SEMIEMPIRICAL QUANTUM MECHANICAL QUANTITATIVE STRUCTURE ACTIVITY RELATIONSHIPS FOR TCDD AND COPLANAR PCBs.

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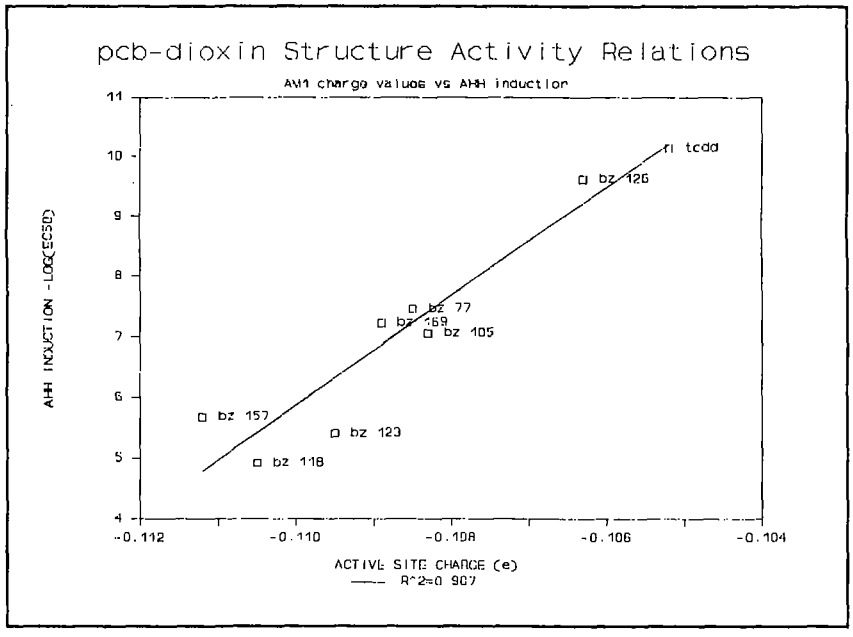
The evidence that toxic halogenated aromatic hydrocarbons exhibit a common biological toxic response, related to aryl hydrocarbon hydroxylase (AHH) induction, mediated by the aryl hydrocarbon (Ah) receptor [1] suggests that the Structure Activity Relationships observed could be based on specific electronic properties of the molecular structures. The semiempirical quantum mechanical model AM1 [2] provides a method capable of calculating molecular electronic charge distribution and enthalpies of formation for the halogenated aromatic hydrocarbons with reasonable computational resources.

We demonstrate a Quantitative Structure Activity Relationship between published AHH induction data and electronic charge distribution for 2,3,7,8-TCDD, and non-ortho and mono-ortho coplanar PCB congeners, calculated using the AM1 Hamiltonian. The relationship of rotational barriers and Ah receptor binding for non-ortho and mono-ortho PCBs is also investigated and preliminary results presented.



(1) Stephen Safe, C. Yao and D. Davis in Organohalo Compounds; vol 2: Dioxin'90-EPRI Seminar O. Hutzinger and H. Fiedler Eds. Ecoinforma Press, 1990

(2) Michael J. S. Dewar, Eve G. Zoebisch, Eamonn F. Healy and James P. Stewart, J. Am. Chem. Soc. 107, 3902-3909 (1985)