized from nicotinic acid and *p*-hydroxybenzoic acid with loss of one carbon atom from the aromatic ring of the latter compound. The intermediate stages of this novel biosynthetic pathway remain to be elucidated.

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Control of Bulk Dipolar Alignment Using Guest–Host Inclusion Chemistry: New Materials for Second-Harmonic Generation

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Second harmonic generation (SHG) is a subset of nonlinear optical properties which is currently under intensive investigation at laboratories around the world.[1] Many polar, acentric organic and inorganic materials are capable of efficient SHG when subjected to intense optical fields encountered under laser irradiation. From a physical organic perspective, it is useful to consider the electronic properties of those materials that have proved to be effective for SHG. Oudar[2] has suggested that a simple two-level model is adequate for predictive use in a search for new materials. Within this framework, polar materials which possess low-lying charge-transfer states, or which experience large changes in molecular dipole moment on photoexcitation, are potential SHG active materials. These are materials that are anticipated to have high molecular second-order polarizability, β, which will contribute to the field-induced dipole moment, μ (eq 1). Physical organic

$$\mu = \mu_0 + \alpha \mathrm{E} + \beta \mathrm{EE} + \gamma \mathrm{EEE} + \ldots \qquad (1)$$

and organometallic chemists can list many small molecules which may be SHG active based on this simple criterion. Unfortunately, many inherently interesting molecules fail to be SHG active in the bulk because their crystal space group is centrosymmetric, and the bulk polarizability of the material vanishes because of symmetry restrictions on the expansion of the bulk polarization **P**, a vectoral quantity (eq 2). To date, methods for engineering

$$\mathbf{P} = \mathbf{P}_0 + \chi^{(1)}\mathbf{E} + \chi^{(2)}\mathbf{EE} + \chi^{(3)}\mathbf{EEE} + \ldots \qquad (2)$$

small polar molecules into acentric environments have been restricted to thin film (Langmuir–Blodgett monolayers,[3] orientation of molecules in polymer glasses[4] using strong electric or magnetic fields, or use of liquid-crystalline mesogens[4]) or directed crystal growth techniques.[5] We now report that polarizable materials whose natural crystal habit may be centrosymmetric (thus incapable of SHG) can be induced to exhibit SHG by inclusion into a host lattice structure[6] which imparts a polar director to the alignment of the molecular dipoles. The use of inclusion compound hosts appears, surprisingly, to be a general method for dipolar alignment of organic and organometallic compounds.[7]

We have found that inclusion hosts such as thiourea, tris(*o*-thymotide) (TOT), and deoxycholic acid, as well as clathrate hosts such as cyclodextrins[7] (CD), are capable of forming polar

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Table I. Relative Second-Harmonic Generation Capabilities of Host–Guest Inclusion Complexes

guest	host:guest	SHG rel to urea
Inclusion Compounds with β-Cyclodextrin		
p-nitroaniline	1:1	2.0–4.0
p-(*N*,*N*-dimethylamino)cinnamaldehyde	1:1	0.4
N-methyl-*p*-nitroaniline	1:1	0.25
2-amino-5-nitropyridine	1:1	0.07
p-(dimethylamino)benzonitrile	1:1	0.015
Inclusion Complexes with Thiourea		
benzenechromium tricarbonyl	3:1	2.3
(fluorobenzene)chromium tricarbonyl	3:1	2.0
(cyclopentadienyl)rhenium tricarbonyl	ND[a]	0.5
(1,3-cyclohexadiene)iron tricarbonyl	3:1	0.4
(1,3-cyclohexadienyl)manganese tricarbonyl	3:1	0.4
(trimethylenemethane)iron tricarbonyl	3:1	0.3
(cyclopentadienyl)manganese tricarbonyl	3:1	0.3
(1,3-butadiene)iron tricarbonyl	ND[b]	1.0
pyrrolylmanganese tricarbonyl	ND[b]	0.2
(cyclopentadienyl)dicarbonylnitrosylchromium	3:1	0.1
(cyclopentadienyl)diethylenerhodium	ND[b]	0.0
(cyclopentadienyl)(1,3-cyclohexadiene)cobalt	3:1	0.0
(cyclopentadienyl)ethylenetetrafluoroethylenerhodium	ND[b]	0.0
Inclusion Complexes with Tris(*o*-thymotide)		
p-(dimethylamino)cinnamaldehyde	2:1	1.0
p-(dimethylamino)benzonitrile	2:1	0.3
(*p*-cyanobenzoyl)manganese pentacarbonyl	ND[c]	0.2
(indane)chromium tricarbonyl	1:1	0.1
(anisole)chromium tricarbonyl	ND[c]	0.1
(tetralin)chromium tricarbonyl	1:1	0.1
benzenemanganese tricarbonyl–tetrafluoroborate	ND[c]	0.1
(pyridine)tungsten pentacarbonyl	2:1	0
Inclusion Complexes with Deoxycholic Acid		
p-nitroaniline	ND	1.0
4-(dicyanomethylene)-2-methyl-6-(*p*-(dimethylamino)styryl)-4*H*-pyran	ND	0.4

[a] Errors in powder SHG intensity measurements can be ±50% because of particle size differences among samples, but relative rankings within a series are probably correct. Note, e.g., the range of values obtained for different preparations of PNA–β-CD; ND = not determined. [b] In some cases volatility of the guest complicates analysis. [c] Cocrystallization of TOT with the complexes prevents accurate analysis.

Table II. X-ray Structures of Selected Complexes

complex	space group
tris(thiourea)–(benzene)chromium tricarbonyl	$R3c$
tris(thiourea)–(1,3-cyclohexadiene)manganese tricarbonyl	$R3c$
tris(thiourea)–(1,3-cyclohexadiene)iron tricarbonyl	$Pna2_1$
TOT_2–(tetralin)chromium tricarbonyl	$Pca2_1$
TOT_2–*p*-(dimethylamino)cinnamaldehyde	$P1$[a]
TOT_2–(pyridine)tungsten pentacarbonyl	$I2/a$

[a] The structure is disordered (in TOT or the aldehyde) and was solved within space group $P\bar{1}$ (a centrosymmetric space group). The observation of SHG is sufficient to assign the correct structure as $P1$ (acentric).

guest–host complexes with a wide variety of organic and organometallic compounds. In most cases a solution containing the guest and host is allowed to crystallize by cooling below ambient temperature or by slow evaporation. In some instances, solvent diffusion techniques have been used to produce adequate crystals. SHG measurements were made by using a modification of the method of Kurtz and Perry,[8] using powder samples (250-μm-thick cell). Urea (90–125 μm) was used as a reference material.[9] A Nd-YAG laser emitting at 1.06 μm was used in all experiments, and the frequency-doubled green beam at 532 nm was observed through band-pass filters. The modifications made to the method ensure that spurious light is not detected as SHG radiation.[10] Table I lists relative magnitudes of SHG, compared to urea, for the series of complexes prepared.

Several points are pertinent. First, with the sole exception of *N*-methyl-*p*-nitroaniline, all of the guests crystallize in centrosymmetric space groups and are incapable of SHG. Of the hosts, both the cyclodextrins and the cholic acid derivatives are chiral and thus crystallize in noncentrosymmetric space groups, but they are not especially polarizable molecules. Therefore, they do not exhibit substantial SHG alone (e.g., β-CD shows SHG 0.001× urea), and SHG observed for the inclusion complexes represents a significant alteration of the nonlinear optical properties of the composite solids. Neither TOT nor thiourea exhibit SHG; both are centrosymmetric solids in their native crystal forms. Second, 28 examples are listed in Table I; only four failed to exhibit SHG. Statistically, an organic or organometallic compound chosen at random has approximately only a 30% probability of crystallizing in an acentric space group.[11] The occurrence of polar, noncentrosymmetric structures in our work is 85%. This surprising generality demonstrates that there must be aspects of the inclusion process which favor construction of polar structures over nonpolar ones. Third, we note the generality of the nature of both the host and the guest. We believe that this is among the first examples of the use of organometallics for nonlinear optics.[12] Fourth, while we have not yet measured the second-order susceptibility ($\chi^{(2)}$) of any of the solids reported, the relative SHG values compared to urea ($\chi^{(2)} \sim 3 \times 10^{-9}$ esu)[1,9] suggest that they can be quite efficient SHG materials, with susceptibilities near those of lithium niobate ($\sim 10^{-8}$ esu),[8,13] potassium dihydrogen phosphate (KDP; $\sim 3 \times 10^{-9}$ esu),[9a,c] or potassium titanyl phosphate (KTP, $\sim 3 \times 10^{-8}$ esu),[14] materials used commonly as frequency doublers in lasers. Organic materials capable of comparable SHG have also been discovered, e.g., 2-methyl-4-nitroaniline (MNA, $\sim 2 \times 10^{-8}$ esu).[15]

X-ray crystal structures[16] have been obtained for some of the composite solids. Structures that have been solved are listed in

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(16) X-ray analyses were performed by Dr. J. Calabrese and Dr. I. Williams of this department. Data were collected on either a Syntex R3 or an Enraf-Norius CAD4 diffractometer, using graphite-monochromated Mo Kα radiation. Crystals, roughly 0.4–0.5 mm along the longest dimension, were prepared by solvent diffusion or slow evaporation techniques. Structures were refined by Patterson (PHASE) methods or by direct methods (MULTAN). Final R factors were in the range 2.9–5%, depending on the sample. Graphics used in the figure were produced using CHEM-X, designed and distributed by Chemical Design Ltd., Oxford, England. The crystallographic coordinates and symmetry parameters were used to generate the packing diagrams. Full details of the structures will be reported separately.

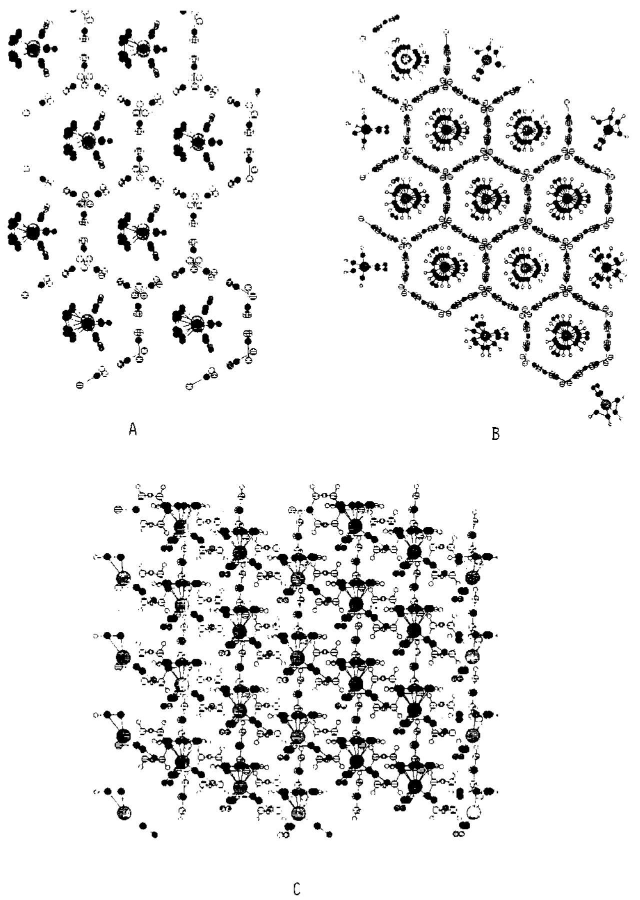

Figure 1. (a) Molecular arrangement of (1,3-cyclohexadiene)Fe(CO)$_3$ within the hexagonal thiourea lattice in tris(thiourea)–(1,3-CHD)Fe(CO)$_3$. (b) A similar view in tris(thiourea)–$C_6H_6Cr(CO)_3$. (c) Another view of tris(thiourea)–$C_6H_6Cr(CO)_3$, perpendicular to the stacking axis, showing the dipolar alignment of the organometallic (the structure of tris(thiourea)–(1,3-CHD)Mn(CO)$_3$ is isomorphous).

Table II. All SHG active materials are members of polar space groups. Several structures will be discussed briefly. Tris(thiourea)–(1,3-cyclohexadiene)iron tricarbonyl crystallized in the orthorhombic space group *Pna*2$_1$. Hexagonal channels of thiourea enclose stacks of the organometallic guest. The (1,3-CHD)Fe(CO)$_3$ molecules are arranged sideways within the channels, with the dipolar axis extending between the carbonyl end of the molecule and the CHD portion directed perpendicular to the channel axis (crystal *c* axis; Figure 1A). Within each channel, the polar director is pointed either 30° up or down with respect to the net polar axis (crystal *a* axis). The structures of the other two thiourea inclusion complexes listed (those with $(C_6H_6)Cr(CO)_3$ and (1,3-CHD)Mn(CO)$_3$) are similar, with respect to the arrangement of the thiourea matrix, but have the dipolar organometallics stacked head to tail within the channel along the polar axis (crystal *c* axis in space group *R*3*c*; Figure 1B,C). Thus the polar director is oriented in a markedly different manner even within this small series of similar complexes. The only inactive inclusion compound for which we have determined the crystal structure, TOT_2–(Pyr)W(CO)$_5$, is centrosymmetric.[17]

The bulk nonlinearity of these complexes arises from their polar, noncentrosymmetric structures. The molecular polarizability which contributes to the SHG is correlated with the degree of charge transfer associated with the excited states of the guests. For the organics, such as *p*-nitroaniline, the donor–acceptor substituents influence the movement of charge on excitation in a predictable way.[1,2] This situation is less clear for the organometallics used here.[12] For some, the position of the d–d transitions with respect to metal-to-ligand or ligand-to-metal transitions is not known. The degree of CT involved in these complexes is also not known. A simple analysis predicts that organometallics whose accessible excited states are d–d localized cannot be highly nonlinearly polarizable, but how close in energy CT states should lie to cause observed nonlinearities is unknown. In addition, possible contributions of the host to the resultant bulk polarization of the complexes in unknown at this time. We believe that a thorough analysis of the series of structures reported here can offer new insights into the molecular and bulk contributions to optical nonlinearity.

The inclusion complex method appears to be a general technique for dipolar alignment. In solution, dipoles prefer to aggregate in a face-to-face, antiparallel arrangement, which minimizes electrostatic repulsion.[18] In a lattice inclusion matrix, dipoles would prefer to arrange themselves in a linear, head-to-tail sequence which minimizes electrostatic interactions in this pseudo-one-dimensional situation. A cofacial, antiparallel arrangement within the channel can be prohibited sterically if the channel width r is smaller than roughly twice the dipole thickness. If the dipoles, once included in a channel, are not able to rotate or rearrange, then a polar alignment will be a stable and favorable arrangement. This can be assured if the dipole length is larger than r. This simple electrostatic and steric mnemonic is useful in choosing guest–host combinations, if other factors, such as hydrogen bonding, are not operative. We are continuing to elaborate both the structural limits of this mnemonic and to study the linear and nonlinear optical properties of these complexes in more detail.

Acknowledgment. We thank Drs. J. Calabrese and I. Williams for X-ray crystallography and Drs. D. L. Thorn and G. R. Meredith for helpful suggestions.

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