ICNTC-2020 Special Issue

J. Indian Chem. Soc.,
Vol. 97, No. 10c, October 2020, pp. 2101-2105

Computational examination of degradation reactions of precious endocrine disruptors molecules through surface

Simal Kurumoglu and Yelda Yalcin Gurkan*

Department of Chemistry, Tekirdag Namik Kemal University, Tekirdag, Turkey

E-mail: yyalcin@nku.edu.tr

Manuscript received online 20 October 2020, revised and accepted 31 October 2020

In this study, the possible reaction paths of Aclonifen, Terbutryn, Quinoxyfen, Heptachlorepoxide, Chlorfenvinfos, Chlorprifos, Trifluralin, Bifenox, Di(2-ethylhexyl)phthalate, Perfluorooctansulfonic acid molecules, which are among the primary endocrine disrupting molecules, were determined. Optimized geometries are drawn with Gauss View 5. Later, with the Gaussian 09 program, geometric optimization was made and the lowest energy states were found. Geometric structure analysis was done and bond lengths and bond angles were calculated. The purpose of this study is to determine the most likely way of interaction of Aclonifen, Terbutryn, Quinoxyfen, Heptachloropoxide, Chlorfenvinfos, Chlorprifos, Trifluralin, Bifenox, Di(2-ethylhexyl)phthalate, Perfluorooctansulfonic acid and OH in the gas and water phase. The effect of solvent water, COSMO is used as the dissolution model and has a stabilizing effect in reducing the energy in the reactions. The lowest energy molecule has the most stable structure. Accordingly, when we list the endocrine disrupter molecules from the most stable to the most unstable; it is listed as Heptachloropoxide, Chlorpyrifos, Perfluorooctanesulfonic acid, Chlorfenvinfos, Bifenox, Quinoxyfen, Trifluralin, Di(2-ethylhexyl)phthalate, Aclonifen, Terbutryn. These results will guide experimental studies and determine the fragmentation mechanism.

Keywords: Priority endocrine disrupting molecules, hydroxyl radical, DFT, Gaussian 09 .

Introduction

Chemicals used today such as food additives, chemicals used in cosmetics and pharmaceutical industries, pesticides, herbicides, cigarette smoke and alcohols threaten human health. These pollutants especially affect the endocrine system by acting like the hormone systems of living things. The endocrine disrupter molecules which are organophosphorus pesticides, herbicides used to increase yield in agricultural products, PFOS, which are used as protective coating material in textile, carpet and paper industry and preferred especially in textile products due to their water and oil repellency properties and phthalates preferred in manufacturing for the processing of plastic products as plasticizers. Although these chemicals, which are highly degradable, are treated in treatment plants, they pollute surface waters at reduced rates. Thus, it participates in the biological cycle and is stored by biomass. Most of these chemicals are carcinogenic, mutagenic, toxic and estrogenic. In addition, they prevent the metabolic activities of hormones such as androgens, estrogens, progesterone, which are involved in reproduction and development, by binding to hormone receptors, acting as a hormone or acting as an anti-hormonal effect and preventing the natural hormone from binding to the specific receptor site. Therefore, it is of great importance to examine primary endocrine disrupting molecules at the molecular level[1,2].

With the development of the industry as a result of rapid population growth; chemicals have entered every area of our lives. As a result, an increase in endocrine disrupting molecule concentrations occurs in surface waters. These molecules are generally found in very low concentrations such as μg/L in surface waters. Since they are resistant to biological treatment available in wastewater treatment plants, they cannot be treated and are continuously discharged to receiving environments, thus polluting the discharge water and surface water. Endocrine disrupting molecules into surface waters; it is mixed with the use of pesticides or discharge of effluents from wastewater treatment plants. Endocrine disrupting molecules in the aquatic environment undergo

changes such as dilution in water, reaction with OH radicals, biodegradation, photolysis, and accumulation in sediment[3].

In this study, the possible reaction pathways of primary endocrine disrupting molecules such as Aclonifen, Terbutryn, Quinoxifen, Heptachlorepoxide, Chlorfenvinfos, Chlorprifos, Trifluralin, Bifenox, Di(2-ethylhexyl)phthalate, Perfluorooctanesulfonic acid molecules between the OH radical were determined. Optimized geometries were drawn with Gauss View 5. Then, the lowest energy states were found by geometric optimization with Gaussian 09 program. These results will guide experimental studies and determine the fragmentation mechanism. Considering that classical biological enhancement methods are insufficient to remove primary endocrine disrupting molecules; Computational analysis of the degradation reactions of primary endocrine disrupting molecules in surface waters that will guide the application of alternative treatment methods to increase the treatment efficiency was carried out.

Molecular orbital calculations

Density functional theory (DFT) is a quantum mechanical modeling method used in physics and chemistry to investigate the electronic structure (principally the ground state) of many-body systems, in particular atoms, molecules, and the condensed phases. DFT is among the most popular and versatile methods available in condensed-matter physics, computational physics, and computational chemistry. The analysis was made on the probable reaction path of Endocrine Disruptors Molecules with OH radicals. The calculation of optimized geometry and the geometric optimization for the determination of the lowest energy status were made via Gauss View 5 and the Gaussian 09 program. Activation energy for the probable reaction paths was calculated and their most stable state from the thermodynamic perspective was determined for the gase and water phase. The aim of this study is to estimate the degradation mechanism of Endocrine Disruptors Molecules in gase and water phase. Calculation of the probable reaction path of the activation energy was made, and their most stable state in the thermodynamic frame was determined for this phase[4,5].

Molecular orbital calculations of the most durable conformer found as a result of molecular mechanics method were made by DFT/B3YLP/6-31G* methods. DFT calculations were made with the hybrid B3LYP function combining the HF and Becke change terms with the Lee-Yang-Parr correlation function. It is the 6-31G(d) basic set used in such calculations. As a result of quantum chemical calculations, geometric parameters, energy, enthalpy and energy without Gibbs, charge density and Mulliken charges in gas phase were determined[6].

OH radical acts like an electrophile in its reaction with any organic molecule and therefore readily attaches the unsaturated bonds known to be the most reactive type in biological systems, goes into reaction with every biomolecule it confronts, including water. Aromatic compounds are good detectors since they hydroxylate. The attack of any hydroxyl radical to an aromatic compound results in the formation of a hydroxylated product. While O radical is a nucleophile, and thus does not attach these bonds. If there is an aliphatic side chain readily bound to an aromatic molecule, radical H attacks O, whereas OH radical preferentially attaches the aromatic ring, which can result in the formation of various products when pH reaches a range in which O radical is the reactant rather than OH radical[7,8].

Results and discussion

According to Fig. 1 the optimized geometric molecular structures of Aclonifen, Terbutryn, Quinoxyfen, Heptachlorepoxide, Chlorfenvinfos, Chlorprifos, Trifluralin, Bifenox, Di(2-ethylhexyl)phthalate, Perfluorooctansulfonic acid, respectively, among the primary endocrine disrupting molecules. Electronegative atoms attached to molecules; O, Cl, F, N are shown in color. The bond lengths, bond angles and Mulliken charges of molecules in Table 1 give preliminary information about the fragmentation sites of molecules. The highest bond lengths and angles of the 10 molecules examined in this study are written in bold in this table.

When the Mulliken loads of the molecules in Table 1 are examined, the atoms with the highest electronegativity N_9, N_4, O_{17}, Cl_{22}, O_{11}, O_{18}, N_{10}, O_{20}, O_{41}, O_{12} are written in bold and red in the table.

Electrochemical calculations in gase and water phase were analyzed for each molecule. The ΔE energy, ΔH enthalpy and ΔG Gibbs free energy values given in Table 2 are given separately for each molecule. When the Gibbs free

values of ΔG were examined, it was seen that the ΔG value of each fragmentation was negative. Thus, we list the endocrine disrupter molecules from the most stable to the most unstable.

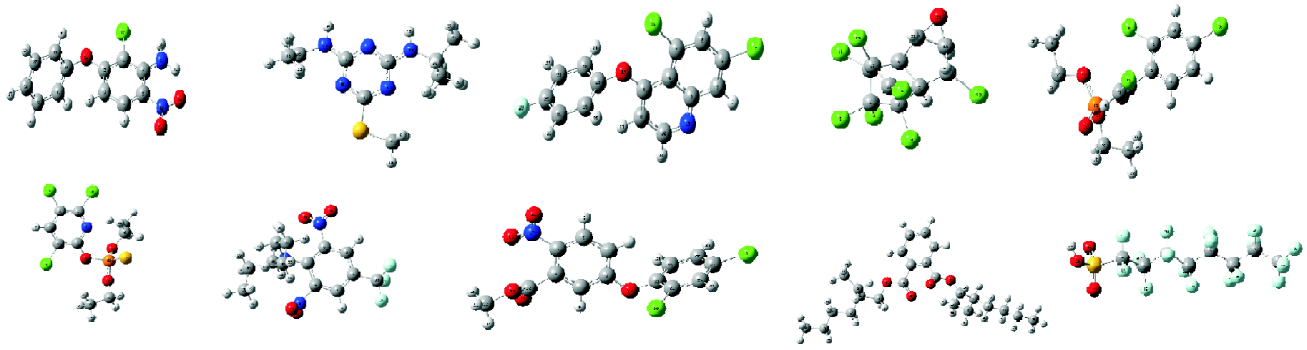

Fig. 1. Optimum geometric structures of the molecules (a: Aclonifen, b: Terbutryn, c: Quinoxyfen, d: Heptachlorepoxide, e: Chlorfenvinfos, f: Chlorprifos, g: Trifluralin, h: Bifenox, ı: Di(2-ethylhexyl)phthalate, i: Perfluorooctansulfonic acid) (yellow, sulphur; blue, nitrogen; light blue, fluorine; green, chlorine; white, hydrogen; red, oxygen; grey, carbon),

Table 1. Bond lengths, angles and Mulliken loads of some optimizeted molecules

Aclonifen	Bond length (Å)		Bond angle (°)		Mulliken loads	Terbutryn	Bond length (Å)		Bond angle (°)		Mulliken loads
$C_{17}O_{16}$	**1.39**	$C_{17}O_{16}C_2$	**120.2**	N_9	**–0.83050**	$N_{14}C_{16}$	1.46	$C_{16}N_{14}C_3$	**124.7**	N_4	**–0.43512**
$O_{16}C_2$	1.35	$Cl_{15}C_1C_6$	**118.6**	O_{13}	**–0.40686**	N_6C_2	1.36	$H_{15}N_{14}C_3$	114.5	N_5	**–0.35795**
C_1Cl_{15}	**1.75**	$H_{10}N_9H_{11}$	**122.1**	O_{14}	**–0.45092**	$N_{14}C_3$	1.36	$C_{16}N_{14}H_{15}$	119.4	N_6	**–0.36126**
N_9C_6	1.35	$H_{10}N_9C_6$	**119.8**	Cl_{15}	0.00957	N_4C_3	1.34	$C_3N_4C_2$	114.5	S_7	0.14121
$N_{12}C_5$	**1.44**	$O_{13}N_{12}O_{14}$	**122.3**	O_{16}	**–0.56024**	S_7C_1	1.78	$C_1N_6C_2$	**113.5**		
						S_7C_8	1.82	$C_3N_5C_1$	113.5		
Quinoxyfen	Bond length (Å)		Bond angle (°)		Mulliken loads	Hepta-chlorepoxide	Bond length (Å)		Bond angle (°)		Mulliken loads
$C_{18}O_{17}$	**1.39**	$F_{28}C_{25}C_{23}$	**118.9**	Cl_{14}	0.04155	Cl_9C_3	1.8	$Cl_{11}C_1C_3$	116.5	Cl_{10}	0.04460
C_8O_{17}	1.36	$C_{18}O_{17}C_8$	**120.4**	Cl_{15}	0.00447	Cl_8C_3	1.79	$\mathbf{Cl_{15}C_{13}C_{12}}$	**127.7**	Cl_{11}	0.04226
C_3N_{16}	1.36	$C_{10}N_{16}C_3$	**117.4**	N_{16}	**–0.53156**	$Cl_{10}C_2$	1.78	$Cl_{14}C_{12}C_2$	124.1	Cl_{14}	0.09677
$Cl_{14}C_5$	**1.76**	$Cl_{14}C_5C_6$	115.1	O_{17}	**–0.58507**	$Cl_{15}C_{13}$	1.71	$Cl_{10}C_2C_{12}$	115.7	Cl_{15}	0.08084
$Cl_{15}C_1$	**1.75**	$C_6C_1Cl_{15}$	**118.4**	F_{28}	**–0.29010**	$\mathbf{Cl_{22}C_{16}}$	**1.81**			Cl_{22}	**–0.03209**
Chlorfenvinfos	Bond length (Å)		Bond angle (°)		Mulliken loads	Chlorprifos	Bond length (Å)		Bond angle (°)		Mulliken loads
$O_{20}P_{17}$	1.71	$C_{28}O_{20}P_{17}$	109.5	Cl_{10}	**–0.01062**	$O_{15}C_{16}$	1.43	$O_{15}C_{16}H_{17}$	109.5	N_6	**–0.42439**
$O_{19}P_{17}$	1.71	$O_{20}P_{17}O_{18}$	109.5	Cl_{11}	0.03262	$O_{15}P_{12}$	**1.71**	$O_{15}P_{12}O_{11}$	109.5	Cl_9	0.04277
$O_{16}P_{17}$	1.71	$O_{18}P_{17}O_{16}$	109.5	Cl_{15}	0.07194	$P_{12}S_{13}$	1.81	$P_{12}O_1C_1$	109.5	Cl_{10}	0.05582
$C_{21}O_{19}$	1.43	$O_{18}P_{17}O_{19}$	109.5	O_{16}	**–0.57630**	$P_{12}O_{11}$	1.71	$C_{23}O_{14}P_{12}$	109.5	O_{11}	**–0.56861**
$O_{20}C_{28}$	1.43	$P_{17}O_{16}C_{12}$	109.5	P_{17}	1.35776	$O_{14}P_{12}$	1.71	$C_5N_6C_1$	117.2	P_{12}	1.05728
$O_{16}C_{12}$	1.43	$Cl_{15}C_{13}C_{12}$	**120.2**	O_{18}	**–0.57694**	$O_{14}C_{23}$	1.43	$N_6C_5C_4$	123.5	S_{13}	**–0.32773**
C_4Cl_{11}	**1.76**	$Cl_{11}C_4C_5$	**120.0**	O_{19}	**–0.54692**	$C_{11}0C_5$	1.76	$Cl_{10}C_5N_6$	115.7	O_{14}	**–0.50271**
C_2Cl_{10}	**1.76**	$Cl_{10}C_2C_1$	**119.0**	O_{20}	**–0.53362**					O_{15}	**–0.50692**

Table-1 (contd.)

Trifularin	Bond length (Å)		Bond angle (º)		Mulliken loads	Bifenox	Bond length (Å)		Bond angle (º)		Mulliken loads
$F_{13}C_{12}$	1.35	$F_{13}C_{12}C_4$	109.5	N_9	0.14543	$O_{11}C_{10}$	1.26	$O_{11}C_{10}C_4$	**120.2**	O_{11}	**–0.47733**
$F_{15}C_{12}$	1.35	$F_{15}C_{12}C_4$	109.5	N_{10}	**–0.42002**	$O_{12}C_{10}$	1.43	$O_{12}C_{10}C_4$	119.9	O_{12}	**–0.49219**
$N_{11}O_{19}$	1.36	$C_2N_{11}O_{17}$	109.5	N_{11}	0.17290	$O_{19}N_{17}$	1.35	$O_{18}N_{17}C_5$	109.5	N_{17}	0.17611
$N_{10}C_1$	**1.47**	$C_2N_{11}O_{19}$	109.5	F_{15}	**–0.26137**	$O_{20}C_2$	1.43	$O_{20}C_2C_1$	120.0	O_{18}	**–0.24038**
$N_{10}C_{30}$	**1.47**	$C_{30}N_{10}C_1$	109.5	O_{16}	**–0.23529**	$O_{20}C_{21}$	1.43	$O_{20}C_{21}C_{22}$	119.2	O_{19}	**–0.33007**
N_9O_{18}	1.36	$C_6N_9O_{16}$	109.5	O_{18}	**–0.32825**	$Cl_{30}C_{22}$	1.74	$Cl_{30}C_{22}C_{21}$	120.0	O_{20}	**–0.57458**
N_9C_6	1.47	$N_9C_6C_5$	**120.0**	O_{19}	**–0.31340**	$Cl_{31}C_{27}$	1.74	$Cl_{31}C_{27}C_{24}$	120.0	Cl_{30}	0.03435
Di(2-ethylhexyl) phthalate	Bond length (Å)		Bond angle (º)		Mulliken loads	Perfluoro-octansulfonic acid	Bond length (Å)		Bond angle (º)		Mulliken loads
$C_{42}O_{41}$	**1.43**	$O_{41}C_{39}O_{40}$	**120.0**	O_{12}	**–0.47598**	S_9O_{11}	1.45	$O_{11}S_9O_{12}$	107.7	S_9	1.14850
$O_{41}C_{39}$	1.42	$O_{12}C_{11}O_{13}$	120.0	O_{13}	**–0.46223**	S_9O_{10}	1.45	$O_{10}S_9O_{12}$	108.2	O_{10}	**–0.48200**
$C_{11}O_{12}$	1.26	$O_{40}C_{49}C_5$	**120.2**	O_{40}	**–0.39920**	S_9O_{12}	1.63	$O_{10}S_9C_8$	108.5	O_{11}	**–0.48199**
$C_{11}O_{13}$	1.43	$O_{12}C_{11}C_6$	120.2	O_{41}	**–0.51857**	$O_{12}H_{13}$	0.98	$S_9O_{12}H_{13}$	107.6	O_{12}	**–0.62955**
$O_{13}C_{14}$	1.43	$C_{42}O_{41}C_{39}$	109.5			S_9C_8	1.89	$O_{11}S_9C_8$	107.3		

Table 2. Gibbs free energy, enthalpy and energy values (Au) for the gase and water phase of optimizeted molecules

Molecule	Phase	ΔE Energy (kcal/mol)	ΔH Enthalpy (kcal/mol)	ΔG Gibbs free energy (kcal/mol)
Aklonifen	Gase	–789253.419	–789252.826	–789291.533
	Water	–789260.055	–789259.462	–789298.430
Terbutryn	Gase	–667789.662	–667789.069	–667830.681
	Water	–667795.580	–667794.988	–667837.226
Quinoxyfen	Gase	–1083331.674	–1083331.081	–1083370.829
	Water	–1083336.388	–1083335.795	–1083375.407
Heptachlorepoxide	Gase	–2309426.247	–2309425.655	–2309465.002
	Water	–2309431.115	–2309430.522	–2309469.932
Chlorfenvinfos	Gase	–1561450.311	–1561449.718	–1561499.599
	Water	–1561205.647	–1561205.055	–1561256.739
Chlorprifos	Gase	–1725639.345	–1725638.752	–1725685.372
	Water	–1725645.532	–1725644.939	–1725692.005
Trifluralin	Gase	–796409.198	–796408.605	–796457.153
	Water	–796414.956	–796414.364	–796462.942
Bifenox	Gase	–1185888.162	–1185887.569	–1185933.569
	Water	–1185896.539	–1185895.946	–1185942.041
Di(2-ethylhexyl)phthalate	Gase	–776711.433	–776710.840	–776775.445
	Water	–776719.007	–776718.414	–776783.620
Perfluorooctansulfonic acid	Gase	–1648028.693	–1648028.100	–1648084.062
	Water	–1648034.993	–1648034.400	–1648090.781

Conclusion

In this study, the possible reaction pathways of primary endocrine disrupting molecules such as Aclonifen, Terbutryn, Quinoxifen, Heptachloropoxide, Chlorfenvinfos, Chlorprifos,

Trifluralin, Bifenox, Di(2-ethylhexyl)phthalate, Perfluorooctanesulfonic acid molecules were determined. For this purpose, geometry optimization of the molecules was made, then the most suitable quantum mechanical method was determined and the possible products were predicted theoretically. The fragmentation reaction requires energy. OH radicals are used to degrade primary endocrine disrupter molecules. The lowest energy molecule has the most stable structure. Accordingly, when we list the endocrine disrupter molecules from the most stable to the most unstable; Heptachlorethoxide, Chlorprifos, Perflurooctansulfonic acid, Chlorfenvinfos, Bifenox, Quinoxifen, Trifluralin, Di(2-ethylhexyl)phthalate, Aclonifene, Terbutryn.

The functional groups of endocrine disrupting molecules and the lowest energies and stability they have are included. Heptachloropoxide molecule with the lowest energy, which has the most stable structure; it is an epoxide containing electronegative Cl atom and alkene structure. Chlorprifos molecule; the aromatic ring is an ether containing P and S atoms and an electronegative Cl atom. Perflurooctansulfonic acid molecule; it is an acid containing an S atom and electronegative O and F atoms. Chlorfenvinfos molecule; the aromatic ring is an ether containing P and electronegative Cl atom. Bifenox molecule; it is an ester containing aromatic ring, carbonyl group, N atom and electronegative O and Cl atoms. Quinoxifen molecule; it is an ether containing an aromatic ring and electronegative O atom. Trifluralin molecule; The aromatic ring is a tertiary amine containing N atom and electronegative O and F atoms. Di(2-ethylhexyl)phthalate molecule; is an ester containing an aromatic ring. Aclonifene molecule; a primary amine containing an electronegative O atom containing aromatic ring, ether group and N atom. The most energetic and least stable Terbutryn molecule; it is triazine containing an S atom.

When the functional groups of molecules are examined, the energies of molecules whose N atoms are attached are high and their stability is low. It is seen that molecules to which electronegative atoms are attached have low energies and high stability.

Our goal was to break down endocrine disrupting molecules down to the smallest harmless substances. As can be seen from the results, this fragmentation took place theoretically. These results will guide experimental studies and determine the fragmentation mechanism.

Acknowledgements

The authors greatly appreciate Tekirdag Namik Kemal University Research Foundation for financial support. Project number: NKUBAP.01.GA.20.260.

References

1. B. E. Kurutaş and M. Kılınç, *Archive Medical Review Journal*, 2003a, **12(3)**.
2. K. Kitchin, *Meth. Find Exptl. Clin. Pharmacol*, 1984, **6**, 303.
3. J. Miles and C. ve Harris, *Pest Monitor J.*, 1971, **5(3)**, 289.
4. P. Popelier, "Atom in Molecules", Pearson Education, USA, 2000.
5. Gaussian 09, Revision B.04, Gaussian, Inc., Pittsburgh, PA, 2009.6. Hinchliffe, A. Modelling molecular structures, John Wiley & Sons, New York, 1997.
7. J. B. Foresman and E. ve Frish, "Exploring chemistry with electronic structure methods", USA, 1996.
8. P. W. Atkins, "Physical Chemistry", 6th ed., Oxford University Press, New York, 1998.
9. B. E. Kurutaş and M. ve Kılınç, *Archive Medical Review Journal*, 2003b, 12.