Structural and electronic properties of polychlorinated biphenyls (PCBs) and polychlorinated diphenyl ethers (PCDEs)

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ABSTRACT

Frontier molecular orbital energies of polychlorinated biphenyls (PCBs) and polychlorinated diphenyl ethers (PCDEs) were calculated using the semi-empirical AM1 method. A significant correlation is found between the toxic properties of PCBs and PCDEs and the energy difference (dE) between lowest unoccupied molecular orbital (LUMO) and the highest occupied molecular orbital (HOMO).

INTRODUCTION

The toxic and entzyme induction responses of PCDDs and related compounds have been explained by similarities in their chemical structures[1], polarizability[2] and by ability to form charge-transfer complexes at the receptor in which these compounds act as electron acceptors[3]. In the present work, a semiempirical AM1 method[4] was utilized in calculating the structural and electronic properties of PCBs and PCDEs. The AM1 procedure was selected because it gives good estimates of molecular energies and the computational time is much shorter than needed by the *ab initio* methods.

PCDEs have been taken with in calculations, because they have been recently shown to have toxic properties similar to the PCBs[5]. PCDEs have been found in several environmental samples so they might reveal to be important environmental toxicants. Therefore, it's important to find quantitative structure activity relationships (QSARs) for these compounds that can be used to predict toxic properties of their different isomers.

EXPERIMENTAL

The semi-empirical AM1 molecular orbital calculations have been performed with a VAX 4000 computer using the AMPAC program package (QCPE No. 506). The C-C and C-O bond lengths were started as 1.40 Å, C-H bond lengths as 1.10 Å, and C-Cl bond lengths as 1.70 Å. All aromatic bond angles were input as 120°. The initial geometry was then optimized by varying bond lengths, bond angles, and dihedral angles to minimize the heat of formation of the molecule with Broyden-Fletcher-Goldfarb-Shanno (BFGS) method. The global energy minima of PCDEs were determined by conformational analysis using 30° intervals of the dihedral angles about two C-O bonds. The optimized geometry is then calculated using dihedral angles of the global energy minima as starting values. The twist angles in PCBs were input as 45°. The AMPAC was run with the following key words: AM1, precise, bonds, T=20000.

RESULTS

The frontier orbital energy gap (E_{HOMO}-E_{LUMO}=dE) is shown to have relation to Ah receptor binding and associated enzyme inducing activities of polychlorinated aromatic hydrocarbons[6]. The toxic 2,3,7,8-substituted PCDDs have lower dE than the other PCDDs. In Figure 2 is shown how dE correlates with the receptor binding values[7] (-logEC_{50}) for PCBs (r=0.726, n=14) and in Figure 2 is presented correlation between dE and the immunosuppressive induction activities of PCDEs in mice[7] (r=0.589, n=7). Pearson[10] has demonstrated that the absolute hardness, η, which is defined by η = dE/2, represents a good measure for reactivity of a molecule. The greater the dE, the higher the stability and inertness of the molecule. This means that the PCDD, PCB and PCDE isomers, that have lower dE, are expected to be more reactive (=toxic) than isomers with greater dE.

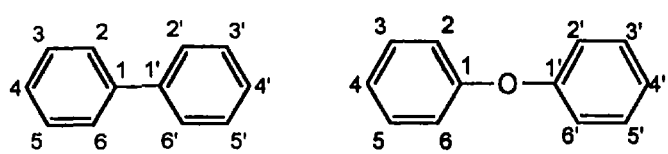

Figure 1. Numbering of biphenyl and diphenyl ether

Table 1. IUPAC numbering[9], AM1 calculated HOMO-LUMO energy gap, dE, and published reseptor binding data and (2-1-1'-2') torsion angles for lowest energy conformation of chlorinated biphenyls and 2,3,7,8-TCDD.

PCB	IUPAC no	dE	$logLC_{50}$	Torsion angle, [°]
2,2',4,4'-	47	9.303	3.89	92.8
2,3,4,5-	61	8.735	3.85	60.0
3,4,4',5-	74	8.433	4.55	41.0
3,3',4,4'-	77	8.440	6.15	138.9
2,3,3',4,4'-	105	8.682	5.37	59.9
2,3,4,4',5-	114	8.625	5.39	60.4
2,3',4,4',5-	118	8.603	5.04	58.0
2',3,4,4',5-	123	8.667	4.85	59.6
3,3',4,4',5-	126	8.405	6.89	138.6
2,2',4,4',5,5'-	153	9.030	4.10	90.5
2,3,3',4,4',5-	156	8.596	5.15	60.5
2,3,3',4,4',5'-	157	8.688	5.30	61.0
2,3',4,4',5,5'-	167	8.583	4.79	58.2
2,3',4,4',5',6-	168	9.099	4.00	90.2
2,3,7,8-TCDD		8.088	8.00	planar

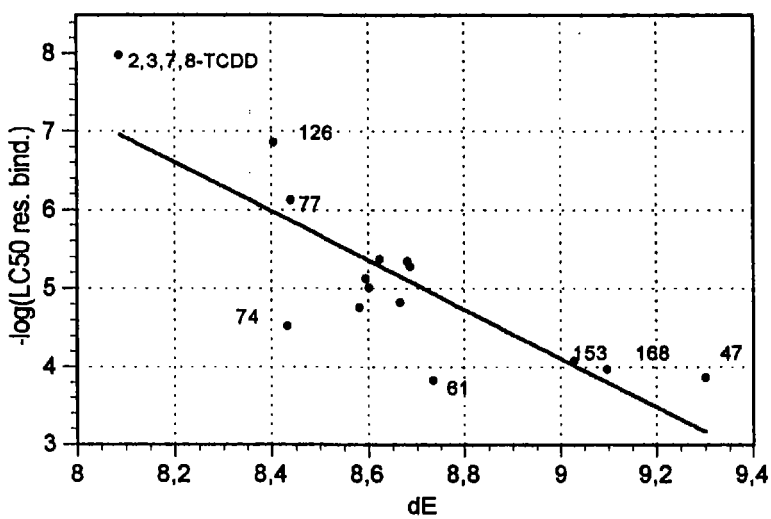

Figure 2. Relation between $-logEC_{50}$ (reseptor binding) values and HOMO-LUMO energy gap, dE, of PCBs.

Table 2. ED_{50} values for immunotoxicity and calculated LUMO-HOMO energy gap, dE for PCDEs and 2,3,7,8-TCDD.

PCDE	IUPAC no*	immunotoxicity ED_{50}, µmol/kg	-log(TEF/ED50 immunotoxicity)	**dE**, [eV]
3,3',4,4'-tetra	77	50.6	4.33	8.710
2,2',4,5,5'-penta	101	258	5.03	8.724
2,3',4,4',5-penta	118	21.8	3.96	8.540
3,3',4,4',5-penta	126	8.8	3.57	8.671
2,2',4,4',5,5'-hexa	153	81.2	4.54	8.555
2,3,3',4,4',5-hexa	156	0.5	2.32	8.453
2,3',4,4',5,5'-hexa	167	0.7	2.47	8.603
2,3,7,8-TCDD		0.0024	0.00	8.088

*Numbering same as for PCBs.

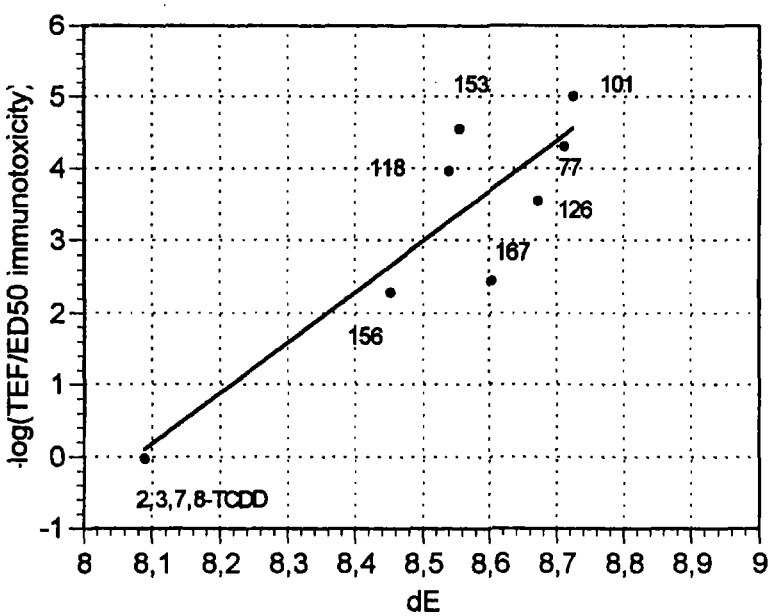

Figure 3. Relation between LUMO-HOMO energy gap, dE and -log(TEF/immunotoxicity) values for PCDEs.

LITERATURE CITED

1. Poland A., Knutson J. 2,3,7,8-tetrachlorodibenzo-*p*-dioxin and related compounds. Examination of the mechanism of toxicity. *Annu. Rev. Pharmacol. Toxicol.* 1982; **22**: 517-554.
2. McKinney J. D., Chae K., McConnell E. and Birnbaum L. S. Structure-induction versus structure toxicity relationships for polychlorinated biphenyls and related aromatic hydrocarbons. *Environ. Health Perspect.* 1985; **60**,:57-68, .
3. Cheney V. B. and Tolly T. Electronic factors affecting receptor binding of dibenzo-*p*-dioxin and dibenzofurans. *Int. J. Quantum Chem.* 1979;**16**:87-110.
4. Dewar M. Zoebish E. Healy E. J. Stewart, AM1: a new general purpose quantum mechanical molecular model. *J. Am. Chem. Soc.* 1985;**107**:3902-9.
5. Becker M., Phillips T. and Safe. S. Polychlorinated diphenyl ethers - a review. *Toxicol. Environ. Chem.* 1991; **33:** 189-200.
6. Nevalainen T. and Kolehmainen E. Semiempirical molecular orbital properties of polychlorinated dibenzo-*p*-dioxins (PCDDs), polychlorinated biphenyls (PCBs) and polychlorinated diphenyl ethers (PCDEs). Manuscript in preparation.
7. Bandiera S. Safe S. Okey A. B.,Binding of polychlorinated biphenyls classified as either phenobarbitone, 3-methylcholantrene or mixed-type inducers to cytosolic Ah reseptor. *Chem.-Biol. Interact.* 1982; **39**: 253-277.
8. Howie L., Dickerson R., Davis D. and Safe S., Immunosuppresive and monooxygenase induction activities of polychlorinated diphenyl ether congeners in C57BL/6N mice: quantitative structure-activity relationships. *Toxicol. Appl. Pharmacol.* 1990; **105**:254-263.
9. Ballschmiter K. and Zell M. Analysis of polychlorinated biphenyls (PCB) by glass capillary gas chromatography. *Fresenius Z. Anal. Chem.* 1980; **302**: 20-31.
10. Pearson R G, Absolute electronegativity and hardness correlated with molecular orbital theory, *Proc. Natl. Acad. Sci. USA* 1986;**83**:8440-8441.