



Theoretical investigation on the kinetics and mechanisms of hydroxyl radical-induced transformation of parabens and its consequences for toxicity: Influence of alkyl-chain length



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ABSTRACT

As emerging organic contaminants (EOCs), the ubiquitous presence of preservative parabens in water causes a serious environmental concern. Hydroxyl radical ($\cdot\text{OH}$) is a strong oxidant that can degrade EOCs through photochemistry in surface water environments as well as in advanced oxidation processes (AOPs). To better understand the degradation mechanisms, kinetics, and products toxicity of the preservative parabens in aquatic environments and AOPs, the $\cdot\text{OH}$ -initiated degradation reactions of the four parabens were investigated systematically using a computational approach. The four studied parabens with increase of alkyl-chain length were methylparaben (MPB), ethylparaben (EPB), propylparaben (PPB), and dibutylparaben (BPB). Results showed that the four parabens can be initially attacked by $\cdot\text{OH}$ through $\cdot\text{OH}$ -addition and H-abstraction routes. The $\cdot\text{OH}$ -addition route was more important for the degradation of shorter alkyl-chain parabens like MPB and EPB, while the H-abstraction route was predominant for the degradation of parabens with longer alkyl-chain for example PPB and BPB. In assessing the aquatic toxicity of parabens and their degradation products using the model calculations, the products of the $\cdot\text{OH}$ -addition route were found to be more toxic to green algae than original parabens. Although all degradation products were less toxic to daphnia and fish than corresponding parental parabens, they could be still harmful to these aquatic organisms. Furthermore, as alkyl-chain length increased, the ecotoxicity of parabens and their degradation products was found to be also increased.

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1. Introduction

In recent years, the presence of emerging organic contaminants (EOCs) in water and wastewater has already become a global public concern in almost all parts of the world (Schwarzenbach et al., 2010, 2006). Parabens, a group of EOCs with antimicrobial and preservative properties, are widely used in toothpastes, cosmetics, textiles, foodstuffs, and beverages (Calafat et al., 2010; Liao et al., 2013b). Approximately 8000 tons of parabens are consumed annually around the world (Ramaswamy et al., 2011), and most are continuously released into the environment during their production, use, and disposal. As such, parabens are now detected in various aquatic environments (Kasprzyk-Hordern et al., 2008; Liao

et al., 2013a; Liu and Wong, 2013), imposing potential risks to aquatic organisms (An et al., 2014a; Terasaki et al., 2009; Yamamoto et al., 2011). Furthermore, parabens have been detected in breast tumor tissue, and may be associated with the formation of these cancers (Darbre and Harvey, 2008; Kuş et al., 2013). Recent studies on a series of parabens, including methyl- (MPB), ethyl- (EPB), propyl- (PPB), and butyl-parabens (BPB) (structures are shown in Fig 1) (Karpuzoglu et al., 2013), have revealed that parabens affect estrogen levels, potentially impacting female reproductive health (Smith et al., 2013). Due to their potential toxicity to aquatic organisms and human beings, it is important to study the transformation and removal of these pollutants from water environments.

Conventional wastewater treatment technologies are still inadequate for removing parabens (Leal et al., 2010). However, advanced oxidation processes (AOPs) have proven to be successful in destroying and mineralizing recalcitrant organic pollutants in

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water (An et al., 2015,2010). Recently, different AOPs including UV irradiation (Błędzka et al., 2012; Sánchez-Martín et al., 2013), photocatalytic (Lin et al., 2009; Yang et al., 2010), photo-sonochemical (Daghrir et al., 2014), electrochemical (Steter et al., 2014), and ozone oxidation (Tay et al., 2010a,2010b), which generate highly reactive hydroxyl radicals ($\cdot\text{OH}$), have been frequently used in experiments to detoxify parabens (Fang et al., 2013). In fact, $\cdot\text{OH}$ is also one of the main photo-generated species involved in the indirect phototransformation of a wide spectrum of EOCs in surface waters (Dong and Rosario-Ortiz, 2012; Wenk et al., 2011). Therefore, the $\cdot\text{OH}$ -initiated reactions of parabens could likely occur, either in surface water environments or in AOP systems.

Recent studies suggest that some of the degradation products from these AOPs and photochemical transformation are found to be more toxic than these parental EOCs (Boxall et al., 2004; Daghrir et al., 2014; Prasse et al., 2012). For parabens, only a fraction of them can be completely oxidized into water and carbon dioxide due to the TOC removal of 43%–80%, and some can be transformed into by-products (Daghrir et al., 2014; Lin et al., 2009). However, there is still very limited attention paid to the transformation products of parabens, as well as their potential toxicity during $\cdot\text{OH}$ -induced transformation of parabens. In our previous experimental study, the acute toxicity was found to be increased during PPB degradation (Fang et al., 2013), suggesting that the transformation products formed in the treatment process maybe more toxic than the parental PPB. However, the study has not identified how PPB's degradation products are formed during $\cdot\text{OH}$ -based oxidation processes, why the transformation products are more toxic than the parental PPB, and what about the cases in the transformation of other parabens. In particular, the alkyl chain length of parabens may significantly affect the transformation products and their consequences for the toxicity toward aquatic organisms. To the best of our knowledge, the systematic research on the relationship among the transformation mechanisms, environmental fate, aquatic toxicity and the alkyl chain length of a series of parabens have not been yet fully explored.

Given the large and ever-increasing number of EOCs, theoretical calculations are found very crucial to evaluate their environmental photodegradation behavior, ecological risk assessment as well as pollution prevention, as experimental methods are costly and time-consuming, and cannot evaluate all emerging chemicals (Zhang et al., 2010; Zhou et al., 2011). It have been demonstrated that computational approaches have provided important information on the reaction intermediates or active species involved in chemical reactions, which are necessary for the mechanism clarification but are difficult to be detected experimentally (An et al., 2015,2014b,2011; Fang et al., 2013). Also, theoretical calculations have successfully used to predict the toxicity assessments of EOCs in water (Gao et al., 2014a,2014b; Madden et al., 2009).

Given this background, in this work, theoretical calculations on the structure-dependency degradation mechanisms and the toxicity of degradation products of different parabens during $\cdot\text{OH}$ -mediated transformation processes were performed based on the density functional theory (DFT), and the mechanisms, kinetics and toxicity evolution of the $\cdot\text{OH}$ -initiated oxidation of four different parabens (MPB, EPB, PPB, and BPB) were systematically compared. The ecological risks posed by parabens as well as their transformation products were evaluated using the most extensively validated and used tool, named the US EPA "ecological structure–activity relationships" (ECOSAR) program. These theoretical results will help explain paraben degradation mechanisms and assess the potential risks associated with their $\cdot\text{OH}$ -mediated degradation processes.

2. Computational methods

2.1. Mechanism and kinetics computations

All quantum chemical calculations were carried out using the Gaussian 03 program (Frisch et al., 2003). The geometrical parameters of reactants (RC), transition states (TS), and products (PC) were optimized at the B3LYP level with a standard 6-31G(d,p) basis set. At the same level, the vibrational frequencies were calculated to

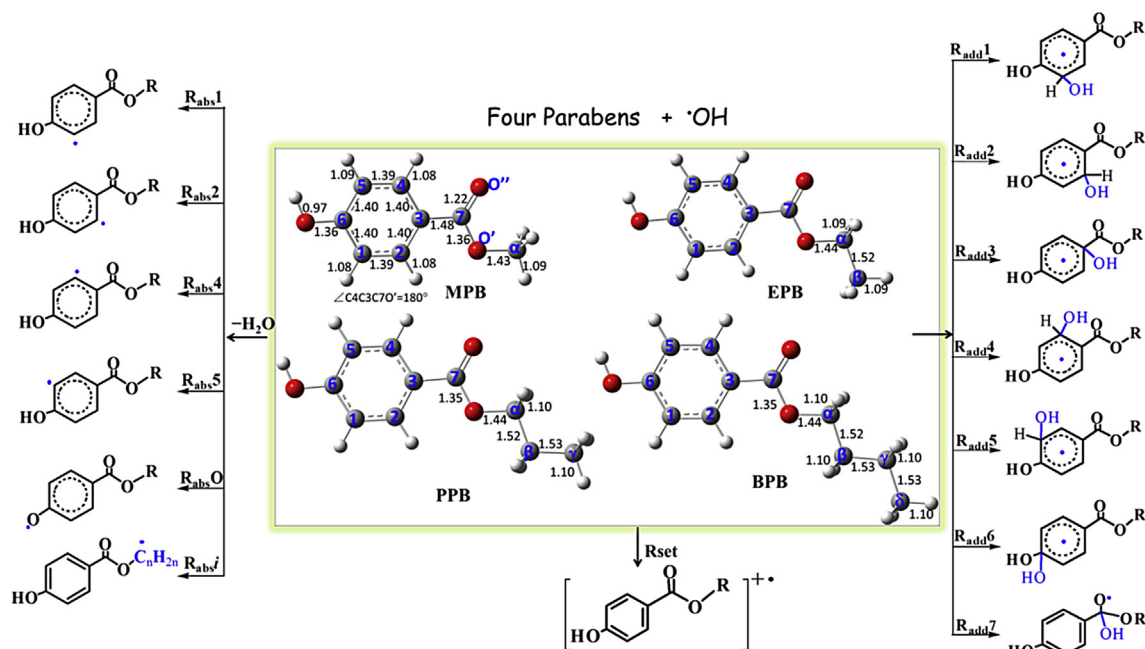


Fig. 1. Four parabens conformation optimized at B3LYP/6-31G (d,p) level, as well as all possible routes for their degradation reactions with $\cdot\text{OH}$. Herein, the same geometrical parameters for the four parabens are listed only in MPB. Bond lengths are in angstroms. \bullet = C, \circ = H, \bullet = O.

identify these stationary points as either minima (with zero imaginary frequency) or *TS* (with one and only one imaginary frequency), to obtain the thermodynamic contributions. Intrinsic reaction coordinate (IRC) calculations were conducted to confirm that each *TS* connected the reactants with its corresponding products. Single-point energy calculations, including the solvent effect, were performed to establish the potential energy surface (PES) at the B3LYP/6–311++G(d,p) level, based on the optimized structures described above. The solvent effect was considered using a conductive polarizable continuum model (CPCM) (Barone and Cossi, 1998). Based on PES information, the reaction kinetics were calculated using conventional transition-state theory (TST), considering solvent cage effects (Okuno, 1997) and diffusion-limited effects (Collins and Kimball, 1949; Gao et al., 2014a).

2.2. Ecotoxicity assessment

The acute and chronic toxicities of parabens and their degradation products were assessed using the ECOSAR program (ECOSAR, 2014). The program can estimate the acute and chronic toxicity to aquatic organisms such as fish, aquatic invertebrates, and aquatic plants by using computerized Structure Activity Relationships (SARs). The usefulness and reliability of ECOSAR has been previously demonstrated, and ECOSAR was ranked as one of the best overall effect-predictive programs to assess the toxicity of many organic pollutants (Madden et al., 2009; Tunkel et al., 2005), and the detail discussion was given in Supplementary Section. Moreover, this tool has been successfully employed to predict the toxicities of various EOCs such as pharmaceuticals (Jones et al., 2002), fragrance materials (Salvito et al., 2002), and bactericides (Gao et al., 2014b). As for parabens and their products investigated conducted in this study, their molecular weights (<1000) and log Kow (ranging from –3 to 8.0) meet the applicability of ECOSAR program, and the risks to aquatic organisms were also considered at three different trophic levels in this work: green algae, daphnia and fish. Acute toxicity is expressed using EC_{50} values (the pollutant concentration that inhibits green algae growth by 50% after 96 h) and LC_{50} values (the pollutant concentration that leads to the death of 50% fish and daphnia after 96 and 48 h exposures, respectively). According to the chemicals White Paper (EU, 2001), the lowest effect concentration was used in the analysis for the most conservative estimation based on the precautionary principle.

3. Results and discussion

3.1. Correlating aquatic toxicity of parabens with molecular structure

Fig. 1 shows the optimized structures of four parabens and their atomic numbering. As seen, four parabens exhibit similar geometrical parameters; all have a planar structure with a dihedral angle of approximately 180.0° between the benzene ring and the side chain. As the alkyl-chain length increases, the C–H bond lengths of four parabens show little change (within 0.01 Å), but the physicochemical properties change significantly. For example, the log Kow of the four parabens (MPB, EPB, PPB, and BPB) were calculated as 2.00, 2.49, 2.98, and 3.47, respectively (Table S1). These results are well consistent with the previous experimental values (1.98, 2.35, 3.00, and 3.32) (Casoni and Sarbu, 2009). These data indicate that as alkyl-chain length increases, the log Kow increases from MPB to BPB.

To further estimate differences in aquatic toxicity of the four parabens, the acute and chronic toxicities were investigated at three trophic levels of aquatic organisms (fish, daphnia, and green algae) (Fig. 2 and Table S1). For all calculations of toxicity (LC_{50} , EC_{50}

and ChV) across all tested aquatic organisms, the aquatic toxicity increases in the order MPB < EPB < PPB < BPB. These computational trends agree well with the early reported experimental observation (Yamamoto et al., 2011). That is, the aquatic toxicities on fish, daphnia, and algae are weaker for the parabens with a shorter alkyl chain than those with a longer alkyl chain. In addition, both acute and chronic toxicities show a linear relationship with log Kow, indicating that the aquatic toxicity increases with increasing hydrophobicity. This finding may be explained that the large hydrophobicity pollutants are more powerful to penetrate the cell membrane (Liu et al., 2015), thereby leading to higher aquatic toxicity.

For acute toxicity (Fig. 2a), all four parabens were found toxic to at least one of the three aquatic organisms; specifically for the daphnia. For example, MPB was toxic to daphnia, and harmful to fish and green algae. These results agree well the experimental observation that *D. magna* growth was more sensitive to paraben exposure than the fathead minnow growth responses (Dobbins et al., 2009). As for chronic toxicity (Fig. 2b), MPB and BPB were harmful and toxic to all three aquatic organisms, respectively; EPB and PPB were harmful for green algae and toxic to daphnia and fish. Moreover, the predicted toxicity values of parabens were fall into the same toxicity class as the experimental measured data (Table S1). As for daphnia, the predicted toxicity values are slightly lower than the experimental data reported by Dobbins et al. (2009),

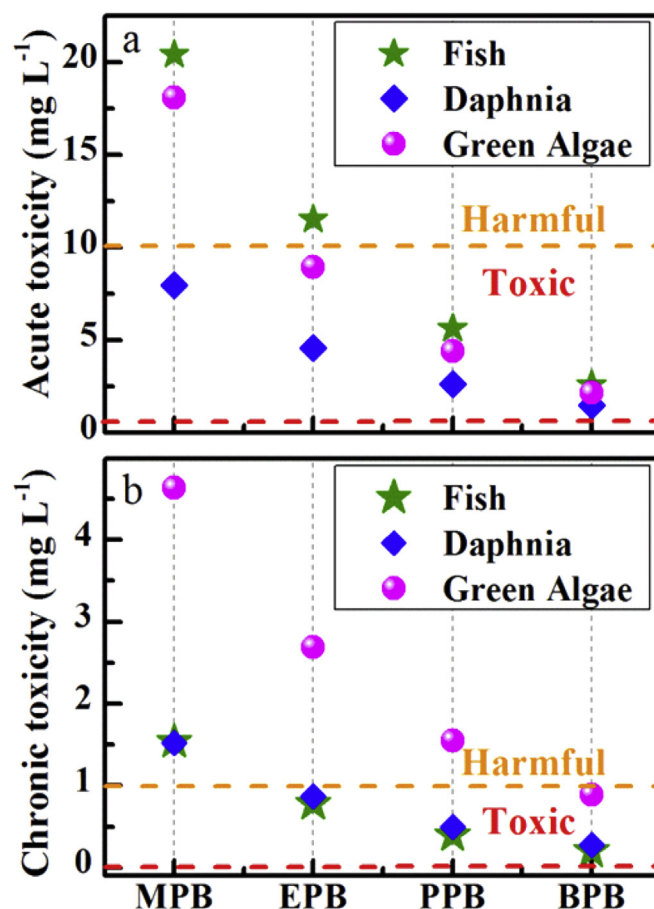


Fig. 2. The acute (a) and chronic (b) toxicity of four different parabens to three trophic levels of aquatic organisms (fish, daphnia, and green algae). According to the European Union criteria and the Chinese hazard evaluation guidelines for new chemical substances (HJ/T 154–2004) (Table S2). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

but it agree well with the experiment by Yamamoto et al. (2007). These results indicate that the ECOSAR program is a suitable method to assess the toxicity of parabens and their transformation products.

In general, from the point of view of their acute and chronic toxicities, all four parabens are considered to be potentially harmful to aquatic environment, and their toxicity to aquatic species at three trophic levels increases with an increase in the alkyl-chain length.

3.2. Advanced oxidative degradation of parabens in water

3.2.1. Mechanisms

In natural waters and aqueous-phase AOPs, $\bullet\text{OH}$ is a well-known highly reactive oxidant, and it can initiate three types of reaction routes with the four parabens, summarized in Fig. 1: (i) $\bullet\text{OH}$ -addition: either onto the C atom of benzene ring (R_{add1-6}) or carbonyl group (R_{add7}); (ii) H-abstraction by $\bullet\text{OH}$: either from benzene ring ($R_{abs1,2,4,5}$), phenolic hydroxyl (R_{absOH}), or alkyl group ($R_{abs\alpha-\delta}$); and (iii) single-electron transfer from parabens molecules to $\bullet\text{OH}$ (R_{set}). Although the electron transfer is not a common mechanism for $\bullet\text{OH}$ reactions (Fang et al., 2000), this route is still considered for the completeness of the transformation mechanisms in this work. These reaction routes occur in parallel, but different degradation routes have a different probability of occurring. As such, it is important to study both the main degradation products and the degradation mechanisms to understand how paraben structure is transformed by degradation.

Table 1 presents the computed reaction energies (ΔG) of the degradation routes of four parabens; Fig. S1 shows the transition state geometries involved in these routes. As Table 1 shows, ΔG of the single-electron transfer routes (R_{set}) were calculated as ranging from 10.55 to 11.01 kcal mol⁻¹ for the four parabens. These positive ΔG values indicate that the single-electron transfer routes are endothermic. Thus, this type of mechanism is less spontaneous than exothermic routes ($\Delta G < 0$ kcal mol⁻¹), and can be ruled out as a viable mechanism. Moreover, this conclusion can well explain our previous experimental results, why the transient spectrum of the single-electron transfer product, the radical cation of propylparaben (PPB^{•+}), was not observed during PPB degradation in AOP systems (Fang et al., 2013). Therefore, there is a very low probability for the electron-transfer reactivity of the four parabens with $\bullet\text{OH}$, regardless of the alkyl-chain length of these parabens. However, this finding does not exclude R_{set} route as a viable route for the reaction of $\bullet\text{OH}$ with other organic contaminants, such as the deprotonated pentachlorophenol (Fang et al., 2000).

For the $\bullet\text{OH}$ -addition routes of the four parabens, R_{add3} and R_{add7} routes have difficulty to occur, because these endothermic reactions are not thermodynamically favored (Table 1). This phenomenon is easy to understand since there exist the electronic and steric hindrance effects of substituents. However, the other five routes ($R_{add1,2,4,5,6}$) have exothermic reactions with a negative ΔG of -5.66 – -3.14 kcal mol⁻¹, suggesting that these routes are thermodynamically feasible for degrading the four parabens. Among these five exothermic routes ($R_{add1,2,4,5,6}$), the lowest energy barrier (ΔG^\ddagger) of 7.53 – 7.93 kcal mol⁻¹ was located in R_{add1} route for degrading the four parabens (Table 2); these were 2.25 – 4.54 kcal mol⁻¹ lower than the ΔG^\ddagger of the other routes ($R_{add2,4,5,6}$). These data imply that the R_{add1} route would be the most favorable $\bullet\text{OH}$ -addition route for degrading the four parabens and more significant than other $\bullet\text{OH}$ -addition ones. This finding can be explained that the phenolic hydroxyl group ($-\text{OH}$) preferentially activates the *ortho* and *para* positions, due to the electron-donating behavior (Yu et al., 2006). Considering the steric hindrance effect, *ortho*-position was more readily attacked by $\bullet\text{OH}$ than *para* position

Table 1

Reaction energies (ΔG , kcal mol⁻¹) for $\bullet\text{OH}$ -initiated degradation of four parabens.

		MPB	EPB	PPB	BPB
$\bullet\text{OH}$ -addition	R_{add1}	-5.65	-5.60	-5.66	-5.12
	R_{add2}	-3.75	-3.51	-3.62	-3.14
	R_{add3}	3.15	2.25	2.10	2.67
	R_{add4}	-4.08	-3.68	-3.38	-3.61
	R_{add5}	-4.45	-4.45	-4.54	-3.76
	R_{add6}	-4.56	-4.62	-4.54	-4.41
	R_{add7}	17.56	17.82	17.90	18.35
H-abstraction	R_{abs1}	-4.34	-4.38	-4.41	-4.47
	R_{abs2}	-6.36	-6.47	-6.44	-6.38
	R_{abs4}	-5.75	-5.79	-5.76	-5.72
	R_{abs5}	-4.65	-4.70	-4.69	-4.64
	R_{absOH}	-29.56	-29.77	-29.78	-29.91
	$R_{abs\alpha}$	-21.12	-24.15	-24.77	-23.68
	$R_{abs\beta}$		-19.28	-24.76	-24.19
	$R_{abs\gamma}$			-21.07	-25.00
	$R_{abs\delta}$				-21.09
	electron transfer	R_{set}	11.01	10.55	10.57

Herein, ΔG was calculated relative to the reactants, parabens and $\bullet\text{OH}$, and the formula was $\Delta G = G_{Products} - G_{Reactants}$.

of parabens. This attack would be also facilitated by the ester group because of its orientation effect (*meta*-directing). Thus, the hydroxylation of the aromatic ring of parabens via $\bullet\text{OH}$ is expected to occur in *ortho* to phenolic OH group of parabens, namely, *meta* to the ester group of parabens. This preference result is in agreement with previous data obtained in similar system (An et al., 2014b; DeMatteo et al., 2005; Tay et al., 2010b). However, there is a slight different with the experimental research that the hydroxylation on the *ortho* to the ester group (Daghrir et al., 2014).

For the H-abstraction routes, the ΔG^\ddagger were calculated to be 12.99 – 16.57 kcal mol⁻¹ for benzene-H-abstraction ($R_{abs1,2,4,5}$), 10.40 – 11.25 kcal mol⁻¹ for phenolic-H-abstraction (R_{absOH}), and 7.11 – 10.44 kcal mol⁻¹ for alkyl-H-abstraction ($R_{abs\alpha-\delta}$) routes (Table 2). These results suggest that the ΔG^\ddagger of H-abstraction from benzene moiety routes are higher by about 2.4 – 9.5 kcal mol⁻¹ than the other H-abstraction routes (Table 1). Thus, routes ($R_{abs1,2,4,5}$) may be ignored, as phenolic-H-abstraction (R_{absOH}) and alkyl-H-abstraction ($R_{abs\alpha-\delta}$) routes would be more significant. Nevertheless, due to the small difference in ΔG^\ddagger of these routes with their corresponding parabens, their contributions were unlikely to be identified based solely on their mechanisms; further kinetics calculations were needed to distinguish their detailed contributions.

Table 2

Energies barrier (ΔG^\ddagger , kcal mol⁻¹) for $\bullet\text{OH}$ -initiated degradation of four parabens.

	Routes	MPB	EPB	PPB	BPB
OH-addition	R_{add1}	7.53	7.59	7.55	7.93
	R_{add2}	10.40	10.57	10.49	11.08
	R_{add3}	10.13	9.84	9.97	10.55
	R_{add4}	10.08	10.16	9.95	10.48
	R_{add5}	11.65	11.50	11.66	12.44
	R_{add6}	11.59	11.56	11.62	11.84
	R_{add7}	23.35	23.52	23.63	24.12
H-abstraction	R_{abs1}	13.14	12.99	13.17	13.81
	R_{abs2}	14.78	15.39	15.51	16.05
	R_{abs4}	13.32	13.18	13.03	13.63
	R_{abs5}	16.07	15.92	15.89	16.57
	R_{absOH}	10.63	10.40	10.48	11.25
	$R_{abs\alpha}$	9.74	9.05	9.34	9.88
	$R_{abs\beta}$		9.27	9.76	10.44
	$R_{abs\gamma}$			7.53	8.23
	$R_{abs\delta}$				7.11
	electron transfer	R_{set}	13.13	12.34	12.37

Herein, ΔG^\ddagger was calculated relative to the reactants, parabens and $\bullet\text{OH}$, and the formula was $\Delta G^\ddagger = G_{Transition\ states} - G_{Reactants}$.

Based on the discussion above, the single-electron transfer route (R_{set}), two $\bullet\text{OH}$ -addition routes (R_{add3} and R_{add7}) and four benzene-H-abstraction routes ($R_{abs1,2,4,5}$) could be ruled out from the degradation pathways of corresponding parabens in $\bullet\text{OH}$ -based processes because of the endothermic reactions and high energy barriers. Therefore, the $\bullet\text{OH}$ -addition (R_{add1}) route and two types of H-abstraction routes ($R_{abs\text{OH}}$ and $R_{abs\alpha-\delta}$) would be the most important in assessing the kinetics and transformation products toxicity of parabens.

3.2.2. Kinetics

To quantitatively evaluate the contribution of each route and provide insights into the fate of the four parabens in water, the rate constants were calculated for the temperature range 273–313 K. Fig. 3 and Table S3 list the second-order rate constants for each route, as well as the total reactions (k_{total} , the sum of rate constants of each route). For the comparison, the available experimental data are also included. The calculated k_{total} of the four parabens were $2.61\text{--}12.3 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ in the 273–313 K range, which were close to the diffusion limit reaction ($10^{10} \text{ M}^{-1} \text{ s}^{-1}$). This indicates that the four parabens could be rapidly degraded by $\bullet\text{OH}$ in natural waters and AOPs through an almost diffusion-controlled process. Nevertheless, the $\bullet\text{OH}$ reactions with the four parabens also depends highly on the steady-state concentrations of $\bullet\text{OH}$ ($[\bullet\text{OH}]$), which are found in freshwaters at $[\bullet\text{OH}]$ ranging from 10^{-18} to 10^{-14} M (Plumlee et al., 2009) and in AOPs applications up to 10^{-10} M (Wang et al., 2012).

As Fig. 3 shows, using k_{total} as a function of the 273–313 K temperature range, the k_{total} of four parabens increased with rising temperature. For example, the k_{total} of the degradation of EPB increased from 3.66×10^9 to $1.01 \times 10^{10} \text{ M}^{-1} \text{ s}^{-1}$. These results suggest that a relatively high temperature could promote the $\bullet\text{OH}$ -initiated degradation of parabens in AOP systems and photochemical transformation in natural waters. To further estimate the rate constants in other experimental temperature ranges, the Arrhenius formulas were also established within the temperature range of 273–313 K (Table S4). From these formulas, the activation energies of the degradation reactions of MPB, EPB, PPB and BPB were obtained as 4.39, 4.33, 3.77, and 2.88 kcal mol^{-1} , respectively, further confirming the easy $\bullet\text{OH}$ -initiated reaction of the four parabens. Moreover, parabens with longer alkyl-chain length are degraded more efficiently. This makes the alkyl-chain length of degradation products particularly important in $\bullet\text{OH}$ -initiated

transformation of parabens in waters.

At room temperature (298 K), the k_{total} were calculated as 5.01×10^9 , 7.34×10^9 , 8.88×10^9 , and $9.58 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ for MPB, EPB, PPB and BPB (Table S3), respectively. This indicates that the total rate constants of the four parabens increase with an increase of the alkyl-chain length; the total rate constants for k_{MPB} is lower than k_{EPB} , which is lower than k_{PPB} , which is lower than k_{BPB} . In addition, these calculated rate constants are close to the available experimental values (Błędzka et al., 2012; Fang et al., 2013; Tay et al., 2010b) with the largest deviation within a factor of 1.3 (Table S3). For instance, the calculated k_{total} for PPB degradation of $8.88 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ was comparable with the experimental values of $8.60 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ (Tay et al., 2010b) and $7.71 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ (Fang et al., 2013). The good agreement between the experimental rate constants and the calculated data validates the reliability of the present calculated models. In addition, several sophisticated methods such as the group contribution methods (GCM) (Minakata et al., 2009; Monod and Doussin, 2008), also exhibit an reasonable ability to predict the reaction rate at room temperature, and the obtained GCM calculated results (Table S3) were also comparable with the experimental data, and the largest deviation is obtained as 1.5. Nevertheless, the prediction of the temperature-dependence rate constants is limited using the GCM, due to lack of the temperature-dependence parameters such as group rate constant and group contribution factor. Thus, the rate constants in this study were still calculated using the quantum chemical calculation and transition-state theory.

3.2.3. Degradation products

To quantitatively estimate the difference in the degradation intermediates of different parabens, the temperature dependence of the branching ratio (Γ) was calculated in the 273–313 K temperature range (Fig. 4). The Γ of each route was determined using the equation, $\Gamma_i = k_i/k_{total}$, where k_i is the reaction rate constant of the i th route. For MPB degradation, the $\bullet\text{OH}$ -addition route (R_{add1}) remained as the dominant one across the investigated temperature range (Gao et al., 2014a). For example, Γ of R_{add1} was 62% at room temperature, which was higher by 28% and 58% than the Γ values of H-abstraction routes ($R_{abs\alpha}$ and $R_{abs\text{OH}}$), shown in Fig. 4a). Therefore, the $\bullet\text{OH}$ -addition route would be the main MPB degradation mechanism, forming $\bullet\text{MPB-OH}_1$ and further producing stable *ortho*-hydroxylated MPB (*o*-OH-MPB). Interestingly, this result is in general agreement with a previous study conducted on toluene, as an aromatic compound with short alkyl-chain length (Hatipoglu et al., 2010).

As Fig. 4b shows, for EPB degradation, the $\bullet\text{OH}$ -addition route (R_{add1}) is also a major degradation route below 313 K, while the contribution of $R_{abs\alpha}$ and $R_{abs\beta}$ becomes more competitive at higher temperature. For example, as temperature increased, Γ of R_{add1} decreased from 37% at room temperature to 31% at 313 K, which is equal to the Γ of $R_{abs\alpha}$ and $R_{abs\beta}$ (31%) at 313 K. Stable products, *ortho*-hydroxylated EPB (*o*-OH-EPB), α -EPB-OH, and β -OH-EPB would be mainly produced accordingly.

As Fig. 4c and d show, different results are obtained for PPB and BPB degradation. The $\bullet\text{OH}$ -addition route (R_{add1}) is no longer the dominant route, and the alkyl-H-abstraction route becomes the largest contribution route to PPB and BPB. As Fig. 4c shows, for PPB degradation, Γ of $R_{abs\gamma}$ of 35% is comparable with that of R_{add1} (30%) at room temperature, while Γ of $R_{abs\alpha}$ and $R_{abs\beta}$ are 20% and 13%, respectively. This result demonstrates that the H-abstraction from the PPB end group $-\text{CH}_3$ ($R_{abs\gamma}$) would be the most important route. Thus, as far as the degradation products are concerned: γ -PPB-OH > α -PPB-OH > β -PPB-OH for PPB degradation (Fig. 4c), and δ -BPB-OH is greater than γ -BPB-OH, which is greater than α -BPB-OH, which is greater than β -BPB-OH for BPB degradation (Fig. 4d).

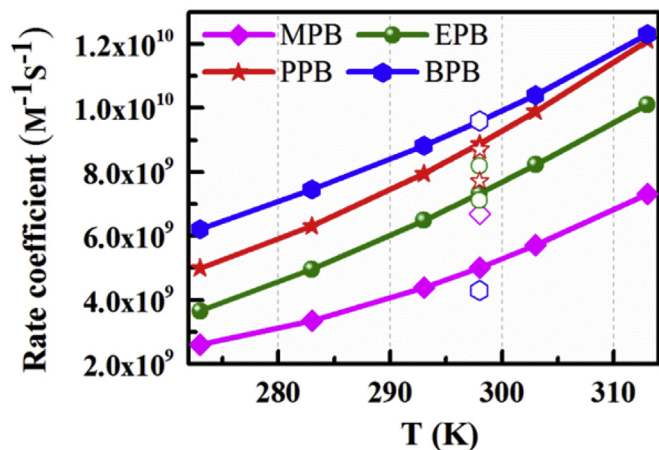


Fig. 3. Calculated total rate constants (solid representation) as well as the experimental data (hollow representation) for four different parabens reacted with $\bullet\text{OH}$ in water, as a function of T in the temperature range of 273–313 K.

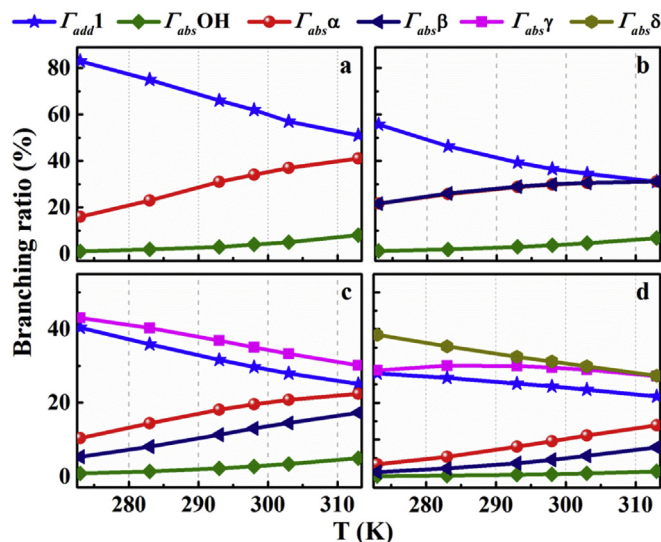


Fig. 4. Calculated branching ratio (Γ) of each route in the reaction between parabens and $\bullet\text{OH}$ in the 273–313 K temperature range. MPB (a); EPB (b); PPB (c); BPB (d).

The result is somewhat different with the reactivity according to the order of C–H bond energies: $D_0(\text{H}-\text{CH}_2\text{R1}) > D_0(\text{H}-\text{CHR1R2}) > D_0(\text{H}-\text{CR1R2R3})$ (Berkowitz et al., 1994). This discrepancy may be explained why the reactivity of the H-abstraction reaction of $\bullet\text{OH}$ in solution is not only related to the C–H bond energies, but also affected by the solvent cage effect, and diffusion-control limit (Minakata et al., 2009), as well as steric effect and electronic effect of the neighboring functional groups within parabens. Although several transformation products have been reported in the experimental research (Daghrir et al., 2014), the branching ratio of these reaction routes is never attempted experimentally so far. Thus, additional experimental studies are needed to obtain better calibration.

In summary, the $\bullet\text{OH}$ -addition route (R_{add1}) would be the dominant one for MPB and EPB degradation, mainly forming hydroxylated products on the aromatic ring. In contrast, the alkyl-H-abstraction route becomes a major route, and the hydroxylated products on the aromatic ring become less significant for PPB and BPB degradation. At room temperature, the contributions of $\bullet\text{OH}$ -addition pathways to the degradation of the four parabens, MPB, EPB, PPB and BPB, were 82%, 58%, 48%, and 34%, respectively (Fig. S2). This finding suggests that with increasing of the alkyl-chain length of parabens, the contribution of the $\bullet\text{OH}$ -addition pathways becomes less significant. As for PPB and BPB degradation, $\bullet\text{OH}$ predominately attacks the alkyl chain rather than the aromatic ring; the H atom on the end $-\text{CH}_3$ group is the most reactive position. This result may be explained that in water environment, hydrogen bonds already exist between water and ester group of parabens, which could inhibit the formation of the hydrogen-bonded complex between the attacking $\bullet\text{OH}$ and the ester group, thereby limiting activating effect of ester group in the aqueous phase. Moreover, the $\bullet\text{OH}$ can be surrounded with H-bonded water molecules, leading to a substantial increase of its effective size (Monod and Doussin, 2008). Due to the steric hindrance effect, the abstraction of H from C atom adjacent to the ester group could be less favorable than the C-terminal ($-\text{CH}_3$) of the alkyl chain. Thus, the solvation effect would result in the most reactive position on the end $-\text{CH}_3$ group, which is different from the hydroxylation of the alkyl chain in gas phase.

3.3. Toxicity evolution during the degradation of parabens

To investigate the potential ecotoxicity of the four parabens and their degradation products in water, the acute and chronic toxicities were also evaluated using three different trophic levels of aquatic organisms (fish, daphnia, and green algae). Fig. 5, Fig. S3–S4 and Tables S5–S7 show the results. For MPB degradation, its $\bullet\text{OH}$ -addition product (*o*-MPB-OH) was harmful to aquatic organisms, but the H-abstraction product (α -MPB-OH) was non-harmful (Gao et al., 2014a). As Fig. 5a–b shows, a more toxic $\bullet\text{OH}$ -addition product (*o*-EPB-OH) was formed during EPB degradation. The acute and chronic toxicity of *o*-EPB-OH to green algae could be about 1.4 and 3 times higher than the original compound EPB, respectively. However, opposite results were observed for daphnia and fish (Fig. 5c–f and Table S5). That is, the $\bullet\text{OH}$ -addition product, *o*-EPB-OH, was not harmful to daphnia, and 2–6 times less harmful to fish. For the H-abstraction products (α -EPB-OH and β -EPB-OH), toxicities for aquatic organisms were lower compared to the original compound EPB. For example, α -EPB-OH and β -EPB-OH to daphnia could be about 7–8 times less toxic than EPB. As such, it is concluded that the aquatic toxicity increased for green algae from $\bullet\text{OH}$ -addition routes as compared with EPB, while it declined for fish and daphnia. Decreasing trends in aquatic toxicity were also obtained for H-abstraction routes at the three levels of aquatic organisms.

As for PPB degradation, similar conclusions were achieved with the calculated results: the acute and chronic toxicities of the $\bullet\text{OH}$ -addition product *o*-PPB-OH increased for green algae as compared with the original compound PPB, and decreased for daphnia and fish (Fig. S3). While the H-abstraction products (α -PPB-OH, β -PPB-OH and γ -PPB-OH) were less toxic than the parental paraben PPB, these products would still be harmful to aquatic organisms at all three trophic levels. This result is in agreement with our previous single experimental observation of PPB (Fang et al., 2013), and gives insight into the possible degradation products with increased toxicity. Nevertheless, the absolutely toxicity values of these degradation products will need further investigation because the toxicity calculation is subject to several uncertainties, i.e., the uncertainty about pollutants with specific mode of action, mixture interactions, bioavailability, and so on (Sanderson et al., 2003). Detailed, peer-reviewed toxicological data concerning the aquatic toxicity of these products are scarce, hindering accurate assessment of the effects of parabens in the environment.

As Fig. S4 shows, different results were obtained in the case of BPB degradation. The aquatic toxicity of BPB $\bullet\text{OH}$ -addition and H-

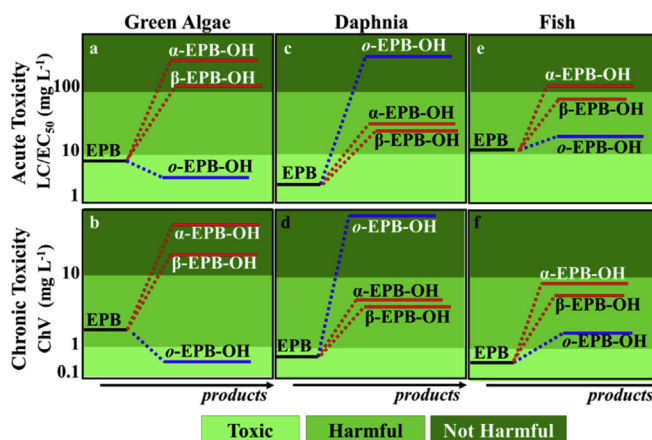


Fig. 5. Acute and chronic toxicity evolution characteristics during EPB degradation.

abstraction products both decreased, except that the chronic toxicity of *o*-BPB-OH increased for green algae (Fig. S4b). The *o*-BPB-OH would be nearly two times more toxic to green algae than BPB, although both compounds were at similar toxic levels.

In sum, for the \bullet OH-initiated transformation of the four parabens, the aquatic toxicity of the transformation products increased from MPB to EPB to PPB to BPB, similar to the parental compounds. All products generated through \bullet OH-addition, *o*-parabens-OH, would be more toxic to green algae than the original compounds. The opposite was observed for daphnia and fish, as well as with the H-abstraction products to aquatic organisms at three trophic levels. However, although all H-abstraction products were less toxic than the corresponding parental compounds, these degradation products were still harmful to aquatic organisms (Daghrir et al., 2014). Furthermore, among these H-abstraction products, the \bullet OH attack route on the terminal $-\text{CH}_3$ group could result in more toxic products than on the $-\text{CH}_2$ group of parabens. For example, β -EPB-OH, γ -PPB-OH and δ -BPB-OH would have the most harmful effects on aquatic organisms among H-abstractions products. In addition, with prolonging of the reaction, several break-down by-products such as 4-Hydroxybenzoic acid, hydroquinone and phenols could be further formed (Daghrir et al., 2014; Tay et al., 2010b). The aquatic toxicity of these break-down by-products were also considered and supplemented in Table S7. As seen, hydroquinone and phenols would have more aquatic toxicity than these obtained hydroxylated products, although the 4-Hydroxybenzoic acid could be non-harmful to aquatic organisms. In all, the adverse effect of these degradation products as well as parabens cannot be ignored during the degradation in AOPs systems or in the aquatic photochemical degradation.

Parabens were found to be widely presented in water environments, e.g., in the urban streams of Guangzhou, South China, MPB and PPB were detected up to 1062 and 2142 ng L⁻¹, respectively (Peng et al., 2008). Therefore, PPB equivalence approach (Yamamoto et al., 2011) was employed to calculate the toxicity values of the two parabens (Table S8). Herein, green algae, as the sensitive species to degradation products, was chosen as the models to assess the potential chronic hazards. The total hazard quotients (HQ) of MPB and PPB in urban streams of Guangzhou were calculated to be 0.016 for green algae. In addition, from the combined results of the kinetics and degradation products, the total HQ of degradation products of MPB and PPB was calculated to be 0.019. The results suggest that the potential risk would slightly increase during the \bullet OH-induced transformation of MPB and PPB, although they are not likely to cause biological effects at environmentally relevant levels in aquatic ecosystems at present. Taking into consideration the fact that the parabens, referred as “pseudo-persistent” contaminants, are continuously discharge into the environment. The multiple component parabens and their products may exert higher ecological risk. On the other hand, there is potential for parabens and their transformation products to elicit estrogenic responses at concentrations lower than those that may cause acute or chronic toxicity. Thus, the estrogenic potential of parabens and their transformation products in aquatic ecosystems are significant topic and all ongoing.

3.4. Fate prediction of parabens in the environment depending on alkyl-chain length

The results above related to the degradation mechanisms and kinetics in \bullet OH-based processes may be used to roughly predict the fate of parabens in the realistic environment depending on the alkyl-chain length. Parabens with longer alkyl chain can be degraded faster in the water environment owing to their higher rate constants. Accordingly, the half-life ($t_{1/2}$) of the \bullet OH-initiated

transformation products of parabens would decrease with an increase of the alkyl-chain length under the same environmental condition. For instance, the $t_{1/2}$ at 298 K was predicted to be 3.84 h for MPB, 2.62 h for EPB, 2.17 h for PPB and 2.01 h for BPB in surface waters with [\bullet OH] of 1.00×10^{-14} M, e.g. in Lake Nichols, northern Wisconsin (Brezonik and Fulkerson-Brekken, 1998). Moreover, considering the increasing aquatic toxicity of parental compounds as well as the transformation products from MPB to EPB to PPB to BPB, the occurrence and aquatic toxicities of transformation products from the long chain paraben are worth studying. Nevertheless, the transformation products from short chain paraben should not be overlooked because the mainly formed intermediates would be form \bullet OH-addition process, which are more toxic to organic organisms than the original compounds.

4. Conclusion

This work found that \bullet OH, as an important oxidant during AOPs or photochemical transformation in natural waters, can initially attack four parabens via the \bullet OH-addition and H-abstraction routes. The \bullet OH-addition route was more important for the degradation of shorter alkyl-chain parabens, while H-abstraction route was predominant for longer alkyl-chain parabens. The calculated total rate constants and activation energies suggest that \bullet OH-initiated reactions of the four parabens can easily occur, and parabens with longer alkyl-chain length can be degraded more efficiently. With the increase of their alkyl-chain length, the aquatic toxicity of parabens and their products increased gradually. Particularly, the \bullet OH-addition products have higher toxicity to green algae than the original parabens. Although all degradation products were less toxic to daphnia and fish than the corresponding parental parabens, they could still be harmful to aquatic organisms. Among the H-abstraction products, the \bullet OH attack on the terminal $-\text{CH}_3$ group of parabens could result in products with the highest toxicity. The environmental impact of parabens and their degradation products during AOP systems or in natural waters should not be ignored in the future experimental studies and environmental assessment.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.watres.2015.12.047>.

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