Asian Journal of Chemistry; Vol. 27, No. 4 (2015), 1199-1204

ASIAN JOURNAL OF CHEMISTRY

http://dx.doi.org/10.14233/ajchem.2015.17146

Adsorption Mechanism of Estrogens on Soil Studies Based on Density Functional Theory and Quantitative Structure-Activity Relationship Model

XIAOYU LIU[1], SHANSHAN LI[2,3], YUHANG CAI[1], LONG JIANG[2], NAN CHENG[1], WENJIN ZHAO[1,*] and YU LI[2]

[1]College of Environment and Resources, Jilin University, Changchun 130012, P.R. China
[2]Resources and Environmental Research Academy, North China Electric Power University, Beijing 102206, P.R. China
[3]Department of Civil and Environmental Engineering, University of Louisville, Louisville, KY 40292, United States of America

*Corresponding author: Tel./Fax: +86 431 85168031; E-mail: zhaowj@jlu.edu.cn

Received: 30 January 2014; *Accepted*: 22 April 2014; *Published online*: 4 February 2015; AJC-16756

The optimum molecular geometries of estrogens (estrone, 17β-estradiol, estriol, 17α-ethynylestradiol and bisphenol-A) were carried out through the B3LYP method of density functional theory (DFT) using 6-31G(d) basis sets and 35 kinds of quantum chemical parameters, such as energy, dipole moment, polarizability and hyperpolarizability *etc*., were calculated based on optimal geometries. The quantitative structure-activity relationship (QSAR) model between the maximum adsorption capacity of estrogens on soil and the estrogens' quantum chemical parameters was established to reveal the adsorption mechanism of estrogens. It was found that the adsorption process of the estrogens on soil was mainly controlled by physical interaction and the polarizability of estrogens was the most principal factor influencing the adsorption of estrogens on soil. The maximum adsorption capacity of bisphenol-A was larger than other estrogens and this could be explained by charge distribution. The charge distribution profiles of estrogen molecules showed that the estrogens with more homogeneous charge distribution possessed stronger adsorption ability on soil. The study could provide a theoretical guidance for removing the estrogens using adsorption method.

Keywords: Density functional theory, Quantitative structure-activity relationship model, Estrogens, Adsorption mechanism.

INTRODUCTION

Environmental estrogens are endocrine disruptor interfering with the hormonal system of human beings and animals. Entering the body, they will demote the reproductive capacity and the immune function[1,2]. In addition, some human diseases and abnormal phenomena of animals, such as feminization of male and reproductive disorders, could be ascribed to their exposure to environmental estrogens[3]. The absorption of estrogens on adsorbent, such as soil, has great influence on estrogens' movement, transformation and biodegradation[4]. Estrogens generally have a low level of solubility and high level of hydrophobicity in water and they can be absorbed on soil through distributional effects. And adsorption has been claimed to be an effective way in removing estrogens from water[5].

In recent years, many achievements have been made in the study of effective adsorption of estrogens. In the sewage treatment process, the removal of estrogens mainly by absorbing the pollutants onto organics, activated sludge and inactivated sludge, as well as the degradation of microorganism in activated sludge[6]. From studying the adsorption mechanism of estrogen in soil - water system, researchers found that the adsorption characteristics of estrogens on different soil had obvious differences[7]. For example, the adsorption of estrogen on soil doped MnO_2 both had physical adsorption and chemical degradation. MnO_2 could be used as the stabilization agent for the soil and prevented secondary pollution of estrogens caused by desorption effectively[8]. However, previous studies on adsorption mechanisms were mainly about the soil compositions on the experimental level. Therefore, it is necessary to investigate the influence of estrogens' physicochemical property on adsorption in the level of quantum chemistry. The quantum chemistry, which is based on quantum mechanics, is a subject to research on chemistry using fundamental theories and methods of quantum mechanics. It has been an effective mean in studying microscopic properties of molecules[9]. The density functional theory (DFT) plays an important role in theoretical arithmetic and prediction on thermodynamic properties of environmental pollutants[10-12].

In this study, five estrogens [estrone (E1), 17β-estradiol (E2), estriol (E3), 17α-ethynylestradiol (EE2) and bisphenol-A (BPA)] were selected. The 35 quantum chemical parameters of estrogens were calculated and based on which, the quantitative

structure-activity relationship (QSAR) model between the maximum estrogens adsorption capacity (Γ_{max}, mg/g) on soil was developed. Our aim was to reveal the adsorption mechanism of estrogens on soil on the level of quantum chemistry and provide a theoretical guidance for the estrogens removal using the adsorption method.

EXPERIMENTAL

Adsorption of estrogens on soil data: The data of maximum adsorption capacity of E1, E2, E3, EE2 and BPA were cited from the previous studies[13]. For each determination, 0.70 ± 0.0001 g of the soil sample was mixed with 40 mL of the estrogen solution at different concentrations; the concentrations of the estrogen were set at 0.4, 0.6, 0.8, 1.0, 2.0, 3.0, 4.0 and 5.0 mg/L. The pH of the estrogen solutions were controlled at 6.70 ± 0.03. The samples were shaken at 250 rpm for 24 h (25 °C). Each sample was filtered with a 0.45 μm membrane filter and transferred into 2 mL amber vials for high performance liquid chromatography (HPLC) analysis. Duplicate experiments were conducted to account for experimental error and to investigate the reproducibility of the results. A blank experiment was also performed. The sorption isotherm of estrogens adsorption on soil was fitted by Langmuir model and the parameters were listed in Table-1.

Quantum chemical parameters of estrogens: The geometries of the studied molecules were optimized using hybrid density functional theory (DFT), B3LYP, with the 6-31G (d) basis set. The 35 quantum chemical parameters were calculated based on optimum molecular geometries with the Gaussian 09 program system. They were the total energy E_{Total} (a.u.), the energy of the lowest unoccupied molecular orbitals E_{lumo} (eV), the energy of the highest occupied molecular orbitals E_{homo} (eV), the difference value between E_{lumo} and E_{homo} ΔE (eV), the extreme value of Millikan charge on hydroxyl radical O_{OH} and H_{OH} (C), the extreme value of Millikan charge on methyl group C_{CH_3} and H_{CH_3} (C), the extreme value of Millikan charge on benzene $C_{Benzene}$ and $H_{Benzene}$ (C), the polarizabilities α_{xx}, α_{xy}, α_{yy}, α_{xz}, α_{yz} and α_{zz} (a.u.), the average polarizability $\bar{\alpha}$ (a.u.), the anisotropy polarizability $\Delta\alpha$ (a.u.) and the first hyperpolarizabilities β_{xxx}, β_{xxy}, β_{xyy}, β_{yyy}, β_{xxz}, β_{xyz}, β_{yyz}, β_{xzz}, β_{yzz} and β_{zzz} (a.u.). All the quantum chemical parameters are shown in Table-4.

QSAR Model method: The quantitative structure-activity relationship (QSAR) model, which combined with theoretical calculation and statistical analysis, is constructed to describe the relationship between the molecular structure of compound and its biological activity[14,15]. The QSAR model was established through a multiple linear regression analysis. The quantum chemical parameters (X_i) were the independent variables and the Γ_{max} of estrogens were the dependent variables. α_i were the coefficients of the independent variables, which reflected the loadings of the quantum chemical parameters. The QSAR model for the adsorption of estrogens on soil was represented as follow:

$$\Gamma_{max} = \alpha_0 + \alpha_1 \times X_1 + \alpha_2 \times X_2 + \ldots + \alpha_i \times X_i$$

RESULTS AND DISCUSSION

Optimum molecular geometries of estrogens: The geometries of the studied molecules were optimized at B3LYP/6-31G(d) level. The estrogens have the optimum molecular geometries for the positive minimum frequency and no imaginary frequency[16]. Fig. 1 was the geometries of estrogens. As it was seen from Fig. 1, E1, E2, E3 and EE2 shared the same tetracyclic molecular framework, which was composed of four rings: a phenol ring (labeled as A), two cyclohexane rings (labeled as B and C) and a cyclopentane ring (labeled as D)[17]. Take E1and E2 as an example, their geometrical parameters calculated were: the average bond distances of ring A, the average bond distances of ring B, C and D and the average valence angles of the whole molecule (Table-2). Dihedral angles of E1 and E2 from computed and experimental values were listed in Table-3. The Nash-Suttcliffe simulation efficiency coefficients (NSC) of E1 and E2 were 0.996 and 0.992. As illustrated in Tables 2 and 3, an excellent agreement could be observed when comparing the calculated with the experimental geometries[18]. Therefore, a further analysis could be made based on the optimum molecular geometries of estrogens. The optimum molecular geometries of estrogens and the atomic numbers were shown in Fig. 2(a).

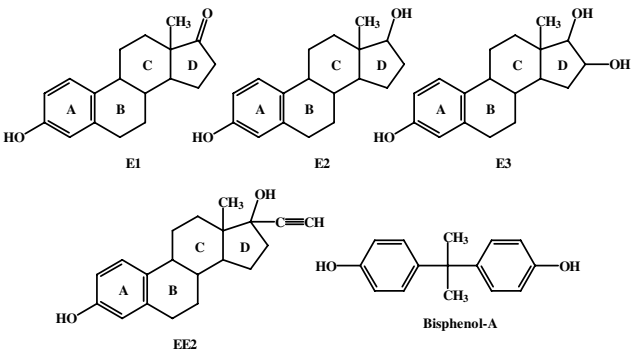


Fig. 1. Structures of estrogens

Correlation analysis between quantum chemical parameters and maximum adsorption: A Pearson correlation analysis between the Γ_{max} and 35 quantum chemical parameters of the estrogens was performed (Table-4). In the field of statistics, the correlation coefficient at $0.01 < P < 0.05$ was

TABLE-1
LANGMUIR ISOTHERM MODELS AND PARAMETERS FOR ADSORPTION OF ESTROGENS ON SOIL[a]

Estrogens	$Q = C_e K\Gamma_{max}/(1 + KC_e)$	K	Γ_{max}	R^2
E1	$Q = 0.0970C_e/(1 + 1.9470\ C_e)$	1.9470	0.0498	0.9031
E2	$Q = 0.0714C_e/(1 + 0.2775\ C_e)$	0.2775	0.2574	0.9865
E3	$Q = 0.0097C_e/(1 + 0.0566\ C_e)$	0.0566	0.1710	0.9934
EE2	$Q = 0.0581C_e/(1 + 0.4744\ C_e)$	0.4744	0.1225	0.9960
BPA	$Q = 0.0067C_e/(1 + 0.0006\ C_e)$	0.0006	11.1345	0.9920

[a]From [Ref. 13]

TABLE-2
BOND DISTANCES AND VALENCE ANGLES OF E1 AND E2

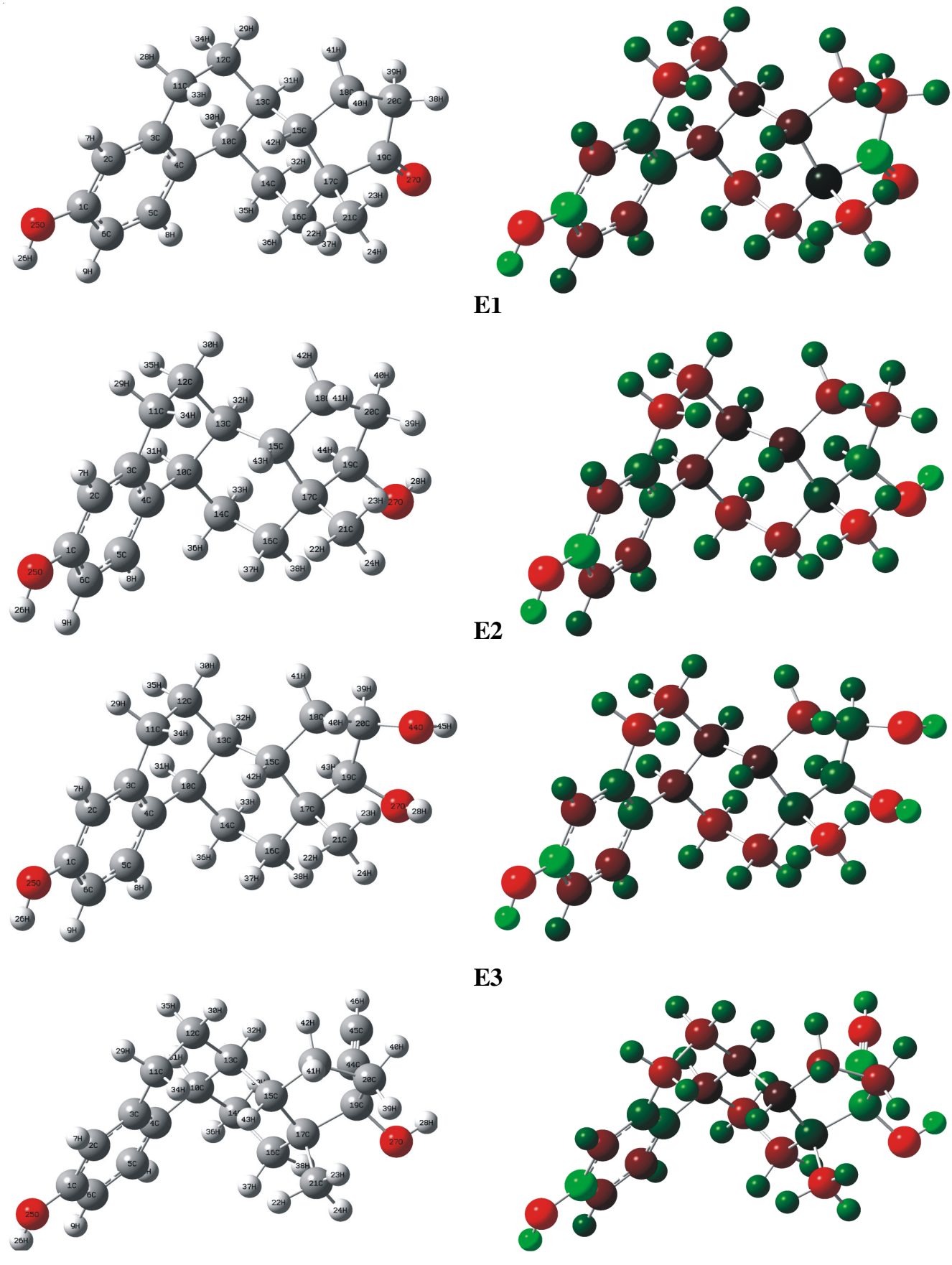
Estrogens	Bond distances, mean (Å)				Valence angles, mean (°)	
	Ring A		Rings B, C and D		Whole molecule	
	Computed	Experimental[a]	Computed	Experimental[a]	Computed	Experimental[a]
E1	1.399	1.391 ± 0.030	1.540	1.529 ± 0.022	111.944	110.940 ± 6.495
E2	1.399	1.486 ± 0.218	1.543	1.527 ± 0.017	111.476	110.667 ± 6.389

[a]From [Ref. 18]

TABLE-3
DIHEDRAL ANGLES OF E1 AND E2

Dihedral angle (°)	E1		E2	
	Computed	Experimental[a]	Computed	Experimental[a]
D(6,1,2,3)	-0.24	0.89	-0.23	3.21
D(25,1,2,3)	179.92	179.21	-179.95	-177.59
D(2,1,6,5)	0.19	1.48	0.15	-4.28
D(25,1,6,5)	-179.98	-176.88	179.96	176.54
D(1,2,3,4)	-0.18	-3.11	-0.11	1.35
D(1,2,3,11)	179.29	177.93	-179.12	-179.70
D(2,3,4,5)	0.63	0.32	0.51	-4.53
D(2,3,4,10)	-176.83	-176.12	176.56	176.40
D(11,3,4,5)	-179.71	-179.45	179.49	176.57
D(11,3,4,10)	4.09	4.11	-4.47	-2.50
D(2,3,11,12)	167.60	165.47	167.26	171.74
D(4,3,11,12)	-13.31	-14.76	-13.74	-9.32
D(3,4,5,6)	-0.69	2.16	-0.60	3.49
D(10,4,5,6)	176.90	178.70	-176.65	-177.44
D(3,4,10,13)	-23.84	-23.18	-23.98	-19.44
D(3,4,10,14)	-149.77	-150.55	-150.04	-144.45
D(5,4,10,13)	160.09	160.49	160.11	161.54
D(5,4,10,14)	34.16	33.12	34.05	36.53
D(4,5,6,1)	0.29	-3.11	0.28	0.87
D(4,10,13,12)	51.50	52.13	51.44	52.05
D(4,10,13,15)	174.88	177.46	174.79	176.85
D(14,10,13,12)	-179.32	-179.82	179.26	179.17
D(14,10,13,15)	-54.30	-54.48	-54.52	-56.03
D(4,10,14,16)	167.45	177.92	168.90	179.54
D(13,10,14,16)	60.09	52.09	58.78	53.70
D(3,11,12,13)	42.71	45.61	43.02	43.14
D(11,12,13,10)	-62.32	-65.68	-62.36	-65.07
D(11,12,13,15)	164.92	173.77	164.60	173.11
D(10,13,15,17)	43.43	60.66	-45.40	-54.15
D(10,13,15,18)	-159.74	-175.72	-162.95	-175.05
D(12,13,15,17)	-167.79	-178.33	-169.52	-177.14
D(12,13,15,18)	-75.90	-54.70	-72.93	-53.53
D(10,14,16,17)	-54.86	-53.39	54.22	61.34
D(13,15,17,16)	-37.15	-63.94	-38.60	-61.32
D(13,15,17,19)	175.75	173.67	173.27	177.97
D(13,15,17,21)	61.53	61.27	60.29	63.00
D(18,15,17,16)	157.54	164.02	160.12	165.80
D(18,15,17,19)	34.64	41.63	38.25	45.10
D(18,15,17,21)	-78.08	-70.77	-78.20	-69.87
D(13,15,18,20)	-166.58	-165.90	-102.13	-159.15
D(17,15,18,20)	-36.19	-38.17	-21.75	-31.94
D(14,16,17,15)	42.76	57.11	43.04	55.25
D(14,16,17,19)	175.23	169.66	172.54	166.14
D(14,16,17,21)	-68.02	-69.84	-65.59	-70.46
D(15,17,19,20)	-21.13	-29.52	-40.96	-41.10
D(15,17,19,27)	159.49	152.73	-164.81	-165.57
D(16,17,19,20)	-146.32	-146.46	-163.62	-157.18
D(16,17,19,27)	34.29	35.78	72.52	78.38
D(21,17,19,20)	95.07	89.75	75.44	77.86
D(21,17,19,27)	-84.32	-88.00	-48.42	-46.59
D(15,18,20,19)	22.99	19.55	3.41	6.06
D(17,19,20,18)	1.04	6.11	27.69	22.28
D(27,19,20,18)	-178.35	-176.02	148.80	150.31
D(17,19,27,28)			175.50	180.00
D(20,19,27,28)			66.48	58.71

[a]From [Ref. 18]



(a) (b)

Fig. 2. Optimum molecular geometries (a) and charge distribution of estrogens (b)

TABLE-4
CORRELATION BETWEEN QUANTUM CHEMICAL PARAMETERS AND Γ_{max} OF ESTROGENS

Quantum chemical parameters	Estrogens					r	Sig. (2-tailed)
	E1	E2	E3	EE2	BPA		
E_{Total}	-849.625	-850.815	-926.028	-926.948	-731.668	0.879	0.050
E_{lumo}	-0.013	0.003	0.000	0.004	-0.002	-0.017	0.978
E_{homo}	-0.212	-0.207	-0.210	-0.206	-0.206	0.582	0.303
ΔE	0.199	0.210	0.210	0.210	0.204	-0.311	0.611
O_{OH}	-0.648	-0.649	-0.648	-0.649	-0.646	0.923	0.025
H_{OH}	0.406	0.405	0.406	0.405	0.406	0.576	0.309
C_{CH3}	-0.468	-0.464	-0.505	-0.467	-0.455	0.489	0.404
H_{CH3}	0.163	0.164	0.160	0.168	0.150	-0.920	0.027
$C_{Benzene}$	0.357	0.356	0.357	0.356	0.351	-0.992	0.001
$H_{Benzene}$	0.129	0.127	0.128	0.127	0.138	0.987	0.002
μ	1.880	1.505	0.881	1.503	2.305	0.728	0.163
Q_{xx}	-126.038	-112.063	-121.110	-121.591	-95.134	0.917	0.028
Q_{yy}	-114.714	-116.750	-122.850	-126.386	-96.318	0.916	0.029
Q_{zz}	-118.377	-121.307	126.705	-129.285	-95.543	-0.141	0.821
Q_{xy}	17.868	11.662	-10.835	-10.740	4.870	0.097	0.876
Q_{xz}	4.065	-4.339	-1.021	-3.102	4.016	0.570	0.316
Q_{yz}	-1.324	1.369	3.912	-1.979	-5.287	-0.735	0.157
$\bar{\alpha}$	179.098	182.120	185.224	198.380	158.281	-0.862	0.060
$\Delta\alpha$	80.004	80.230	79.888	78.857	82.370	0.914	0.030
α_{xx}	218.586	223.134	227.522	238.391	206.703	-0.776	0.123
α_{xy}	10.405	10.944	-9.139	-11.522	0.435	0.013	0.984
α_{yy}	181.074	181.318	182.780	187.101	142.011	-0.992	0.001
α_{xz}	-17.602	-17.816	-17.948	-24.671	20.907	0.987	0.002
α_{yz}	8.610	7.652	-5.477	-7.384	-1.646	-0.150	0.809
α_{zz}	137.632	141.908	145.370	169.647	126.127	-0.630	0.254
β_{xxx}	214.005	211.627	-178.920	-183.878	39.693	0.055	0.930
β_{xxy}	-6.036	-11.346	-28.090	-9.492	195.752	0.995	0.000
β_{xyy}	-45.821	-41.265	49.099	48.388	-11.733	-0.138	0.825
β_{yyy}	-9.284	10.539	-10.580	5.603	101.079	0.982	0.003
β_{xxz}	-34.306	-75.869	70.239	76.787	25.236	0.104	0.868
β_{xyz}	-7.641	-3.106	-2.589	-15.565	23.209	0.937	0.019
β_{yyz}	-4.210	-12.376	10.782	1.049	14.861	0.646	0.239
β_{xzz}	57.654	49.094	-39.009	-72.352	0.840	0.017	0.979
β_{yzz}	42.572	46.906	30.925	49.101	-20.214	-0.970	0.006
β_{zzz}	-34.530	-48.061	79.062	74.315	13.052	-0.037	0.953

regarded as very significant and the correlation coefficient at $P < 0.01$ was regarded as extremely significant. In Table-4, it was very clear that the correlation coefficients of E_{Total}, O_{OH}, H_{CH_3}, Q_{xx}, Q_{yy}, $\Delta\alpha$ and β_{xyz} were at level of $0.01 < P < 0.05$ and the correlation coefficients of $C_{Benzene}$, $H_{Benzene}$, α_{yy}, α_{xz}, β_{xxy}, β_{yyy} and β_{yzz} were at the level of $P < 0.01$. The above fourteen quantum chemical parameters exhibited significant relationships with Γ_{max} and they were preliminarily selected for the construction of QSAR model between the Γ_{max} of estrogens on soil and the estrogens' quantum chemical parameters.

QSAR model construction: Regression equation was obtained *via* Statistic Package for Social Science (SPSS). The QSAR model for the relationship between the Γ_{max} and the quantum chemical parameters of the estrogens was established as follows:

$$\Gamma_{max} = 48.348 - 0.263\alpha_{yy}$$

As seen in Table-5, the R^2_{adj} of the QSAR model was 0.978, which implied that the model was robust. With the $P = 0.001$ ($P < 0.01$), it showed good statistical significance of the model.

Shown in Table-6, the regression coefficients of constant and α_{yy} were 48.348 and -0.263, respectively. The model has a very good level of linear significance ($P < 0.01$). The points of standardized residual in Fig. 3 tended to cluster along the 45° tangent line. It indicated that the standardized residual obeyed the normal distribution approximately and the QSAR model between the Γ_{max} of estrogens on soil and the estrogens' quantum chemical parameters was reliable.

TABLE-5
QSAR MODEL EVALUATION PARAMETERS

R^2_{adj}	Std. Error of the Estimate	F	Sig.
0.978	0.732	177.163	0.001

TABLE-6
REGRESSION COEFFICIENTS OF QSAR MODEL

Model	B	Std. Error	t	Sig.
(Constant)	48.348	3.472	13.927	0.001
α_{yy}	-0.263	0.020	-13.310	0.001

Adsorption mechanism of estrogens on soil: As was presented in the QSAR model, the Γ_{max} of estrogens on soil had a negative linear correlation with α_{yy}, which meant that the polarizability of estrogens was the most principal factor influencing the adsorption of estrogens on soil and it was also

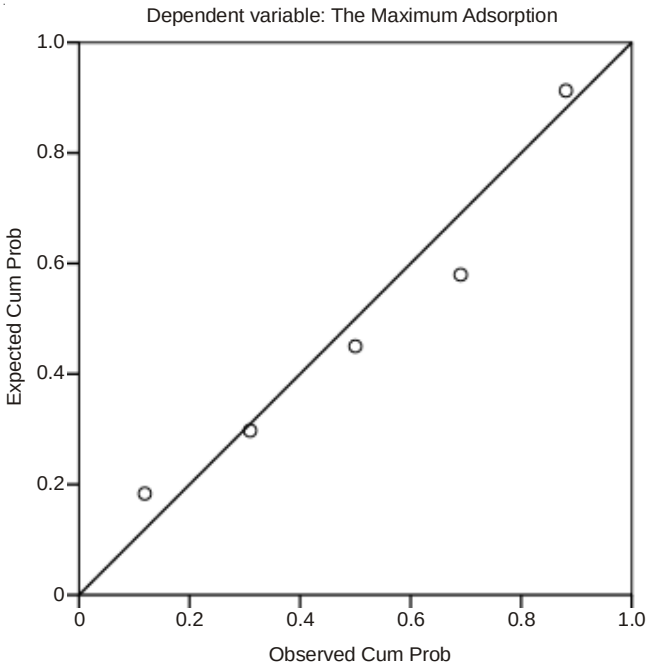


Fig. 3. Normal P-P plot of regression standardized residual

an important physical parameter used to measure the intensity of polarization under the action of electric field. This was consistent with the conclusion of Li *et al.*[8] that the adsorption process of the estrogens on soil was mainly controlled by physical interaction.

Moreover, the Γ_{max} of bisphenol-A was much greater than other estrogens (Table-1) and this could be explained by charge distribution theory. Fig. 2 (b) illustrated the charge distribution profiles for estrogens based on Mulliken population analysis[19]. The red atom had a negative charge and the green atom had a positive charge. The brighter colour indicated greater charge while the darker colour indicated smaller charge. It could be seen from Fig. 2 that bisphenol-A was tetrahedral structure centering on the ^{21}C and it had a high level of spatial symmetry and charge distribution. It illustrated that charge distribution influenced the adsorption capacity of estrogens and the estrogens with more homogeneous charge distribution possessed stronger adsorption capability on soil.

Conclusion

The optimum molecular geometries of estrogens were obtained through DFT and 35 quantum chemical parameters were calculated. The QSAR model between the maximum adsorption capacity of estrogens on soil and the estrogens' quantum chemical parameters was established. It was found that the adsorption process of the estrogens on soil was mainly controlled by physical interaction and the polarizability of estrogens was the most principal factor influencing the adsorption of estrogens on soil. The charge distribution profiles of estrogen molecules showed that the estrogens with more homogeneous charge distribution possessed stronger adsorption ability to soil.

ACKNOWLEDGEMENTS

Financial support was provided by the Ministry of Science and Technology China ('973' Project No. 2004CB3418501).

REFERENCES

1. T. Colborn, F.S. vom Saal and A.M. Soto, *Environ. Health Perspect*., **101**, 378 (1993).
2. M. Yokosuka, R. Ohtani-Kaneko, K. Yamashita, D. Muraoka, Y. Kuroda and C. Watanabe, *Toxicol. in vitro*, **22**, 1 (2008).
3. D. Terri, B. Sue, B. Aake, K. Robert and V.K. Glen, World Health Organization: Global Assessment of the State-of-the-Science of Endocrine Disruptors, Geneva, pp. 4/33-4/50 (2002).
4. C.A. Staples, P.B. Dome, G.M. Klecka, S.T. Oblock and L.R. Harris, *Chemosphere*, **36**, 2149 (1998).
5. Y.P. Zhang and J.L. Zhou, *Water Res*., **39**, 3991 (2005).
6. O. Braga, G.A. Smythe, A.I. Schäfer and A.J. Feitz, *Environ. Sci. Technol*., **39**, 3351 (2005).
7. A. Mohammed, Y.S. Yang, X.Q. Du, M.X. Yang and A. Musa, *J. Jilin Univ. (Earth Sci. Ed.)*, **43**, 574 (2013).
8. Y. Li, C. Zhang, J.L. Liu, X.P. Li and X.J. Wang, *Chem. J. Chinese Univ*., **34**, 634 (2013).
9. D. Nori-Shargh, F.R. Ghanizadeh, M.M. Hosseini and F. Deyhimi, *J. Mol. Struct.-Theochem*., **808**, 135 (2007).
10. J.E. Lee, W. Choi and B.J. Mhin, *J. Phys. Chem. A*, **107**, 2693 (2003).
11. X.W. Li, E. Shibata and T. Nakamura, *J. Chem. Eng. Data*, **48**, 727 (2003).
12. J. Tomasi, B. Mennucci and R. Cammi, *Chem. Rev*., **105**, 2999 (2005).
13. J.L. Liu, Study on the Adsorption Behaviors and Biodegradation of Estrogen Chemicals in Soil System, North China Electric Power University, Beijing, China (2012).
14. C. Hansch, A. Leo and R.W. Taft, *Chem. Rev*., **91**, 165 (1991).
15. H. Gao, J.A. Katzenellenbogen, R. Garg and C. Hansch, *Chem. Rev*., **99**, 723 (1999).
16. W.J. Hehre, L. Radom, P.R. Schleyer and J.A. Pople, *ab initio* Molecular Orbital Theory, John Wiley & Sons, New York, p. 227 (1986).
17. E.V. Rokhina and R.P.S. Suri, *Sci. Total Environ*., **417-418**, 280 (2012).
18. C. Kubli-Garfias, *J. Mol. Struc-Theochem*., **452**, 175 (1998).
19. P.B. Nagabalasubramanian, M. Karabacak and S. Periandy, *Spectrochim. Acta A*, **82**, 169 (2011).