For a sample of high optical density, the height of the sample volume is less than that imaged into the spectrometer and saturation does not result in a decrease in intensity of the analyte bands but only increases the Raman intensity from the transparent solvent and internal standard in the bleached sampling volume.

Note Added in Proof. Recently we reassigned the ca. 1000 cm^{-1} and 800 cm^{-1} substituted benzene Raman peaks to the ν_{12} and ν_1 modes of benzene, respectively. We have avoided dwelling on this reassignment in this paper because it would confuse comparisons with data cited by other workers. Details on this reassignment are found in ref 12.

Acknowledgment. We gratefully acknowledge partial support of this work from NIH grant 1R01GM30741-04. Sanford A. Asher is an Established Investigator of the American Heart Association; this work was done during the tenure of an Established Investigatorship of the American Heart Association and with funds contributed in part by the American Heart Association, Pennsylvania affiliate.

Registry No. Phenol, 108-95-2; tyrosine, 60-18-4; tryptophan, 73-22-3.

Cadmium-113 Shielding Tensors of Cadmium Compounds. 3. Single-Crystal Studies on Cadmium Glycinate Monohydrate and Cadmium Dinitrato Bis(1,1,3,3-tetramethyl-2-thiourea)

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Abstract: Cadmium glycinate monohydrate and cadmium dinitrato bis(1,1,3,3-tetramethyl-2-thiourea) have been investigated by single-crystal oriented ^{113}Cd NMR. The cadmium shielding tensor elements for the two sulfur–four oxygen system in $Cd(C_5H_{12}N_2S)_2(NO_3)_2$ are −340, +308, and +327 ppm for σ_{11}, σ_{22}, and σ_{33}, respectively. The 438 ppm anisotropy and the extreme magnitude of σ_{11} are discussed in terms of cadmium–sulfur and cadmium–nitrate interactions. The orientation of the shielding tensor is in agreement with previous results for oxo–cadmium crystals. The ^{113}Cd shielding tensor elements for $Cd(NH_2CH_2CO_2)_2{\cdot}H_2O$ were determined to be −116, +200, and +256 ppm relative to solid $Cd(ClO_4)_2$. The orientation of the tensor in this two nitrogen–four oxygen system was found to be dominated by the glycinate chelate moieties.

Substitution of Cd^{2+} for Ca^{2+} in parvalbumin,[1] troponin,[2,3] calmodulin,[4] insulin,[5] and concanavalin A[6] places cadmium in an all-oxygen coordination environment. The ^{113}Cd NMR spectroscopy of these cadmium-substituted metalloproteins gives rise to anomalously shielded isotropic chemical shifts (for a review of NMR of calcium-binding proteins, see ref 7). Because of our interest in the development and utilization of cadmium magnetic resonance as a probe of calcium sites in the muscle proteins troponin and calmodulin, we have undertaken an extensive investigation of the structural factors responsible for this characteristic cadmium chemical shielding. In particular we have been interested in how cadmium–oxygen bond length dispersion and variation in the source of oxygen ligands are manifest in the magnitude and orientation of individual shielding tensor elements. Previous solution and solid-state work[8-10] on oxo–cadmium model compounds indicates that the isotropic average of the cadmium shielding tensor is not sufficiently discriminating to establish structure–shift correlations.

Preliminary single-crystal oriented ^{113}Cd NMR of seven oxo–cadmium compounds has demonstrated four tensor element–structure correlations.[11,12] First, tensor elements of comparable magnitude have similar orthogonal environments. Second, the least shielded tensor element is aligned nearly orthogonal to planes containing water oxygens. Third, if the cadmium coordination sphere is devoid of water oxygens, then the least shielded element is oriented to maximize the short cadmium–oxygen bond shielding contribution. Fourth, the most shielded tensor element is nearly perpendicular to the longest cadmium–oxygen bond.

These data suggest the following interpretation of cadmium chemical shielding. The isolated closed-shell Cd^{2+} ion is the most shielded species possible. Any perturbation of this configuration via bond formation results in a "deshielding" of the cadmium nucleus. Long cadmium–oxygen bonds, typically associated with poor ligands such as nitrate and sulfate, indicate weak bonding interactions. Tensor elements reflecting contributions from these types of interactions are therefore shielded relative to the hexaaquo species, $Cd(ClO_4)_2$. Conversely, more covalent cadmium–nitrogen and cadmium–sulfur bonding interactions represent greater perturbations of the closed-shell configuration. Tensor elements reflecting shielding contributions from these ligands are therefore expected to fall in the deshielded region of the chemical shift range.

In order to refine these arguments, the orientation of the ^{113}Cd shielding tensor in single cyrstals of cadmium glycinate monohydrate and cadmium nitrate tetramethylthiourea was determined. For the establishment of tensor element–structure correlations, these two crystals represent excellent two nitrogen–four oxygen and two sulfur–four oxygen systems. The orientation of the least

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Table I. Direction Cosines Relating the Principal Elements of the ^{113}Cd Shielding Tensor to the Molecular Reference Frame in Cadmium Nitrate Tetramethylthiourea

tensor element,[a] ppm		direction cosines			angle, deg		
		a'	*b*	*c'*	*a'*	*b*	*c'*
σ_{11}	−340	0.0228	−0.9995	−0.0227	89	178	91
σ_{22}	308	0.1859	−0.0181	0.9824	79	91	11
σ_{33}	327	−0.9823	−0.0266	0.1854	169	92	79
$\bar{\sigma}$	98						

[a] All shifts are reported relative to solid $Cd(ClO_4)_2$.

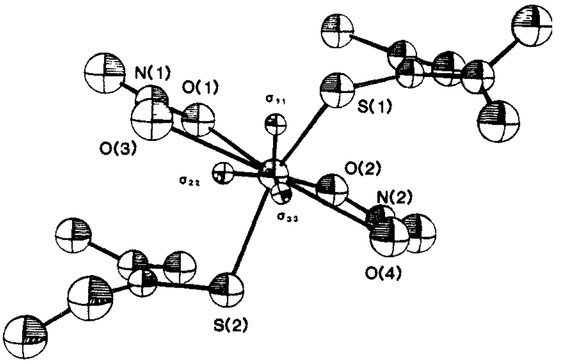

Figure 1. ORTEP drawing showing the orientation of ^{113}Cd shielding tensor in the cadmium nitrate tetramethylthiourea reference frame.

shielded element relative to "deshielding" ligands can be studied. Conversely, the orientation of the most shielded tensor element reported to date (−340 ppm) relative to the extremely long Cd–O–(NO_2) bonds in the nitrate tetramethylthiourea complex is discussed first.

Experimental Section

Cadmium dinitrato bis(1,1,3,3-tetramethyl-2-thiourea) crystals were collected from an aqueous solution containing cadmium nitrate tetrahydrate and thiourea in a 1:2 molar ratio. Crystals are monoclinic (a = 12.510 Å, b = 7.27 Å, c = 21.67 Å, β = 95.42°, Z = 4) and belong to the $P2_1/c$ space group.[13] The crystals were coated with an acetonitrile-based glue to slow decomposition. Cadmium glycinate monohydrate was crystallized from an aqueous solution containing a 1:2 molar ratio of cadmium chloride:glycine. The crystals are monoclinic (a = 14.86 Å, b = 5.30 Å, c = 10.0 Å, β = 90.4°, Z = 4). The crystal structure was solved under the space group $I2/a$.[14]

NMR data were collected on a wide-bore WP-200 spectrometer[15] employing a Doty-designed probe (Doty Scientific Inc.). Data acquisition was via a standard Hartman–Hahn spin-locked cross-polarization pulse sequence.[16] An acquisition time of 102.4 ms preceded by a 5-ms contact was employed in each case. Both the extraction of the elements of the chemical shielding tensor from the ^{113}Cd shift data and the crystallographic determination of the orientation of the unit cell reference frame relative to the cube frame have been described previously.[11,12]

Results and Discussion

$Cd(C_5H_{12}N_2S)_2(NO_3)_2$. Cadmium nitrate tetramethylthiourea crystallizes in the monoclinic space $P2_1/c$. Griffith, Rodesiler, and Amma[13] solved the crystal structure with cadmium in general position. The point group symmetry operators are expected to generate two magnetically distinguishable tensors. Experimentally, a single resonance was found in all rotation spectra. The ^{113}Cd shielding tensor and the corresponding direction cosines are given in Table I, where σ_{11}, the most shielded tensor element reported to date, is seen to be coincidental with the unique crystallographic axis. While the alignment of an element with the twofold is required to account for the reduction in the number of distinguishable tensors, it should be noted that the C_1 site symmetry imposes no constraints on the tensor orientation. Again, in Table I, the shielding tensor is seen to be an η = 0.04 tensor with an anisotropy of 438 ppm. Now, with the near-axial tensor symmetry and the very large anisotropy we expect the lattice site to be composed of two distinct shielding environments.

Table II. Structural Data for Cadmium Nitrate Tetramethylthiourea: Interatomic Distances and Angles for the Cadmium Primary Coordination Sphere and Details of Tensor–Ligand Geometry

interatomic distances, Å		interatomic angles, deg		tensor element–ligand angles, deg	
Cd–O(1)	2.290	O(1)–Cd–O(2)	93	σ_{11}–Cd–O(1)	70
Cd–O(2)	2.299	O(1)–Cd–O(3)	51	σ_{11}–Cd–O(2)	105
Cd–O(3)	2.681	O(1)–Cd–O(4)	143	σ_{11}–Cd–O(3)	68
Cd–O(4)	2.686	O(1)–Cd–S(1)	110	σ_{11}–Cd–O(4)	115
Cd–S(1)	2.497	O(1)–Cd–S(2)	109	σ_{11}–Cd–S(1)	41
Cd–S(2)	2.499			σ_{11}–Cd–S(2)	149
		S(1)–Cd–O(2)	109		
		S(1)–Cd–O(3)	89	σ_{22}–Cd–O(1)	59
		S(1)–Cd–O(4)	86	σ_{22}–Cd–O(2)	141
				σ_{22}–Cd–O(3)	23
		S(2)–Cd–O(2)	106	σ_{22}–Cd–O(4)	141
		S(2)–Cd–O(3)	87	σ_{22}–Cd–S(1)	106
		S(2)–Cd–O(4)	86	σ_{22}–Cd–S(2)	66
		S(1)–Cd–S(2)	125	σ_{22}–Cd–O(1)	141
				σ_{33}–Cd–O(2)	125
				σ_{33}–Cd–O(3)	92
				σ_{33}–Cd–O(4)	75
				σ_{33}–Cd–S(1)	53
				σ_{33}–Cd–S(2)	71

The cadmium coordination sphere is illustrated in Figure 1 and detailed in Table II. The coordination sphere consists of four oxygen atoms from a pair of bidentate nitrate anions and two sulfurs from a pair of monodentate tetramethylthiourea. Several structural features are significant when considering the shielding of this cadmium nucleus: (1) the coplanar arrangement of the two nitrate ligands; (2) the large Cd–O–(NO_2) bond length dispersion, the Cd–O(1) and –O(2) distances are normal at 2.290 and 2.299 Å while the Cd–O(3) and –O(4) distances of 2.681 and 2.686 Å are extremely long; (3) the "axial" position of S(1) and S(2) relative to the plane containing both nitrate ligands.

The orientation of the ^{113}Cd shielding tensor in the nitrate tetramethylthiourea reference frame is illustrated in Figure 1. Details are given in the final column of Table II. With the above structural features in mind, both the orientation and relative magnitude of the tensor elements are readily understood. From previous work,[17–19,24] Cd–S bonding is known to represent the most deshielding influences on cadmium chemical shifts, while the converse is true for nitrate ligands. Now, if we recall that a tensor element reflects the shielding environment normal to the element, then the "more orthogonal" orientation of σ_{11} (distinctly the most shielded element) with the nitrate planes is anticipated. σ_{11} makes an angle of 66° with the plane defined by O(1), Cd, and O(4) while σ_{22} and σ_{33} are directed 23° and 8°, respectively, from the same plane. Similarly, the orientation of the deshielded elements

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Table III. Structural Data for Cadmium Glycinate Monohydrate: Selected Interatomic Distances and Angles for the Cadmium Coordination Sphere and Details of the ^{113}Cd Shielding Orientation within the Molecular Frame

interatomic distances, Å		interatomic angles, deg		tensor element–ligand angle, deg	
Cd–O(1)	2.3	N(1)–Cd–O(1)	78	σ_{11}–Cd–N(1)	82
Cd–O(2)	2.5	N(1)–Cd–O(2)	93	σ_{11}–Cd–O(1)	76
Cd–N(1)	2.3	N(1)–Cd–O(1′)	102	σ_{11}–Cd–O(2)	164
		N(1)–Cd–O(2′)	87		
				σ_{22}–Cd–N(1)	9
				σ_{22}–Cd–O(1)	84
		O(1)–Cd–O(2)	88		
		O(1)–Cd–O(2)	88	σ_{22}–Cd–O(2)	87
		O(2)–Cd–O(1)	92		
				σ_{33}–Cd–N(1)	94
				σ_{33}–Cd–O(1)	164
				σ_{33}–Cd–O(2)	100

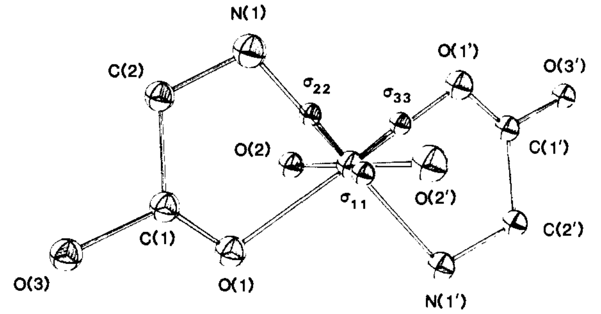

Figure 2. ORTEP drawing illustrating the orientation of the principal shielding directions of the ^{113}Cd shielding tensor in the cadmium glycinate monohydrate reference frame. Primed labels indicate inversion-related atoms.

with respect to the Cd–S(1) and Cd–S(2) internuclear vectors is consistent with the large positive eigenvalues (σ_{22} = 308 and σ_{33} = 327). Note that σ_{22} and σ_{33} are oriented 74°, 114° and 53°, 71° from the Cd–S(1) and Cd–S(2) vectors, while σ_{11} makes angles of 139°, 31° with the same two vectors.

Finally, a comment on the magnitude of σ_{11} is in order. The −340 ppm value of σ_{11} is the most shielded element reported to date. By comparison with cadmium nitrate tetrahydrate (see Tables IV and V of ref 11), this element is 116 ppm more shielded than σ_{11} in the simple nitrate. In the tetramethylthiourea nitrate crystal, the shielded element reflects major contributions from Cd–O(NO$_2$) bonds with distances of 2.290, 2.299, 2.681, and 2.686 Å. As Amma et al.[13] point out, the extremely long bond represents such weak covalent interactions that the coordination approaches a 2S–2O system. With weaker bond interactions (or the complete loss of two Cd–O bonds) relative to cadmium nitrate, the extremely shielded value of −340 ppm is understandable, if not expected.

$Cd(NH_2CH_2CO_2)_2{\cdot}H_2O$. The cadmium glycinate monohydrate structure was determined by projection. Low, Hirschfeld, and Richards[14] solved the structure with cadmium on a space group (*I*2/*a*) center of symmetry. The cadmium coordination sphere is illustrated in Figure 2. Details are found in Table III. Figure 2 shows the coordination geometry to be approximately octahedral with bonding distances varying from 2.3 to 2.5 Å. As mentioned above, the primary coordination sphere consists of four oxygens and two nitrogens. If we consider the O(2) and O(2′) positions to be axial, then the equatorial plane contains O(1), O(1′), N(1), and N(1′) from two chelate rings. The chelate moieties are approximately planar and are center-related.

The static ^{113}Cd powder spectrum at 200 MHz (see Figure 3) reveals an η = 0.26 tensor with three distinct principal elements (σ_{11} = −115, σ_{22} = 196, and σ_{33} = 258 ppm) in accordance with the $\bar{1}$ site symmetry. The small anisotropy indicates that the deshielded elements, σ_{22} and σ_{33}, should have comparable orthogonal environments, while σ_{11}, distinctly the most shielded element, should reflect a unique direction. Further, nitrogen is known to be a deshielding ligand relative to oxygen.[20-24] With these arguments in mind, one would predict the shielding tensor to be oriented such that σ_{11} is coincidental with the N(1)–Cd–N(1′) line and the two deshielded elements are orthogonal to this same line. This is *not* what was found experimentally.

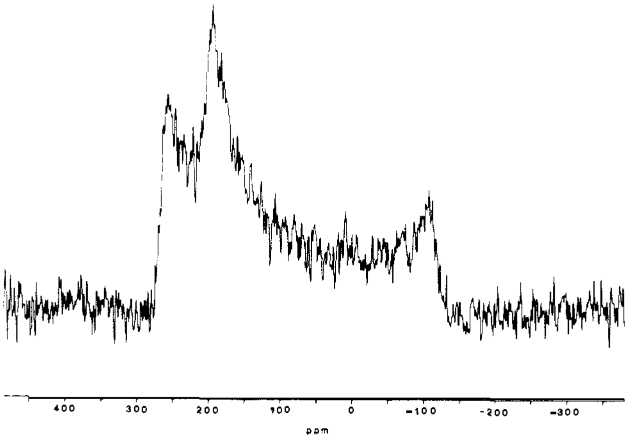

Figure 3. Nonaxial (η = 0.26) ^{113}Cd powder spectrum of cadmium glycinate monohydrate. The spectrum was taken at 200 MHz. Discontinuities occur at −115, 196, and 258 ppm.

Table IV. Principal Elements of the ^{113}Cd Shielding Tensors and Corresponding Direction Cosines[a] for the Two Distinguishable Tensors in Cadmium Glycinate Monohydrate

tensor element, ppm		direction cosines[a]			angles, deg[a]		
		a′	*b*	*c′*	*a′*	*b*	*c′*
σ_{11}	−117	0.5760	0.2752	0.7697	55	74	40
σ_{22}	199	−0.7513	0.5492	0.3659	139	57	69
σ_{33}	255	−0.3220	−0.7891	0.5231	109	142	58
$\bar{\sigma}$	112						
σ_{11}	−116	−0.5688	0.3035	−0.7644	125	72	140
σ_{22}	200	0.7614	0.5459	−0.3497	40	57	110
σ_{33}	256	0.3112	−0.7810	−0.5416	72	141	123
$\bar{\sigma}$	113						

[a] Angles are relative to the orthogonalized monoclinic cell.

The principal elements of the ^{113}Cd shielding tensor and the corresponding direction cosines are given in Table IV. Referring to Figure 2, one sees that the tensor orientation in the glycinate is not dominated by the shielding influence of the carboxylate oxygens or the deshielding due to nitrogen ligands. Rather, the orientation is dominated by shielding associated with the chelate rings. Note that the most shielded element makes an angle of 82° with the best least-square plane BLP containing atoms from both chelate rings. Conversely, the deshielded elements reflect minimal shielding contribution from the chelate units: σ_{22} and σ_{33} make angles of 7° and 14°, respectively with the chelate BLP. This data indicates that for ligands from chelate units, two effects must be considered: first, the shielding influence due to direct bond formation, and, second, shielding due to current densities located on the ligand support structure.

Two magnetically distinguishable tensors are generated by the 2/*m* point group symmetry operators. Table IV provides the principal elements of the ^{113}Cd shielding tensor and the corresponding direction cosines for the two distinguishable lattice sites. Referring to Table IV, one can readily see the twofold relationship between the two sets of eigenvectors. In this case the tensor–lattice site assignments were based upon the orientational dependence

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of the direct ^{113}Cd–^{14}N dipolar contribution to the ^{113}Cd line width.[25]

As shown in Figure 2, cadmium is bound to two inversion-related nitrogen atoms. The ^{113}Cd–^{14}N direct dipolar interaction will lead to splitting of the cadmium resonance at ν_0. As a result of this coupling, multiple resonances would be observed at frequencies given by

$$\nu = \nu_0 + D(1 - 3\cos^2\theta)M \qquad (1)$$

where M is the total ^{14}N spin quantum number ($M = -2, -1, 0, 1, 2$) and θ is the angle the $N(1)$–Cd–N(1′) vector makes with B_0. D is the ^{113}Cd–^{14}N dipolar coupling constant. Since D for the dipolar coupling between ^{113}Cd and ^{14}N is only 147 Hz,[25] the splittings are not resolved experimentally. The effect of this interaction is a broadening of the two cadmium resonances corresponding to the two distinguishable twofold related tensors. The magnitude of the broadening will be orientation-dependent. The tensor assignement takes advantage of this dependence.

If we take the frequency difference between the $M = +1$ and $M = -1$ resonances as an approximation of the ^{113}Cd line width, $\nu_{1/2}$, due to direct dipolar interaction, then this contribution to the line width is given as

$$\nu_{1/2} = 2D(1 - 3\cos^2\theta) \qquad (2)$$

For rotation about the $(5\bar{1}0)$ direction, a maximum line width of 400 Hz at goiniometer rotation angles of 80° for cadmium at position xyz and 100° for cadmium at position $\bar{x}y\bar{z}$ would be predicted. Experimentally, the maximum dipolar line width contribution was 420 ±20 Hz and occurred at 80° and 100°. This allowed unambiguous assignment of individual rotation plots to lattice sites in the crystal.

Conclusion

The orientation of the ^{113}Cd shielding tensor in cadmium glycinate and cadmium nitrate tetramethylthiourea was determined. These crystals represent 2N–4O and 2S–4O systems, respectively. In the latter case the general features of the tensor orientation relative to the primary coordination sphere could be predicted by employing the tensor element–structure correlations observed in the oxo–cadmium compounds. In addition, the −340 ppm magnitude of the most shielded tensor element for this crystal can be understood in terms of structural parameters, specifically the extremely long Cd–O(NO_2) bonds. The shielding tensor orientation in the glycinate reference frame was not anticipated. These data indicate that to correctly interpret the shielding in terms of structural parameters both the shielding influence due to direct bond formation and shielding due to current densities originating on structure adjacent to the direct bond (e.g., glycinate chelate ring) must be considered.

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Registry No. $Cd(NH_2CH_2CO_2)_2{\cdot}H_2O$, 19476-62-1; $Cd(C_5H_{12}N_2S)_2(NO_3)_2$, 85040-98-8.

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Comparative Analysis of the Electrostatic Potentials of Dibenzofuran and Some Dibenzo-*p*-dioxins

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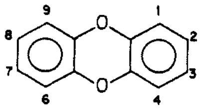
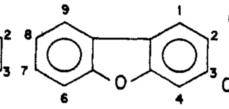
Abstract: Electrostatic potential maps of dibenzofuran, dibenzo-*p*-dioxin, 2,8-dichloro-3,7-dimethyldibenzo-*p*-dioxin, 2,3,7,8-tetrafluorodibenzo-*p*-dioxin, and 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) are presented and compared. The biological activities of these molecules increase from zero for the first two to very strong for the highly toxic TCDD. The analysis of the electrostatic potentials suggests certain key features that may be necessary for the effective interaction of these classes of compounds with a cytosolic receptor, which is believed to be the initial step leading to various toxic responses and other biological activity.

Dibenzo-*p*-dioxin (I) and dibenzofuran (II) are the parent compounds for large families of derivatives, having halogens and other substituents at various positions. For example, considering just chlorine as a substituent, there are 75 possible derivatives of I (containing 1–8 chlorines) and 135 such derivatives of II. When bromine, fluorine, and other types of substitution are taken into account, there are clearly hundreds of possible compounds. These have varying degrees of toxicity, ranging from zero to very high; the latter is exemplified by the notorious 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD, III). The toxic responses elicited by these compounds include gastric lesions, hepatotoxicity, carcinogenesis, loss of lymphoid tissue, acute loss of weight, and chloracne.[1,2]



I



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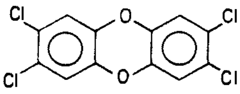

III

To differing extents, the substituted dibenzo-*p*-dioxins and dibenzofurans also induce aryl hydrocarbon hydroxylase (AHH) activity.[3] This is a microsomal monooxygenase system that is involved in the metabolic conversion of carcinogenic aromatic hydrocarbons to their active forms.[4]

Studies of a series of halogenated dibenzo-*p*-dioxins and dibenzofurans have revealed a good correlation between potency

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